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GEC-ESTRO Basic TC

Modern Brachytherapy Techniques

Firenze 13 – 16 March 2016

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Firenze 2016

Welcome to the

29th

GEC-ESTRO Brachytherapy Course

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GEC-ESTRO-BT Teaching Course
Firenze 2016

Local Organisators:
- Lorenzo Livi
- Isacco Desideri

Teaching Staff :
- Dimos Baltas (GE)
- Peter Hoskin (UK)
- Renaud Mazeron
- Bradley Pieters (NL)
- Erik Van Limbergen (BE)

ESTRO School :
- Luis Teixeira

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GEC-ESTRO-BT Teaching Course
Firenze 2016

The Programme

Evaluation Forms

MCQ examination

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Exhibitors :

- Elekta (Nucletron)

- Varian Medical Systems

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General aspects of brachytherapy

Erik Van Limbergen, MD, PhD

GEC-ESTRO Teaching Course

Firenze 2016

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Βραχυθεραπεια

- Brachus = short by

  - ➢ Interstitial brachytherapy
  - ➢ Contact brachytherapy
    - → surface mould
    - → intracavitary
    - → endoluminal

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History of Brachytherapy (1)

1896 Becquerel

1898 Marie Sklodowska-Curie

1901 Danlos and Block : Paris

1905 Abbe : US Radium implantations

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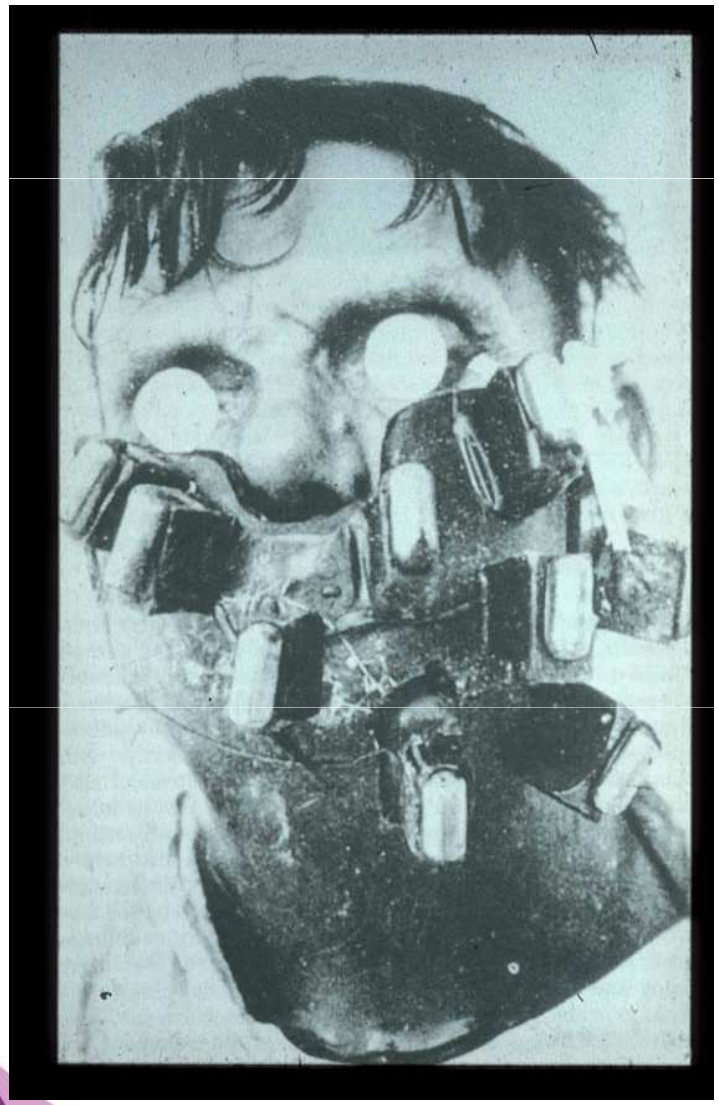
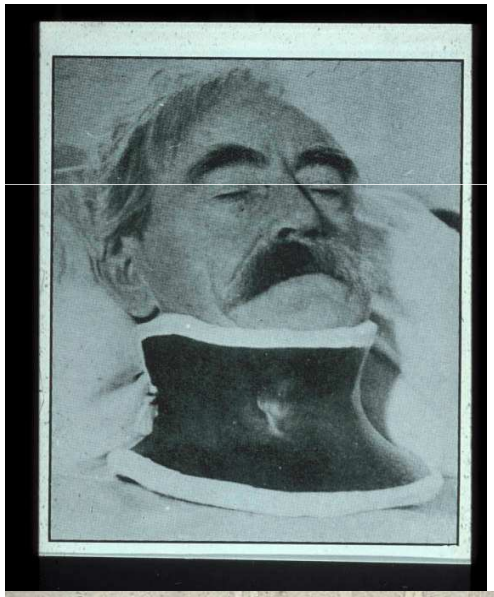
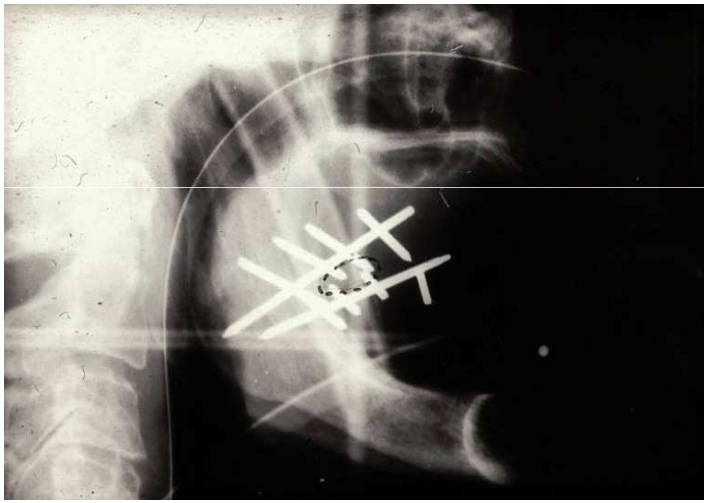
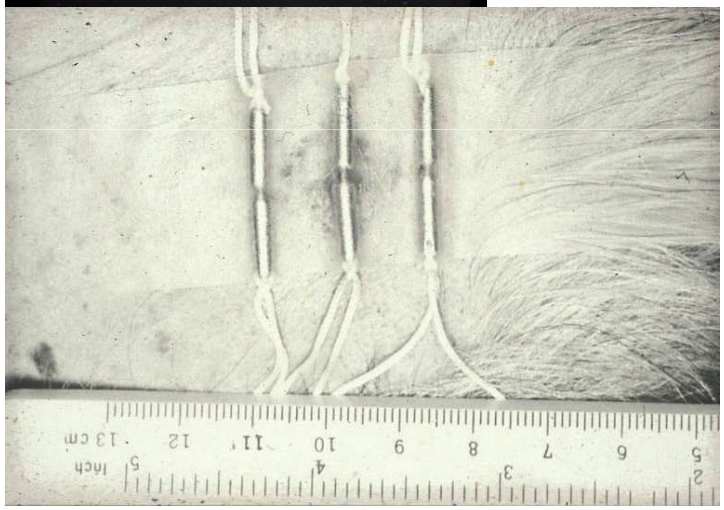
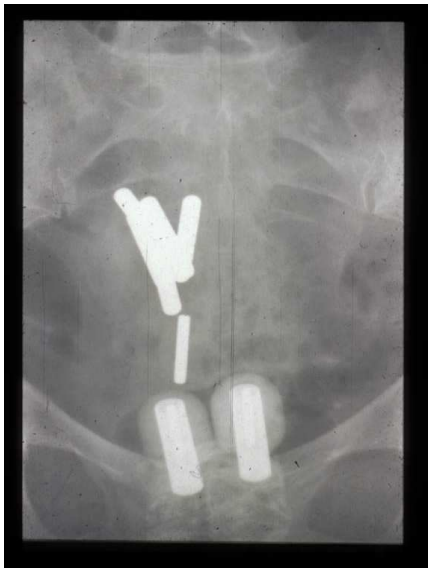
History of Brachytherapy (2)











Radium 226 tubes and needles

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[20.4] Radium plaques being applied in the Skin Department, St. Vincent's Hospital, Melbourne, Australia in 1905[19].

Different schools of brachytherapy

- Radiumhemmet Stockholm
- Memorial Hospital New York
- Institut du Radium Paris

Different empirical methods and rules

- Stockholm method for Gyne (1914)
- Paris method for Gyne (1919)
- Manchester system (1934) Paterson-Parker,Meredith
- Paris System for IS : Pierquin,Chassagne,Dutreix

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History of Brachytherapy (3)

Discovery of artificial radioactive isotopes

- *1934* *Irene Curie - Fréderic Joliot*
- *1958* *Iridium I92: U. Henschke*

Development of afterloading concept

- *58 - 65* *U. Henschke - D. Chassagne*

Development of 3D dosimetry and fundamental rules of dosimetry

- *1965* *B. Pierquin - D. Chassagne - A. Dutreix*

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Artificial Isotopes

	Radium 226	Iridium 192
• Half life	1640 years	72.4 days
• Radioprotection:		
➢ HVL	20 mm Pb	6 mm Pb
➢ Consistency	powder Radon gas	metal wires non contaminating
• Accessibility	Rigid sources large diameter	flexible sources small sizes

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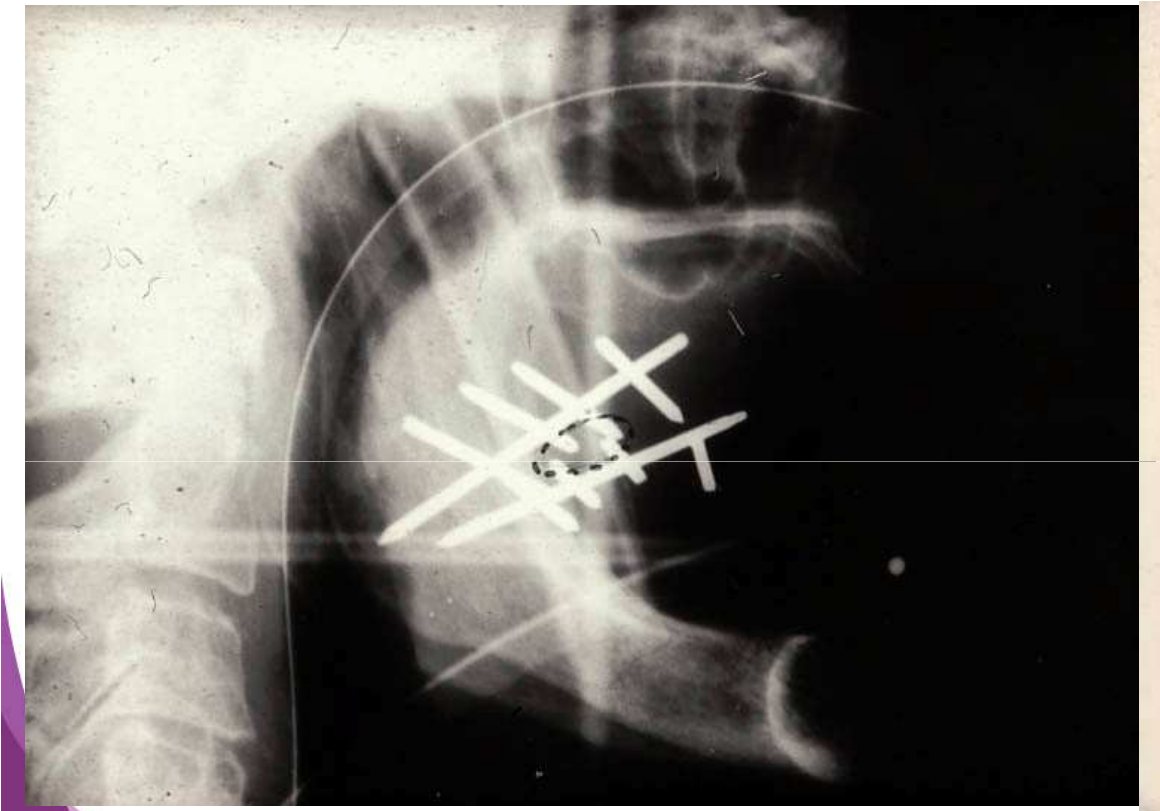
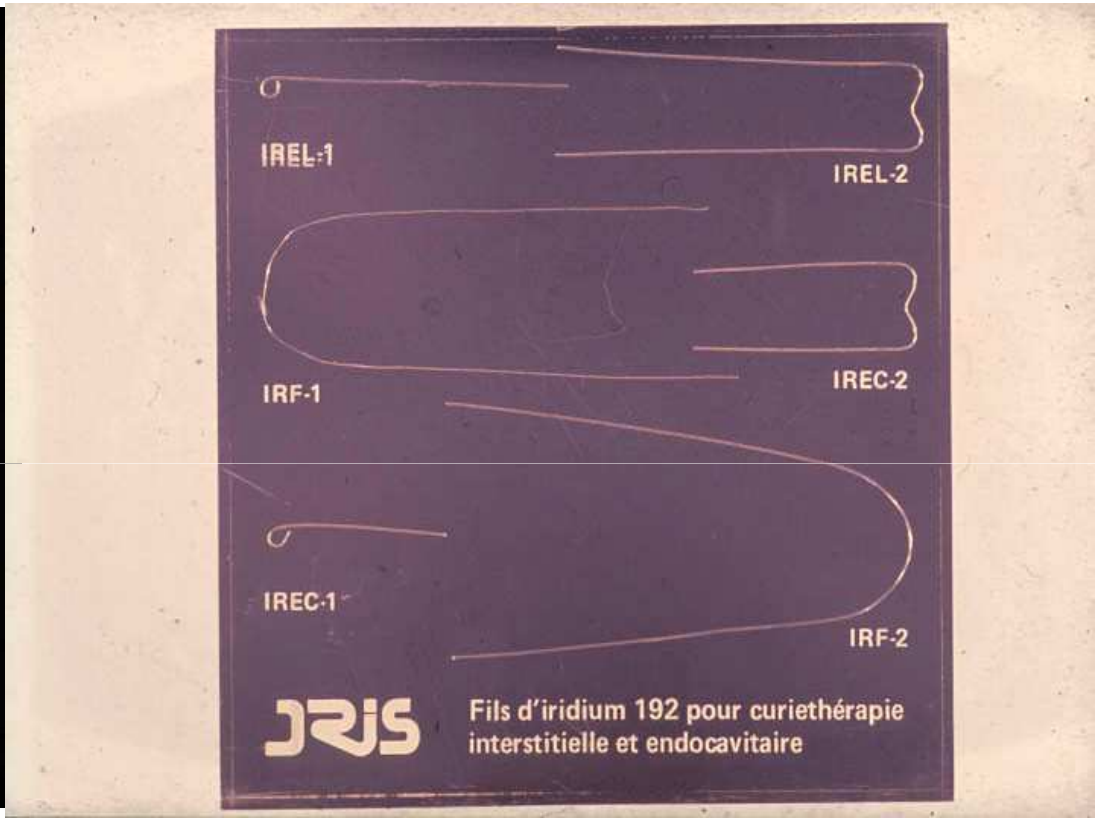
Artificial Isotopes

Radium 226



Iridium 192



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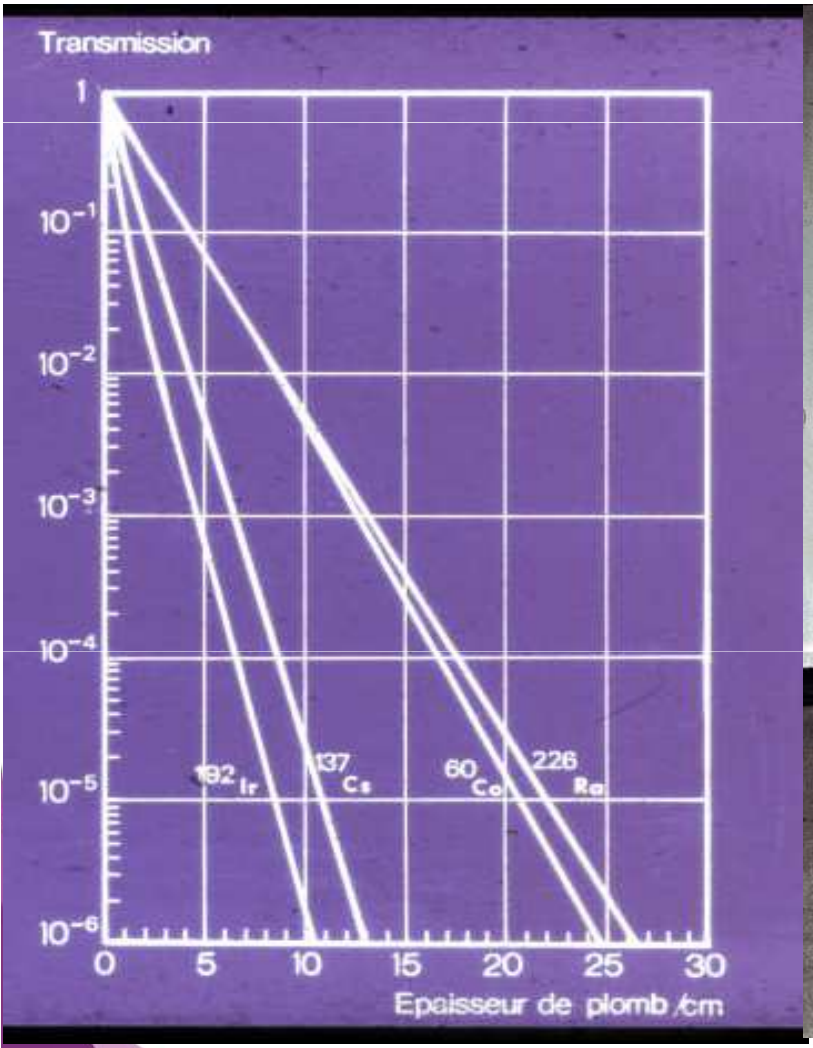
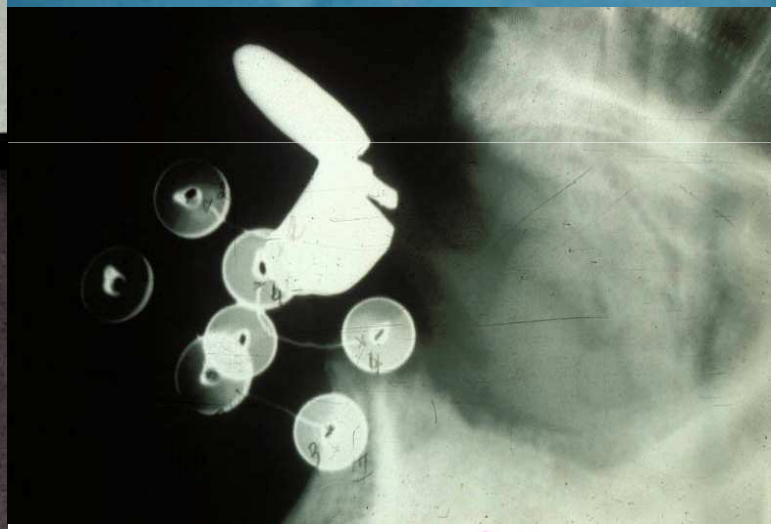
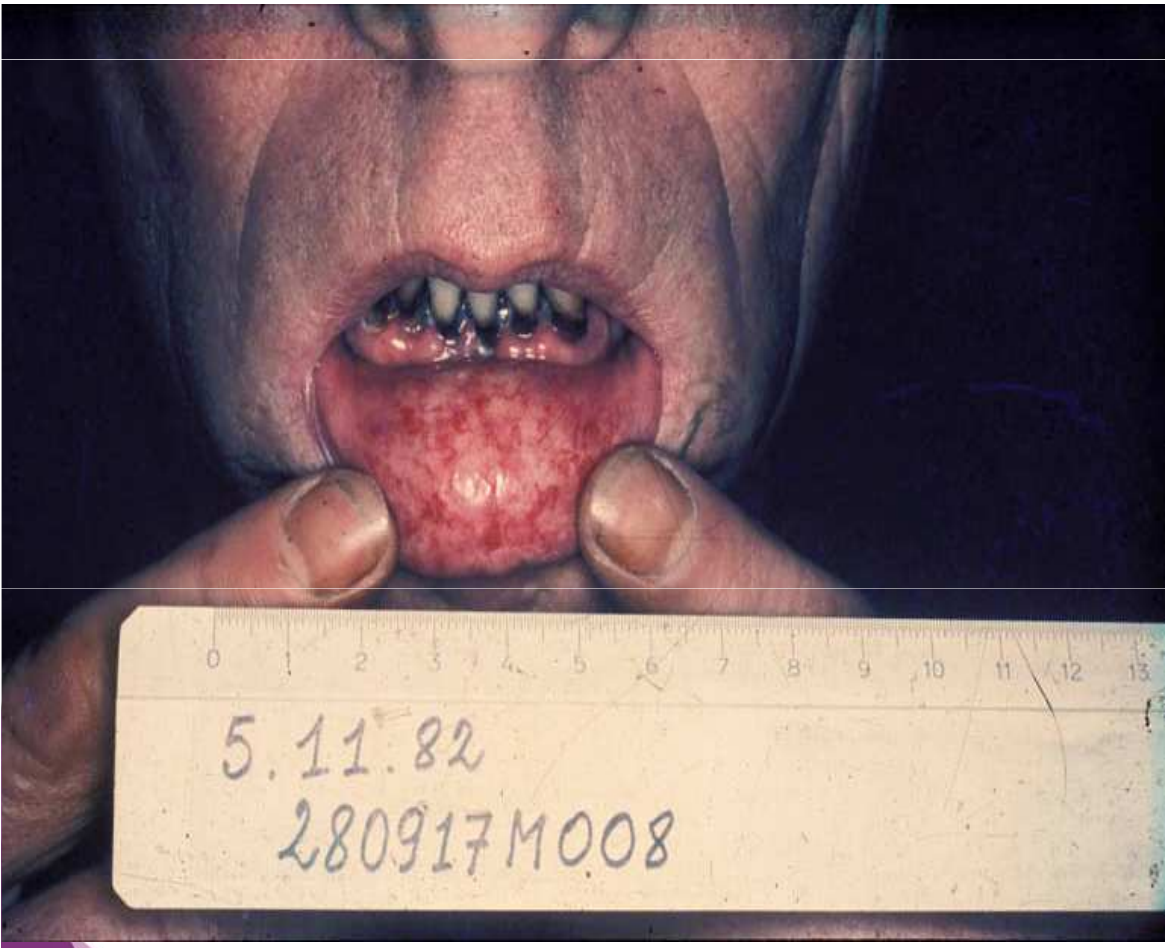
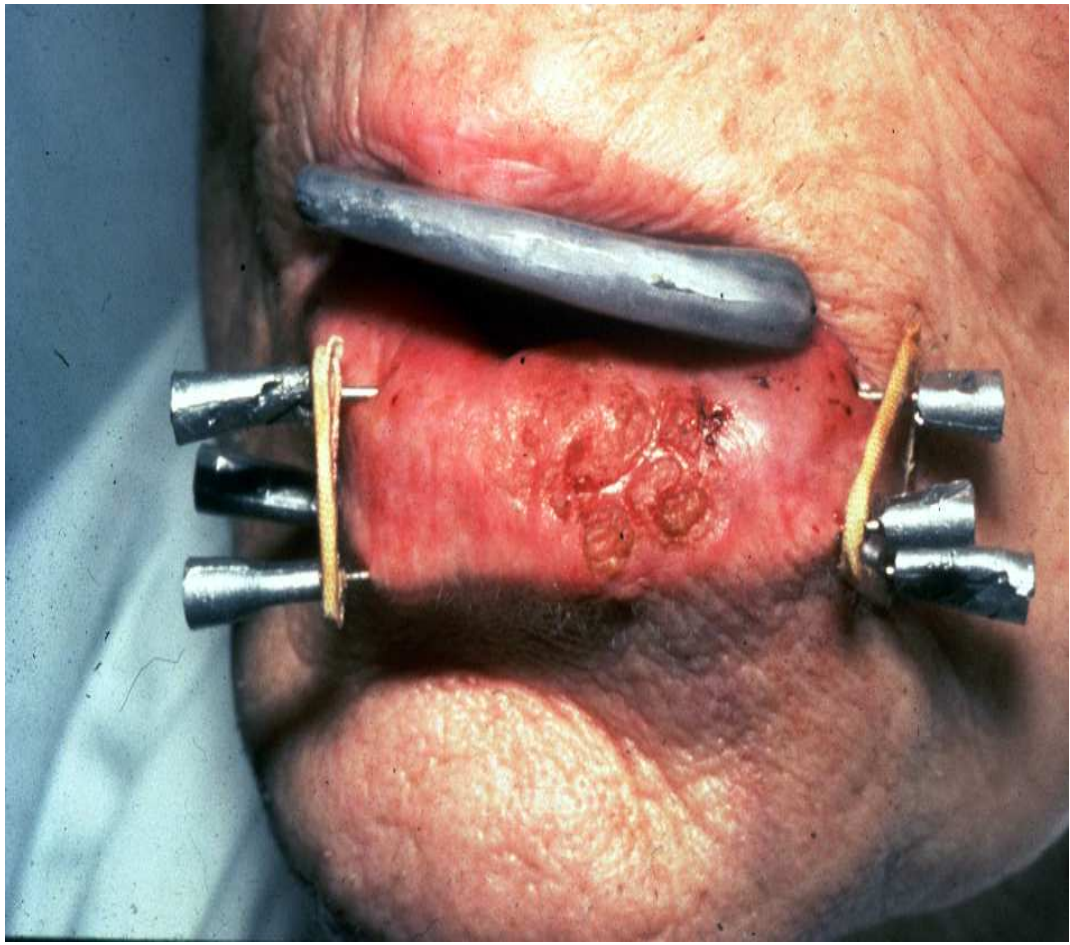
Iridium 192 versus Radium 226





Iridium 192 versus Radium 226





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Place of Brachytherapy

- Organ sparing, curative treatment

- Ballistic selectivity : limited target volumes

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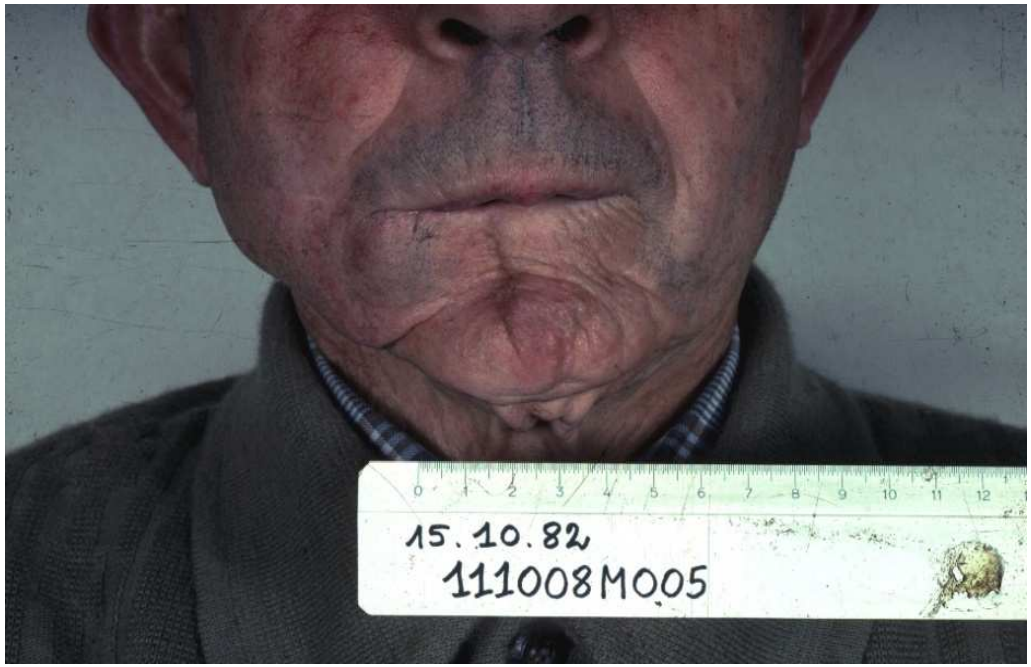
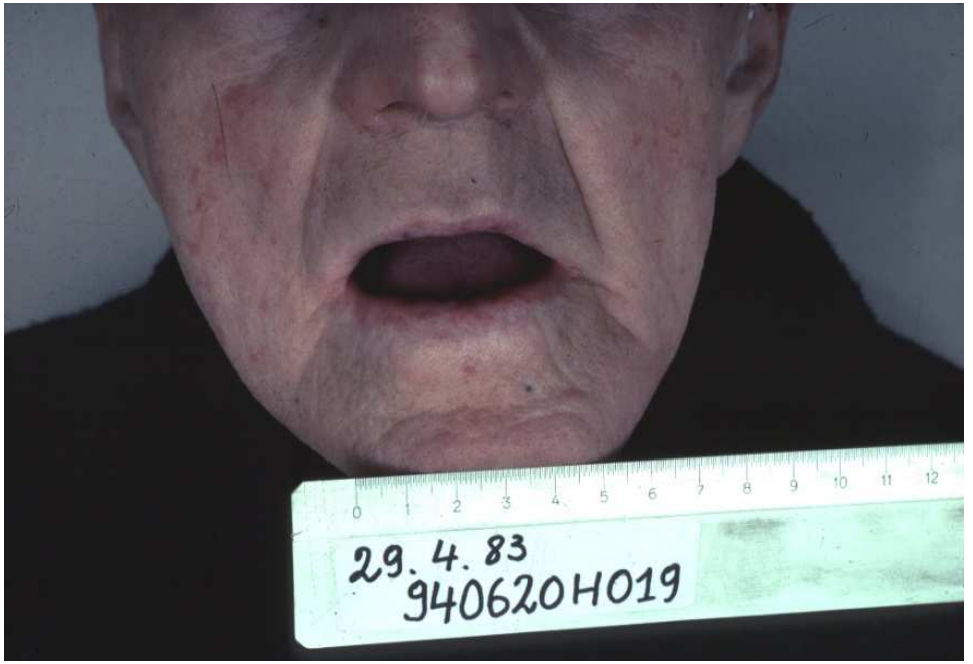
Place of Brachytherapy

- Organ sparing, curative treatment





- Ballistic selectivity : limited target volumes

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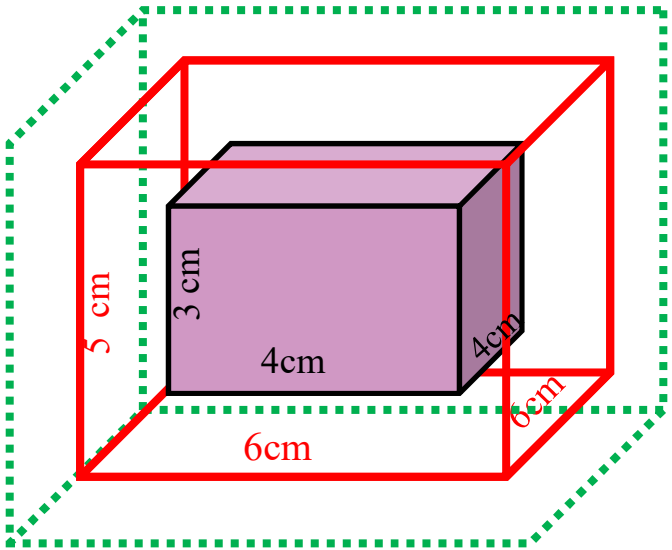
Volume effect of CTV=PTV



PTV margin:	**+ 5mm**	**+ 10 mm**
CTV	**48 cm^3**	**48 cm^3**
PTV	**100 cm^3**	**180cm^3**

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General indications of brachytherapy

- Organ sparing possibility versus surgery

- Ballistic selectivity CTV = PTV
- Small conformal treated volumes
- Critical position of organs at risk

- Accessible for application or implantation technique

- Growing interest because of progress in technology : image guided brachytherapy

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Types of BT

Temporary implants

Dose rates :	**LDR**	**0.4 – 1 Gy/h**
	MDR	**1 - 12Gy/h**
	HDR	**> 12 Gy/h**
	PDR	**0.5 – 2Gy/h**

Permanent implants

VLDR

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Advantages of afterloading technique

- Radioprotection
  - medical staff
  - nurses
  - visitors

- Quality of the implant
  - careful placement of source carriers
  - adjustments possible

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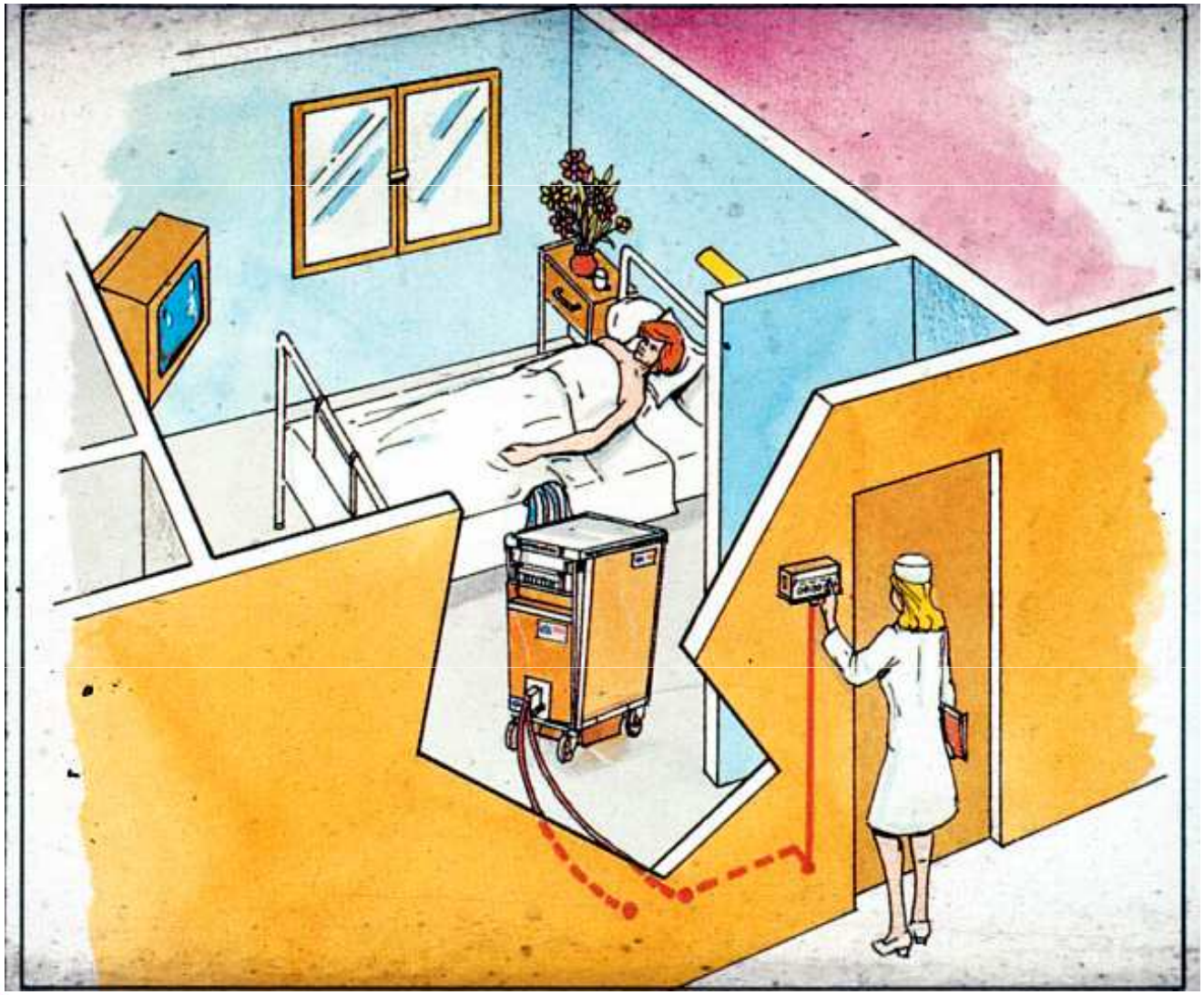
Remote control afterloaders



Mechanical (Cs)

Pneumatical (Cs)

Stepping source
Ir 192, Co 60, …..

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Stepping source afterloaders

- Gammamed

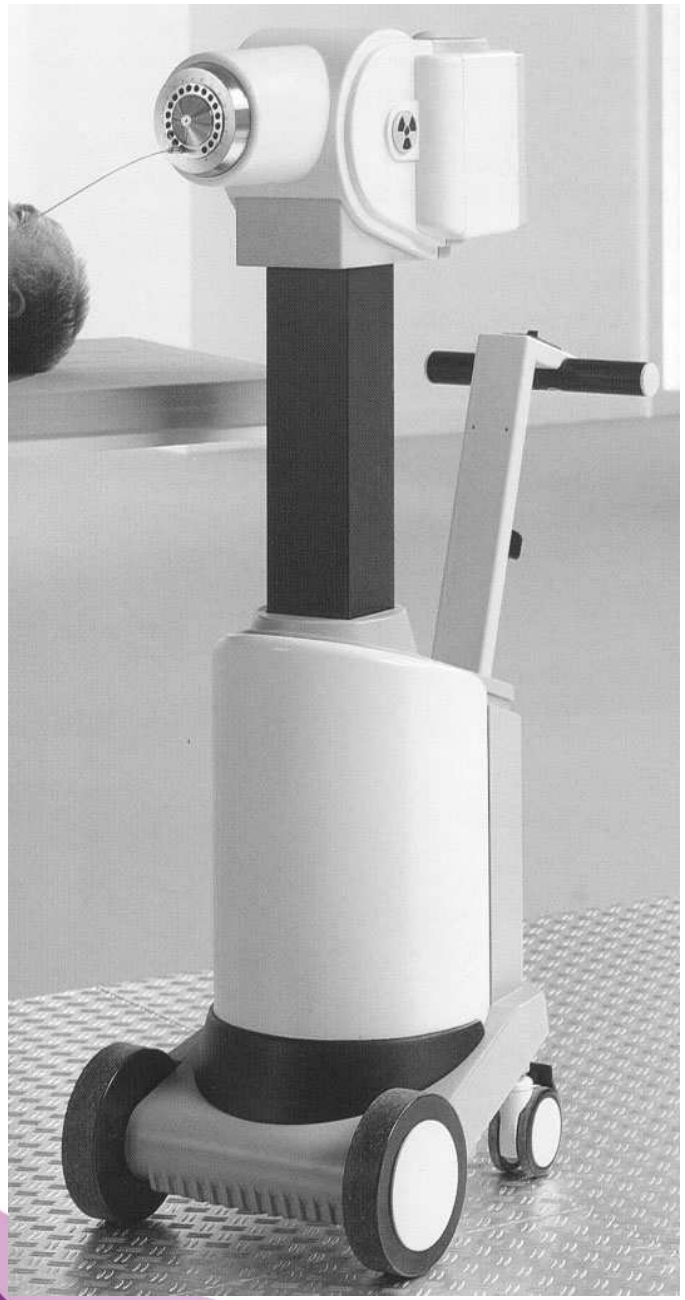
- Varisource

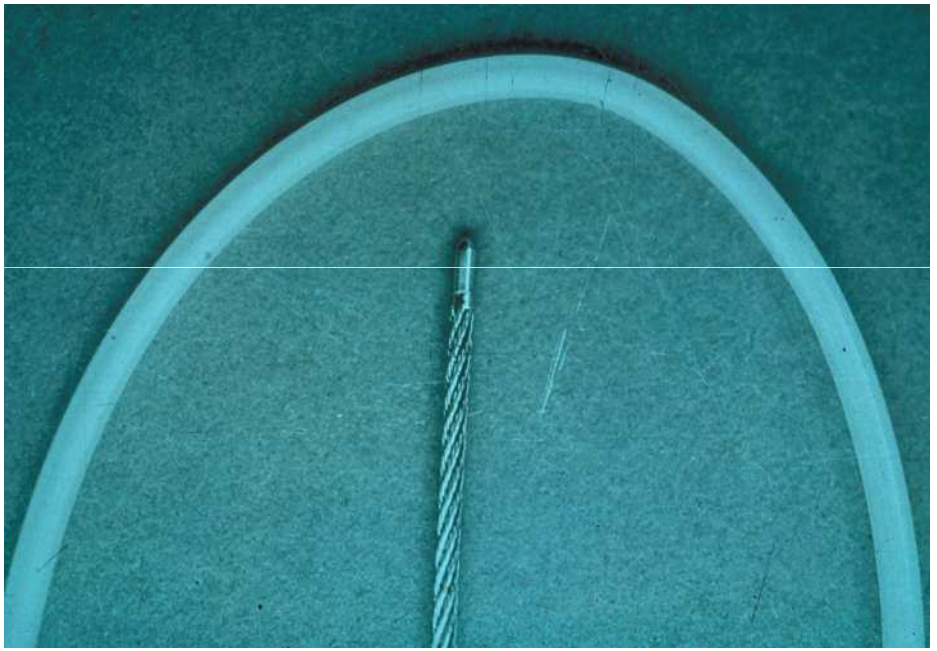
- Multisource

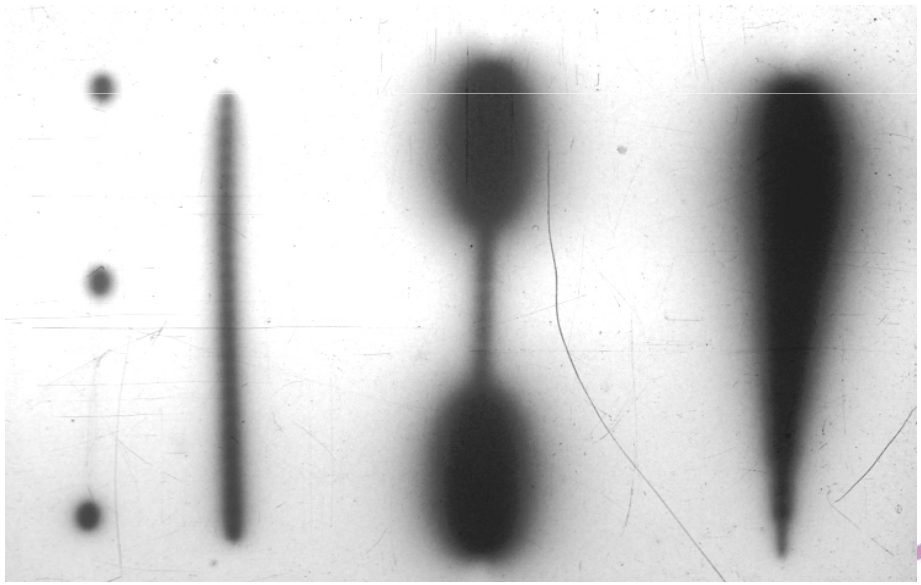
- Microselectron

- Flexitron

Stepping Source afterloaders







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Advantages of stepping source technology

Full radioprotection

Only one source replacement needed

Easy individual adaption of source track lengths

Optimization possibilities

HDR and PDR

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Afterloading techniques

- Remote control afterloading

  a hugh variety in dedicated applicator types

  gyne applicators
  guide needles : straight and curved
  plastic tubes , plastic needles
  moulds, masks with plastic tubes
  skin surface applicators
  endoluminal catheters

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Intrauterine-vaginal applicators

- Fletcher - Suit - Delclos
  Tandem + ovoids
- Stockholm derived
  Tandem + ring
- Personalised moulds
  Pierquin – Chassagne

  Shielded or not shielded

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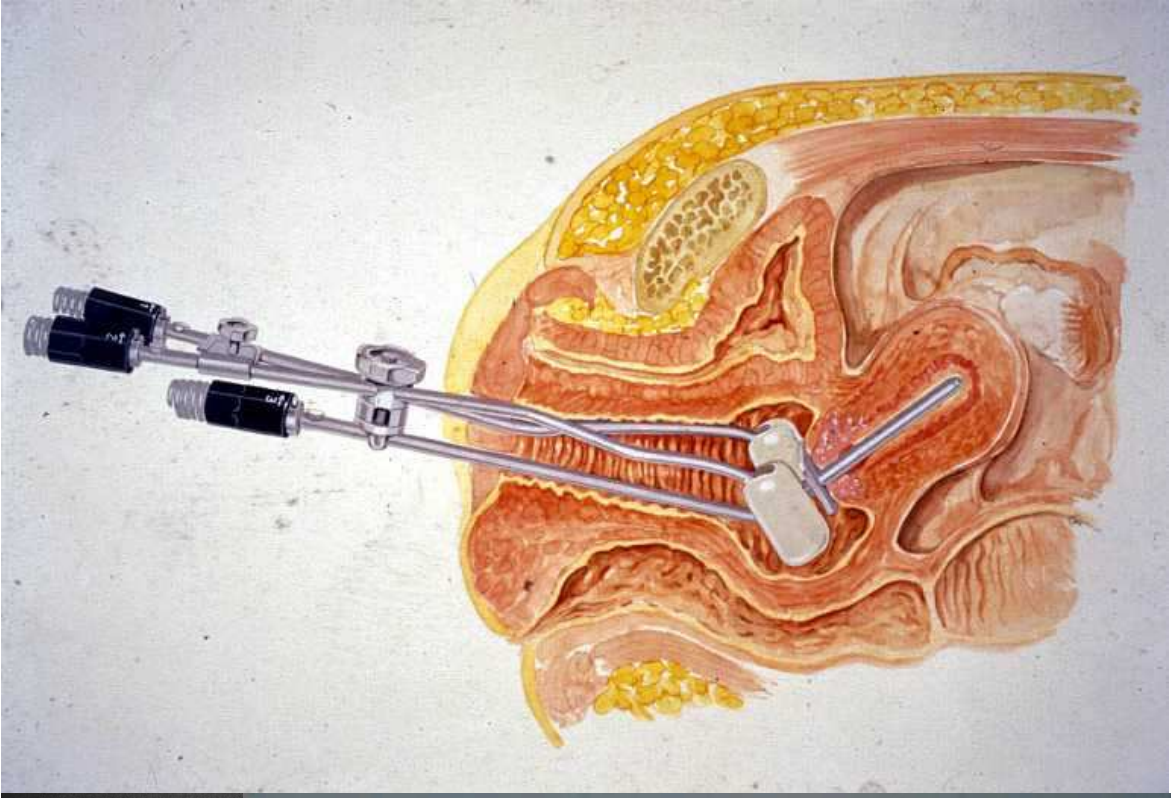
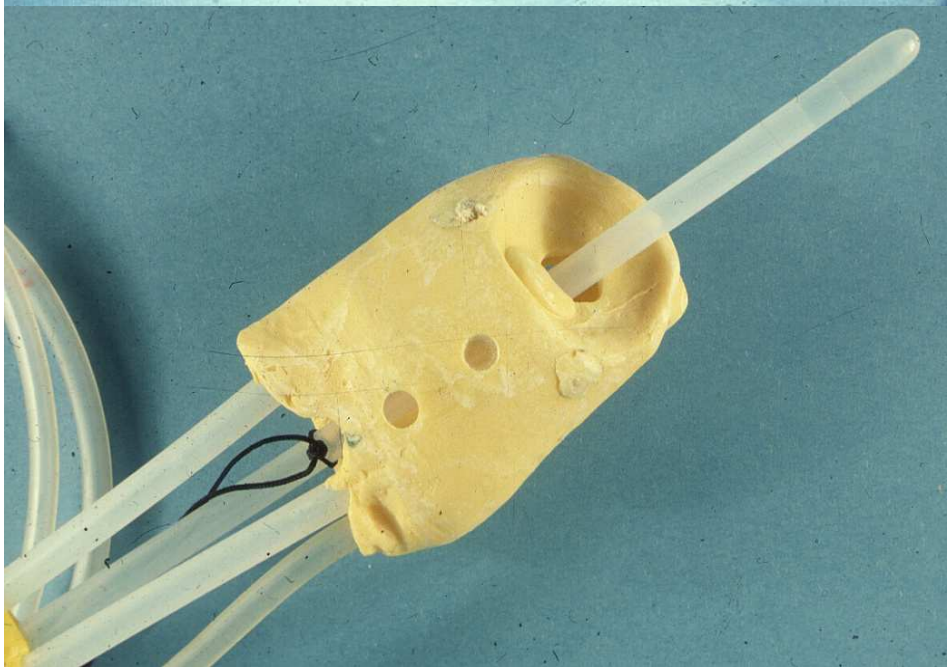
IU-IV Applicators





Guide needles

- Metal or Rigid plastic needles
- External diameter 1.6 - 2 mm
- HDR, PDR afterloaders
- Used in : breast
  anal canal
  interstitial gyne

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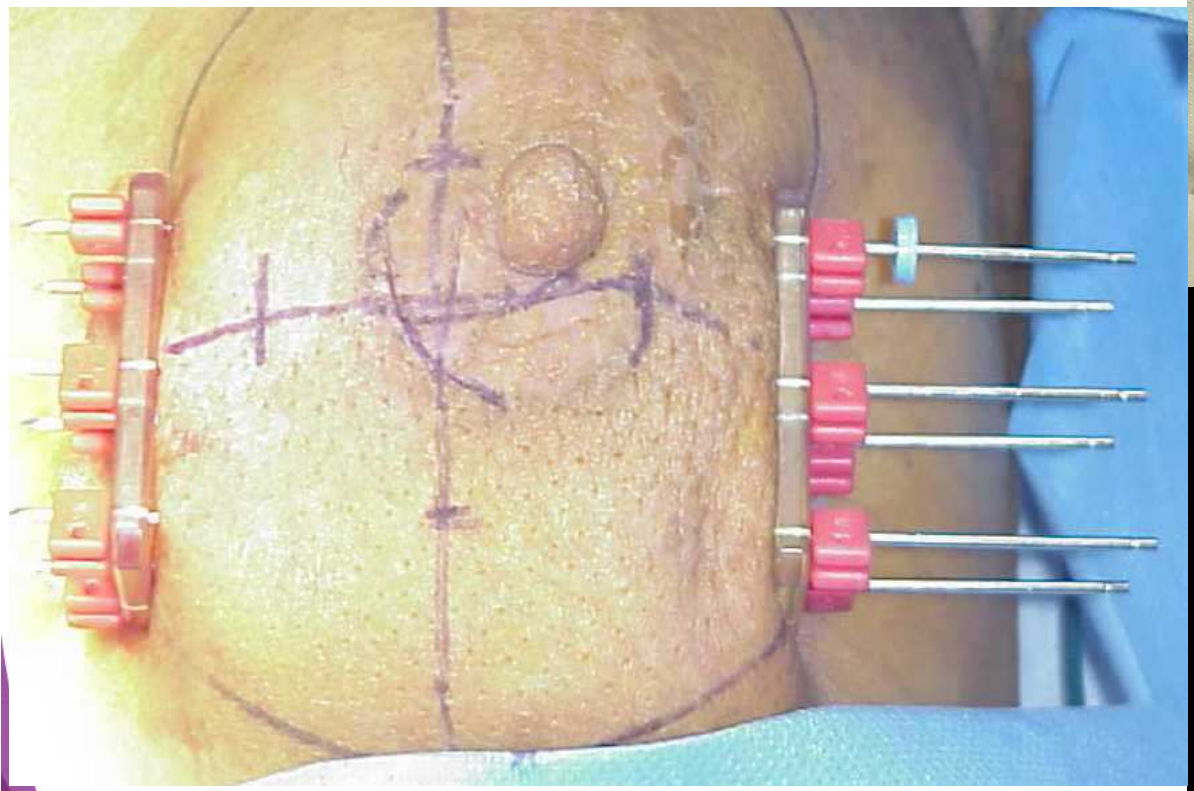
Guide needles



Plastic tubes, plastic needles

- Thin and supple tubes

  1.6 to 1.9 mm thick

  Head and Neck

  Soft Tissue Sarcomas

  Bladder

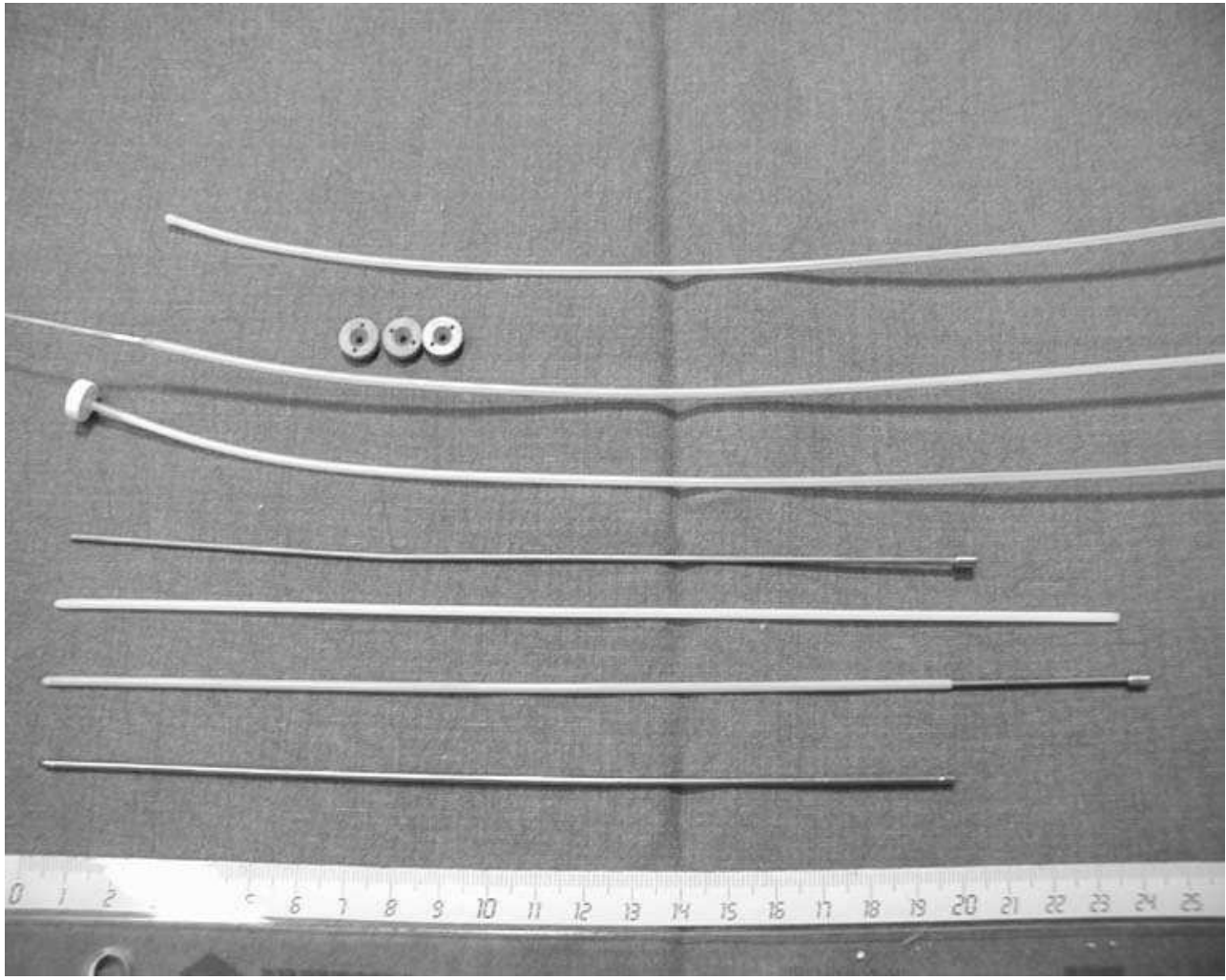
  CORT

- Rigid needles

  Interstitial Gyne

  Prostate

  Anal canal



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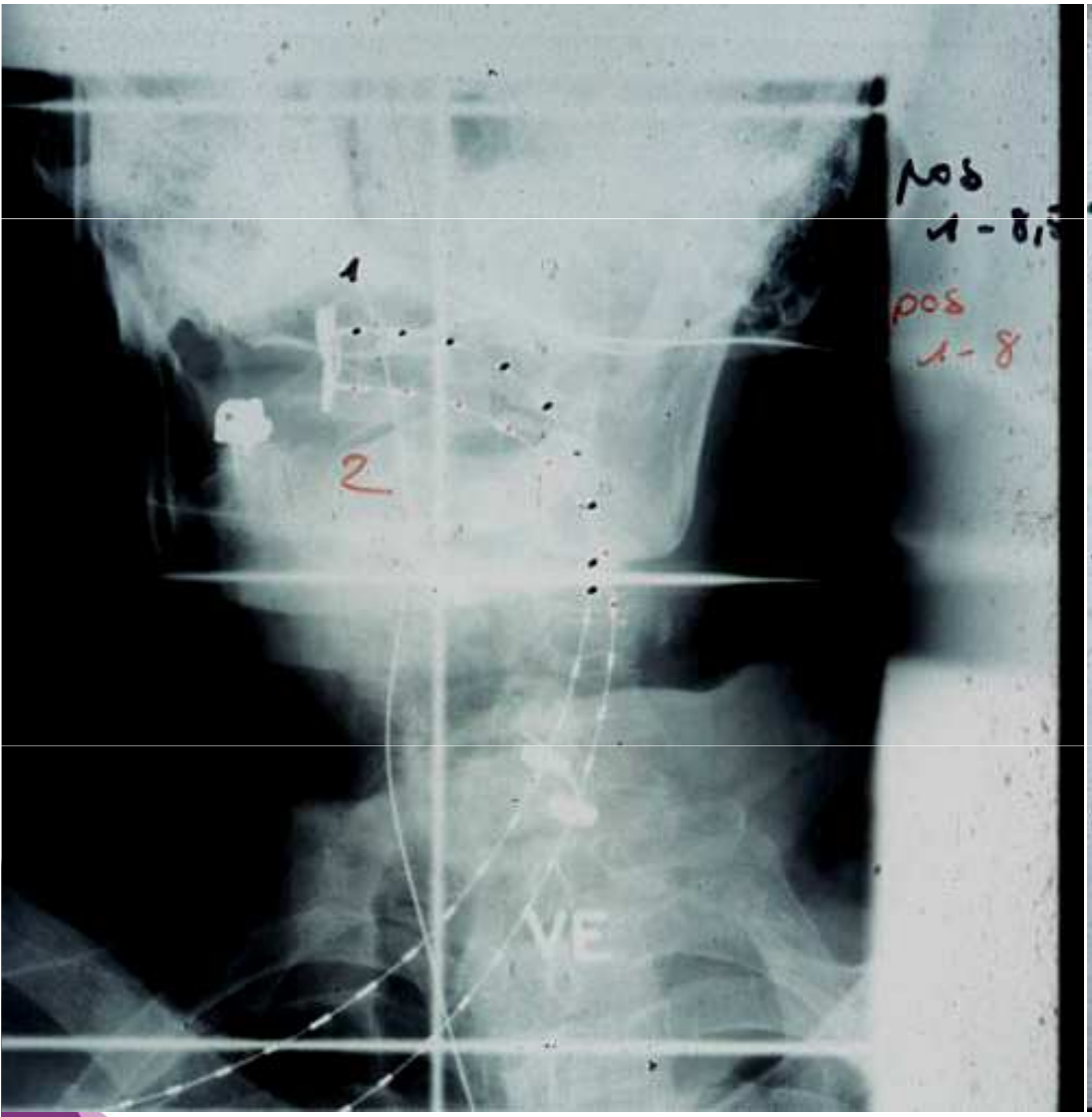
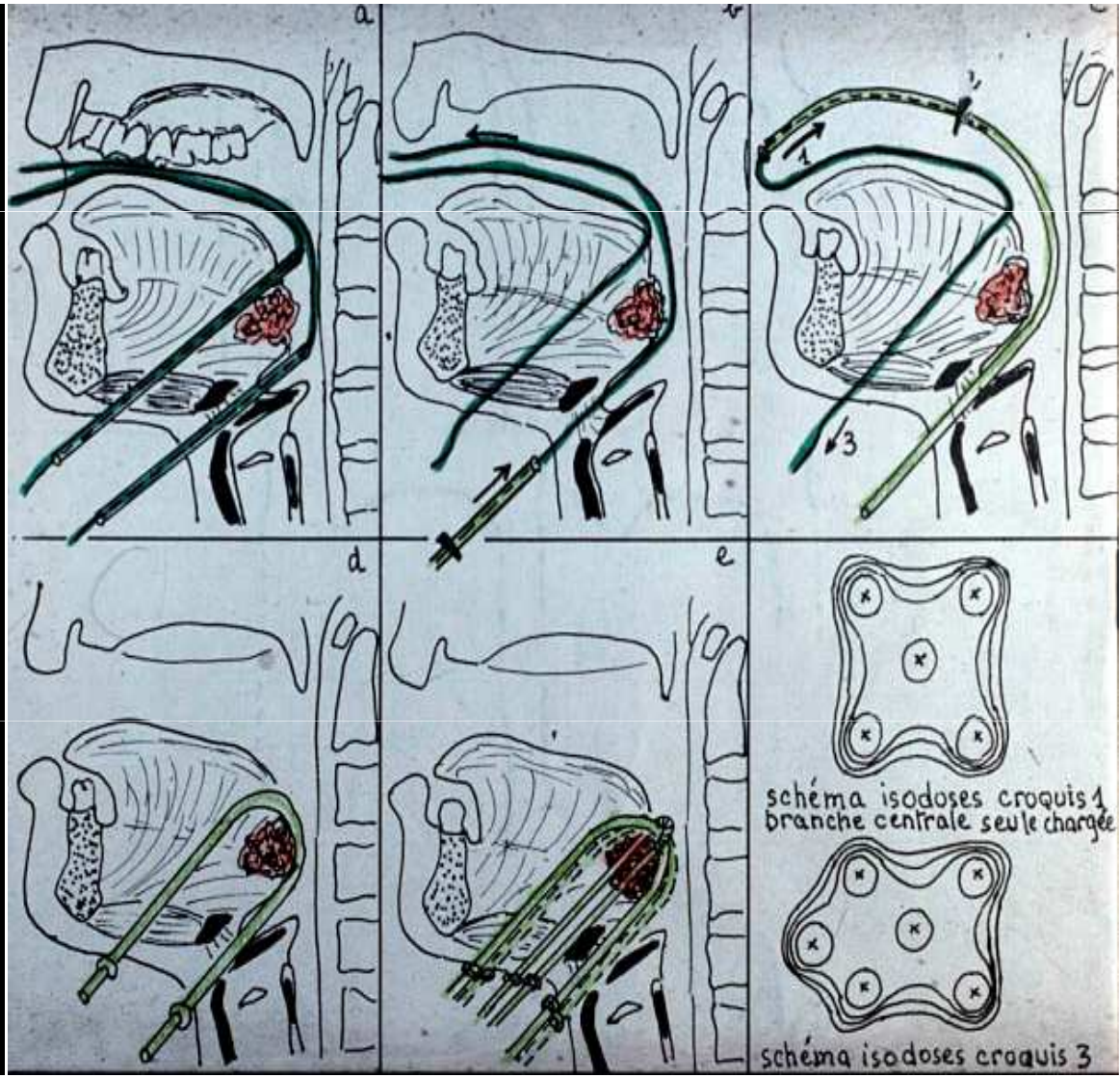
Plastic tubes





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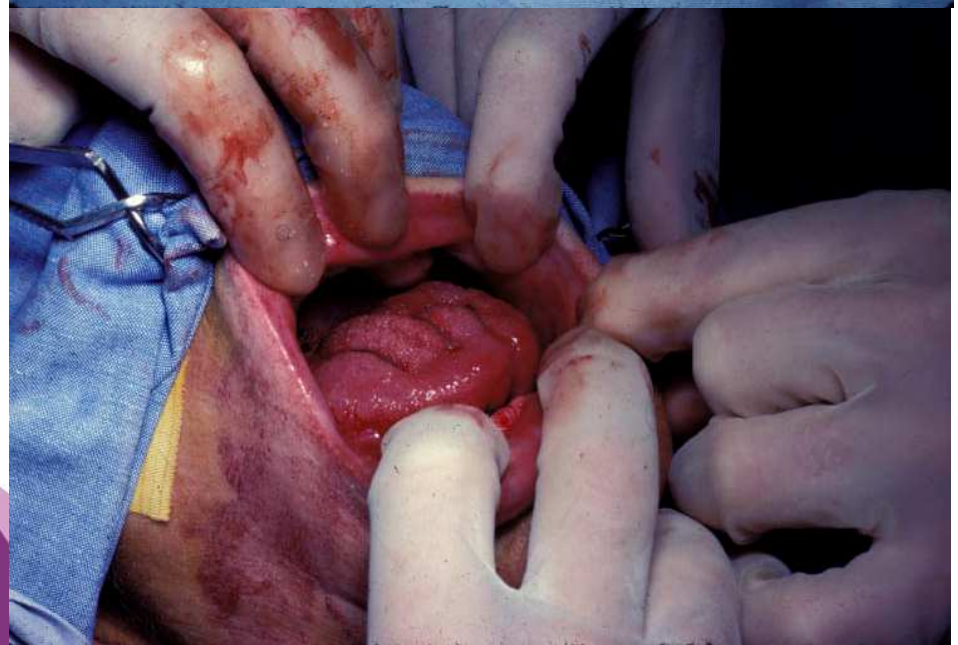
Plastic tubes



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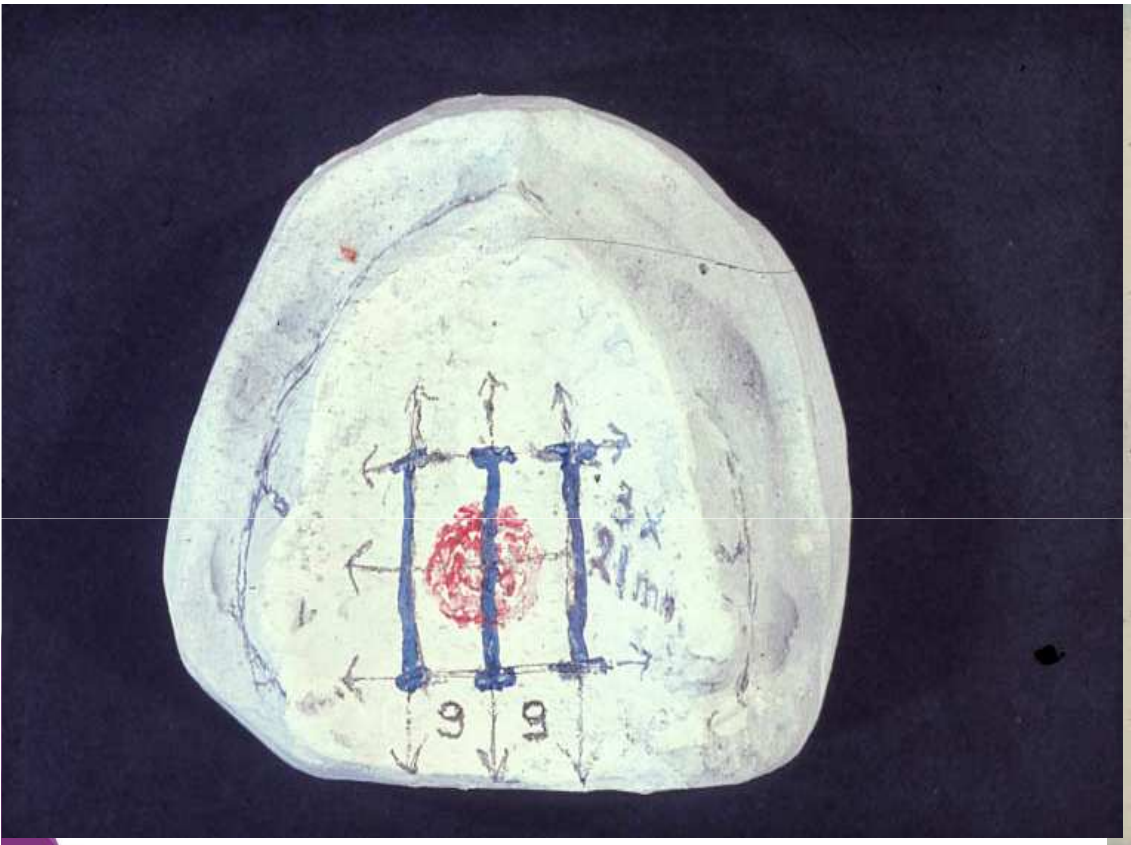
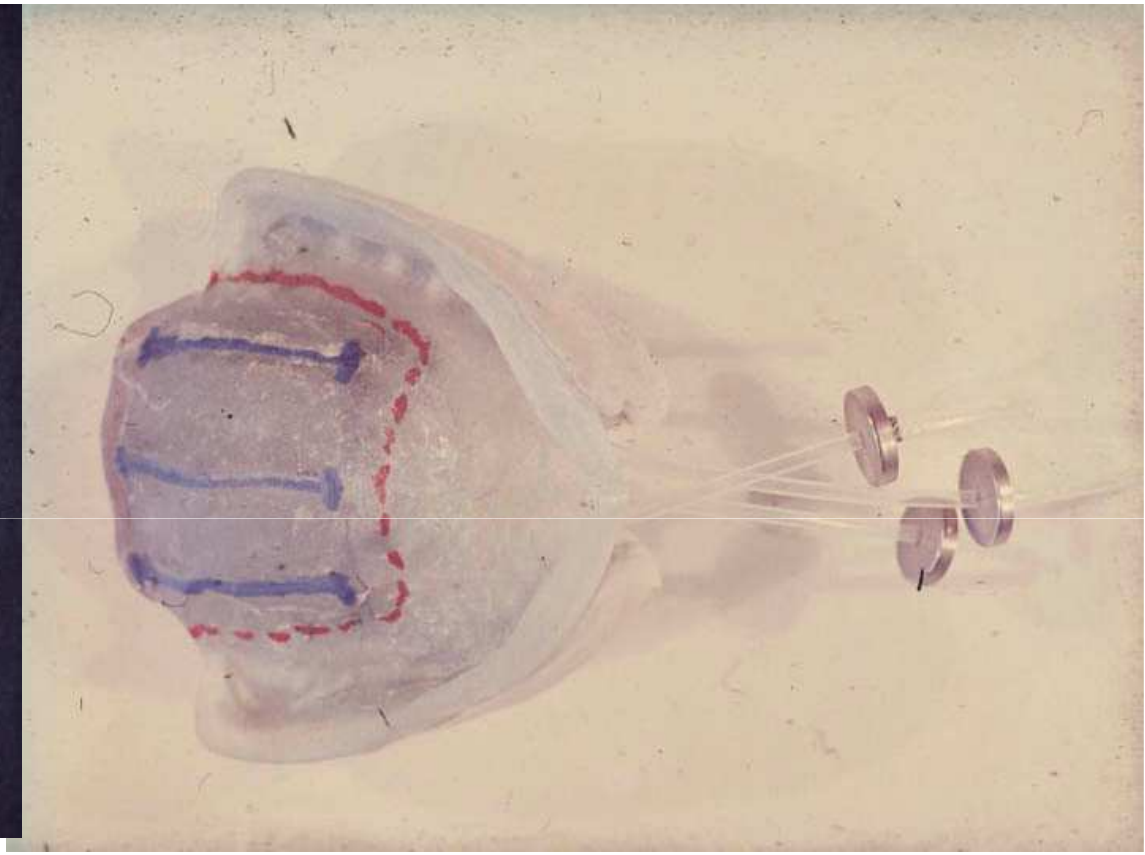
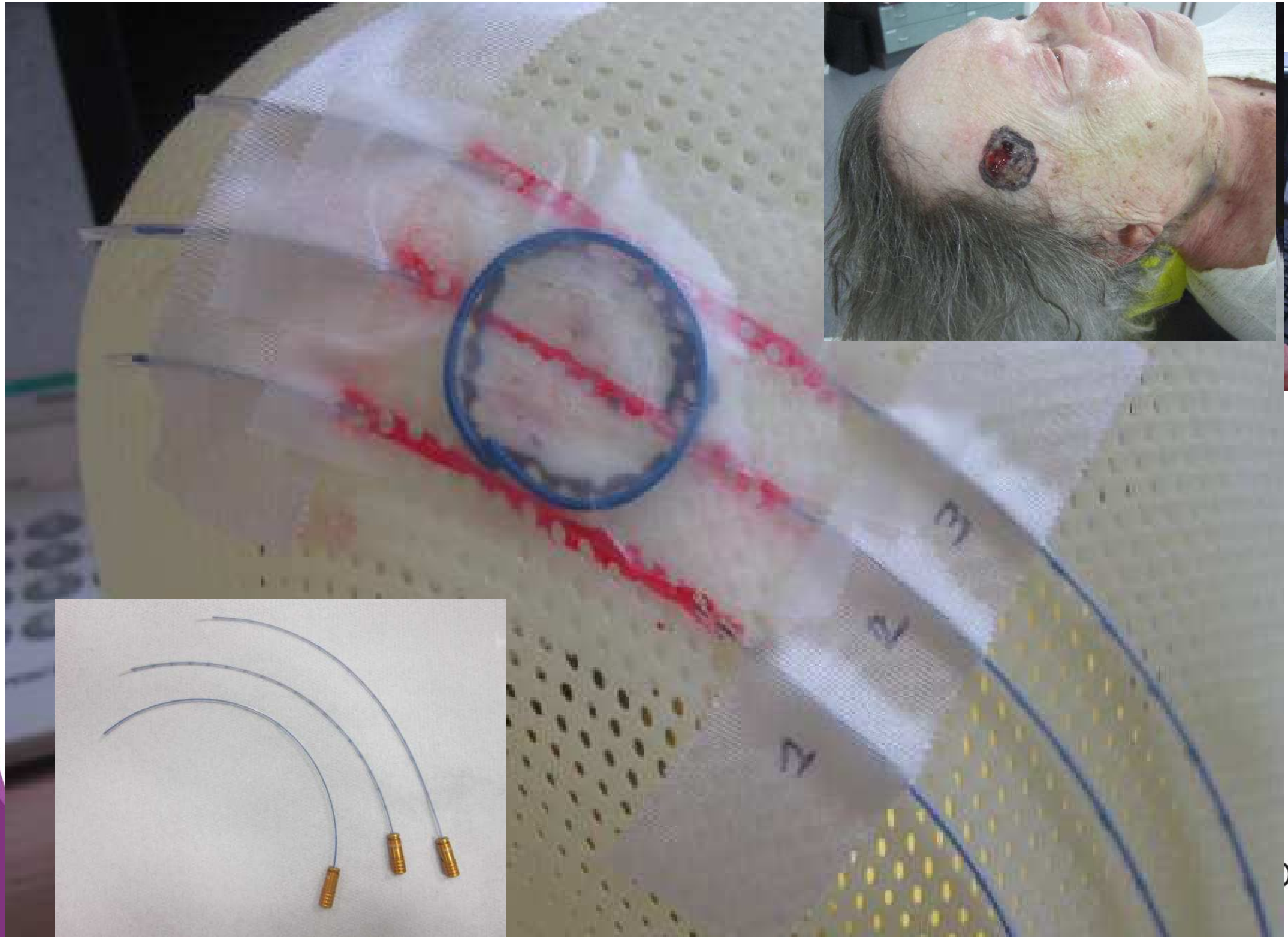
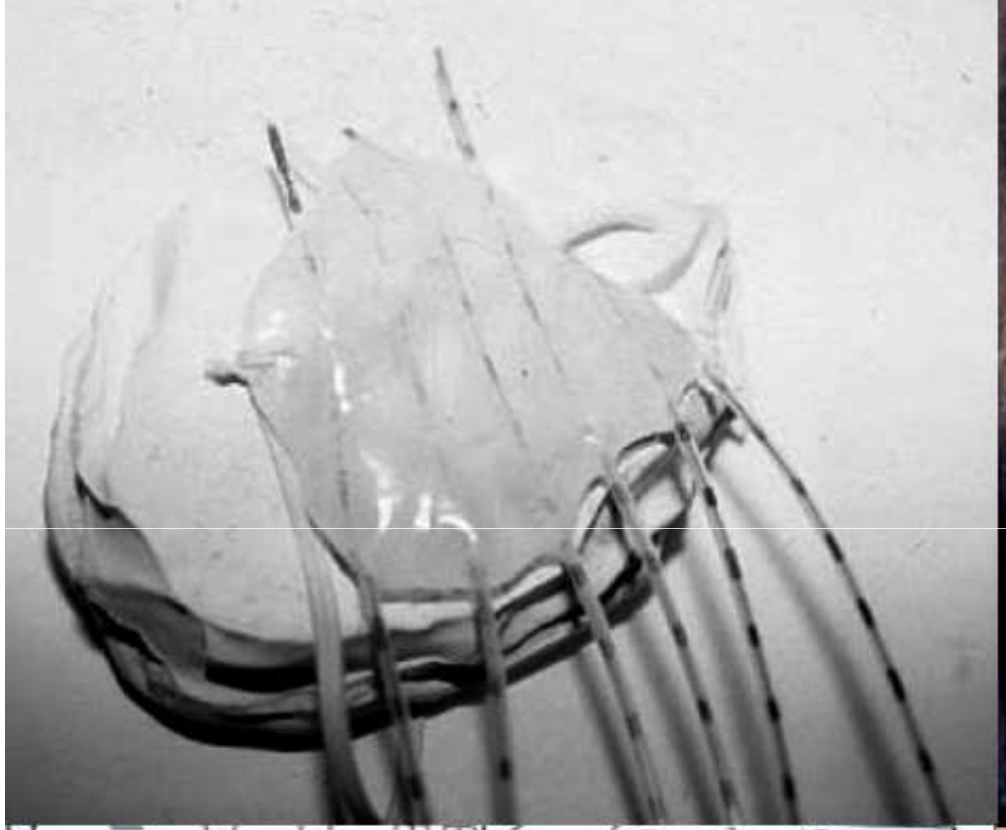
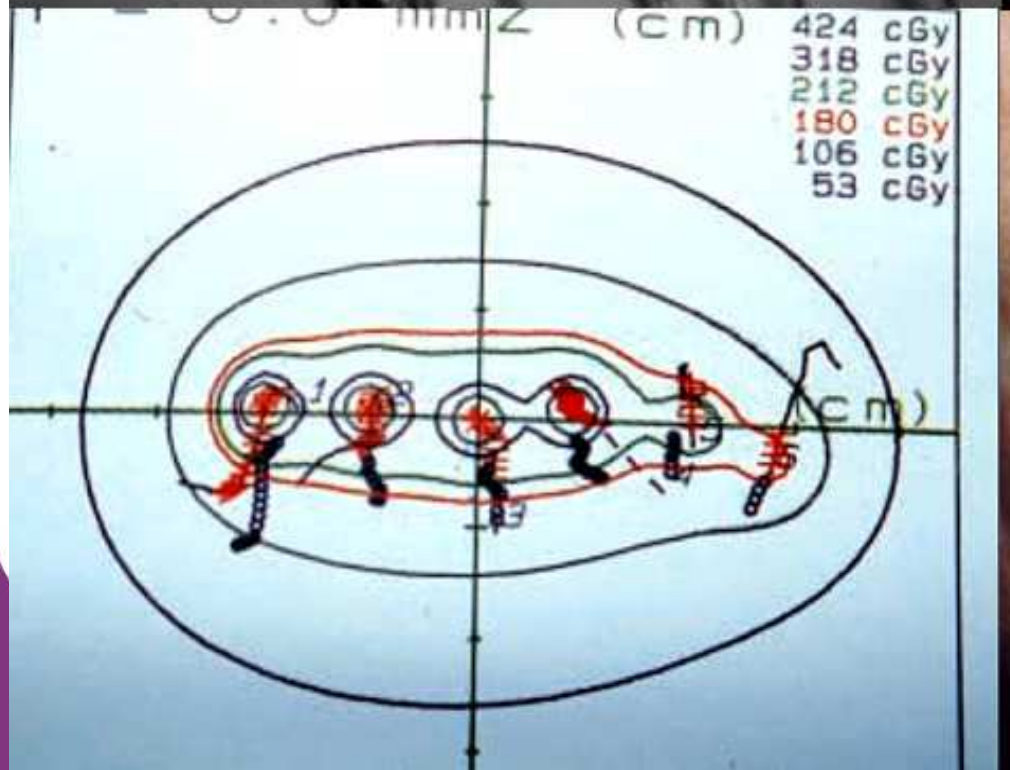
Mould applicators







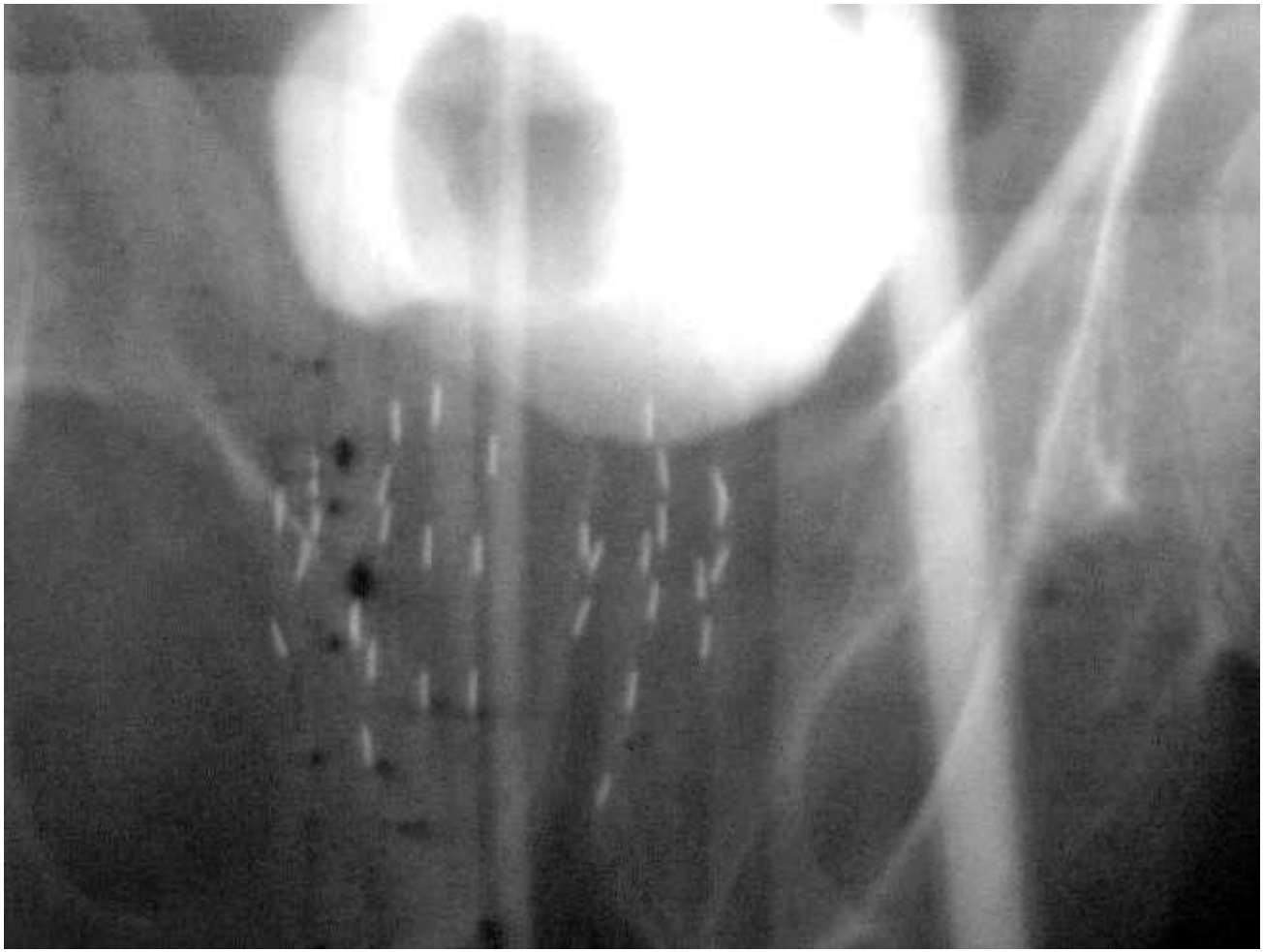



(cm)
424 cGy
318 cGy
212 cGy
180 cGy
106 cGy
53 cGy
(cm)

Leipzig Applicator

Permanent Seeds

- Permanent implant
- Very low dose rate



- Iodine 125, Palladium 103

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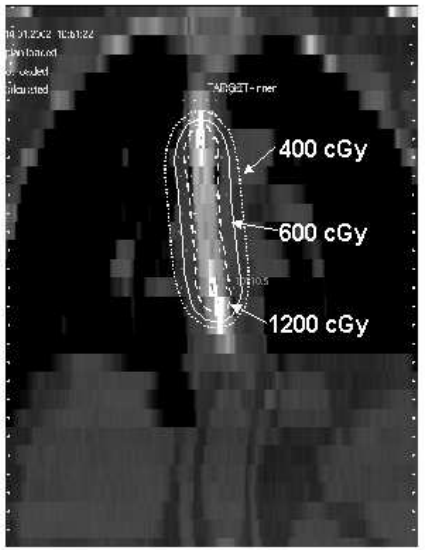
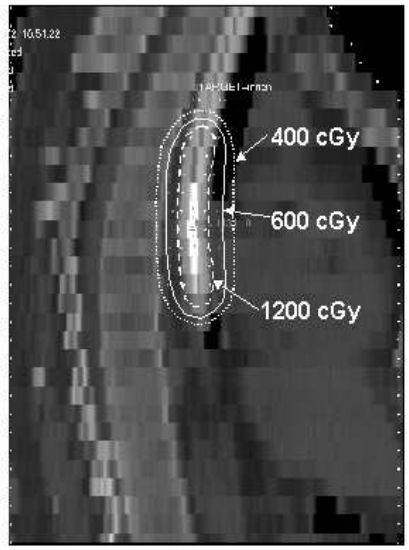
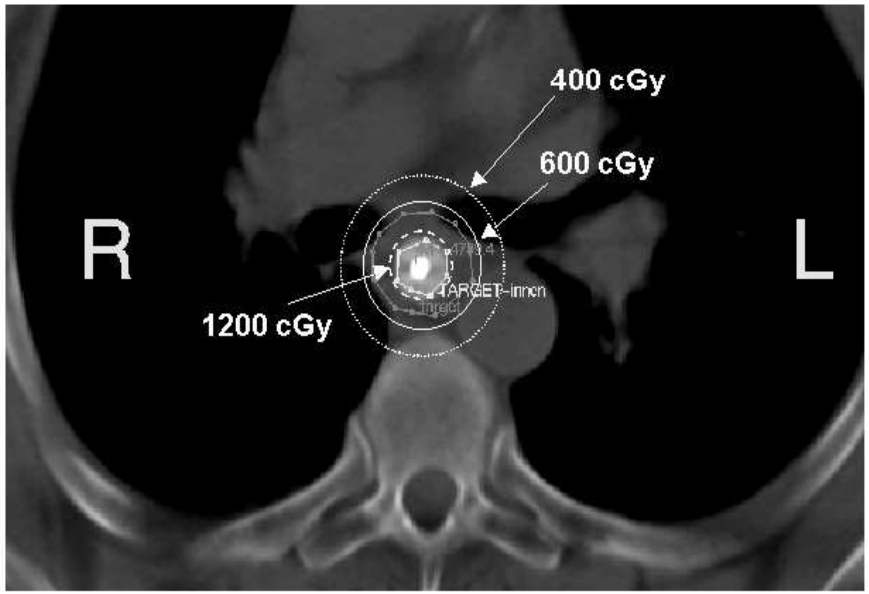
Endoluminal afterloading applicators

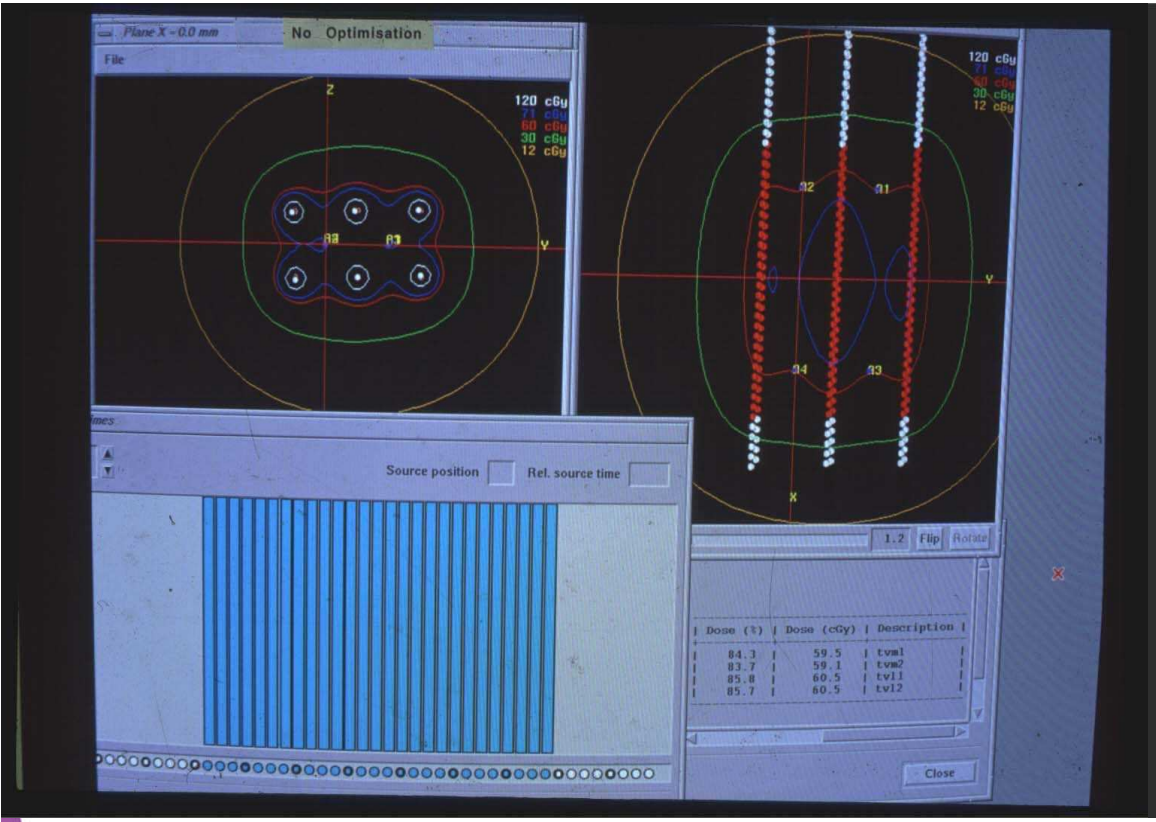
- Bronchus
- Esophagus
- Biliary tract

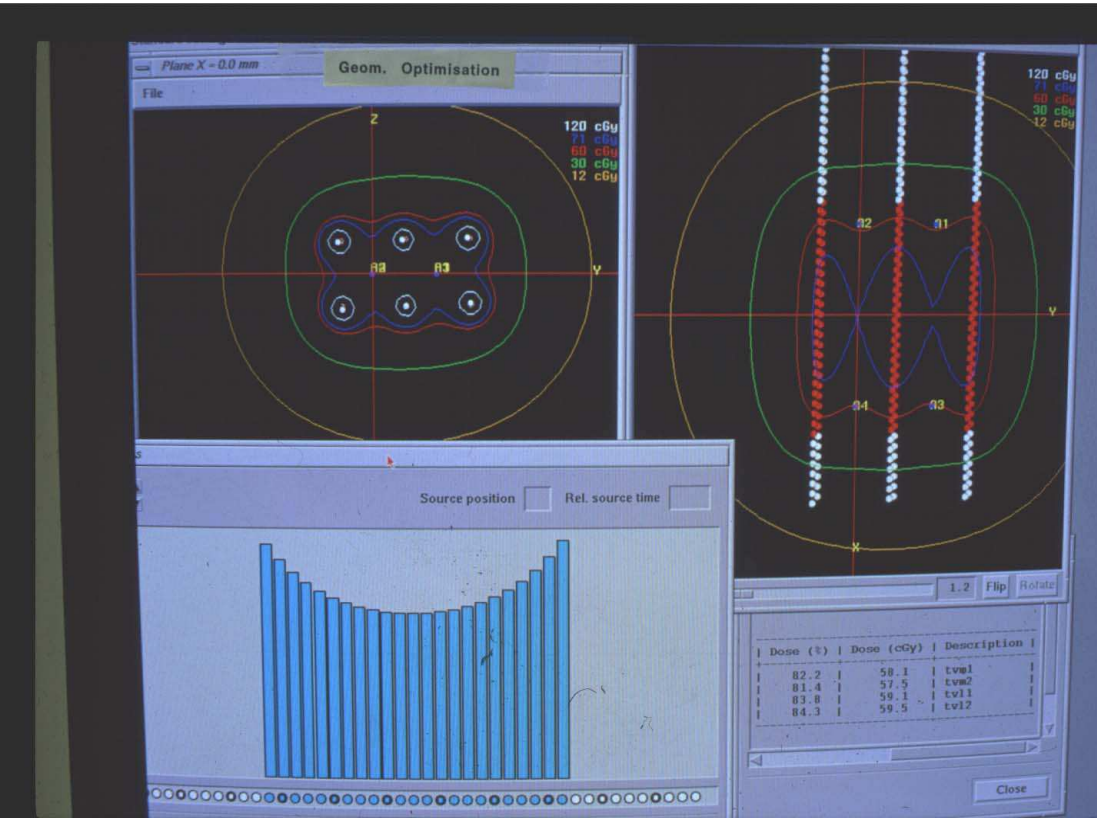






Dwell time optimization can make a good implant better





ASL 70mm: Target covered
Skin doses too high

ASL 60 mm: Target covered
Skin doses acceptable

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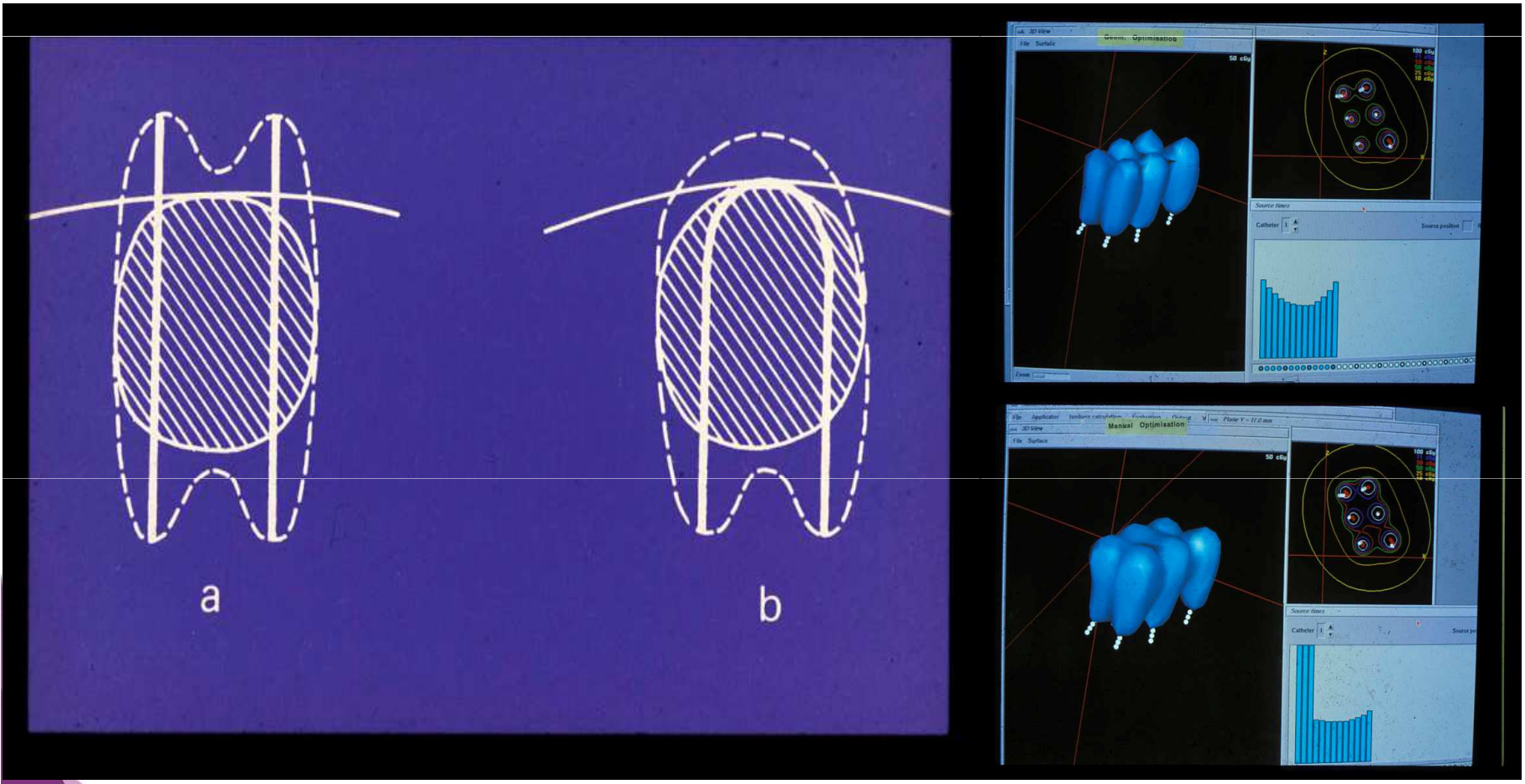
Dwell time optimization can make a good implant better



Geometrical optimization

Manual optimization

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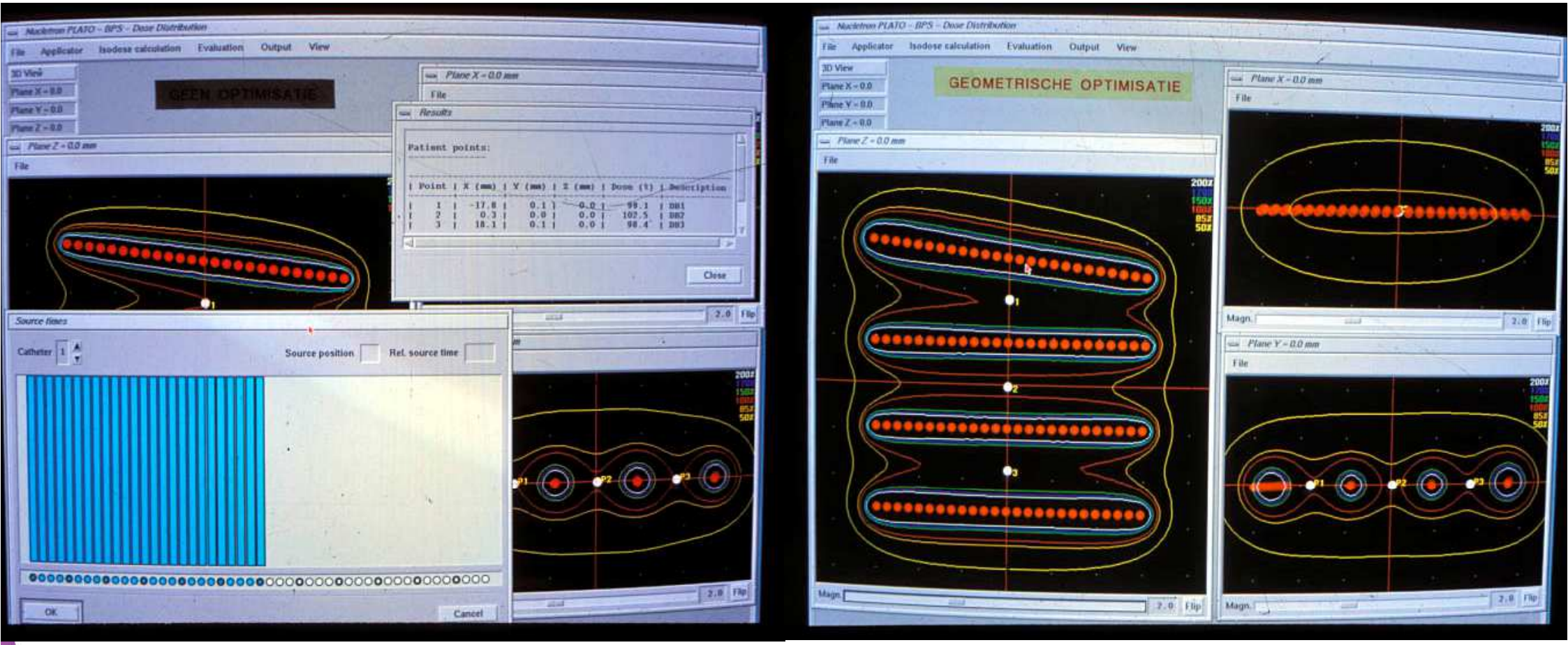
Correction of slight deviations



Slight divergence of source carriers

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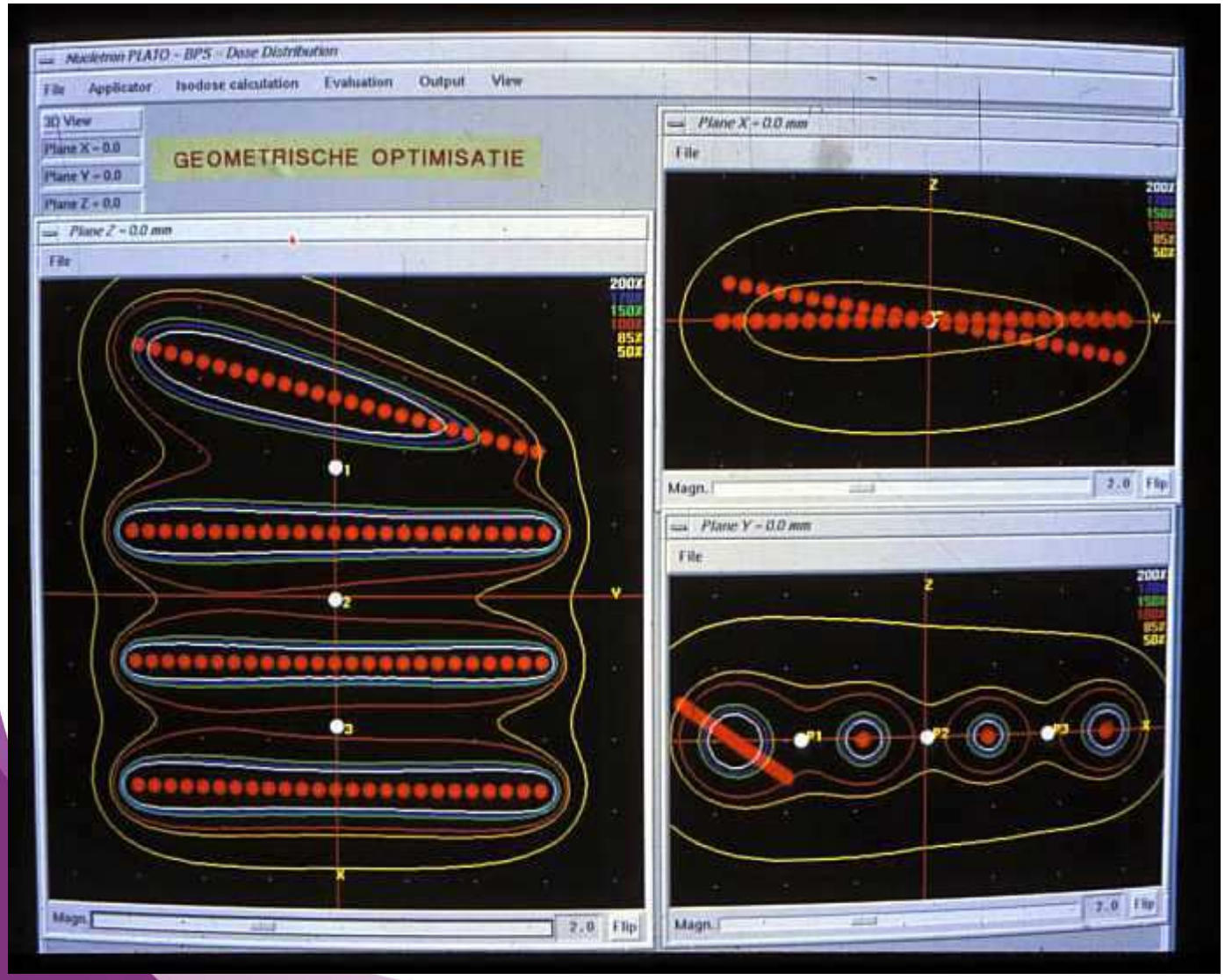
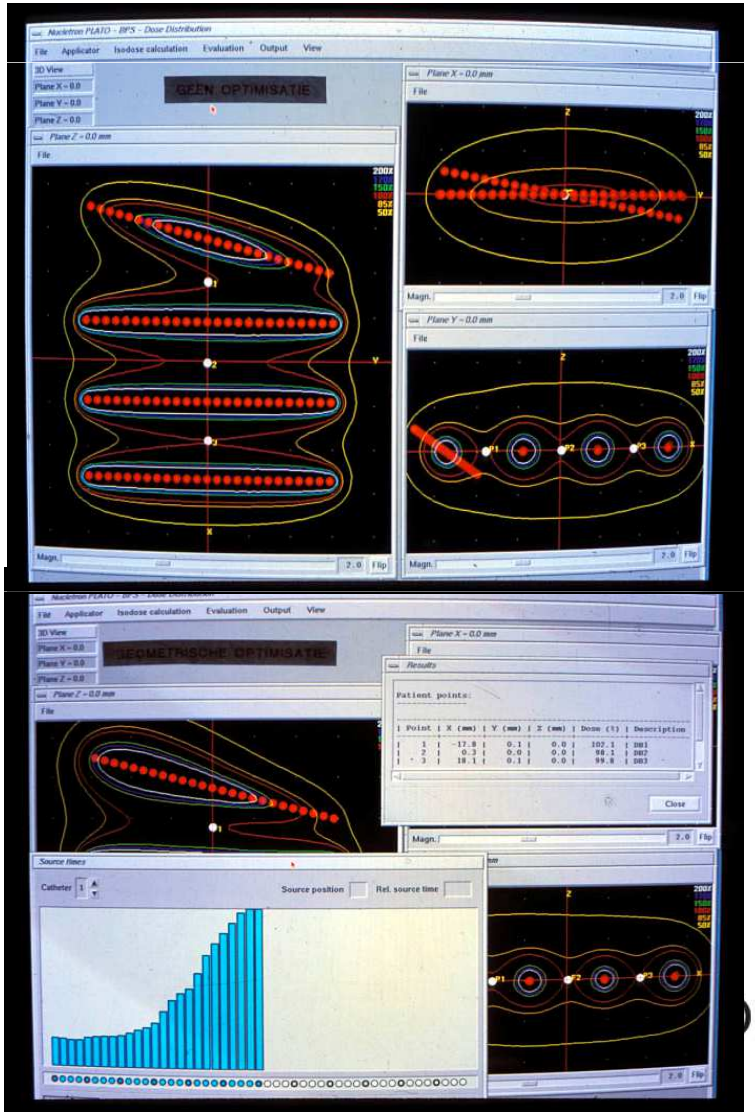
Dwell time optimization can never make a bad implant good





Modern Image guided 3D brachytherapy

- Modern imaging techniques:
  - US, CT, MRI

- 3D dosimetry
  - more accurate dose distribution
  - DVH relation to outcome
    for target + OAR

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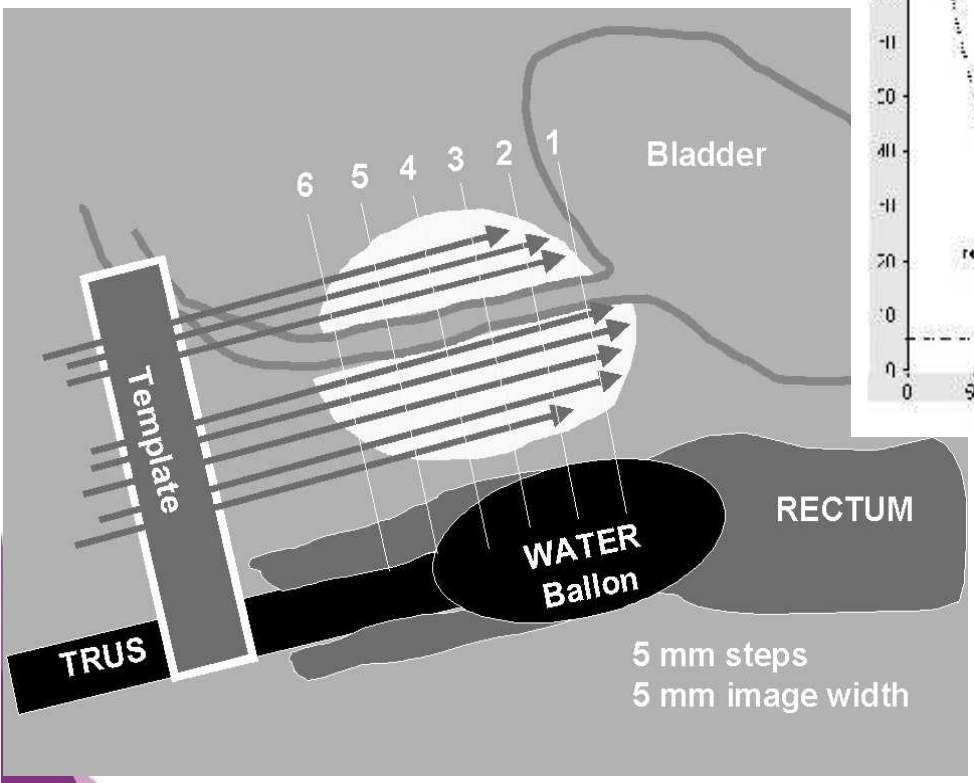
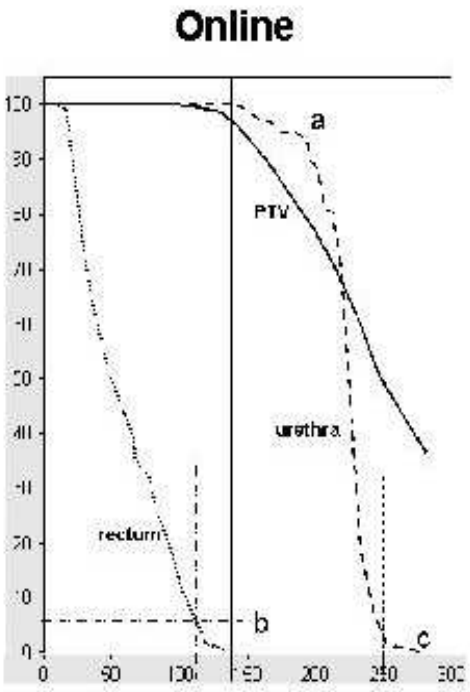
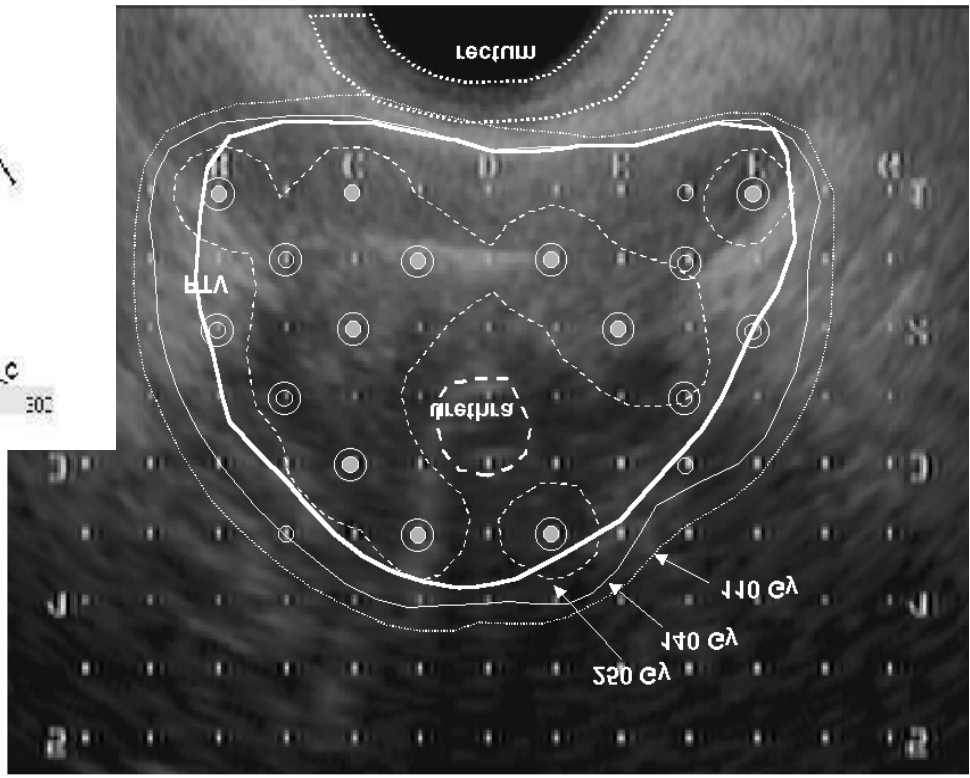
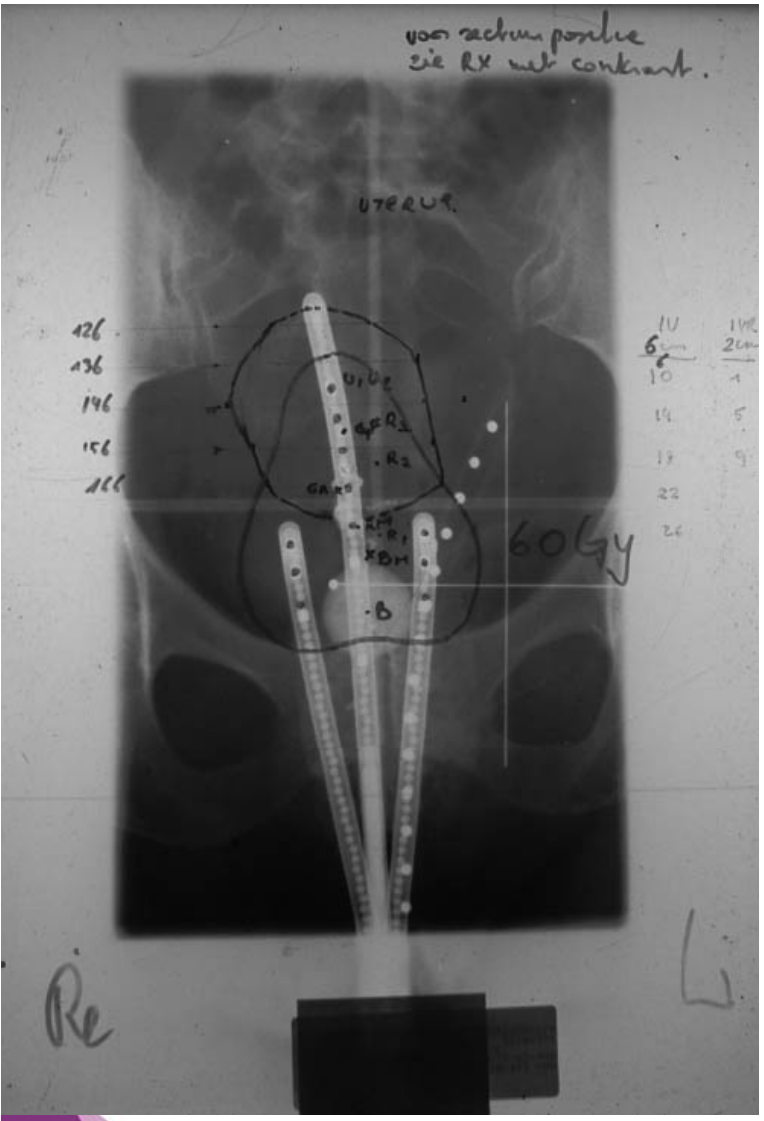
Ultra sono guided brachytherapy







2D X Rays



3D CT guidance

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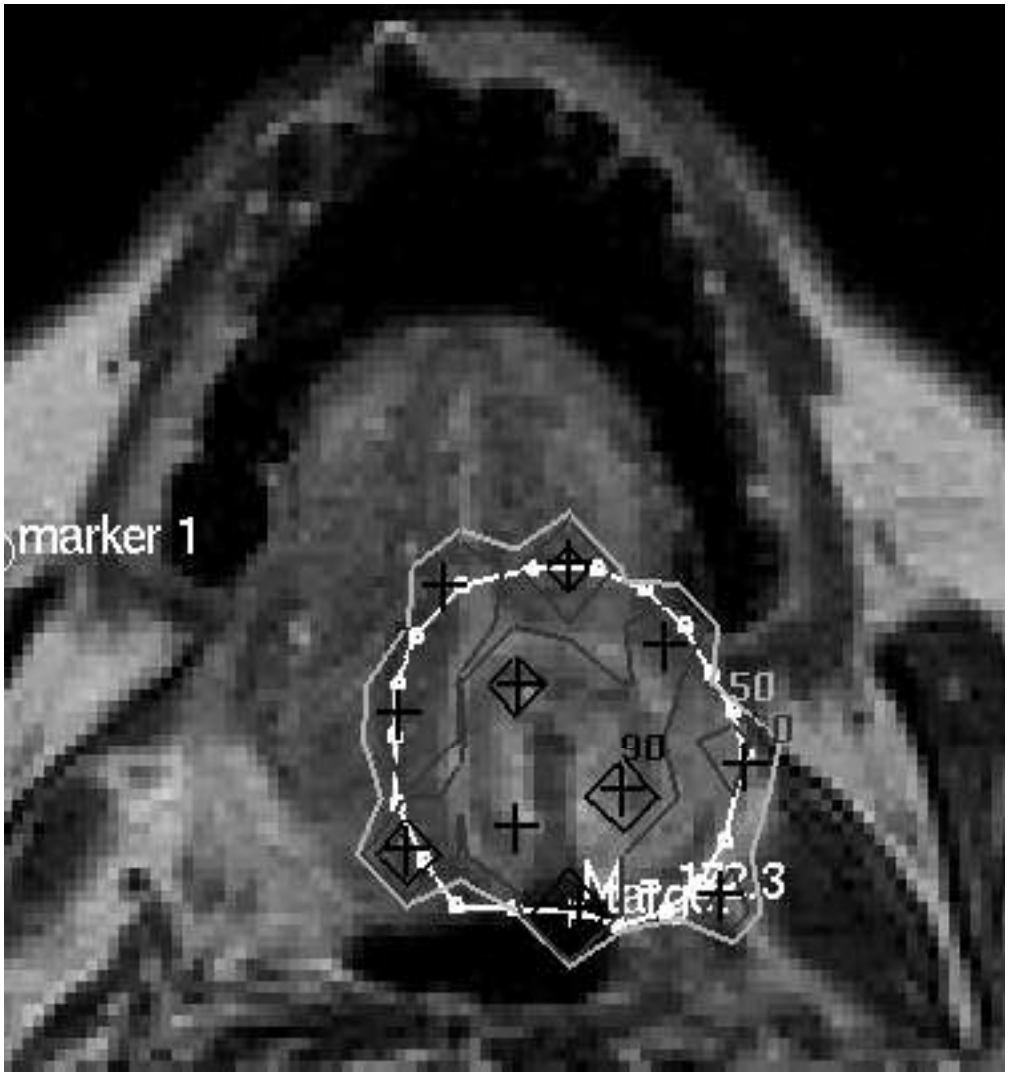
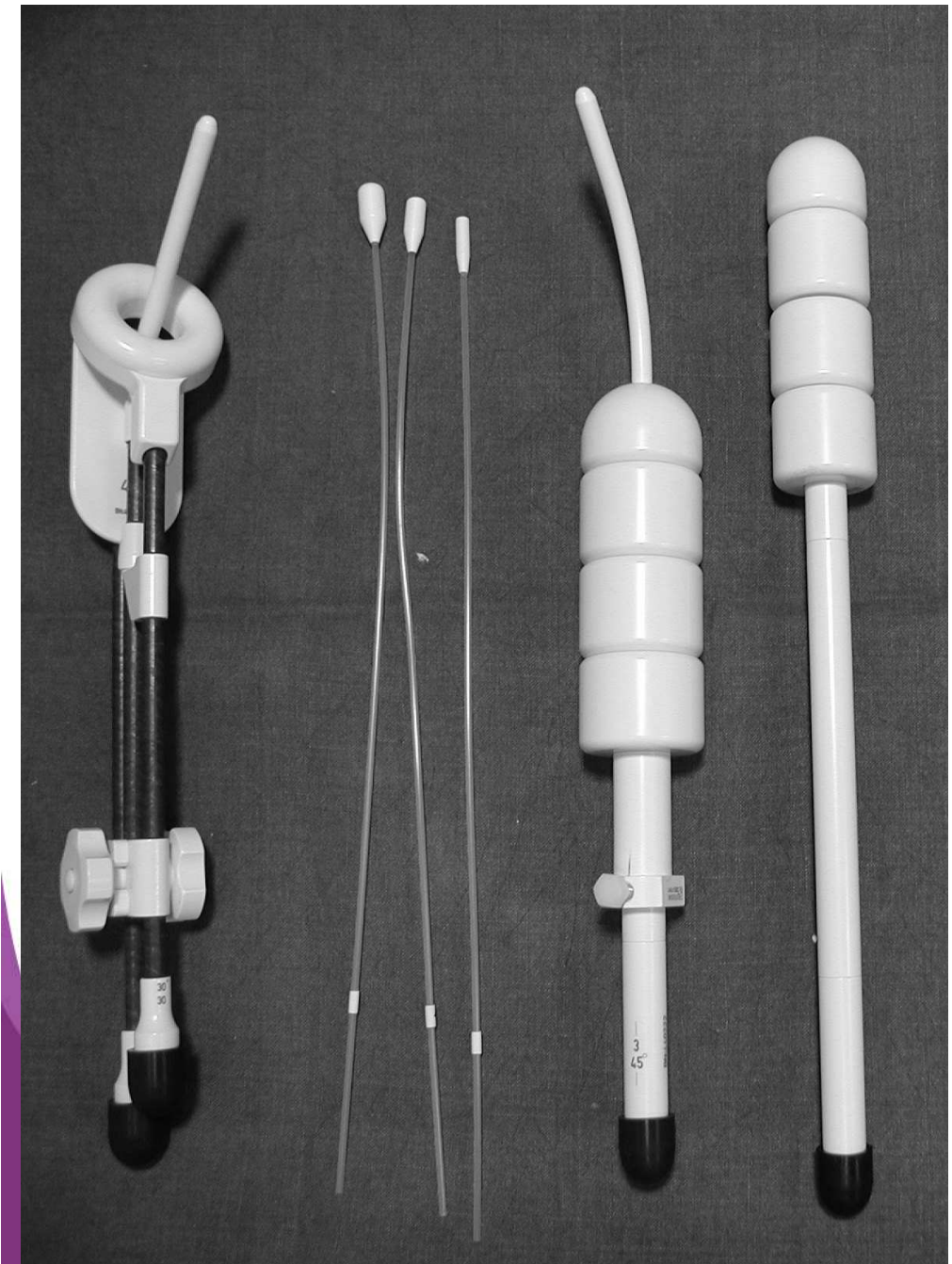
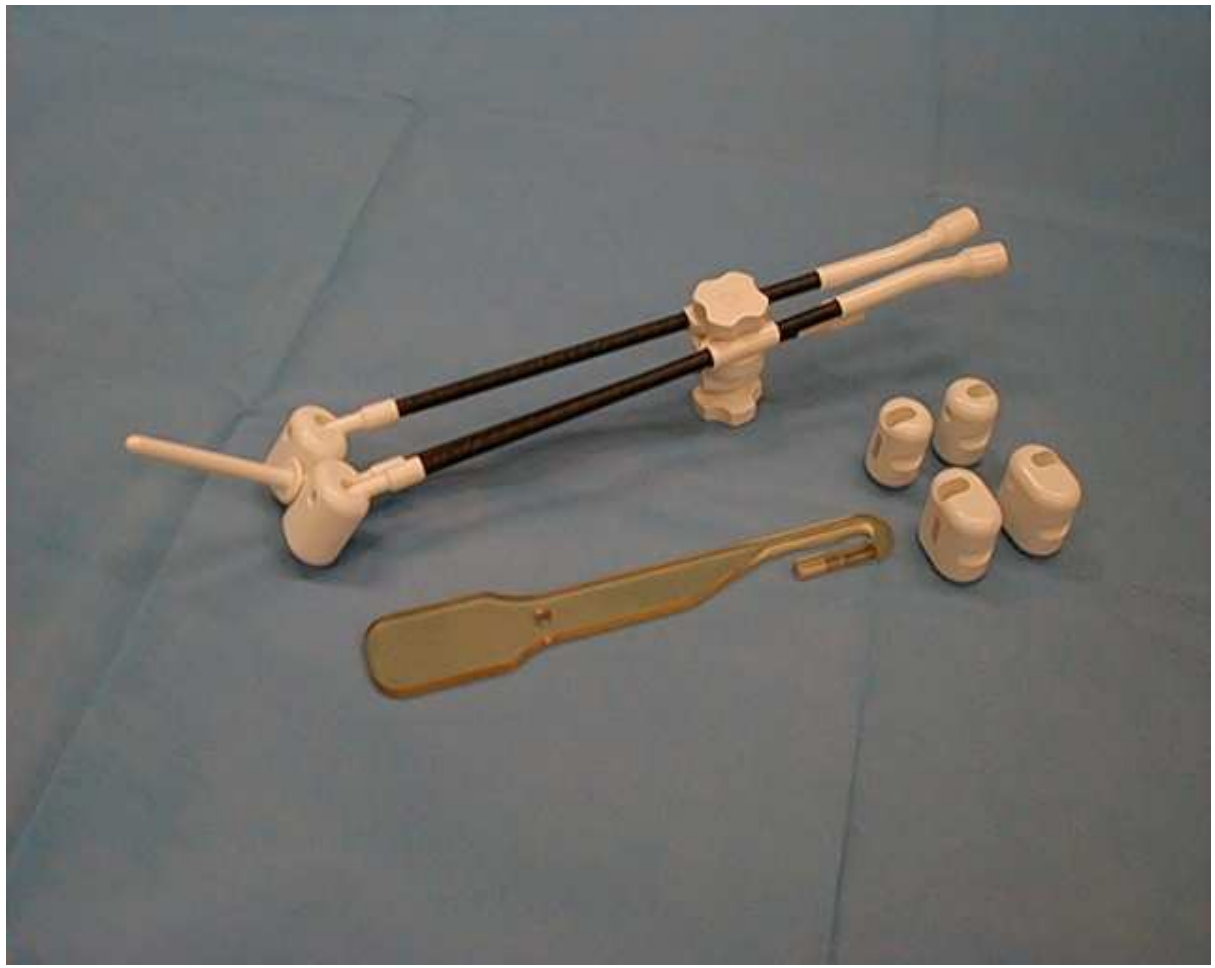
MRI guidance



MRI compatible applicators





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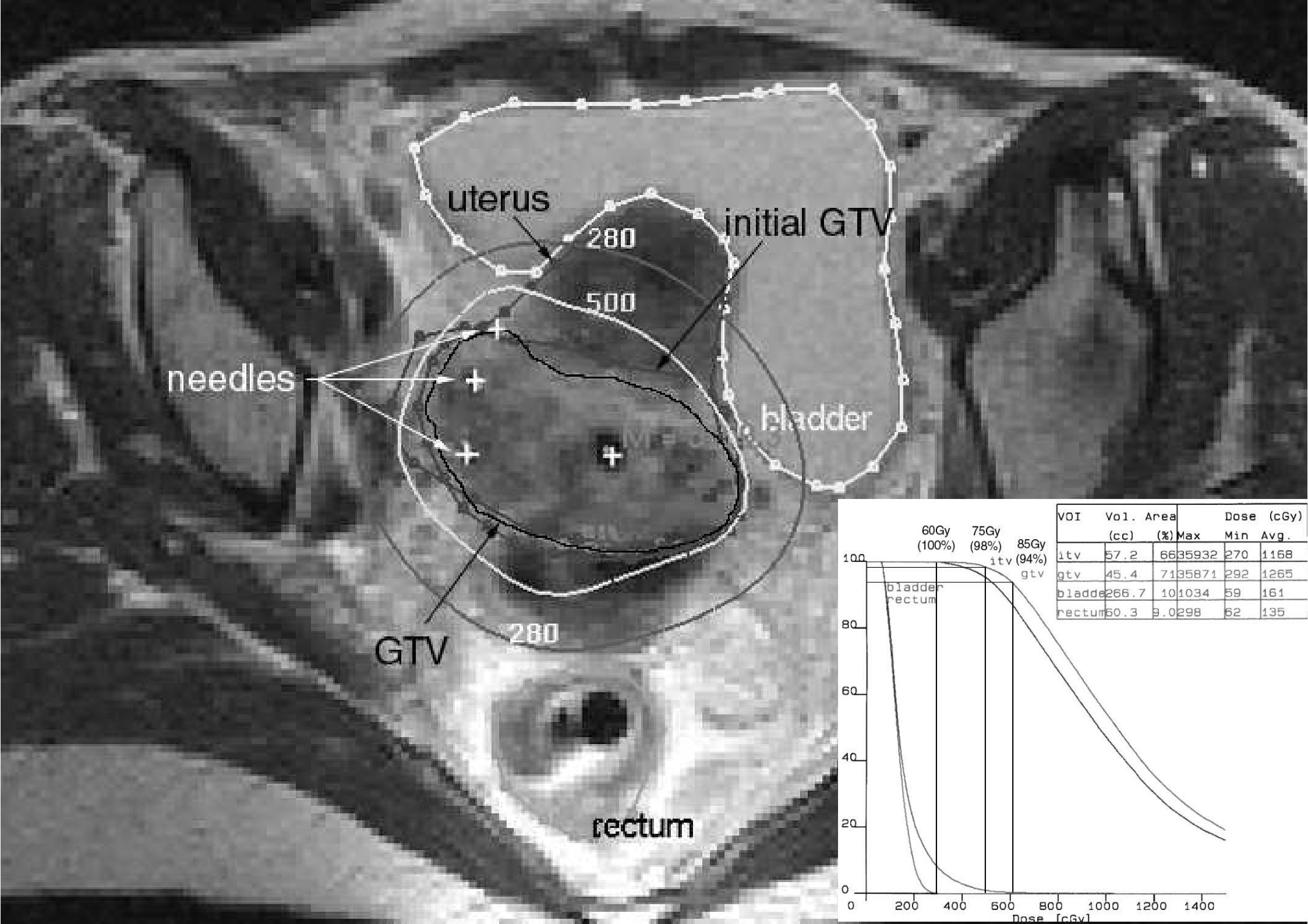

VOI	Vol. (cc)	Area (%)	Dose (cGy) Max	Min	Avg.
itv	57.2	66	35932	270	1168
gtv	45.4	71	35871	292	1265
bladde	266.7	10	1034	59	161
rectum	60.3	9.0	298	62	135

Different schools in brachytherapy

"a system"

- based on large experience
  - patient selection
  - special applicator types and techniques
  - specific loading patterns
  - specific dose rates

- be carefull with "own modifications"

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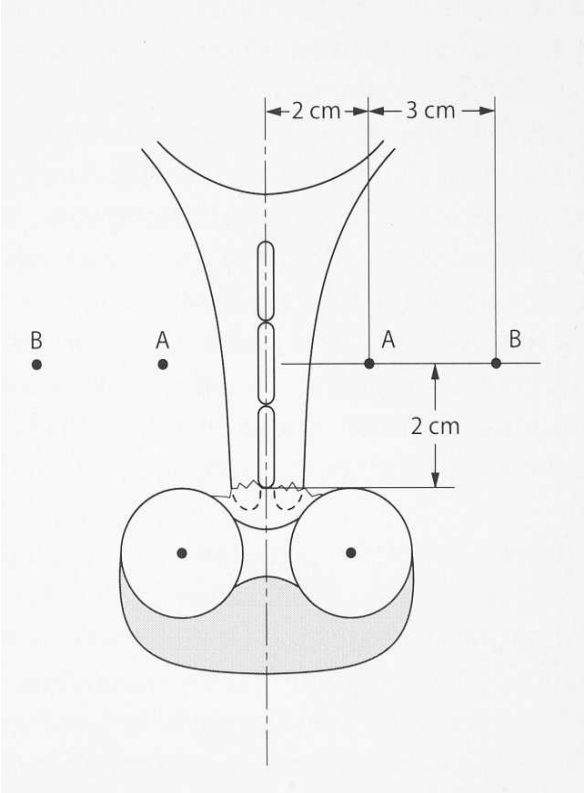
Endocavitary brachytherapy

- mgh
- doses to selected points :
  Manchester A – B



- doses to reference volumes
  reference points in critical organs
  ICRU 38

- **doses to 3D target (image guided)**

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Interstitial brachytherapy

- Patterson and Parker
- Quimby system
- Paris system

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Common Language

- Different schools
- Common language needed for recording and reporting

- General philosophy
  prescribe dose according to school – system

  report according to international accepted reference points and volumes

Recommendations for recording and reporting

1985 ICRU 38 :	Gynecological brachytherapy
1997 ICRU 58 :	Interstitial and intraluminal brachytherapy
2000 GEC-ESTRO Rec:	Prostate Permanent Implants
2001 GEC-ESTRO Rec:	Endovascular brachytherapy
2005 GEC-ESTRO Rec :	Prostate Temporary Implants
2005 GEC-ESTRO Rec :	3D GYNE (1)
2006 GEC-ESTRO Rec :	3D GYNE (2)
2008 GEC-ESTRO Rec:	Head and Neck
2010 GEC-ESTRO Rec:	Selection criteria APBI
2015 GEC-ESTRO Rec:	Target delineation on Breast Ca

2015 ICRU 88 -GEC-ESTRO Rec: Recording and reporting on Gyn BT

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Conclusion 1

Modern brachytherapy with is high ballistic selectivity and adaptivity is a competitive tool in the multidisciplinary treatment of cancer patients

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Conclusion 2

A strong collaboration between

- radiation oncologists
- organ specialists
- medical physicists
- radiation technologists

is necessary to obtain optimal results for the patient(s)

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Conclusion 3

To fully exploit the strength of BT, Specific training in

- radiation oncology
- medical physics
- radiobiology
- techniques

is needed for all members of the "brachytherapy team"

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Florence, March 13-16 2016

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Modern Brachytherapy Techniques

WWW.ESTRO.ORG/SCHOOL

Sources and Afterloaders Used in Brachytherapy

ESTRO Teaching Course

Florence, 2016

Dimos Baltas

E-mail: dimos.baltas@uniklinik-freiburg.de

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Topics

- **Some History**
- Radionuclides
- Does it mater which Radionuclide?
- Sources and Source Types
- Afterloaders
- New Developments

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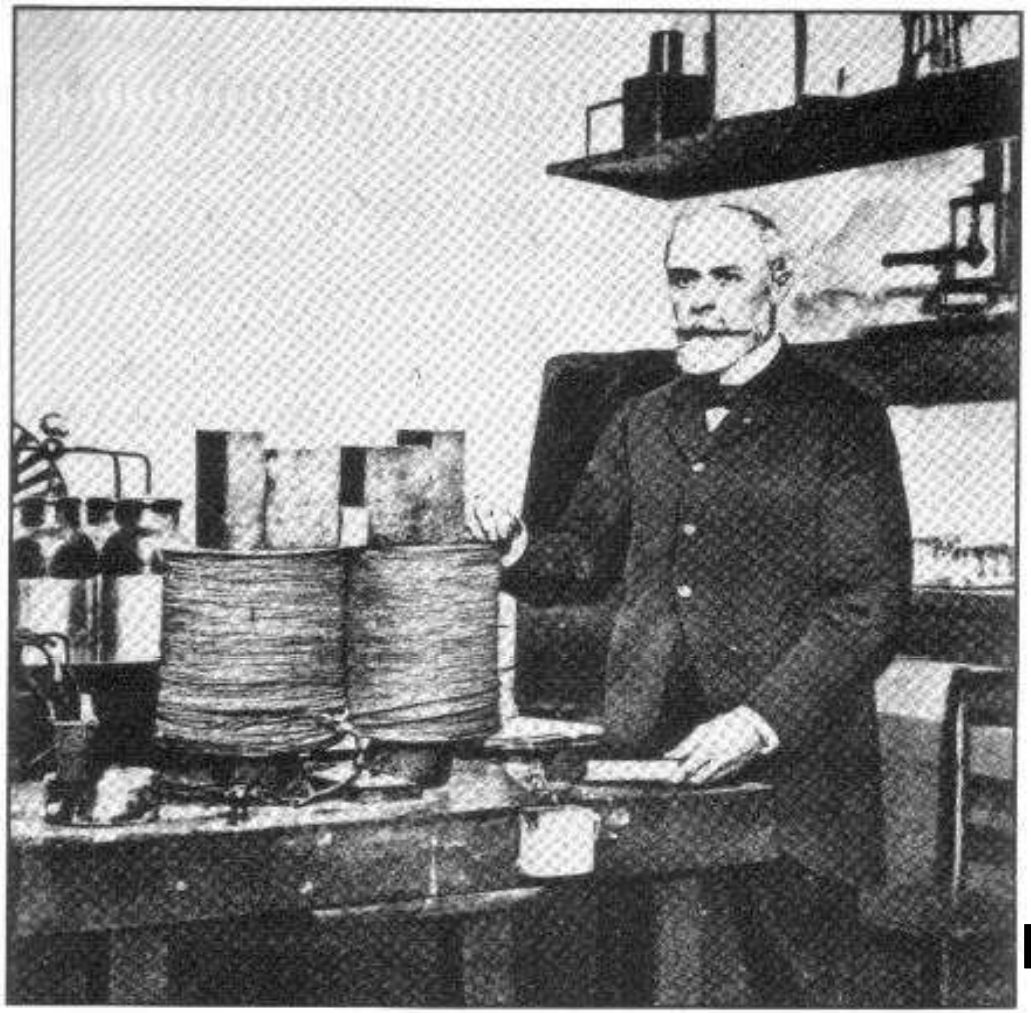
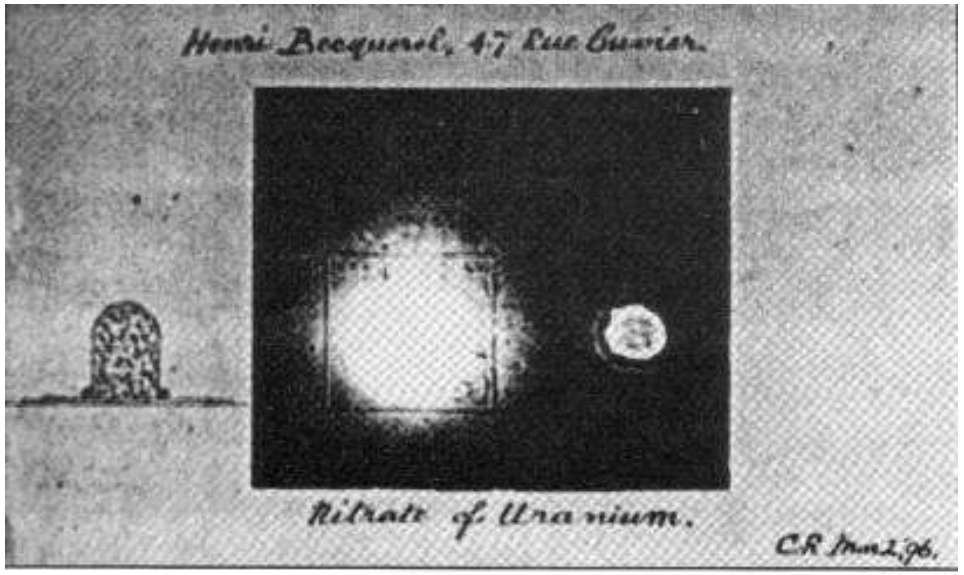
History: Radioactivity & Radium

Henri Becquerel: 1852–1908



[2.1] Antoine Henri Becquerel in his laboratory. (Courtesy: Museum Marii Sklodowskiej-Curie, Warsaw.)



Discovery of Radioactivity
1st March 1896

(photographic film blackening that proved the existence of the emission of spontaneous radiations from uranium)

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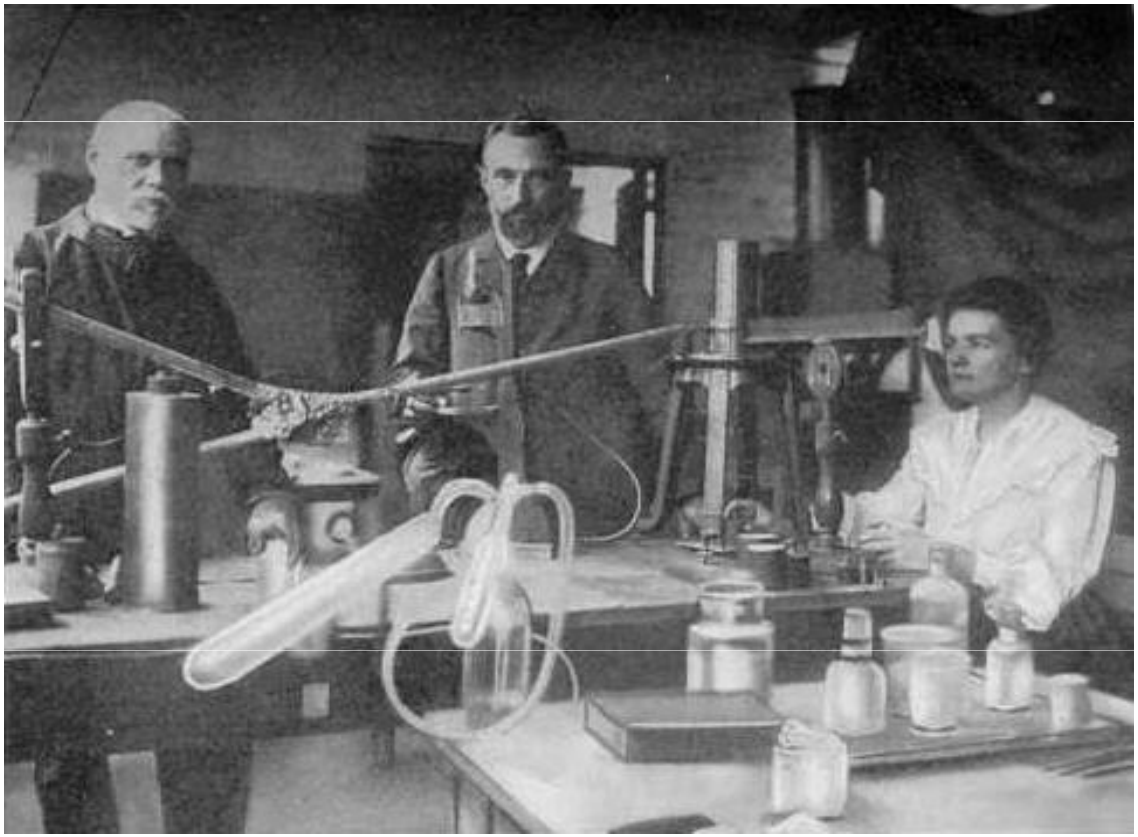
History: Radioactivity & Radium



Curies in their Laboratory where Radium was discovered

Discovery of Radium
December 1898

Pierre and Marie Curie

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History: Radioactivity & Radium

A view of the extraction of Radium in the old shed where the first Radium was obtained

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History: The Birth of (Interstitial) Brachytherapy

1903, two years later and completely independent from Pierre Curie, Alexander Graham Bell proposed the Publisher of *Archives Roentgen Ray,* to place radioactive material in form of thin fragments of Radium and encapsulated in thin glass tubes, directly into the tumour tissue.

Dear Dr. Sowers:

I understand from you that the Röntgen rays, and the rays emitted by radium, have been found to have a marked curative effect upon external cancers, but that the effects upon deep-seated cancers have not this far proved satisfactory.

It has occurred to me that one reason for the unsatisfactory nature of these latter experiments arises from the fact that the rays have been applied externally, thus having to pass through healthy tissues of various depths in order to reach the cancerous matter.

The Crookes' tube, from which the Röntgen rays are emitted, is of course too bulky to be admitted into the middle of a mass of cancer, *but there is no reason why a tiny fragment of radium sealed up in a fine glass tube should not be inserted into the very heart of the cancer, thus acting directly upon the diseased material.* Would it not be worth while making experiments along this line?

[Signed] Alexander Graham Bell

Fig. 1. Alexander Graham Bell [1], suggesting the concept of brachytherapy.

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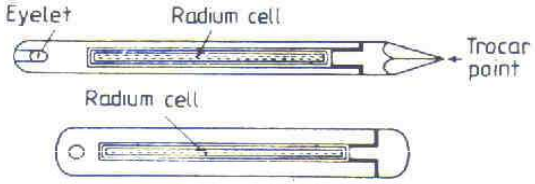
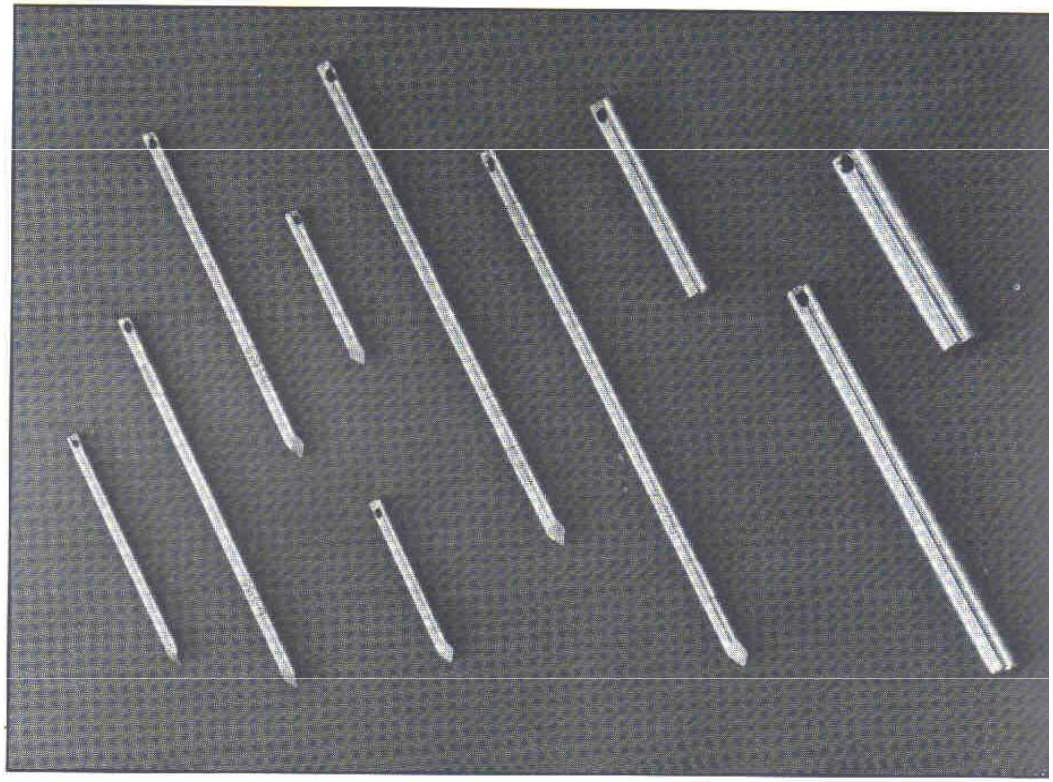
History: Radioactivity & Radium



[3.17] Although there was a large range of linear radium sources, tubes and needles, in terms of geometrical and active length and linear activity (milligram radium/cm), the basic design from the early 1920s was essentially that shown in the schematic diagram. Eyelets were used to suture a needle to the patient's tissue to prevent the possibility of its involuntary removal before the end of treatment, or to attach string threads to a tube to enable removal, such as from the uterus or vagina after gynaecological brachytherapy had been completed. Some designs had removeable screw-on ends so that different radium cells could be placed in the outer container, depending on the required treatment. Union Minière du Haut Katanga, the Belgian company, supplied such sources in the 1920s, but by the 1950s the Radiochemical Centre, Amersham (later Amersham International), who were then the major supplier of radium sources, had no screw-on end designs and certainly did not supply any radium cells which, because of their very thin walls, were of a much greater hazard that the sealed sources illustrated here. These are the well known G-tubes which were 2 cm geometrical length, and available with different milligram radium contents



such as 10 mg, 15 mg, 20 mg and 25 mg. When radium was replaced by artificially produced radionuclides, such G-tubes then contained caesium-137 with an actively specified in terms of milligram radium equivalent [20.12, 20.56].

radium needles and tubes (original design)

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Topics

- Some History
- **Radionuclides**
- Does it mater which Radionuclide?
- Sources and Source Types
- Afterloaders
- New Developments

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History: Radioactivity & Radium

Radium Sources: Financial Point of View

TABLE 5.1

Prices for 1 g of ^{226}Ra at the Beginning of the Twentieth Century

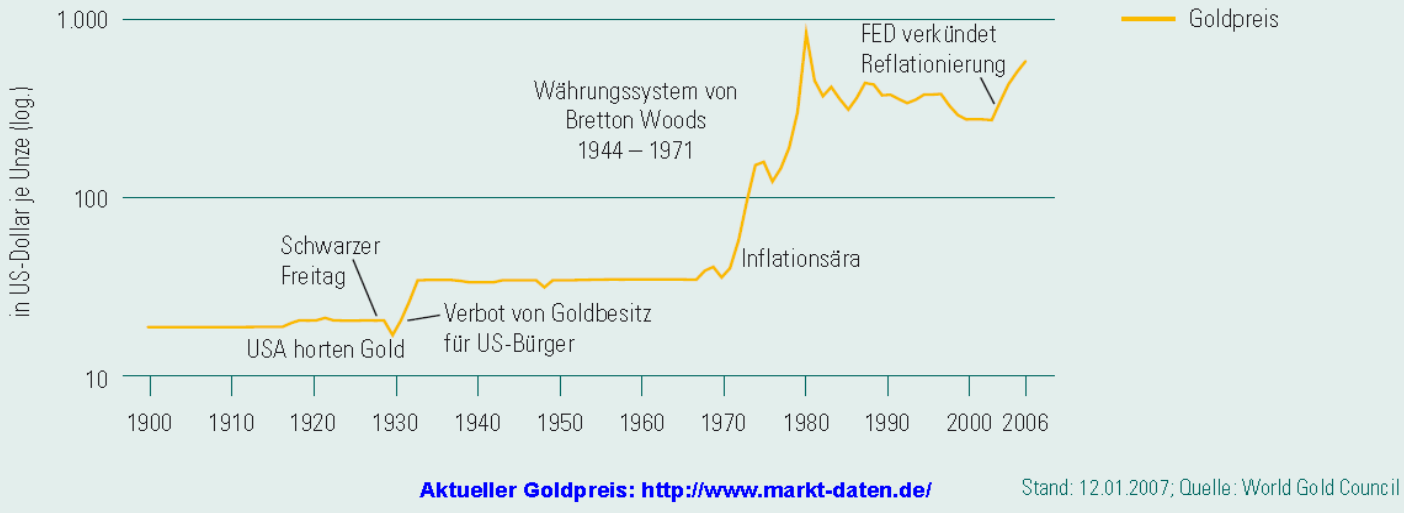
Year	U.S. Dollars
1902	3,000.00
1904	18,600.00
April 1906	50,000.00
August 1906	70,000.00
December 1906	90,000.00
1911	120,000.00
1914	150,000.00

Source: From Towpik, E. and Mould, R.F., *J. Oncol.*, Nowotwory, Warsaw, 1998.

1g pure Gold 1900-1923: 0.67 U.S. Dollars

Jahrhundertrückblick auf Gold

1 Ounce= 28,3495231 Gramm



Aktueller Goldpreis: http://www.markt-daten.de/

Stand: 12.01.2007; Quelle: World Gold Council

Radionuclides: the different "Characters"

TABLE 5.3

Radionuclide Physical Properties

Physical Property	Relevance to Brachytherapy
Radiation emitted	Source geometry and structure
Half-life $T_{1/2}$	Determines if permanent or temporary implant or both are practical
Specific activity	Source size, dose rate
Energy of emitted radiation	Dose distribution within tissue, radiation protection requirements
Density and atomic number	Radiographic visibility/localization, isotropy/anisotropy of dose distribution

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Radionuclides: All we have ?

Table 5.12 Physical characteristics of radionuclides used in brachytherapy. Photon energy ranges, mean and effective photon energies are according to Table 5.3 to Table 5.11, where only penetrating energies above 10 keV have been considered. The maximum specific activity is calculated for ideal (point) pure radionuclide sources using Eq. 2.60.

Radionuclide				Density[a] ρ (g.cm^3)	Decay	Half life[a] $T_{1/2}$	Photon energy range (MeV)	Mean photon energy E_{mean} (MeV)	Effective energy E_{eff} (MeV)	Mean γ-energy (MeV)	HVL[c] (mm Pb)	Maximum specific activity (GBq.mg^{-1})	Γ_δ[e] (μGy.h^{-1}.MBq^{-1}.m^2)	Type of implant
Name	Symbol	Z	A											
Caesium	Cs	55	131	1.873	EC	9.689 d[b]	0.029 – 0.034	0.030	0.030	---	0.030	3809.13	0.0151	Permanent
Caesium	Cs	55	137	1.873	β^-	30.07 a	0.032 – 0.662	0.615	0.652	0.662	7.0	3.202	0.0771	Temporary
Cobalt	Co	27	60	8.90	β^-	5.27 a	0.347 – 2.159	1.253	1.257	1.253	12.0	41.91	0.3059	Temporary
Gold	Au	79	198	19.32	β^-	2.695 d	0.069 - 1.088	0.406	0.417	0.415	2.8	9055.12	0.0545	Permanent
Iodine	I	53	125	4.93	EC	59.49 d	0.027 - 0.035	0.028	0.028	0.035	0.025	650.15	0.0348	Permanent or temporary
Iridium	Ir	77	192	22.42	β^-, EC	73.81 d	0.061 -1.378	0.355	0.398	0.372	3.0	340.98	0.1091	Temporary
Palladium	Pd	46	103	12.02	EC	16.991 d[b]	0.020 - 0.497	0.021	0.021	0.137	0.008	2763.13	0.0361	Permanent
Radium	Ra	88	226	5.00	α	1600 a[b]	0.047 - 2.45	0.830[f]	---	0.830[f]	13.0	0.0366	---	Temporary
Thulium	Tm	69	170	9.321	β^-, EC	128.6 d[b]	0.048 – 0.084	0.066	0.067	0.084	0.17[g]	221.07	0.00053	Temporary
Ytterbium	Yb	70	169	6.73	EC	32.015 d	0.021 - 0.773	0.093	0.131	0.143	0.23[g]	893.29	0.0431	Permanent or temporary

[a] According to NIST Physical Reference Data, on line version, 2004[14, 15]

[b] According to NUDAT Vs. 2.0 on line tables, 2004[3], [c] Half Value Layer (first) values most taken from ICRP 21 Figures 50 and 51[16]

[d] According to Granero et al., 2005[18] and Lymperopoulou et al., 2006[21]

Activity

2.6.2 Activity

In order to describe quantitatively the time rhythm of the occurrence of spontaneous nuclear transformations (decays) of an amount of a specific radionuclide, the *activity* A (s^{-1}) is defined as

$$A = \frac{dN}{dt} \tag{2.55}$$

where dN is the number of decays observed during the time interval dt. The special name for the unit of activity is becquerel (Bq). Until recently, the unit used to describe activity has been the *curie* (Ci): $1\ Ci = 3.7 \times 10^{10}$ Bq, but the use of this unit is no longer recommended even if it is still present in several publications.

Definition of 1Ci: Activity contained in 1g ^{226}Ra

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Activity

- Molar mass of ^{226}Ra is 226,02 g/mol
- $T_{1/2}$ of decay for ^{226}Ra is 1600 a

$$A_{spec} = \lambda \frac{N_A}{M} = \frac{ln2}{T_{1/2}} \cdot \frac{N_A}{M}$$

- Thus considering 1a = 365x24x60x60s
- and N_A = 6,022 x10^{23} mol^{-1} (Avogadro-Number)
- A_{spec} for ^{226}Ra is 3,7x10^{10} Bq/g = 37GBq/g =1Ci/g

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Radionuclides: A Review

^{60}Co: containing radioactive needles, Wiiliam Myers, Ohio State University 1947 (cobanic: 45% Co & 55% Ni): 1mm small diameter and could be bent!

^{137}Cs: Longer half life than ^{60}Co (30 vs. 5 years), lower energy than ^{60}Co (0.662 vs. 1.25 MeV)

^{198}Au: replaces ^{222}Rn seeds since 1910.

^{192}Ir: since 1958 as seed by Ulrich Henscke. From early 1960s mainly as wire (IGR, Paris-group). High speicifc activity and thus appropriate as Miniaturized stepping source.

^{125}I: since late 60s as seeds for interstitial applications.

^{103}Pd: shorter half life than ^{125}I (17 vs. 59 days) and very high specific activity.

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Radionuclides: A Review

Table 5.12 Physical characteristics of radionuclides used in brachytherapy. Photon energy ranges, mean and effective photon energies are according to Table 5.3 to Table 5.11, where only penetrating energies above 10 keV have been considered. The maximum specific activity is calculated for ideal (point) pure radionuclide sources using Eq. 2.60.

Radionuclide				Density[a] ρ ($g.cm^3$)	Decay	Half life[a] $T_{1/2}$	Photon energy range (MeV)	Mean photon energy E_{mean} (MeV)	Effective energy E_{eff} (MeV)	Mean γ-energy (MeV)	HVL[c] (mm Pb)	Maximum specific activity ($GBq.mg^{-1}$)	Γ_δ [e] ($\mu Gy.h^{-1}.MBq^{-1}.m^2$)	Type of implant
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Iodine	I	53	125	4.93	EC	59.49 d	0.027 - 0.035	0.028	0.028	0.035	0.025	650.15	0.0348	Permanent or temporary
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Palladium	Pd	46	103	12.02	EC	16.991 d [b]	0.020 - 0.497	0.021	0.021	0.137	0.008	2763.13	0.0361	Permanent

[a] According to NIST Physical Reference Data, on line version, 2004[14, 15]

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[d] According to Granero et al., 2005[18] and Lymperopoulou et al., 2006[21]

Radionuclides: A Review

Sources: ^{60}Co

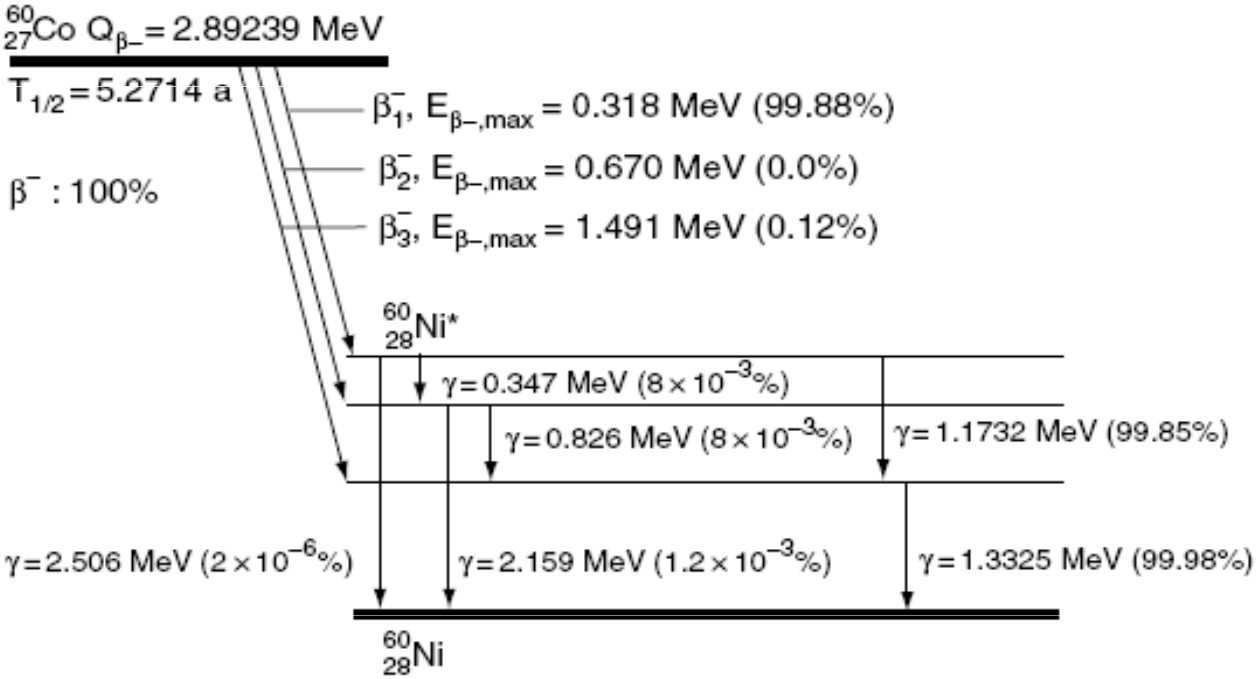

FIGURE 5.3
Schematic representation of β^- decay of $^{60}_{27}$Co which decays almost totally (99.92%) to the third excited state of $^{60}_{28}$Ni. The disintegration energy for the decay is $Q_{\beta^-} = 2.8239$ MeV. The two main γ-rays are 1.1732 and 1.3325 MeV, both with an intensity of approximately 100%.[3] On average, two photons are emitted per disintegration with energy above 10 keV (see Table 5.4c). The half-life for $^{60}_{27}$Co decay is 5.2714 years.[14]

Radionuclides: A Review

Sources: ^{60}Co

5.3.1 Teletherapy

^{60}Co as a teletherapy source was considered as an alternative to both deep x-ray therapy tubes and sources of some 5 to 10 gm ^{226}Ra for treating deep-seated tumors. The economics for the new ^{60}Co was a major consideration. A ^{60}Co teletherapy machine could be constructed with costs for the required activity of the ^{60}Co source of 50,000 U.S.$. For an equivalent ^{226}Ra source the costs were a factor of 1000 higher.

In 1949, the Canadians started two independent ^{60}Co teletherapy projects: in Ottawa and in Saskatoon. The first patient was treated on October 27, 1951 by the Eldorado machine in Ottawa and on November 8 of the same year, a patient was treated at the University of Saskatchewan in Saskatoon.

Radionuclides: A Review

Sources: ^{60}Co

5.3.2 Brachytherapy

In a letter to the journal *Science* in June 1948 on "Radioactive Needles Containing Cobalt 60", William Myers from the Department of Medicine, Ohio State University,[2] described studies with ^{60}Co started in October 1947.

For the production of ^{60}Co radioactive needles, an alloy wire composed of 45% cobalt and 55% nickel, the so-called cobanic, was used in order to overcome the machining difficulties related to pure cobalt. In this work, needles of a very small diameter, 1.0 mm, are described. The half-value thickness of the gamma irradiation of this type of source was 0.41″ (10.41 mm) Pb.

Myers also stated that the expected benefit when using ^{60}Co sources when compared to ^{226}Ra should be that the ^{60}Co radioactive wires can be bent to conform to the shape of tumors which are in a difficult anatomical environment (e.g., bones) and that there is no danger of loss by leaks or breakages. This was the worldwide first use of ^{60}Co radioactive needles for cancer therapy.

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Radionuclides: A Review

Sources: ^{137}Cs

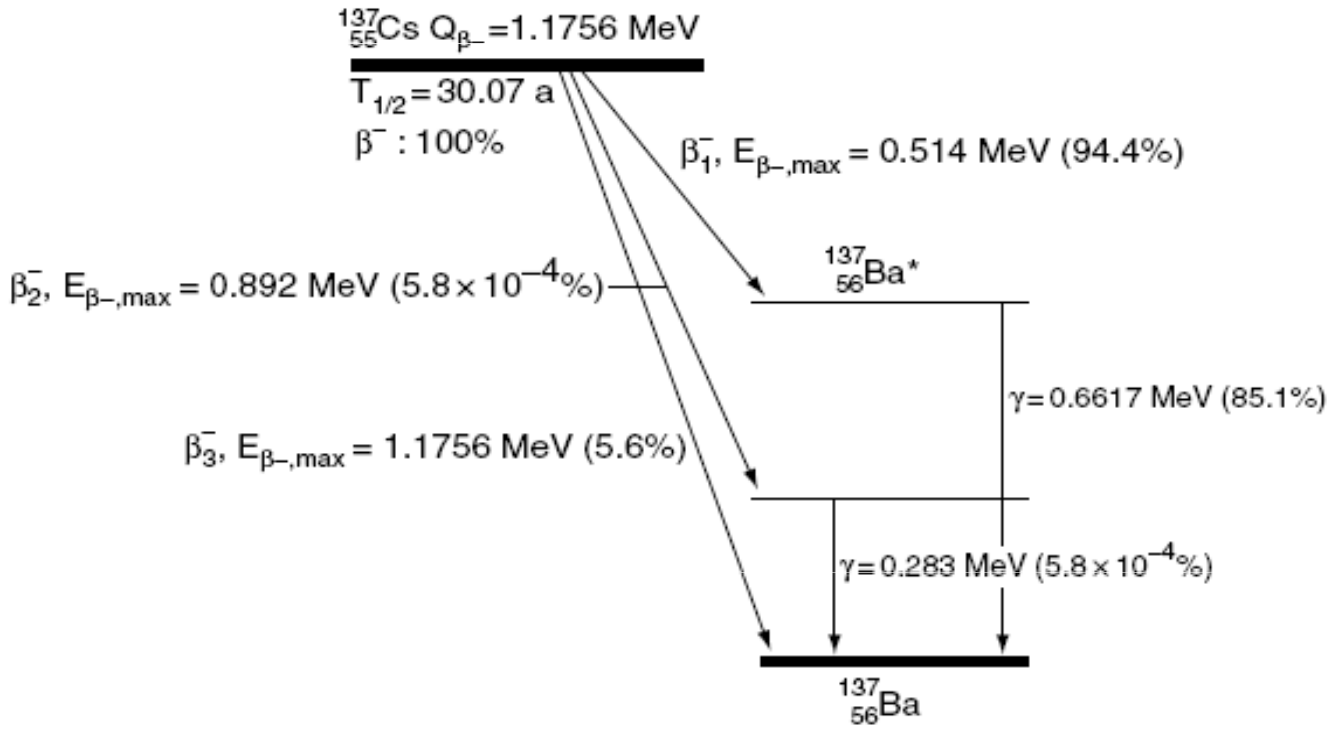

FIGURE 5.4
Schematic representation of β^- decay of $^{137}_{55}Cs$ which decays mainly (94.4%) to the second excited state of $^{137}_{56}Ba$. The disintegration energy for the decay is $Q_{\beta^-} = 1.1756$ MeV. There is practically a single γ-ray emitted of 0.6617 MeV with an absolute intensity of 85.1%.[3] On average, 0.9 photons are emitted per disintegration with energy above 10 keV (see Table 5.5c). The half-life for $^{137}_{55}Cs$ decay is 30.07 years.[14]

Radionuclides: A Review

Sources: ^{137}Cs

5.4 ^{137}Cesium

^{137}Cs was discovered in the late 1930s by Glenn Seaborg and Margaret Melhase. It was first introduced as a ^{226}Ra substitute firstly for intracavitary brachytherapy for gynecological tumors and secondly for interstitial treatments. The principal advantages of ^{137}Cs over ^{226}Ra are the reduced amount of shielding required (see Table 5.2 for half-value layer values) and the absence of a gaseous daughter product.

The longer half-life of 30.07 years for ^{137}Cs, when compared to 5.27 years for ^{60}Co, enables the clinical use of ^{137}Cs sources over a long period of time before replacement is necessary: at least for 10 years. This feature, and the lower production costs of ^{137}Cs sources, as well as the smaller amount of shielding required when compared to ^{60}Co (see Table 5.2 for half-value layer values), made ^{137}Cs the main ^{226}Ra substitute in brachytherapy in the early 1960s.

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Radionuclides: A Review

Sources: ^{198}Au

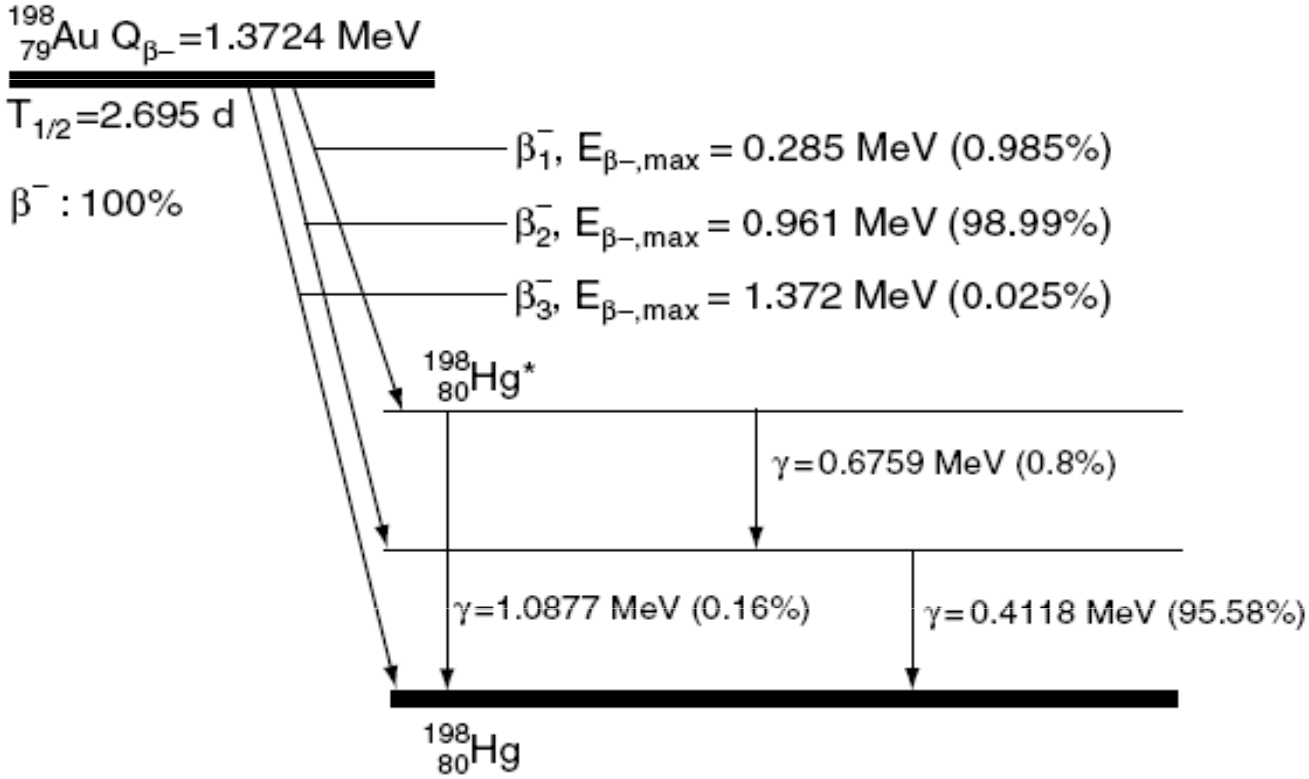

FIGURE 5.5
Schematic representation of β^- decay of $^{198}_{79}$Au which decays mainly (98.99%) to the second excited state of $^{198}_{80}$Hg. The disintegration energy for the decay is $Q_{\beta^-} = 1.3724$ MeV. There is mainly a γ-ray emitted of 0.412 MeV with an intensity of 95.58%.[3] On average, 1.0 photon is emitted per disintegration with energy above 10 keV (see Table 5.6c). The half-life for $^{198}_{79}$Au decay is 2.695 days.[14]

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chool

Radionuclides: A Review

Sources: ^{198}Au

5.5 ^{198}Gold

In 1952, ^{198}Au seeds[4] replaced ^{222}Rn seeds which had been used since approximately 1910. The original design of ^{222}Rn seed was a small glass capillary tube containing the radioactive gas, but in the 1920s the design was improved by using gold instead of glass. This prevented accidents due to breakages. The ^{222}Rn seeds had to be implanted into the tumor singly but an advantage of using ^{198}Au seeds, or grains as they were sometimes termed, was that a special gun was designed to contain a cartridge of 14 ^{198}Au grains. This improved the probability of obtaining the required spatial distribution of the sources.

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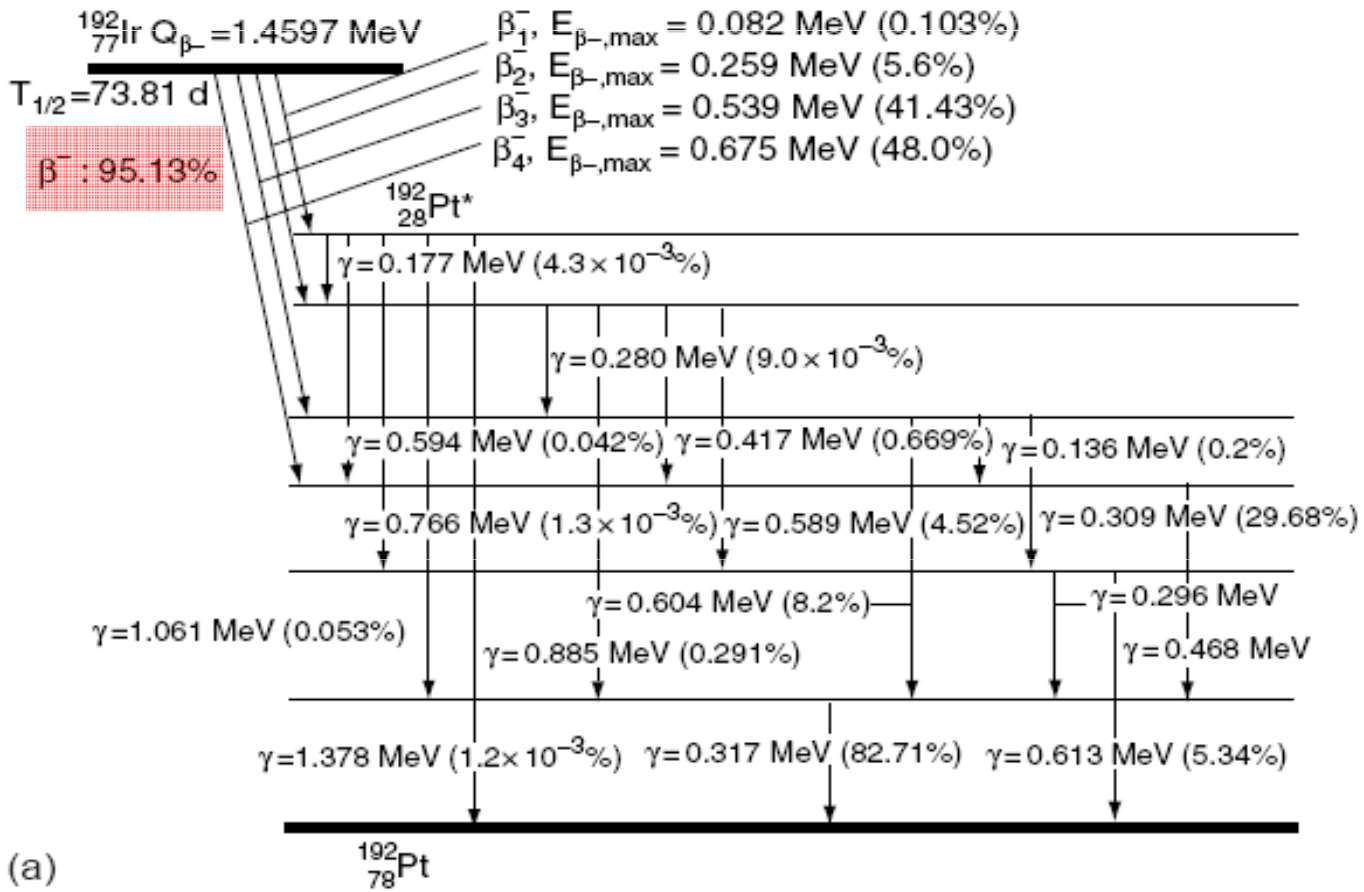
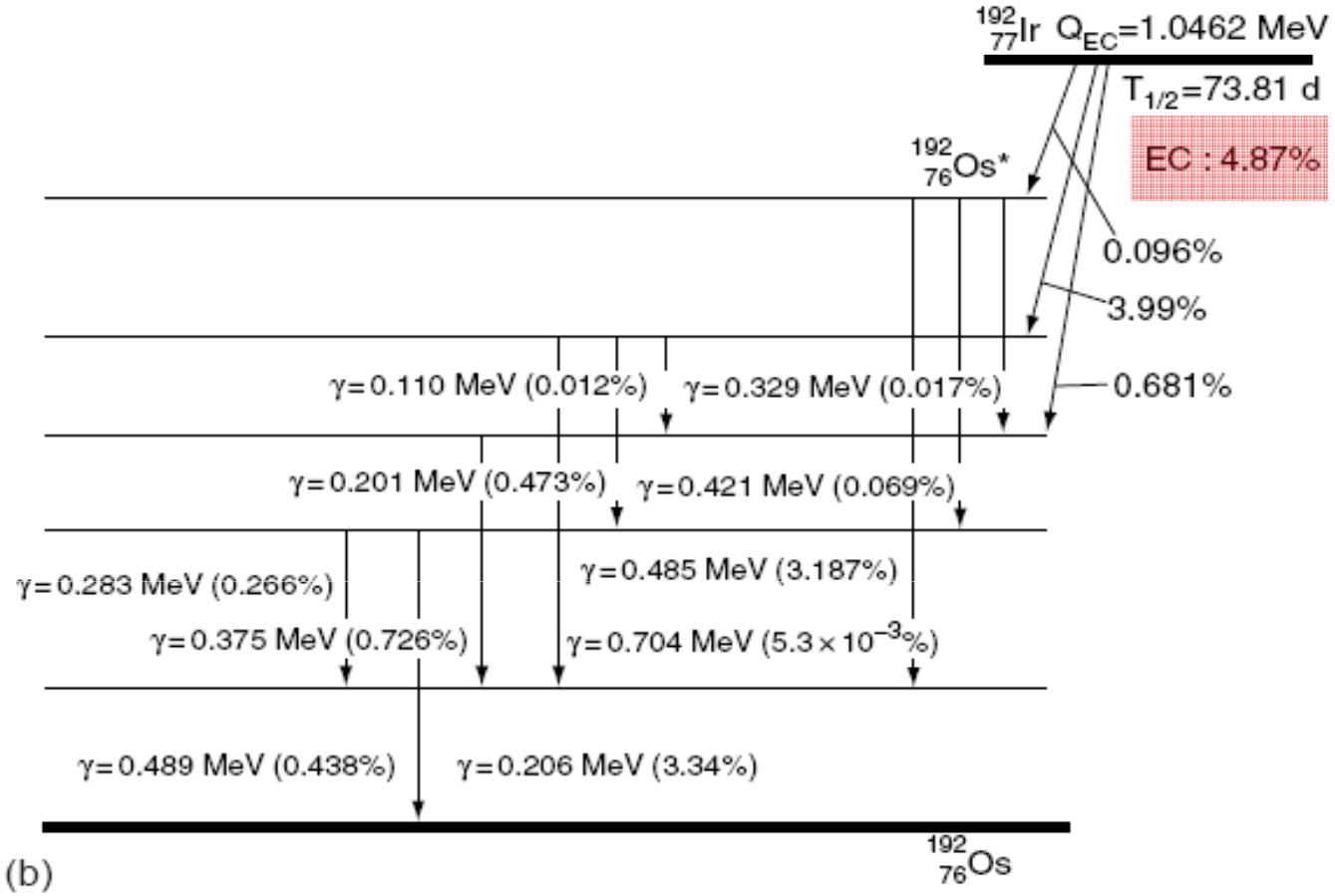
Radionuclides: A Review

Sources: ^{192}Ir



Radionuclides: A Review

Sources: ^{192}Ir



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Radionuclides: A Review

Sources: ^{192}Ir

5.6 ^{192}Iridium

Iridium has been used in brachytherapy since 1958, firstly as seeds by Ulrich Henschke and then, from the early 1960s, mainly as ^{192}Ir wires, forming the basis of the Paris System developed by Bernard Pierquin, Daniel Chassagne, Andree Dutreix, and others, mainly from the Institut Gustave Roussy.

Without doubt, ^{192}Ir has now become the most popular radionuclide as a replacement for ^{226}Ra.[5] Its half-life of 73.81 days allows ^{192}Ir to be easily used for temporary implants by making decay corrections of approximately 1% per day. The high specific activity of ^{192}Ir (see Table 5.2) makes it practical to supply sources of a very wide spectrum of activities to hundreds of GBqs. This makes very short treatment durations possible.

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Radionuclides: A Review

Sources: ^{125}I

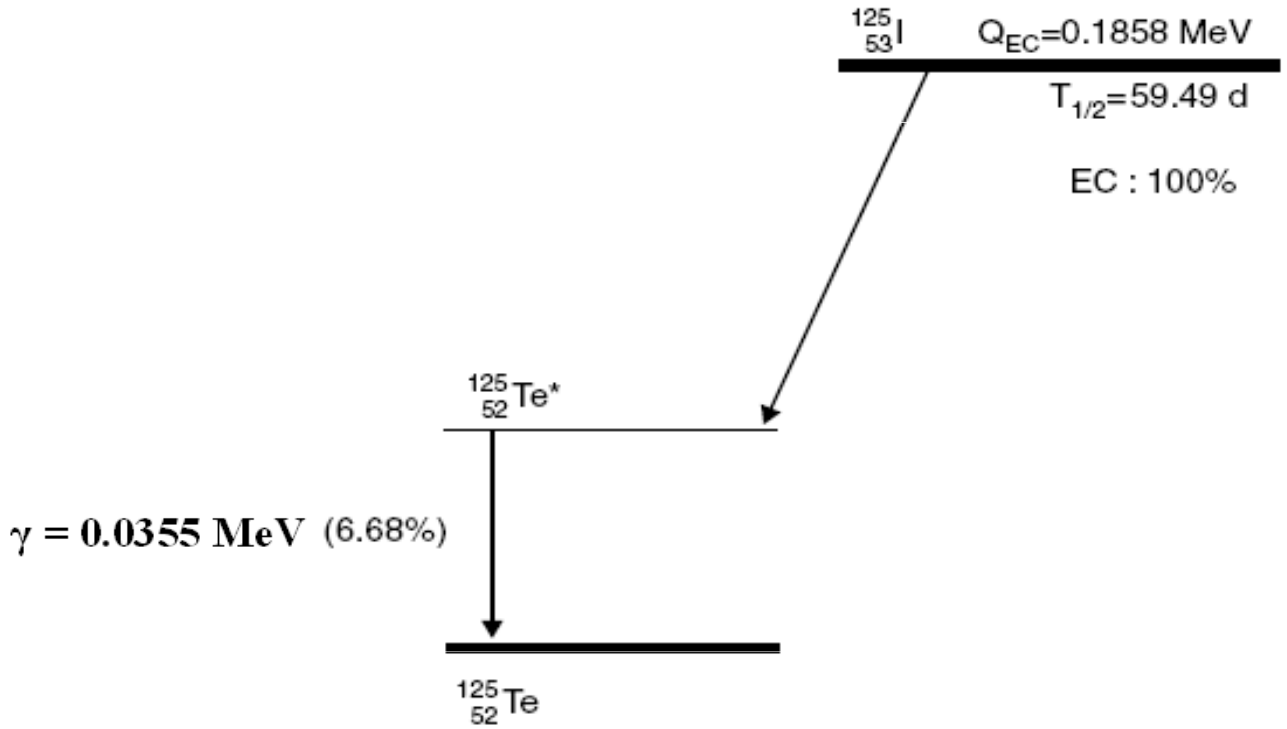

FIGURE 5.7
Schematic representation of EC decay of $^{125}_{53}$I to the first excited state of $^{125}_{52}$Te. The disintegration energy for the decay is $Q_{EC} = 0.1858$ MeV. There is a single γ-ray of 0.035 MeV with an intensity of 6.68% emitted, whereas there are several characteristic x-rays emitted in the range 0.027 to 0.032 MeV as a result of IC processes (see also Table 5.10b).[3] The average number of photons emitted per disintegration with energy above 10 keV is 1.4. The half-life for $^{125}_{55}$I decay is 59.49 days.[14]

Radionuclides: A Review

Sources: ^{125}I

5.7 ^{125}Iodine

Allen Reid and Albert Keston discovered the ^{125}I radionuclide in 1946,[6] but it took almost 20 years until ^{125}I sources became clinically available for interstitial brachytherapy.

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Sources: ^{103}Pd

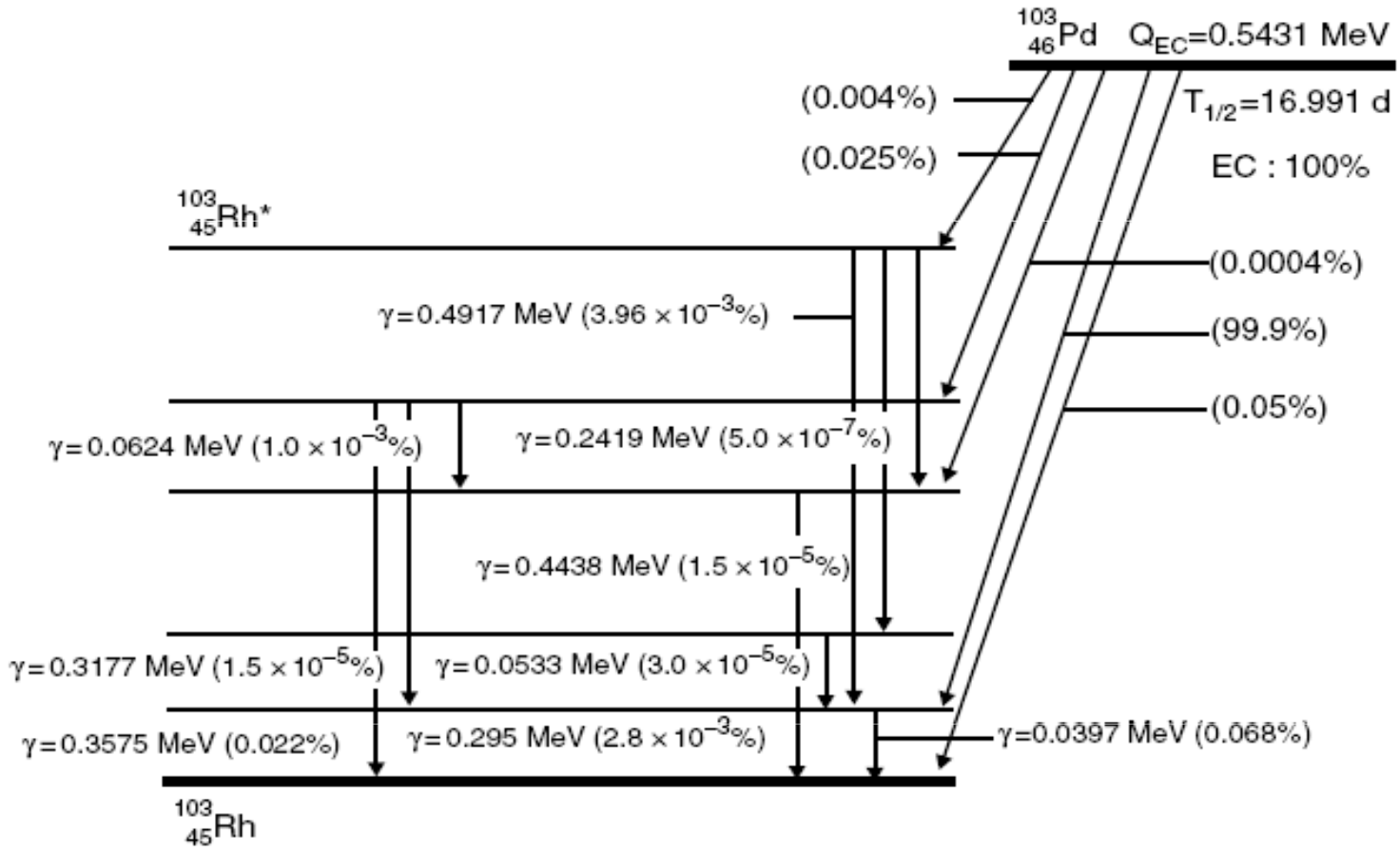

FIGURE 5.8
Schematic representation of EC decay of $^{103}_{46}$Pd to the different excited states and the ground state of $^{103}_{45}$Rh. The disintegration energy for the decay is $Q_{EC} = 0.5431$ MeV. The γ-rays emitted have very low, almost negligible intensities. There are several characteristic x-rays emitted in the range 0.020 to 0.023 MeV (see also Table 5.11b).[3] The average number of photons emitted per disintegration with energy above 10 keV is 0.8. The half-life for $^{103}_{46}$Pd decay is 16.991 days.[3]

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Radionuclides: A Review

Sources: ^{103}Pd

5.8 ^{103}Palladium

Brachytherapy seed sources containing ^{103}Pd have been introduced as replacements for ^{125}I sources for permanent implants. Its very short half-life of approximately 17 days makes ^{103}Pd only appropriate for permanent implant treatments. Its very high specific activity (see Table 5.2) in combination with its short half-life enables dose delivery at an initial dose rate higher than that obtained when using ^{125}I. This feature should be of benefit when it is used for interstitial implantation of rapidly proliferating tumors, since the accumulation of dose with ^{103}Pd occurs in a shorter time period than for ^{125}I.

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Topics

- Some History
- Radionuclides
- **Does it mater which Radionuclide?**
- Sources and Source Types
- Afterloaders
- New Developments

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Many different radionuclides

- Does it matter which Radionuclide?

Let’s have a closer look at some issues

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Does it matter which Radionuclide?

Emission type:

- **Photon radiation: +++ (penetration)**
- **Electrons: - - - (dose near the source; used in endovascular)**

Emission energy:

- **High energy photons useful in temporary implants, at the expense of higher shielding costs.**
- **Low energy photons useful in permanent implants, with limited radiation to the surrounding of the patient.**

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Radionuclides: Related Costs, shielding

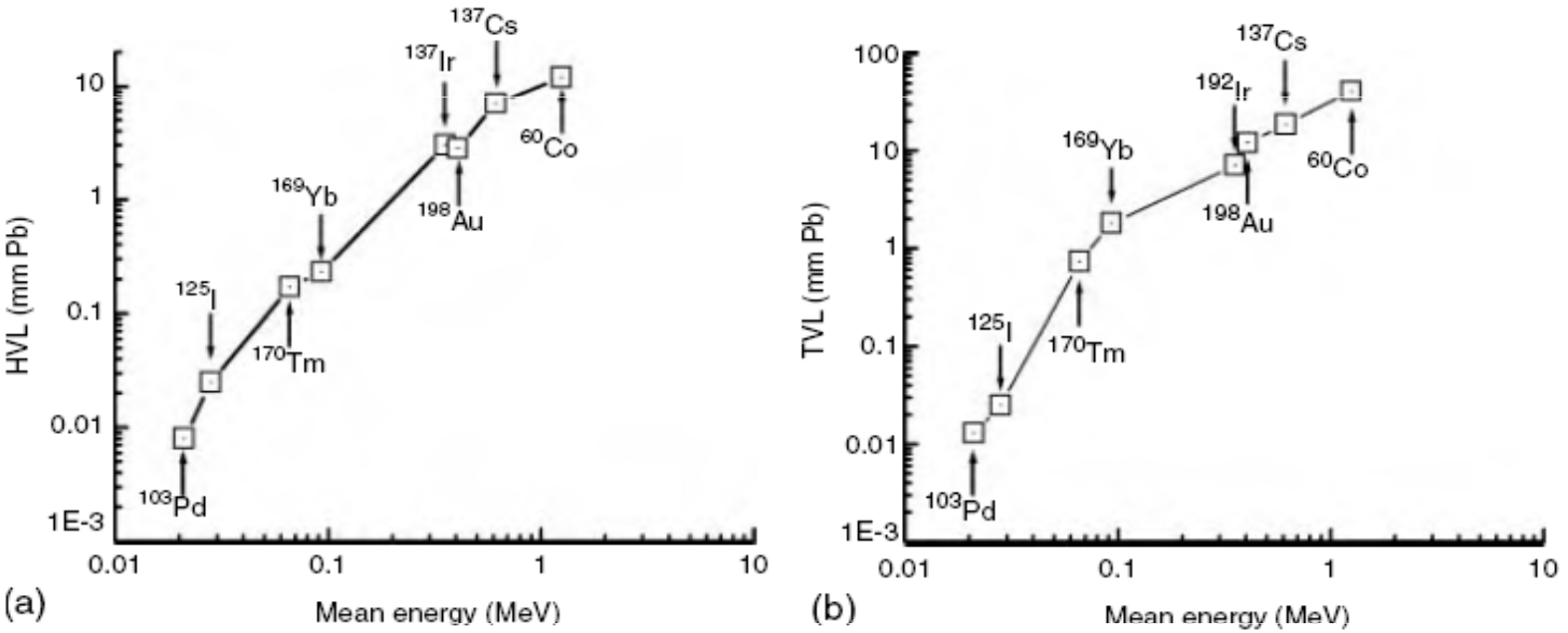

FIGURE 5.2

Thickness of lead required (a) for 50% transmission, HVL, and (b) for 10% transmission, TVL for the different radionuclides handled in this chapter. HVL values are according to the data presented in Table 5.2, where the tenth value layer data are according to Williamson.[19] The TVL values for ^{169}Yb and ^{170}Tm according to Granero et al.[18] (for ^{169}Yb and ^{192}Ir see also Lymperopoulou et al.[21]).

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Shielding calculations in brachytherapy

Radiation transmission data for radionuclides and materials relevant to brachytherapy facility shielding

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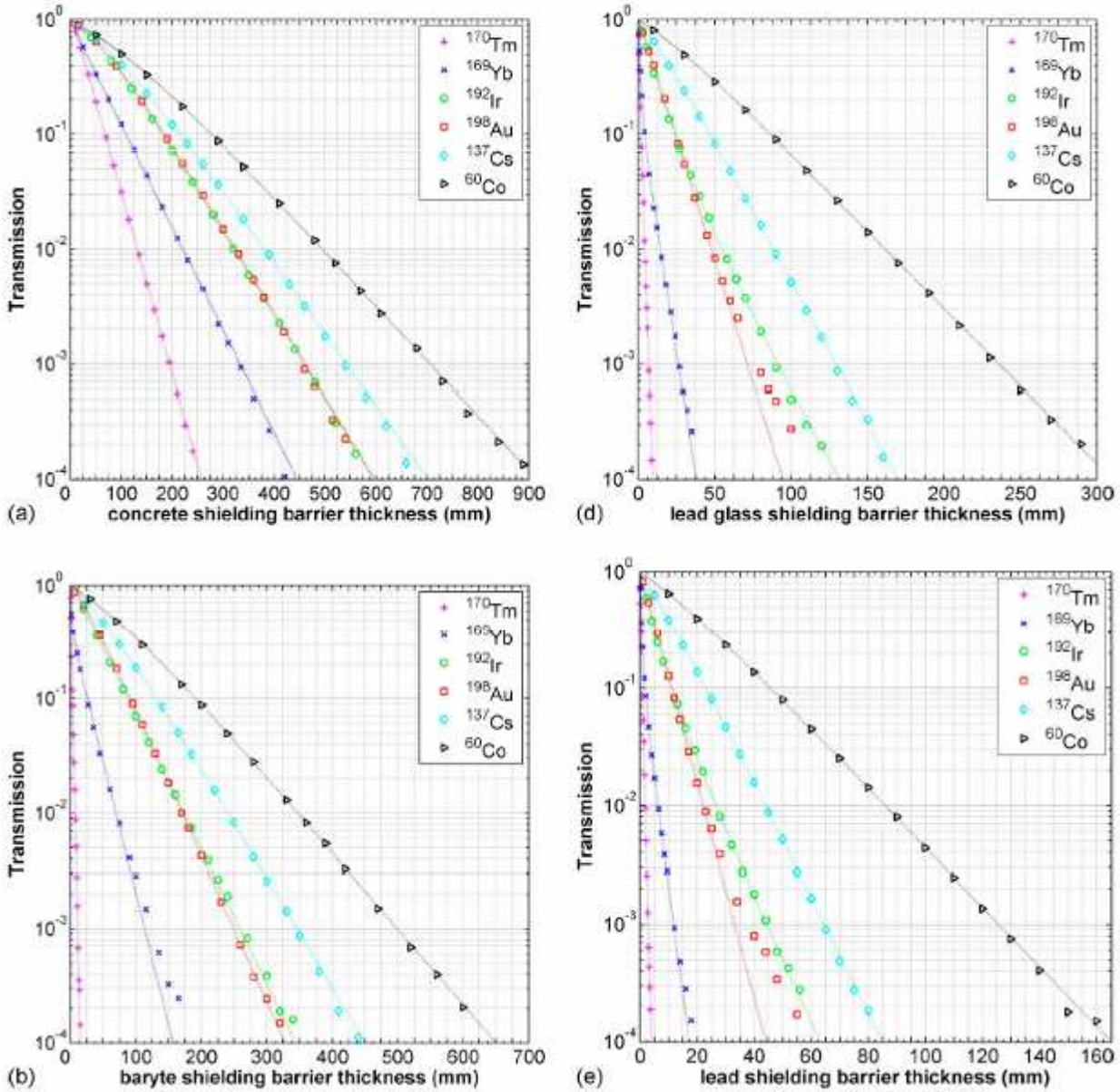
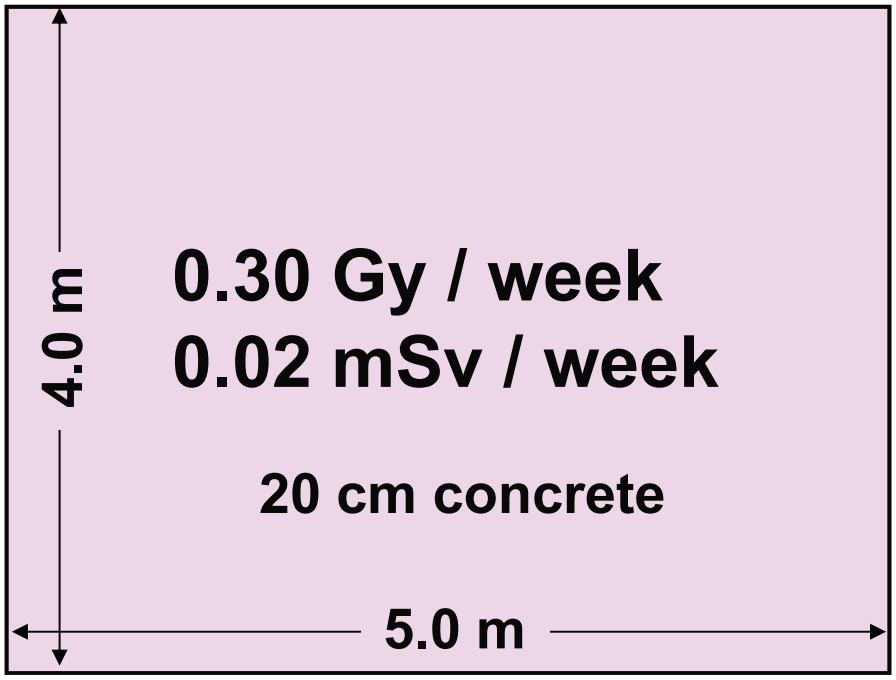
(Received 2 July 2008; revised 26 August 2008; accepted for publication 27 August 2008; published 14 October 2008)



Radionuclides: Related Costs, shielding

Energy ←→ Radiation Protection
Mobility / Flexibility / Costs



^{192}Ir *versus* ^{169}Yb

3.5 cm vs. 1.0 cm Pb

ca. 45 k€

^{192}Ir *versus* ^{170}Tm

3.5 cm vs. 0.5 cm Pb

only Material Costs
of ca. 52 k€

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Does it matter which Radionuclide?

Long half life:

- Associated with low specific activity A_{spec} (Bq/g)
- Radioactive waste
- If too long, not useful with permanent implants

Short half life:

- Smaller source size possible (high A_{spec})
- More frequent source exchange
- Possible higher radiobiological response

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Many different radionuclides

- Does it matter which Radionuclide?

A forgotten Perspective - RBE

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Does it mater which Radionuclide?
A forgotten Perspective - RBE

RBE

ERT		BRT	
MV-X-rays	= 1.0	^{60}Co	= 1.0
p^+	≈ 1.1	^{192}Ir	≈ 1.3[a]
C-ions	≈ 2.0-4.0	^{241}Am	≈ 2.1[a]
		^{125}I	≈ 2.1[a] - 1.4[b]
		^{103}Pd	≈ 2.3[a] - 1.9[b]
		40-50 kVp X	≈ 1.4 - 1.5[c]

[a] Wuu et al., *Int J Rad Oncol Biol Phys*, 36, 689-697, 1996
[b] Ling et al., *Int J Rad Oncol Biol Phys*, 32, 373-378, 1995
[c] Reniers et al., *Phys Med Biol*, 53, 7125-7135, 2008

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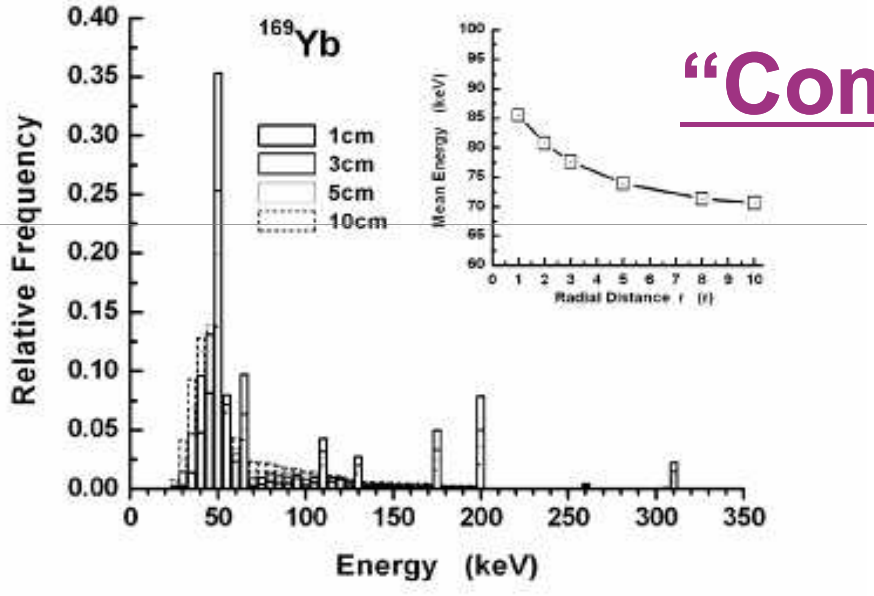
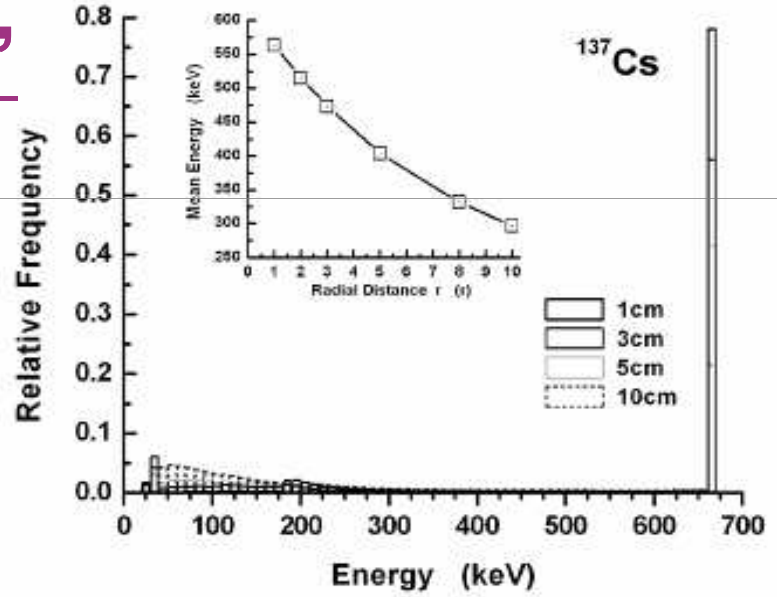
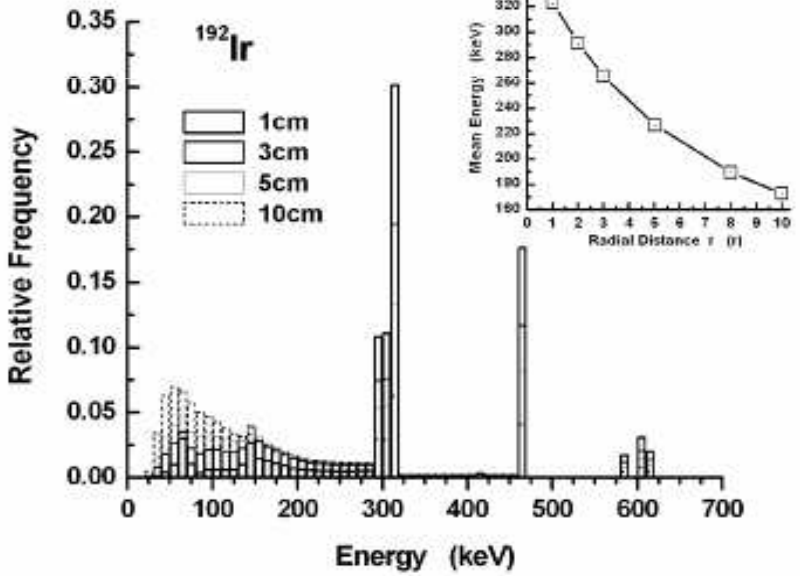
RBE and Energy Shift

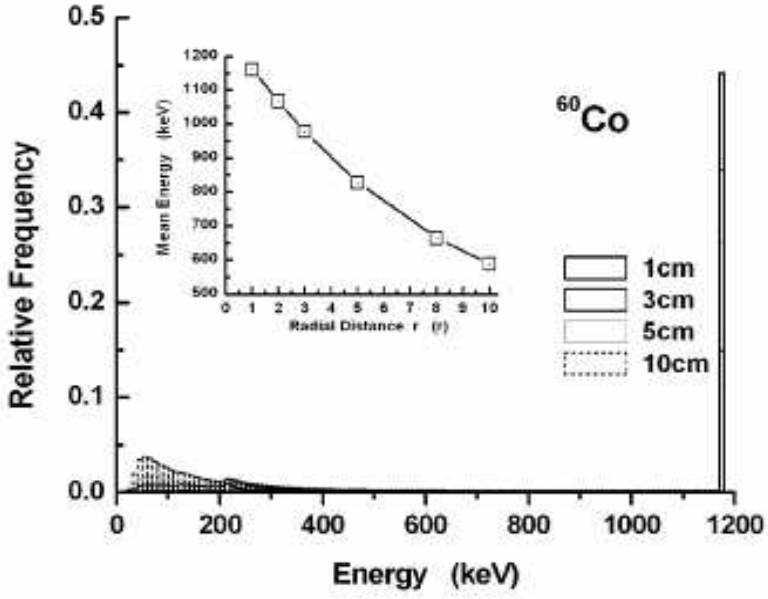
"Compton"

Point Sources

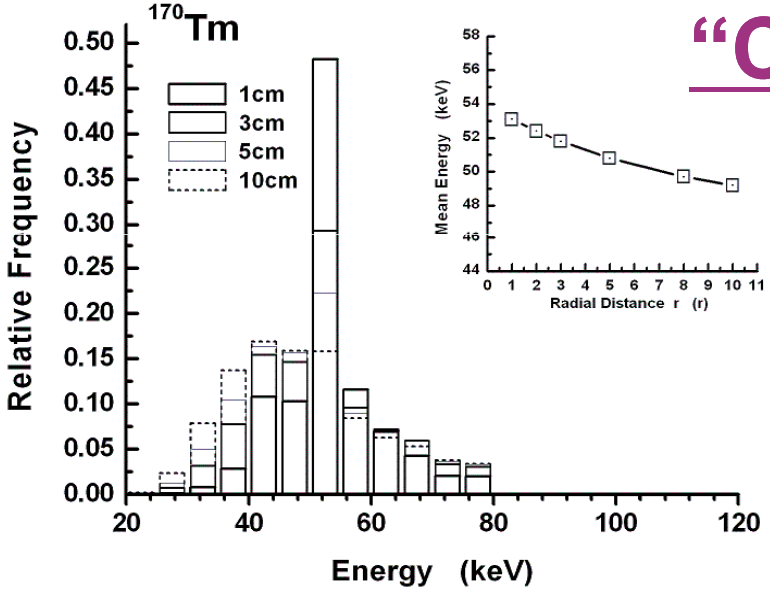






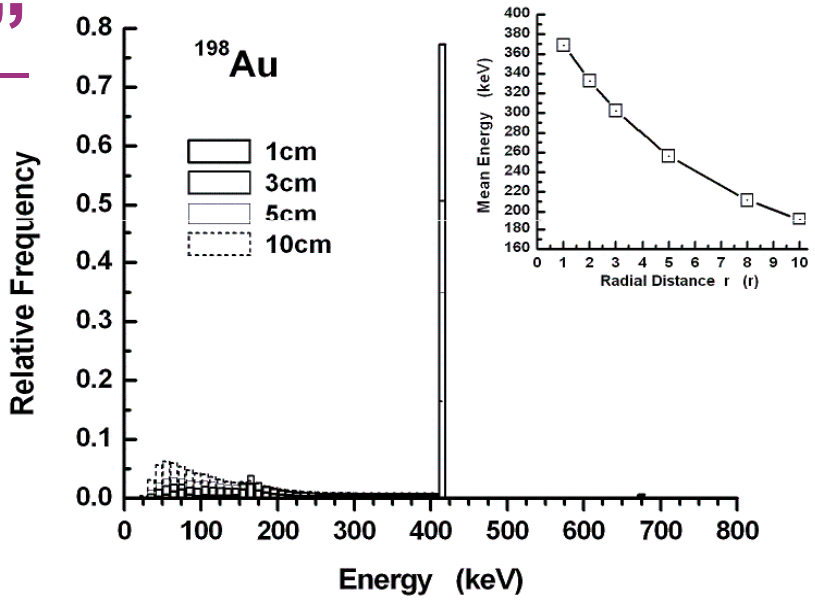


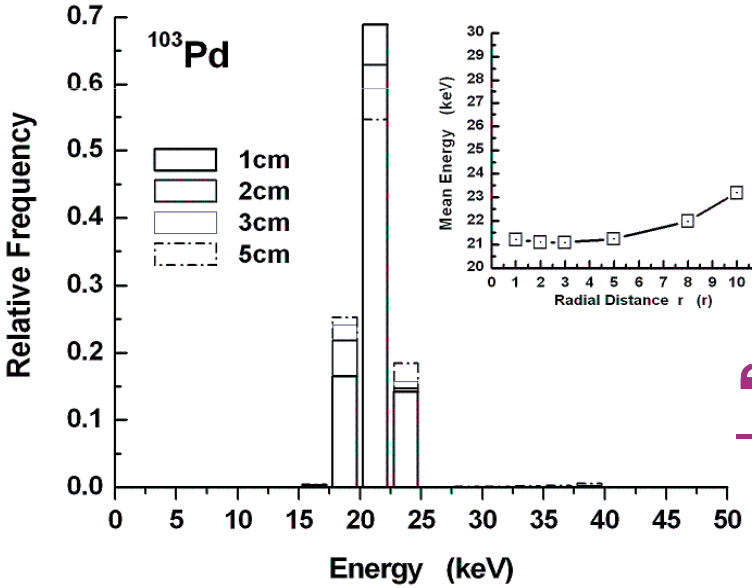
RBE and Energy Shift



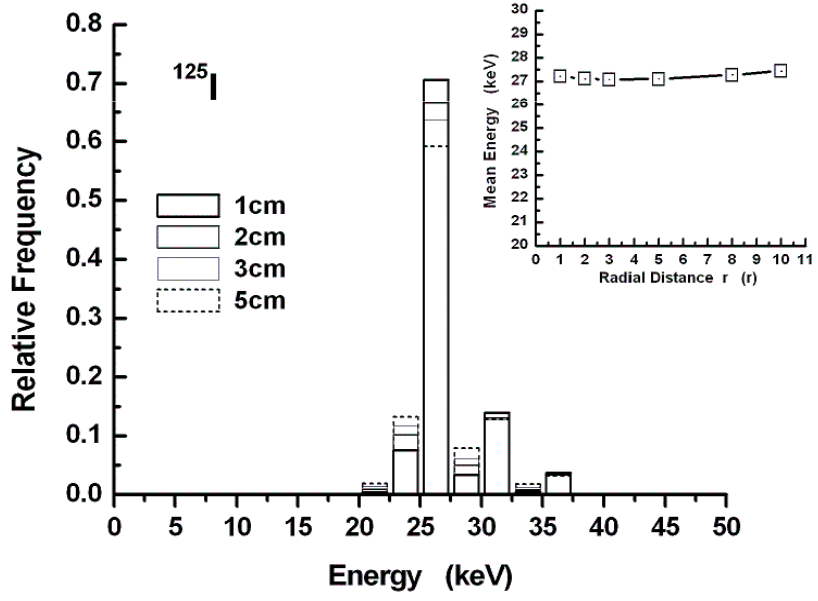
"Compton"

Point Sources





"Photo"



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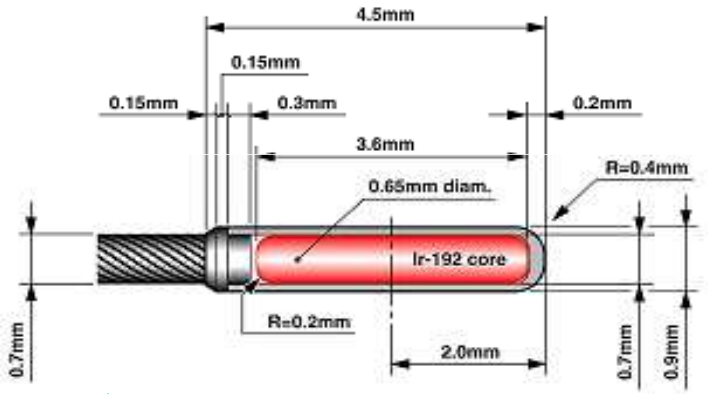
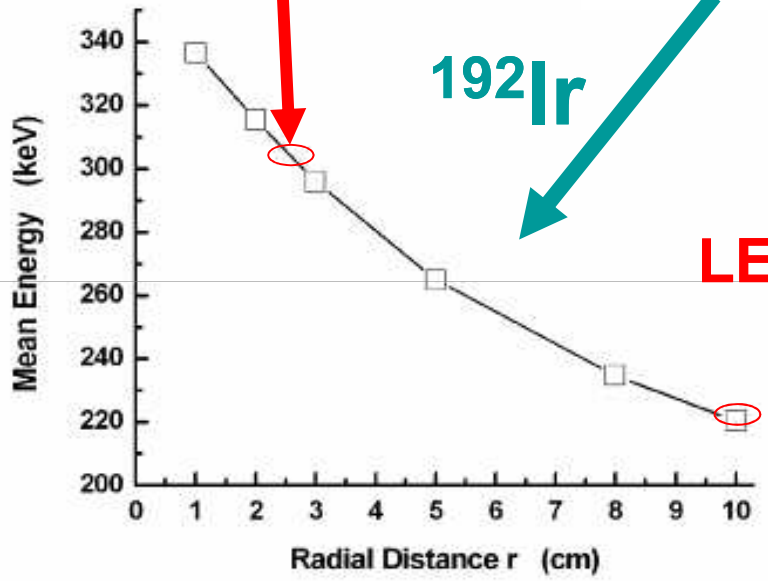
RBE and Energy Shift

e^- ≈ 81 keV
LET≈0.48 keV/µm



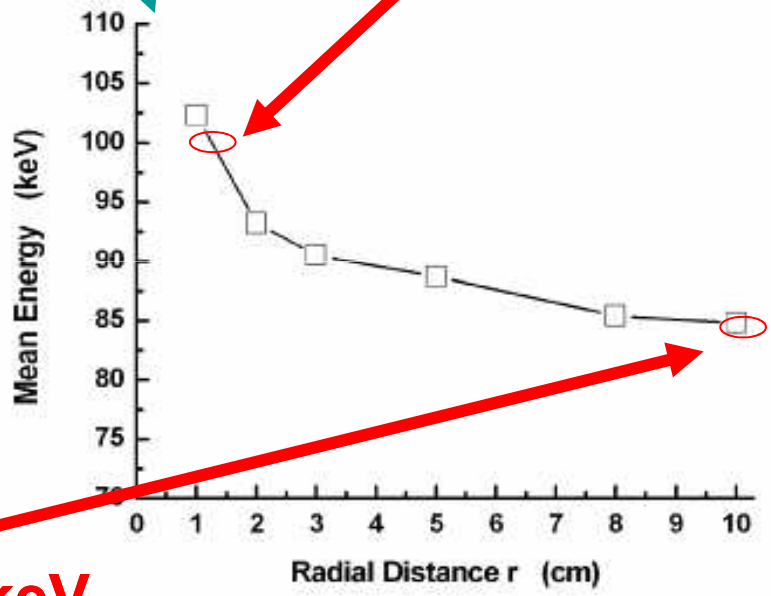
^{192}Ir



e^- ≈ 43 keV
LET≈0.78 keV/µm

e^- ≈ 14 keV
LET≈1.6 keV/µm

^{169}Yb



e^- ≈ 10 keV
LET≈2.3 keV/µm

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A Summary of the Basic Physics behind Sources and Dosimetry in Brachytherapy:

The Role of Energy

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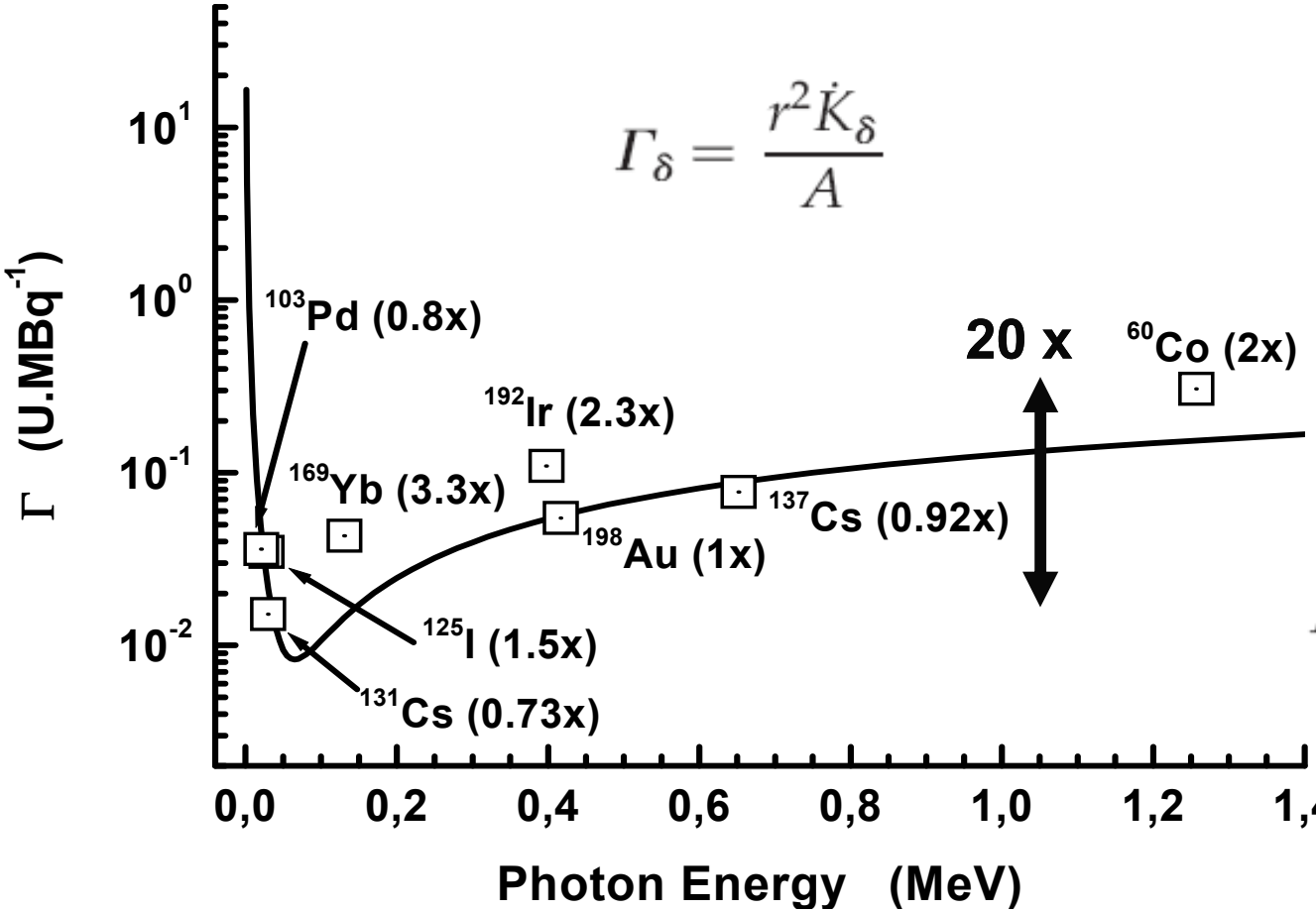
The Air Kerma-Rate Constant Γ_δ

$$\Gamma_\delta = \frac{r^2 \dot{K}_\delta}{A}$$



$$\Gamma_\delta = \left(\frac{1}{4\pi}\right) \sum_i \left\{ n_i E_i \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i} \right\}$$

FIGURE 5.1
Energy dependence of the air kerma-rate constant Γ_δ for mono-energetic point sources calculated using Equation 2.63. Mass energy absorption coefficients for dry air are according to Hubbell and Seltzer,[17] where a log–log interpolation has been applied to these tables. Γ_δ values plotted against photon energy. The Γ_δ values ($\delta = 10$ keV) for the seven radionuclides of interest in brachytherapy are also plotted according to their effective energy, E_{eff} as in Equation 5.2. The numbers in parenthesis are the mean number of photons emitted per decay for each radionuclide considering only photons emitted with energy above the cut-off value of $\delta = 10$ keV (Table 5.2).

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The Role of Specific Activity and Density ρ and Energy

Maximal S_k from 1 mm³ of Radionuclide Material

• ^{192}Ir	➔	2	1.0 (7.7 TBq)	2 ➔ 1.0 (834 mGy.h^{-1}.m²)
• ^{137}Cs	➔	7	8 x 10^{-4}	6 ➔ 6 x 10^{-4}
• ^{60}Co	➔	5	5 x 10^{-2}	4 ➔ 0.1 x
• ^{198}Au	➔	1	23 x	1 ➔ 11 x
• ^{170}Tm	➔	4	0.3 x	5 ➔ 10^{-3}
• ^{169}Yb	➔	3	0.8 x	3 ➔ 0.3 x
• ^{204}Tl	➔	6	3 x 10^{-2}	7 ➔ 4 x 10^{-5}

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The Tissue (water) Effect

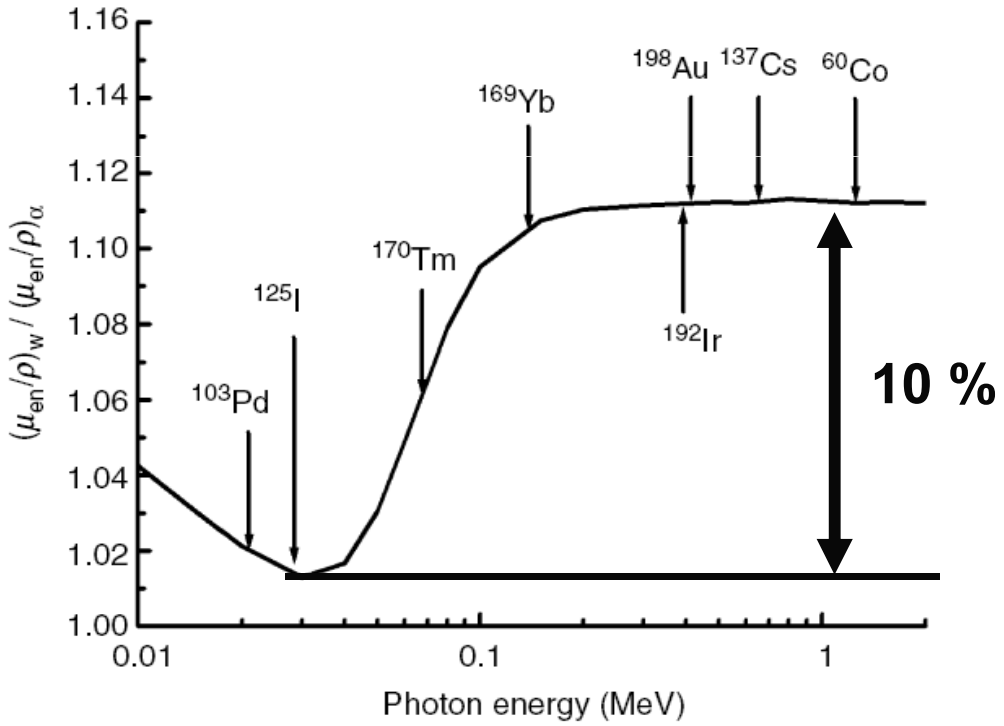

FIGURE 8.4
Energy dependence of the ratio of mass energy absorption coefficients of water to that of air, $(\mu_{en}/\rho)^w_\alpha$, in the brachytherapy related energy range 0.01 to 2.0 MeV. The mass energy absorption coefficients for dry air and liquid water considered are according to Hubbell and Seltzer.[19] The corresponding values for the different brachytherapy radionuclides calculated using their effective energies as listed in Table 5.15, and a log–log interpolation in the tables of Hubbell and Seltzer,[19] are also indicated.

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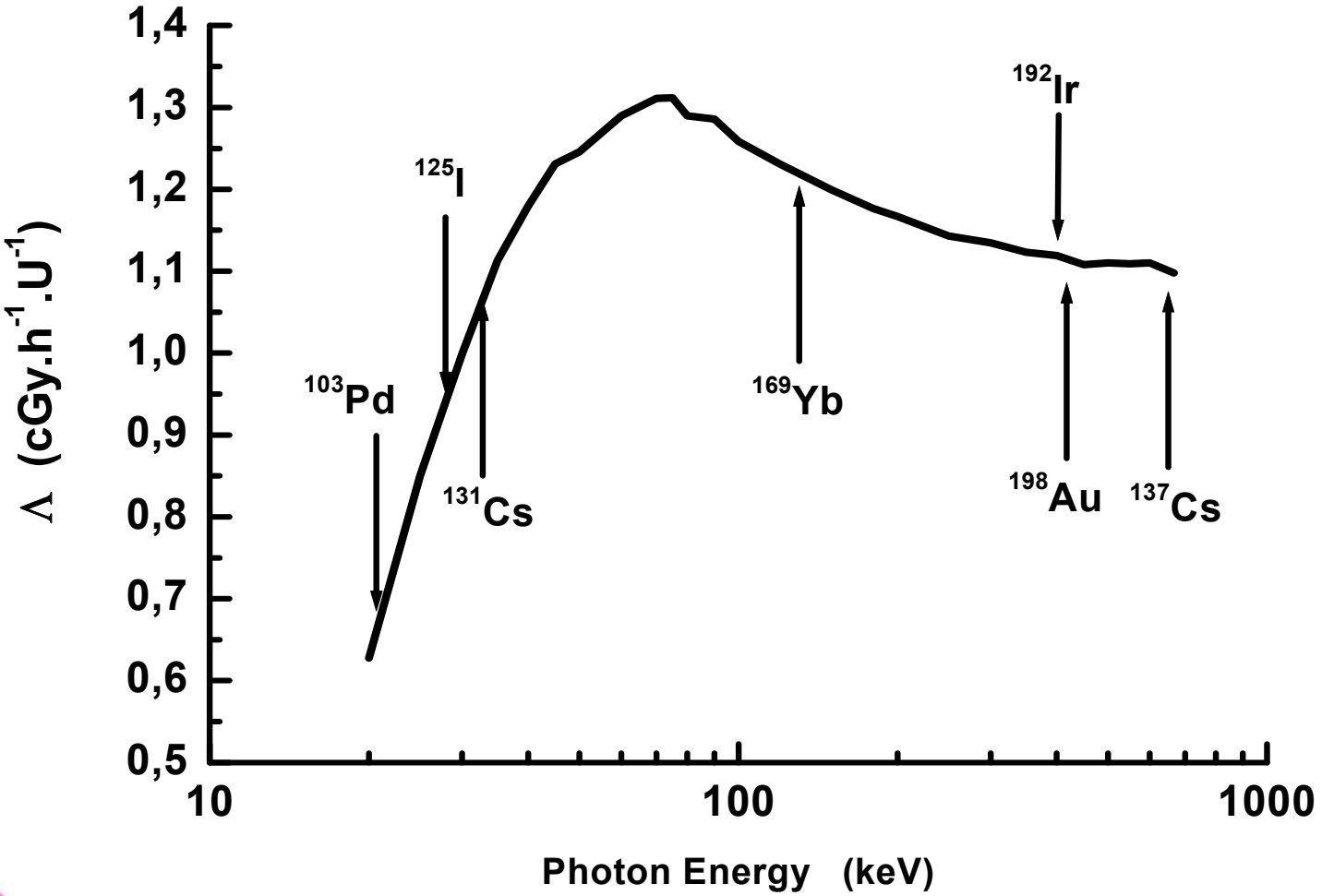
The Dose Rate Constant Λ

(Dose Rate per Unit Source Strength at 1cm & 90°)



$$\Lambda = \frac{\dot{D}(r_0, \theta_0)}{S_K}$$

$(r_0, \theta_0) = (1\text{cm}, 90°)$

Topics

- Some History
- Radionuclides
- Does it mater which Radionuclide?
- **Sources and Source Types**
- Afterloaders
- New Developments

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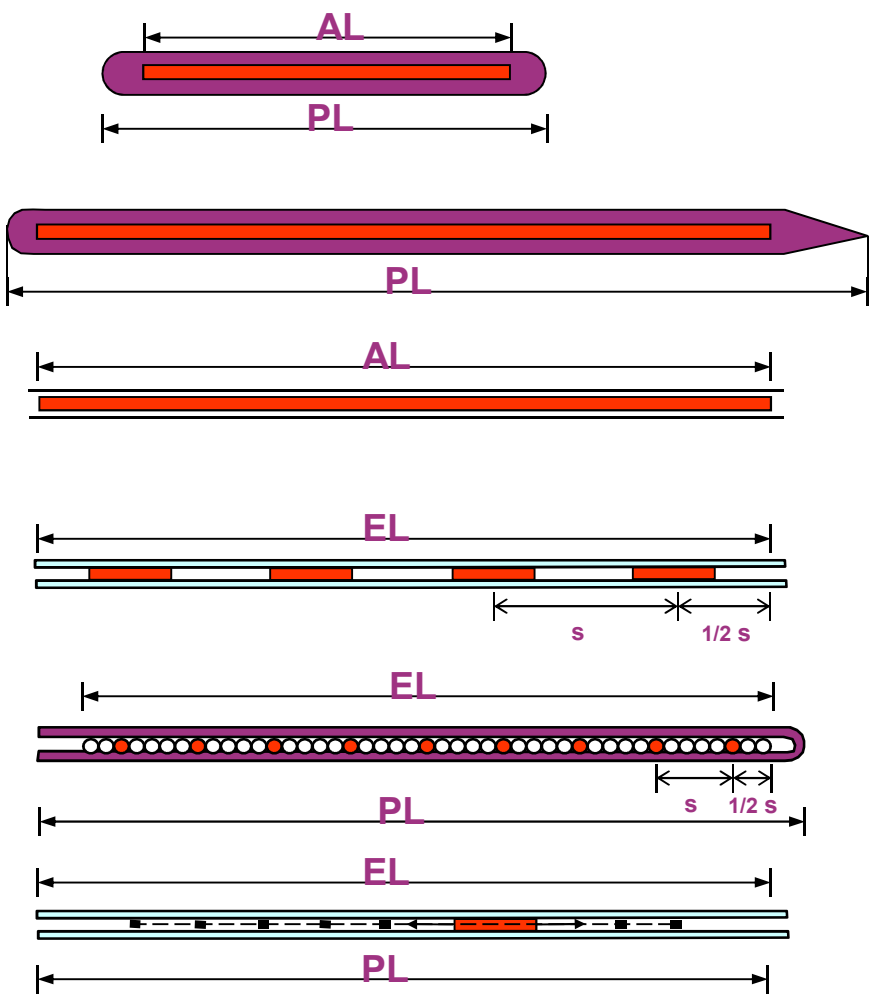
Sources & Source Types: Sealed Sources

Physical Forms (schematically)



Tube

Needle

Wire

Seed Ribbon

Source Train

Stepping source

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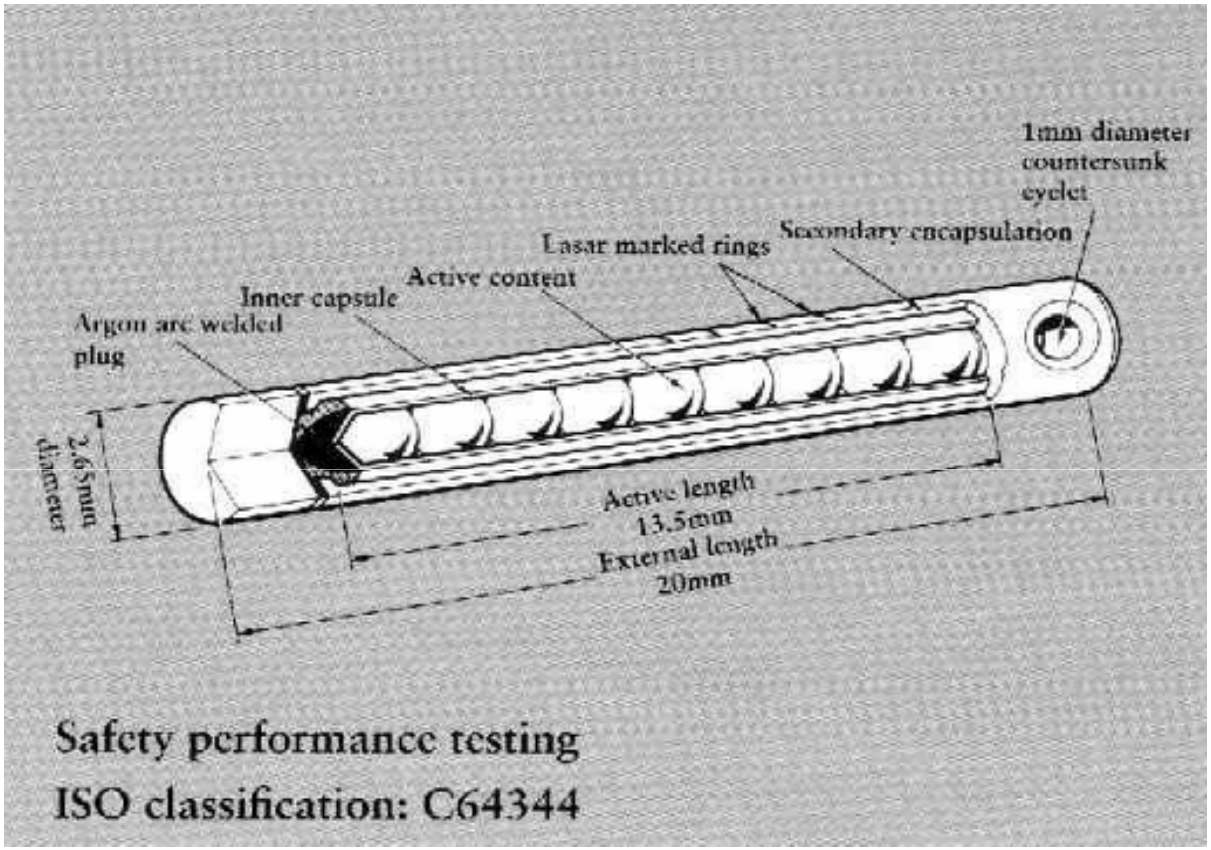
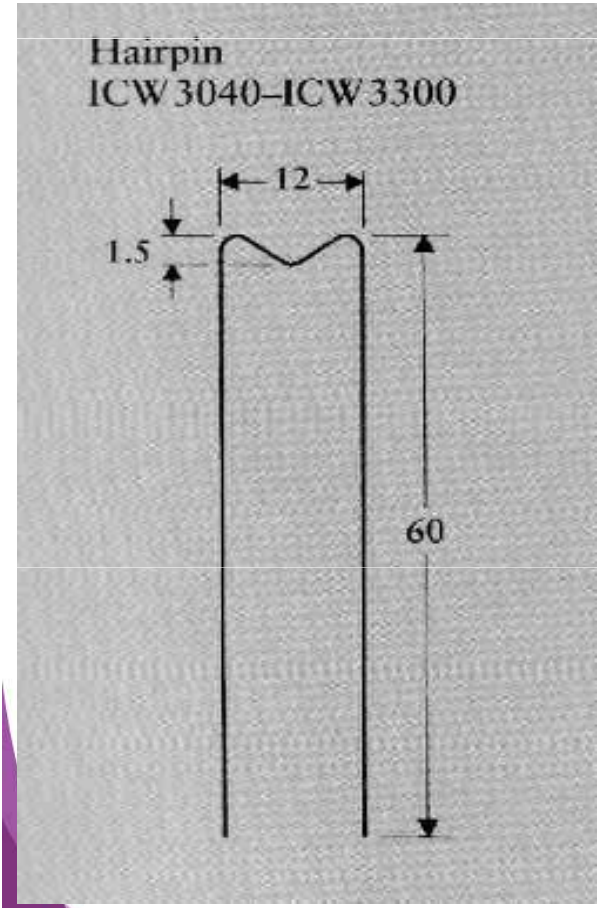
Sources & Source Types:
Sealed Sources

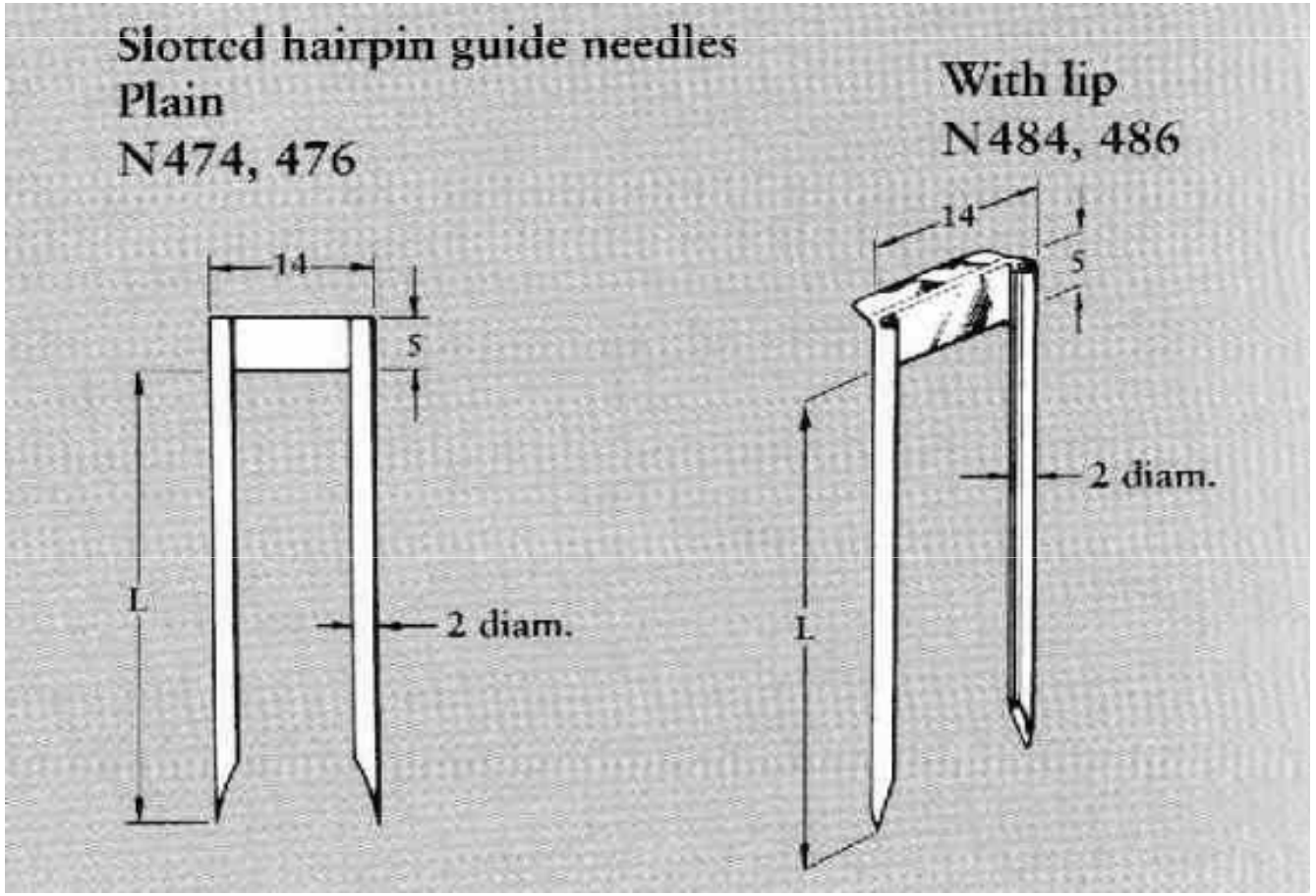
Example of a 2 cm length tube source, Cs-137
Note the difference in active length and external length



Sources & Source Types: Sealed Sources

Special forms of ^{192}Ir sources





Left: example of a wire-type source, in the form of a "hairpin", Ir-192 (low dose rate, e.g., for tongue implants) Right: guiding needles for "hairpin"

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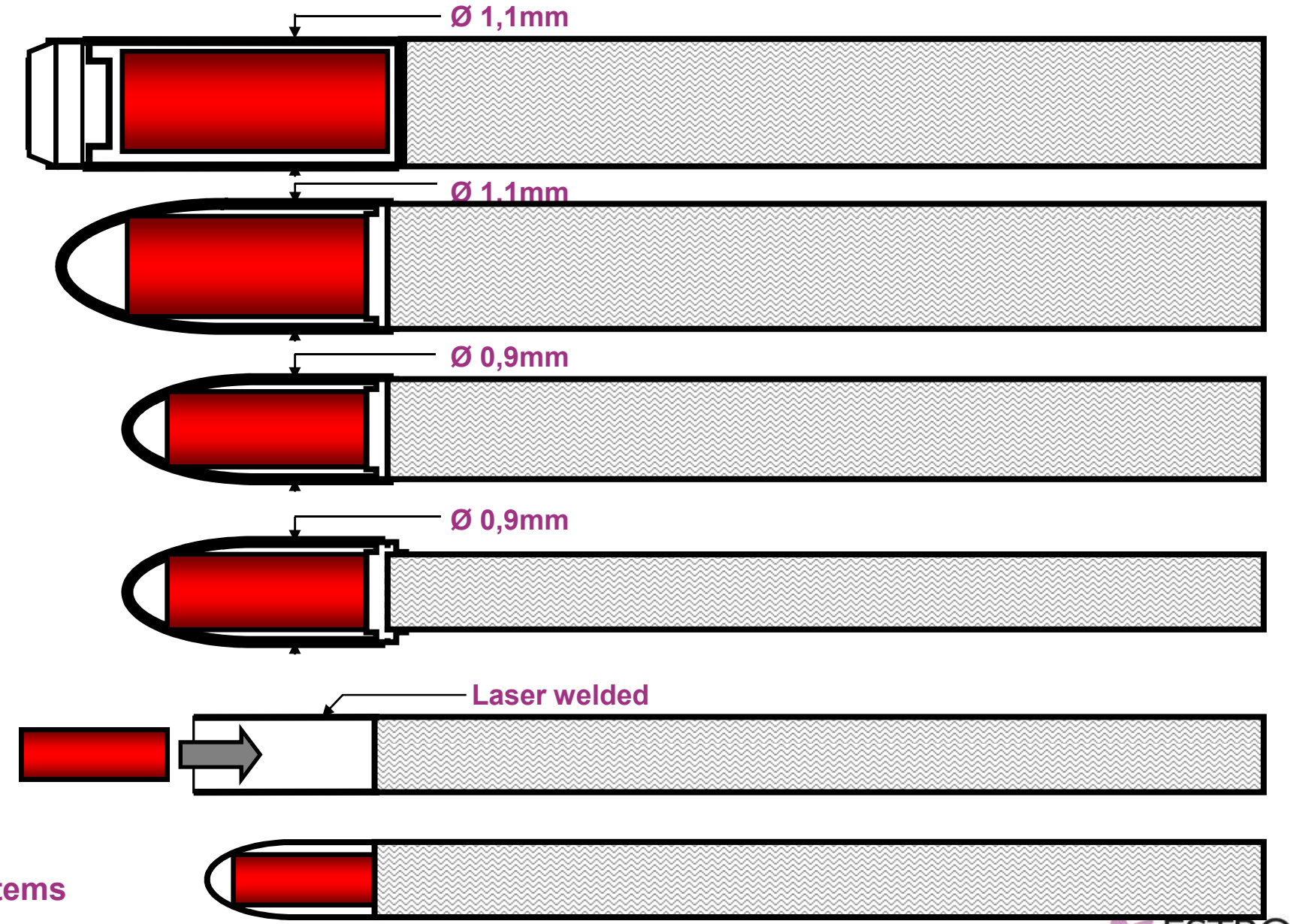
Sources & Source Types:
Sealed Sources - Afterloading - ^{192}Ir



HDR & PDR have identical dimensions

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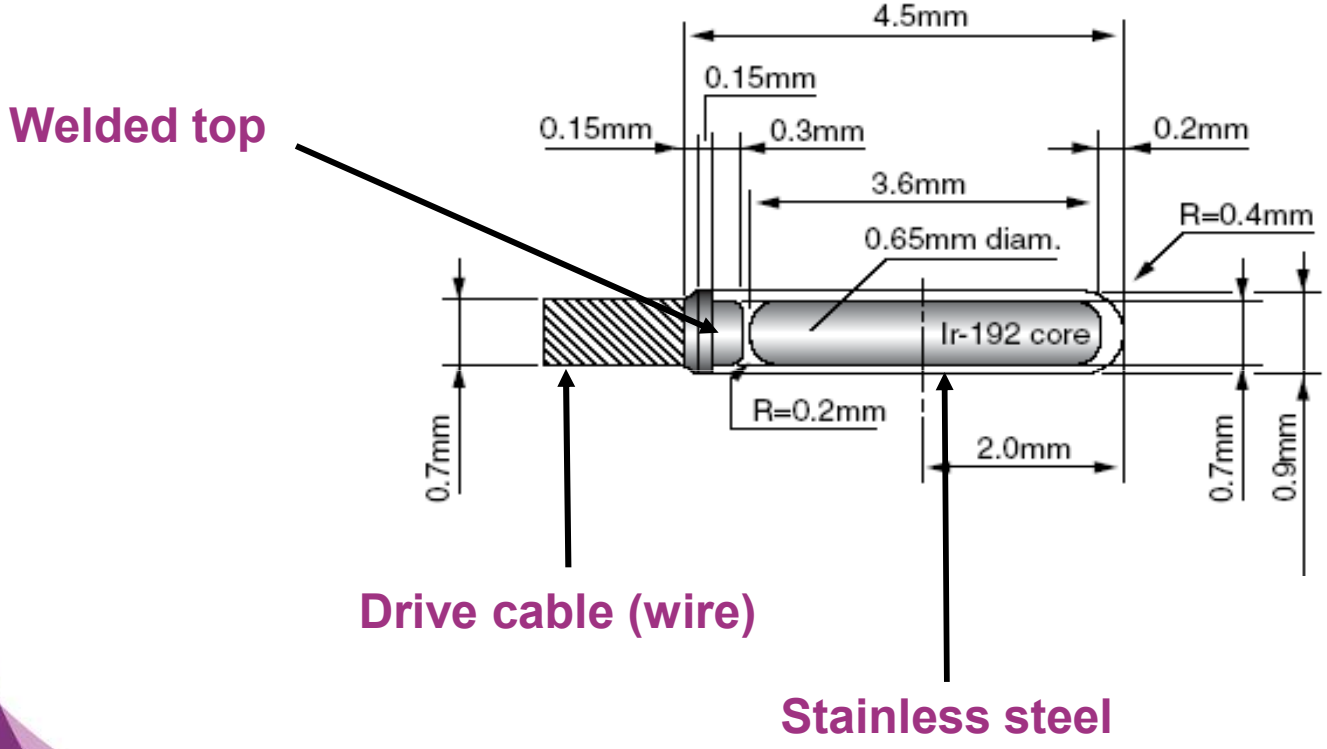
Sources & Source Types:
Sealed Sources - Afterloading

Example of design of a miniaturized high dose rate (HDR) ^{192}Ir-source, welded to the end of a drive cable



Sources & Source Types: Sealed Sources

Permanent implants

e.g., for prostate

These sources are using Radionuclides combining a short half life with low energy

Examples:

^{125}I **(59.5 days; 28 keV)**

^{103}Pd **(17 days; 21 keV)**

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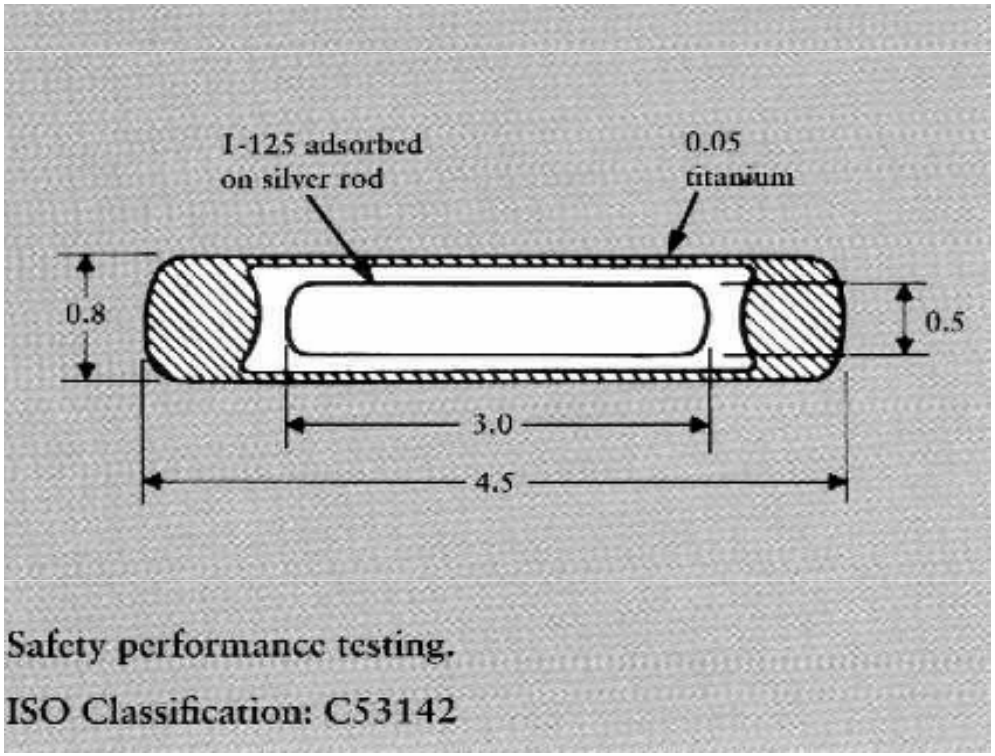
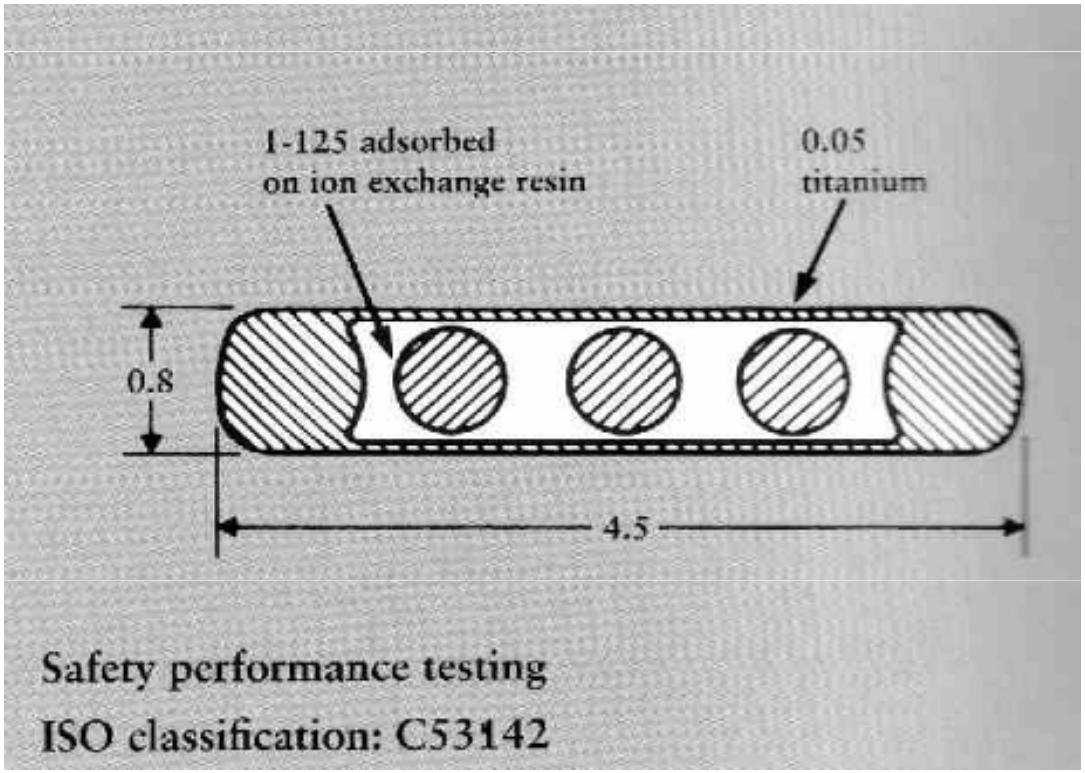
Sources & Source Types: Sealed Sources

Details of ^{125}I seed sources





Two examples of ^{125}I sources for permanent implants:
Left: model 6711 (silver rod acts as X-ray marker)
Right: model 6702 (no X-ray marker)

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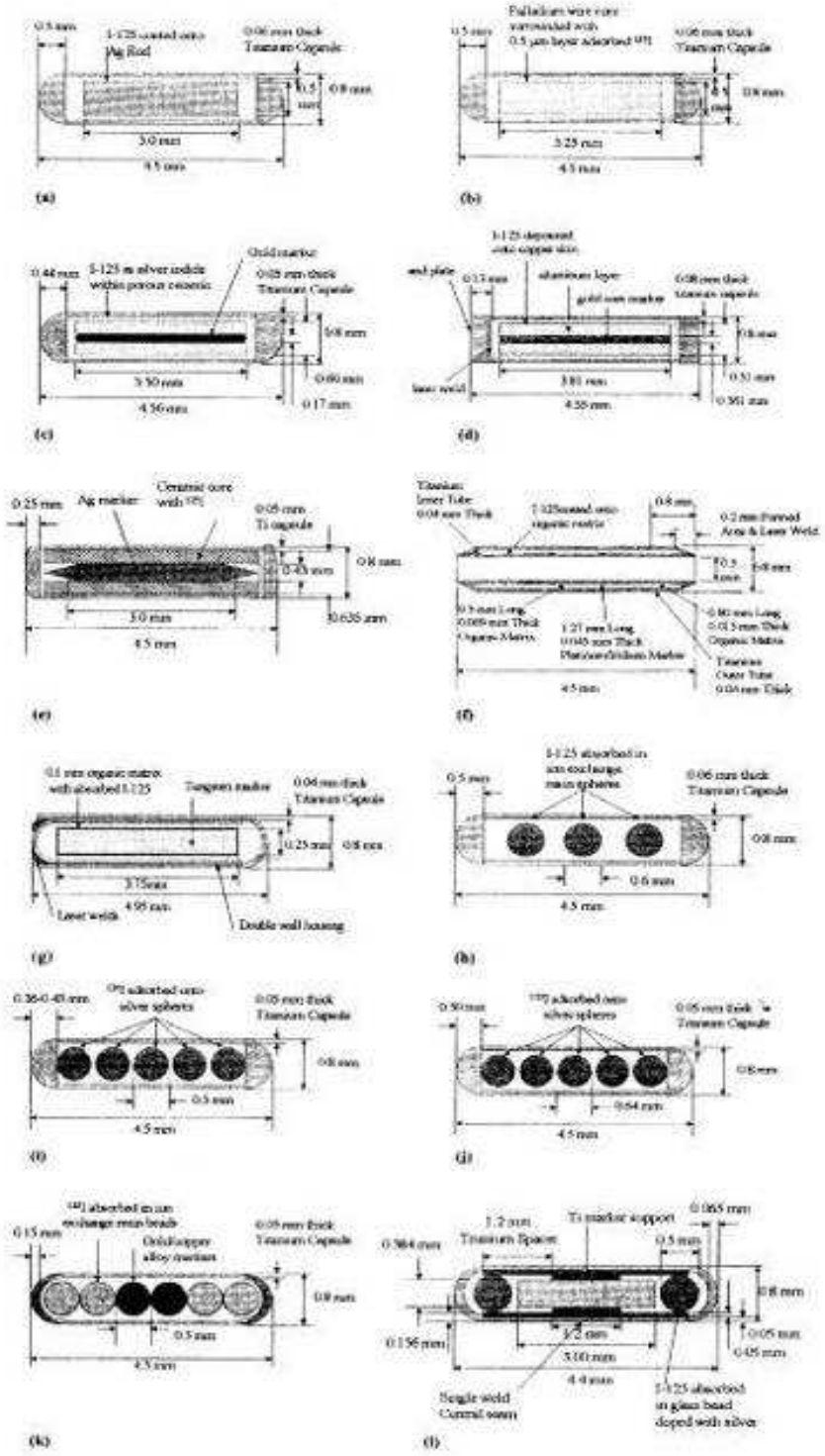

But, there are many, many ^{125}I and ^{103}Pd source types commercially available….

So, take care of using the correct dosimetric data

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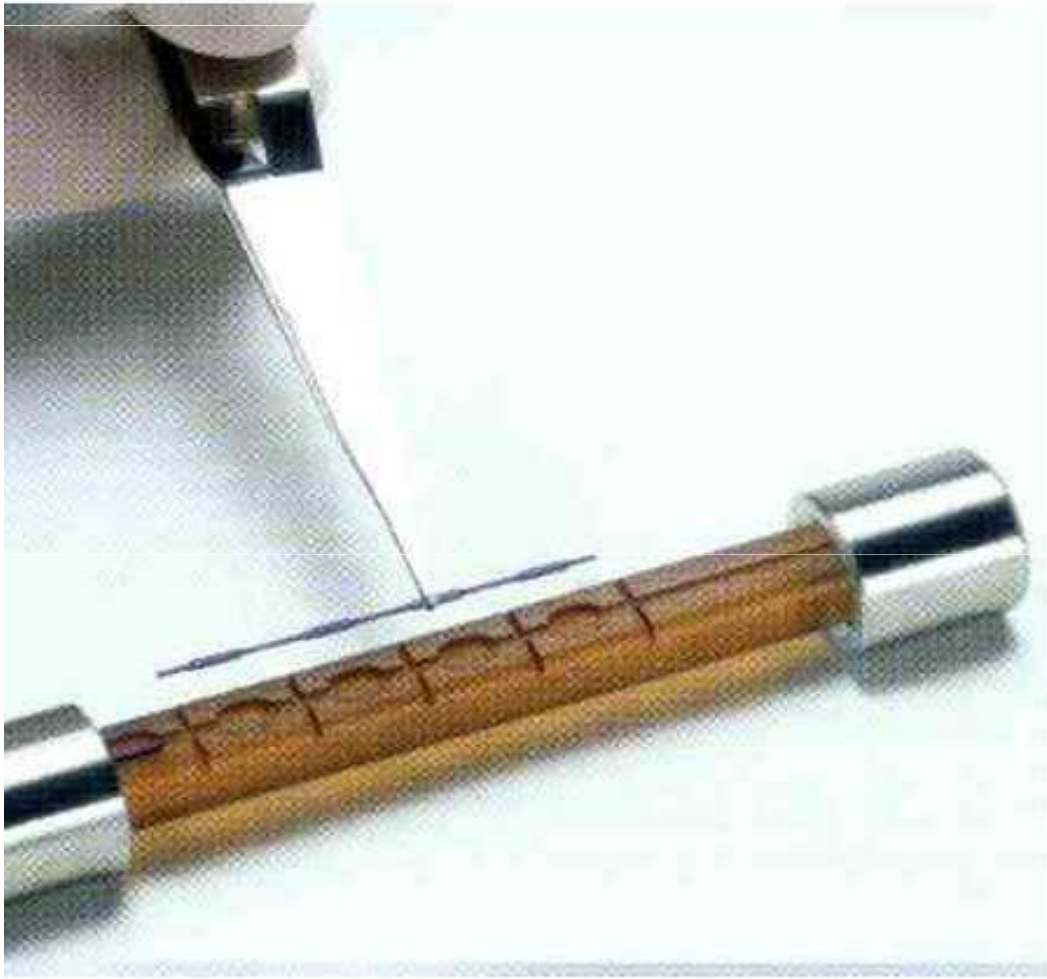
Sources & Source Types: Sealed Sources

“stranded” seeds

A “Rapidstrand” seed ribbon technique with the ^{125}I sources connected in a suture



Sources & Source Types:
Sealed Sources

Details of ^{103}Pd seed source

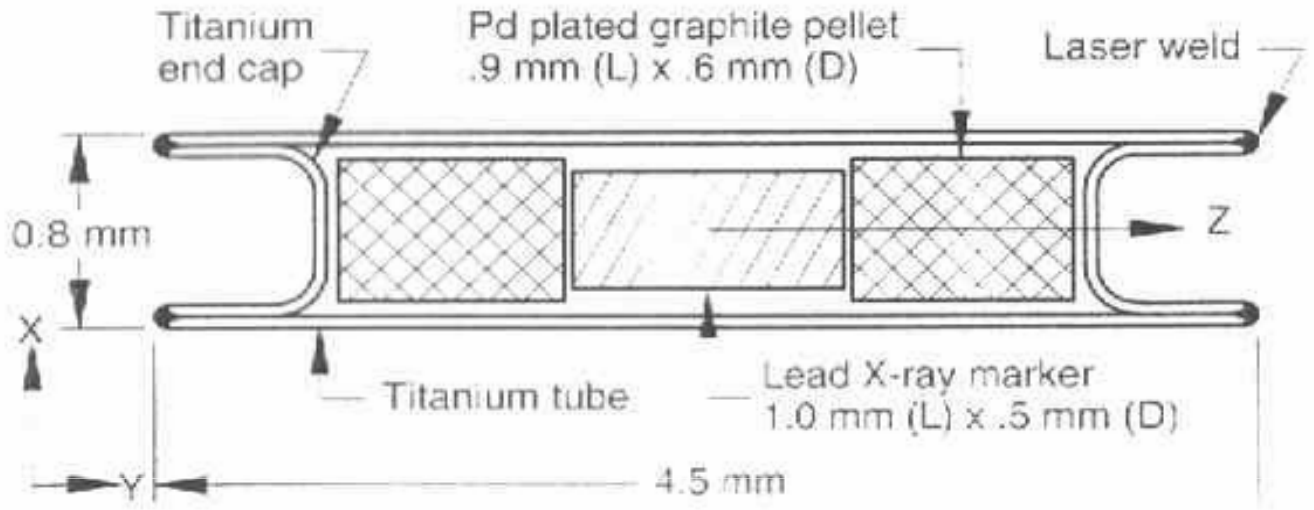


Figure 2a. Schematic of palladium-103 seeds. (Reproduced with permission of Theragenics Corporation).

Example of a Palladium-103 seed source containing 2 active pellets separated by a lead marker

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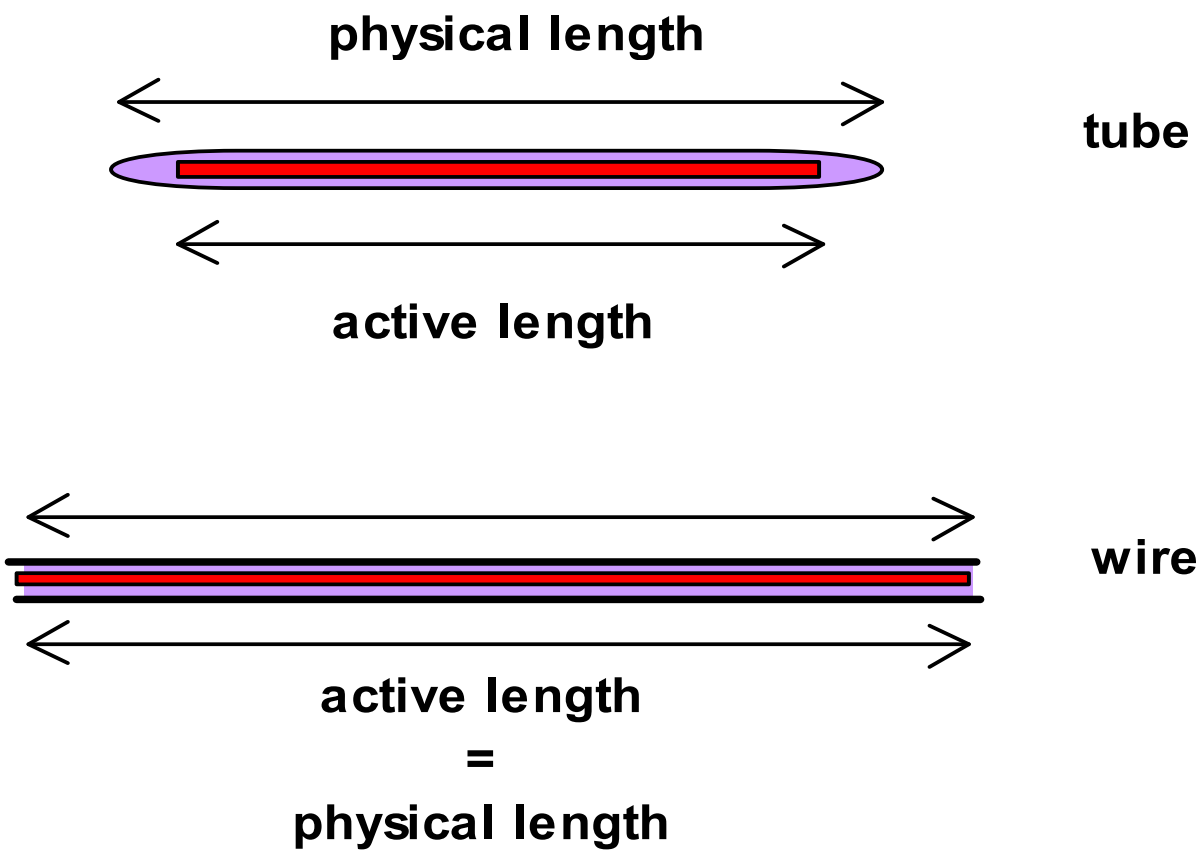
Definition of “length”



Definition of “length”

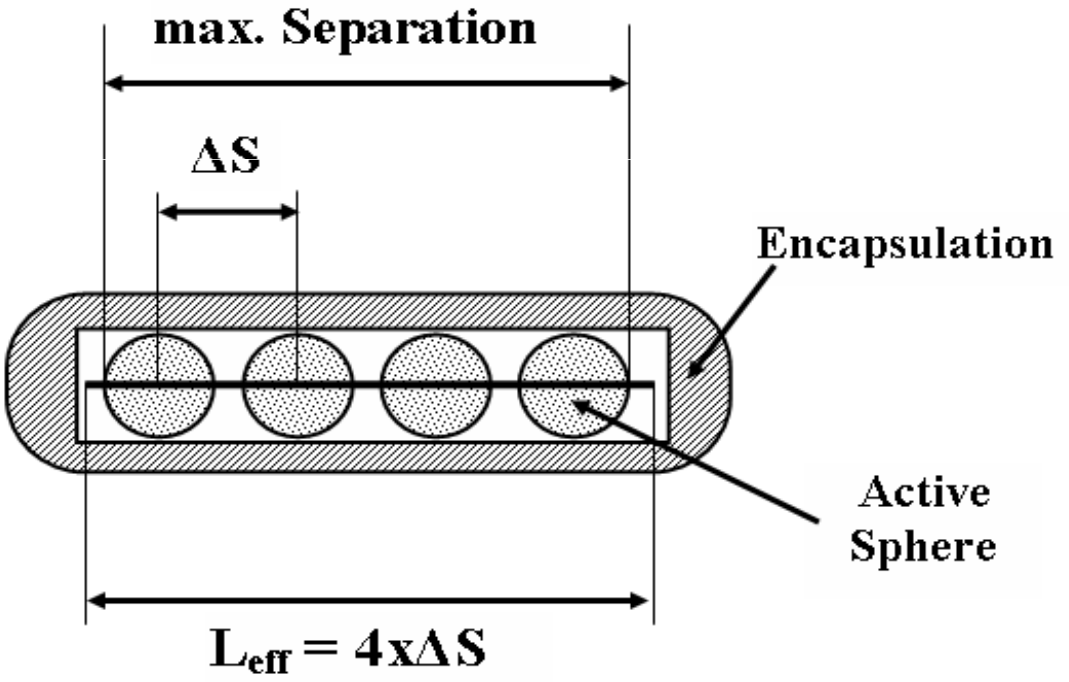


FIGURE 8.14
Graphical demonstration of the determination of the effective source length L_{eff} according to TG-43 U1[13] for the example of a seed source containing four uniformly spaced radioactive spheres. ΔS is the center-to-center spacing of the radioactive spheres. In this specific case the effective source length L_{eff} is longer than maximum separation of the radioactivity defined as the distance between the most distal edges of the radioactive spheres (1st and 4th spheres).

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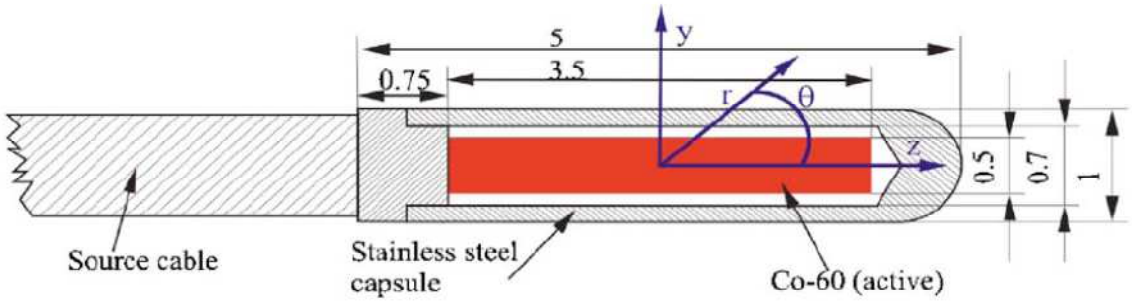
Possible “revival” of ^{60}Co?



BEBIG ^{60}Co-60 HDR – Model Co0.A86

Technical note: Dosimetric study of a new Co-60 source used in brachytherapy

D. Granero and J. Pérez-Calatayud
Physics Section, Radiation Oncology Department, “La Fe” University Hospital, Avenida Campanar 21, E46009 Valencia, Spain

F. Ballester[a)]
Department of Atomic, Molecular and Nuclear Physics and IFIC, University of Valencia-CSIC, Dr. Moliner 50, E46100 Burjassot, Spain

3485 Med. Phys. 34 (9), September 2007

Manufactured by Eckert & Ziegler BEBIG GmbH Berlin, Germany

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Possible "revival" of ^{60}Co?

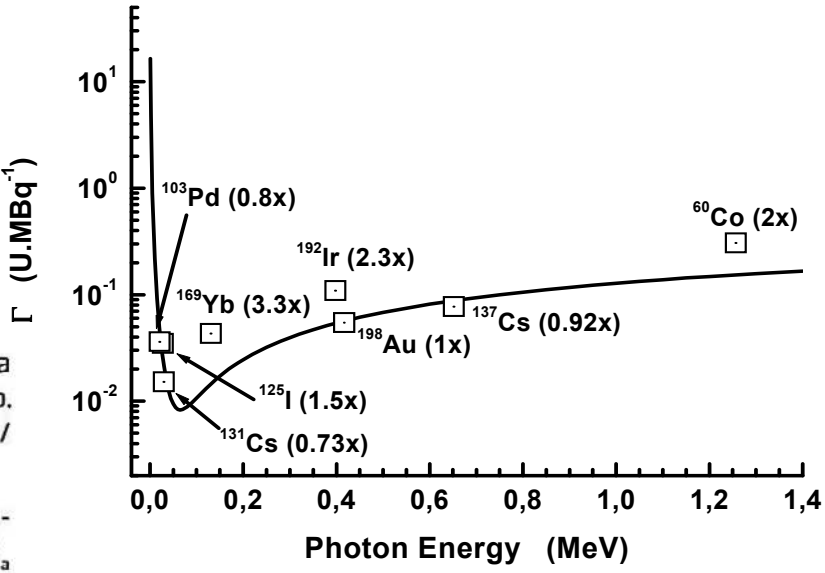

Table 1. Maximal and mean energy of beta radiation, energy range and mean energy of gamma radiation, half life time, dose rate constant Λ and air kerma rate $\dot{K}_a$ per mCi for ^{192}Ir and ^{60}Co. Data from Brookhaven National Laboratory, National Nuclear Data Center, NuDat 2.3 (http://www.nndc.bnl.gov/nudat2) and [1, 5].

Tabelle 1. Maximale und mittlere Energie der Betastrahlung, Energiebereich und mittlere Energie der Gamma-Strahlung, Halbwertszeit, Dosisleistungskonstante Λ und Luftkermarate $\dot{K}_a$ pro mCi für ^{192}Ir und ^{60}Co. Daten aus Brookhaven National Laboratory, National Nuclear Data Center, NuDat 2,3 (http://www.nndc.bnl.gov/nudat2) und [1, 5].

Nuclide	$E_{max,\beta}$ (MeV)	$\bar{E}_\beta$ (MeV)	E_γ (MeV)	$\bar{E}_\gamma$ (MeV)	$T_{1/2}$	Λ (cGy h^{-1}U^{-1})	$\dot{K}_a$ mCi^{-1} (UmCi^{-1})
^{192}Ir	0.675	0.181	0.136–1.062	0.375	73.8 d	1.12	4.13
^{60}Co	0.318	0.096	1.17–1.33	1.25	5.27 a	1.09	11.36

Table taken from:

Comparison of ^{60}Cobalt and ^{192}Iridium Sources in High Dose Rate Afterloading Brachytherapy

Jürgen Richter, Kurt Baier, Michael Flentje[1]

Strahlenther Onkol 2008 · No. 4 © Urban & Vogel

An older paper with similar contents:

Some theoretical derivations relating to the tissue dosimetry of brachytherapy nuclides, with particular reference to iodine-125

R. G. Dale

176 **Med. Phys. 10 (2), Mar/Apr 1983**

Possible “revival” of ^{60}Co?

Advantage:

- Long Half-Time
- Source Exchange every few years (simplified logistics)

Disadvantage:

- High Energy
- Radiation Protection
- International Regulations

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Topics

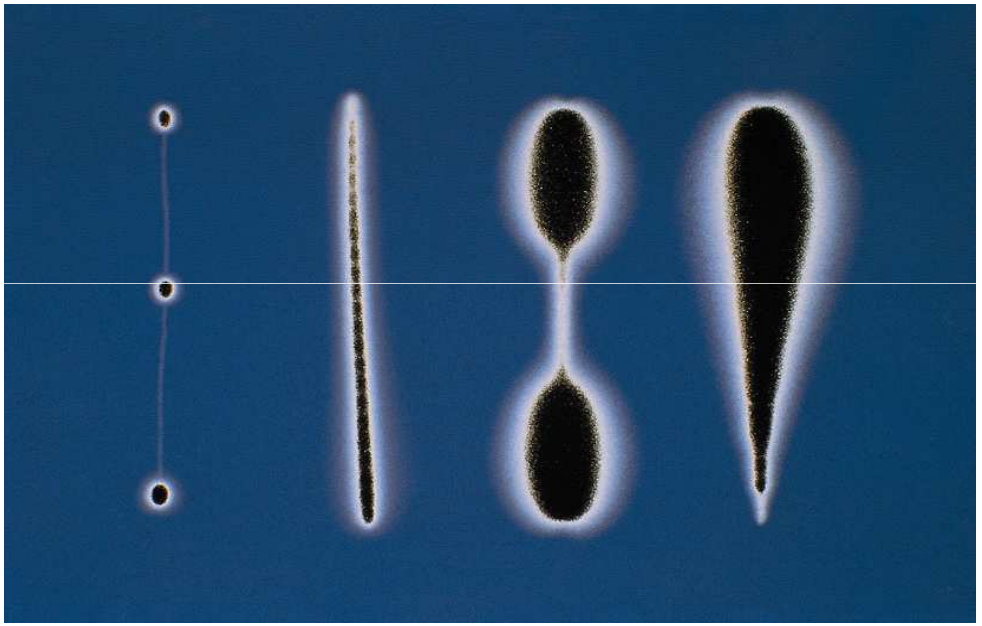
- Some History
- Radionuclides
- Does it mater which Radionuclide?
- Sources and Source Types
- **Afterloaders**
- New Developments

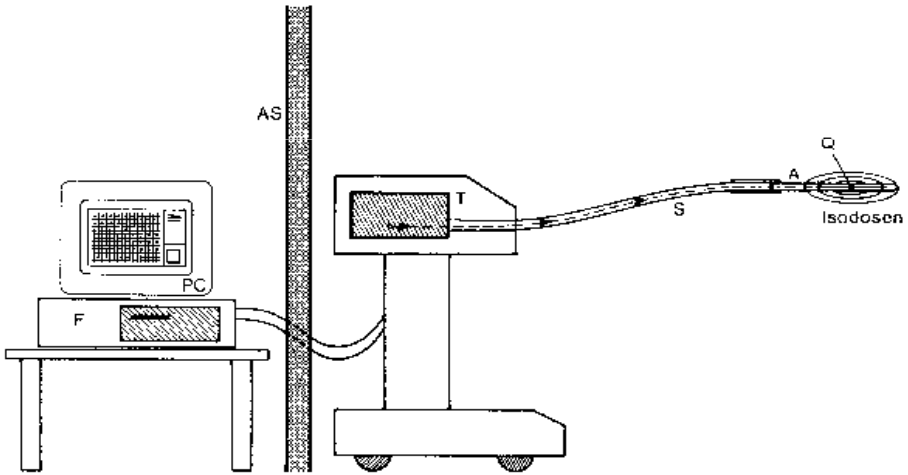
ESTRO School

Contents

- Some history
- **Afterloaders**
- Radionuclides
- Sources

Dose Distribution





The main principle of the afterloader

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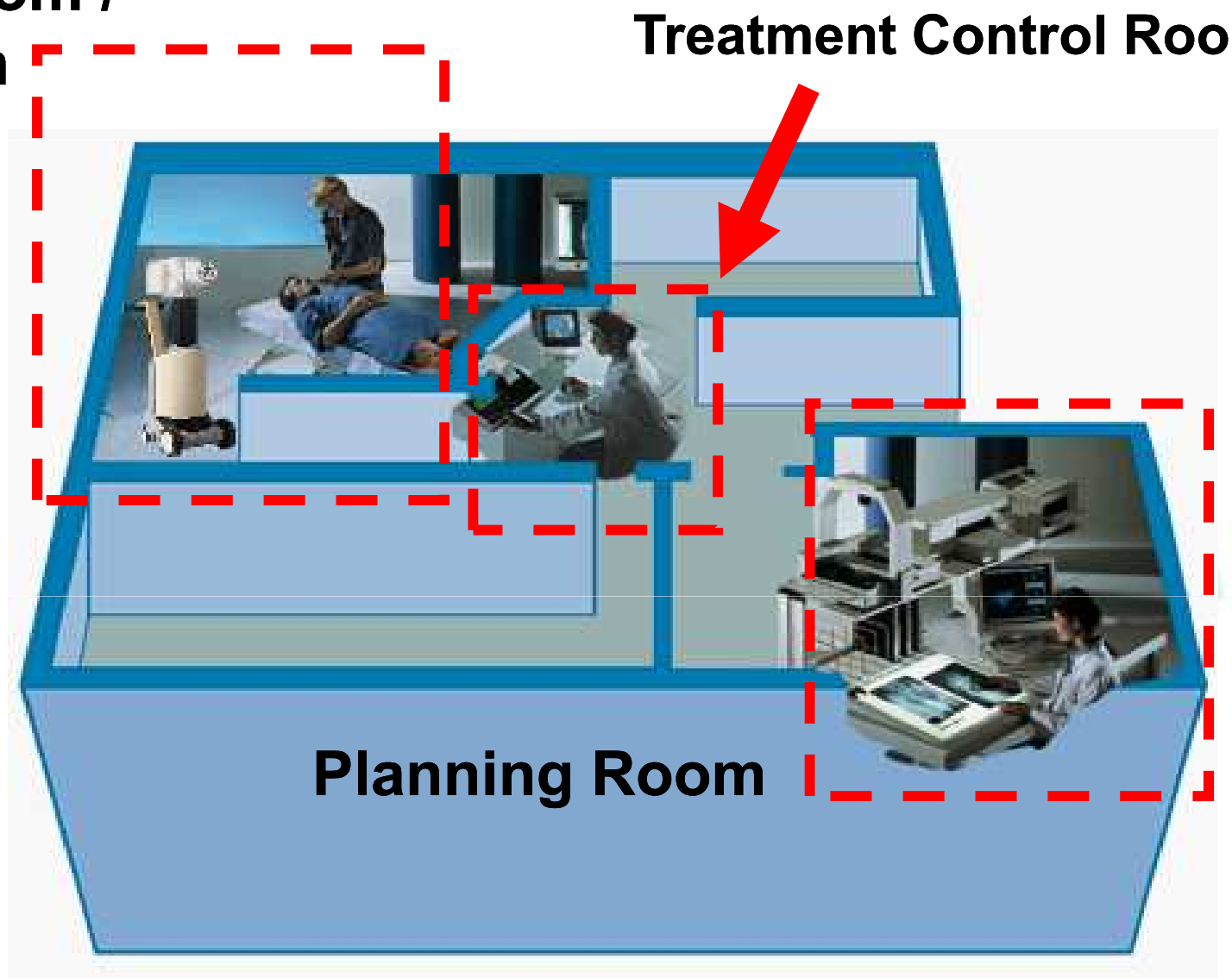
Afterloaders: The Main Principle



Afterloaders

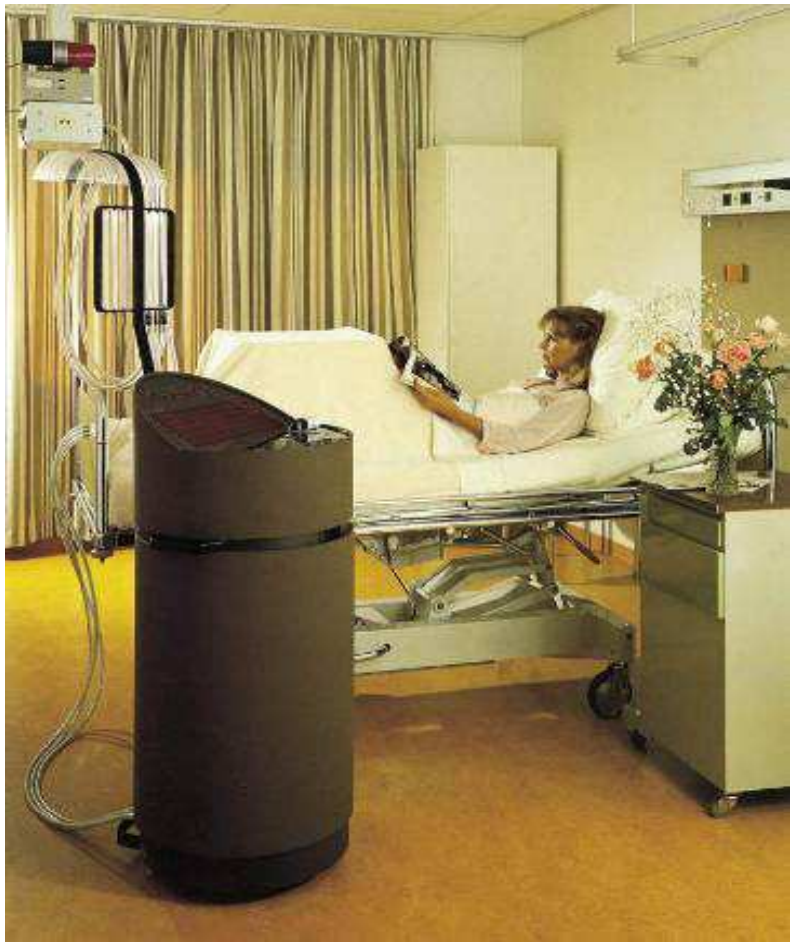
Selectron LDR

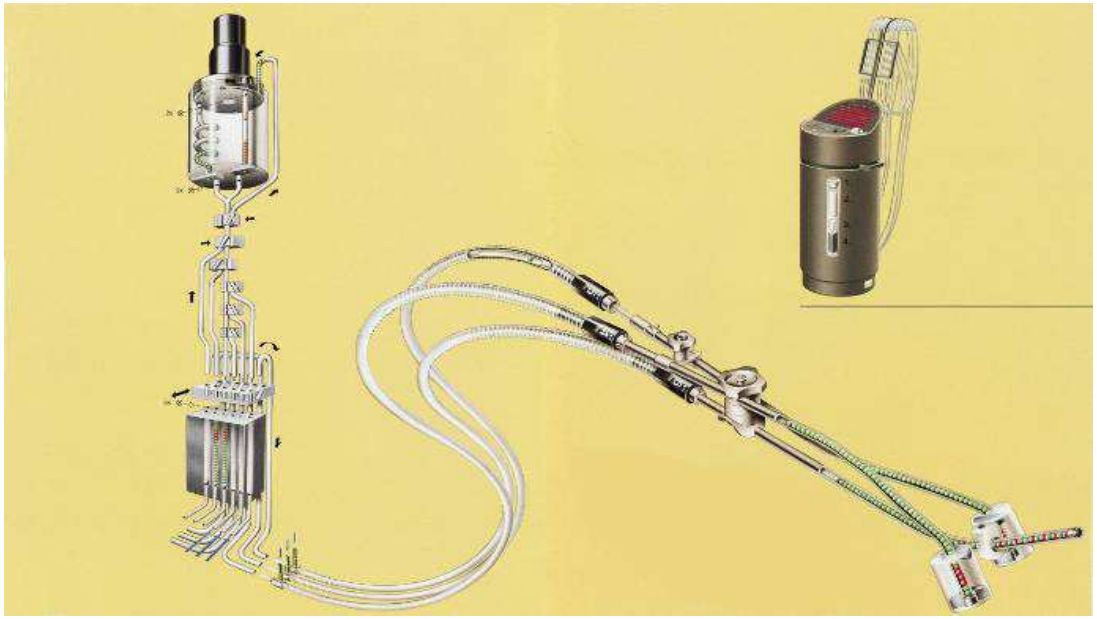
3 or 6 channels

Maximum:

48 Cs-137 sources

(pellets of 2.5 mm)





Cs-137 pellet source afterloader

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Afterloaders: Overview (HDR & PDR)

Varian, GammaMed Plus

Varian, Varisource

Varian, Varisource

Nucletron, MicroSelectron Vs. 3

Nucletron, Flexitron

Nucletron, MicroSelectron Vs. 3 Nucletron, Flexitron

BEBIG, SagiNova®

BEBIG, MultiSource

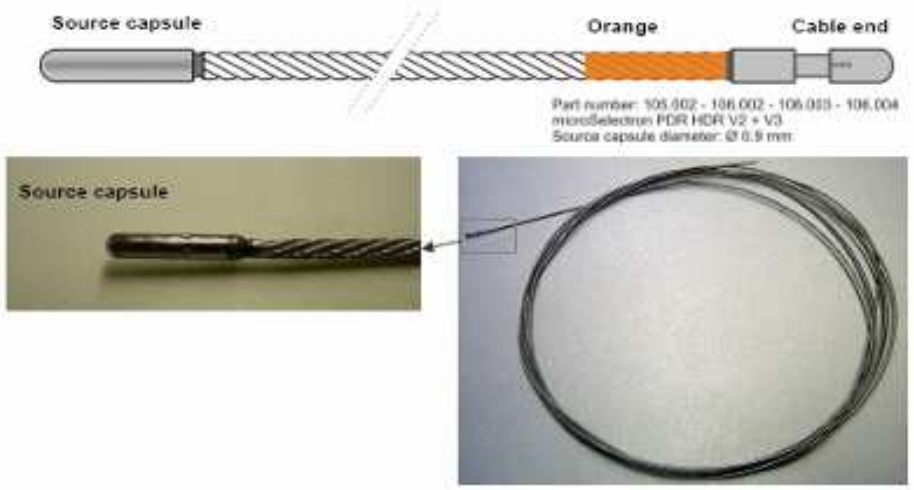
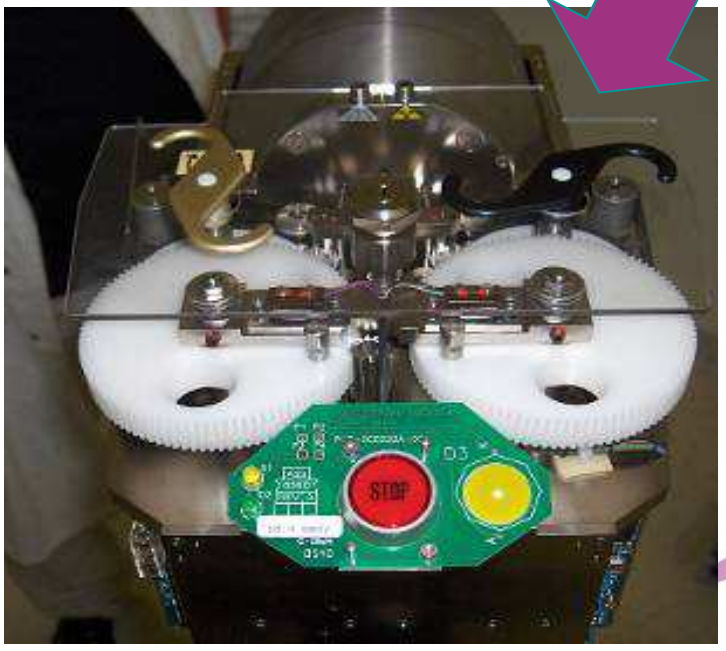


Figure 2: Source cable: microSelectron HDR V2 + V3

Modern Afterloaders: Some Details



Nucletron, MicroSelectron Vs. 3

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Afterloaders: properties

TABLE 2.1 Features of Modern HDR and PDR Afterloading Equipment

1. Vendor and Product Specification					
Name of Vendor	Nucletron B.V.	Nucletron B.V.	Eckert & Ziegler BEBIG GmbH	Varian Medical Systems Inc.	Varian Medical Systems Inc.
Website	www.nucletron.com	www.nucletron.com	www.ibt-bebig.eu	www.varian.com	www.varian.com
Name of product(s)	microSelectron Digital 6CH - 18CH - 30CH	Flexitron 40CH	MultiSource: 20 channels (extended to 40 channels in 2011) GyneSource: with 5 channels but same specs as MultiSource	Varisource iX	GammaMedplus iX; GammaMedplus iX 3/24 with 3 channels but same specs
Specify capability for use as HDR and/or PDR	HDR and PDR	HDR and PDR	HDR only	HDR only	HDR for iX models, PDR for non iX models
2. Specifications of Source or Sources					
Single or dual source capability	2 drives	3 drives	Single source	Single source	Single source
Possible types of source (radionuclide), available now and/or under development	^{192}Ir	^{192}Ir	Co-60: source type Co0.A86 Ir-192: source type Ir2.A85-2	^{192}Ir	^{192}Ir

(continued)

Refs:

Thomadsen 2000, Achieving Quality in Brachytherapy.

ESTRO Booklet 8 2004, A Practical Guide to QC of Brachytherapy Equipment.

Table taken from chapter 2 of: Comprehensive Brachytherapy 2013, (Eds. Venselaar, Baltas, Meigooni, Hoskin).

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TABLE 2.1 (Continued) Features of Modern HDR and PDR Afterloading Equipment

2. Specifications of Source or Sources					
Maximum source strength for each possible radionuclide, with approval for marketing by authorities	HDR: 57 mGy.h−1 @ 1m (518 GBq (14Ci) of Ir-192) PDR: 10.2 mGy.h−1 @ 1m (92.5 GBq (2.5 Ci) of Ir-192) Maximum storage source capacity: 518 GBq (14 Ci)	HDR: 49 mGy.h−1 @ 1m (444 GBq (12 Ci) of Ir-192) PDR: 10.2 mGy.h−1 @ 1m (92.5 GBq (2.5 Ci) of Ir-192) Maximum storage capacity: 814 GBq (22 Ci) of Ir192	Co0.A86: 22.6 mGy.h−1 @ 1m (2 Ci, 74 GBq) values + 10 % Ir2.A85-2: 40 mGy.h−1 @ 1m (10 Ci, 370 GBq) values +30 % − 10 %	44.8 mGy.h−1 @ 1m (11 Ci, 407 GBq)	61.1 mGy.h−1 @ 1m (15 Ci, 555 GBq) Local regulations may prohibit to install more than 10 Ci
Source outer dimensions for each of the source types (L = length, OD = outer diameter, in mm)	3.5 mm active length × 0.6 mm diameter Source capsule outer diameter: 0.9mm	3.5 mm active length × 0.6 mm diameter Source capsule outer diameter: 0.86 mm	Co0.A86 1.0(OD) × 5(L) mm Ir2.A85-2 0.9(OD) × 5(L) mm	0.59(OD) × 5(L) mm	HDR: 0.9(OD) × 4.52(L) mm; PDR: 0.9(OD) × 2.97(L) mm
Guarantee for the maximum number of source transfers, or source cycles	25,000 cycles	30,000 cycles	Co0.A86 100,000 (>400.000 tested) Ir2.A85-2 25,000	1,000	5,000
3. Specification of Applicators					
Outside diameter of the applicators (needles and or tubes, in mm)	Needles 1.3 mm Flexibles 4F	Needles 1.3 mm Flexibles 4F	needles 1.5 mm (17G) catheters 1.65mm for both sources	18G (1.27 mm) needles constructed from robust think wall tubing. 4.7F robust thick walled catheters	17G (1.5 mm) needles. 5F catheters.
Minimum curvature of an applicator (plastic loop radius, e.g. for an 180 degree curve, in mm)	13 mm for all applicators with a fixed geometry and an inner diameter of 2.5 mm or larger; 15 mm for flexible applicators with an inner diameter of 1.5 mm or higher; 20 mm for flexible applicators with an inner diameter of 1.3 mm up to 1.5 mm	13 mm for applicators with a fixed geometry; 15 mm for flexible applicators with an inner diameter of 1.2 mm and outer diameter of 1.5mm or higher;	10 mm (loop of 90°) 15 mm (loop of 180°) for both sources	17 mm	13 mm
4. Source to Cable Attachment					
Method of source attachment to cable	Laser welded to ultra flexible drive wire	Laser welded to ultra flexible drive wire, including weld protection	Laser welded	Embedded in the Nitinol (nickel-titanium) source drive wire	Laser welded to ultraflexible drive cable
5. Source Extension and Movement					
Maximum source extension (in mm from the indexer)	1500 mm	1400 mm	1500 mm	1500 mm	1300 mm
Speed of source movement, in seconds over maximum source extension	500 mm/s, typ. outdrive time 4 s for 1500 mm	1400mm in 3.7 sec	300 mm/s 5 s for 1500 mm	600 mm/s	630 mm/s
6. Number of Channels					
Number of hardware applicator channels	30	40	MultiSource: 20 GyneSource: 5	20	iX model: 24; iX 3/24 model: 3
Maximum number of channels that can be used in one plan/treatment	90	40	MultiSource (2011): 40 GyneSource model: 5	unlimited	unlimited

(*continued*)

And 2 pages more……

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Afterloaders: Overview (HDR & PDR)

Stand, 2015

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Afterloaders: Special Solutions

A seed Afterloader in Prostate Brachytherapy: Robotic Assisted Seed Delivery

Seed Selectron, a development designed specifically for permanent prostate afterloading
(by Nucletron B.V., The Netherlands)

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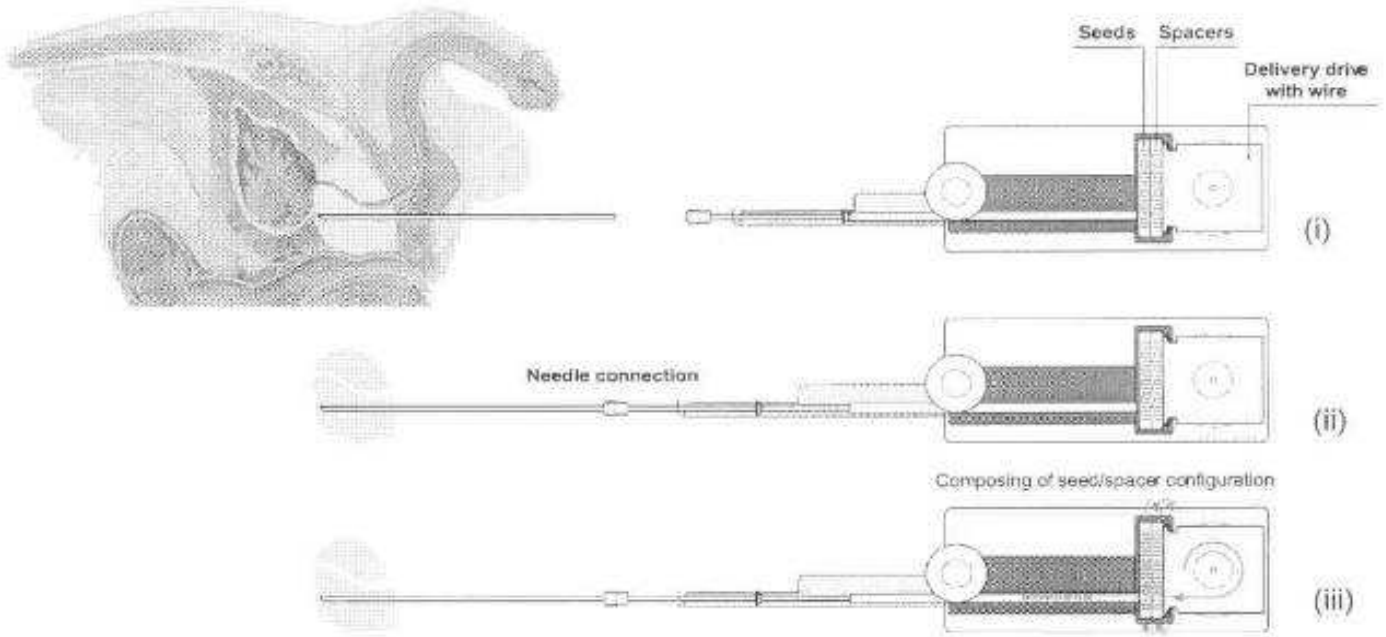
Afterloaders: Special Solutions

A seed Afterloader in Prostate Brachytherapy: Robotic Assisted Seed Delivery

Principle of loading of a needle

Application of the seed afterloader



Cassettes with ^{125}I sources and spacers

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Topics

- Some History
- Radionuclides
- Does it mater which Radionuclide?
- Sources and Source Types
- Afterloaders
- **New Developments**

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New Developments in Sources in Brachytherapy: Radionuclides

Part I: Energy

- ➔ **Homogeneity**
- ➔ **Conformity (PTV, OARs)**
- ➔ **Shielding Costs**

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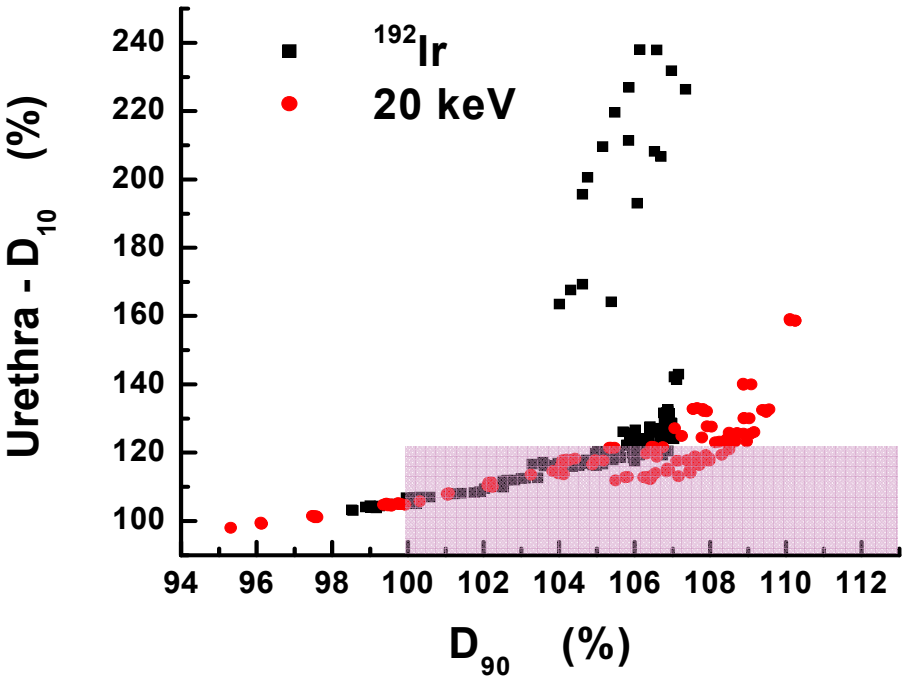
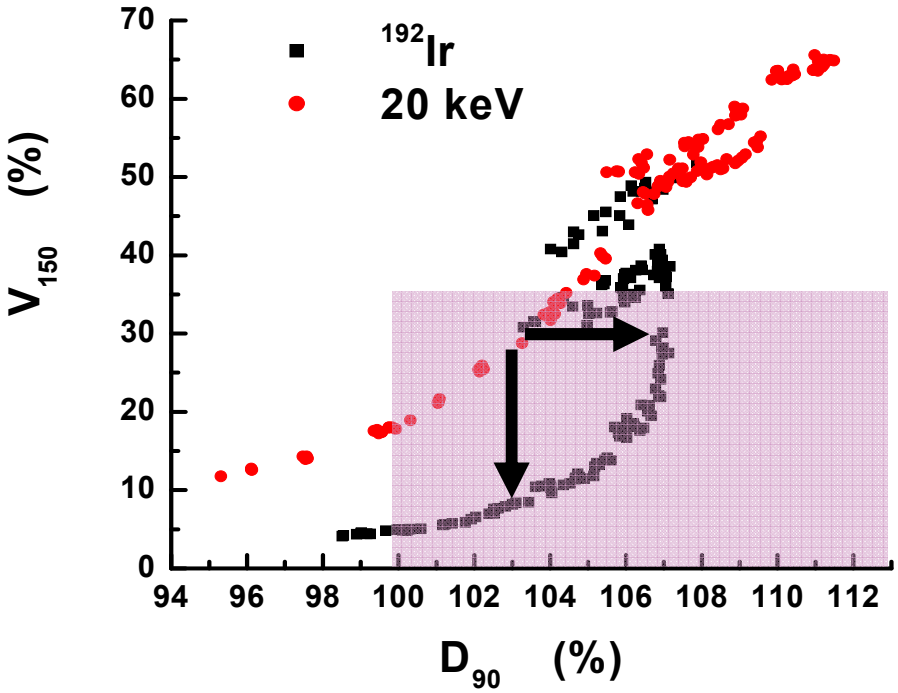
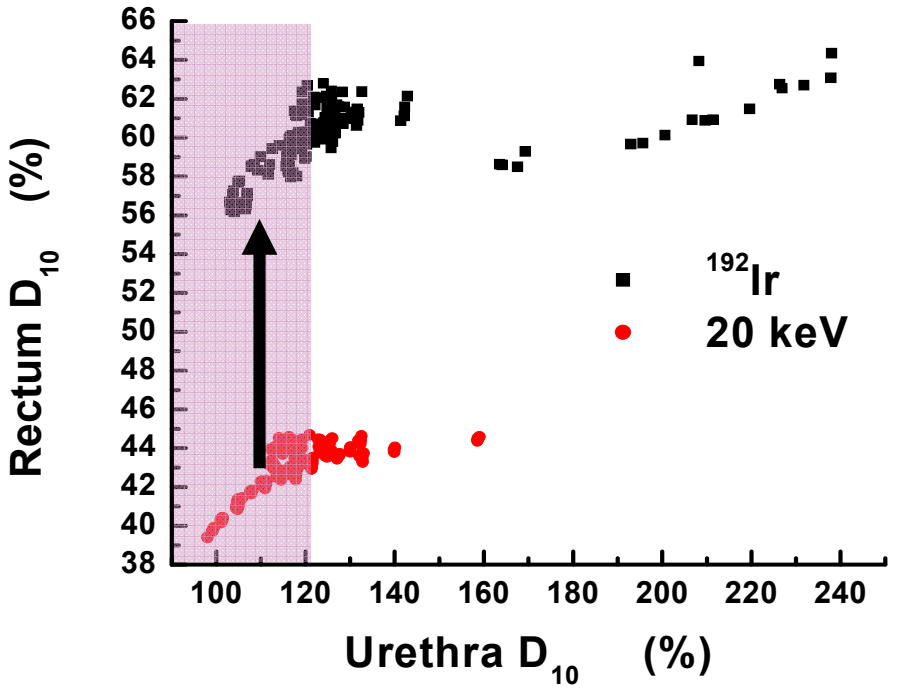
Example of Prostate Implants: Homogeneity & Conformity versus Energy







Example of Prostate Implants: Homogeneity Conformity

Multi-species prostate implant treatment plans incorporating ^{192}Ir and ^{125}I using a Greedy Heuristic based 3D optimization algorithm

V. Chaswal
Department of Engineering Physics and Department of Medical Physics, University of Wisconsin-Madison, Madison, Wisconsin 53706

S. Yoo
Department of Radiation Oncology, Duke University Medical Center, Durham, North Carolina 27710

B. R. Thomadsen
Department of Engineering Physics, Department of Medical Physics, University of Wisconsin-Madison, and Department of Human Oncology, University of Wisconsin Medical School, Madison, Wisconsin 53706

D. L. Henderson[a)]
Department of Engineering Physics and Department of Medical Physics, University of Wisconsin-Madison, Madison, Wisconsin 53706

(Received 1 June 2006; revised 20 September 2006; accepted for publication 26 October 2006; published 10 January 2007)

The goals of interstitial implant brachytherapy include delivery of the target dose in a uniform manner while sparing sensitive structures, and minimizing the number of needles and sources. We investigated the use of a multi-species source arrangement (^{192}Ir with ^{125}I) for treatment in interstitial prostate brachytherapy. The algorithm utilizes an "adjoint ratio," which provides a means of ranking source positions and is the criterion for the Greedy Heuristic optimization. Three cases were compared, each using 0.4 mCi ^{125}I seeds: case I is the base case using ^{125}I alone, case II uses 0.12 mCi ^{192}Ir seeds mixed with ^{125}I, and case III uses 0.25 mCi ^{192}Ir mixed with ^{125}I. Both multi-species cases result in lower exposure of the urethra and central prostate region. Compared with the base case, the exposure to the rectum and normal tissue increases by a significant amount for case III as compared with the increase in case II, signifying the effect of slower dose falloff rate of higher energy gammas of ^{192}Ir in the tissue. The number of seeds and needles decreases in both multi-species cases, with case III requiring fewer seeds and needles than case II. Further, the effect of ^{192}Ir on uniformity was investigated using the 0.12 mCi ^{192}Ir seeds in multi-species implants. An increase in uniformity was observed with an increase in the number of 0.12 mCi ^{192}Ir seeds implanted. The effects of prostate size on the evaluation parameters for multi-species implants were investigated using 0.12 mCi ^{192}Ir and 0.4 mCi ^{125}I, and an acceptable treatment plan with increased uniformity was obtained. © *2007 American Association of Physicists in Medicine.*
[DOI: 10.1118/1.2400827]

New Developments in Sources in Brachytherapy (Radionuclides):

Part II: Half-Life $T_{1/2}$

- ➔ **Better Adaptation to Tumour Radiobiology (permanent implants)**
- ➔ **Logistics/Complexity (source exchanges/year, authorities/legal issues)**

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New Developments in Sources in Brachytherapy (permanent implants):

Example: ^{131}Cs *versus* ^{125}I & ^{103}Pd

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Seeds with ^{131}Cs Radioactive Isotope

- ^{131}Cs isotope was suggested for BRT use back in 1960s (Henschke & Lawrence 1965)
- Based on Invention made by Donald C. Lawrence in 1967
- Developed by IsoRay, Inc. (Richland, WA, USA)
- Received FDA 510(k) clearance in 2003
- In 2009 FDA clearance for head & neck, lung and other sites (Proxcelan™ ^{131}Cs Brachytherapy Seeds)

Seeds with ^{131}Cs Radioactive Isotope

Evaluation of the new cesium-131 seed for use in low-energy x-ray brachytherapy

Mark K. Murphy,[a] R. Kim Piper,[a] and Lawrence R. Greenwood
Pacific Northwest National Laboratory, Richland, Washington 99352

Michael G. Mitch, Paul J. Lamperti, and Stephen M. Seltzer
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University of Washington, Seattle, Washington 98195

(Received 9 June 2003; revised 2 April 2004; accepted for publication 2 April 2004; published 25 May 2004)

Characterization measurements and calculations were performed on a new medical seed developed by IsoRay Inc. in Richland, Washington, that utilizes the short-lived isotope ^{131}Cs. This model has recently received FDA 510(k) clearance. The objective of this work was to characterize the dosimetric properties of the new seed according to the AAPM Task Group 43 recommendations. Cesium-131 is a low-energy x-ray emitter, with the most prominent peaks in the 29 keV to 34 keV region. The intended application is brachytherapy for treating cancers in prostate, breast, head and neck, lung, and pancreas. The evaluations performed included air-kerma strength, radial dose function, anisotropy in phantom, half-life, energy spectra, and internal activity. The results indicate the CS-1 seeds have a dose-rate constant of 0.915 cGy hr^{-1} U^{-1} in water, dose penetration characteristics similar to ^{125}I and ^{103}Pd, anisotropy function values on the order of 0.71 at short distances and small angles, and an average anisotropy factor of 0.964. The overall dosimetric characteristics are similar to ^{125}I and ^{103}Pd seeds with the exception of half-life, which is 9.7 days, as compared to 17 days for ^{125}I. The shorter half-life may offer significant advantages in

© *2004 American Association of Physicists in Medicine.*

2]

trength, anisotropy function, brachytherapy, brachytherapy seed, cesium-
ıt, dosimetry, Monte Carlo, radial dose function, thermoluminescent

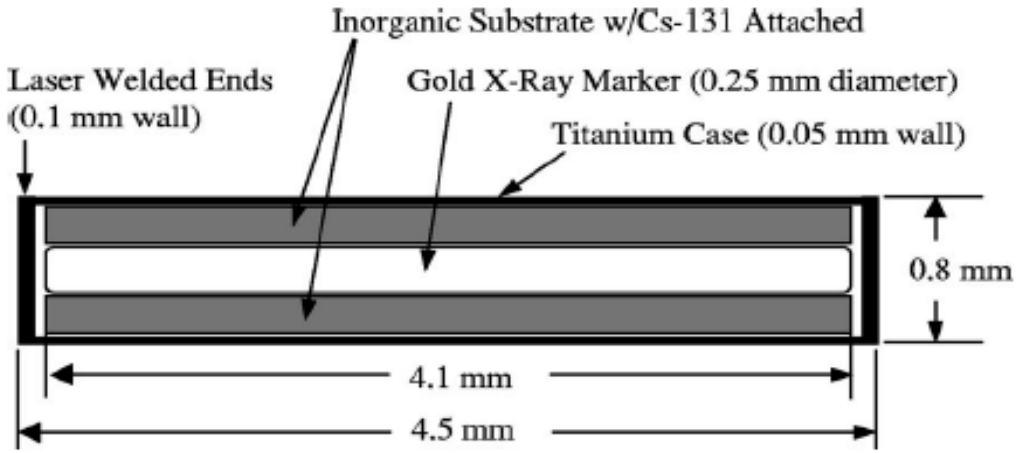

FIG. 1. Schematic drawing of the cross section containing the symmetry axis of the cylindrically shaped CS-1 ^{131}Cs seed.

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Seeds with ^{131}Cs Radioactive Isotope

Dosimetric characterization of model Cs-1 Rev2 cesium-131 brachytherapy source in water phantoms and human tissues with MCNP5 Monte Carlo simulation

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Hualin Zhang
Department of Radiation Medicine, The Ohio State University, Columbus, Ohio 43210

(Received 16 October 2007; revised 15 January 2008; accepted for publication 15 January 2008; published 24 March 2008)

A recently developed alternative brachytherapy seed, Cs-1 Rev2 cesium-131, has begun to be used in clinical practice. The dosimetric characteristics of this source in various media, particularly in human tissues, have not been fully evaluated. The aim of this study was to calculate the dosimetric parameters for the Cs-1 Rev2 cesium-131 seed following the recommendations of the AAPM TG-43U1 report [Rivard *et al.*, Med. Phys. **31**, 633–674 (2004)] for new sources in brachytherapy applications. Dose rate constants, radial dose functions, and anisotropy functions of the source in water, Virtual Water™, and relevant human soft tissues were calculated using MCNP5 Monte Carlo simulations following the TG-43U1 formalism. The results yielded dose rate constants of 1.048, 1.024, 1.041, and 1.044 cGy h^{-1} U^{-1} in water, Virtual Water™, muscle, and prostate tissue, respectively. The conversion factor for this new source between water and Virtual Water™ was 1.02, between muscle and water was 1.006, and between prostate and water was 1.004. The authors' calculation of anisotropy functions in a Virtual Water™ phantom agreed closely with Murphy's measurements [Murphy *et al.*, Med. Phys. **31**, 1529–1538 (2004)]. Our calculations of the radial dose function in water and Virtual Water™ have good agreement with those in previous experimental and Monte Carlo studies. The TG-43U1 parameters for clinical applications in water, muscle, and prostate tissue are presented in this work. © *2008 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2868754]

Key words: brachytherapy, cesium-131, Monte Carlo, MCNP5, tissue water conversion factor

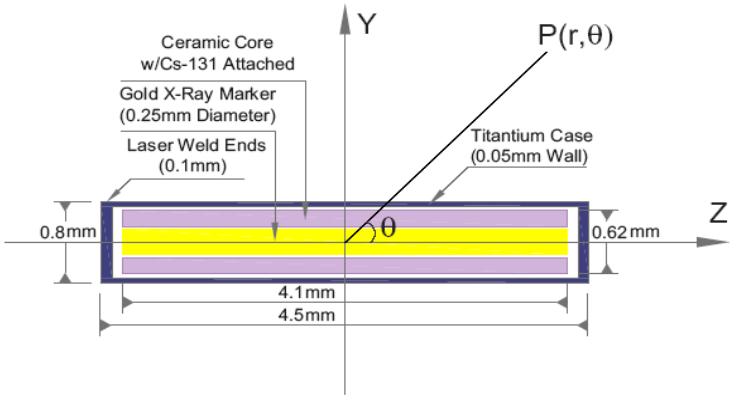
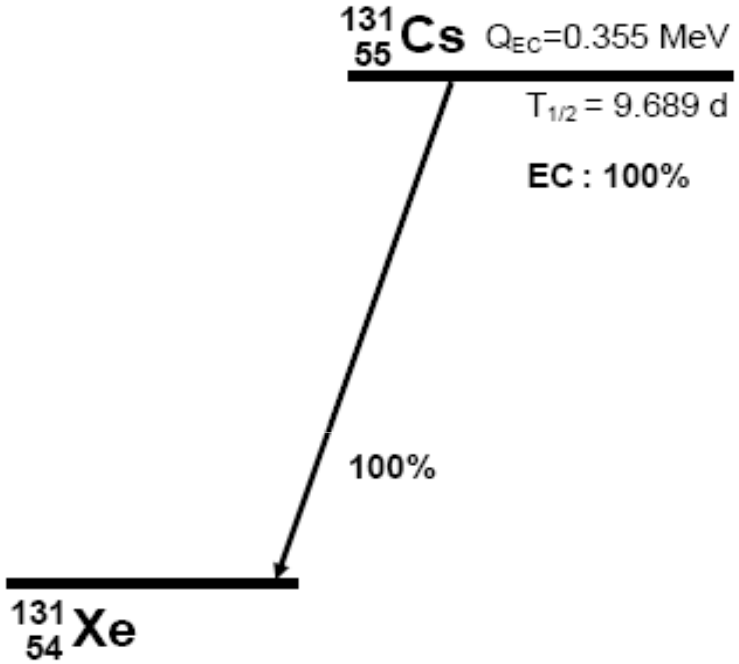
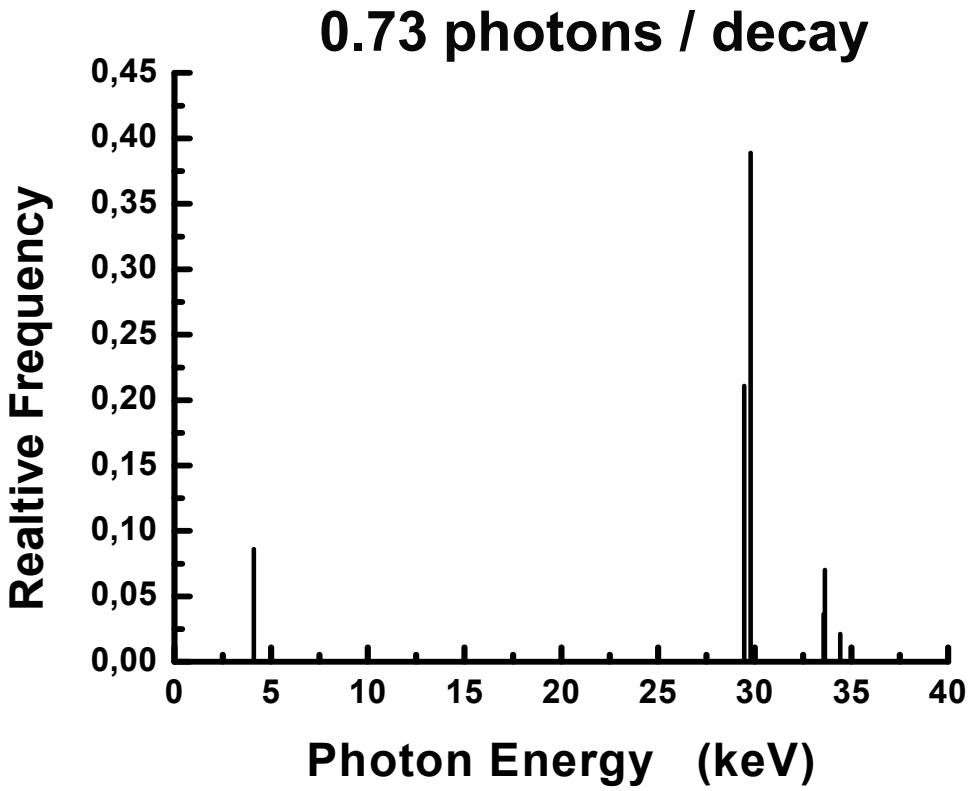


FIG. 1. Schematic diagram of model Cs-1 Rev2 cesium-131 source.

Seeds with ^{131}Cs Radioactive Isotope





Effective Energy: 30keV

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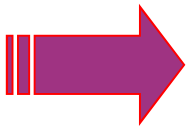
Seeds with ^{131}Cs Radioactive Isotope

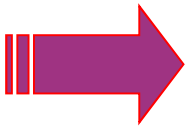
- **Shorter $T_{1/2}$ compared to ^{125}I and ^{103}Pd**
  9.689d *vs.* 59.49d and 16.991d



Biological Effectiveness

- **Higher Energy**

  30keV *vs.* 28keV and 21keV



Dose Homogeneity

- **Apparent Activity Conversion Factor**

  0.638 $U.mCi^{-1}$

  versus

  1.27 $U.mCi^{-1}$ for ^{125}I and 1.29 $U.mCi^{-1}$ for ^{103}Pd

ESTRO School

Seeds with ^{131}Cs Radioactive Isotope

- Apparent Activity Conversion Factor

  0.638 $U.mCi^{-1}$

  versus

  1.27 $U.mCi^{-1}$ for ^{125}I and 1.29 $U.mCi^{-1}$ for ^{103}Pd

- **Initial Dose Rate (at the prostate surface)**

  30 $cGy.h^{-1}$

  versus

  7 $cGy.h^{-1}$ for ^{125}I and 20 $cGy.h^{-1}$ for ^{103}Pd

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Seeds with ^{131}Cs Radioactive Isotope

- **Biological Effectiveness**

ELSEVIER

0360-3016/03/$–see front matter

PII S0360-3016(02)04208-6

BIOLOGY CONTRIBUTION

THE DETERMINATION OF RADIOBIOLOGICALLY OPTIMIZED HALF-LIVES FOR RADIONUCLIDES USED IN PERMANENT BRACHYTHERAPY IMPLANTS

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Purpose: To use tumor growth kinetics and other biologic parameters in an extended version of the linear-quadratic (LQ) formulation to determine radiobiologically optimized half-lives of radionuclides which might be used in permanent brachytherapy implants.

Methods and Materials: A version of the LQ model suitable for the analysis of permanent brachytherapy implants has been modified to investigate the radionuclide half-lives that will maximize the biologically effective dose (BED) delivered to tumors with repopulation rates (K values) in the range 0.01–1.1 $Gyday^{-1}$. The method assumes that part of the physical dose delivered to the tumor may be radiobiologically wasted because of the repopulation phenomenon, whereas adjacent normal tissues will exhibit little or no wastage. To perform the analysis, it is necessary to stipulate α/β ratios and sublethal damage recovery rates together with the normal tissue tolerance BED. The analysis also takes into account a range of likely relative biological effectiveness (RBE) values.

Results: Rapidly growing tumors require the shortest radionuclide half-lives, but even slow-growing tumors such as prostate adenocarcinomas can be satisfactorily treated with radionuclides possessing half-lives substantially less than that associated with I^{125}. The likelihood that prostate tumors possess an α/β value which is comparable with, or lower than, that associated with late-responding normal tissues would also mitigate against the use of long-lived radionuclides. Although a number of parameter assumptions are involved, the results suggest that, for a wide range of tumor types, shorter-lived radionuclides are more versatile for achieving reasonable clinical results. The theoretically derived optimum half-lives typically range from around 0–5 days for fast-repopulating tumors (K 1.1 $Gyday^{-1}$) to approximately 14–50 days for slow-growing tumors (K ~ 0.1 $Gyday^{-1}$ or less). For prostate implantation, ^{103}Pd is overall a better choice than ^{125}I.

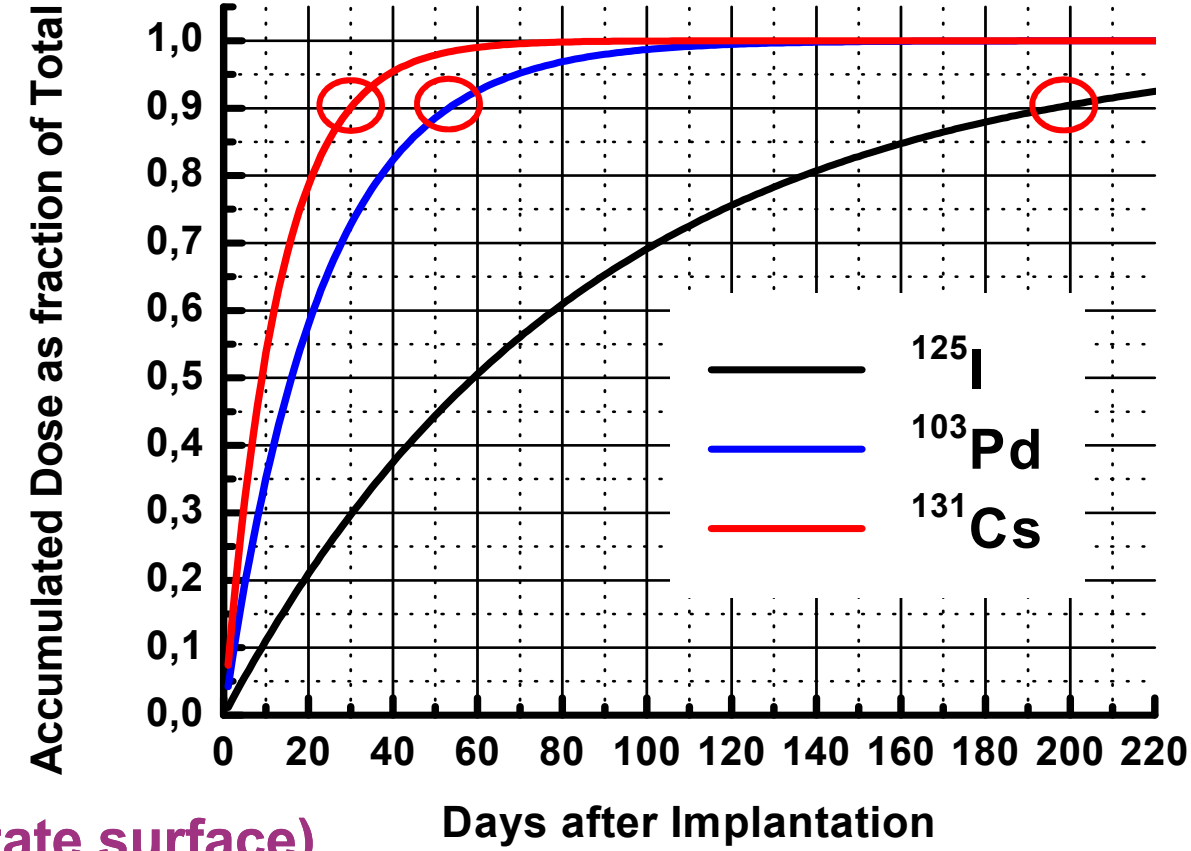
Conclusion: With so many variables and parameter uncertainties, it is not appropriate to attempt to define optimum radionuclide half-lives too closely. However, this study suggests that half-lives in the approximate range 4–17 days are likely to be significantly better for a wide range of tumor types for which the radiobiologic characteristics may not be precisely known in advance. © 2003 Elsevier Science Inc.

Seeds with ^{131}Cs Radioactive Isotope

- **Biological Effectiveness**

Total Dose (100%)

- **145 Gy**
- **125 Gy**
- **115 Gy**



- **Initial Dose Rate (at the prostate surface)**
  30 cGy.h^{-1}
  versus
  7 cGy.h^{-1} for ^{125}I and 20 cGy.h^{-1} for ^{103}Pd

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Seeds with ^{131}Cs Radioactive Isotope

- **Dose Homogeneity**

Cancer Biother Radiopharm. 2009 Dec;24(6):701-5.

Dosimetric study of Cs-131, I-125, and Pd-103 seeds for permanent prostate brachytherapy.

Yang R, Wang J, Zhang H.

Department of Radiation Oncology, Cancer Center, Peking University Third Hospital, Beijing, China.

Abstract

As a well-established single-modality approach for early-stage prostate cancer, transperineal interstitial permanent prostate brachytherapy (TIPPB) has gained increasing popularity due to its favorable clinical results. Currently, three isotopes, namely Cs-131, I-125, and Pd-103, are commercially available for TIPPB. This is the first study to systematically explore the dosimetric difference of these three isotopes for TIPPB. In total, 25 patients with T1-T2c prostate cancer previously implanted with I-125 seeds were randomly selected and replanned with Cs-131, I-125, and Pd-103 seeds to the prescription doses of 115, 145, and 125 Gy, respectively. The planning goals attempted were prostate V(p)100 approximately 95%, D(p)90 >or= 100%, and prostatic urethra D(u)10 <or= 150%. The dosimetric parameters, as well as the number of seeds and needles required, were analyzed and compared. The mean homogeneity index (HI) was 0.59, 0.56, and 0.46 for Cs-131, I-125, and Pd-103 plans, respectively. The average D(u)10 was 124.6%, 125.7%, and 129.7%, respectively. The average rectum V(r)100 was 0.19, 0.22, and 0.31 cc, respectively. In addition, the average number of seeds was 57.9, 63.0, and 63.7, and the average number of needles required was 31.6, 32.9, and 33.6 for Cs-131, I-125, and Pd-103 seeds, respectively. This study demonstrates that TIPPB, utilizing Cs-131 seeds, allows for better dose homogeneity, while providing comparable prostate coverage and sparing of the urethra and rectum, with a comparable number of, or fewer, seeds and needles required, compared to I-125 or Pd-103 seeds. Further biological and clinical studies associated with Cs-131 are warranted.

PMID: 20025550 [PubMed - indexed for MEDLINE]

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Seeds with ^{131}Cs Radioactive Isotope

- **Recommendations**

Brachytherapy. 2008 Oct-Dec;7(4):290-6. Epub 2008 Sep 7.

Recommendations for permanent prostate brachytherapy with (131)Cs: a consensus report from the Cesium Advisory Group.

Bice WS, Prestidge BR, Kurtzman SM, Beriwal S, Moran BJ, Patel RR, Rivard MJ; Cesium Advisory Group.

Foundation for Medical Physics Research, San Antonio, TX 78216, USA.

Abstract

PURPOSE: Published clinical information on the safety and efficacy of (131)Cs implants is limited. We provide consensus recommendations for (131)Cs prostate brachytherapy based on experience to date.

METHODS AND MATERIALS: The Cesium Advisory Group (CAG) consists of experienced (131)Cs users. Recommendations are based on three clinical trials, one of which has completed accrual and has been published in the peer reviewed literature, and combined CAG experience of more than 1200 (131)Cs implants.

RESULTS: We recommend using 1.059cGyh(-1)U(-1) as the dose rate constant for the IsoRay source. The prescription for monotherapy implants is 115Gy and when combined with 45-50Gy external beam it is 85Gy. Suggested individual source strength ranges from 1.6 to 2.2U. The release criterion for (131)Cs implants is 6mRh(-1) at 1m. (131)Cs brachytherapy should be performed differently from (125)I and (103)Pd brachytherapy: source placement is further from the urethra and rectum, the prostate V(150) should be < or =45%; sufficient margins may be obtained while limiting source placement to the capsule or close to the capsule. The increased dose rate may cause degradation of postimplant quantifiers due to edema. However, large variability in the magnitude and rate of resolution of edema make determination of the most representative postoperative imaging time impossible. The CAG recommends postimplant imaging on the day of the implant. Recommended postimplant evaluation goals include prostate D(90) greater than the prescription dose; maintaining D(u)(,30)<140% of the prescription dose and keeping V(r)(,100)<0.5cm(3).

CONCLUSION: It was the consensus of the CAG that optimal (131)Cs implants should be performed differently from those performed with (125)I or (103)Pd. Guidelines have been established to allow for safe and effective delivery of (131)Cs prostate brachytherapy.

PMID: 18782682 [PubMed - indexed for MEDLINE]

Seeds with ^{131}Cs Radioactive Isotope

NEWSFEED

Jun 16, 2010

More centres adopt IsoRay's Cs-131 for lung cancer treatment

1

RICHLAND, WA, (Marketwire), 15 June 2010 - IsoRay, Inc. (AMEX: ISR) announced today that doctors at Curtis and Elizabeth Anderson Cancer Institute and WellSpan Health's York Cancer Center are now using Cesium-131 Brachytherapy seeds for the treatment of lung cancer.

Brachytherapy is a type of radiation therapy that is used to kill cancer cells and shrink tumors. Known as internal radiation therapy, radioactive material is placed next to or inside the tumor. However, not all seed Brachytherapy radioisotopes are the same. Cesium-131 Brachytherapy seed gives physicians and their patients a new choice in treatment with important benefits.

World's first Cesium-131 implant for recurrent head and neck cancer performed

2

28. September 2009 09:14

IsoRay, Inc. (Amex: ISR) announced today that on August 5, 2009, Dr. Bhupesh Parashar from the Department of Radiation Oncology, Dr. David Kutler of the Department of Otorhinolaryngology, and Dr. Jason Spector of the Department of Plastic Surgery at Weill Cornell Medical Center performed the world's first Cesium-131 implant for a recurrent head and neck cancer (buccal mucosa).

Alternatives for Cancer
Immune System Therapy
Breast/Prostate/Lung Cancer
www.immunerecovery.net

California Proposition 65
Testing, risk mgt, consulting, product assessments & screening
www.intertek.com/prop65

Urologie Unispital Basel
Laparoskopie, HIFU, Brachy bei PCA
Nervenschonende Prostatektomie
www.uro-basel.ch

Ion Implant Service
Specializing in high energy implants for the GaAS industry
www.tss-ion-implant.com

Ads by Google

The implant was performed using Vicryl®-embedded seeds on a 66-year-old patient who had received a full course of radiation to the head and neck several years ago. Cesium-131 was chosen for its short half-life and the higher dose rate. The patient tolerated the implant procedure well, and has had no adverse effects that can be attributed to the use of Cs-131 seeds. There is no evidence of cancer recurrence to date.

Dr. Parashar stated, "We are very pleased to date with this patient's progress. Having Cs-131 with its combination of short half-life and high energy gave us another option for treating this patient's recurring buccal mucosa cancer."

Dr. Dattatreyudu Nori, the Chairman of the Department of Radiation Oncology at Weill Cornell Medical Center, and a pioneer in the field of brachytherapy, performed some of the initial Cesium-131 prostate implants in 2005.

Until now clinical experience with Cesium-131 has been focused on prostate cancer and ocular melanoma. However, Cesium-131 has been cleared by the FDA for use in the treatment of malignant disease (e.g., prostate, ocular melanoma, head and neck, lung, brain, breast, etc.) and may be used in surface, interstitial, and intracavitary applications for tumors with known radiosensitivity.

Dwight Babcock, IsoRay's CEO, stated, "This is another example supporting our strategy to expand the use of Cesium-131 seeds to a larger population of patients with varying cancers. The use of Cs-131 is a very attractive alternative to other treatment options, and physicians continue to broaden the scope of this isotope for use in minimally invasive treatments."

http://www.isoray.com

ESTRO School

New Developments in Sources in Brachytherapy (Afterloading Technology):

- **Radionuclides / Sources of intermediate & low Energy (≤100 keV)**
- **Miniaturised X-Ray-Sources**

New Developments in Sources in Brachytherapy (Afterloading Technology):

Radionuclides / Sources of intermediate & low Energy

➔ **Lower Energy than ^{192}Ir**

➔ **Half-Life $T_{1/2}$?**

(source exchanges/year)

ESTRO School

Energy ←→ Radiation Protection

Mobility / Flexibility / Costs

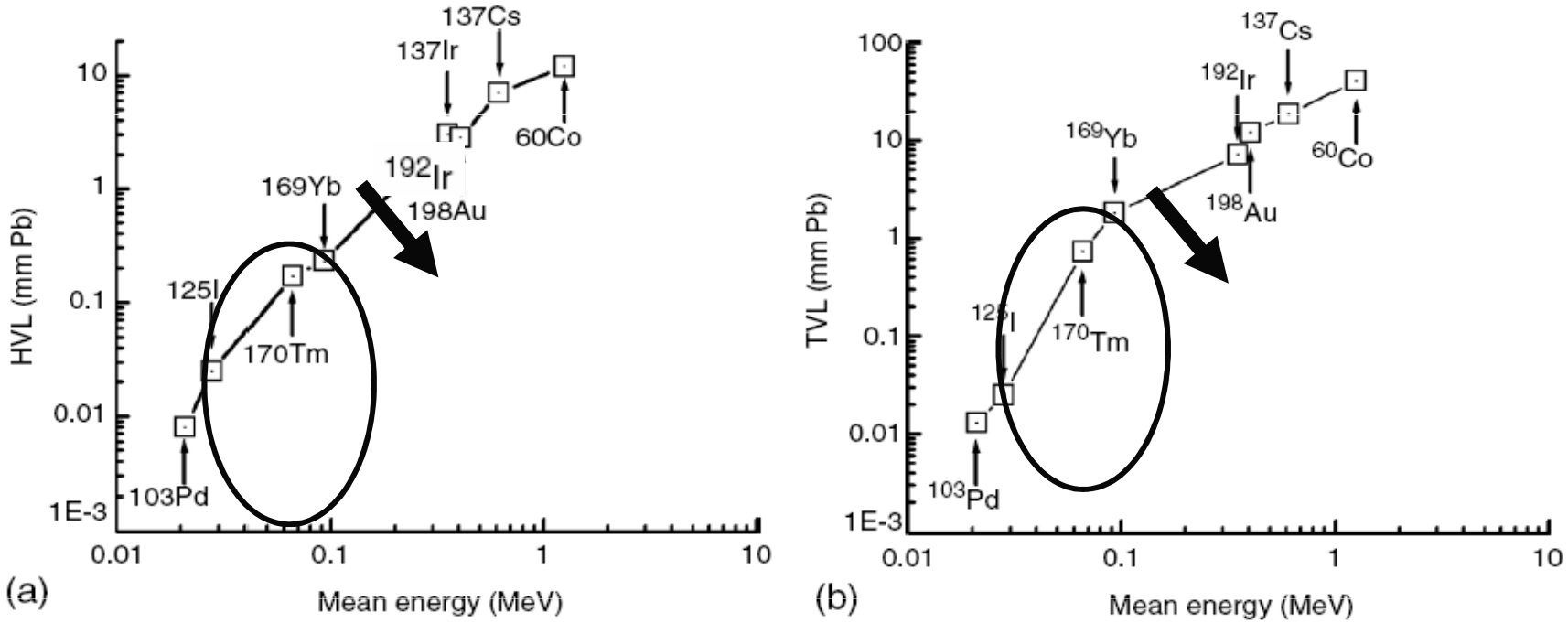

FIGURE 5.11
Thickness of lead required (a) for 50% transmission, HVL, and (b) for 10% transmission, TVL for the different radionuclides handled in this chapter. HVL values are according to the data presented in Table 5.15, where the tenth value layer data are according to Williamson.[19] The TVL values for ^{169}Yb and ^{170}Tm according to Granero et al.[18] (for ^{169}Yb and ^{192}Ir see also Lymperopoulou et al.[21]).

ESTRO School

New Developments in Sources in Brachytherapy (Afterloading Technology):

Radionuclides / Sources of intermediate & low Energy

- → ^{169}Yb
- → ^{170}Tm
- → ^{204}Tl
- → ^{101}Rh

Ytterbium was discovered in 1878 from the Swiss Chemist Jean Charles Galissard de Marignac.

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Ytterbium is never found in nature as free element. Its abundance in Earth's crust by is weight of 3200 ppb (parts per billion – 10^9). Ytterbium is found in the ore monazite sand [(Ce, La, etc.)PO4] and an ore containing small amounts of all the rare earth metals. It is also found in the ores euxenite and xenotime. It is difficult to separate from other rare earth elements.
Ion exchange and solvent extraction techniques developed since the 1940's have lowered the cost of production.

Natural abundance: ^{168}Yb 0.13%, ^{170}Yb 3.04%, ^{171}Yb 14.28%, ^{172}Yb 21.83%, ^{173}Yb 16.13%, ^{174}Yb 31.83%, ^{176}Yb 12.76%

Melting point: 824 ° C, Density: 6.73 g.cm^{-3}

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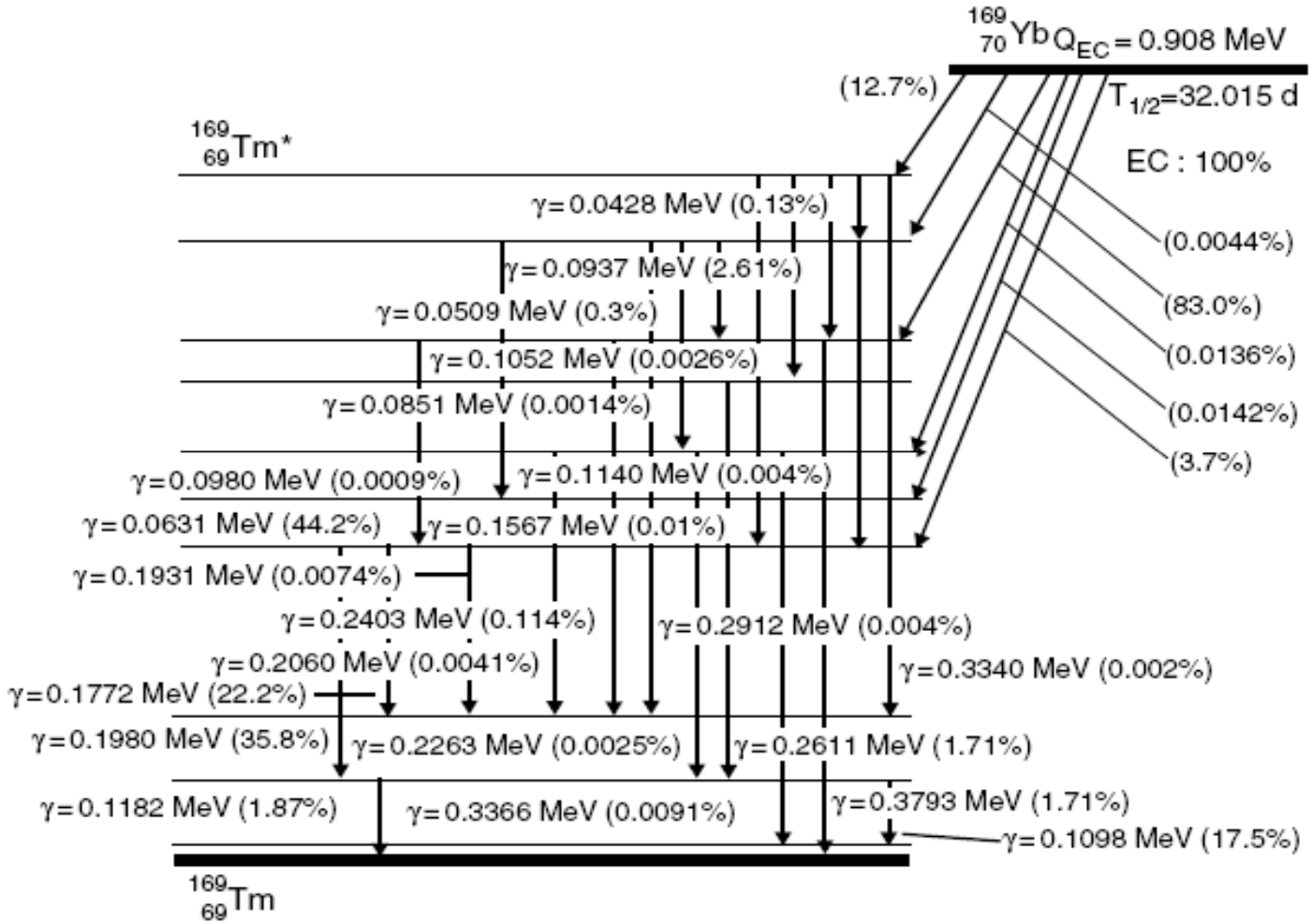
Sources: ^{169}Yb



Sources: ^{169}Yb

5.9 ^{169}Ytterbium

^{169}Yb was discovered using artificial activation techniques in 1946, but its initial applications were industrial. It was not until 1990 that the first clinical application of ^{169}Yb sources took place in London, Ontario, Canada. This was followed in 1993 by a detailed report on the clinical application of the new ^{169}Yb brachytherapy seed source.[8] These seeds have been manually loaded in preimplanted catheters (for a temporary perineal implant) and also, using a total activity of approximately 3700 MBq, for treatment of a recurrence of rectal adenocarcinoma.

^{169}Yb is potentially applicable for permanent or temporary implants due to its intermediate half-life of 32 days and its relative high specific activity which is higher than that of ^{192}Ir and ^{125}I but lower than that of ^{103}Pd.

Radionuclides / Sources of intermediate & low Energy → ^{169}Yb

A dosimetric comparison of ^{169}Yb versus ^{192}Ir for HDR prostate brachytherapy

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(Received 14 July 2005; revised 6 September 2005; accepted for publication 29 September 2005; published 29 November 2005)

For the purpose of evaluating the use of ^{169}Yb for prostate High Dose Rate brachytherapy (HDR), a hypothetical ^{169}Yb source is assumed with the exact same design of the new microSelectron source replacing the ^{192}Ir active core by pure ^{169}Yb metal. Monte Carlo simulation is employed for the full dosimetric characterization of both sources and results are compared following the AAPM TG-43 dosimetric formalism. Monte Carlo calculated dosimetry results are incorporated in a commercially available treatment planning system (SWIFT^{TM}), which features an inverse treatment planning option based on a multiobjective dose optimization engine. The quality of prostate HDR brachytherapy using the real ^{192}Ir and hypothetical ^{169}Yb source is compared in a comprehensive analysis of different prostate implants in terms of the multiobjective dose optimization solutions as well as treatment quality indices such as Dose Volume Histograms (DVH) and the Conformal Index (COIN). Given that scattering overcompensates for absorption in intermediate photon energies and distances in the range of interest to prostate HDR brachytherapy, ^{169}Yb proves at least equivalent to ^{192}Ir irrespective of prostate volume. This has to be evaluated in view of the shielding requirements for the ^{169}Yb energies that are minimal relative to that for ^{192}Ir. © *2005 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2126821]

A dosimetric comparison of ^{169}Yb and ^{192}Ir for HDR brachytherapy of the breast, accounting for the effect of finite patient dimensions and tissue inhomogeneities

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(Received 19 July 2006; revised 28 September 2006; accepted for publication 18 October 2006; published 17 November 2006)

Monte Carlo simulation dosimetry is used to compare ^{169}Yb to ^{192}Ir for breast high dose rate (HDR) brachytherapy applications using multiple catheter implants. Results for bare point sources show that while ^{169}Yb delivers a greater dose rate per unit air kerma strength at the radial distance range of interest to brachytherapy in homogeneous water phantoms, it suffers a greater dose rate deficit in missing scatter conditions relative to ^{192}Ir. As a result of these two opposing factors, in the scatter conditions defined by the presence of the lung and the finite patient dimensions in breast brachytherapy the dose distributions calculated in a patient equivalent mathematical phantom by Monte Carlo simulations for the same implant of either ^{169}Yb or ^{192}Ir commercially available sources are found comparable. Dose volume histogram results support that ^{169}Yb could be at least as effective as ^{192}Ir delivering the same dose to the lung and slightly reduced dose to the breast skin. The current treatment planning systems' approach of employing dosimetry data precalculated in a homogeneous water phantom of given shape and dimensions, however, is shown to notably overestimate the delivered dose distribution for ^{169}Yb. Especially at the skin and the lung, the treatment planning system dose overestimation is on the order of 15%–30%. These findings do not undermine the potential of ^{169}Yb HDR sources for breast brachytherapy relative to the most commonly used ^{192}Ir HDR sources. They imply, however, that there could be a need for the amendment of dose calculation algorithms employed in clinical treatment planning of particular brachytherapy applications, especially for intermediate photon energy sources such as ^{169}Yb. © *2006 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2392408]

Key words: brachytherapy, breast, ^{169}Yb, ^{192}Ir, Monte Carlo simulation

On the use of high dose rate ^{192}Ir and ^{169}Yb sources with the MammoSite® radiation therapy system

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Medical Physics Department, Medical School, University of Athens, 75 Mikras Asias, 11527, Athens, Greece

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G. Lymperopoulou, E. Pantelis, and L. Sakelliou
Particle Physics Section, Physics Department, University of Athens, Panepistimioupolis, Ilisia, 157 71 Athens, Greece

(Received 19 March 2007; revised 27 June 2007; accepted for publication 27 June 2007; published 23 August 2007)

Ample literature exists on the dose overestimation by commercially available treatment planning systems in MammoSite® applications using high dose rate ^{192}Ir sources for partial breast brachytherapy as monotherapy, due to their inability to predict the dose reduction caused by the radiographic contrast solution in the balloon catheter. In this work Monte Carlo simulation is used to verify the dose rate reduction in a balloon breast applicator which does not vary significantly with distance and it is 1.2% at the prescription distance for the reference simulated geometry of 10% diluted radiographic contrast media and 2.5 cm balloon radius. Based on these findings and the minimal hardening of the initially emitted photon spectrum for ^{192}Ir, a simple analytical method is proposed and shown capable for correcting dosimetry planning in clinical applications. Simulations are also performed to assess the corresponding dose reduction in applications of balloon breast applicators using high dose rate ^{169}Yb sources that have recently become available. Results yield a far more significant and distance dependent dose reduction for ^{169}Yb (on the order of 20% at the prescription distance for the abovementioned reference simulation geometry). This dose reduction cannot be accounted for using simple analytical methods as for ^{192}Ir due to the significant hardening of the initially emitted ^{169}Yb photons within the diluted radiographic contrast media. Combined with results of previous works regarding the effect of altered scatter conditions (relative to treatment planning system assumptions) on breast treatment planning accuracy, which is more pronounced for ^{169}Yb relative to ^{192}Ir, these findings call for the amendment of dose treatment planning systems before using ^{169}Yb high dose rate sources in balloon breast applicators. © *2007 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2760306]

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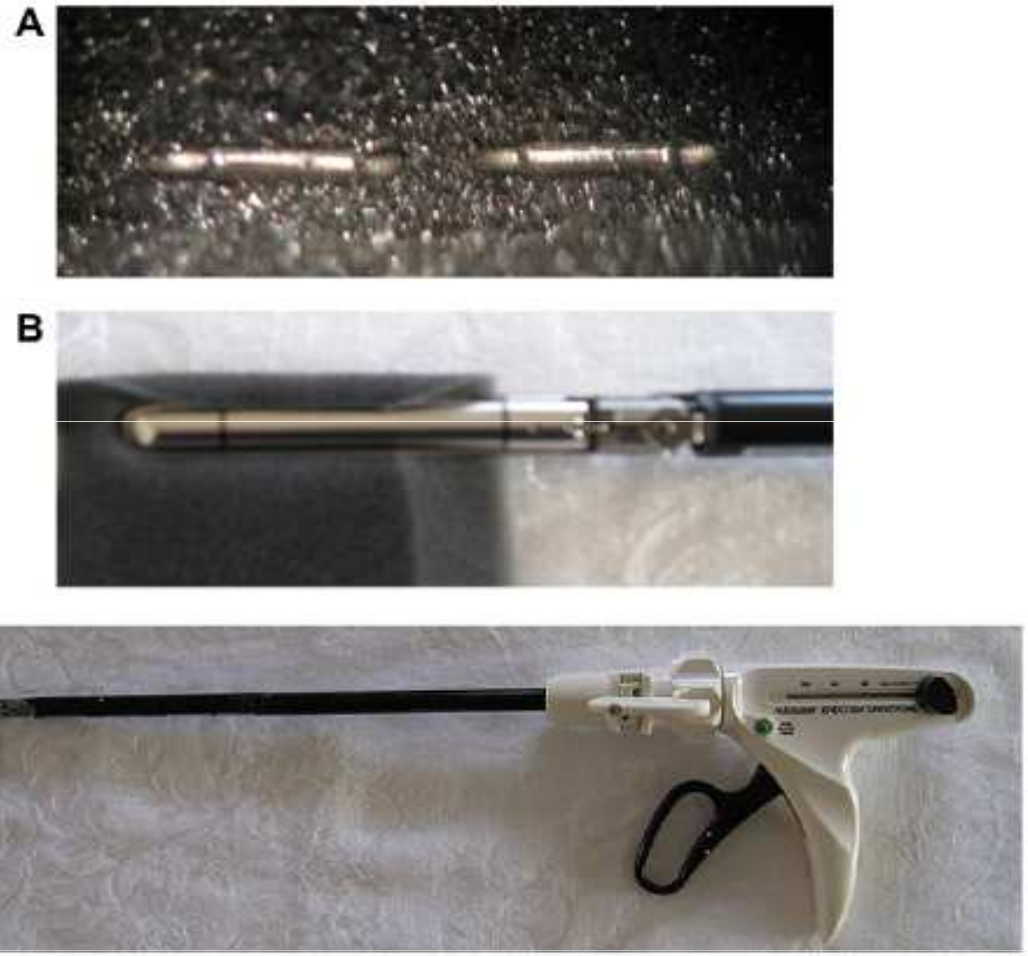

Fig. 6. Magnified view of source/staples placed in a tissue phantom (A) using commercially available surgical stapler widely used for video-assisted thoracoscopic surgery (B and C).

ELSEVIER Brachytherapy 10 (2011) 163–169

A novel ytterbium-169 brachytherapy source and delivery system for use in conjunction with minimally invasive wedge resection of early-stage lung cancer

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[1]Department of Radiation Oncology, Tufts Medical Center, Tufts University School of Medicine, Boston, MA
[2]Department of Radiation Oncology, Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI
[3]Source Production & Equipment Co., Inc (SPEC), St Rose, LA

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New Developments in Sources in Brachytherapy (Afterloading Technology):

Table 2. Characteristics of the ^{57}Co, ^{101}Rh and ^{192}Ir sources

	^{57}Co	^{101}Rh	^{192}Ir
Specific activity (TBq/g)	312	397	341
Half-life	272 days	3.3 years	74 days
Photon energy (keV)	122, 136	121.5 (average)	360 (average)
Yield (photons/disintegration)	1.61	2.37	2.36
Air kerma strength per activity (U/mCi)	0.46	1.09 ± 0.01	3.62
Dose rate constant (cGy/(hU))	1.215	1.18 ± 0.08	1.114
Half-value layer in lead (mm)	0.298	0.0331	2.97

Pakravan, Ghorbani, Meigooni, *Journal Contemp Brachytherapy* 7 (2), 171-180- (2015)

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Neues in der Physik der Brachytherapie: Radionuklide / Strahler

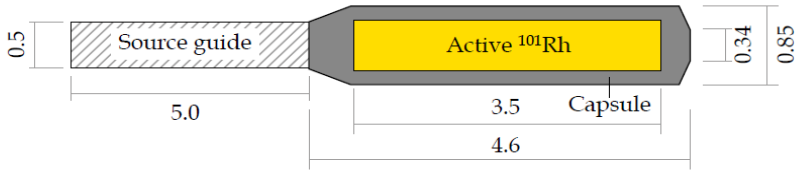

Fig. 1. Geometric design of the ^{101}Rh hypothetical source (all dimensions are in millimeters). This figure is not to

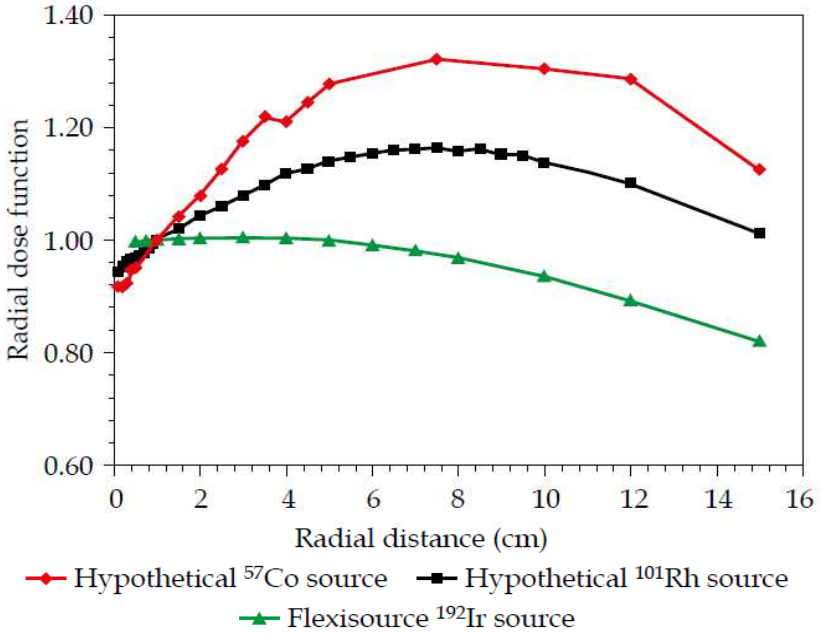

Fig. 2. A comparison of the radial dose function for the hypothetical ^{101}Rh source, hypothetical ^{57}Co source and Flexisource ^{192}Ir source

Conclusions

Advantages of ^{101}Rh to ^{192}Ir are having relatively longer half-life (3.3 years versus 74 days), higher specific activity (397 TBq/g versus 341 TBq/g)k, and very low half-value layer (0.0331 mm in lead versus 2.97 mm of lead). These adequate physical characteristics make this radionuclide interesting as a possible brachytherapy source. Air kerma strength per activity for hypothetical ^{101}Rh source is about twice than that of hypothetical ^{57}Co source and it has a dose rate constant comparable to hypothetical ^{57}Co and ^{192}Ir sources. Radial dose function for the ^{101}Rh hypothetical source is greater than that of ^{192}Ir source for distances greater than 1.0 cm. The 2D anisotropy function of ^{101}Rh is very similar to that of ^{192}Ir, which can be taken into account as another advantage of this new proposed source. With these suitable physical properties, ^{101}Rh could be considered as potential candidate in brachytherapy.

Pakravan, Ghorbani, Meigooni, *Journal Contemp Brachytherapy* 7 (2), 171-180- (2015)

ESTRO School

New Developments in Sources in Brachytherapy (Afterloading Technology):

Miniaturised X-Ray-Sources (Electronic Brachytherapy, eBX)

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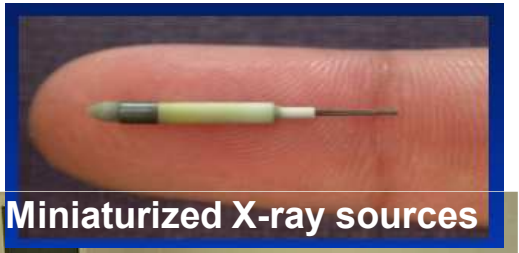
Afterloaders: electronic Brachytherapy (eBx)

Intrabeam

Carl Zeiss Meditec. Inc.



Miniaturized X-ray sources

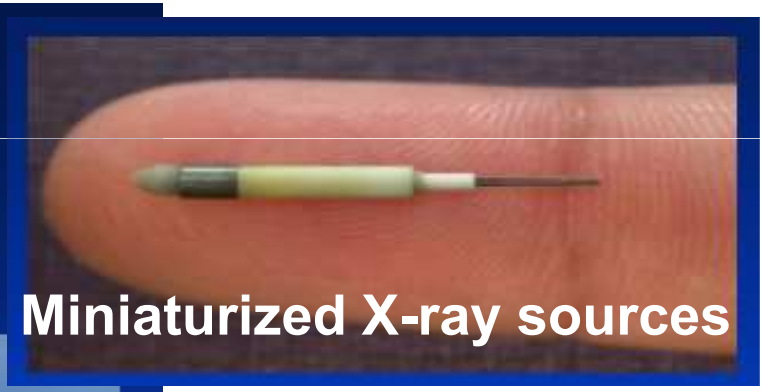
Xoft Inc.

ESTRO School

Miniaturised X-Ray-Source

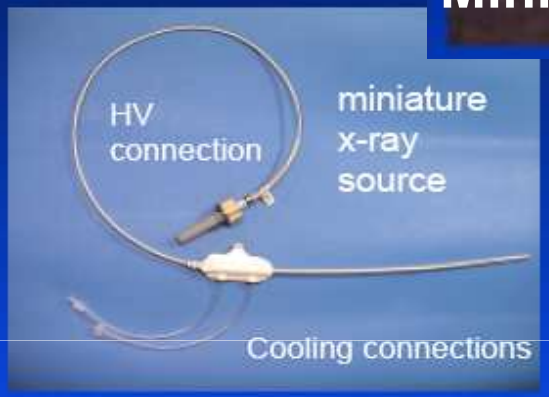
Electronic Brachytherapy (eBx)

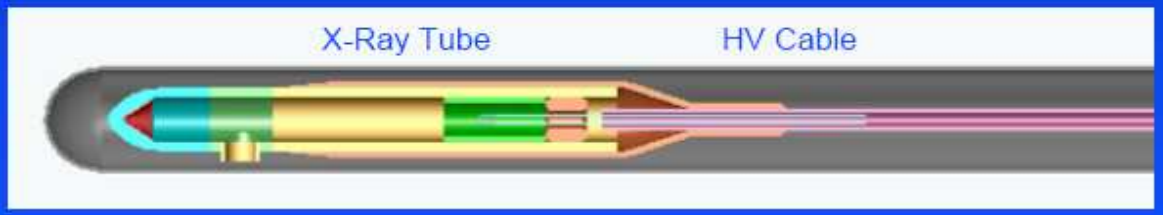
Xoft Inc.



Miniature x-ray source inserted into a flexible cooling catheter

- High vacuum x-ray tube technology
- 50 kV max. operating potential
- Water cooled
- Fully disposable device





X-ray source tip detail

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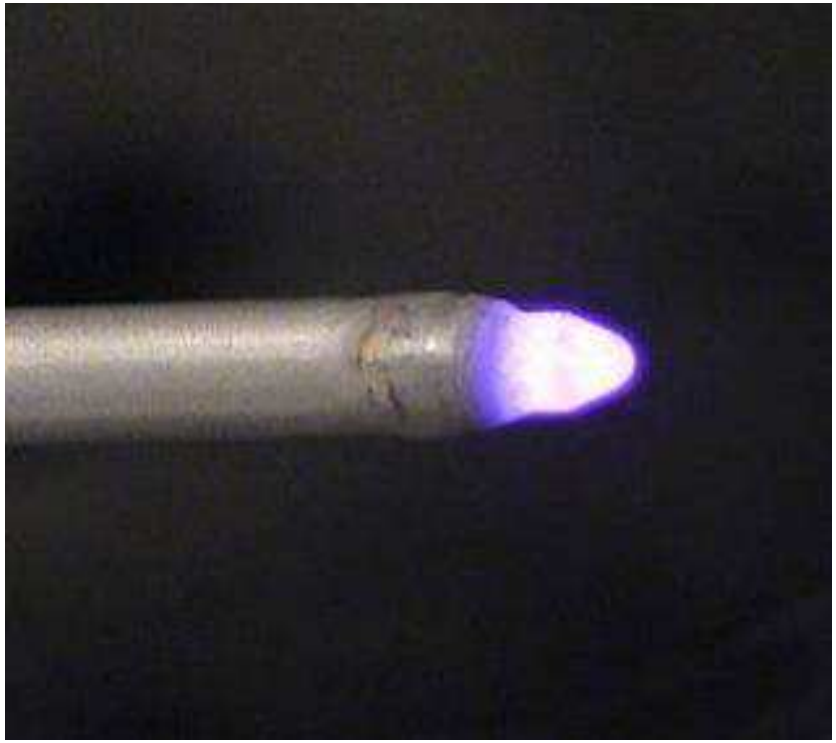
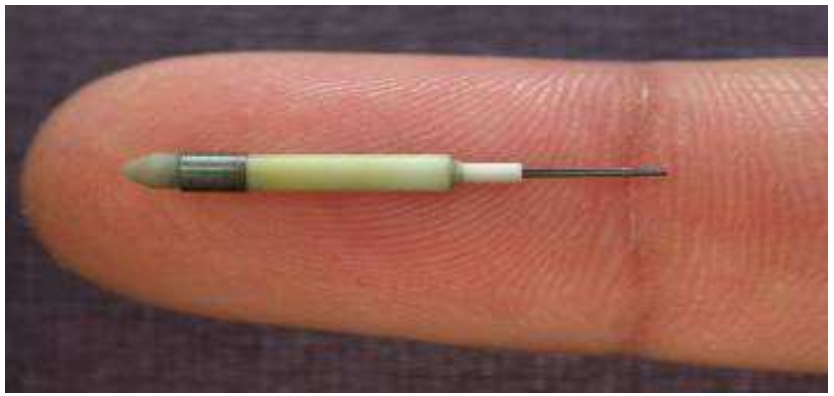
Miniaturised X-Ray-Source

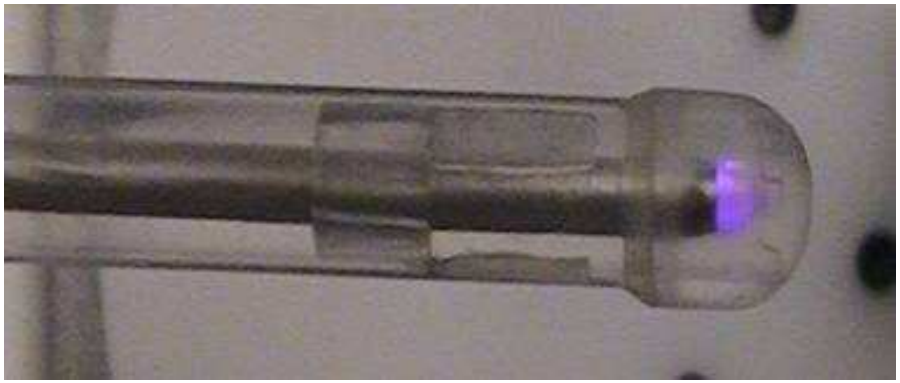
Electronic Brachytherapy (eBx)



Light emission from e^- and x-ray interactions with anode



X-ray tube size



X-ray source in cooling catheter

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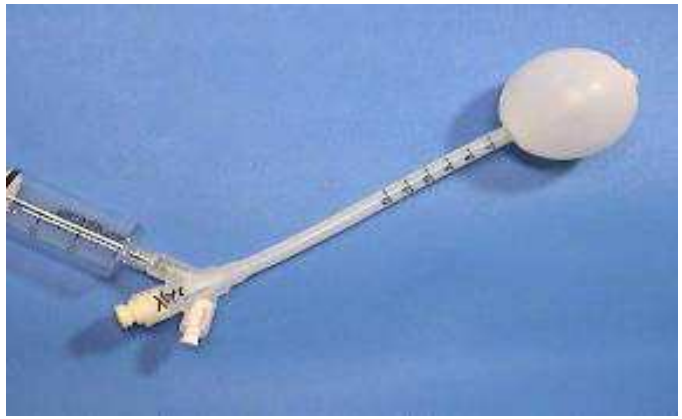
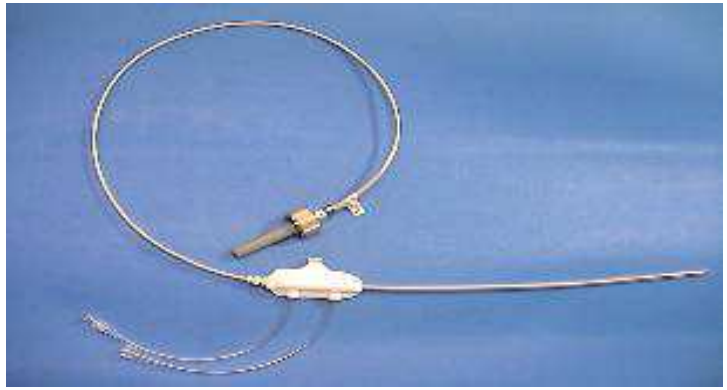
Miniaturised X-Ray-Source

Electronic Brachytherapy (eBx)





Xoft Inc.

APBI System Components

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Miniaturised X-Ray-Source

Electronic Brachytherapy (eBx)

Similarities of Modern Teletherapy and Electronic Brachytherapy

Feature	Teletherapy		Brachytherapy	
	^{60}Co	Linacs	Radionuclides	Axxent
Dose conformity	O	●	◗	●
IORT capable	◗	◗	◗	●
No radionuclide handling/waste	O	●	O	●
Can turn on and off easily	O	●	O	●
Has selectable energies	O	●	O	●
Easily adjustable dose rates	O	●	O	●

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POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Miniature x-ray tubes will ultimately displace Ir-192 as the radiation sources of choice for high dose rate brachytherapy

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Colin G. Orton, Ph.D., Moderator

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OVERVIEW

Recent advances in the development of miniature x-ray tubes have made electronic brachytherapy a feasible alternative to conventional high dose rate brachytherapy with high activity Ir-192 sources. Because of the obvious radiation safety and security advantages, it is conceivable that the miniature x-ray tube might displace Ir-192 as the source of choice for HDR brachytherapy. This is the proposition debated in this month's Point/Counterpoint.

Arguing for the Proposition is Randall W. Holt, Ph.D. Dr. Holt earned his Ph.D. in Biomedical Engineering at Case Western Reserve University, specializing in 3D-image analysis, after which he received postdoctoral training at the USC Department of Radiation Oncology, specializing in virtual simulation and 3D dosimetry software. Currently Dr. Holt is the Director of Physics for North Valley Radiation Oncology, which provides a broad range of medical physics services to clinics in Northern California. He is board certified by the ABR in radiation therapy physics.

Arguing against the Proposition is Bruce R. Thomadsen, Ph.D. Dr. Thomadsen earned his M.S. and Ph.D. degrees in Medical Physics at the University of Wisconsin—Madison, where he is currently an Associate Professor in the Department of Medical Physics. He is board certified by the ABR in Radiological Physics, by the ABHP in Comprehensive Health Physics, and by the ABMP in Radiation Oncology Physics. His major research interests include all aspects of radiation therapy physics but especially brachytherapy. Dr. Thomadsen currently serves on numerous AAPM committees and task groups and chairs the Radiation Safety Subcommittee and the Special Brachytherapy Modalities Working Group, and is a member of the Board of Editors of *Medical Physics*.

FOR THE PROPOSITION: Randall W. Holt, Ph.D

Opening statement

To displace Ir-192, miniature x-ray sources must deliver therapeutic radiation as well as, or potentially better than, Ir-192, under safer conditions, and with favorable economics.

Current electronic brachytherapy (eBx) source technology provides dose rates comparable to 7-Ci Ir-192 sources, with similar cylindrically symmetric dose distributions, using miniature x-ray tubes small enough to be inserted into the human body via catheter guides.[1] Energy is the distinguishing characteristic, with eBx sources ranging from 20 to 50

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A recent point / counterpoint discussion in Medical Physics

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Further reading

A Century of X-Rays and Radioactivity in Medicine. 2003. R.F. Mould. CRC Press.

Achieving Quality in Brachytherapy. 2000. B.R. Thomadsen. Institute of Physics Publishing. Medical Science Series. Bristol and Philadelphia.

A Practical Guide to QC of Brachytherapy Equipment. 2004. J. Venselaar, J. Perez-Calatayud (eds). ESTRO Booklet 8. ESTRO, Brussels.

Comprehensive Brachytherapy; Physical and Clinical Aspects. 2013. J. Venselaar et al (eds). CRC Press, Taylor&Francis Group. Boca Raton (FL): Chapt 2 Standard Technology in Brachytherapy 9-28. Chapt 3 Radionuclides in Brachytherapy: Current and Potential New Sources 29-42. Chapt 26 Special Brachytherapy Modalities 397-408. Chapt 27 Advanced Brachytherapy Technologies: Encapsulation, Ultrasound, and Robotics 409-26.

The Physics of Modern Brachytherapy for Oncology. 2007. D. Baltas, S. Sakelliou, N. Zamboglou. CRC Press, Taylor&Francis Group, New York.

Radiation Transmission Data for Radionuclides and Materials Relevant to Brachytherapy Facility Shielding. 2008. P. Papagiannis et al. Med Phys 35(11): 4898-906.

Comparison of ^{60}Cobalt and ^{192}Iridium Sources in High Dose Rate Afterloading Brachytherapy. 2008. J. Richter et al. Strahlentherapie No 4.

Brachytherapy with Miniature Electronic X-ray Sources. 2005. M.J. Rivard, L.A. DeWerd, H.D. Zinkin. Chapter 51 in: Brachytherapy Physics, Second edition, Proceedings AAPM/ABS Summer school. Medical Physics Monograph No 3: 889-900.

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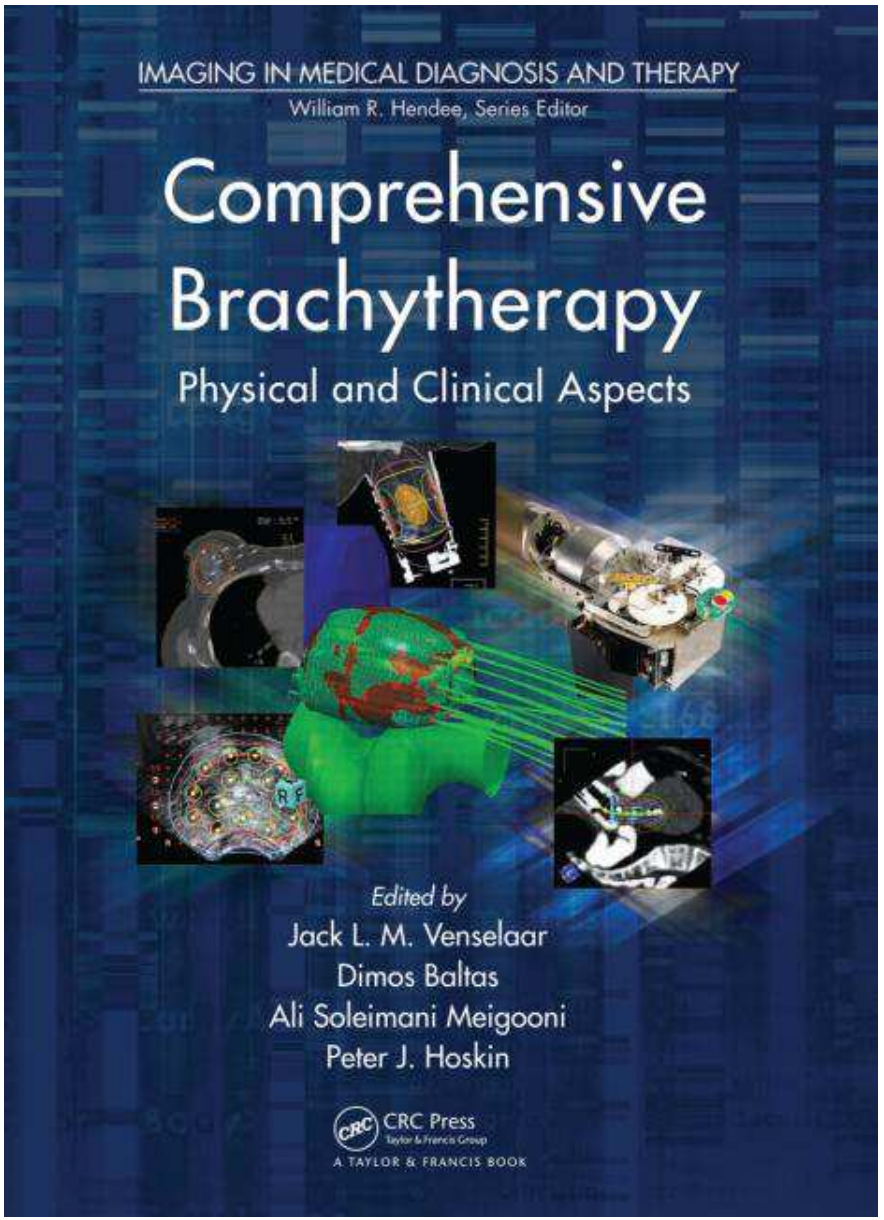
Further reading



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Radiobiology of LDR – HDR Brachytherapy

Erik Van Limbergen, MD, PhD

GEC-ESTRO Teaching Course

Firenze 2016

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Time Scale of Effects of ionising radiation

- Physical phase — 10^{-18} - 10^{-12} sec
  - excitation
  - ionisation
- Chemical phase — 10^{-12} - 10^{-6} sec
- Biological phase
  - enzyme reactions
  - repair processes — hours
  - cell repopulation — days - weeks

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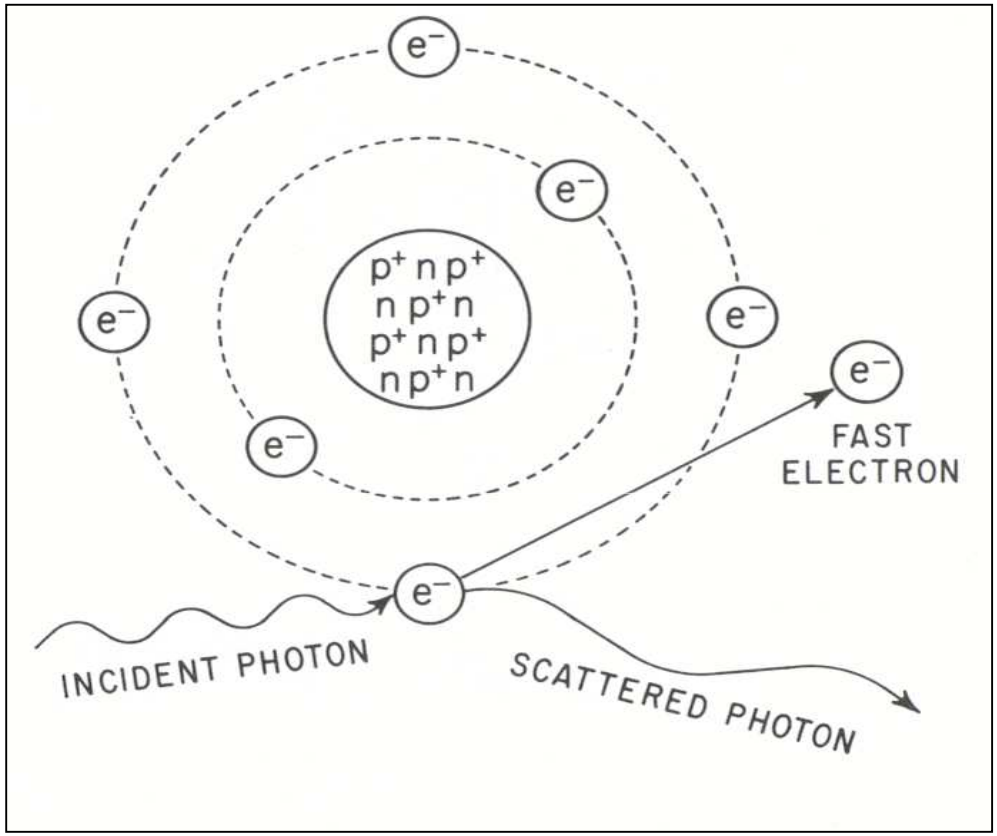
DNA Damage by ionising irradiation

Physical phase

excitation

ionisation

- Photoelectric absorbtion
- Compton effect
- Pair formation



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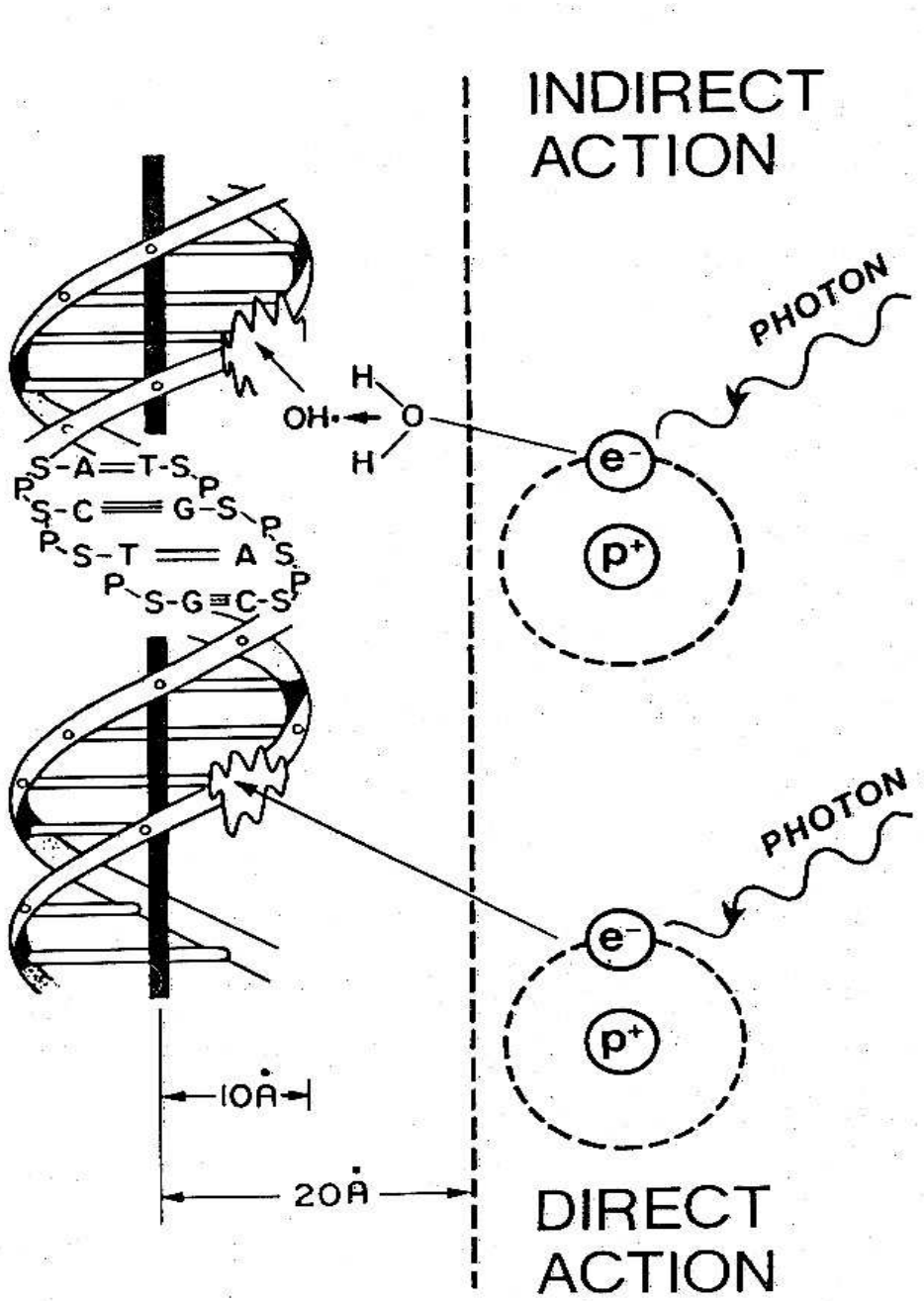
DNA Damage by ionising irradiation

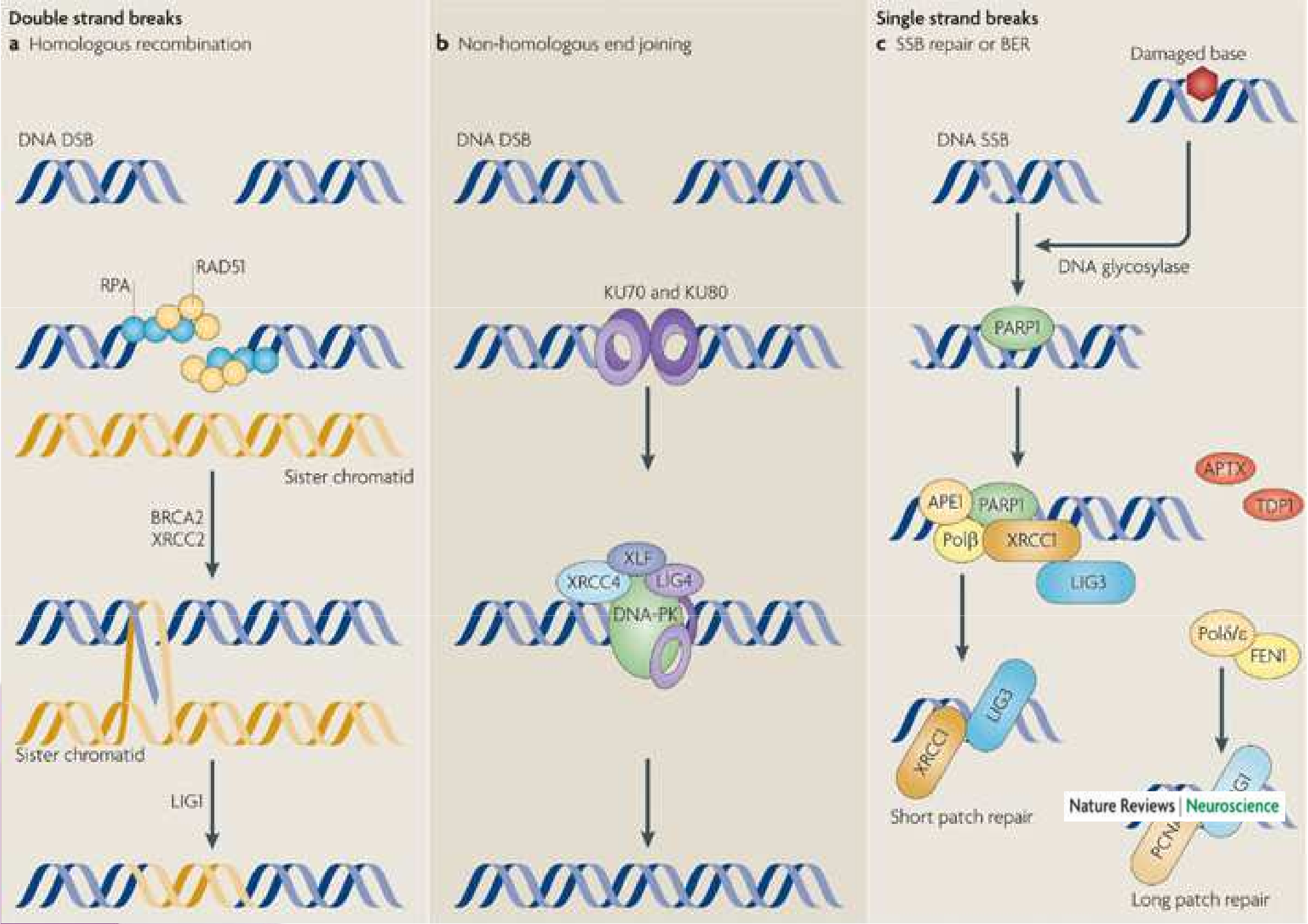
Chemical phase

direct and indirect action

free radicals

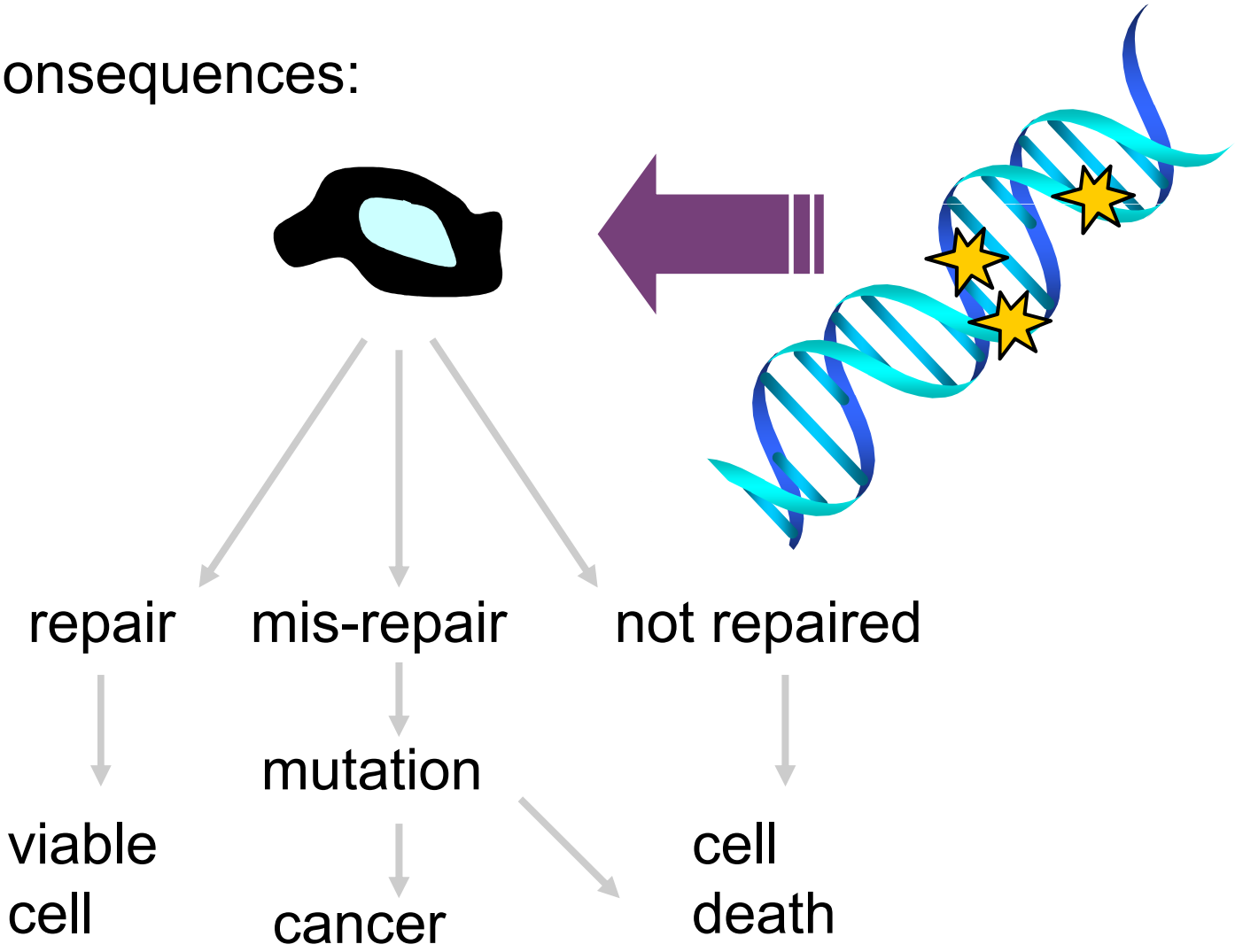
damage fixation




Double strand breaks
a Homologous recombination
DNA DSB
RPA
RAD51
Sister chromatid
BRCA2
XRCC2
Sister chromatid
LIG1
b Non-homologous end joining
DNA DSB
KU70 and KU80
XLF
XRCC4
LIG4
DNA-PK
Single strand breaks
c SSB repair or BER
Damaged base
DNA SSB
DNA glycosylase
PARP1
APTX
TDP1
APE1
PARP1
Polβ
XRCC1
LIG3
XRCC1
LIG3
Short patch repair
Polδ/ε
FEN1
PCNA
Long patch repair
Nature Reviews | Neuroscience

Radiation damage to a cell

Consequences:



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Clonogenic Cell kill by radiation

- Mitotic catastrophy
  - Direct or delayed
- Intermitotic cell death
  - Apoptosis
  - Autophagy
  - Senescence
  - Necrosis

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4 R'S of Radiobiology

Redistribution in the cell cycle

Repair of sublethal damage

Reoxygenation

Repopulation

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Redistribution

- It might be the most important process below 1 Gy/min.
- It can lead to cell synchronisation in G2 and M stages (G2 block), and consequently to an increase in radiosensitivity,

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Reoxygenation

- is a relatively slow process, that could be a disadvantage in low dose rate irradiation.The total duration of the irradiation usually does not exceed a few days, that is not sufficient to allow the tumour to significantly shrink.

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Repopulation

- is the slowest process and is of significance only below 1 Gy/min
- Important in early reactions

  not occurring in late responding NT during the 6-7 weeks irradiation,
- little effect in tumours for TT < 3 - 4 weeks,

  past this period, accelerated repopulation of fast-growing tumours can be observed

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Dose M to compensate for repopulation

	Time				
Tpot	5 d	10 d	20 d	30 d	40 d
2 d	5 Gy	10 Gy	20 Gy	30 Gy	40 Gy
5 d	2 Gy	4 Gy	8 Gy	12 Gy	16 Gy
10 d	1 Gy	2 Gy	4 Gy	6 Gy	8 Gy

With M = 2 Gy.T/Tpot

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Effects of repopulation

- During one-week irradiation:

  0 Gy

- During 4-8 week irradiation:

  tumour: 15 Gy

  late effects: 0 Gy

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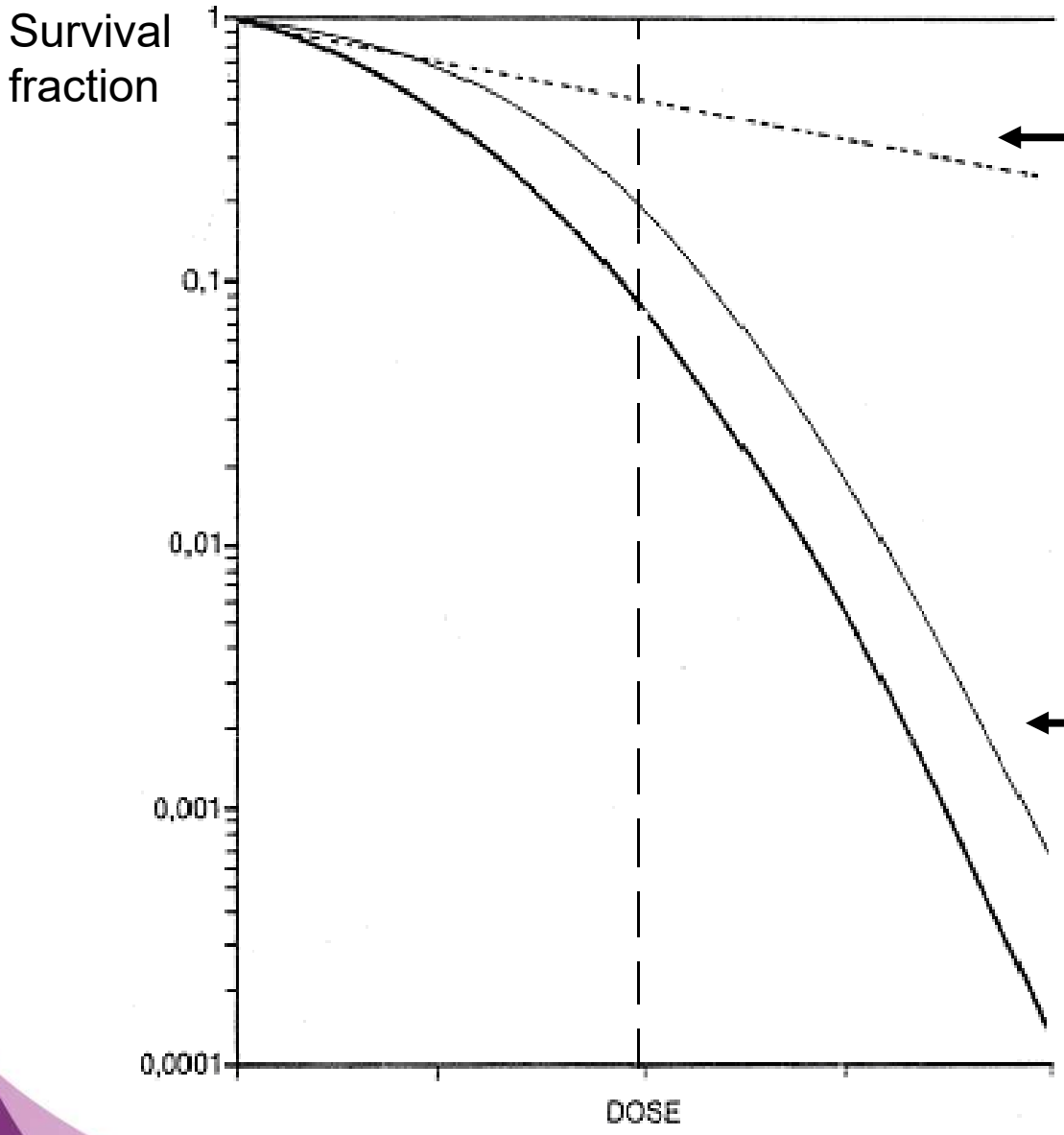
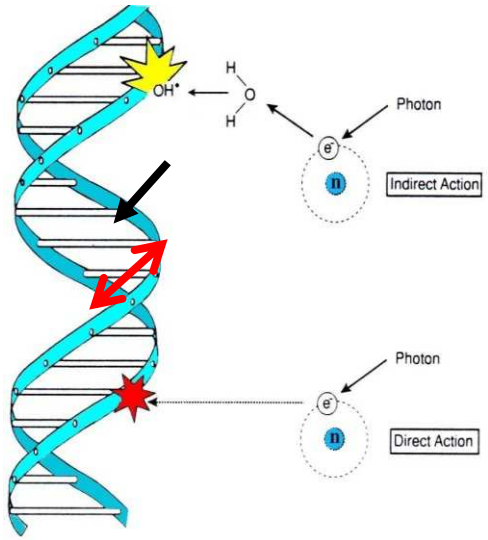
LQ Repair-Model



Linear component



Quadratic component

Linear quadratic

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Linear quadratic model

$E = \alpha D$ lethal non repairable linear term

$E = \beta D^2$ sublethal repairable quadratic term

Total Effect $E = \alpha D + \beta D^2$

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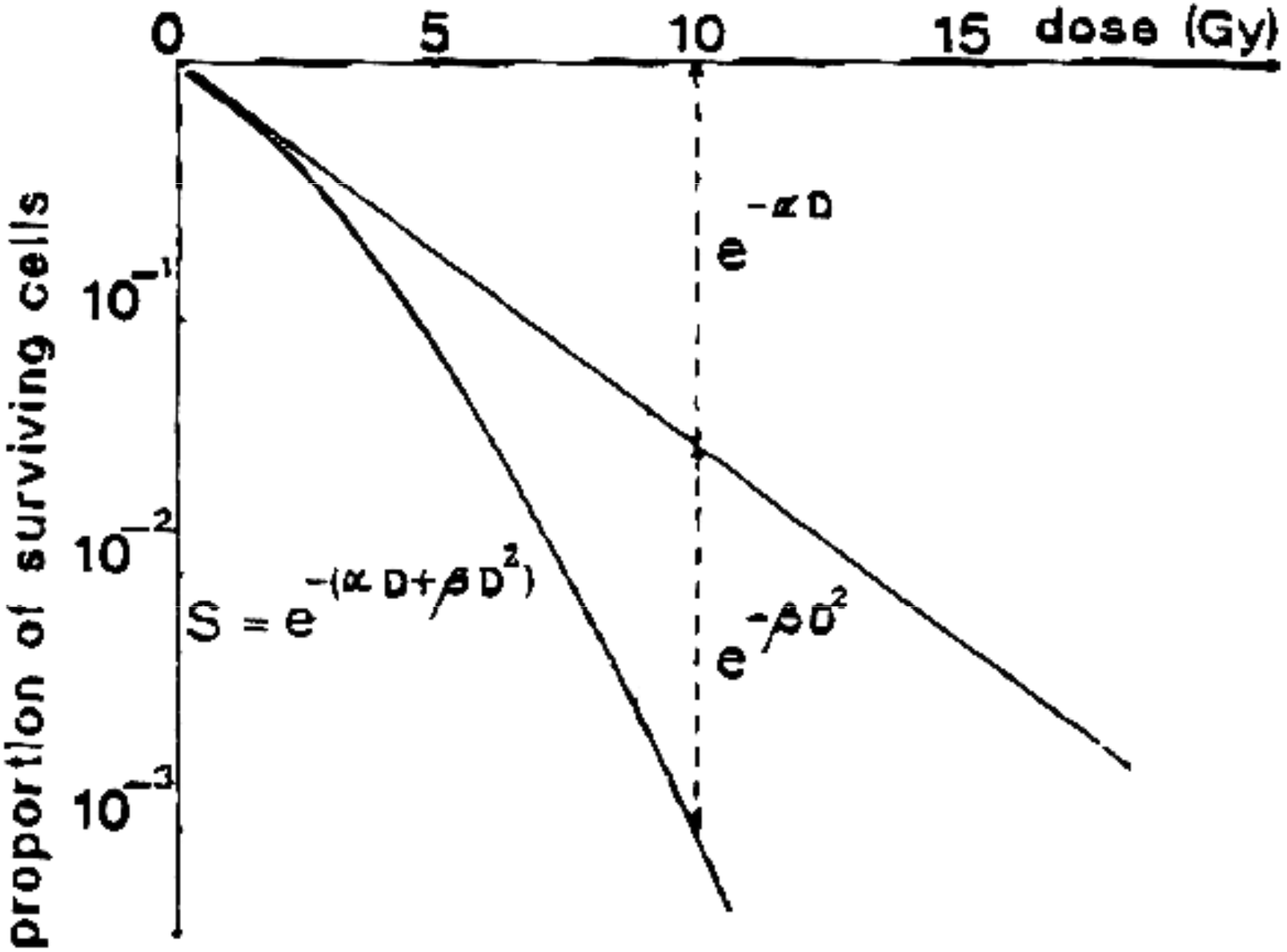
Repaircapacity : α/β ratio



Repair capacity

- The shoulder reflects the relative importance of repair capacity

- A large shoulder means a large repair capacity
- And thus a large sensibility to changes in dose per fraction

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BE of EBRT and BT

- The biological effects strongly depend on
  - Total dose
  - Fraction size
  - Dose Rate
  - Total Treatment Time
  - Treated Volume
  - Dose Distribution

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Radiobiological effects

Strongly different for BT

as compared to EBRT

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DOSE - VOLUME Differences BT- EBRT

EBRT

- Volume Treated usually quite large.
- Variation in Dose is kept minimal

  - homogeneous dose distribution

  - with < 5% lower doses

  and < 7% higher doses in TV

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DOSE- VOLUME Differences BT-EBRT

BT

- Treated Volume is rather small
- Dose prescribed to a MT isodose encompassing the PTV,
- Very inhomogeneous dose distribution within the TV

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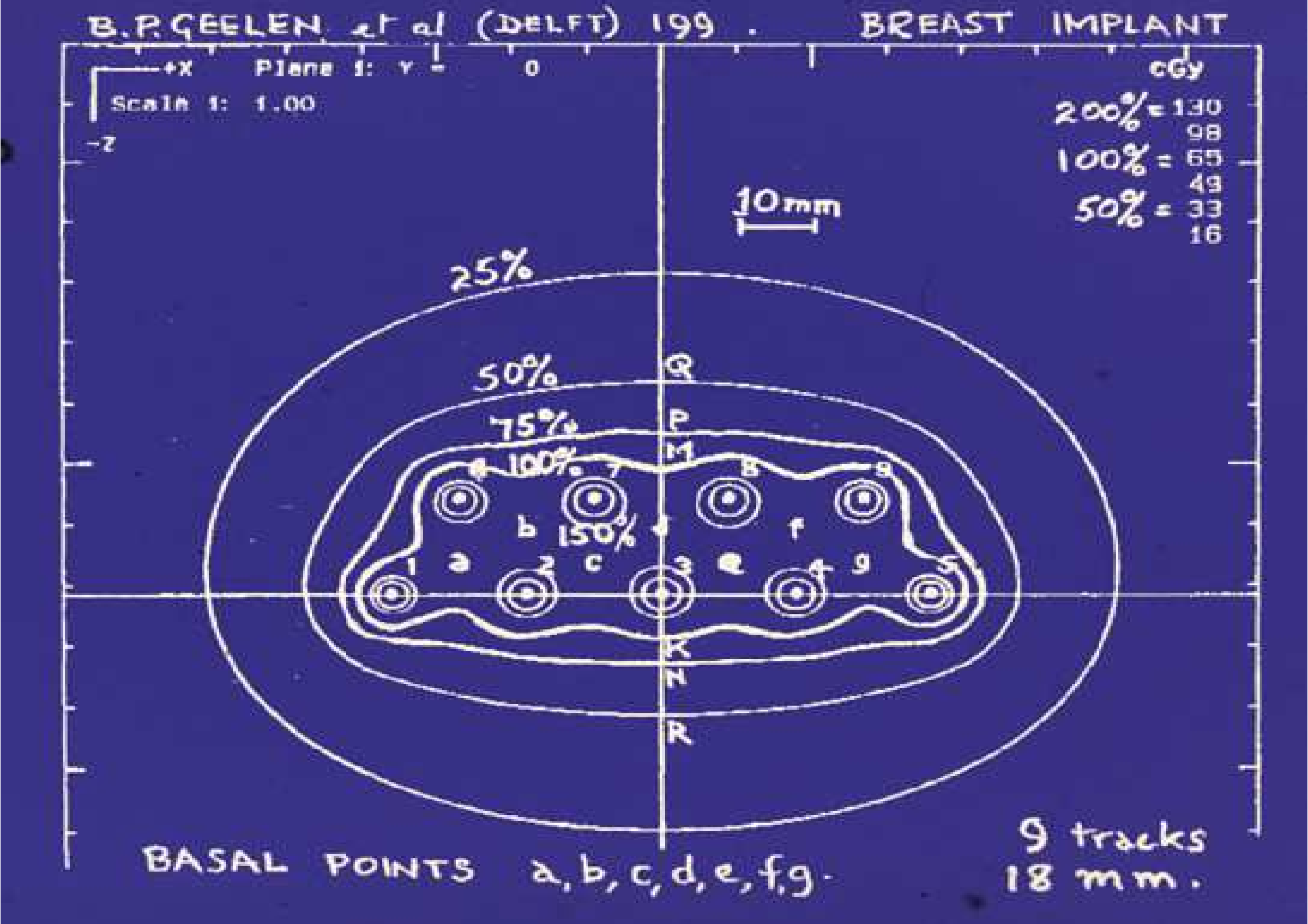
B.P.GEELEN et al (DELFT) 199 . BREAST IMPLANT
+X
Plane 1: Y = 0
Scale 1: 1.00
-Z
cGy
200% = 130
98
100% = 65
49
50% = 33
16
10mm
25%
50%
75%
100%
150%
Q
P
M
K
N
R
a
b
c
d
e
f
g
1
2
3
4
5
6
7
8
9
BASAL POINTS a, b, c, d, e, f, g.
9 tracks
18 mm.

DOSE-VOLUME Differences BT-EBRT

- The **integral** dose given by BT is much higher than the prescribed dose
- Never been tolerated by normal tissues in volume as large as treated with EBRT,

  because of the volume-effect relationship

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DOSE RATE and

OVERALL TREATMENT TIME

- EBRT, small HDR fractions over several weeks, with full repair between fractions,

- BT dose delivered at
  - continuous LDR
  - or PDR, with incomplete repair
  - or large HDR fractions

- over a short treatment time (a few days)

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Dose Rate Effects

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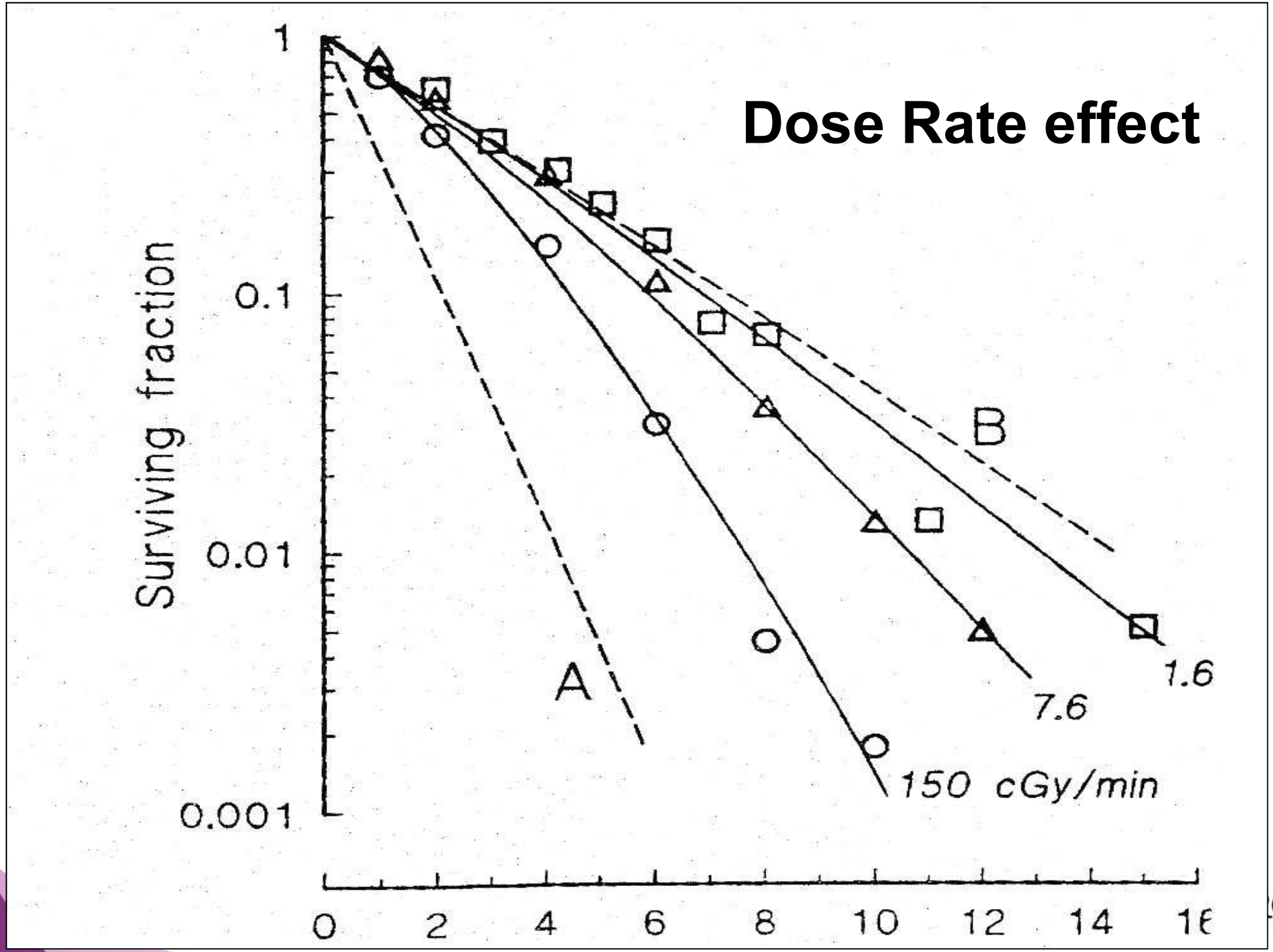
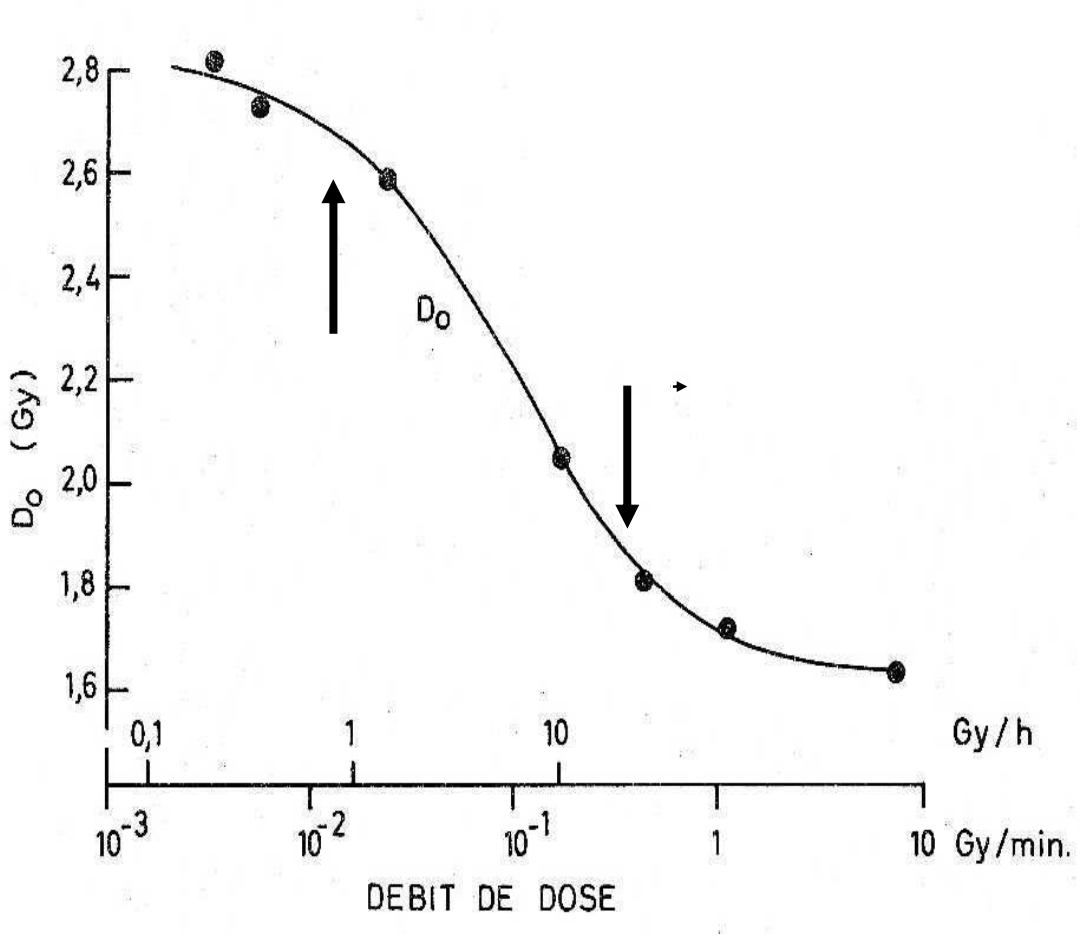
Dose Rate effect



Dose Rate Effect



ICRU – GEC ESTRO report 88

Dose Rate definitions

LDR 0.4 - 1 Gy/h

MDR 1 Gy - 12 Gy/h

HDR $\geq$ 12 Gy/h
($\geq$ 0.2 Gy/min)

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Changing Dose Rate in ICBT

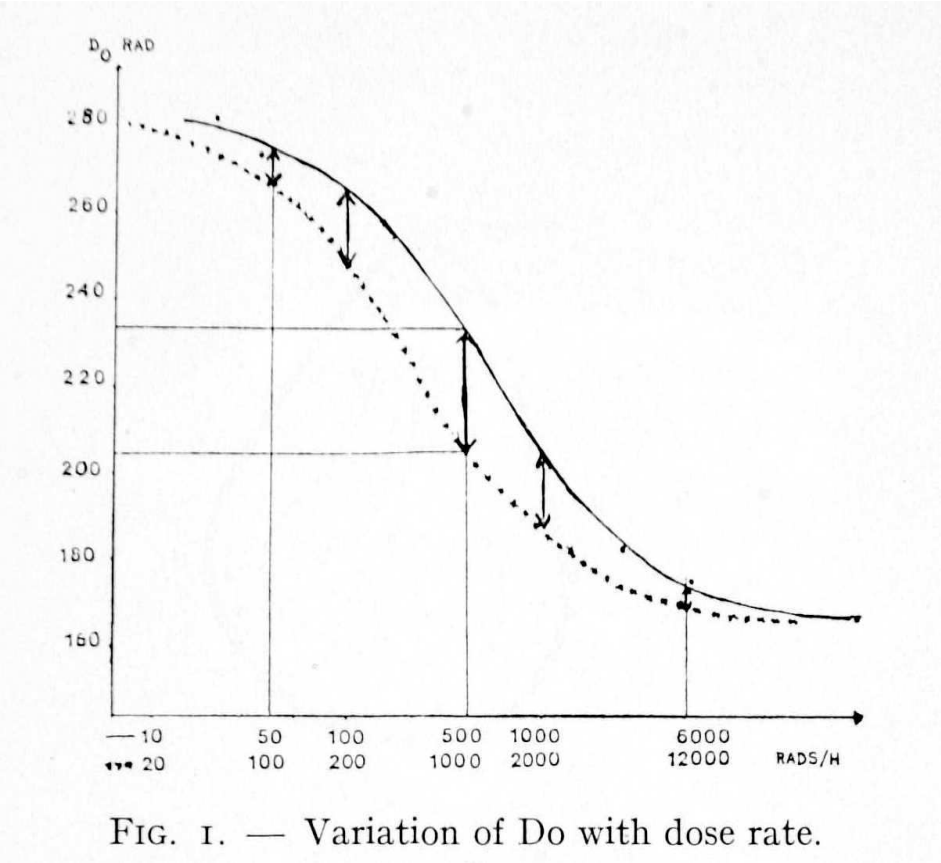
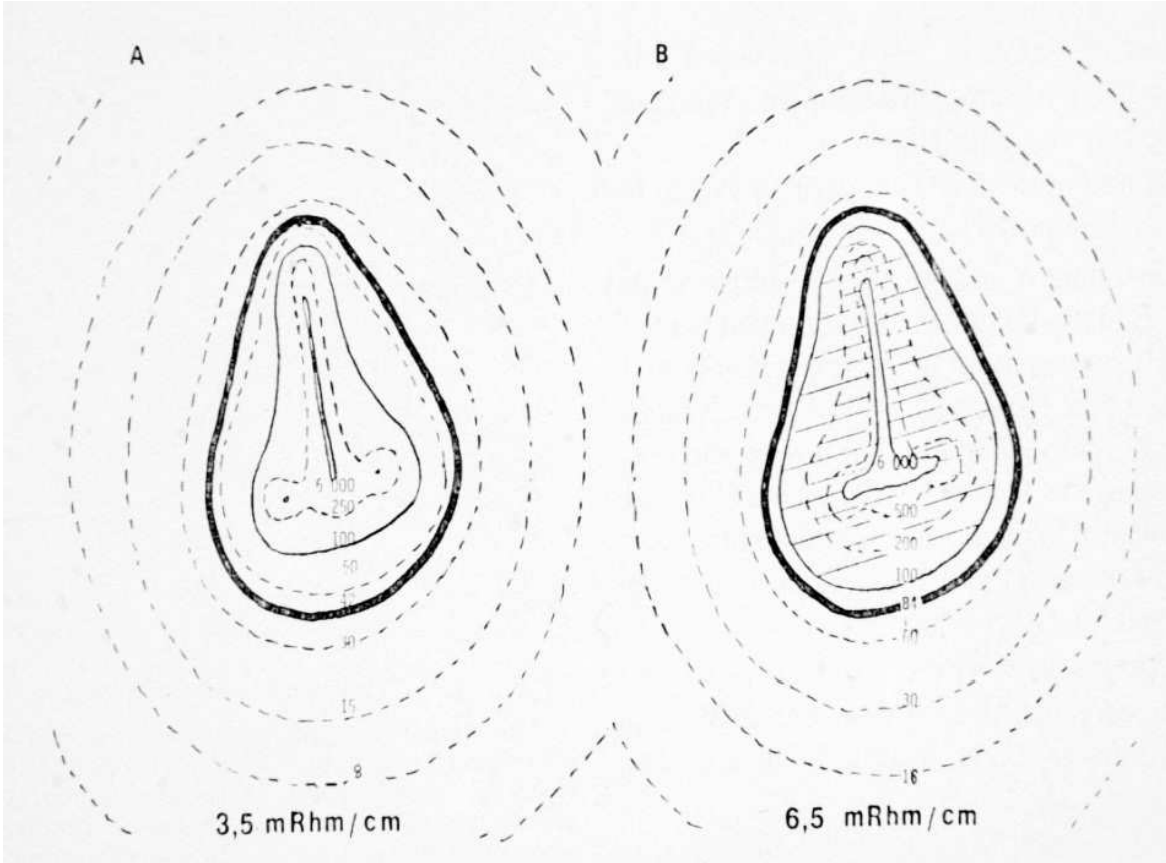


FIG. 1. — Variation of Do with dose rate.



Different spatial effect
of changing DR in ICBT

Van Limbergen et al 1985

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HDR

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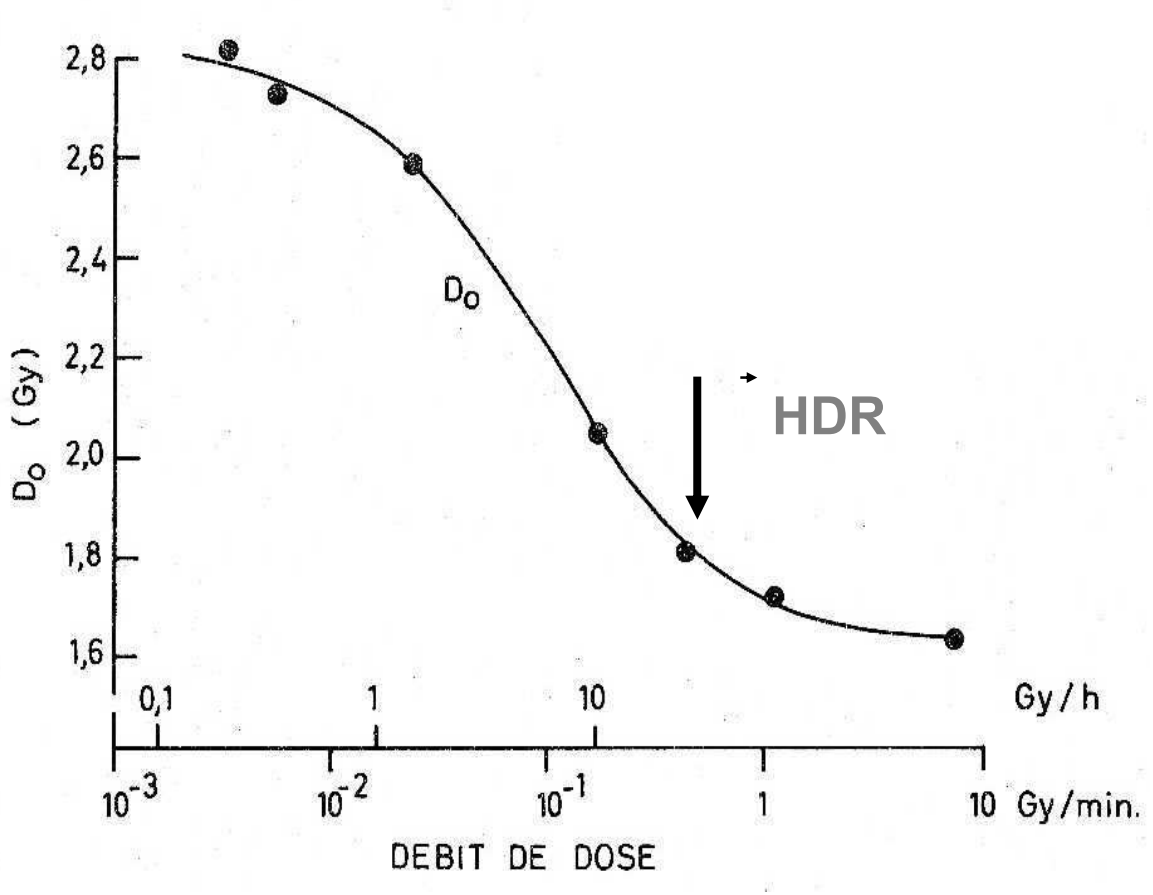
Dose Rate Effect

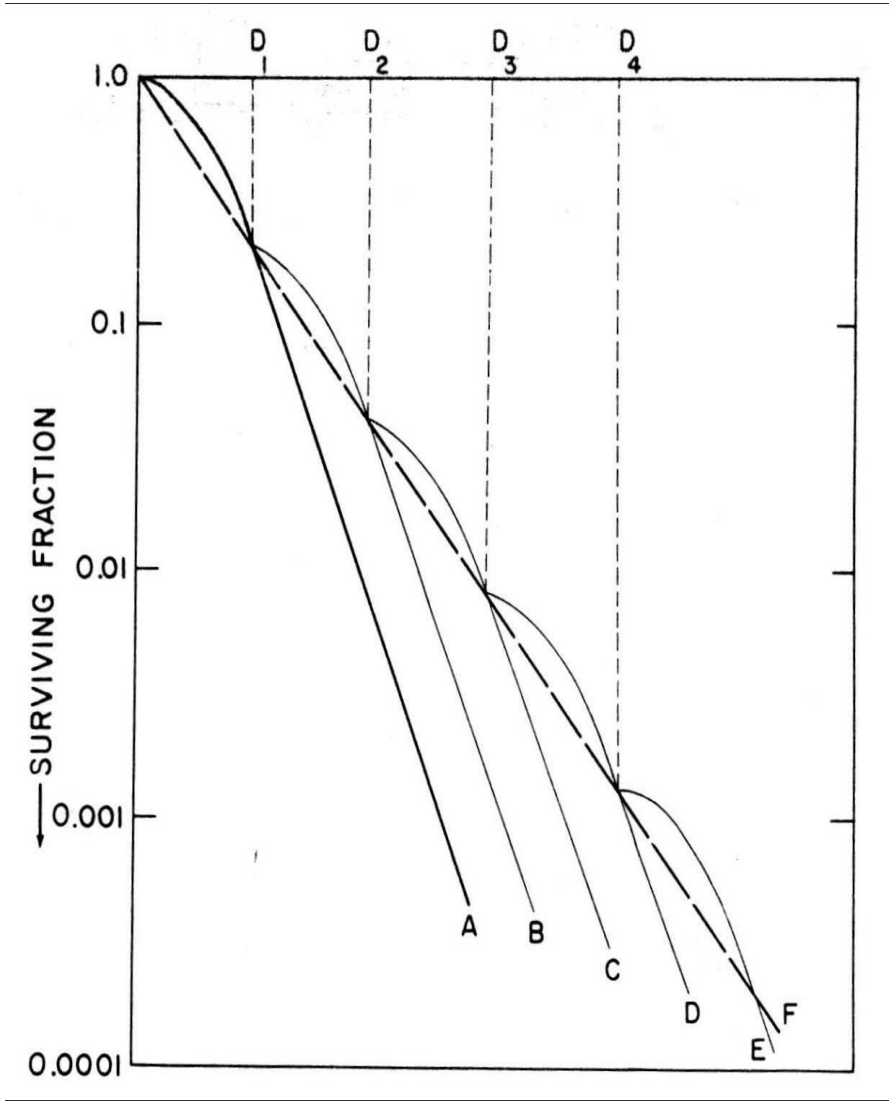


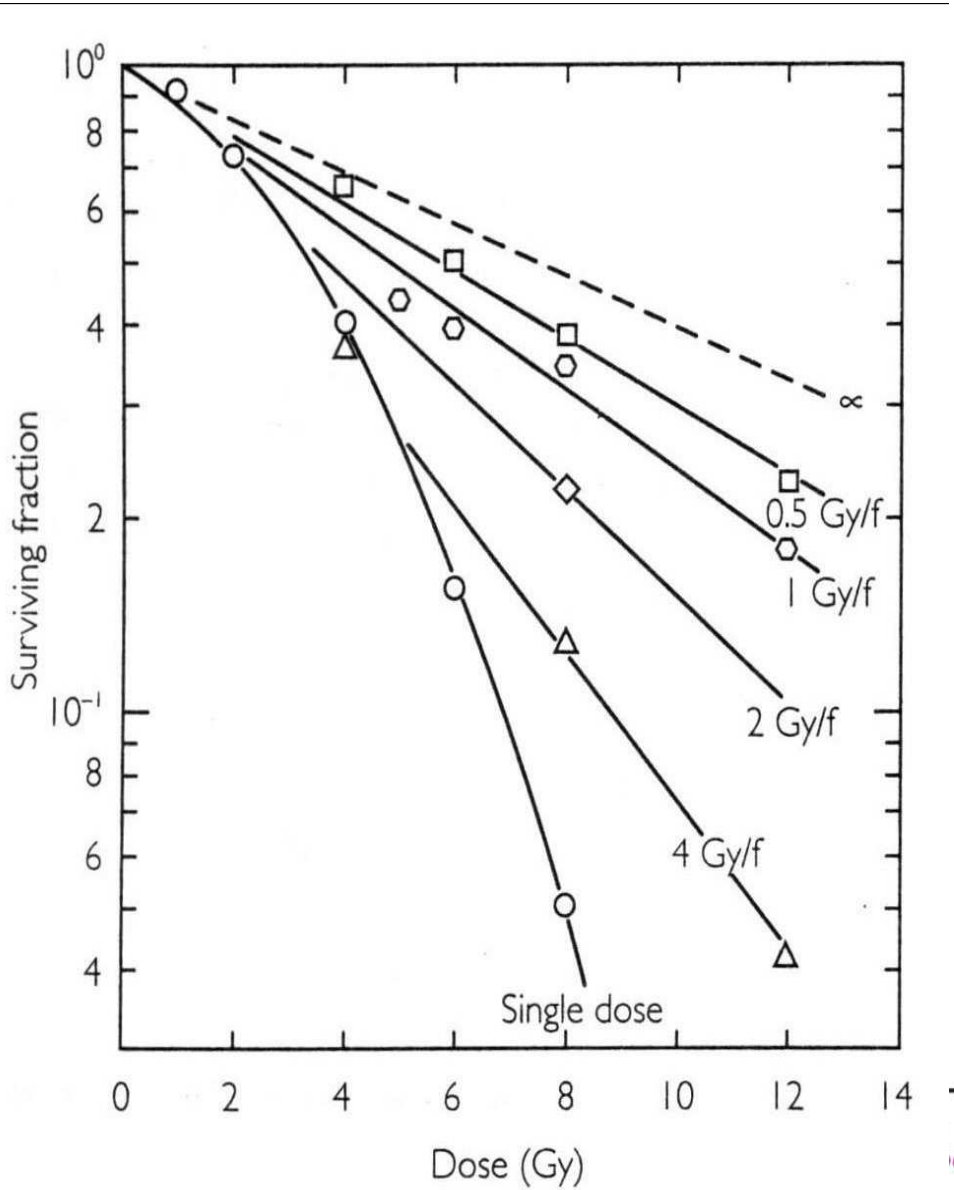
HDR

≥ 12 Gy/h

(≥ 0.2Gy/min)

High dose rate (HDR) brachytherapy





HDR BT cervixca

Importance of fraction size (to point A)

Complications:	< 7 Gy	> 7Gy
G 2 - 4	7.6%	11.2%
G 3 - 4	1.3%	3.4%

Orton, 1991

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LDR

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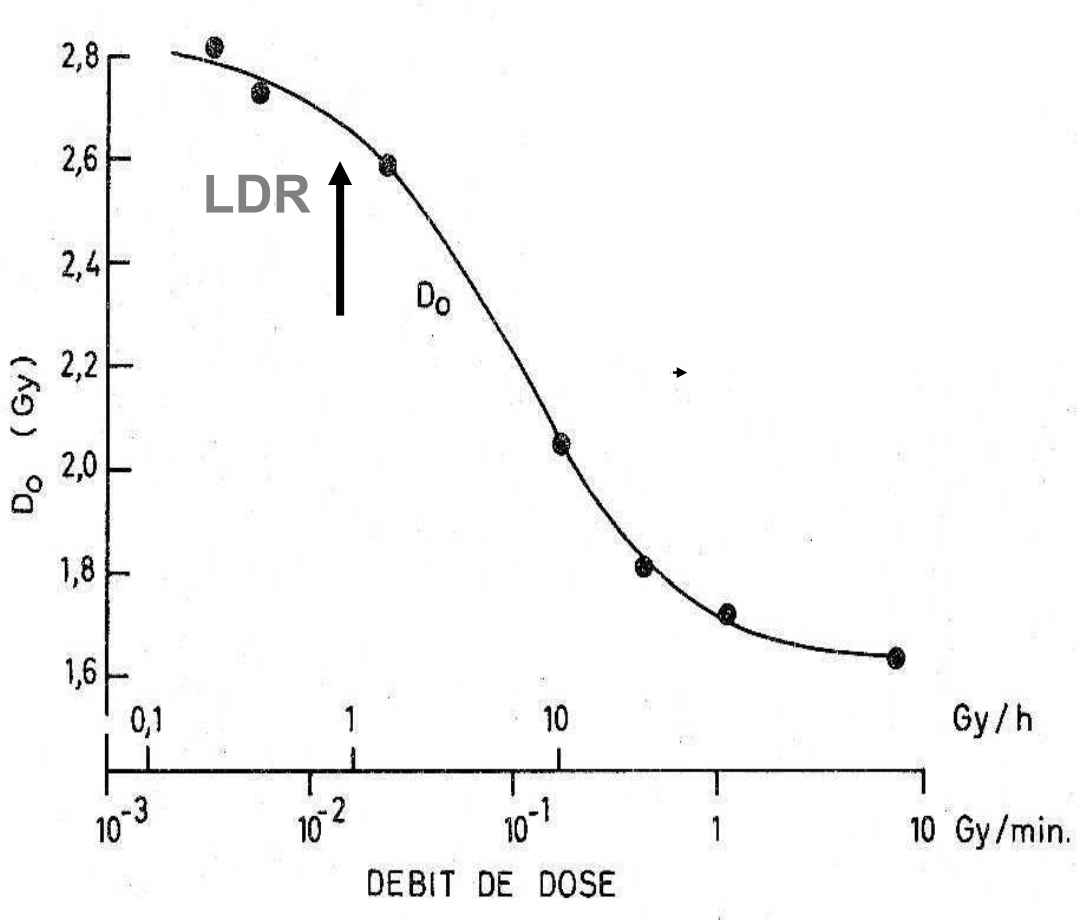
Dose Rate Effect



LDR

0.4 - 1 Gy/h

LDR brachytherapy

- SLD Repair is the fastest process, that takes place at < 1Gy/min
- is the most significant effect between 1 Gy/min, and 1Gy/h

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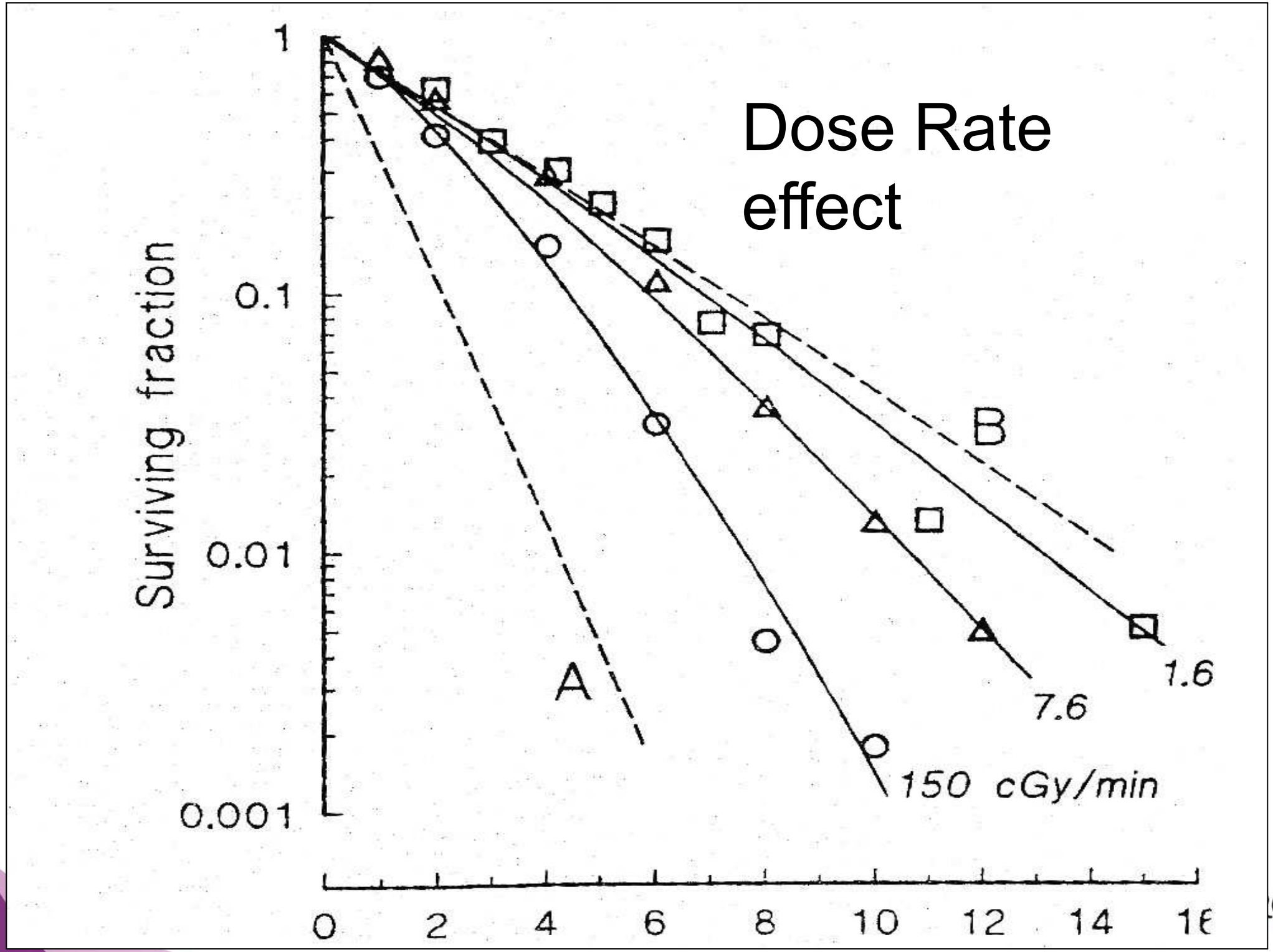
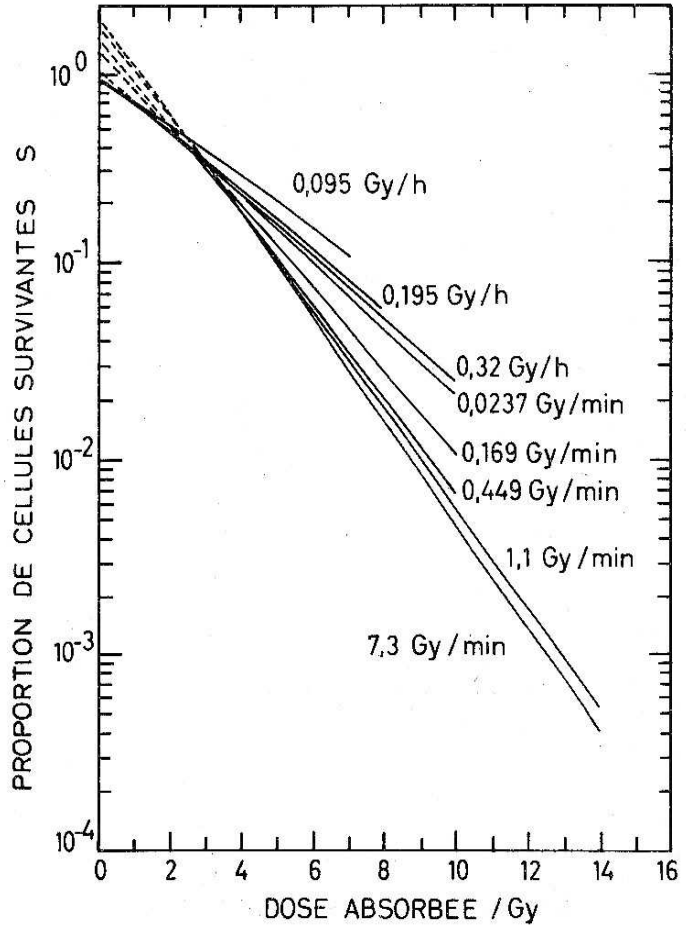

Dose Rate effect
Surviving fraction
1
0.1
0.01
0.001
0
2
4
6
8
10
12
14
A
B
1.6
7.6
150 cGy/min

Linear quadratic model

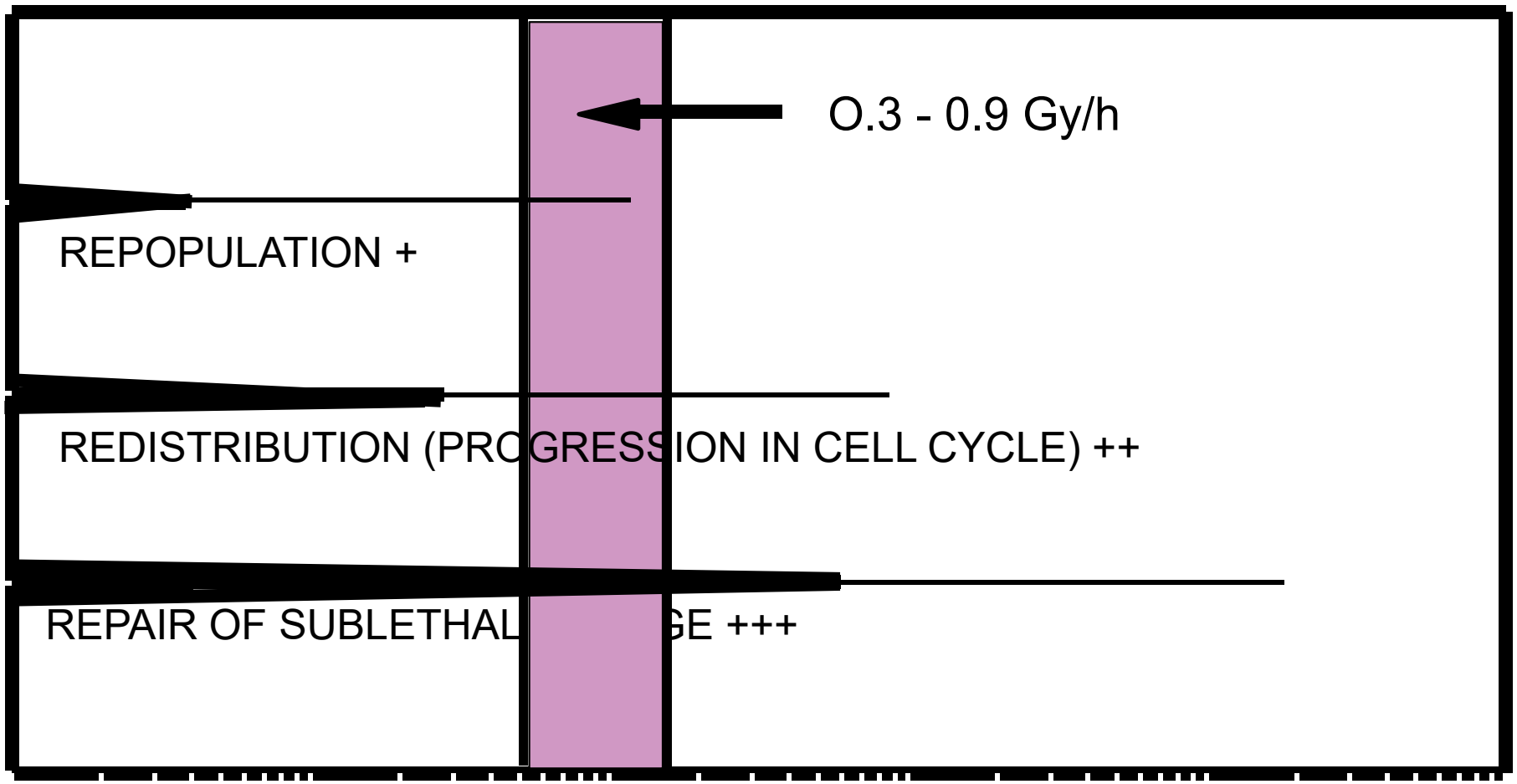
$$E = \alpha D + g \beta D^2$$

$$g = \frac{2\left(\mu t - 1 + e^{(-\mu t)}\right)}{(\mu t)^2}$$

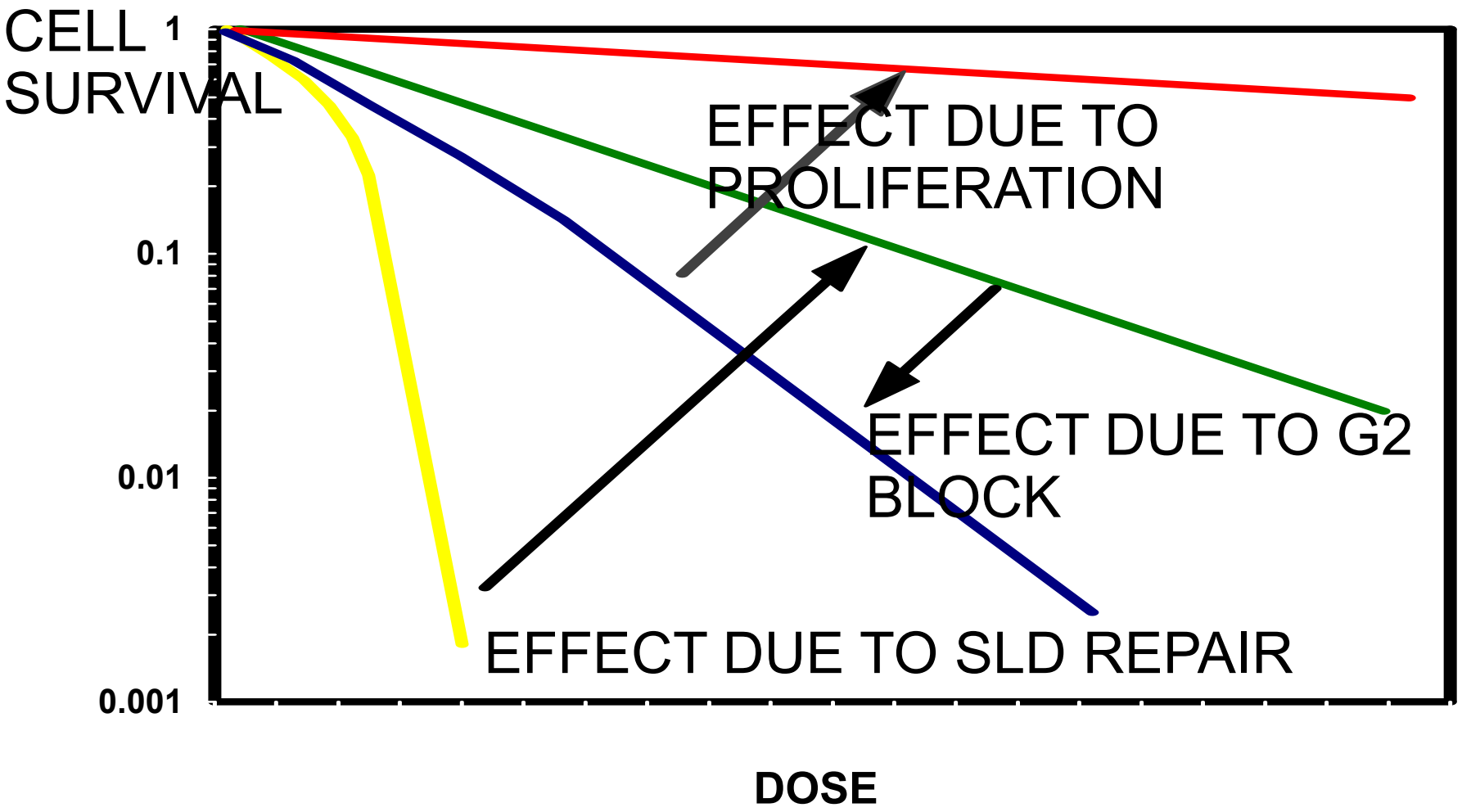
$$\mu = 0.693 / T_{1/2}$$



Low dose rate brachytherapy



Low dose rate



French Cooperative Study

Grade 3-4 complications (%)
related to Dose Rate

	< 60 cGy/h	**> 60 cGy/h**	
Ref. bladder dose	0.8 %	5.3 %	p = 0.001
Ref. rectal dose	1.7 %	6.5 %	p = 0.01
Mean rectal dose	2.3 %	8.5 %	p = 0.01

J.C. Horiot,ea 1993

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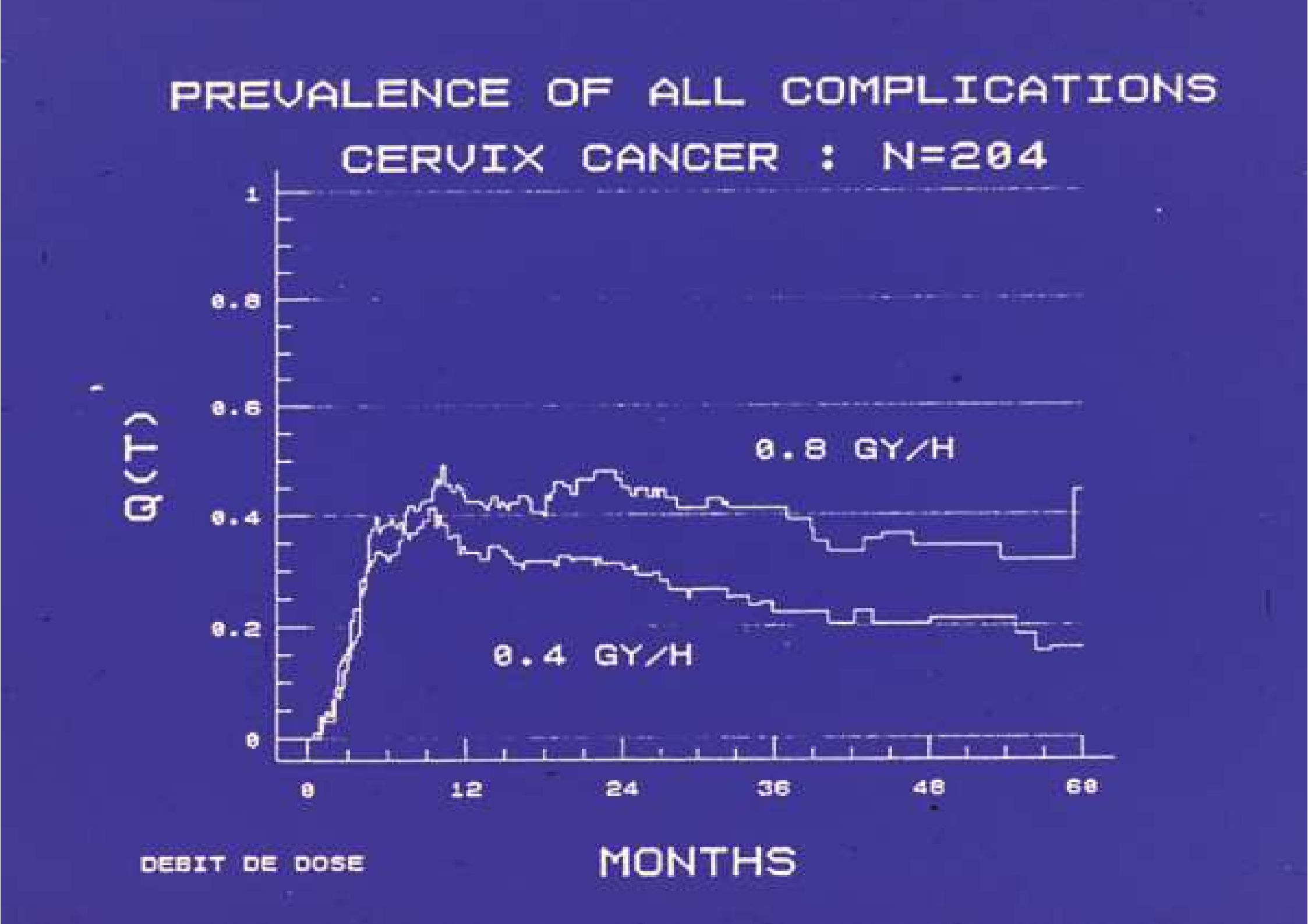
IGR phase III trial

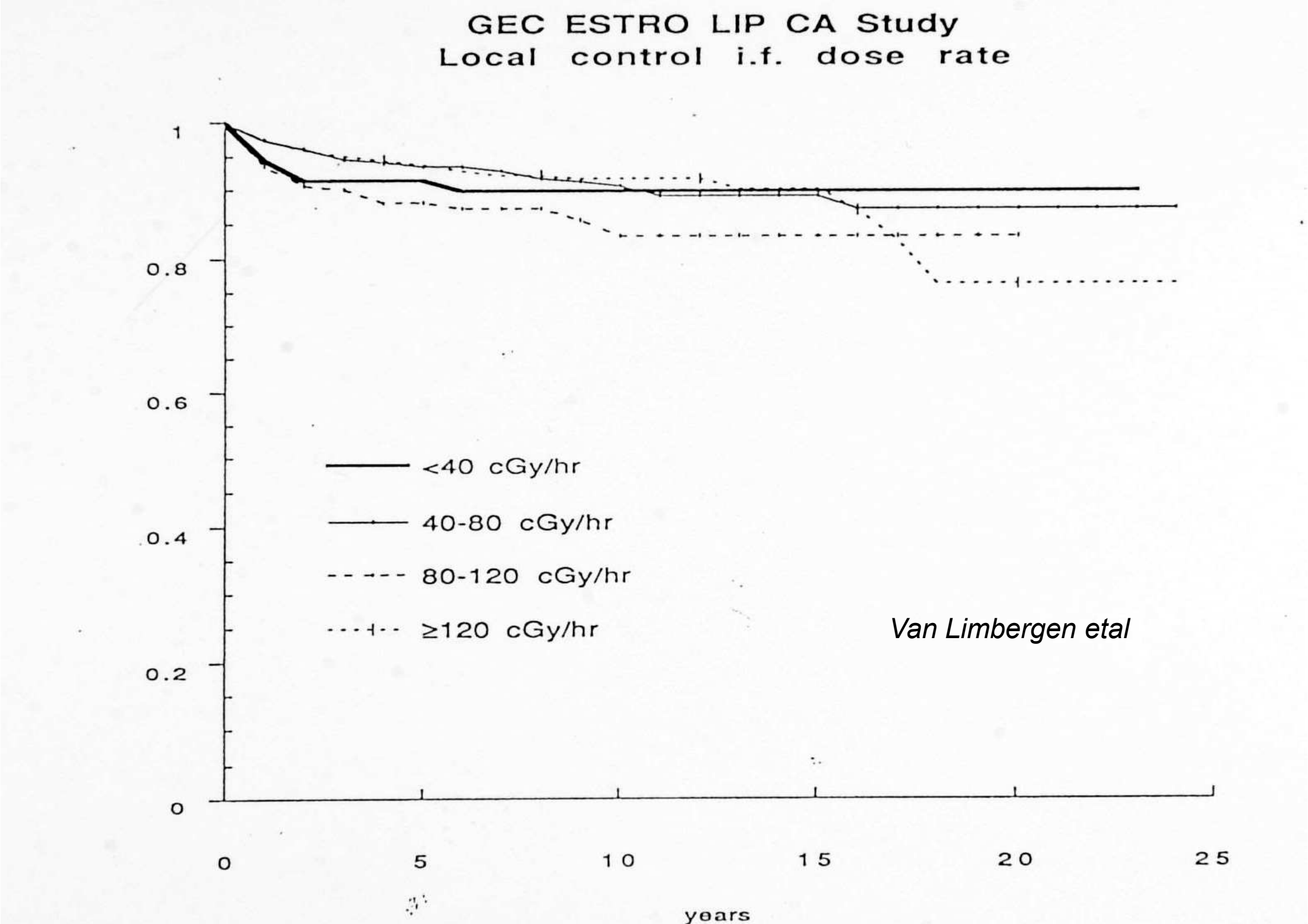
CONCLUSIONS :

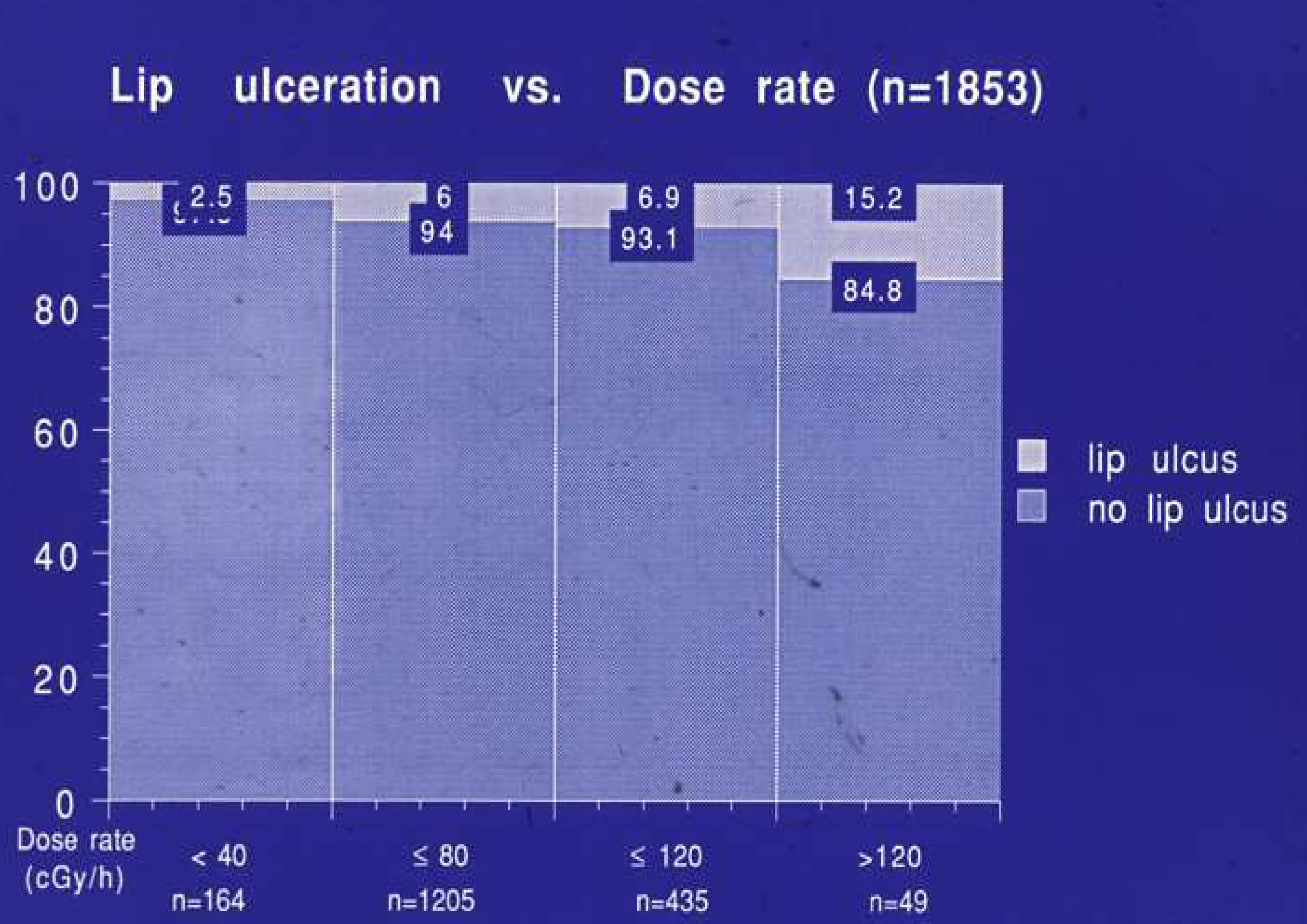
Cs 37 cGy/h versus 73 cGy/h

- No DRE for surgical difficulties at operation except for delayed surgery in stage II
- No DRE for tumor sterilisation in specimen except for medium size tumors
- No DRE for relapse free survical
- Higher complications prevalence in the higher dose rate group

Haie et al., 1994


PREVALENCE OF ALL COMPLICATIONS
CERVIX CANCER : N=204
G(T)
1
0.8
0.6
0.4
0.2
0
0.8 GY/H
0.4 GY/H
0
12
24
36
48
60
MONTHS
DEBIT DE DOSE


GEC ESTRO LIP CA Study
Local control i.f. dose rate
1
0.8
0.6
0.4
0.2
0
<40 cGy/hr
40-80 cGy/hr
80-120 cGy/hr
≥120 cGy/hr
Van Limbergen etal
0
5
10
15
20
25
years


Lip ulceration vs. Dose rate (n=1853)
100
80
60
40
20
0
2.5
94
6
93.1
6.9
84.8
15.2
lip ulcus
no lip ulcus
Dose rate (cGy/h)
< 40
n=164
≤ 80
n=1205
≤ 120
n=435
>120
n=49

Mobile tongue and floor of mouth

Iridium 192 alone	local failure	necrosis
≥ 62.5 Gy - ≥ 0.5 Gy/h	7 %	44 %
≥ 62.5 Gy - < 0.5 Gy/h	13 %	19 %
< 62.5 Gy - ≥ 0.5 Gy/h	21 %	37 %
< 62.5 Gy - < 0.5 Gy/h	48 %	5 %

J.J. Mazeron et al, Radiother. Oncol. 21, 39, 1991

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Faucial arch tumors

Grade 2-3 complications:

Dose rate < 0.6 Gy/h (288 pts)	6 %
Dose rate > 0.6 Gy/h (52 pts)	10 %

p = 0.006

M. Pernot, et al., IJROBP, 30, 1051, 1994

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Clinical data on DRE in LDR brachytherapy

- No large DRE on tumor control
- No DRE for early complications
- Significant DRE for late complications

  Magnitude ? - Dose specification

  - Dose - Dose Rate correlated

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Effect of dose rate

IN PRACTICE :

- Dose adjustments are unnecessary in the range 0.3-0.9 Gy/hr.

- A decrease in dose rate may be beneficial to normal tissue tolerance without significantly affecting local control.

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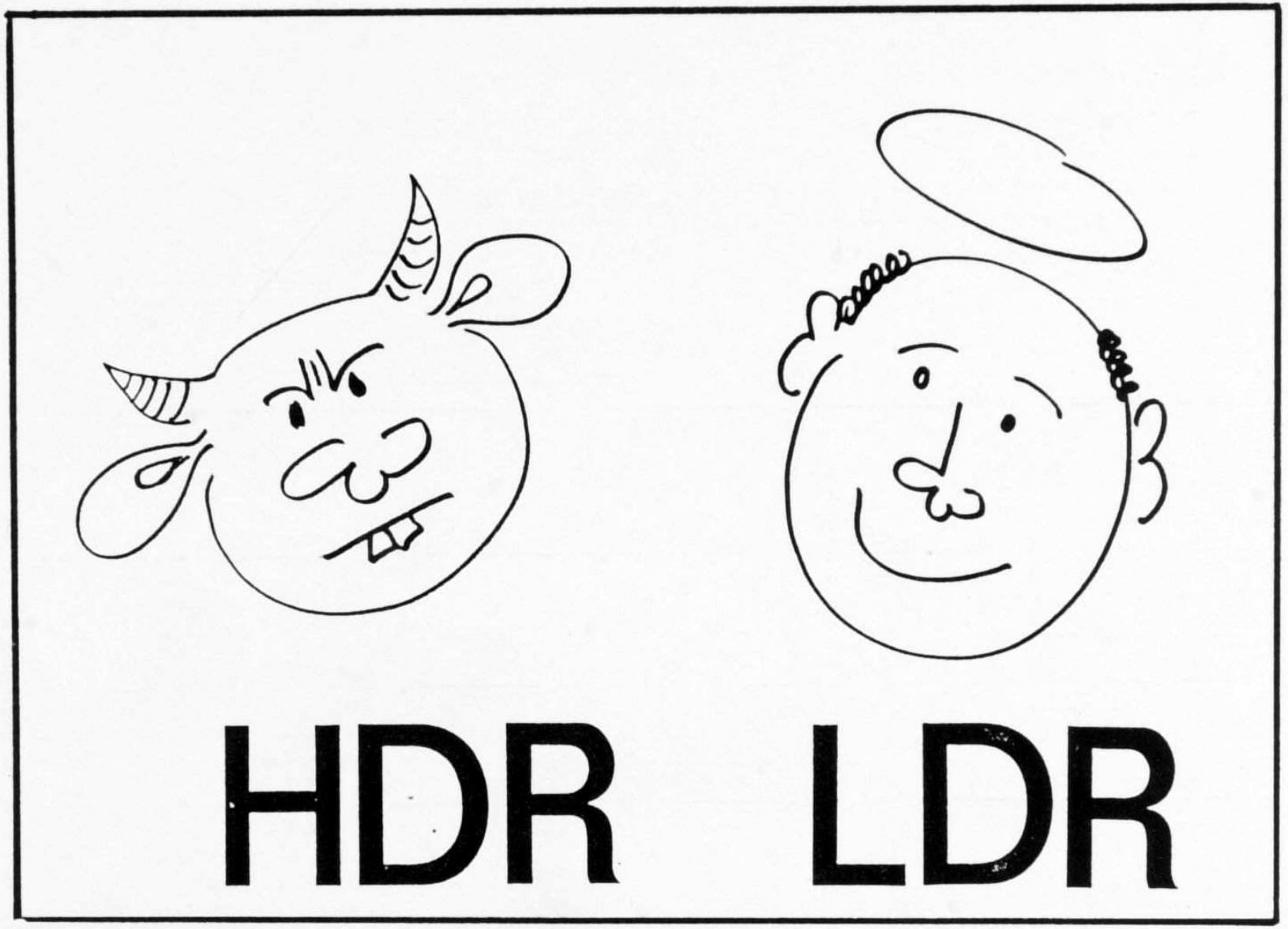

HAS LOW DOSE RATE VIRTUES BY ITSELF ?

HDR- ICBT: late complications

- Clinical Data HDR vs LDR

➢ Review literature *				
(Fu and Phillips 1990)	G2-4	12 %	18 %	
➢ Meta-analysis 17 068 pts				
(Orton 1991)	G3-4	2.2%	5.3%	p<0.001
➢ Randomised Phase III				
(Patel 1994)	G1-4	6.4%	19.9%	p<0.001
	G3-4	0.4%	2.4%	p> 0.05

* majority Fx 7.8 Gy to point A

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Conclusion HDR

- Main factors are
  - TOTAL DOSE
  - FRACTION SIZE
  - TOTAL TREATMENT TIME
- $TE = (d + \alpha/\beta) D$
- $M = 2\ Gy\ .\ T/\ Tpot$

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Conclusion LDR

- Main factors are
  - TOTAL DOSE
  - DOSE RATE

- $TE = (\alpha/\beta + 2.9.T½.DR)D$

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Common Language EQD2

$$EQD2 = D\ (\alpha/\beta + d) / (\alpha/\beta + 2)$$

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Biologically equivalent dosis of 30 Gy / 10 fractions

Reference: 2 Gy / fraction

- EQD2 = 30 (α/β + 3) / (α/β + 2)
- Tumour (Squamous cell ca – early responding normal tissues):α/β = 10 Gy EQD2 = 30 x 13 / 12 = 32.5 Gy
- Late responding normal tissues: α/β = 3 Gy EQD2 = 30 x 6 / 5 = 36 Gy

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Equivalence formula : carcinoma

$T_{1/2} = 1$ hr

$d = 2.89 \cdot T_{1/2} \cdot DR$

3 Gy / fraction = 1 Gy / hr

1.8 Gy / fraction = 0.6 Gy / hr

1.2 Gy / fraction = 0.4 Gy / hr

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Equivalence formula : late effects

$T_{1/2}$ = 1.5 hr

$d = 2.89 \cdot T_{1/2} \cdot DR$

- 4.5 Gy / fraction = 1 Gy / hr
- 2.4 Gy / fraction = 0.6 Gy / hr
- 1.8 Gy / fraction = 0.4 Gy / hr

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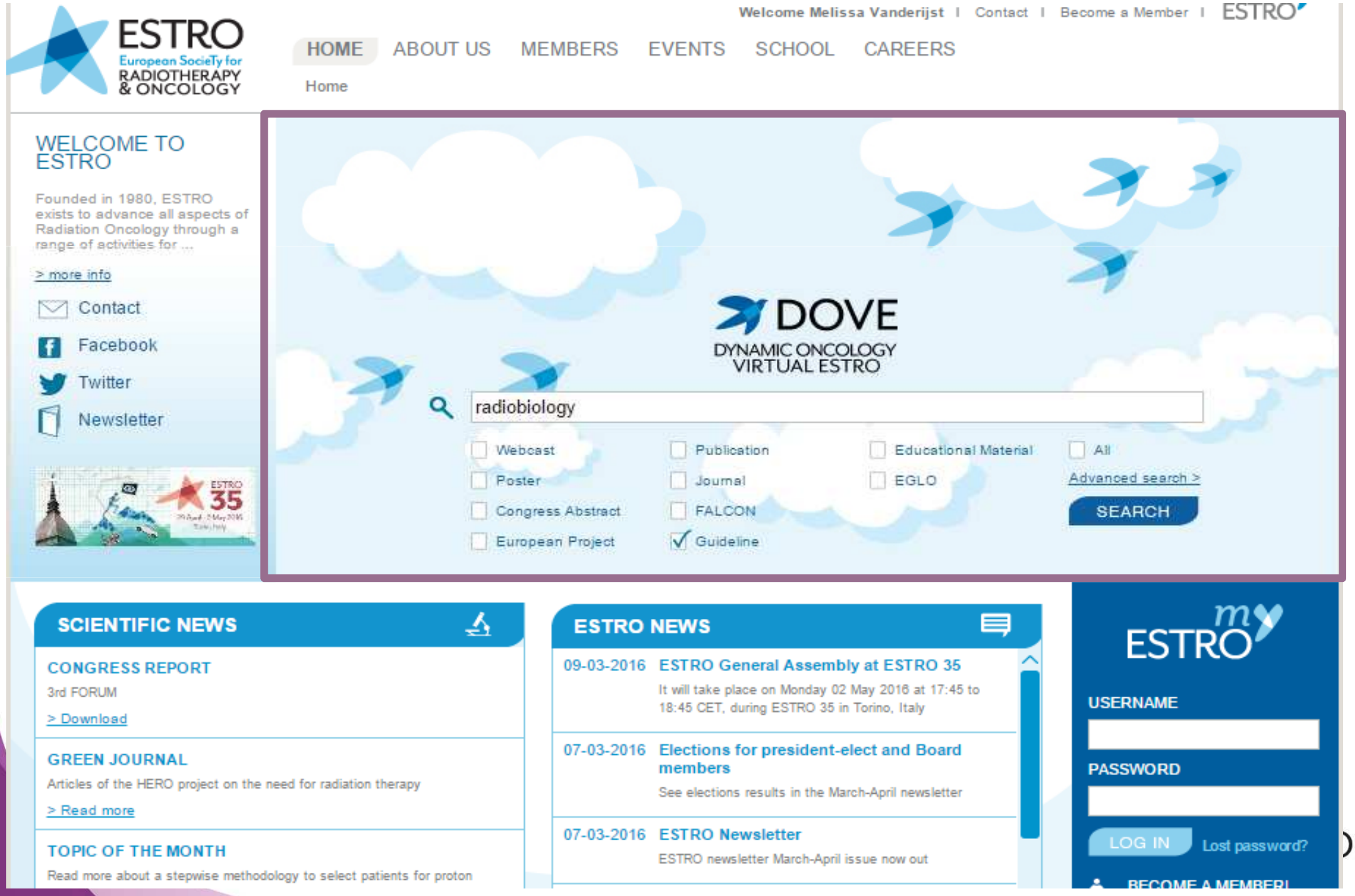
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FALCON
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European Project
Guideline
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CONGRESS REPORT
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GREEN JOURNAL
Articles of the HERO project on the need for radiation therapy
> Read more
TOPIC OF THE MONTH
Read more about a stepwise methodology to select patients for proton
ESTRO NEWS
09-03-2016 ESTRO General Assembly at ESTRO 35
It will take place on Monday 02 May 2016 at 17:45 to 18:45 CET, during ESTRO 35 in Torino, Italy
07-03-2016 Elections for president-elect and Board members
See elections results in the March-April newsletter
07-03-2016 ESTRO Newsletter
ESTRO newsletter March-April issue now out
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Endovascular brachytherapy is a new, rapidly growing field of interest in radiotherapy for the prevention of neointimal hyperplasia after angioplasty in both coronary and peripheral arteries.[...more]

Intercomparison of treatment concepts for MR image assisted brachytherapy of cervical carcinoma based on GYN GEC-ESTRO recommendations. Gu

Stefan S Lang, An A Nulens, Edith E Briot, Christian C Kirisits, Marisol M De Brabandere, Isabelle I Dumas, Johannes J Dimopoulos, Peter P Petrow, Dietmar D Georg, Erik E Van Limbergen, Christine C Haie-Meder, Richard R Pötter

[1]Department of Radiotherapy and Radiobiology, Medical University of Vienna, Austria

PURPOSE: To perform a multicentre intercomparison study of treatment concepts for MRI assisted brachytherapy of cervix cancer based on recommendations of the Gynaecological GEC-ESTRO Working Group.[...more]

The GEC ESTRO Handbook of Brachytherapy: Radiobiology of LDR, HDR, PDR and VLDR Brachytherapy (2nd edition - November 12, 2015) Gu

Erik Van Limbergen , Michael Joiner , Albert Van der Kogel , Wolfgang Dörr

Brachytherapy (BT) differs from external beam therapy (EBRT) in two main ways: the distribution of the absorbed dose and the time-dose patterns.

[...more]

GEC-ESTRO Handbook Radiobiology (1st edition, 2002) Gu

NEW EDITION AVAILABLE HERE [...more]

Muscle-Invasive Bladder Cancer

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TURB / Partial Cystectomy
EBRT + Brachytherapy

B. Pieters
Academic Medical Center / University of Amsterdam

Pioneers

- Herberger & Sauer, 1941
- Barringer, 1947
- Breur, 1951
- van der Werf-Messing, 1965

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MIBC

Standard

Radical cystectomy ± neo-adjuvant chemotherapy

Alternative in selected cases

Bladder preserving treatment

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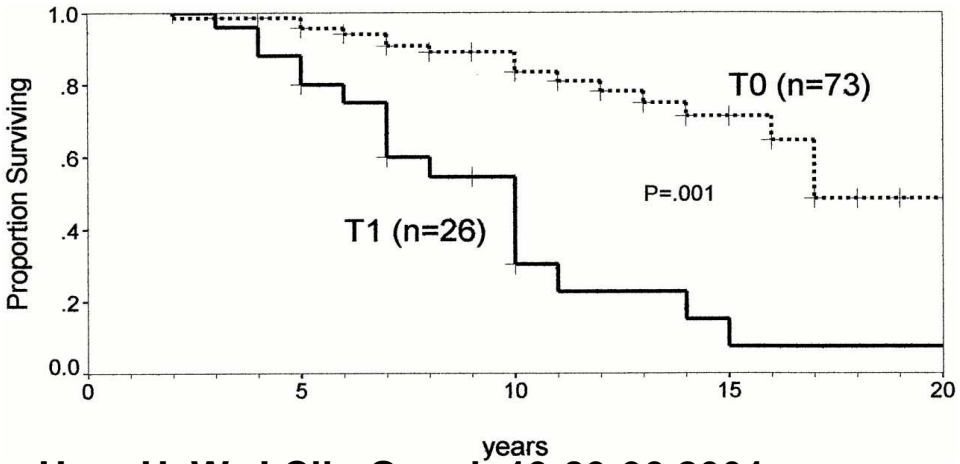
Bladder preservation



Herr, H. W. J Clin Oncol; 19:89-93 2001

Local progression-free survival with a bladder distribution of 99 patients with muscle-invasive bladder cancer treated by TUR, stratified by no tumor (T0) or non-muscle-invasive tumor (T1) on restaging TUR

TURB alone if invasion limited to superfcial muscle layers.
TURB alone is not a curative option in most patients
EAU guidelines 2014

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Improvement in bladder sparing approaches External Beam Radiotherapy

1) Chemoradiation, - addition of sensitizing chemotherapy to radiation

2) Improved radiation techniques

- Improved tumor delineation,
- Improved RT accuracy and
- Improved dosimetry

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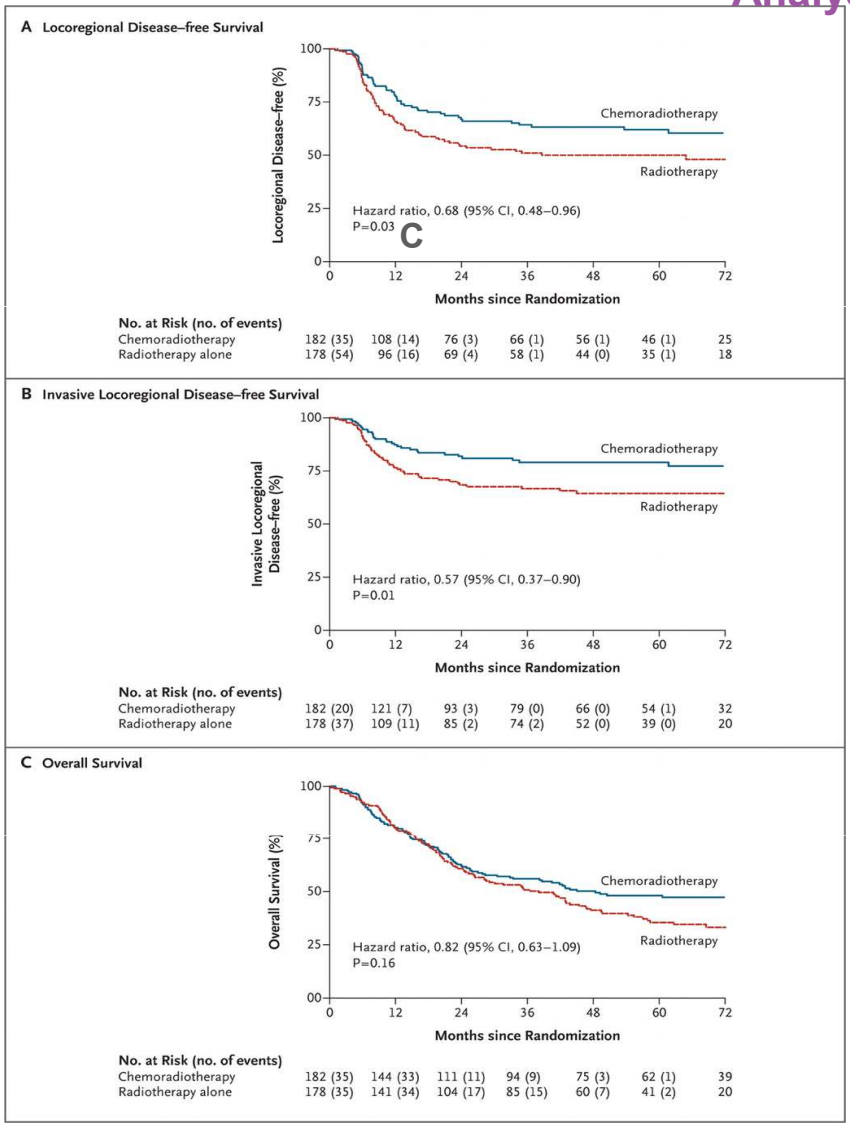
Chemoradiation

Analysis of Survival.



James ND et al. N Engl J Med 2012;366:1477-1488.

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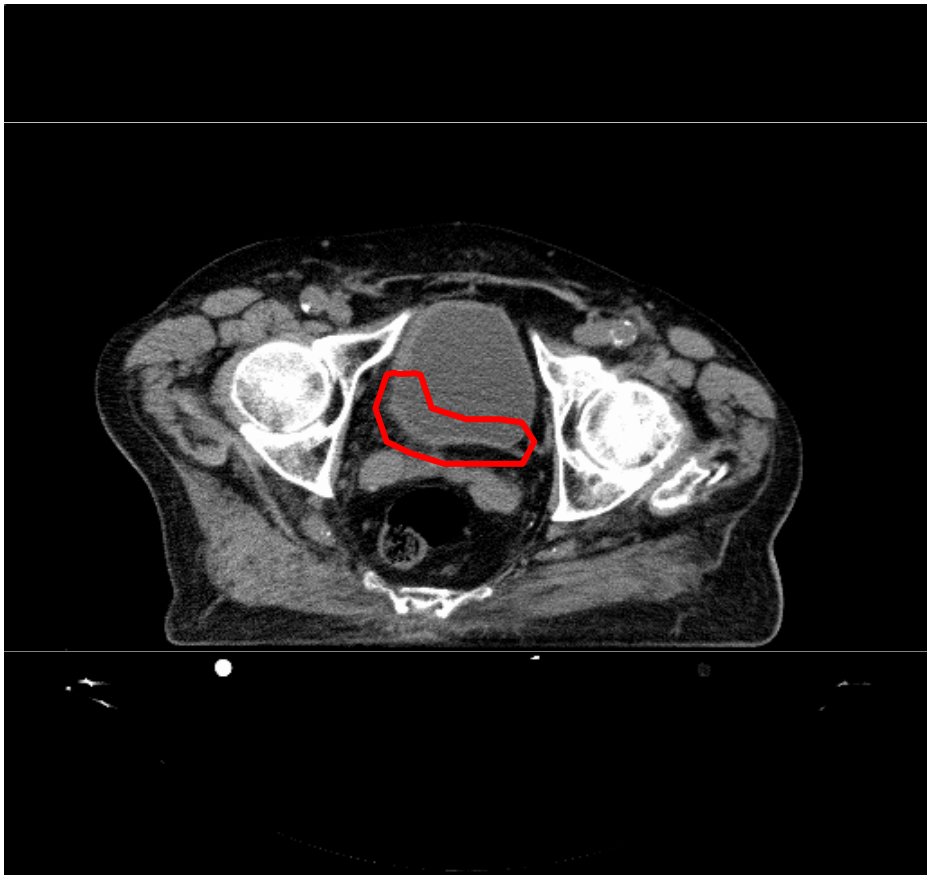
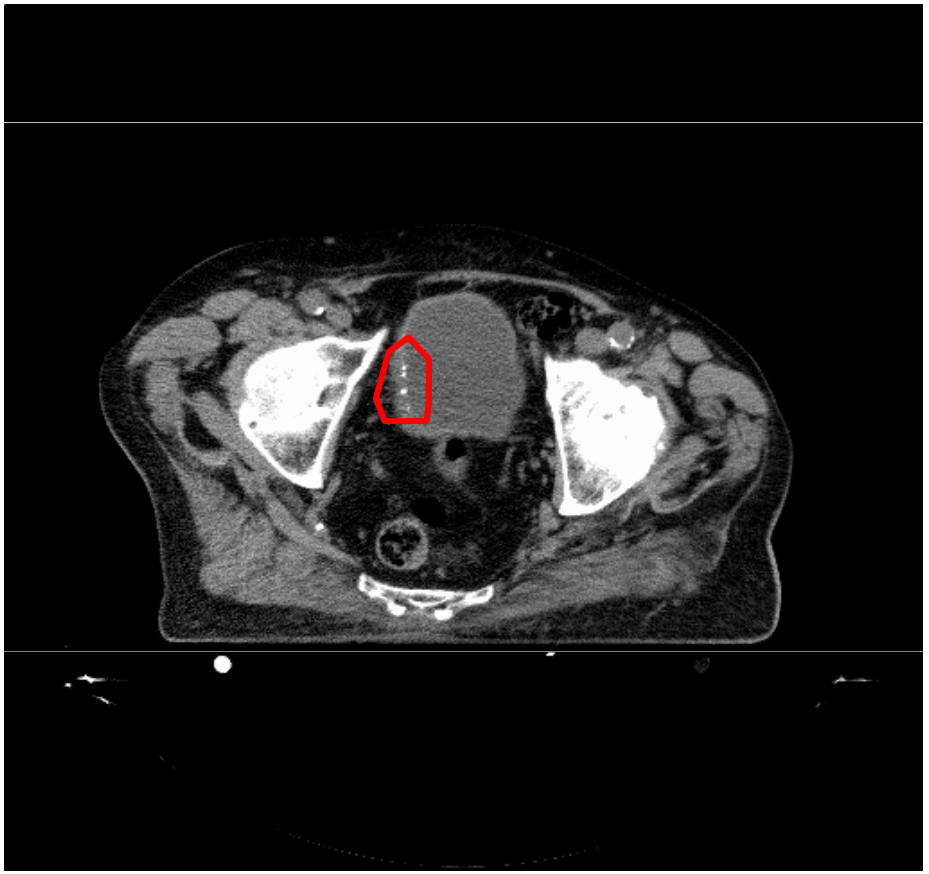
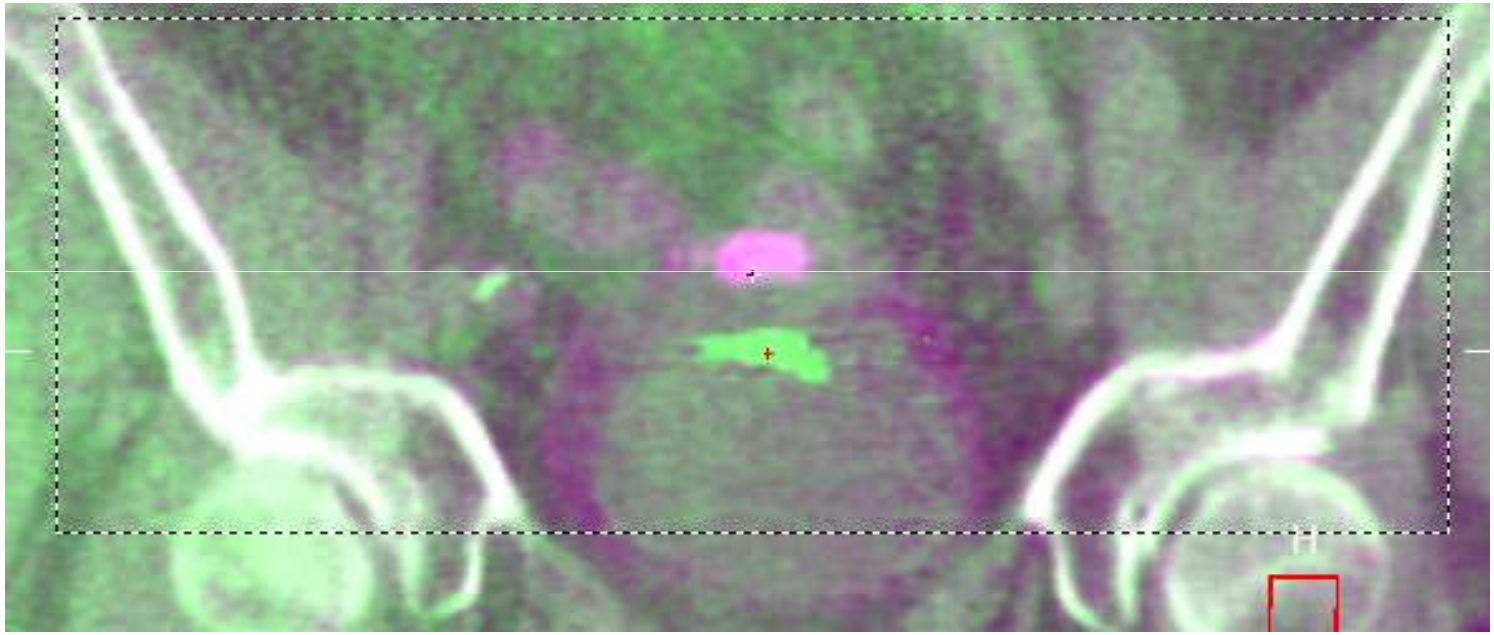
Use of fiducial markers: → improved tumordelineation
→ positional verification possible



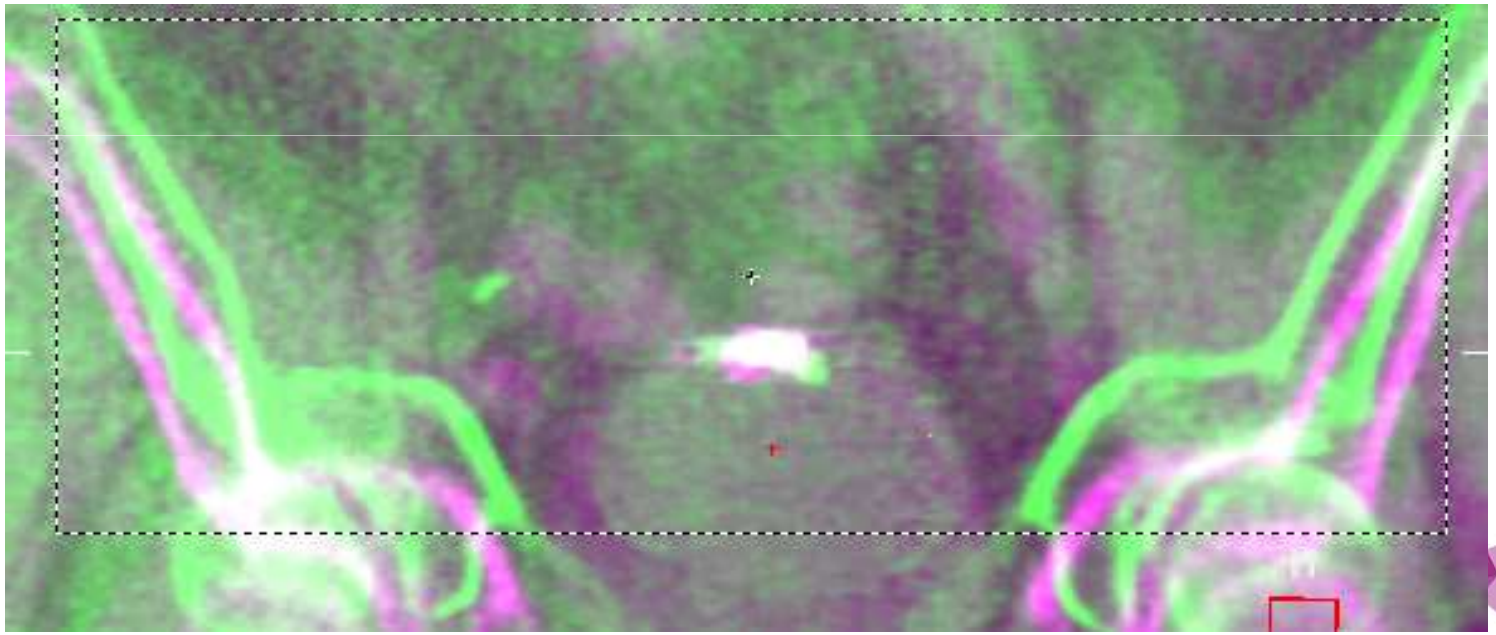


Daily match on tumorposition

Bony match



Tumor match



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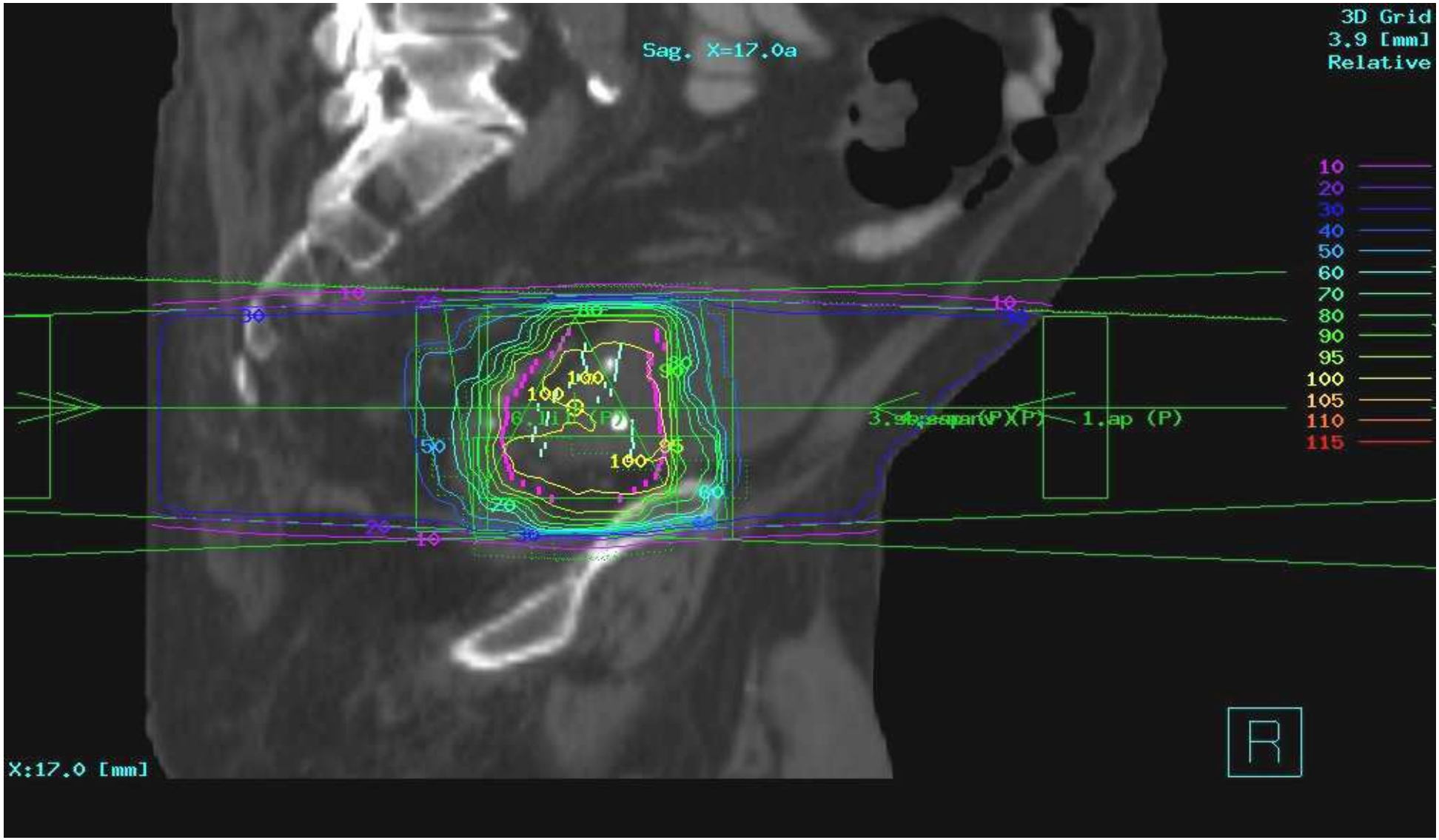
IMRT

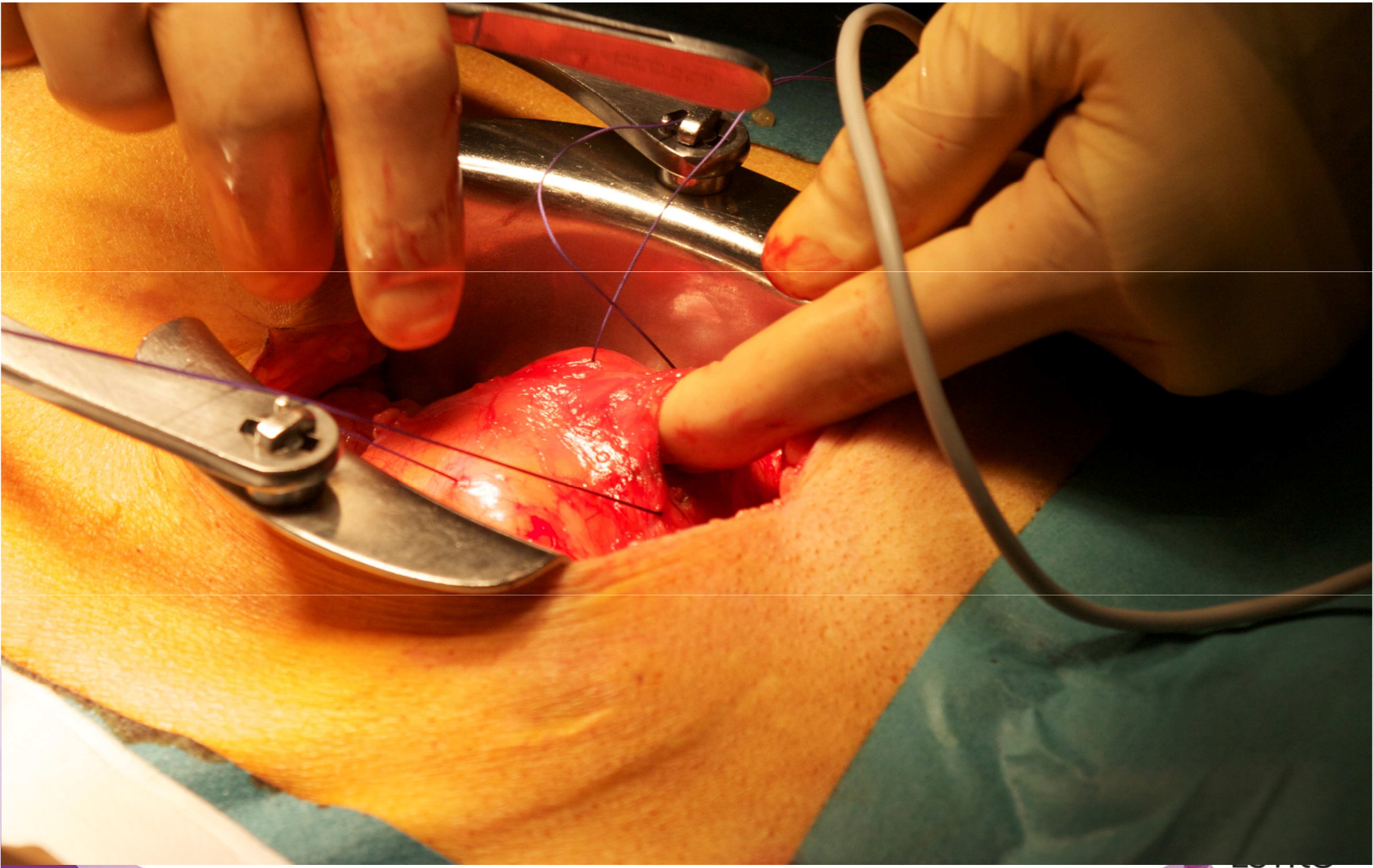

Sag. X=17.0a
3D Grid
3.9 [mm]
Relative
10
20
30
40
50
60
70
80
90
95
100
105
110
115
1.ap (P)
R
X:17.0 [mm]

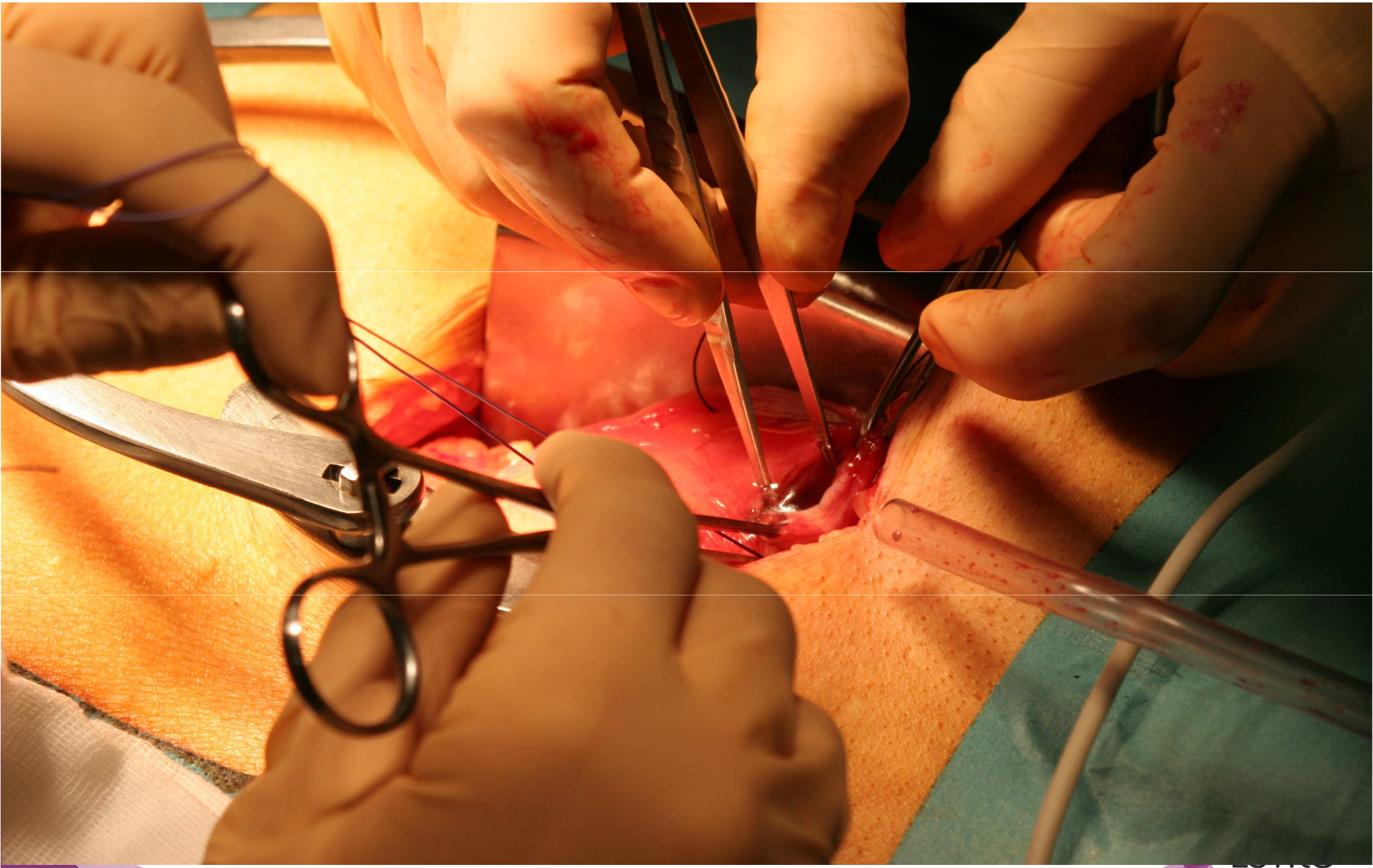
Bladder Preservation with Brachytherapy

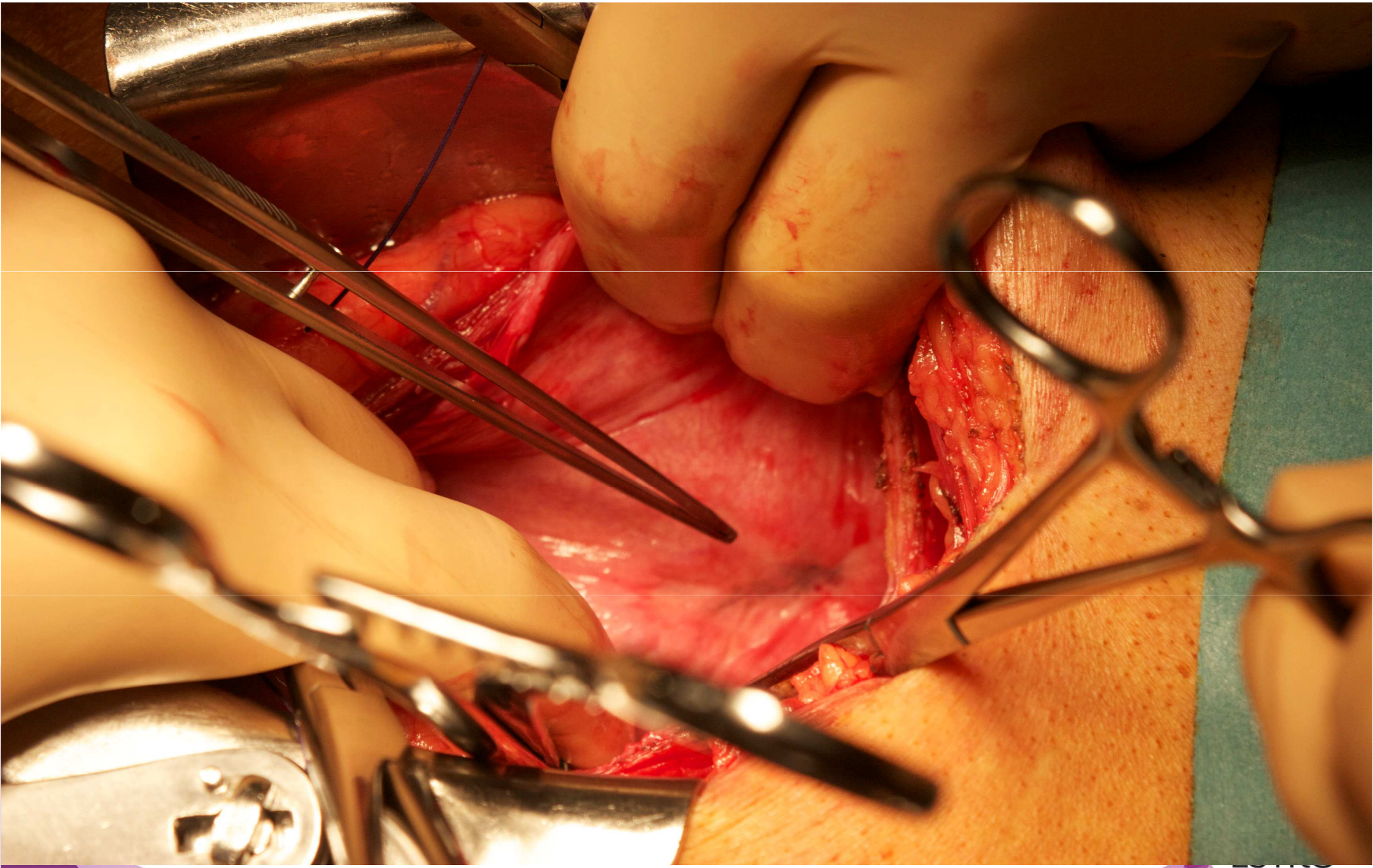
Techniques

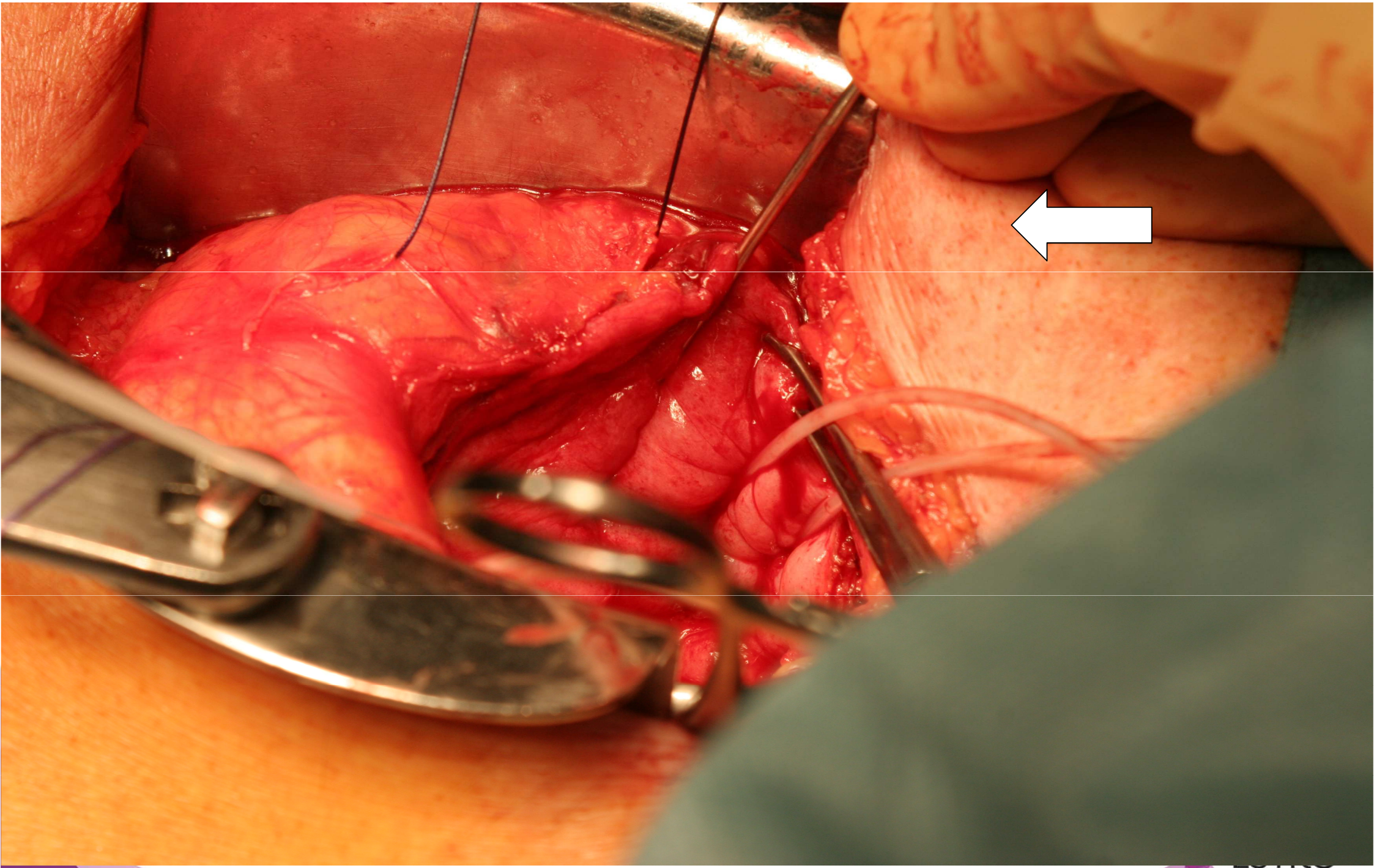
- Sectio alta
- Laparoscopic

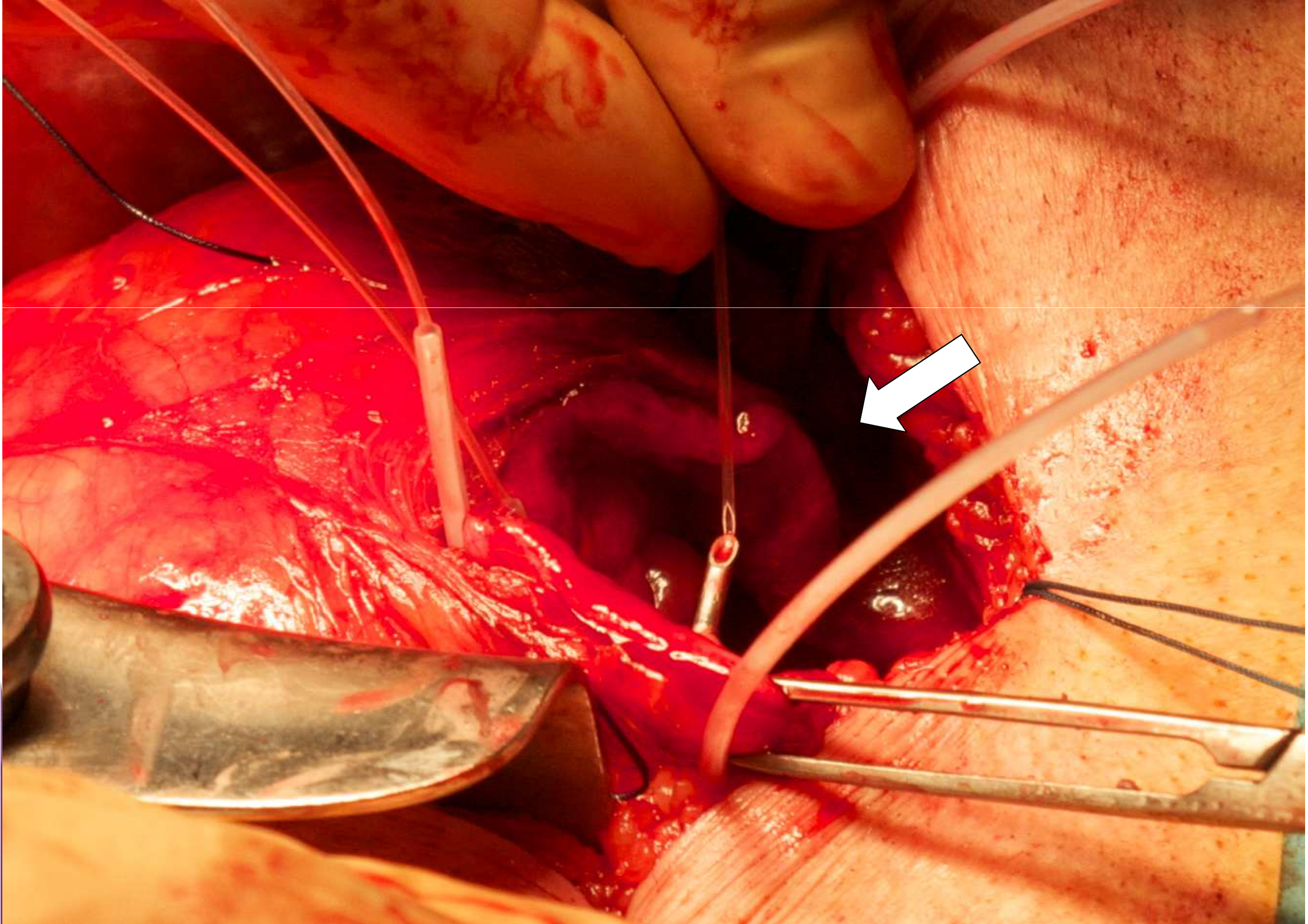
SECTIO ALTA

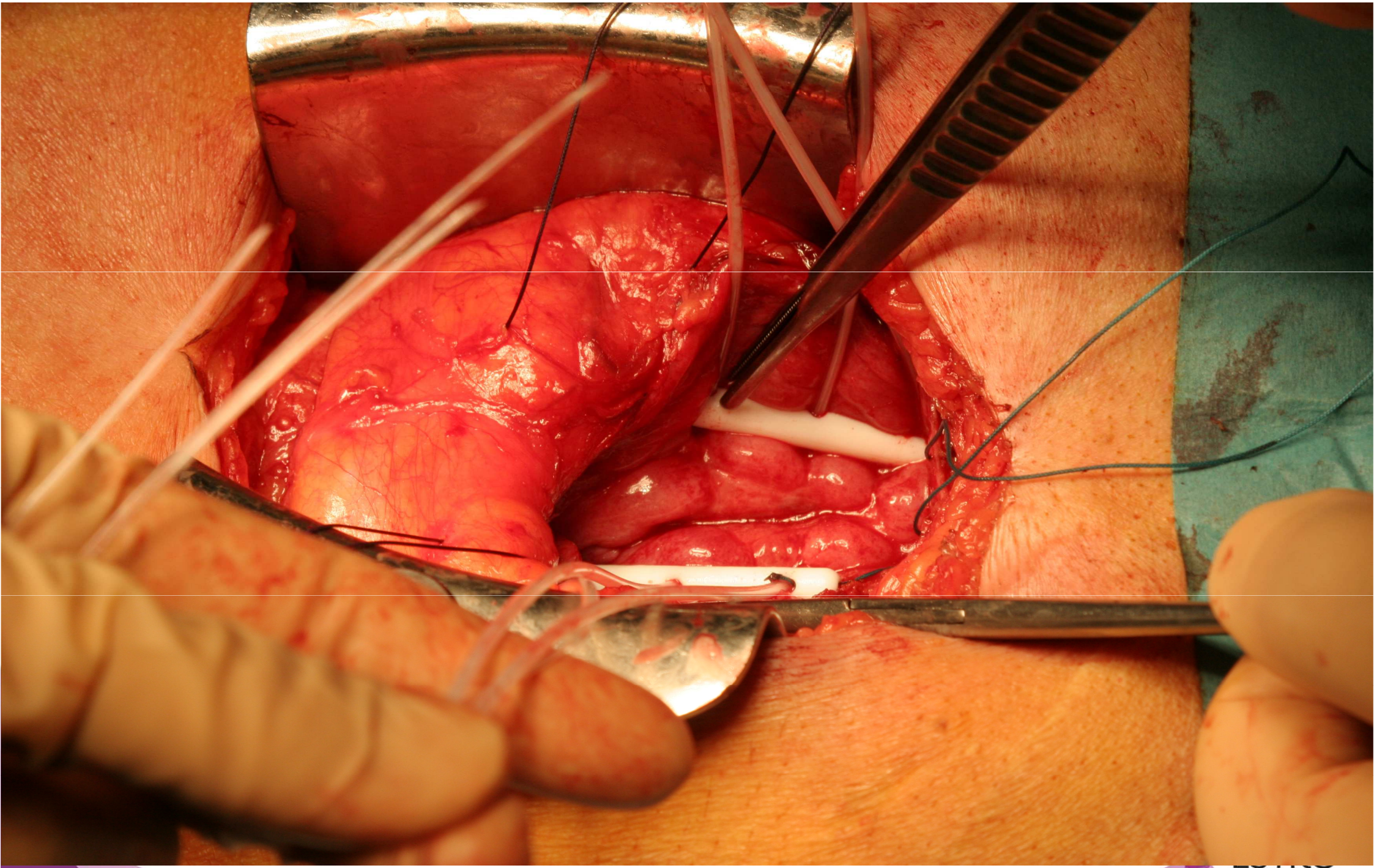


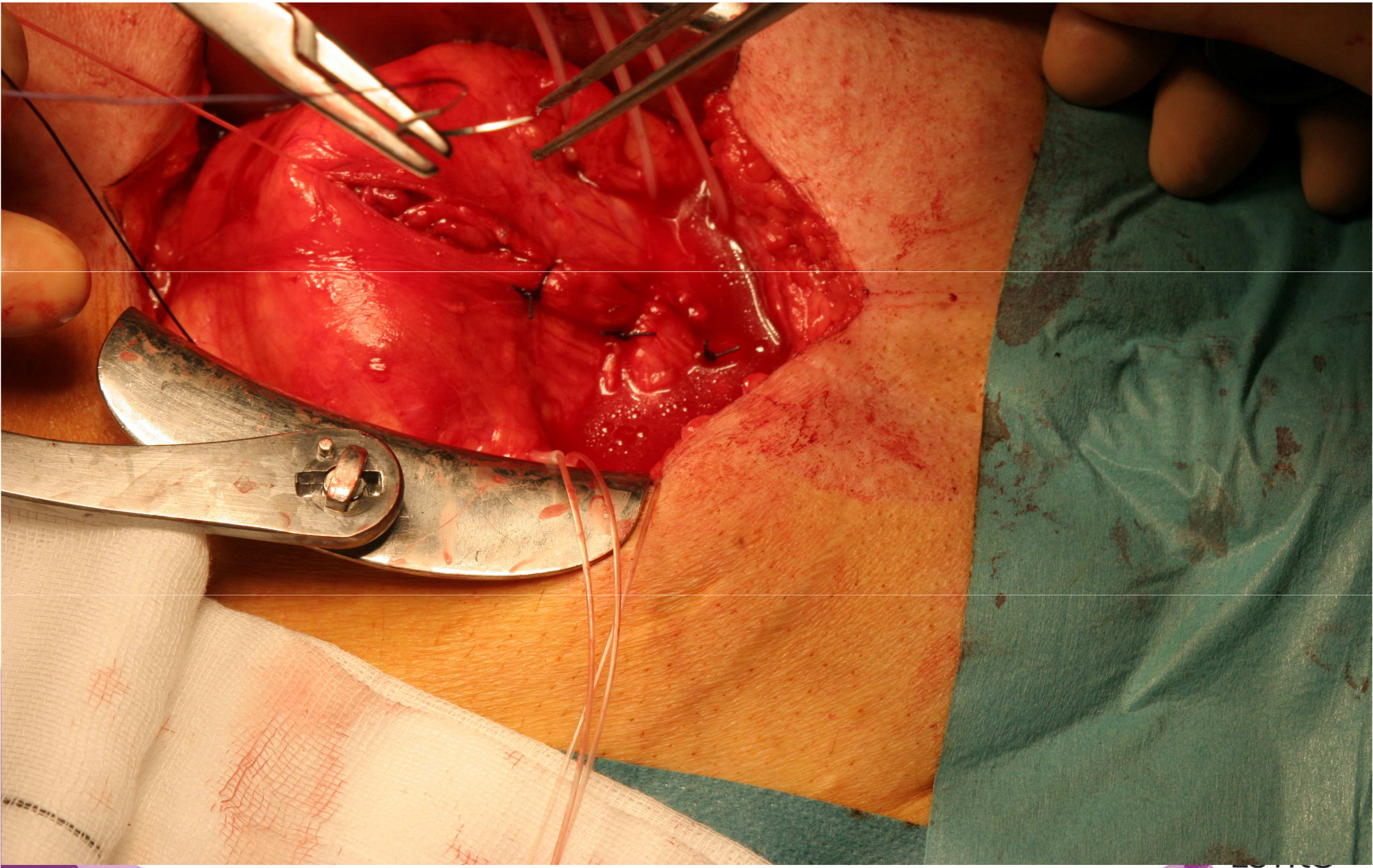


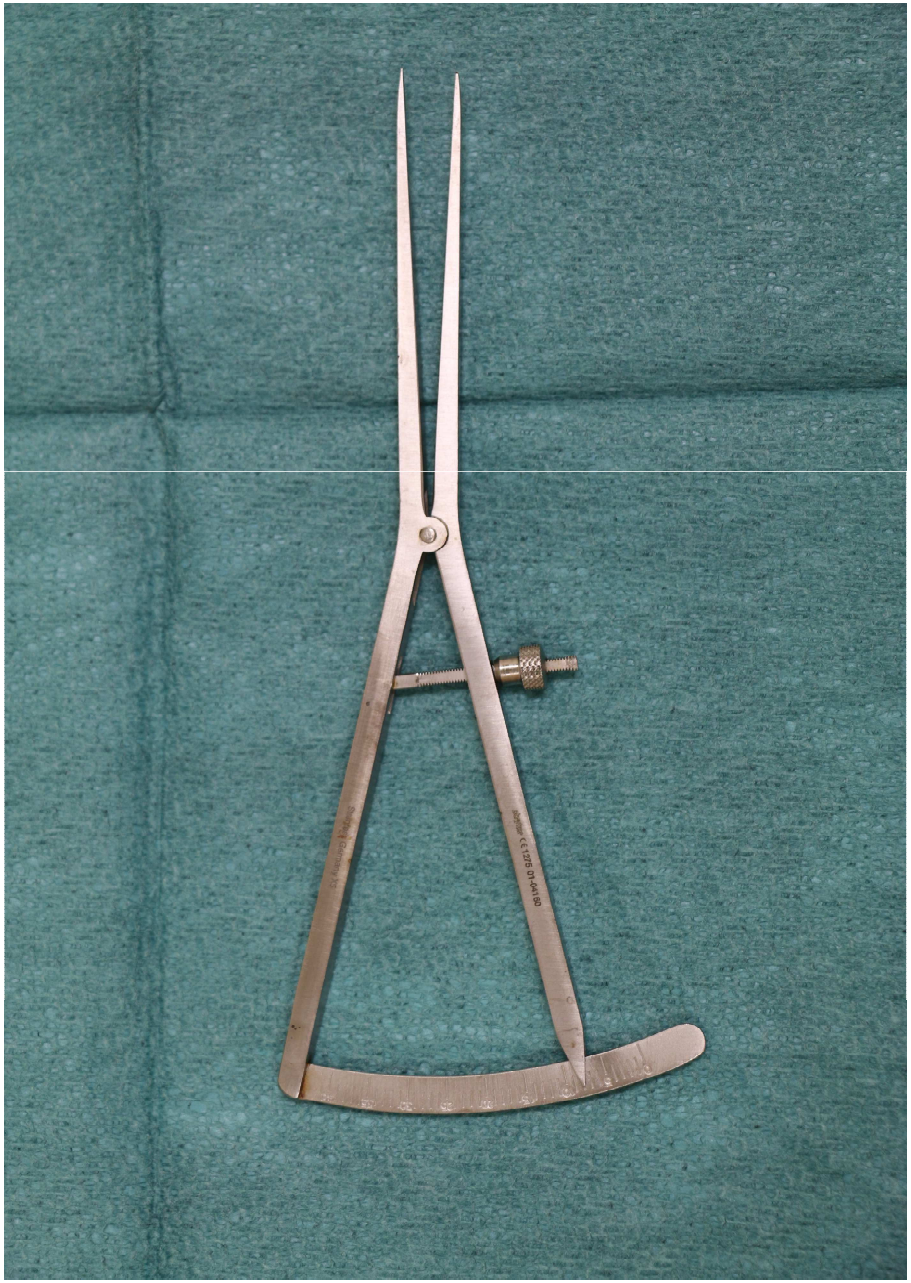


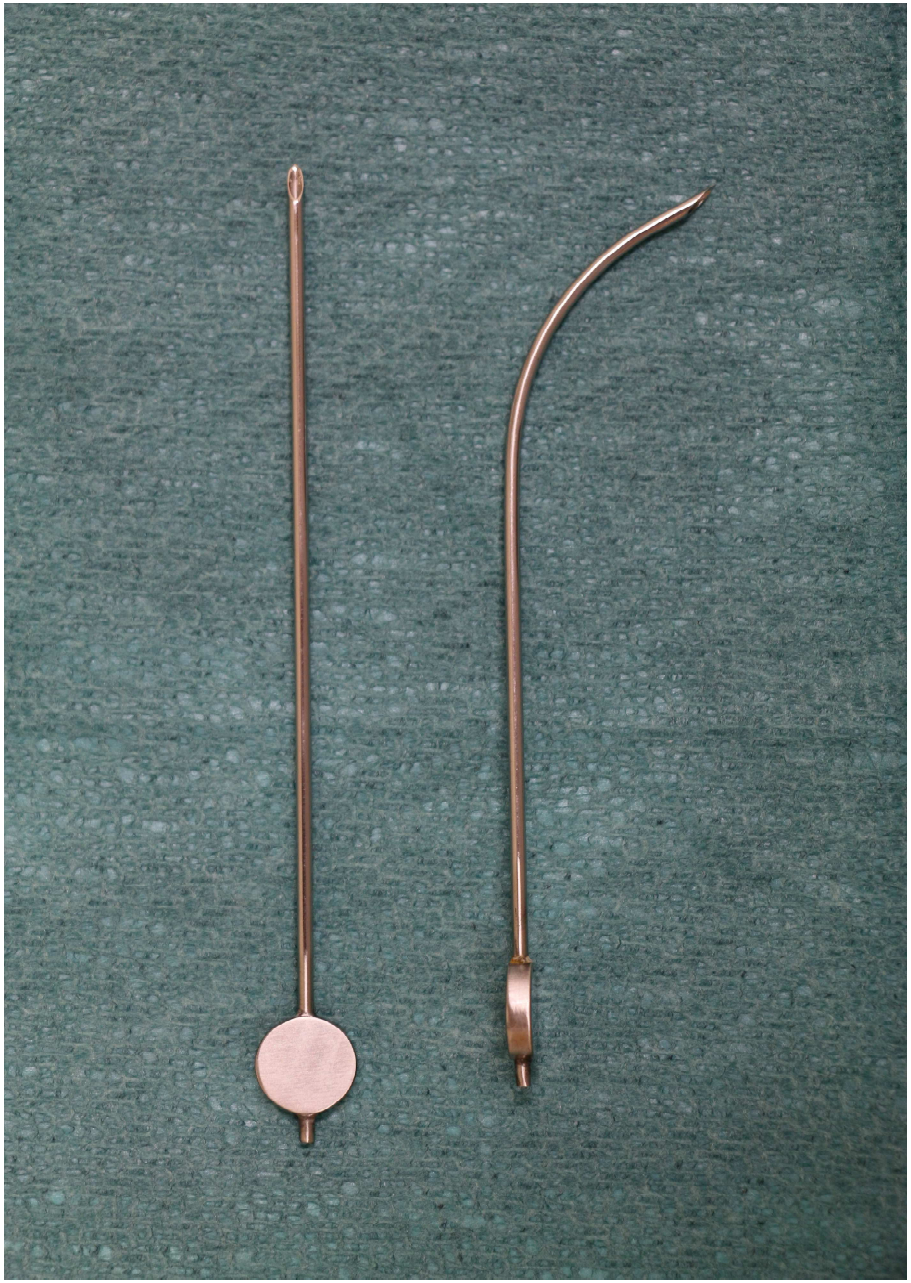


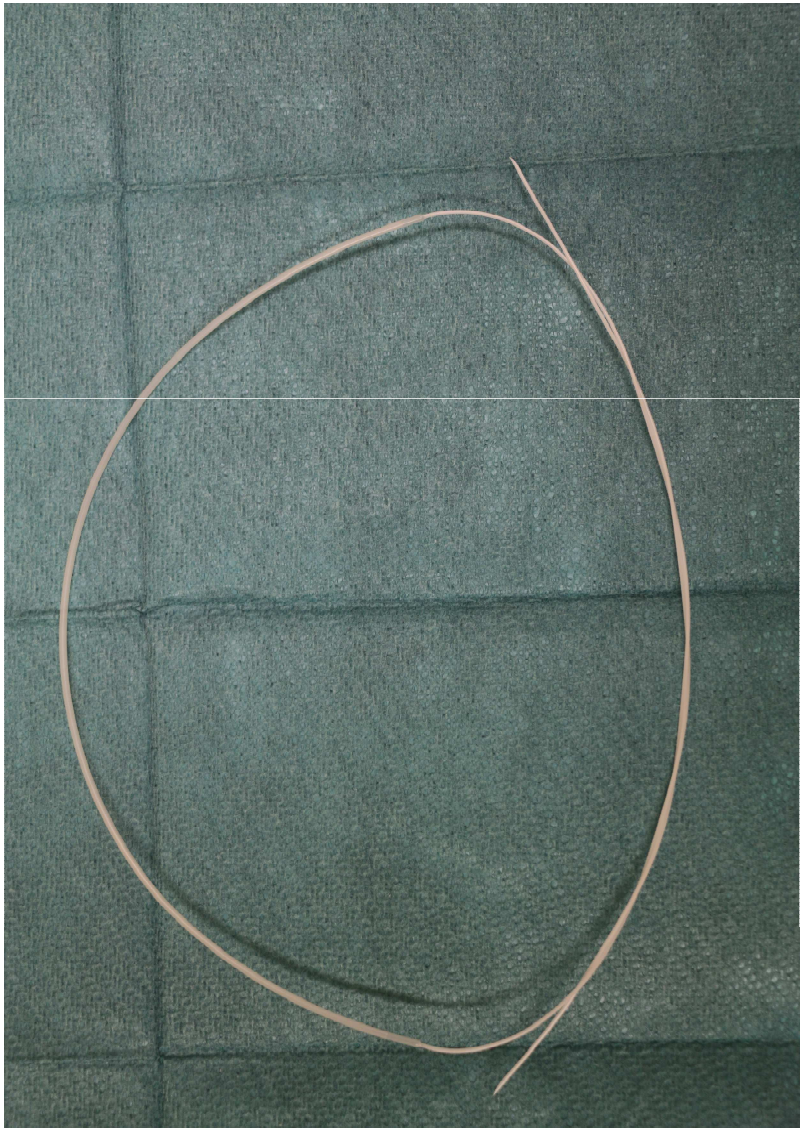


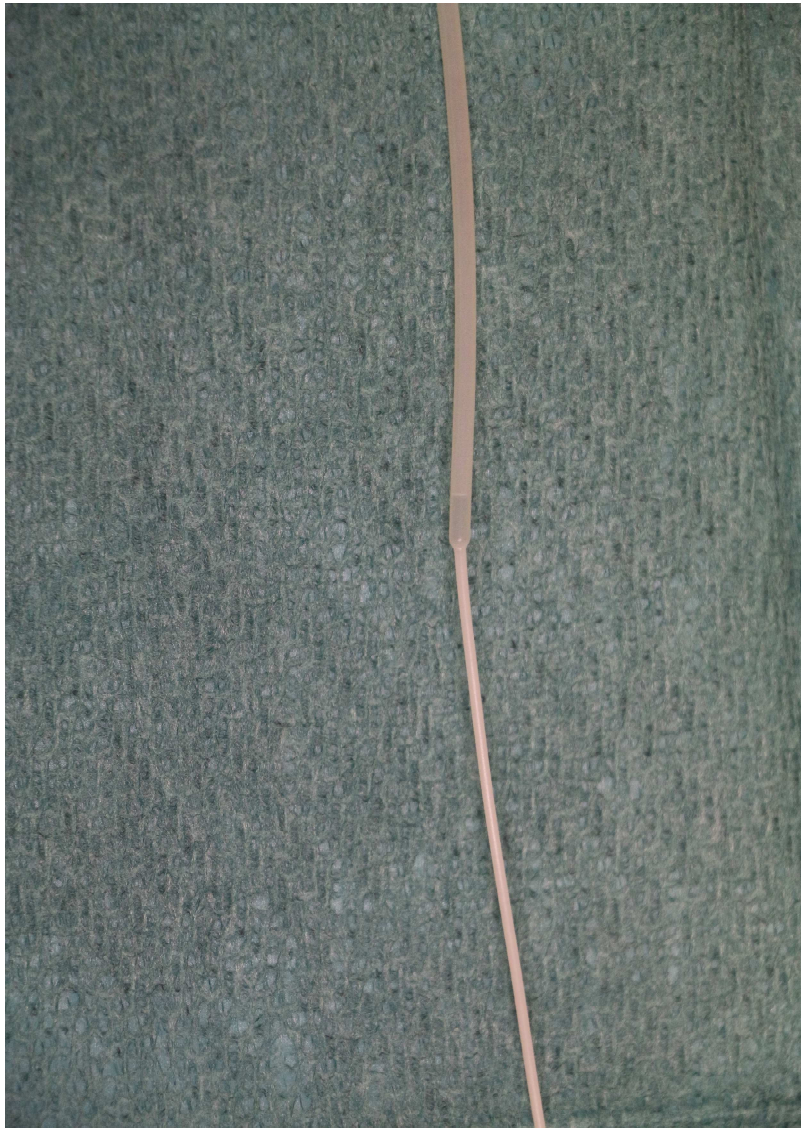












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LAPAROSCOPIC ROBOT-ASSISTED

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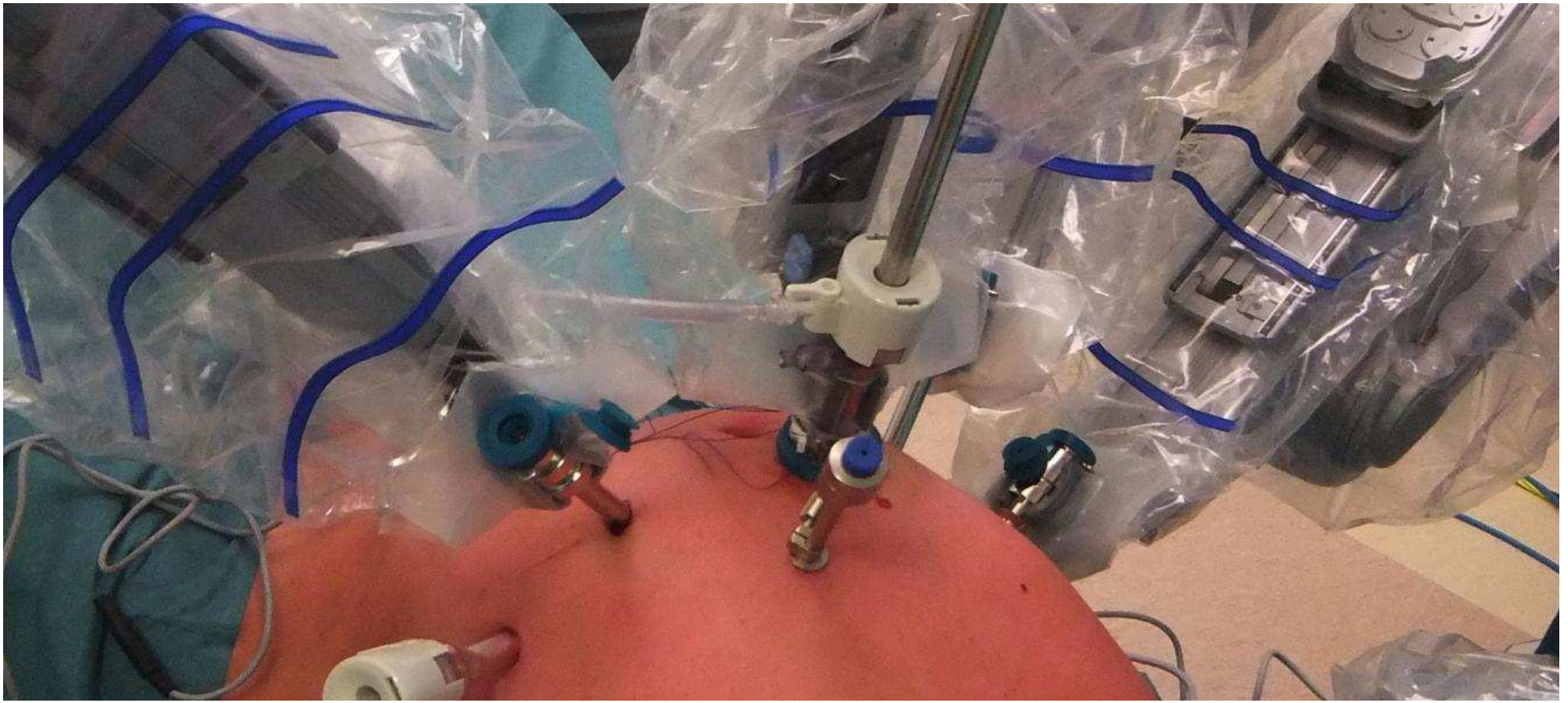
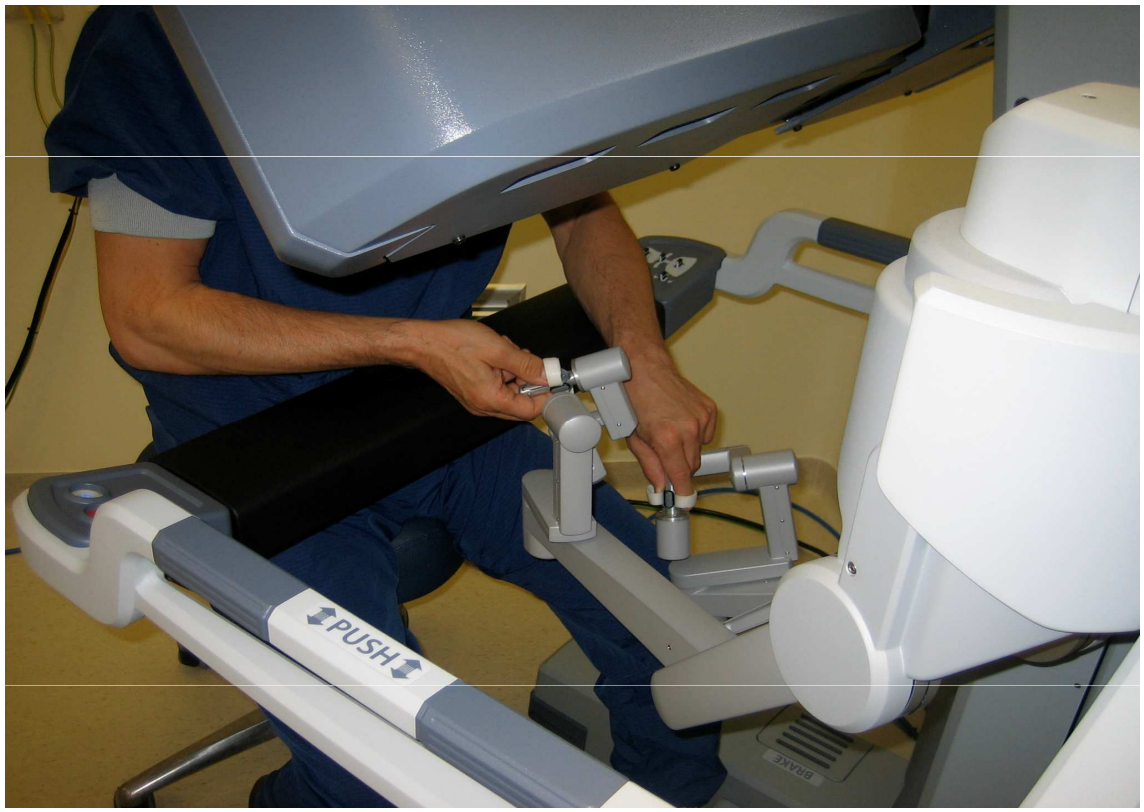


Courtesey of:
G. Smits
E. Van der Steen-Banasik

Courtesey of:
G. Smits
E. van der Steen-Banasik



Courtesey of G. Smits

Laparoscopic view

Cystoscopic view

Courtesey of G. Smits

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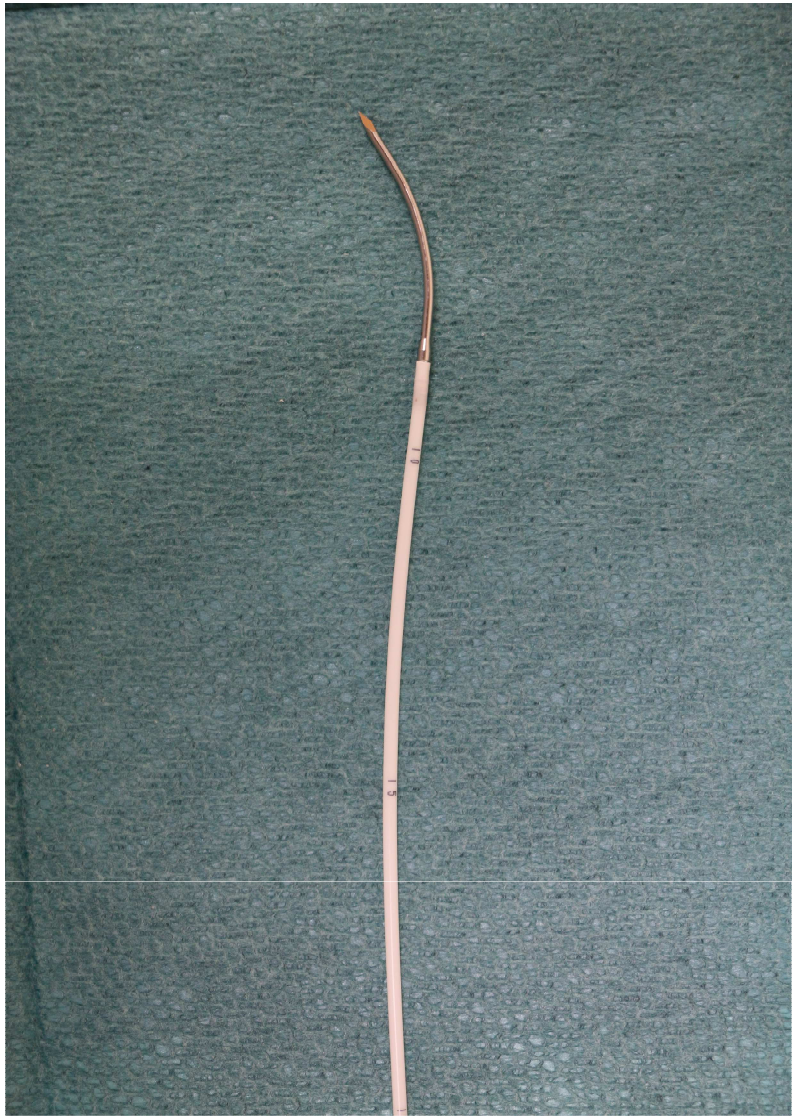

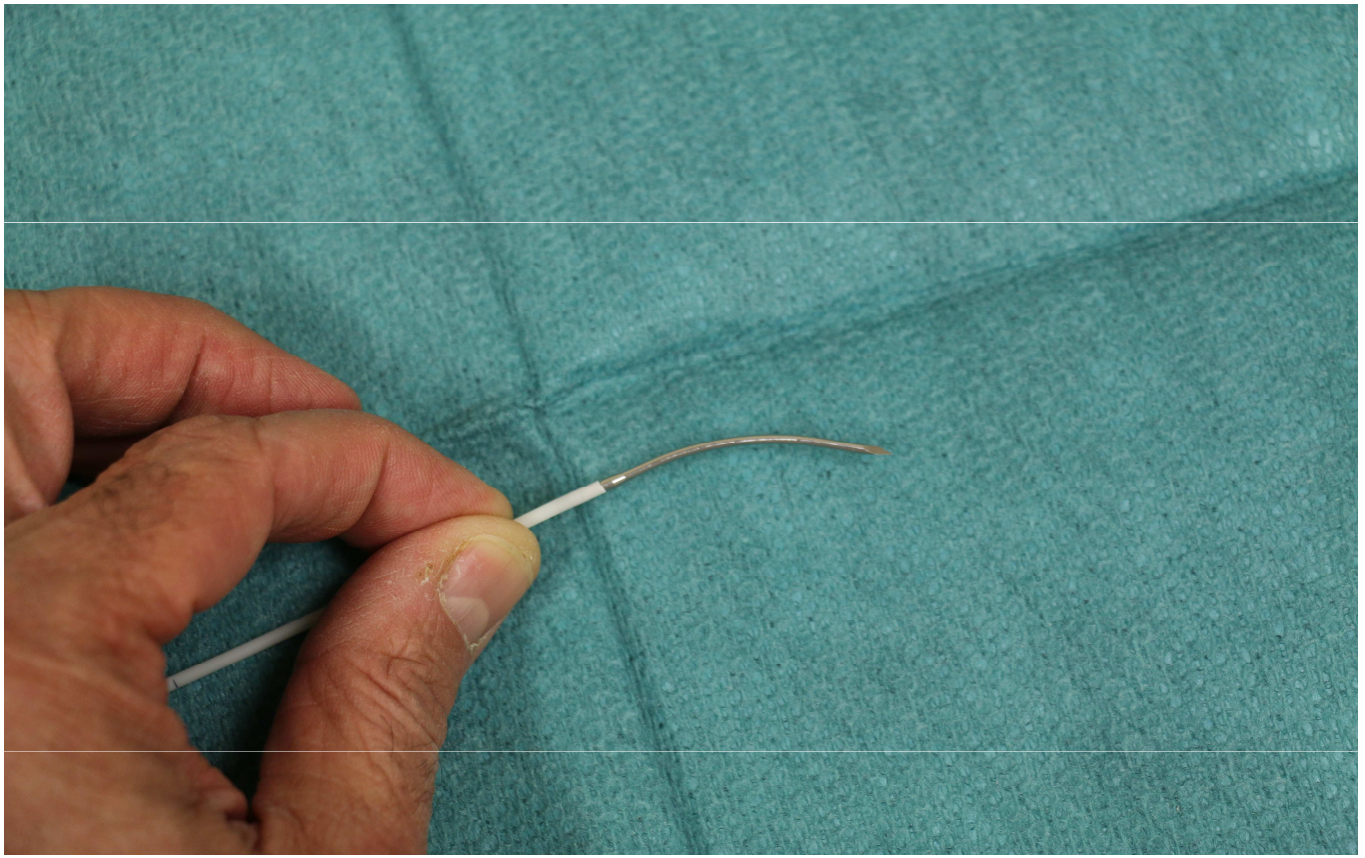

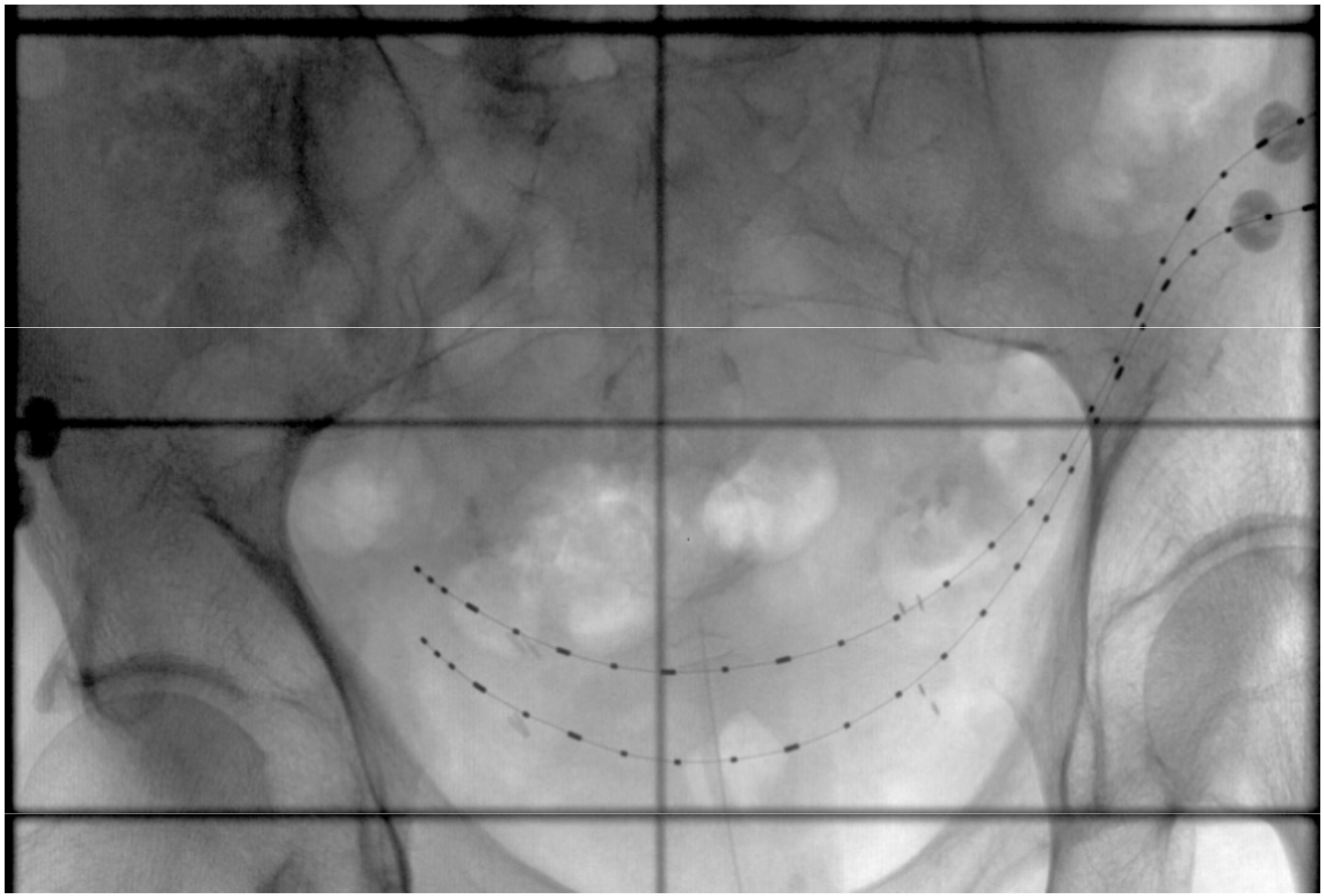

Laparoscopic implant

Courtesey of E. van der Steen-Banasik

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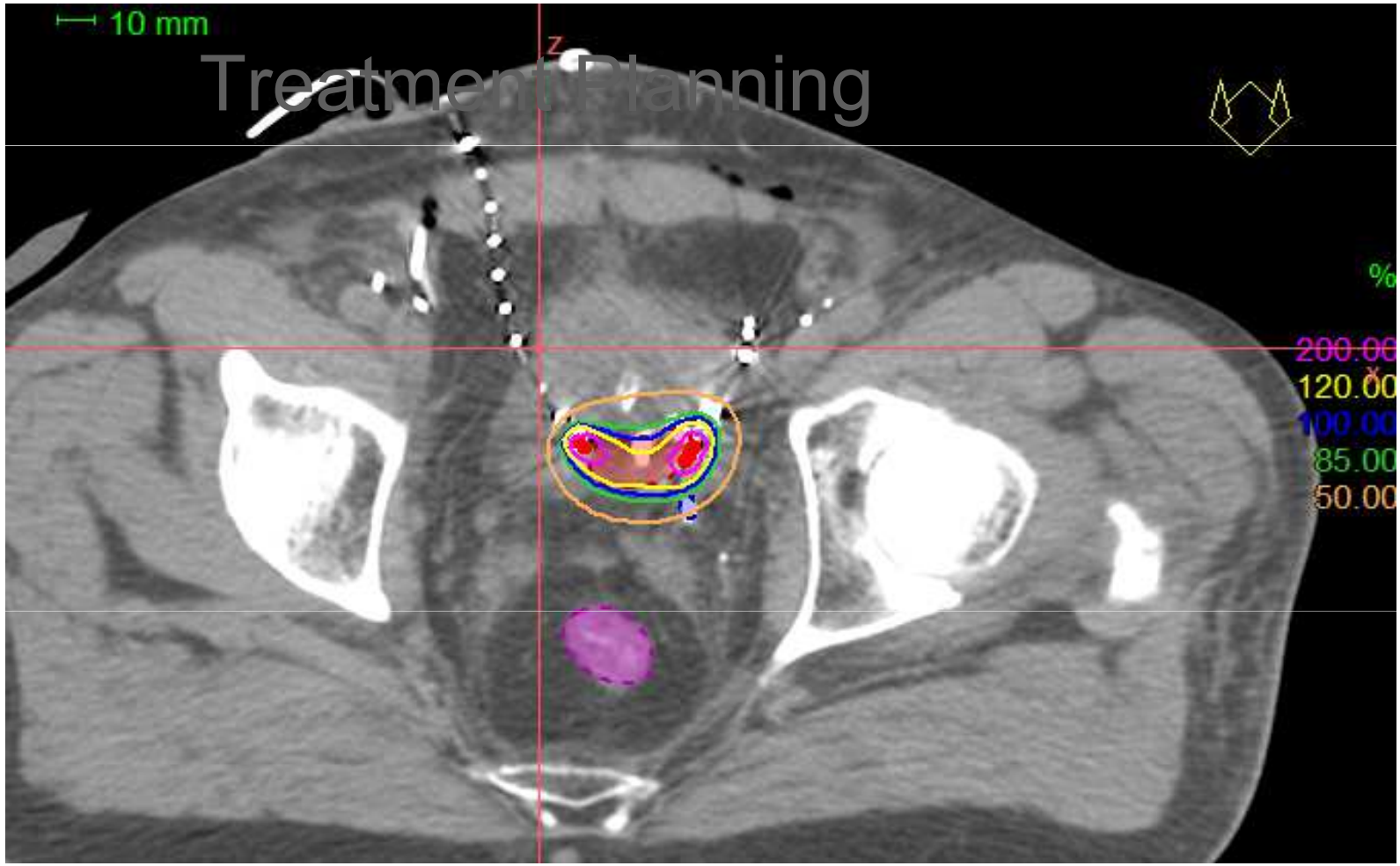
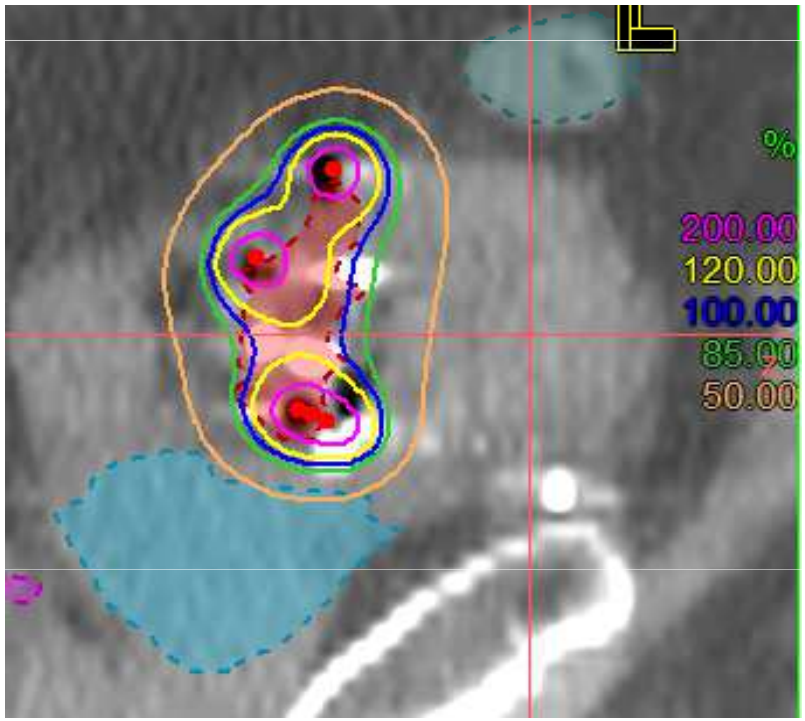
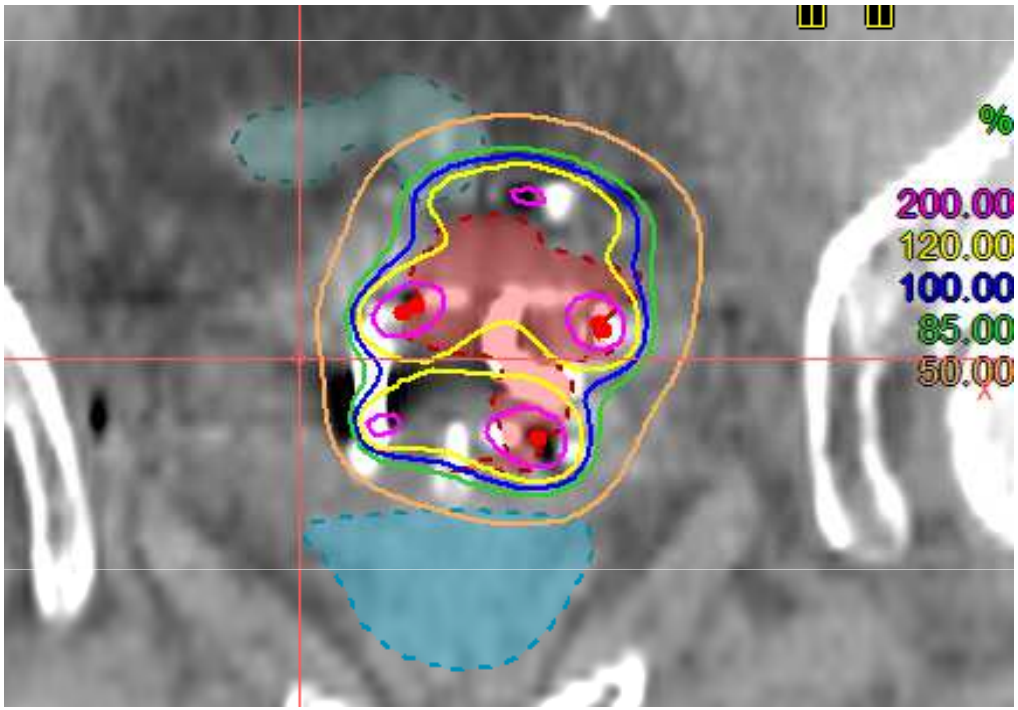
Treatment Planning







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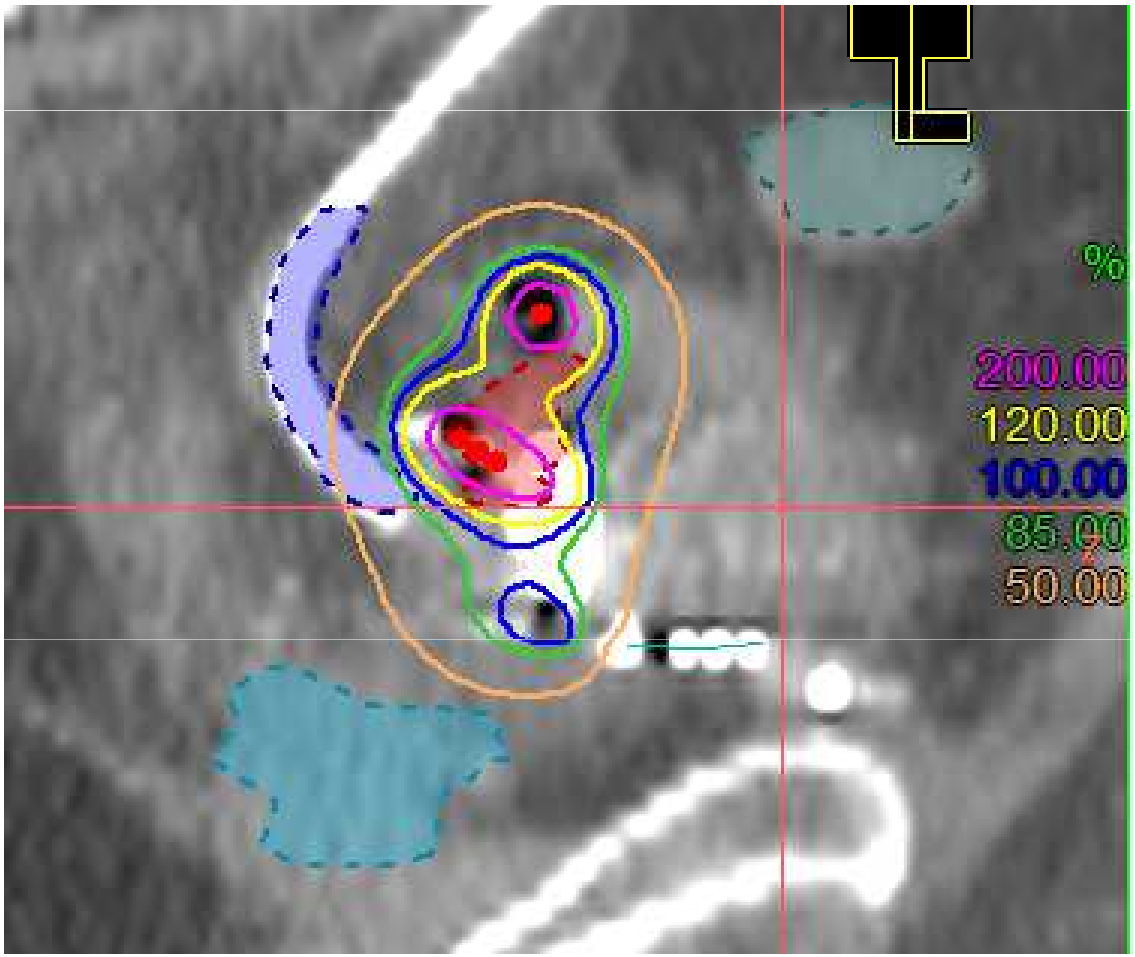
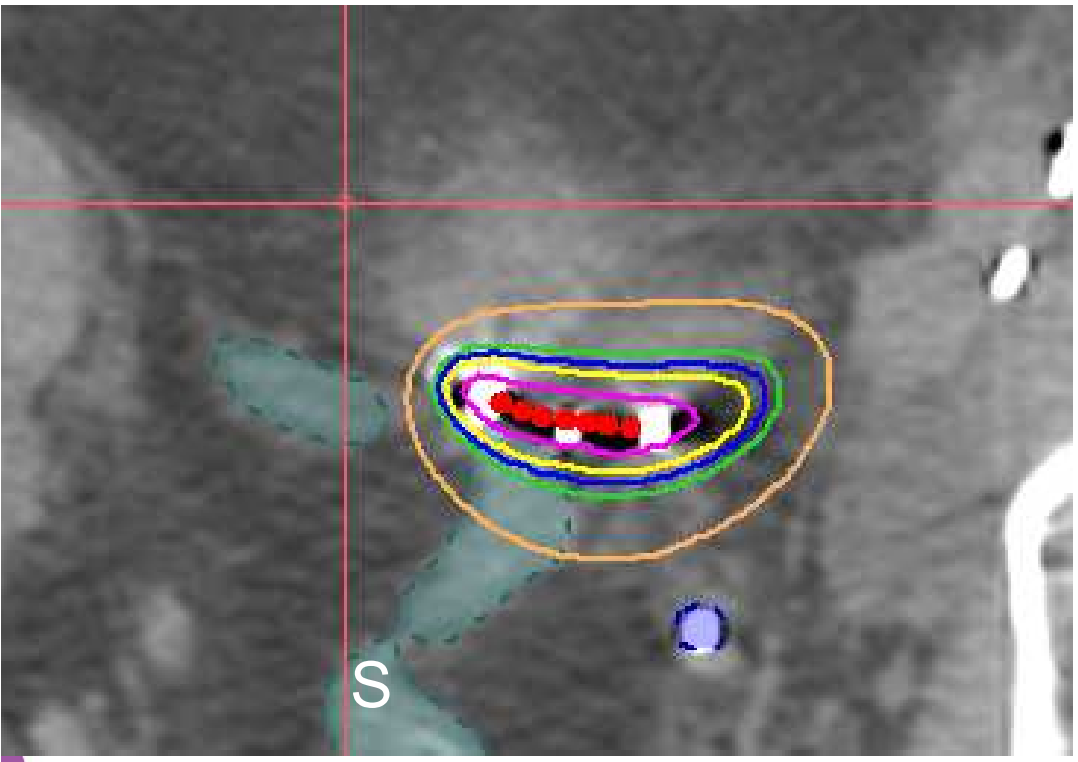
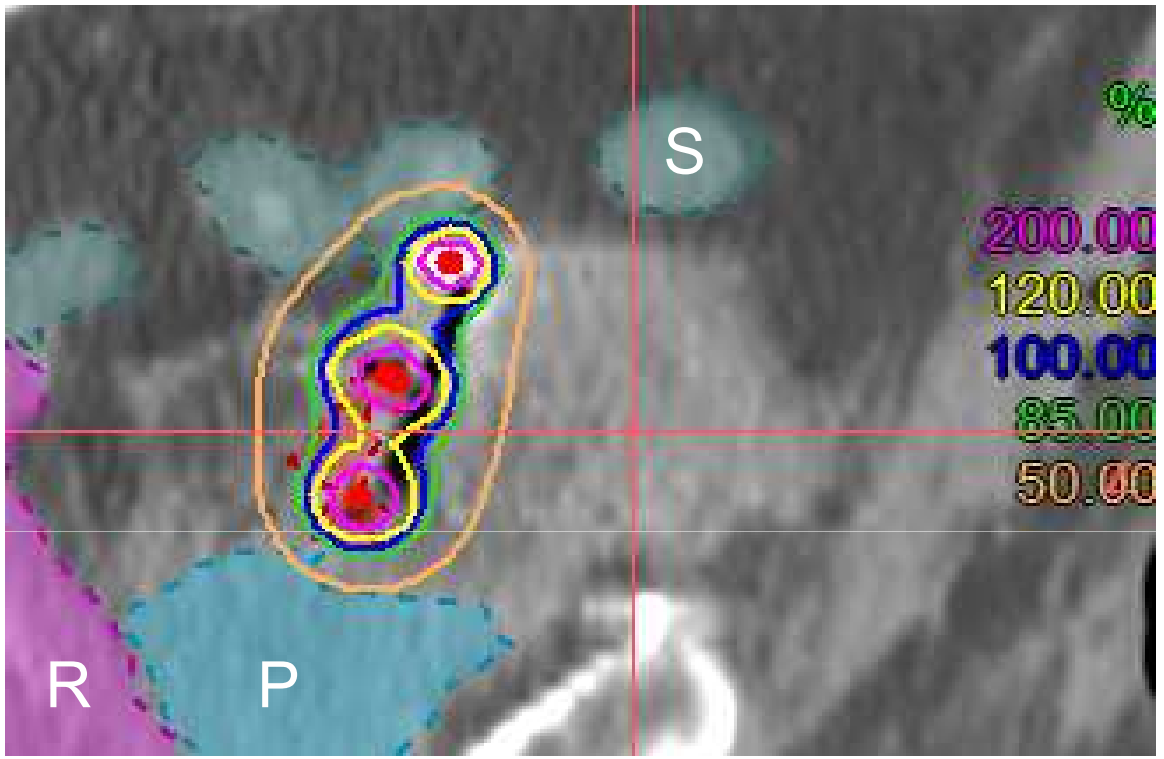
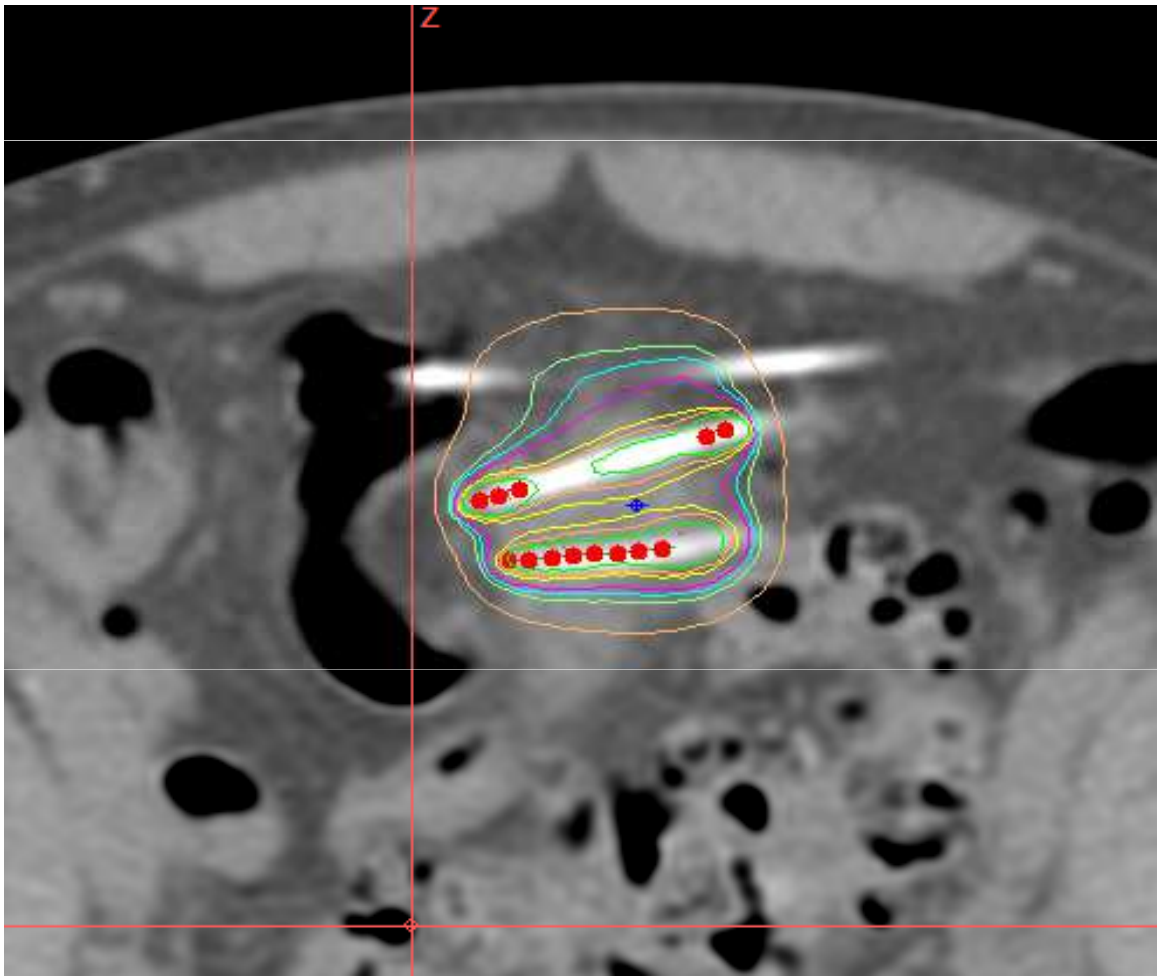

%
200.00
120.00
100.00
85.00
50.00

Sigmoid






Z

- Solitary tumors
- ≤ 5 cm
- pT1-2, (small pT3)
- Preferably not located in the bladder neck for sectio alta technique. For robot-assisted less problematic

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Recent Publications
Results

Author	Reference	Year	Number of patients		5-year		
					Local control	Cause-specific survival	Overall survival
De Crevoisier	(33)	2004	58	T1 T2 T3	100% 65% 62%	100% 70% 38%	69% 60% 38%
Nieuwenhuijzen	(30)	2005	108	T1-T2	-	75%	65%
Blank	(20)	2007	122	T1-T3	76%		73%
Onna	(34)	2008	111	T1-T2	-	82%	70%
van der Steen-Banasik	(22)	2009	89	T1-T2	-	71%	57%
Koning	(21)	2012	1040	T1-T3	75%	-	62%
Aluwini	(31)	2013	192	T2-T3	80%	75%	66%

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original article

Annals of Oncology 0: 1–6, 2012
doi:10.1093/annonc/mds126

Brachytherapy after external beam radiotherapy and limited surgery preserves bladders for patients with solitary pT1–pT3 bladder tumors

C. C. E. Koning,[1*,†] L. E. C. M. Blank[1], C. Koedooder[1], R. M. van Os[1], M. van de Kar[1], E. Jansen[1], J. J. Battermann[2], M. Beijert[3], C. Gemaat[4], K. A. M. van Herpen[5], C. Hoekstra[6], S. Horenblas[7], J. J. Jobsen[4], A. D. G. Krol[8], M. L. M. Lybeert[9], I. E. W. van Onna[10], R. C. M. Pelger[11], P. Poortmans[12], F. J. Pos[7], E. van der Steen-Banasik[13], A. Slot[14], A. Visser[13] & B. R. Pieters[1]

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Tumor characteristics

	≤ 3 cm	> 3 cm, ≤5cm	> 5cm	unknown
Tumor size	725 (70%)	224(22%)	10(1%)	61(5,9%)
	pT1	pT2	pT3	pTx/T4
pTNM	126(12%)	797(77%)	100(9,5%)	15(1,5%)
Differentiation	Well diff	Mod diff	Poorly diff	
	13(1,3%)	167(16%)	824(79%)	
Histology	Transitional cc	Papillair trans	adenoca	
	863(83%)	114(11%)	37(3.6%)	

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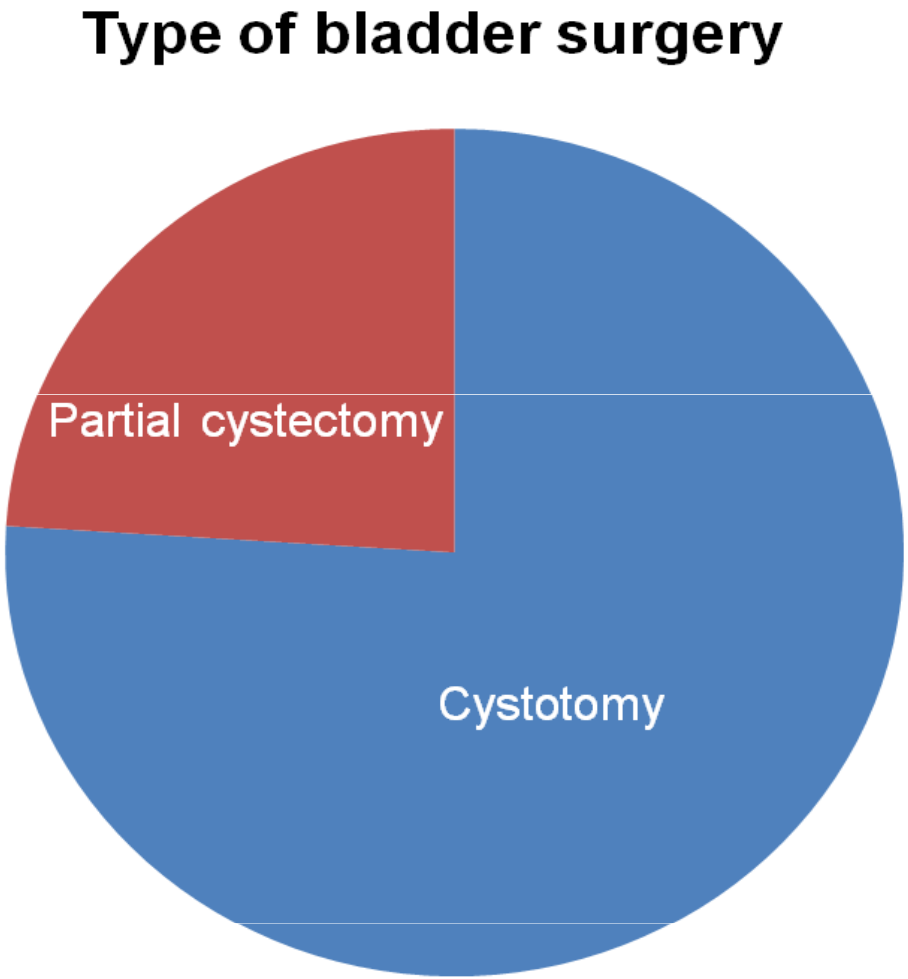
Treatment



Suprapubic cystotomy 791 (76%)

Partial cystectomy 247 (24%)

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Treatment Schedule

Low grade / low stage tumors
High grade small tumors

pT1 G1-3 pT2 G1-2 and < 3 cm	
EBRT	10 Gy
Brachytherapy	50-60 Gy

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Treatment Schedule

High grade large tumors
Low grade / low stage, large tumors
High stage

pT1 G3 and > 3 cm pT2 G1-2 and > 3 cm pT2 G3 small pT3	
EBRT	30-40 Gy
Brachytherapy	25-40 Gy

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Results

Multivariate analysis

Local recurrences: brachytherapy technique

(P<0.005)

Metastasis: tumor diameter and tumor grade

(P=0.05 and P< 0.001)

Overall survival: age, grade and tumor diameter

(P< 0.001, P=0.02, P=0.02)

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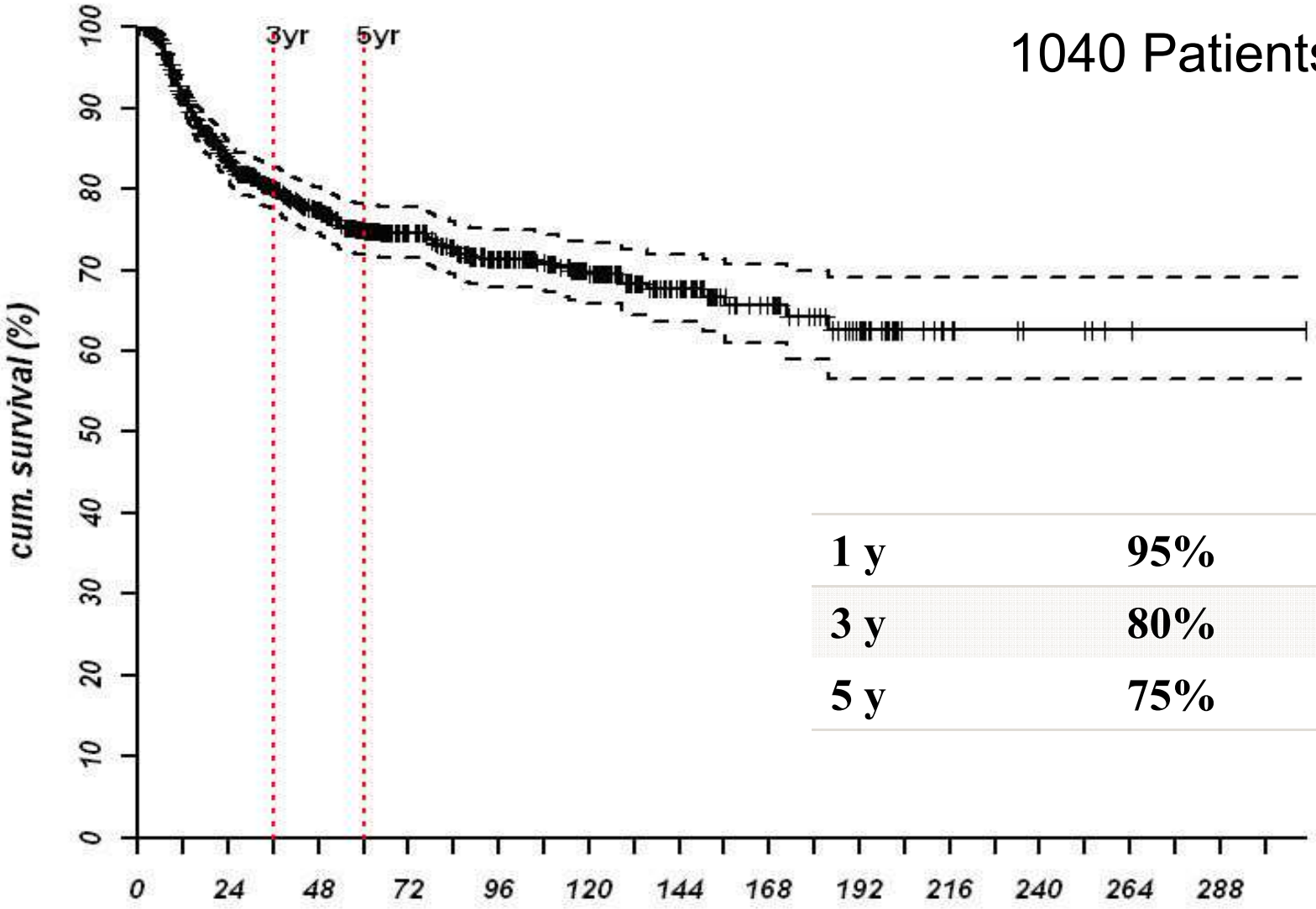
Local recurrence free survival

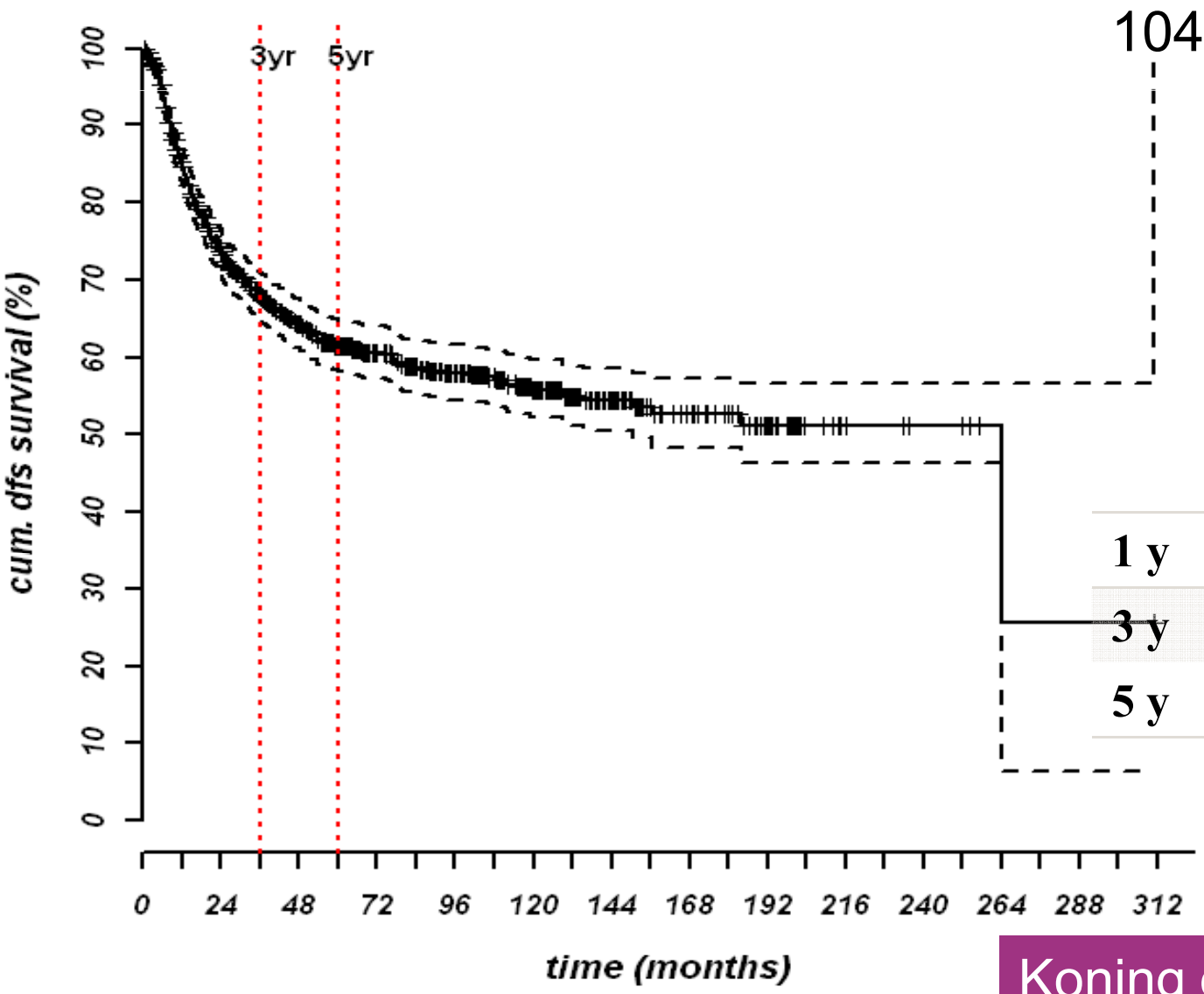


1040 Patients

1 y	95%
3 y	80%
5 y	75%

Koning et al. Ann Oncol 2012;23:2948-2953

Disease free survival

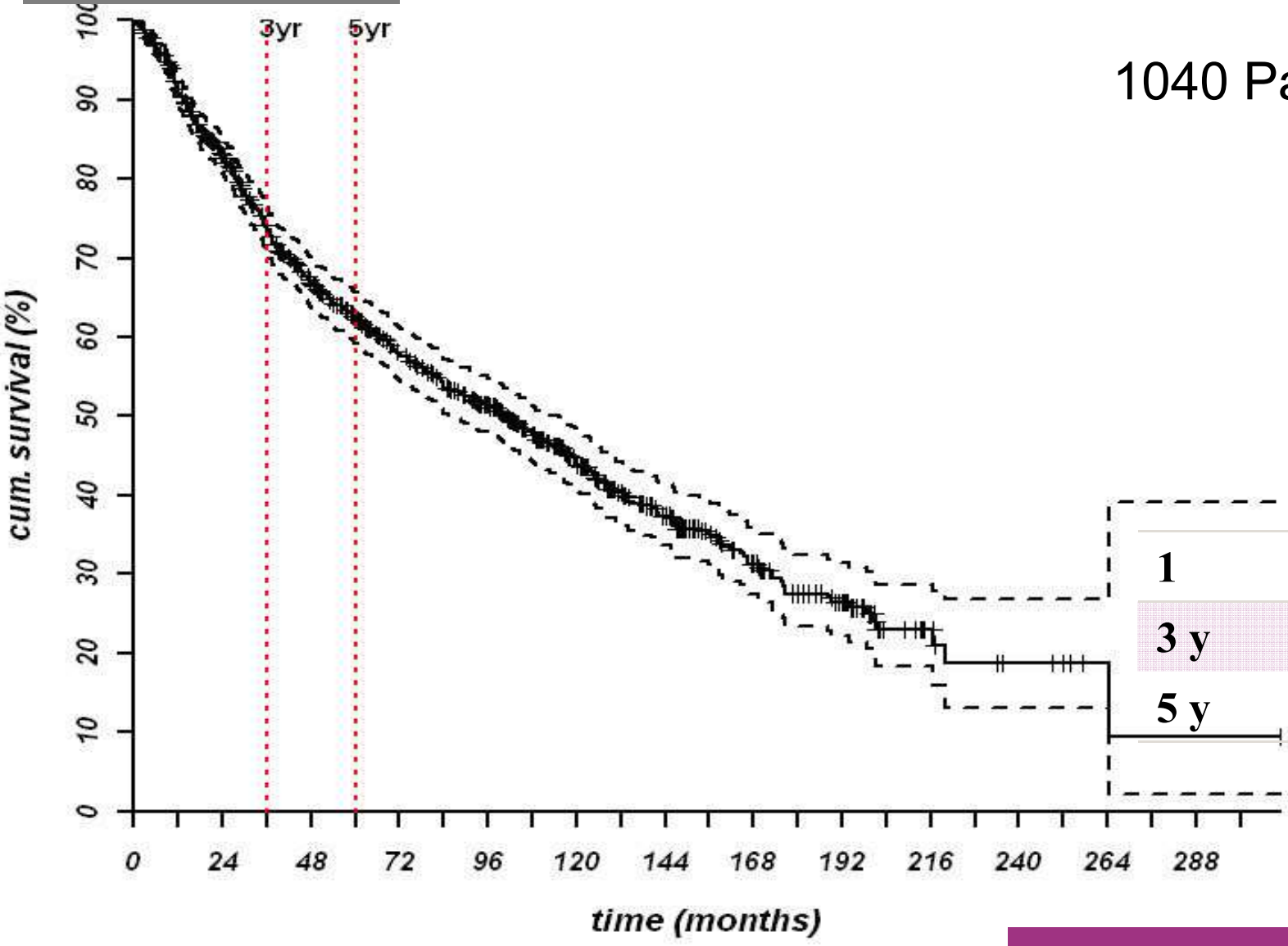


1040 Patients

1 y	85%
3 y	68%
5 y	61%

Koning et al. Ann Oncol 2012

Overall survival



1040 Patients

1	91%
3 y	74%
5 y	62%

Koning et al. Ann Oncol 2012

Cystectomy series

	Year	N	5y RFS (%)	10 y OS (%)	Local recurrence only (%)
Stein	2001	1176	68	43	7
Madersbacher	2003	552	62	37	8
Hautmann	2006	841	65	45	9

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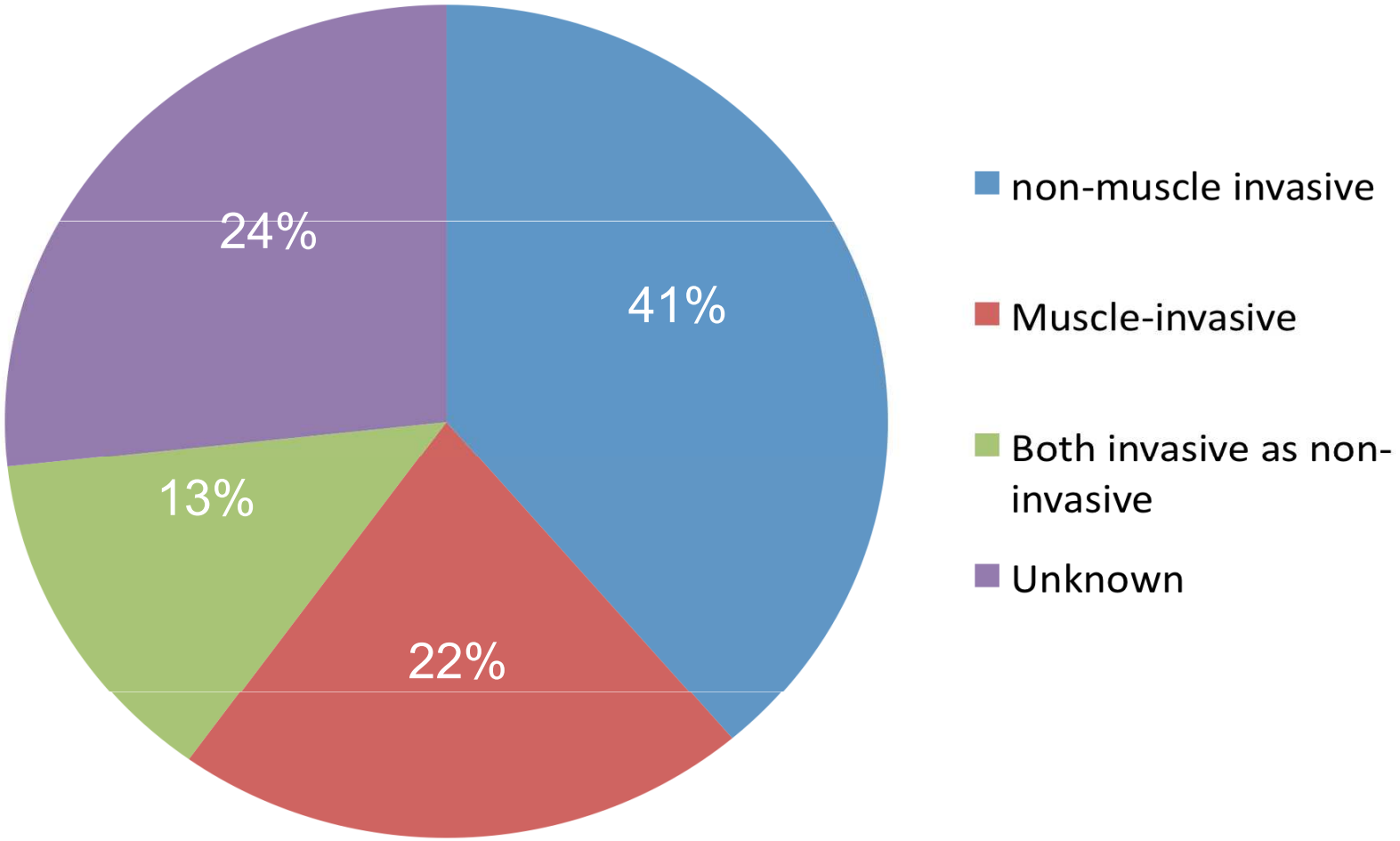
Relapse

232 (22%) bladder relapses



8% invasive relapses

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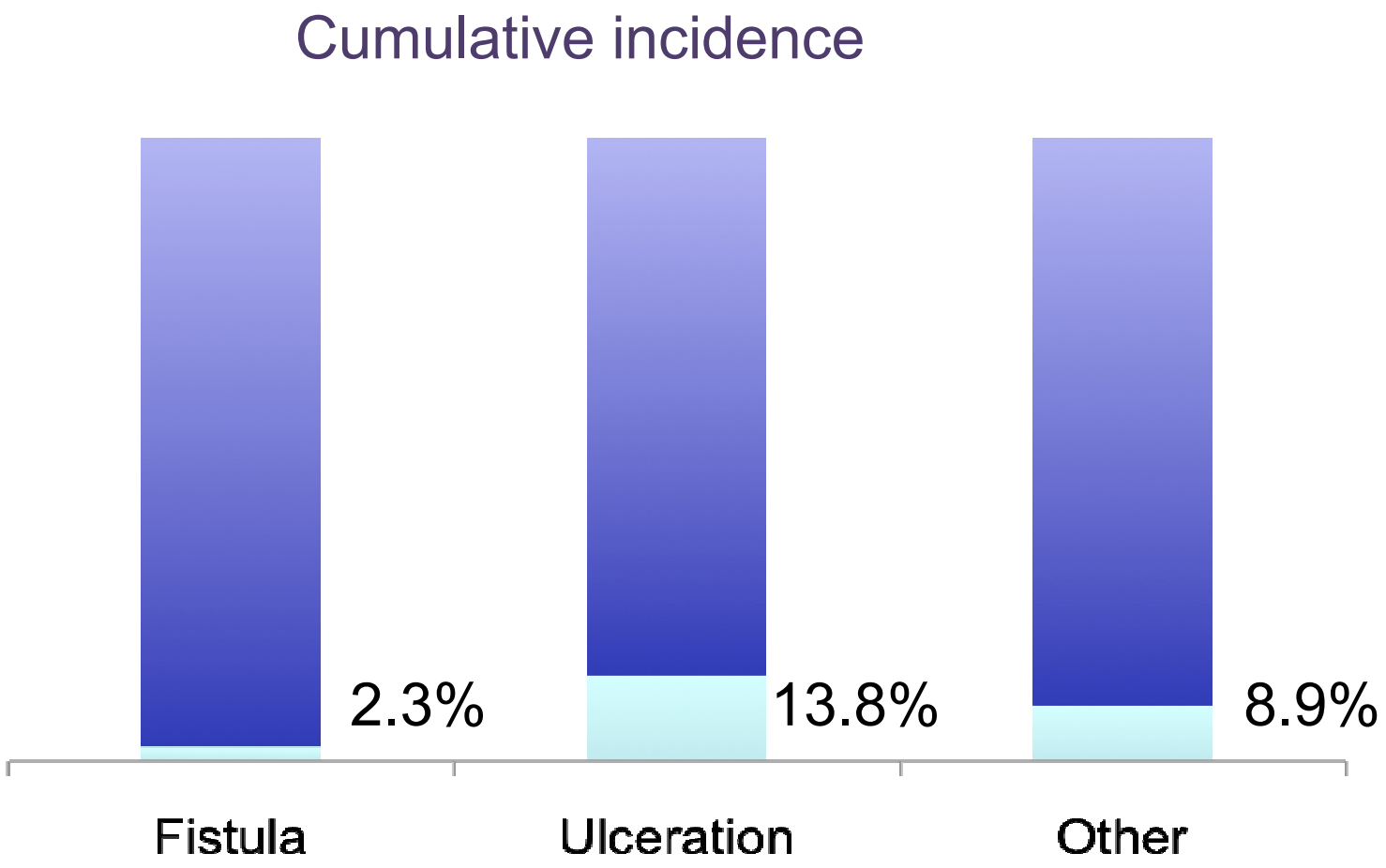
Cumulative incidence
2.3%
13.8%
8.9%
Fistula
Ulceration
Other

Conclusion

Largest cohort on bladder brachytherapy

Local control at 5 years: 75%

Comparable to cystectomy series

Brachytherapy should be offered and discussed with patients

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Conclusion

- Bladder brachytherapy a solution for bladder preservation in MIBC
- Laparoscopic / Robot-assisted technique is emerging
- Start a team-work with an urologist and radiation oncologist

The AMORE Protocol: a concept for local treatment of Orbital and H&N RMS of childhood

Bradley Pieters

Academic Medical Center / University of Amsterdam

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Outline

1. The AMORE concept
2. Examples
3. Results Up-front AMORE 1993-2007
4. AMORE as Salvage treatment
5. Conclusions

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The AMORE Concept

- Ablatio
- MOld technique Brachytherapy
- REconstruction

in 1 week

Dilemmas in local therapy of non-orbital HNRMS

- **1. Naive patients:**
  - -delayed surgery
    - risk of mutilation
    - difficult accessibility parameningeal sites
  - -external beam radiation therapy (EBRT)
    - high-doses, wide fields, young children
    - serious sequelae
- **2. Relapsed patients:**
  - -effective salvage strategies lacking!

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Methods AMORE: First Surgical Session Day 1

- **Macroscopically complete resection** (microscopic residual)
- Sparing normal tissue
- Adequate exposure brachytherapy

- **Insert brachytherapy mold(s)**

  material: -Gutta Percha

  -FastForm Percha (polymer; FastForm Research Ltd)

  -Flexible catheters (Polyethylene)

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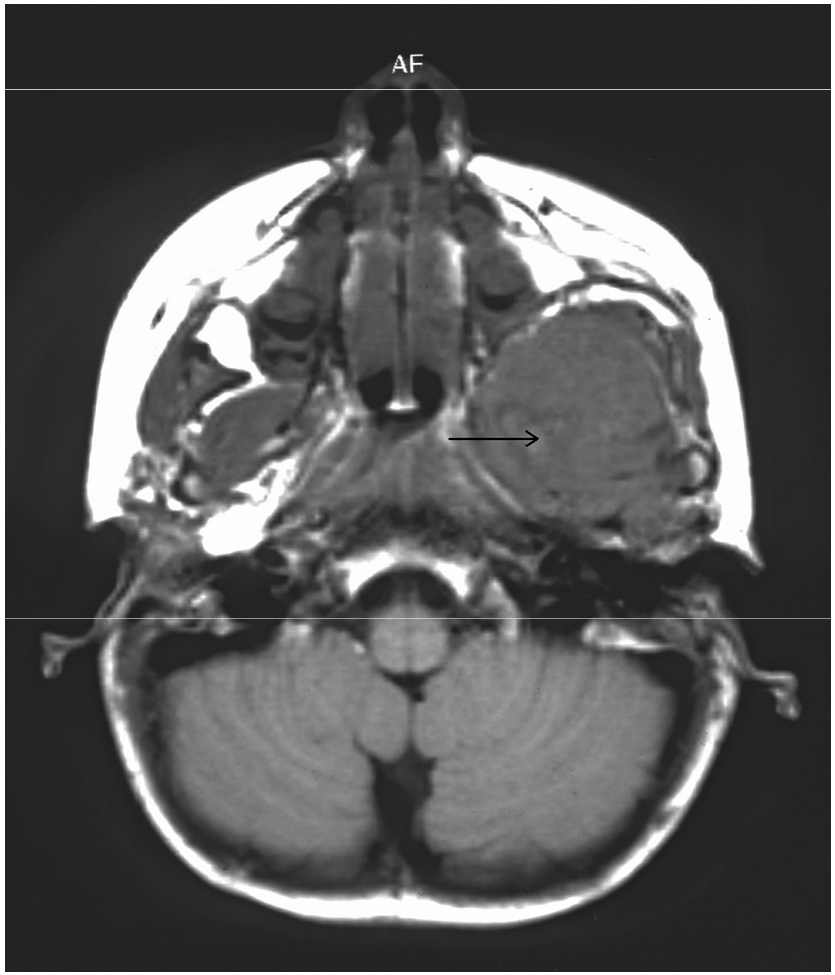
RMS in left pterygoid fossa



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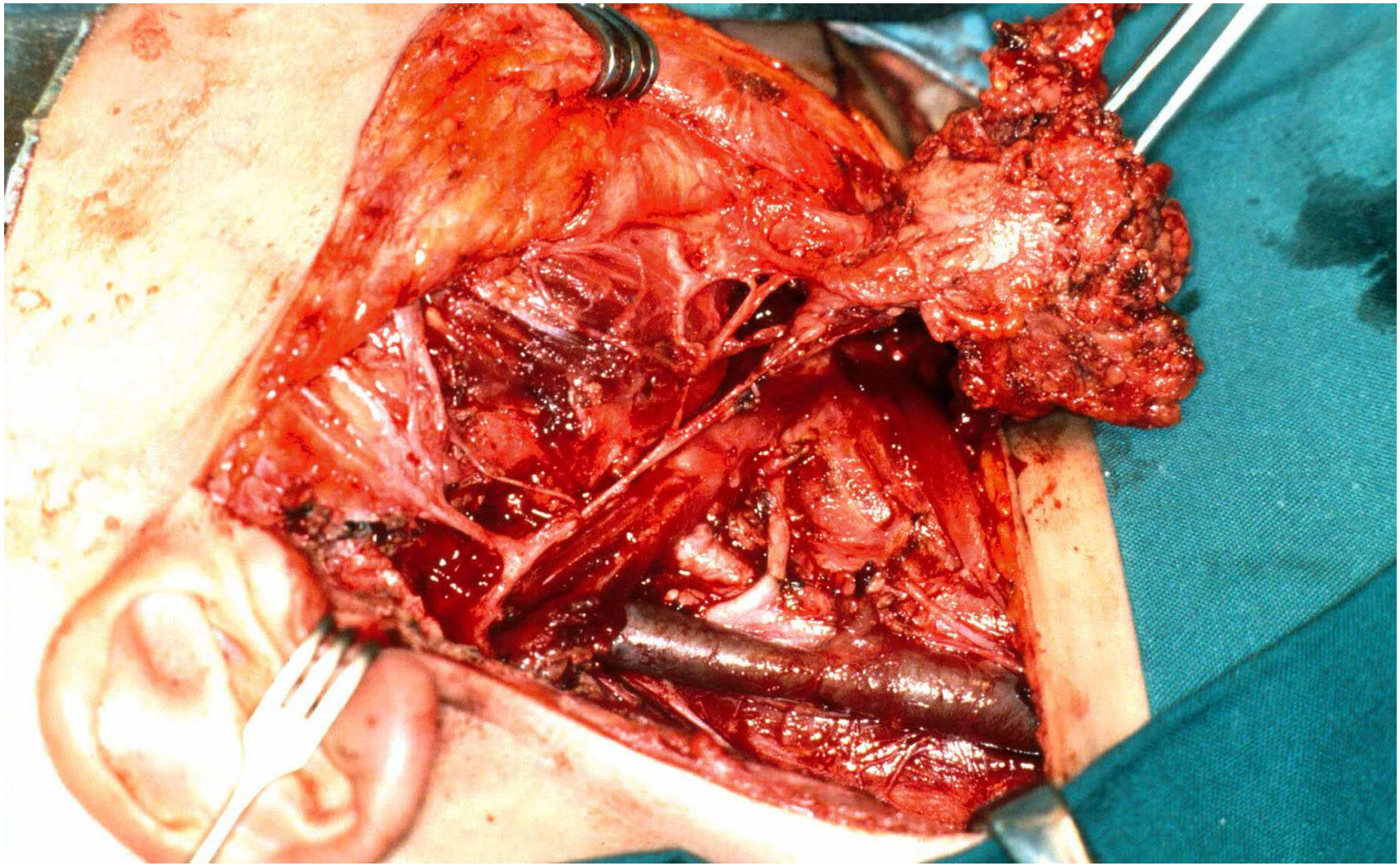
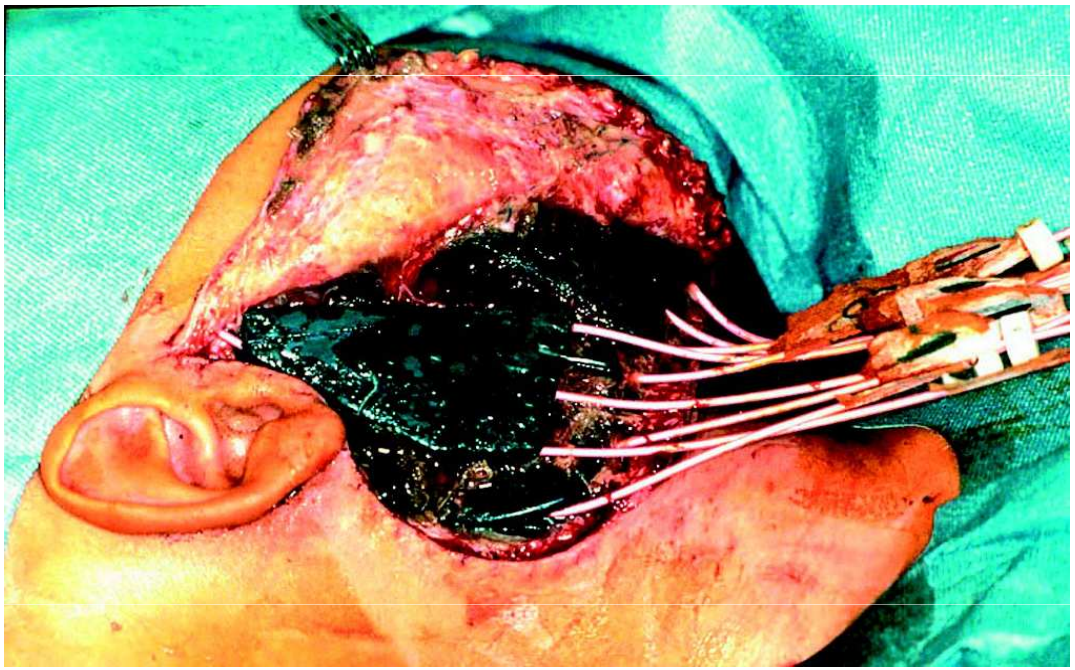
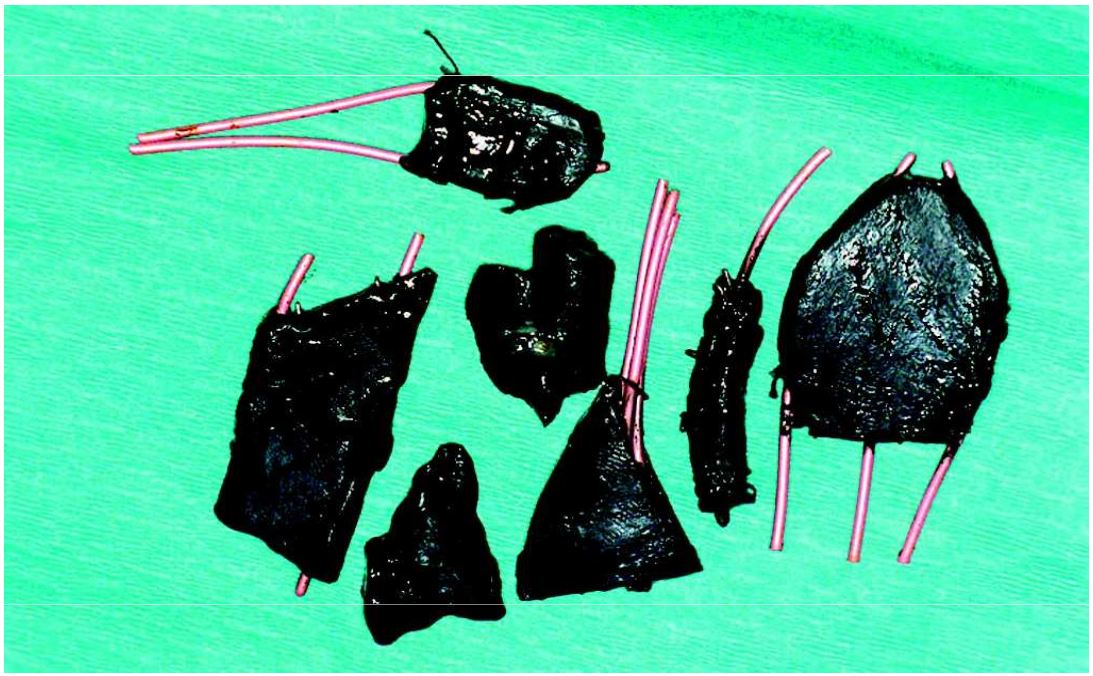
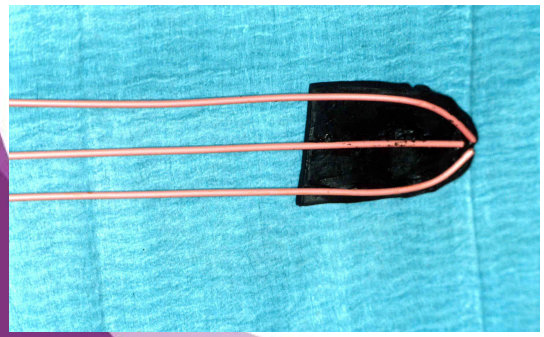
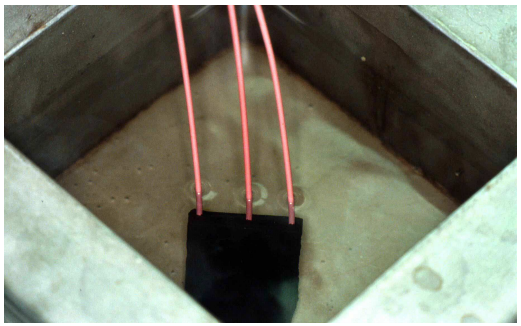


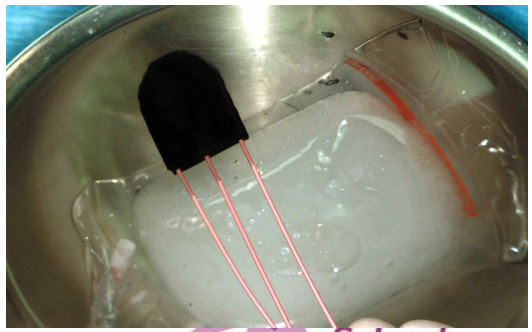
MOld placement





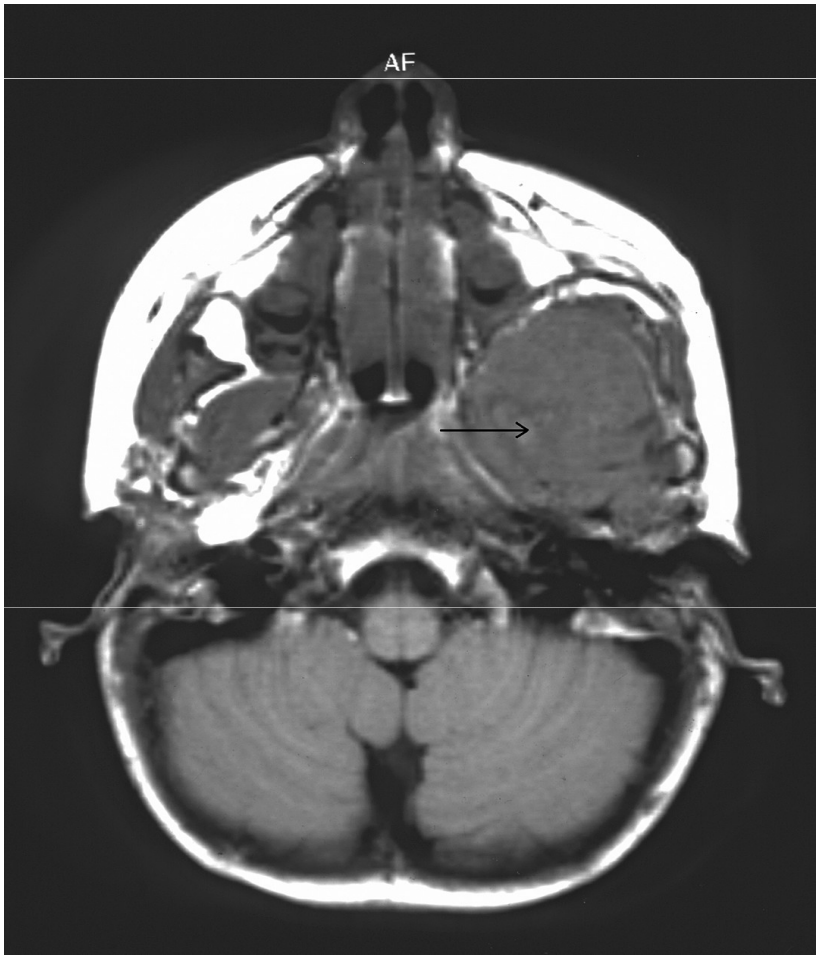


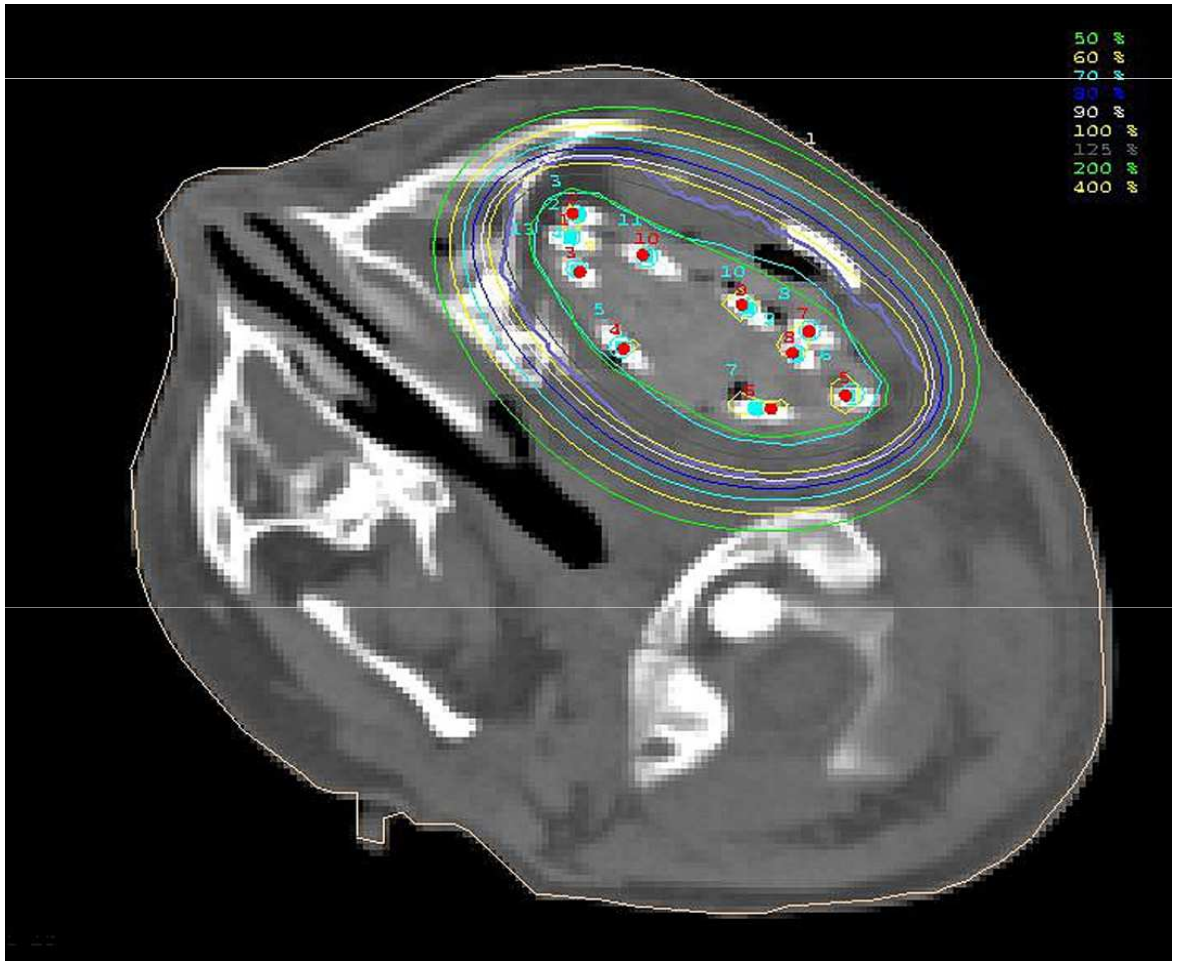




Postoperative AMORE Day 1

Planning of dose distribution





Brachytherapy (day 3-5)

- Verification mold position in relation to Clinical Target Volume

- Computer-aided dose planning (LDR/PDR)
  - 40-45 Gy to CTV
  - 5mm from surface of the mold

- Afterloading Iridium192
  - dose delivery 3-4 days

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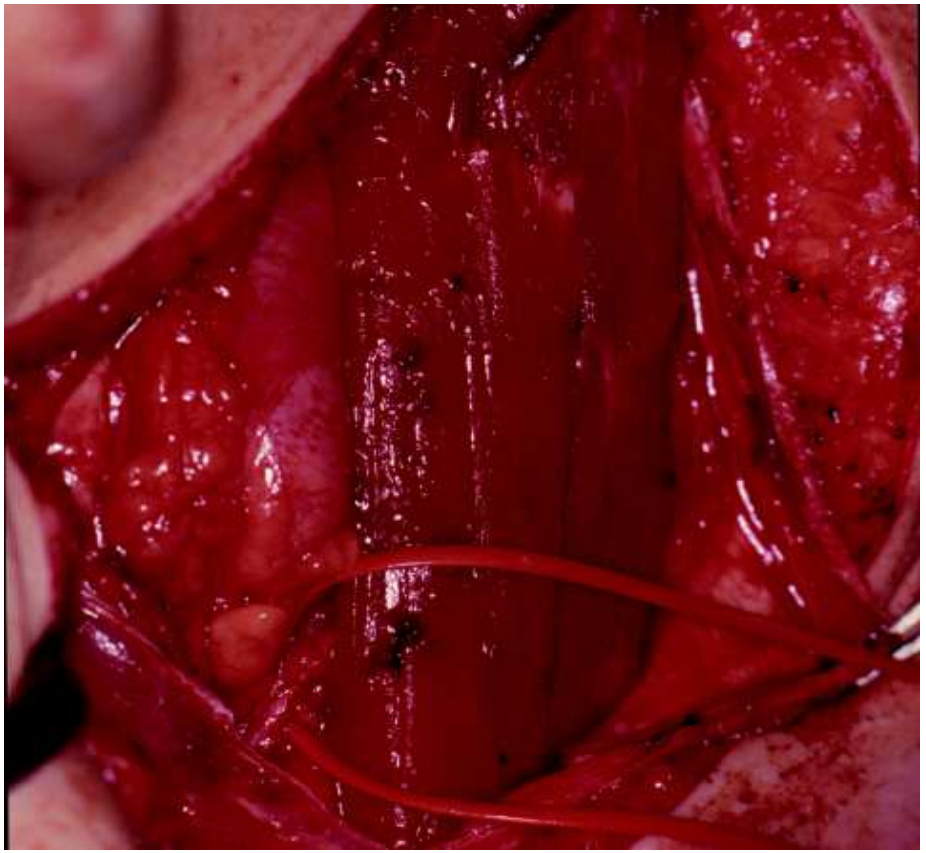
REconstruction: AMORE II

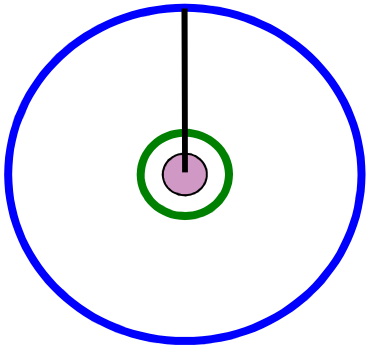
- Remove mold
- Surgical reconstruction

  -Free vascularised (microanastomosis)

  or -Transpositional muscle flap

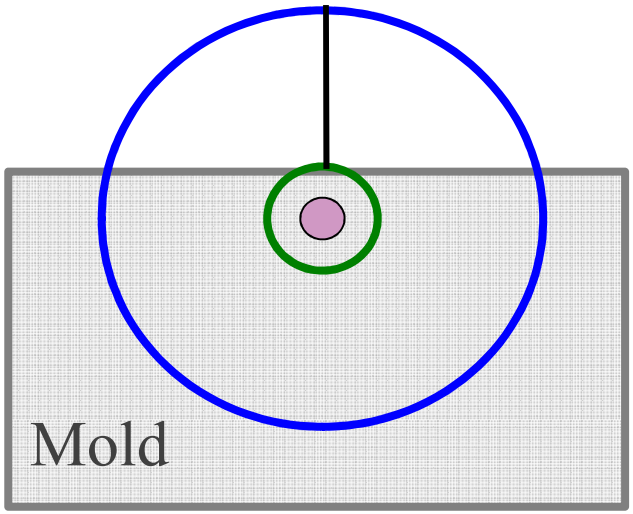
REconstrucion

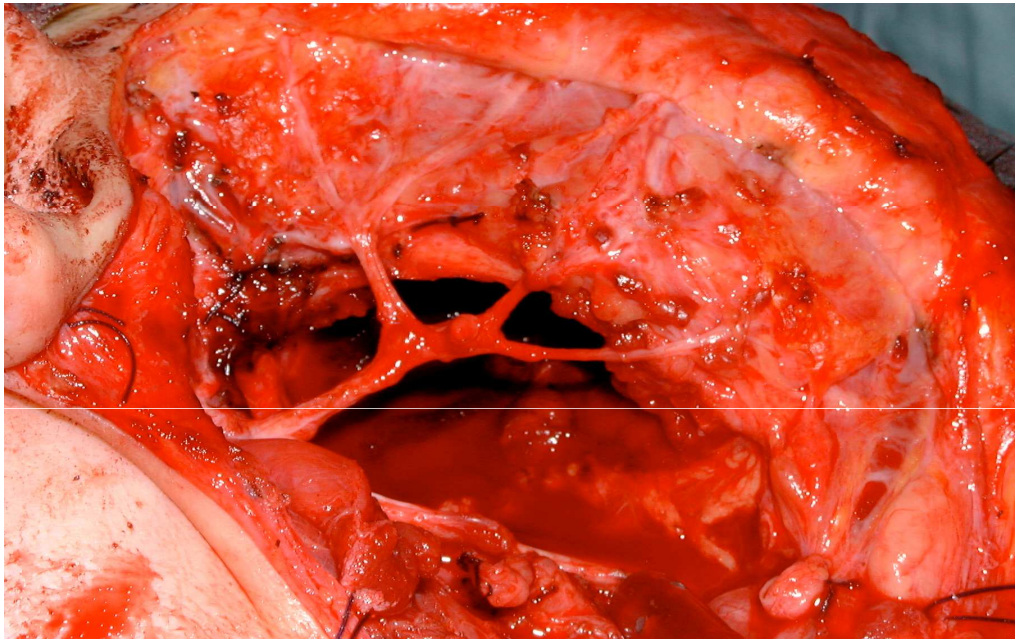


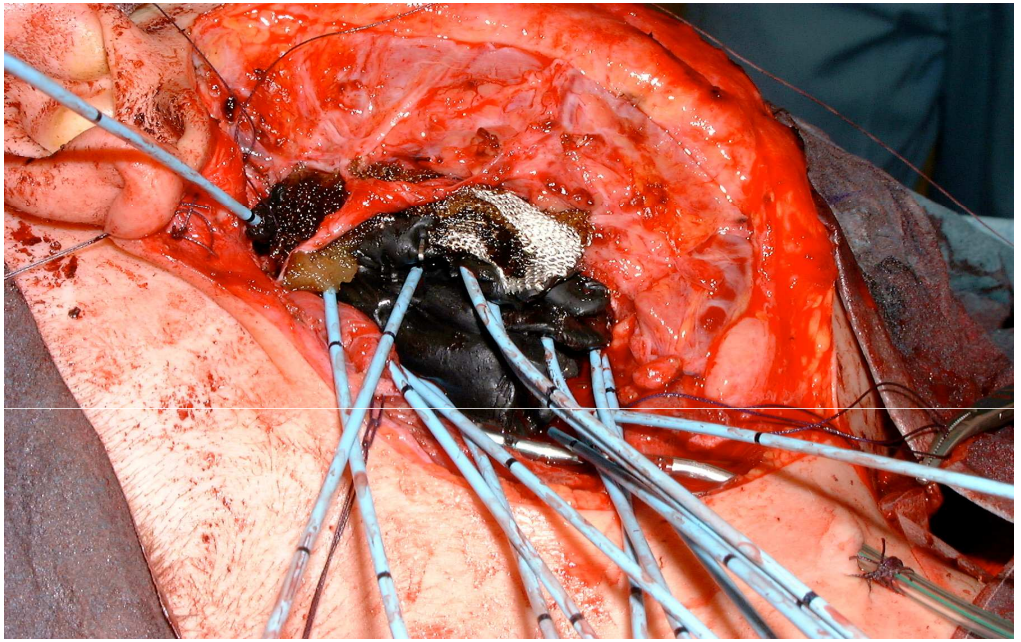


100% isodose

200% isodose







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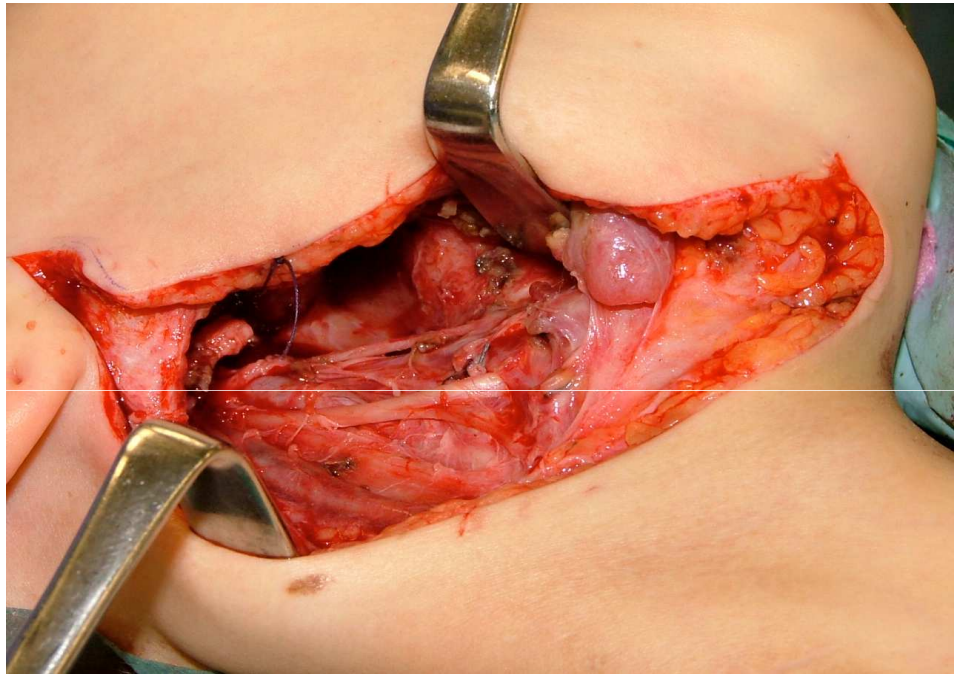
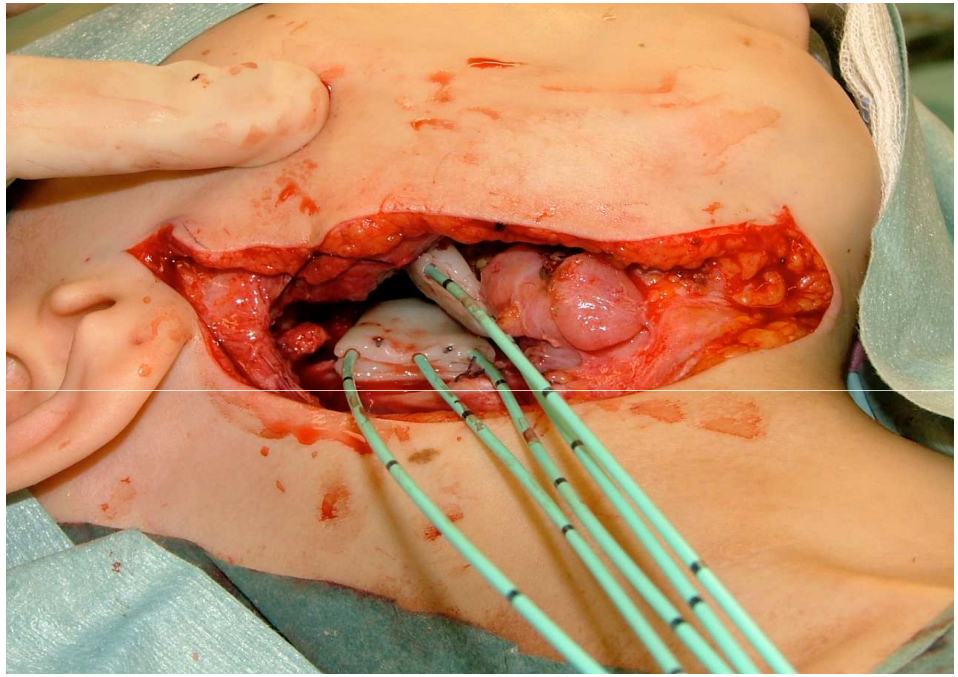
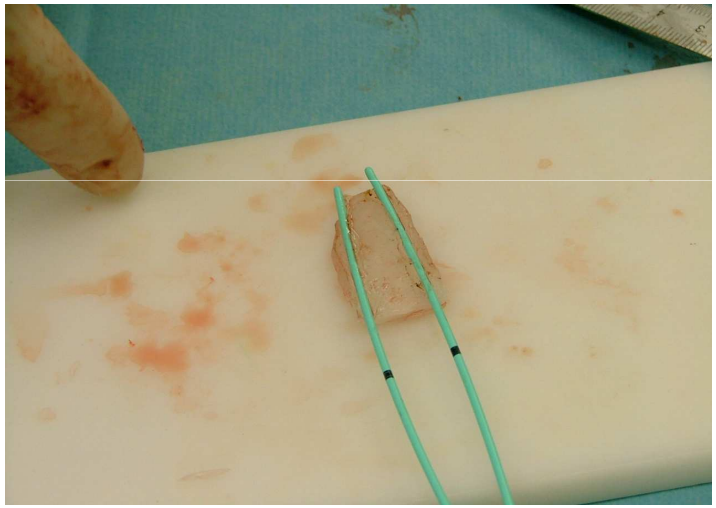
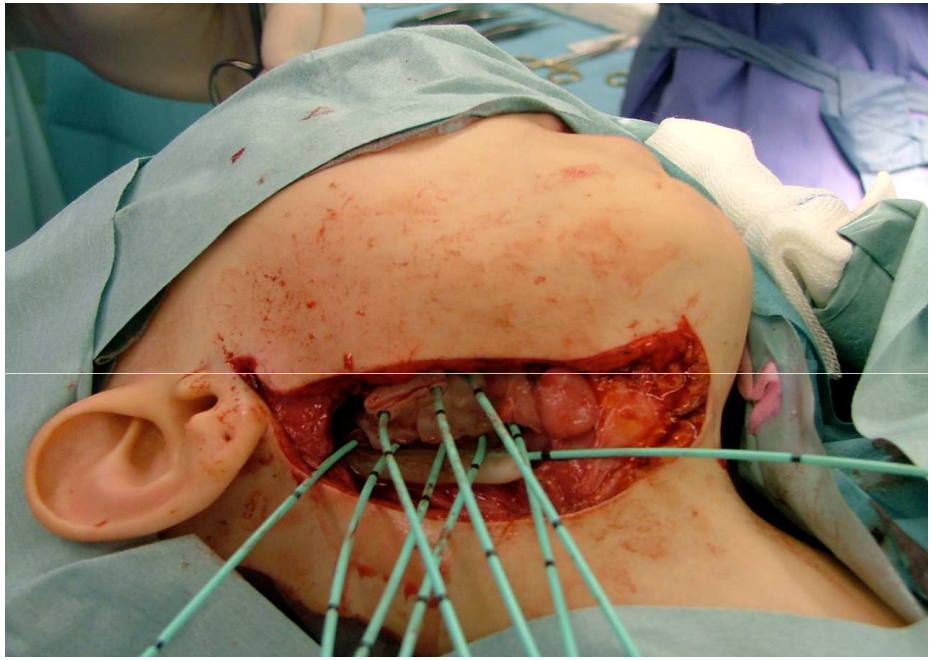


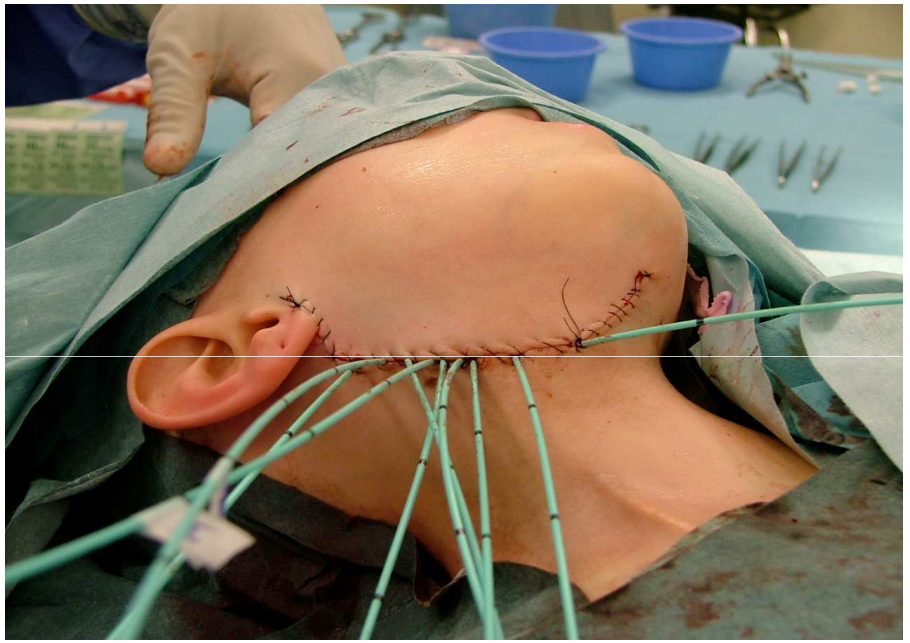


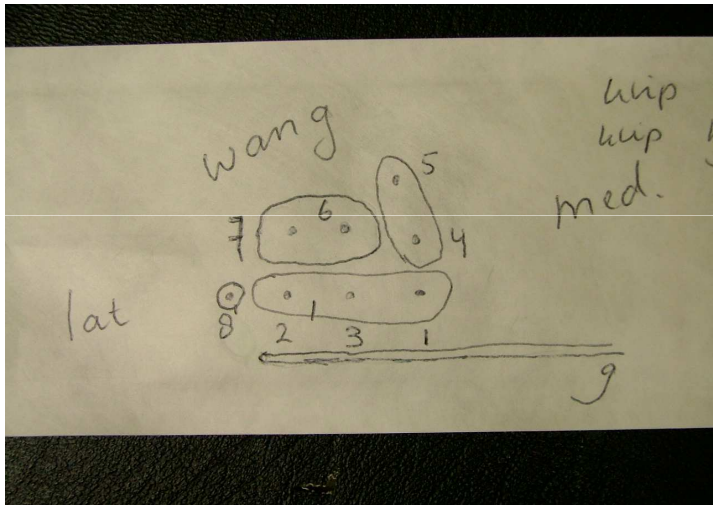


FastForm Percha

FastForm Research Ltd



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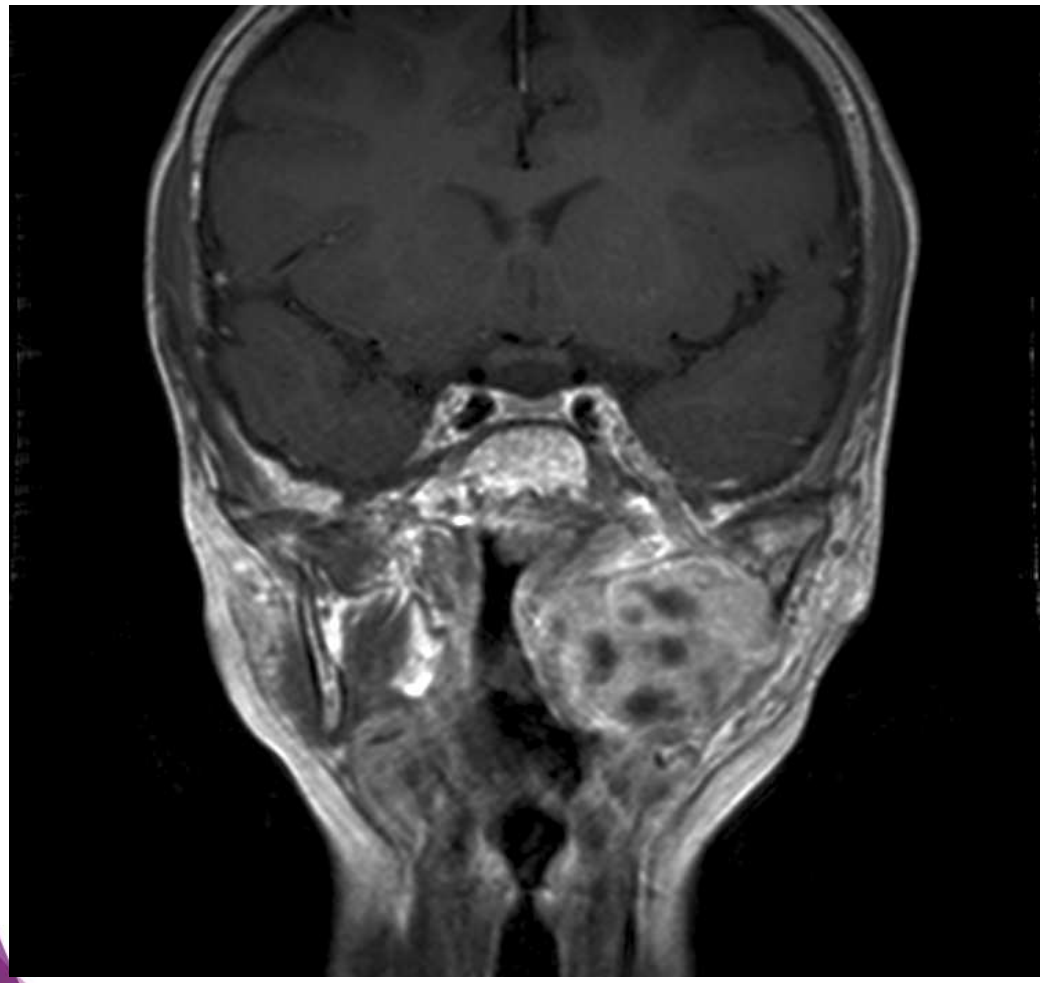
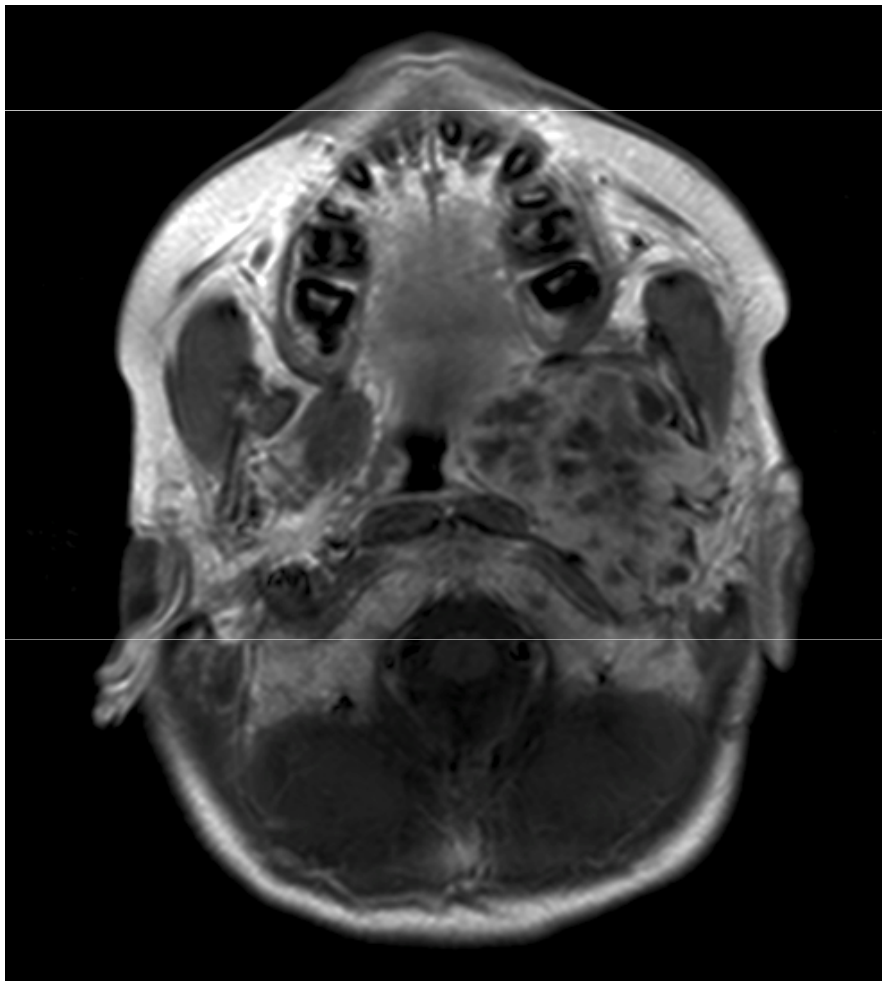
Recurrence after chemotherapy and EBRT





Before salvage chemotherapy

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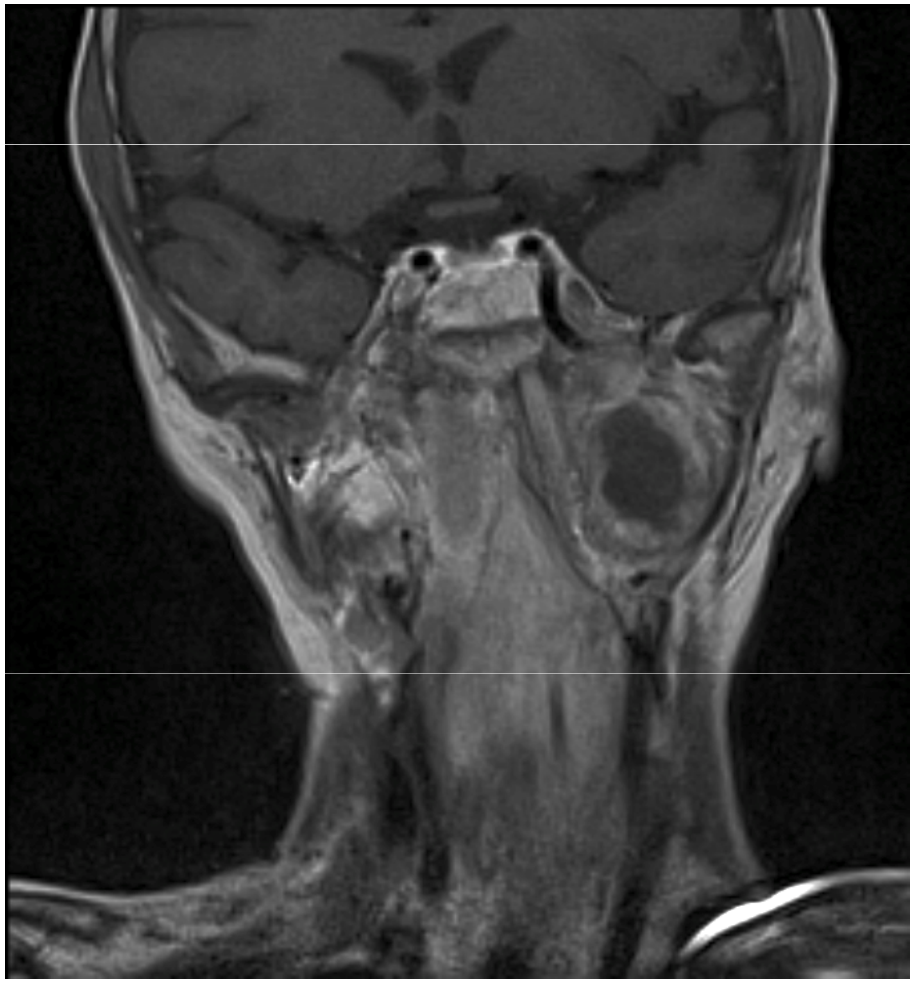

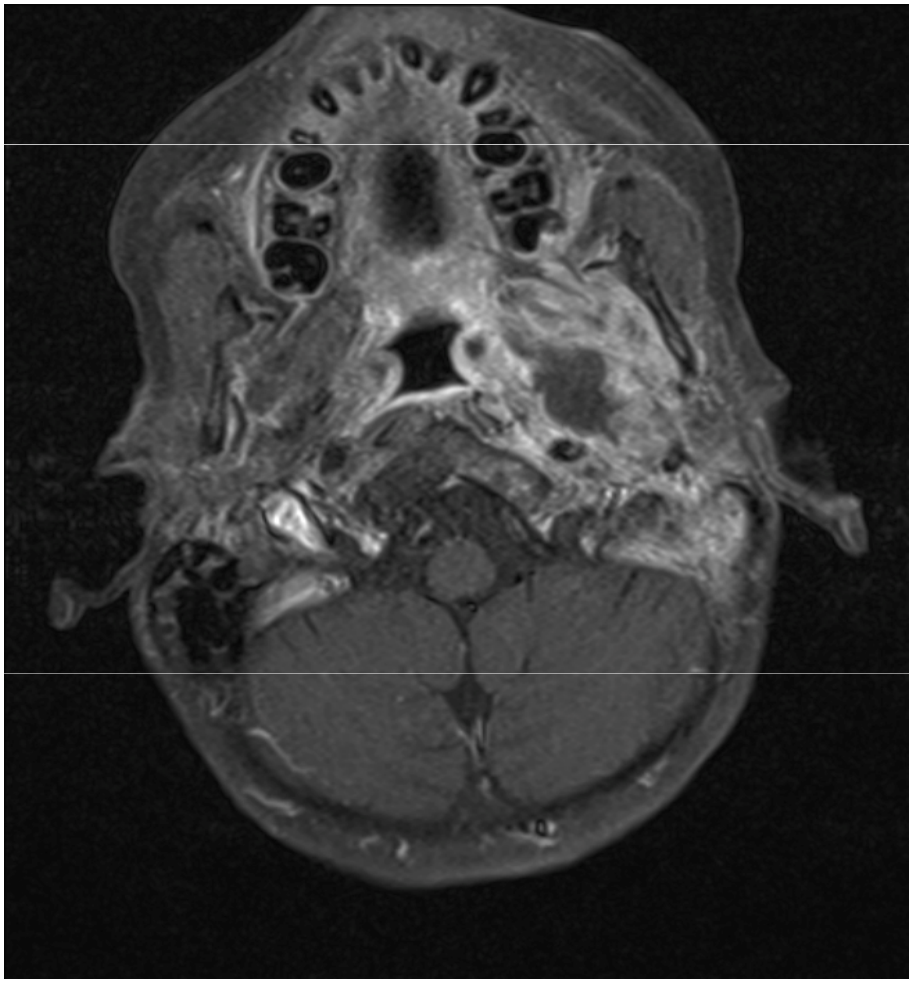

After salvage chemotherapy

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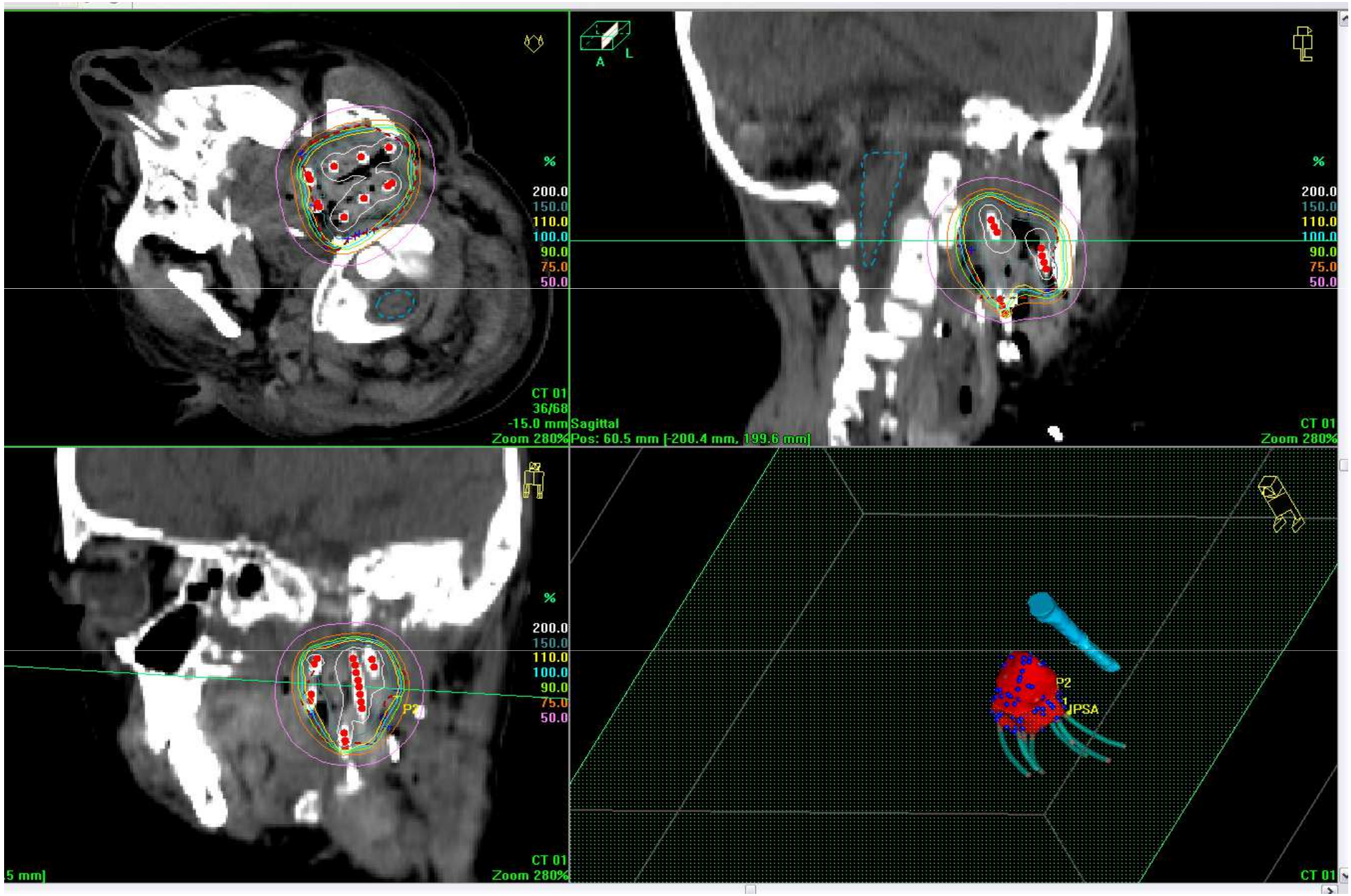

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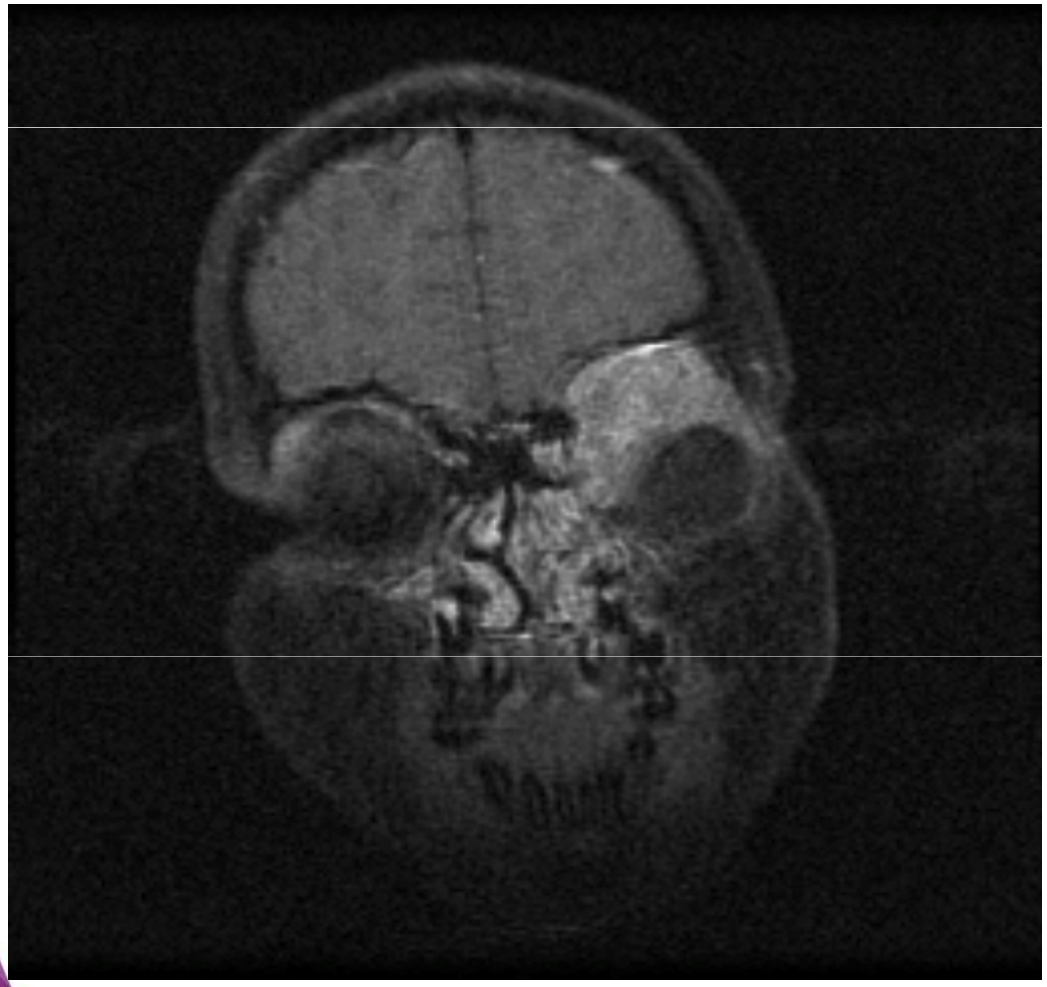
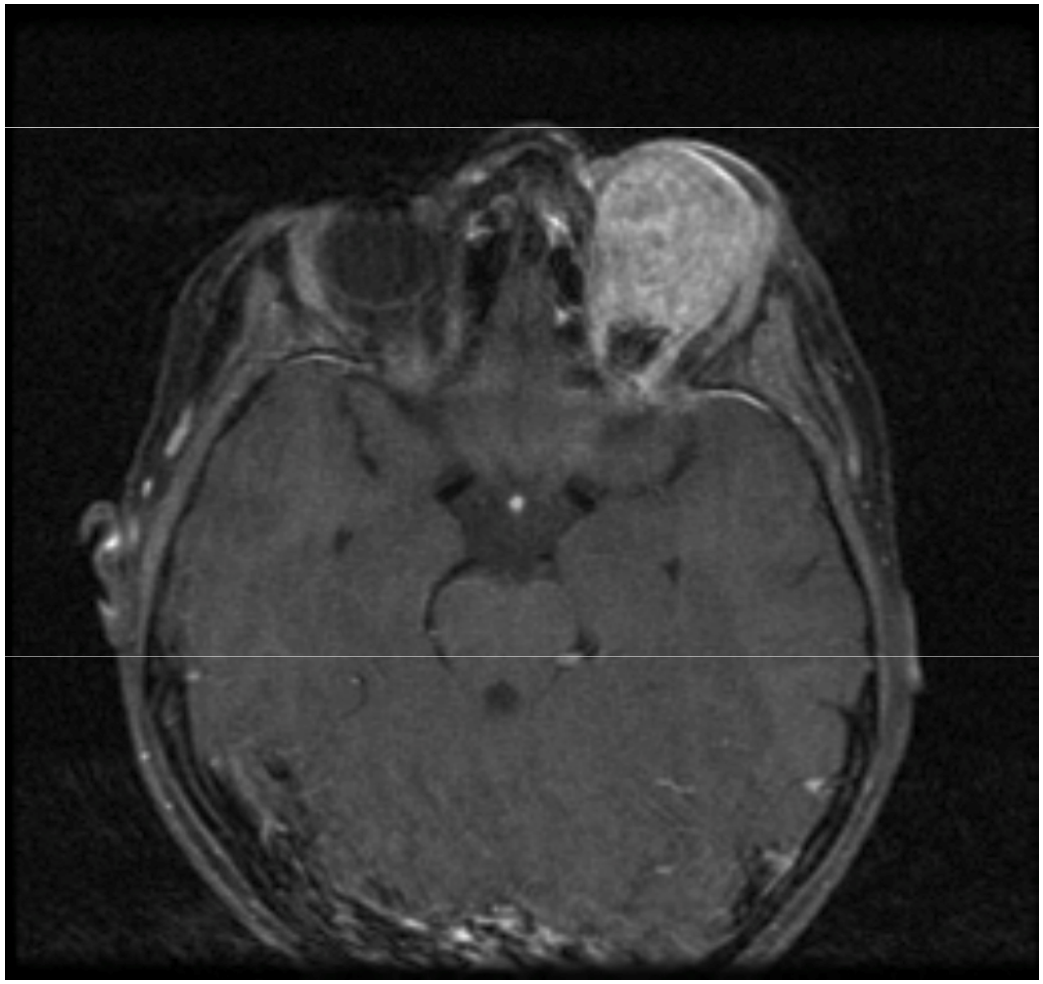
Orbital RMS





Before chemotherapy

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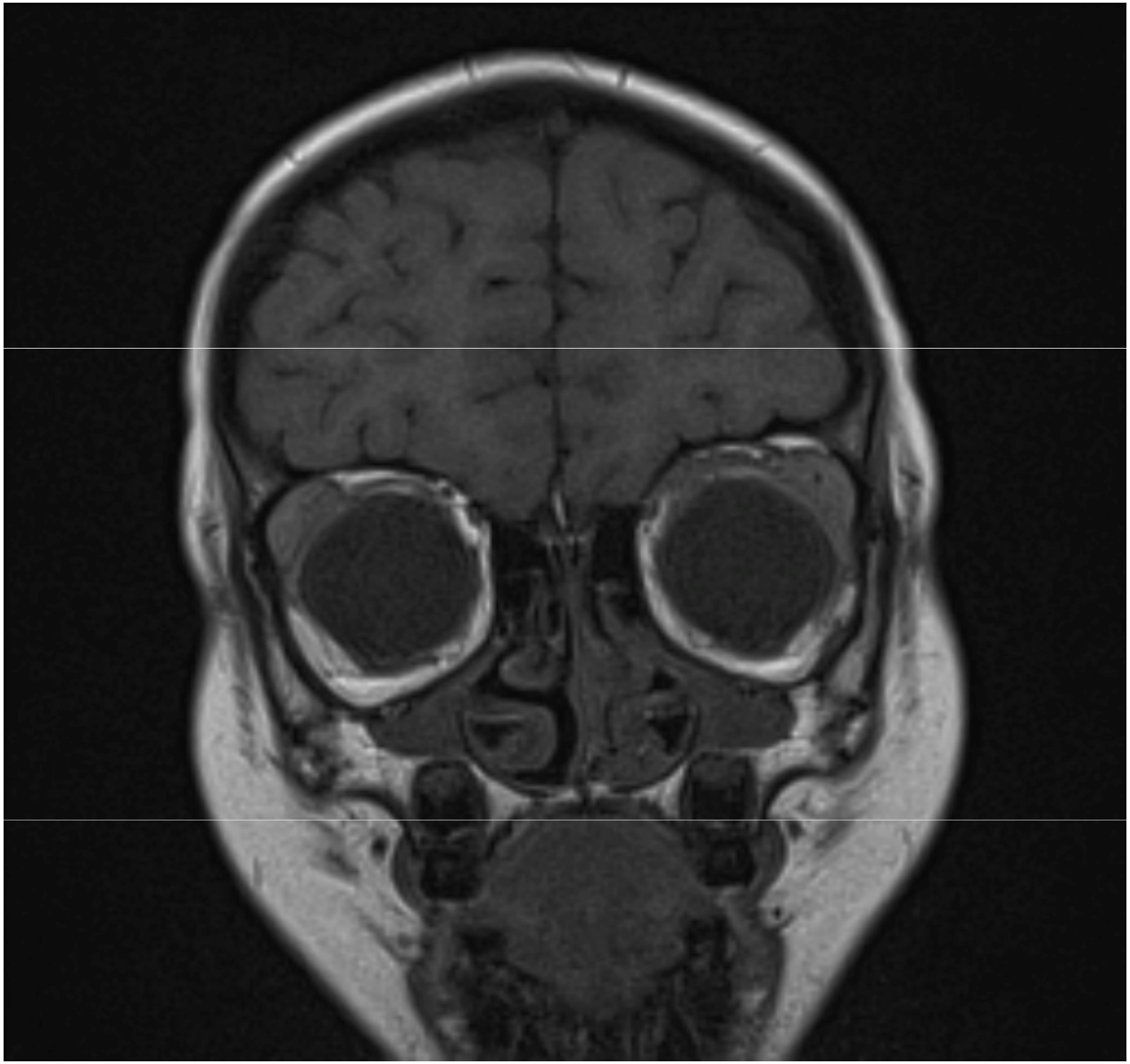
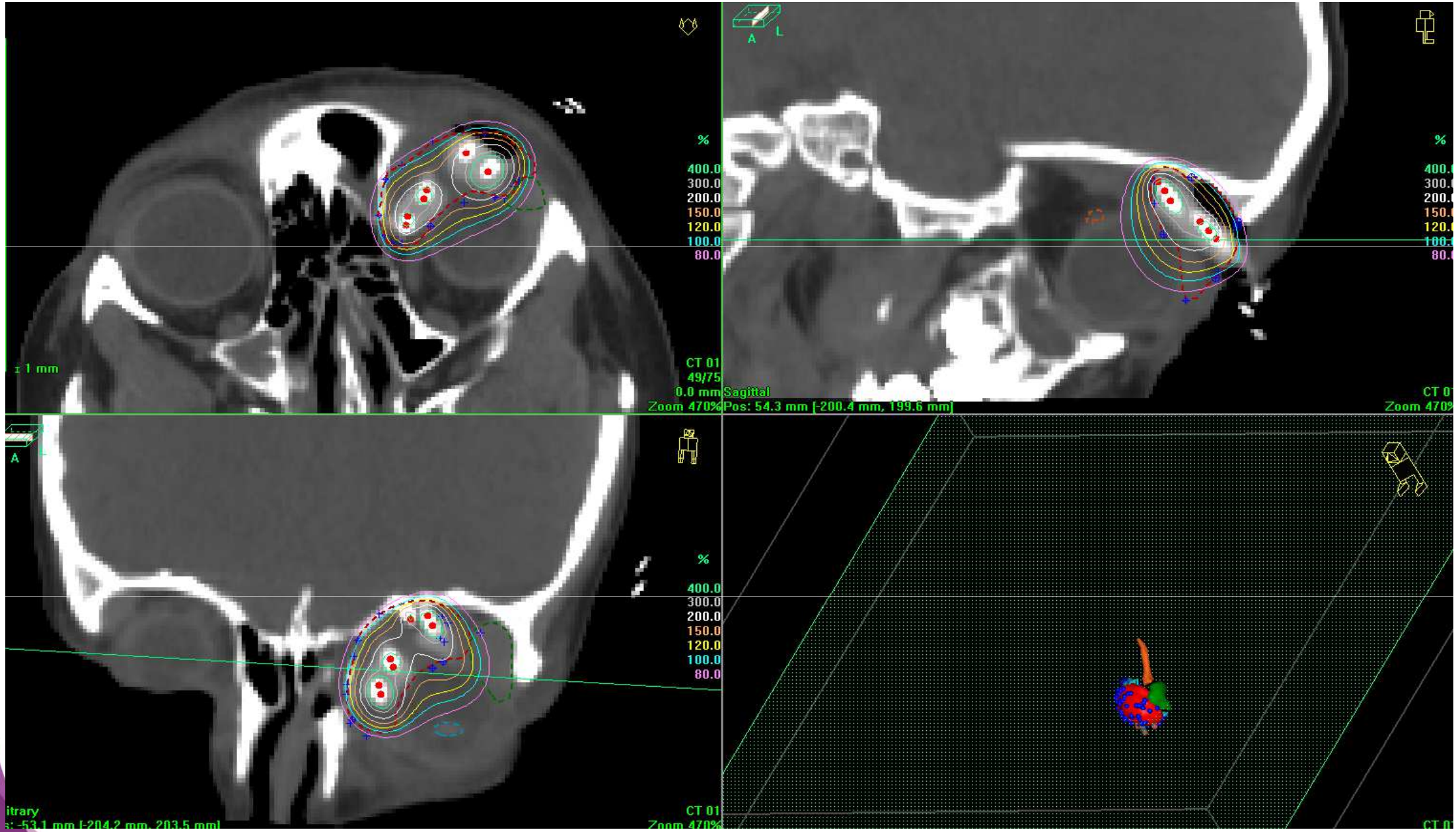


After chemotherapy



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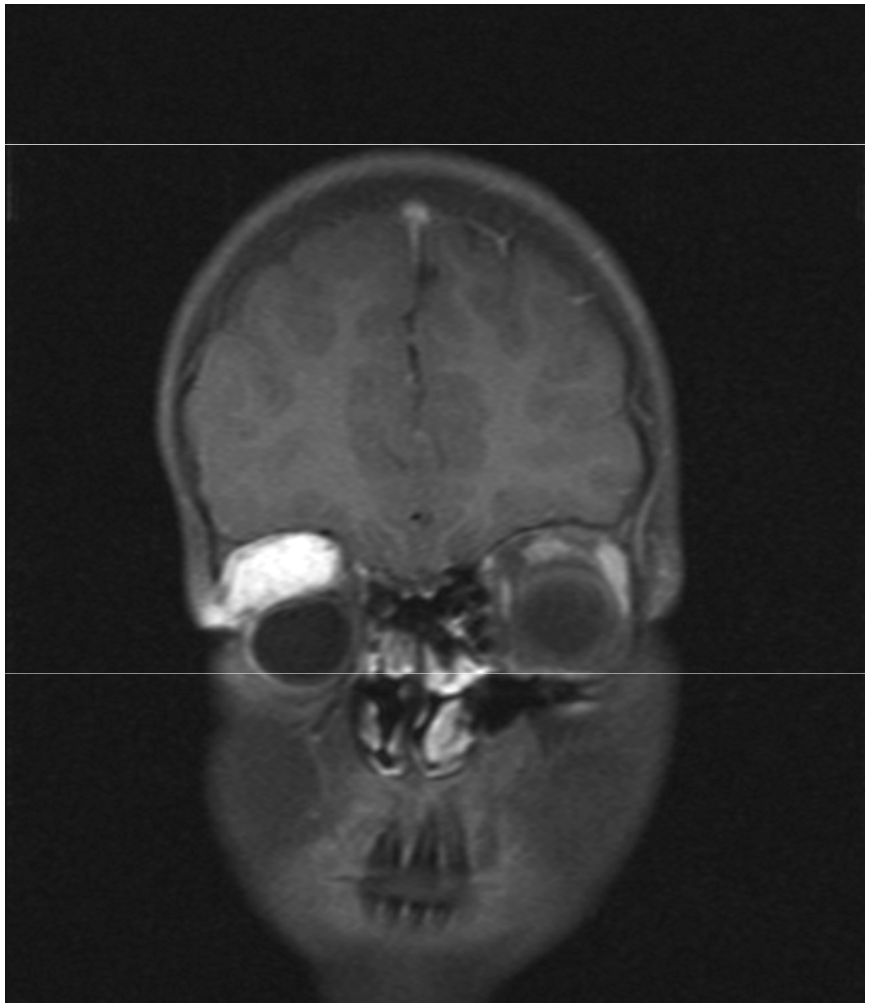
Recurrence after chemotherapy and EBRT



Before salvage chemotherapy

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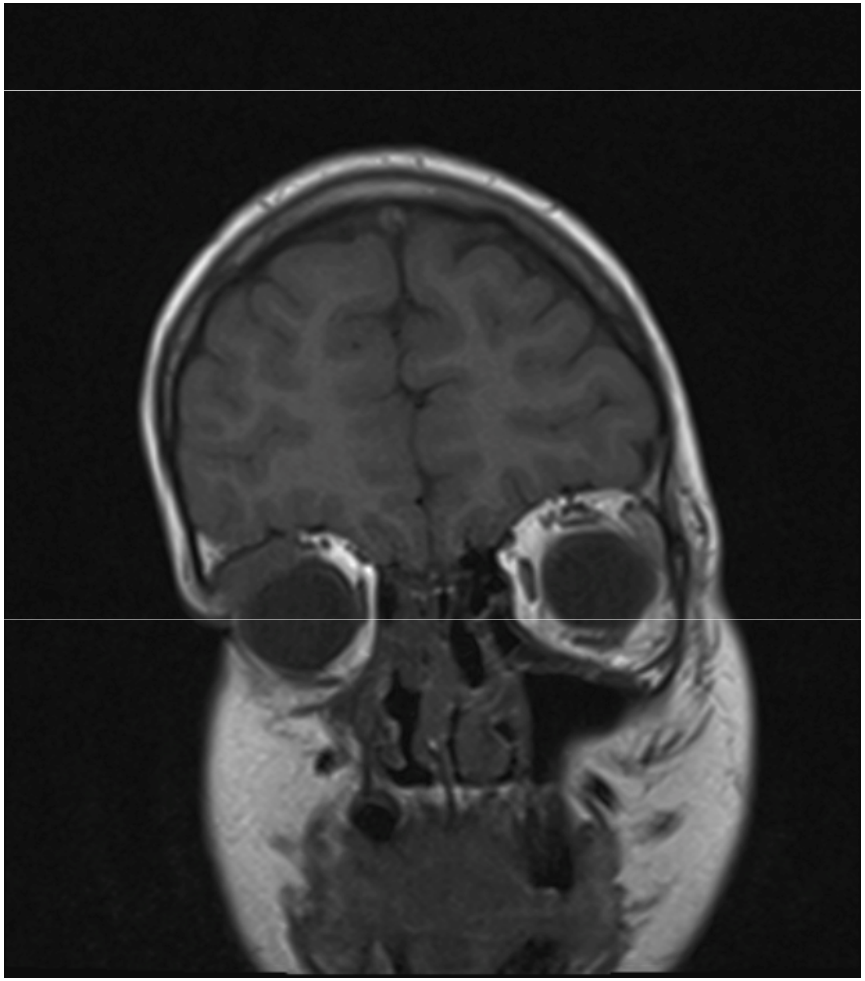

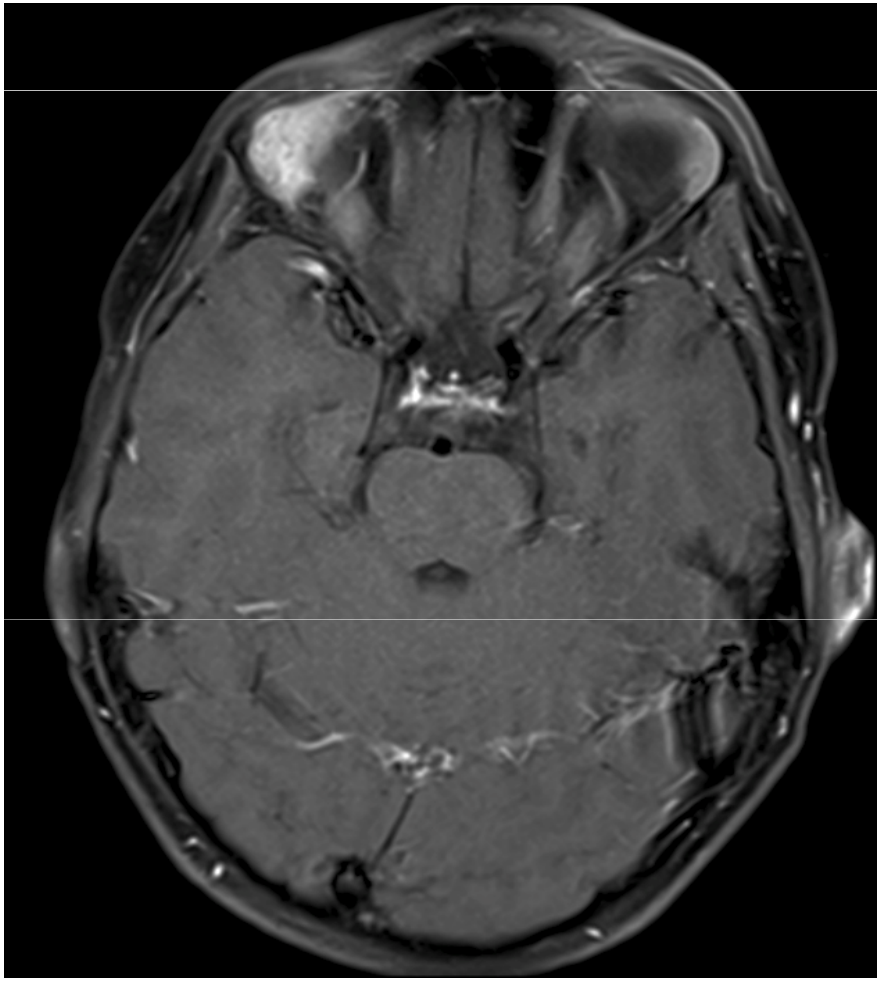

After salvage chemotherapy

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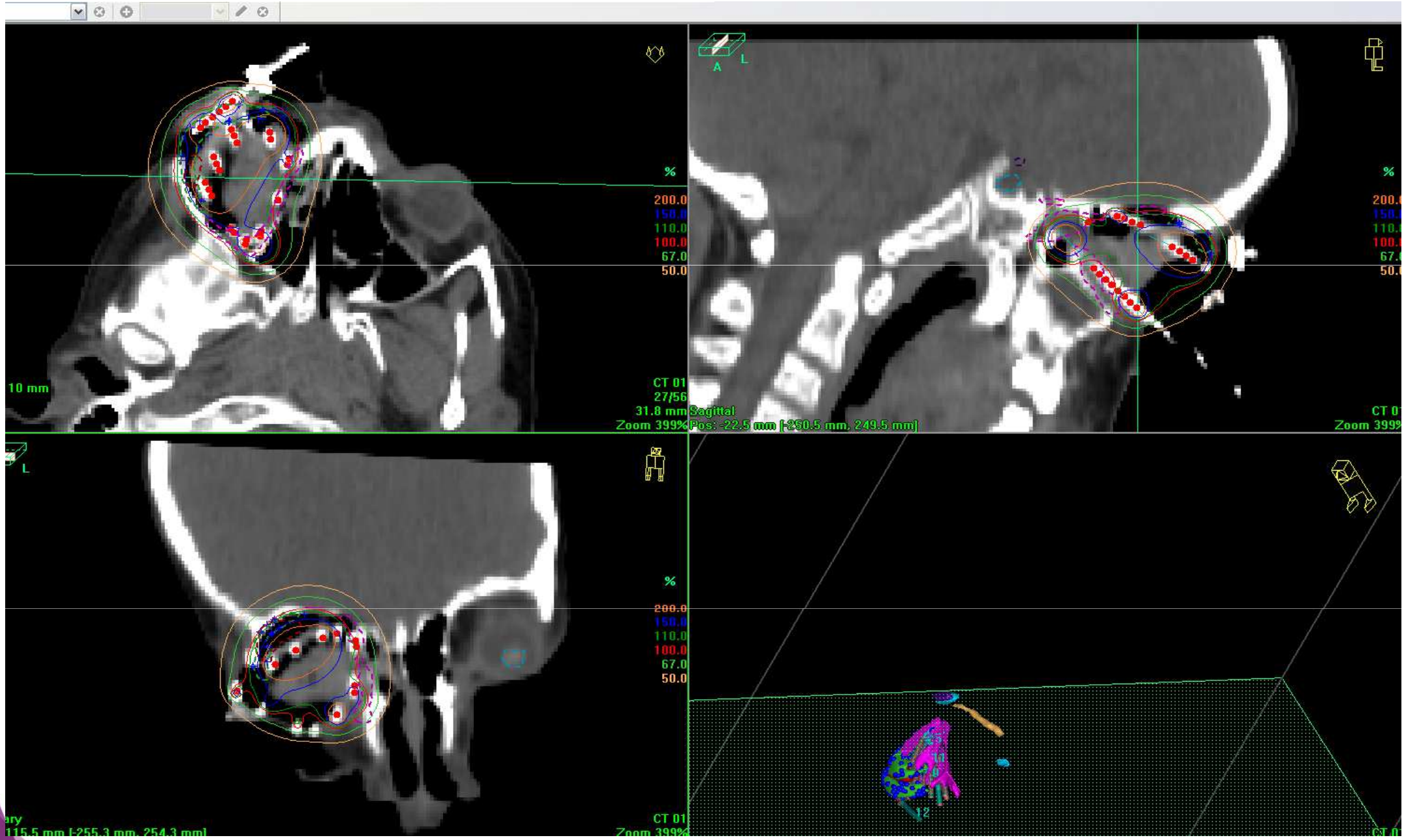
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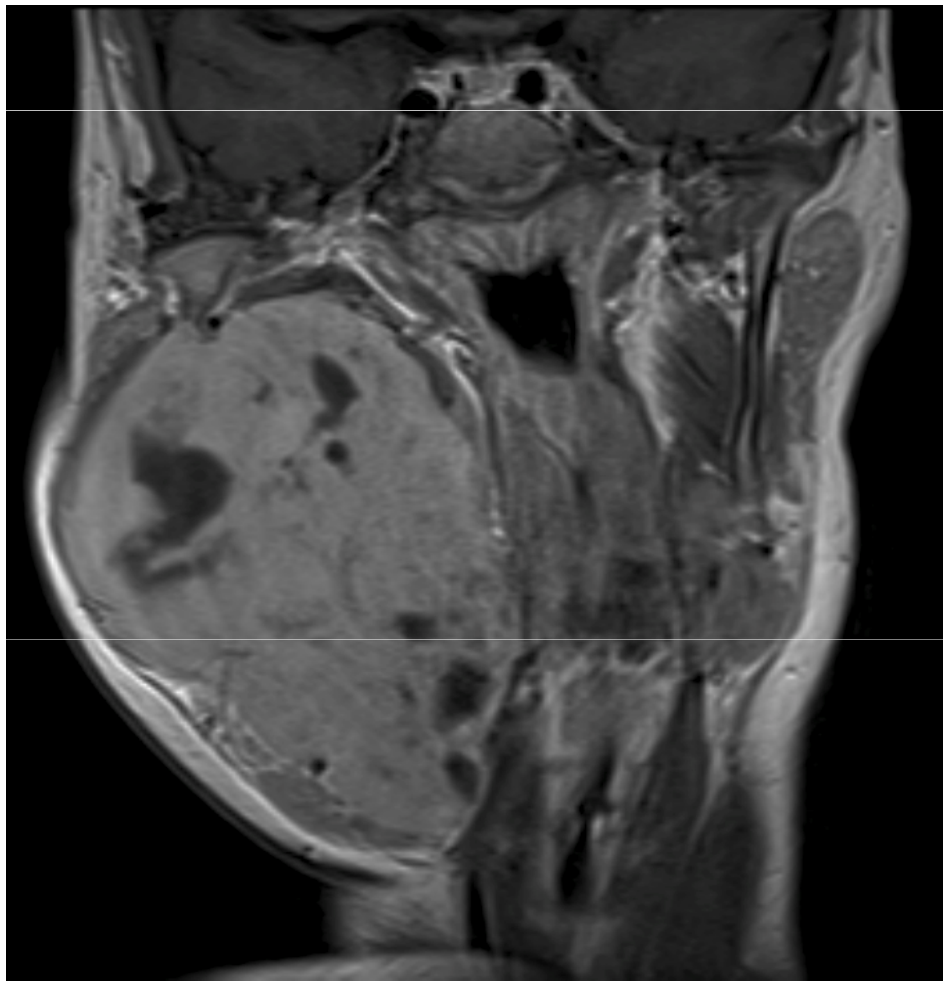
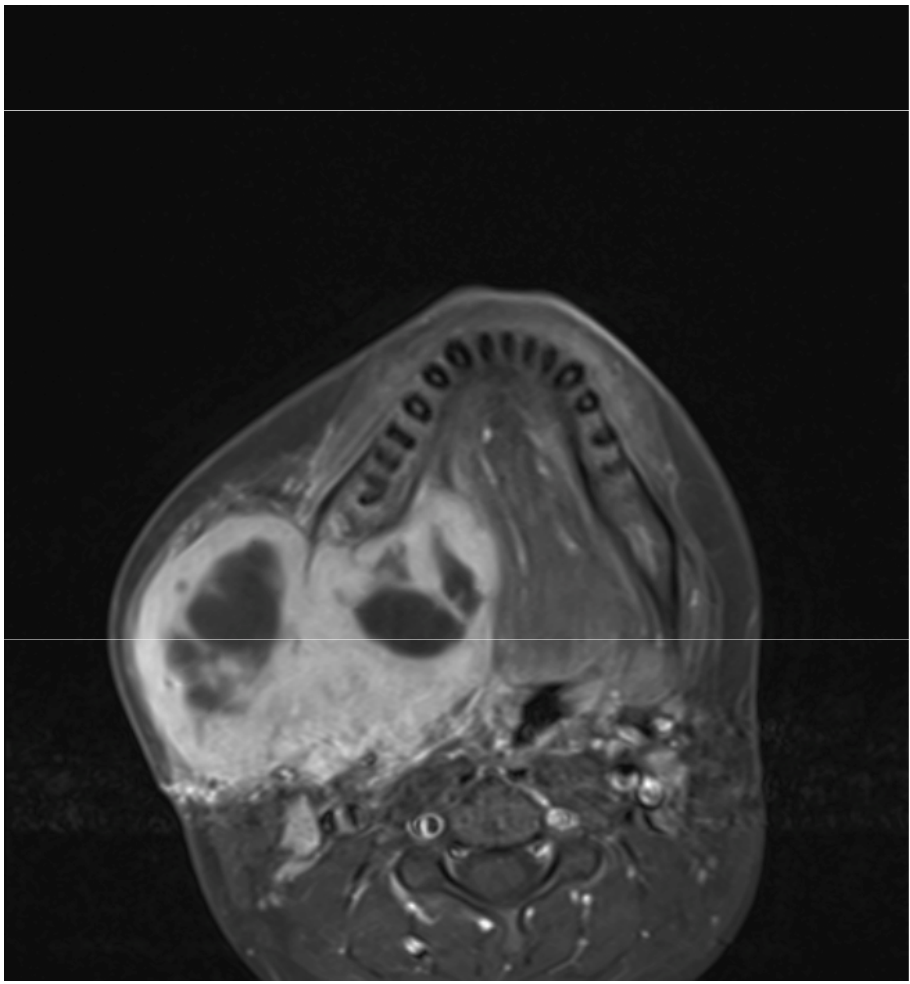
110.0
100.0
67.0
50.0
10 mm
CT 01
27/56
31.8 mm
Zoom 399%
A
L
Sagittal
Pos: -22.5 mm [-250.5 mm, 249.5 mm]
CT 01
Zoom 399%
L
%
200.0
150.0
110.0
100.0
67.0
50.0
CT 01
Zoom 399%

Undifferentiated sarcoma





After Chemotherapy

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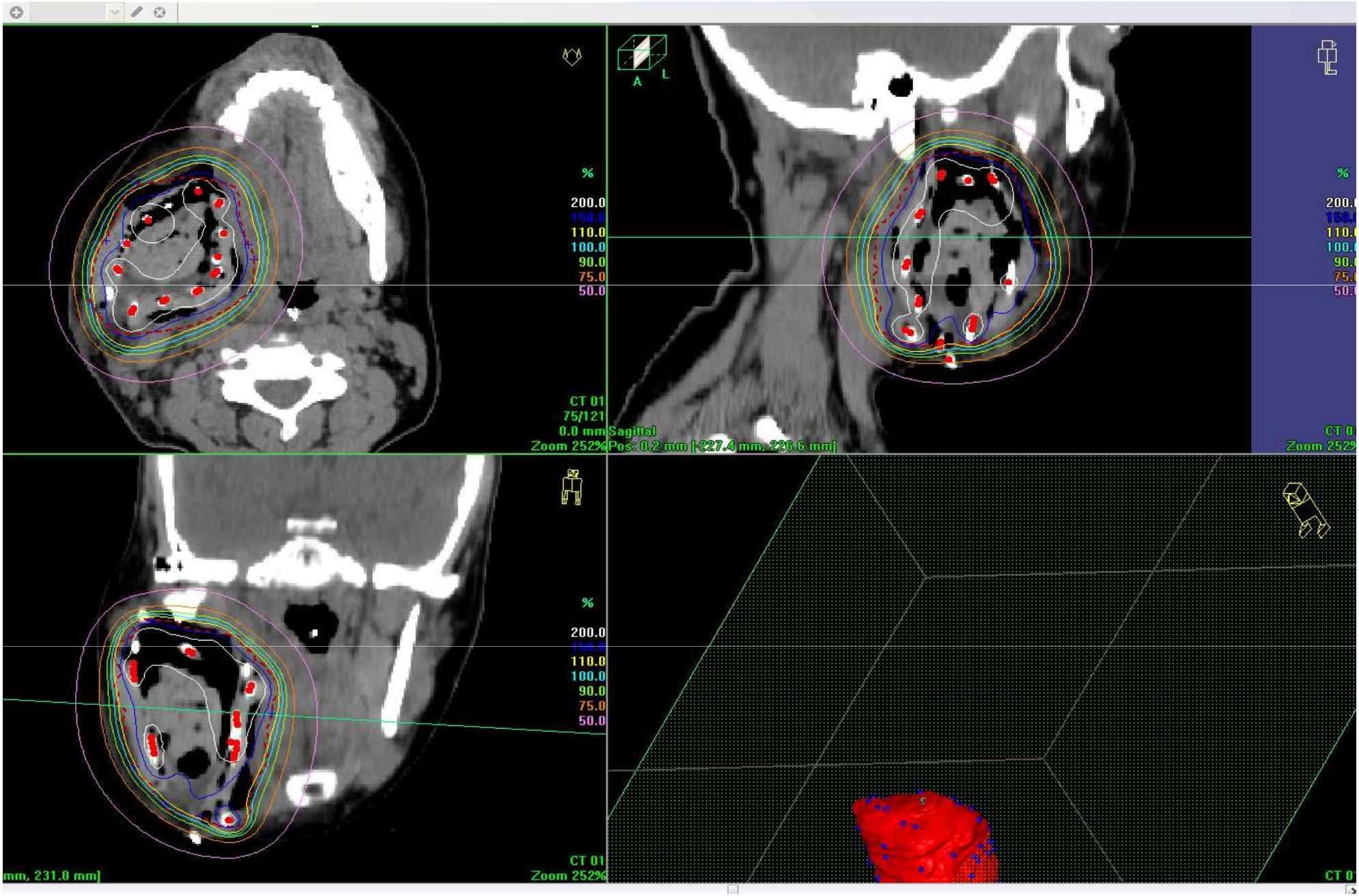
%
200.0
150.0
110.0
100.0
90.0
75.0
50.0
CT 01
75/121
0.0 mm Sagittal
Zoom 252% Pos: 0.2 mm [-227.4 mm, 226.6 mm]
A
L
CT 01
Zoom 252%
mm, 231.0 mm]

Results Up-front AMORE 1993-2007

Int J Rad Onc Biol Phys 2009; 24(5):1555-1562

Eur J Cancer 2003, 39 (11) 1594 -1602

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31 Patients

- 13 females and 18 males
- Age: 1.2-13.6 years, mean 6.1 years
- 25 the Netherlands, 6 abroad
- 24 PMN, 7 non-PMN
- TNM stage I (2), II (21), III (8)
- 26 Embryonal, 3 Alveolar, 2 NOS

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Chemotherapy

- 10 MMT-89
- 18 MMT-95
- 1 CWS-91, 1 COG-D9803, 1 E*p*SSG-2005

- Total of 4-8 courses pre-AMORE
- All completed chemotherapy according to protocols

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Ablatio

- 22 macroscopic radical resection
- 6 compartment resection or explorative surgery
- 1 macroscopically irradical resection
- 2 patients exact surgical report missing

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Brachytherapy

- Low-dose rate technique: 1993-2001
- Pulsed Dose Rate technique: 2002-2007
- CTV: 5 mm of tissue starting from surface of the mold encompassing the microscopically residual tumor volume
- Dose: 40-50 Gy depending on peroperative findings regarding vital structures

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REconstruction

- 26 patients
- Majority free vascularized flaps
- Minority pedicled flaps

Follow-up

- 0.2-14.5 years (mean 5.7)
- Analysis performed October 2007

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Survival of 24 PMN

- 1 distant relapse
- 5 local relapse (2 AWD > 4 years after)
- 3 combined local/distal relapse
- 7 Died of disease
- 1 Mucoepidermoid carcinoma contralateral parotid gland 4.8 yrs after AWD 7 years later
- **5-year DFS 59%**
- **5-year OS 65%**

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Survival of 7 Non-PMN

- One local recurrence with pulmonary metastases died
- **5-year DFS 90%**
- **5-year OAS 90%**

Late effects

- Partial N. VII palsy: 4
- N. IX, N. XI lesion: 1 each
- Malocclusion: 3
- Dental problems: 4
- Trismus: 1
- Severe fibrosis, xerostomia or osteonecrosis: not observed

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AMORE as Salvage Treatment
1993-2007

Int J Rad Onc Biol Phys, 2009; 24(5):1555-1562

Eur J Surg Oncol 2004; 30(8):884-892

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11 Salvage patients

- 5 PMN: 2 Residual disease
  3 LR (1 second LR; 1 with single lung met)
  All had previous EBRT
- 6 Non-PM: All LR (1 second LR after previous EBRT)

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11 Salvage patients

- 5 females, 6 males
- Age: 2.4-16.9 years (mean 7.7)
- Follow-up: 0.7-14.1 years (mean 6.3)

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Results AMORE as Salvage

- 2 distant metastasis
  - One with local recurrence

- **5-y DFS and OS: 82%**

Conclusions AMORE as Salvage

- 5-year disease-free and OAS 82%
- Feasible, even after prior external beam
- Limited complications AMORE without prior EBRT
- Promising local control rate

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Overall Conclusions AMORE

- Feasible technique (!Experienced multidisciplinary team!)
- Adequate concept
- Local control upfront treatment compares to conventional strategies
- Promising results salvage treatment even after EBRT
- Low incidence disorders craniofacial growth
- Further evaluation late effects in progress

ESTRO School

Florence, March 13-16 2016

ESTRO School

Modern Brachytherapy Techniques

WWW.ESTRO.ORG/SCHOOL

Physics and Dose Calculation in Brachytherapy

ESTRO Teaching Course

Florence, 2016

Dimos Baltas

E-mail: dimos.baltas@uniklinik-freiburg.de

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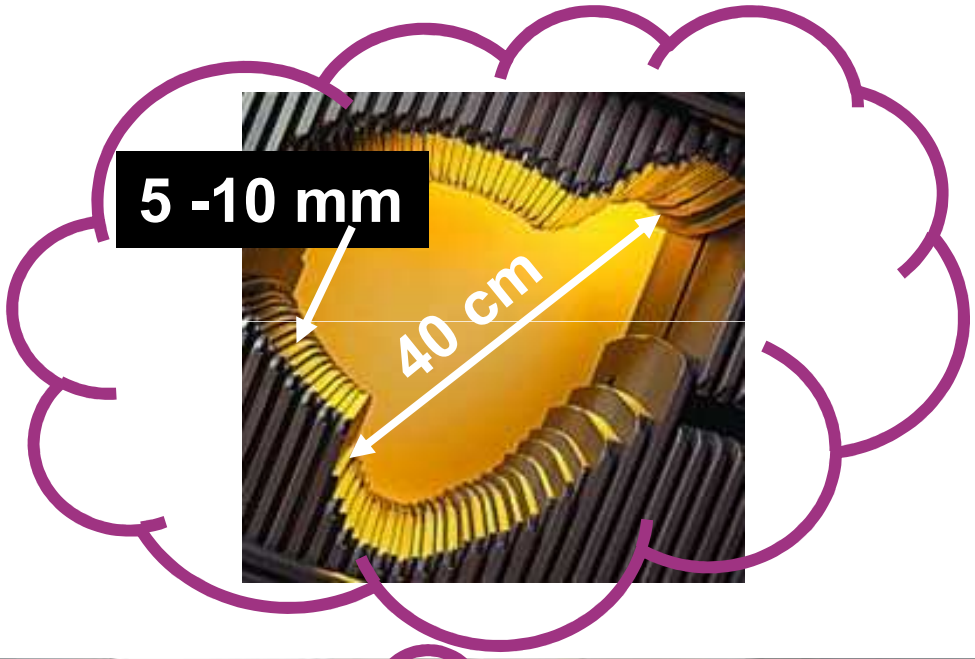
ERT *versus* BRT from Technology and Physics/Dosimetry

Point of View:

Similarities and Differences

ERT



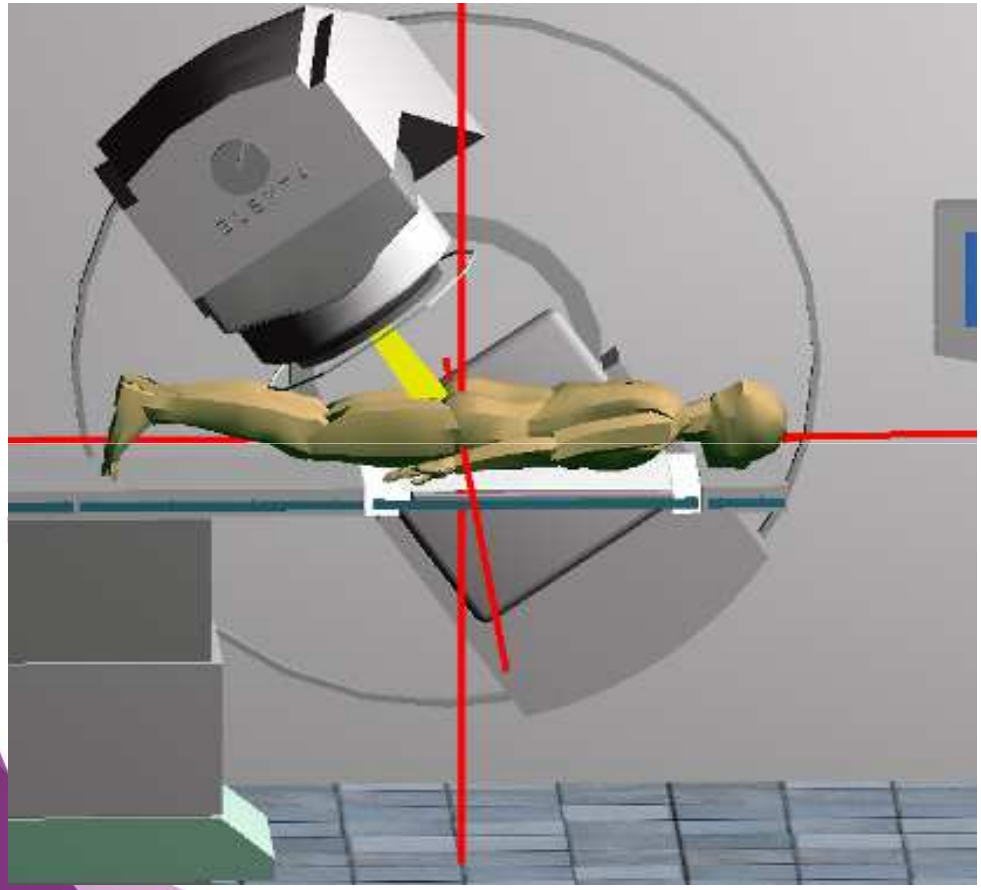
BRT

TRO

Modern Radiation Therapy

The Field / Beam:

ERT



BRT

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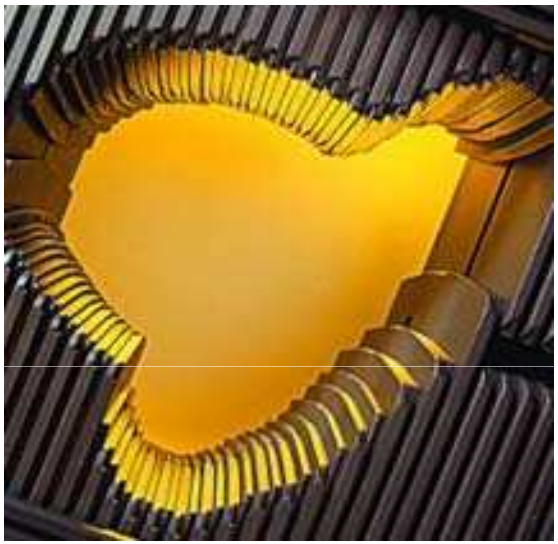
Modern Radiation Therapy

Beam Shaping: Plane

Field

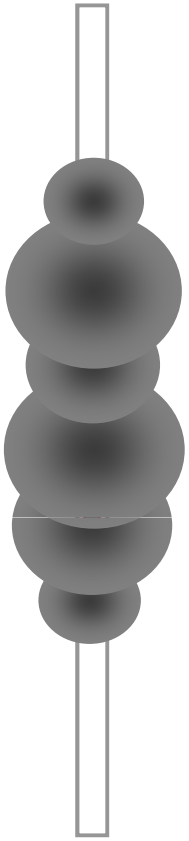


MLC

2.5 mm
or
5.0 mm
or
10.0 mm

ERT

Needle/Catheter



MSS

- 1.0 mm
- 2.5 mm
- 5.0 mm
- 10.0 mm
- ?? mm

BRT

ESTRO School

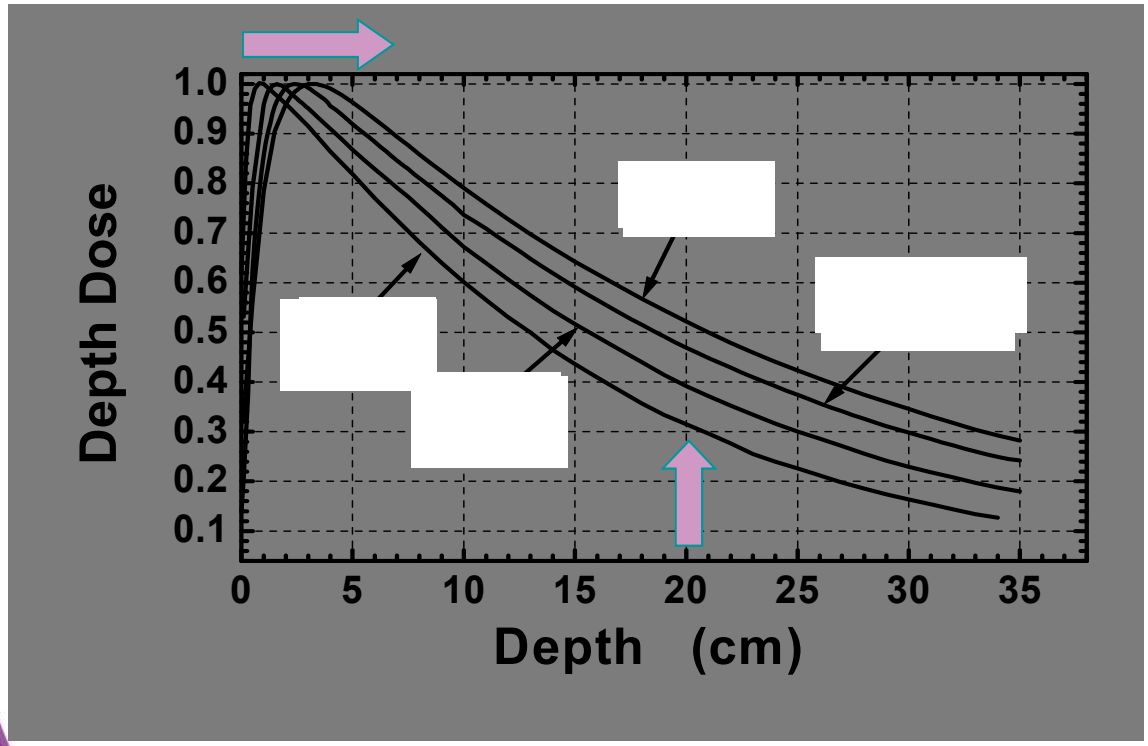
Modern Radiation Therapy

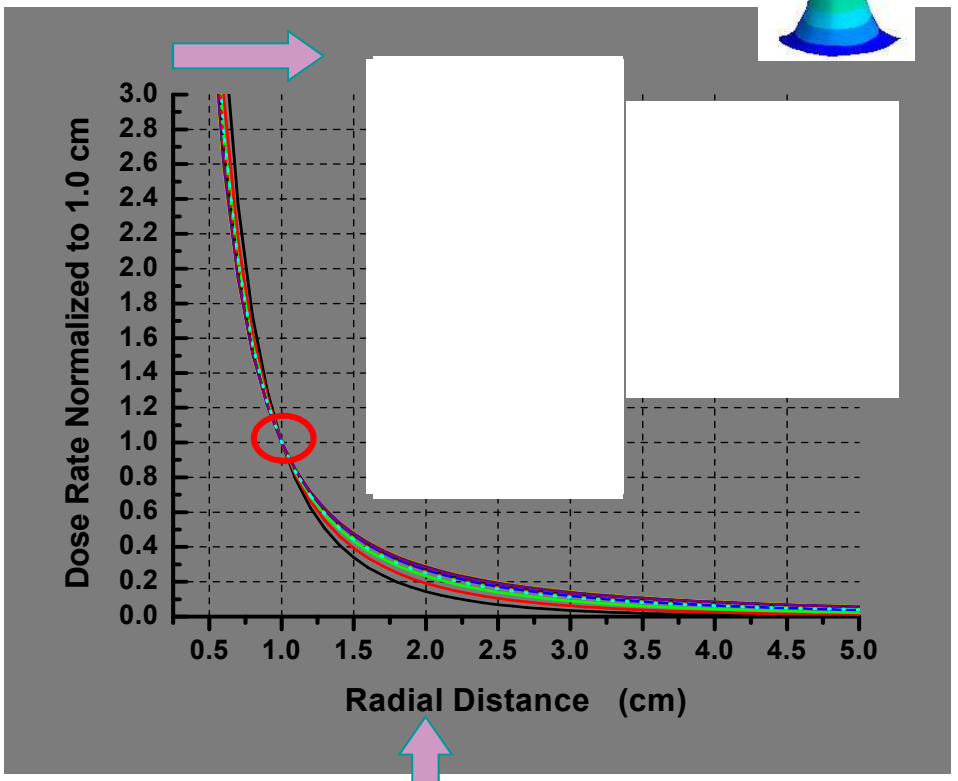
Dosimetric Kernel

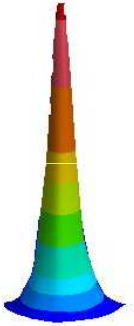
ERT

10 : 1

BRT







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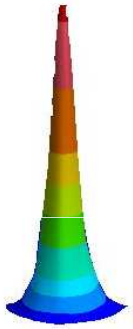
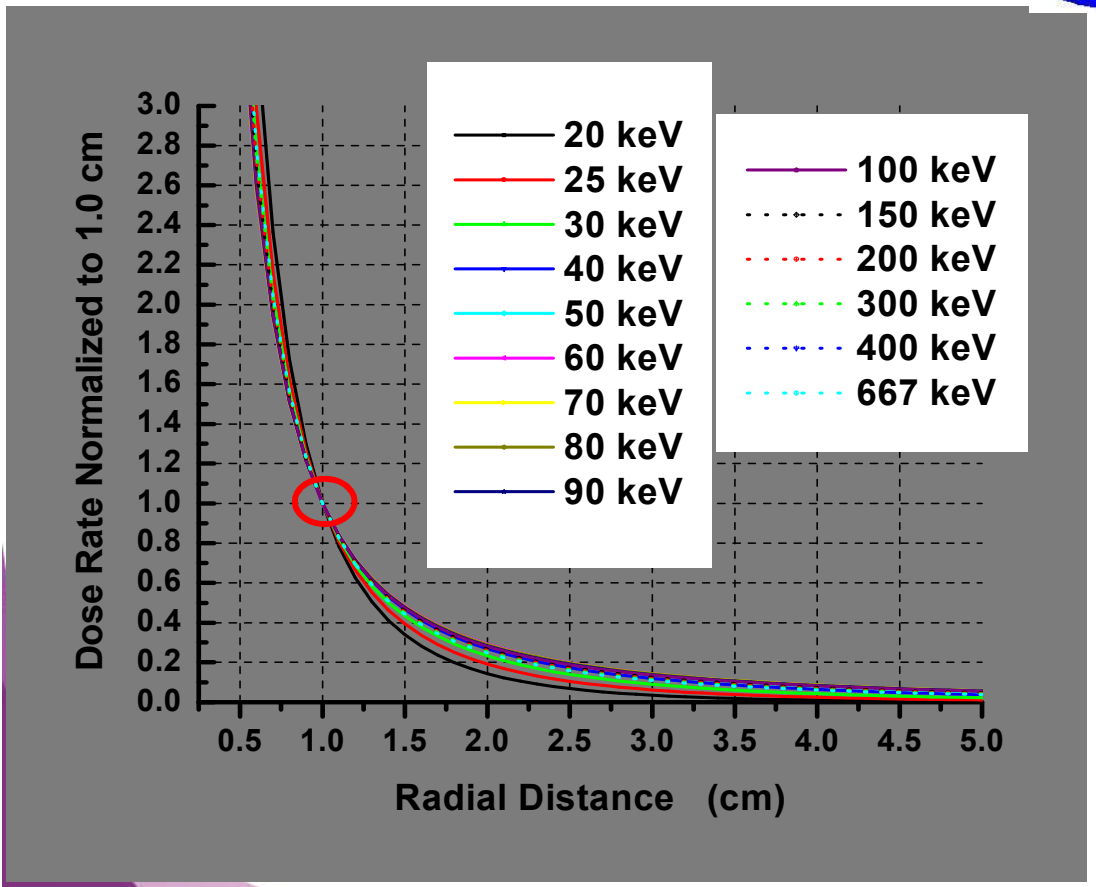
Modern Radiation Therapy

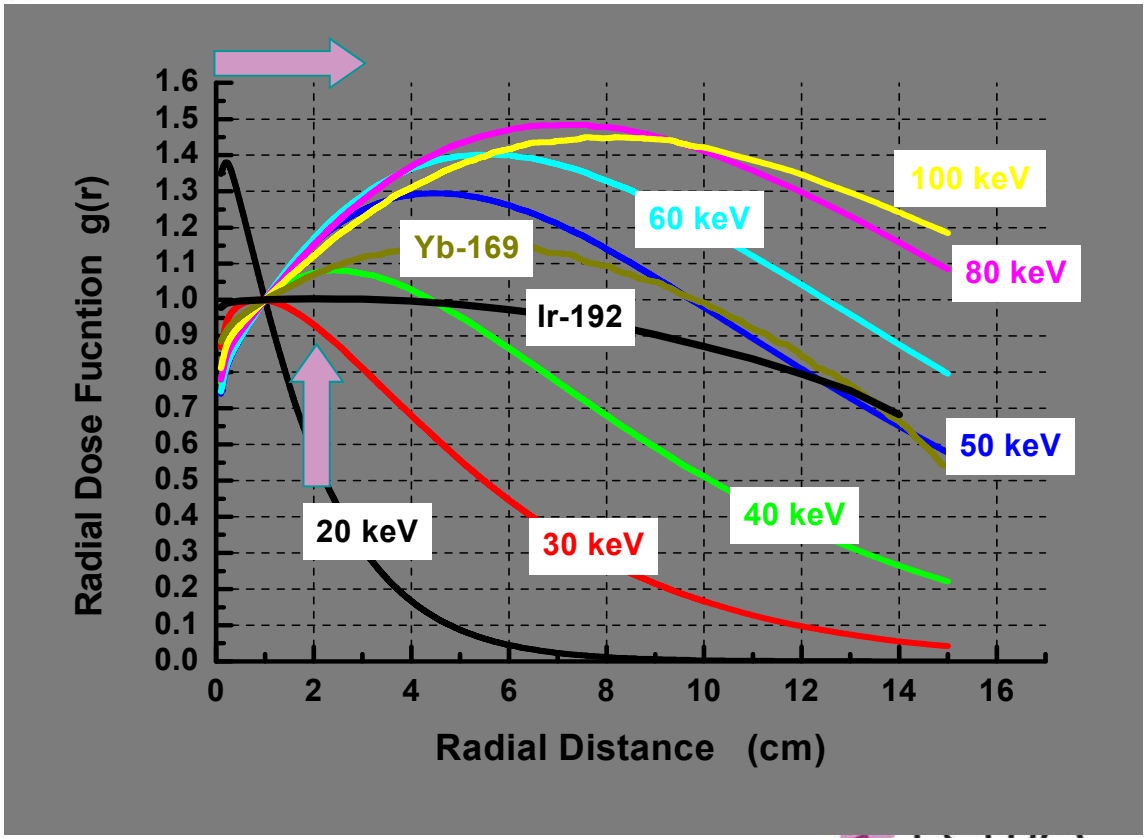
Dosimetric Kernel



BRT



BRT



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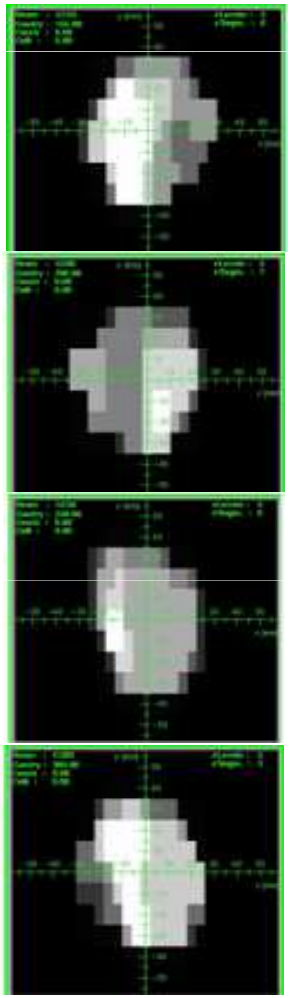
Modern Radiation Therapy

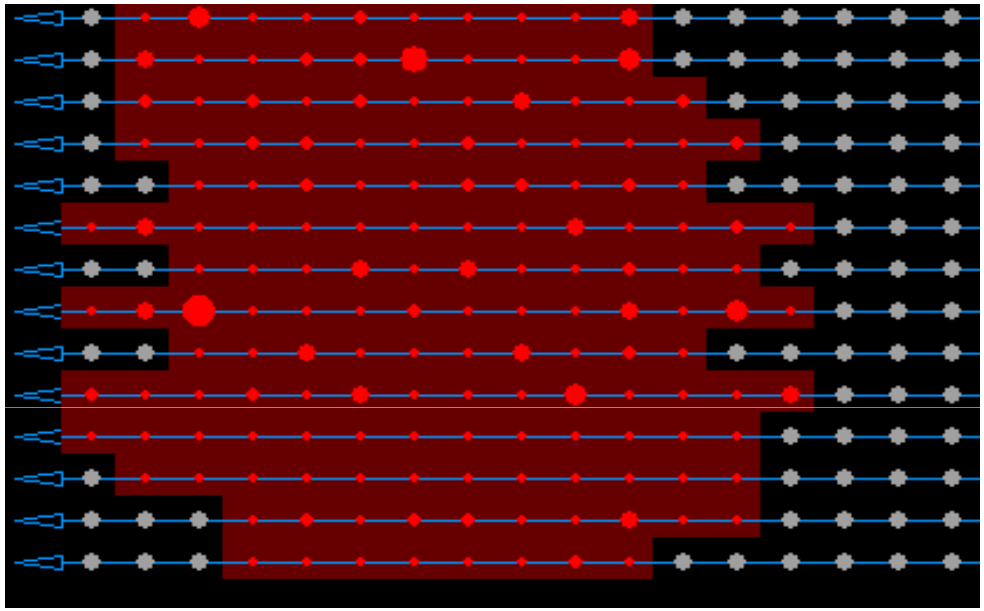
Dose Shaping: Intensity Modulation (2D)

ERT



BRT

MSS: Step & Shoot



"Bixel" ⇔ Dwell Position

"MUs" ⇔ Dwell Time

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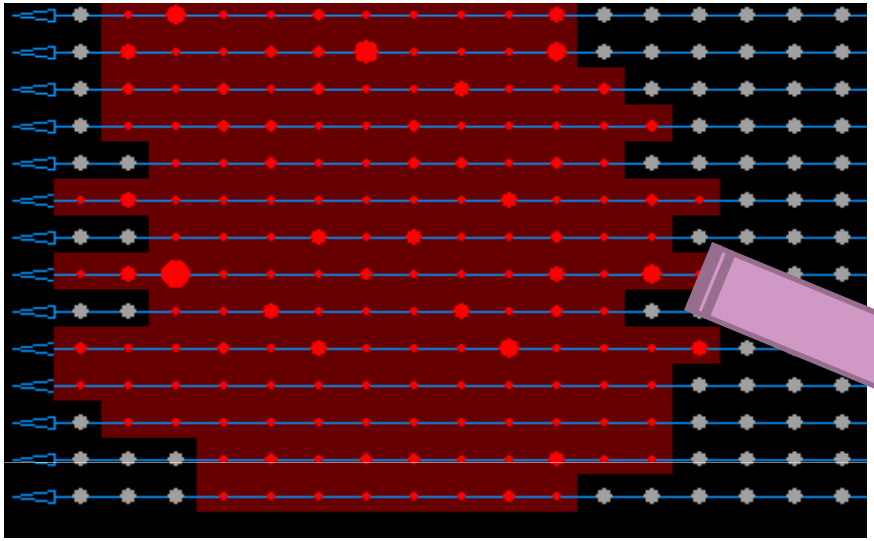
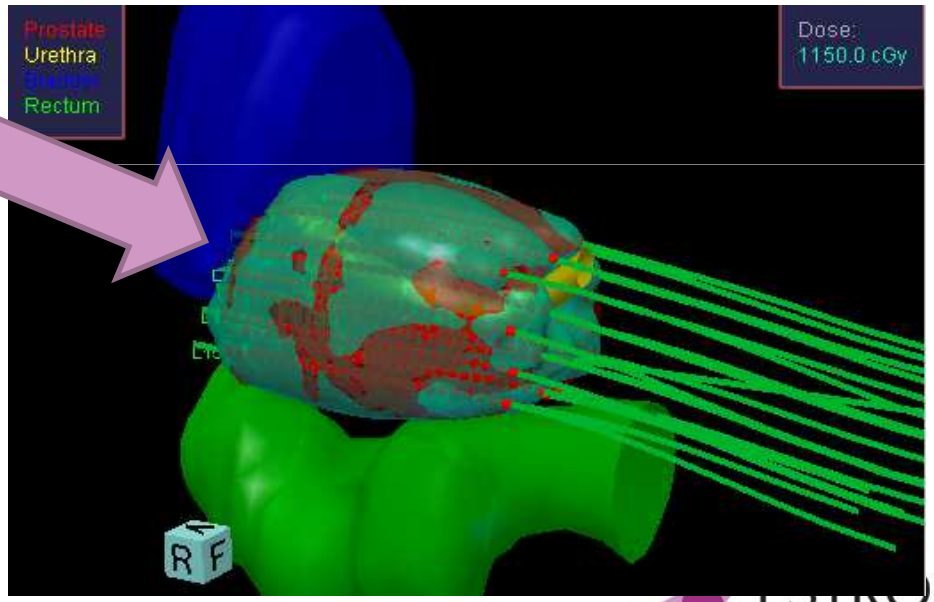
Dose Shaping: Intensity Modulation (2D)

MSS: Step & Shoot



”Spot”



Step and Shoot in BRT: How does it work ?

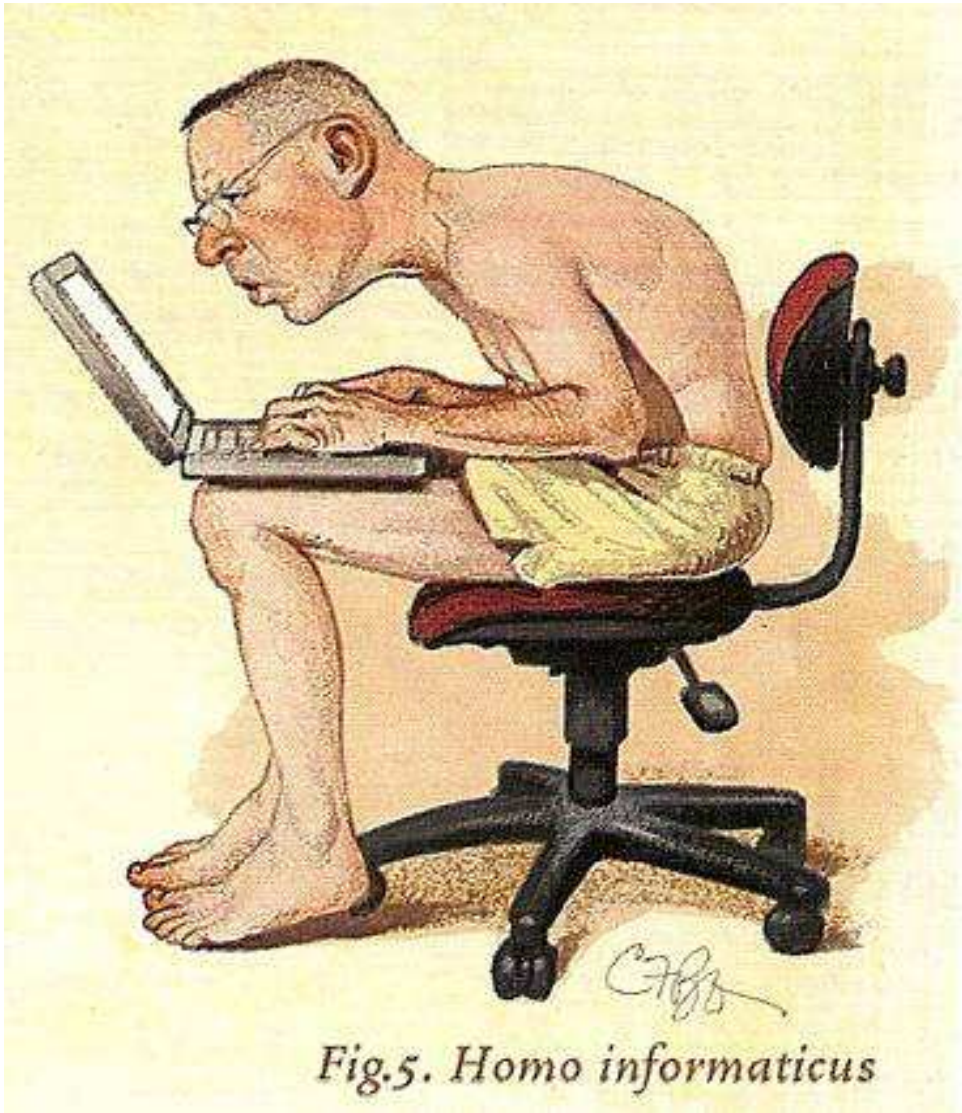
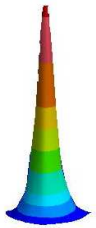
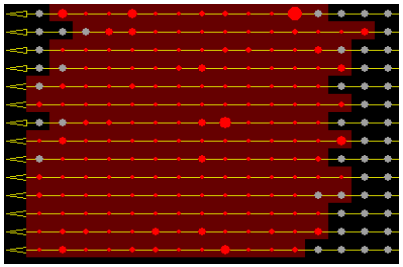


Fig.5. Homo informaticus

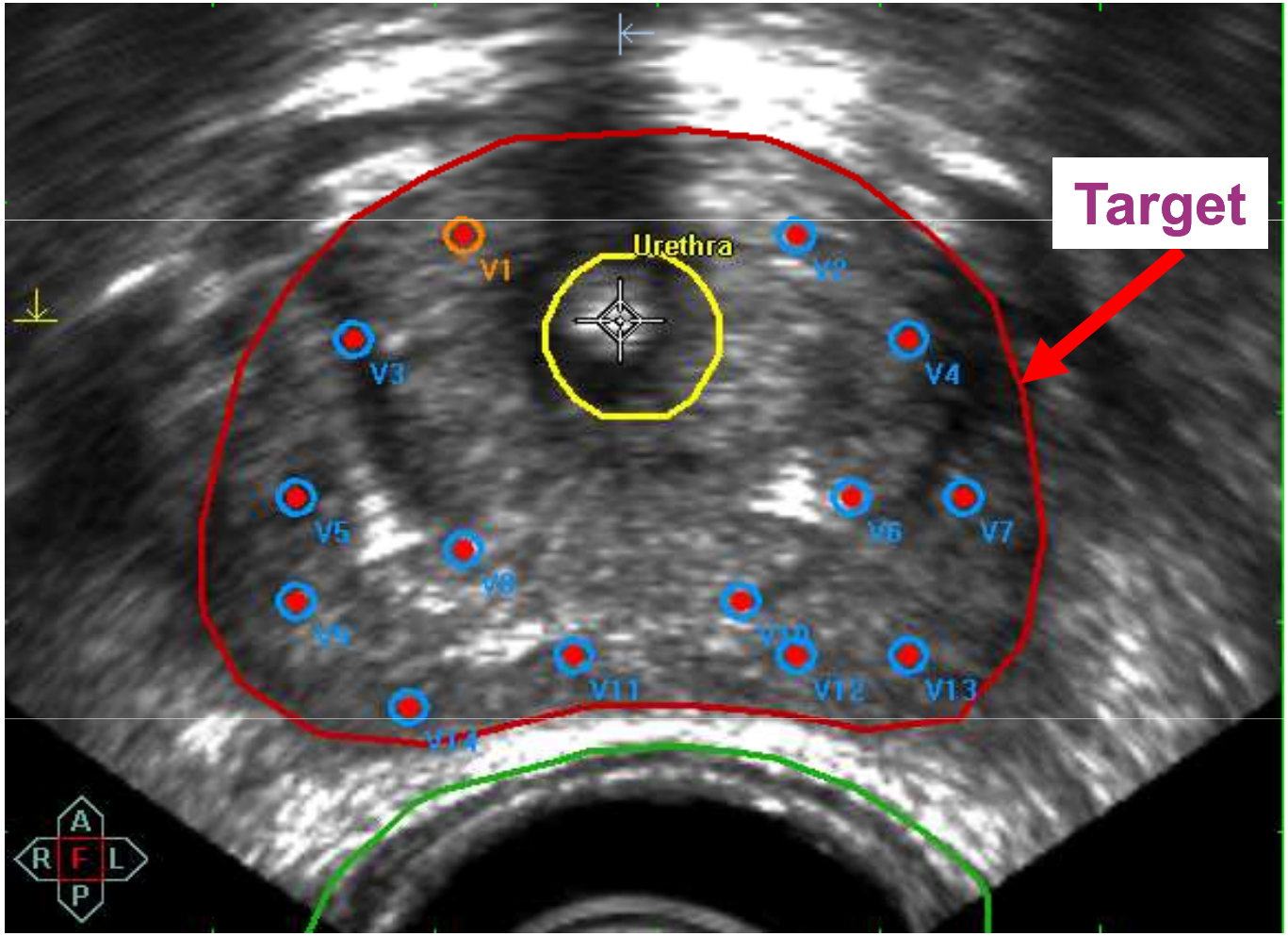
Treatment Delivery



Spot = Shoot



Intensity Pattern



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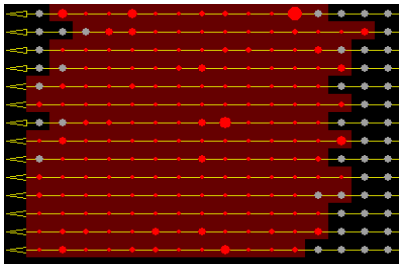
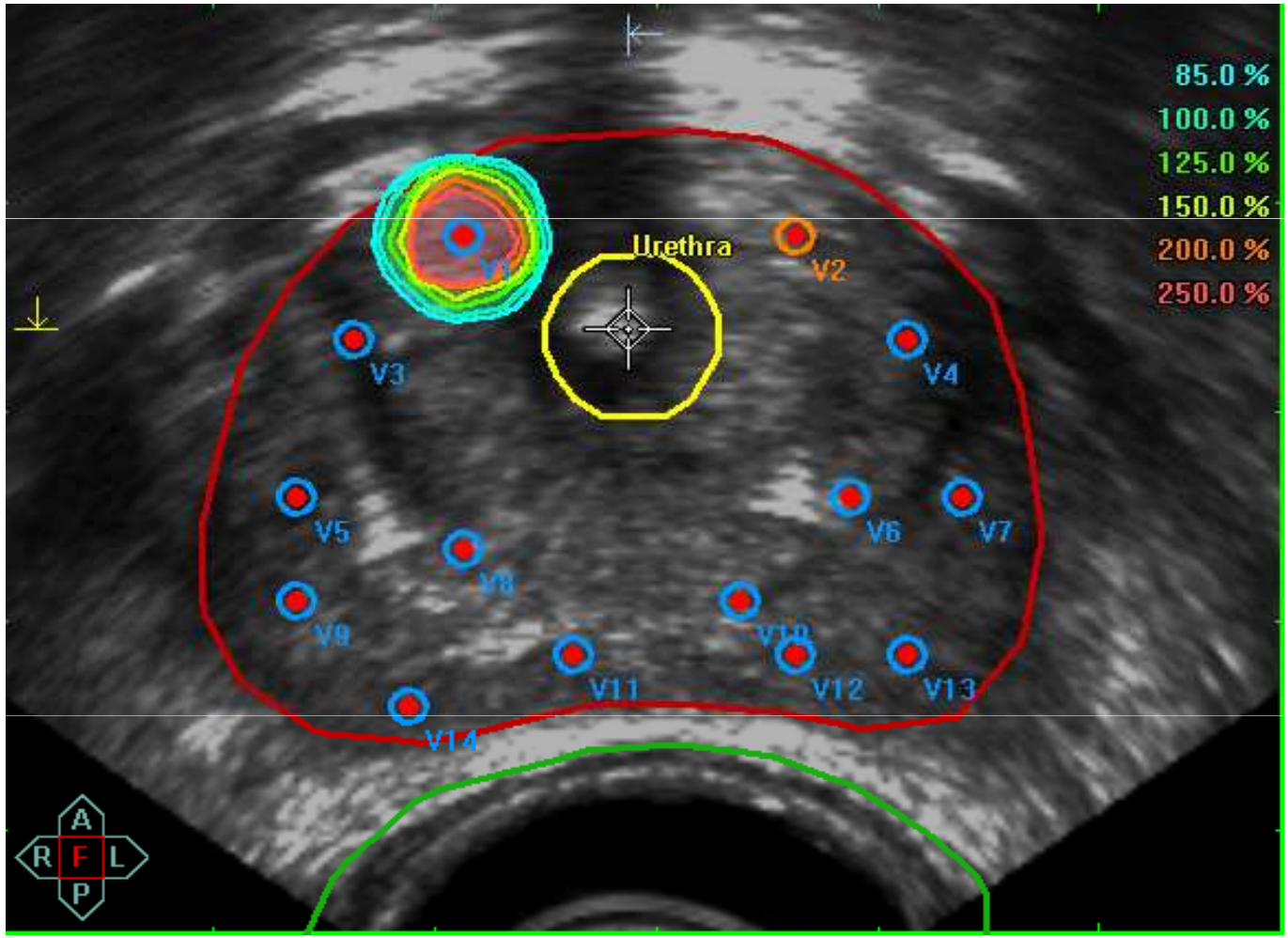
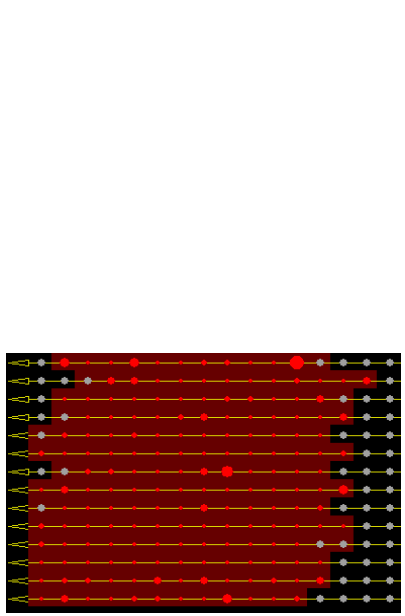
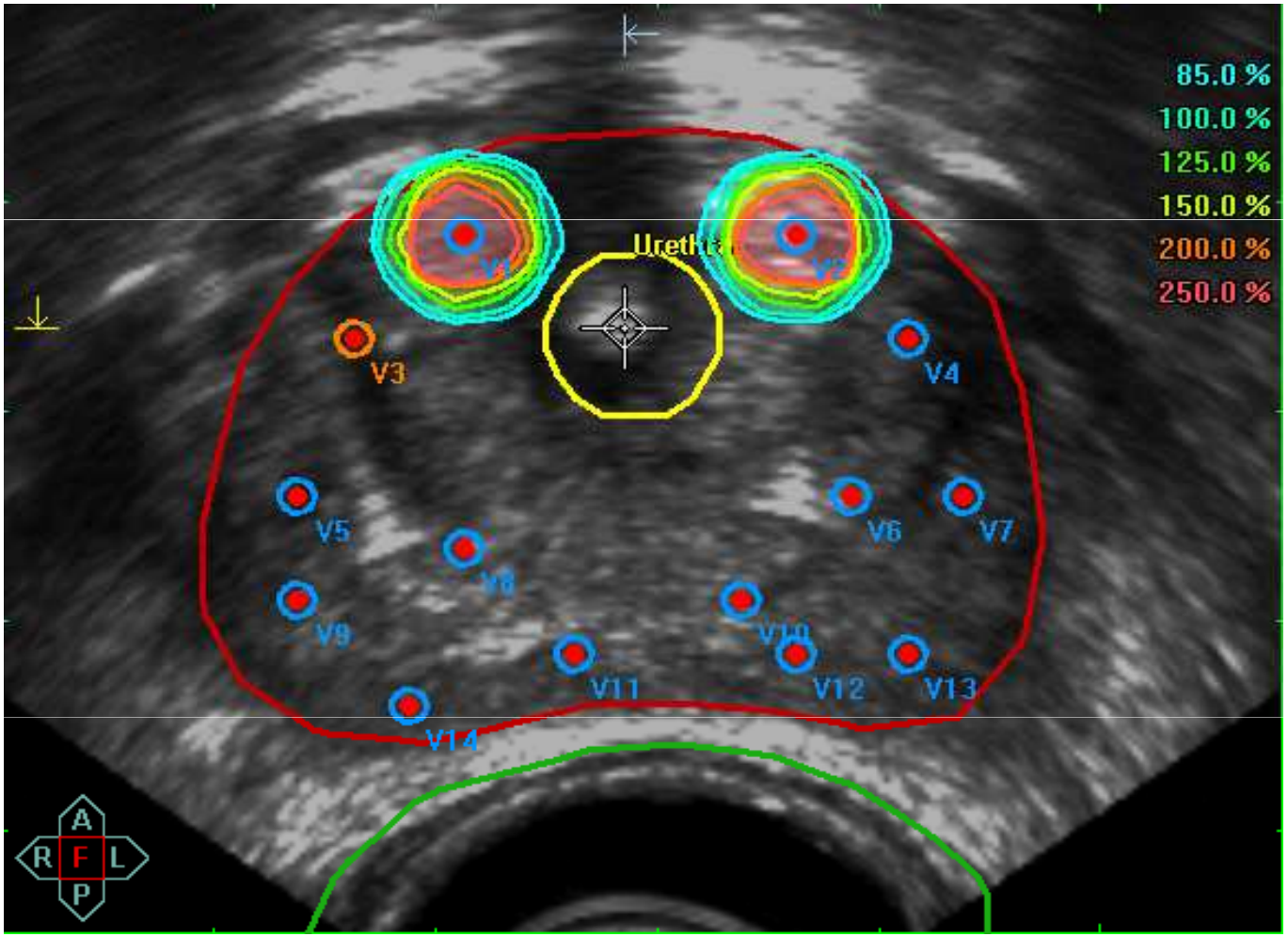
Treatment Delivery => Step and Shoot



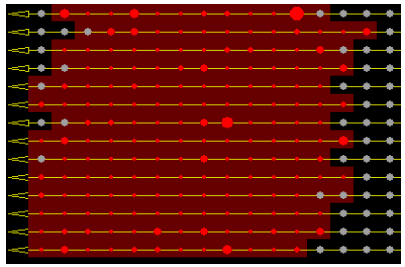


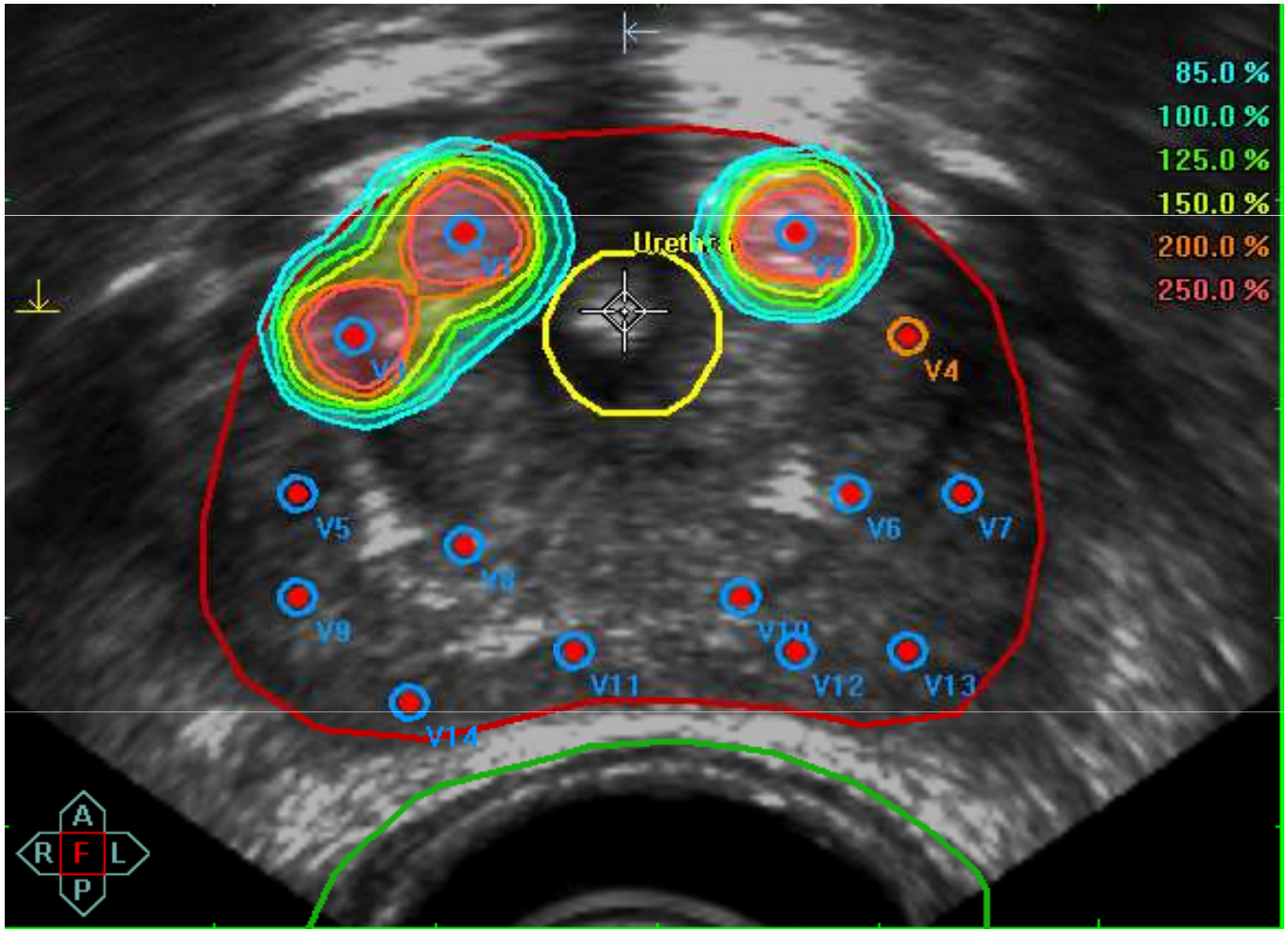
Treatment Delivery => Step and Shoot



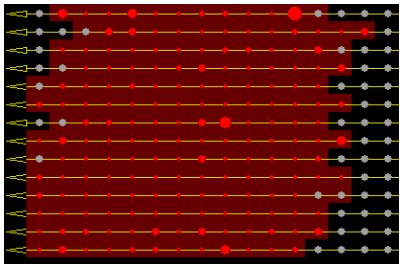


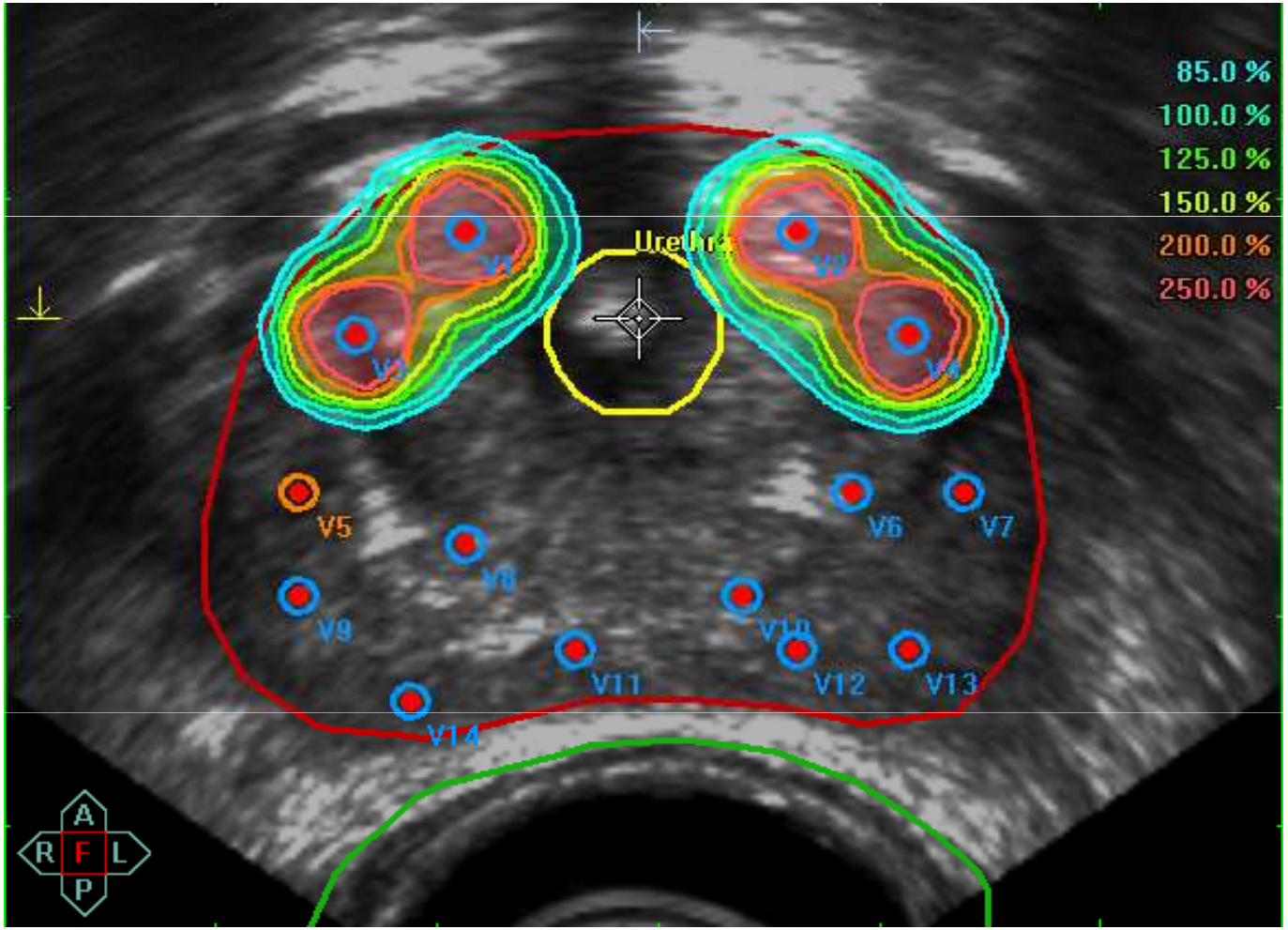
Treatment Delivery => Step and Shoot



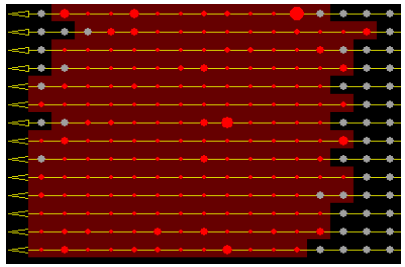


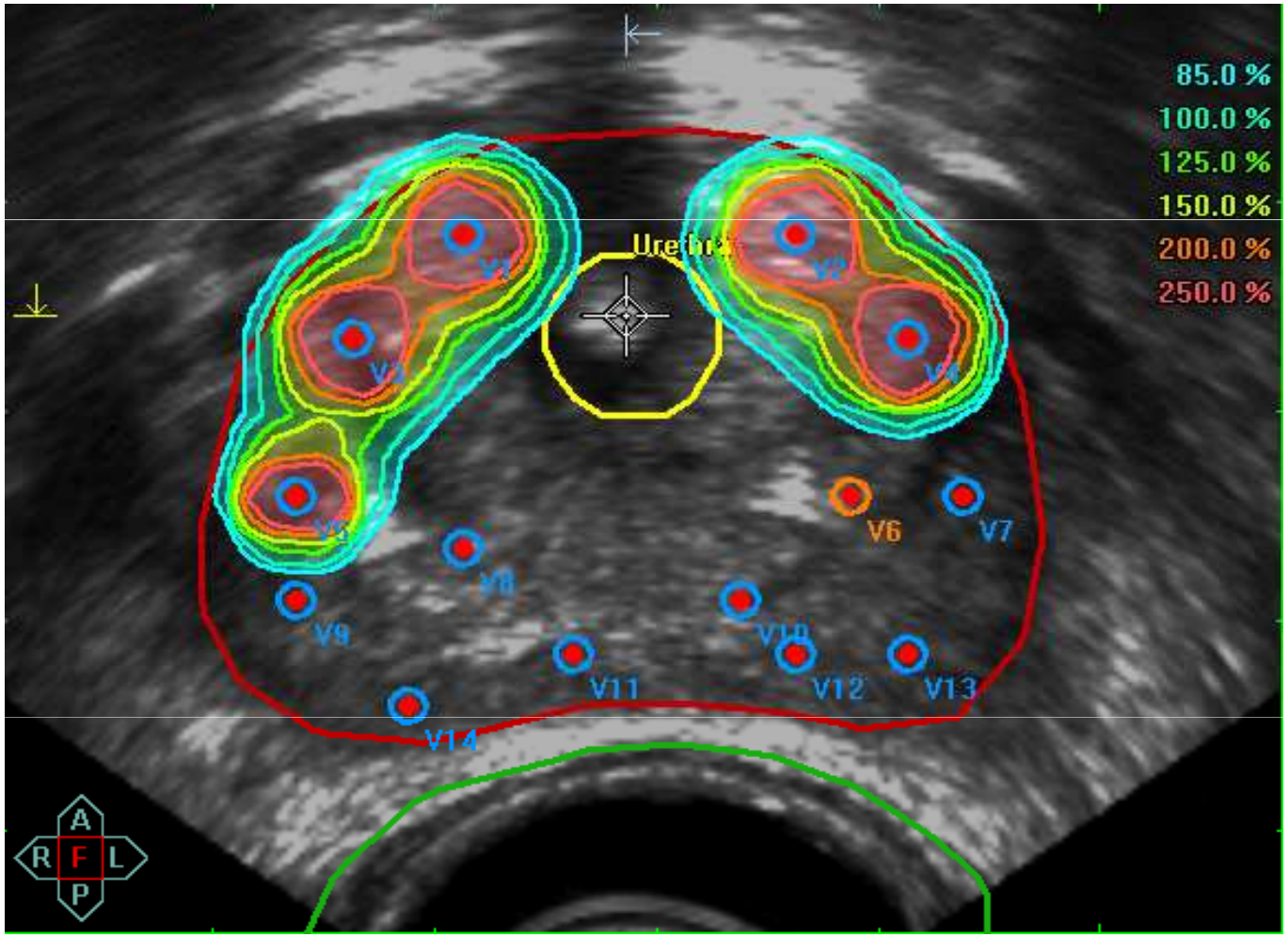
Treatment Delivery => Step and Shoot



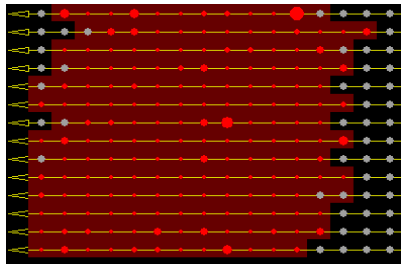


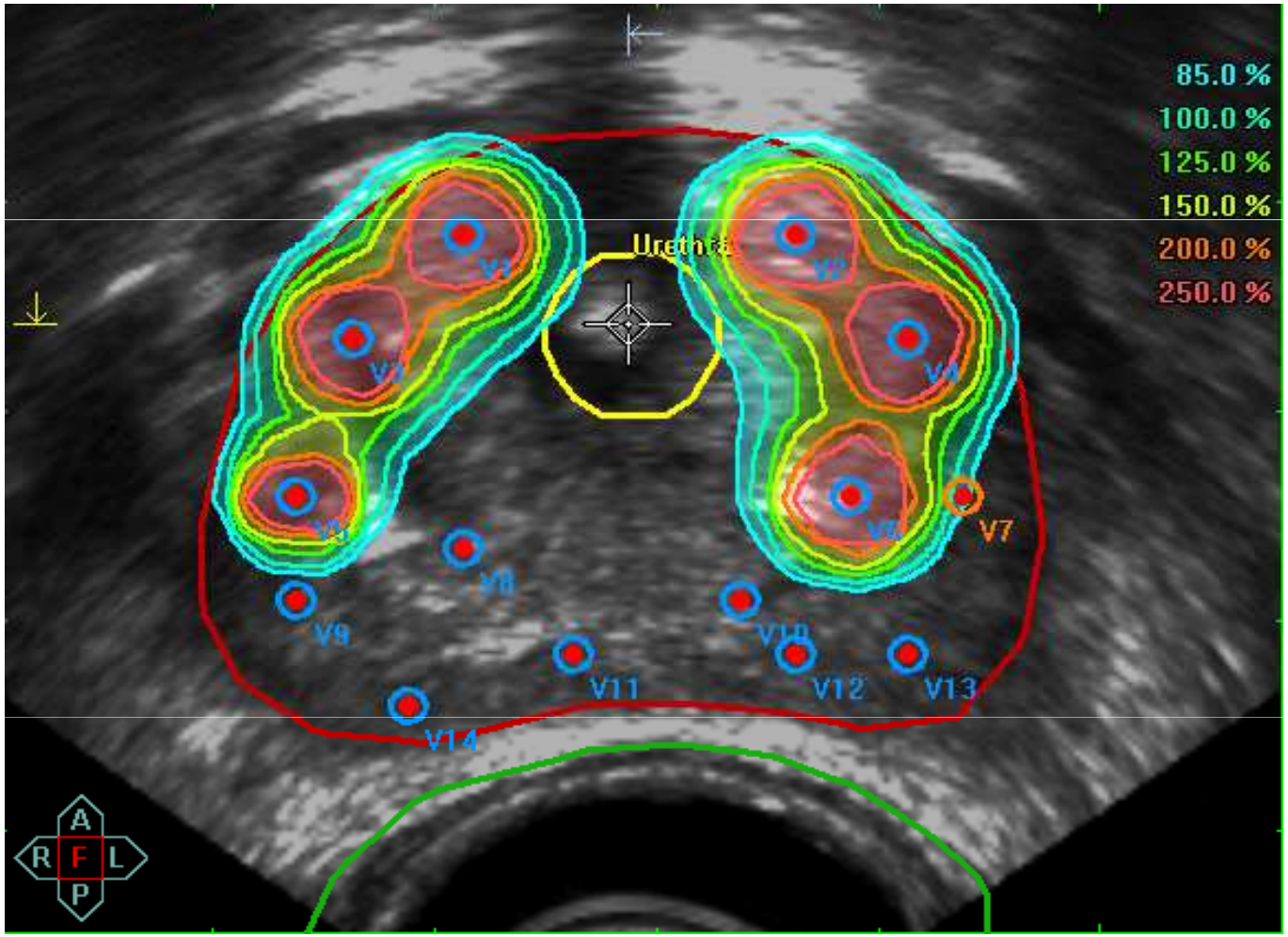
Treatment Delivery => Step and Shoot



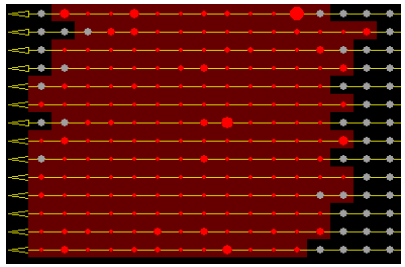


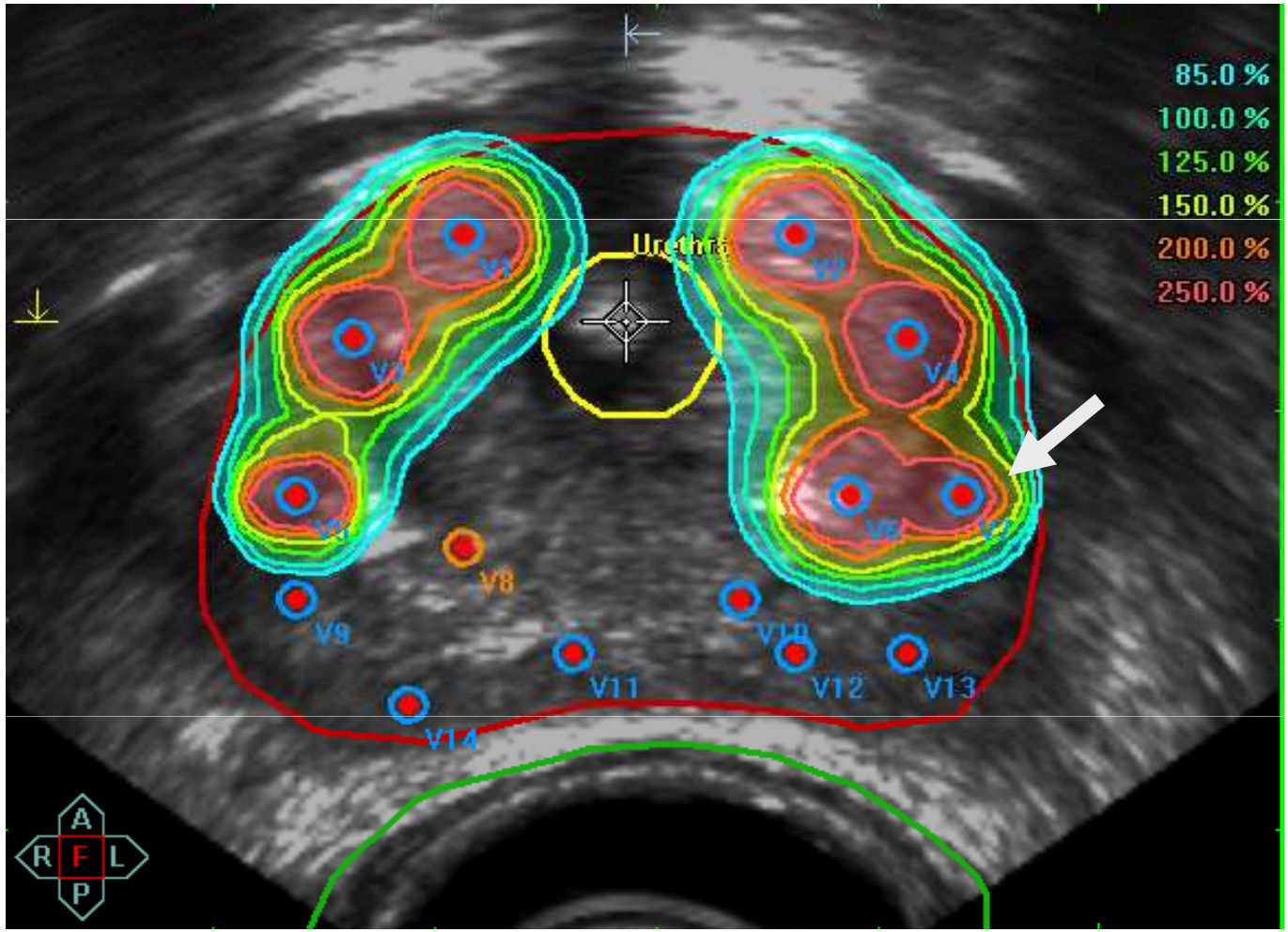
Treatment Delivery => Step and Shoot



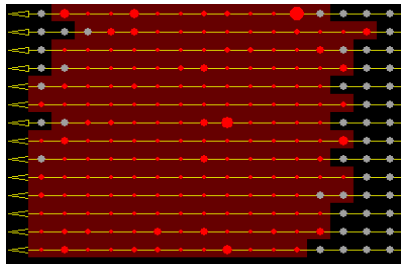


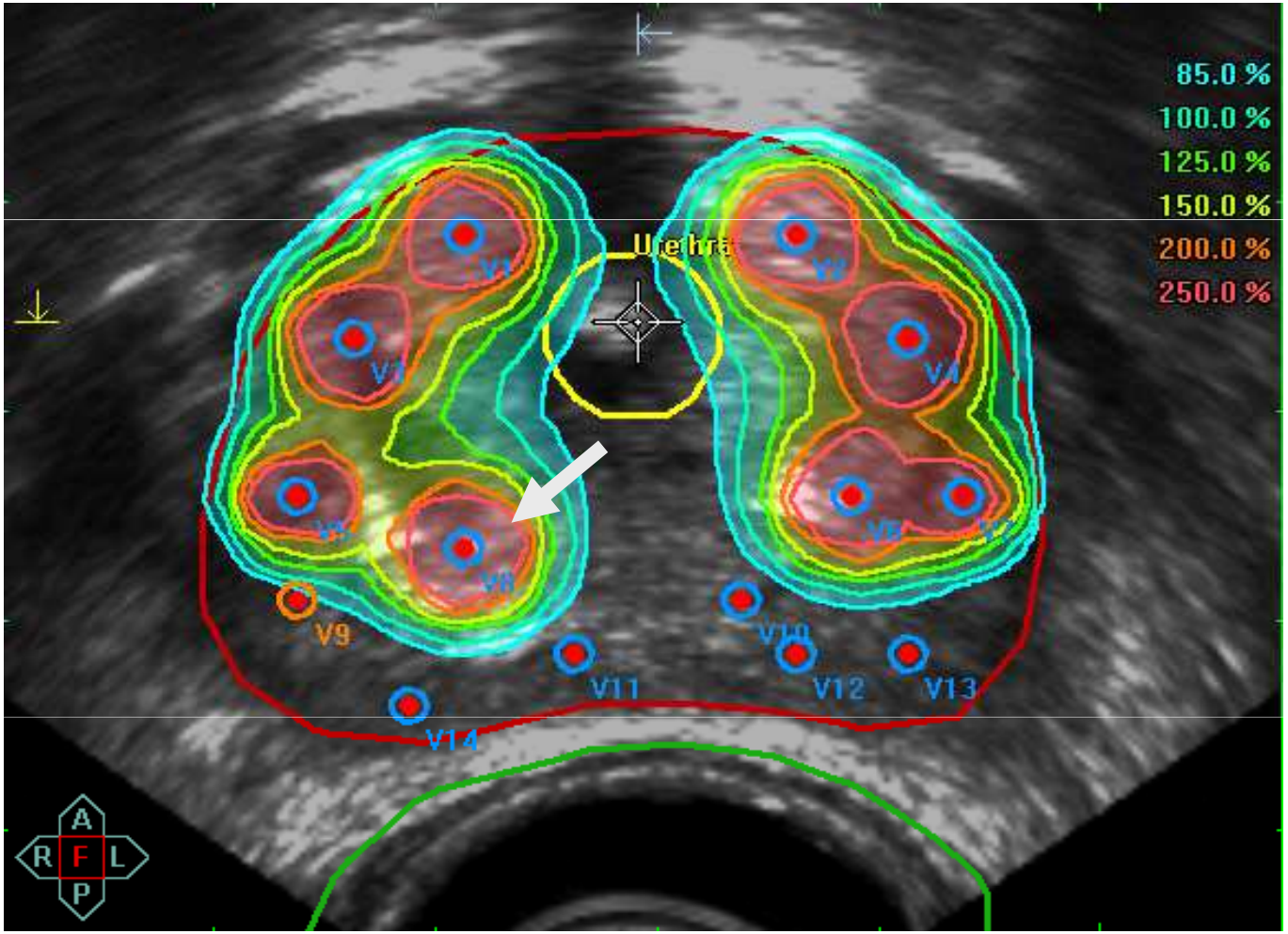
Treatment Delivery => Step and Shoot





Treatment Delivery => Step and Shoot





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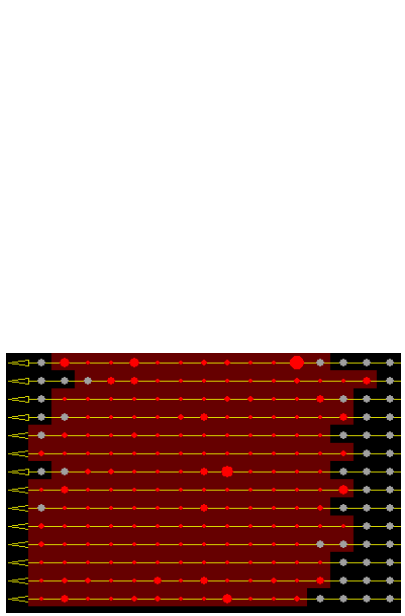
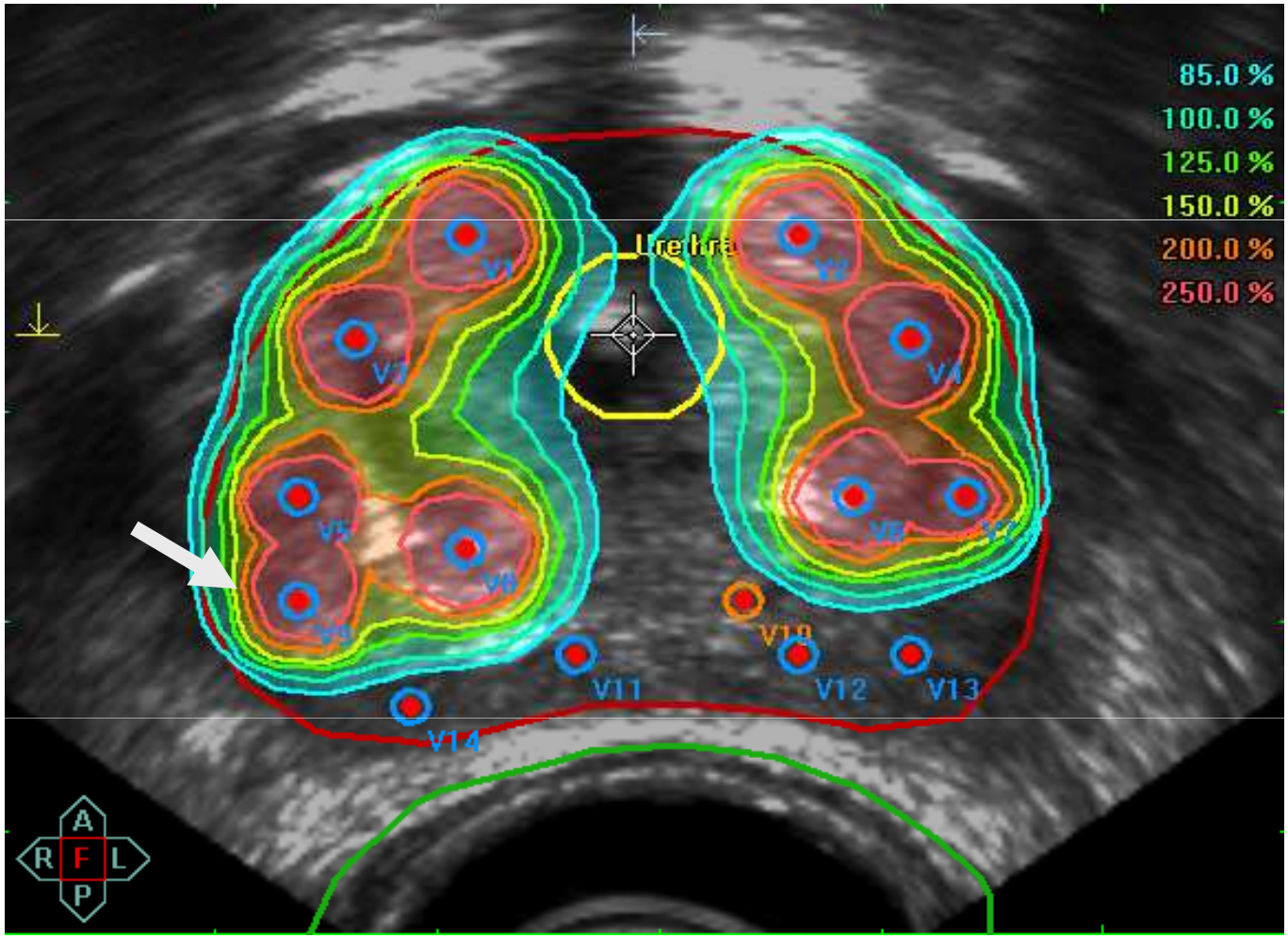
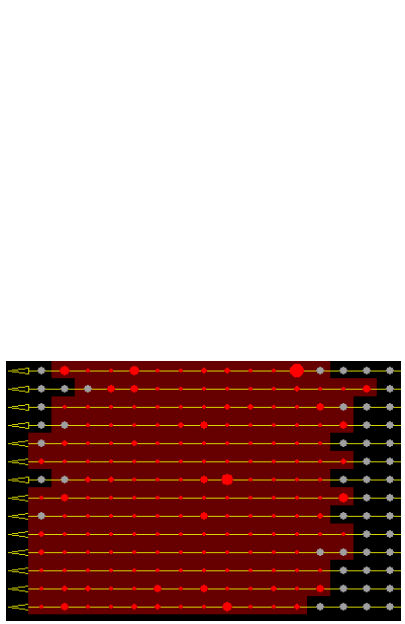
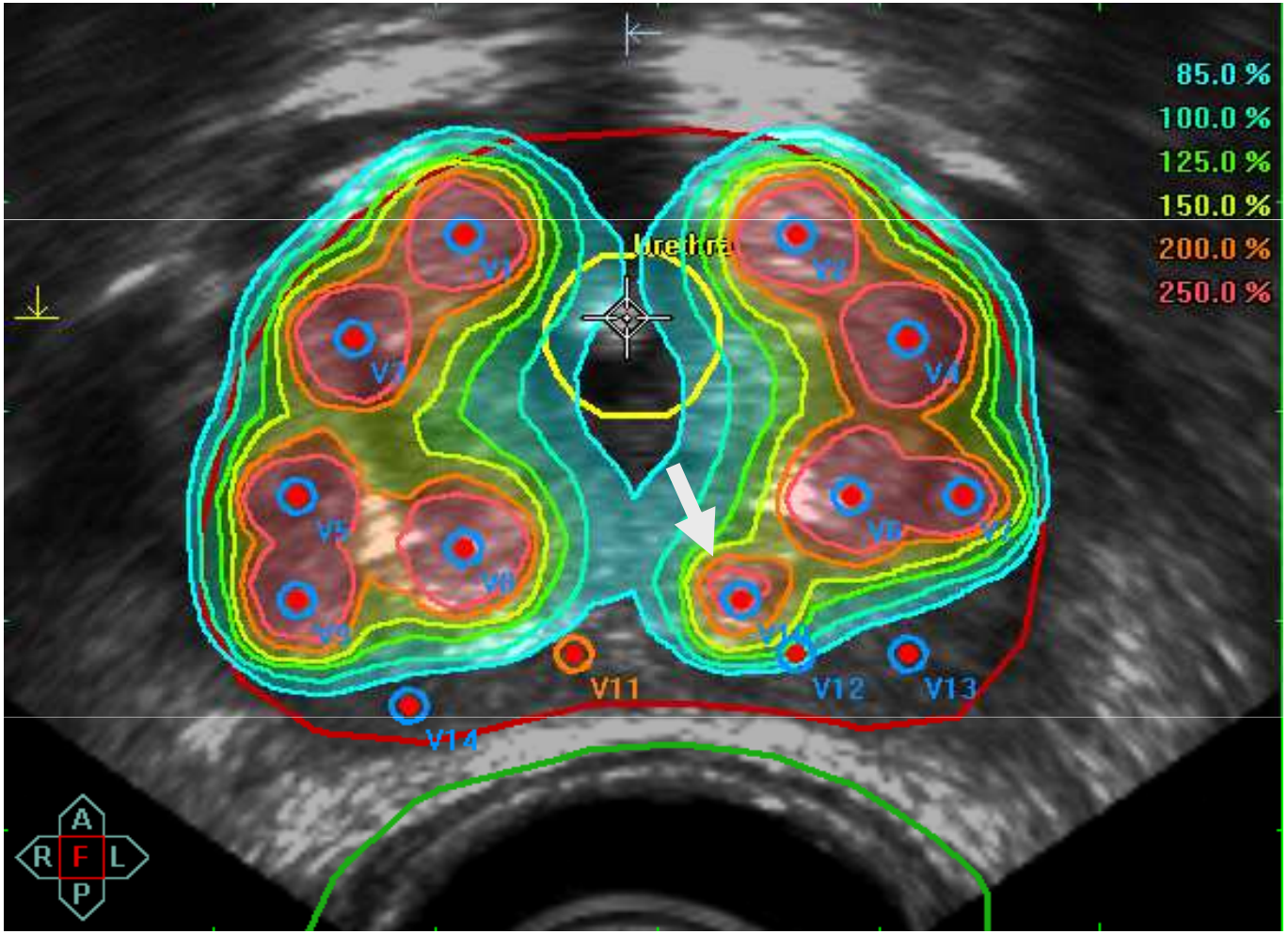
Treatment Delivery => Step and Shoot



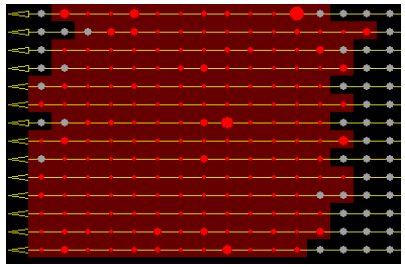


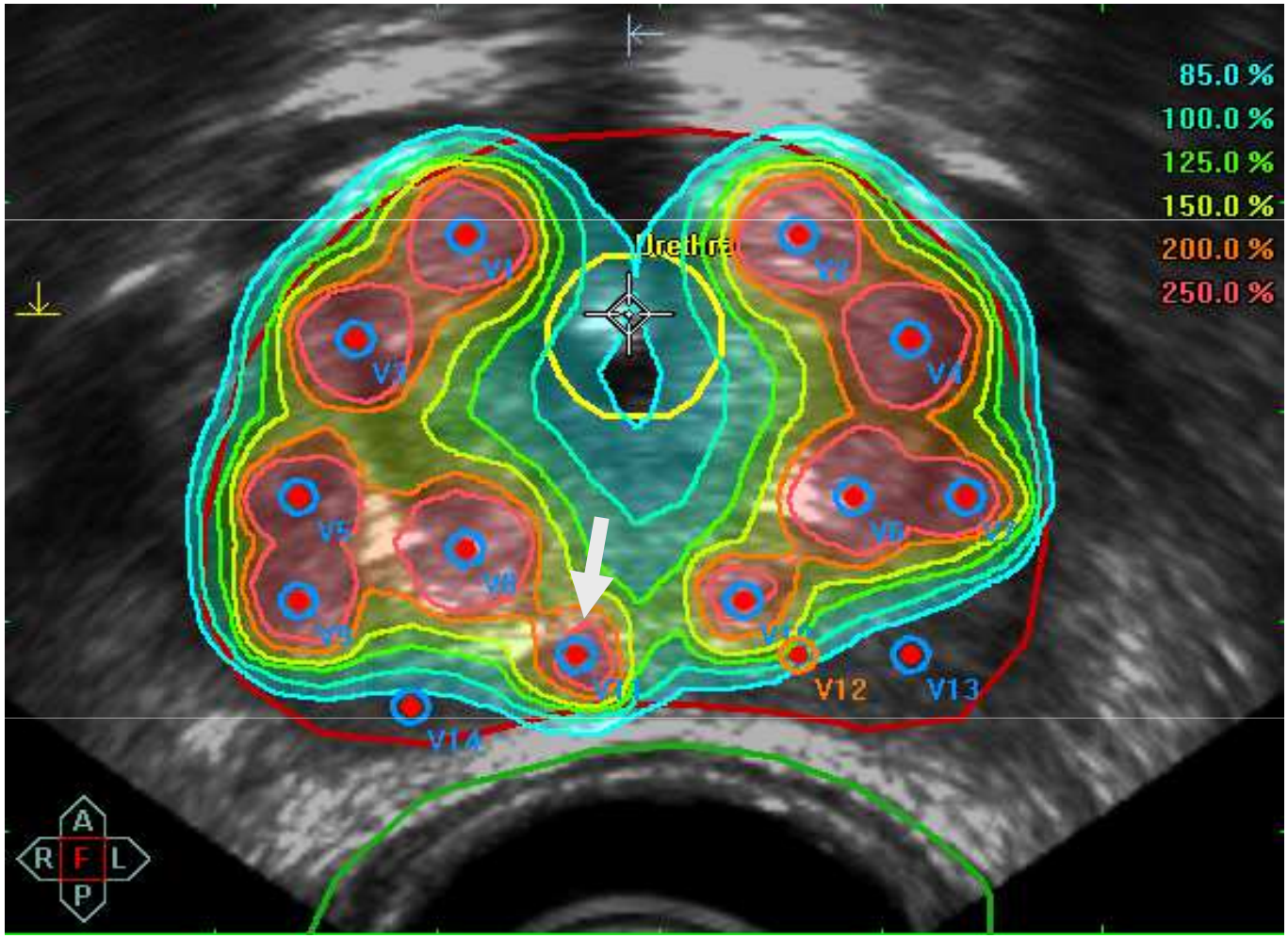
Treatment Delivery => Step and Shoot



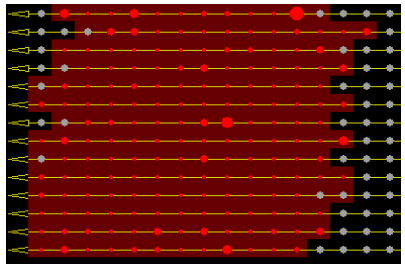


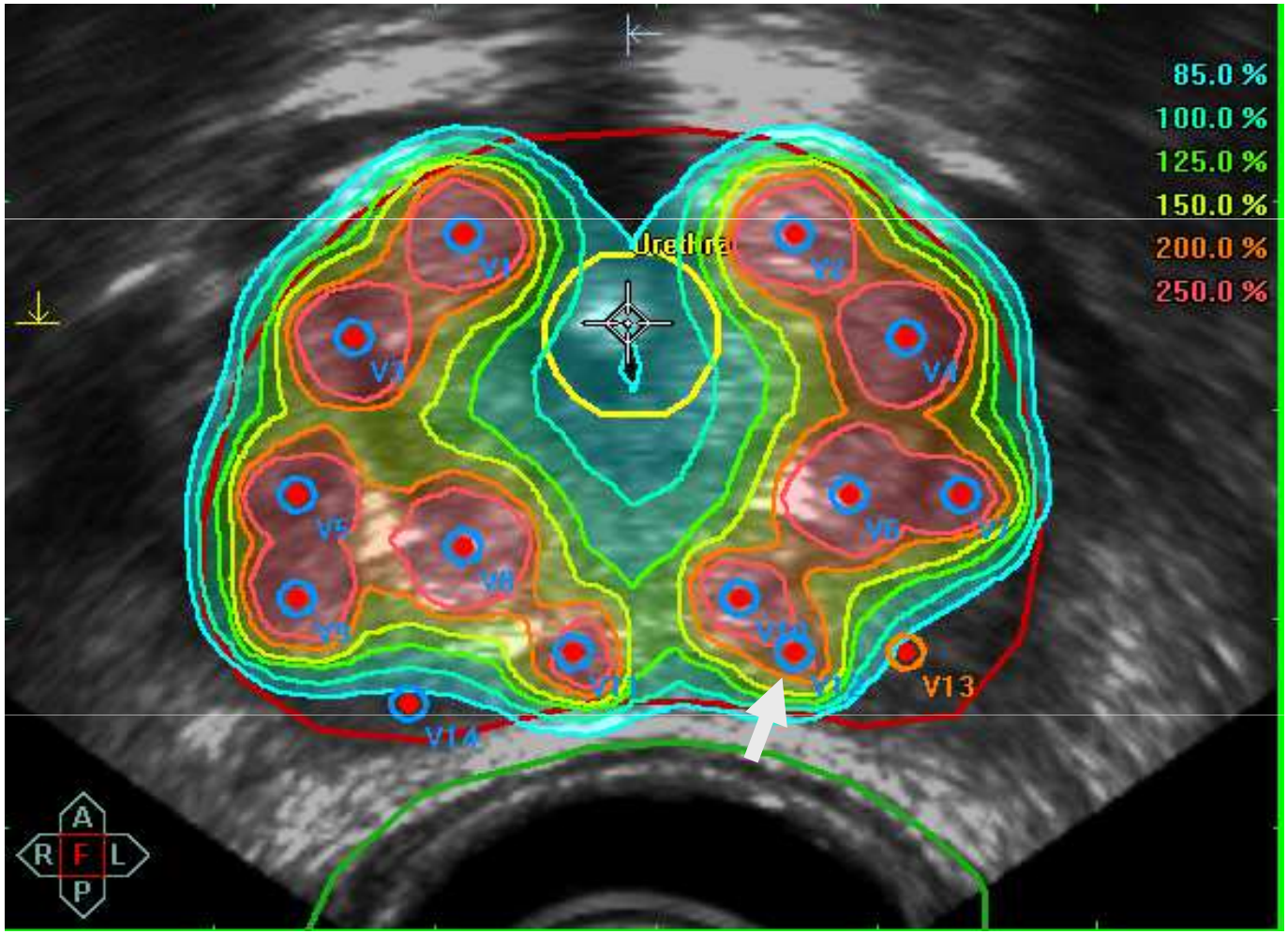
Treatment Delivery => Step and Shoot



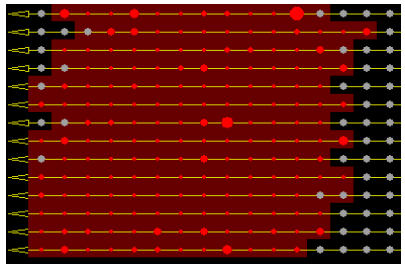


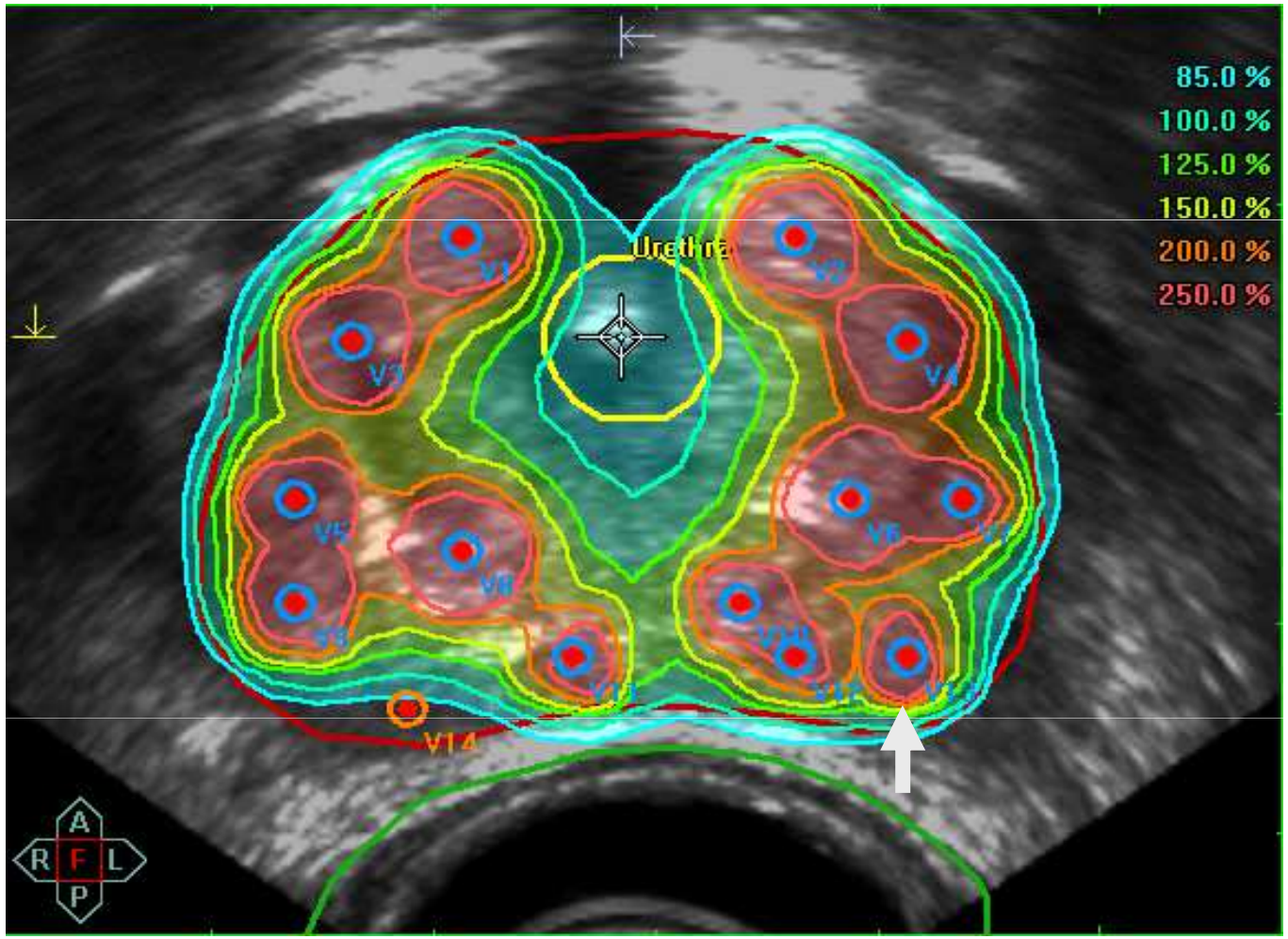
Treatment Delivery => Step and Shoot



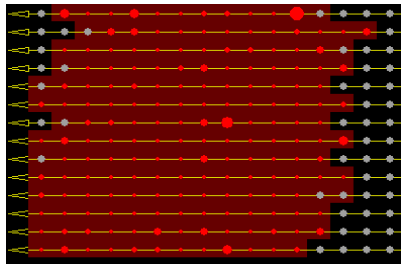


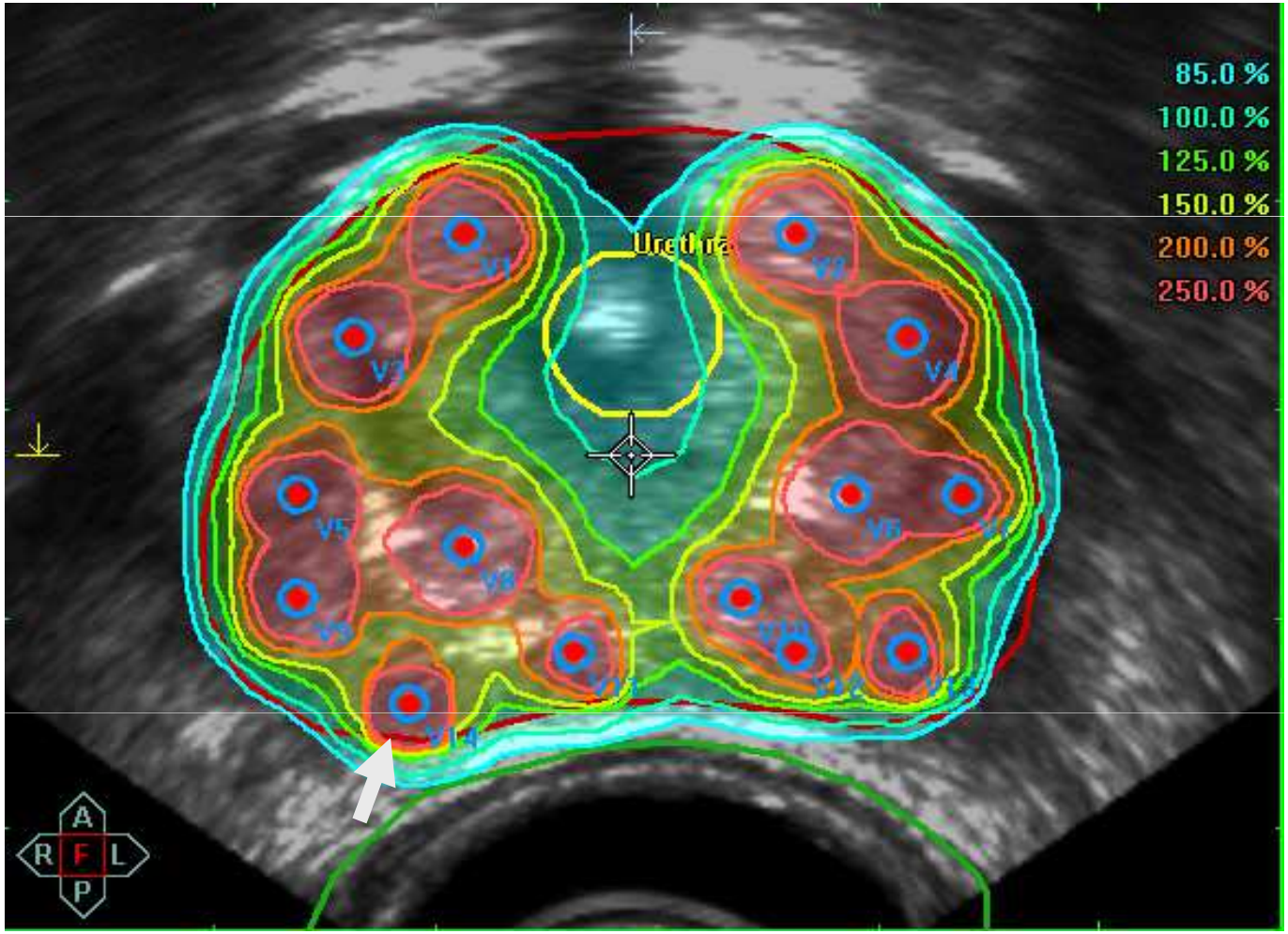
Treatment Delivery => Step and Shoot





Treatment Delivery => Step and Shoot

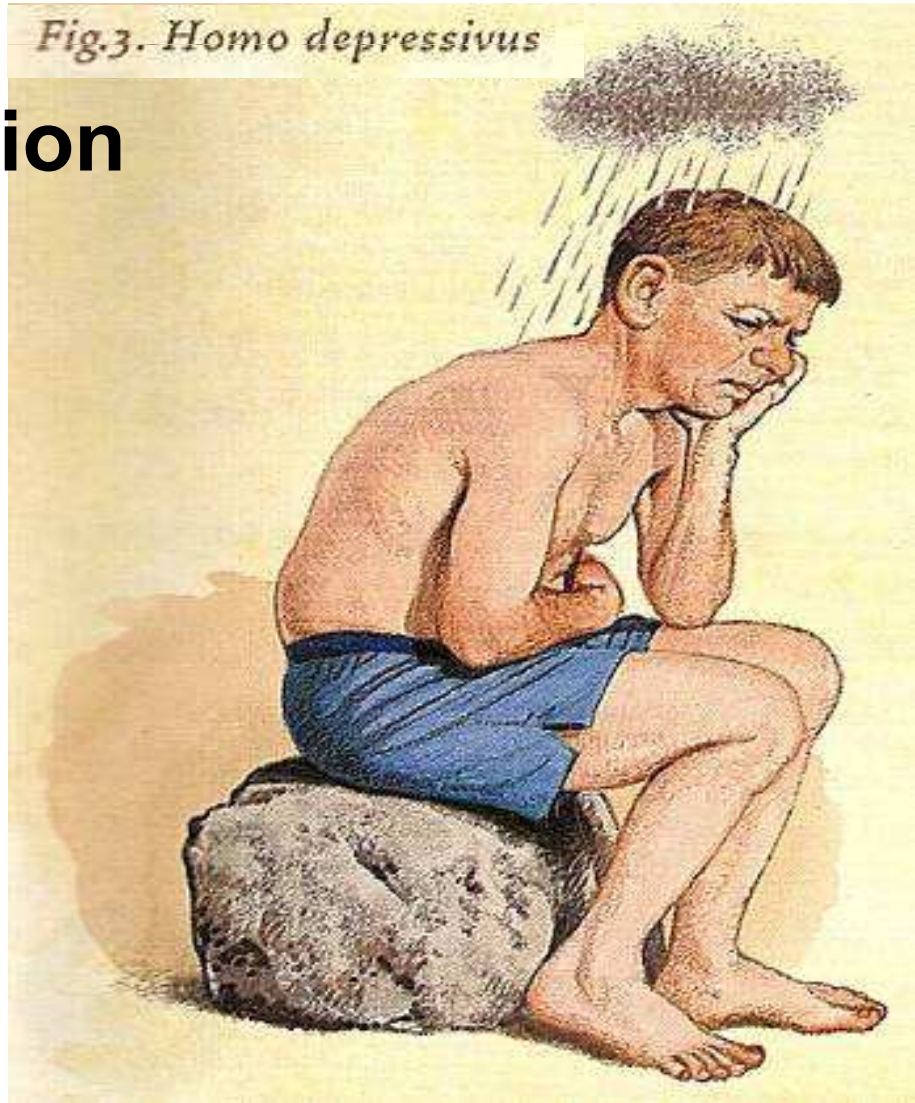




Topics:

- **Definition of Quantities**
- **Dosimetry and Dose Calculation**
  (for a one-source geometry)
- **Localization techniques**

  (…only if there is enough time)



Relevant Quantities:

- **Source Decay**
- **Source Strength:**

  Activity (mCi, GBq), Exposure Rate,

  Air Kerma Rate (K_a, S_K)

- **Absorbed Dose Rate**

  Attenuation and Diffusion
  (Absorption and Scatter)

- **Absorbed Dose**

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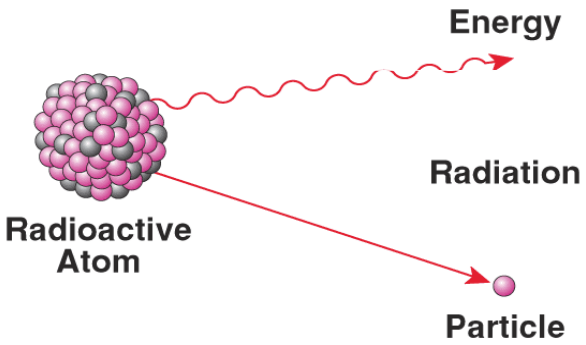
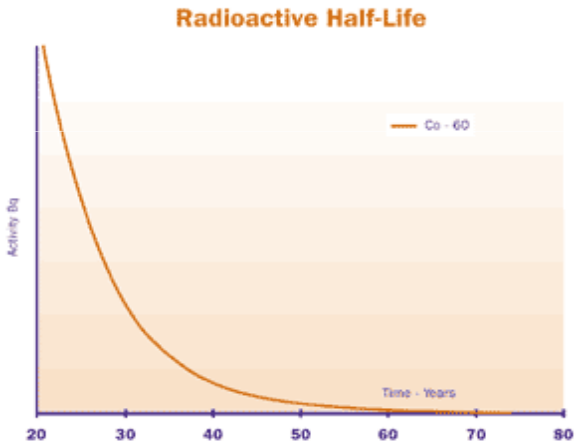
Radioactivity, decay calculation:





Half-life: The period of time it takes for radioactivity to reduce by half

- ***Number of nuclei prone to decay:***

$$N(t) = N_0 \cdot e^{-\lambda t}$$

- ***Activity:***

$$A(t) = -\Delta N(t) / \Delta t \approx N(t)$$

$$A(t) = A_0 . e^{-\lambda t}$$

- ***Decay constant:***

$$\lambda = \ln(2) / T_{1/2} = 0.693 / T_{1/2}$$

- ***Half life of the source:***

$$A(t = T_{1/2}) = \tfrac{1}{2} \cdot A_0$$

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Half Life $T_{1/2}$ of Radionuclides

Table 5.12 Physical characteristics of radionuclides used in brachytherapy. Photon energy ranges, mean and effective photon energies are according to Table 5.3 to Table 5.11, where only penetrating energies above 10 keV have been considered. The maximum specific activity is calculated for ideal (point) pure radionuclide sources using Eq. 2.60.

Radionuclide				Density[a] ρ (g.cm³)	Decay	Half life[a] $T_{1/2}$	Photon energy range (MeV)	Mean photon energy E_{mean} (MeV)	Effective energy E_{eff} (MeV)	Mean γ-energy (MeV)	HVL[c] (mm Pb)	Maximum specific activity (GBq.mg^{-1})	Γ_δ [e] (μGy.h^{-1}.MBq^{-1}.m²)	Type of implant
Name	Symbol	Z	A											
Caesium	Cs	55	131	1.873	EC	9.689 d [b]	0.029 – 0.034	0.030	0.030	---	0.030	3809.13	0.0151	Permanent
Caesium	Cs	55	137	1.873	β^-	30.07 a	0.032 – 0.662	0.615	0.652	0.662	7.0	3.202	0.0771	Temporary
Cobalt	Co	27	60	8.90	β^-	5.27 a	0.347 – 2.159	1.253	1.257	1.253	12.0	41.91	0.3059	Temporary
Gold	Au	79	198	19.32	β^-	2.695 d	0.069 - 1.088	0.406	0.417	0.415	2.8	9055.12	0.0545	Permanent
Iodine	I	53	125	4.93	EC	59.49 d	0.027 - 0.035	0.028	0.028	0.035	0.025	650.15	0.0348	Permanent or temporary
Iridium	Ir	77	192	22.42	β^-, EC	73.81 d	0.061 -1.378	0.355	0.398	0.372	3.0	340.98	0.1091	Temporary
Palladium	Pd	46	103	12.02	EC	16.991 d [b]	0.020 - 0.497	0.021	0.021	0.137	0.008	2763.13	0.0361	Permanent
Radium	Ra	88	226	5.00	α	1600 a [b]	0.047 - 2.45	0.830[f]	---	0.830[f]	13.0	0.0366	---	Temporary
Thulium	Tm	69	170	9.321	β^-, EC	128.6 d [b]	0.048 – 0.084	0.066	0.067	0.084	0.17[d]	221.07	0.00053	Temporary
Ytterbium	Yb	70	169	6.73	EC	32.015 d	0.021 - 0.773	0.093	0.131	0.143	0.23[d]	893.29	0.0431	Permanent or temporary

[a] According to NIST Physical Reference Data, on line version, 2004[14, 15]

[b] According to NUDAT Vs. 2.0 on line tables, 2004[3], [c] Half Value Layer (first) values most taken from ICRP 21 Figures 50 and 51[16]

[d] According to Granero et al., 2005[18] and Lymperopoulou et al., 2006[21]

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The “Strength” of a Source

Previously, source strength specification was based on “contents”, # of disintegrations per time unit

- **By Definition: 1 Ci (3.7×10^{10} s^{-1}) Activity of 1 g Ra-226**
- **In SI-units: 1 Disintegration per s = 1 Bq**

(mostly using a prefix: MBq, GBq)

Example: 1 mCi = 37 MBq

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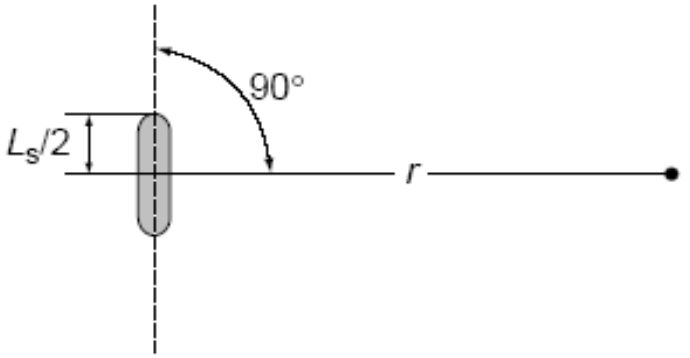
The “Strength” of a Source

Now, Specification of Sources in terms of Energy Deposition, per unit of time at a given distance:

- exposure rate: R. h^{-1} @ 1cm
- **in Air Kerma Rate: μGy . h^{-1} @ 1 m**



For linear sources this can be expressed in

- exposure rate per unit of length, or
- **Air Kerma Rate units per unit of length**

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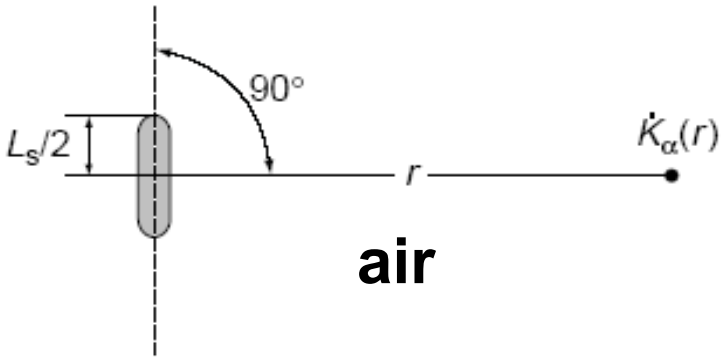
The “Strength” of a Source

Reference Air Kerma Rate K_R

$$K_R = K_a(r = 1m)$$



r = 1m

The reference air kerma rate of a source is defined as the air kerma rate in air at a reference distance of 1 m from the center of the source, corrected for attenuation and scattering in air. This is the air kerma rate *in vacuo*. For rigid sources usually considered in the practice of brachytherapy (as distinct from malleable wire sources), the direction from the source center to the reference point at 1 m has to be at right angles to the long axis of the source.

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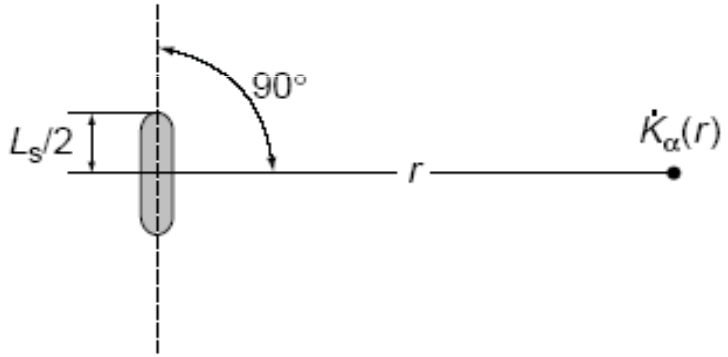
The “Strength” of a Source

Air Kerma Strength S_K



AAPM, North America

$$S_K = \dot{K}_\alpha(r) r^2$$

If r = 1m then we have in the above Equation the Reference Air Kerma Rate K_R

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The "Strength" of a Source

Air Kerma Rate Constant Γ_δ

Let us consider a source of irradiation being a point in free space (vacuum), an *ideal point source*, consisting of a specific radionuclide and having an activity A. If $\dot{K}_\delta$ is the air kerma rate due to photons of energy greater than a certain cut-off value δ at a distance r from that point source, the *air kerma-rate constant* Γ_δ (J kg^{-1} m^2) of that radionuclide is defined as

$$\Gamma_\delta = \frac{r^2 \dot{K}_\delta}{A} \qquad (2.61)$$

Using the special names gray (Gy) for the kerma and becquerel (Bq) for the activity, the unit of the air kerma-rate constant is Gy s^{-1} Bq^{-1} m^2.

For monoenergetic Source:

$$\Gamma_\delta = \left(\frac{1}{4\pi}\right) E \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha,E}$$

For Source with known Spectrum:

$$\Gamma_\delta = \left(\frac{1}{4\pi}\right) \sum_i \left\{ n_i E_i \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha,E_i} \right\}$$

The "Strength" of a Source

Table 5.12 Physical characteristics of radionuclides used in brachytherapy. Photon energy ranges, mean and effective photon energies are according to Table 5.3 to Table 5.11, where only penetrating energies above 10 keV have been considered. The maximum specific activity is calculated for ideal (point) pure radionuclide sources using Eq. 2.60.

Radionuclide				Density[a] ρ (g.cm³)	Decay	Half life[a] $T_{1/2}$	Photon energy range (MeV)	Mean photon energy E_{mean} (MeV)	Effective energy E_{eff} (MeV)	Mean γ-energy (MeV)	HVL[c] (mm Pb)	Maximum specific activity (GBq.mg^{-1})	Γ_δ[e] (μGy.h^{-1}.MBq^{-1}.m²)	Type of implant
Name	Symbol	Z	A											
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Gold	Au	79	198	19.32	β^-	2.695 d	0.069 - 1.088	0.406	0.417	0.415	2.8	9055.12	0.0545	Permanent
Iodine	I	53	125	4.93	EC	59.49 d	0.027 - 0.035	0.028	0.028	0.035	0.025	650.15	0.0348	Permanent or temporary
Iridium	Ir	77	192	22.42	β^-, EC	73.81 d	0.061 -1.378	0.355	0.398	0.372	3.0	340.98	0.1091	Temporary
Palladium	Pd	46	103	12.02	EC	16.991 d [b]	0.020 - 0.497	0.021	0.021	0.137	0.008	2763.13	0.0361	Permanent
Radium	Ra	88	226	5.00	α	1600 a [b]	0.047 - 2.45	0.830[f]	---	0.830[f]	13.0	0.0366	---	Temporary
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[a] According to NIST Physical Reference Data, on line version, 2004[14, 15]

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[d] According to Granero et al., 2005[18] and Lymperopoulou et al., 2006[21]

TABLE 7.2

Summary of Recommended Values of the Air Kerma Rate Constant Γ_δ for the Brachytherapy Radionuclides and for Ideal Point Sources

	Air Kerma Rate Constant Γ_δ (μGy h^{-1} MBq^{-1} m^2 = U MBq^{-1})			
Radionuclide	ICRU Report 58[8]	AAPM Report 51[15]	Table 5.2 (δ = 10 keV)	Real Sources Literature
$^{137}_{55}$Cs	0.0772	—	0.0771	
$^{60}_{27}$Co	0.306	—	0.3059	
$^{198}_{79}$Au	0.0559	—	0.0545	
$^{125}_{53}$I	0.0337	0.0358/ 0.0355[a]	0.0348	0.0206 − 0.0219[b], 0.0217[c]
$^{192}_{77}$Ir	0.108 [0.100, 0.116]	0.111	0.1091	0.0993 − 0.975[d], 0.1027[e], 0.110[f], 0.0973[g], 0.0979[h], 0.1025[i], 0.107[j], 0.0992[k]
$^{103}_{46}$Pd	0.0343	0.035/ 0.0361[a]	0.0361	0.0173[l]
$^{170}_{69}$Tm	—	—	0.00053	
$^{169}_{70}$Yb	—	—	0.0431	0.0427[25] (δ = 10 keV), 0.0359[m], 0.0297[n] (δ = 10 keV),

Γ_δ values which are given in the literature for commercially available sources are also listed.

[a] Revised values using a cut-off value of δ = 5 keV in AAPM Report TG-43 update.[17]

[b] STM1251-^{125}I-seed.[21]

[c] selectSeed-^{125}I.[23]

[d] PDR source designs for the microSelectron-PDR afterloader system from Nucletron B.V., The Netherlands considering δ = 11.3 keV.[18]

[e] HDR source design (5 mm active length) for the VariSource afterloader from Varian Oncology Systems, USA.[19]

[f] HDR and PDR source designs for the microSelectron afterloaders from Nucletron B.V., The Netherlands.[20]

[g] New design for the microSelectron-HDR afterloader considering δ = 11.3 keV.[26]

[h] Old design for the microSelectron-HDR afterloader considering δ = 11.3 keV.[26]

[i] Old HDR source design (10 mm active length) for the VariSource afterloader considering δ = 11.3 keV.[26]

[j] Seed source from Best Industries Inc., U.S.A. considering δ = 11.3 keV.[26]

[k] Seed source from Alpha-Omega Services, Inc., U.S.A., considering δ = 11.3 keV.[26]

[l] Model 200-^{103}Pd-seed.[22]

[m] X1267-^{169}Yb.[24]

[n] Model HDR 4140 ^{169}Yb by Implant Sciences Corporation, U.S.A., considering δ = 10 keV.[79]

Baltas et al., Taylor & Francis, 2007

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The "Strength" of a Source

Units and Conversion Factors

TABLE 7.1

Units and Unit Conversion Factors for Reference Air Kerma Rate and Air Kerma Strength

Source Strength Quantity	Symbol	SI	Current Unit	Conversion Factor
Reference air kerma rate	$\dot{K}_R$	$Gy\ s^{-1}$	$\mu Gy\ h^{-1}$	$(1/3600) \times 10^{-6}\ Gy\ s^{-1} = 2.778 \times 10^{-10}\ Gy\ s^{-1}$
			$mGy\ h^{-1}$	$(1/3600) \times 10^{-3}\ Gy\ s^{-1} = 2.778 \times 10^{-7}\ Gy\ s^{-1}$
			$mGy\ h^{-1}$	$1.0 \times 10^{3}\ \mu Gy\ h^{-1}$
Air kerma strength	S_K	$Gy\ m^2\ s^{-1}$	U, 1 U = 1 $\mu Gy\ m^2\ h^{-1}$ = 1 cGy $cm^2\ h^{-1}$	$(1/3600) \times 10^{-6}\ Gy\ m^2\ s^{-1} = 2.778 \times 10^{-10}\ Gy\ m^2\ s^{-1}$
Air kerma rate constant	Γ_δ	$J\ kg^{-1}\ m^2$ or $Gy\ s^{-1}\ Bq^{-1}\ m^2$	$\mu Gy\ h^{-1}\ MBq^{-1}\ m^2$	$(1/3600) \times 10^{-12}\ Gy\ s^{-1}\ Bq^{-1}\ m^2 = 2.778 \times 10^{-16}\ Gy\ s^{-1}\ Bq^{-1}\ m^2$
			$\mu Gy\ h^{-1}\ MBq^{-1}\ m^2$	$1.0\ U\ MBq^{-1}$

Baltas et al., Taylor & Francis, 2007

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The “Strength” of a Source

Apparent Activity A_{app}:

S_K

$$A_{app} = 10^{-6}\left(\frac{1}{3600}\right)\frac{\dot{K}_R r_{ref}^2}{\Gamma_\delta}$$

usually in MBq

where $\dot{K}_R$ is the reference air kerma rate expressed in μGy h^{-1} and r_{ref} is the reference distance of 1 m.

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The “Strength” of a Source

Reference Air Kerma Rate K_R

Air Kerma Strength S_K

Note:

The quantity of preference to specify the source strength would be the “absorbed dose to water at a specified distance in a full water geometry” (as it is the case for ERT). This is, however, until now not achievable in practice.

Currently the dosimetry systems (e.g. Well Type Chambers) are calibrated at least for Reference Air Kerma Rate K_R or equivalently for Air Kerma Strength S_K.

!

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Dosimetry of Sealed Radioactive Sources*

Dose Calculation around a Sealed Source*

*Photon emitting sources

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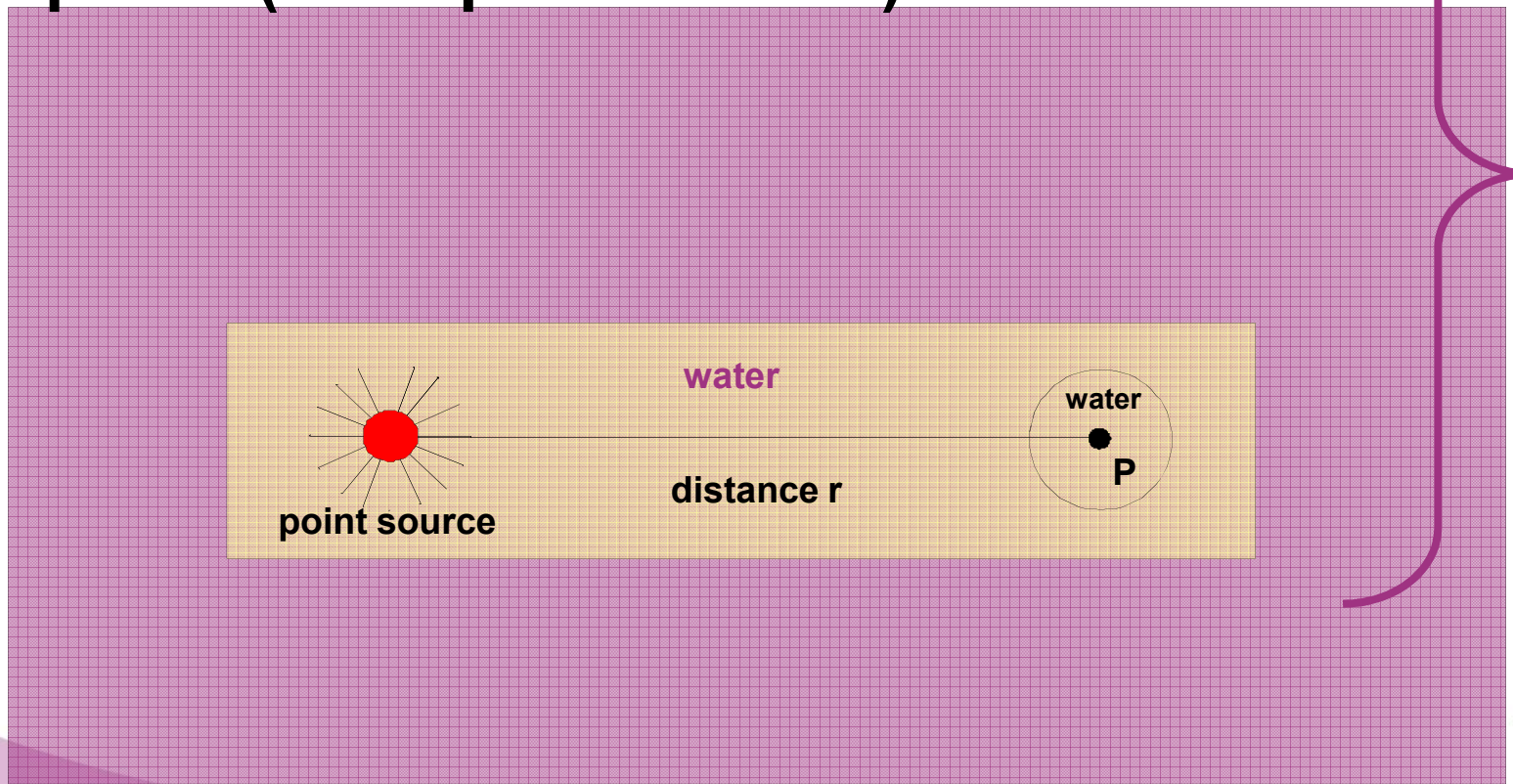
Dosimetry in homogeneous, full scatter phantom:

This is what we want to know:

***Absorbed Dose-to-water at a point P in water medium*, taking into account scatter and absorption (ideal point source)**



4 x Steps

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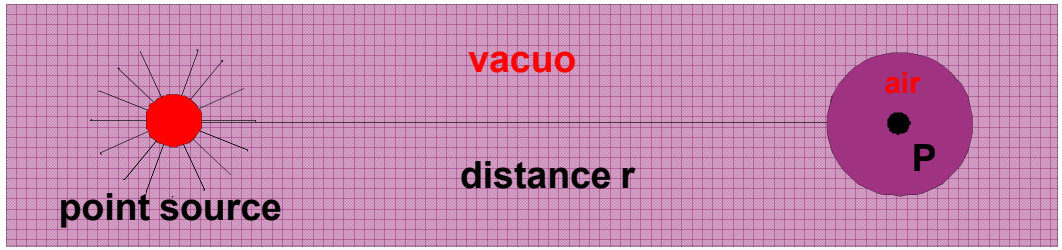
Absorbed Dose-to-water

This is what we know:

Step 1: At the place of point of interest P, at a distance r (Figure 8.3a) from the source *in vacuo*, a small air volume containing an air mass dm_α is considered.

Step - 1

$$\dot{K}_\alpha(r) = \dot{K}_R\left(\frac{r_0}{r}\right)^2$$



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Absorbed Dose-to-water

Step - 2

Step 2: The absorbed dose rate to air in the air volume dV, $D_\alpha(r)$, is given by the collision kerma rate (see Equation 2.42 and Section 2.5) $\dot{K}_{\mathrm{col},\alpha}(r)$ in that air volume

$$\dot{D}_\alpha(r) = \dot{K}_{\mathrm{col},\alpha}(r) = \dot{K}_\alpha(r)(1 - g_\alpha)$$

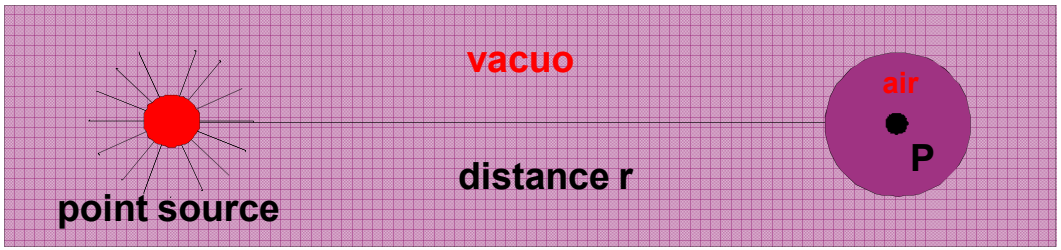
g_α is the fraction of the energy of the electrons liberated by photons in air that is lost due to radiative processes (bremsstrahlung and fluorescence). Values of g_α for different photon energies are given in Table 7.9, where for almost all radionuclides g_α is practically 0.

Considering Equation 8.1 and Equation 8.2, the absorbed dose rate to air *in vacuo* is

$$\dot{D}_\alpha(r) = \dot{K}_\mathrm{R}(1 - g_\alpha)\left(\frac{r_0}{r}\right)^2 \qquad (8.3)$$

or

$$\dot{D}_\alpha(r) = S_\mathrm{K}(1 - g_\alpha)\left(\frac{1}{r}\right)^2 \qquad (8.4)$$



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Absorbed Dose-to-water

Step 3: Consider now the situation demonstrated in Figure 8.3b, where the volume element dV is filled with water containing a water mass dm_w. Assuming secondary particle (electron) equilibrium, CPE, conditions,[1] the absorbed dose rate to water $\dot{D}_w(r)$ at the point P *in vacuo* can be calculated from the absorbed dose to air $\dot{D}_\alpha(r)$ at the same place, by correcting for the differences in the mass absorption coefficients between the two media:[1]

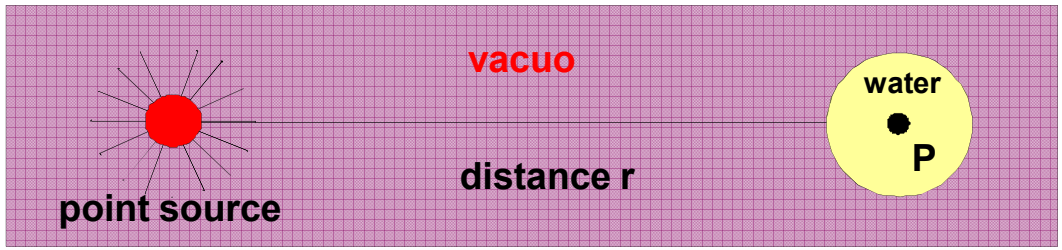
$$\dot{D}_w(r) = \dot{D}_\alpha(r)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w$$

Step - 3

or

$$\dot{D}_w(r) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{r_0}{r}\right)^2$$

$$\dot{D}_w(r) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{1}{r}\right)^2$$



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Absorbed Dose-to-water

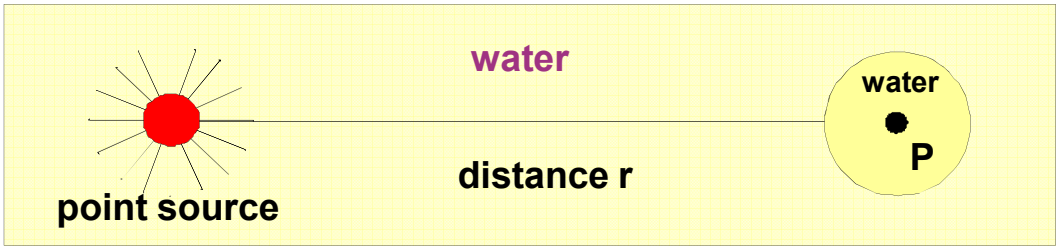
Step 4: Finally, the situation is considered where the space around source and point of interest P(r) is also filled with water (Figure 8.3c). In contrast to the situation *in vacuo*, in water there are attenuation and scatter effects that influence the radiation field at the distance r from the source.

Step - 4

or

$$\dot{D}_w(r) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{r_0}{r}\right)^2 f_{as,w}(r)$$

$$\dot{D}_w(r) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{1}{r}\right)^2 f_{as,w}(r)$$



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Absorbed Dose-to-water

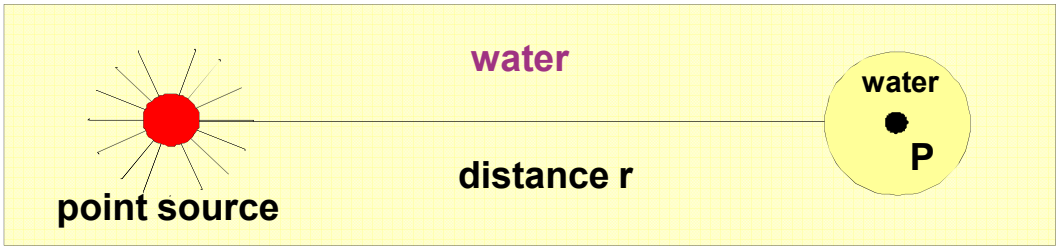
$f_{as,w}(r)$ is the correction for the absorption and scattering effects of the photons emitted from the source at the distance r in water, when compared to the same point in *vacuo*.

Step - 4

or

$$\dot{D}_w(r) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{r_0}{r}\right)^2 f_{as,w}(r)$$

$$\dot{D}_w(r) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{1}{r}\right)^2 f_{as,w}(r)$$



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$$\dot{D}_w(r) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{r_0}{r}\right)^2 f_{as,w}(r)$$

$$\dot{D}_w(r) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w\left(\frac{1}{r}\right)^2 f_{as,w}(r)$$

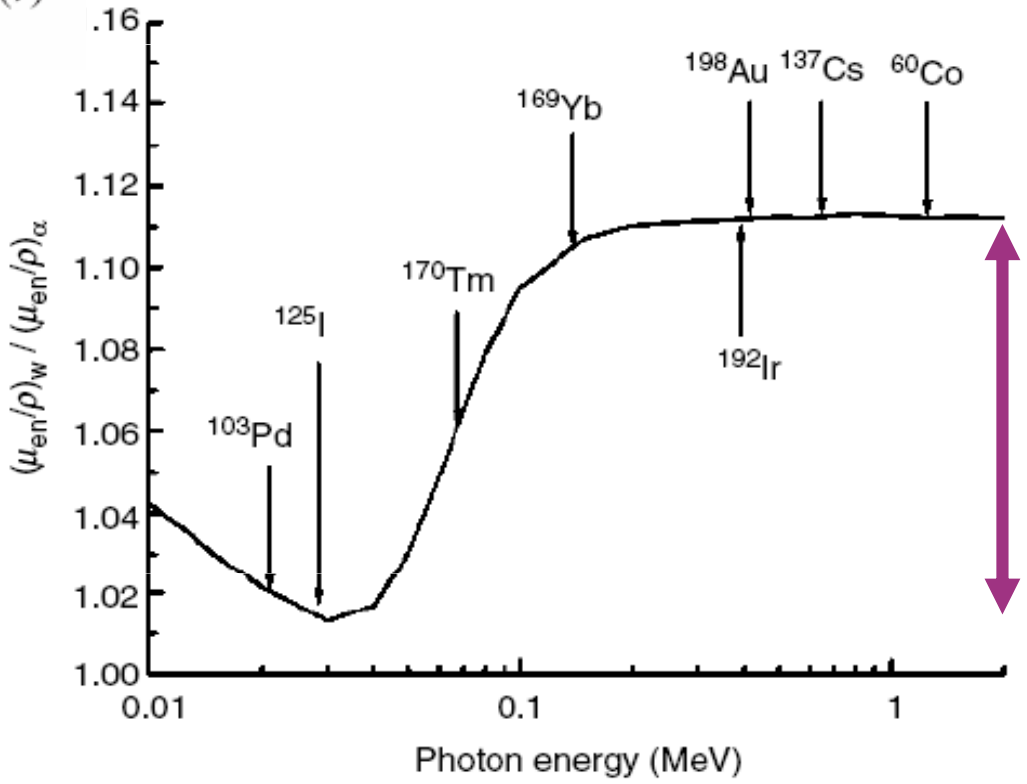

FIGURE 8.4
Energy dependence of the ratio of mass energy absorption coefficients of water to that of air, $(\mu_{en}/\rho)_\alpha^w$, in the brachytherapy related energy range 0.01 to 2.0 MeV. The mass energy absorption coefficients for dry air and liquid water considered are according to Hubbell and Seltzer.[19] The corresponding values for the different brachytherapy radionuclides calculated using their effective energies as listed in Table 5.2, and a log–log interpolation in the tables of Hubbell and Seltzer,[19] are also indicated.

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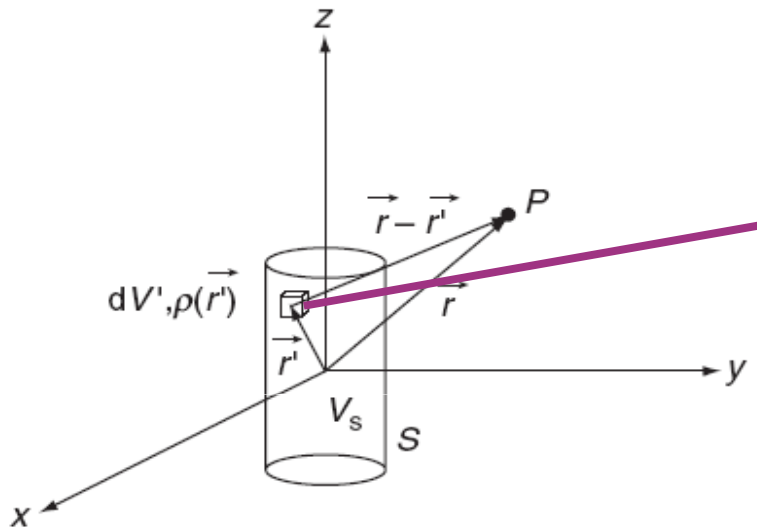
Absorbed Dose-to-water

Real Sources



Spatial distribution

$$d\dot{K}_\alpha(\vec{r}) = \dot{K}_R \left[\frac{\rho(\vec{r}\,')}{\int_{V_s} \rho(\vec{r}\,')dV'} \right] \left(\frac{r_0}{|\vec{r} - \vec{r}\,'|} \right)^2$$

$$d\dot{K}_\alpha(\vec{r}) = S_K \left[\frac{\rho(\vec{r}\,')}{\int_{V_s} \rho(\vec{r}\,')dV'} \right] \left(\frac{1}{|\vec{r} - \vec{r}\,'|} \right)^2$$

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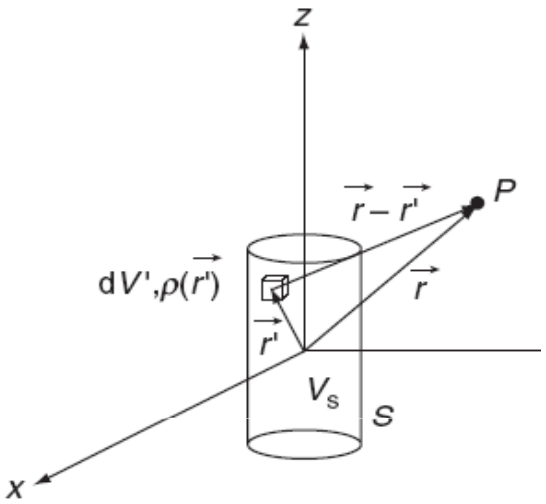
Absorbed Dose-to-water

Real Sources

Spatial distribution



$$\dot{K}_\alpha(\vec{r}) = \int_{V_s} d\dot{K}_\alpha(\vec{r})dV' = \dot{K}_R \left[\frac{\int_{V_s} \frac{\rho(\vec{r}')dV'}{|\vec{r}-\vec{r}'|^2}}{\int_{V_s} \rho(\vec{r}')dV'} \right] r_0^2 \qquad (8.9)$$

or based on the air kerma strength S_K:

$$\dot{K}_\alpha(\vec{r}) = \int_{V_s} d\dot{K}_\alpha(\vec{r})dV' = S_K \left[\frac{\int_{V_s} \frac{\rho(\vec{r}')dV'}{|\vec{r}-\vec{r}'|^2}}{\int_{V_s} \rho(\vec{r}')dV'} \right] \qquad (8.10)$$

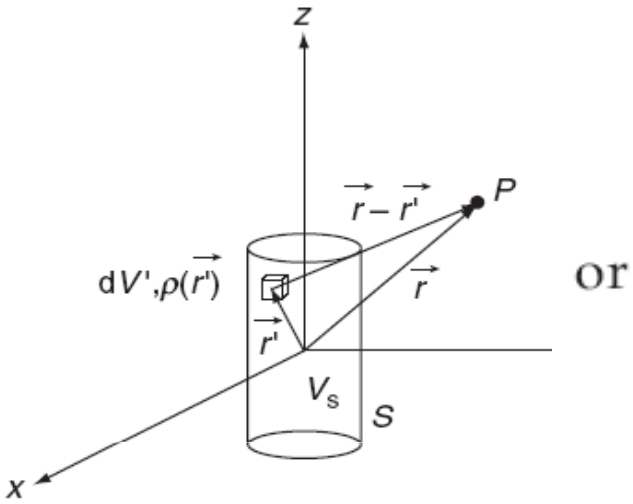
It has been established to name the fraction in the brackets in the above two equations as geometry function, $G(\vec{r})$:

$$G(\vec{r}) = \frac{\int_{V_s} \frac{\rho(\vec{r}')dV'}{|\vec{r}-\vec{r}'|^2}}{\int_{V_s} \rho(\vec{r}')dV'} \qquad (8.11)$$

!

Absorbed Dose-to-water

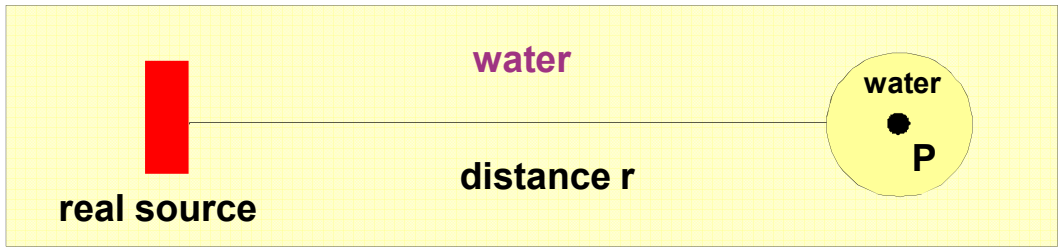
Real Sources



or

$$\dot{D}_w(\vec{r}) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w r_0^2 G(\vec{r}) f_{as,w}(\vec{r})$$

$$\dot{D}_w(\vec{r}) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w G(\vec{r}) f_{as,w}(\vec{r})$$



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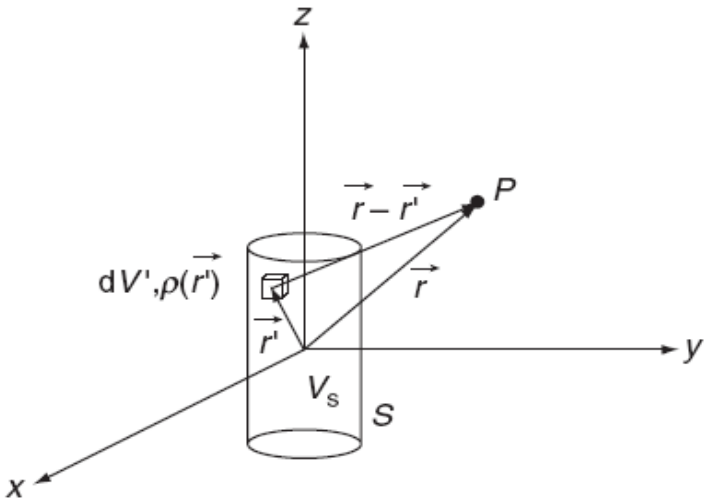
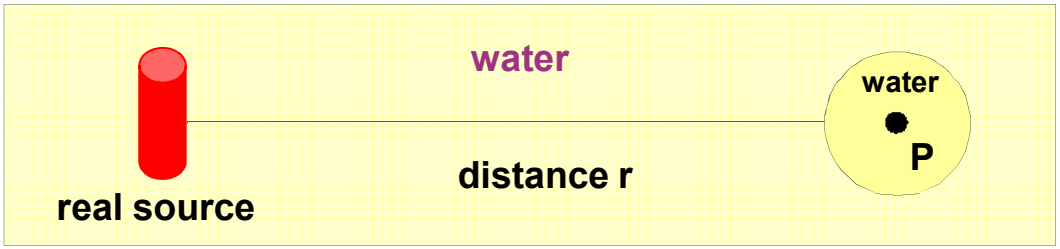
Absorbed Dose-to-water

Real Sources: Cylindrical Geometry



$$\dot{D}_w(r,\theta) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)^w_\alpha r_0^2 G(r,\theta) f_{as,w}(r,\theta)$$

$$\dot{D}_w(r,\theta) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)^w_\alpha G(r,\theta) f_{as,w}(r,\theta)$$



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Absorbed Dose-to-water

$$\dot{D}_w(r,\theta) = \dot{K}_R(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w r_0^2 G(r,\theta) f_{as,w}(r,\theta)$$

$$\dot{D}_w(r,\theta) = S_K(1-g_\alpha)\left(\frac{\mu_{en}}{\rho}\right)_\alpha^w G(r,\theta) f_{as,w}(r,\theta)$$

Note: these expressions can be found in text books, are very helpful to understand the underlying Physics, but are not recommended and have been essentially replaced in commercial TPSs with the AAPM TG43 formalism….

!

A short introduction to the

AAPM-TG43 Formalism

Dose calculation – AAPM-TG43

AAPM-TG43 formalism

The generally accepted formalism for brachytherapy Applied for Afterloader, Seeds, Wires, Tubes (Medical Physics in 1995, revised Version in 2004, > 50keV in 2012)

Why this formalism???

- **Introduction of revised calibration standards**
- **Source strength specification quantities**
- **Dose calculation formalisms**
- **Confusion with regard to dosimetric data**
- **Only quantities from dose rates in water medium near the actual source to be used**

Dose calculation – AAPM-TG43

Avoid Confusion !!!!!!

Summary of Recommended Values of the Air Kerma Rate Constant Γ_δ for the Brachytherapy Radionuclides and for Ideal Point Sources

	Air Kerma Rate Constant Γ_δ (μGy h^{-1} MBq^{-1} m^2 = U MBq^{-1})			
Radionuclide	ICRU Report 58[8]	AAPM Report 51[15]	Table 5.2 (δ = 10 keV)	Real Sources Literature
$^{137}_{55}$Cs	0.0772	—	0.0771	
$^{60}_{27}$Co	0.306	—	0.3059	
$^{198}_{79}$Au	0.0559	—	0.0545	
$^{125}_{53}$I	0.0337	0.0358/ 0.0355[a]	0.0348	0.0206 – 0.0219[b], 0.0217[c]
$^{192}_{77}$Ir	0.108 [0.100, 0.116]	0.111	0.1091	0.0993 – 0.975[d], 0.1027[e], 0.110[f], 0.0973[g], 0.0979[h] 0.1025[i], 0.107[j], 0.0992[k]
$^{103}_{46}$Pd	0.0343	0.035/ 0.0361[a]	0.0361	0.0173[l]
$^{170}_{69}$Tm	—	—	0.00053	
$^{169}_{70}$Yb	—	—	0.0431	0.0427[25] (δ = 10 keV), 0.0359[m], 0.0297[n] (δ = 10 keV),

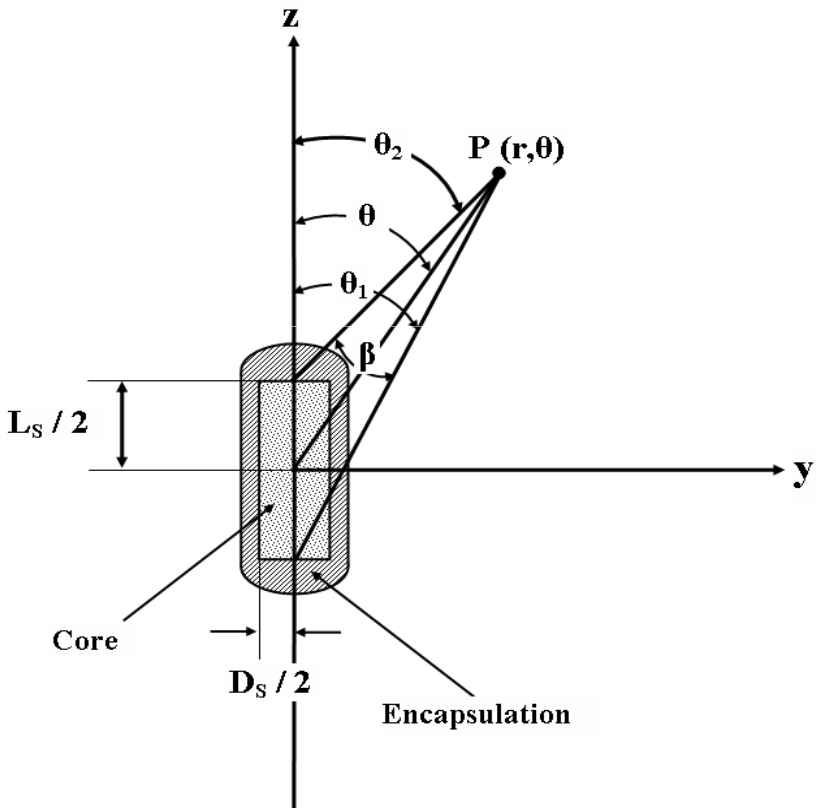
45% 12% 52% !

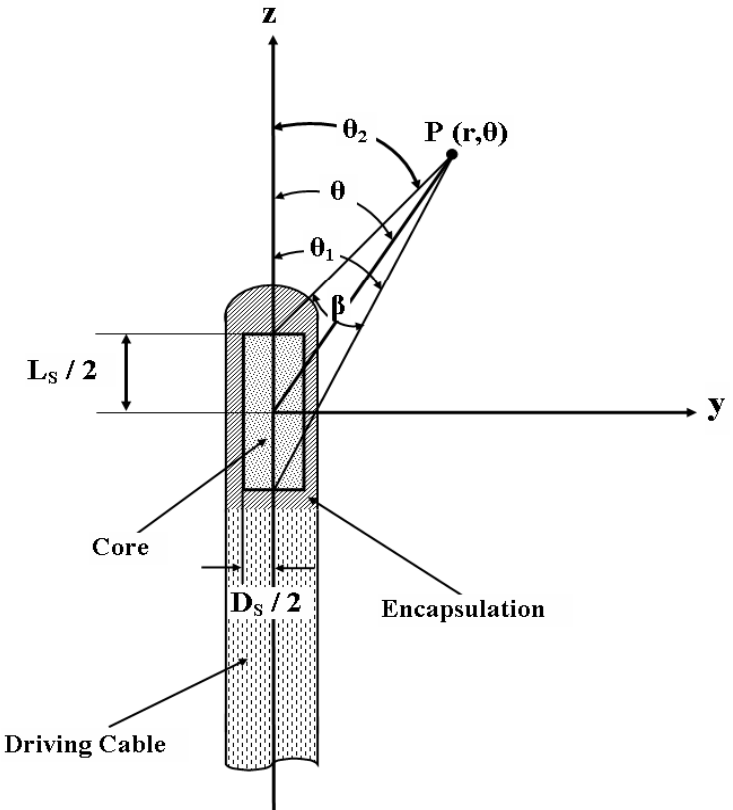
Dose calculation – AAPM-TG43

$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

5 x Multiplications
1 x Division

Cylindrically Symmetric Source





Dose calculation – AAPM-TG43:

More Details …..

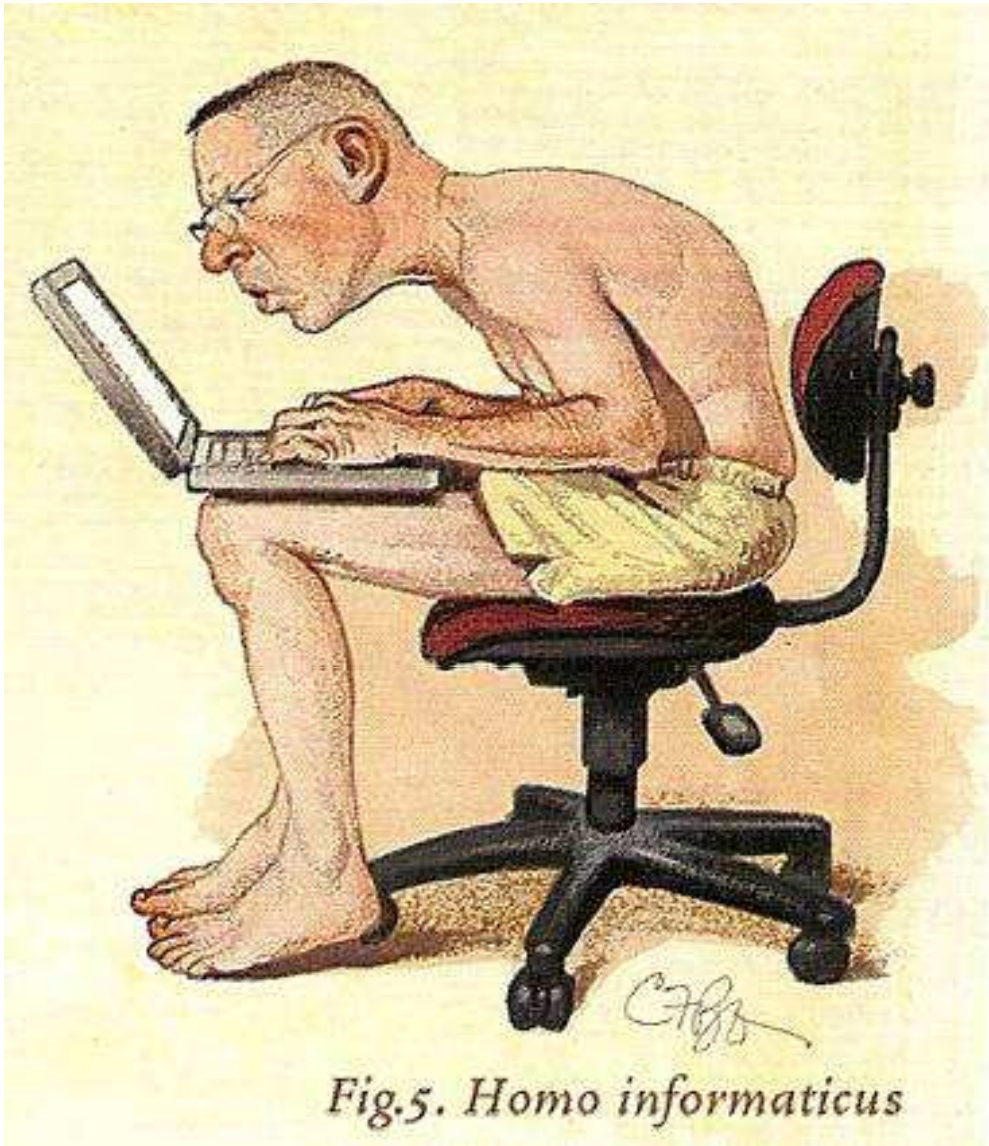
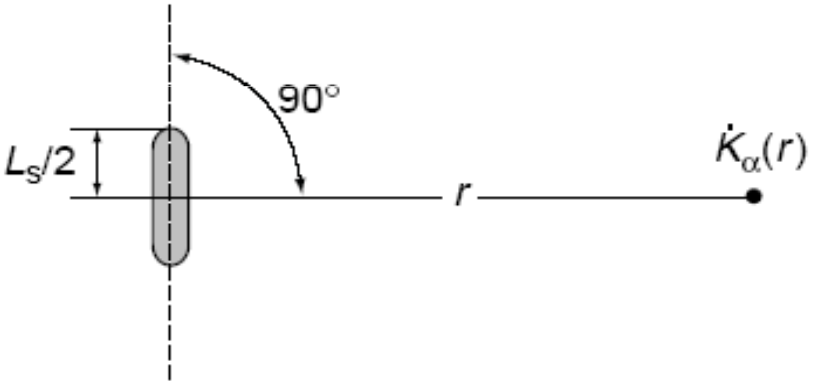


Fig.5. Homo informaticus

Dose calculation – AAPM-TG43

$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

That is, the air kerma strength, S_K, defined as the product of the air kerma rate in free space at a measurement distance r from the source center along the perpendicular bisector, $K_a(r)$, and the square of the distance r.



$$S_K = \dot{K}_\alpha(r) r^2$$

S_K: The air kerma strength in U, $1\,U = 1\,\mu Gy\,m^2\,h^{-1} = 1\,cGy\,cm^2\,h^{-1}$

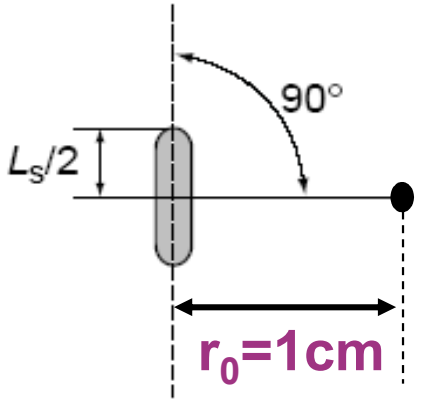
Dose calculation – AAPM-TG43

$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

Λ: The dose rate constant in water. Λ is expressed in units of $cGy\,h^{-1}\,U^{-1}$.

The dose rate constant, Λ, is defined as the dose rate to water in water at the reference point, namely at a distance of r_0 = 1 cm on the transverse axis (θ = 90°), per unit air kerma strength, S_K:

$$\Lambda = \frac{\dot{D}(r_0,\theta_0)}{S_K}$$



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Dose calculation – AAPM-TG43

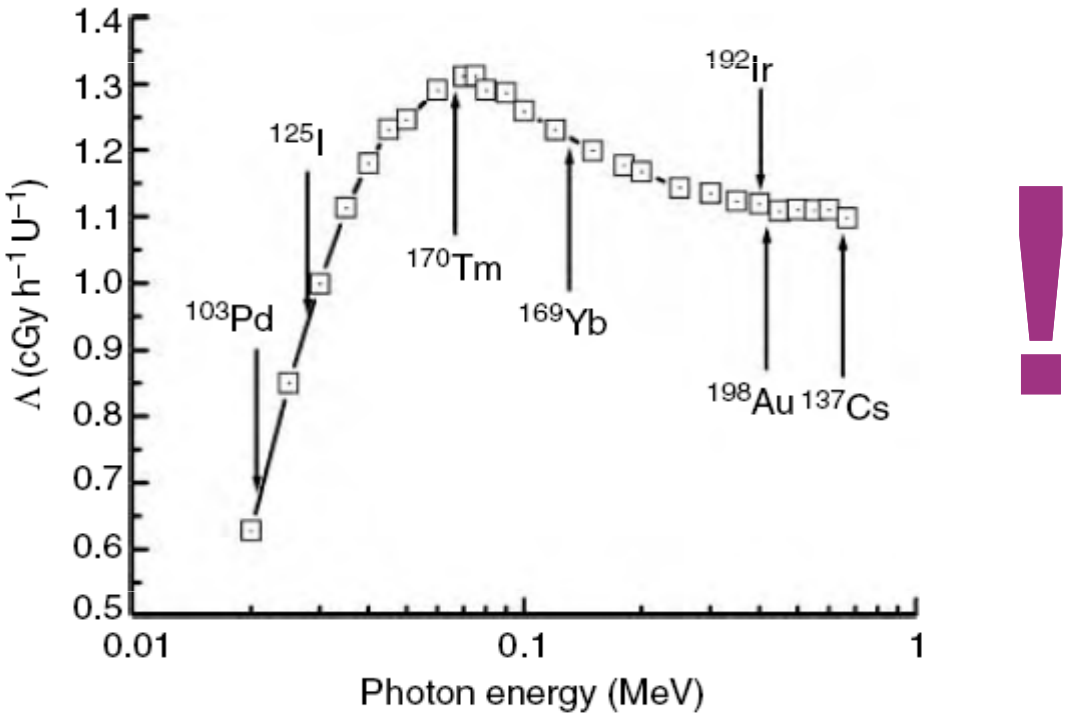

FIGURE 8.7
Energy dependence of the dose rate constant Λ expressed in cGy h^{-1} U^{-1} for monoenergetic point sources in the energy range of 0.020 to 0.700 MeV. The Λ values for the effective energies E_{eff}, see Equation 5.2, of the brachytherapy relevant radionuclides listed in Table 5.2 are indicated by arrows. The dose rate constant values shown have been calculated using MC simulations.

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Dose calculation – AAPM-TG43

$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

G(r,θ): The geometry function at radial distance r and polar angle θ. It is a dimensionless quantity.

- **From a physics point of view the geometry function simply provides an effective inverse square-law correction based upon the spatial distribution of radioactivity within the source core.**
- **It depends only on the 3D volume shape of the active core of the source and not on the radionuclide, nor on the encapsulation!**
- **It neglects scattering and attenuation!**

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Dose calculation – AAPM-TG43

Point Source Approximation

$$G(r,\theta) = G(r) = \frac{1}{r^2} \quad \mathbf{G_P(r,\theta)}$$

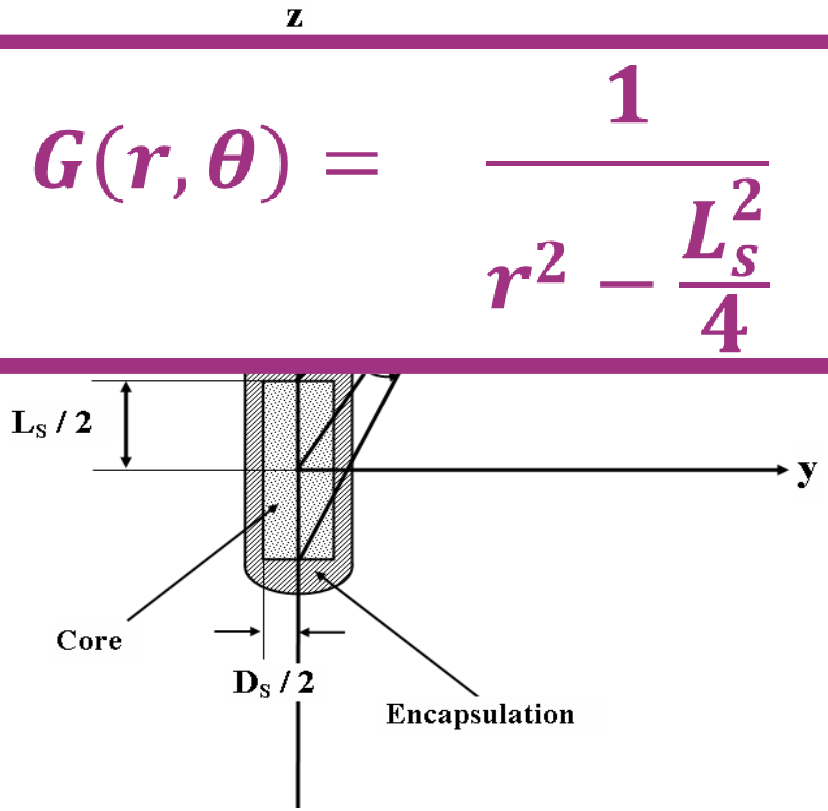
Line Source Approximation

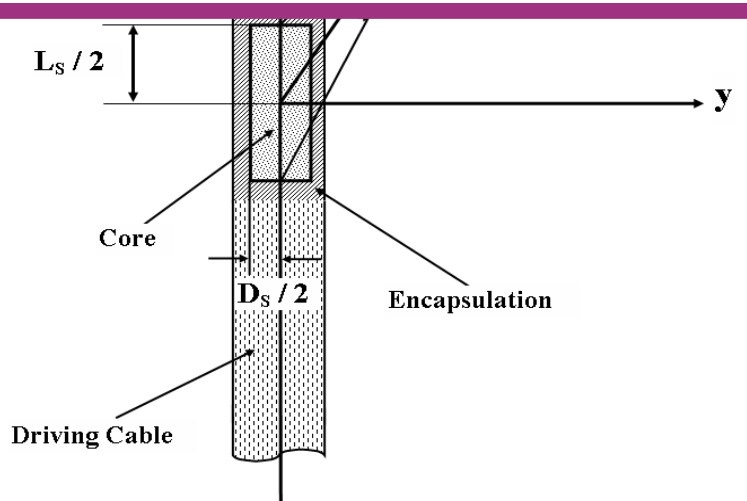
$$G(r,\theta) = \frac{\beta}{L_s r \sin\theta} \quad \mathbf{G_L(r,\theta)}$$

$$\beta = \theta_2 - \theta_1$$

Cylindrically Symmetric Source

$$G(r,\theta) = \frac{1}{r^2 - \frac{L_s^2}{4}} \quad for\ \theta = 0°\ or\ 180°$$

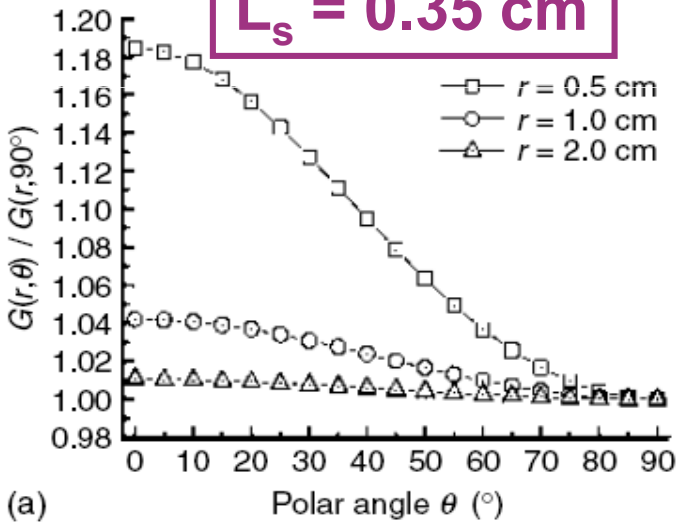




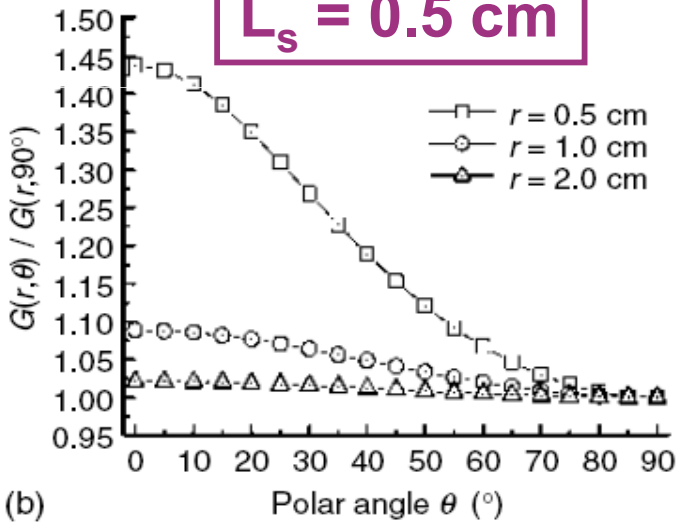
Dose calculation – AAPM-TG43

The geometry function G(r,θ)

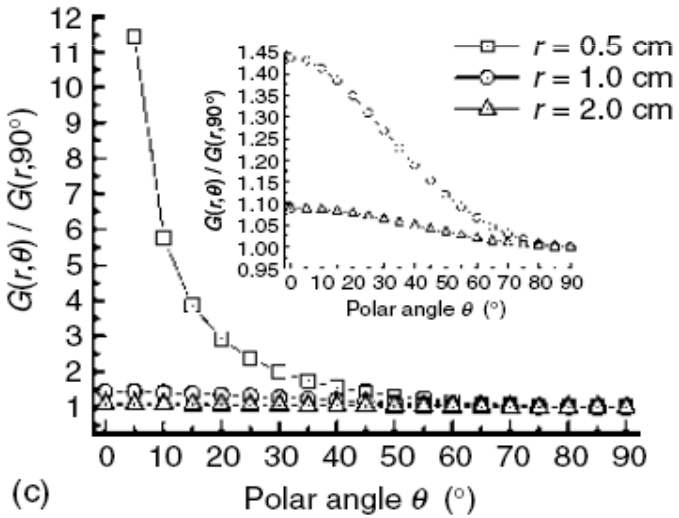
L_s = 0.35 cm



L_s = 0.5 cm



L_s = 1.0 cm



$$G(r,\theta)r^2 \approx 1.0 \;\forall_r > 3L_s$$

!

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Dose calculation – AAPM-TG43

The geometry function $G_L(r,\theta)$

HEBD > 50keV in 2012

$$G_L(r,\theta) = \frac{\cos^{-1}\left(\frac{r\cos\theta - \frac{L}{2}}{\sqrt{r^2 + \left(\frac{L}{2}\right)^2 - Lr\cos\theta}}\right) - \cos^{-1}\left(\frac{r\cos\theta + \frac{L}{2}}{\sqrt{r^2 + \left(\frac{L}{2}\right)^2 + Lr\cos\theta}}\right)}{Lr\sin\theta}. \quad (6)$$

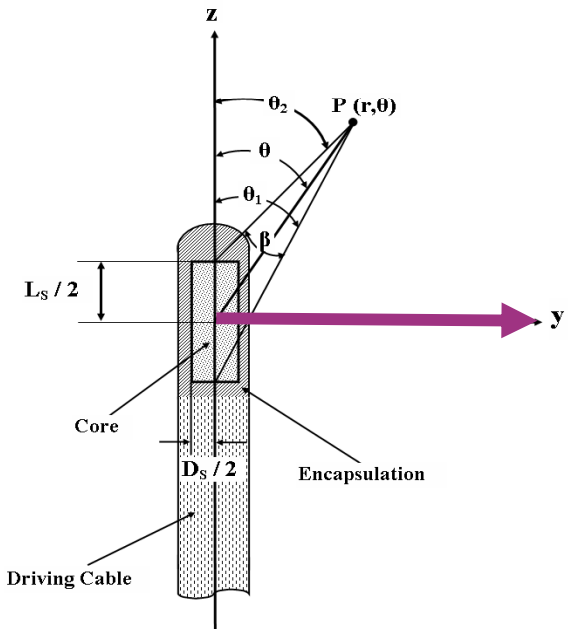
Dose calculation – AAPM-TG43

$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

g(r): The radial dose function that considers the distance dependence of absorption and scatter of the photon rays in the water medium along the transversal axis, that is the y-axis or equivalently for θ =90° . g(r) is a dimensionless quantity.

!

It is always g(r=1cm) = 1.00



g(r)

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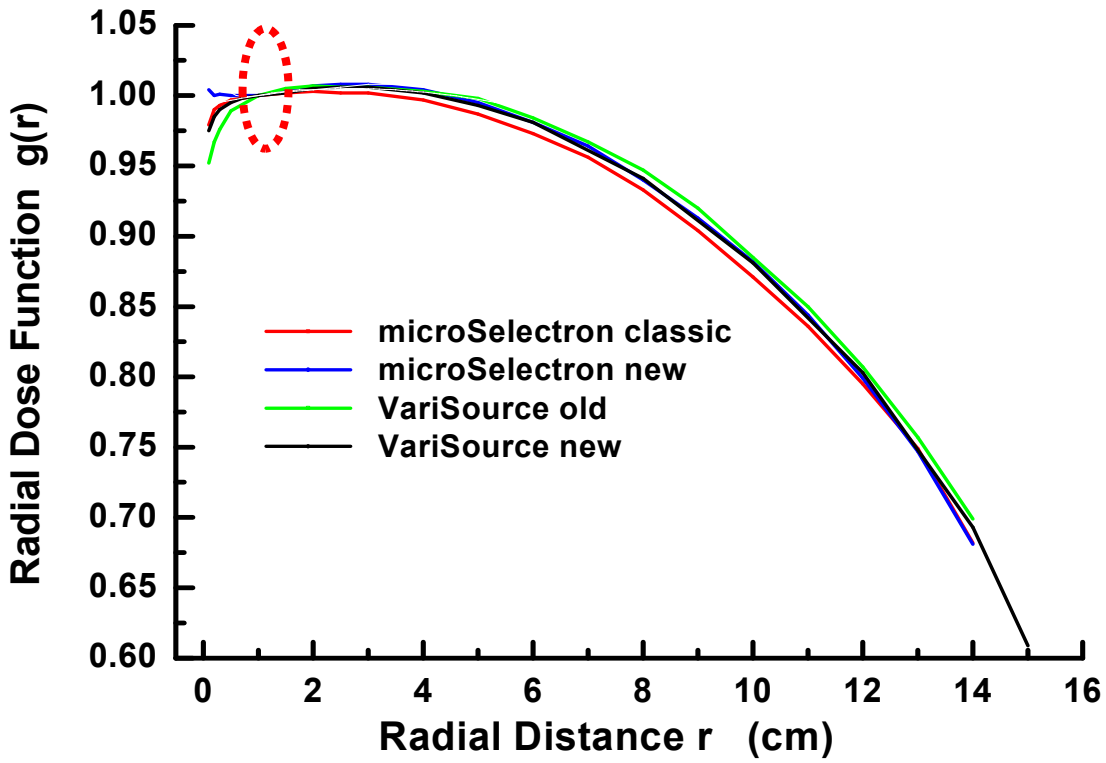
Dose calculation – AAPM-TG43

^{192}Ir – HDR Sources



Different Sources

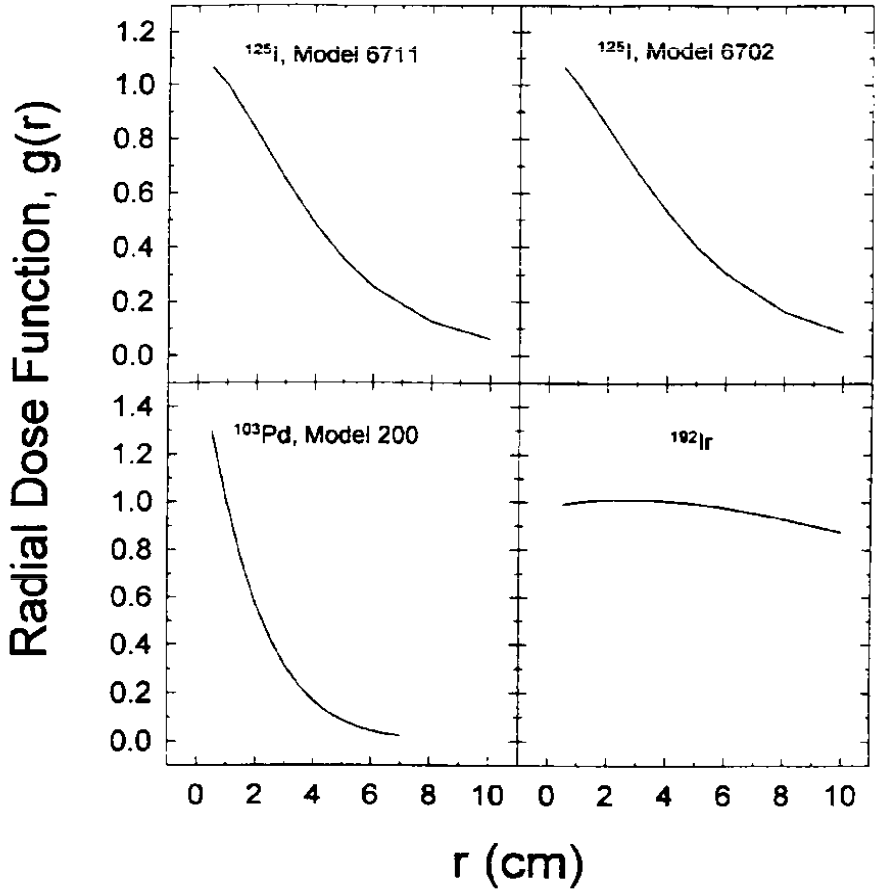


FIG. 2. Radial dose functions in a Solid Water medium for ^{103}Pd, ^{125}I, and ^{192}Ir sources.

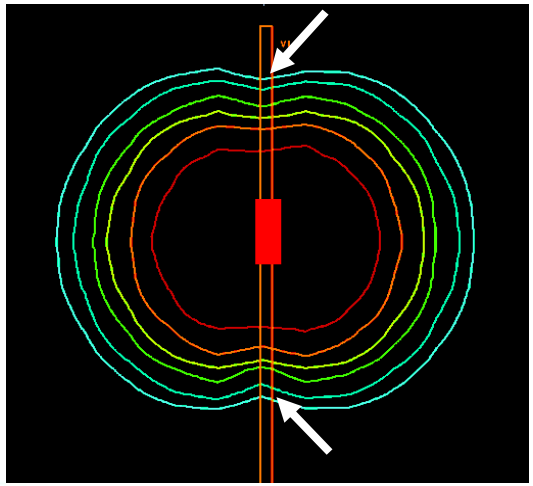
Dose calculation – AAPM-TG43

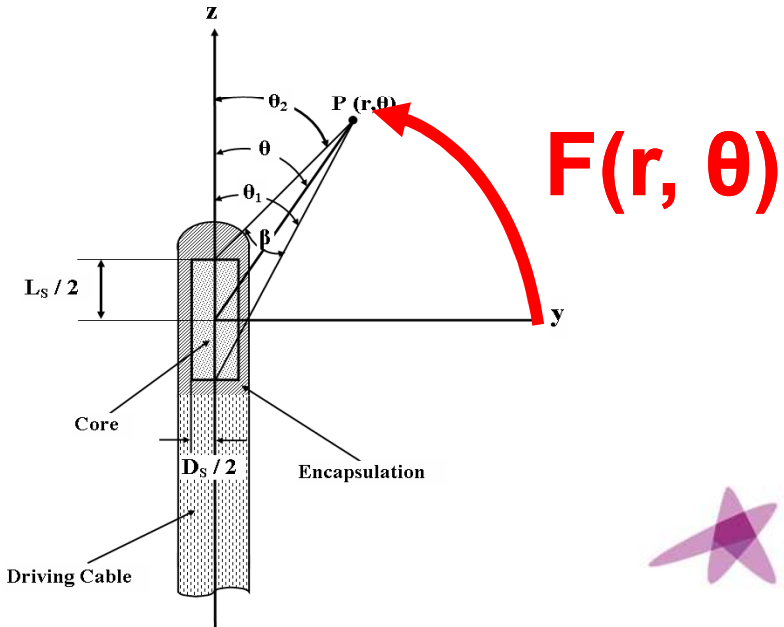
$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

F(r, θ): The anisotropy function that considers the effect of absorption and scatter of the photons within the source active core and encapsulation material as well as part of the driving cable if any. F(r, θ) is a dimensionless quantity.

!

It is always F(r, θ=90°) = 1.00





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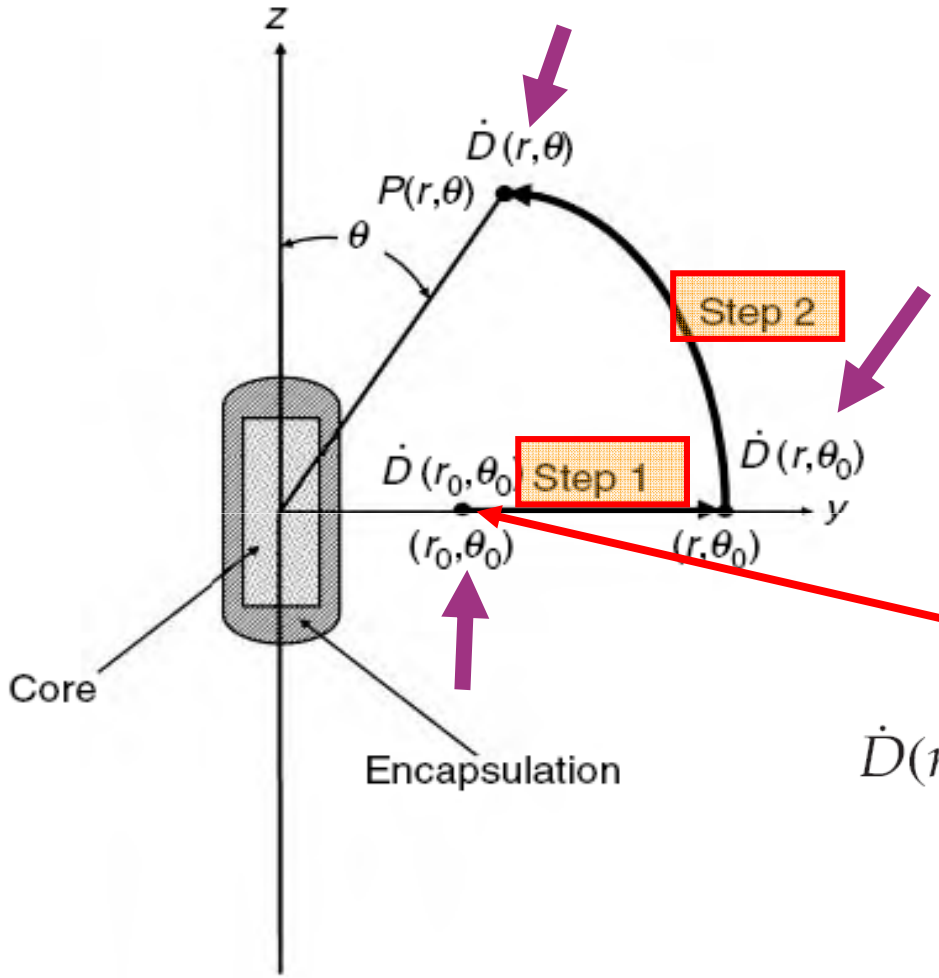
Dose calculation – AAPM-TG43

Summary:

- **It is a Two-Step 2D - Calculation Method**



(r_0, θ_0): (1.0cm, 90°)

$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

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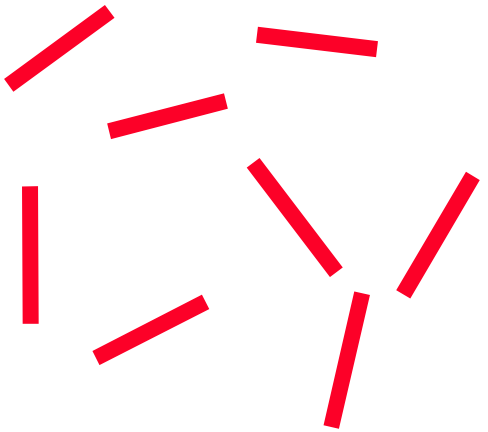
Dose calculation – AAPM-TG43

The 1D Approximation

$$\dot{D}(r) = S_K \Lambda \frac{G(r, \theta_0)}{G(r_0, \theta_0)} g(r) \varphi_{an}(r)$$

Anisotropy factor:
Independent of orientation



!

With randomly oriented seeds, orientation is not known: use $\varphi_{an}(r)$ instead of $F(r, \theta)$.

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Dose calculation – AAPM-TG43

The 1D Approximation

$$\dot{D}(r) = S_K \Lambda \frac{G(r, \theta_0)}{G(r_0, \theta_0)} g(r) \varphi_{an}(r)$$

The anisotropy factor $\varphi_{an}(r)$ is thus defined as the ratio of the dose rate at distance r, averaged with respect to solid angle, to the dose rate on the transverse y-axis ($\theta = \theta_0 = 90^\circ$)) at the same distance.

$$\varphi_{an}(r) = \frac{\int_0^\pi \dot{D}(r, \theta) \sin\theta \, d\theta}{2\dot{D}(r, \theta_0)}$$

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Dose calculation – AAPM-TG43

Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations

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2003; published 27 February 2004)

A. General 2D formalism

The general, two-dimensional (2D) dose-rate equation from the 1995 TG-43 protocol is retained,

$$\dot{D}(r,\theta) = S_K \cdot \Lambda \cdot \frac{G_L(r,\theta)}{G_L(r_0,\theta_0)} \cdot g_L(r) \cdot F(r,\theta), \qquad (1)$$

B. General 1D formalism

While a 1D isotropic point-source approximation [Eq. (9)] only approximates the true complex 2D dose distribution, it simplifies source localization procedures by eliminating the need to determine the orientation of the source longitudinal axis from imaging studies.

$$\dot{D}(r) = S_K \cdot \Lambda \cdot \frac{G_X(r,\theta_0)}{G_X(r_0,\theta_0)} \cdot g_X(r) \cdot \phi_{\text{an}}(r). \qquad (9)$$

Users should adopt one of the following implementations of Eq. (9):

$$\dot{D}(r) = S_K \cdot \Lambda \cdot \left(\frac{r_0}{r}\right)^2 \cdot g_P(r) \cdot \phi_{\text{an}}(r), \qquad (10)$$

or

$$\dot{D}(r) = S_K \cdot \Lambda \cdot \frac{G_L(r,\theta_0)}{G_L(r_0,\theta_0)} \cdot g_L(\mathrm{r}) \cdot \phi_{\text{an}}(r). \qquad (11)$$

Dose calculation – AAPM-TG43

Supplement to the 2004 update of the AAPM Task Group No. 43 Report

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published 24 May 2007)

$$\phi_{an}(r) \approx \frac{\phi_{an}(r_{\min})}{r^2 G_L(r,\theta_0)} \quad \text{for } r < r_{\min}. \qquad (1)$$

$$\phi_{an}(r) \approx \phi_{an}(r_{\min}) \frac{\int_{4\pi} G_L(r,\theta_0)\,d\Omega}{\int_{4\pi} G_L(r_{\min},\theta_0)\,d\Omega} \quad \text{for } r < r_{\min}. \qquad (2)$$

When using Eq. (2) instead of Eq. (1) for sources in this report and the TG-43U1 report, extrapolating from $\phi_{an}(r_{\min} = 1\text{ cm})$ to $\phi_{an}(0.25)$ and $\phi_{an}(0.50)$ improved the average extrapolation accuracy by 8.8% and 0.2%, respectively, as

Dose calculation – AAPM-TG43

Erratum: "Supplement to the 2004 update of the AAPM Task Group No. 43 Report" [Med. Phys. 34, 2187–2205 (2007)]

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This erratum clarifies one point and corrects a typographical error in the supplement to the updated AAPM Task Group No. 43 Report (AAPM TG-43U1S1).[1] In Sec. III.B., clarifications on recommended interpolation and extrapolation methods for the 1D anisotropy function $\phi_{an}(r)$ were presented. Equations (1) and (2) of the TG-43U1S1 report demonstrated extrapolation methods of $\phi_{an}(r)$ for $r < r_{min}$. However, Eq. (1) should have been

$$\phi_{an}(r) \approx \phi_{an}(r_{min}) \frac{r_{min}^2 G_L(r_{min}, \theta_0)}{r^2 \cdot G_L(r, \theta_0)} \quad \text{for } r < r_{min}. \tag{1}$$

Equation (2) contained a typographical error and should have been

$$\phi_{an}(r) \approx \phi_{an}(r_{min}) \frac{\int_{4\pi} G_L(r, \theta) d\Omega / G_L(r, \theta_0)}{\int_{4\pi} G_L(r_{min}, \theta) d\Omega / G_L(r_{min}, \theta_0)} \quad \text{for } r < r_{min}, \tag{2}$$

where the extrapolated $\phi_{an}(r)$ is the product of $\phi_{an}(r_{min})$ and the ratio of the geometry function integrated over all space divided by the geometry function on the transverse plane at r and r_{min}.

These equations were used correctly to calculate the data in columns 4 and 5 of Table XII of TG-43U1S1, but were included incorrectly in the report text. The AAPM Low Energy Brachytherapy Source Dosimetry Work Group appreciates the contributions to this erratum from Dr. Keith Furutani, who brought the errors to our attention.

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[1]M. J. Rivard, W. M. Butler, L. A. DeWerd, M. S. Huq, G. S. Ibbott, A. S. Meigooni, C. S. Melhus, M. G. Mitch, R. Nath, and J. F. Williamson, "Supplement to the 2004 Update of the AAPM Task Group No. 43 Report," Med. Phys. **34**, 2187–2205 (2007).

Dose calculation – AAPM-TG43

Dose calculation for photon-emitting brachytherapy sources with average energy higher than 50 keV: Report of the AAPM and ESTRO

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Dose calculation – AAPM-TG43

Table III. Interpolation and extrapolation recommendations for high-energy and (*low-energy*)[3] brachytherapy sources for the line-source approximation.

	$r < r_{min}$	$r_{min} < r \leq r_{max}$	$r > r_{max}$
Parameter	Extrapolation	Interpolation	Extrapolation
$g_L(r)$	nearest neighbor or zeroth-order extrapolation	linear (*log-linear*) using datapoints immediately adjacent to the radius of interest	Linear using data of last two tabulated radii (*single exponential function based on fitting $g_L(r)$ datapoints for the furthest three r values*).
$F(r,\Theta)$	nearest neighbor or zeroth-order extrapolation.	bilinear (*bilinear*) interpolation method for $F(r, \theta)$	nearest neighbor or zeroth-order r-extrapolation.

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Dose calculation – AAPM-TG43

V.A. Preparation of dosimetry parameters

For the high energy sources, e.g., HDR ^{192}Ir sources, dosimetric parameters should be tabulated for 2D formalisms. Exceptions include spherical pellets (eg. ^{137}Cs Selectron from Nucletron) where a 2D model can not be formulated. Regardless of the dimensionality of the formalism adopted, the line-source approximation should always be used for computing the geometry function (with the obvious exception of spherically symmetric sources), $G_L(r,\theta)$, and $g_L(r)$. For reader convenience, we include the following alternative expression for $G_L(r,\theta)$:

$$G_L(r,\theta) = \frac{\cos^{-1}\left(\frac{r\cos\theta - \frac{L}{2}}{\sqrt{r^2 + \left(\frac{L}{2}\right)^2 - Lr\cos\theta}}\right) - \cos^{-1}\left(\frac{r\cos\theta + \frac{L}{2}}{\sqrt{r^2 + \left(\frac{L}{2}\right)^2 + Lr\cos\theta}}\right)}{Lr\sin\theta} \qquad (6)$$

Dose calculation – AAPM-TG43

Summary:

- 2D Method
- 1D Approximation if Source Orientation missing
- Requires individual Parameters for each Source design
- It is based on measured or MC-calculated and experimentally verified data !
- It is based on Air Kerma Strength S_K

Dose from Dose-Rate

TG-43 derives the Dose Rate

$$D(r,\theta) = \dot{D}(r,\theta,t_0)\,\tau\left(1 - e^{-\frac{T}{\tau}}\right)$$

t_0 : is the time of the begin of the treatment

$\tau = T_{1/2} / \ln 2$, with $T_{1/2}$ the half-life of the Radionuclide

T : is the duration of the Treatment (placement of the source)

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Dose from Dose-Rate

TG-43 derives the Dose Rate: $T \ll \tau$

$$D(r, \theta) = \dot{D}(r, \theta, t_0) T k_u$$

k_u : is a units conversion factor to convert the dose rate expressed in cGy h^{-1} and considering the time unit of the value T to the desired dose unit, Gy or cGy.

! This is e.g. the case for HDR or PDR treatments with ^{192}Ir or HDR treatments with ^{60}Co

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Dose from Dose-Rate

TG-43 derives the Dose Rate: T >> τ

$$D(r,\theta) = \dot{D}(r,\theta,t_0)\tau k_u$$

k_u : is a units conversion factor to convert the dose rate expressed in cGy h^{-1} and considering the time unit of the value T to the desired dose unit, Gy or cGy.

$\tau = T_{1/2} / \ln 2$, with $T_{1/2}$ the half-life of the Radionuclide

This is e.g. the case for permanent implants with ^{125}I or ^{103}Pd

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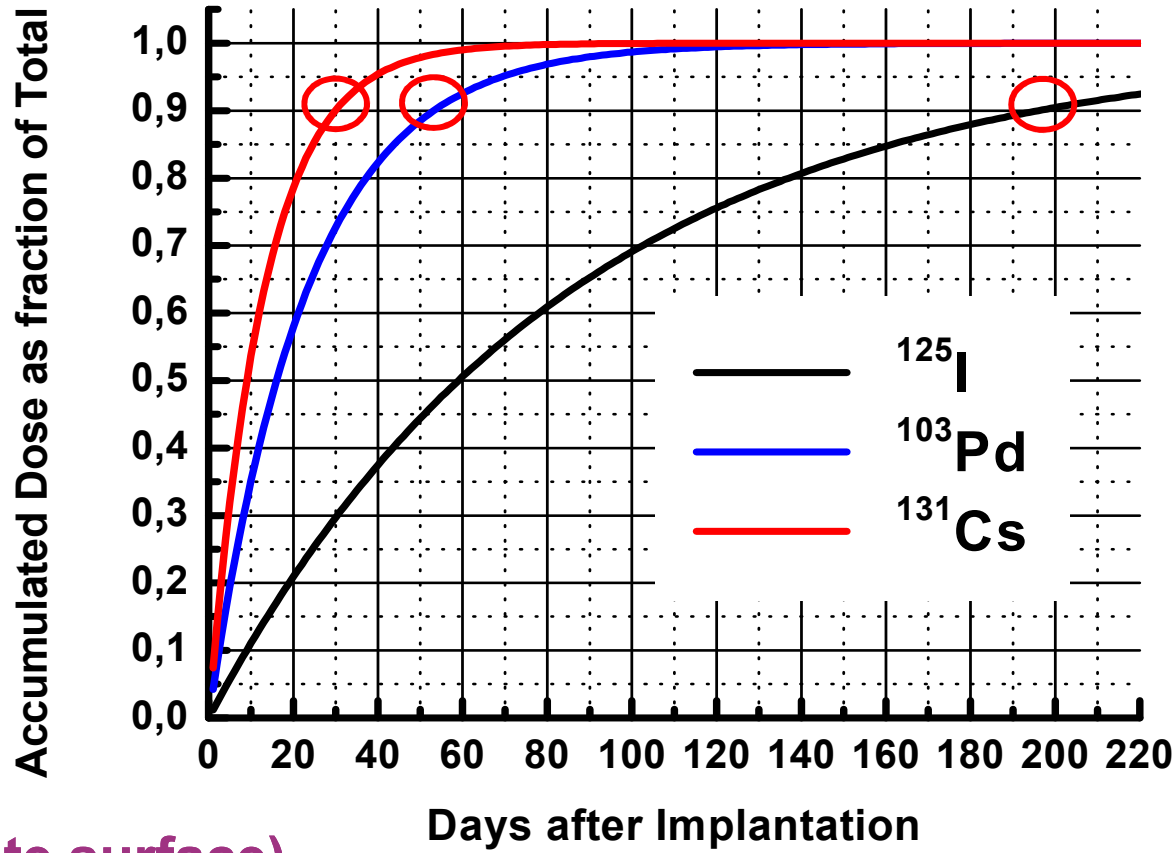
Dose from Dose-Rate: Accumulation over Time

Total Dose (100% = 1.0)

- **145 Gy**
- **125 Gy**
- **115 Gy**



- **Initial Dose Rate (at the prostate surface)**
  30 cGy.h^{-1}
  versus
  7 cGy.h^{-1} for ^{125}I and 20 cGy.h^{-1} for ^{103}Pd

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Dose from Dose-Rate

TABLE 8.14

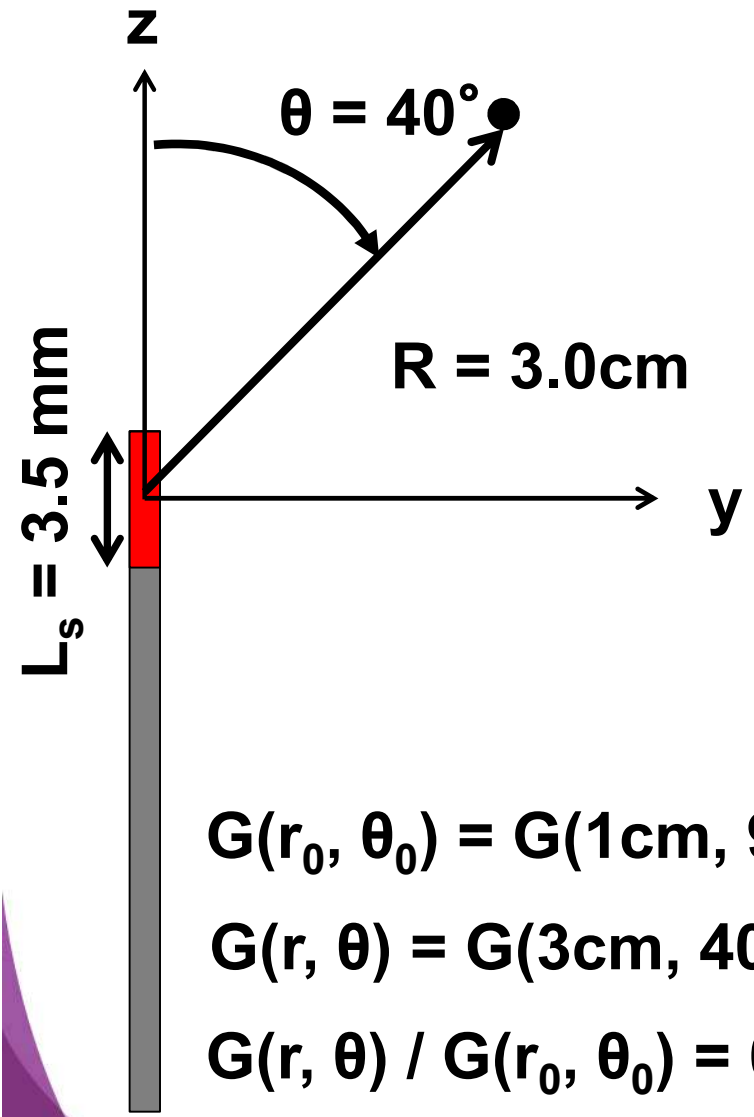
Units Conversion Factor k_u Considered in Equation 8.57 and Equation 8.58 for Converting the Dose Value into the Desired Dose Unit, cGy or Gy

Dose Unit	Source Dwell Time T Unit (Equation 8.57)	Source Mean Life τ Unit (Equation 8.58)	Conversion Factor
cGy	sec	d	$1/3{,}600 = 2.778 \times 10^{-4}$ h sec^{-1}
	min		$1/60 = 1.667 \times 10^{-2}$ h min^{-1}
	h		1.000
	d		24 h d^{-1}
Gy	sec	d	$1/3600 \times 10^{-2} = 2.778 \times 10^{-6}$ h sec^{-1} Gy cGy^{-1}
	min		$1/60 \times 10^{-2} = 1.667 \times 10^{-4}$ h min^{-1} Gy cGy^{-1}
	h		1.0×10^{-2} Gy cGy^{-1}
	d	y	0.24 h d^{-1} Gy cGy^{-1}

Based on the calculated initial dose rate value expressed in cGy h^{-1} and the source dwell time T expressed either in seconds or minutes or hours or days, or source mean life τ expressed in days (see also Table 2.3).

Baltas et al., Taylor & Francis, 2007

Practical Example: Bebig ^{192}Ir-HDR Source



$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

S_K = 40.000 U

Λ = 1,108 cGy/(hU)

$$G(r,\theta) = \frac{\beta}{L_s r \sin\theta}$$

$G(r_0, \theta_0) = G(1cm, 90^o) = 0{,}99\ cm^{-2}$

$G(r, \theta) = G(3cm, 40^o) = 1/r^2 = 1/9\ cm^{-2} = 0{,}11111\ cm^{-2}$

$G(r, \theta) / G(r_0, \theta_0) = 0{,}012346\ cm^{-2} / 0{,}99\ cm^{-2} = 0{,}1122334$

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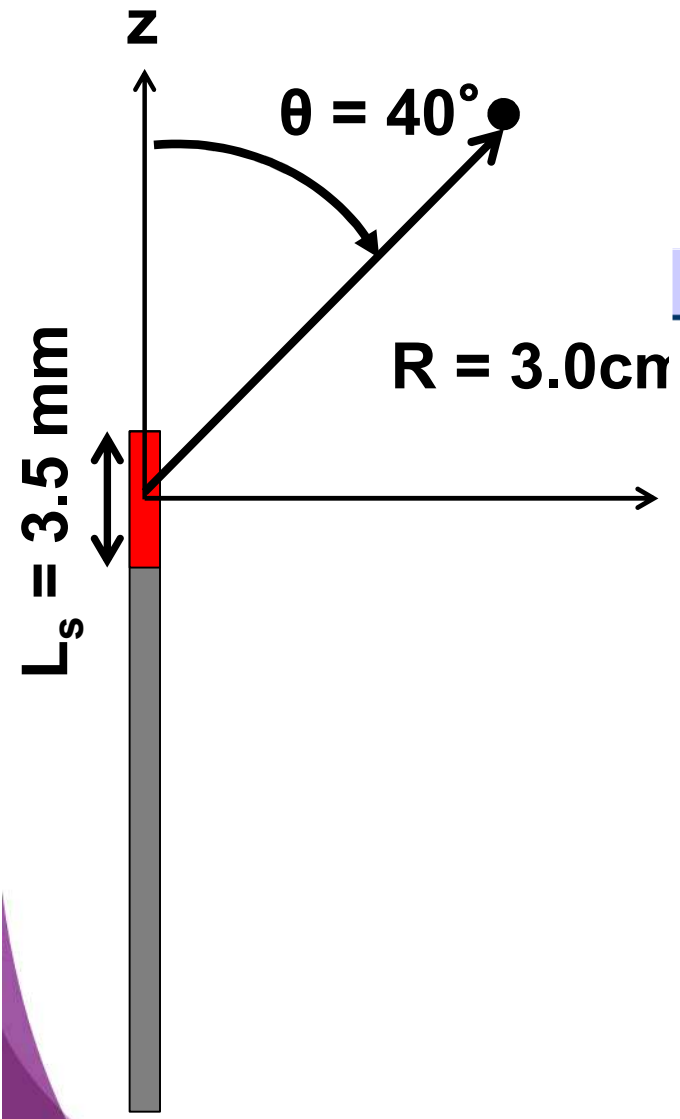
Practical Example: Bebig ^{192}Ir-HDR Source



$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

Radial dose function: g(r)

Ir-192 HDR Bebig

r(cm)	g (r)
0.25	0.9903
0.5	0.9964
0.75	0.9984
1	1.0000
1.5	1.0025
2	1.0035
3	1.0052
4	1.0035
5	0.9990
6	0.9915
7	0.9814
8	0.9682
10	0.9352
12	0.8944
15	0.8214
20	0.6867

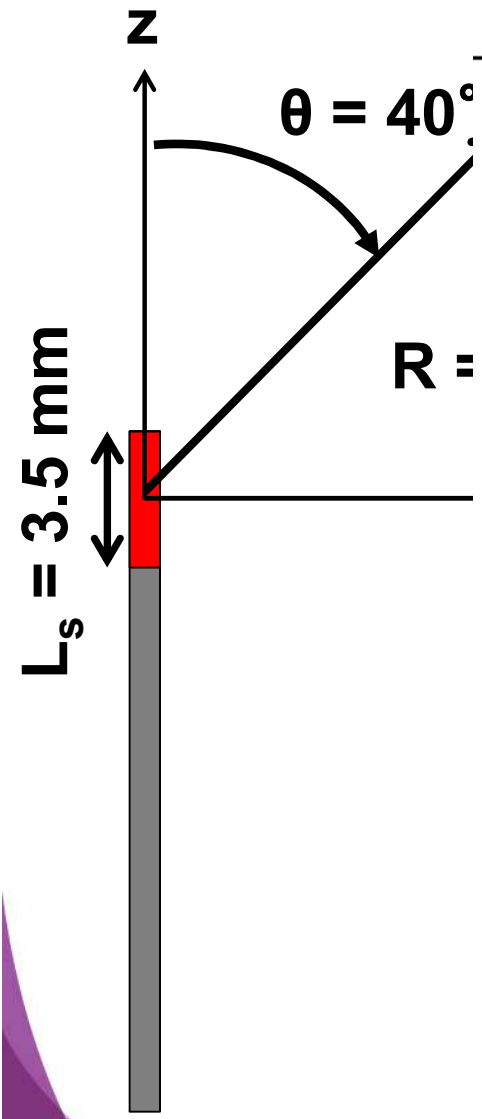
Fitted to: $g(r) = a_0 + a_1 r + a_2 r^2 + a_3 r^3 + a_4 r^4 + a_5 r^5$

Range: 0.25 to 20 cm

a_0= 0.9924
a_1= 9.064E-03
a_2= -1.465E-03
a_3= -2.230E-05
a_4= 2.642E-06
a_5= -4.603E-08

4

Practical Example: Bebig ^{192}Ir-HDR Source



Ir-192 HDR Bebig

θ	r (cm)															
	0.25	0.5	0.75	1	1.5	2	3	4	5	6	7	8	10	12	15	20
0	---	0.643	0.610	0.598	0.599	0.605	0.633	0.655	0.679	0.698	0.714	0.728	0.763	0.775	0.801	0.838
1	---	0.645	0.617	0.608	0.611	0.618	0.644	0.667	0.689	0.707	0.724	0.738	0.769	0.783	0.811	0.837
2	---	0.651	0.626	0.621	0.626	0.637	0.660	0.683	0.704	0.719	0.739	0.753	0.777	0.797	0.823	0.843
3	---	0.654	0.633	0.631	0.638	0.649	0.672	0.695	0.714	0.729	0.748	0.761	0.784	0.805	0.828	0.852
4	---	0.658	0.643	0.643	0.652	0.663	0.685	0.707	0.724	0.741	0.757	0.771	0.793	0.813	0.834	0.856
5	---	0.667	0.656	0.654	0.662	0.674	0.695	0.717	0.734	0.750	0.765	0.777	0.799	0.818	0.840	0.860
6	---	0.678	0.667	0.668	0.675	0.686	0.707	0.727	0.744	0.760	0.773	0.784	0.805	0.822	0.843	0.865
8	---	0.701	0.693	0.695	0.704	0.714	0.733	0.750	0.765	0.779	0.791	0.801	0.820	0.835	0.852	0.872
10	---	0.728	0.722	0.725	0.732	0.741	0.758	0.772	0.787	0.798	0.808	0.819	0.834	0.849	0.865	0.881
15	---	0.796	0.790	0.792	0.797	0.803	0.814	0.824	0.834	0.842	0.849	0.856	0.869	0.878	0.890	0.900
20	---	0.848	0.842	0.843	0.845	0.850	0.857	0.865	0.871	0.877	0.883	0.887	0.896	0.903	0.910	0.918
25	---	0.887	0.881	0.881	0.883	0.886	0.891	0.896	0.901	0.904	0.909	0.912	0.918	0.923	0.929	0.933
30	---	0.915	0.911	0.910	0.910	0.912	0.916	0.919	0.923	0.926	0.928	0.931	0.935	0.938	0.943	0.945
40	---	0.950	0.948	0.948	0.948	0.949	0.951	0.953	0.955	0.956	0.957	0.958	0.960	0.962	0.964	0.965
50	---	0.972	0.971	0.971	0.971	0.972	0.973	0.973	0.974	0.975	0.976	0.976	0.977	0.978	0.980	0.980
60	0.990	0.985	0.985	0.986	0.985	0.986	0.986	0.986	0.988	0.987	0.988	0.988	0.988	0.989	0.989	0.989
70	0.996	0.994	0.994	0.995	0.995	0.996	0.995	0.995	0.996	0.995	0.996	0.996	0.996	0.996	0.996	0.996
80	0.999	0.998	0.997	0.998	0.998	0.998	0.999	0.999	0.999	0.999	0.999	0.999	0.999	0.999	0.999	0.999
90	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
100	0.999	0.998	0.998	0.999	0.999	0.999	0.999	0.998	0.999	0.999	0.999	0.998	0.999	0.999	0.999	0.999
110	0.996	0.993	0.993	0.994	0.994	0.994	0.994	0.995	0.995	0.995	0.995	0.995	0.995	0.995	0.995	0.995
120	0.991	0.985	0.986	0.986	0.986	0.986	0.986	0.986	0.987	0.987	0.988	0.987	0.987	0.988	0.989	0.988
130	---	0.972	0.971	0.972	0.971	0.972	0.973	0.973	0.974	0.975	0.976	0.977	0.977	0.978	0.979	0.979
140	---	0.951	0.949	0.949	0.949	0.950	0.952	0.953	0.955	0.956	0.958	0.959	0.960	0.962	0.964	0.965
150	---	0.916	0.911	0.911	0.912	0.914	0.916	0.919	0.923	0.925	0.927	0.930	0.934	0.937	0.942	0.945
155	---	0.889	0.883	0.883	0.884	0.887	0.892	0.896	0.901	0.905	0.908	0.911	0.916	0.921	0.927	0.931
160	---	---	0.843	0.842	0.843	0.848	0.855	0.862	0.868	0.874	0.880	0.885	0.892	0.900	0.908	0.915
165	---	---	---	0.789	0.792	0.797	0.807	0.817	0.827	0.835	0.843	0.850	0.862	0.872	0.882	0.895

$$F(r, \theta)$$

40.000 U

cGy/(hU)

0,1122334

= 1,0052

F(r=3.0cm, 40°) = 0,951

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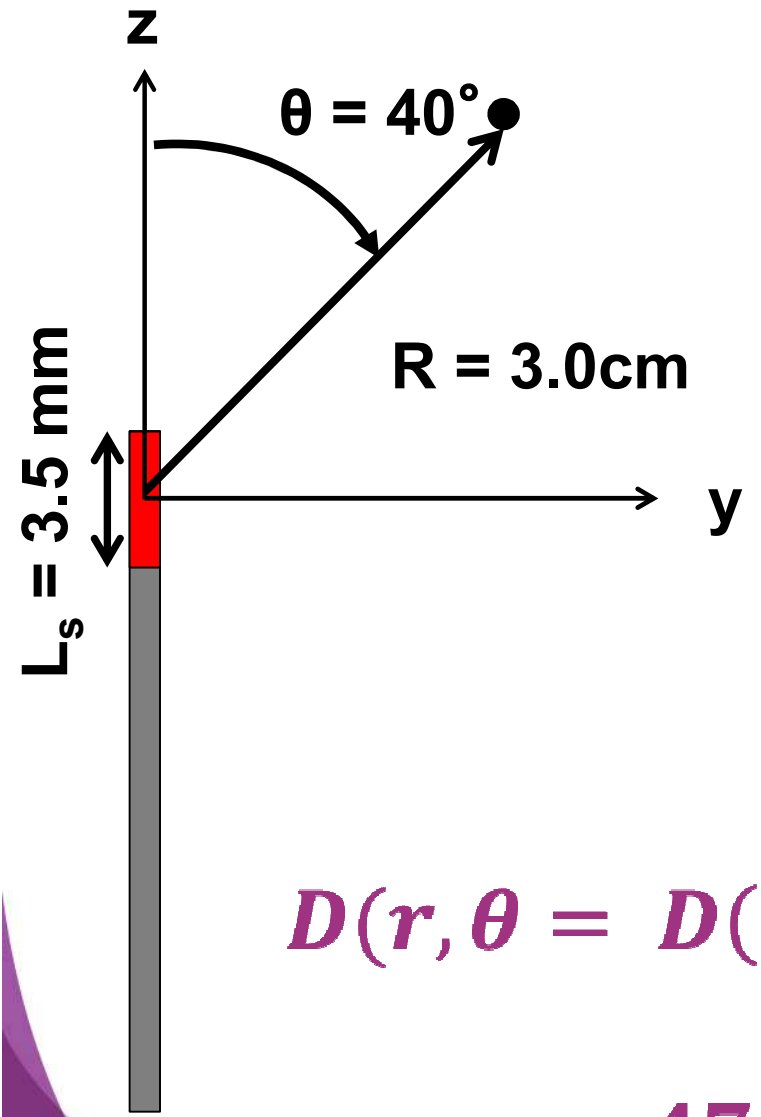
Practical Example: Bebig ^{192}Ir-HDR Source



$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

S_K = 40.000 U

Λ = 1,108 cGy/(hU)

$G(r, \theta) / G(r_0, \theta_0)$ = 0,1122334

g(r=3.0cm) = 1,0052

F(r=3.0cm, 40°) = 0,951

$$D(r,\theta = D(3cm, 40°) = 4755,1 \frac{cGy}{h} =$$

$$= 47,551 \frac{Gy}{h} = 0,793 \frac{Gy}{min}$$

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Complexity …..

Many Catheters/Needles, Many Sources …

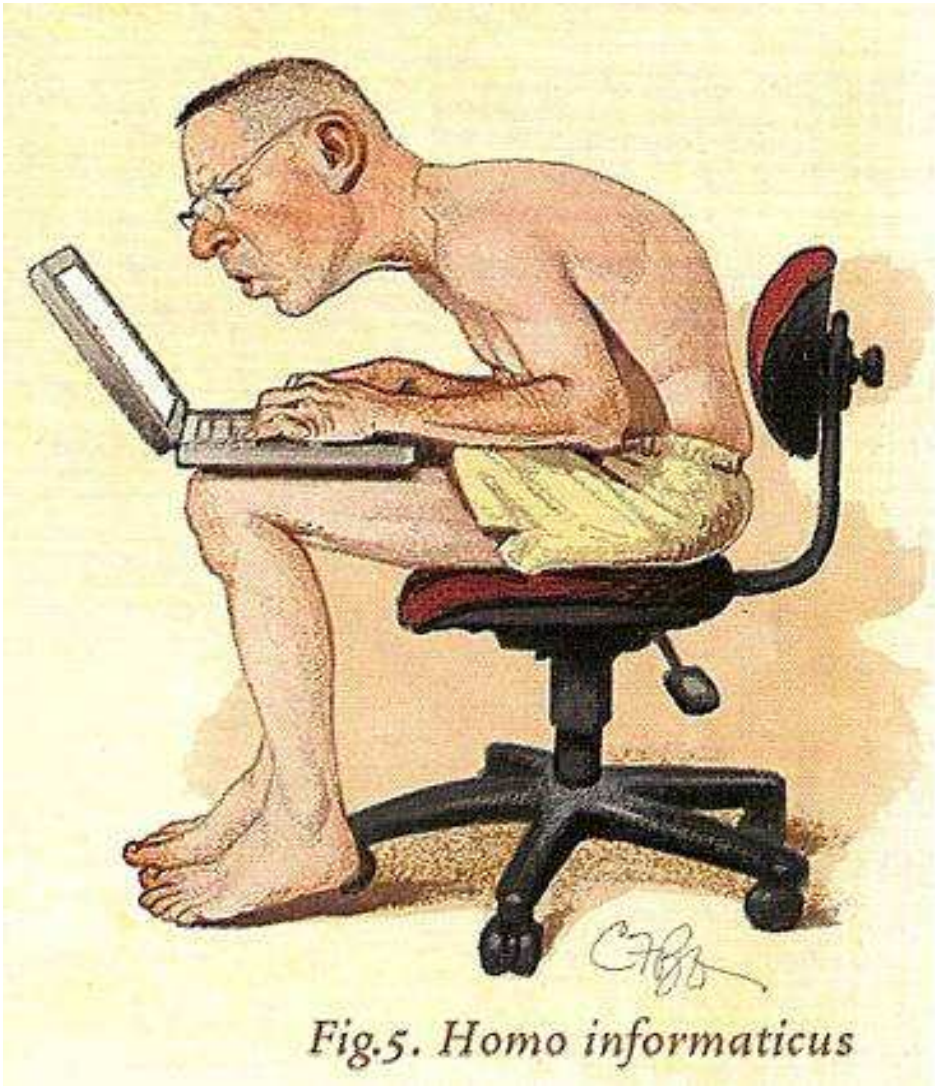
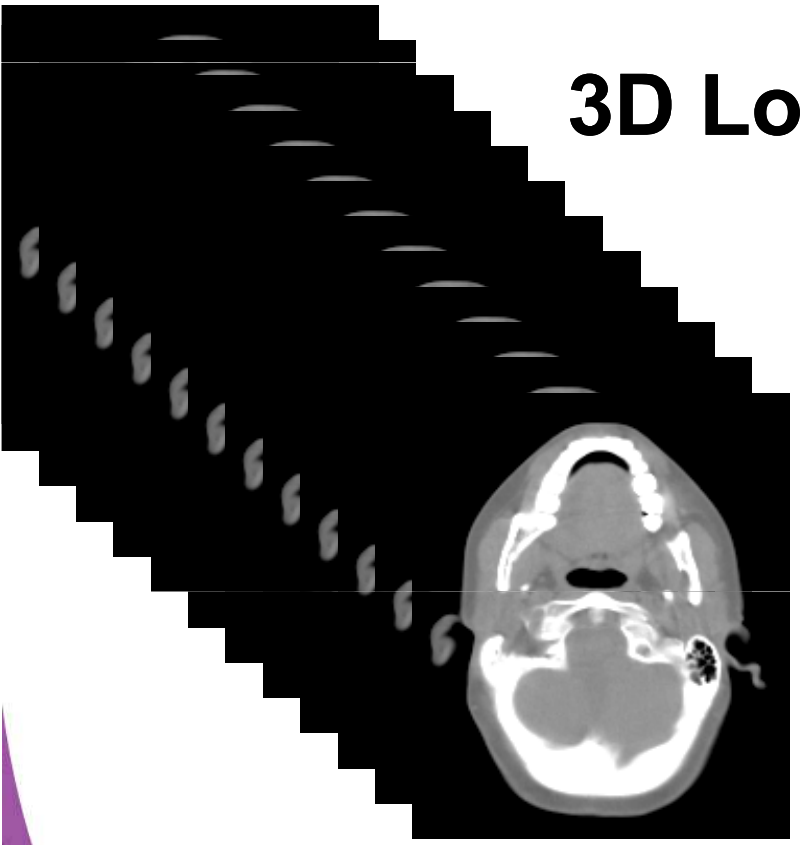
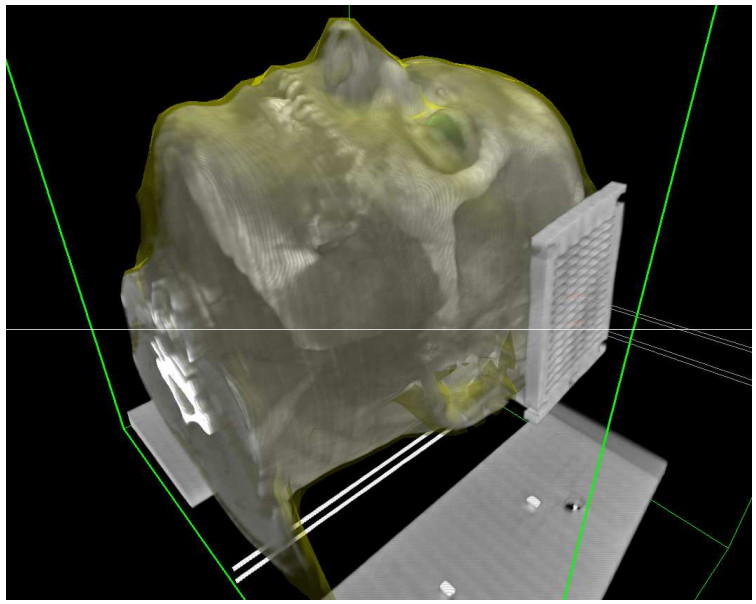


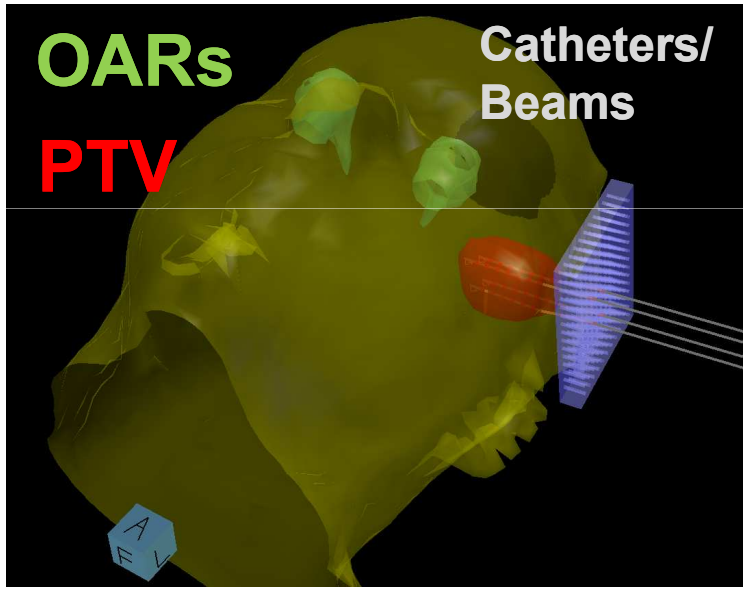
Fig.5. Homo informaticus

We have to identify our fields and the related Anatomy ….



3D Localization →





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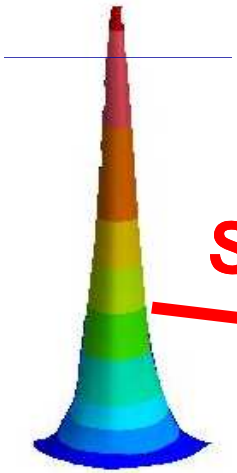
Dose / Dose Rate Calculation at a Point

$$D(P) = \sum_{i=1}^{N_{catheters}} \sum_{j=1}^{M_{sources,i}} t_{i,j}\dot{D}_{i,j}(P) \quad with \quad \dot{D}_{i,j}(P) = \left\{ S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta) \right\}_{P,i,j}$$



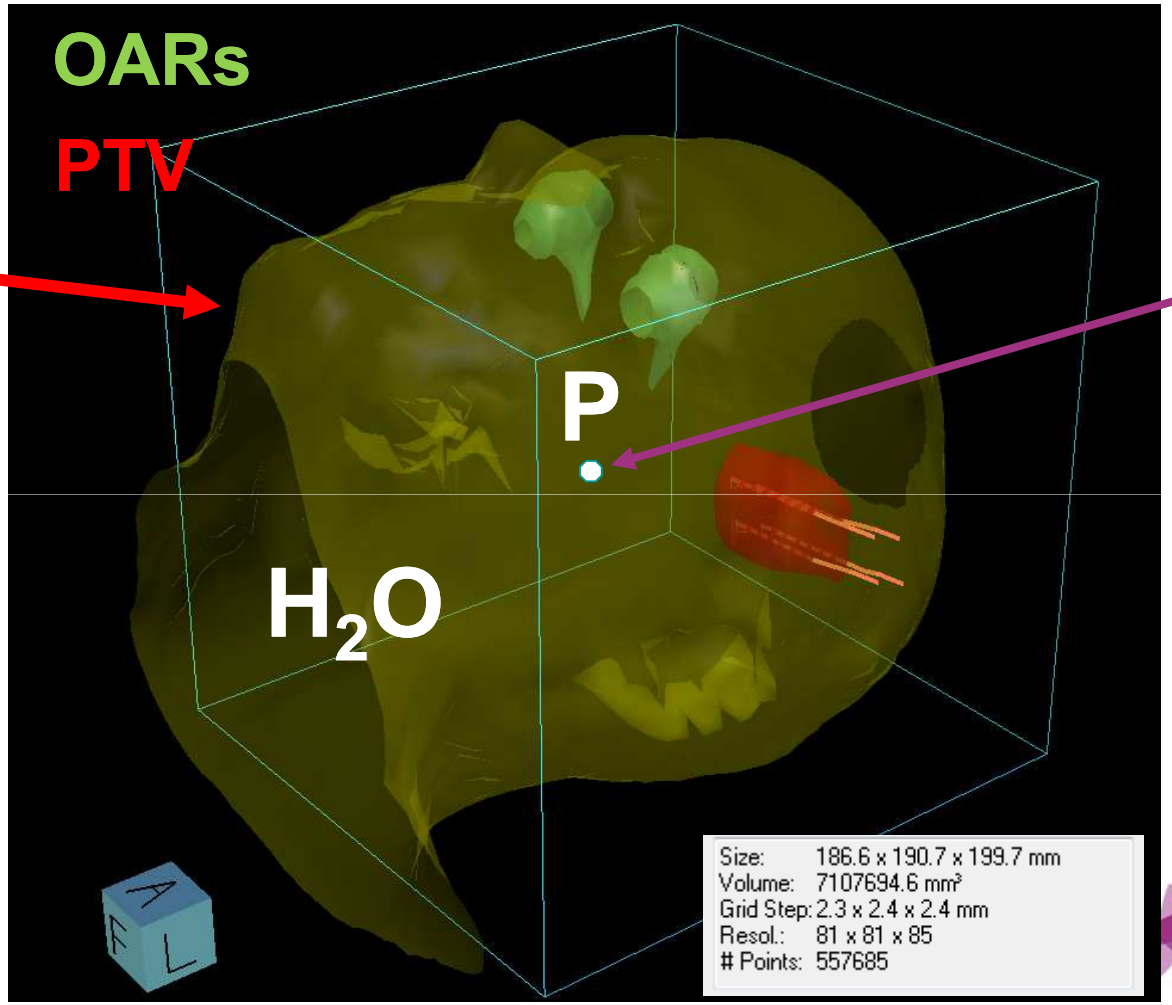
Superposition

^{192}Ir

^{60}Co

^{169}Yb

…



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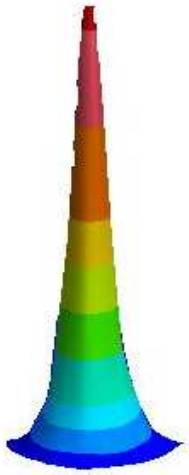
2D Dose Distribution

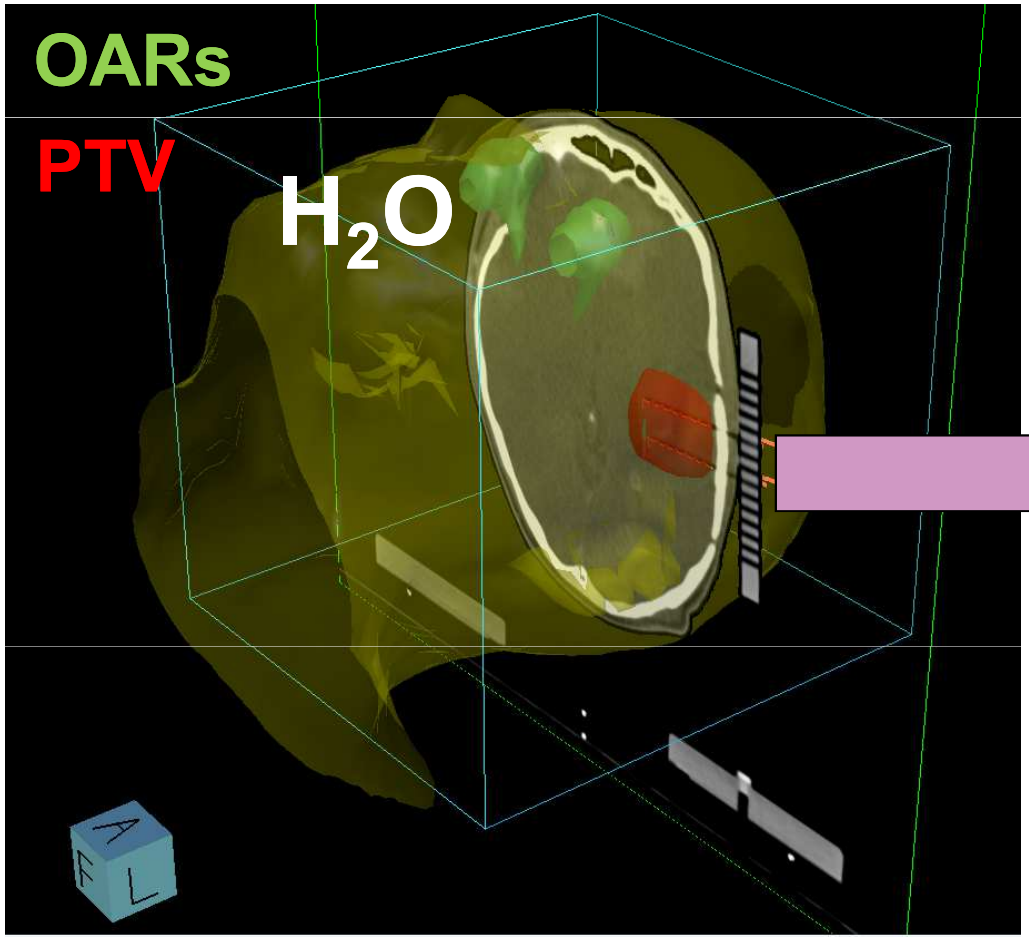


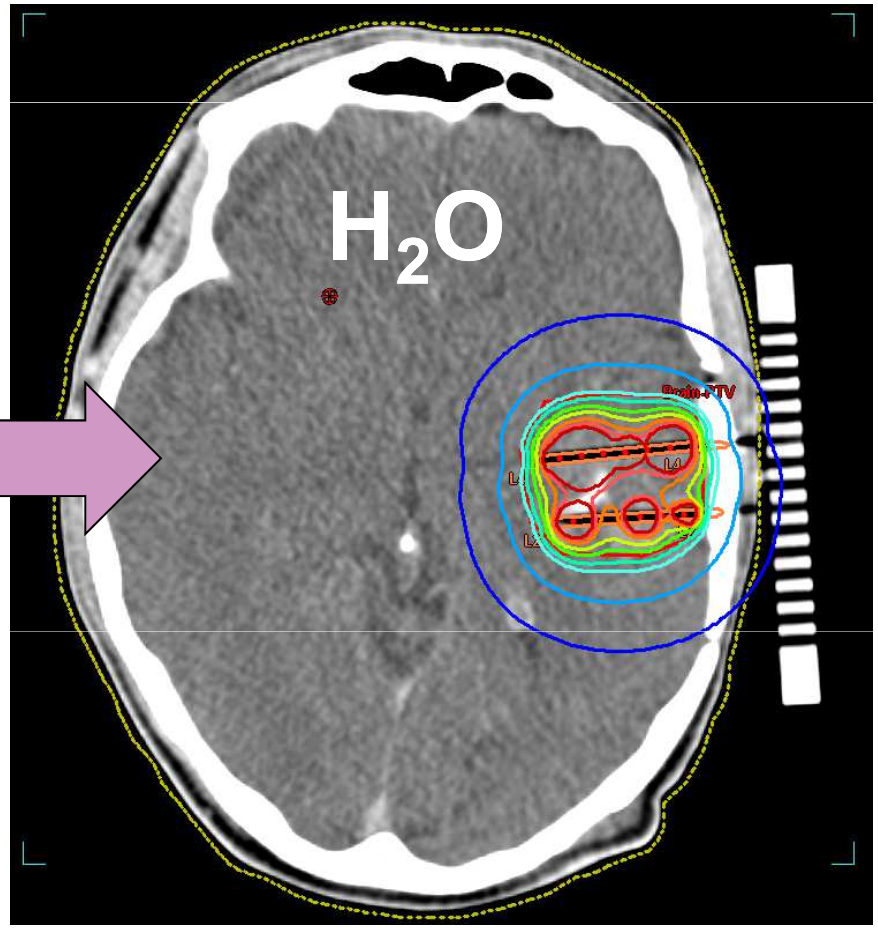
^{192}Ir

^{60}Co

^{169}Yb

...





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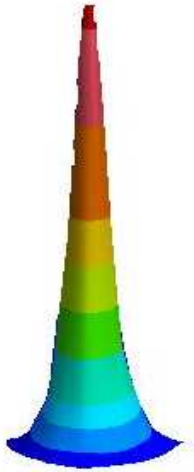
3D Dose Distribution

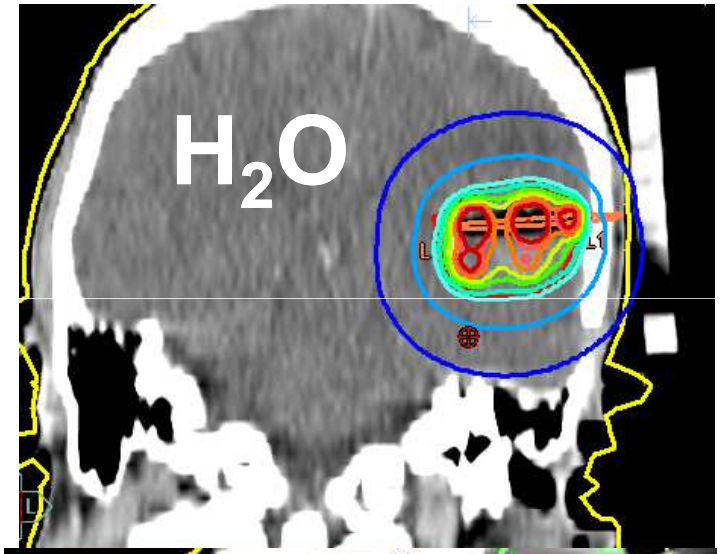


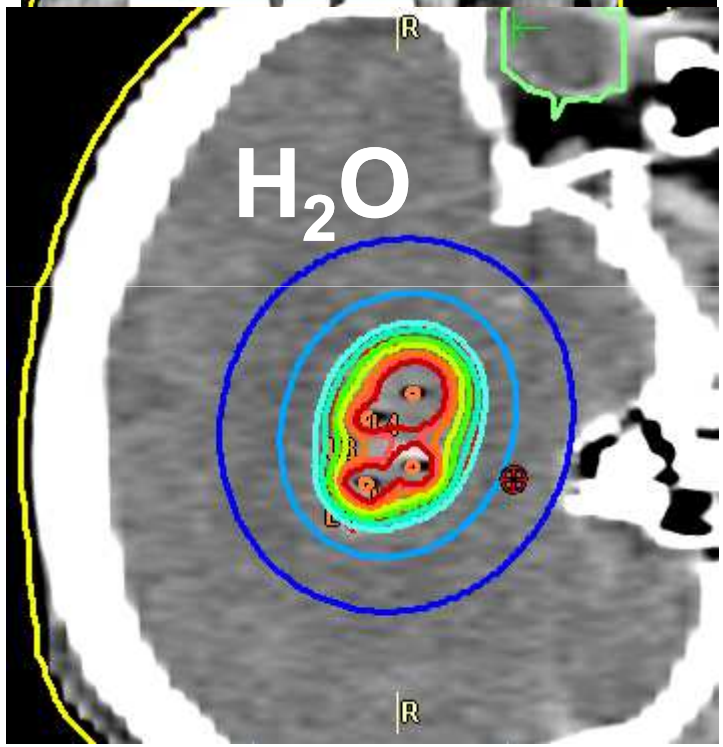
^{192}Ir

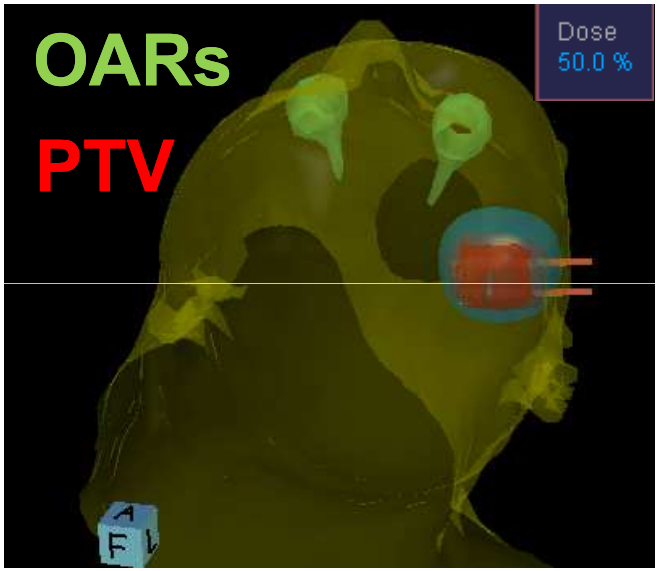
^{60}Co

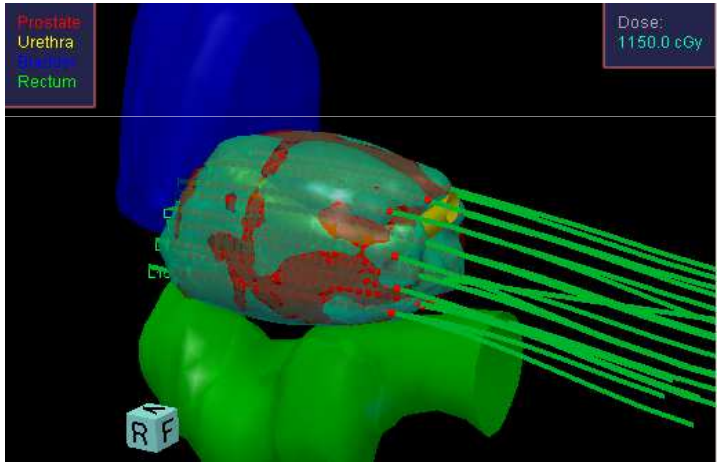
^{169}Yb

...









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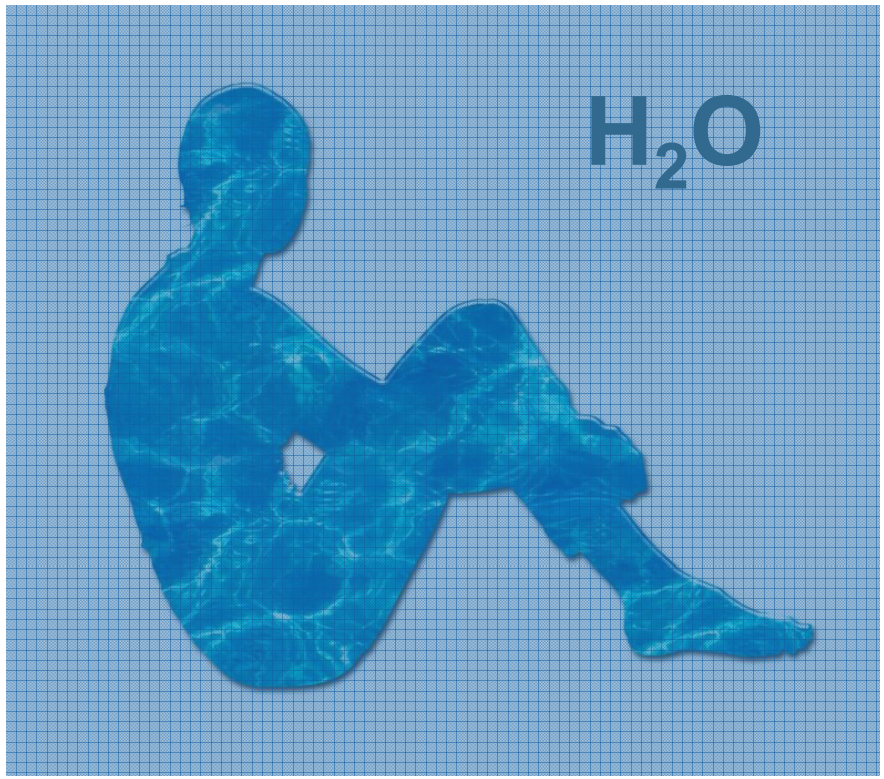
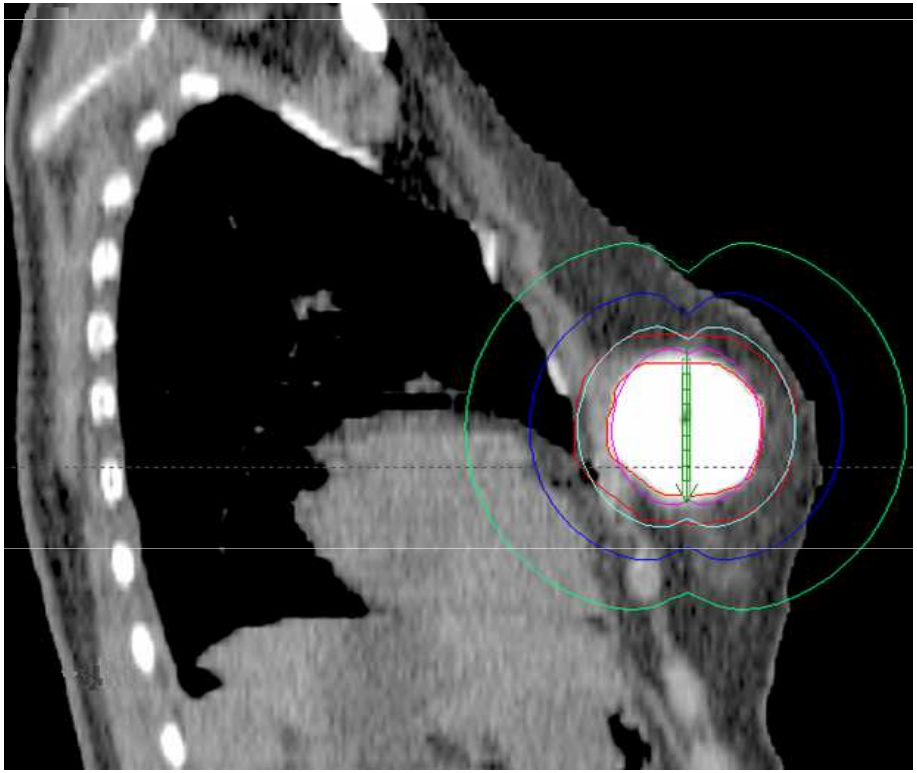
Limitations of TG-43 based Dose Calculation

Assumptions !!!

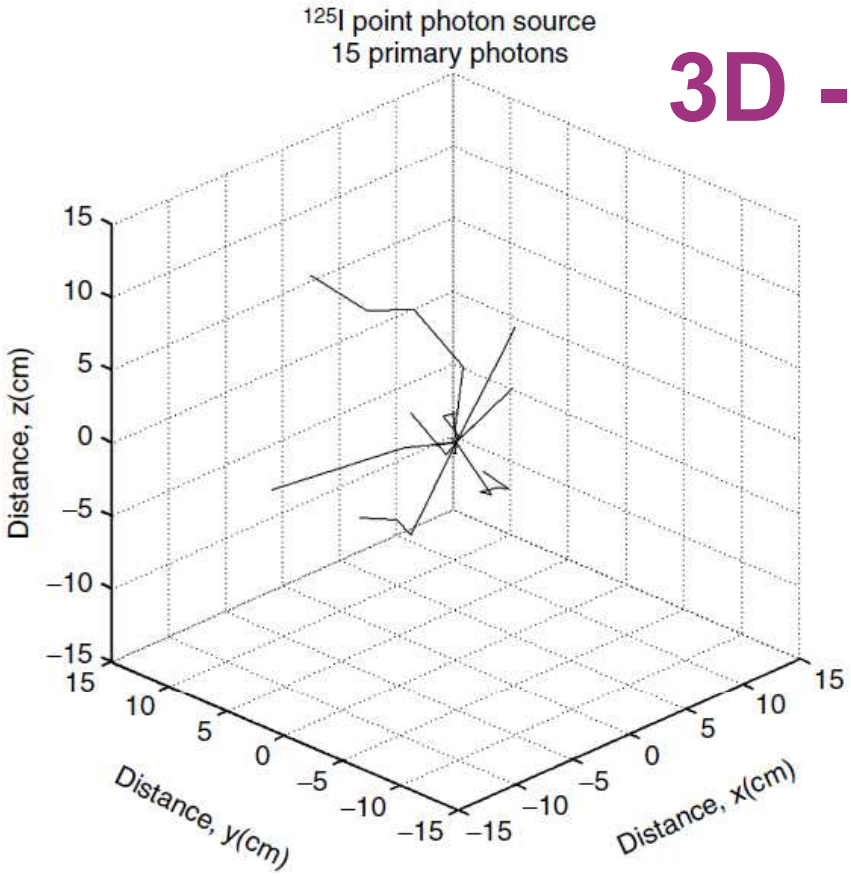


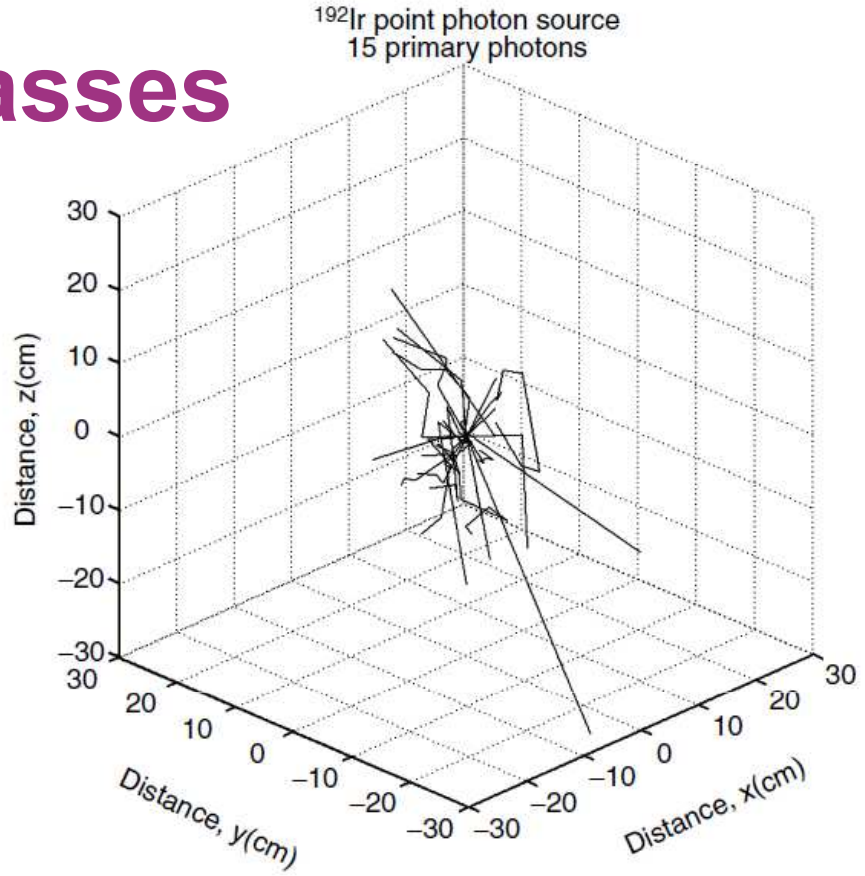
≠



Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

3D - Glasses





Figures from: Baltas, Sakelliou, Zamboglou (Eds), The Physics of modern brachytherapy for oncology, Taylor & Francis Books Inc, 2006 / TG186: Beaulieu et al , Med. Phys. 39(10), 6208 (2012)

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Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

Sensitivity of Anatomic Sites to Dosimetric Limitations of Current Planning Systems

anatomic site	photon energy	absorbed dose	attenuation	shielding	scattering	beta/kerma dose
prostate	high					
	low	XXX	XXX	XXX		
breast	High			X	XXX	
	low	XXX	XXX	XXX		
GYN	high			XXX		
	low	XXX	XXX			
skin	high			XXX	XXX	
	low	XXX		XXX	XXX	
lung	high				XXX	XXX
	low	XXX	XXX		XXX	
penis	high				XXX	
	low	XXX			XXX	
eye	high			XXX	XXX	XXX
	low	XXX	XXX	XXX	XXX	

Rivard, Venselaar, Beaulieu, *Med Phys* 36, 2136-2153 (2009)

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Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

Is that important for the Clinic?

Site / Application	Importance
Shielded Applicators	Huge
Eye plaque	-10 to -30% (TG129)
Breast Brachy	-5% to -40%
Prostate Brachy	-2 to -15% on D90
GYN	Depends on applicators

- **Rivard, Venselaar, Beaulieu, *Med Phys* 36, 2136-2153 (2009)**
- **Beaulieu *et al* (TG-186), *Med Phys* 39, 2012**

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Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

Rule of thumb

Energy Range	Effect
^{192}Ir	Scatter condition
	Shielding (applicator related)
^{103}Pd / ^{125}I / eBx	Absorbed dose (μ_{en}/ρ)
	Attenuation (μ/ρ)
	Shielding (applicator, source)

Rivard, Venselaar, Beaulieu, *Med Phys* 36, 2136-2153 (2009)

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Thank you very much for your Attention

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THE PARIS SYSTEM

Interstitial brachytherapy

Renaud Mazeron

Gustave Roussy

Paris System

- Dedicated to interstitial brachytherapy
- ≠ Paris Method (Gyne) / isodose envelop
- Developped in the 1960s / complete system
- Created for I ^{192} wires
- Set of rules tacking into account
  - The geometry and method of application
  - the source strength
  - In order to get a suitable dose distribution

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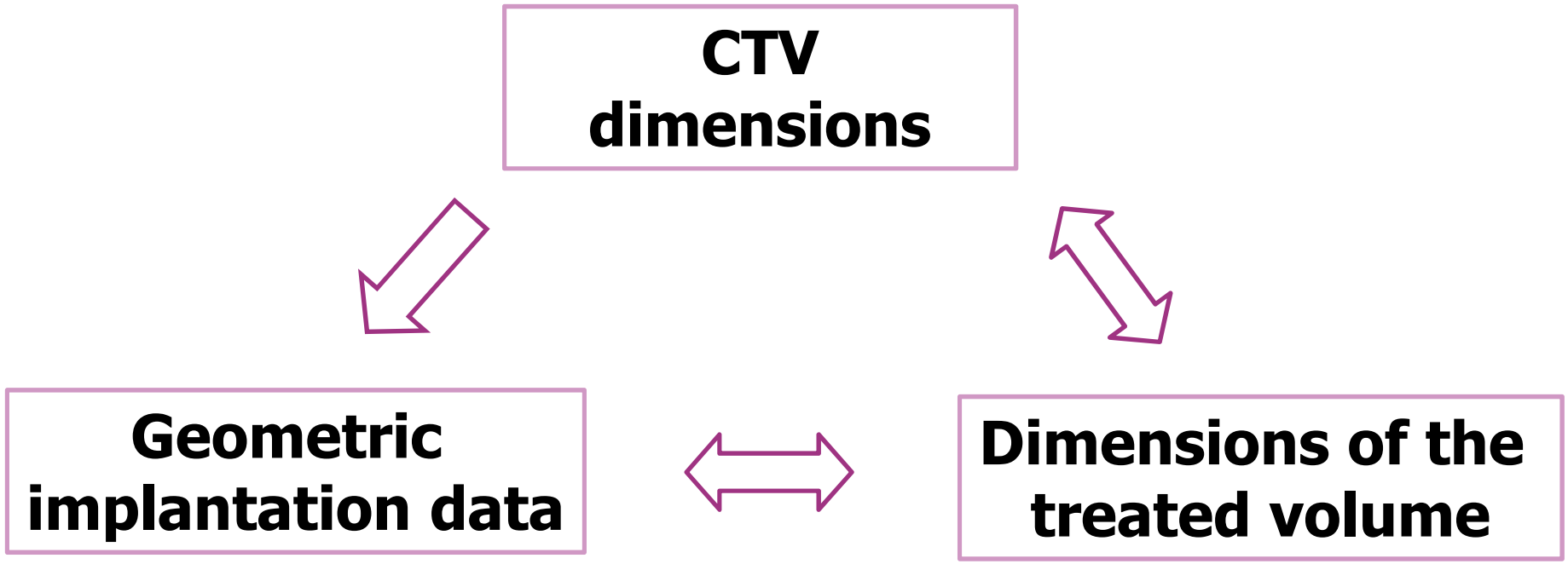
Predictive implant system

Forecast dosimetry



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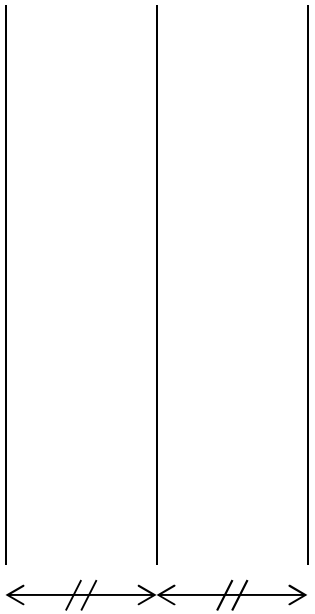
Paris system: Basic principles (1)

1. Linear activity is (LDR):

   - uniform along each line
   - identical for all the lines

2. Radioactive sources are:

   - parallel
   - straight
   - equidistant



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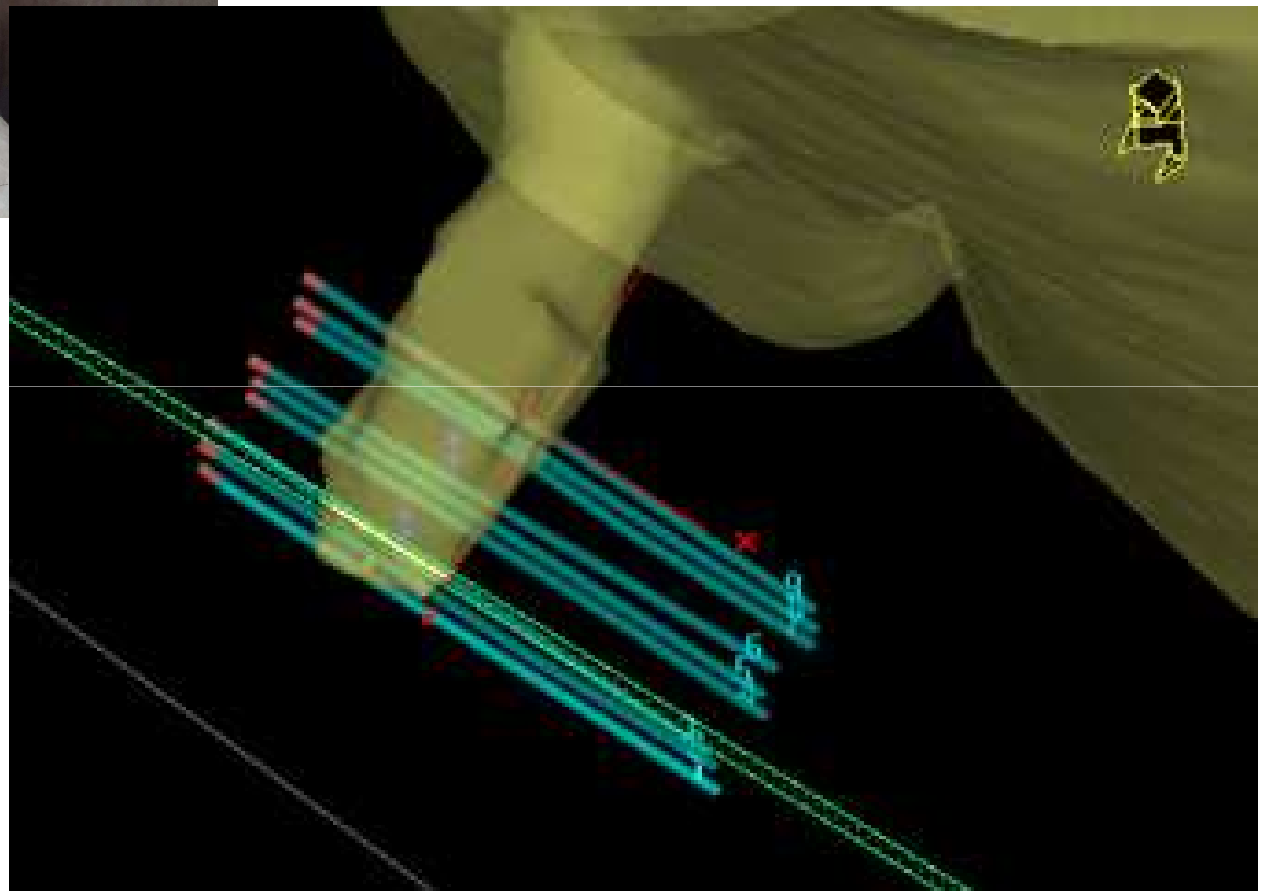
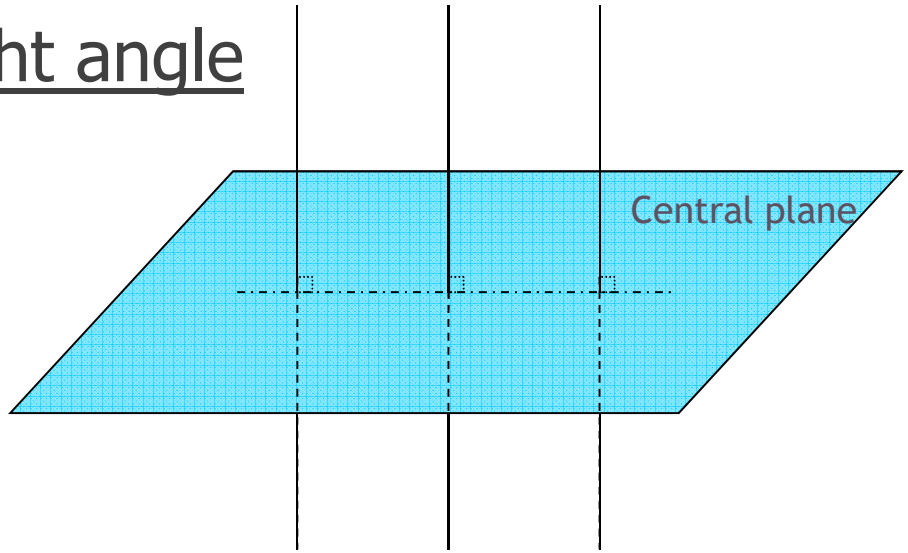


Paris system: Basic principles (2)

3. Dose specification Central plane

the plane on which the mid-points of the sources lie, should be at the right angle to the axis of each source



PS: Sources are equally separated but source separation varies from one implant to an other

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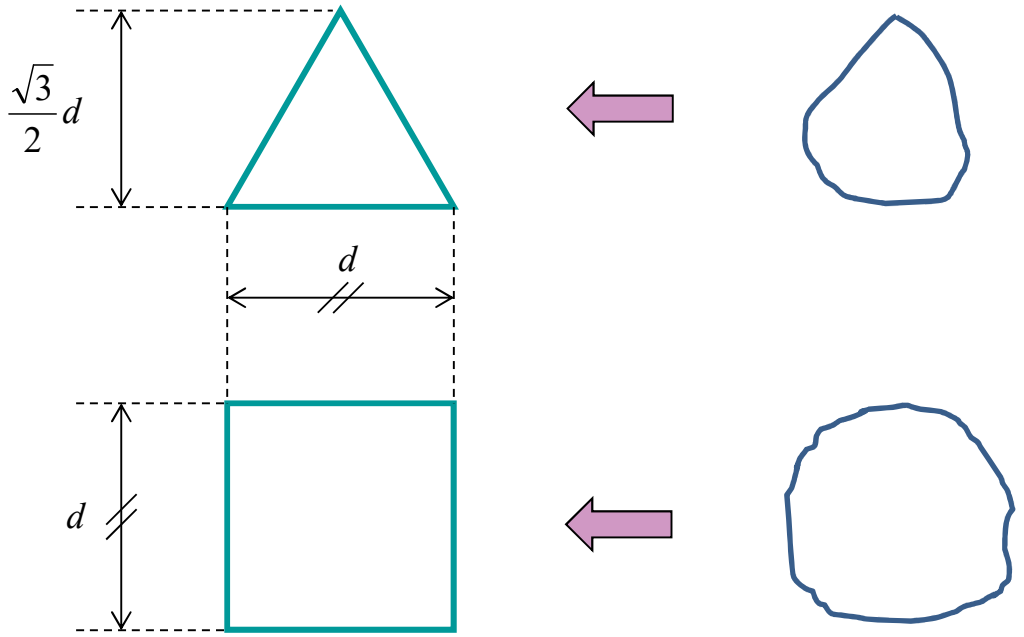
Paris system: Forecast dosimetry

- Tumoral thickness determination

  If >12 mm: 2 or more planes as implantation pattern

  Tumor shape determines whether an implantation is arranged in «squares» or in «triangles».



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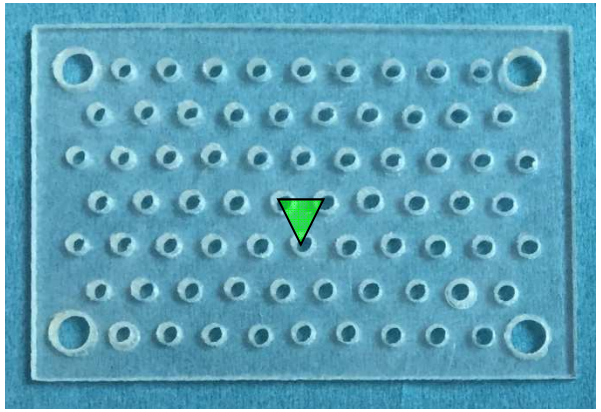
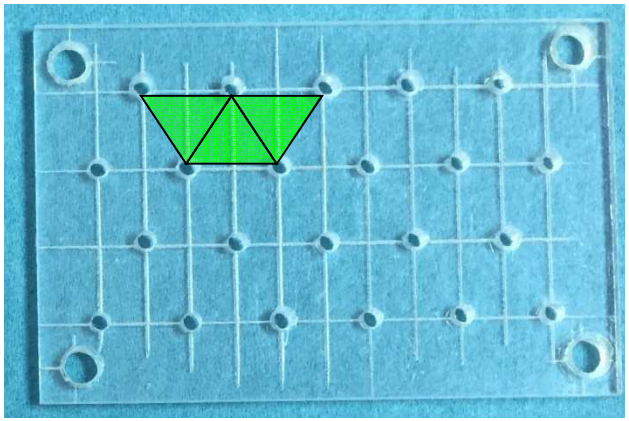
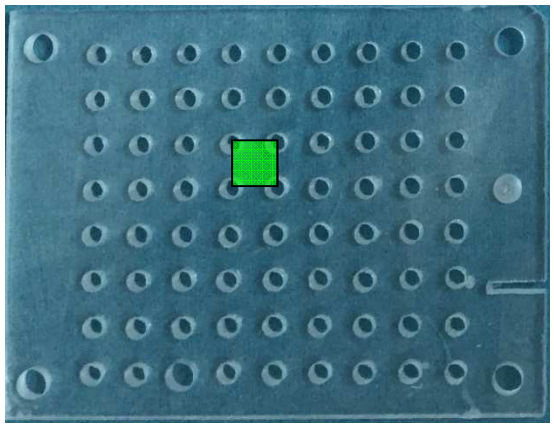
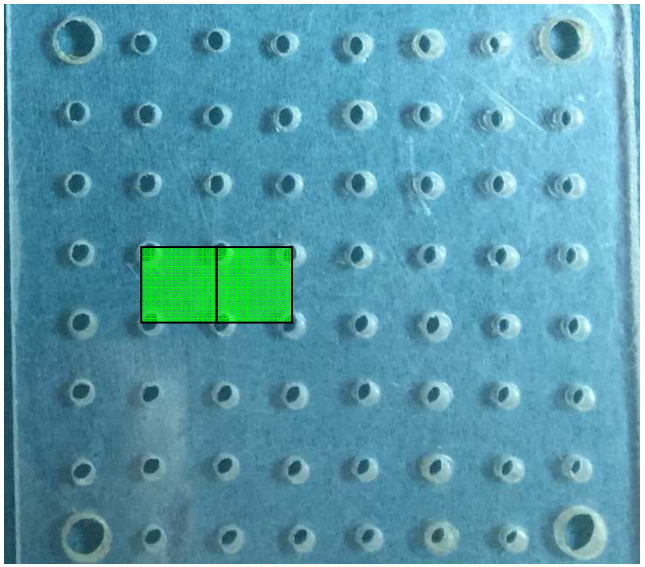
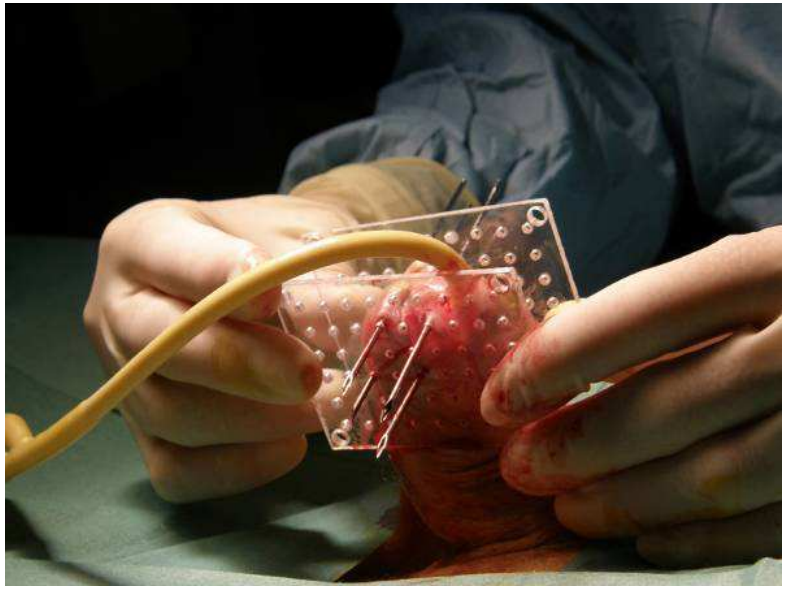
Templates

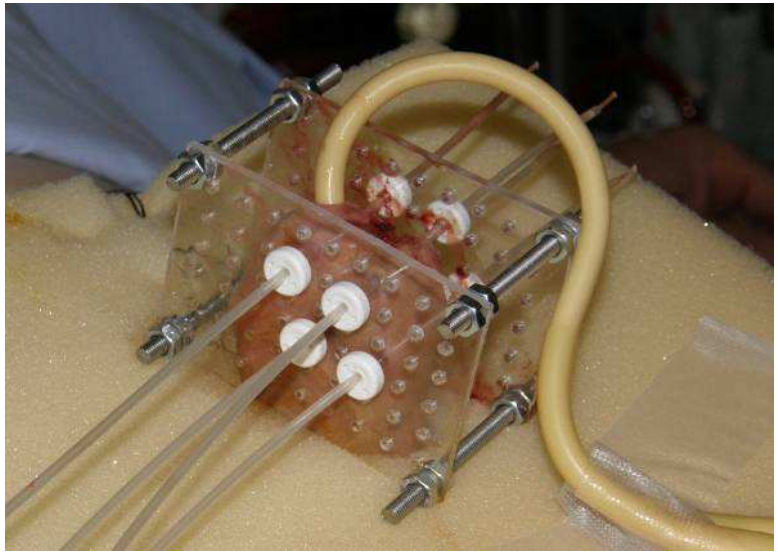












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Ratios of source spacing to target thickness and source length to target length

4. Source spacing is a function of thickness

- Single plane

- Spacing = 2 x target thickness (2 sources)
- Spacing = 1.67 x target thickness (3 or more sources)

- Double plane

- Square spacing = 0.62 to 0.64 x target thickness
- Triangles spacing = 0.75 to 0.79 x target thickness

5. Source length is a function of target length

- radio active Length = 1.33 to 1.54 x target length

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Paris system forecast relationships

Implant type	Treated length / radioactive length	Treated thickness/ spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.7	0.5	0.37	-
n lines in 1 plane	0.7	0.6	0.33	-
n lines in «square»	0.7	1.55 - 1.60	-	0.27
n lines in triangle	0.7	1.3	-	0.20

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Paris system: V100%

Empirical relation between the treated volume (in cm^3) and the geometric implantation data

$$V_T = k.N.E^2.L$$

N = number of lines
E = spacing of lines (cm)
L = active length
k = 0.47 for planar implants and for patterns in « triangles »
0.57 for patterns in « squares »

Validity limits for the Paris system

Active length (mm)	Minimum Separation (mm)	Maximum Separation (mm)
10 to 40	8	15
50 to 90	10	20
≥ 100	15	25

Is the Paris system valid for stepping sources?

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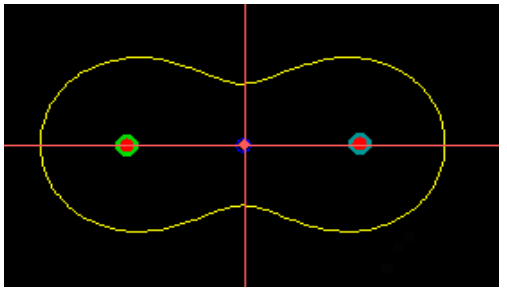
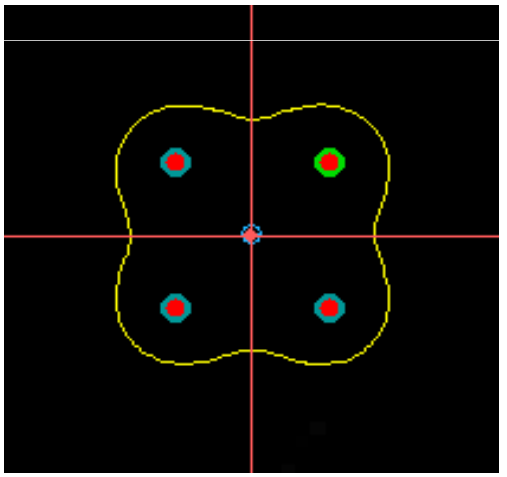
Method

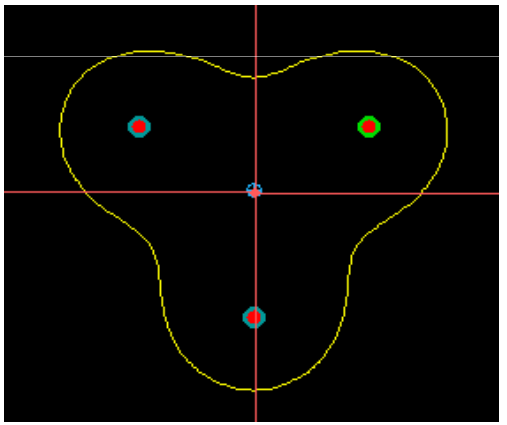
- Recalculation of the ratios with stepping sources
  - Length / width / margins
  - Single plan / triangle / square

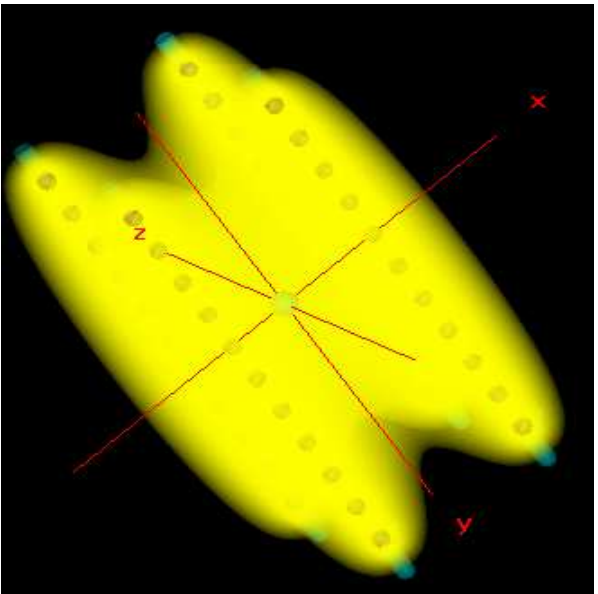
- Comparison to those reported orgininally with I^{192} wires

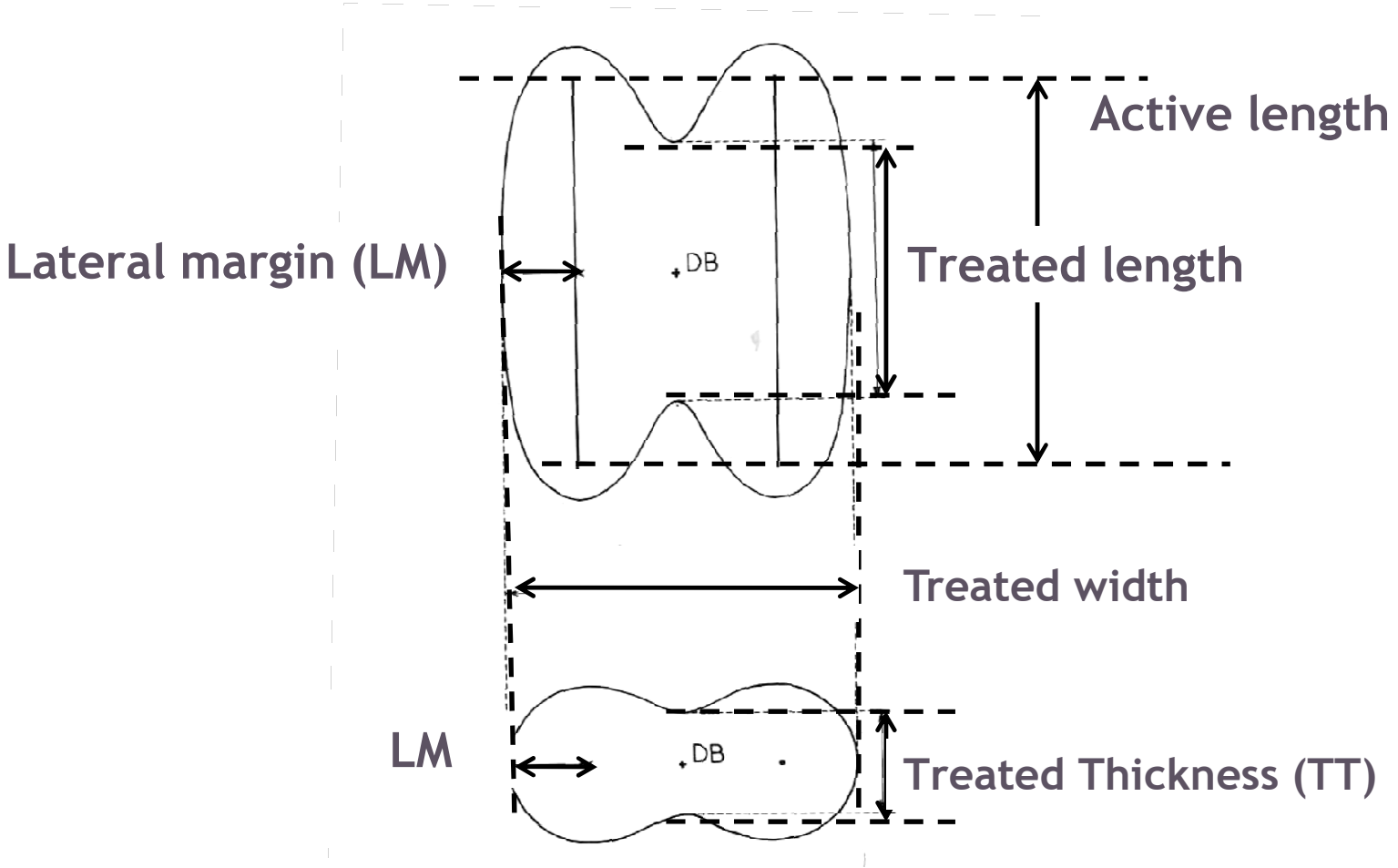
(Dutreix et al. – Dosimétrie en curiethérapie – Ed. Masson, 1982)

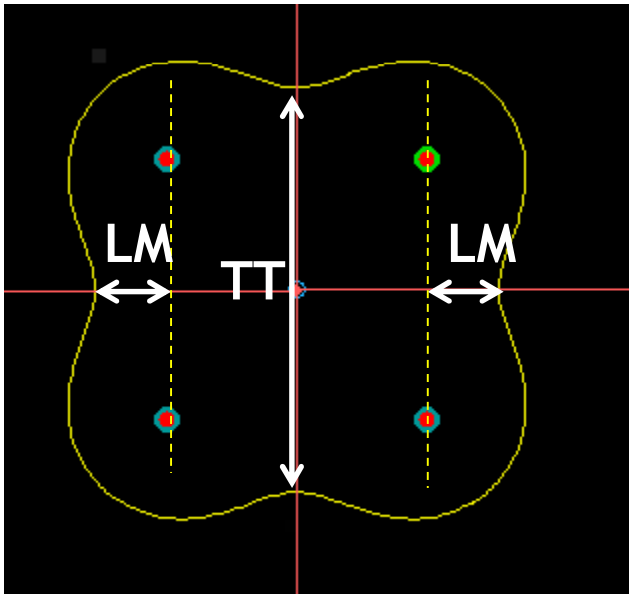




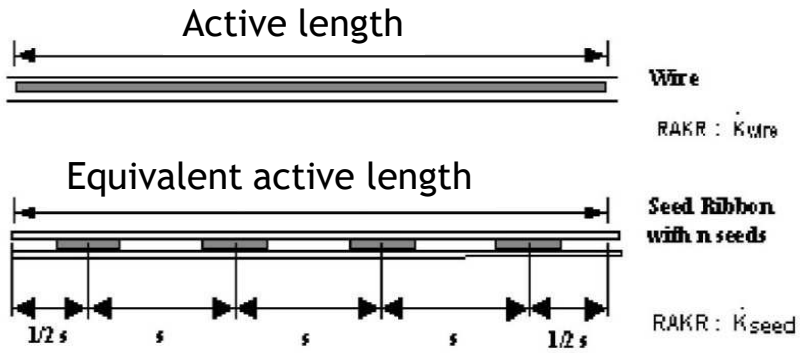


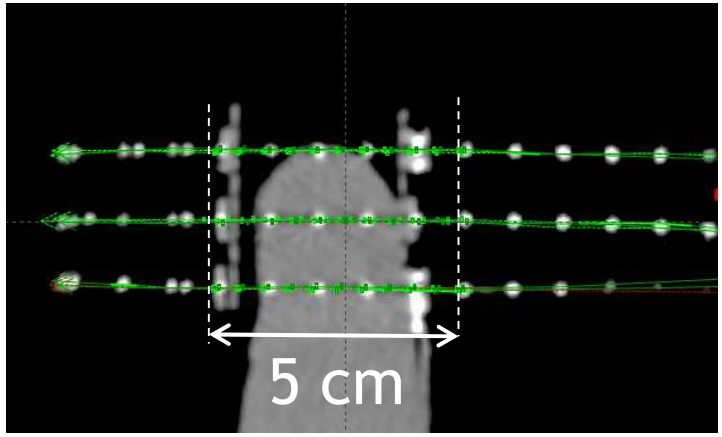

x
z
y


Active length
Lateral margin (LM)
DB
Treated length
Treated width
LM
DB
Treated Thickness (TT)


LM
TT
LM

Equivalent active length



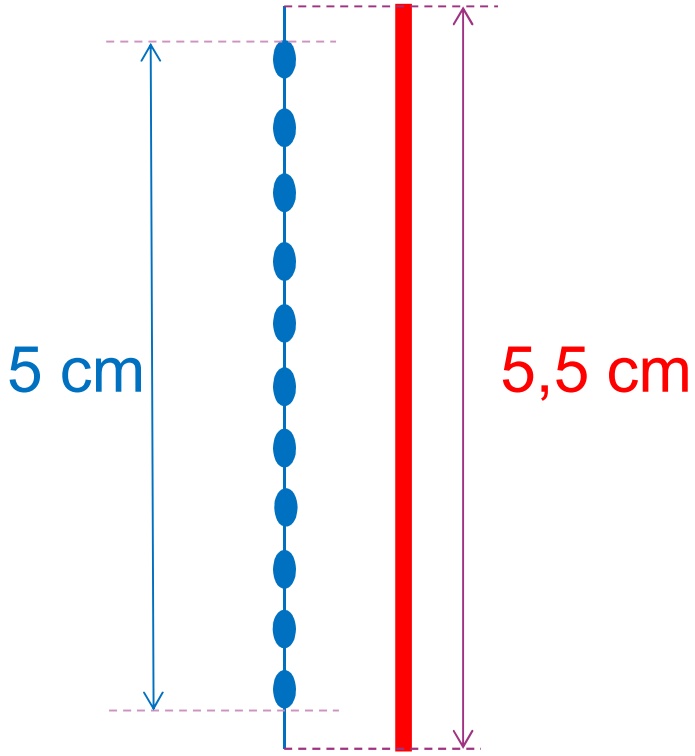


$$AL = EAL = n \times s$$

AL = 5 cm ➡ Stepping source

EAL = n x s = 11 x 0,5 cm

= 5,5 cm ➡ Ir-192 wire



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Paris System

	Arrangement		
	1 Plan	Triangle	Square
TL/AL	0,7		
Th/Sp	0,6	1,3	1,6
LM/Sp	0,35	/	/
SM/Sp	/	0,2	0,27

Ratio Treated length/ Active lenght

	Ecartement	L/LAe [Stepping source]	L/LAe [Dutreix et al.]
1 PLAN	1	0,80	0,77
	1,2	0,78	0,75
	1,4	0,74	0,74
	1,6	0,73	0,72
	1,8	0,70	0,70
	2	0,69	0,69
	Moyenne	**0,74**	**0,73**
	Ecart type	0,04	0,03
1 CARRE	1	0,74	0,73
	1,2	0,71	0,72
	1,4	0,69	0,70
	1,6	0,67	0,69
	1,8	0,66	0,67
	2	0,65	0,66
	Moyenne	**0,69**	**0,70**
	Ecart type	0,03	0,03
1 Triangle	1	0,77	0,75
	1,2	0,74	0,73
	1,4	0,72	0,71
	1,6	0,70	0,70
	1,8	0,69	0,69
	2	0,67	0,67
	Moyenne	**0,71**	**0,71**
	Ecart type	0,04	0,03

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Paris system

	Arrangement		
	1 Plan	Triangle	Square
TL/AL		0,7	
Th/Sp	0,6	1,3	1,6
LM/Sp	0,35	/	/
SM/Sp	/	0,2	0,27

Ratio Treated length/ Active lenght

	Ecartement	L/LAe [Stepping source]	L/LAe [Dutreix et al.]	L/LA [Stepping source]
1 PLAN	1	0,80	0,77	0,88
	1,2	0,78	0,75	0,86
	1,4	0,74	0,74	0,82
	1,6	0,73	0,72	0,80
	1,8	0,70	0,70	0,77
	2	0,69	0,69	0,75
	Moyenne	**0,74**	**0,73**	**0,81**
	Ecart type	0,04	0,03	0,05
1 CARRE	1		0,73	0,81
	1,2		0,72	0,78
	1,4		0,70	0,76
	1,6		0,69	0,74
	1,8		0,67	0,73
	2		0,66	0,71
	Moyenne	**0,69**	**0,70**	**0,76**
	Ecart type	0,03	0,03	0,04
1 Triangle	1	0,77	0,75	0,85
	1,2	0,74	0,73	0,81
	1,4	0,72	0,71	0,79
	1,6	0,70	0,70	0,77
	1,8	0,69	0,69	0,76
	2	0,67	0,67	0,73
	Moyenne	**0,71**	**0,71**	**0,79**
	Ecart type	0,04	0,03	0,04

≈ 0,8

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Paris system

	Arrangement		
	1 Plan	Triangle	Square
TL/AL	0,7		
Th/Sp	0,6	1,3	1,6
LM/Sp	0,35	/	/
SM/Sp	/	0,2	0,27

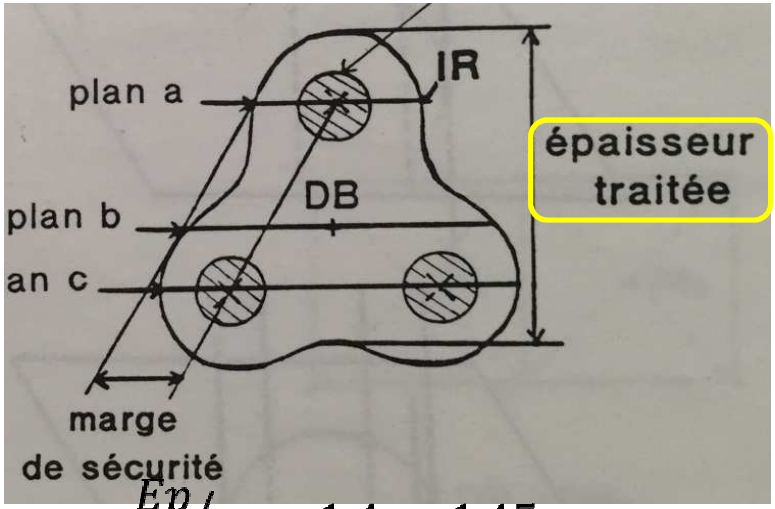
Treated Thickness / Spacing

	Ecartement	Ep/Ec [Stepping source]	Ep/Ec [Dutreix et al.]	
1 PLAN	1	0,60	0,58	
	1,2	0,58	0,57	
	1,4	0,57	0,56	
	1,6	0,56	0,55	
	1,8	0,56	0,54	
	2	0,55	0,54	
	Moyenne	**0,57**	**0,56**	≈ 0,6
	Ecart type	0,02	0,02	
1 CARRE	1	1,58	1,57	
	1,2	1,58	1,57	
	1,4	1,57	1,56	
	1,6	1,56	1,56	
	1,8	1,56	1,56	
	2	1,56	1,55	
	Moyenne	**1,57**	**1,56**	≈ 1,55-1,6
	Ecart type	0,01	0,01	
1 Triangle	1	1,46	1,29	
	1,2	1,45	1,29	
	1,4	1,43	1,28	
	1,6	1,45	1,28	
	1,8	1,42	1,27	
	2	1,44	1,27	
	Moyenne	**1,44**	**1,28**	??
	Ecart type	0,01	0,01	

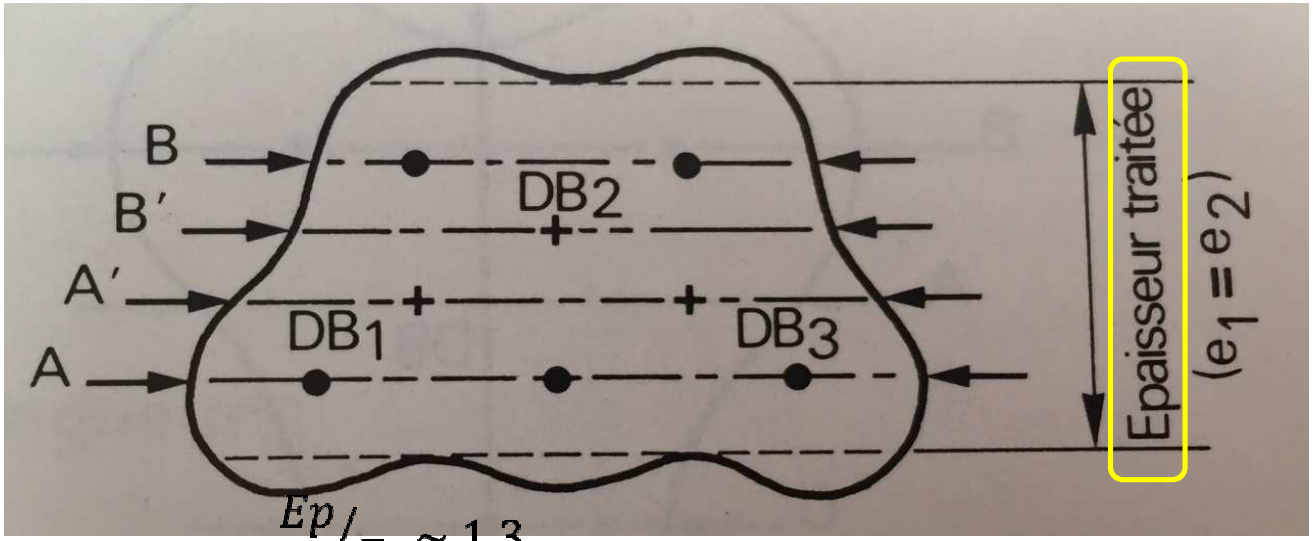
Paris system

	Arrangement		
	1 Plan	Triangle	Square
TL/AL	0,7		
Th/Sp	0,6	1,3	1,6
LM/Sp	0,35	/	/
SM/Sp	/	0,2	0,27

Treated thickness / Spacing



$Ep/_{Ec} \sim 1,4 - 1,45$



$Ep/_{Ec} \sim 1,3$

1 Triangle

Ecartement	Ep/Ec [Stepping source]	Ep/Ec [Dutreix et al.]
1	1,46	1,29
1,2	1,45	1,29
1,4	1,43	1,28
1,6	1,45	1,28
1,8	1,42	1,27
2	1,44	1,27
Moyenne	**1,44**	**1,28**
Ecart type	0,01	0,01

ESTRO School

Paris system

Safety margins / Spacing

	Arrangement		
	1 Plan	Triangle	Square
TL/AL	0,7		
Th/Sp	0,6	1,3	1,6
LM/Sp	0,35	/	/
SM/Sp	/	0,2	0,27

	Ecartement	MS/Ec [Stepping source]	MS/Ec [Dutreix et al.]	
1 PLAN	1	0,350	0,330	
	1,2	0,358	0,338	
	1,4	0,350	0,346	
	1,6	0,363	0,354	
	1,8	0,356	0,362	
	2	0,370	0,370	
	Moyenne	**0,36**	**0,35**	≈ 0,35
	Ecart type	0,008	0,015	
1 CARRE	1	0,300	0,282	
	1,2	0,283	0,281	
	1,4	0,271	0,279	
	1,6	0,281	0,278	
	1,8	0,272	0,276	
	2	0,265	0,275	
	Moyenne	**0,28**	**0,28**	0,28
	Ecart type	0,012	0,003	
1 Triangle	1	0,230	0,240	
	1,2	0,233	0,237	
	1,4	0,250	0,234	
	1,6	0,213	0,231	
	1,8	0,228	0,228	
	2	0,220	0,225	
	Moyenne	**0,23**	**0,23**	0,23
	Ecart type	0,013	0,006	

Paris system forecast relationship
--
Stepping source

Implant type	Treated length / radioactive length	Treated thickness /spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	**0.8**	0.5	0.37	-
n lines in one plane	**0.8**	0.6	0.33	-
n lines in «square»	**0.8**	1.55 to 1.60	-	0.27
n lines in triangle	**0.8**	1.3	-	0.20

ESTRO School

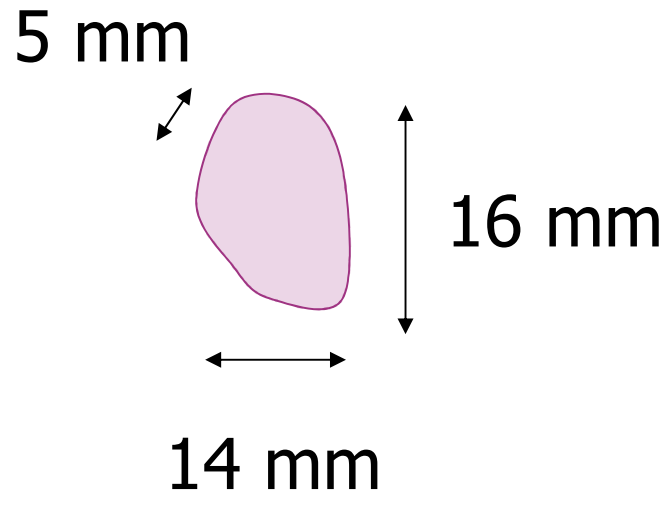
Paris system

Practical example

Basal cell carcinoma

CTV : 16 mm x 14 mm x 5 mm

L x W x T



ESTRO School

1st Step: number of planes

Tumoral thickness determination

CTV : 16 mm x 14 mm x 5 mm

L x W x T

ESTRO School

1st Step

Tumoral thickness determination
If it exceeds 12 mm: two or more planes as implantation pattern.

CTV : 16 mm x 14 mm x 5 mm
L x W x T

ESTRO School

1st Step

One plane is enough

CTV : 16 mm x 14 mm x 5 mm
L x W x T

ESTRO School

2nd Step: spacing

Source spacing selection as a function of tumoral thickness ⟶ total line number deduction

CTV : 16 mm x 14 mm x 5 mm
L x W x T

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Paris system forecast relationship 2.0

Implant type	Treated length / radioactive length	Treated thickness /spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.8	**0.5**	0.37	-
n lines in one plane	0.8	0.6	0.33	-
n lines in «square»	0.8	1.55 to 1.60	-	0.27
n lines in triangle	0.8	1.3	-	0.20

ESTRO School

2nd Step: spacing

Source spacing selection as a function of tumoral thickness ⟶ total line number deduction

CTV : 16 mm x 14 mm x 5 mm
L x W x T

Source spacing

- Single plane : T (5)/ spacing = 0.5
- Spacing = 2 x target thickness (2 sources)

ESTRO School

2nd Step: spacing

Source spacing selection as a function of tumoral thickness ⟶ total line number deduction

CTV : 16 mm x 14 mm x 5 mm
L x W x T

Source spacing

- Single plane : T (5)/ spacing = 0.5
- Spacing = 2 x target thickness (2 sources)

ESTRO School

2nd Step: spacing

Source spacing selection as a function of tumoral thickness ⟶ total line number deduction

CTV : 16 mm x 14 mm x 5 mm
L x W x T

Source spacing

- Single plane
- Spacing = 2 x 5mm (2 sources)

ESTRO School

2nd Step

Line spacing to treated 5 mm: 10 mm

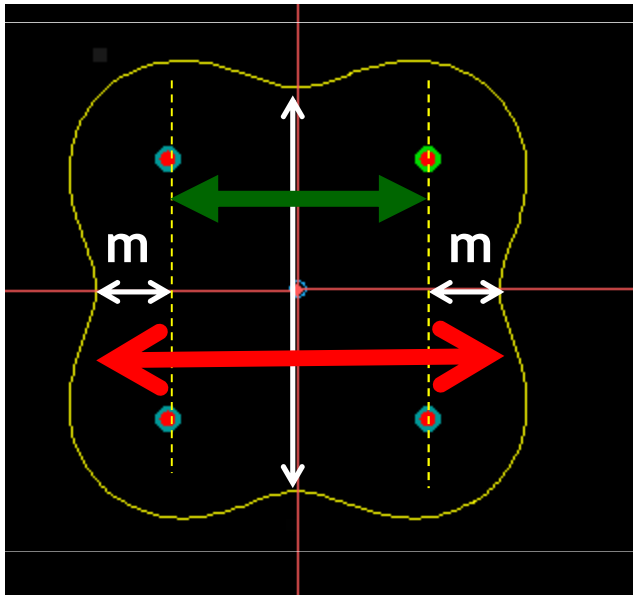
What will be the treated width?

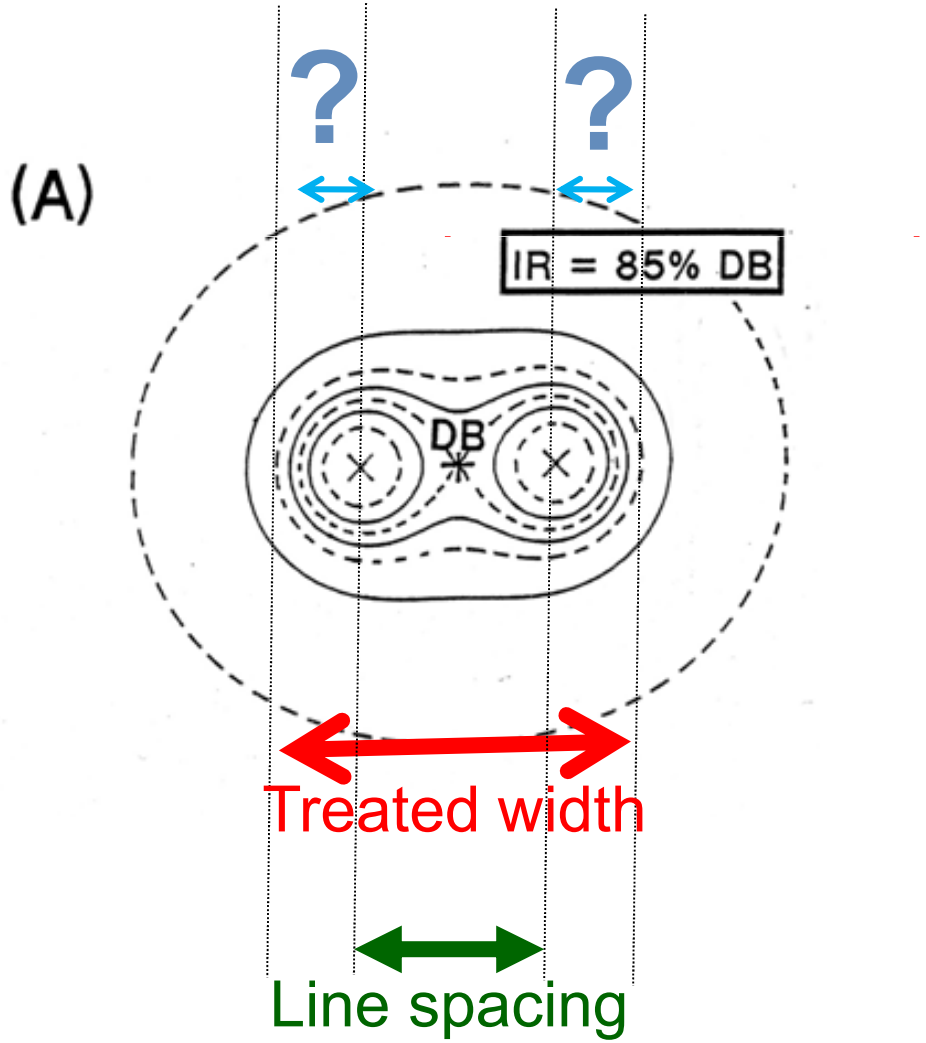
Is 10 mm enough?

CTV : 16 mm x 14 mm x 5 mm
L x W x T

ESTRO School

Lateral Margins





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Paris system forecast relationship

Implant type	Treated length / radioactive length	Treated thickness /spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.7	0.5	0.37	-
n lines in one plane	0.7	0.6	0.33	-
n lines in «square»	0.7	1.55 to 1.60	-	0.27
n lines in triangle	0.7	1.3	-	0.20

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2nd Step

Line spacing : 10 mm

Ratio Lateral margin/separation = 0.37

This spacing corresponds to a lateral margin of 3.7mm

The treated width is :

10 mm + 2 x (3.7 mm) = 17 mm

CTV : 16 mm x 14 mm x 5 mm

L x W x T

ESTRO School

3rd Step

What is the required radioactive length?

CTV : 16 mm x 14 mm x 5 mm
L x W x T

The radioactive length is:
16 mm / 0.8 = **20 mm**

Implant type	Treated length / Radioactive length
2 lines	0.8
n lines in one plane	0.8
n lines in «square»	0.8
n lines in triangle	0.8

ESTRO School

Paris system

CTV : 16 mm x 14 mm x 5 mm
L x W x T

2 lines :
10 mm apart
20 mm long

ESTRO School

Practical example 2

Lip cancer
Squamous cell carcinoma
CTV : 2.5 cm x 1.5 cm x 1.3 cm
L x T x W

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1st Step: number of planes?

Lip cancer
Squamous cell carcinoma
CTV : 2.5 cm x 1.5 cm x 1.3 cm
L x T x W

ESTRO School

1st Step

Tumoral thickness determination
If it exceeds 12 mm, two or more planes as implantation pattern

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

ESTRO School

1st Step

TWO planes

Squamous cell carcinoma

CTV : 25 mm x 15 mm x 13 mm

L x T x W

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1st Step: geometry

Tumoral thickness determination
Square or triangle ?

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

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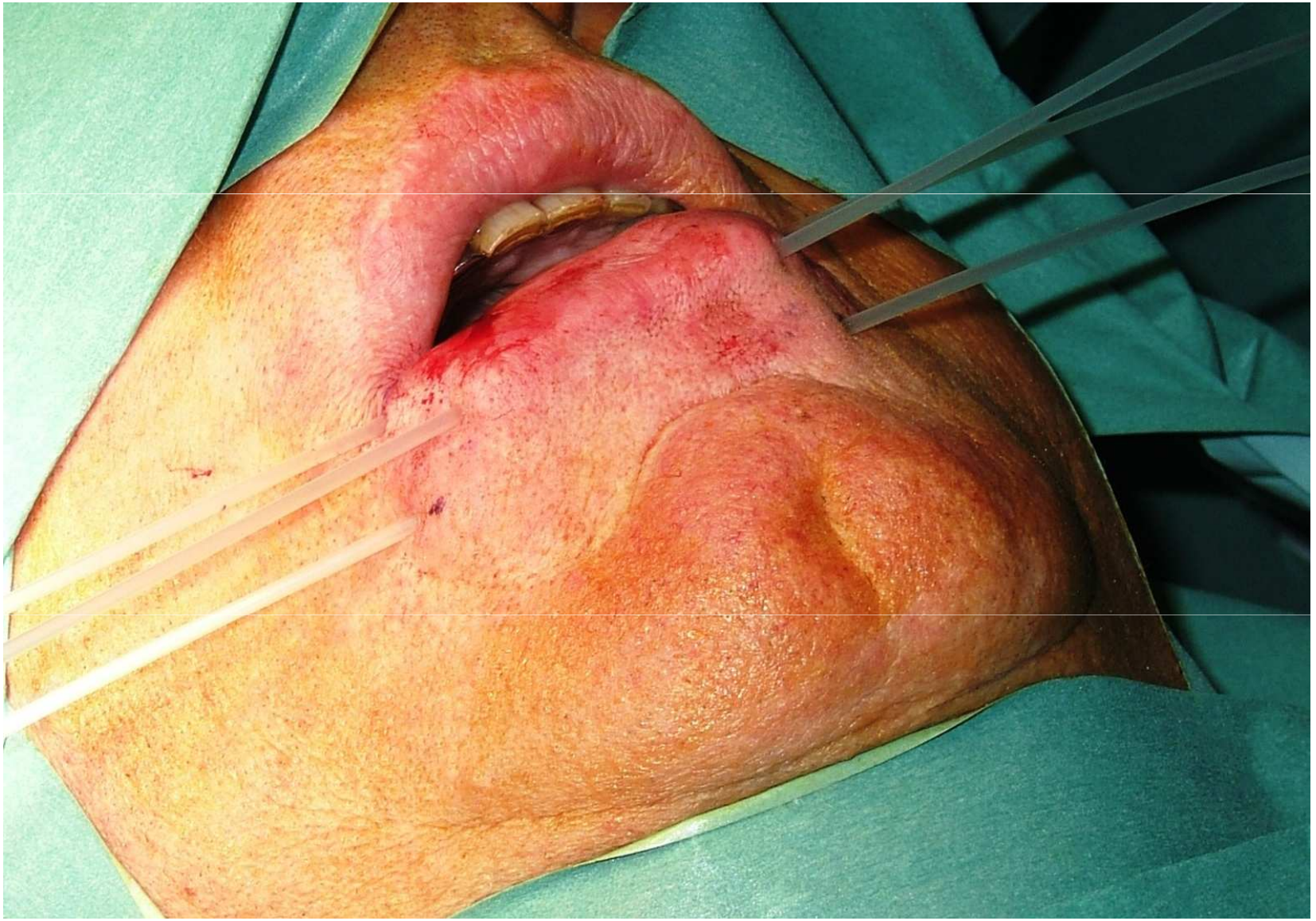
Geometry = shape



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2nd Step: Spacing

Source spacing selection as a function of tumoral thickness

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

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Paris system forecast relationship

Implant type	Treated length / radioactive length	Treated thickness /spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.8	0.5	0.37	-
n lines in one plane	0.8	0.6	0.33	-
n lines in «square»	0.8	1.55 to 1.60	-	0.27
n lines in triangle	0.8	1.3	-	0.20

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2nd Step: Spacing

Source spacing selection as a function of tumoral thickness

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

Source spacing:
15 / 1.3 = **12 mm**

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3rd Step: lengh

Radioactive length ?

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

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Paris system forecast relationship

Implant type	Treated length / radioactive length	Treated thickness /spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.8	0.5	0.37	-
n lines in one plane	0.8	0.6	0.33	-
n lines in «square»	0.8	1.55 to 1.60	-	0.27
n lines in triangle	0.8	1.3	-	0.20

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3rd Step: lenght

Radioactive length ?

25 / 0.8 = 31.3 mm

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

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Safety margins?

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

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Paris system forecast relationship

Implant type	Treated length / radioactive length	Treated thickness /spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.7	0.5	0.37	-
n lines in one plane	0.7	0.6	0.33	-
n lines in «square»	0.7	1.55 to 1.60	-	0.27
n lines in triangle	0.7	1.3	-	0.20

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Safety margins?

Lip cancer
Squamous cell carcinoma
CTV : 25 mm x 15 mm x 13 mm
L x T x W

Safety margins:
12 x 0.2 = 2.4 mm
Treated width:
12 + (2x2.4)=16.8 mm

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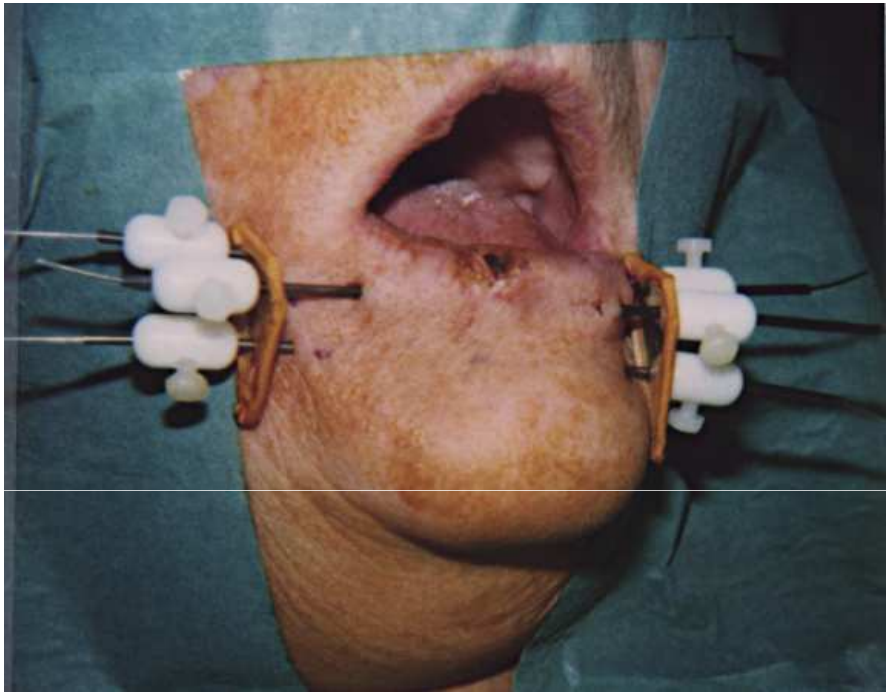
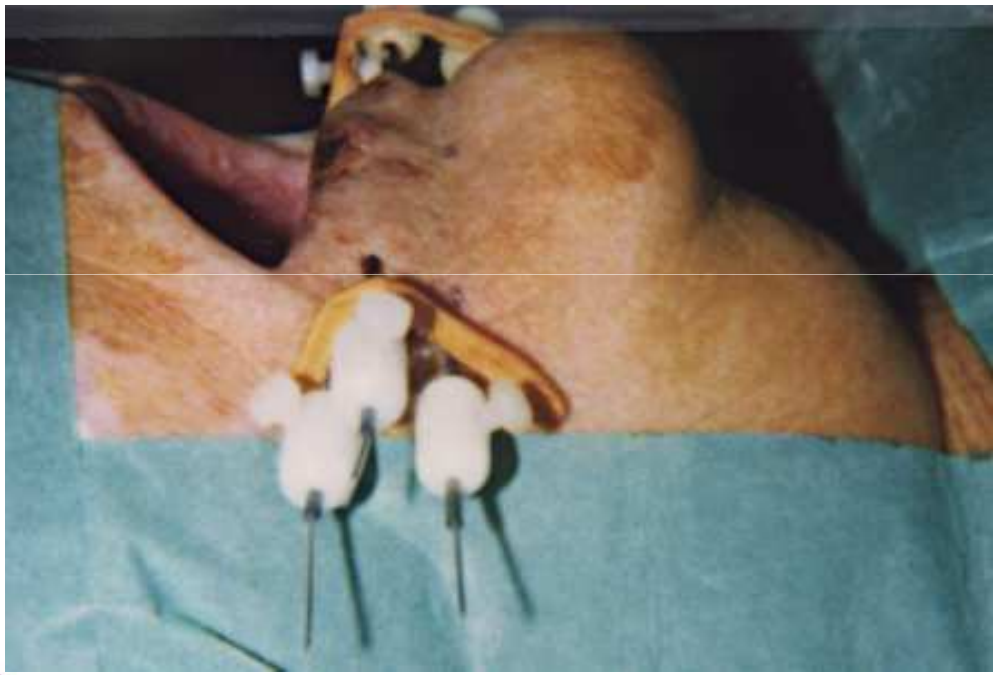
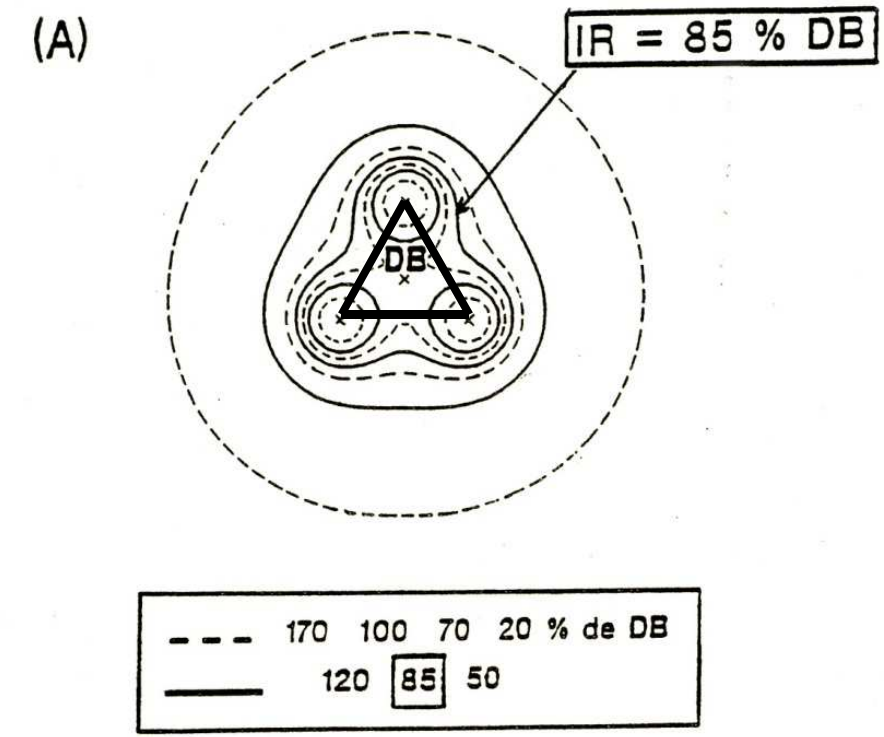
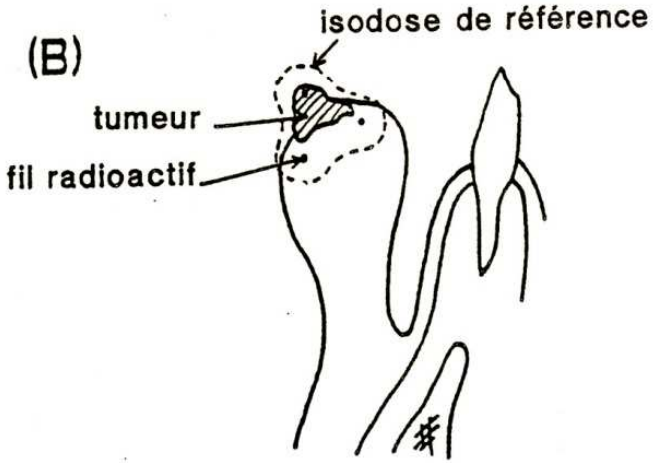


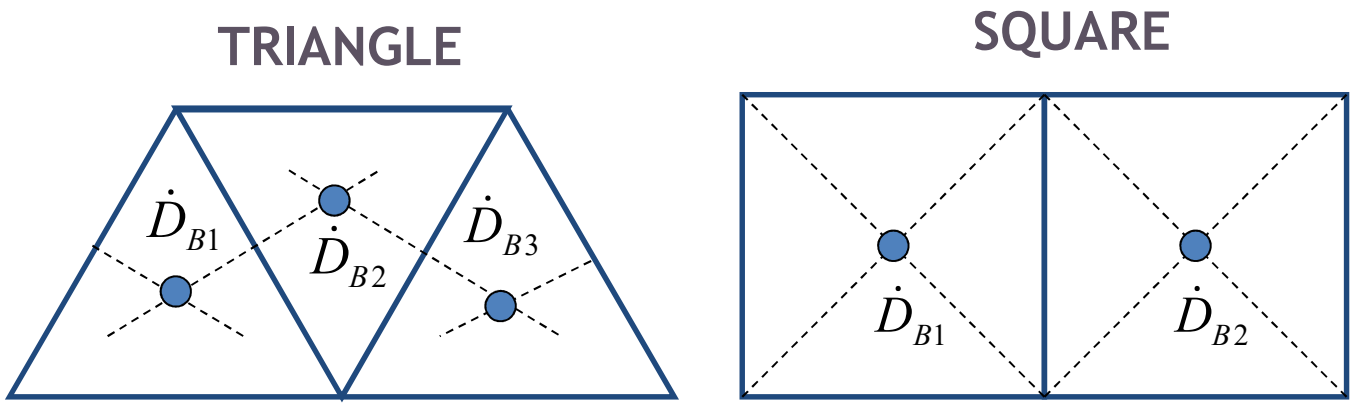



(A)
IR = 85 % DB
DB
170 100 70 20 % de DB
120 85 50


(B)
isodose de référence
tumeur
fil radioactif

Paris system: Dosimetry

- Is based on the dose-rate in the **central plane** of the treatment volume as implanted.
- The **basal dose-rate** is the **minimum dose-rate** between a group of sources in the central plane



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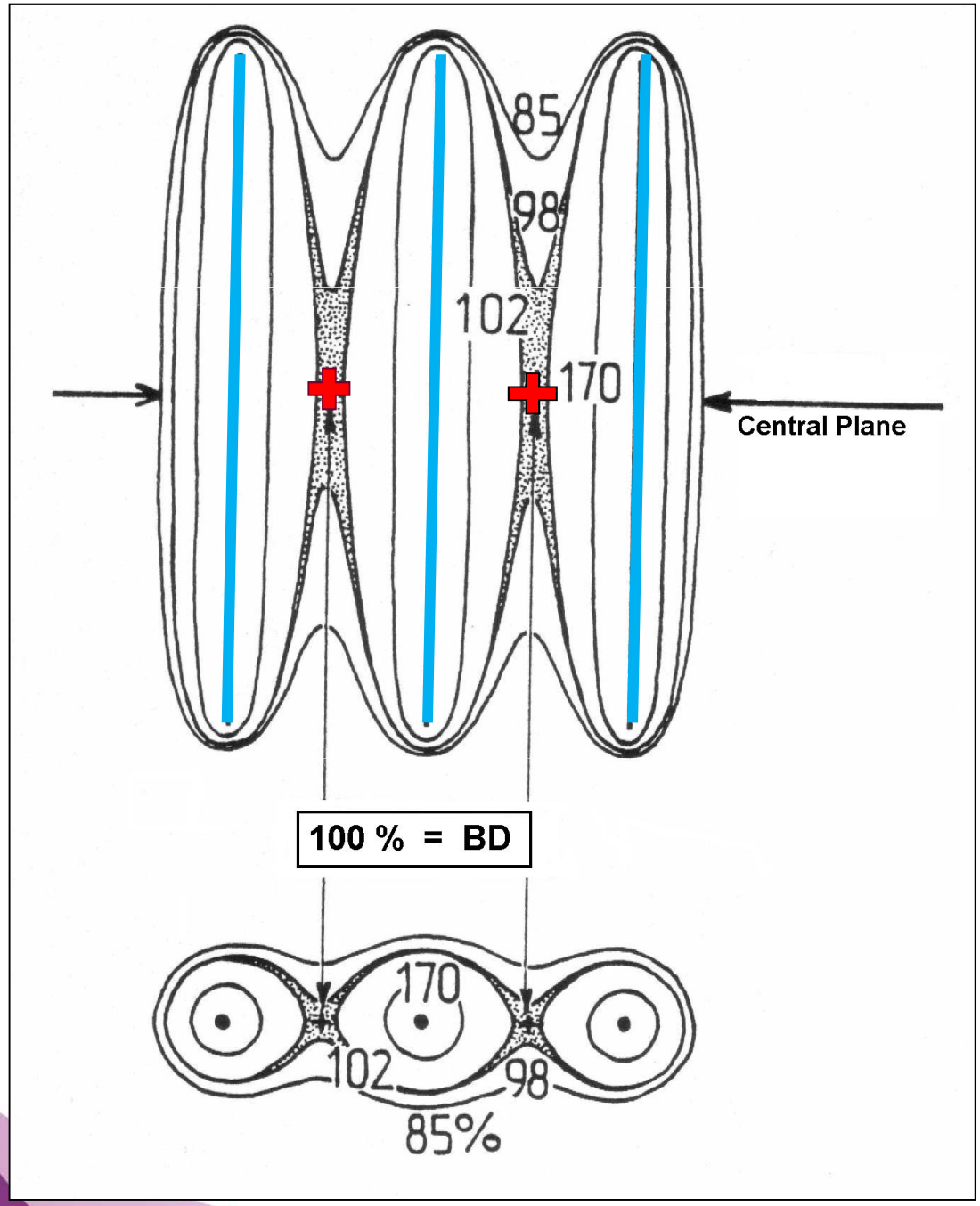
Basal dose rate calculation



Dose distribution in the central plane and in the plane of three linear and coplanar sources

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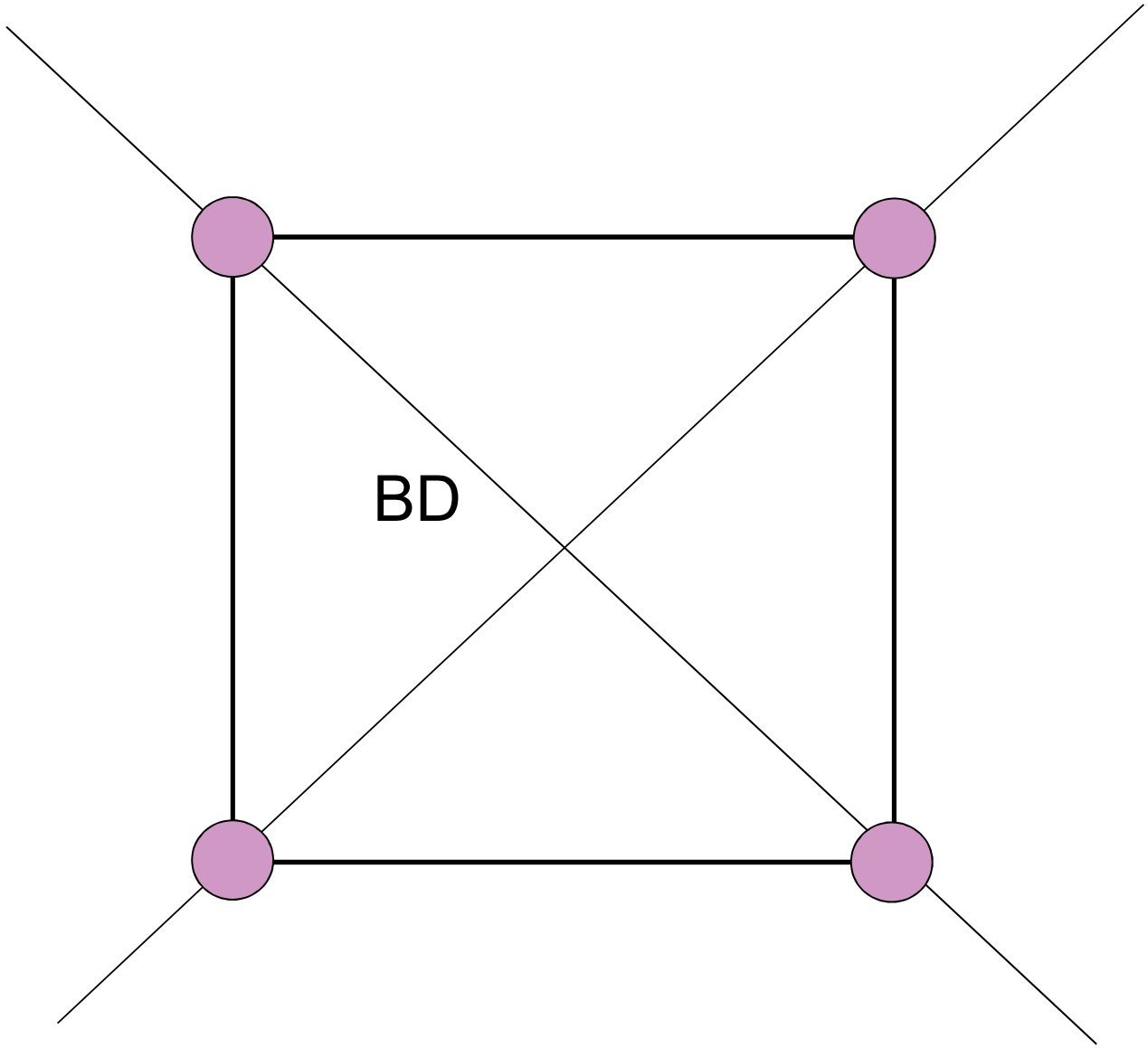
Paris system



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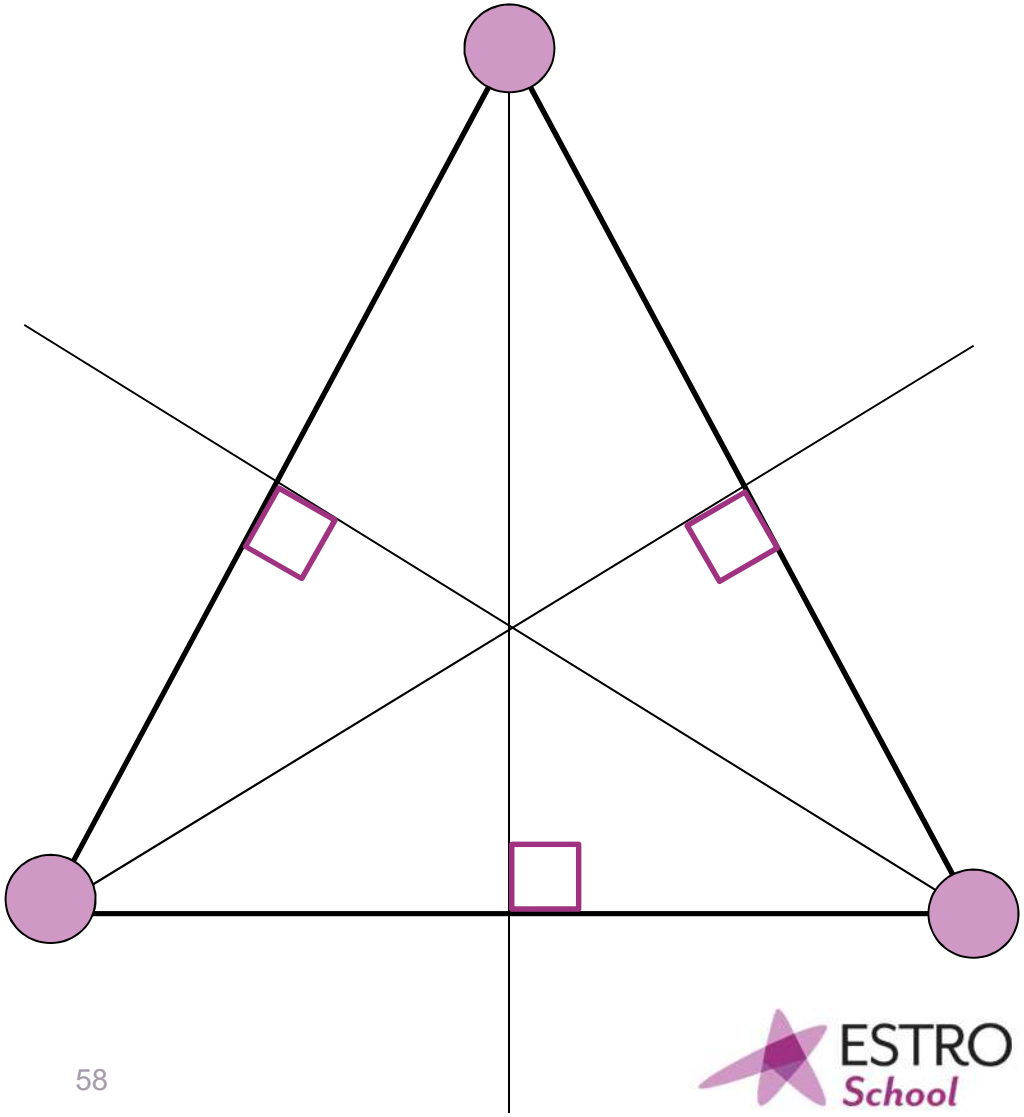
Paris system: Triangle

The **basal dose rate** is calculated at the intersection point of the perpendicular bisectors of the triangle sides



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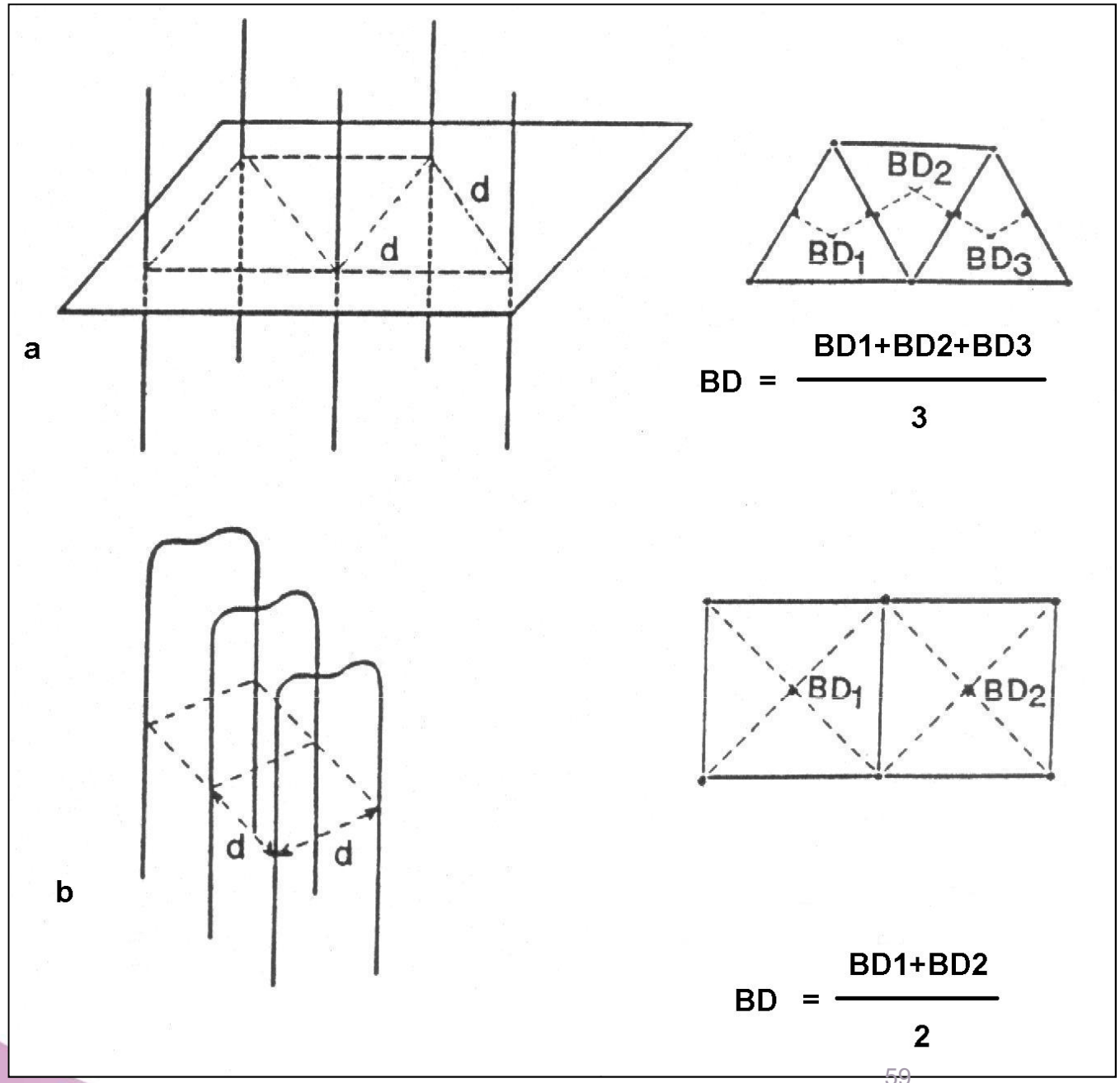
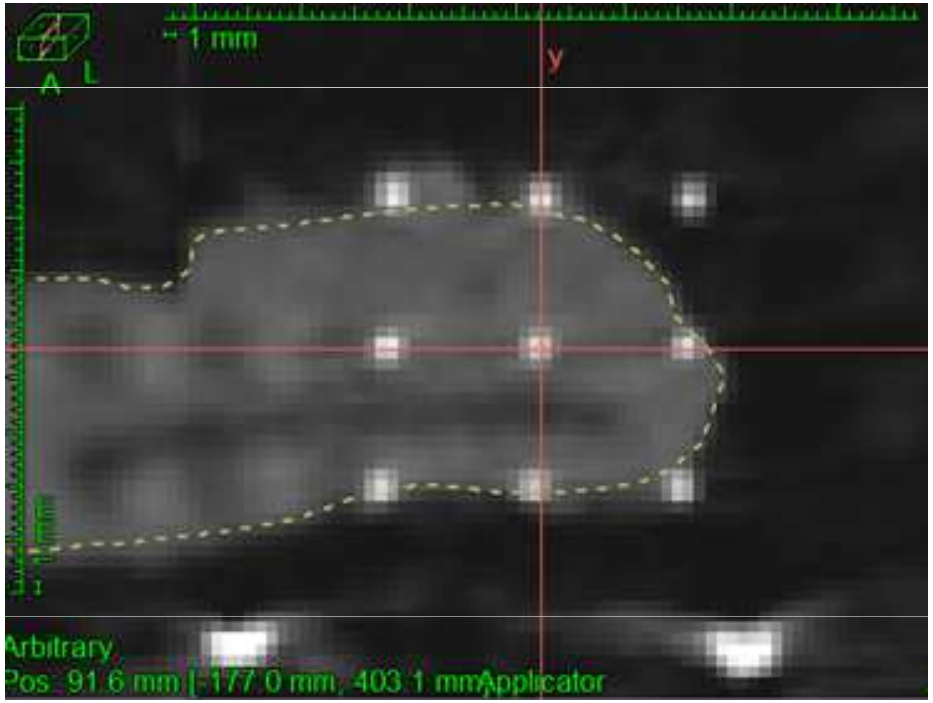
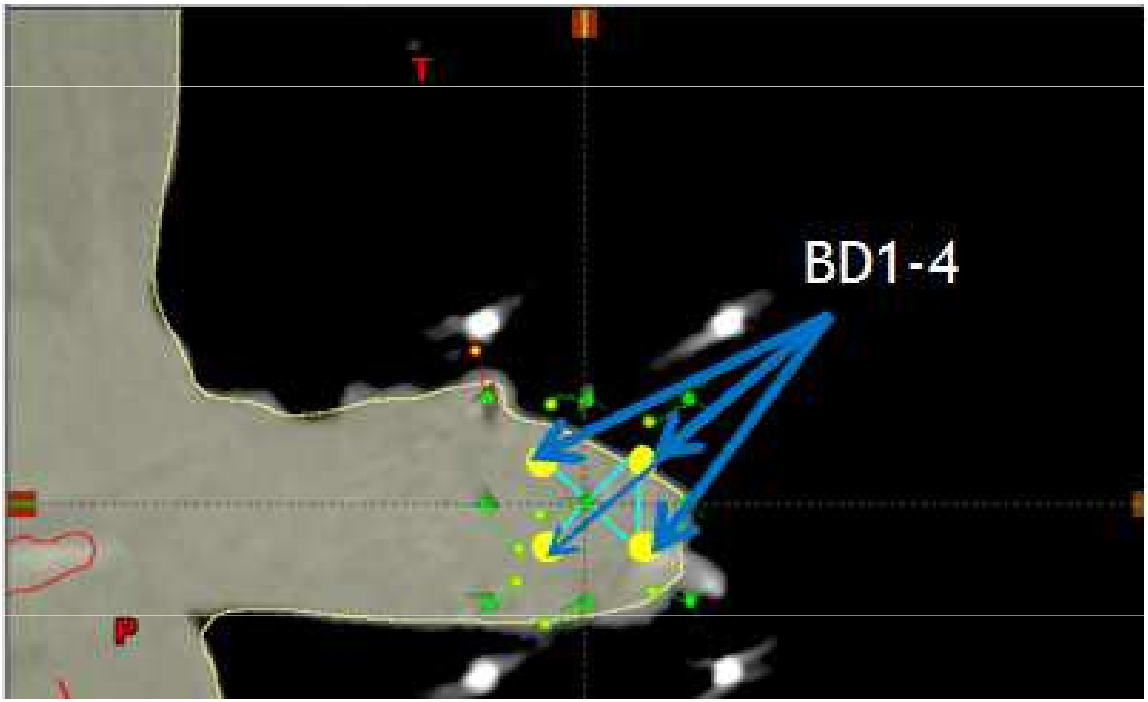
Multiple squares / triangles



a : triangles
b : squares

BD points definitions





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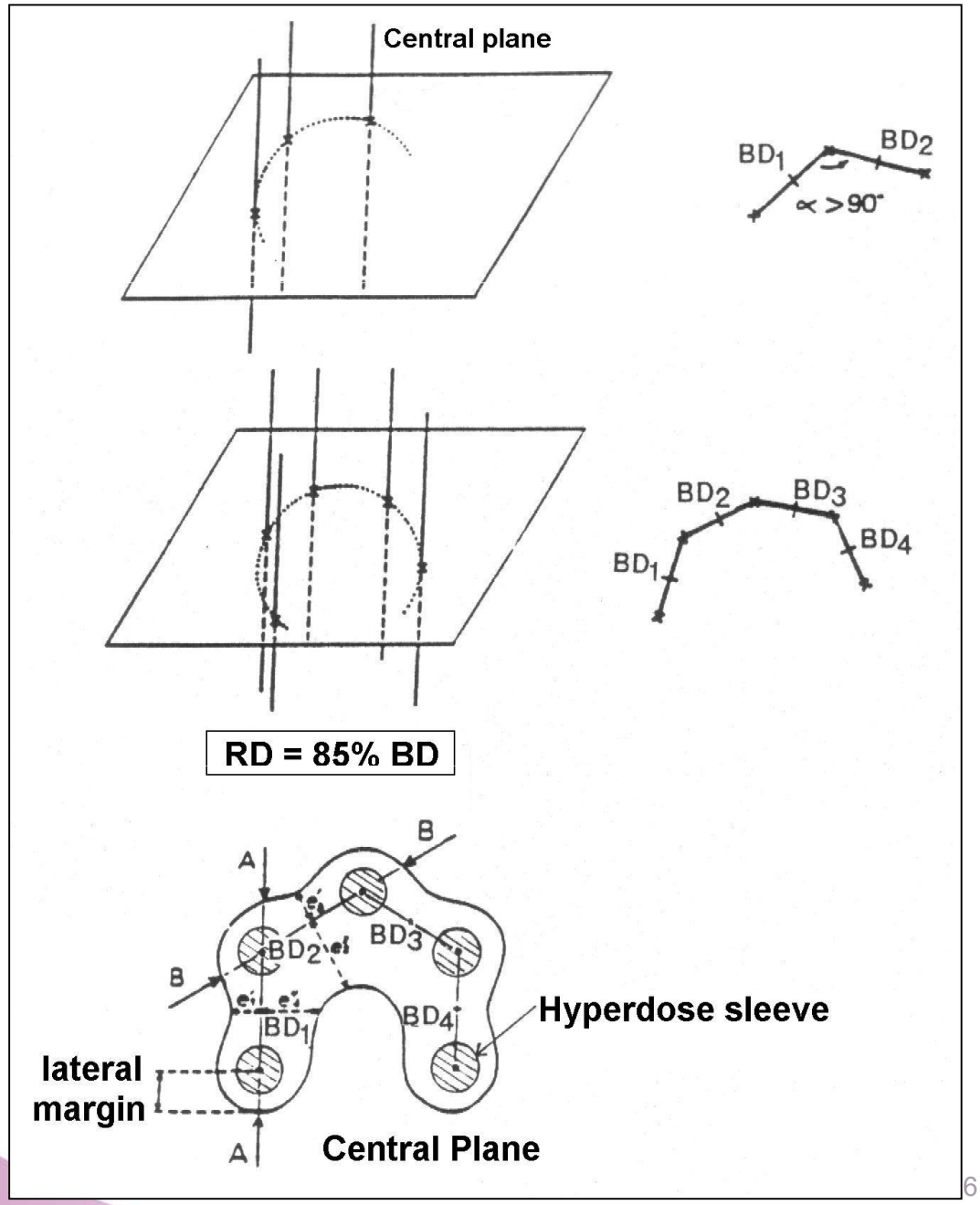
Basal/reference dose rate calculation



Example with curved plane line arrangement

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Paris system

Reference dose-rate : DR

DR = 0.85 x DB

Treatment volume = volume enclosed by the 85 % reference isodose

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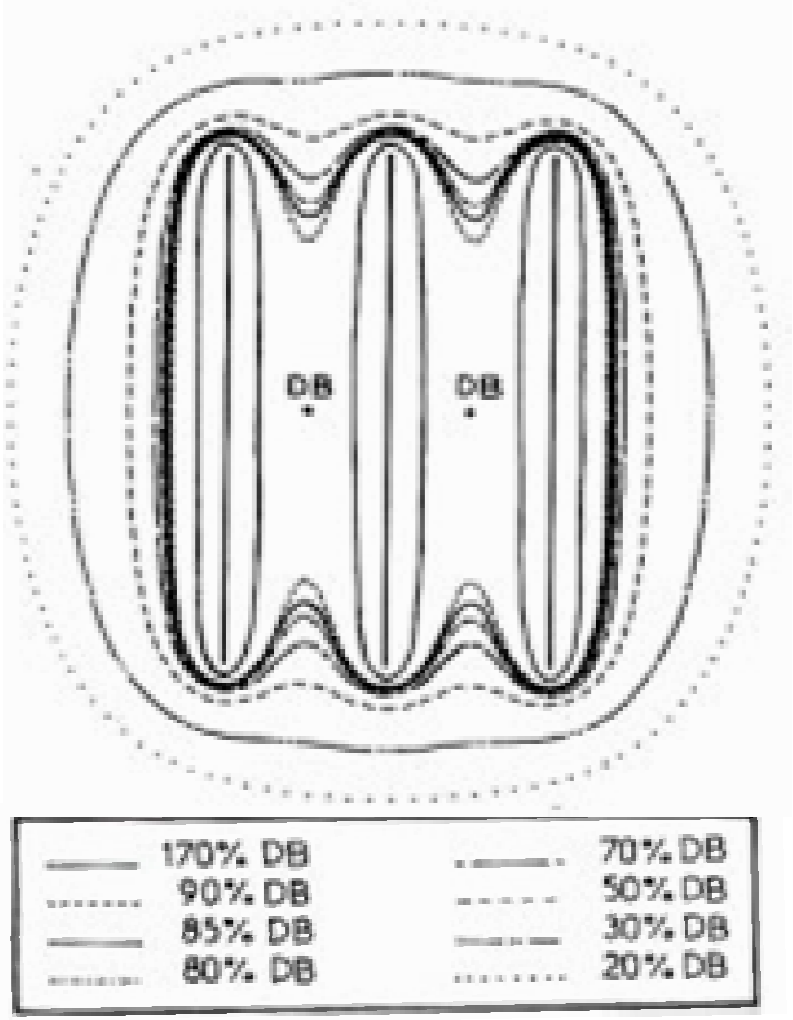
Why 85%?

$$\dot{D}_{REF} = 0{,}85 \times \dot{D}_{B}$$



- Based on clinical experience + compromise!
  - High isodose

➔ **Good homogeneity**

  - Low isodose

➔ **Shape / coverage**

➔ **Measurements on real cases**

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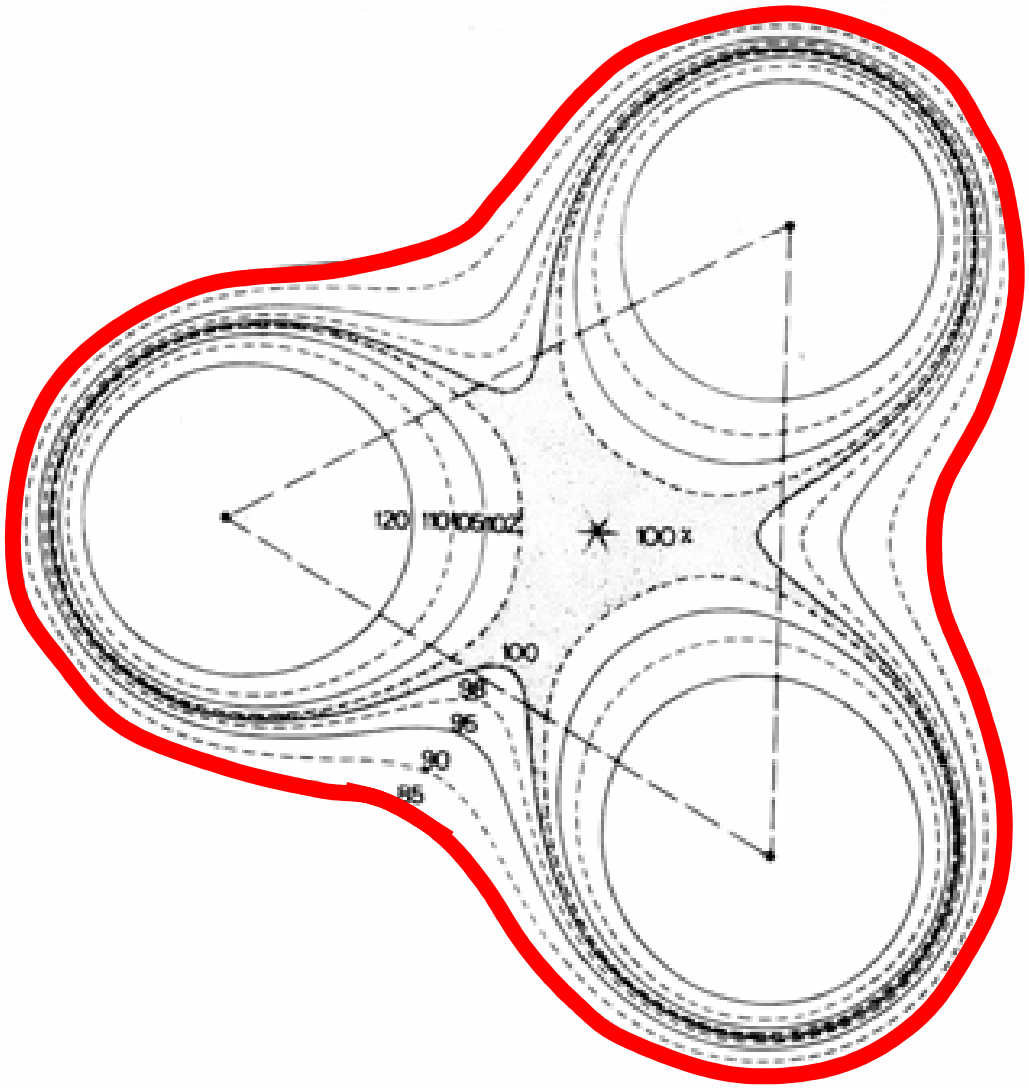
D_{Ref} = 0.85 x BD



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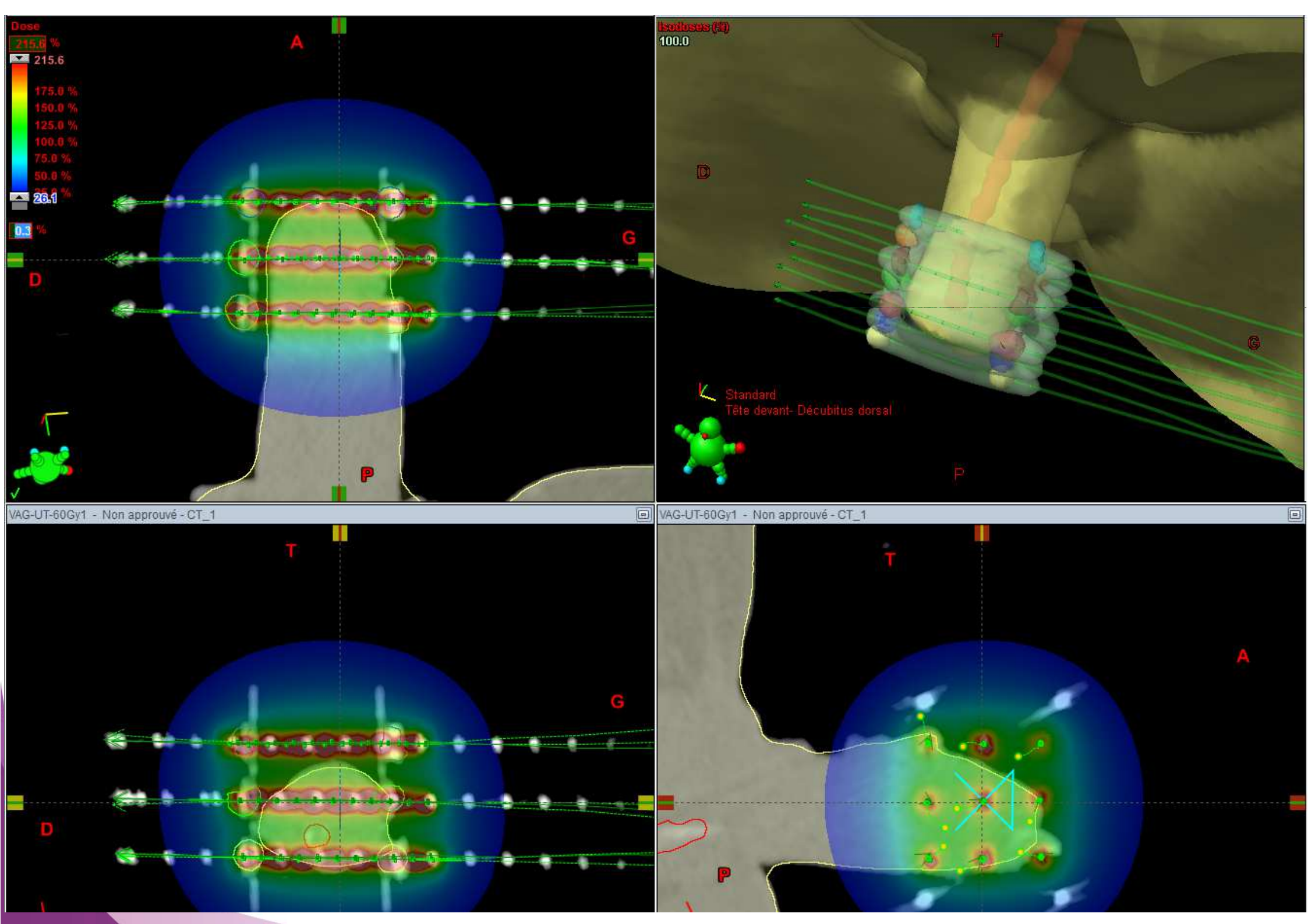

Dose
215.6 %
215.6
175.0 %
150.0 %
125.0 %
100.0 %
75.0 %
50.0 %
26.1
0.3 %
A
G
D
P
Isodoses (%)
100.0
T
D
G
Standard
Tête devant- Décubitus dorsal
P
VAG-UT-60Gy1 - Non approuvé - CT_1
T
G
D
VAG-UT-60Gy1 - Non approuvé - CT_1
T
A
P

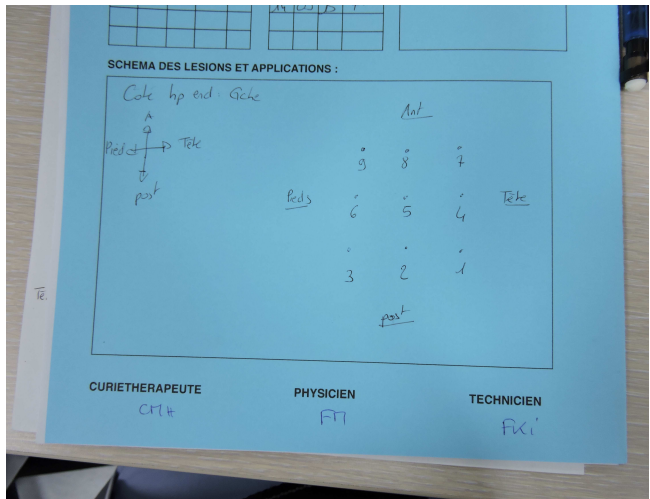
Steps after the implantation

- Imaging: CT / MRI / X-rays

- Source distribution determination in the central plane

  - catheter localization from Images
  - Slice through the central plane

- Basal dose-rate points definition
- Reference dose-rate calculation
- Total duration for the implant
- Radioactive decay correction (Iridium, LDR)



Example: 70 Gy (lip tumor)

- Reference dose rate = 0.52 Gy / hour
- 70 (Gy) / 0.52 (Gy /h) = 134.6 hours
- = 5.6 days (5 days and 14 hours and 24 minutes)

- Time adjustment: 3 hours
- Treatment time = 5 days 18 hours
- decay = 1.5 – 2 Gy….

Table 2.12: Time adjustment (Δt) for the total irradiation time (t) of iridium-192 LDR implants.

Treatment time t (days)	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
Δt (hours)	1	2	3	4	5.5	7	9	12	15

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Is optimization required?

- Strict following of the rules
  - Good coverage of the target
  - Homogeneity
  - Conformity to LDR experience

- Optimizing
  - Contra balance geometrical limits
    - Anatomical constraints (parallelism)
    - Material : plastic tubes (divergence / convergence)
    - Skills (operator)
    - impossibility of using templates
  - Adaptive BT
    - Planning aims
    - Boosts (GTV/CTV)

Always start with a good implant!

And then

IMPROVE IT

with optimization!!!

Don’t optimize to correct a bad implant!

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Paris system

An implant is considered

acceptable when :

$$BD - 10\% < BD\ i < BD + 10\%$$

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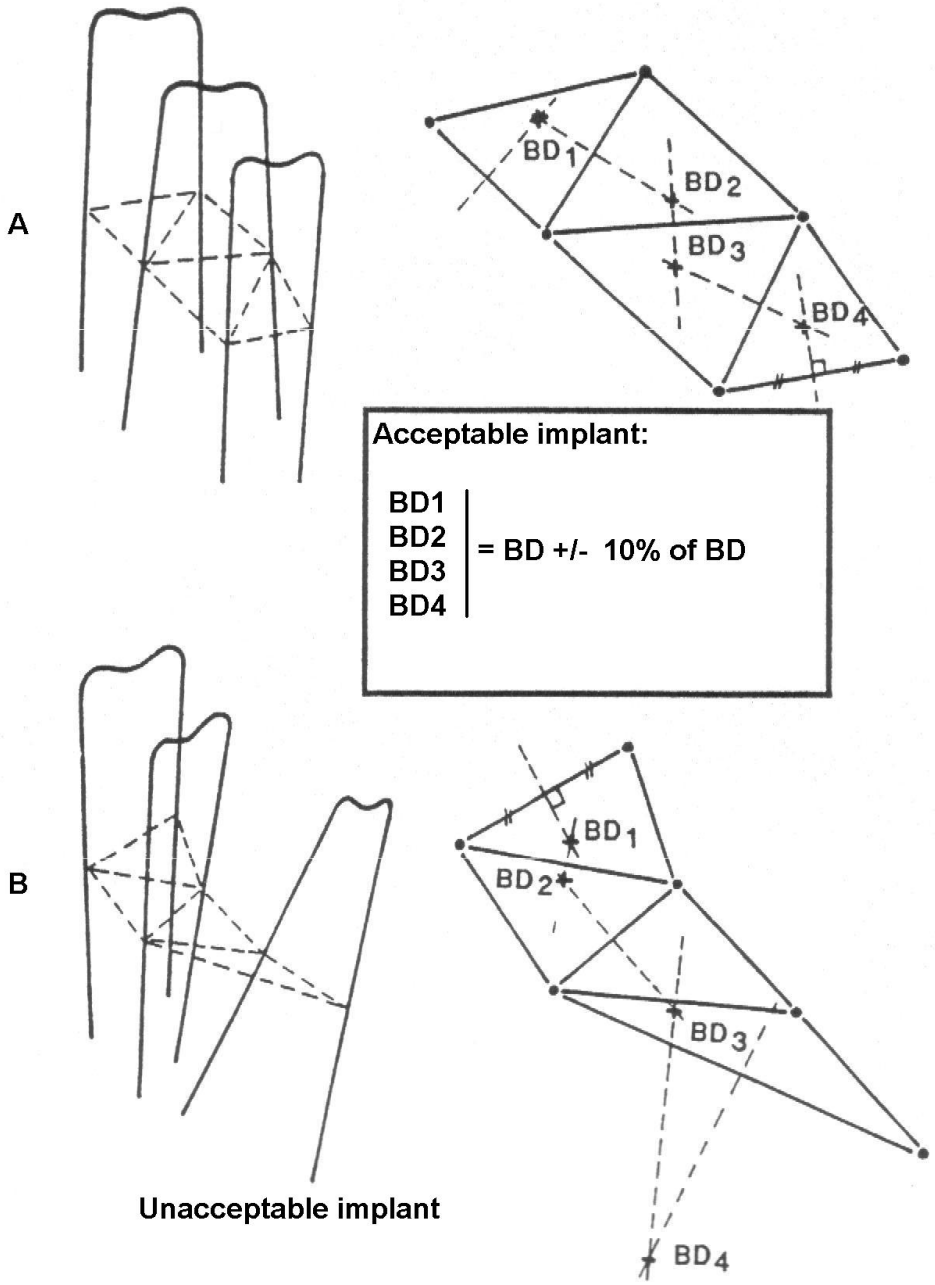
Basal dose rate calculation



implants with imperfect geometry

Acceptable if
0.9 BD<BDi<1.10 BD

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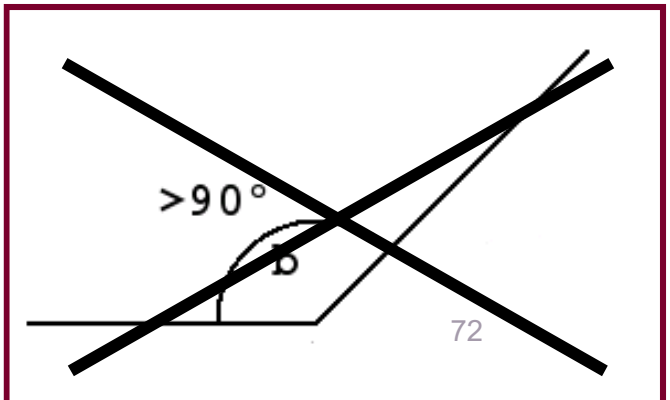
Paris system

In a **perfect** implantation, triangles should be **equilateral**

Applications might be considered as **unacceptable** when triangles have an **obtuse angle**

inevitable **underdosage** of the area of the longest triangle side

Hyperdosage along the catheters to compensate



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ICRU Report 58 (1997)

« Dose and volume specification for

reporting interstitial therapy »

- A. DUTREIX, D. CHASSAGNE
- D. ASH, W.F. HANSON
- A.G. VISSER, J.F. WILSON
- A. WAMBERSIE

ICRU Report 58

AIM was

- to develop a *common language*
- to provide a method of *dose and volume specification and reporting* which can be used for implants of all types and common to interstitial therapy performers
- description of what has been performed, possible intercomparison

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ICRU report 58

Recommended parameters for reporting are closely related to the Paris system : reported doses defined in the central plane

Basal dose = Mean Central Dose

Reference dose = Minimum Target Dose

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Characteristics of brachytherapy doses for the LDR/HDR - boost treatment

Long-term results (10 years) of intensive breast conserving therapy including a high-dose and large-volume interstitial brachytherapy boost (LDR/HDR) for T1/T2 breast cancer

Alexandra Resch[a,*], Richard Pötter[a], Erik Van Limbergen[b], Eva Biber[a], Tanja Klein[a], Claudia Fellner[a], Leonore Handl-Zeller[a], Gudrun Langbauer[a], Helmut Schürer-Waldheim[c], Alfred Staffen[c], Raimund Jakesz[c], Ernst Kubista[d], Stephan Lehr[e], Wolfgang Seitz[a]

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[c]*Department of Surgery, Vienna University, Medical School, General Hospital of Vienna, Vienna, Austria*
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Received 26 July 2001; received in revised form 27 January 2002; accepted 14 February 2002

Radiother Oncol 63:47-58;2002

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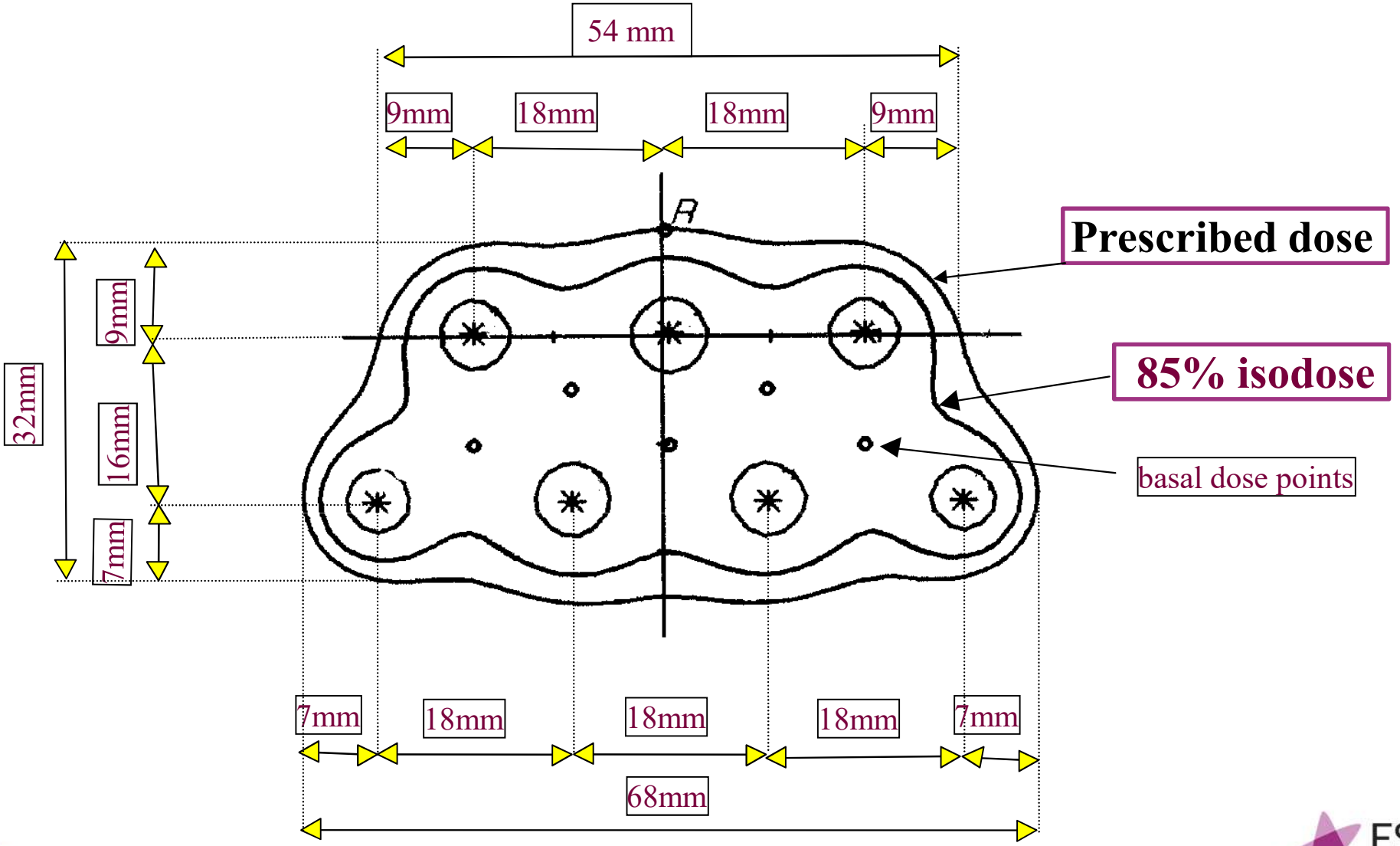
Interstitial breast brachytherapy central plane dose recording*- implant with 7 needles -



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Characteristics of brachytherapy doses for the LDR - boost treatment : 410 patients

doses in Gy	mean ± s	range
„prescribed dose" rate / hour	0,7 ± 0,2	0,3 - 1,1
„total prescribed dose"	**19,9 ± 4,9**	9,9 - 27,0
mean central dose / hour	1,0 ± 0,3	0,4 - 1,5
total mean central dose	27,9 ± 7,1	12,6 - 39,4
85% of mean central dose		
dose rate per hour	0,9 ± 0,3	0,3 - 1,3
total 85 % of mean central dose	**23,7 ± 6,0**	10,7 - 33,5

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Paris system conclusion

Implant type	Treated length / radioactive length	Treated thickness/spacing	Lateral margin / spacing	Safety margin / spacing
2 lines	0.8	0.5	0.37	-
n lines in one plane	0.8	0.6	0.33	-
n lines in «square»	0.8	1.55 - 1.60	-	0.27
n lines in triangle	0.8	1.3	-	0.20

Paris system

- Relationships confirmed for stepping sources
- Treated length / active length = 0.8
- The Paris system is:
  - Old (B. Pierquin, ‘60)
  - Simple
  - Robust
  - Ingenious
  - Provisional
  - Safe
  - ou dated
  - Only val fo Ir-192 wires

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Image Guided Brachytherapy

Bradley Pieters

Academic Medical Center / University of Amsterdam

Image Guided Brachytherapy

Imaging in Brachytherapy: General Introduction
Image Guided Determination Target and Organs at Risk
Image Guided Evaluation of Target and OAR
Image Guided Application
Uncertainties when using BT Imaging
Clinical Relevance: Prostate, Gynaecology
New Developments

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Imaging in Brachytherapy

clinical examination remains important (!)

IMAGE ASSISTED PROVISIONAL TREATMENT PLANNING

(treatment simulation and provisional dose calculation)
conventional radiography (CR);
sectional imaging: MRI, CT, US, (PET)
light imaging: endoscopy (ES)

IMAGE GUIDED APPLICATION

CR, MRI, CT, US, ES (with or without on-line treatment planning)

IMAGE ASSISTED DEFINITIVE TREATMENT PLANNING ("guided")

Imaging after application for definitive treatment planning
(CR, US, CT, MRI, PET)

IMAGE ASSISTED QUALITY CONTROL OF DOSE DELIVERY

Imaging for quality control during or after brachytherapy
(CR, CT, MRI)

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Imaging in brachytherapy

„Treatment machine“

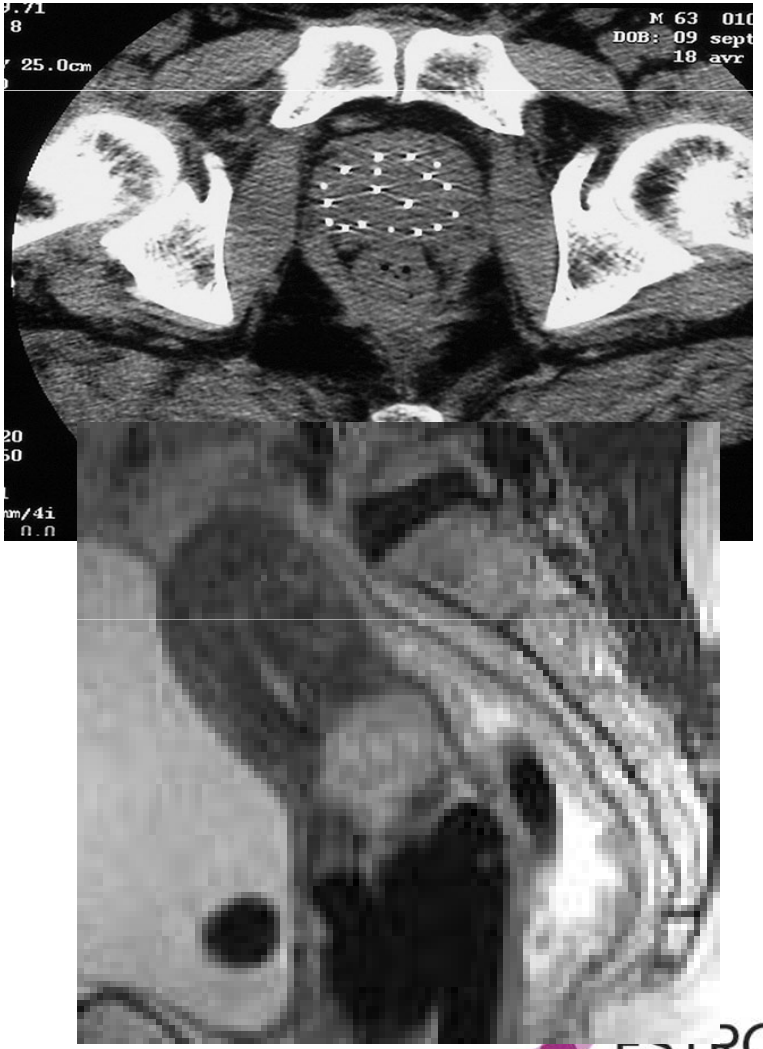
Applicator/sources

plus GTV, CTV….

plus Organs at Risk

Imaged at the same time

Depicted on the same image



Applicator Impact on Imaging in brachytherapy (I)

on adjacent topography

GTV, CTV and OAR

dilatation (endoluminal BT)
oedema (interstitial BT, time factor)
cervix/vaginal topography (intracavitary BT)

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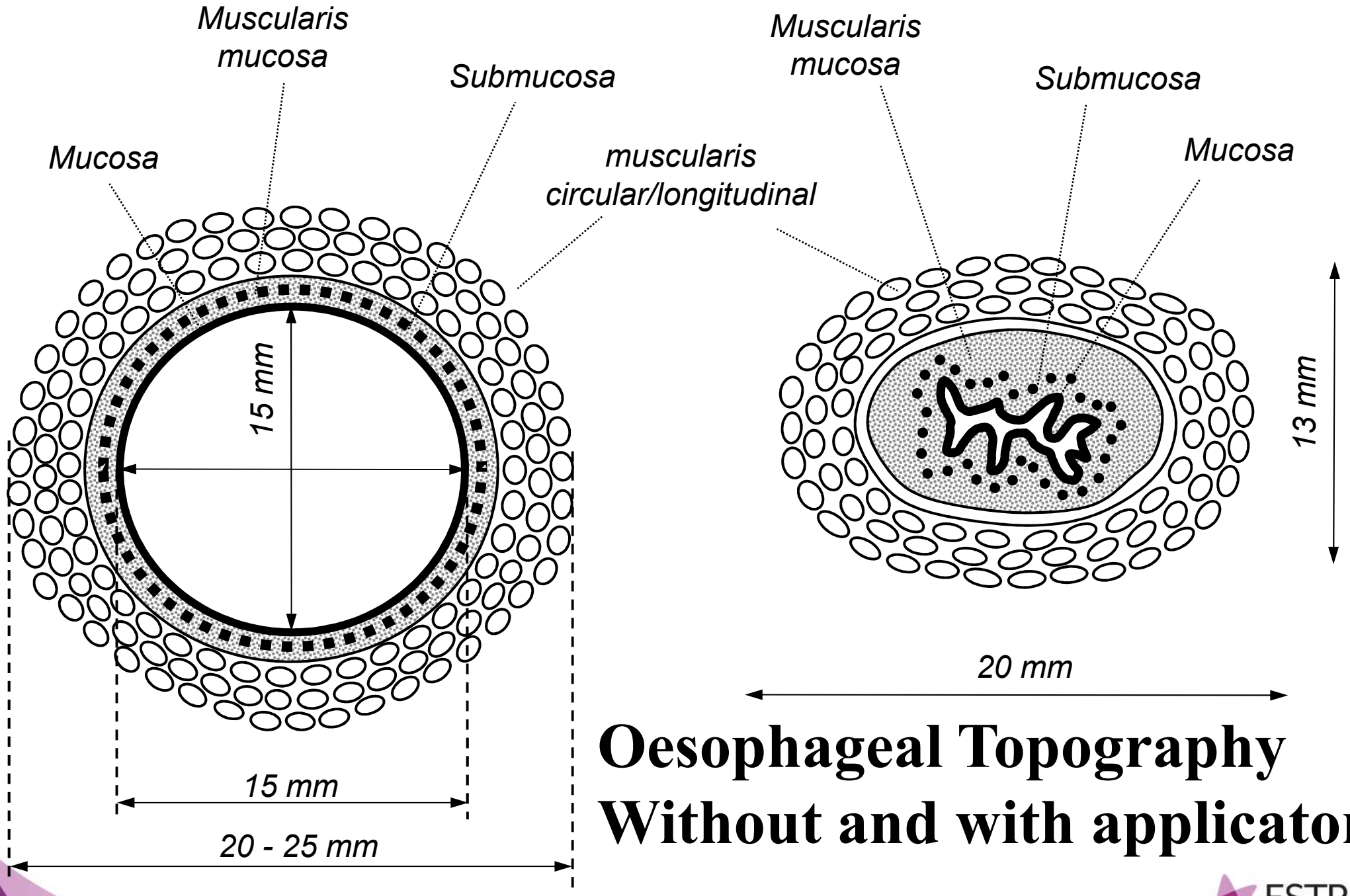

Oesophageal Topography Without and with applicator

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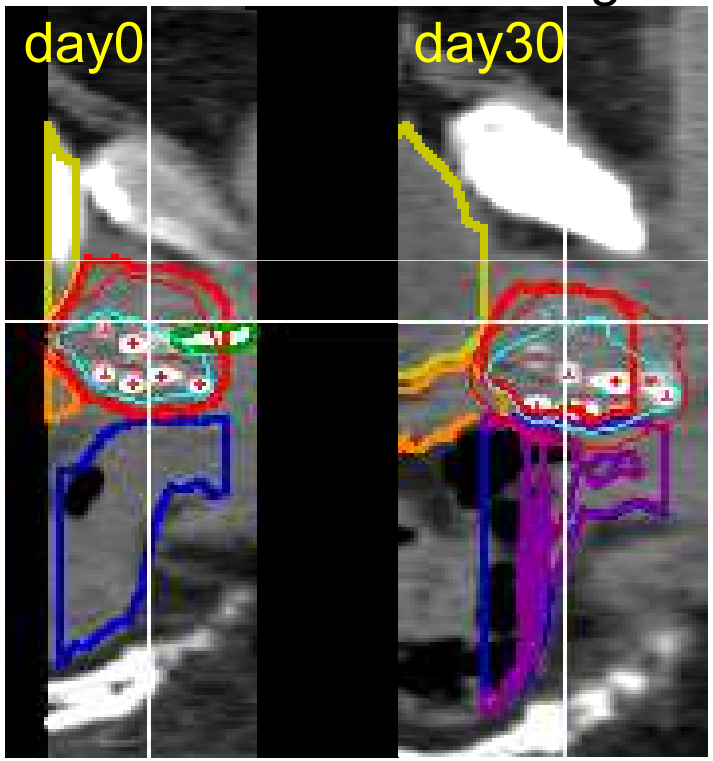
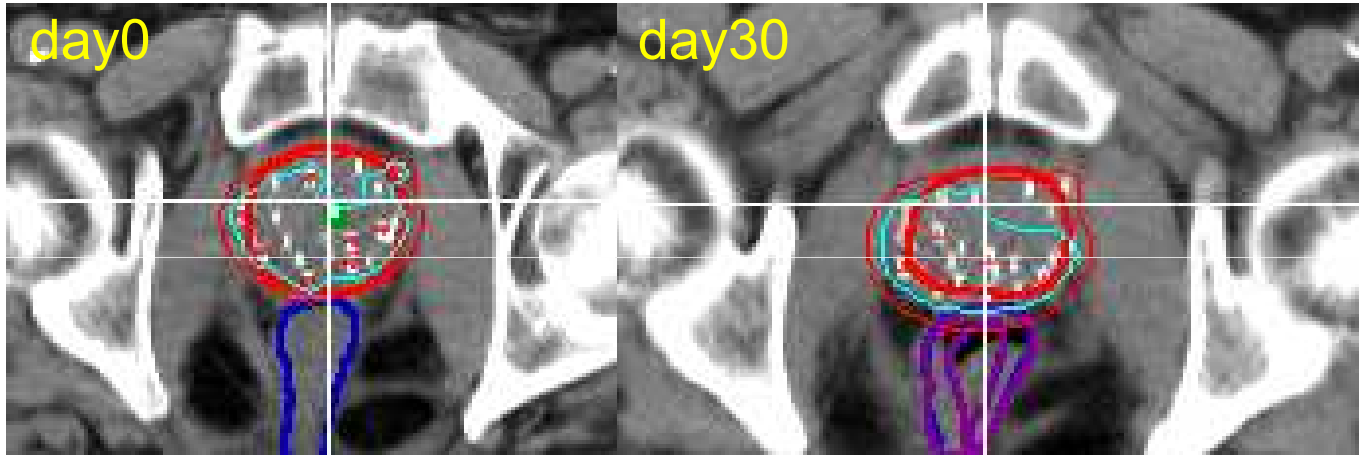
Decongest prostate edema: decreasing the volume

sagittal

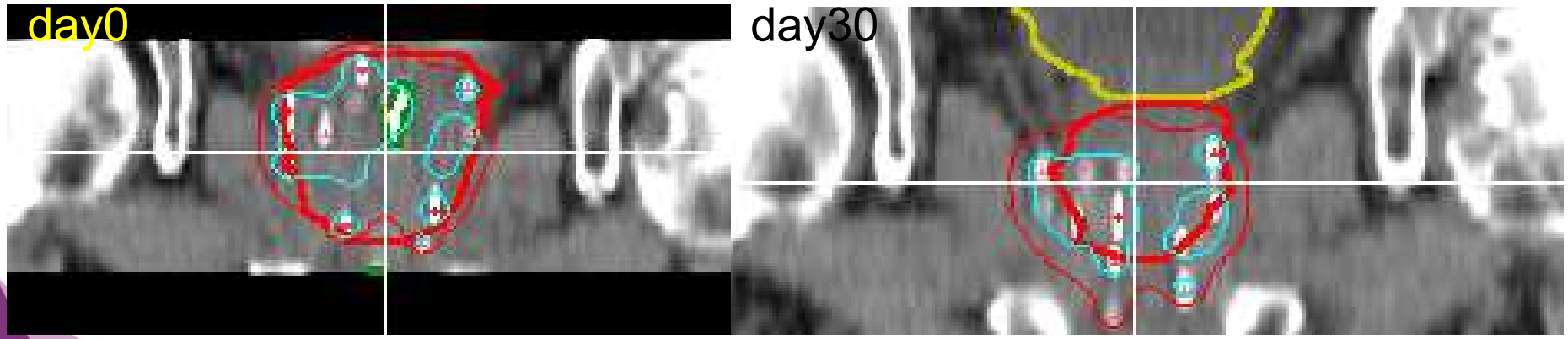


transverse



	Volume ↓	**D90 ↑**	**V100↑**
Day 0:	70cm^3	137Gy	87%
Day30:	39cm^3	197Gy	99%

coronal



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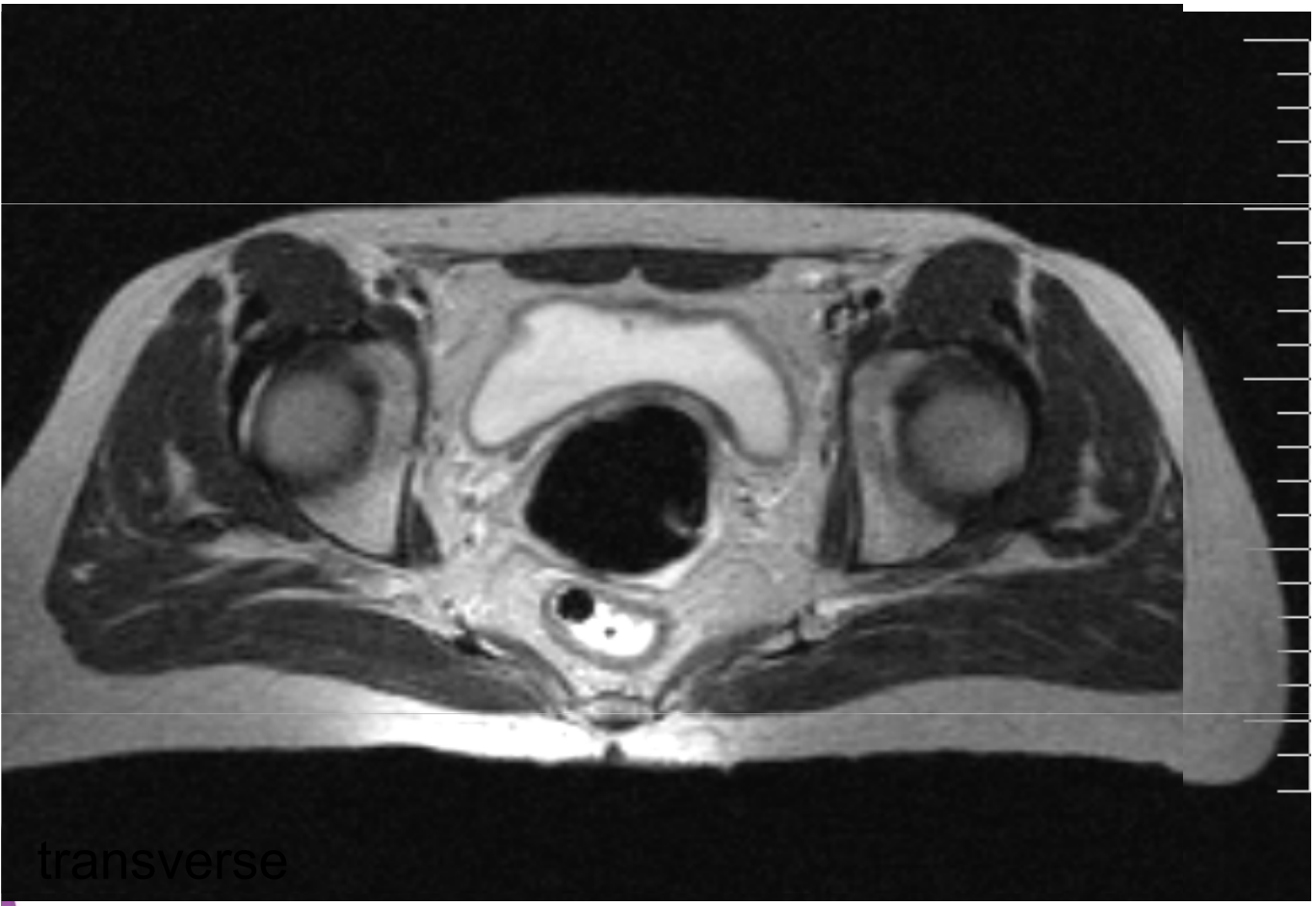
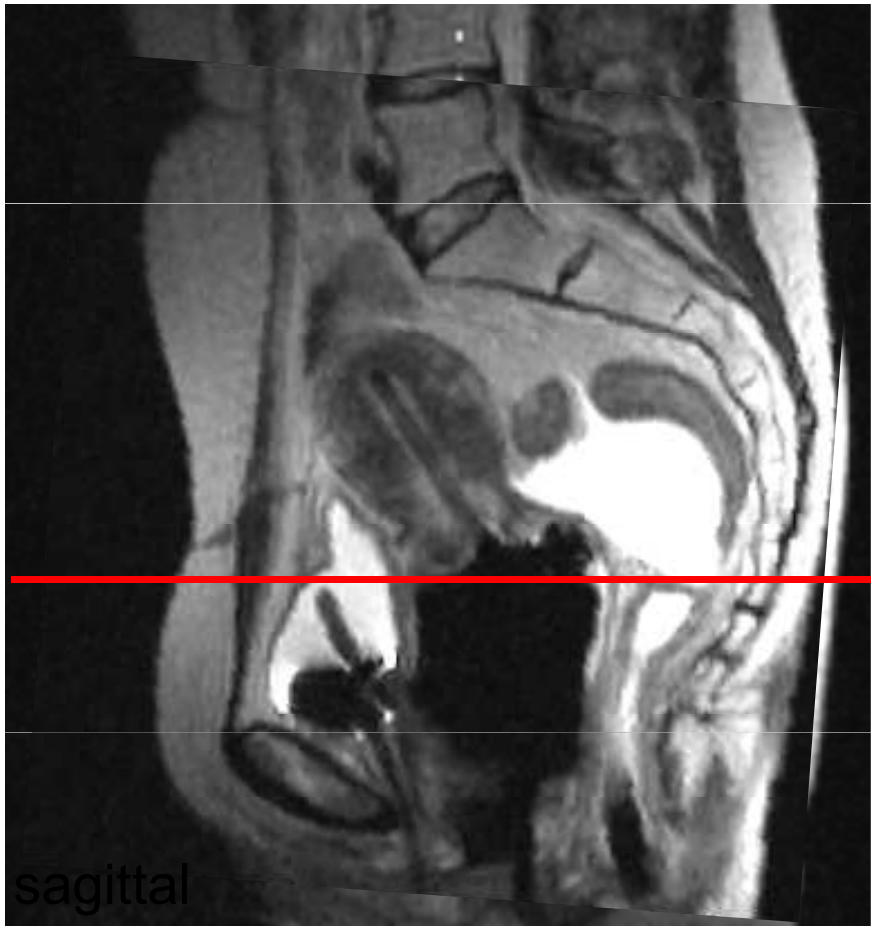
Impact of insertion of a Tandem-Ring Applicator on topography

before brachytherapy





without/with applicator

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Applicator Impact on Imaging in brachytherapy (II)

Interdependence between

Applicator and Imaging System:

X-ray, CT, MRI, US, ...

feasibility of imaging (e.g. metallic tubes)

visibility (dependent on image system)

validity

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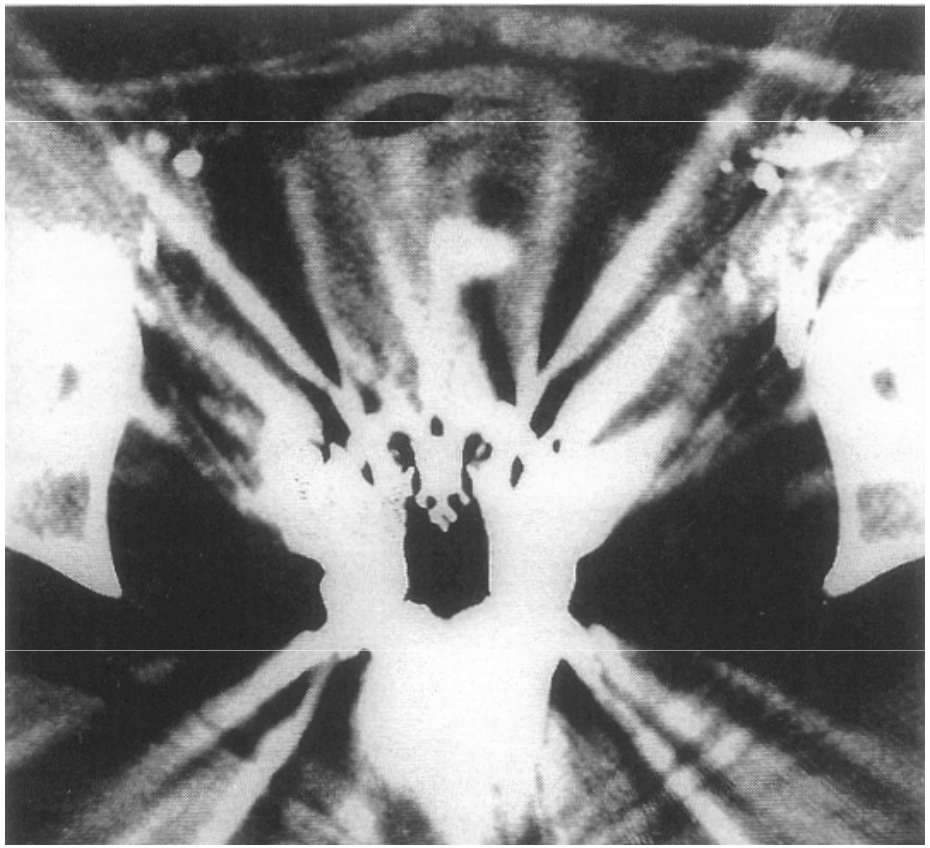
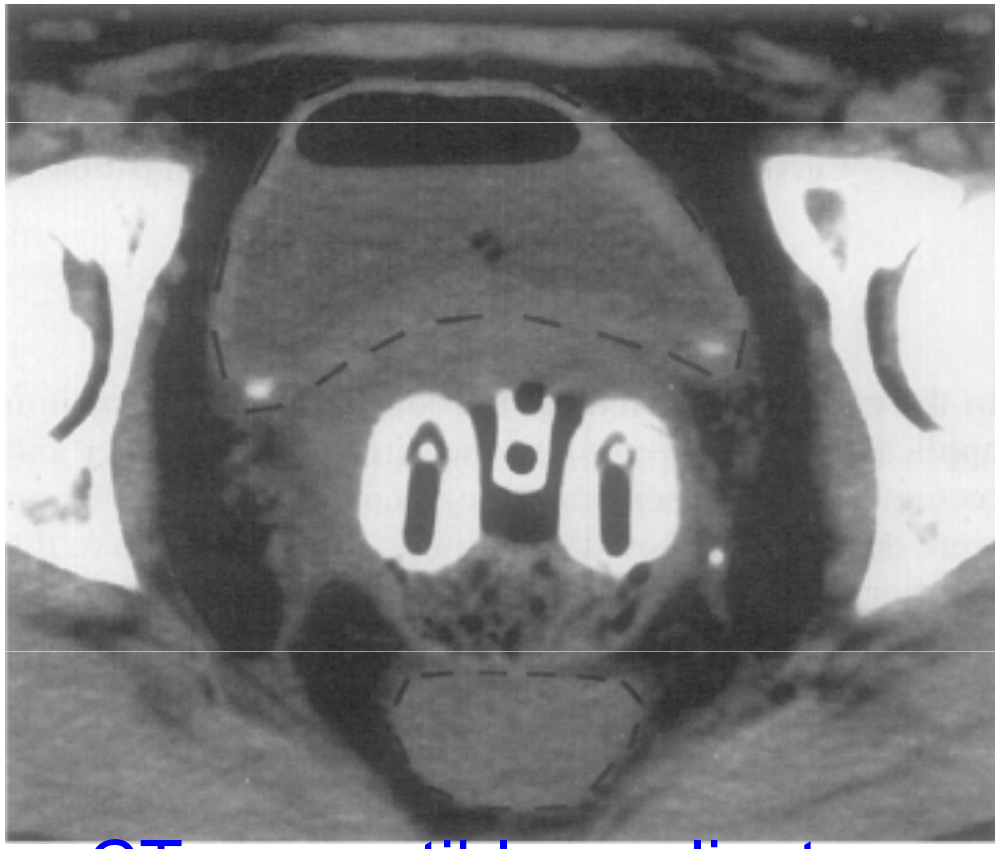
Computed tomography
Applicator depiction



Metallic Applicator Artefacts



CT-compatible applicator
optimal depiction quality

Steggerda et al. J. Brachytherapy Int. 1998

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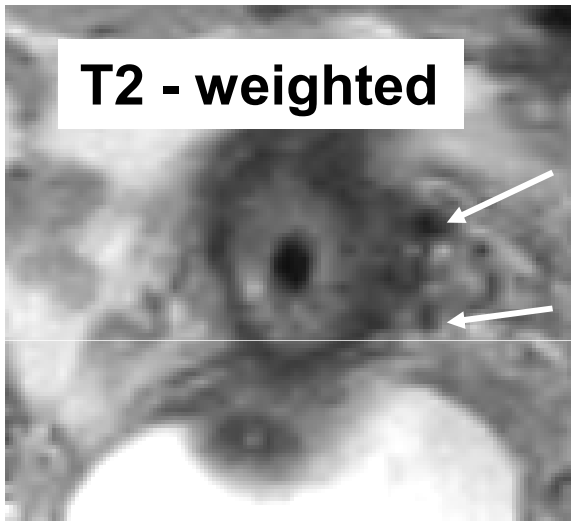
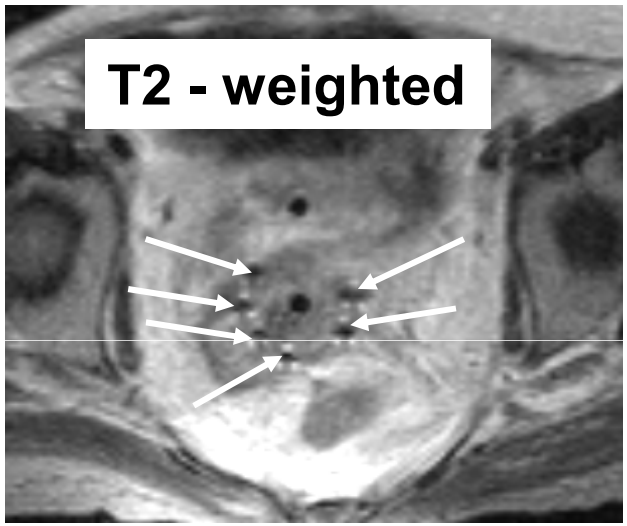
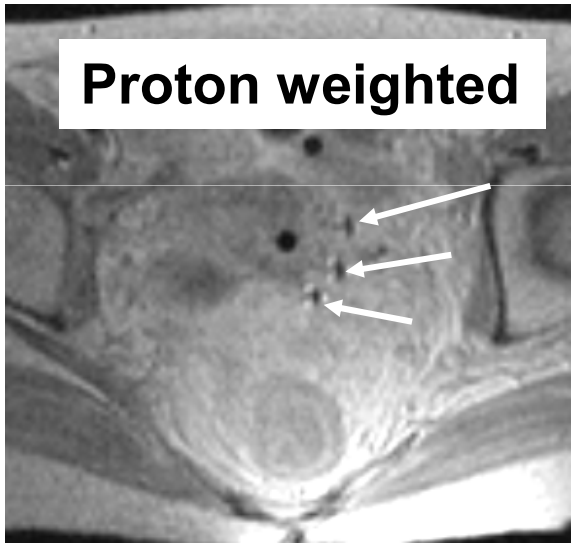
Needle Depiction

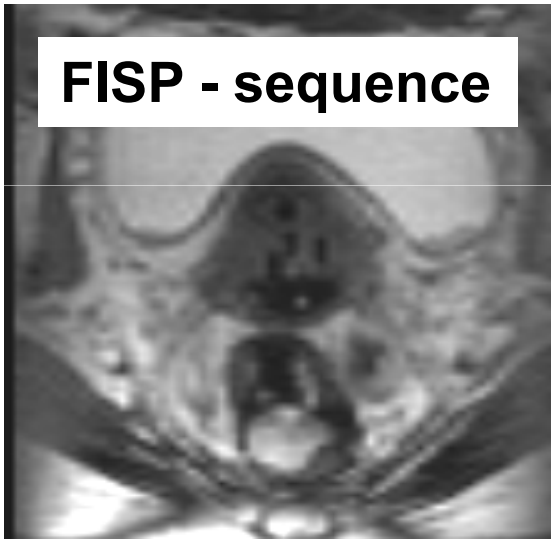


poor quality



excellent depiction





improvement for needles / loss of soft tissue depiction quality

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Imaging in brachytherapy

Orientation of imaging

aim: „systematic“ relation (according to „axes“)

source position(s) and adjacent anatomy

„Brachytherapy Eye View“ („BEV“)

Allowing for

Precise and reproducible source allocation

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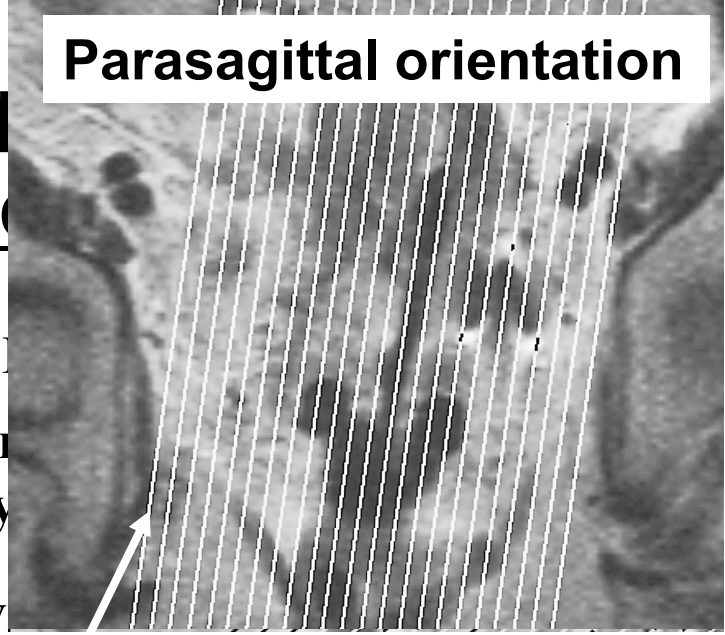
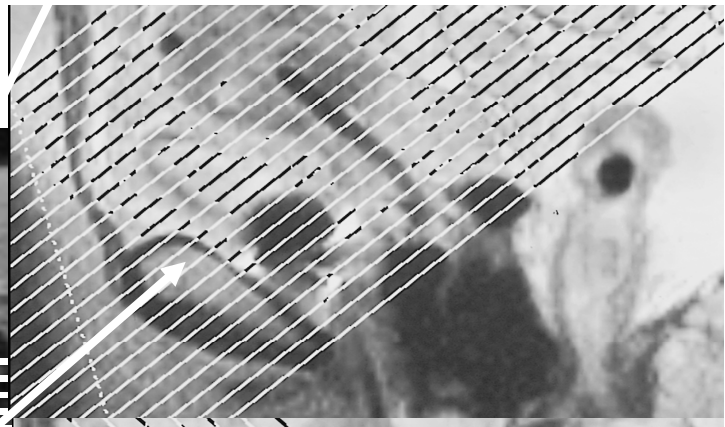
3D-MRI assisted image acq
Multiplanar capability-specifi

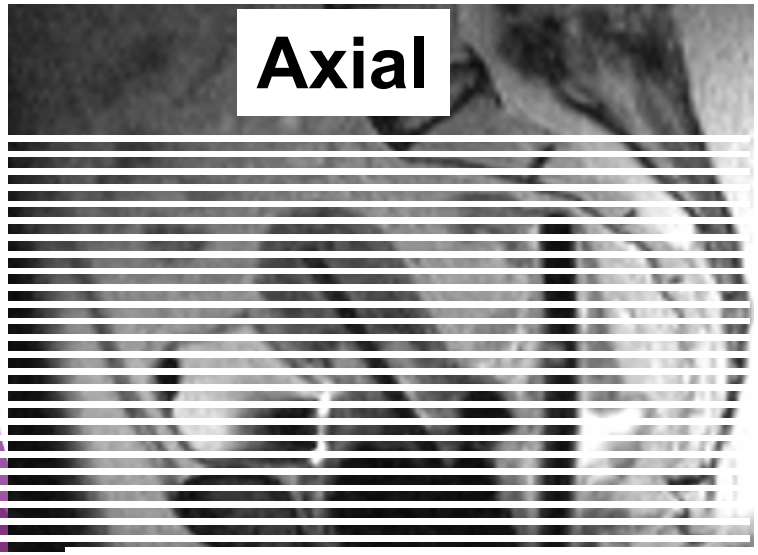
PLANE	COVERAGE-BO
T2 axial	discus L5
T2 sagittal	pelvic wall (obturator muscle)
T2 frontal or frontal oblique	entire uterus - cervix - vagina - tumor

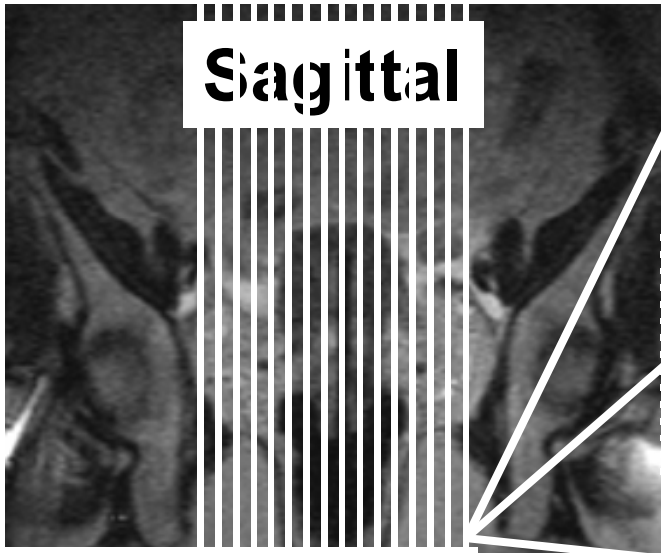
infer
of sy
pelv



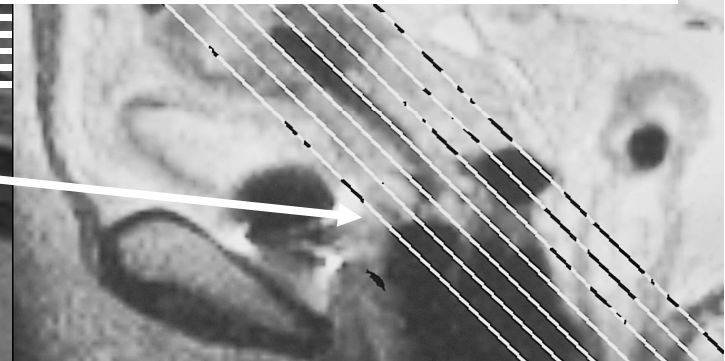
Paratransverse orientation



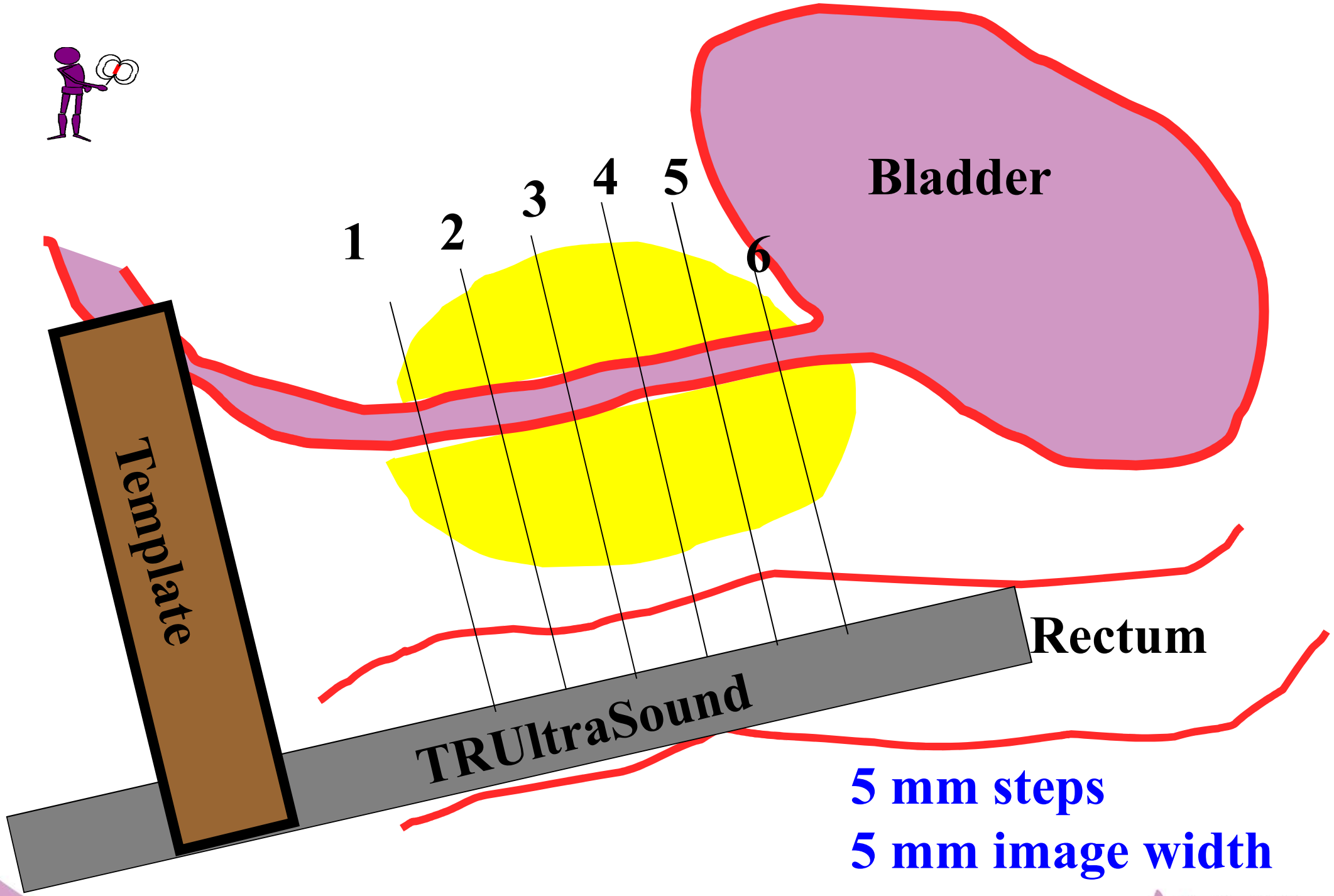




Paracoronal orientation



Slice orientation parallel/orthogonal to applicator axis


Bladder
1
2
3
4
5
6
Template
TRUltraSound
Rectum
5 mm steps
5 mm image width

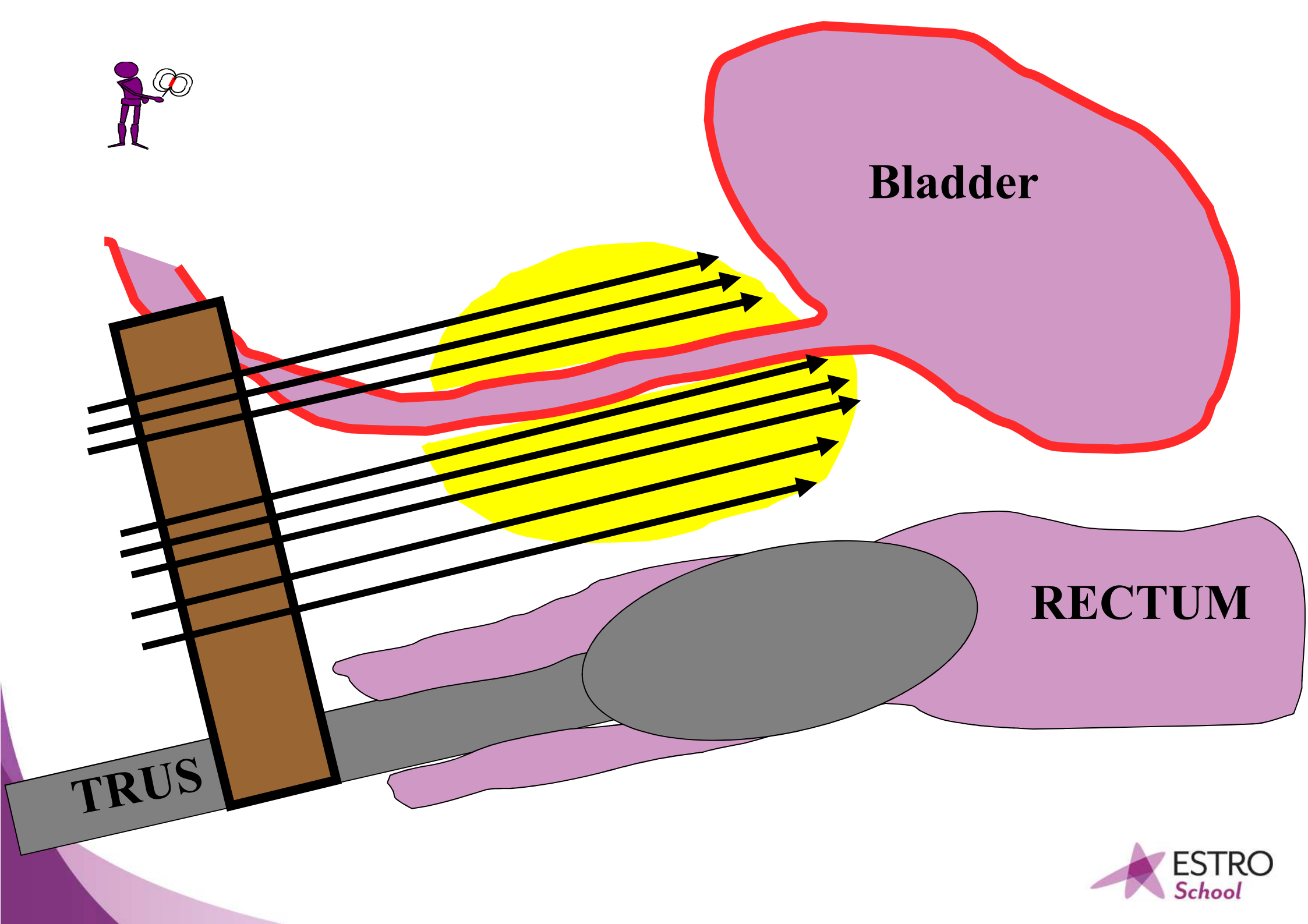
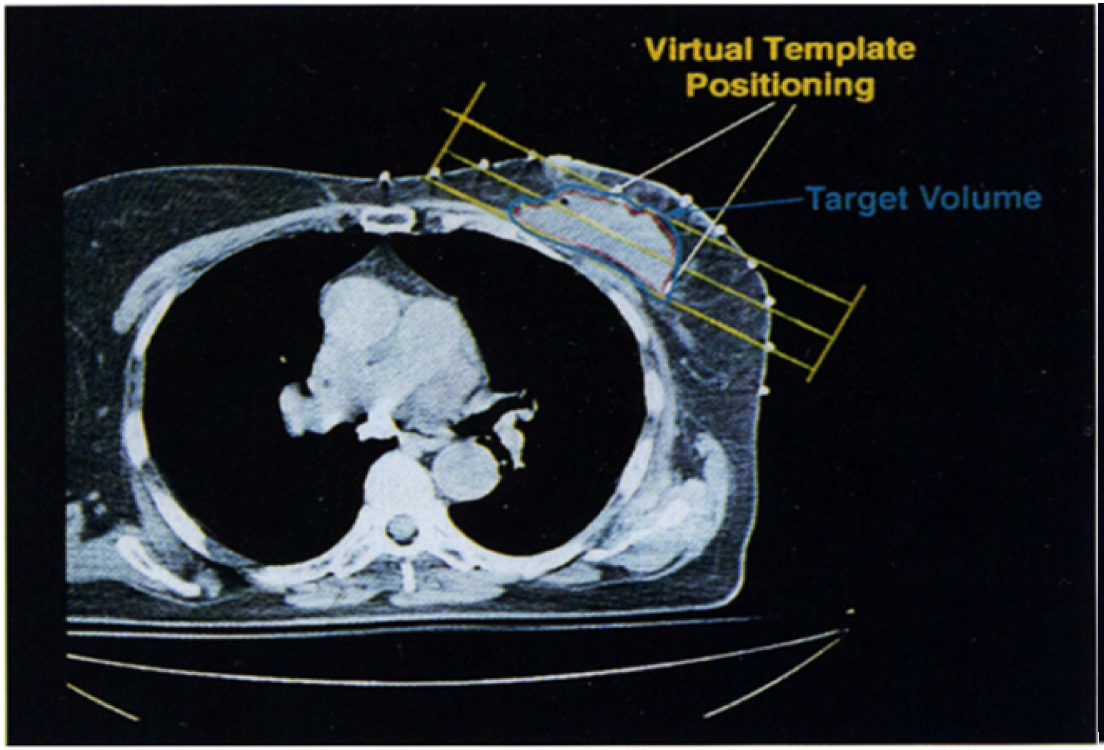
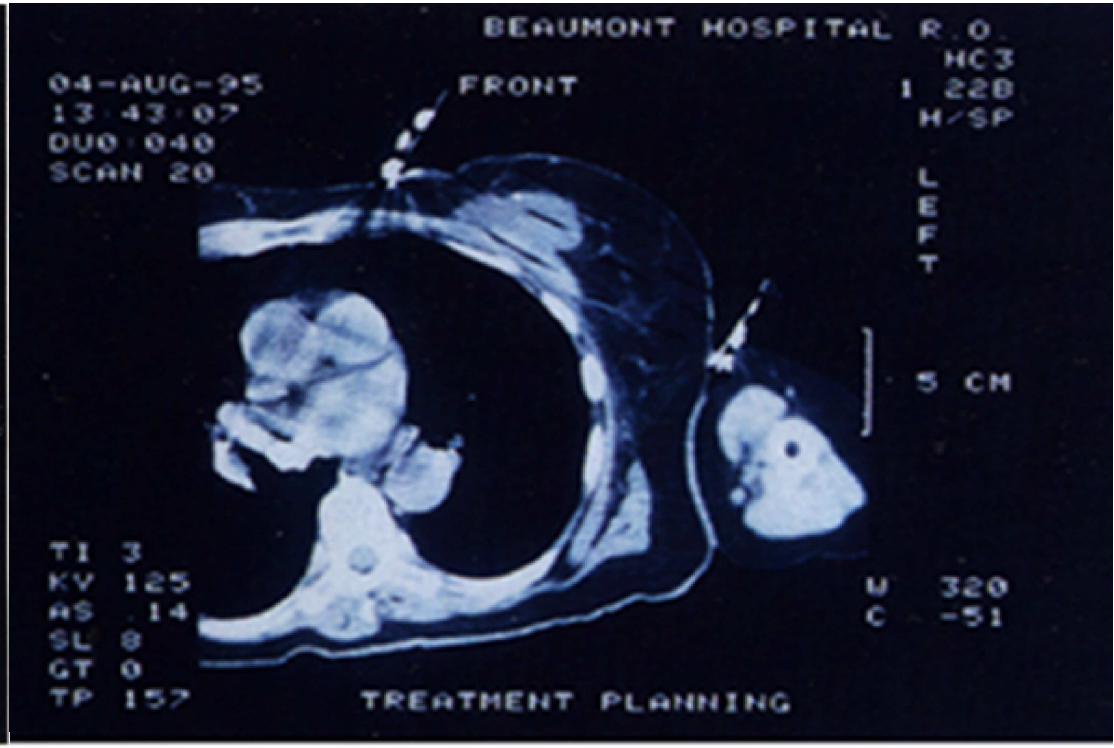

Bladder
RECTUM
TRUS

Image Guidance





F.A. Vicini. Int J Radiat Oncol Biol Phys, 1998;40:629-635

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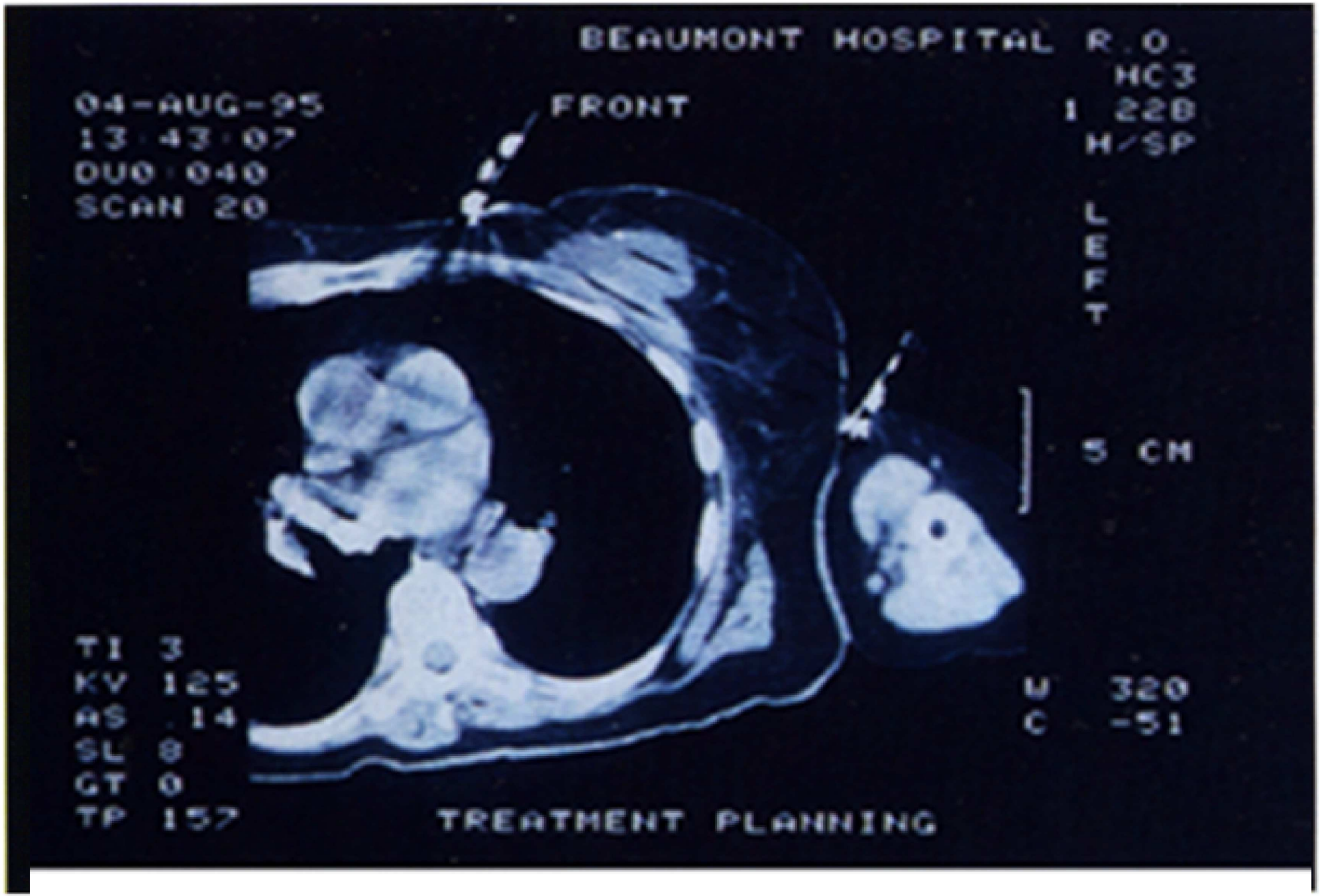
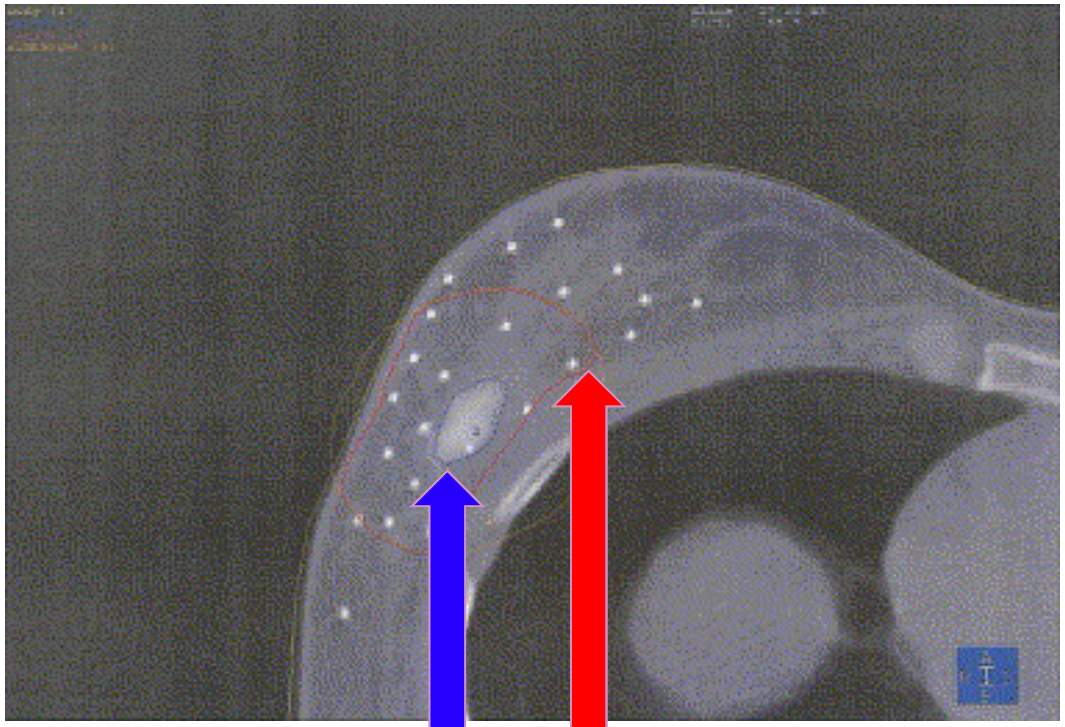
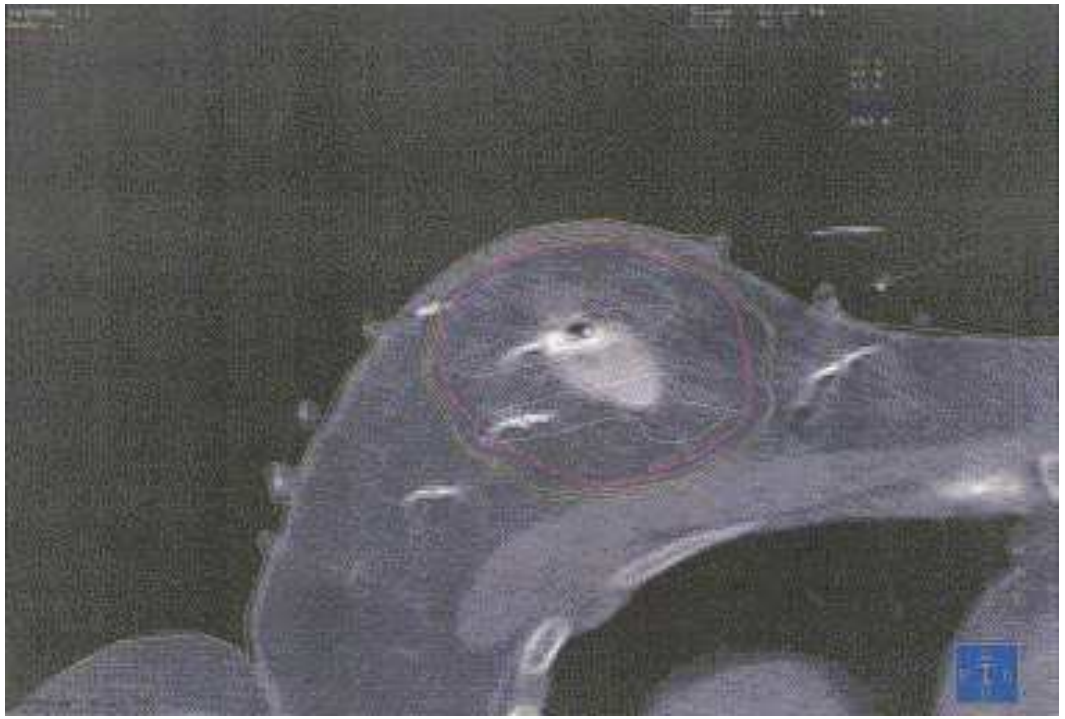

BEAUMONT HOSPITAL R.O.
HC3
1 22B
H/SP
04-AUG-95
13:43:07
DUO:040
SCAN 20
FRONT
LEFT
5 CM
TI 3
KV 125
AS 14
SL 8
GT 0
TP 157
W 320
C -51
TREATMENT PLANNING





Lumpectomy cavity

CTV

R.K. Das Int J Radiat Oncol Biol Phys, 2004;59:1224-1229

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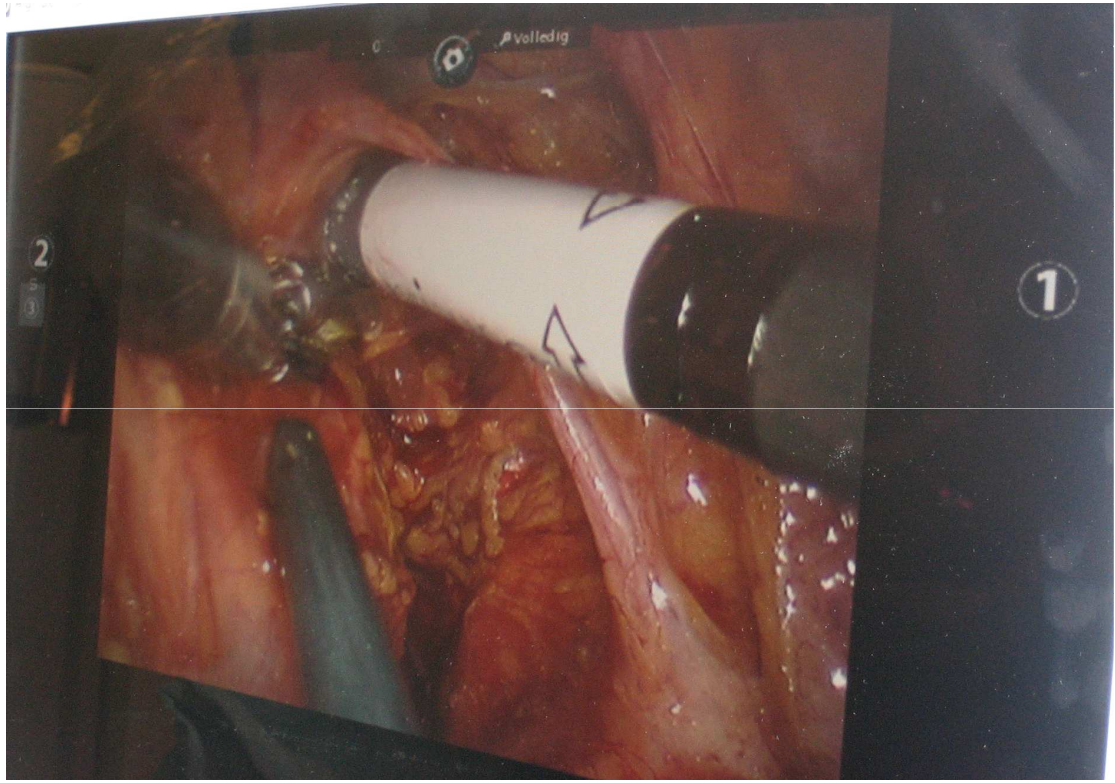
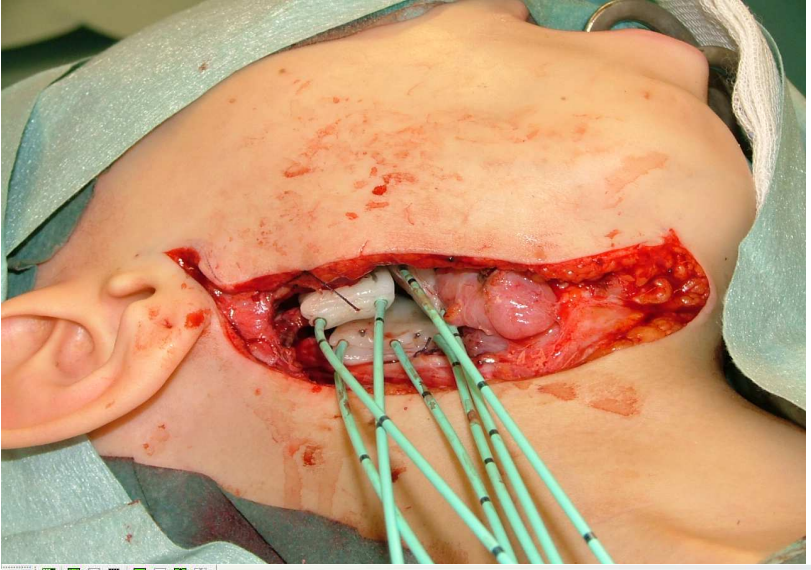
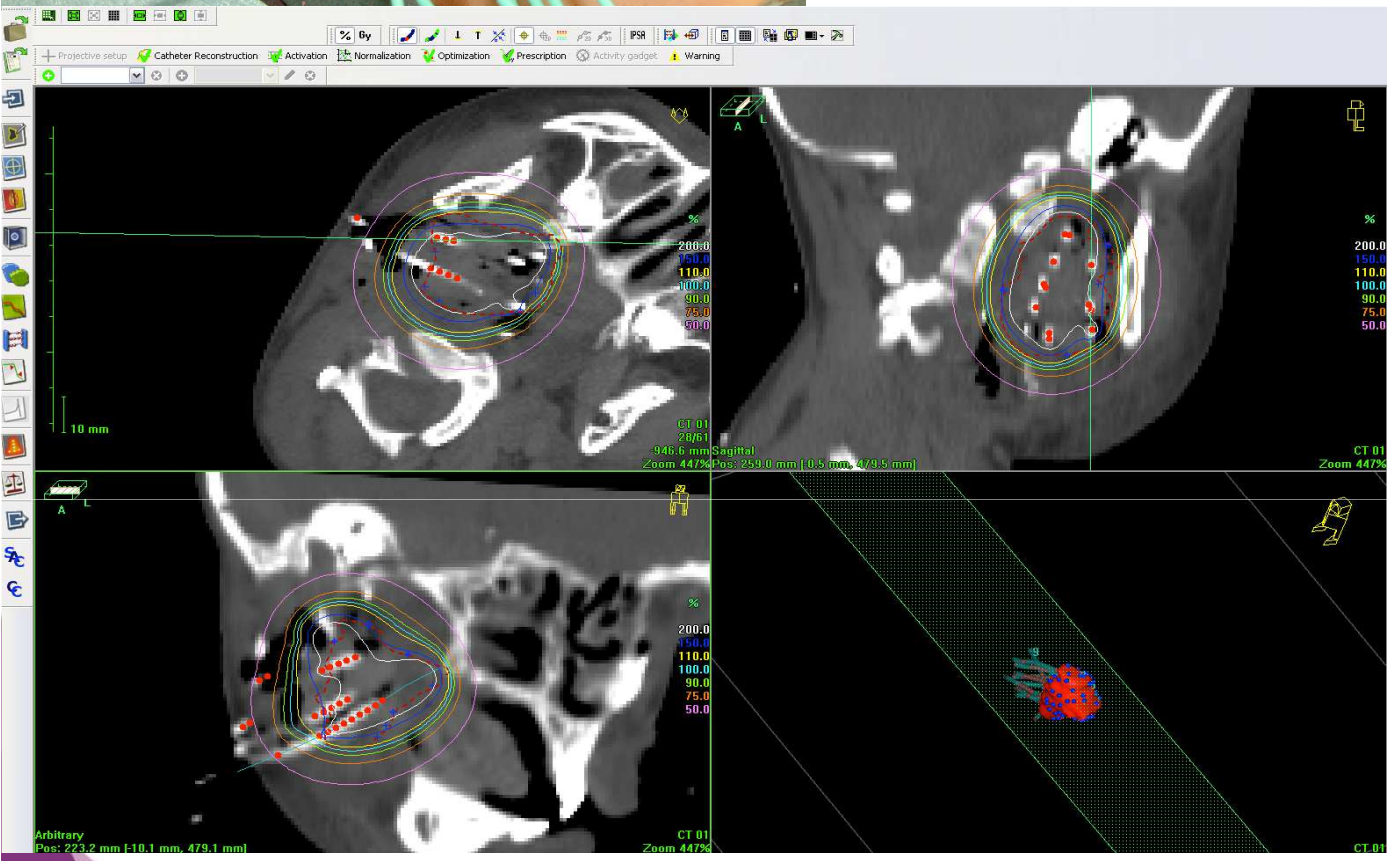
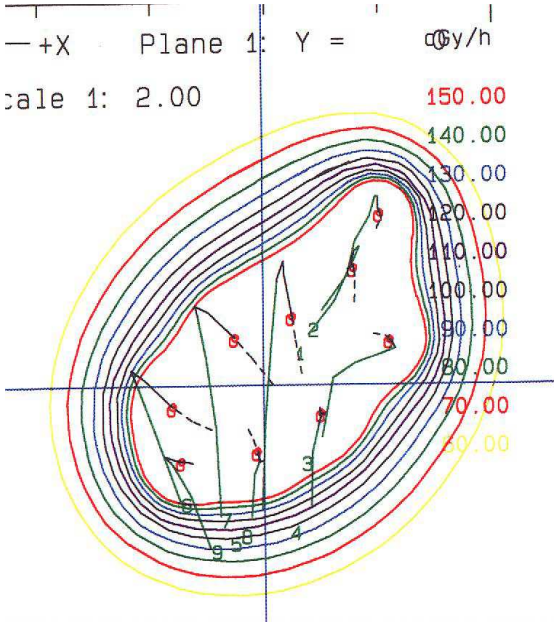

volledig
2
1



Present





Past

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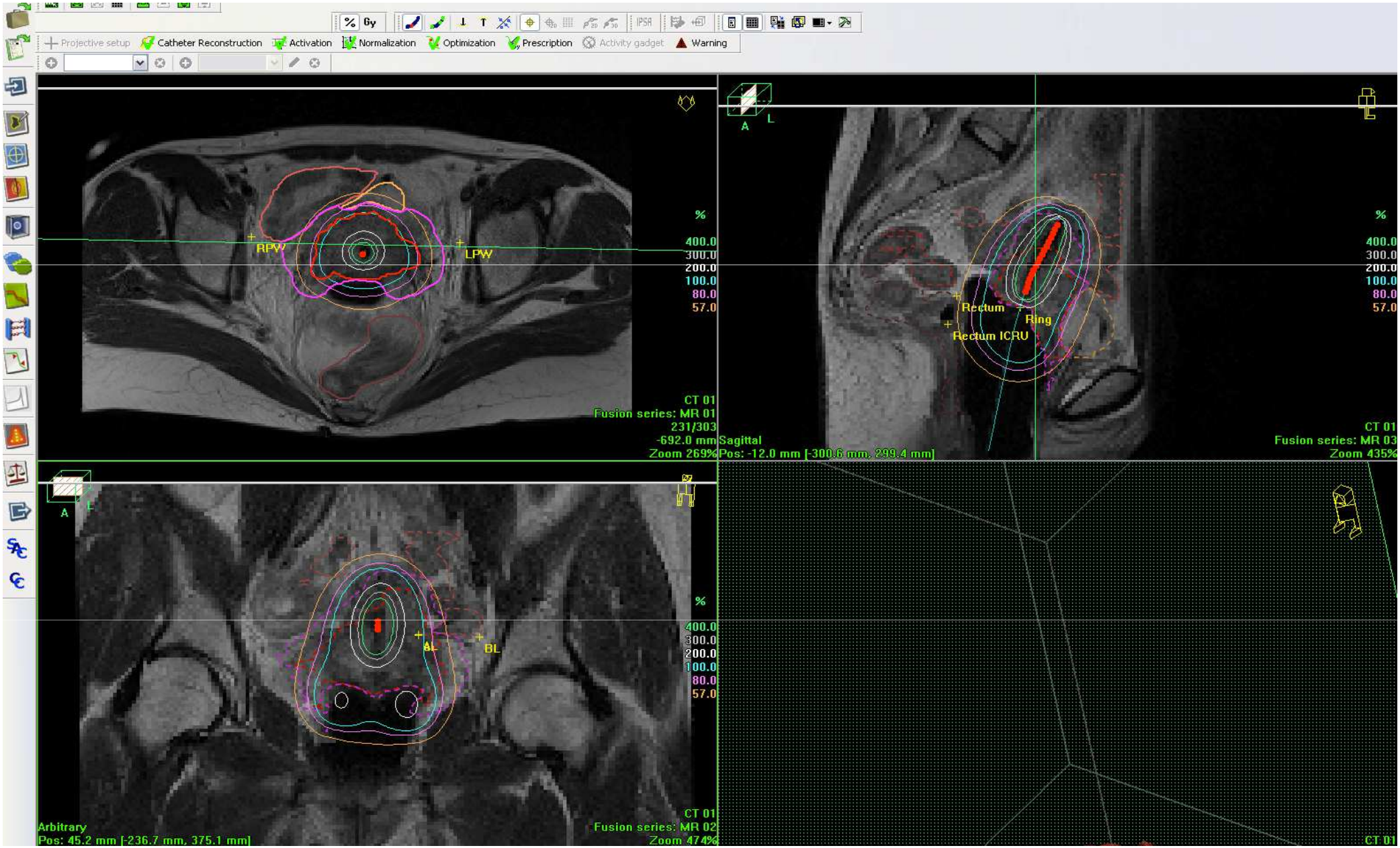

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Errors
Deviations
Distorsions
Spatial and Temporal Uncertainties

Image processing and usage

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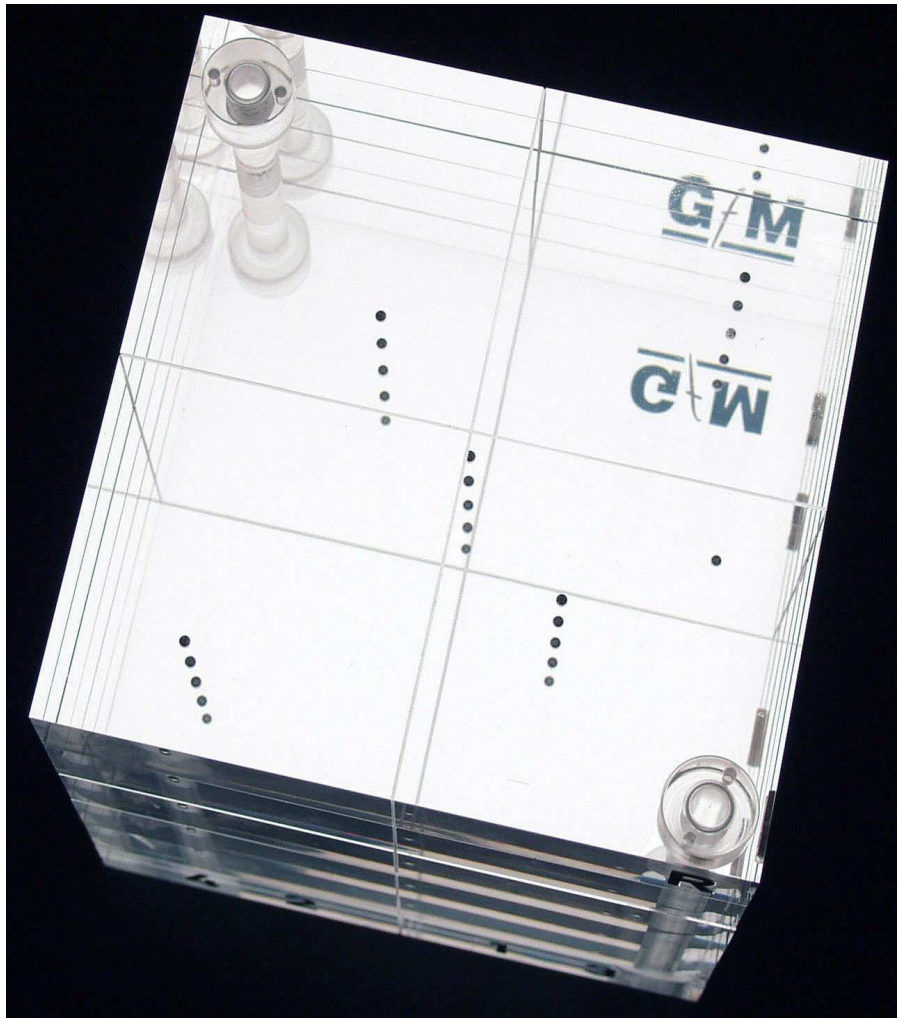
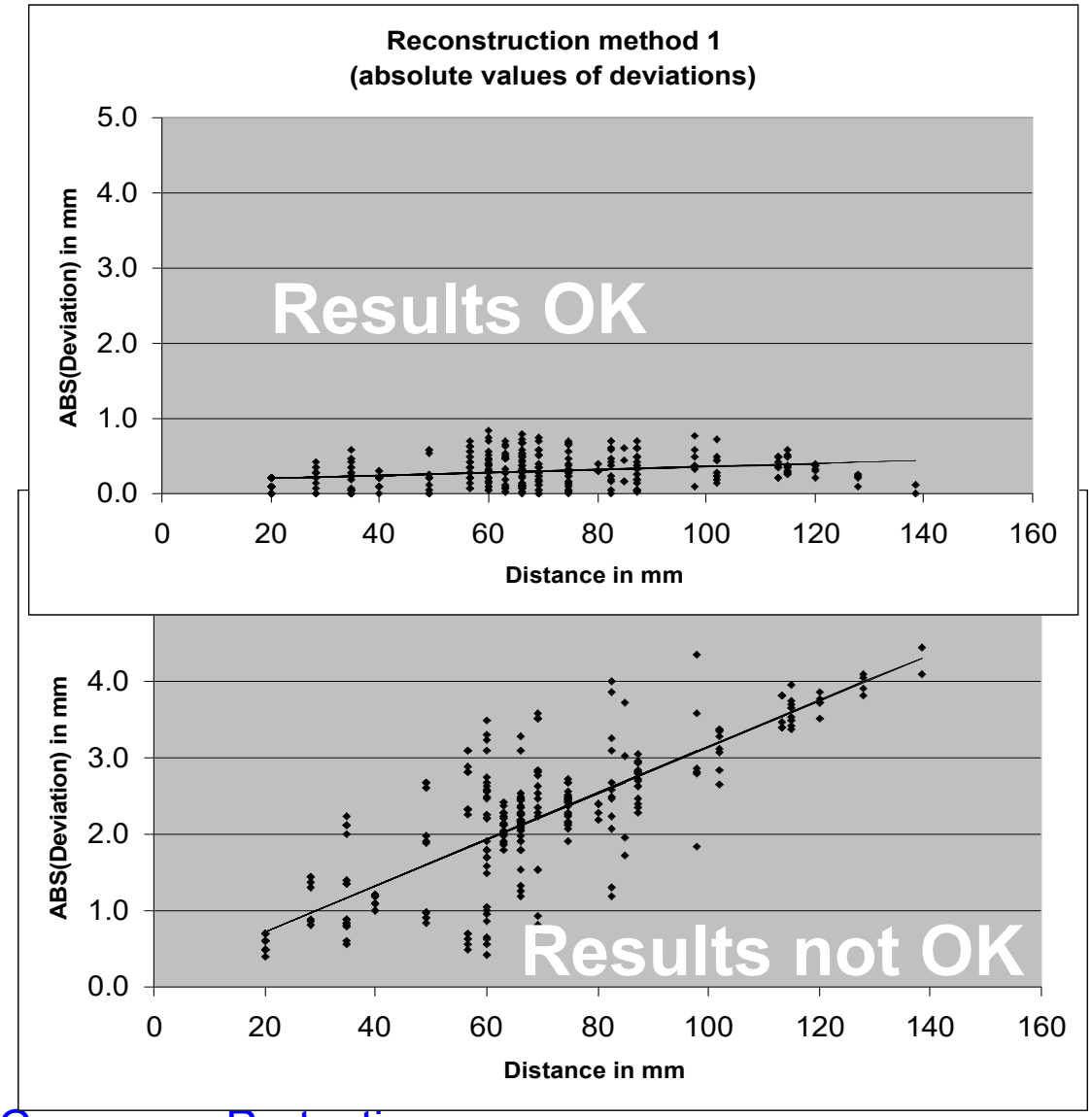
BRAPHYQS, Geometric test





EUROPEAN COMMISSION
Directorate General Health and Consumer Protection
- Europe Against Cancer Programme

Roué, R&O, 2006;78:78-83

ESQUIRE Project:
Education, **S**cience and **QU**ality assurance **I**n **R**adiotherapy in **E**urope

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Contouring Uncertainties

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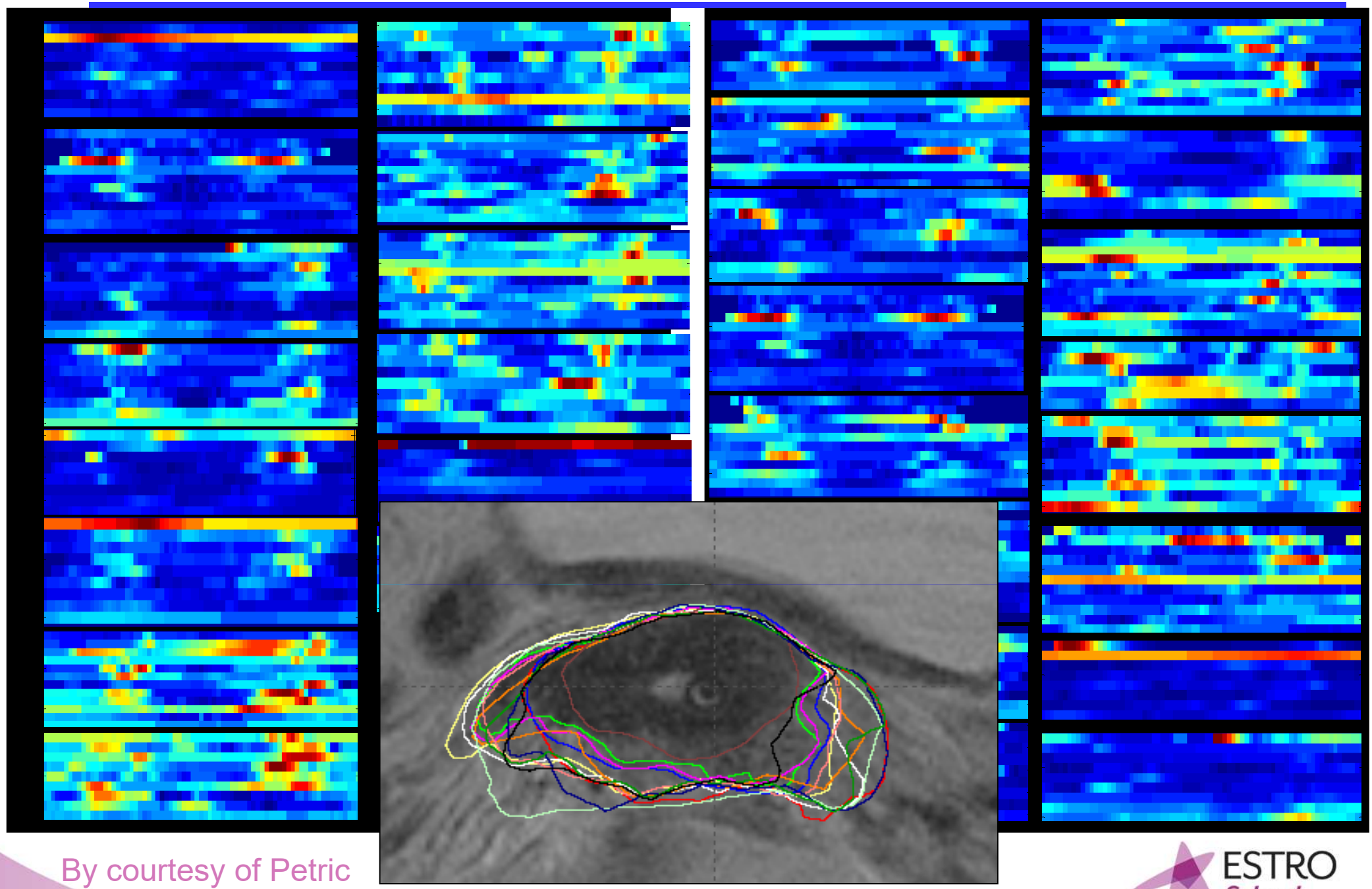
WHERE do observers differ?



By courtesy of Petric

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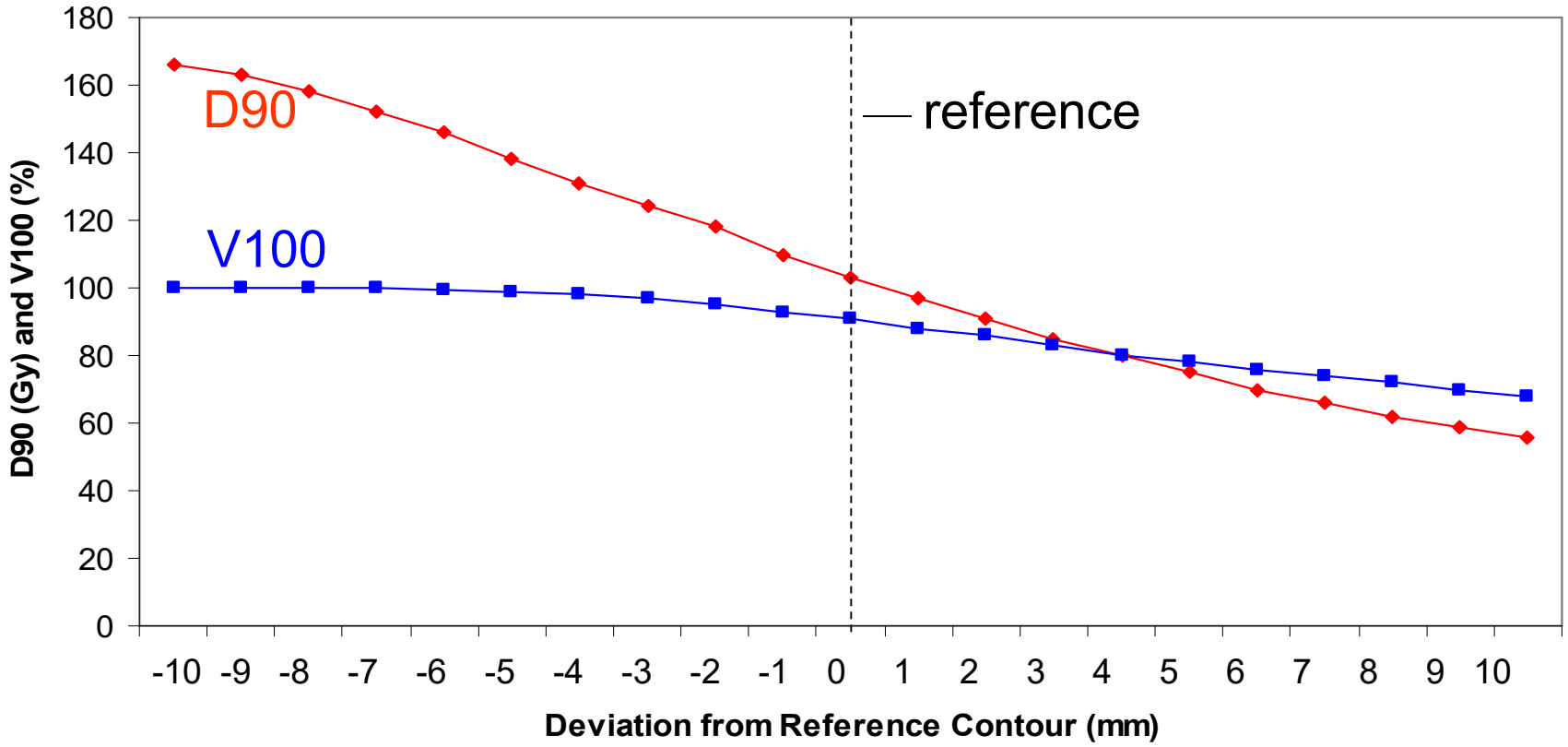
How big is 1mm in terms of Dose?



Variation per mm *lateral* contour displacement*

D90: 3 % – 8 % (nominal ~ 0.5 – 2 Gy)

V100: up to 3%

*Estimation! Valid for this example

By courtesy of Petric

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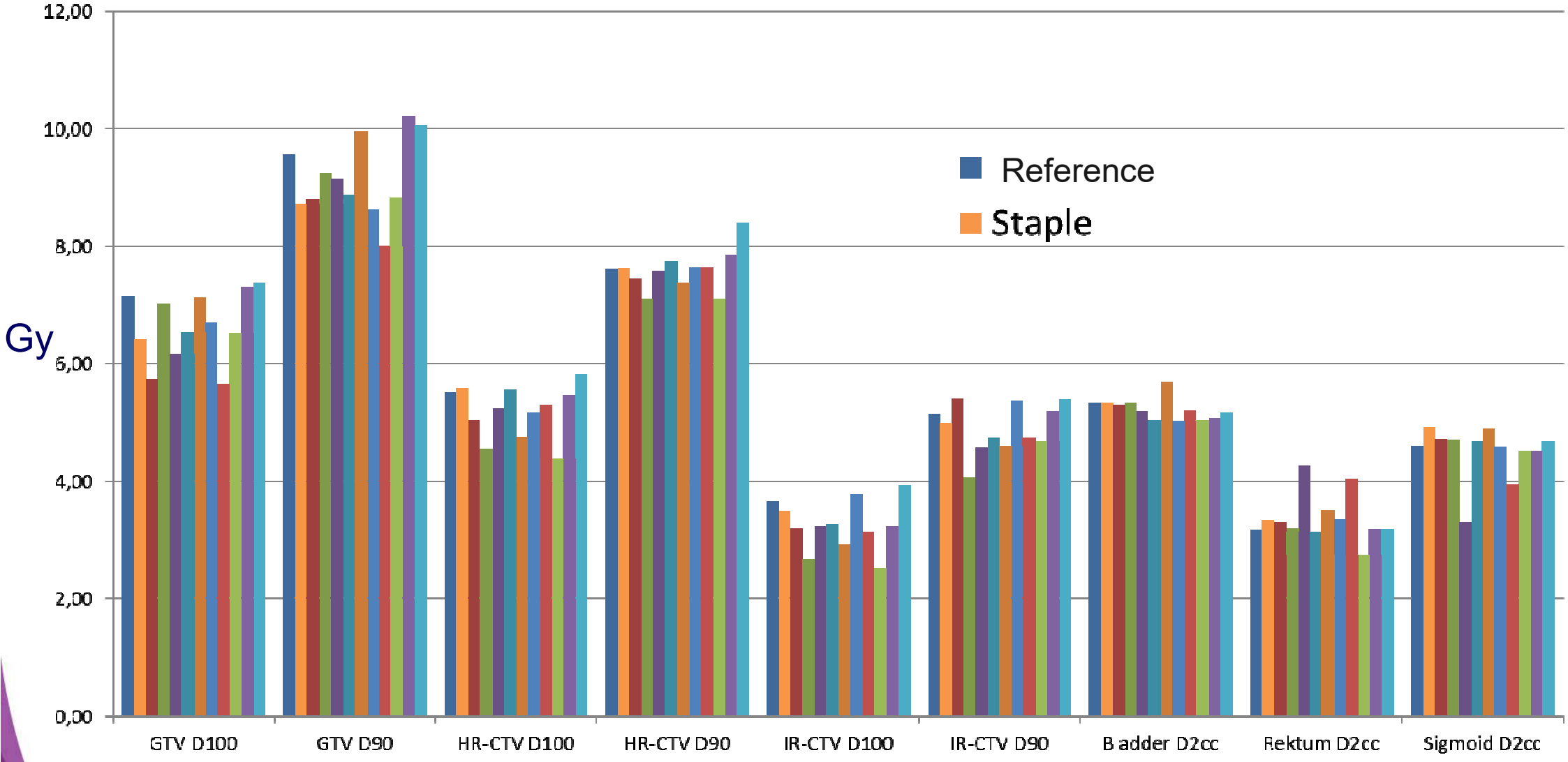
LJU1



Mean (Gy)	6,61	9,18	5,13	7,59	3,19	4,88	5,21	3,39	4,45
SD (Gy)	0,62	0,71	0,45	0,38	0,44	0,45	0,20	0,45	0,47
Rel.SD (%)	9,3	7,7	8,8	5,0	13,6	9,1	3,9	13,3	10,6

By courtesy of Hellebust

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SD (in %) for all cases

Not including reference value and STAPLE

Case	GTV D100	GTV D90	HR-CTV D10	HR-CTV D90	CTV D100	IR-CTV D90	Bladder D2cc	Rektum D2cc	Sigmoid D2cc
LJU1	9,3	7,7	8,8	5,0	13,6	9,1	3,9	13,3	10,6
LJU2	17,3	8,6	16,8	10,3	15,6	13,5	3,6	3,6	21,6
LJU3	11,8	7,8	24,4	12,5	20,6	10,9	8,7	17,1	7,9
VIE1	26,7	13,3	27,2	12,7	20,5	19,3	6,2	2,4	8,9
VIE2	16,5	7,6	18,3	7,9	16,8	11,6	4,9	4,0	4,6
VIE3	18,3	11,5	20,3	11,7	24,8	13,6	5,2	4,8	13,3
Range	9,3 – 26,7	7,6 – 13,3	8,8 – 27,2	5,0 – 12,7	3,6 – 24,8	9,1 – 19,2	3,6 – 8,7	2,4 – 13,3	4,6 – 21,6

By courtesey of Hellebust

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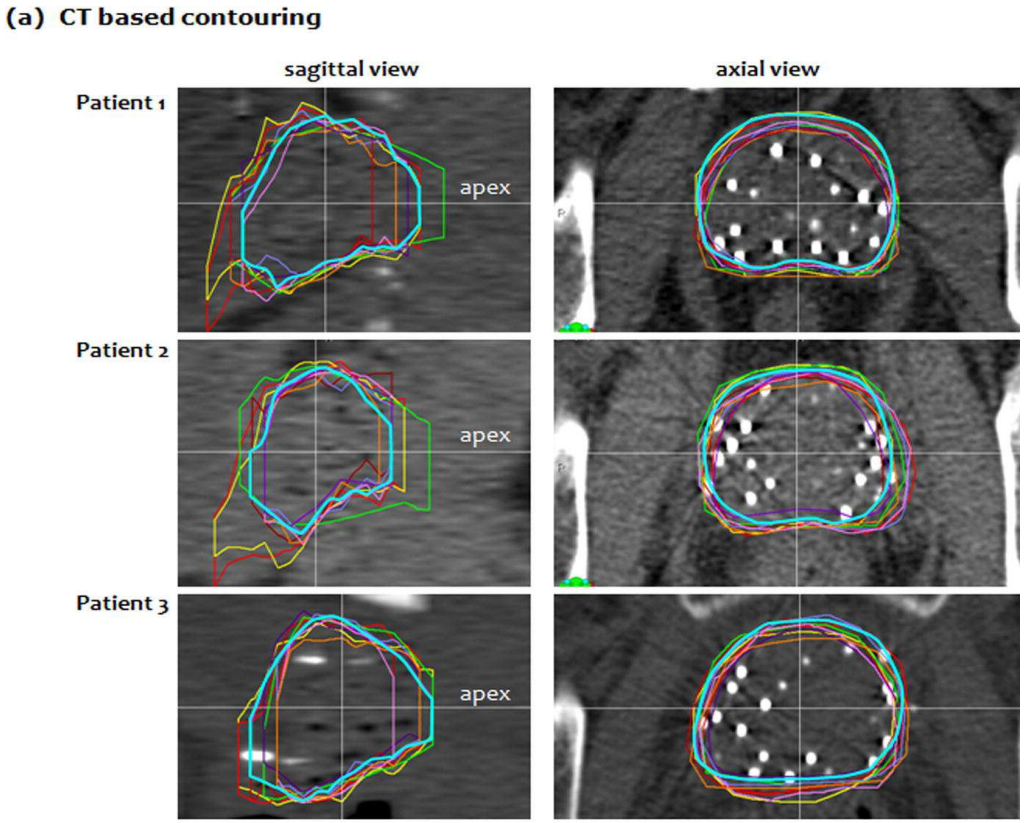
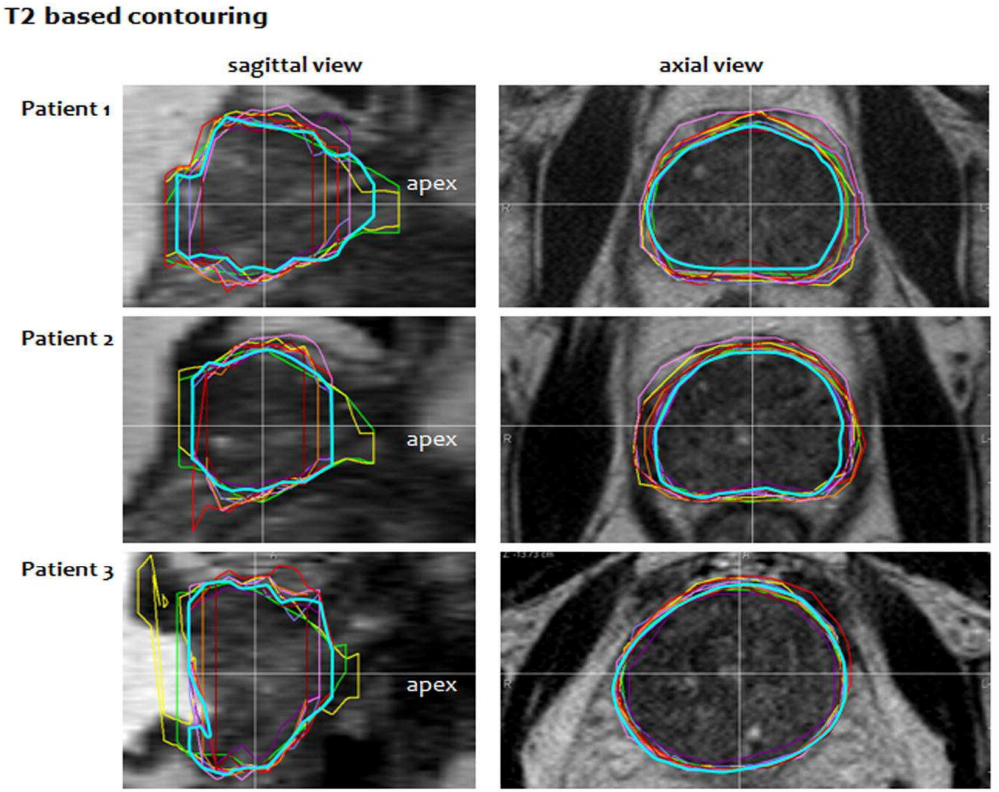
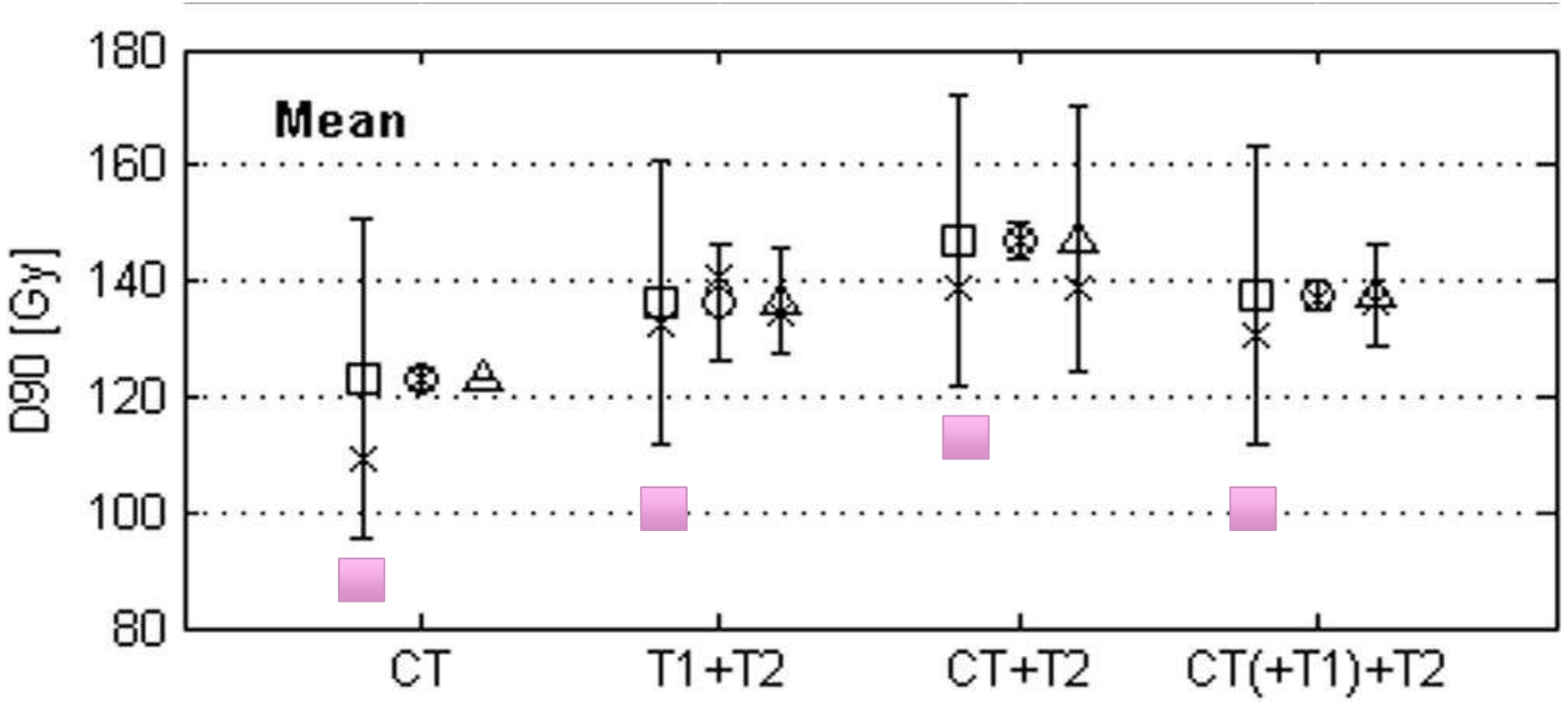
Contouring Uncertainty Prostate





De Brabandere, R&O 2012; 104,192-198

ESTRO School



De Brabandere, R&O 2012; 104,192-198

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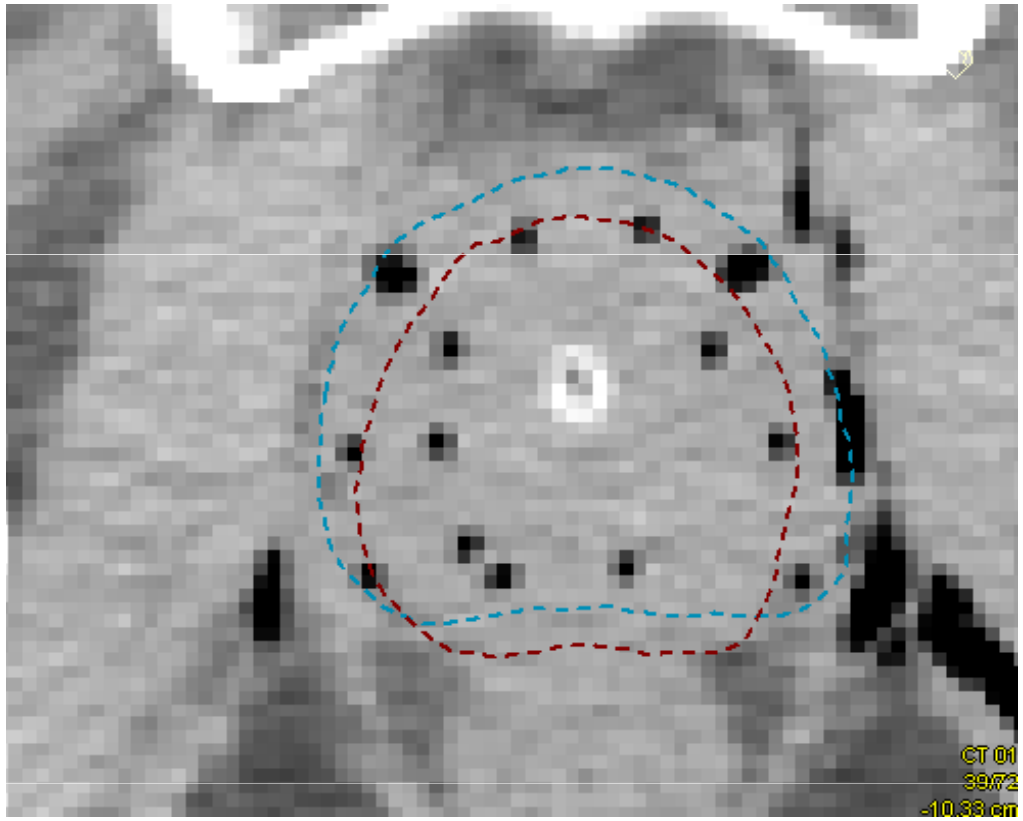
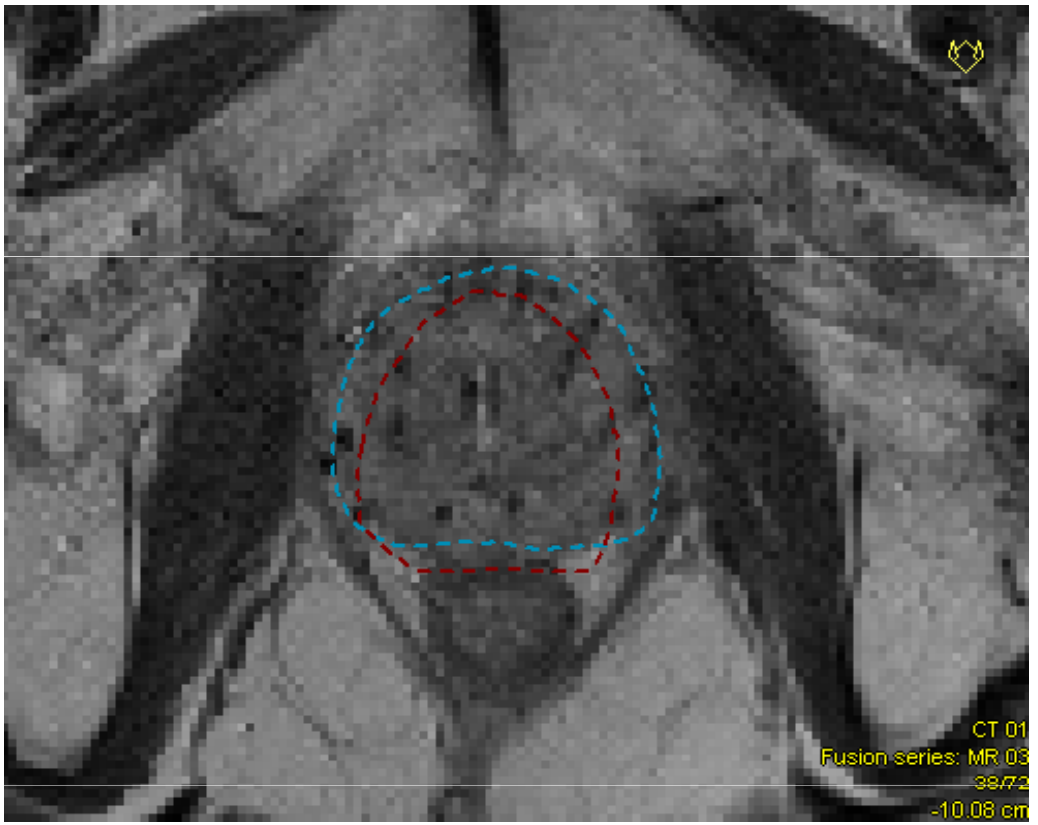
Comparison Treatment Planning on CT vs MR





PTV-MRI vs PTV-CT

A. Dinkla, Acta Oncol 2013;52:658-665

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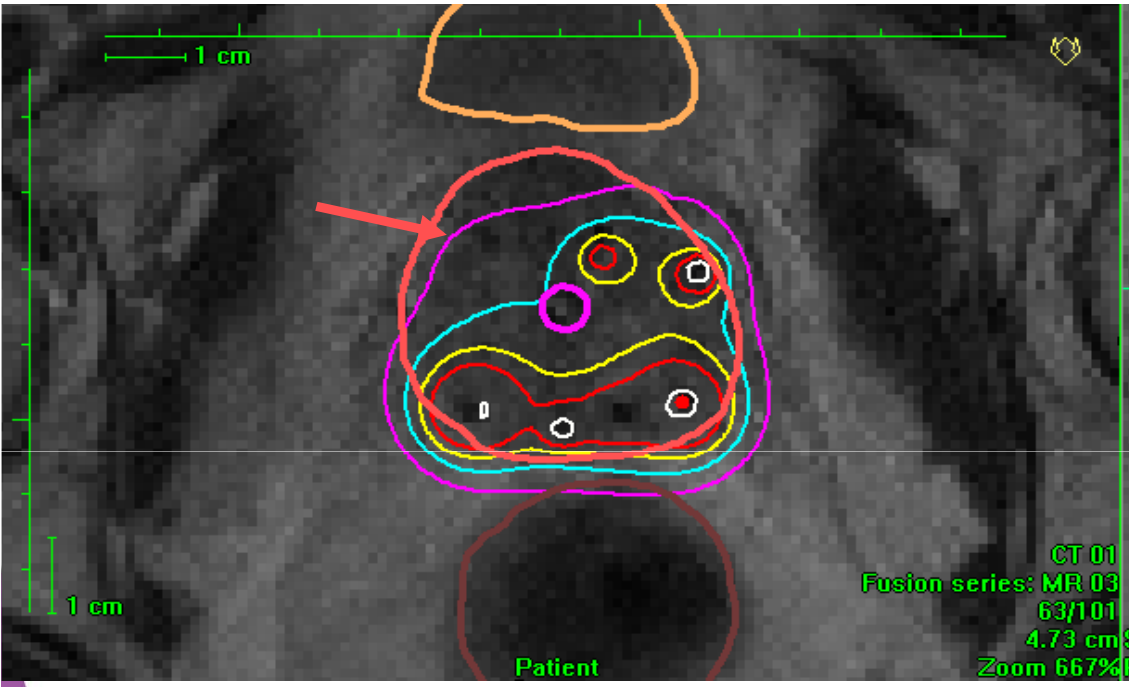
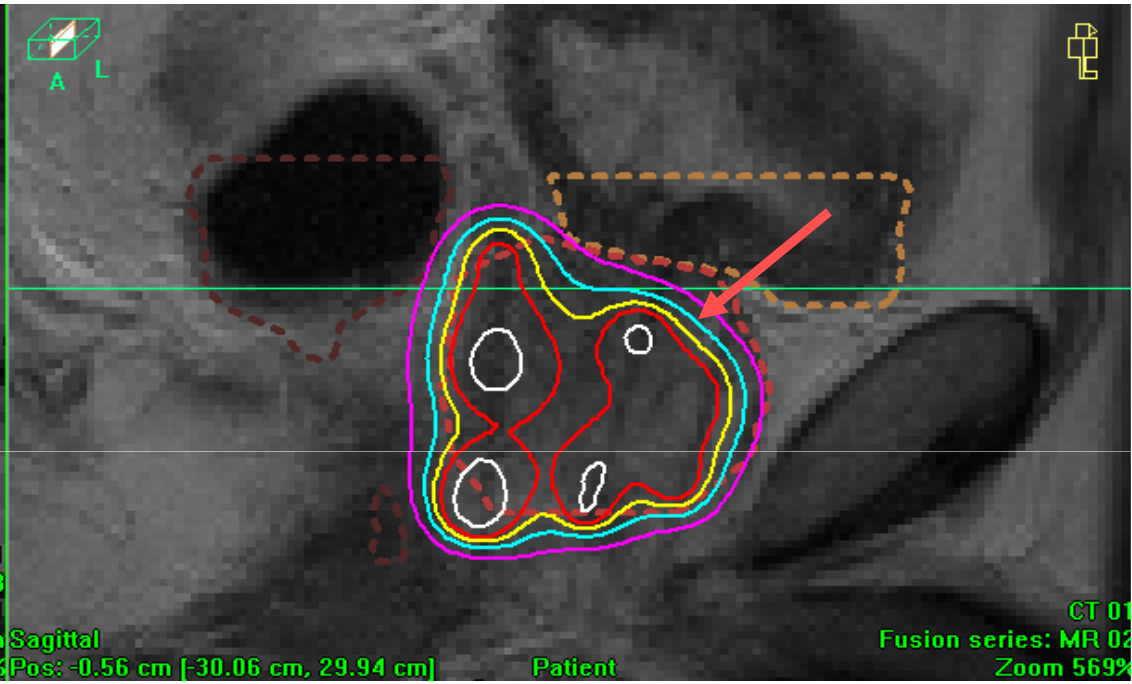
Example

CT-plan, projected on MRI contours:

- Missing coverage ventral side (1)
- At basal side of prostate (2)



(1)



(2)

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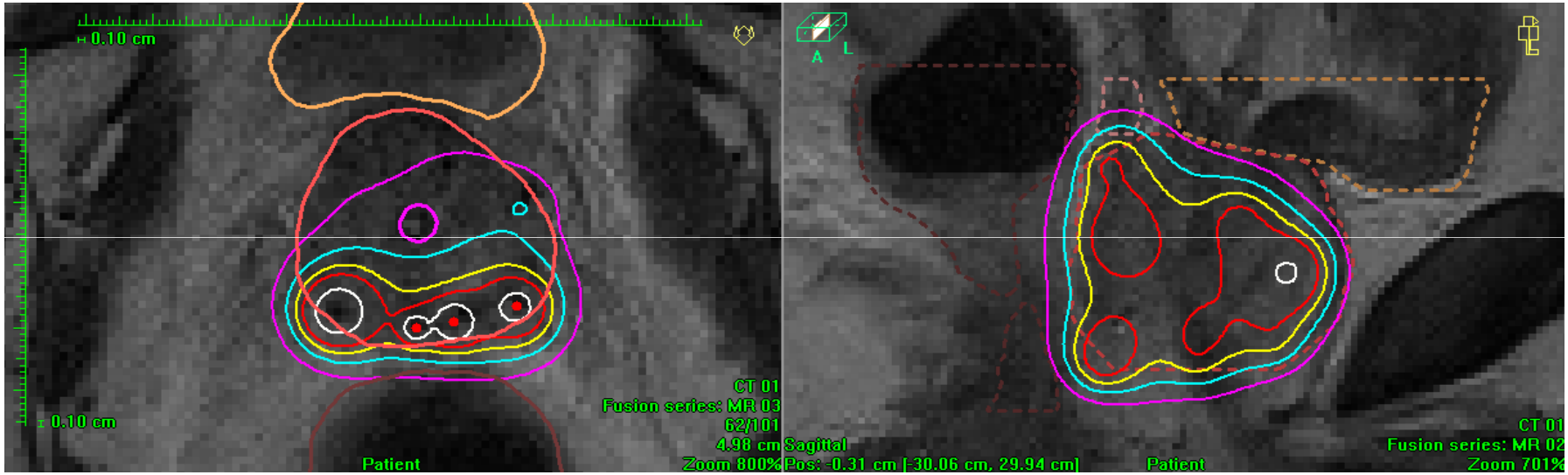
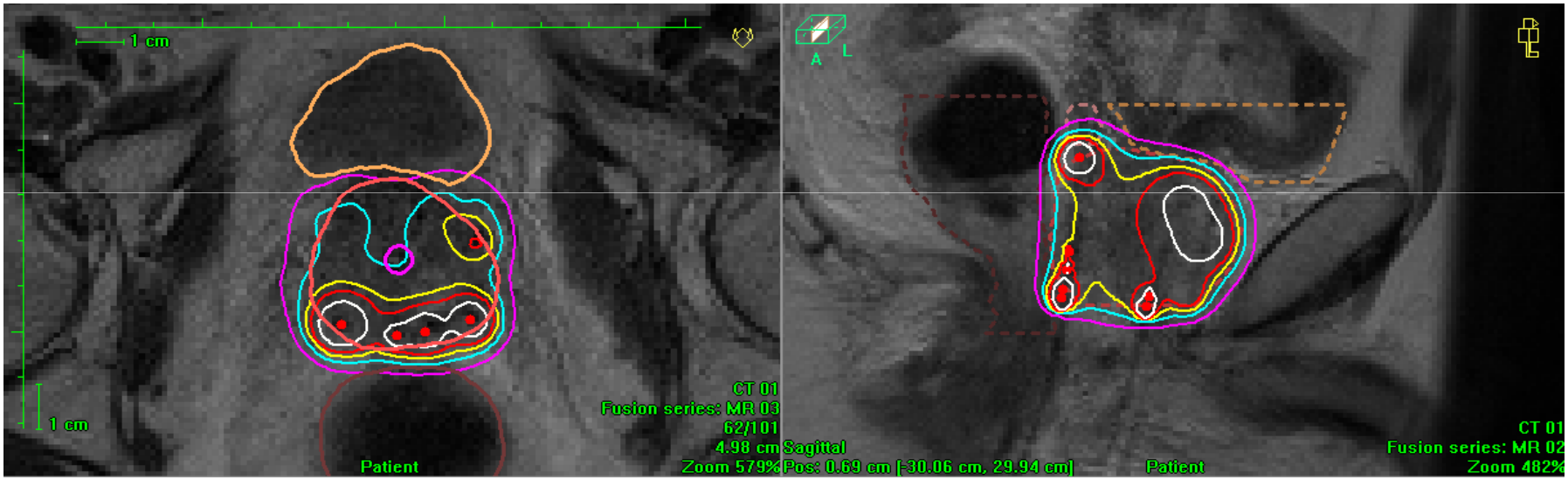
Example: Improved coverage with MRI-based planning

CT-based plan



MRI-Based plan



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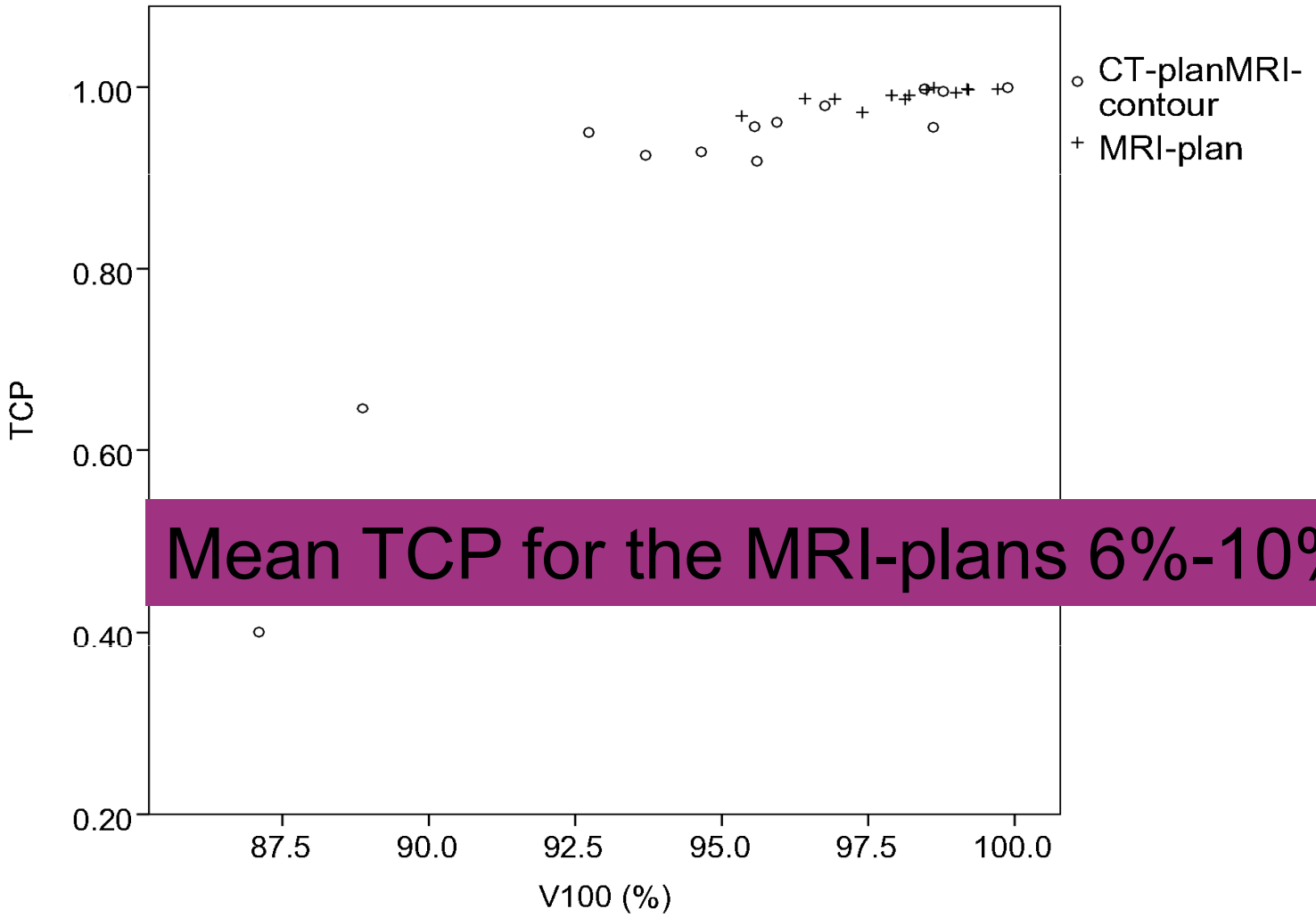
TCP vs $V_{100\%}$ for α/β = 1.5 Gy



Mean TCP for the MRI-plans 6%-10% higher

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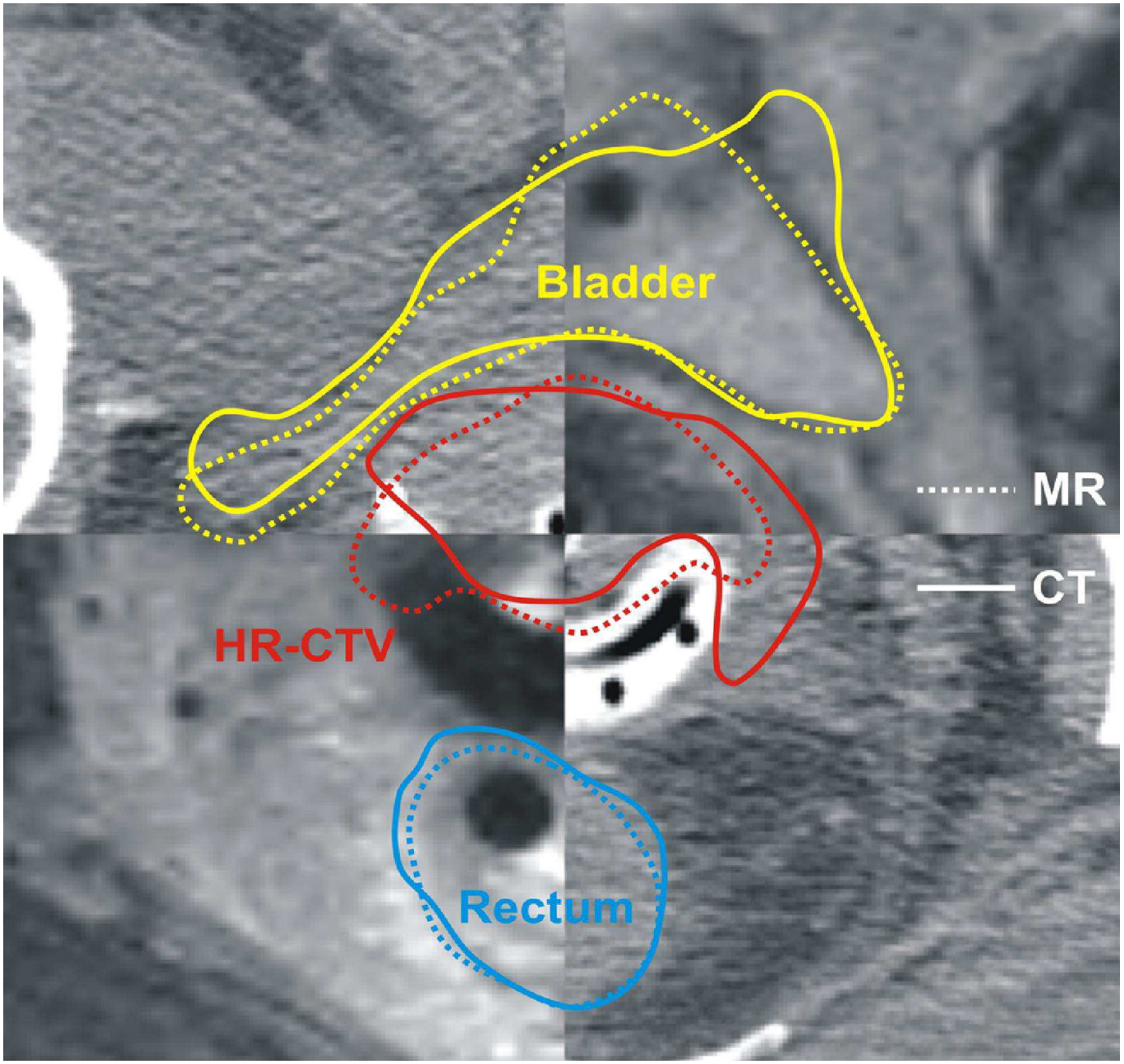

Viswanathan et al, Int J Radiat Oncol Biol Phys 2007;68:491-498

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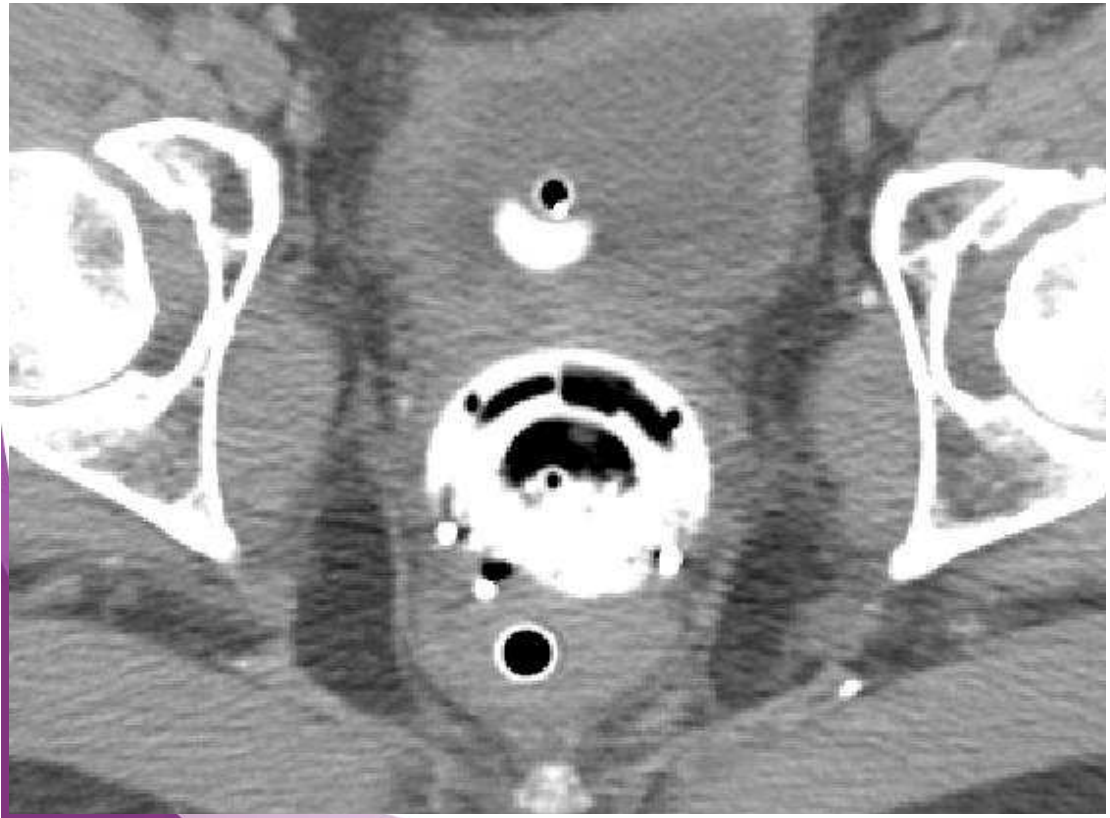
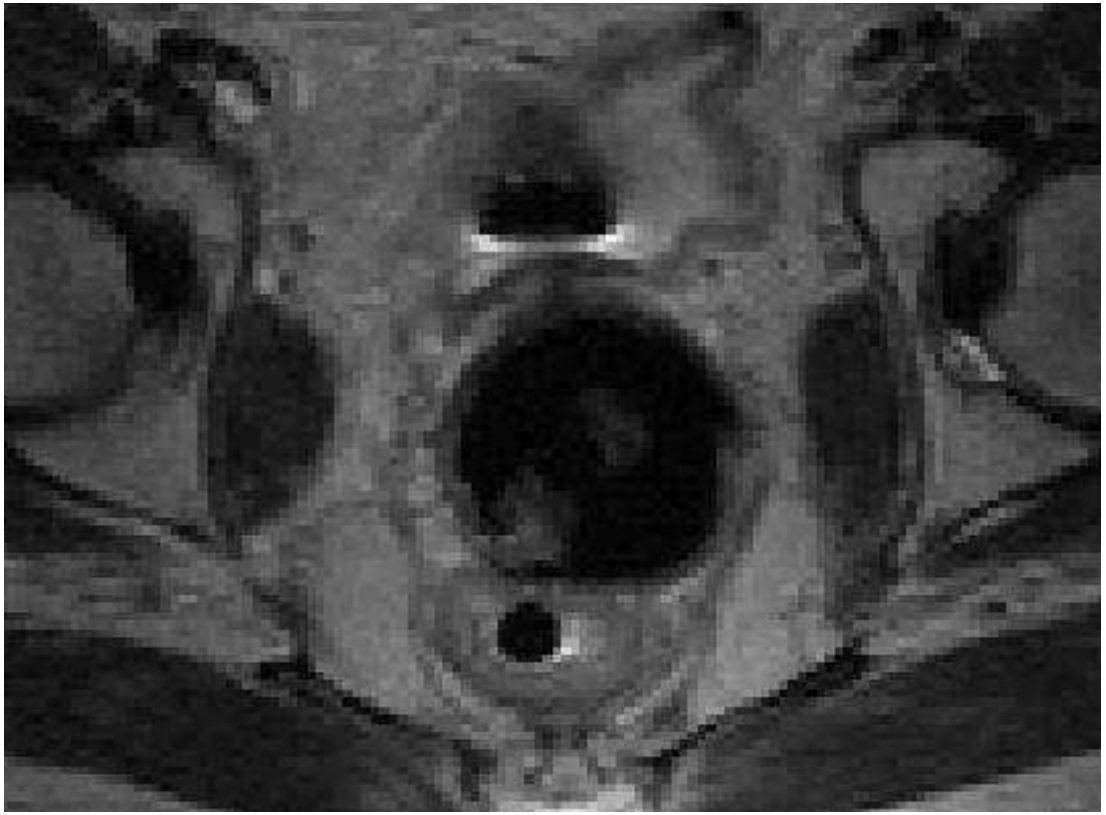
Applicator reconstruction

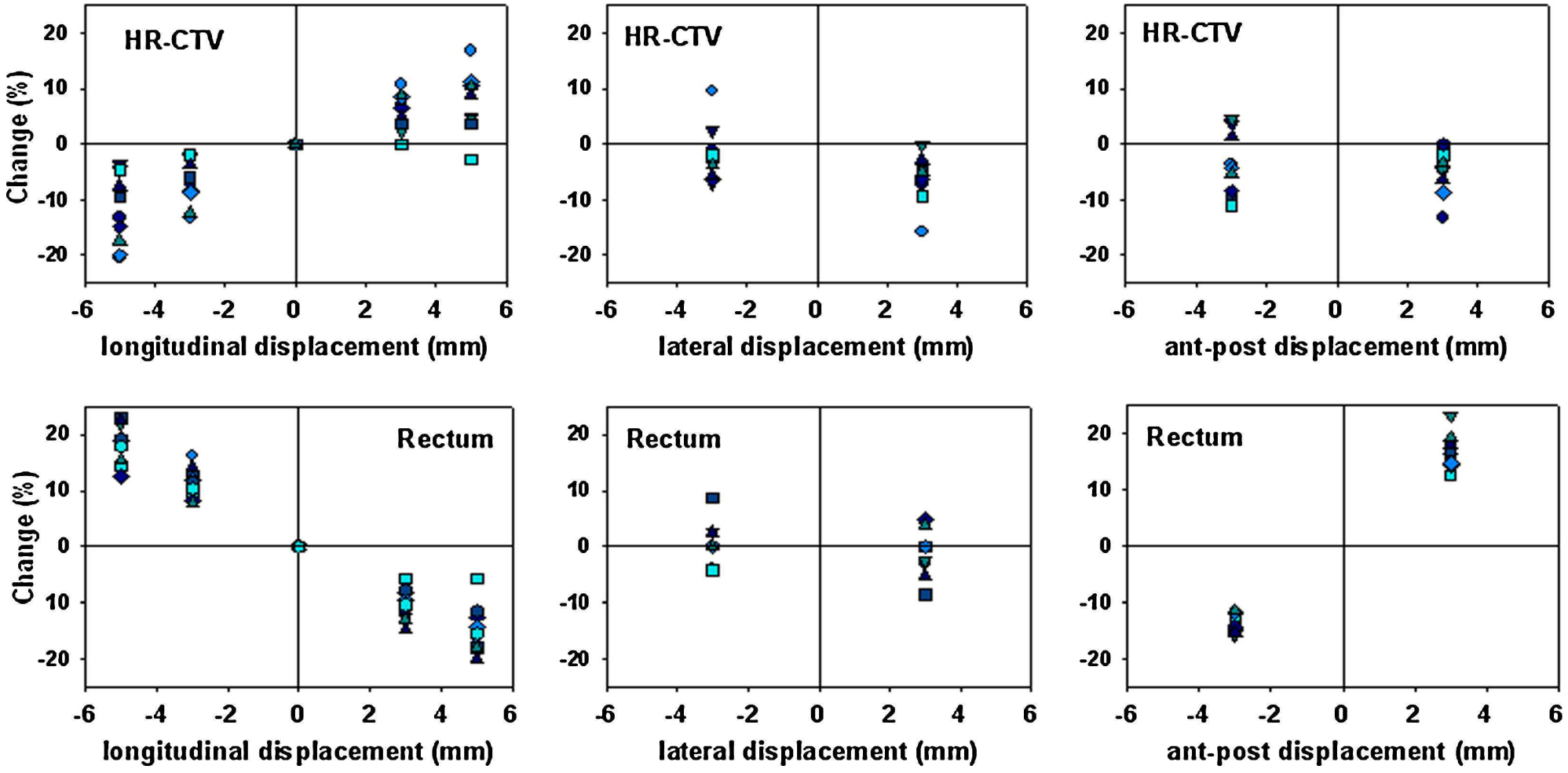
Target and OAR delineation on T2 MRI

Reconstruction on MRI only possible if applicator position and orientation is clearly visible





Intracavitary Applicator Reconstruction Uncertainties



Tanderup Radiother Oncol 2008

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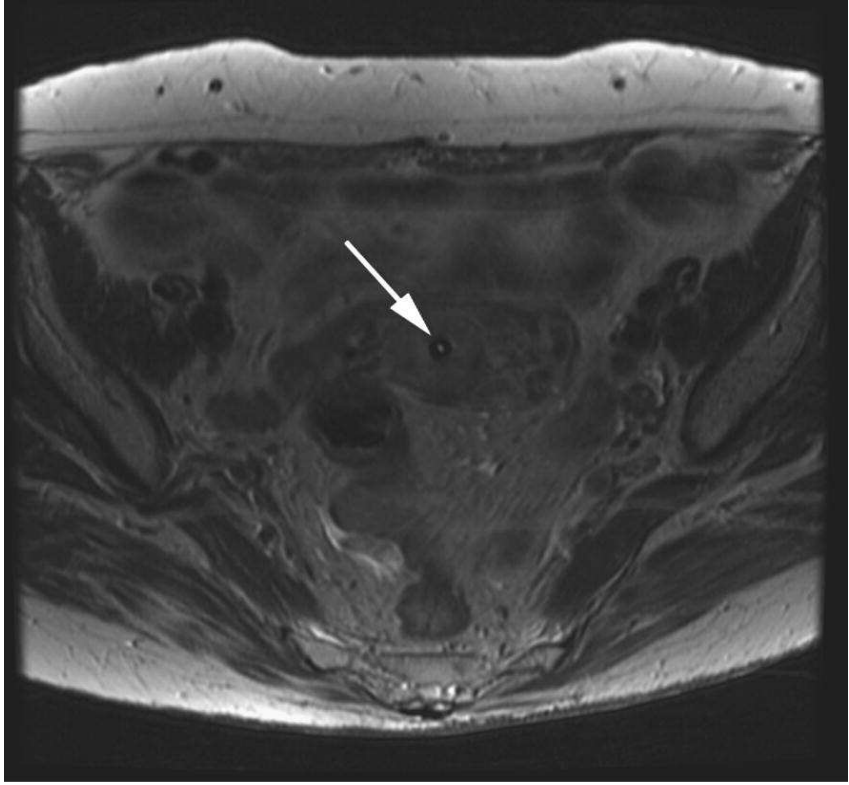
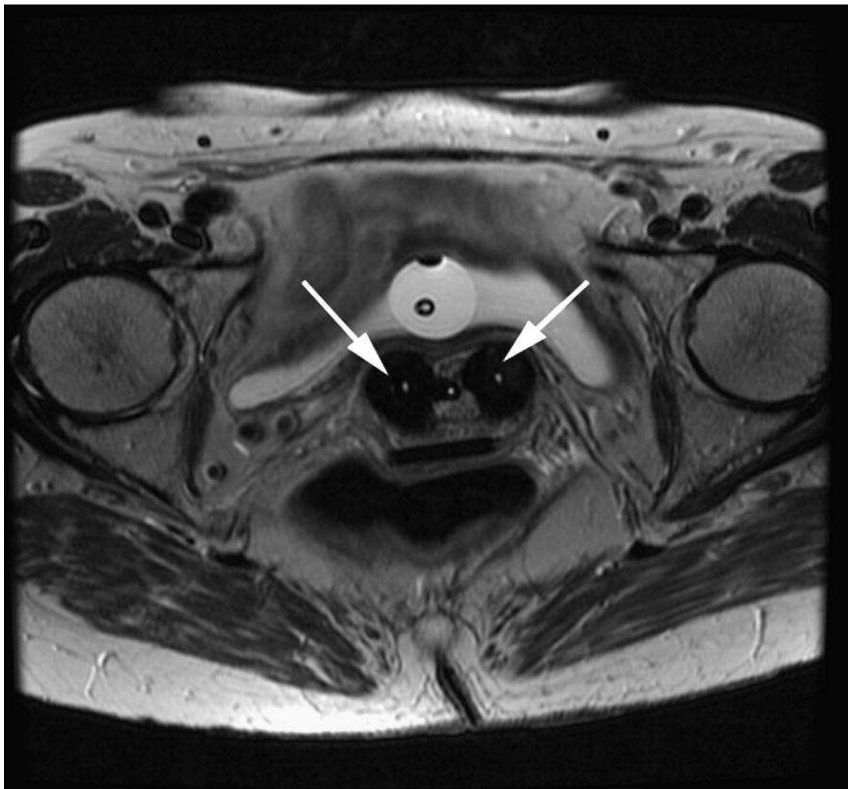
Visible MRI dummy sources for reconstrucion of source positions

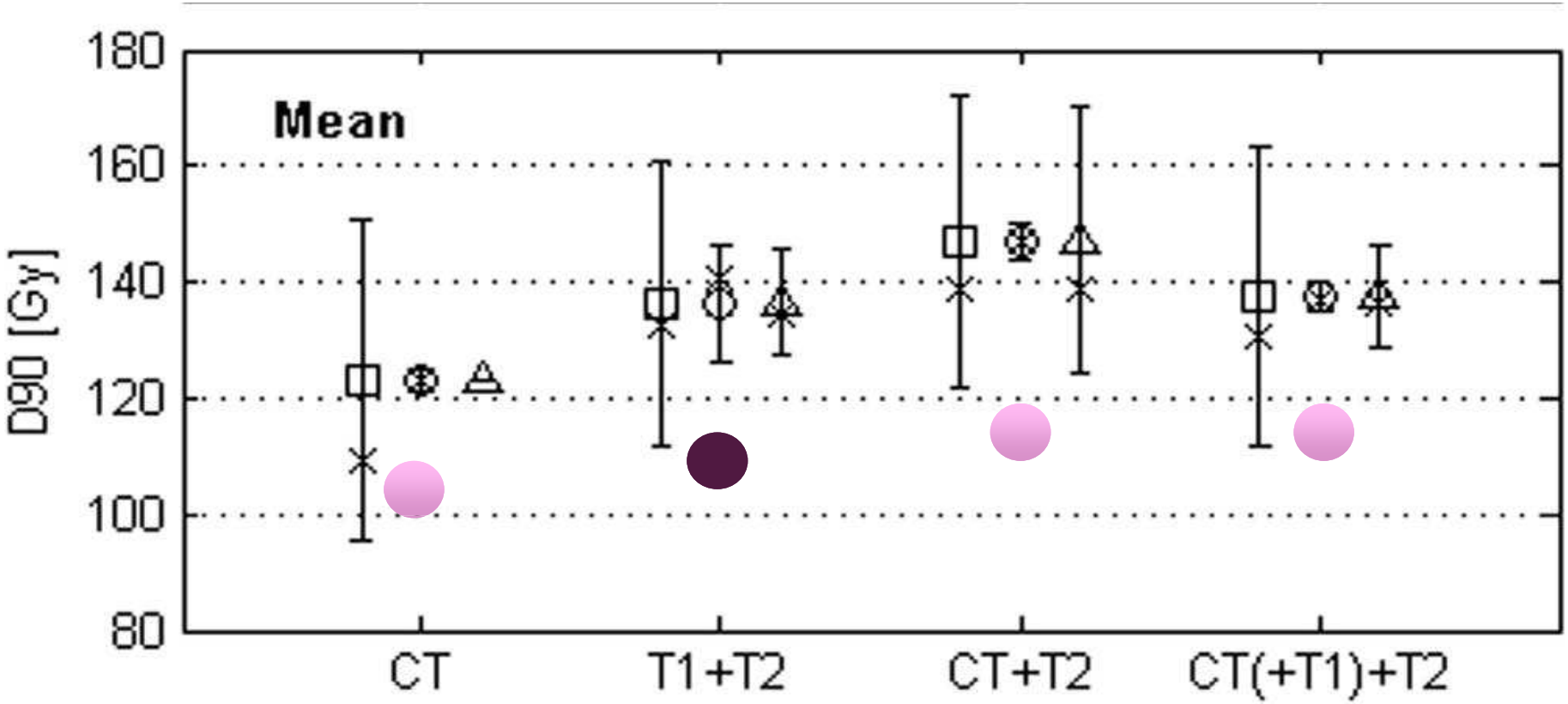




Dose calculation is based on the geometry of the source positions!

Perez-Calatayud Radiother Oncol 2009

Seed Reconstruction Prostate Brachytherapy



De Brabandere, R&O 2012; 104,192-198

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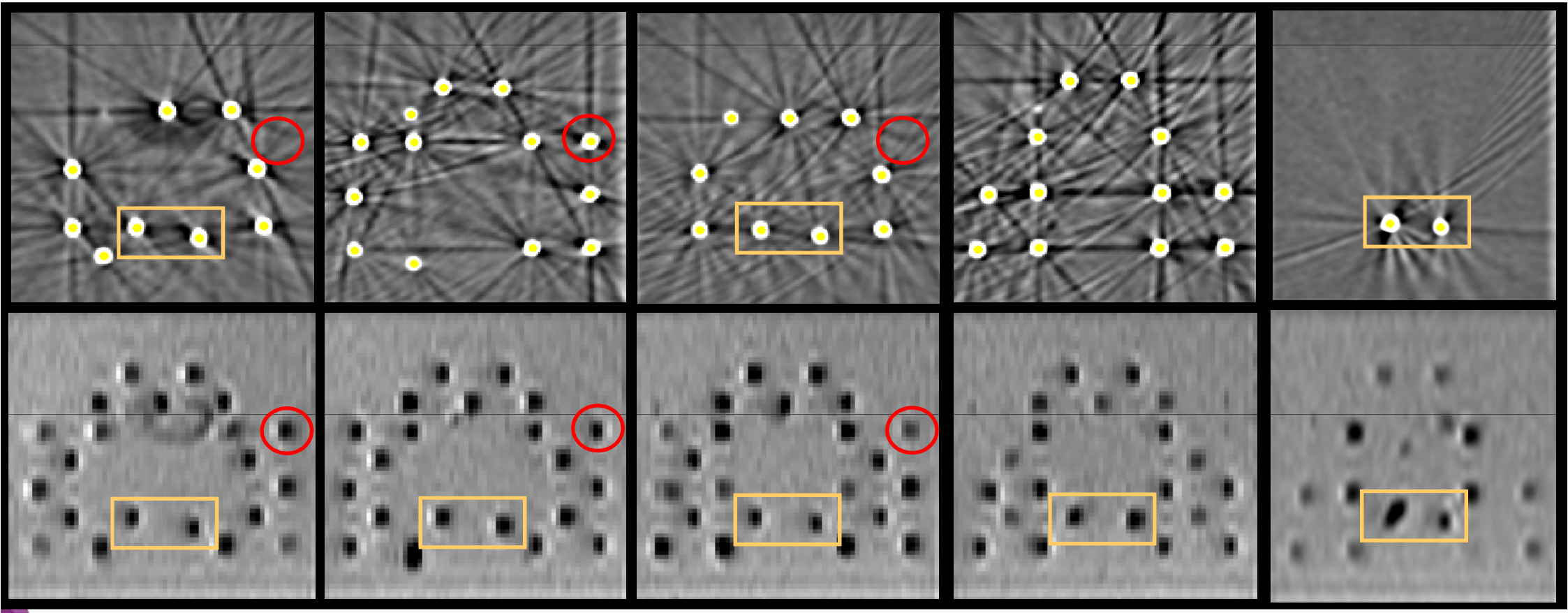
Positioning Deviation

Comparison of CT and MR seed imaging for 5 consecutive slices taken with 5 mm interslice distance



de Brabandere et al. R&O 2006;79:190-197

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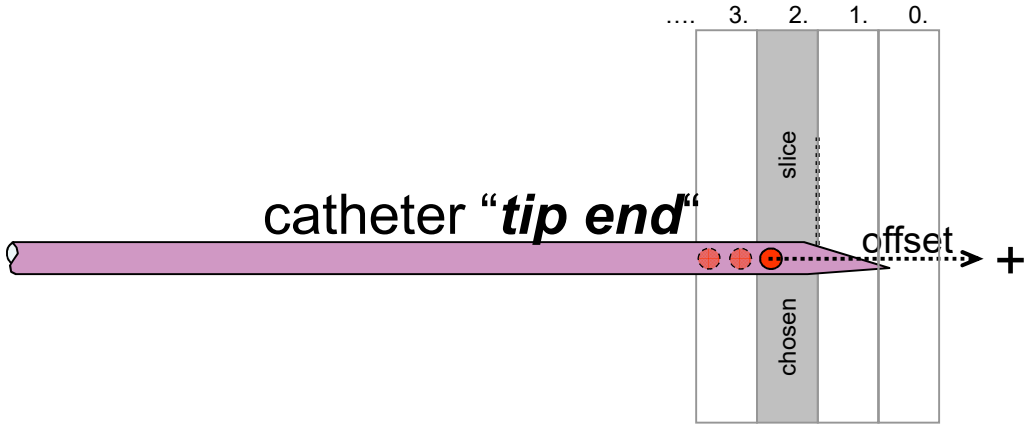
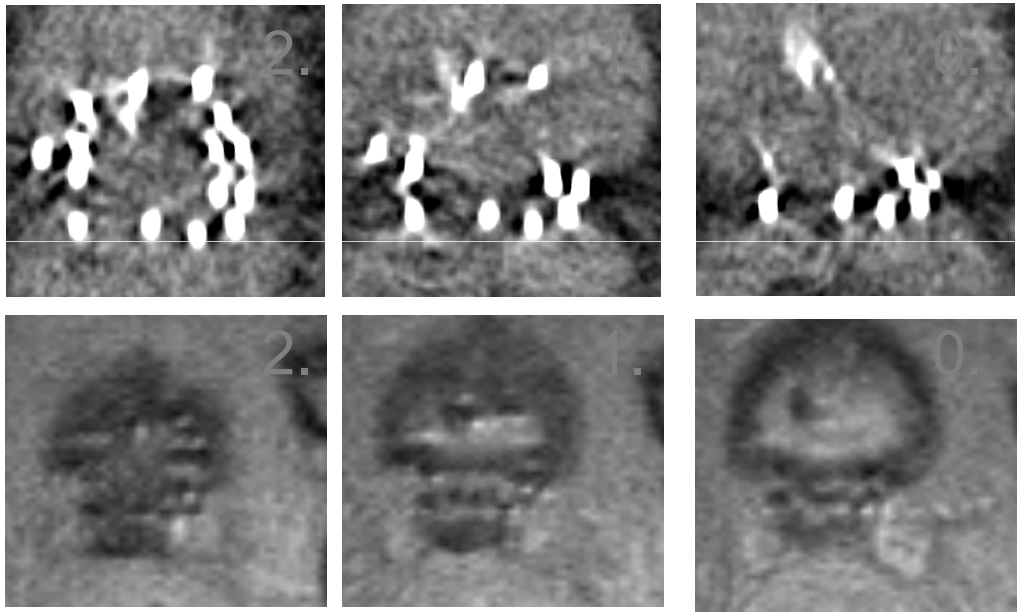
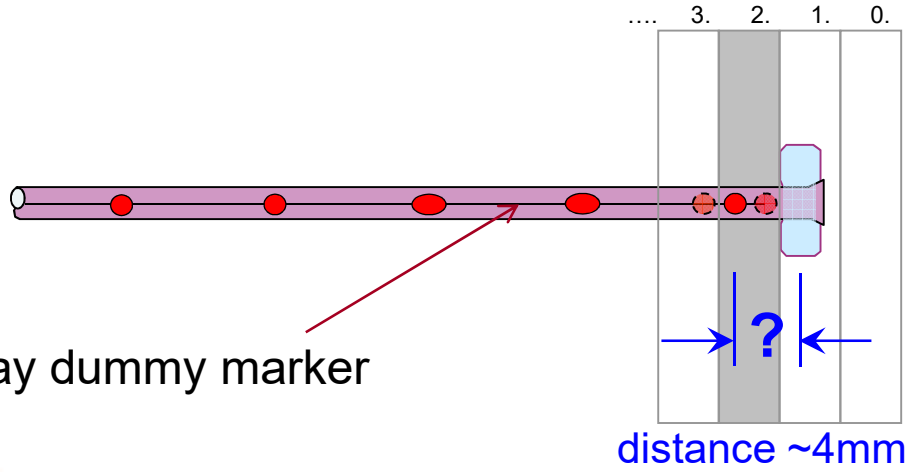
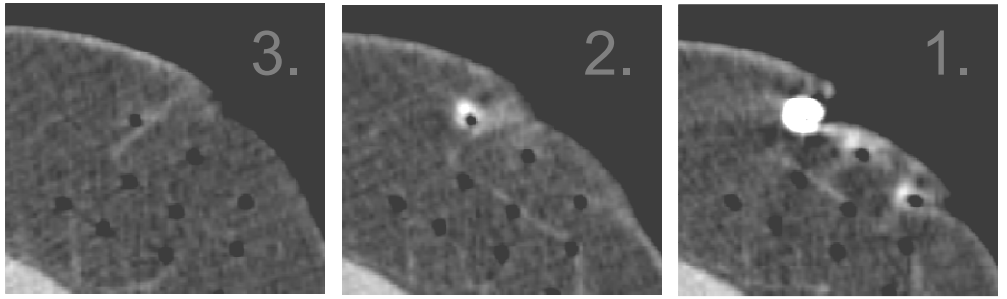
Direct reconstruction by using CT or MR images

the first dwell position is a problem !









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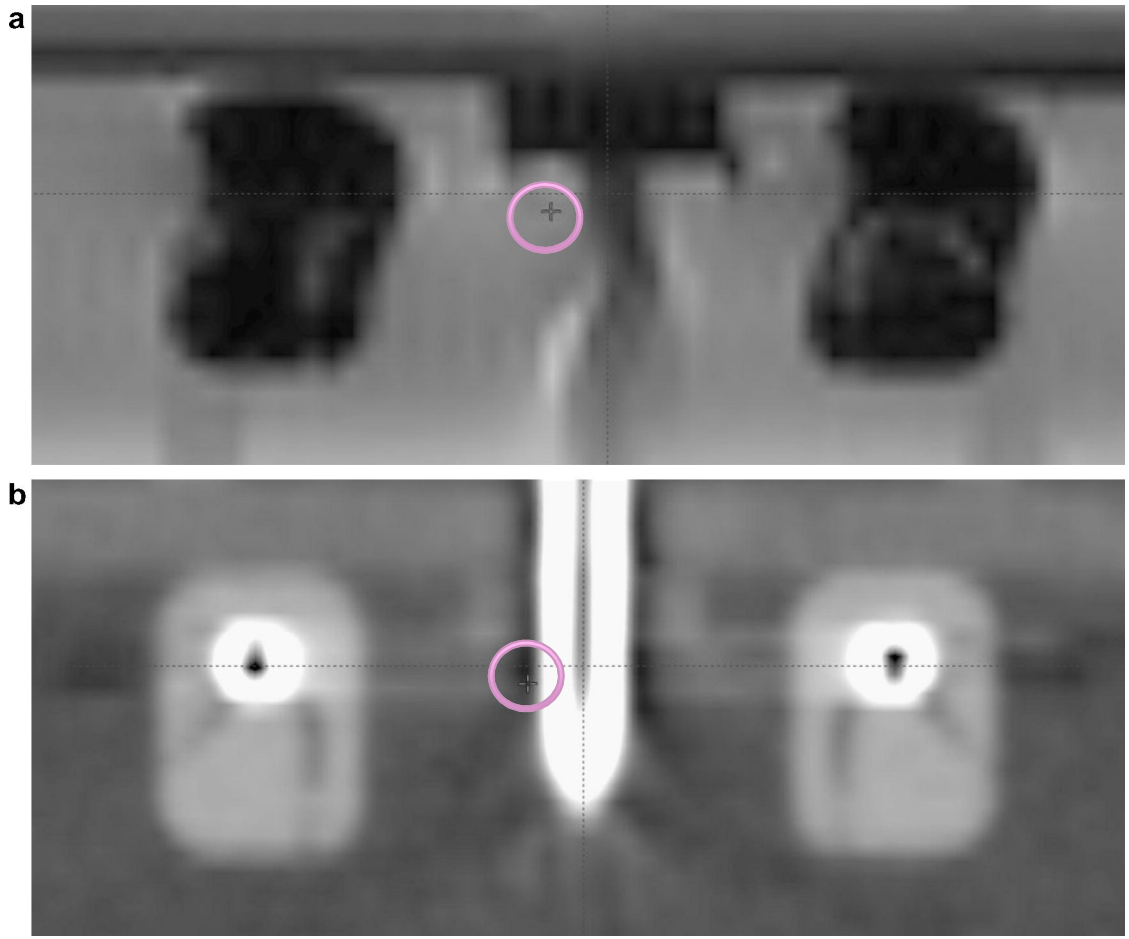
MR Distorsions

T1W MRI

CT



Titanium applicator

Haack et al. Radiother Oncol 2009;91:187

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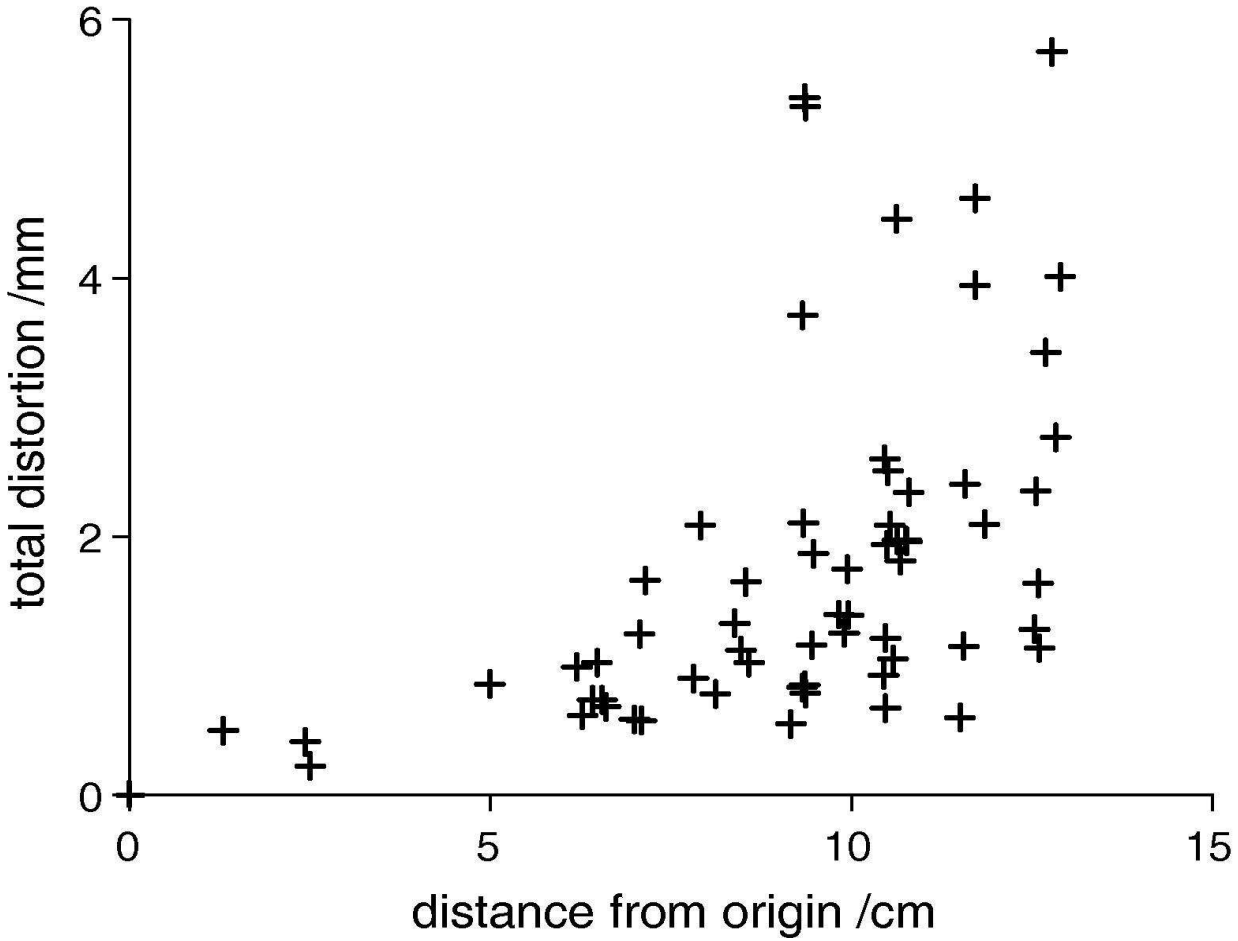
MR Distorsions



Wills et al. Radiother Oncol 2009;94:346-352

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Uncertainties and Errors

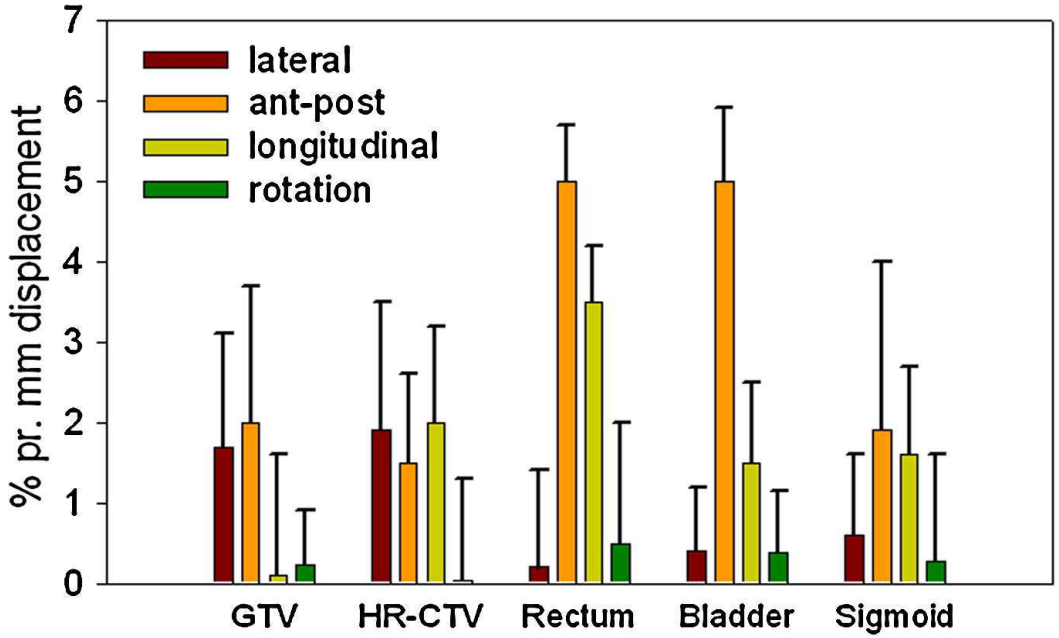
Systematic errors

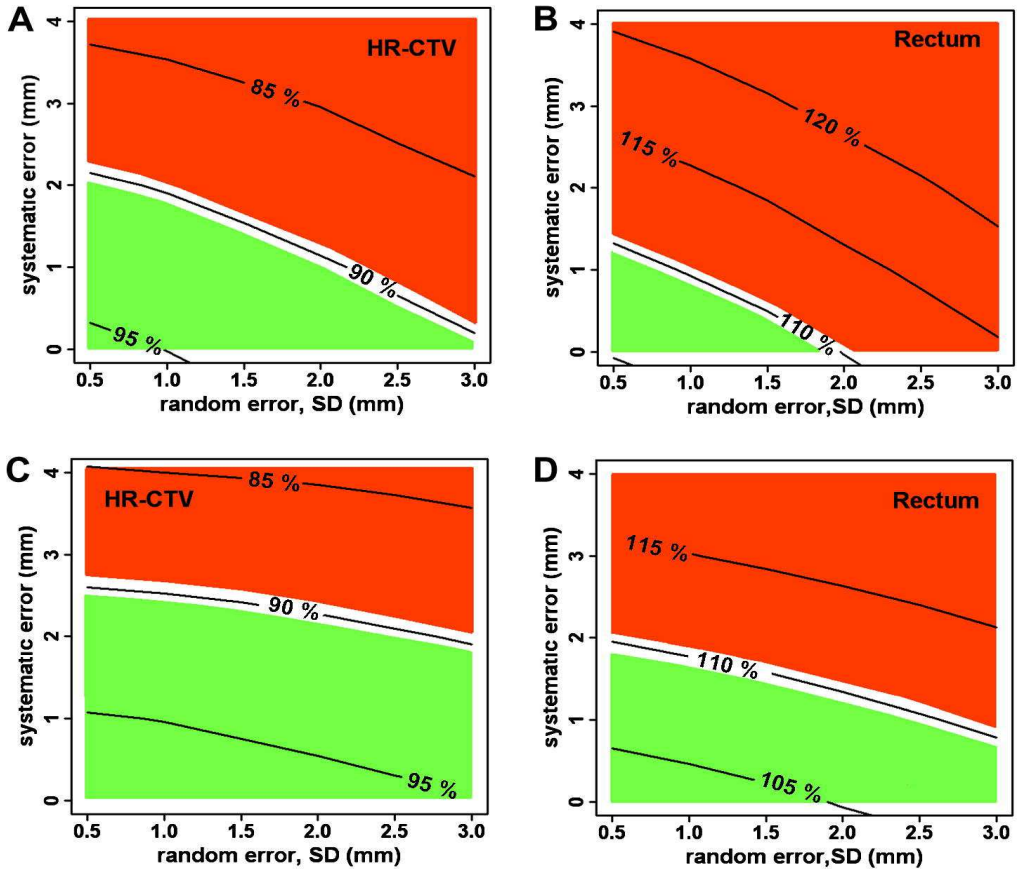
- Have the same influence in every brachytherapy fraction
  - Errors in application commissioning process
  - MR distorsions
  - Incorrect reconstruction procedure
  - Magnification errors

Random errors

- Uncertainties that differ between brachytherapy sessions
  - Visibility of the applicator
  - Accuracy of image fusion
  - MR distorsions related to patient specific interaction with magnetic field

1 fraction





4 fractions

Tanderup Radiother Oncol 2008

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Temporal Uncertainties

Inter-application variation

Variation occuring between subsequent applications

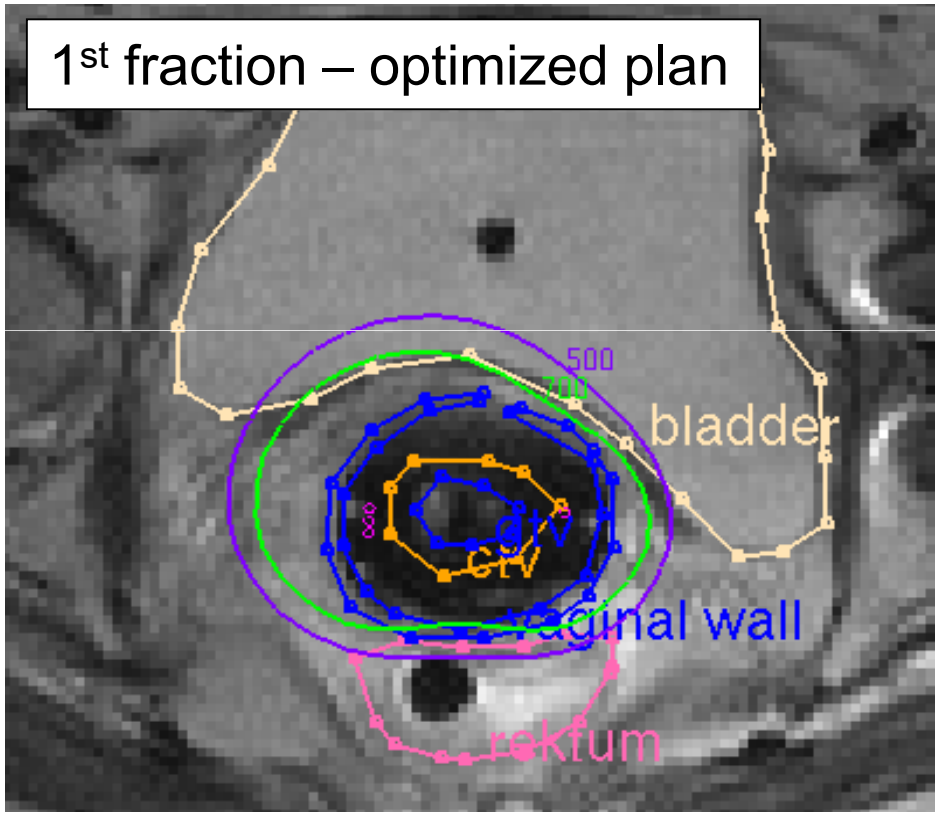
Intra-application variation

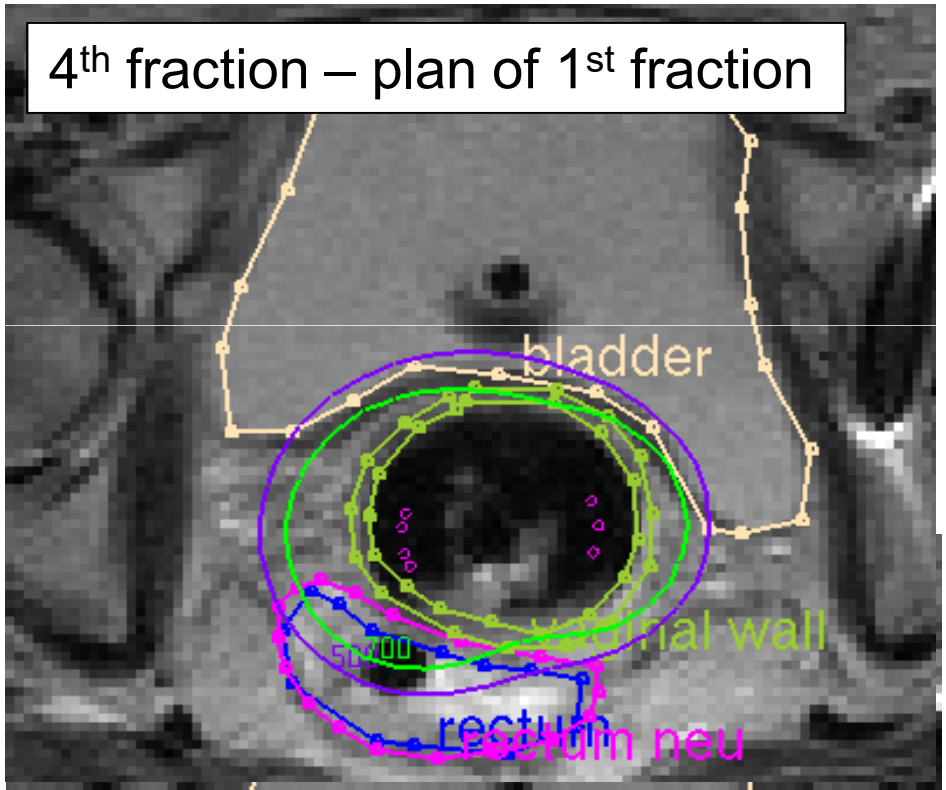
Variation during the same applicator insertion

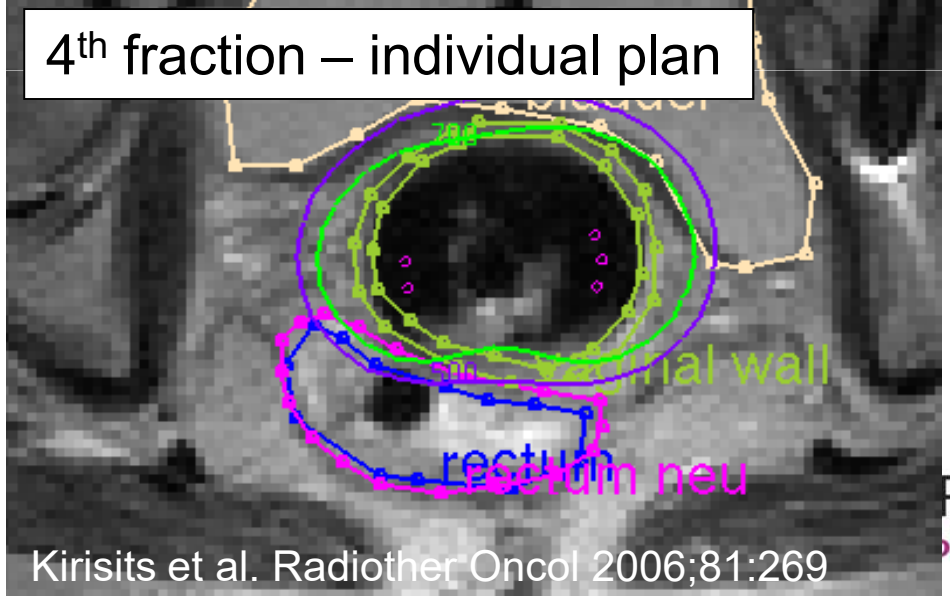
Variation between imaging and dose delivery

- LDR and PDR brachytherapy
- Fractionated HDR brachytherapy (prostate/Gyn)

Inter-application variation



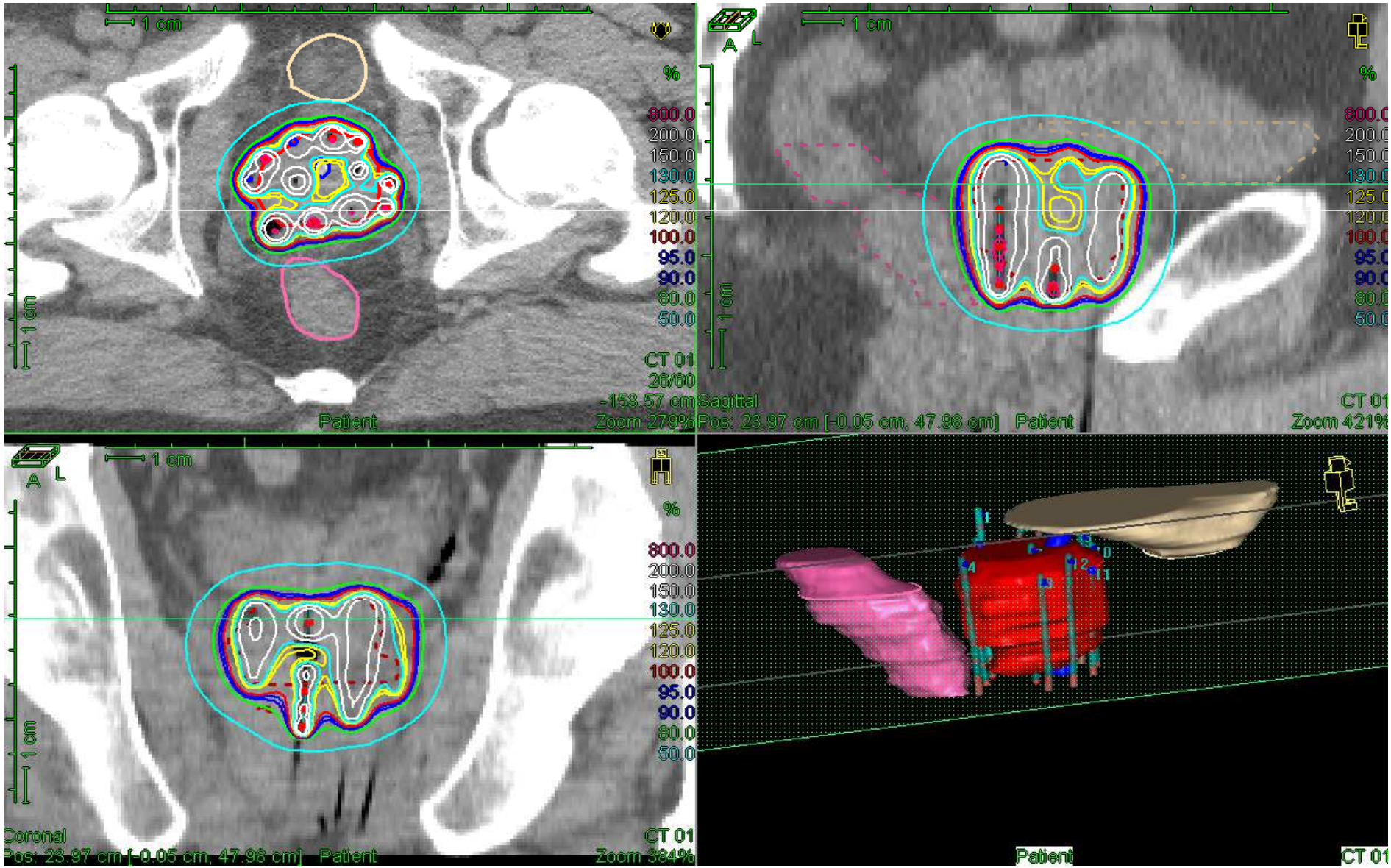




Rectum	D_{2cc} [Gy]	ICRU [Gy]
1st fraction	4.7	3.3
4th fraction		
plan of 1st frac.	8.3	6.5
individual plan	4.9	3.6

Kirisits et al. Radiother Oncol 2006;81:269

Rectum Dose Variation



By courtesy of A. Dinkla

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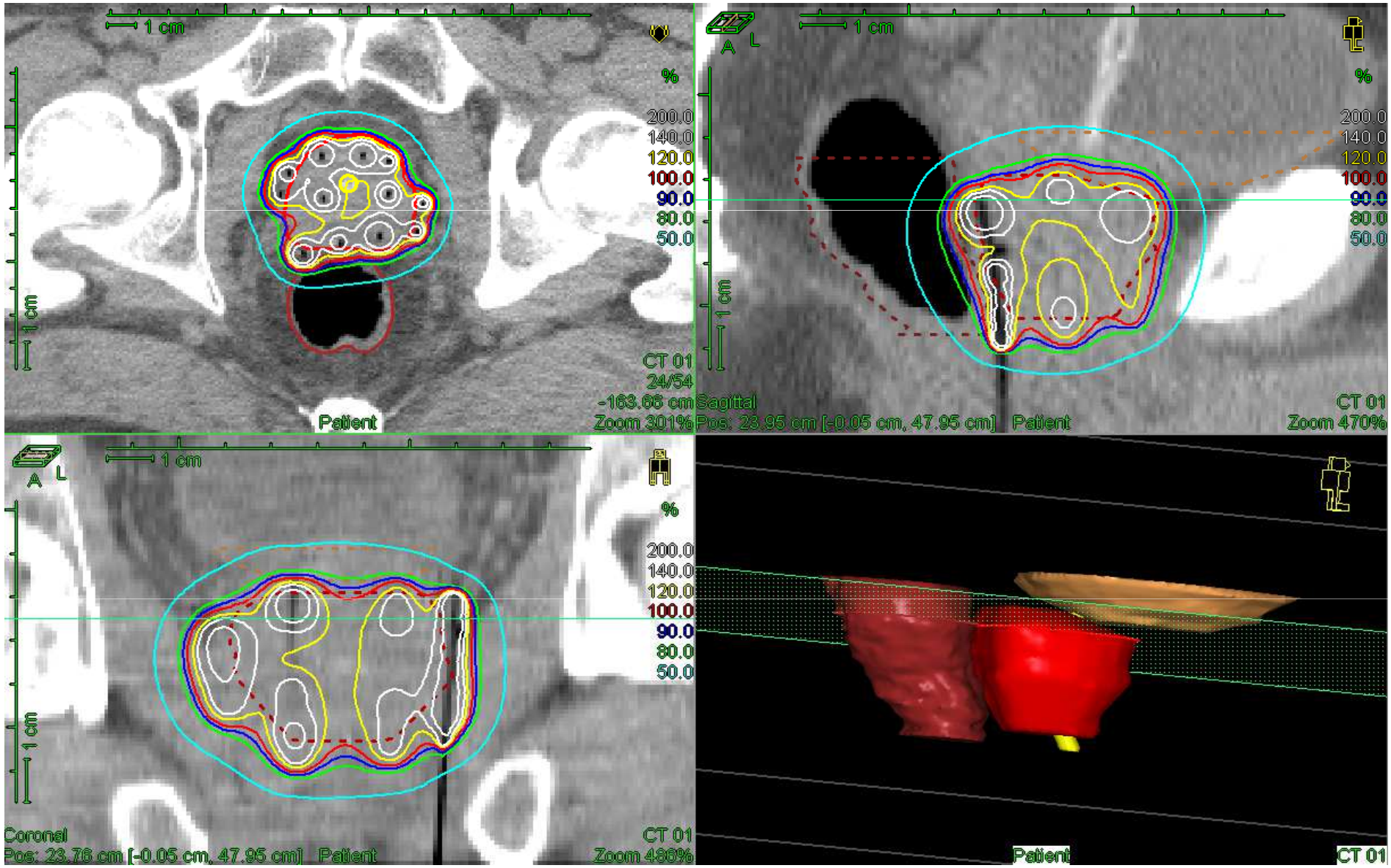
Rectum Dose Variation



By courtesy of A. Dinkla

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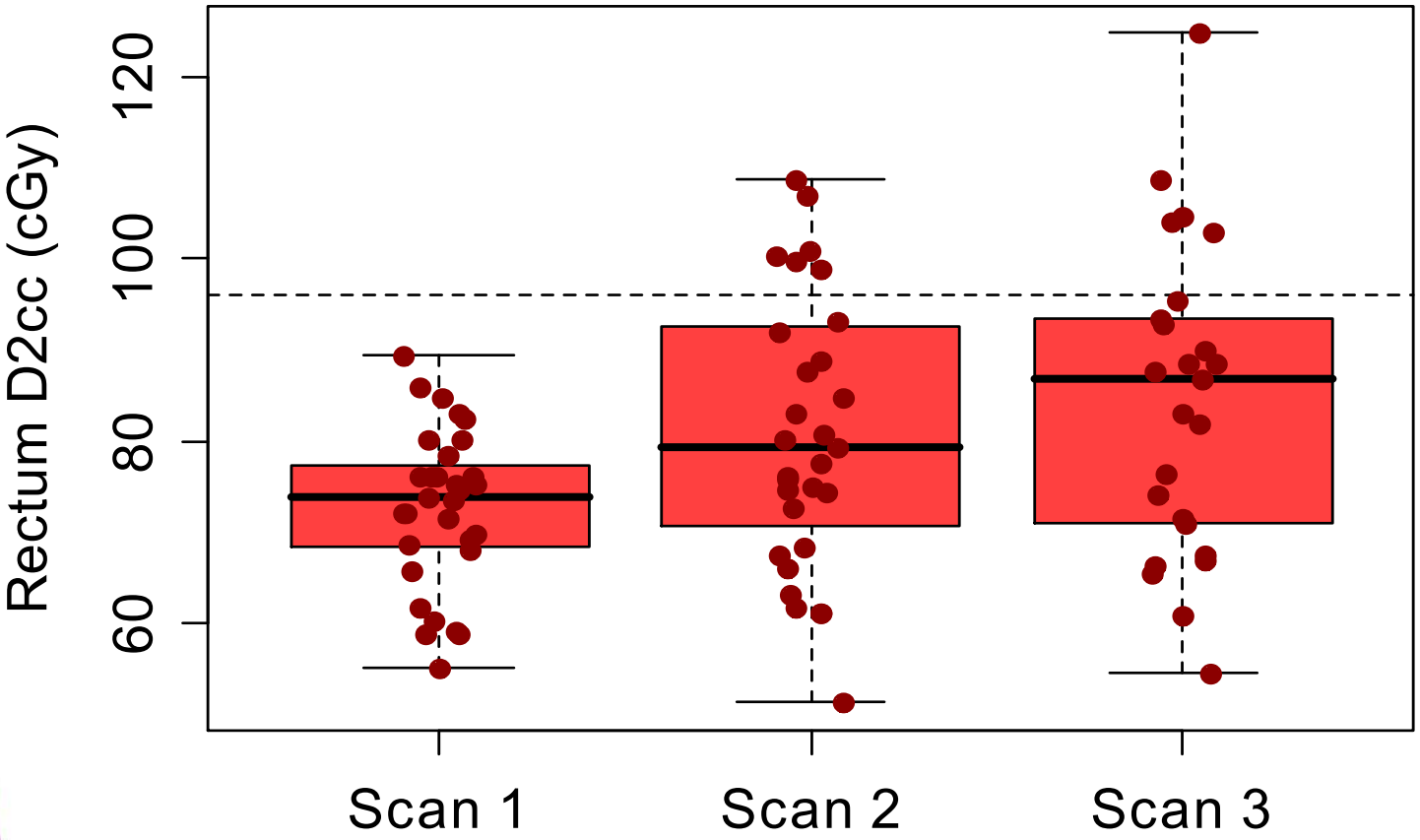
Variation rectum D2cc

Rectum dose underestimated at planning



A. Dinkla. Radiother Oncol 2013;107: 106-111

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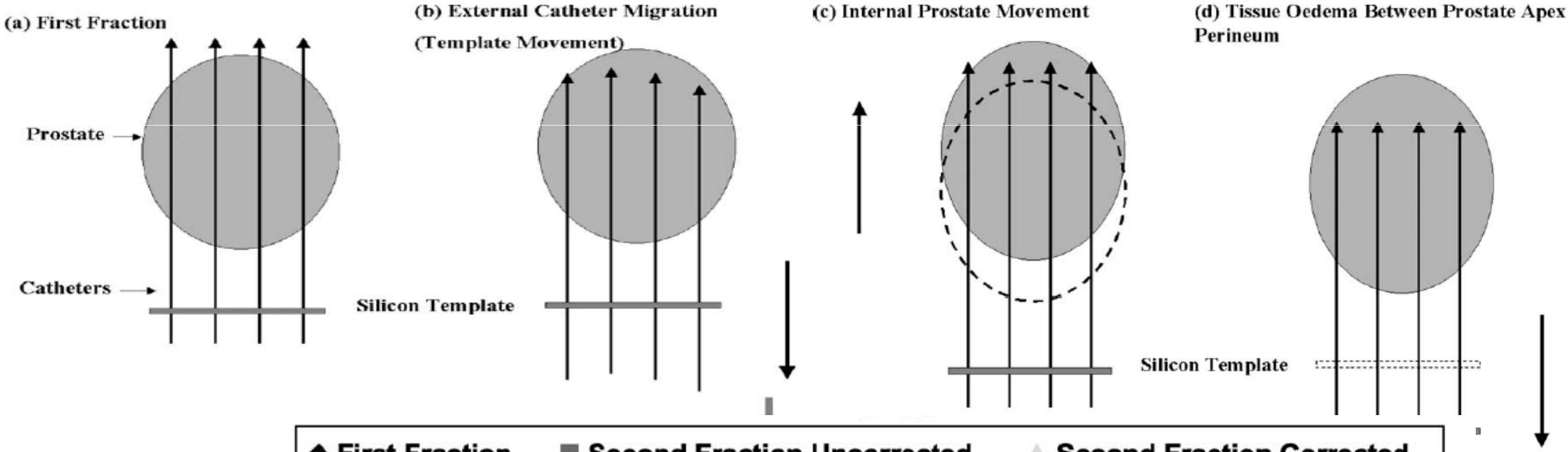
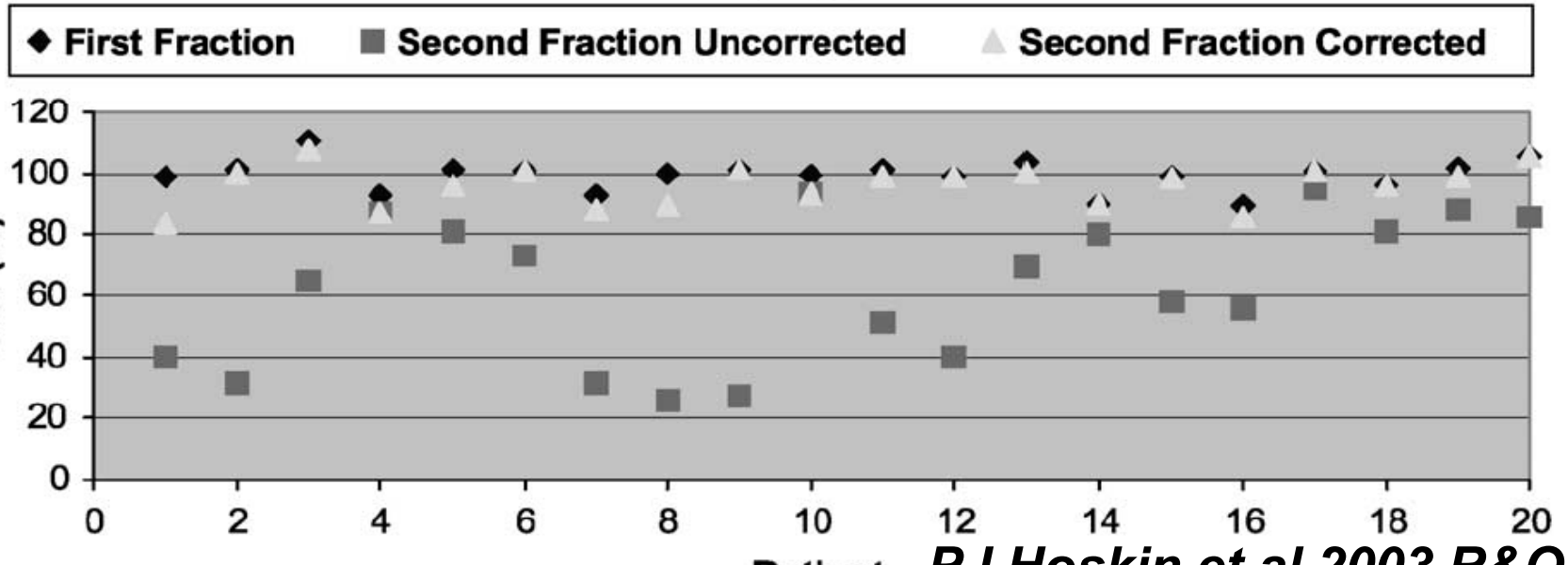
Fractionated HDR afterloading BT for prostate cancer: **intra-application variation**: catheter and gland movement between fractions





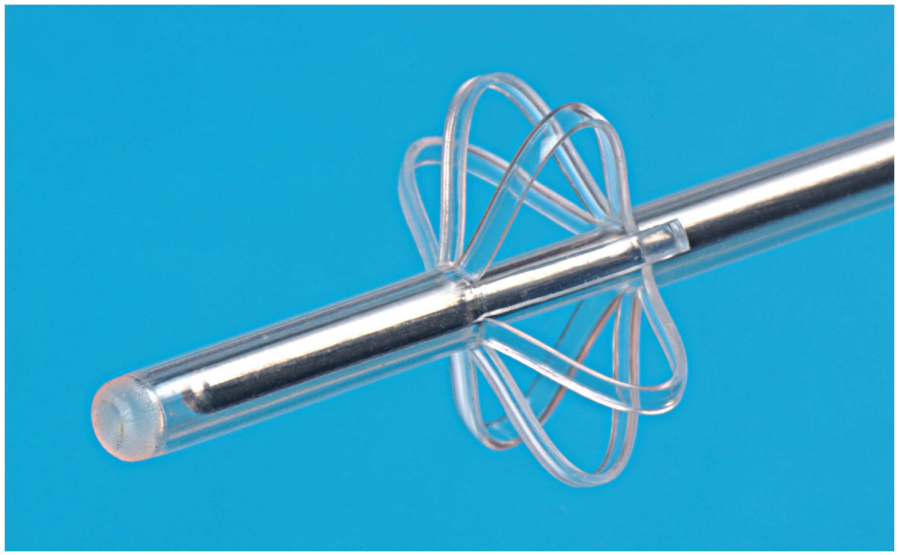
First fraction
Second fraction no corrective action
Second fraction afte corrective action

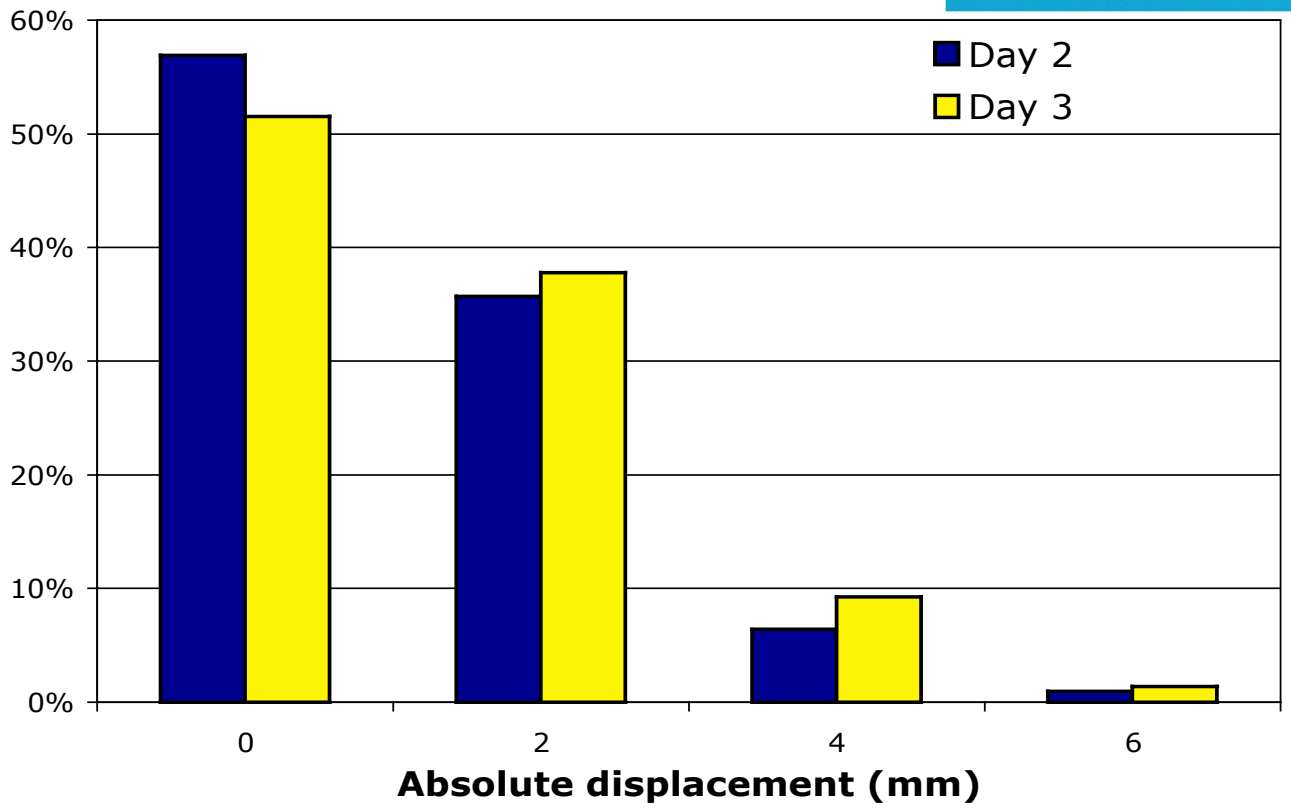
e (Gy)
7 (6.4)
(6.5)
4 (6.35)

TRO ool

PJ Hoskin et al 2003 R&O

Catheter Displacement





602 measurements

Mean absolute displacement
Day 2: 1.0 mm
Day 3: 1.2 mm

Pieters et al, R&O, 2006;80:69

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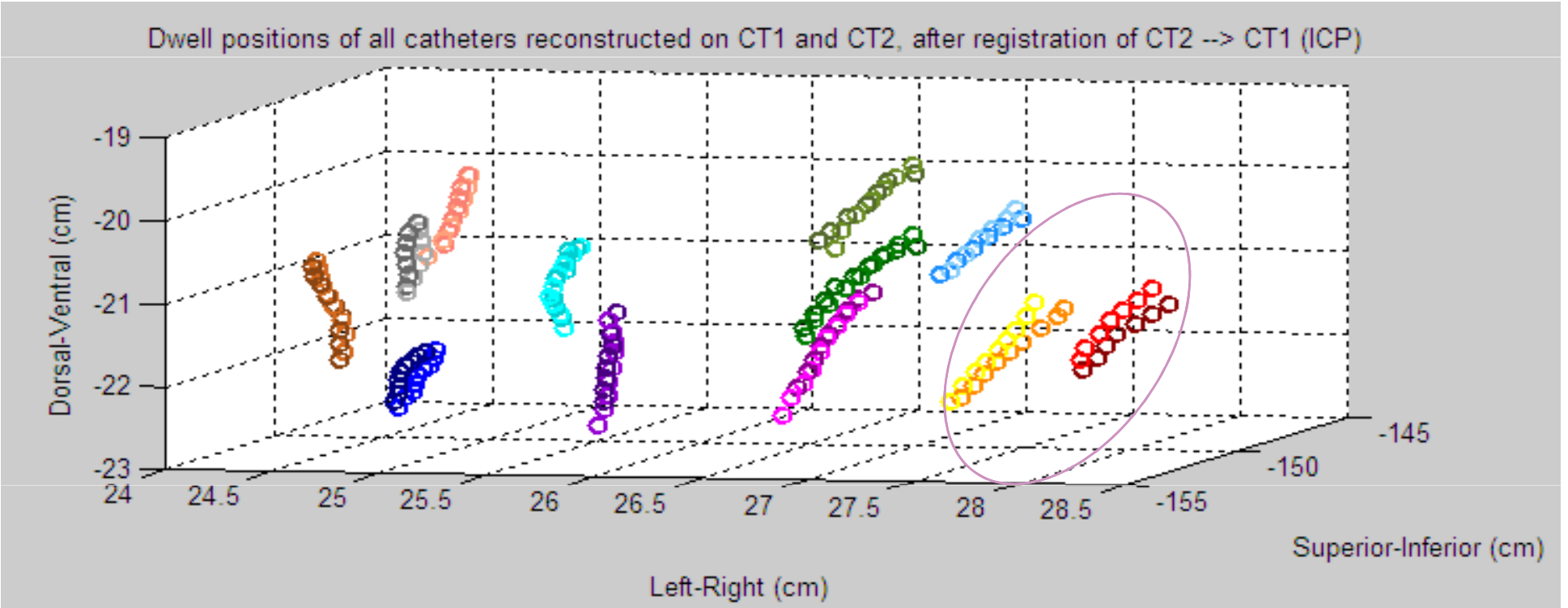
No shift of dwell positions during treatment



By courtesy of A. Dinkla

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Planned dose vs averaged over 3 scans

	Planning CT	Average	Mean difference	p
V100 (%)	95.5 [94.1-96.9]	94.2 [93.0-95.3]	-1.2 [-1.9:-0.6]	NA
V100 (cc)	32.4 [28.6-36.1]	31.8 [28.3-35.4]	-0.5 [-0.9:-0.1]	0.02
D90 (cGy)	132.1 [129.6:134.7]	128.9 [126.8:130.9]	-3.3 [-4.8:-1.8]	0.00

PTV remains constant

V100 and D90 lower on follow-up scans

No large decrease in V100

A. Dinkla. Radiother Oncol 2013;107: 106-111

Dosimetric impact of inter- and intra-fractional anatomical variations

Structure ΔD2cm3 between 2 acquisitions [%] (fixed plan, variable anatomy)

	Intra-application only		Inter-application only		Total	
	Mean	SD	Mean	SD	Mean	SD
Bladder	.3	±7.7	0.1	±21.2	0.6	±19.5
Rectum	.8	±20.5	.3	±22.3	4.1	±21.7
Sigmoid	2.3	±23.5	.8	±30.2	1.6	±26.8

ΔD90 between 2 acquisitions [%] (fixed plan, variable anatomy)

	Intra-application only		Inter-application only		Total	
	Mean	SD	Mean	SD	Mean	SD
HR CTV	-2.5	±10.8	0.4	±15.1	-1.1	±13.1

System Random

Cervix cancer

Nesvacil et al. Radiother Oncol 2013;107:20-25

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Image Guided Brachytherapy basic issues

„CTV is equal to PTV“:

Applicators/sources move with the target as they are fixed into the target tissue

Minor geometric uncertainties

Consider

Contouring uncertainties

Reconstruction uncertainties/errors

Distorsions

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Image Guided Brachytherapy basic issues

Internal Organ motion and **changes induced by intervention**

represent major uncertainties:
oedema (prostate/Gyn),
organ filling status: bladder, (rectum), sigmoid, bowel
organ movement: sigmoid, bowel

Consider
Interapplication variation
Interfractional variation

Results Retropubic Prostate Implants

MSKCC

- Local failure 48%

NKI

- Local failure 52%

Poor seed distribution. Quality of implant poor.
Abandonment in early 80s

Biochemical control in low risk prostate cancer treated by seeds implant

D'Amico	*1998*	*85%*
Blasko	*2000*	*92%*
Merrick	*2001*	*96%*
Potters	*1999*	*92%*
Zelefsky	*2000*	*88%*
Blank	*2000*	*95%*
Grimm	*2001*	*85%*

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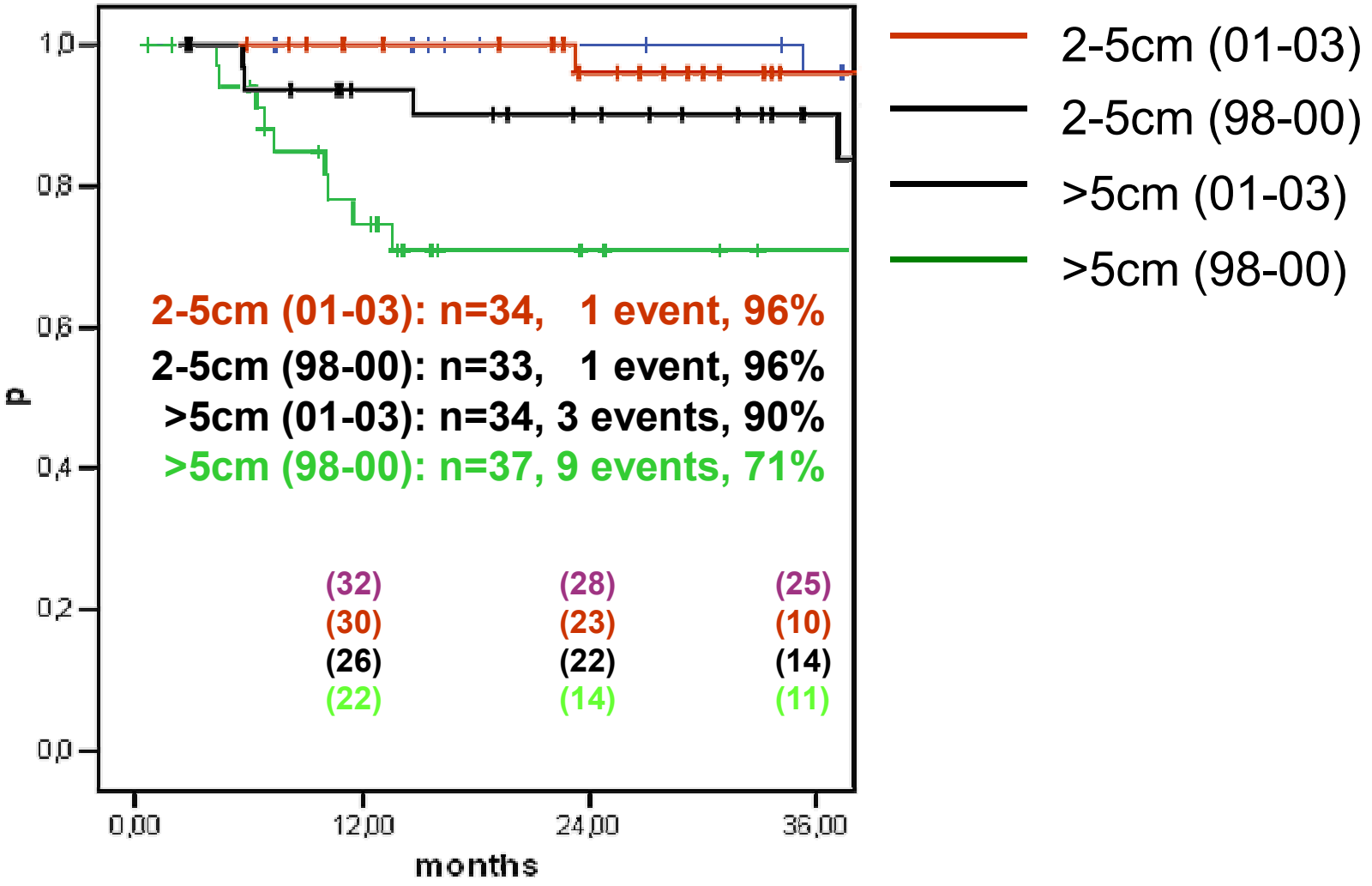
Dose Optimization with MRI Based Planning

	X-ray	MRI/optimized
HR-CTV D90	76 Gy	79 Gy
IR-CTV D90	65 Gy	69 Gy
Bladder D2cc	86 Gy	82 Gy
Rectum D2cc	59 Gy	62 Gy
Sigmoid D2cc	70 Gy	68 Gy

Mean values

De Brabandere Radiother Oncol 2008

Cervix Cancer: MRI based Brachytherapy + 3D CRT +/- Chth
Vienna series 1998-2003: n=145
CCR true pelvis / treatment period and tumor size



Pötter et al. R&O, 2007;83:148-155

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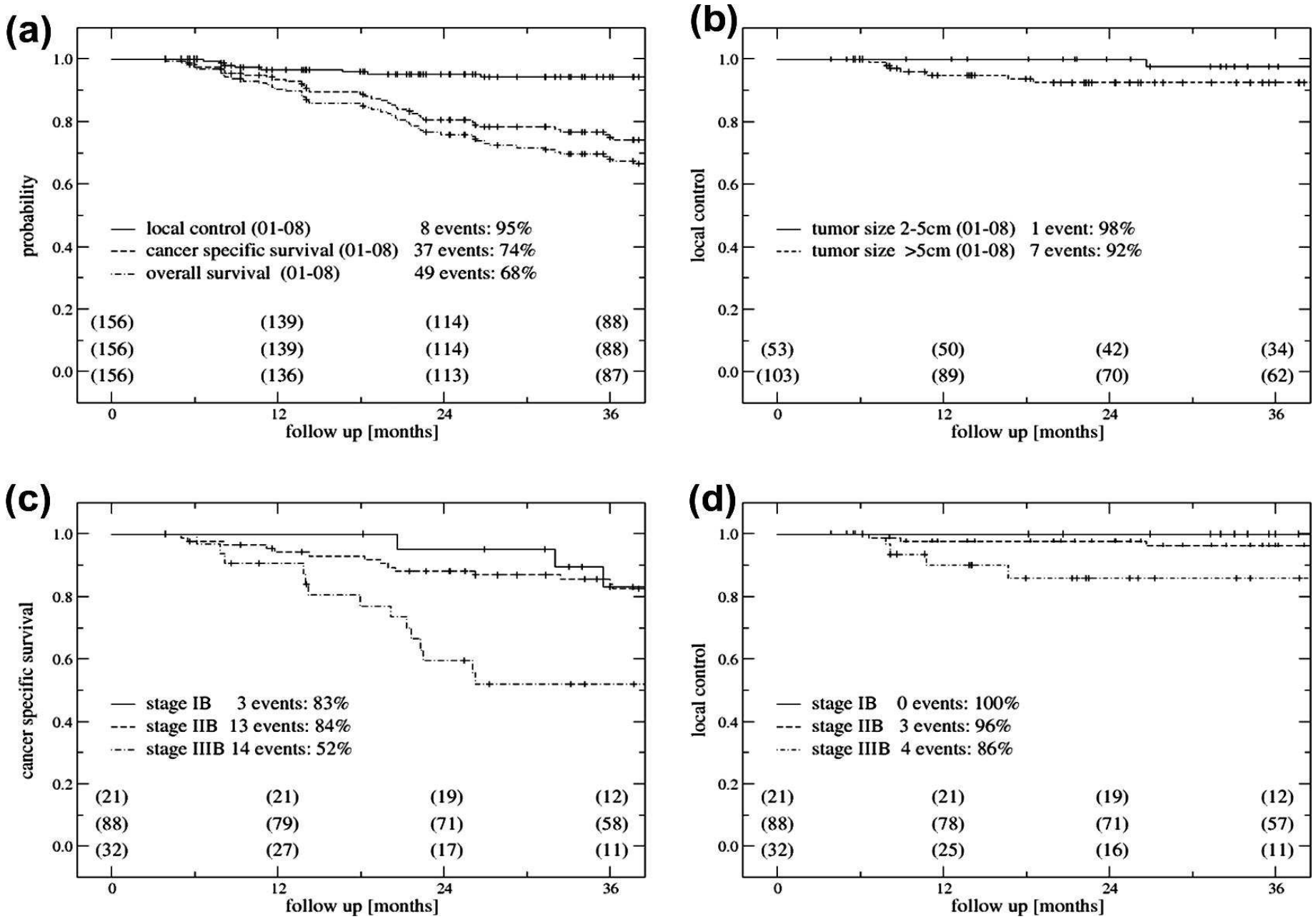

Pötter et al. Radiother Oncol, 2011;100:116-123

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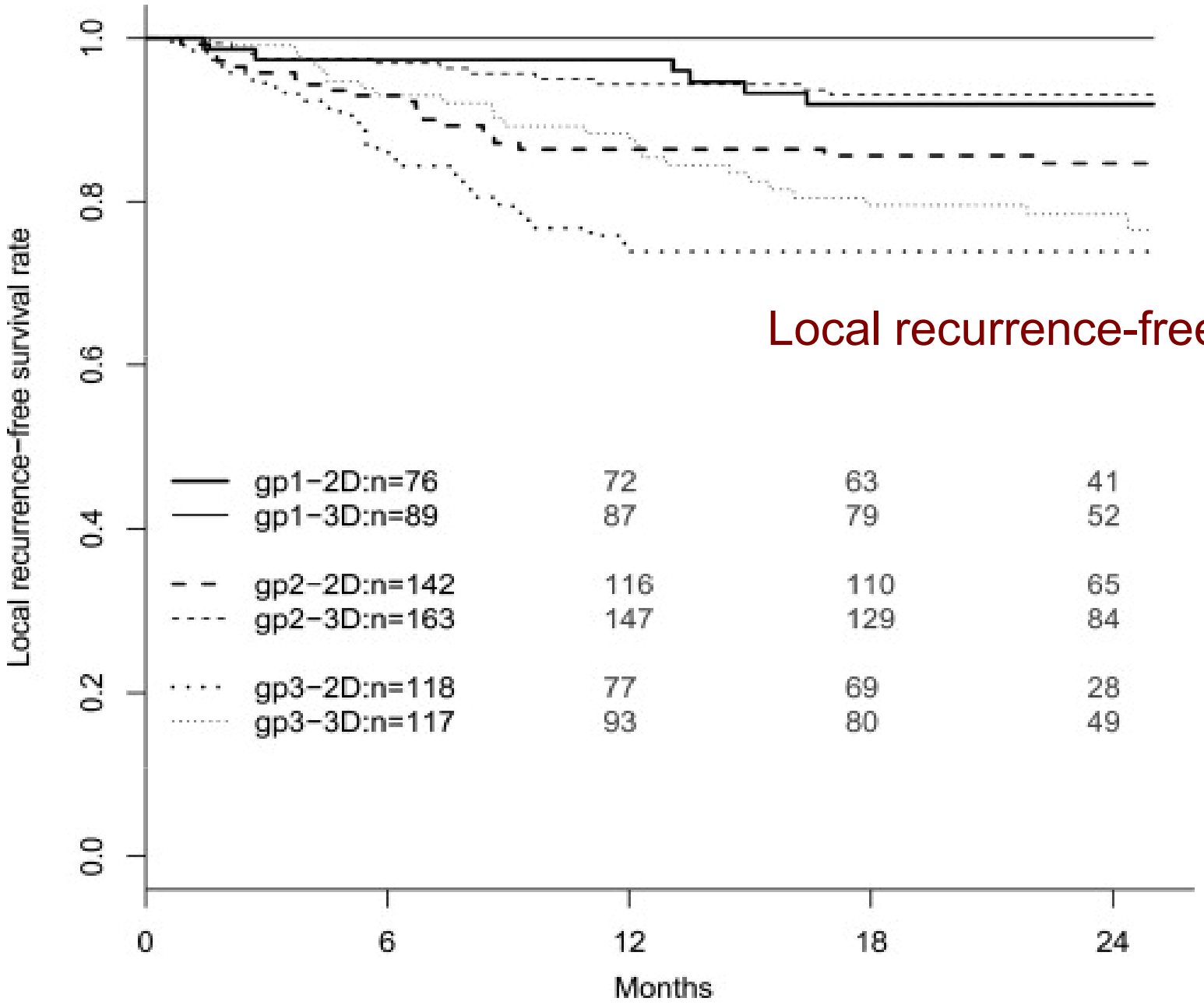

Local recurrence-free survival

Multicenter French study

Charra-Brunaud, R&O 2012;103, 305-313

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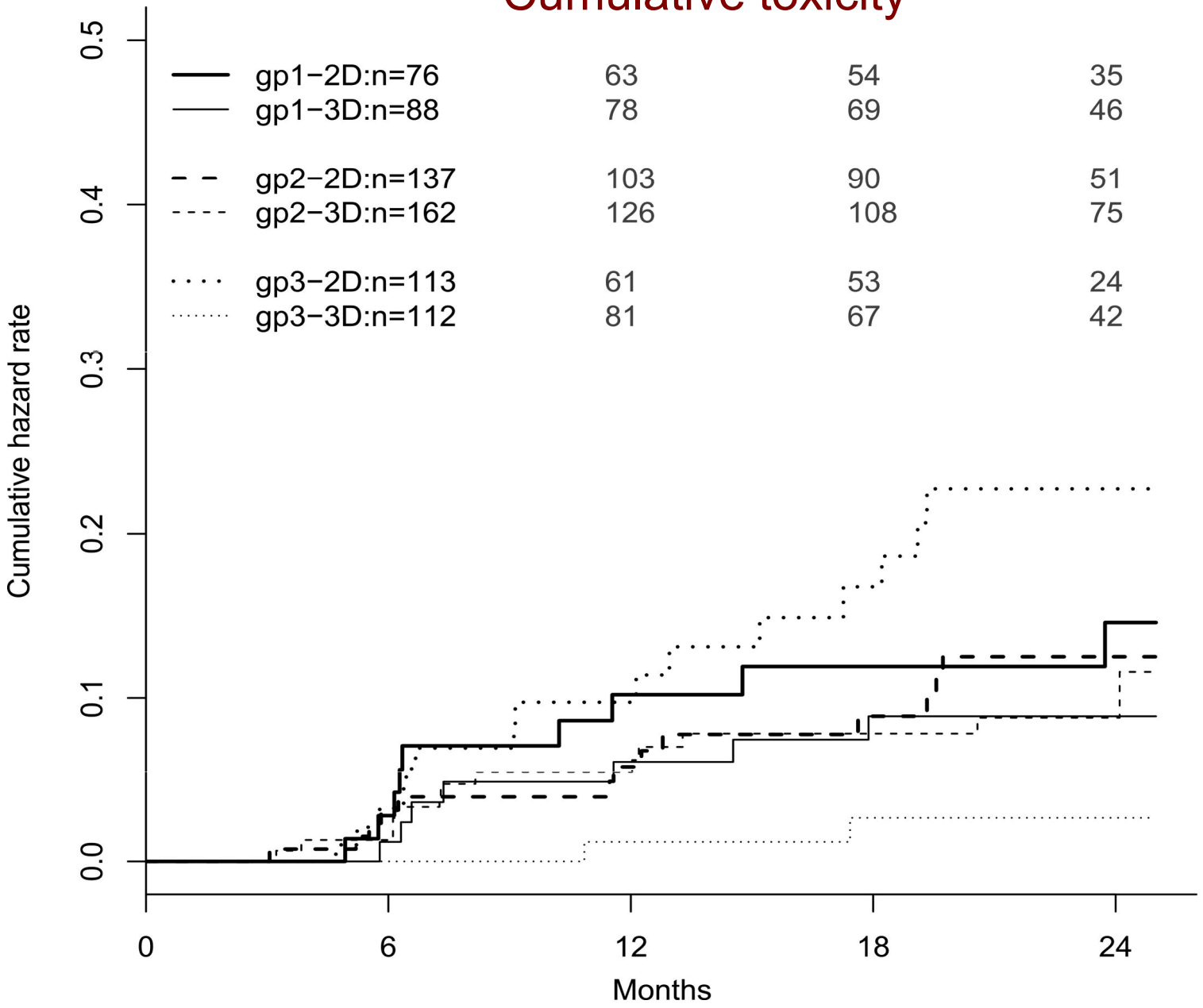
Cumulative toxicity



Multicenter French study

Charra-Brunaud, R&O 2012;103, 305-313

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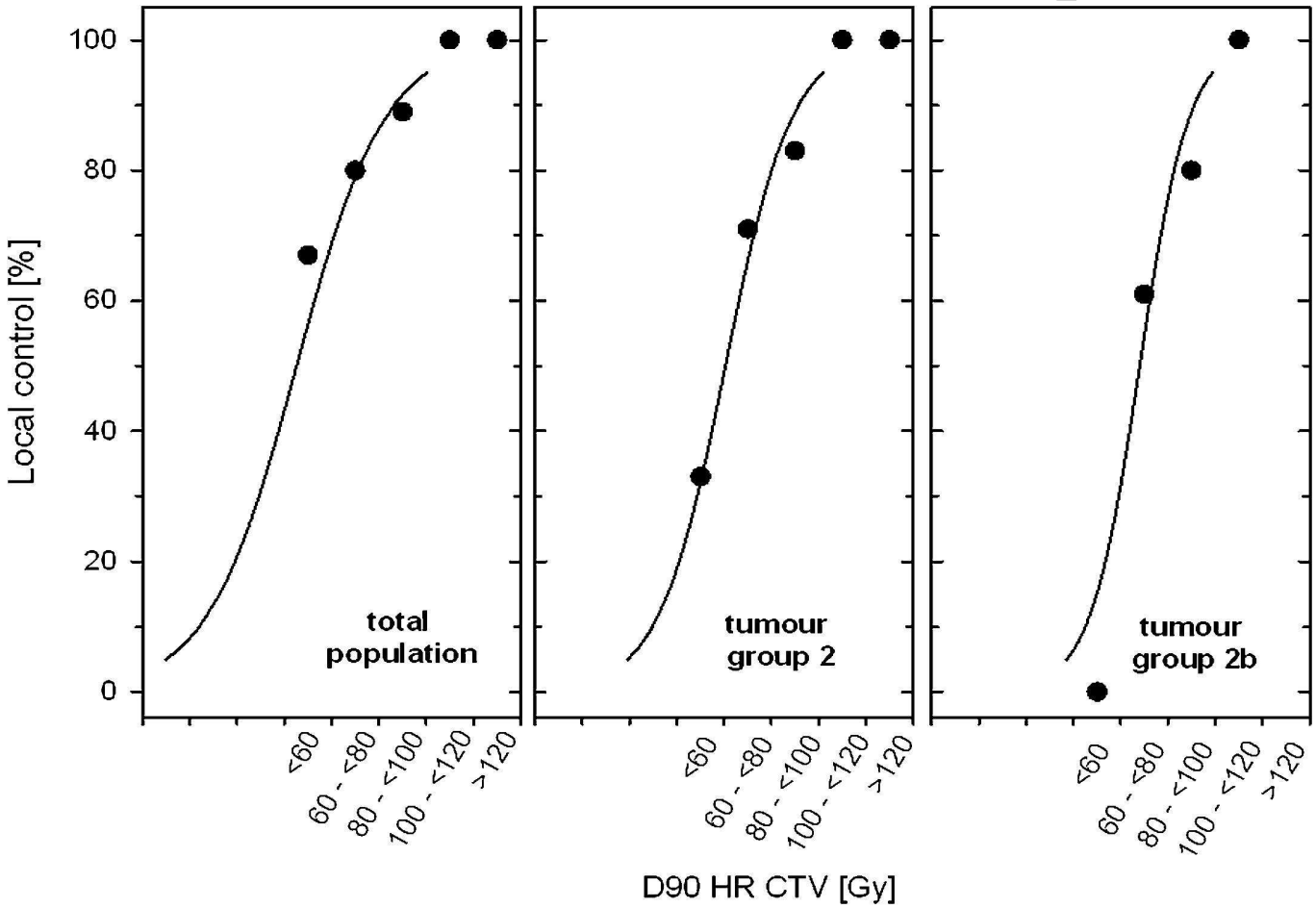
Dose-effect relationship



Dimopoulos et al., Radiother Oncol 2009;93:311

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New Developments

Image-guided Brachytherapy

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DCE-MRI

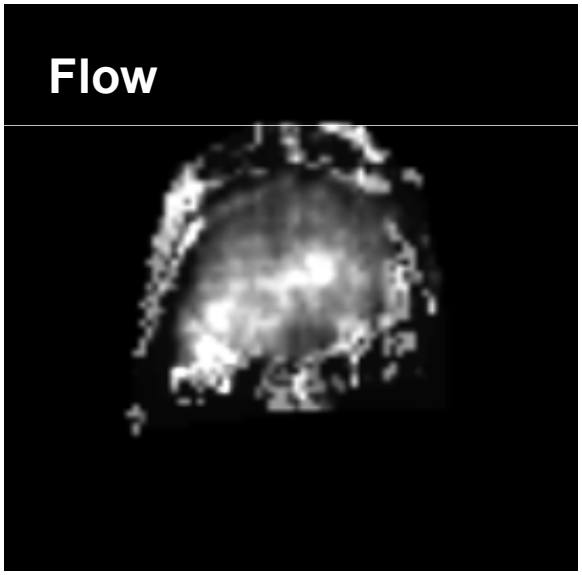
Microvessels in carcinoma versus benign tissue: ratio 2.0

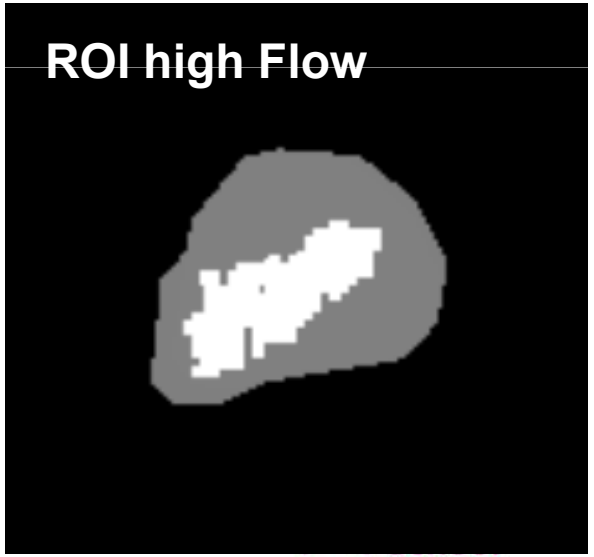
(Bigler 1993)

Probably due to angiogenesis

Degree of vascularization corresponds with

- aggressive behavior
- risk of metastasis





Resolution: high

Measuring time: short (5 min)

Treshold e.g.Flow > 20 ml/100g

By courtesy of van Vulpen

DWI-MRI

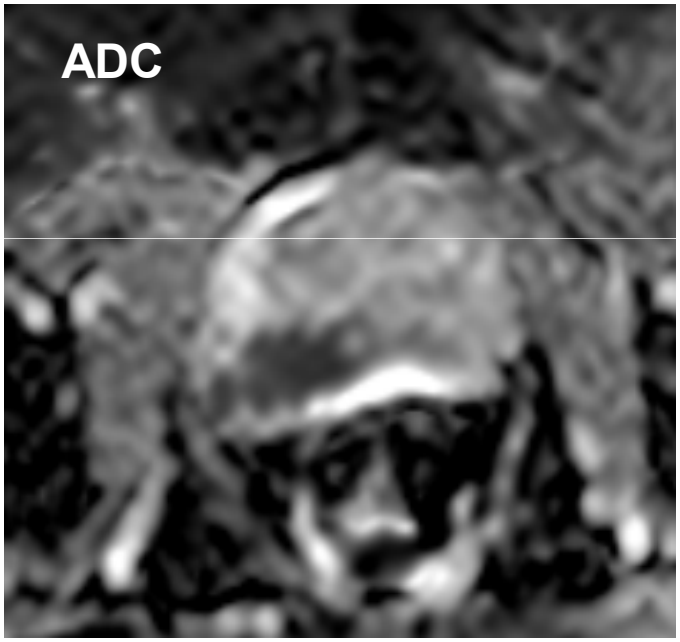
Is water diffusion in tissue

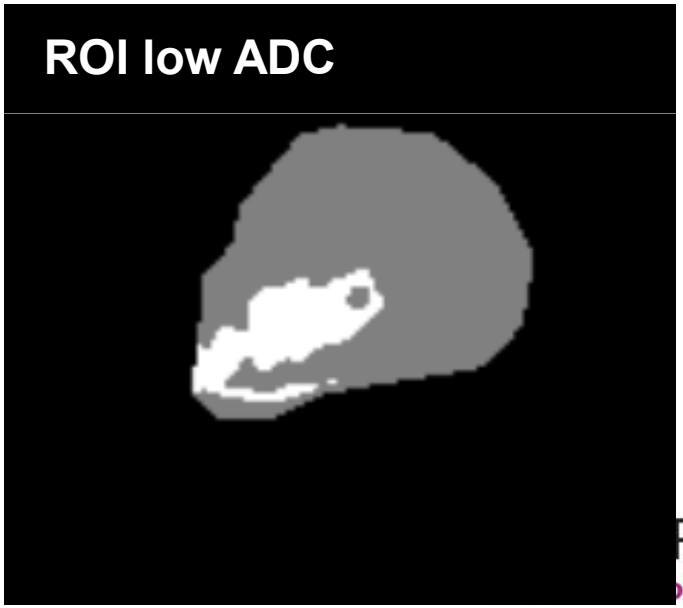
decreased diffusion =
- increased cell density =
- higher malignancy grade

Resolution: high

Measuring time: short (4 min)

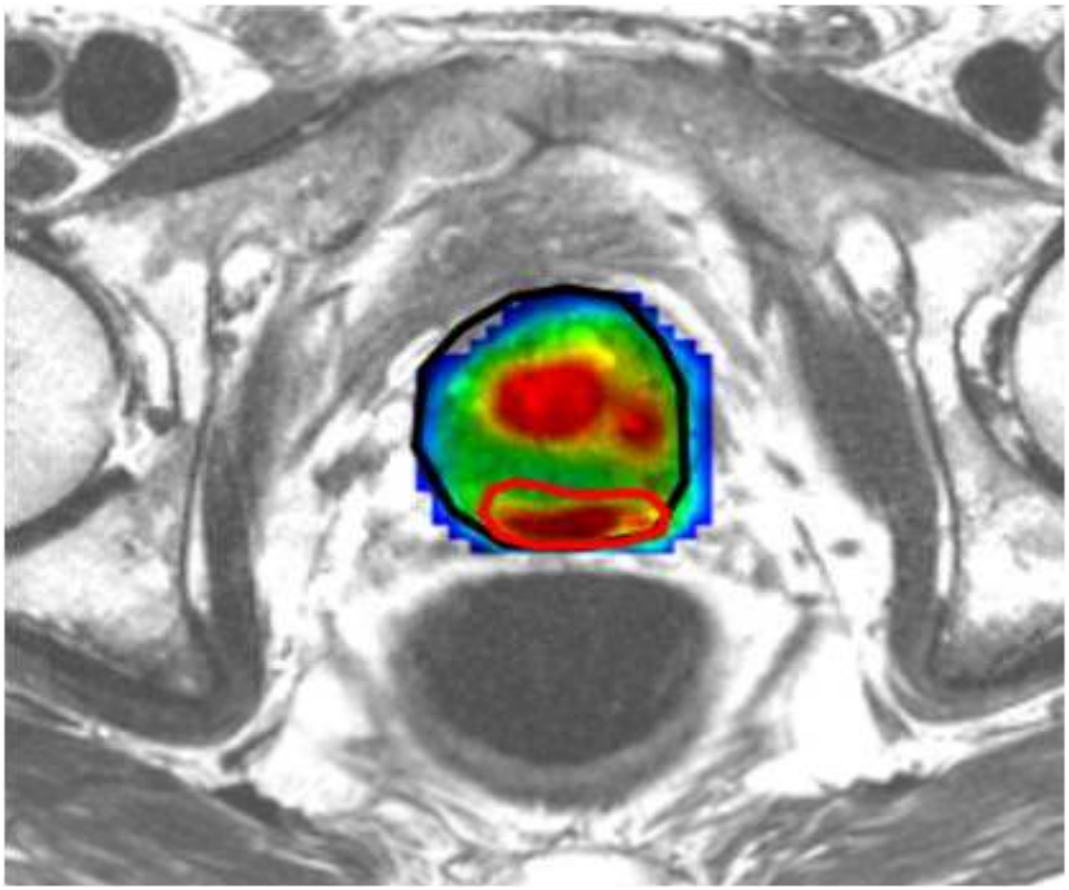
Treshold e.g. ADC < 10^{-3} mm^2/s

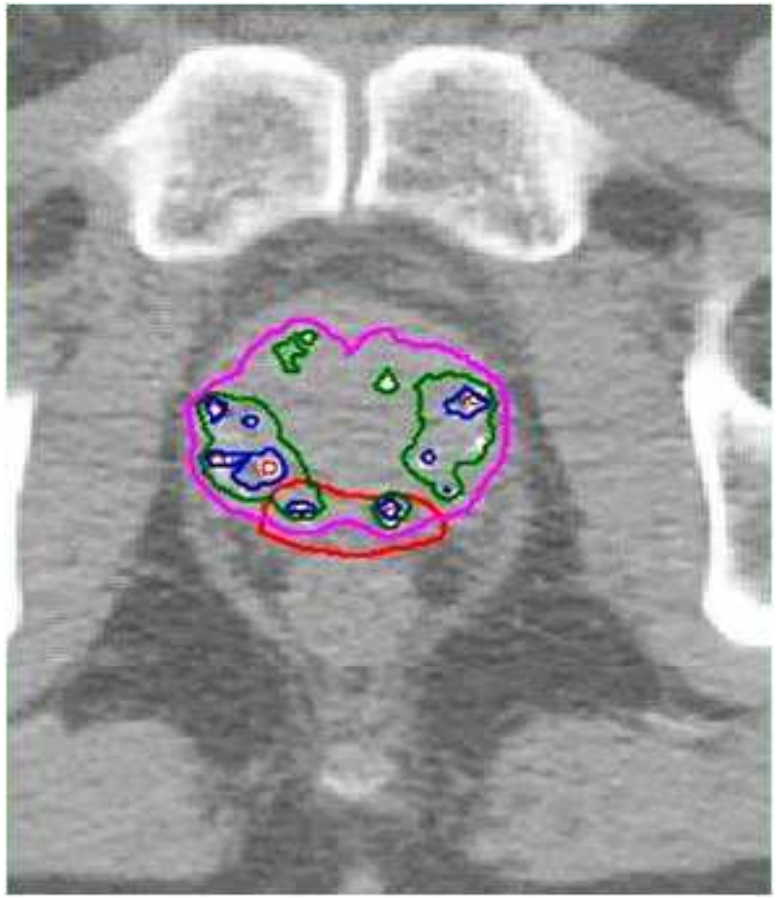




By courtesy of van Vulpen

Establish a I-125 dose effect relationship





By courtesy of van Vulpen

Focal salvage using HDR

Many focal salvage possibillities:

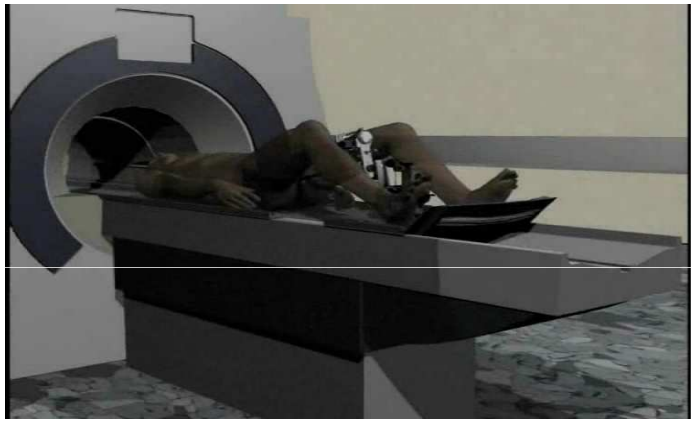
HDR

I-125

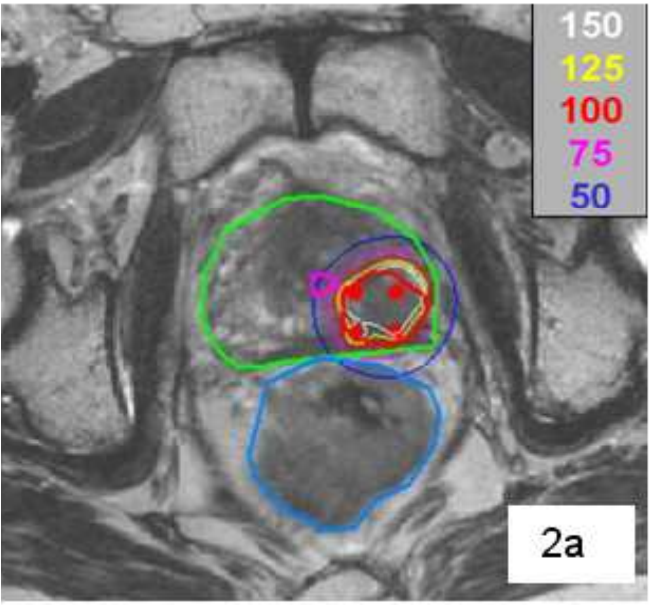
Cryo

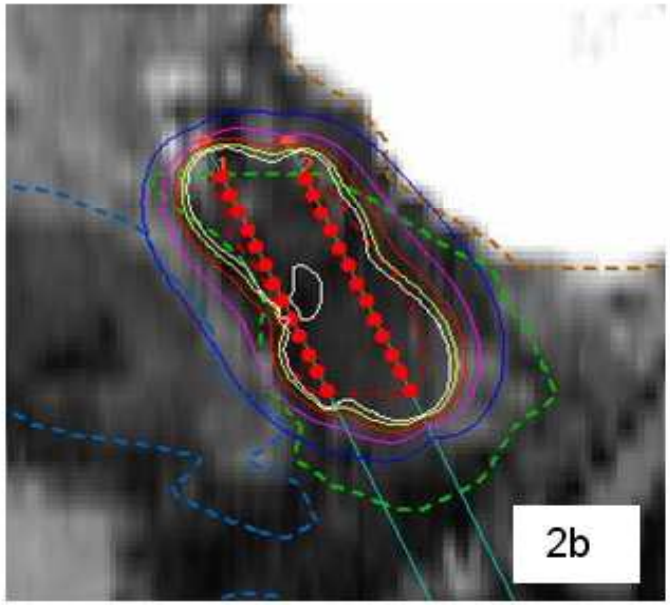
HYFU

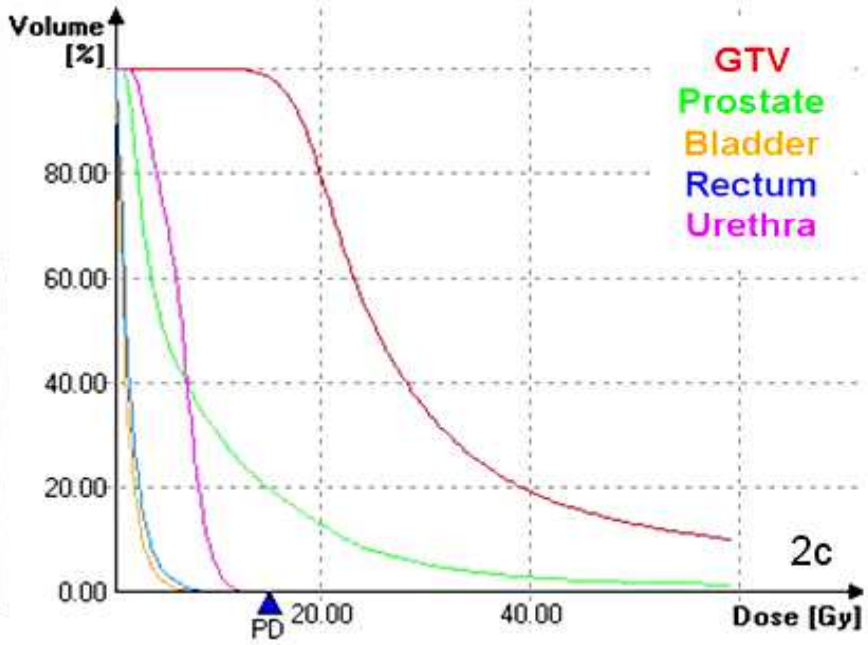
Etc…



(Moman 2009)







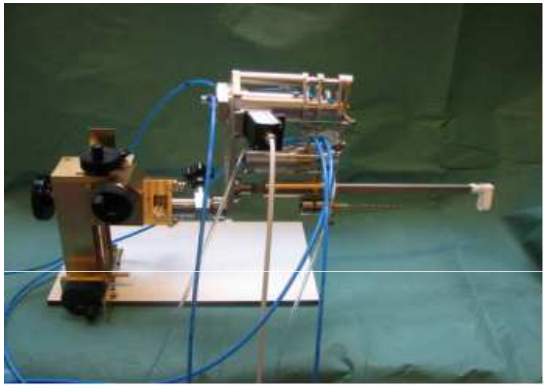
By courtesy of van Vulpen

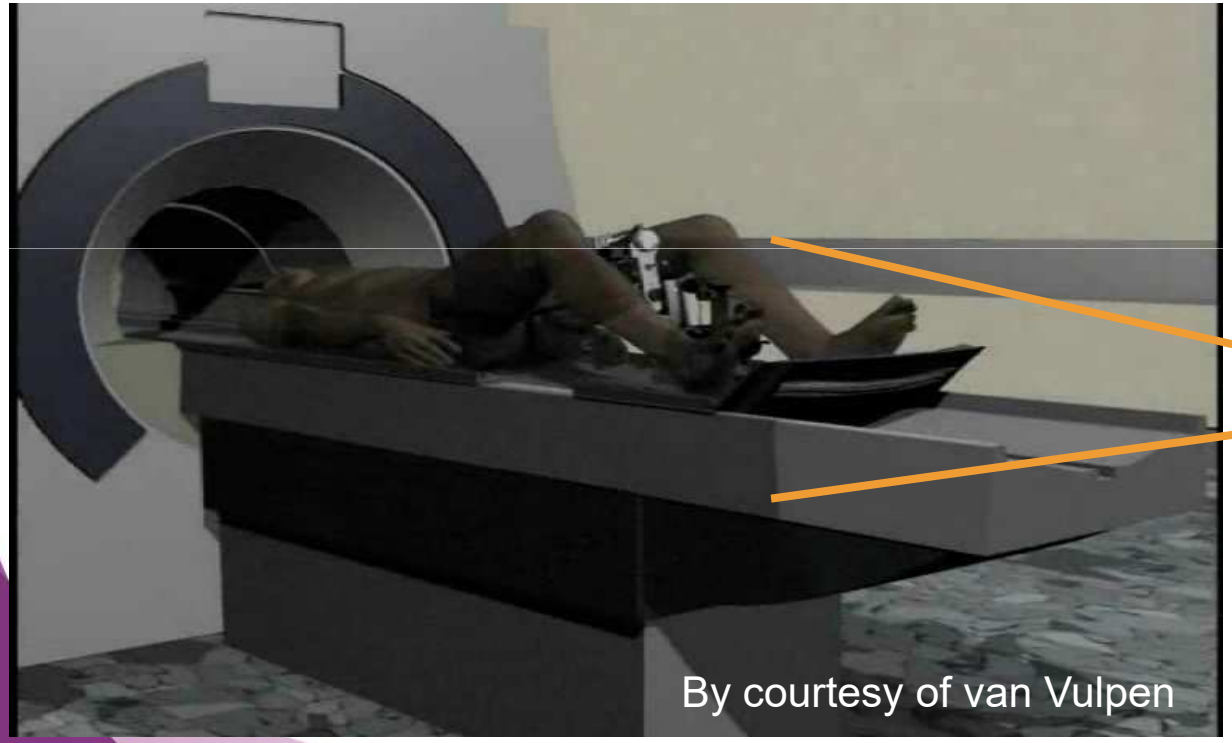
Brachytherapy: MRI compatible robot

MRI guided inverse planning
- Avoid bulbus + neurovasc. bundle

MRI guided brachytherapy
- HDR
- LDR (I-125)

MRI guided biopsies





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Sonovue (Bracco) contrast agent

Philips IU22 ultrasound device

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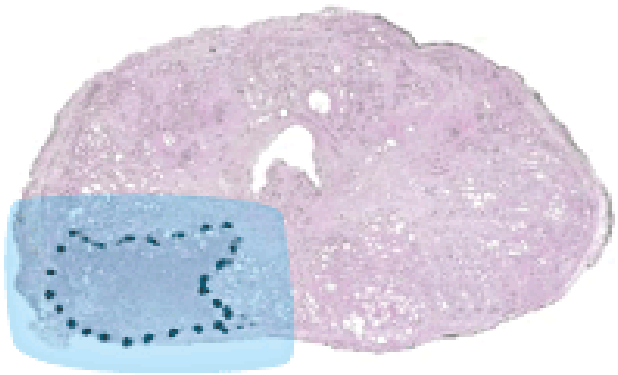
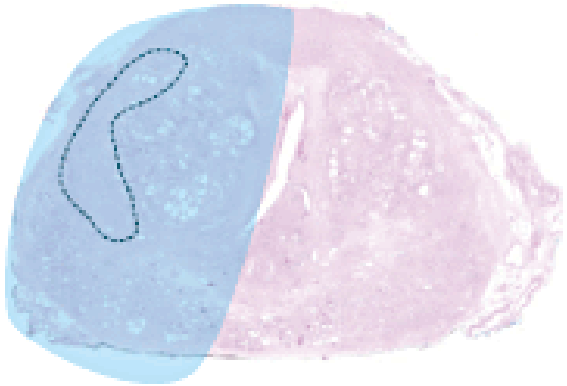
Contrast Enhanced Ultrasound Microvessel Imaging

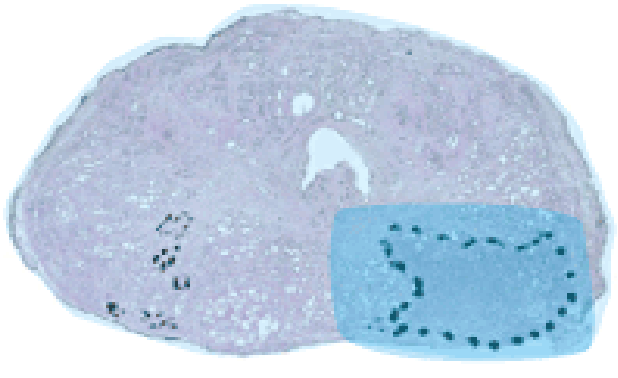
Treatment Plan / Target



Ultra-Focal Therapy



Focal Therapy



Focused Therapy

Langley et al. BJU International 2012

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WWW.ESTRO.ORG/SCHOOL

Brachytherapy for breast cancer

E. Van Limbergen MD, PhD

University Hospital Gasthuisberg

Leuven, Belgium

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Brachytherapy for breast cancer

- BT- Boost Irradiation
  - Postoperative
  - Peroperative
- Accelerated Partial Breast Irradiation
  - Interstitial
  - Intracavitary Balloon

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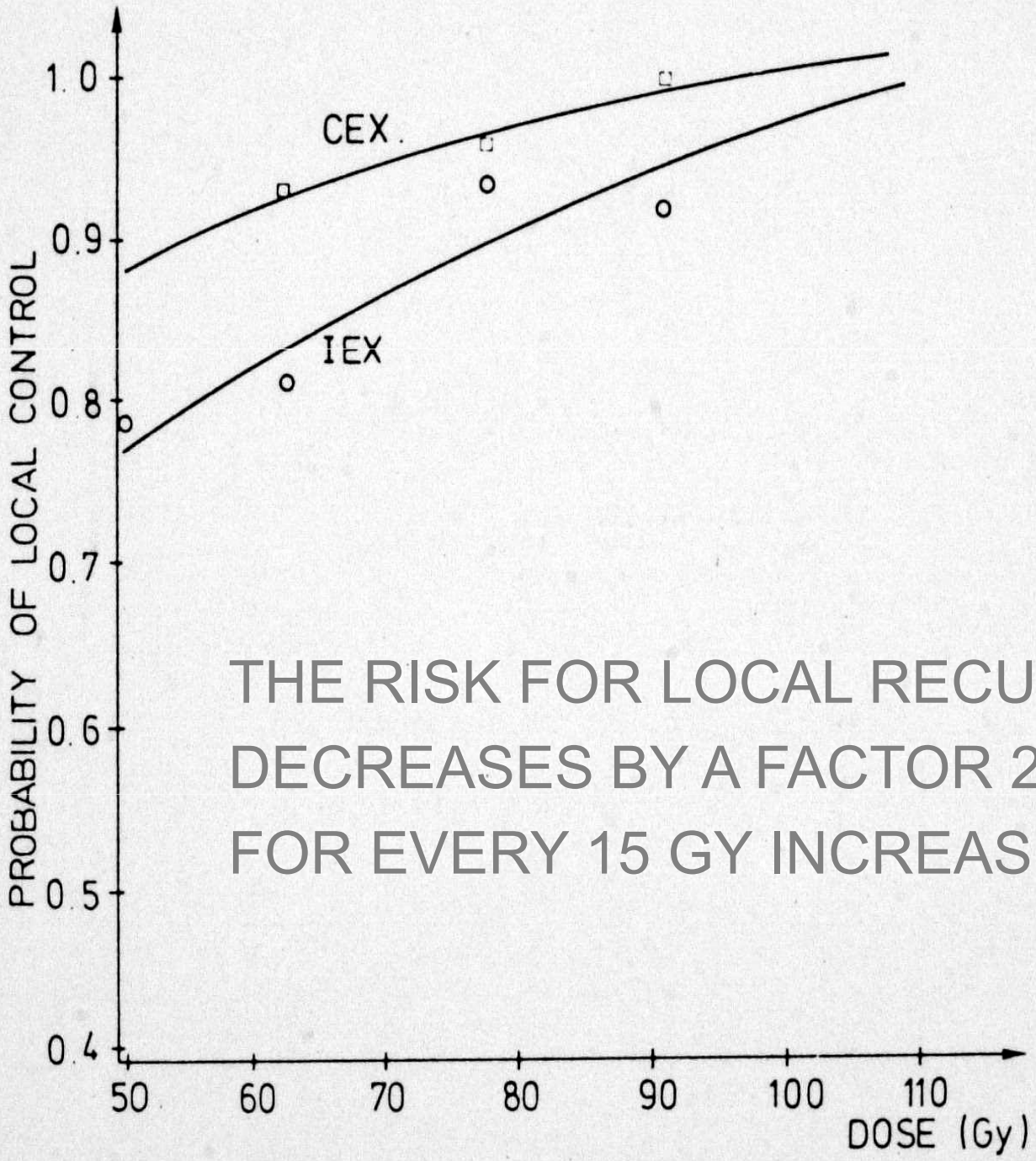


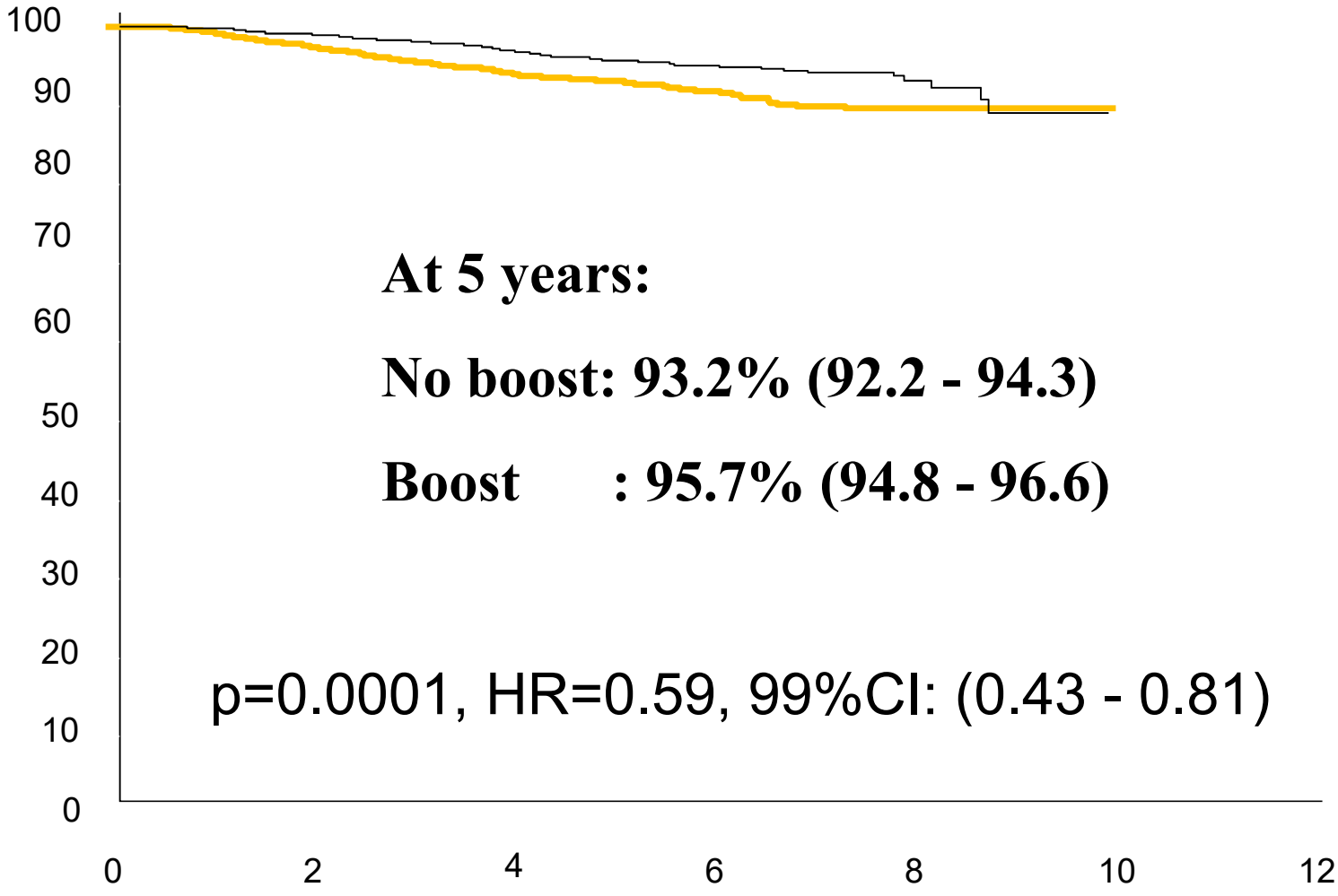
THE RISK FOR LOCAL RECURRENCE
DECREASES BY A FACTOR 2
FOR EVERY 15 GY INCREASE IN DOSE.

Local recurrences after BCS + RT BOOST versus NO BOOST

Randomised Trials		no boost	boost	H.R. :
• Lyon n = 1024	5 y	4.5 %	3.6 % (10 Gy)	0.8 *p = 0.044*
• French M.C. n = 664	5 y	6.8 %	3.6 % (16Gy)	0.53 *p = 0.13*
• EORTC 10801a n = 5569	5 y	6.8 %	3.4% (15Gy)	0.59 *p = 0.0001*
• EORTC 10801b	7y	19%(10 Gy)	9% (25Gy)	

Local Control

EORTC



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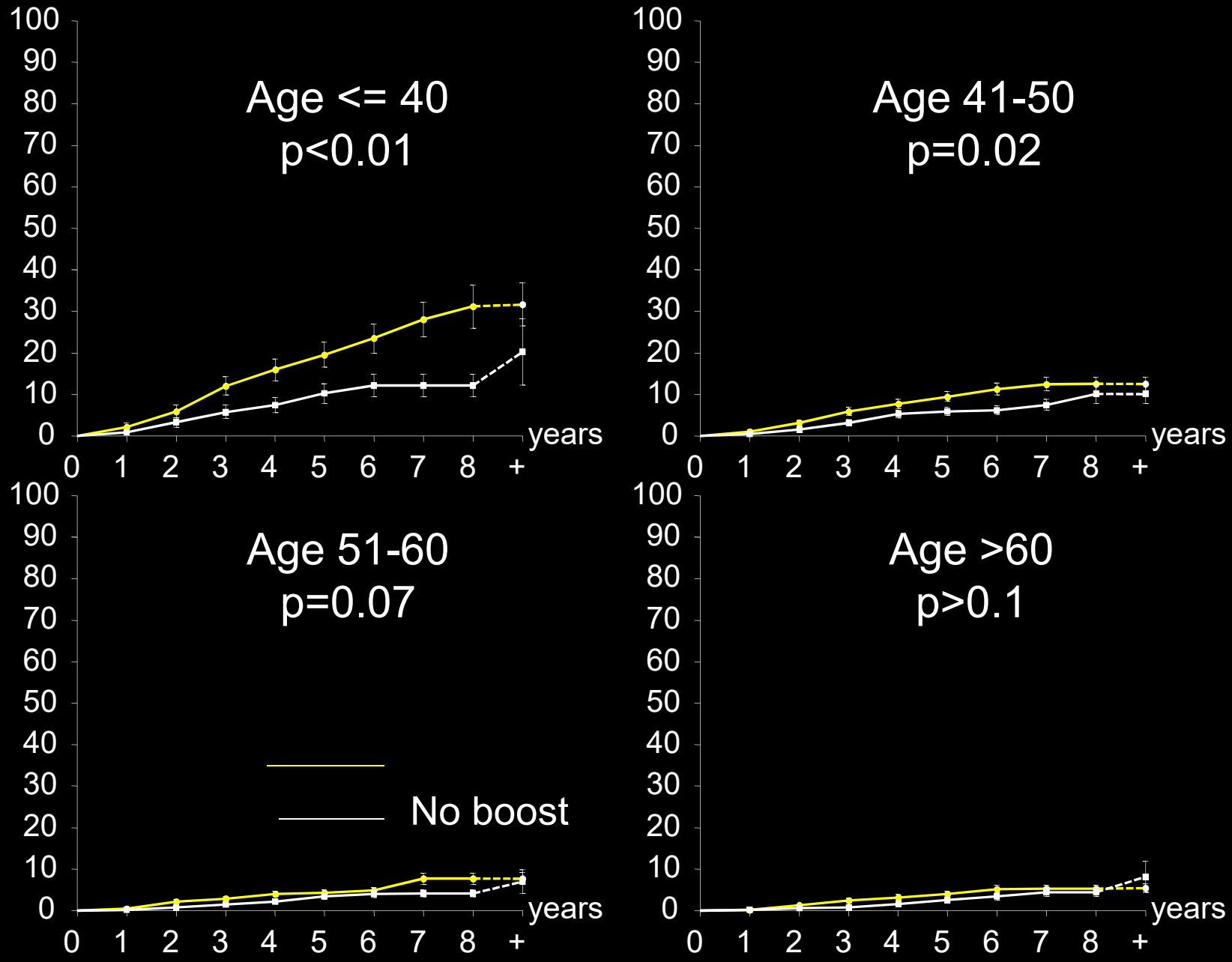
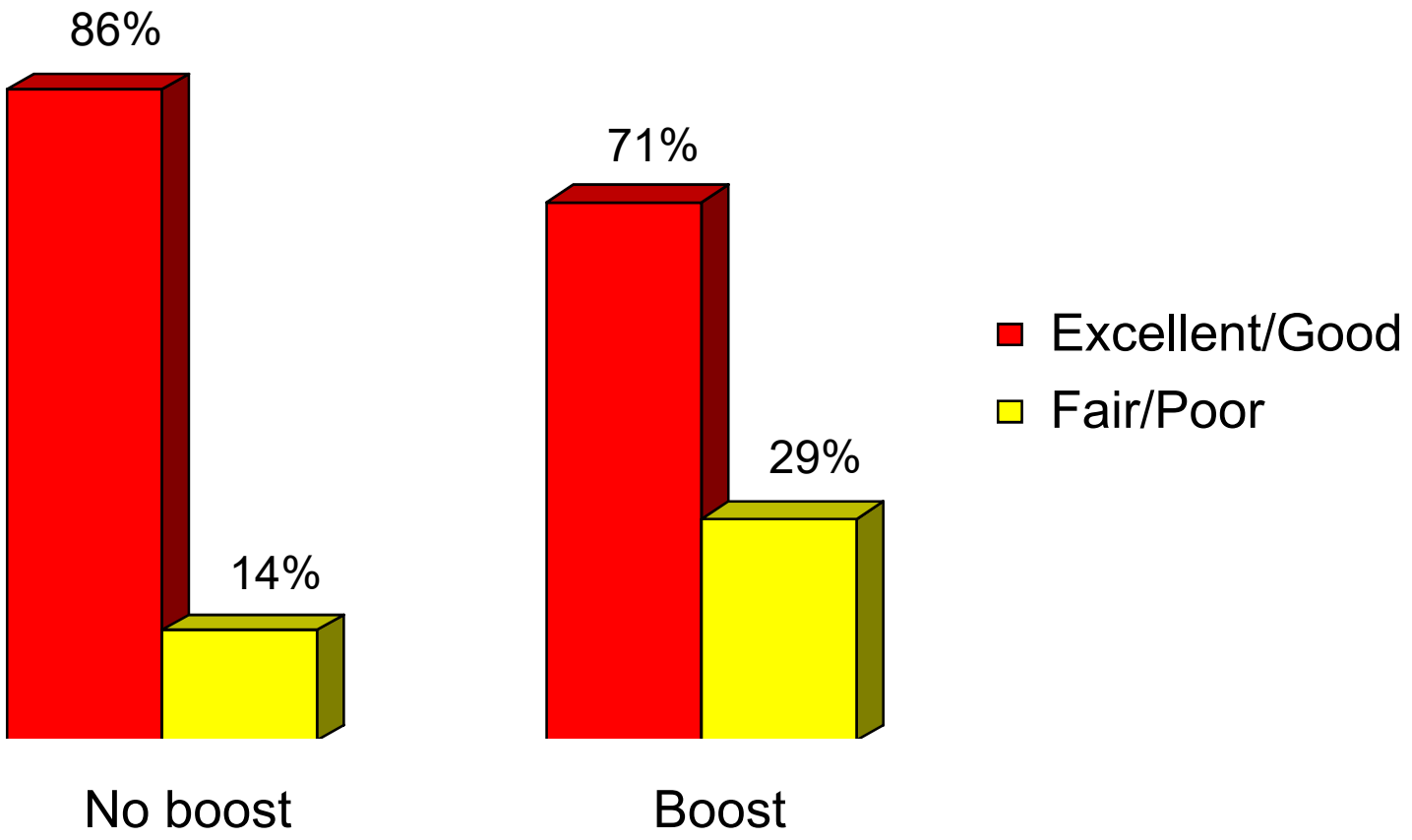
Local failure by age: boost vs no boost



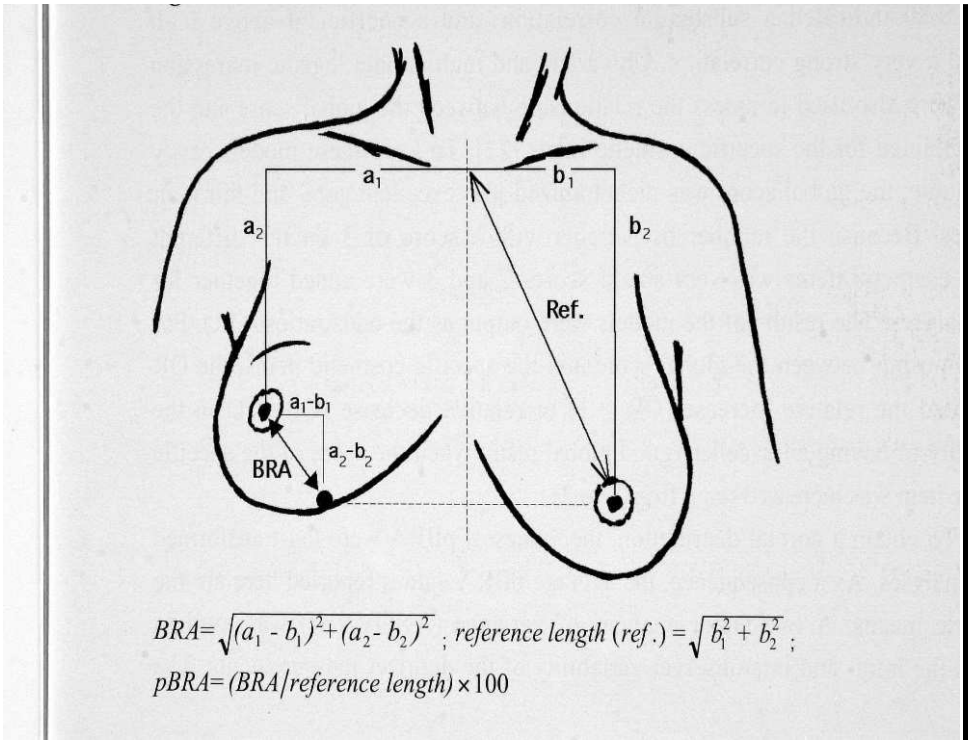
Global score by boost treatment



COSMETIC DAMAGE BY RADIOTHERAPY

↑RADIATION FIBROSIS
BREAST RETRACTION

VISIBLE SKIN
TELEANGIECTASES



$BRA=\sqrt{(a_1 - b_1)^2+(a_2 - b_2)^2}$; $reference\ length\ (ref.)=\sqrt{b_1^2 + b_2^2}$;

$pBRA= (BRA/reference\ length) \times 100$

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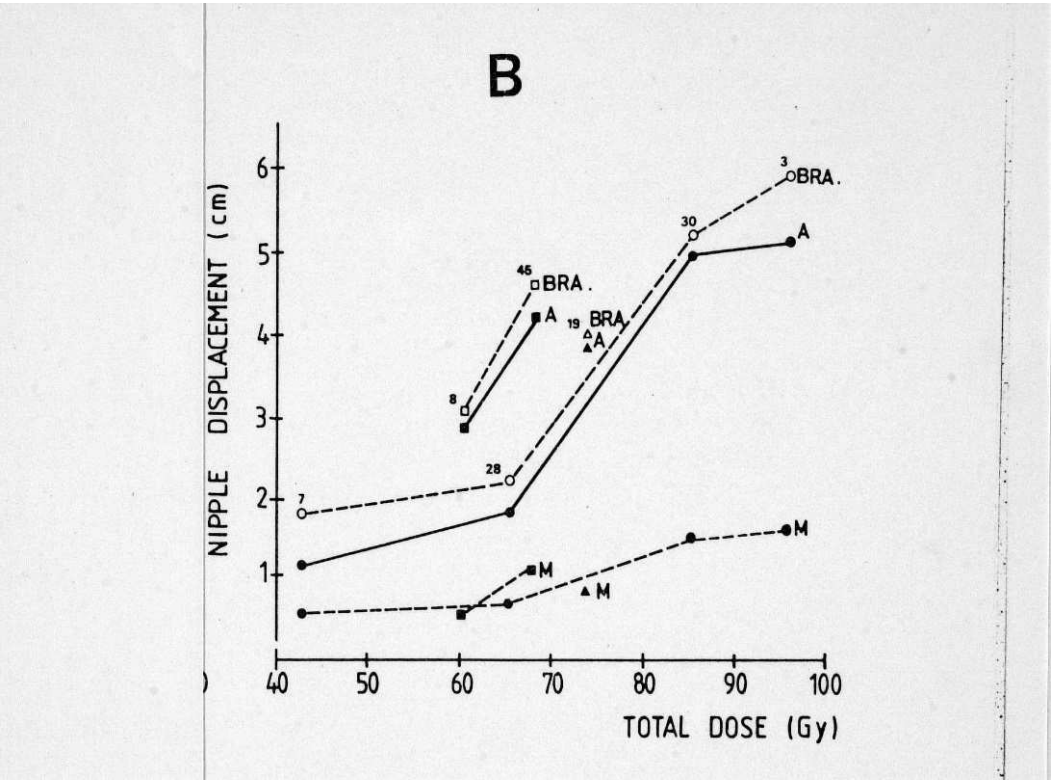
FIBROSIS



- **DOSE DEPENDENT**

  Leuven 1968-1980

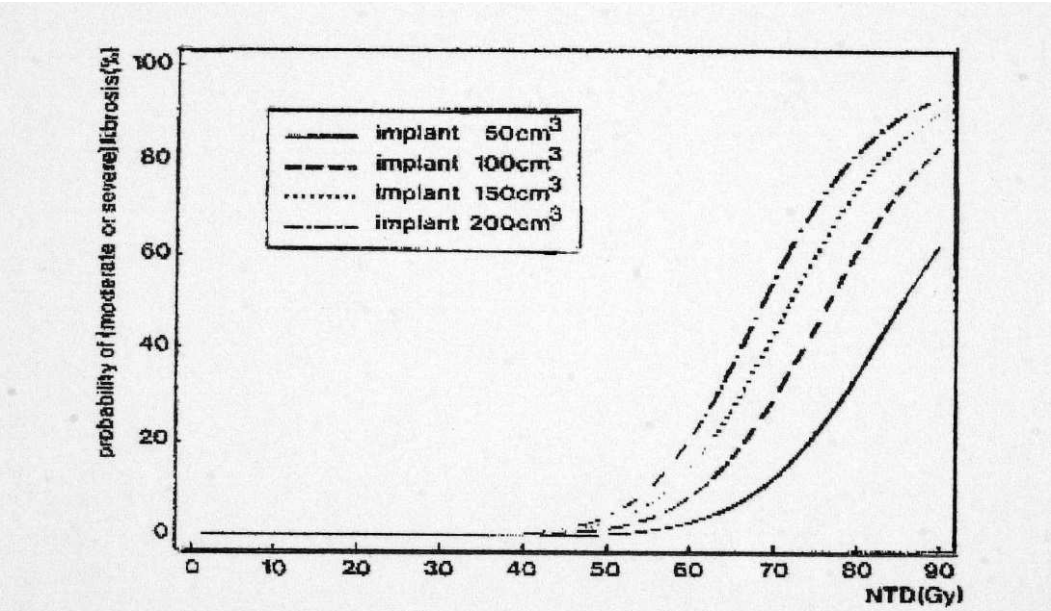


Fig. 3. Probability of fibrosis (grade 2 and 3) as a function of normalized total dose and implant volume. Bold parts of the curves depict the dose range studied in this analysis.

- **VOLUME DEPENDENT**

  Amsterdam 1985-1989

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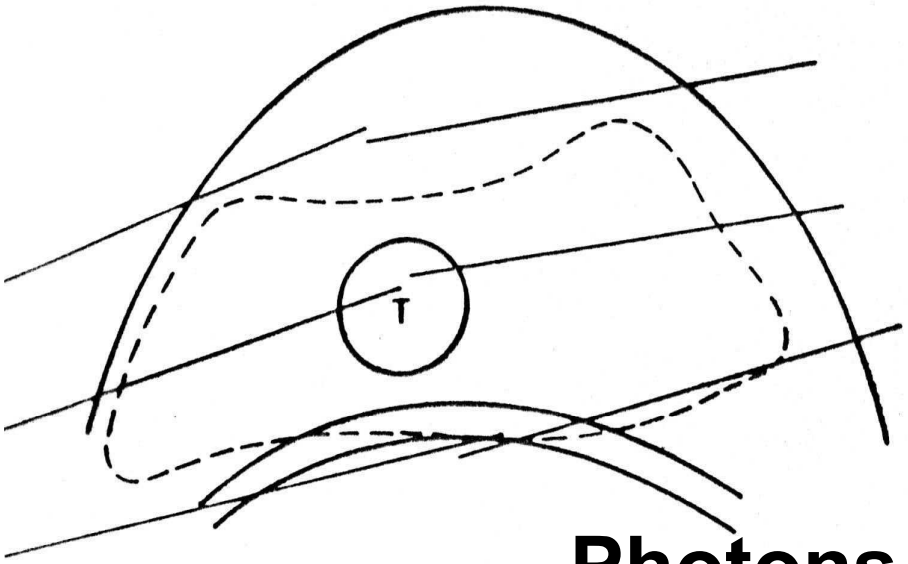
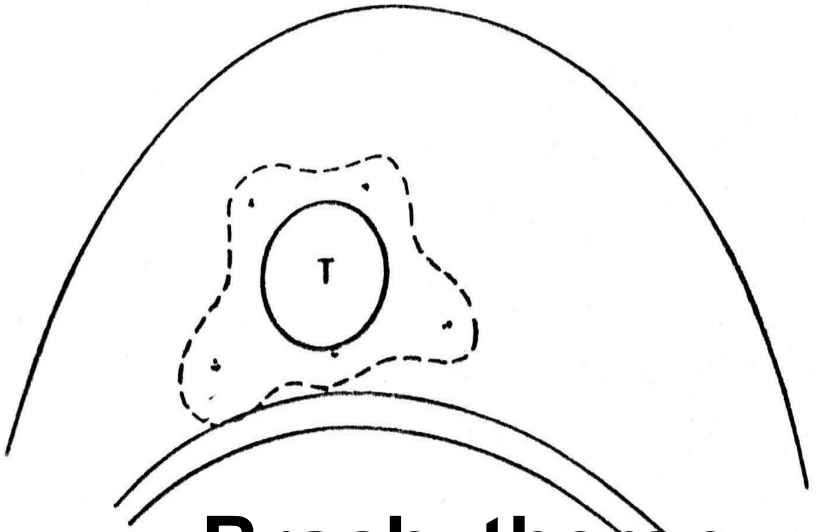
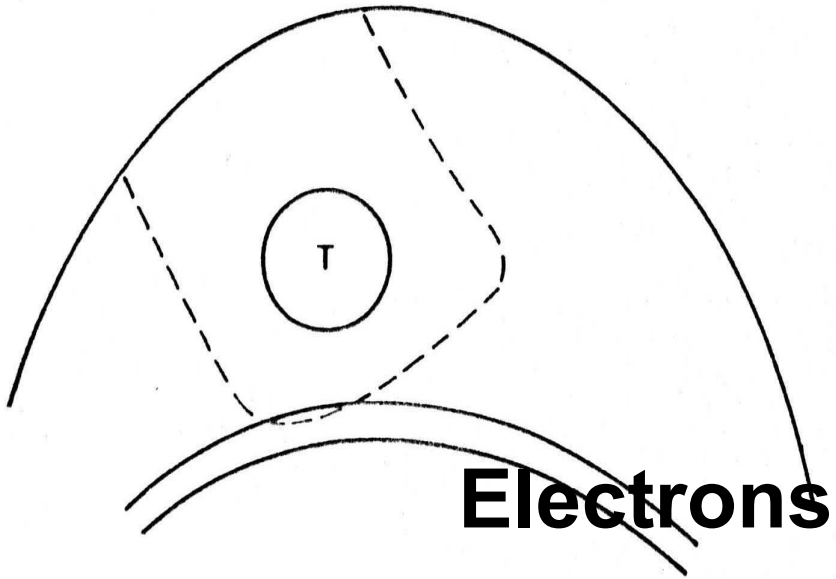
BOOST MODALITIES



Photons



Brachytherapy



Electrons

- Conformally covering the target
- As small volumes as possible
- As much skin sparing as possible

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BALLISTIC SELECTIVITY OF BOOST MODALITIES

	Electrons	Interstitial
EORTC TRIAL 10882		
M. Ptaszynski 1995	50 - 300 cm^3	25 - 90 cm^3
AMC DATA		
G. Van Tienhoven 1995	150 cm^3	48(12-76) cm^3
GRAZ-LINZ STUDY		
Hammer et Al. 1995	70 - 130 cm^3	26 - 64 cm^3

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BCT local failure rates
EB versus BT boost

- RT ONLY

		EBB	BTB	
Fourquet 1995	5y	30%	16%	

- BCS + RT

Mansfield 1990	5y	8.0%	7.0%	
	10y	18.0%	8.0%	*p= 0.2*
Touboul 1995	5y	8.8%	5.5%	*p= 0.32*
Hammer 1995	5y	8.2%	4.3%	*p= 0.03*
Hammer 2010	10y	7,2%	5,9%	
Van Tienhoven 1995	5y	8.2%	2.8%	
EORTC 2001	5y	4.5%	2.5%	*p= 0.09*
Polgar 2001	5y	5.8%	7.7%	*p= 0.69*
Verhoeven 2015	10y	2.5%	0.7%	*p= 0.0*

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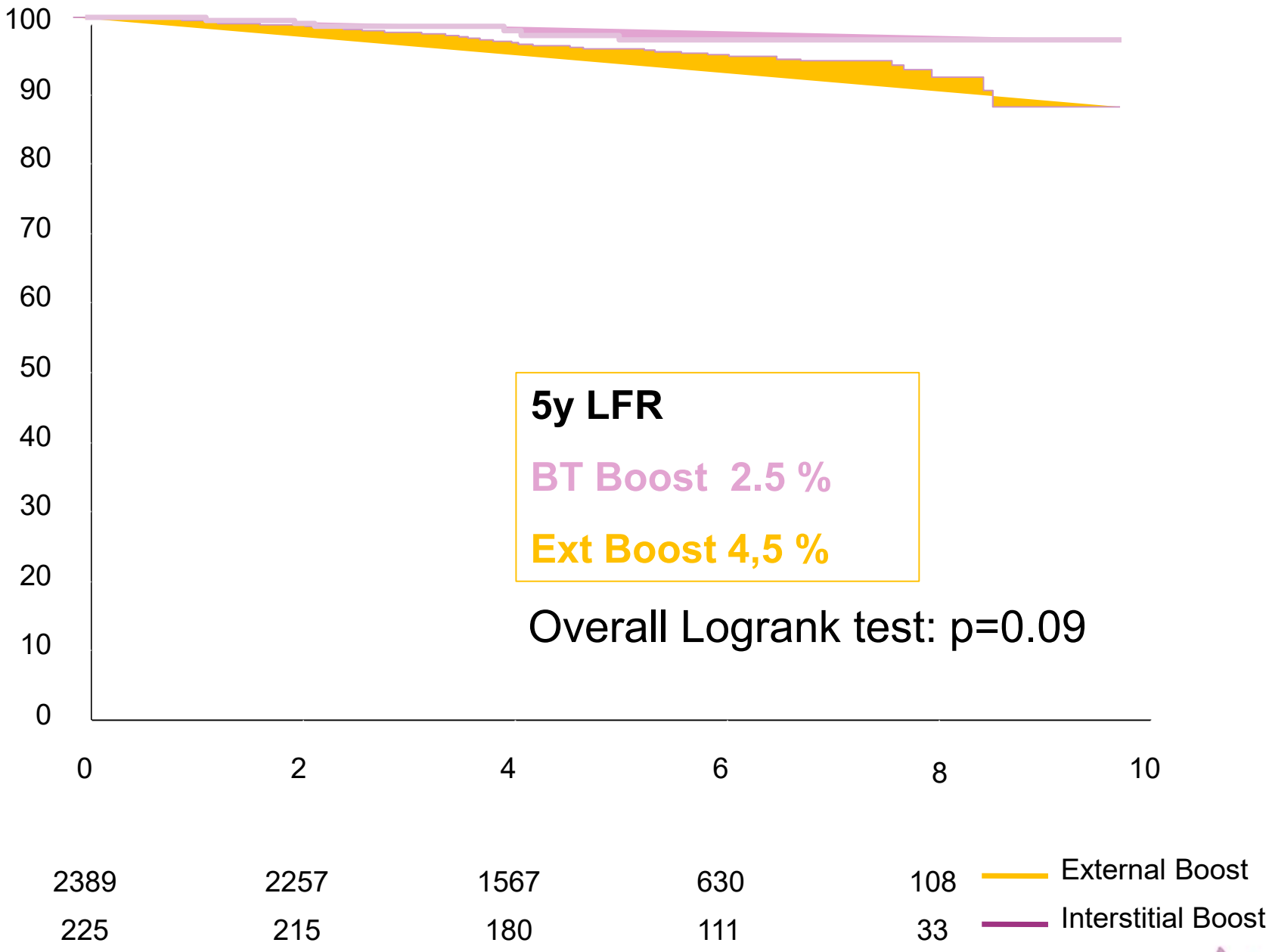
Local control by Type of Boost

EORTC

10882



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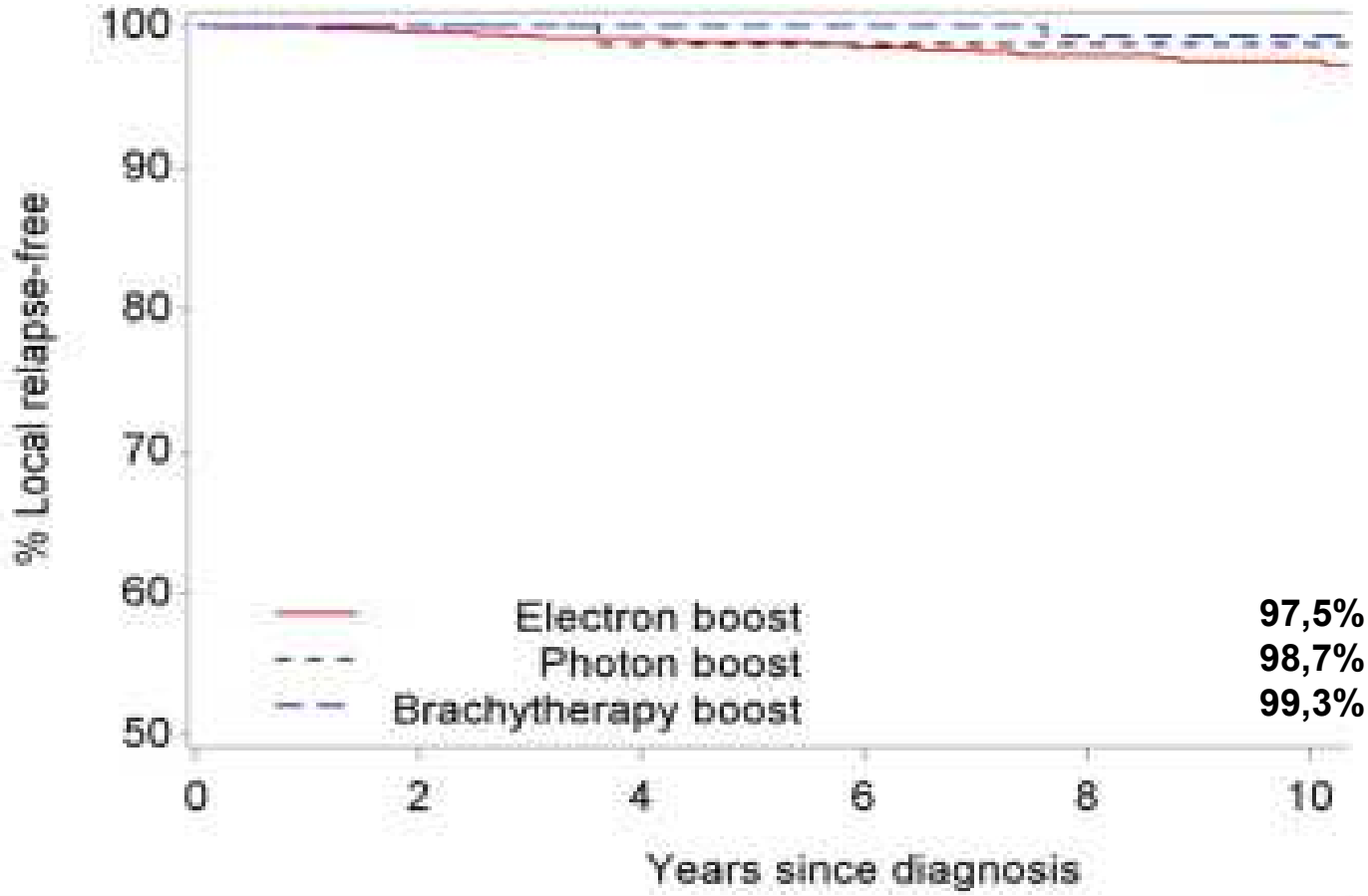
The Breast

Volume 24, Issue 4, August 2015, Pages 391–396

Original article

A comparison of three different radiotherapy boost techniques after breast conserving therapy for breast cancer

Karolien Verhoeven[a], [1], Isabelle Kindts[a], [1], Annouschka Laenen[b], Stéphanie Peeters[a], Hilde Janssen[a], Erik Van Limbergen[a], Caroline Weltens[a]



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GRAZ-LINZ STUDY
420 PTS T1-T2

	Electrons	Interstitial
BOOST DOSE	5,6 X 1,8 GY-2 GY	10 Gy HDR
VOLUME	70-130 cm^3	21 - 64 cm^3
LOC REC (5 Y)	8.2 %	4.3 %
MEAN COSMETIC SCORE *P<0.0005*	1.49	1.15
GOOD TO EXCELLENT *p<0.001*	70 %	88 %
FIBROSIS	29 %	17 %
TELEANGIECTASES	28 %	9 %

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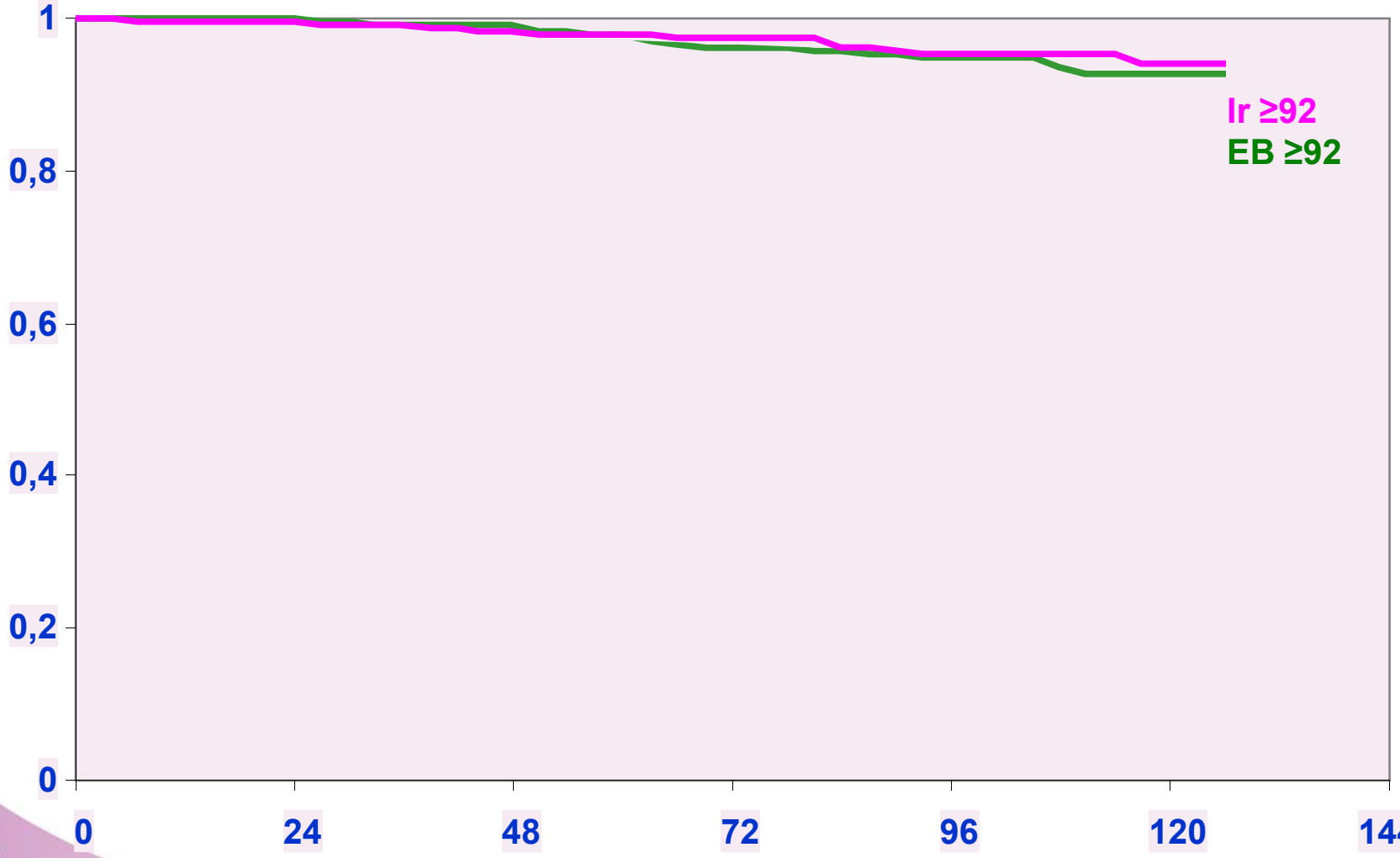
Linz II study (*Courtesy Joe Hammer*)

1635 cases
Local Control **EB ≥1992 vs. Ir ≥1992**



JH – BHS Linz

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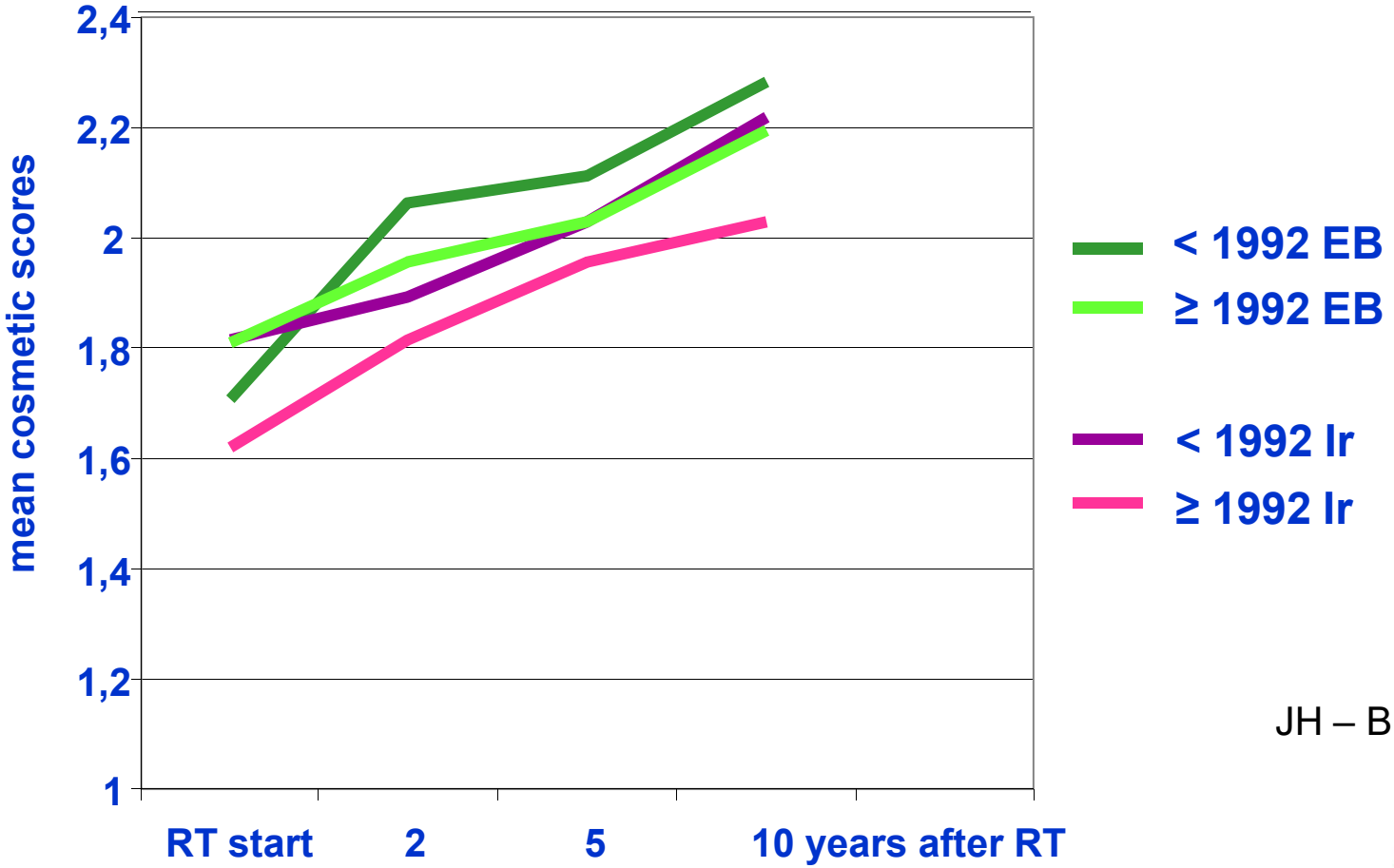
Linz II study (*Courtesy Joe Hammer*)

1635 cases

Cosmetic Evaluation Score 1 to 4



JH – BHS Linz

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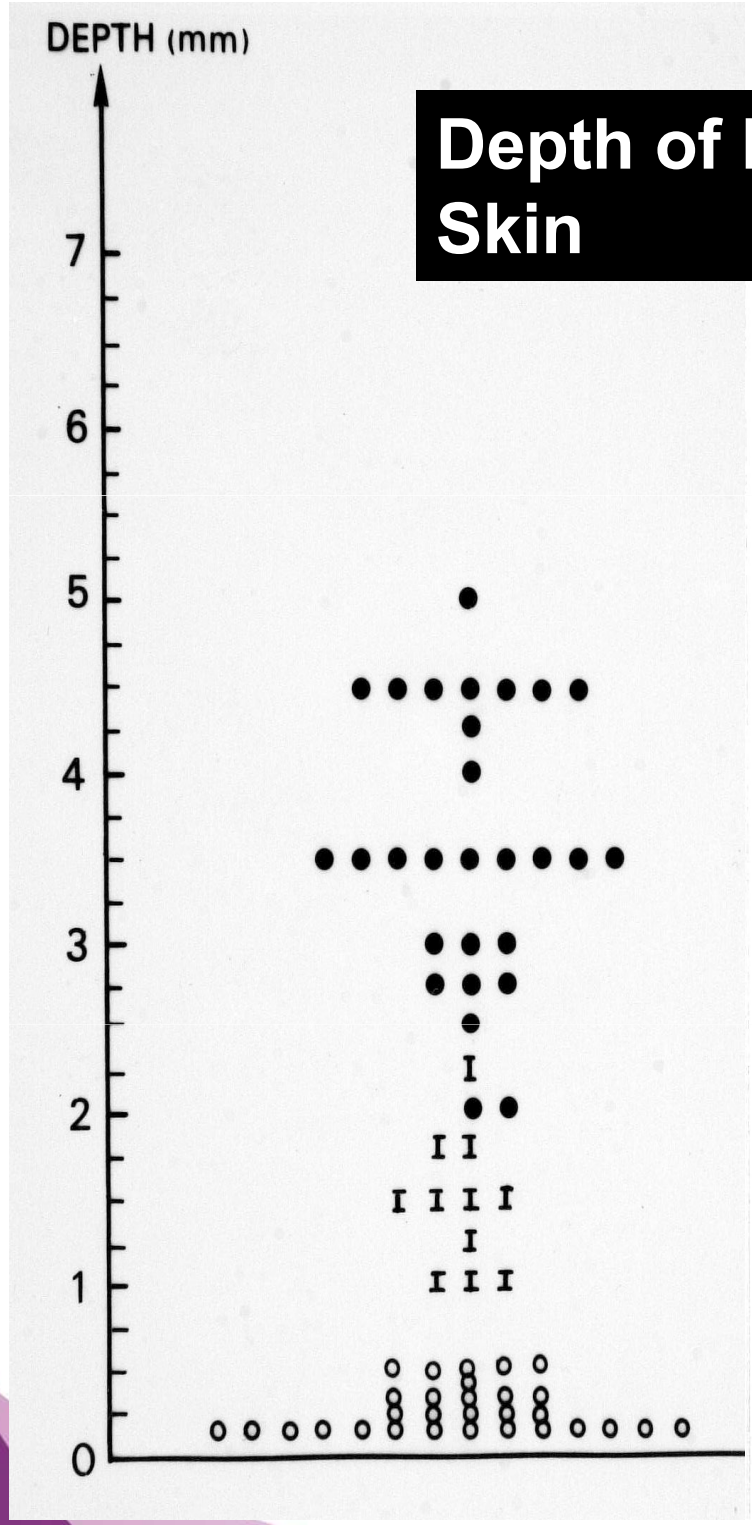
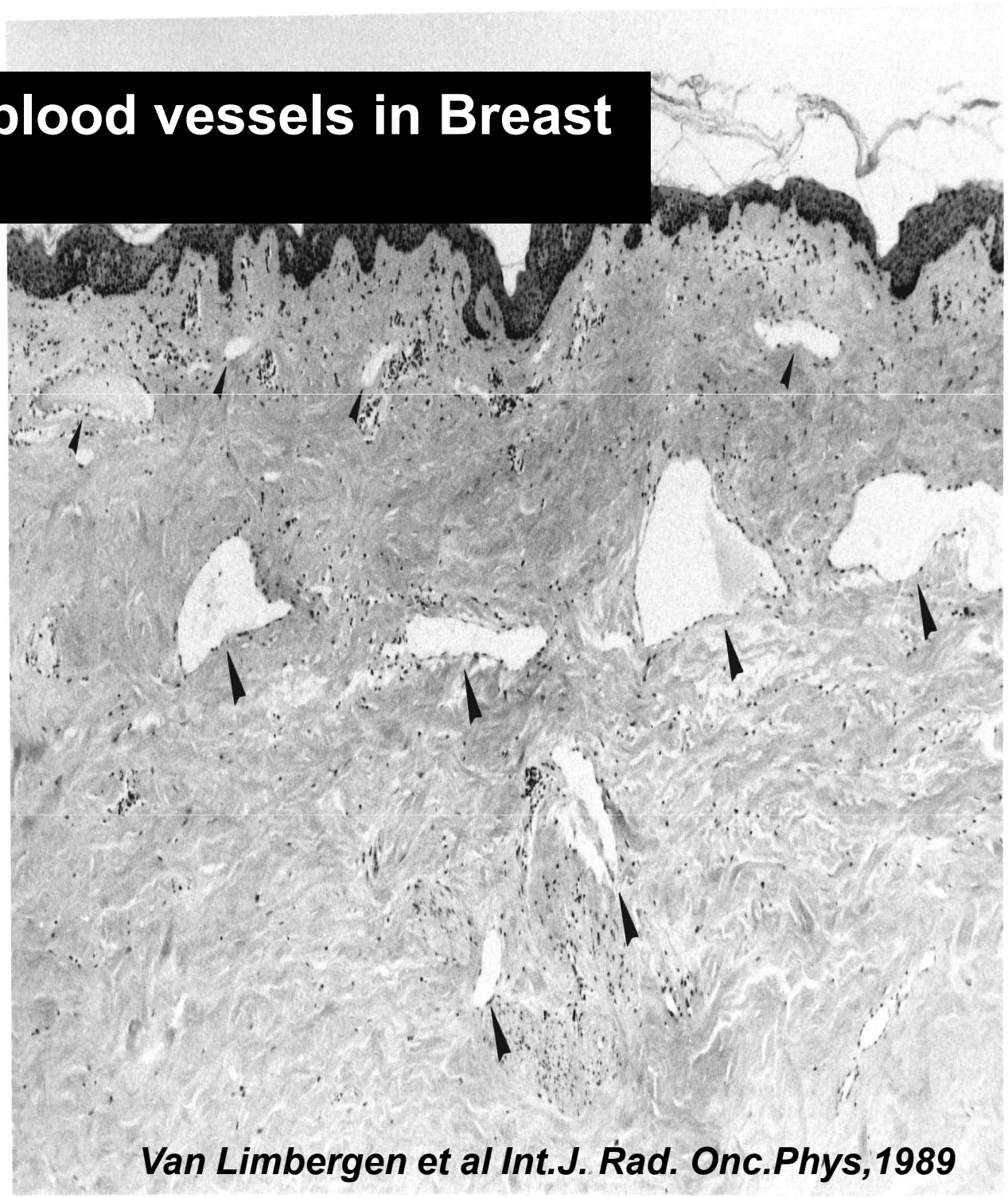
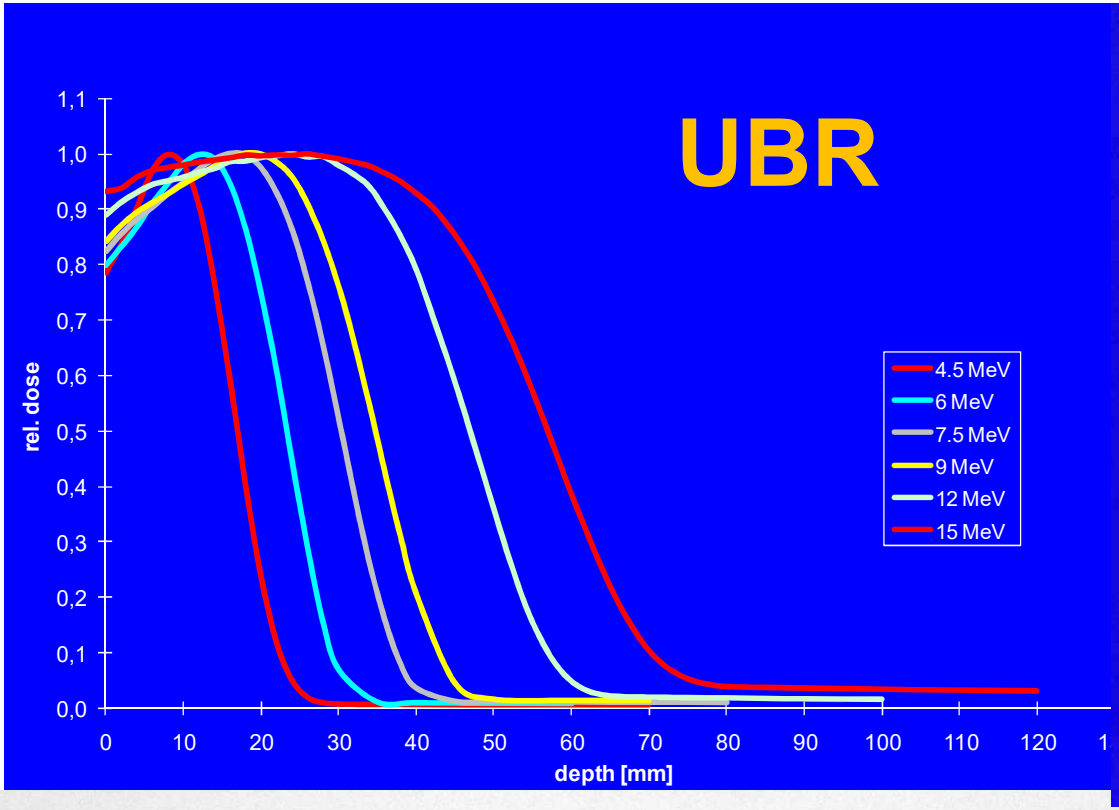
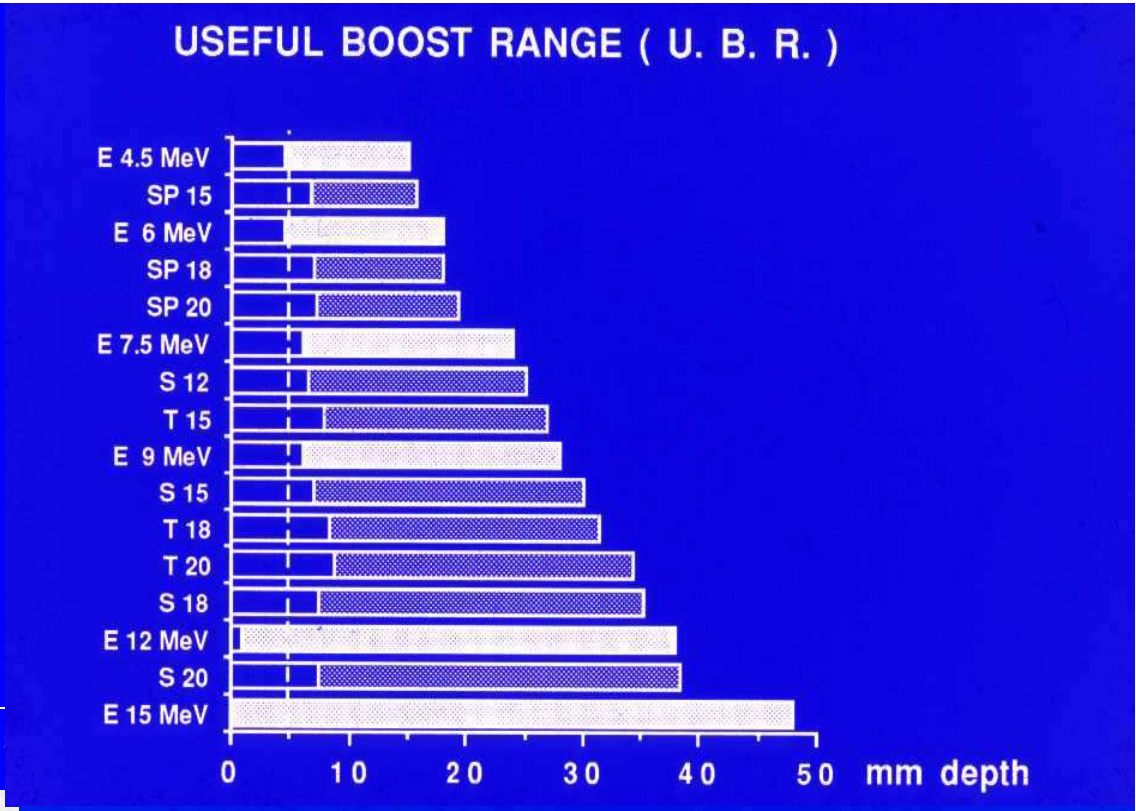
Depth of blood vessels in Breast Skin

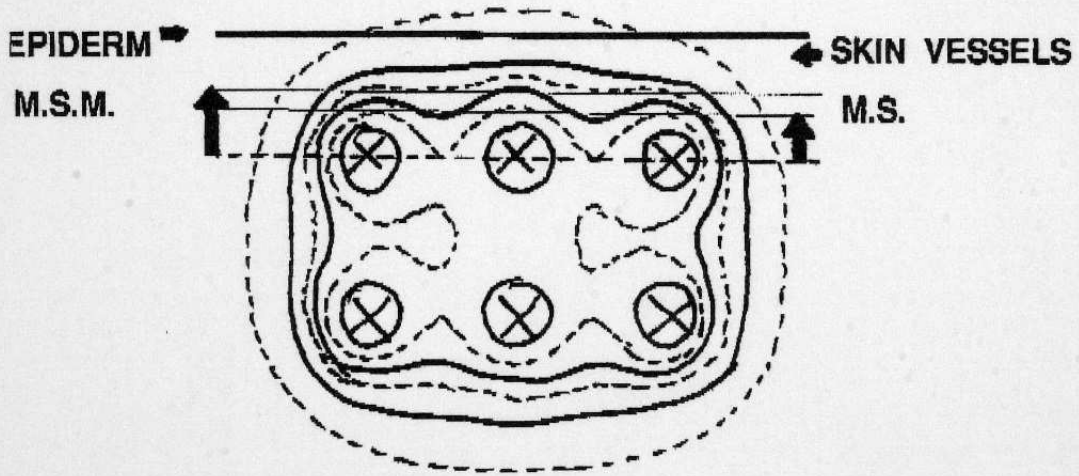


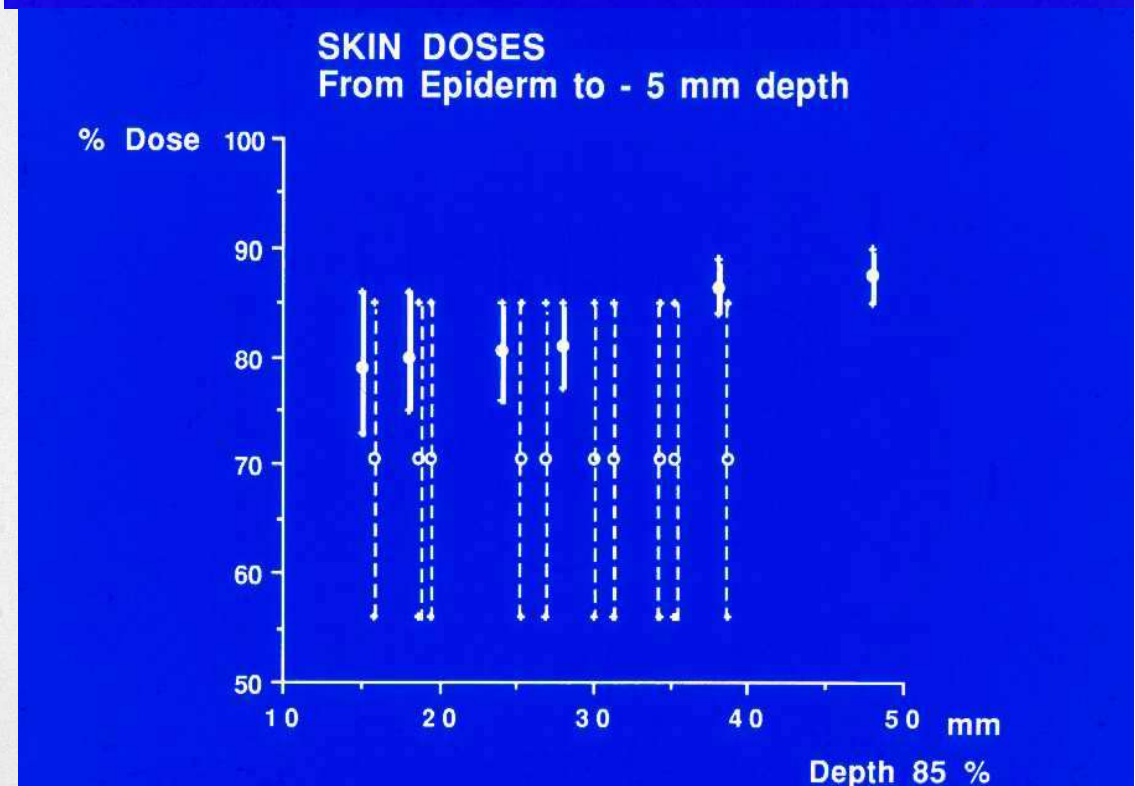


Van Limbergen et al Int.J. Rad. Onc.Phys,1989


UBR
rel. dose
depth [mm]
4.5 MeV
6 MeV
7.5 MeV
9 MeV
12 MeV
15 MeV


USEFUL BOOST RANGE (U. B. R.)
E 4.5 MeV
SP 15
E 6 MeV
SP 18
SP 20
E 7.5 MeV
S 12
T 15
E 9 MeV
S 15
T 18
T 20
S 18
E 12 MeV
S 20
E 15 MeV
mm depth


EPIDERM
SKIN VESSELS
M.S.M.
M.S.


SKIN DOSES
From Epiderm to - 5 mm depth
% Dose
mm
Depth 85 %

INCIDENCE OF SKIN TELEANGIECTASES (at 5 y)

	50 Gy	60 Gy
Score > 1	30 %	60 %
Score > 2	12 %	30 %
Score > 3	0 %	5 %

Turesson and Notter Int. J. Rad. Onc. Biol. Ph. 10, 599-606, 1984.

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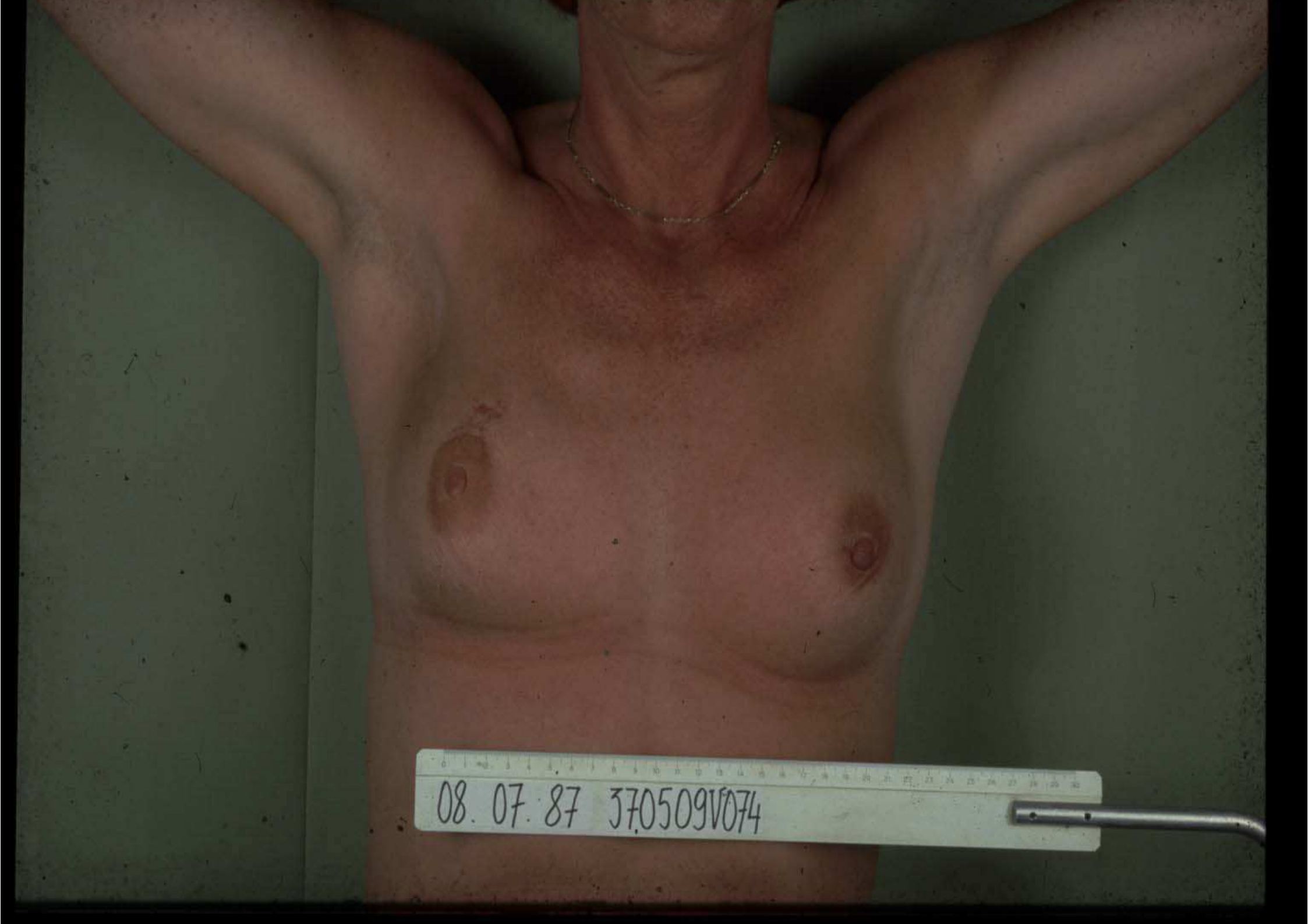
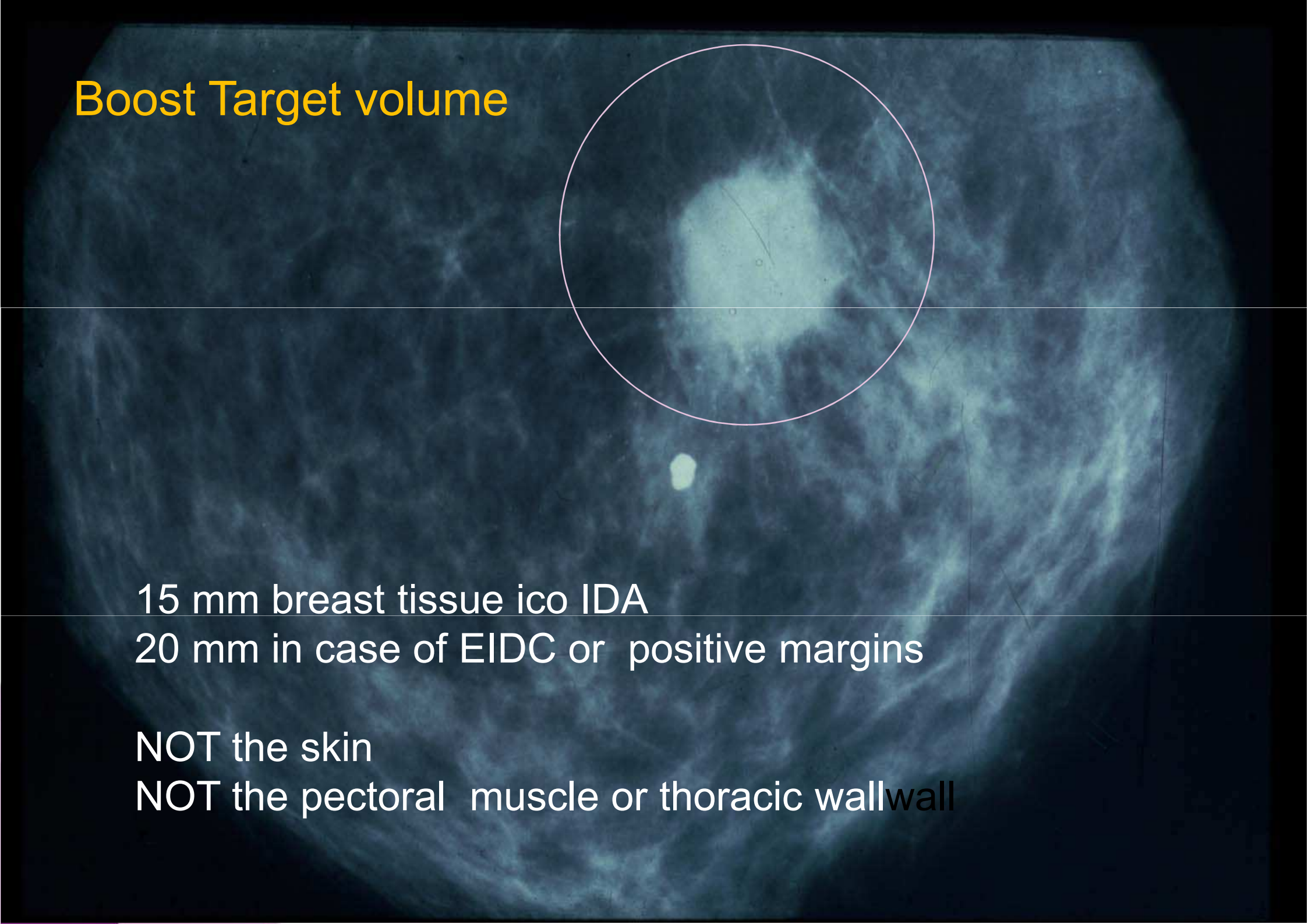

08. 07. 87 37.0509V074

Boost Target volume



15 mm breast tissue ico IDA
20 mm in case of EIDC or positive margins

NOT the skin
NOT the pectoral muscle or thoracic wallwall

Radiotherapy and Oncology

Volume 115, Issue 3, June 2015, Pages 342–348

GEC ESTRO Recommendations

Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery

Vratislav Strnad[a], Jean-Michel Hannoun-Levi[b], Jose-Luis Guinot[c], Kristina Lössl[d], Daniela Kauer-Dorner[e], Alexandra Resch[e], György Kovács[f], Tibor Major[g], Erik Van Limbergen[h], On behalf of Working Group Breast Cancer of GEC-ESTRO

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Boost target localisation

- Clinical examination
- Preoperative mammograms
- Surgical - pathological reports
- Scar position
- Clips
- Ultrasound
- CAT-scan

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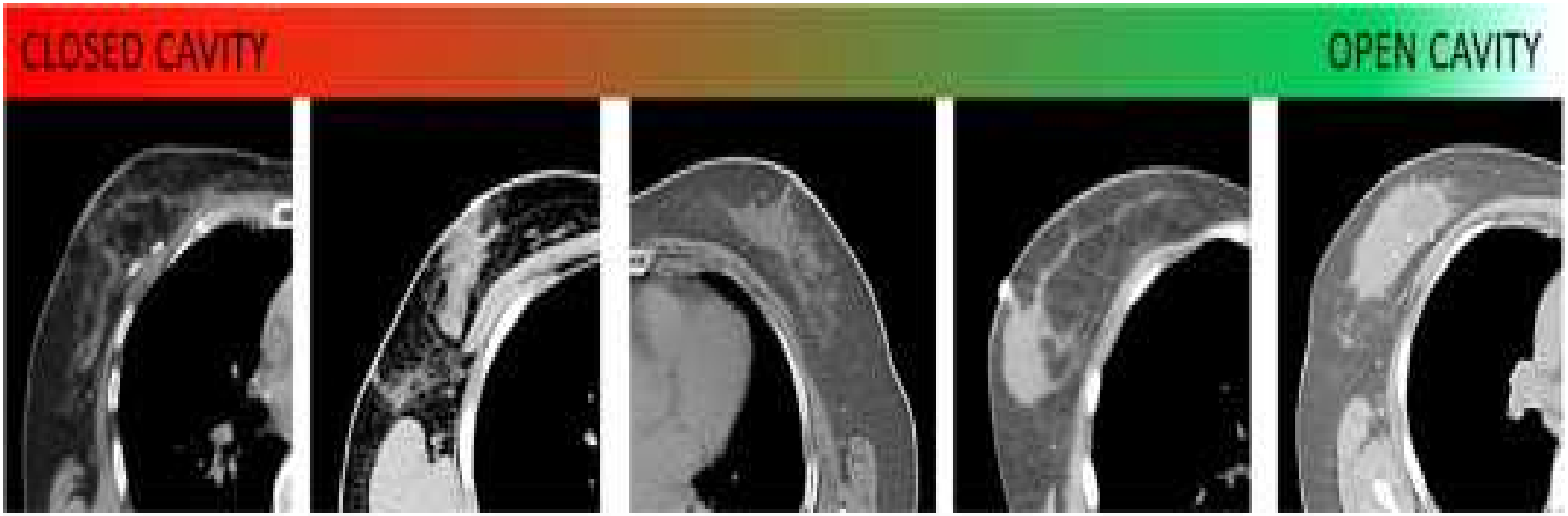
Closed vs Open cavity



CVS 1	CVS2	CVS3	CVS4	CVS5
No cavity	Heterogenous cavity with indistinct margins	Heterogenous cavity with some indistinct margins	Mildly heterogenous cavity with mostly distinct margins	Homogenous cavity with clearly identified margins

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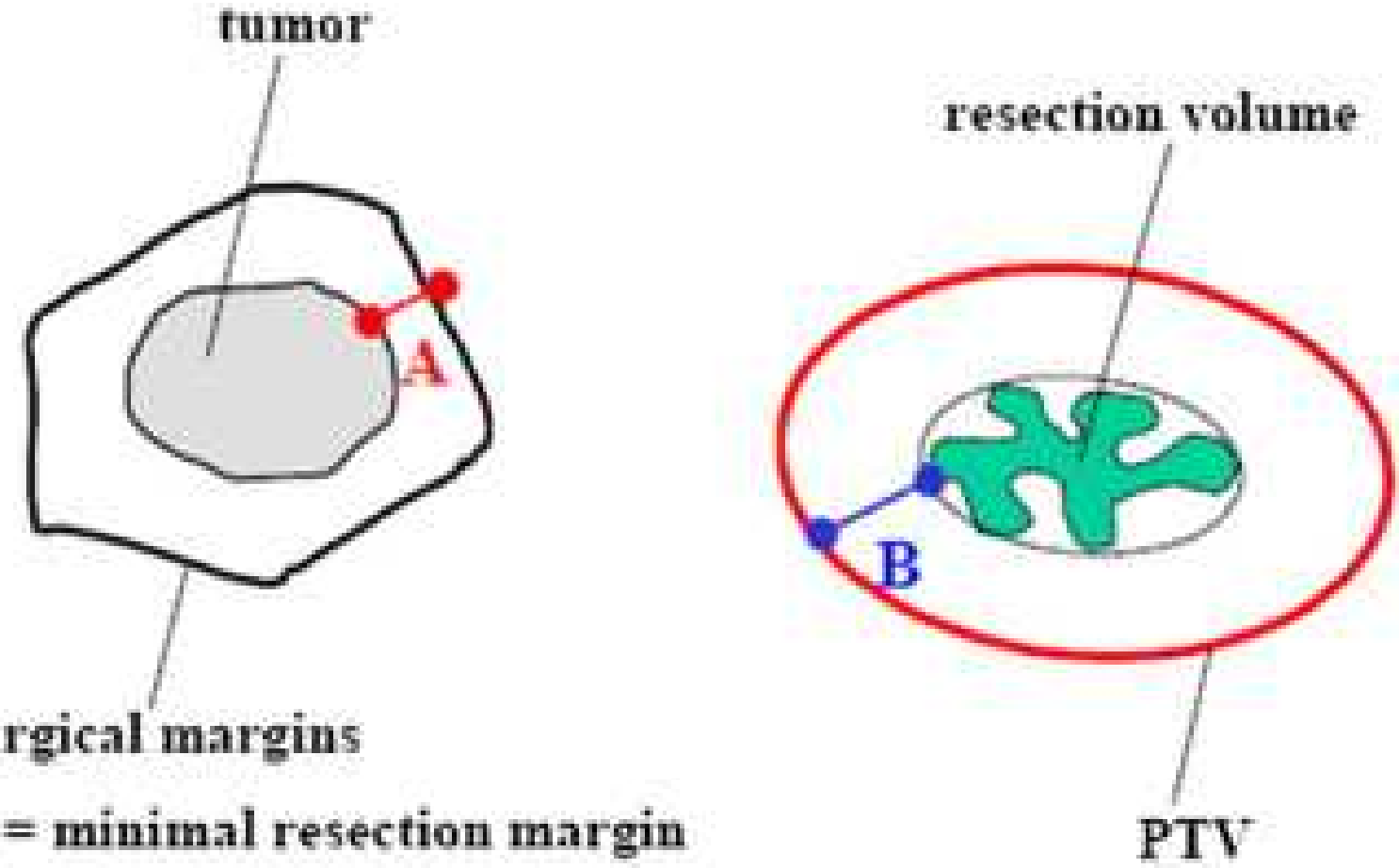
GEC-ESTRO Breast Working Group Recommendations



A = minimal resection margin

B = safety margin

B = >20 mm minus A

Strnad et al Rad Onc 2015

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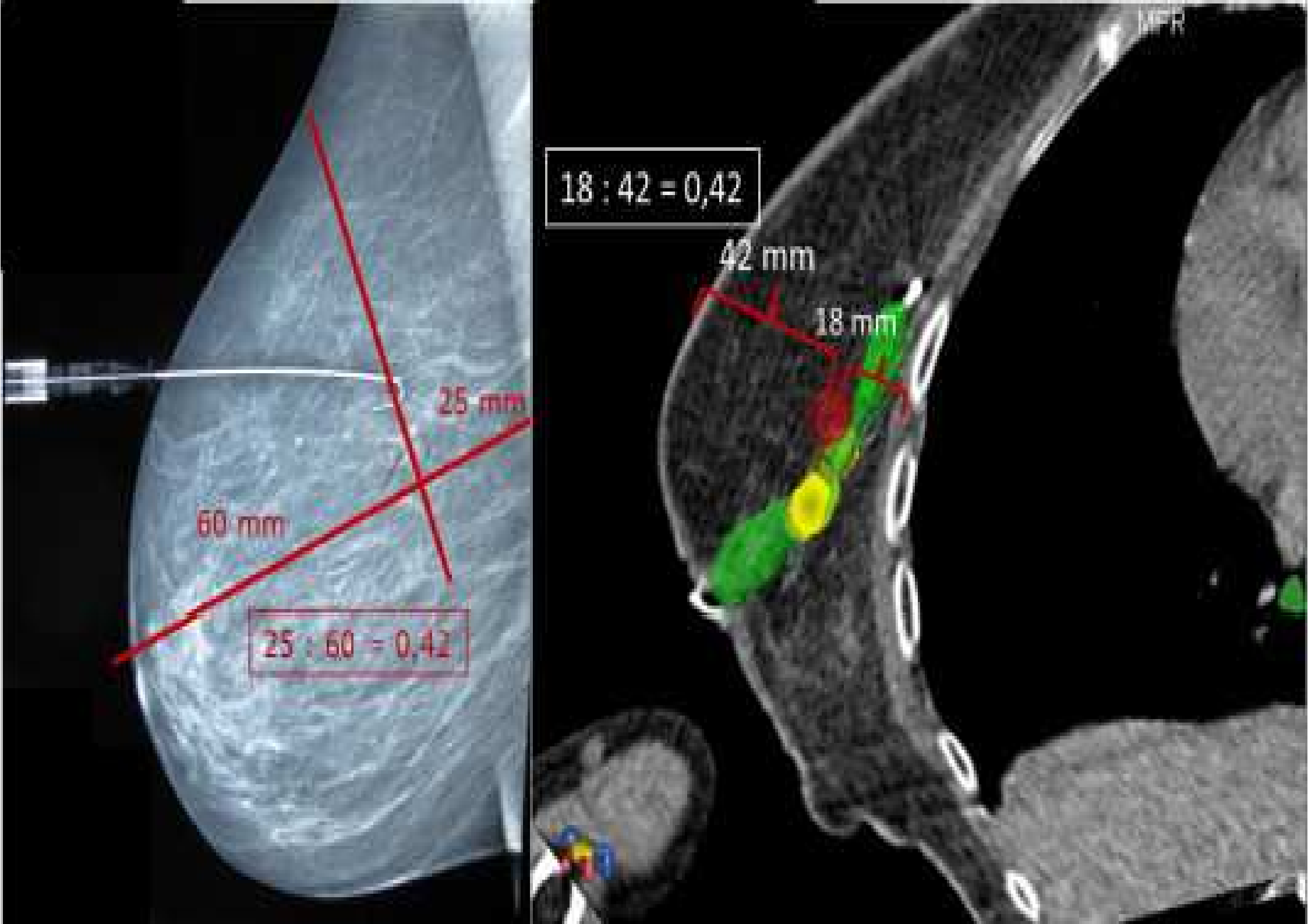
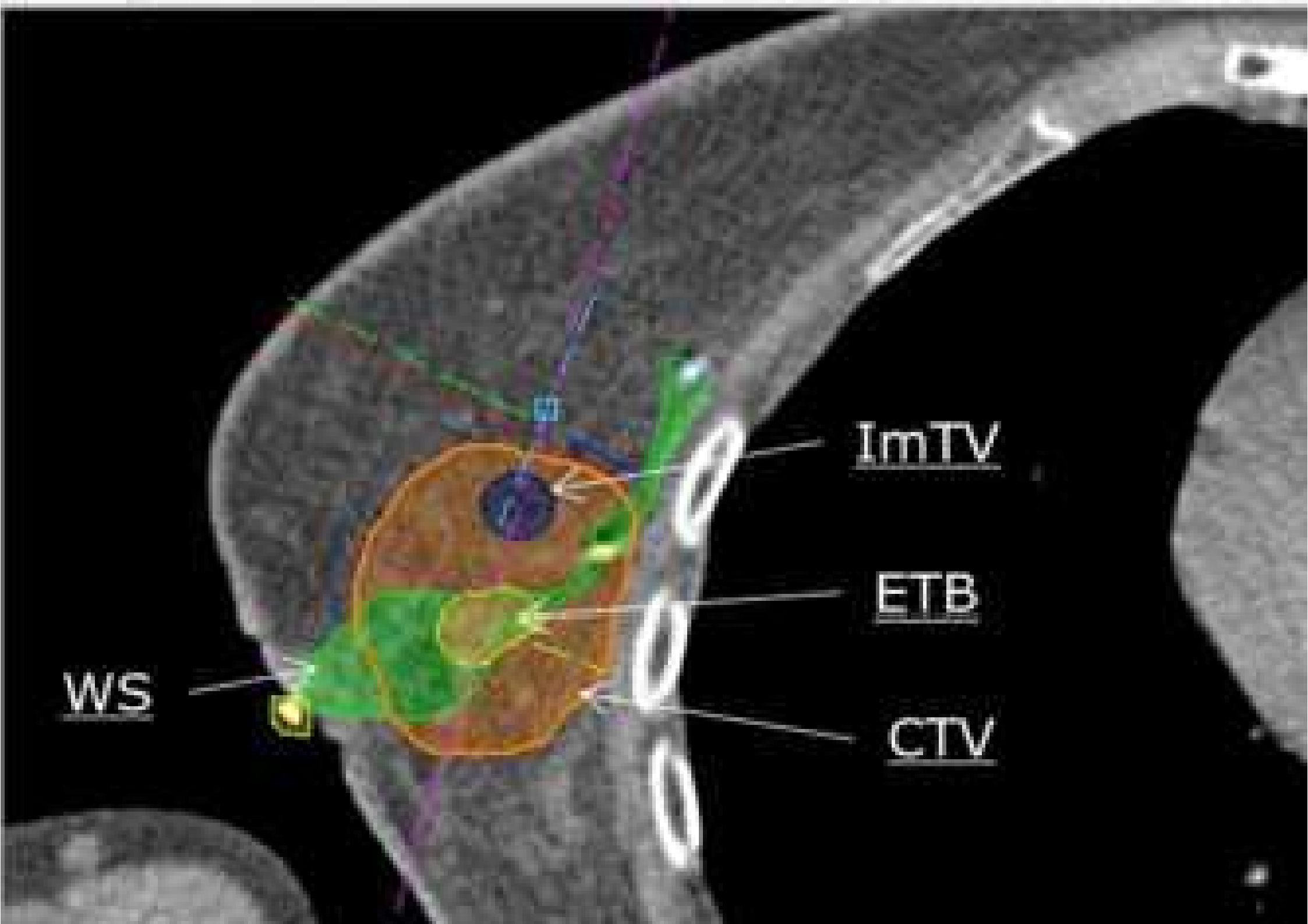

25 mm
60 mm
25 : 60 = 0,42
18 : 42 = 0,42
42 mm
18 mm


ImTV
ETB
WS
CTV

For target delineation after closed cavity surgery GEC-ESTRO recommend the following steps

- 1. Perform a CT with marks on the scar.
- 2. Delineation of clips.
- 3. Delineation of surgical bed – whole surgical scar (WS) inside breast.
- 4. Delineation of ImTV (Imaging correlated Target Volume).
- 5. Delineation of ETB (Estimated Tumour Bed).
- 6. Delineation of CTV (Clinical Target Volume).
- 7. Delineation of PTV (Planning Target Volume).

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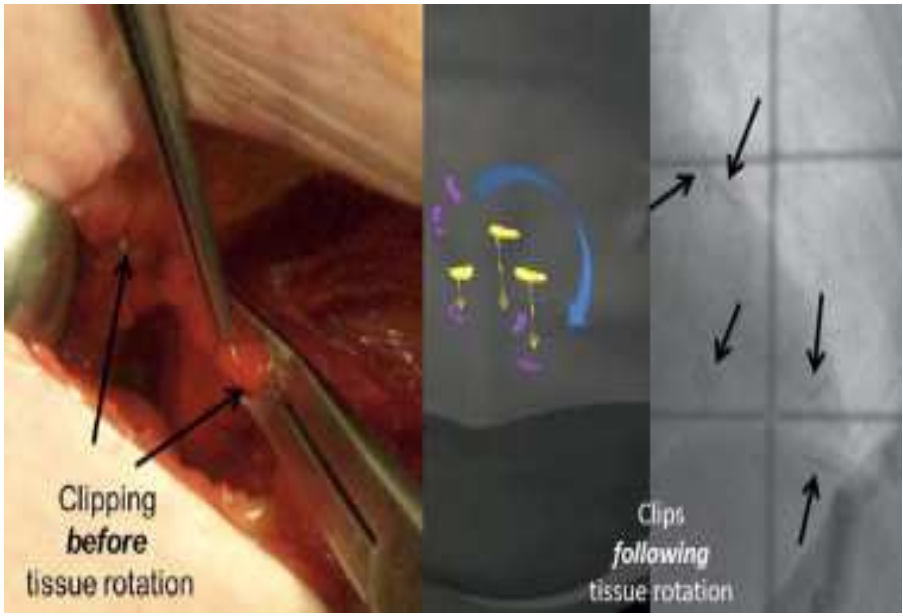
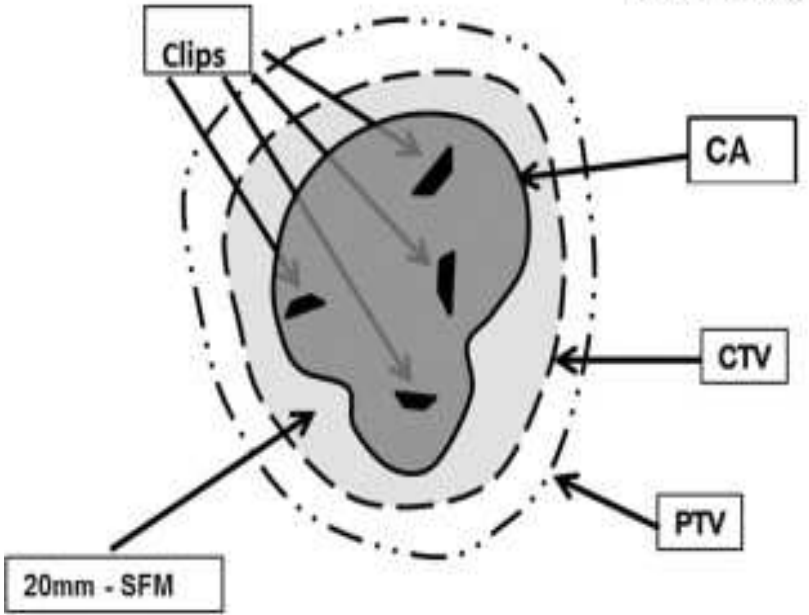
MCBT after Oncoplastic surgery

- In case of oncoplastic surgery no recommendations can be given.
- Only in selected cases of limited rotational flaps the CTV can be defined as the sum of the clipped area (CA) and the distance of 20 mm minus the smallest surgical free margin (SFM) defined by the pathologist (CTV = CA + (20-SFM).
- The PTV is defined as the CTV + 10 mm.



CTV = CA + (20-SFM)
PTV = CTV + 10 mm



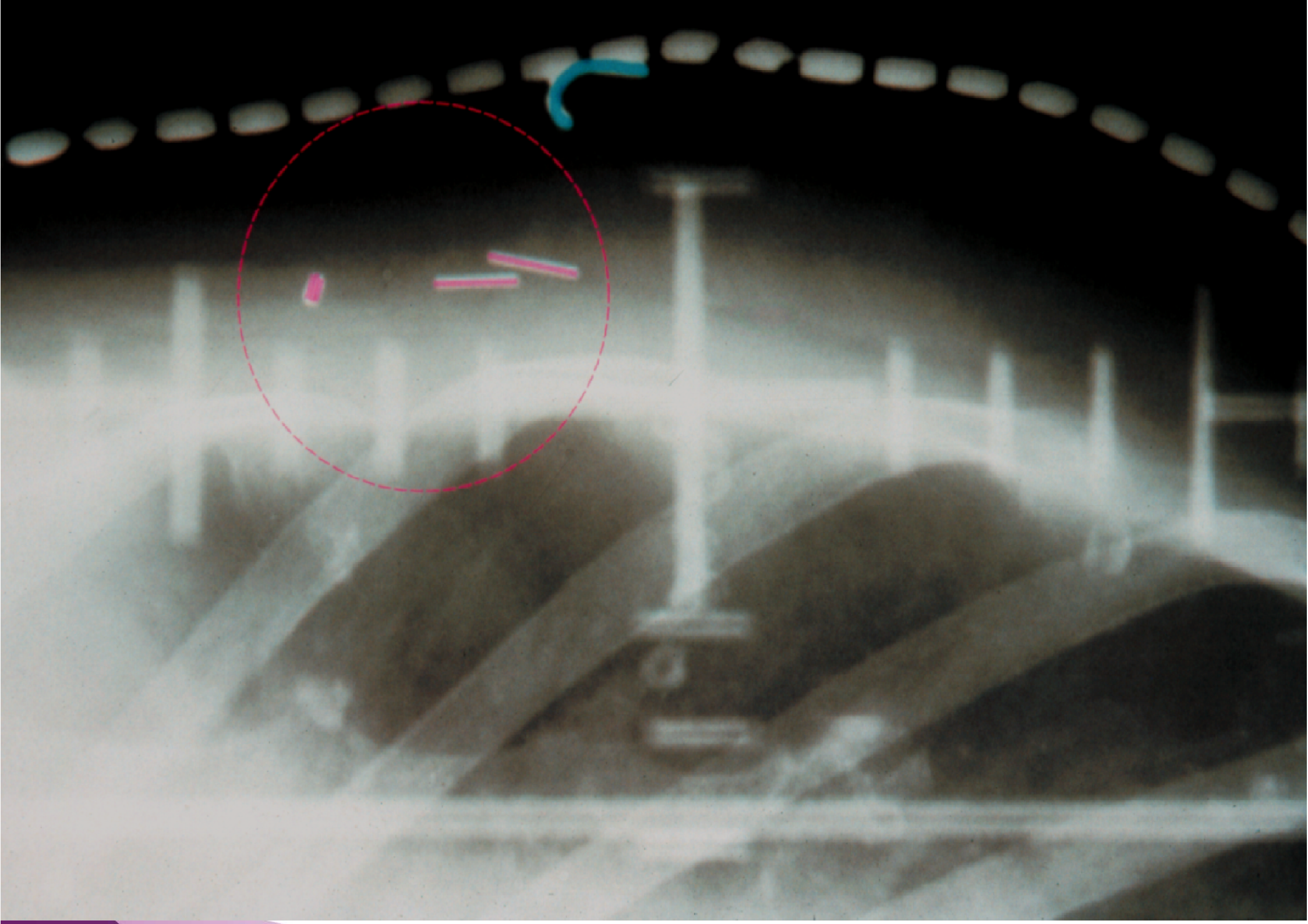
Localisation of needle entrance and exit points :

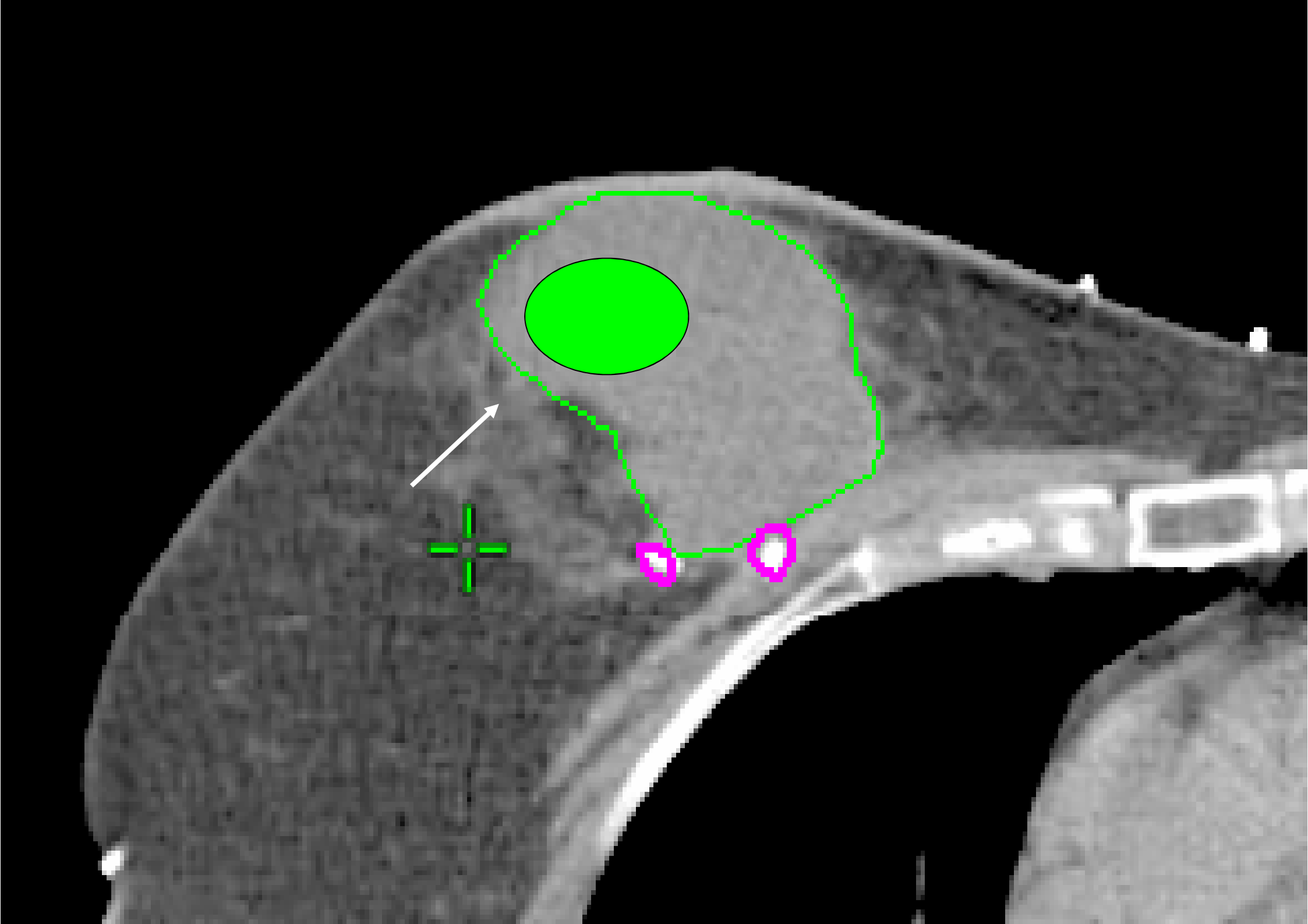
Define implant isocentre:

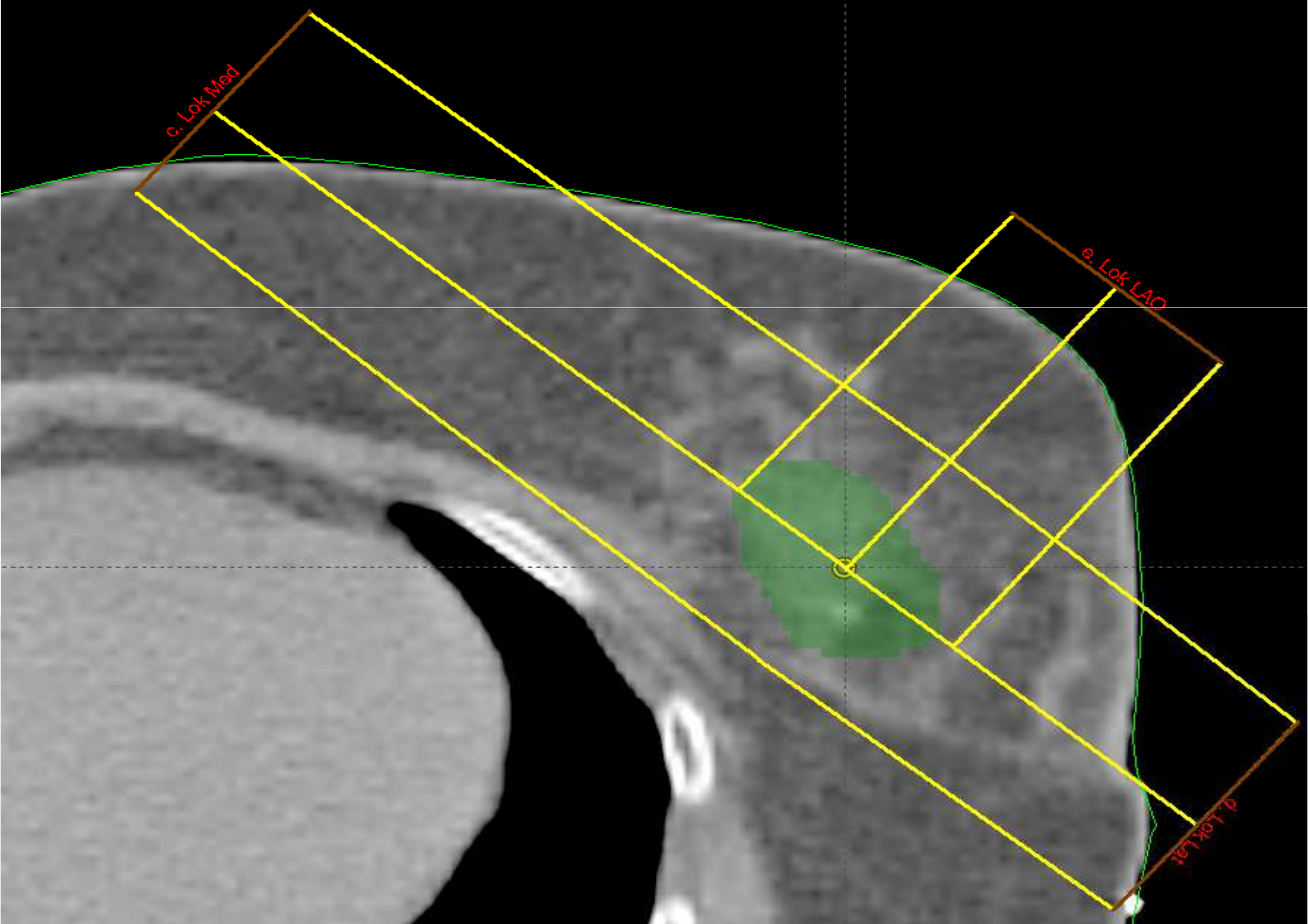
mammography

clips

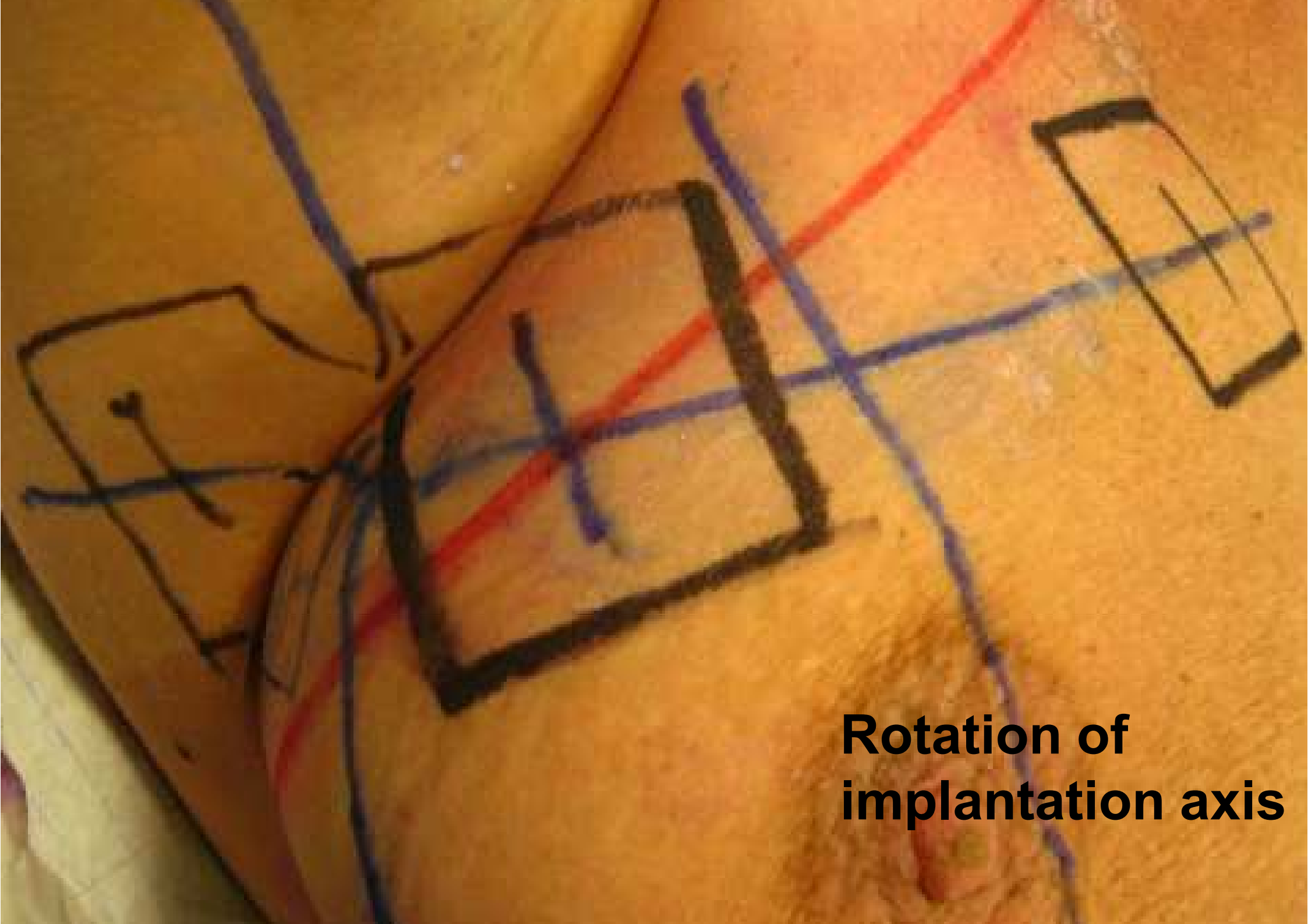
CAT

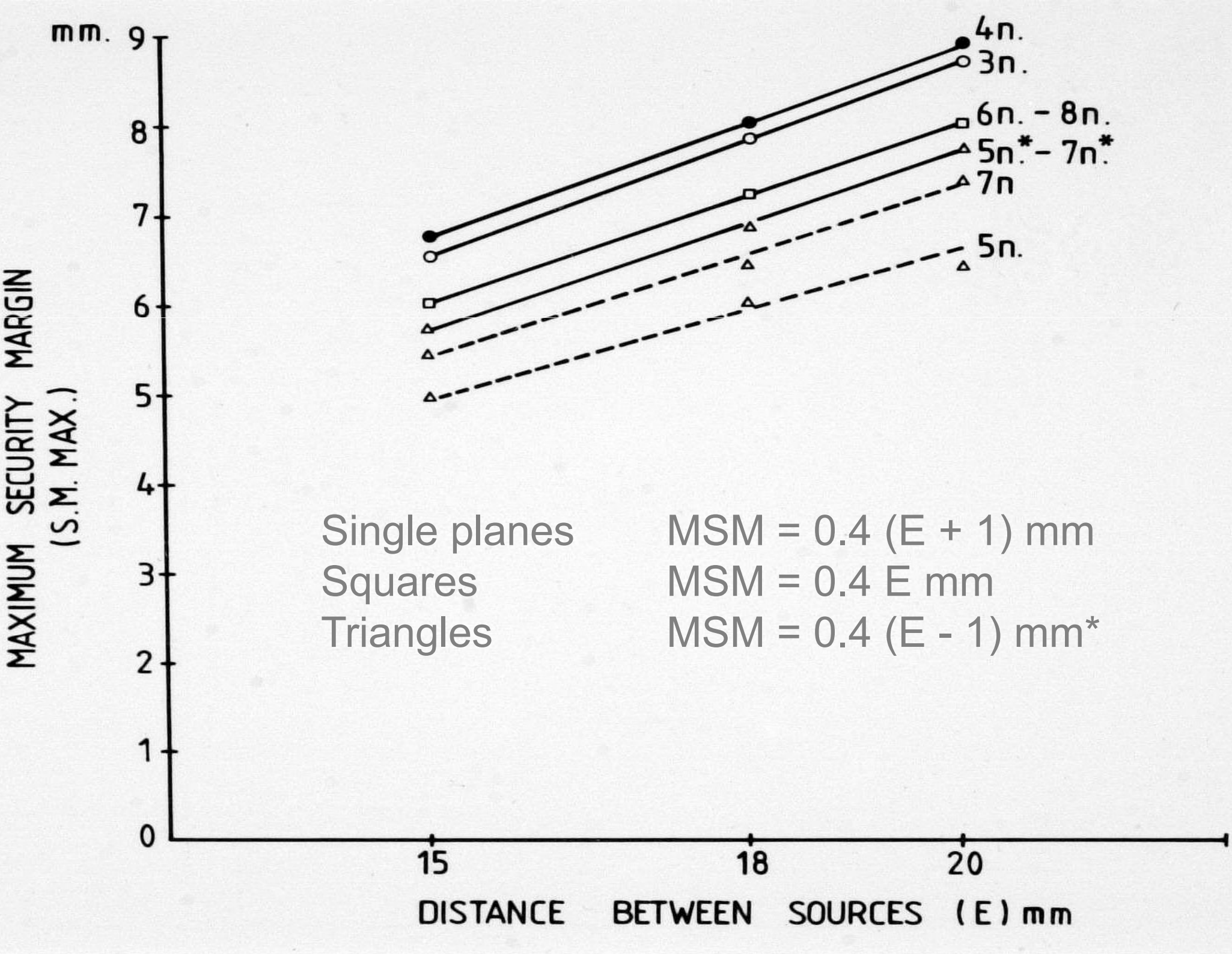




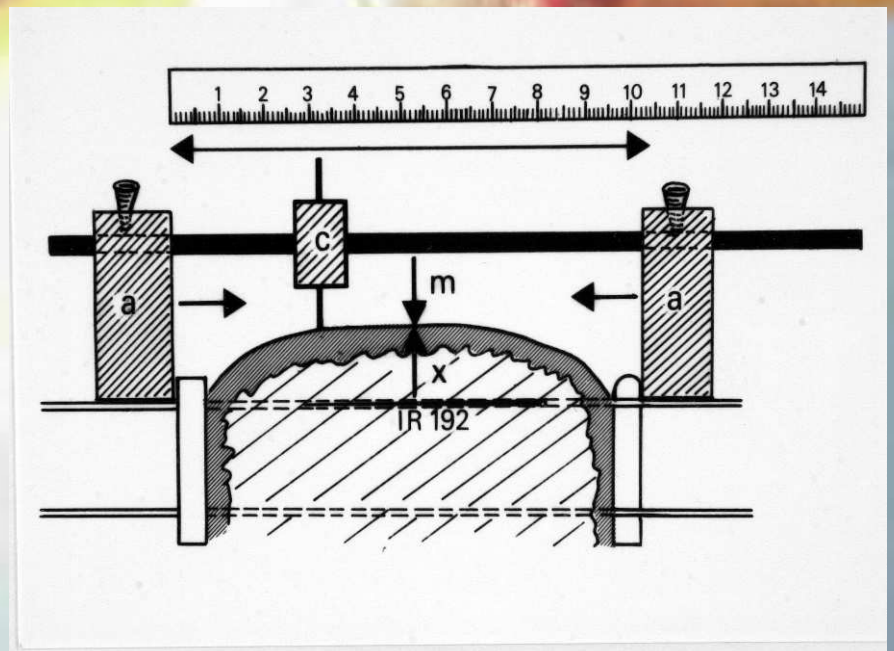

c. Lok Med
e. Lok LAO
d. Lok Lat

Tilting of
coronal plane


Rotation of
implantation axis

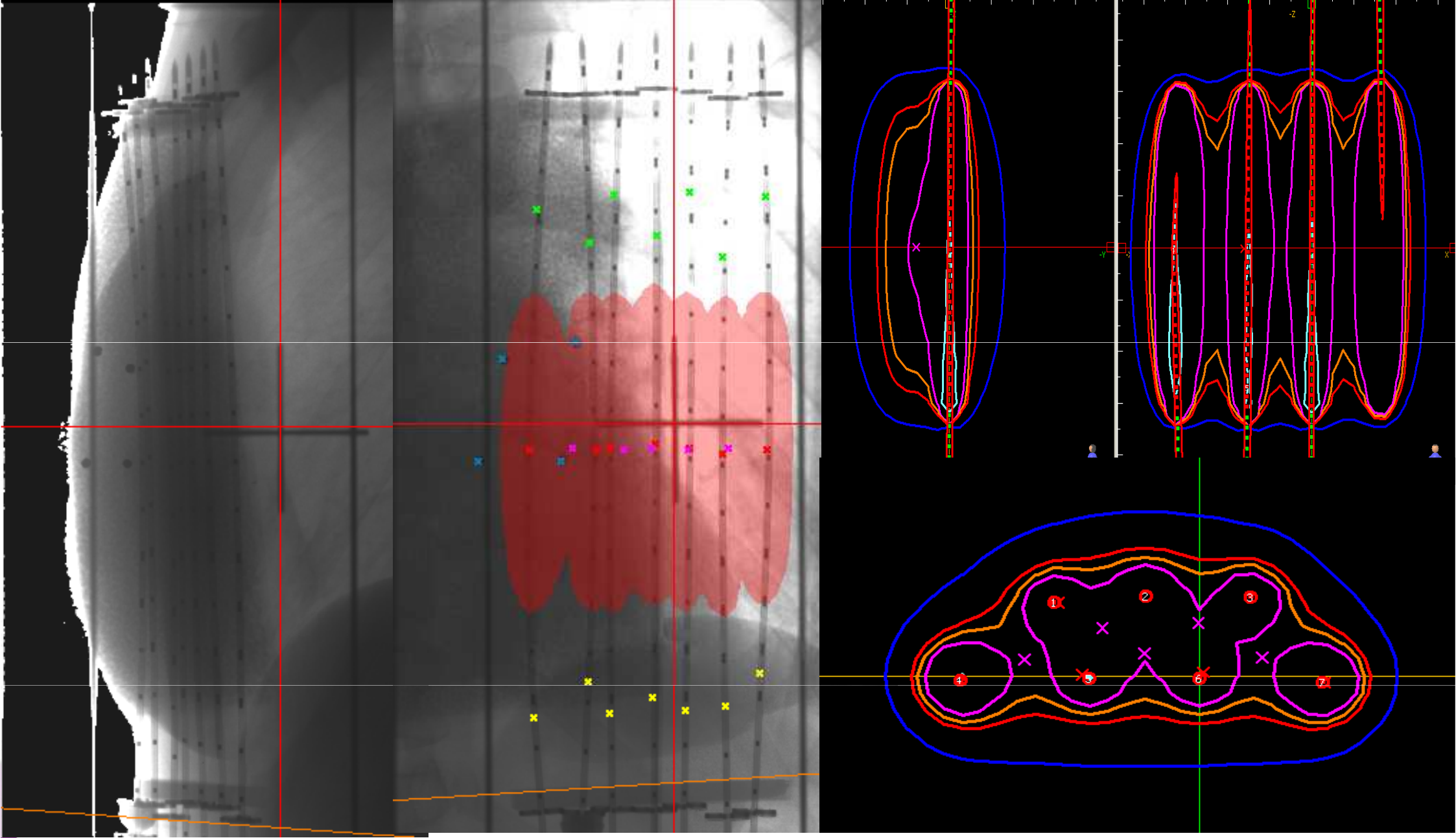

mm.
9
8
7
6
5
4
3
2
1
0
MAXIMUM SECURITY MARGIN
(S.M. MAX.)
4n.
3n.
6n. - 8n.
5n.* - 7n.*
7n
5n.
Single planes MSM = 0.4 (E + 1) mm
Squares MSM = 0.4 E mm
Triangles MSM = 0.4 (E - 1) mm*
15
18
20
DISTANCE BETWEEN SOURCES (E) mm

The Skin Source Measuring Bridge



Van Limbergen et al

Int. J. Rad.Onc. Biol. Phys 1989



8.5 Gy HDR
on D90 CTV BOOST

Skin Max Dose < 7.5 Gy

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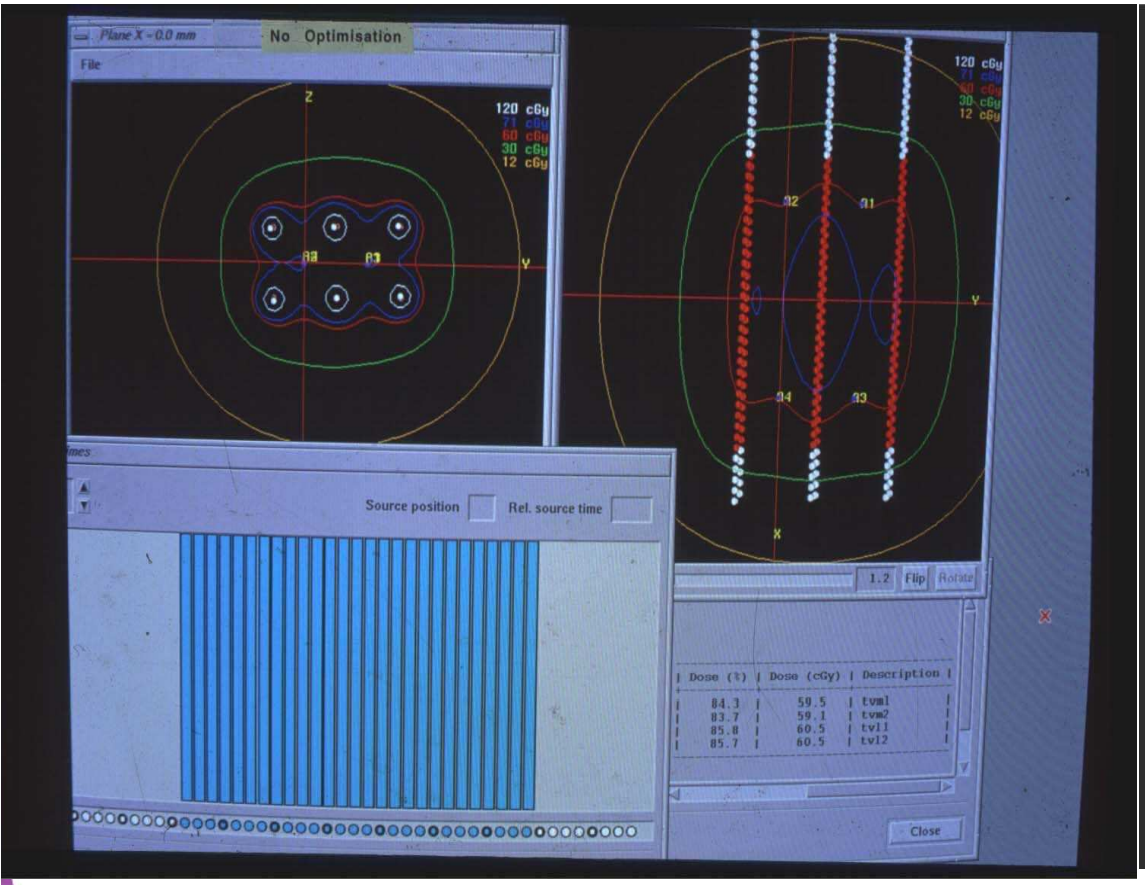
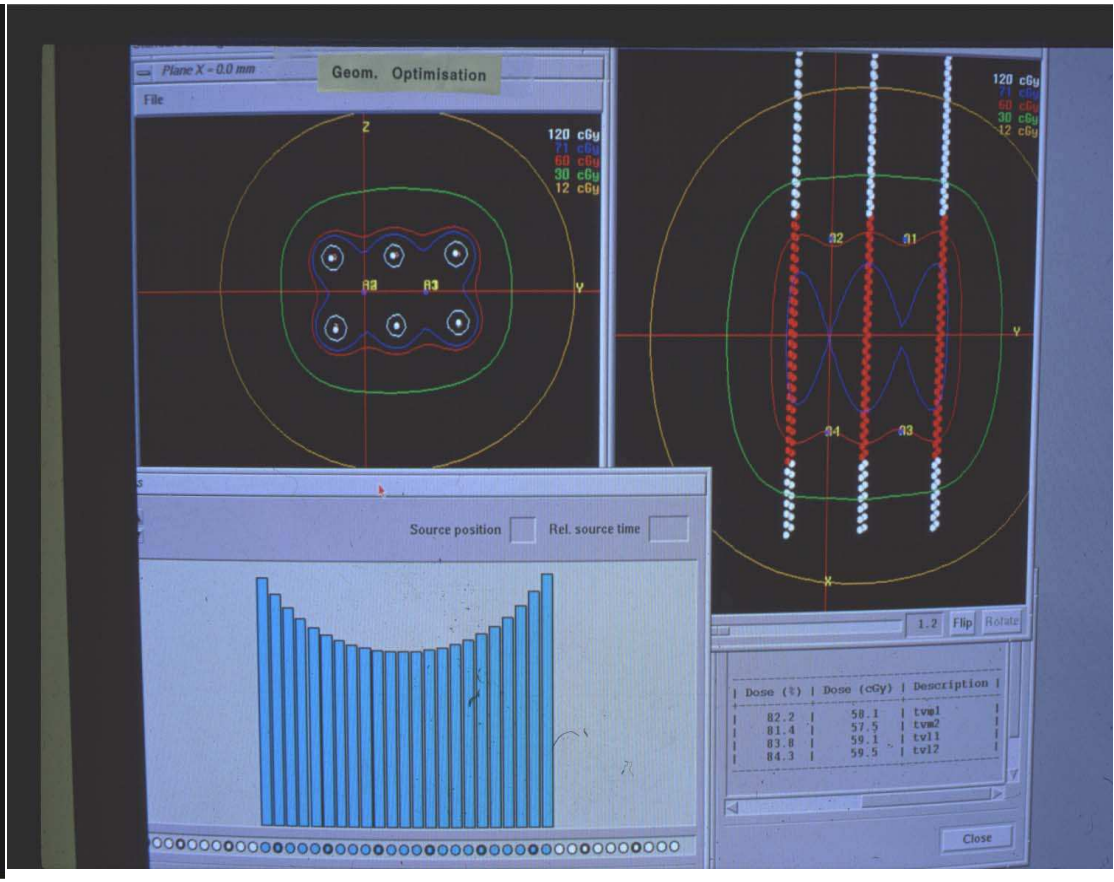
Optimization of Breast implant





Target covered
with **70mm** ASL
Skin doses too high

Target covered
with **50mm** ASL
Skin doses acceptable

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LEUVEN Data Material - Methods

426 T_{1-2} N_0N_1 breast ca pts,

Treated between 1983 - 1996
with BCS + Radiotherapy (442 Breasts)

Age 45 y (27-82 y)

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Breast Brachytherapy Boost Leuven 1983 - 1996

Teleangiectases in the breast skin

	no bridge	bridge	15 Gy bridge
Above implant	60 %	11.0 %	**4.5** %
Exit points	22 %	5.5 %	**2.8** %

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Boost target localisation
Intraoperative Boost

- Direct visualisation
  - no geographical miss ?
  - better cosmesis ?
- Shorter treatment time
- Reduced hospitalisation time

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Intra-operative Boost
Local recurrences

			local failures	
		n	5 y	10 y
Hennequin	LDR	954	7 %	16 %
	HDR	108	5.1 %	
Mansfield	LDR 20 Gy	1070	7 %	15 %
Krishnan	No long term data		2 /102 at 36 mos	

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Cosmesis
Intra - operative Boost

		Eo	Fair	Poor
Hennequin:	LDR	49 %	40 %	11 %
	HDR	63.2 %	31 %	
	postop	79.5 %		
	perop	**54.0 %**		

p=0.042

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Challenges to 3D-C MCBT

- Technically more demanding
- More complex treatment planning
- Considerable training and experience are essential
- No commercial hype as for MSB

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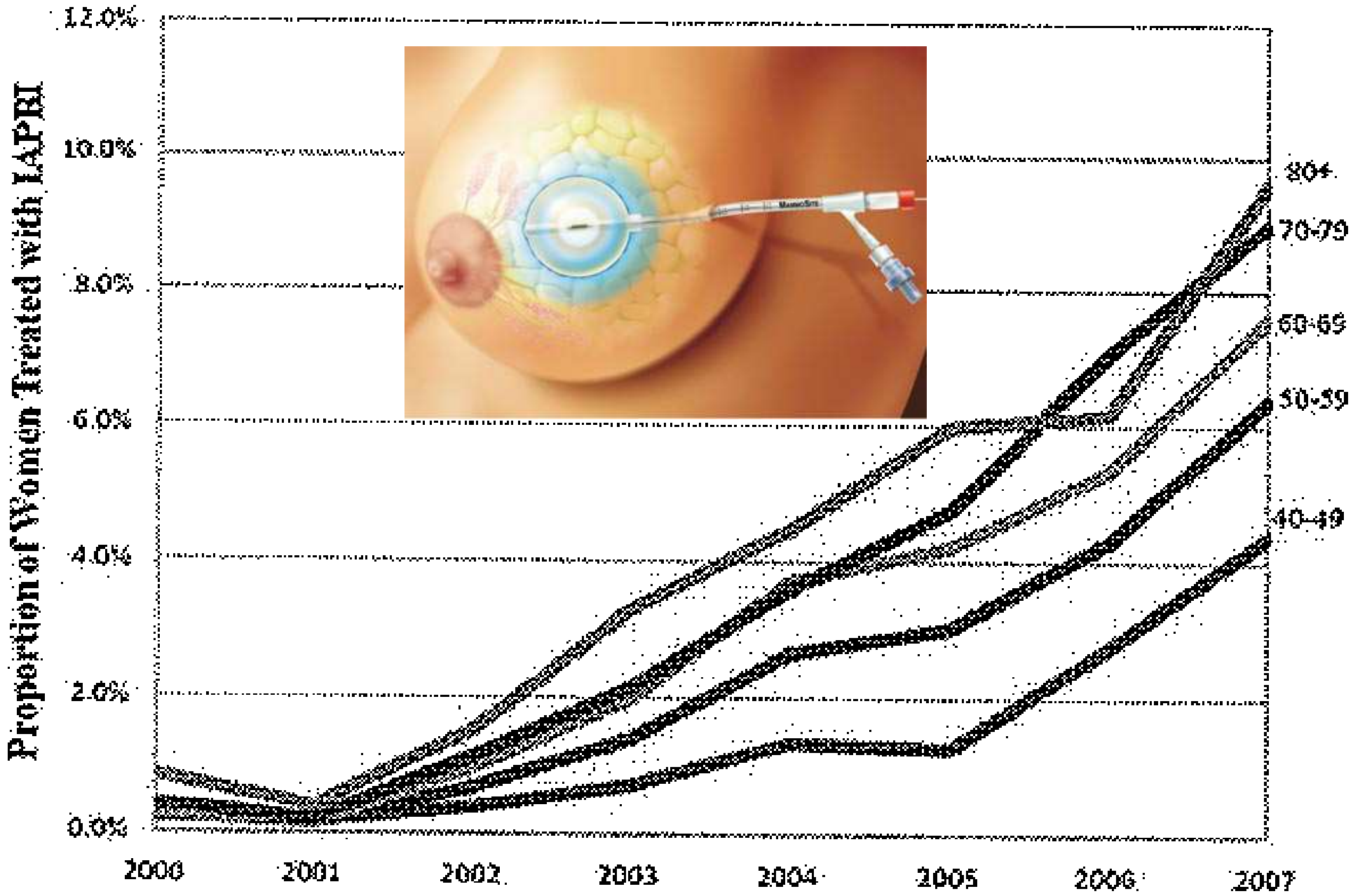


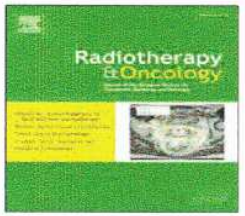
Figure 2. Implantable accelerated partial breast irradiation (IAPBI) use is shown by patient age from 2000 through 2007.

Radiotherapy and Oncology 91 (2009) 147–149

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Editorial

Accelerated partial breast irradiation with intracavitary balloon brachytherapy may be not as simple as it was supposed to be

Erik Van Limbergen *

Initially : skin – balloon spacing > 5mm is recommended
(Our prediction was : spacing should be at least 15 mm)

2004: Keish et al 34 % teles at 3 year spacing should be > 6mm
2005: Chao et al recommend >7 mm
2006: Jerusz et al recommend > 7mm
2006: Niehoff > 5mm : 16 % in boost and 36.5% in APBI
2007: Belcacémy > 17mm is needed to avoid any TA

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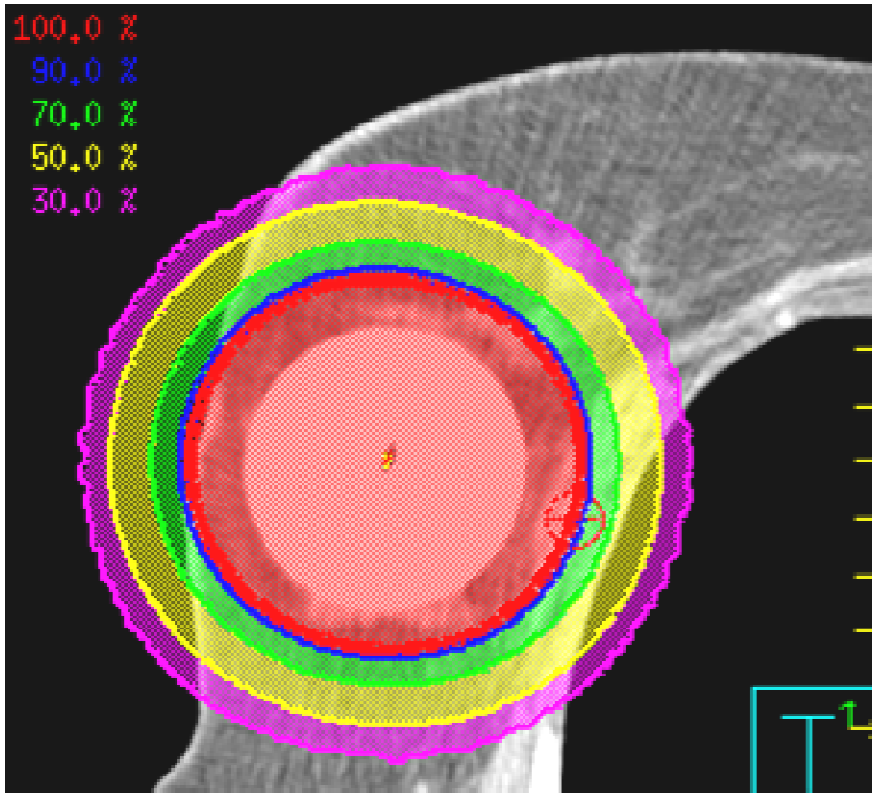
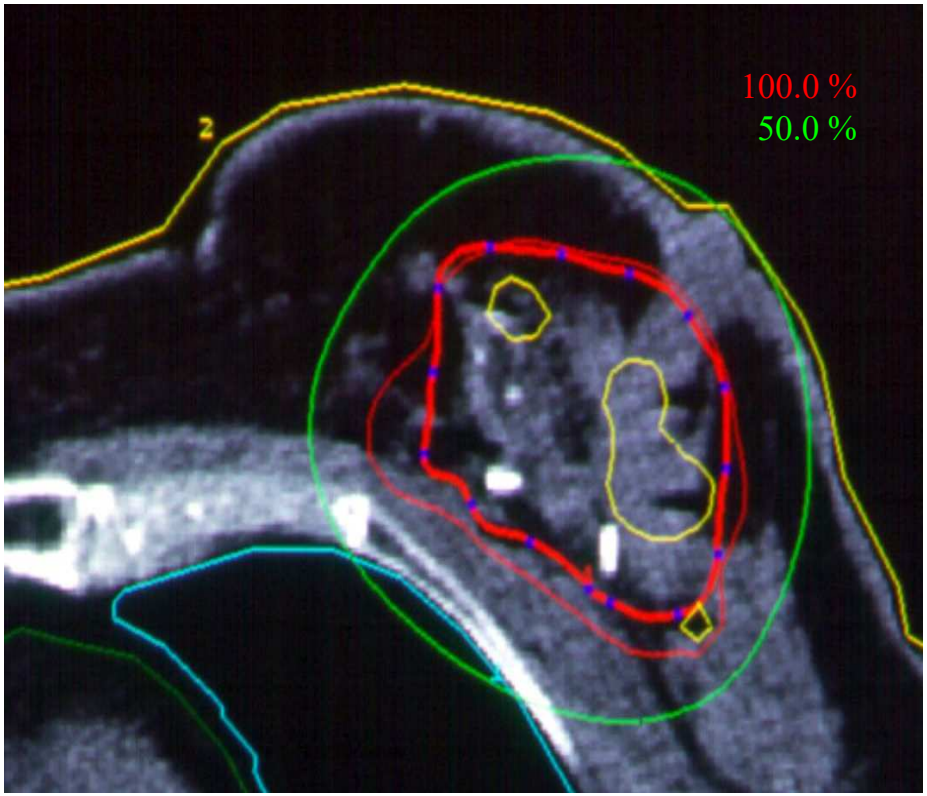
Comparison of dose distributions

MammoSite



Max. skin dose > 100%

Interstitial brachytherapy



Max. skin dose = 50%

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Conclusion

- MCBT has a high ballistic selectivity
  and potentially for the same nominal dose :
  - Better local control rates
  - Less fibrosis (volume effect)
  - Less teleangiectasia (skin dose)

- Technical performance is critical :
  - Target localisation
  - Avoidance of skin irradiation

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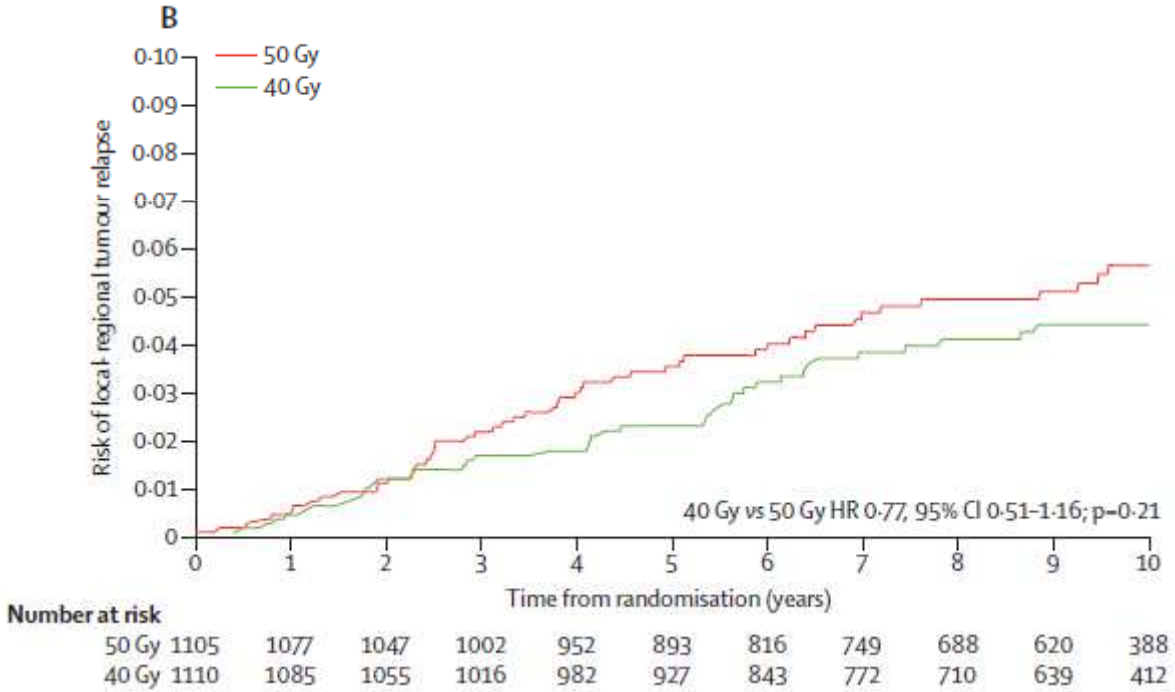
Accelerated Partial Breast Irradiation (APBI)

Peter Hoskin

Mount Vernon Cancer Centre

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Lancet Oncol 2013; 14: 1086–94



The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Lancet Oncol 2013; 14: 1086–94

	Moderate or marked events (n/patients; %)	Estimated proportion of patients with event by 5 years (%; 95% CI)	Estimated proportion of patients with event by 10 years (%; 95% CI)	Crude hazard ratio (95% CI)	p value*
Breast shrinkage†					
50 Gy	256/1003 (25·5%)	15·8% (13·6–18·3)	31·2% (27·9–34·9)	1·00	..
40 Gy	221/1006 (22·0%)	11·4% (9·5–13·6)	26·2% (23·1–29·6)	0·80 (0·67–0·96)	0·015
Breast induration (tumour bed)†					
50 Gy	153/1003 (15·3%)	12·1% (10·2–14·4)	17·4% (14·9–20·3)	1·00	..
40 Gy	129/1006 (12·8%)	9·6% (7·9–11·6)	14·3% (12·1–16·9)	0·81 (0·64–1·03)	0·084
Telangiectasia					
50 Gy	52/1081 (4·8%)	3·8% (2·8–5·2)	5·8% (4·4–7·7)	1·00	..
40 Gy	34/1094 (3·1%)	1·8% (1·1–2·8)	4·2% (2·9–5·9)	0·62 (0·40–0·96)	0·032
Breast oedema†					
50 Gy	86/1003 (8·6%)	8·1% (6·6–10·1)	9·0% (7·3–11·0)	1·00	..
40 Gy	49/1006 (4·9%)	4·7% (3·5–6·2)	5·1% (3·9–6·7)	0·55 (0·39–0·79)	0·001
Shoulder stiffness‡					
50 Gy	4/73 (5·5%)	2·9% (0·7–11·0)	8·2% (2·9–21·8)	1·00	..
40 Gy	3/81 (3·7%)	3·1% (0·8–11·9)	3·1% (0·8–11·9)	0·76 (0·17–3·39)	0·71
Arm oedema‡					
50 Gy	7/73 (9·6%)	6·0% (2·3–15·3)	13·5% (6·4–27·0)	1·00	..
40 Gy	3/81 (3·7%)	2·8% (0·7–10·7)	4·7% (1·5–14·0)	0·42 (0·11–1·63)	0·21

Rationale for APBI

- WLE and WB RT results in low rates of local recurrence
- Most local recurrences (up to 85%) occur near the original tumour bed
- WB RT results in significant morbidity

Patient selection for APBI

Organization	Appropriate age (years)	Maximum tumour size (cm)	Histology	Lymph-node involvement	Margin status
American Brachytherapy Society[31]	≥50	≤3	Infiltrating ductal carcinoma	No; by SLN or axillary dissection	Negative (at inked margin)
American Society of Breast Surgeons[32]	≥45	≤2	Invasive ductal carcinoma or DCIS	No; by SLN or axillary dissection	Negative (>2 mm)
NSABP B-39/RTOG-0413[33]	≥18 (on protocol)	≤3	Invasive ductal carcinoma or DCIS	Yes; allows for 0–3 nodes (no extracapsular extension allowed); axillary staging required for patients with invasive breast cancer	Negative (at inked margin)
ASTRO: 'suitable' patients outside of a clinical trial[34]	≥60	≤2	Invasive ductal carcinoma or favourable subtype (mucinous, tubular, and colloid)	No; by SLN or axillary dissection	Negative (>2 mm)

Radiotherapy and Oncology 94 (2010) 264–273

Patient selection for APBI

ASTRO consensus statement

Factors	Suitable criteria	Cautionary criteria	Unsuitable criteria
Age (years)	≥60	50–59	<50
Tumour size (cm)	≤2.0	2.1–3.0	>3.0
LN status	pN0	NS	pN1, pN2, pN3
Margin status	Negative (>2 mm)	Close (<2 mm)	Positive
Grade	Any	NS	NS
ER status	Positive	Negative	NS
DCIS	Not allowed	≤3 cm	>3 cm
LVSI	Not present	Limited or focal	Extensive
EIC	Not allowed	≤3 cm	≥3 cm
Multicentricity	Unicentric	NS	Present
Multifocality	Unifocal with total size ≤2 cm	Clinically unifocal with total size 2.1–3.0 cm	>3 cm or if clinically multifocal
BRCA mutation	Not present	NS	Present

Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 4, pp. 987–1001, 2009

Patient selection for APBI

GEC-ESTRO recommendations on patient selection for accelerated partial-breast irradiation.

Characteristic	A/low-risk group – good candidates for APBI	B/intermediate-risk group – possible candidates for APBI	C/high-risk group – contraindication for APBI
Patient age	>50 years	>40–50 years	⩽40 years
Histology	IDC, mucinous, tubular, medullary, and colloid cc.	IDC, ILC, mucinous, tubular, medullary, and colloid cc	–
ILC	Not allowed	Allowed	–
Associated LCIS	Allowed	Allowed	–
DCIS	Not allowed	Allowed	–
HG	Any	Any	–
Tumour size	pT1–2 (⩽30 mm)	pT1–2 (⩽30 mm)	pT2 (>30 mm), pT3, pT4
Surgical margins	Negative (⩾2 mm)	Negative, but close (<2 mm)	Positive
Multicentricity	Unicentric	Unicentric	Multicentric
Multifocality	Unifocal	Multifocal (limited within 2 cm of the index lesion)	Multifocal (>2 cm from the index lesion)
EIC	Not allowed	Not allowed	Present
LVI	Not allowed	Not allowed	Present
ER, PR status	Any	Any	–
Nodal status	pN0 (by SLNB or ALND[a])	pN1mi, pN1a (by ALND[a])	pNx; ⩾pN2a (4 or more positive nodes)
Neoadjuvant chemotherapy	Not allowed	Not allowed	If used

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……..choosing the wrong patients for APBI

Results of APBI studies using suboptimal patient selection criteria with adequate (⩾4 years) follow-up.

Institution	Technique	Median FUP (years)	LR% (*n*)	Annual LR% (*n*)	Comments on patient selection
Uzsoki hospital [37]	MDR	12	24 (17 of 70)	2	Max. tumour size: 5 cm; 100% unknown margins; 30% unknown pathological axillary status (pNx); 4% node positive; 10% lobular ca.; multifocal tumours, LVI and EIC allowed; no patient age limitation
Christie hospital[a] [20]	EBI	8	20 (69 of 353)	2.5	Max. tumour size: 4 cm; 100% unknown margins; no surgical axillary staging; lobular ca., LVI and EIC allowed; no patient age limitation
Cookridge hospital[a] [11]	EBI	8	12 (10 of 84)	1.5	Max. tumour size: 4.5 cm; 41% node positive; lobular ca., LVI and EIC allowed; no patient age limitation
London Reg. Ca. C. [30]	HDR	7.6	15 (6 of 39)	2	Max. tumour size: 4.5 cm; 31% close margins; 15% node positive; 5% pNx; 8% EIC pos.; no patient age limitation
Tufts university [16]	HDR	7	9.1 (3 of 33)	1.30	45% Close margins; 9% node positive; 55% EIC pos.; no patient age limitation
Guy's hospital I [12]	LDR	6	37 (10 of 27)	6.2	Max. tumour size >4 cm; 56% positive margins; 44% node positive, 41% EIC positive; lobular ca. and LVI allowed; patient age >40 years
Guy's hospital II [13]	MDR	6.3	18 (9 of 49)	2.9	Max. tumour size: 4 cm; 43% positive margins; 45% node positive; 14% lobular ca., LVI and EIC allowed, no patient age limitation
Osaka Med. center [26]	HDR	4.3	5.0 (1 of 20)	1.15	15% Positive margins; 35% EIC pos.; 5% lobular ca.; 10% DCIS; no patient age limitation (25% with age ⩽45 years)
Florence hospital [10]	LDR	4.2	6 (7 of 115)	1.4	Max. tumour size: 5 cm; 8% positive and 7% unknown margins; 38% node positive; 20% lobular ca.; LVI and EIC allowed, no patient age limitation
All patients		4.2–12	17 (132 of 790)	1.15–6.2	

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……..choosing the right patients for APBI

Trial	*n*	Median follow up (years)	Dose delivery, prescription	IBTR (%)	Good-to-excellent cosmesis (%)
King *et al.* (2000)[35]	51	6.25	LDR over 4 days (45 Gy) or HDR of 4 Gy for 8 fractions	2	75
Antonucci *et al.* (2009)[95]	199	9.6	LDR of 0.52 Gy/h for 96 h or HDR of 4 Gy for 8 fractions or HDR of 3.4 Gy for 10 fractions	5	98
Arthur *et al.* (2008)[39]	99	7	LDR of 0.4–0.54 Gy/h for 3.5–5 days or HDR of 3.4 Gy for 10 fractions	4	NR
Ott *et al.* (2011)[96], (2007)[97]	274	5.25	PDR over 5 days at 0.6 Gy/h or HDR of 4 Gy for 8 fractions	2.9	94
Polgár *et al.* (2007)[50], (2010)[98]	45	12	HDR of 4.33 Gy for 7 fractions or 5.2 Gy for 7 fractions	8.9	77.8

Treatment modalities for APBI

- External beam radiotherapy
  - 3D CRT
  - IMRT
  - SBRT
- Brachytherapy
  - Interstitial multicatheter
  - Balloon catheter
- Intra-operative radiotherapy
  - TARGIT
  - electrons

Comparison of three accelerated partial breast irradiation techniques: Treatment effectiveness based upon biological models

Joseph Bovi, X. Sharon Qi, Julia White, X. Allen Li*

Radiotherapy & Oncology 2007

- NSABP-B39/RTOG Phase III Trial
- External Beam 50-50.4Gy (1.8-2.0Gy per #)

  vs

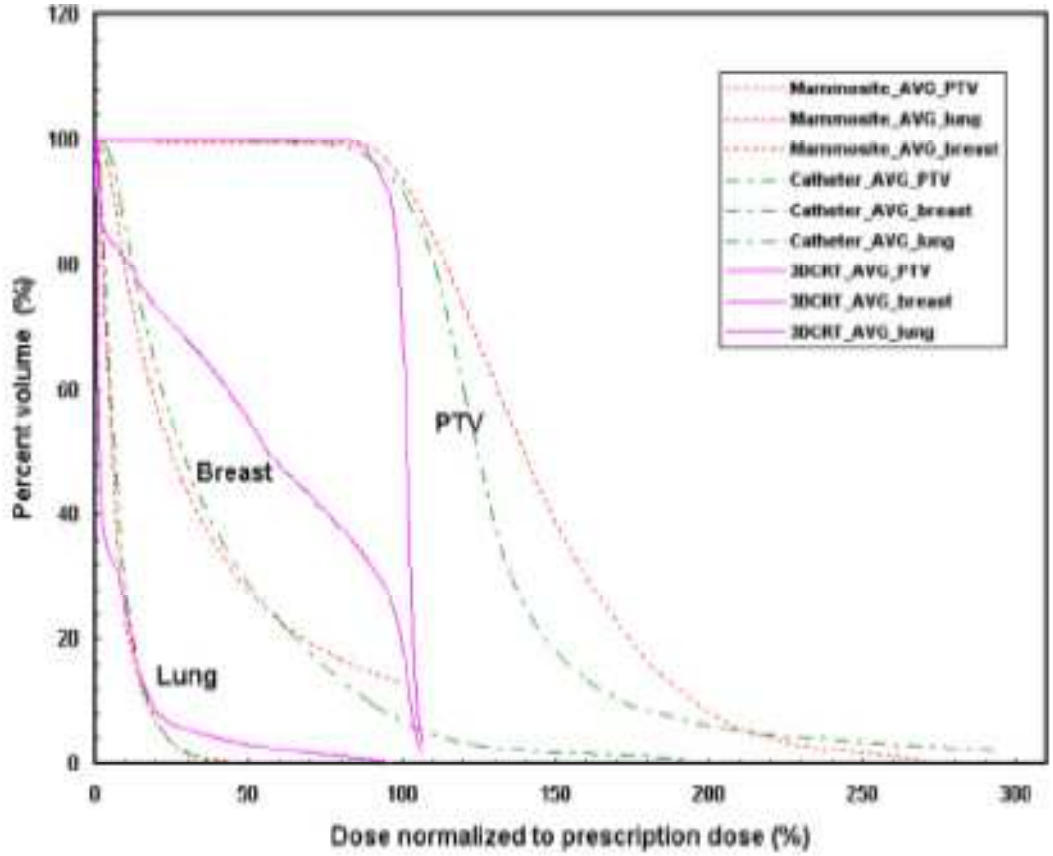
- ABPI

Multicatheter interstitial MCT):	34Gy	10f	5days
Mammosite (MST):	34Gy	10f	5days
External beam (3DCRT):	38.5Gy	10f	5days

Comparison of three accelerated partial breast irradiation techniques: Treatment effectiveness based upon biological models

Joseph Bovi, X. Sharon Qi, Julia White, X. Allen Li*

Radiotherapy & Oncology 2007



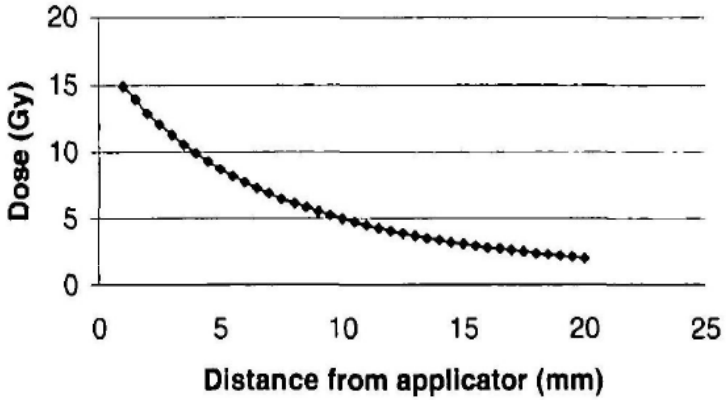
Average DVHs of the five patients in each of the three APBI modalities for PTV, breast, and lung.

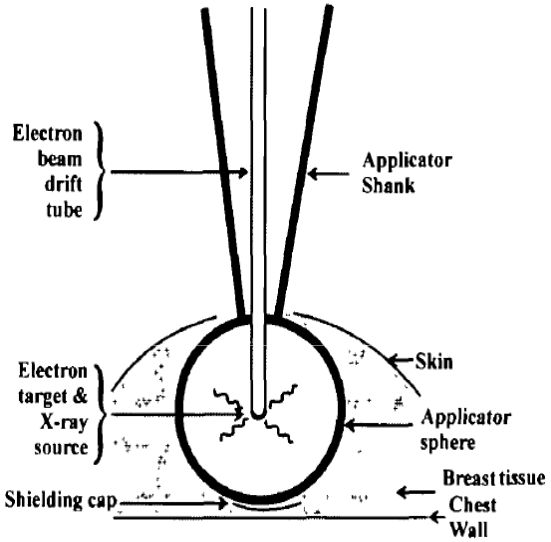
The INTRABEAM® Photon Radiotherapy System for the adjuvant treatment of early breast cancer: a systematic review and economic evaluation

HEALTH TECHNOLOGY ASSESSMENT

VOLUME 19 ISSUE 69 AUGUST 2015

Jo Picot,* Vicky Copley, Jill L Colquitt, Neelam Kalita, Debbie Hartwell and Jackie Bryant



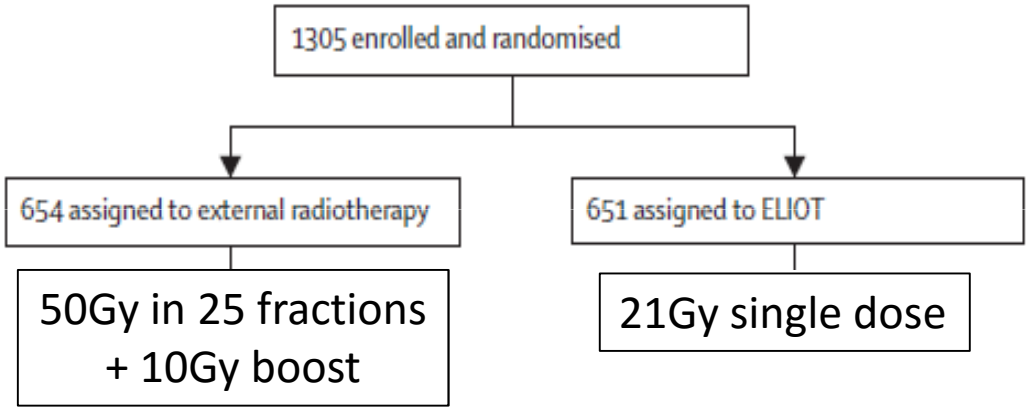


Local recurrence	INTRABEAM events/*n*; 5-year cumulative risk (%) (95% CI)[65]	WB-EBRT events/*n*; 5-year cumulative risk (%) (95% CI)[65]	Absolute difference in Kaplan–Meier estimate at 5 years; *p*-value
Whole group ($n = 3375$)[a]	23/1679; 3.3 (2.1 to 5.1)	11/1696; 1.3 (0.7 to 2.5)	12 (2.0%); $p = 0.042$
Pre-pathology stratum ($n = 2234$)[a]	10/1107; 2.1 (1.1 to 4.2)	6/1127; 1.1 (0.5 to 2.5)	4 (1.0%); $p = 0.31$
Post-pathology stratum ($n = 1141$)[a]	13/572; 5.4 (3.0 to 9.7)	5/569; 1.7 (0.6 to 4.9)	8 (3.7%); $p = 0.069$

Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Lancet Oncol 2013; 14: 1269–77

Umberto Veronesi, Roberto Orecchia, Patrick Maisonneuve, Giuseppe Viale, Nicole Rotmensz, Claudia Sangalli, Alberto Luini, Paolo Veronesi, Viviana Galimberti, Stefano Zurrida, Maria Cristina Leonardi, Roberta Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella, Bettina Ballardini



Pathological size‡		
≤1 cm	194 (30%)	199 (31%)
1–1·5 cm	235 (36%)	243 (38%)
1·5–2 cm	115 (18%)	120 (19%)
>2 cm	103 (16%)	83 (13%)

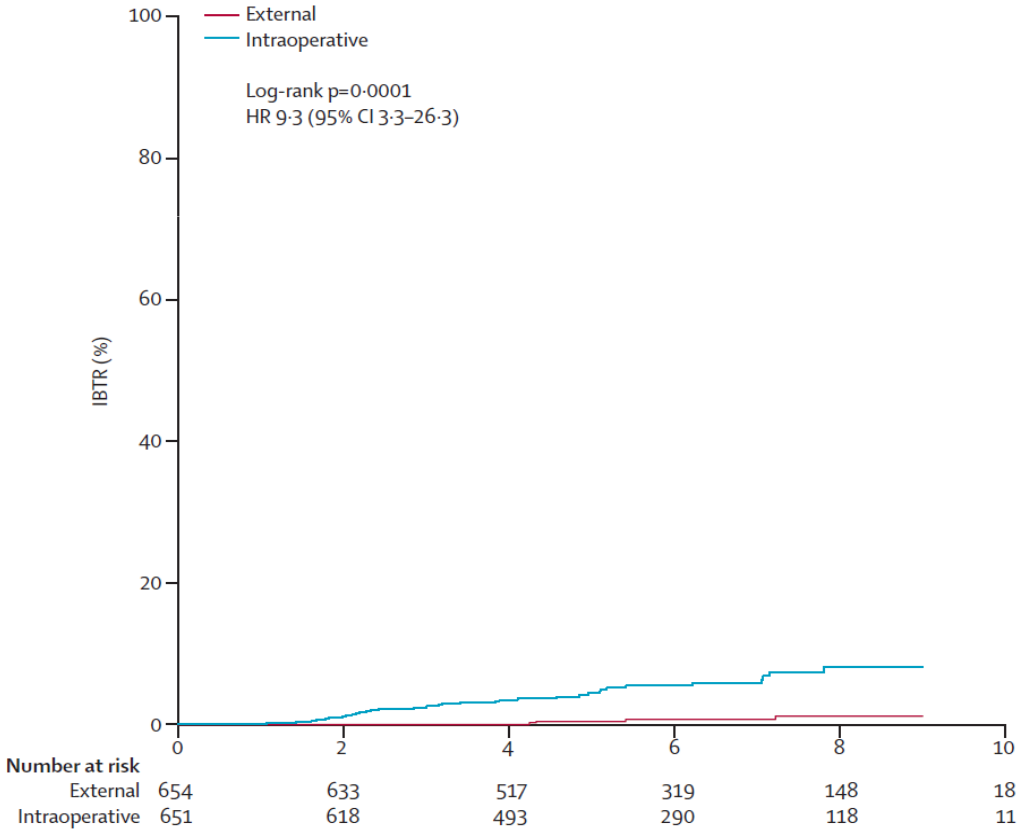
Number of positive nodes†		
None	471 (73%)	478 (74%)
1–3	138 (21%)	138 (21%)
≥4	38 (6%)	31 (5%)

Tumour grade§		
G1	160 (25%)	196 (31%)
G2	328 (52%)	305 (48%)
G3	145 (23%)	129 (20%)

Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Lancet Oncol 2013; 14: 1269–77

Umberto Veronesi, Roberto Orecchia, Patrick Maisonneuve, Giuseppe Viale, Nicole Rotmensz, Claudia Sangalli, Alberto Luini, Paolo Veronesi, Viviana Galimberti, Stefano Zurrida, Maria Cristina Leonardi, Roberta Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella, Bettina Ballardini



	External radiotherapy	intraoperative radiotherapy with electrons	p value†
Any skin toxicity			
No	427	401	..
Yes, acute	32	5	..
Yes, chronic	5	6	0·0002
Erythema			
No	7	24	..
Grade 1–2	35	5	..
Grade 3	2	0	..
Grade 4	3	0	..
Grade 5	0	0	<0·0001
Dryness			
No	128	147	..
Grade 1–2	20	10	..
Grade 3–5	0	0	0·04
Hyper-pigmentation			
No	138	146	..
Grade 1–2	36	11	..
Grade 3-5	0	0	0·0004

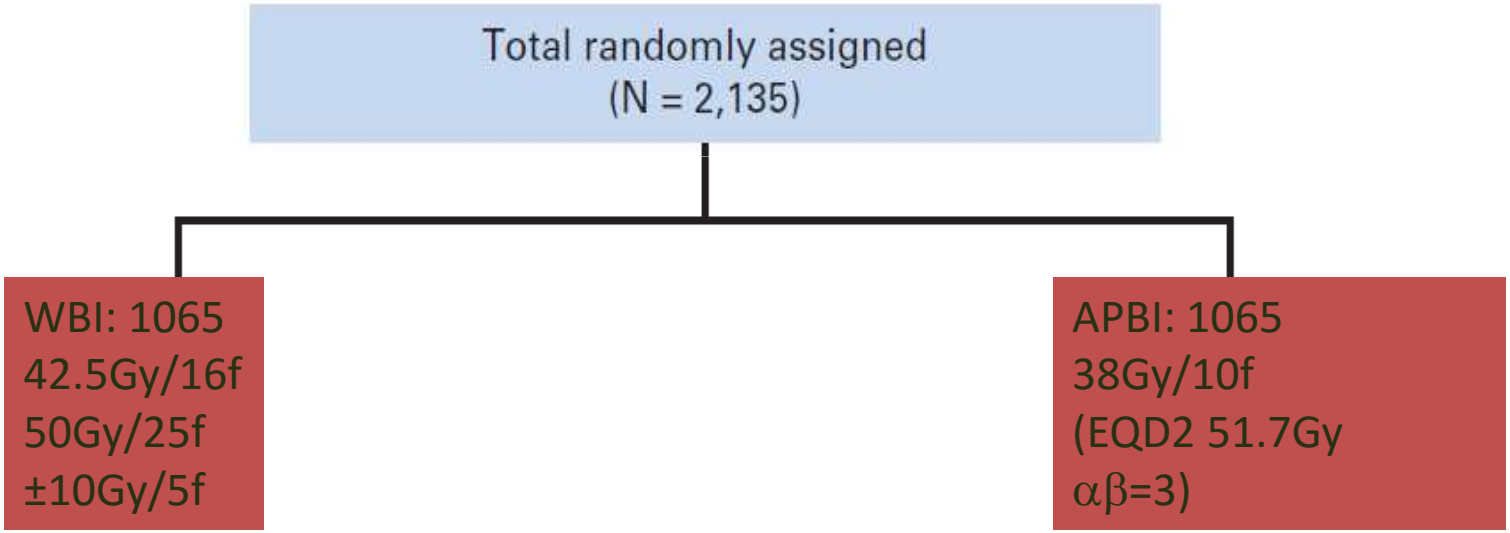
APBI with external beam techniques

Series	*n*	Median follow up (years)	EBRT dose (bid fractionation)	IBTR (%)	Good-to-excellent cosmesis (%)
Chen *et al.* (2010)[40]	94	4.2	3.85 Gy for 10 fractions	1.1	89
Hepel *et al.* (2009)[59]	60	1.25	3.85 Gy for 10 fractions	NR	81.7
Vicini *et al.* (2010)[105]	58	4.5	3.85 Gy for 10 fractions	6	NR
Jagsi *et al.* (2010)[60]	32	2.5	3.85 Gy for 10 fractions	NR	79.5
Shah *et al.* (2012)[106]	192	4.8	3.85 Gy for 10 fractions	0	81
Formenti *et al.* (2012)[63]*	47	1.5	6 Gy for 5 fractions (10 days)	0	89

Interim Cosmetic and Toxicity Results From RAPID: A Randomized Trial of Accelerated Partial Breast Irradiation Using Three-Dimensional Conformal External Beam Radiation Therapy

Ivo A. Olivotto, Timothy J. Whelan, Sameer Parpia, Do-Hoon Kim, Tanya Berrang, Pauline T. Truong, Iwa Kong, Brandy Cochrane, Alan Nichol, Isabelle Roy, Isabelle Germain, Mohamed Akra, Melanie Reed, Anthony Fyles, Theresa Trotter, Francisco Perera, Wayne Beckham, Mark N. Levine, and Jim A. Julian

J Clin Oncol 31:4038-4045. © 2013



Interim Cosmetic and Toxicity Results From RAPID: A Randomized Trial of Accelerated Partial Breast Irradiation Using Three-Dimensional Conformal External Beam Radiation Therapy

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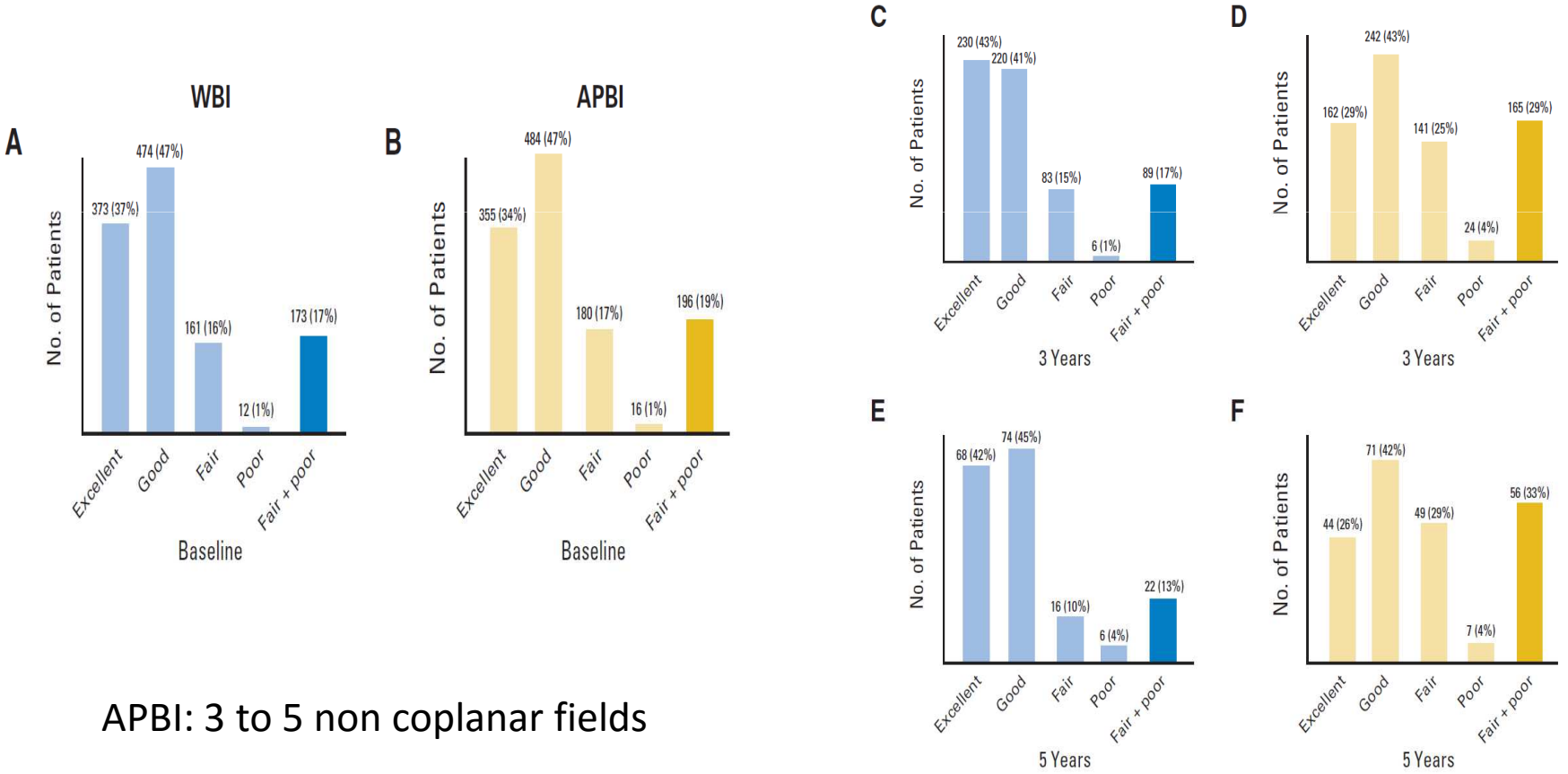
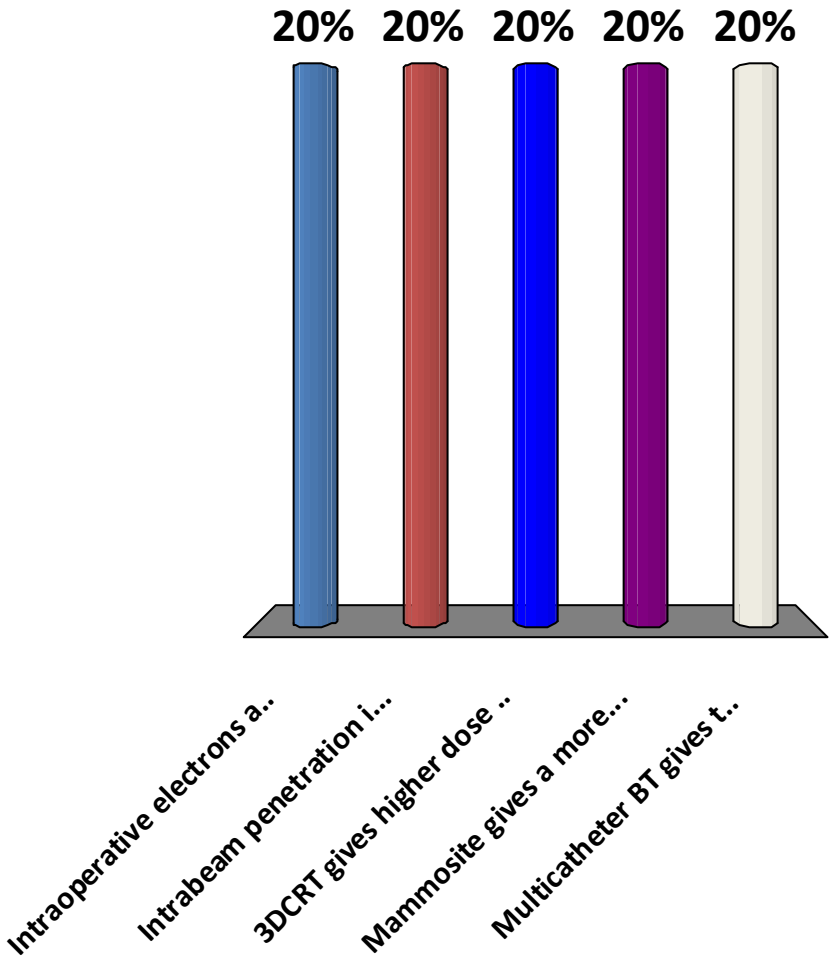
J Clin Oncol 31:4038-4045. © 2013



APBI: 3 to 5 non coplanar fields

Treatment modalities for APBI……

A. Intraoperative electrons are equivalent to EBRT
B. Intrabeam penetration is 50% at 10mm
C. 3DCRT gives higher dose to the breast than BT
D. Mammosite gives a more conformal dose than BT
E. Multicatheter BT gives the lowest skin dose



Treatment modalities for APBI

- External beam radiotherapy
  - 3D CRT
  - IMRT
  - SBRT
- Brachytherapy
  - Interstitial multicatheter
  - Balloon catheter
- Intra-operative radiotherapy
  - TARGIT
  - electrons

Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery

Radiotherapy and Oncology 115 (2015) 342–348

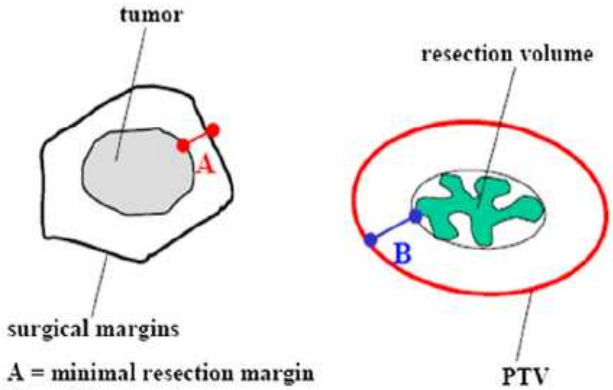
CVS 1
No cavity

CVS2
Heterogenous cavity with indistinct margins

CVS3
Heterogenous cavity with some indistinct margins

CVS4
Mildly heterogenous cavity with mostly distinct margins

CVS5
Homogenous cavity with clearly identified margins



A = minimal resection margin
B = safety margin

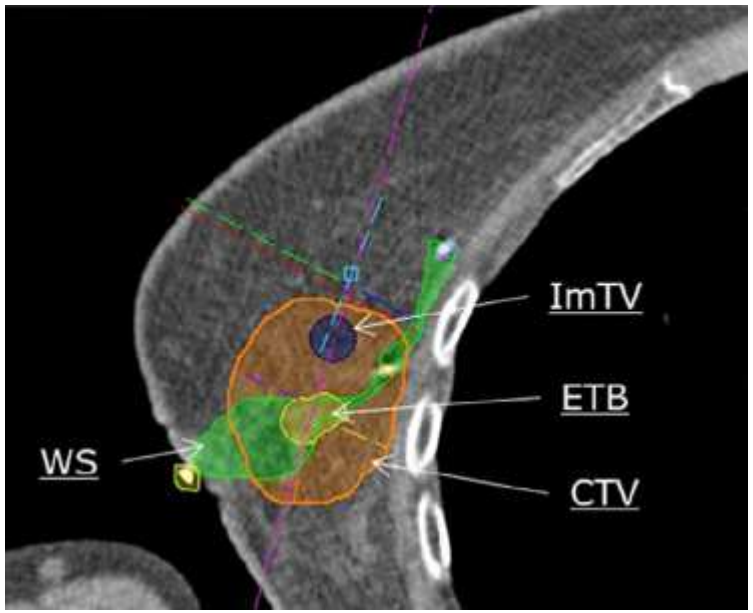
B = >20 mm minus A

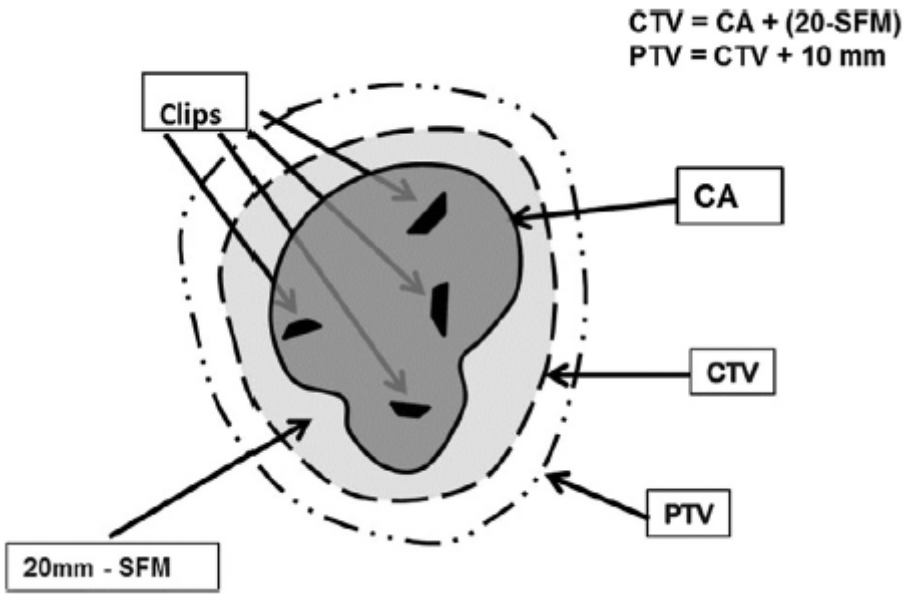
Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery

Radiotherapy and Oncology 115 (2015) 342–348

Recommendations

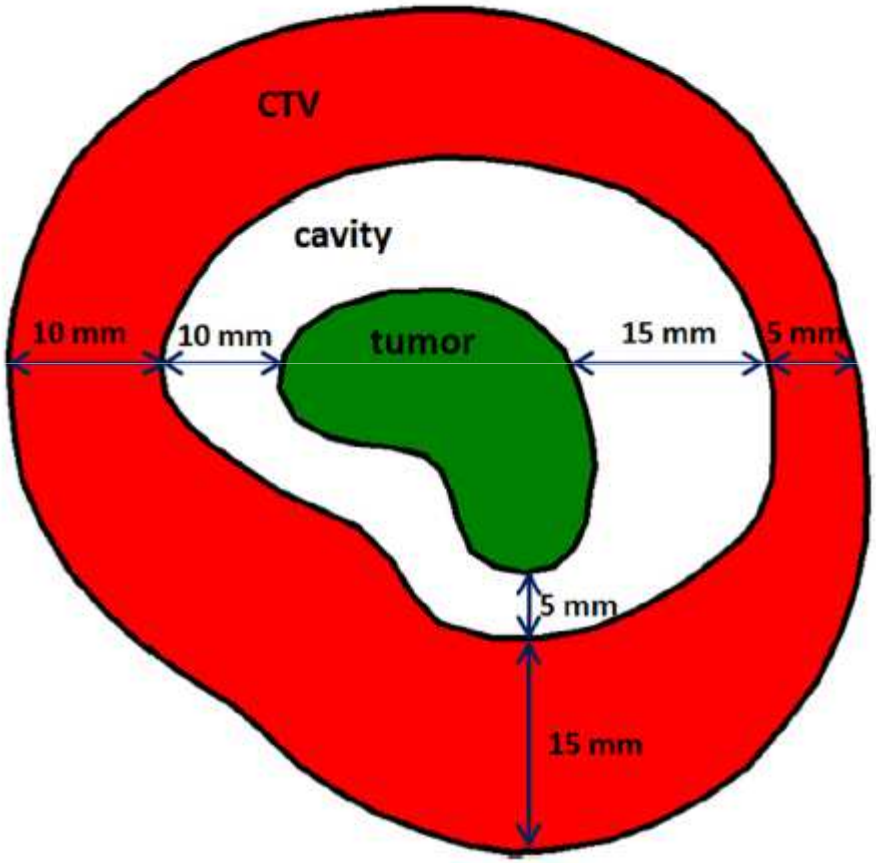
1. Perform a CT with marks on the scar.
2. Delineation of the clips.
3. Delineation of surgical bed – whole surgical scar (WS) inside breast.
4. Delineation of ImTV (Imaging correlated Target Volume).
5. Delineation of ETB (Estimated Tumour Bed).
6. Delineation of CTV (Clinical Target Volume).
7. Delineation of PTV (Planning Target Volume).



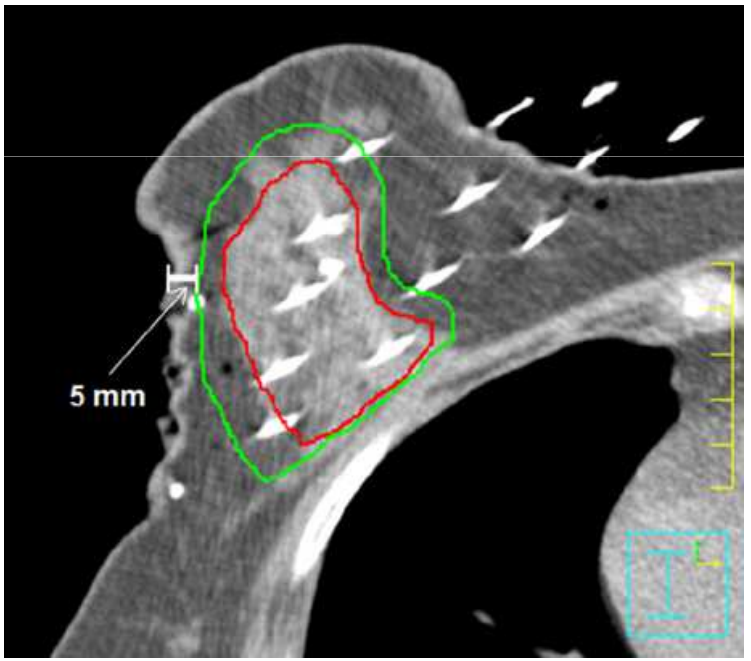


Recommendations from GEC ESTRO Breast Cancer Working Group (II): Target definition and target delineation for accelerated or boost partial breast irradiation using multicatheter interstitial brachytherapy after breast conserving open cavity surgery

Radiotherapy and Oncology xxx (2016) xxx–xxx



Tumour margins defined by preresection CT and post resection clips



Limited to chest wall and 5mm from skin

Brachytherapy with interstitial catheters

Trial	*n*	Median follow up (years)	Dose delivery, prescription	IBTR (%)	Good-to-excellent cosmesis (%)
King *et al.* (2000)[35]	51	6.25	LDR over 4 days (45 Gy) or HDR of 4 Gy for 8 fractions	2	75
Antonucci *et al.* (2009)[95]	199	9.6	LDR of 0.52 Gy/h for 96 h or HDR of 4 Gy for 8 fractions or HDR of 3.4 Gy for 10 fractions	5	98
Arthur *et al.* (2008)[39]	99	7	LDR of 0.4–0.54 Gy/h for 3.5–5 days or HDR of 3.4 Gy for 10 fractions	4	NR
Ott *et al.* (2011)[96], (2007)[97]	274	5.25	PDR over 5 days at 0.6 Gy/h or HDR of 4 Gy for 8 fractions	2.9	94
Polgár *et al.* (2007)[50], (2010)[98]	45	12	HDR of 4.33 Gy for 7 fractions or 5.2 Gy for 7 fractions	8.9	77.8

Brachytherapy with balloon catheters

Mammosite

Trial	*n*	Median follow up (years)	HDR dose (bid fractionation)	IBTR (%)	Good-to-excellent cosmesis (%)
Khan *et al.* (2012)[99]	1,440	5	3.4 Gy for 10 fractions	3.6 (women >70 years 3.7% and younger women 3.3%)	At 3 years, 92.4% for women aged >70 years and 93.4% for younger women
Cuttino *et al.* (2008)[100]	483	2	3.4 Gy for 10 fractions	1.2	91
Benitez *et al.* (2007)[38]	43	5.4	3.4 Gy for 10 fractions	0	83.3
Wilkinson *et al.* (2012)[101]	45	3.7	7 Gy for 4 fractions	0	98
Dragun *et al.* (2007)[102]	90	2	3.4 Gy for 10 fractions	2.2	90

Multi-lumen catheters

Trial	*n*	Median follow up (months)	Device(s)	IBTR (%)
Lee *et al.* (2012)[56]	26	9	MammoSite® ML and Contura®	NR
Fisher *et al.* (2012)[55]	40	13	SAVI®	NR
Israel *et al.* (2012)[103]	46	36	Contura®	2
Yashar *et al.* (2011)[104]	102	21	SAVI®	1

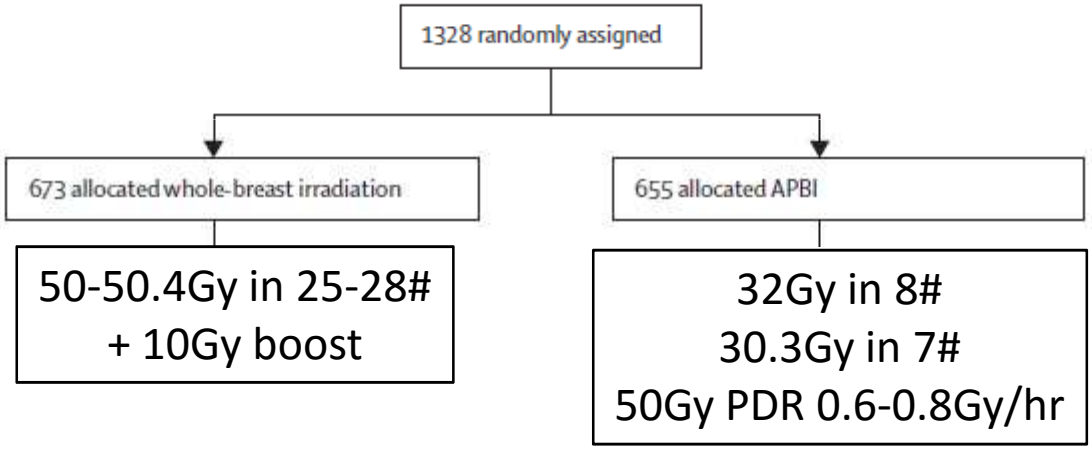
APBI phase III trials

Trial	Design	Patients planned	Inclusion criteria	APBI technique	Control arm
NSABP B-39/RTOG 0413	Equivalence (closed to low-risk arm)	4,300	Age ≥18 years; DCIS or invasive adenocarcinoma; stage 0, I, II (T <3 cm); lumpectomy; margins free of tumour; ≤3 positive nodes	34 Gy in 10 fractions using MIB or MammoSite® /MammoSite® ML/ SAVI® or 38.5 Gy over 10 fractions using 3D-CRT	WBI: 50–50.4 Gy in 25 or 28 fractions with optional 10–16 Gy boost (no brachytherapy boost permitted)
TARGIT	Equivalence (completed enrollment)	2,232	Age ≥45 years; T1, small T2, N0, N1; ductal; non-lobular and no EIC	20 Gy in 1 fraction, IORT low energy X-rays (50 Kv)	WBI according to treating institutions guidelines
ELIOT	Equivalence	824	Age ≥48 years; T ≤2.5 cm, N0; invasive carcinoma; quadrantectomy	21 Gy in 1 fraction, IORT, electrons up to 9 MeV	WBI: 50 Gy in 25 fractions with optional 10 Gy boost
RAPID (OCOG)	Equivalence	2,128	Age ≥40 years; T <3 cm, N0; DCIS or invasive carcinoma; negative margins	38.5 Gy in 10 fractions (5–8 days) using 3D-CRT	WBI: 42.5 Gy in 16 fractions. Large breast to receive 50 Gy in 25 fractions. Boost irradiation of 10 Gy in 4–5 fractions for moderate-risk to high-risk patients as per local cancer centre guidelines
GEC-ESTRO	Non-Inferiority, non-irrelevant, 3% difference	1,300	Age ≥40 years; T ≤3 cm, pN0-Nmi; stage 0, I, II; DCIS, ductal or lobular carcinoma; margin ≥2 mm	32 Gy in 8 fractions or 30.3 Gy in 7 fractions MIB HDR or 50 Gy MIB PDR (1 pulse/h, 24 h/day; 0.6–0.8 Gy/h)	WBI: 50–50.4 Gy in 25/28 fractions with optional 10 Gy boost
IMPORT-LOW	Non-inferiority	1,935	Age ≥50 years; T ≤3 cm, node negative; invasive adenocarcinoma; margin ≥2 mm	IMRT; supine position Arm 1: 40 Gy in 15 fractions to primary tumour region + 36 Gy in 15 fractions to low-risk region (EBRT) Arm 2: 40 Gy in 15 fractions to primary tumour region (EBRT)	WBI: 40 Gy in 15 fractions
IRMA	Non-inferiority	3,302	Age ≥49 years; T <3 cm, N0; invasive carcinoma; margins ≥2 mm	38.5 Gy in 10 fractions using 3D-CRT	WBI, 45 Gy in 18 fractions or 50–50.4 Gy in 25/28 fractions

5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial

Lancet 2016; 387: 229–38

Vratislav Strnad, Oliver J Ott, Guido Hildebrandt, Daniela Kauer-Dorner, Hellen Knauerhase, Tibor Major, Jaroslaw Lyczek, Jose Luis Guinot, **et al**



T stage		
pTis (DCIS)	36 (6%)	24 (4%)
pT1mi	0	4 (1%)
pT1a	30 (5%)	21 (4%)
pT1b	187 (30%)	182 (33%)
pT1c	313 (49%)	262 (48%)
pT2 (≤3 cm)	67 (11%)	58 (11%)

Grading		
1	248 (39%)	217 (39%)
2	319 (50%)	288 (52%)
3	57 (9%)	42 (8%)
No data	9 (1%)	4 (1%)

5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial

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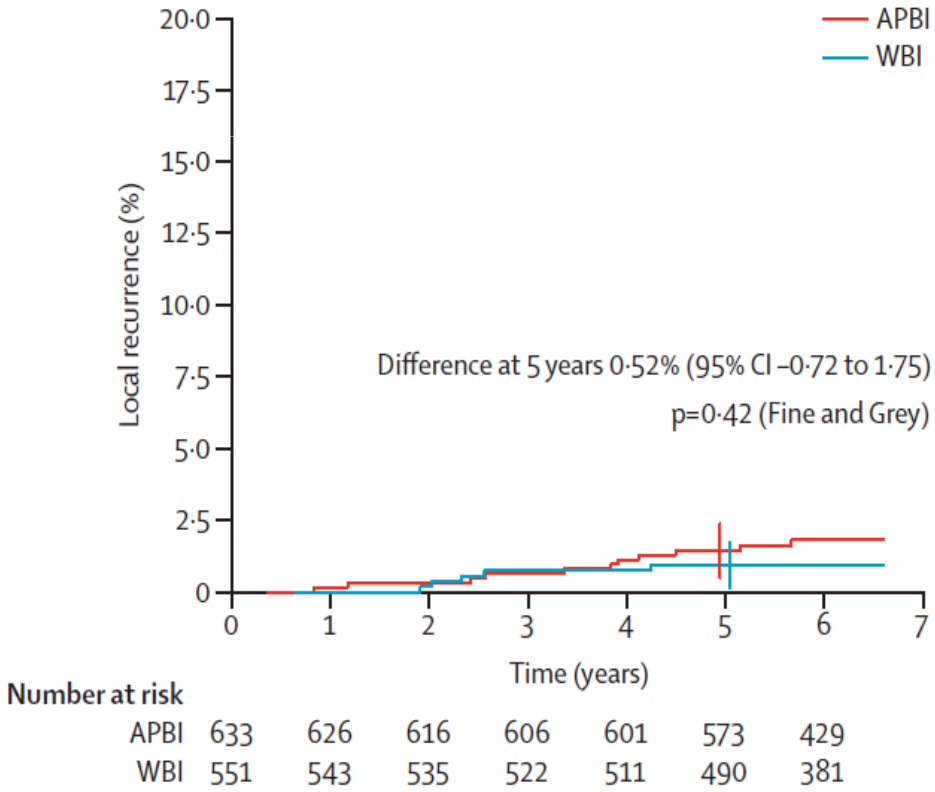


Late Toxicity	WBRT	ABPI
Grade 2/3 skin	6%	3%
Grade 2/3 subcut	6%	8%
Grade 3 fibrosis	0.23%	0
NO grade 4 events		

Florence, March 13-16 2016

ESTRO School

Modern Brachytherapy Techniques

WWW.ESTRO.ORG/SCHOOL

Optimization in Interstitial Treatment Plans

ESTRO Teaching Course

Florence, 2016

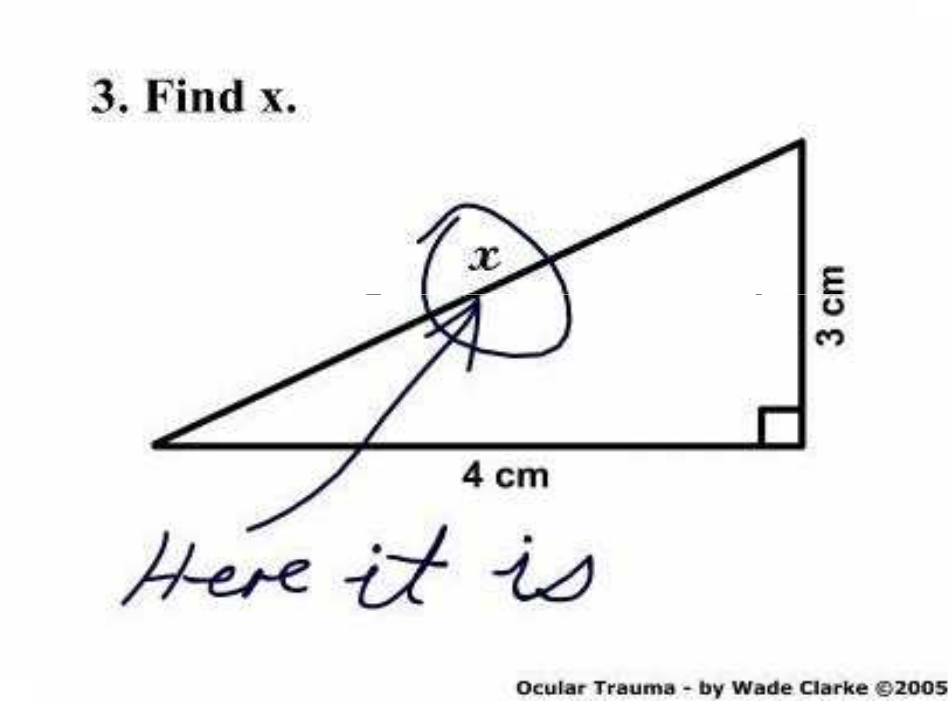
Dimos Baltas

E-mail: dimos.baltas@uniklinik-freiburg.de

ESTRO School

Introduction on Dose Optimization

What do we really mean with Optimisation,
Inverse Optimisation or
Inverse Planning ?



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Introduction on Dose Optimization

Bridge "inverter"between China and Hong Kong, since the traffic flows in Hong Kong on the left.

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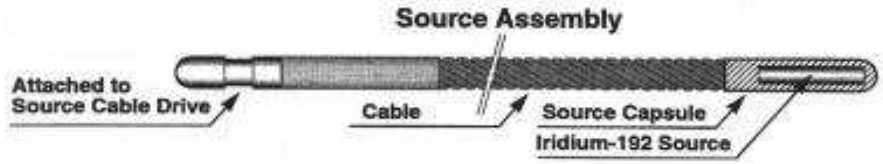
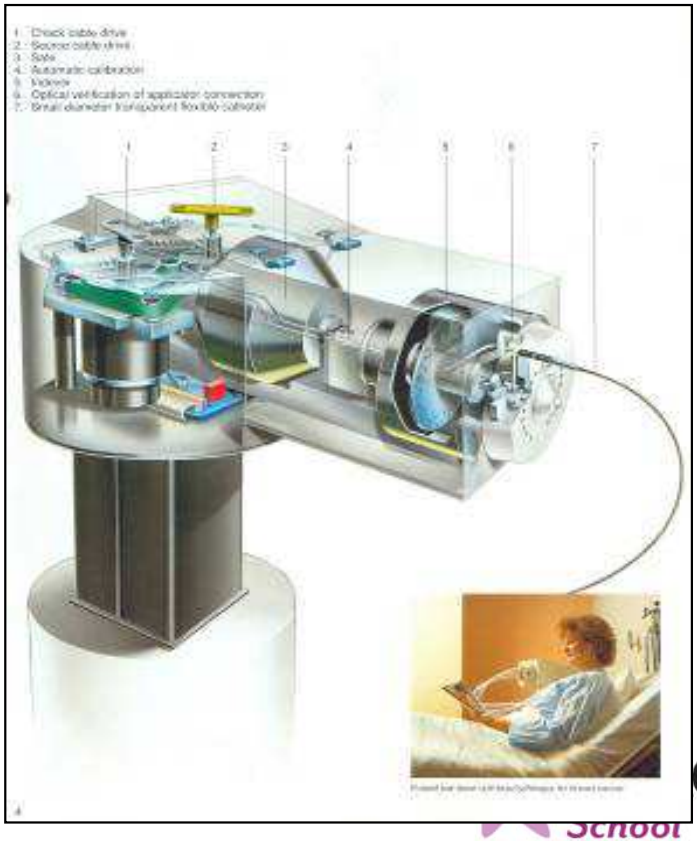
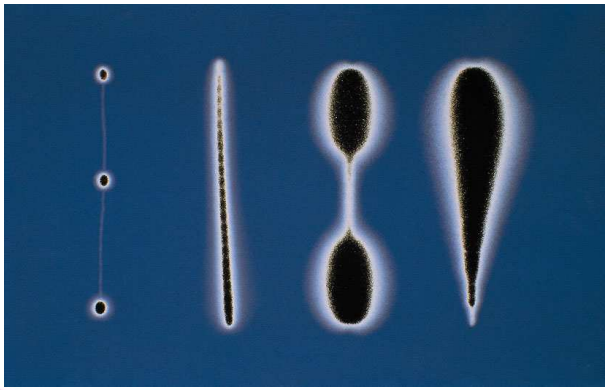
Optimization in interstitial Brachytherapy

- Temporary interstitial brachytherapy
- HDR and PDR afterloading techniques
- Single stepping Iridium-192 source (^{60}Co):
  - positioned at dwell positions
  - dwell times freely chosen







Topics

- **Introduction on Dose Optimization in Brachytherapy**
- Forward Planning & Techniques
- Inverse Optimization and Planning
- Dose Evaluation
- Quality Parameters and Indices

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Introduction on Dose Optimization

The *Forward* and the *Inverse* Problem

Physical Theories allow us to make Predictions:

Given a complete Description of a Physical System =>
We can predict the Outcome of some Measurements.

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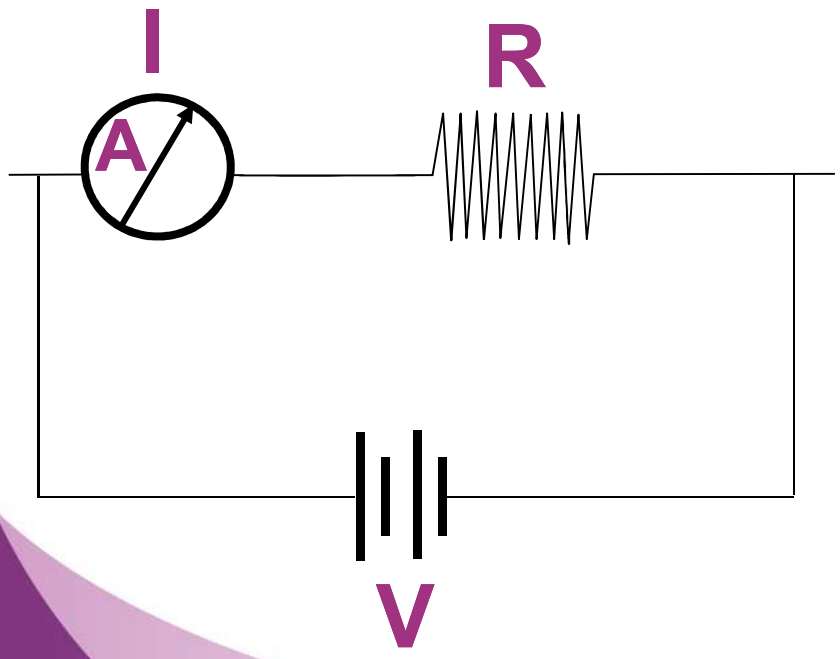
Introduction on Dose Optimization

Given a complete Description of a Physical System =>
We can predict the Outcome of some Measurements.



Ohm's Law: For given R and known V we can predict the measurement of current I:

$$I = V / R$$

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Introduction on Dose Optimization

The *Forward* and the *Inverse* Problem

This Problem of Predicting the Result of a Measurement is called:

The *Modelization* Problem or
The *Simulation* Problem or
The *Forward* Problem.

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Introduction on Dose Optimization

The *Forward* and the *Inverse* Problem

The *Inverse* problem consists of using the actual Result of some Measurements to infer the values of the Parameters that characterize the System:

The *Inverse* Problem.

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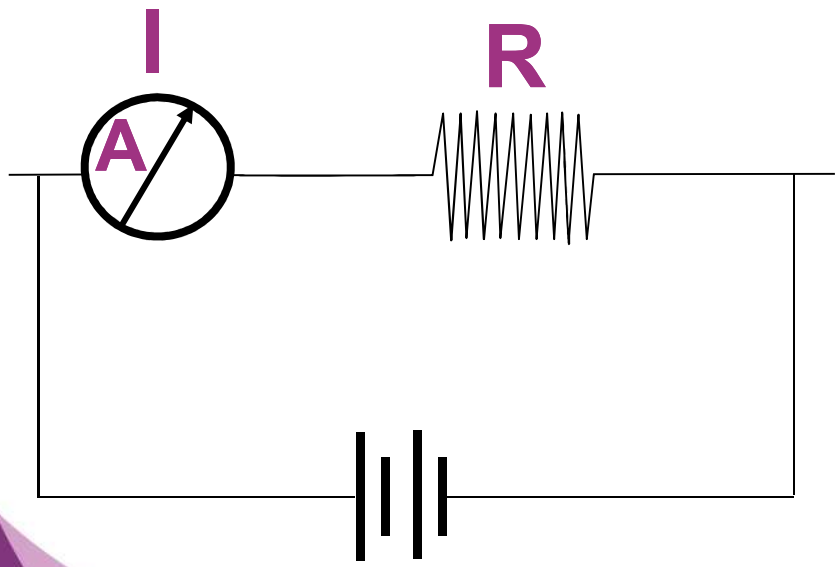
Introduction on Dose Optimization

The *Inverse* problem consists of using the actual Result of some Measurements to infer the values of the Parameters that characterize the System:



For a measured value of current I infer values of the parameters R and V:

$$V = I \times R$$

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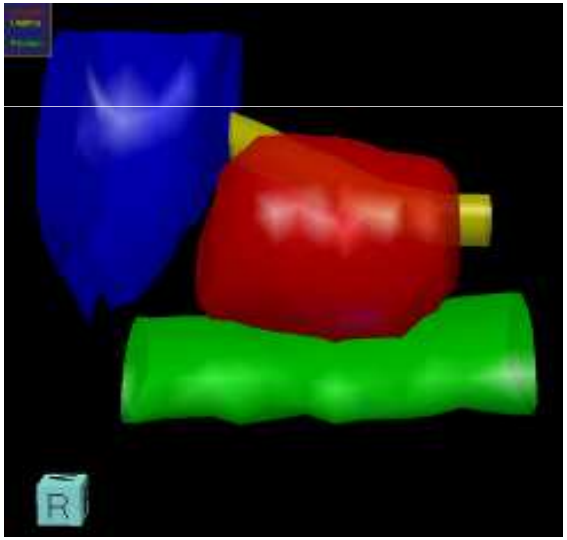
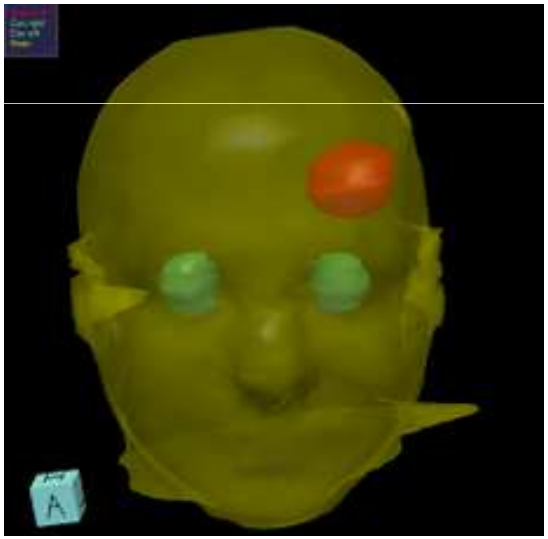
Introduction on Dose Optimization

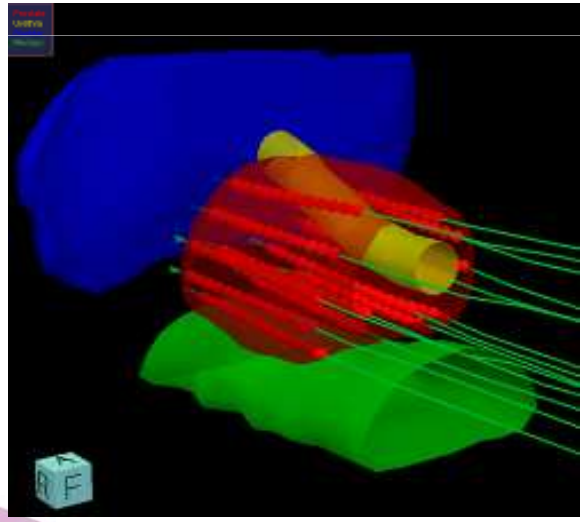
Our “System” in Brachytherapy

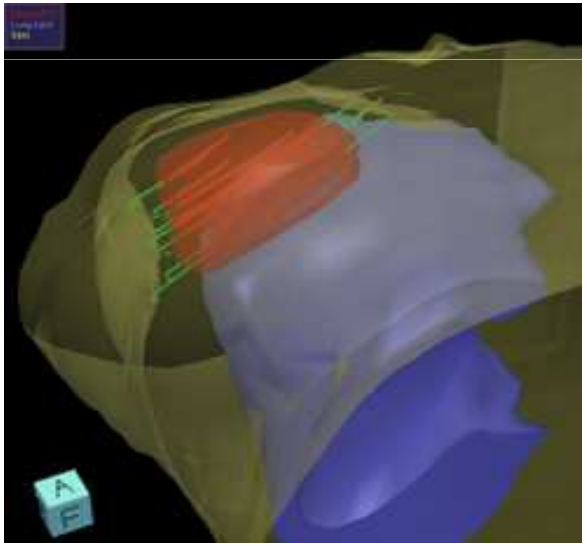
Anatomy

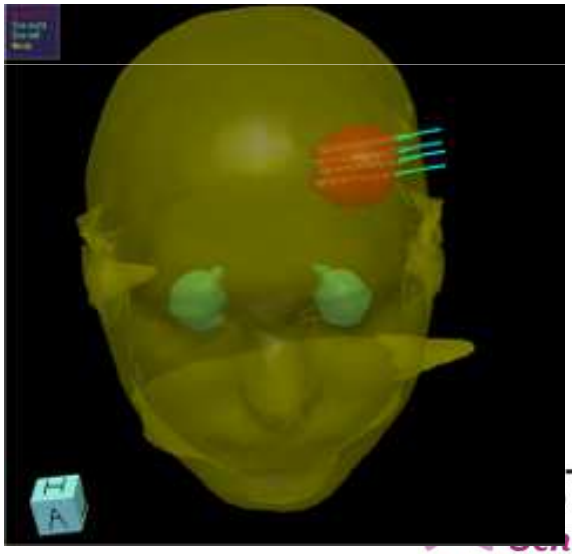




Catheters & Source Dwell Positions



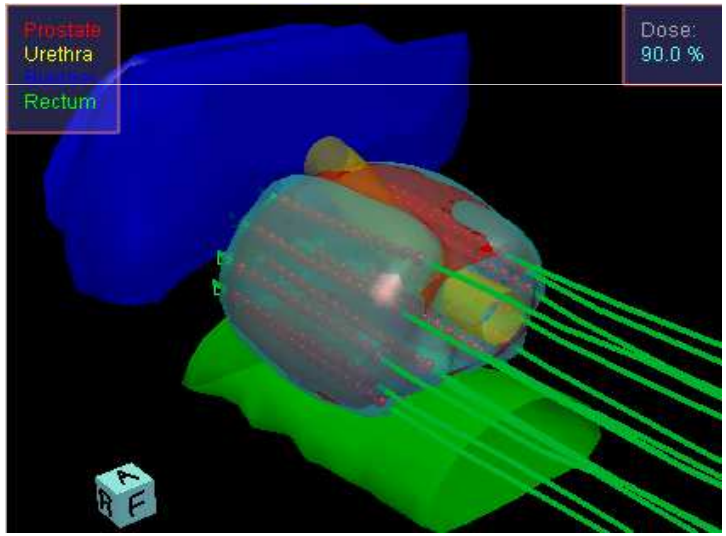


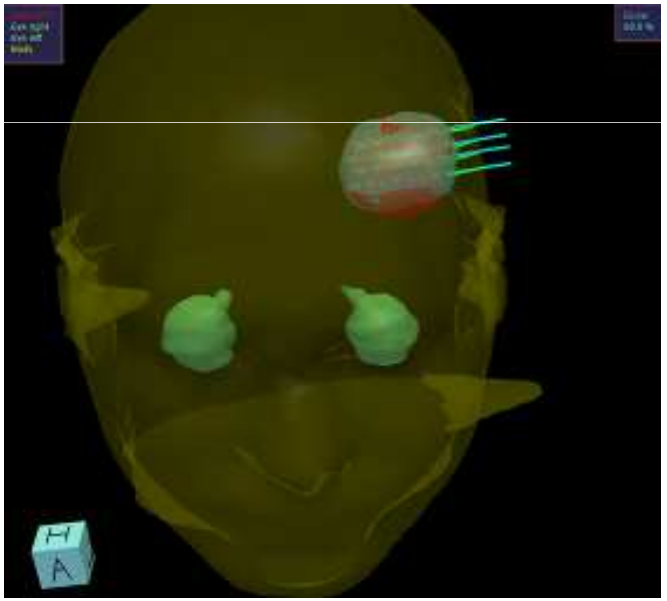


Introduction on Dose Optimization

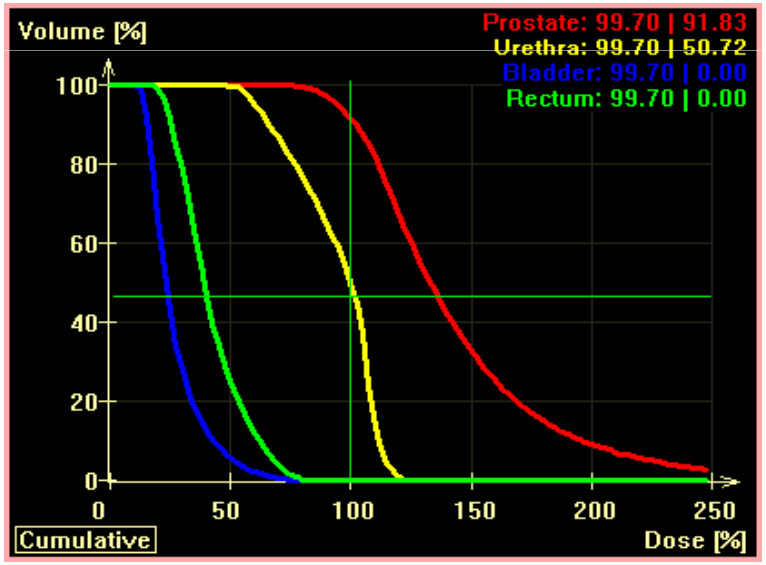
Our “Result” in Brachytherapy

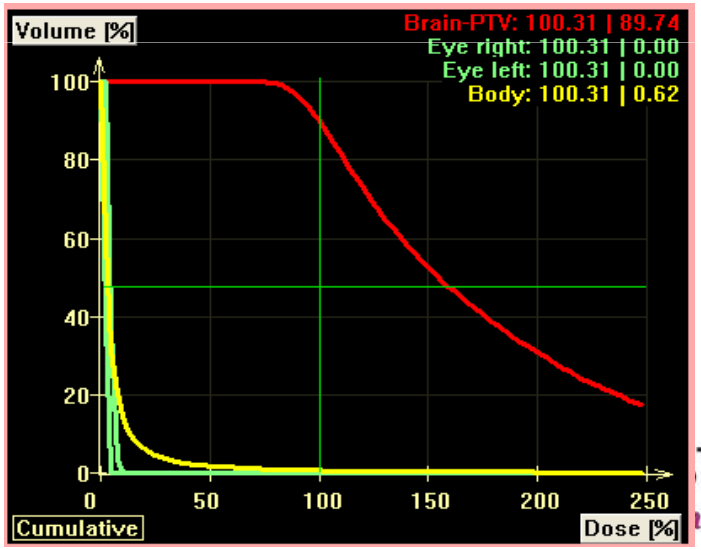
Spatial Dose Distribution 2D & 3D





Anatomy based Dose Evaluation DVHs



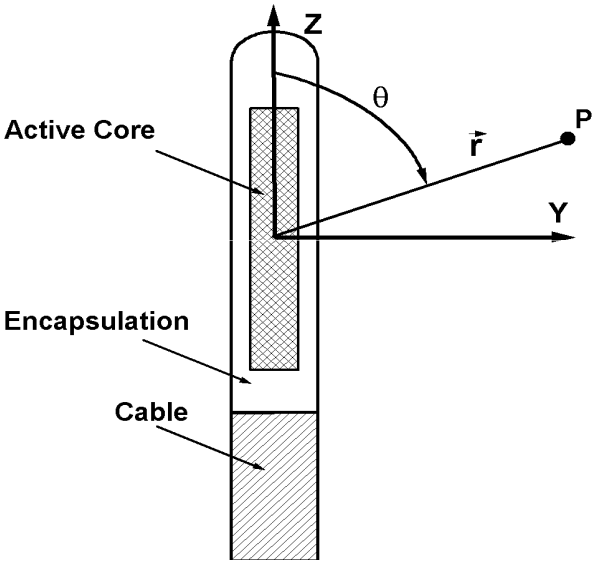


Introduction on Dose Optimization

The "System-Law" in Brachytherapy: the Dosimetric Kernel

TG-43, Nath R et al, 1995
TG-43 U1, Rivard M et al, 2004

$$\dot{D}(r,\theta) = S_K \cdot \Lambda \cdot \frac{G_L(r,\theta)}{G_L(r_0,\theta_0)} \cdot g_L(r) \cdot F(r,\theta)$$



S_K : ***Source Strength***

Λ: ***Dose Rate Constant***

G(r,θ): ***Geometry Function***

g(r): ***Radial Dose Function***

F(r,θ): ***Anisotropy Function***

(r_0, θ_0): ***(1.0cm, 90°)***

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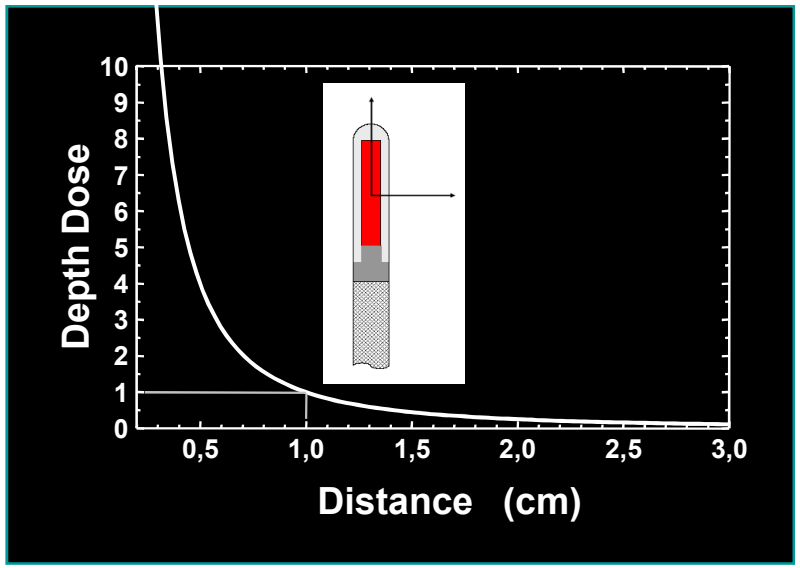
Introduction on Dose Optimization

The "System-Law" in Brachytherapy: the Dosimetric Kernel

^{192}Ir

^{60}Co

…



$$D \approx T \cdot \frac{1}{r^2}$$

Approximation: dose is proportional with time and inversely proportional with square of distance

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Introduction on Dose Optimization

The "Ohm's-Law" in Brachytherapy: the Dosimetric Kernel

TG-43, Nath R et al, 1995
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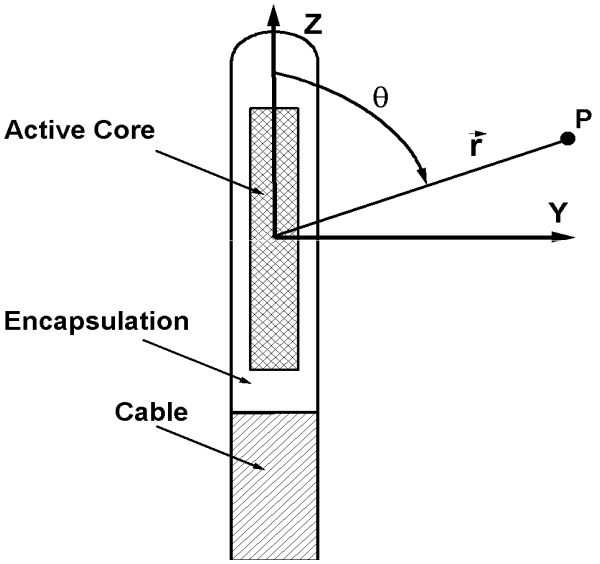

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Introduction on Dose Optimization

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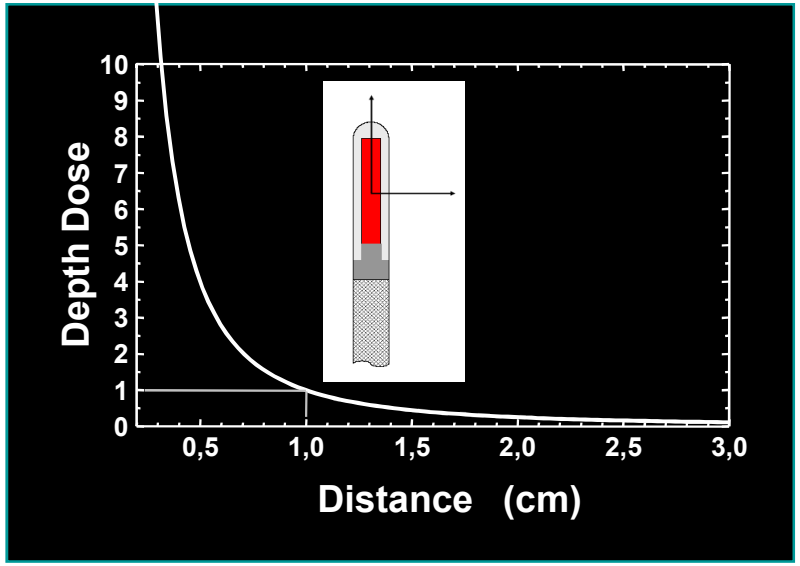

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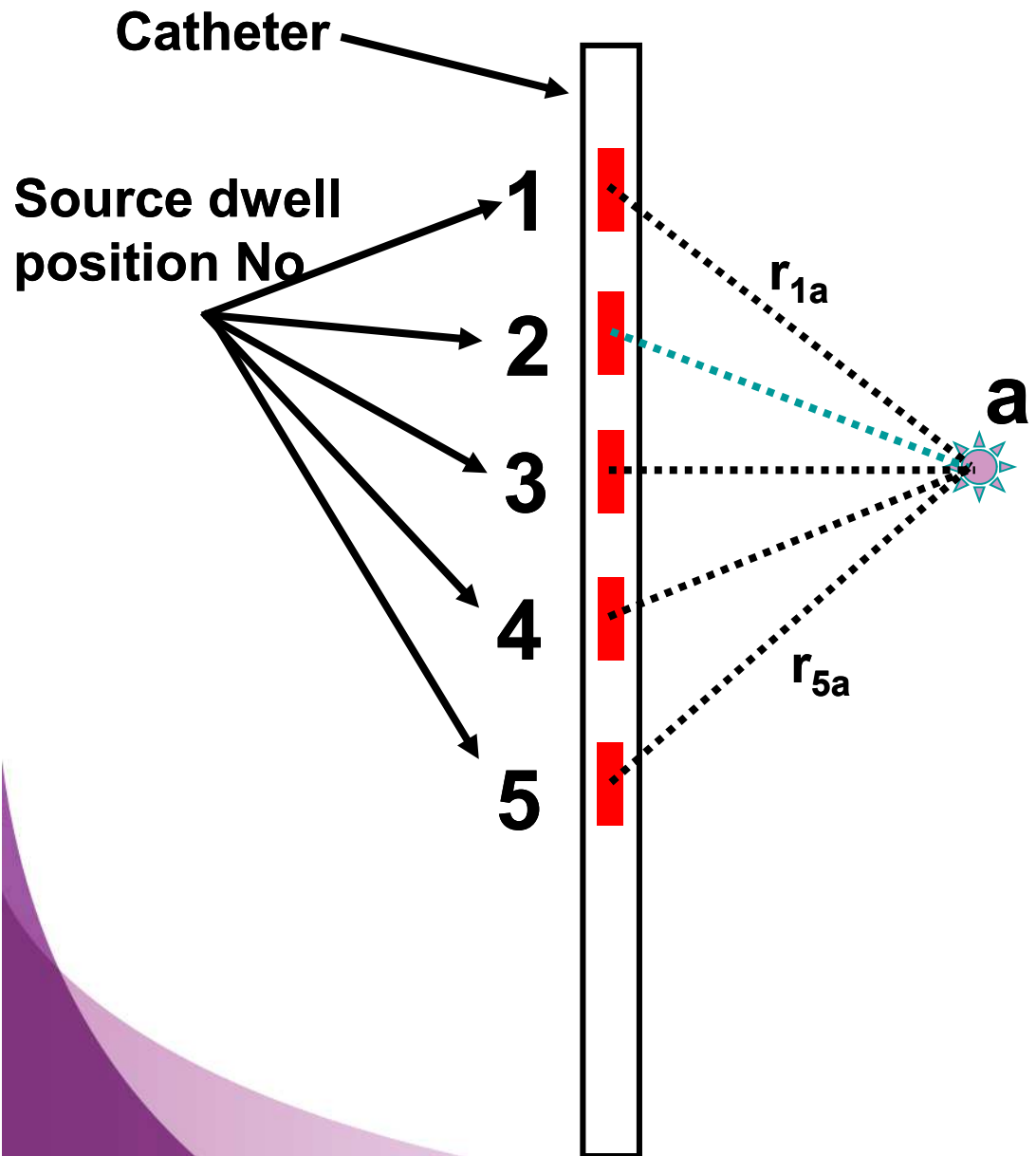
Introduction on Dose Optimization



Dose Calculation at a Point D_a

$$D_a \approx \left(T_1 \cdot \frac{1}{r_{1a}^2}\right) + \left(T_2 \cdot \frac{1}{r_{2a}^2}\right) +$$

$$\left(T_3 \cdot \frac{1}{r_{3a}^2}\right) + \left(T_4 \cdot \frac{1}{r_{4a}^2}\right) + \left(T_5 \cdot \frac{1}{r_{5a}^2}\right)$$

T_1, T_2,… T_5 are the dwell times of the source at the 5 dwell positions

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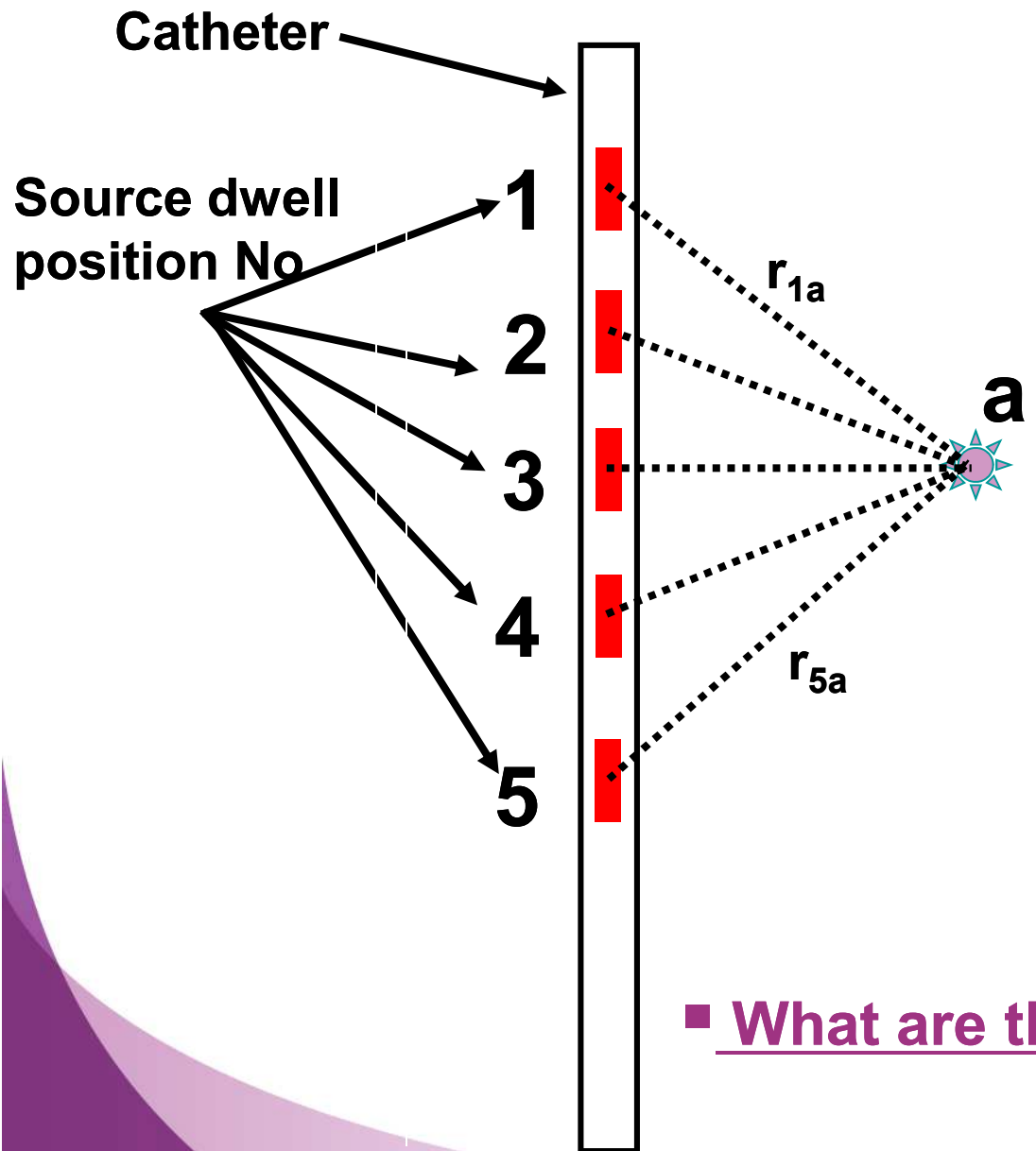
Introduction on Dose Optimization



Dose Calculation at a Point D_a

- Catheters and Source Dwell Positions are given
- The free adjustable Parameters for varying the Dose D_a at the Point "a" are the Dwell Times of the Source T_i

- What are the adequate Source Dwell Times T_i ?

Introduction on Dose Optimization

Lets summarize:

- **The "System-Law" is given:** $D \approx T \cdot \frac{1}{r^2}$
- **The known System parameters (mandatory) are the Source Dwell Positions (SDPs) in 3D space { $(x, y, z)_i$ }**
- **<u>What are the adequate Source Dwell Times T_i ?</u>**

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Introduction on Dose Optimization

- To answer this Question, we have to define our wished “Result”, the wished dose distribution, our “Goal”.
- Then the Dwell Times of the Source, T_i, have to be adjusted so that the wished dose distribution is resulted.

This “Adjustment” of Dwell Times to achieve our “Goal” is called “Optimization”.

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Introduction on Dose Optimization

All developed methods and algorithms in the past 20 years have been influenced by the following factors:

- **A detailed 3D description of the implanted catheters is pre-assumed and is mandatory (reconstruction, SDPs)**
- **Is a detailed 3D description of the relevant anatomy (Targets, OARs) available (3D anatomy model)?**
- **Can the wished dose distribution be expressed in numbers? (Computers and Algorithms understand only numbers not "thoughts")**
- **Can we find a mathematical formulation combining the "wishes" and the Source stepping ability (dwell times, step & shoot) which can then be used to automatically set-up the Source stepping in the catheters (dwell times), to solve the inverse problem?**
- **…..**

Topics

- Introduction on Dose Optimization in Brachytherapy
- **Forward Planning & Techniques**
- Inverse Optimization and Planning
- Dose Evaluation
- Quality Parameters and Indices

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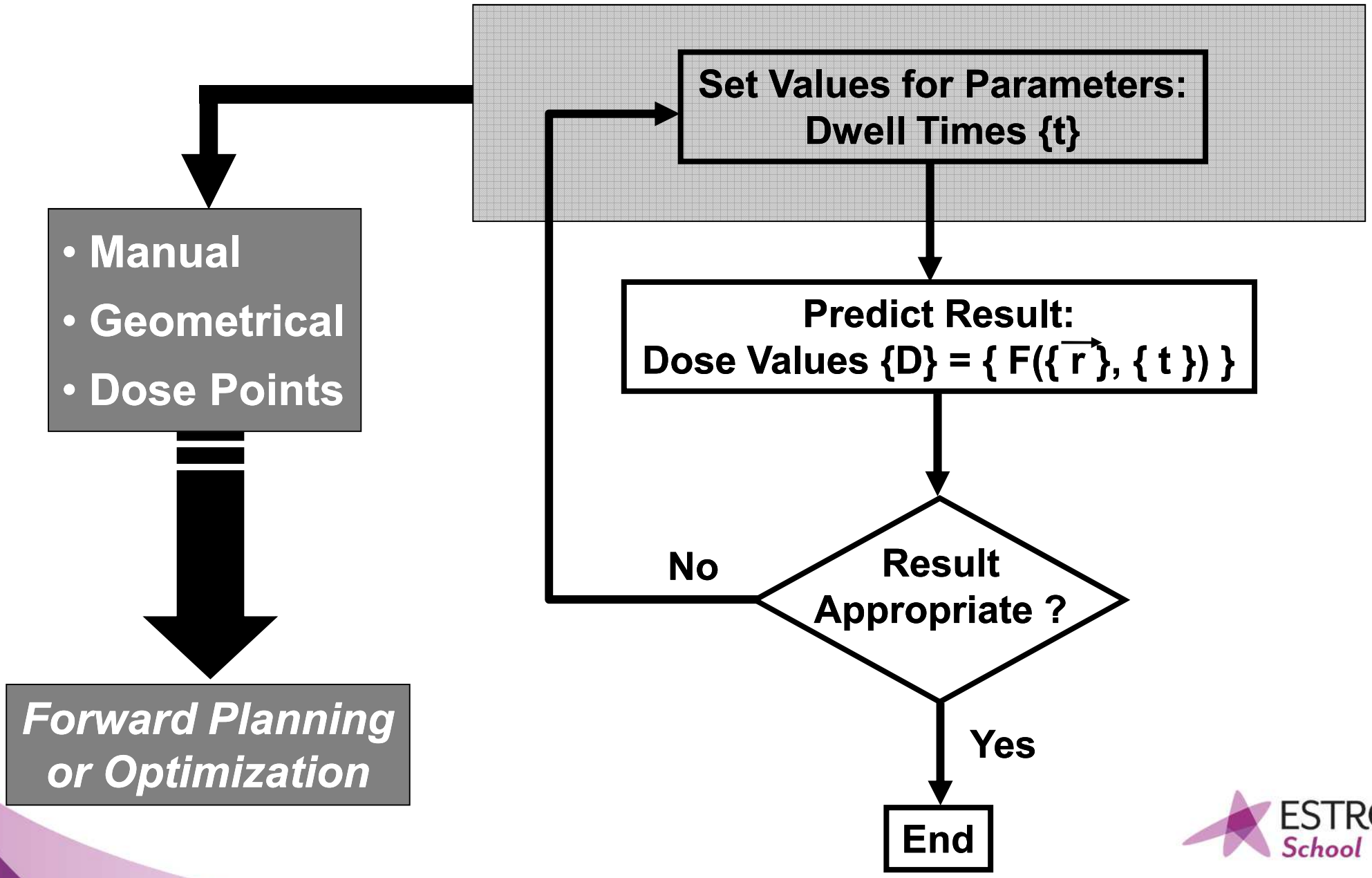
Our "Forward Problem" in Brachytherapy



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Forward Planning / Optimization

- **Manual Selection / Adjustment of Dwell Times T_i**
- **Automatic Selection / Adjustment of Dwell Times T_i**

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Forward Planning / Optimization

Manual Selection / Adjustment of Dwell Times T_i

- It is based on Clinical Experience and Planner Expertise
- It is time consuming / Human Resources intensive
- It is Expert-dependent
- The “wished” dose distribution is not mandatory to be pre-defined (Expertise):
  - Visual inspection of 2D dose distributions (isodose lines)
  - Inspection of resulted doses to some “representative” points
  - Inspection of DVH curves
  - Inspection of Dose-Volume-Parameters
  - …

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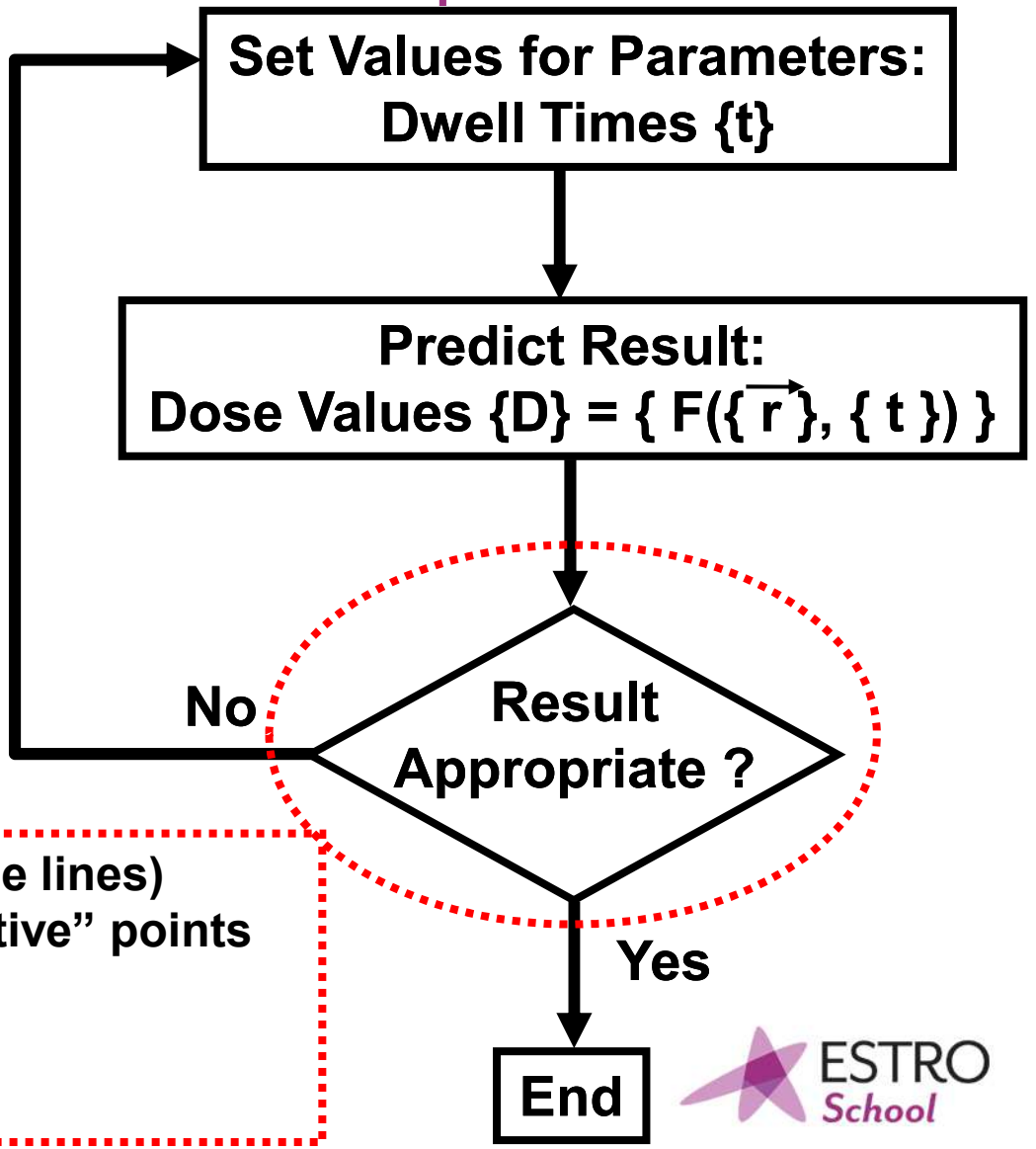
Forward Planning / Optimization

Manual Selection / Adjustment of Dwell Times T_i



- Visual inspection of 2D dose distributions (isodose lines)
- Inspection of resulted doses to some “representative” points
- Inspection of DVHs
- Inspection of Dose-Volume-Parameters
- …

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Forward Planning / Optimization

Automatic Selection / Adjustment of Dwell Times T_i

- **It requires that user somehow defines "wishes"**
  - **User defines/selects rules for the dwell times T_i (e.g. Geometrical Optimization)**
  - **User defines the dose level at some "representative" points (Dose Point Optimization, Graphical Optimization)**
- **Since both "rules" and "representative" points can not describe fully a 3D dose distribution, planner goes over several loops (changing rules, combining with dose points) as in the case of manual adjustment, until a clinical acceptable plan is created.**

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Forward Planning / Optimization

Catheter Geometry-based Adjustment of Dwell Times T_i (Geometrical "*Optimisation*", GO, G. Edmundson, 1990)

- It is a "Catheter-Centric" Method
- The Basic Principe is: Each SDP shall "feel" the Existence of neighbours (SDPs socialisation)
- Developed by G. Edmundson at a period, where no 3D anatomy model was available for planning (late 80's)
- ***If*** dose distribution around catheters is adequate ***and if*** catheter geometry fits to anatomy-topology, then the dose distribution is clinically acceptable with respect to anatomy

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Forward Planning / Optimization

Catheter Geometry-based Adjustment of Dwell Times T_i (Geometrical "*Optimisation*", GO)

- **The "best" planner can achieve is pre-defined by the "Implanter": Catheter-Geometry ⇔ Anatomy-Topology**
- **GO Offers an automatic method to "concentrate" dose around catheters, following their geometry**
- **"The American Optimisation"!**

Forward Planning / Optimization

Geometrical "*Optimisation*", GO

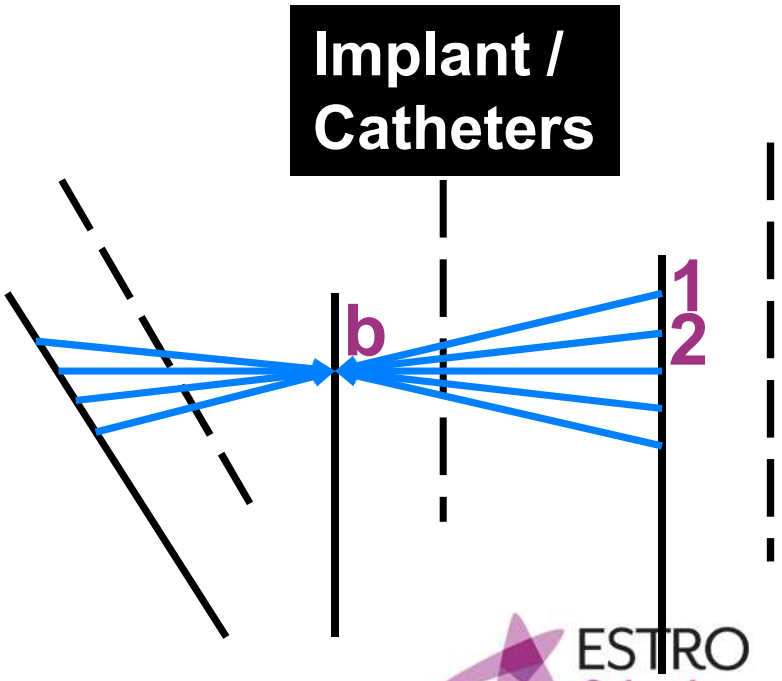
- The dwell time of the source at a dwell position is inversely proportional to the dose contribution of neighboring source dwell positions.
- Points a, b, c, … are source dwell positions (SDPs).

1 $$D_b \approx \left(T_1 \cdot \frac{1}{r_{1b}^2}\right) + \left(T_2 \cdot \frac{1}{r_{2b}^2}\right) + \left(T_3 \cdot \frac{1}{r_{3b}^2}\right) \ldots$$

2 $$T_b := \left(\frac{1}{D_b}\right)$$

If D_b large → T_b small

3 T_i equal to 1 at start, iteratively calculated until nothing changes anymore.



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Forward Planning / Optimization

Geometrical "*Optimisation*", GO

- **The dwell time of the source at a dwell position is inversely proportional to the dose contribution of neighboring source dwell positions.**

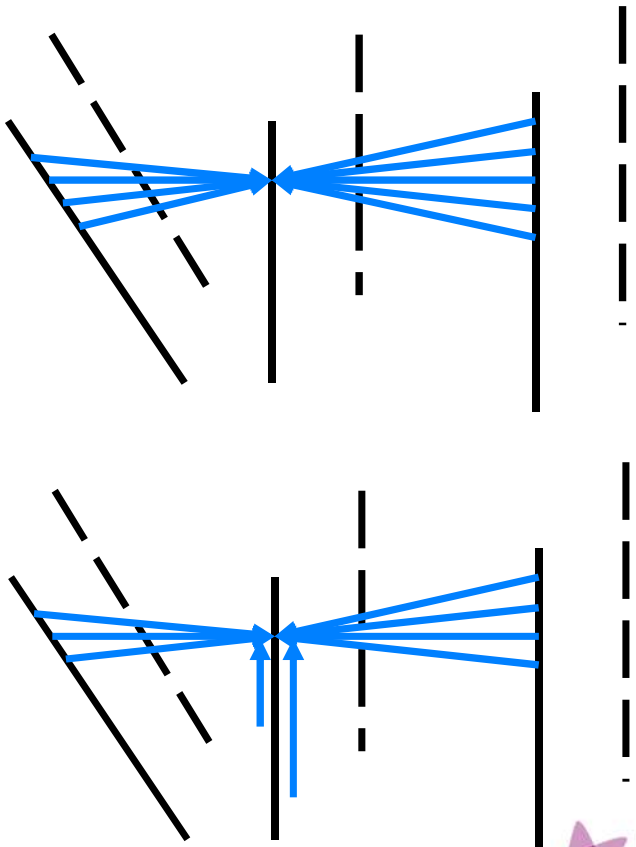
- **Volume:**

  only SDPs in others catheters are taken into account

- **Distance:**

  all other SDPs

  are taken into account



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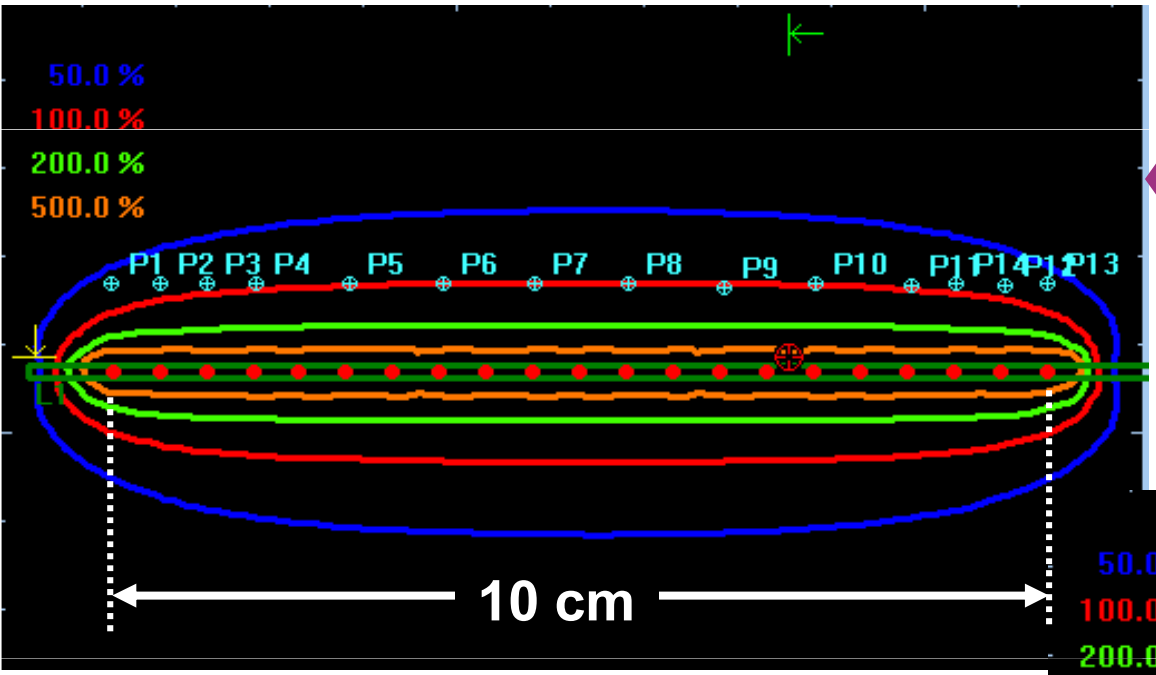
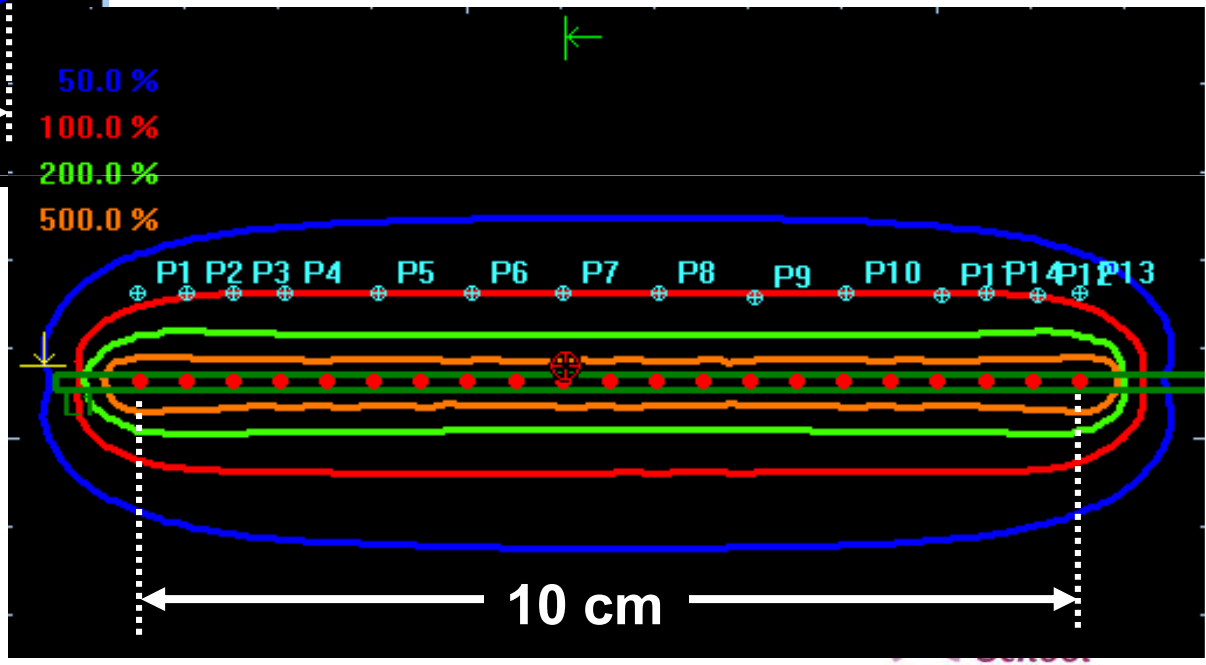
Forward Planning / Optimization

Geometrical "*Optimisation*", GO



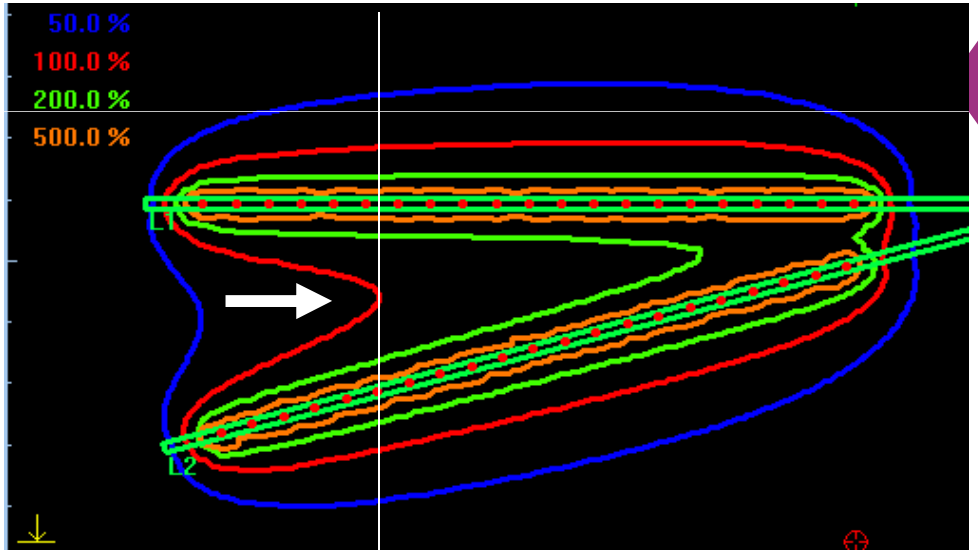
Equal Dwell Times

GO - Distance



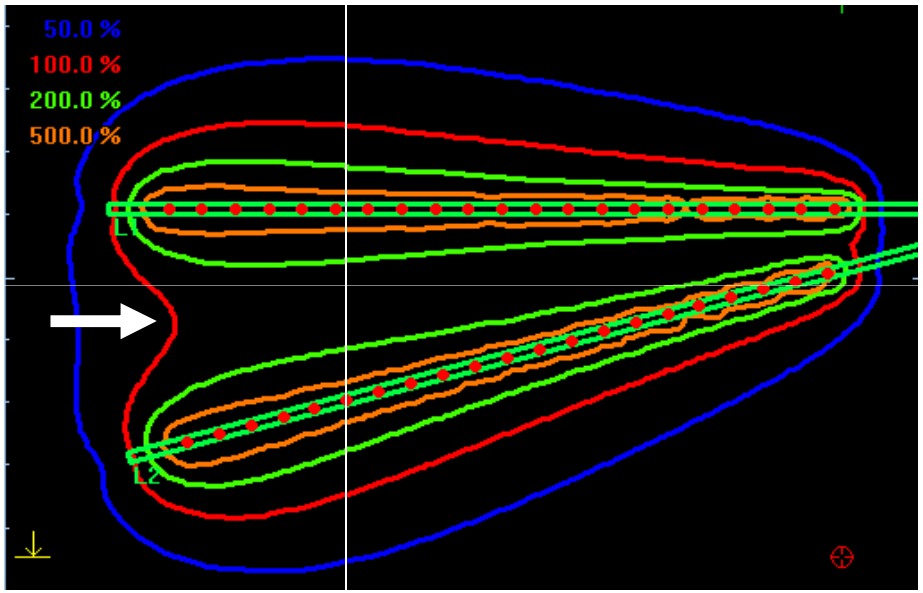
Forward Planning / Optimization

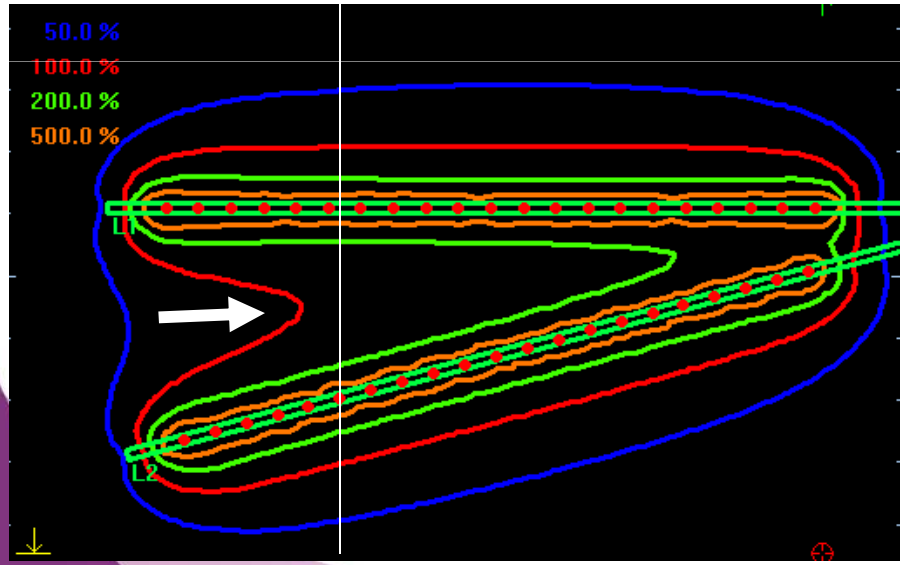
Geometrical "*Optimisation*", GO



Equal Dwell Times

GO - Volume





GO - Distance

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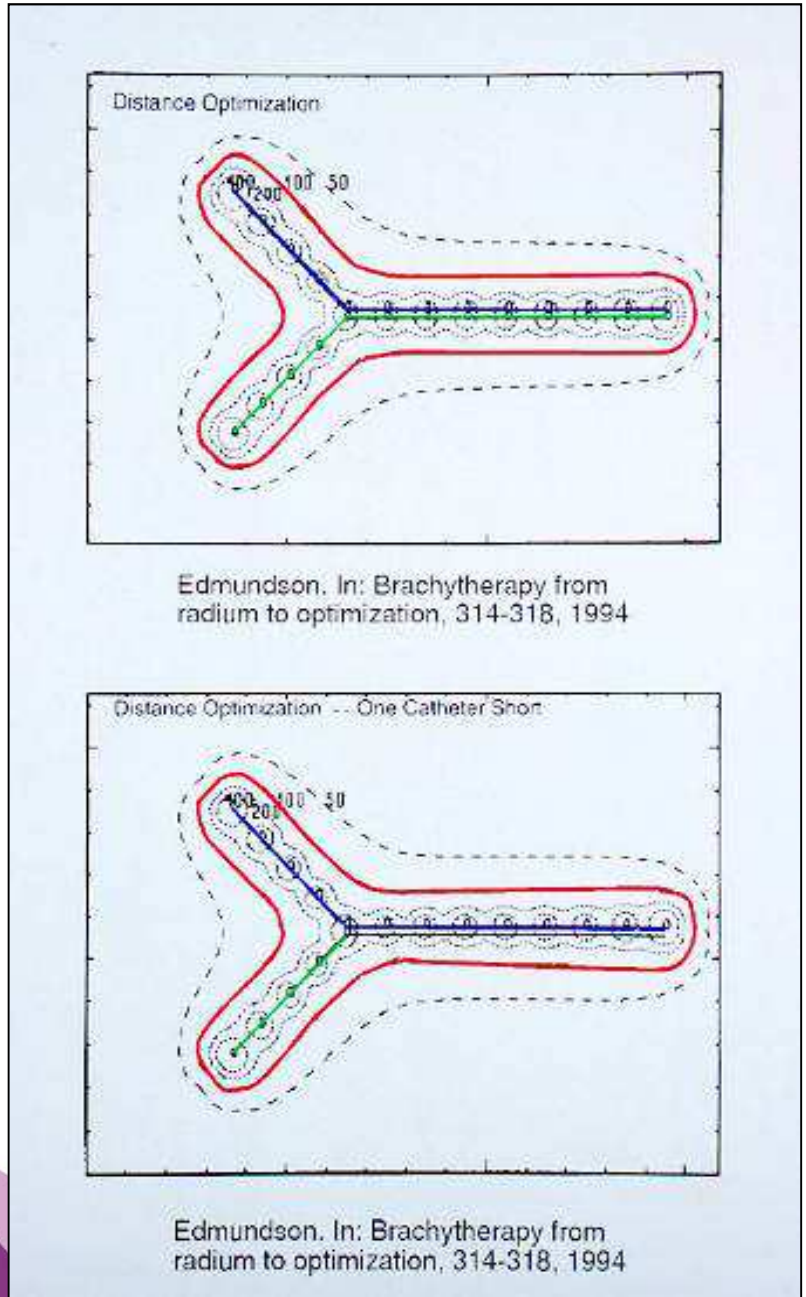
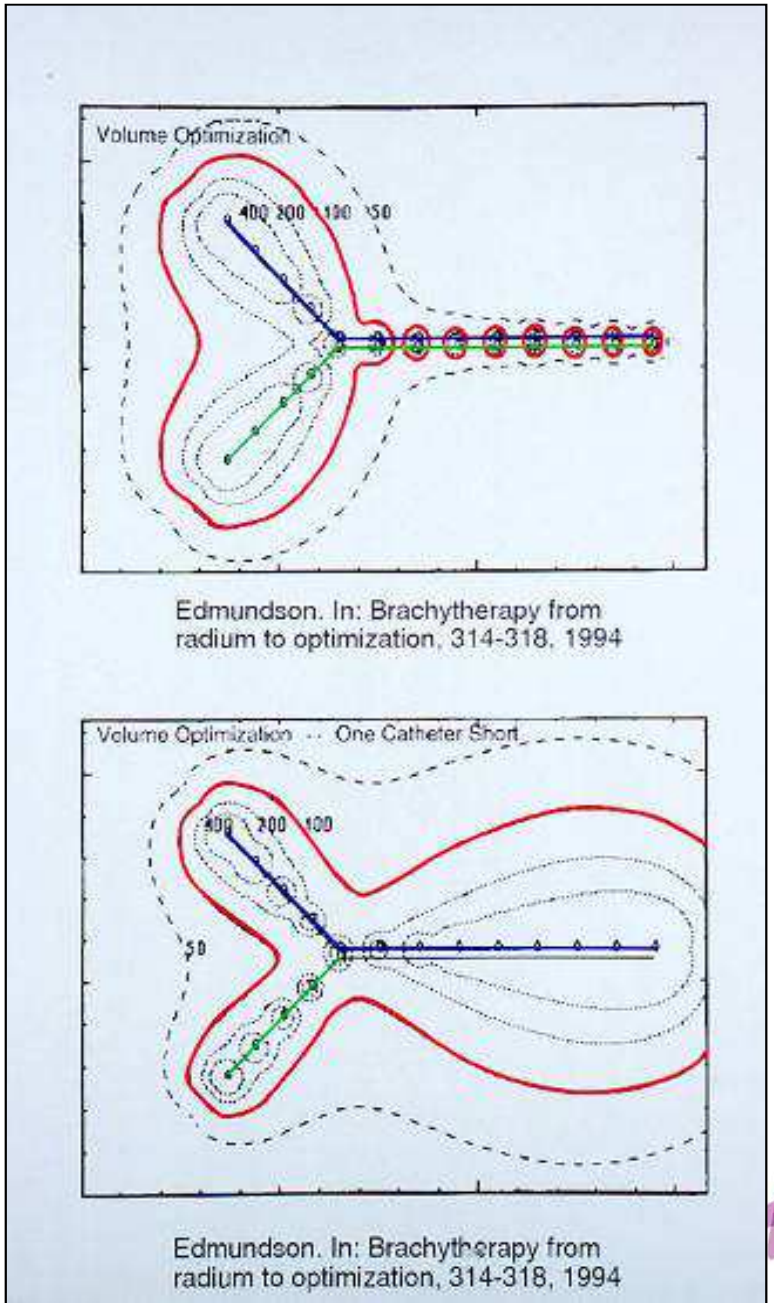
Forward Planning / Optimization

Geometrical "*Optimisation*", GO





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Forward Planning / Optimization

Catheter Geometry-based Adjustment of Dwell Times T_i (Geometrical “Optimisation”, GO)

Lets summarize (I):

GO does not need anatomical information. It’s goal is to homogenize the dose distribution around the catheters. Assuming that the catheters are inserted in such a way that their geometrical distribution fits to the geometry of the PTV, then the resulted dose distribution is expecting to fit more or less to the anatomy.

=> It is planner‘s responsibility to evaluate the dose distribution with respect to anatomy, GO does not understand it!

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Forward Planning / Optimization

Catheter Geometry-based Adjustment of Dwell Times T_i (Geometrical “Optimisation”, GO)

Lets summarize (II):

- **This is a catheter orientated Method for Adjustment of { T_i }**
- **Source Dwell Positions (SDPs) are virtually considered as Dose Points (DPs)**
- **GO – Volume has been developed to enable filing in cold volumes between catheters. It is a useful attribute but extreme care should be taken by reviewing the results.**

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Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

- **A representative set of points is defined (DPs)**
  - **Originally, DPs were defined relative to catheters**
  - **DPs can also be defined relatively to anatomy**
- **Planner defines the dose value, that has to be achieved to DPs ➔ a common value**

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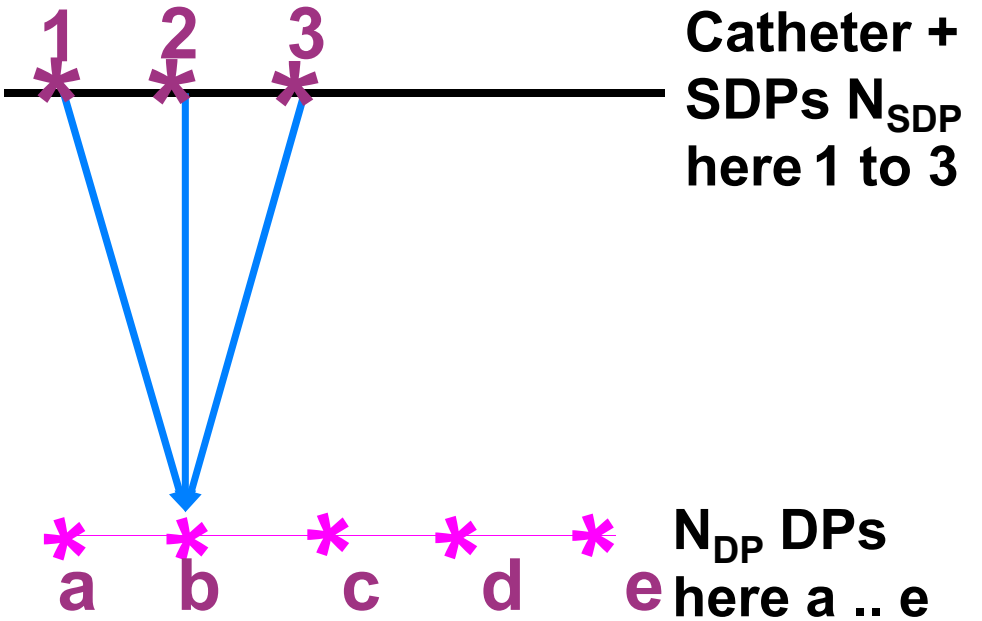
Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

$$D \approx T \cdot \frac{1}{r^2}$$



$$D_{a,b,..e} \approx \left(T_1 \cdot \frac{1}{r_{1a}^2}\right) + \left(T_2 \cdot \frac{1}{r_{2a}^2}\right) + \left(T_3 \cdot \frac{1}{r_{3a}^2}\right)$$

Where $D_a = D_b = \ldots D_e = 100\% =$ e.g. 10 Gy

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Dose Points-based Adjustment of Dwell Times T_i (DPO)

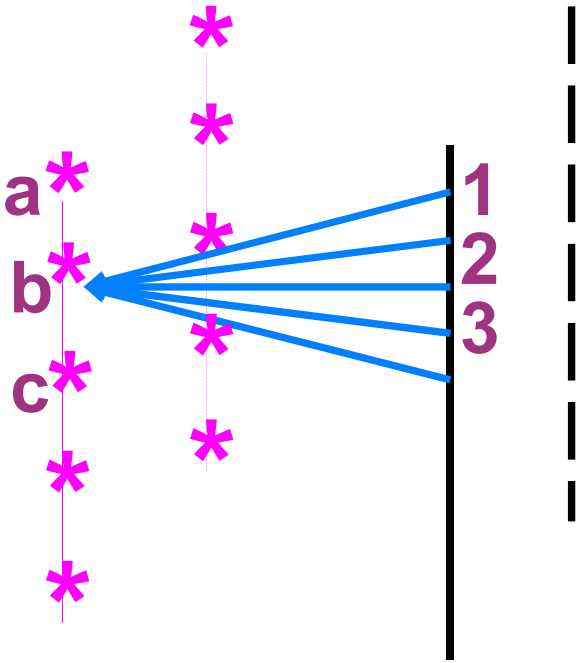
$$D_b \approx \left(T_1 \cdot \frac{1}{r_{1b}^2}\right) + \left(T_2 \cdot \frac{1}{r_{2b}^2}\right) + \left(T_3 \cdot \frac{1}{r_{3b}^2}\right) \ldots = 10\,\text{Gy}$$

$$D_a \approx \left(T_1 \cdot \frac{1}{r_{1a}^2}\right) + \ldots = 10\text{Gy}$$

$$D_c \approx \left(T_1 \cdot \frac{1}{r_{1c}^2}\right) + \ldots = 10\text{Gy}$$

N_{DP} Equations with

N_{SDP} unknown Dwell Times T_i



DPO = Solve the N_{DP} Equations for the T_i , i=1, N_{SDP}

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Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

- **Some Traps …**

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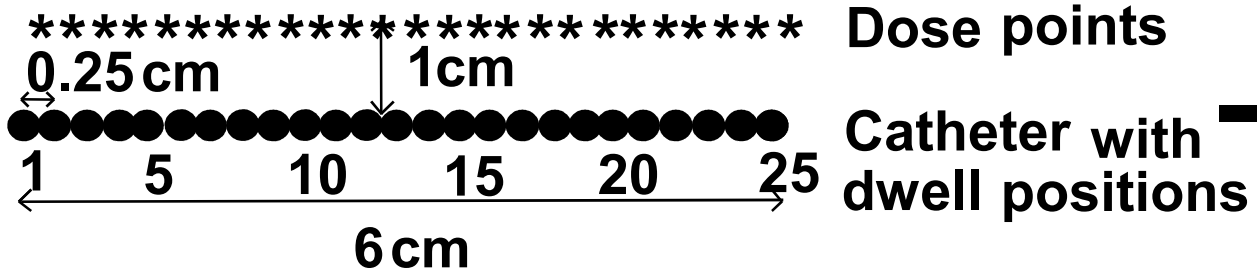
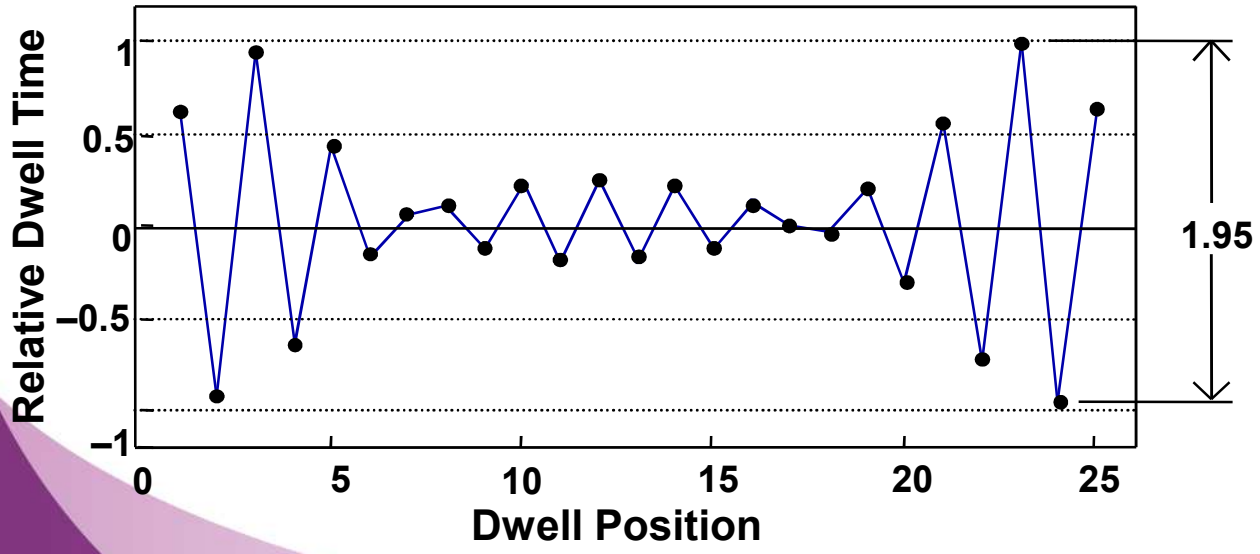
Dose Points-based Adjustment of Dwell Times T_i (DPO)

- The “Black Holes” or the “Mystery” of negative Dwell Times





DPO Solution

Negative T_i: Mathematically Feasible, Physically Nonsense

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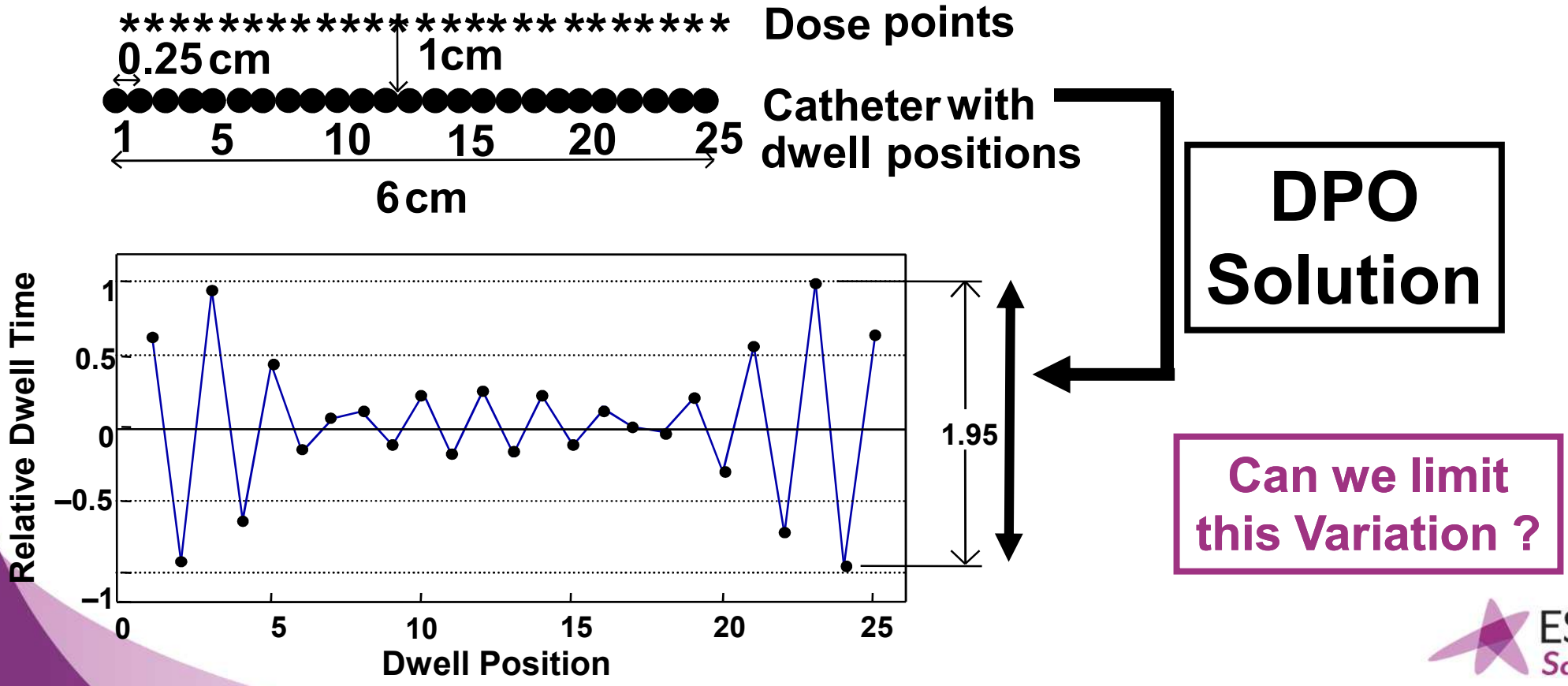
Dose Points-based Adjustment of Dwell Times T_i (DPO)

- How can we avoid “Black Holes”- Negative Dwell Times?



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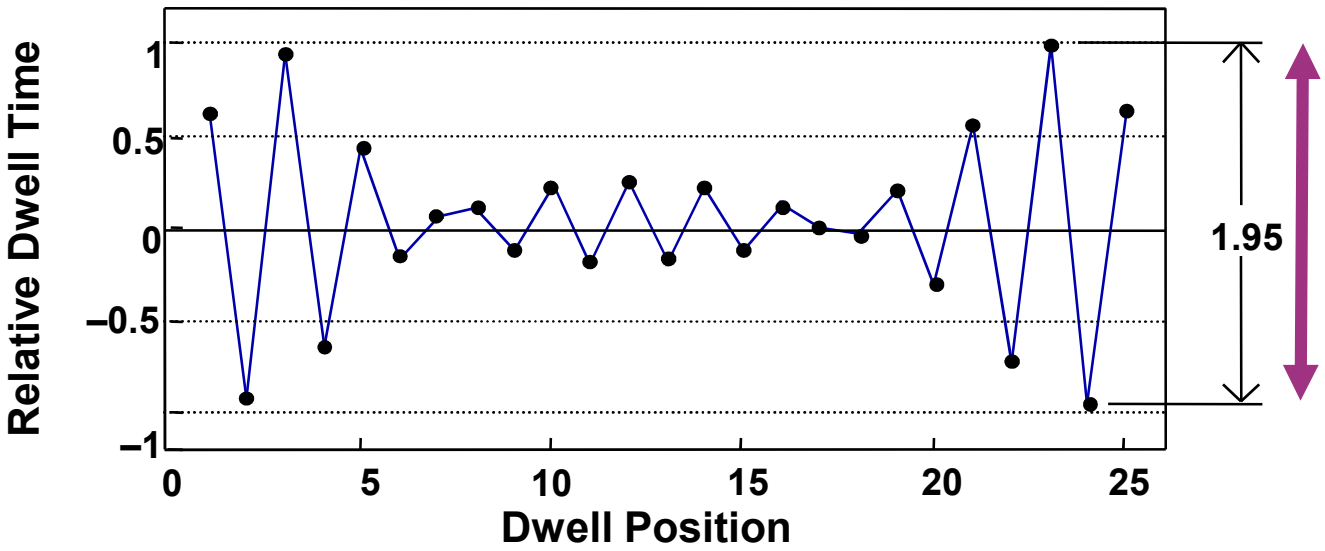
Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

- **How can we avoid "Black Holes"- Negative Dwell Times?**



Can we limit this Variation ?

Define Dwell Time Gradient as: and try to restrict it (DTGR)

$$DTGR \approx \sum_{i=1}^{N_{SDP}-1} [T_{i+1} - T_i]^2$$

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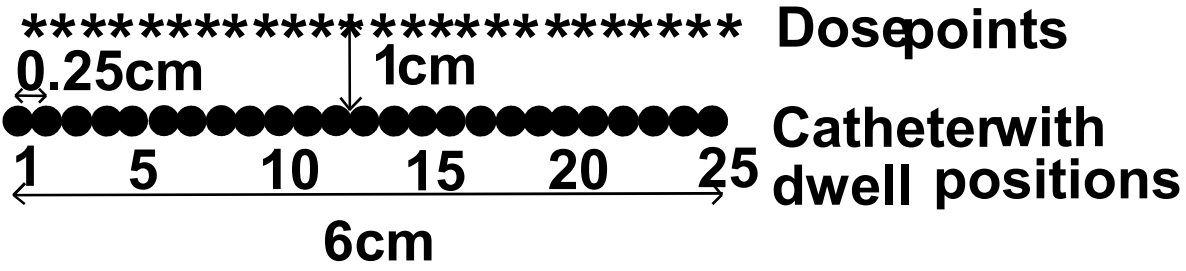
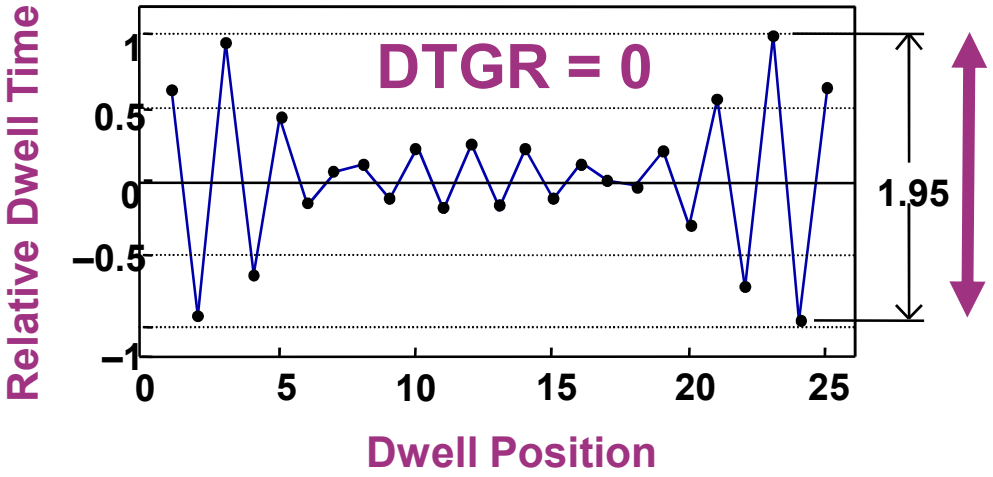
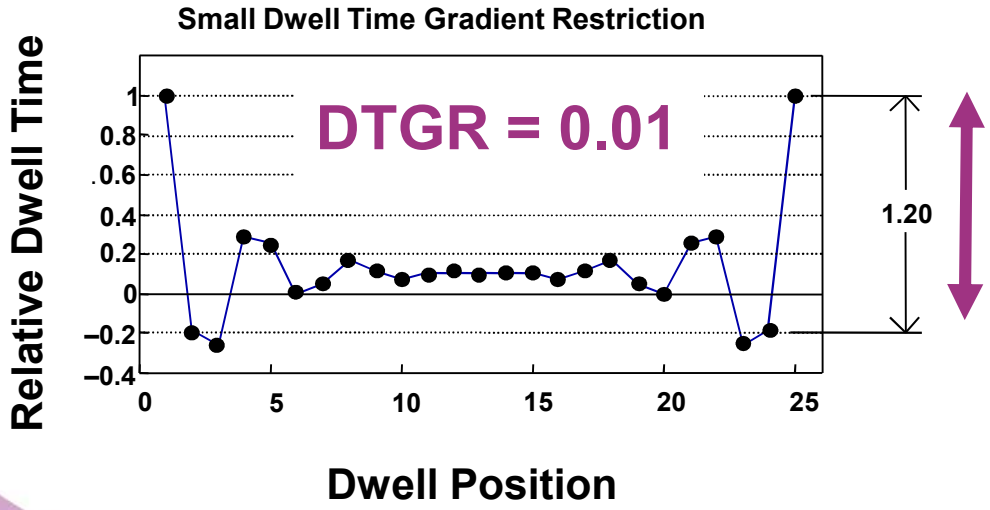
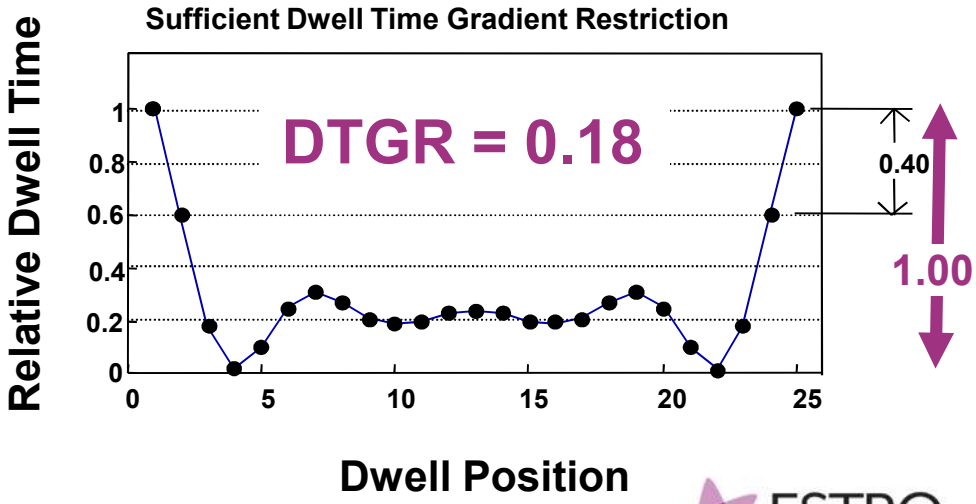
Dose Points-based Optimisation (DPO)

Avoid Negative Dwell Times?









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Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

- **How can we avoid "Black Holes"- Negative Dwell Times?**

  - **As long as the linear Form of Equations, $D \approx T \times 1/r^2$, is used (mathematically attractive) there is no guarantee for non negative T_i**

  - **DTGR is a method to moderate but *not* to solve the problem**

  - **There exist also other methods trying to limit negative T_i, e.g. Polynomial description of T_i within a catheter…**

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Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

- **How can we avoid "Black Holes"- Negative Dwell Times?**
  - **The simplest secure way to guarantee non negative Dwell Times is the following simple transformation:**

$$t_i = \sqrt{T_i} \quad \text{and} \quad \text{thus} \quad T_i = t_i^2$$

  - **Solving the problem of NDP Equations with NSDP unknown t_i the Dwell Times T_i are calculated as $T_i = t_i^2$, and thus $T_i \geq 0$, for each t_i.**
  - **The Mathematical Attractiveness of linearity is then lost!**

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Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i: Graphical Optimisation

- Similar to DPO
- Practical for Fine Tuning a dose distribution
- User-Friendly: Drag and Drop of an Isodose Line
- Planner “feels” he is manipulating isodoses instead of handling DPs (more native action).

Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i: Graphical Optimisation

- **Planner takes an isodose line and shifts it to another position:**
  - **Take a line: Starting Point defines the final Dose Level, D_{final}**
  - **Shift to another position: This point becomes the DP of the "optimisation" and has at the time of planner action the dose D_{start}.**
  - **The Dwell Times T_i have to be adjusted in such a way, that our DP gets instead of D_{start} the dose level D_{final}.**
- **The Dwell Times (all or part of them) are then adjusted according to:**

$$\delta D = D_{final} - D_{start}$$

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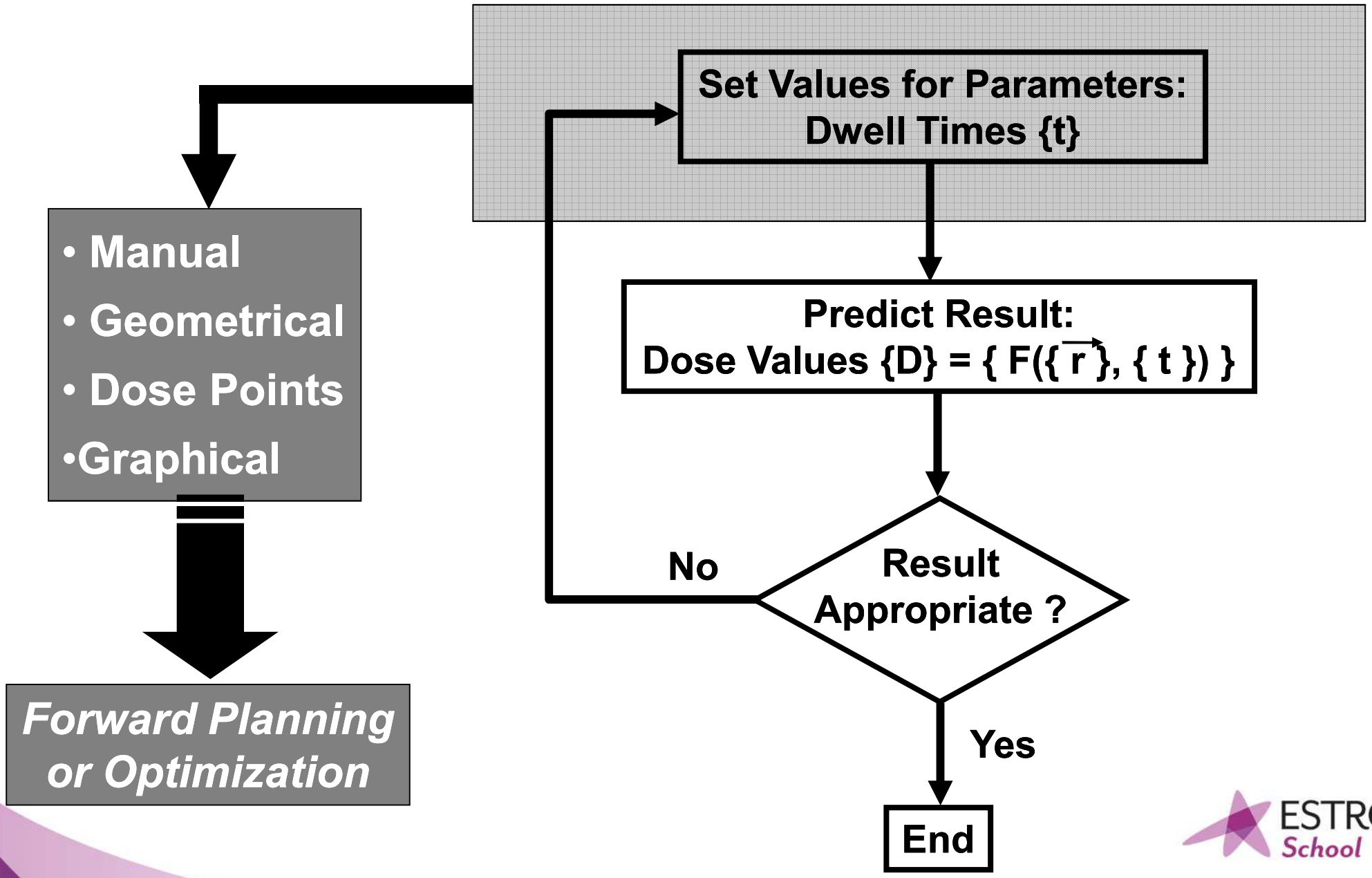
Our "Forward Problem" in Brachytherapy



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Topics

- Introduction on Dose Optimization in Brachytherapy
- Forward Planning & Techniques
- **Inverse Optimization and Planning**
- Dose Evaluation
- Quality Parameters and Indices

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Inverse Optimization and Planning

Automatically estimate the implant parameters:
Catheters, Dwell Positions and Dwell Times T_i which result to a 3D dose Distribution that fulfils Clinical Dosimetric Criteria

- **Inverse Optimization:**
  for given { $\vec{r}$ } find adequate { t }
- **Inverse Planning:**
  find adequate { $\vec{r}$ } and { t }

3D Dose Distribution fits / fulfils Dosimetric Criteria

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Inverse Optimization and Planning

It presupposes:

- **A complete 3D anatomical model**
  VOIs: Target(s), OARs
- **Dosimetric wishes – objectives for all VOIs**
- **Dosimetric objectives have to be arithmetically defined**

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Inverse Optimization and Planning

Planner freedom is limited due to:

- **The particular implemented Algorithm, since it defines the kind of “wishes” planner can express**
- **The arithmetic interpretation of “wishes”**

<u>But keep in mind: This is Nothing different to IMRT</u>

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Inverse Optimization and Planning

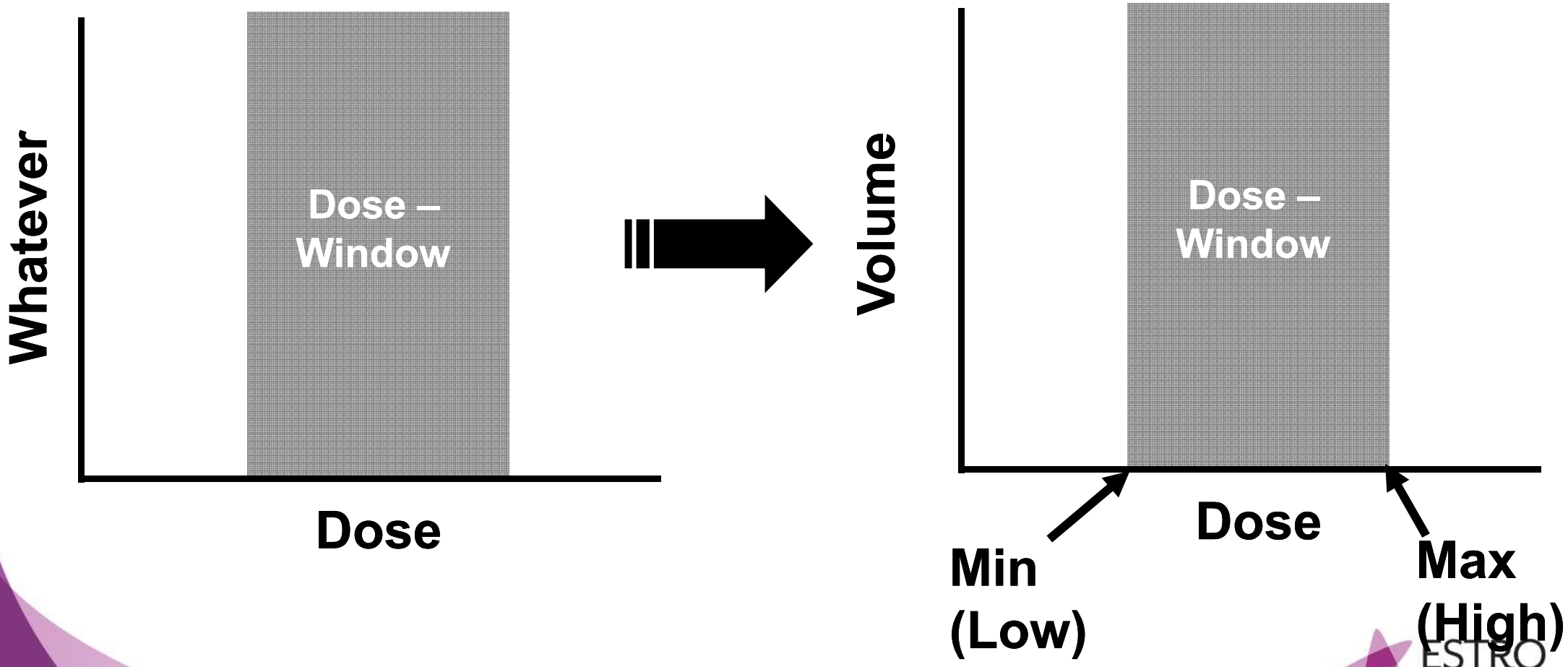
Planner “Wishes”:

The “Wish”, “Wished Result” is here a “clinically accepted dosimetry”, a protocol, rather than an “ideal” dose distribution.

Due to the fact, that in BRT we deliver a huge spectrum of dose values, the clinical protocol, Considers some “representative” dose-volume values for the 3D dose distribution.

Inverse Optimization and Planning

Our Wishes: “ideal” Dose Distribution



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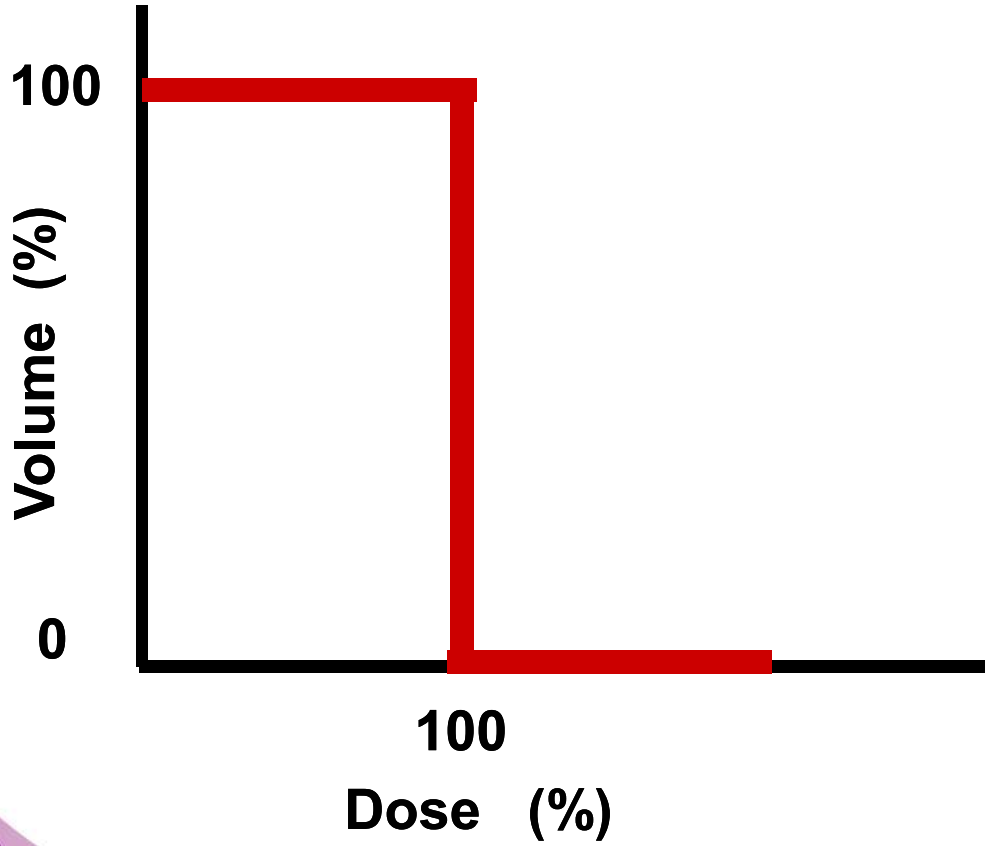
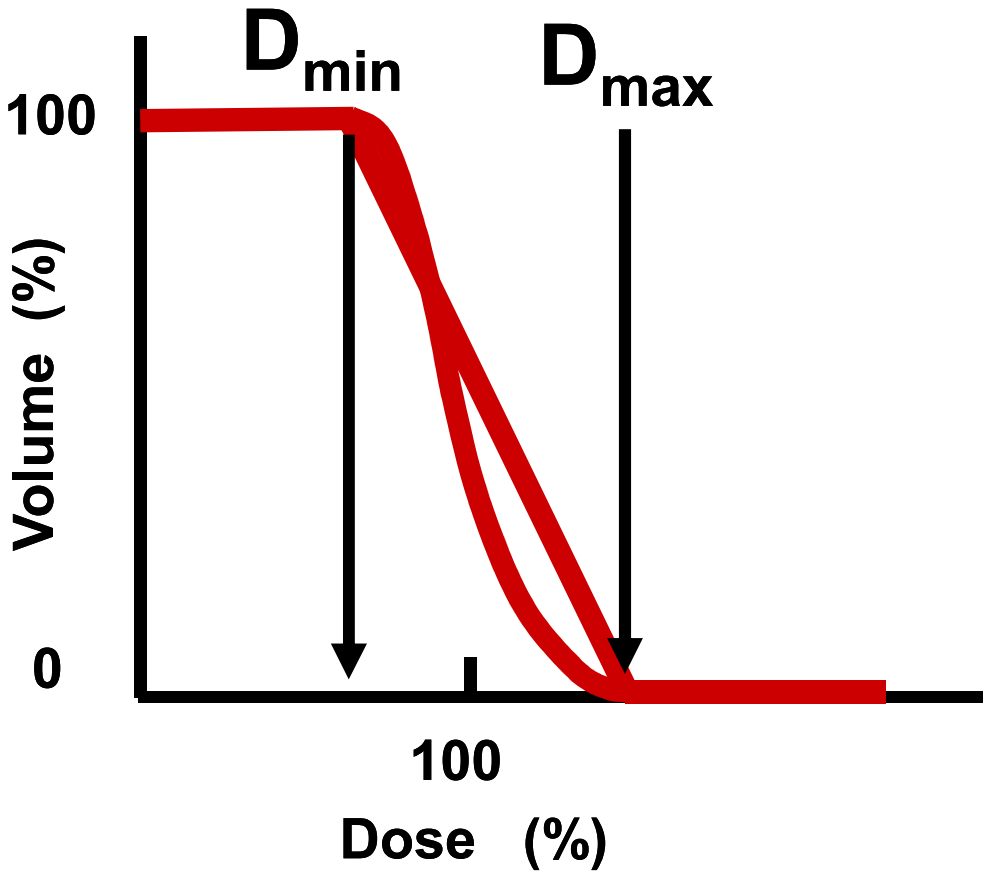
Inverse Optimization and Planning

“ideal” Dose Distribution: GTV/CTV/PTV





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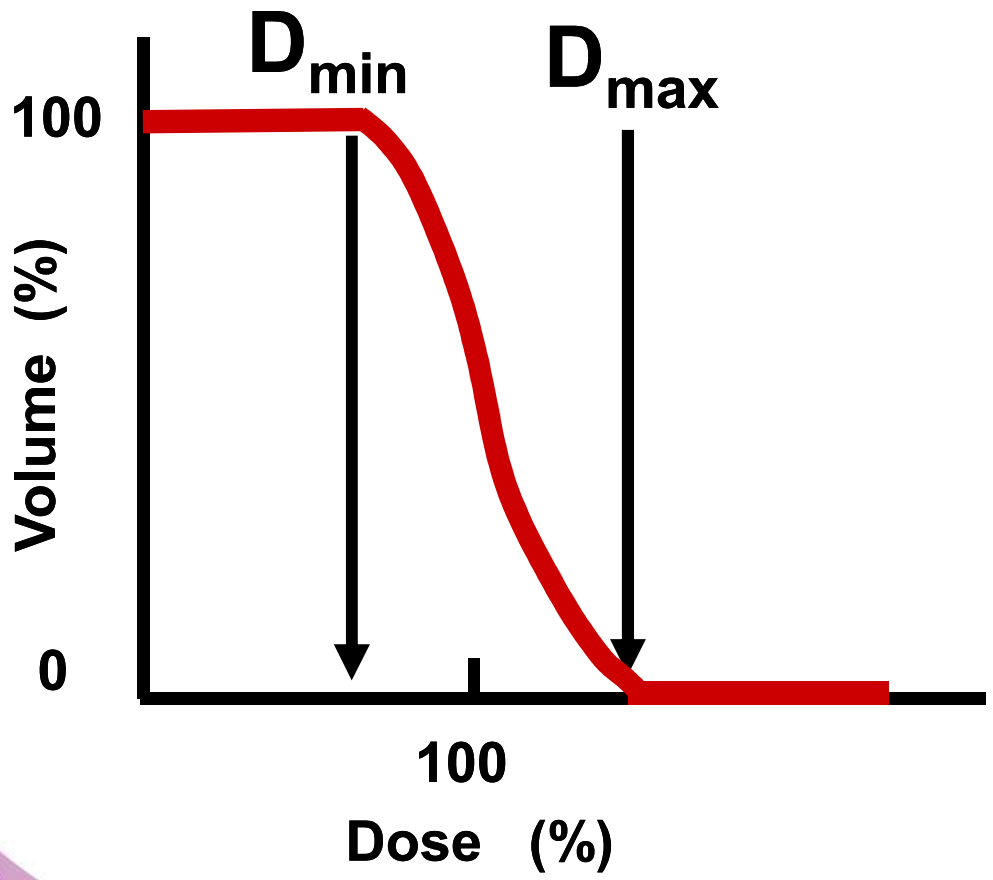
Inverse Optimization and Planning

"ideal" Dose Distribution: GTV/CTV/PTV



D_{min}:100% Volume
with dose ≥ D_{min}
(D_V, V), V=100%
(Low-Limit)

D_{max}: 0% Volume
with dose ≥ D_{max}
(D_V, V), V=0%
(High-Limit)

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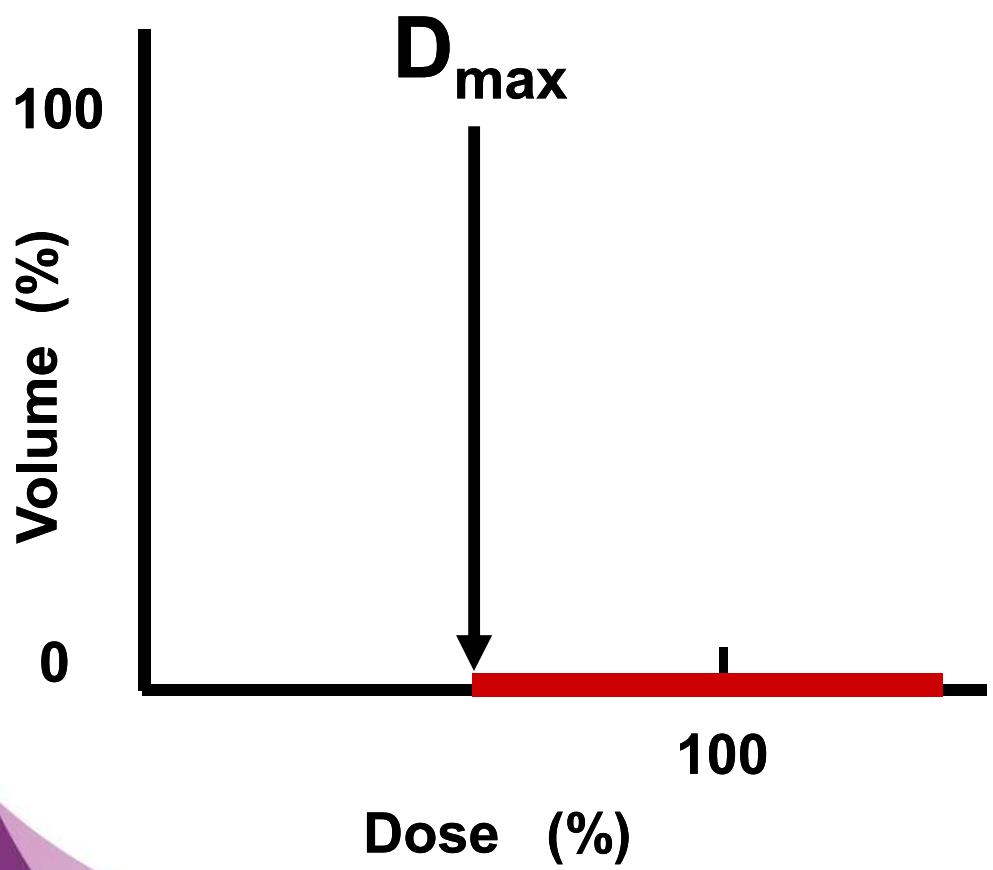
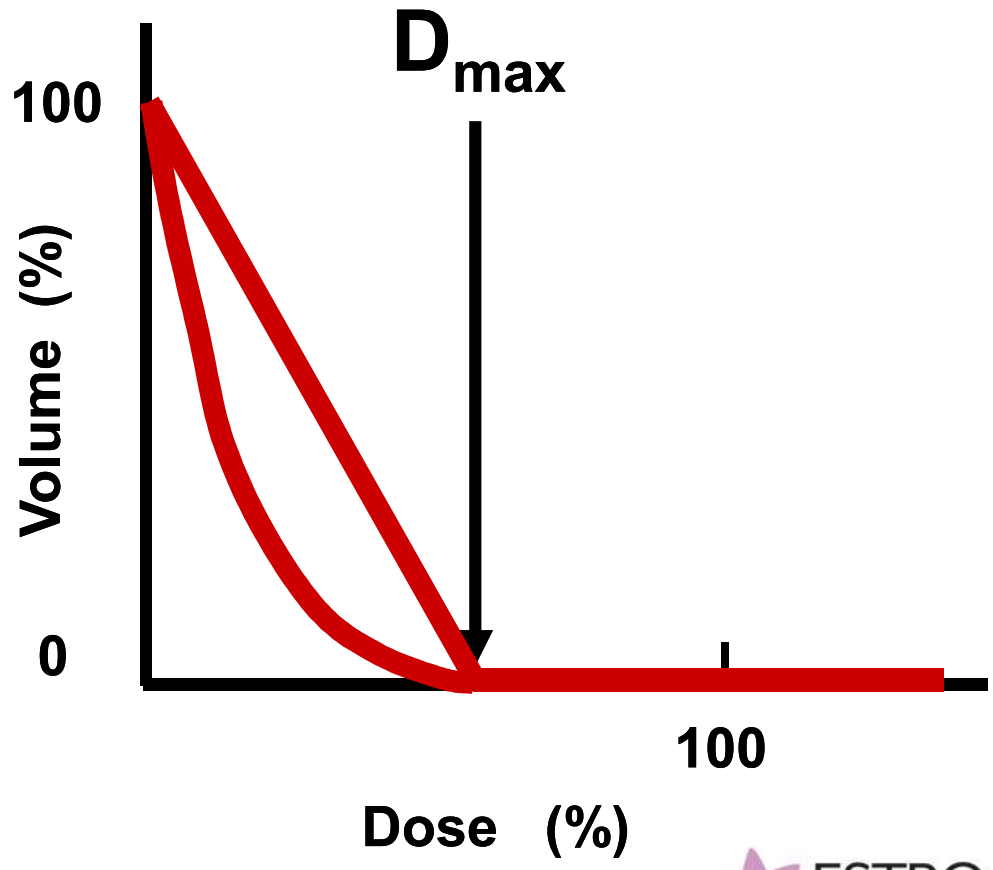
Inverse Optimization and Planning

"ideal" Dose Distribution: OARs





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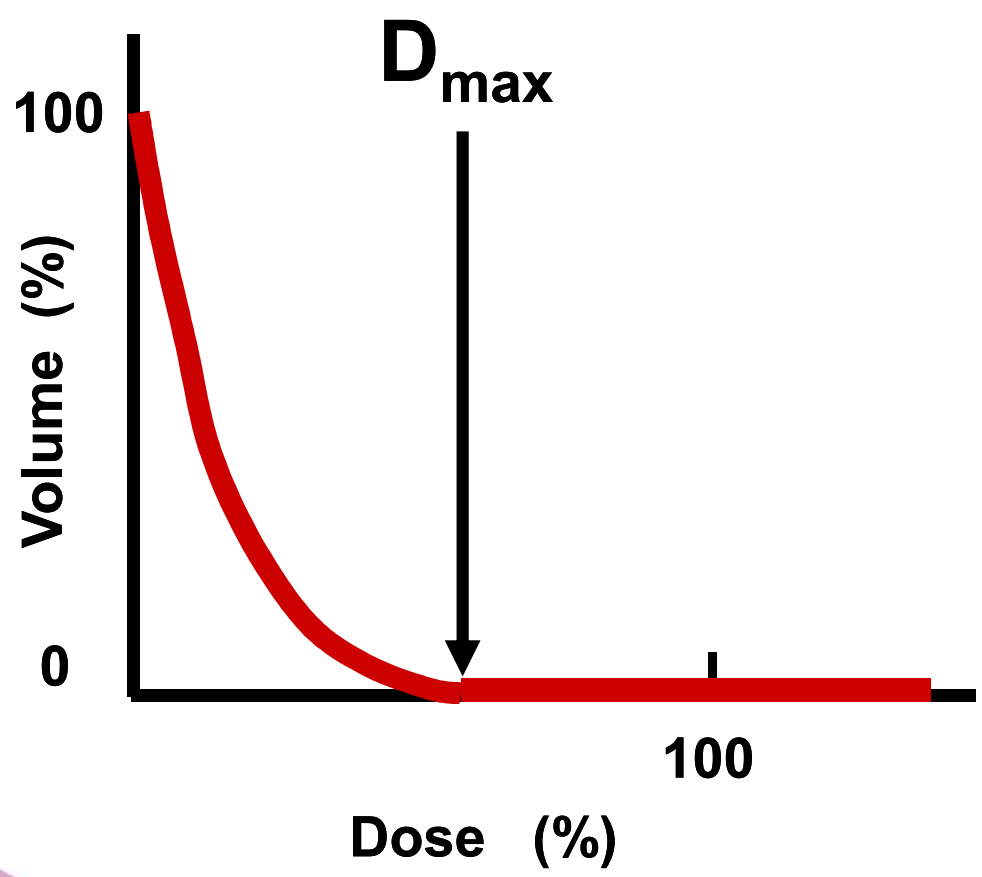
Inverse Optimization and Planning

"ideal" Dose Distribution: OARs



D_{max}: 0% Volume with dose ≥ D_{max}

(D_V, V), V=0% (High-Limit)

(D_V, V)

For V = 0% =>

D_H^{OAR} or D_{crit}^{OAR}

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Inverse Optimization and Planning

Due to the fact, that in BRT we deliver a huge spectrum of dose values, the clinical protocol, considers simply some "representative" values for the 3D dose distribution:

Dose - Volume - Pairs

(D_V, V)

For GTVs, CTV/PTV, OARs, …

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Inverse Optimization and Planning

The DEF-Scheme

- Define the "Optimum", $\{ (D_V, V)_i \}_{VOI\text{-}j}$
- Express the Deviation from "Optimum"

  by a Mathematical Expression f
  (Cost Function, Objective Function)

- Find $\{ t \}$ or $[\{ \vec{r} \}, \{ t \}]$
  to minimize Deviation, Cost Function

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Inverse Optimisation and Planning

General Form of a *Dose Objective Function*

Low-Objective
$D_L = D_V$ for $V_{100\%}$

$$f_i = \frac{1}{N_i}\sum_{j=1}^{N_i}\left[\left[D_L^i - d_j^i(\mathbf{x})\right]^p\right] \quad \forall \; d_j^i(\mathbf{x}) < D_L^i$$

High-Objective
$D_H = D_V$ for $V_{0\%}$

$$f_i = \frac{1}{N_i}\sum_{j=1}^{N_i}\left[\left[d_j^i(\mathbf{x}) - D_H^i\right]^p\right] \quad \forall \; d_j^i(\mathbf{x}) > D_H^i$$

d^i_i is the dose at the jth-sampling point for the ith-objective function:

$$d_j^i(\mathrm{x}) = \sum_{k=1}^{N_{cath}}\sum_{l=1}^{N_{ASDP}^k} x_{lk}^2\,\tilde{d}^{\,i}_{jkl}$$

Catheters/ Needles/ Applicators — **Active SDPs** — **Dwell time t_{lk}**

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Inverse Optimisation and Planning

General Form of a *Dose Objective Function*

d^i_j is the dose at the jth-sampling point for the ith-objective function:

$$d^i_j(\mathrm{x}) = \sum_{k=1}^{N_{cath}} \sum_{l=1}^{N^k_{ASDP}} x^2_{lk} \tilde{d}^{\,i}_{jkl}$$

Catheters Active SDPs Dwell time t_{lk}

- $x^2_{lk} = t_{lk}$ to avoid negative (non-physical) dwell time values t_{lk}
- $\tilde{d}^{\,i}_{jkl}$ can (should) be calculated in a pre-process step and are then available in a sense of a Look-Up-Table for the optimisation process. Implementations in this way (HIPO) make optimiser independent of the dose calculation engine considered (TG 43, MC-LUTs, CC, other Solvers)

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Inverse Optimisation and Planning

General Form of a *Dose Objective Function*

Low-Objective
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$$f_i = \frac{1}{N_i}\sum_{j=1}^{N_i}\left[\left[D_L^i - d_j^i(\mathbf{x})\right]^p\right] \quad \forall \; d_j^i(\mathbf{x}) < D_L^i$$

High-Objective
$D_H = D_V$ for $V_{0\%}$

$$f_i = \frac{1}{N_i}\sum_{j=1}^{N_i}\left[\left[d_j^i(\mathbf{x}) - D_H^i\right]^p\right] \quad \forall \; d_j^i(\mathbf{x}) > D_H^i$$

The Norm Factor *p*

p = 0 : Volume Objective Function

1 : Linear

2 : Variance based Objective Function

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Inverse Optimisation and Planning

Create a single Objective Function via weighted Aggregation

The M *objective functions* f_m *are* combined into a *single objective function f,* by using a *weighted sum (aggregation)* of all objectives:

$$f = \sum_{m=1}^{M} w_m \, f_m = f(\{\vec{r}\},\{t\},\{w\})$$

w_m : the *Importance Factors* (IFs) for the individual *Objective Functions* f_m or *Penalties* for the *penalisation* of the *violation of the individual objectives*.

These are considered as a measure of the significance of each of the objectives / objective functions in the optimisation process.

The optimisation process equals then the minimisation of the *Aggregated Objective Function f*.

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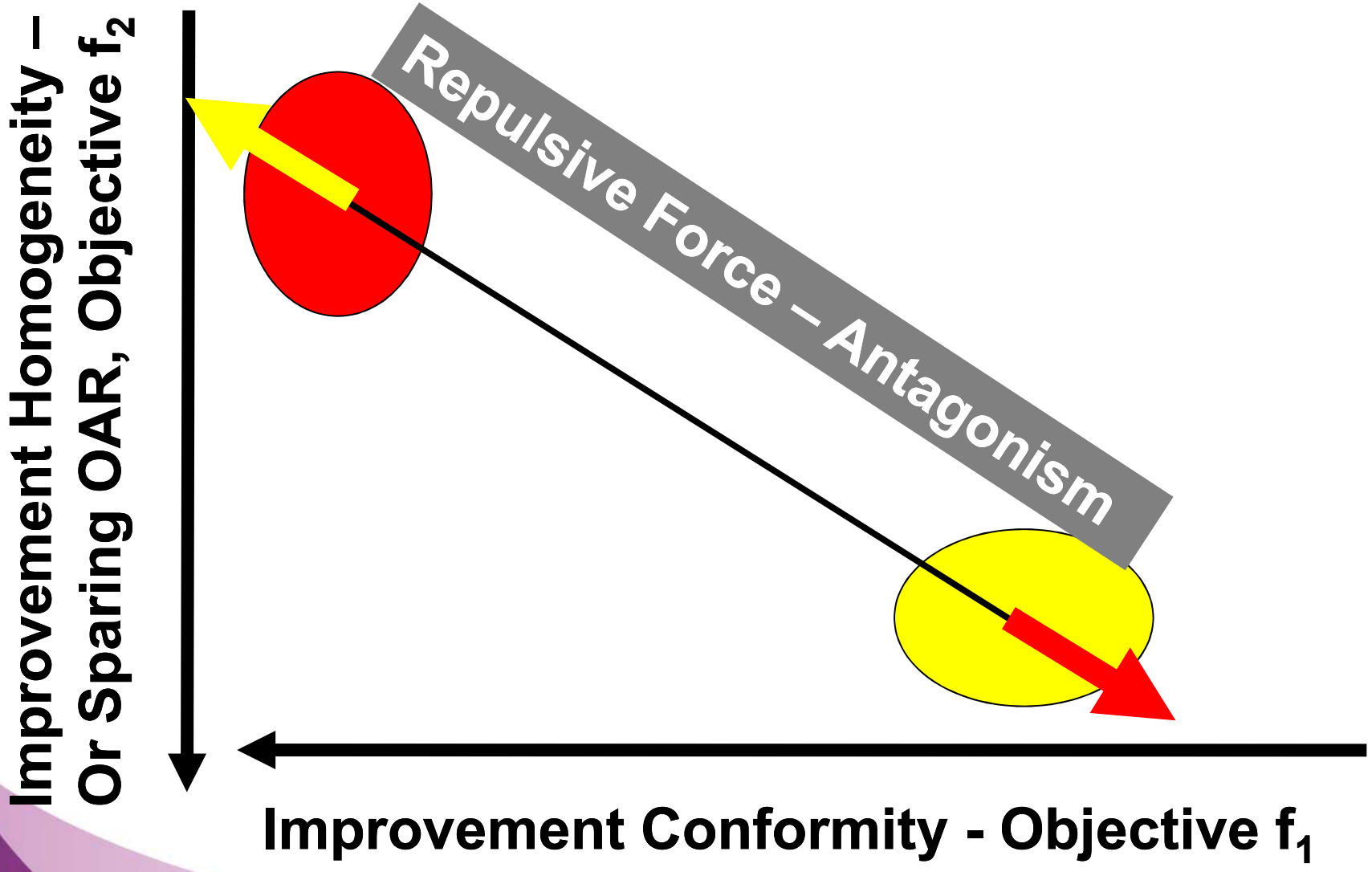
Inverse Optimization and Planning

A Multi-Objective (MO) Problem



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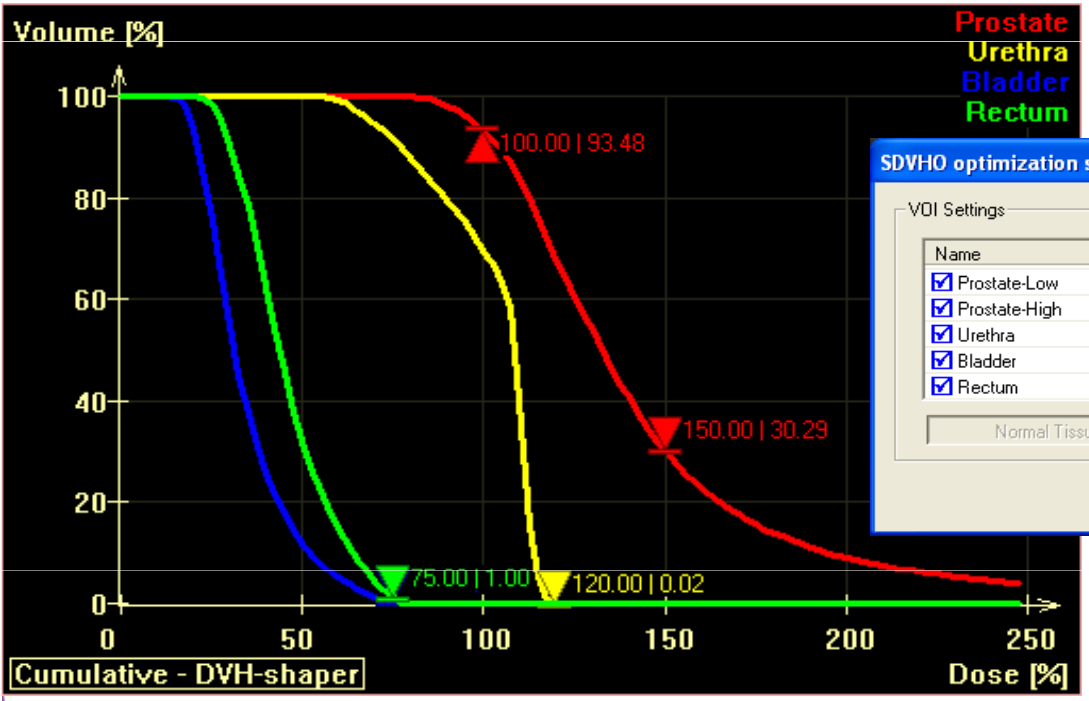
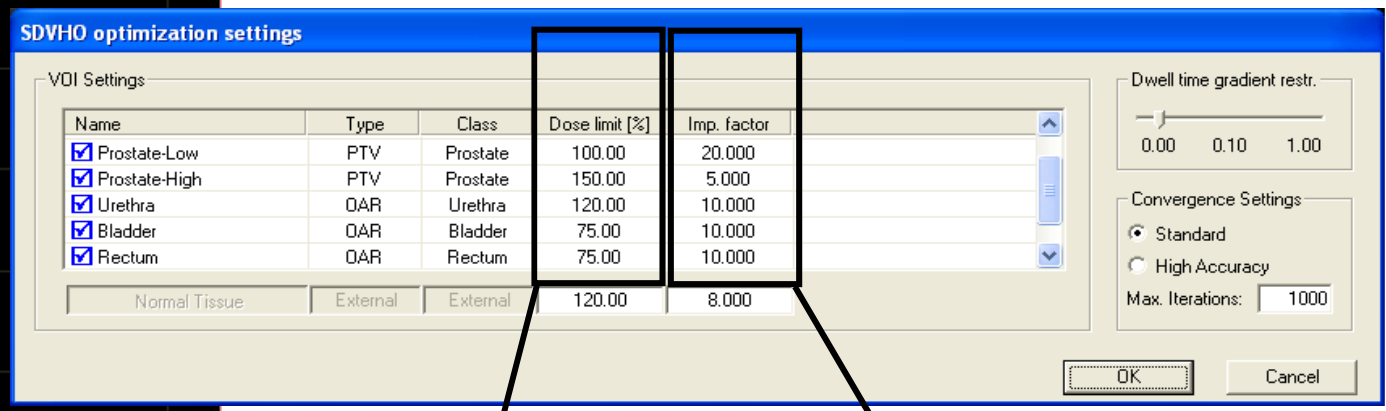
Due to the fact that it is a multi-objective procedure, there is no Guarantee that all Planner-defined Objectives (“Wishes”) will be fulfilled simultaneously (at the same degree).
The solution will represent a “good” compromise among all wishes/objectives!

Inverse Optimization and Planning

Example of User-Interface of State of the Art Optimizers*





Dose limits in % of D_{ref}

Penalties if limits are exceeded

*HIPO/DVHO, Oncentra Prostate OcP

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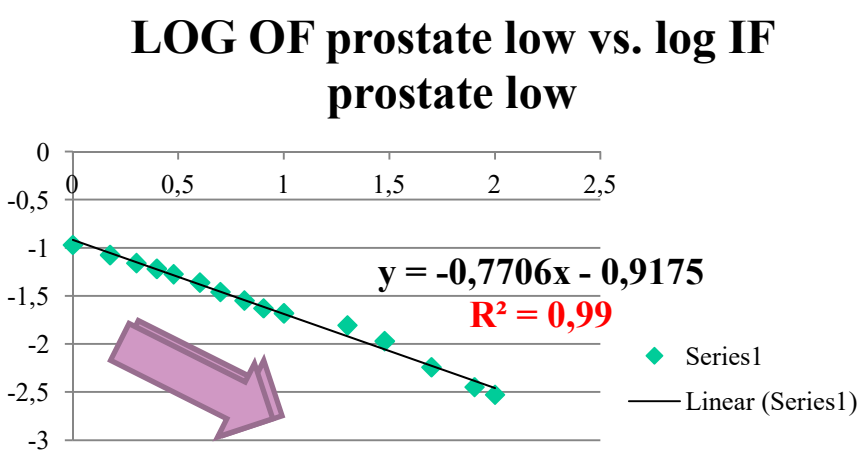
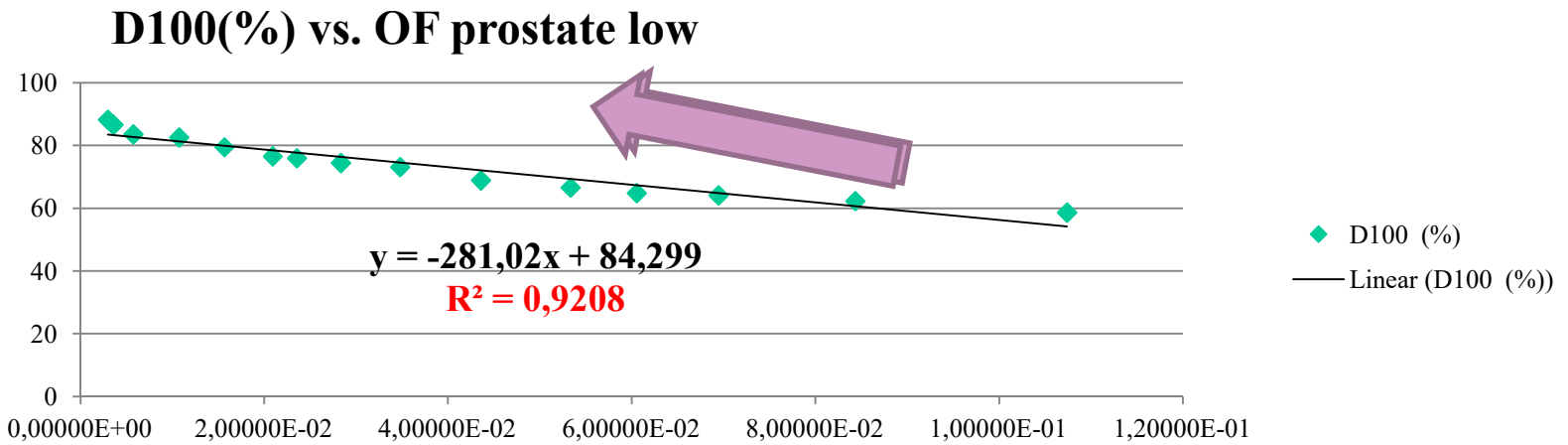
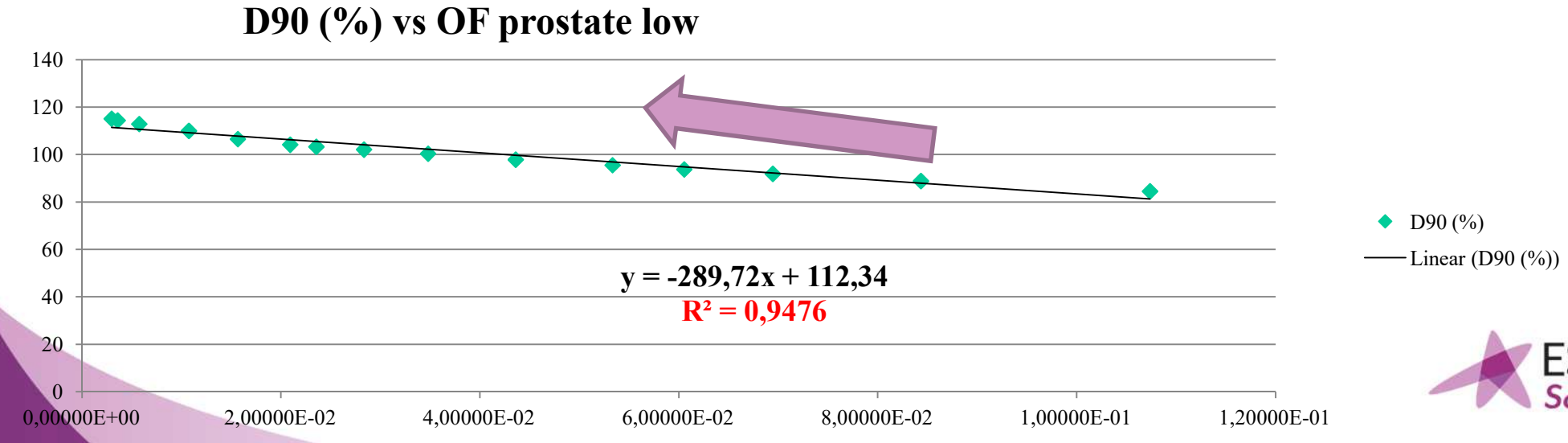


Do “Mathematics” work Compatible to clinical Expectations ?





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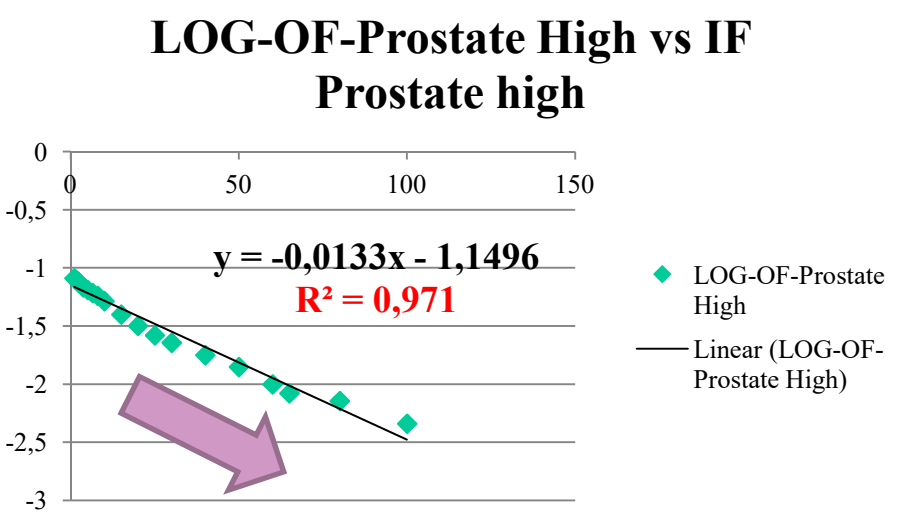

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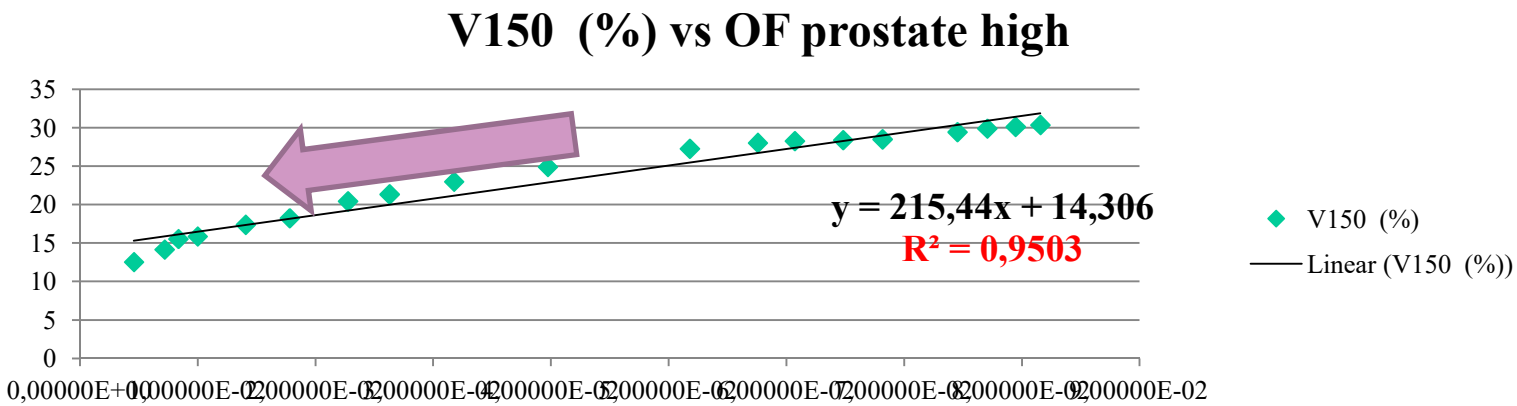

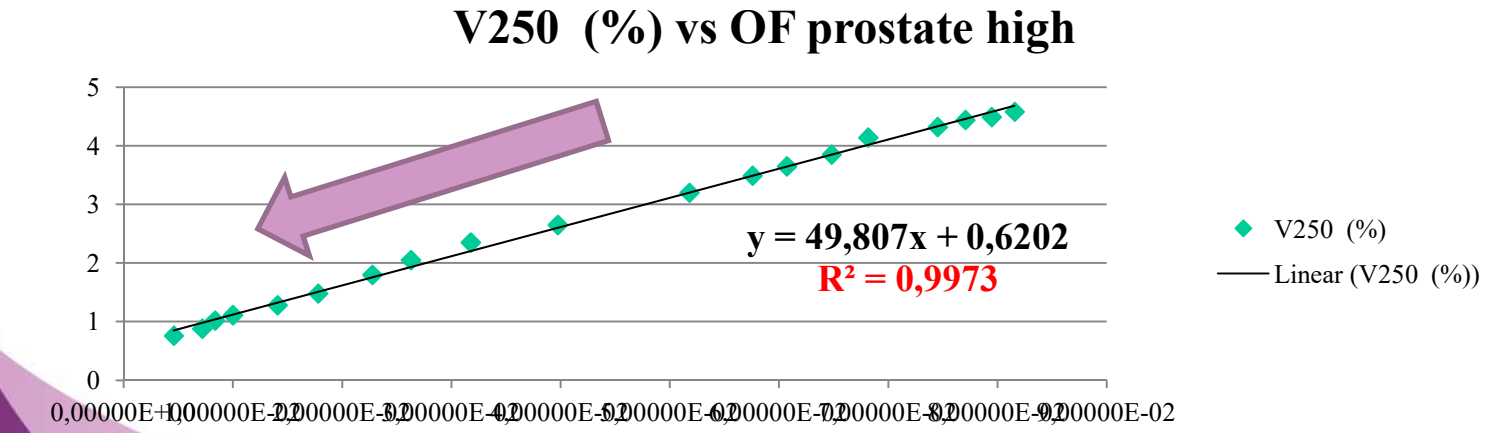

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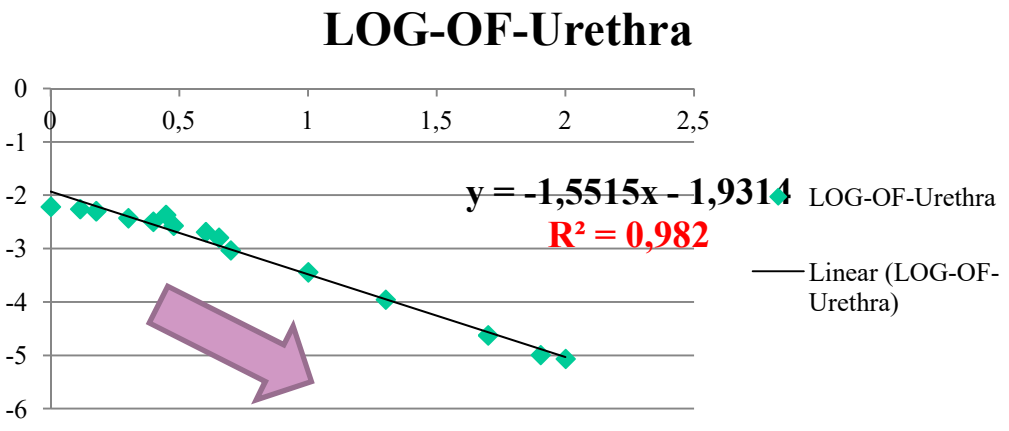

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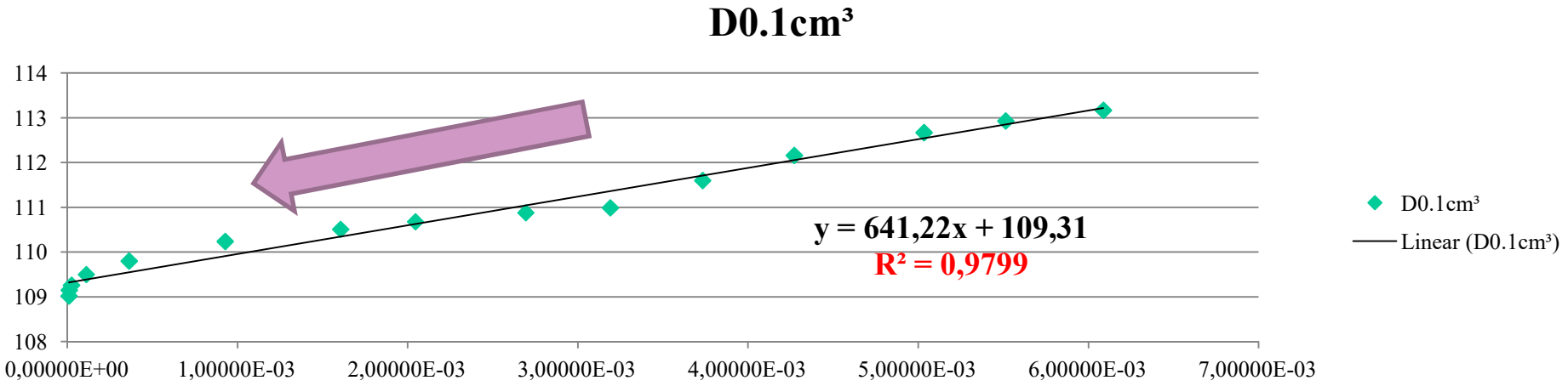

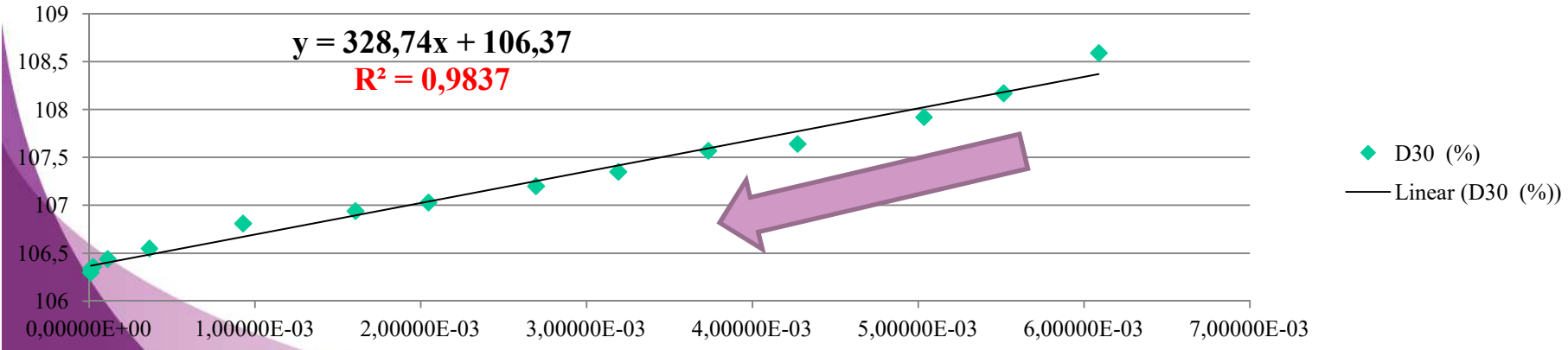

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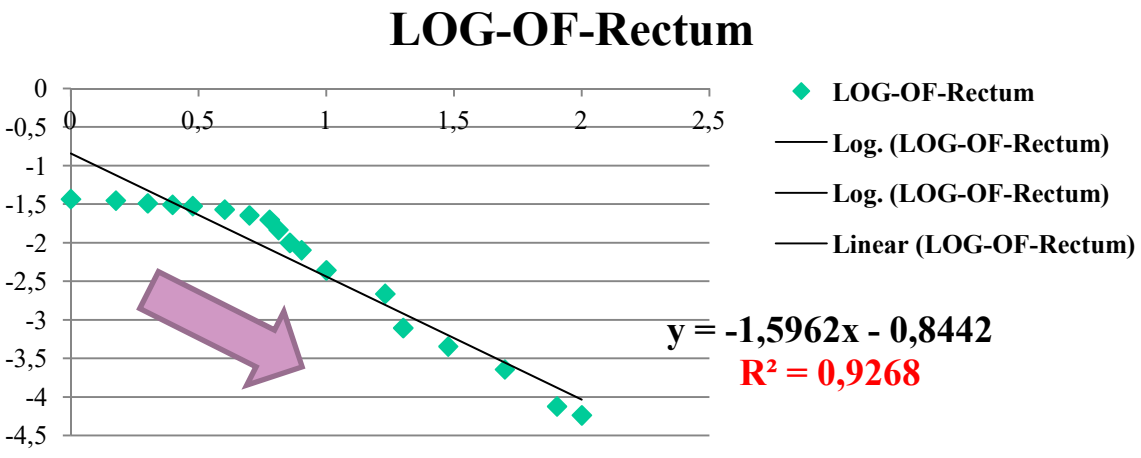
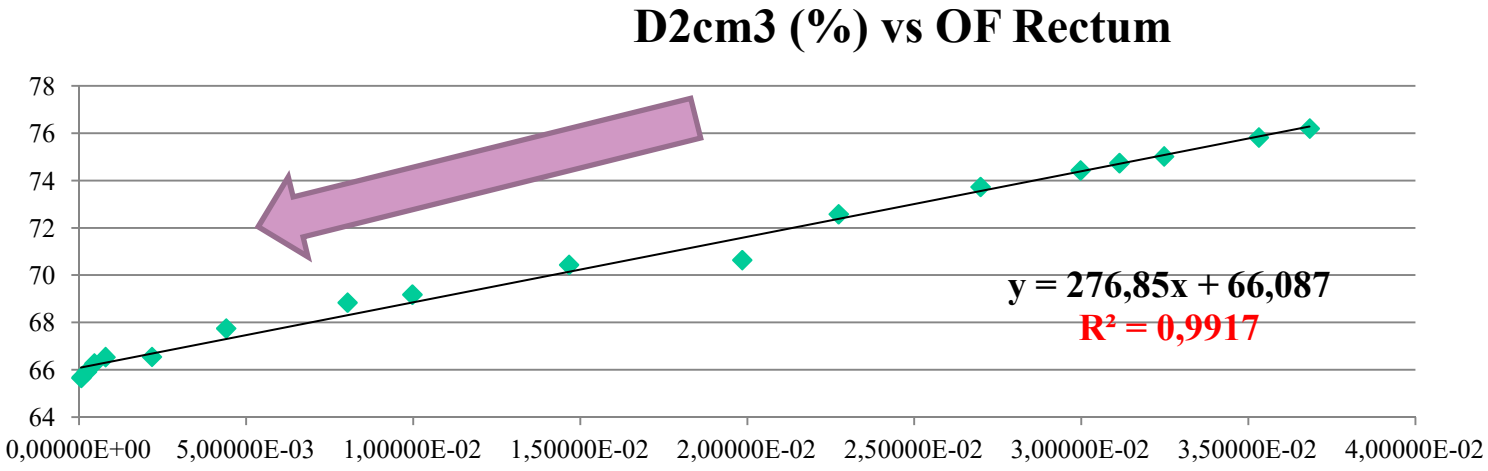
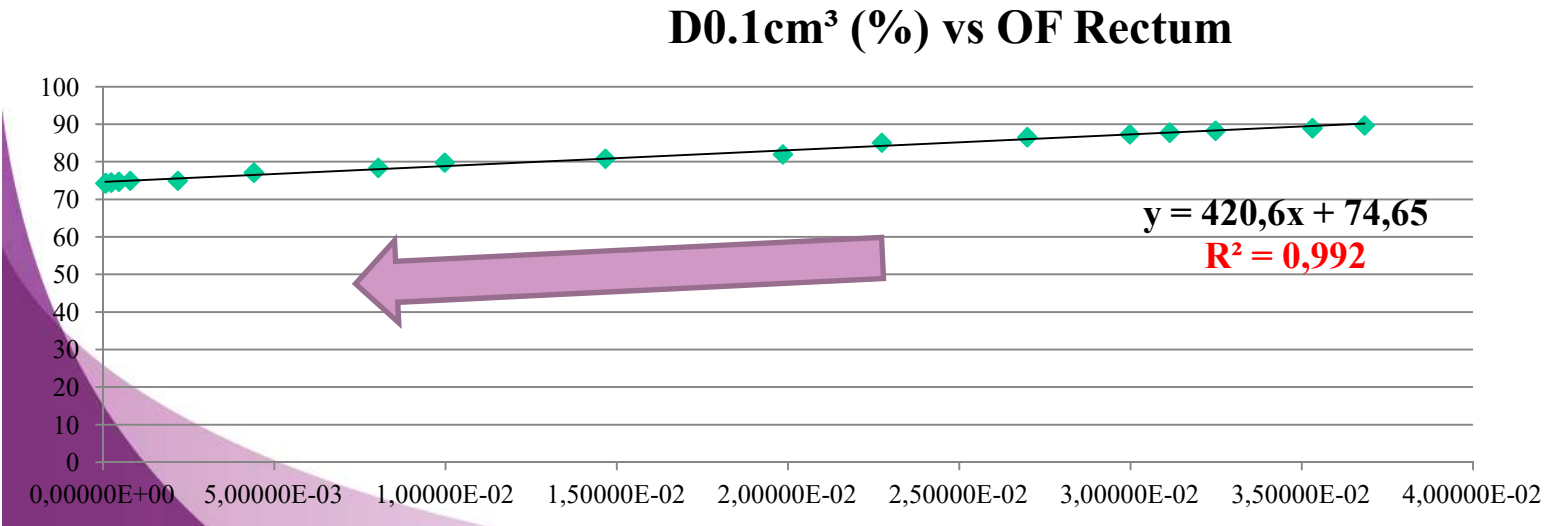


Do “Mathematics” work Compatible to clinical Expectations ?





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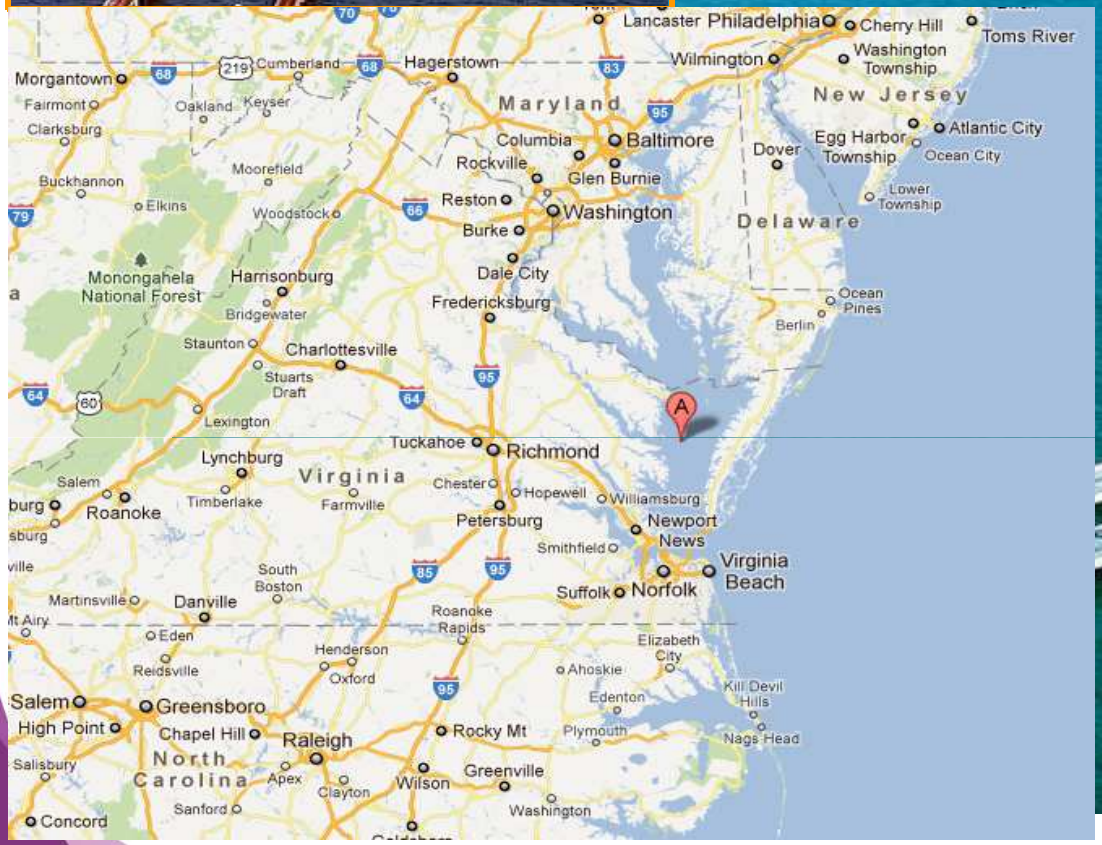

Bridges, tunnels into the Chesapeake Bay, which allow the passage of warships of the base in Norfolk.

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DEMO on a Prostate Implant

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Radiobiology in PDR

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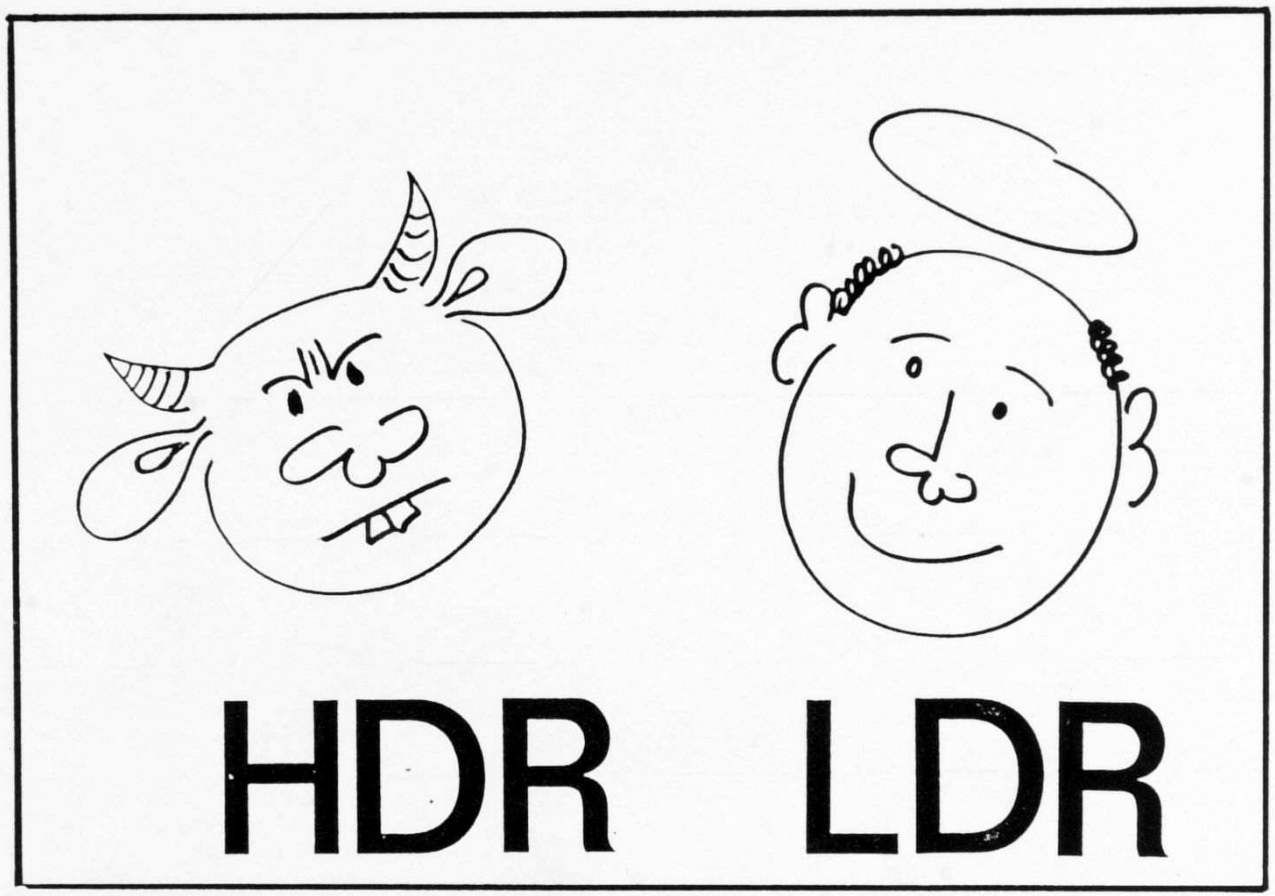
Bradley Pieters
Academic Medical Center / University of Amsterdam

Erik van Limbergen
Catholic University Leuven



HAS LOW DOSE RATE VIRTUES BY ITSELF ?

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PULSED LOW DOSE RATE

THE BEST OF BOTH WORLDS …….

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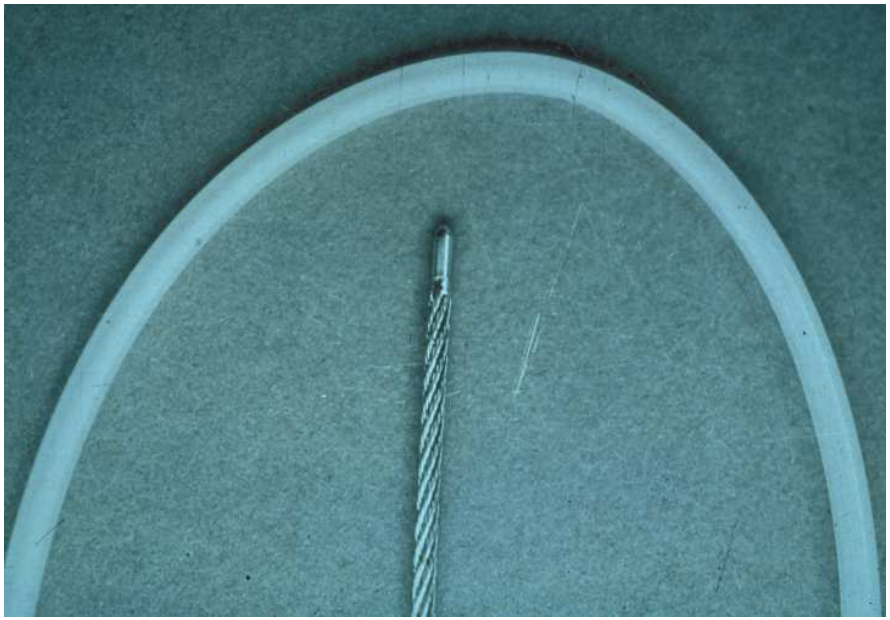
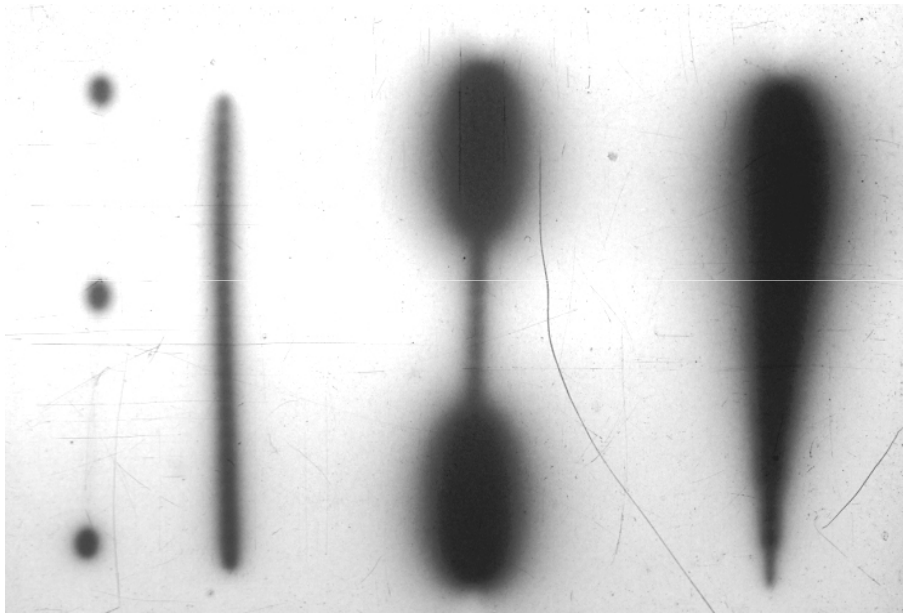
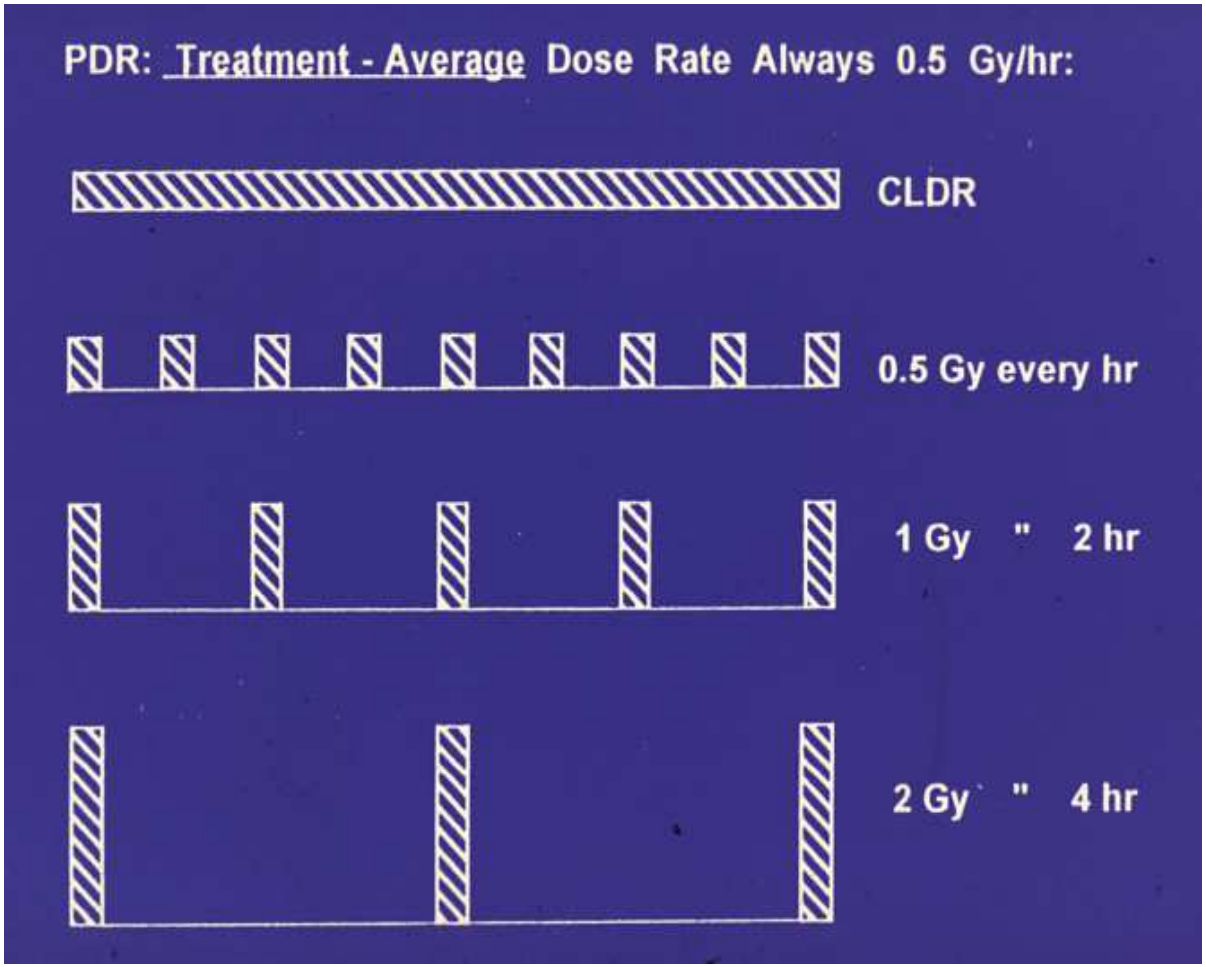
ADVANTAGES P.D.R.

HDR stepping source technology





Mimicking LDR radiobiology



FACTORS CONTRIBUTING TO BIOLOGICAL EFFECTS IN PDR BRACHYTHERAPY

- total dose
- total time
- dose per pulse
- interval
- dose rate in the pulse

- repair capacity (α/β ratio of target cells)
- repair velocity (T 1/2 SLD repair)

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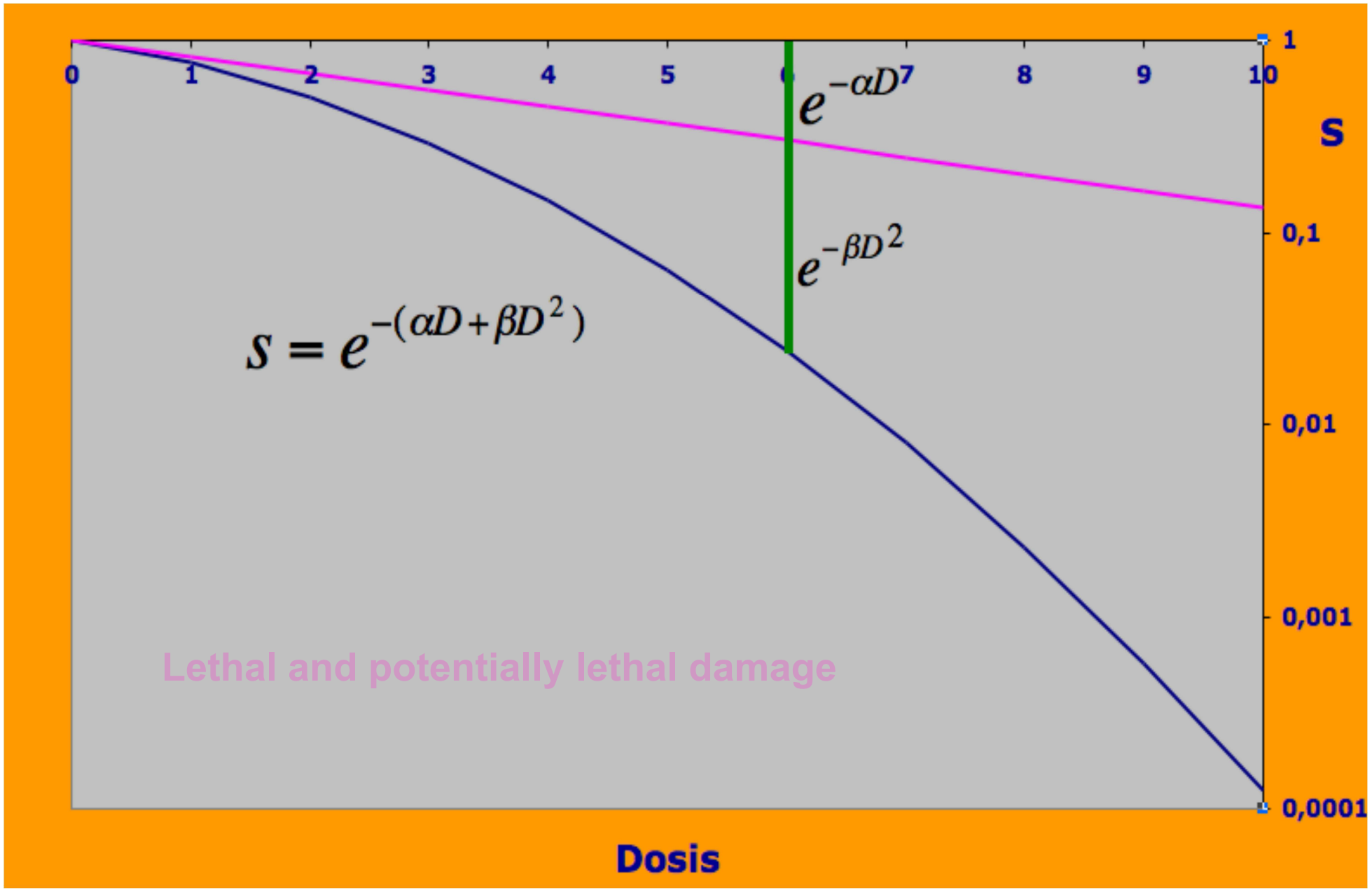
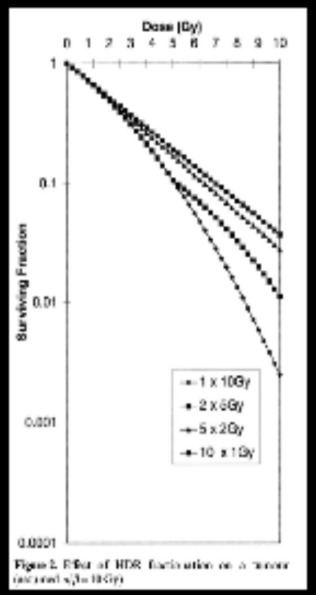
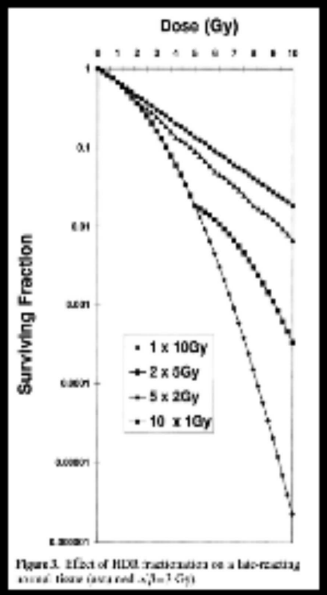
An hourly pulse dose schedule of 50 cGy in 15 minutes has more biological effect than 100 cGy in 45 minutes

A. True
B. False

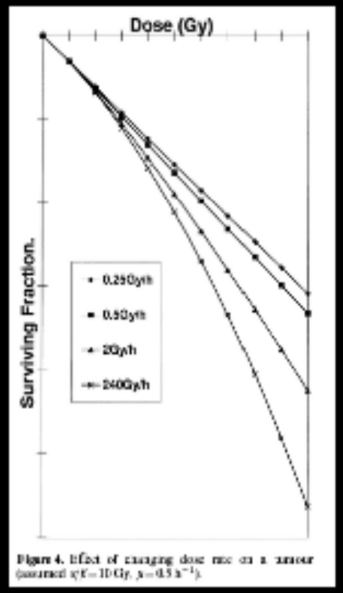

0
1
2
3
4
5
6
7
8
9
10
1
0,1
0,01
0,001
0,0001
S
$e^{-\alpha D^7}$
$e^{-\beta D^2}$
$S = e^{-(\alpha D + \beta D^2)}$
Lethal and potentially lethal damage
Dosis

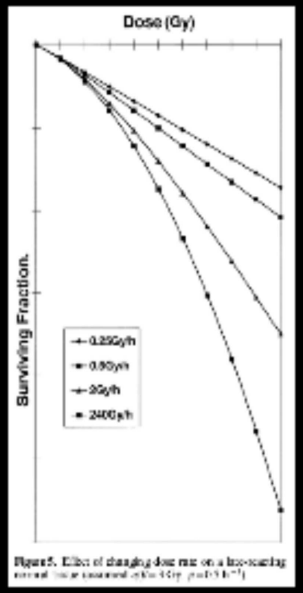
α/β= 10 Gy α/β= 3 Gy





10 x 1 Gy
5 x 2 Gy
2 x 5 Gy
1 x 10 Gy





25 cGy/u
50 cGy/u
200 cGy/u
24000 cGy/u

Dale
Br J Radiol 1998

EQUIVALENCY PDR - CLDR

Mathematical modeling		
Fowler and Mount 1992	α/β 3 - 15 Gy	0.5 Gy/h
In vitro		
Brenner and Hall 1991	36 human cell lines	0.5 Gy/h
Armour et al. 1992	9 L gliosarcoma cells	
In vivo		
Mason et al. 1993	mice jejunum	0.5-0.7 Gy/h
Moulder J. et al. 1996	rat kidney	
	rat tumours	

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PDR Survival curve

- $S = \exp - (\alpha D + \beta d \,.\, (1 + Hm) \,.\, D)$
- With:

  D = total dose

  d = dose per pulse

  Hm = incomplete repair factor

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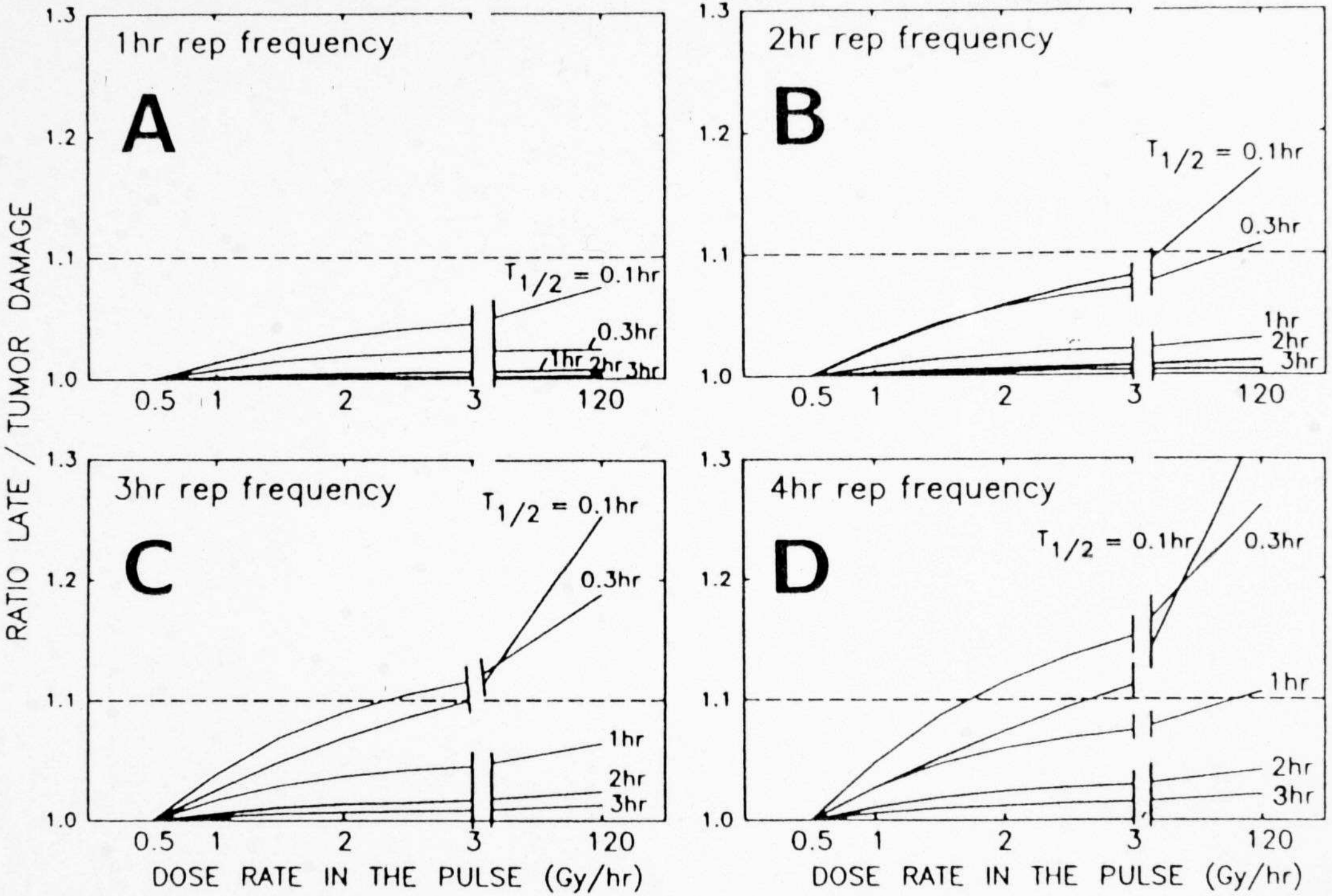
1hr rep frequency
A
2hr rep frequency
B
3hr rep frequency
C
4hr rep frequency
D
RATIO LATE / TUMOR DAMAGE
DOSE RATE IN THE PULSE (Gy/hr)
DOSE RATE IN THE PULSE (Gy/hr)
T1/2 = 0.1hr
0.3hr
1hr
2hr
3hr
1.3
1.2
1.1
1.0
0.5
1
2
3
120

BIOLOGICAL EFFECTIVENESS PDR
Same physical dose - same overall time

PDR $\geq$ CLDR

ONLY A FEW % DIFFERENCE

IF: - small pulses 0.5 - 1 Gy

- pulse dose rate < 3 Gy/hr
- SLD repair T 1/2 > 1 h

Fowler and Mount 1992

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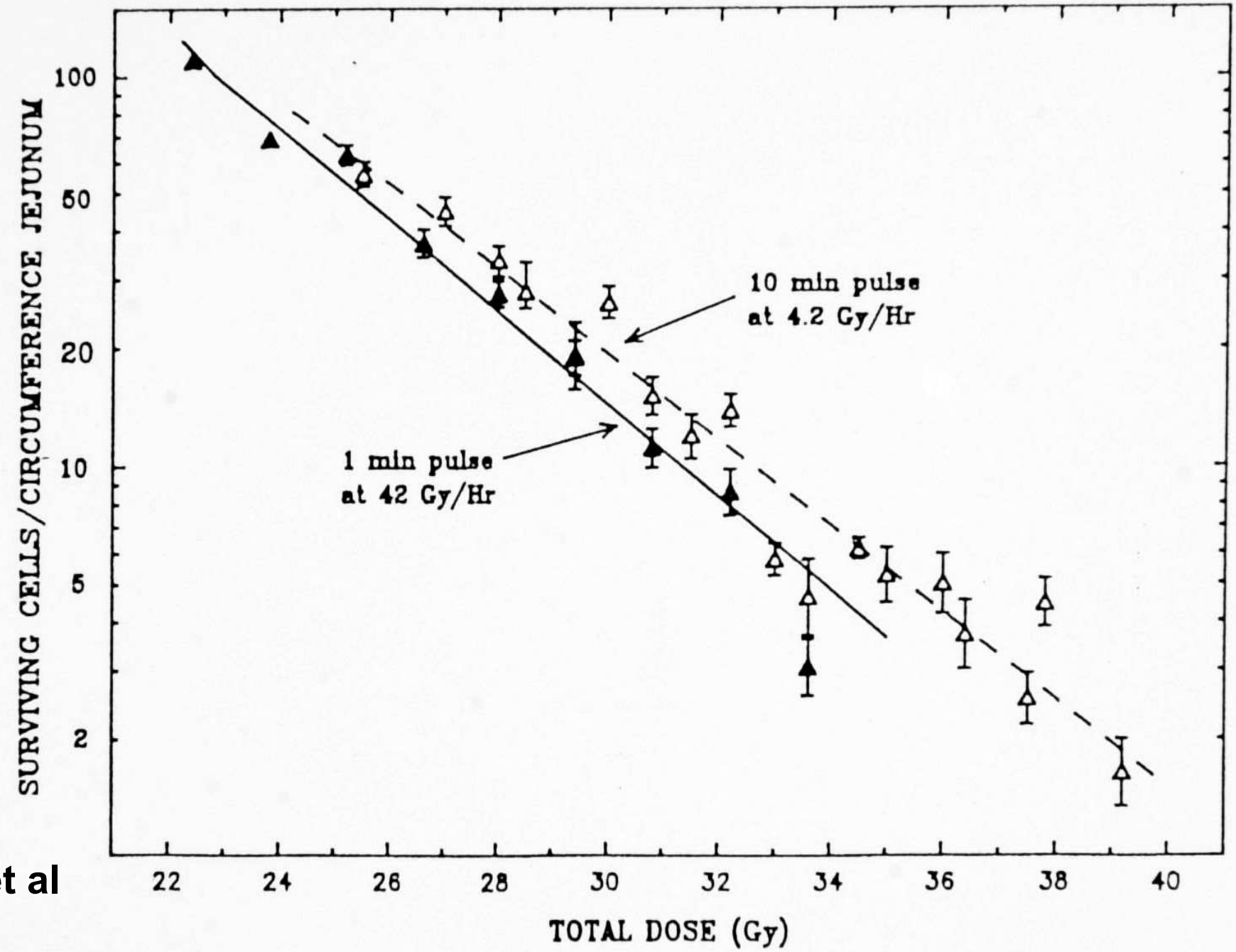

Mason et al

Fig. 2. Surviving cells per circumference of jejunum plotted as a function of total dose on semilogarithmic coordinates. (△) 10 min pulses at 4.2 Gy/h; (▲) 1 min pulses at 42 Gy/h. Both groups were treated at an average dose rate of 0.7 Gy/h.

ISO EFFECT DOSES FOR DIFFERENT PULSE DOSE RATES WITH CONSTANT AVERAGE DOSE RATE (0.7/hr)

Pulse dose rate	Pulse width	Interval	Iso-effect at cell survival level of		
			50%	20%	10%
42 Gy/h	1 min	1h	25.4	28.7	31.3
4.2 Gy/h	10 min	1h	26.2	29.8	32.6

Mason K. e.a. 1994

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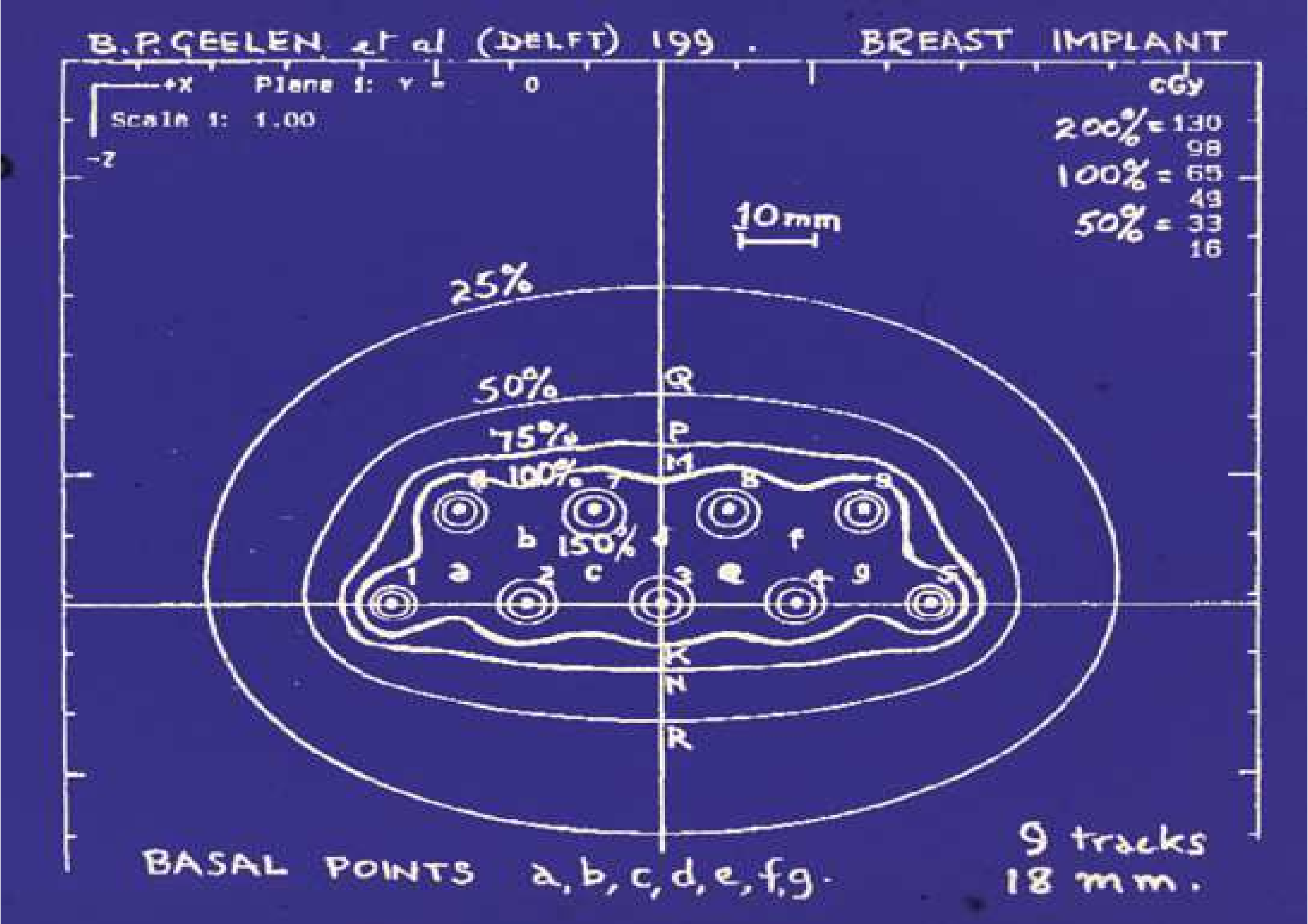
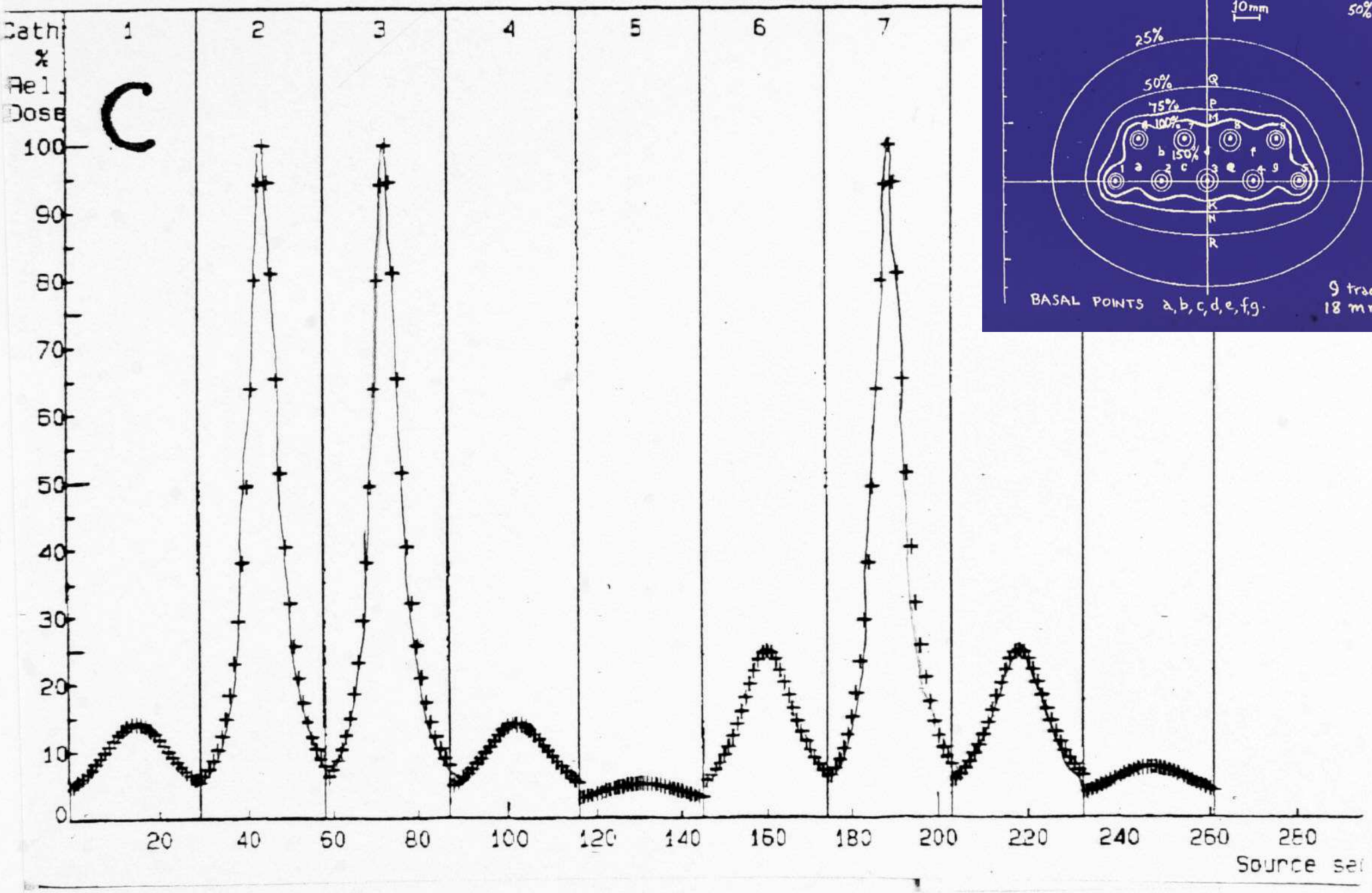
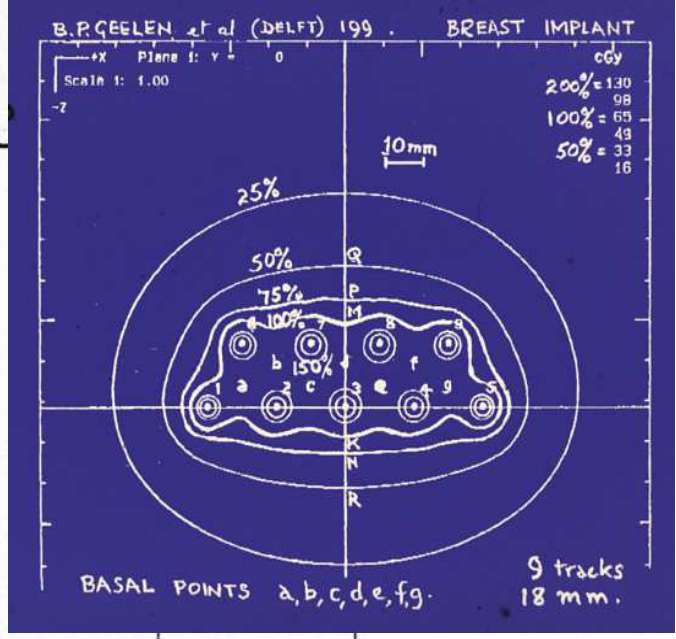

B.P.GEELEN et al (DELFT) 199 . BREAST IMPLANT
+X
Plane 1: Y = 0
Scale 1: 1.00
-Z
cGy
200% = 130
98
100% = 65
49
50% = 33
16
10mm
25%
50%
75%
100%
150%
Q
P
M
K
N
R
a
b
c
d
e
f
g
1
2
3
4
5
7
8
9
BASAL POINTS a, b, c, d, e, f, g.
9 tracks
18 mm.


Cath
%
Rel
Dose
C
1
2
3
4
5
6
7
100
90
80
70
60
50
40
30
20
10
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
Source sa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Plane 1: Y = 0
Scale 1: 1.00
cGy
200% = 130
98
100% = 65
49
50% = 33
16
10mm
25%
50%
75%
100%
150%
BASAL POINTS a,b,c,d,e,f,g.
9 tracks
18 mm.

INSTANTANEOUS DOSE RATES IN PDR INTERSTITIAL IMPLANTS

Distance from the source	1 Curie	0.5 Curie
at 5 mm	170 Gy/hr	85 Gy/hr
at 14.6 mm	20 Gy/hr	10 Gy/hr
at 20.7 mm	10 Gy/hr	5 Gy/hr

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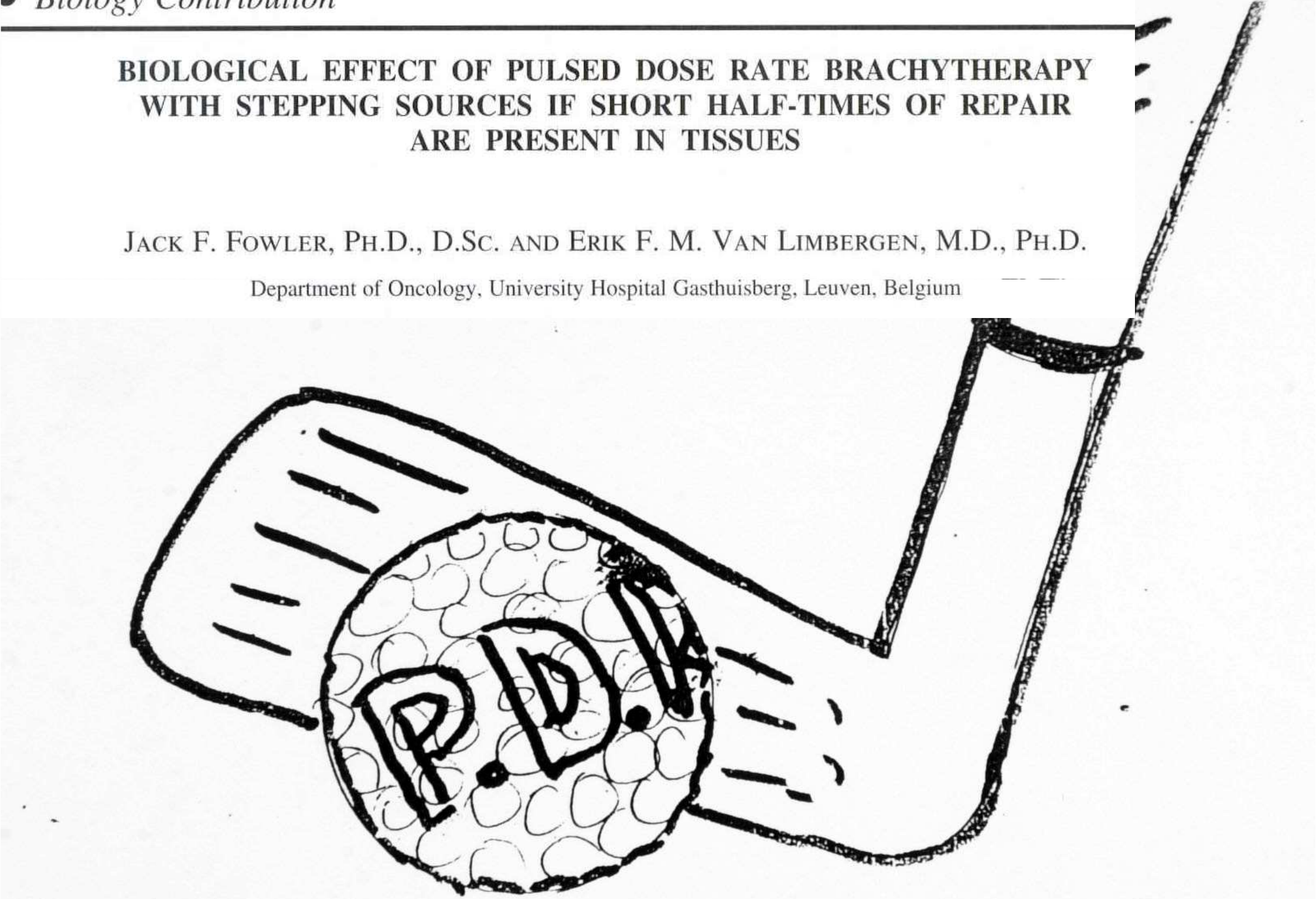
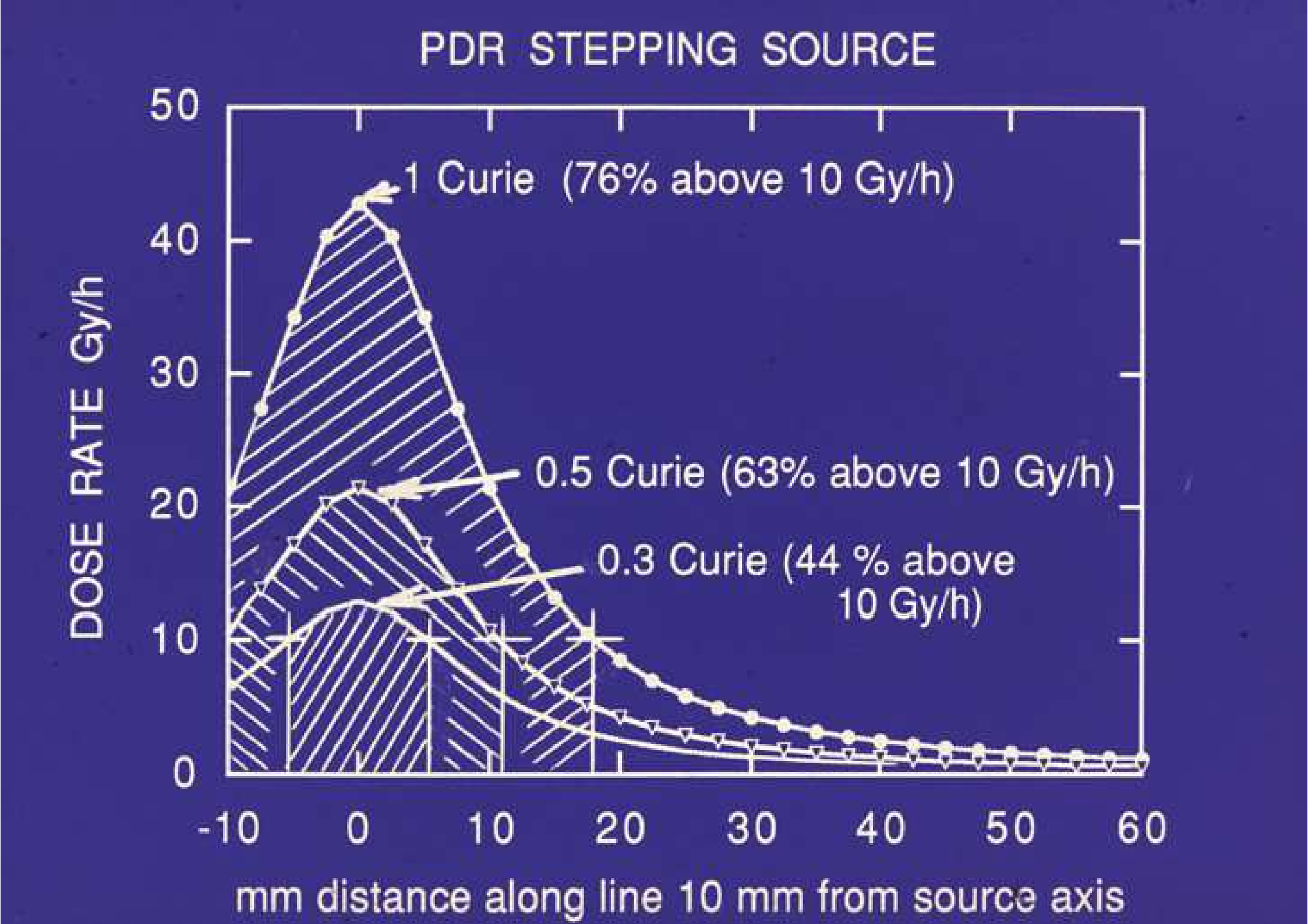
BIOLOGICAL EFFECT OF PULSED DOSE RATE BRACHYTHERAPY WITH STEPPING SOURCES IF SHORT HALF-TIMES OF REPAIR ARE PRESENT IN TISSUES

JACK F. FOWLER, PH.D., D.SC. AND ERIK F. M. VAN LIMBERGEN, M.D., PH.D.

Department of Oncology, University Hospital Gasthuisberg, Leuven, Belgium




PDR STEPPING SOURCE
DOSE RATE Gy/h
50
40
30
20
10
0
1 Curie (76% above 10 Gy/h)
0.5 Curie (63% above 10 Gy/h)
0.3 Curie (44 % above
10 Gy/h)
-10
0
10
20
30
40
50
60
mm distance along line 10 mm from source axis

PDR DOSE RATE EFFECTS
In the range 0.4 Gy/hr - 120 Gy/hr

DALE's EQUATION

α/β 3 Gy for late en 10 Gy for acute effects

mono exponential repair T 1/2: 2 min. - 1.5 hr

RE calculated to 70 Gy - 140 hr, CLDR

4 PDR schedules 0.5 Gy - 1hr

1 Gy - 2 hr

1.5 Gy - 3 hr

2 Gy - 4 hr

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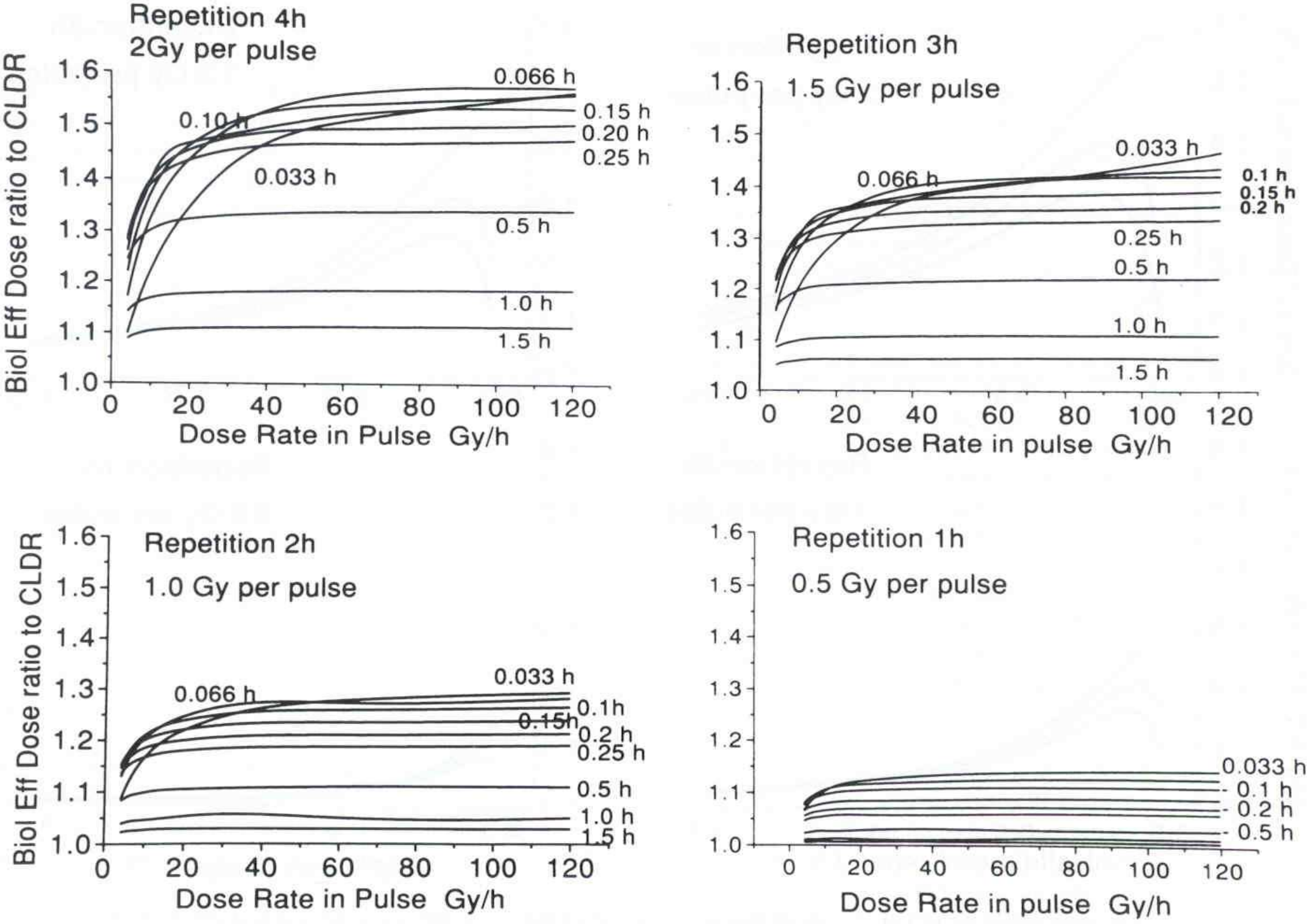
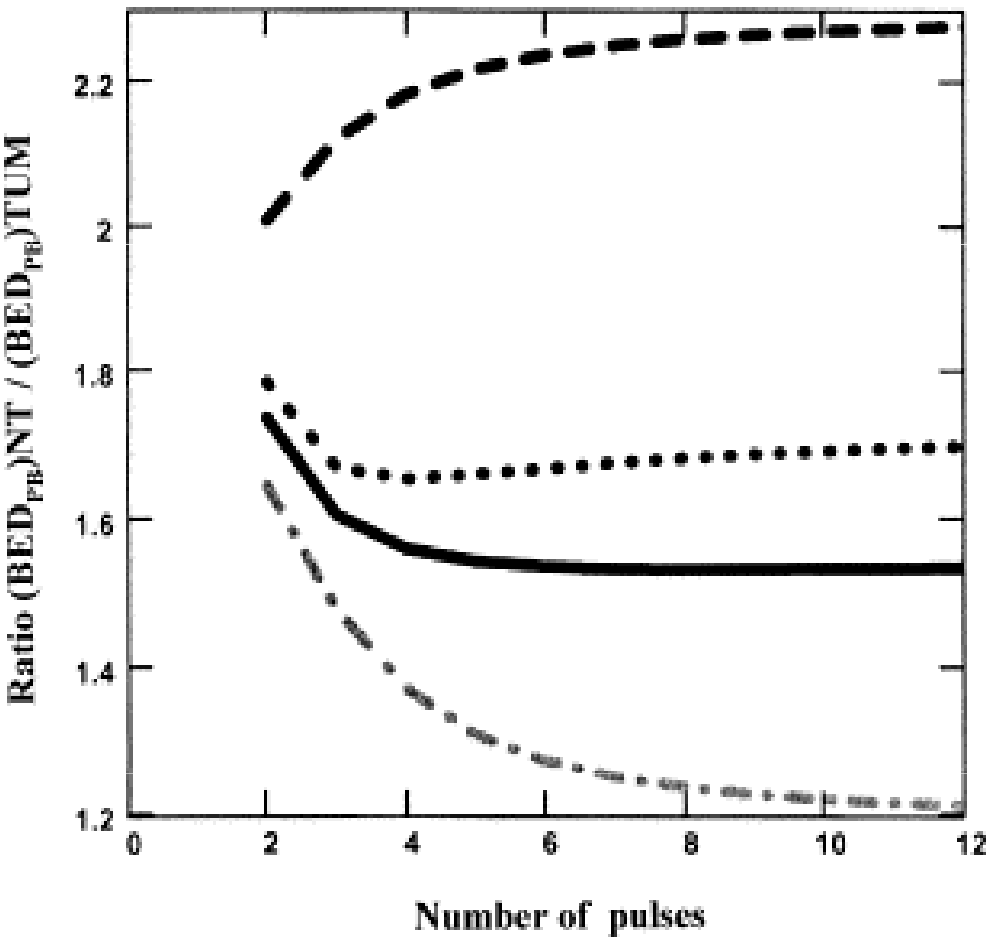

Repetition 4h
2Gy per pulse
Biol Eff Dose ratio to CLDR
Dose Rate in Pulse Gy/h
0.066 h
0.10 h
0.15 h
0.20 h
0.25 h
0.033 h
0.5 h
1.0 h
1.5 h
Repetition 3h
1.5 Gy per pulse
Dose Rate in pulse Gy/h
0.033 h
0.066 h
0.1 h
0.15 h
0.2 h
0.25 h
0.5 h
1.0 h
1.5 h
Repetition 2h
1.0 Gy per pulse
Biol Eff Dose ratio to CLDR
Dose Rate in Pulse Gy/h
0.033 h
0.066 h
0.1h
0.15h
0.2 h
0.25 h
0.5 h
1.0 h
1.5 h
Repetition 1h
0.5 Gy per pulse
Dose Rate in pulse Gy/h
0.033 h
0.1 h
0.2 h
0.5 h

Variation in values for T1/2



T1/2 normal tissue = 3 h

T1/2 tumour = 0.5 h

T1/2 normal = 1 h, T1/2 tumour = 1 h

T1/2 normal tissue = 0.5 h

Sminia, R&O 2001;59:273-280

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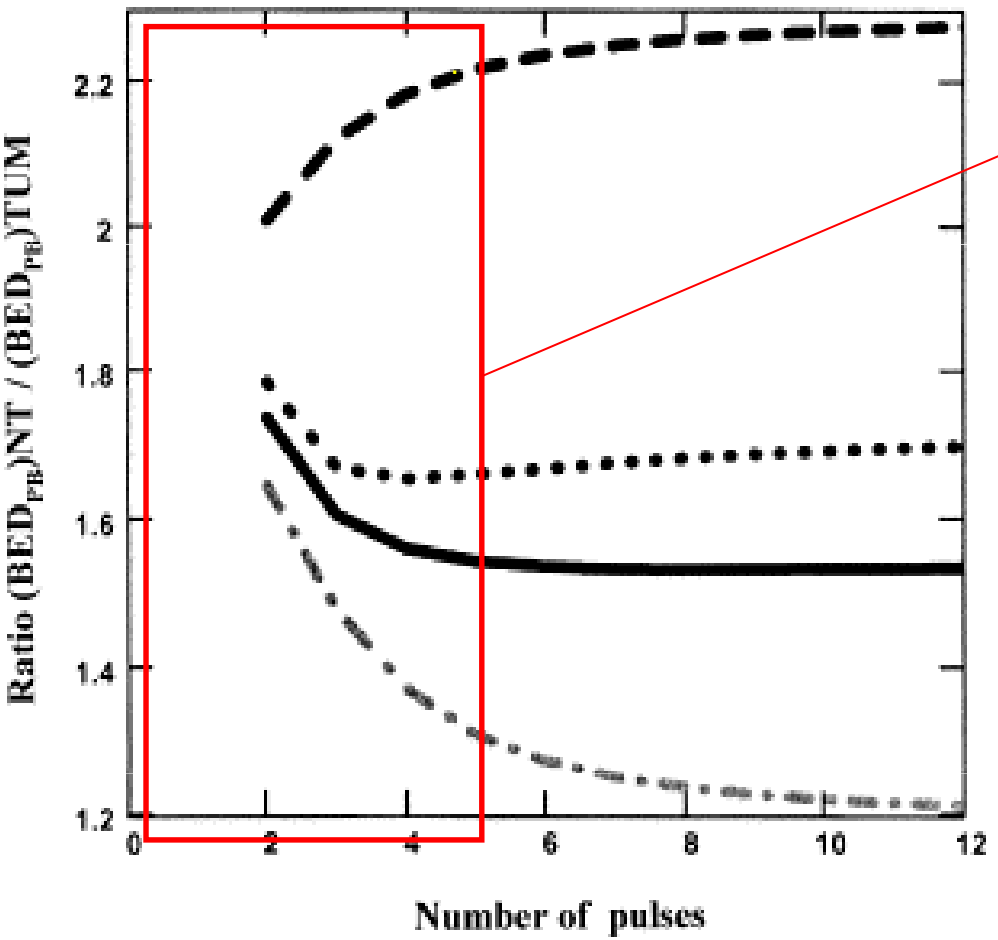
Variation in values for T1/2



T1/2 normal tissue = 3 h

Highly variable BED_{NT} / BED_{TUM}

T1/2 tumour = 0.5 h

T1/2 normal = 1 h, T1/2 tumour = 1 h

T1/2 normal tissue = 0.5 h

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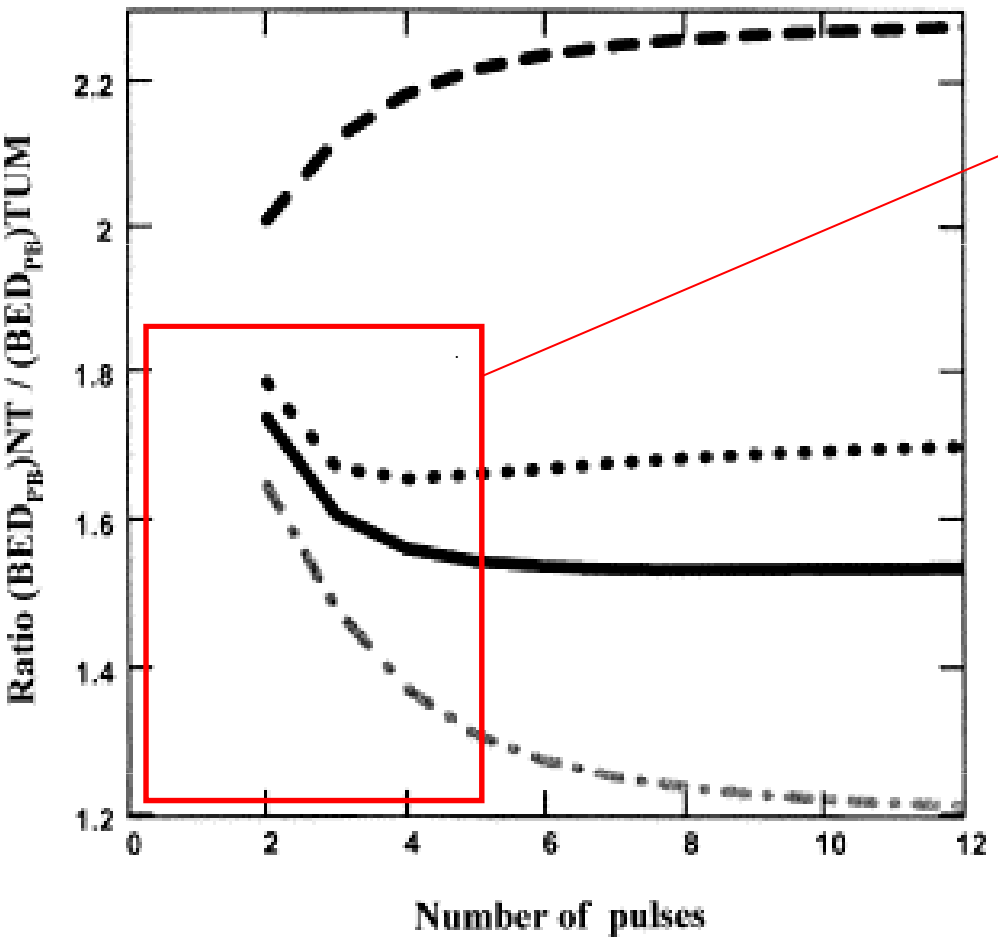
Variation in values for T1/2



T1/2 normal tissue = 3 h

Higher toxicity at small number of pulses

T1/2 tumour = 0.5 h

T1/2 normal = 1 h, T1/2 tumour = 1 h

T1/2 normal tissue = 0.5 h

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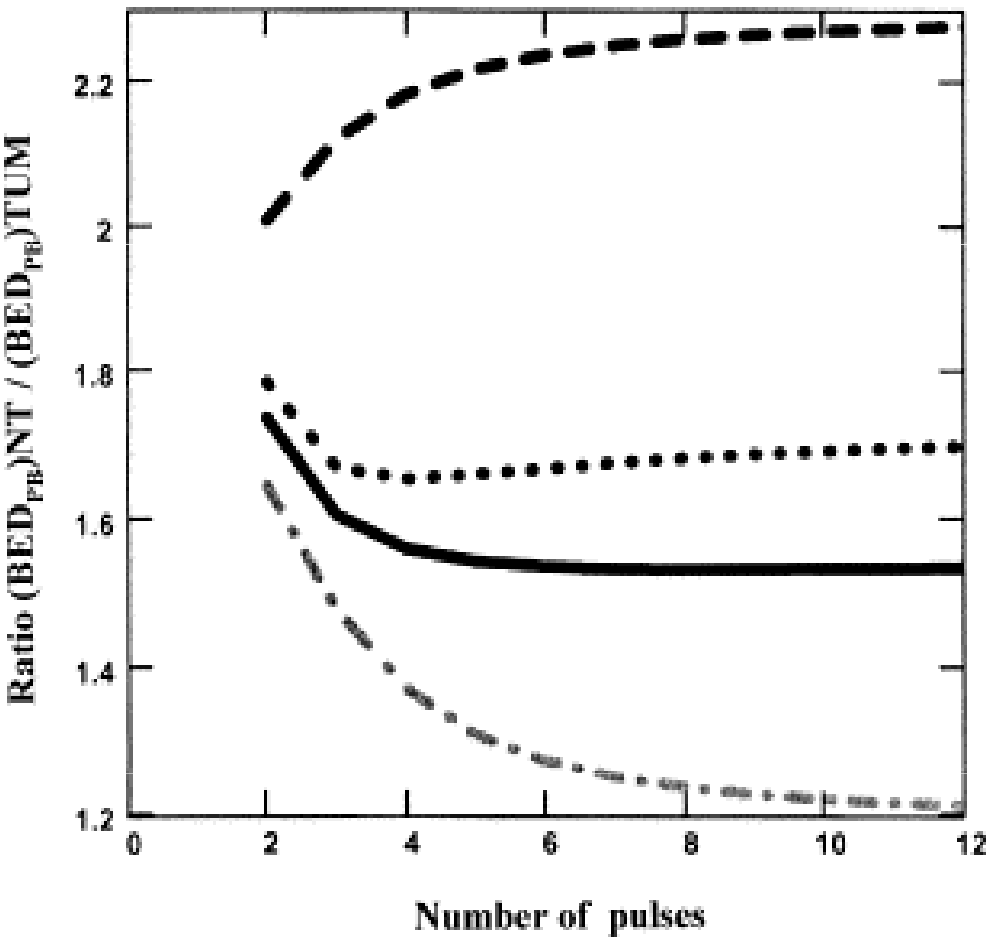
Variation in values for T1/2



T1/2 normal tissue = 3 h

Conclusion:

Design of PDR protocol is more safe at higher number of pulses

$t_{1/2}$ tumour = 0.5 h

T1/2 normal = 1 h, T1/2 tumour = 1 h

T1/2 normal tissue = 0.5 h

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CONCLUSION (1)

Dose rate effects > 10 Gy/hr are not substantially different from HDR

More than 40 - 75 % of the time, and much more of the dose is delivered at > 10 Gy/hr HDR

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CONCLUSION (2)

Pulse size and not pulse dose rate is the dominant factor

PDR behaves as (hyperfractionated) HDR but with incomplete repair between fractions.

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CONCLUSION (3)

The enhanced effects are especially seen in tissues

- with small α/β
- fast T 1/2 (<0.5hr)

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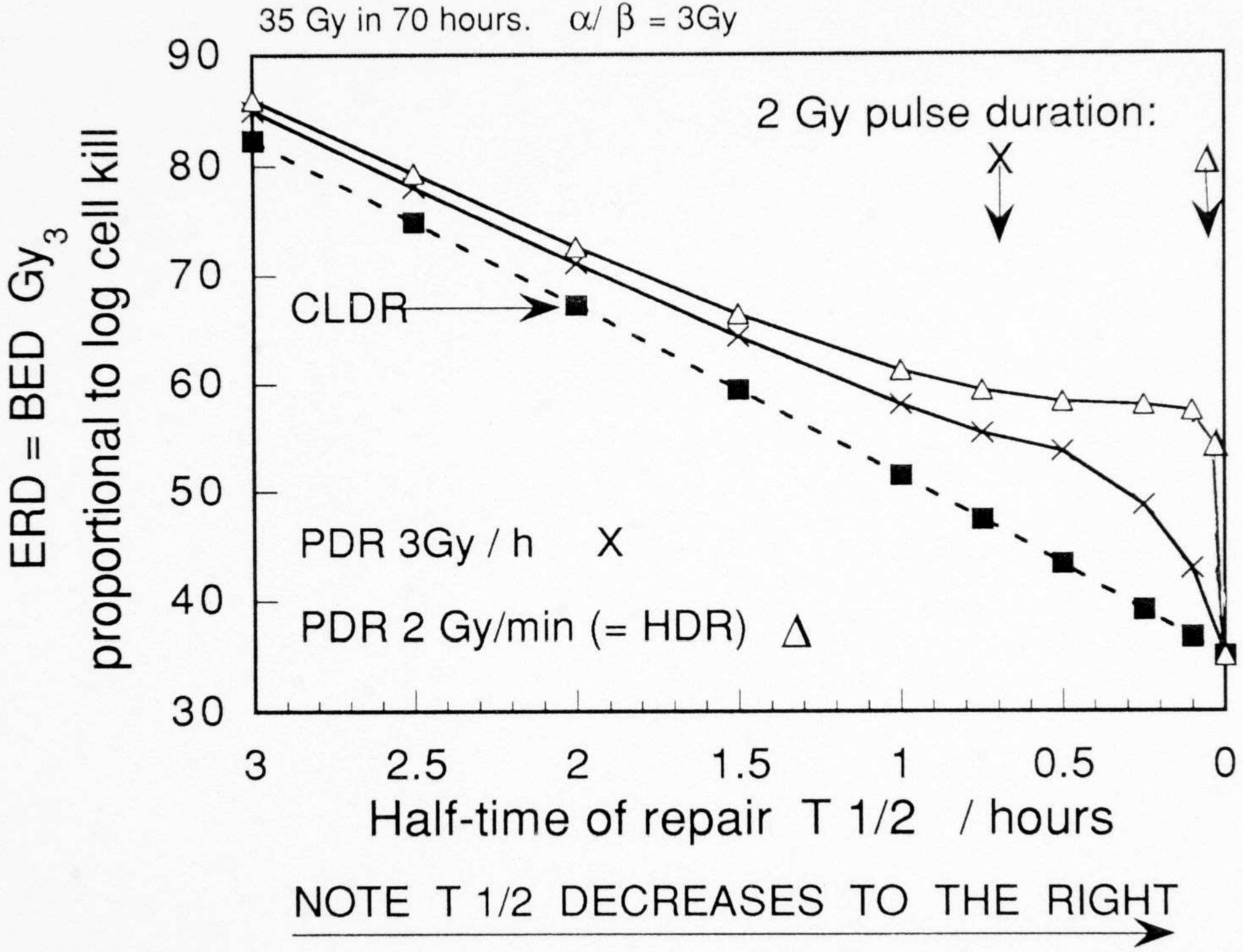
35 Gy in 70 hours. α/ β = 3Gy
90
80
70
60
50
40
30
ERD = BED Gy3
proportional to log cell kill
2 Gy pulse duration:
X
CLDR
PDR 3Gy / h X
PDR 2 Gy/min (= HDR) Δ
3
2.5
2
1.5
1
0.5
0
Half-time of repair T 1/2 / hours
NOTE T 1/2 DECREASES TO THE RIGHT

2 COMPONENT REPAIR

	FAST	20-45’	SLOW	75’	ERT
				200-300’	LRT
human skin	50%	25’	50%	75’	ERT
Turesson-Thomas				210-320’	LRT
rat spinal cord	38%	42’	62%	228’	LRT
Ang					
rat kidney	30%	35’	70%	130-200’	LRT
Moulder + Fish					
rodent lung	7-6%	24’	24%	216’	LRT
van Rongen					

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PDR in Clinical Practice

Breast
Uterovaginal
Anal canal
Head and Neck
Bladder
Sarcoma
Endometrial
Pelvic interstitial
Orbital tumors
Childhood cancers (rhabdomyosarcomas)

An hourly pulse dose schedule of 50 cGy in 15 minutes has more biological effect than 100 cGy in 45 minutes

A. True
B. False

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WWW.ESTRO.ORG/SCHOOL

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

UNIVERSITÉ PARIS SUD
FACULTÉ DE MÉDECINE

ÉCOLE DES SCIENCES DU CANCER
GUSTAVE ROUSSY

Pediatrics

Gustave Roussy experience

Renaud Mazeron

Gustave Roussy

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Brachytherapy in pediatric malignancies

Tumor characteristics

- High chemosensitivity
- High cure rate
- Complication rate /sequelae = important issue
- Fertility preservation

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Brachytherapy in paediatric malignancies

Indications

- Tumor **accessible** to BT
- Used whenever brachytherapy is:
  - an **alternative to EBRT**
  - complementary to surgery allowing a **conservative approach**

Contra-indications

- **Bony structures vicinity**
- **Nervous structures vicinity**
- **Extremities**
- **Tumor size > 50 mm**

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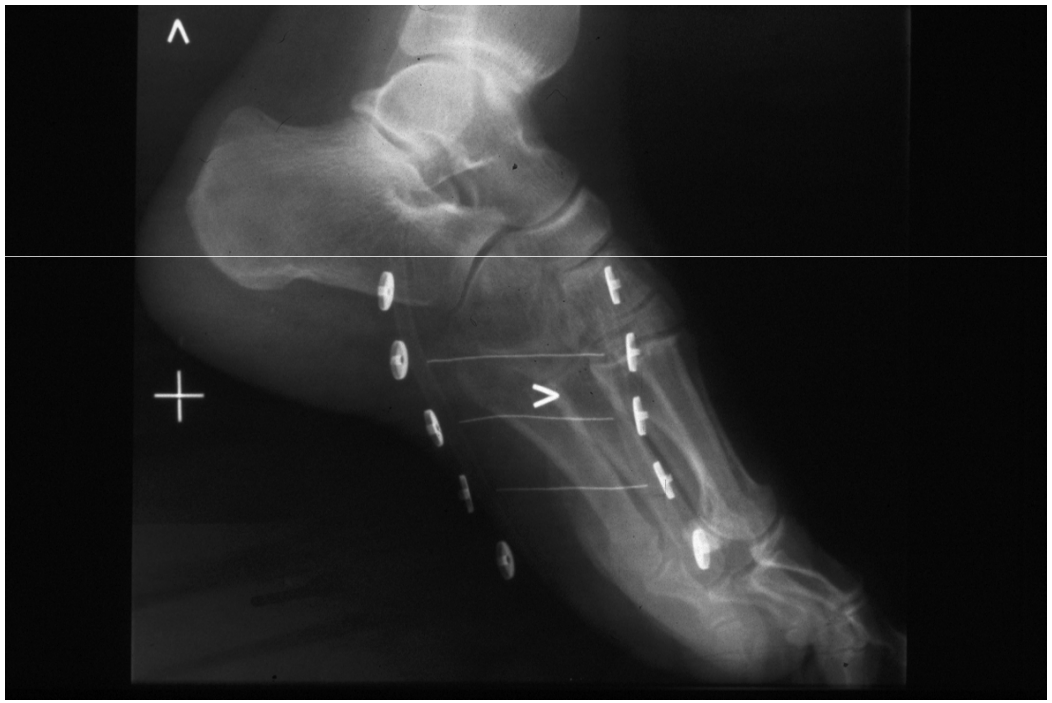
Brachytherapy in paediatric malignancies



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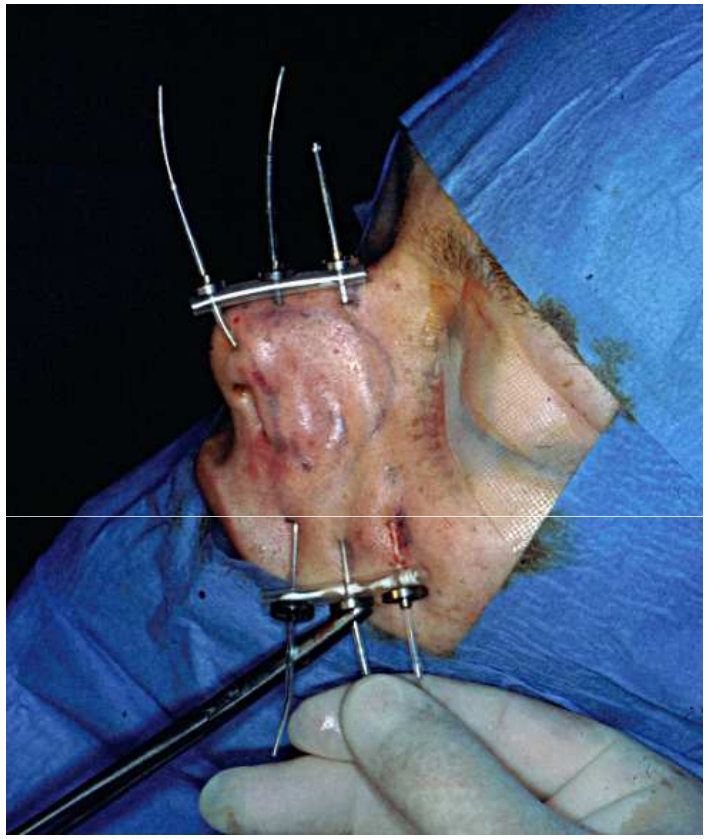
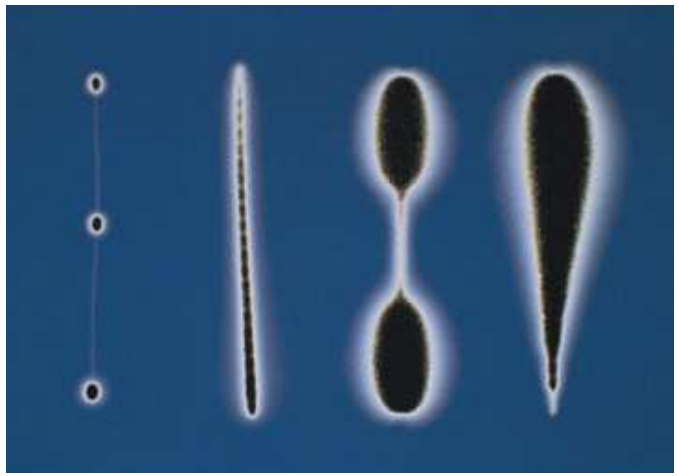
IGR experience: LDR

- Based on adult experience
- Long follow-up
- LDR Constraints:
  - **Parents / Radioprotection**
  - **Hospitalization**
  - **Limited optimization**



PDR brachytherapy

- Optimization
- Limitation: age
- Radioprotection / Visits
- Ir-192 wires abandoned



Treatment strategy

- **Chemotherapy :** tumor reduction

- **Surgery :**
  - tumor resection
  - ovarian transposition

- **Brachytherapy :**
  - interstitial / intracavitary
  - LDR / PDR

Local Treatment

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IGR Experience

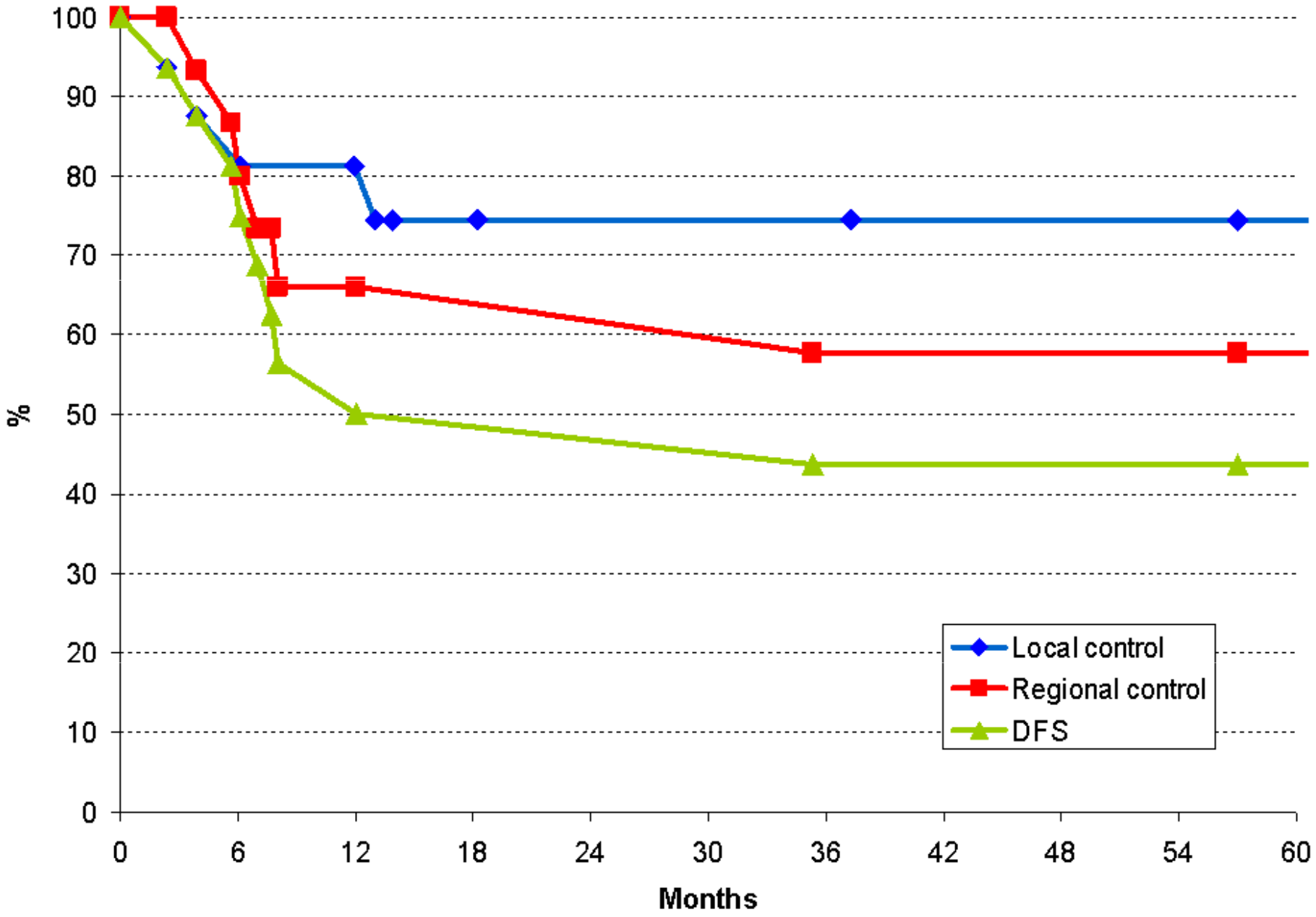
- Head and neck: RMS of the naso labial fold
- Pelvis: RMS of the prostate / bladder neck
- Pelvis: RMS of the vagina

Naso-labial fold

- RMS
- ^{192} I wires
- Interstitial implantation
- Paris System rules
- Per operative implantation
- Dose : 50 to 70 Gy
  - Response
  - Resection quality (cosmetic outc.)
- Volume : 6 cm^3 (2.7-18.1)
- Dose rate : 0.48 Gy/ h, (0.32-0.66)

Patients characteristics

Male / Female	8 / 8
Embryonal / Alveolar	10 / 6
Age	5 months to 13.5 years
0 – 4 years	12 / 16
Initial tumour diameter	20 mm (6-45)
Tumour diameter at BT	11 mm (0-26)
IRSS IIA	2 /16
IRSS III	14 / 16
BT in first line treatment	14 / 16
BT as salvage treatment	2



Mazeron et al. Ped Blood Cancer 2014

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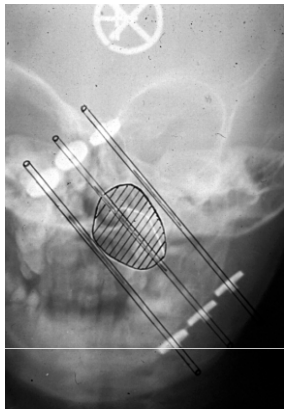
Relapses according to RMS subtypes

	Embryonal	Alveolar
n	10	6
Local	3 / 10 (30%)	1 / 6 (17%)
Regional	2 / 10 (20%)	4 / 6 (67%)
Metastatic	1 / 10 (10%)	1 / 6 (17%)
total	4 / 10 (40%)	5 / 6 (83%)



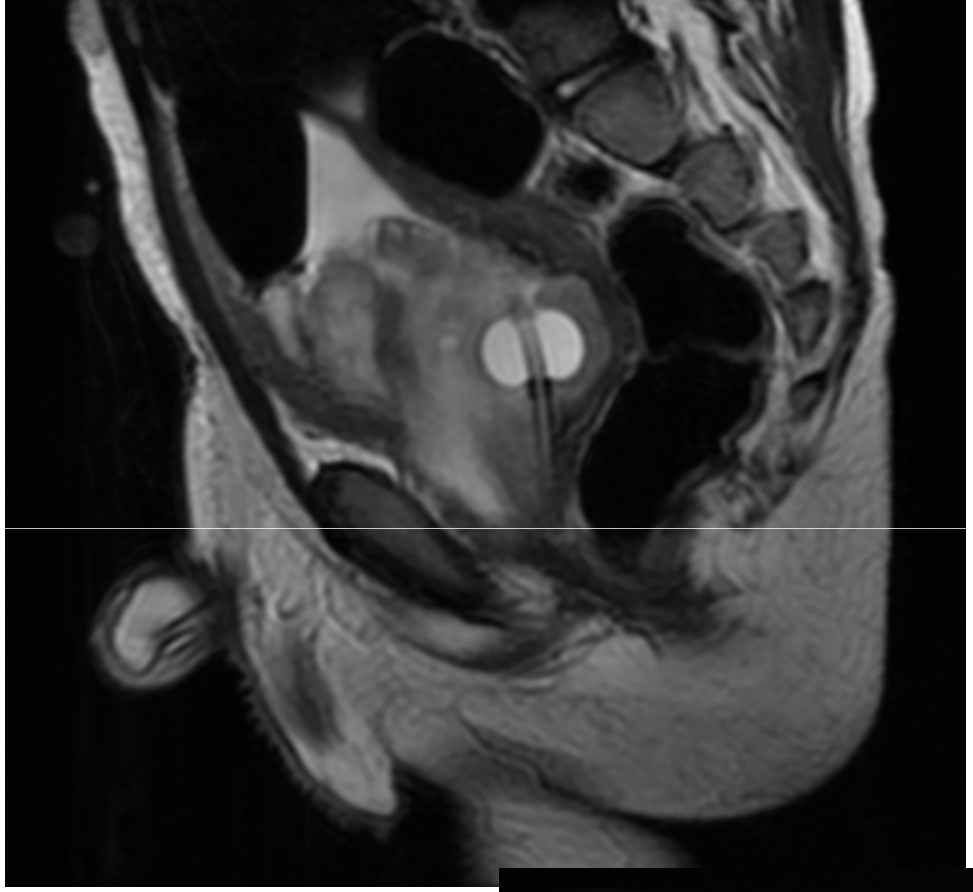
Cosmetic results

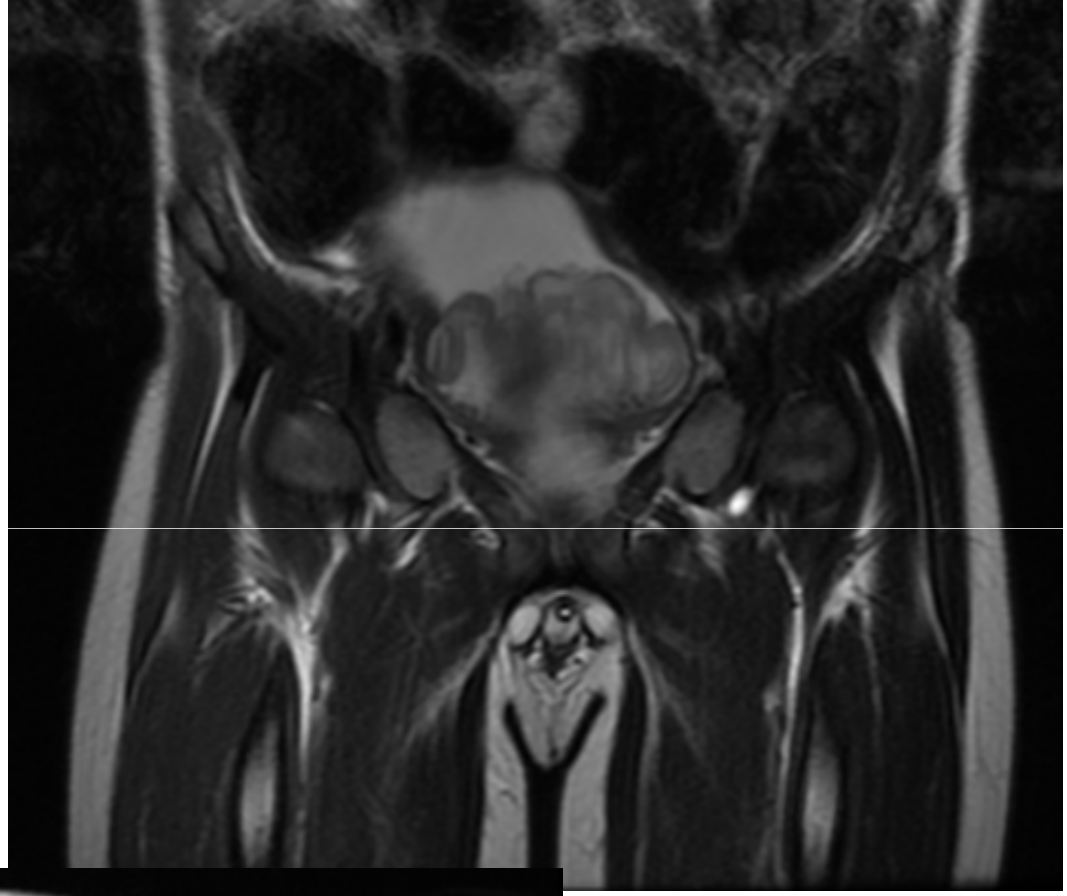
Prostate/bladder RMS

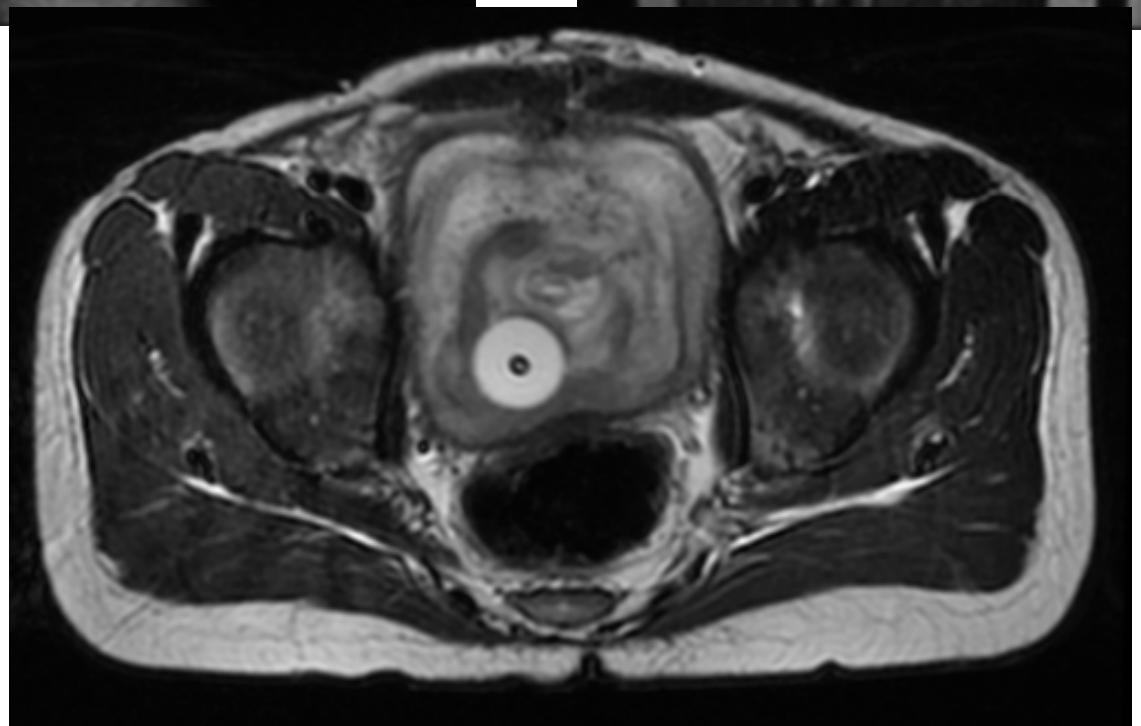
BT selection :

- Assessed on MRI / cystoscopy findings
- Tumor size (< 4cm)
- Tumor extension : bladder/prostate
- Treatment performed on the residuum after chemotherapy

- Aim: avoid mutilating surgery and incontinence







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Chemotherapy

↓

Evaluation

↓

Conservative treatment feasable?

Surgery: free margin at the upper part (bladder)

BT: No extension above the level of the trigona

↓

Partial prostatectomy

Partial cystectomy

+ BT

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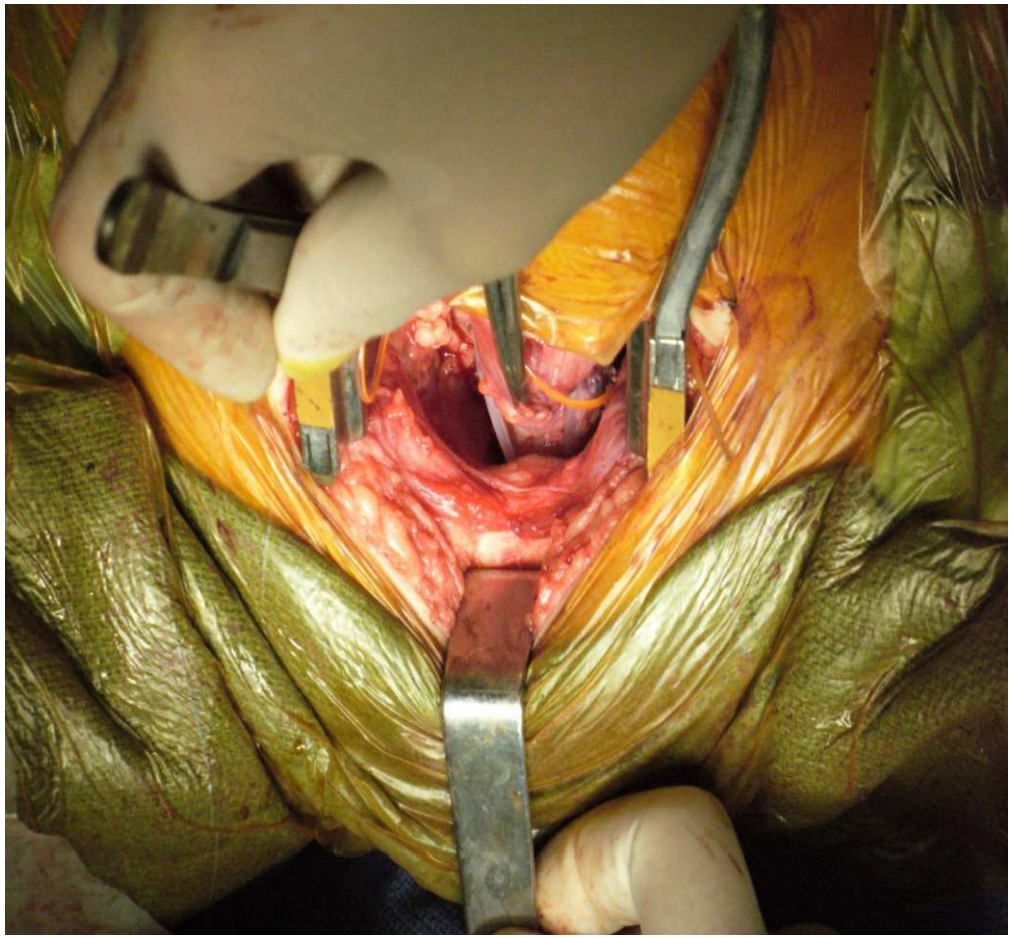
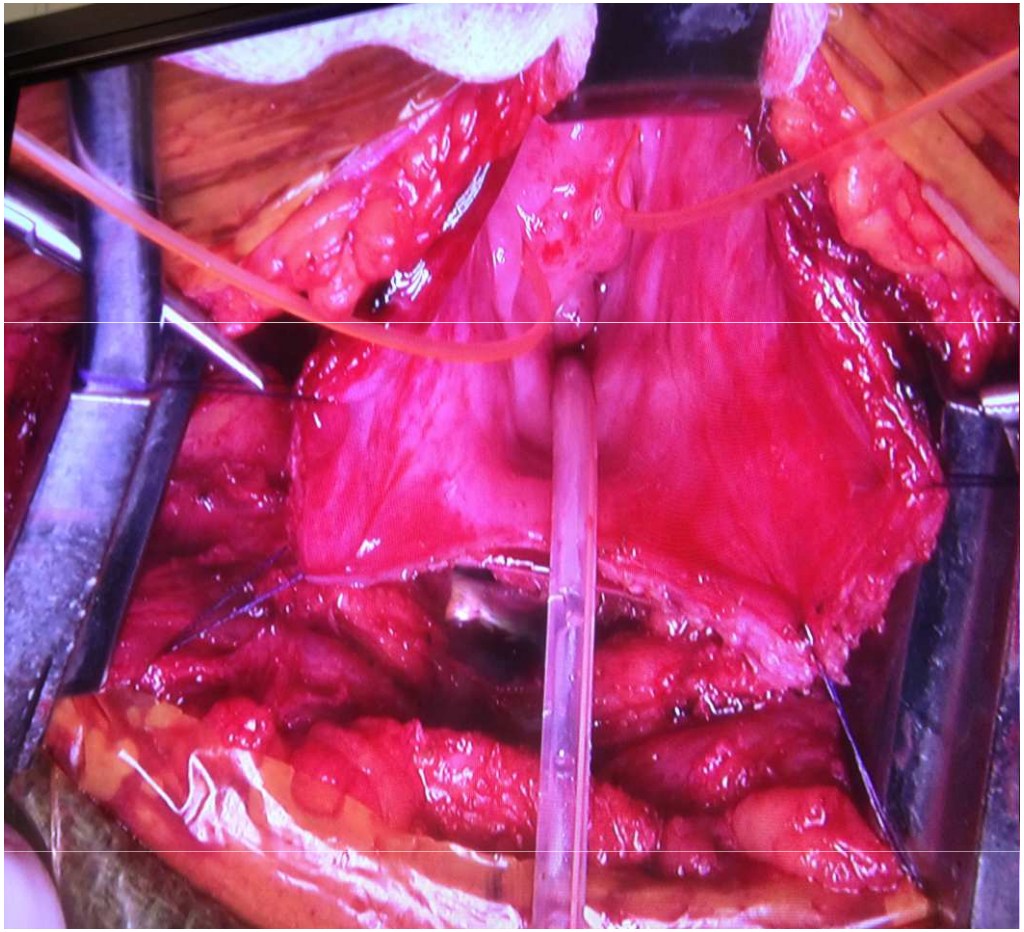
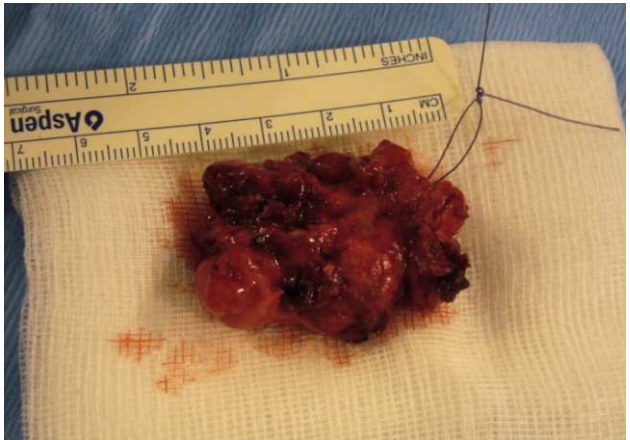
Prostate/bladder RMS







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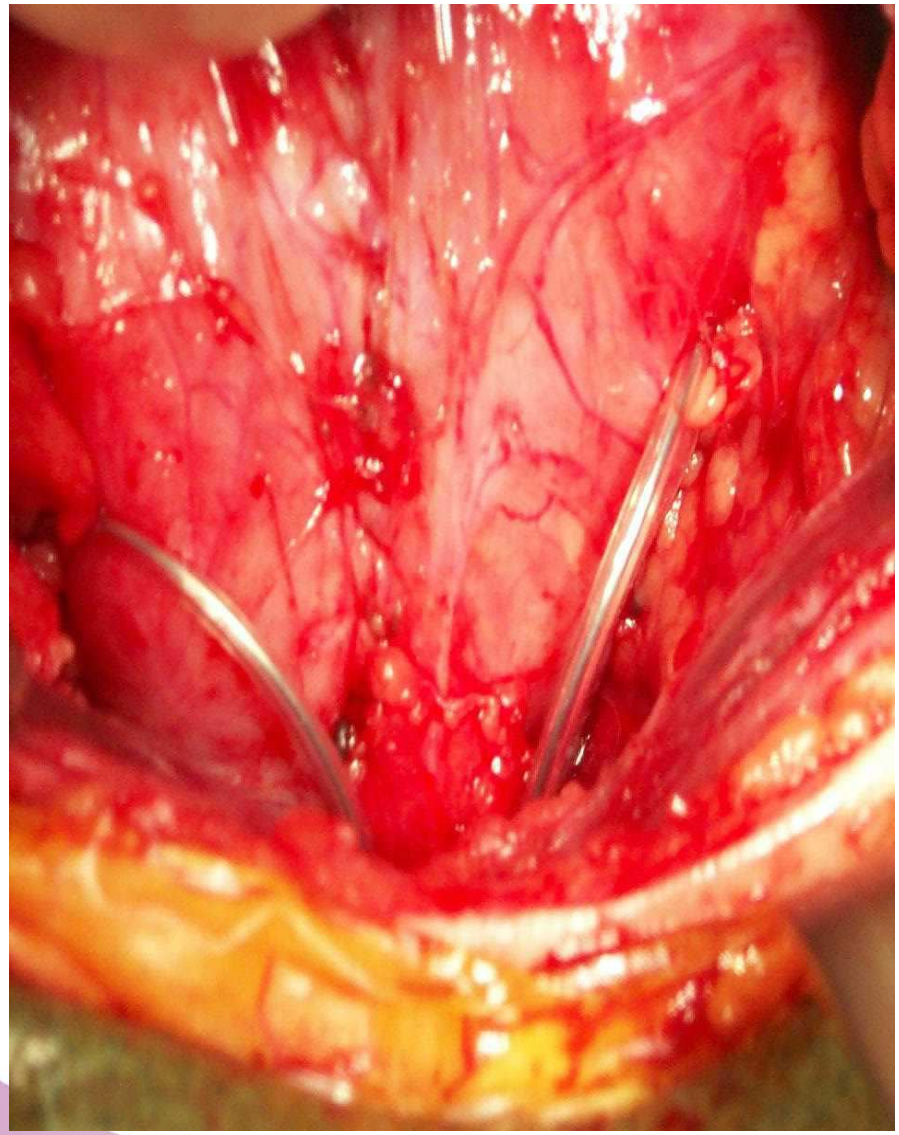
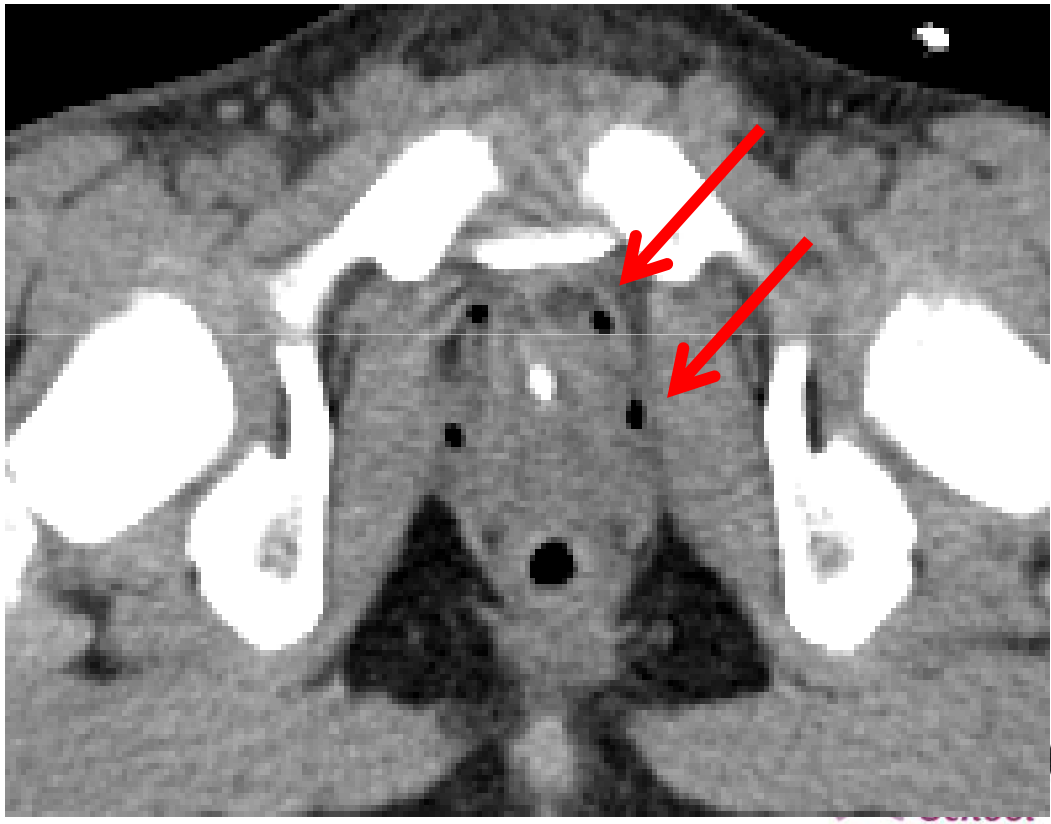
Prostate/bladder RMS

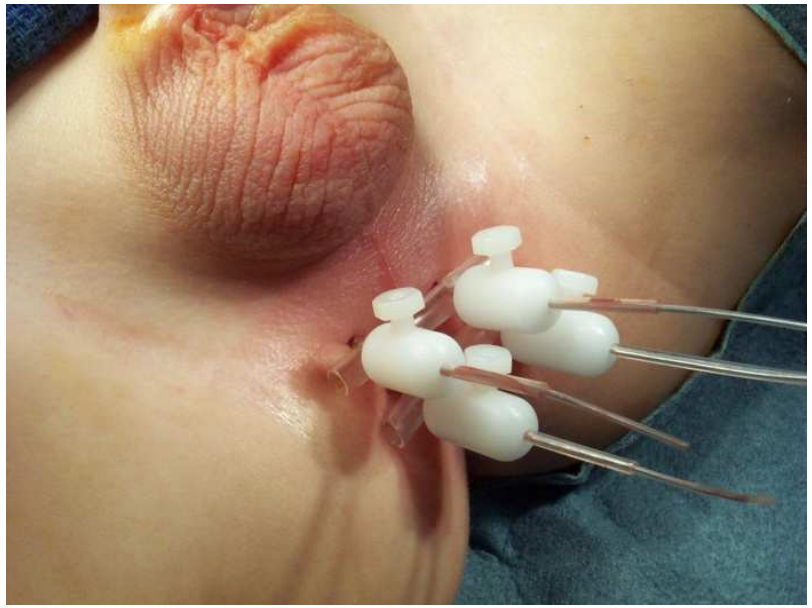


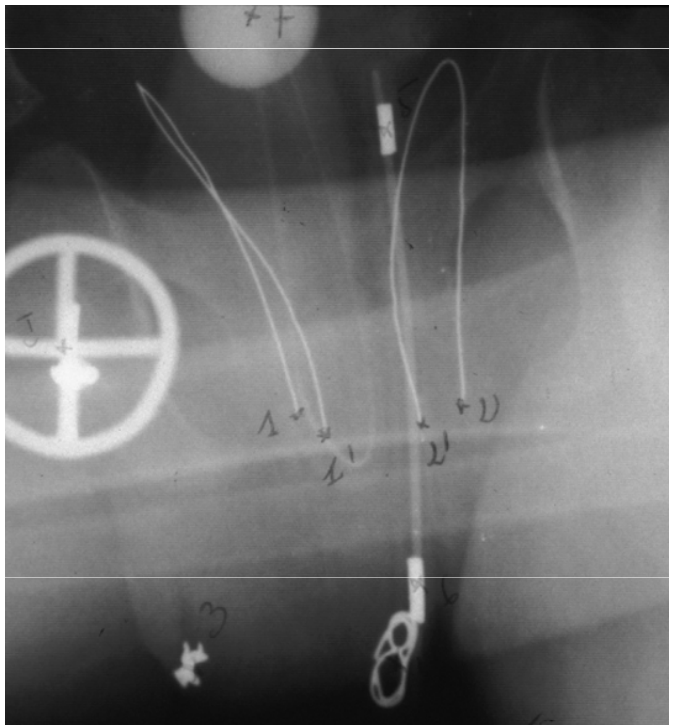
- 2 sagital loops
- Encompassing the prostate
- Perineal approach

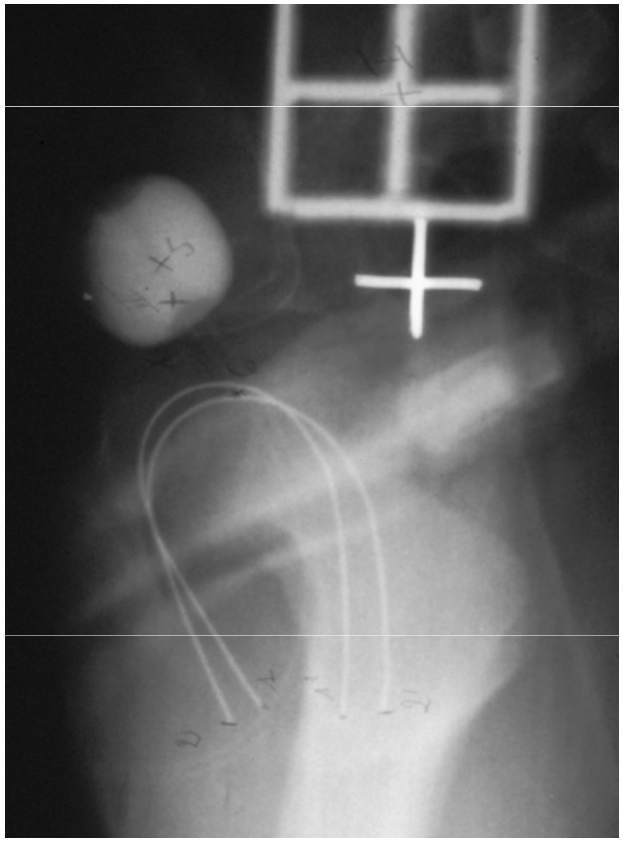


Per-operative implantation: perineal approach

Prostate/bladder RMS: loops techniques







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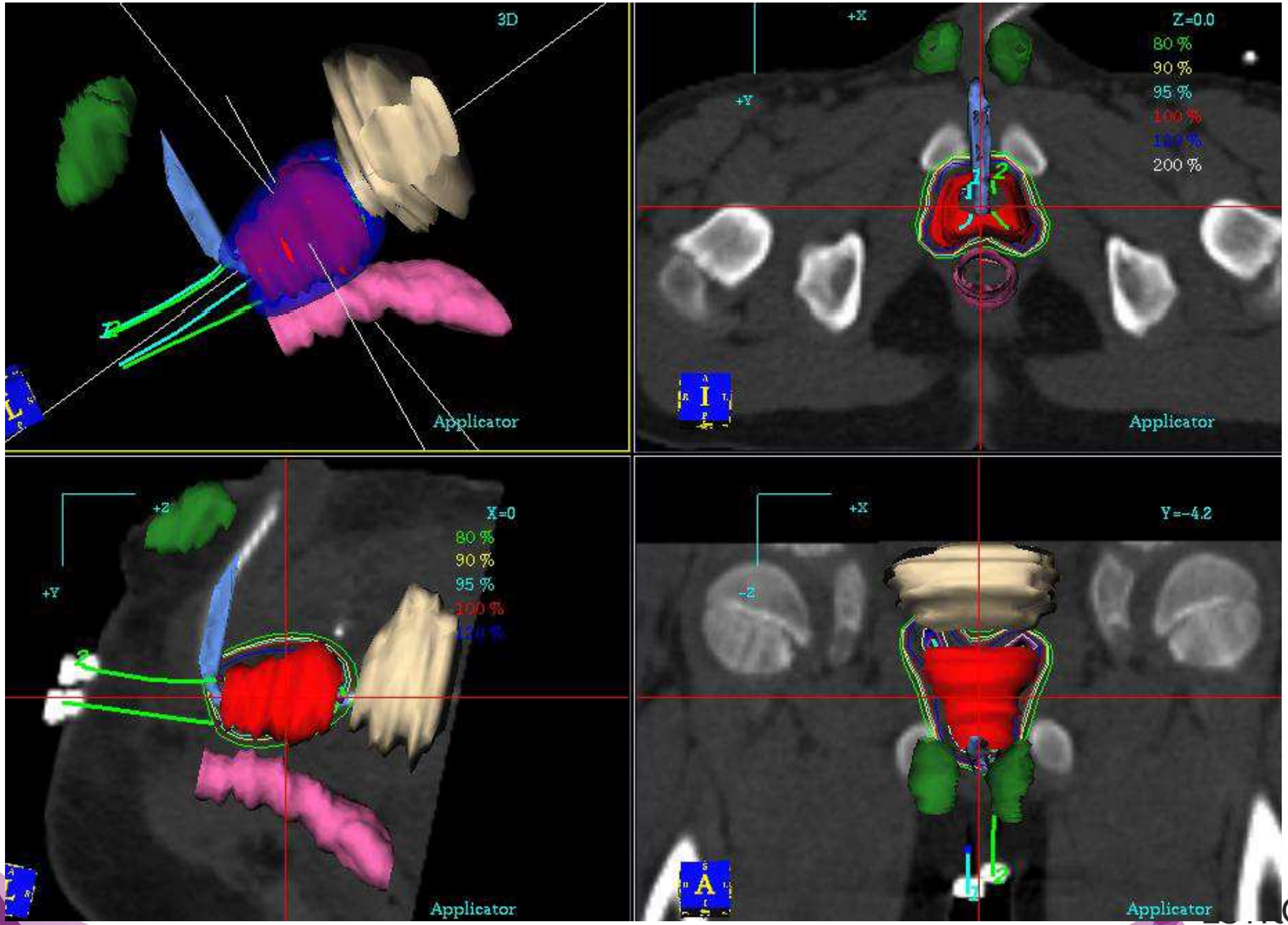
3D
Applicator
+X
Z=0.0
80 %
90 %
95 %
200 %
+Y
Applicator
+Z
X=0
80 %
90 %
95 %
+Y
Applicator
+X
Y=-4.2
-Z
Applicator

Loops technique

- Mimicking the LDR experience
  - 2 tubes and sagittal large loops
- Large couverture
  - Enough for afterloaders
  - But one case of obstruction
- Technique adaptation
  - PDR
  - Paris system
  - 4 tubes

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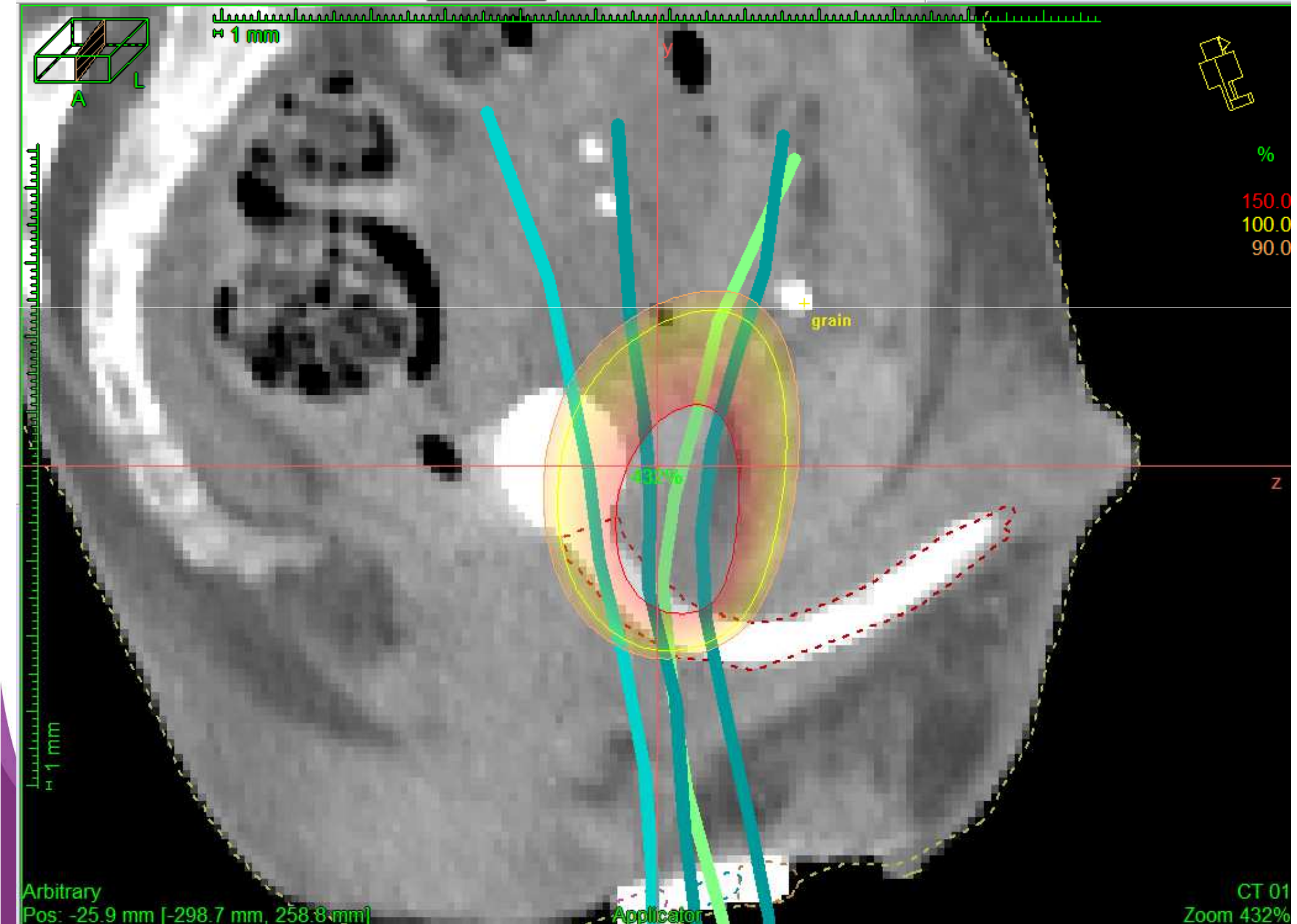
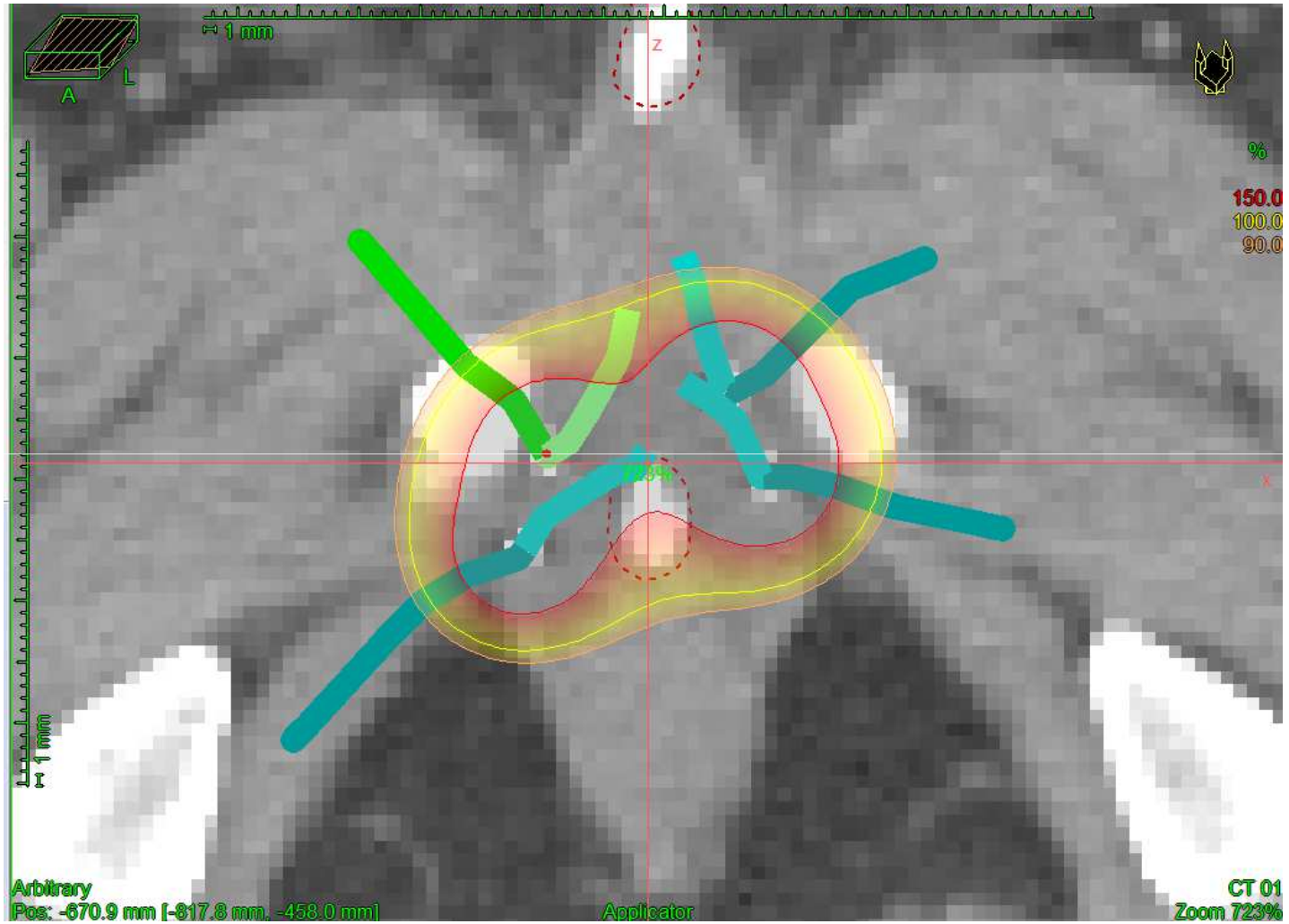

A
L
1 mm
y
%
150.0
100.0
90.0
grain
z
1 mm
Arbitrary
Pos: -25.9 mm [-298.7 mm, 258.8 mm]
Applicator
CT 01
Zoom 432%

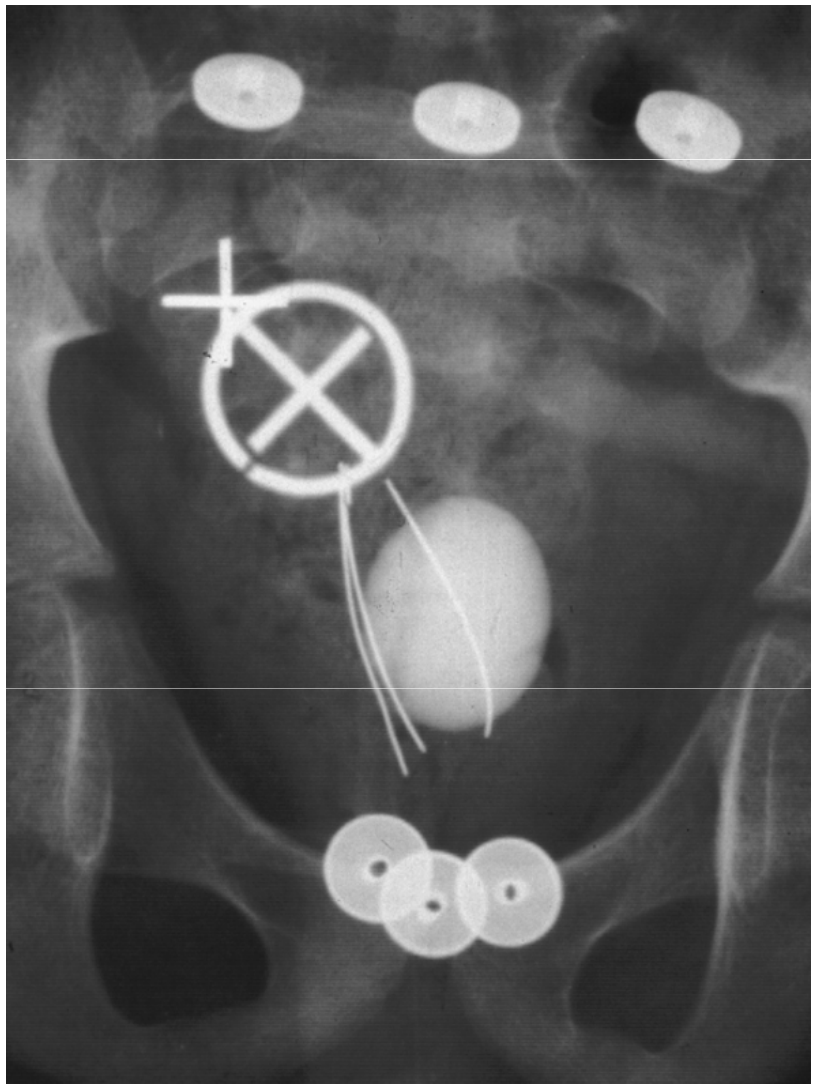


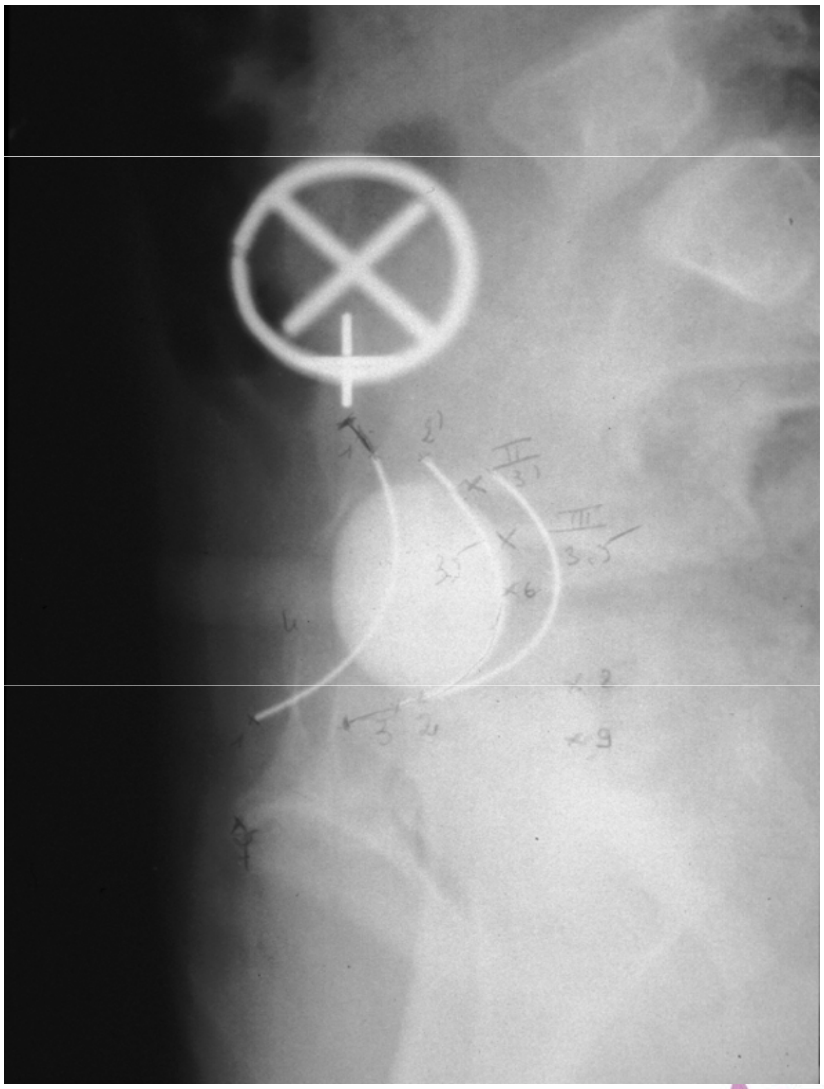
Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	8	-19.6	-750.6	149.1	1.00	0.00	23.82	
1	9	-19.1	-754.6	146.1	1.00	0.00	23.82	
1	10	-18.7	-758.6	143.1	1.00	0.00	23.82	
1	11	-18.6	-763.0	140.7	0.84	0.00	20.00	
1	12	-18.5	-767.4	138.3	0.84	0.00	20.00	
1	13	-18.0	-772.1	136.6	0.84	0.00	20.00	
2	5	-31.4	-725.9	139.3	1.00	0.00	23.82	

Prostate/bladder rhabdomyosarcoma

- Bladder RMS :
  - Different technique
  - Guide needles
  - Encompassing the limits of partial cystectomy

Prostate/bladder rhabdomyosarcoma





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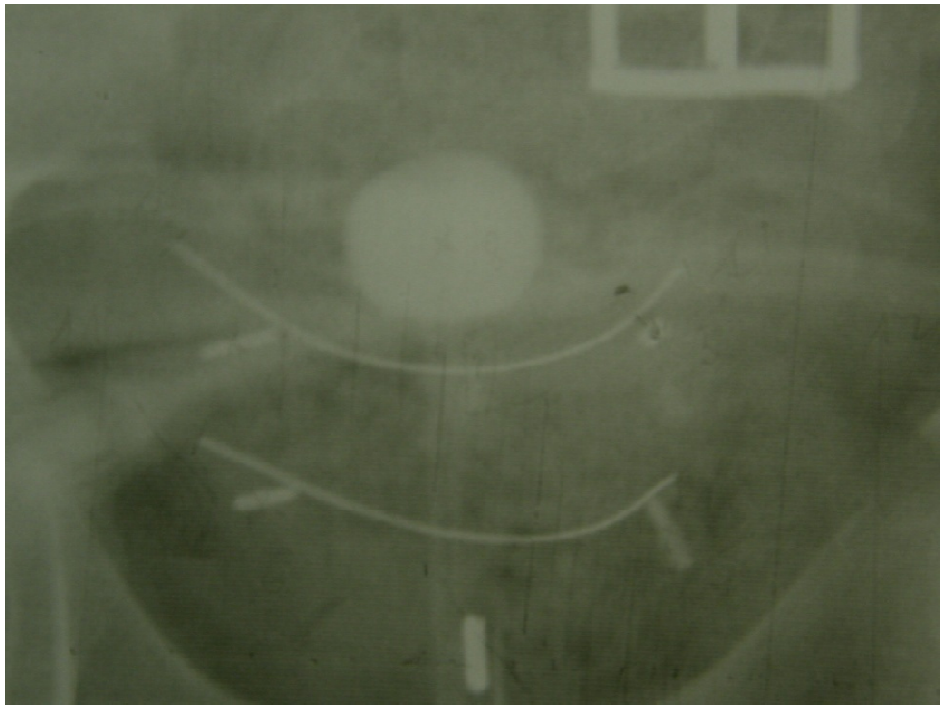
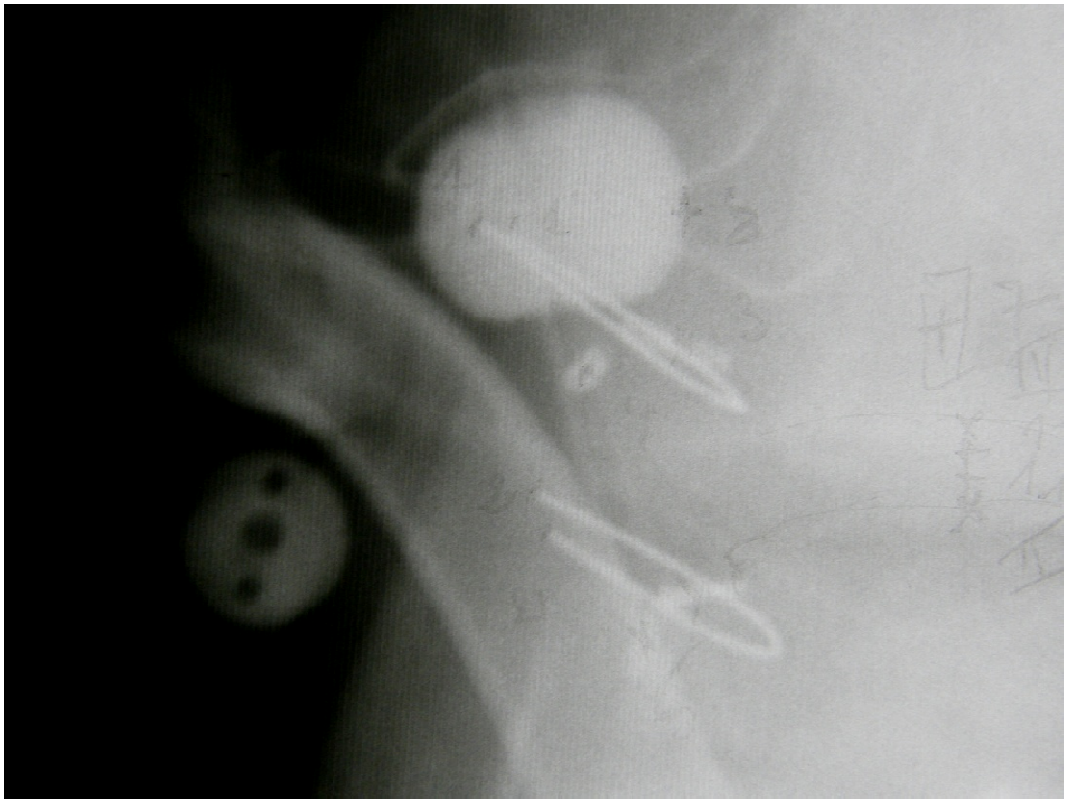
Prostate/bladder rhabdomyosarcoma





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Prostate/bladder RMS

- 1976 - 2009
- 67 children
  - 1976-1989 : 16
  - 1990-1999 : 12
  - 2000-2009 : 39
- 59 first-line treatment
- 12 different countries
  - Median age : 20 months (3 months-15 years)
  - 51% initial tumor size > 5 cm

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Prostate/bladder rhabdomyosarcoma

- Partial prostatectomy +/- partial cystectomy (65%)
- partial cystectomy alone: 20%
- One boy : radical cystoprostatectomy
- No complete resections
- 85% viable immature tumor cells in the resection area

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Prostate/bladder RMS

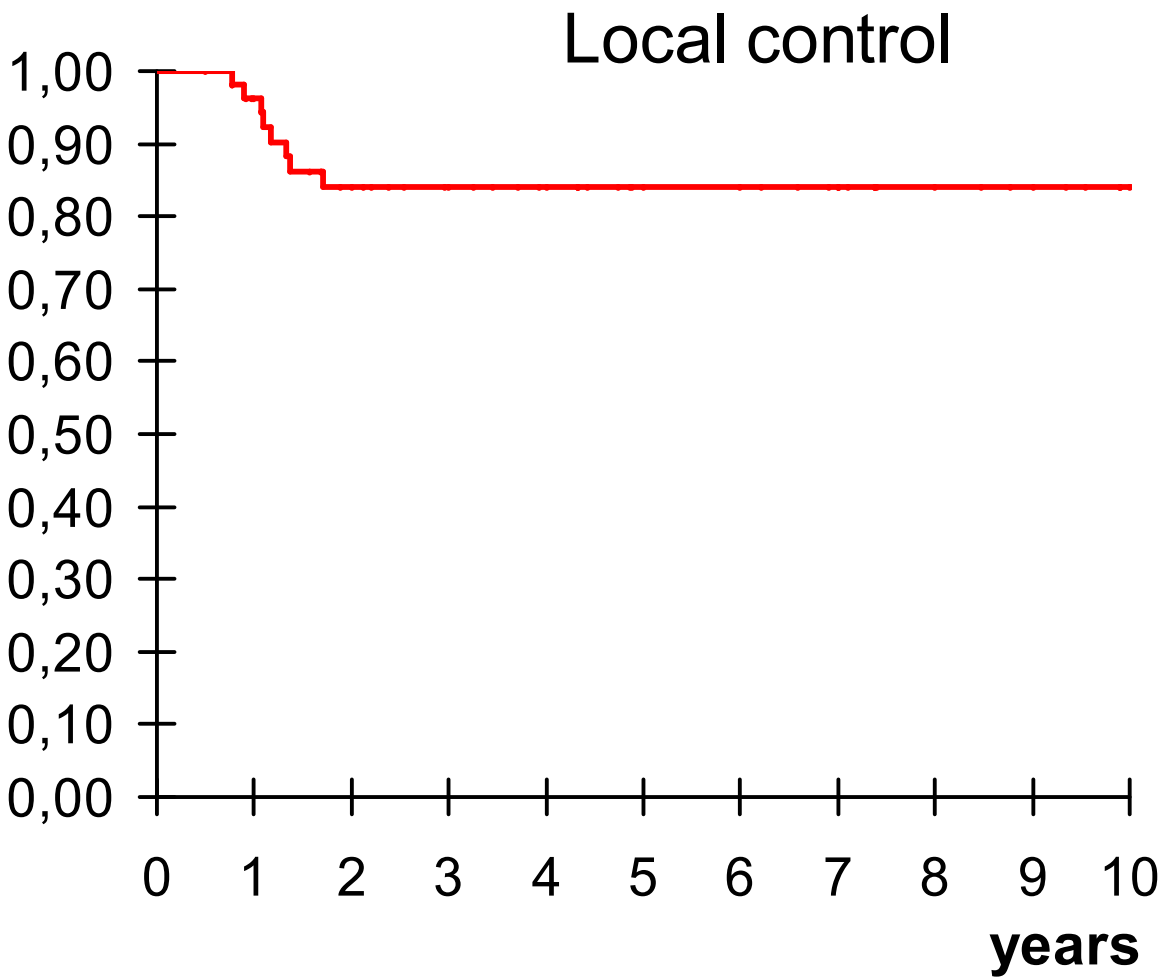
- Mean interval surgery-loading : 6 days
- Median prescribed dose: 60 Gy
- Paris system : 85% of basal dose
- Mean isodose volume : 29 cm^3
- 4 had a combination of external irradiation and brachytherapy (20-30 Gy + pelvic EBRT, 45 Gy)
- Mean bladder dose : 35 Gy
- Mean rectal dose : 35 Gy
- Mean testis dose : 3 Gy

Prostate/bladder RMS

- Mean follow-up : 6.6 years (0.5-28.3)
- 7 recurrences within or above the treated BT volume (3 combined with regional/metastasis):
  - 5 before 2000 (out of 28)
  - 2 after 2000 (out of 39)
- Mean time to failure : 10.3 months

  (range : 5.2-14.1 months)
- 2 salvaged by surgery + chemotherapy

Prostate/bladder rhabdomyosarcoma



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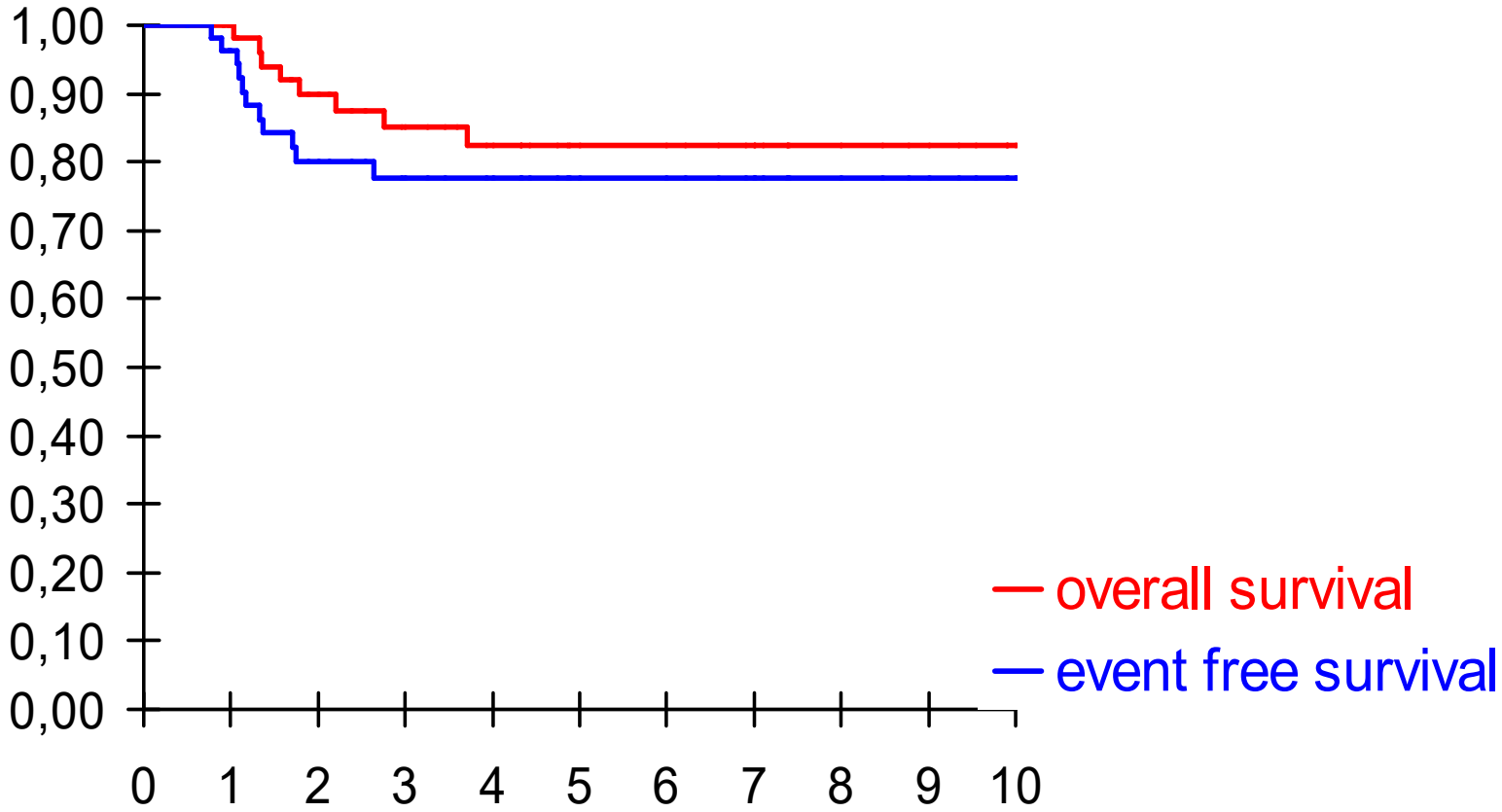
Prostate/bladder rhabdomyosarcoma



At risk

overall survival	55	51	41	35	30	24	24	21	16	14	10
event free survival	55	49	37	32	29	23	23	20	15	13	9

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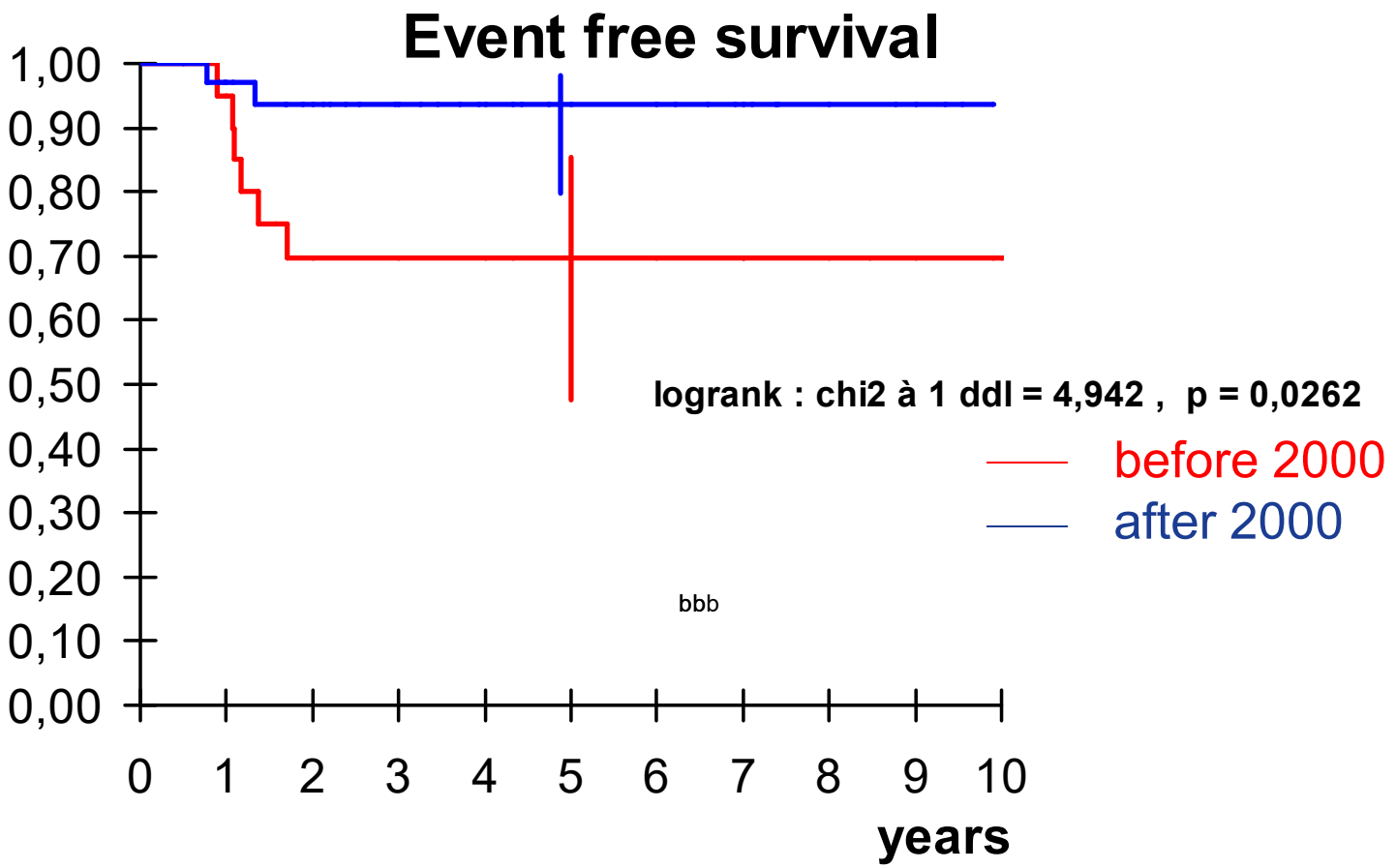
Prostate/bladder rhabdomyosarcoma



At risk

20	19	13	13	13	12	12	12	11	10	9
35	30	25	20	16	11	11	8	4	3	

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Long term follow-up: Qol evaluation

- 22 males contacted: 18 answered
- Median age at local treatment: 2 years (14m-11y)
- Median FU: 10 years (5-21)
- Medean age at time of study: 13 y (7-25y)

Qol

13: normal Qol
- 9: no incontinence
- 4: rare dribbling

4: protections
1: intermittent catheterism (neurogenic bladder)

Sexuality

All pubertal patients have normal erections

3 sexually active
- Satisfying sex
- 2 normal ejaculations
- No baby so far

Martelli Brachy 2016

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Gynaecological tumours

- Chemotherapy role
- Initial examination by radiation oncologist
- Ovarian transposition
- Brachytherapy on **residual disease**
- Dose 50 - 60 Gy

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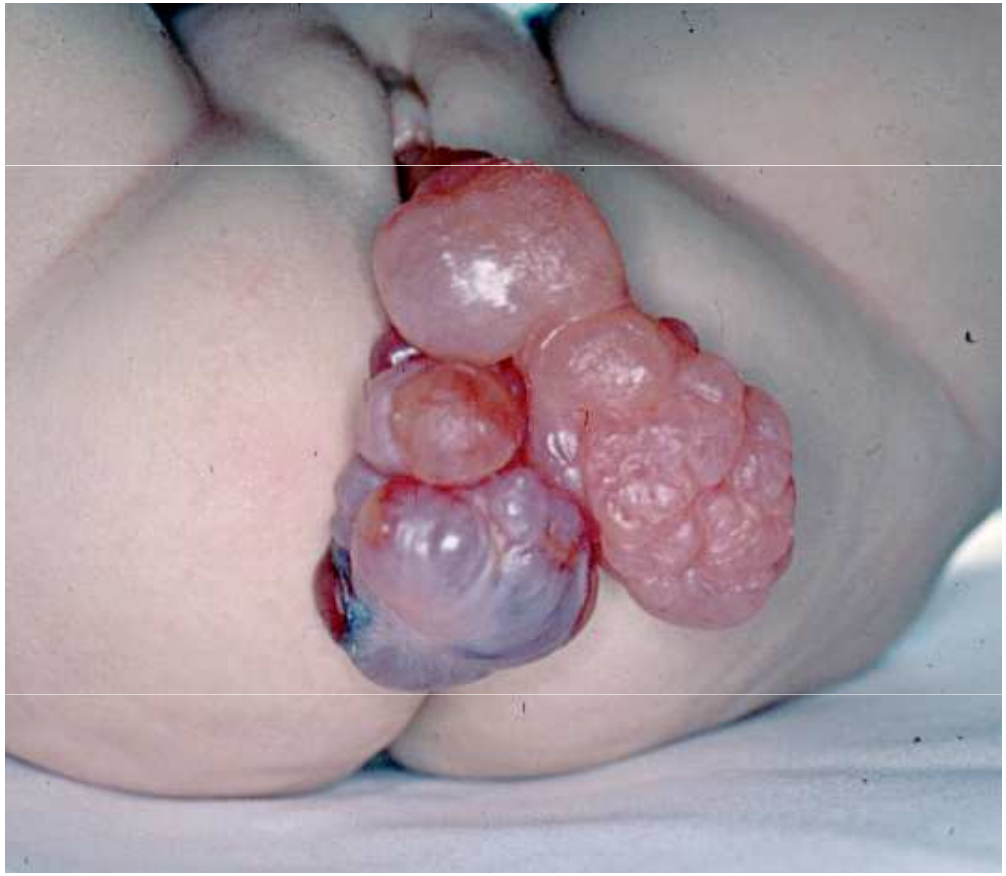
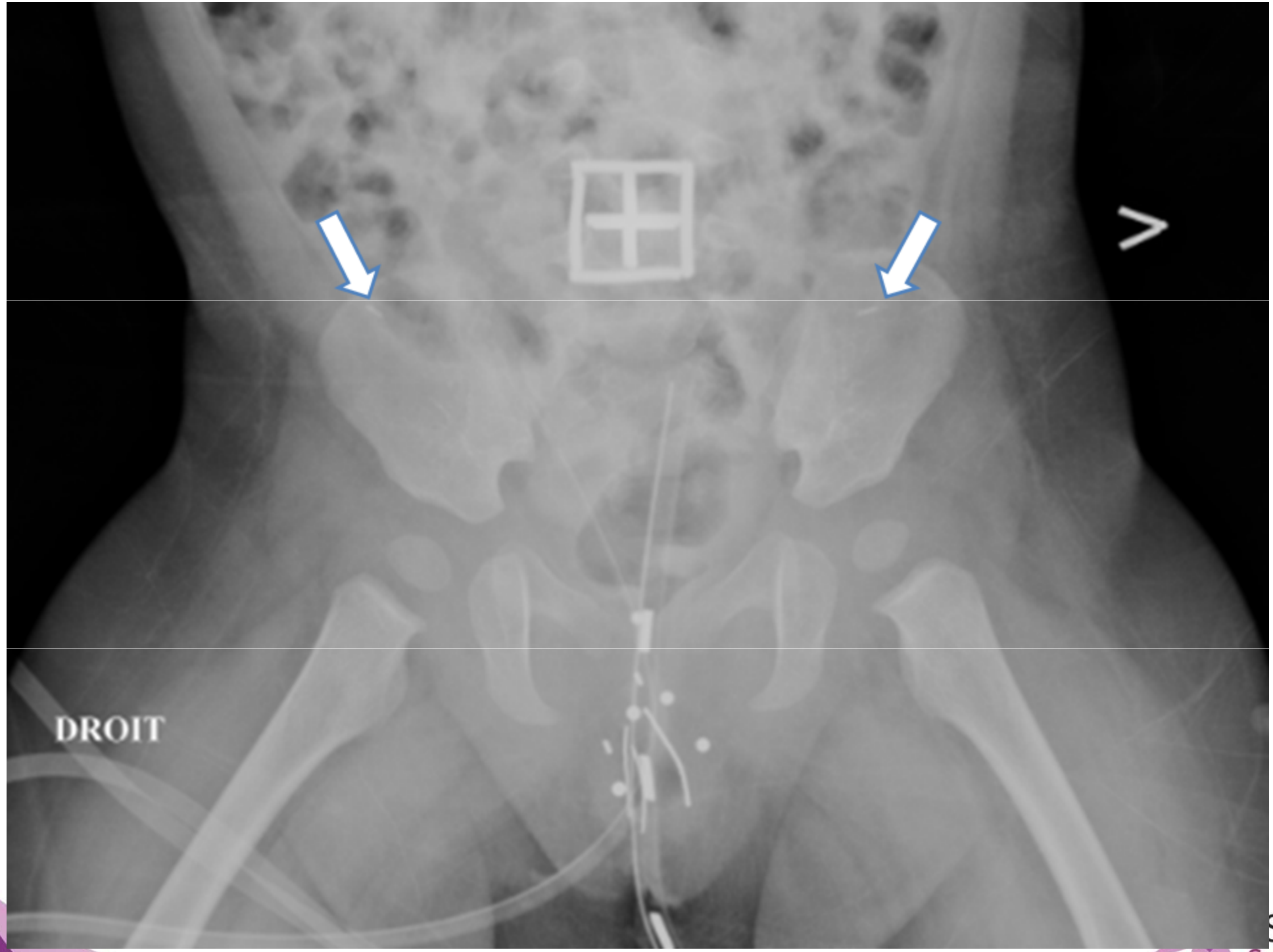


« Grape bunches »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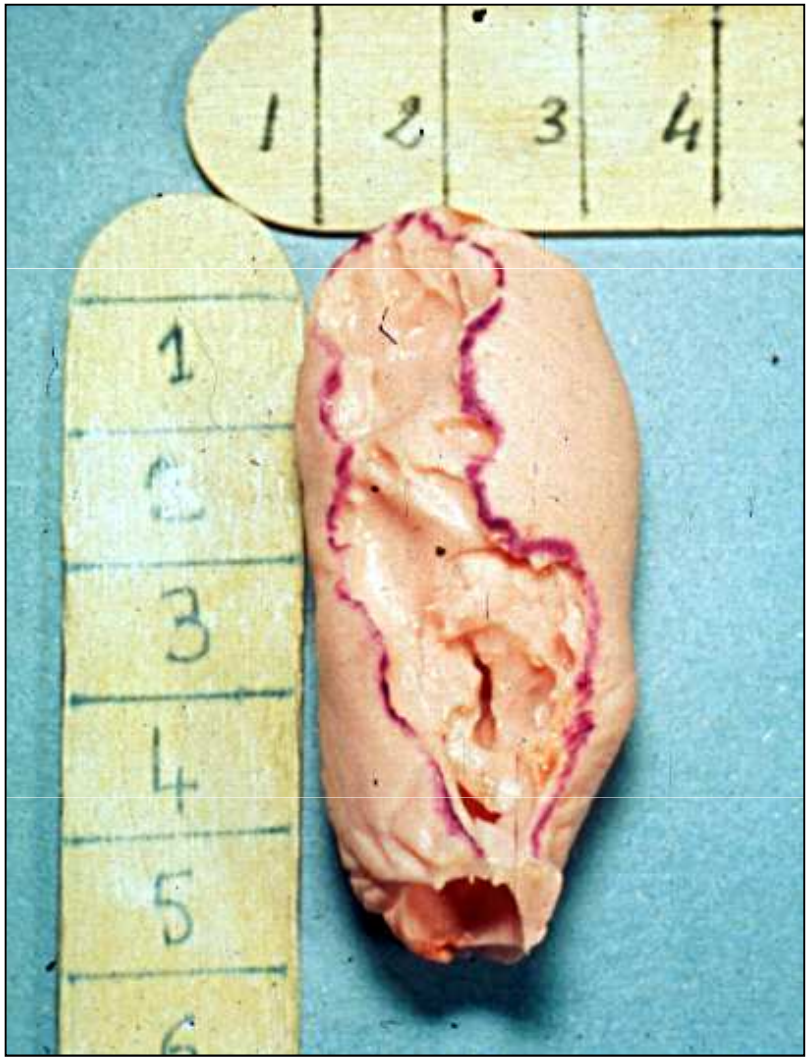
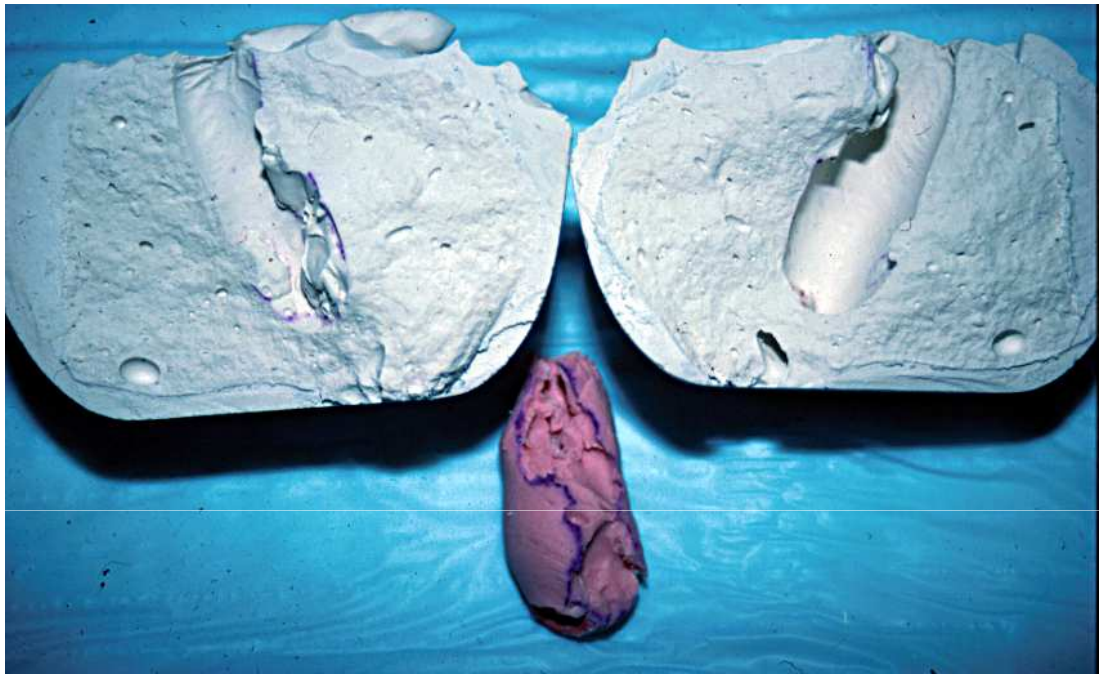
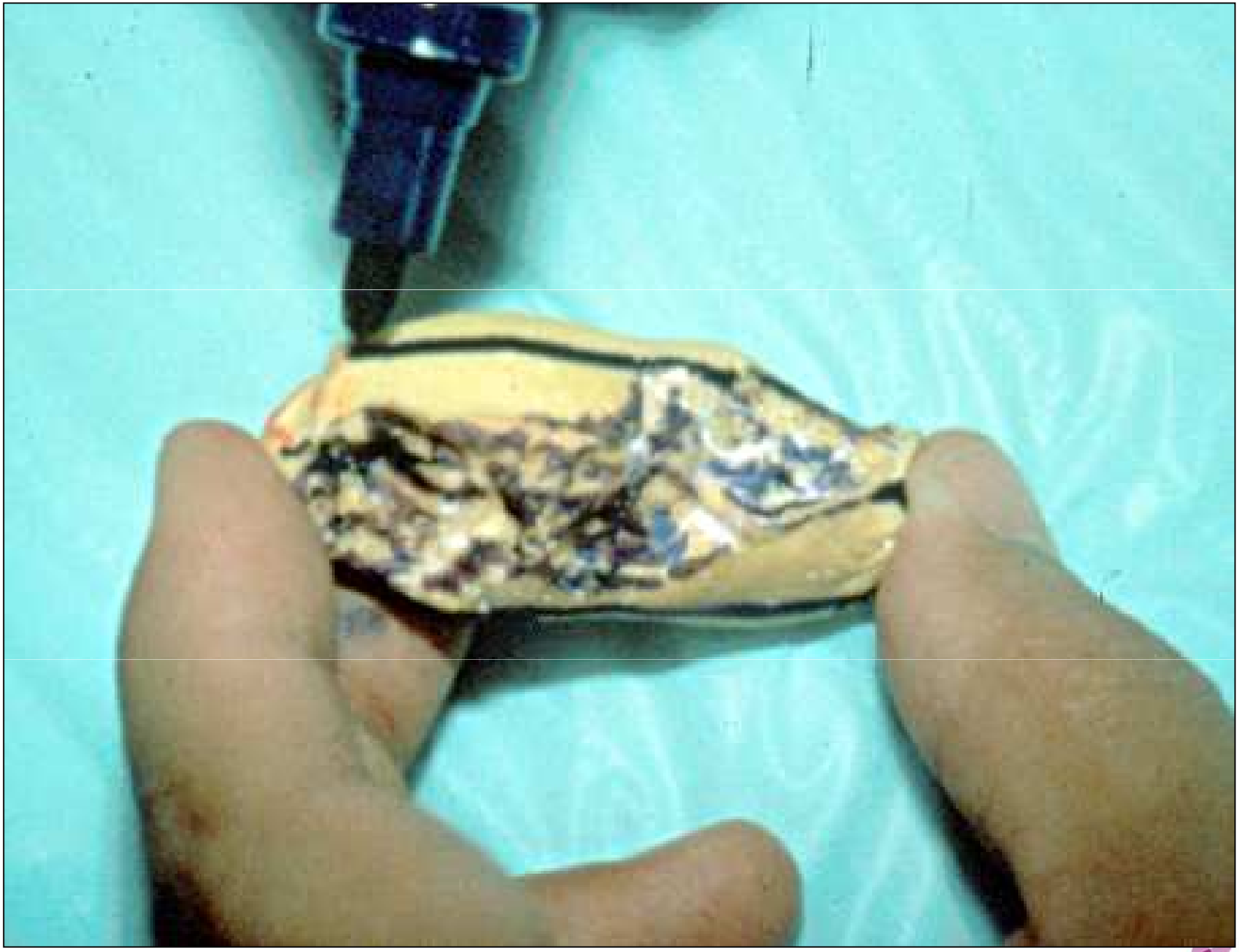
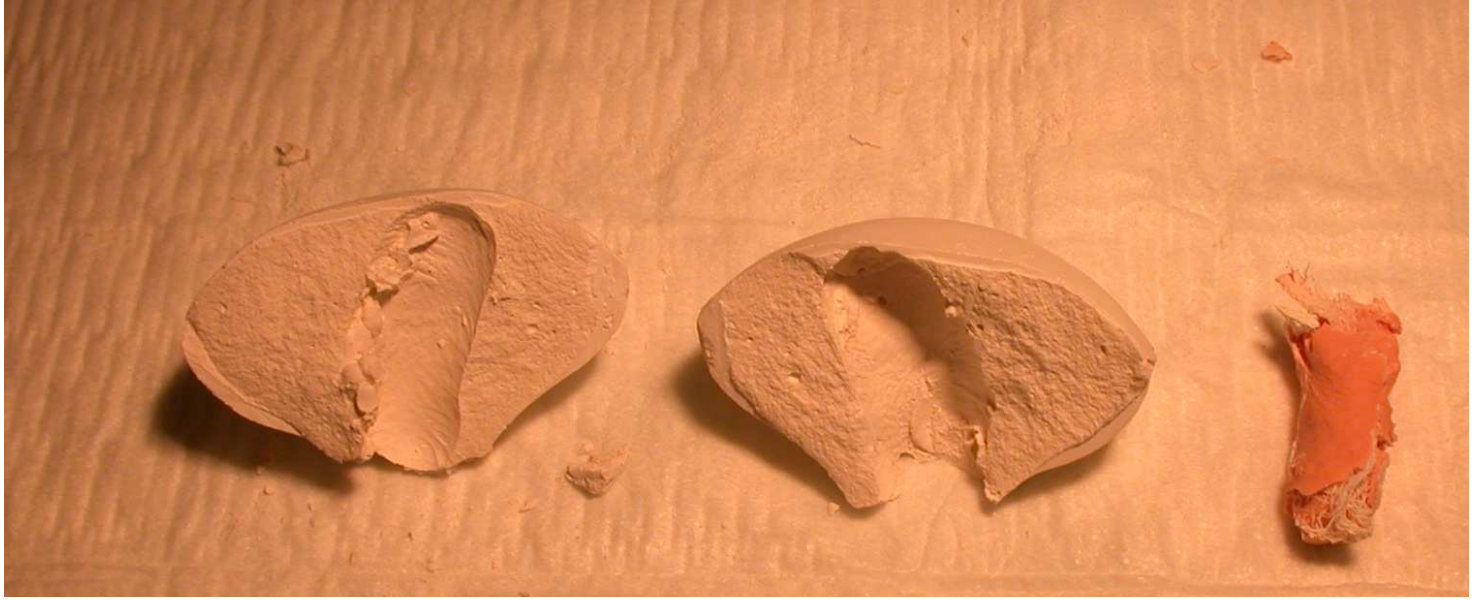
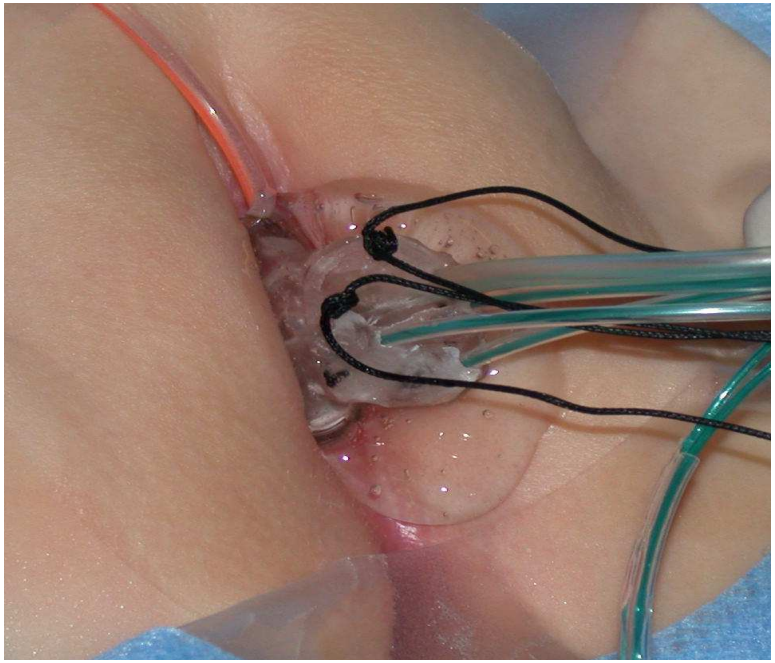
Vaginal impression

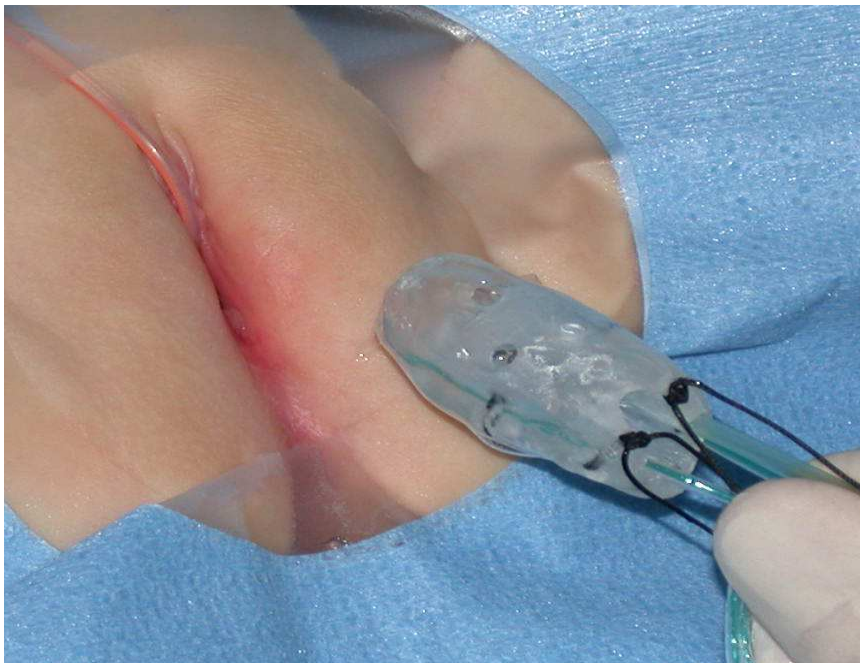


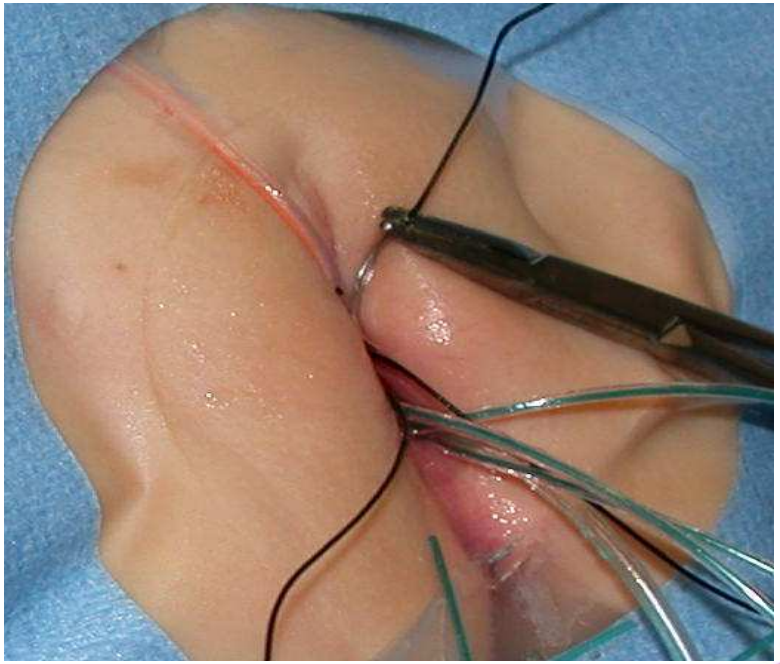


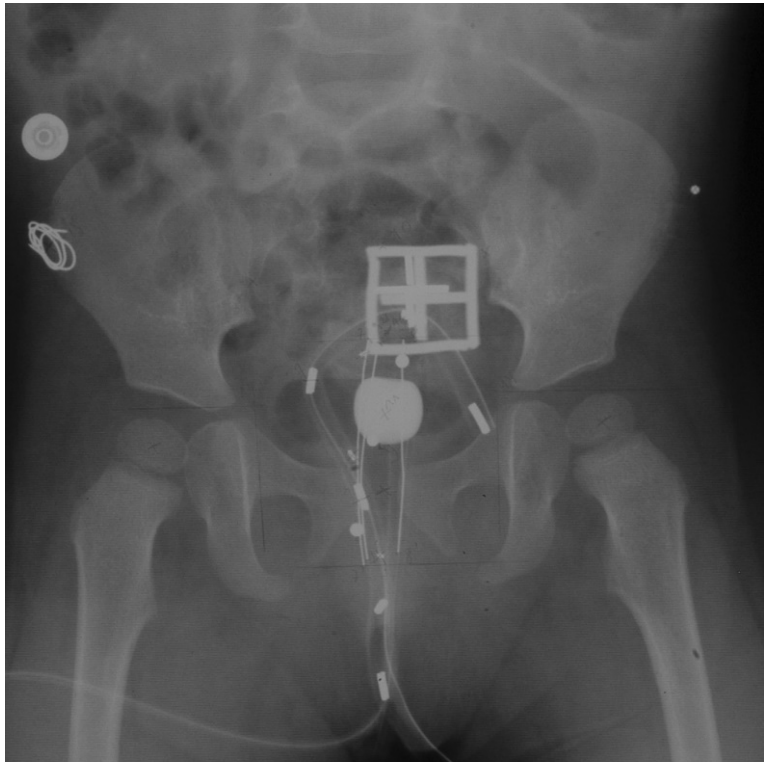


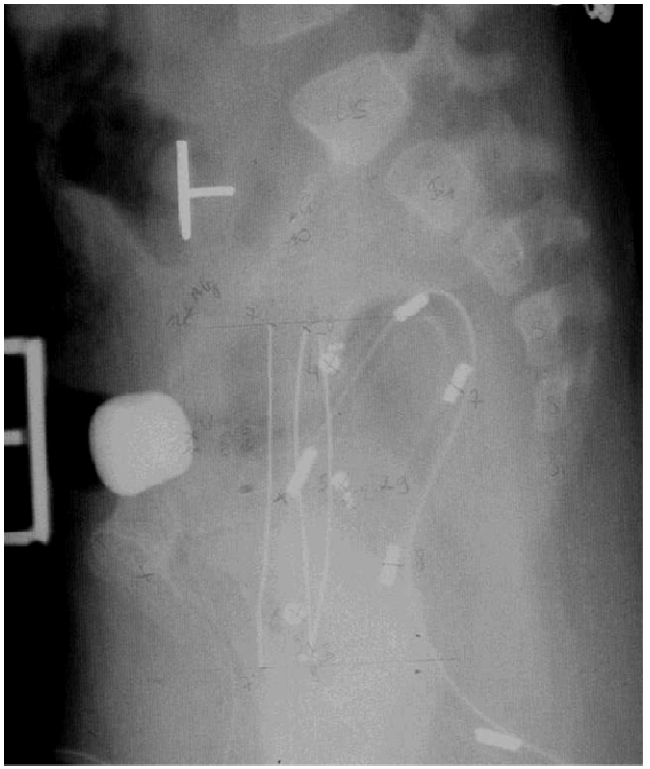


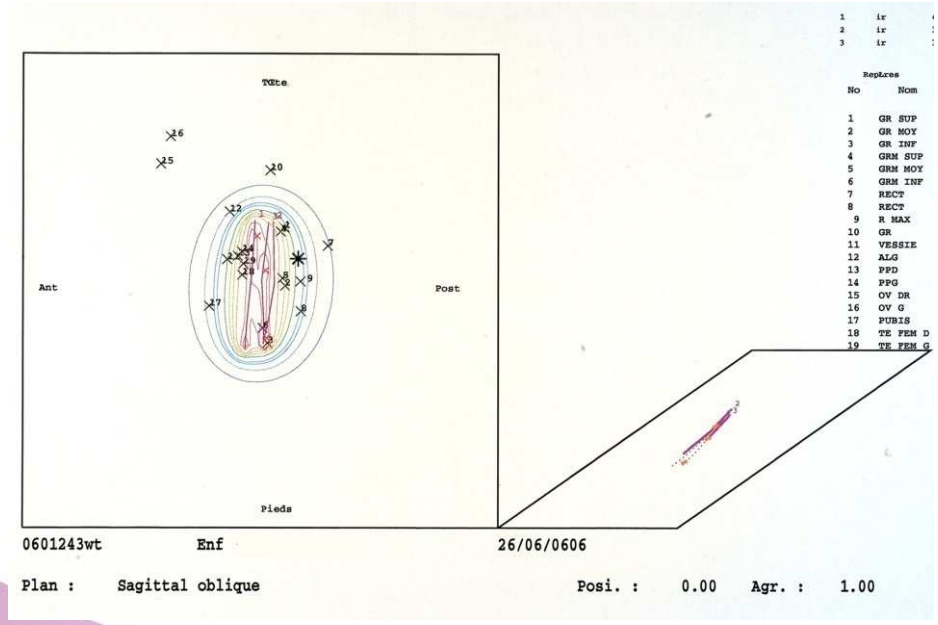








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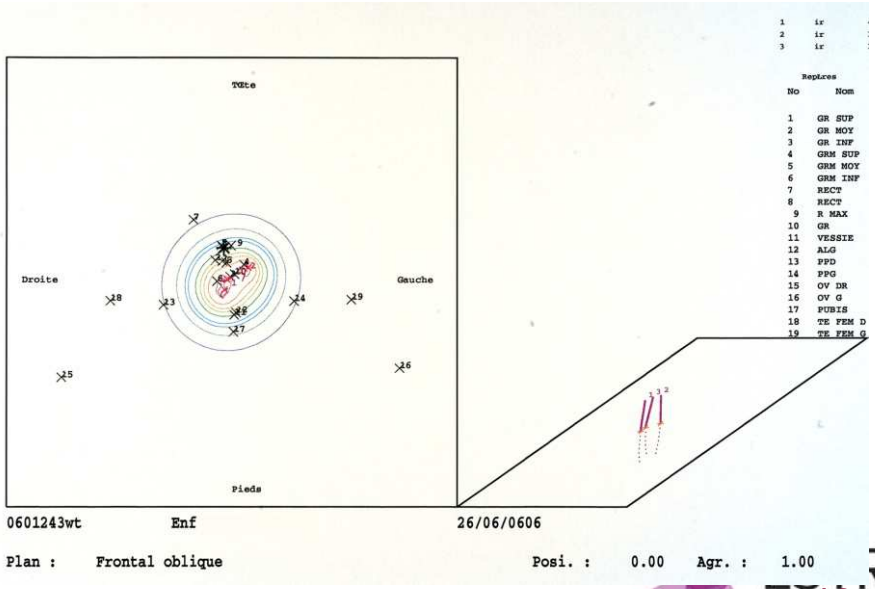
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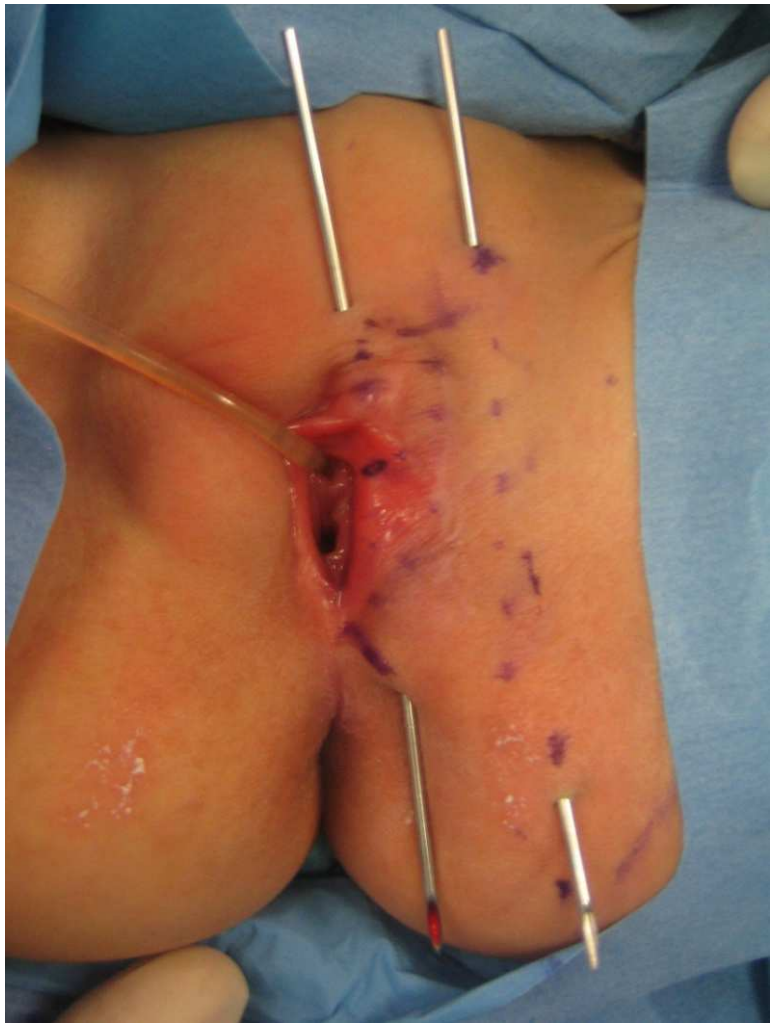
17 PUBIS
18 TE FEM D
19 TE FEM G

BT in gynaecological RMS

- Interstitial BT
  - ➢ Vaginal mould technique
  - ➢ Low dose-rate 0.5 Gy/hr
  - ➢ Tumour dose: 60-65 Gy in 1 to 3 applications



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BT in gynaecological RMS

- From 1971 to 2005
- 39 children treated with BT as a part of treatment
- multiagent chemotherapy, surgery and BT
- 20 children before 1990 and 19 after 1990
- Initial physical examination (under anesthesia)
- Before 1990, the initial tumoral extension was included in the BT volume
- Then, the CTV was limited to the residual disease

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BT in gynaecological RMS

- Median age: 1.4 years (0.4-14.3)
- Tumor exteriorisation : in 29 pts
- Tumor site :
  - Vagina : 26 pts
  - Vulva : 6 pts
  - Vulva and vagina : 7 pts
- Histological type :
  - Botryoid in 31 pts
  - Alveolar in 5 pts
  - Embryonal in 3 pts

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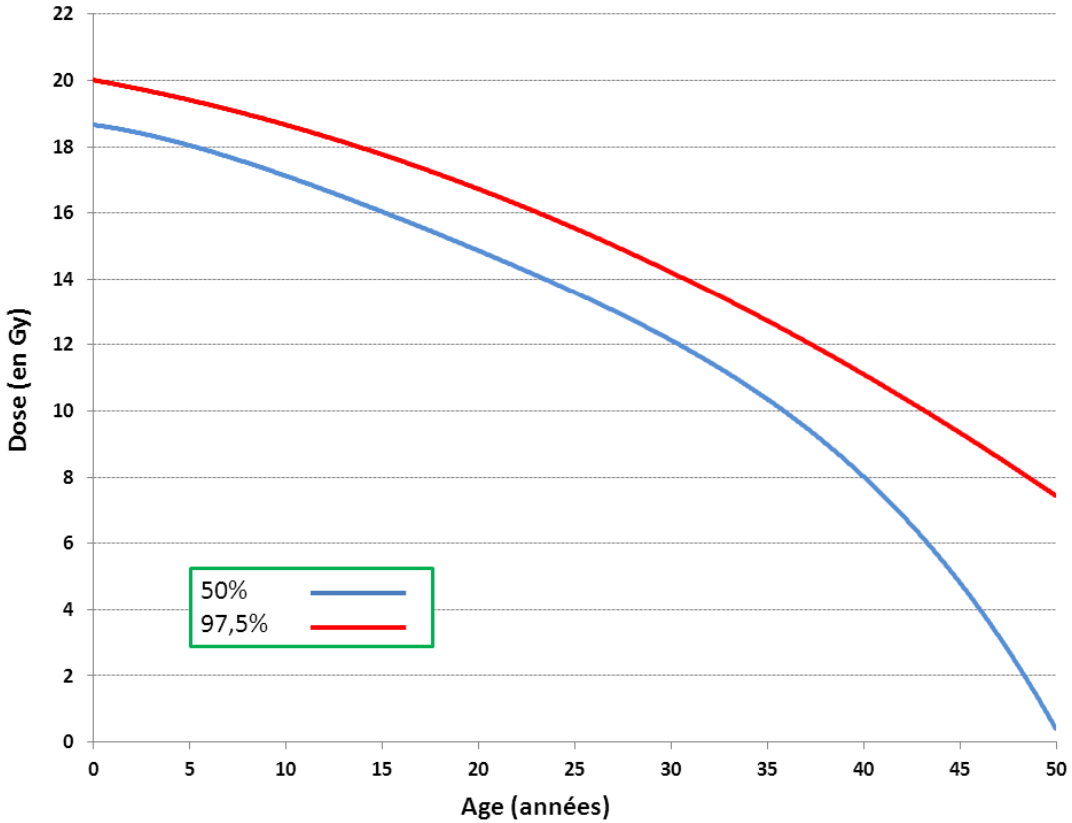
BT in gynaecological RMS

- Ovarian transposition before BT : 33 pts
- Mean dose delivered (Gy) : 68.8
- Mean treated volume (cm^3) : 46
- Mean ICRU bladder point (Gy) : 31
- Mean ICRU rectal point (Gy) : 34
- Mean ovaries dose (Gy): 2.8



BT in gynaecological RMS

- Long term follow-up not always easy
- Median FU : 8.4 years (0.8-30)
- Patterns of failure

Local	:	5.1%
Pelvic	:	2.6%

- At last follow-up: 20 ≥ 12 y. 17 have menstruations and 3 delivered 4 normal babies.

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BT in gynaecological RMS

- Among 20 patients treated before 1990 :
  - Acute grade 1-2 renal/genitourinary function symptoms : 6 pts
  - All transient acute side effects
  - 75 % presented sequelae in terms of vaginal or urethral sclerosis or stenosis (3 requiring plastic surgery)

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BT in gynaecological RMS

- Among 19 patients treated after 1990 :
  - ➢ acute side effects with maximal grade 1-2 renal/genitourinary function symptoms : 2
  - ➢ 20% had vaginal or urethral sclerosis or stenosis (0 surgery)

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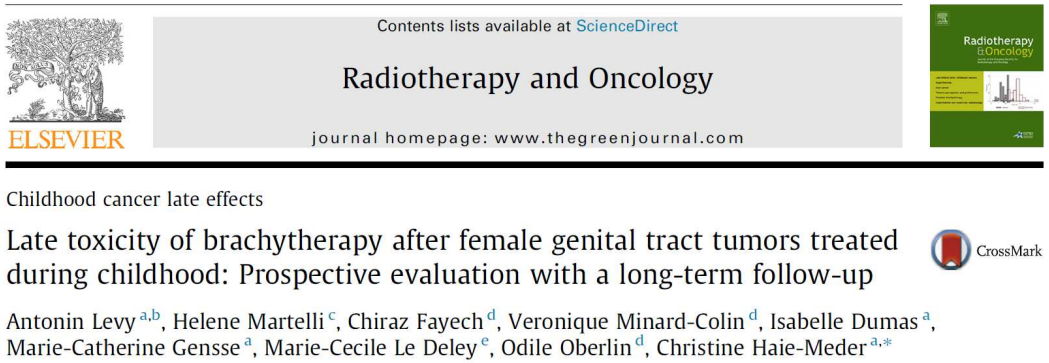
Long term Quality of life

- 42 patients contacted: 51% answered
- Age at treatment: 1.7 (0-16) years
- Median FU: 15 years
- 90%: good or very good QoL
- Dichotomy before and after 1990
- No endocrine disorder or puberty delay
- 1 second malignancy (uterine sarcoma)
- Late Side effect mainly urologic and gynecologic
- 28% had grade 3-4 events



Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

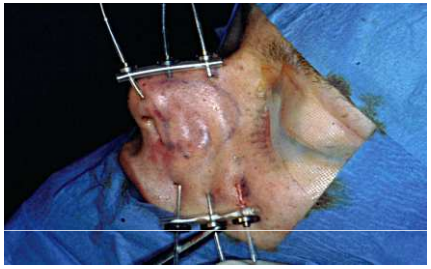
Childhood cancer late effects

Late toxicity of brachytherapy after female genital tract tumors treated during childhood: Prospective evaluation with a long-term follow-up

Antonin Levy [a,b], Helene Martelli [c], Chiraz Fayech [d], Veronique Minard-Colin [d], Isabelle Dumas [a], Marie-Catherine Gensse [a], Marie-Cecile Le Deley [e], Odile Oberlin [d], Christine Haie-Meder [a,*]

	Median total number of late effects (range)			
	G3–4		All grades	
	r_s	p	r_s	p
Brachytherapy period[a]	–	*0.008*	–	*0.005*
<1990	1 (0–8)		5 (0–16)	
⩾1990	0 (0–1)		1 (0–10)	
Cumulative dose[b]	*0.36*	*0.02*	*0.34*	*0.03*
⩽60 Gy	0 (0–8)		1 (0–14)	
>60 Gy	2 (0–8)		7 (1–16)	
Brachytherapy volume[b]	*0.45*	*0.02*	*0.43*	*0.03*
<11 cm^3	0 (0–4)		2 (0–9)	
>11 cm^3	1 (0–8)		6 (0–16)	
Maximal dose to ovaries[b]	*0.36*	*0.04*	*0.53*	*0.002*
<1.7 Gy	0 (0–4)		1 (0–6)	
>1.7 Gy	1 (0–8)		8 (0–16)	

Summary

	Vagina (1)	Prostate/ Bladder (2)	H & N (3)
			
N	39	26	16
FU	8.4 y	4 y	4.4 y
OS	91%	92%	50%
Local control	95%	85%	75%
Histo	Botryoid 80%	Emb: 77%	Emb: 63%

(1) Magné N, Int J Radiat Oncol Biol Phys. 2008 Nov 1;72(3):878-83

(2) Martelli H, J Pediatr Surg. 2009 Jan;44(1):190-6.

(3) Mazeron R, Ped Blood Cancer. 2014 Jul;61(7):1162-7

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Brachytherapy in pediatric malignancies

Conclusions

- **Muldisciplinary approach**
- **Avoid mutilating surgery / alterative to EBRT**
- **Radiation oncologist involved from the beginning**
- **Role of imaging (CT-Scan, MRI)**
- **Intra-operative brachytherapy**
- **Limited volume**
- **PDR**

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WWW.ESTRO.ORG/SCHOOL

Head & neck Techniques

Renaud Mazeron

Gustave Roussy

BT in Squamous cell carcinomas

- Lip
- Mobile tongue
- Floor of mouth

} Oral cavity

- Base of tongue
- Tonsillar area
- Soft palate

} Oropharynx

3

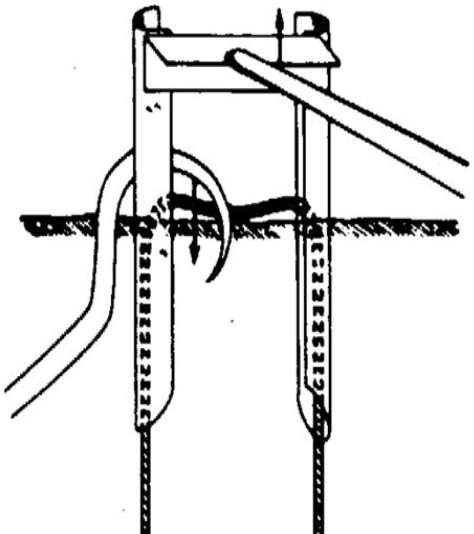
Brachytherapy Technique

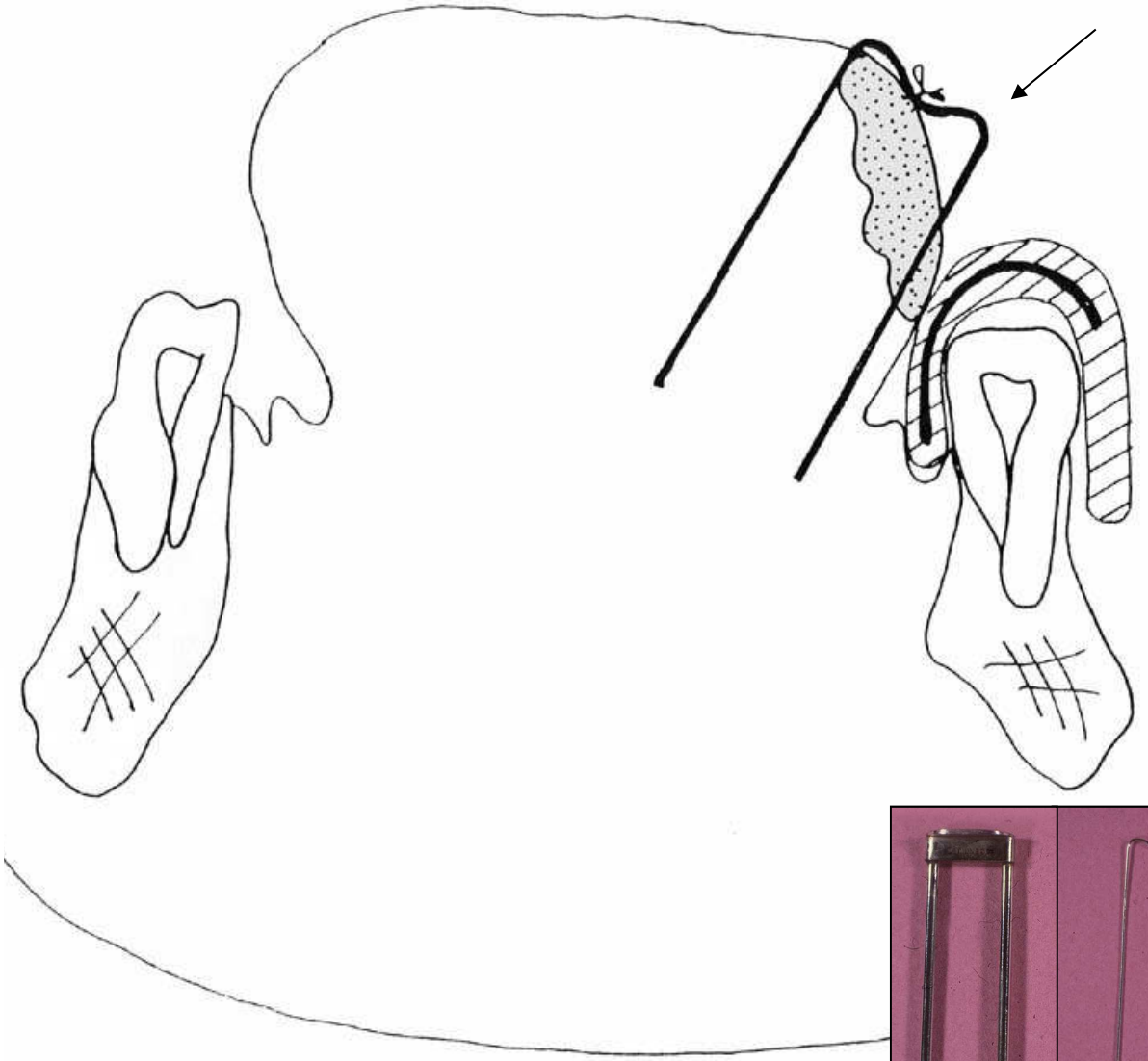
Guide Gutter technique

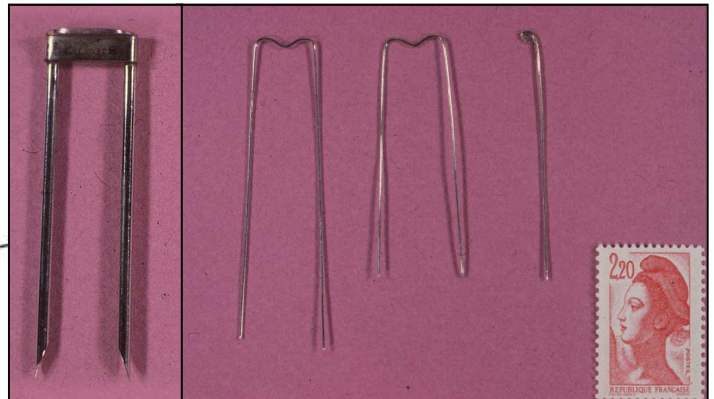
- Iridium 192 hairpins
- Local anesthesia
- Immediate loading
- Limited tumours

Guide gutter technique

I^{192} hairpin







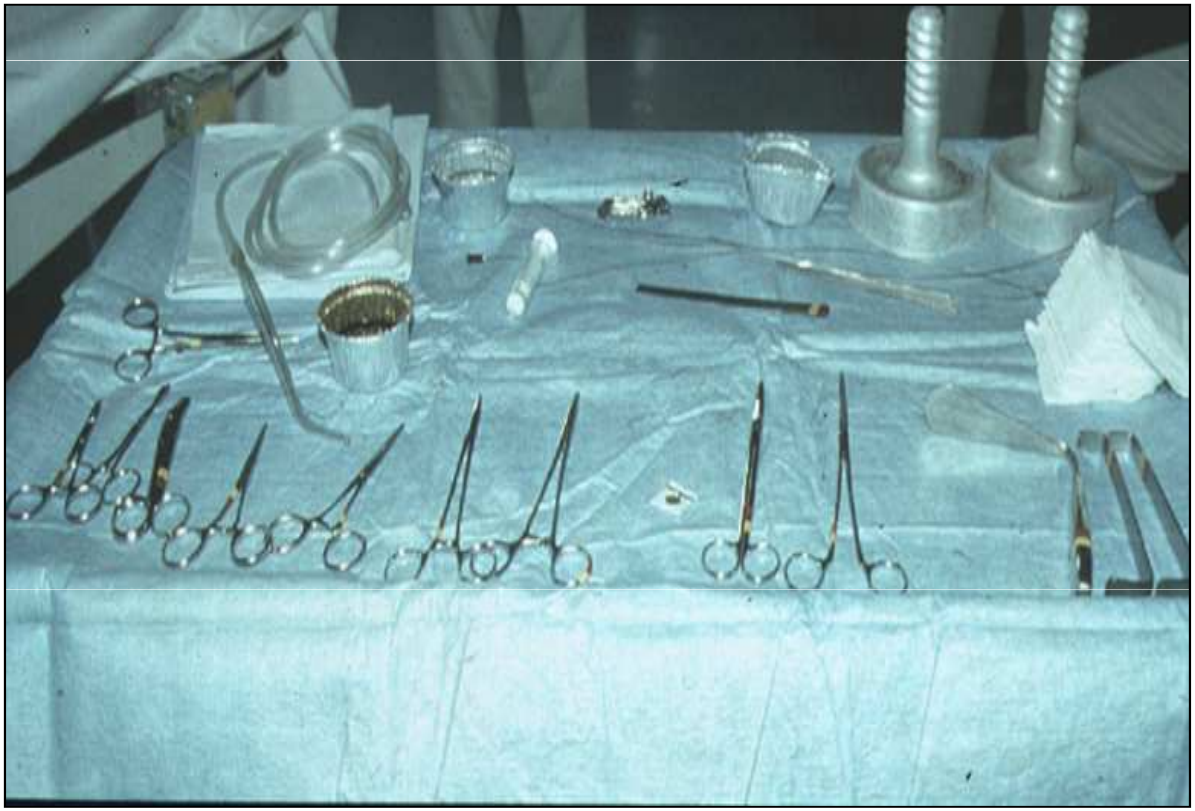
Plastic tube technique

- Iridium 192 wires or seeds (PDR/HDR)
- General anesthesia
- Loading postponed to 24 hours
- Moderately extensive tumors

7

Plastic tube technique

- OT
- General anesthesia
- 2 physicians
- Aspiration
- Light
- Nasal intubation
- Removal: OT



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Clinical examination

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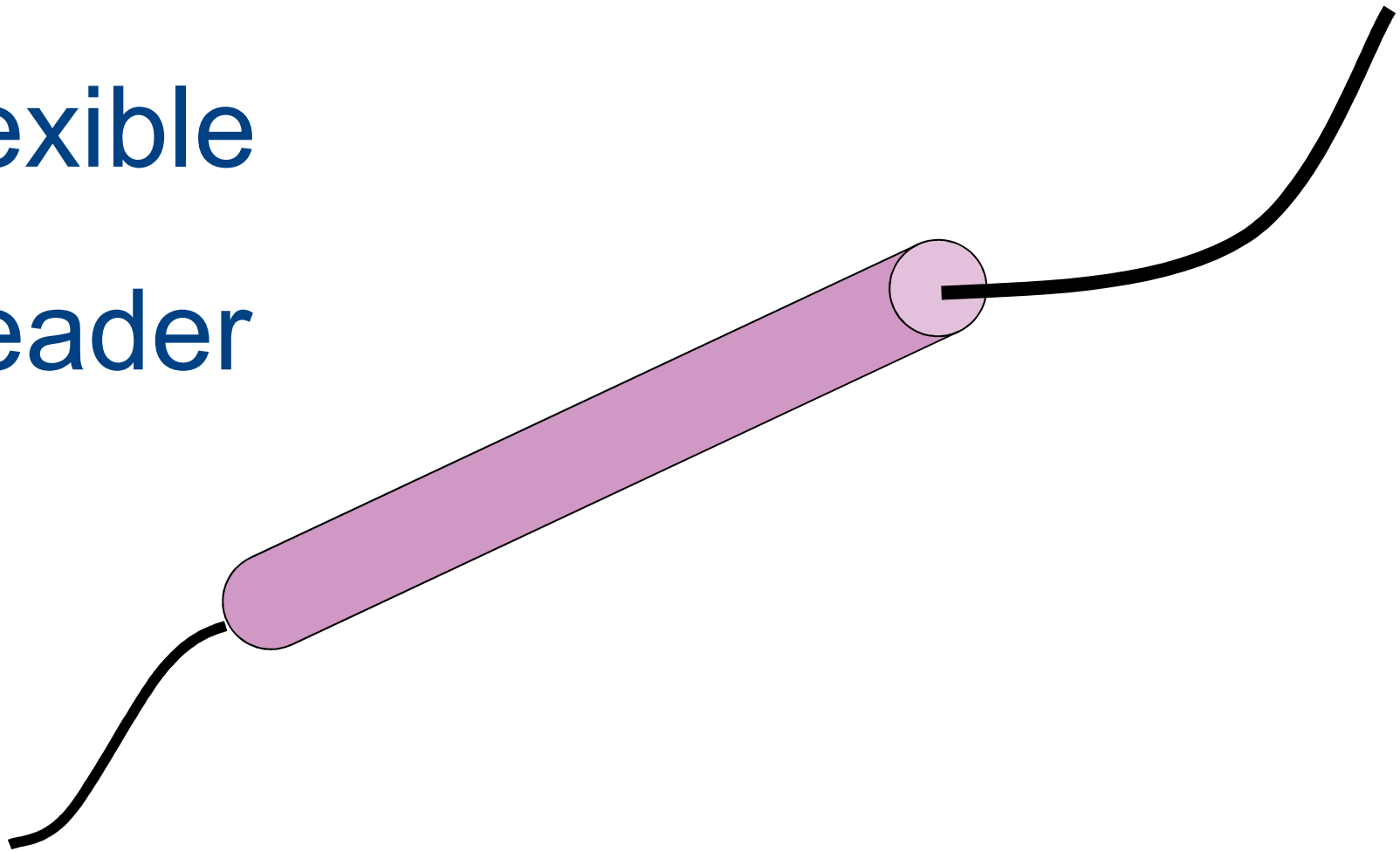
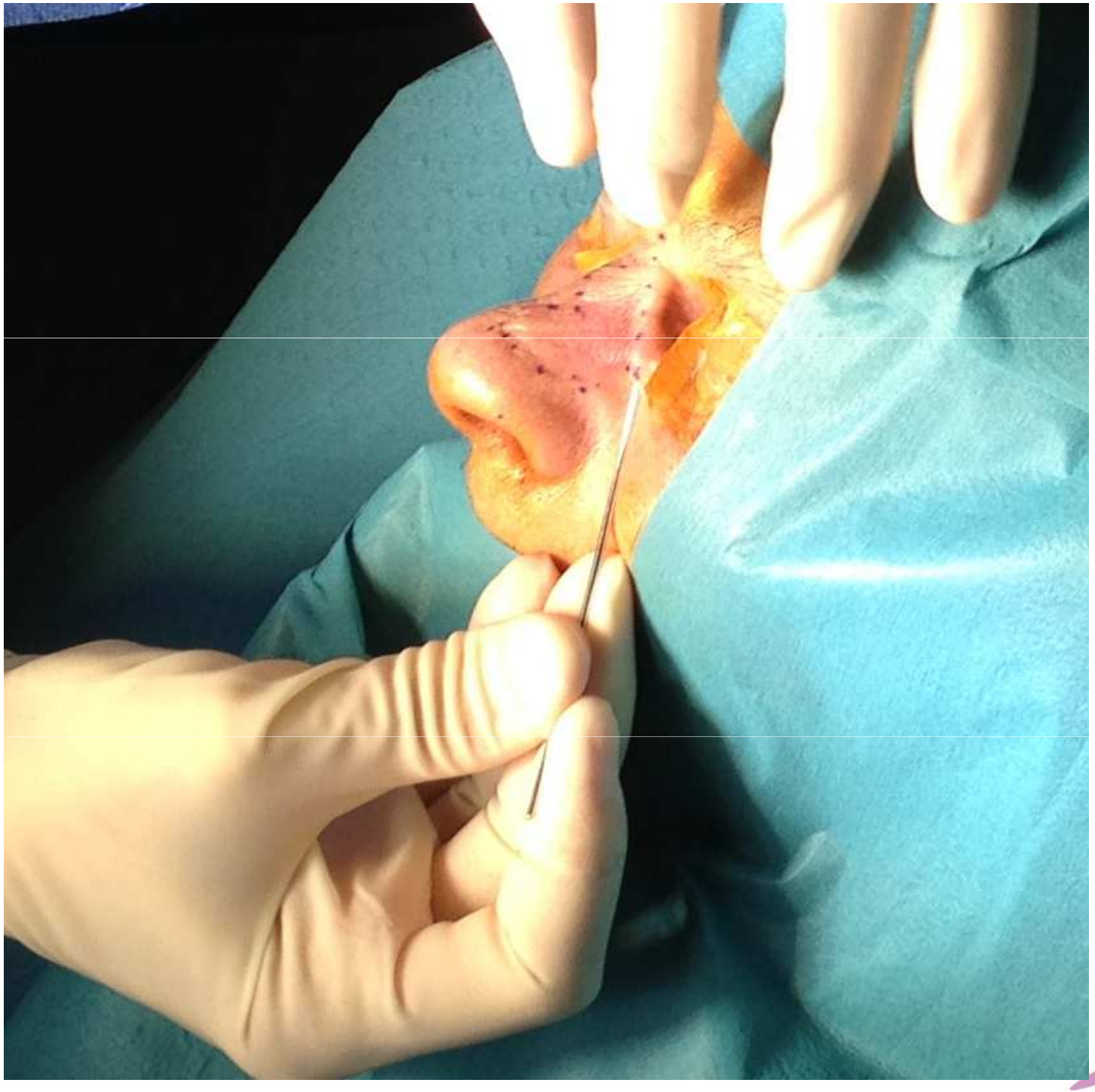
Plastic tubes

- Flexible
- Leader





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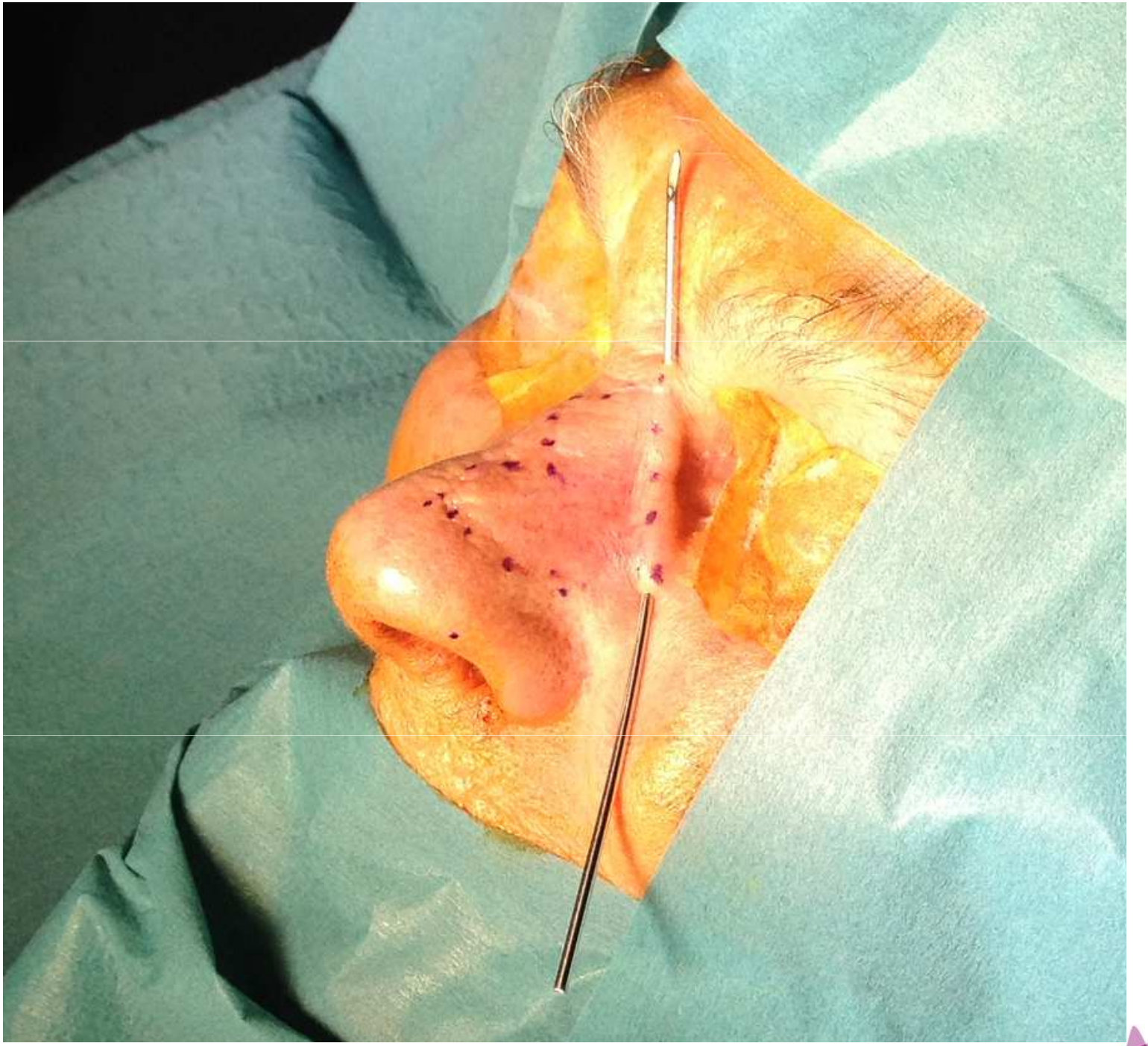

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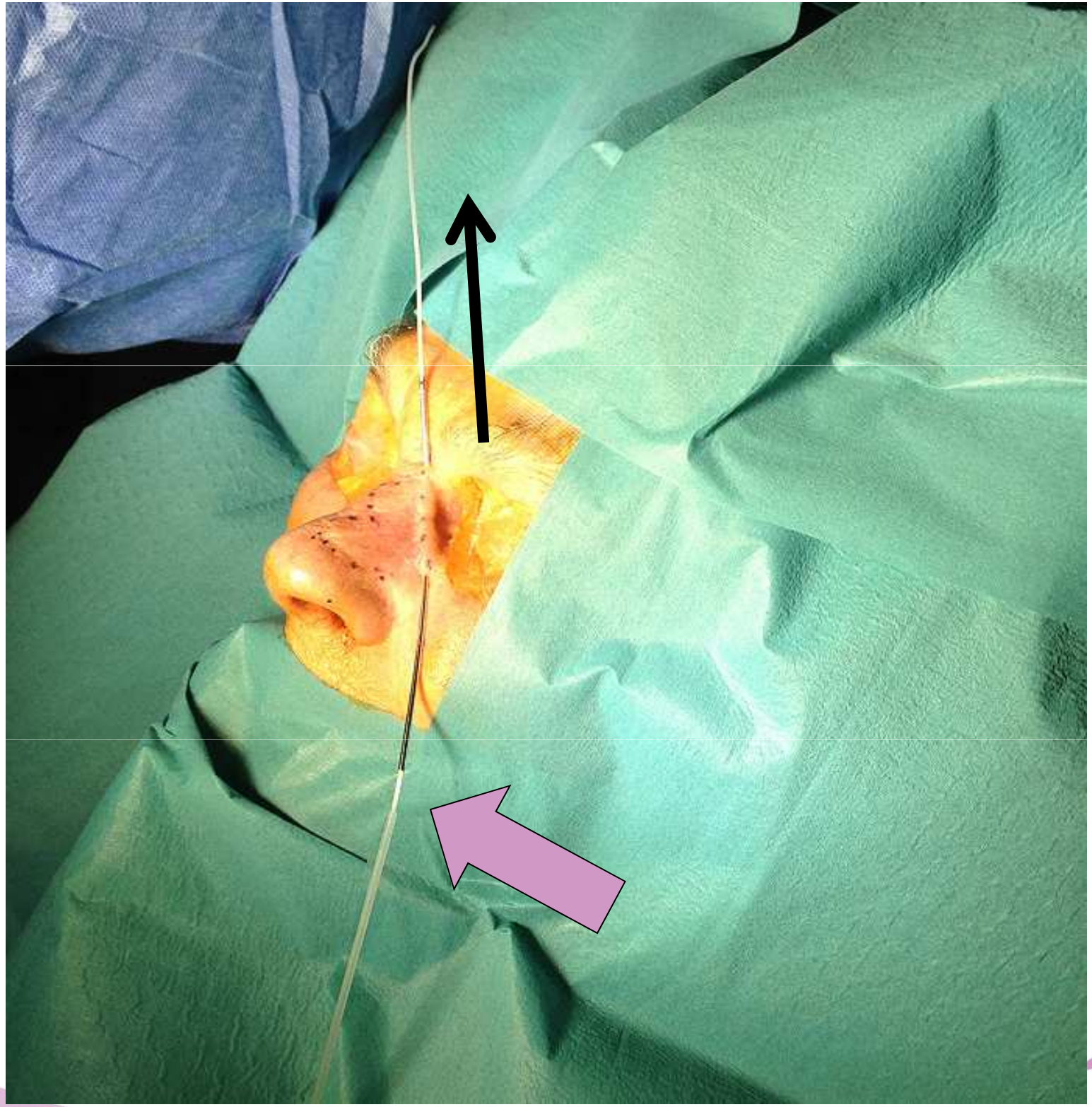

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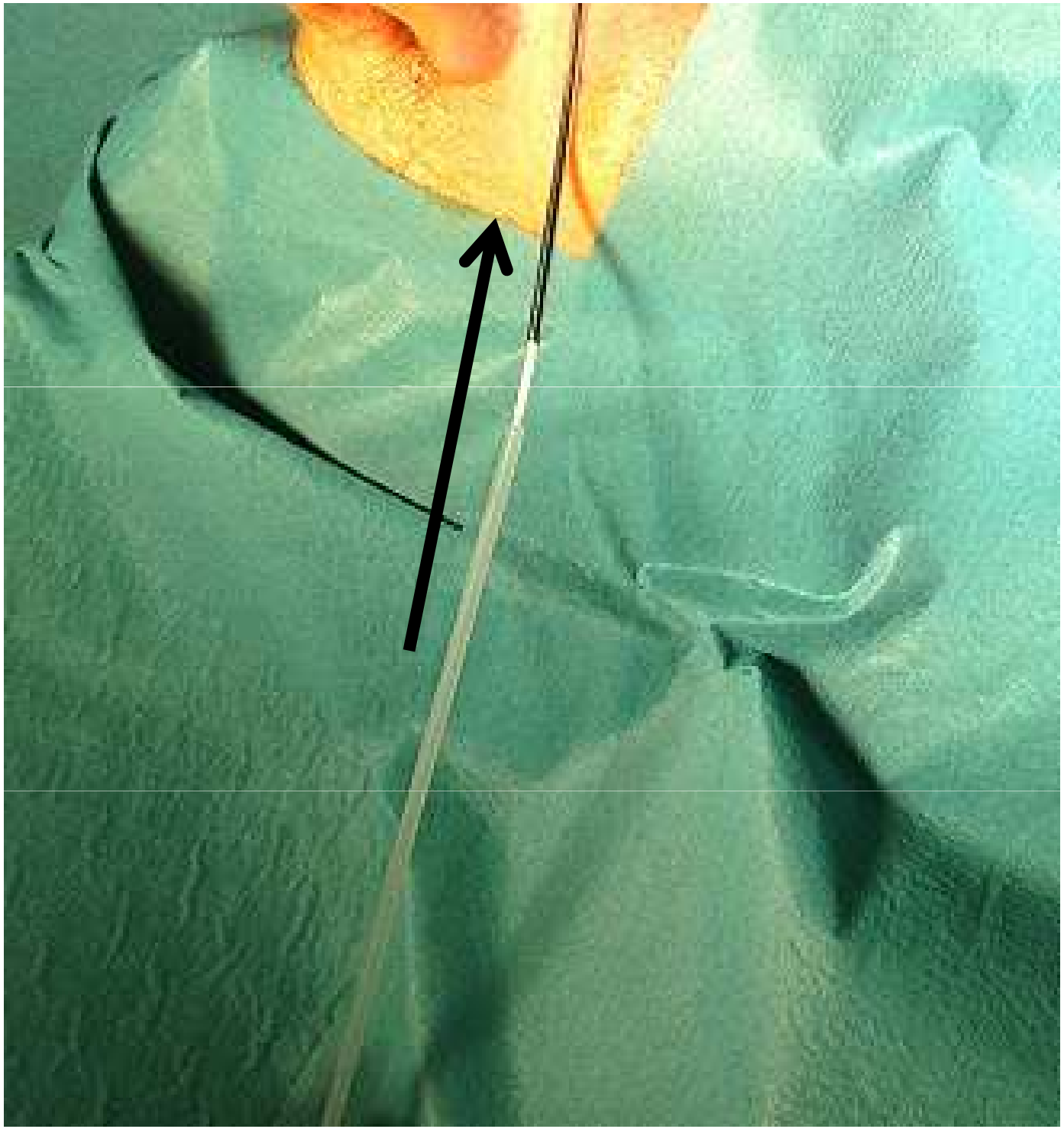

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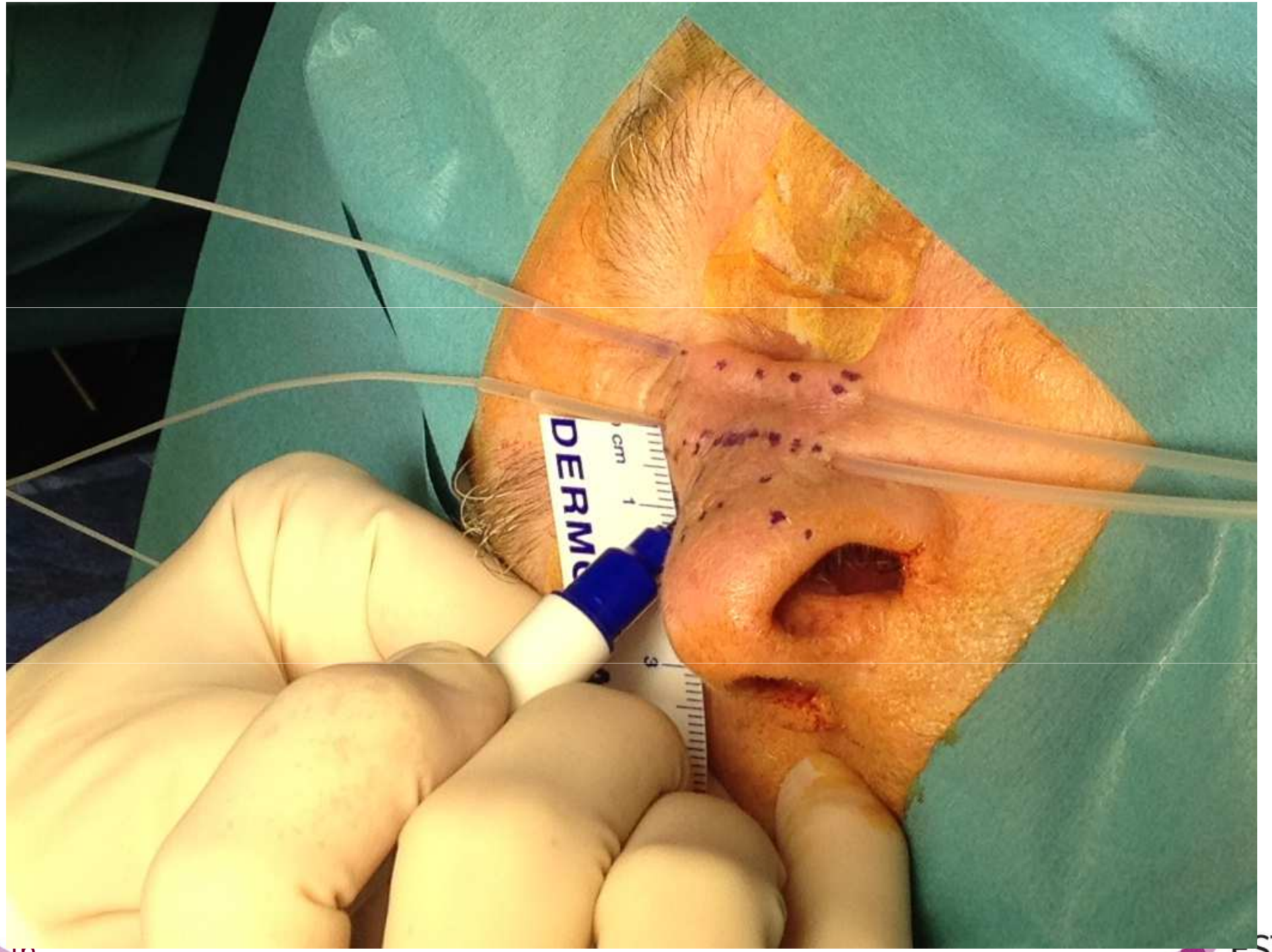
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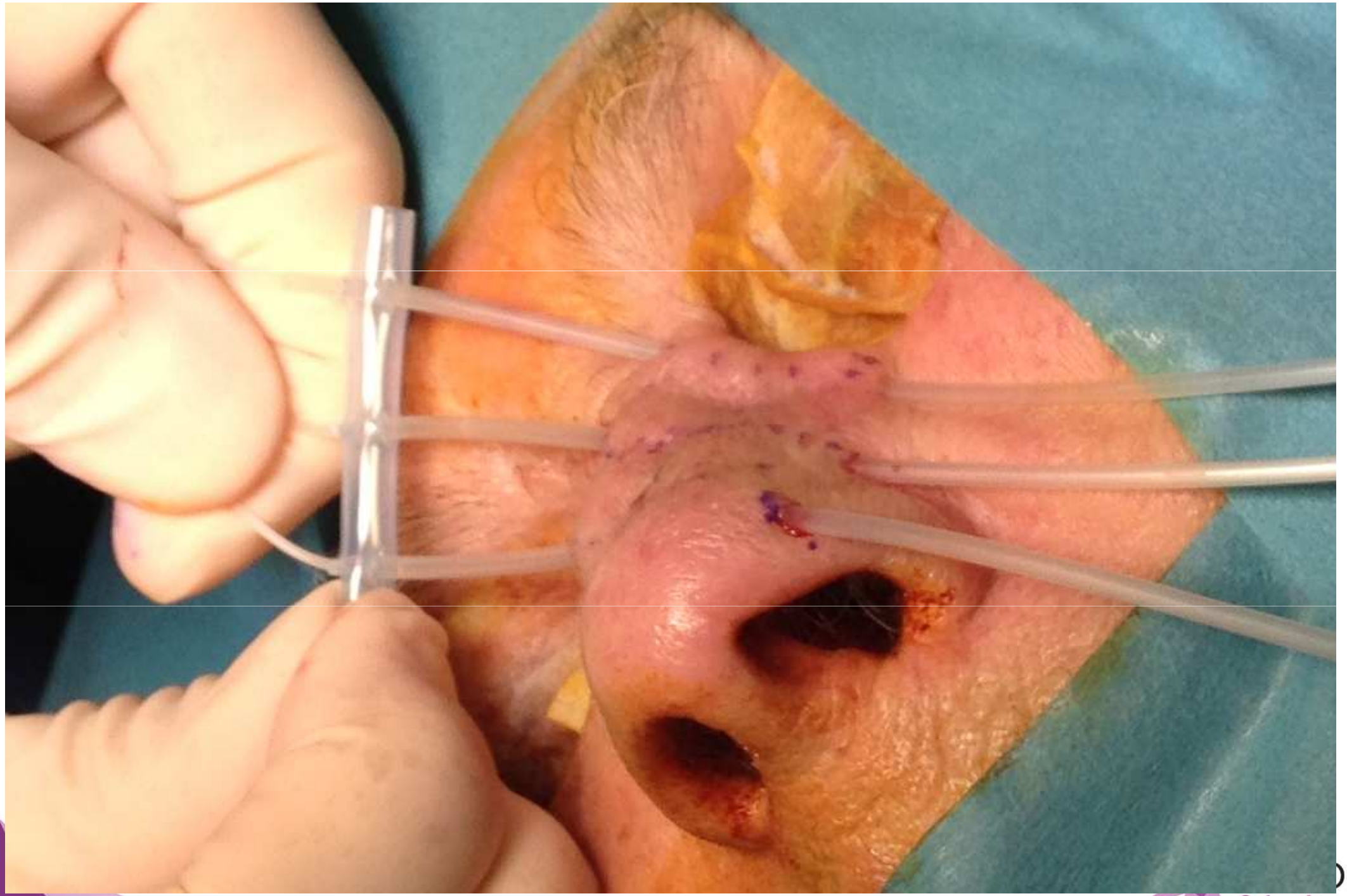

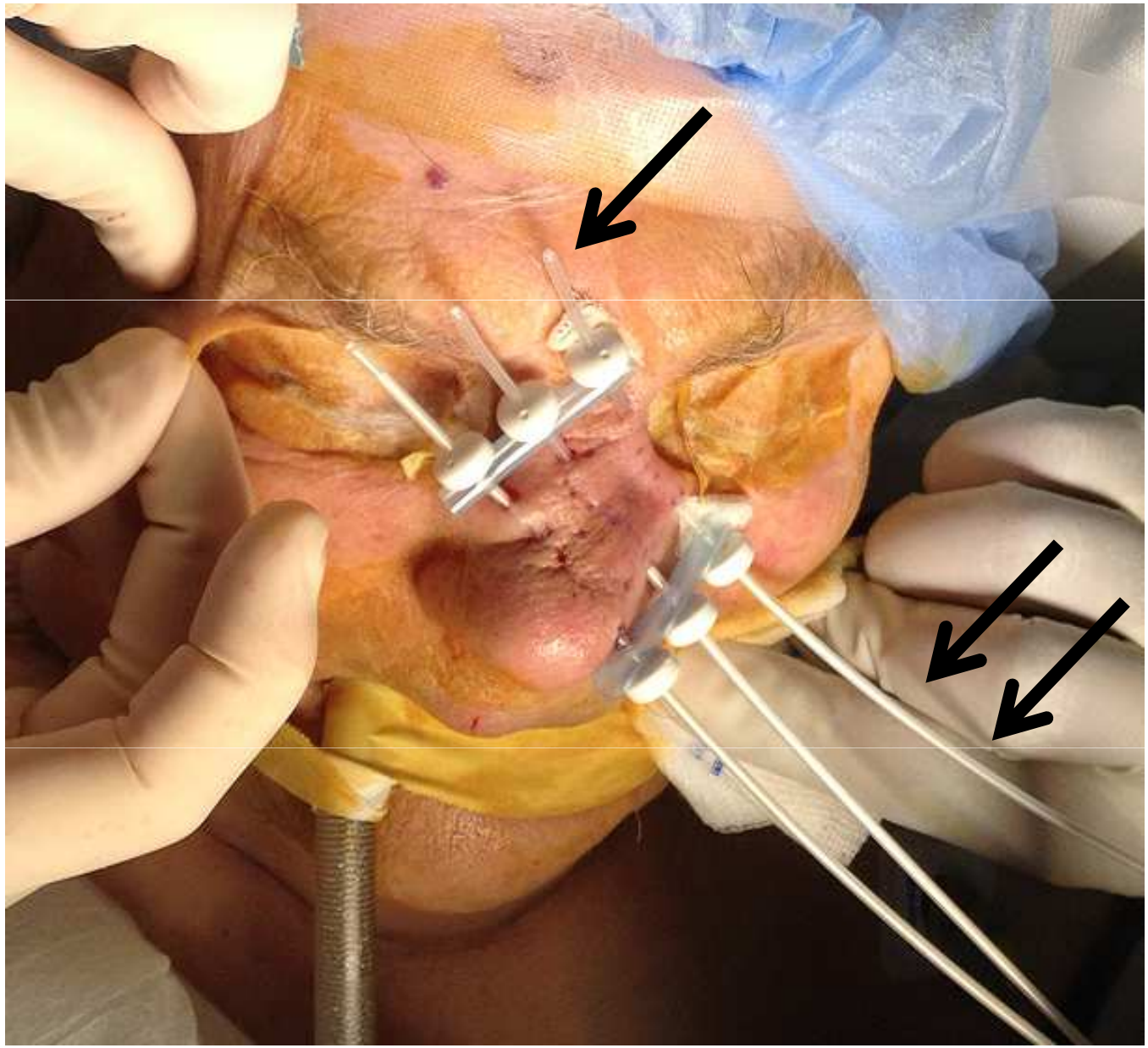

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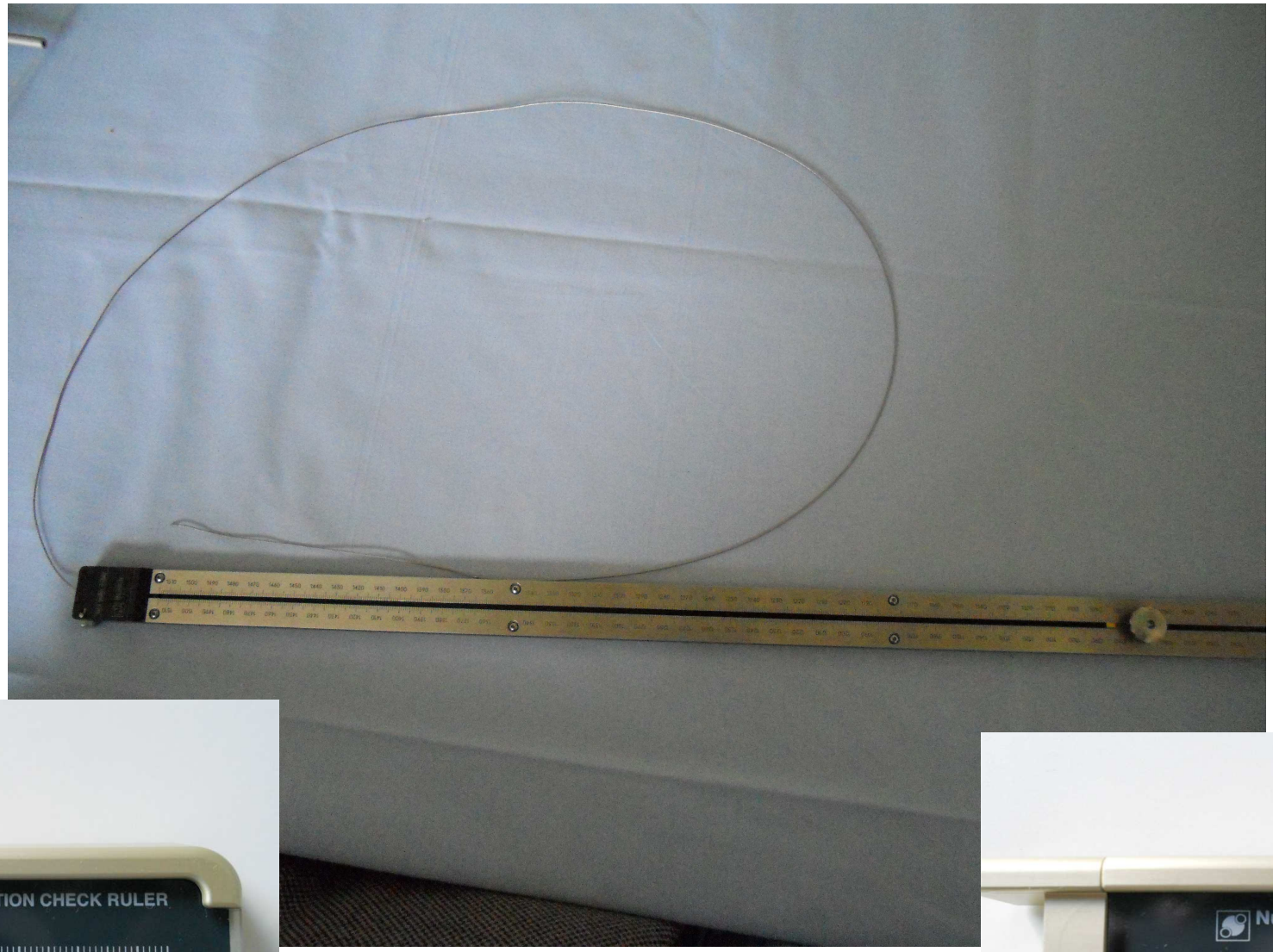
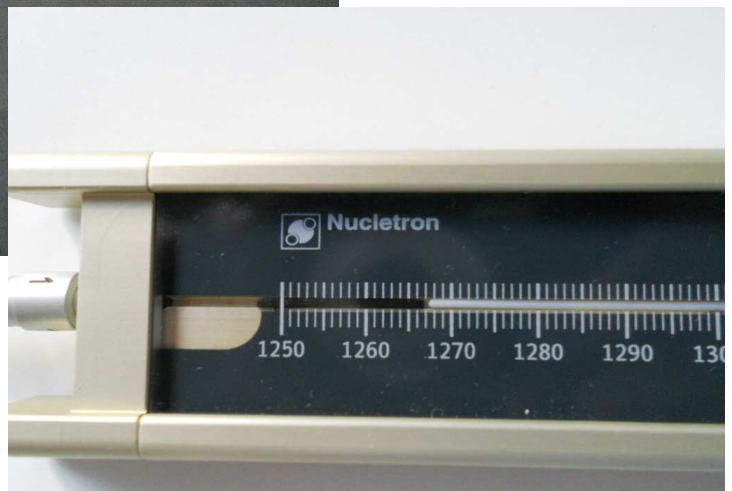
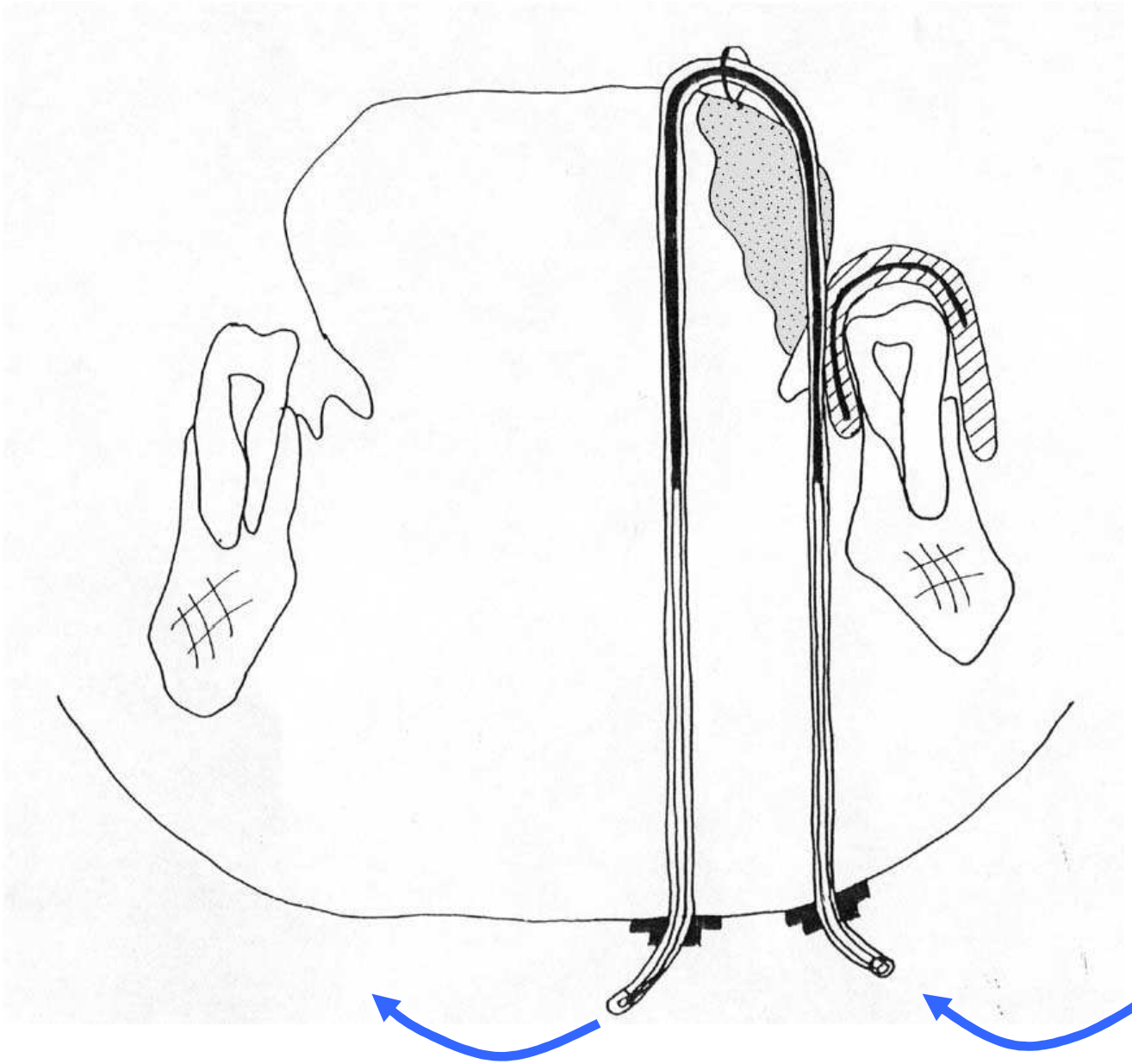
Stretching of plastic tube…

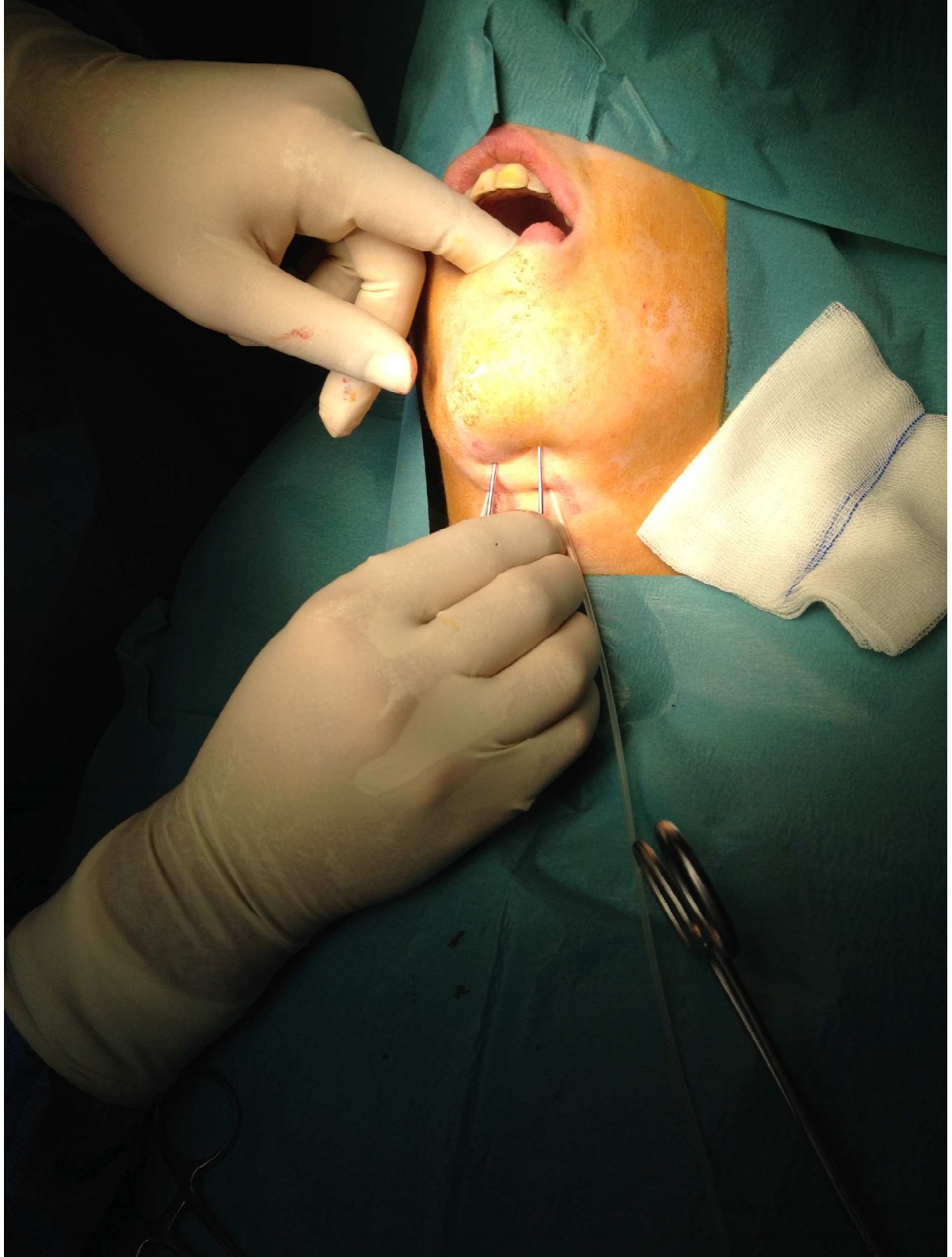




Plastic tube technique : loops



21



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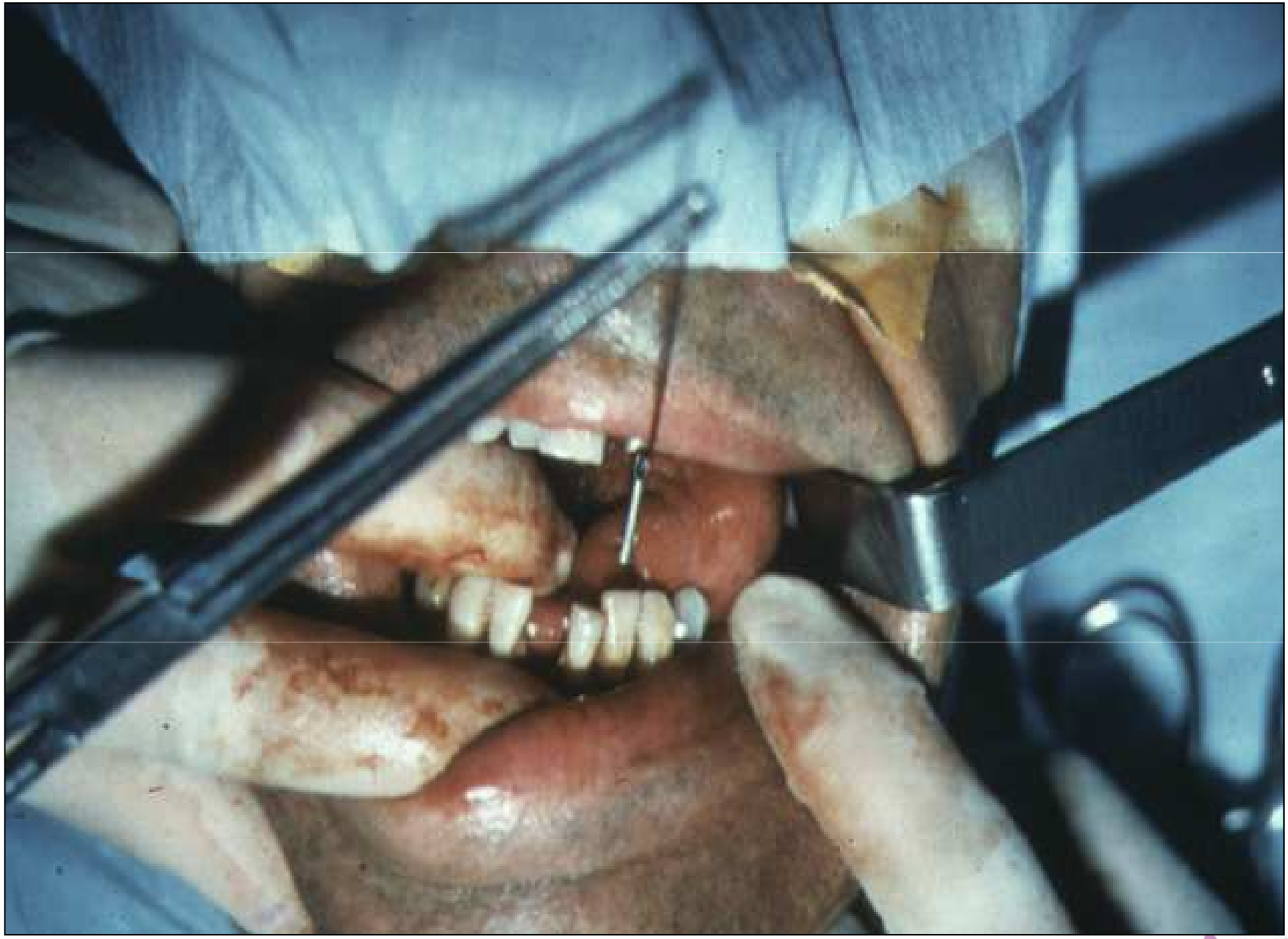
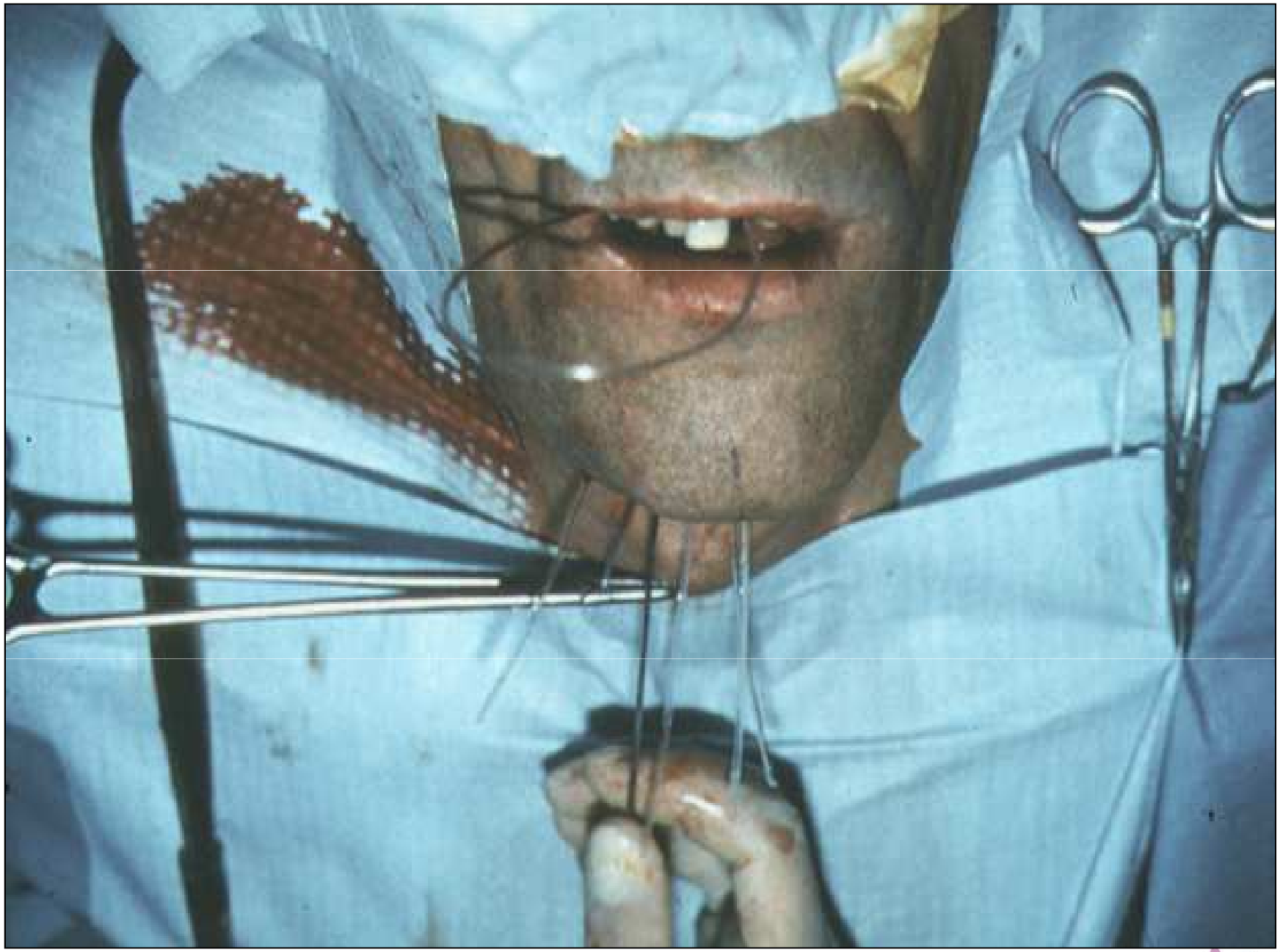
ESTRO School

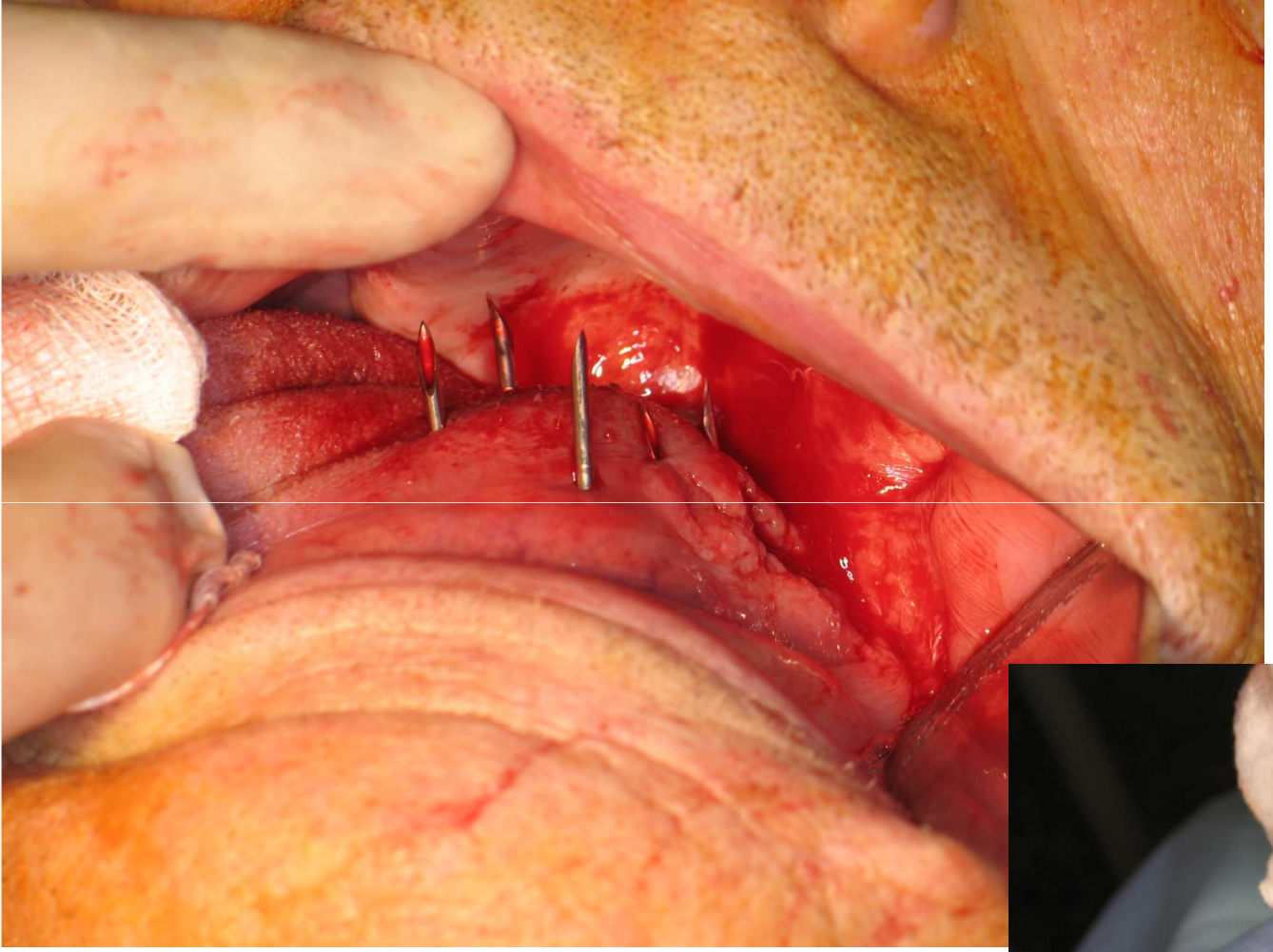


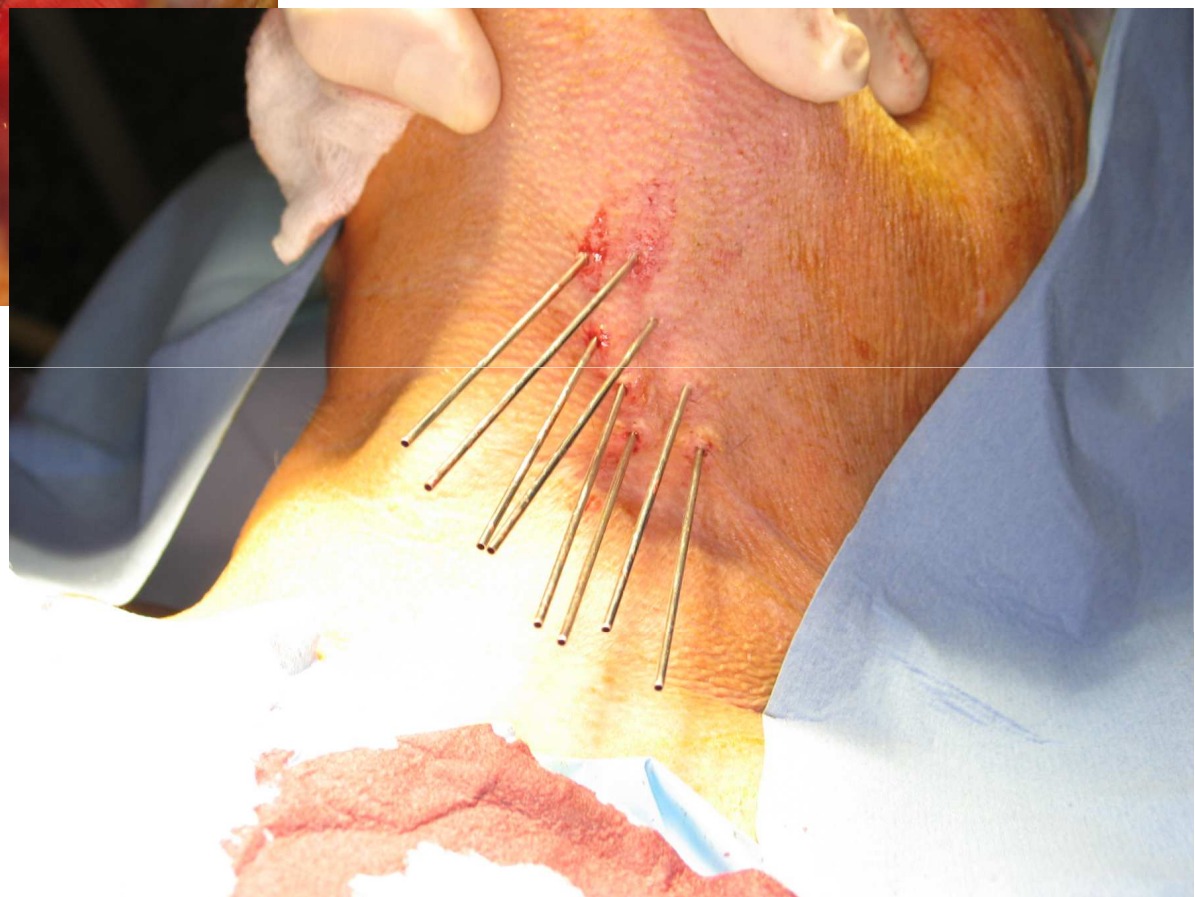
ESTRO School



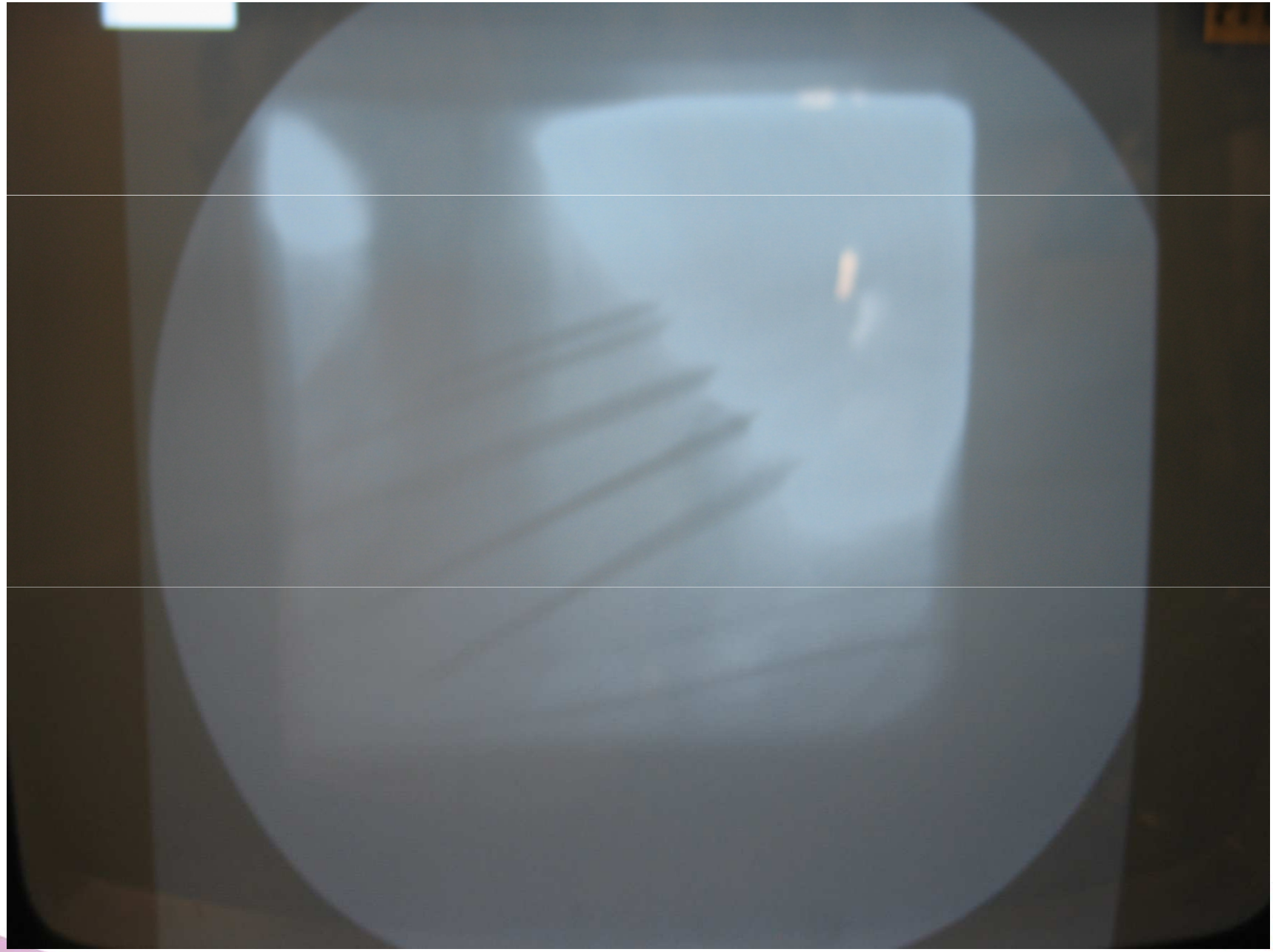
ESTRO School

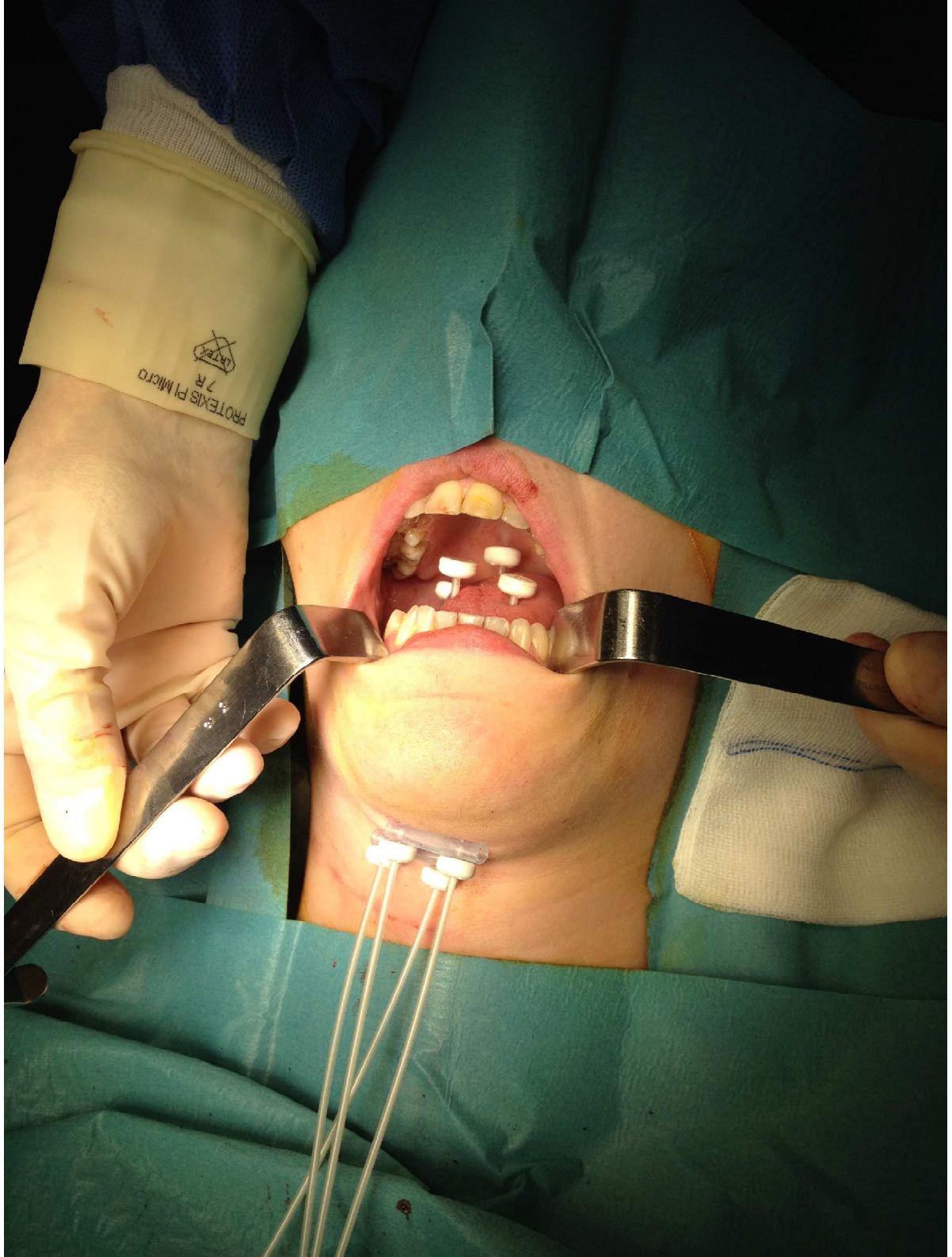
ESTRO School



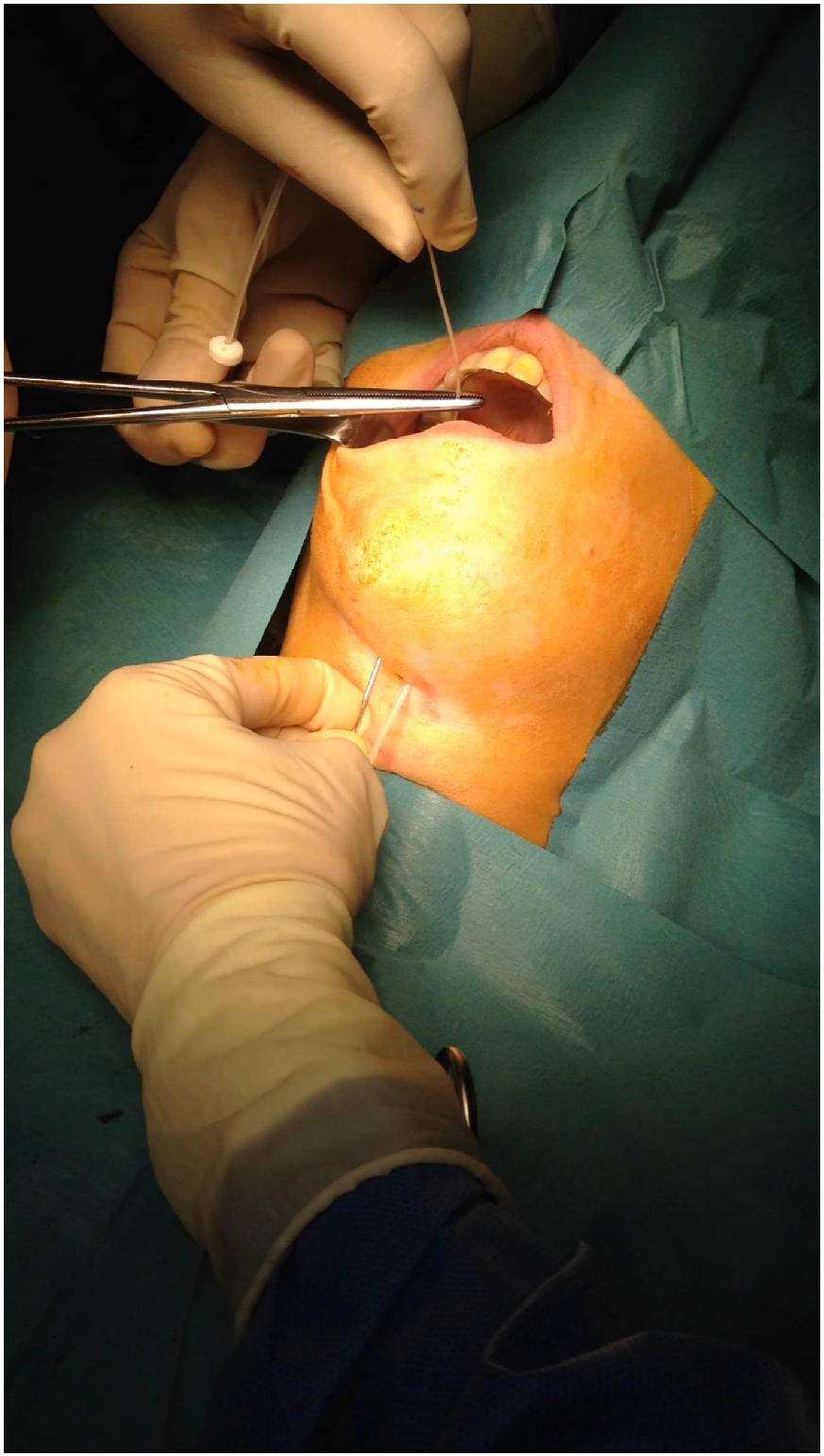


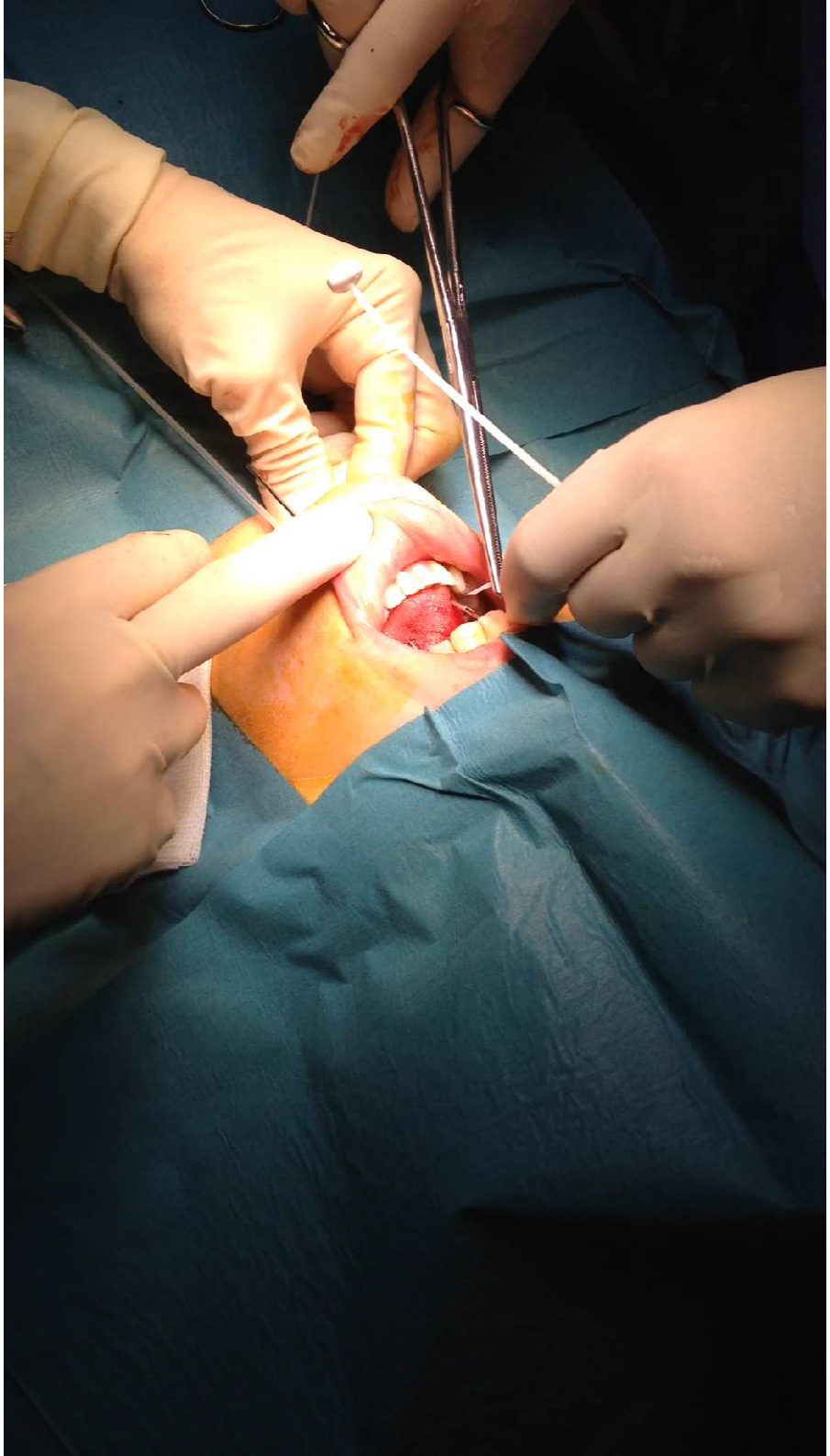
⇢ Fluoroscopy guidance





ESTRO School





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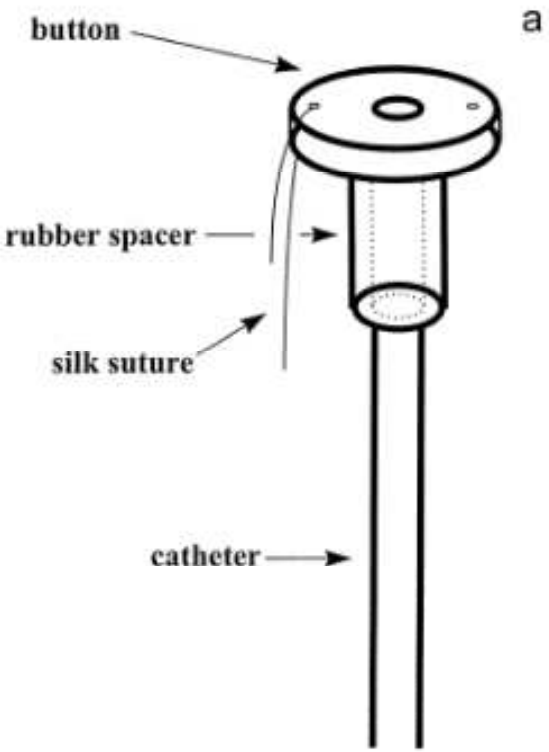
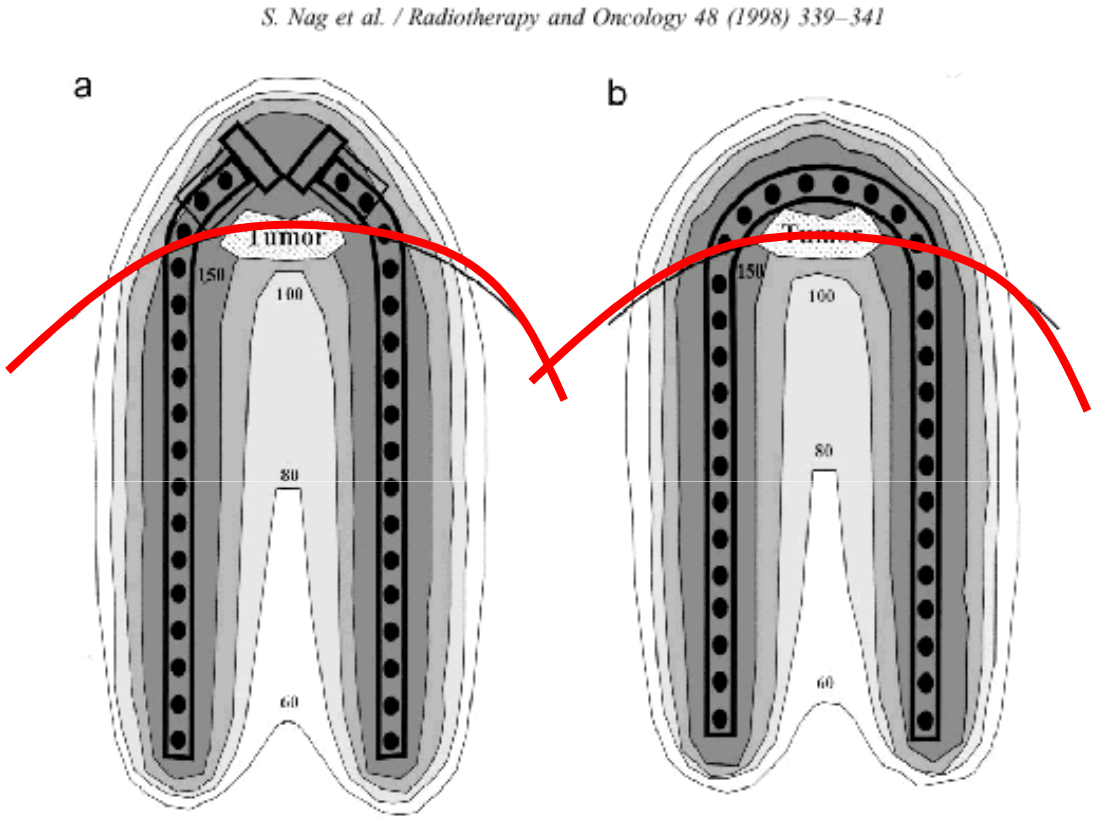
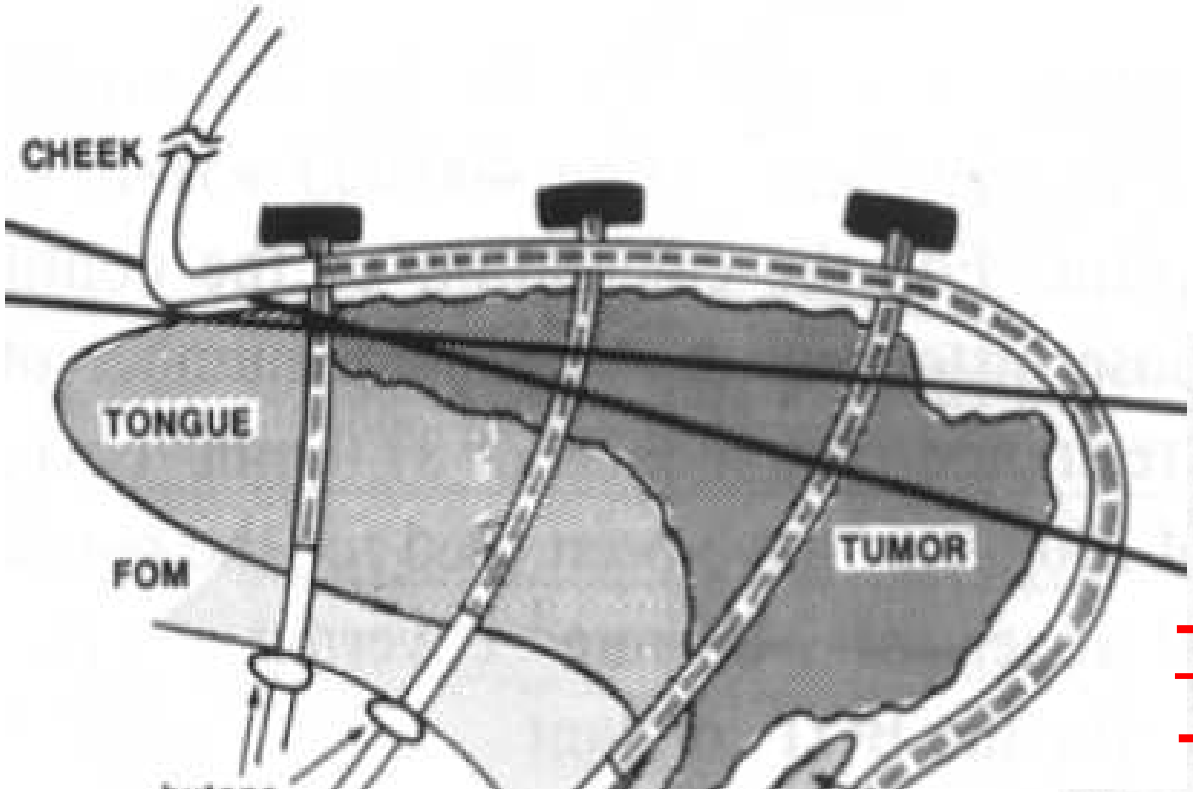
PDR / HDR After-loaders

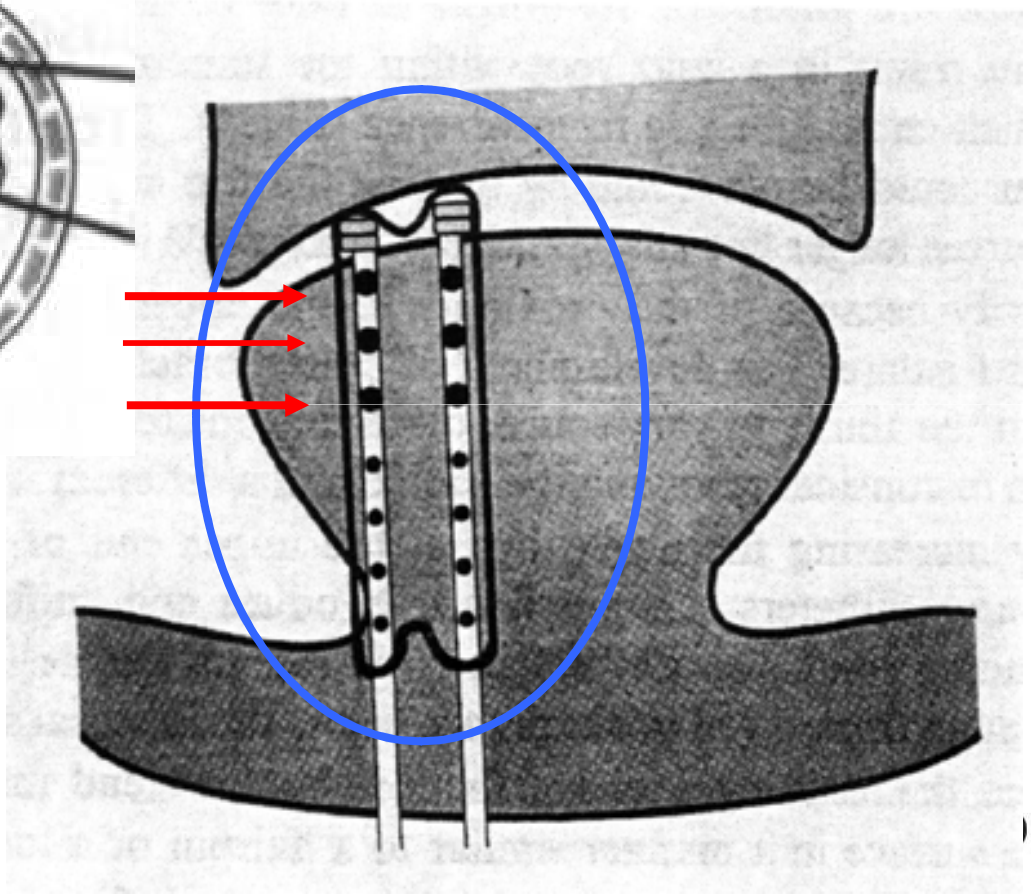
- Difficulties with loops
- Edema
- Fold



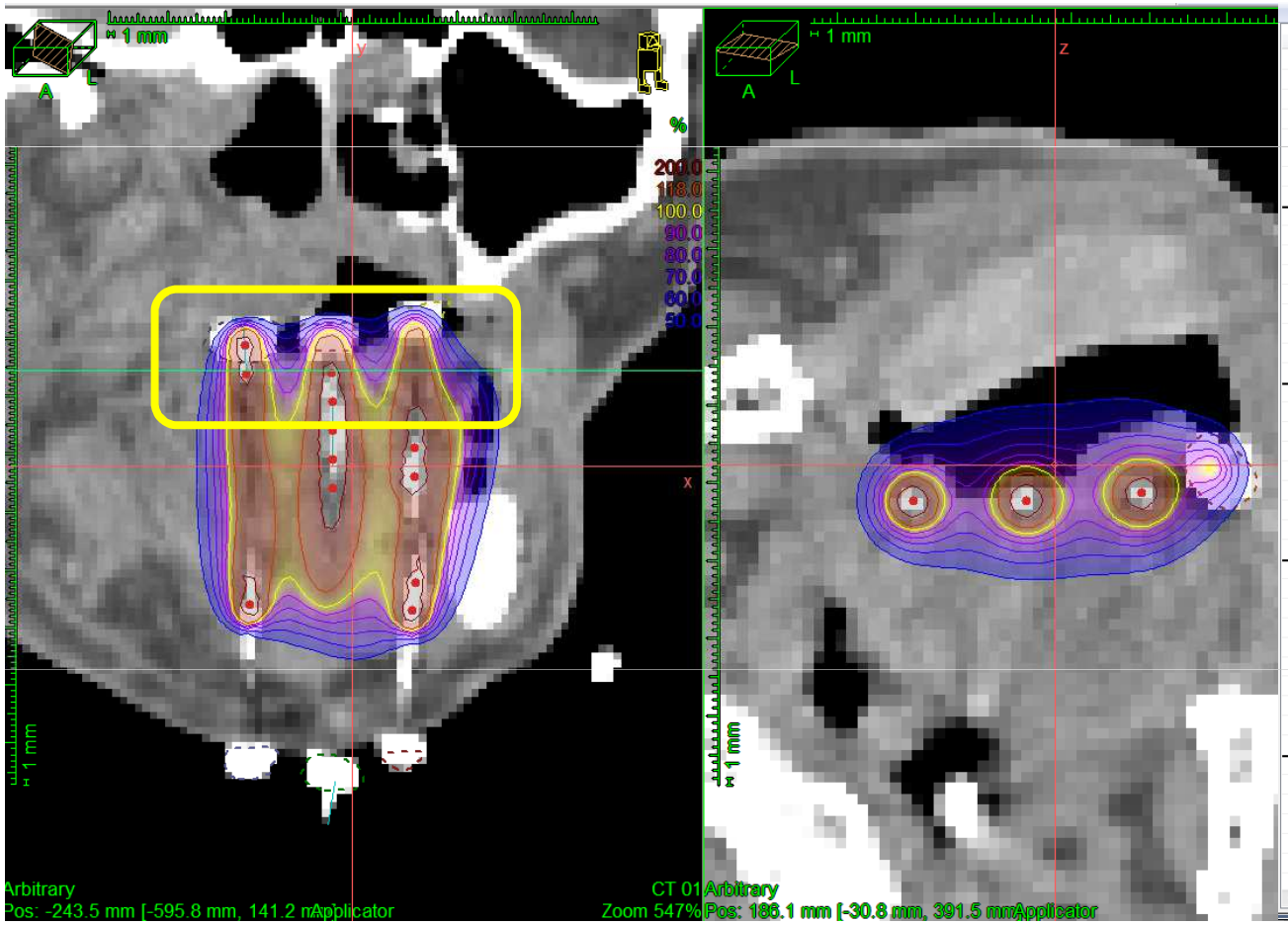


PDR / HDR





Paris system



Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	1	4.1	229.9	248.2	1.00	0.00	4.33	
1	2	3.5	225.5	250.4	1.00	0.00	4.33	
1	3	3.0	220.8	252.1	1.00	0.00	4.33	
1	4	2.1	216.2	253.6	1.00	0.00	4.33	
1	5	1.0	211.5	255.1	1.00	0.00	4.33	
1	6	-0.1	206.9	256.4	1.00	0.00	4.33	
1	7	-1.0	202.0	257.4	1.00	0.00	4.33	
1	8	-1.9	197.2	258.3	1.00	0.00	4.33	
2	1	19.8	229.9	264.7	1.00	0.00	4.33	
2	2	17.3	225.6	264.0	1.00	0.00	4.33	
2	3	15.7	221.1	262.9	1.00	0.00	4.33	
2	4	14.1	216.4	261.8	1.00	0.00	4.33	
2	5	12.6	211.7	261.5	1.00	0.00	4.33	
2	6	11.1	206.9	261.2	1.00	0.00	4.33	
2	7	9.6	202.2	260.9	1.00	0.00	4.33	
2	8	8.8	197.3	260.3	1.00	0.00	4.33	
2	9	8.3	192.4	259.6	1.00	0.00	4.33	
3	1	32.2	234.3	262.1	1.00	0.00	4.33	
3	2	30.2	229.7	261.3	1.00	0.00	4.33	
3	3	28.2	225.2	260.6	1.00	0.00	4.33	
3	4	26.5	220.6	259.9	1.00	0.00	4.33	
3	5	25.1	215.8	259.4	1.00	0.00	4.33	
3	6	23.8	211.0	259.2	1.00	0.00	4.33	
3	7	22.6	206.1	259.4	1.00	0.00	4.33	
3	8	21.5	201.3	259.7	1.00	0.00	4.33	
3	9	20.3	196.4	259.9	1.00	0.00	4.33	
4	1	4.5	241.7	234.6	1.00	0.00	4.33	
4	2	3.6	236.9	236.0	1.00	0.00	4.33	
4	3	2.3	232.3	237.3	1.00	0.00	4.33	
4	4	1.0	227.6	238.6	1.00	0.00	4.33	
4	5	0.6	222.8	239.8	1.00	0.00	4.33	
4	6	0.1	218.0	241.1	1.00	0.00	4.33	
4	7	-0.4	213.1	242.1	1.00	0.00	4.33	
4	8	-1.2	208.2	242.5	1.00	0.00	4.33	
4	9	-2.0	203.3	243.0	1.00	0.00	4.33	
4	10	-2.4	198.3	243.4	1.00	0.00	4.33	
5	1	15.9	241.5	243.7	1.00	0.00	4.33	
5	2	15.6	236.6	244.4	1.00	0.00	4.33	
5	3	15.2	231.7	245.0	1.00	0.00	4.33	
5	4	14.8	226.7	245.4	1.00	0.00	4.33	
5	5	14.5	221.7	245.7	1.00	0.00	4.33	
5	6	13.9	216.8	246.1	1.00	0.00	4.33	
5	7	13.2	211.8	246.4	1.00	0.00	4.33	

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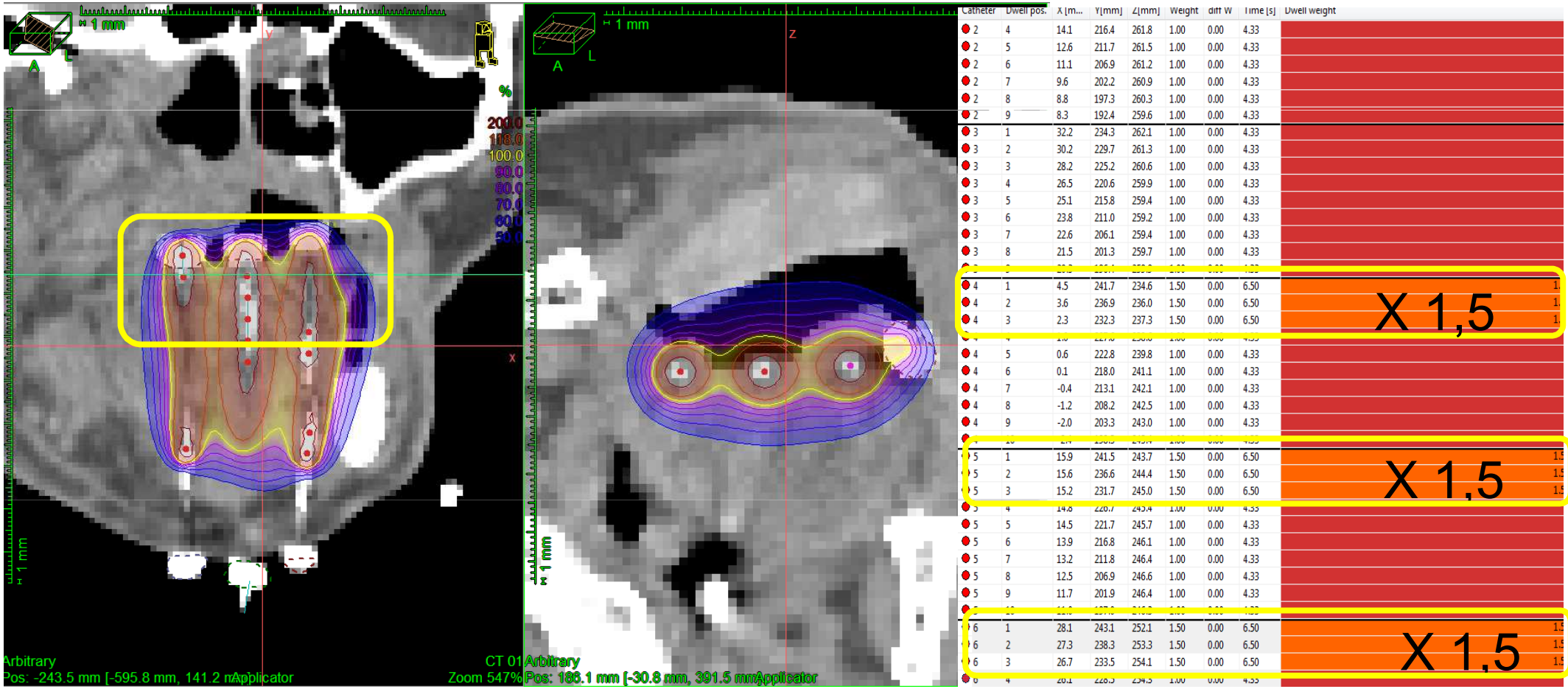
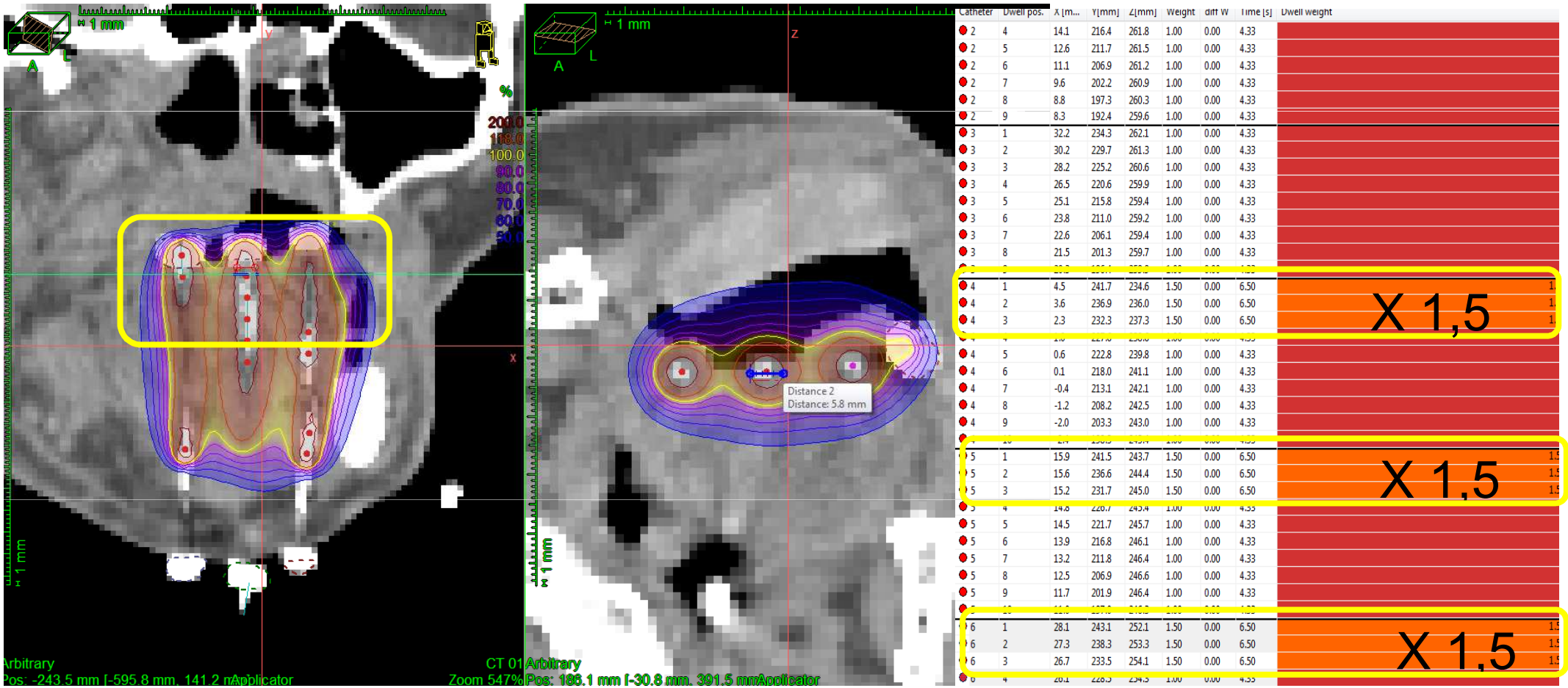
Optimization on distal dwell positions



Check the hyperdosage sleeves



Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
2	4	14.1	216.4	261.8	1.00	0.00	4.33	
2	5	12.6	211.7	261.5	1.00	0.00	4.33	
2	6	11.1	206.9	261.2	1.00	0.00	4.33	
2	7	9.6	202.2	260.9	1.00	0.00	4.33	
2	8	8.8	197.3	260.3	1.00	0.00	4.33	
2	9	8.3	192.4	259.6	1.00	0.00	4.33	
3	1	32.2	234.3	262.1	1.00	0.00	4.33	
3	2	30.2	229.7	261.3	1.00	0.00	4.33	
3	3	28.2	225.2	260.6	1.00	0.00	4.33	
3	4	26.5	220.6	259.9	1.00	0.00	4.33	
3	5	25.1	215.8	259.4	1.00	0.00	4.33	
3	6	23.8	211.0	259.2	1.00	0.00	4.33	
3	7	22.6	206.1	259.4	1.00	0.00	4.33	
3	8	21.5	201.3	259.7	1.00	0.00	4.33	
4	1	4.5	241.7	234.6	1.50	0.00	6.50	
4	2	3.6	236.9	236.0	1.50	0.00	6.50	
4	3	2.3	232.3	237.3	1.50	0.00	6.50	
4	5	0.6	222.8	239.8	1.00	0.00	4.33	
4	6	0.1	218.0	241.1	1.00	0.00	4.33	
4	7	-0.4	213.1	242.1	1.00	0.00	4.33	
4	8	-1.2	208.2	242.5	1.00	0.00	4.33	
4	9	-2.0	203.3	243.0	1.00	0.00	4.33	
5	1	15.9	241.5	243.7	1.50	0.00	6.50	
5	2	15.6	236.6	244.4	1.50	0.00	6.50	
5	3	15.2	231.7	245.0	1.50	0.00	6.50	
5	5	14.5	221.7	245.7	1.00	0.00	4.33	
5	6	13.9	216.8	246.1	1.00	0.00	4.33	
5	7	13.2	211.8	246.4	1.00	0.00	4.33	
5	8	12.5	206.9	246.6	1.00	0.00	4.33	
5	9	11.7	201.9	246.4	1.00	0.00	4.33	
6	1	28.1	243.1	252.1	1.50	0.00	6.50	
6	2	27.3	238.3	253.3	1.50	0.00	6.50	
6	3	26.7	233.5	254.1	1.50	0.00	6.50	

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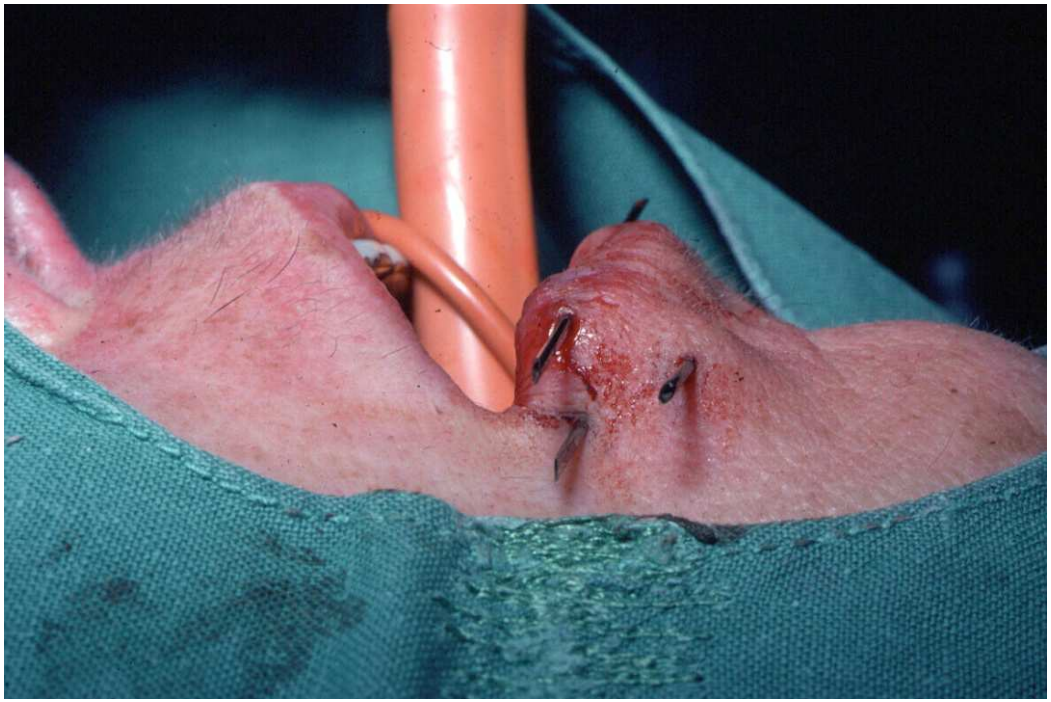
Hypodermic needles



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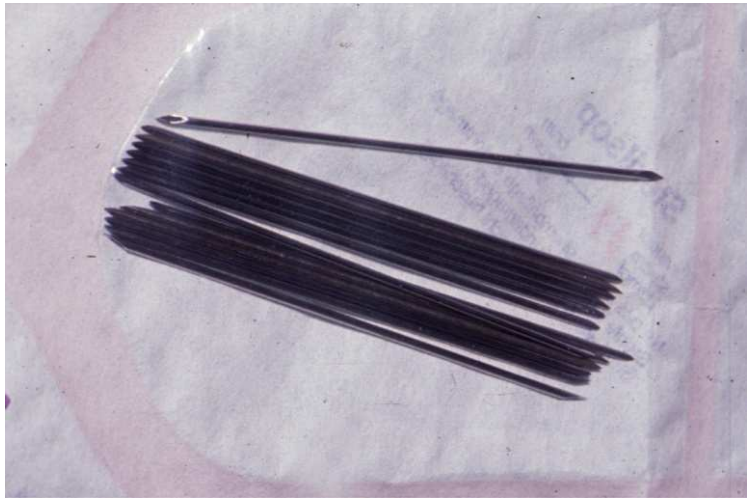
Hypodermic needles



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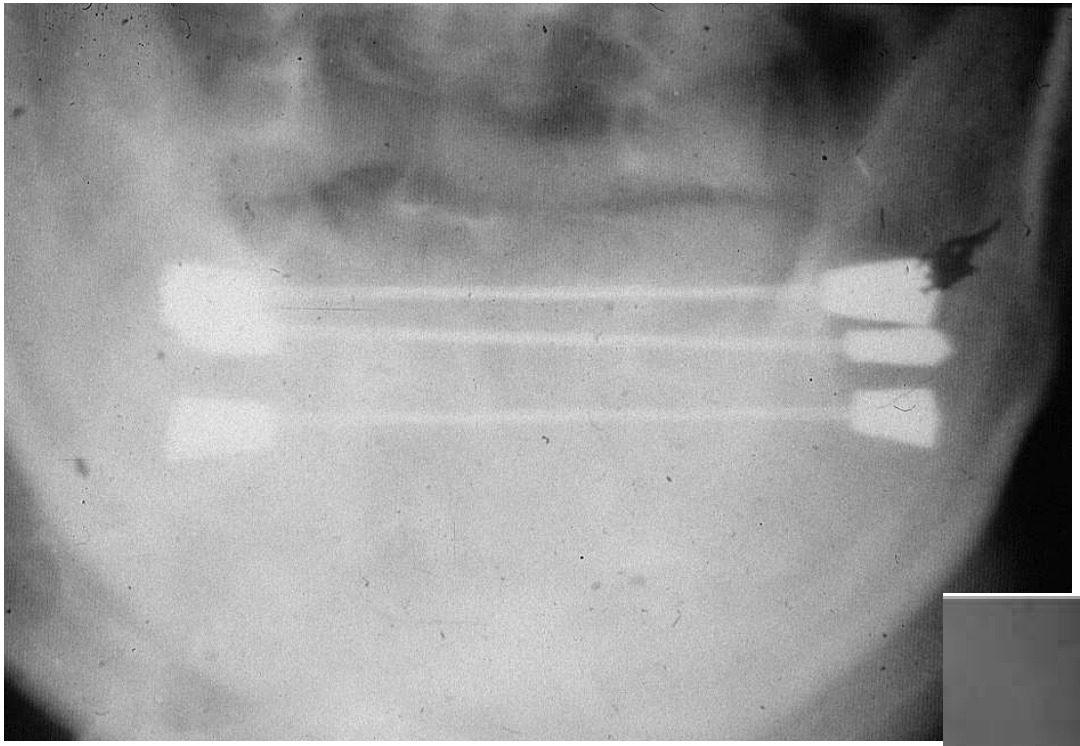
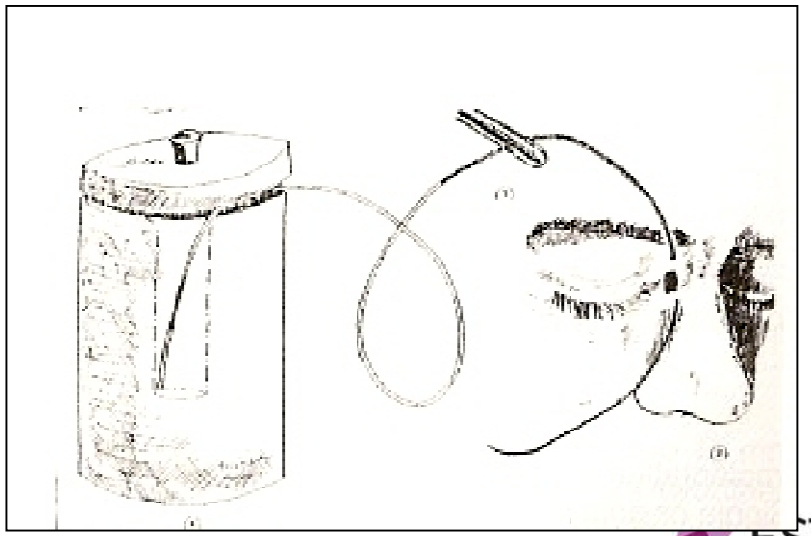
⇢ Hypodermic needles



Brachytherapy Technique

Silk wire

- 0.4 mm
- Iridium 192 wires
- Face / curvatures
- Preloading
- Preparation



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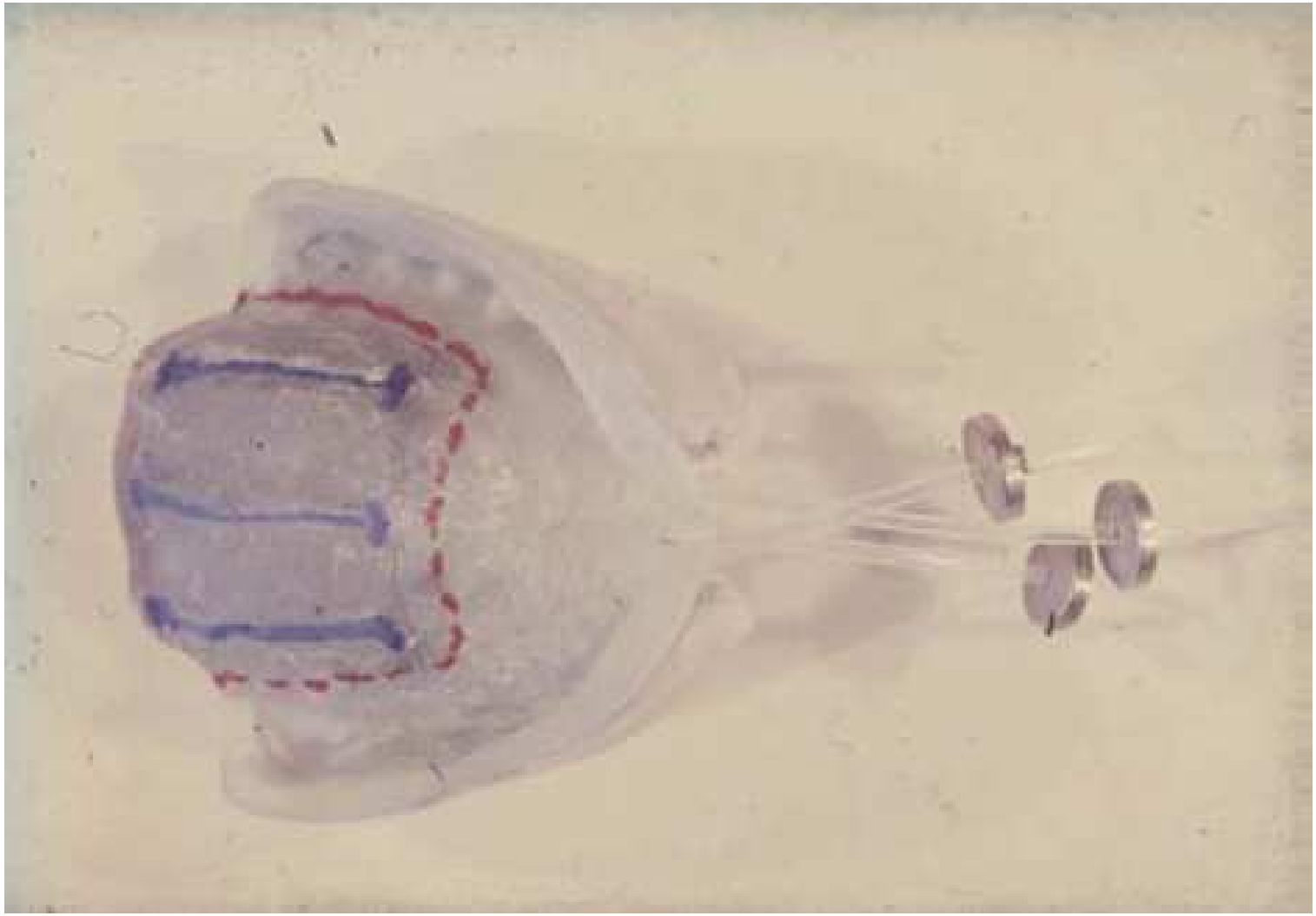
⇢ Intracavitary technique



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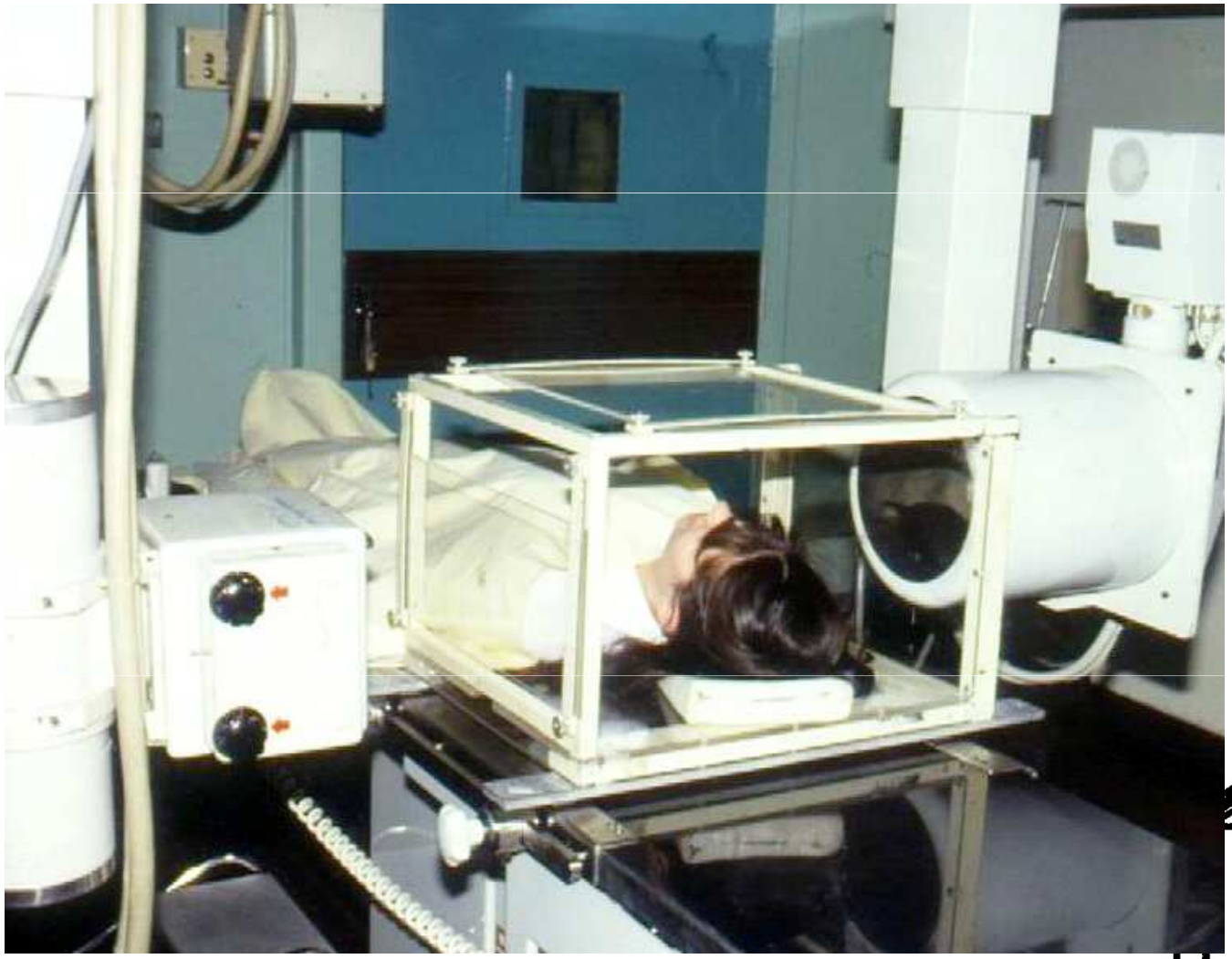
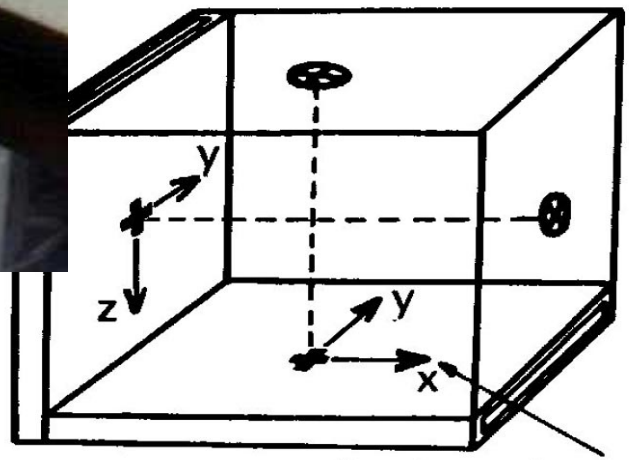
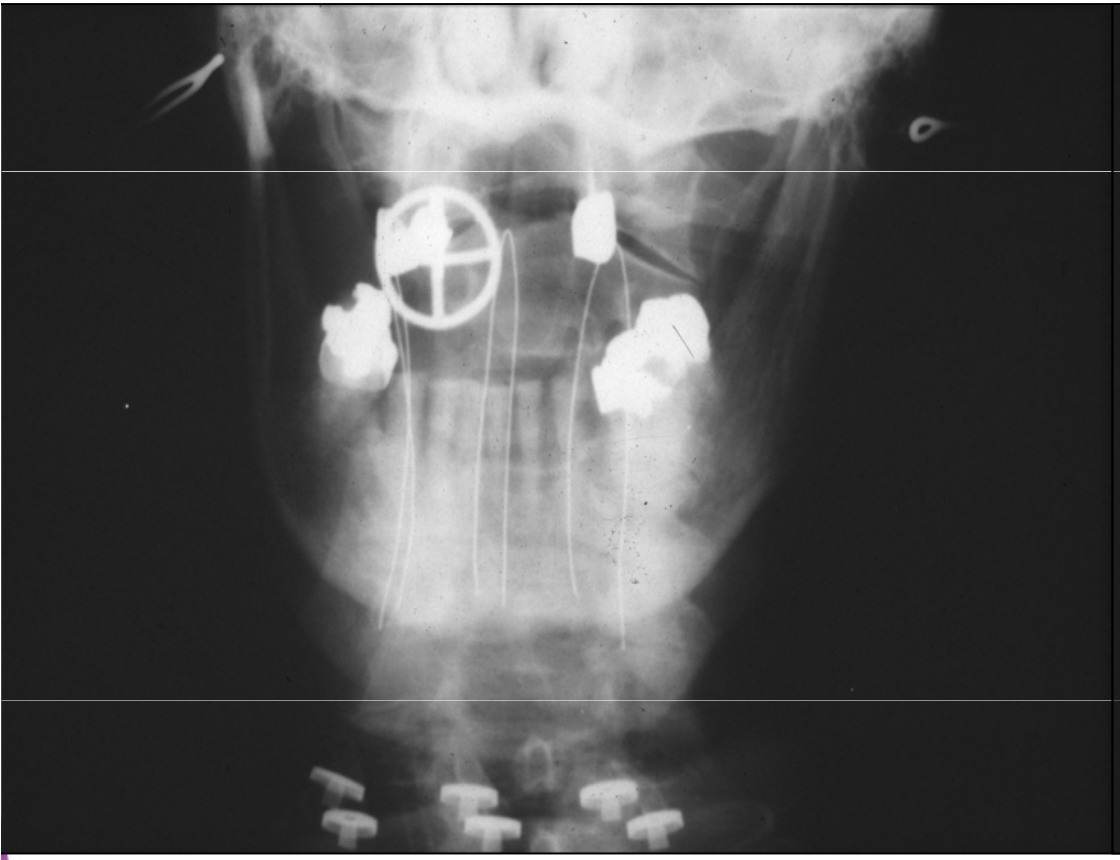
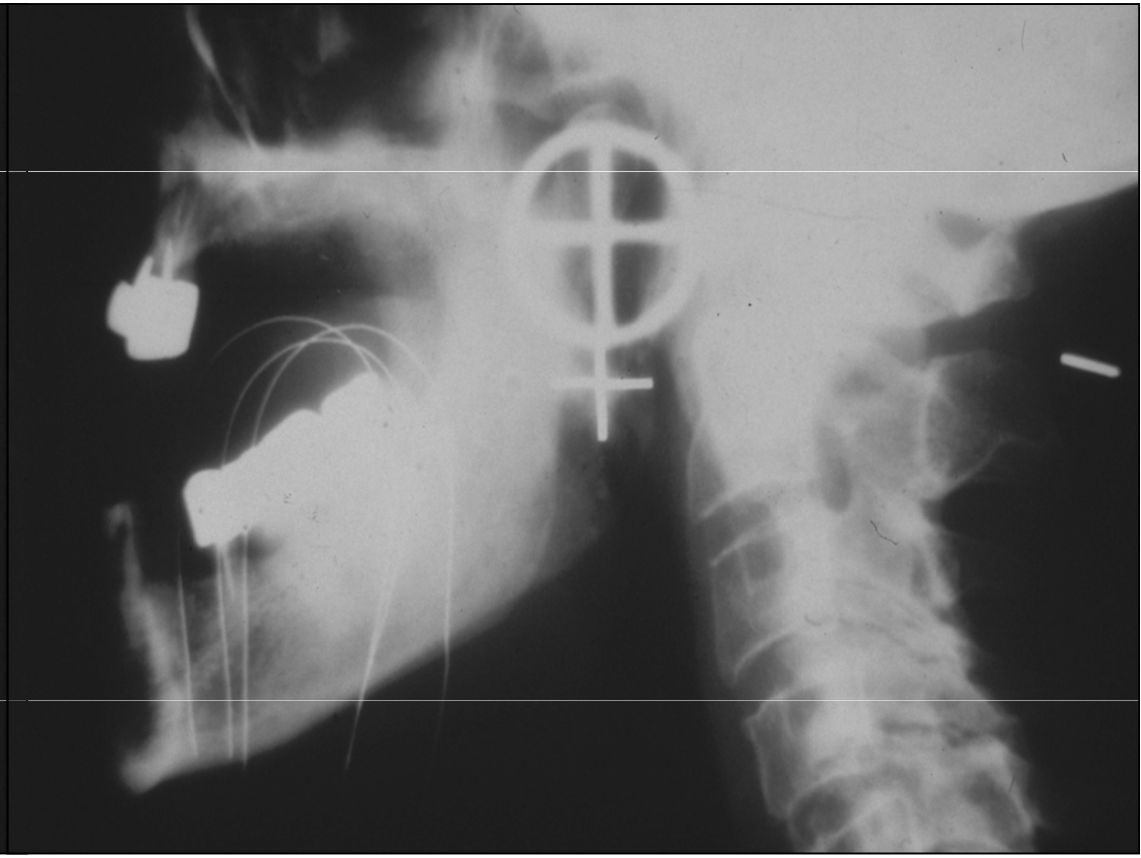
Orthogonal X rays

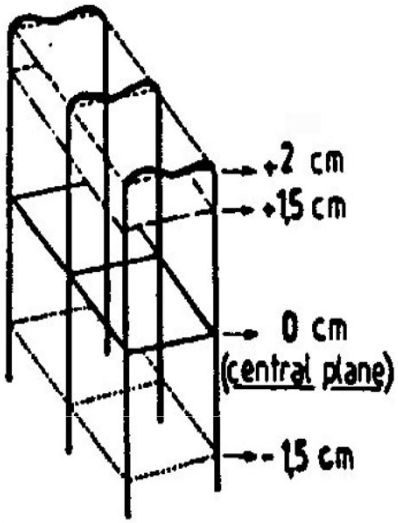


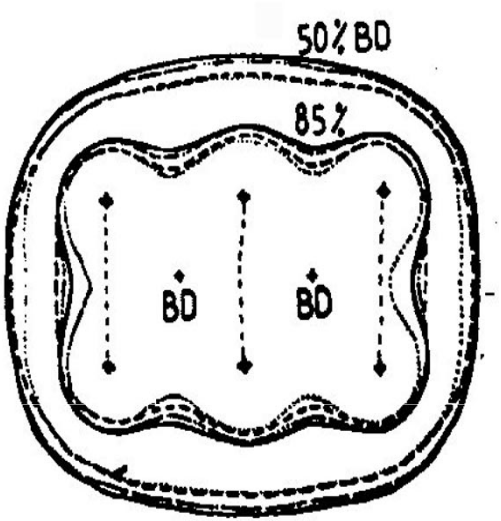






2D dosimetry



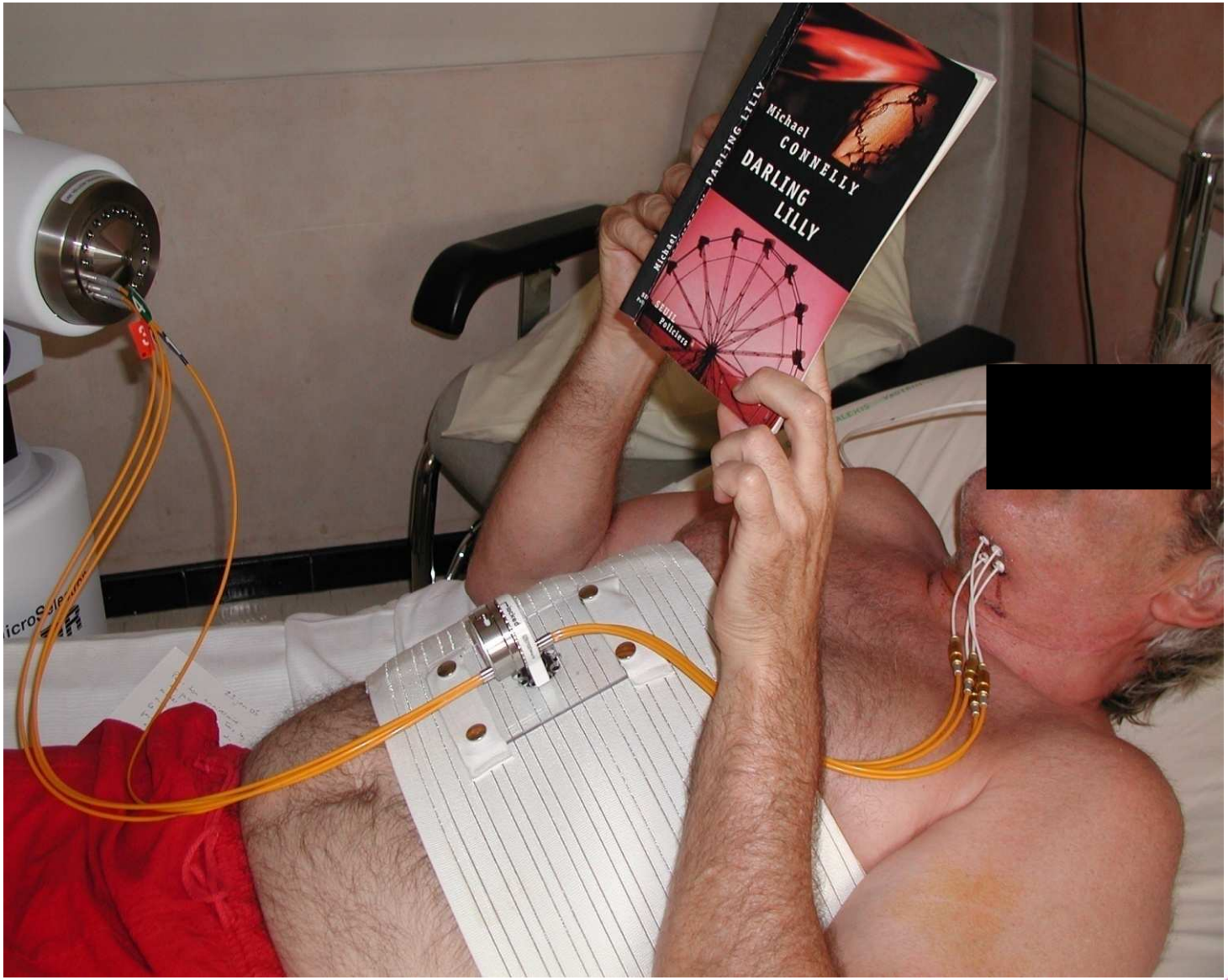


ESTRO School

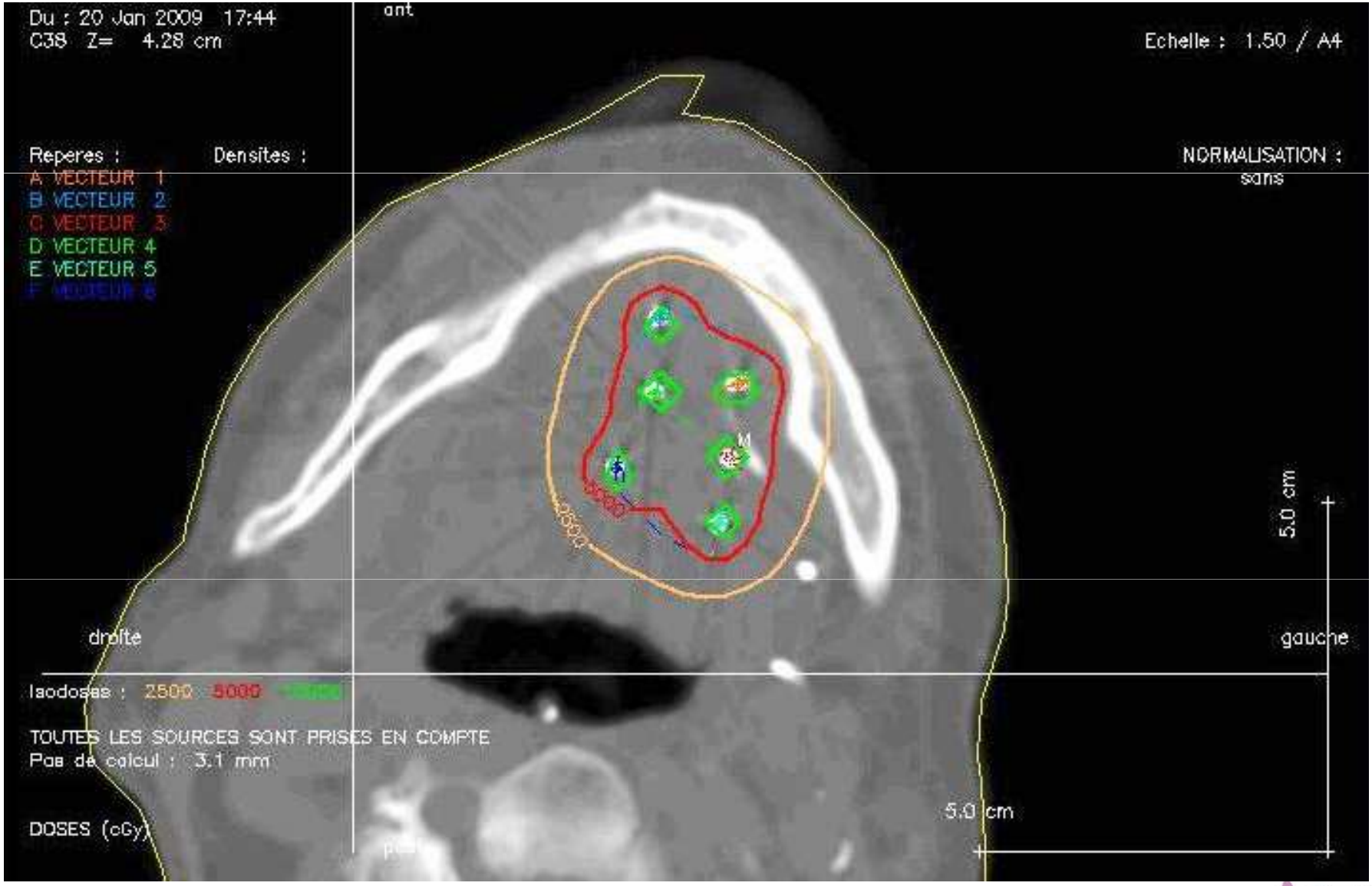
PDR / HDR

- Radioprotection
- 3D dosimetry
- Optimization (does not replace a bad implantation)
- DVH
- Pitfalls: loops
- PDR: experience from LDR / Modulation of dose rate (outcomes and morbity)
- HDR: less experience

PDR



ESTRO School


Du : 20 Jan 2009 17:44
C38 Z= 4.28 cm
ant
Echelle : 1.50 / A4
Reperes :
Densites :
A VECTEUR 1
B VECTEUR 2
C VECTEUR 3
D VECTEUR 4
E VECTEUR 5
NORMALISATION :
sans
5.0 cm
droite
gauche
Isodoses : 2500 5000
TOUTES LES SOURCES SONT PRISES EN COMPTE
Pas de calcul : 3.1 mm
DOSES (cGy)
5.0 cm

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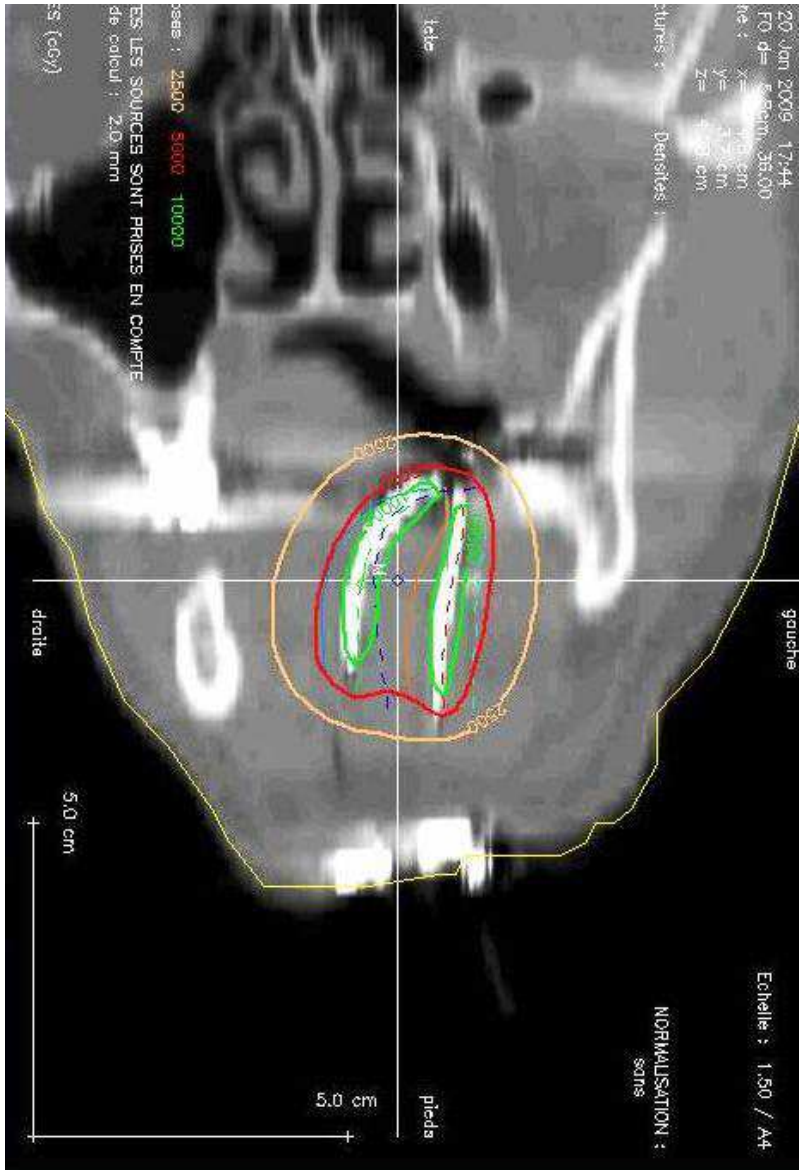
3D dosimetry



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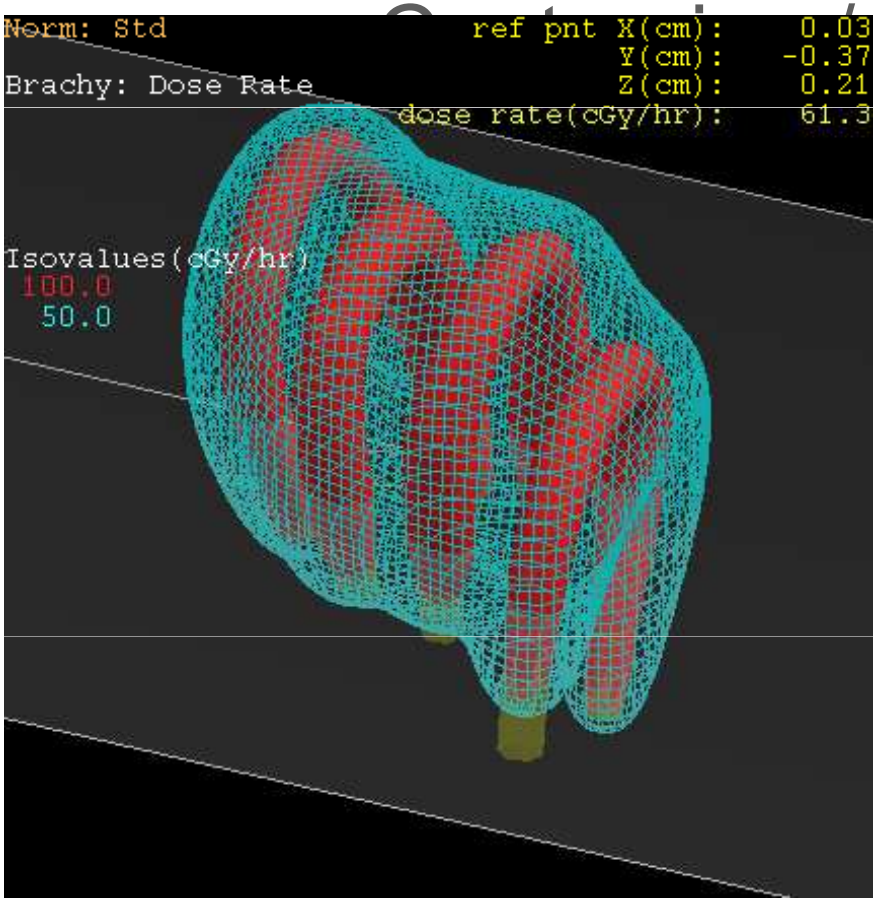
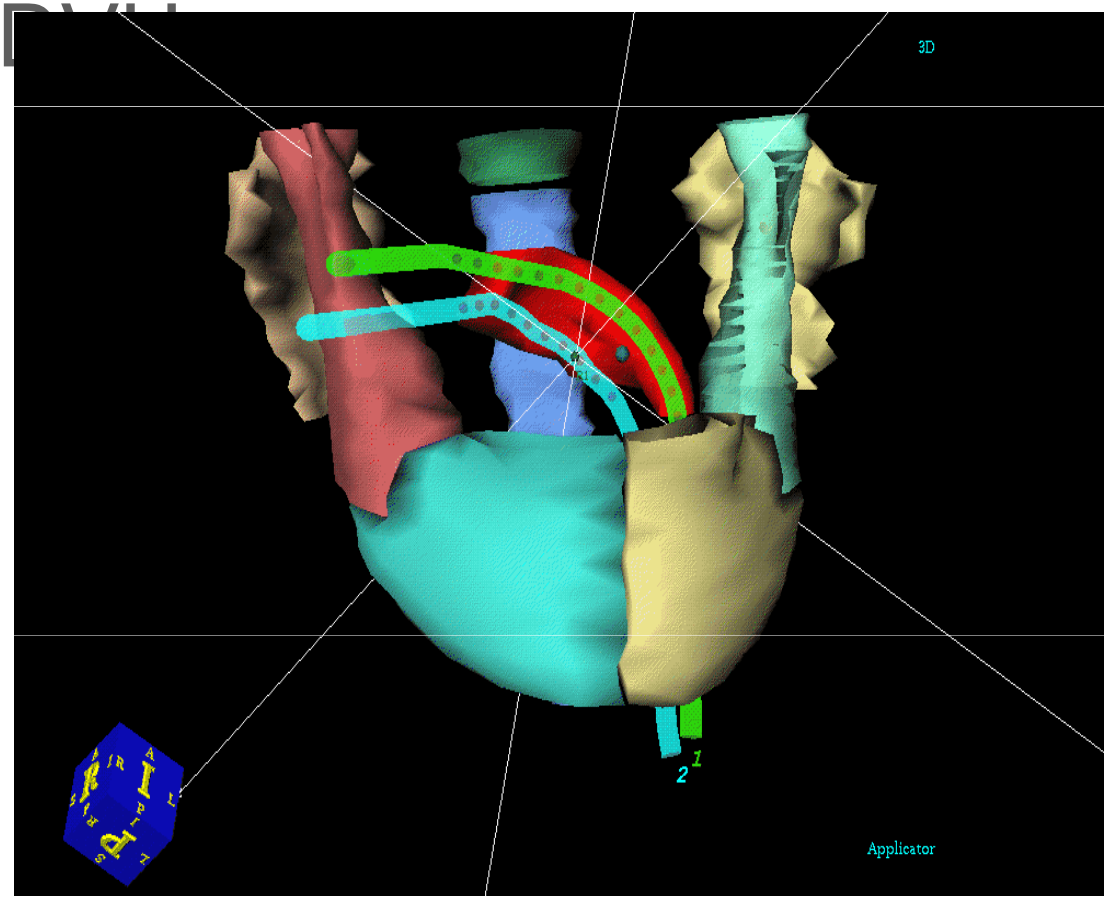
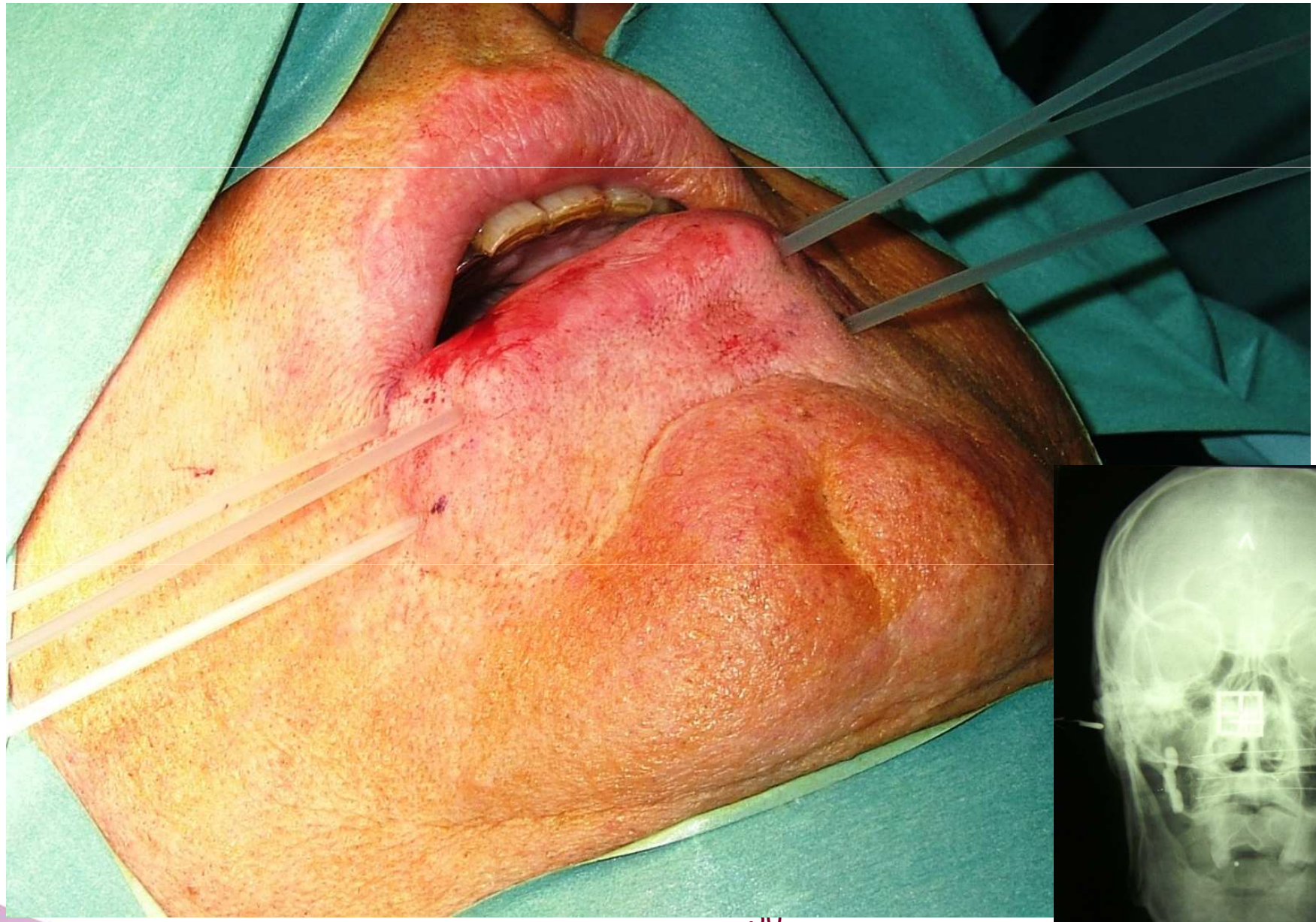

Norm: Std
ref pnt X(cm): 0.03
Y(cm): -0.37
Z(cm): 0.21
Brachy: Dose Rate
dose rate(cGy/hr): 61.3
Isovalues(cGy/hr)
100.0
50.0


3D
Applicator

49

Lip



⇢ Lip

- Width: no limit
- Discuss EBRT from 5 cm
- CTV = visible lesion + at least 5-10 mm safety margins
- Upper lip or commisura : plastic tubes better
- Lower lip: rigid needles technique +/- template or plastic tubes
- Protector device: mandibule and opposite lip
- 60-75 Gy

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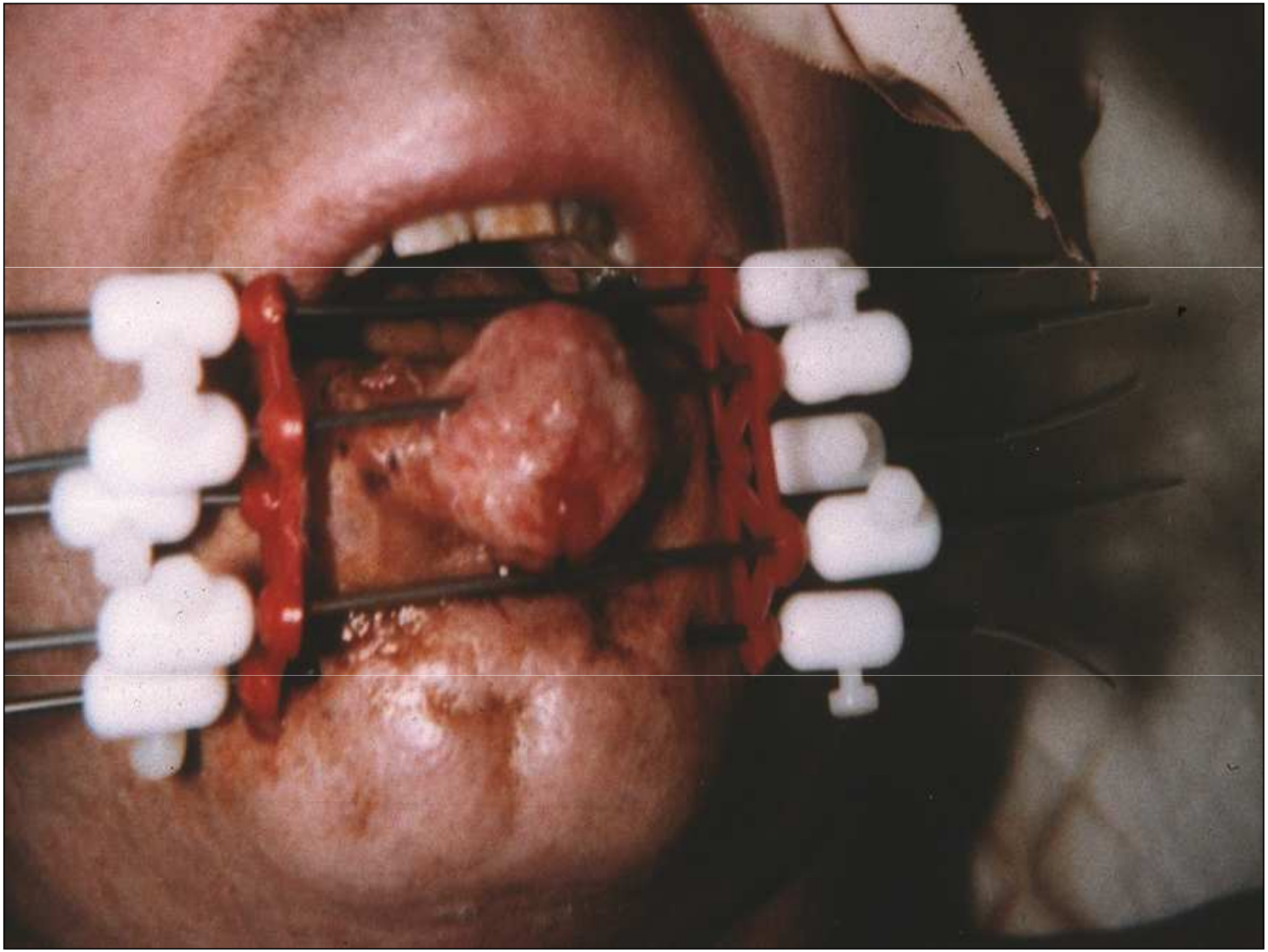
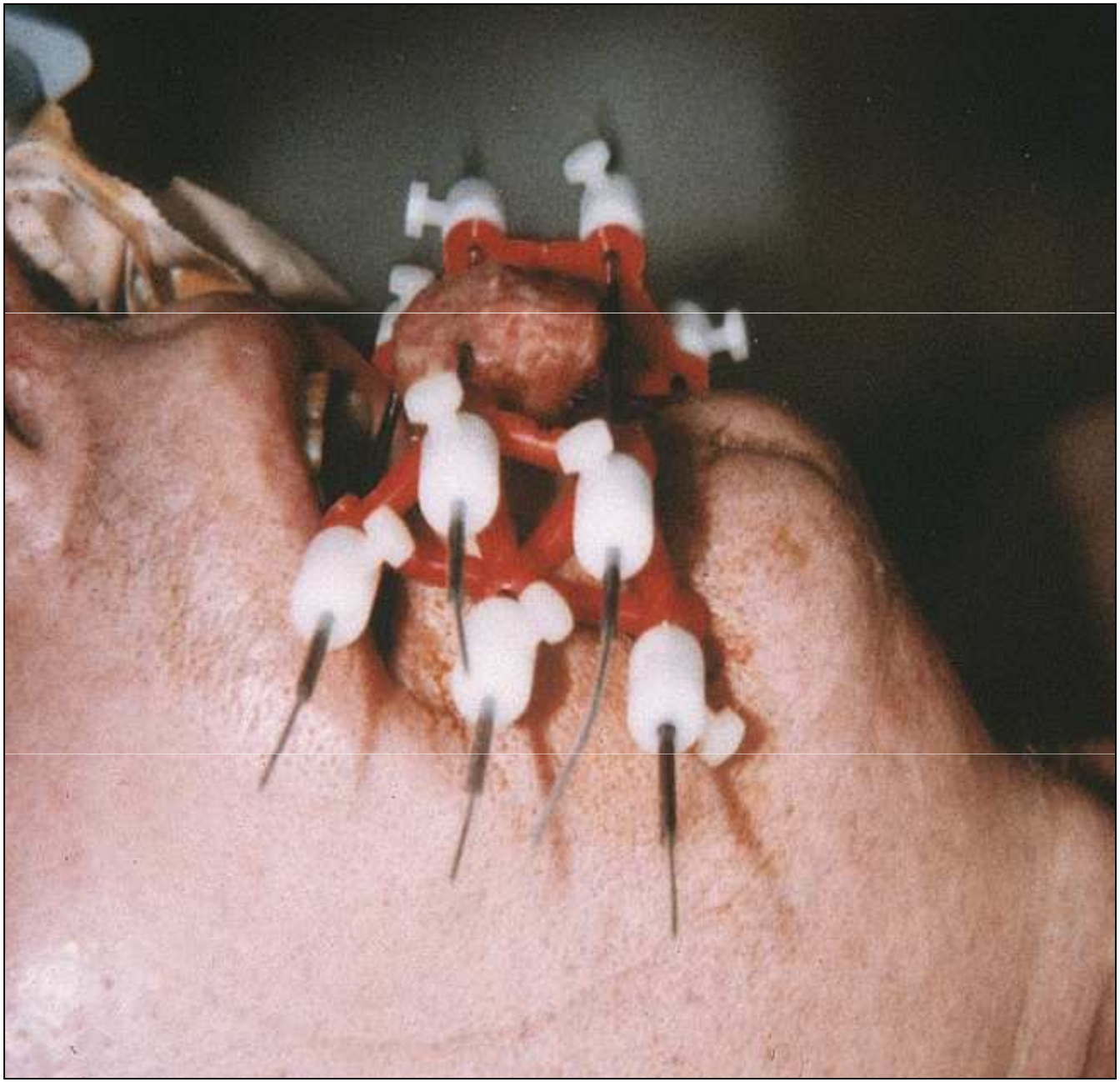
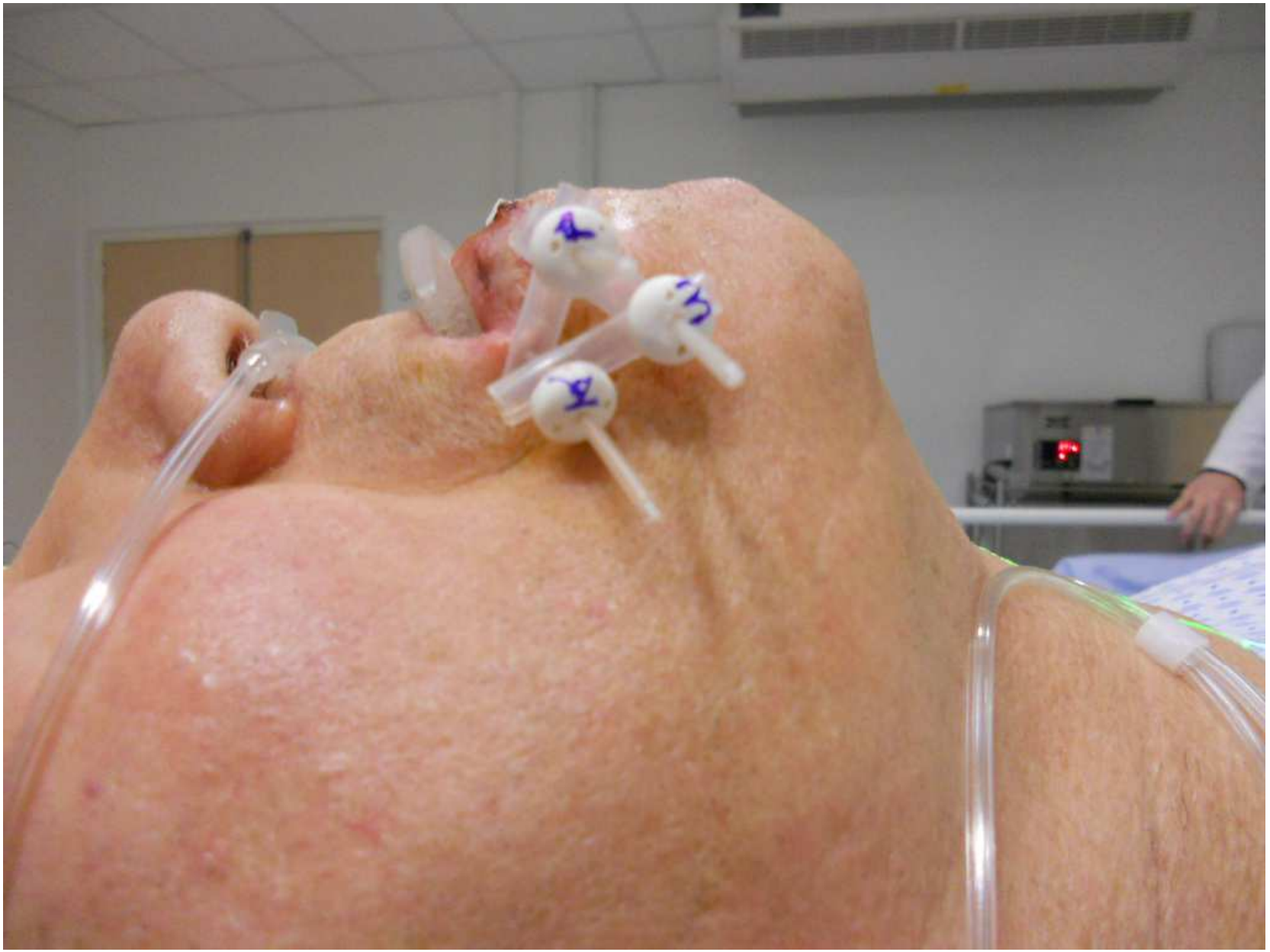


ESTRO School



ESTRO School



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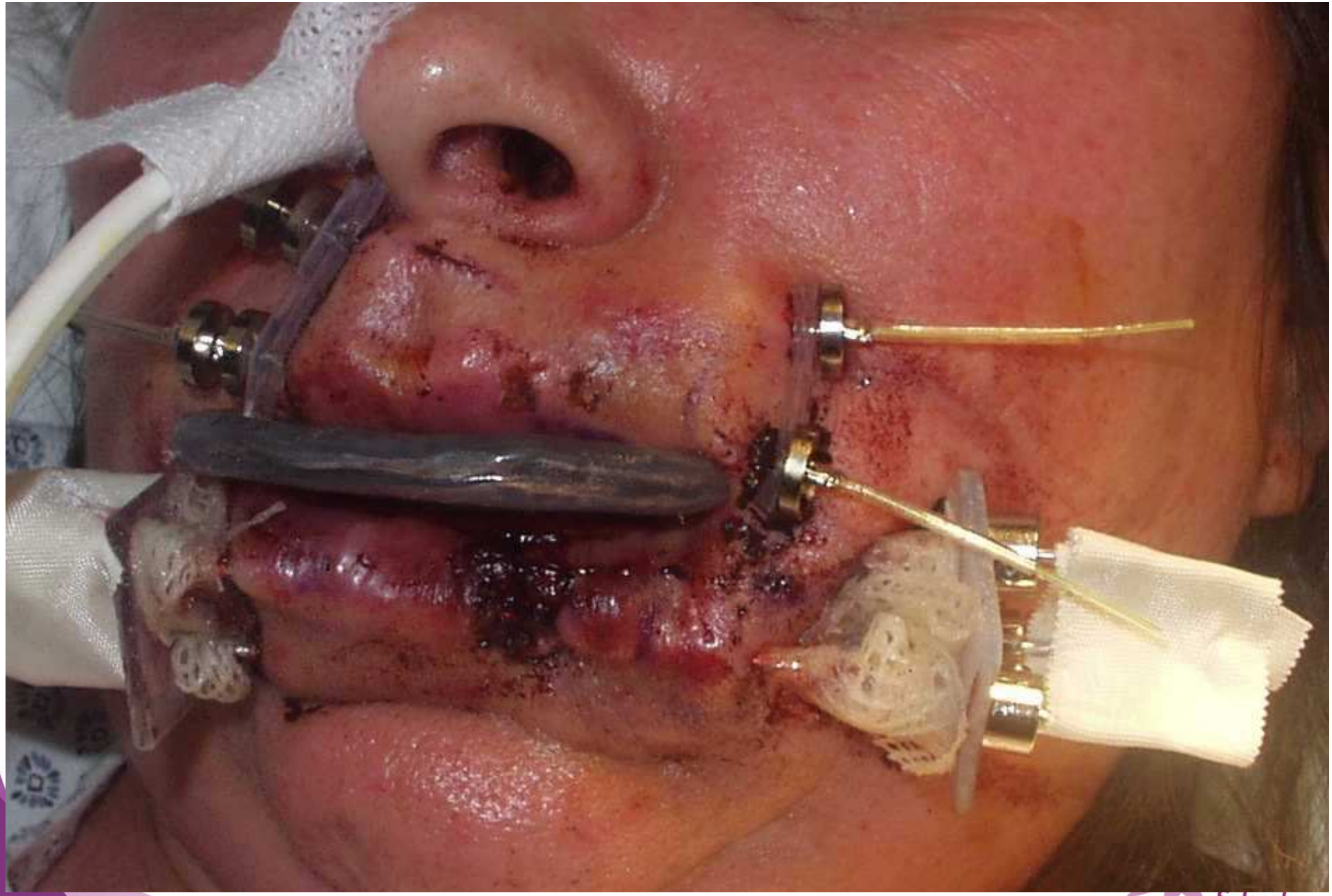
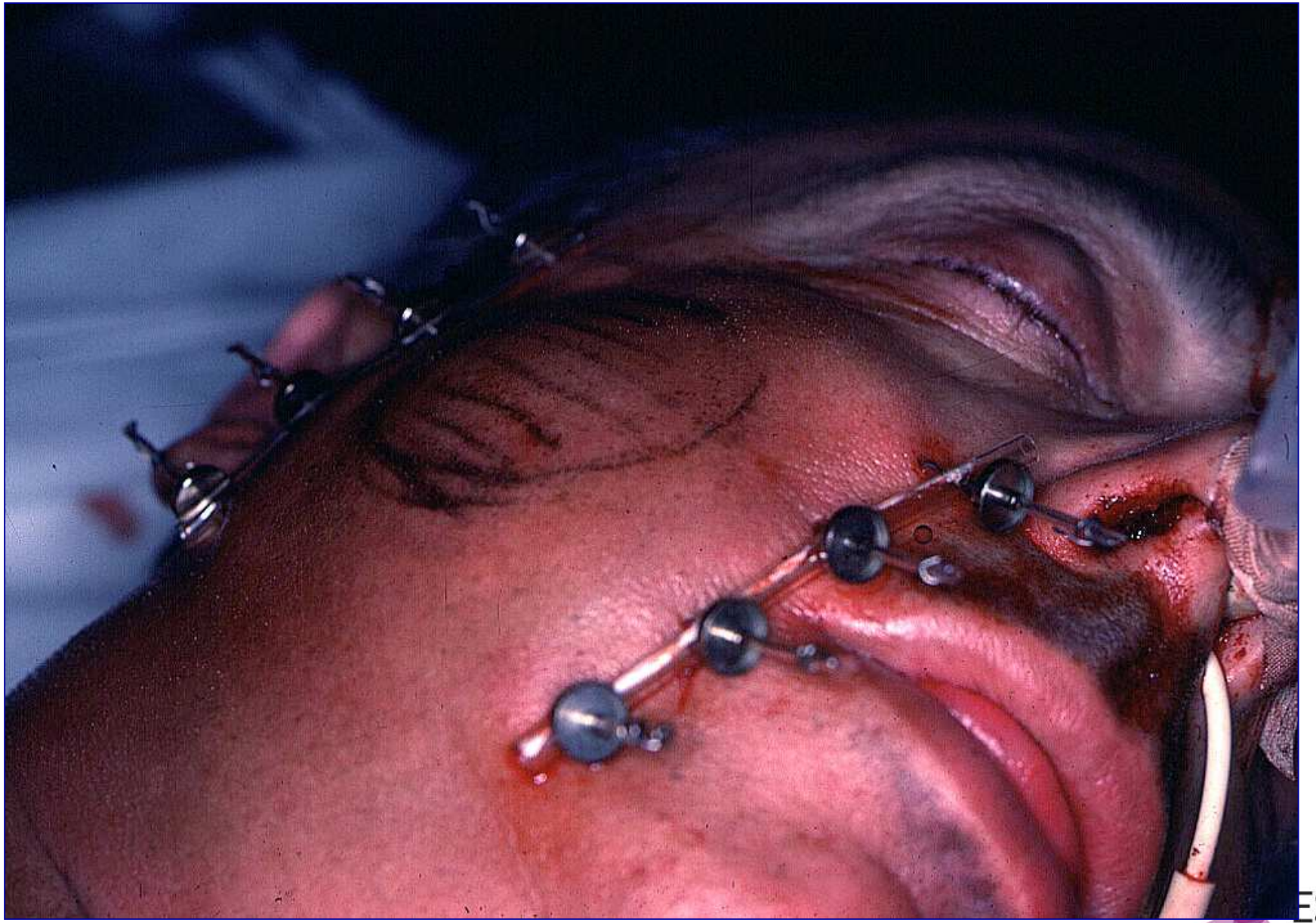
Lip

ESTRO School



Oral mucosa



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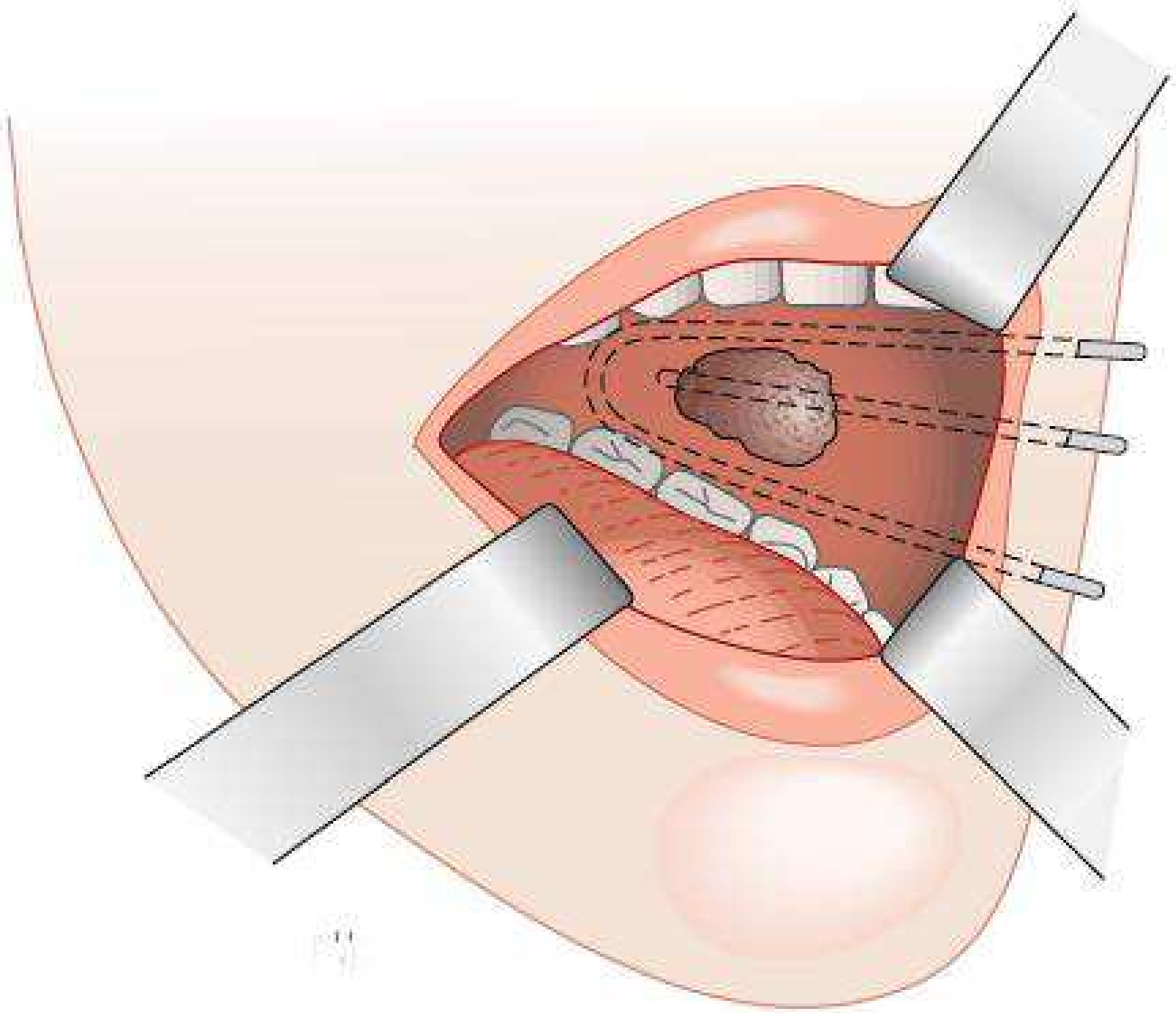
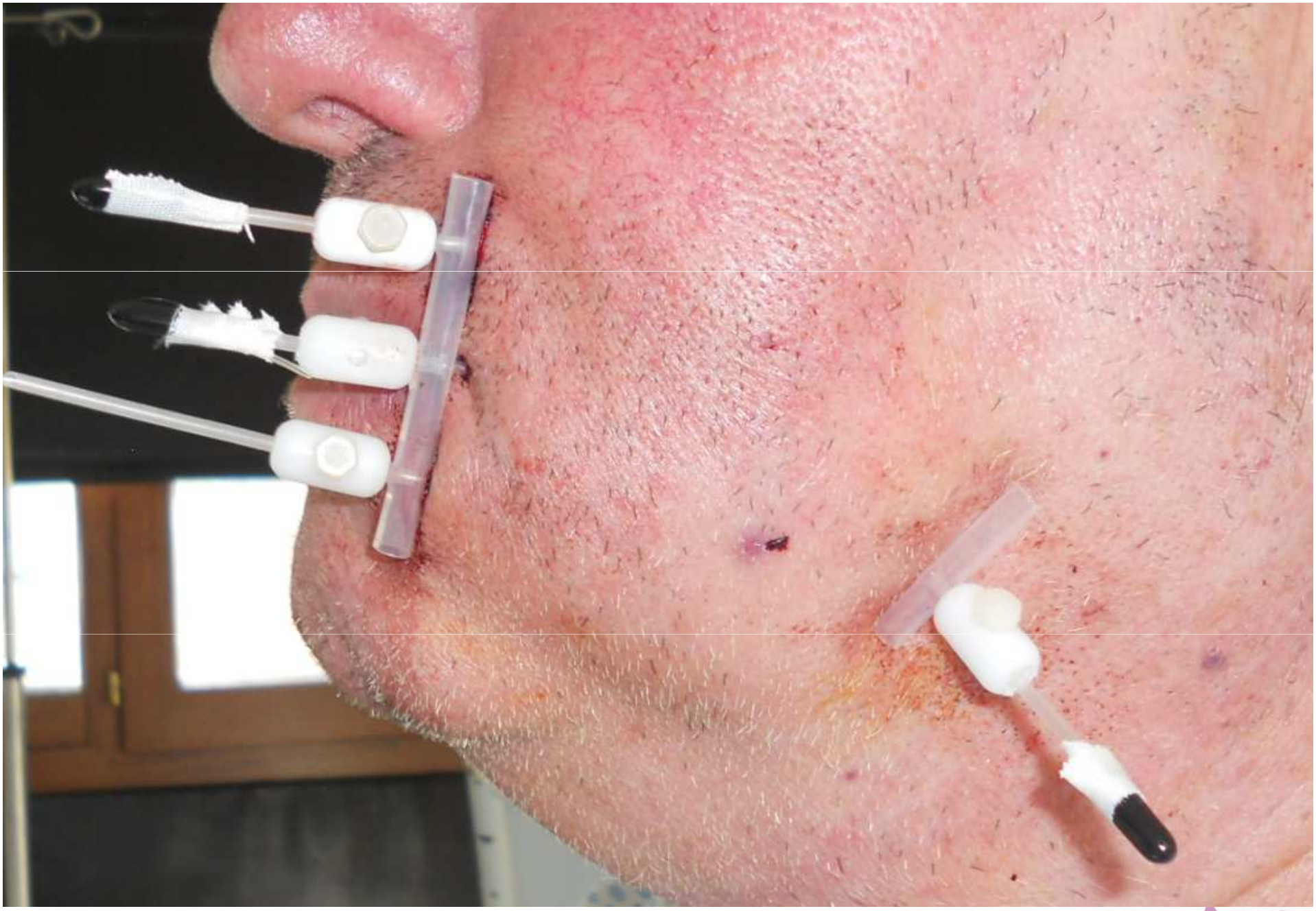
ESTRO School





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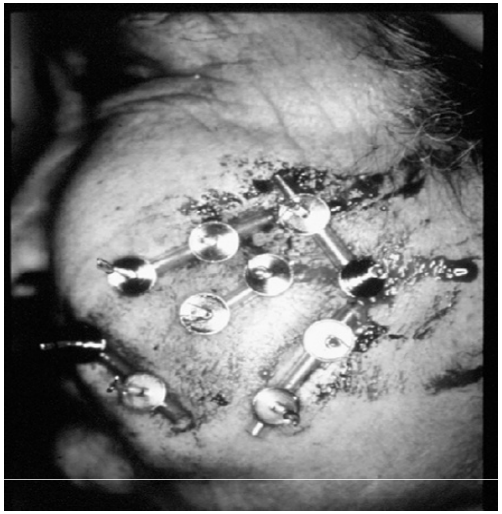
Oral Mucosa



Recommendations

- Width < 4 cm
- Thickness < 1.5 cm
- No extent in bucco-alveolar sulcus or the intermaxillary commisure
- Safety margins: 5-10 UD, 10 mm AP

65-70 Gy (25-30 Gy after EBRT)

Lymph node involvement uncommon

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Oral cavity: indication

- **Lip :**
  - **no tumor size. limit: T1-T3**
  - **contra-indication : bone extension**

- **Buccal mucosa**
  - **tumor up to 4 cm: T1, limited T2**
  - **no extent in the gingivobuccal sulcus**

BT as sole treatment

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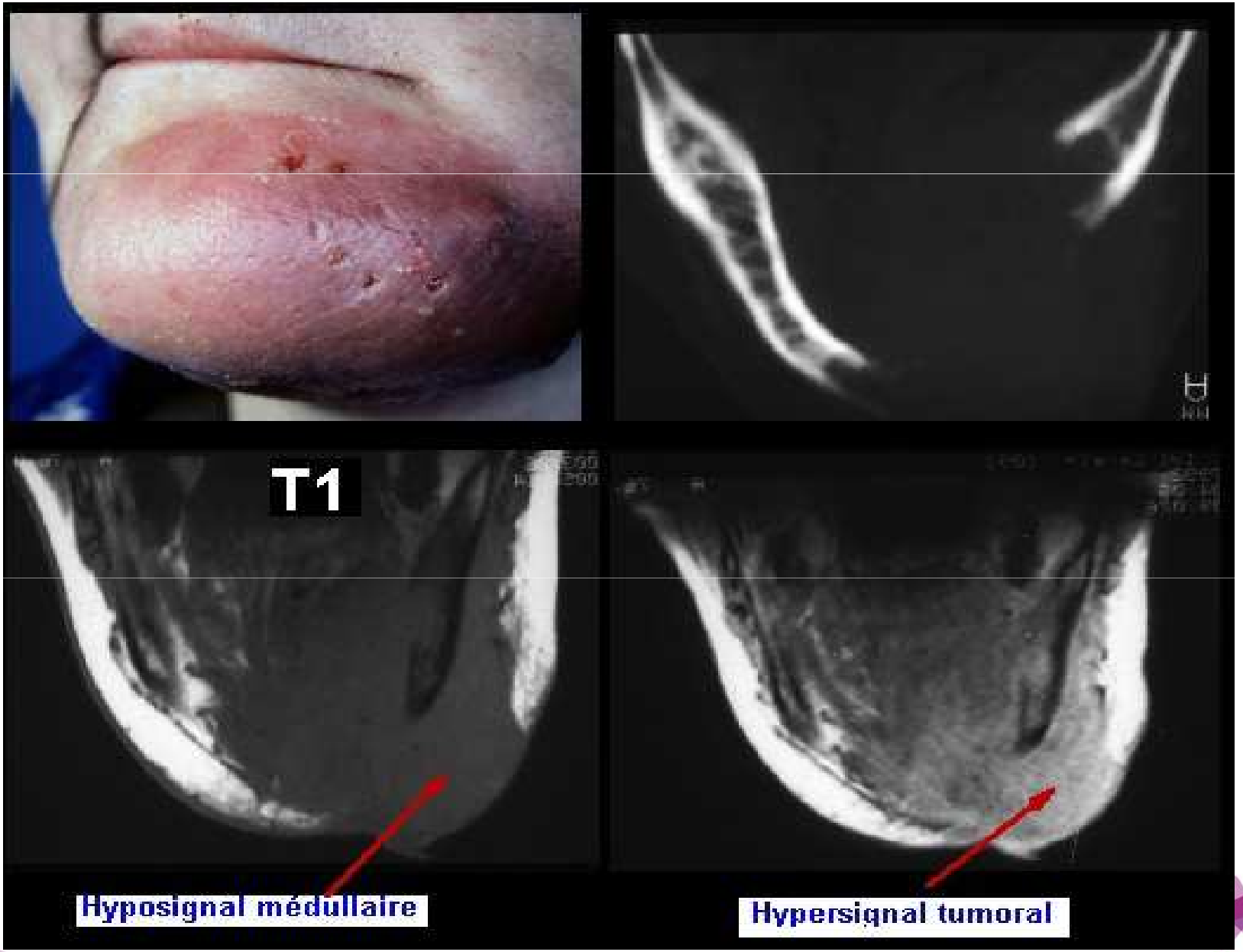
Bone extension



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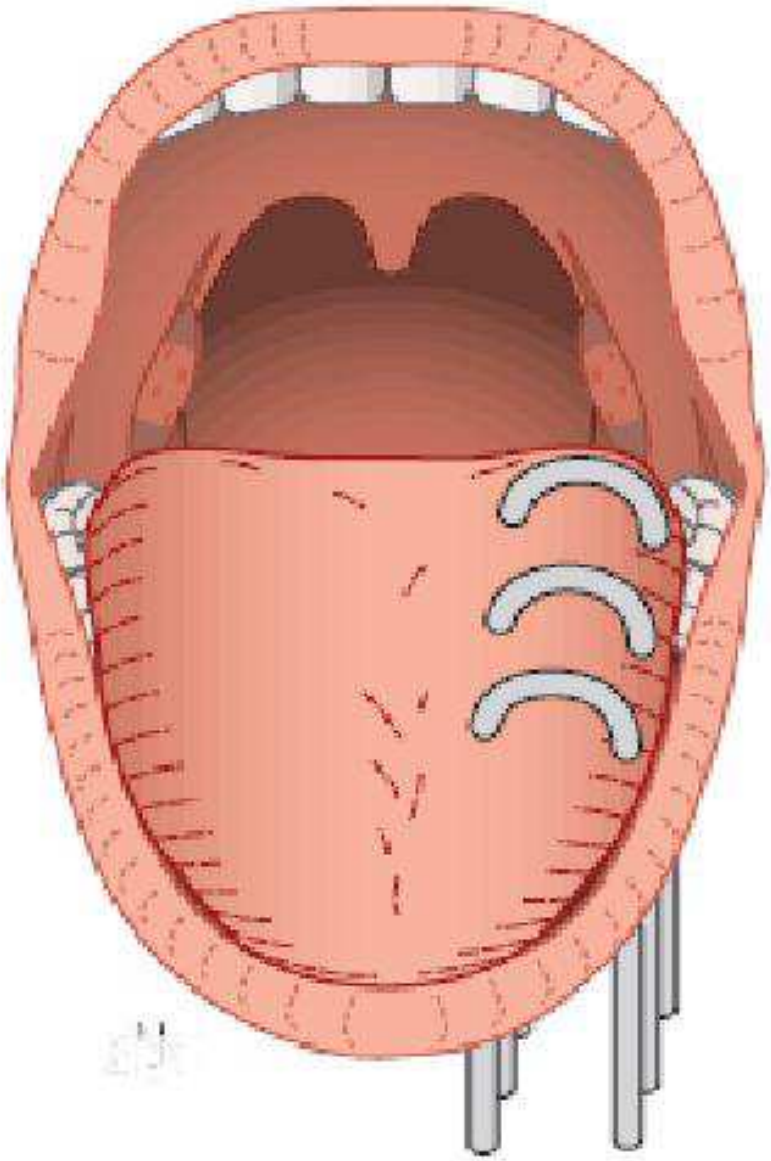
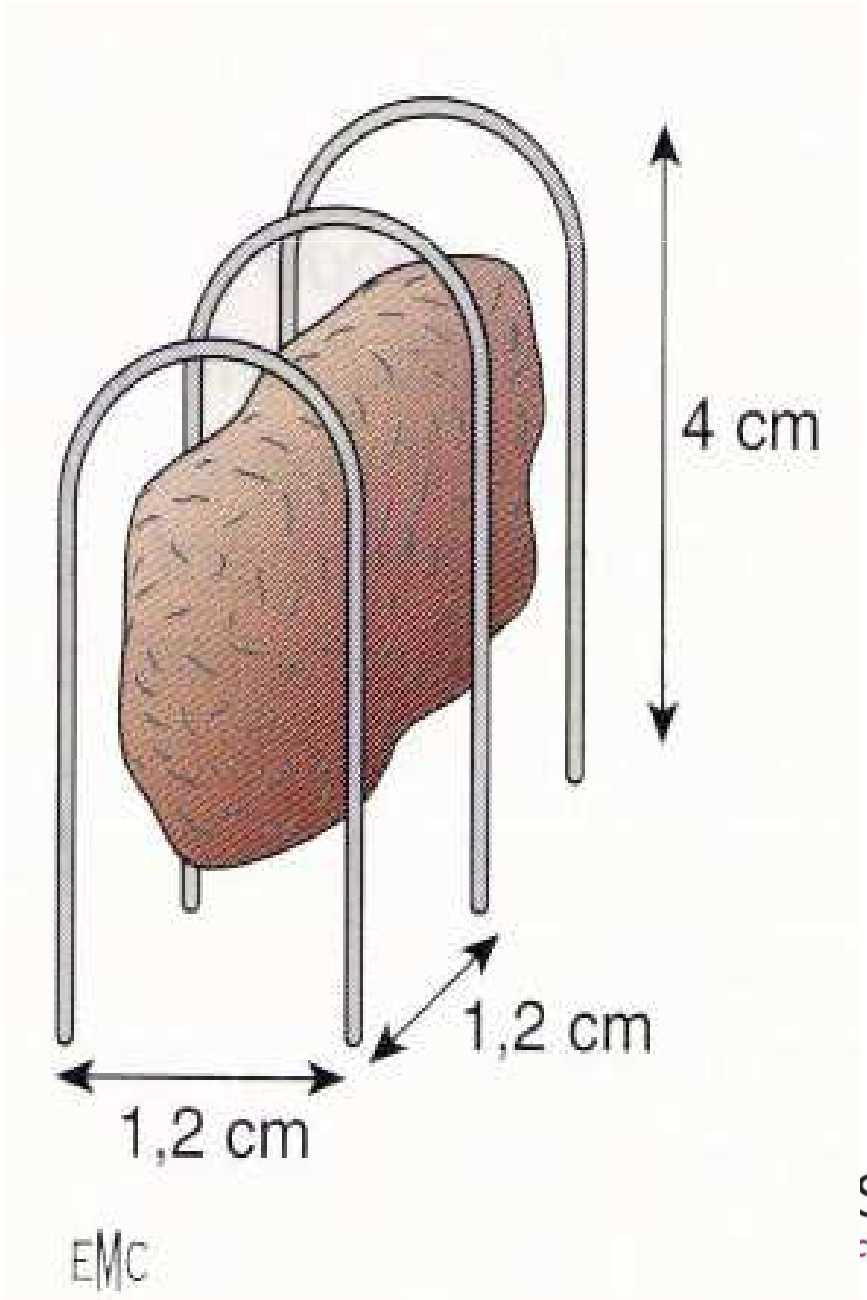
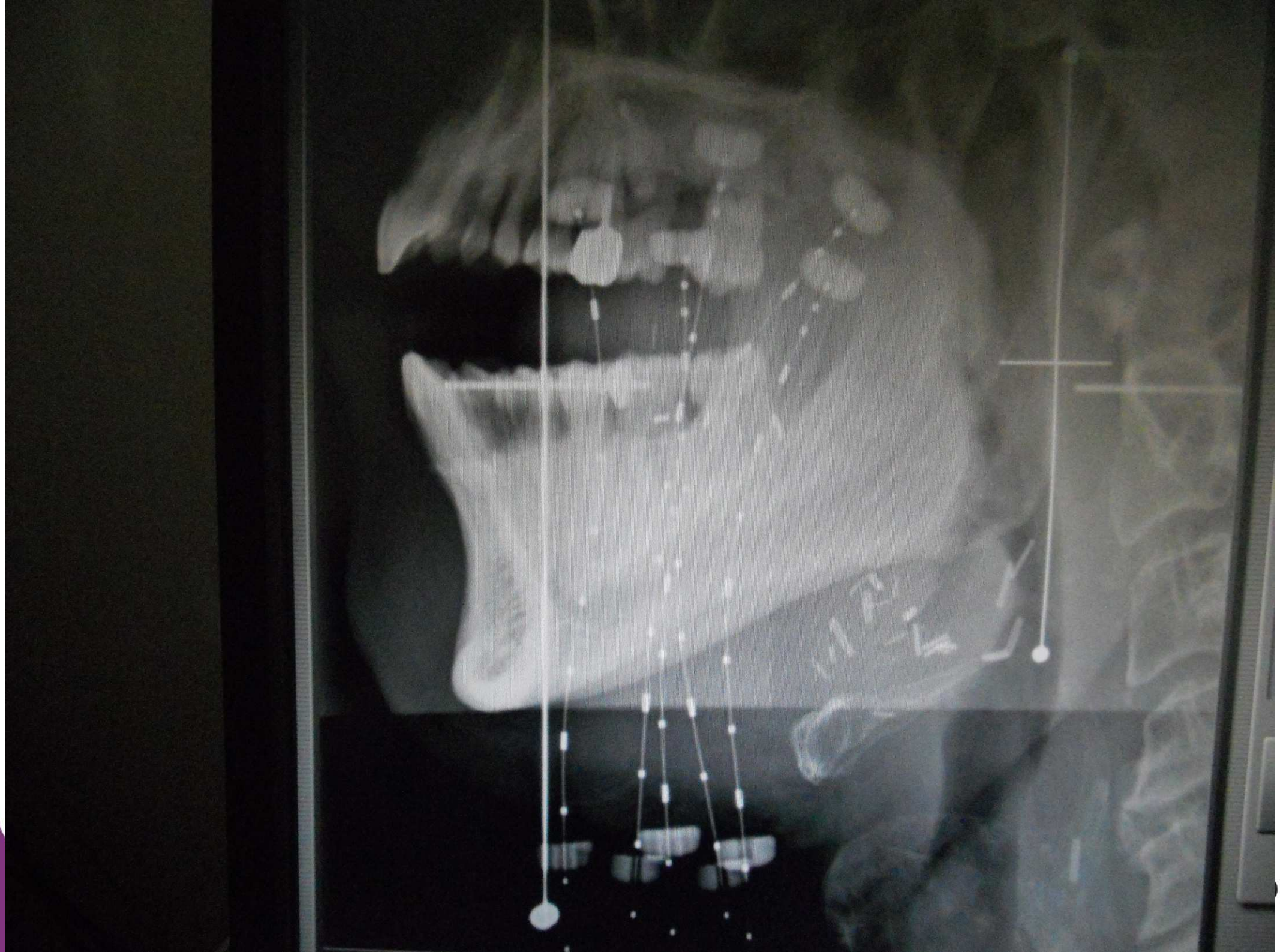
Mobile Tongue

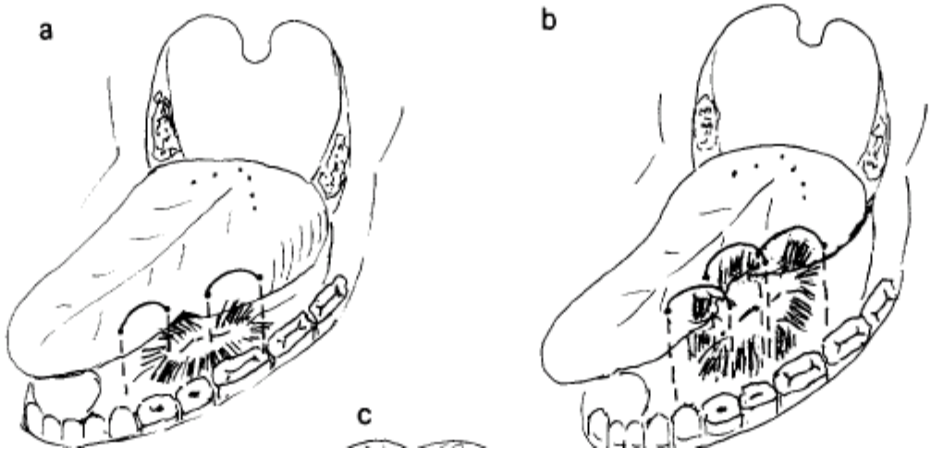






Oral cavity: indication

- Mobile tongue:
  - tumor up to 4 cm in size
  - T1, limited T2



- Floor of mouth:
  - less than 3 cm in size
  - Vicinity of less than 1 cm with the maxillary bone
  - T1,very limited T2

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Mobile tongue cancer

Iridium 192 implantation alone

	local failure
Superficial tumours (108 pts)	9 %
Infiltrating tumours (90 pts)	22 %

$p < 0.001$

J.J. Mazeron et al, IJROBP 19, 1369, 1990

⇢ Mobile tongue and floor of mouth

Iridium 192 alone	at 5 years	
Intersource spacing	local fail.	necrosis
9-14 mm (204 pts)	14 %	33 %
15-20 mm (70 pts)	24 %	44 %
	p=0.13	p=0.04

J.M. Simon et al, Radiother. Oncol. 26, 19, 1993

Mobile tongue and floor of mouth

T1-2 without gingival extension:

- Primary tumor: 65-70 Gy implant.
- Neck node areas: either close follow-up or neck dissection (+ 50-65 Gy if N+, with a shielding of the implanted area).

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Oral cavity

Floor of mounth

- Safety margin: at least 5 mm
- 65 Gy (or EBRT 45-50 + BT 15-25 Gy)
- Post-op: 50-65 (10-25 with EBRT)
- Salvage 60-65 Gy

Mobile tongue:

- Safety margin: at least 5 mm
- 65-75 Gy (or 25-30 Gy after EBRT)
- Post-op: 50-60 Gy
- Salvage: 60 gy
- Dose rate / pulse : 0.3 – 0.7 Gy / h

Osteonecrosis

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Lead Gutter

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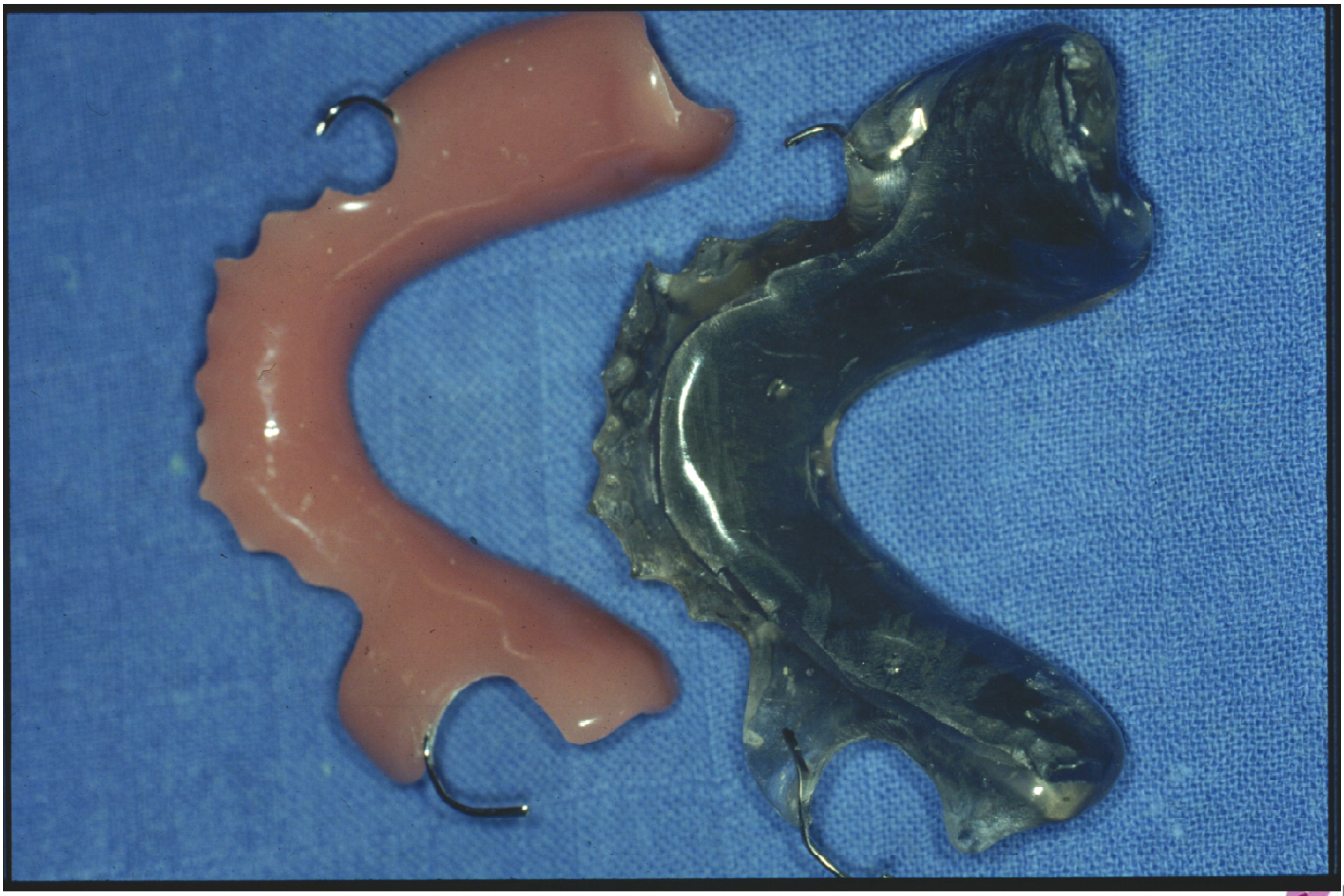
Lead gutter



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Oropharynx

General recommendations

- Tonsila, Soft palate, Base of tongue
- Tumors ≤ 5 cm
- Contra indicated if extension to retromolar trigone, nasopharynx, larynx, hypopharynx, bone
- BT may be used as sole treatment in exophytic tumor ≤ 1 cm, in recurring or new cancer in previously irradiated area
- BT as a boost / Combinated with EBRT.

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General recommandations

- CTV = GTV + at least 1 cm
- Plastic tube technique
- Lead gutter if invasion of mobile tongue
- Implant removal in the operating room
- Antibiotics and steroids may be indicated

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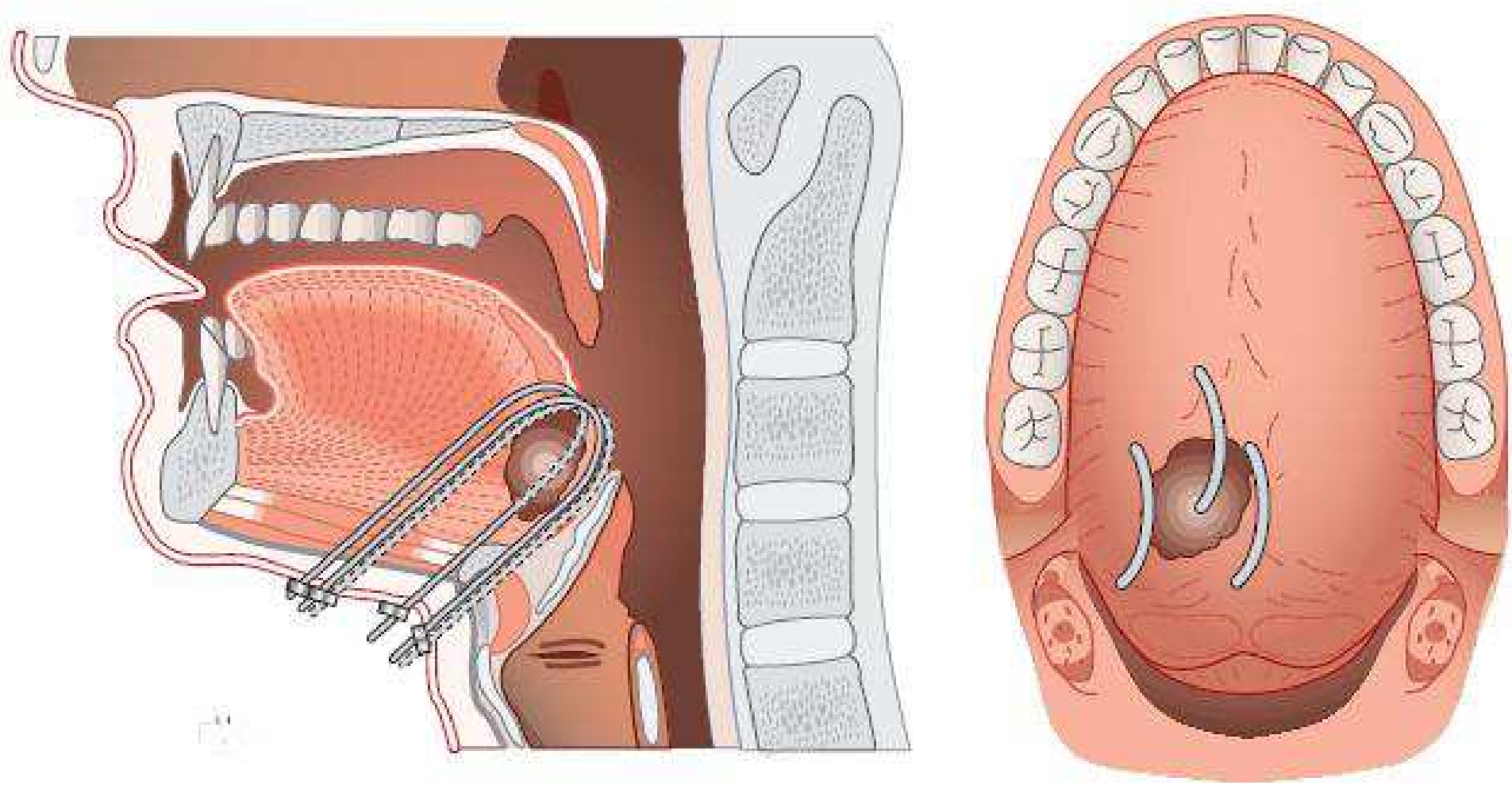
Base of tongue



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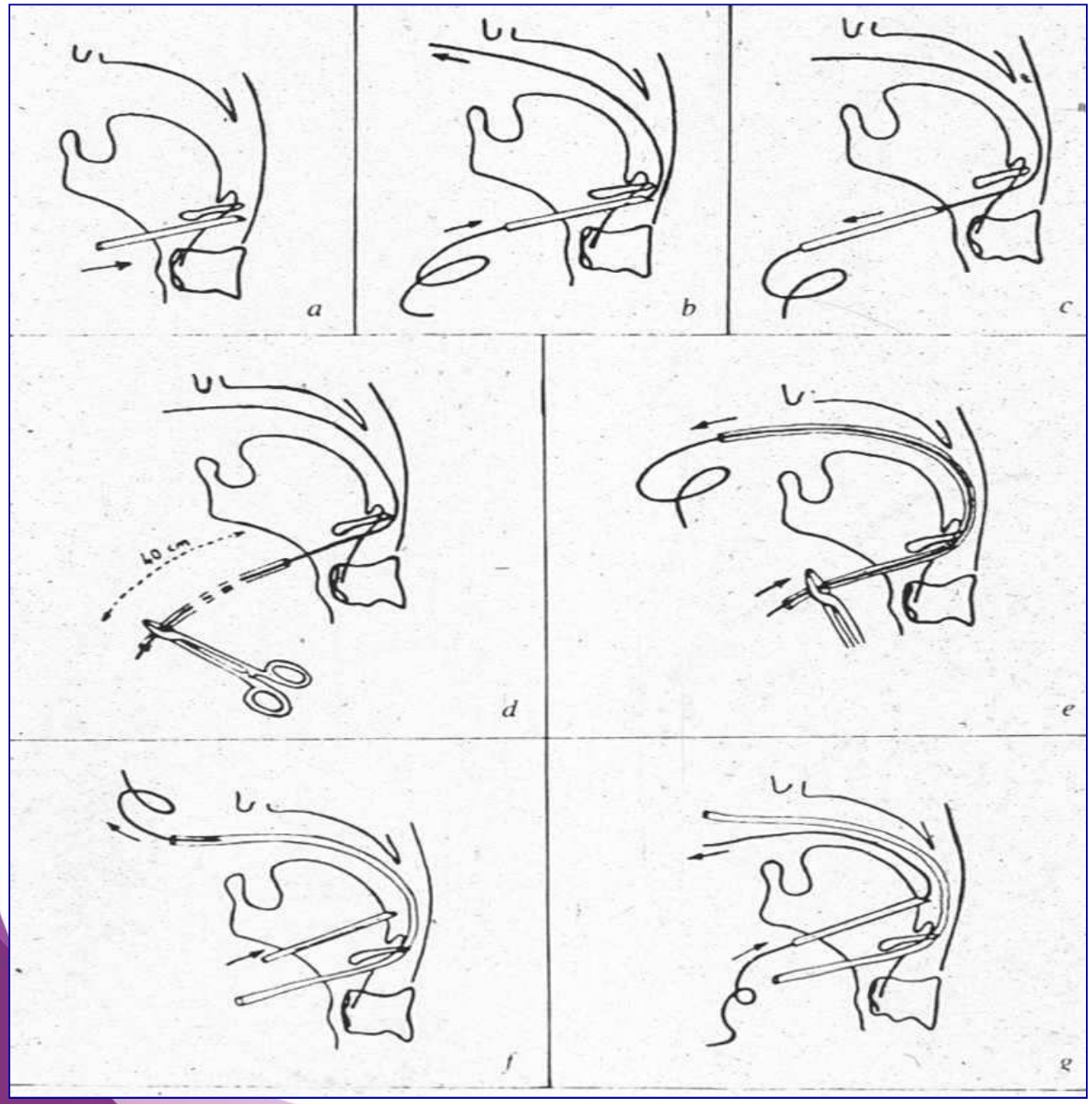
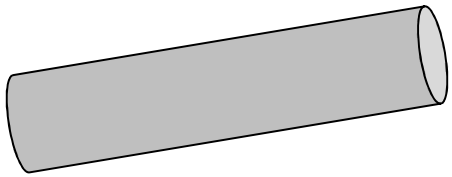
Base of tongue



Vascular guide wire



Tube leader

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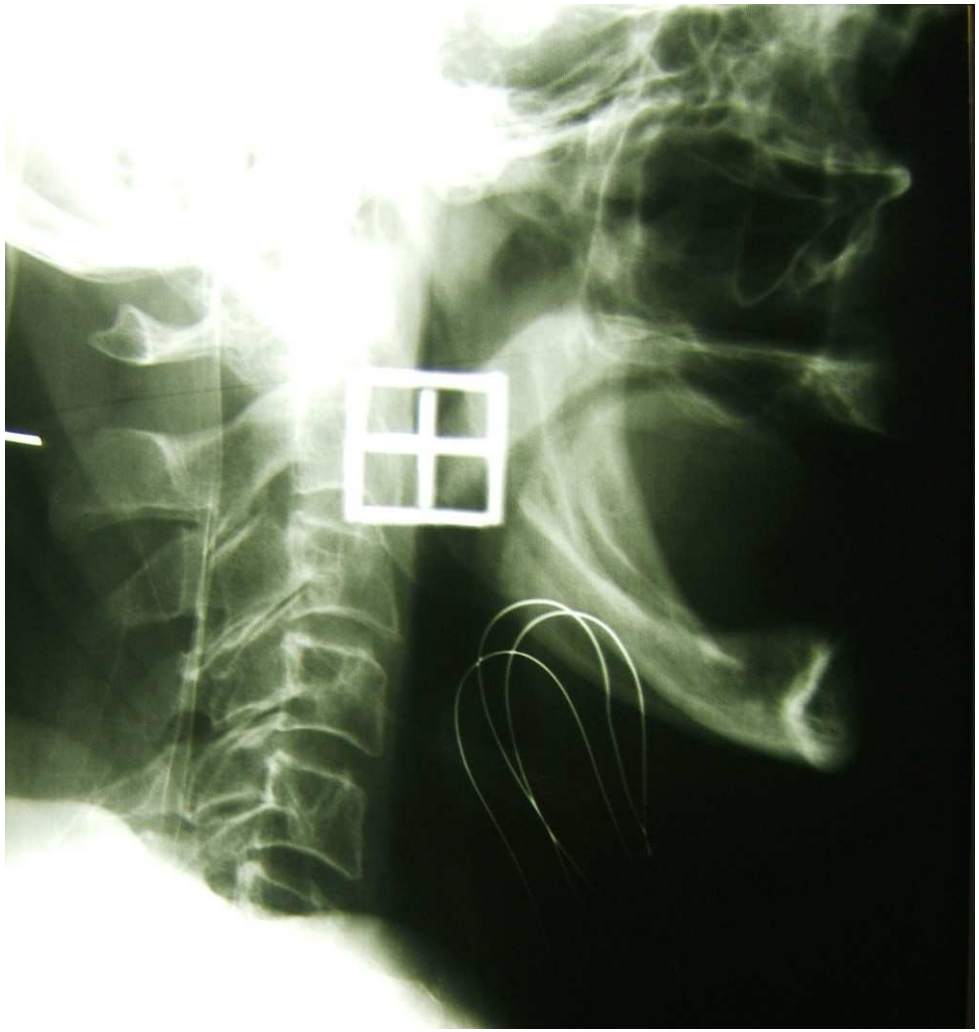
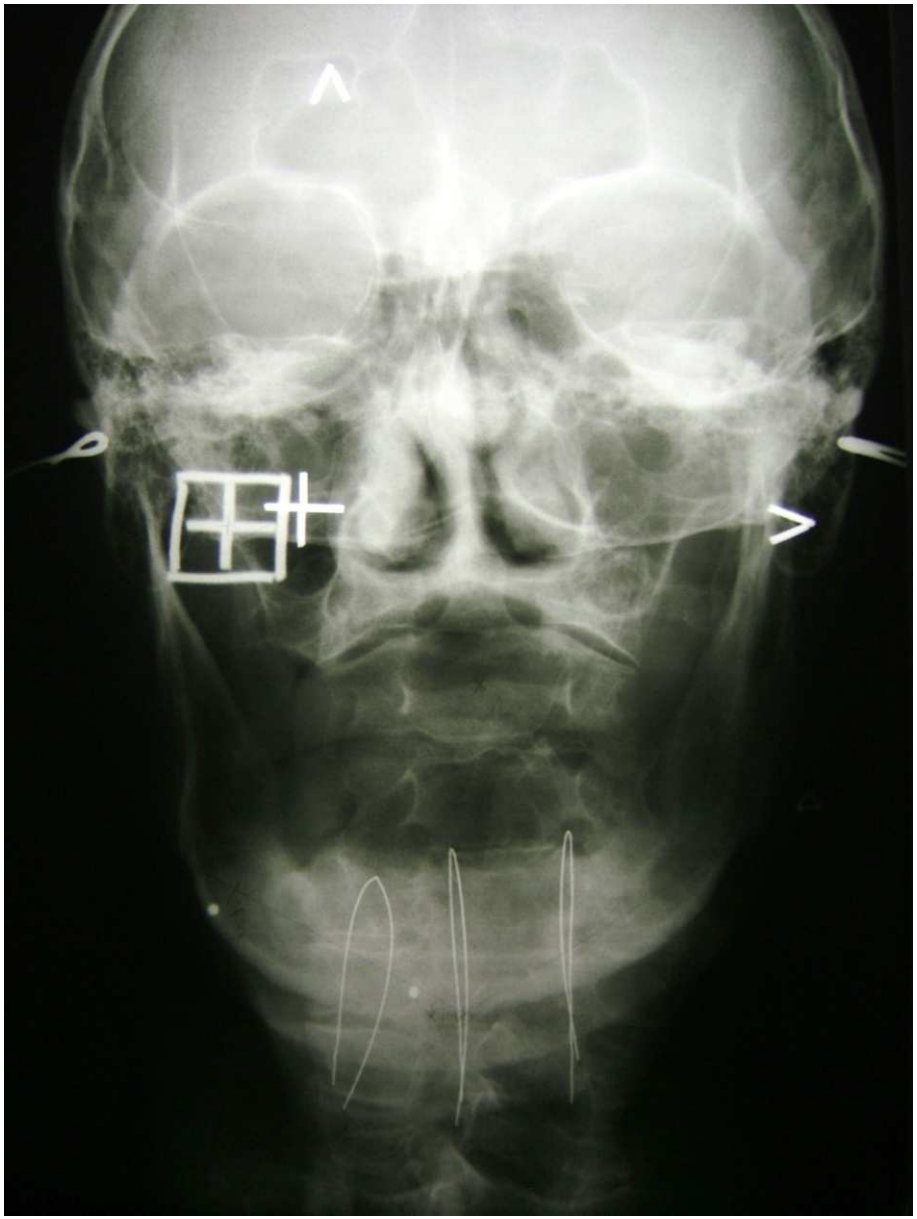
Base of tongue





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Faucial arch

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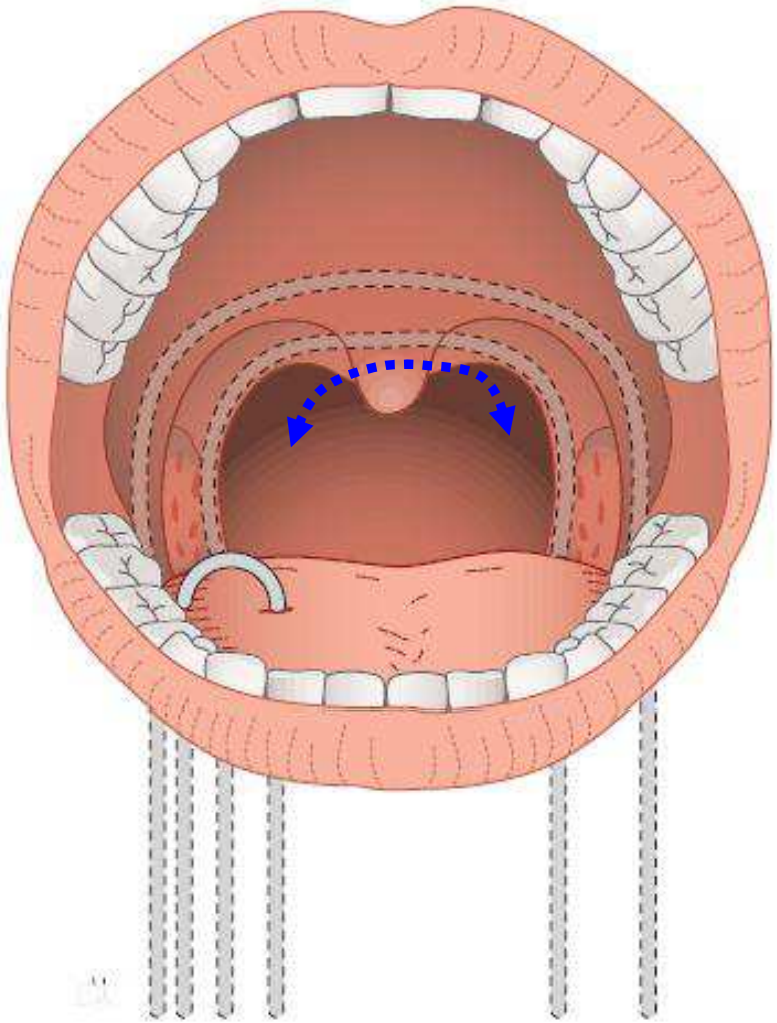
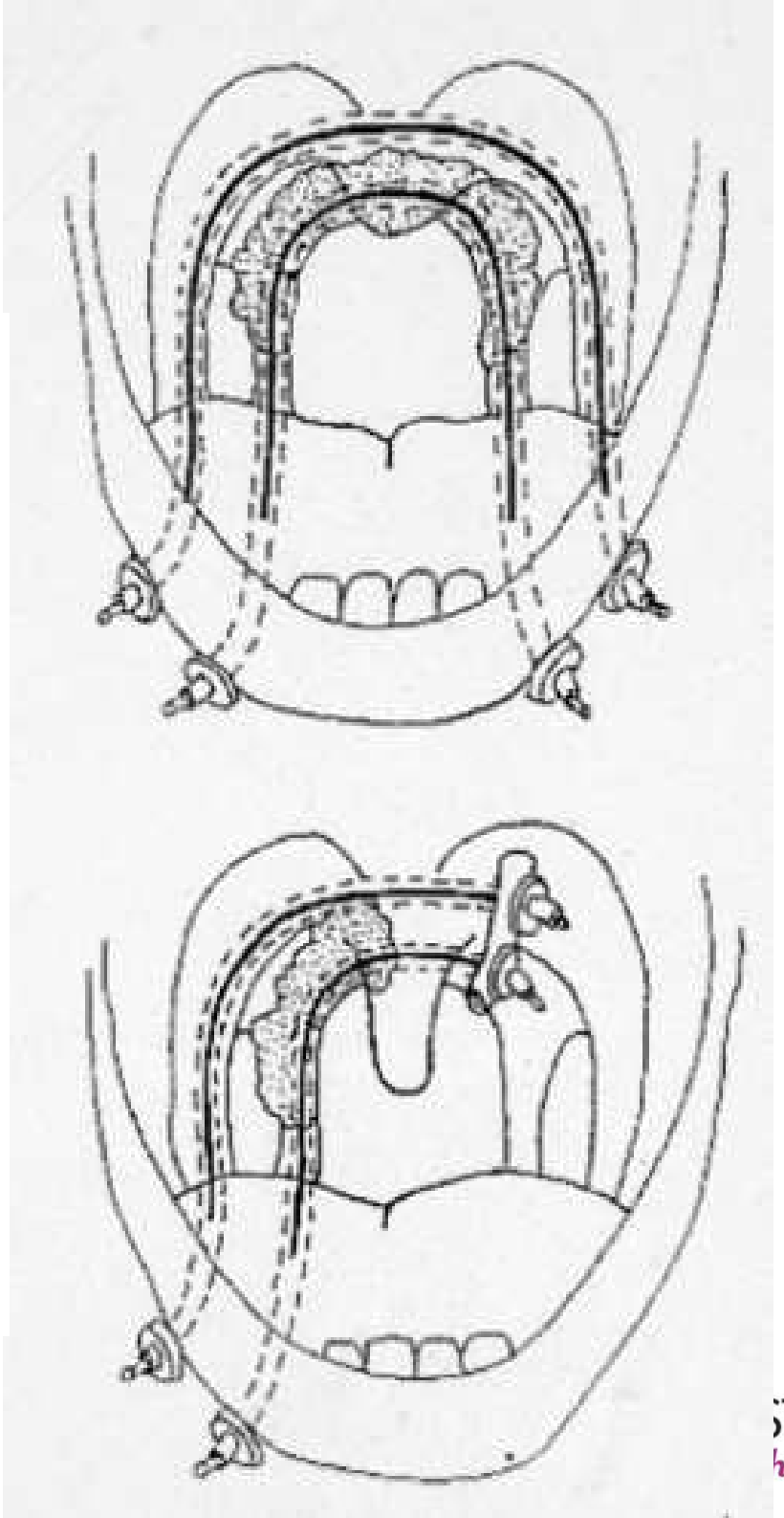
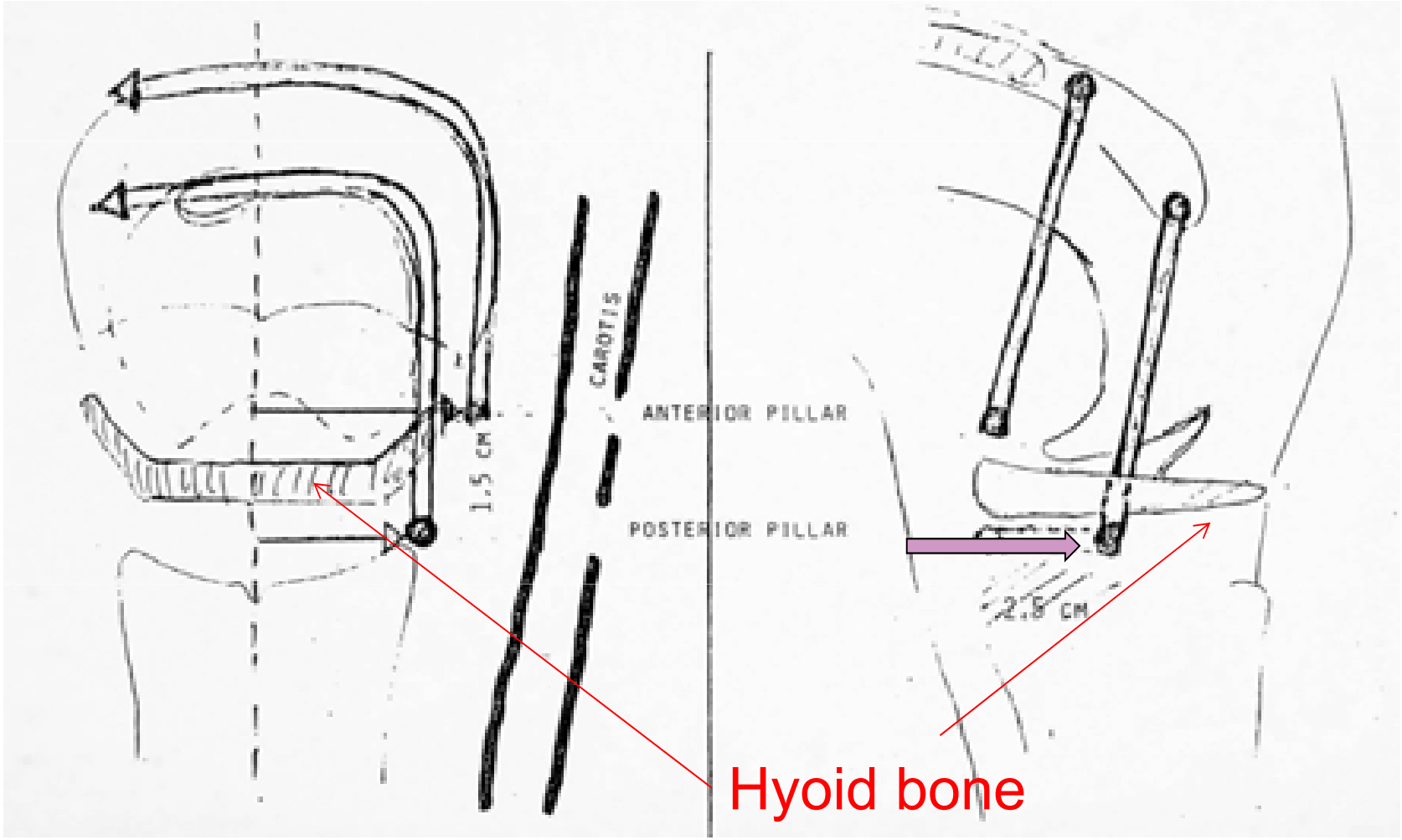
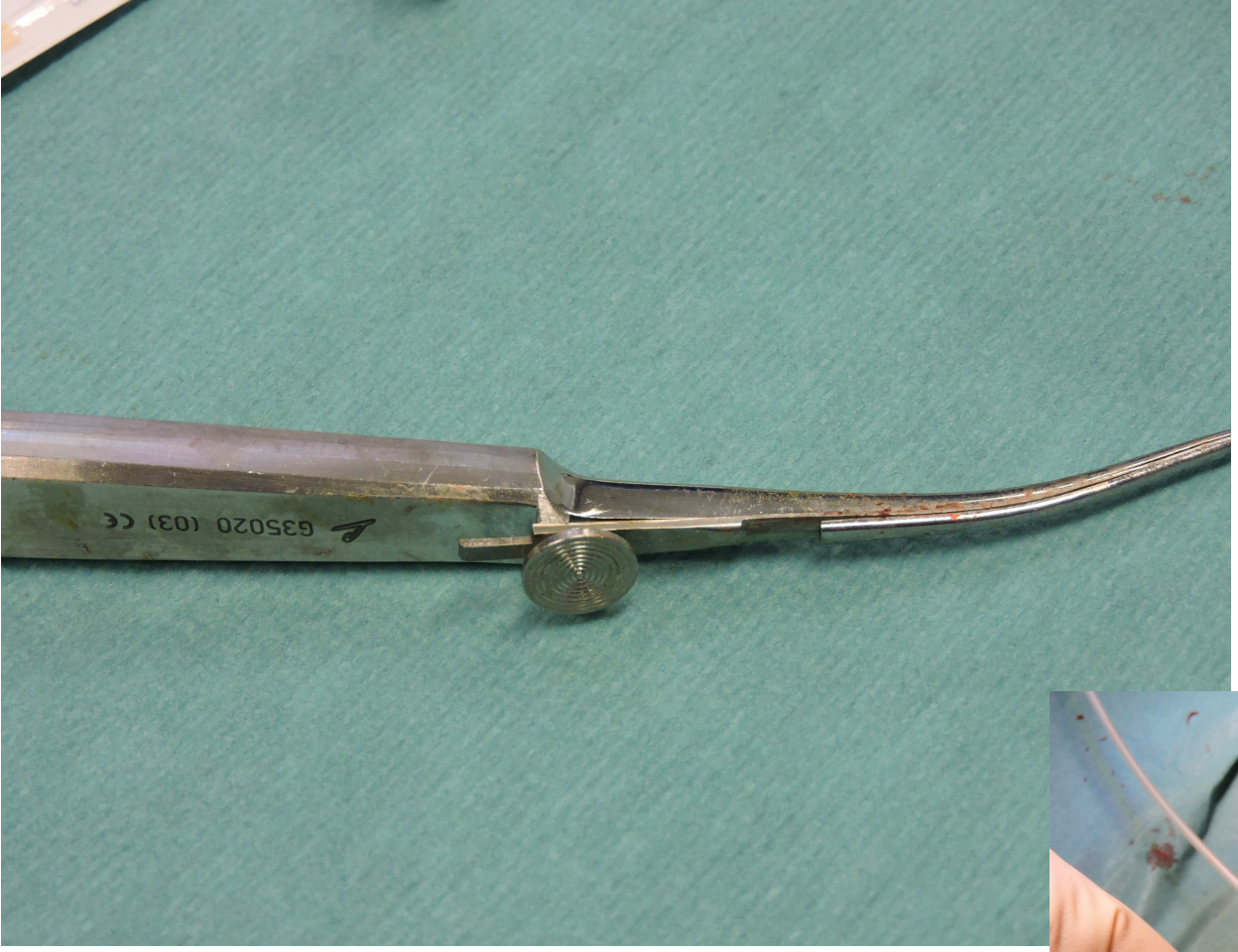


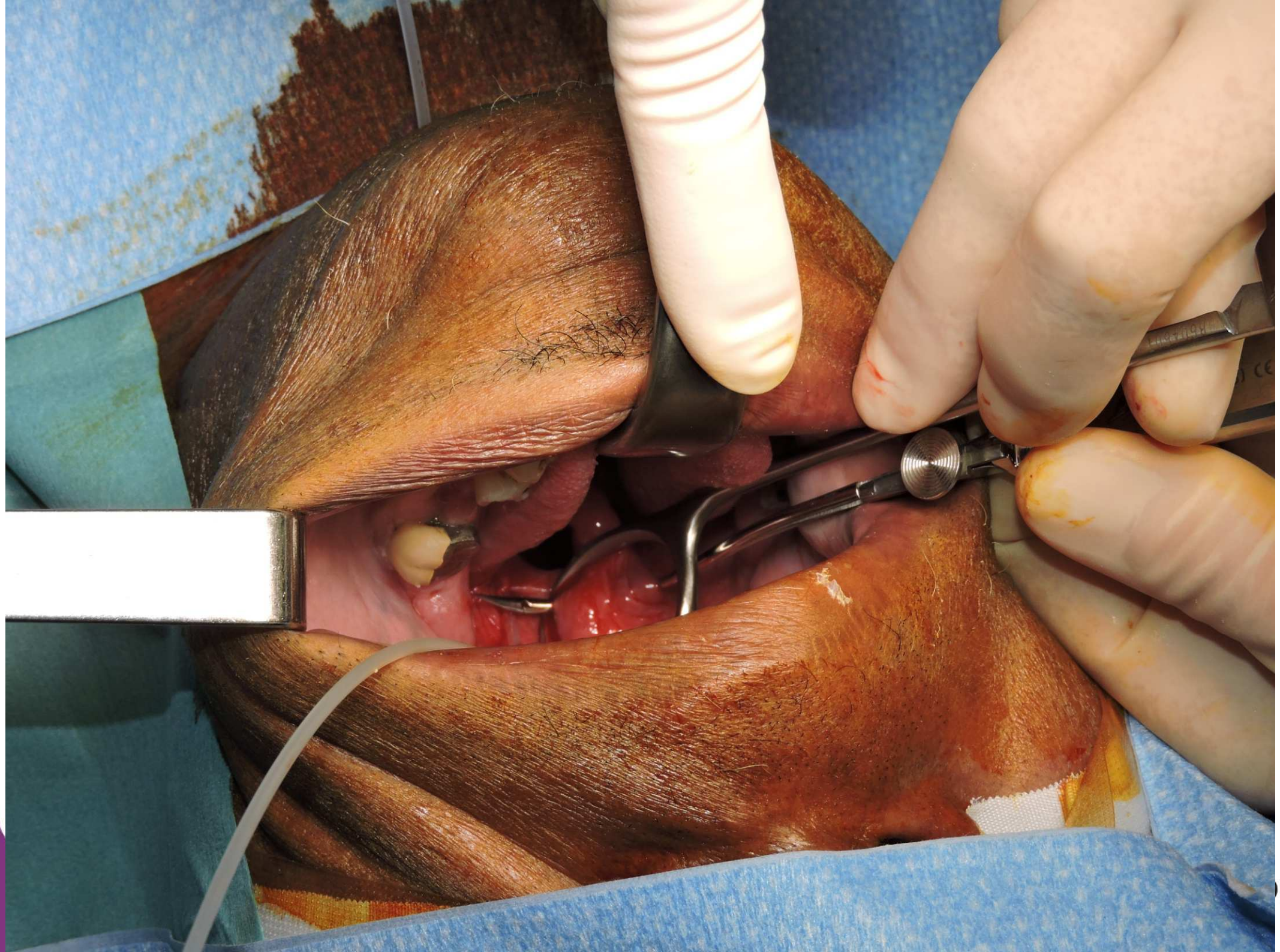


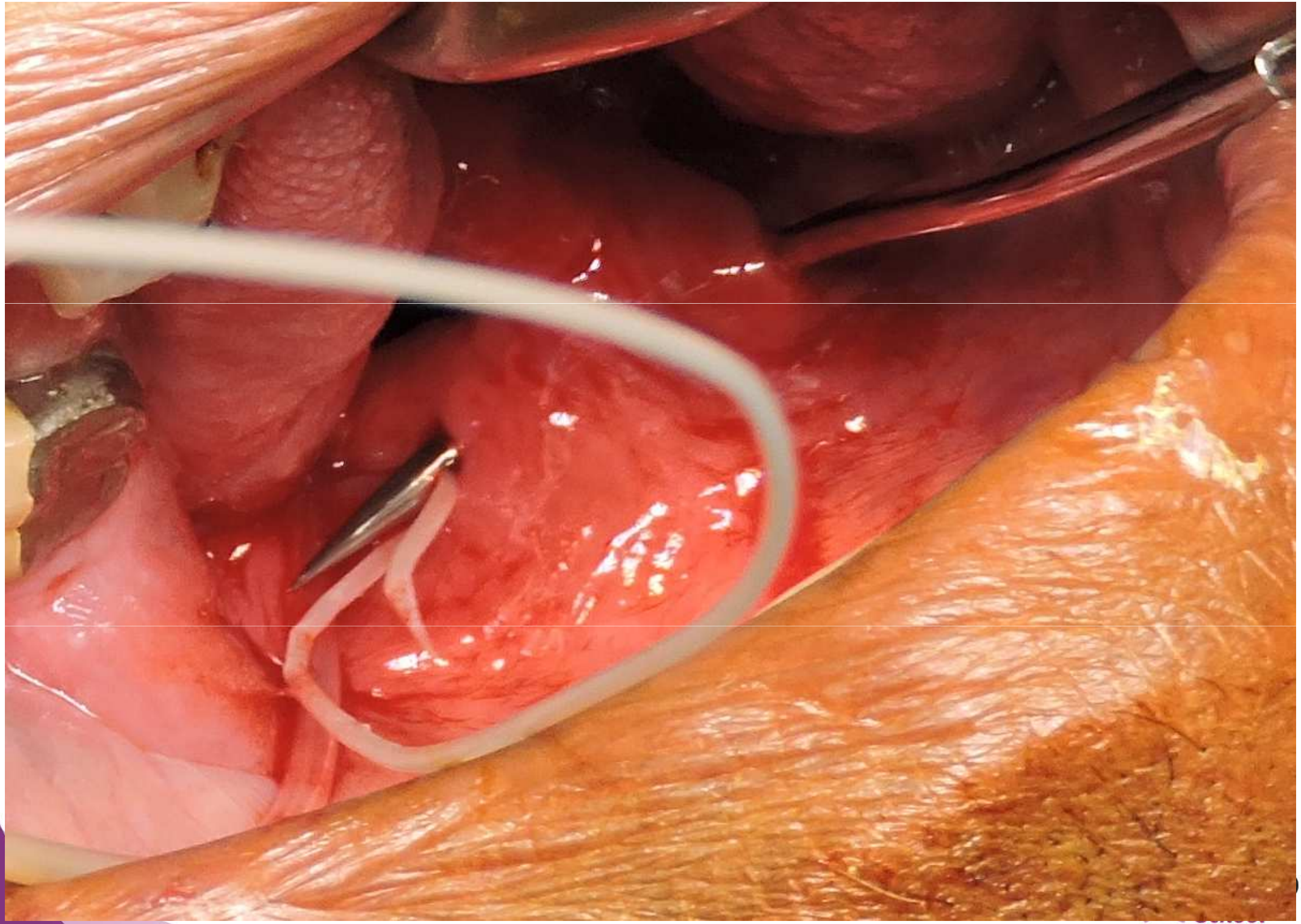
Insertion points

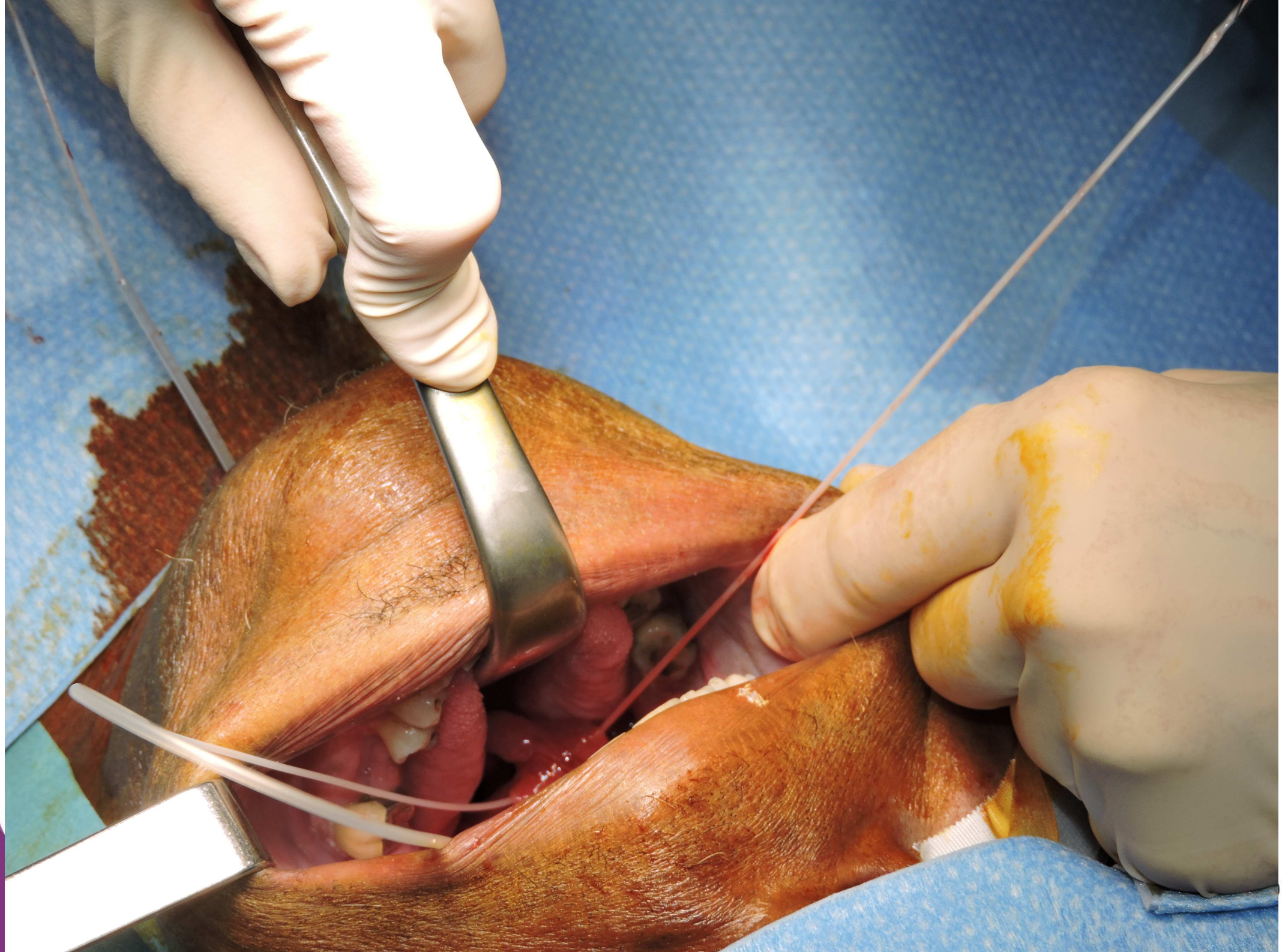


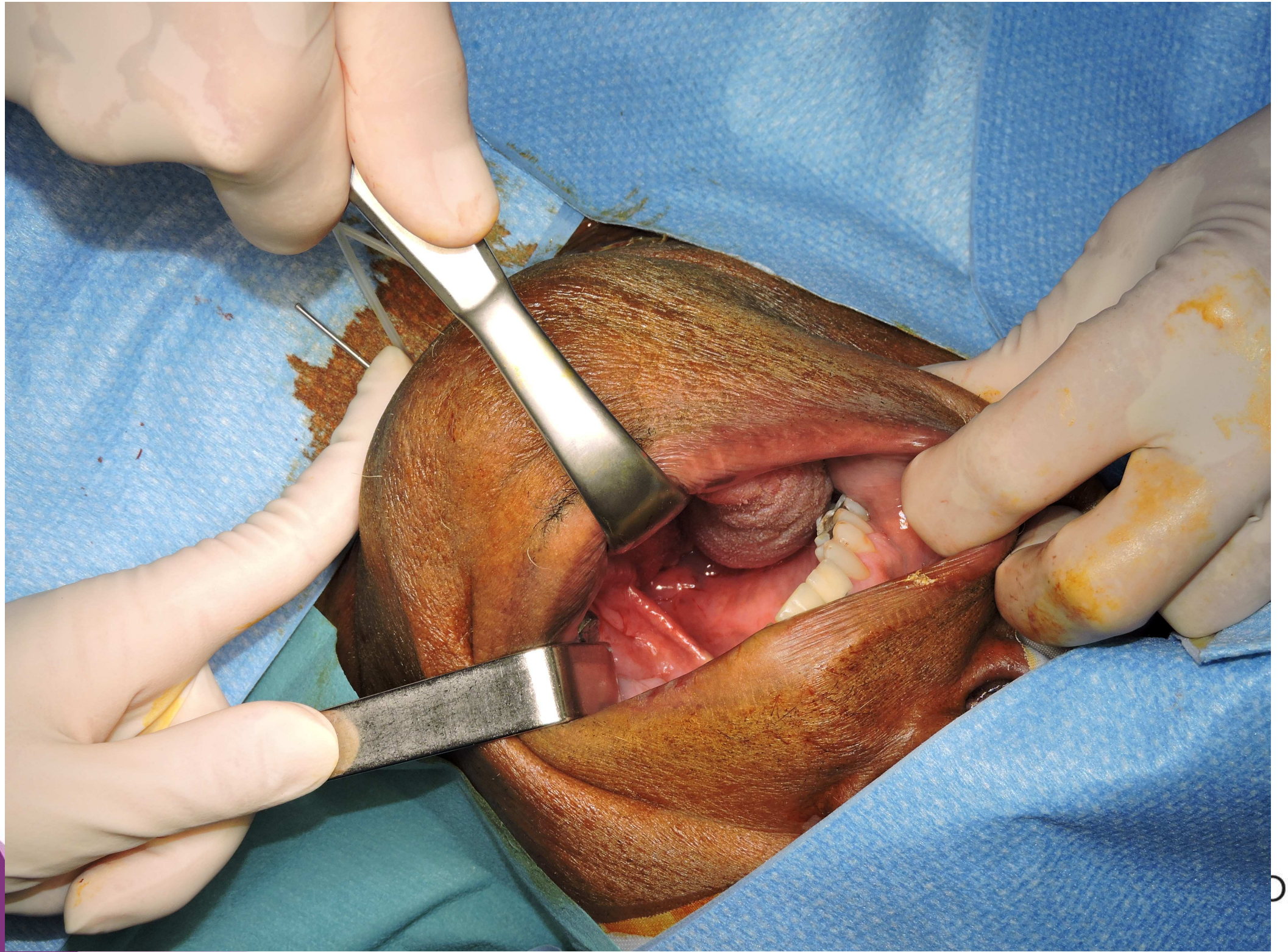
Reverdin suture instrument

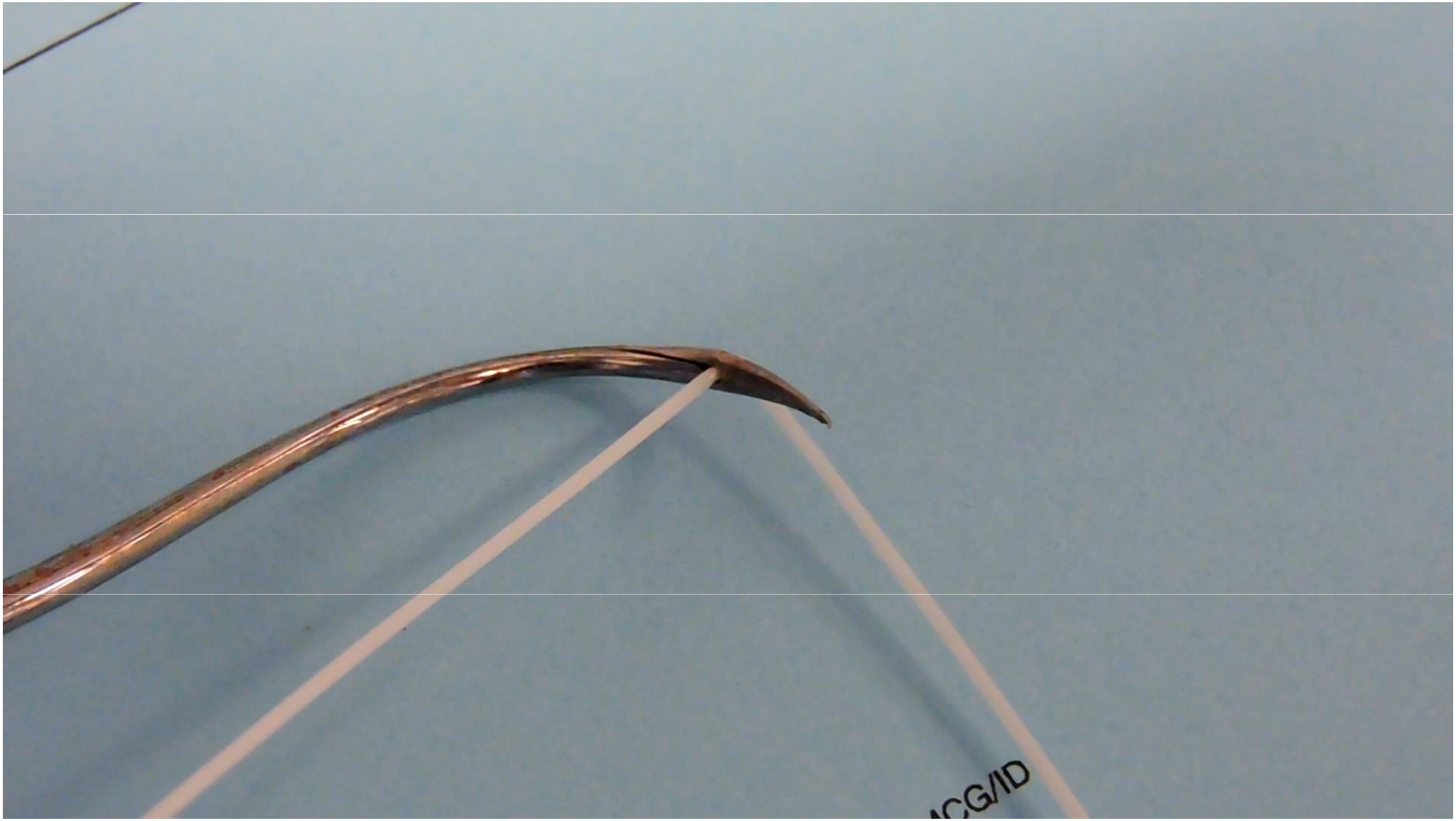

G35020 (03) CE







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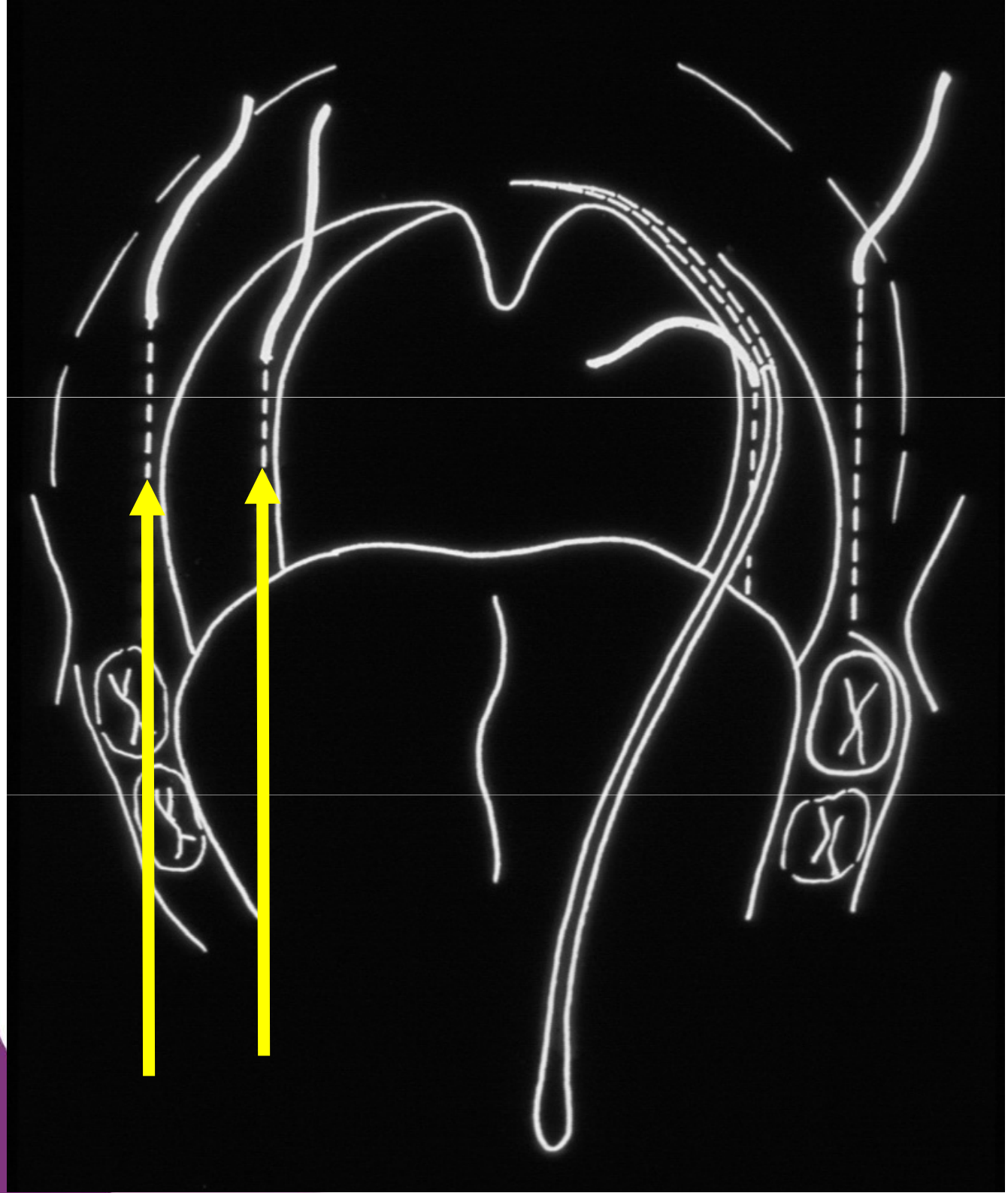
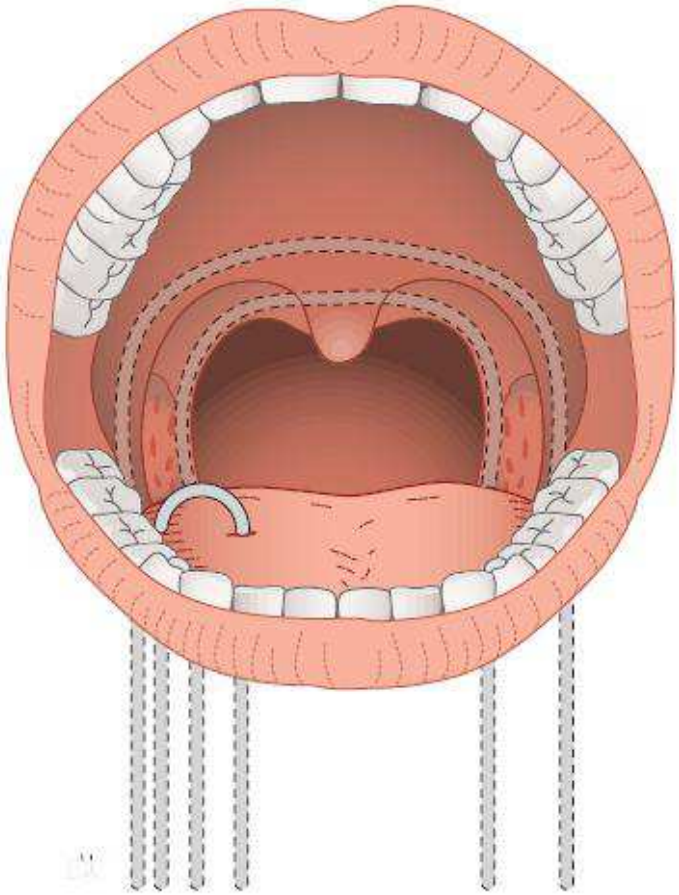
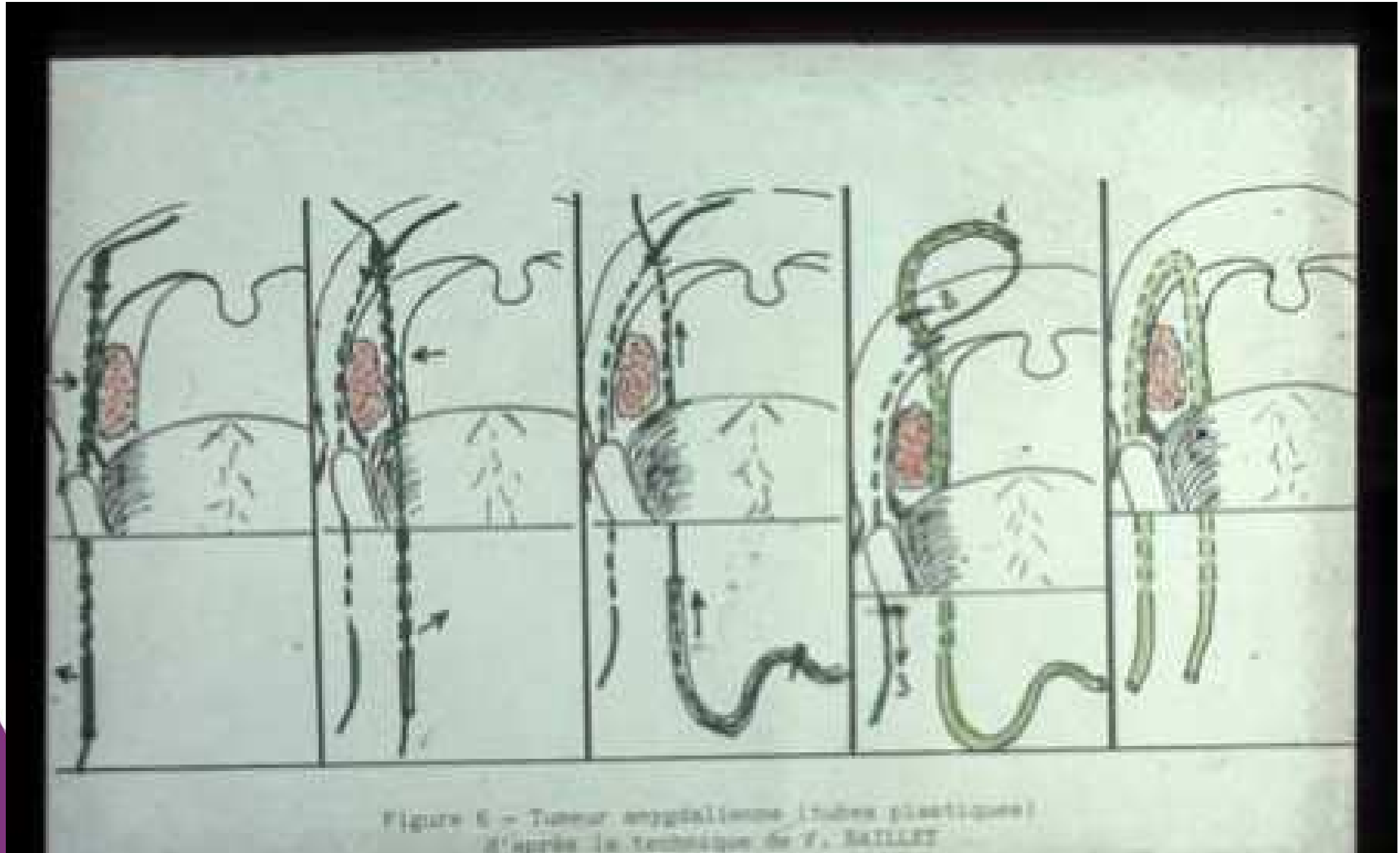
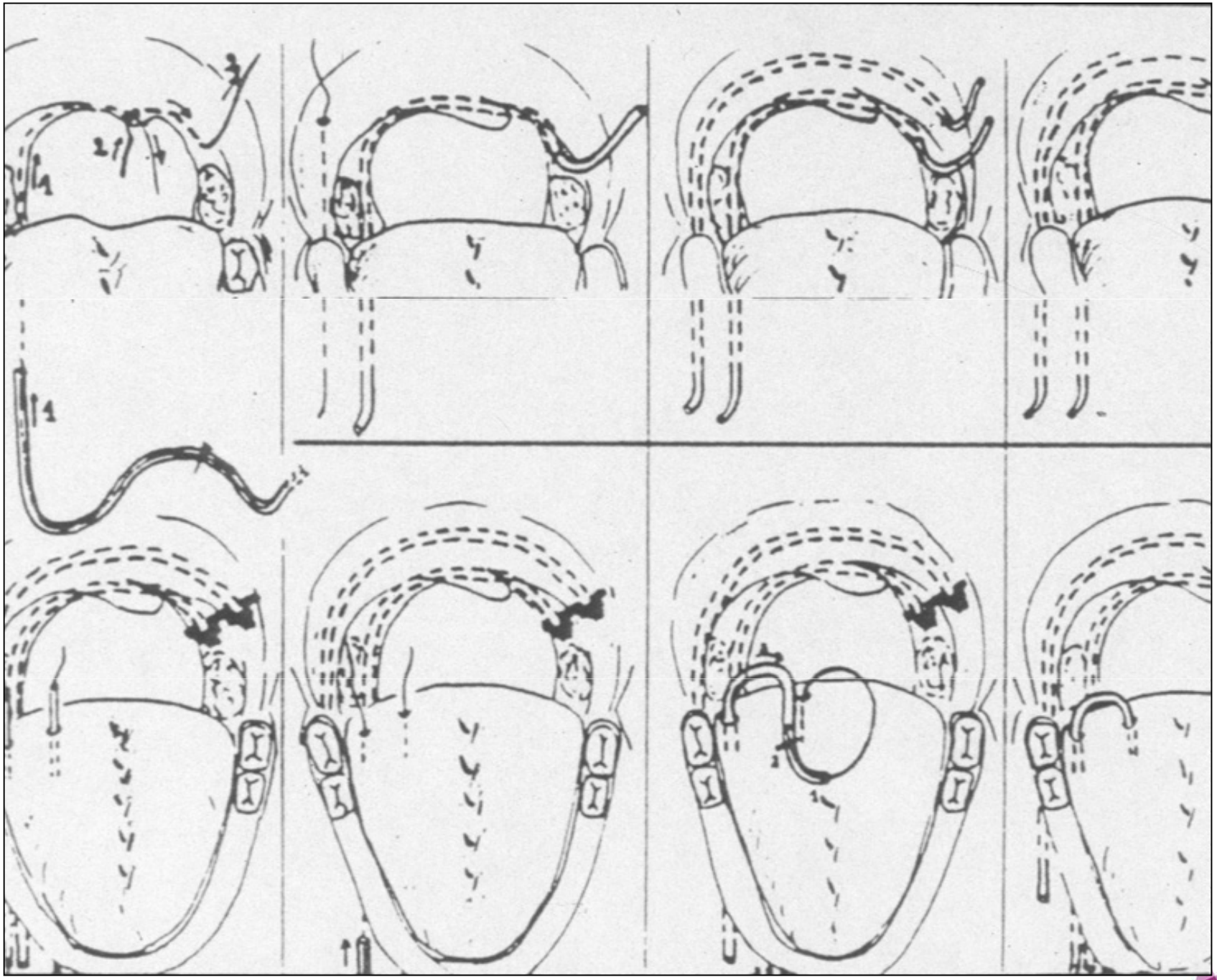


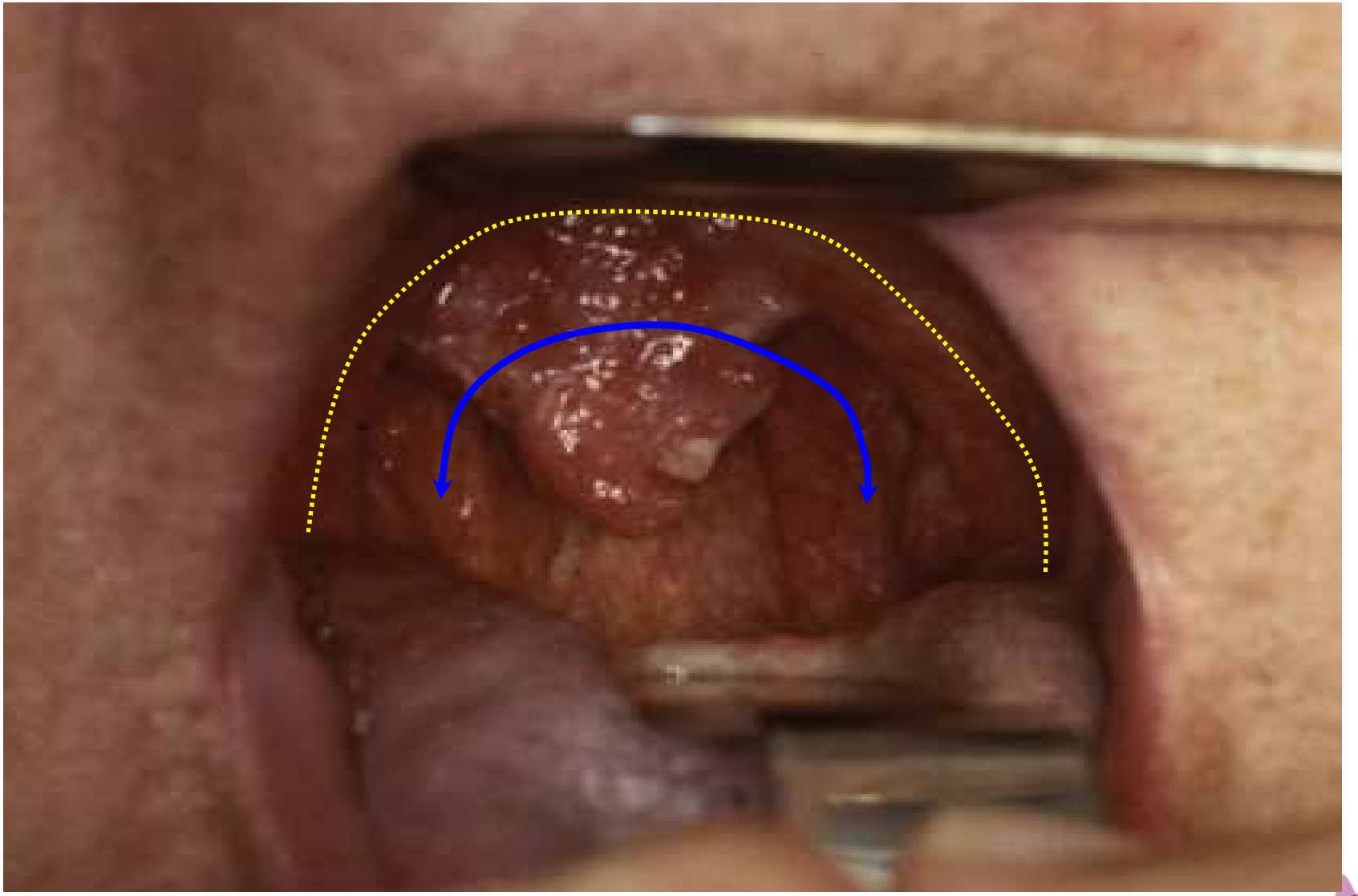


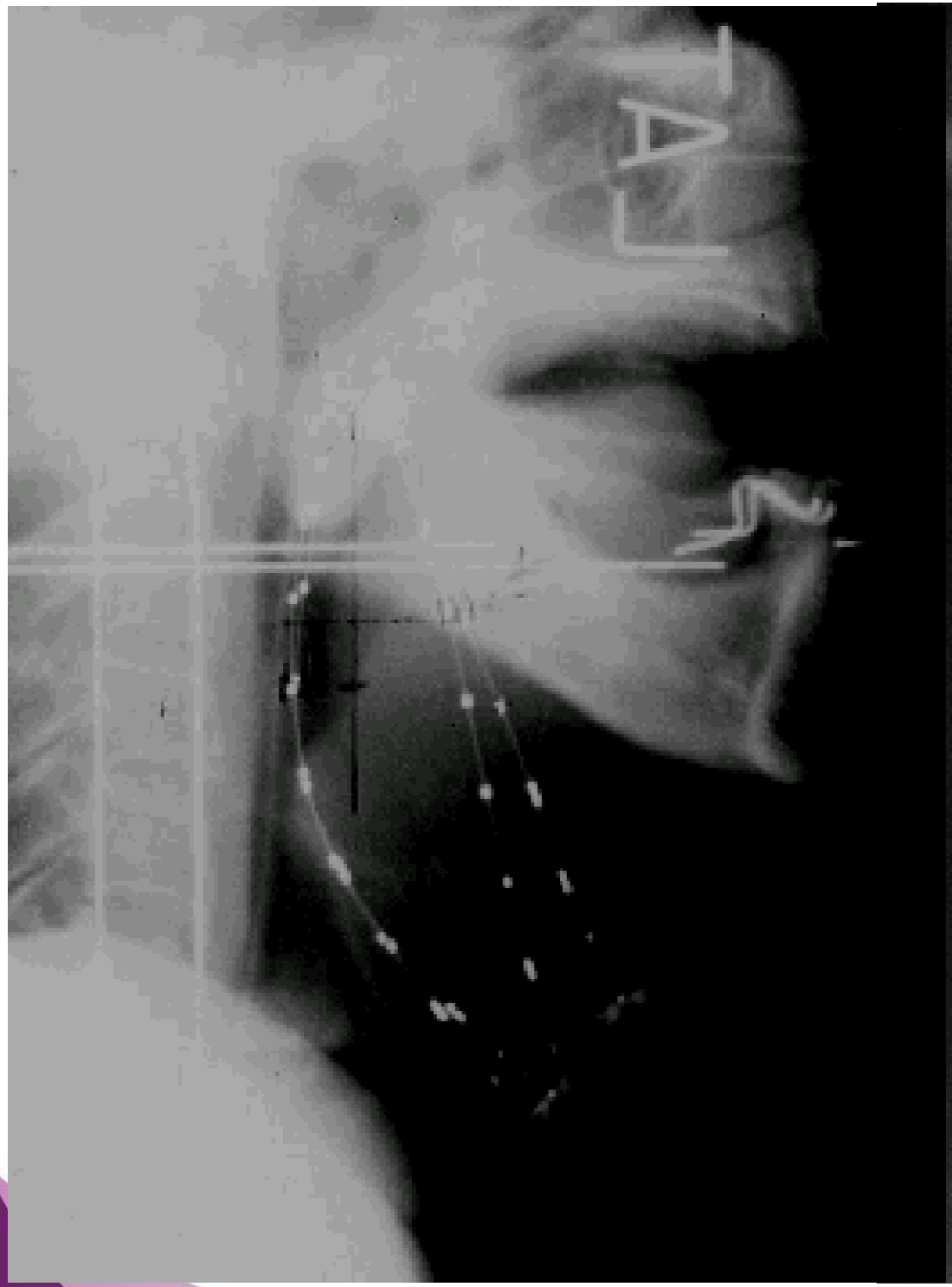
Tonsillar lesions





Uvula

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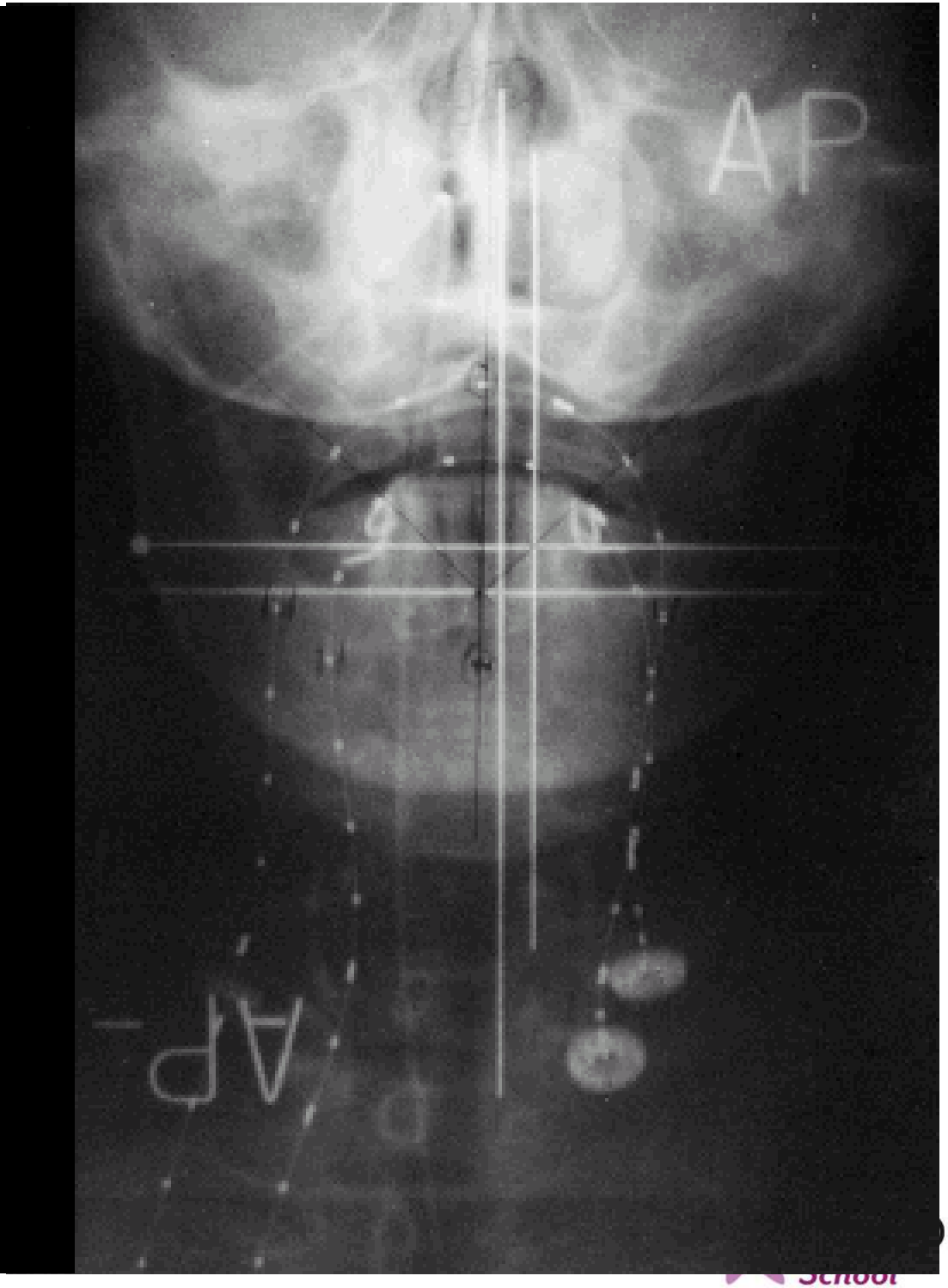
AP
AP

Oropharynx: indications

Indications

- **Base of tongue : T1-T3 (< 5cm)**
- **Soft palate : T1, T2**
- **Tonsillar fossa : T1, T2**
- **Vallecula : T1**

Contra-indications :
Extension to retromolar trigone / nasopharynx / larynx / hypopharynx
No bone involvement

BT usually combined with ERT

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Oropharynx

EBRT: 45-50 Gy (tumor and neck nodes)

- Tonsilar: 25-30 Gy
- Base of tongue: 30-35 Gy (whole base to 65-70 and tumor site to 75-80 Gy)
- HDR: 22.4-33.6 Gy in 4 fractions

Re-irradiation:

- 60 Gy

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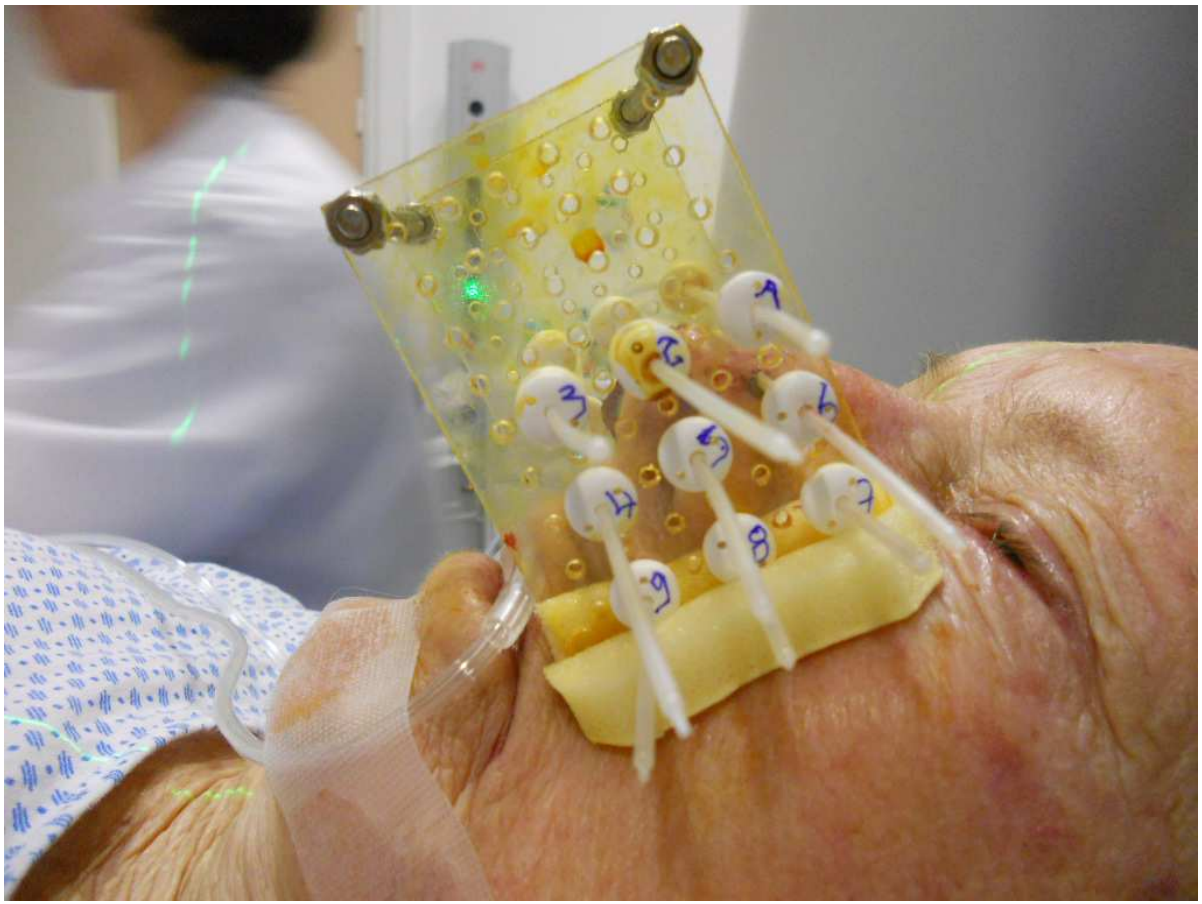
⇢ Miscellaneous



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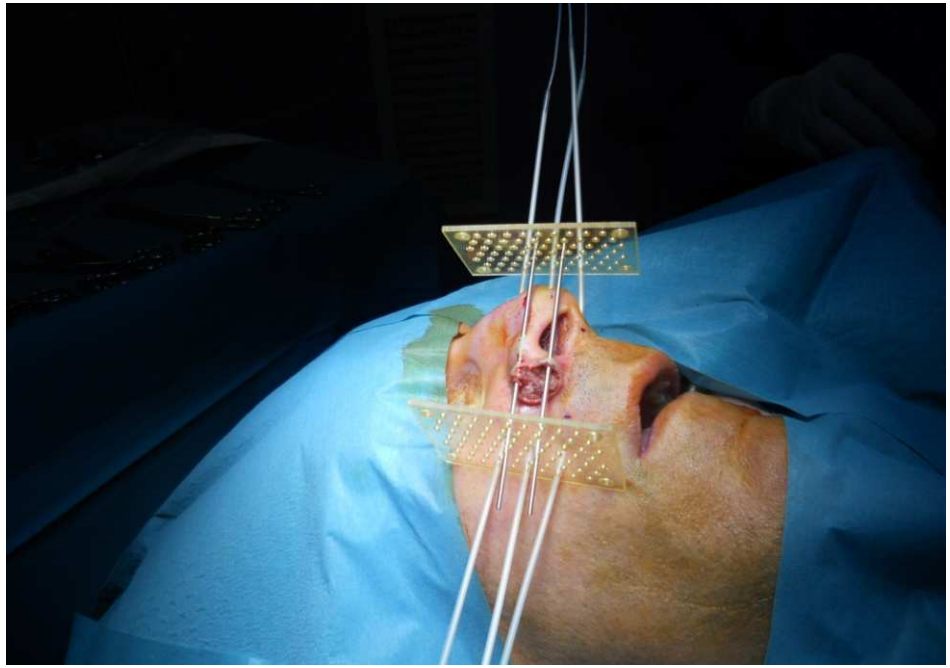

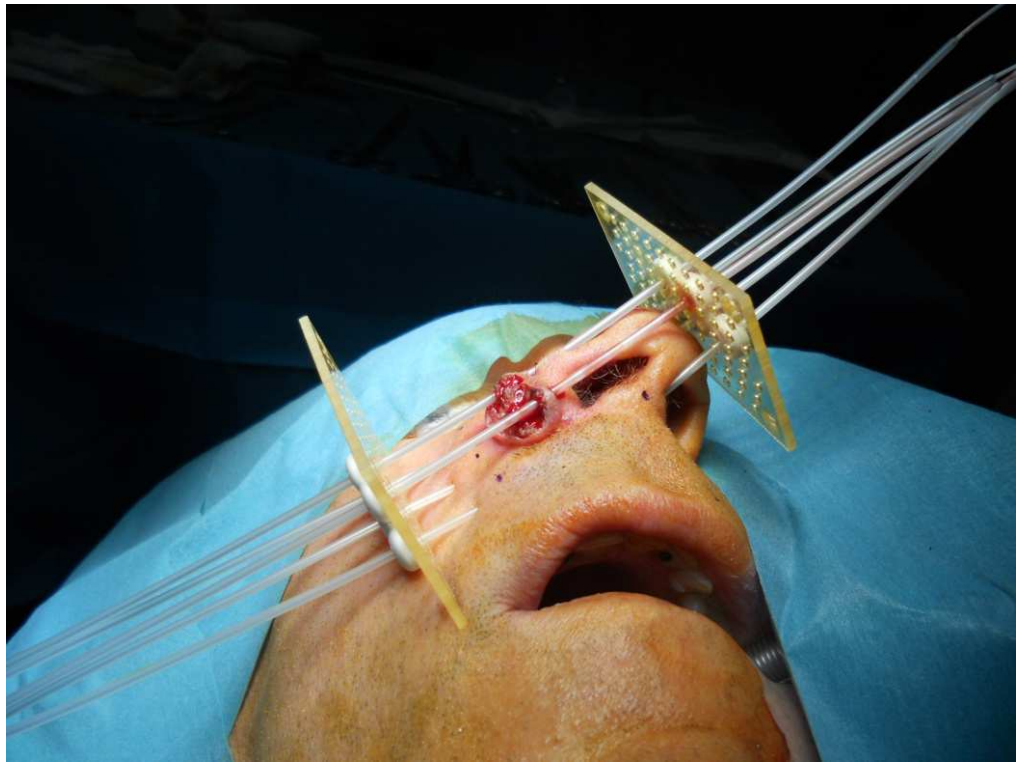

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Radiobiological factors influencing outcome in Head and Neck Brachytherapy

Erik Van Limbergen
Dep of Radiation Oncology
University Hospital Gasthuisberg
Leuven, Belgium

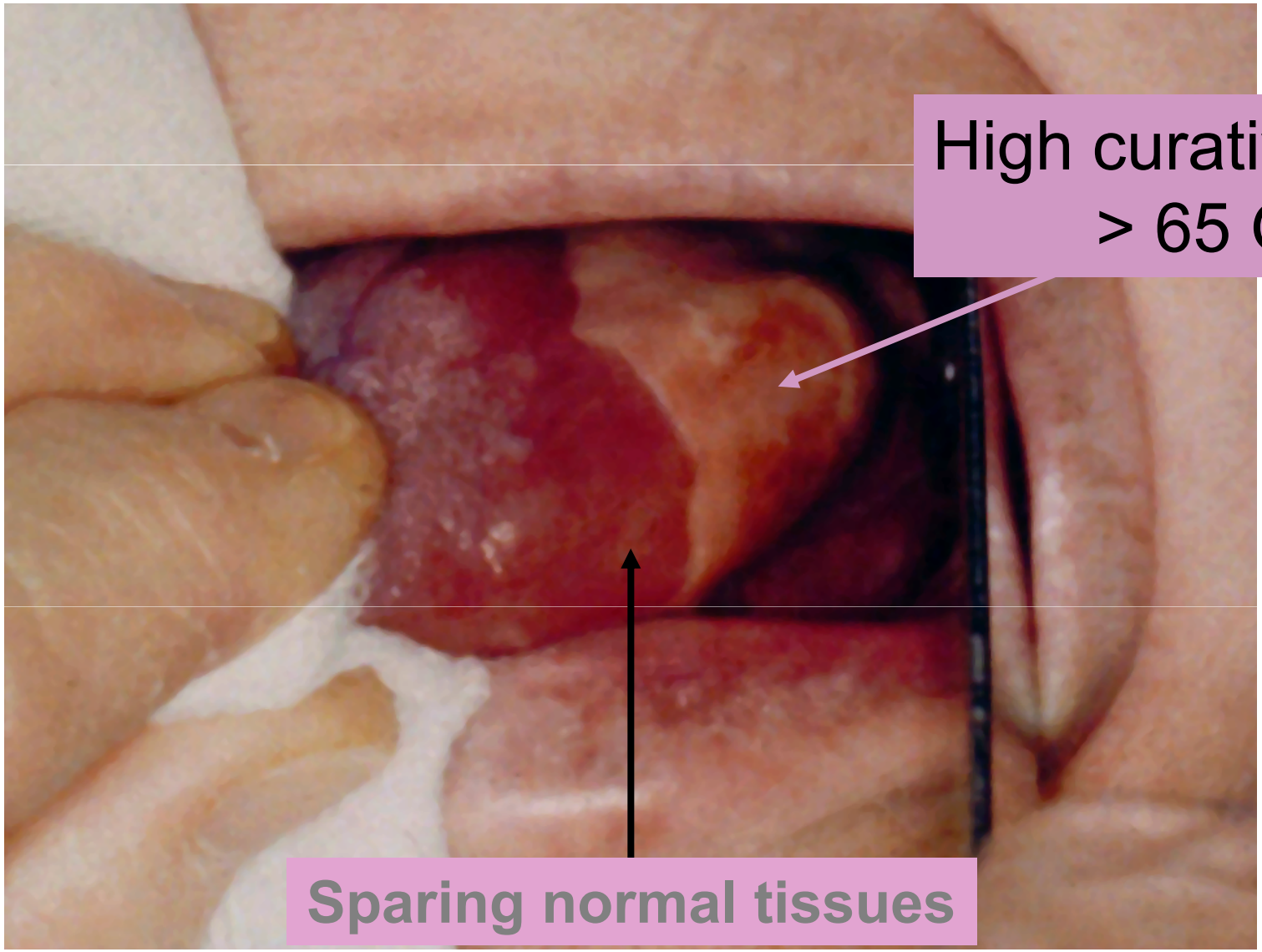
LDR (< 1 Gy/h)
« classical golden standard »

- pro:
  - Radiobiology
  - Clinical data
    - Long follow up+++

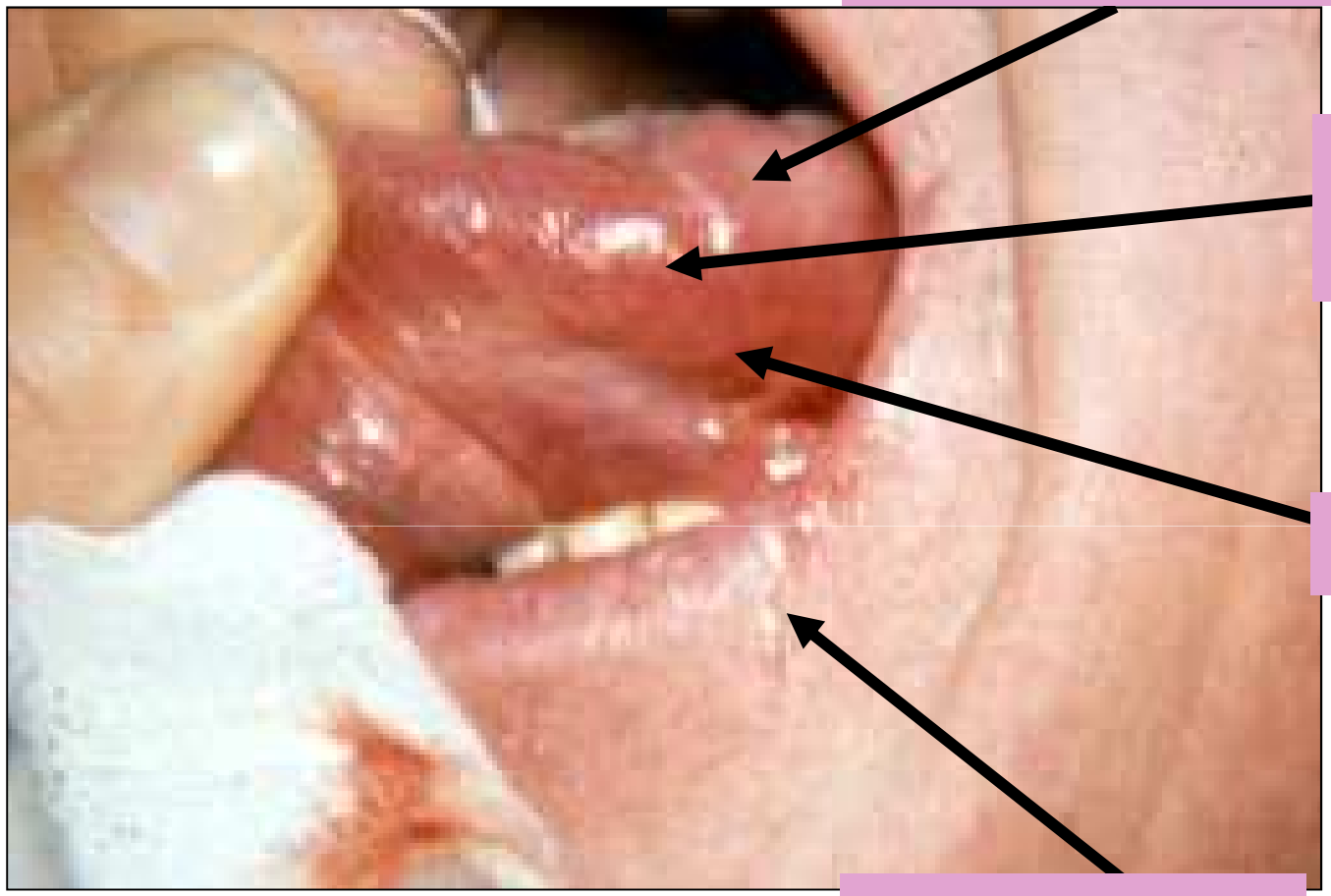
Contra:

- Manual « optimisation »
- Radioprotection

MUCOSITIS (3-6 Weeks)



Healing after 2 Months



Factors influencing local control

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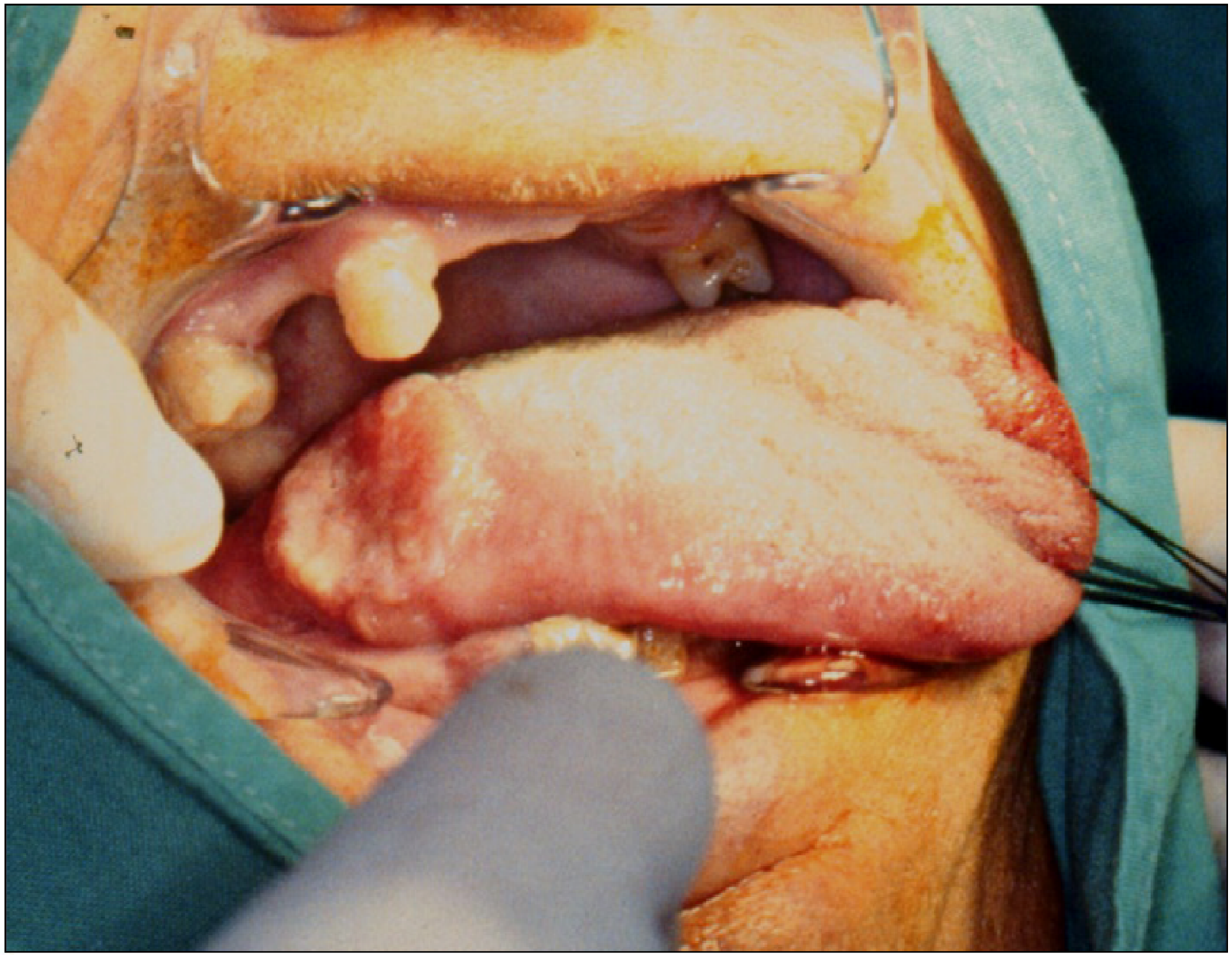
Mobile tongue Tumors



M.Tongue: Iridium Series >100pts (LDR)

	# pts	Technique	Local control	Late complic	5 y.survival
Decroix	*602*	BT +/-EBI+/-Surg	**76%**	13%	36%
Haie	*269*	**BT** EBI + BT	**87%** **49%**	 8%	62% 30%
Mazeron	*121*	**BT** 55-60 Gy **BT** 65-75 Gy	**73%** **92%**	T2 N0 7%	
Wendt	*103*	**BT** BT+ EBI <40 Gy BT+ EBI >40 Gy EBI	**65%** **92%** **69%** **28%**	0 4% 17% 0	89% 78% 71% 57%
Nareyama	*130*	BT EBI + BT	**86%**		
Shibuya	*370*	**BT** BT + EBI	**75%** **48%**	4%	
Lefebvre	*283*	**BT**	**83%**	6%	NP
Pernot	*448*	BT EBI + BT	 **68%**	9% (3 % grade 3)	 44%
Matsura	*173*	**BT** EBI + BT	**84 - 95%** **74 - 80%**		69 - 84%
		2500 Patients	65-95%		

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M.Tongue:
Dose response of brachytherapy

	Brachy dose	EBI dose	5 y. local control
Mendenhall	> 35 Gy	NA	60%
(Florida)	< 35 Gy	NA	40%
Wendt	NA	< 40 Gy	92%
(MD Anderson)	NA	>40 Gy	62%

Wendt et al : IJROBP 1990;18:1287–1292

Mendenhall et al : Radiother Oncol 1989;16:275–281

M.Tongue:

Exclusive brachytherapy is better!

T2 N0 series: 5 y. local control

	# patients	Brachy alone	EBI + Brachy
Pernot (Nancy)	**147**	**90%**	**51%**
Benk (Paris)	**110**	**88%**	**36%**
Haie (Villejuif)	**77**	**93%**	**80%**

Pernot et al : Radiother Oncol; 1992;23: 223- 228
Benck et al : Radiother Oncol; 1990;18: 339- 347
Haie et al : Actual Carcinol Cervicofac;1983;9: 52- 57

M.Tongue: Prognostic factors for local control

- Brachytherapy Alone
- Dose effect: Brachytherapy D. > 62.5 Gy
- Dose rate 0.3-0.5 Gy/h

  Mazeron et al : Radioth Oncol 1991;21;39–47

  Coche-Dequeant et al : Bull Cancer / Radiother 1995;82:203

  Pernot et al : IJROBP 1994;29:673–679

- (Pre-) Concept of quality index:

  Treated V. > 120 % of GTV (2D concept)

  5 y - local control: 75 % vs 52 %

  Pernot et al : IJROBP 1994;29:673–679

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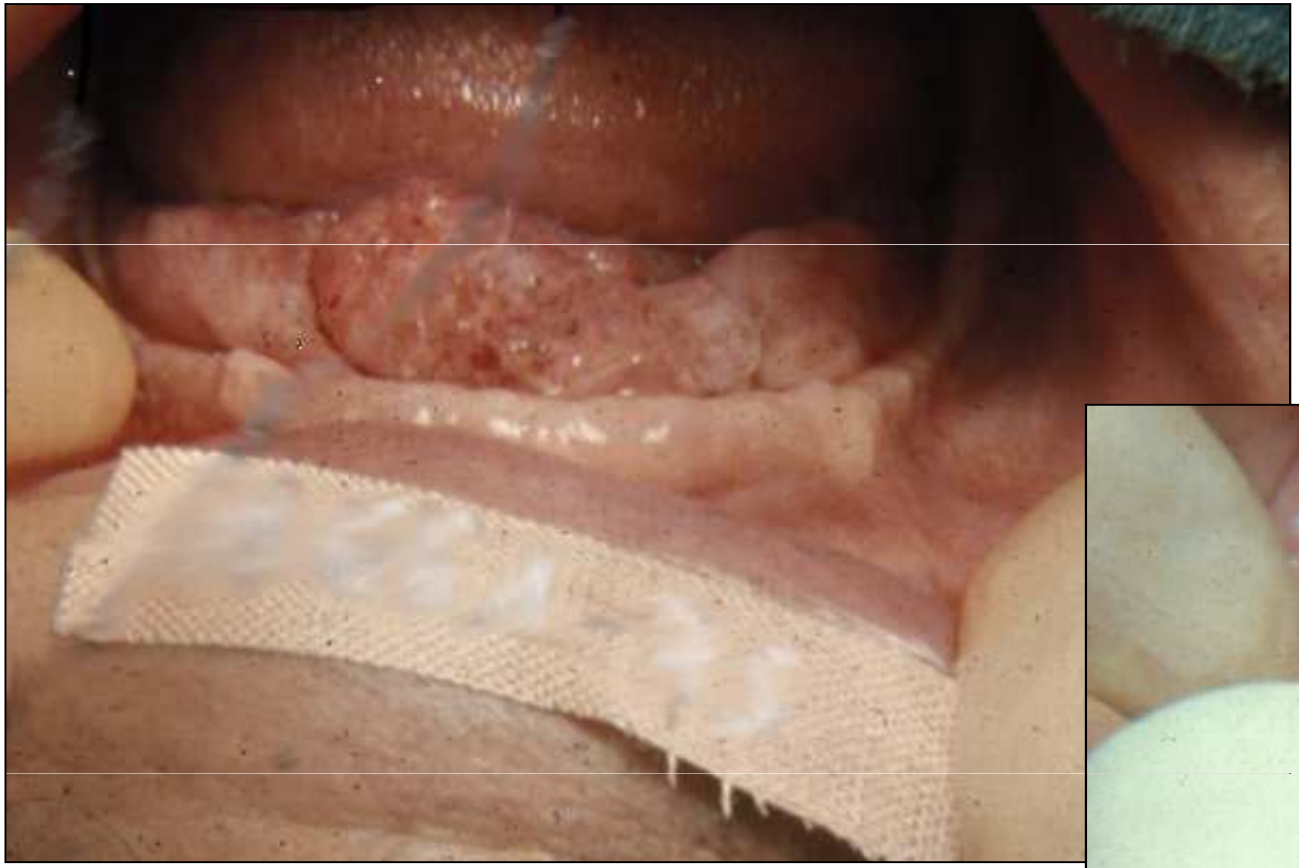
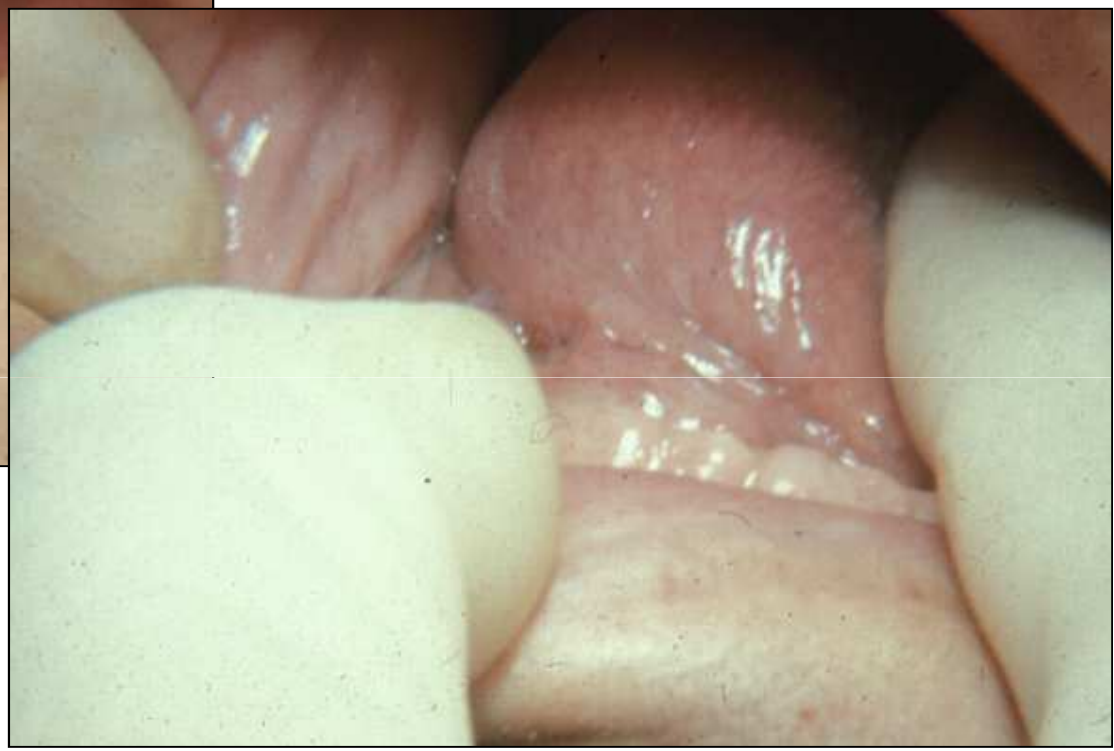
Floor of Mouth





Floor of mouth:

Iridium Series >100pts (LDR)

	#pts	Technique	Local control	5 y. survival
Baillet	966	BT+EBI	71%	T1T2N0 = 60%
Bolla	239	EBI + BT	T1 = 90% T2 = 80%	T1 = 65% T2 = 55%
Volterrani	175	BT	70%	44%
Marsiglia	206	BT EBI+BT	89% 59%	74% 34%
Cole	162	EBI+BT	89%	
Lefebvre	146	BT	80%	
Pernot	207	BT	T1 = 97% T2 = 72% T3 = 51%	71% 42% 36%

Floor of mouth:

Exclusive brachytherapy is better!

T2 N0 series: 5 y. local control

Author	#pts	BT alone	EBI+BT
Grimard	67	74%	70%
Pernot	79	92%	53% *

* 5 y. survival : 76% and 35%

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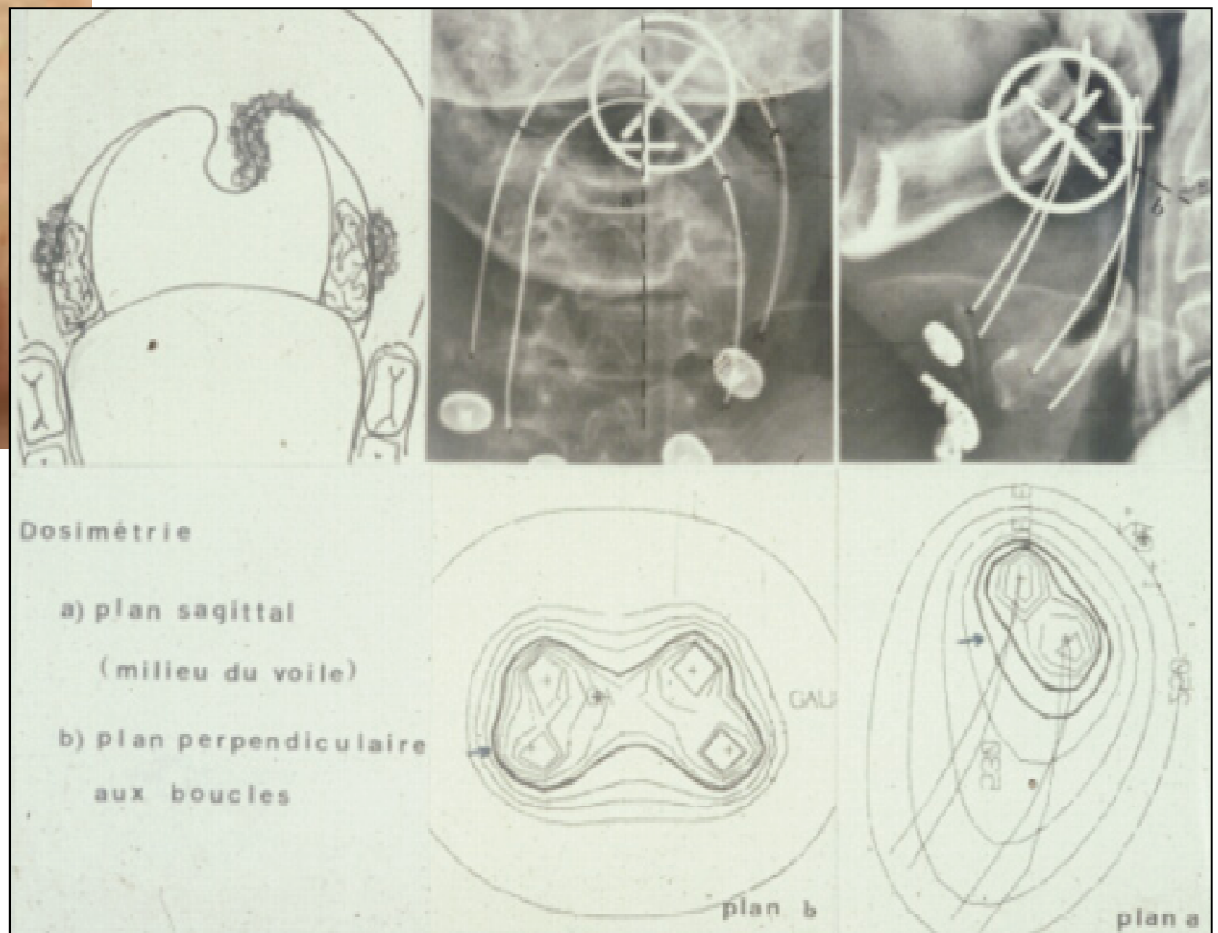
Velotonsillar Arch



From Pernot

Soft palate: LDR series

	#pts	Technique	Local control	5 y. survival
Eschwege	1 28 19	BT ± EBI	68%	23%
Sealy	22	BT	89%	
Mazeron	16 14 29	EBI BT EBI+ BT	75% 100% 82%	
Esche T1 T2	43	EBI±BT (14 + 29)	92%	OS 37% DFS 64%

Tonsil : LDR series

	# pts	Technique	Local control	5 y.survival
Mendenhall	136T1-T4	EBI ± BT	76%	42%
Behar	37	EBI ± BT	95%	64%
Puthawala	80	EBI ± BT	84% at2 y.	72% at 3 y.
Mazeron	41	EBI	58%	23%
	11 T1-T2	BT	100%	50%
	106	EBI + BT	91%	60%
Pernot	271 T1T2	EBI + BT	87%	
	90 T3		67%	

Mazeron et al IJROBP1993;27:251-277

Velotonsillar arch: EBRT series

T3-T4: 5y.local control

		T3	T4	
Calais	137 pts	57%	11%	*Ann Radiol 1989;32:55*
Fayos	353 pts	53%	25%	*I J R O B P 1983;9:134*
Gelinas	399 pts	79%	65%	*Radiology 1973;108:383*
Nong	150 pts	58%	50%	*I J R O B P 1989;16:657*
Withers	319 pts	60%	50%	*I J R O B P 1995;33:549*
Horiot	356 pts (T2-T3) Hyperfraction Conventionnal	 59% 40%		*Radiat Oncol 1992;25:231*

Velotonsillar arch: prognostic factors for local control

- Overall time of treatment < 55 days
- Gap < 20 days
  - 5y local control: 88% vs 74%
  - 5y survival: 63% vs 44%

Hoffstetter et al: Radiother Oncol 1997;45:141–148

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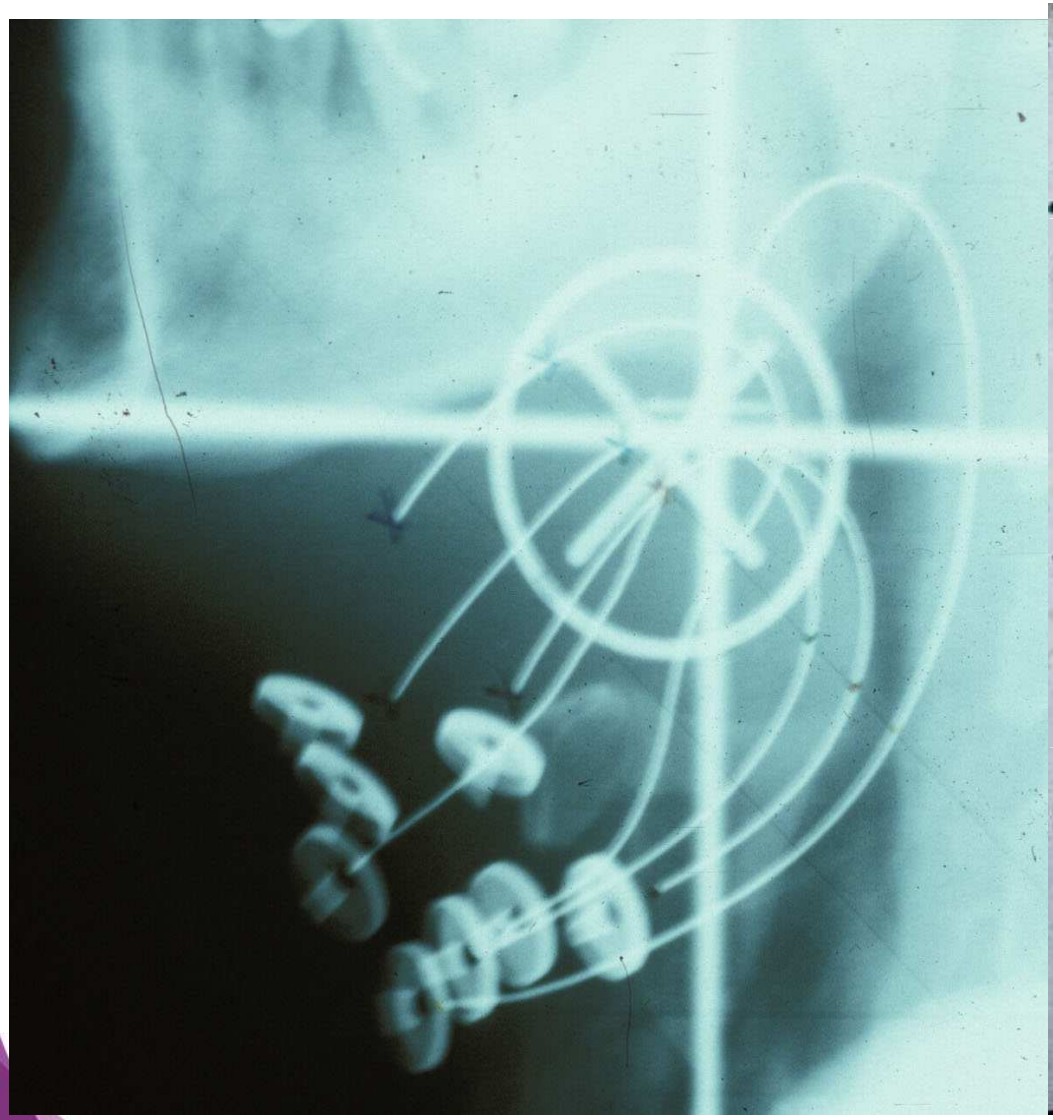
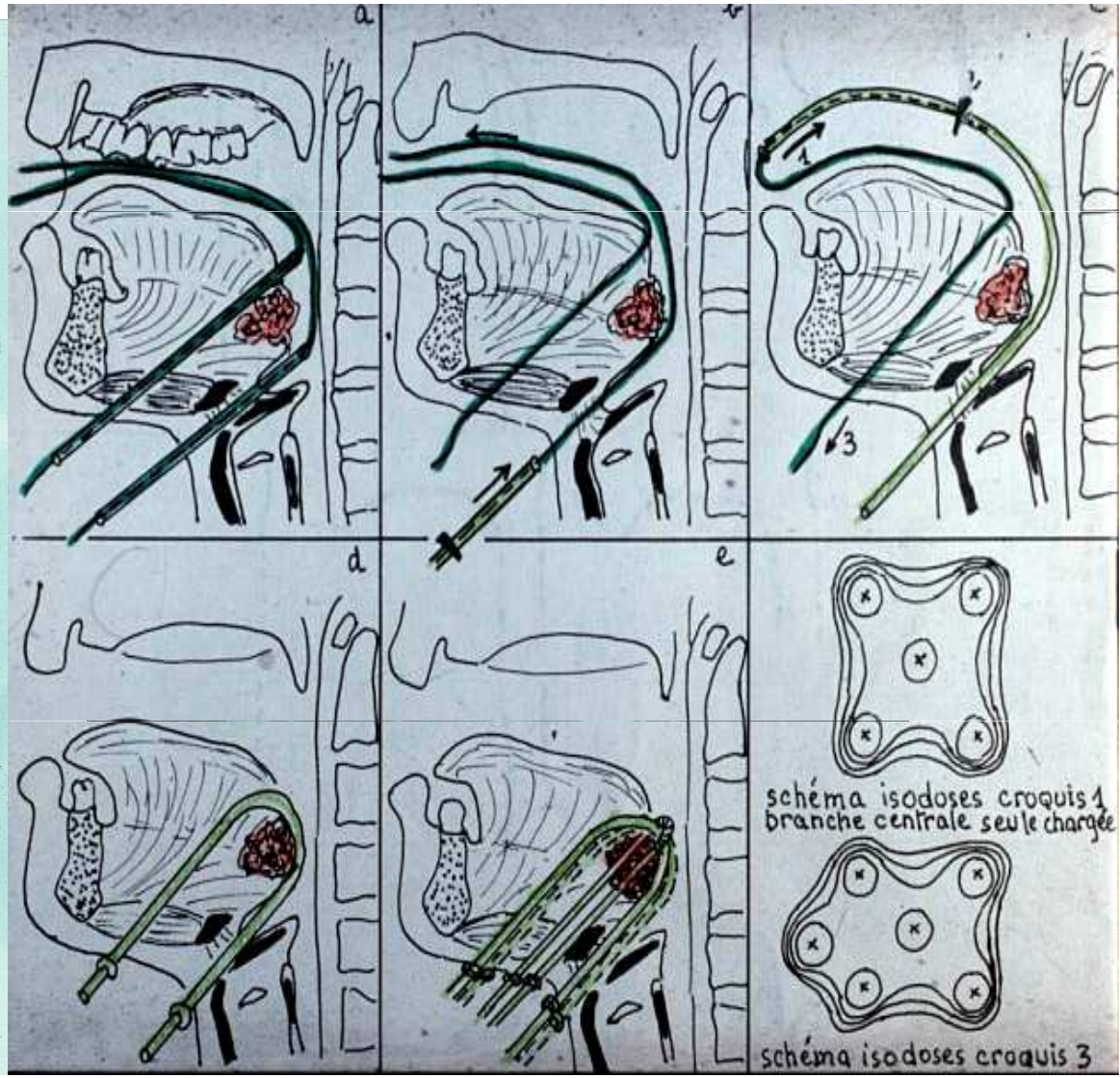
Base of tongue





Base of tongue: LDR series

	#pts	Treatment	Local control		5 y. survival
Goffinet	14	EBI + BT	71%		70%
	14	Surg. + EBI	36%		50%
Housset	54	EBI	57%		17%
	29	EBI + BT	T1 : 100%		52%
			T2-3: 74%		
	27	Surg. +EBI	81%		49%
Crook	T1 13	EBI + BT	85%		
	T2 35		71%		
Puthawala	T1 2	EBI + BT	2/2		35%
	T2 16		88%		
	T3 40		75%		
	T4 12		67%		
Lusinchi	T1 18	EBI + BT	83%		26%
	T2 39		51%		
	T3 51		69%		
Hoffstetter			2 y	5 y	
T1 T2 T3	45	EBI	28%	19%	19%
	72	EBI + BT	71%	39%	44%
	19	Surg + EBI	51%	32%	45%
Lee	68	EBI + BT	88%		86%

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Local control in Oropharyngeal cancer

- Benefit of brachy dose
- BT Dose ~ 65 Gy
- Dose rate = 0.5 Gy /h
- Local control 80 – 95 %

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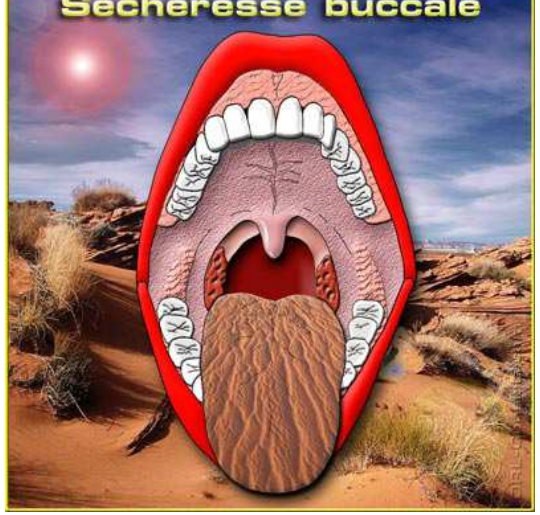

LOCAL CONTROL

COMPLICATIONS

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Factors influencing late complications

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Late complications

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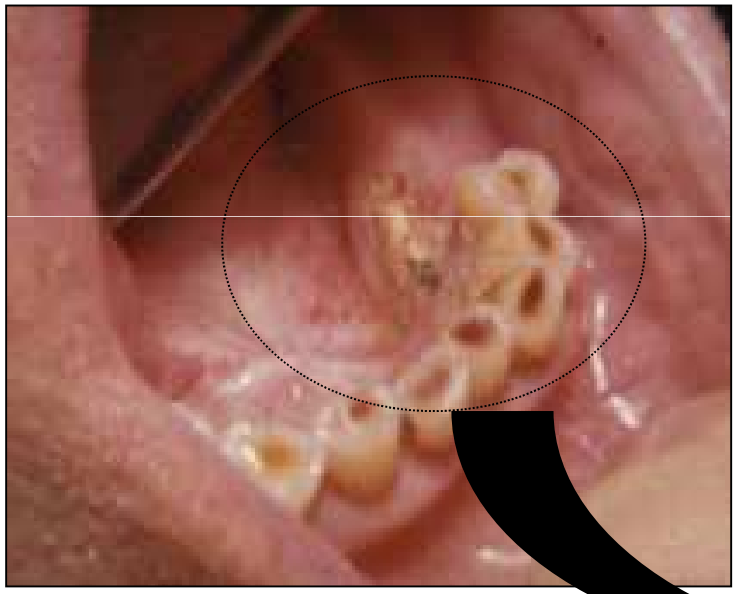
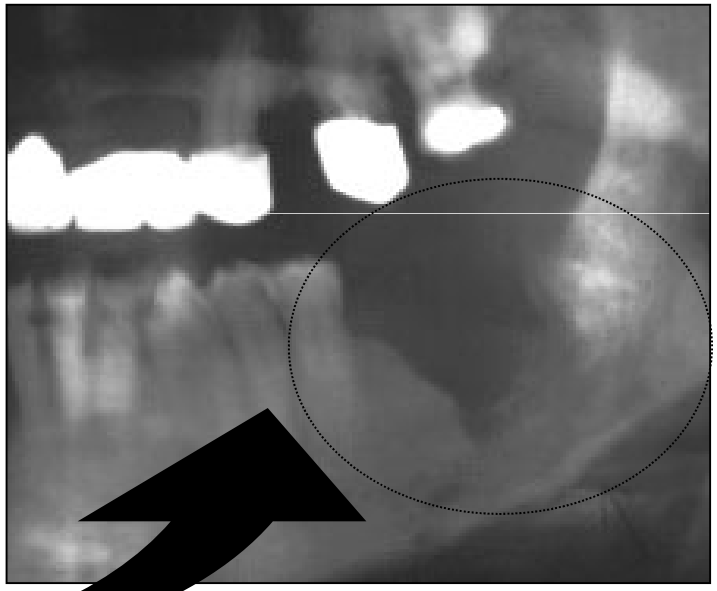
Osteoradionecrosis



Clinical radionecrosis



Radiologic bone defect

Pathologic devascularised bone sequester

Incidence of Late complications Grade 3

- Oral cavity : 3-6%
- Velotonsillar: ; 1-2%
- Base of tongue: 5%
- Post operative:
  - Exclusive BT : 3%
  - Combined with EBI: 12%

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Mobile Tongue

Prognostic factors for late complications

- Dose rate ≥ 0.5 Gy/h
- Treated surface ≥ 8 cm^2 or > 12 cm^2
- Catheter spacing ≥ 15 mm
- Total dose of exclusive brachytherapy ≥ 65 Gy
- Total dose of EBI + brachytherapy > 80 Gy

  Pernot et al : *Radiother Oncol 1995;35:177–185*
  IJROBP 1994;29:973–679
  Mazeron et al : *IJROBP 1990;18:1299–1306*
  IJROBP 1990;19:281–285
  Radiother Oncol 1991 ;21:38–47

- Lead protection of the mandible

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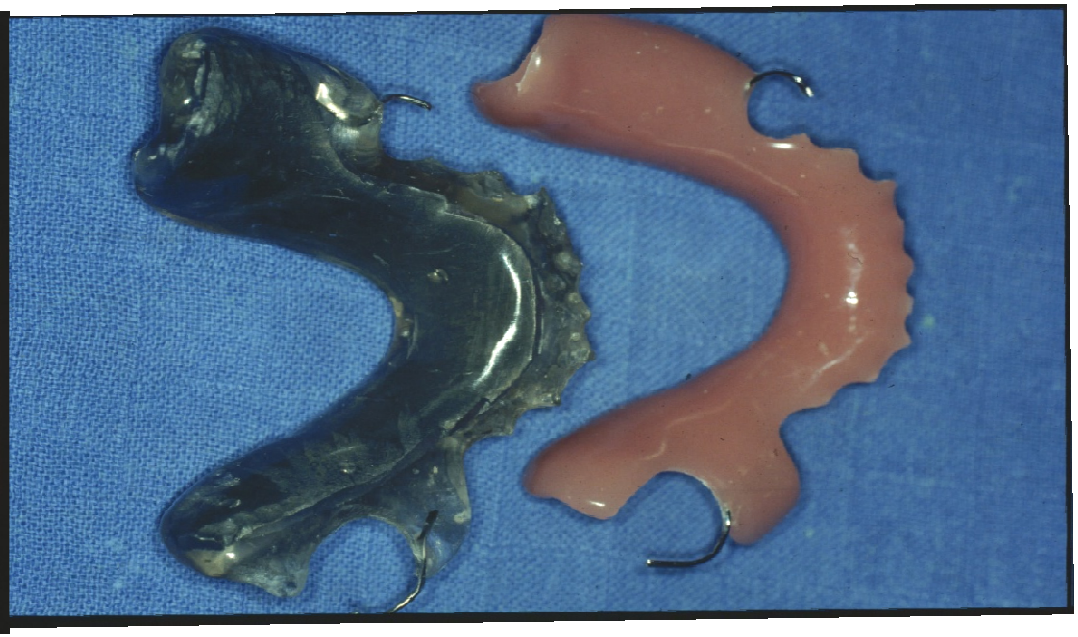
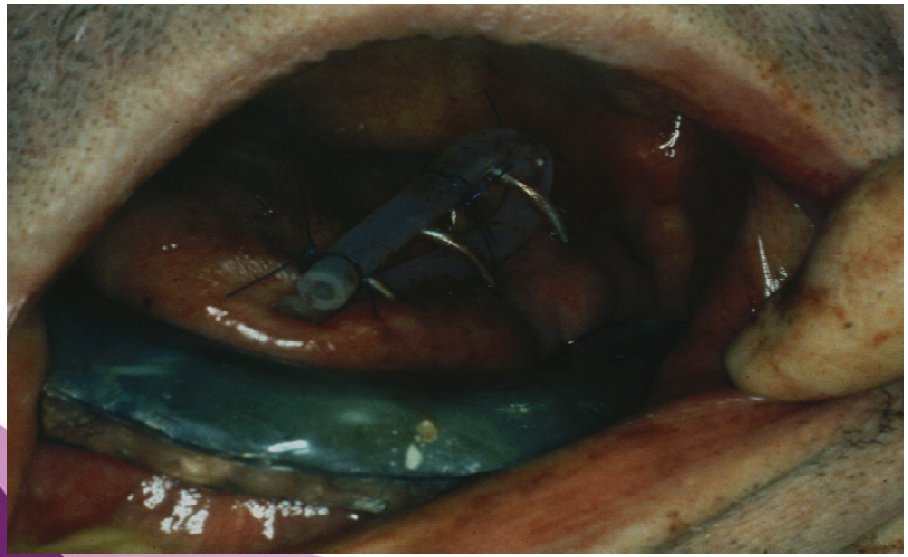
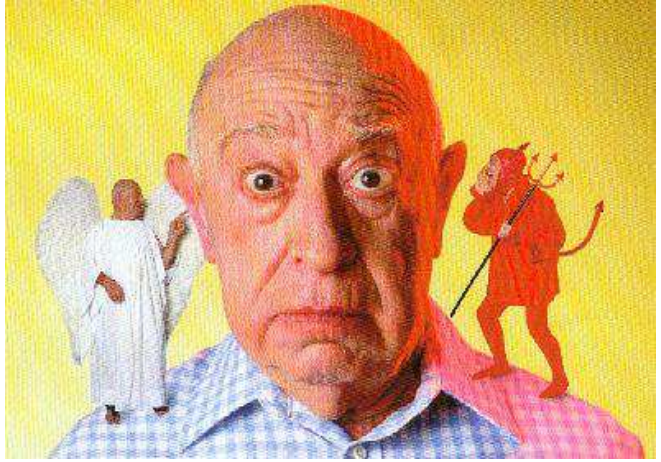
Lead shielding

- Tailored for each patient







Prophylaxis

- General measures
  - Alcohol / Tobacco abstinence
  - Balanced diet
  - Mouth baths

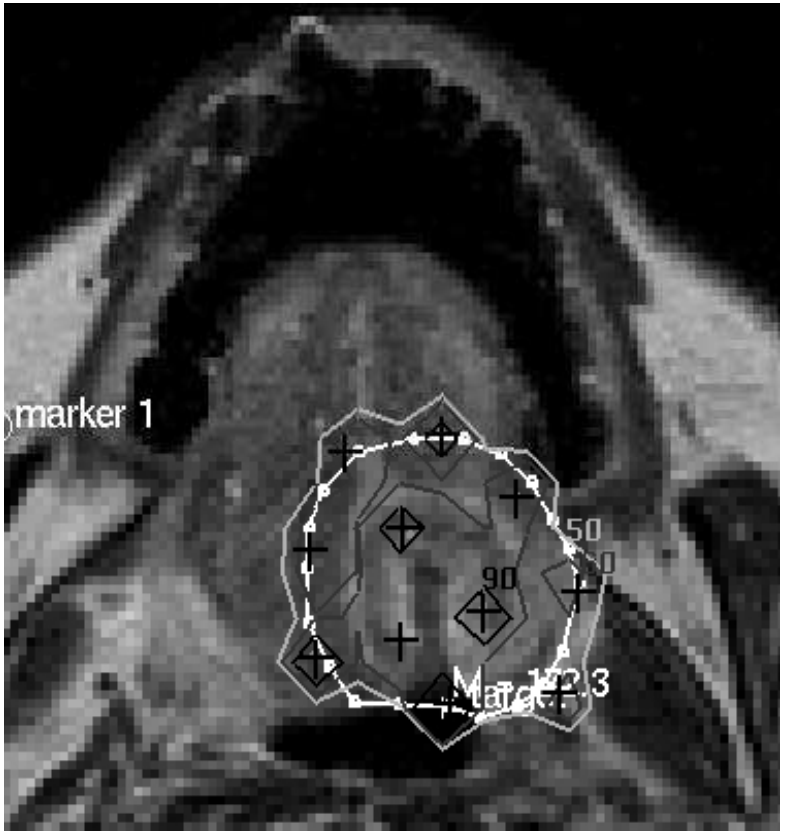
- Dental Prophylaxis
  - Pre implantation tooth extraction:
    - Suture of the gum
    - 2-week delay for healing

- Mandibular Leaded protections

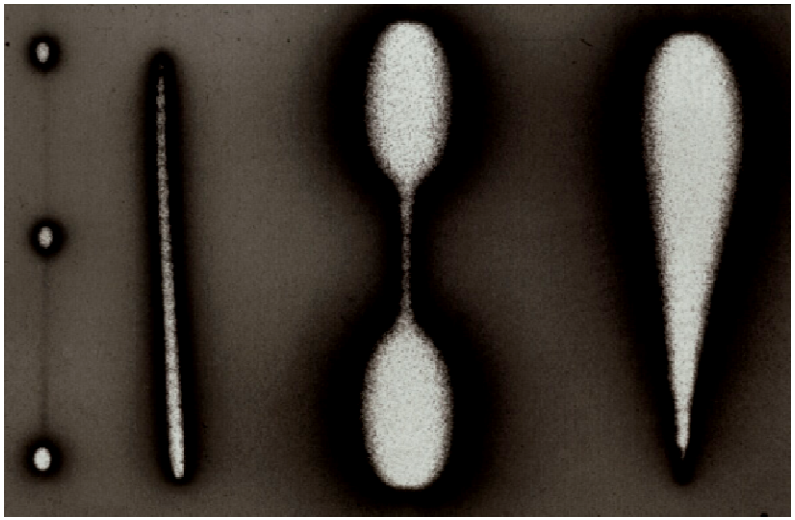
  50 % decrease of the dose transmitted to the bone

Nowadays

3D Imaging : CT / MRI



Stepping sources Technology



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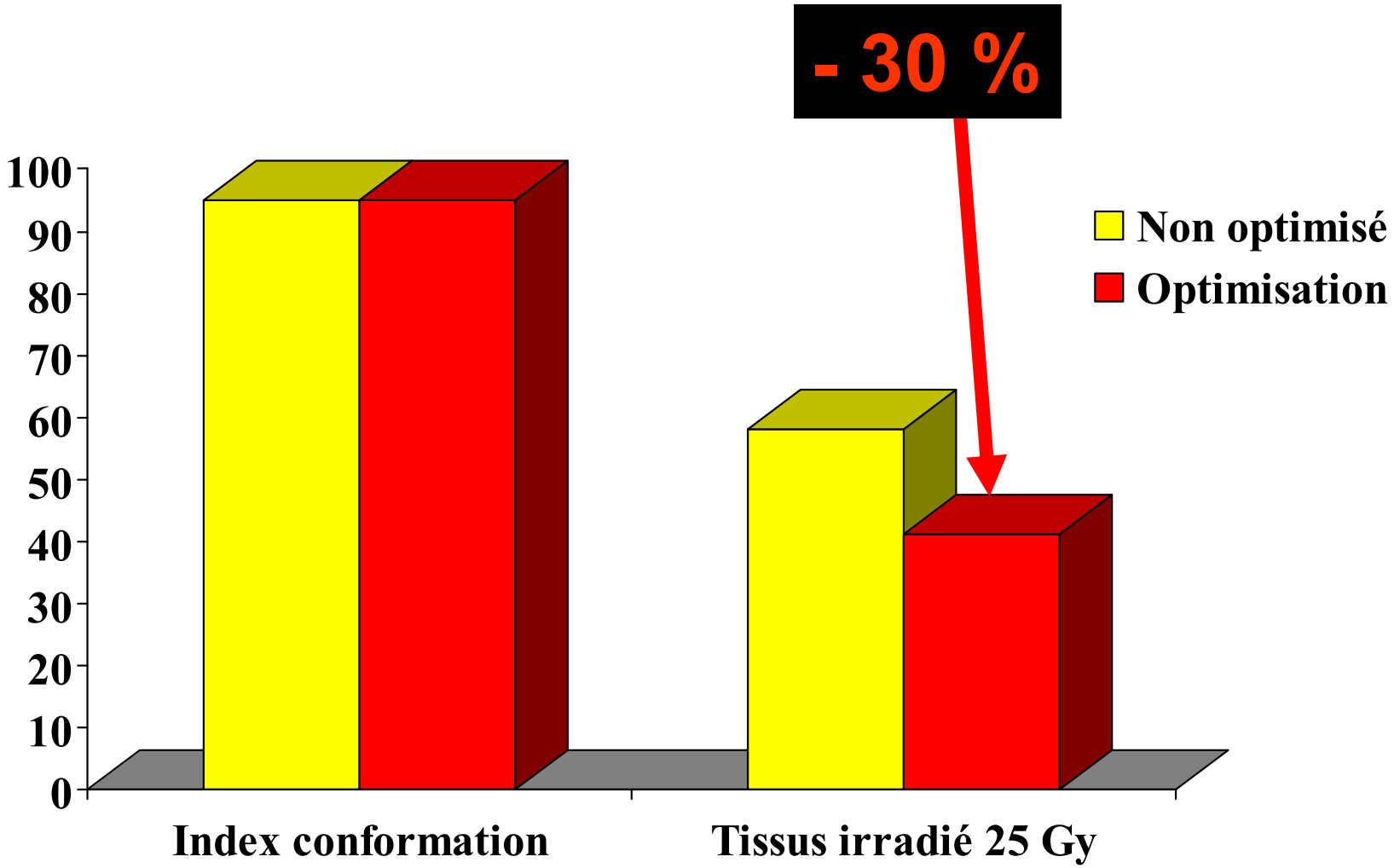
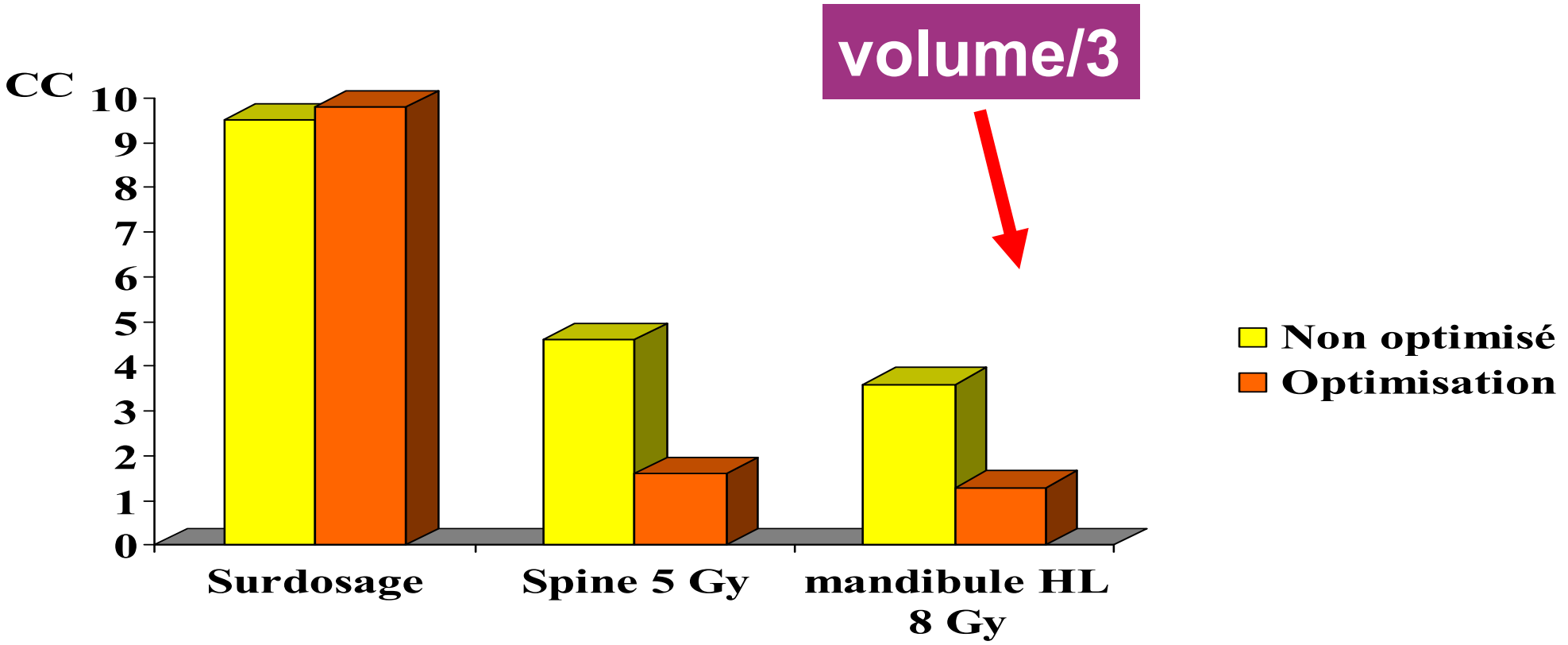
Conformal index- irradiated tissues



F. Ahmad, M. Lapeyre 2004

Benefit of optimisation homolateral mandibule dose



F. Ahmad, M. Lapeyre 2004

PDR series in H&N

Authors	pts	Gy/h	*fract/ d*	Dose EB+BT	local C %	Compl %
Levendag 1997	19	<2	*4-8*	56-70 +20-28	100	0 G3
De Pree 1999	17	.4-.75	/	41 m	59	6
Strnad 2000	40	.5 .7	*24*	50 +24	92	5
Peiffert 2001	30	.5	*24*	45 +16-35	83	16 G2-3
Ziemlew 2007	45 50% lip	.6 –1	*24*	70 +10	88	23

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PDR H&N

- Patients : 236
  Post-op=192
- Dose :
  BT alone: 56 Gy (144 pts)
  Boost : 24 Gy (92 pts)
- DR: 0.4-0.7 Gy/h
  1 pulse/h, 24 h

Tumor site	Tumor(number of patients) T1	T2	T3	T4	Tx	Total
Lip	4	3	0	0	0	7
Floor of mouth	38	18	2	8	1	67
Oral tongue	36	54	7	2	4	103
Base of tongue	1	13	5	4	2	25
Tonsil	6	9	3	1	0	19
Soft palate	3	3	0	0	0	6
Others	2	3	1	1	2	9
Total	90	103	18	16	9	236

- 5 y. survival T1-2 : 82-73% T3-4 : 56%
- 5y. RF T1-2 : 93-83 % T3-4 : 83%
- Soft tissue necrosis : 9,7%
- Bone necrosis: 7,2%

V. Strnad, W. Melzner, Strahlenther Onkol 2005;181:762–7

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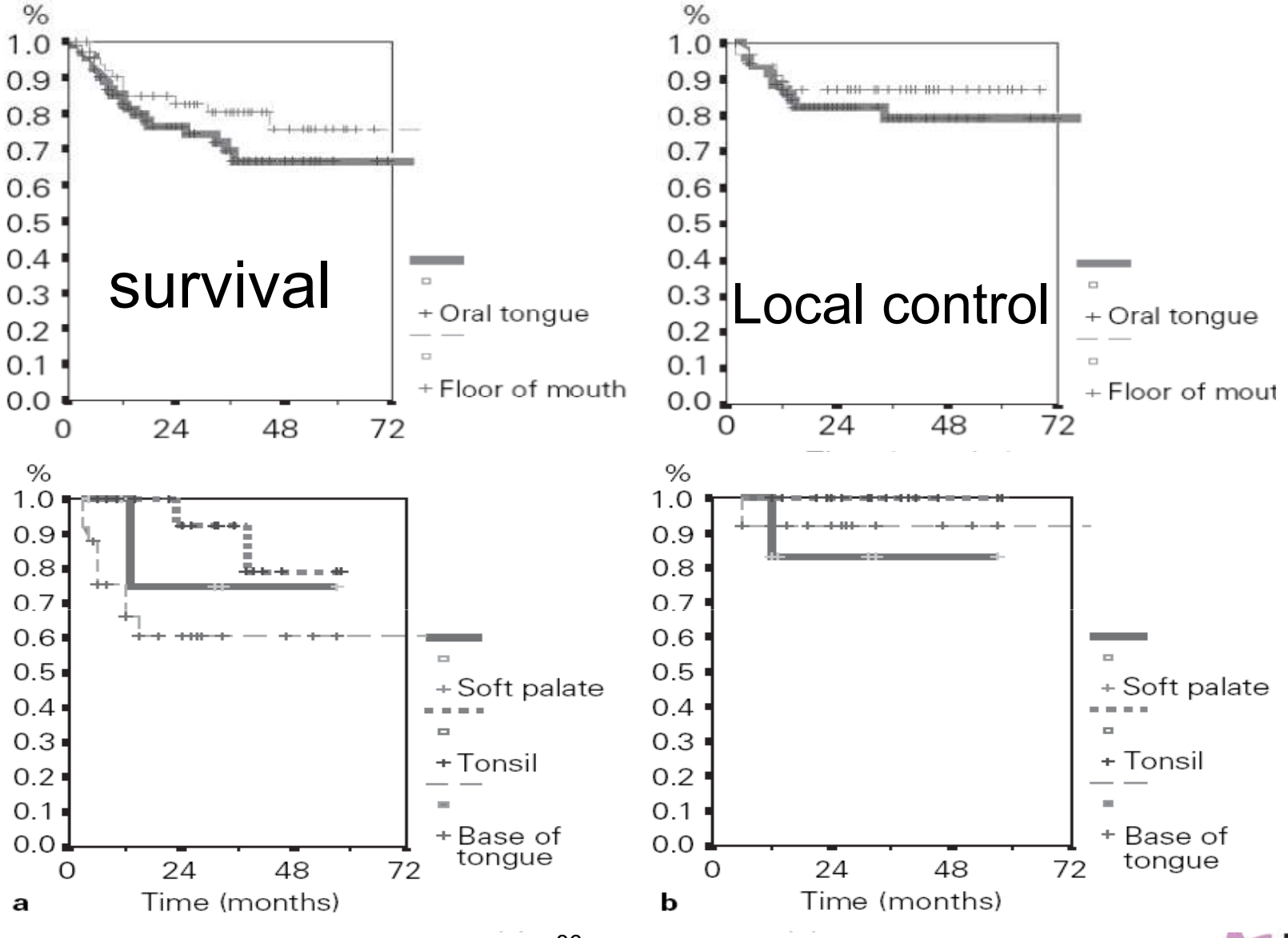
PDR in H&N



V. Strnad, W. Melzner, Strahlenther Onkol 2005;181:762–7

PDR H&N
prognostic factors

- 2000 à 2004 : 210 pts
- Implantation : Paris System
- MCD 100% and Reference : 85%
- Pulse: 0.5 Gy/h

• Local Control : 80% at 4 year		
– Quality index	< 1.72	*(p = 0,02)*
– intersource distance	< 11.8 mm	*(p= 0,01)*
• Soft tissues necrosis : 11%		
– V85	> 26,8 ml	*(p = 0,01)*
– Quality index	> 1,72	*(p = 0,04)*
– intersource distance	> 16,9 mm	*(p= 0,07)*
• ORN : 7,6%		
– Prescribed Dose :	> 0.64 Gy/h	*(p= 0,03)*
– High dose	> 80,3 Gy/h	*(p= 0,04)*

Winfrid J. Melzner, Radiotherapy and Oncology 82 (2007) 167–173.

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ELSEVIER

BRACHYTHERAPY

Brachytherapy ■ (2014) ■

A case–control study of patients with squamous cell carcinoma of the oral cavity and oropharynx treated with pulsed-dose-rate brachytherapy

Alain Haddad[1,*], Didier Peiffert[1], Michel Lapeyre[2], Valentin Harter[3], Isabelle Buchheit[4], Pierre Graff[1]

[1]*Département de Radiothérapie, Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France*
[2]*Département de Radiothérapie, Centre Jean Perrin, Clermont-Ferrand, France*
[3]*Unité d'Activité et de Statistiques Médicales, Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France*
[4]*Département de Physique, Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France*

- 36 consecutive patients treated with PDR BT
- randomly matched to
- 72 control patients treated with cLDR BT

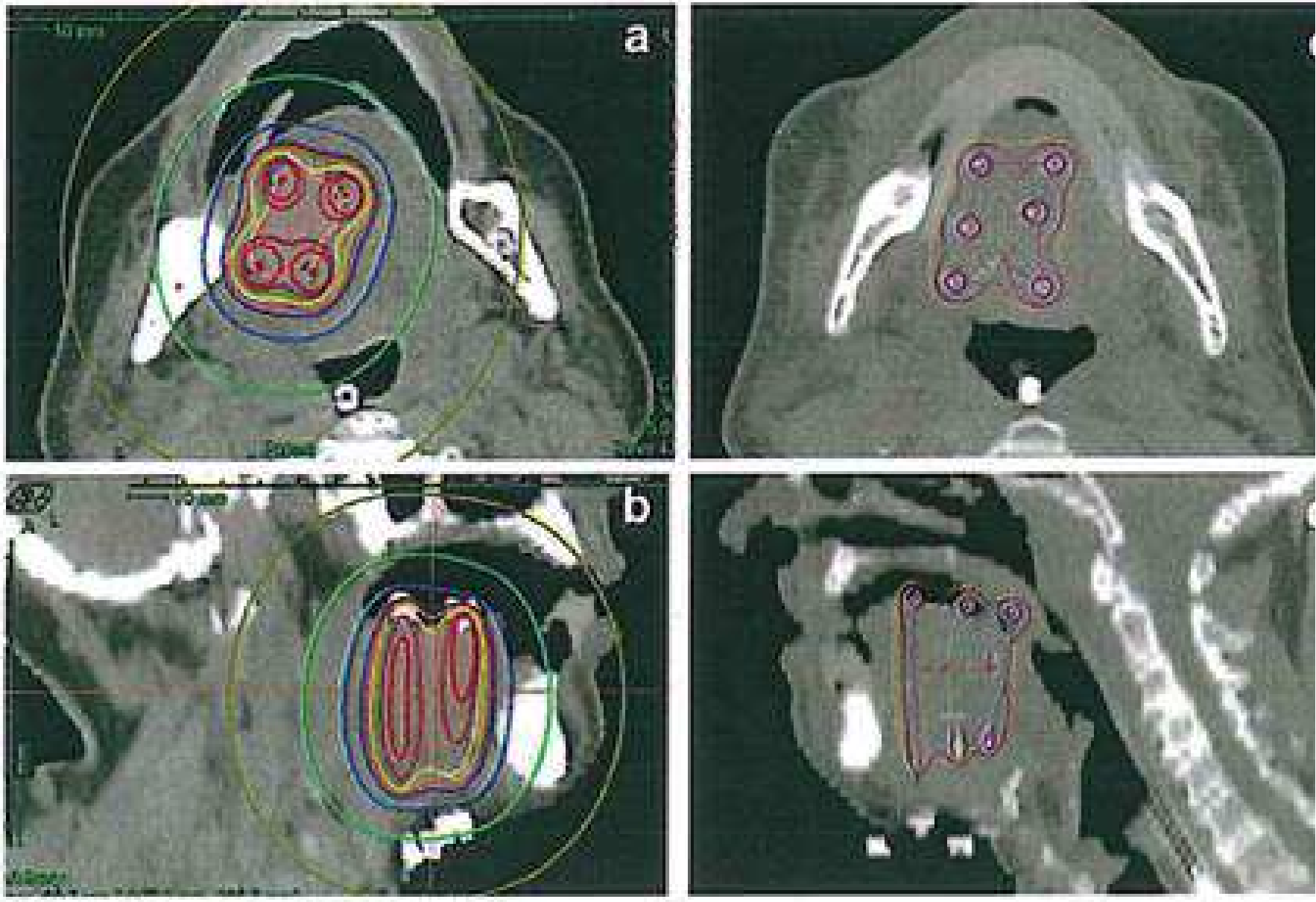

Fig. 1. Typical implant dose distributions. Left: (a) PDR 4-line implant in transverse and (b) sagittal views. Right: (c) LDR 6-l
(d) sagittal views. PDR = pulsed-dose-rate; LDR = low-dose-rate.

cLDR vs PDR

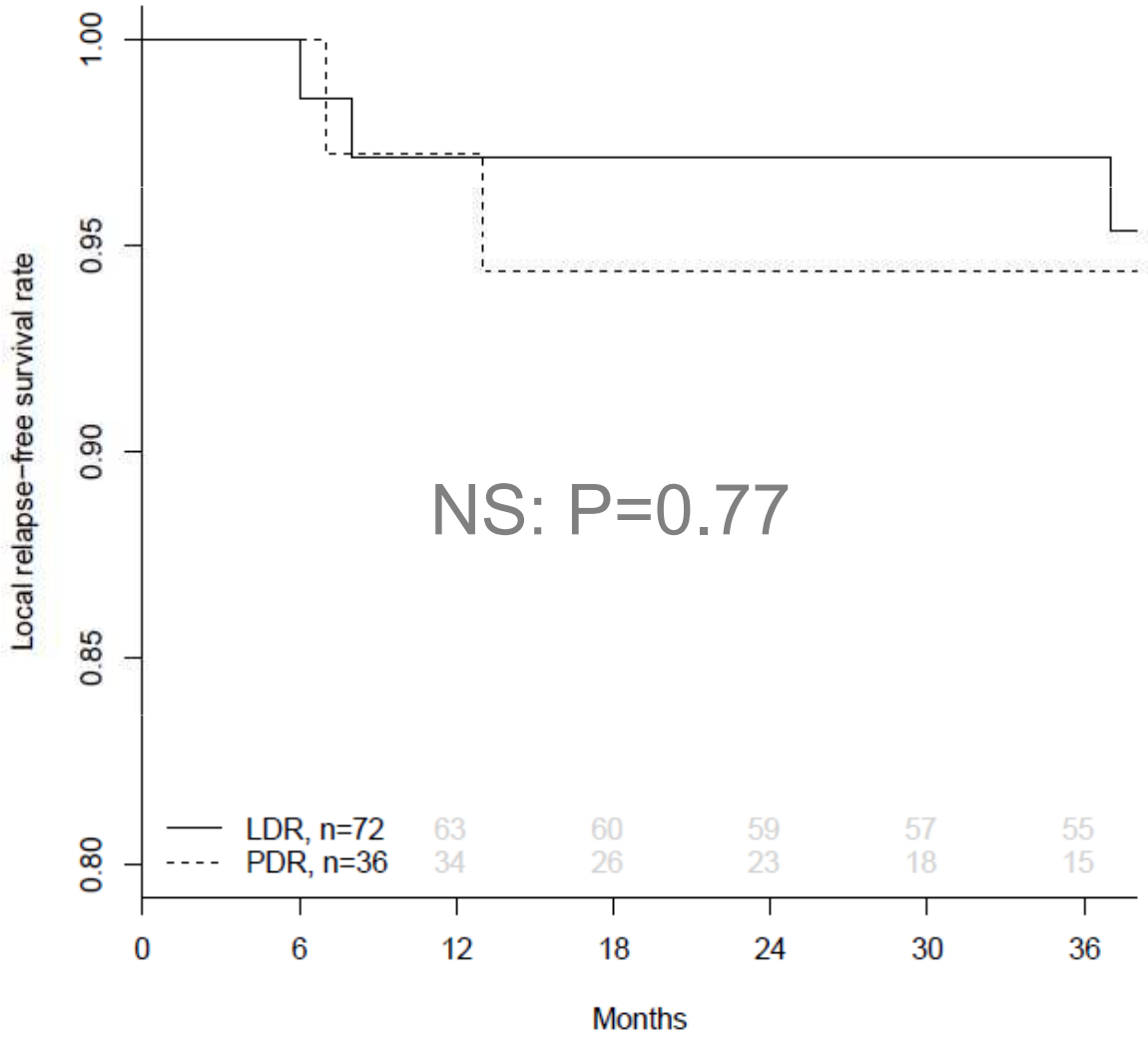

Figure 1 : Kaplan-Meier estimates of the Local Recurrence Free Survival (LRFS) for patients treated with Pulsed-Dose Rate (PDR) or continuous Low Dose Rate (cLDR) brachytherapy, showing no statiscally significant difference at 3 years (p=0.77).

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cLDR vs PDR

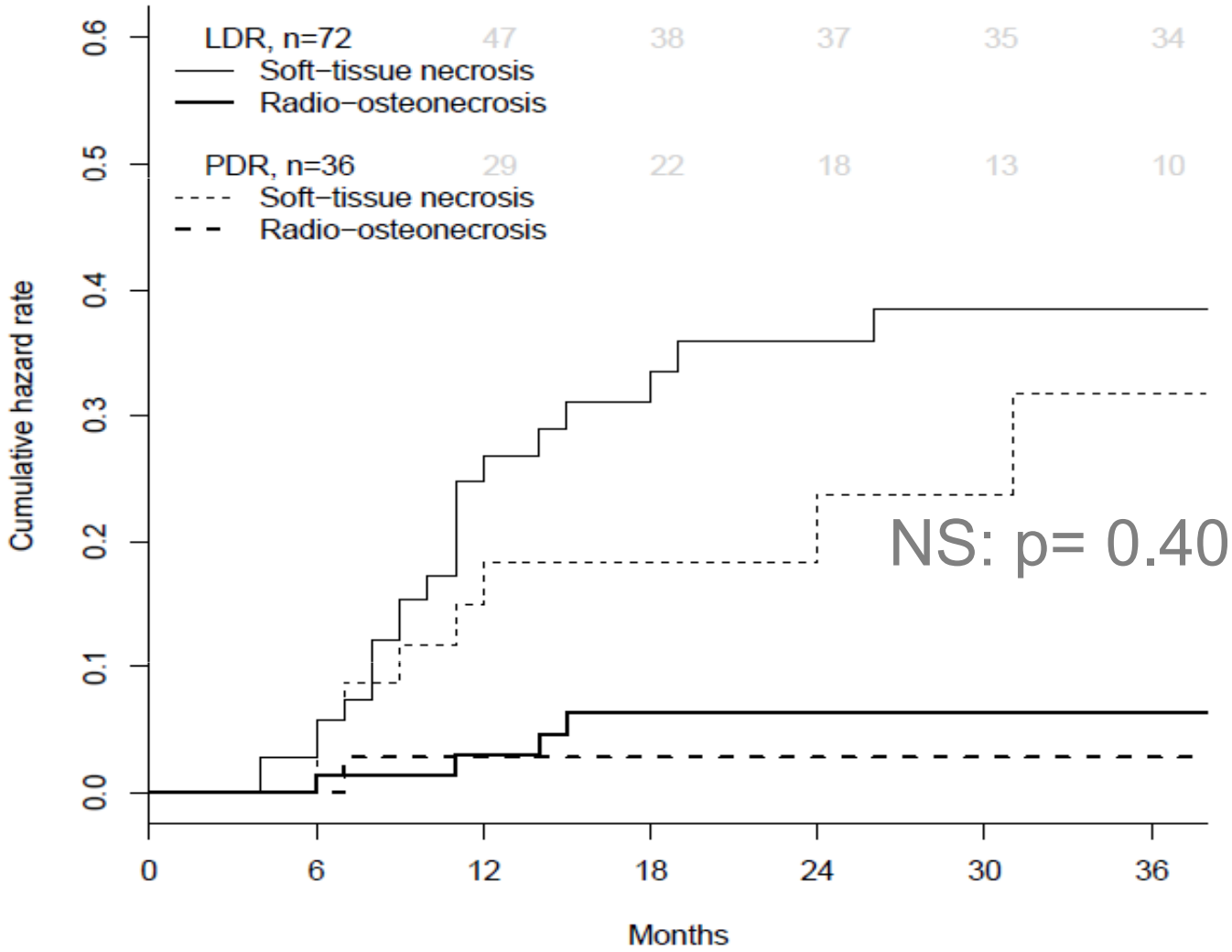

Figure 2 : Kaplan-Meier estimates of the cumulative risk of late grade 2-3 complications following Pulsed-Dose Rate (PDR) or continuous Low Dose Rate (cLDR) brachytherapy, showing no statistically significant difference at 3 years (p=0.4).

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OPEN ACCESS Freely available online

PLOS ONE

High Dose Rate versus Low Dose Rate Brachytherapy for Oral Cancer – A Meta-Analysis of Clinical Trials

Zhenxing Liu, Shengyun Huang, Dongsheng Zhang*

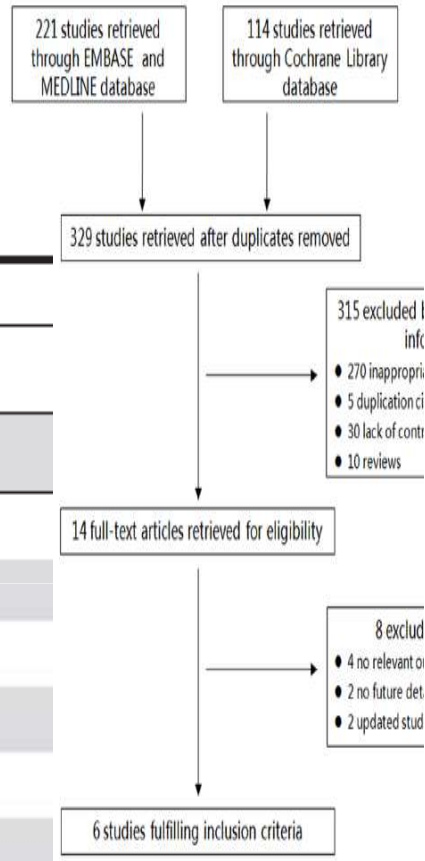
Department of Oral and Maxillofacial Surgery, Provincial Hospital Affiliated to Shandong University, Jinan, China

Table 2. Characteristics of literatures investigating LDR vs. HDR for oral cancer.

Author	Year	Anatomy	LOE	LDR			HDR		
				Pts	Implants	Dose(Gy)	Pts	Implants	Dose(Gy)
Ghadjar[13]	2011	Lip	2b	70	^{192}Ir	60	33	^{192}Ir	36
Arrate[14]	2010	Lip	2b	100	^{192}Ir	60–70	21	^{192}Ir	45–50
Umeda[15]	2005	Tongue	2b	78	^{226}Rd/^{137}Cs	61	26	^{192}Ir	59
Kakimoto[16]	2003	Tongue	2b	61	^{192}Ir	69	14	^{192}Ir	49
Inoue[17]	2001	Tongue	1b	26	^{192}Ir	70	25	^{192}Ir	60
Inoue[18]	1997	Floor of mouth	2b	41	^{198}Au	72	16	^{192}Ir	53

LOE: levels of evidence, Pts: patients.

doi:10.1371/journal.pone.0065423.t002



1. PRISMA flow chart of the meta-analysis.

371/journal.pone.0065423.g001

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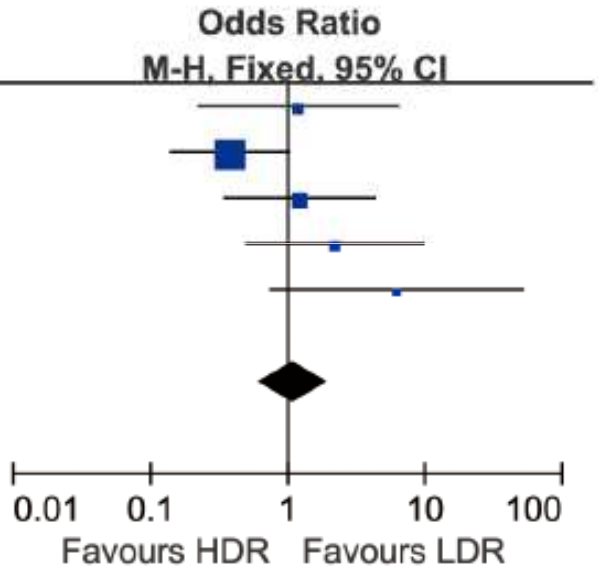
Local Recurrence LDR/HDR

a.

Study or Subgroup	LDR Events	LDR Total	HDR Events	HDR Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Ghadjar 2011	5	70	2	33	11.7%	1.19 [0.22, 6.49]	2011
Umeda 2005	13	78	9	26	52.3%	0.38 [0.14, 1.03]	2005
Kakimoto 2003	20	61	4	14	20.3%	1.22 [0.34, 4.37]	2003
Inoue 2001	6	26	3	25	10.9%	2.20 [0.48, 9.98]	2001
Inoue 1997	12	41	1	16	4.7%	6.21 [0.74, 52.39]	1997
Total (95% CI)		**276**		**114**	**100.0%**	**1.12 [0.62, 2.01]**	
Total events	56		19				

Heterogeneity: $Chi^2 = 7.77$, df = 4 (P = 0.10); $I^2 = 48\%$

Test for overall effect: Z = 0.38 (P = 0.71)



b.

Study or Subgroup	LDR Events	LDR Total	HDR Events	HDR Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Ghadjar 2011	5	70	2	33	17.1%	1.19 [0.22, 6.49]	2011
Umeda 2005	13	78	9	26	27.9%	0.38 [0.14, 1.03]	2005
Kakimoto 2003	20	61	4	14	23.0%	1.22 [0.34, 4.37]	2003
Inoue 2001	6	26	3	25	19.4%	2.20 [0.48, 9.98]	2001
Inoue 1997	12	41	1	16	12.6%	6.21 [0.74, 52.39]	1997
Total (95% CI)		**276**		**114**	**100.0%**	**1.21 [0.49, 2.98]**	
Total events	56		19				

Heterogeneity: $Tau^2 = 0.50$; $Chi^2 = 7.77$, df = 4 (P = 0.10); $I^2 = 48\%$

Test for overall effect: Z = 0.41 (P = 0.68)

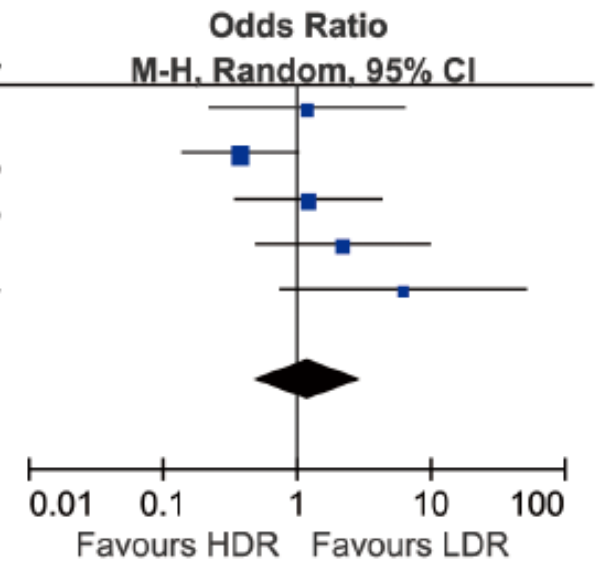


Figure 3. Local recurrence of oral cancer treated with LDR vs. HDR brachytherapy (a. fixed effects model; b. random effects model).

doi:10.1371/journal.pone.0065423.g003

Complications LDR/HDR

Study or Subgroup	LDR Events	LDR Total	HDR Events	HDR Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Ghadjar 2011	38	70	19	33	36.7%	0.88 [0.38, 2.02]	2011
Arrate 2010	32	100	7	21	24.4%	0.94 [0.35, 2.56]	2010
Kakimoto 2003	15	61	3	14	11.4%	1.20 [0.29, 4.86]	2003
Inoue 2001	1	26	3	25	9.1%	0.29 [0.03, 3.03]	2001
Inoue 1997	13	41	6	16	18.3%	0.77 [0.23, 2.59]	1997
Total (95% CI)		**298**		**109**	**100.0%**	**0.86 [0.52, 1.42]**	
Total events	99		38				

Heterogeneity: $Chi^2 = 1.09$, $df = 4$ ($P = 0.90$); $I^2 = 0\%$

Test for overall effect: $Z = 0.60$ ($P = 0.55$)

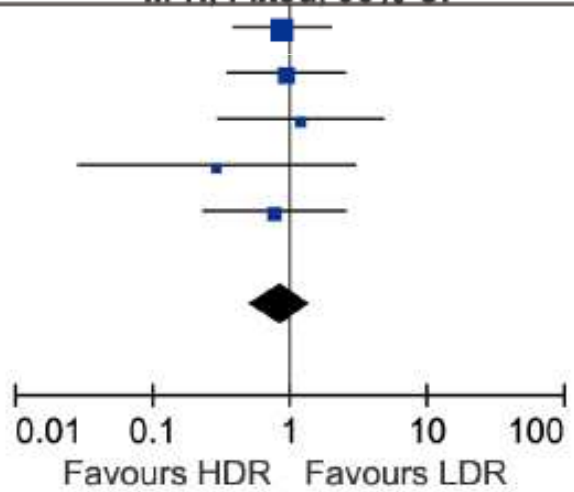


Figure 5. Grade 3 or Grade 4 complications of oral cancer treated with LDR vs. HDR brachytherapy.
doi:10.1371/journal.pone.0065423.g005

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Mortality LDR/HDR

Study or Subgroup	LDR Events	LDR Total	HDR Events	HDR Total	Weight	Odds Ratio M-H. Fixed. 95% CI	Year
Ghadjar 2011	16	70	7	33	24.1%	1.10 [0.40, 3.00]	2011
Umeda 2005	21	78	11	26	39.6%	0.50 [0.20, 1.27]	2005
Kakimoto 2003	34	61	8	14	18.9%	0.94 [0.29, 3.05]	2003
Inoue 2001	6	26	3	25	7.7%	2.20 [0.48, 9.98]	2001
Inoue 1997	13	41	3	16	9.7%	2.01 [0.49, 8.30]	1997
Total (95% CI)		**276**		**114**	**100.0%**	**1.01 [0.61, 1.66]**	
Total events	90		32				

Heterogeneity: $Chi^2 = 4.15$, $df = 4$ ($P = 0.39$); $I^2 = 4\%$

Test for overall effect: $Z = 0.03$ ($P = 0.98$)

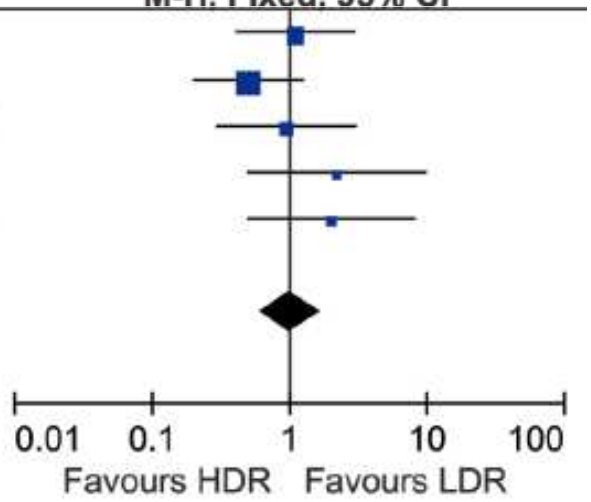

Figure 4. Overall mortality of oral cancer treated with LDR vs. HDR brachytherapy.
doi:10.1371/journal.pone.0065423.g004

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Conclusion

- Brachytherapy is effective in H&N tumours
  - High dose
  - Conformal
  - Accelerated
- Competitive with external beam irradiation
- Competitive with surgery

- PDR similar LC, less complications than LDR
- HDR sligthly lower control , but more complications than LDR

Proper fractionation schedules to be elaborated

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Florence, March 13-16 2016

ESTRO School

Modern Brachytherapy Techniques

Safety in Brachytherapy: Some Aspects with regard to Advance Techniques and Advance Imaging

ESTRO Teaching Course

Florence, 2016

Dimos Baltas

E-mail: dimos.baltas@uniklinik-freiburg.de

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Safety in Life ! Mexico, To be continued …

In 2013, "a truck carrying a highly radioactive source **used for cancer treatments** was stolen by thieves on its way to a waste storage facility."

July 2014: "Mexican authorities on Friday found a load of dangerous radioactive material that was in a stolen pick-up, a top civil protection official said.
The load of iridium 192 was found abandoned on a street a few miles from where the truck was stolen in the industrial Mexico City suburb of Tlalnepantla, Luis Felipe Puente, the head of the country's civil protection agency, said on Twitter.
Military troops mounted a security perimeter around the small container emblazoned with logos for hazardous materials until it was removed from the site by the country's nuclear safety commission, according to media reports.
The material, normally used in industrial radiography, was housed in a specialized container and would only pose a health risk if the housing was tampered with, Mexico's interior ministry said in a statement. "

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Safety in Life ! Mexico, To be continued …

"A container of Iridium-192 used for industrial radiography was taken from a truck in the town of Cardenas in Tabasco state."

16 April 2015

"A container of Iridium-192 used for industrial radiography was taken from a transporter in the town of San Juan del Río in Querétaro state."

29 Februar 2016

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What do we mean with *Safety*?

"Safety is the condition of a "steady state" of an organization or place doing what it is supposed to do. "What it is supposed to do" is defined in terms of public codes and standards, associated architectural and engineering designs, corporate vision and mission statements, and operational plans and personnel policies. For any organization, place, or function, large or small, safety is a normative concept. It complies with situation-specific definitions of what is expected and acceptable."

***Charles G. Oakes*, PhD, Blue Ember Technologies, LLC.*"Safety versus Security in Fire Protection Planning,"* The American Institute of Architects: Knowledge Communities, May 2009. Retrieved on June 22, 2011.

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“It complies with situation-specific definitions of what is expected and acceptable.”

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What do we mean with *Safety*?

The UK Health and Safety Executive defines Safety Culture as:

A more succinct definition has been suggested:
"Safety culture is how the organization behaves when no one is watching."

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“… when no one is watching.”

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What do we mean with *Safety*?

The International Basic Safety Standards defines Safety Culture as:

"The assembly of characteristics and attitudes in organisations and individuals which establishes that, as an over-riding priority, protection and safety issues receive the attention warranted by their significance."

"Have I done all that I reasonably can to reduce (unnecessary) radiation exposure?"

Prevention of High-dose-rate Brachytherapy Accidents, Volume 35 No. 2, 2005

The main Steps/Procedures in Modern Brachytherapy

- **Localisation (*Imaging*)**
- **(Pre-)Planning of the procedure (*Imaging/RTP*)**
- **Implantation (*Imaging, Guidance/Navigation, IO-RTP*)**
- **Treatment Planning (*Imaging, RTP*)**
- **Treatment Delivery (*Afterloading*)**
- ***Treatment Delivery Verification (Imaging, …?)***

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Advance Imaging resulted to:

- **More accurate Localisation/Delineation of the Target(s) (common to ERT: CT, MR, PET, 3D-U/S)**
- **Better Visualisation of Catheters/Applicators**
- **More accurate and safe Placement of Catheters/Applicators**
- **More accurate Localisation of Catheters/Applicators**
- ***More accurate Dose Calculation (?)***

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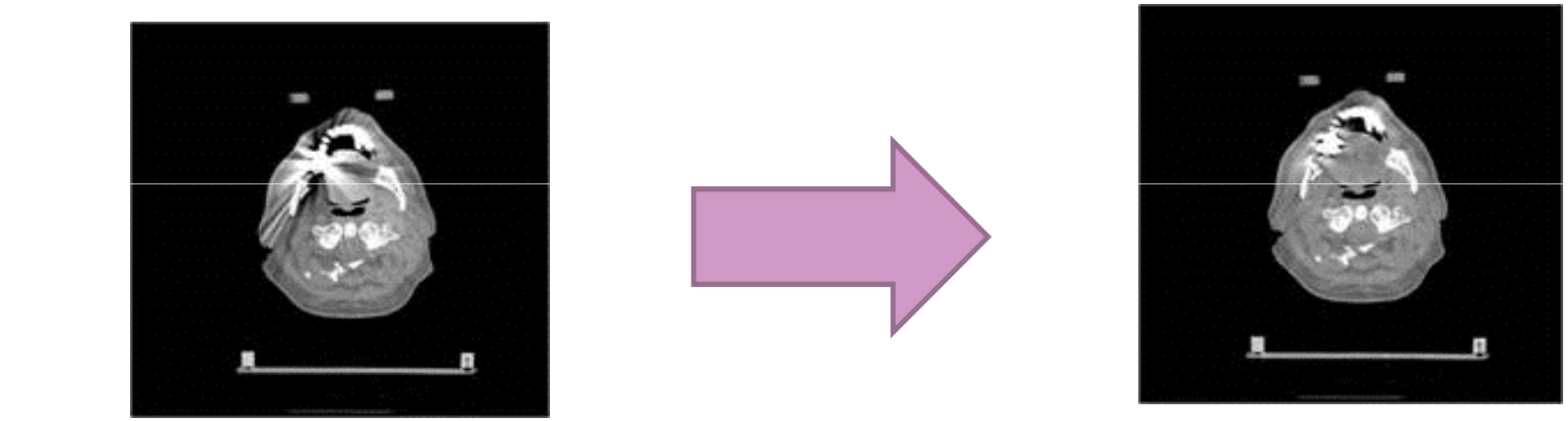
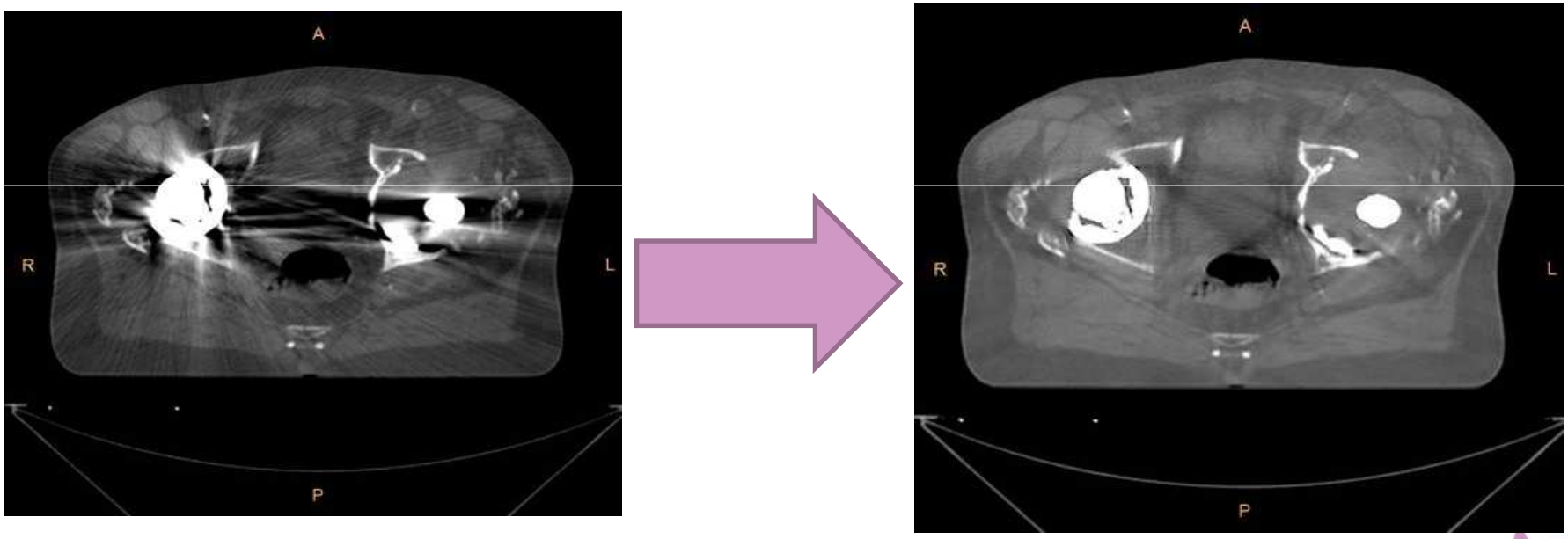
Advance Imaging: Metallic Artefacts





By Courtesy of Philips CT Imaging

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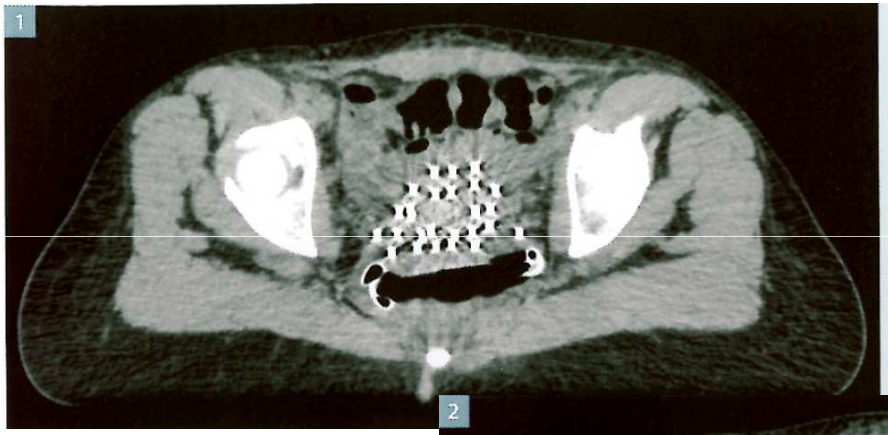
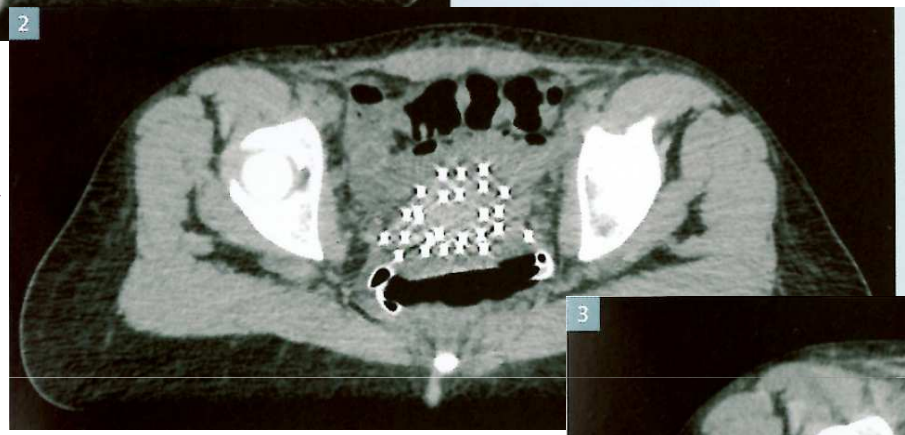
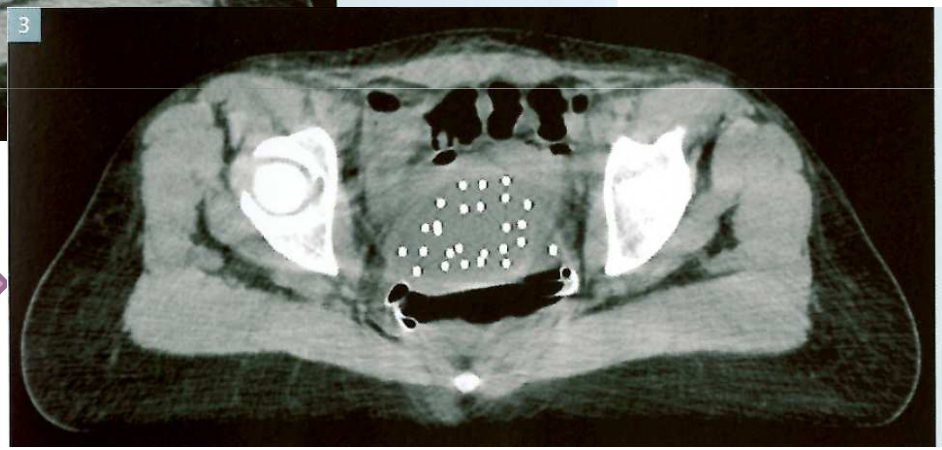
Advance Imaging: Metallic Artefacts



1 Interstitial brachytherapy treatment with no iMAR reconstruction.



2 Interstitial brachytherapy treatment with spine implant iMAR reconstruction.



3 Interstitial brachytherapy treatment with neuro coil iMAR reconstruction.

SIEMENS Healthcare, Germany: SOMATOM Definition AS Open – RT Pro edition

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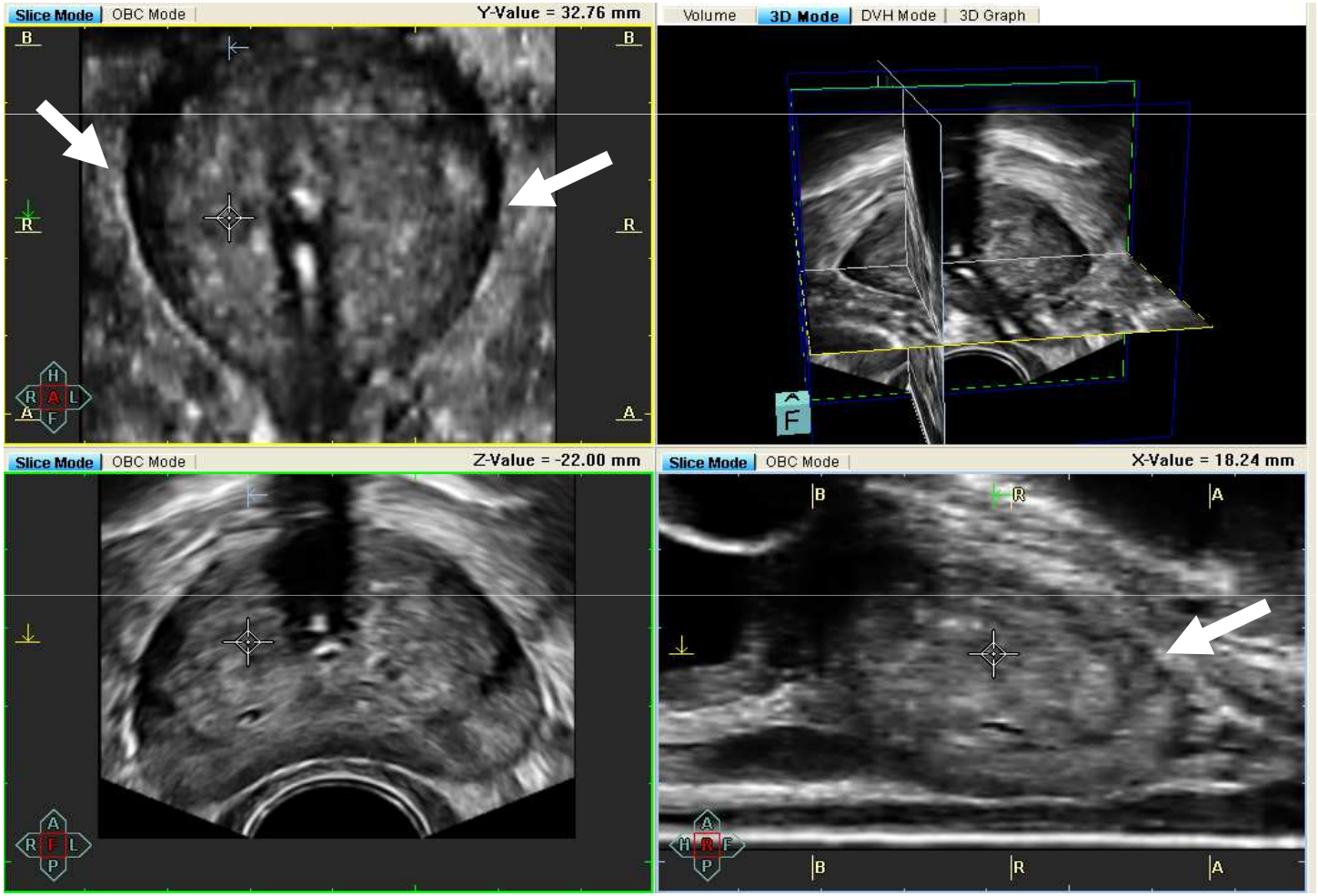
Advance Imaging

2D and 3D U/S-Acquisition



Clinical Data and Images by courtesy of Dept. of Radiation Oncology, Offenbach
Using BiopSee(R) by MedCom GmbH

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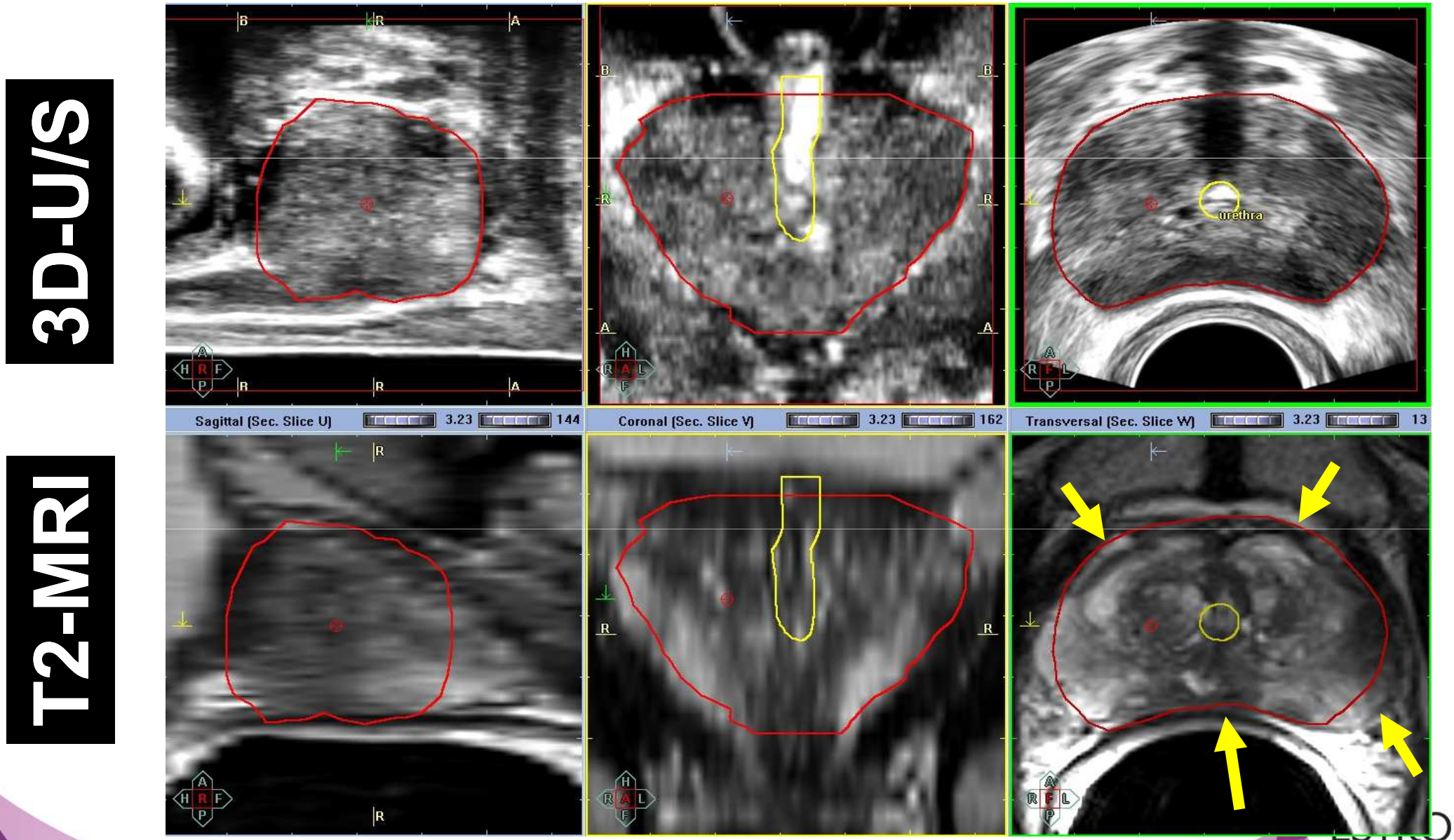
Advance Imaging: Multi-Modality Imaging



Advance Imaging: Applicators

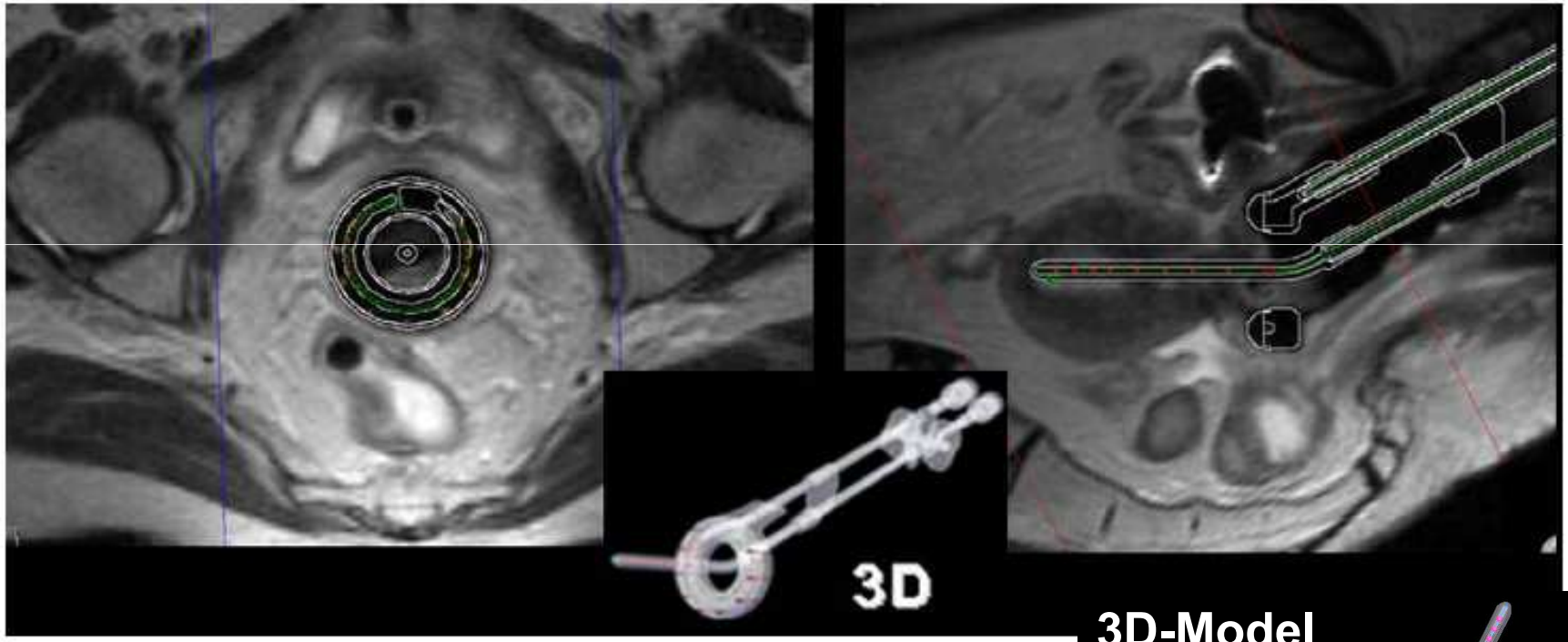
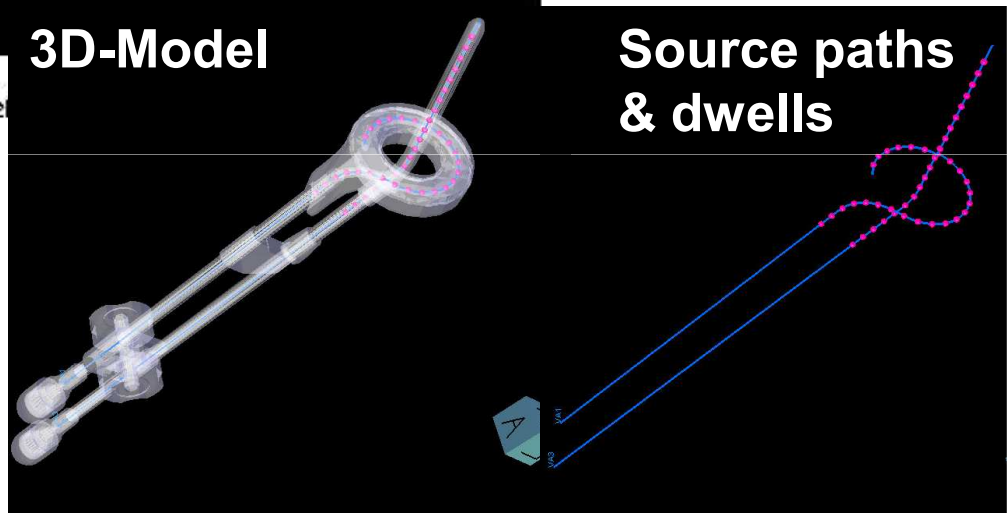


Fig. 7. Position of a library applicator (in the middle) in the transversal (le



Robust back-projection!!!

GEC-ESTRO Recommendations, Hellebust T., Kirisits, C., Berger, D., et al.
Radiotherapy & Oncology 95, 153-160, 2010

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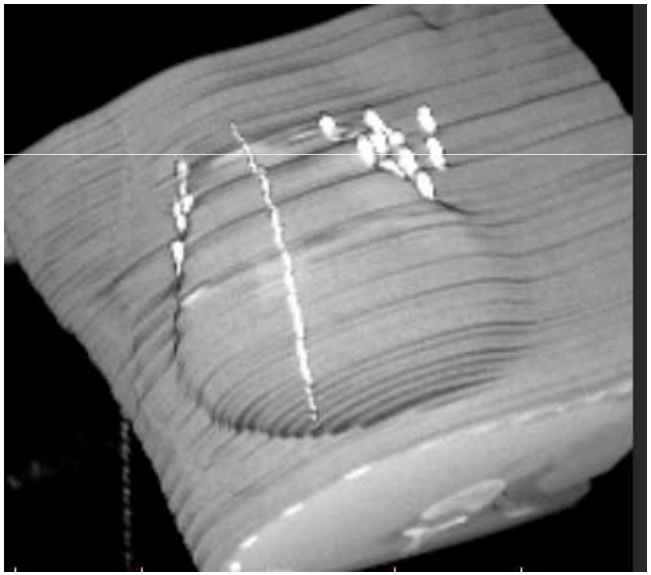
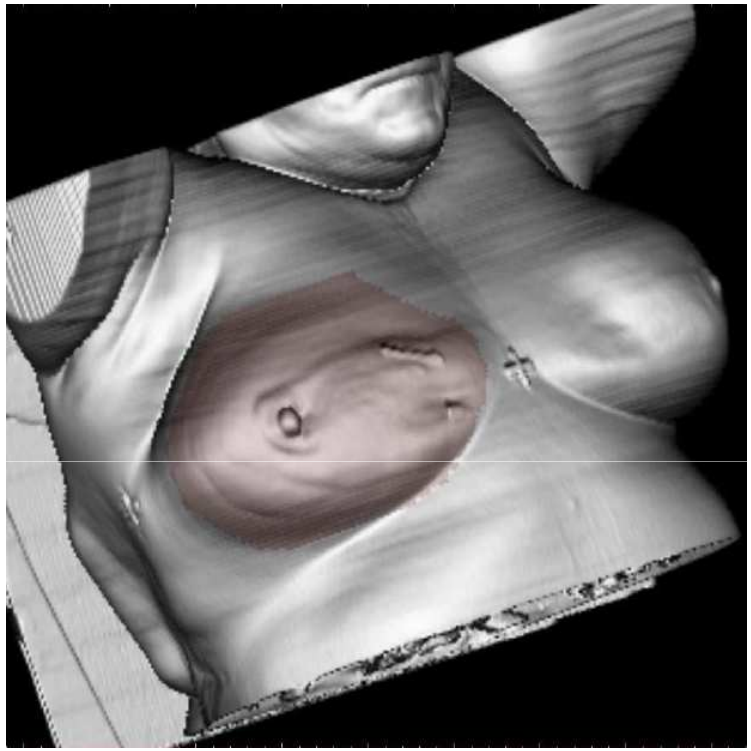
Advance Imaging: Applicator Localisation



?



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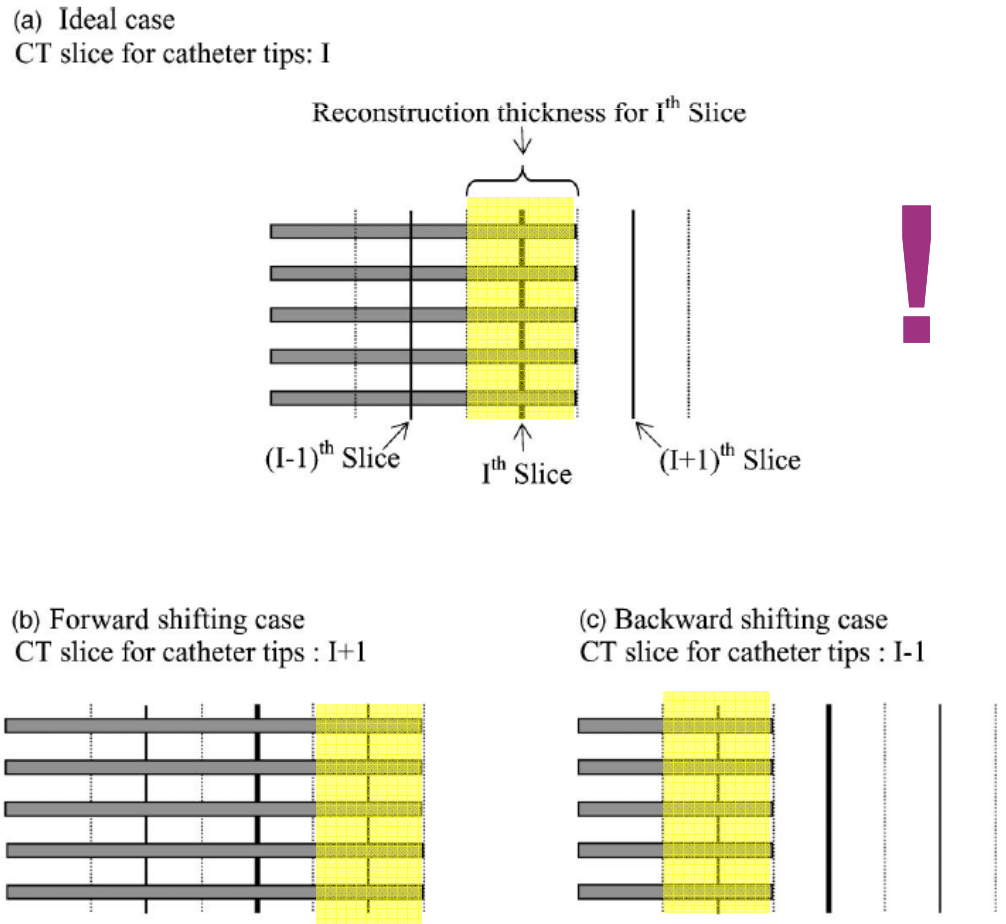
Advance Imaging: Applicator Localisation

The partial-volume-effect



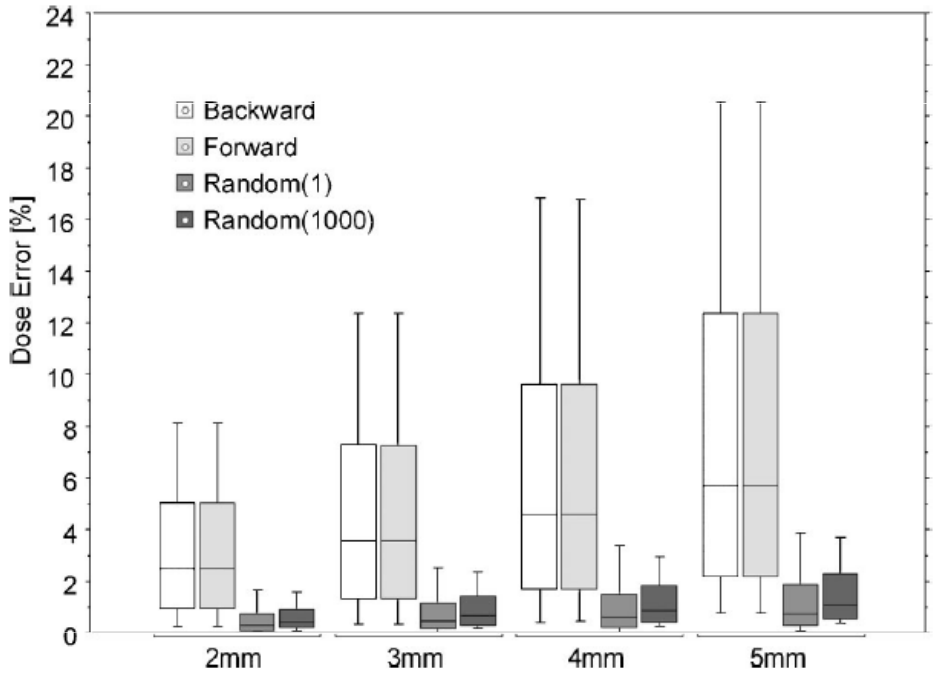


FIG. 3. Statistical representation of dose uncertainty for four different types of simulations. The data was obtained from five patients for the various CT slice thickness from 2 to 5 mm. Random(1) is a random shifting of catheters and Random(1000) is the thousand times random shifting of catheters. (Each parallel bar indicates 10, 25, 50, 75, and 90 percentiles from the lowest to the highest).

Kim Y, Hsz IC, Lessard E, Pouliot J, "Dose uncertainty due to CT slice thickness in CT-based HDR-BRT of PCA, *Medical Physics*, 2004

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Advance Technology:
Medical Physics / Dosimetry

- **High level of Standardization**
- **Wide Availability of Dosimetry Laboratories (P & S*)**
- **Availability of Easy to Use Dosimetry Systems**

*** Primary & Secondary**

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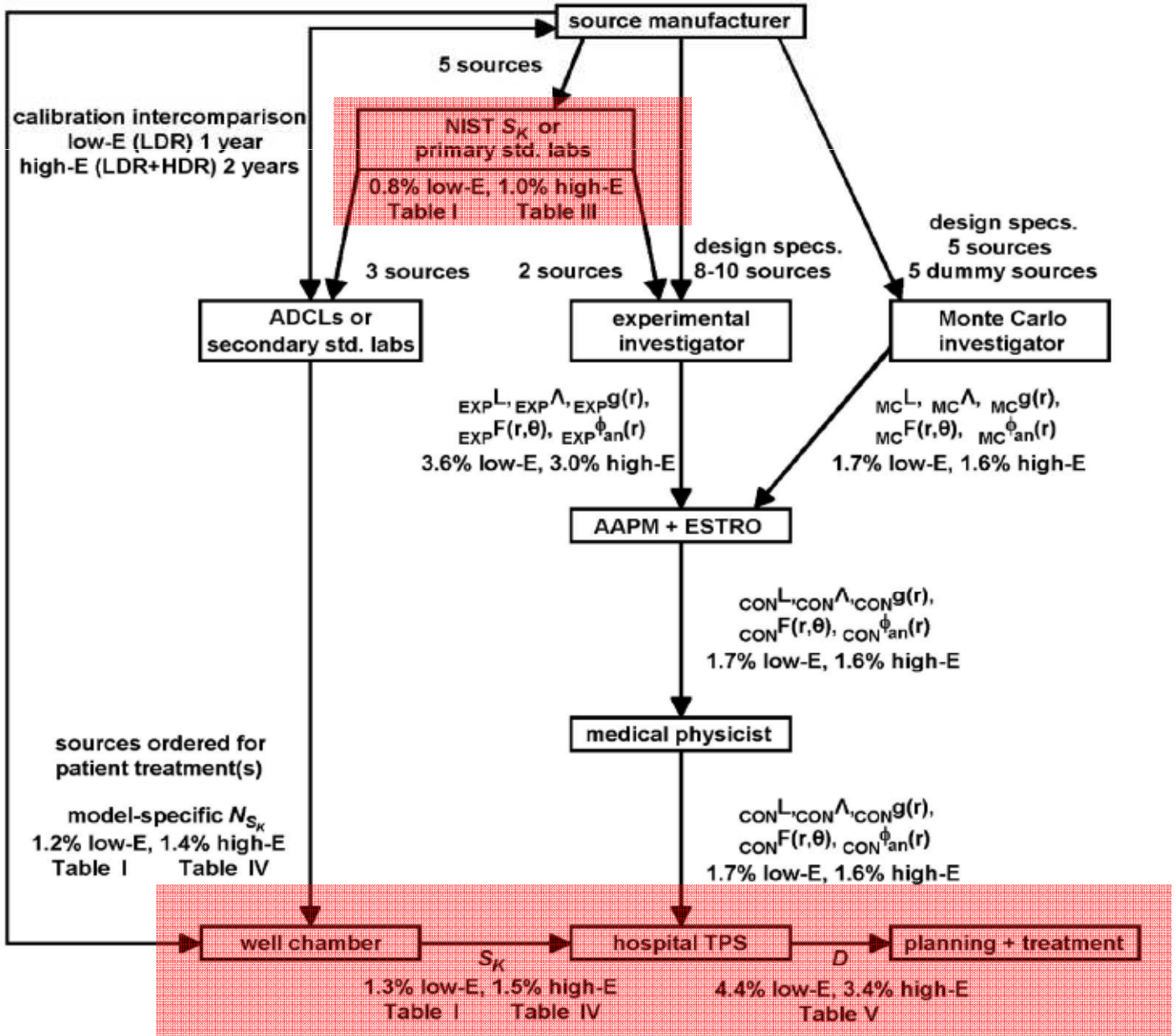
A dosimetric uncertainty analysis for photon-emitting brachytherapy sources: Report of AAPM Task Group No. 138 and GEC-ESTRO

782 Med. Phys. 38 (2), February 2011 0094-2405/2011/38(2)/782/20/$30.00 © 2011 Am. Assoc. Phys. Med.



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Advance Technology: Modern Afterloaders

- **Their use results to reduction of exposure to the Staff**

- ***High Strength Sources***
- ***Source Transports / Exchanges***
- ***Malfunctions ?***

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Statistics over 50 years: Accidents

- More than 50% of the severe accidents occur in industrial facilities
- 1/5th in the Research Field
- 1/8th in nuclear power civilian applications
- *1/10th in Medicine*

Jean-Claude Nenot:“ Radiation accidents over the last 60 years” J. Radiol. Prot. 29: 301-320, 2009.

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Statistics over 50 years: Number of Victims

- **In industrial facilities often only one Victim**
- ***In Radiation Oncology Accidents related to overdoses imply classically a series of Patients***

Jean-Claude Nenot:“ Radiation accidents over the last 60 years” J. Radiol. Prot. 29: 301-320, 2009.

Some Issues on Safety

A. HDR treatment delivery misadventures and types of errors

The Task Group prefers the term ''misadventure'' to describe treatments which deviate from the safety or accuracy criteria at the foundation of the institution's QA program. An event or incident is a misadventure if it has the potential to compromise the patient's clinical outcome, safety of the patient, caregivers; or public, or if uncorrected, has the potential to compromise safety or clinical efficacy of future treatments. A misadventure may be a treatment delivery error, delivery of an incorrect or unintended therapeutic dose, or failure to adhere to established procedures, which if repeated could result in future delivery errors. The Task Group believes good clinical judgment must be used to identify misadventures; it is neither useful nor possible to set exact criteria for such events. Most HDR brachytherapy misadventures are caused by human errors or misjudgments made during treatment planning and delivery, rather than by failure or malfunction of equipment. Generally, treatment delivery errors fall into systematic and random errors.

HDR-BRT treatment delivery: Report of AAPM TG-59.

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ICRP Publication 97 (HDR)

- **More than 1000 centres**
- **Over 1500 Machines (over 400 in developing Countries)**
- **Over 10,000 high activity sources/year**
- **Over 500,000 treatments annually**
- ***More than 500 Events have been recorded!***

Prevention of High-dose-rate Brachytherapy Accidents, Volume 35 No. 2, 2005

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ICRP Publication 97 (HDR)

Origin of the different Events:

- Handling and Transport of Sources
- Inadequate Structural Shielding

} Human

- Sources in transit (remaining in the safe, in the patient, along the transfer tubes)

- Treatments given to wrong patients
- Incorrect prescription or delivery of dose, repeated treatments to the same patient

} Human

Prevention of High-dose-rate Brachytherapy Accidents, Volume 35 No. 2, 2005

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ICRP Publication 97 (HDR)

Human Errors:

- Incorrect Indication
- Patient Identification
- Diagnosis or Area of Treatment
- Dose Prescription
- Data Entry
- Catheter or Applicator

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Human Errors ?:

Hospital delivers radiation to wrong spots in 100 cancer treatment cases

December 26, 2013

Tweet 8 g+1 3

THE ASAHI SHIMBUN

ISEHARA, Kanagawa Prefecture--One hundred patients received radiation treatments for cancerous tumors for the wrong parts of their bodies, Tokai University Hospital disclosed Dec. 25.

It said the errors were found in cases involving brachytherapy, a procedure in which a radioactive source is placed into or adjacent to the area requiring treatment.

In the mistakenly treated cases, the radioactive substances were placed about 3 centimeters from the area they were intended to target. The hospital said the errors were caused by a problem with medical devices used in the procedure.

The hospital has set up an investigation board, which also includes third parties, to determine what precisely went wrong.

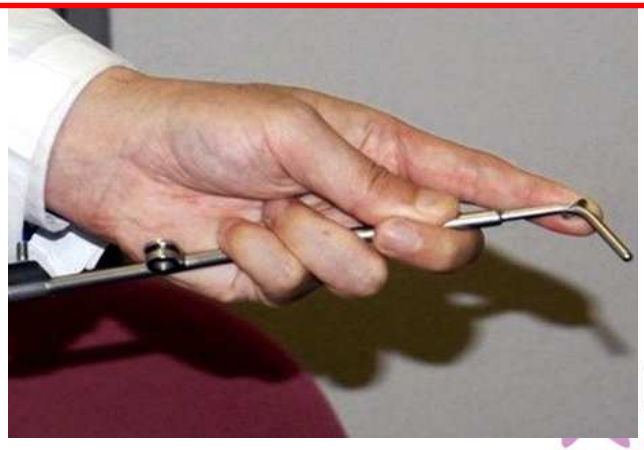
Tokai University Hospital officials said the patients were all women, ranging in age from 30 to 89, who underwent treatment for uterine cancer between May 2007 and November 2013.

In brachytherapy, a small tube is inserted into the patient's body and a radioactive substance less than 2 millimeters in diameter is transferred to the tip of the tube by using a wire.

In November, hospital staff members, after ascertaining there was a problem, checked the therapeutic instruments and confirmed that radioactive materials had been inserted in wrong spots.

2007 – 2013, 100xPts

They said that between 12 and 30 sieverts of radiation was probably delivered to bladders or other body areas without any tumors. That may also have led to a decrease of around 10 percent in the amount of radiation exposure to cancer cells.



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Human Errors ?:

March 2013: Radiation Oncology Dept. in Germany found out that 7 cases have been mistakenly treated using HDR-BRT.
This was an under-dosage for all 7 cases.
After a further research in the patient files, the amount of those cases was increased to 10.
It was the result of malfunction of the RTP and the resulting faulty user operation.
Further investigation:

- **Manual adjustment of dwell times**
- **wrong representation /interpretation of the dose distribution in the RTP**
- **Manufacturer has then fixed the problem**
- ***New training and education of the staff***

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Solutions

- **Guidelines**
- **Courses**
- **Education / Training Sides**
- **?????**

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Braphyqs

BRAchytherapy PHYsics Quality assurances System

UNCERTAINTY IN MODERN BRACHYTHERAPY - ANALYSIS CONCEPT

The Braphyqs physicist network in Europe is a Working Group of GEC-ESTRO

Dose Delivery by Afterloader

Positional accuracy

[mm-1xSD] for straight applicator

~ 0 mm for accuracy, and ~ ±1 mm (1 SD) for precision

Temporal accuracy

dwell time delivery 1%
rounding error 1%,
transit dose 1%
(estimate level for confidence of 65%!)

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Uncertainties related to

1. Source calibration	~ 1,5 %
2. a) Dose calculation in water	~ 4 %
b) Systematic effects	*up to 10 %*
3. Accuracy of afterloader performance (time/spatial distribution)	~ 2 %
Mainly site specific	
4. Imaging (localisation, volume interpolation,…)	5 %
5. Contouring	x %
6. Variations at patient level (inter- and intrafraction variations, organ movement/swelling)	up to ~50%

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Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and AAPM

Radiotherapy and Oncology xxx (2013) xxx–xxx

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Original article

Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and the AAPM ☆

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ABSTRACT

Background and purpose: A substantial reduction of uncertainties in clinical brachytherapy should result in improved outcome in terms of increased local control and reduced side effects. Types of uncertainties have to be identified, grouped, and quantified.

Methods: A detailed literature review was performed to identify uncertainty components and their relative importance to the combined overall uncertainty.

Results: Very few components (e.g., source strength and afterloader timer) are independent of clinical disease site and location of administered dose. While the influence of medium on dose calculation can be substantial for low energy sources or non deeply seated implants, the influence of medium is of minor importance for high energy sources in the pelvic region. The level of uncertainties due to target, organ, applicator, and/or source movement in relation to the geometry assumed for treatment planning is highly dependent on fractionation and the level of image guided adaptive treatment. Most studies to date report the results in a manner that allows no direct reproduction and further comparison with other studies. Often, no distinction is made between variations, uncertainties, and errors or mistakes. The literature review facilitated the drafting of recommendations for uniform uncertainty reporting in clinical BT, which are also provided. The recommended comprehensive uncertainty investigations are key to obtain a general impression of uncertainties, and may help to identify elements of the brachytherapy treatment process that need improvement in terms of diminishing their dosimetric uncertainties. It is recommended to present data on the analyzed parameters (distance shifts, volume changes, source or applicator position, etc.), and also their influence on absorbed dose for clinically relevant dose parameters (e.g., target parameters such as D_{90} or OAR doses). Publications on brachytherapy should include a statement of total dose uncertainty for the entire treatment course, taking into account the fractionation schedule and level of image guidance for adaptation.

Conclusions: This report on brachytherapy clinical uncertainties represents a working project developed by the Brachytherapy Physics Quality Assurances System (BRAPHYQS) subcommittee to the Physics Committee within GEC ESTRO. Further, this report has been reviewed and approved by the American Association of Physicists in Medicine.

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Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and AAPM

Vaginal Cylinder

Table 1
Example 1 HDR ^{192}Ir BT source for vaginal cylinder applicator.

Category	Typical level (%)	Assumptions
Source strength	2	PSDL traceable calibrations
Treatment planning	3	Reference data with the appropriate bin width
Medium dosimetric corrections	1	Valid for applicator without shielding and if CTV located inside pelvis; an advanced dose calculation formalism should be used if this assumption false
Dose delivery including registration of applicator geometry to anatomy	5	Accurate QA concept for commissioning and constancy checks, especially for source positioning and applicator/source path geometry, appropriate imaging techniques (either small slice thickness, 3D sequences or combination of different slice orientations), applicator libraries (either by using software solutions or manual)
Interfraction/Intrafraction changes between imaging and dose delivery	5*	For one treatment plan per applicator insertion and measures to detect major variations for subsequent fractions
Total dosimetric uncertainty ($k = 1$)	8	For treatment delivered with the same BT source

* Estimated value based on expert discussion.

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Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and AAPM

Intracavitary Cervical BRT

Table 2
Example 2 HDR ^{192}Ir source for intracavitary, image-guided cervical cancer BT.

Category	Typical level (%)	Assumptions
Source strength	2	PSDL traceable calibrations
Treatment planning	3	Reference data with the appropriate bin width
Medium dosimetric corrections	1	Applicator without shielding and CTV inside pelvis (concerning for scatter); an advanced dose calculation formalism should be used if this assumption false
Dose delivery including registration of applicator geometry to anatomy	4	Accurate QA concept for commissioning and constancy checks, especially for source positioning and applicator/source path geometry, appropriate imaging techniques (either small slice thickness, 3D sequences or combination of different slice orientations), applicator libraries (either by using software solutions or manual)
Interfraction/Intrafraction changes *(including contouring uncertainties)*	11	For one treatment plan per applicator insertion but several subsequent fractions if only one fraction is applied the remaining uncertainty between imaging and dose delivery should be at least smaller than this interfraction variation
Total dosimetric uncertainty *(including contouring uncertainties)* ($k = 1$)	**12**	For treatment delivered with the same BT source note that in cervix cancer BT, both HDR and PDR schedules consist of several fractions, reducing the random uncertainties (see text)

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Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and AAPM

Permanent Seeds Implants PCA

Table 4
Example 4 LDR ^{125}I sources for permanent prostate BT.

Category	Typical level (%)	Assumptions
Source strength	3	PSDL traceable calibrations
Treatment planning	4	Reference data with the appropriate bin width
Medium dosimetric corrections	5	No consideration is given for calcifications or their composition in the patient
Inter-seed attenuation	4	An advanced dose calculation formalism may indicate source models and orientations cause the largest effects
Treatment delivery imaging	2	US QA performed according to AAPM TG-128
Target contouring uncertainty	2	Using CT or CT + T2 imaging
Anatomy changes between dose delivery and post-implant imaging	7*	Post-implant imaging using CT, with a scalar correction factor for edema correction
Total dosimetric uncertainty ($k = 1$)	**11**	For treatment delivered without excreted seeds

* Estimated value based on expert discussion.

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Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and AAPM

Temporary HDR-Implants PCA (U/S-based)

Table 5
Example 5 HDR ^{192}Ir source for temporary prostate BT.

Category	Typical level (%)	Assumptions
Source strength	2	PSDL traceable calibrations
Treatment planning	3	Reference data with the appropriate bin width
Medium dosimetric corrections	1	Full scatter conditions in the pelvic region and for the prostate location are assumed
US-based Treatment planning and delivery: Catheter reconstruction and source positioning accuracy	2	Assuming usage of dedicated catheter reconstruction tools (catheter free-length measurement based methods) for an accurate (0.7 mm) reconstruction of catheter tip and 1.0 mm source positioning accuracy by the afterloader for straight catheters and transfer tubes
US-based 2D and 3D-imaging overall effect	2	US QA performed according to AAPM TG-128 report
Changes of catheter geometry relative to anatomy between intraoperative treatment planning and intraoperative treatment delivery	2	Assuming that new image acquisition and treatment plan calculation is done always before each fraction. It is also required that no manipulation of the implant and anatomy occurs, as it is the case when removing/manipulating the US-probe or moving the patient from the operation table before treatment delivery
Target contouring uncertainty	2	Using CT or CT + T2 imaging
Total dosimetric uncertainty ($k = 1$)	**5**	For treatment delivery without patient movement and changes in the lithotomic set-up and with the US probe at the position of the acquisition (transversal plane at the prostate base)

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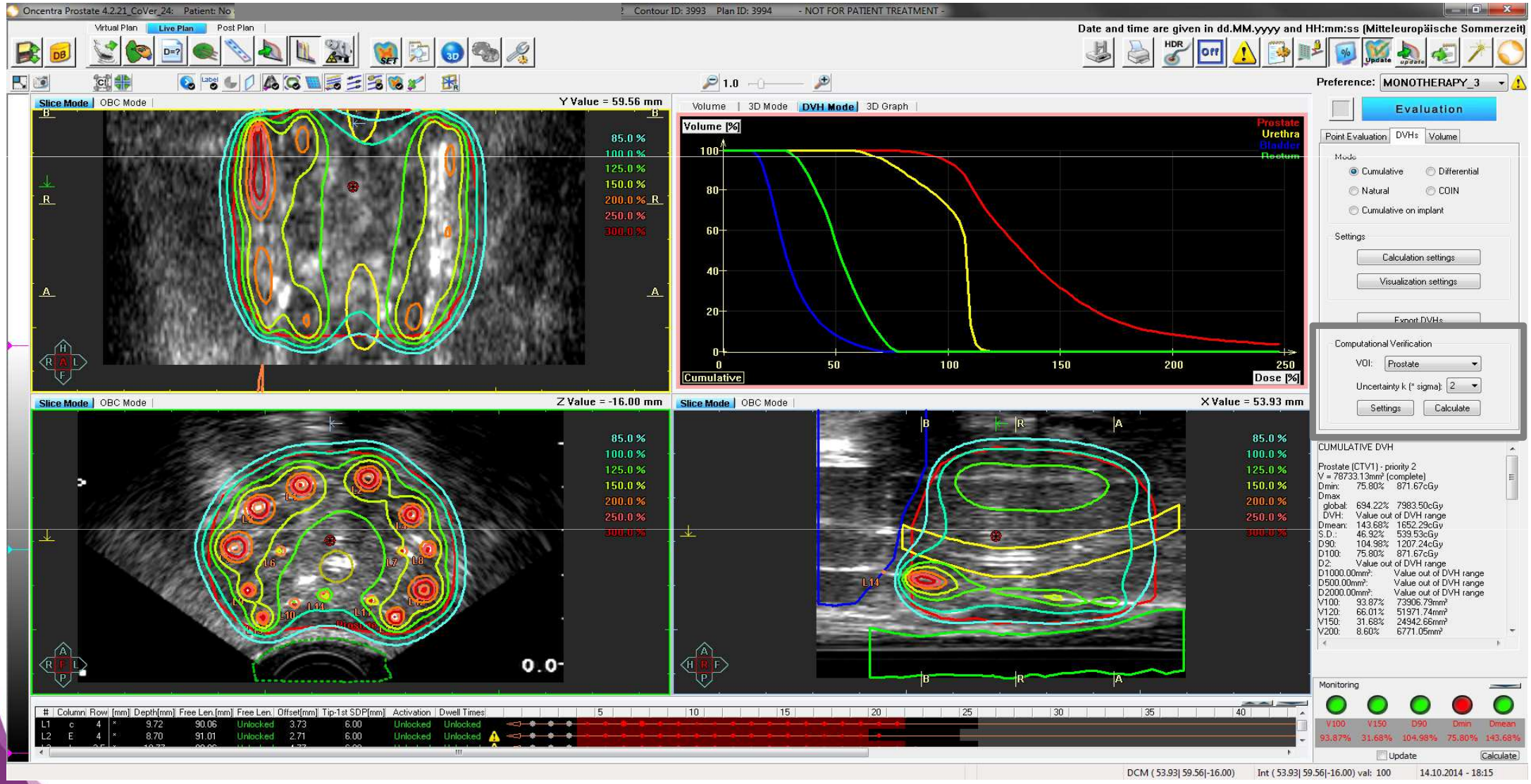
Computational Verification: Incorporate uncertainties into the Dose Calculation!



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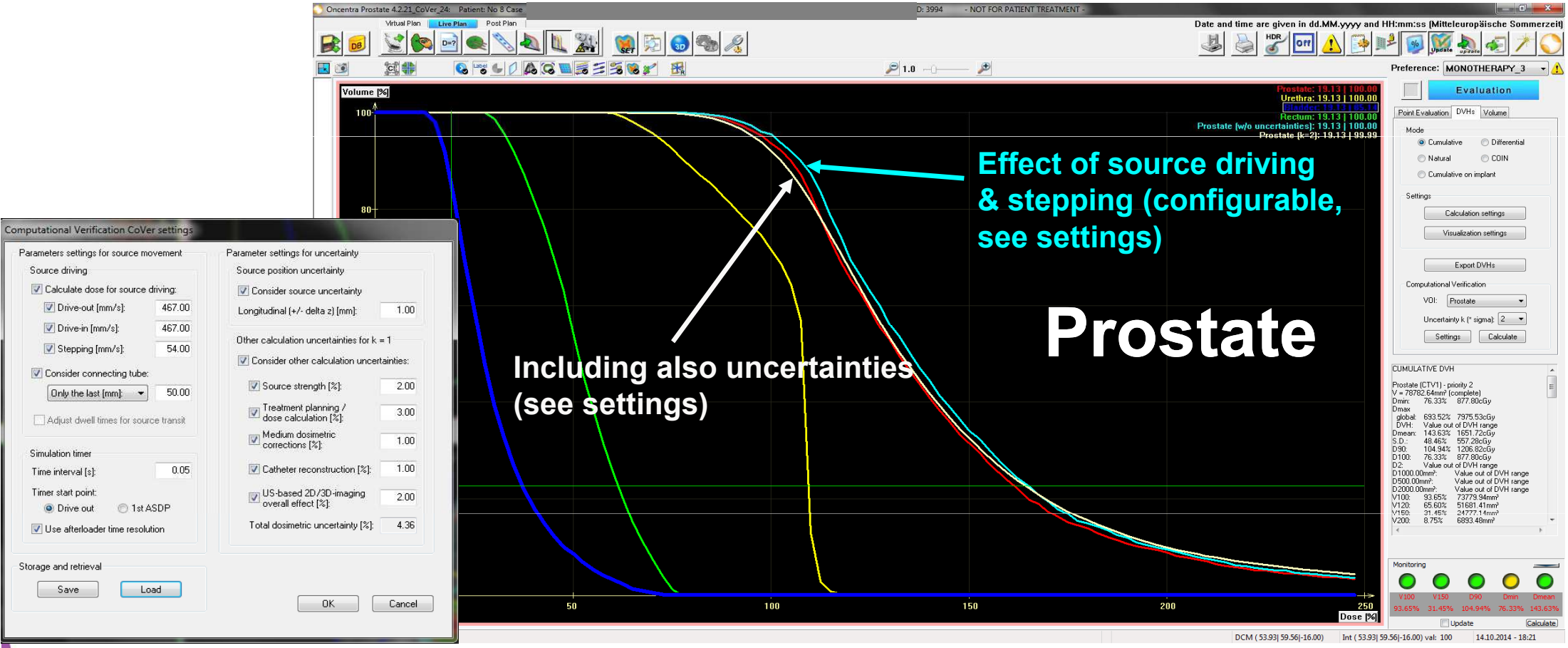
Computational Verification: Incorporate uncertainties into the Dose Calculation!



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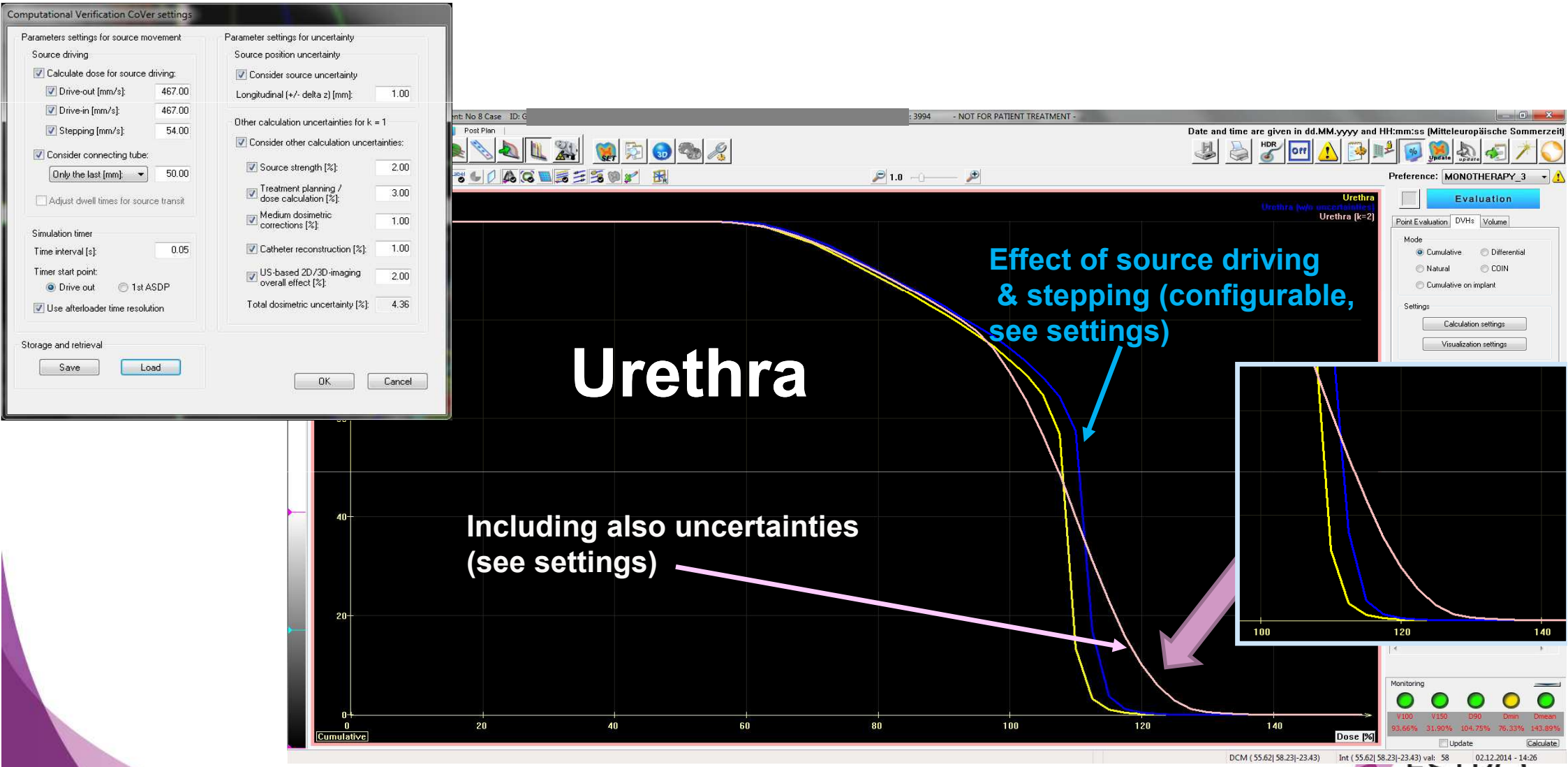
Computational Verification: Incorporate uncertainties into the Dose Calculation!



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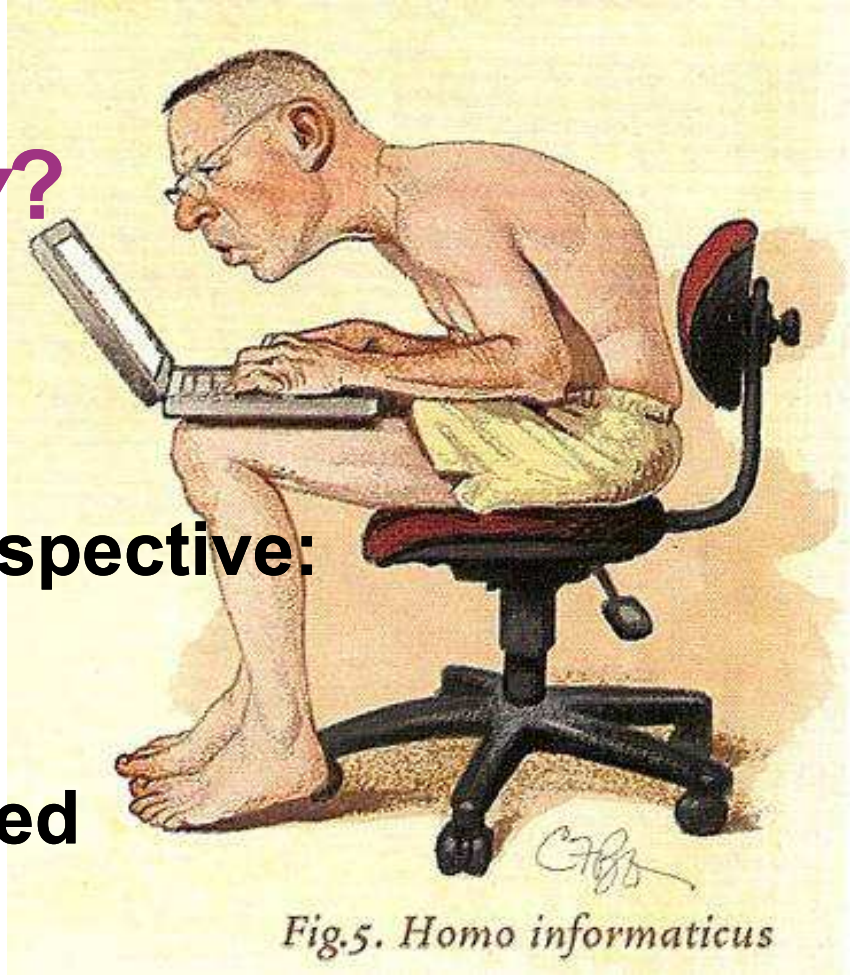
What do we mean with *Safety*?



Do we include also the Question/Perspective:

?

Delivered = Planned

Even if we treat the correct Patient at the Correct Location, with the Correct Applicator/Catheters, with the Correct Plan and with a 100% secure Device and safe Treatment Suite!!!

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Delivered $\stackrel{?}{=}$ Planned

Answer only when

- **Imaging of Anatomy (same as in ERT: EPID, kV-CBCT, MV-CBCT,…)**
- **Imaging & Localisation of Catheters/Applicators (ERT: Beams)**
- **Imaging & Localisation**

under Treatment Conditions is realized*

***in the Treatment Room**

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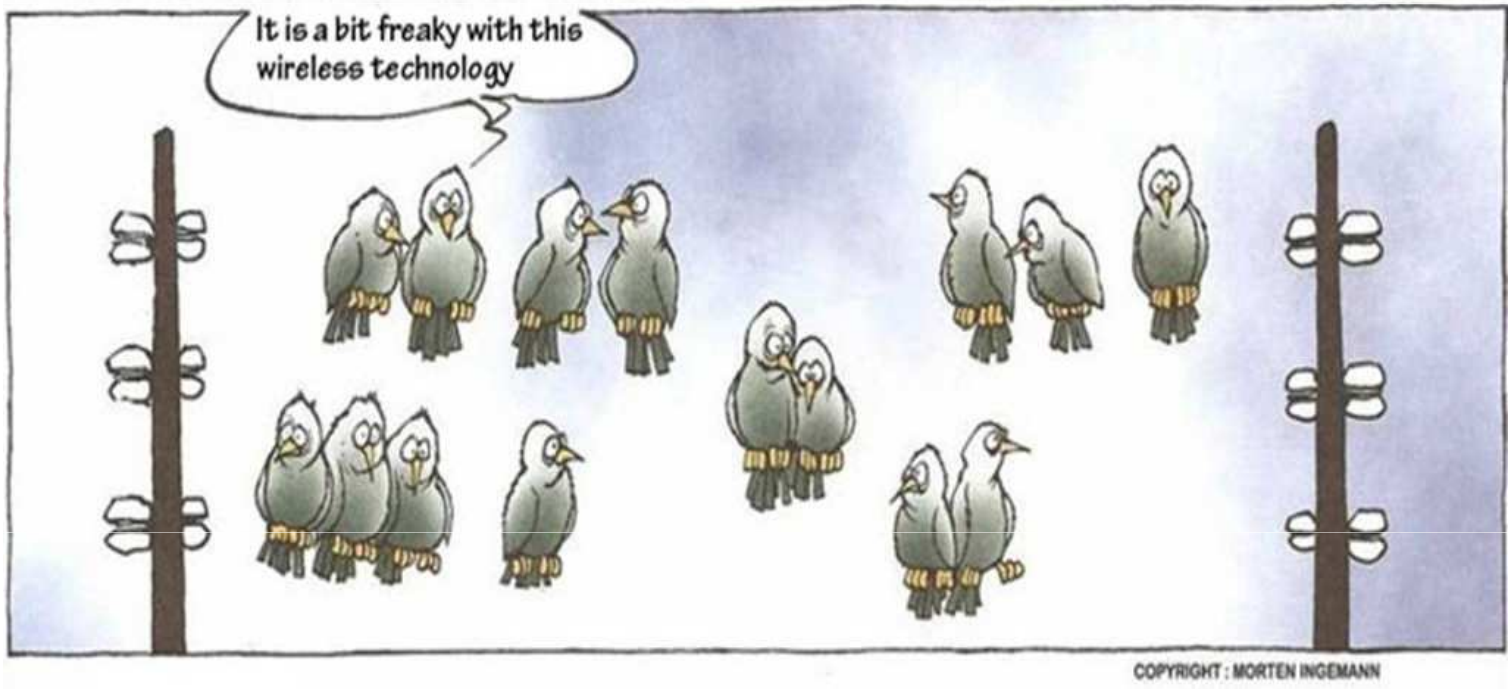
Delivered ≟ Planned

Some Perspectives

- **Advance 2D- & 3D-U/S Imaging Systems using Synthetic Techniques (abdominal & transrectal Imaging) for Gynecology & Prostate**
- **EM-Tracking systems for catheters/applicators**
- **Advance Verification Systems utilizing time-resolved in-Vivo-Dosimetry Techniques**
- **…..**

Thank you very much for your Attention



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Brachytherapy in Anal Cancer

Erik Van Limbergen
Dep.Radiation Oncology
University Hospital Gasthuisberg
Leuven/ Belgium

With courtesy to Didier Pfeiffert
Dep of Radiotherapy
Centre Alexis Vautrin, Nancy, France

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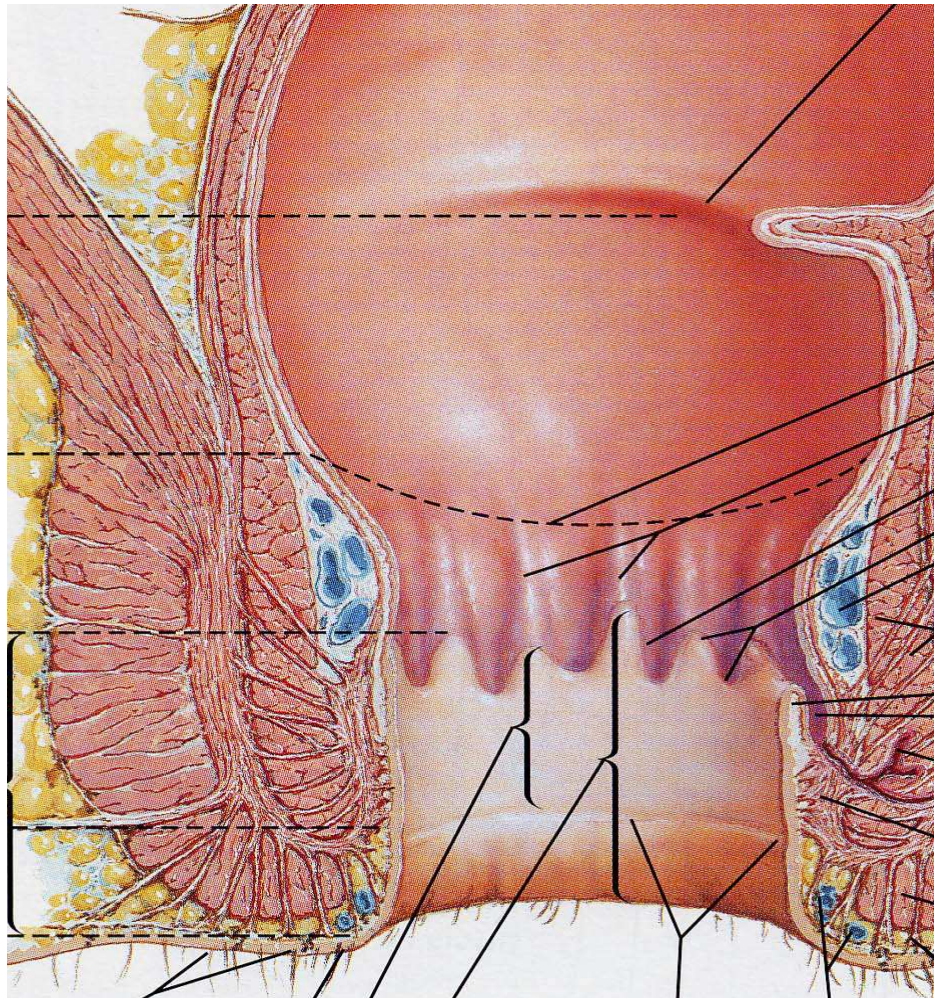
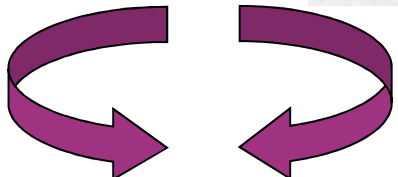
Anatomical Definitions

- **ANAL CANAL** :
  - 3 - 4 cm long
  - from the anorectal jonction
  - to the peri-anal skin

  pectinate (dentate) line is at mid-canal



- **ANAL MARGIN** :
  - From the canal –margin jonction
  - To the skin (5 cm diameter)



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Epidemiology

- Incidence 1 / 100 000
- 3000 new cases/year in Europe
- 1, 2 % digestive Ca.

- 75 % females - after 60 years
- 5-10 % metastatic at diagnosis
- Homosexuality, HPV(types 16,18)

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Pathology

Squamous-cell Ca. = 95 %

- keratinizing
- non keratinizing
  - (transitional)
  - (cloacogenic)
- basaloïd

Adenocarcinomas

Sarcomas

Lymphomas

Melanomas

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Lymphatic Spread

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Work up

- Detailed clinical examination and sketch
- Rigid anorectal endoscopy & tatooing
- Biopsy
- CT-Scan
- Endorectal ultrasonography
- MRI & PET CT

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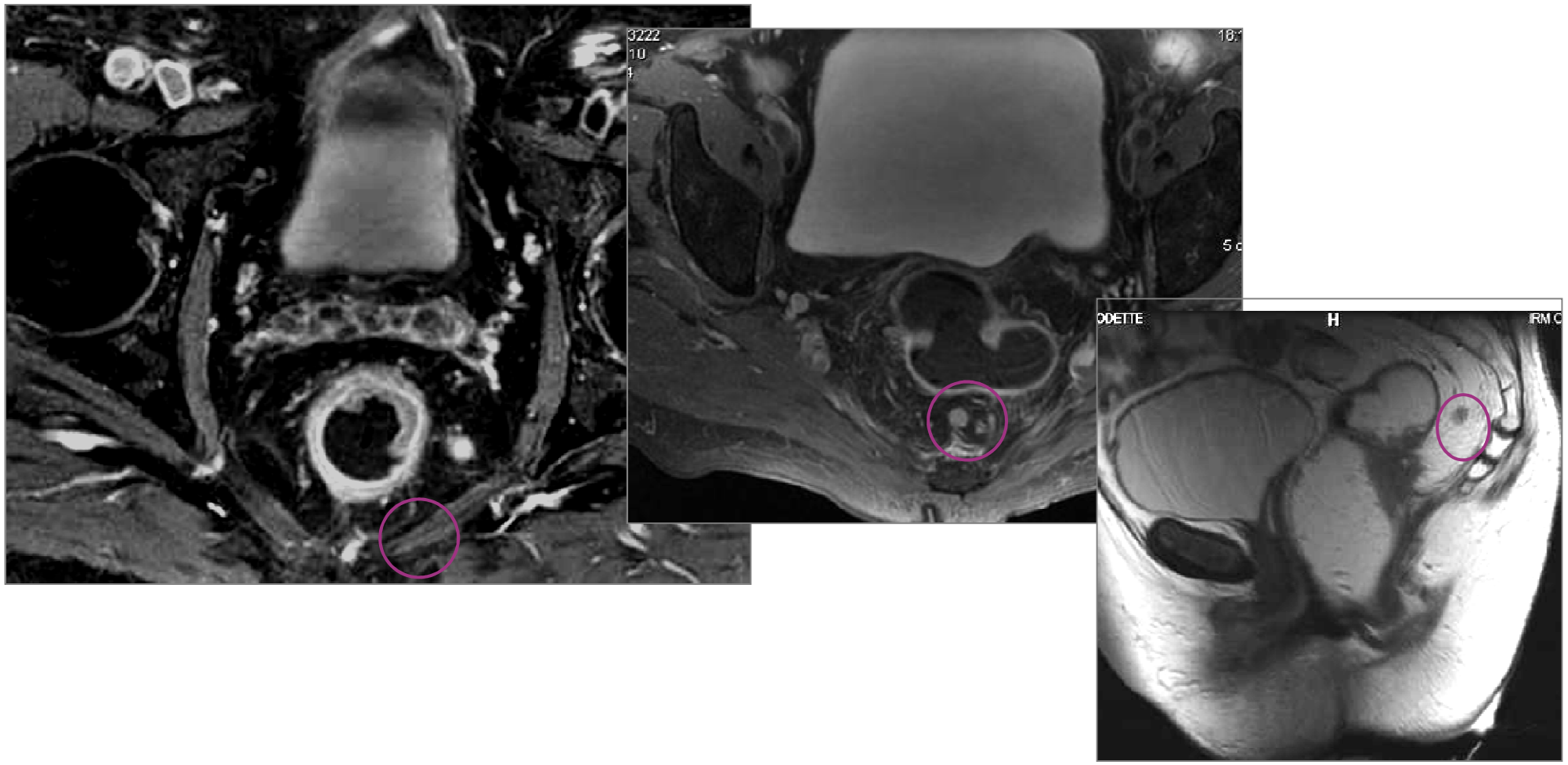
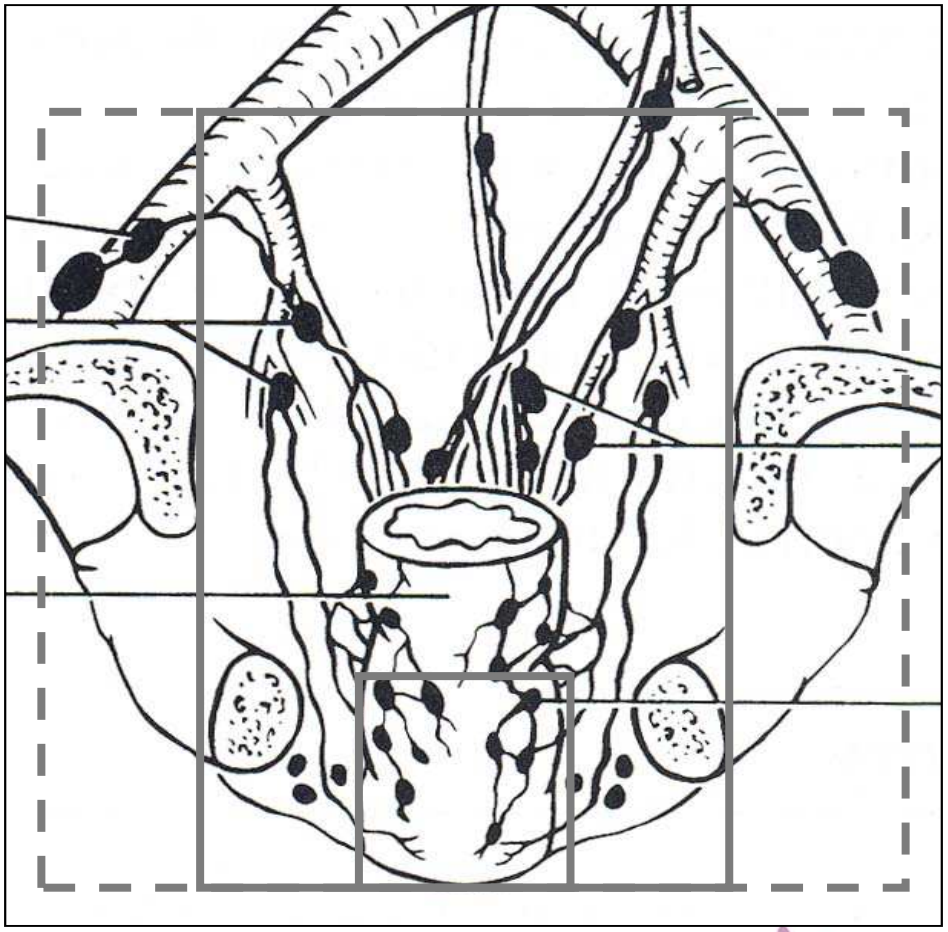
Pararectal nodes



Bellin MF, Roy C, Kinkel K et al. Lymph nodes metastases. Safety and effectiveness of MR Imaging with ultrasmall superparamagnetic iron oxide particles-Initial Clinical Experience.Radiology 1998 , 207 : 799-808.
Bellin MF, Beigelman C, Precetti-Morel S et al. Iron Oxyde –enhanced MR lymphography : initial experience. Eur J radiol 2000; 34 : 257-264.

Target Volumes

- PTV 1:
  - Anal canal
    - Lower rectum
    - Anal margin
  - Pelvic Nodes
    - Para-rectal nodes
    - Presacral nodes
    - Inguinal nodes
- PTV2:
  - Tumor bed
  - Involved nodes



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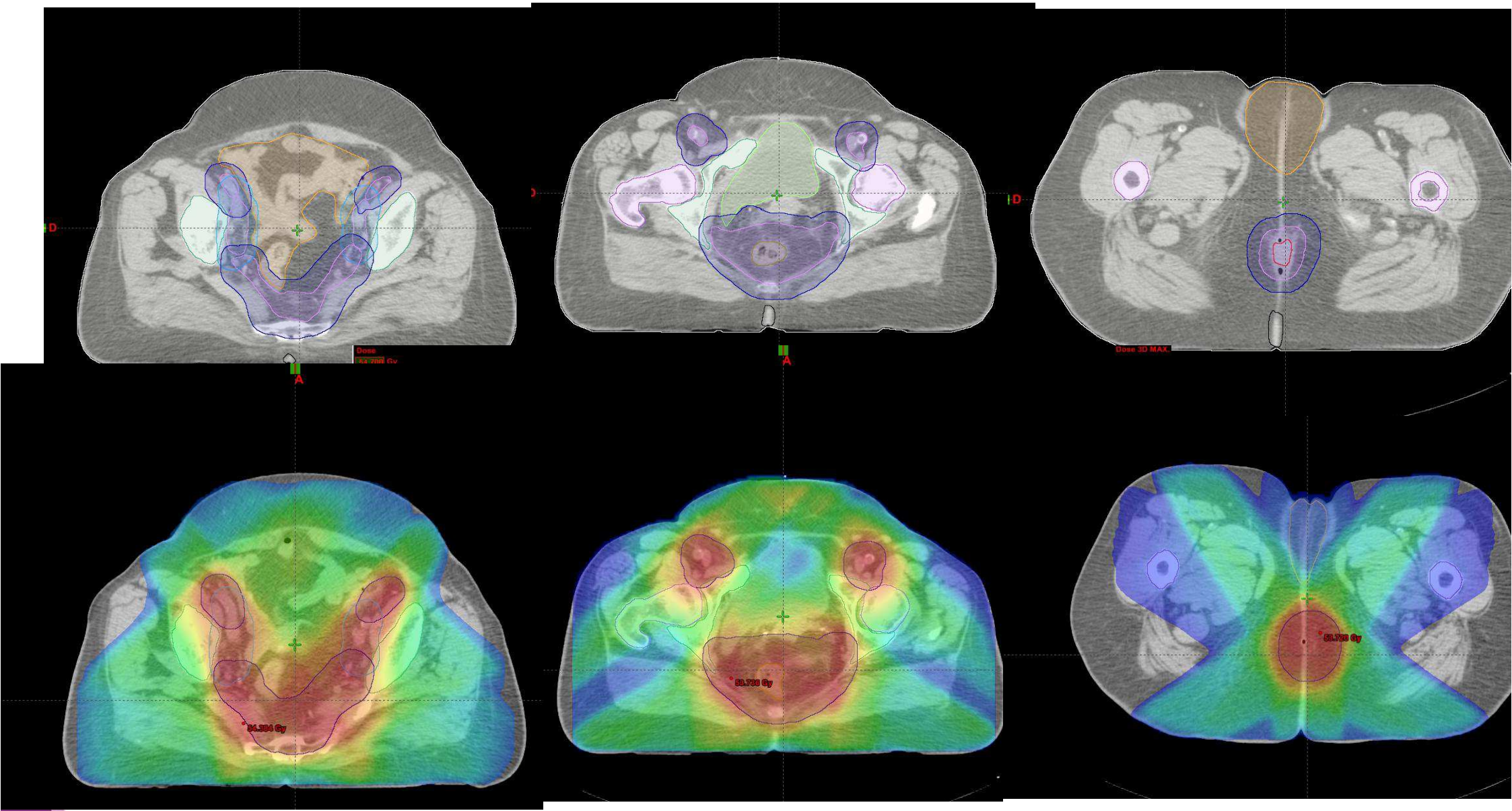
YSE (201003280) - Planification de radiothérapie - [CanalAnal_45G - Retiré - Transversale - Etude1 (Moy)]
Links Modifier Affichage Insérer Planification Outils Fenêtre Aide
CanalAnal_45G - Retiré - Transversale - Etude1 (Moy)
Isodoses (Gy)
45.000
42.750
A
D
P
42.8
45.0
49.140 Gy
OS
os sain
pli interfessier
PTV ING D
PTV1 ILE D
PTV1 ILE G
PTV1 ING G
PTV1T
périné
Rectum
Somme PTV1
Uterus
Vagin
Vessie
vessie saine
Standard
Tête devant- Décubitus dorsal

IMRT Anal Canal dp 2011



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Evaluation

- Survival
- Cure of the Cancer
- Local control
- Sphincter preservation
- Functional results
- Quality of life

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Exclusive irradiation(> 60 Gy) (1984-96) including a boost

Authors	Nb pts	Relapses	5 year Surv
Salmon	183	34 %	58 %
Eschwege	64	19 %	46 %
Papillon *	159	12 %	65 % (crude)
Touboul	270	20 %	74 %
Allal *	125	20 %	65 %
Gérard *	108	17 %	64 %
Peiffert *	118	20 %	60 %
Total =	1027		

* brachytherapy

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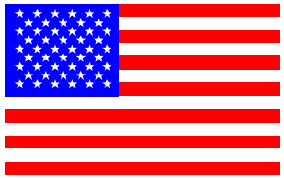

Concomitant Radiochemo (≤ 50 Gy)

with no boost

Authors	Nb pts	Contrôle T	Compl. gr. IV	Survival
Nigro	104	90 %		78 %
Sischy	79	61 %	1 sténose	73 %
Michaelson	37	81 %	non	80%
Cummings	69	90 %	5 AAP	sp. 76 %
Flam	30	85 %	1 sténose	27 NED
Habr-Gamma	30	87 %	non	80 %
Hugues	25	78 % T1-3 33 % T4	1 DCD	/
Marti	52	≤ 4 cm 96 % > 4 cm 85 %	3 AAP	≤ 4 cm 100 % > 4 cm 80 %
Tanum	106	84 histo	14 (2 DCD)	70 %

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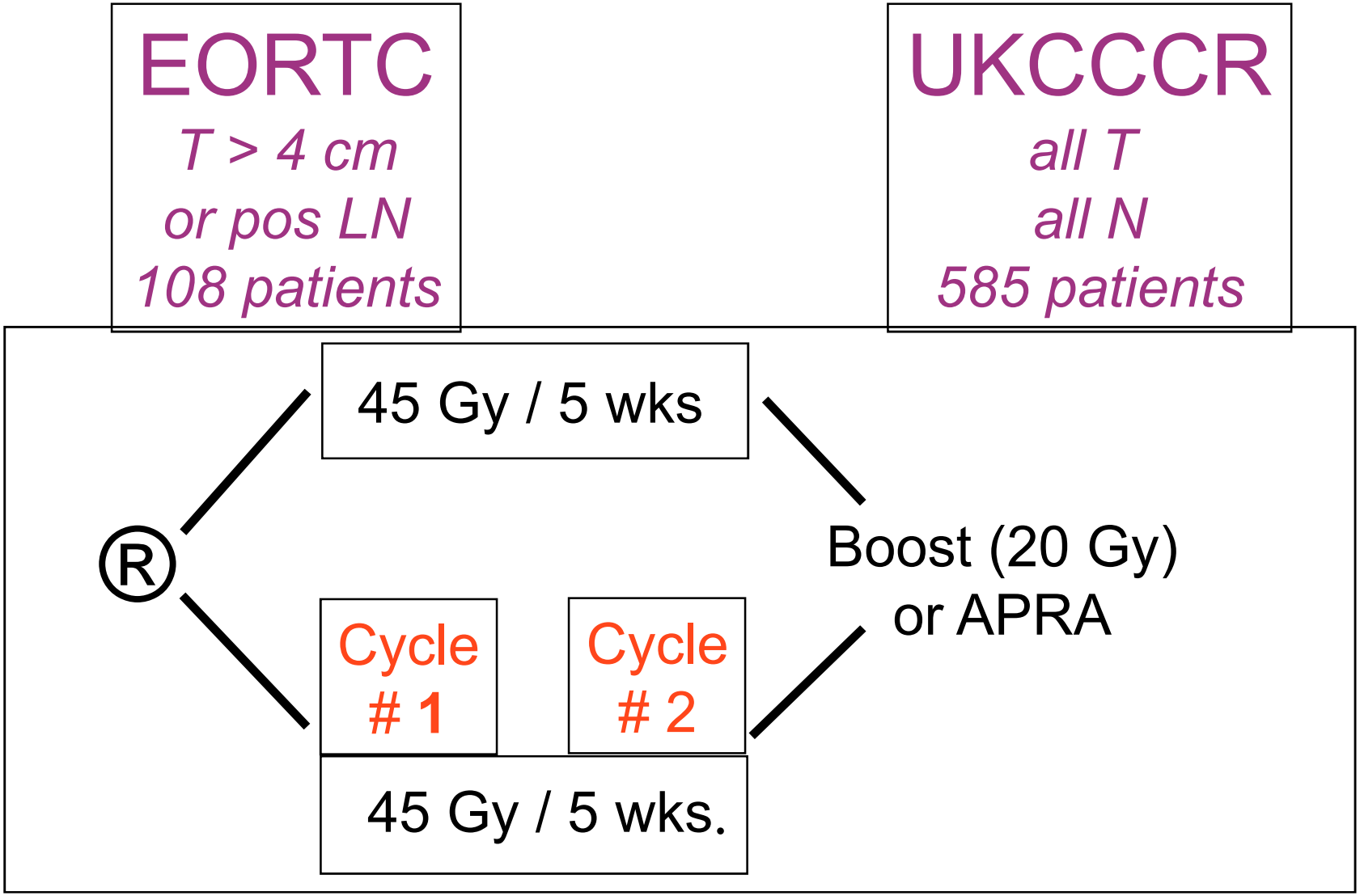
Which patients benefit from High Dose irradiation and concomitant chemotherapy?



5 FU = 750 mg /m^2 d 1-4 et d 29 - 32
MITO = 15 mg/m^2 d 1

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Which patients benefit from High Dose irradiation and concomitant chemotherapy?

		Local Control	Surv. w/o colostomy	Disease spec. Survival	Survival
EORTC	Radio	55 % p = 0,02	40 % p = 0,002		55 % NS
	Radio-chemo	68 %	72 %		57 %
UKCCCR	Radio	39 % p		61 % p = 0,02	58 % p = 0,25
	Radio-chemo	<0,0001 61 %		72 %	65 %

Ref. : Bartelink : J Clin Oncol 1997;5:2040–2049

: UKCCCR : Lancet 1996;348:1049–1054

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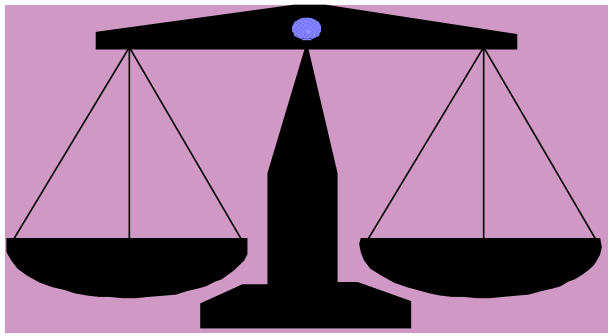
To boost or not to boost?

Local Control



- First site of failure is the anus
- Only 50% of Local failures can be salvaged
- Boost increases the local control

Complications

Increase with the total dose

Increase with the treated volume

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When to boost ?

- **Yes** if exclusive irradiation

- If radiochemotherapy
  - Early stages: NO/YES
  - Large tumors or poor responders:YES

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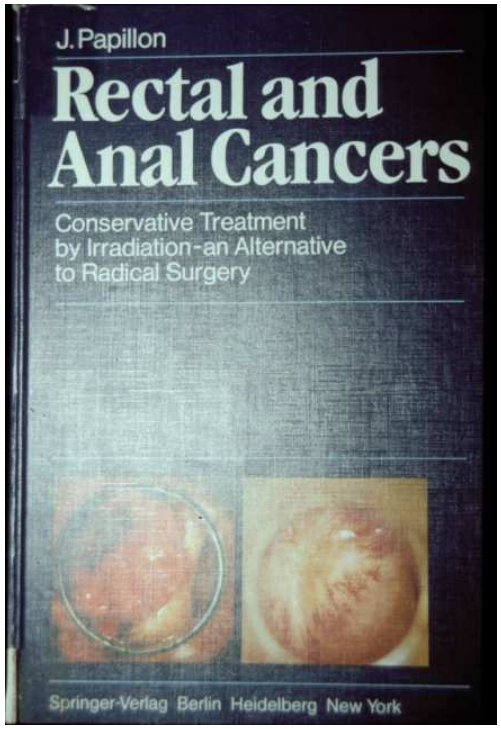
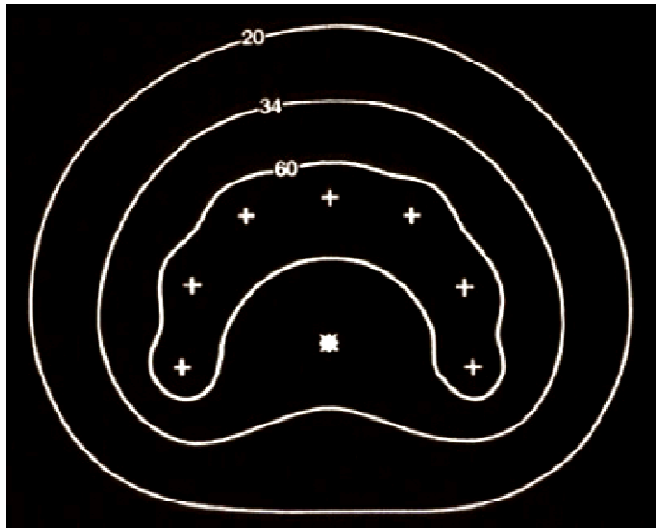
Goals of brachy



- Reduce overall treatment time
- Increase the dose
  - On a small conformal volume
- Spare the controlateral sphincter
  - To increase the functional results



Impact of brachy

Local reccurence

I. J. Radiation Oncology ● Biology ● Physics Volume 80, Number 3, 2011

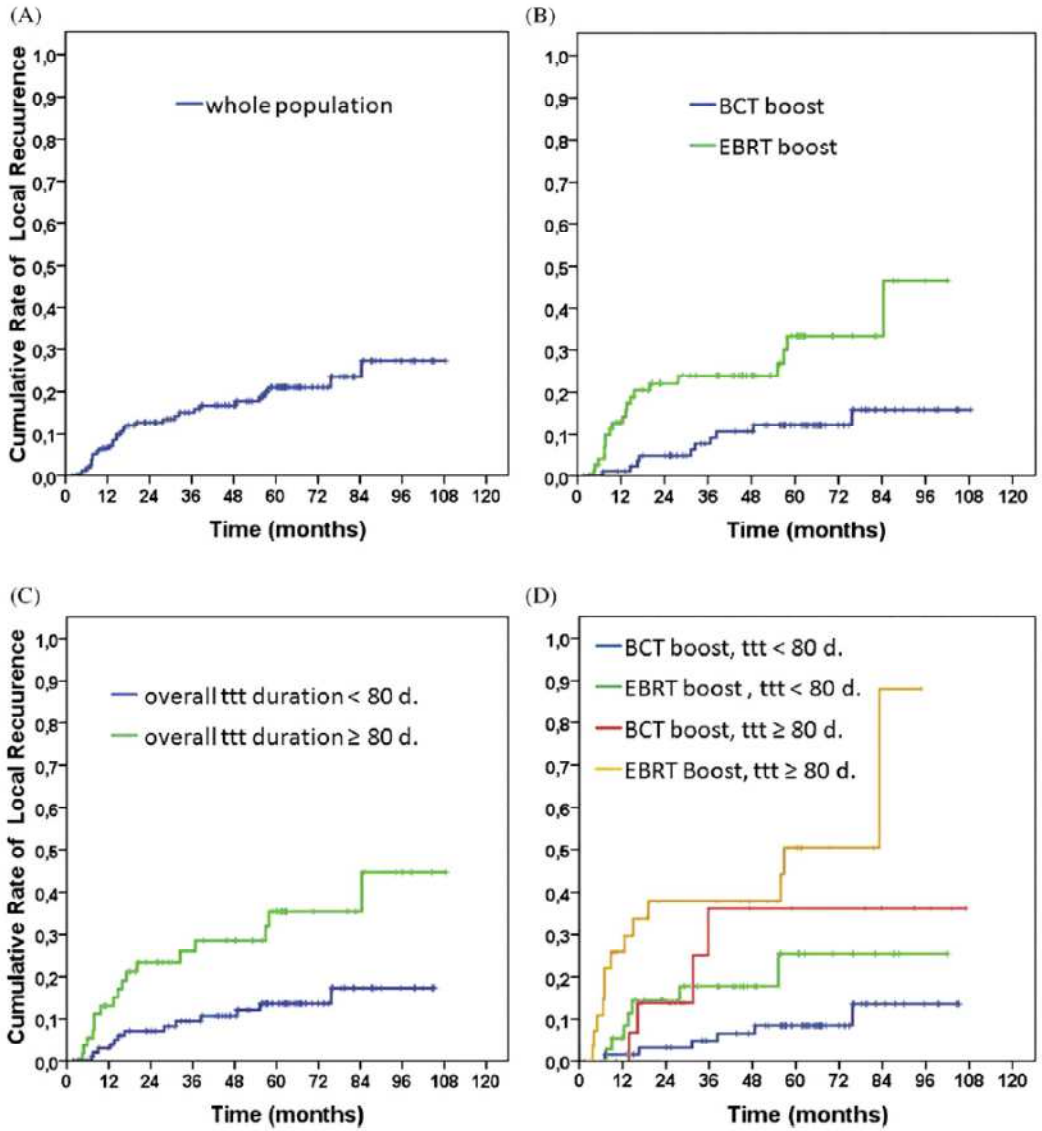


Fig. 3. Cumulative rate of local recurrence for the whole population (A), regarding the boost technique: brachytherapy (BCT) vs. external-beam radiotherapy (EBRT) (B), regarding the overall treatment time (<80 days vs. ≥80 days) (C), and combining boost technique and overall treatment time (D).

survival

I. J. Radiation Oncology ● Biology ● Physics Volume 80, Number 3, 2011

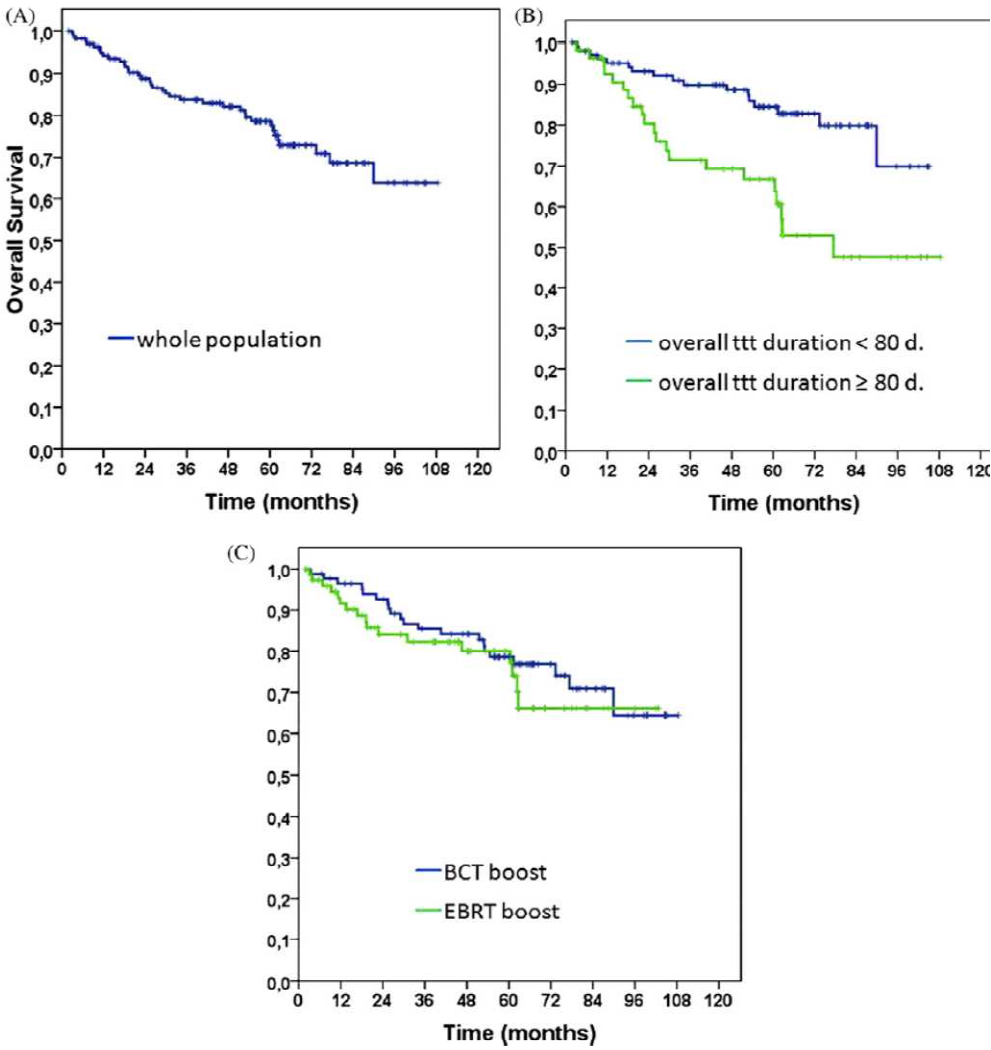


Fig. 2. Overall survival for the whole population (A), regarding the overall treatment time < 80 days vs. ≥80 days (B according to the boost technique: brachytherapy (BCT) vs. external-beam radiotherapy (EBRT) (C).

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Impact of brachy

HIGH-DOSE SPLIT-COURSE RADIATION THERAPY FOR ANAL CANCER: OUTCOME ANALYSIS REGARDING THE BOOST STRATEGY (CORS-03 STUDY)

JEAN-MICHEL HANNOUN-LEVI, M.D., PH.D.,*†† CÉCILE ORTHOLAN, M.D.,* MICHEL RESBEUT, M.D.,†††

Table 2. Treatment features

Treatment feature	EBRT boost $n = 76$ (%)	BCT boost $n = 86$ (%)	p value	Whole population $n = 162$ (%)
Neoadjuvant chemotherapy				
Yes	7 (9)	10 (12)	0.80	17 (10)
No	69 (91)	76 (88)		145 (90)
Concurrent chemotherapy				
Yes	50 (66)	62 (72)	0.39	112 (69)
No	26 (34)	24 (28)		50 (31)
Field size of EBRT first course				
Small field*	5 (7)	11 (13)	0.06	16 (10)
Pelvic field	41 (54)	31 (36)		72 (44)
Pelvic field + inguinal nodes	30 (39)	44 (51)		74 (46)
Mean dose of EBRT first course (Gy) (minimum–maximum)	45.4 (39.5–50)	44.9 (40–50)	0.10	45.1 (39.5–50)
Mean boost dose (Gy) (minimum–maximum)	18.3 (8–25)	17.4 (10–25)	0.07	17.9 (8–25)
Mean overall treatment time† (days) (minimum–maximum)	82 (45–143)	69 (37–128)	<0.001	75 (37–143)
Mean gap duration‡ (days) (minimum–maximum)	39 (0–106)	30 (2–89)	0.02	36 (0–106)

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Indications for Brachytherapy

- 1-3 weeks gap after pelvic irradiation
- Stages
  - ✓ T1,T2
  - ✓ T3 lower than 2/3 circumference
  - ✓ T4 (without vaginal involvement)

- After Partial or Complete response:
- 15 to 20 Gy boost

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Technique

Rigid or Plastic Needles (MRI guided BT)

- 4 to 6

Ring template

- Spacing : 10 to 15 mm

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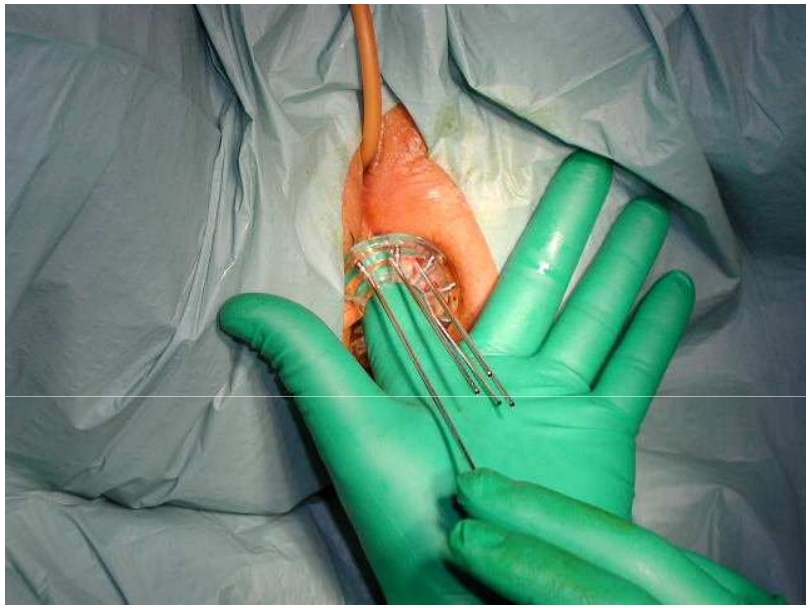
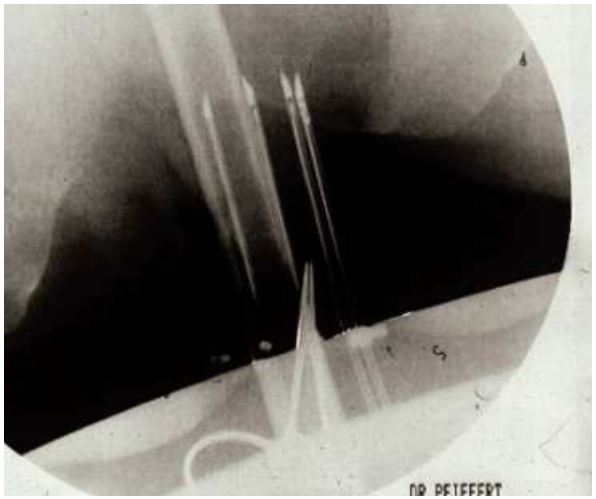
Implantation

Under digital control

- Under the mucosa
- 3-5 mm depth





- Rectal tube or cylinder to remove controlateral sphincter/mucosa

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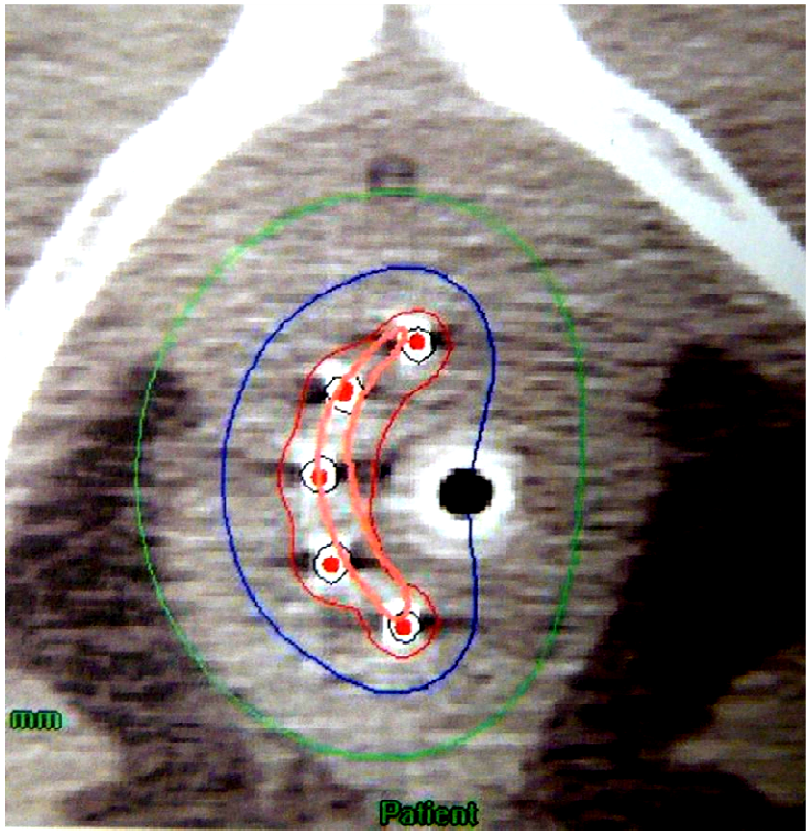
Dose distribution



Paris System

85% Ref isodose if 15mm spacing

- 9 mm thick
- 6 mm inside
- 3 mm outside

PDR

- prescription of the optimal pulse size 0.5 Gy/h
- Geometrical and target related optimization

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Pulsed Dose Rate

- Roed et al: Rad Oncol 1996;41:131
  - High rate of Late complic
    - Volume
    - Total dose (Paris system)
- Gerard et al : Rad Oncol 1999;51:129
  - Acute toxicity
  - Tumor response
- Bruna et al: Rad Oncol 2006
  - 2 years follow up

ELSEVIER

Radiotherapy and Oncology 41 (1996) 131–134

RADIOTHERAPY & ONCOLOGY

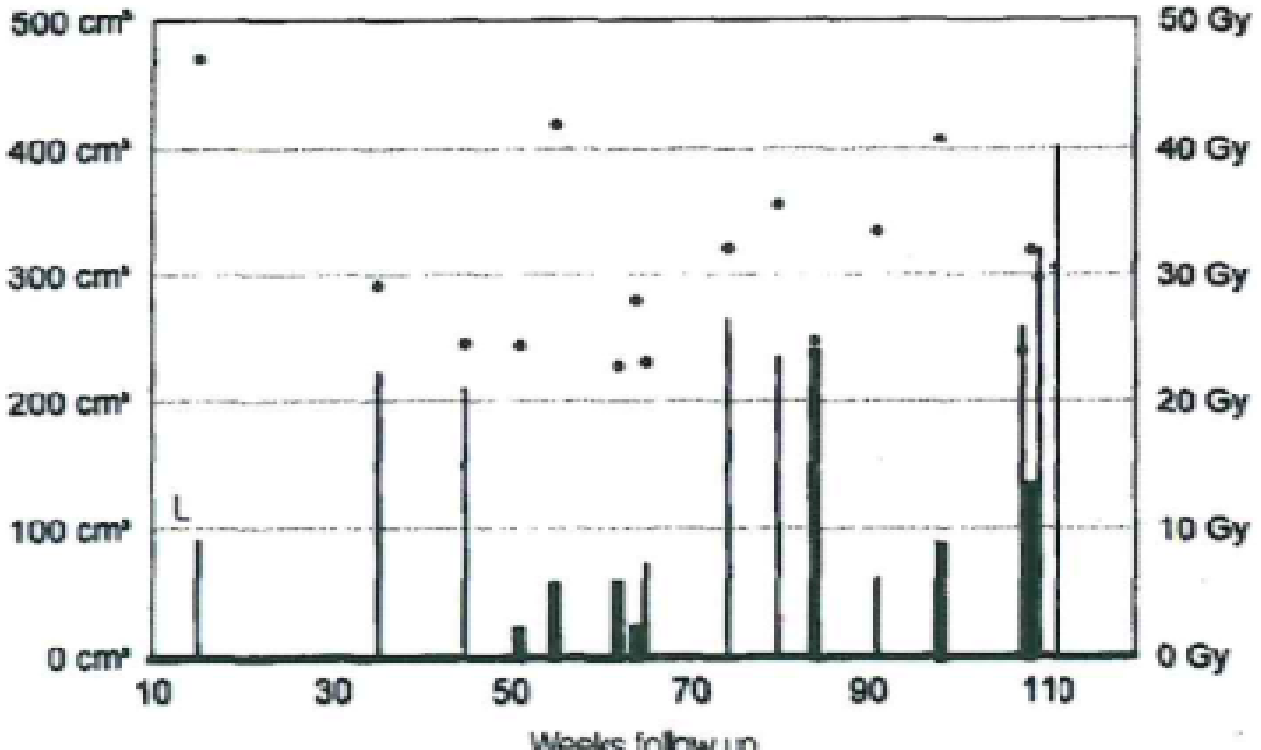
Short communication

Pulsed dose rate (PDR) brachytherapy of anal carcinoma

Henrik Roed[a,*], Svend A. Engelholm[a], Lars B. Svendsen[b], Flemming Rosendal[a], Kjeld J. Olsen[a]

[a]*The Finsen Center 5074, Copenhagen University Hospital, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark*
[b]*Department of Surgical Gastroenterology C. Copenhagen University Hospital, Copenhagen, Denmark*

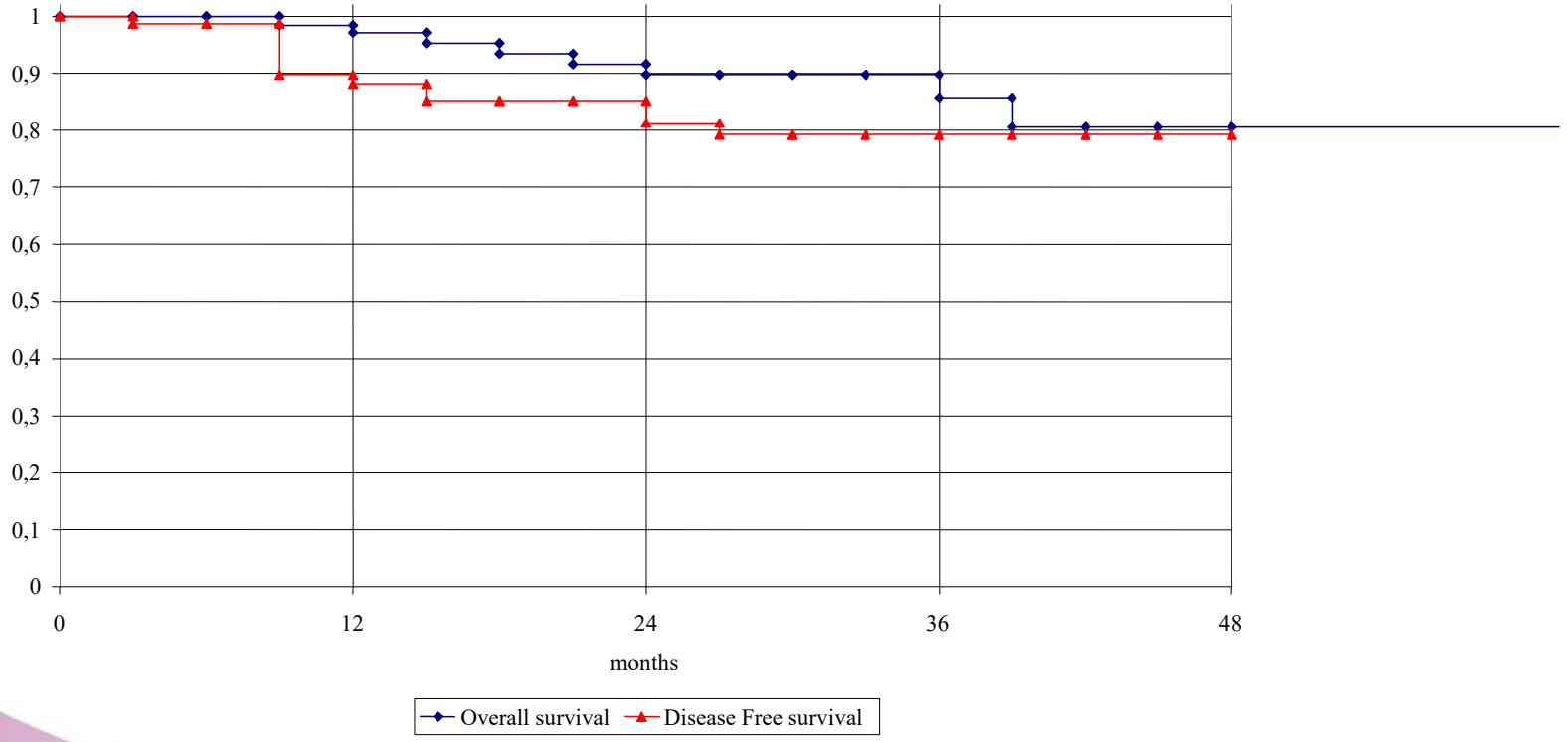
Received 6 February 1996; revised 25 June 1996; accepted 27 July 1996



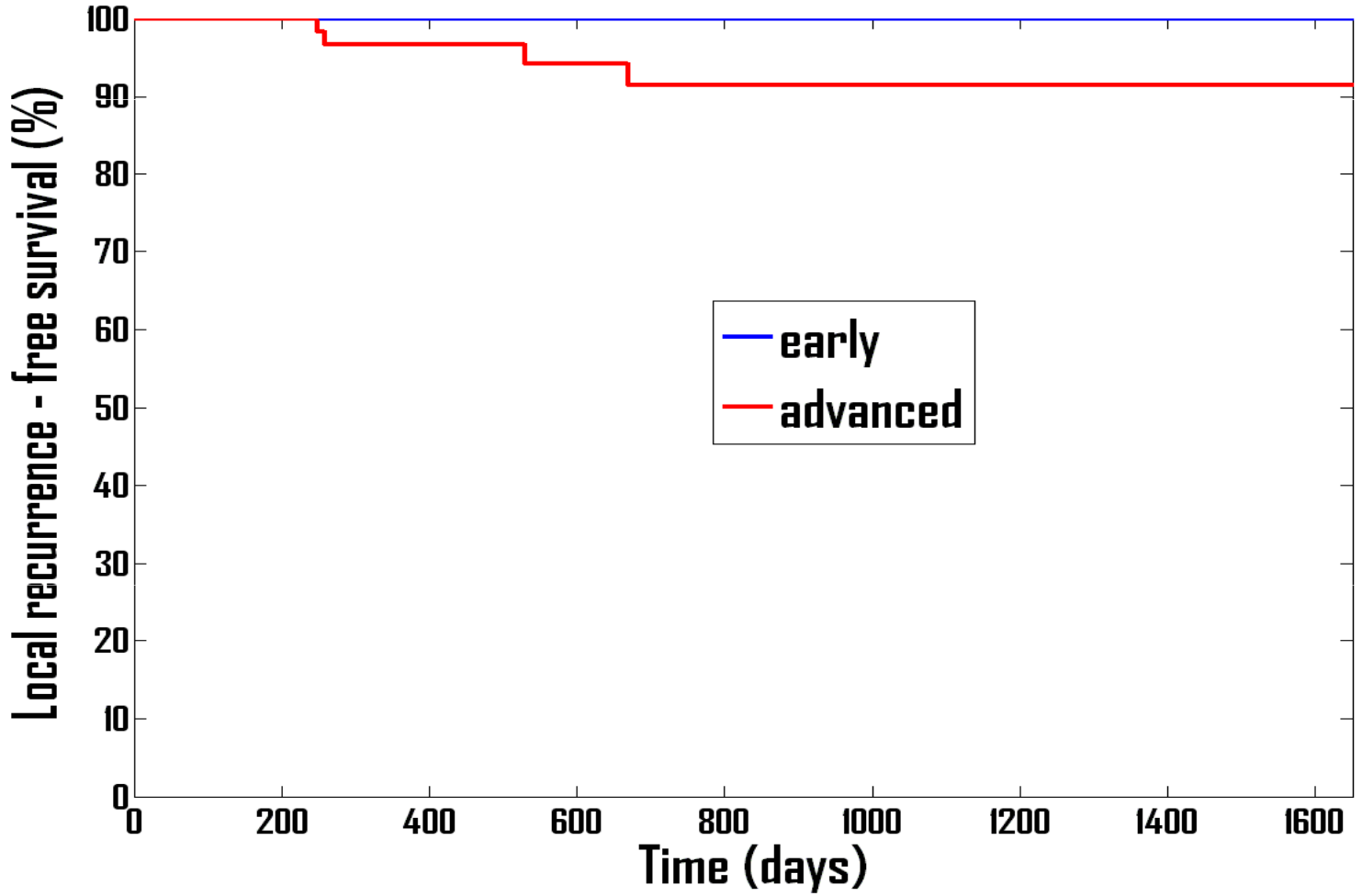
Treatment of squamous cell anal canal carcinoma (SCACC) with pulsed dose rate brachytherapy: A retrospective study

Antoine Bruna[a,*], Pauline Gastelblum[b,e], Laurence Thomas[c], Olivier Chapet[b], Marc A. Bollet[a], Jean-Michel Ardiet[b], Jean-Pierre Gérard[d], Didier Peiffert[a]

[a]*Brachytherapy Department, Centre Alexis Vautrin, Vandoeuvre Lès Nancy, France,* [b]*Brachytherapy Department, Hôpital Lyon-Sud, Pierre Bénite, France,* [c]*Brachytherapy Department, Bordeaux, France,* [d]*Radiotherapy Department, Centre Antoine Lacassagne, Nice, France,* [e]*Radiotherapy Department, Institut Bordet, Brussels, Belgium*



Leuven PDR series:
83 pts



Van Brussel S, Janssen H , Van Limbergen E 2011

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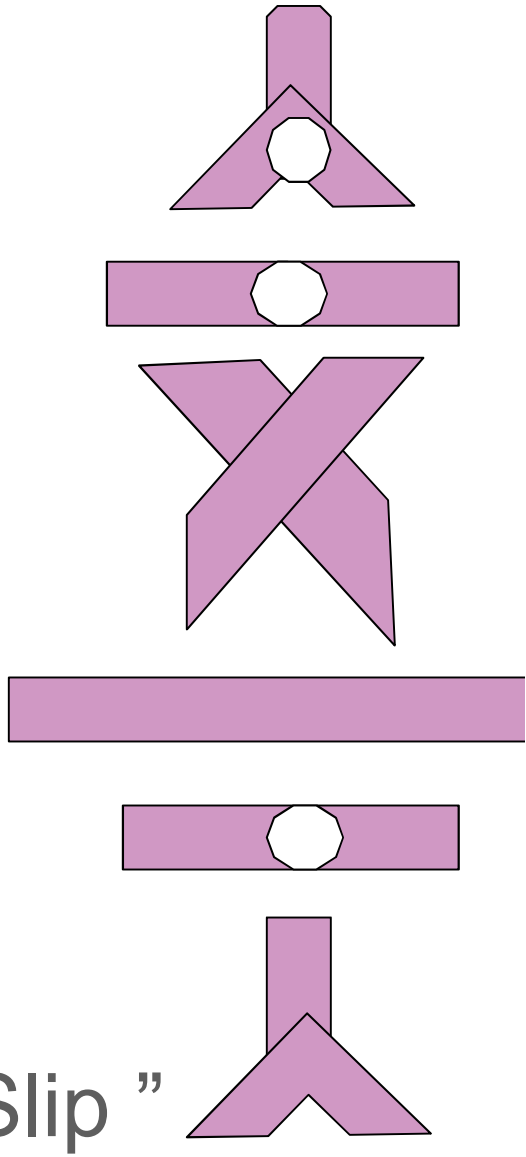
7 Layers



The “ Leuven Elastoplast Brachy Fixation Slip ”

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HDR

- Kapp et al:I.J.R.O.B.P2001;49:997
  - Split course (50 Gy)
  - Concomitant chemo 5FU MITO
  - HDR 6 Gy

Effects on normal tissues

Acute / Late

- Epidermitis,
- Cystitis,
- Rectal dyscomfort

Necrosis if :

- ✓ High dose ,
- ✓ Implantation through the mucosa
- ✓ !! Relapse !!

- ✓ Incontinence
- ✓ Pain
- ✓ Bleeding : no biopsy

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Management of late complications

- Exam under general anestesia
  - Excision of necrosis
  - BIOPSIES
- Local desinfection
- Antibiotics
- Hyperbaric oxygen therapy
- Temporary colostomy

Conclusion

- Brachytherapy is an optimal technique to boost most anal canal tumors
- Precise technique and indications
- Local control
- Risk of necrosis
  - Dose
  - Dose rate (PDR)
  - Volume

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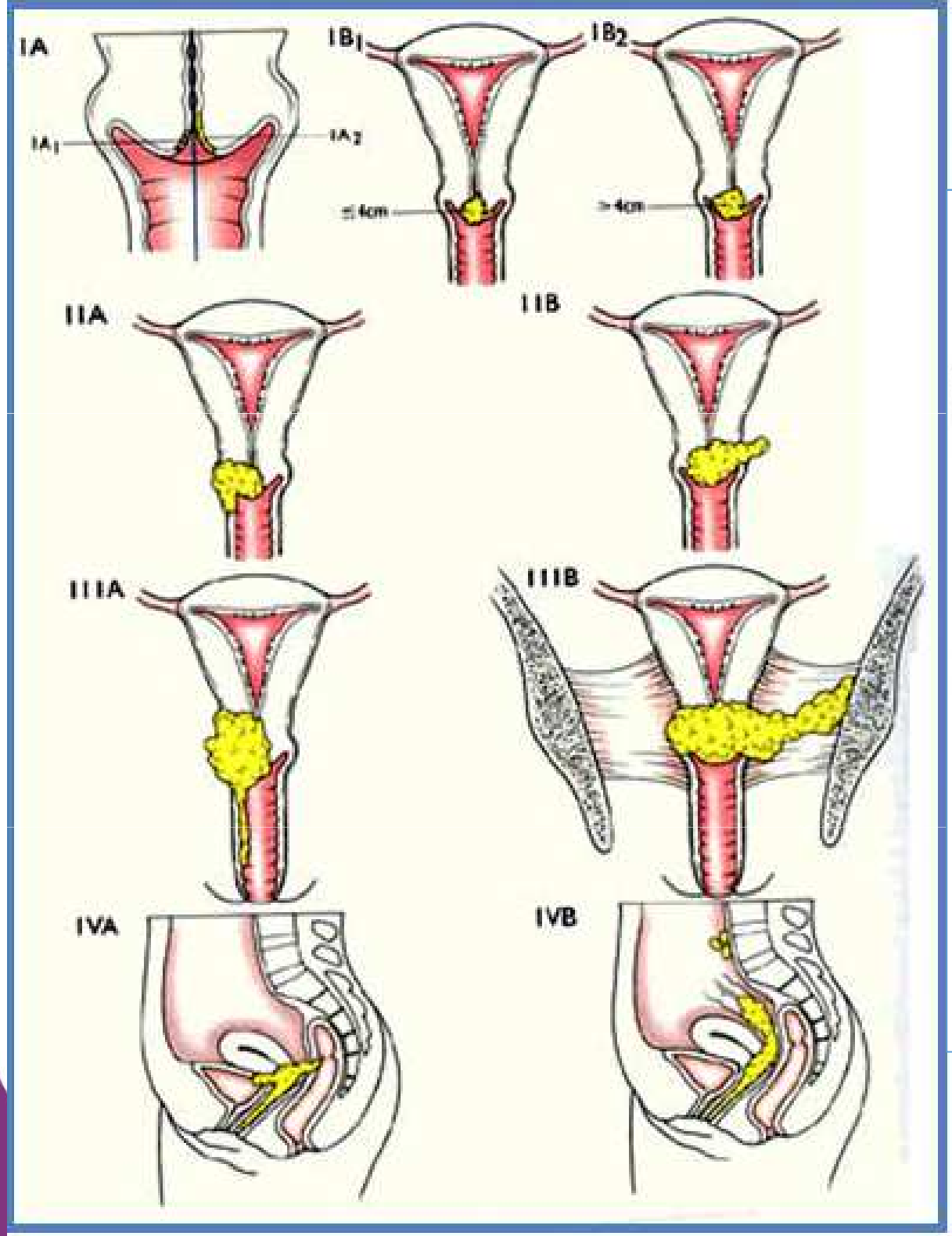
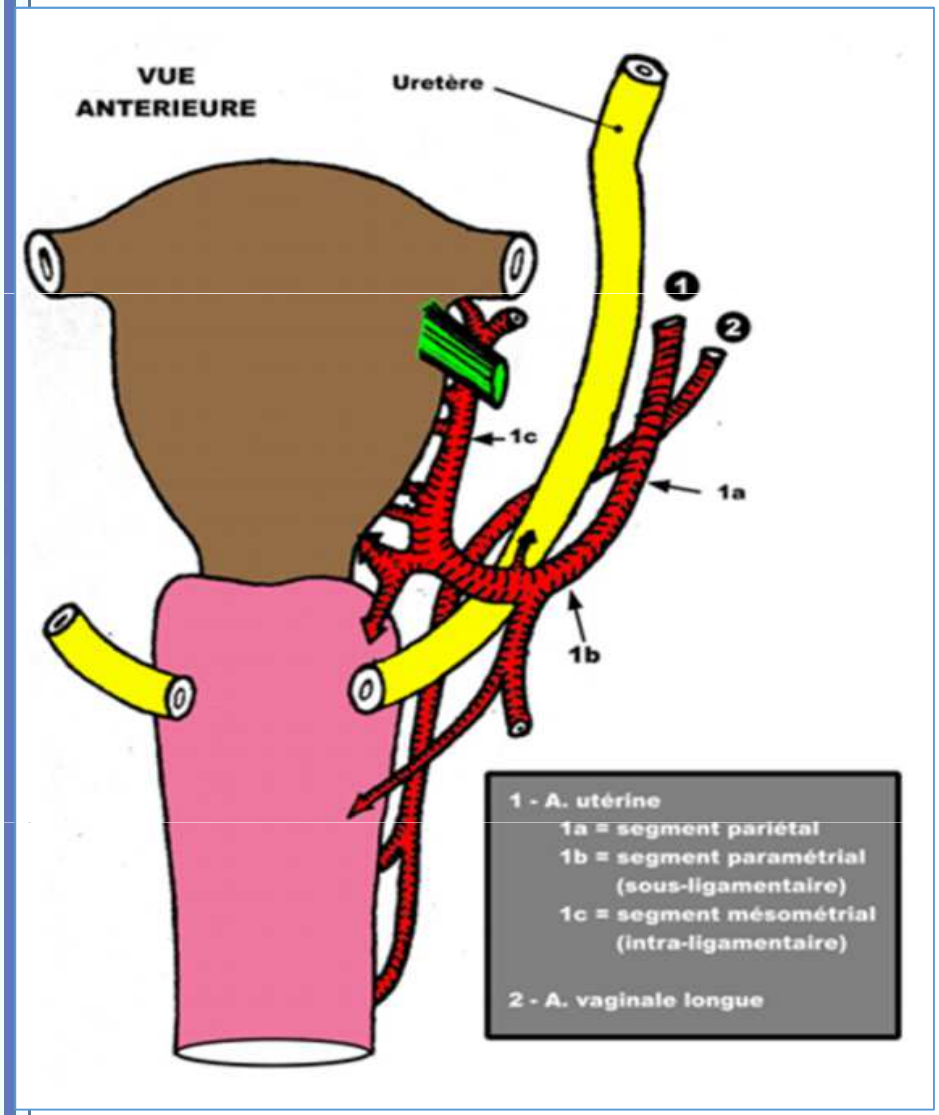
Techniques in cervix brachytherapy

Renaud Mazeron

Gustave Roussy





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Introduction

- Tumors < 4 cm : no standard
  - Surgery
  - EBRT followed by BT
  - BT followed by Surgery
  - Fertility preservation: trachelectomy (<2cm, N-)
- Tumors > 4 cm : Chemoradiation followed by BT

International Journal of
Radiation Oncology
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EDITORIAL

Curative Radiation Therapy for Locally Advanced Cervical Cancer: Brachytherapy Is NOT Optional

Kari Tanderup, PhD,*,† Patricia J. Eifel, MD,‡ Catheryn M. Yashar, MD,§
Richard Pötter, MD,‖ and Perry W. Grigsby, MD*

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Crucial role of BT

Outcomes
1973, 1978, 1983

Komaki IJROBP 31 : 973 - 82 ; 1995
1686 patients
stage III (262 pts)

	1973 n = 114	1978 n = 115	1986 n = 33	p
BT	60.5 %	76.5 %	87.9 %	< 0.001
Linacs	28 %	60 %	87 %	
OS at 5 years	25 %	39 %	47 %	0.02

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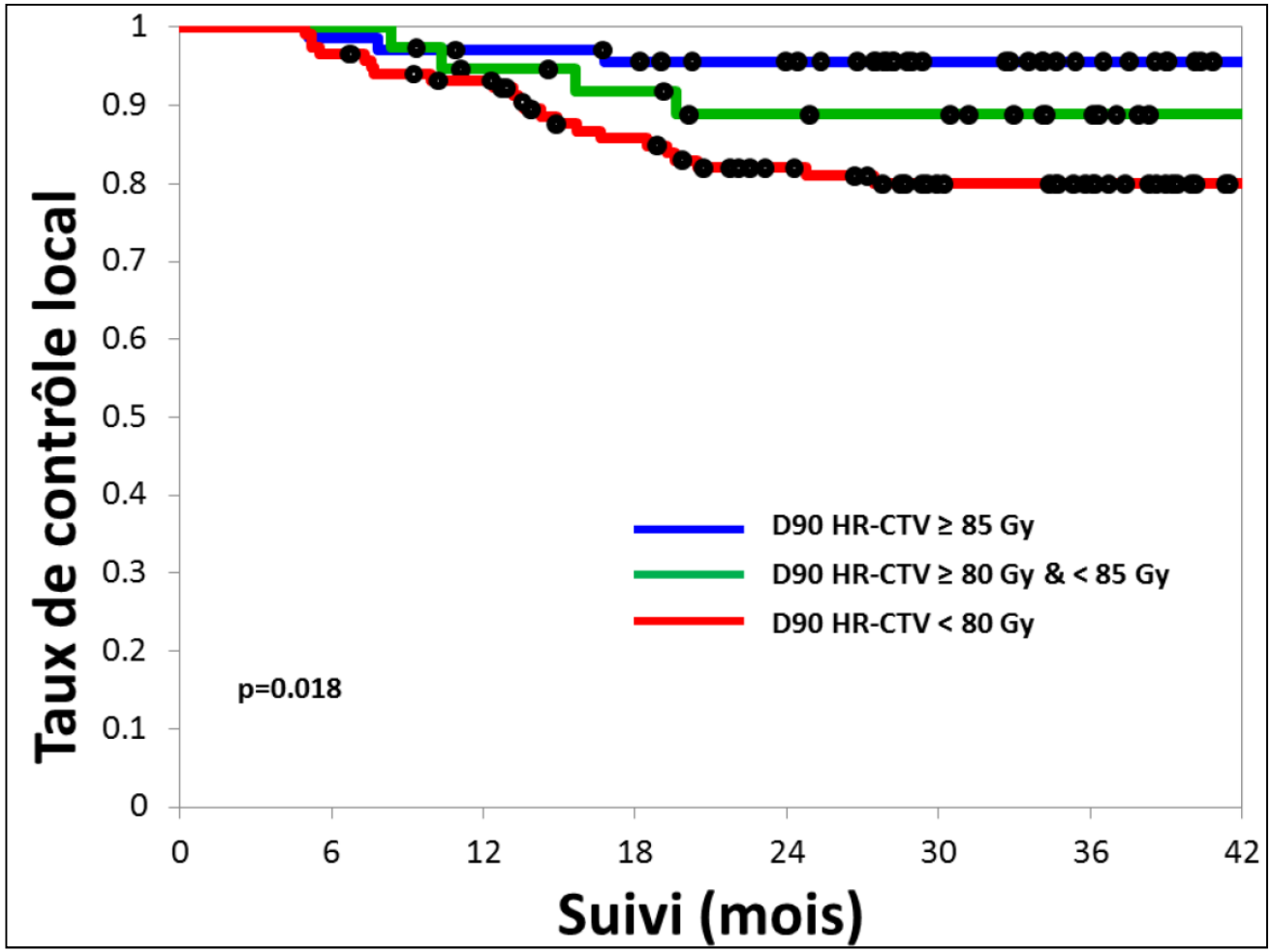
Dose / Local failures
Perez IJROBP 21 : 885 - 96 ; 1991
1211 patients

Dose point A	Stage IIB n = 347	%	Stage III n = 282	%
< 6 000	8/12	67	18/25	72
6000 - 9000	61/261	23	71/180	39
> 9000	10/74	14	27/77	35

Dose-volume effect

- Gustave Roussy
- 225 patients
- 50%: IIB lesions
- Concom chemo
- IGABT
- Median FU: 3 y



Castelnau-Marchand Gynecol Oncol 2015

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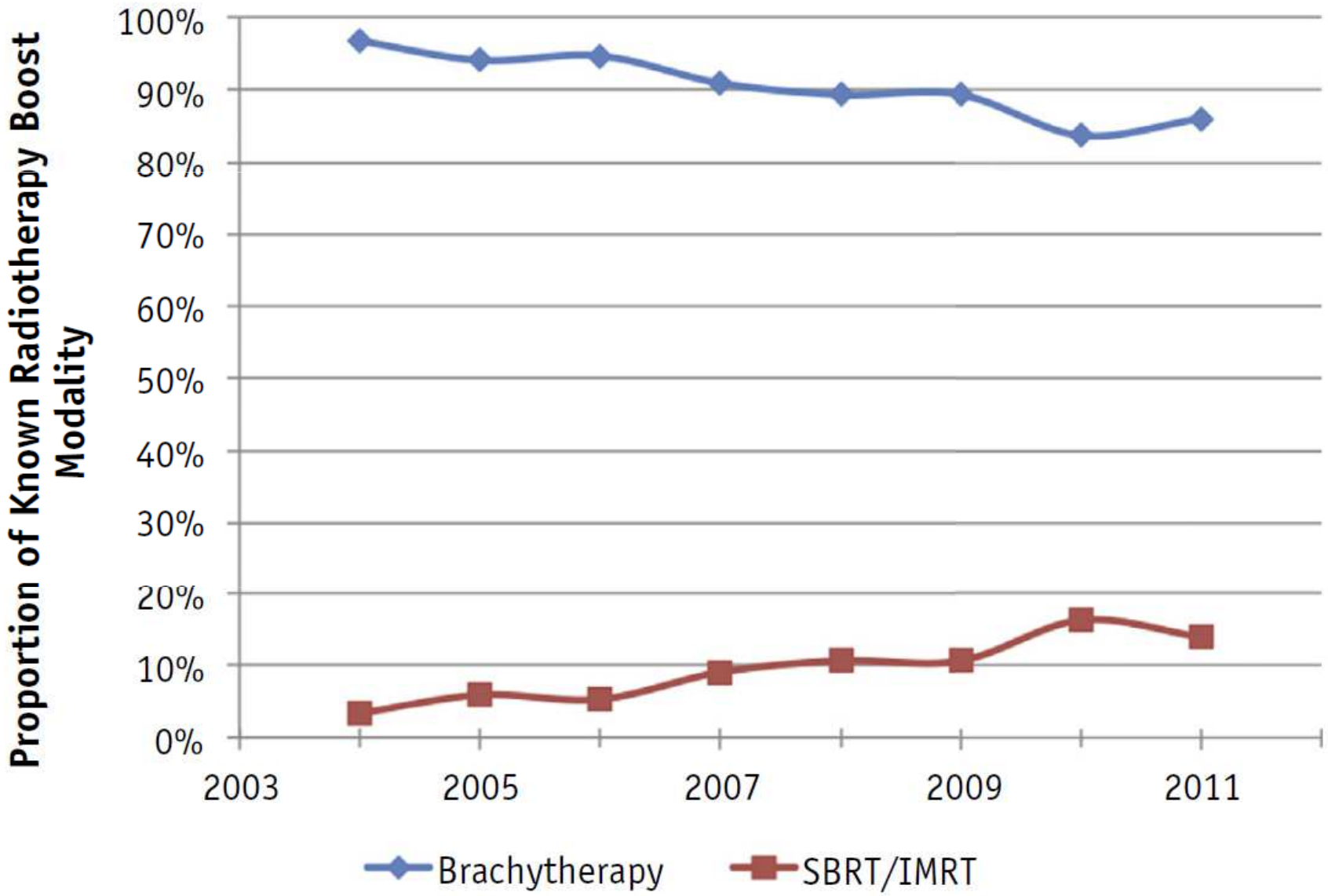
Decreasing use of BT in USA



Gill IJROBP 2014

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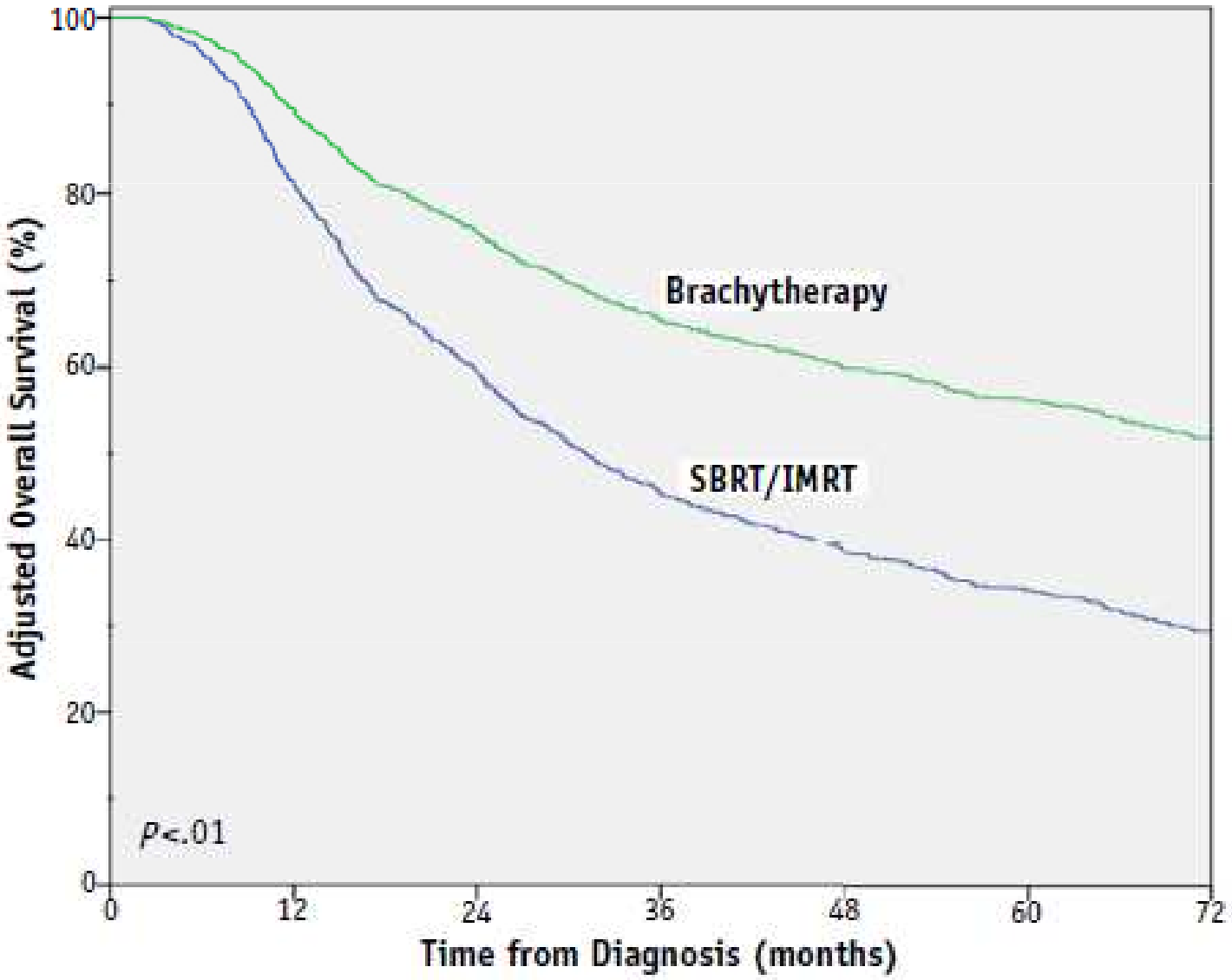
Consequences



Gill IJROBP 2014

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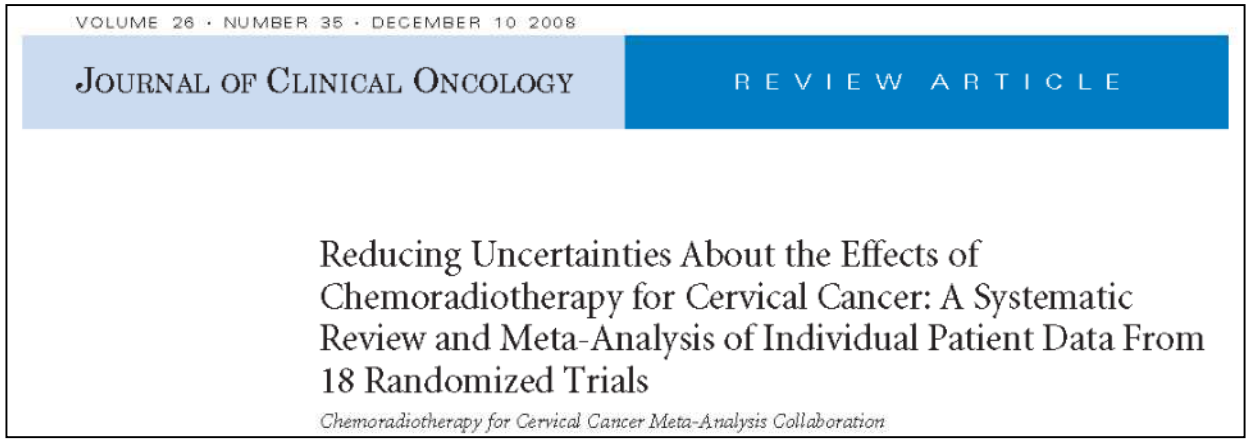
Concomitant chemotherapy



	HR	IC 95%	p	Gain absolu à 5 ans
DFS	0,78	0,70-0,87	0,000005	**8 %**
Regional control	0,76	0,68-086	0,000003	**9 %**
Distant disease free surv	0,81	0,72-0,91	0,0004	**7 %**
Overall survival	**0,81**	**0,71-0,91**	**0,0006**	**6 %**

Concomitant chemoradiation

- No effect of patient age
- Cisplatinium does not do better
- No influence
  - Nodal status
  - Histological subtype
  - Grade
- Decreasing efficacy with increasing FIGO stage
  - Marginal in stage III
    - Ib - IIa = + 10 %
    - IIb = + 7 %
    - III et IVa = + 3 %

Combining EBRT and brachytherapy

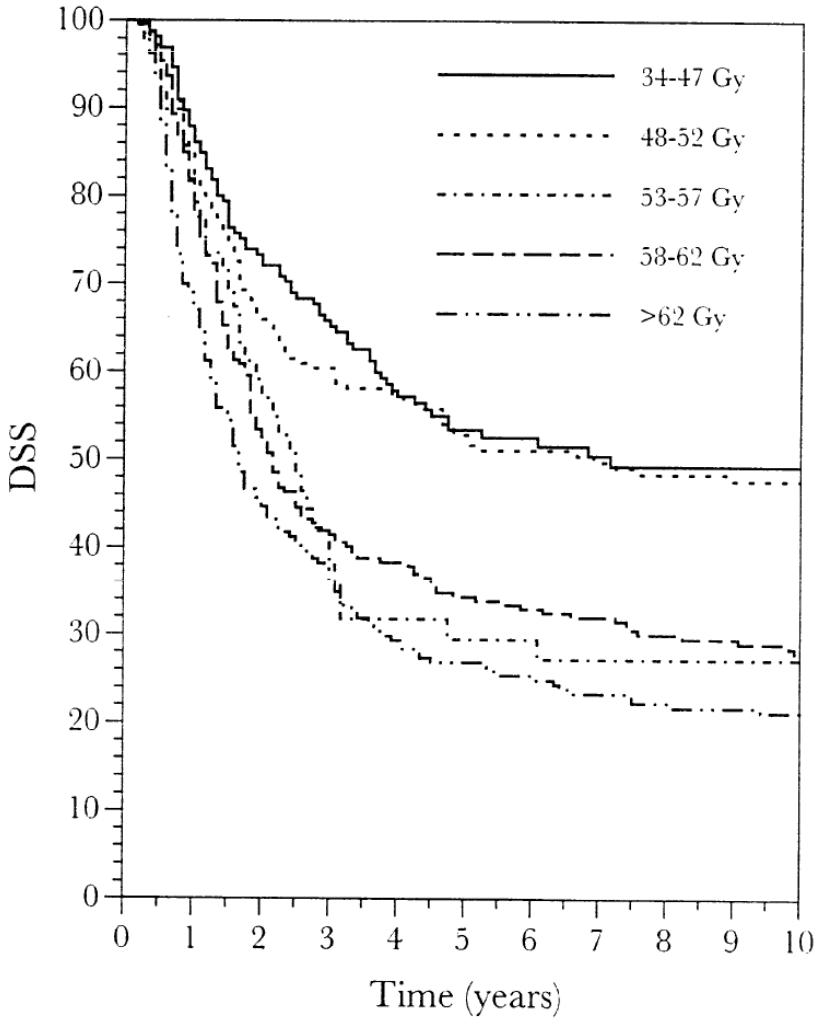
- Both modalities contribuate
- important balance
- EBRT: Low risk CTV
  - Aim: delivery of 45 – 50 Gy: microscopic disease
  - Tumor shrinkage
  - Nodal boost required
- Brachytherapy: dose escalation
  - Cervical disease
  - Sparing of OAR
  - Also contribuates to treat node metastasis

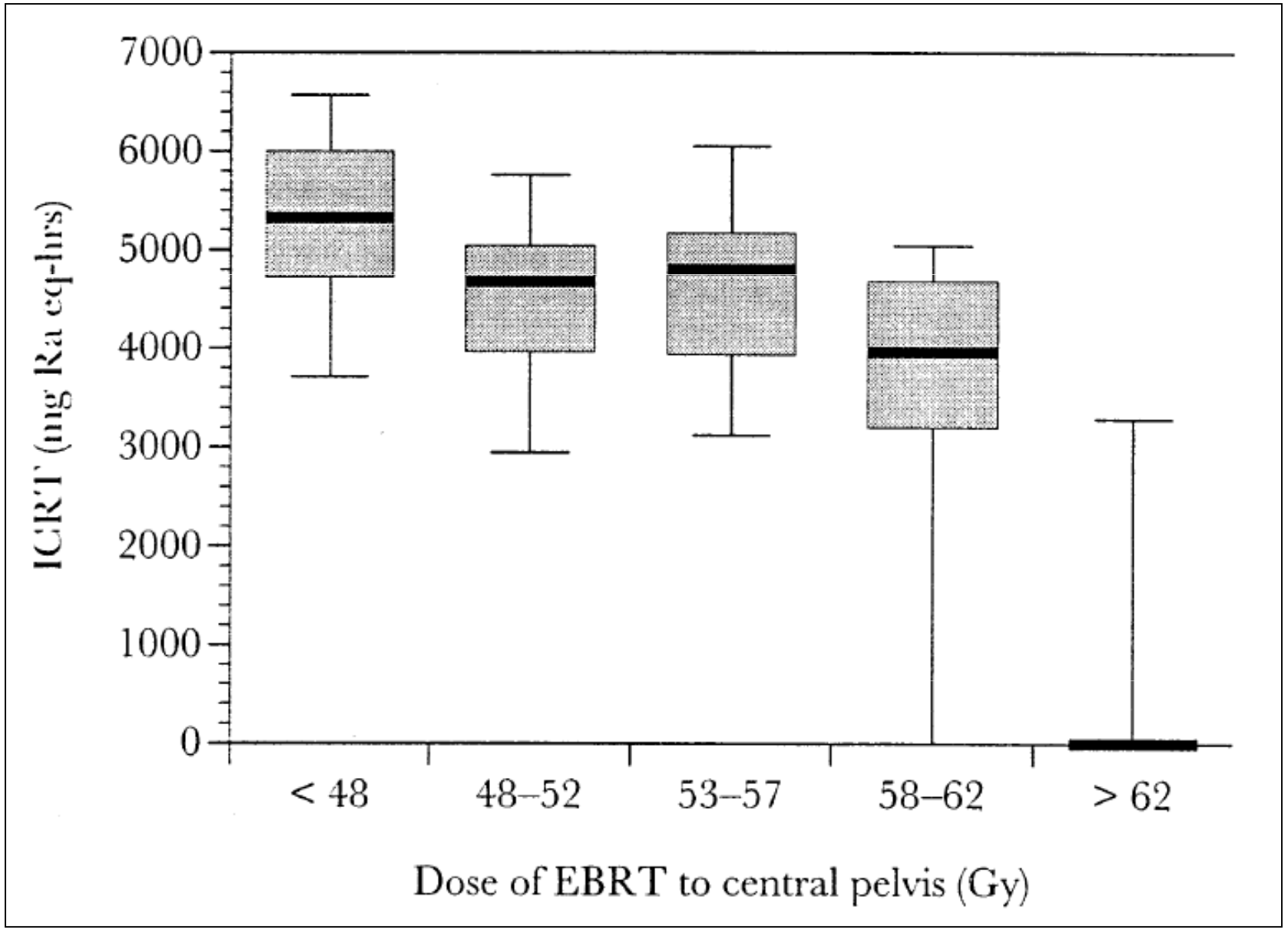
FIGO IIIB SQUAMOUS CELL CARCINOMA OF THE CERVIX: AN ANALYSIS OF PROGNOSTIC FACTORS EMPHASIZING THE BALANCE BETWEEN EXTERNAL BEAM AND INTRACAVITARY RADIATION THERAPY

MARK D. LOGSDON, M.D., AND PATRICIA J. EIFEL, M.D.

Division of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX

- 907 patients
- Stage IIIB
- Different periods
- High EBRT doses
  - Low DSS
  - Increased morbidity



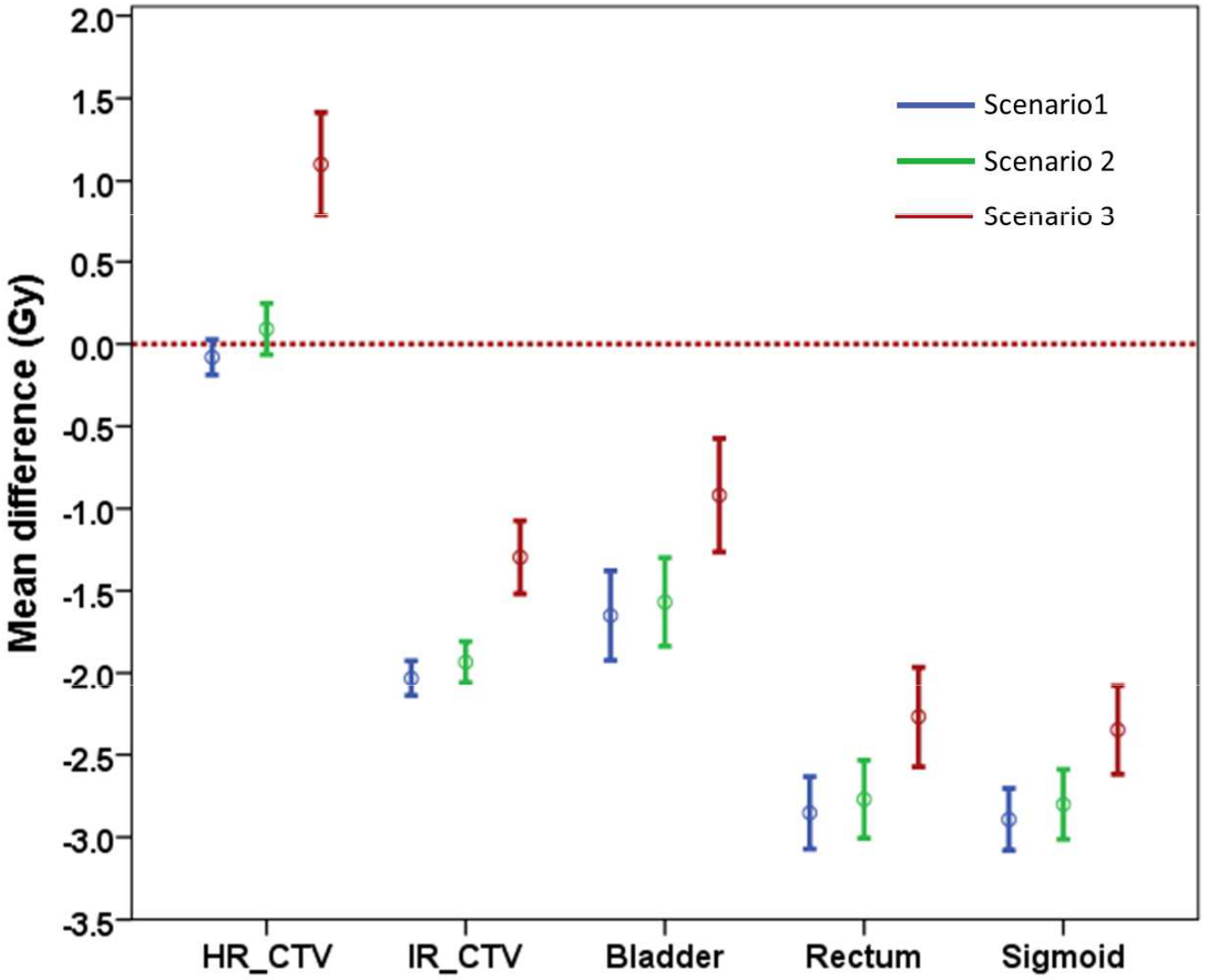

7000
6000
5000
4000
3000
2000
1000
0
ICRT (mg Ra eq-hrs)
< 48
48–52
53–57
58–62
> 62
Dose of EBRT to central pelvis (Gy)

45 or 50 Gy, Which is the Optimal Radiotherapy Pelvic Dose in Locally Advanced Cervical Cancer in the Perspective of Reaching Magnetic Resonance Image-guided Adaptive Brachytherapy Planning Aims?

R. Mazeron *†, C. Petit *, E. Rivin *, E. Limkin *, I. Dumas ‡, P. Maroun *, P. Annede *, F. Martinetti ‡, T. Seisen *, D. Lefkopoulos †‡, C. Chargari *, C. Haie-Meder *

- 120 optimized plans
- Multiplication of pulses until planning aims are reached or a dose contraint not respected
  - Using a pelvic EBRT dose of 45 Gy in 25 fractions
  - Or 50.4 Gy in 28 Gy
- 3 sets of planning aims
  - Usual : B: 90, R and S: 75
  - Intermediate
  - EMBRACE II

Results: 45 Gy plan – 50.4 Gy plan

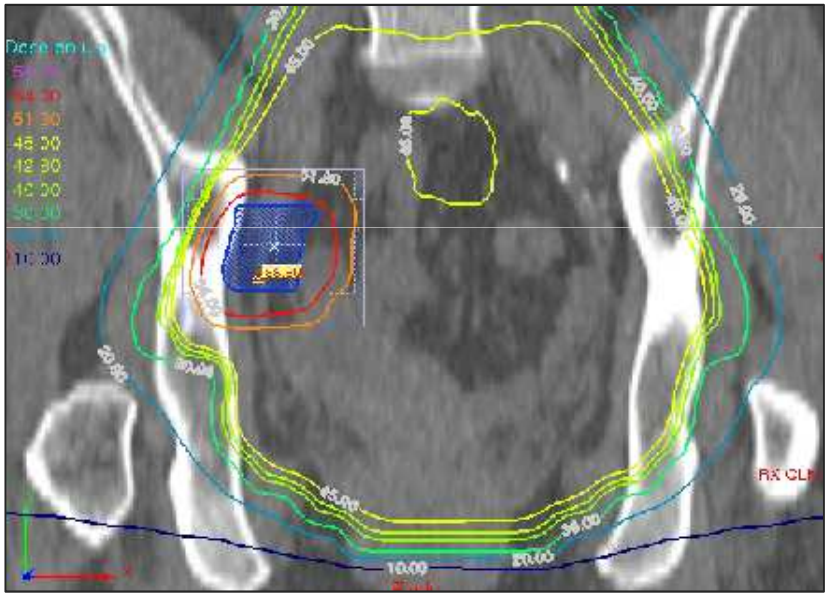


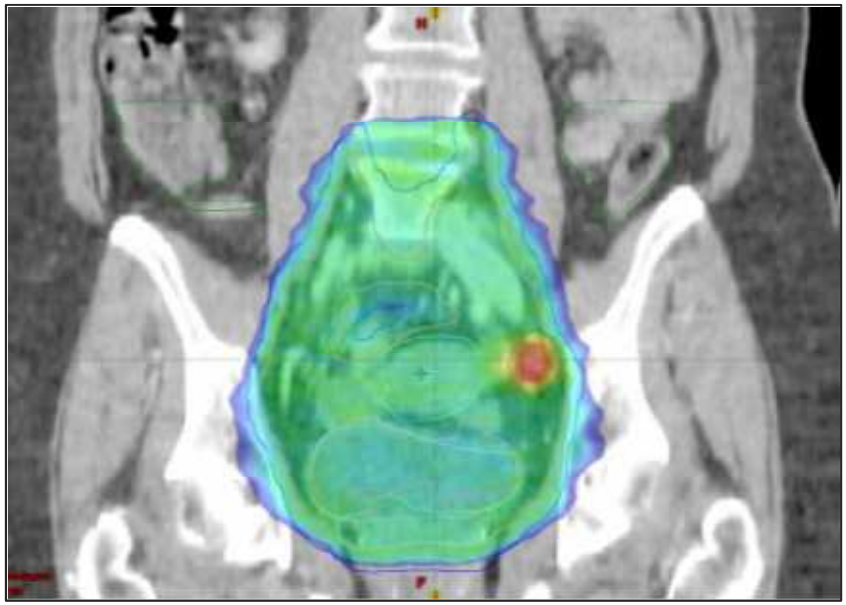
Balance EBRT / BT

- Privilege BT
  - Better coverage of CTV_{HR}
  - Better sparing of OAR
- DO NOT USE: cervical SIB
- AVOID parametrial boosts / Trust in IS BT
- 50.4 Gy is not enough to treat nodal metastasis

Nodal boost

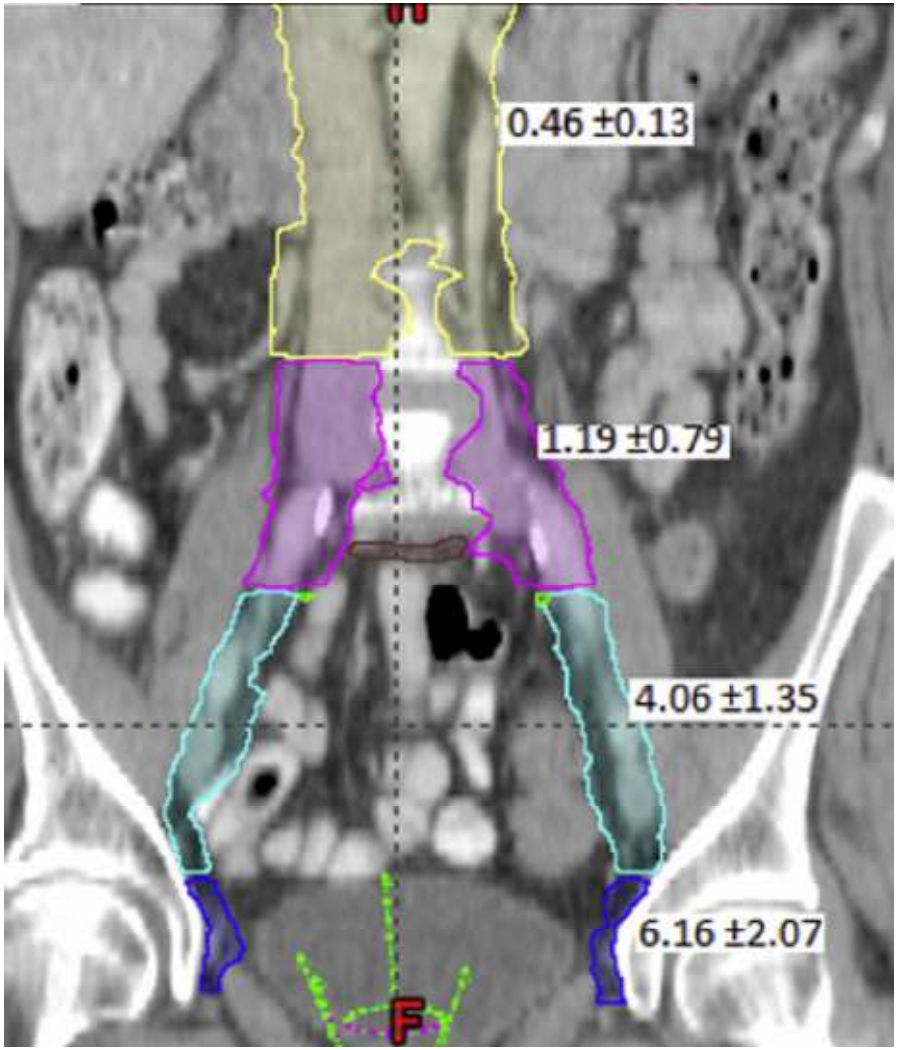
- Planning aim : 60 Gy / Lack of data
- Sequential: after BT, based on calculations of its contribution
- SIB: based on an evaluation of BT contribution





Simultaneous intregated boost

- Decrease treatment time
- Ext/int iliac
  - SIB: 2.2 x 25 = 55 Gy
- Prim iliac
  - 2.3 x 25 = 57.5 Gy
- Para aortic
  - Negligible contribution
  - 2.4 ?
- Lack of data on long term activity



Mohamed Brachy 2015

Excessive overall treatment time

Author	Year	# pts	Threshold	Impact on local control
Lanciano et al	1993	837	55 jours	⇓ 0.85 % / jour
Petereit et al	1995	202	55 jours	⇓ 0.7 % / jour
Perez et al	1995	1224	49 jours	⇓ 0.85 % / jour
Girinsky et al	1993	386	52 jours	⇓ 1.1 % / jour
Song et al. *	2013	113	56 jours	Non rapporté
Mazeron et al. *	2015	225	56 jours	⇓ 0.6 % / jour

Pelvis 45 Gy = 35-37 days

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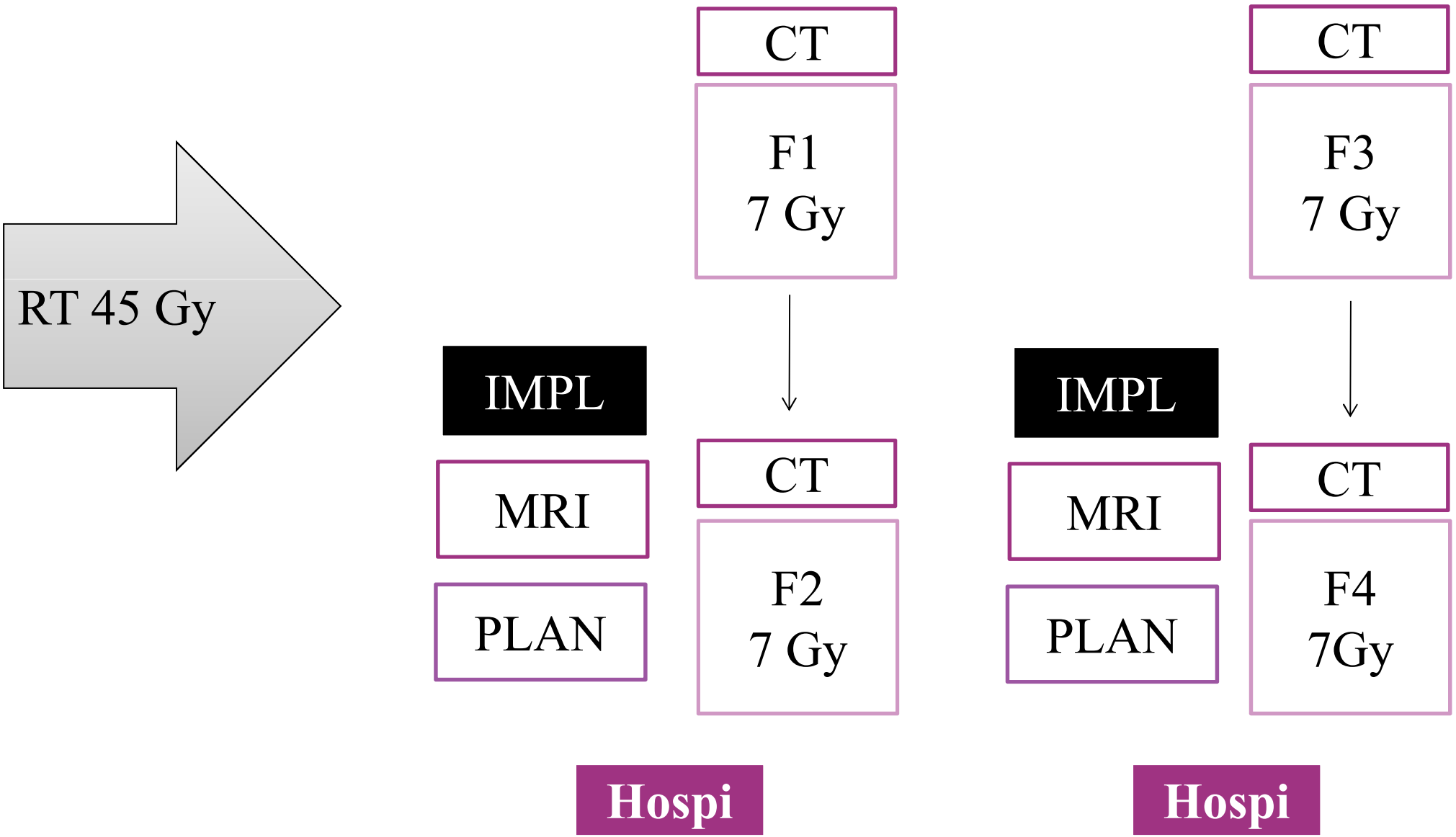
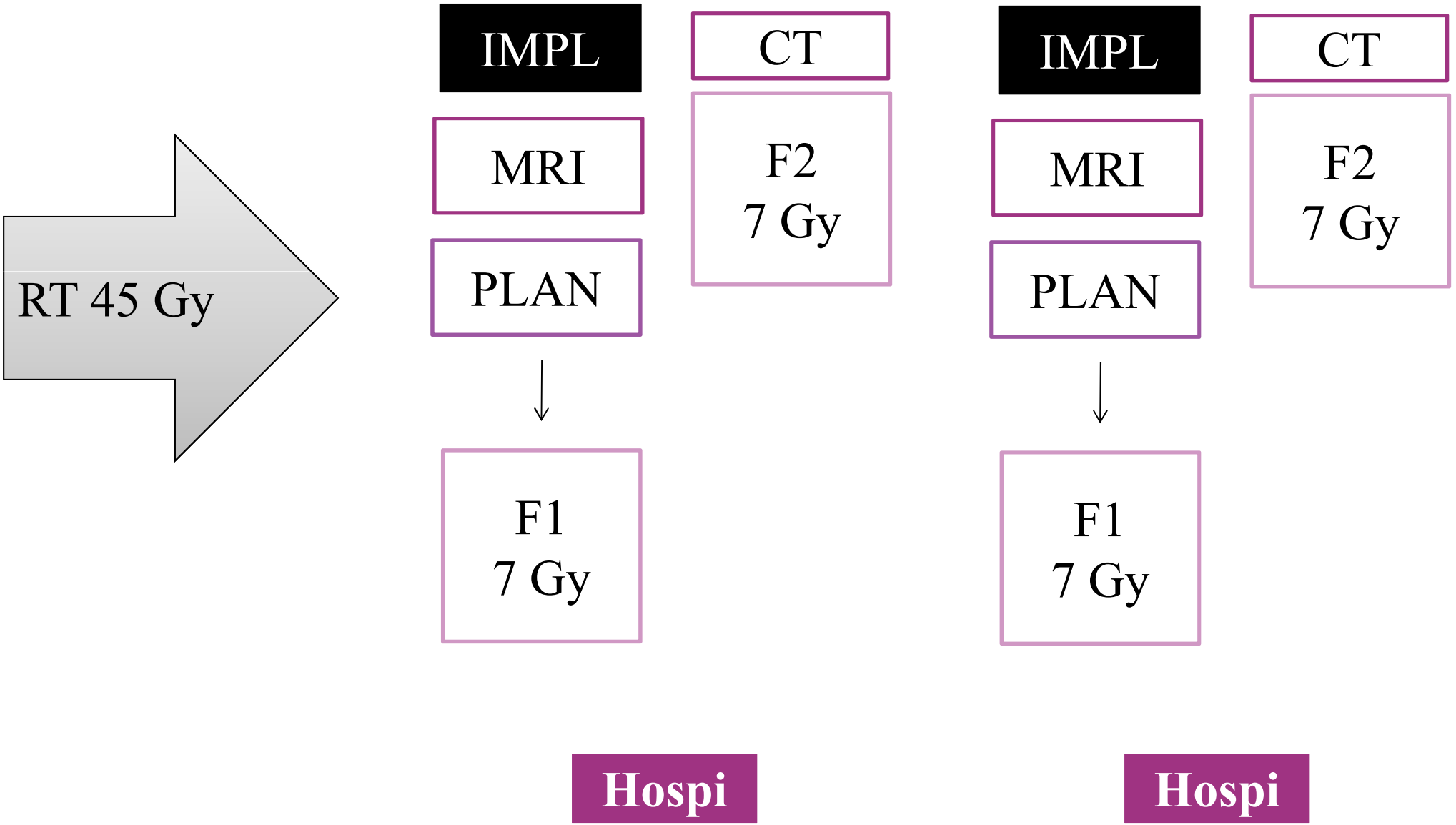

RT 45 Gy
CT
F1
7 Gy
IMPL
MRI
PLAN
CT
F2
7 Gy
Hospi
CT
F3
7 Gy
IMPL
MRI
PLAN
CT
F4
7Gy
Hospi


RT 45 Gy
IMPL
MRI
PLAN
F1
7 Gy
CT
F2
7 Gy
Hospi
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MRI
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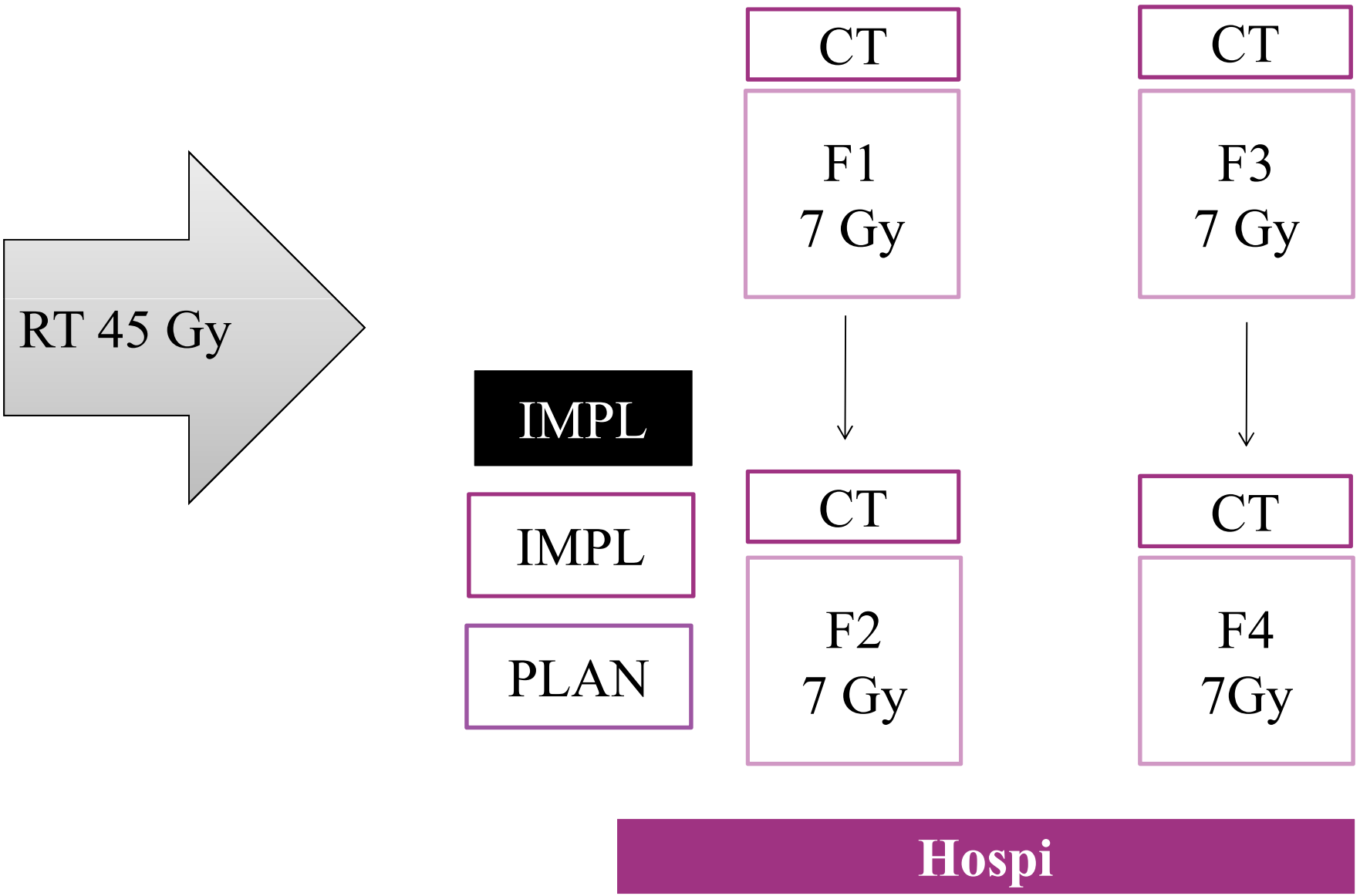
F1
7 Gy
CT
F2
7 Gy
Hospi


RT 45 Gy
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7 Gy
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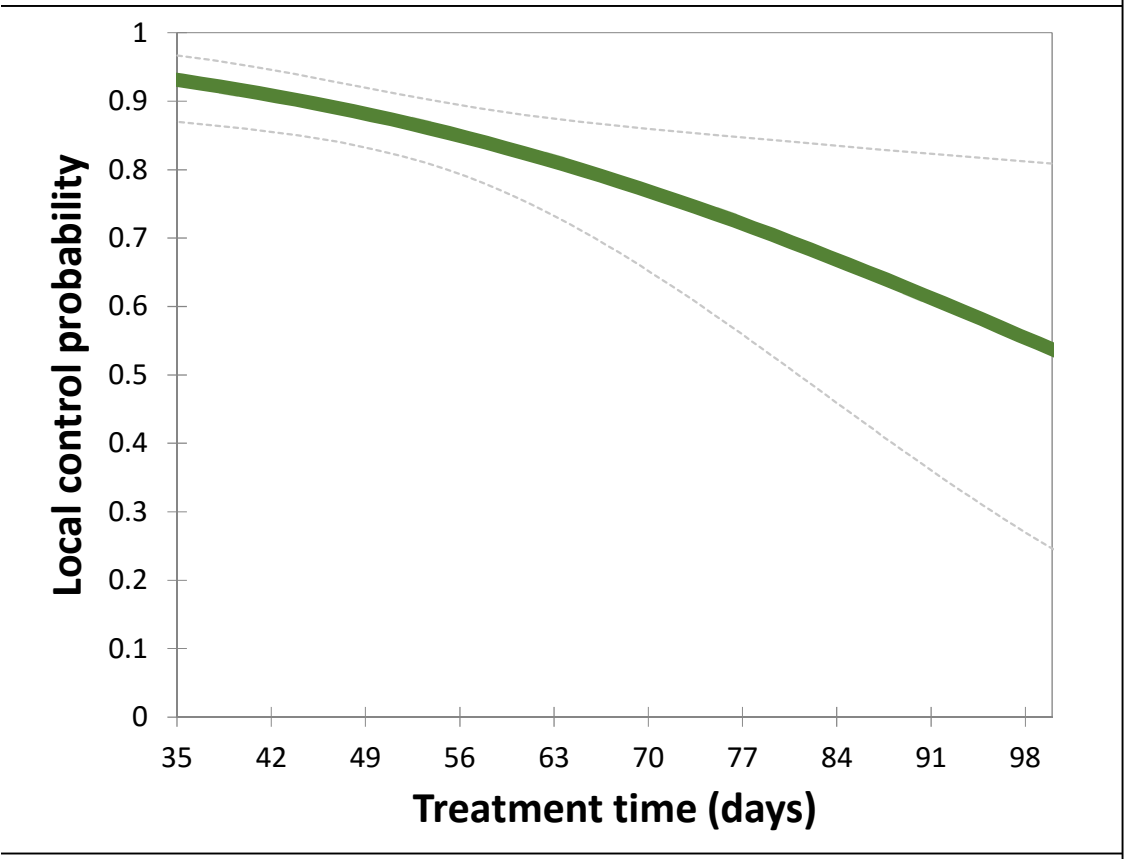
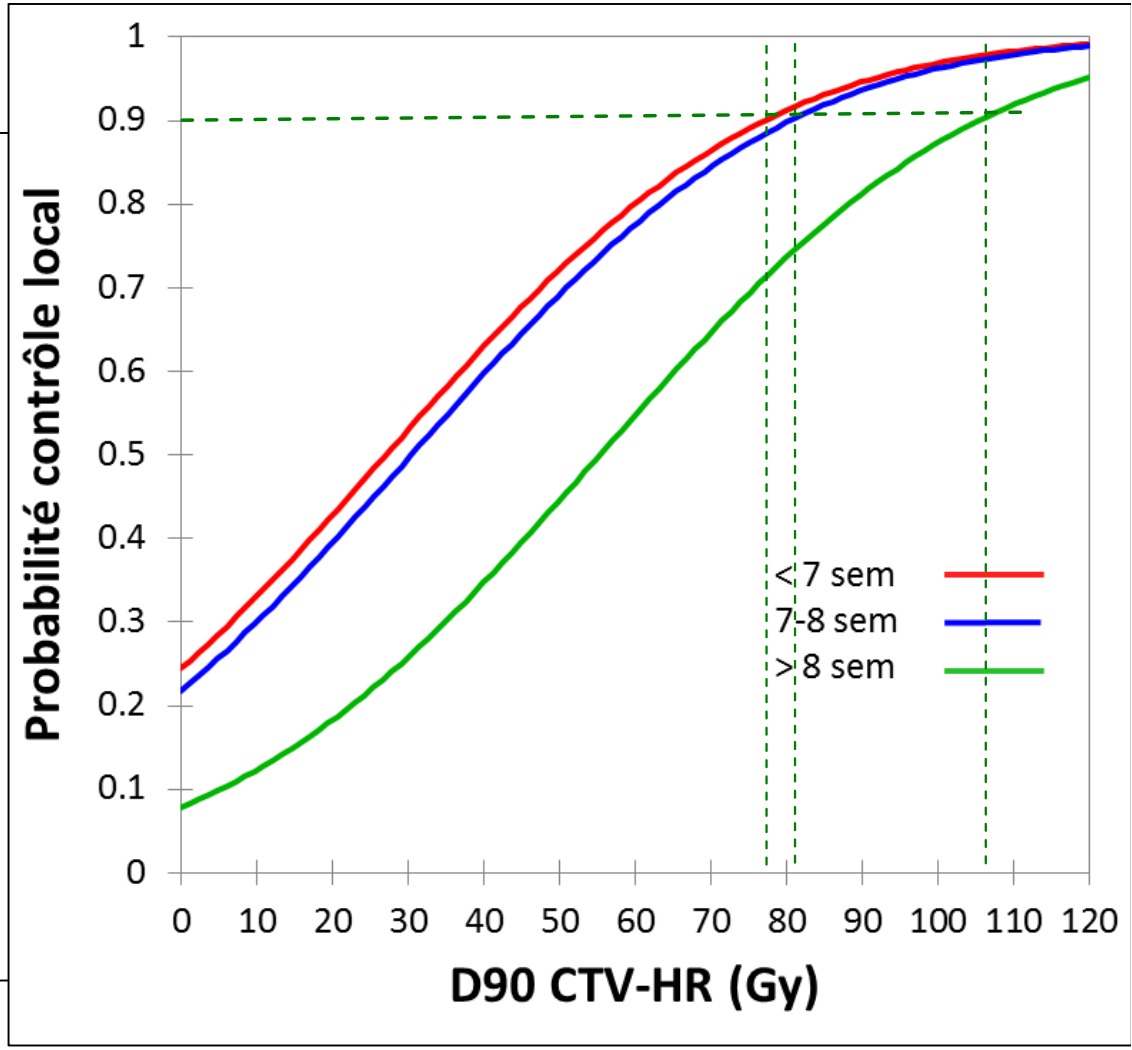
F2
7 Gy
CT
F4
7Gy
Hospi

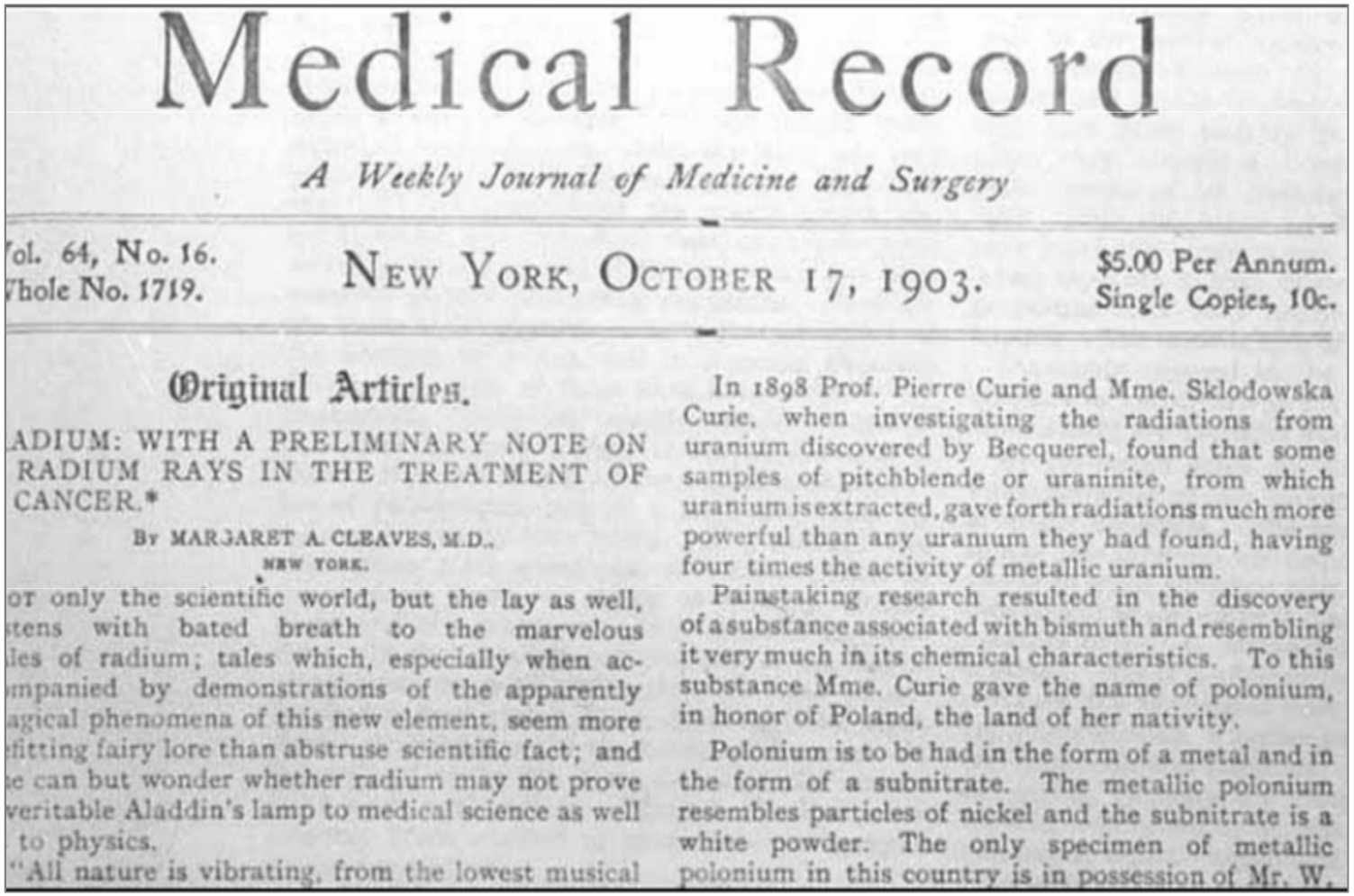




Beyond **55 jours / -0.63% per day**

≈ 4.41% per week.

Techniques



Medical Record

A Weekly Journal of Medicine and Surgery

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Original Articles.

ADIUM: WITH A PRELIMINARY NOTE ON RADIUM RAYS IN THE TREATMENT OF CANCER.*

By MARGARET A. CLEAVES, M.D., NEW YORK.

or only the scientific world, but the lay as well, tens with bated breath to the marvelous les of radium; tales which, especially when ac- mpanied by demonstrations of the apparently agical phenomena of this new element, seem more fitting fairy lore than abstruse scientific fact; and e can but wonder whether radium may not prove veritable Aladdin's lamp to medical science as well to physics.

"All nature is vibrating, from the lowest musical

In 1898 Prof. Pierre Curie and Mme. Sklodowska Curie, when investigating the radiations from uranium discovered by Becquerel, found that some samples of pitchblende or uraninite, from which uranium is extracted, gave forth radiations much more powerful than any uranium they had found, having four times the activity of metallic uranium.

Painstaking research resulted in the discovery of a substance associated with bismuth and resembling it very much in its chemical characteristics. To this substance Mme. Curie gave the name of polonium, in honor of Poland, the land of her nativity.

Polonium is to be had in the form of a metal and in the form of a subnitrate. The metallic polonium resembles particles of nickel and the subnitrate is a white powder. The only specimen of metallic polonium in this country is in possession of Mr. W.

Treatment planning for intracavitary treatments based on clinical examination and X-ray images

Brachytherapy characteristics :
high dose gradient (10 % per mm)

→ many difficulties in expressing the dose in IC BT

Historically :

- Paris method and Stockholm system : mgh radium implant
- Manchester system : fixed distances related to anatomy and applicator reference points : A and B

Treatment planning for intracavitary treatments based on clinical examination and X-ray images

Differences in point A definition between centres
If chosen as the dose specification point

⟶ point A definition = unequivocal

Point A: applicator-based

Treatment planning for intracavitary treatments based on clinical examination and X-ray images

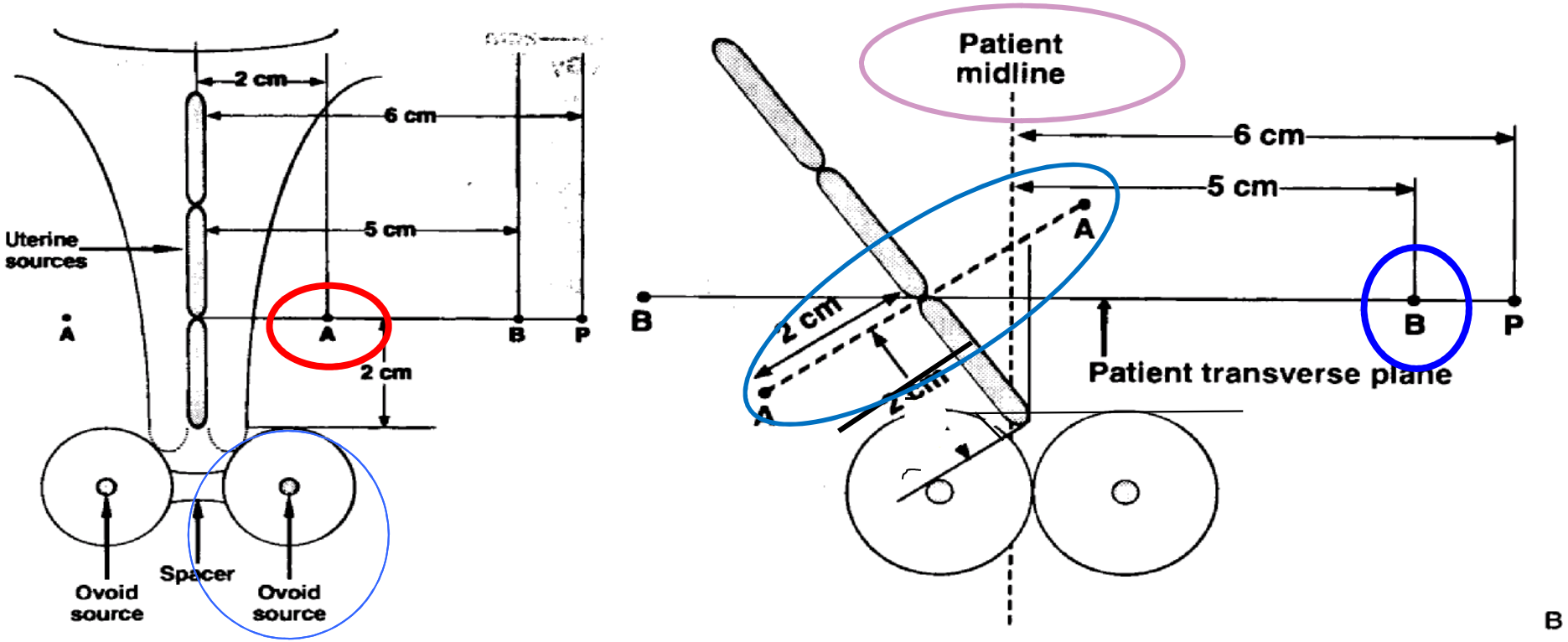
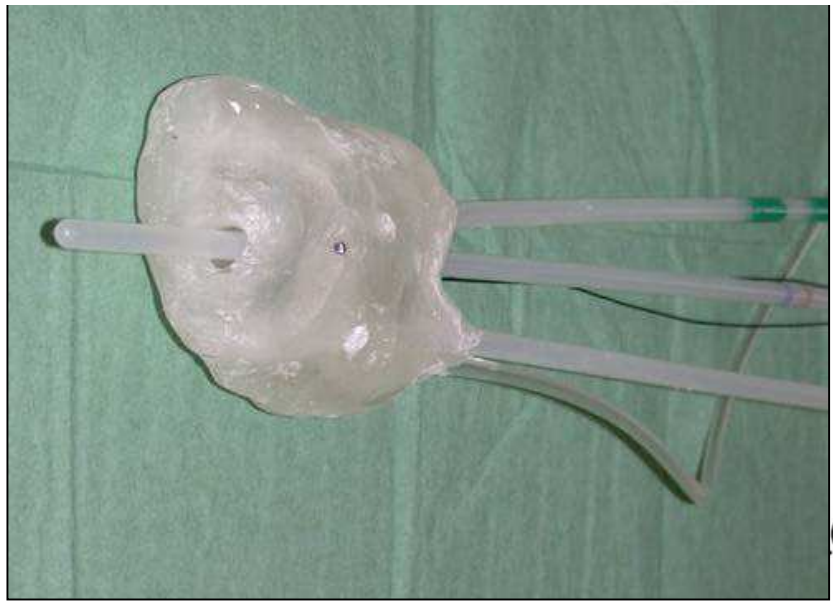


FIGURE 15–34. Definition of points A and B in an ideal application (**A**) and a distorted application (**B**) that is displaced to the left of the patient's mid-line and a uterus that is tilted toward the right. Note that point A is carried with the uterus, whereas points B and P are defined to be 5 and 6 cm, respectively, to the right and left of the patient's mid-line. Point P is used by the Mallinckrodt Institute of Radiology system to specify minimum dose to the pelvic lymph nodes. (Meredith WJ, ed: Radium Dosage: The Manchester System, ed 2. Edinburgh, Scotland, E & S Livingston, 1967)

Applicators

- Combine an intrauterine tandem
- And vaginal sources
- Initially designed for Radium
- Modified for Iridium and Cesium
- Modified to become CT / MRI compatible
- Modified for Interstitial brachytherapy

Applicators



Applicator: Ring

Historical background

Classical "Stockholm method":

- flexible intrauterine tube and a flat box (plate)
- containing Radium sources
- implanted independently – no fixed geometry

Modern "Stockholm" based technique (1960s)

- rigid uterine tandem with a ring applicator for
- afterloading devices (Cs^{137}- I^{192})
- intrauterine tube and ring fixed to each other (fixed geometry)

several applicator types, also MR/CT compatible

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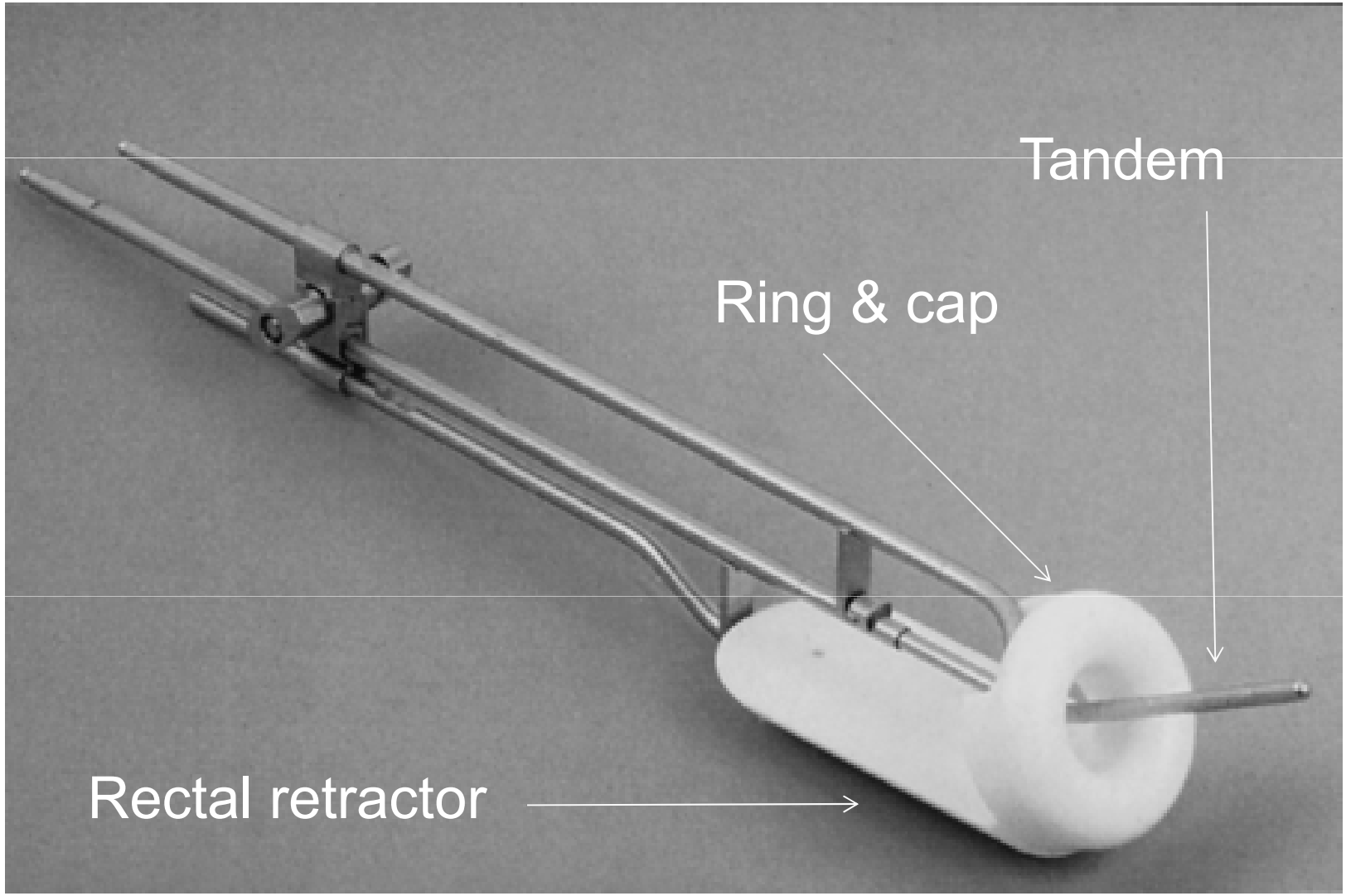
Ring



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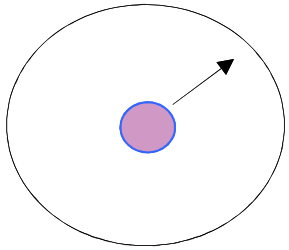
Ring

- Diameter of the ring: anatomy
- Length of the tandem: uterus anatomy
- Angle between ring and vagina: anatomy
- Cap: reduce the dose to vagina
- Packing



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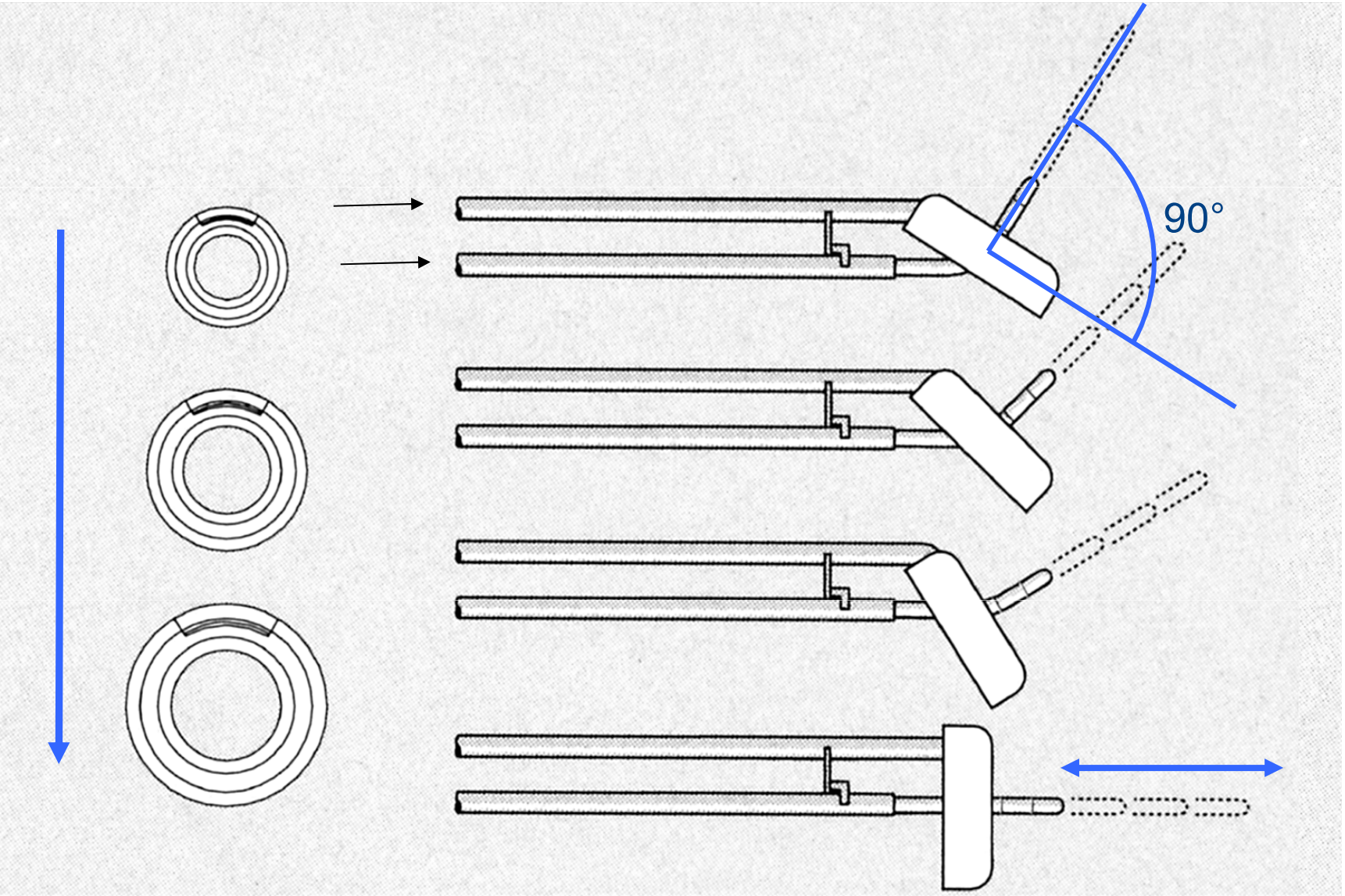
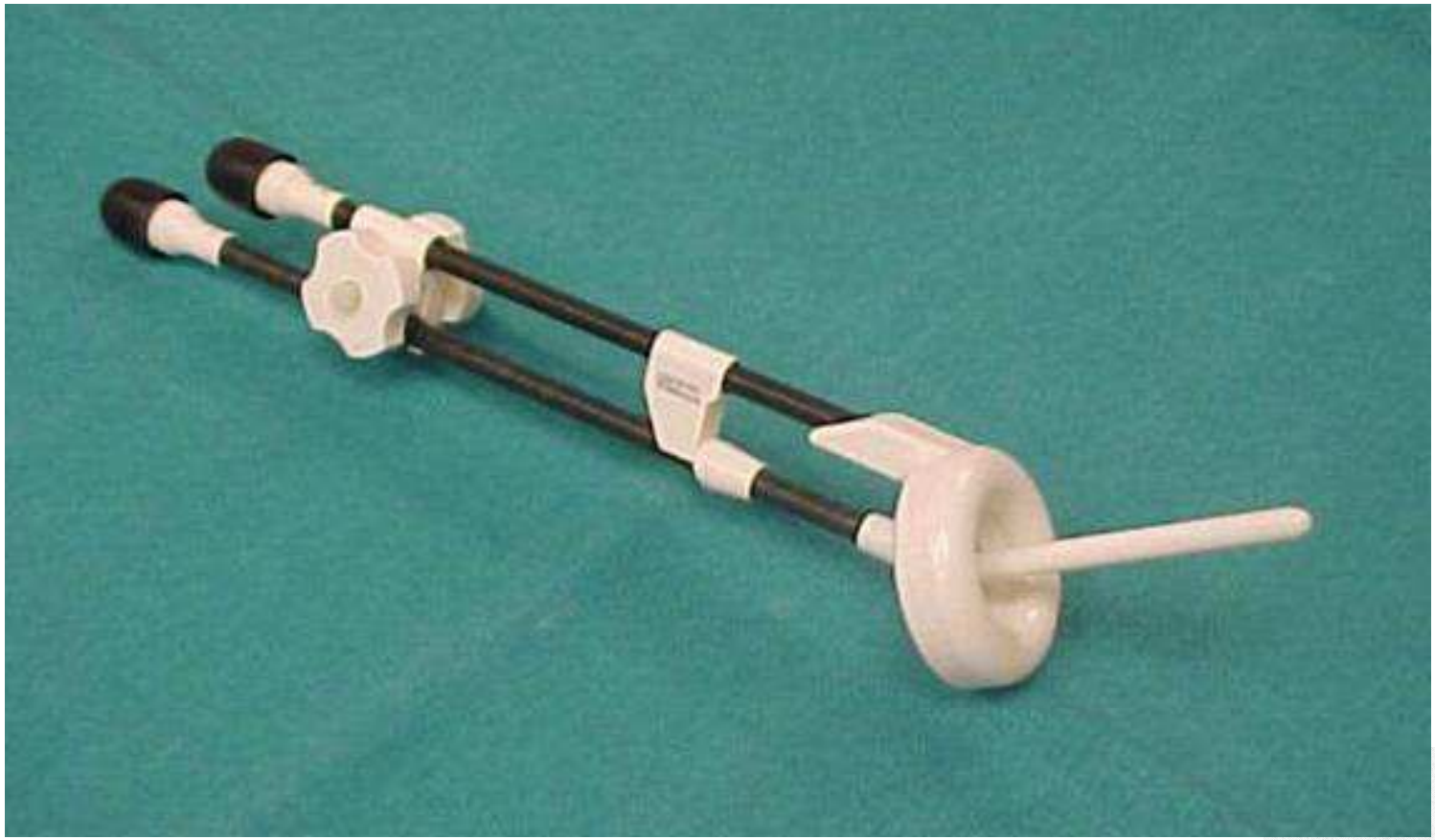
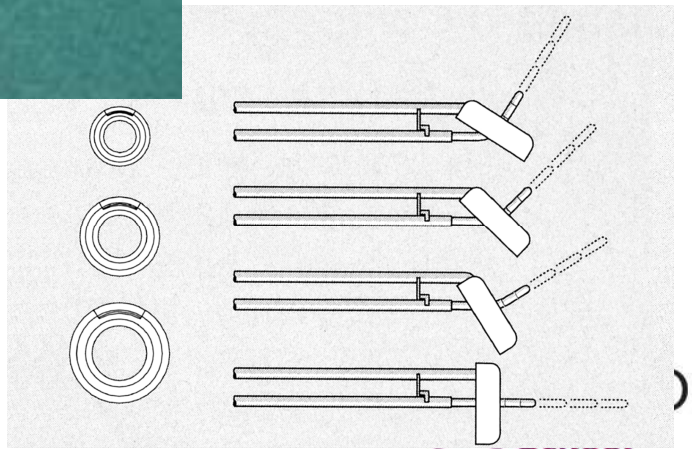
Construction: Tandem, Ring (+ cap)



Nucletron – MR/CT compatible





Varian (Gammamed) – MR/CT compatible

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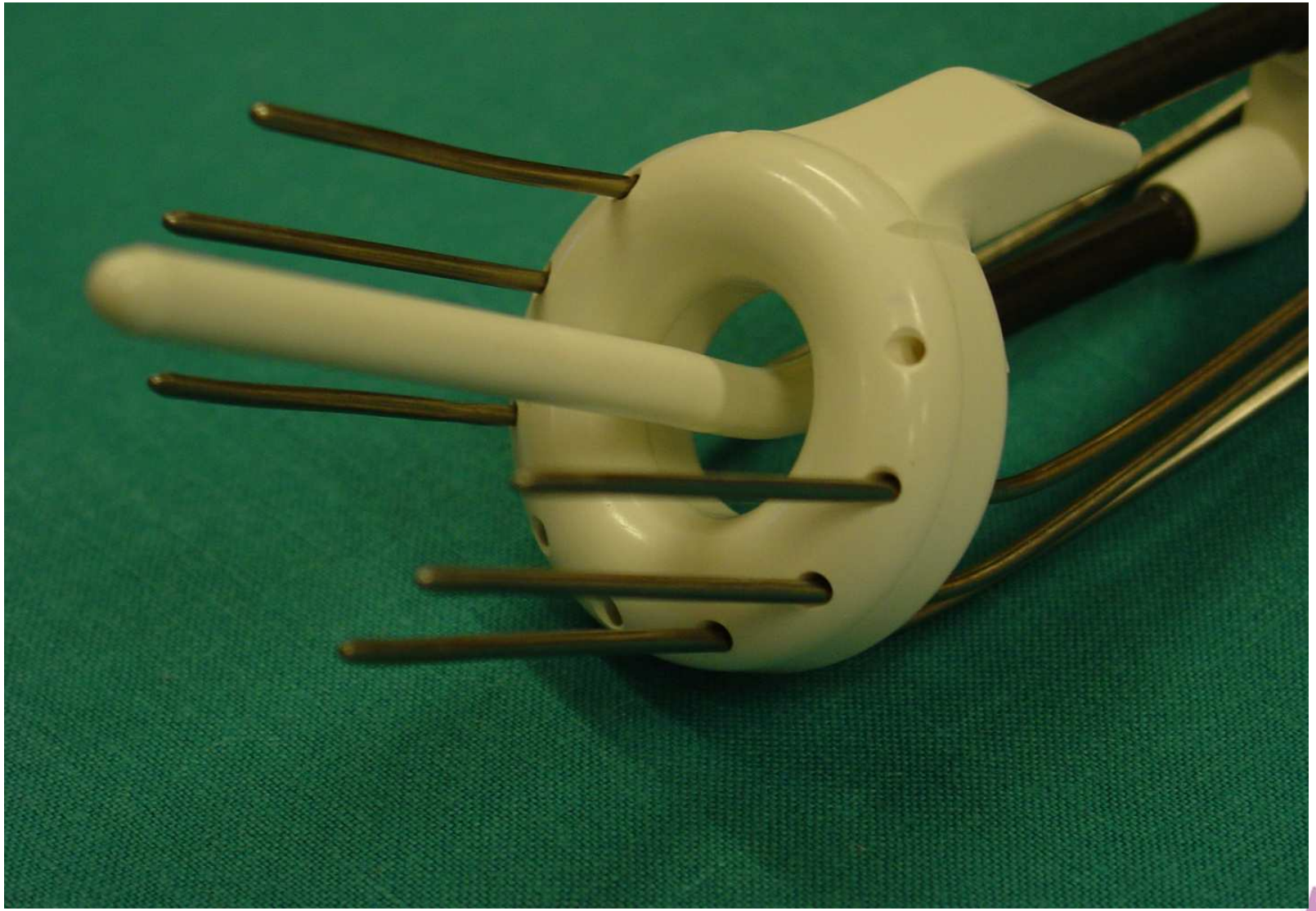
Vienna applicator



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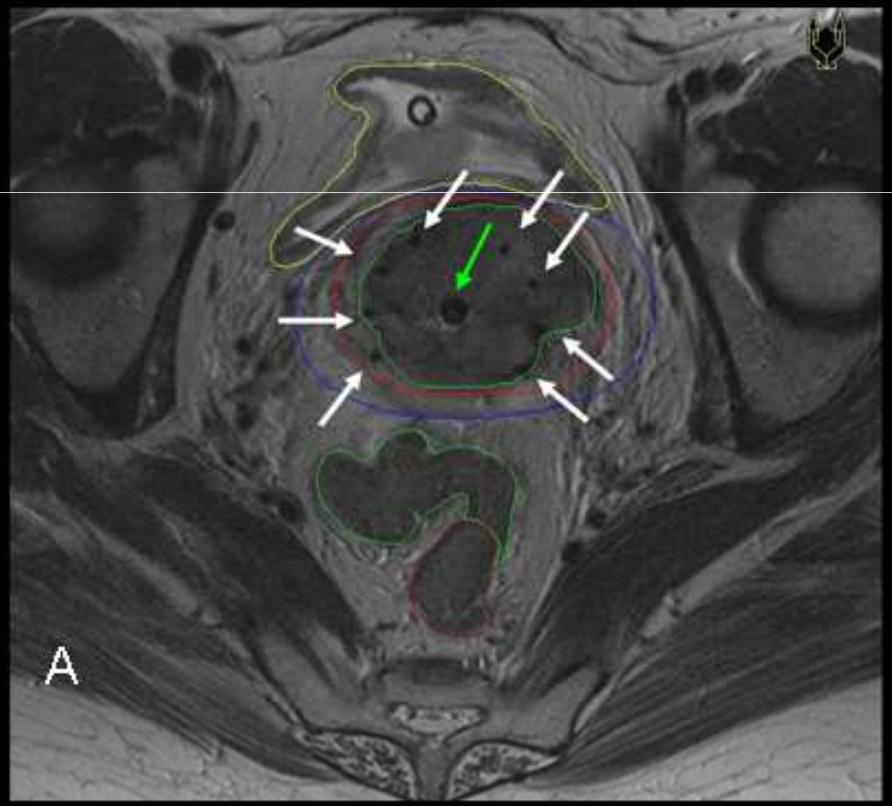
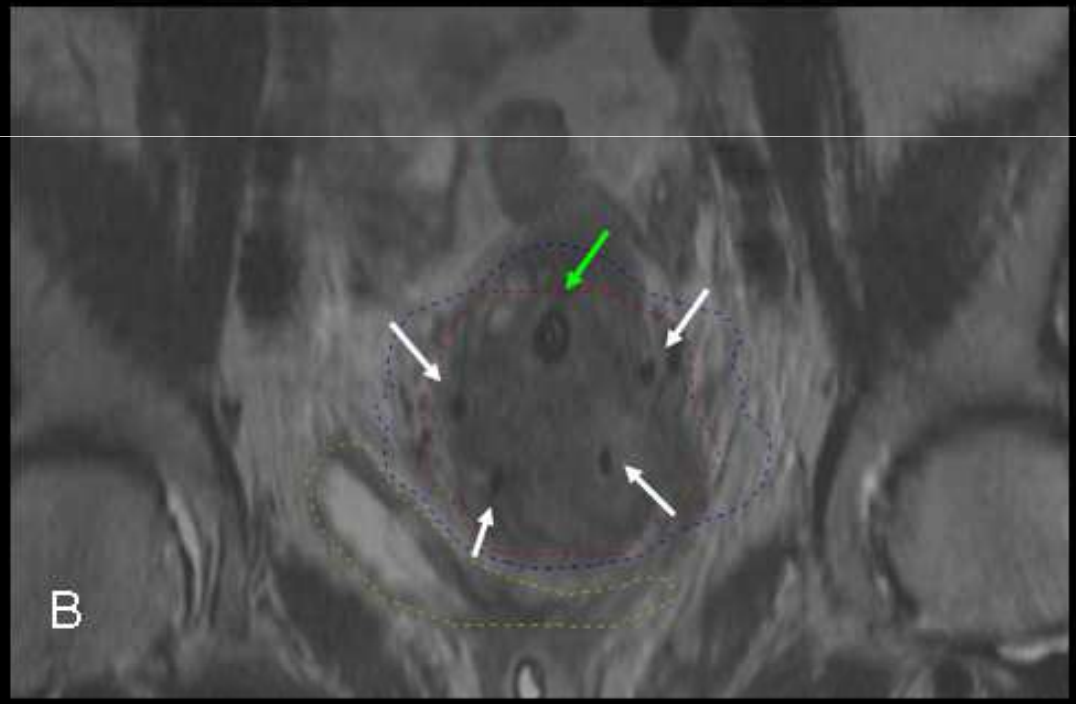
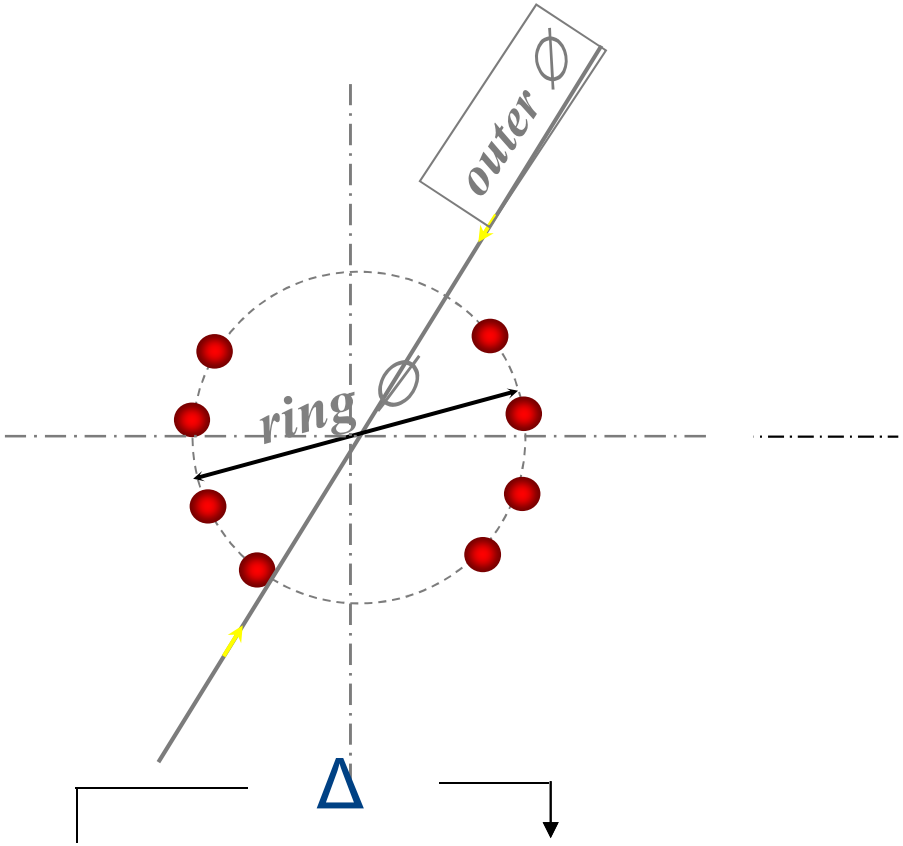

A


B

Tandem-ring dimensions



ring diameter (based on sources)	outer diameter
26 mm	38 mm
30 mm	42 mm
34 mm	47 mm

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Standard loading pattern

Tandem loading

Similar to Manchester or Fletcher loading

15 + 10 + 10 mg Ra = more active dwell positions at tip

Ring loading

Similar to Fletcher loading: 20 on each side of the ring

Active dwell positions on both lateral sides of the ring

Difference

Different sizes of ovoids vs. constant ring thickness, only distance between vaginal sources different (diameter) – number of active dwell positions constant to limit vaginal dose

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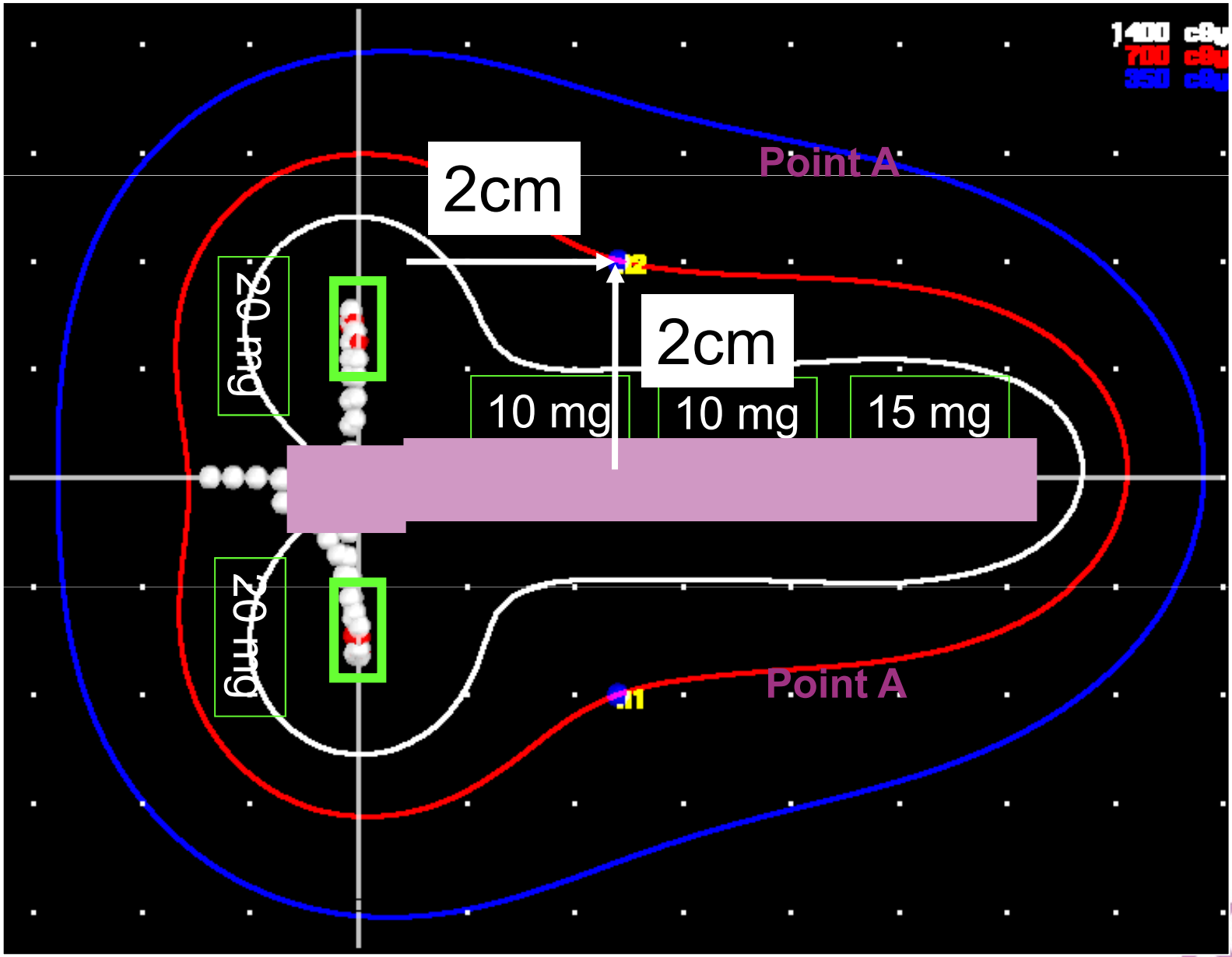
Ring standard loading pattern



Manchester / Fletcher systems

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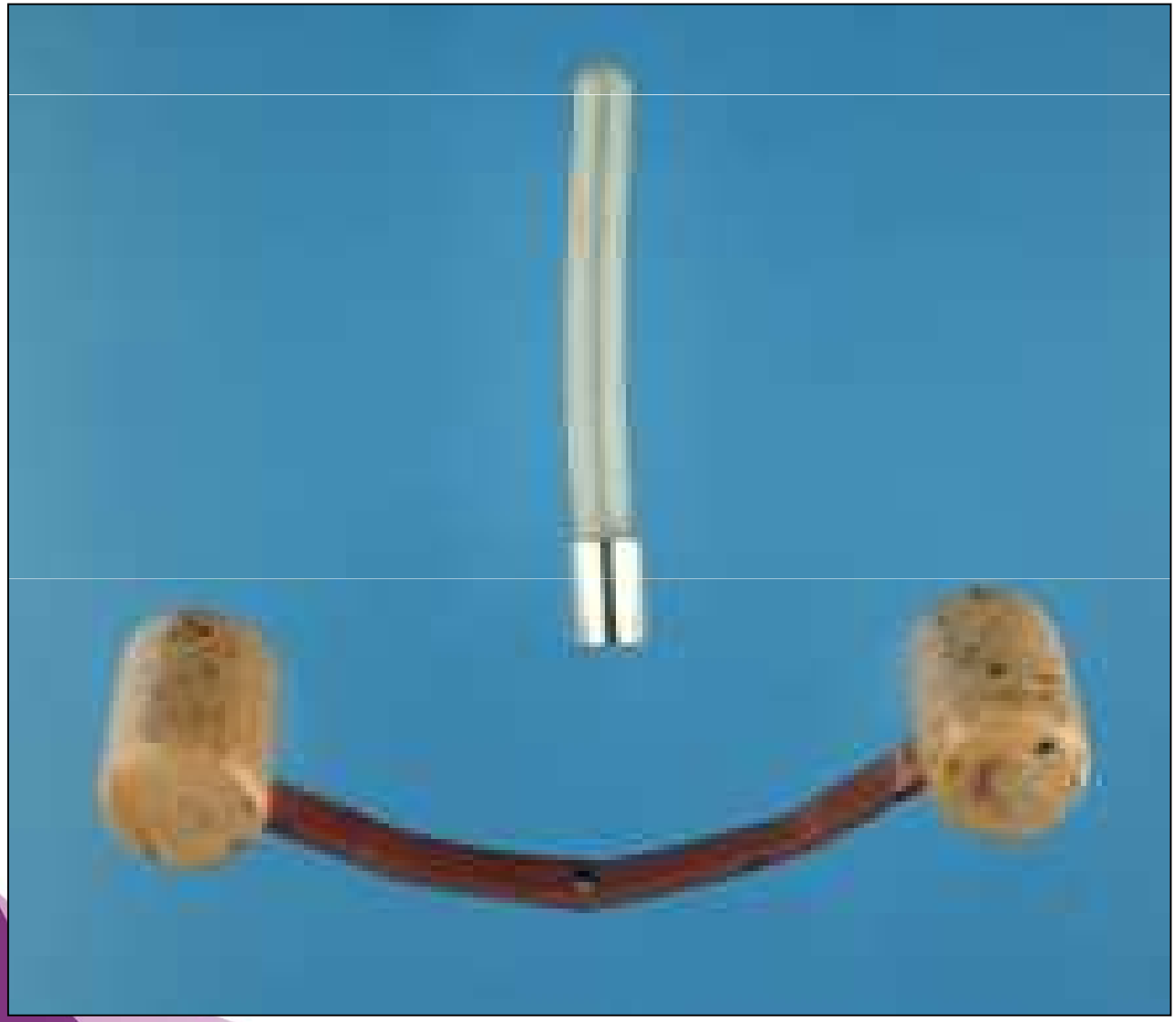
HISTORICAL PARIS METHOD
(≠ Paris system)



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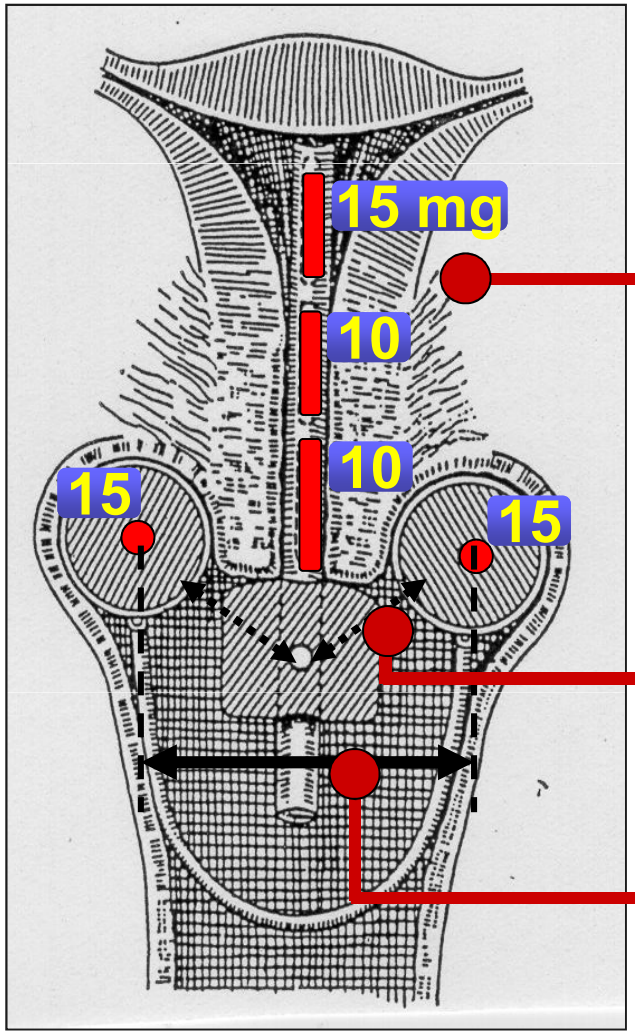
HISTORICAL PARIS TECHNIQUE

^{226}Ra manual preloading



- Ratio: tandem / corks: 0.7-1.5
- X mg of ^{226}Ra for Y hours
- Prescribing, reporting: mgh
- Tandem and vaginal sources not connected
- Distance between vaginal sources not fixed

HISTORICAL MANCHESTER SYSTEM

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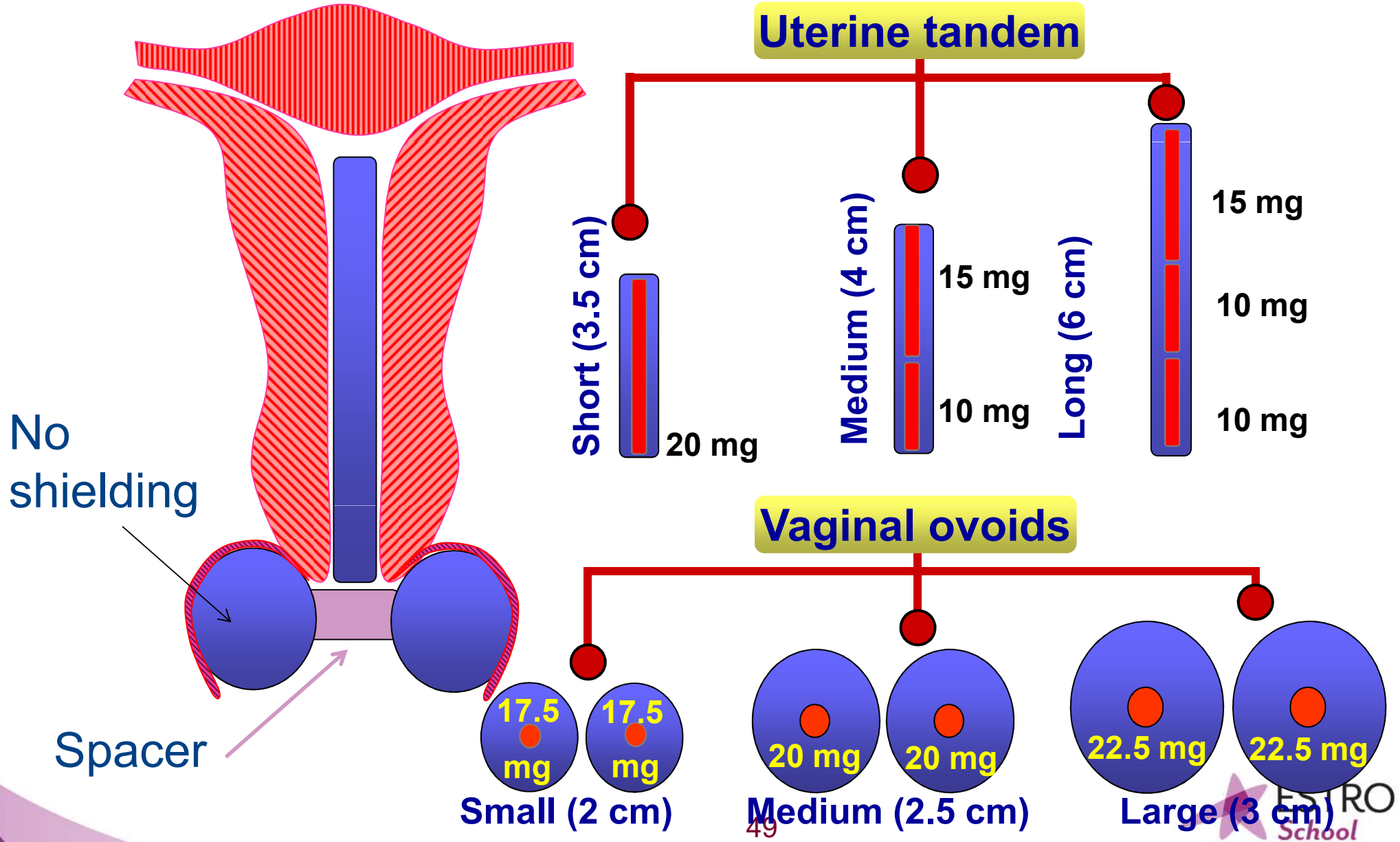
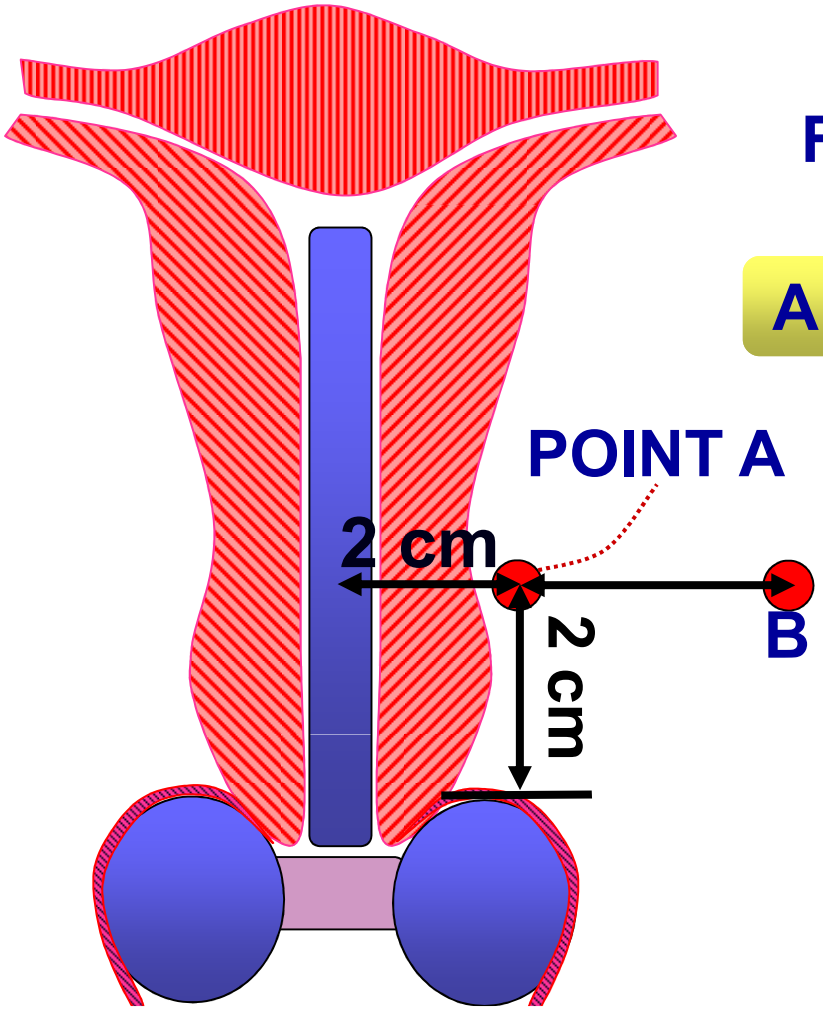
Tandem/ovoids manual preloading: ^{226}Ra



HISTORICAL MANCHESTER SYSTEM



Point A

FOR A GIVEN TUMOUR VOLUME

A set of rules

- source strength
- application duration
- source geometry

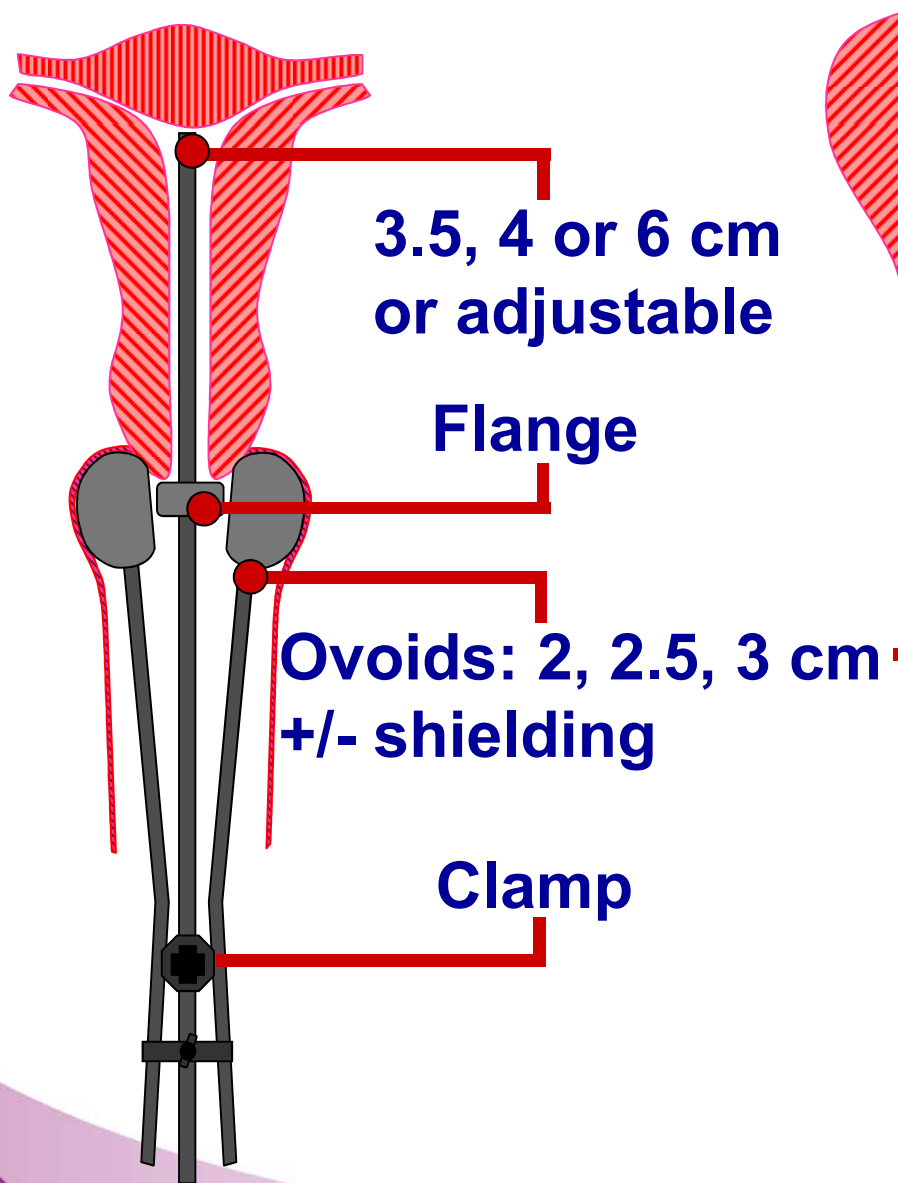
CERTAIN POINT A DOSE (R)

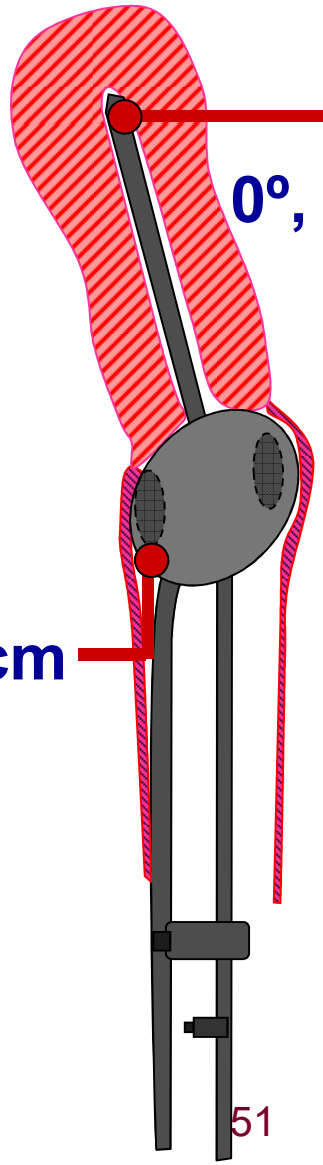
CLASSICAL APPLICATION:

144 hours (2 sessions) for 8000 R at point A (dose rate 53 R/h)

Meredith WJ, ed. Radium dosage. The Manchester system. Edinburgh;1947.

Mimicking historical system





137Cs, 192Ir sources

Loading patterns:
mg Ra equivalent

D-rate at point A:
^{137}Cs ~ 50 cGy/h
^{192}Ir: PDR or HDR

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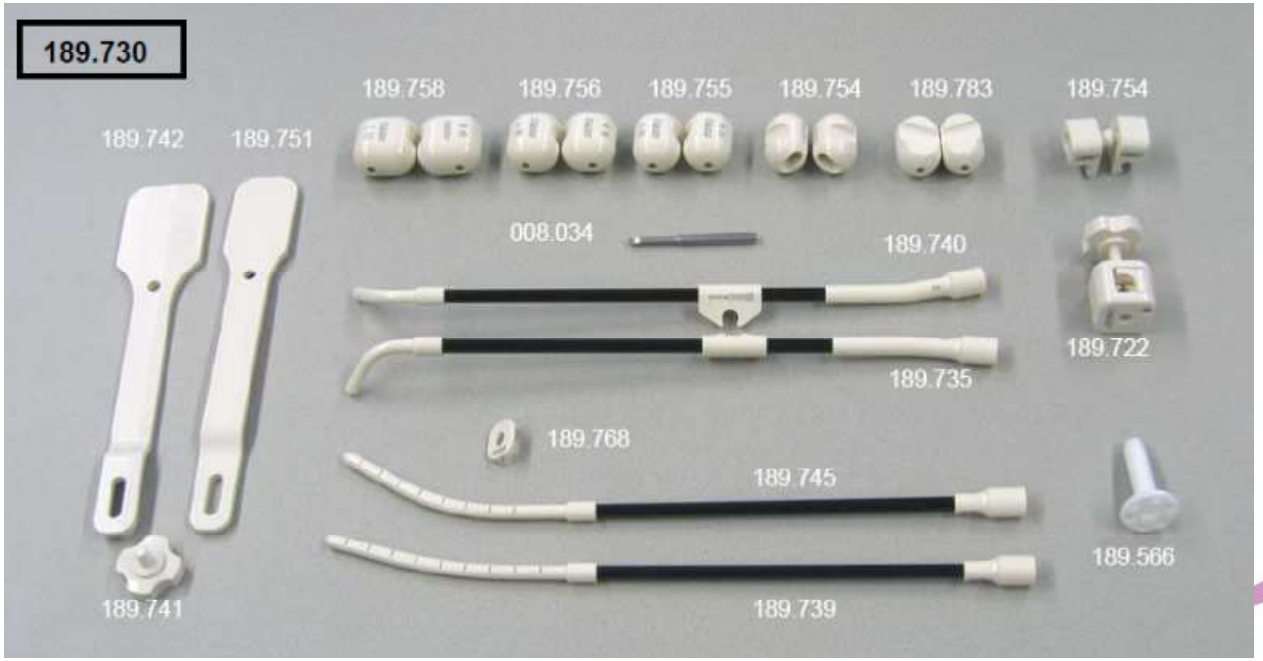
MRI / CT compatible



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Ovoids

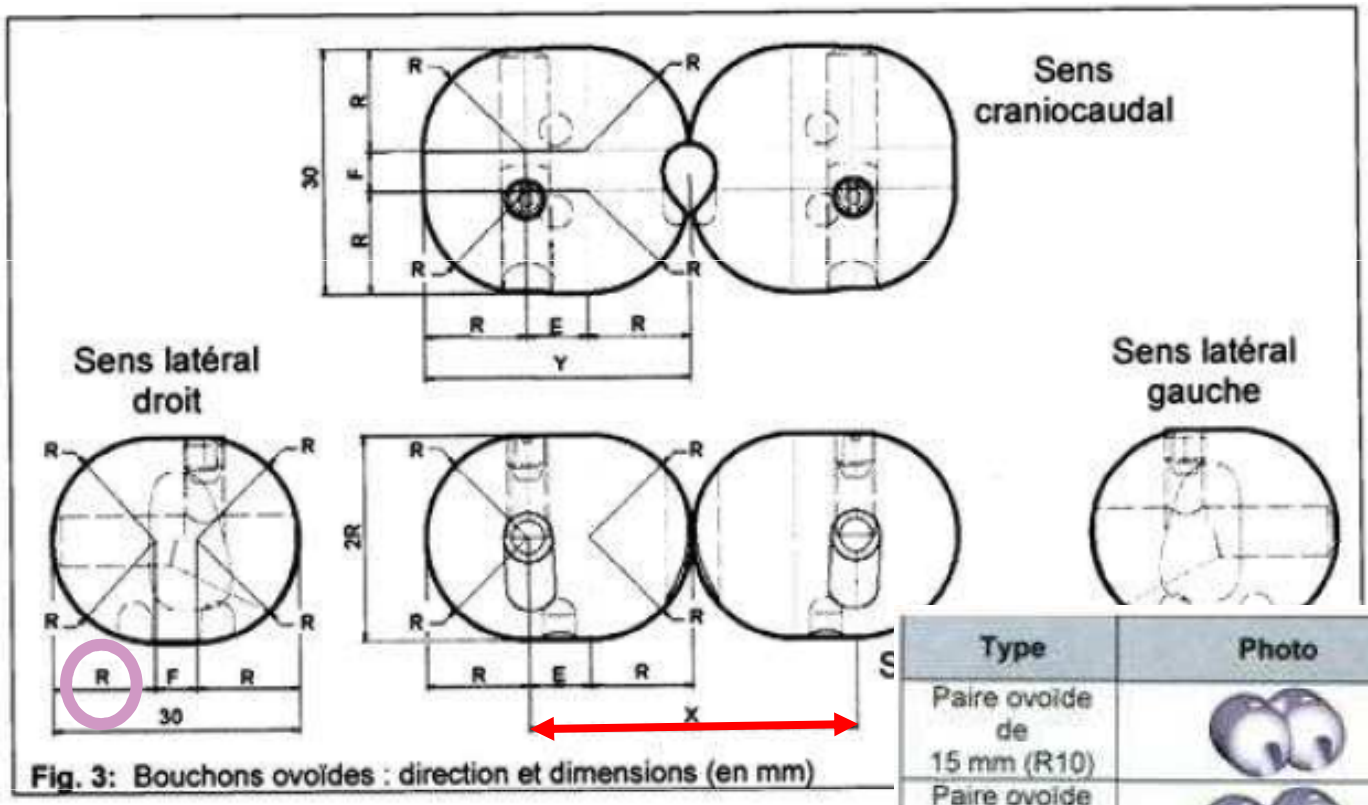

Fig. 3: Bouchons ovoïdes : direction et dimensions (en mm)

Type	Photo	X (mm)	R (mm)	E (mm)	F (mm)	Y (mm)
Paire ovoïde de 15 mm (R10)		15	10	0	10	17,5
Paire ovoïde de 20 mm (R10)		20	10	0	10	20
Paire ovoïde de 25 mm (R10)		25	10	2,5	10	22,5
Paire ovoïde de 30 mm (R10)		30	10	5	10	25
Paire ovoïde de 35 mm (R10)		35	10	7,5	10	27,5
Paire ovoïde de 40 mm (R10)		40	10	10	10	30

Wavelet progressive : Maximum

“Fletcher” based techniques

- Initially designed for Radium
- Rigid metallic tandem
- Cylindrical colpostats perpendicular to the axis of the vagina
- Against the cervix
- Adapted by Delclos and Suit for afterloading machines (Cs and Ir)

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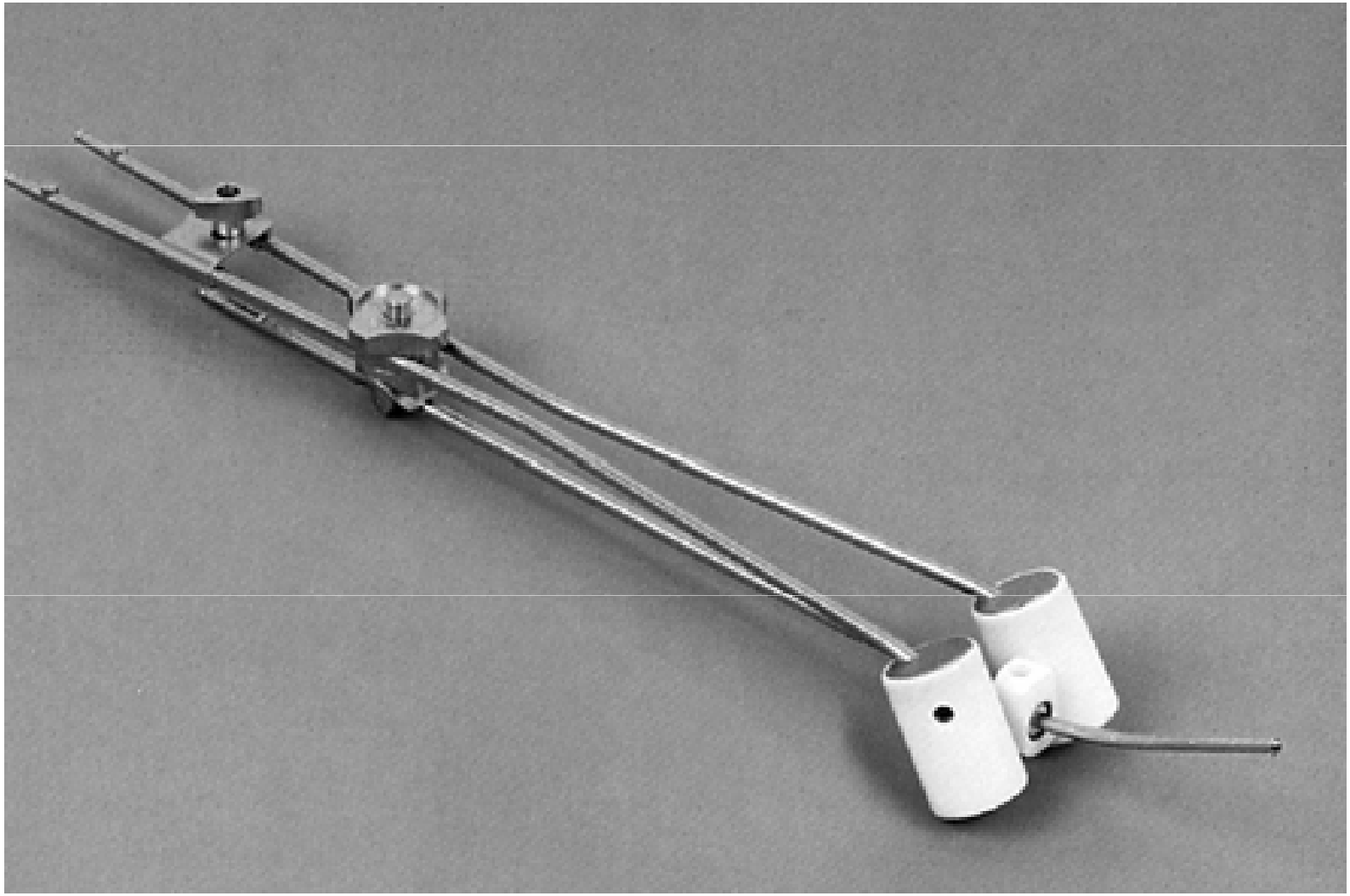
Classical Fletcher Applicator



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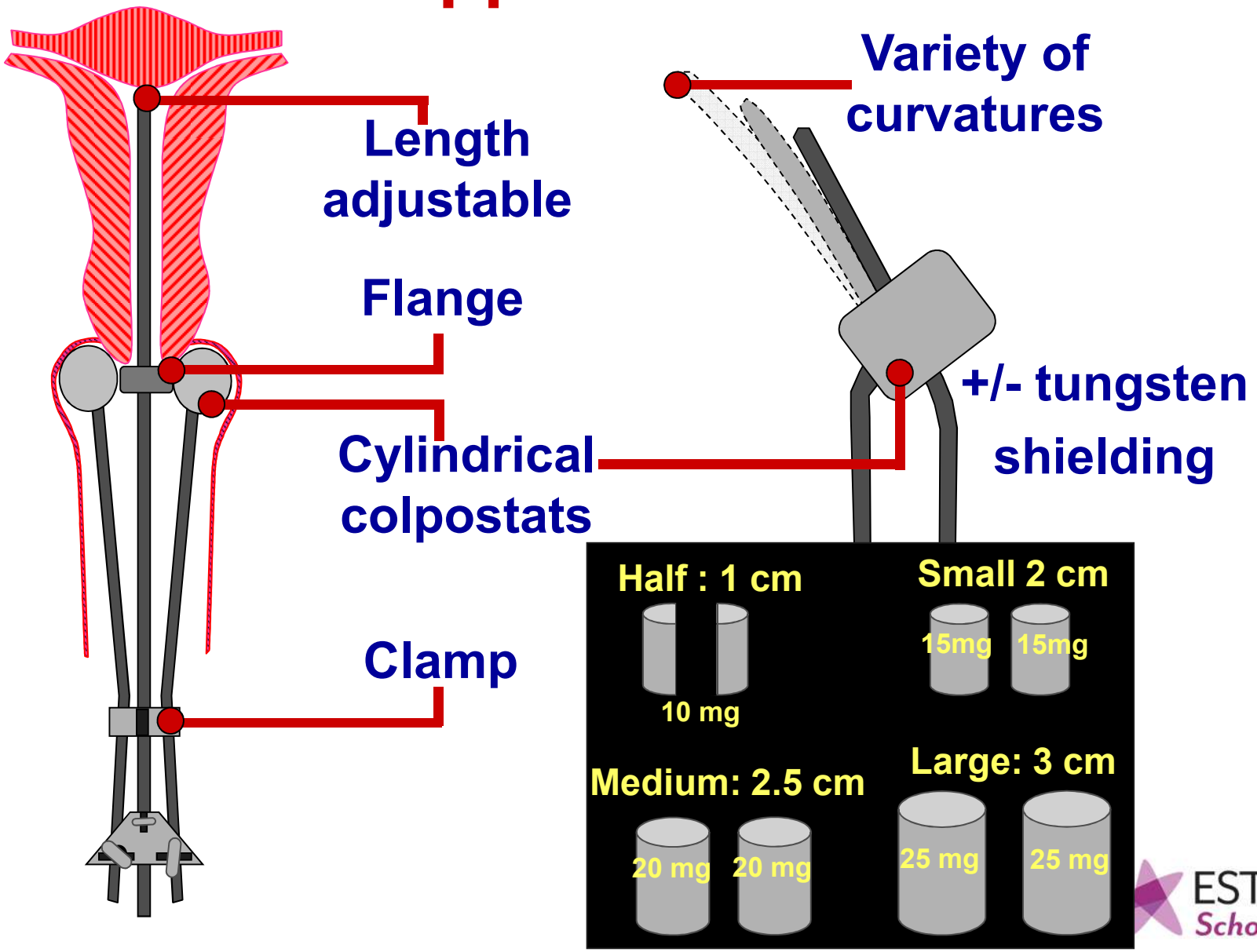
FLETCHER-SUIT-DELCLOS- STYLE TECHNIQUES

Applicators



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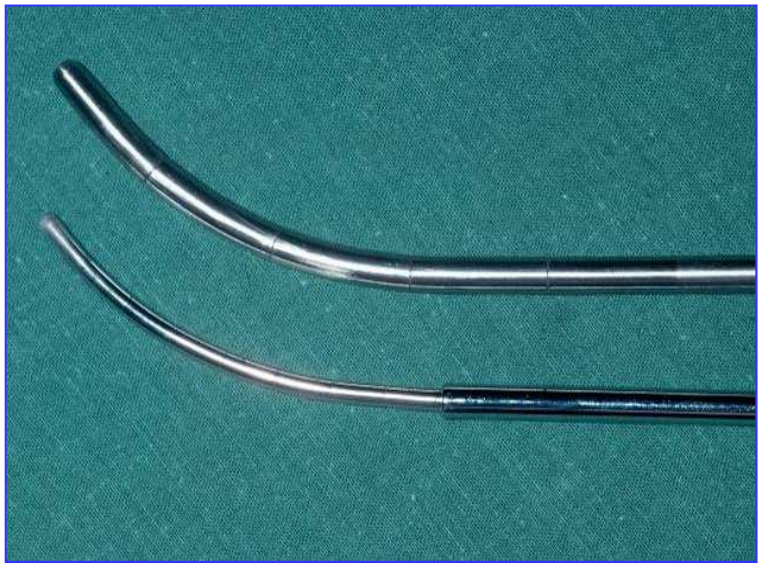
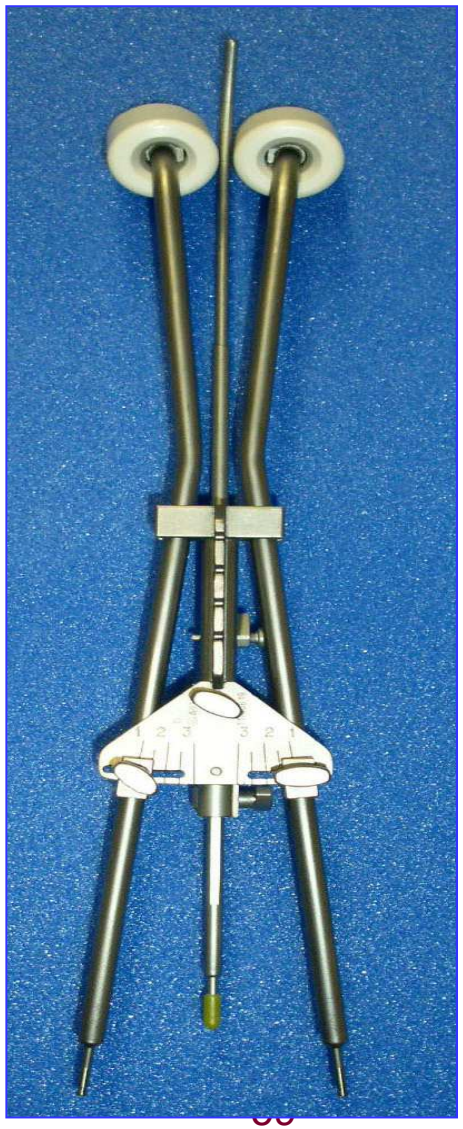
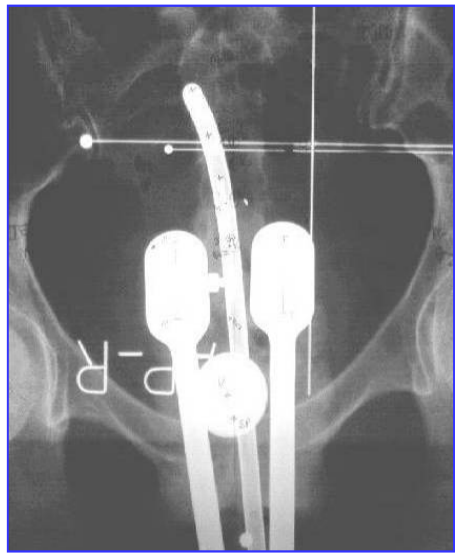
FLETCHER-SUIT-DELCLOS- STYLE TECHNIQUES

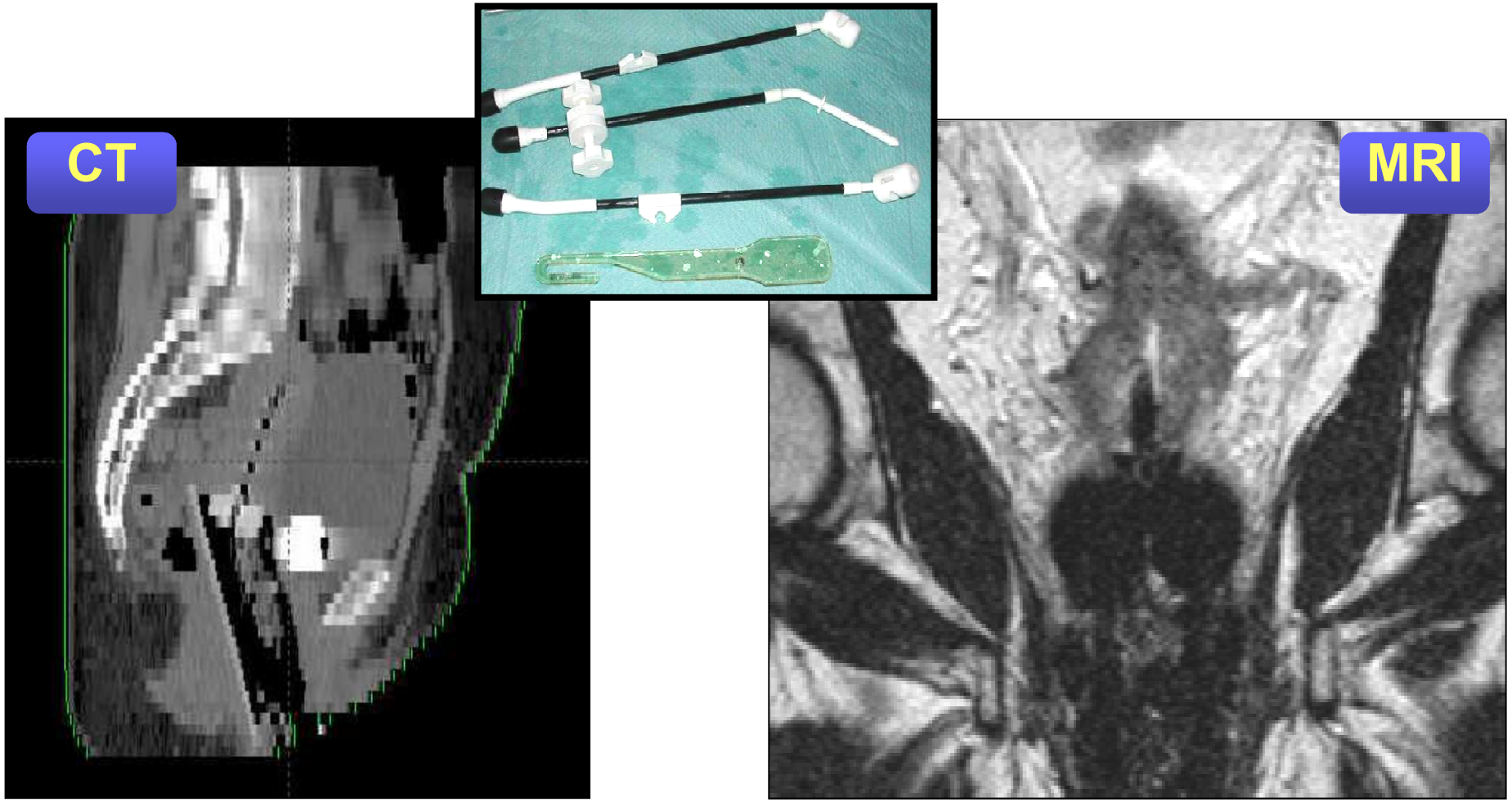
Applicators







Applicators – CT, MRI compatibility



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Summary

Historical systems

- Sets of rules: activity (mg ^{226}Ra), duration (h), geometry
- Non-fixed geometry
- Limited possibility for individualisation
- Large amount of clinical experience
- Basis for development of modern techniques

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Summary

Modern techniques

- Mimicking historical systems
- Fixed geometry, capability of adjusting components
- Tandem: adjustable lengths, varying curvatures+/- tungsten shielding in the ovoids
- Introduction of ^{137}Cs and ^{192}Ir, afterloading
- CT, MRI compatibility
- Novel approaches with interstitial component added
- Increasing possibility for individualized adaptation

Vaginal mould

Personalized vaginal mould

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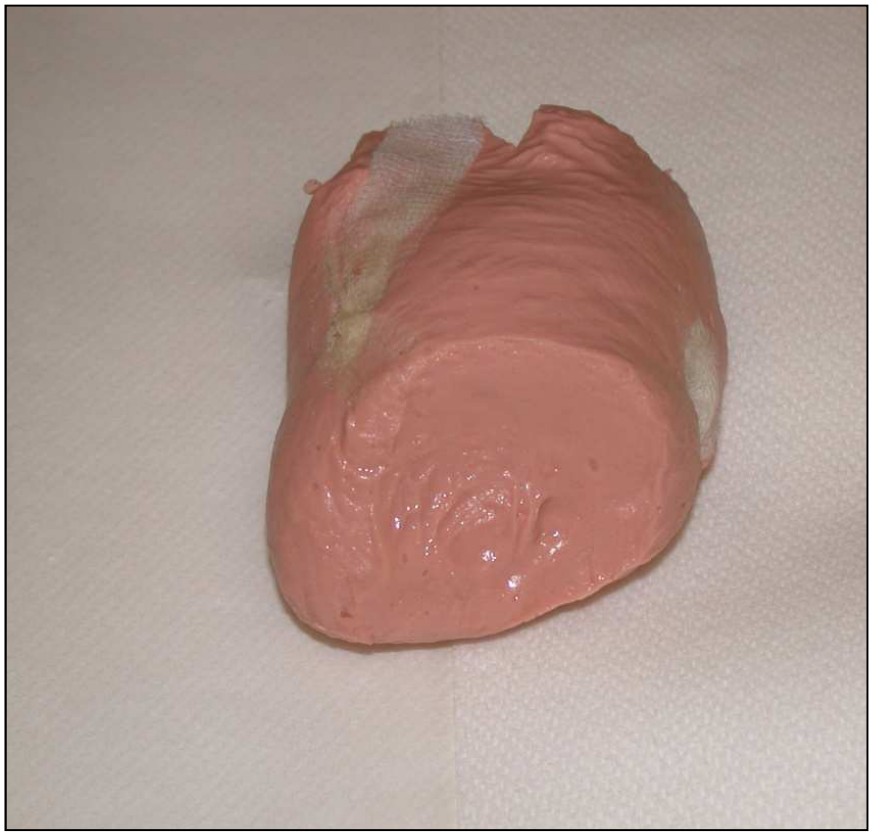
Empreinte vaginale



solidification (2 min)

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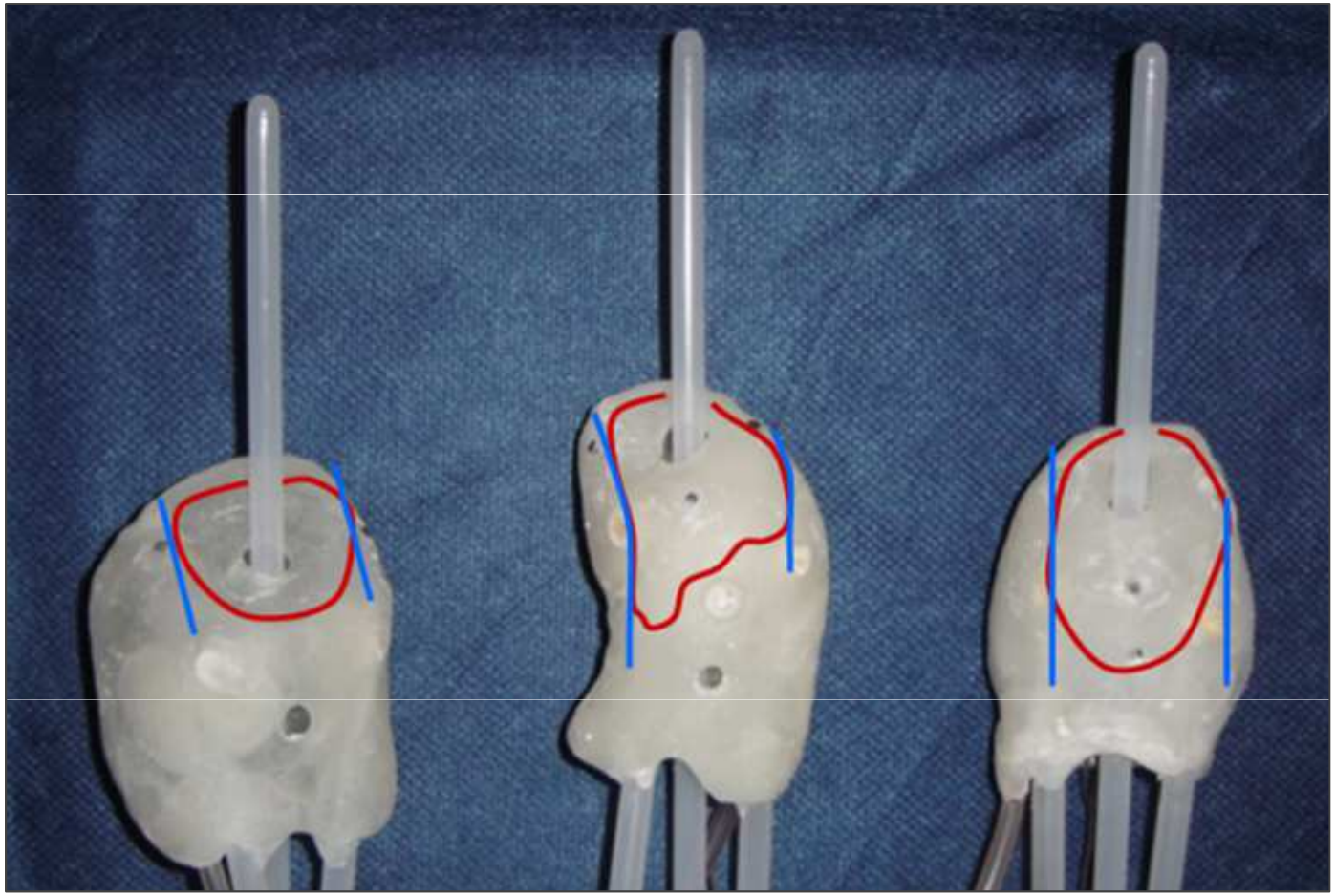
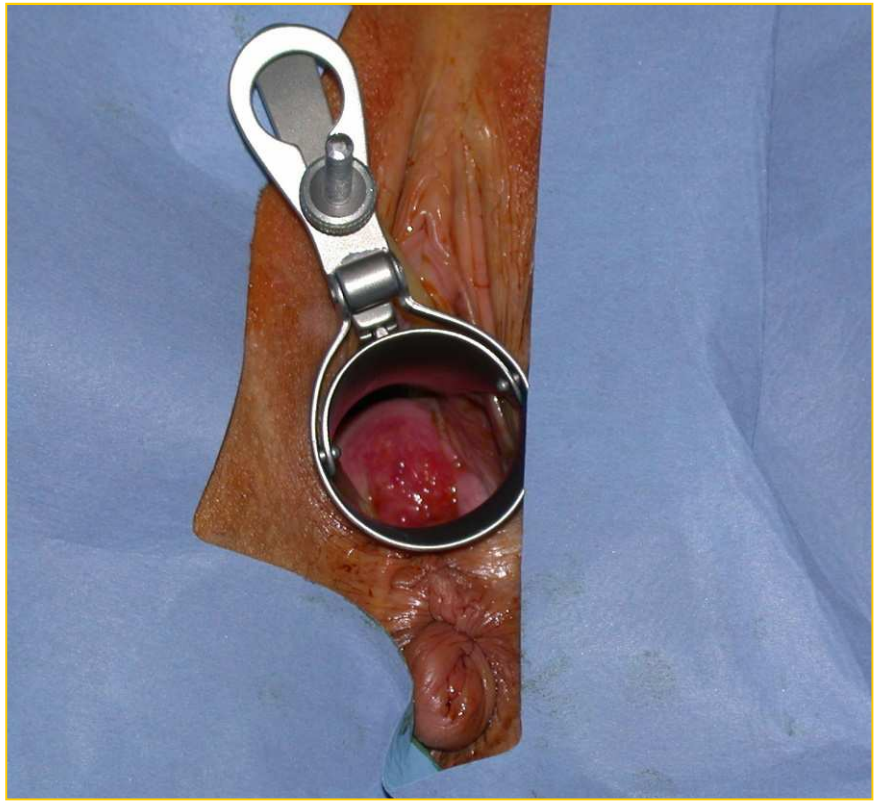


Implantation



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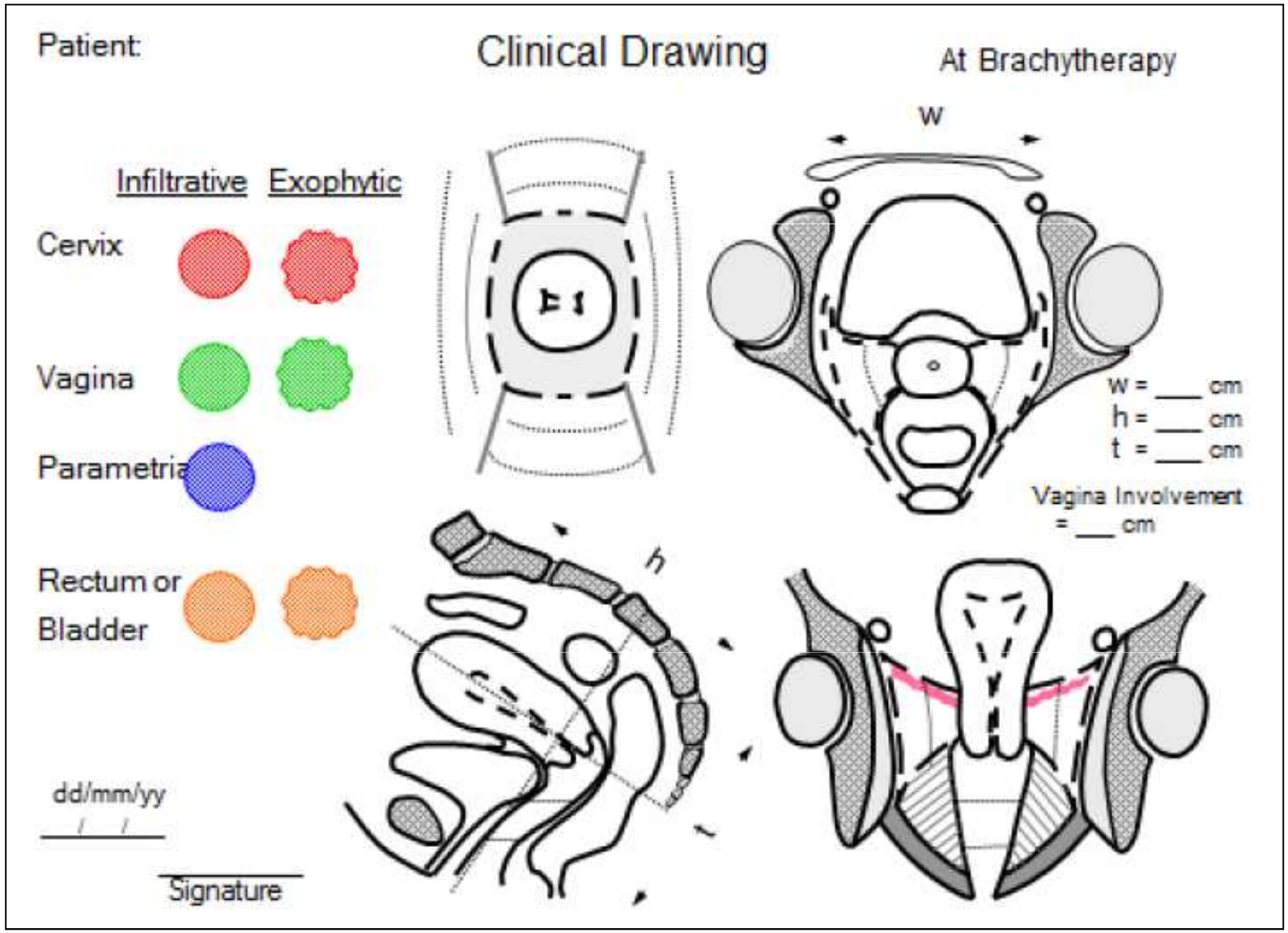
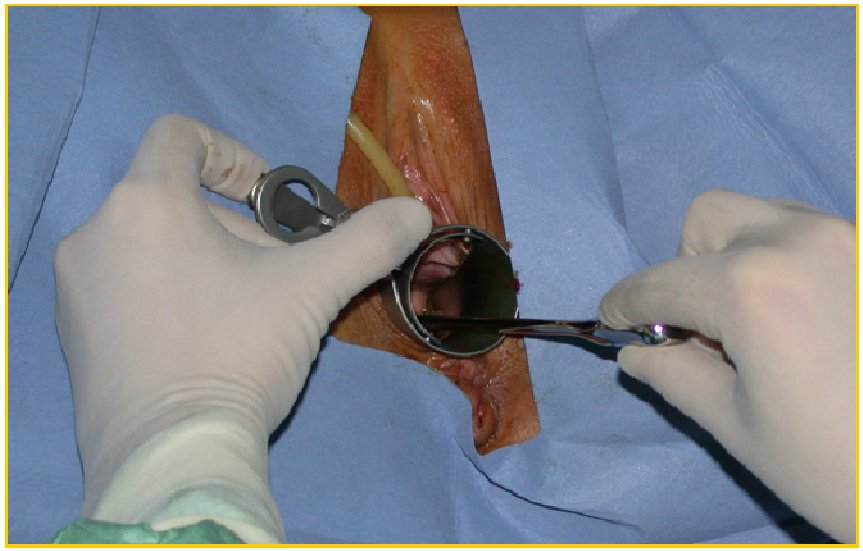
Bladder repletion

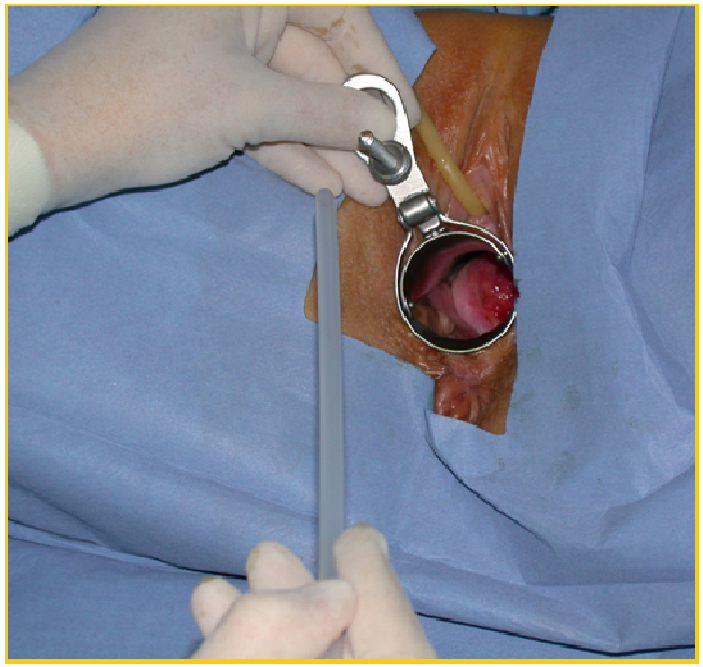
- Impacts the dose delivered to the bladder: ↑
- Impacts the dose delivered to the small bowel: ↓
- No impact on the doses delivered to
  - CTVs
  - Rectum
  - Sigmoïd colon
- Ensure a good reproducibility
  - PDR: empty bladder
  - HDR: controled fill in

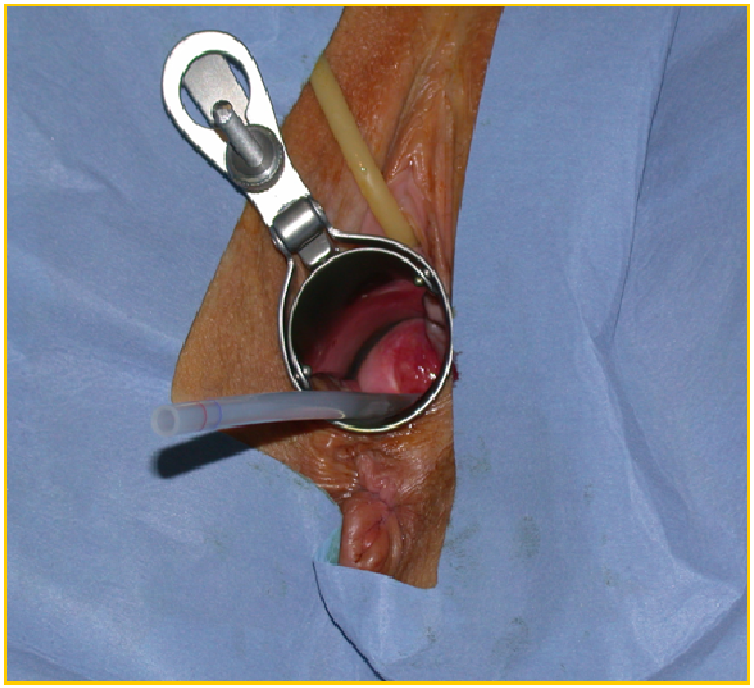
Clinical examination





Dilatation up to the catheter diameter





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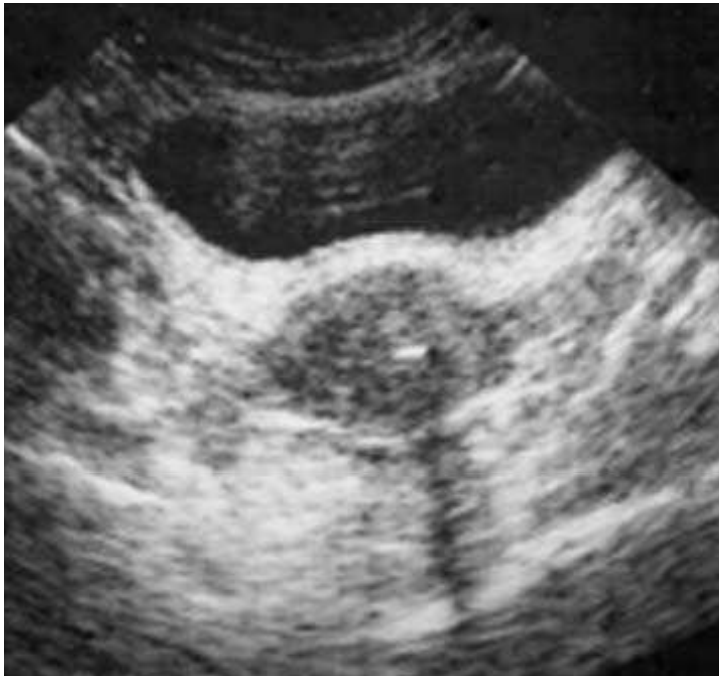

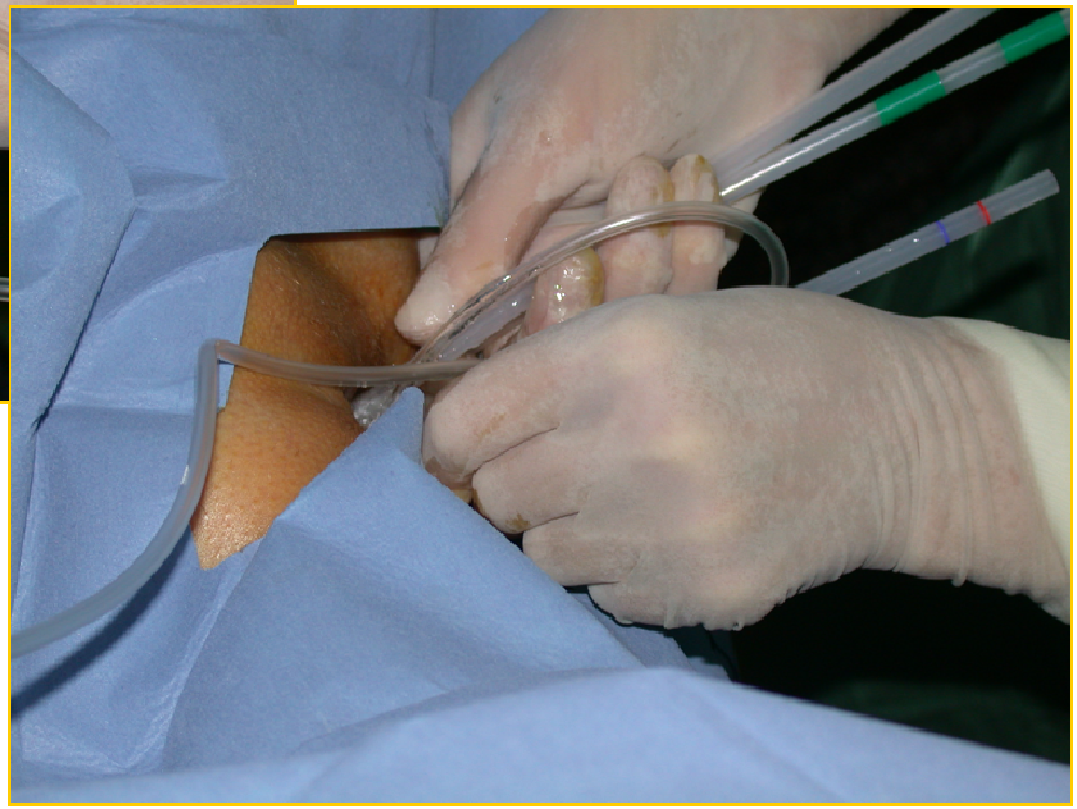

Vaginal applicator insertion

no packing

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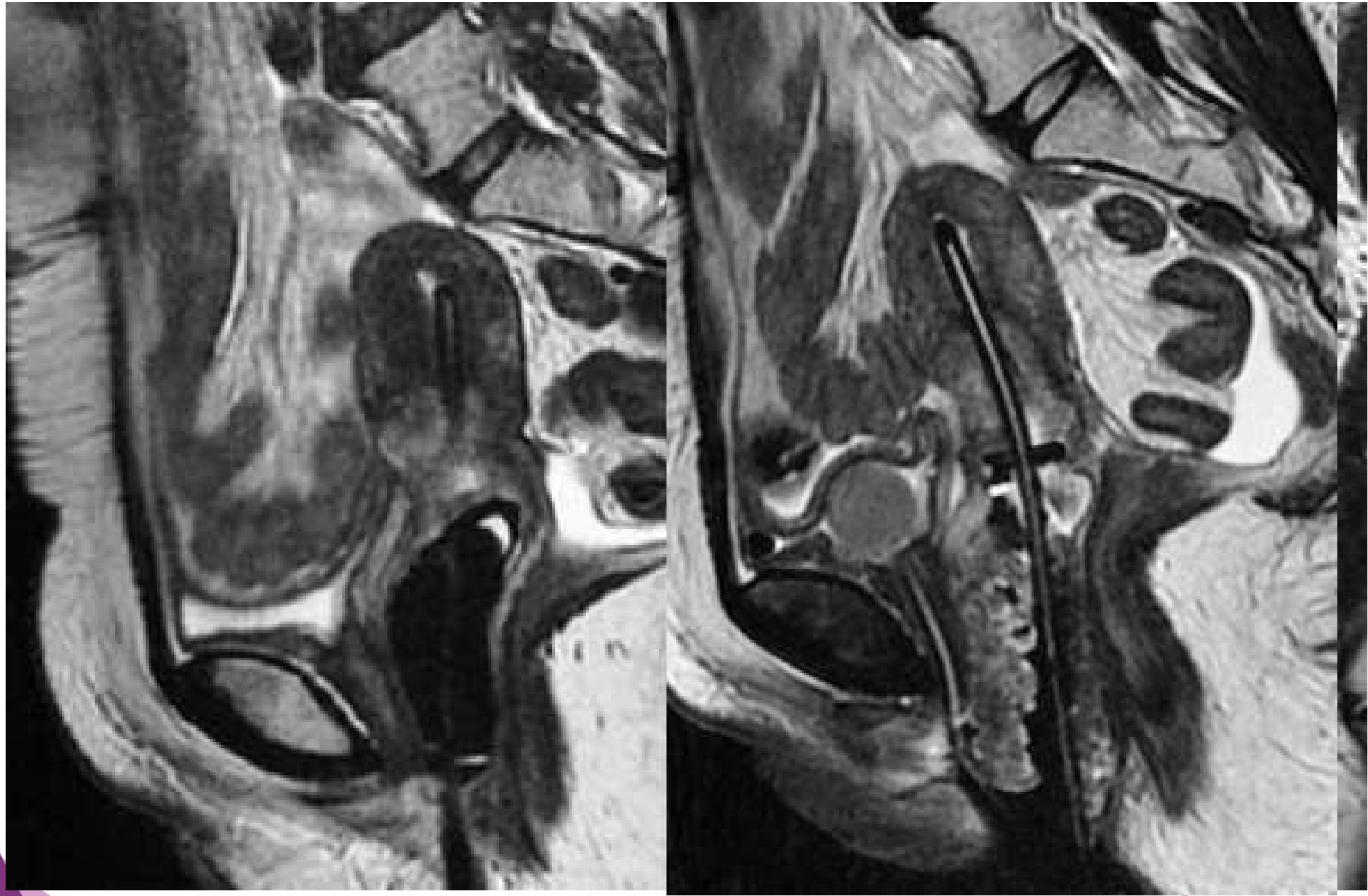
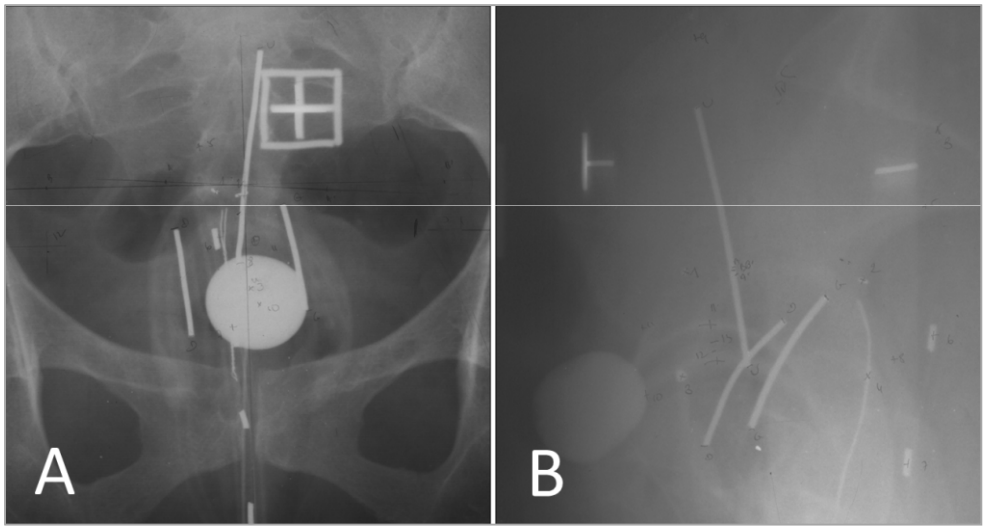


A

B

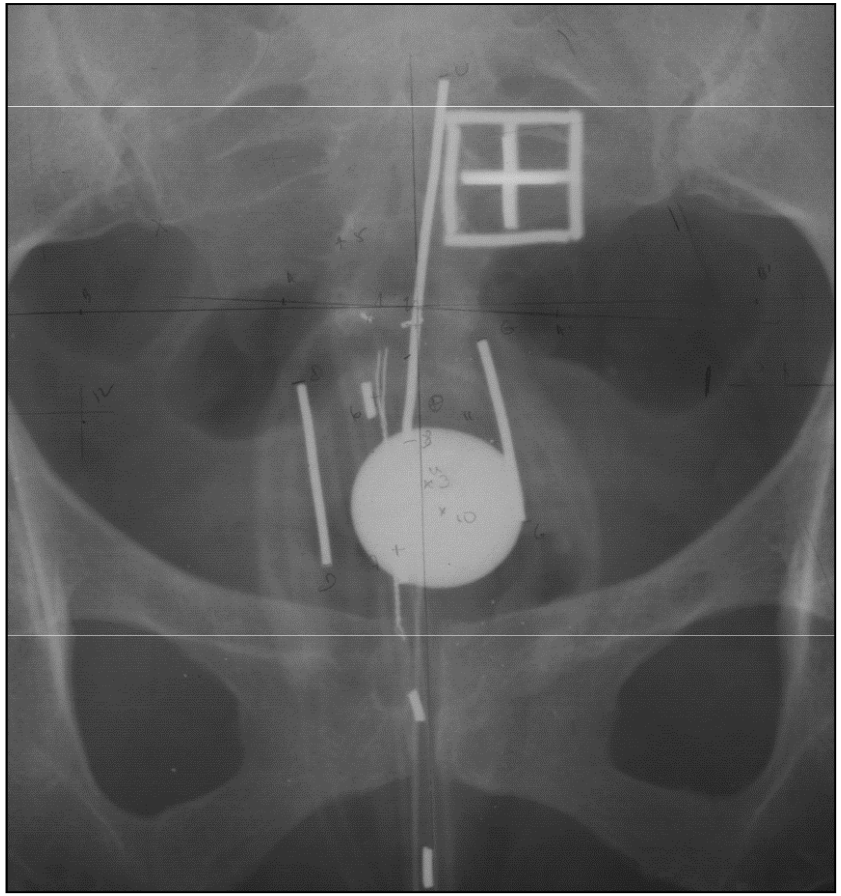

A
B

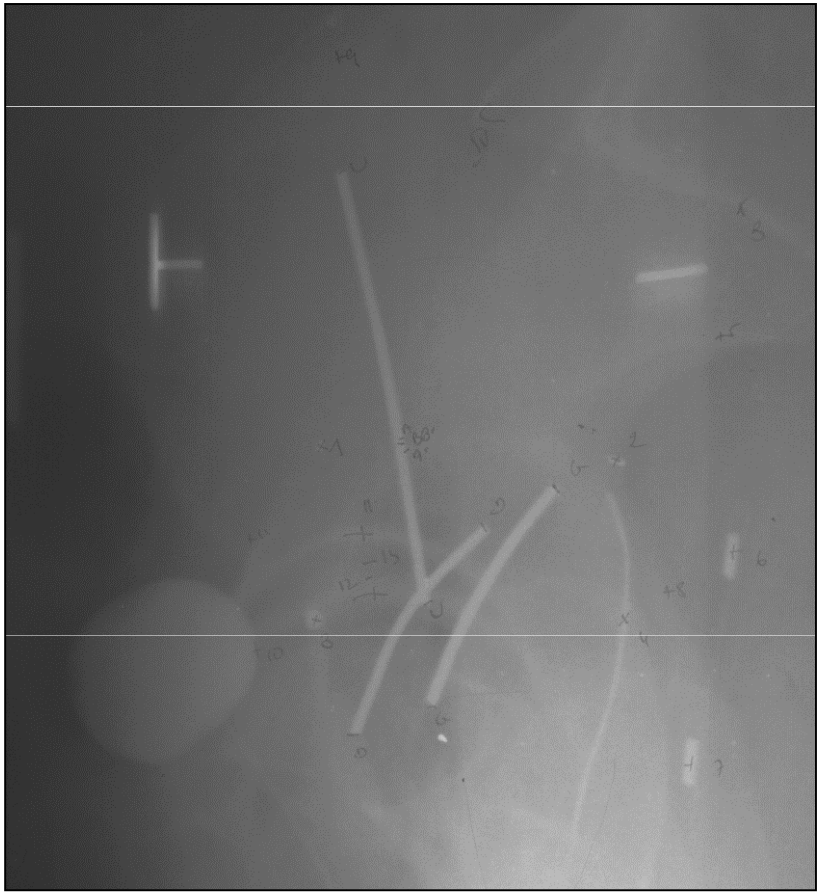
3D image acquisition

- MRI
  - T2 Sequences: axial, sagittal, frontal
  - Dummy sources
    - Water + iodo povidone (bubles)
    - Facilitate the applicator reconstruction
    - Localize accuratly the tip dwell position
- CT
  - Axial slice
  - Iodine enhancement

A
B
C

Classical Paris technique: orthogonal X rays





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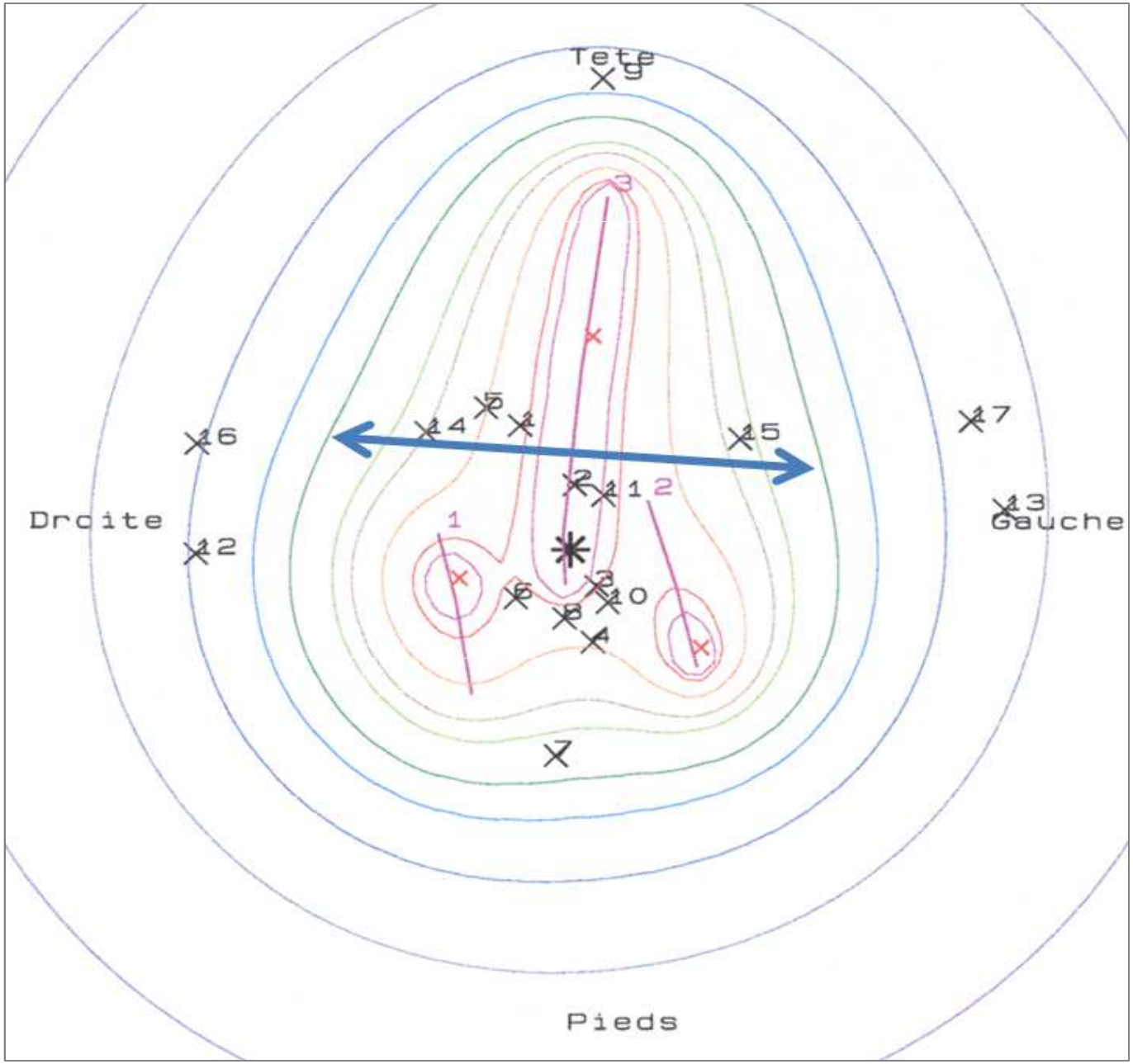
Prescription system



Standard Pattern Loading

- The dimensions of the pear shaped isodose depend on:
  - Applicator
  - Loading pattern

- Different standard loading patterns will result in different tumour and OAR doses

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Standard pattern loading

Dimensions of the isodose going through point A

	Manchester small ovoids 40 Gy ERT 32.5 Gy	Fletcher Dijon colpostats 20 mm 40 Gy ERT 42 Gy in 72 h	Vienna small ring 45 Gy ERT 4 x 7 Gy	Paris moulage 45 Gy ERT 15 Gy
H	9.5	10.0	8.7	8.9
W	6.7	6.3	5.7	5.7
T	4.2	4.0	4.2	4.3
HxWxT	267	252	208	218
Volume	133	126	104	109

Standard pattern loading

Dimensions of the isodose going through 60 Gy isodose

	Manchester small ovoids 40 Gy ERT 32.5 Gy	Fletcher Dijon colpostats 20 mm 40 Gy ERT 42 Gy in 72 h	Vienna small ring 45 Gy ERT 4 x 7 Gy	Paris moulage 45 Gy ERT 15 Gy
H	11.6	11.7	10.6	10.7
W	8.7	7.6	7.7	7.5
T	7.2	6.3	6.7	6.6
HxWxT	726	560	546	529
volume	363	280	273	264

Conclusion

- Different schools
  - Different applicators
  - Different prescription methods
  - But also similarities
- Clinical outcomes not so different
- Need for a common language
- Development of image-guided brachytherapy
- An opportunity to harmonize the reporting
- GEC-ESTRO recommendations

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Recommendations for reporting:

Target and OAR dose-volumes in cervix ca brachytherapy ICRU-38 1985 and GEC ESTRO 2005 -2006 and upcoming ICRU –GEC ESTRO report 88

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Dose specification in Brachytherapy for Cervix Cancer

Classical

- **Point A Dose (“Manchester”)**
- **60 Gy isodose level (ICRU 38)**

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Dose Specification in Cervix Ca Brachytherapy

NOW: Based on 3 D imaging

- GTV, CTV, PTV
- Organs at Risk, OARs

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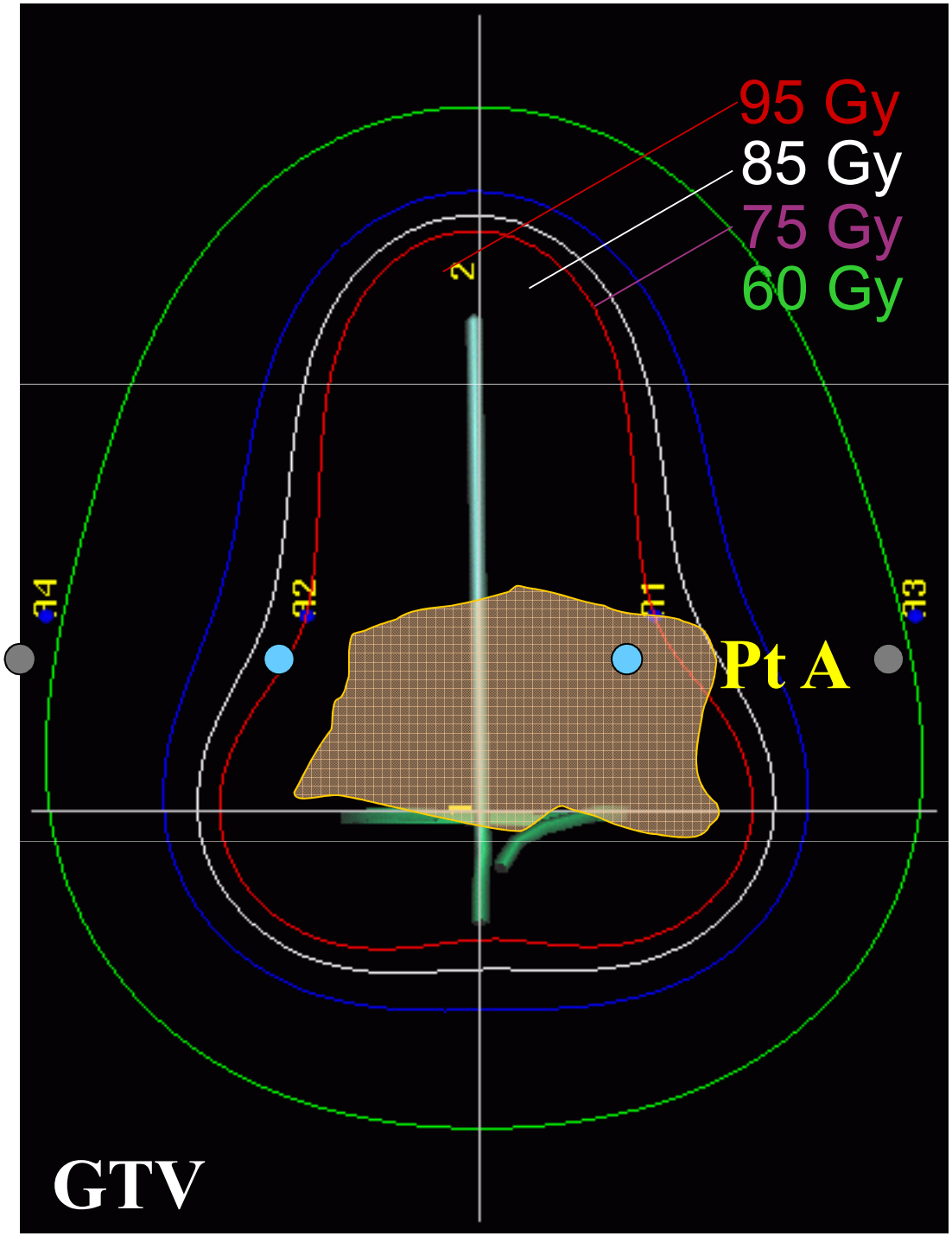
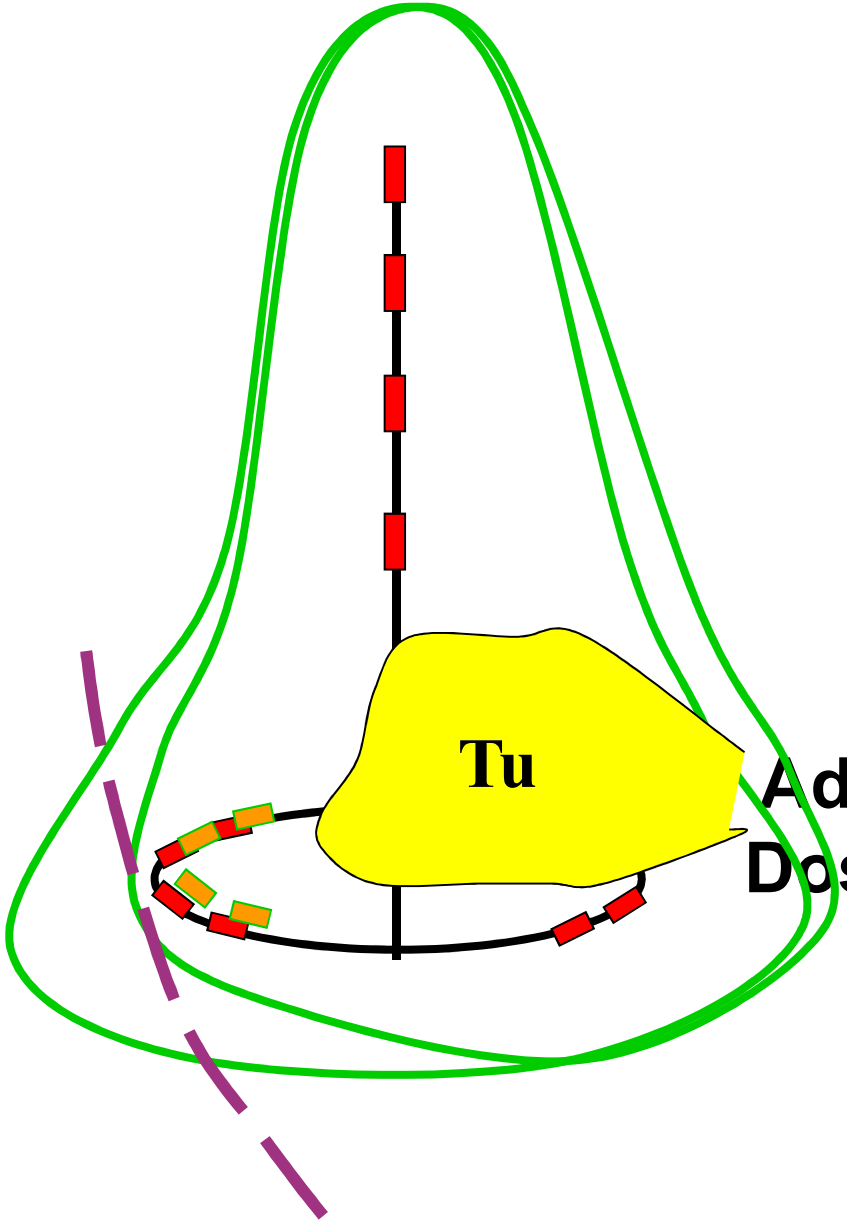

95 Gy
85 Gy
75 Gy
60 Gy
2
34
32
31
33
Pt A
GTV

Individual Adaptation to Anatomy

based on clinical examination and 3D imaging

Adaptation of
Dose to Rectum
And Bladder



Adaptation of
Dose toTumour

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Short History of the upcoming ICRU/GEC ESTRO Report (88)

1985 ICRU Report 38: Gynaecologic Brachytherapy

1999 ICRU report committee on 38 Revision

due to various developments in the field,

e.g. imaging, treatment planning, dose rates

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Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group* (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV

Christine Haie-Meder[a,*], Richard Pötter[b], Erik Van Limbergen[c], Edith Briot[a], Marisol De Brabandere[c], Johannes Dimopoulos[b], Isabelle Dumas[a], Taran Paulsen Hellebust[d], Christian Kirisits[b], Stefan Lang[b], Sabine Muschitz[b], Juliana Nevinson[e], An Nulens[c], Peter Petrow[f], Natascha Wachter-Gerstner[b]

Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

Richard Pötter[a,*], Christine Haie-Meder[b], Erik Van Limbergen[c], Isabelle Barillot[d], Marisol De Brabandere[c], Johannes Dimopoulos[a], Isabelle Dumas[b], Beth Erickson[e], Stefan Lang[a], An Nulens[c], Peter Petrow[f], Jason Rownd[e], Christian Kirisits[a]

RT&O 2005,2006

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Short History of the upcoming ICRU/GEC ESTRO Report (88)

2005/2006 Gyn GEC ESTRO Recommendations I/II

wide dissemination and acceptance

2009 Relaunch ICRU report committee 38 revision

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Purpose of the upcoming ICRU/GEC ESTRO Report (88)

To provide common concepts and terms

*** for volumes, in particular initial/residual GTV**

initial/adaptive CTV, PTV, OAR (3D/4D)

*** for radiobiological variations**

*** for dose volume parameters (3D/4D)**

*** for the process: planning aims to prescription**

*** for dose point parameters (2D)**

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GEC-ESTRO GYNE Group TARGET CONCEPT

- **Based on Tumor load**
  - **GTV**
  - **I-CTV Significant microscopic disease**
  - **L-CTV Potential microscopic spread**

- **Changes in time**
  - **At time of diagnosis**
  - **At time of brachytherapy**

- **Assessment**
  - **By clinical examination**
  - **By 3D MR imaging**

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GEC-ESTRO GYNE Group BT-TARGET Definitions

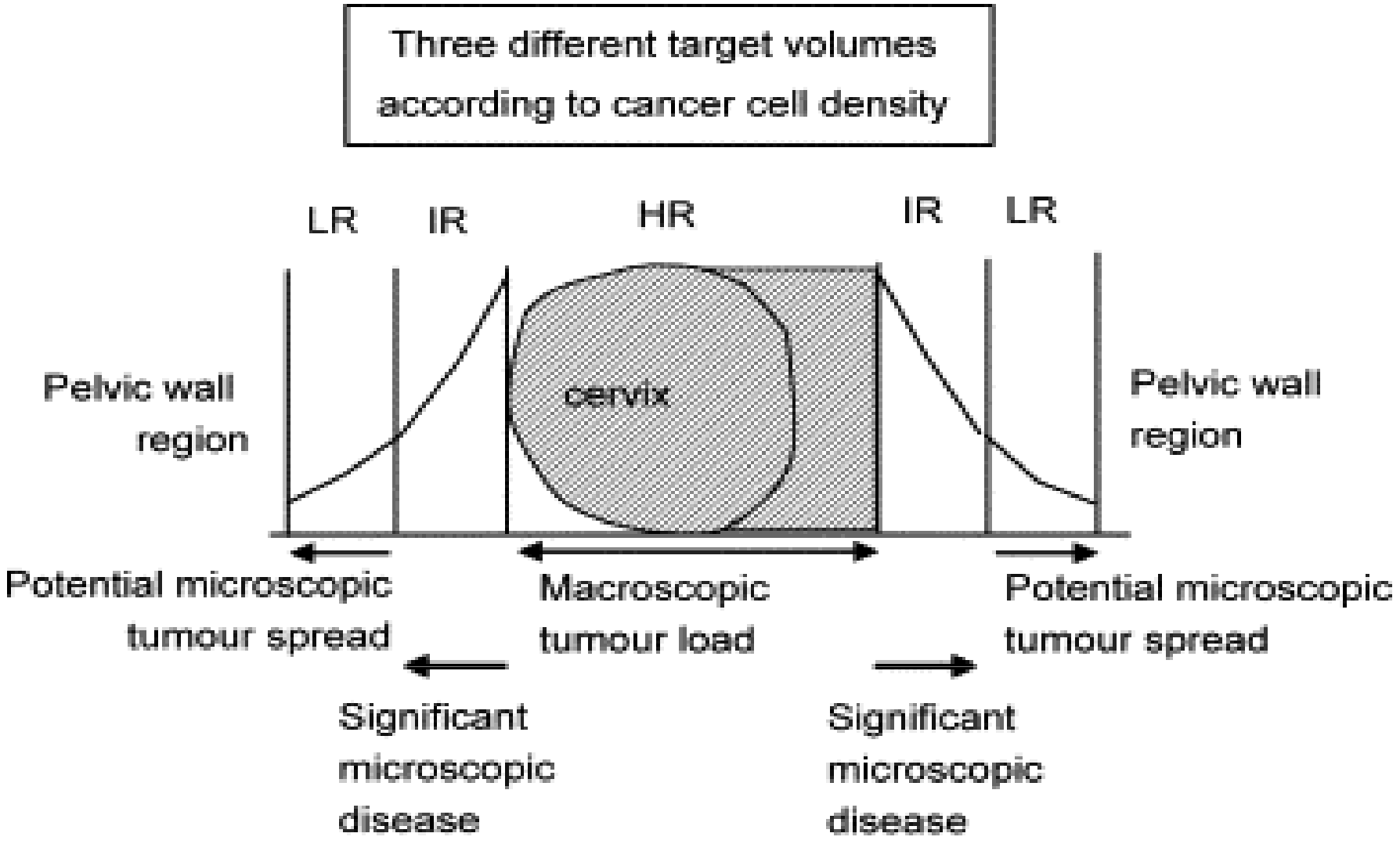
GTV : Macroscopic Tumor at BT

HIGH Risk CTV : Whole cervix assumed residual tumor

INTERMED. Risk CTV : Significant microscopic disease at time BT: = area of ca. at diagnosis

LOW Risk CTV : Potential microscopic = possible tumor at time of spread diagnosis

GEC ESTRO guidelines for gynae brachytherapy



Potter et al RT&O2005

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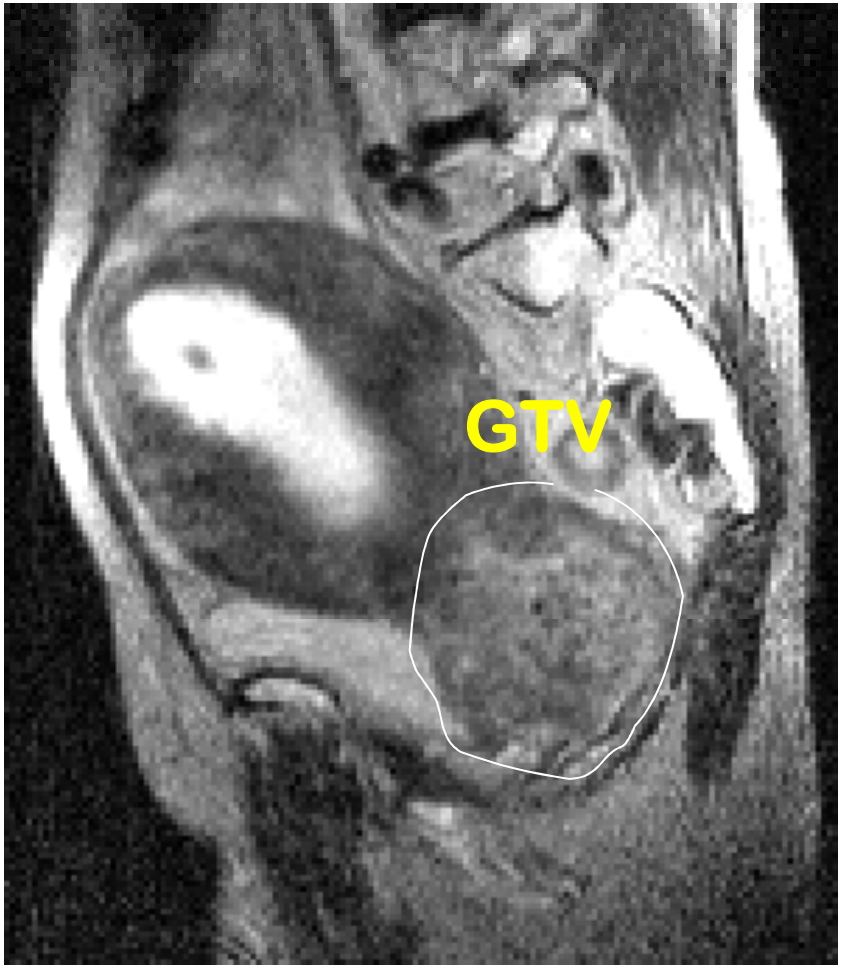
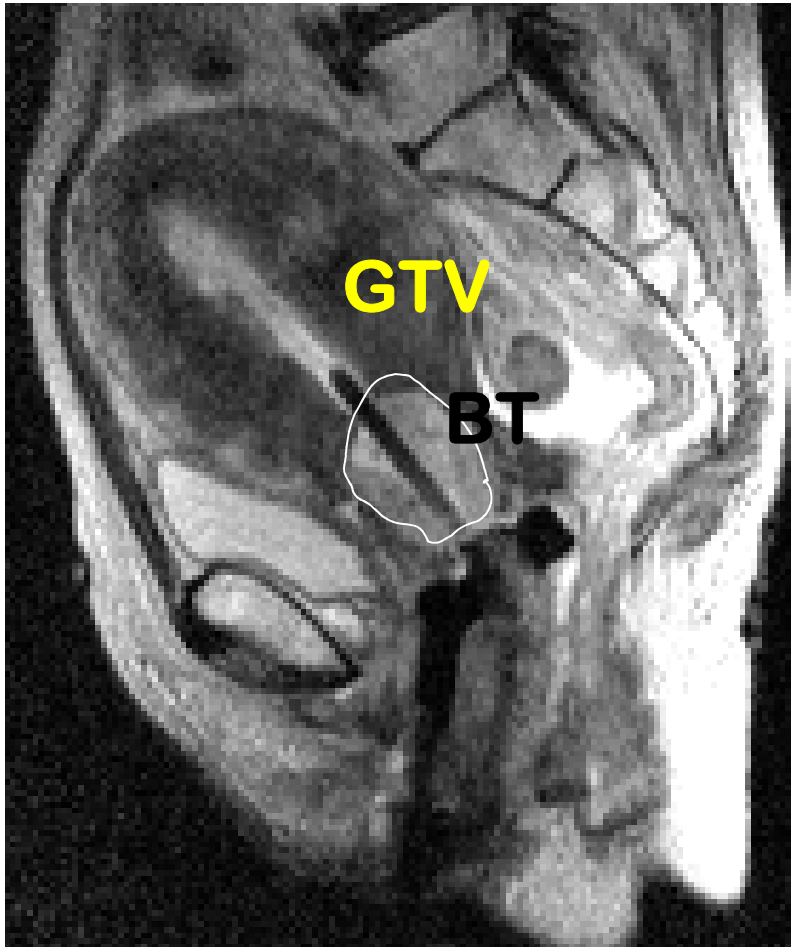
Cervix Cancer FIGO IB2
significant remission after EBRT





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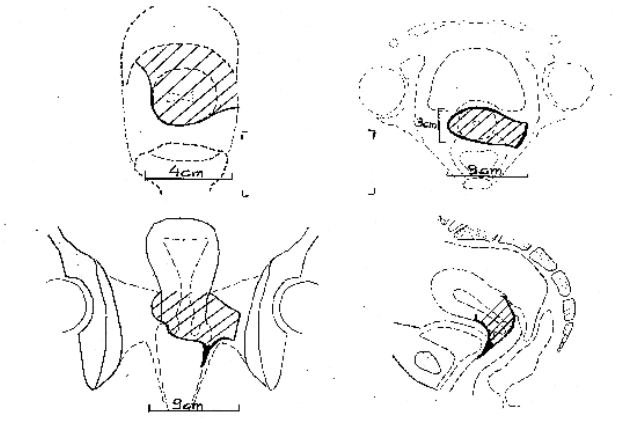
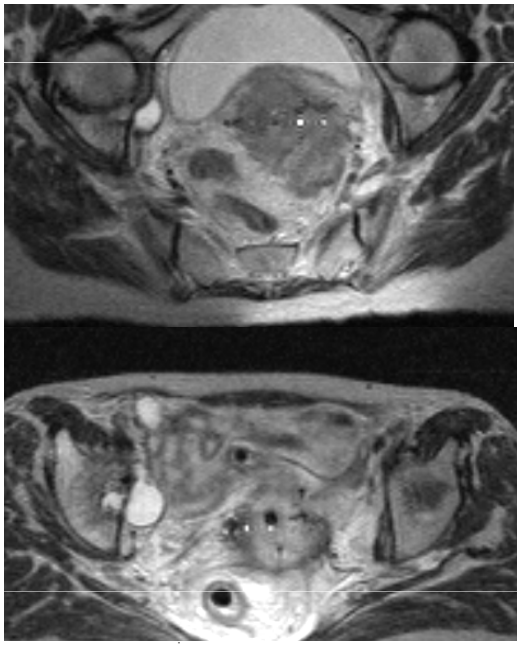
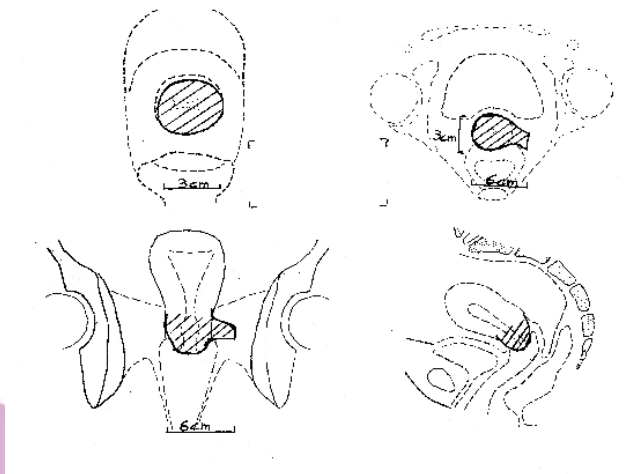
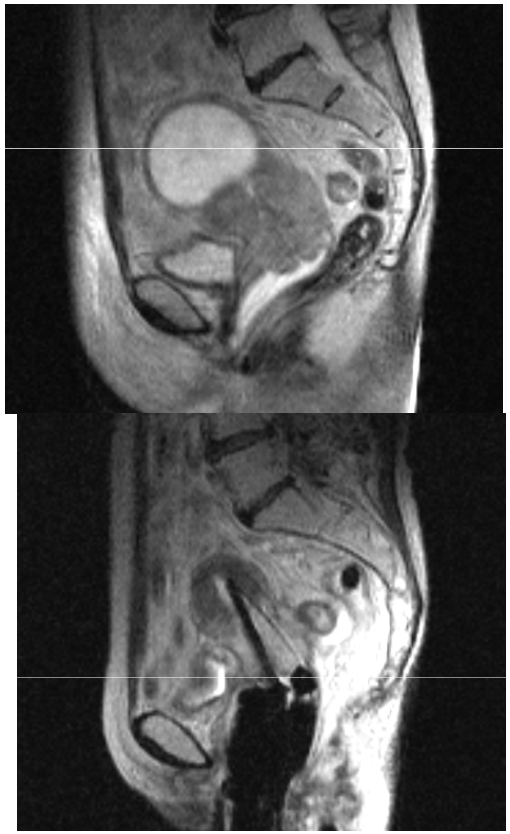






At diagnosis



At time of Brachytherapy

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Definition of GTV

CLINICAL EXAMINATION

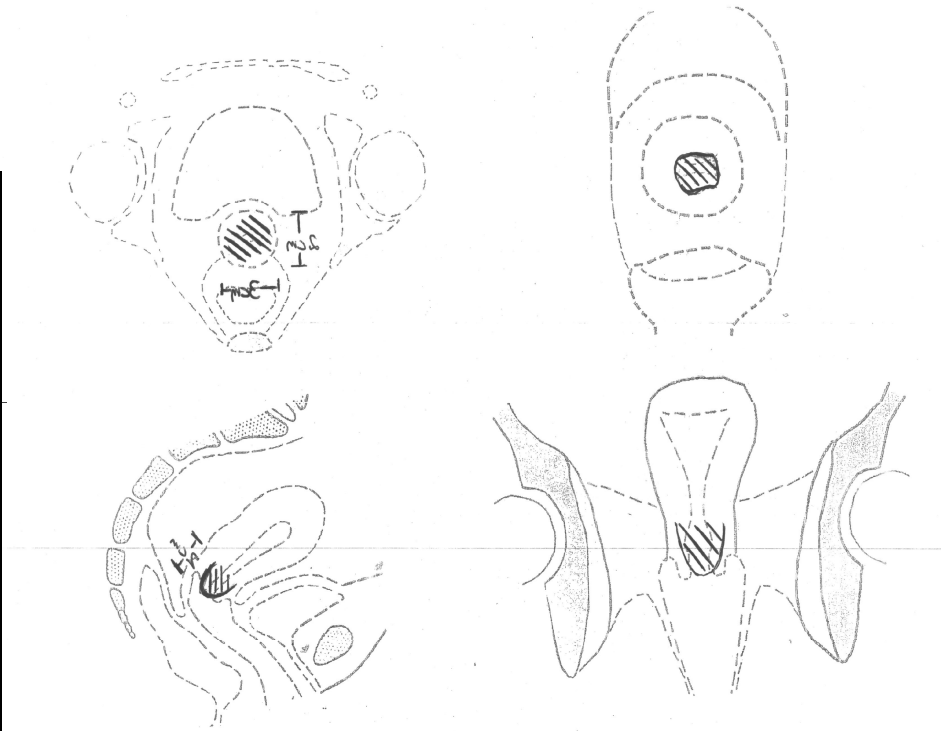
Assessment TUMOUR SIZE
TOPOGRAPHY

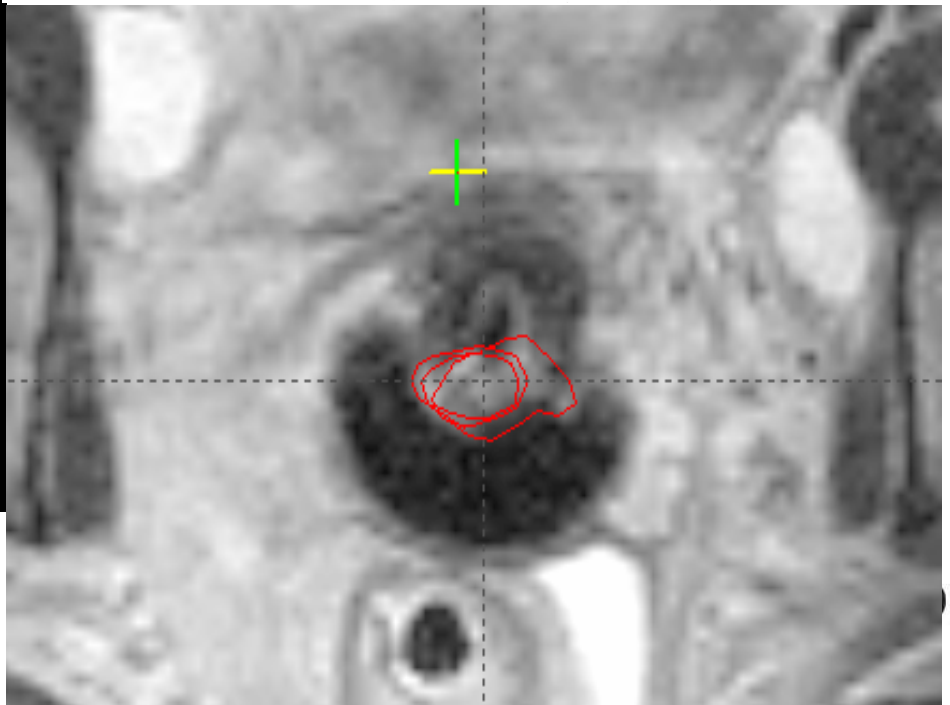
Accurate and reproducible

DOCUMENTATION

MR IMAGING

high signal intensive zones
in cervix and surroundings





Definition of HIGH RISK CTV:

Persistent GTV,
Always whole cervix
Presumed tumour extension
Residual edematous zones at CE
Residual grey zones on MRI

NO SAFETY MARGIN

DOSE HIGH ENOUGH TO STERILIZE MACROSCOPIC TUMOUR

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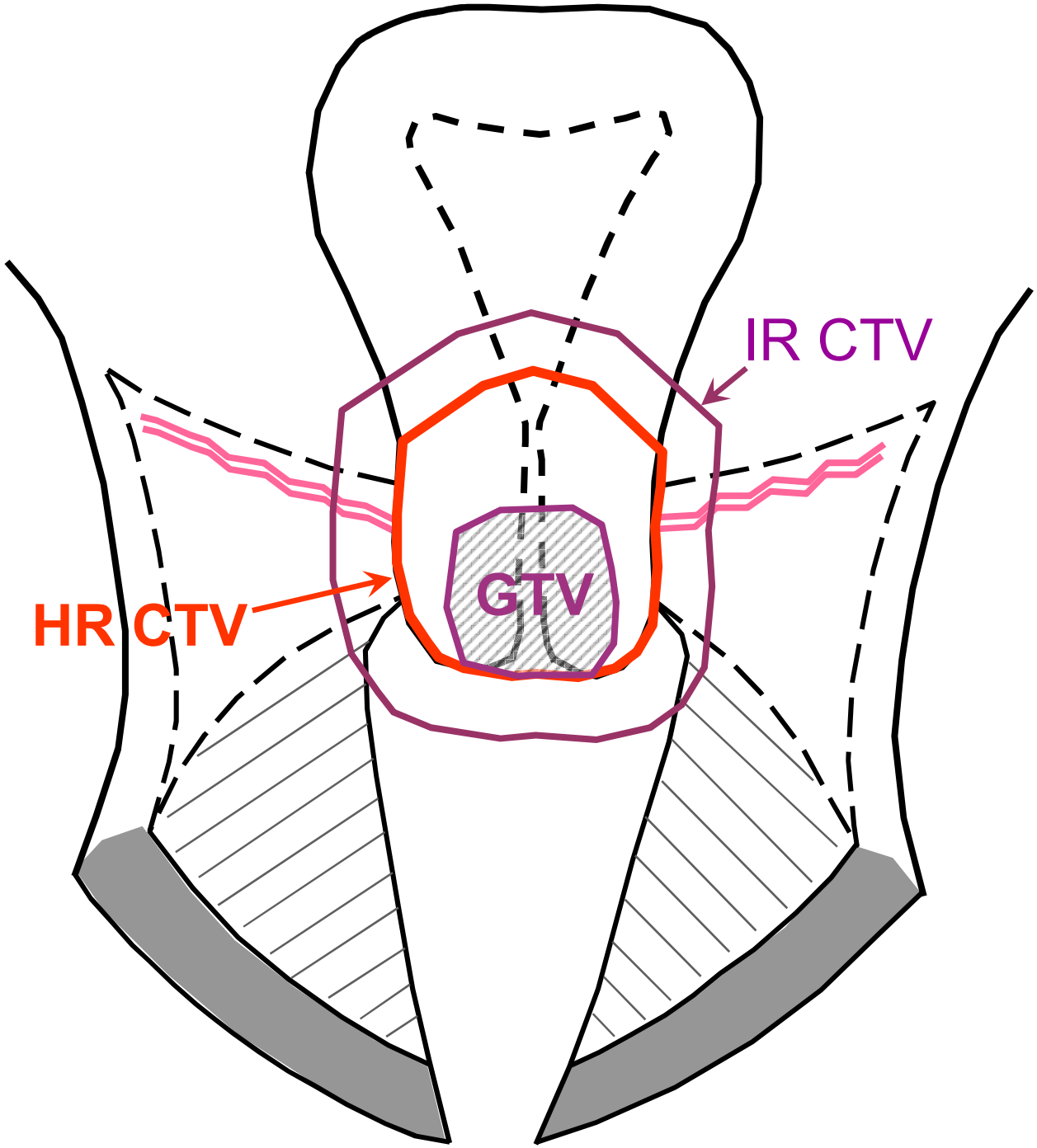
Definition of
INTERMEDIATE RISK CTV:

Stage I disease

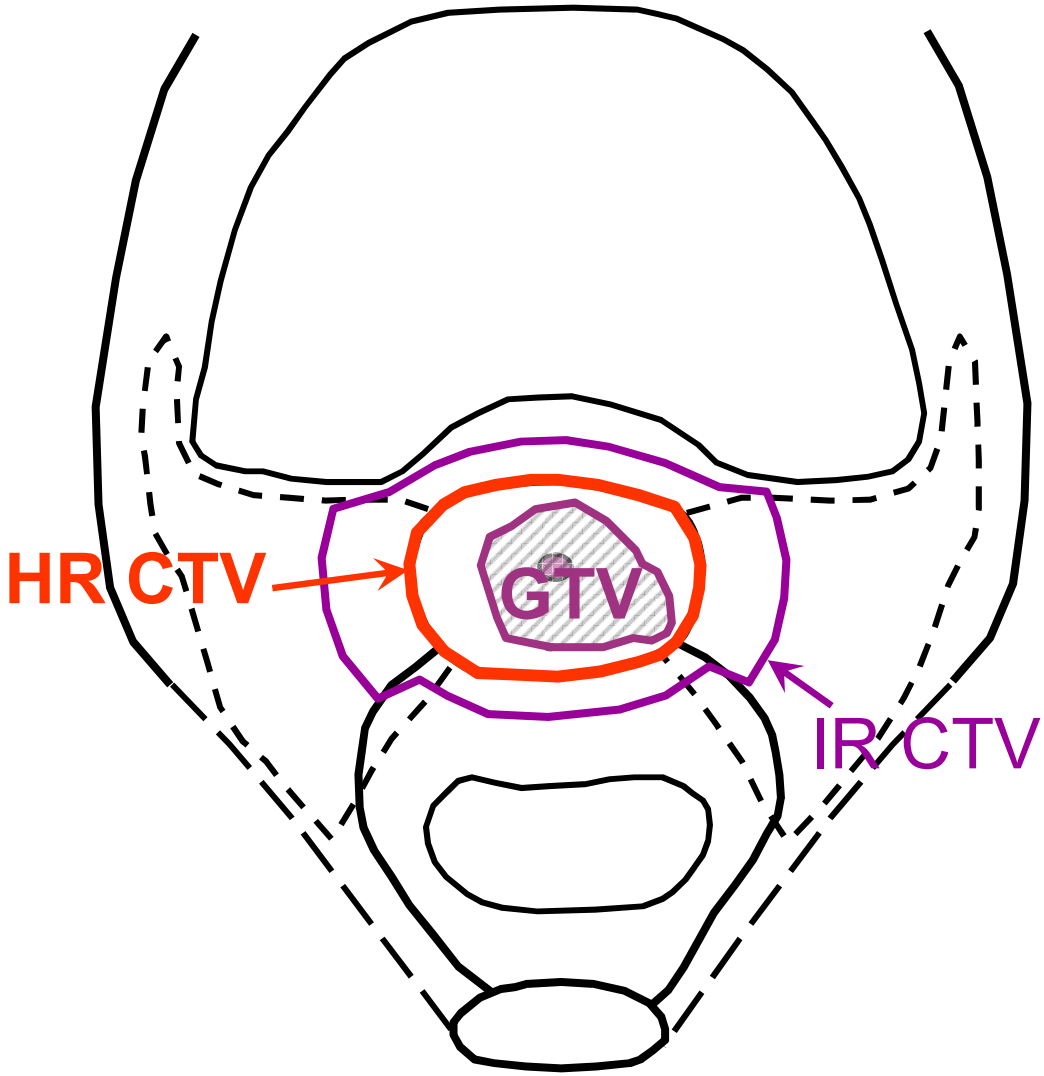
SAFETY MARGINS (5 - 15 mm)
around HR CTV according to potential tumour spread

- up to 5 mm AP, limited by bladder or rectum
- 10 mm cranially in uterine corpus
  + 5 mm if endocervical tumour in BT only
- 10 mm laterally into parametria
  + 5 mm if lateralised I B in BT only

Stage IB



Stage IB



Definition of INTERMEDIATE RISK CTV

Extensive disease:

Encompasses High Risk CTV

SAFETY MARGINS (5 - 10 mm) according to

- Initial tumor spread
- Tumor regression
- Always respecting anatomical borders

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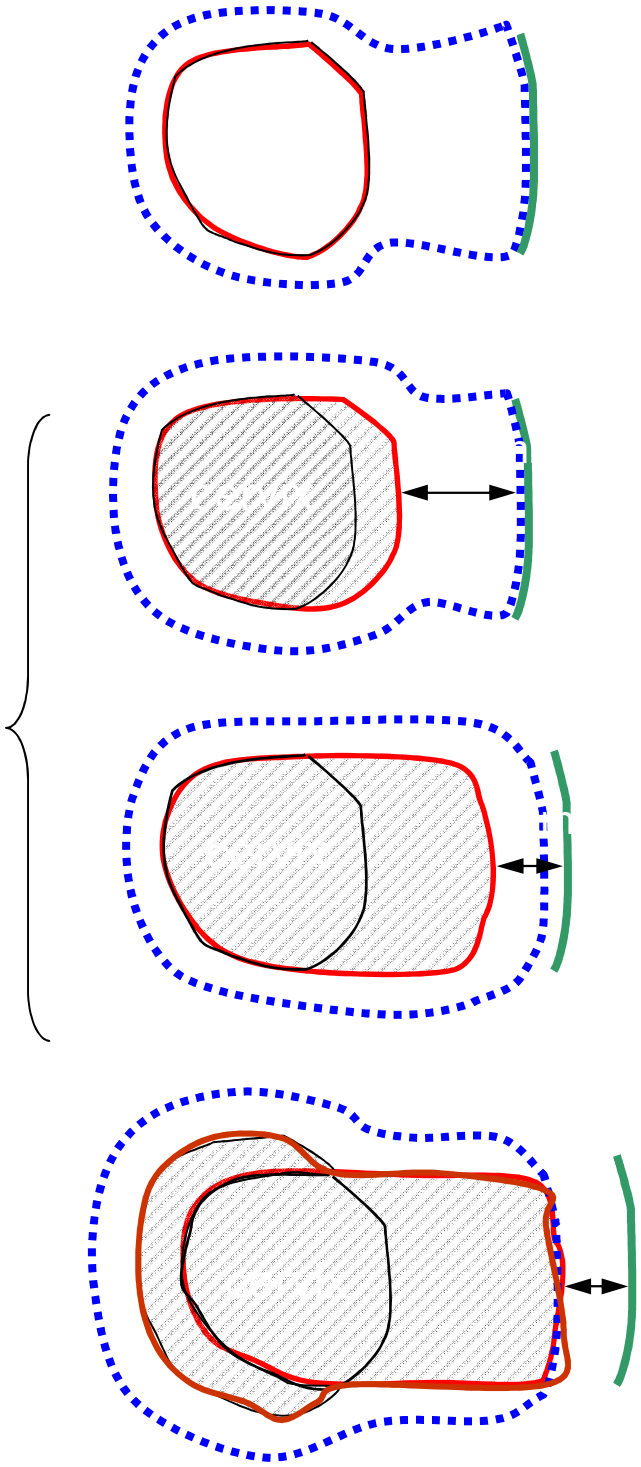
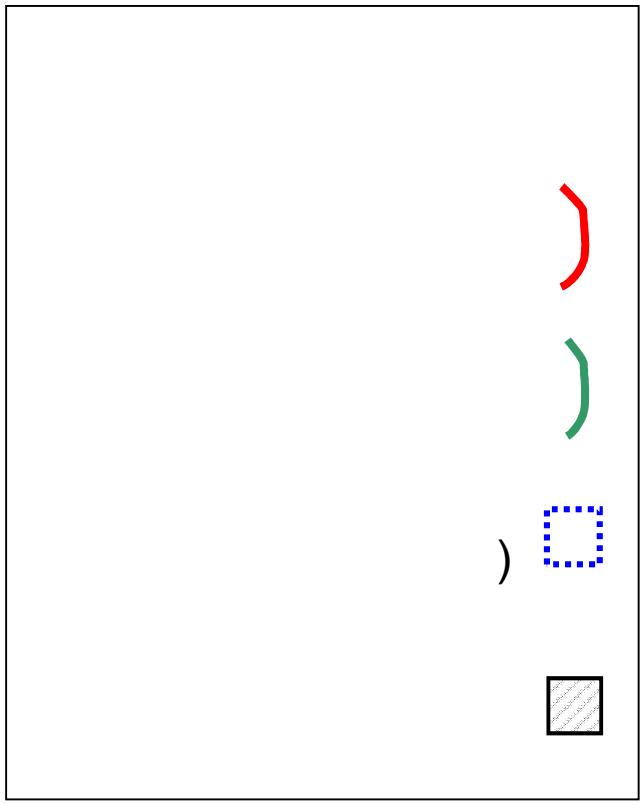
CTV BT



Extensive Disease



Stage II A-IV A

High Risk CTV:

- always whole cervix

  plus (presumed) residual disease in adjacent tissues

Intermediate Risk CTV *: HR CTV + adjacent tissue

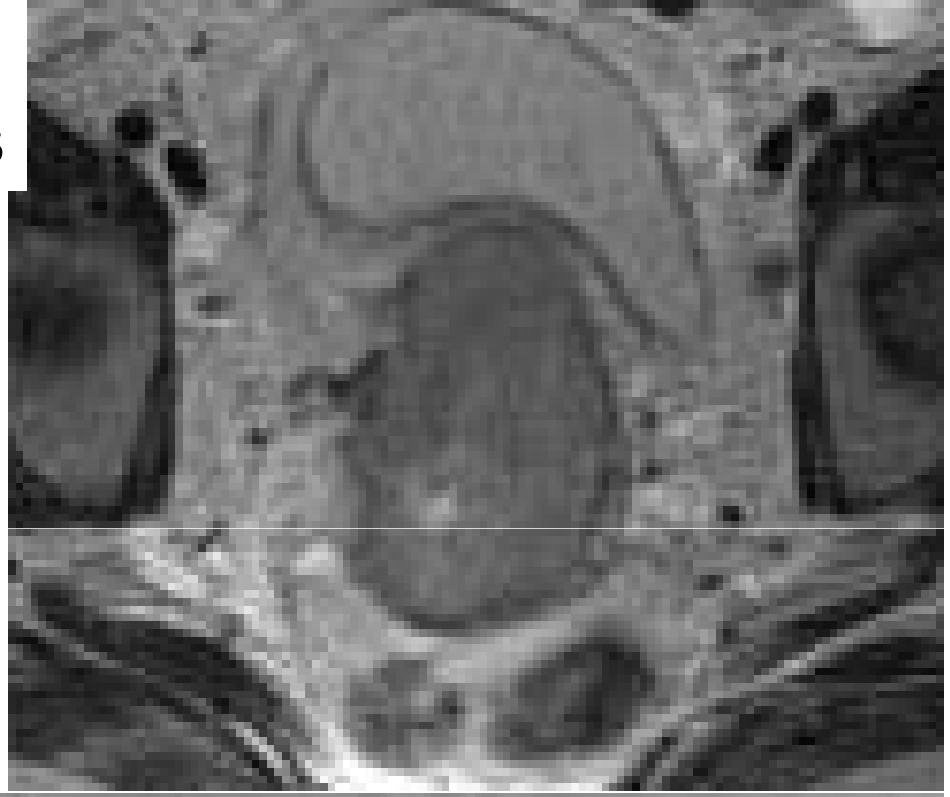
-medial parametria (at least 10 mm* beyond HR CTV)

-upper vagina (at least 10 mm below os level or HR CTV *)

-nearby uterine corpus (at least10 mm* beyond HR CTV)

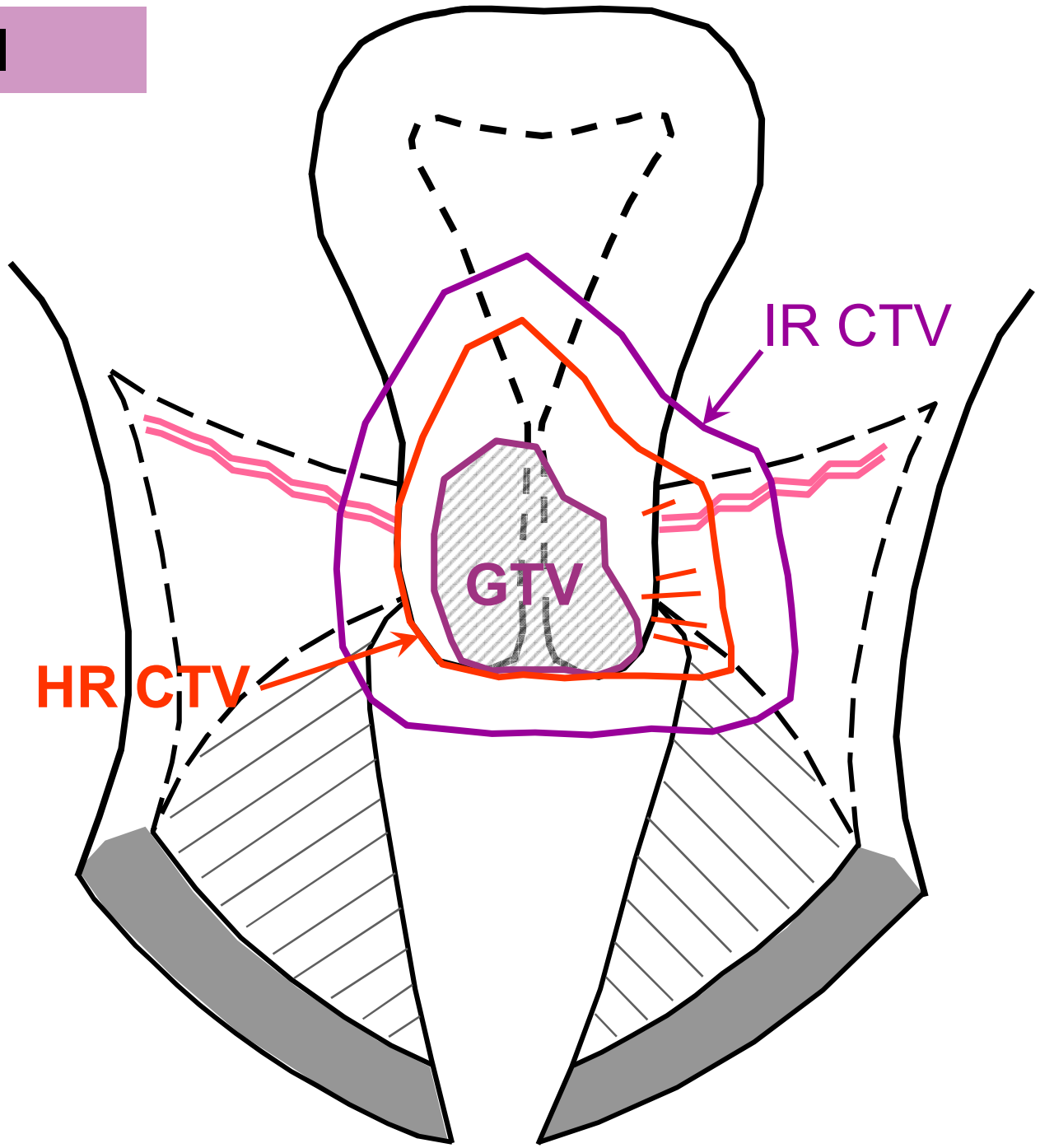
*Always including previously involved anatomical sites (GTV at diagnosis) and respecting anatomical borders

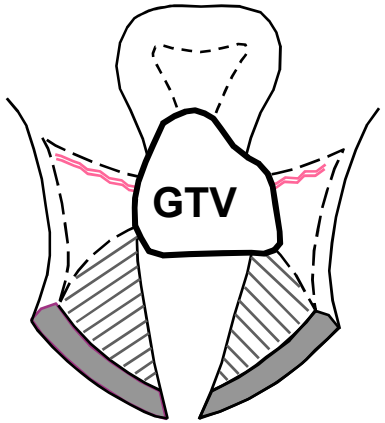
At diagnosis



At Brachy therapy

STAGE II





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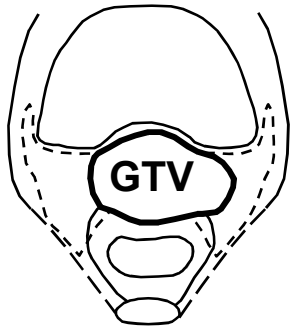
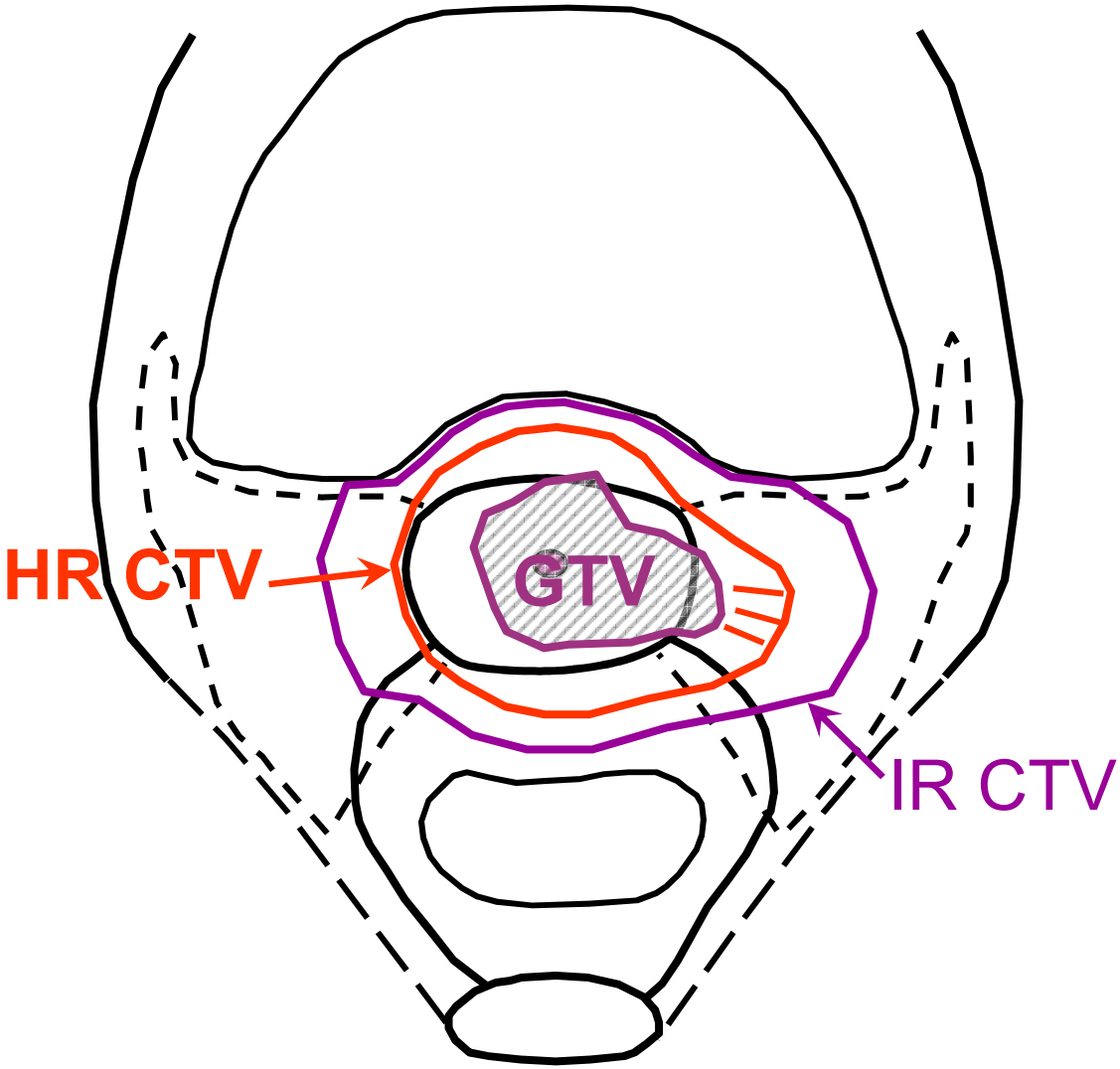
Stage II





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Dogma in Brachytherapy
CTV = PTV

- Most likely true for HDR Brachytherapy

- Questionable for LDR/PDR and fractionated HDR Brachytherapy (one application)
  * Target
  * Different OAR: Rectum, Sigmoid, Bladder

Very few data!
Prospective 3D Image based evaluation needed

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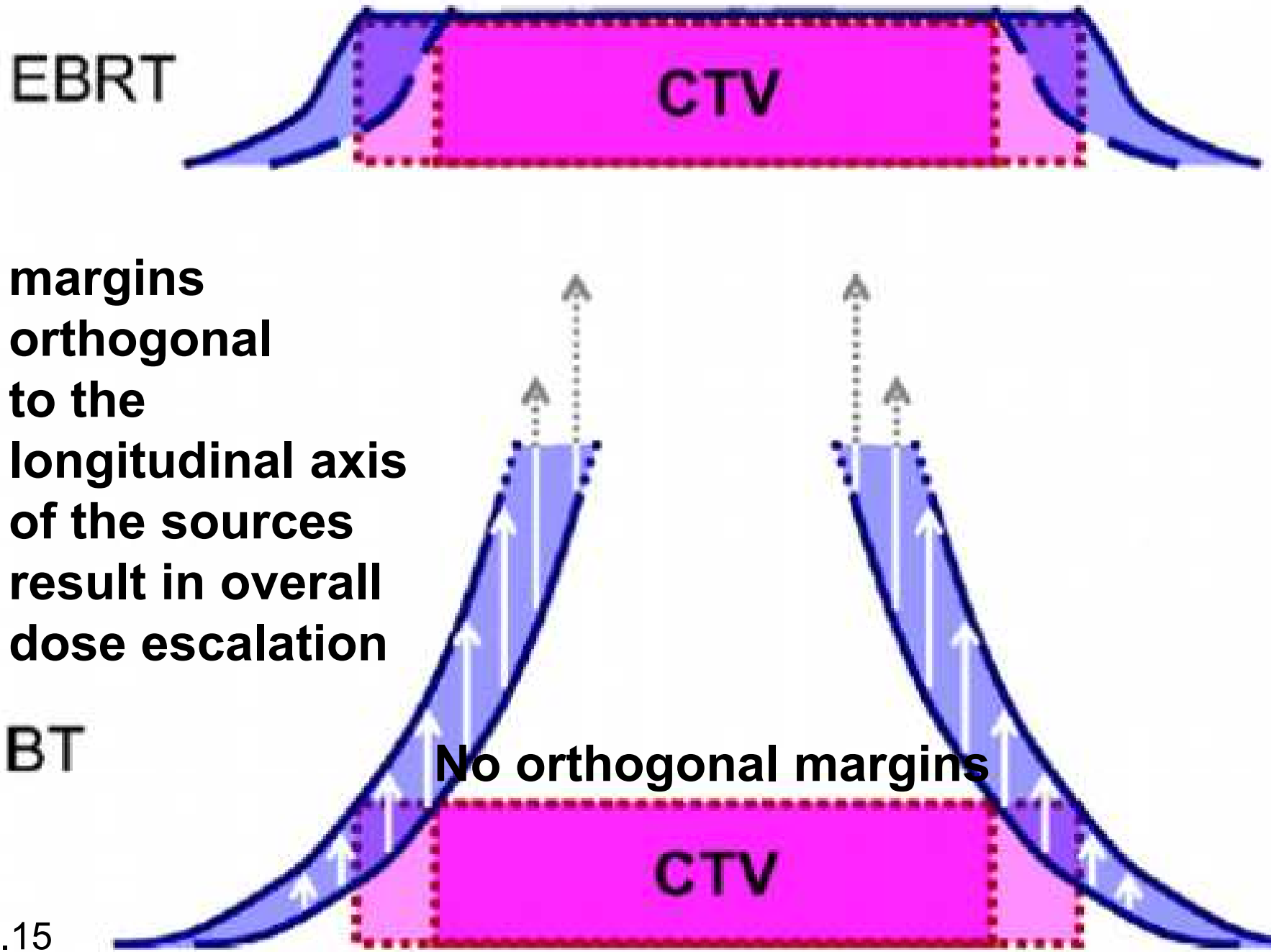
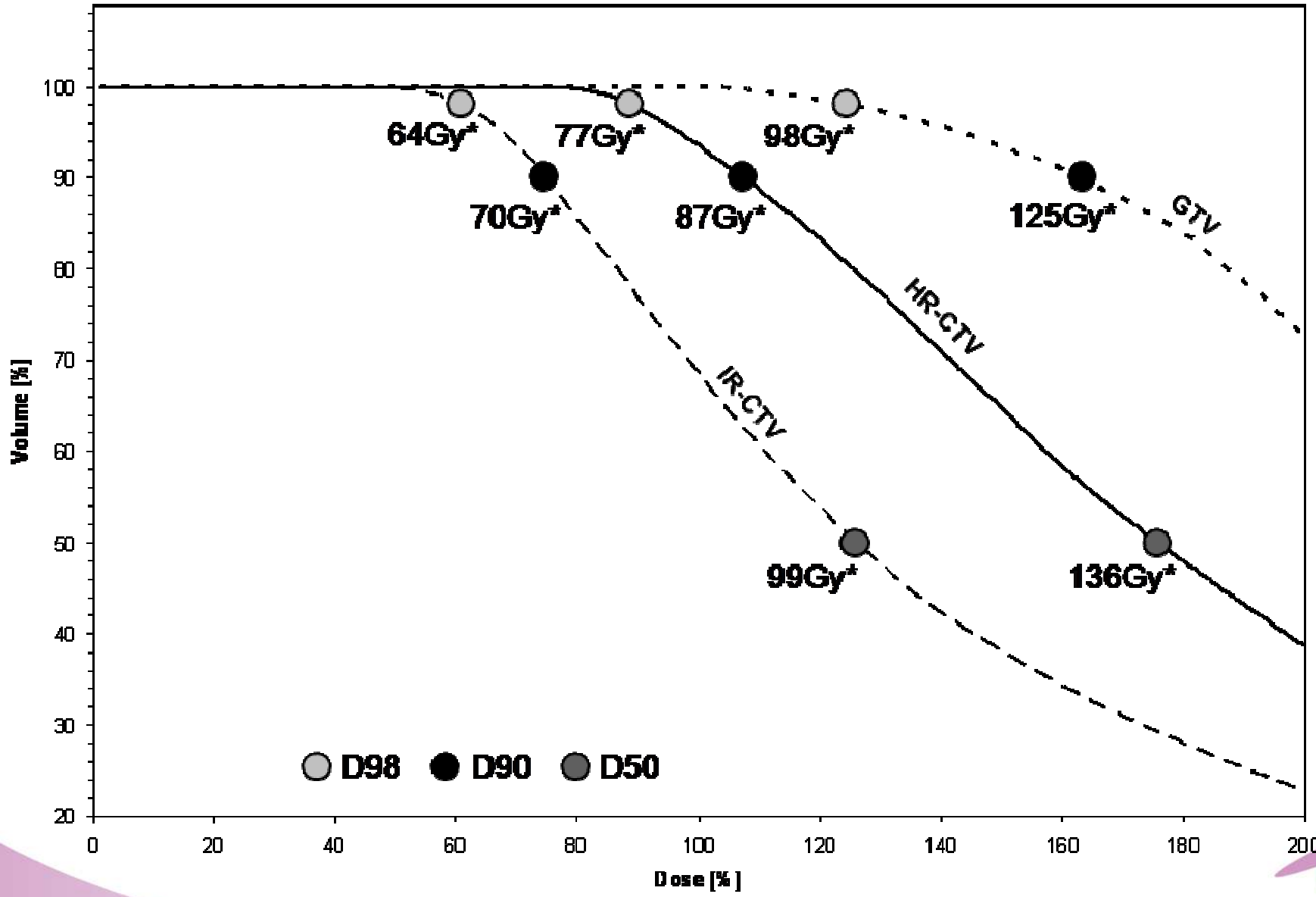

EBRT
CTV
margins
orthogonal
to the
longitudinal axis
of the sources
result in overall
dose escalation
BT
No orthogonal margins
CTV

Fig. 5.15

DVH for target volumes



ORGANS at Risk

Bladder and Rectum,

Sigmoid, Vagina

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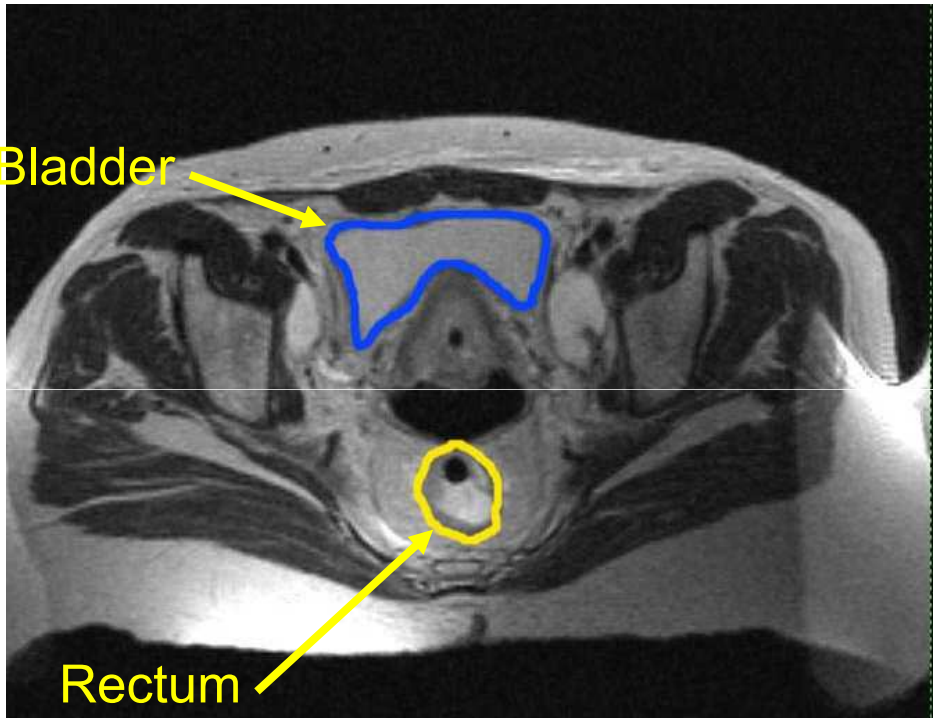
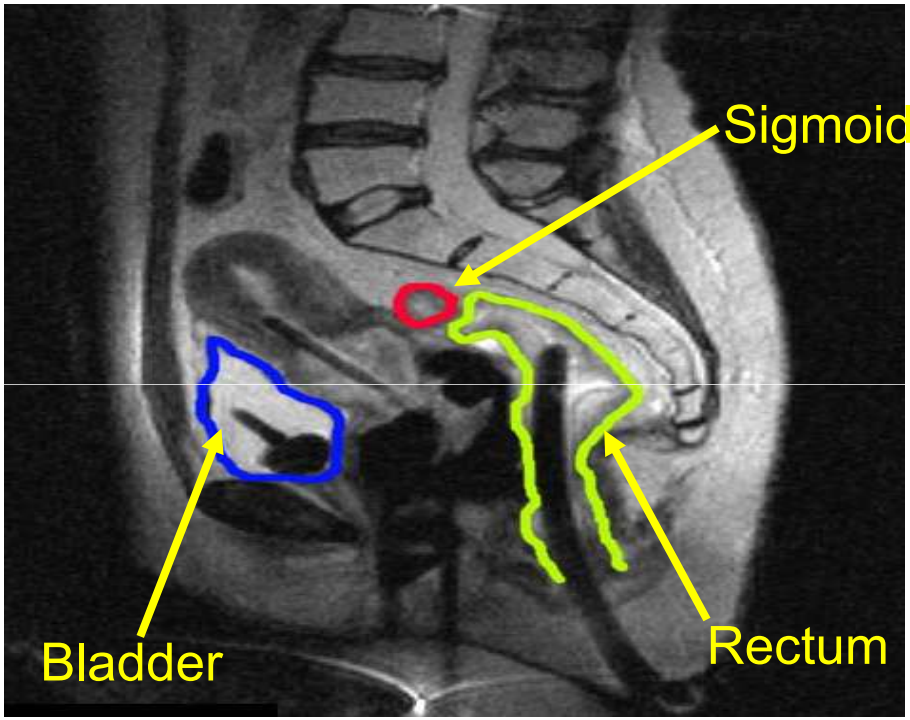
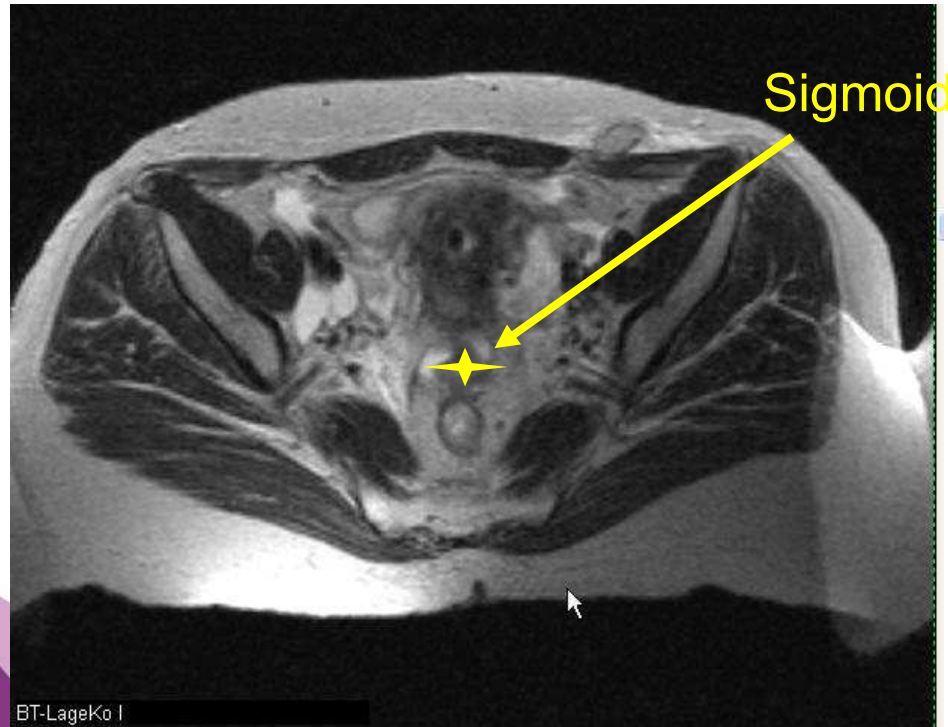
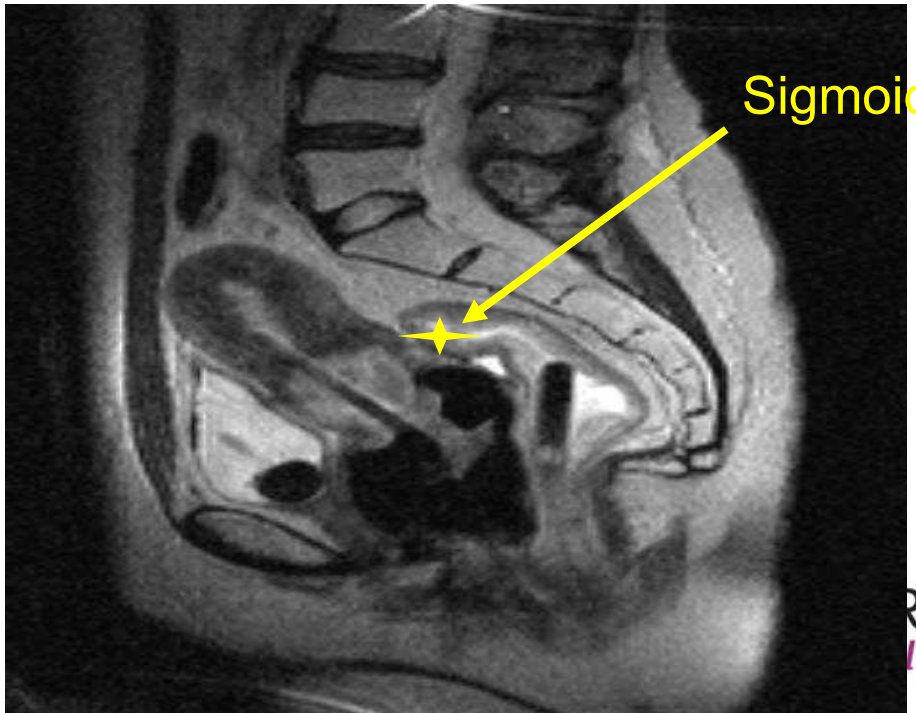
IMAGE GUIDED BT: specific GEC-ESTRO GYNE Group protocol

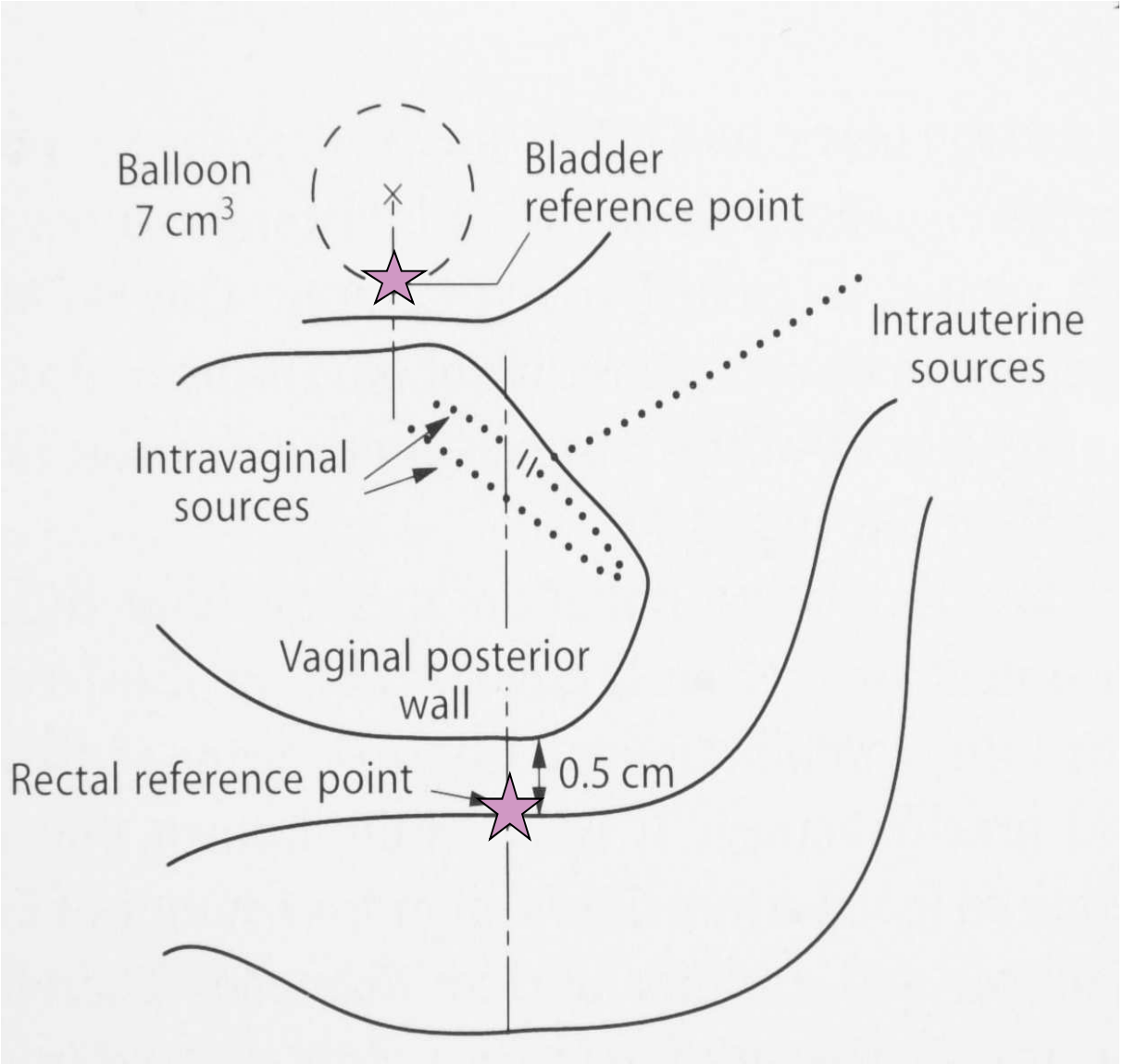








ICRU 38: Organs at risk



Defined in the 1985 report

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ICRU BLADDER REFERENCE POINT

- EASILY REPRODUCIBLE,

But…

- POOR CORRELATION WITH BLADDER COMPLICATIONS

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CORRELATION OF ICRU BLADDER REFERENCE POINT AND BLADDER COMPLICATIONS SHOWN TO BE POOR

YES	Crook e.a. 1987
	Montana e.a. 1989
NO	Stryker e.a. 1988
	Cunningham e.a. 1981
	Pourquier e.a. 1987
	Sinistrero e.a. 1993
	Arthur e.a. 1996

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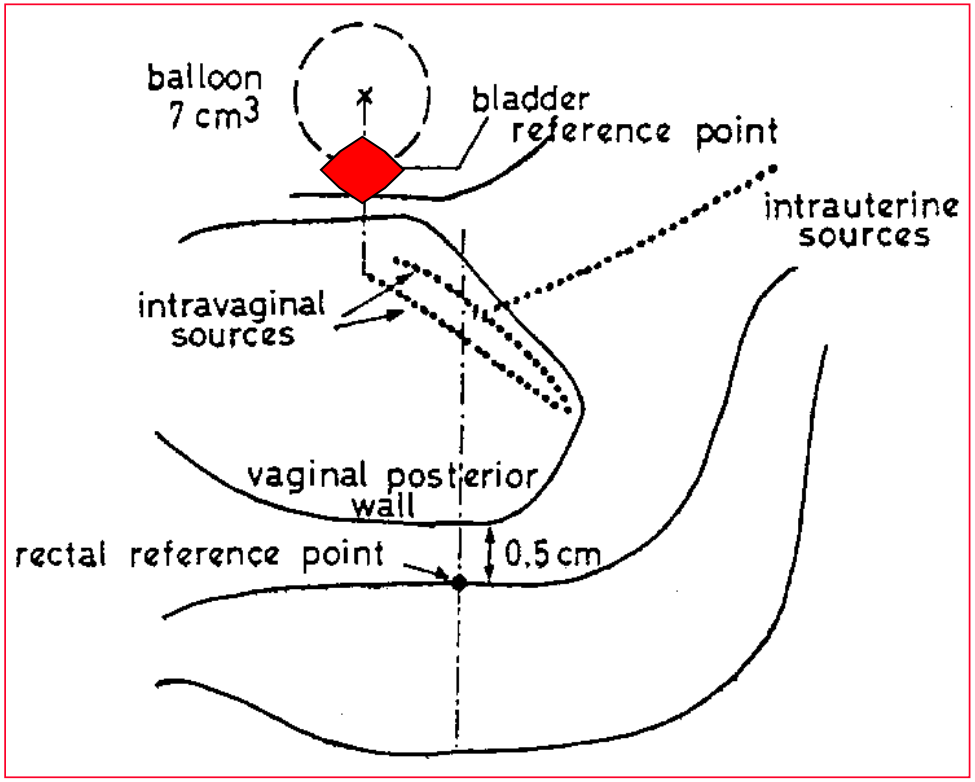
"ICRU BLADDER REFERENCE POINT UNDERESTIMATES MAXIMUM BLADDER DOSE"



Reported by, e.g.:

Hunter ea 1986

Kuipers and Visser 1986

Ling ea 1987

Kapp ea 1992

Barillot ea 1994

Tan ea 1996

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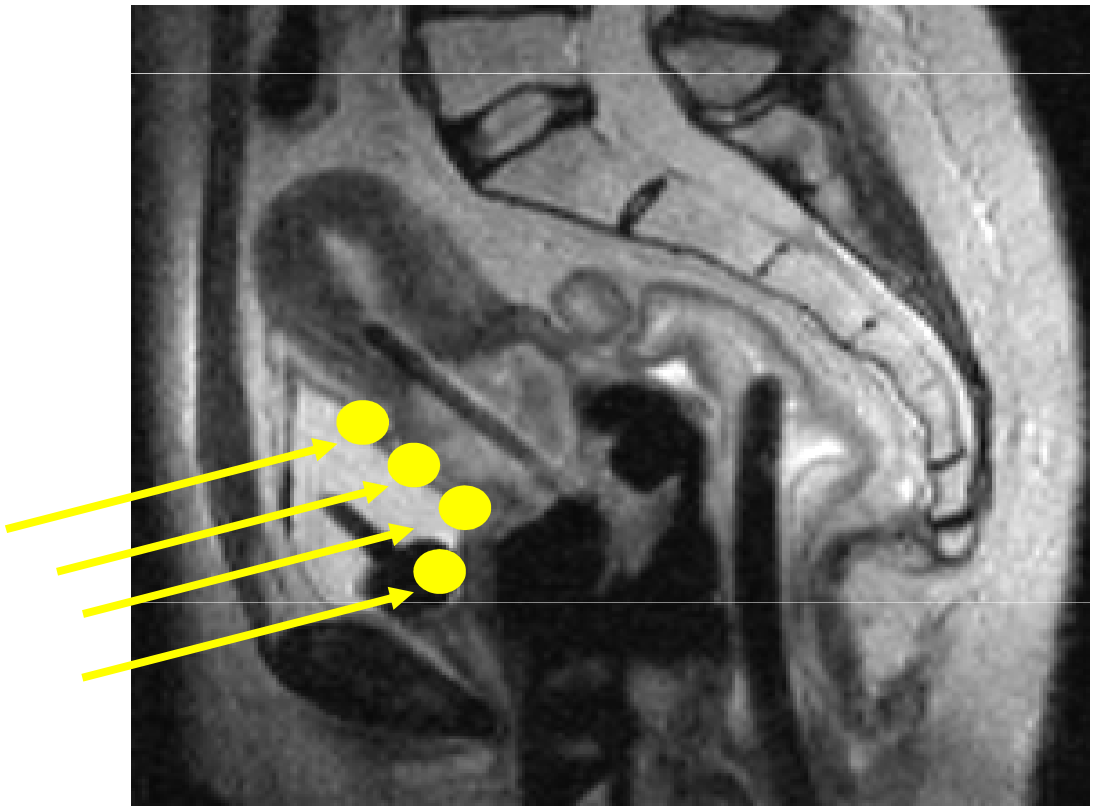
MAXIMUM BLADDER DOSES

Suggestions by, e.g.:

- Hunter ea 1986
- Ling ea 1987
- Barillot ea 1994



USUALLY 2 to 3 CM more CRANIALLY and LATERALLY at the OVOIDS

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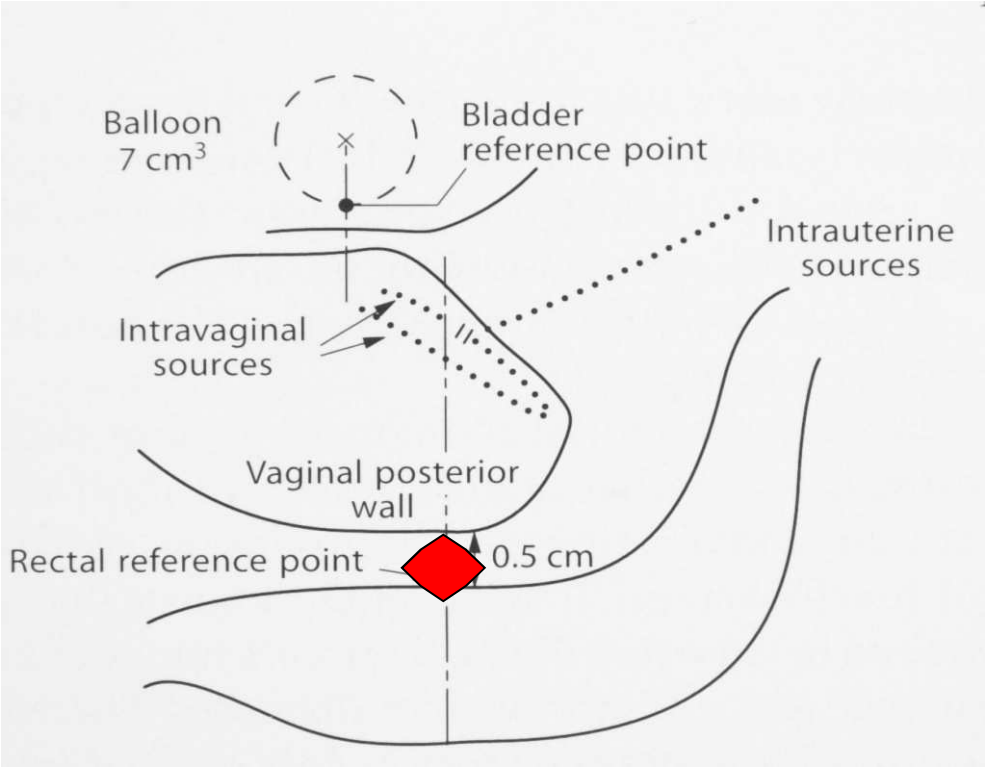
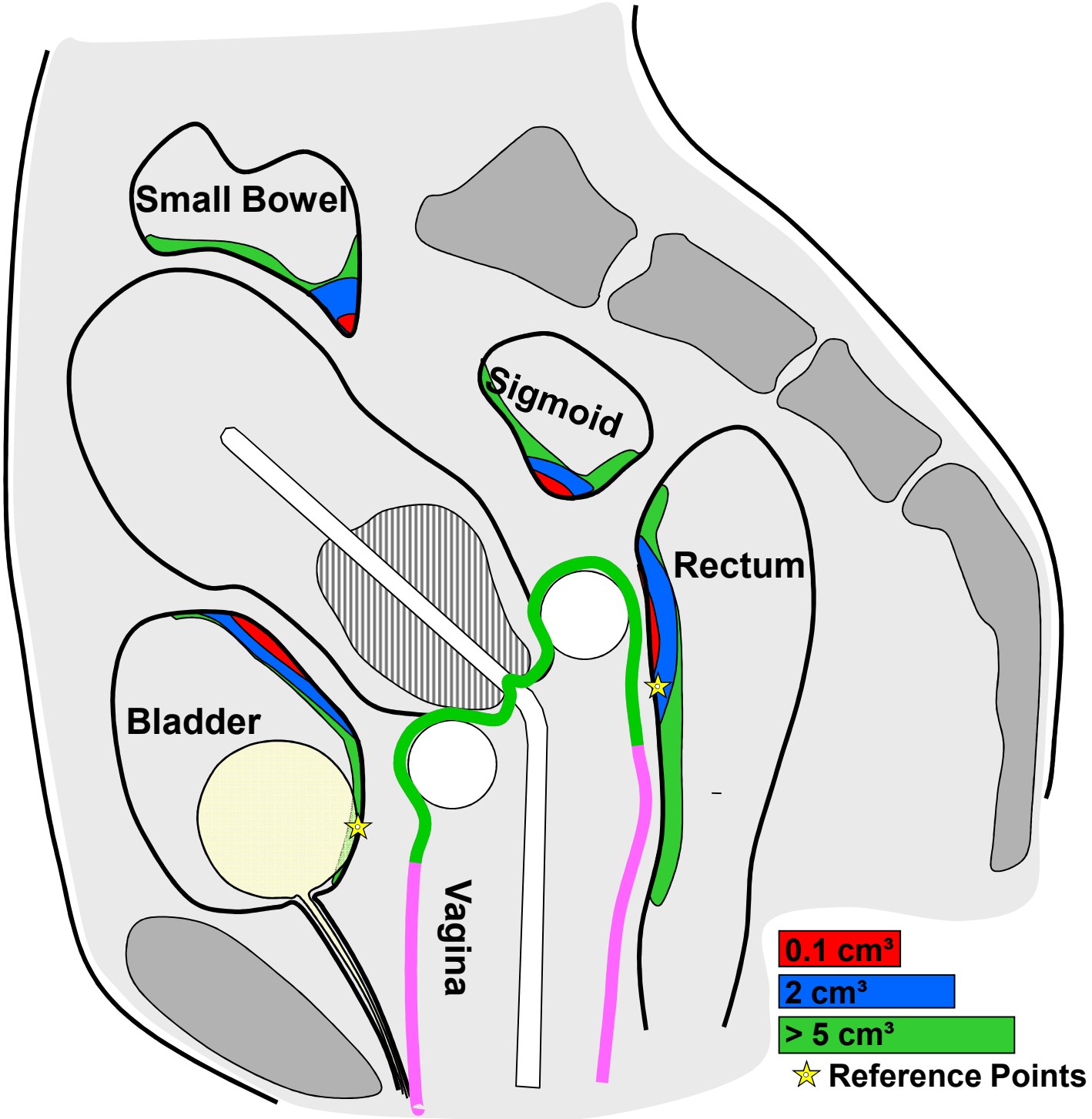
CORRELATION RECTAL COMPLICATIONS TO ICRU RECTUM REFERENCE POINT



YES	Orton and Rosenblum 1986
	Crook ea 1987
	Pourquier ea 1987
	Joslin ea 1989
	Sinistrero ea 1993
NO	Arthur ea 1996


Small Bowel
Sigmoid
Rectum
Bladder
Vagina
0.1 cm³
2 cm³
> 5 cm³
Reference Points

Outer Organ Contour

or

Organ wall contouring ????

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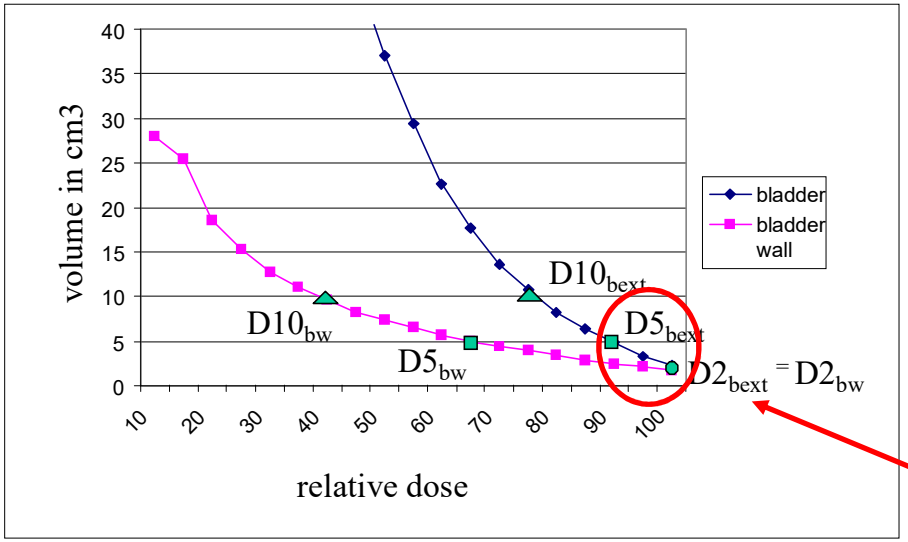
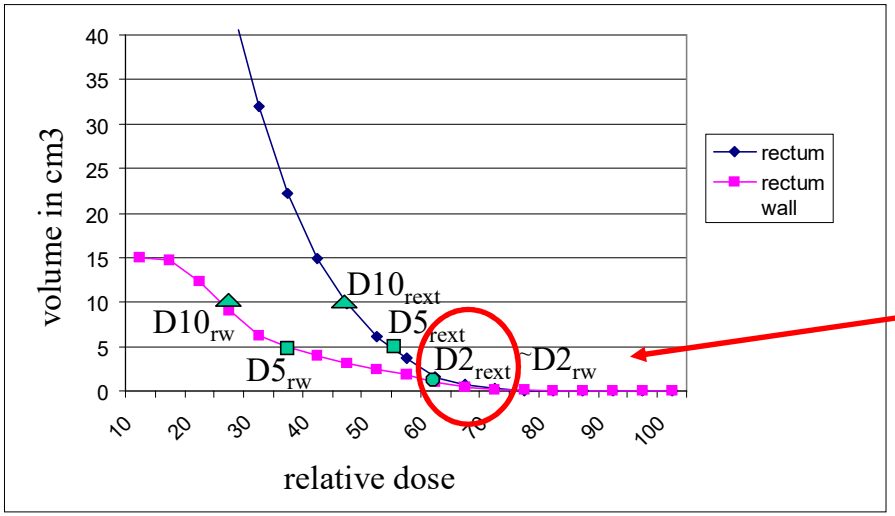
The usefulness of organ or organ-wall contouring

in the small-volume-part of the graphs,
the curves tend to come very close together



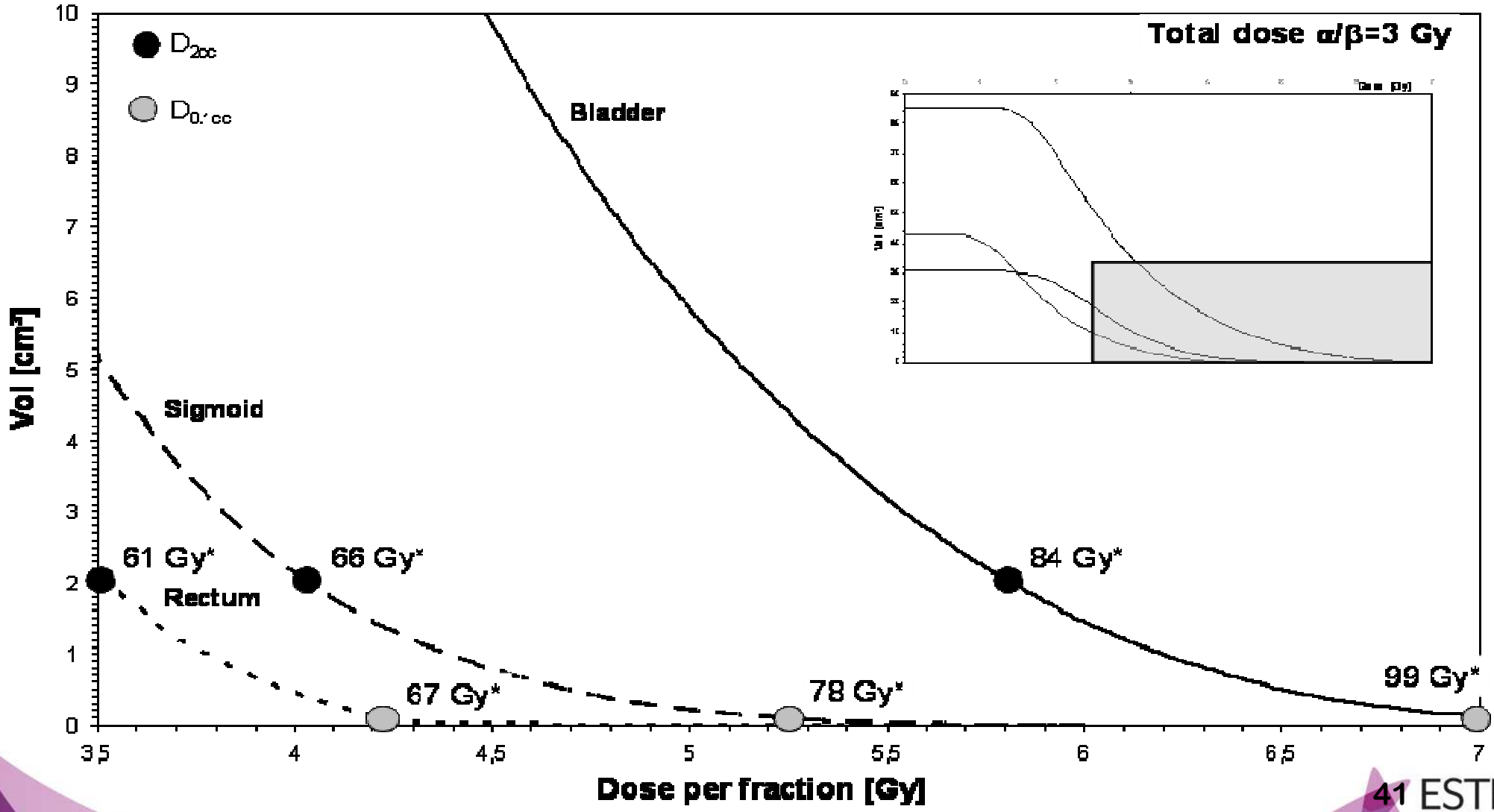


Cut off -volume 2-3 cc

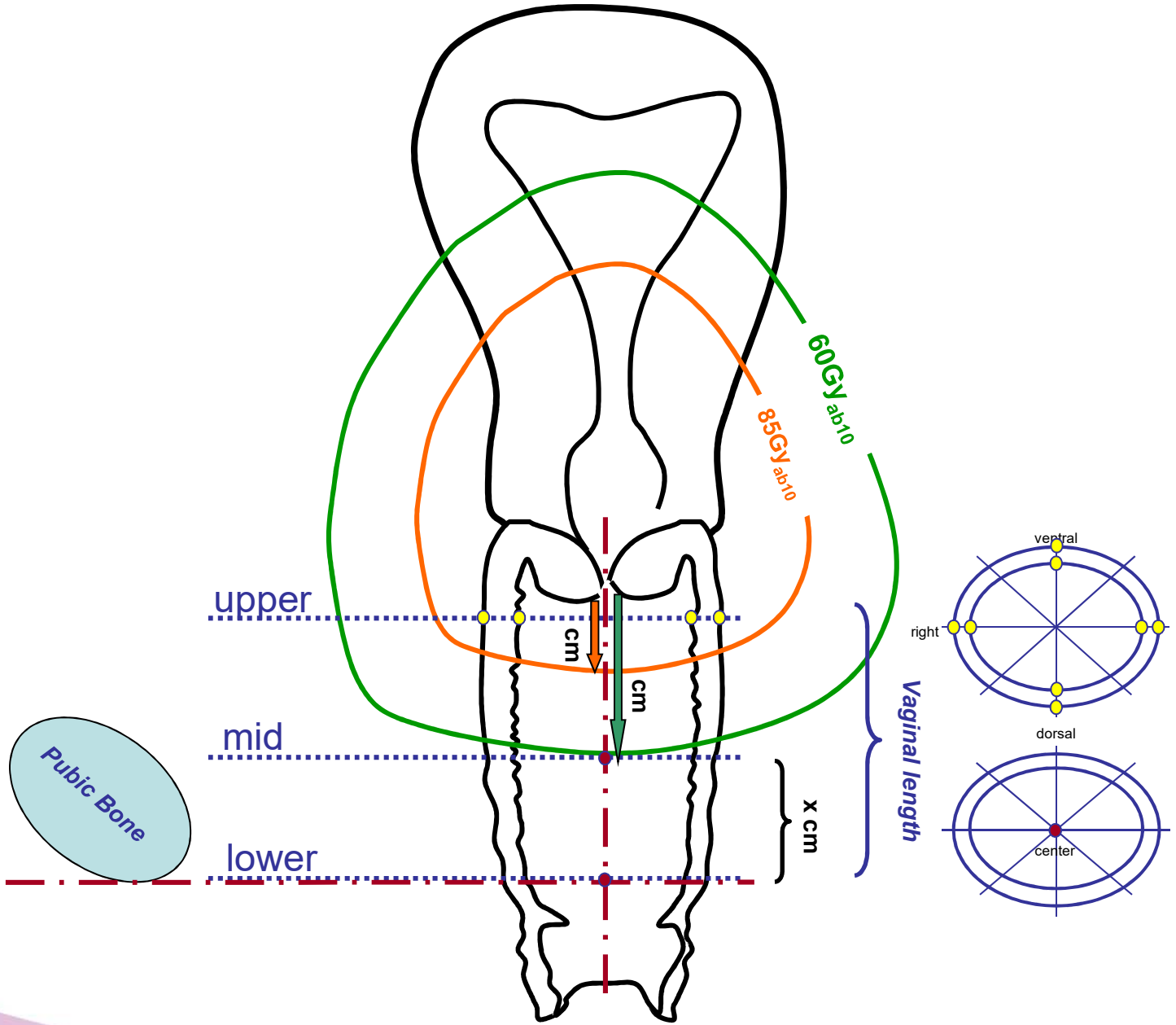
Fig.1

(Wachter-Gerstner et al. R&O 2003)

DVH for OAR


Total dose α/β=3 Gy
D2cc
D0.1cc
Bladder
Sigmoid
Rectum
61 Gy*
66 Gy*
67 Gy*
78 Gy*
84 Gy*
99 Gy*
Vol [cm³]
Dose per fraction [Gy]
10
9
8
7
6
5
4
3
2
1
0
3,5
4
4,5
5
5,5
6
6,5
7

Vaginal dose – DVH, Dose surface histogram, points, dimensions



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WWW.ESTRO.ORG/SCHOOL

Treatment planning
In
Cervix brachytherapy

Renaud Mazeron

Gustave Roussy

GEC-ESTRO recommendations

A first target related to the extent of GTV at diagnosis:

intermediate dose: 60 Gy

Intermediate-risk CTV → isodose envelope prescription

A second target related to the extent of GTV at time of BT:

high dose: 85 Gy

High-risk CTV → Point A prescription

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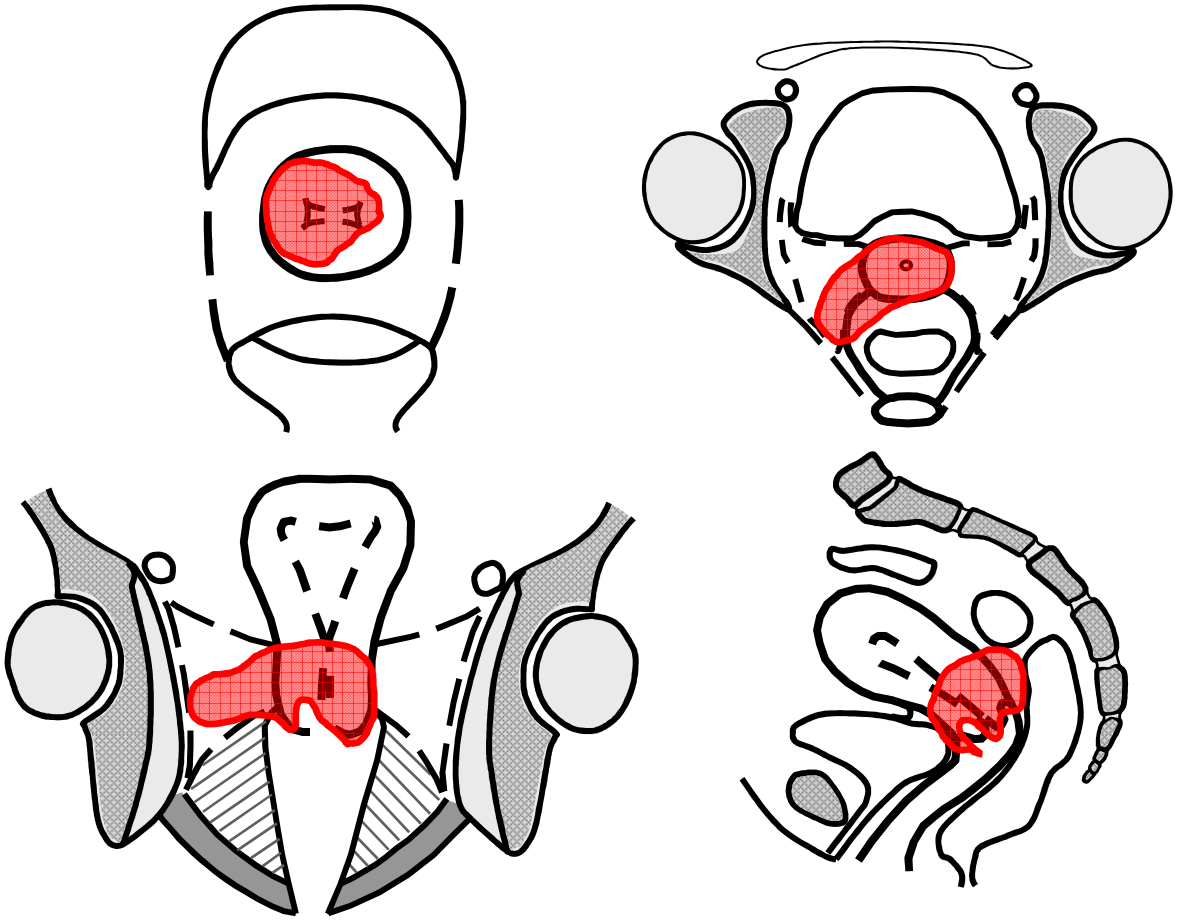
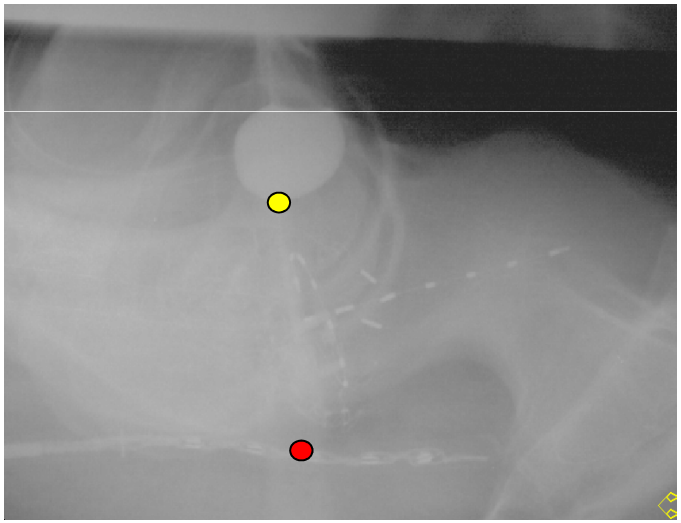
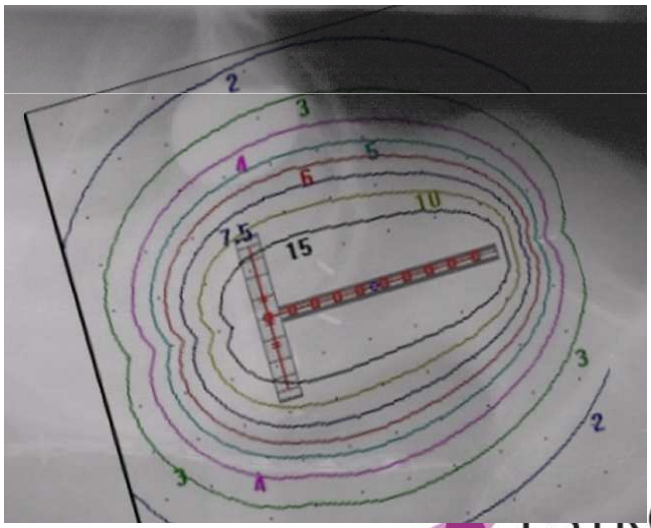
Optimisation on 2D radiographs

- Clinical examination
- ICRU rectum and bladder points







Courtesy of Kari Tanderup

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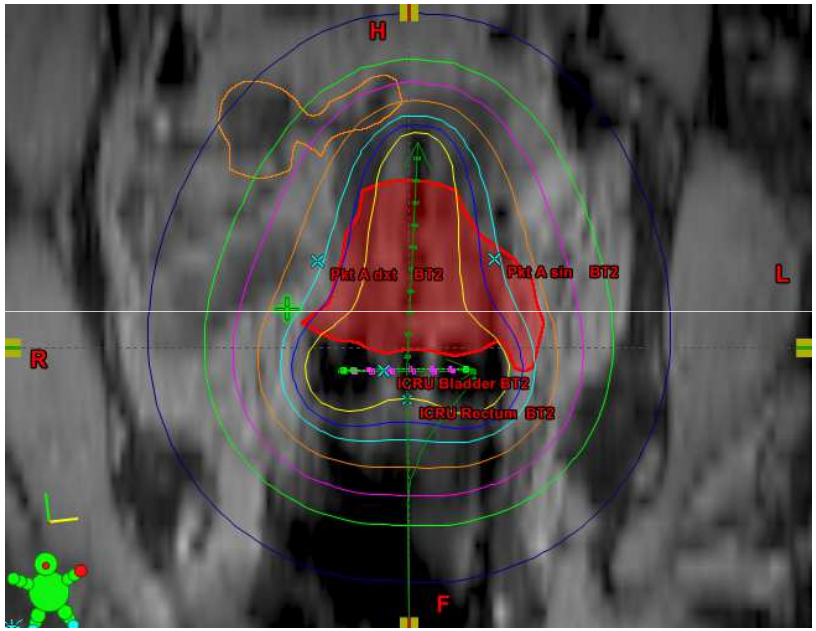
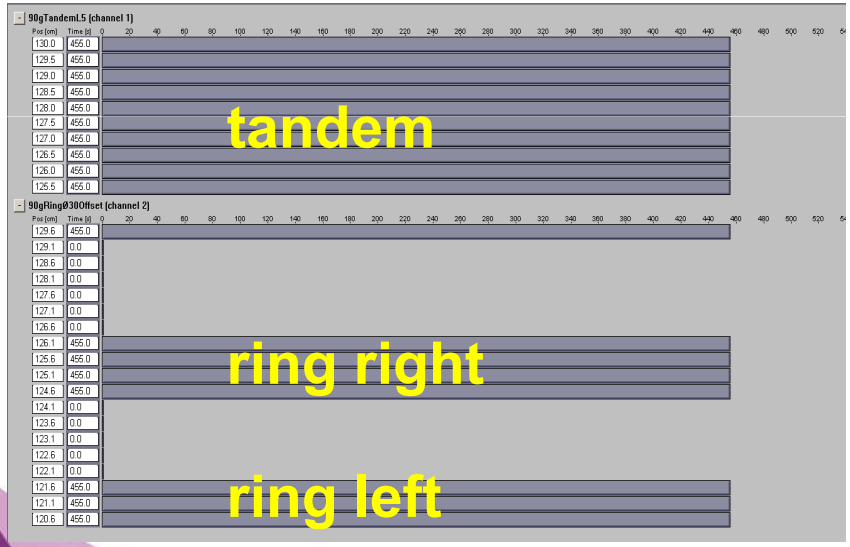
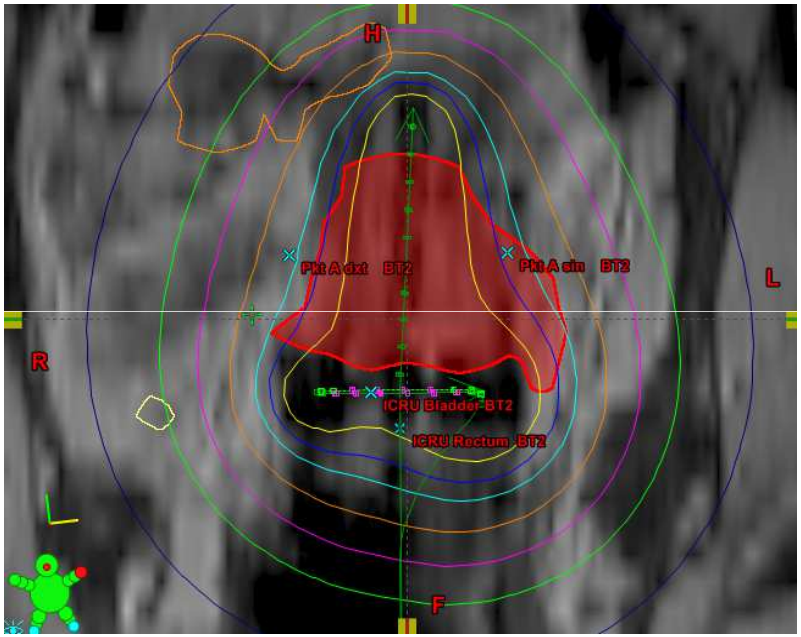
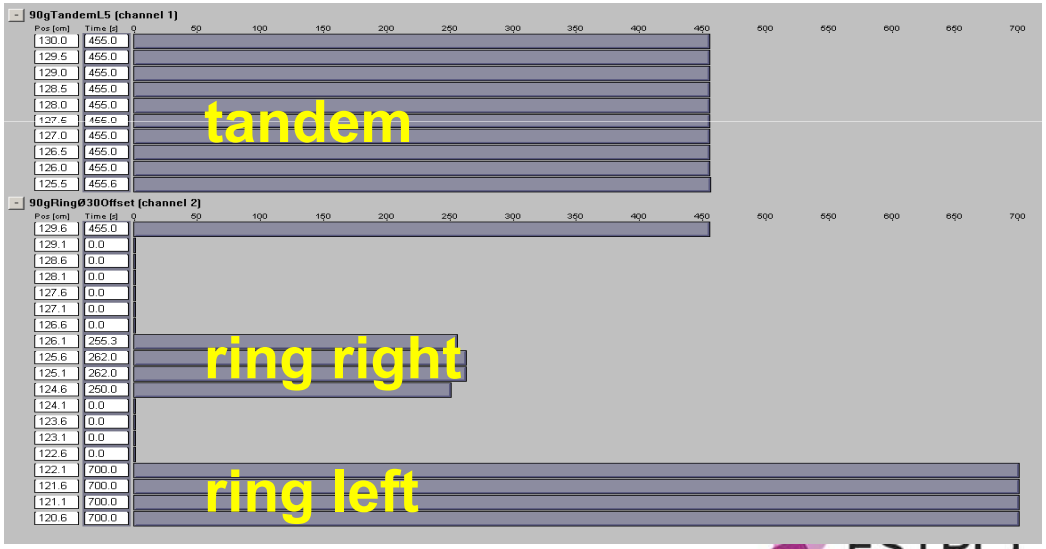
Standard





Optimised





3D MRI (CT) dose optimization

- Adaptation to size of target
  - Large tumours: increased irradiated volume
  - Small tumours: decreased irradiated volume to spare normal tissue
- Adaptation to shape of target
  - Re-distribution of dwell positions and dwell times
- Adaptation to organs at risk
- Adaption of planning aims
  - Response to EBRT
  - Volume, width
  - Treatment time

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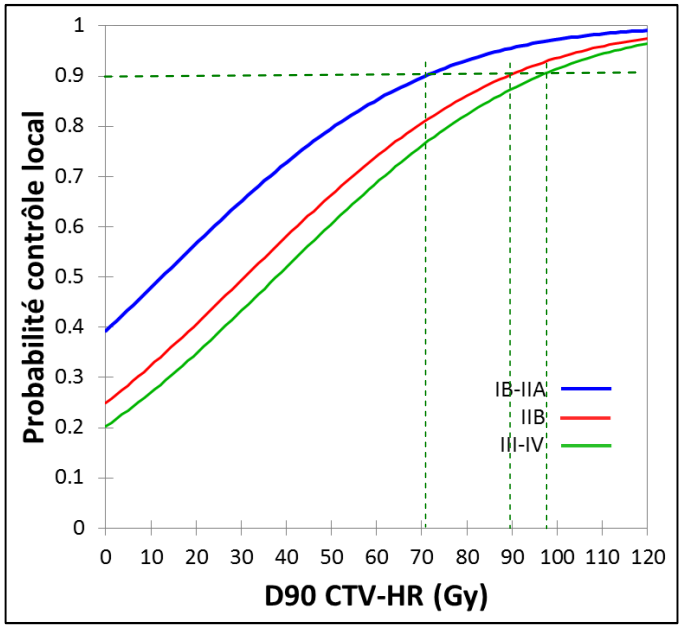
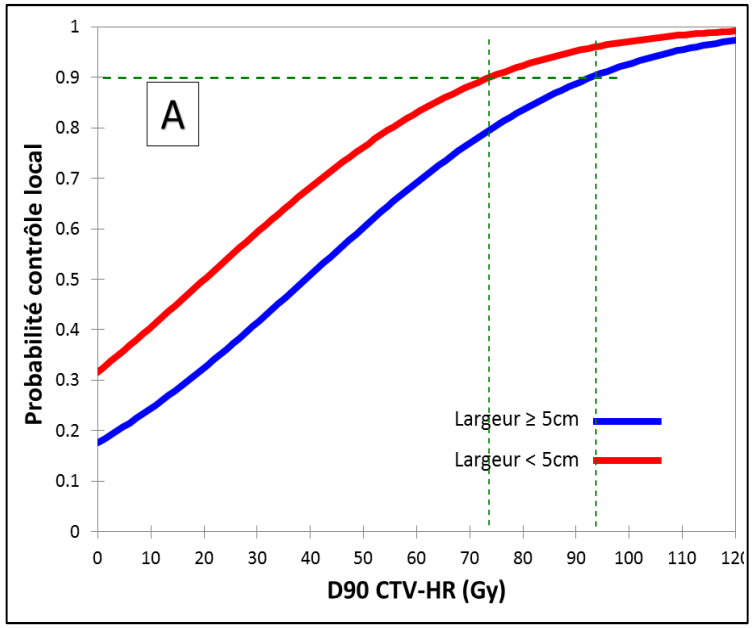
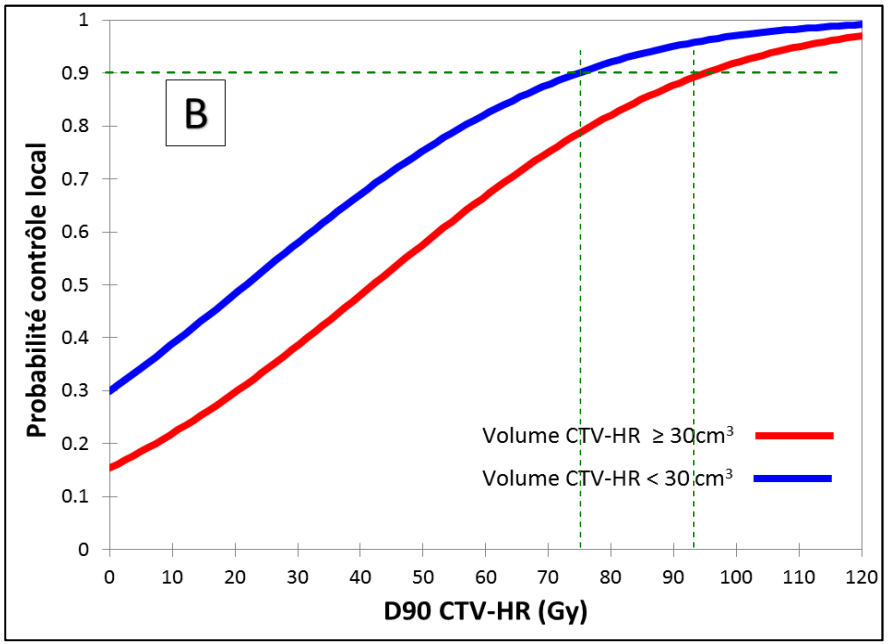
Adaptation to tumour characteristics







Mazeron Radioth Oncol 2015
Tanderup Radioth Oncol 2016

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Definitions

- EBRT and BT doses are summed
  - BT volumes received 100% EBRT prescribed dose
  - IMRT: inhomogeneity!
  - Dummy volume

- Worst case assumption
  - $2cm^3$ is stable
    - Treatment delivery
    - In between fractions

- EQD2
  - α/β = 10 Gy for tumor
  - α/β = 3 Gy for OAR

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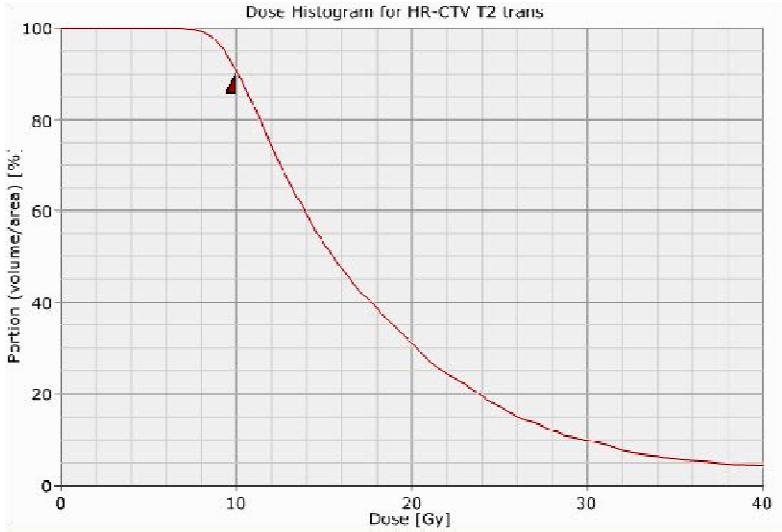
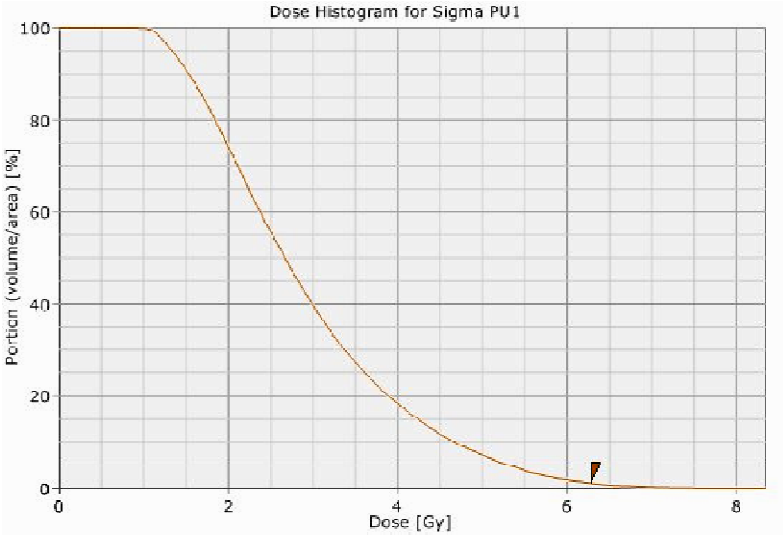
DVH constraints on total dose

- EQD_2 calculations
  - Tumor: α/β = 10 Gy
  - OAR: α/β = 3 Gy
  - T½ = 1.5 h

- Tumour, D90, planning AIMS
  - HR-CTV ≥ 85 Gy
  - IR-CTV > 60 Gy

- OAR, D_{2cm3}
  - Bladder ≤ 85-90 Gy
  - Rectum ≤ 70-75 Gy
  - Sigmoid ≤ 70-75 Gy



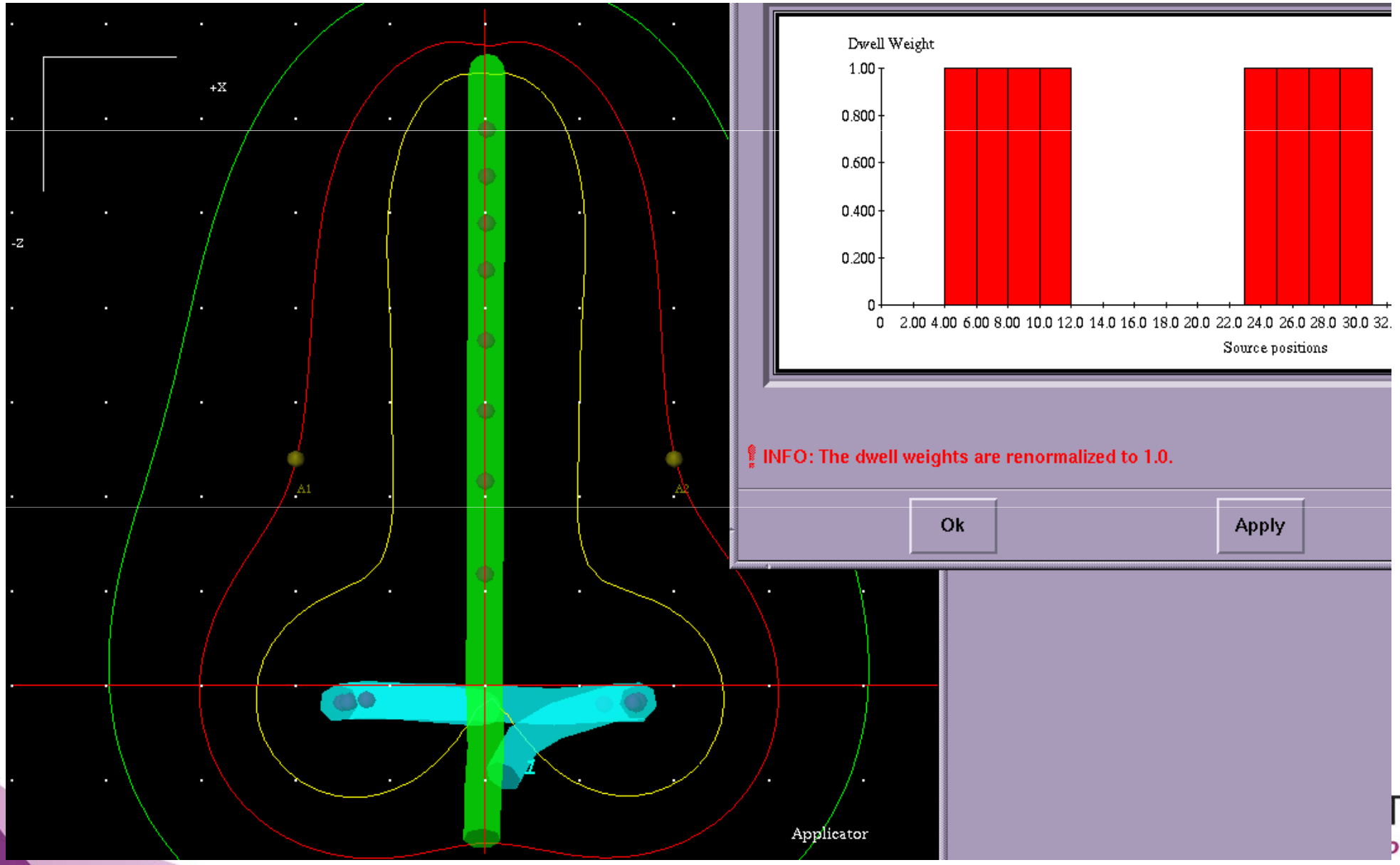


Tools for dose optimization

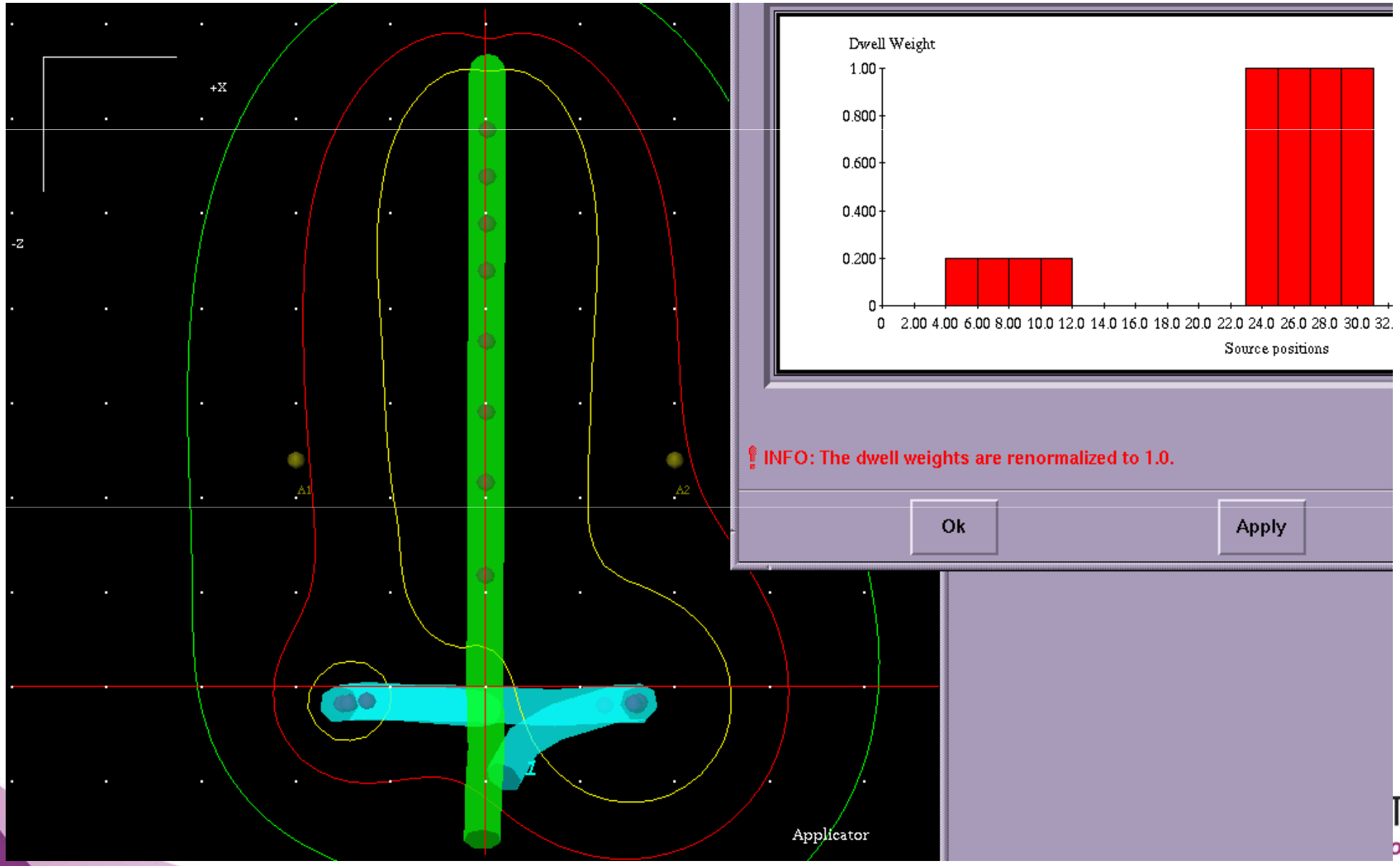
- 1. Manual dose optimization
- 2. Graphical optimization / Dose shaper
- 3. Inverse planning

⇢1. Manual optimization

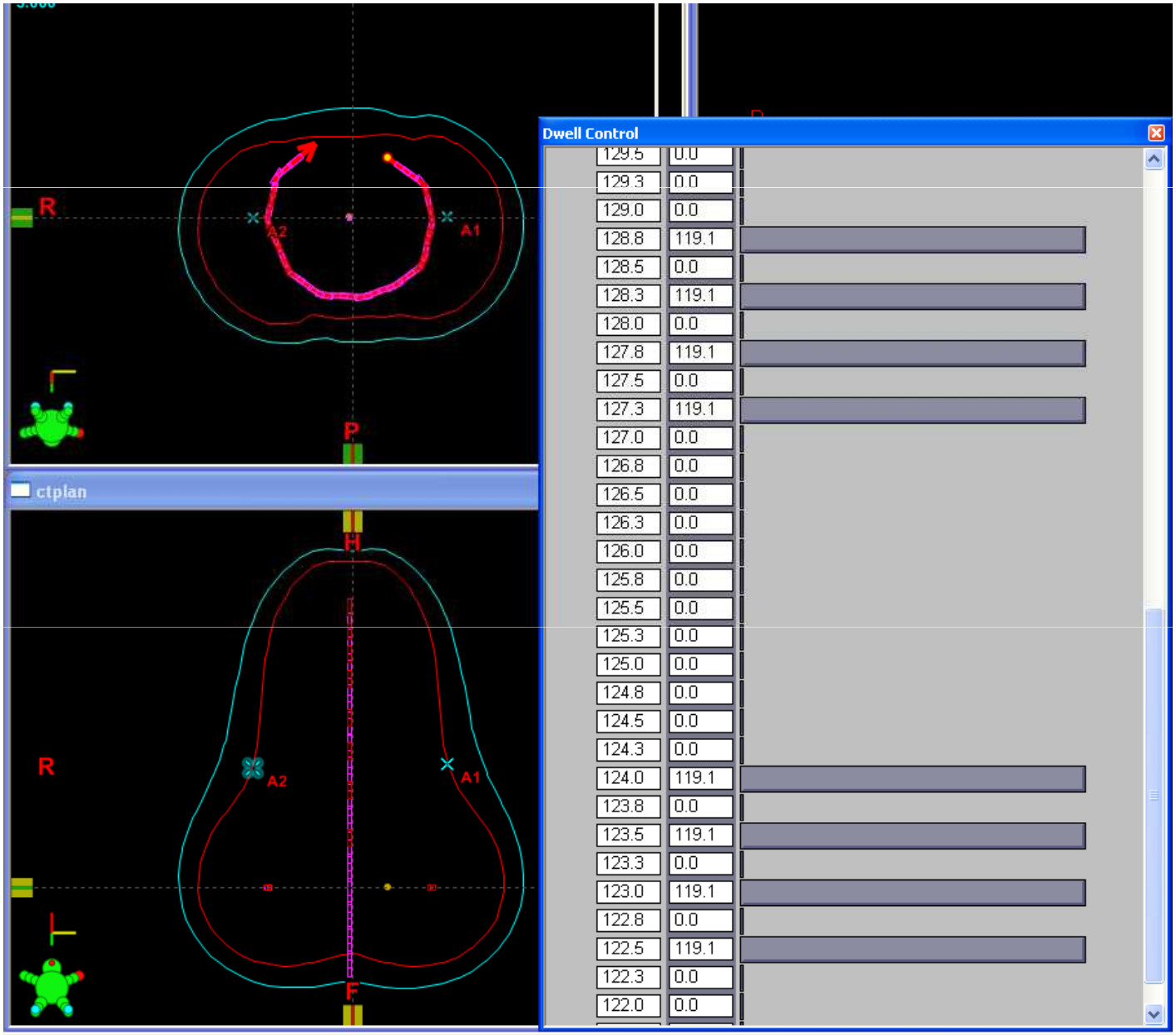
Normalisation on reference points = Standard loading



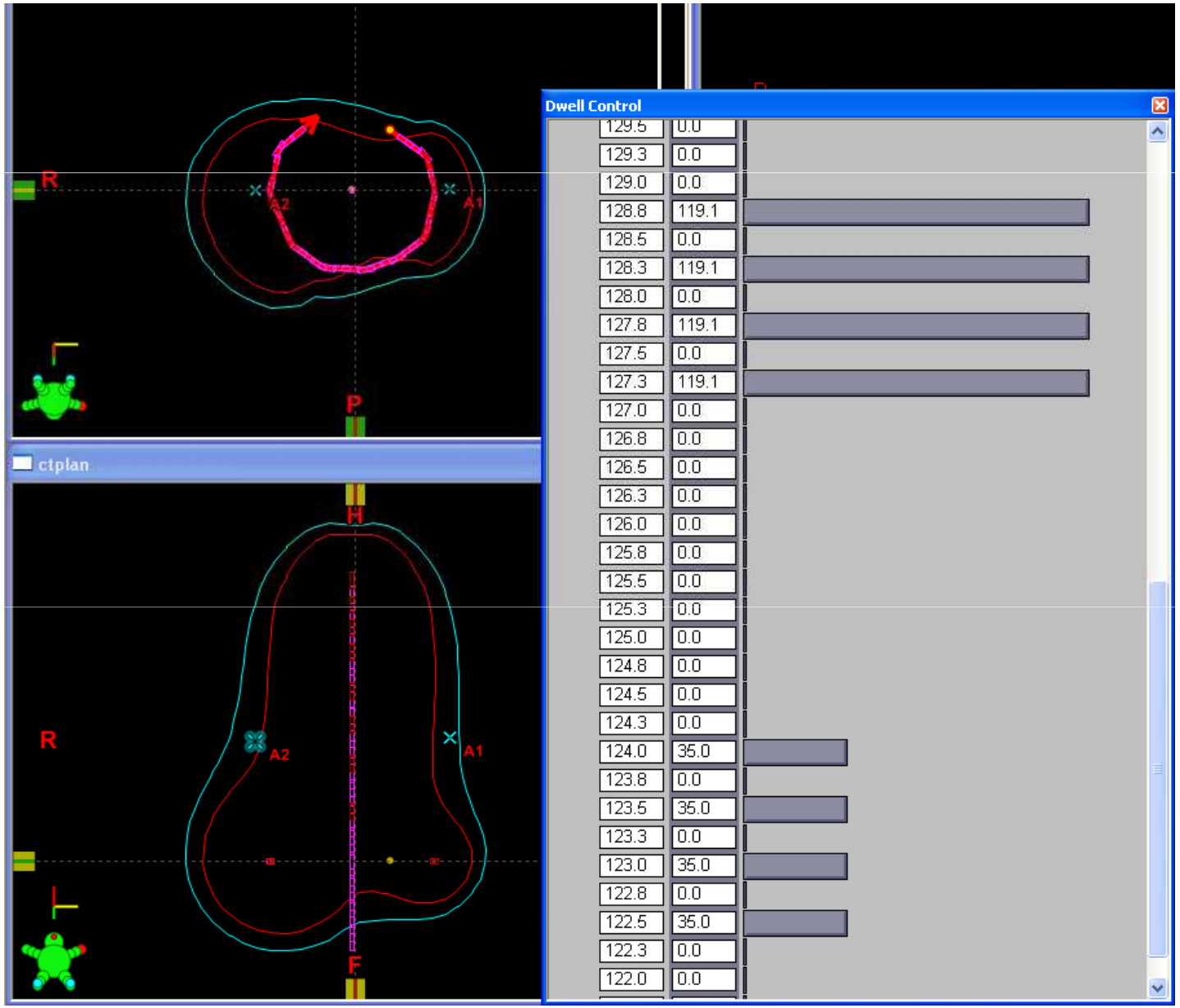
⇢ Normalisation on reference points
Modified loading

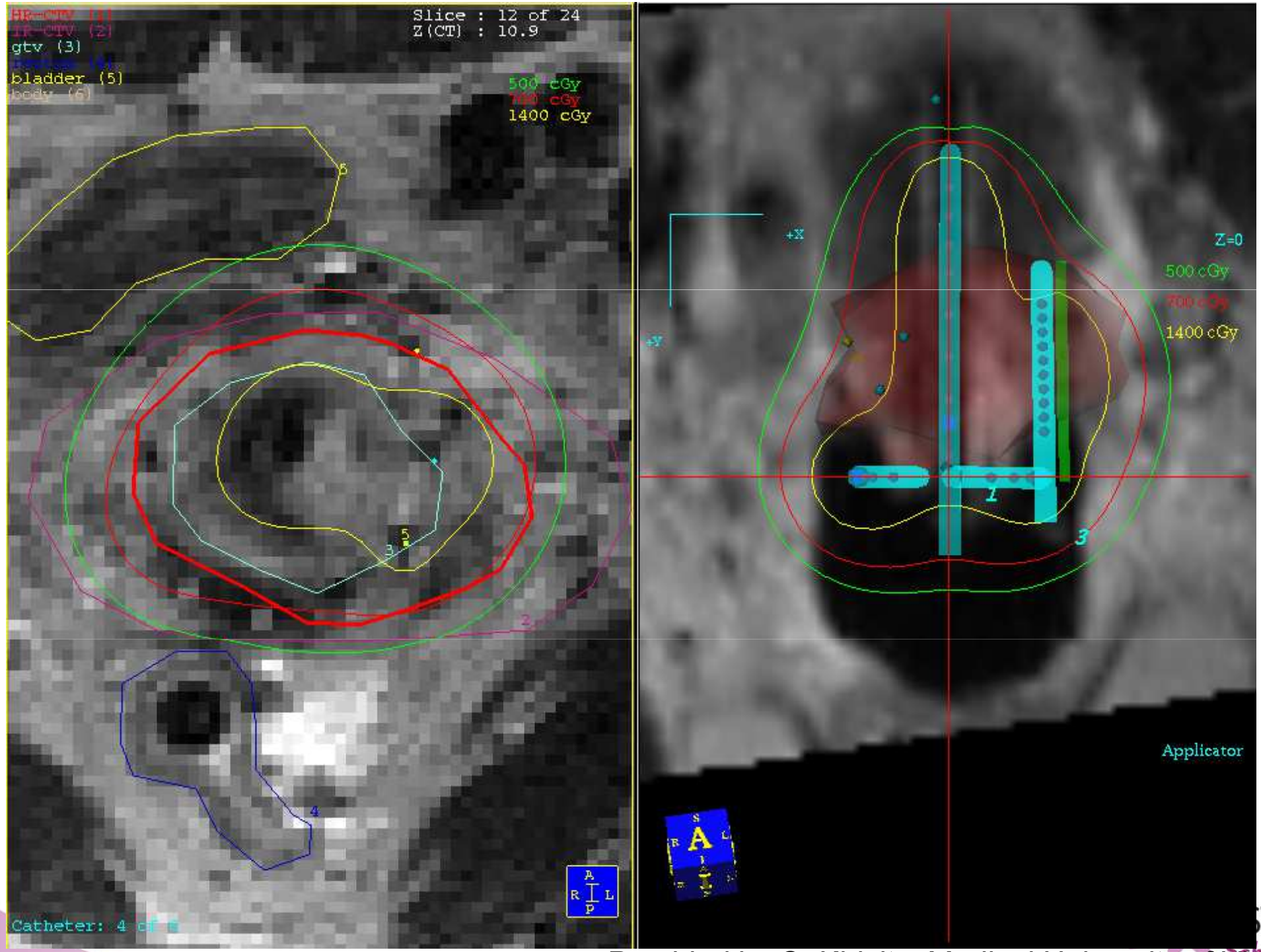


- **Absolute dwell times**
  Standard loading pattern

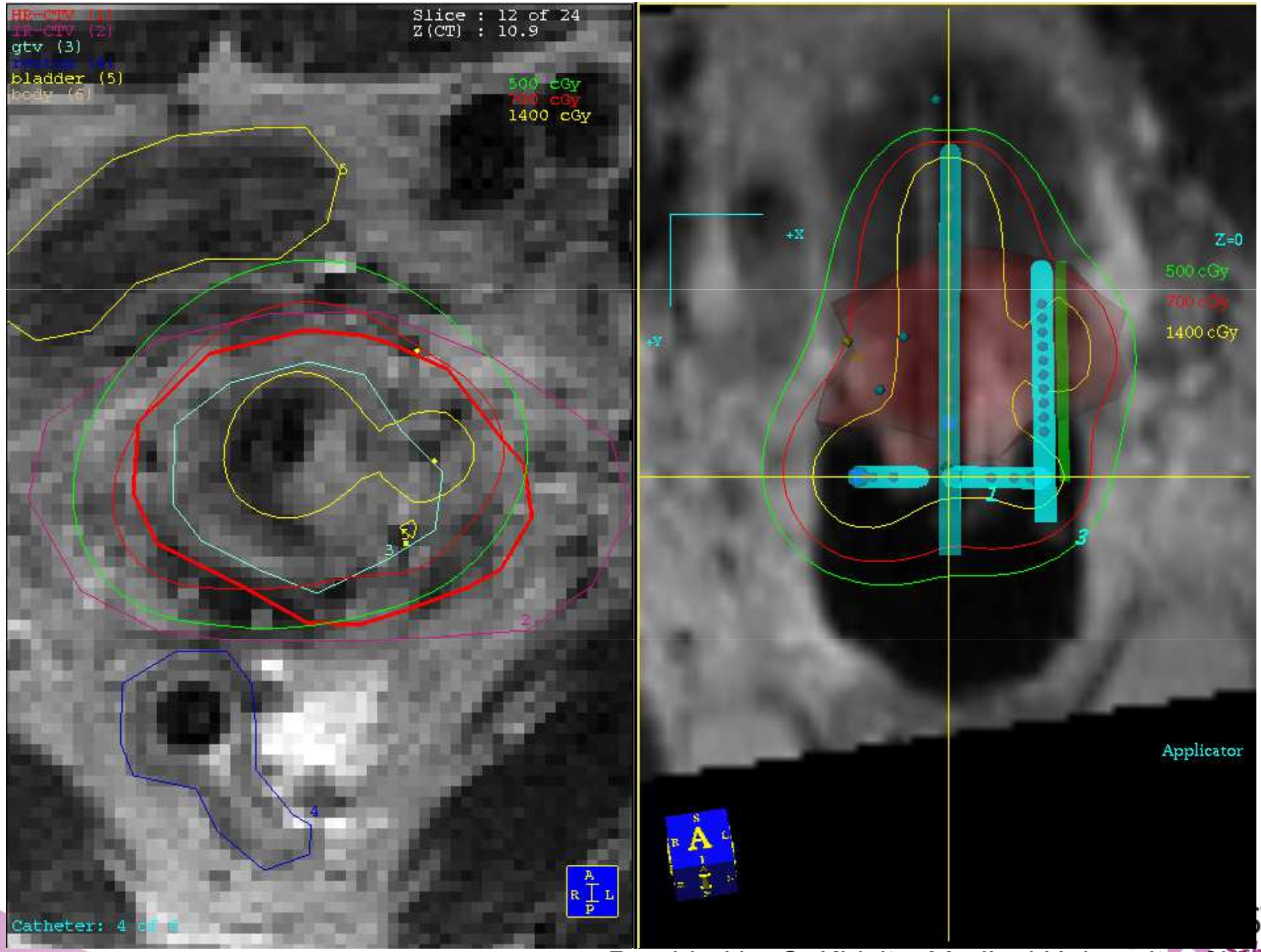


- **Absolute dwell times**
  Modified loading pattern

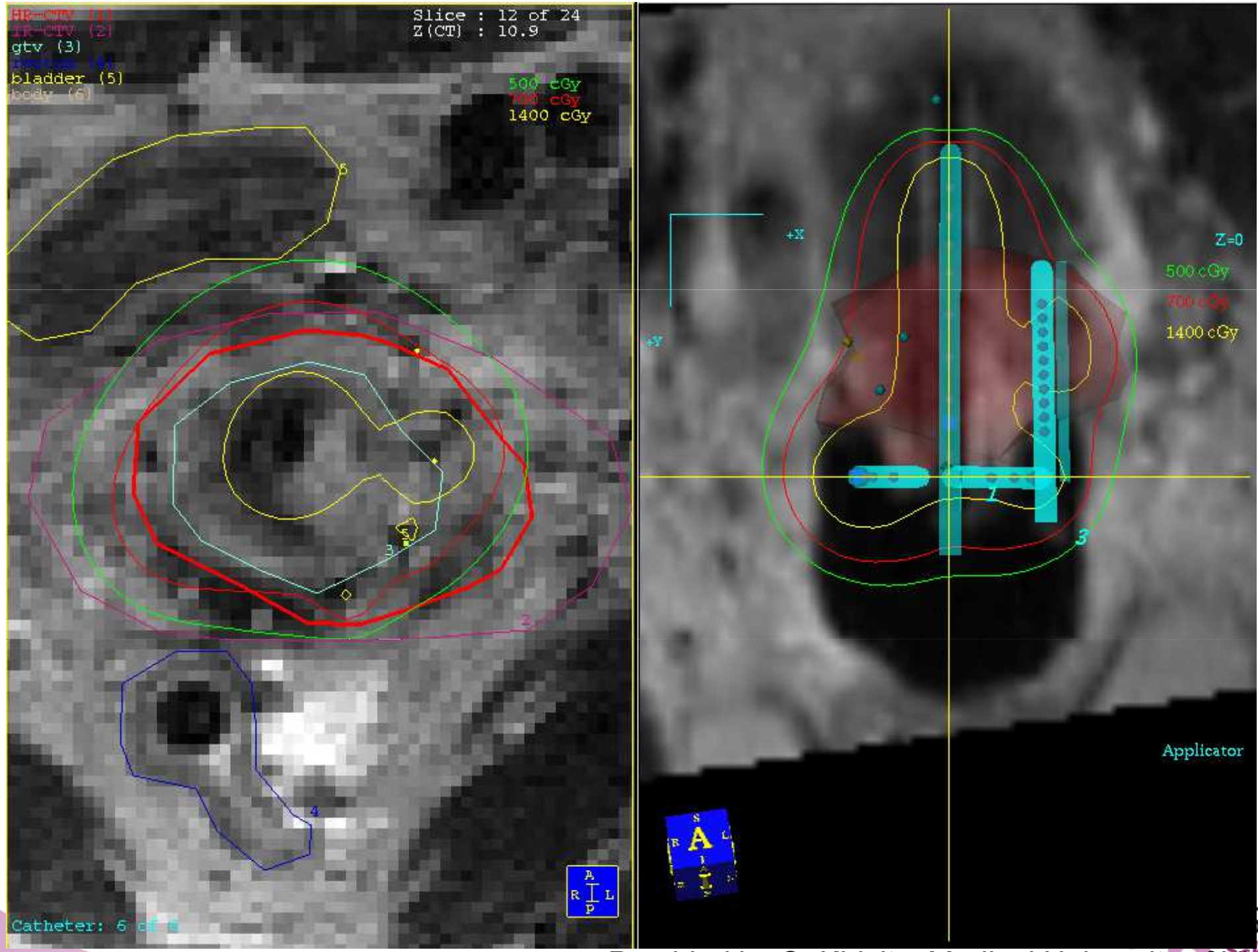




Provided by C. Kirisits, Medical University of Vienna



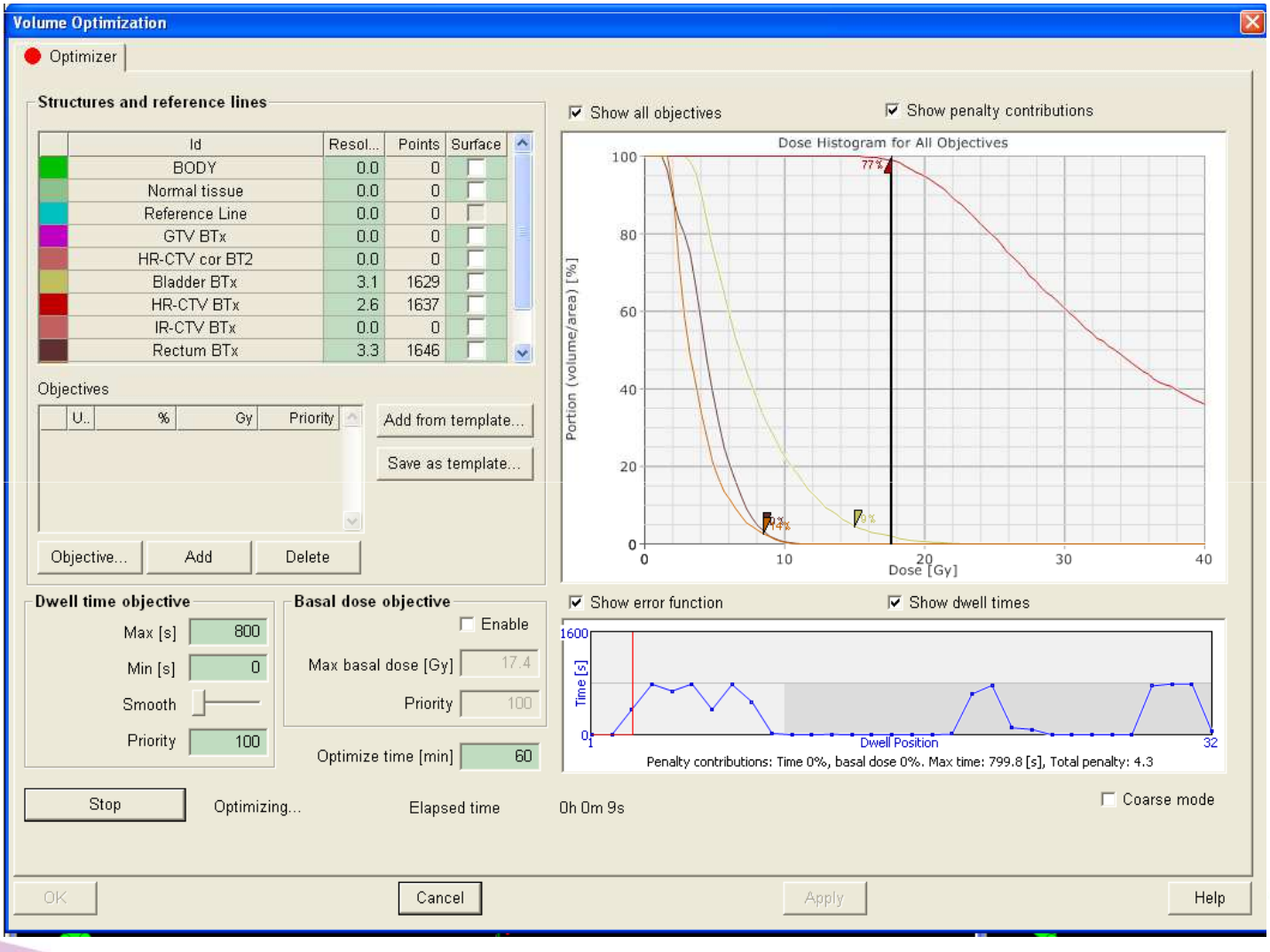
Provided by C. Kirisits, Medical University of Vienna



Provided by C. Kirisits, Medical University of Vienna

3. Inverse dose optimisation

- Controlled by DVH constraints
- Weighting factors for different structures



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Case from real life

- FIGO IIB with posterior involvement of the bladder
- Pelvic EBRT 45 Gy
- Concomitant chemotherapy
- MRI guided BT
- Intracavitary
- Vaginal mould
- PDR (imagine % for HDR users)
- HR-CTV = 38 cm^3
- Brachyvision ® (Varian Medical System)

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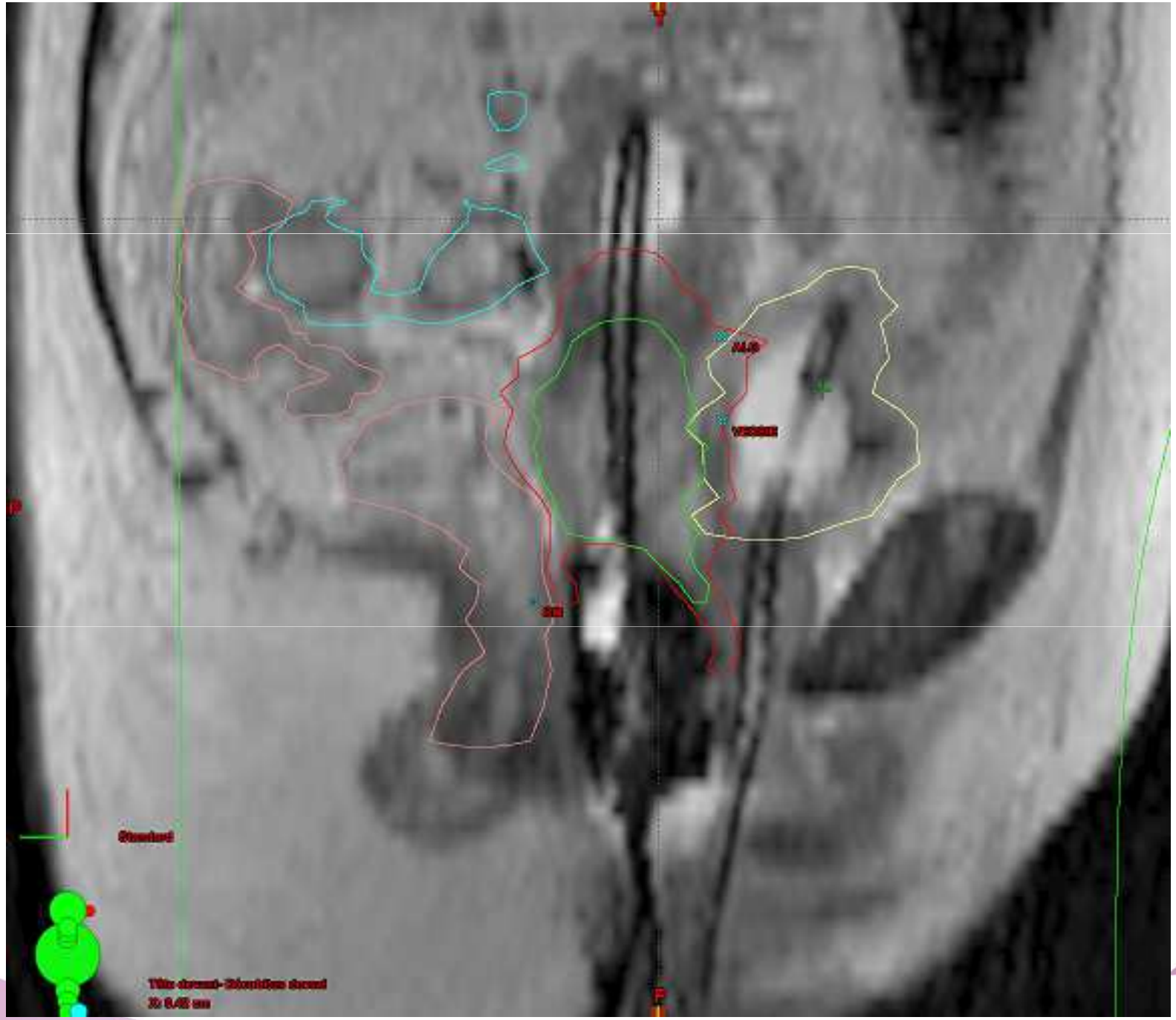
Delineation



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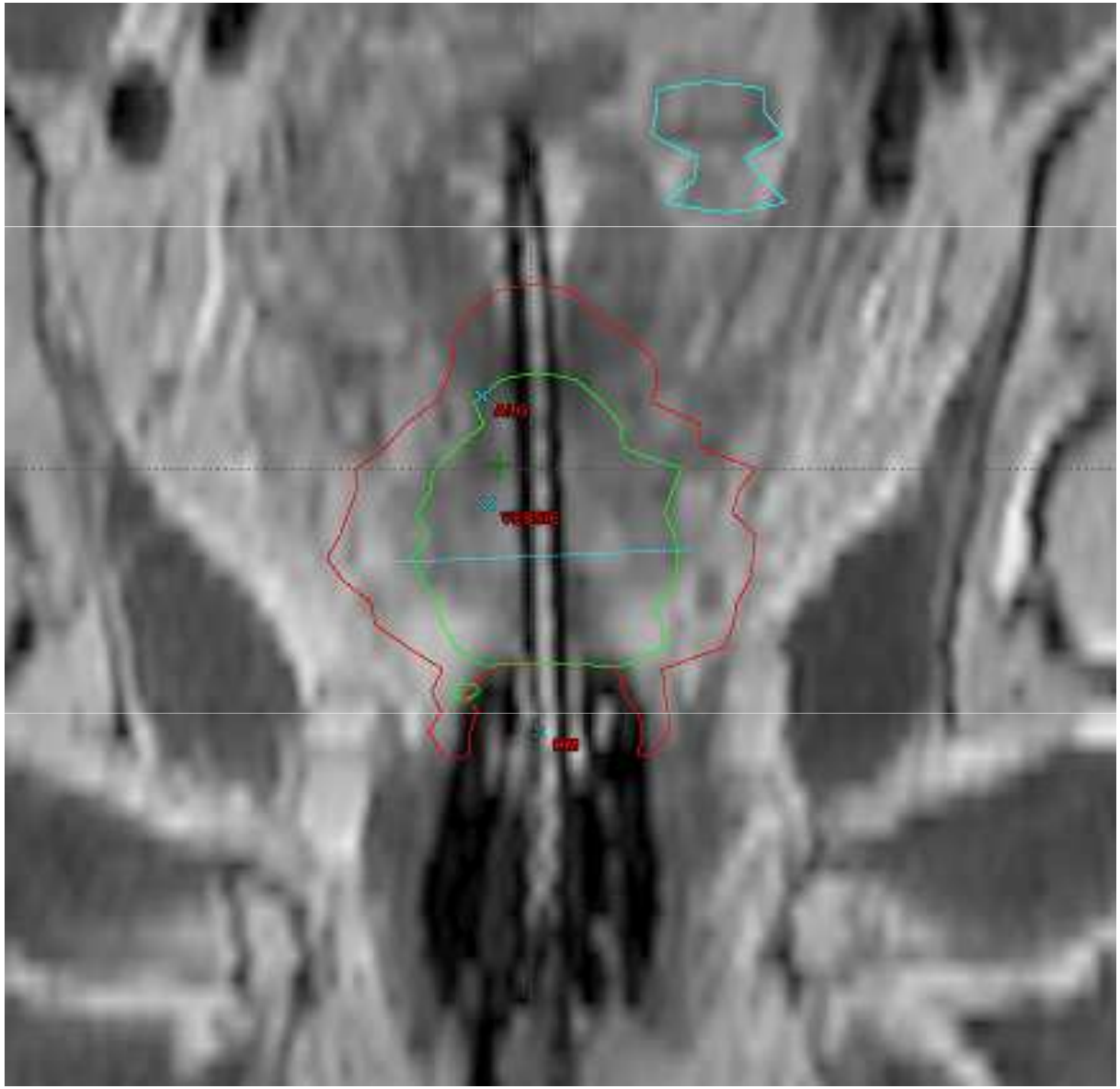
Delineation (2)



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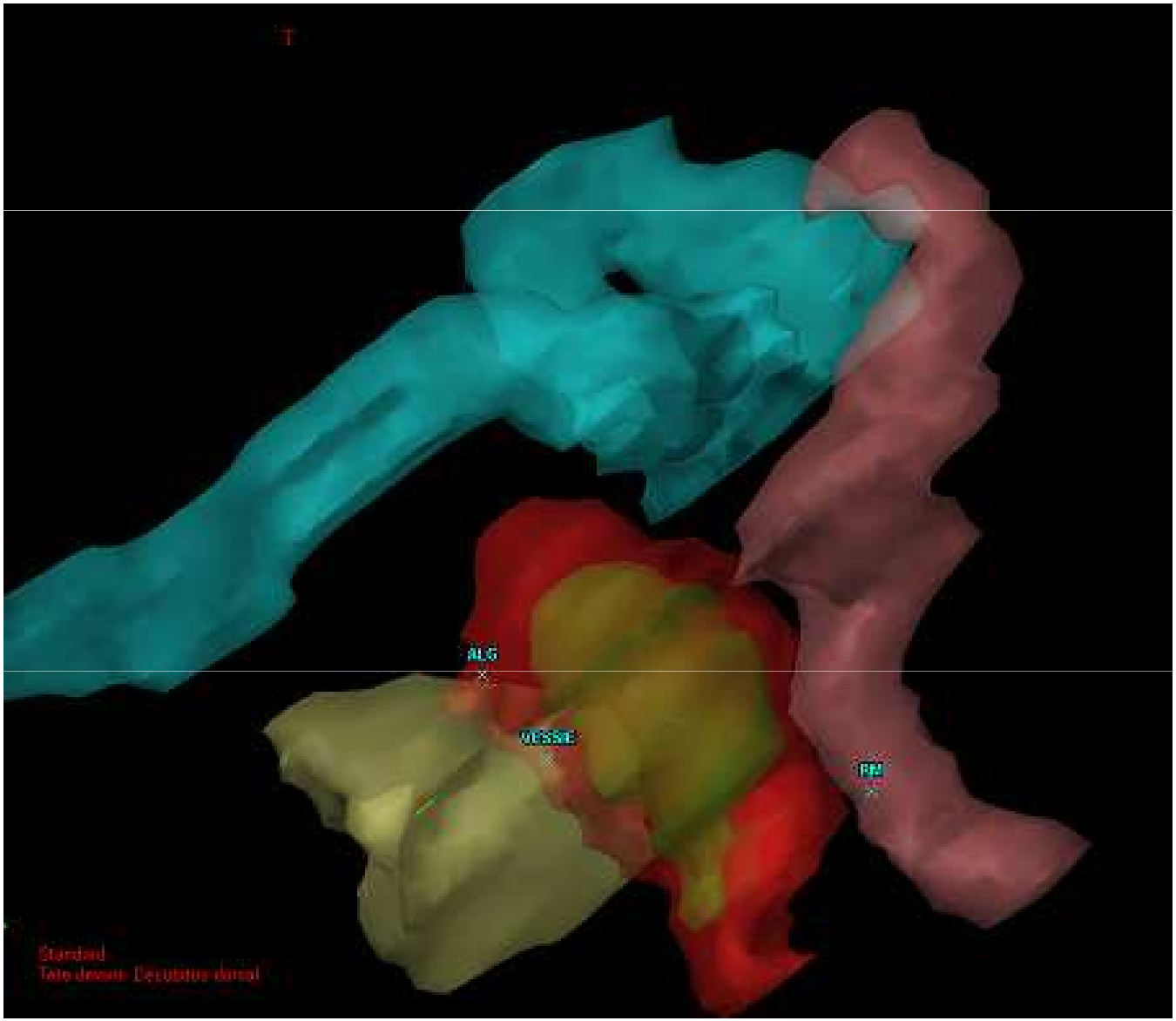
3D view



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Planning aims

EQD2	HDR
• D_{90} CTV_{HR} ≥ 85 Gy	≈ 7 Gy x 4
• D_{90} CTV_{IR} > 60 Gy	≈ 3.5 Gy x 4
• D_{2cm3} Bladder ≤ 85 Gy	≈ 5,9 Gy x 4
• D_{2cm3} Rectum ≤ 70-75 Gy	≈ 5 Gy x 4
• D_{2cm3} Sigmoid ≤ 70-75 Gy	≈ 5 Gy x 4

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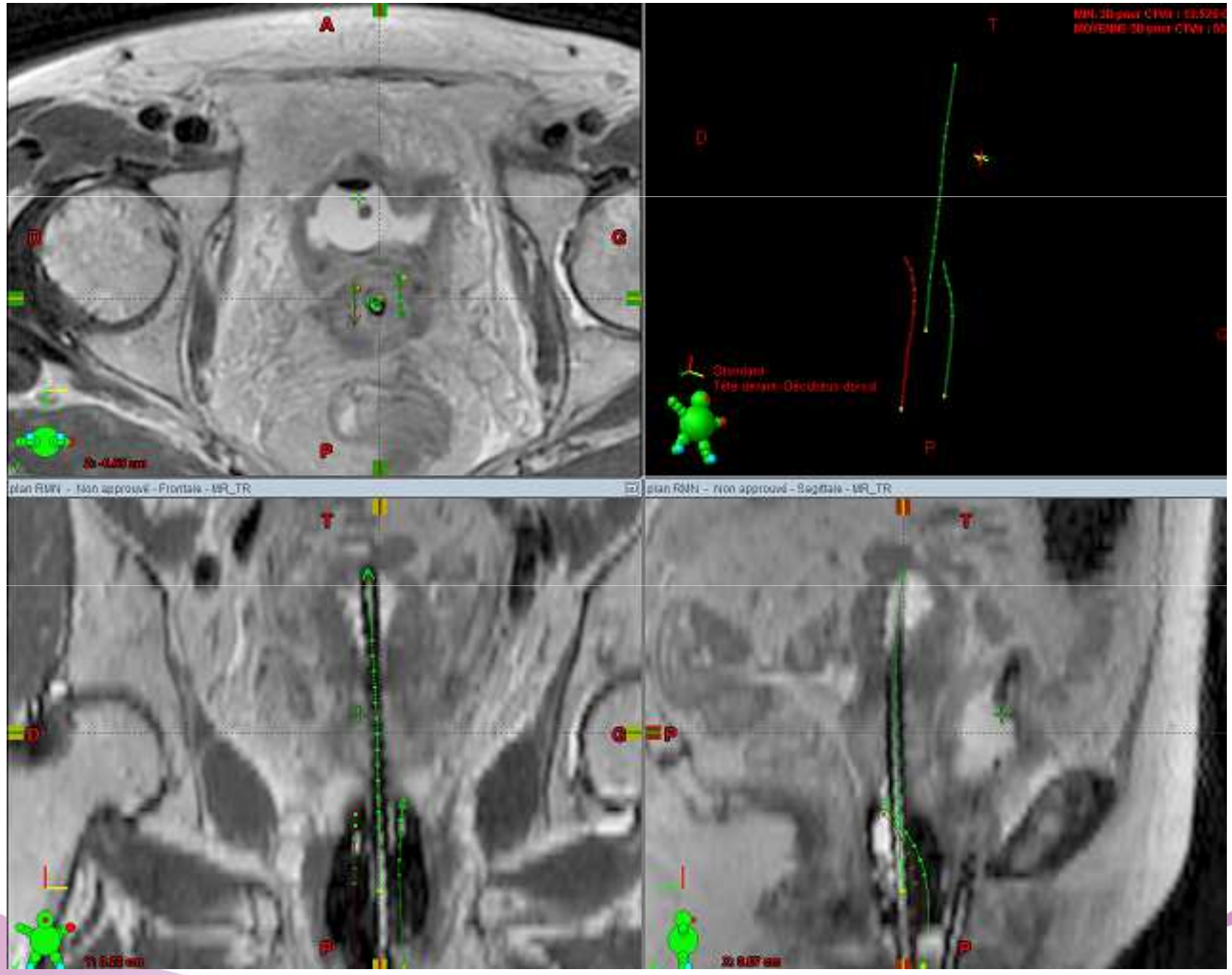
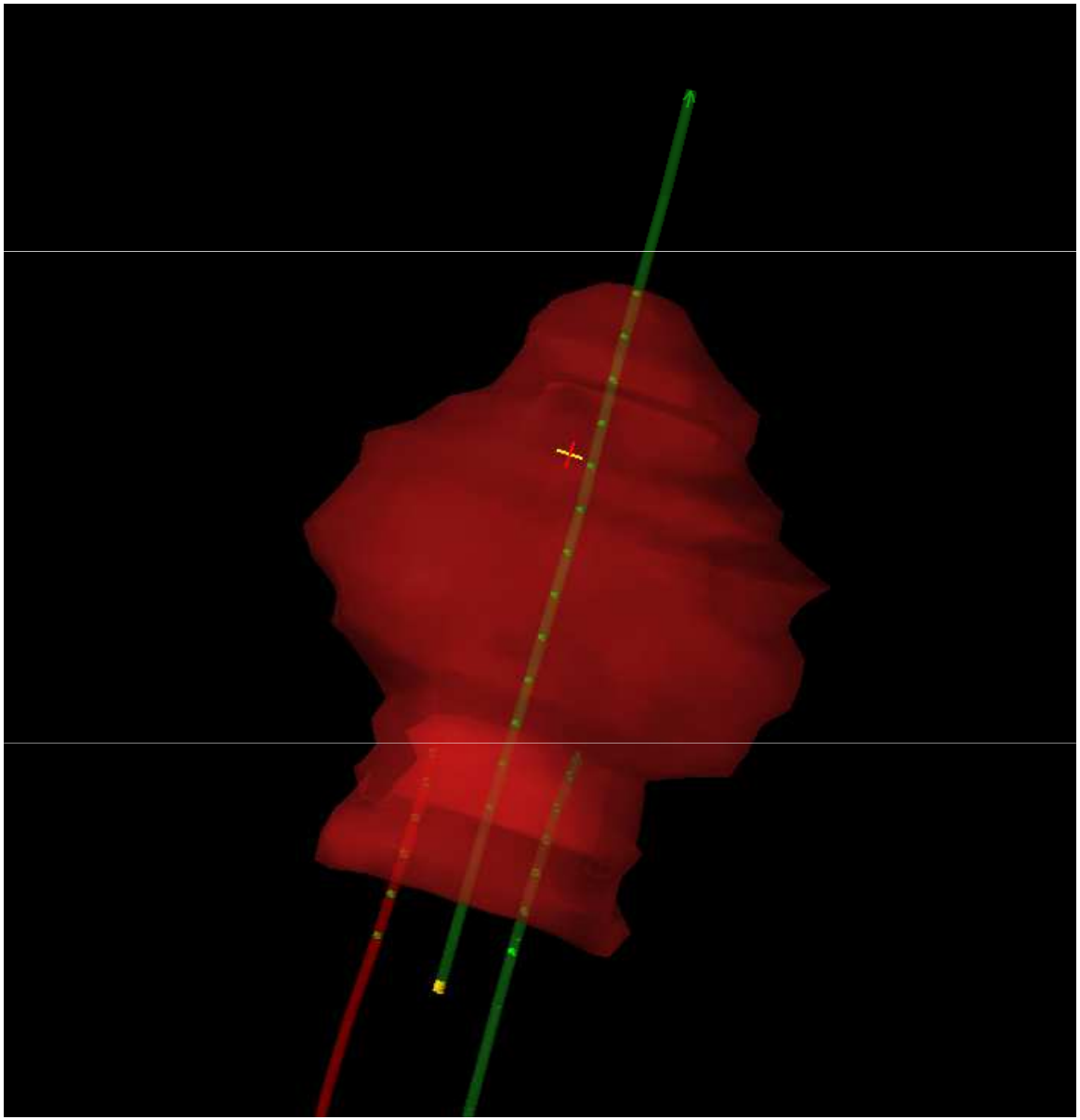
1 st setp: Applicator reconstruction



2 nd step: Activation



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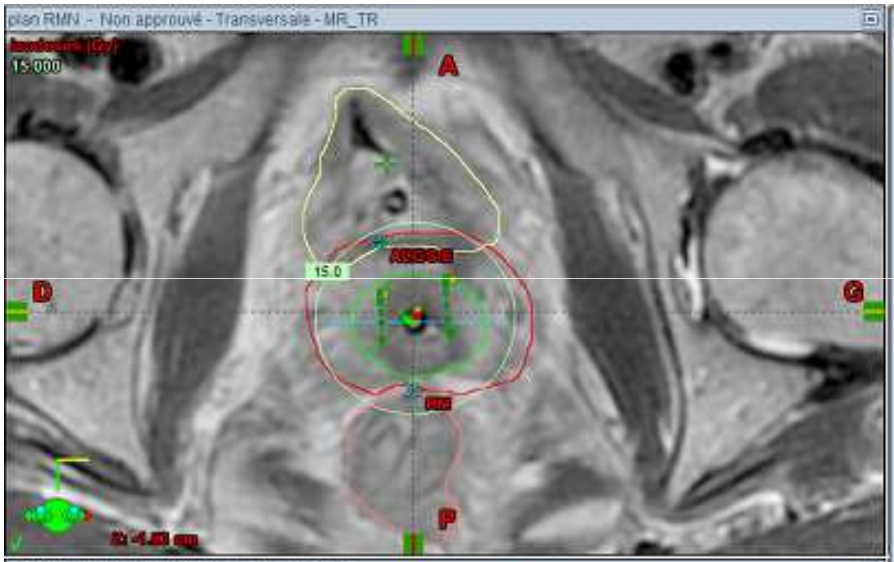
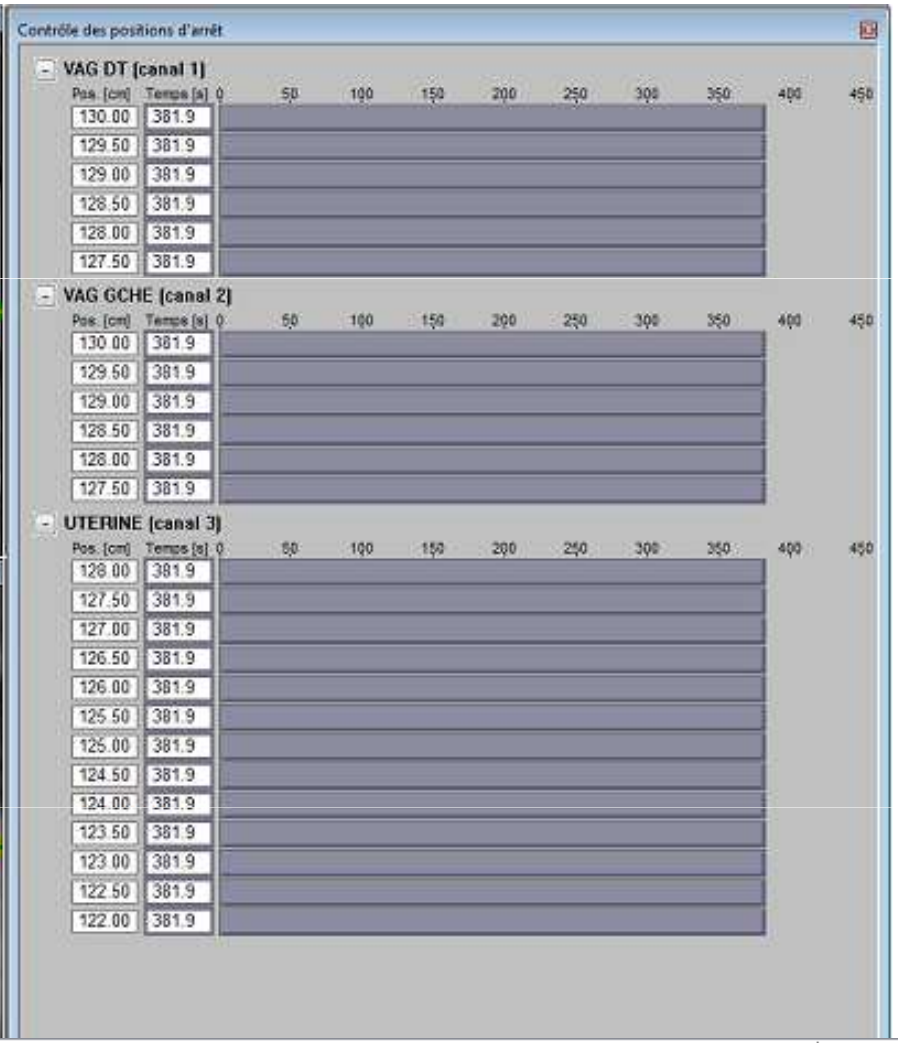
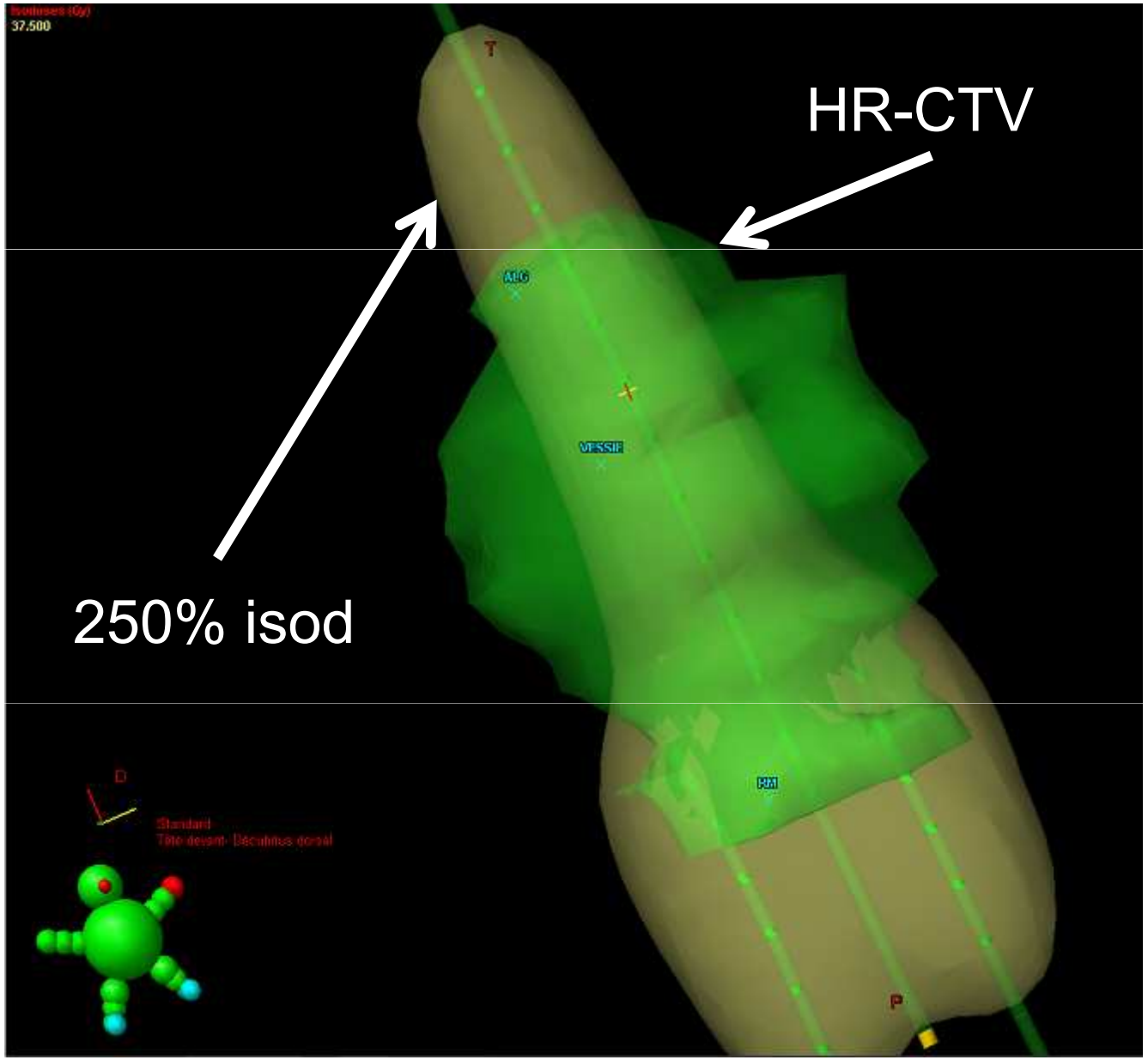
3 rd step: Plannification





Structure	Index		Valeur cible	Valeur réelle
CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	77.94
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	43.55
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	17.50
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	18.24
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	7.44
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	106.83

Manual optimization



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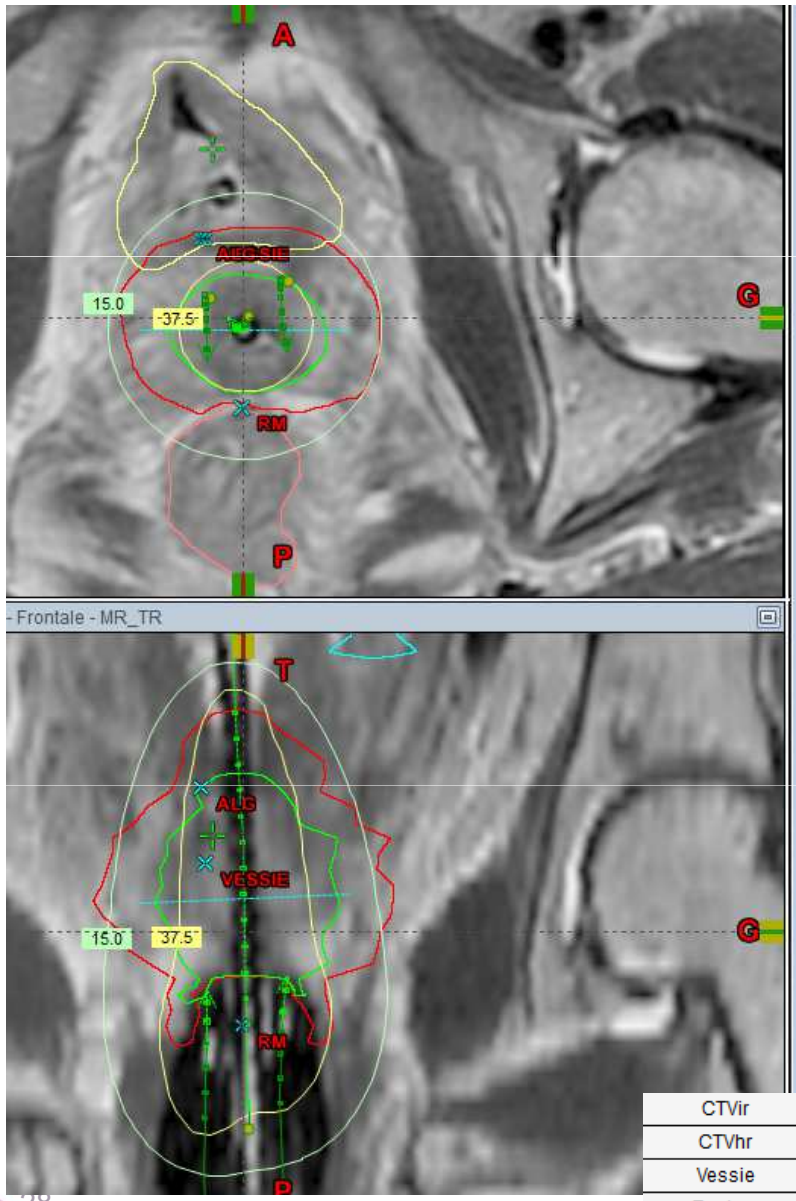
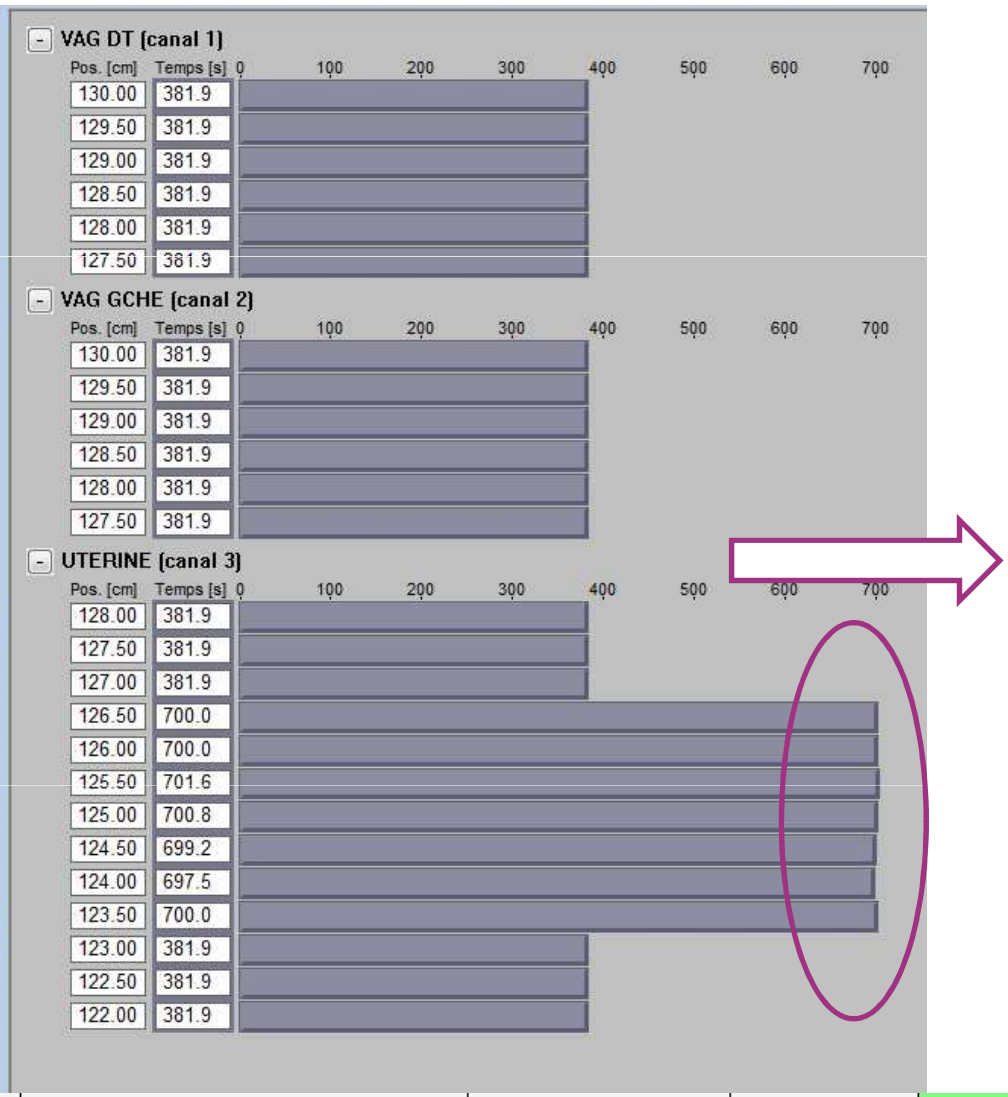
Manual optimization (2)





CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	96.41
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	74.75
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	24.26
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	21.41
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	9.94
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	147.91

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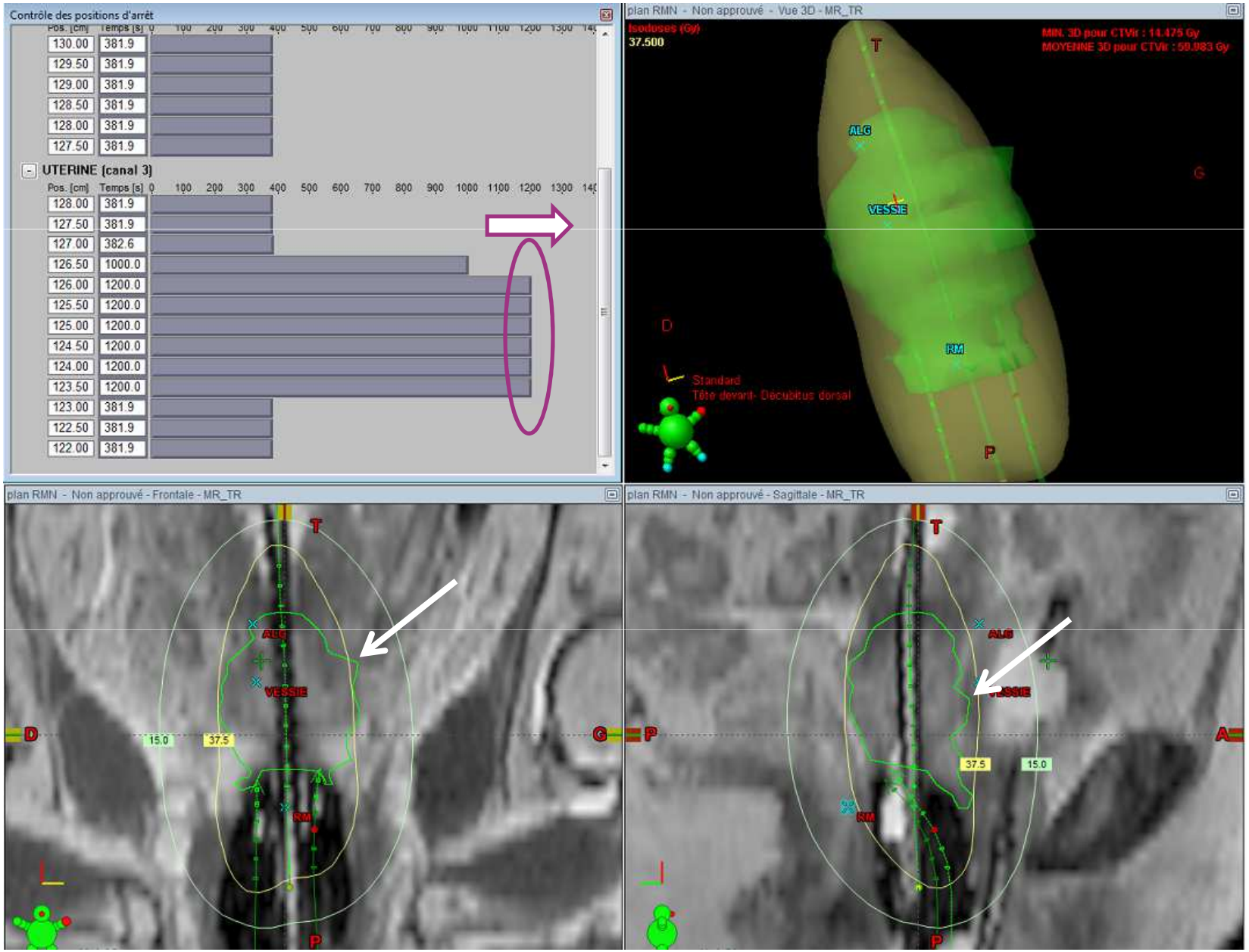
Manual optimization (3)



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Manual optimization (4)

Structure	Index		Valeur cible	Valeur réelle
CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	100.00
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	97.21
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	34.58
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	26.49
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	13.50
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	212.95

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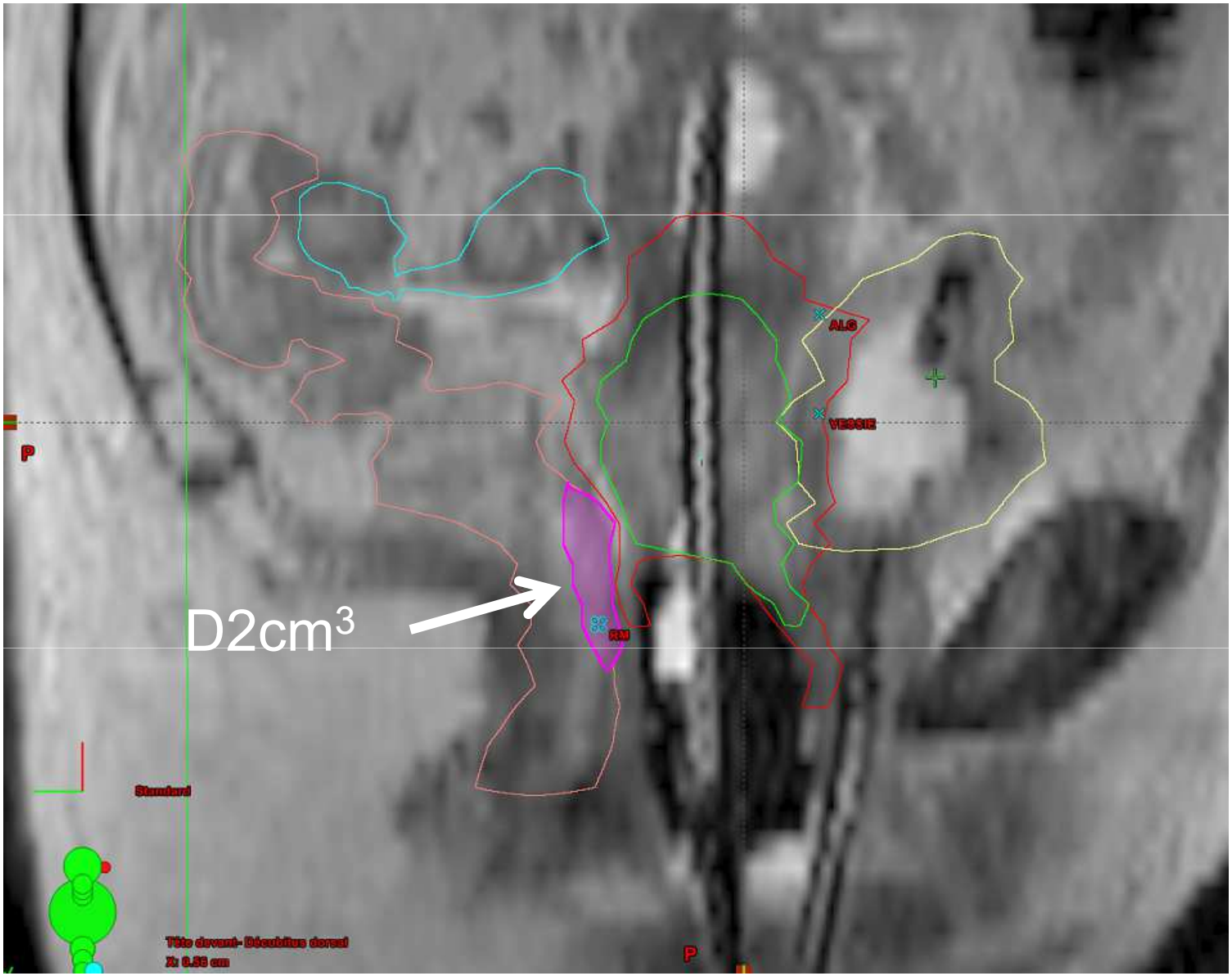
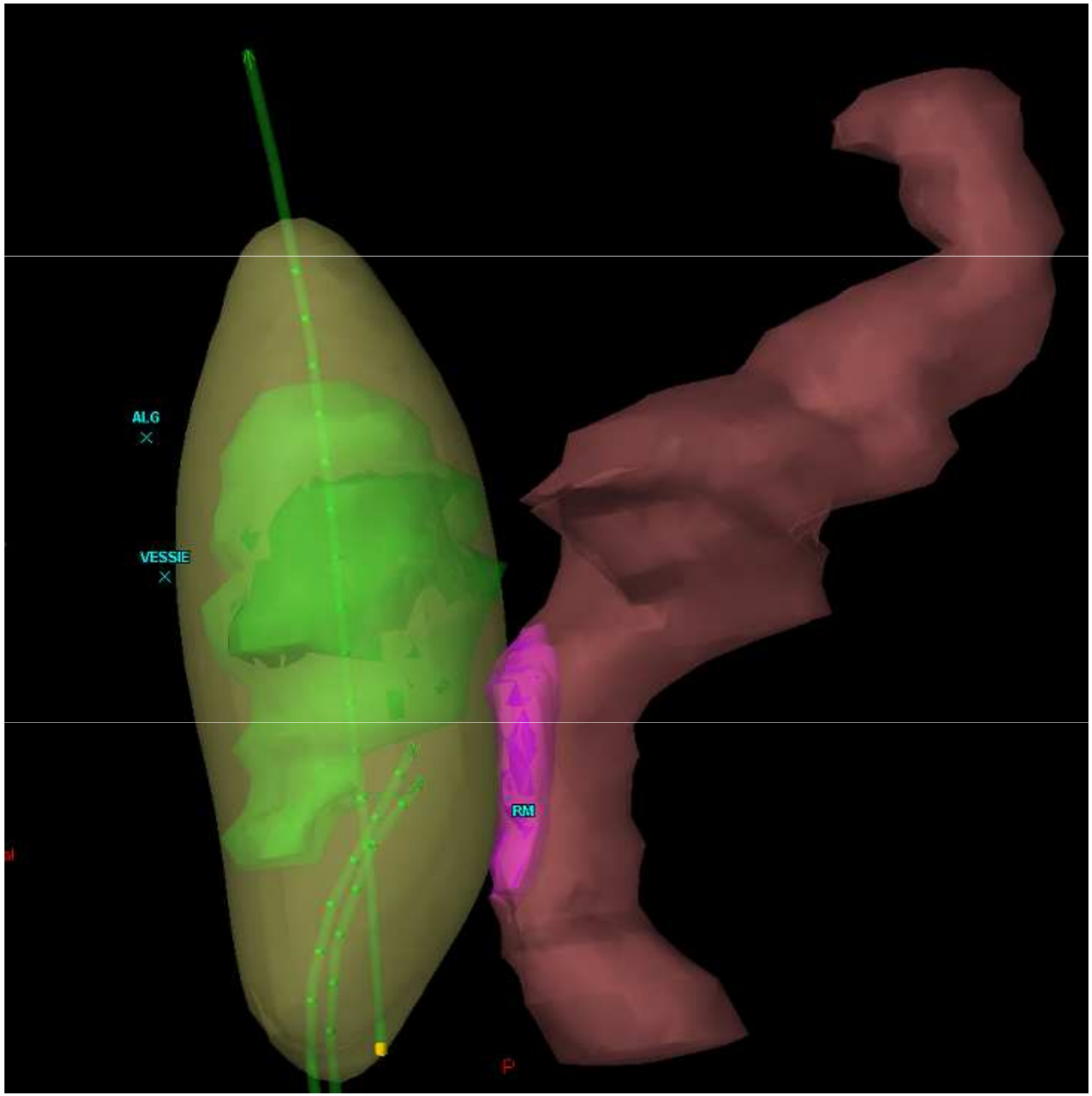
Manual optimization (5)



Manual optimization (6)



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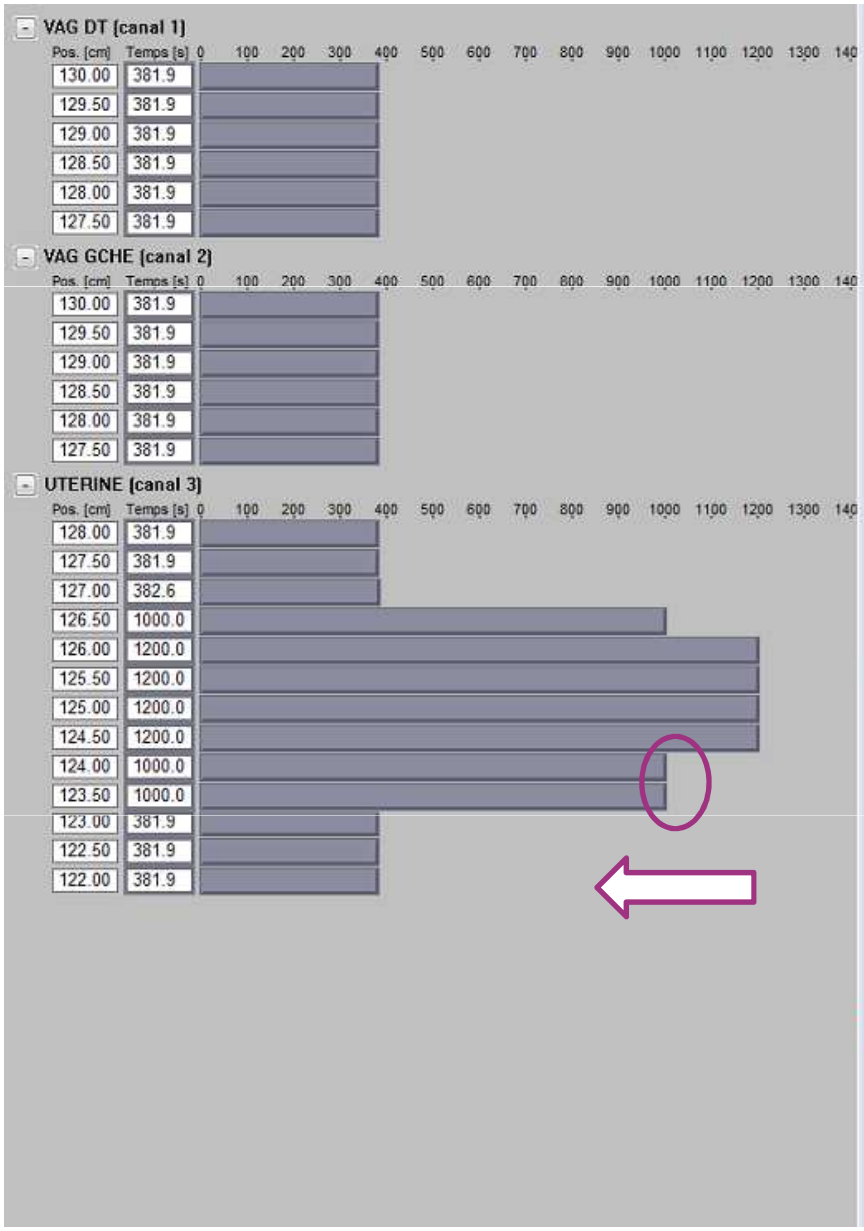
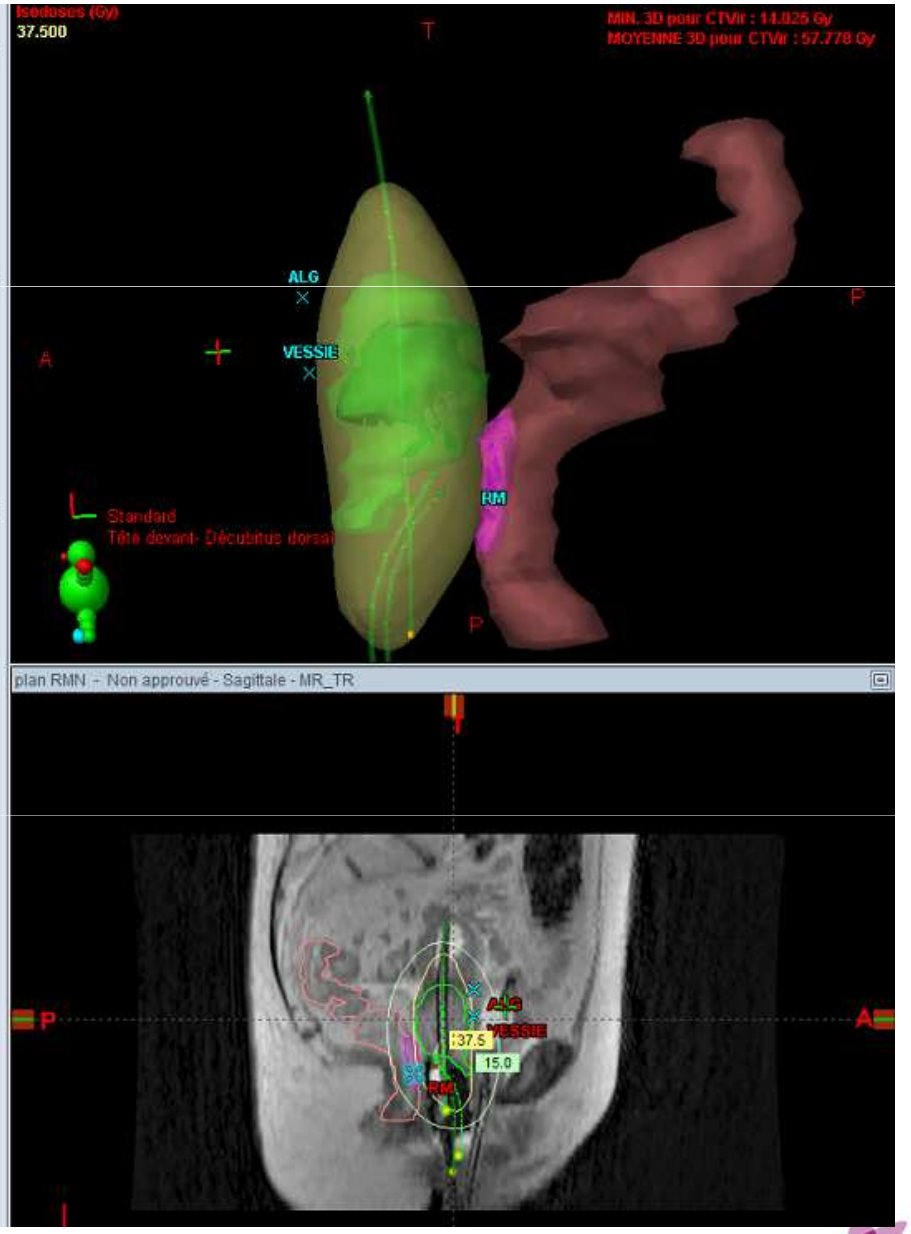
Manual optimization (7)





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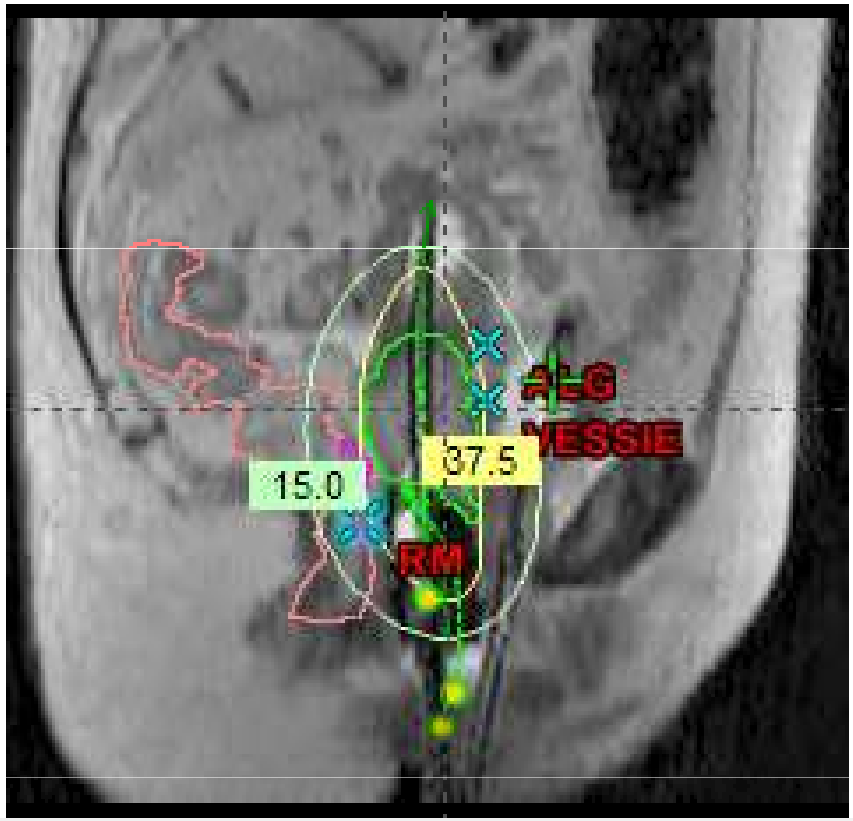
Manual Optimization (8)



Structure	Index		Valeur cible	Valeur réelle
CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	100.00
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	95.96
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	33.23
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	25.56
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	13.25
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	204.69

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PDR specificity

- Adaptation of the number of pulses
- Respect max dose / pulse of 0.5 – 0.6 Gy
- Number of pulses ranging from 30 to 60
- Example: 60 pulses

- Dose per pulse:

Structure	Index		Valeur cible	Valeur réelle
CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	99.98
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	95.14
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	0.54
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	0.42
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	0.22
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	202.19

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EqD2 (1)

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	α/β [Gy]	10		Department of Radiotherapy and Radiobiology, Medical University of Vienna										
2	$T_{1/2}$ [h]	1.5		Neither the authors nor anybody else can accept any legal responsibility or liability for any errors or omissions that may be made.										
3	μ [1/h]	0.46												
4														
5	**EBRT 1**		BED	EQD_2		**EBRT 2**		BED	EQD_2		**TOTAL EBRT**			
6			[Gy]	[Gy]				[Gy]	[Gy]			BED	EQD_2	
7	number of fractions n					number of fractions n						[Gy]	[Gy]	
8	dose / fraction d [Gy]		0.0	0.0		dose / fraction d [Gy]		0.0	0.0		EBRT 1+2	0.0	**0.0**	
9	TOTAL	0.0	0.0	**0.0**		TOTAL	0.0	0.0	**0.0**					
10														
11	**PDR 1**		BED	EQD_2		**PDR 2**		BED	EQD_2					
12			[Gy]	[Gy]				[Gy]	[Gy]		**TOTAL PDR**			
13	pulse dose $d_{p,1}$ [Gy]					pulse dose $d_{p,2}$ [Gy]						BED	EQD_2	
14	number of pulses n_1					number of pulses n_2						[Gy]	[Gy]	
15	pulse repetition time [h]					pulse repetition time [h]					PDR 1+2	0.0	**0.0**	
16	pulse irradiation time t_1 [h]					pulse irradiation time t_2 [h]								
17	dose fraction 1 d_1 [Gy]	0.0	0.0	**0.0**		dose fraction 2 d_2 [Gy]	0.0	0.0	**0.0**		**TOTAL EBRT + PDR**			
18														
19												BED	EQD_2	
20												[Gy]	[Gy]	
21											EBRT + PDR	0.0	**0.0**	
22														
23														
24						**treatment planning**	d	BED	EQD_2					
25						**EBRT + PDR**	[Gy]	[Gy]	[Gy]					
26														
27						total dose constraint		0.0						
28						**dose / pulse PDR**	**#DIV/0!**							
29														
30														

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EqD2 (2)

	Absolute dose	EqD2	EBRT + BT	Planning aims
D90 HR-CTV	41.35	44.4	**88.7**	85
D90 IR-CTV	23.20	22.4	**66.7**	60
D2cm^3 Bladder	32.48	34.1	**77.3**	80
D2cm^3 Rectum	25.20	24.0	**67.2**	70
D2cm^3 Sigmoid	13.08	10.4	**53.6**	70?

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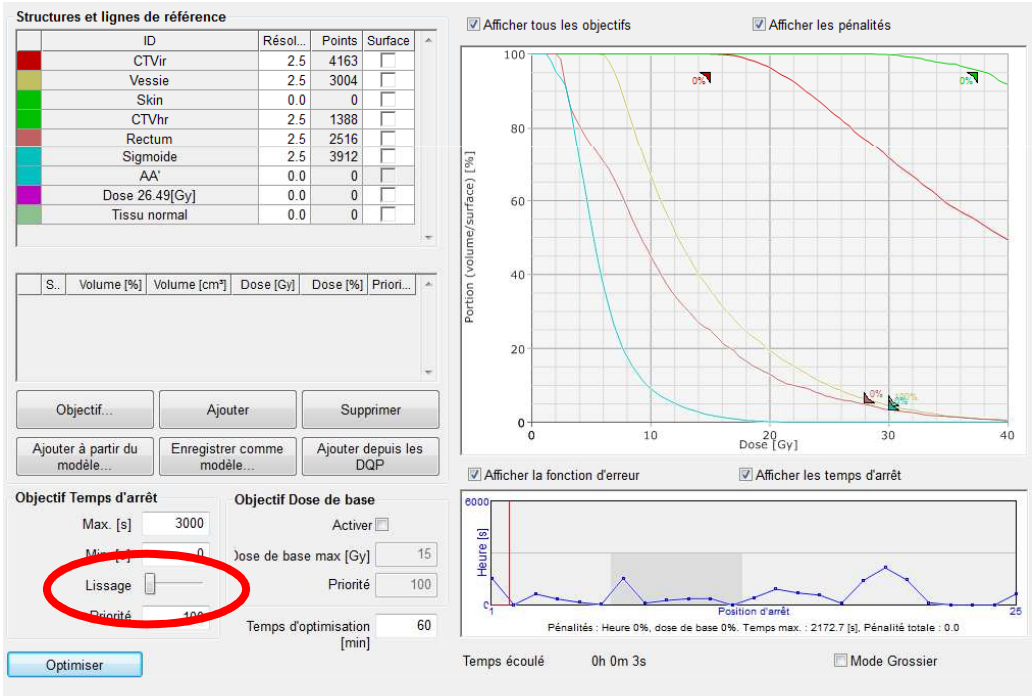
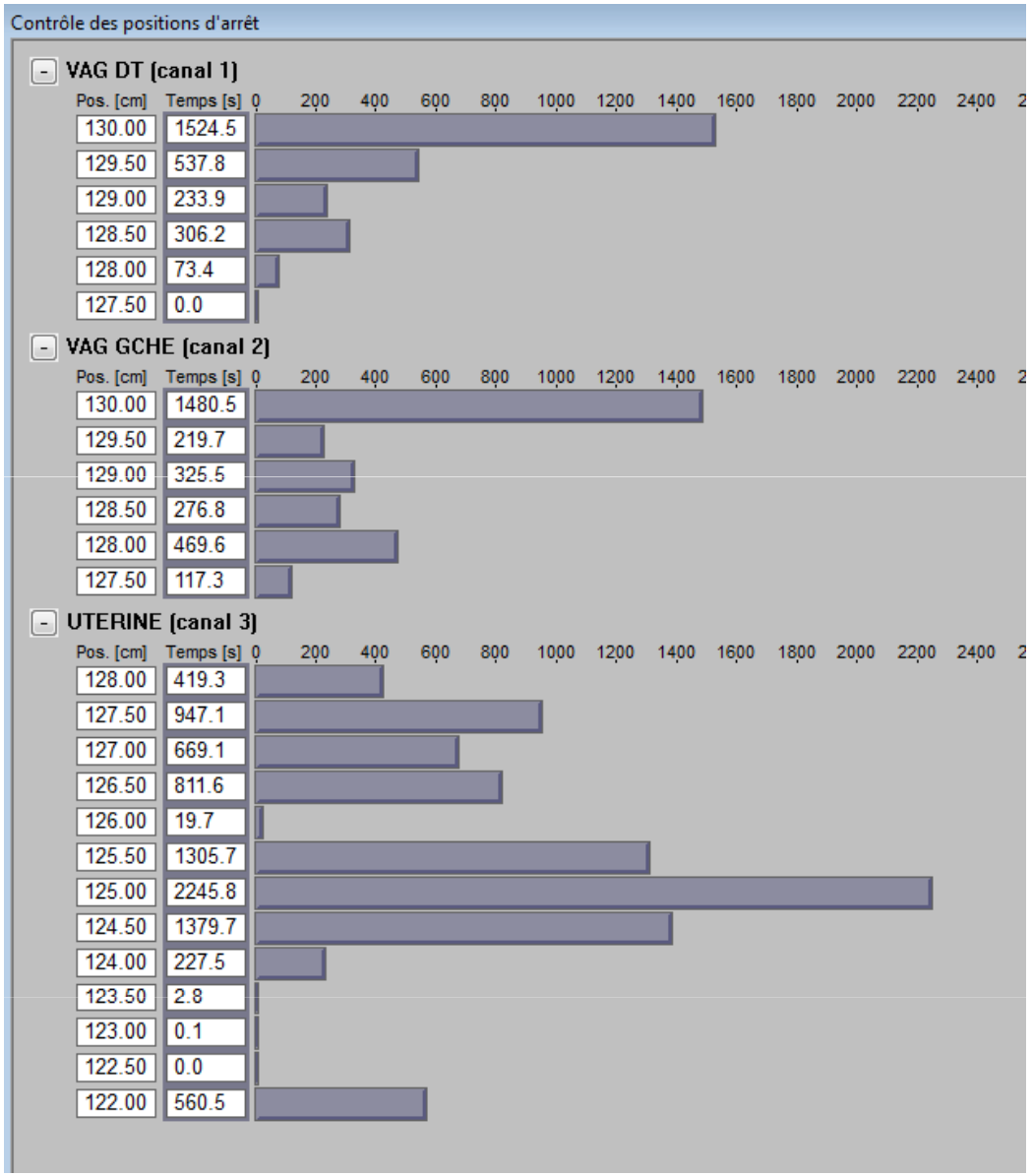
Inverse planning (1)





Structure	Index		Valeur cible	Valeur réelle
CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	99.99
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	94.38
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	30.50
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	27.45
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	13.74
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	194.40

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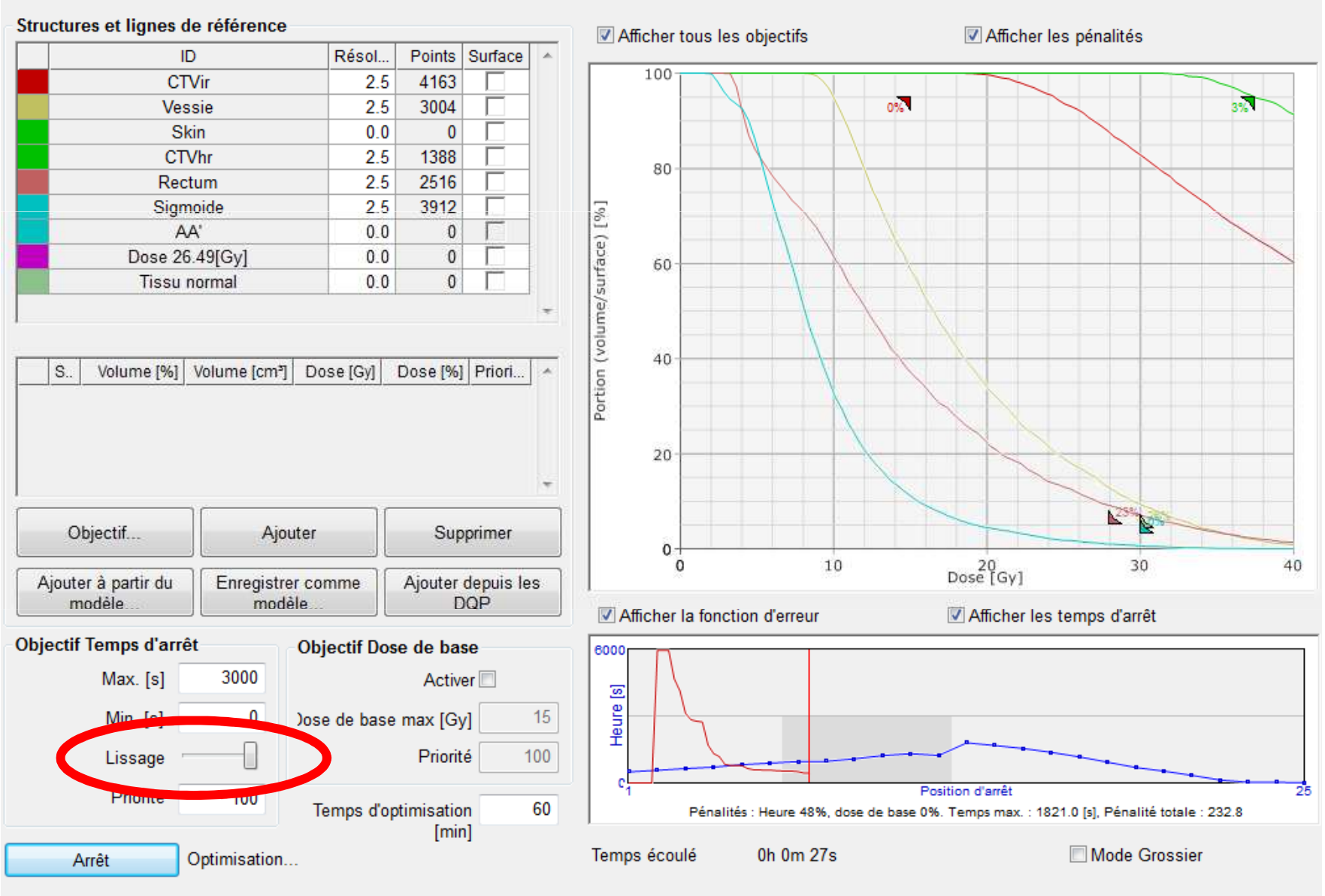
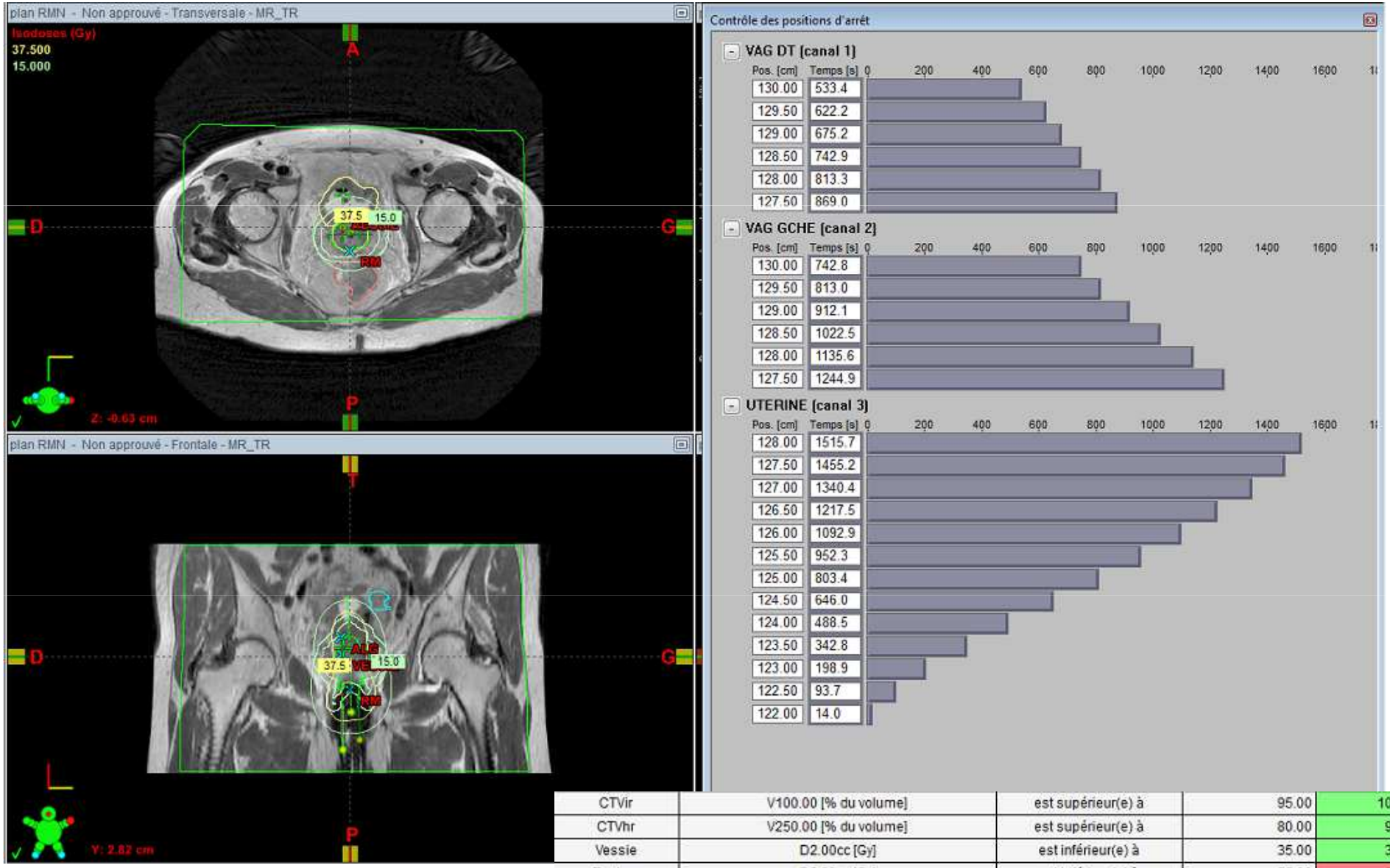
Inverse planning (2)

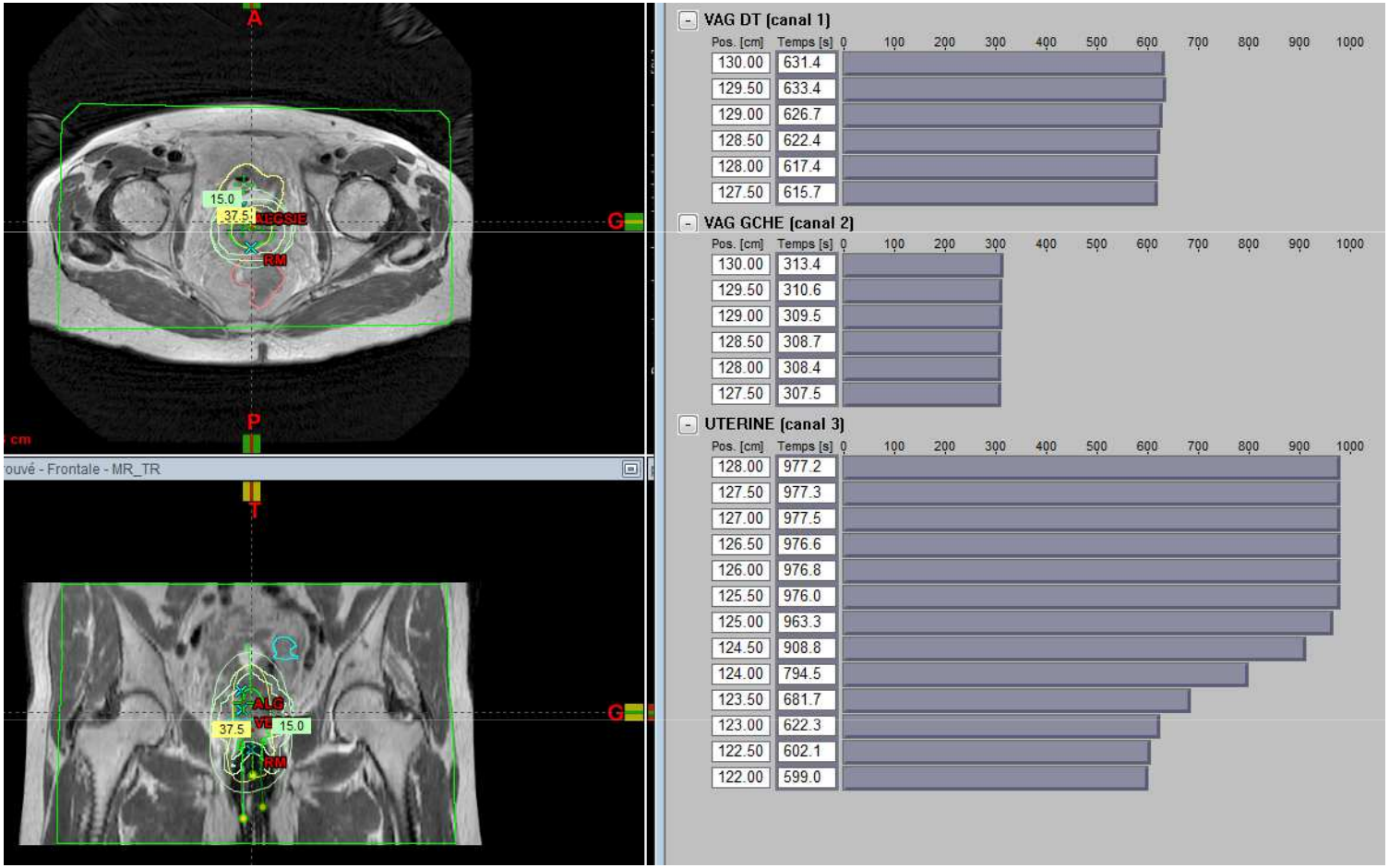


Inverse planning (3)



CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	100.00
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	94.45
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	33.85
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	31.46
Sigmoïde	D2.00cc [Gy]	est inférieur(e) à	25.00	20.04
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	330.28

Inverse planning (4)



Structure	Index		Valeur cible	Valeur réelle
CTVir	V100.00 [% du volume]	est supérieur(e) à	95.00	100.00
CTVhr	V250.00 [% du volume]	est supérieur(e) à	80.00	94.49
Vessie	D2.00cc [Gy]	est inférieur(e) à	35.00	33.05
Rectum	D2.00cc [Gy]	est inférieur(e) à	25.00	28.27
Sigmoide	D2.00cc [Gy]	est inférieur(e) à	25.00	16.44
Skin	V100.00 [cm³]	est inférieur(e) à	250.00	246.47

Inverse planning (5)

	Manual	IP full	IP moy	IP low
D90 IR-CTV (%)	100	100	100	100
D90 HR-CTV (%)	97.2	94.4	94.5	94.5
D2cm^3 bladder (Gy)	34.6	30.5	33.1	33.9
D2cm^3 Rectum (Gy)	26.5	27.5	28.3	31.5
D2cm^3 Sigmoid (Gy)	13.5	13.4	16.4	20.0
V15 Gy (cm^3)	213	194.40	246.5	333.3

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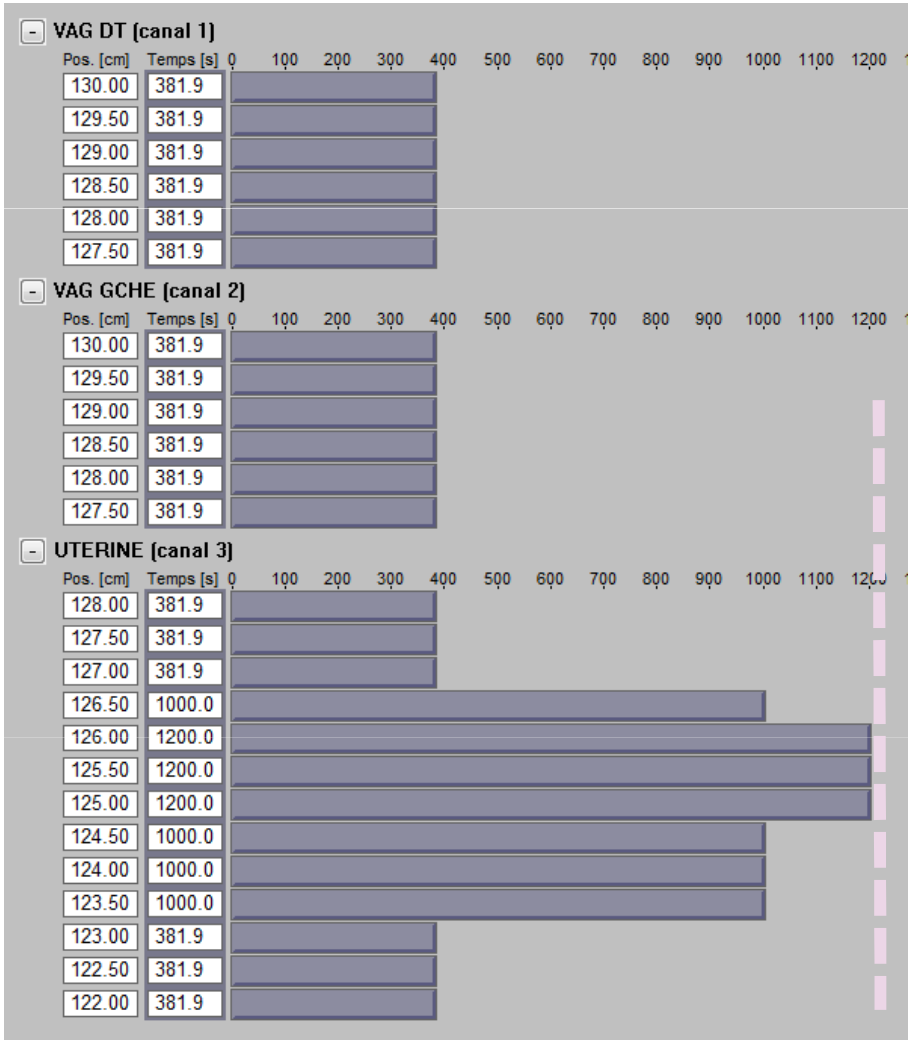
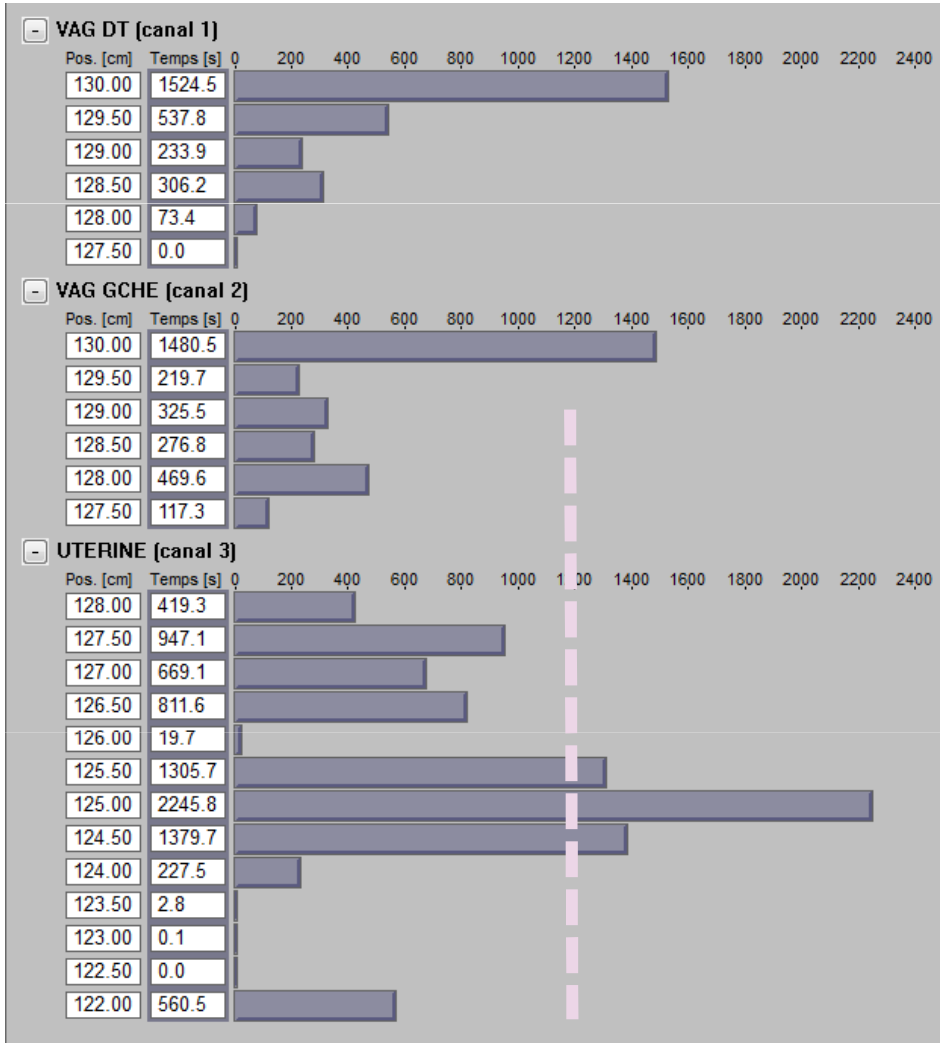
Equivalent plans?





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Should we give up the points?

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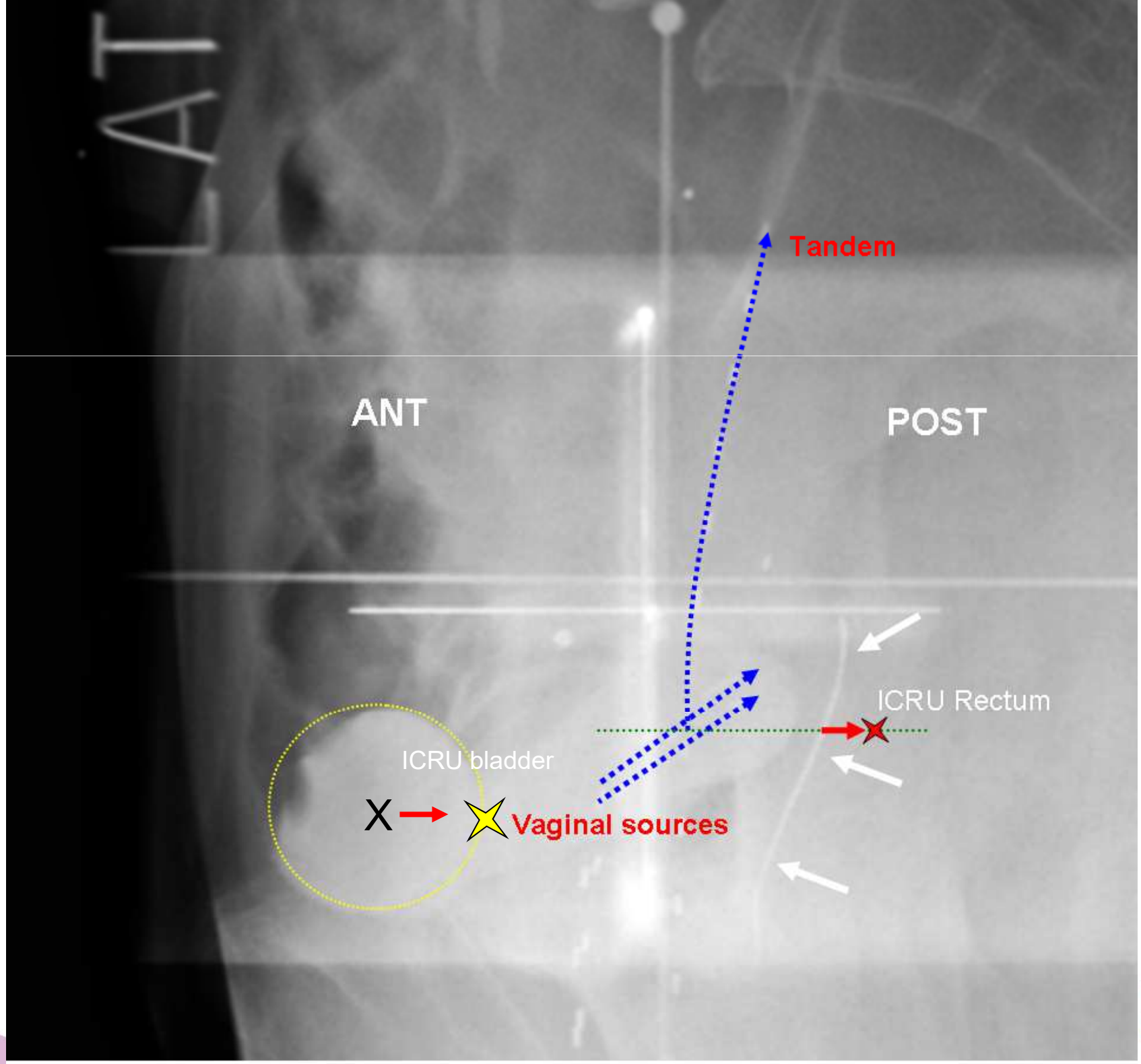

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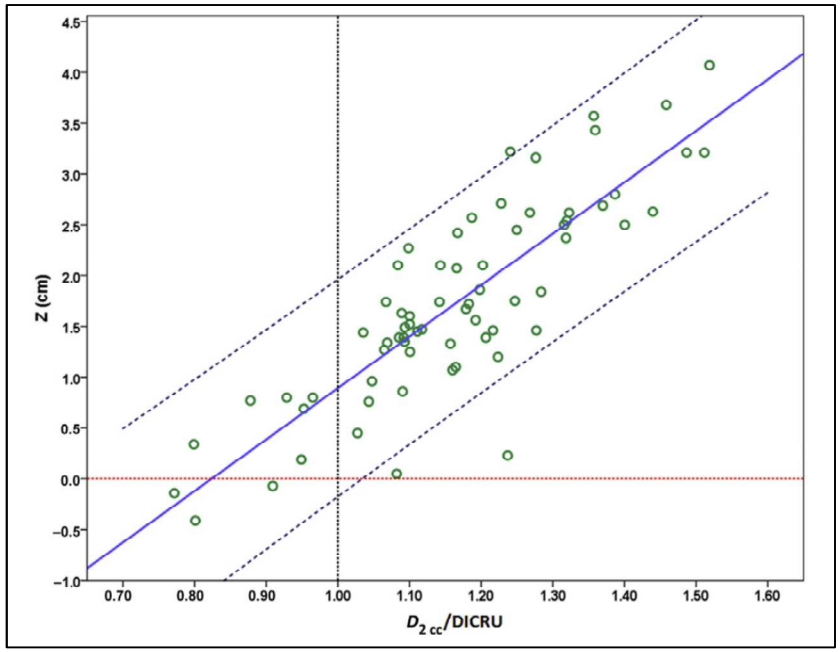
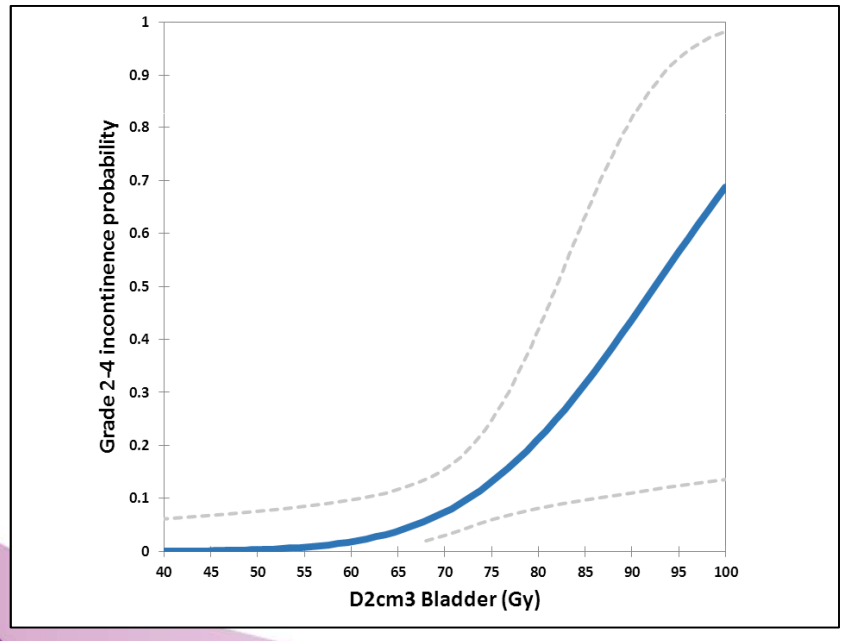
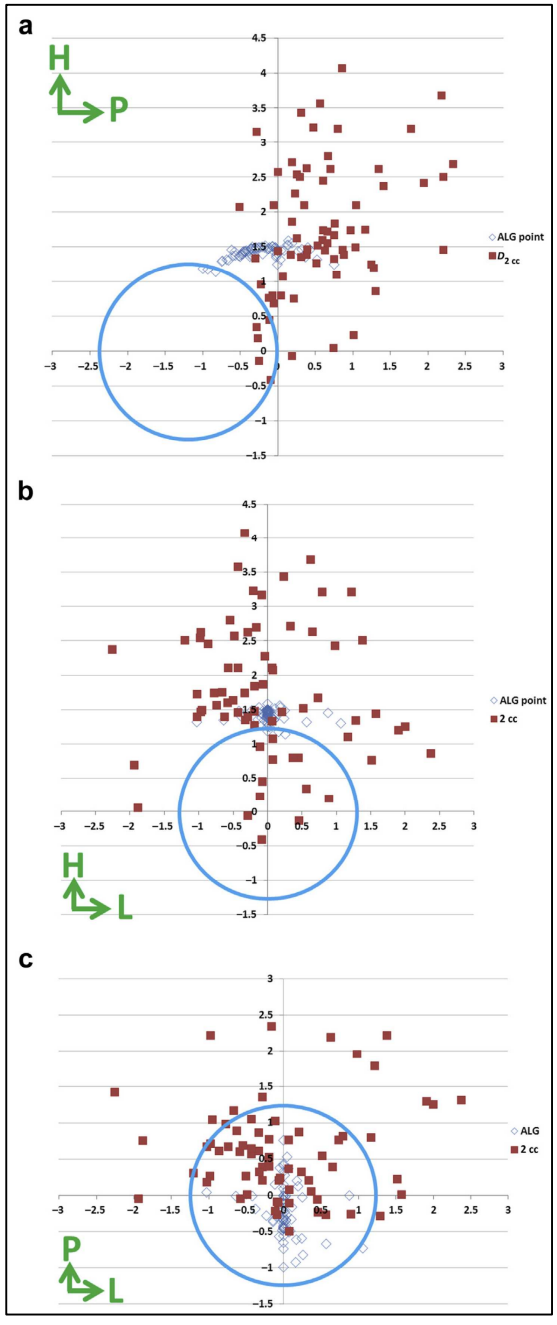
ICRU bladder point







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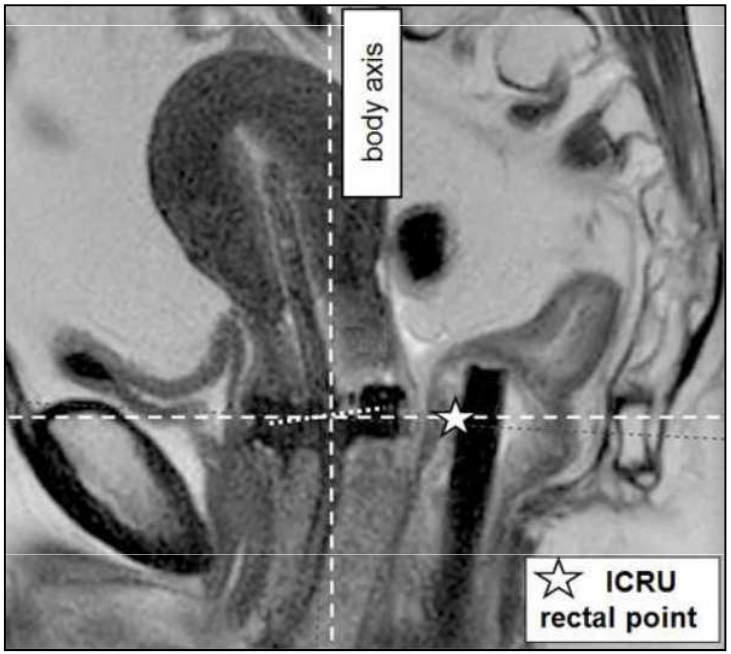
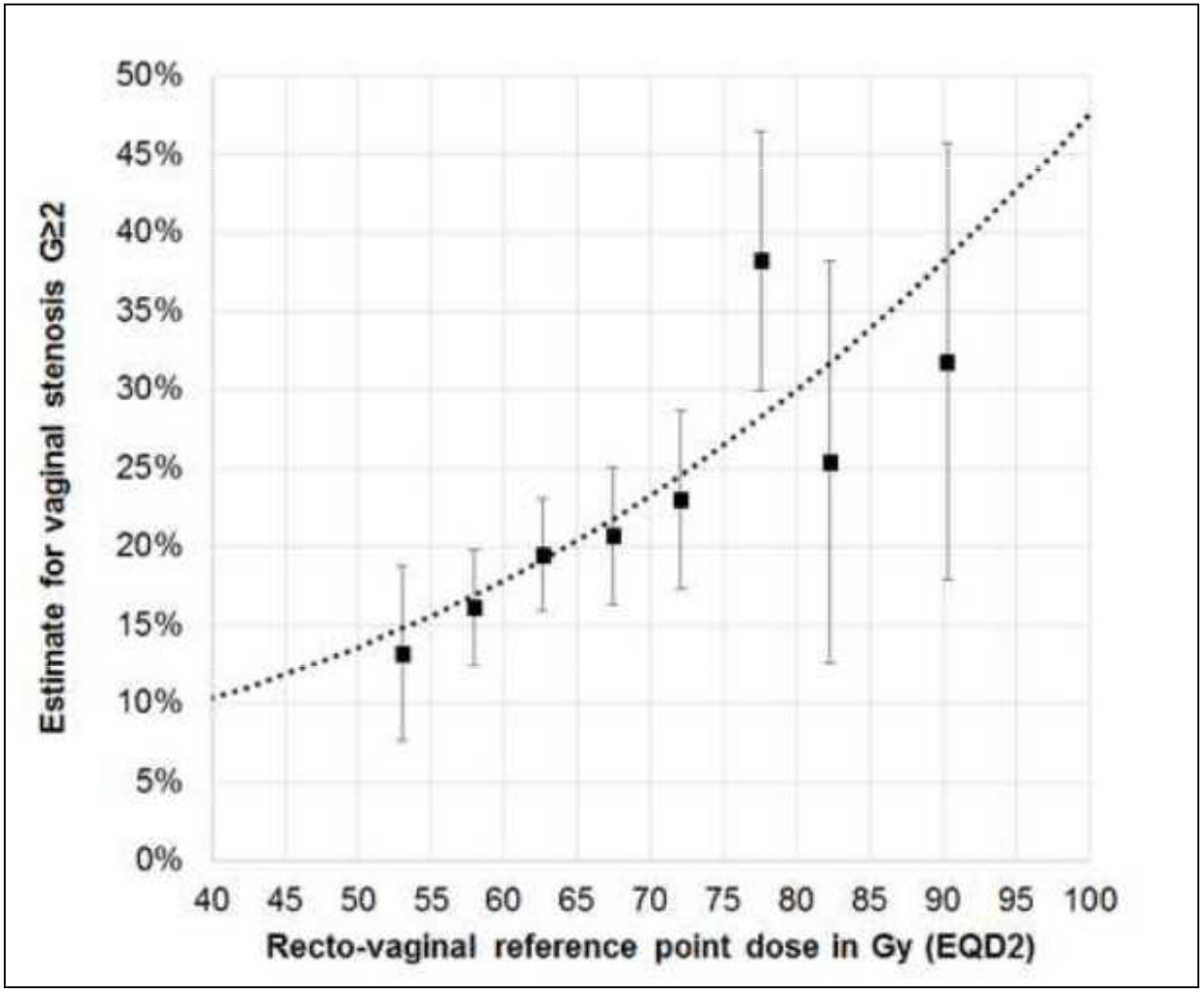
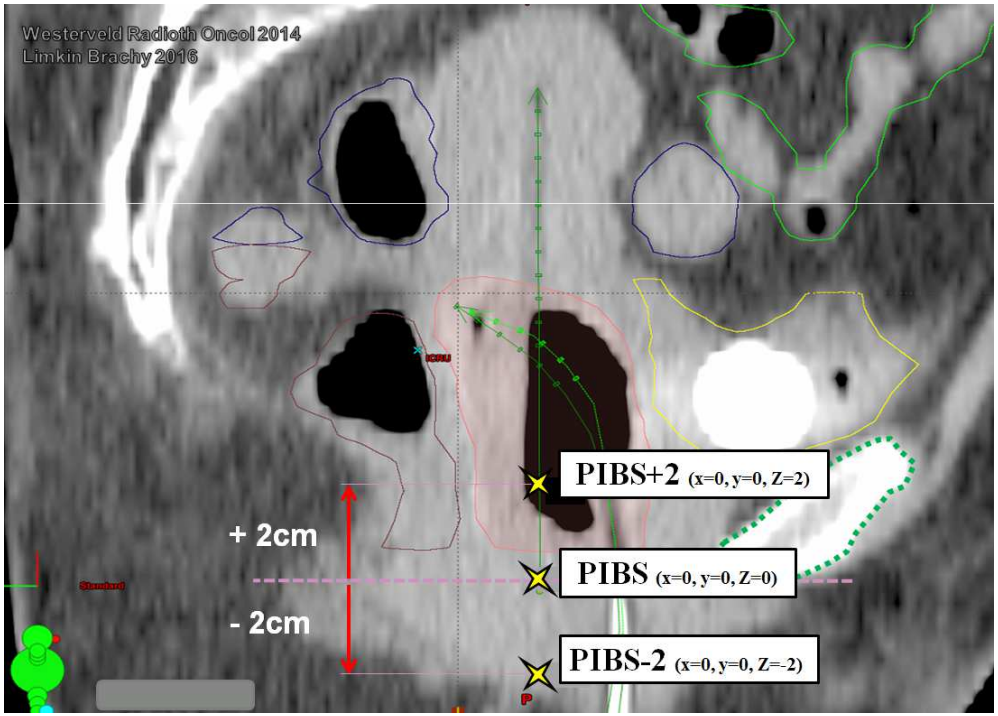
ICRU recto-Vaginal point

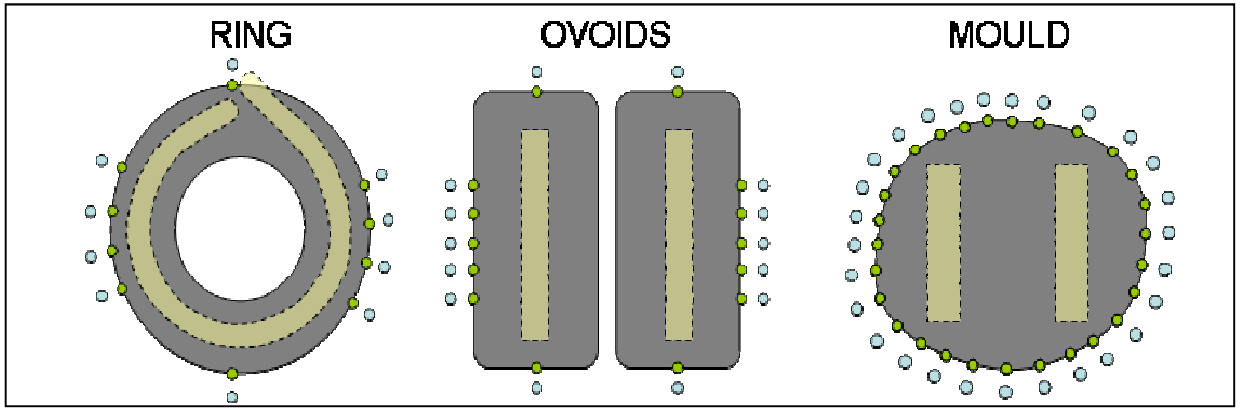




Kirchheiner et al. Radiother Oncol 2016

Even more points…





EMBRACE II

Target	D90 CTV_{HR} $EQD2_{10}$	D98 CTV_{HR} $EQD2_{10}$	D98 GTV_{res} $EQD2_{10}$	D98 CTV_{IR} $EQD2_{10}$	Point A $EQD2_{10}$
Planning Aims	> 90 Gy < 95 Gy	> 75 Gy	>95 Gy	> 60 Gy	> 65 Gy
Limits for Prescribed Dose	> 85 Gy	-	>90 Gy	-	-
OAR	Bladder D_{2cm^3} $EQD2_3$	Rectum D_{2cm^3} $EQD2_3$	Recto-vaginal point $EQD2_3$	Sigmoid D_{2cm^3} $EQD2_3$	Bowel D_{2cm^3} $EQD2_3$
Planning Aims	< 80 Gy	< 65 Gy	< 65 Gy	< 70 Gy*	< 70 Gy*
Limits for Prescribed Dose	< 90 Gy	< 75 Gy	< 75 Gy	< 75 Gy*	< 75 Gy*

+ ICRU recto-vaginal point ≤ 65 Gy

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Conclusion

- From 2D to 3D and image guided BT
- GEC-ESTRO recommendations
- Continuous and progressive development over 100 years
- Looking forward for
  - Clinical outcomes
  - Morbidity
  - Dose constraints
  - Nomograms / Personalization of planning aims

Results and complications of 3D brachytherapy for cervical cancer

Peter Hoskin
Mount Vernon Cancer Centre

Advantages of 3D brachytherapy

- Point doses shown to be unrepresentative
- Cross sectional imaging enables
  - Accurate verification of applicator position
  - Accurate definition of normal tissue dosimetry
  - Opportunity for conformal dose distributions to tumour volume

Results and complications of 3D brachytherapy for cervical cancer

- Dosimetric
- Tumour control
- Complications

Potential of dose optimisation in MRI-based PDR brachytherapy of cervix carcinoma

Marisol De Brabandere[a,*], Amr Gaber Mousa[b], An Nulens[a], Ans Swinnen[a], Erik Van Limbergen[a]

[a]Department of Radiation Oncology, University Hospital Leuven, Belgium, [b]Radiation Therapy Department, National Cancer Institute, Cairo University, Egypt

RT&O 2008

16 patients planned with conventional x-rays
Reconstructed on MR images and replanned to optimise with following constraints:

HR CTV:	**D90**	**$\geq 85Gy_{10}$**
Rectum D2cc		**$75Gy_3$**
Sigmoid D2cc		**$75Gy_3$**
Bladder D2cc		**$85Gy_3$**

Potential of dose optimisation in MRI-based PDR brachytherapy of cervix carcinoma

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RT&O 2008

Tumour dose

HR CTV D90 <85Gy$_{10}$

X-ray: 13/16

Optimised: 11/16

Mean dose increase 3Gy optimised

Dose and coverage values for the three target values as calculated after projection of the X-ray based dose grid on MR-images (X-ray based), and as obtained with MRI-based dose optimisation (optimised)

	Mean ± 1SD	
	X-ray based	Optimised
Point A dose [$Gy_{\alpha/\beta 10}$]	80 ± 6	79 ± 5
GTV (volume = 6 ± 7 cc)		
D100 [$Gy_{\alpha/\beta 10}$]	94 ± 31	89 ± 19
D90 [$Gy_{\alpha/\beta 10}$]	118 ± 43	103 ± 24
D50 [$Gy_{\alpha/\beta 10}$]	191 ± 95	138 ± 36
HR-CTV (volume = 48 ± 19 cc)		
D100 [$Gy_{\alpha/\beta 10}$]	61 ± 6	64 ± 6
D90 [$Gy_{\alpha/\beta 10}$]	76 ± 9	79 ± 7
D50 [$Gy_{\alpha/\beta 10}$]	108 ± 18	105 ± 10
V(85 $Gy_{\alpha/\beta 10}$) [%]	74 ± 16	79 ± 13
V(80 $Gy_{\alpha/\beta 10}$) [%]	81 ± 15	86 ± 11
IR-CTV (volume = 112 ± 44 cc)		
D100 [$Gy_{\alpha/\beta 10}$]	55 ± 3	58 ± 3
D90 [$Gy_{\alpha/\beta 10}$]	65 ± 5	69 ± 4
D50 [$Gy_{\alpha/\beta 10}$]	89 ± 11	92 ± 7
V(60 $Gy_{\alpha/\beta 10}$) [%]	96 ± 5	99 ± 2
Reference volumes		
V_{ref}(100 $Gy_{\alpha/\beta 10}$) [cc]	67 ± 15	73 ± 13
V_{ref}(85 $Gy_{\alpha/\beta 10}$) [cc]	101 ± 21	112 ± 18
V_{ref}(60 $Gy_{\alpha/\beta 10}$) [cc]	339 ± 106	410 ± 95

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RT&O 2008

Normal tissues

Dose values for the organs at risk as calculated after projection of the X-ray based dose grid on MR-images (X-ray based), and as obtained with MRI-based dose optimisation (optimised)

	Bladder Mean ± 1SD [$Gy_{\alpha\beta3}$]		Rectum Mean ± 1SD [$Gy_{\alpha\beta3}$]		Sigmoid colon Mean ± 1SD [$Gy_{\alpha\beta3}$]	
	X-ray based	Optimised	X-ray based	Optimised	X-ray based	Optimised
ICRU pt	76 ± 11	74 ± 15	63 ± 5	66 ± 9	–	–
$D_{0.1cc}$	120 ± 24	100 ± 12	64 ± 4	68 ± 7	90 ± 28	82 ± 13
D_{1cc}	93 ± 10	86 ± 7	61 ± 3	64 ± 5	75 ± 16	72 ± 9
D_{2cc}	86 ± 9	82 ± 6	59 ± 3	62 ± 4	70 ± 12	68 ± 7
Ratios	Mean ± 1SD		Mean ± 1SD			
$D_{0.1cc}/D_{icru}$	1.60 ± 0.31	1.34 ± 0.18	1.01 ± 0.08	1.02 ± 0.10	–	–
D_{1cc}/D_{icru}	1.25 ± 0.17	1.16 ± 0.14	0.96 ± 0.06	0.95 ± 0.08	–	–
D_{2cc}/D_{icru}	1.16 ± 0.16	1.10 ± 0.14	0.94 ± 0.06	0.92 ± 0.07	–	–

Exceeding constraints	Xray	Optimised
Bladder	10/16	None
Sigmoid	7/16	None

MRI-guided treatment-planning optimisation in intracavitary or combined intracavitary/interstitial PDR brachytherapy using tandem ovoid applicators in locally advanced cervical cancer

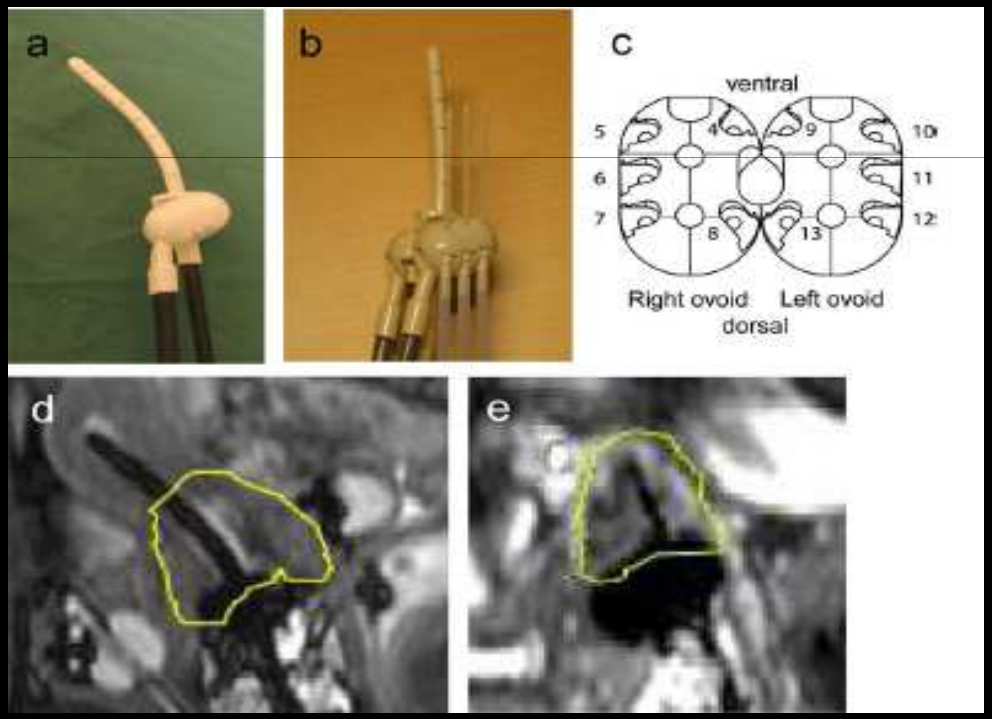
Ina M. Jürgenliemk-Schulz *, Robbert J.H.A. Tersteeg, Judith M. Roesink, Stefan Bijmolt, Christel N. Nomden, Marinus A. Moerland, Astrid A.C. de Leeuw

Department of Radiation Oncology, University Medical Centre Utrecht, The Netherlands

RT&O 2009

24 patients
Ib to Iva Ca Cx

Standard plans using orthogonal films
vs
MR defined volumes and optimisation



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Department of Radiation Oncology, University Medical Centre Utrecht, The Netherlands

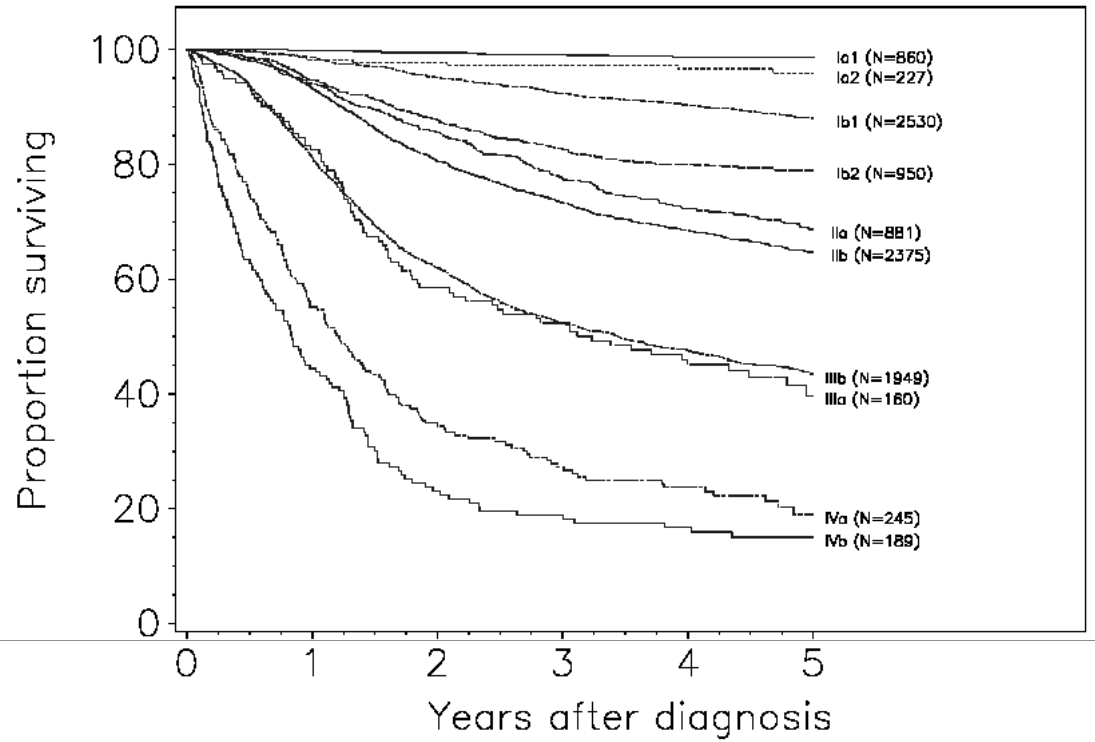
RT&O 2009

	Prescription dose 84Gy	
	Standard	Optimised
HRCTV D90	79Gy	89Gy
BladderD2cc	77Gy	81Gy
Rectum D2cc	61Gy	66Gy
Sigmoid D2cc	60Gy	61Gy
Bowel D2cc	65Gy	62Gy

Results: The average gain of MRI-guided optimisation expressed in D90 HR-CTV was $4 \pm 9\ Gy_{\alpha\beta 10}$ ($p < 0.001$) and $10 \pm 7\ Gy_{\alpha\beta 10}$ ($p = 0.003$) in the two periods. The dose to 2 cm^3 of the OAR met the constraints. In the group that was treated with the combined IC/IS approach, we could increase the D90 HR-CTV for the second PDR fraction with $5.4 \pm 4.2\ Gy_{\alpha\beta 10}$ ($p = 0.005$) and the D100 with $4.8 \pm 3.1\ Gy_{\alpha\beta 10}$ ($p = 0.07$).

Results and complications of 3D brachytherapy for cervical cancer

- Dosimetric
- Tumour control
- Complications

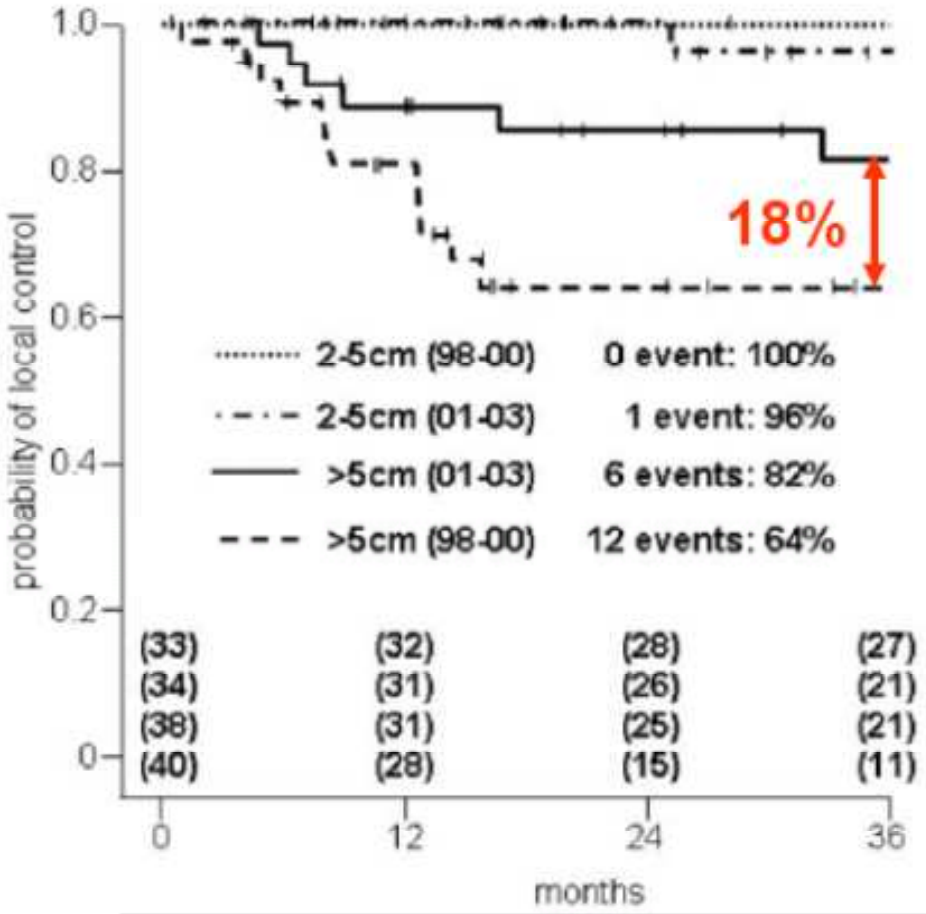


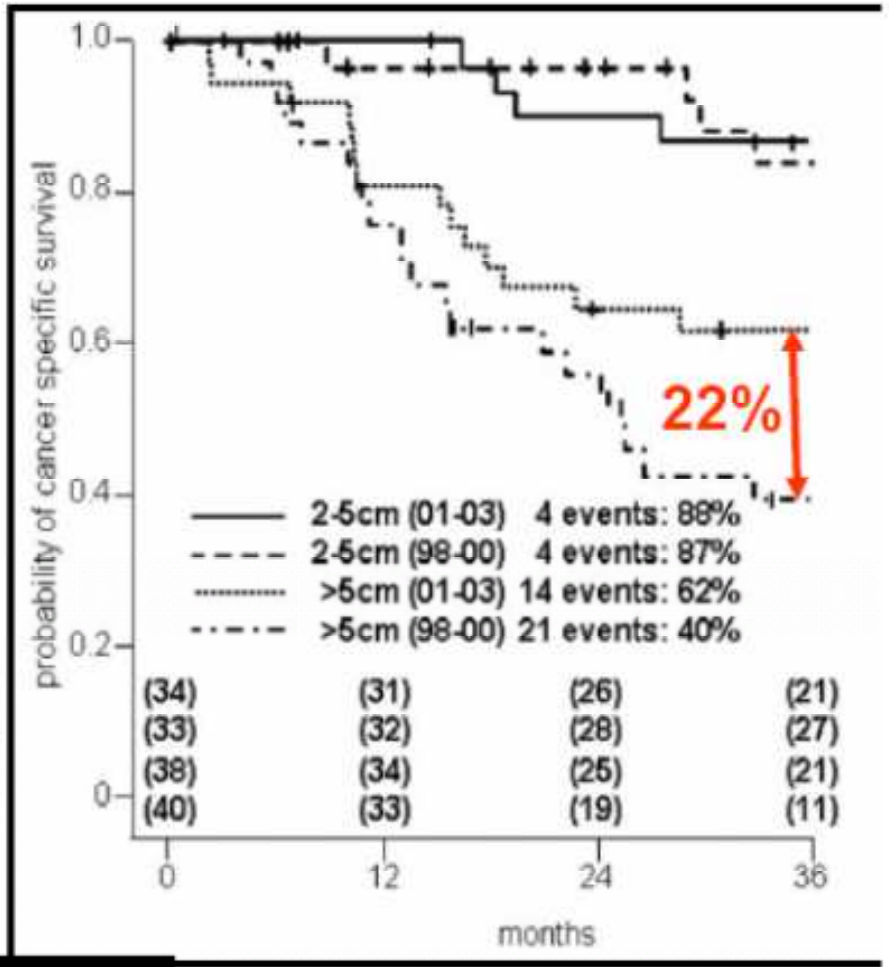
Stage	Patients (n)	Mean age (yr)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	860	44.3	99.8	99.5	99.1	98.7	98.7	0.1 (0.1–0.2)
Ia2	227	45.5	98.2	97.7	97.2	96.7	95.9	0.3 (0.1–0.5)
Ib1	2530	48.3	98.7	95.1	92.3	90.4	88.0	Reference
Ib2	950	47.4	94.8	87.8	82.6	79.9	78.8	
IIa	881	56.5	94.1	85.6	77.6	72.3	68.8	2.4 (2.1–2.8)
IIb	2375	54.1	93.3	80.7	73.4	68.5	64.7	2.9 (2.6–3.3)
IIIa	160	60.1	82.8	58.8	52.6	45.3	40.4	5.2 (4.0–6.6)
IIIb	1949	56.4	81.5	62.2	52.6	47.6	43.3	5.7 (5.0–6.4)
IVa	245	60.0	56.1	35.6	27.9	24.1	19.5	12.6 (10.5–15.1)
IVb	189	56.6	45.8	23.9	19.6	17.2	15.0	19.2 (15.8–23.4)

[a]Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country.

Fig. 9. Carcinoma of the cervix uteri: patients treated in 1996–98. Survival by FIGO stage, $n = 10366$.

Image guided adpative brachytherapy (IGBT) cervix cancer local control and cancer specific survival (1998-2003) TREATMENT PERIOD (-/+ IGABT) AND TUMOUR SIZE





mean 81 Gy vs. 90 Gy in HR CTV

Pötter R. et al Radiother Oncol 2007

TRUE PELVIS CONTROL
DVH DATA ON 141 PATIENTS

18 true pelvis recurrences (median follow up 50 months)

	V HR-CTV	D_{90}HR-CTV	D_{100}HR-CTV
GROUP I RECCURENCES	**50(±24) cm^3**	**76(±12) Gy**	**60(±10) Gy**
GROUP II NO RECCURENCES	**33(±23) cm^3**	**88(±16) Gy**	**66(±7) Gy**

Cut off level 87 Gy for D_{90} HR-CTV
3 vs. 15 rec., p=0.006:predictive value 96%

(Dimopoulos et al. ESTRO 2006)

Brachytherapy of cervical cancer

Clinical outcome of protocol based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer

Richard Pötter[a,*], Petra Georg[a], Johannes C.A. Dimopoulos[b], Magdalena Grimm[a], Daniel Berger[a], Nicole Nesvacil[a], Dietmar Georg[a], Maximilian P. Schmid[a], Alexander Reinthaller[c], Alina Sturdza[a], Christian Kirisits[a]

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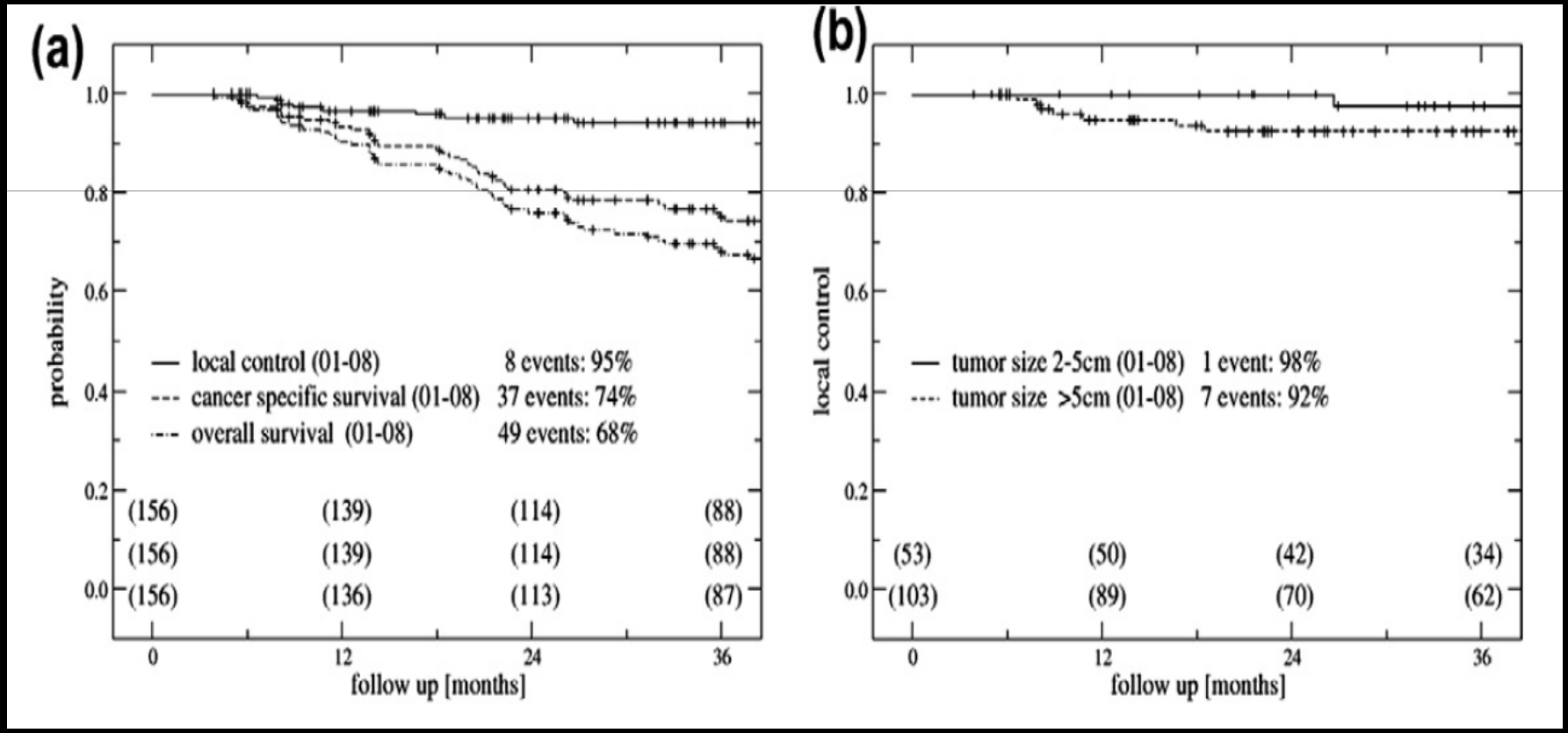
Radiotherapy and Oncology 100 (2011) 116–123



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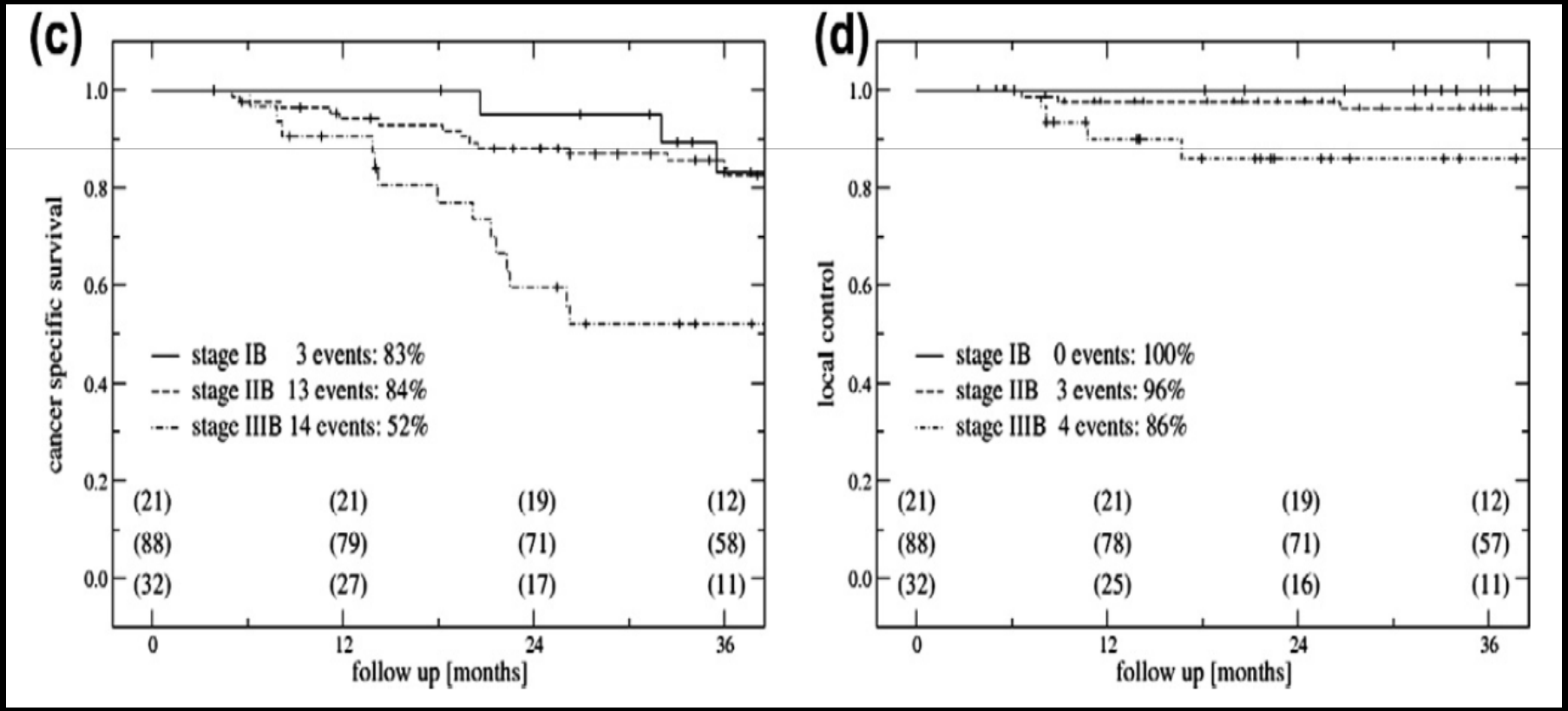
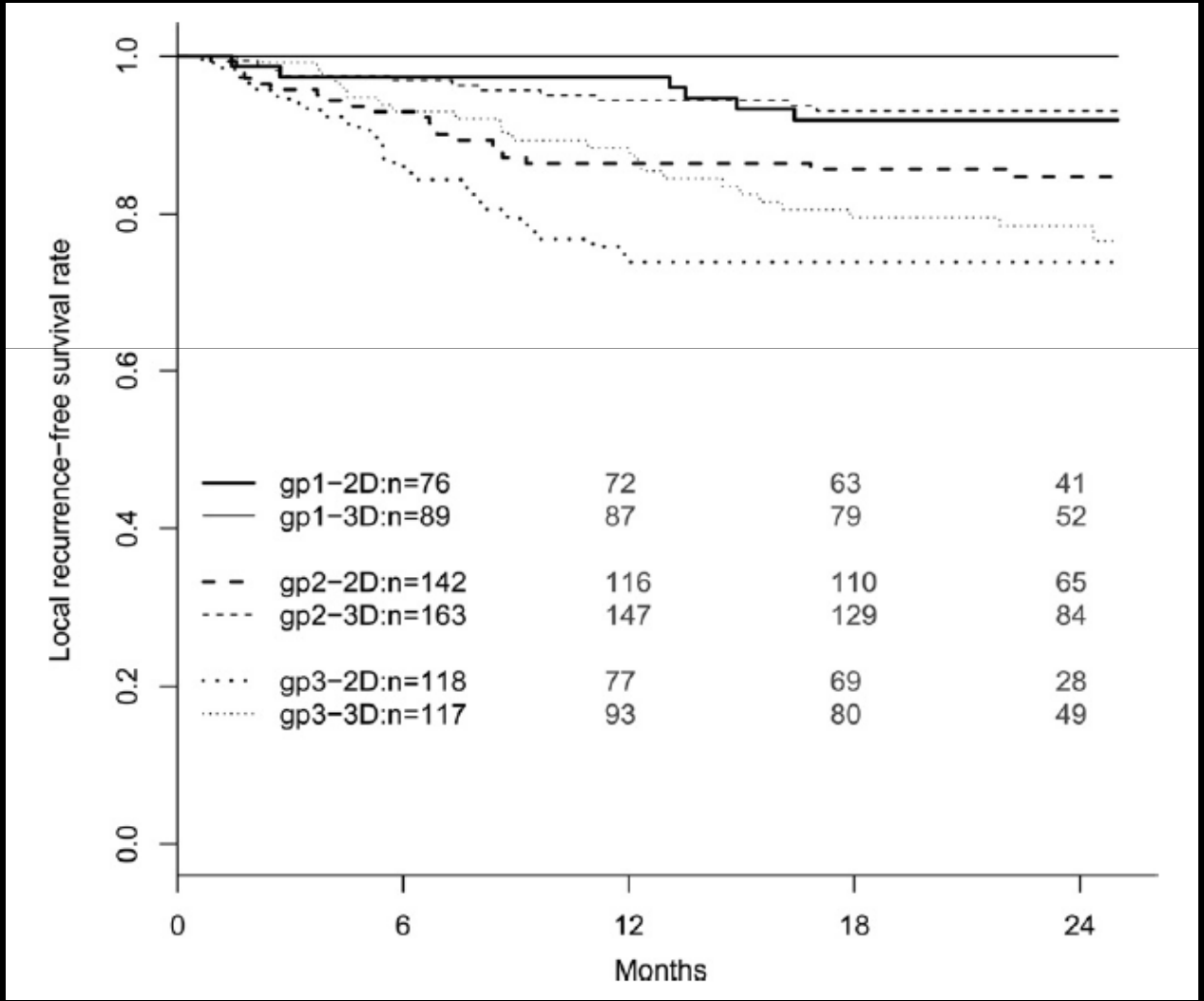


Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: Results of the French STIC prospective study ☆

Radiotherapy and Oncology 103 (2012) 305–313

Local recurrence free survival

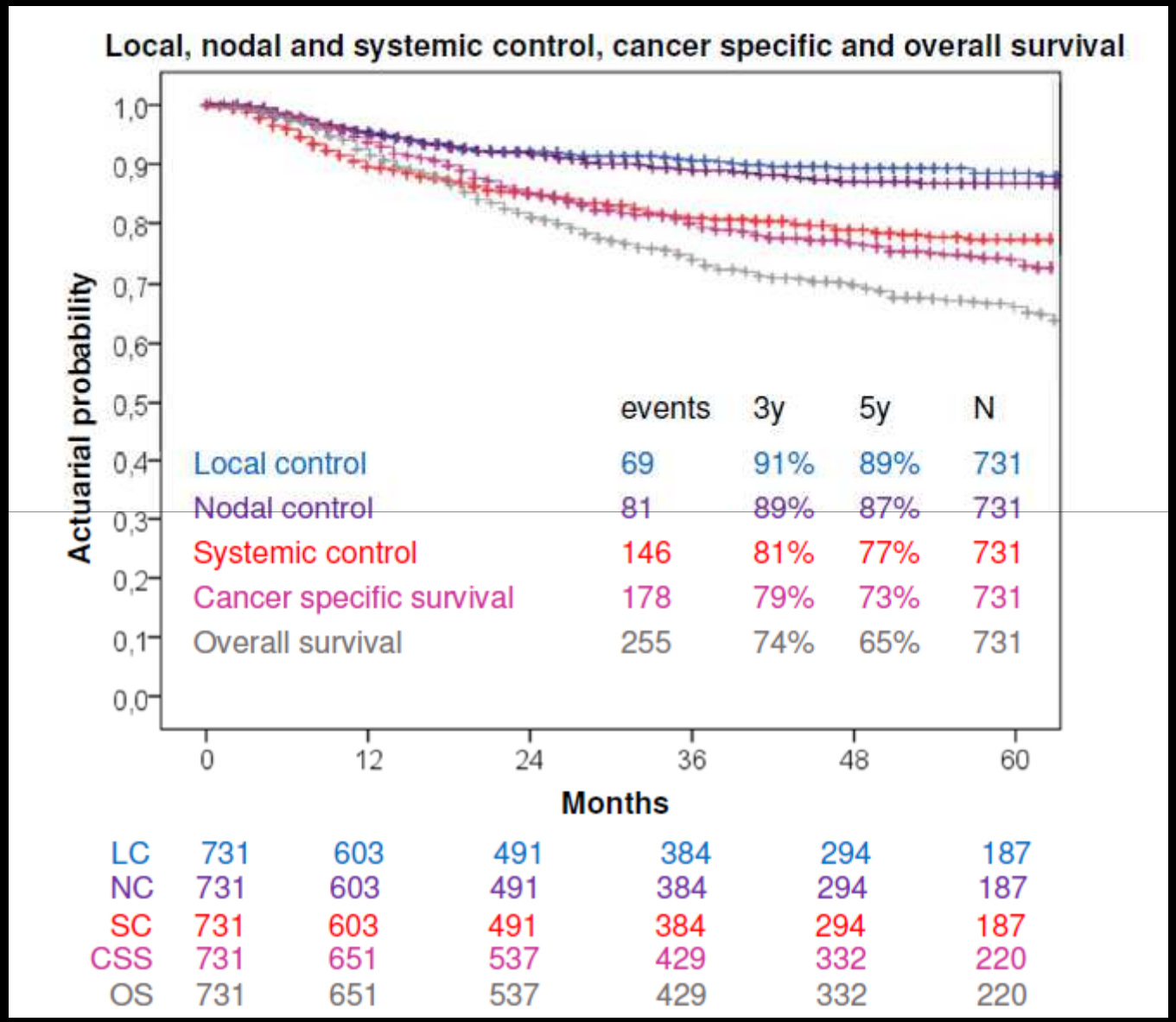


Validation of GEC ESTRO Guidelines

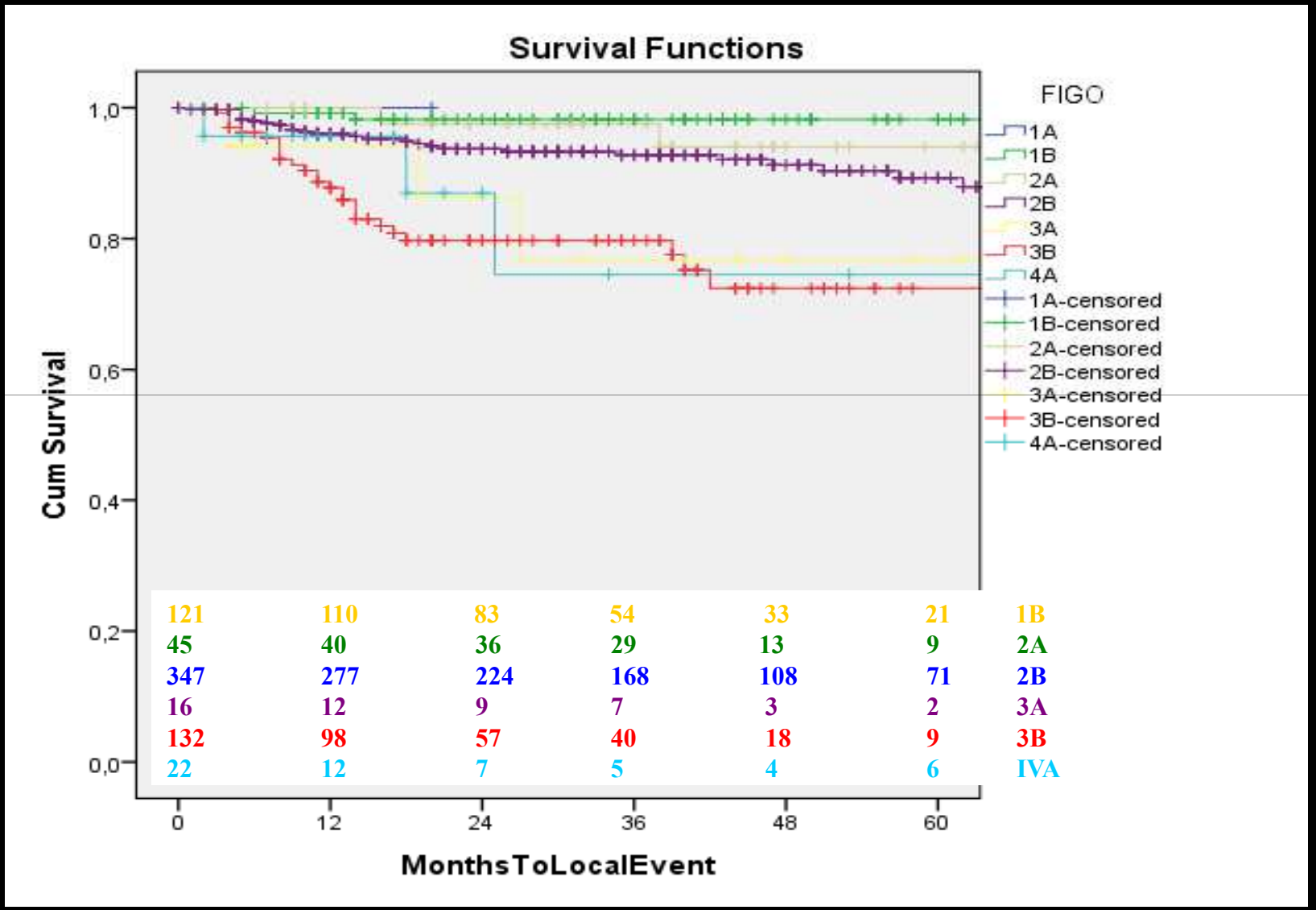
EMBRACE

A
European study on
MRI-guided
brachytherapy in locally advanced
cervical cancer

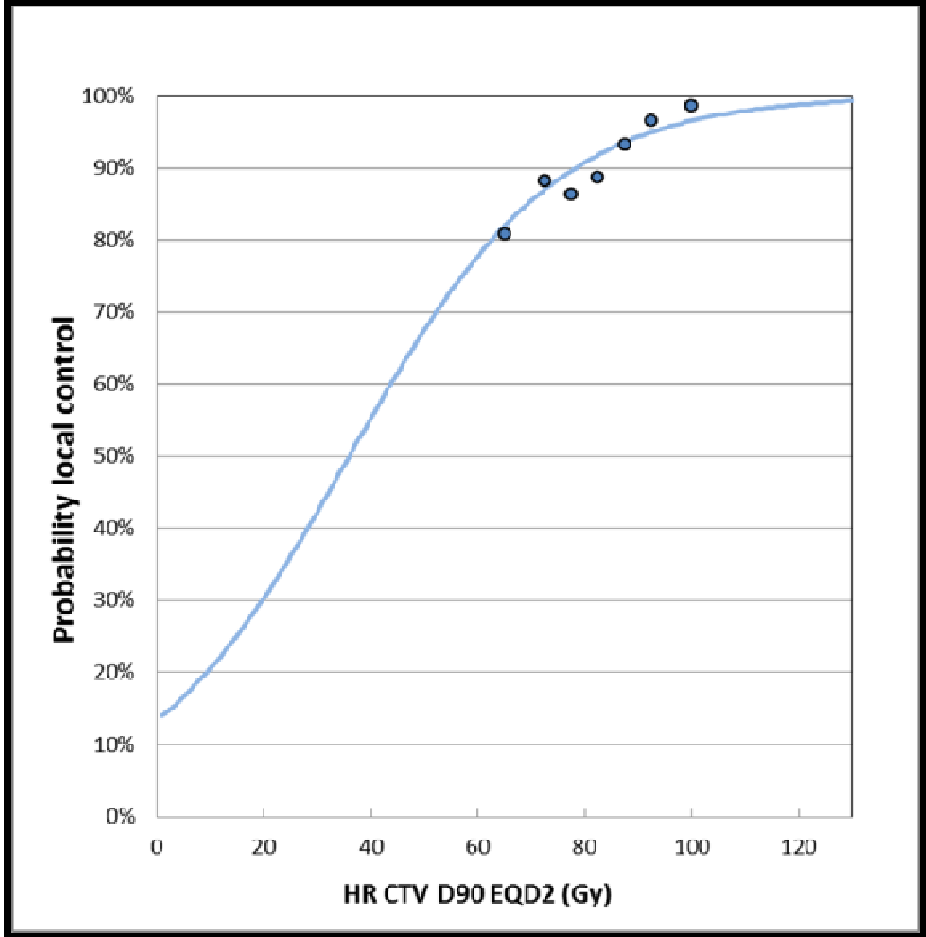
IntErnational study on
MR guided BRachytherapy in
Locally Advanced CErvical Cancer


Local, nodal and systemic control, cancer specific and overall survival
Actuarial probability
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
events 3y 5y N
Local control 69 91% 89% 731
Nodal control 81 89% 87% 731
Systemic control 146 81% 77% 731
Cancer specific survival 178 79% 73% 731
Overall survival 255 74% 65% 731
0 12 24 36 48 60
Months
LC 731 603 491 384 294 187
NC 731 603 491 384 294 187
SC 731 603 491 384 294 187
CSS 731 651 537 429 332 220
OS 731 651 537 429 332 220

Stage related local control



Dose Response forlocal control (RetroEMBRACE)



Relationship between EBRT-C+BT dose and local control

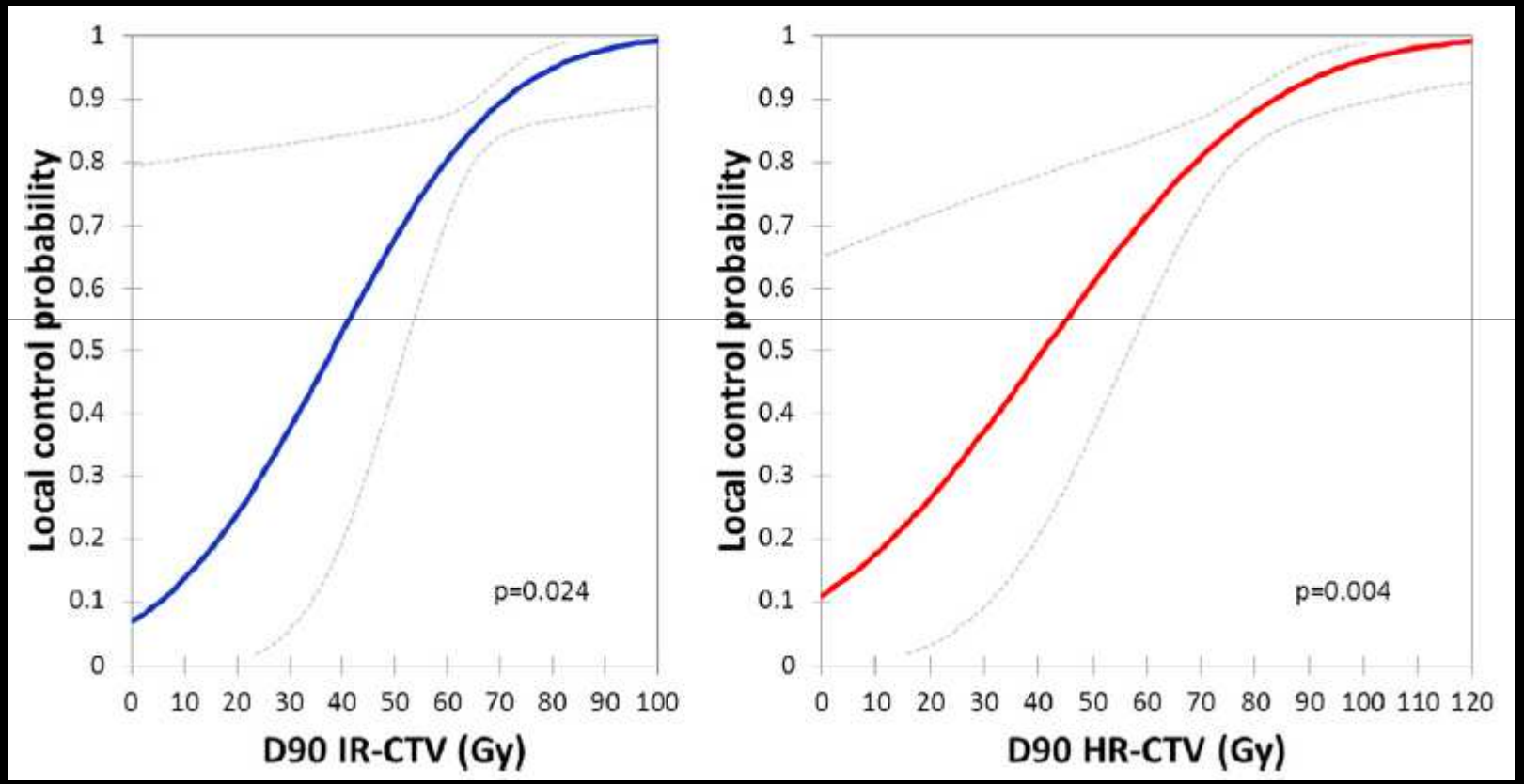
Based on retroEMBRACE, n=592 patients

(Tanderup et al, ESTRO Geneva 2013)

Impact of treatment time and dose escalation on local control in locally advanced cervical cancer treated by chemoradiation and image-guided pulsed-dose rate adaptive brachytherapy

Renaud Mazeron [a,b,*], Pauline Castelnau-Marchand [a], Isabelle Dumas [c], Eleonor Rivin del Campo [a], et al

Radiotherapy and Oncology xxx (2014) xxx–xxx



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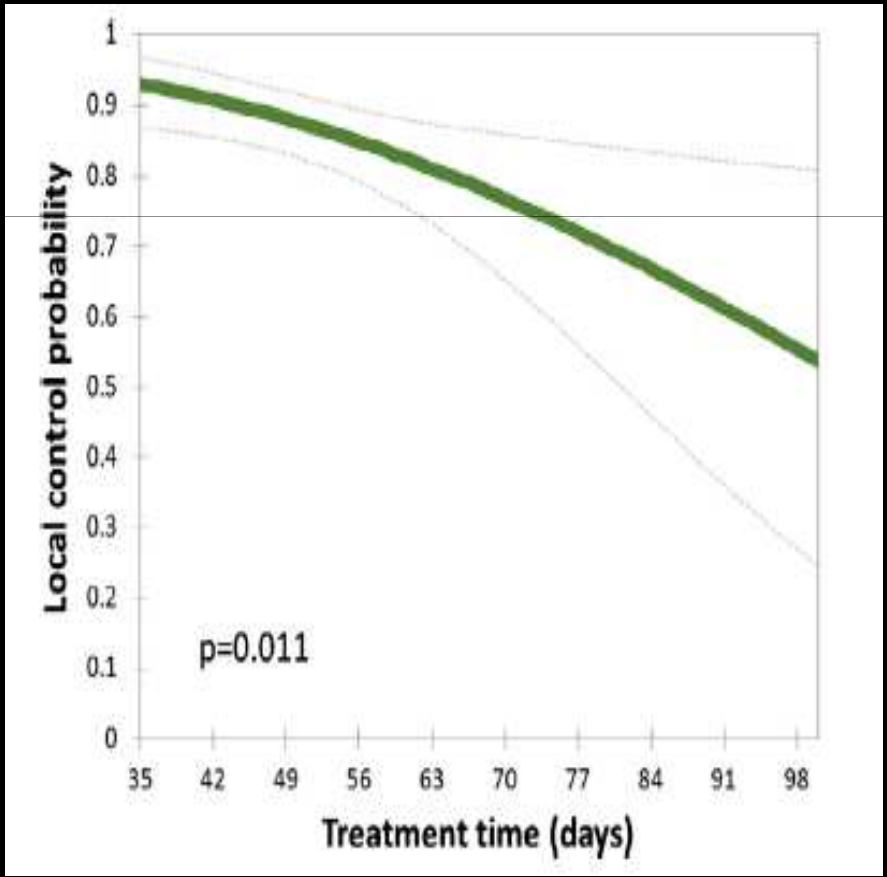
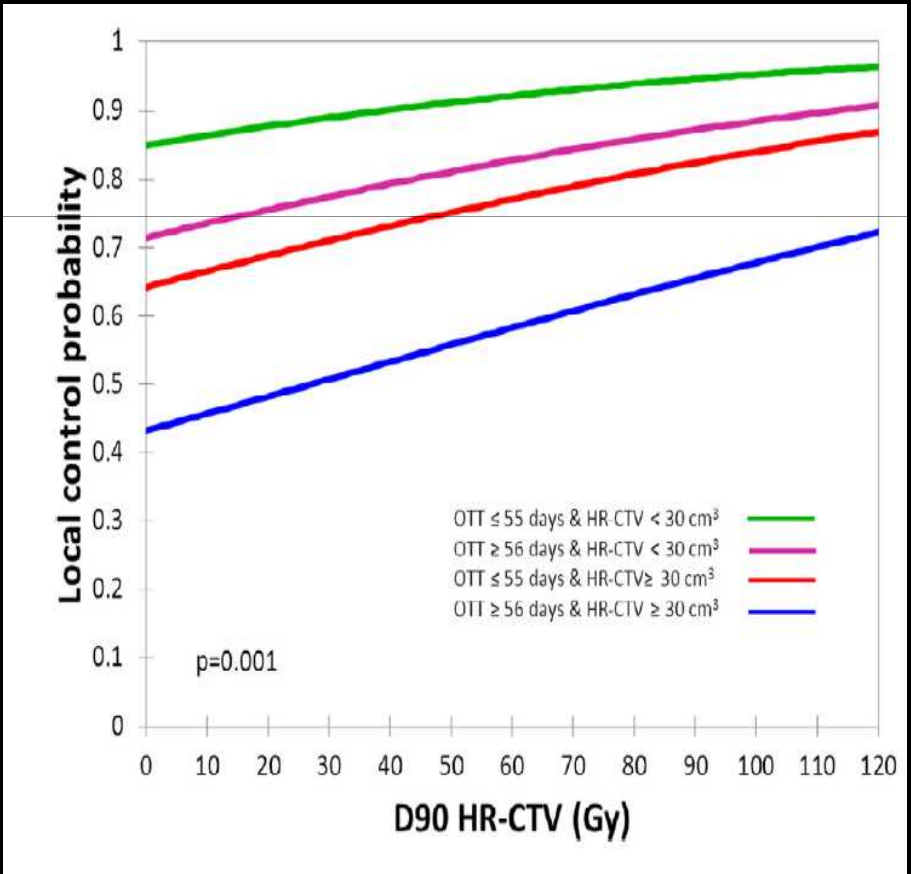
Radiotherapy and Oncology xxx (2014) xxx–xxx

225 patients: 25% IB2, 50% IIB, 10% IIIB





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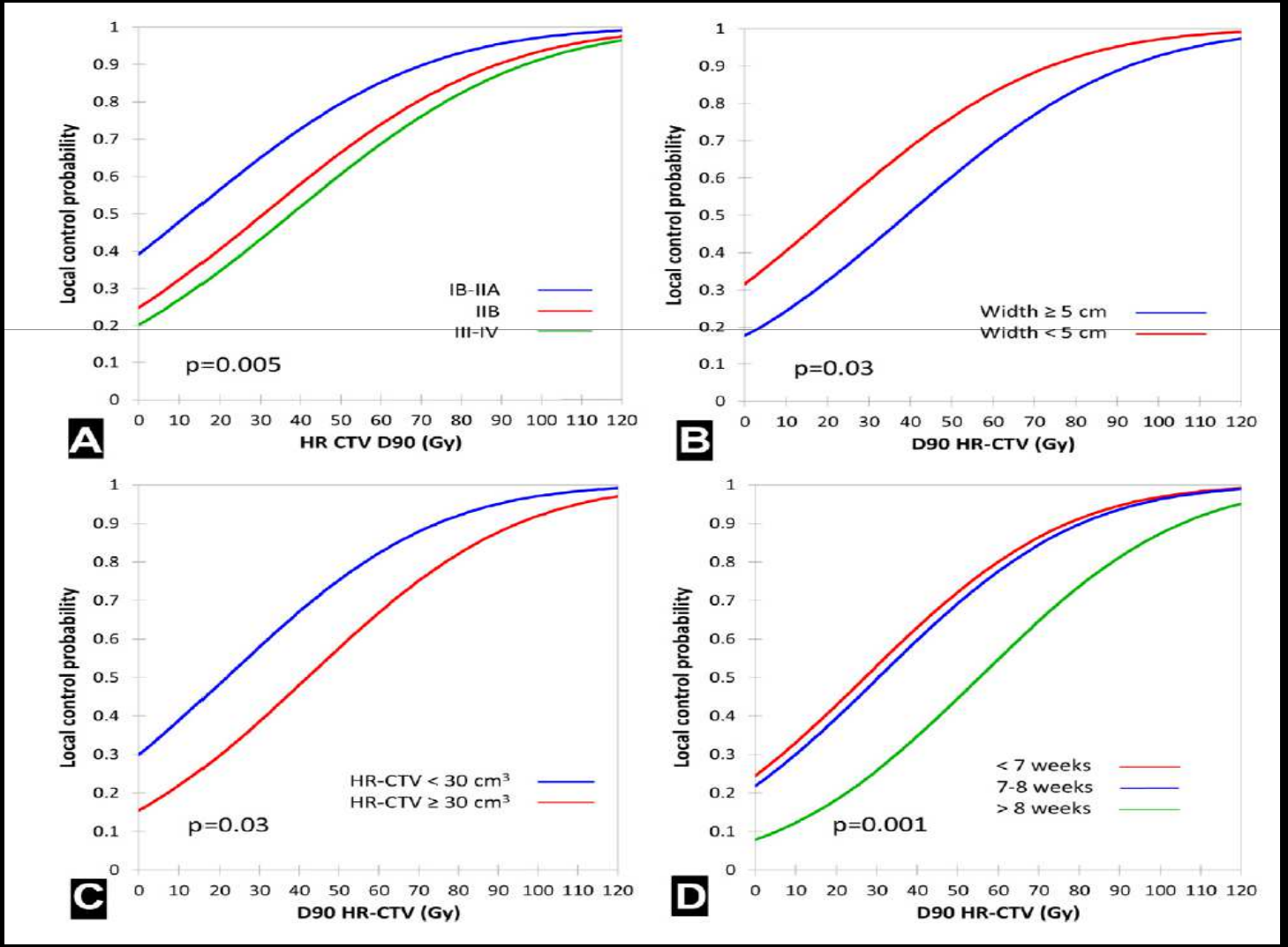


Results and complications of 3D brachytherapy for cervical cancer

- Dosimetric
- Tumour control
- Complications

THE PREDICTION OF LATE RECTAL COMPLICATIONS IN PATIENTS TREATED WITH HIGH DOSE-RATE BRACHYTHERAPY FOR CARCINOMA OF THE CERVIX

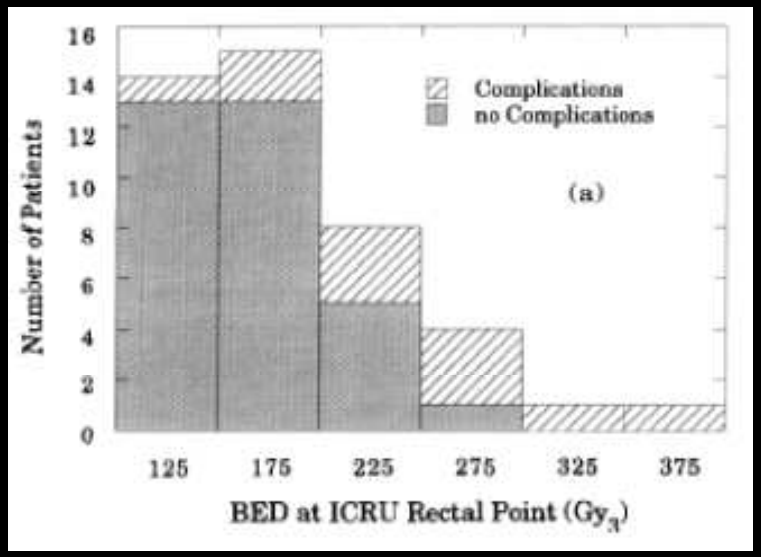
BRENDA G. CLARK, PH.D.,[†] LUIS SOUHAMI, M.D.,[†] TED N. ROMAN, M.D.,[†]
RICK CHAPPELL, PH.D.,[¶] MICHAEL D. C. EVANS, M.SC.,[†] JACK F. FOWLER, PH.D., D.SC.[*]

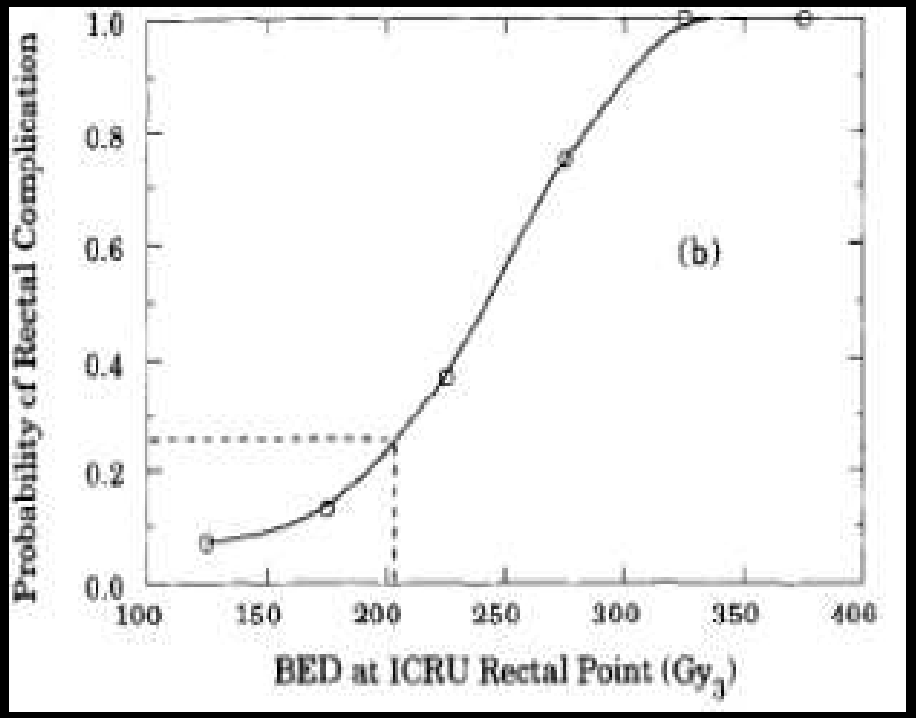
[†]Department of Oncology, McGill University, Montréal, Canada; [¶]Departments of Statistics and Biostatistics, University of Wisconsin, Madison, WI; [*]UZ Gasthuisberg, Belgium.

IJROB 1997

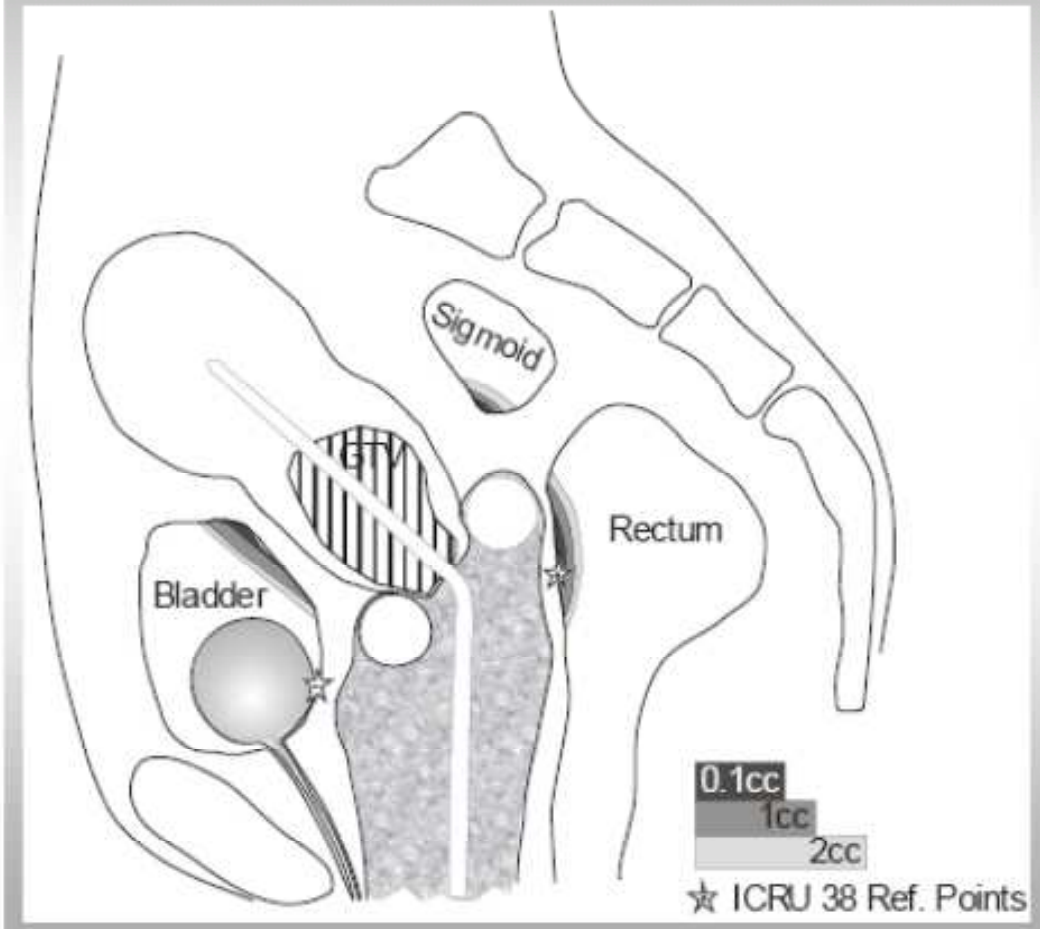
46 patients ca cx

46Gy/23f
3 x 10Gy HDR

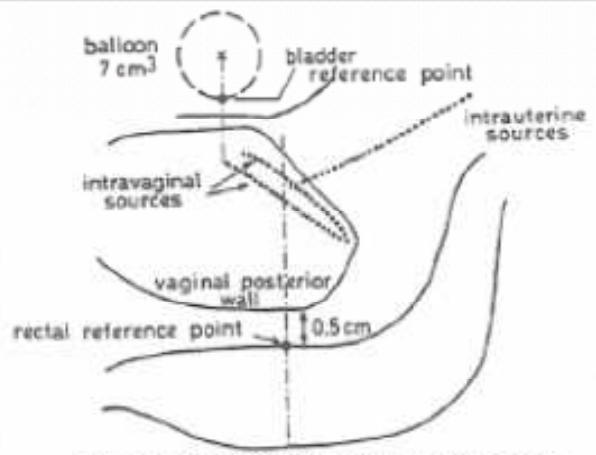




3D radiotherapy:dose to volumes and morbidity



Pötter et al. Radioth and Oncol 2006



ICRU Report 38, 1985, Bethesda

Correlation between ICRU point doses and rectal and bladder toxicity unpredicatble

KBD

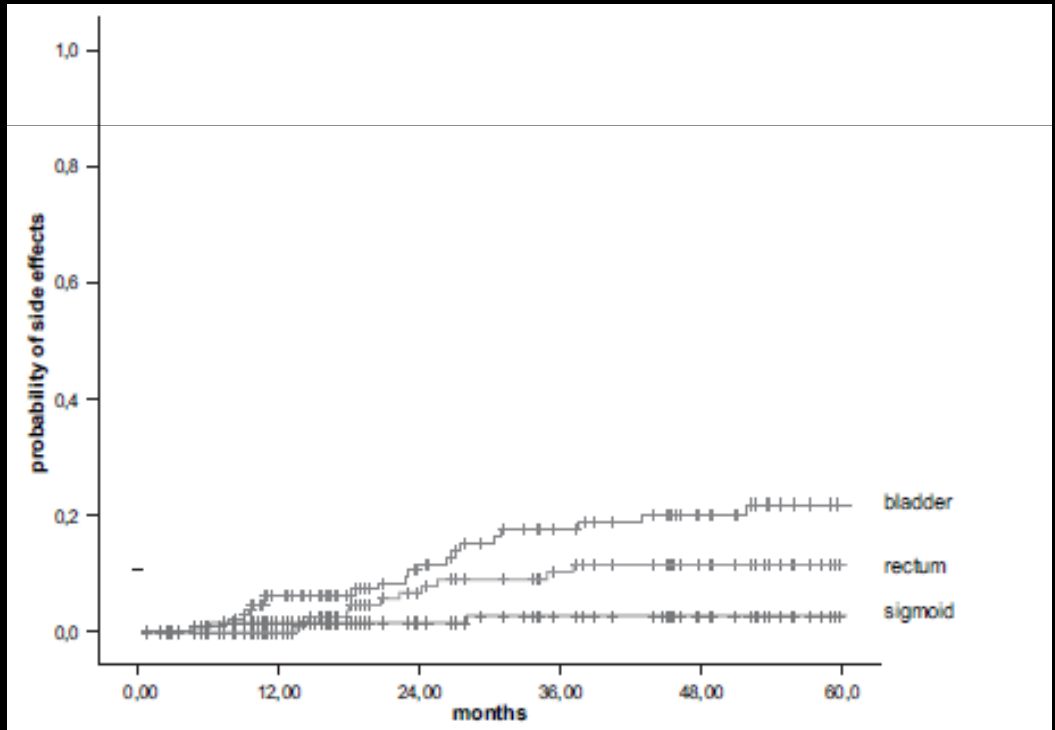
DOSE–VOLUME HISTOGRAM PARAMETERS AND LATE SIDE EFFECTS IN MAGNETIC RESONANCE IMAGE–GUIDED ADAPTIVE CERVICAL CANCER BRACHYTHERAPY

PETRA GEORG, M.D.,* STEFAN LANG, PH.D.,* JOHANNES C. A. DIMOPOULOS, M.D.,* WOLFGANG DÖRR, D.V.M., PH.D.,*† ALINA E. STURDZA, M.D.,* DANIEL BERGER, PH.D.,* DIETMAR GEORG, PH.D.,* CHRISTIAN KIRISITS, D.SC.,* AND RICHARD PÖTTER, M.D.*

*Department of Radiotherapy, Medical University of Vienna, Vienna, Austria; and †Department of Radiotherapy and Radiation Oncology, Medical Faculty Carl Gustav Carus, University of Technology Dresden, Dresden, Germany

IJROB 2011

141 patients: Median follow up 51 months
45Gy + 28Gy IGBT



. Five-year actuarial rates for late adverse side effects (Grade 1–4) of the rectum, sigmoid colon, and bladder.

Brachytherapy of cervical cancer

Clinical outcome of protocol based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer

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Radiotherapy and Oncology 100 (2011) 116–123

Late adverse effects	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
	n	*n*	*n*	*n*	*n*
Vagina	23	84	44	2	1
Bladder	121	20	12	3	0
Rectum	137	8	6	2	3
Bowel/Sigmoid	152	2	2	0	0
Total		114	64	7	4
without vagina		30	20	5	3

Rectum D2cc

Georg et al 2011, 141 pts
≥G2 (mainly rectal bleeding)

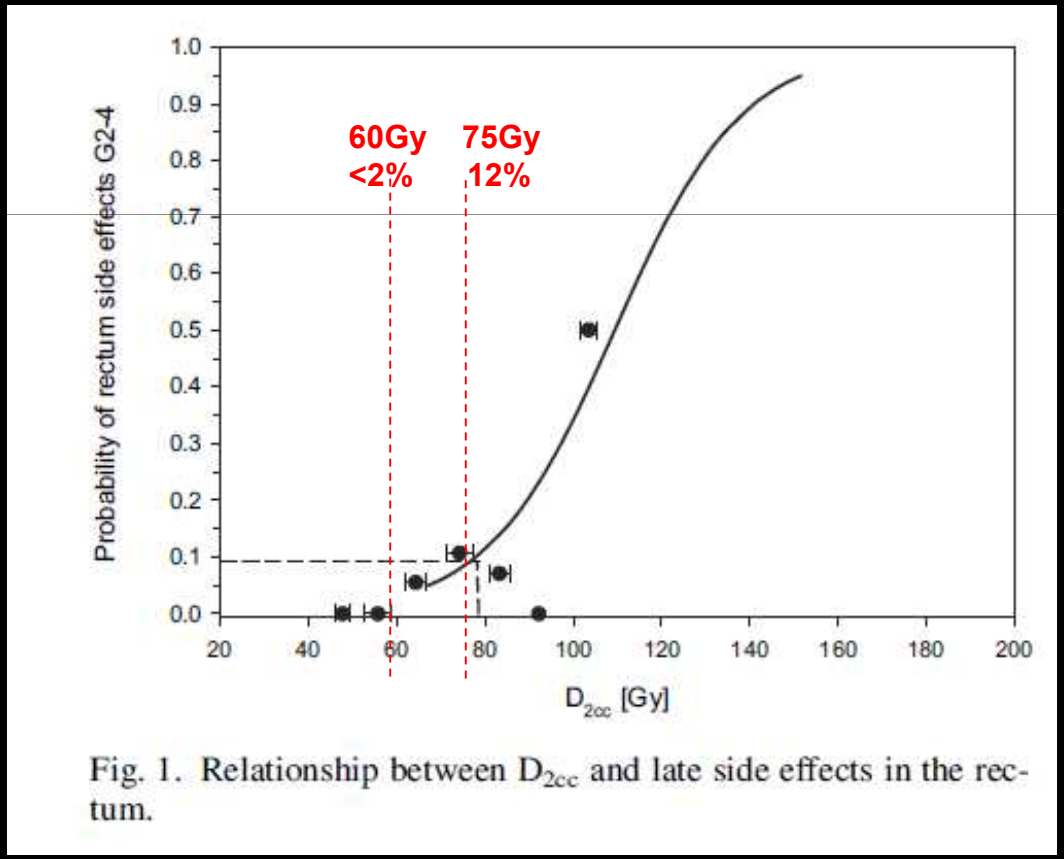
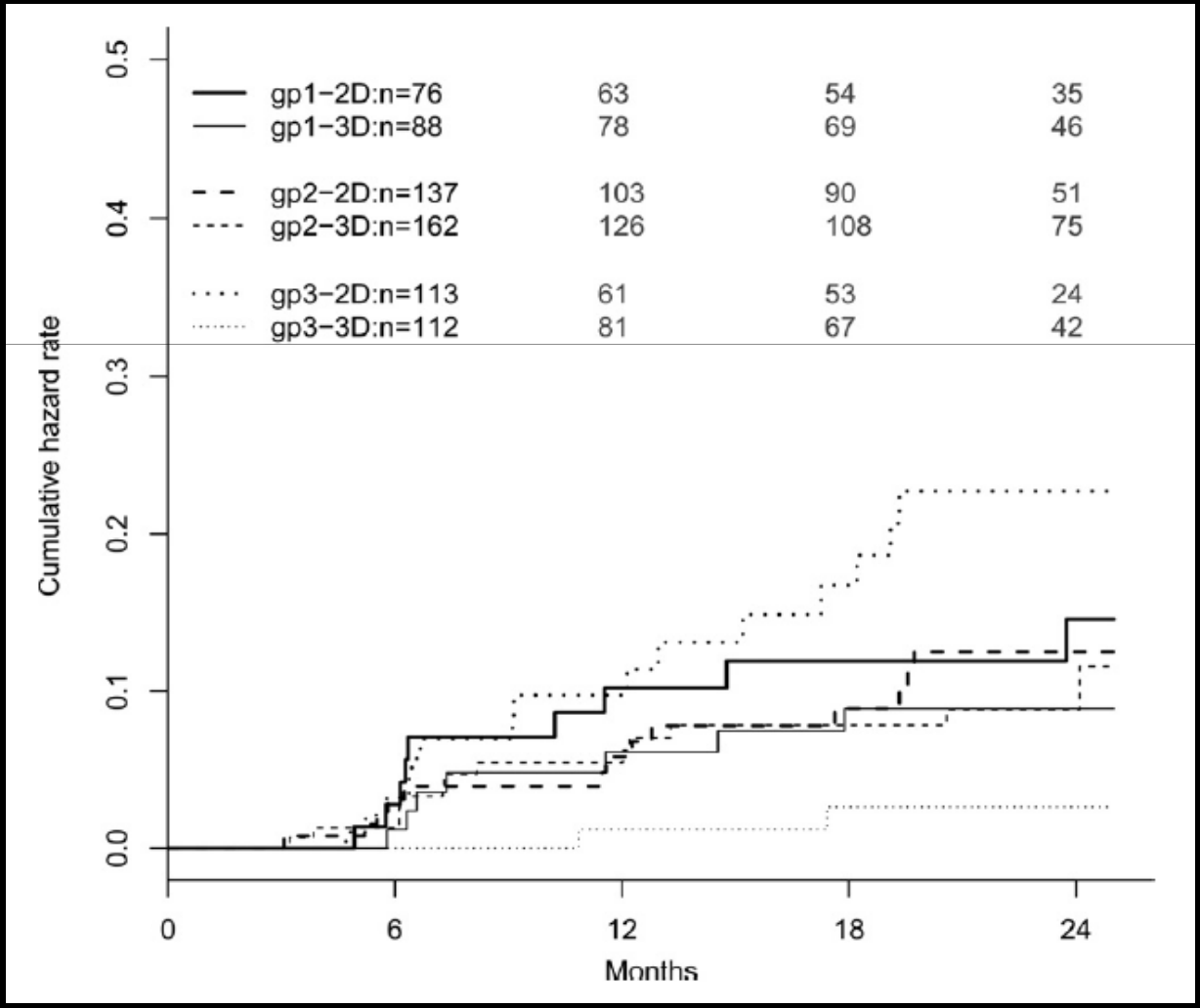


Fig. 1. Relationship between D_{2cc} and late side effects in the rectum.

Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: Results of the French STIC prospective study ☆

Radiotherapy and Oncology 103 (2012) 305–313

Toxicity



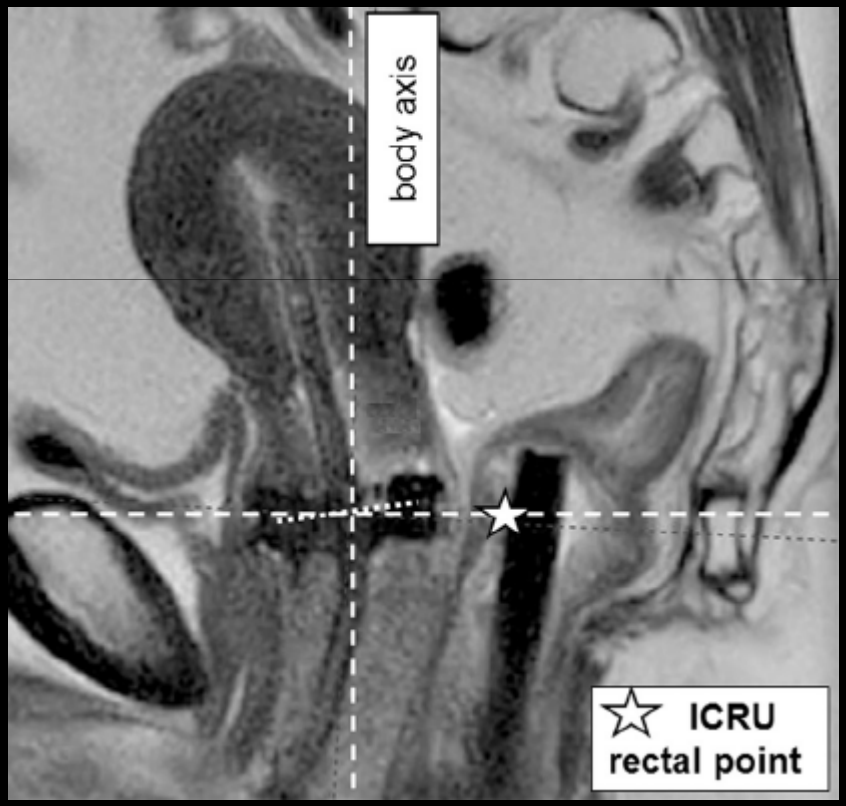
3D radiotherapy:dose to volumes and morbidity
Recommended constraints
associated with late side effects

- Rectum: D2cc < 70-75 Gy EQD2
- Sigmoid: D2cc < 70-75 Gy EQD2
- Bladder: D2cc < 90 Gy EQD2
- Vagina: ???

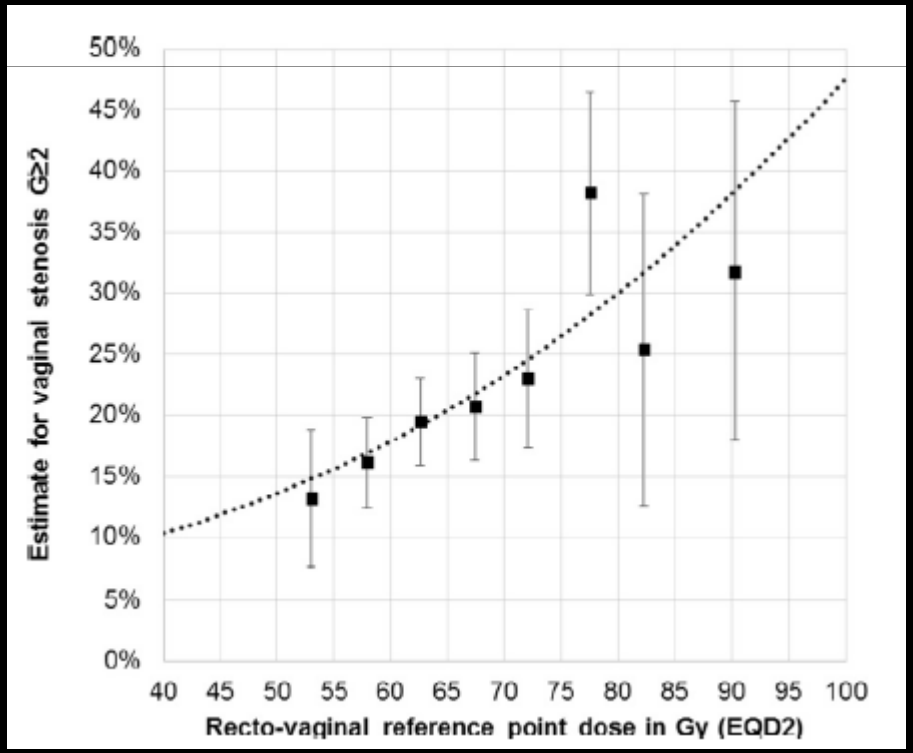
Dose–effect relationship and risk factors for vaginal stenosis after definitive radio(chemo)therapy with image-guided brachytherapy for locally advanced cervical cancer in the EMBRACE study

Radiotherapy and Oncology xxx (2016) xxx–xxx

Kathrin Kirchheiner [a,*], Remi A. Nout [b], Jacob C. Lindegaard [c], Christine Haie-Meder [a], et al.

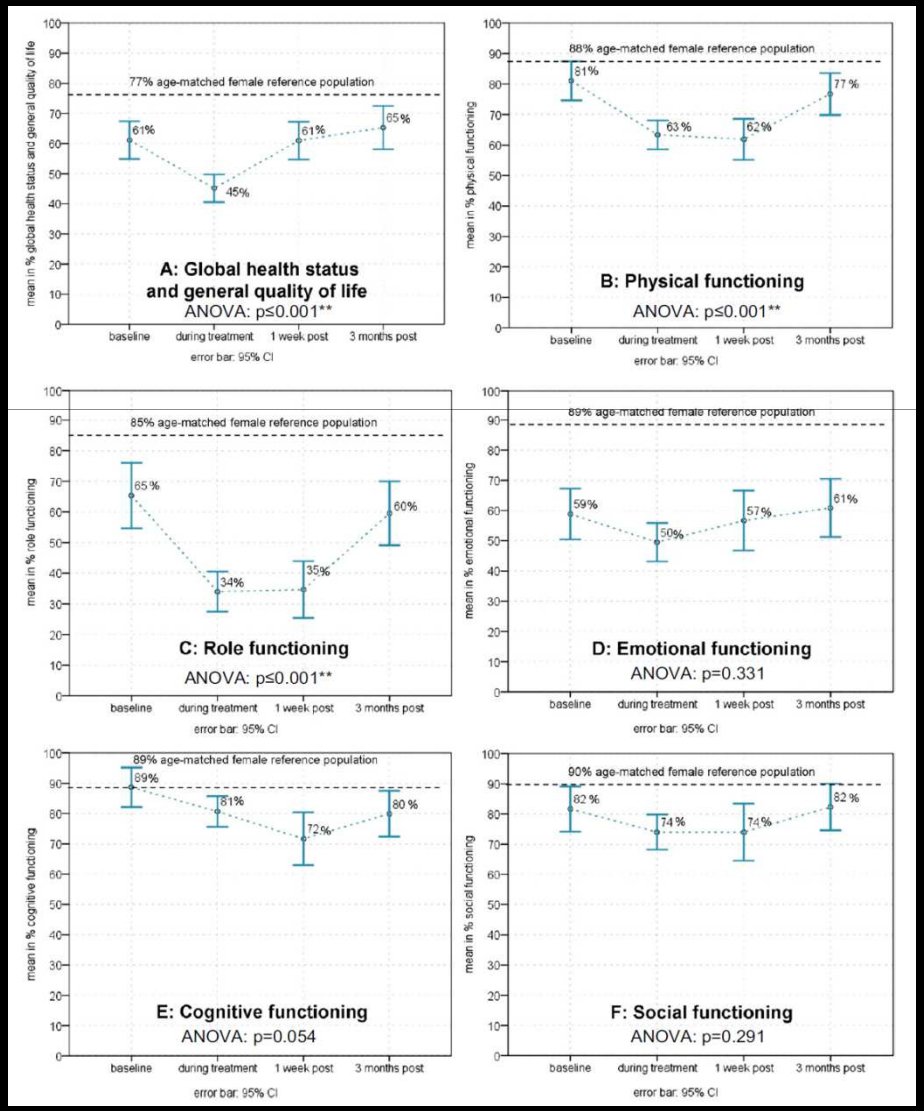


Vaginal stenosis greater when Stage IIa IIIa or EBRT >45Gy



Health related quality of life and patient reported symptoms before and during definitive radio(chemo)therapy using image-guided adaptive brachytherapy for locally advanced cervical cancer and early recovery — A mono-institutional prospective study

Kathrin Kirchheiner [a,*], Remi A. Nout [b], Agnieszka Czajka-Pepl [a], Elisabeth Ponocny-Seliger [c], et al



N=50
EORTC QLQ C30
EORTC QLQ Cx24

Gynecologic Oncology 136 (2015) 415–423

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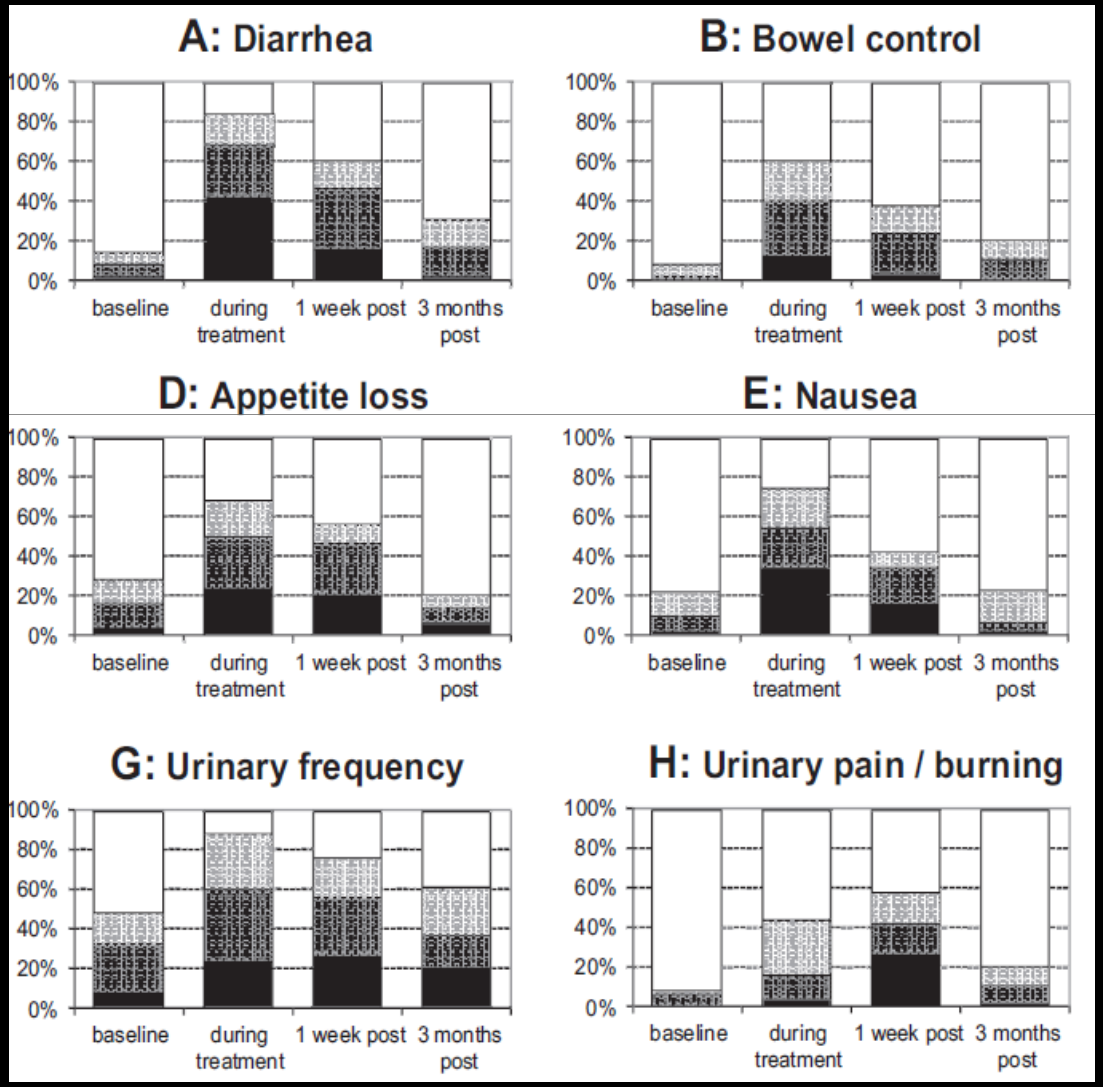

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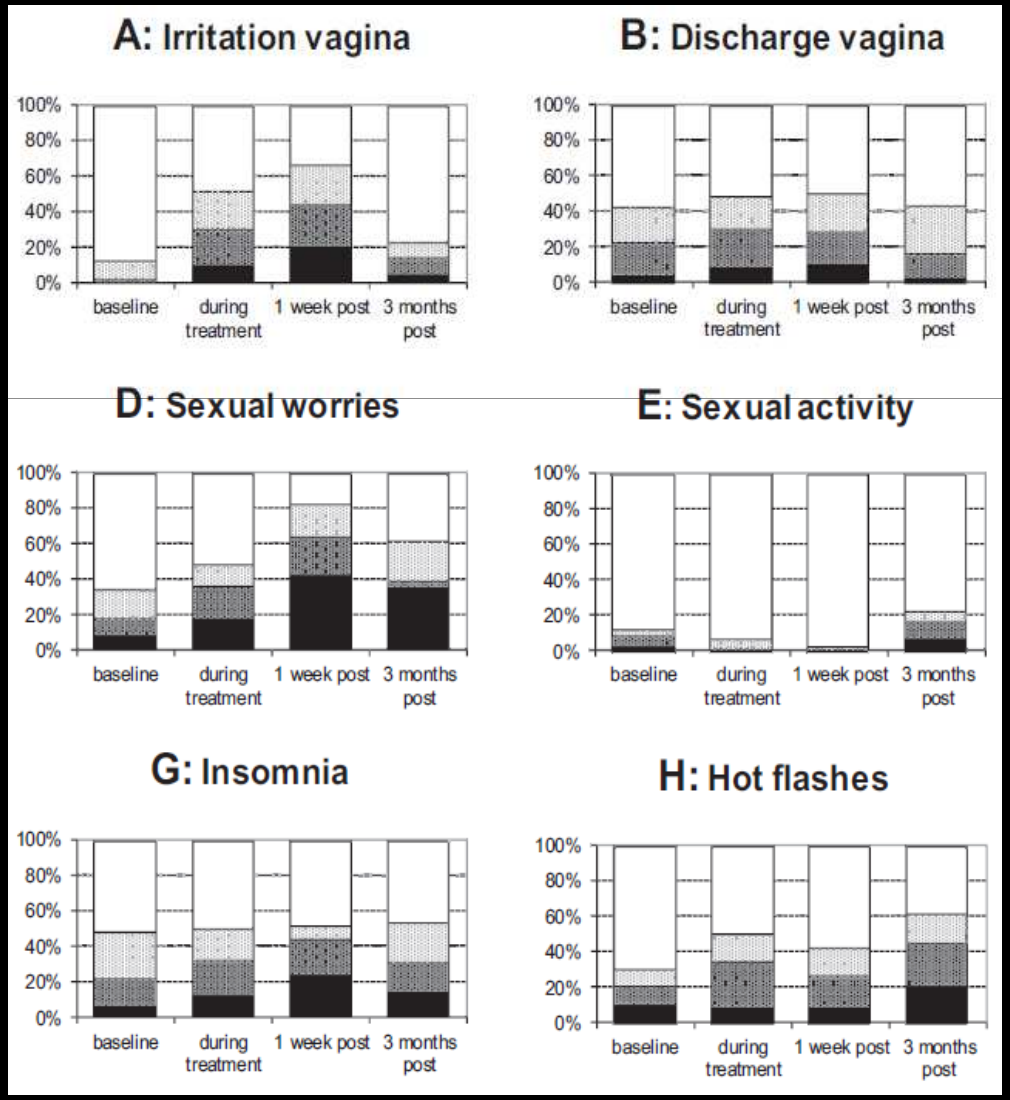
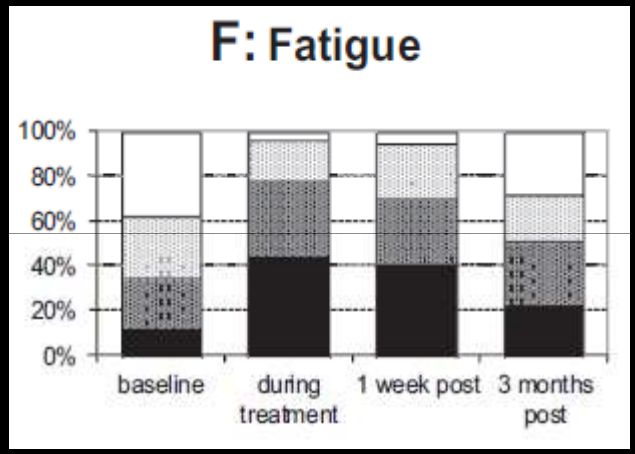


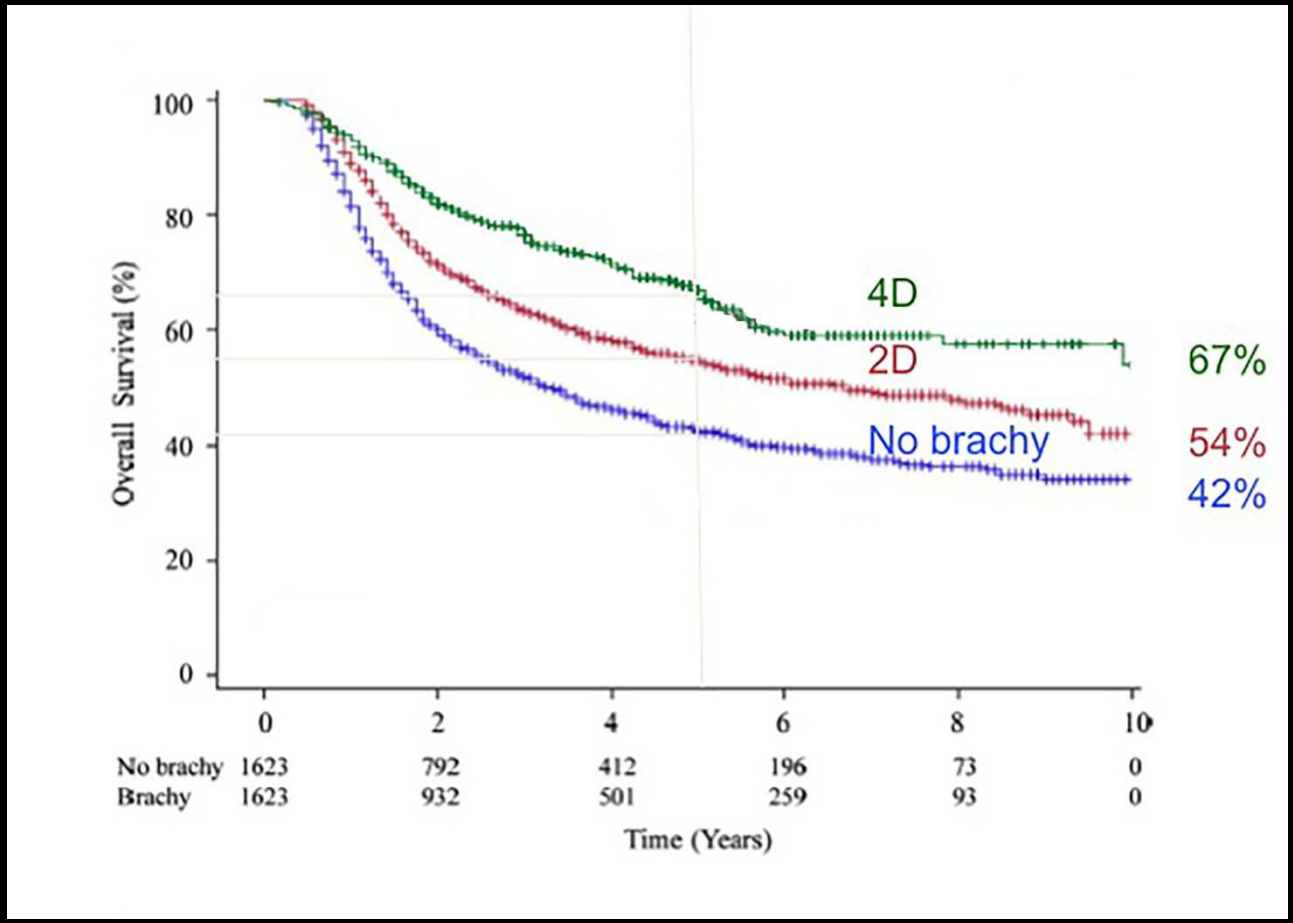


N=50
EORTC QLQ C30
EORTC QLQ Cx24

Gynecologic Oncology 136 (2015) 415–423

Overall Survival locally advanced cervical cancer: the impact of brachytherapy

Total
25% increase in
Overall Survival



Han et al Int J Radiation Oncol Biol Phys 2013;87:111-119
Sturdza et al. Improved local control and survival in LACC through Image guided adaptive brachytherapy, submitted

Re-irradiating head and neck cancers and pelvic recurrences: from brachytherapy to SBRT

Isacco Desideri,

Radiation Oncology Departement – University of Florence

Outline

- The burden of loco-regional recurrence
- Re-irradiation: is there any evidence?
  - **after salvage surgery**
  - **unresectable disease**
- Open issues & future perspectives

Where do we fail in head and neck cancer?

MARCH[1]

MACH-NC[2]

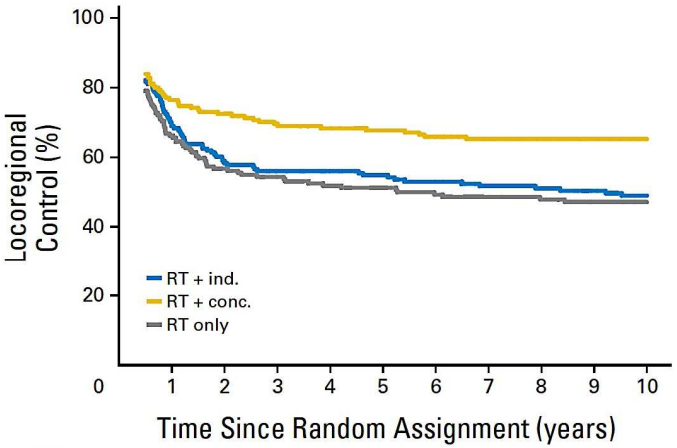
104 trials (1965 – 2000)	**Patients, N (number of comparisons)**	**Locoregional events**	
		N	% in first 2 years
Radiotherapy	6515 (17)	**51%**	92
Concomitant chemotherapy	9530 (56)	**50%**	93
Induction chemotherapy	4631 (32)	**47%**	91
Adjuvant chemotherapy	2068 (11)	**27%**	91

[1]*Bourhis J, Lancet 2006*

[2]*Pignon JP, Radiother Oncol 2009*

Michiels S, Lancet Oncol 2009

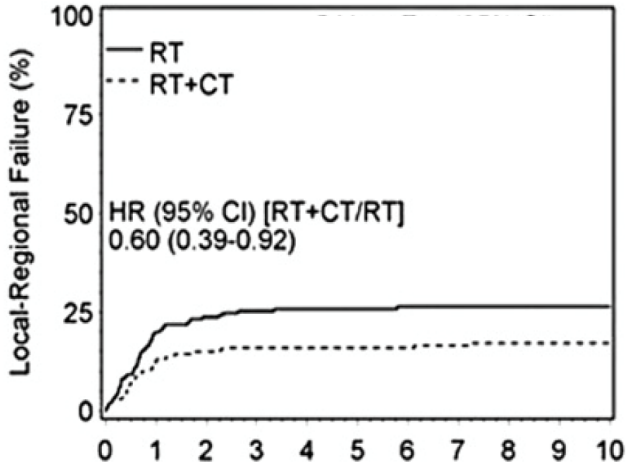
RTOG 91-11



No. at risk
RT + ind.
RT + conc.
RT only

46% vs 33% vs 49% (5-y)

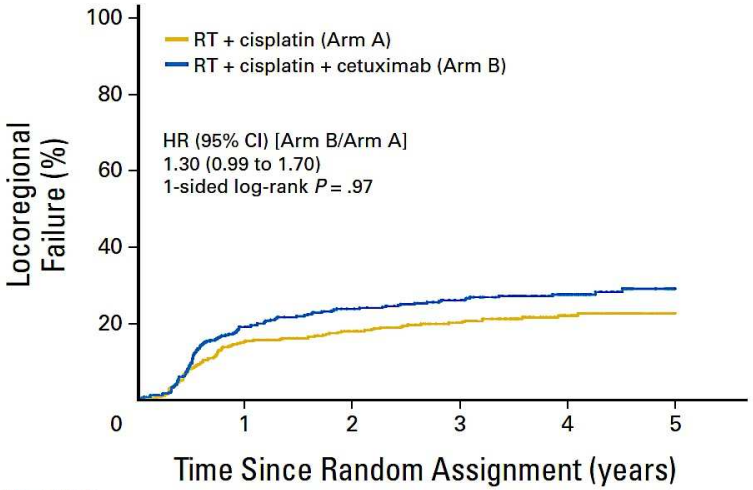
RTOG 95-01



Patients
RT
RT+CT

25% vs 16% (5-y)

RTOG 0522

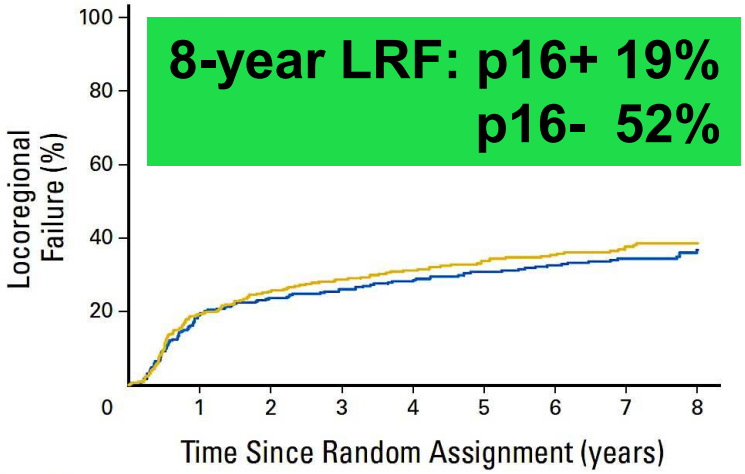


No. at risk
Arm A
Arm B

20% vs 26% (3-y)

RTOG 0129

8-year LRF: p16+ 19%
p16- 52%



No. at risk
SFX
AFX-C

31% vs 34% (5-y)

The burden of loco-regional recurrence

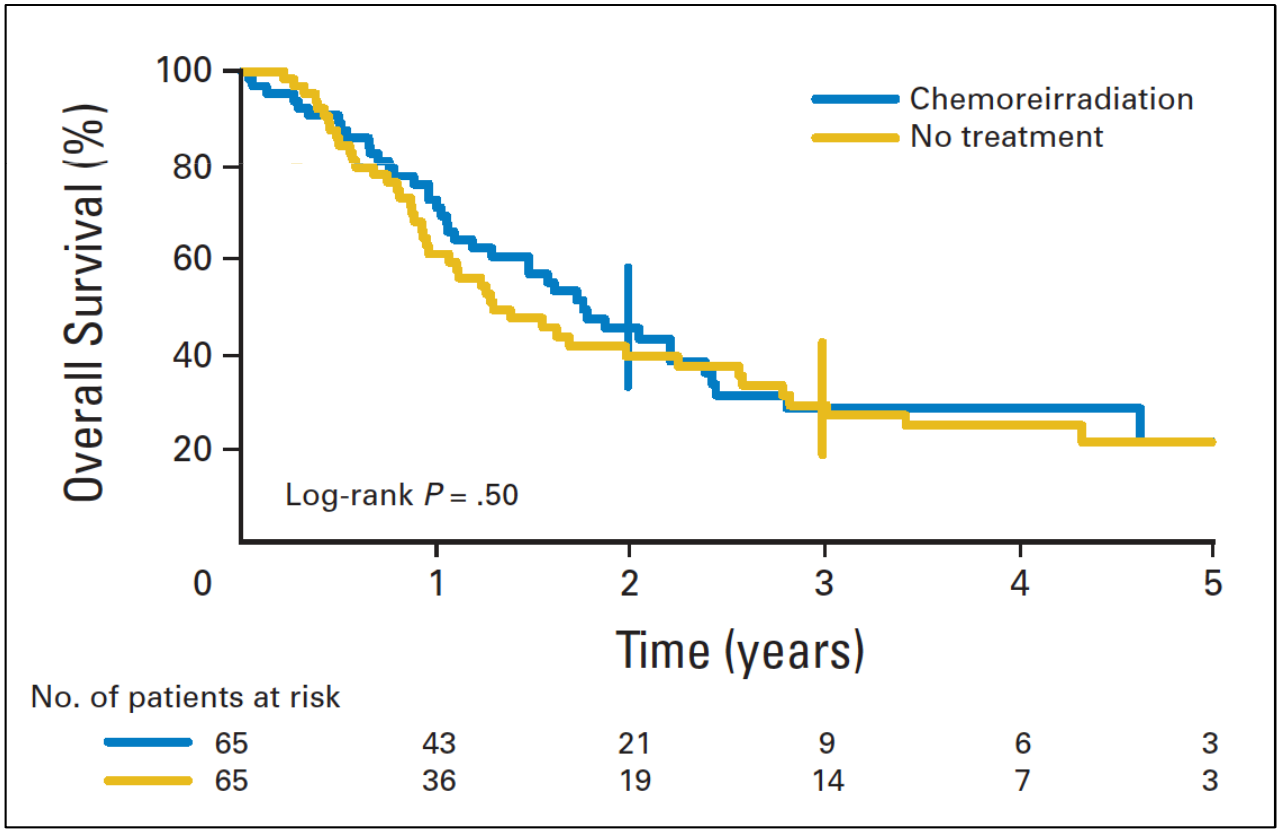
- Surgery: the most effective curative-intent tx
  - half or less of pts are amenable to salvage
  - ≥ 25%: major post-op complications
- Long-term survival achieved in 1/3 of cases
  - best if: rT1; larynx vs other sites
  - meta-analysis on 1080 pts: 5-y DFS 39%

Goodwin WJ, Laryngoscope 2000

- Rate of 2nd recurrence still high (up to 60%)
  - poor outcome if adverse pathologic features

Re-irradiation after salvage surgery

- 130 pts randomized to 60 Gy, 2 Gy/fx (d 1–5; 9-d break) with concomitant HU, FU vs observation



- LRC: HR 2.73 (95% CI, 1.66 to 4.51; p < .0001)
- G3/G4 late toxicity (2-y): 39% vs 10%
- DFS: HR 1.68 (95% CI, 1.13 to 2.50; p <.01)

Janot F, J Clin Oncol 2008

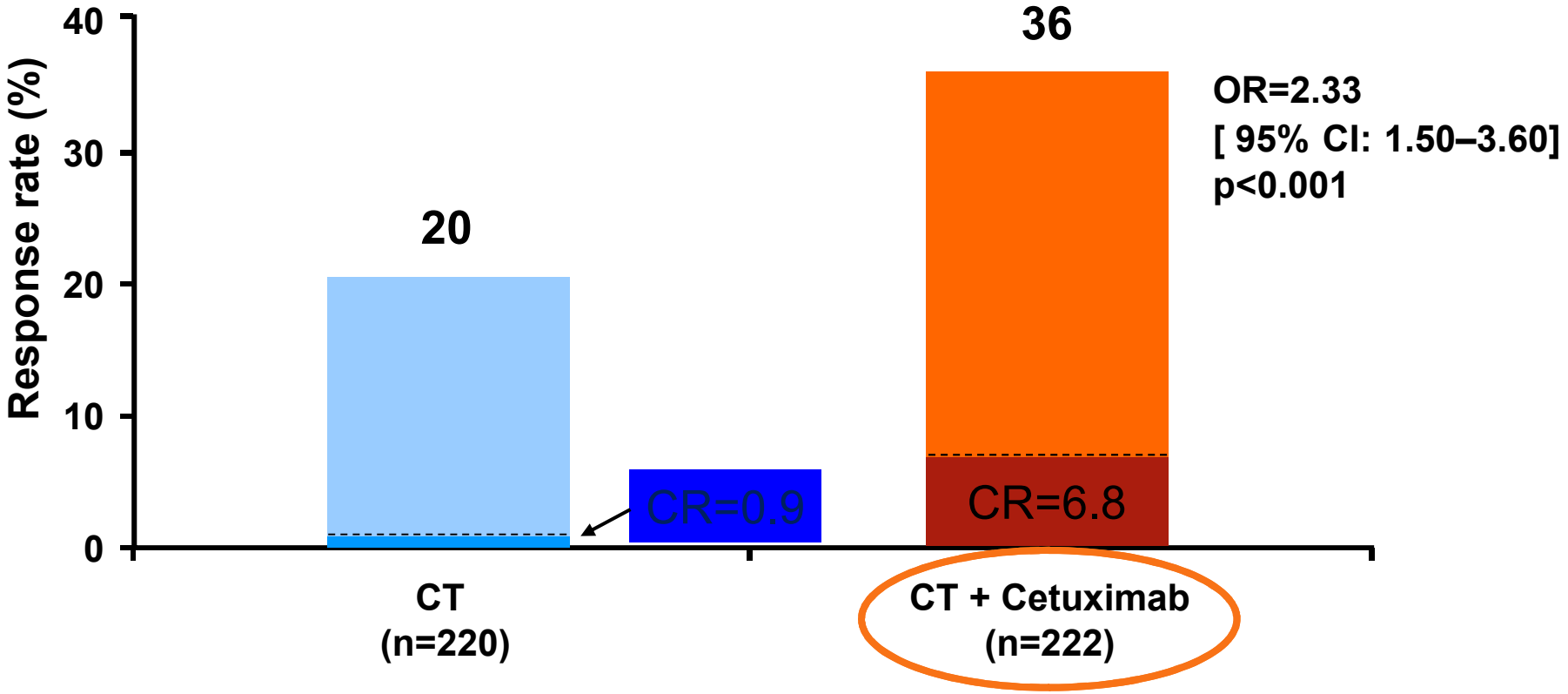
So, is it standard practice?

- Selected pts with high risk features (R1, ECE) should be considered for post-op re-RT
- 40-50% OS @ 2 years may be achieved
- Severe toxicity in > 1/3 of pts; treatment mortality up to 8%

1. **60 Gy/2 Gy fx, split-course over 11 weeks?**
2. **role of chemotherapy?**
3. **impact of hyperfractionation? IMRT?**

Unresectable recurrence: real world scenario

Median **PFS: 5.6 mo** with cetuximab vs 3.3 mo without (HR 0.54; 95% CI, 0.43 to 0.67; p < 0.001)



Vermorken J, N Eng J Med 2008

Unresectable recurrence: real world scenario

	Cetuximab plus Platinum–Fluorouracil (N = 222)	Platinum–Fluorouracil Alone (N = 220)
Extent of disease — no. (%)		
Only locoregionally recurrent	118 (53)	118 (54)
Metastatic with or without locoregional recurrence	104 (47)	102 (46)

- no difference in OS between pts with metastatic/recurrent and locoregional recurrence only p=0.06

Vermorken J, N Eng J Med 2008

Re-irradiation for unresectable disease

- **3D-CRT**
- **IMRT**
- **Brachytherapy**
- **SBRT**

Benchmark data: 3D-CRT

Author	N, study type	Interval to ReRT (months)	Re-irradiation	CT	G3/G4 late toxicity, TRD	2-year outcome
Salama et al, 2006[23] (1986–2001)	66, prospective	N.S.	TD 66–67 Gy, 2 Gy/fx q.d. or 1.5 Gy/fx b.i.d. (d 1–5 → 9-d break) Reirradiation volume: GTV + 10 mm ± ELN-RT	HU + 5FU, CDDP, gemcitabine, paclitaxel, irinotecan	N.S.	3-y LRC, 36% 3-y OS, 11%
Langer et al, 2007[28] (2000–2003)	99, prospective RTOG 9911	40 (6–318)	TD_{median} 60 Gy, 1.5 Gy/fx b.i.d. (d 1–5 → 9-d break) Reirradiation volume: GTV + ≥20 mm	CDDP + paclitaxel	N.S. TRD, 8%	OS, 25.9%
Spencer et al, 2008[27] (1996–1999)	79, prospective RTOG 9610	30 (7–238)	TD 60 Gy, 1.5 Gy/fx b.i.d. (d 1–5 → 9-d break) Reirradiation volume: GTV + ≥20 mm	HU + 5FU	At 2–5 y, 9.4% TRD, 7.6%	OS, 25.9%
Berger et al, 2010[48] (1997–2007)	57‡, prospective	16 (7.5–188)	TD 40 Gy, 2 Gy/fx (wk 2 + 3, 5 + 6) *or* TD 49.6 Gy, 2 Gy/fx (wk 2 + 3, 5 + 6, CB with 1.6 Gy 2nd fx after 28 Gy) Reirradiation volume: PTV = GTV + 10 mm	CDDP + docetaxel	40% TRD, 7%	40 Gy group: OS, 16%† 49.6 Gy group: OS, 31%
Tortochaux et al, 2011[26] (1999–2005)	30¶, randomized GORTEC 98-03	N.S.	TD_{median} 60 Gy, 2 Gy/fx, (d 1–5 → 9-d break) Reirradiation volume: GTV + ≥2 cm + ELN-RT	HU + 5FU	37% TRD, 7%	OS, 8%†

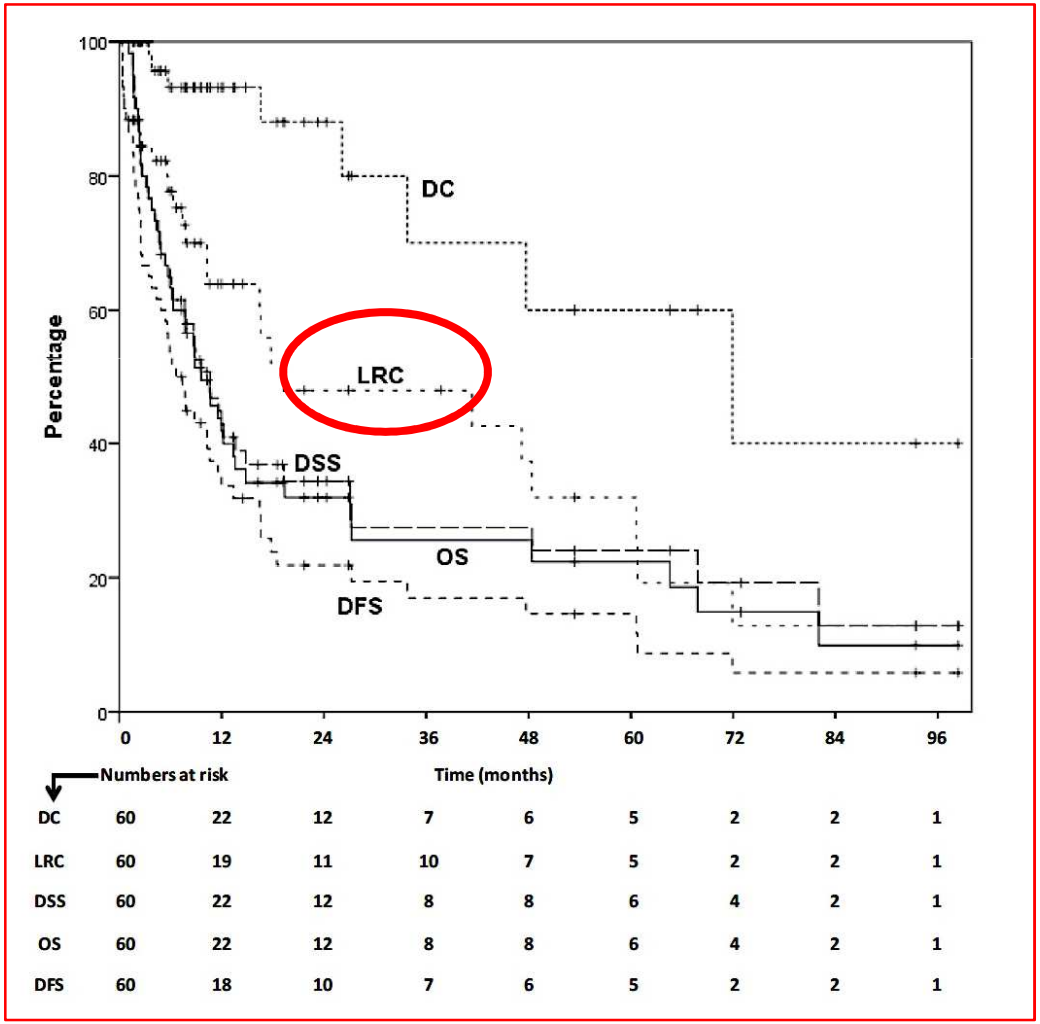
?

?

G3/G4: up to **40%**
2-year OS: 10 to **30%**
TRD: up to **10%**

IMRT: Gent University

- 60 patients (1997 – 2011); 69.1 Gy/212 cGy fx



- LRC:
  - 1-y: 64%
  - 2-y: 48%
- PFS (median): 6.7 months
- G3/G4 late toxicity: 27% (2-y)

Duprez F, Radiother Oncol 2014

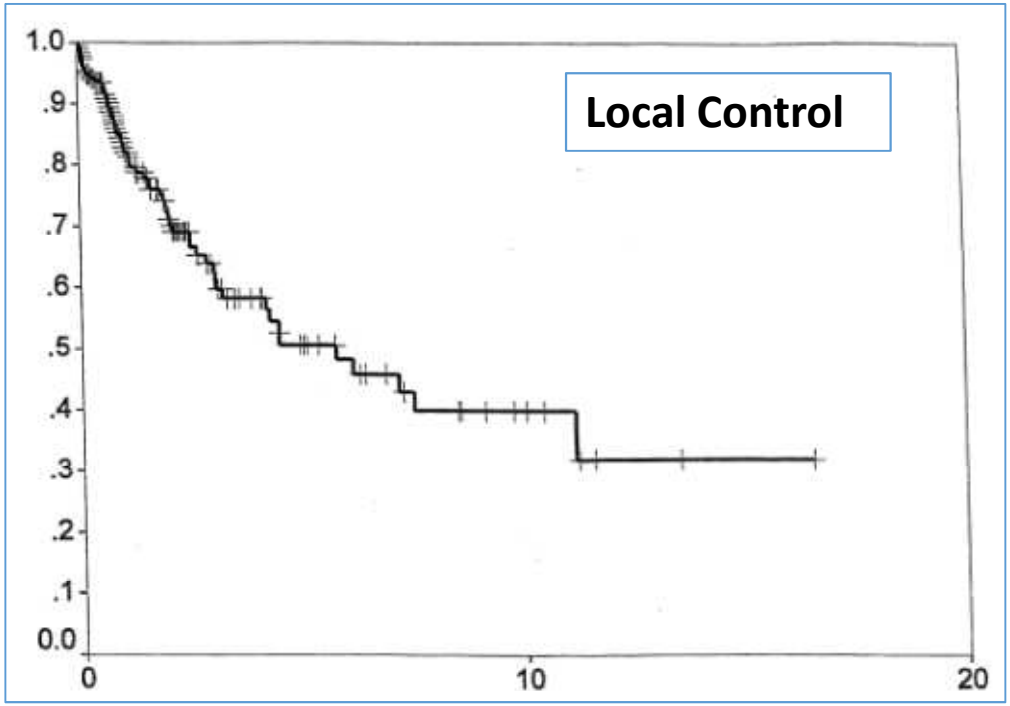
Brachytherapy

INTERSTITIAL LOW-DOSE-RATE BRACHYTHERAPY AS A SALVAGE TREATMENT FOR RECURRENT HEAD-AND-NECK CANCERS: LONG-TERM RESULTS

AJMEL PUTHAWALA, M.D., FACR,*† A. M. NISAR SYED, M.D., FRCS (LON & EDIN),*† SHERIEF GAMIE, M.D.,* YI-JEN CHEN, M.D., PH.D.,*† ADINA LONDRC, M.D.,* AND VAUGHN NIXON, M.D.‡

- 220 patients treated between 1979 and 1997 for recurrent SCCHNC originating from various sites
- Median retreatment dose: 53 Gy
- Mean tumor Volume: 68.75 cc
- Interstial Hyperthermia: 60% of patients
- Concurrent chemotherapy: 40% patients

Puthawala et al , Int J Radiat Oncol Biol Phys 2001



- 2-year LC: 67%

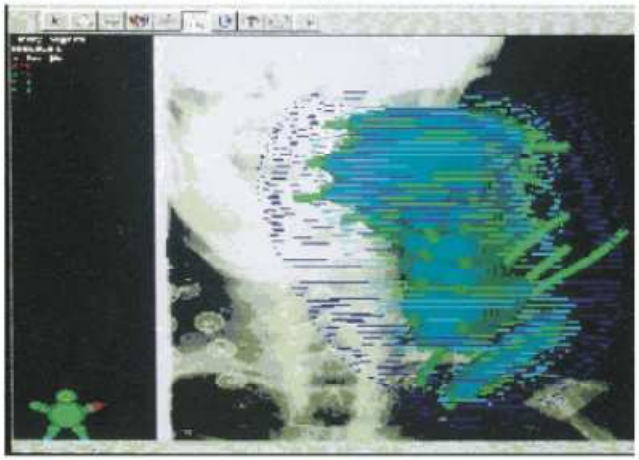
Type	Number of patients
Soft tissue necrosis	28
Osteoradionecrosis	17
Orocutaneous fistulae	3
"Woody" fibrosis	7
Carotid "blowout"	4
Tongue atrophy	6
Dysphagia	8
Severe trismus	4
Hemorrhage	3
Total	80*/220 (36%)

- 27% G3/G4 late toxicity
- Most frequent toxicity: Mandibular radionecrosis (56%)

SALVAGE HIGH-DOSE-RATE (HDR) BRACHYTHERAPY FOR RECURRENT HEAD-AND-NECK CANCER

JAROSLAW T. HEPEL, M.D.,* A. M. NISAR SYED, M.D., F.R.C.S., F.A.C.R.,†
AJMEL PUTHAWALA, M.D., F.A.C.R.,† ANIL SHARMA, PH.D.,† AND PAUL FRANKEL, PH.D.‡

(a)



(b)

- 30 patients previously irradiated by EBRT
- 36 sites of disease treated with HDR-IBT
- Mean tumor dose 34 Gy (18-48 Gy)
- Bid fractions (300/400 cGy)
- 1 year-LC: 69%
- 2-years DFS: 45%
- 2-years OS: 37%
- G3/G4 toxicity: 16%

Head and neck brachytherapy

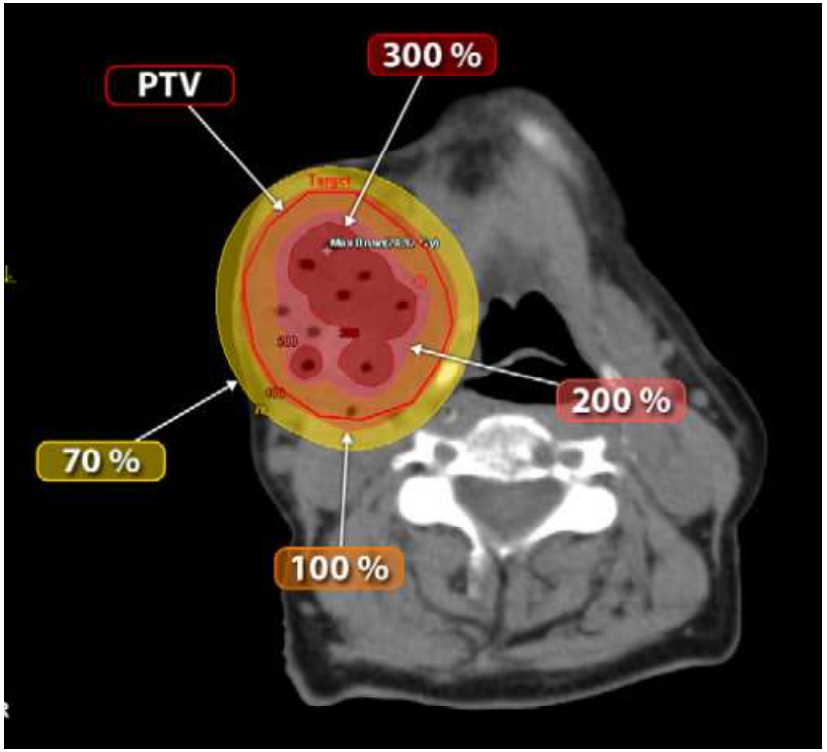
Hypofractionated accelerated CT-guided interstitial ^{192}Ir-HDR-Brachytherapy as re-irradiation in inoperable recurrent cervical lymphadenopathy from head and neck cancer

Nikolaos Tselis [a,*], Markus Ratka [a], Hans-Georg Vogt [a], Christos Kolotas [b], Mehran Baghi [c], Dimos Baltas [d], George Fountzilas [e], Vassilios Georgoulias [f], Hanns Ackermann [g], Nikolaos Zamboglou [a]

- From 2000 to 2007, 74 patients were treated for inoperable recurrent cervical lymphadenopathy.
- All patients had previously been treated with radical radiotherapy or chemoradiation with or without surgery.
- The HDR-BRT delivered a median salvage dose of **30.0 Gy** (range, 12.0–36.0 Gy) in **twice-daily fractions** of 2.0–5.0 Gy in 71 patients and of 30.0 Gy (range, 10.0–36.0 Gy) in once-daily fractions of 6.0–10.0 Gy in three patients.

Tselis et al. Radiother Oncol 2011

- The overall and disease-free survival rates at one, two and three years were 42%, 19%, 6%, and 42%, 37% and 19%, respectively.
- The local control probability at one, two and three years was 67% at all three time points.
- Grade III–IV complications occurred in 13% of patients.



- At a median follow-up of 10 months, a total of 17 (23%) patients experienced neck disease progression. Of those, 11 patients had progression on the periphery or outside the implanted volume and six patients within the implanted volume.

Tselis et al. Radiother Oncol 2011

LDR and HDR-brachytherapy for recurrent cancer of the head and neck

Study	Patients (N)	Salvage treatment	Toxicity Grade III-IV	Outcome
Kupferman et al.	22	Surgery + ^{192}Ir-LDR-BRT median 60 Gy (range 20-60 Gy)	23%	2 y OS = 57% 2 y LC = 67%
Housset et al.	23	^{192}Ir-LDR-BRT 65 Gy in two session separated by 1 month (35 Gy + 30 Gy)	36%, 4% Grade V toxicity	1 y OS = 26% 2 y OS = 13%
Bollet et al.	84	a) ^{192}Ir-LDR-BRT mean 56.5 Gy (range 30-112 Gy) / (n = 72) b) ^{192}Ir-LDR-BRT + EBRT mean 38 Gy (range 23.6-50 Gy) / (n = 12)	35%, 7% Grade V toxicity	1 y OS = 33% 2 y LC = 31%
Cornes et al.	39	Surgery + ^{192}Ir-LDR-BRT mean 49.5 Gy in 5 days	23%	2 y OS = 38% 1 y LC = 63%
Puthawala et al.	220	^{192}Ir-LDR-BRT median 53 Gy (range 35-65 Gy)	27%	2 y OS = 43% 2 y LC = 69%
Hepel et al.	30	^{192}Ir-HDR-BRT mean 34 Gy (range 18-48 Gy)	16%	2 y OS = 37% 2 y LC = 45%
Narayana et al.	30	a) Surgery + ^{192}Ir-HDR-BRT 34 Gy / (n = 18) b) ^{192}Ir-HDR-BRT 40 Gy / (n = 9) c) EBRT 40-50 Gy + ^{192}Ir-HDR-BRT 20 Gy / (n = 3)	13% no Grade IV toxicities	2 y OS = 63% 2 y LC = 71%
Tselis et al.	74	a) ^{192}Ir-HDR-BRT median 30 Gy (range 12-36 Gy) / (n = 69) b) ^{192}Ir-HDR-BRT + EBRT median 30.6 Gy (range 20-45 Gy) / (n = 5)	13%	2 y OS = 19% 2 y LC = 67%
Kolotas et al.	49	^{192}Ir-HDR-BRT mean 31.5 Gy (range 30-36 Gy)	4% no Grade IV toxicities	2 y OS = 31%
Rudzkiankas et al.	30	a) Surgery + ^{192}Ir-HDR-BRT 30 Gy / (n = 13) b) ^{192}Ir-HDR-BRT 30 Gy / (n = 17)	3%	2 y OS = 47% 2 y LC = 67%

Interstitial PDR brachytherapy (1)

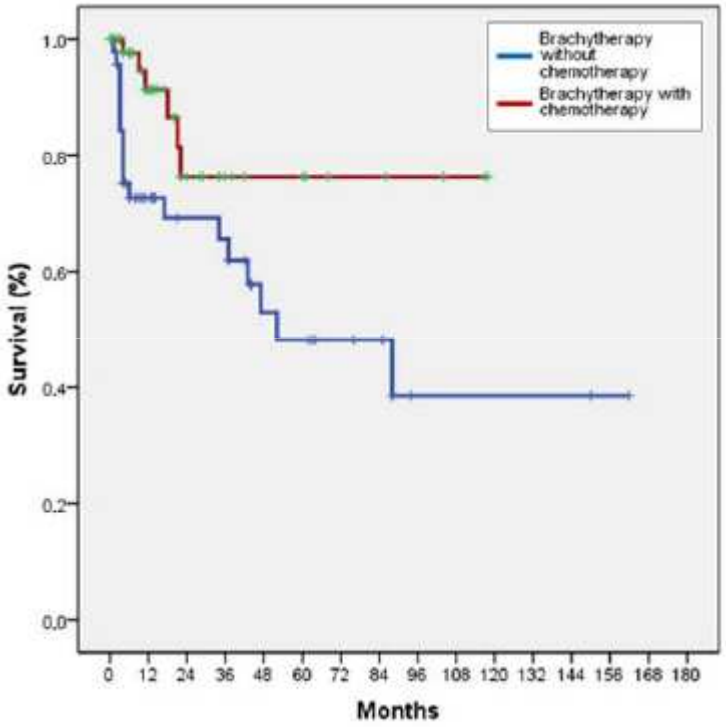
- 104 patients (1999 – 2008), PDR up to **55 Gy**
  - 51%: after R1/R2 salvage surgery
  - 26%: SPT's
  - 60% oral cavity
  - median implant volume 26 cm^3

- LRC:
  2-year: 92%

- G3/G4 toxicity:
  10 – 18%

Strnad V, Strahlenter Onkol 2015

Interstitial PDR brachytherapy (2)



- Salvage brachytherapy in combination with external beam radiotherapy (EBRT) was performed in 23/104 patients (32 %)
- Concomitant chemotherapy was administered in 58/104 (55.8 %) patients

Strnad V et al. Strahlenther Onkol 2015

Stereotactic body radiotherapy

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 5, pp. 1493–1500, 2009
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0360-3016/09/$–see front matter

doi:10.1016/j.ijrobp.2008.12.075

CLINICAL INVESTIGATION **Head and Neck**

STEREOTACTIC BODY RADIOTHERAPY FOR RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK: RESULTS OF A PHASE I DOSE-ESCALATION TRIAL

Dose tier	Subjects (*n*)	Prior RT dose (mean Gy/no. of fx)	Prior spinal cord dose (mean Gy)	Dose/fx (Gy)	No. of fx	Total dose (Gy)	Mean volume of GTV receiving PD (%)
1	3	69.2/36	45.5	5	5	25	98.4
2	3	69.6/35	45.2	6.4	5	32	96.7
3	3	66/30	40.7	7.2	5	36	95
4	6	68.5/36	44.6	8.0	5	40	92
5	10	66.8/35	45.1	8.8	5	44	94

Prescription @80% IDL, 90% coverage
Dose constraints:
Spinal cord <= 8 Gy
Larynx <= 20 Gy
Mandible <= 20 Gy
Brainstem <= 8 Gy
Oral cavity no reported

Heron et al. IJROBP 2009

Table 3. Patient responses by dose tier

	Dose (Gy)					
Response	25	32	36	40	44	Total
Complete response	1	0	1*	0	0	2
Partial response	1*	0	1*	1	2	5
Stable disease	0	3	0	3	6	12
Progressive disease	0	0	0	2	2	4
Not evaluable	1	0	1	0	0	2

* Responses not confirmed.

- The overall response rate in this group of heavily pre-treated patients was 28% (CR + PR).
- No Grade 3 or 4 toxicities were noted

Table 4. Tumor response to SBRT by RECIST and PET

Response	RECIST	PET
CR/CMR	2	2
PR/PMR	5	10
SD/SMD	9	1
PD/PMD	5	6
Total	23	19

Metabolic response may precede anatomic response seen on CT good agreement between PET and CT for the assessment of CR and PD.

Heron et al. IJROBP 2009

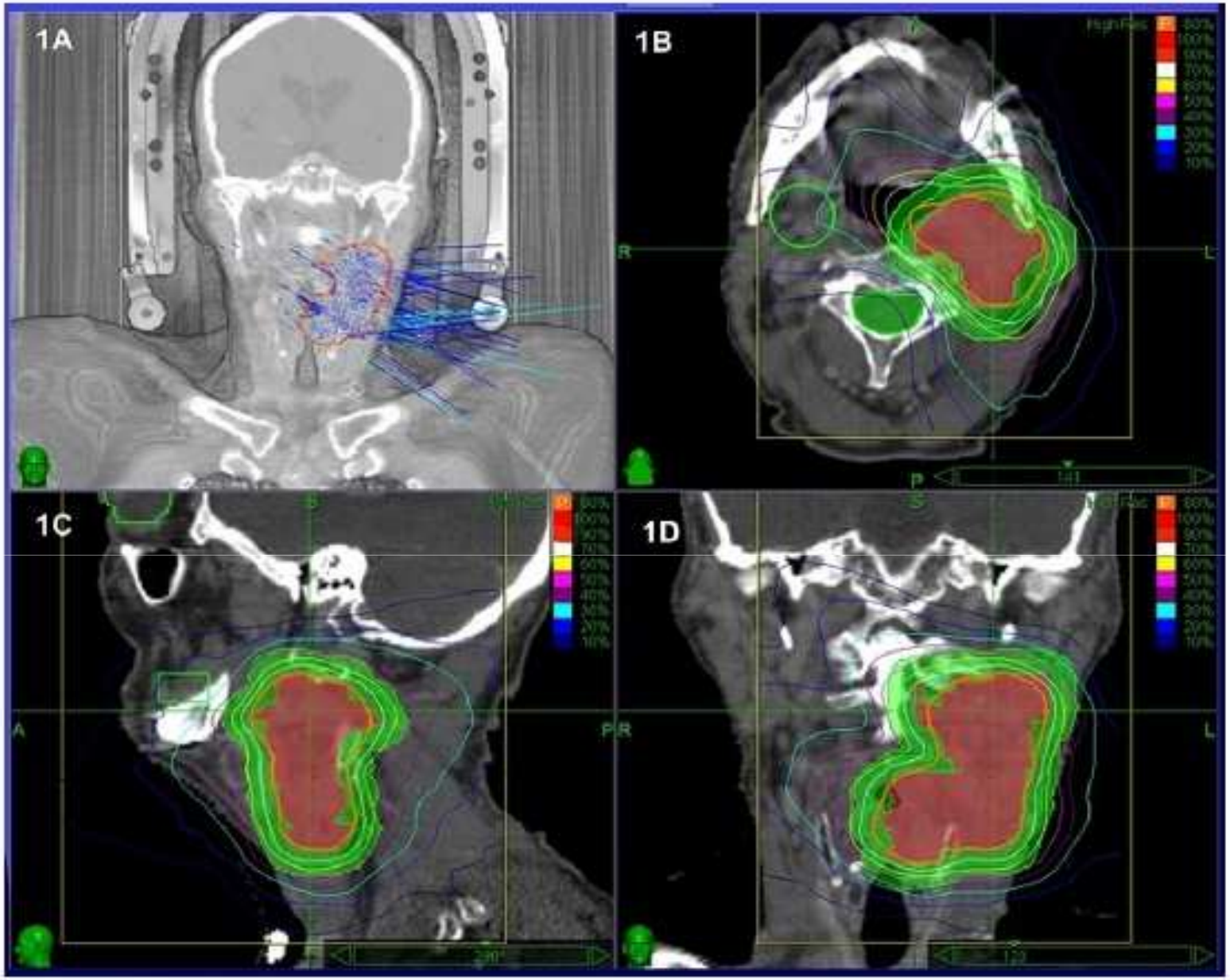


Fig. 3. Representative stereotactic body radiotherapy plan for case shown in Fig. 1. Note sharp dose gradient between gross tumor volume (GTV) and spinal cord.

Heron et al. IJROBP 2009

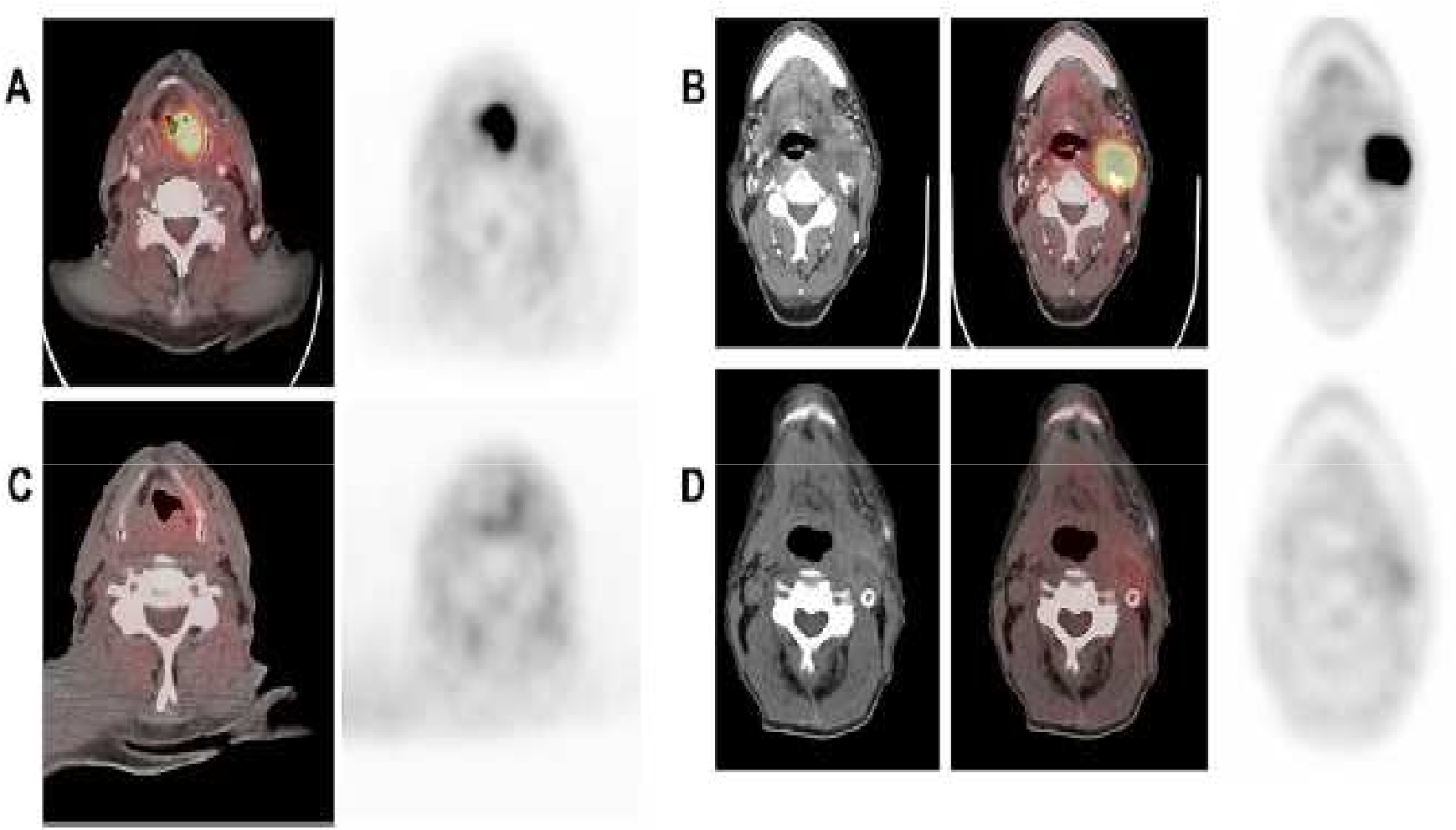


Fig. 1. Positron emission tomography–computed tomography (PET-CT) scans of recurrent squamous cell carcinoma of the head and neck: primary (A, C) and cervical (B, D) metastatic disease before (A, B) and after (C, D) stereotactic body radiotherapy.

Heron et al. IJROBP 2009

Phase II trial

Multi institutional phase II study of concomitant stereotactic reirradiation and cetuximab for recurrent head and neck cancer

Eric F. Lartigau [a,*], Emmanuelle Tresch [a], Juliette Thariat [b], Pierre Graff [c], Bernard Coche-Dequeant [a], Karen Benezery [b], Luis Schiappacasse [a], Marian Degardin [a], Pierre-Yves Bondiau [b], Didier Peiffert [c], Jean-Louis Lefebvre [a], Thomas Lacornerie [a], Andrew Kramar [a]

[a] *Centre Oscar Lambret, University Lille II & ONCOLille Consortium;* [b] *Centre Antoine Lacassagne, Nice; and* [c] *Centre Alexis Vautrin, Vandoeuvre-lès-Nancy Cedex, France*

CTV=GTV+5mm PTV=CTV+1mm

6 x 6 Gy @ 85% in 95% of PTV

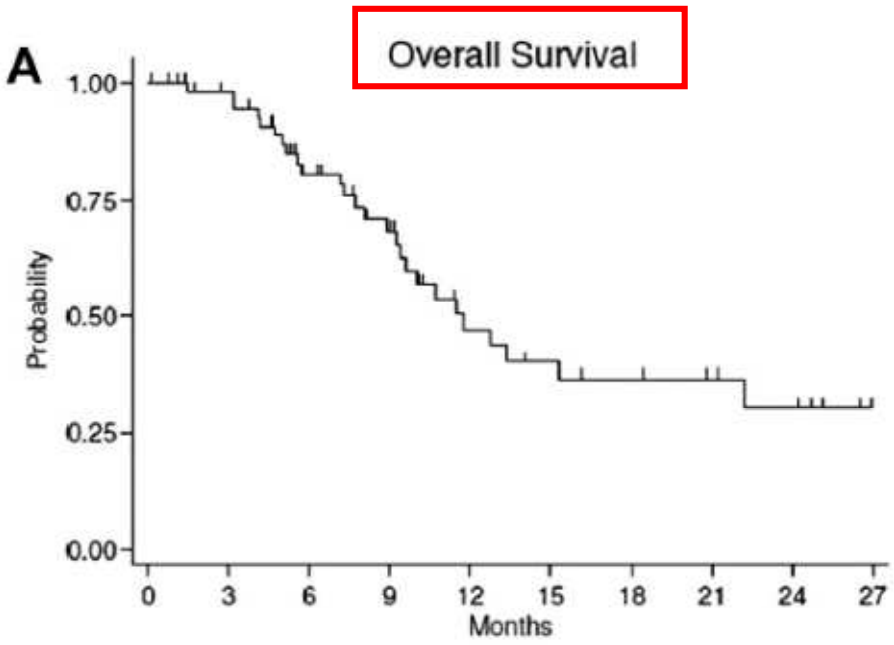
Treatment duration 11 to 12 days

Only spinal cord dose constraint of Dmax <= 6 Gy

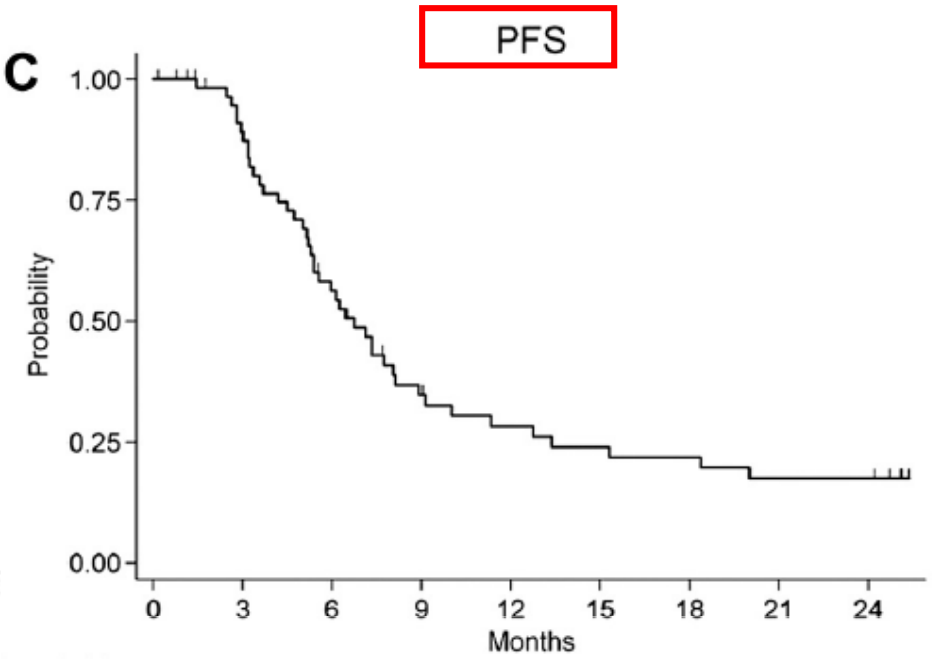
Concurrent cetuximab: 400mg/qm loading dose, then 4x 250 mg/qm

Comet et al. IJROBP 2011

Lartigau et al. Radiother Oncol 2013



Median OS 11.8 months



Median PFS 7.1 months.

- G3 toxicity: 18 patients
- G5: 1 patient (bleeding and malnutrition)

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doi:10.1016/j.ijrobp.2010.04.027

CLINICAL INVESTIGATION **Head and Neck**

SALVAGE REIRRADIATON WITH STEREOTACTIC BODY RADIOTHERAPY FOR LOCALLY RECURRENT HEAD-AND-NECK TUMORS

MUSTAFA CENGIZ, M.D.,* GÖKHAN ÖZYIĞIT, M.D.,* GÜZDE YAZICI, M.D.,* ALI DOĞAN, M.S.,* FERAH YILDIZ, M.D.,* FARUK ZORLU, M.D.,* MURAT GÜRKAYNAK, M.D.,* IBRAHIM H. GULLU, M.D.,† SEFIK HOSAL, M.D.,‡ AND FADIL AKYOL, M.D.*

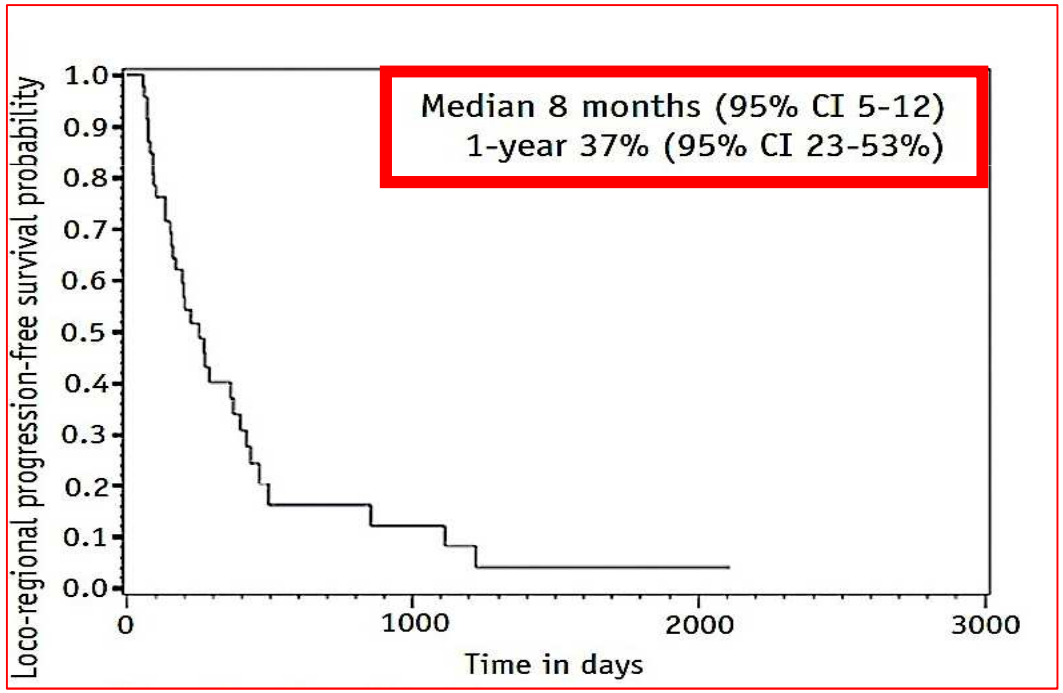
Departments of *Radiation Oncology, †Medical Oncology, and ‡Ear, Nose, and Throat Surgery, Hacettepe University, Faculty of Medicine, Ankara, Turkey

- Treatment-related carotid blow-out syndrome was observed in 8 patients (17.8%), 7 (15.2% of whom died of bleeding from carotid.
- Bleeding was not statistically significantly related to tumor volume ($p = 0.682$), response to treatment ($p = 1.00$), sex ($p = 0.698$), or time elapsed between SBRT and previous radiotherapy ($p = 0.113$). However, when the dose received by the carotid artery was grouped as <100% of the prescribed dose, a significant relation was observed between the carotid artery dose and bleeding ($p = 0.021$). None of the patients with carotid artery dose <100% experienced carotid blow-out syndrome.
- Bleeding occurred only in patients whose carotid artery walls were circumscribed by the tumor with a degree of >180 ($p = 0.073$).

Cengiz et al. IJROBP 2011

SBRT: Pittsburgh phase II

- 50 patients (2007 – 2013)
  - 40/44 Gy in 5 fx + 3 cycles Cetuximab
- Endpoint: 1-year locoregional PFS from 35% to 55%



- PFS (median): 7 months
- G3/G4 late toxicity: 6% (no G4)

- local progression-free survival: 60% (1-y)

Vargo A, Int J Radiat Oncol Biol Phys 2015

Table 3 Cross-trial comparisons for SBRT plus cetuximab, conventional reirradiation plus chemotherapy, and chemotherapy alone with or without cetuximab

Study (ref)	Conventional reirradiation plus chemotherapy	PFS (mo)	OS (mo)	% of cases of toxicity grade 3+
RTOG 9610 (9)	60-Gy hyperfractionated plus 4 cycles of 5FU and hydroxyurea	NR	8.5	85%
RTOG 9911 (10)	60-Gy hyperfractionated plus 4 cycles of cisplatin plus paclitaxel	7.8	12.1	85%†
Chemotherapy with or without Cetuximab				
EXTREME (14)*	Platinum plus 5FU × 6 cycles	3.3	7.4	76%
EXTREME (14)*	Platinum plus 5FU plus cetuximab × 6 cycles	5.6	10.1	82%
SBRT plus cetuximab				
UPCI 06-093	SBRT plus 3 cycles of cetuximab	6.7	10.0	12%
Lartigue et al (21)	SBRT plus 5 cycles of cetuximab	7.1	11.8	30%

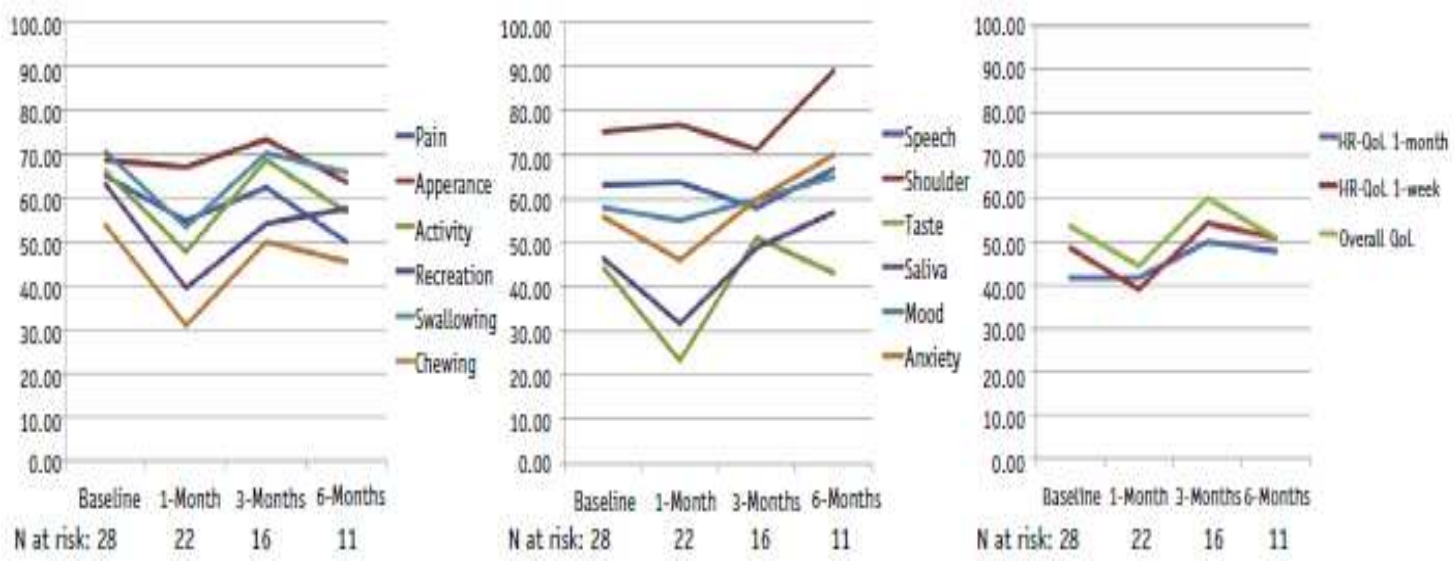
Abbreviations: 5FU = 5 fluorouracil; OS = overall survival; PFS = progression-free survival; RTOG = Radiation Therapy Oncology Group; SBRT = stereotactic body radiation therapy.

* Both recurrent and metastatic patients were included in this trial.

† Estimated in the first 2 years, the crude rates of acute grade 3+ toxicity were 78% and 37% grade 3+ late toxicity.

No grade IV toxicity present study
No carotid blow out syndrome
difference in oropharyngeal cancer patients(HPV +)
between the French trial (80%) and the presented study
(42%) may explain the slight survival differences

Vargo et al, IJROBP 2015



- There were no significant differences in local control, distant control, or overall survival by reirradiation interval, treatment platform (cyberknife /Triology/ Truebeam), or second primary versus local recurrence.
- Recurrent GTV (<25 cm3) was associated with significantly improved locoregional PFS (1 year, 53%, and 22%, p 0.029%) and overall survival (1 year, 70%, and 22%,p <0.01).
- The combination of 40 to 44 Gy over 5 fractions plus 3 doses of Cetuximab translated into a 67% relative increase in median OS (10 vs. 6 months) with acceptable toxicity compared to previous phase I study.
- Short overall treatment time and low rates of acute toxicity which allow patients with a generally poor prognosis to complete a potentially aggressive salvage therapy without compromising QoL

Vargo et al, IJROBP 2015

Study (year)	n	Re-RT dose	Time to re-RT (median)	Margins	Tumor volume (median)	LC	OS
Voynov *et al.* (2006)	22	10–36 Gy in 1–8 fx	n/a	PTV = GTV	19.1 cc (range: 2.5–140.3 cc)	2 years 26%	2 years 22%
Roh *et al.* (2009)	36	18–40 Gy in 3–5 fx	24 months	PTV = GTV + 2–3 mm	22.6cc (range: 0.2–114.9 cc)	2 years 52%	2 years 31%
Heron *et al.* (2009)	25	25–44 Gy in 5 fx	13 months	PTV = GTV	44.8 cc (range: 4.2–216.6 cc)	17% (response rate)	Median 6 months
Siddiqui *et al.* (2009)	21	18–48 Gy in 1–8 fx	19 months	PTV = GTV/CTV	15.5 cc (range: 1.7–155 cc)	2 years 40%	2 years 14%
Unger *et al.* (2010)	65	21–35 Gy in 2–5 fx	26 months	PTV = CTV = GTV + 2–10 mm	75 cc (range: 7–276 cc)	2 years 30%	2 years 41%
Rwigema *et al.* (2011)	96	15–50 Gy in 5 fx	19.4 months	PTV = GTV	24.3 cc (range: 2.5–162 cc)	2 years 31%	2 years 28%
Kodani *et al.* (2011)	21	19.5–42 Gy in 3–8 fx	n/a	PTV = GTV/ITV	11.6 cc (range: 0.7–78.1 cc)	29% (complete response rate)	2 years 58%
Cengiz *et al.* (2011)	46	18–35 Gy in 1–5 fx	38 months	PTV = GTV	45 cc (range: 3–206 cc)	1 year 84%	1 year 47%
Ozyigit *et al.* (2011)	24	30 Gy in 5 fx	38 months	PTV = GTV	63.4 cc (range: 26.3–170.4 cc)	2 years 82%	2 years 64% (CSS)
Vargo *et al.* (2012)	34	30–44 Gy in 5 fx	53 months	PTV = GTV	19.6 cc (range: 4.5–103.9 cc)	1 year 59%	1 year 59%
Lartigau *et al.* (2013)	60	36 Gy in 6 fx + cetuximab'	38 months	PTV = CTV + 1 mm CTV = GTV + 5 mm	n/a	3 months 92%	1 year 47%
Khan *et al.* (2015)	7	35–48 Gy in 5–6 fx	n/a	PTV = GTV + 2–3 mm	3.7 cm (range: 1–10 cm, diameter)	1 year 50%	1 year 60%
Vargo *et al.* (2015)	50	40–44 Gy in 5 fx + cetuximab	18 months	PTV = GTV + 3–5 mm	36.5 cc (range: 3.6–209.2 cc)	1 year 60%	1 year 40%

Potential pitfalls when reirradiating H&N tumors

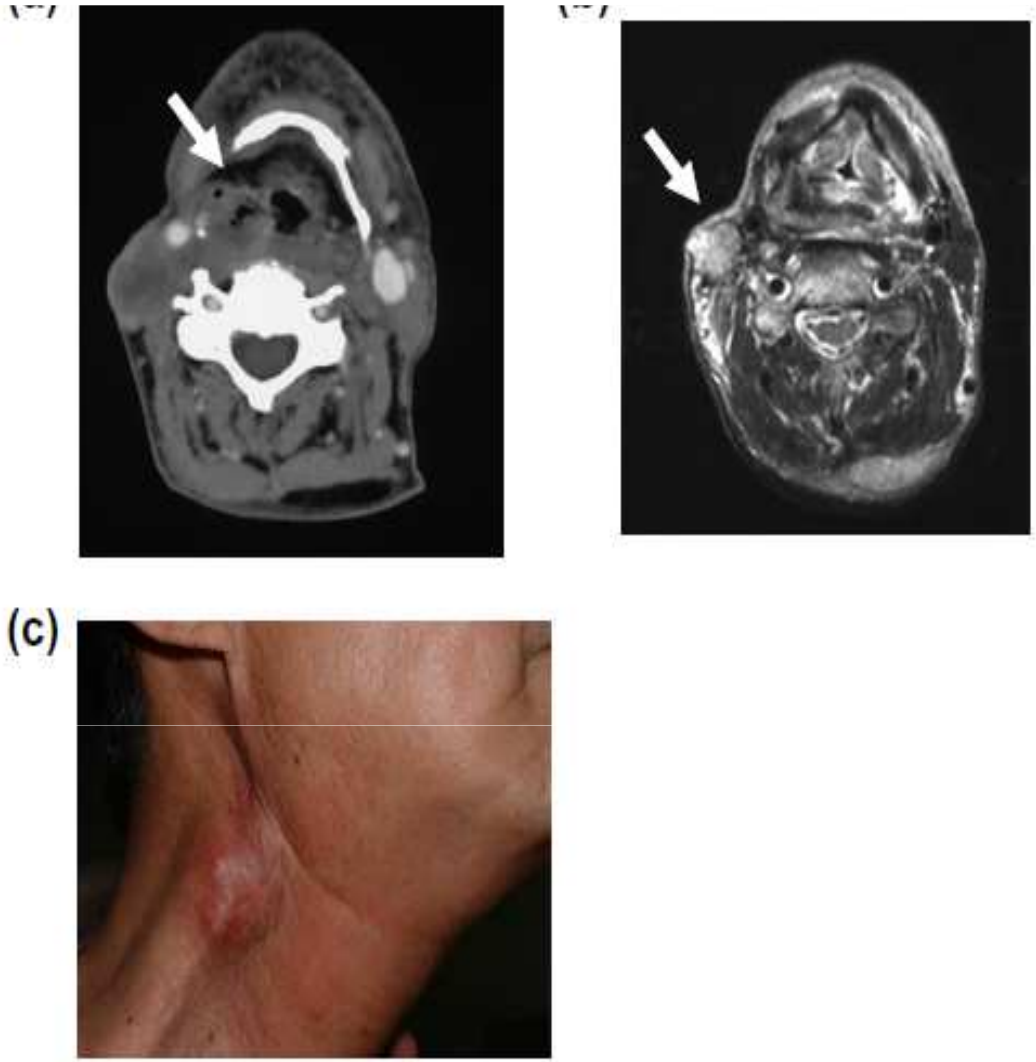


Fig. 1. Case of carotid blow out syndrome (CBOS). A 65-year-old male with hypopharyngeal cancer (moderately differentiated squamous cell carcinoma) with a pathological stage of t3n2c underwent surgery (primary cancer and bilateral radical neck dissection) and was followed up with postoperative radiotherapy at 60 Gy/30 fractions. He showed a recurrent tumor at the primary site and multiple neck nodes (rT3N2b) 8 months later. Then, he received 27 Gy in five fractions by CyberKnife SBRT. He showed all three risk factors prescribed by the CBOS index: radiotherapy to lymph node areas, a tumor involving <180° of the carotid artery, and presence of ulceration and PTV (49.3 cm^3). He developed CBOS 2 months after treatment and died the next day. (a) CT image. Arrow indicates ulceration in primary tumor recurrence. (b) MRI image. Arrow indicates lymph node metastasis with skin invasion. (c) Photograph of lymph node metastasis with skin invasion.

Yamazaki et al. radiotherapy and oncology 2015

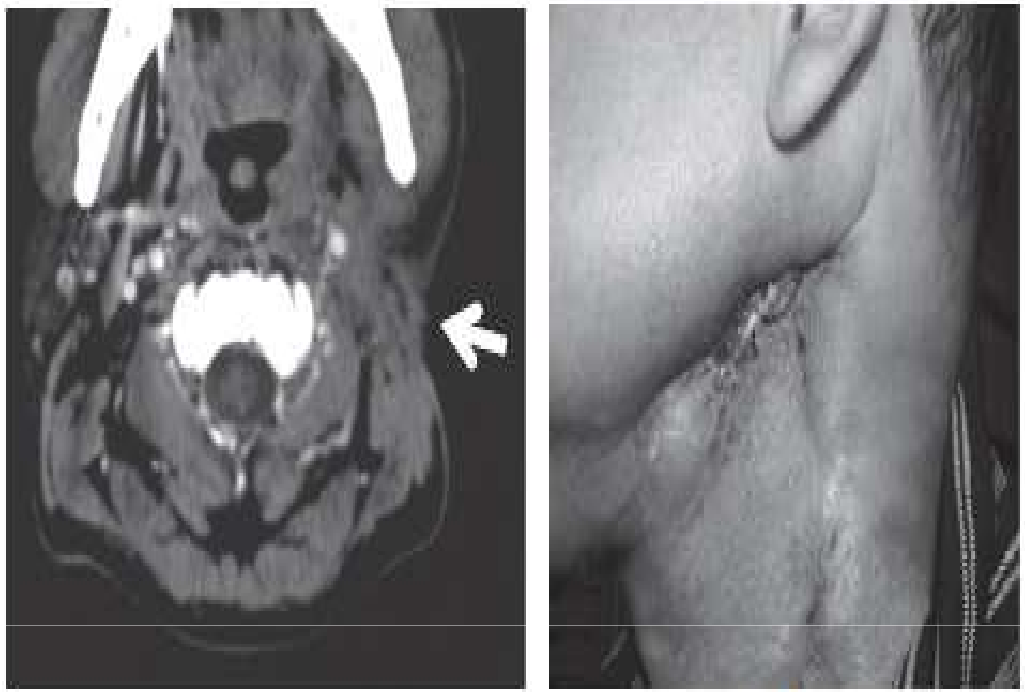


Fig. 1. Case of skin invasion. This patient showed lymph node recurrence after resection of tongue cancer and neck dissection at left neck following postoperative external radiotherapy (60 Gy/30 fractions). CyberKnife hSRT was prescribed with 39 Gy in 5 fractions. He suffered from CBS five months later, which resulted in death one day after bleeding. (a) Contrast enhanced CT image before re-irradiation. (b) Photograph of skin invasion.

Yamazaki et al. radiotherapy and oncology 2013

Characteristics and treatment factors of patients.

Variables	Strata	CBS (−) n = 60		CBS (+) n = 12		p-Value
		No. or mean ± SD, Median (range)	(%)	No. or median (range)	(%)	
Age		63 (45–83)		60 (44–66)		NS
Gender	Female	13	(76)	4	(24)	NS
	Male	47	(85)	8	(15)	
Disease	Nasopharyngeal cancer	38	(88)	5	(12)	NS
	Oropharyngeal cancer	14	(78)	4	(22)	
	Hypopharyngeal cancer	8	(73)	3	(27)	
Irradiated area	Primary	47	(89)	6	(11)	**p = 0.042**
	Lymph node	13	(68)	6	(32)	
	Lymph node only	5	(71)	2	(29)	
	Primary and lymph node	8	(67)	4	(33)	
Ulceration	(−)	52	(91)	5	(9)	**p = 0.001**
	(+)	8	(53)	7	(47)	
Surgical history	(−)	44	(86)	7	(14)	NS
	(+)	16	(76)	5	(24)	
Involvement carotid circumferential	0–180°	22	(100)	0	(0)	**p = 0.03**
	None	14	(100)	0	(0)	
	−180°	8	(100)	0	(0)	
	180–360°	38	(76)	12	(24)	
	180°<	25	(81)	6	(19)	
	Circumferential	13	(68)	6	(32)	
Planning target volume	cm^3	13.5 (1–339)		52 (5.2–139)		**p = 0.02**
Interval	Months	17.6 (3.1–122)		24 (8.3–86.2)		NS
Prescribed dose	Gy	30 (15–39)		30 (12–40)		NS
Number of fractions		5 (3–8)		5 (1–8)		
EQD2 (prescribed dose)	Gy ($\alpha/\beta = 3$)	54 (24–124)		45.3 (24–124)		NS
Maximal dose to carotid	Gy	26.8 (7.5–43.8)		30.2 (14.1–47.7)		NS
EQD2 (maximal dose to carotid)	Gy ($\alpha/\beta = 3$)	54 (4.3–116.3)		54.7 (21.9–119.8)		NS
Prescribed previous dose	Gy	64.8 (40–74.8)		60 (40–70.2)		NS
Previous number of fractions		35 (20–62)		30 (20–58)		
*Cumulative EQD2	Gy ($\alpha/\beta = 3$)	117 (88–190)		105 (90–192)		NS

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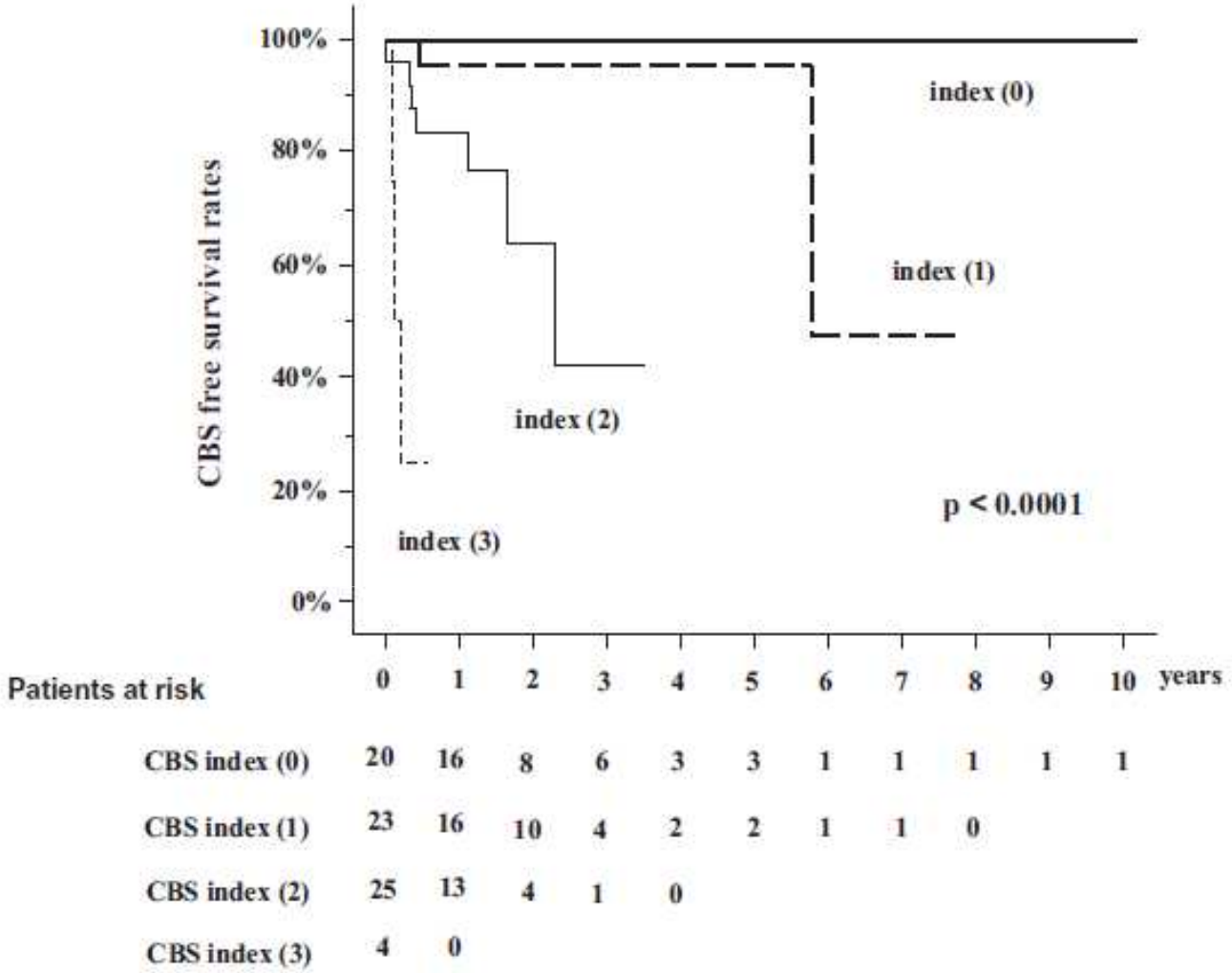


Fig. 2. CBOS-free survival rates in this matched pair model. (a) The CBOS-free survival rates in this matched pair model, according to the risk classification (CBOS index). The CBOS index was defined as the summation of each risk factor (0 or 1) (carotid invasion >180°, presence of ulceration, and lymph node area irradiation). Risk factor groups (0), (1), and (2) were associated with CBOS-free survival rates of 100%, 95%, and 84% at 12 months, respectively, and risk group (3) was associated with a CBOS-free survival rate of 25% at 6 months ($p < 0.0001$).

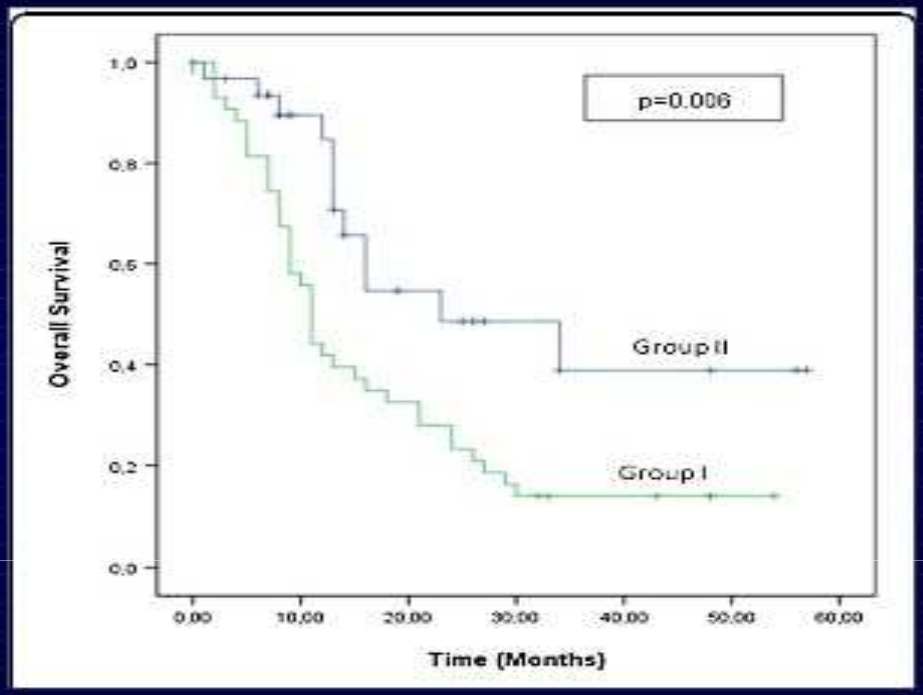
Yamazaki et al. radiotherapy and oncology 2015

Prevention of Carotid blowout syndrome (Re-RT=75)

Group=1:
- Daily SBRT
- N=43
- CBS= 7
- Median OS= 11 mo

Group=2
- Alternate day SBRT
- N=32
- CBS= 4
- Median OS= 23 mo

Reduce CBS:
- Alternate day SBRT
- Carotid contact <180deg
- Max Carotid dose <34Gy
- Skin intact
- No infection
- Low Vol rec disease



Yazici et al. Radiation Oncology 2013

Alternated day treatment is better: Sequentially 16% developed CBOS, whereas only 12% patients who received treatment every alternate day (group II) developed CBOS. Only 14% patients with CBOS survived in group I, whereas 50% in group II who developed CBOS survived.

Table 2
Frequency and mortality of carotid blow-out syndrome according to irradiated site.

	Tx no.	Pt no.	Bleeding	Bleeding/ Tx (%)	Bleeding/ Pt no (%)	Death	Death/ Pt no (%)
NPC	120	97	9	7.5%	9.3%	4	4.1%
OPC	120	99	8	6.7%	8.1%	6	6.1%
HPC	34	34	2	5.9%	5.9%	2	5.9%
Rouviere lymph node	85	61	2	2.4%	3.3%	2	3.3%
Other lymph node	125	90	11	8.8%	12.2%	8	8.9%
Total	484	381	32	6.6%	8.4%	22	5.8%

Tx = treatment session, no. = number, Pt = patient, NPC = nasopharyngeal cancer, OPC = oropharyngeal cancer, HPC = hypopharyngeal cancer.

mortality rate from CBS was 5.8% (22/381), and of the total number of CBS patients, the mortality rate was 68.8% (22/32). The median survival time after CBS was 0.1 month and the 1-year survival rate was 37.5%

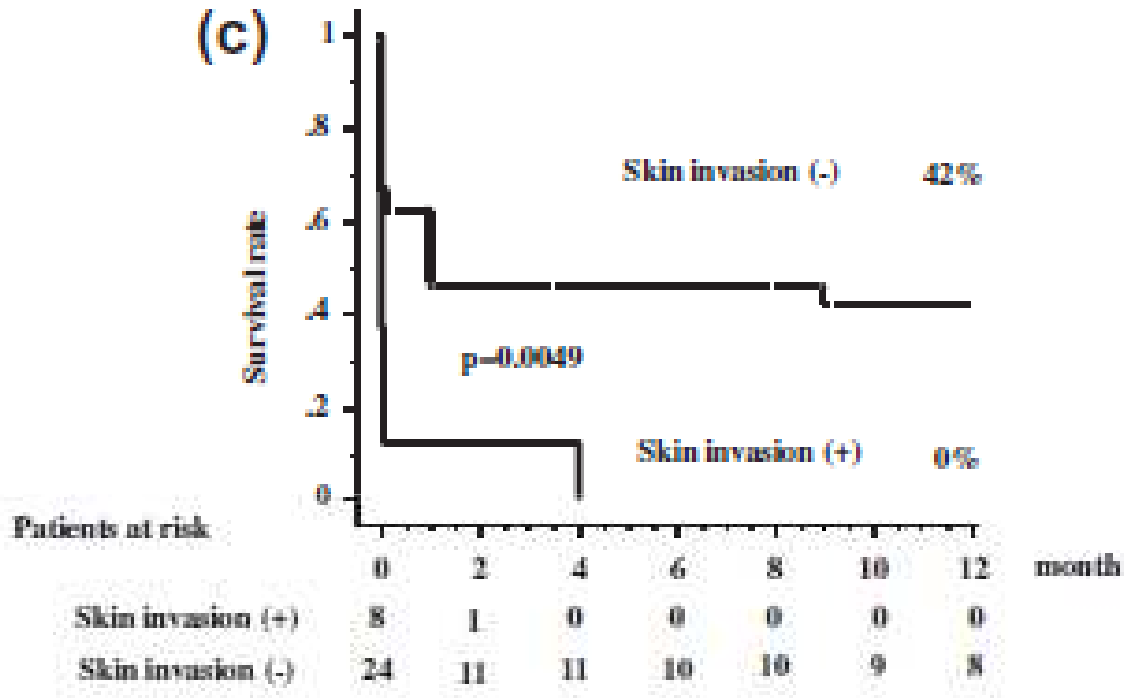
Yamazaki et al. radiotherapy and oncology 2013

Results of multivariate Cox proportional hazards model.

Variable	Strata	Odds ratio	95% confidence interval	p-Value
Age	≦58 vs. 58<	1.645	0.54–4.93	0.37
BED ($\alpha/\beta = 3$)	≦195 vs. 195<	2.044	0.75–5.55	0.16
Surgery	− vs. +	1.093	0.20–5.85	0.91
Skin invasion	− vs. +	1.963	1.059–11.16	0.039
Nasopharynx or other	Nasopharynx vs. other	1.016	0.16–6.27	0.98
Infection/ necrosis	− vs. +	3.864	0.56–6.88	0.09

In multivariate analysis, only skin invasion is identified as statistically significant prognostic factor after CBS

Yamazaki et al. radiotherapy and oncology 2013



-The 1-year survival rate for the skin invasion (-) group was 42%, whereas no patient with active skin invasion survived beyond
4 months (0% at 1 year, p = 0.0049)
- Patients with necrosis/infection formation at CBS onset showed 17% of 1-year survival rate, whereas 67% of value was identified in counterpart (p = 0.003)

Yamazaki et al. radiotherapy and oncology 2013

Patients treated 1.8–2-Gy daily fractions or 1.2-Gy twice daily fractions rate of CBS was 1.3%.

Patients treated with 1.5-Gy twice daily fractions over alternating weeks or with delayed accelerated hyperfractionation received concurrent chemotherapy, and the rate of CBS was 4.5% ($p = 0.002$).

Intensity-modulated radiation therapy (IMRT) series reported bleeding rates of 0–3%.

6.6% of CBS ratio in SBRT seems to be higher than conventional Fraction.

Careful attention should be paid to the occurrence of CBS if the tumor is located adjacent to the carotid artery. The presence of skin invasion at CBS onset is ominous sign of lethal consequences.

Yamazaki et al. radiotherapy and oncology 2013

Radiotherapy and Oncology 106 (2013) 90–95

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Radiotherapy and Oncology

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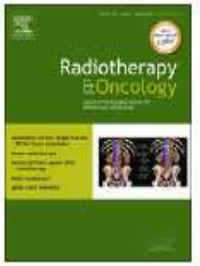


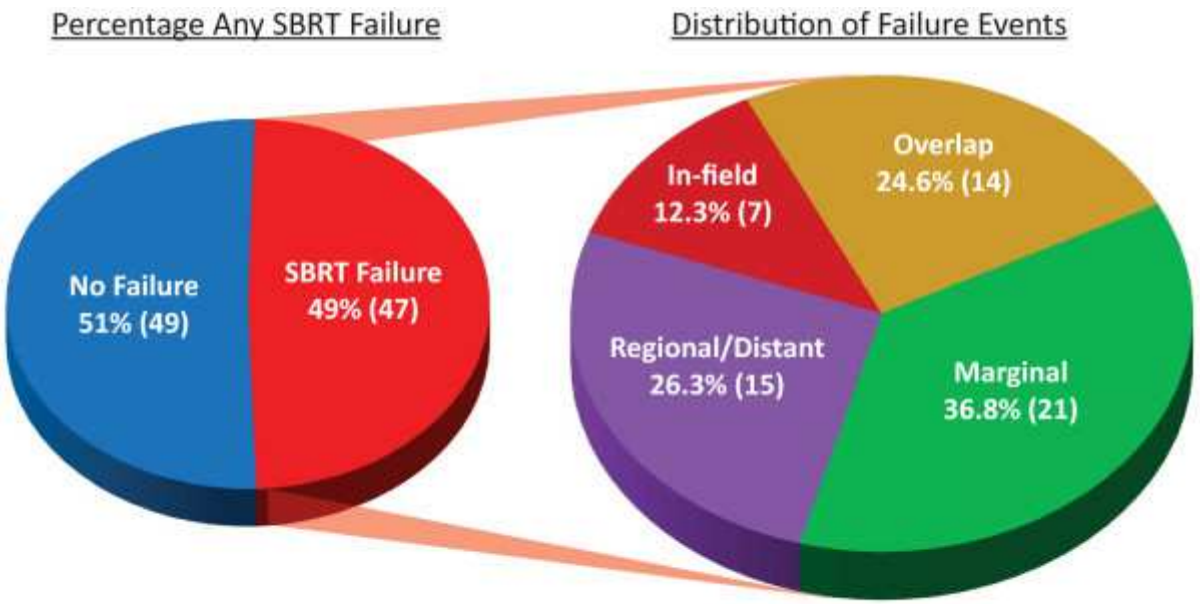
Head and neck cancer

Target delineation in stereotactic body radiation therapy for recurrent head and neck cancer: A retrospective analysis of the impact of margins and automated PET-CT segmentation

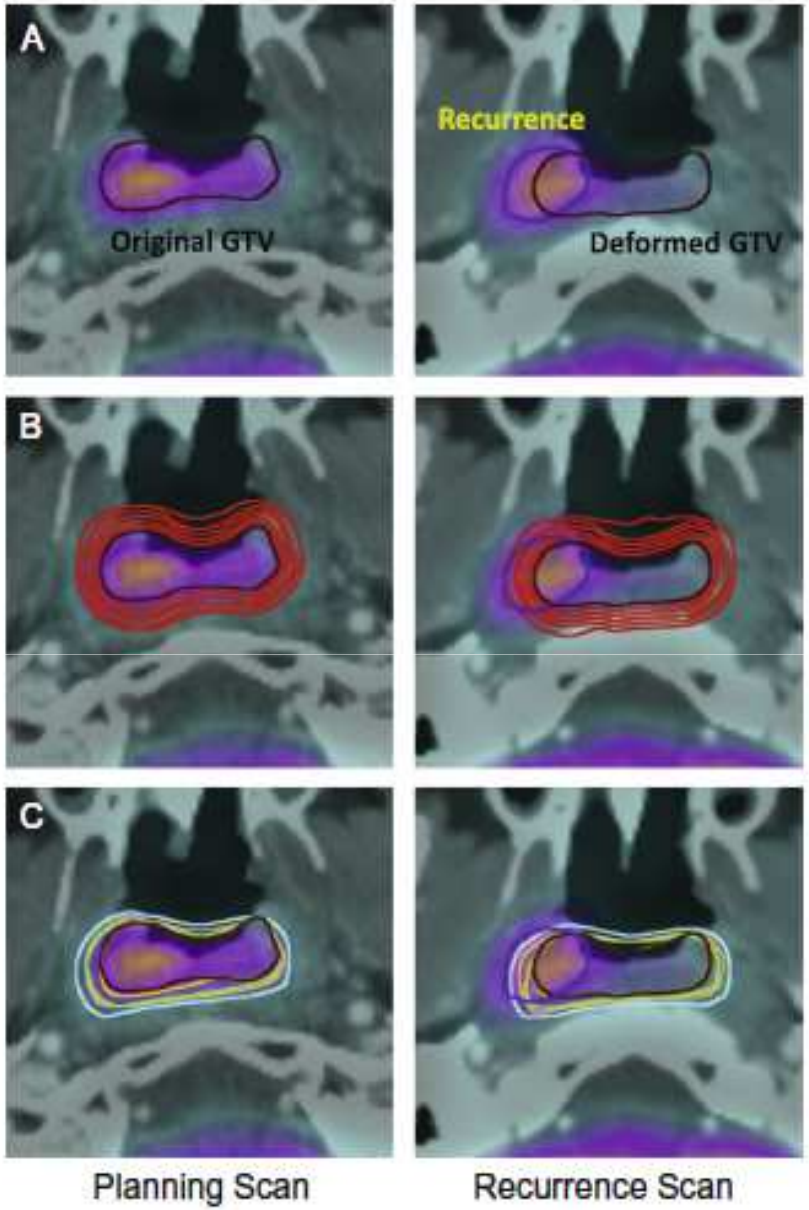
Kyle Wang [a], Dwight E. Heron [a,b,*], David A. Clump [a], John C. Flickinger [a,c], Gregory J. Kubicek [a], Jean-Claude M. Rwigema [a], Robert L. Ferris [a,b], James P. Ohr [d], Annette E. Quinn [a], Cihat Ozhasoglu [a], Barton F. Branstetter [b,e]

Assessment of the impact of retrospectively adding margins/automated PET volumes to the gross tumor volume (GTV) in patients with post-SBRT recurrences.

Target Volume delineation

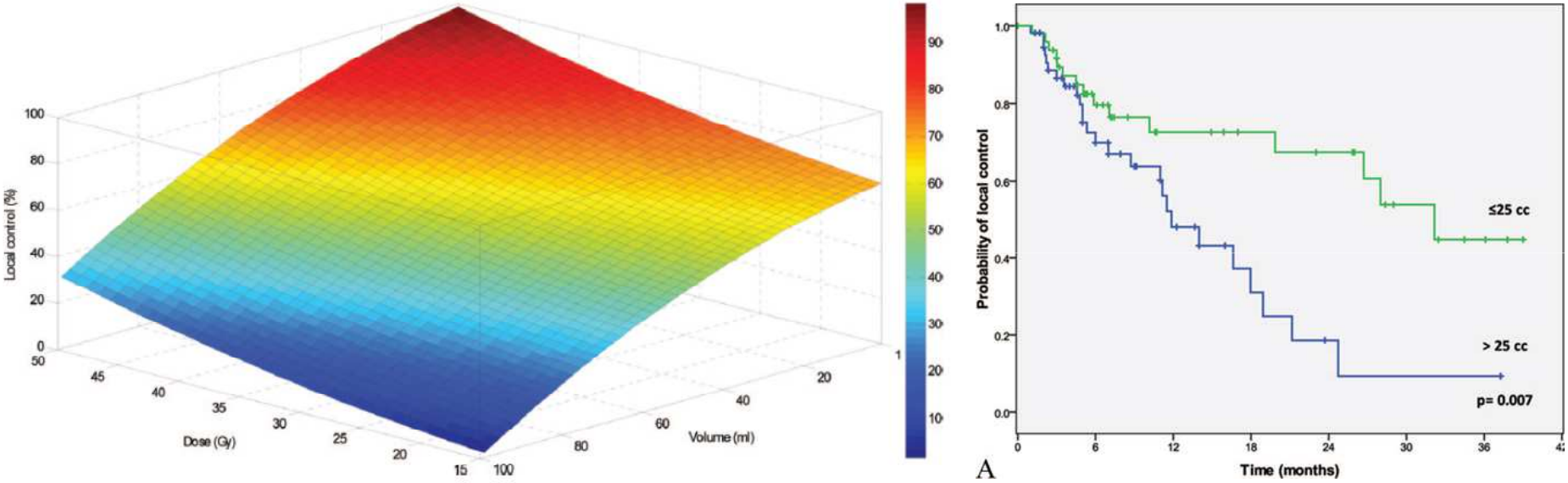


- Pre-treatment planning scans and GTVs were deformed to posttreatment follow-up scans -> Use of deformable registration to analyze patterns of failure.
- Recurrent tumors were categorized: In-field (>75% inside GTV), Overlap (20–75% inside GTV), Marginal (<20% inside GTV but closest edge within 1 cm of GTV), or Regional/Distant (more than 1 cm from GTV). In-field, Overlap, and Marginal failures were considered local failures



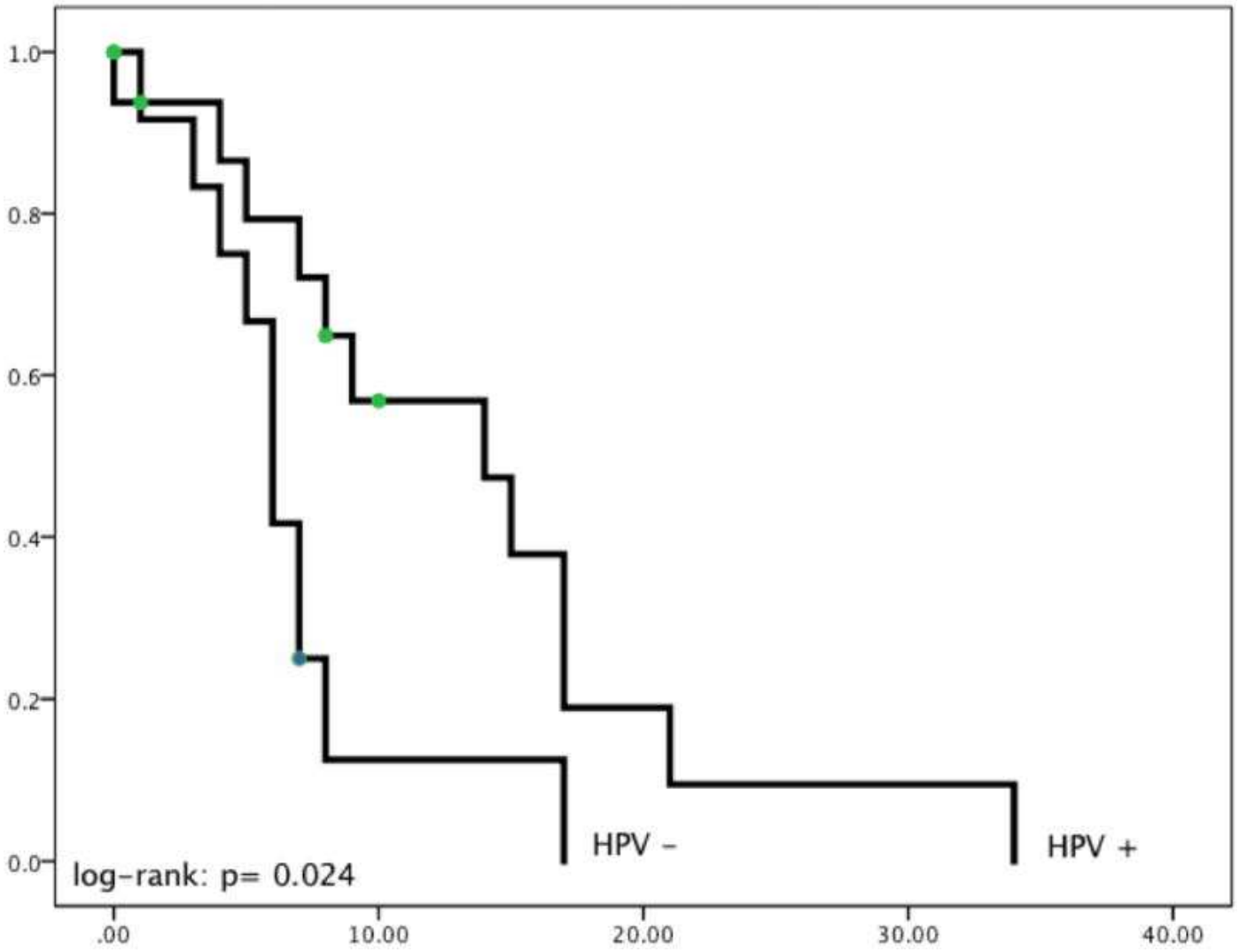
If internal physiological variations such as respiration and swallowing movements were anticipated, the contour was slightly overdrawn especially in the superior–inferior direction and was defined as the internal target volume (ITV).

Re-irradiation & local control: size DOES matter



Rwigema JCM et al AJCO 2011

New concepts: HPV status as predictor factor of response to SBRT



Davis KS et al. Oral Oncology 2014

So, is it standard practice?

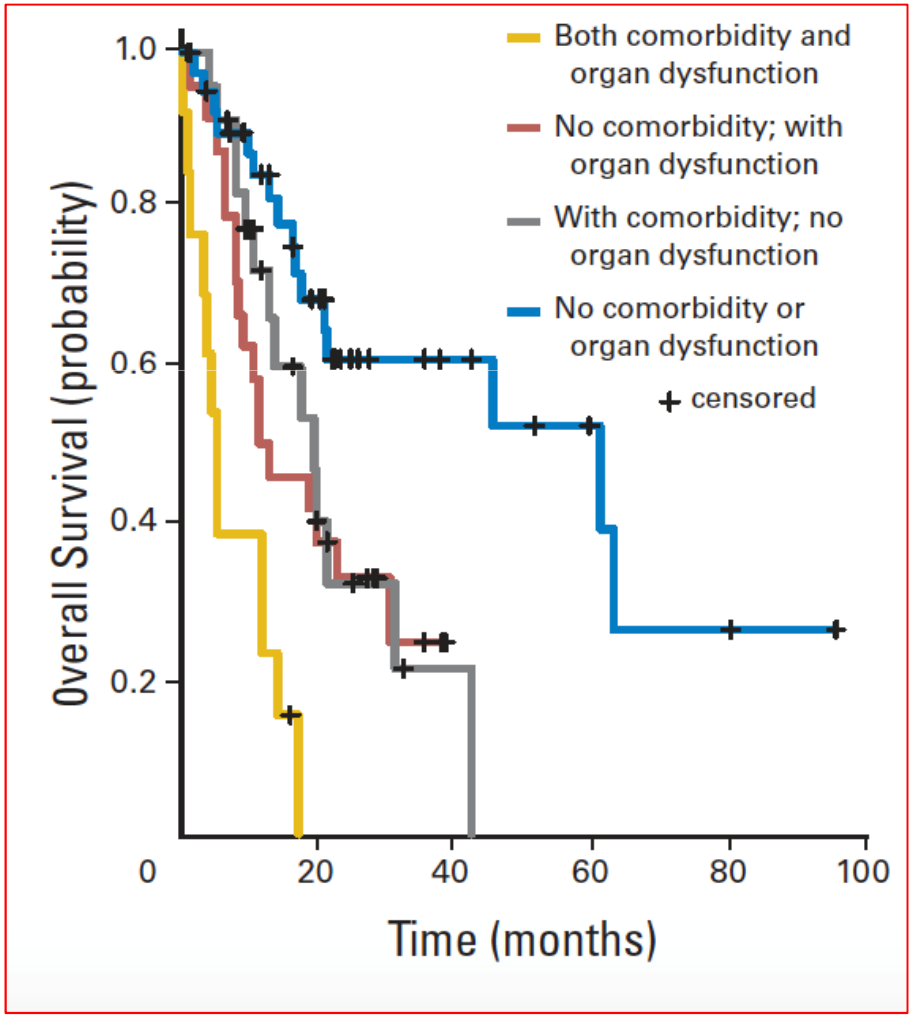
NO

- **Lack of high quality data to recommend re-RT for unresectable disease**
  - heterogeneity
  - case mix
  - significant sources of bias
  - difficult interpretation

Open issues

- Technical feasibility: challenging
  - dose constraints? Normal tissues recovery?
  - GTV-CTV expansion? Volumes?
- Recurrent SCCHN: heterogeneous group
  - HPV positive
  - HPV negative
  - SPT's
- Integration with CT
  - what drugs? Sequential or concurrent schedule? Maintenance?

Who may then benefit from re-RT?



- Organ dysfunction
- Comorbidity
- Interval from 1st RT: ≥ 6 mo
- rT stage: ≤ T2
- Tumor bulk: ≤ 25 cm^3
- Re-RT dose: ≥ 60 Gy

Tanvetyanon T, J Clin Oncol 2009
Riaz N, Radiother Oncol 2014

Future perspectives

A Feasibility Study on Adaptive 18F-FDG-guided Radiotherapy for Recurrent and Second Primary Head and Neck Cancer in the Previously Irradiated Territory.

This study is currently recruiting participants. (see Contacts and Locations)

Verified June 2015 by University Hospital, Ghent

ClinicalTrials.gov Identifier:
NCT01427010

Reirradiation With MK-3475 in Locoregional Inoperable Recurrence or Second Primary Squamous Cell CA of the Head and Neck

This study is currently recruiting participants. (see Contacts and Locations)

Verified January 2015 by University of Maryland

Sponsor:
Dan Zandberg

Collaborator:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Dan Zandberg, University of Maryland

ClinicalTrials.gov Identifier:
NCT02289209

First received: October 17, 2014
Last updated: January 21, 2015
Last verified: January 2015
History of Changes

Verified July 2015 by University of Pittsburgh

Sponsor:
University of Pittsburgh

Information provided by (Responsible Party):
University of Pittsburgh

NCT02057107

First received: January 30, 2014
Last updated: July 29, 2015
Last verified: July 2015
History of Changes

Summary #1

- **Proper patients' selection: crucial factor**

- **Re-irradiation after salvage surgery: increases LRC but also late toxicity**

- **Re-irradiation for unresectable disease: tailored decision on a case-by-case basis**

Summary #2

- **Urgent need to fill the gap of evidence**

- **Prospective data required to assess:**
  - **technical issues**
  - **patterns of failure**
  - **late toxicity**
  - **imaging & translational research**

PELVIC RECURRENCES

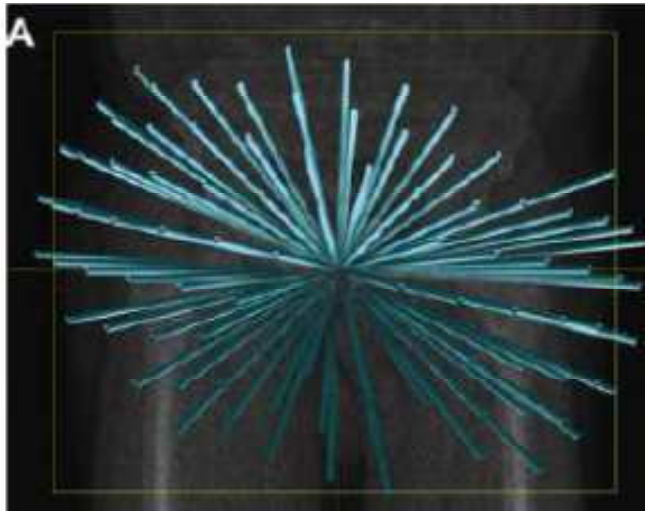
SBRT re-treatment of pelvic recurrences: a different scenario

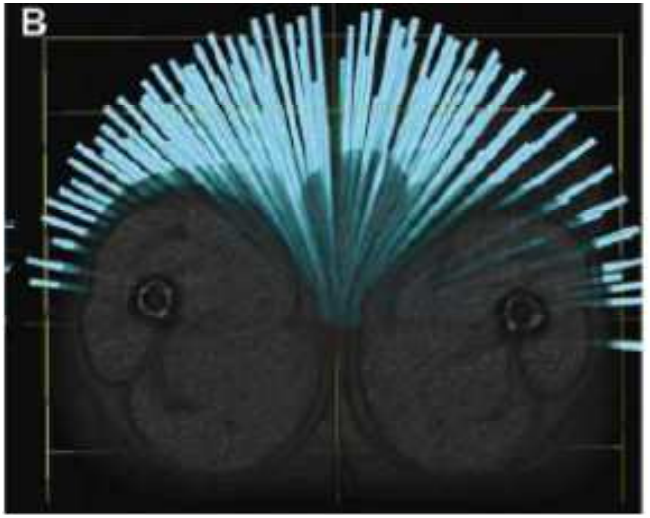
Authors	*n*	Primitive tumor	Previous RT dose	Re-irradiation dose	Survival (months)	LC (%)	OS (%)	G3/G4 Toxicity
Dewas et al.	16	Anal cancer : 6 Rectum : 4 Col : 4 Endomètre : 1 Bladder : 1	45 Gy (20–96)	6 × 6 Gy/3 week	10,6	51,4	46	none
Deonato et al.	6	Cancer du col : 3 Endomètre :2 Ovaire : 1	50,2 Gy (37,5–65)	5 × 4–6 Gy	17,5	81,8	50	none
Abusaris et al.	27	Miscellaneous	31-83 Gy	2–6 × 6–20 Gy	15	53	37	none
Kunos et al.	5	Gynaecological cancer	32-62 Gy	3 × 5–8 Gy	7,5	100	80	none
Jereczek-Fossa et al.	27	Prostate LR : 15 anastomosis : 4 nodal relapses : 8	NR	30 Gy in 5 fractions	16,9	89	NR	none
Defoe et al.	14	Presacral recurrences (rectum)	50,4 Gy (20-81)	3 ×12 Gy or 1 × 12–18 Gy	16,5	68, 2	78,8	none

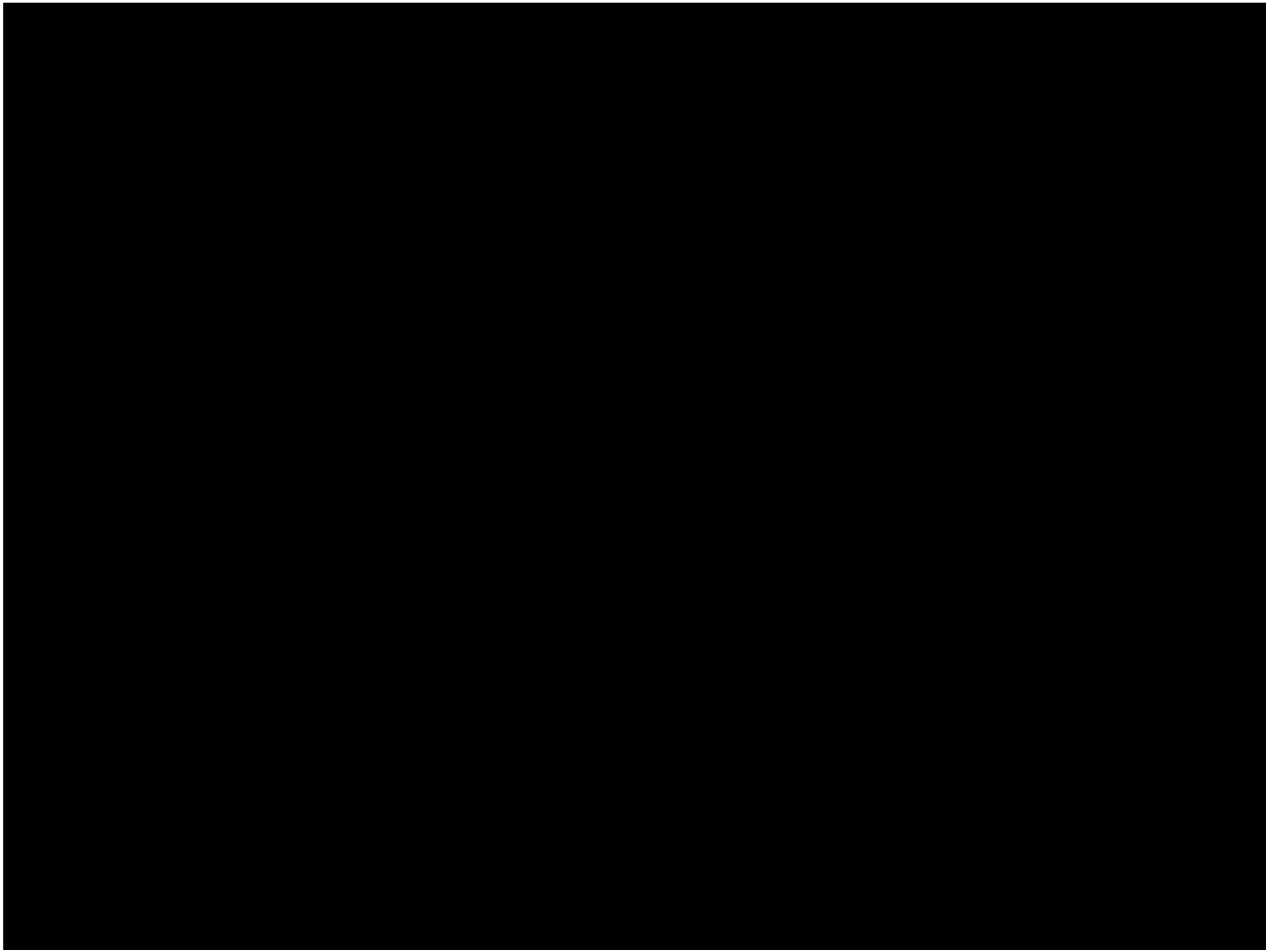
Mazeron R 2014

Phase I-Study:

PROSPECTIVE EVALUATION OF CYBERKNIFE STEREOTACTIC RADIOSURGERY FOR LOCALLY ADVANCED CERVICAL CANCER PATIENTS: EMULATING HDR BRACHYTHERAPY DOSIMETRY







Endometrial cancer
Primary Radiotherapy

Peter Hoskin
Mount Vernon Cancer Centre

Endometrial Cancer: staging UICC 2009

Stage I: confined to uterus

- Ia: invasion <50% myometrial depth
- Ib: invasion >50% myometrial depth

Stage II: invasion of cervix

Stage III: Extension outside uterus within pelvis

Stage IV: Invasion of bladder rectum or distant spread

Endometrium Cancer: Principles of management

- Stage I, II and III: **Surgery +/- postop RT**

  Total Abdominal Hysterectomy plus
  Bilateral salpingo-oophorectomy
  +/- lymph node sampling or dissection

- **Stage I, II and III, unfit for surgery**
  Stage IV

  Primary radiotherapy

Endometrial cancer: uterus in situ

- Surgery contraindicated:
  - gross obesity
  - general frailty
  - coexisting medical conditions:
    - diabetes
    - cardiovascular
    - thrombosis

Primary radiotherapy

- Stage I/II: Low/intermediate risk
  - BRACHYTHERAPY alone

- Stage I/II: High risk
- Stage III & IV
  - External beam to CTV including whole uterus and pelvic nodes: 45 - 50.4Gy
  - BRACHYTHERAPY boost

Endometrial cancer: uterus in situ……applicators

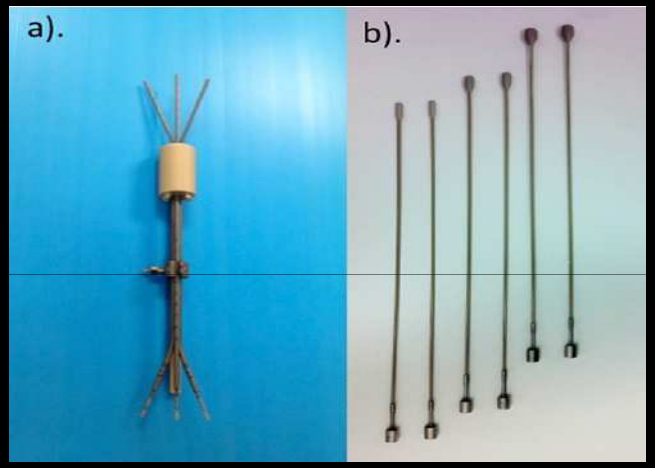
- Classical method: Heymann's capsules
- Modified tube & ovoids
- Rotte Y applicator
- HDR: Heymanns capsules (Norman-Simon)
  Multistem Y intrauterine applicator
  Single line source: weighted dwells

Image-guided high-dose-rate brachytherapy in inoperable endometrial cancer

Br J Radiol;87:2014

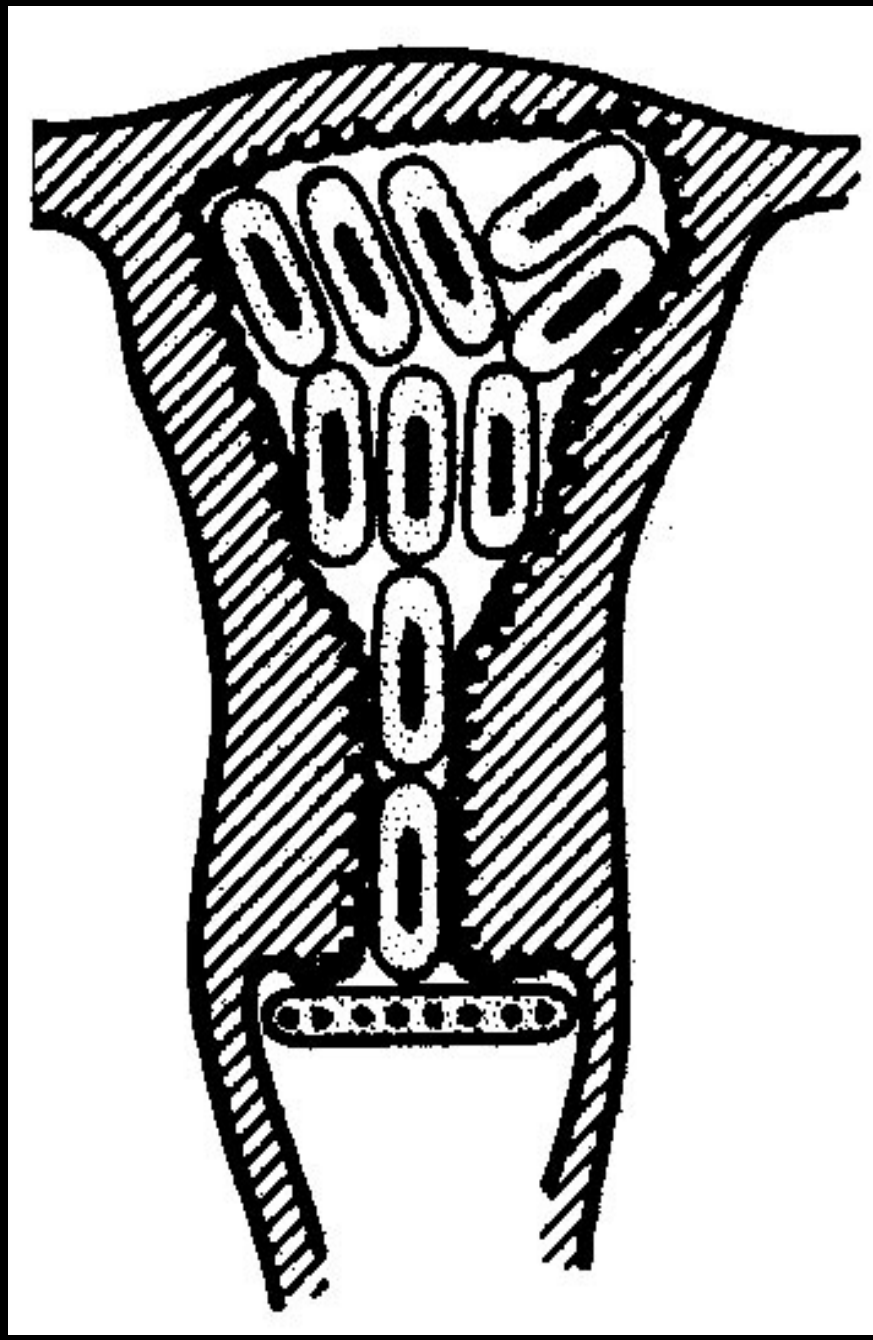
[1,2]P DANKULCHAI, MD, [1]J PETSUKSIRI, MD, [1]Y CHANSILPA, MD and [2]P J HOSKIN, MD

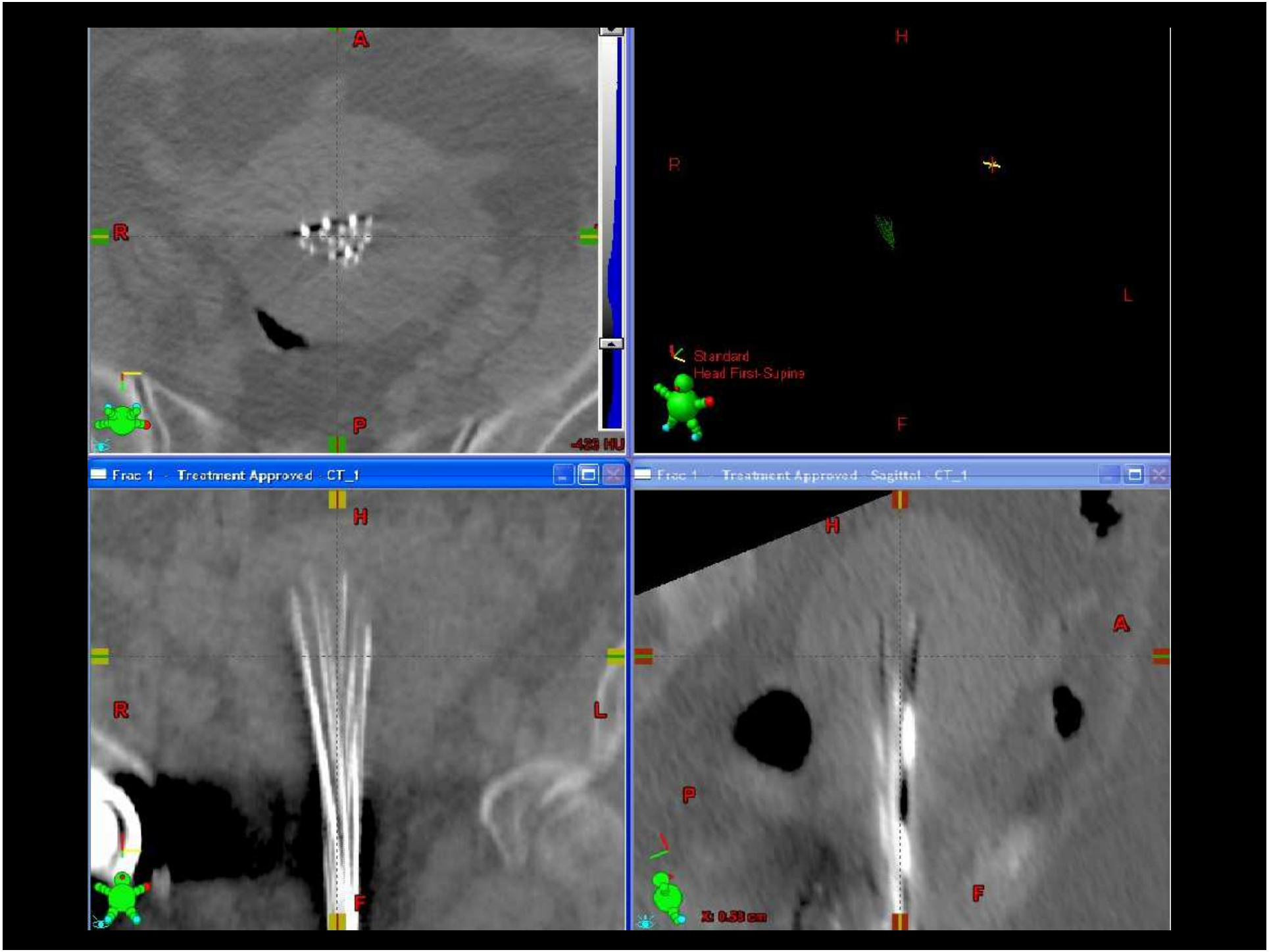
[1]Division of Radiation Oncology, Department of Radiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
[2]Mount Vernon Cancer Centre, Northwood, Middlesex, UK

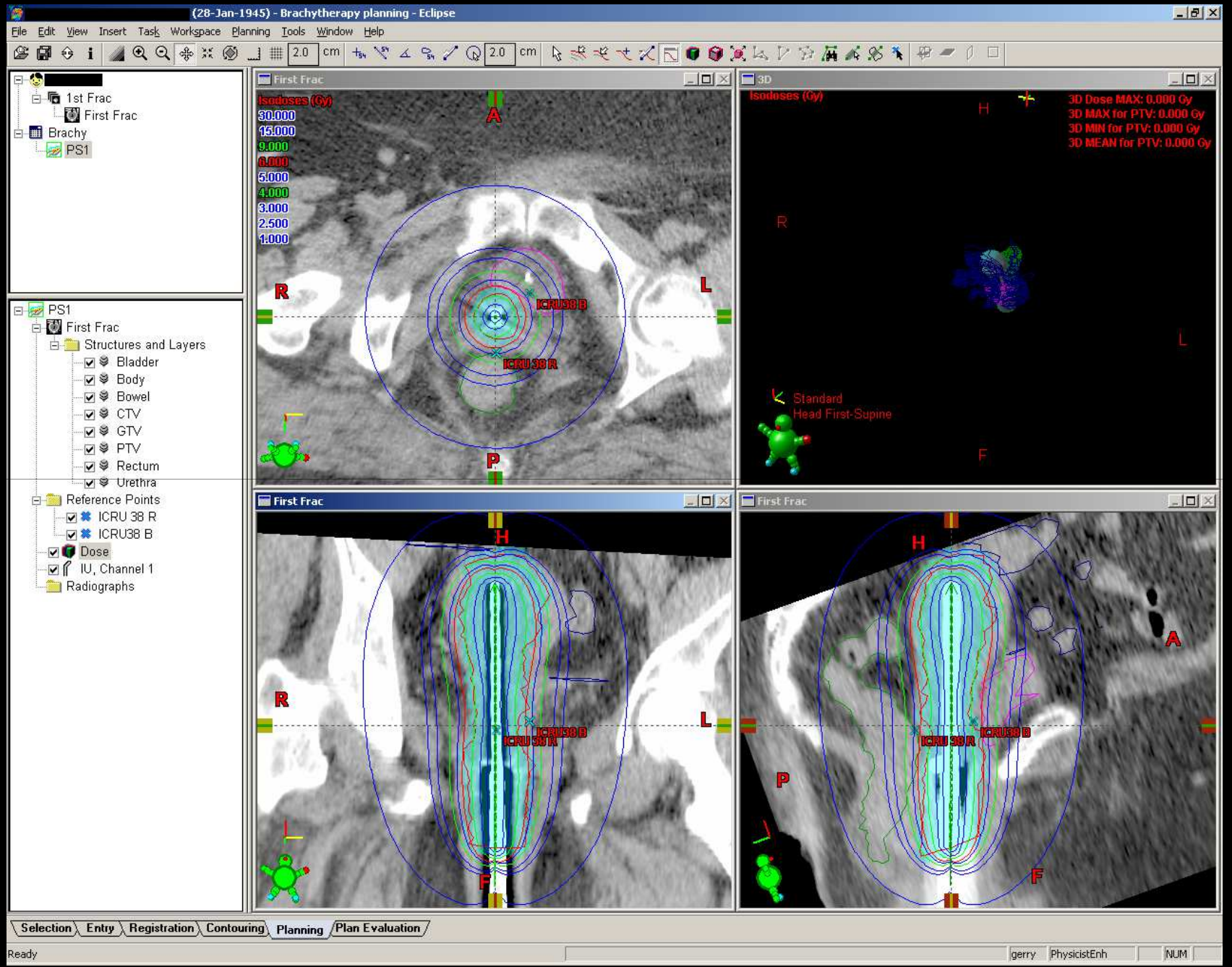


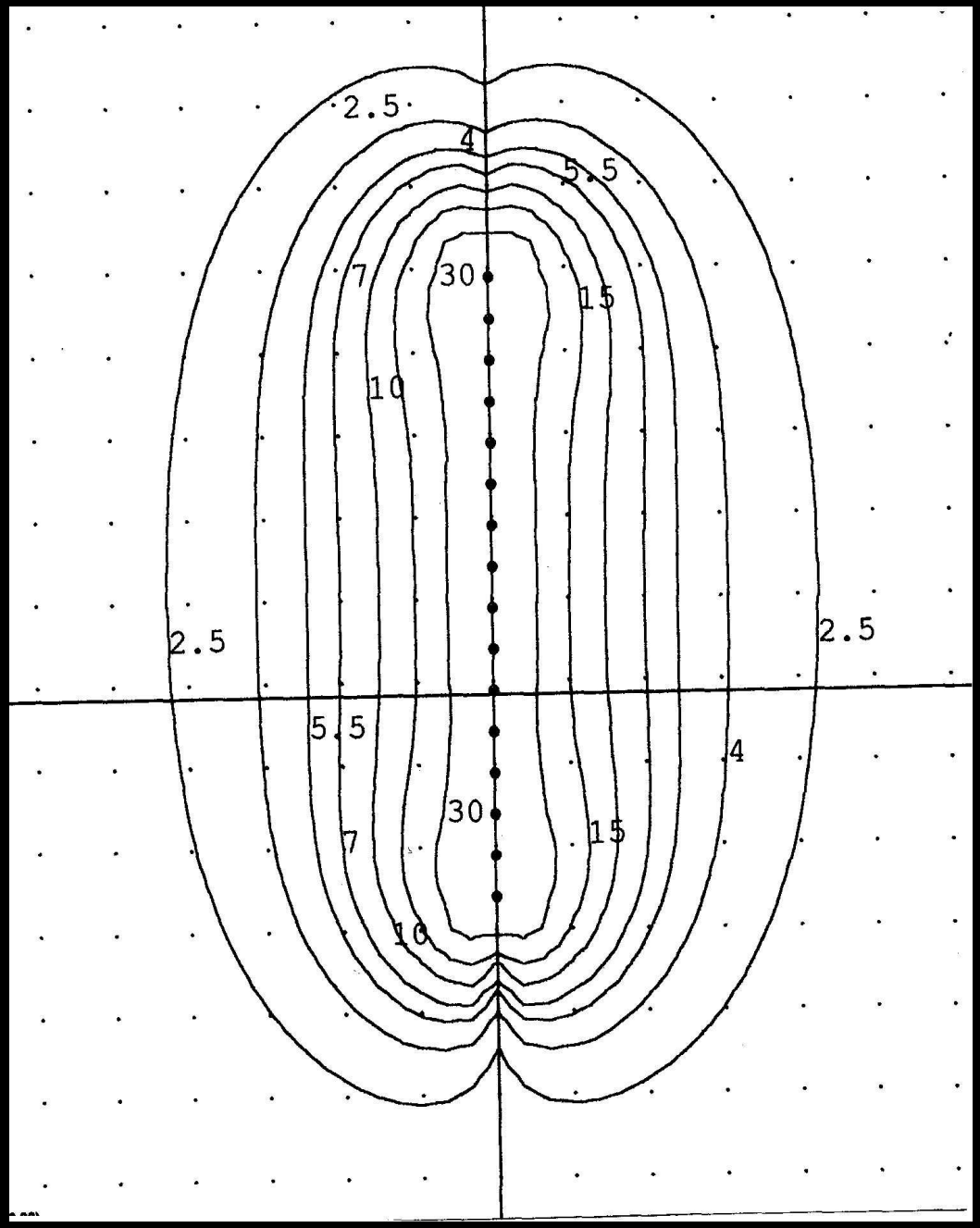
Aspects	Standardized applicator	Individual packing applicator
Insertion	Easy and convenient	Difficult
	Need to know the length of uterine cavity	Need more skill and experience
Optimization	Difficult owing to only 1–3 channels	Easy, depends on place of applicators
Dose distribution	Optimal dose in craniocaudal and lateral directions	Better individually appropriate dose distribution
	Suboptimal in the anteroposterior direction	
	May be a problem for the tolerance dose of the organs at risk	

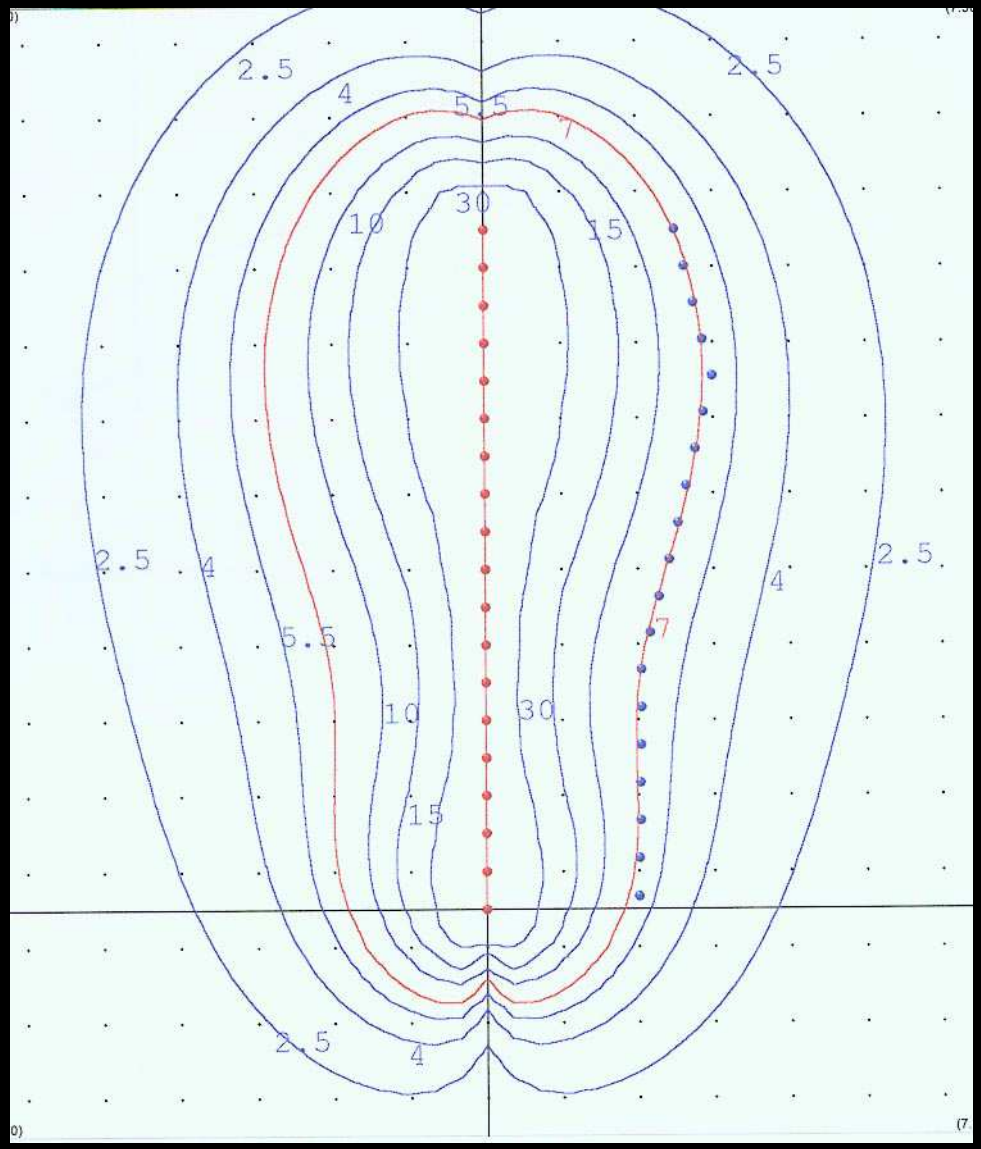
Heymans capsules
In situ




A
R
P
-423 HU
H
R
L
Standard
Head First-Supine
F
Frac 1 - Treatment Approved - CT_1
H
R
L
F
Frac 1 - Treatment Approved - Sagittal - CT_1
H
A
P
F
X: 0.38 cm


(28-Jan-1945) - Brachytherapy planning - Eclipse
File Edit View Insert Task Workspace Planning Tools Window Help
1st Frac
First Frac
Brachy
PS1
PS1
First Frac
Structures and Layers
Bladder
Body
Bowel
CTV
GTV
PTV
Rectum
Urethra
Reference Points
ICRU 38 R
ICRU38 B
Dose
IU, Channel 1
Radiographs
First Frac
Isodoses (Gy)
30.000
15.000
9.000
6.000
5.000
4.000
3.000
2.500
1.000
ICRU38 B
ICRU 38 R
3D
Isodoses (Gy)
3D Dose MAX: 0.000 Gy
3D MAX for PTV: 0.000 Gy
3D MIN for PTV: 0.000 Gy
3D MEAN for PTV: 0.000 Gy
Standard
Head First-Supine
Selection
Entry
Registration
Contouring
Planning
Plan Evaluation
Ready
gerry
PhysicistEnh
NUM


2.5
4
5.5
7
30
15
10
2.5
2.5
5.5
4
30
7
15
10



point no.	time (s)
1	62.1
2	63.1
3	63.7
4	65.5
5	60.9
6	52.4
7	42.1
8	28.7
9	21.2
10	16.9
11	14.9
12	14.5
13	14.4
14	14.1
15	13.9
16	18.3
17	30.8
18	50.0
19	55.0

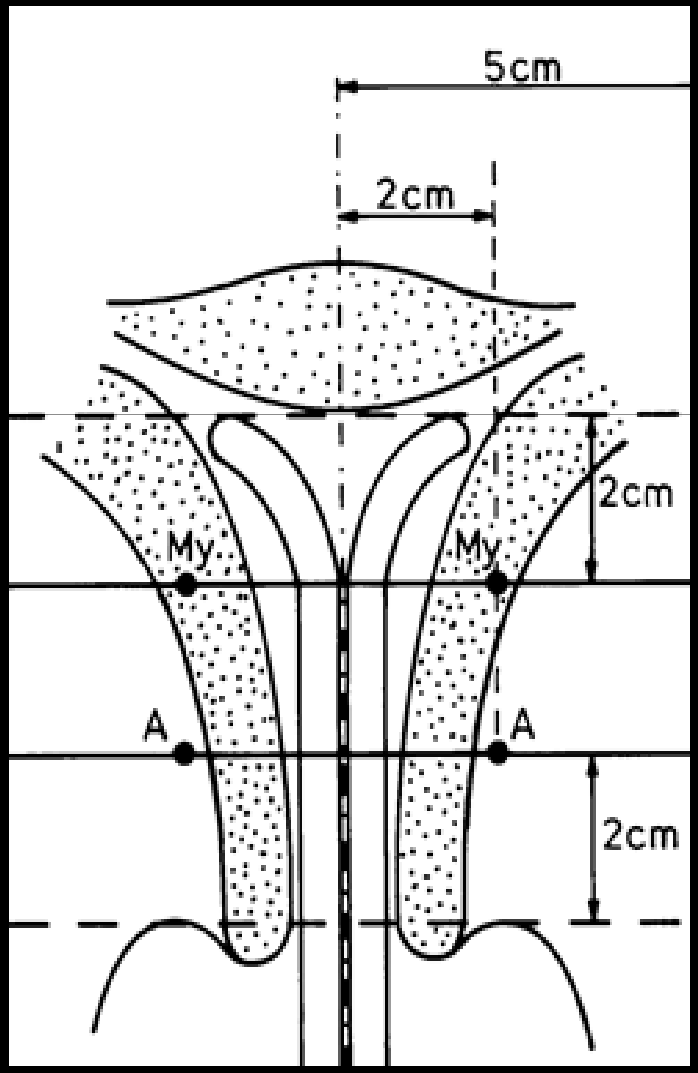
well times: 702.5 seconds

dose reference posi	
wanted(Gy)	calc. (Gy)
7.00	6.92
7.00	7.17
7.00	7.15
7.00	6.90
7.00	6.52
7.00	6.86
7.00	7.06
7.00	7.12
7.00	7.08
7.00	7.00
7.00	6.91
7.00	6.88
7.00	6.96
7.00	6.80
7.00	6.77
7.00	6.83
7.00	6.86
7.00	6.72
7.00	6.27

Dose calculation and prescription

- Accurate definition of CTV only possible on cross sectional imaging
- On MR HRCTV and IRCTV can be defined
- If 3D imaging not available at brachy should be reconstructed from diagnostic films

Dosimetry points for uterine BT



My = prescription point

Image-guided high-dose-rate brachytherapy in inoperable endometrial cancer

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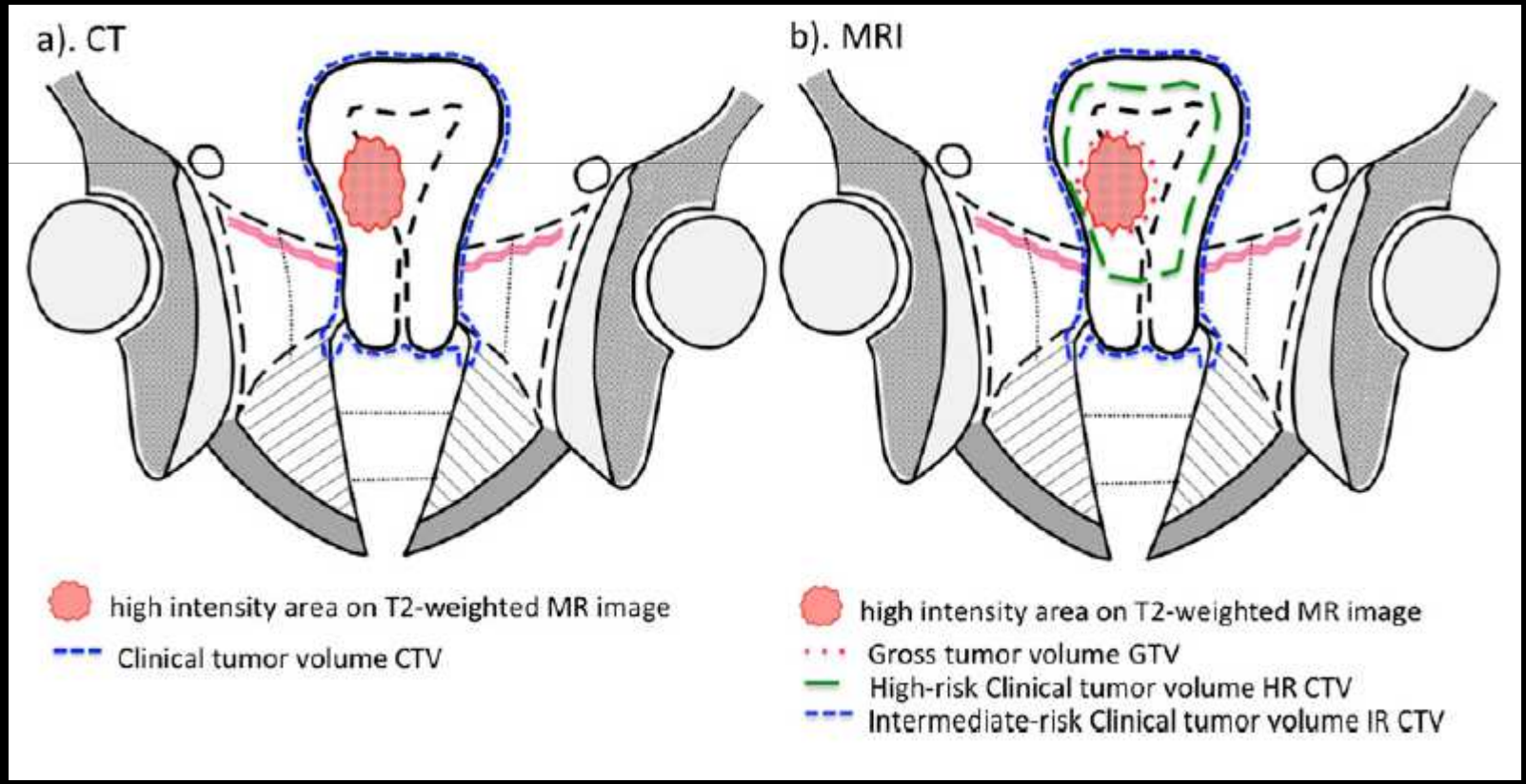
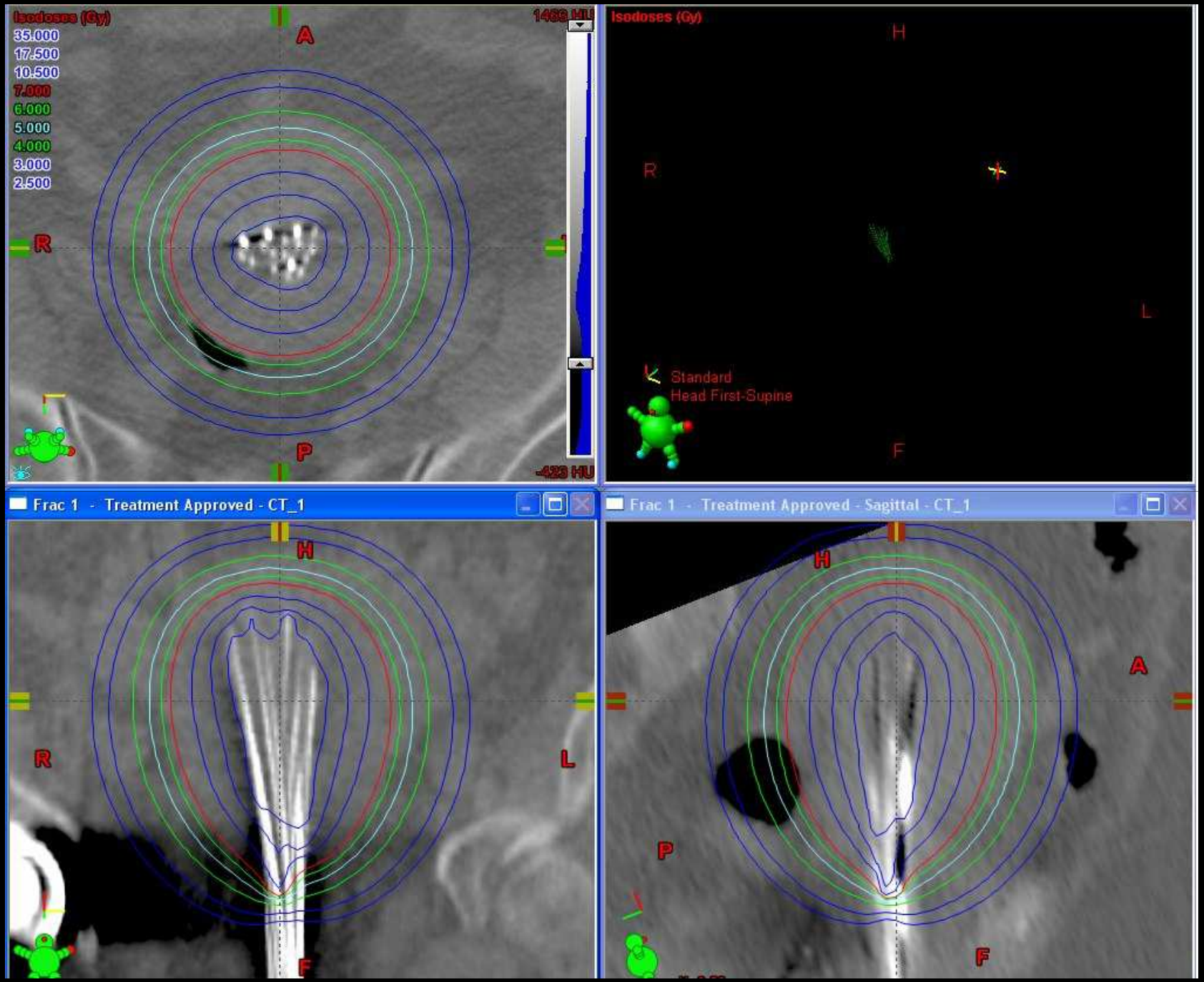



Isodoses (Gy)
35.000
17.500
10.500
7.000
6.000
5.000
4.000
3.000
2.500
1438 HU
-423 HU
A
R
P
Isodoses (Gy)
H
R
L
F
Standard
Head First-Supine
Frac 1 - Treatment Approved - CT_1
H
R
L
F
Frac 1 - Treatment Approved - Sagittal - CT_1
H
A
P
F

Actual dosimetry using modified Heyman's capsules Weitmann et al 2005

	Min CTV dose	D90CTV dose	MinGTV dose	Bladder D2cc	Rectum D2cc
1	4.6	9.7	126.5	10.3	X
2	10.5	24.2	38.3	29.8	16.4
3	10.8	24.5	77.7	7.9	18.9
4	10.6	26.2	34.9	31.4	6.3
5	17.4	35.3	99.1	41.6	17.8
6	19.5	41.8	79.3	78.6	17.1
7	29.8	58.7	48.8	44.6	8.7
8	18.8	45.1	76.1	77.7	11.0
9	20.0	27.5	36.7	144.6	21.1
10	48.4	82.6	74.4	67.3	63.2
11	52.6	65.9	99.3	117.4	59.7
12	52.8	66.2	172.8	72.1	X
13	9.3	22.5	35.5	37.0	5.5
14	14.0	30.0	71.8	79.3	7.3
15	11.0	24.0	33.3	14.7	11.4
16	53.0	58.5	70.6	67.1	62.2

Uterus volume covered by reference volume

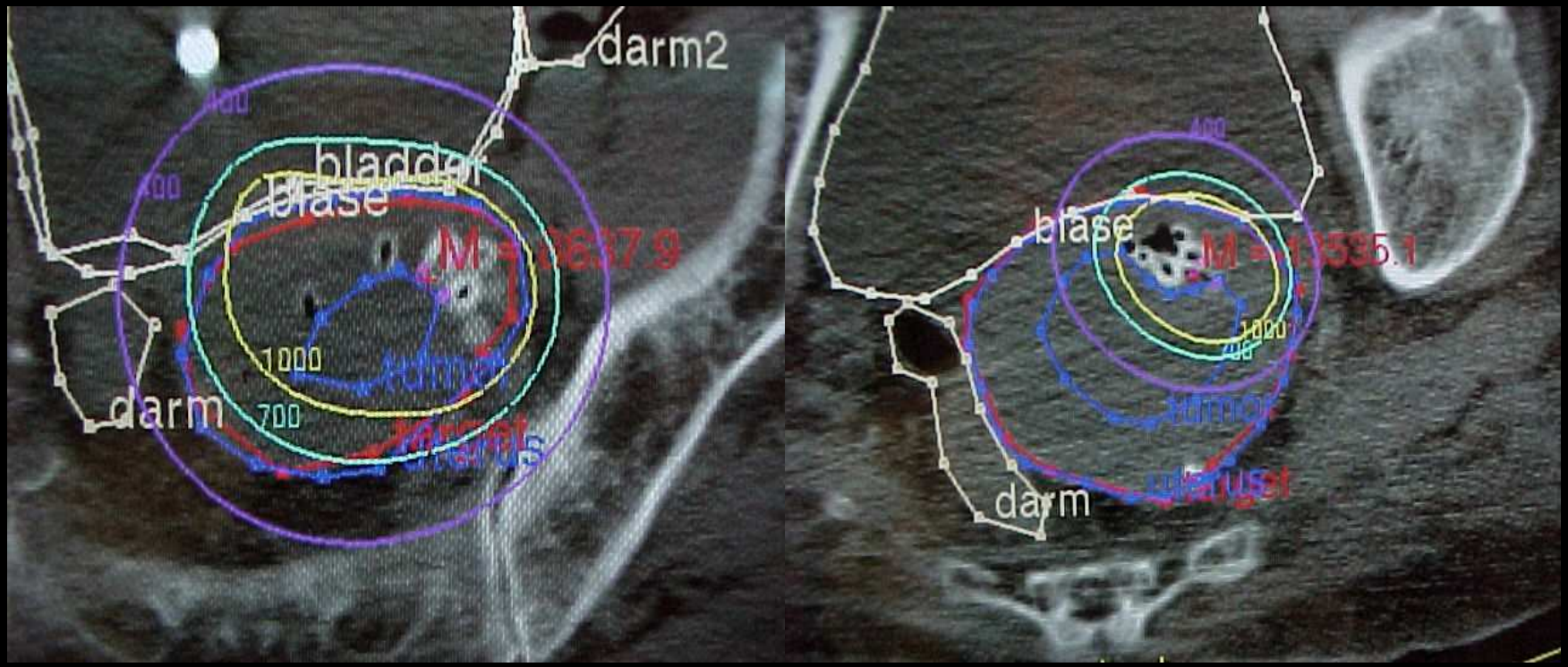
Mock et al. Strahlenther Onkol 1998

uterus volume outside reference isodose

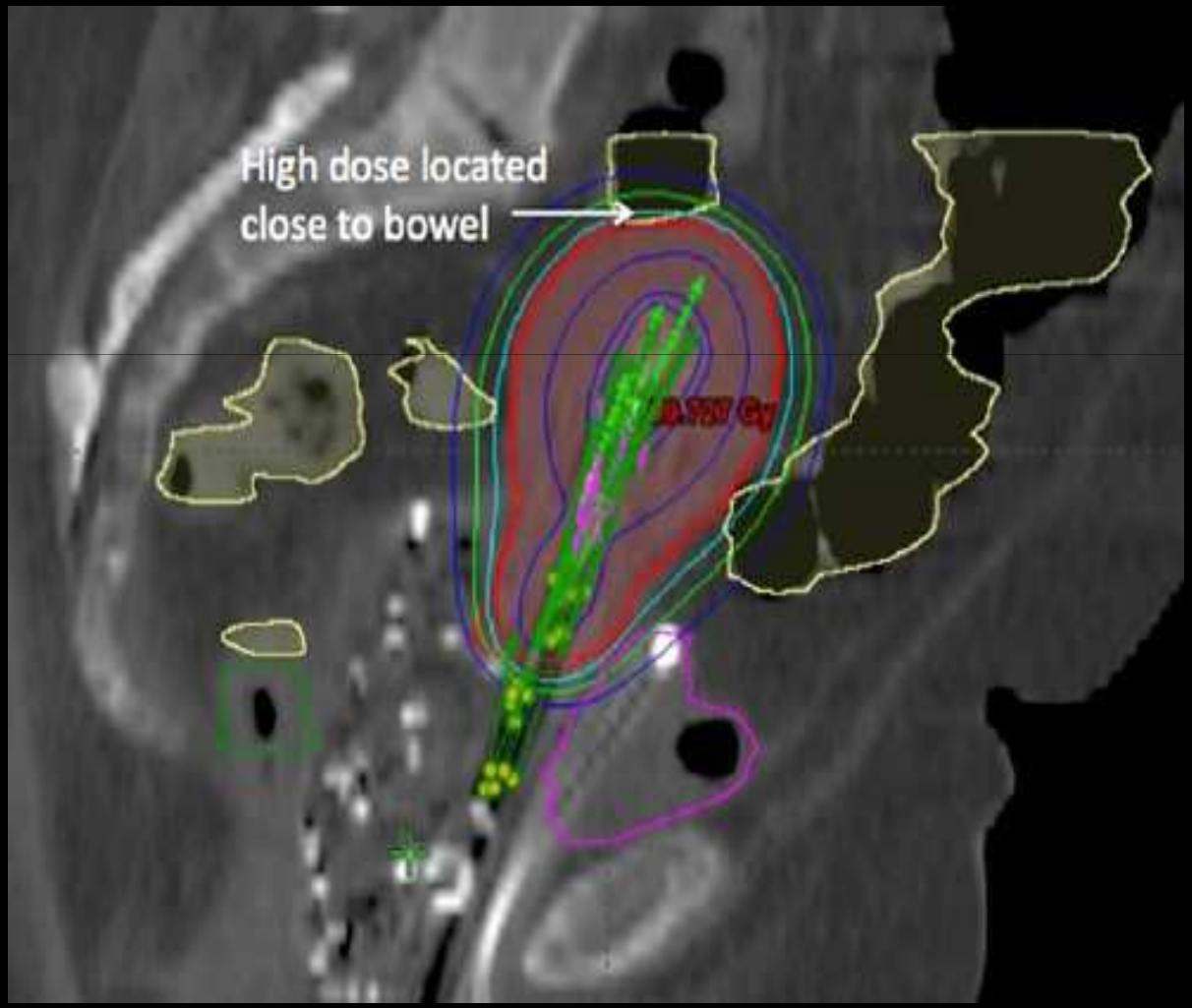
reference isodose outside uterus volume

Poor dose distribution

Weitmann et al. IJROB 2005



OAR limitations



GEC ESTRO Gyn tolerances used:

Rectum<75Gy
Sigmoid < 70-75Gy
Bladder < 80Gy

Image assisted BT for endometrial carcinoma

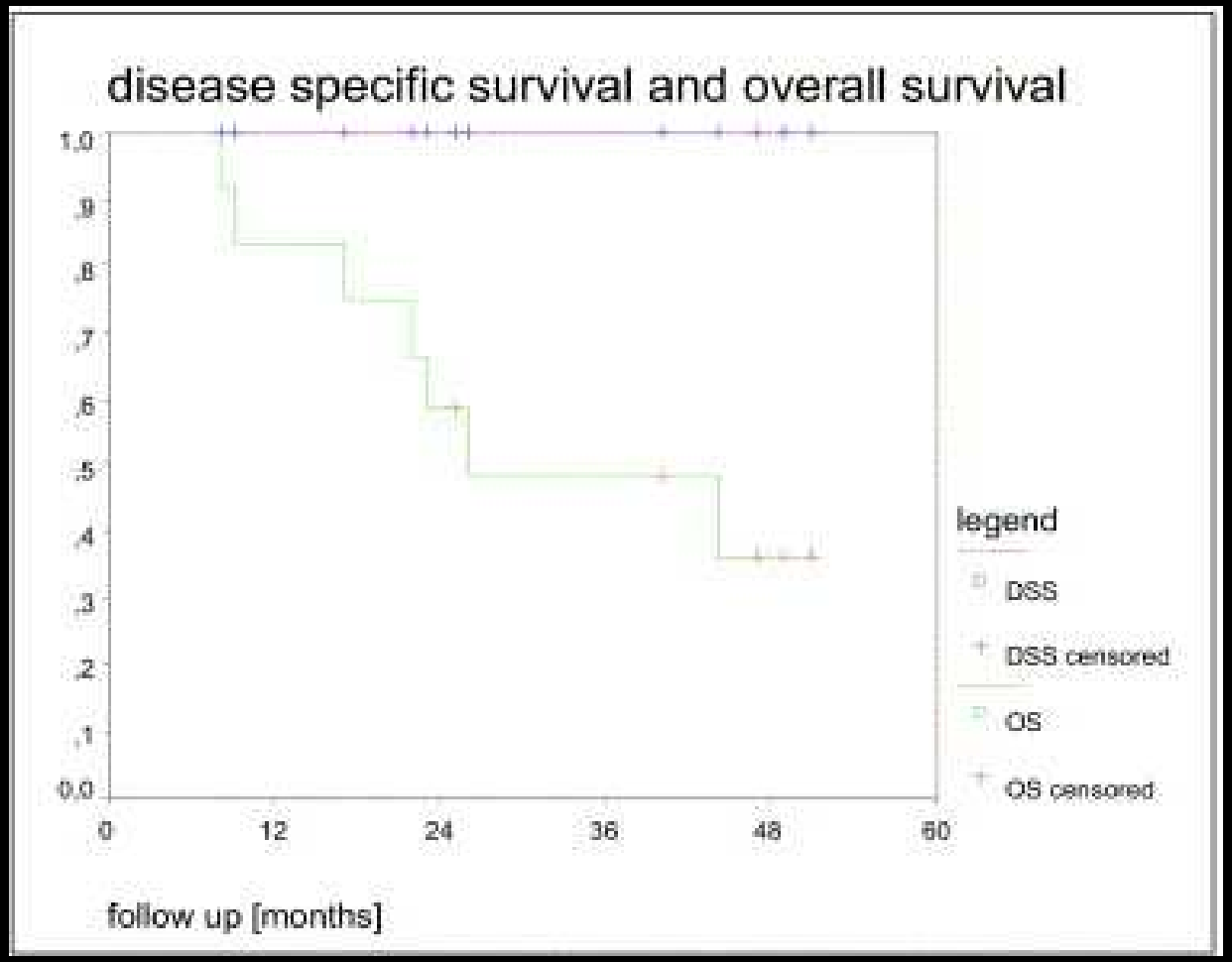
Weitmann et al. IJROB 2005

- Large parts of CTV (uterus) and GTV could be encompassed by the 60 Gy and 100 Gy isodose, respectively……but D90 reached 60Gy or more in only 68%
- Majority of patients with local tumor control.
- Side effects are negligible, because significant high doses in the OAR can be reduced or avoided.

Treatment outcome: Heymann's capsules alone for endometrial cancer

Weitmann et al 2005

16 patients



Intracavitary brachytherapy for endometrium

PDR	HDR	2Gyeq $\alpha\beta 10$	2Gyeq $\alpha\beta 3.5$
BRACHYTHERAPY ALONE			
75Gy/2f	42Gy/6f	59.5Gy	
80.2Gy			
AFTER 45Gy EXT BEAM			
22Gy/1f	28Gy/4f	83.9Gy	
96.9Gy			

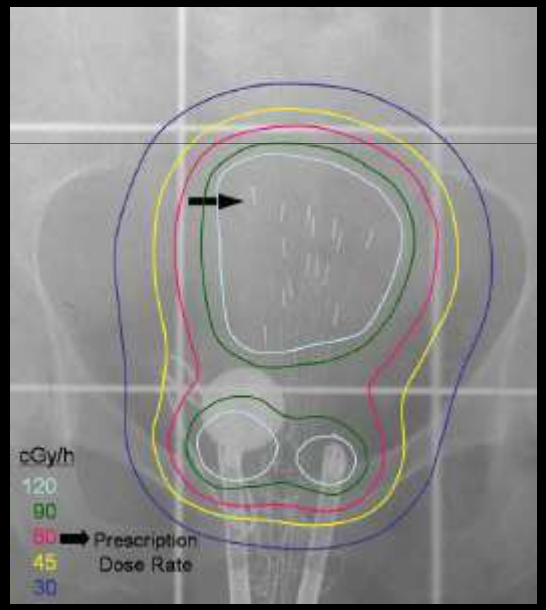
The management of inoperable Stage I endometrial cancer using intracavitary brachytherapy alone: A 20-year institutional review

Carey B. Shenfield*, Robert G. Pearcey, Sunita Ghosh, George S. Dundas

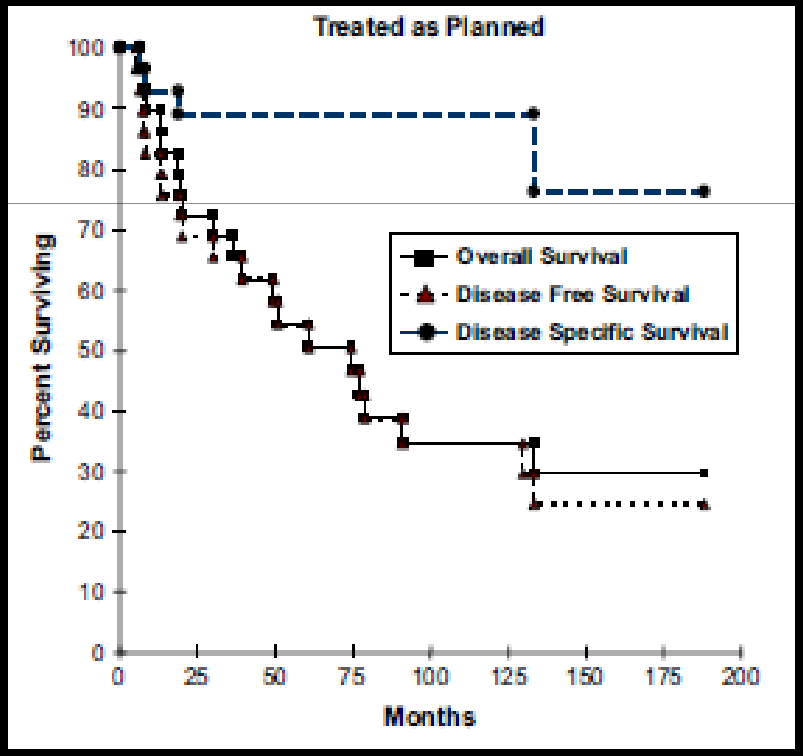
Department of Radiation Oncology, Cross Cancer Institute, University of Alberta, Edmonton, Alberta, Canada

Brachytherapy 2009

1986-2006
44 PATIENTS



6000cGy LDR
(2 X 3000cGy)



Vienna 1981-1992

HDR 8.5Gy x 4-5

Knocke et al 1997]

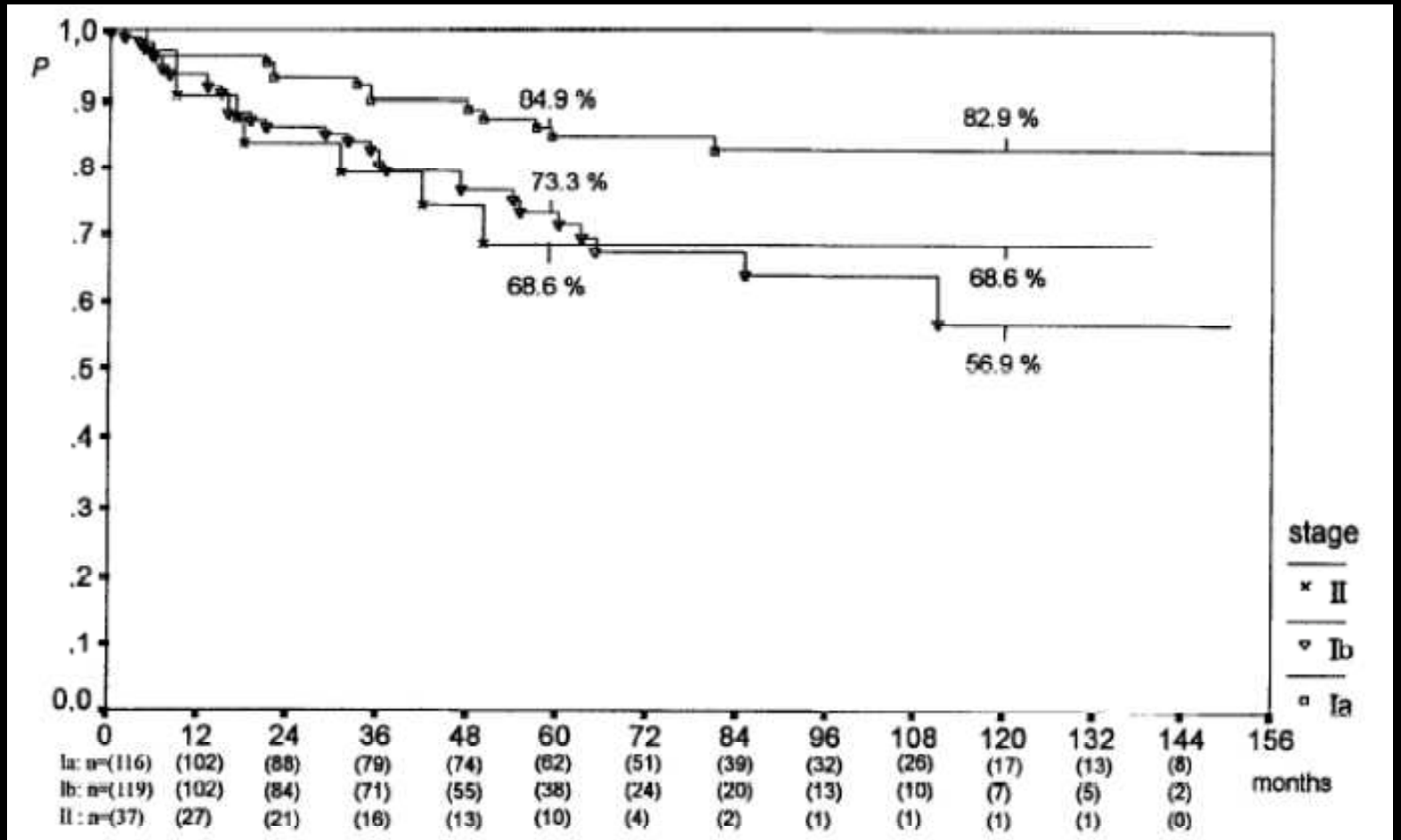
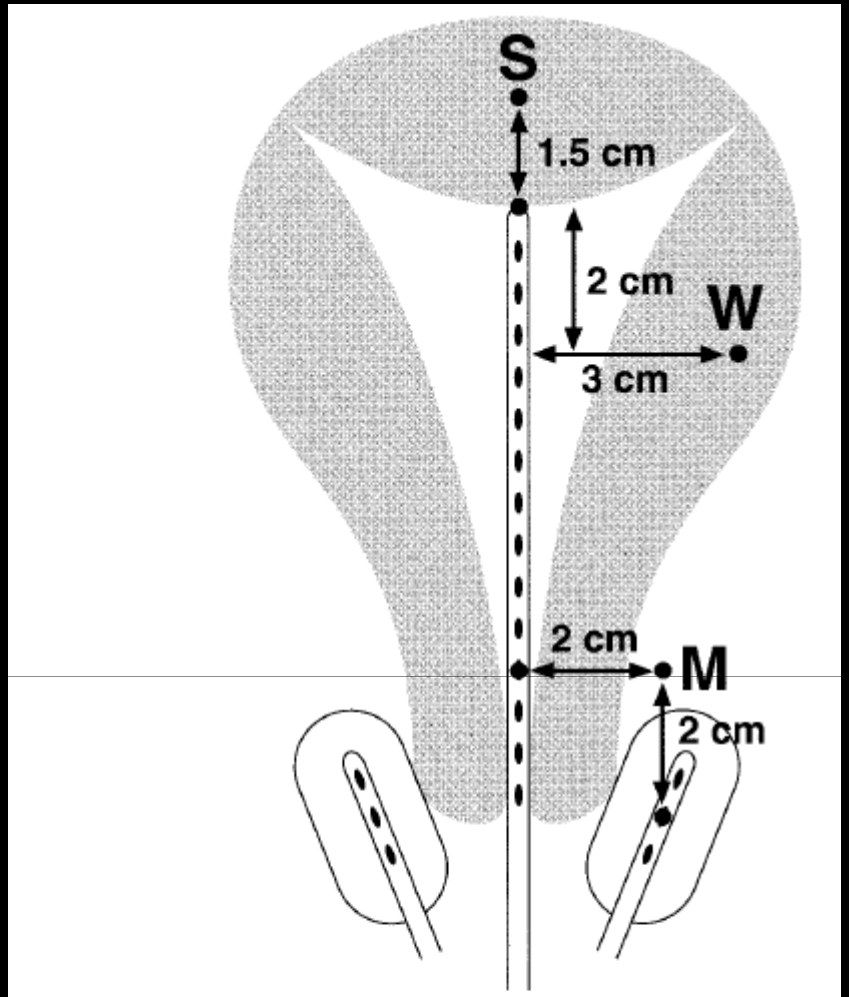


Fig. 3. Disease-specific survival in Stages Ia, Ib, and II. $n = 272$.

Late side effects (actuarial)

(Knocke et al. IJROBP 1997)

	mild	moderate	severe	Total
bladder	2.1 %	0.7 %	0.4 %	3.2 %
rectosig	7.9 %	3.8 %	0.4 %	12.1 %
small bowel	1.9 %	1.4 %	2.1 %	5.4 %
vulvo-vaginal	7.2 %	2.1 %	0.7 %	10.0 %
Total	19.1 %	8.0 %	3.6 %	30.7 %



Prescription Point *5 fractions*	Dose *Gy*
S	5.7
W	7.0
Vaginal mucosa	8.2
M	9.2

FIG. 1. Original fractionation schedules and dose prescription points.

Inoperable stage I endometrial cancer

Wisconcin method

Van Nugyen et al 1998

Inoperable stage I endometrial cancer

Van Nugyen et al 1998

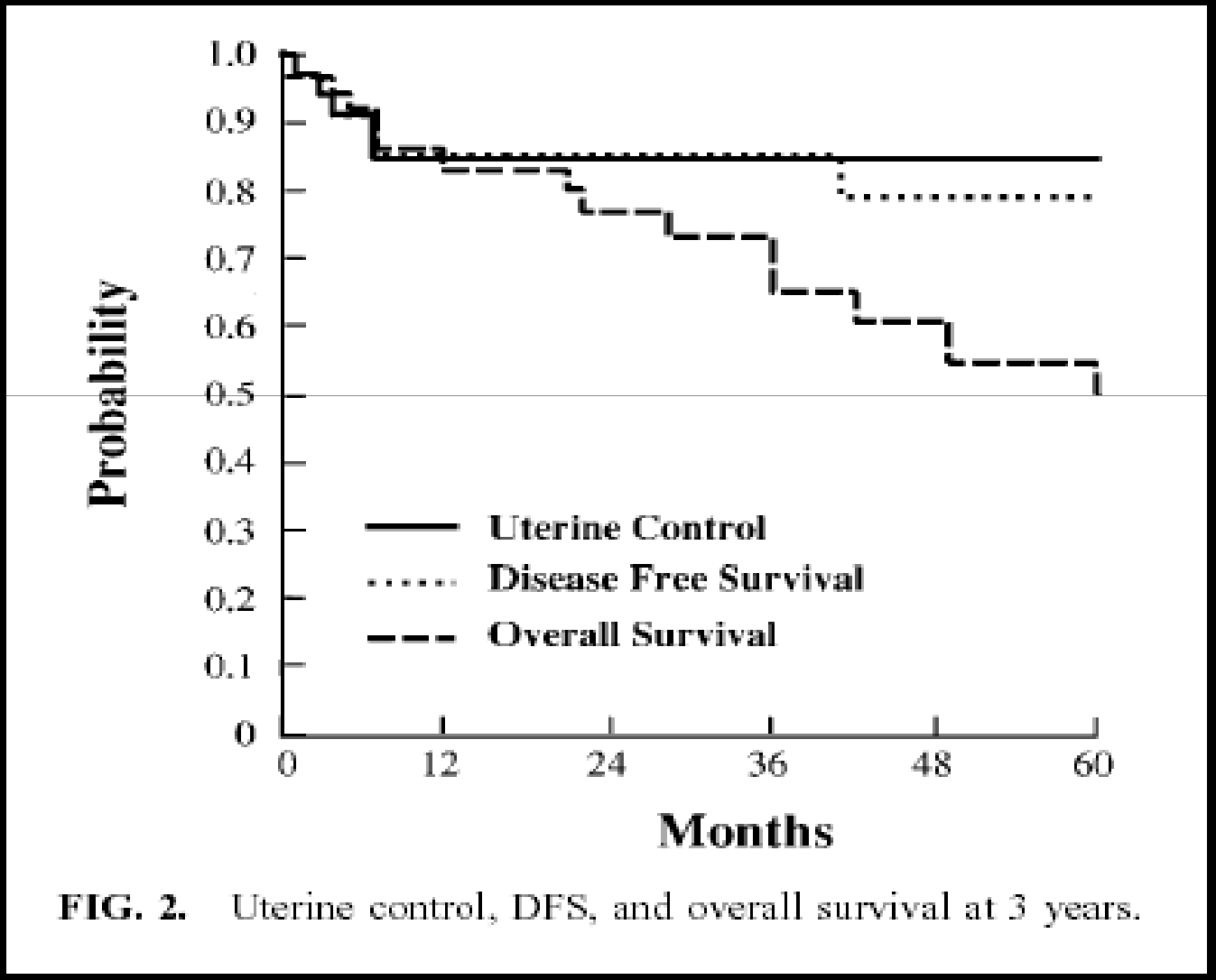
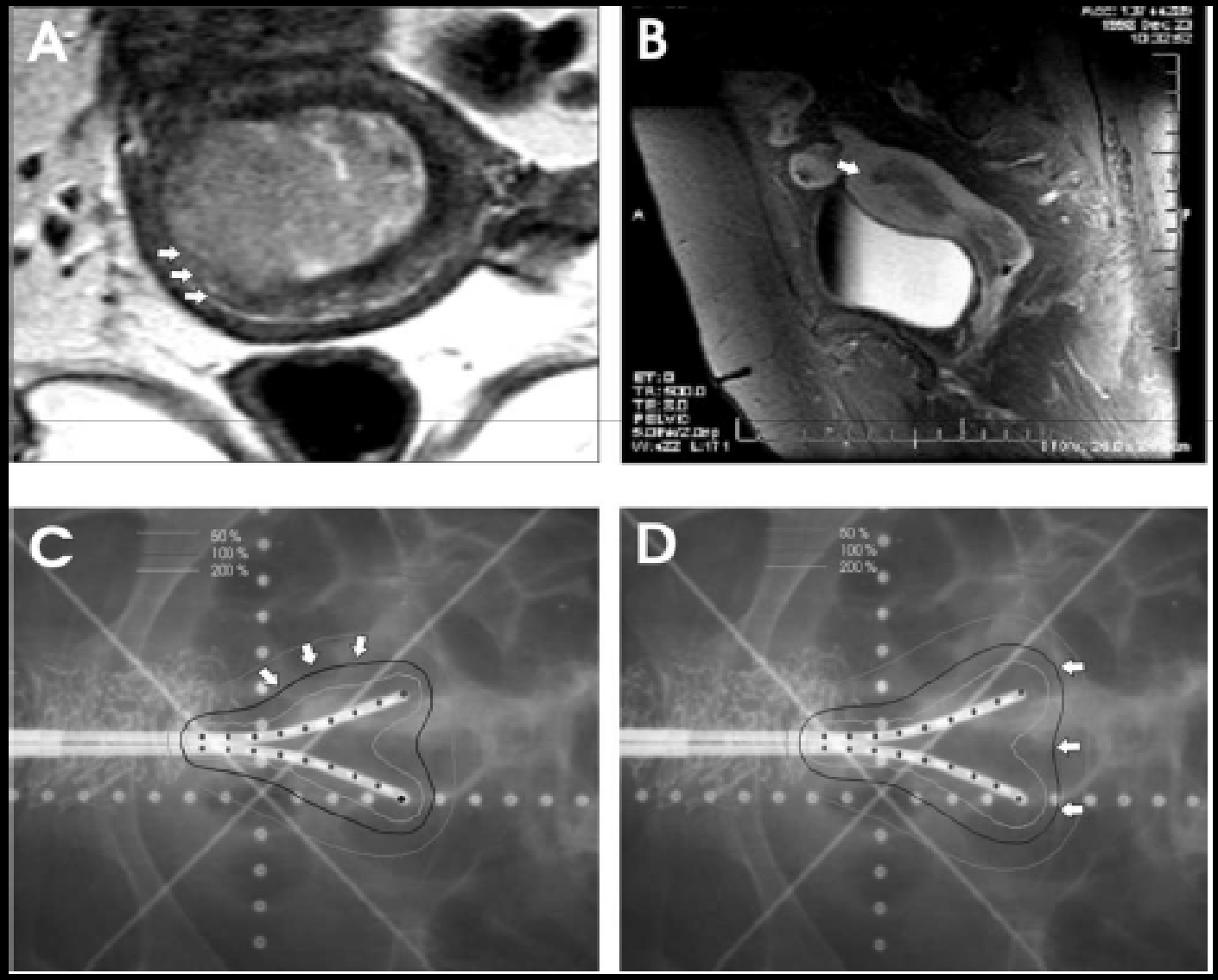


FIG. 2. Uterine control, DFS, and overall survival at 3 years.

Inoperable endometrial cancer (Quebec)

Nyazi et al 2005



Inoperable endometrial cancer (Quebec)

Nyazi et al 2005

n=38

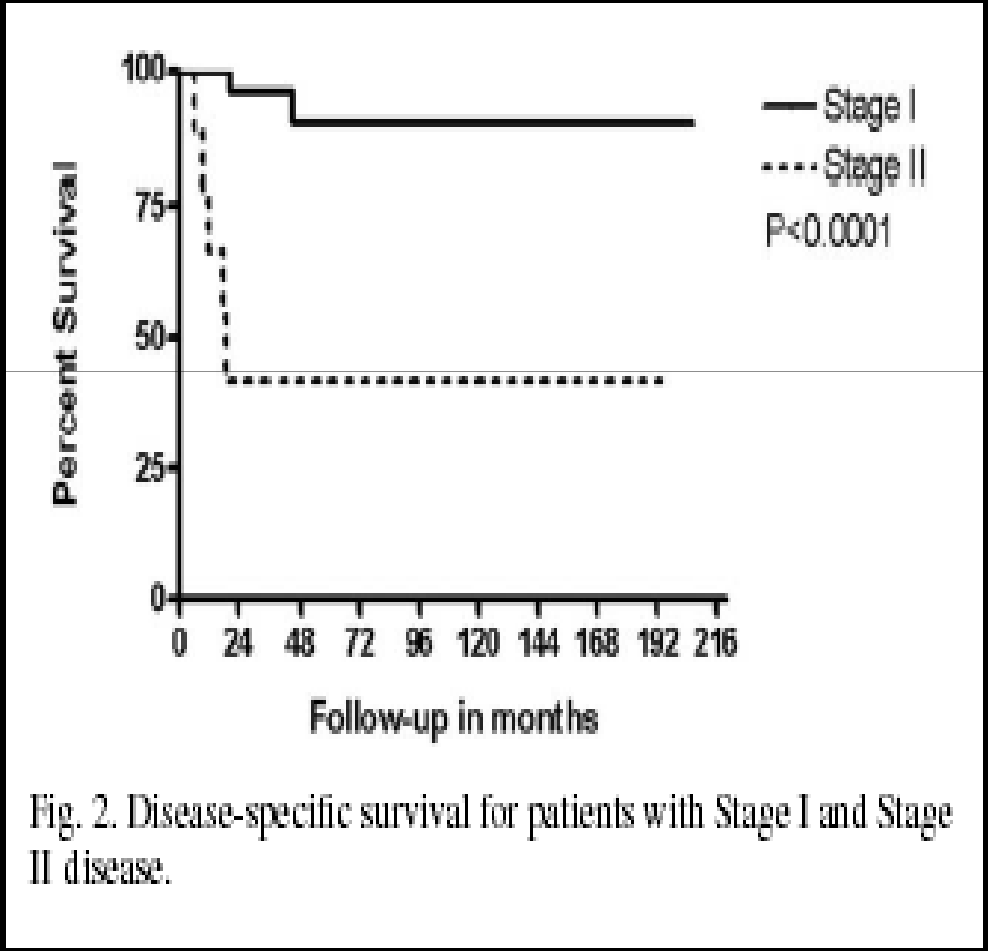


Fig. 2. Disease-specific survival for patients with Stage I and Stage II disease.

Table 3. Cause of death after treatment

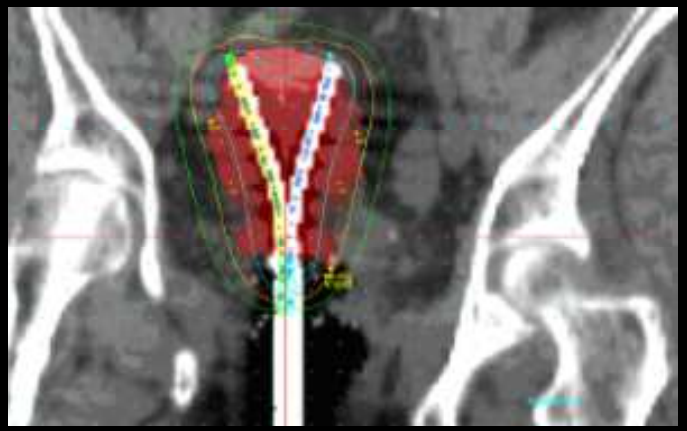
Cause	Number of patients
Endometrial cancer	7
Coronary artery disease	5
Second malignancies	3
Others	6
Not recorded	1

HIGH-DOSE-RATE ROTTE "Y" APPLICATOR BRACHYTHERAPY FOR DEFINITIVE TREATMENT OF MEDICALLY INOPERABLE ENDOMETRIAL CANCER: 10-YEAR RESULTS

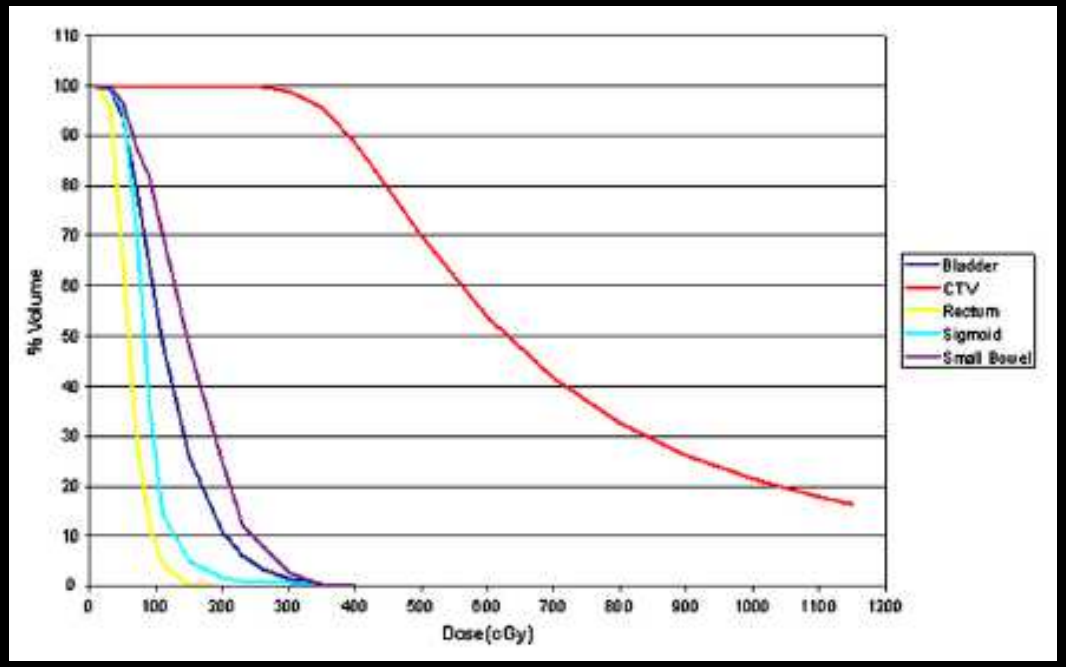
DEVIN COON, B.A.,* SUSHIL BERIWAL, M.D.,* DWIGHT E. HERON, M.D.,* JOSEPH L. KELLEY, M.D.,† ROBERT P. EDWARDS, M.D.,† PANITI SUKUMVANICH, M.D.,† KRISTIN K. ZORN, M.D.,† AND THOMAS C. KRIVAK, M.D.†

* Department of Radiation Oncology and †Division of Gynecologic Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA

IJROB 2008



Ext beam 45-50Y + 5x4Gy HDR (35)
HDR alone 7Gyx5 (14)



49 patients

Hypertension	32 (65.3)
Diabetes	23 (46.9)
Hyperlipidemia	13 (26.5)
CAD/MI	12 (24.5)
Hypothyroidism	8 (16.3)
CVA	4 (8.2)
DVT	4 (8.2)
CHF	2 (4.1)

84% BMI>35kg/m2

HIGH-DOSE-RATE ROTTE "Y" APPLICATOR BRACHYTHERAPY FOR DEFINITIVE TREATMENT OF MEDICALLY INOPERABLE ENDOMETRIAL CANCER: 10-YEAR RESULTS

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* Department of Radiation Oncology and † Division of Gynecologic Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA

IJROB 2008

	3yr	5yr
Cause specific survival	93%	87%
Overall survival	83%	42%
Late Grade 2 or more toxicity	13%	13%

Image-based three-dimensional conformal brachytherapy for medically inoperable endometrial carcinoma

Brachytherapy 13 (2014) 542–547

Beant S. Gill[1], Hayeon Kim[1], Chris Houser[1], Adam Olsen[1], Joseph Kelley[2], Robert P. Edwards[2], John Comerci[2], Paniti Sukumvanich[2], Alexander B. Olawaiye[2], Marilyn Huang[2], Madeleine Courtney-Brooks[2], Sushil Beriwal[1,*]

[1]*Department of Radiation Oncology, Magee-Womens Hospital of University of Pittsburgh Medical Center, Pittsburgh, PA*
[2]*Department of Gynecologic Oncology, Magee-Womens Hospital of University of Pittsburgh Medical Center, Pittsburgh, PA*

38 patients: 20 BT alone 37.5Gy in 5-6#
18 EBRT 45Gy + BT 20Gy in 4-5 #

Characteristics	All patients (n = 38)	BT alone (n = 20)	EBRT + BT (n = 18)
GTV, mean ± SD			
Volume (cc)	6.8 ± 4.5	5.4 ± 1.9	8.9 ± 6.5
D_{90} EQD_2 (Gy)	160.0 ± 62.1	172.3 ± 59.6	138.0 ± 64.6
CTV, mean ± SD			
Volume (cc)	85.7 ± 25.9	82.0 ± 28.0	87.6 ± 24.0
D_{90} EQD_2 (Gy)	59.9 ± 13.3	48.6 ± 5.6	72.4 ± 6.0
Rectum D_{2cc} EQD_2 (Gy)			
Mean ± SD	42.2 ± 18.3	26.3 ± 8.9	59.8 ± 4.0
Sigmoid D_{2cc} EQD_2 (Gy)			
Mean ± SD	52.4 ± 13.6	41.5 ± 8.6	64.6 ± 4.9
Bladder D_{2cc} EQD_2 (Gy)			
Mean ± SD	58.6 ± 15.2	46.8 ± 10.4	71.7 ± 6.1

CTV = uterus, cervix, upper half vagina ± lymph nodes

Image-based three-dimensional conformal brachytherapy for medically inoperable endometrial carcinoma

Brachytherapy 13 (2014) 542–547

Beant S. Gill[1], Hayeon Kim[1], Chris Houser[1], Adam Olsen[1], Joseph Kelley[2], Robert P. Edwards[2], John Comerci[2], Paniti Sukumvanich[2], Alexander B. Olawaiye[2], Marilyn Huang[2], Madeleine Courtney-Brooks[2], Sushil Beriwal[1,*]

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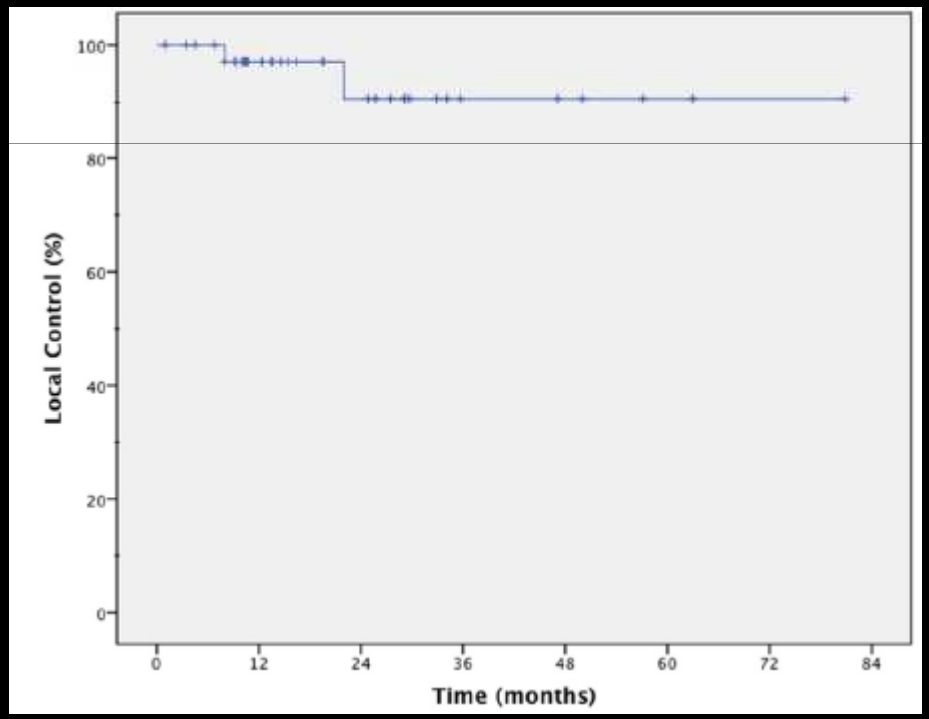
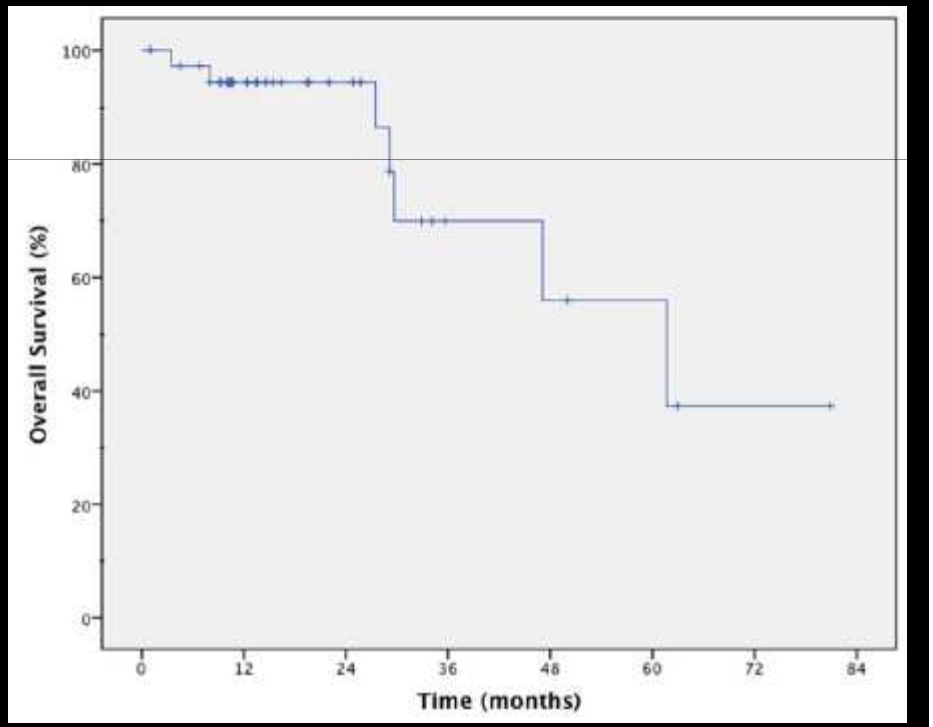




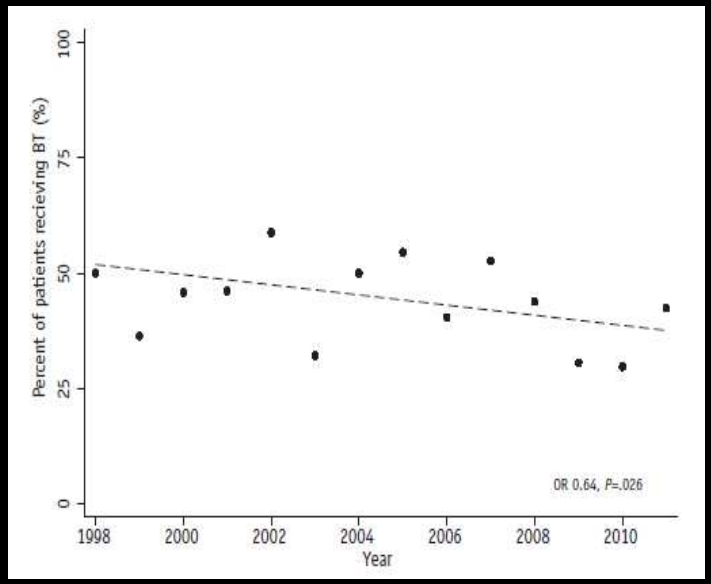
Brachytherapy Is Associated With Improved Survival in Inoperable Stage I Endometrial Adenocarcinoma: A Population-Based Analysis

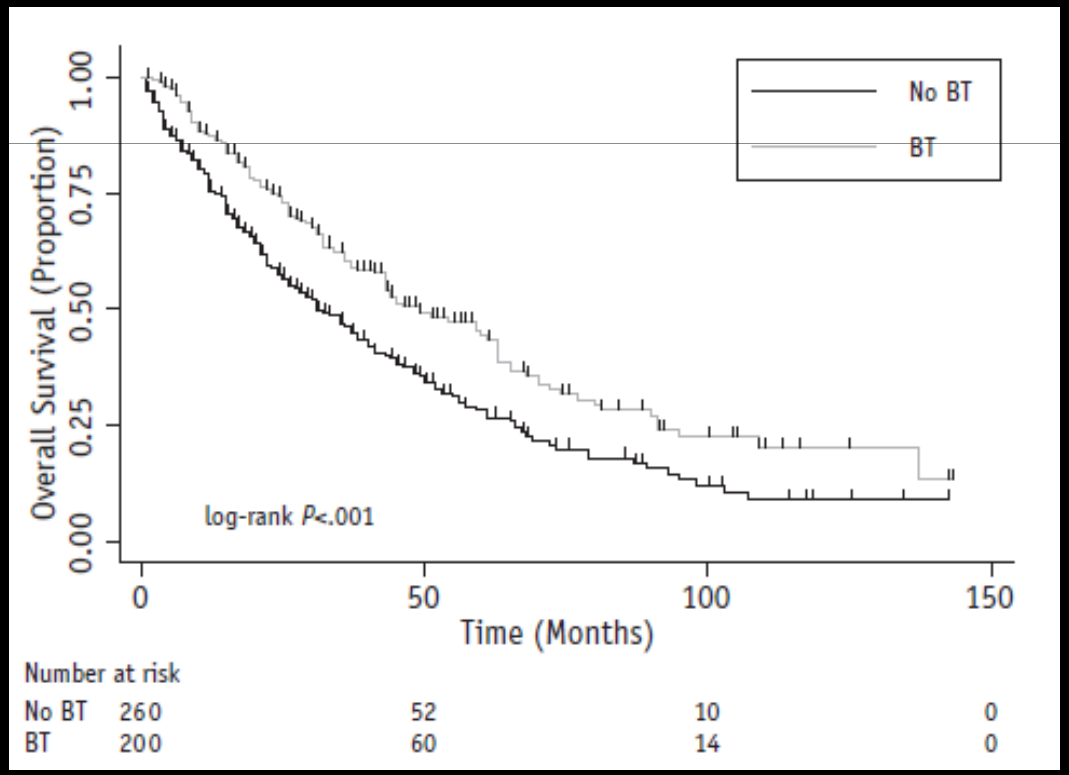
Int J Radiation Oncol Biol Phys, Vol. 93, No. 3, pp. 649–657, 2015

Sahaja Acharya, MD,* Stephanie M. Perkins, MD,* Todd DeWees, PhD,* et al

SEER analysis: 460 patients

Use of brachytherapy





Endometrial Cancer: brachytherapy

- Primary treatment of Stage I / II
  - Alone for Low/intermediate risk
  - After external beam for high risk

- Post operative treatment of Stage I / II
  - Alone for intermediate risk
  - After external beam for high risk with cervical involvement

- Primary treatment of Stage III / IV
  - with external beam

Endometrial cancer Postoperative brachytherapy

Peter Hoskin
Mount Vernon Cancer Centre

Adenocarcinoma of uterine mucosa

- Prognostic factors:
  - Stage:
    - depth of myometrial infiltration
    - tumour beyond the uterus
    - nodal involvement
  - Pathology
    - high tumour grade
    - serous papillary and clear cell variants
    - lymphovascular invasion

Endometrial Cancer: staging UICC 2009

Stage I: confined to uterus

- Ia: invasion <50% myometrial depth
- Ib: invasion >50% myometrial depth

Stage II: invasion of cervical stroma

Stage III: Extension outside uterus within pelvis

Stage IV: invasion of bladder rectum or distant spread

Endometrium Cancer: Principles of management

- **Stage I, II and III:** **Surgery +/- postop RT**

  Total Abdominal Hysterectomy plus
  Bilateral salpingo-oophorectomy
  +/- lymph node sampling or dissection

- **Stage I, II and III, unfit for surgery**

  Primary radiotherapy

Adjuvant post-hysterectomy treatment for localised endometrial cancer

Risk based on:

- Grade 2 or 3
- Myometrial invasion greater than 50%
- Cervical stromal invasion (Stage 2)
- Lymphovascular space invasion (LVSI):

- LOW: none of these
- INTER: one of these
- HIGH: two or more

Adjuvant post-hysterectomy treatment for localised endometrial cancer

Additional considerations:

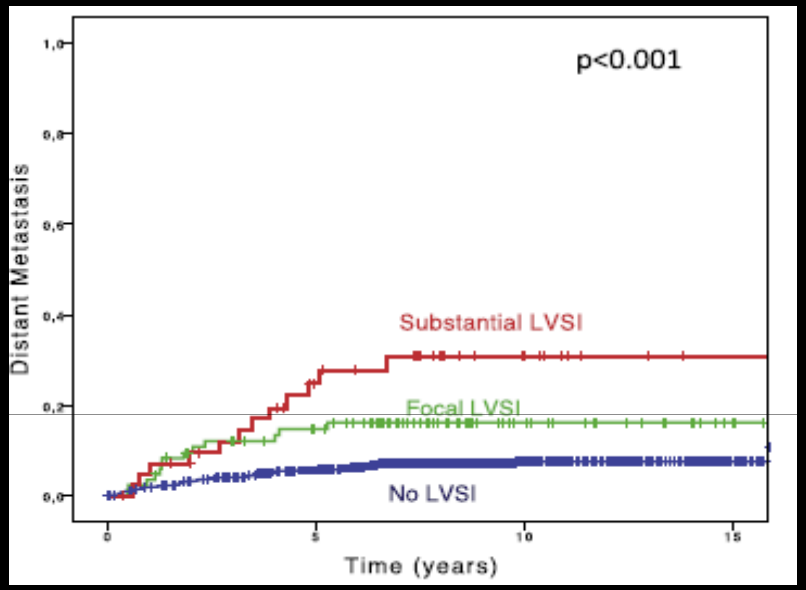
- High intermediate: two of the following……
  - Age>60, G3, IB, LVSI

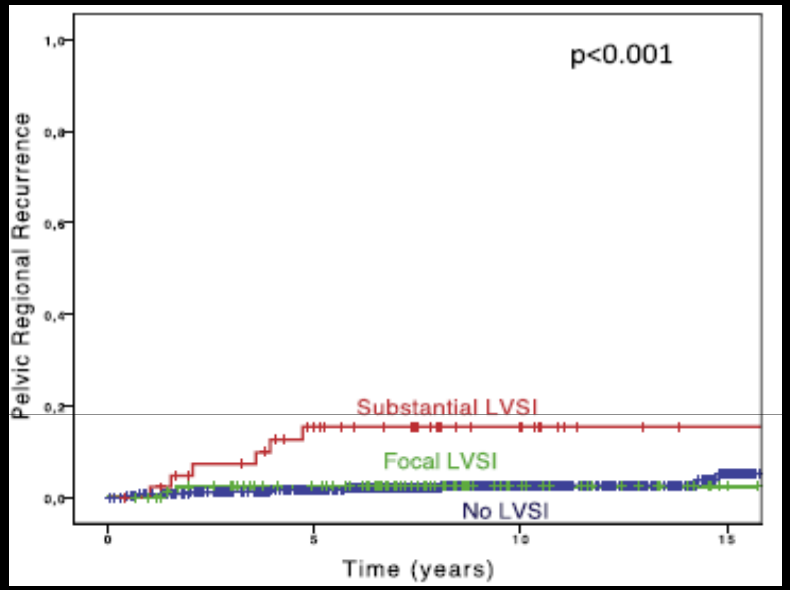
• Type I & 2 based on obesity, hyperlipidaemia, late menopause, anovulatory bleeding, infertility

- Genomic analysis

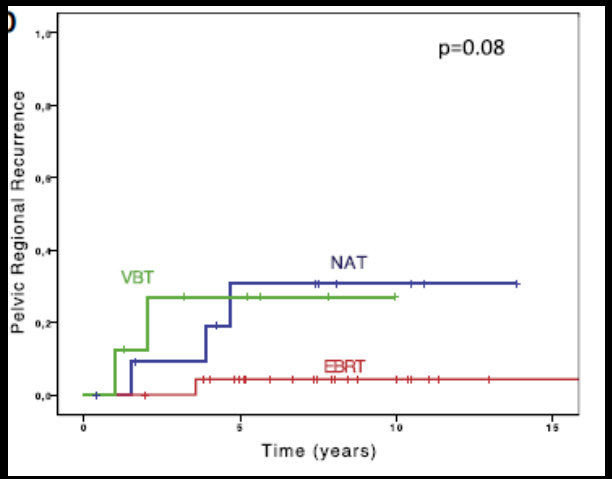
Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer – A pooled analysis of PORTEC 1 and 2 trials

Bosse et al European Journal of Cancer (2015) 51, 1742–1750





Subset all with Substantial LVSI



Adjuvant post-hysterectomy treatment for localised endometrial cancer

- No treatment
- Vaginal vault BT
- External beam
- External beam + VV BT

Intravaginal Brachytherapy in FIGO Stage I Low-Risk Endometrial Cancer: A Controlled Randomized Study.

Bengt et al IJ GYNAEC ONCOL 2009,

- 645 patients: Grade 1 or 2; Stage IA or IB

	Surgery n=326	Surgery + VBT n=319
Vaginal relapse [p=0.114]	3.1%	1.2%
G1/2 urinary toxicity	0.6%	2.8%

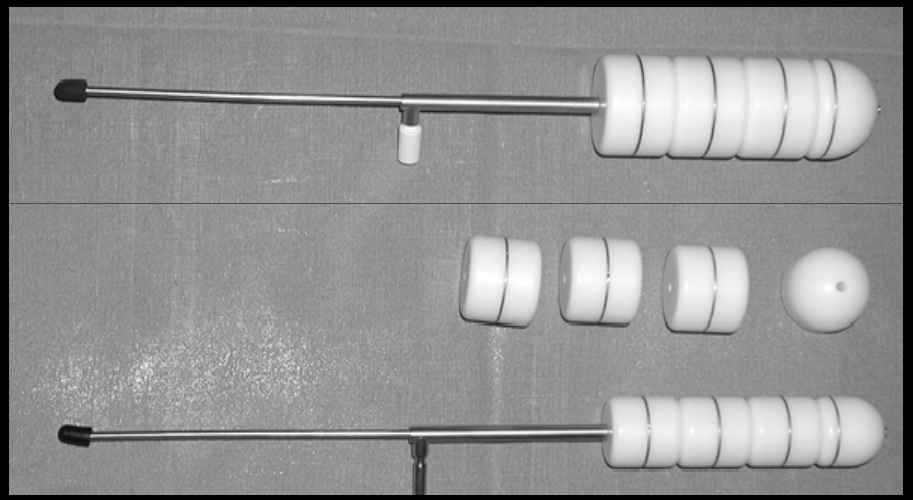
Adjuvant post-hysterectomy treatment for localised endometrial cancer

- No treatment:
  - low risk
- Vaginal vault BT:
  - intermediate risk, no LVSI
- External beam:
  - intermediate risk with LVSI, high risk
- External beam + VV BT:
  - high risk with stage II

Applicators

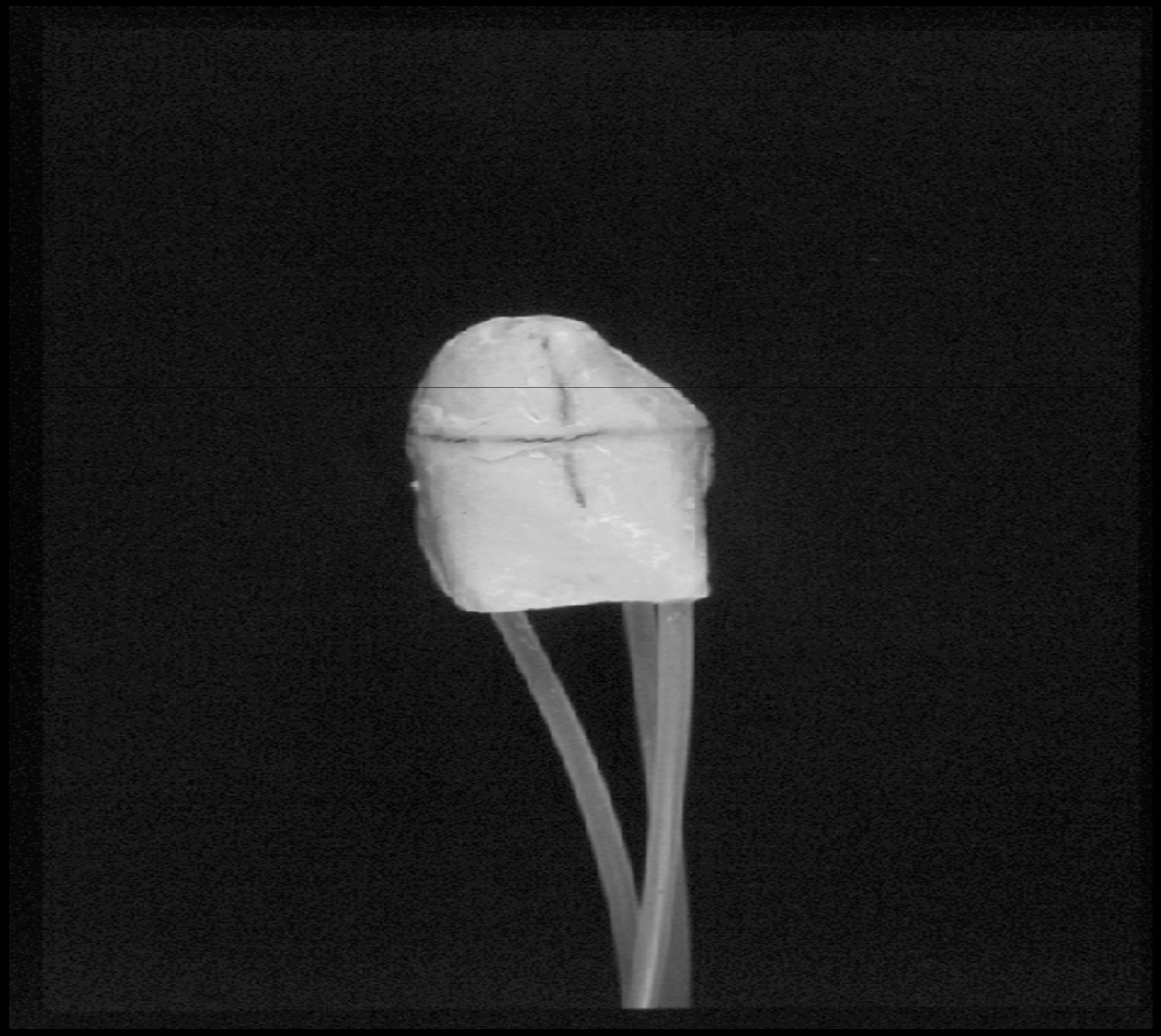
- Standard
  - Cylindrical single line source
  - Ovoids
  - Ring
  - Multichannel
- Customised
  - Individual moulds

Vaginal Cylindrical Single line source



Vaginal multichannel applicator

Mould Applicator (IGR Paris) postoperative vaginal Brachytherapy



Vault brachytherapy:CTV

- Vaginal scar
- Submucosal lymphatics to 5mm depth
- ? vaginal length
  - Cuff only
  - Upper one third
  - Upper two thirds
  - Entire vagina

- Typical volume:
  - 3 to 5 cms length
  - 5mm depth

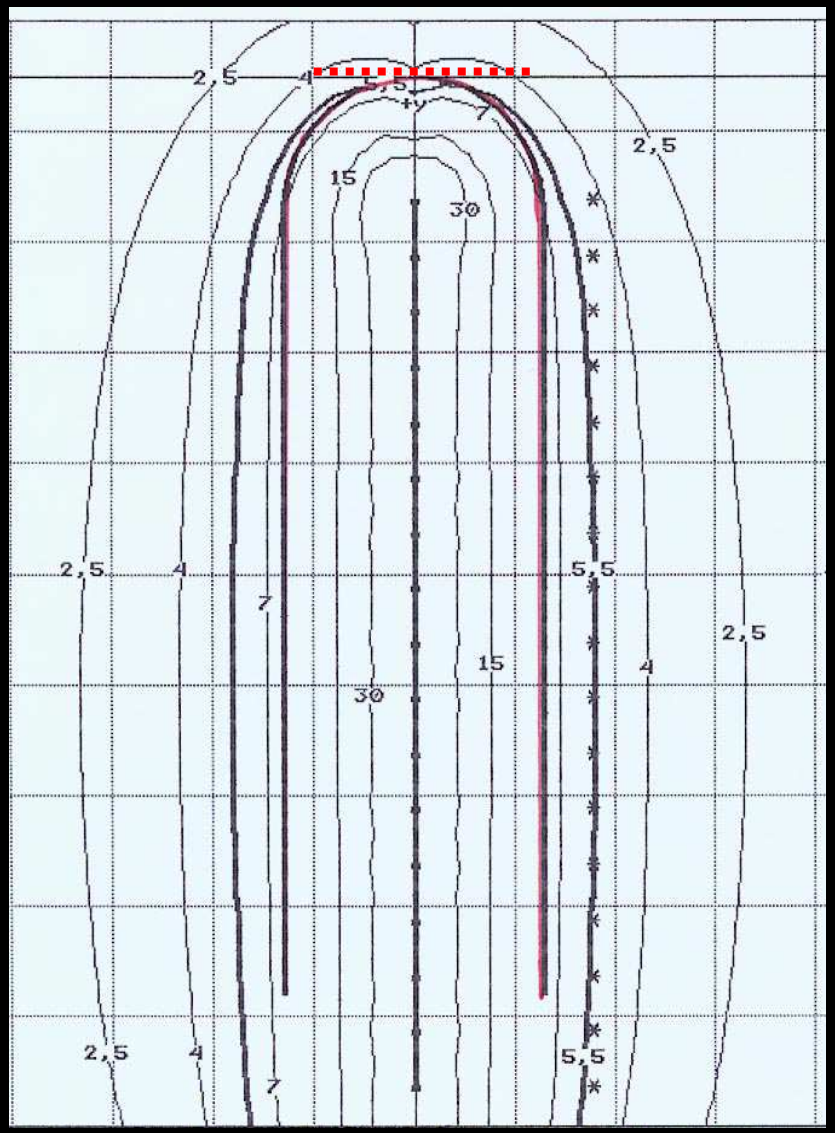
Dosimetry for post operative vaginal vault brachytherapy

Reference Volume encompassed by the **Reference Isodose** at 5 mm from the applicator surface

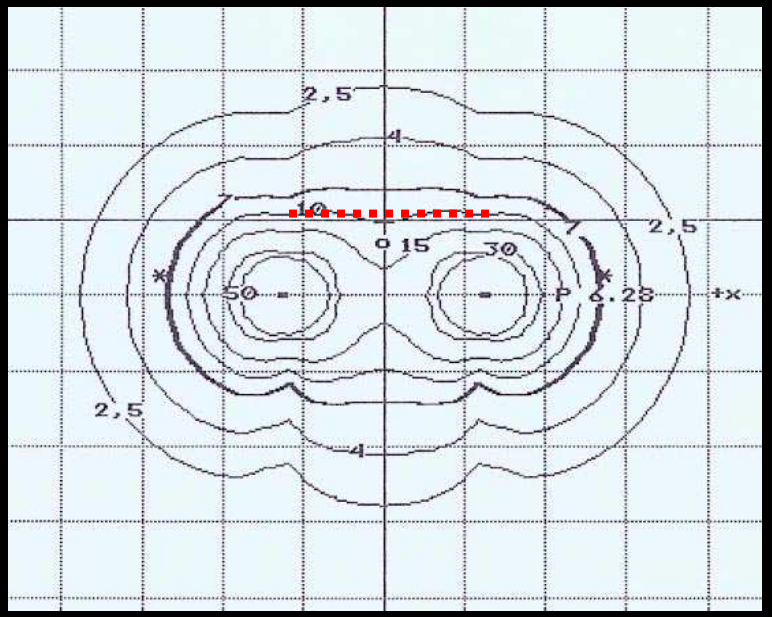
Length of the Reference Volume:

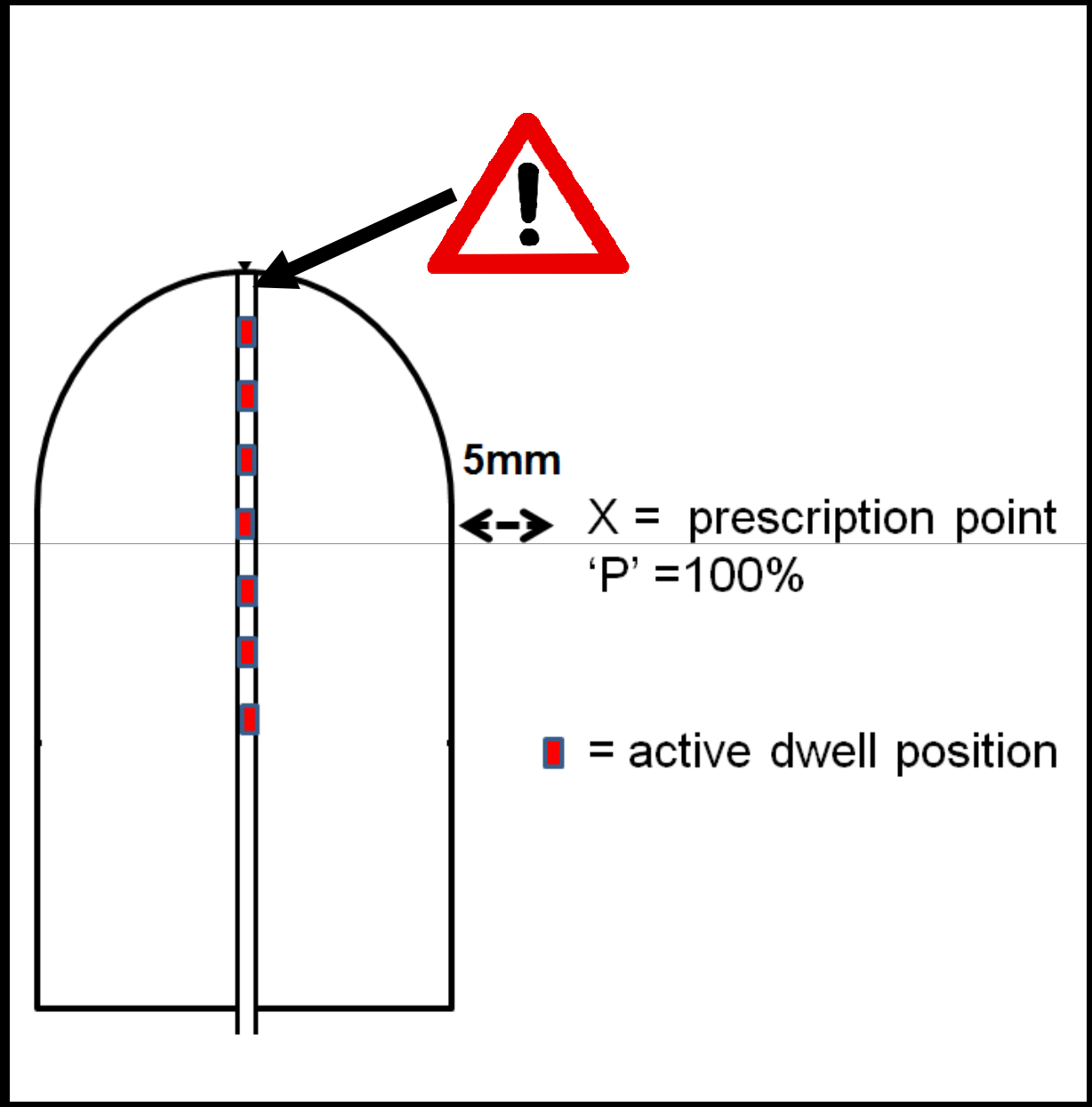
- 2-5cm
- Upper third of vagina

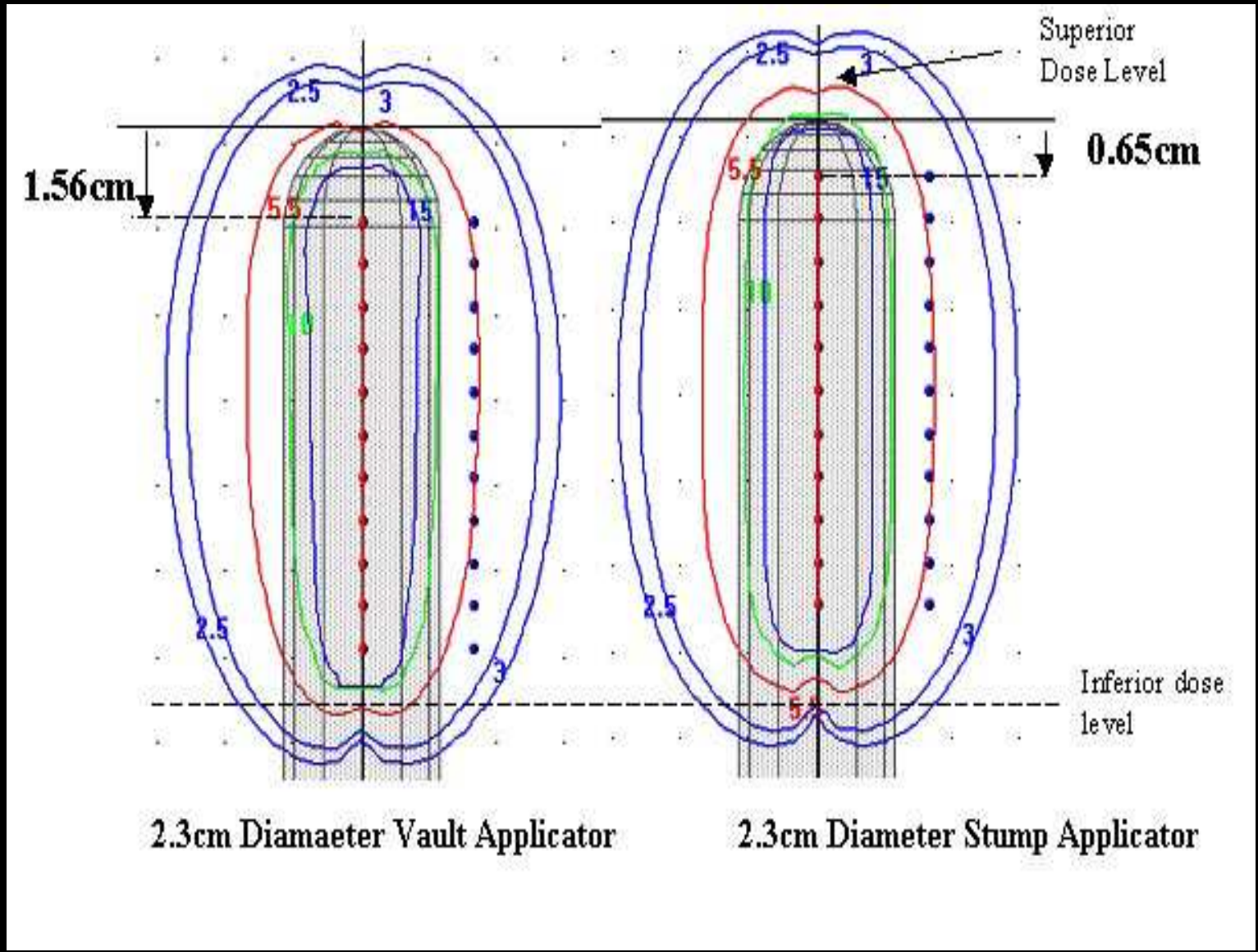
Weighted cylinder

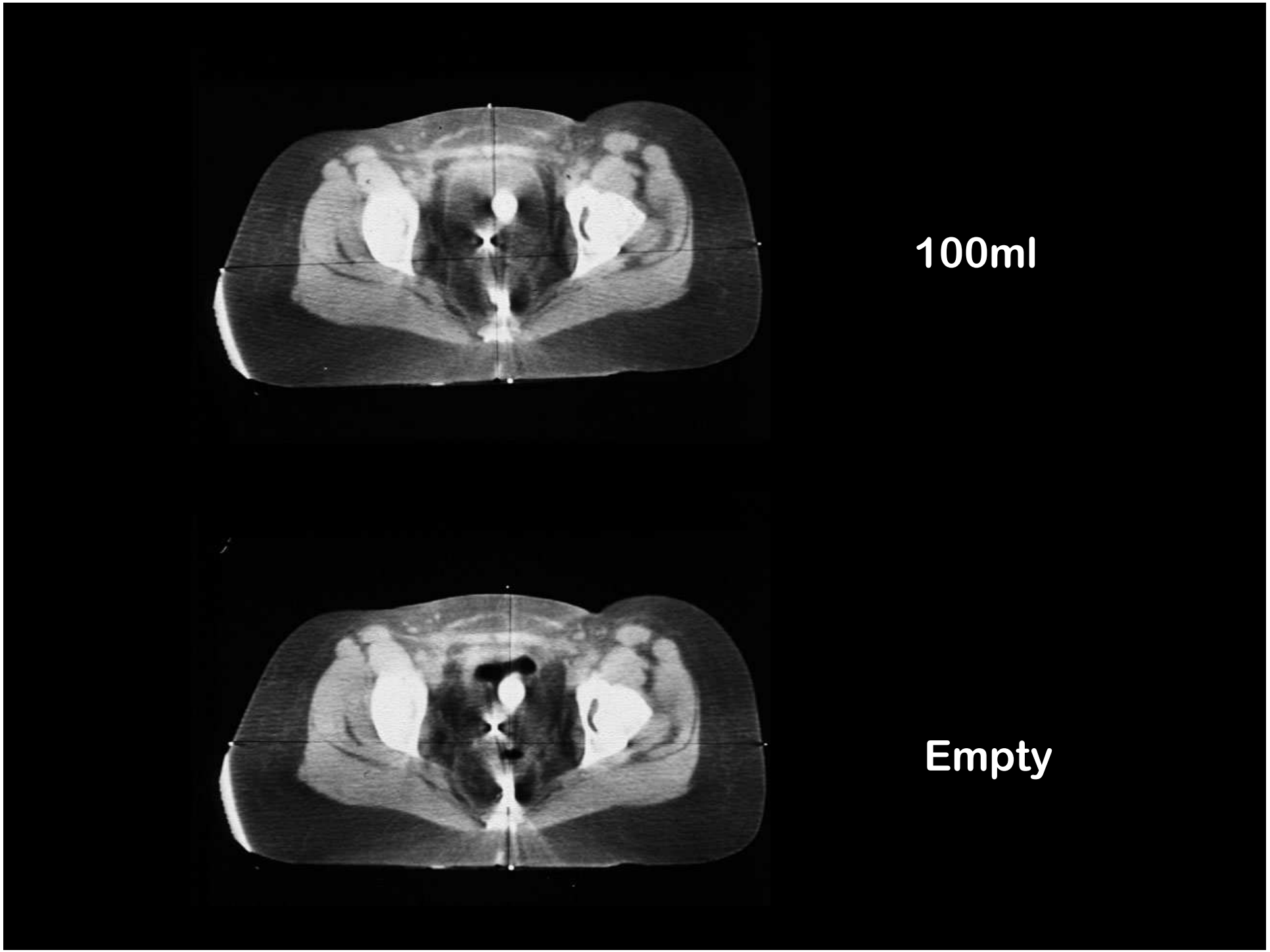


Ovoids




5mm
X = prescription point
'P' =100%
= active dwell position


Superior
Dose Level
1.56cm
0.65cm
Inferior dose
level
2.3cm Diamaeter Vault Applicator
2.3cm Diameter Stump Applicator


100ml
Empty

Effect of bladder volume

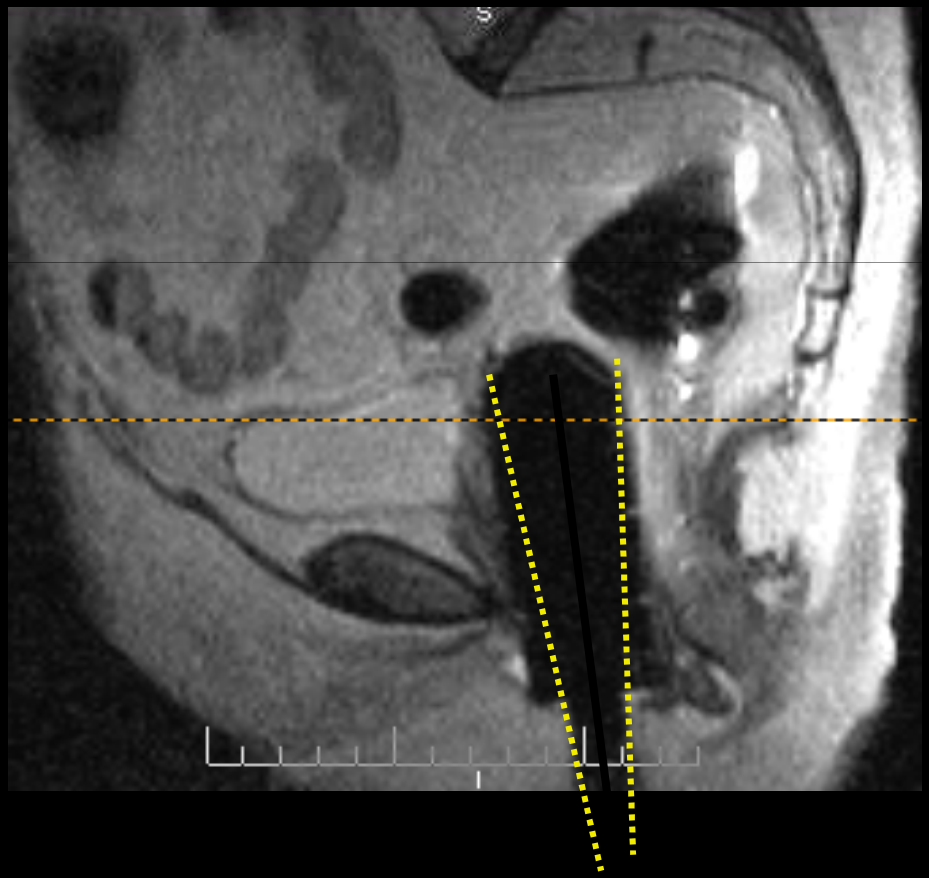
Max bladder dose Empty	70ml	Small bowel volume reduction with 70ml
5.2Gy	5.9Gy	45%

(5.5Gy at 0.5cm prescription)

Importance of applicator angle

Neutral position increases rectal dose

Clamping parallel to couch minimises bladder and rectal doses



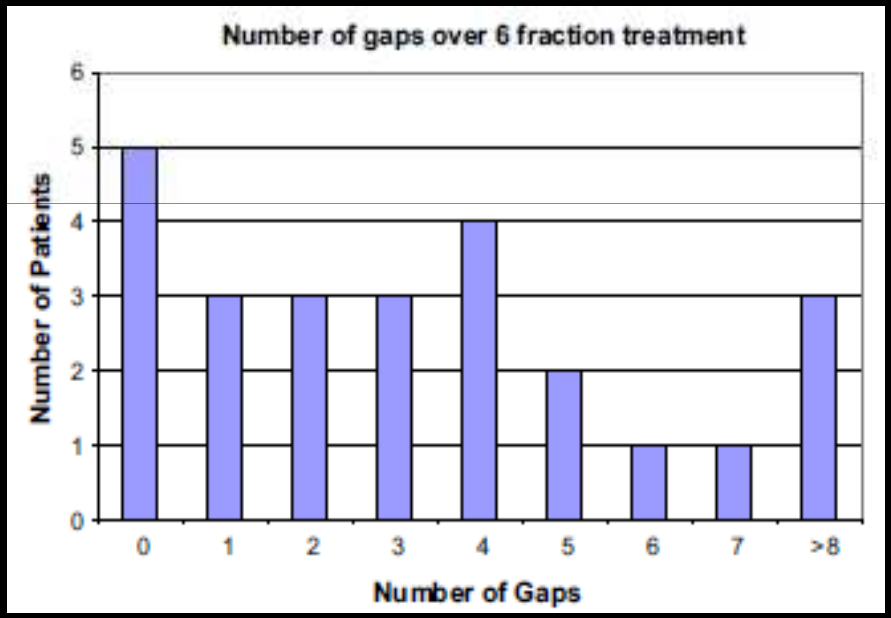
DOSIMETRIC EFFECTS OF AIR POCKETS AROUND HIGH–DOSE RATE BRACHYTHERAPY VAGINAL CYLINDERS

SUSAN RICHARDSON, PH.D., GEETHPRIYA PALANISWAAMY, PH.D., AND PERRY W. GRIGSBY, M.D.

Department of Radiation Oncology, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO

IJROB 2010

25 PATIENTS: 6FRACTION VAULT BRACHYTHERAPY



90 AIRPOCKETS IN 150 PROCEDURES (60%)

DOSIMETRIC EFFECTS OF AIR POCKETS AROUND HIGH–DOSE RATE BRACHYTHERAPY VAGINAL CYLINDERS

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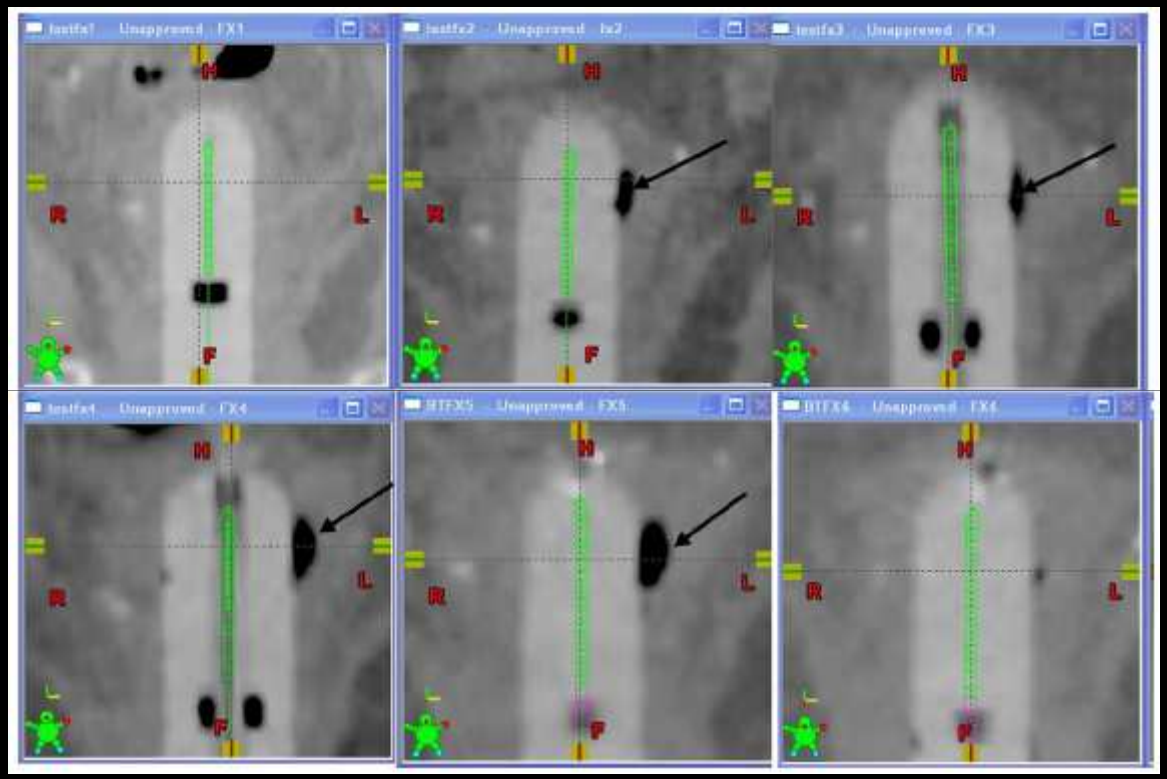
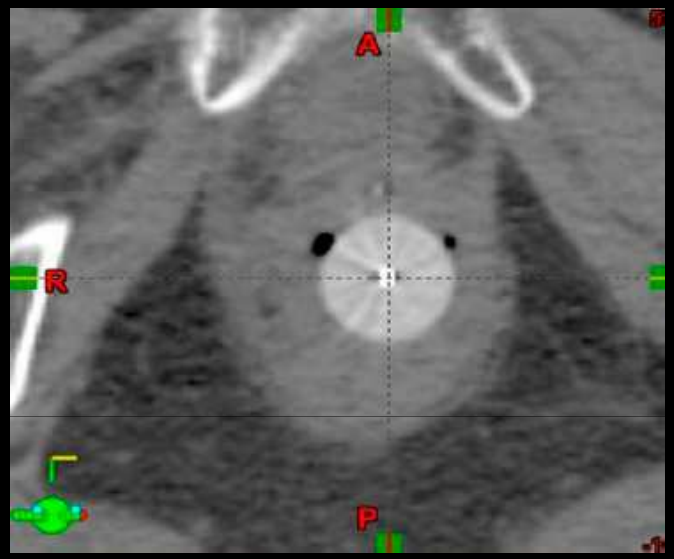


Persistent air pockets over 6 fractions

Average dose reduction 27% (9-58%)

Vaginal vault brachytherapy in endometrial cancer: verifying target coverage with image-guided applicator placement

105 consecutive patients: 21.6Gy/4f
All CT imaged before fraction 1



Study	Applicator diameters (cm)					% air gaps >2 mm
	2	2.3	2.6	3.0	3.5	
Bristol 2008 Cameron et al [1]	4%	0%	40%	36%	20%	32%
Washington 2010 Richardson et al [2]	0%	0%	96%	4%	0%	72%
Bristol, present study	0%	1%	16%	54%	30%	11% 7% after repositioning

Humphries et al. BJR 2013

ELSEVIER

BRACHYTHERAPY

Brachytherapy 11 (2012) 58–67

American Brachytherapy Society consensus guidelines for adjuvant vaginal cuff brachytherapy after hysterectomy

William Small Jr.[1,*], Sushil Beriwal[2], D. Jeffrey Demanes[3], Kathryn E. Dusenbery[4], Patricia Eifel[5], Beth Erickson[6], Ellen Jones[7], Jason J. Rownd[6], Jennifer F. De Los Santos[8], Akila N. Viswanathan[9], David Gaffney[10]

[1]*Department of Radiation Oncology, The Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL*
[2]*Department of Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA*
[3]*Department of Radiation Oncology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA*
[4]*Department of Radiation Oncology, University of Minnesota Medical Center, Minneapolis, MN*
[5]*Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*
[6]*Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI*
[7]*Department of Radiation Oncology, University of North Carolina, Chapel Hill, NC*
[8]*Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL*
[9]*Department of Radiation Oncology, Brigham and Women's Hospital, Boston, MA*
[10]*Department of Radiation Oncology, Huntsman Cancer Institute, Salt Lake City, UT*

- **Proximal 3 to 5 cm vagina treated**
- **Dose prescribed to surface or 0.5cm**
- **Definitive recommendations for dosimetry imaging 'an open question'**
- **Dose recommendations …unhelpful**

American Brachytherapy Society consensus guidelines for adjuvant vaginal cuff brachytherapy after hysterectomy

Brachytherapy 11 (2012) 58–67

Results of postoperative adjuvant cuff radiation therapy with brachytherapy alone

Author/reference	*N*	Treatment	Control/survival	Total pelvic recurrences (%)[a]	Vaginal recurrences (%)	Complications
Sorbe and Smeds (5)	404		5-y OS, 92%	3.0	0.7	6.9%, clinically signi
Noyes et al. (6)	63	16.2 Gy × 2 ovoids at surface	OS, 98.5%	1.6	0	No, Grade 3/4
Fanning et al. (7)	60	7 Gy × 3 at 0.5 cm	3-y NED, 100%	0	0	No, Grade 3/4
Kloetzer et al. (8)	108	10 Gy × 4 to 0.5 or 1.0 cm	3-y OS, 96%	0	0–3	0–12.6%, Grade 3/4
Hong et al. (9)	44	7 Gy × 3 at 0.5 cm	5-y DFS, 92%	0	2.9	No, Grade 3/4
MacLeod et al. (10)	141	8.5 Gy × 4 at surface		2	1.4	No, Grade 3/4
Weiss et al. (11)	122	7 Gy × 3 at surface	5-y NED, 94%	4.1	1.6	No, Grade 3/4
Petereit et al. (12)	191	16.2 Gy × 2 ovoids at surface	4-y OS, 95%	0.5	0	0.5%, Grade 4
Chadha et al. (13)	38	7 Gy × 3 at 0.5 cm	5-y OS, 93%	0	0	No, Grade 3/4
Eltabbakh et al. (14)	332	30 Gy at 0.5 cm (LDR)	5-y DFS, 98.9%	0.6	0	2.1%, Grade 3/4
Anderson et al. (15)	102	5 Gy × 3 at 0.5 cm	5-y OS, 84%	1.9	1	No, Grade 3/4
Horowitz et al. (16)	164	7 Gy × 3 at 0.5 cm	5-y OS, 87%	0.6	1.2	No, Grade 3/4
Rittenberg et al. (17)	53	5.6 Gy × 3 at 0.5 cm	5-y OS, 91%	0	0	No, Grade 3/4
Jolly et al. (18)	50	5 Gy × 5 at 0.5 cm	4-y OS, 97%	2	2	No, Grade 3/4
Alektiar et al. (19)	382	7 Gy × 3 at 0.5 cm	5-y OS, 93%	0	0.8	0.5%, Grade 3; 0.25%, Grade 4
Solhjem et al. (20)	100	7 Gy × 3 at 0.5 cm	3-y OS, 97.9%	0	0	No, Grade 3/4
Cengiz et al. (21)	31	7 Gy × 3 at 0.5 cm (HDR) or 70 Gy at surface (LDR)	5-y OS, 93%	3.2	0	No, Grade 3/4
Atahan et al. (22)	128	5.5 Gy × 5 at 0.5 cm	5-y OS, 96%	1.6	0	No, Grade 3/4
Lin et al. (23)	42	7 Gy × 3 at 0.5 cm (HDR) 65 Gy at surface, 30 Gy at 0.5 cm (LDR)		0	2	No, Grade 3/4
McCloskey et al. (24)	75	7 Gy × 3 at 0.5 cm		2.6	1.3	
Aalders et al. (25)	277	60 Gy at surface (LDR)	5-y OS, 89%	6.9[b]		1%, Grade 4
Knocke et al.[c] (26)	325	8.5 Gy × 4–5 with intrauterine and 7 Gy × 1–2 with intravaginal at 2 cm from the center of the source	5-y OS, 52.7%	13.8[b]		3.1%, Grade 3/4
PORTEC-2[d] (3)	213	7 Gy × 3 at 0.5 cm (HDR) 30 Gy at 0.5 cm (LDR)	5-y, 84.8%	3.8	1.8	2.3%, Grade 3; no, Grade 4

American Brachytherapy Society consensus guidelines for adjuvant vaginal cuff brachytherapy after hysterectomy

Brachytherapy 11 (2012) 58–67

Results of postoperative adjuvant cuff radiation therapy with EBRT and vaginal brachytherapy

Author/reference	*N*	Treatment[a]	Control/survival	Pelvic recurrences (%)	Vaginal recurrences (%)	Complications
Lybeert et al. (27)	291 Postop	40 Gy EBRT + 5 Gy × 4 at 0.5 cm (HDR)	5-y NED I: 88% II: 68% III/IV: 50%	2.7	2.7	No, Grade 3/4
Nori et al. (28)	300	40 Gy EBRT + 7 Gy × 3 at 0.5 cm (HDR)	20-y DFS, 96%	0.3	2	No, Grade 3/4
Algan et al.[b] (29)	81	45 Gy EBRT + 4 Gy × 3 at 0.5 cm (HDR) or 30 Gy surface (LDR)	5-y OS, 83%	3	4	
Cannon et al. (30)	50	45–51 Gy EBRT + 5 Gy × 3/7.8 × 2 at surface (HDR)	5-y OS, 82%	4	0	2%, Grade 3; 2%, Grade 4
Fayed et al. (31)	1179	50.4 Gy EBRT + 2 Gy × 6 at 0.5 cm (HDR)/60–70 Gy total at surface (LDR)[c]	5-y OS, 70% (LDR) and 68% (HDR)	9 (LDR); 14 (HDR)[d,e]		1.9%, Grade 3/4
Aalders et al. (25)	263	40 Gy EBRT 60 Gy at surface (LDR)	5-y OS, 91%	2[e]		0.7%, Grade 5; 0.4%, Grade 4

Prescription dose

Brachytherapy alone

PDR: (0.5Gy/hr)	30Gy at 5 mm
HDR :	21Gy in 3 fr. at 5 mm (7 Gy per fraction)

Prescription dose

Brachytherapy in combination with EBRT after 40-45Gy in 20-25f EBRT

PDR: 20Gy (0.5Gy per hour)

HDR:	**Total dose (2Gy equ)**	
	$\alpha\beta$**10**	$\alpha\beta$**3.5**
45Gy/25f + 15Gy/3f	**63.0**	**72.7**
48.6Gy/27f + 8Gy/2f	**57.1**	**57.6**

Vaginal vault brachytherapy: doses

- Sole treatment

	PDR	HDR
surface	45Gy/30hrs	35Gy/3f
5mm	30Gy/30hrs	21Gy/3f

- Boost after 40-45Gy external beam

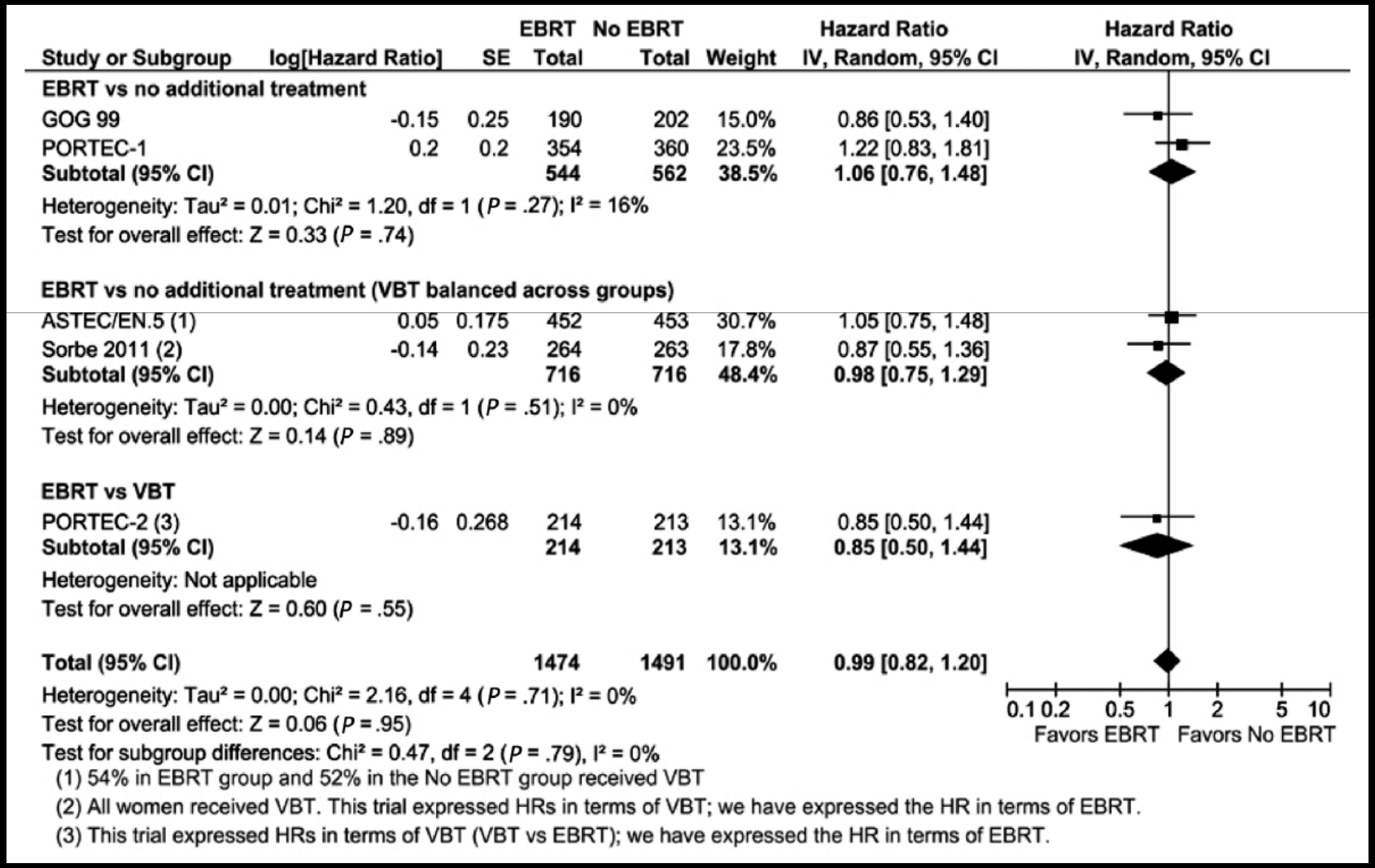
	PDR	HDR
surface	30Gy/20hrs	22Gy/3f
5mm	20Gy/20hrs	15Gy/3f

Adjuvant Radiotherapy for Stage I Endometrial Cancer: An Updated Cochrane Systematic Review and Meta-analysis

Anthony Kong,* Nick Johnson, Henry C. Kitchener, Theresa A. Lawrie*

J Natl Cancer Inst 2012;104:1625–1634

Overall survival



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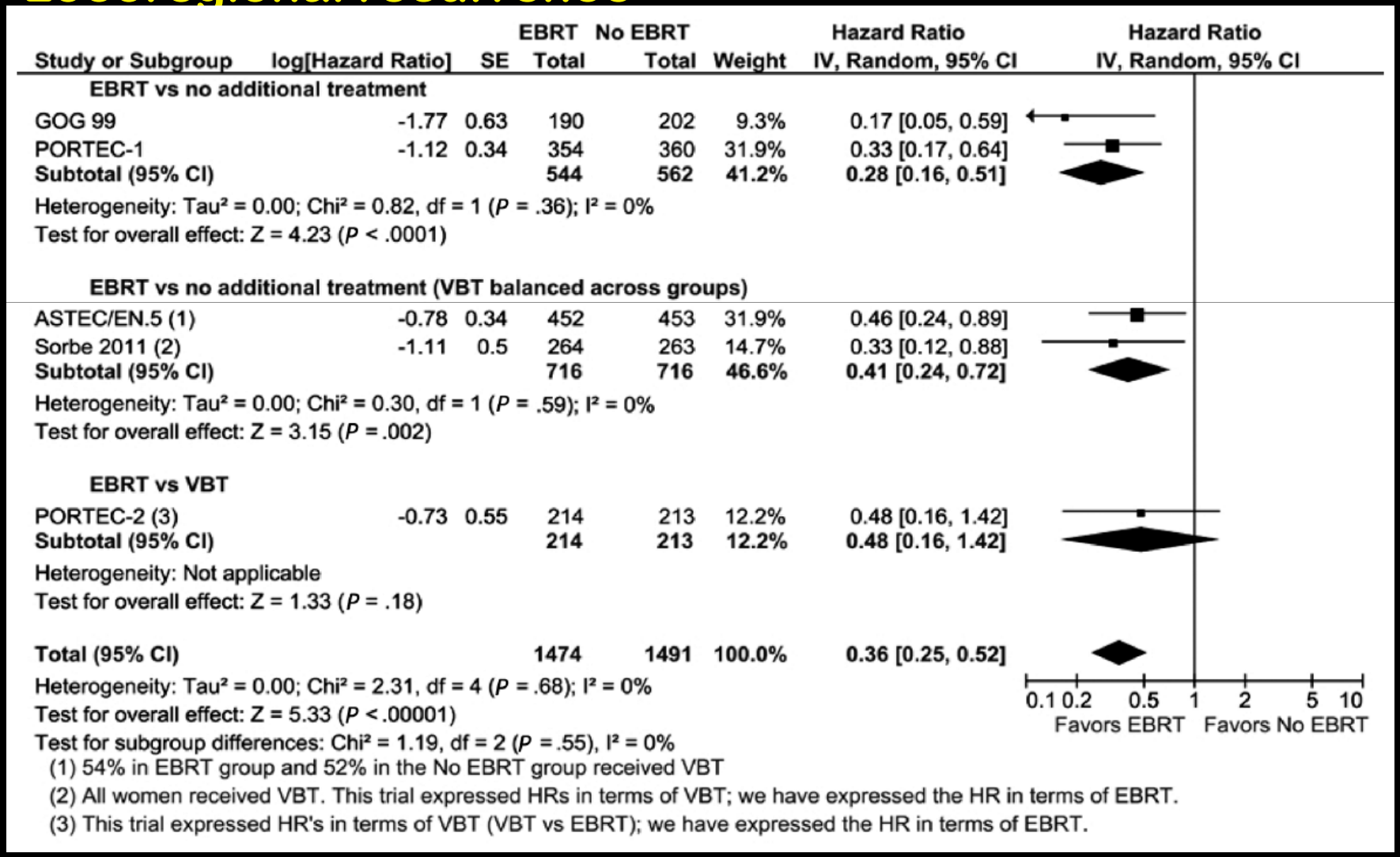
Locoregional recurrence



(1) 54% in EBRT group and 52% in the No EBRT group received VBT

(2) All women received VBT. This trial expressed HRs in terms of VBT; we have expressed the HR in terms of EBRT.

(3) This trial expressed HR's in terms of VBT (VBT vs EBRT); we have expressed the HR in terms of EBRT.

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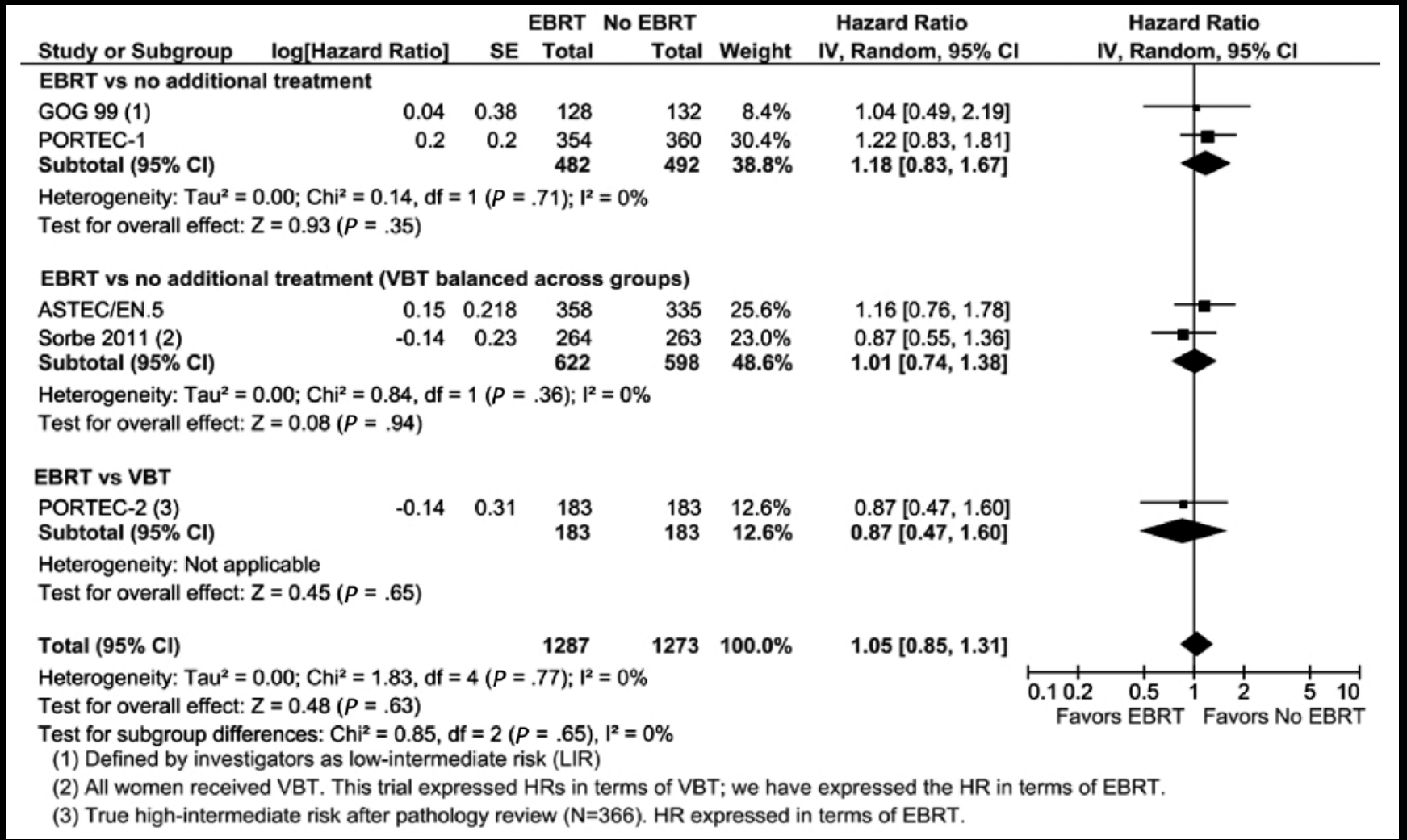
J Natl Cancer Inst 2012;104:1625–1634

Overall survival: intermediate risk



(1) Defined by investigators as low-intermediate risk (LIR)

(2) All women received VBT. This trial expressed HRs in terms of VBT; we have expressed the HR in terms of EBRT.

(3) True high-intermediate risk after pathology review (N=366). HR expressed in terms of EBRT.

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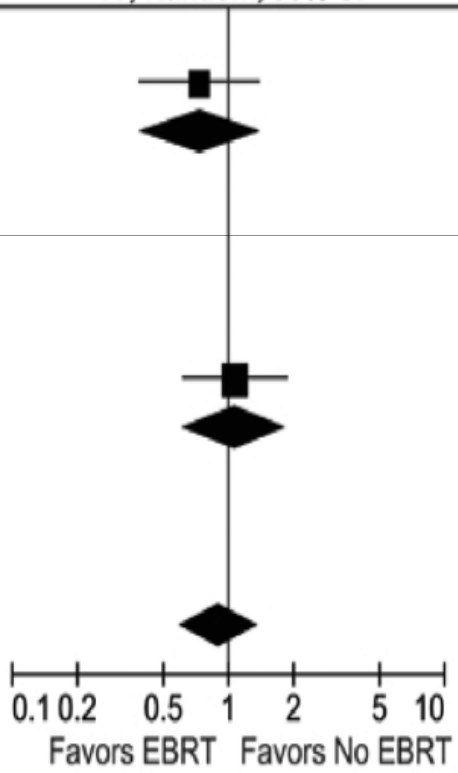
J Natl Cancer Inst 2012;104:1625–1634

Overall survival: high risk

Study or Subgroup	log[Hazard Ratio]	SE	EBRT Total	No EBRT Total	Weight	Hazard Ratio IV, Random, 95% CI
EBRT vs no additional treatment						
GOG 99 (1)	-0.31	0.33	62	70	43.1%	0.73 [0.38, 1.40]
Subtotal (95% CI)			**62**	**70**	**43.1%**	**0.73 [0.38, 1.40]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (*P* = .35)						
EBRT vs no additional treatment (VBT balanced across groups)						
ASTEC/EN.5	0.07	0.287	89	113	56.9%	1.07 [0.61, 1.88]
Subtotal (95% CI)			**89**	**113**	**56.9%**	**1.07 [0.61, 1.88]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (*P* = .81)						
Total (95% CI)			**151**	**183**	**100.0%**	**0.91 [0.60, 1.39]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.75$, df = 1 (*P* = .38); $I^2 = 0\%$						
Test for overall effect: Z = 0.43 (*P* = .67)						
Test for subgroup differences: $Chi^2 = 0.75$, df = 1 (*P* = .38), $I^2 = 0\%$						

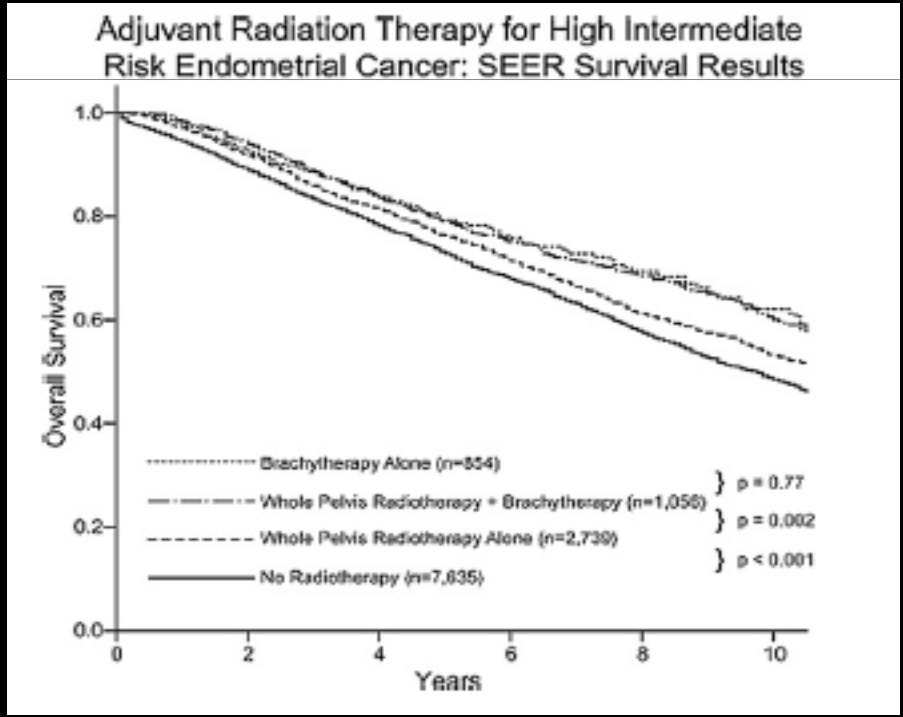
(1) Defined by investigators as high-intermediate risk (HIR)



Brachytherapy for Stage I Endometrial Cancer: Survival Results from the SEER Registry

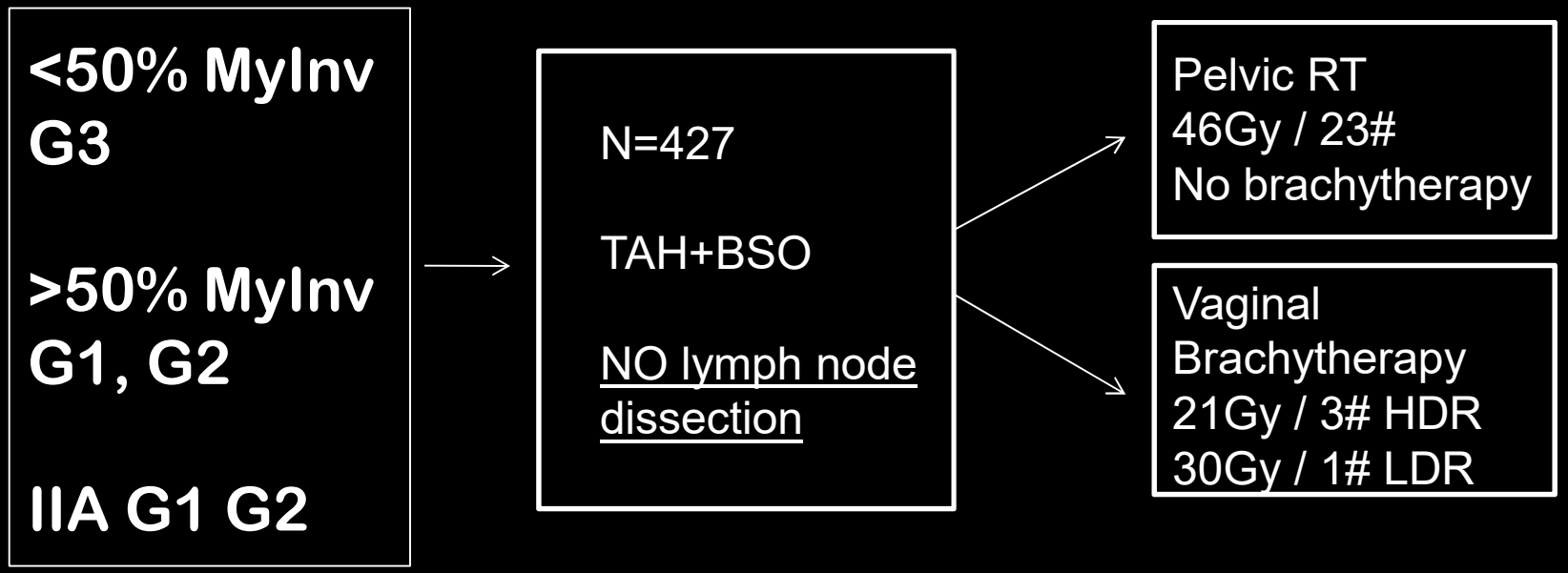
Junzo P. Chino, M.D.[1], Ellen L. Jones, M.D., Ph.D.[2], Andrew Berchuck, M.D.[3], Laura J. Havrilesky, M.D., M.H.Sc.[3] [1]Radiation Oncology, Duke University Medical Center, Durham, NC; [2]Radiation Oncology, University of North Carolina School of Medicine, Chapel Hill, NC; [3]Obstetrics and Gynecology, Division of Gynecologic Oncology, Duke University Medical Center, Durham, NC

12,284 patients Stage 1 endometrial cancer 1988-2006
Clear cell, papillary serous and sarcomatoid excluded



Brachytherapy 2010

PORTEC 2 study



	EBRT	VBT	
3 yr overall survival	84%	84%	p=0.55
3 yr disease specific survival	89%	89%	p=0.38

Patient characteristics

	EBRT	VBT
Age		
<60 yrs	4	4
>60 yrs	96	96
Stage		
IB	8	7
IC	80	81
IIA	11	12
Grade		
1	46	48
2	45	44
3	8	8

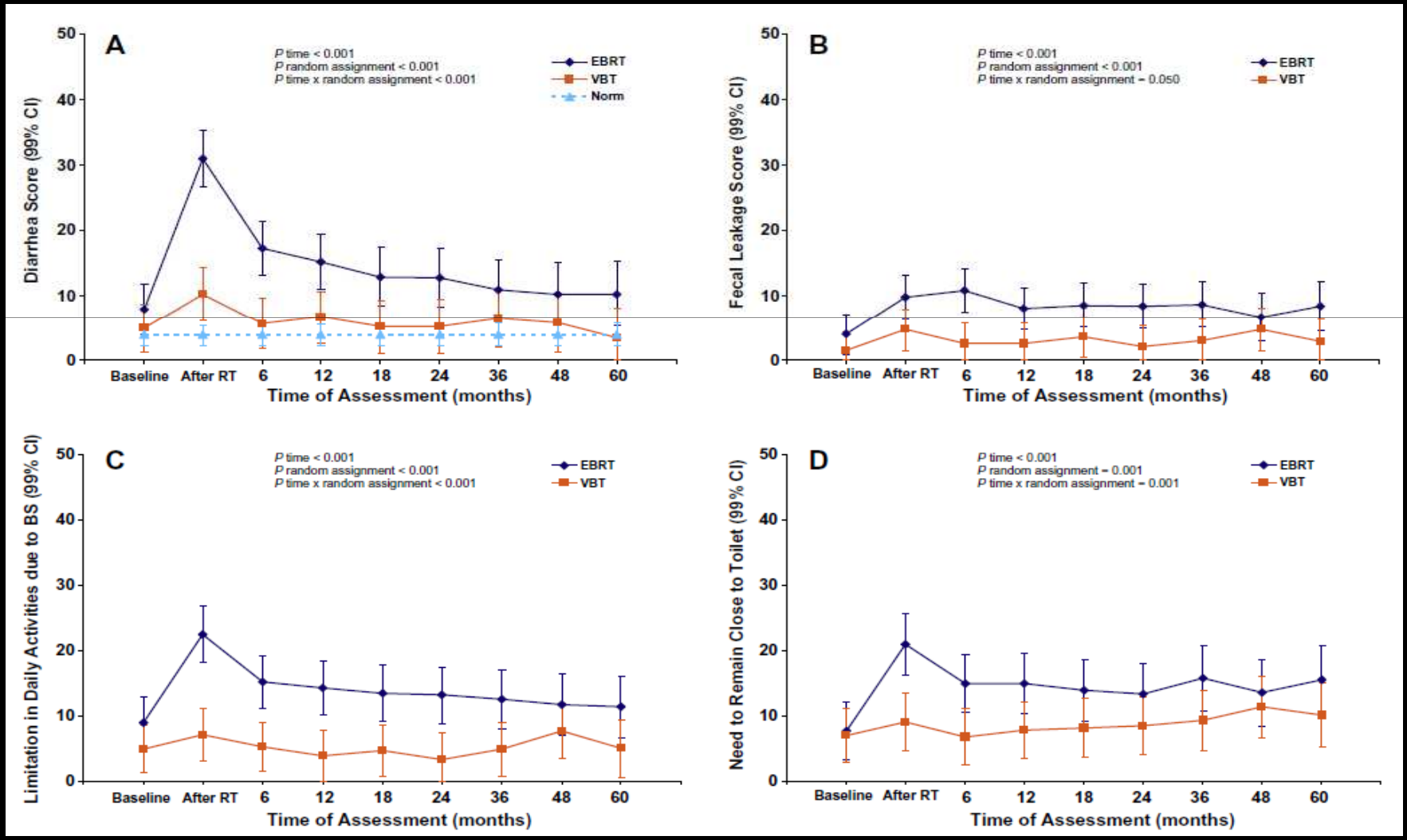
PORTEC 2 – results

Median follow-up 45 months

	5 YEAR ACTUARIAL RATES	
	EBRT	VBT
	(n=214)	(n=213)
Vaginal relapse	1.8%	1.6%
Pelvic relapse	2.1%	5.1%
1st site relapse		
Vagina	1.1%	0.9%
Pelvis	0.5%	1.5%
Distant	5.7%	8.3%

Five-year quality of life of endometrial cancer patients treated in the randomised Post Operative Radiation Therapy in Endometrial Cancer (PORTEC-2) trial and comparison with norm data ☆

EUROPEAN JOURNAL OF CANCER 48 (2012) 1638–1648



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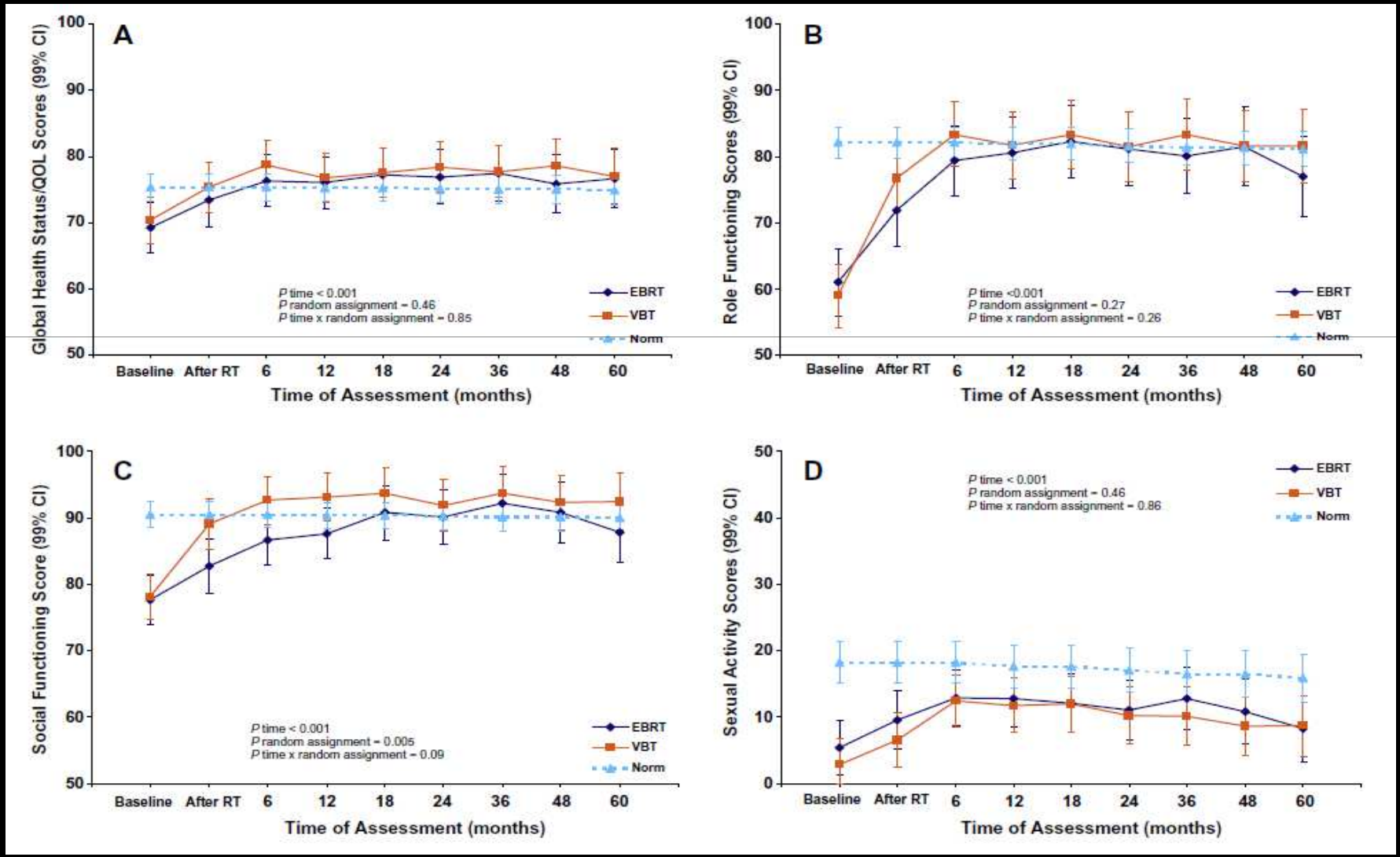


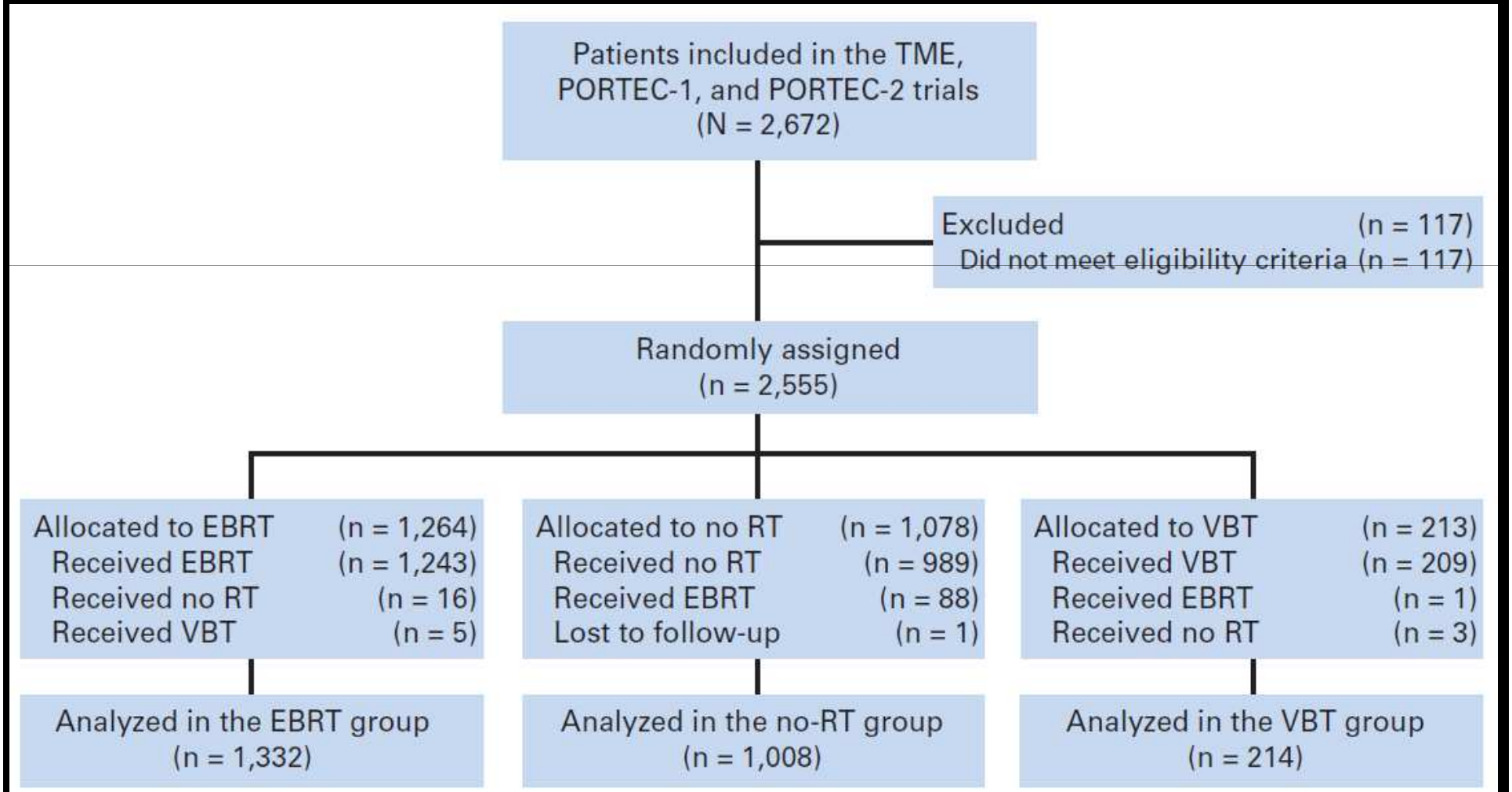
Conclusions of PORTEC-2

- No difference in OS or DFS
- Results of EBRT arm comparable to PORTEC-1 (and ASTEC and GOG-99)
- Brachytherapy effective in preventing vaginal relapse
- More pelvic relapse after VBT but usually associated with distant relapse
- Quality of life improved with VBT

No Increased Risk of Second Cancer After Radiotherapy in Patients Treated for Rectal or Endometrial Cancer in the Randomized TME, PORTEC-1, and PORTEC-2 Trials

Lisette M. Wiltink, Remi A. Nout, Marta Fiocco, Elma Meershoek-Klein Kranenbarg, Ina M. Jürgenliemk-Schulz, Jan J. Jobsen, Iris D. Nagtegaal, Harm J.T. Rutten, Cornelis J.H. van de Velde, Carien L. Creutzberg, and Corrie A.M. Marijnen

J Clin Oncol 32. © 2014



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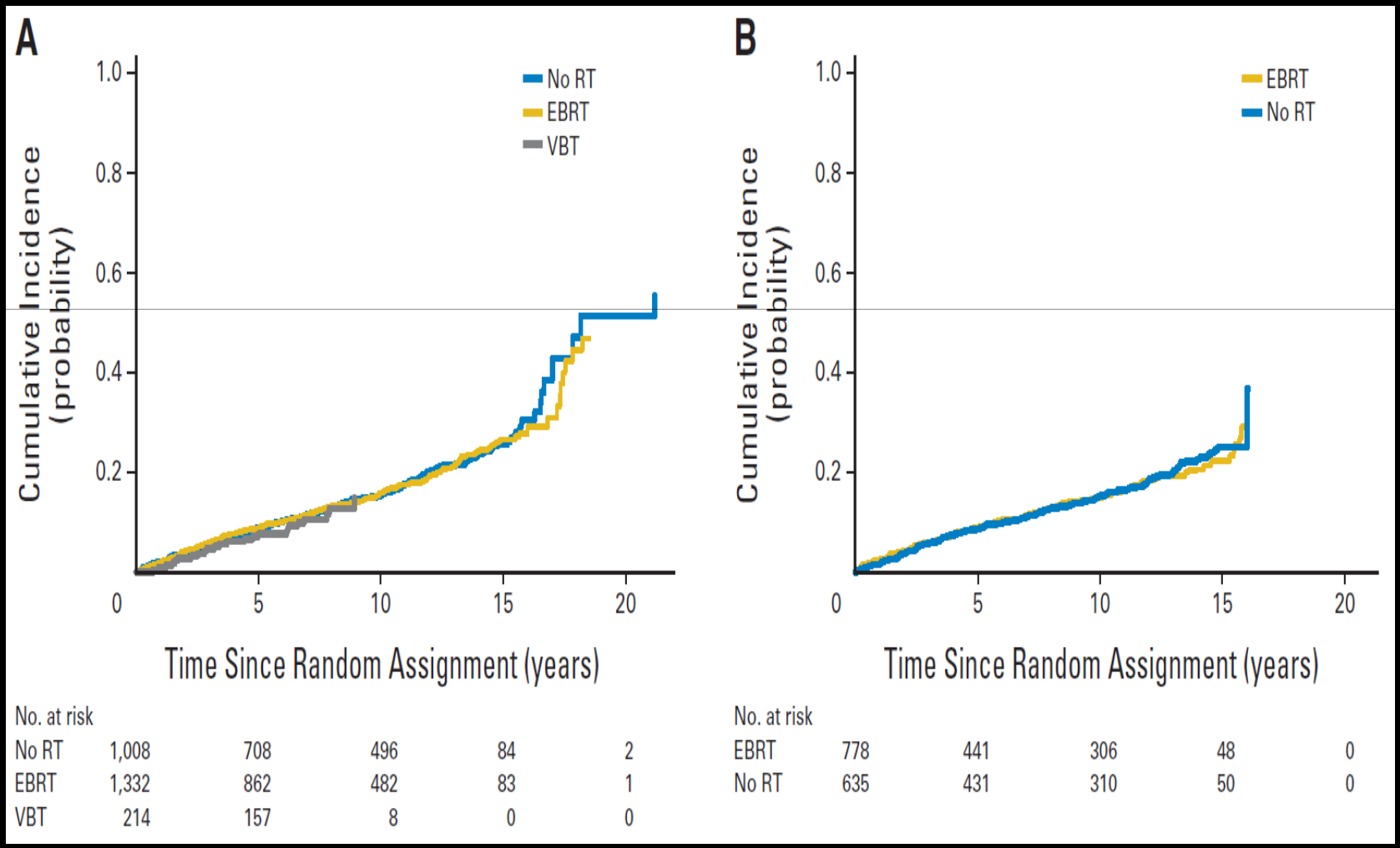


RECURRENT ENDOMETRIAL CANCER AFTER SURGERY ALONE: RESULTS OF SALVAGE RADIOTHERAPY

BARBARA JERECZEK-FOSSA, M.D., PH.D.,*† ANDRZEJ BADZIO, M.D.,* AND JACEK JASSEM, M.D., PH.D.*

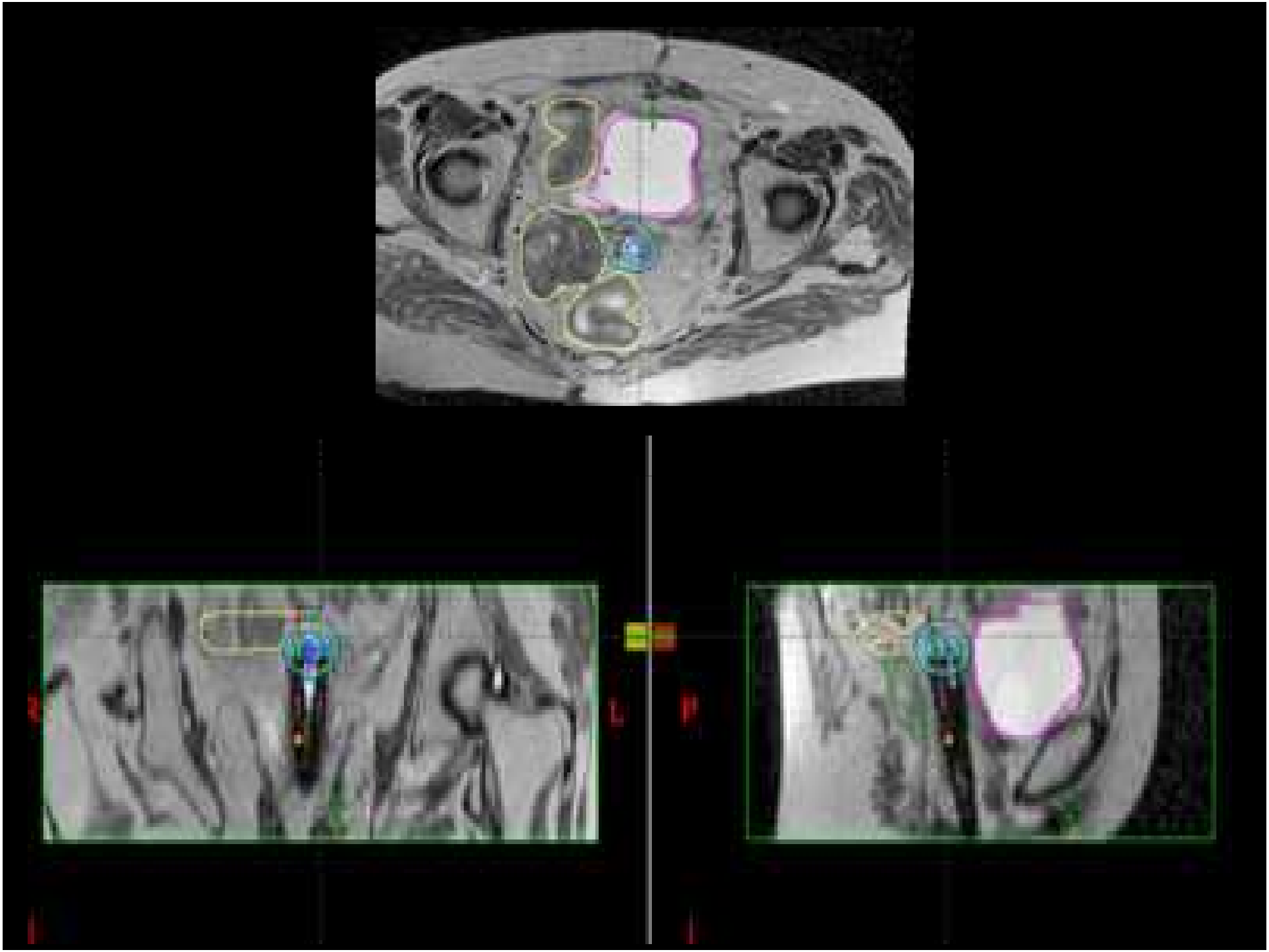
1975-1995: 725 patients endometrial cancer
NO post op RT

73 pelvic relapses

I	Limited to vaginal mucosa	5 (7%)
II	Extravaginal extension without pelvic wall involvement	43 (59%)
IIa	Subvaginal infiltration	24 (33%)
IIb	Lateral parametrial involvement	19 (26%)
III	Pelvic wall involvement	25 (34%)

29 patients vaginal relapse
66% at apex
33% distal suburethral

FIGO I	56 (77%)
IA	3
IB	11
IC	10
Ix—unknown	32
II	4 (5%)
IIA	1
IIB	2
IIx—unknown	1
III	9 (13%)
IIIA	6
IIIB	1
IIIC	1
IIIx—unknown	1
IV	4 (5%)
IVA	2
IVB	2
Myometrial infiltration (MI)	
MI = 0	3 (4%)
MI ≤ ½	9 (12%)
MI > ½	21 (29%)
MIx—unknown	40 (55%)
Grade	
G1	14 (19%)
G2	12 (17%)
G3	20 (27%)
Gx—unknown	27 (37%)
Histotype	
Adenocarcinoma	41 (56%)
Papillary adenocarcinoma	17 (23%)
Adenosquamous carcinoma	10 (14%)
Adenoacanthoma	2 (3%)
Solid/anaplastic carcinoma	2 (3%)
Clear cell carcinoma	1 (1%)



Reirradiation using high-dose-rate brachytherapy in recurrent carcinoma of uterine cervix

Brachytherapy 13 (2014) 548–553

Umesh Mahantshetty*, Nikhil Kalyani, Reena Engineer, Supriya Chopra, Swamidas Jamema, Yogesh Ghadi, Deepak Deshpande, Shyamkishore Shrivastava

Department of Radiation Oncology and Medical Physics, Tata Memorial Centre, Mumbai, India

30 patients; central recurrence after previous RT post TAH

Reirradiation details and clinical outcome	
Time gap between two irradiation (mo)	
Median	25
Interquartile range	13–49
Brachytherapy doses (Gy, EQD2)	
Mean	41.2
Median	42
Interquartile range	37–46
Brachytherapy doses (EQD2; [*n* (%)])	
<40 Gy	14 (46)
>40 Gy	16 (54%)
Response [*n* (%)]	
Complete response	23 (76)
Partial response	5 (18)
Stable disease	1 (3)
Progressive disease	1 (3)
Status at last followup [*n* (%)]	
Disease free	13 (43)
Loco-regional recurrence	3 (10)
Local recurrence	10 (33)
Local recurrence and distant metastasis	2 (7)
Distant metastasis	2 (7)

Toward four-dimensional image-guided adaptive brachytherapy in locally recurrent endometrial cancer

Brachytherapy 13 (2014) 554–561

Lars Fokdal[1,*], Gitte Ørtoft[2], Estrid S. Hansen[3], Lisbeth Røhl[4], Erik Morre Pedersen[4], Kari Tanderup[1,5], Jacob Christian Lindegaard[1]

[1]*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark*

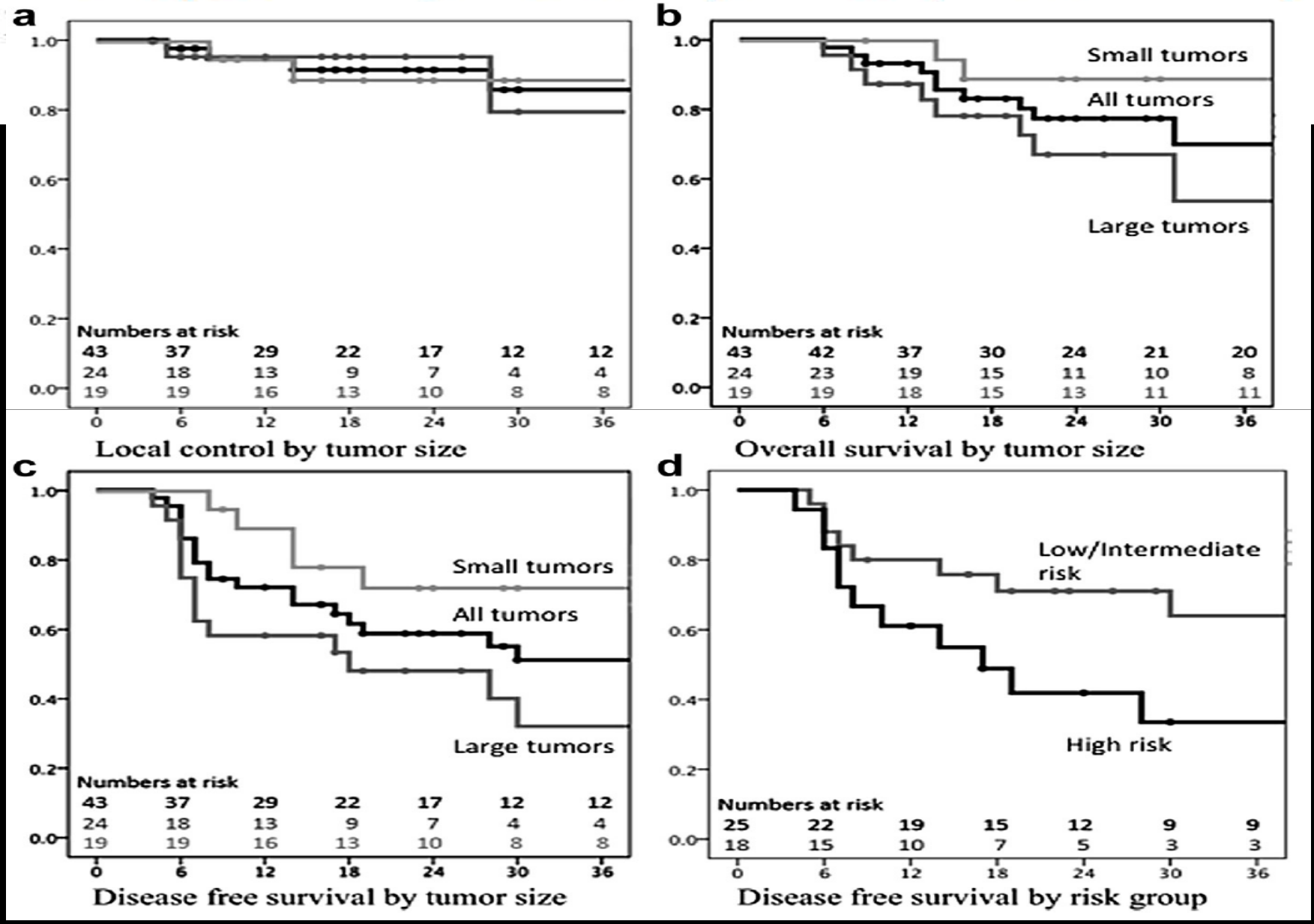
43 patients post TAH: no RT

Location of vaginal recurrence, %	
Upper 1/3	72
Middle 1/3	7
Lower 1/3	21
Parametrial involvement at recurrence, %	
No	69
Proximal	19
Distal/pelvic wall	12
Hydronephrosis at recurrence, %	
No	95
Yes	5
Bladder or rectal involvement at recurrence, %	
No	93
Yes	7

45-50Gy EBRT ……..ICBT 19; ISBT 24 ……10-17.5Gy PDR

Toward four-dimensional image-guided adaptive brachytherapy in locally recurrent endometrial cancer

Brachytherapy 13 (2014) 554–561



Vaginal vault brachytherapy for endometrial cancer

- Alone:
  - Intermediate risk patients
- With external beam:
  - High(er) risk patients with cervical involvement
    - Stage IB G3
    - Stage II/III
    - LVSI

    ….? Role chemorads….PORTEC 3
- Local recurrence: effective salvage

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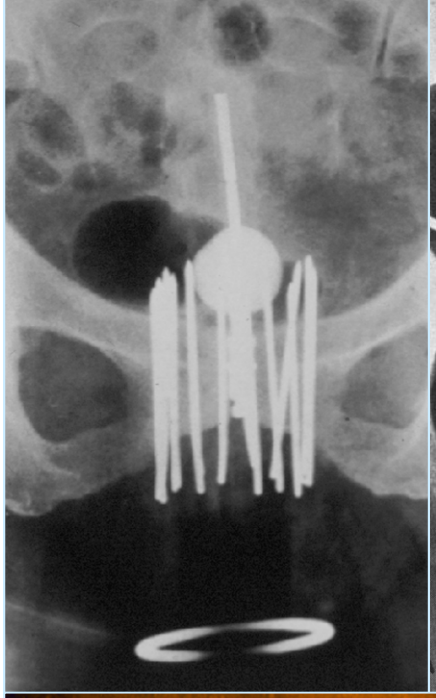
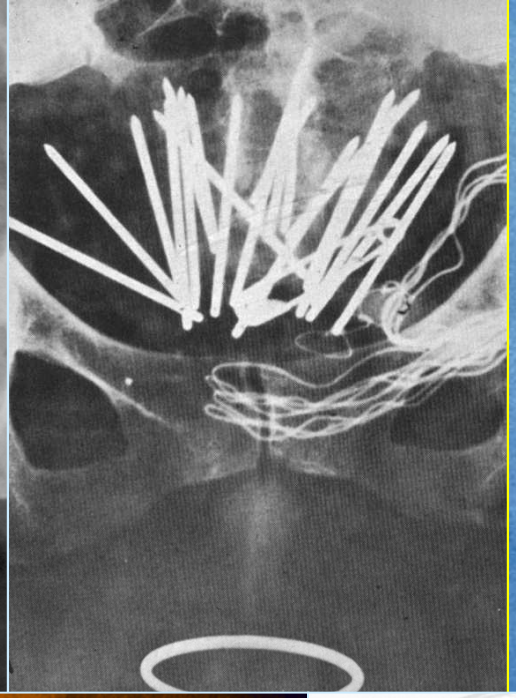
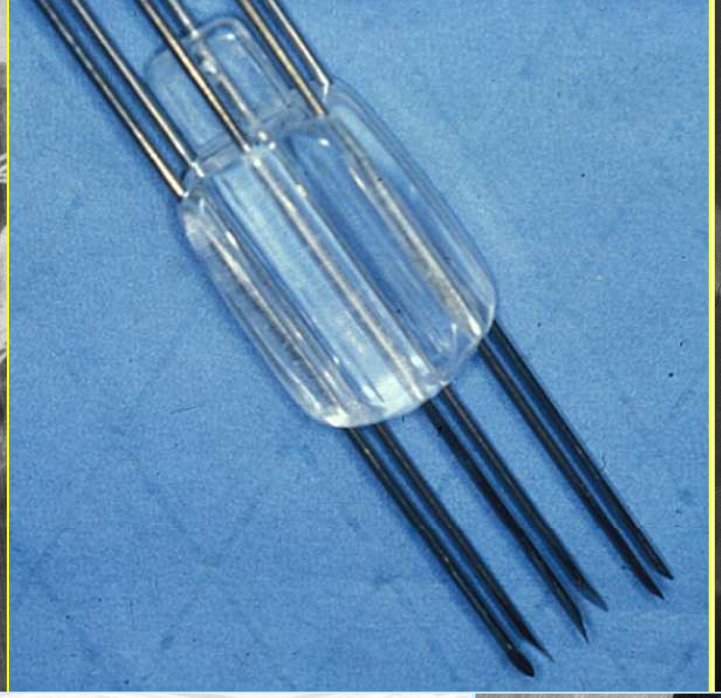
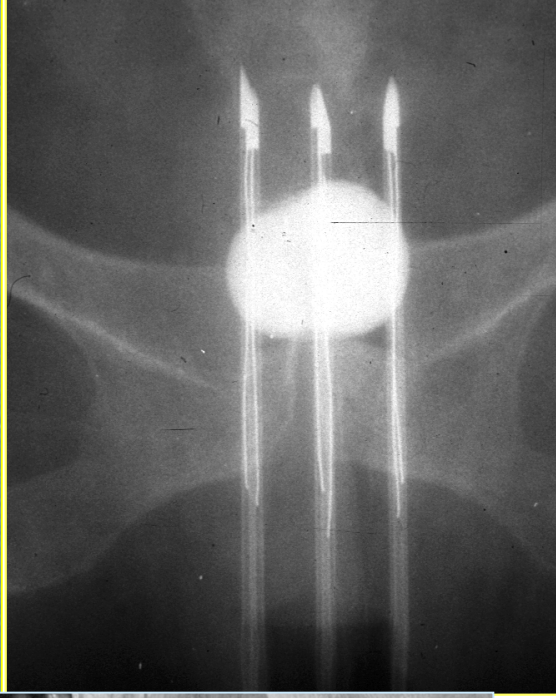
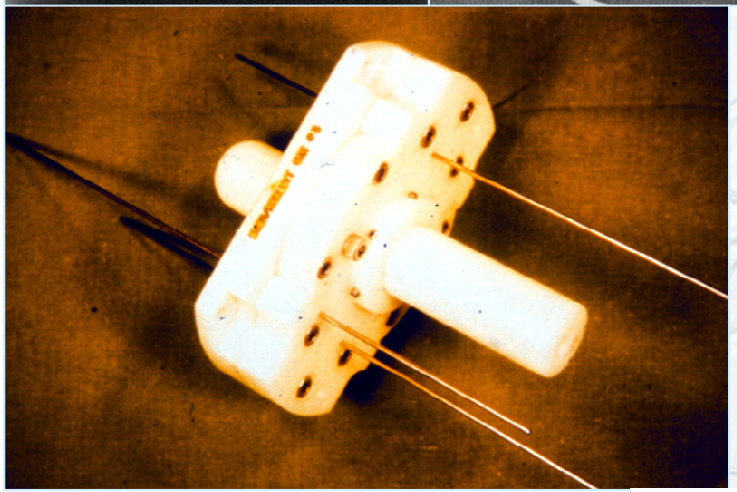
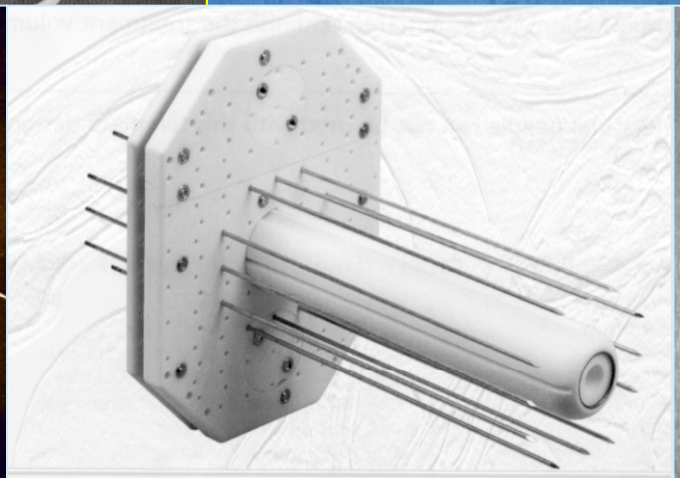
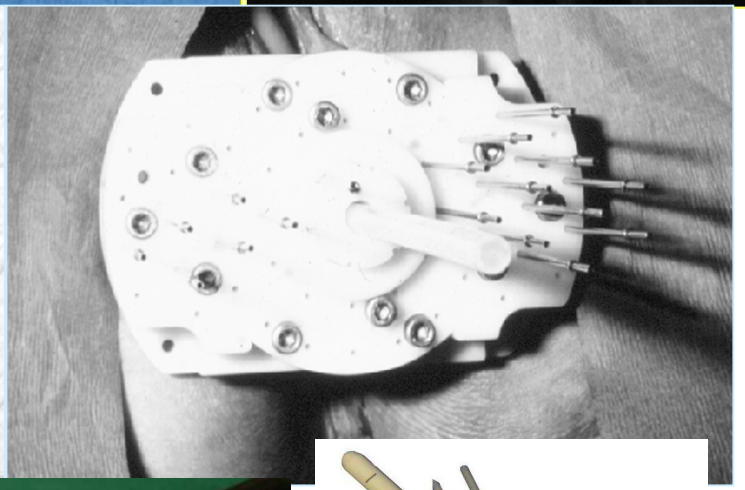
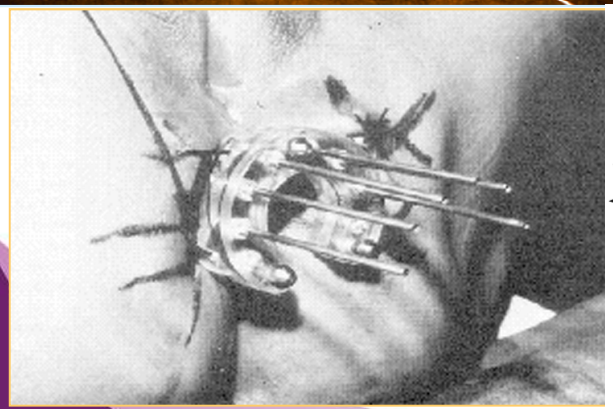
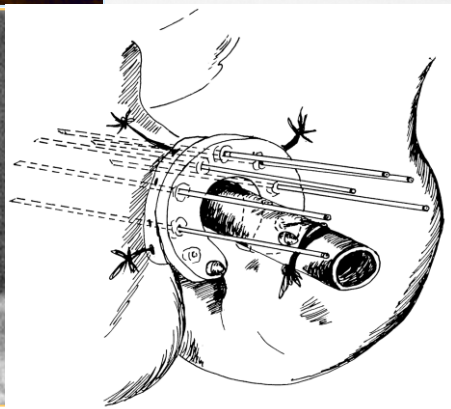
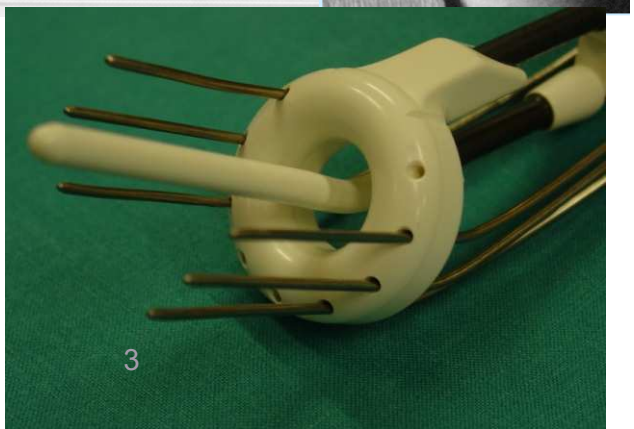
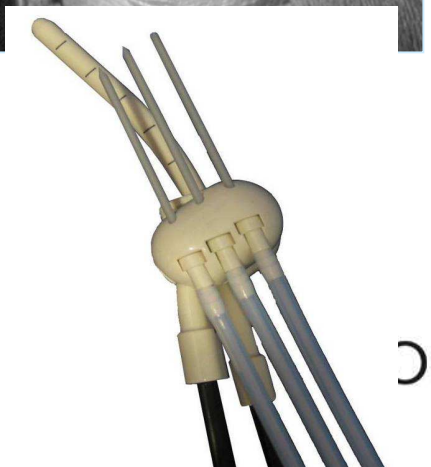
WWW.ESTRO.ORG/SCHOOL

Interstitial Brachytherapy Techniques

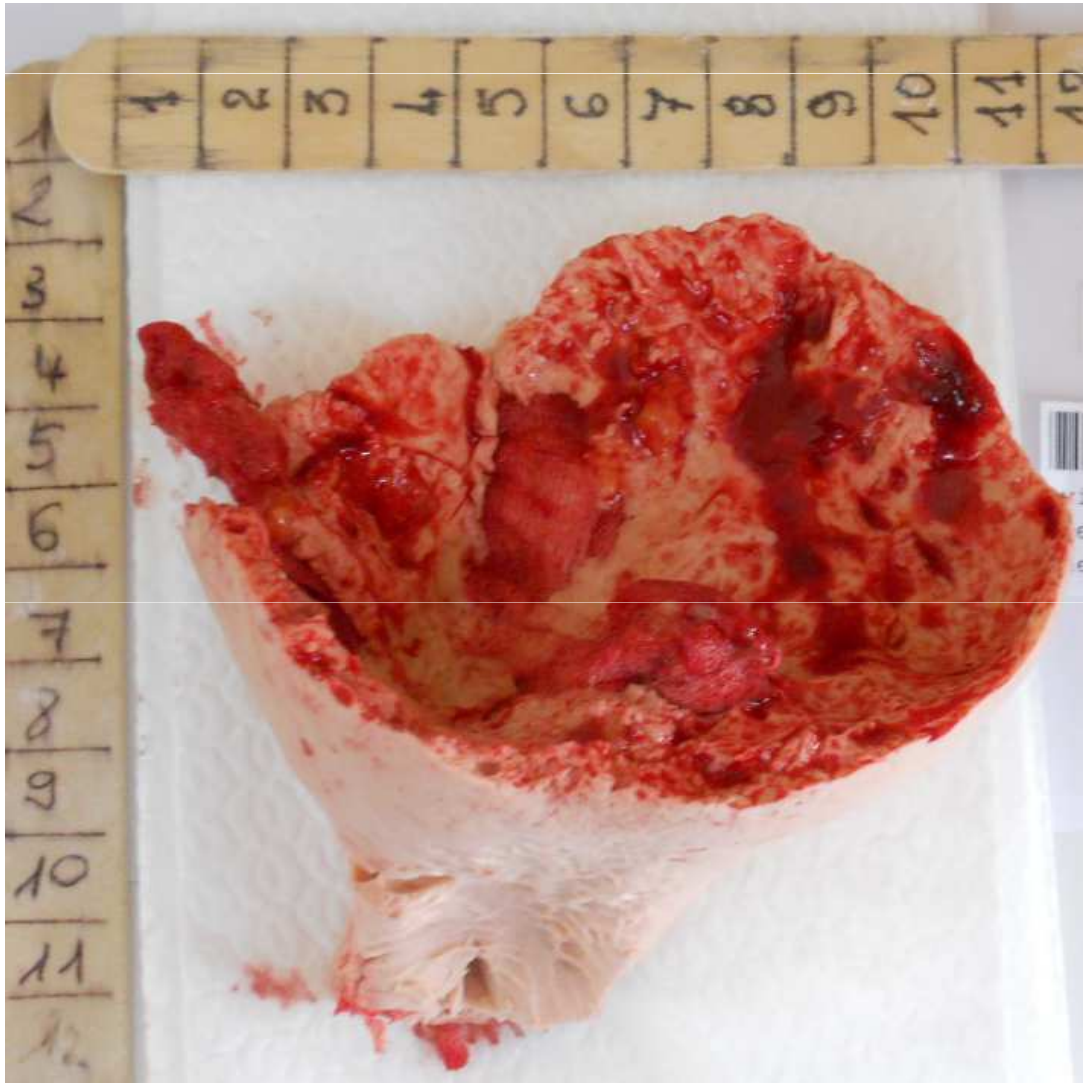
Gynecological tumors

Renaud Mazeron

Gustave Roussy

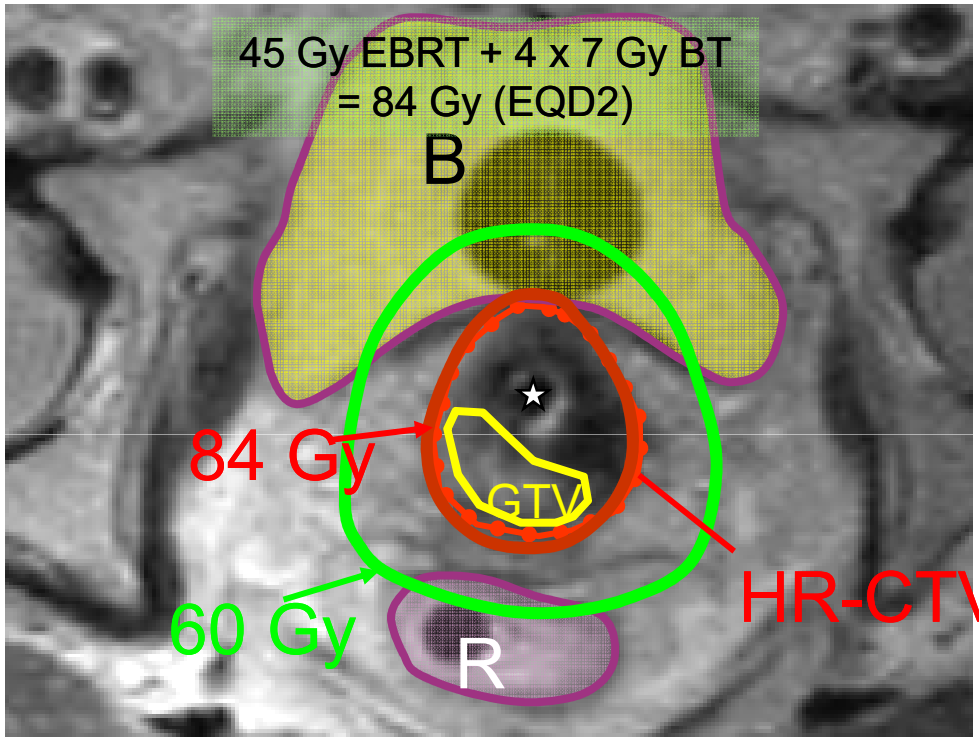
Cervical carcinomas



Brachytherapy

The second component of definitive cervical cancer treatment

integration of EBRT and Brachytherapy



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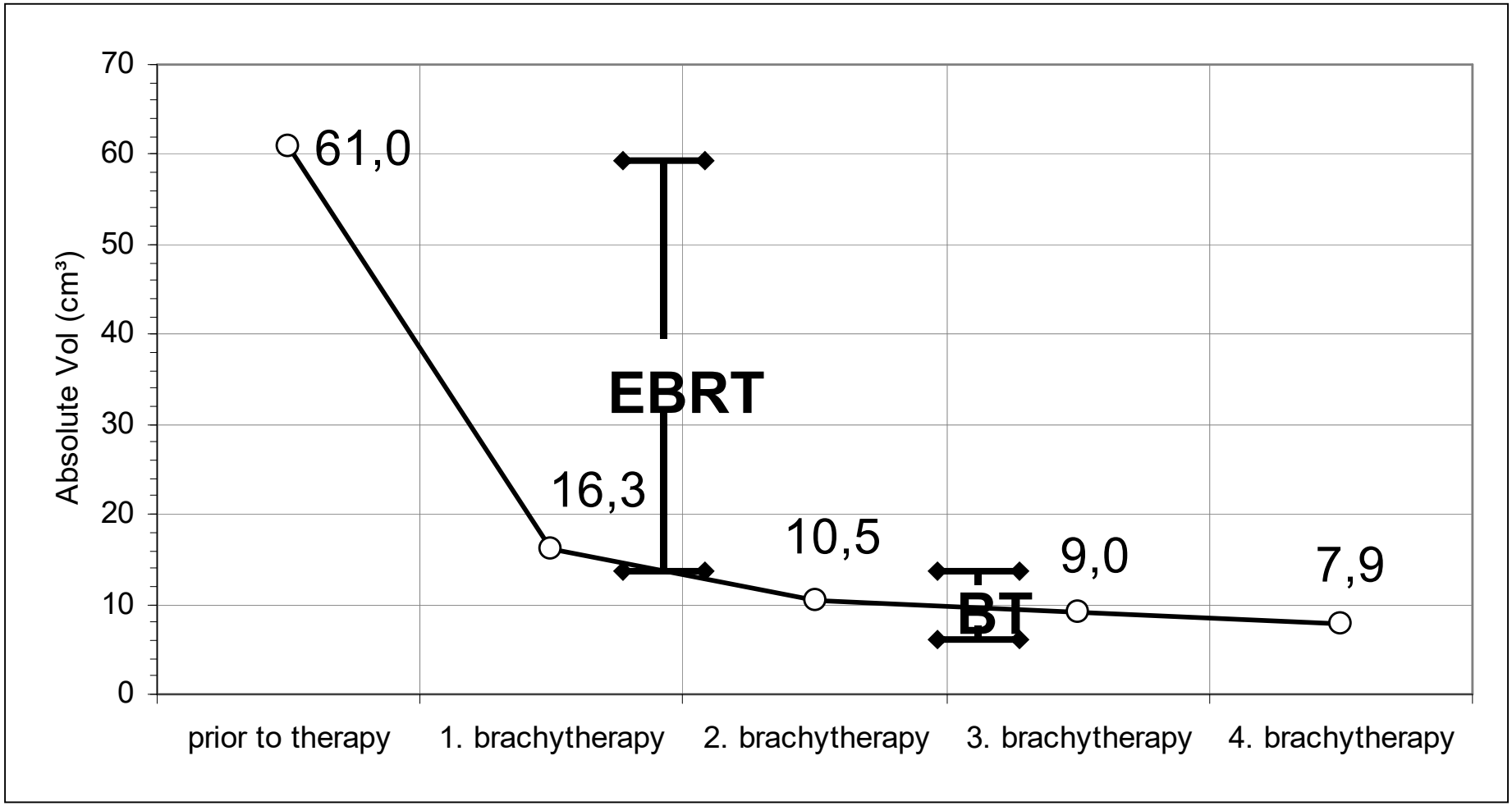
EBRT: tumor regression 75%
Brachytherapy: tumor regression 10%



Dimopoulos et al. Strahlenther Onkol 2009

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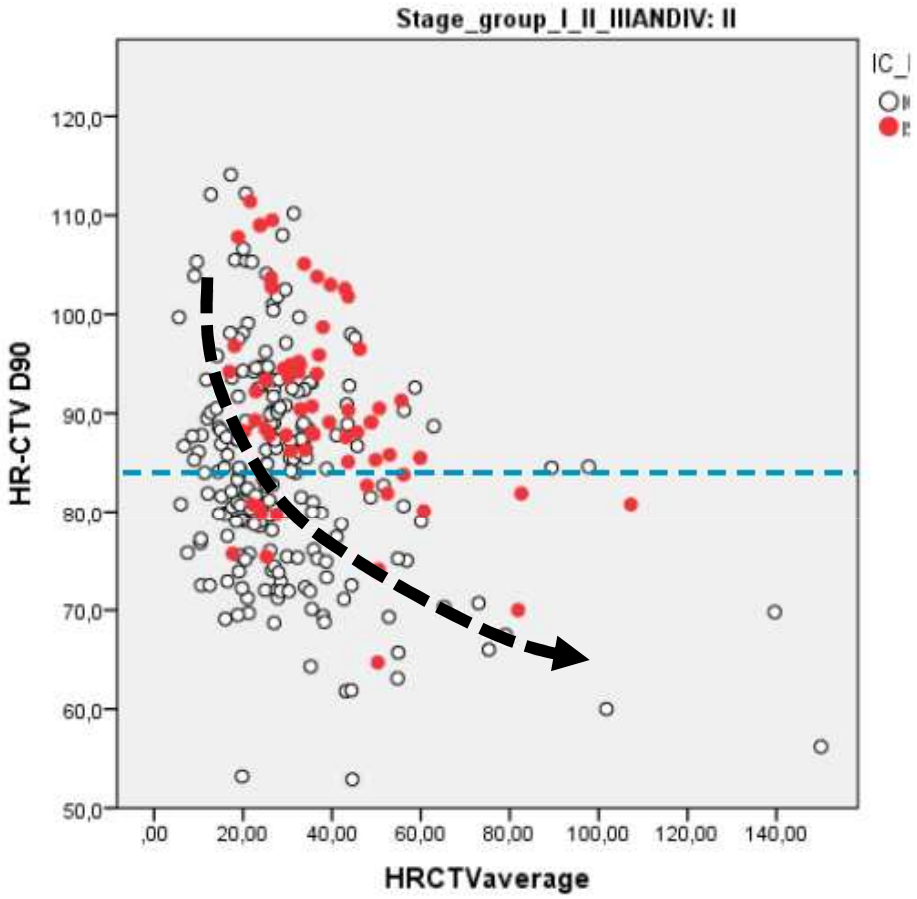
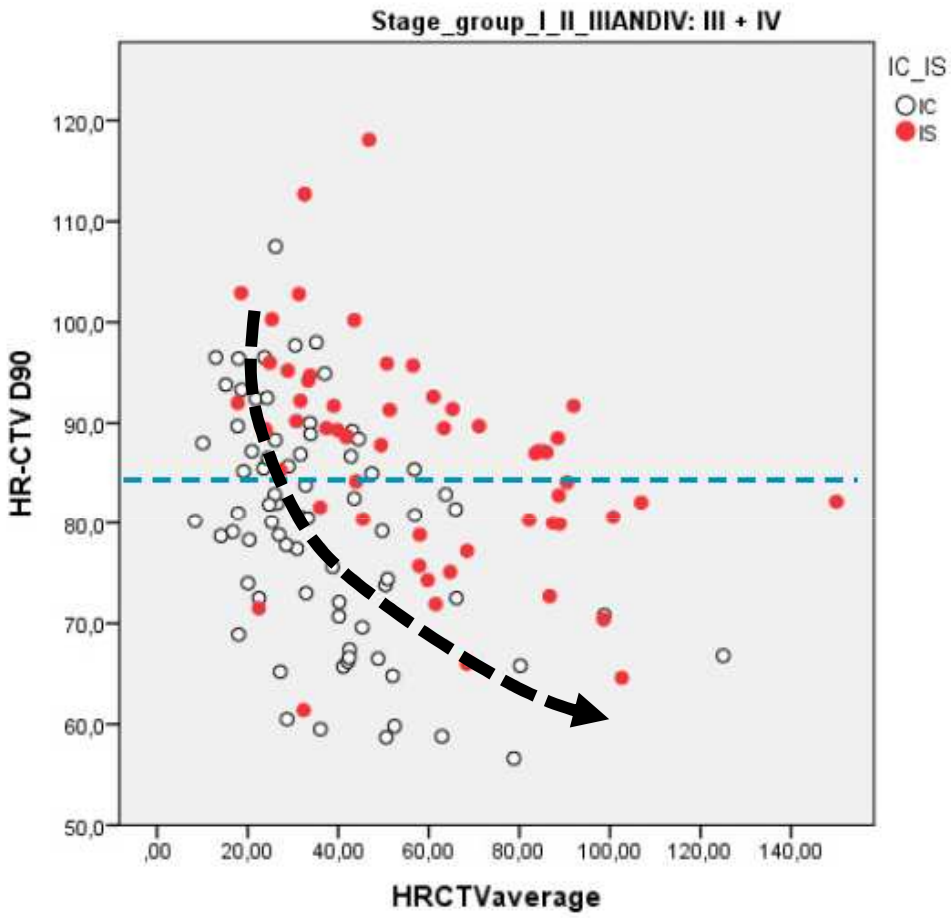
Importance of needles

Stage II



Stage III+IV



K Tanderup

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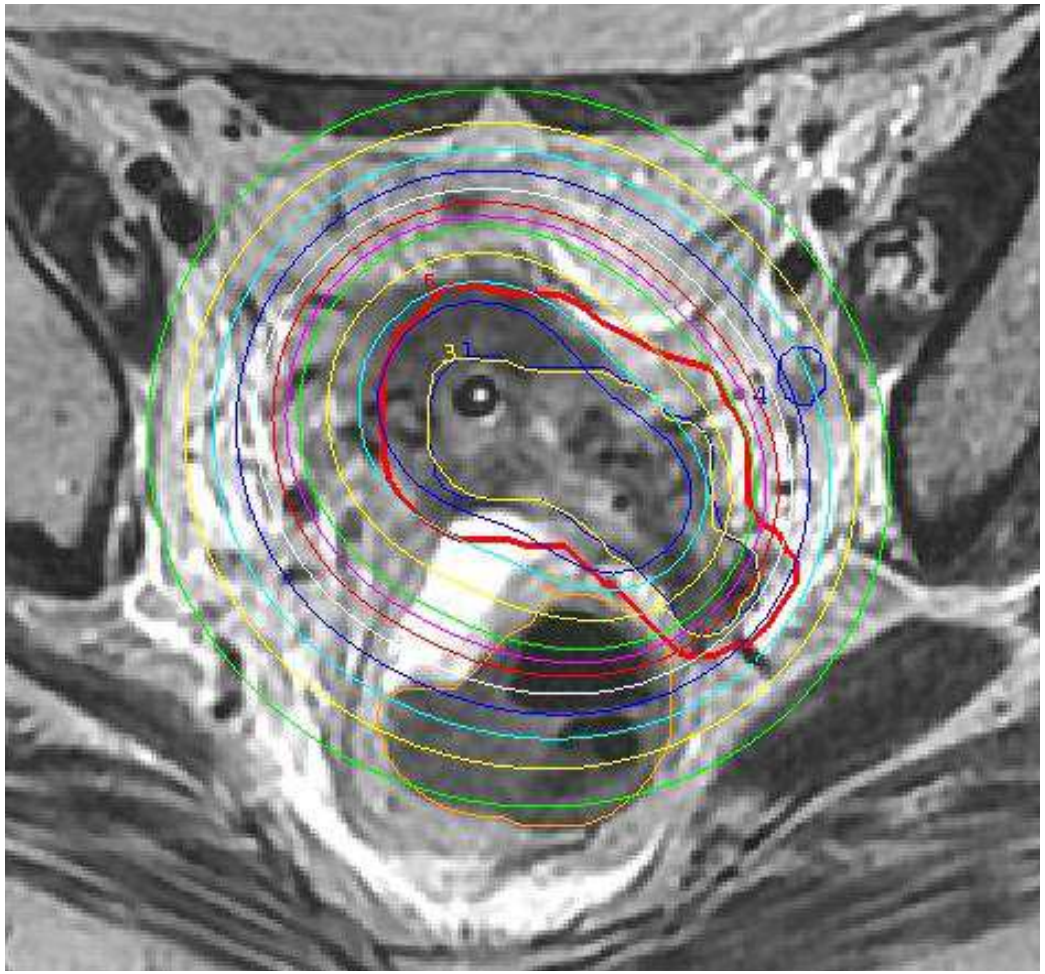
Interstitial Brachytherapy

- HR-CTV not properly covered
- ≈ 25-30% of the cases
- HR-CTV ≥ 30 cm3
- Decrease the irradiated volume
- Improve the conformity index



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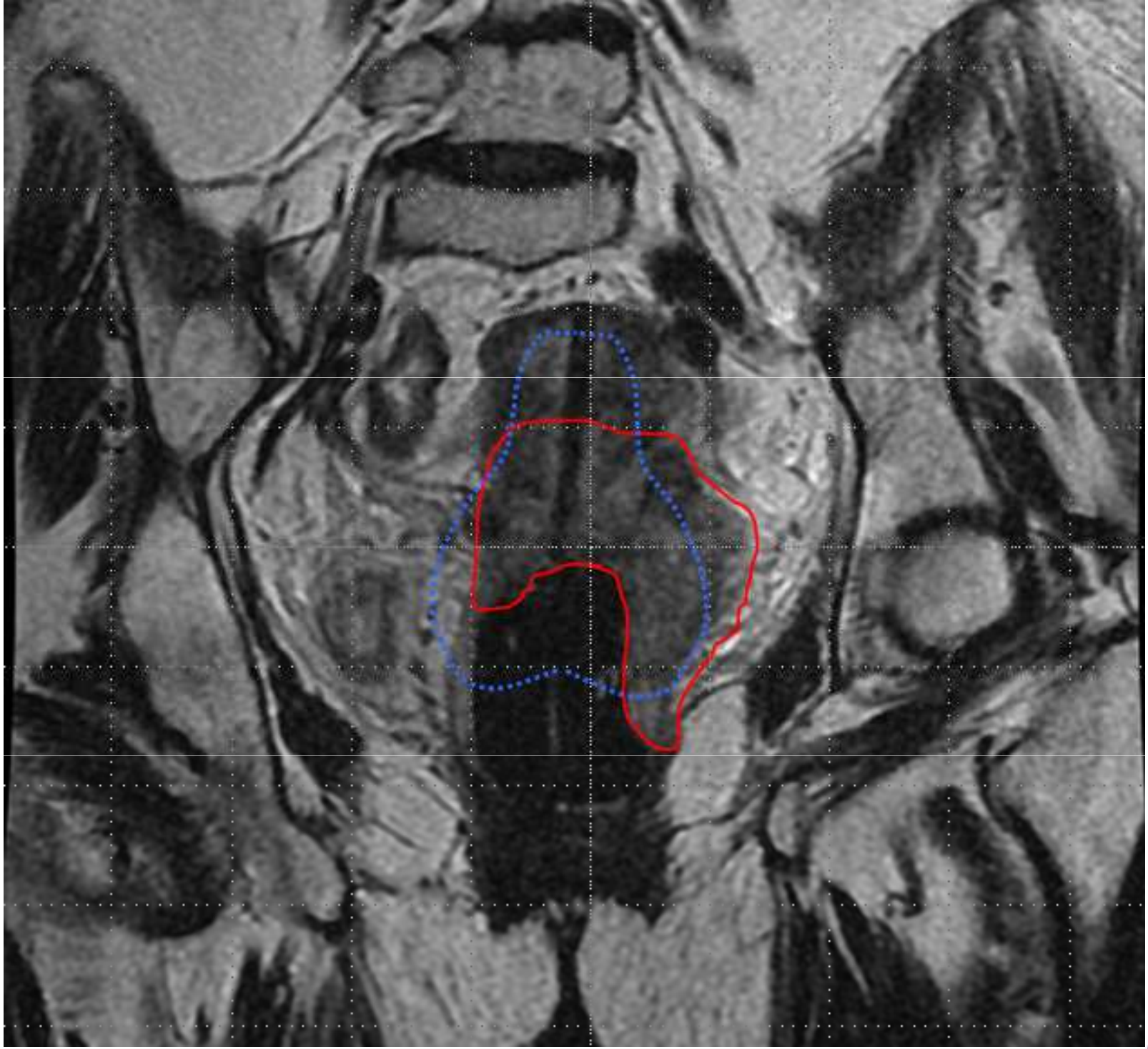

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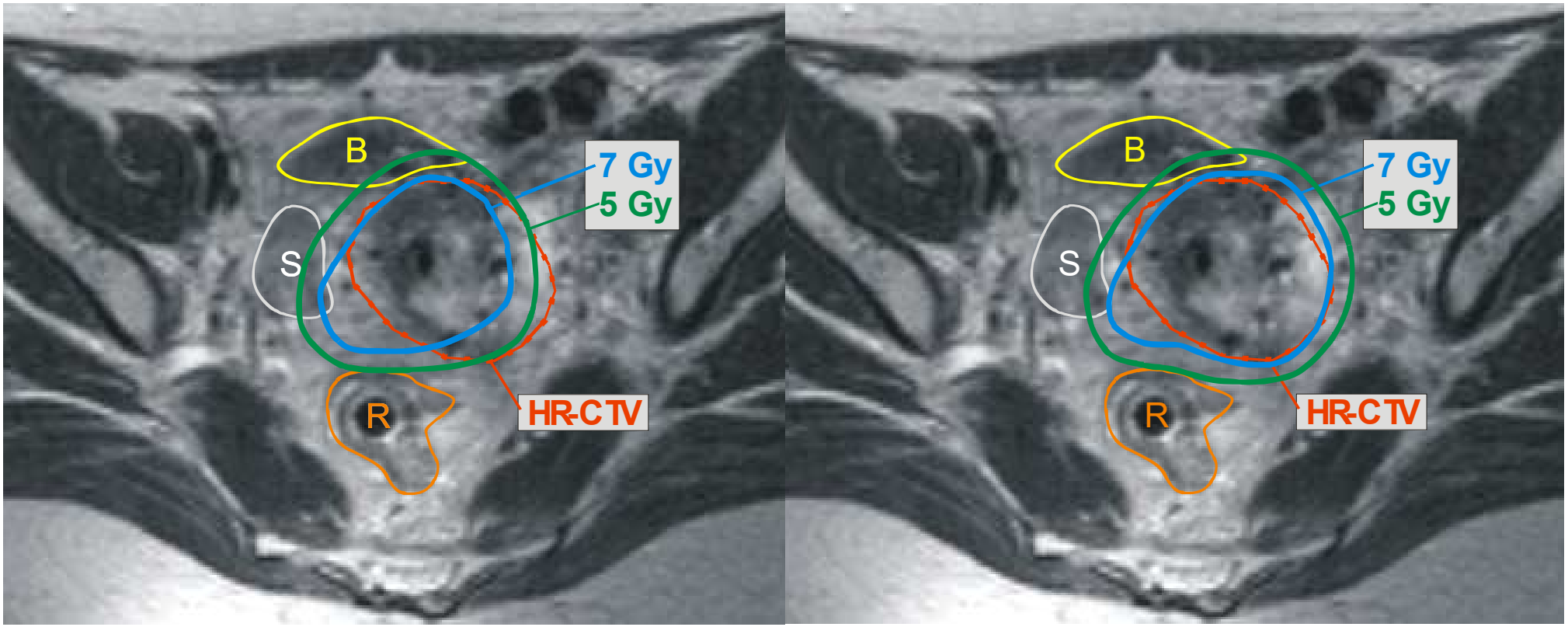
Clinical example - interstitial treatment

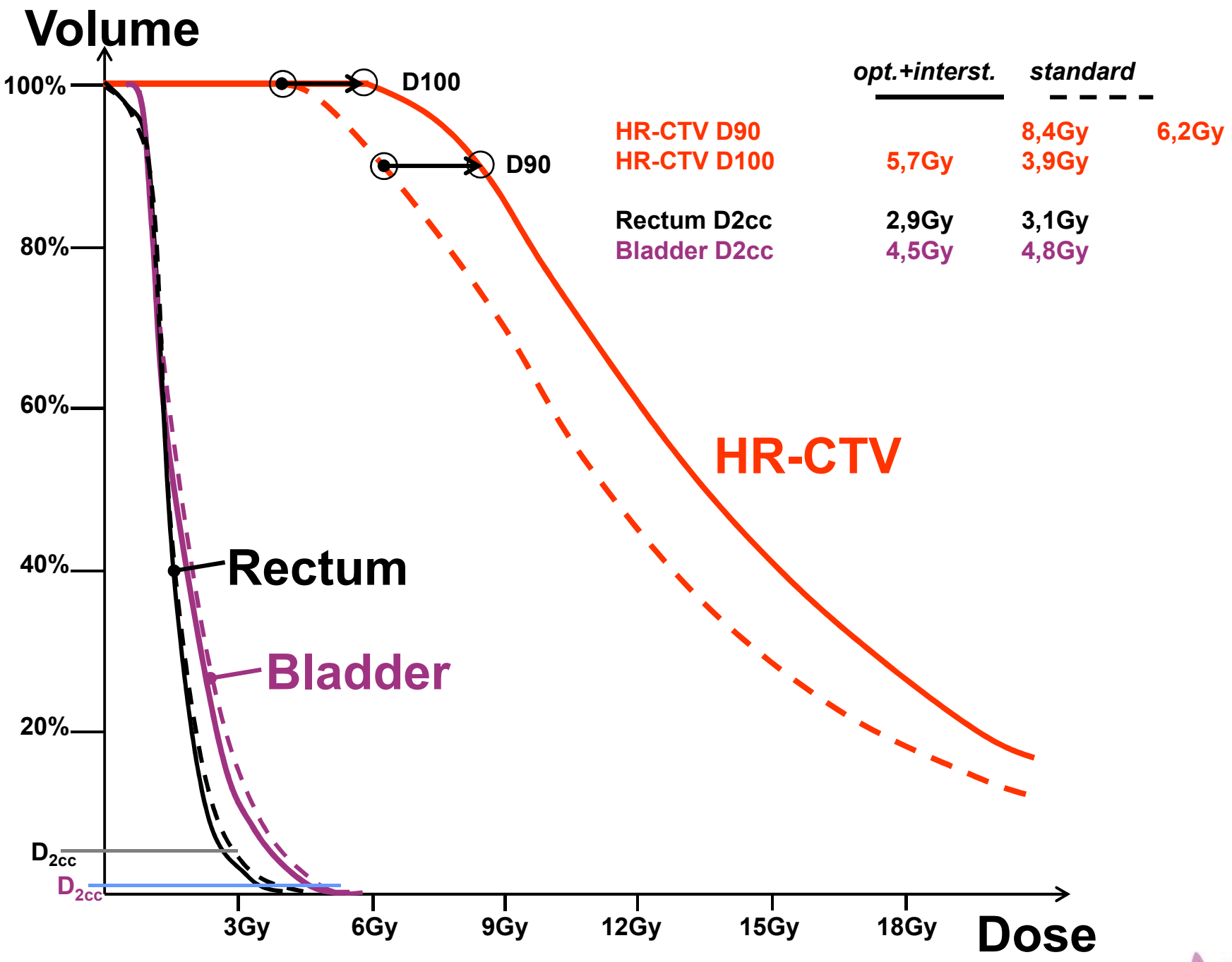
MRI based treatment planning plus novel application technique

standard treatment plan **optimized interstitial**



intracavitary plus needles left parametrium

Improved placement control - Low number of needles – Combined with MRI based treatment planning



	opt.+interst.	standard	
HR-CTV D90		8,4Gy	6,2Gy
HR-CTV D100	5,7Gy	3,9Gy	
Rectum D2cc	2,9Gy	3,1Gy	
Bladder D2cc	4,5Gy	4,8Gy	

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Intracavitary techniques limitations with conventional applicators

- distal vaginal + parametrial extension
- para-vaginal tumor
- middle/distal parametrial tumor extension
- unfavourable topography/unfavourable relation to the applicator
- unfavourable topography of organs at risk

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INTERSTITIAL TECHNIQUES
AIMS IN LOCALLY ADVANCED DISEASE

- *accurate and reproducible placement of needles*
- *tailor positions of needles to the target*
- *tailor dose distribution to target and OAR*
  - *adequate target coverage*
  - *spare OAR*

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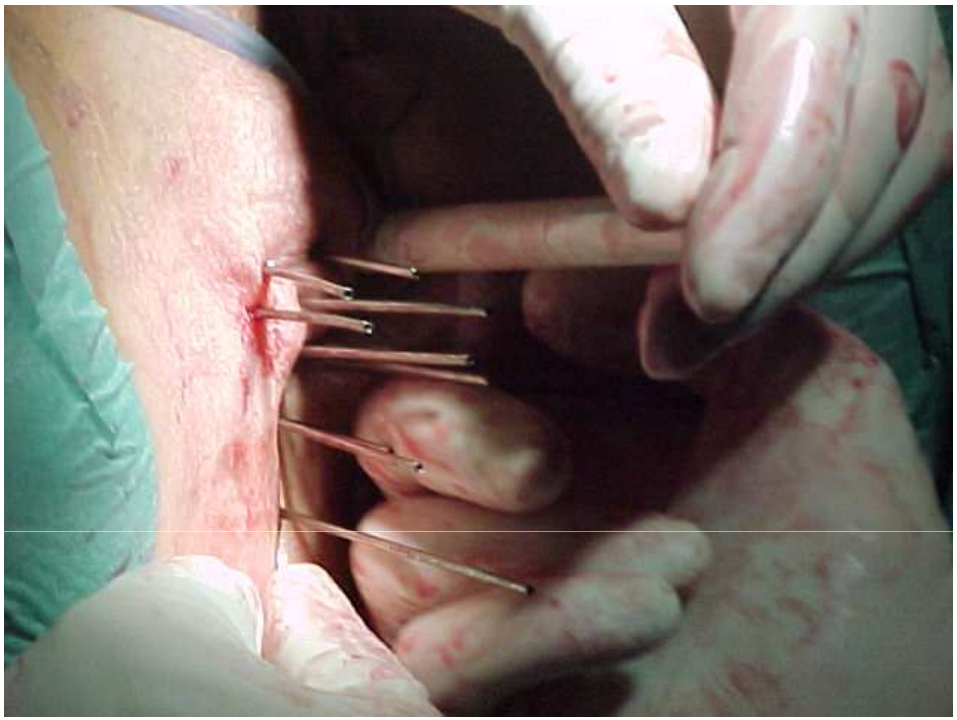
CLASSICAL INTERSTITIAL TECHNIQUES
FREEHAND PLACEMENT



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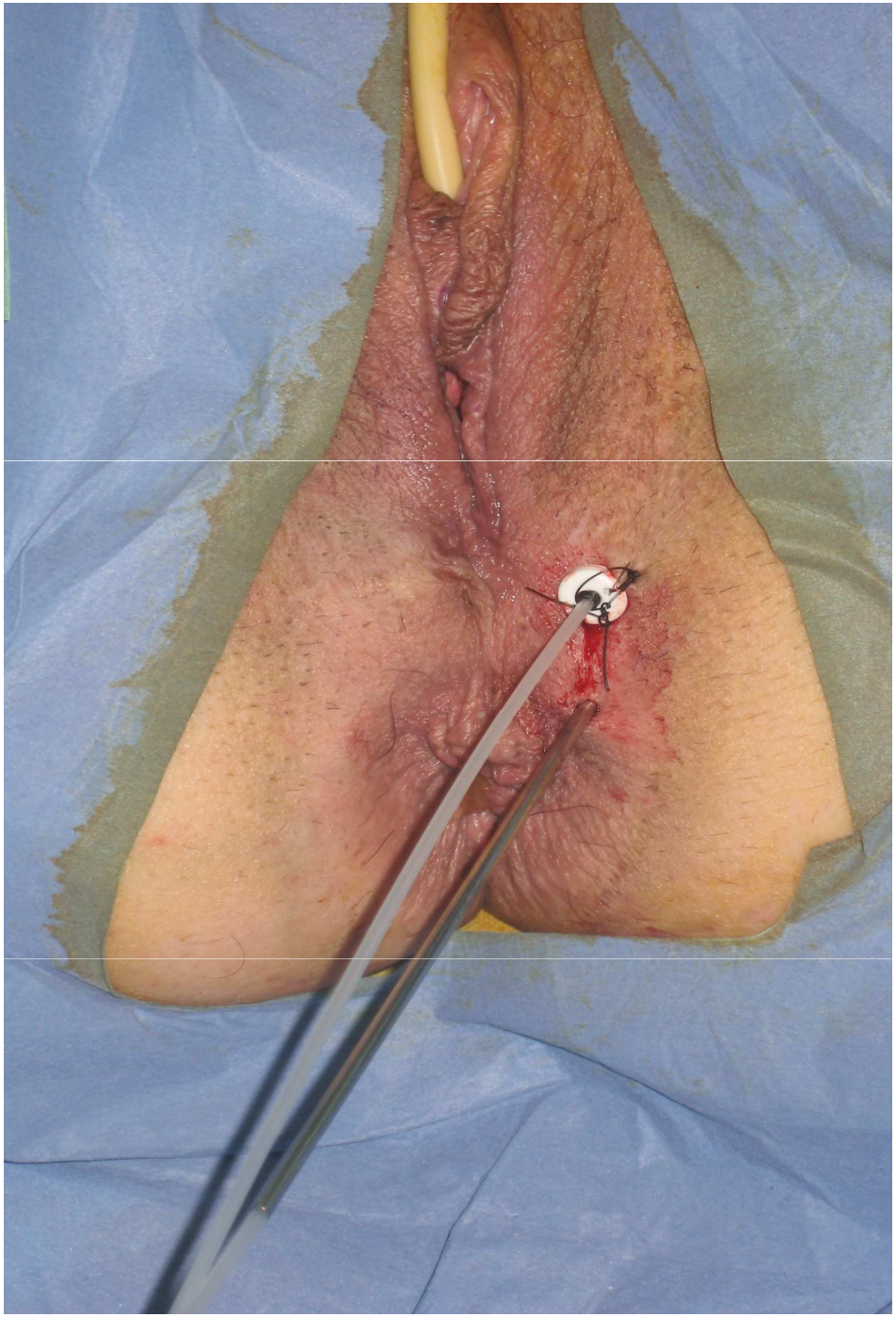
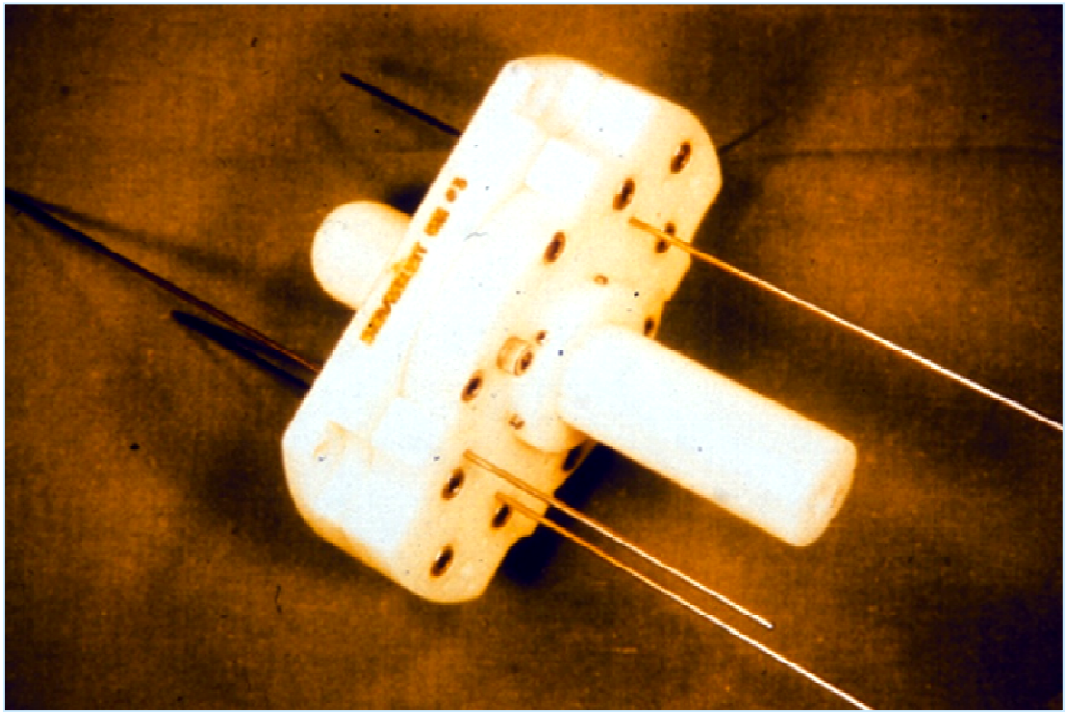
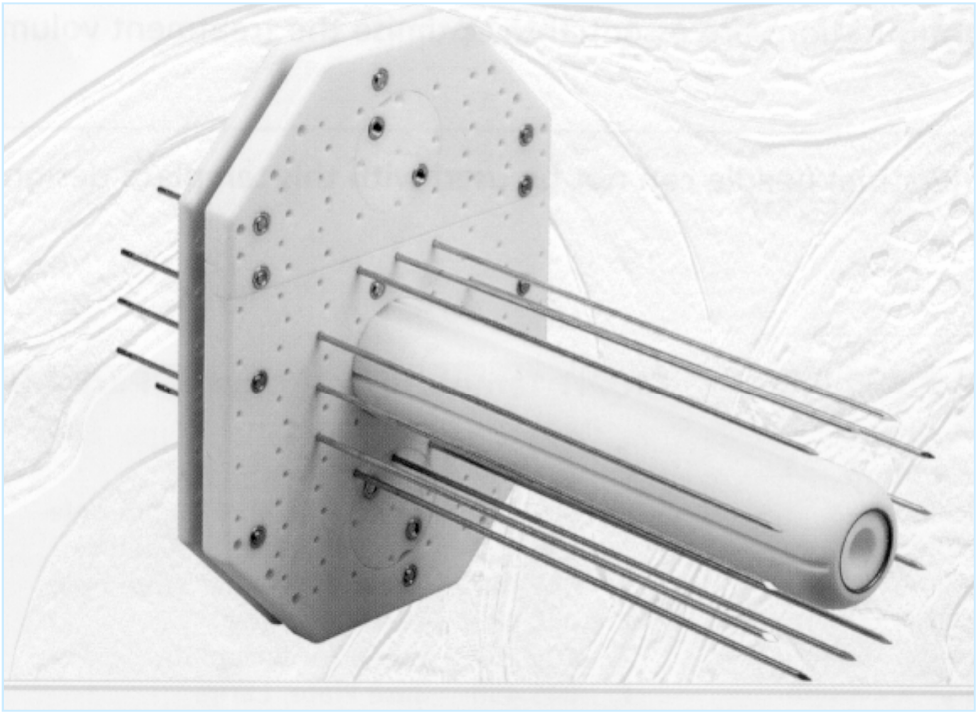


CLASSICAL INTERSTITIAL TECHNIQUES
PERINEAL TEMPLATES

SYED



MUPIT



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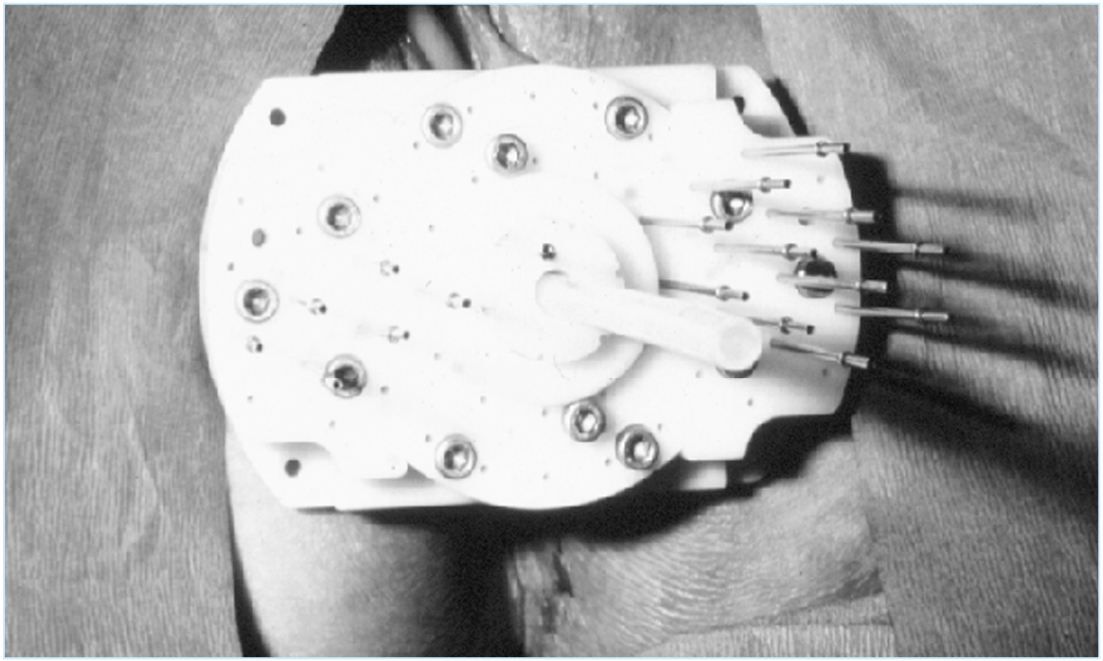
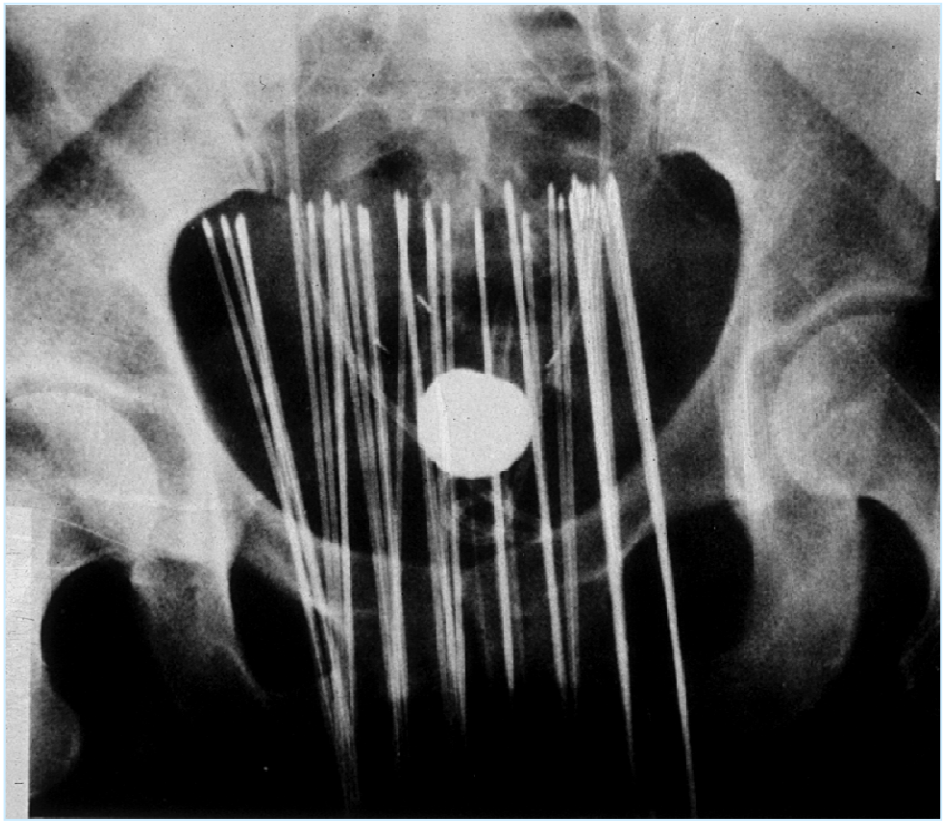
CLASSICAL INTERSTITIAL TECHNIQUES
PERINEAL TEMPLATES

SYED





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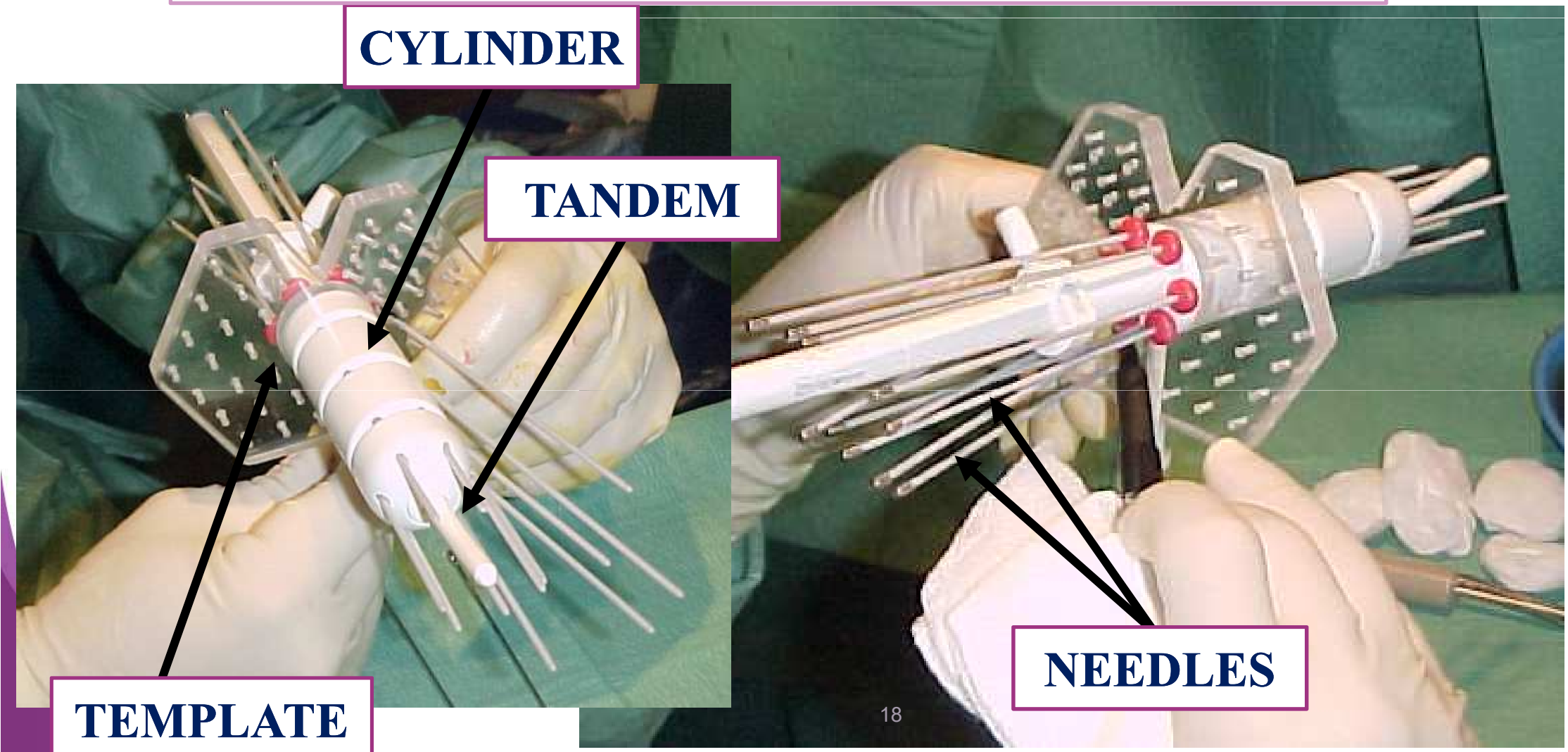
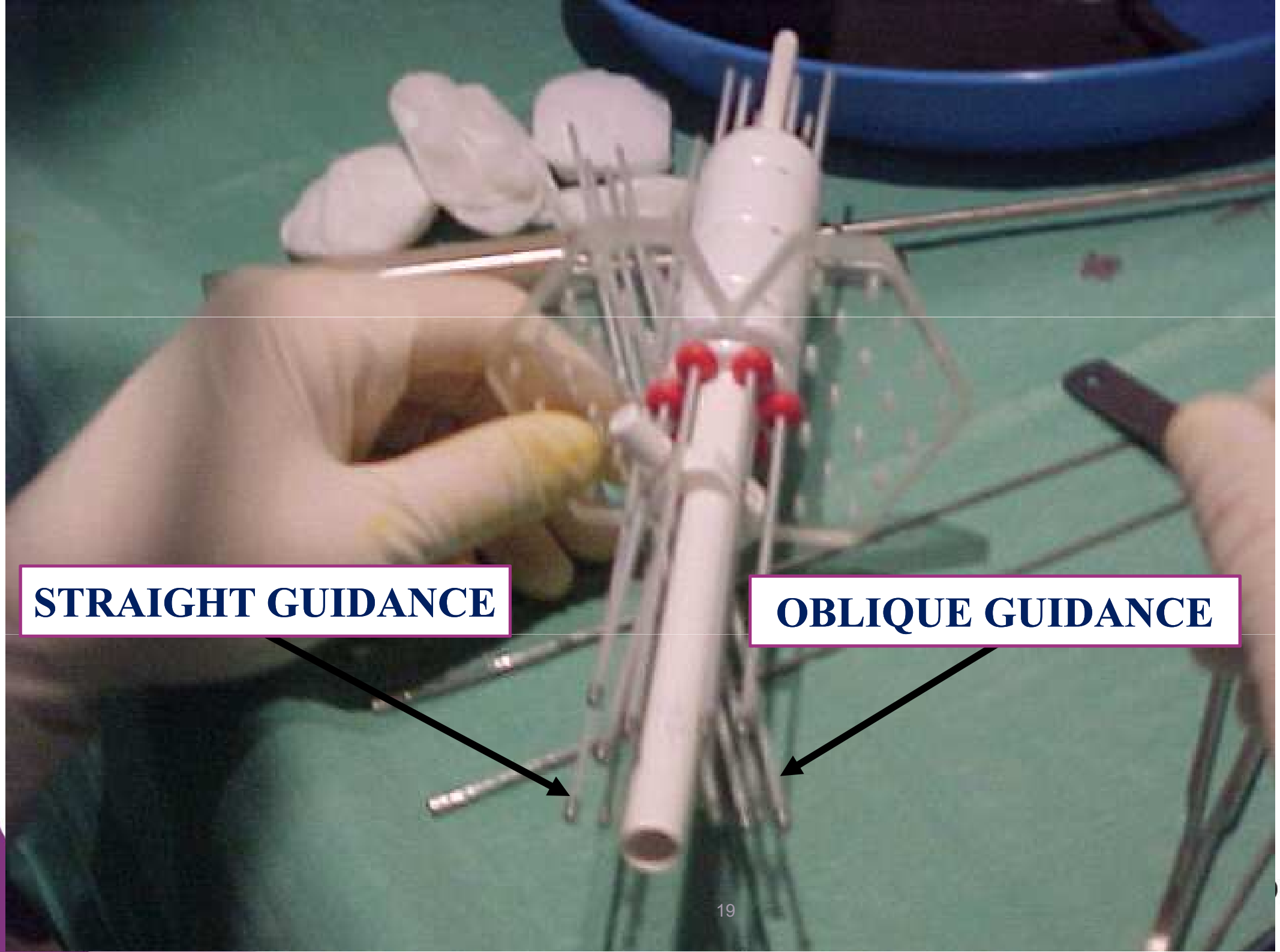
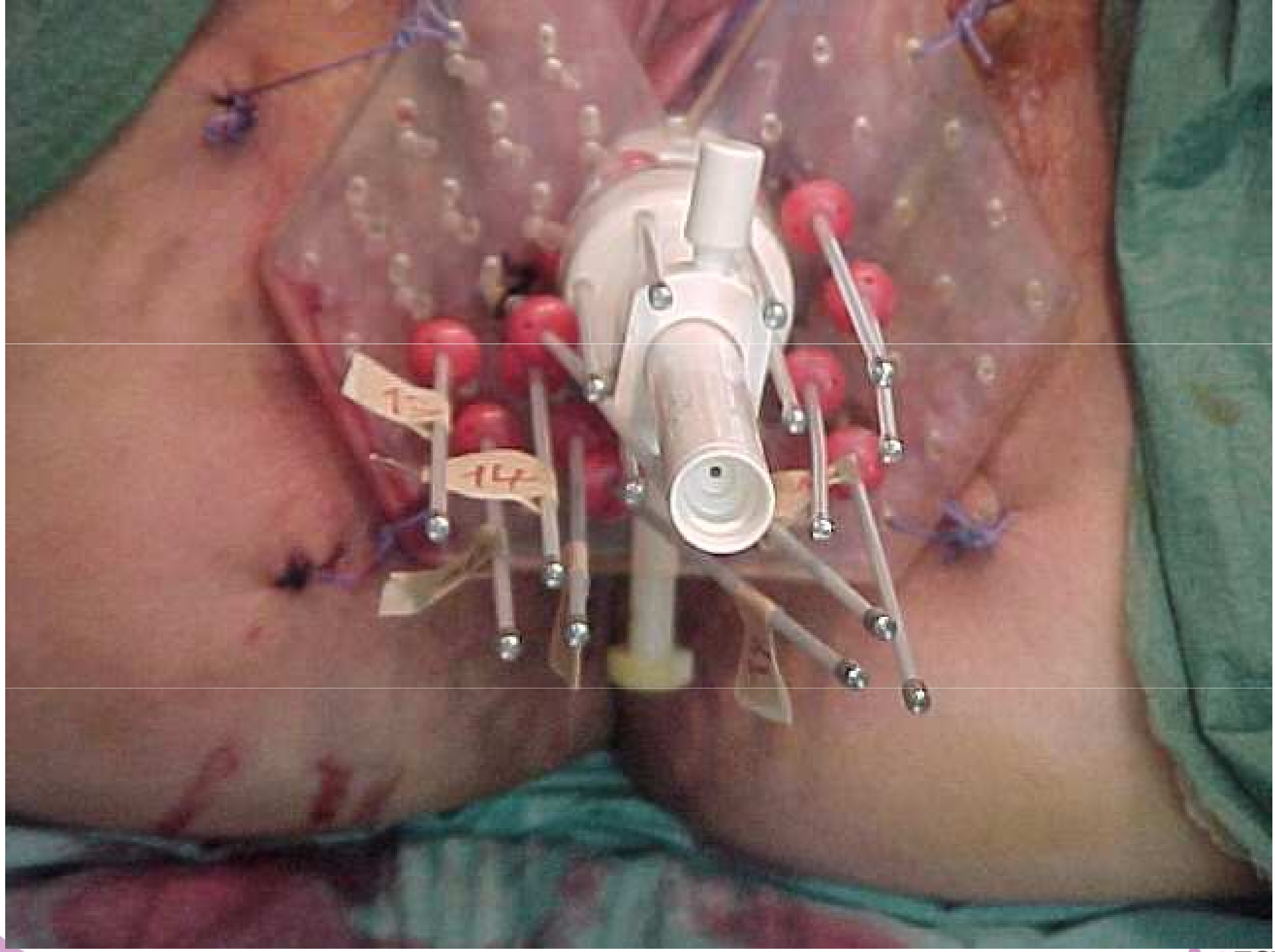
MODIFIED CLASSICAL INTERSTITIAL TECHNIQUES

MRI-compatible cylinder + tandem + template




STRAIGHT GUIDANCE
OBLIQUE GUIDANCE



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CLASSICAL INTERSTITIAL TECHNIQUES

DRAWBACKS

- *Accurate freehand implantation is difficult*
  -operator-depedent
  -positioning often inaccurate
  -loss of parallelism
  -not reproducible

- *Perineal templates (Syed, MUPIT, others)*
  - high number of needles used
  - long distances between template and target (loss of parallelism, inaccurate positioning)
  - impediment for general acceptance: considerable risk of serious acute/late complications

NOVEL INTERSTITIAL TECHNIQUES

Aims

- *improve control over the placement of needles: short distance between template and the target (accurate and reproducible insertion)*
- *lower number of needles to achieve an adequate target coverage*
- *to be combined with individualised MRI based treatment planning to tailor the dose distribution (improve local control without increasing side effects)*

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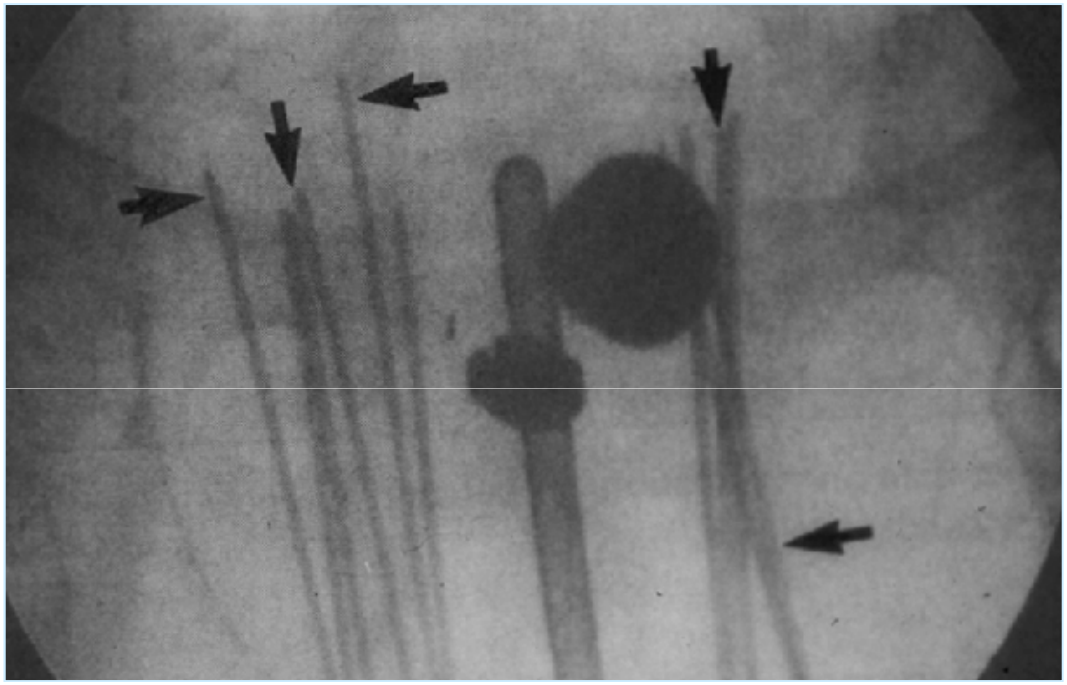
INTERSTITIAL TECHNIQUES
ATTEMPT TO IMPROVE PLACEMENT

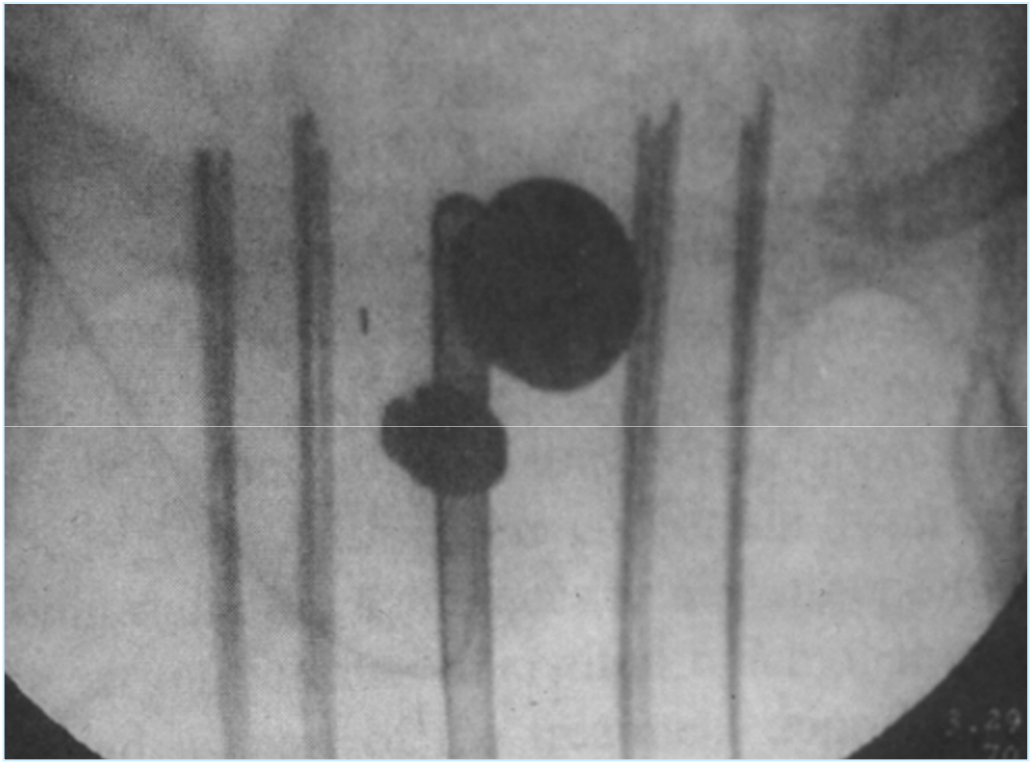
NEEDLE PLACEMENT ACCURACY

- *Fluoroscopy*
- *Computed tomography*
- *MRI: open MRI*
- *Laparotomy guided implants*
- *Laparoscopy*
- *Transabdominal ultrasonography*
- *Transrectal ultrasonography*

INTERSTITIAL TECHNIQUES
ATTEMPT TO IMPROVE PLACEMENT

NEEDLE PLACEMENT ACCURACY: FLUOROSCOPY





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INTERSTITIAL TECHNIQUES
ATTEMPT TO IMPROVE PLACEMENT

NEEDLE PLACEMENT ACCURACY: FLUOROSCOPY

Nag IJROBP 40:415-20;1998

71 pts Syed template

- *Repositioning in all cases*
- *Anterior-posterior plane only*
- *Possible misalignment in the sagittal plane*
- *Problem of tumor coverage*

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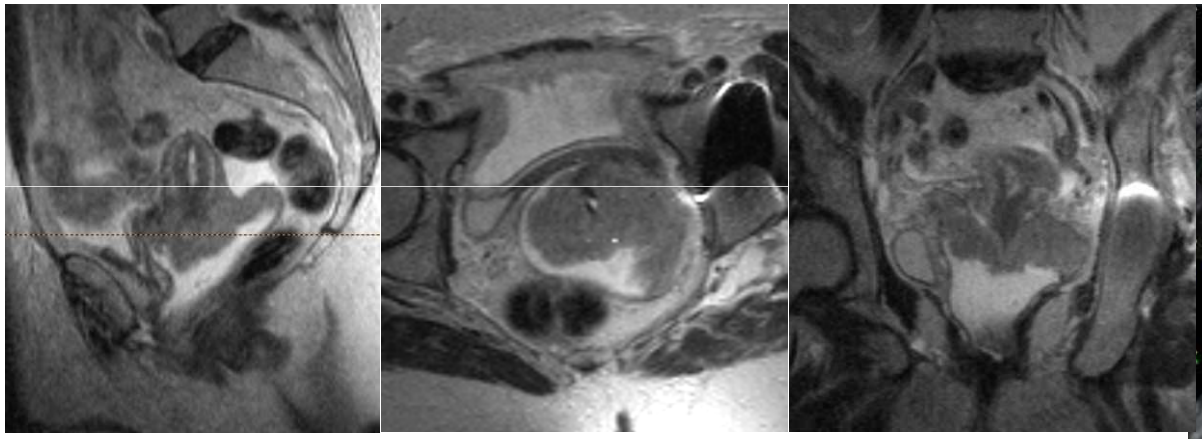
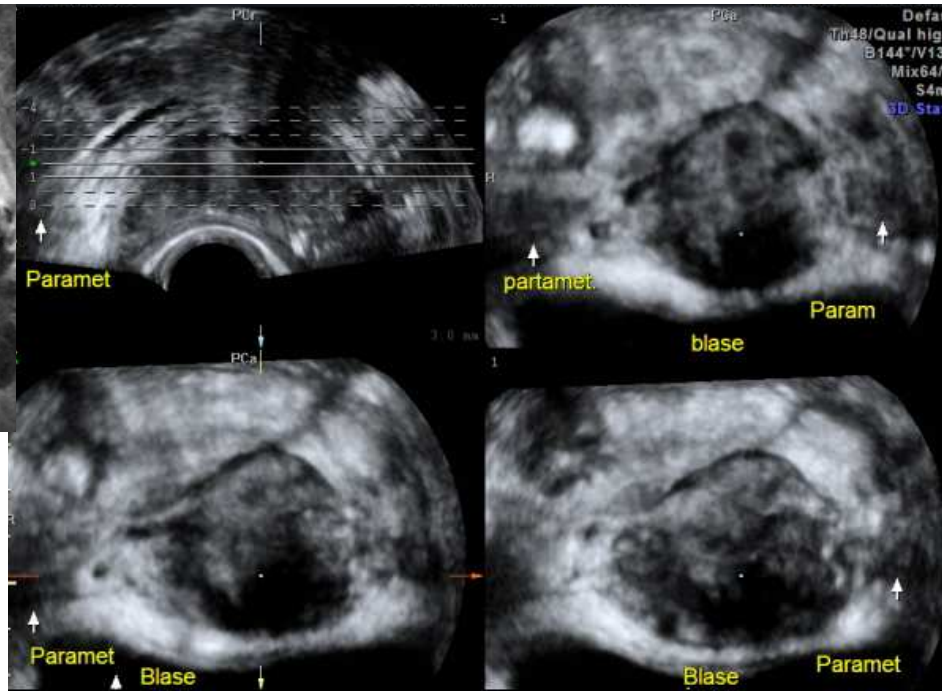
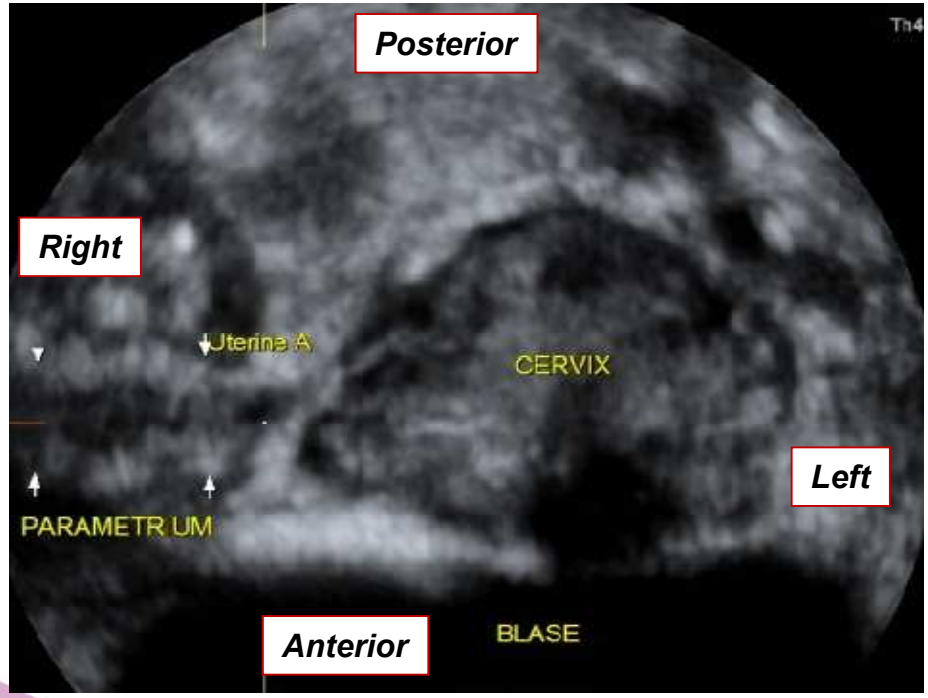
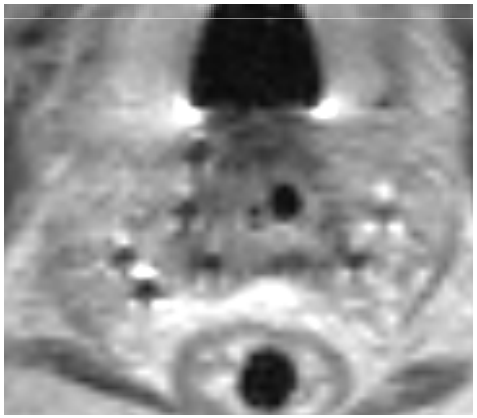
INTERSTITIAL TECHNIQUES
POTENTIAL OF MODERN US TECHNIQUES









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INTERSTITIAL TECHNIQUES
ATTEMPT TO IMPROVE PLACEMENT

NEEDLE PLACEMENT ACCURACY: OPEN LAPAROTOMY

Disaia, Endocurie/Hypertherm. Oncol. 6:251-6;1990

- *Visualization from an intraperitoneal view*
- *Extraperitoneal structures (bladder, cervix, vagina) not visualized*
- *Agressive procedure*

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INTERSTITIAL TECHNIQUES
ATTEMPT TO IMPROVE PLACEMENT

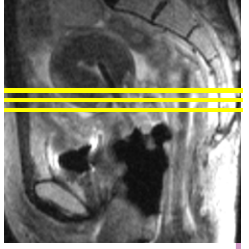
NEEDLE PLACEMENT ACCURACY: OPEN MRI

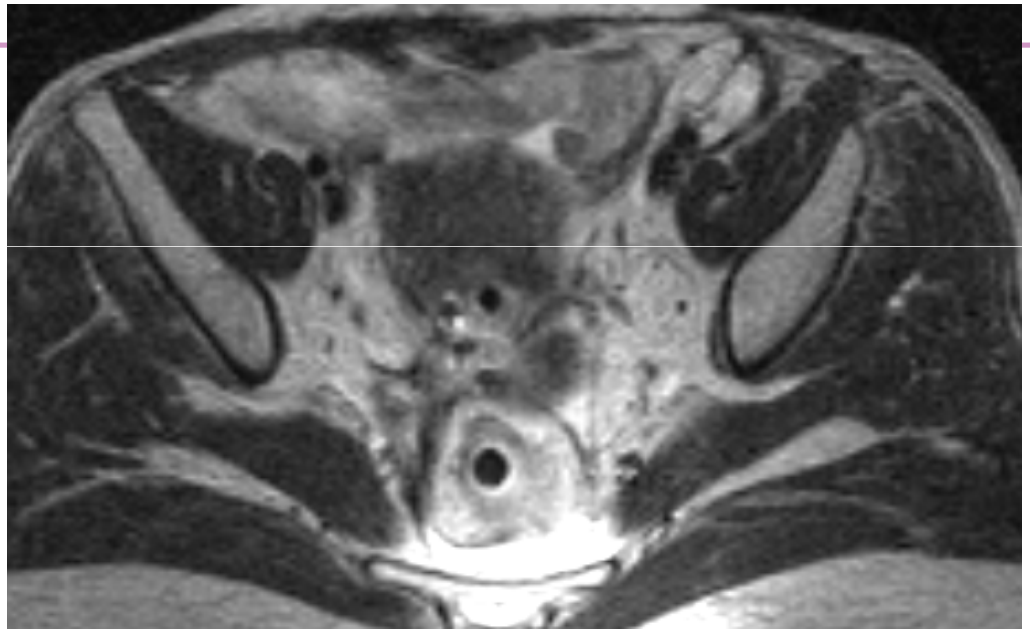
Needle placement accuracy : open MRI with Titanium-Zirconium needles

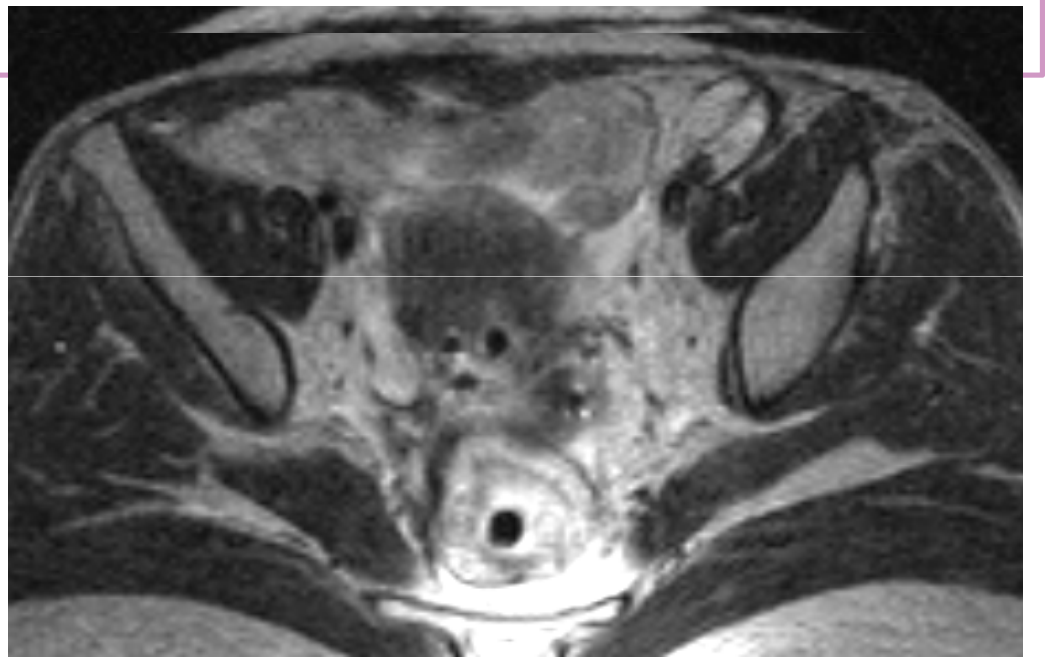
Popowski, IJROBP 47:759-65;2000 6 pts

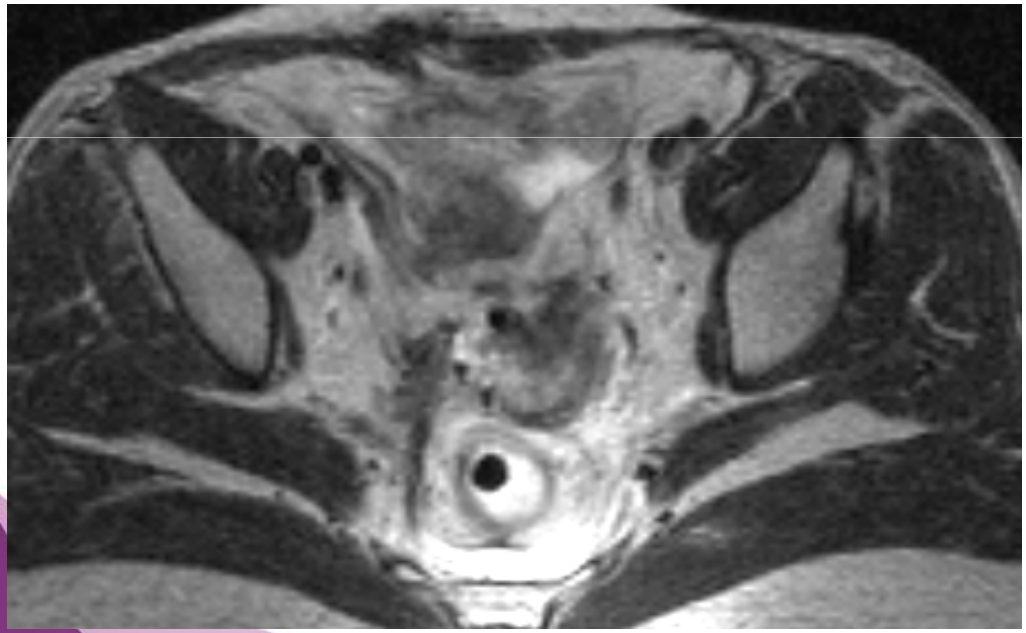
- *Improvement in the treatment quality*
- *Implantation accuracy*
- *Critical organ avoidance*
- *Non magnetic material*

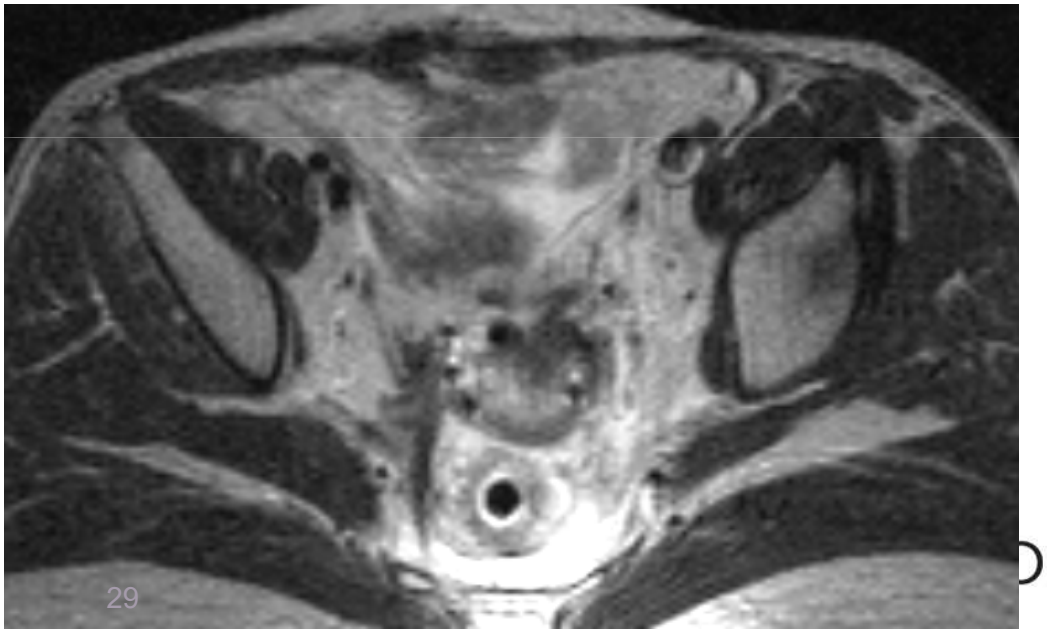
INTERSTITIAL TECHNIQUES
ATTEMPT TO IMPROVE PLACEMENT



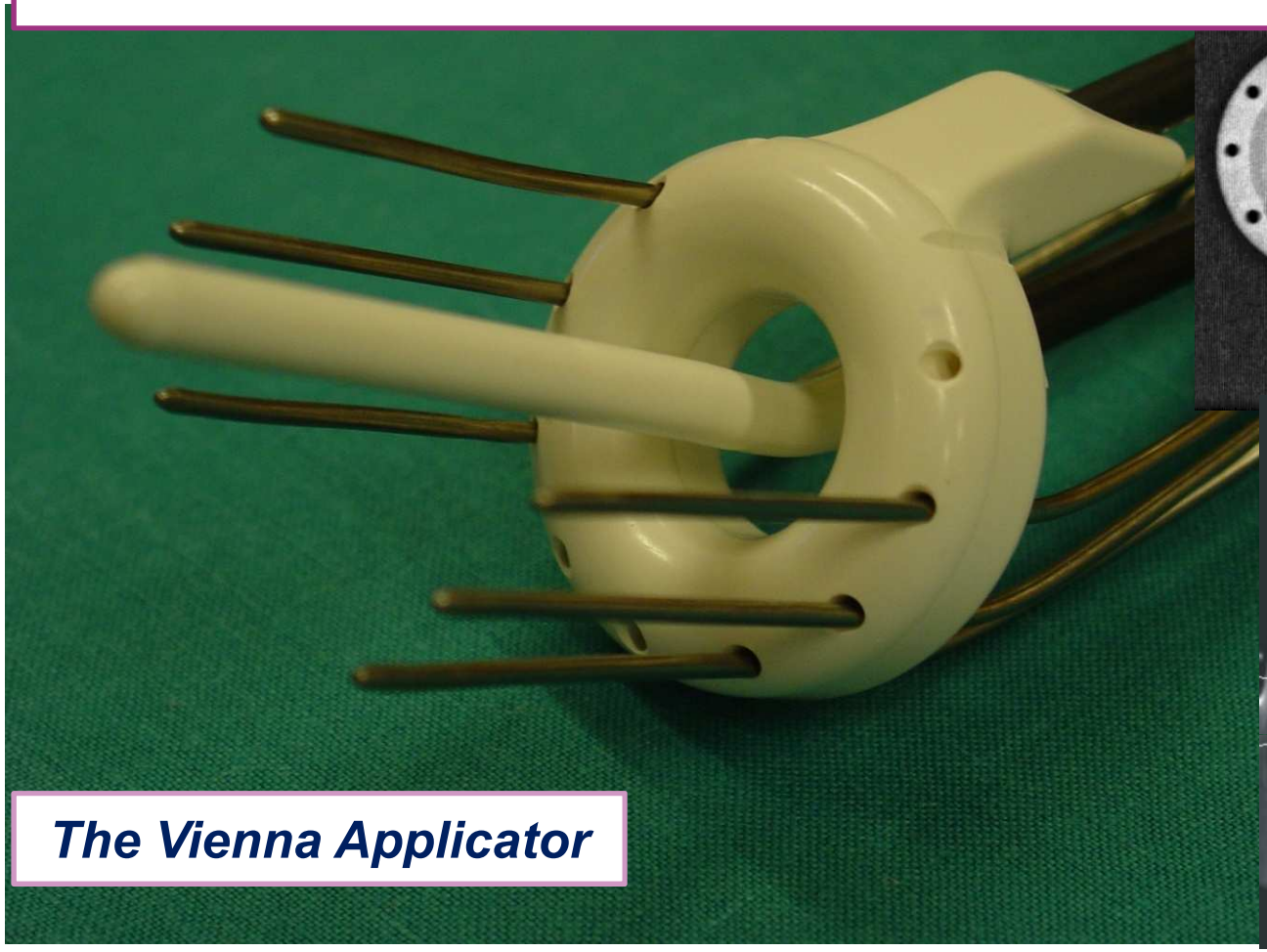




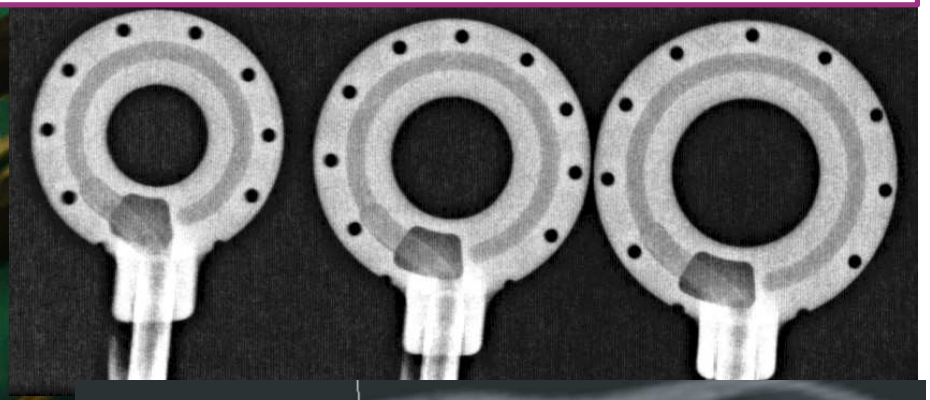


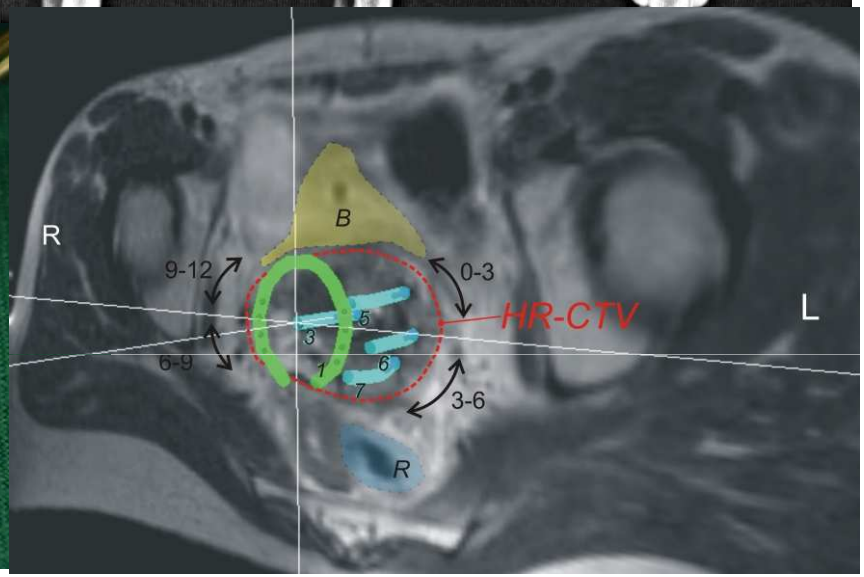


NOVEL INTERSTITIAL TECHNIQUES



The Vienna Applicator





Kirisits et al. IJROBP 2006

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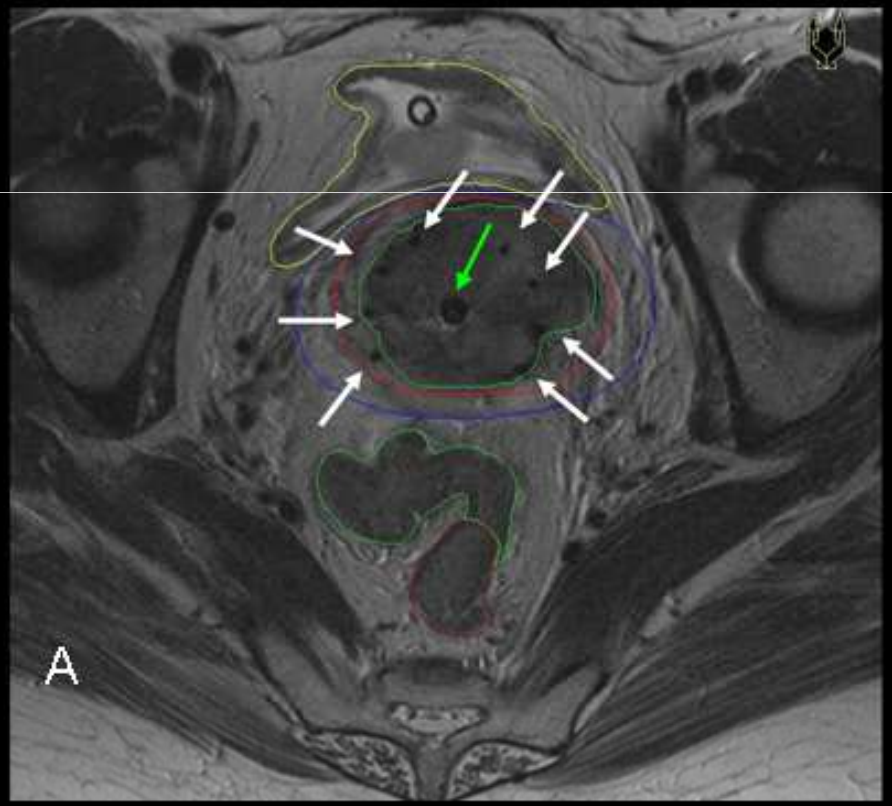
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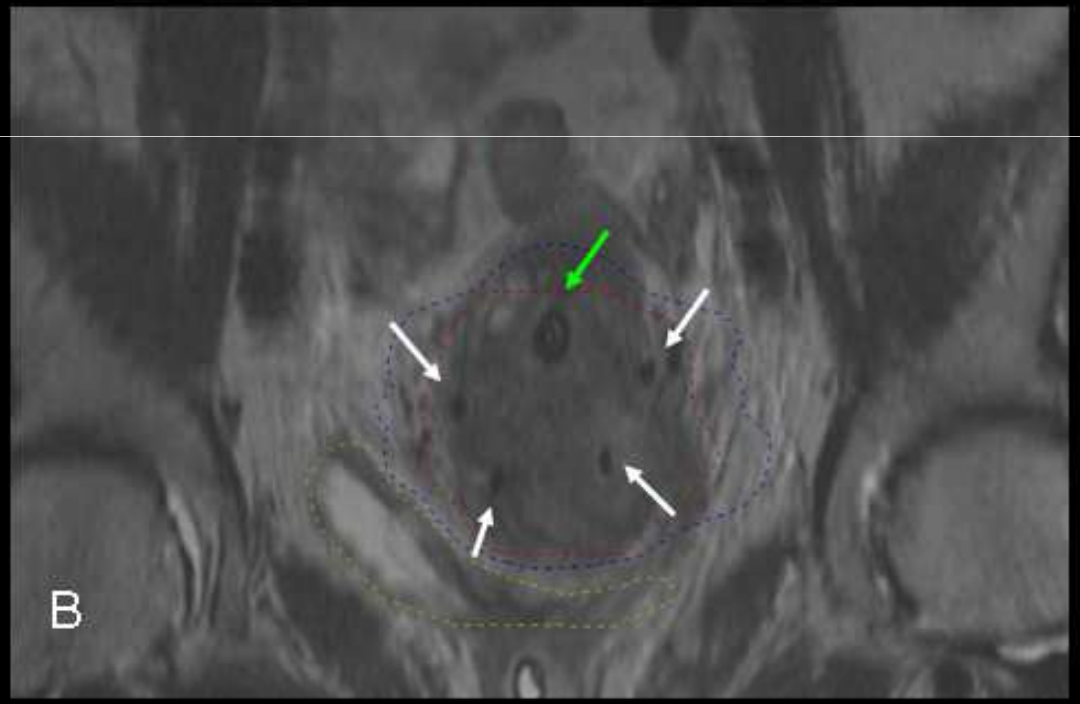
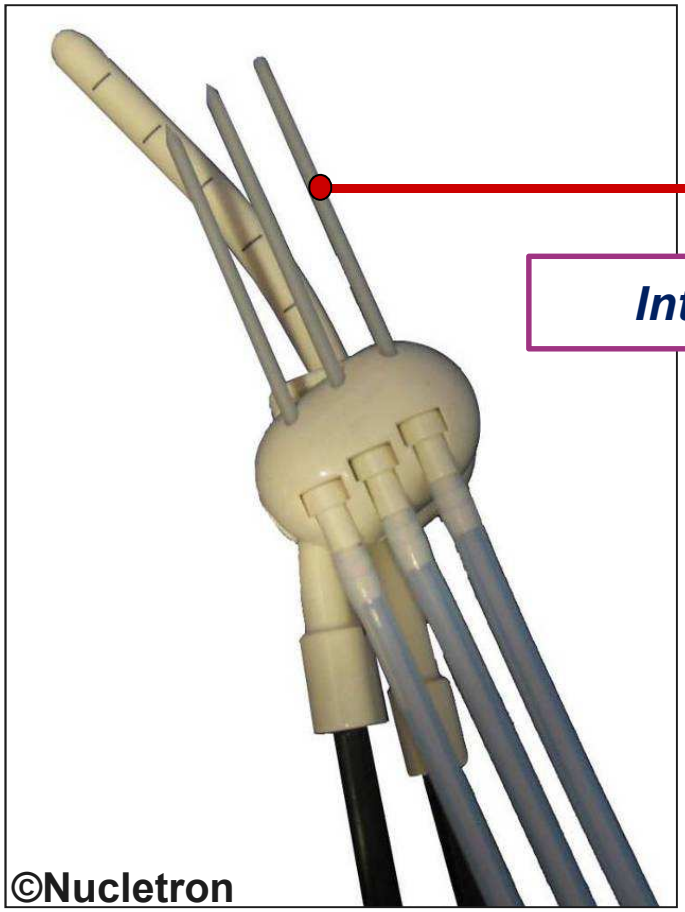

B

NOVEL INTERSTITIAL TECHNIQUES

The Utrecht Applicator



Interstitial needles

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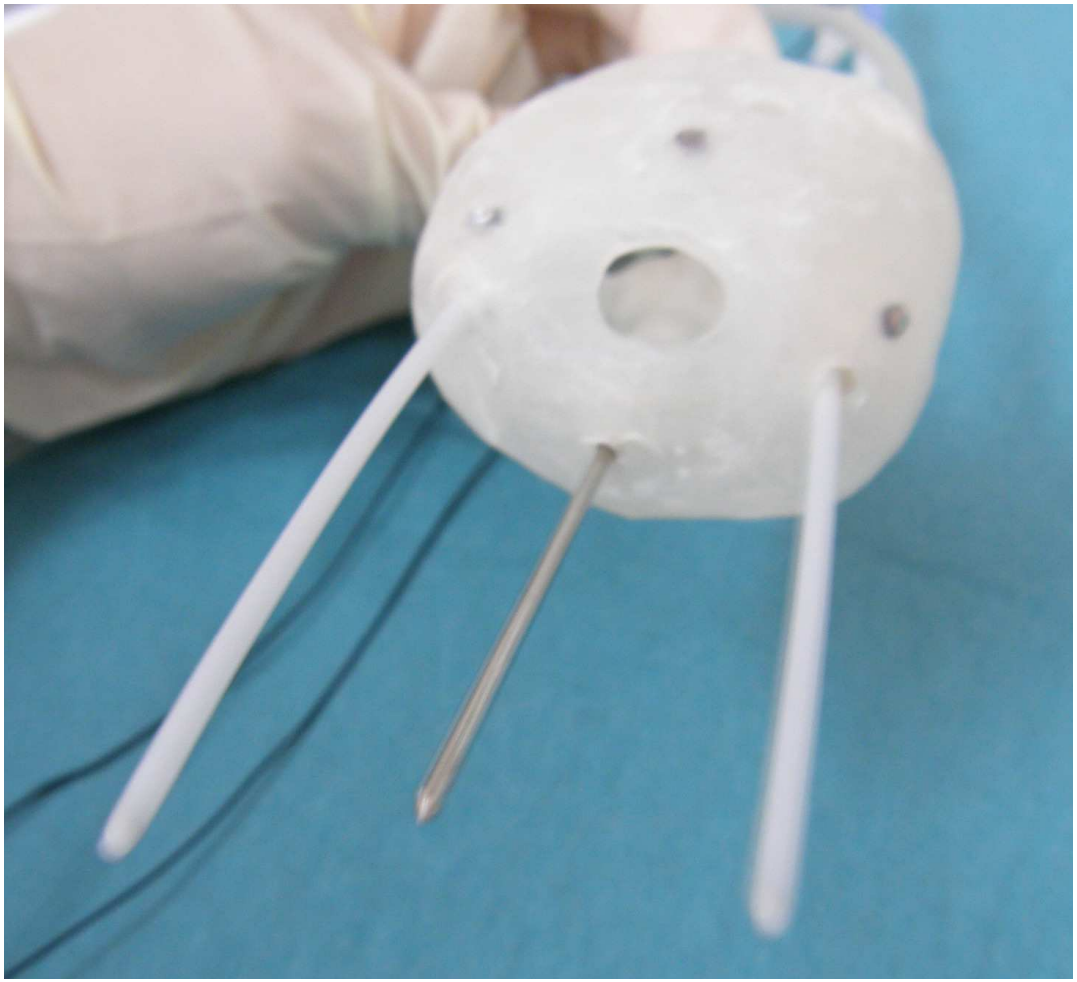
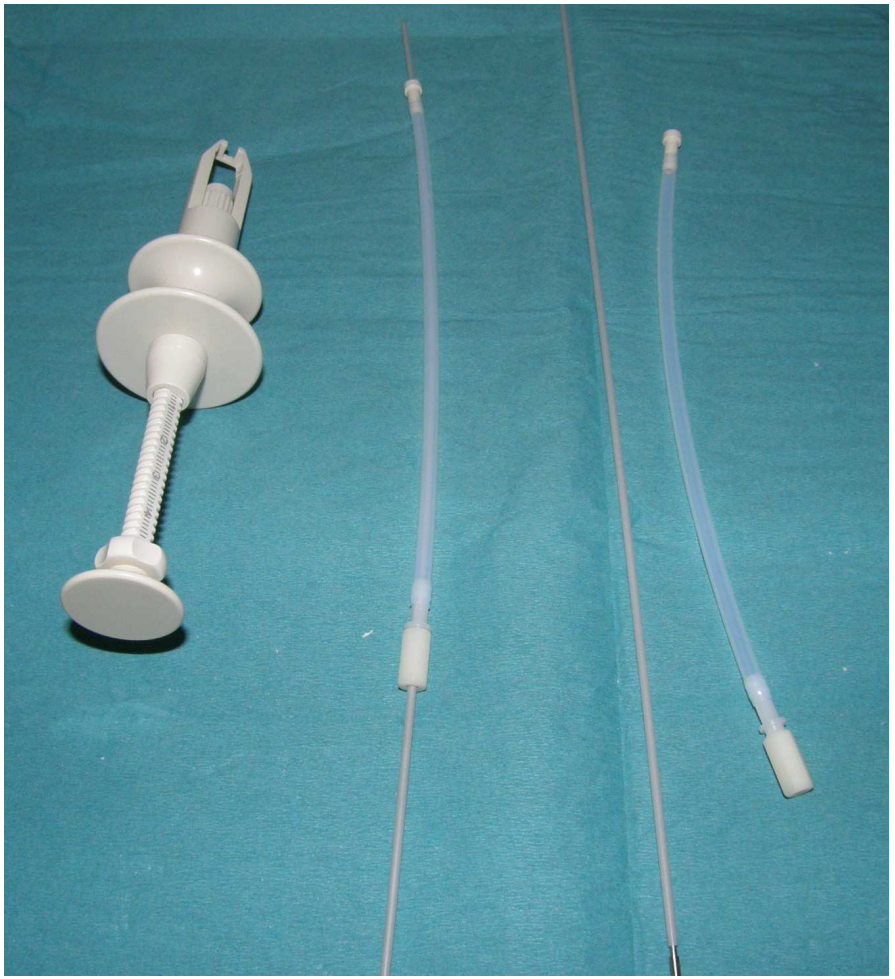
Mould adaptation for interstitial brachytherapy





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modern application techniques

- improve control over the placement of needles: short distance between template and the target (accurate and reproducible insertion)
- lower number of needles to achieve an adequate target coverage
- to be combined with individualised CT/MRI based treatment planning to tailor the dose distribution (improve local control without increasing side effects)

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INTERSTITIAL TECHNIQUES
SELECTION OF APPLICATION TECHNIQUE

Based on clinical examination and sectional imaging:

At the time of diagnosis

-initial tumor extension

During EBRT

-Quantitative and qualitative tumor regression

At the time of brachytherapy

-Topography of tumor in relation to the applicator / DVH

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Pre-plan?

- Anticipation.
  - How many needles
  - Positions?
  - Deapth
- Insertion of ring applicator and dosimetric study
- 24 patients
- PDR, 2 fractions

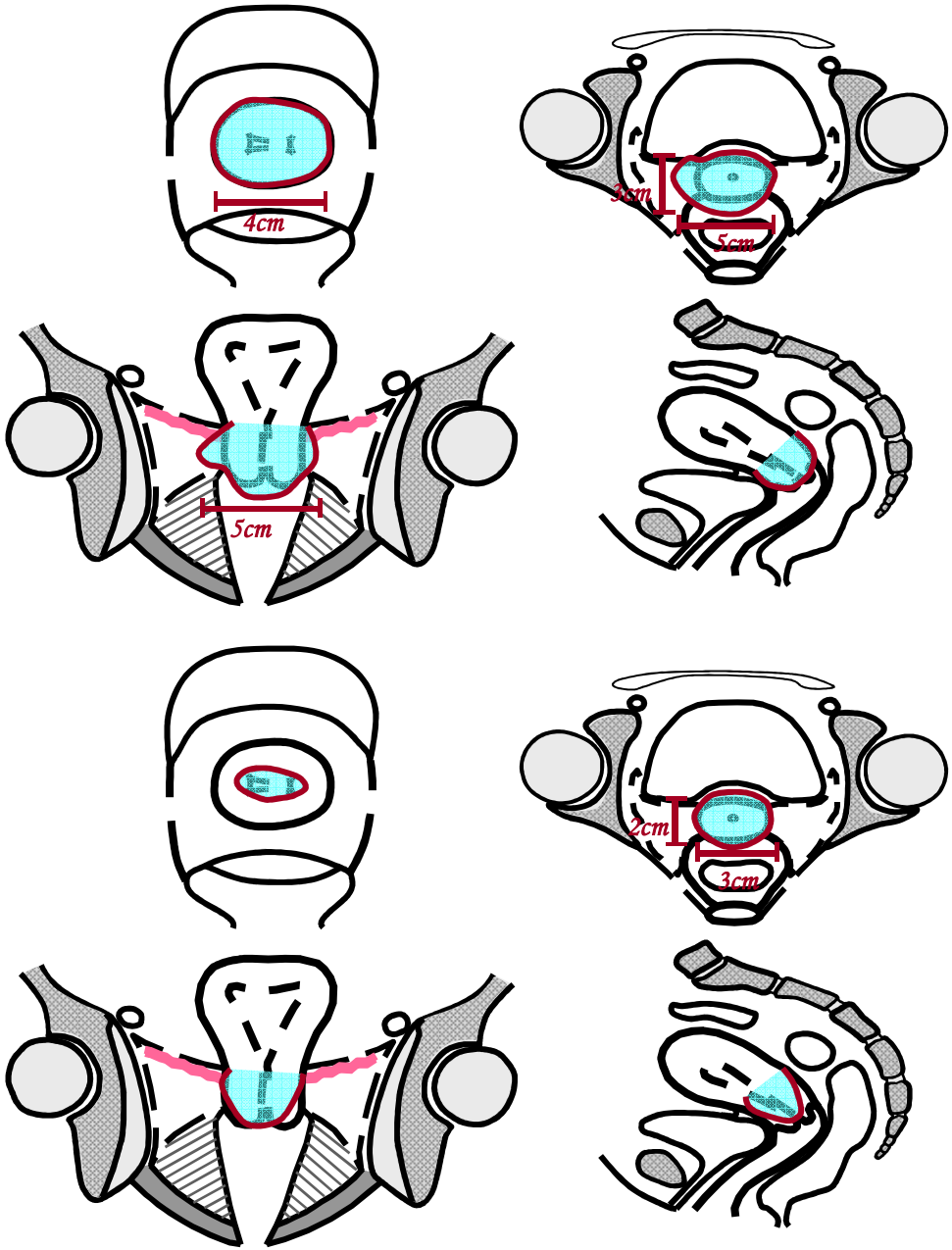
Dose Gy (EQD2)*		Pre-plan IC	Pre-plan IC/IS			BT1 + BT2		
		Mean	Mean	Δdif.ς	P**	Mean	Δdif.ς	P**
HR CTV	D90	85.1 ± 9.0	89.6 ± 5.0	4.5 ± 8.4	0.02	90.0 ± 3.7	4.9 ± 9.0	<0.01
	D100	66.2 ± 7.3	72.6 ± 5.7	6.4 ± 8.5	0.01	72.6 ± 5.1	6.3 ± 8.0	<0.01
IR CTV	D90	65.9 ± 5.0	66.4 ± 3.7	0.5 ± 5.1	0.65	66.3 ± 2.7	0.4 ± 5.3	0.70
Bladder	D2cc	74.7 ± 9.5	73.9 ± 8.7	−0.9 ± 8.9	0.64	72.1 ± 4.9	−2.6 ± 8.7	0.15
Rectum	D2cc	65.6 ± 6.4	64.0 ± 5.8	−1.7 ± 5.8	0.17	64.1 ± 5.2	−1.6 ± 6.1	0.21
Sigmoid	D2cc	67.6 ± 7.8	65.6 ± 6.6	−2.0 ± 5.1	0.03	62.8 ± 5.3	−4.8 ± 7.0	<0.01
Bowel	D2cc	64.3 ± 13.2	60.9 ± 9.3	−3.4 ± 6.3	<0.01	59.6 ± 6.8	−4.7 ± 9.9	0.04

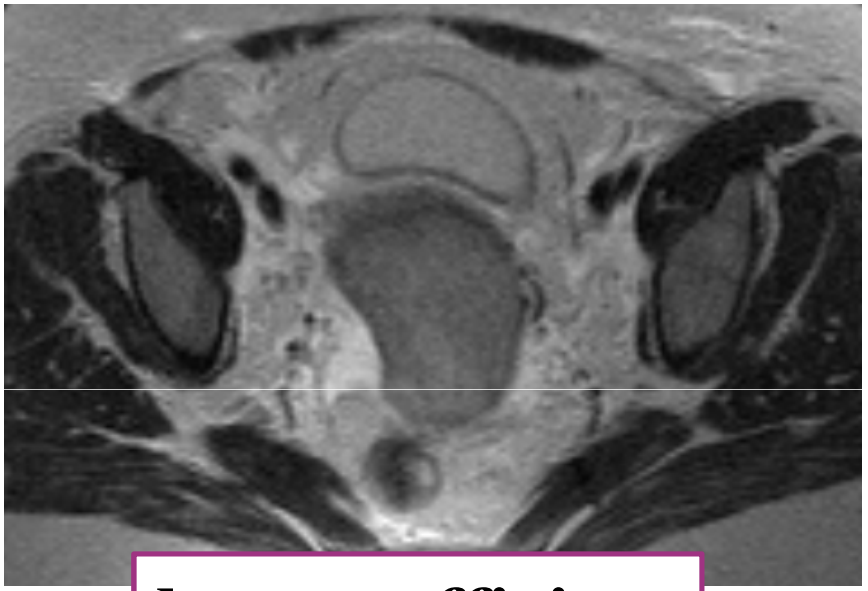
ς Difference between Pre-plan IC/IS or BT1 + BT2 and Pre-plan IC.

* EQD2: T1/2(h) = 1.5, α/β = 10 Gy (tumour), α/β = 3 Gy (normal tissue). Dose of EBRT is included. For BT0 it was assumed that the same plan was delivered twice.

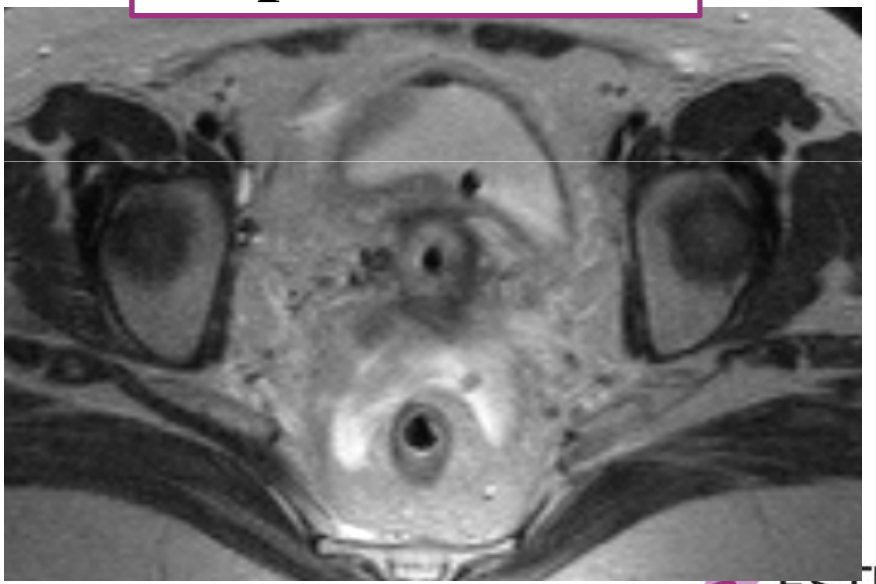
** Matched pairwise two tailed *t*-test statistics.

Pattern of tumor regression I





large sufficient proximal



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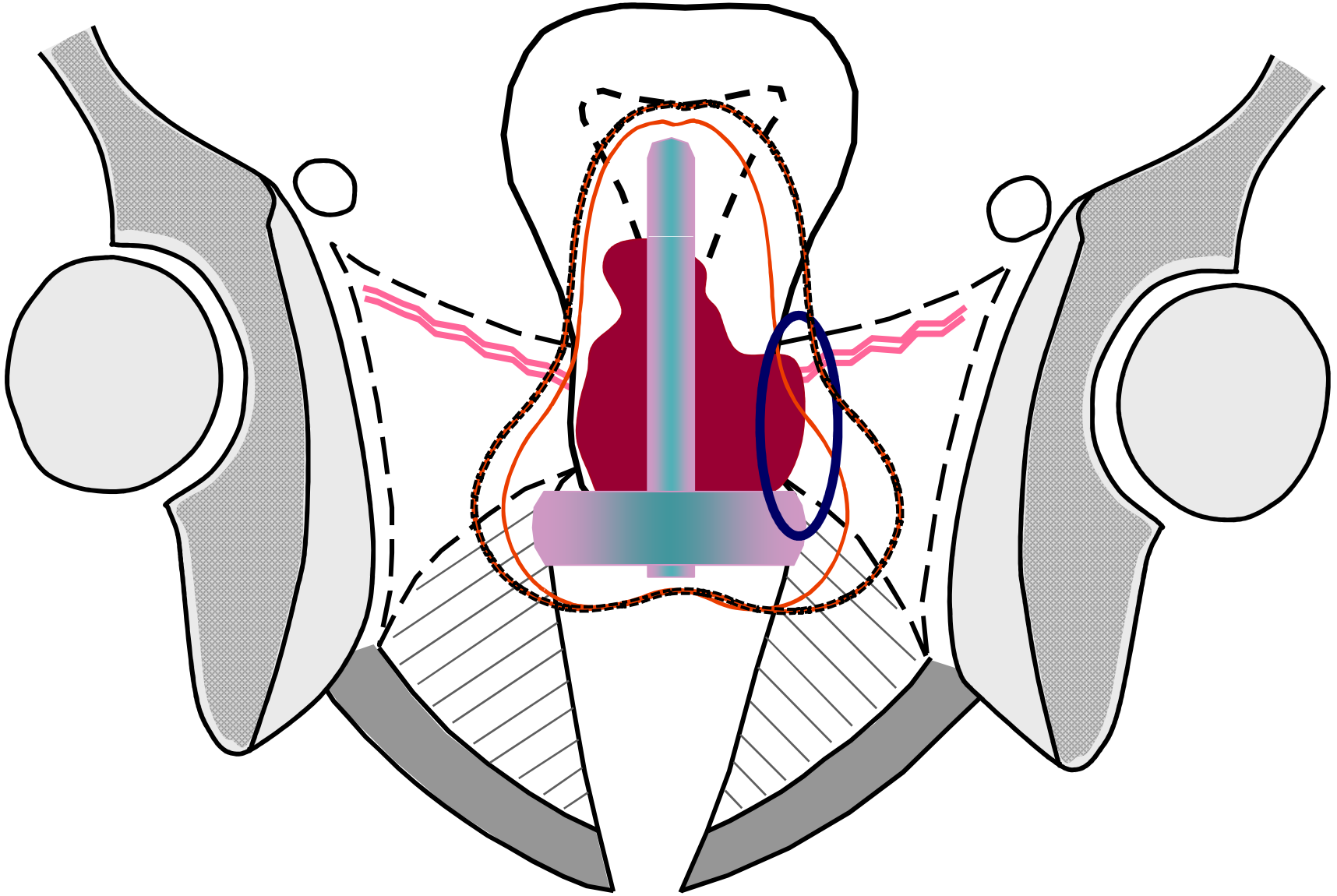
Lateral tumoral extension coverage



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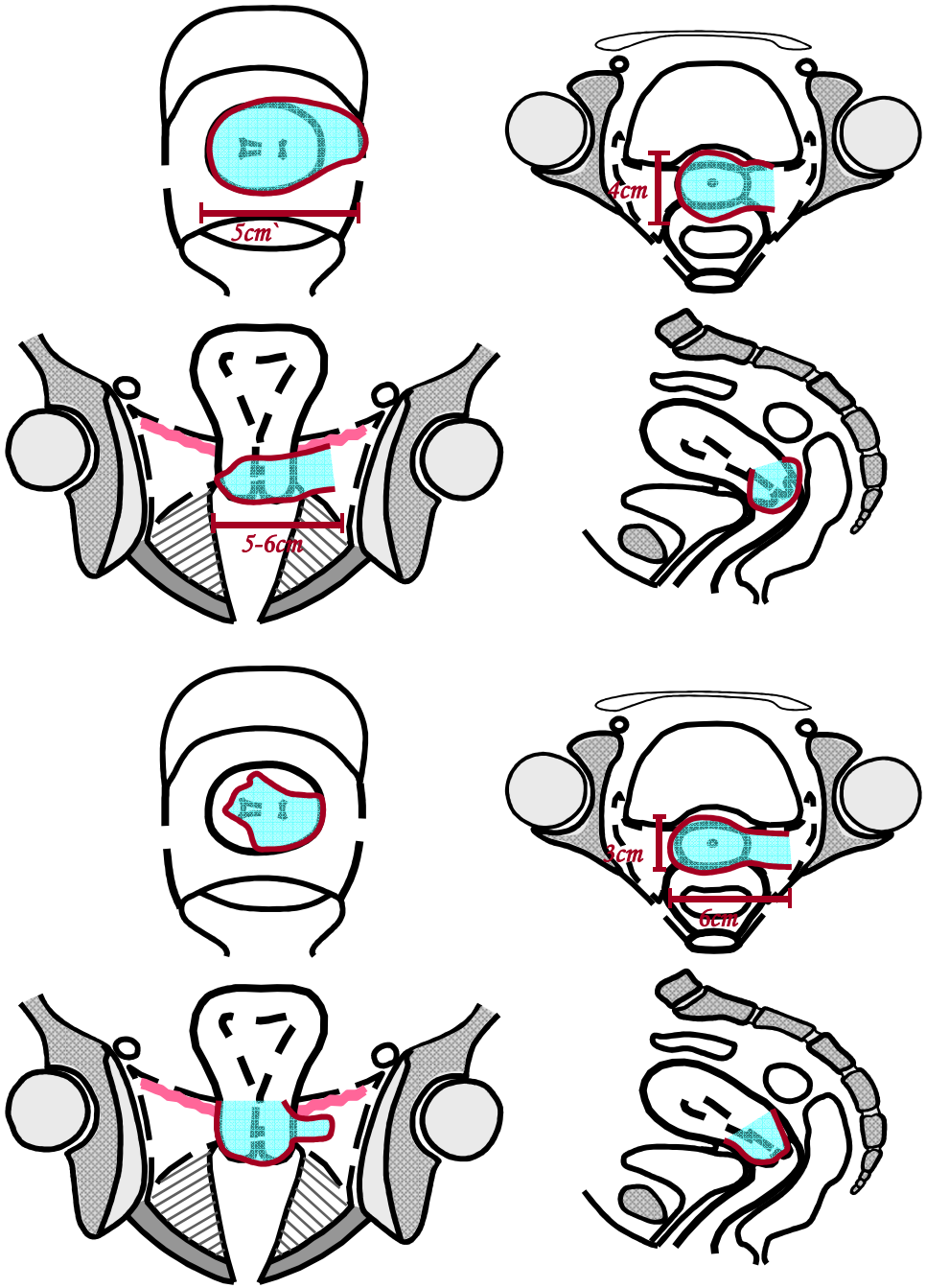
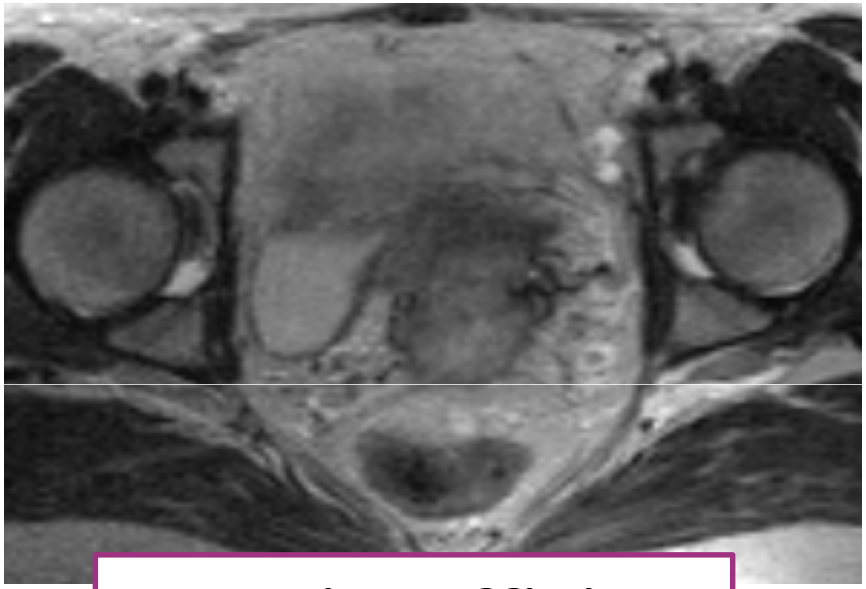
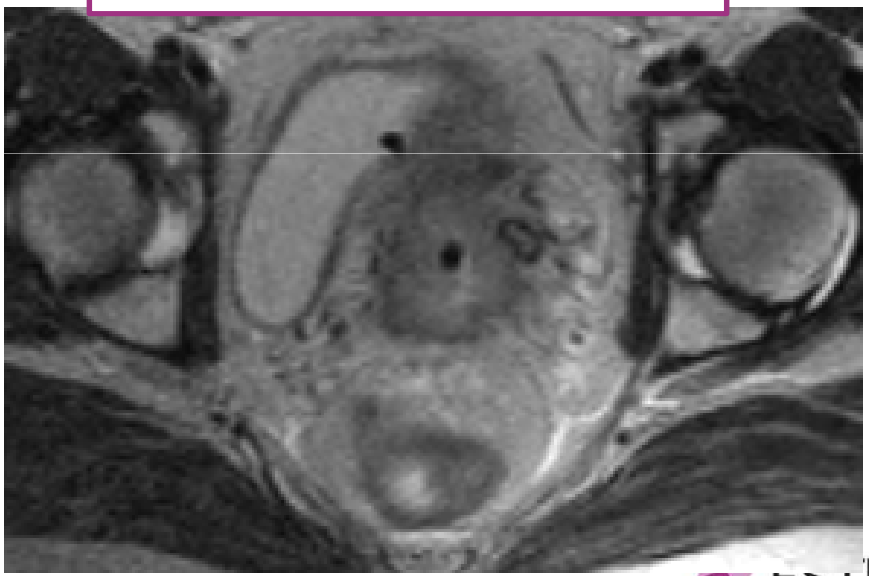
Pattern of tumor regression II





large insufficient middle



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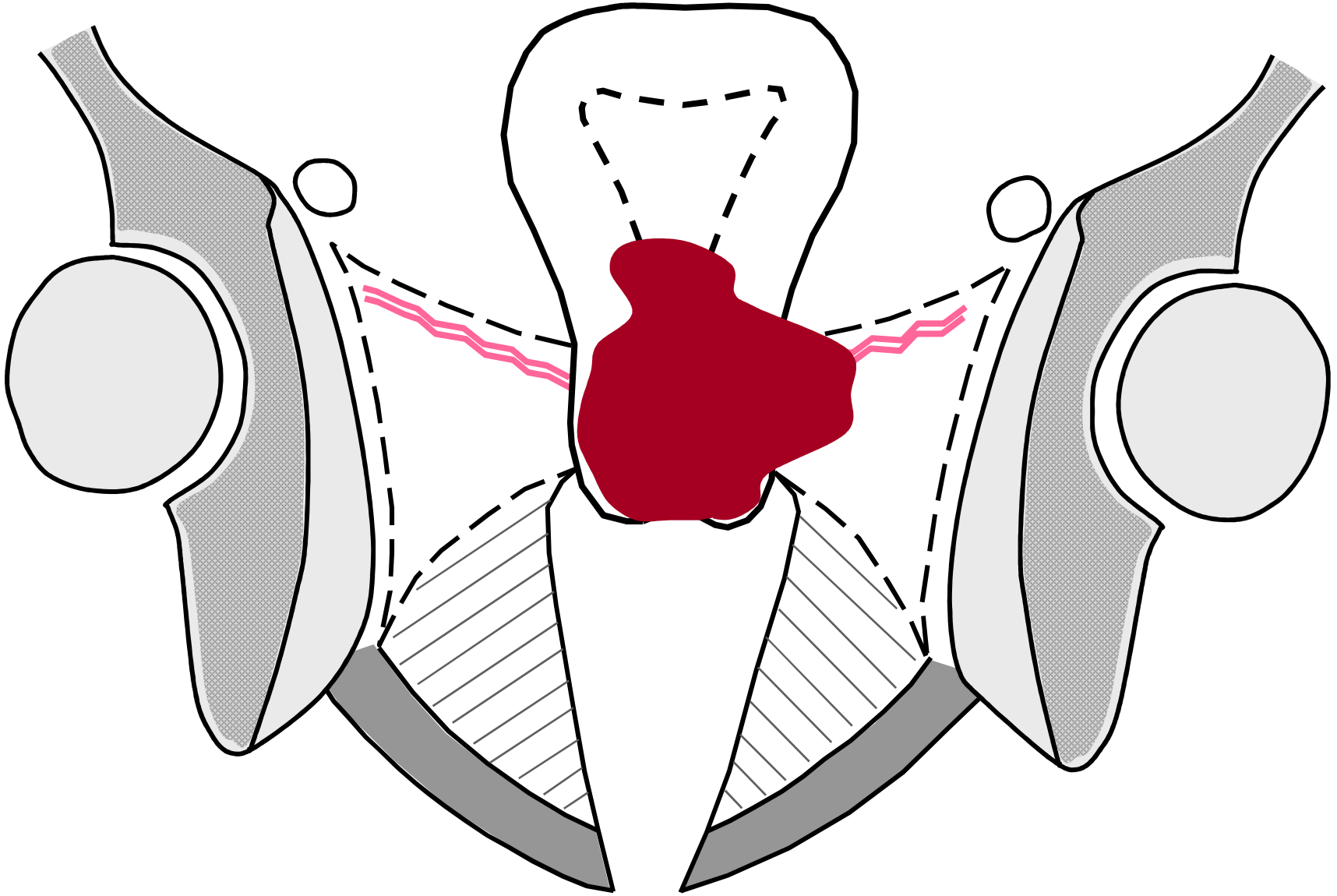
Pattern of tumor regression II



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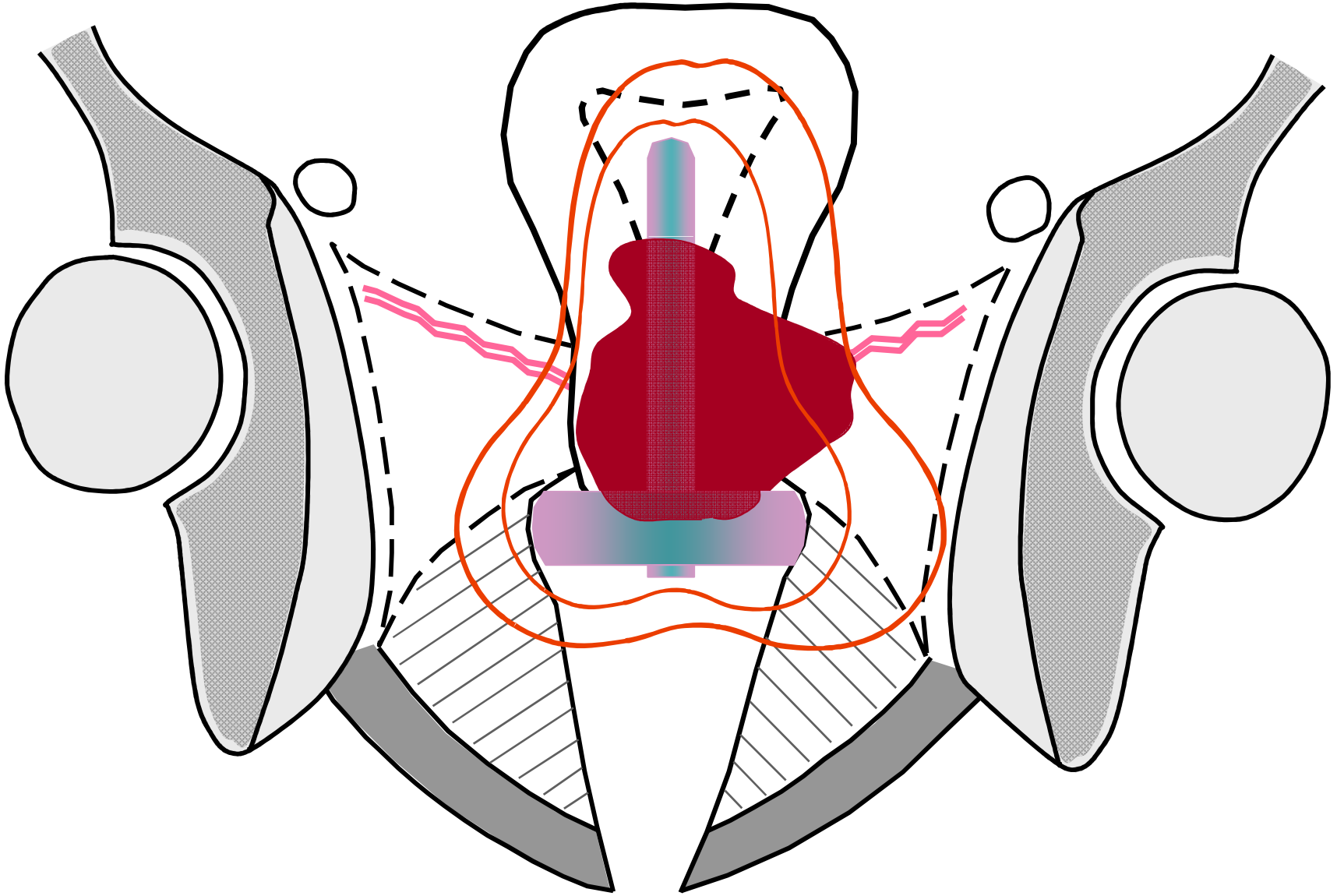
Pattern of tumor regression II



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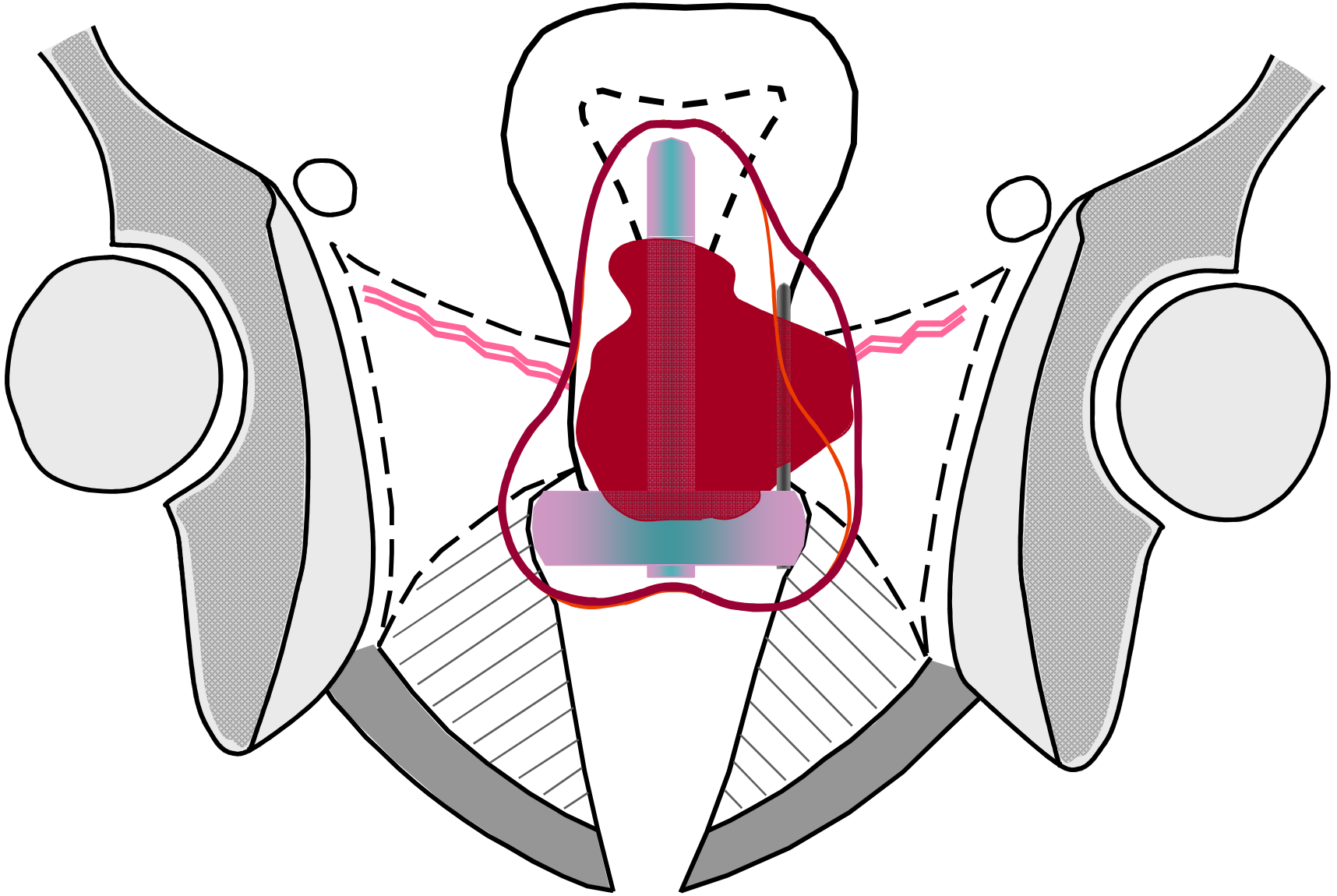
Pattern of tumor regression II



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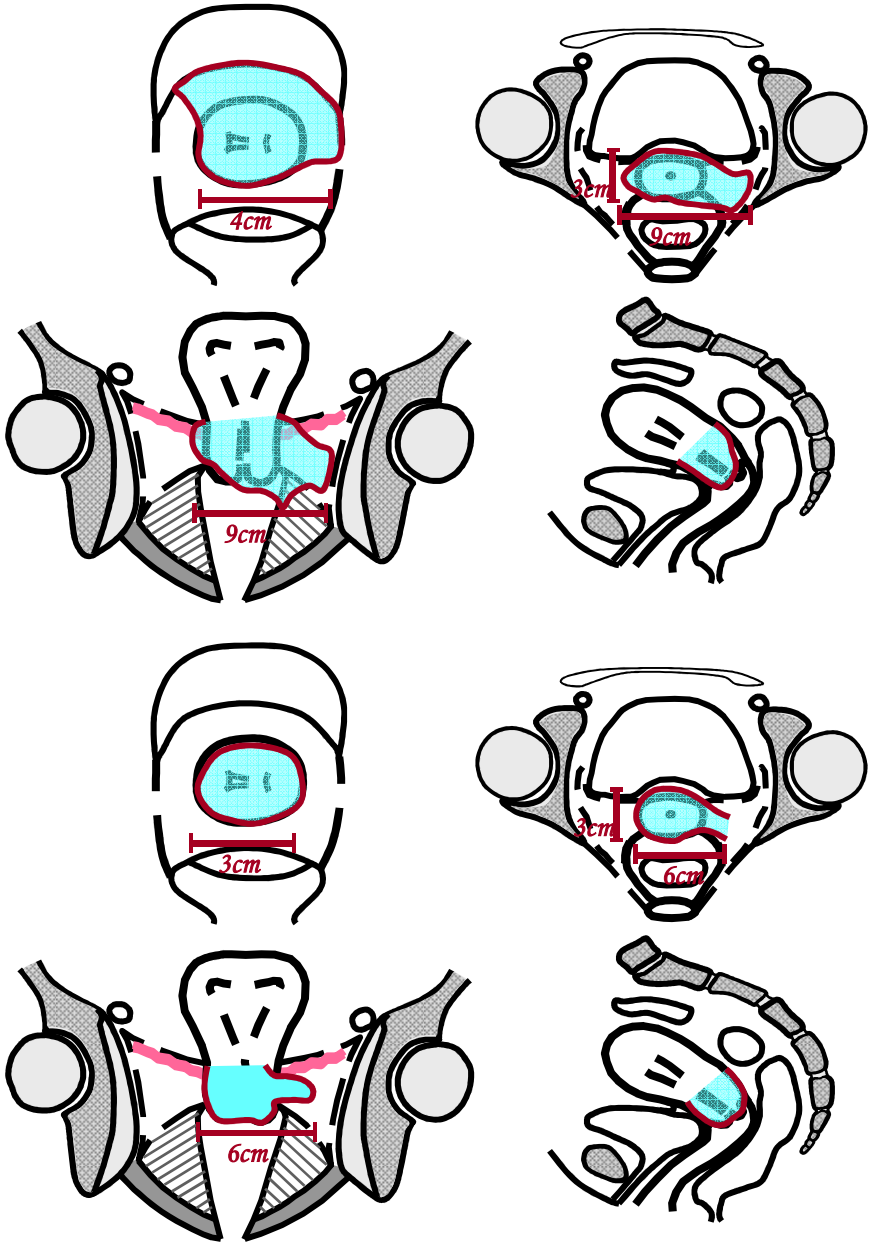
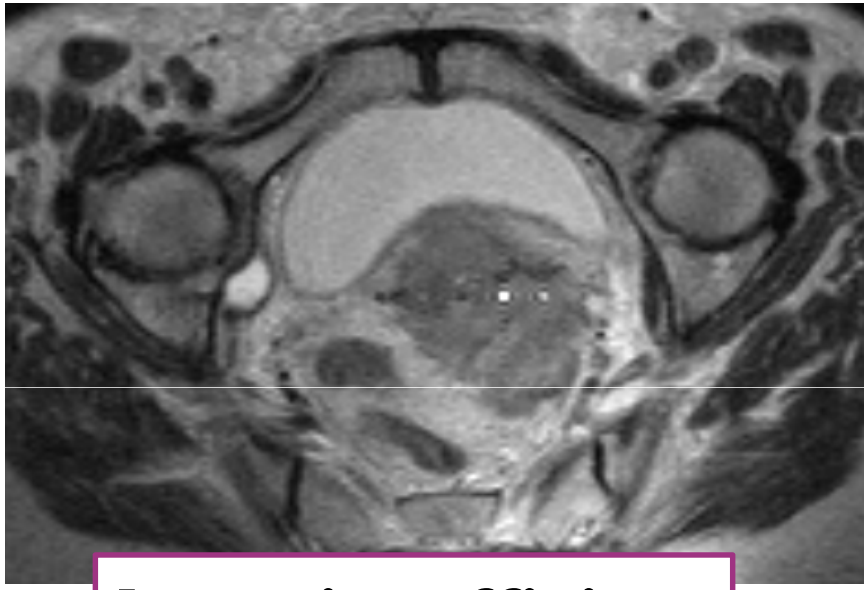
Pattern of tumor regression III





large insufficient distal

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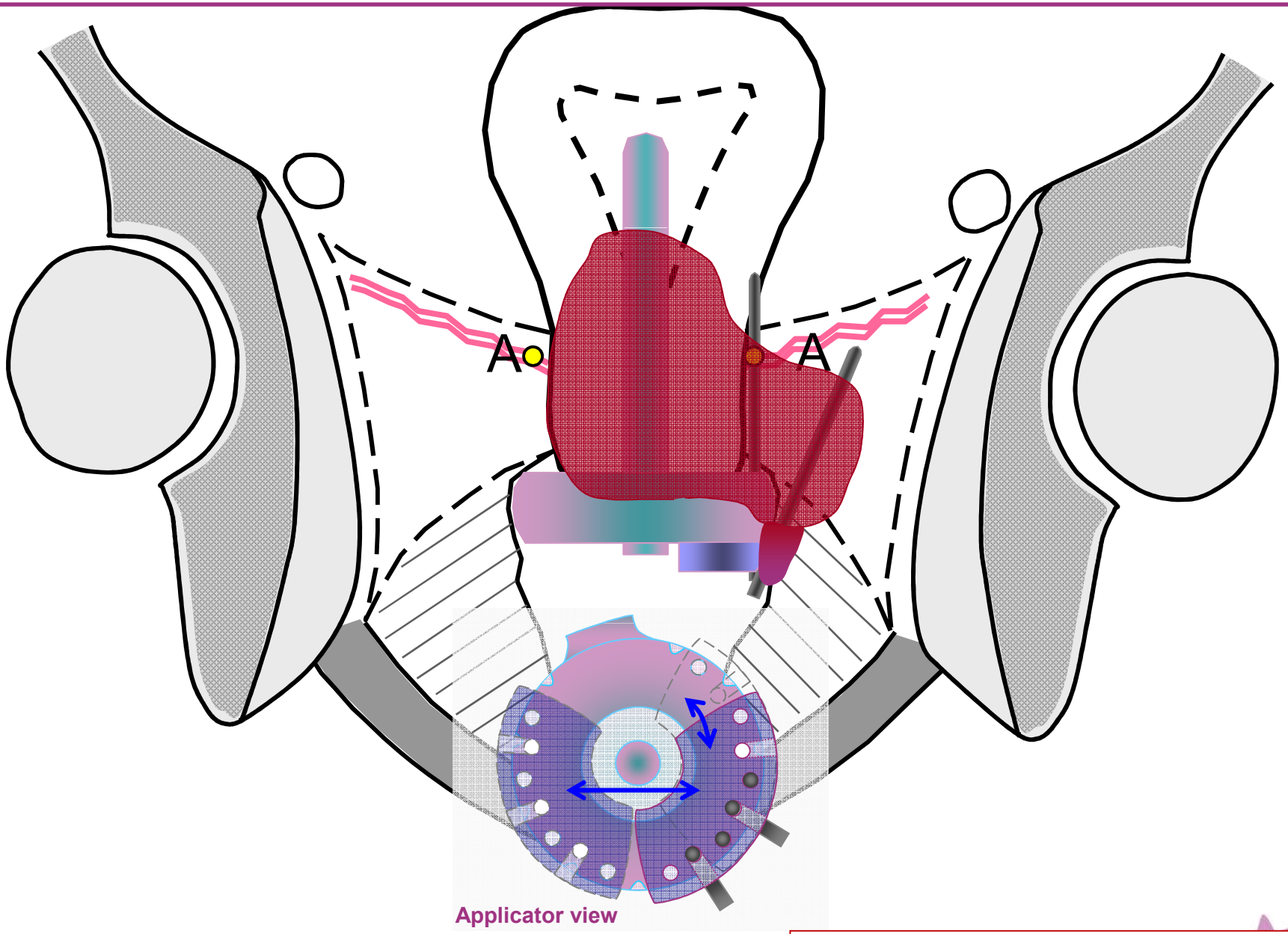
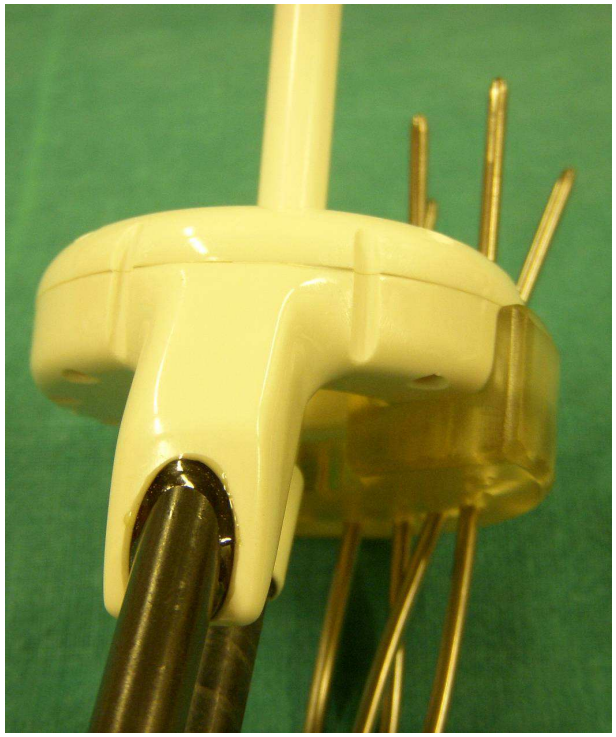
Applicator for distal parametrial disease

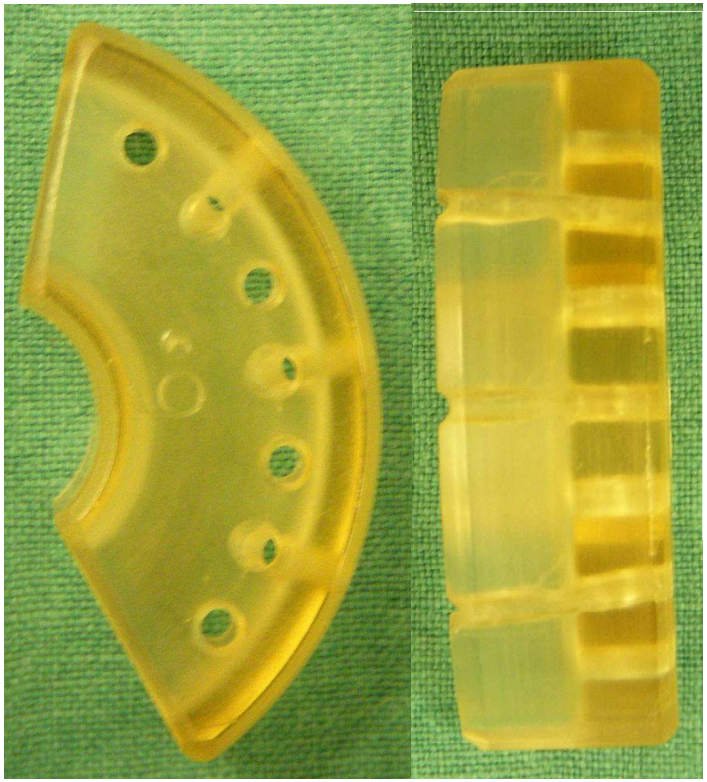
additional parallel and divergent template guided needles

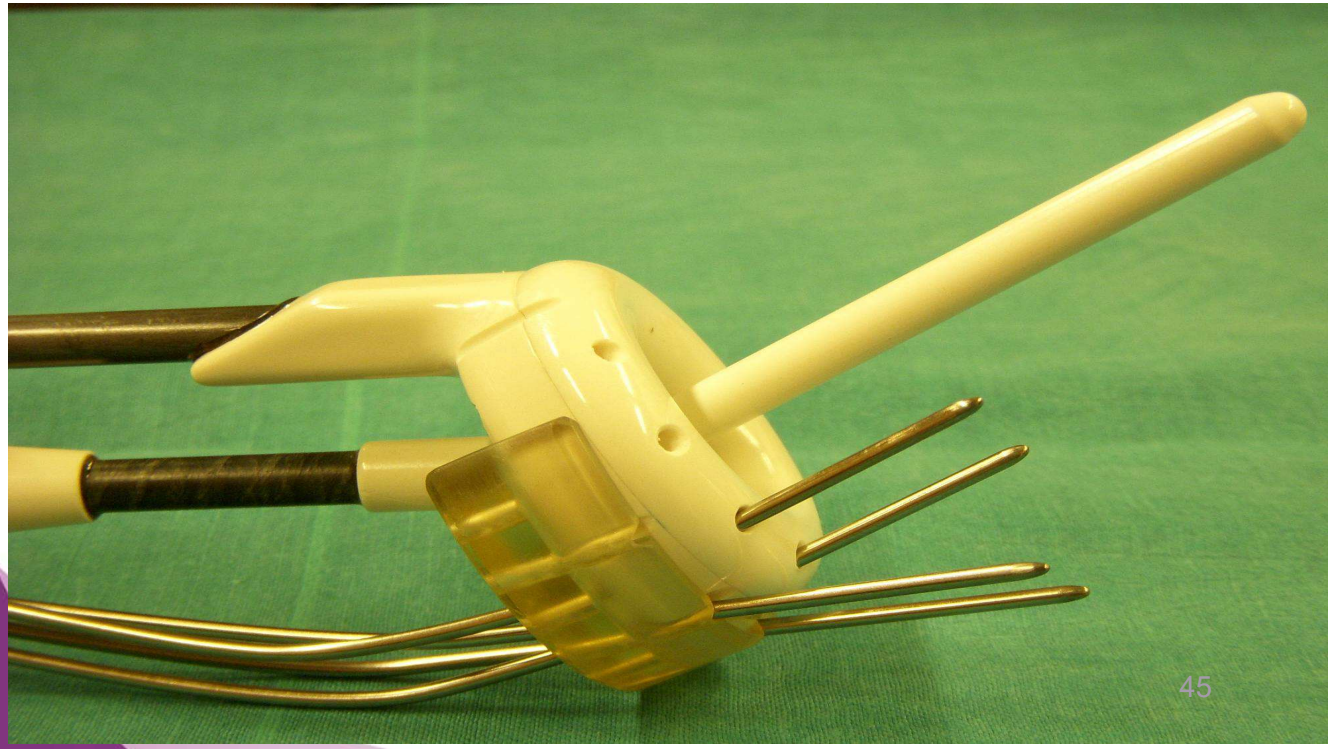


The Vienna II Applicator



Modified Vienna Ring
Vienna II





Provided by Dimopoulos et al

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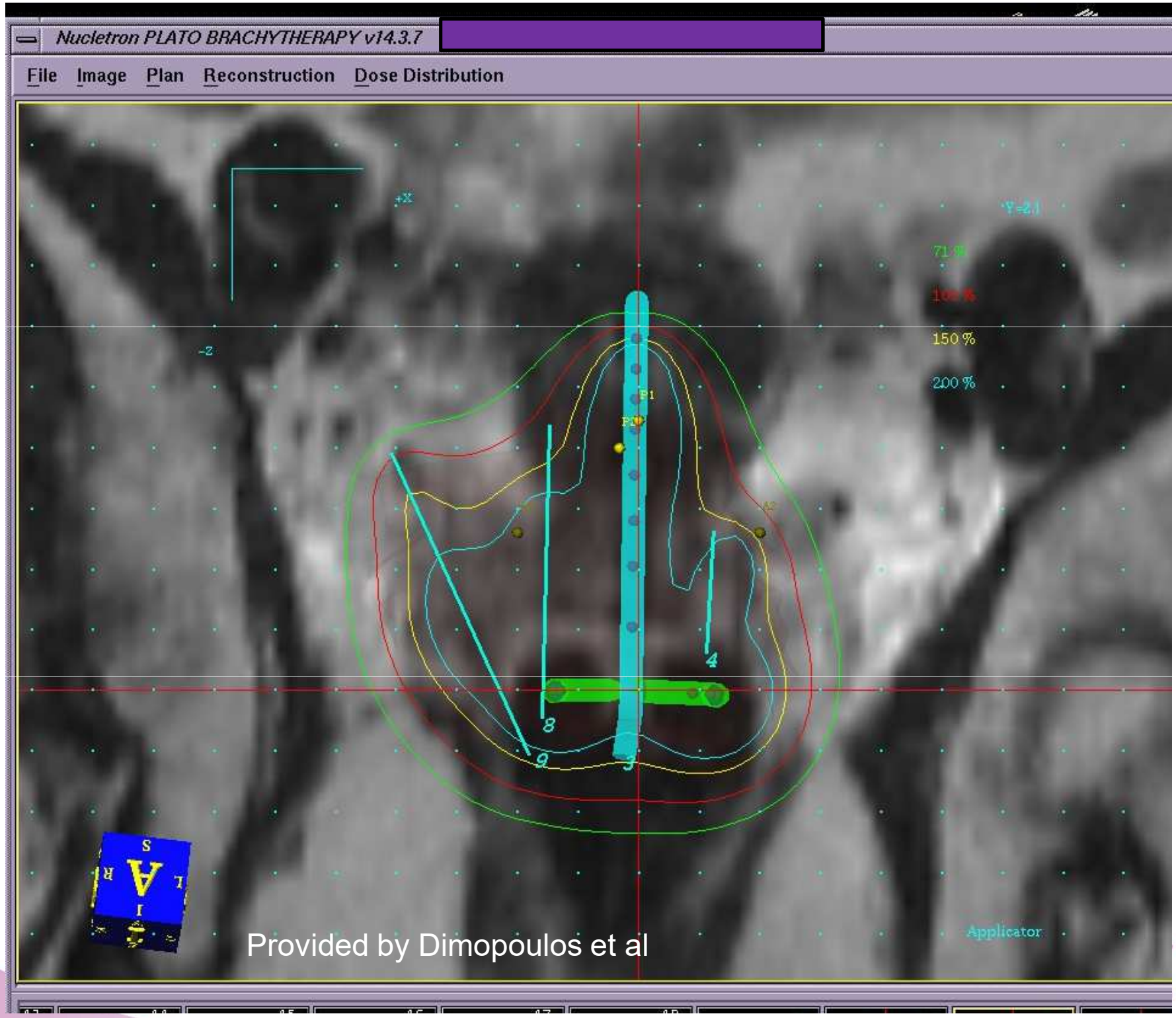

Provided by Dimopoulos et al

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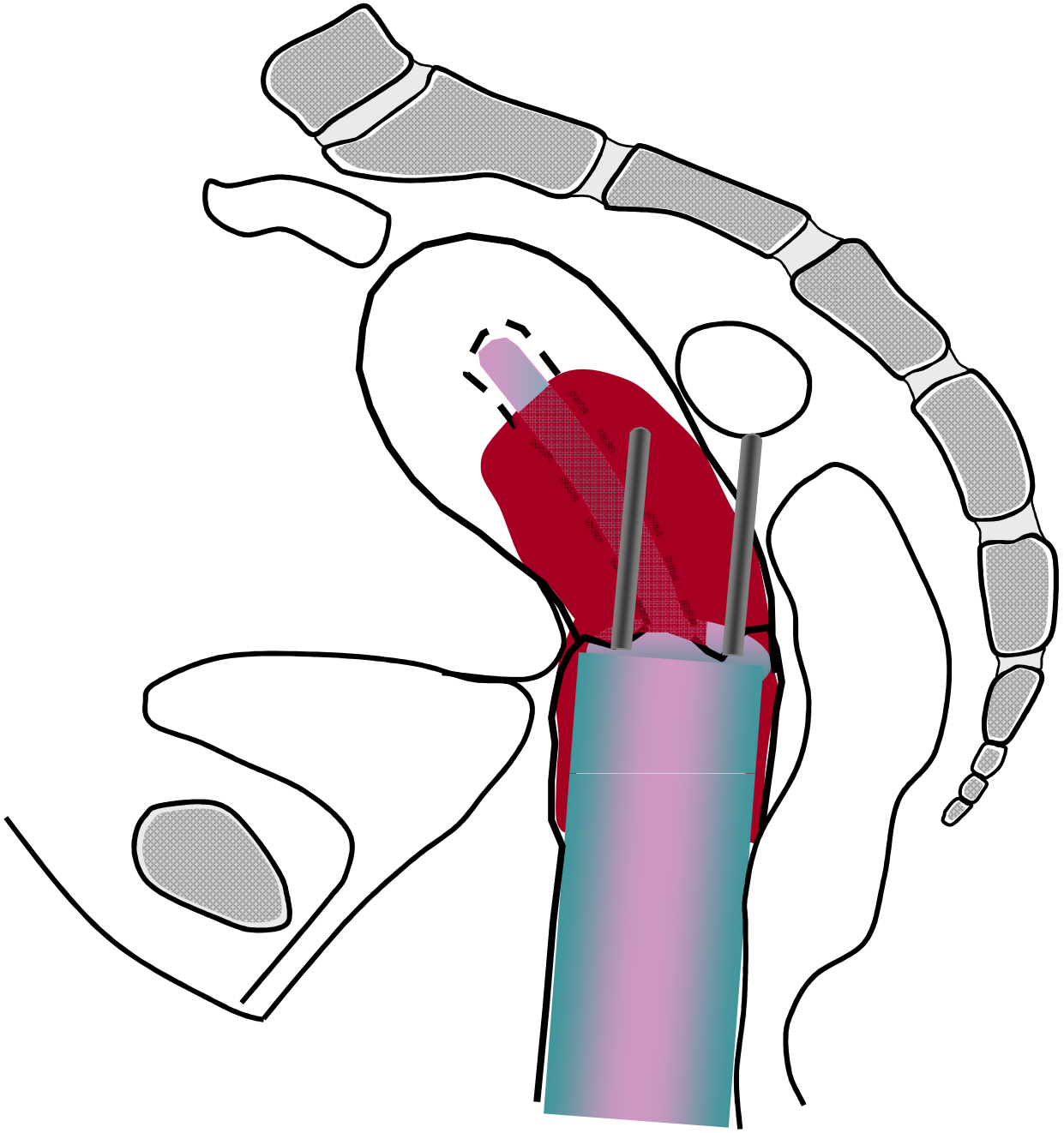
Limitations



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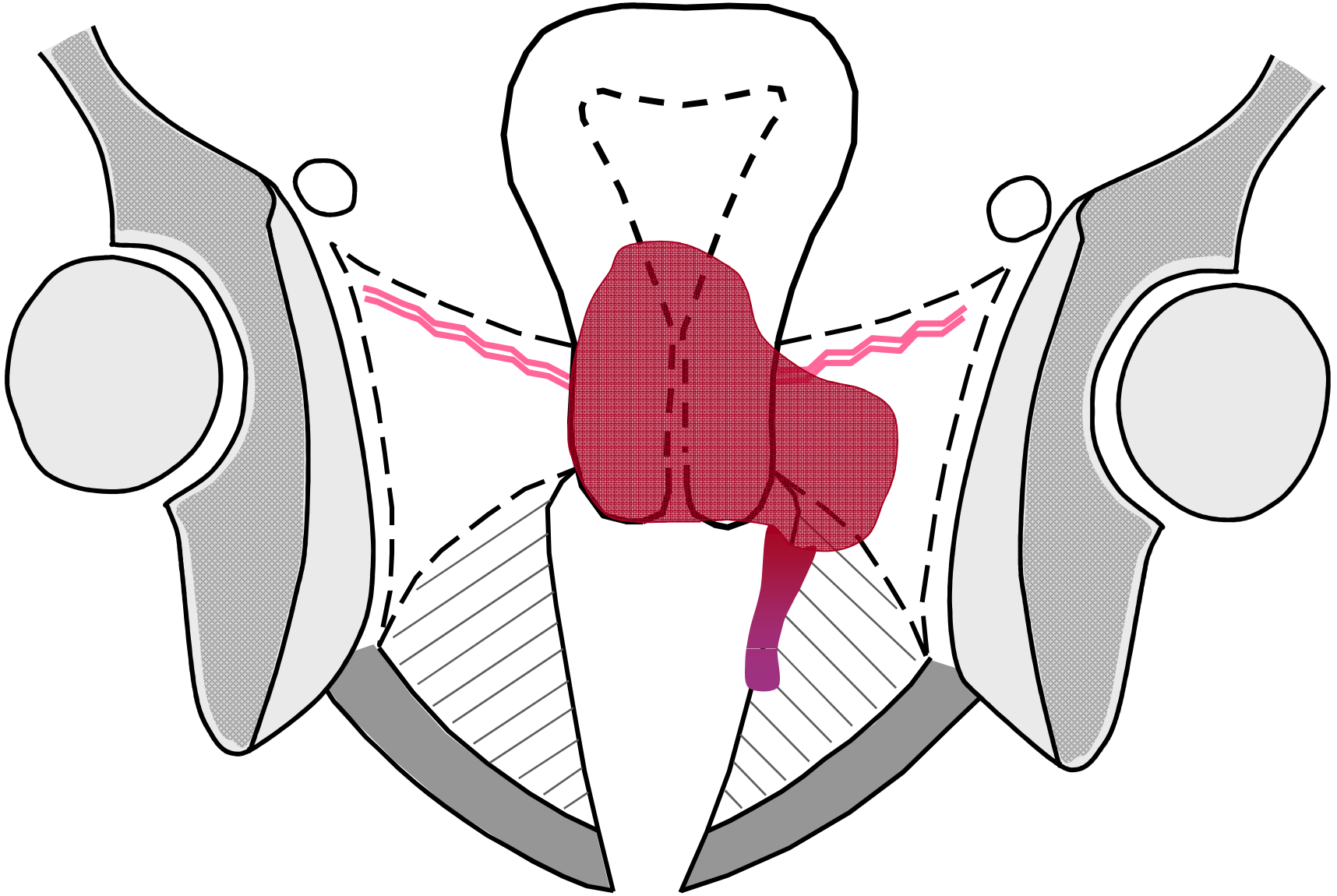
Applicator for distal parametrial disease additional parallel and divergent template guided needles



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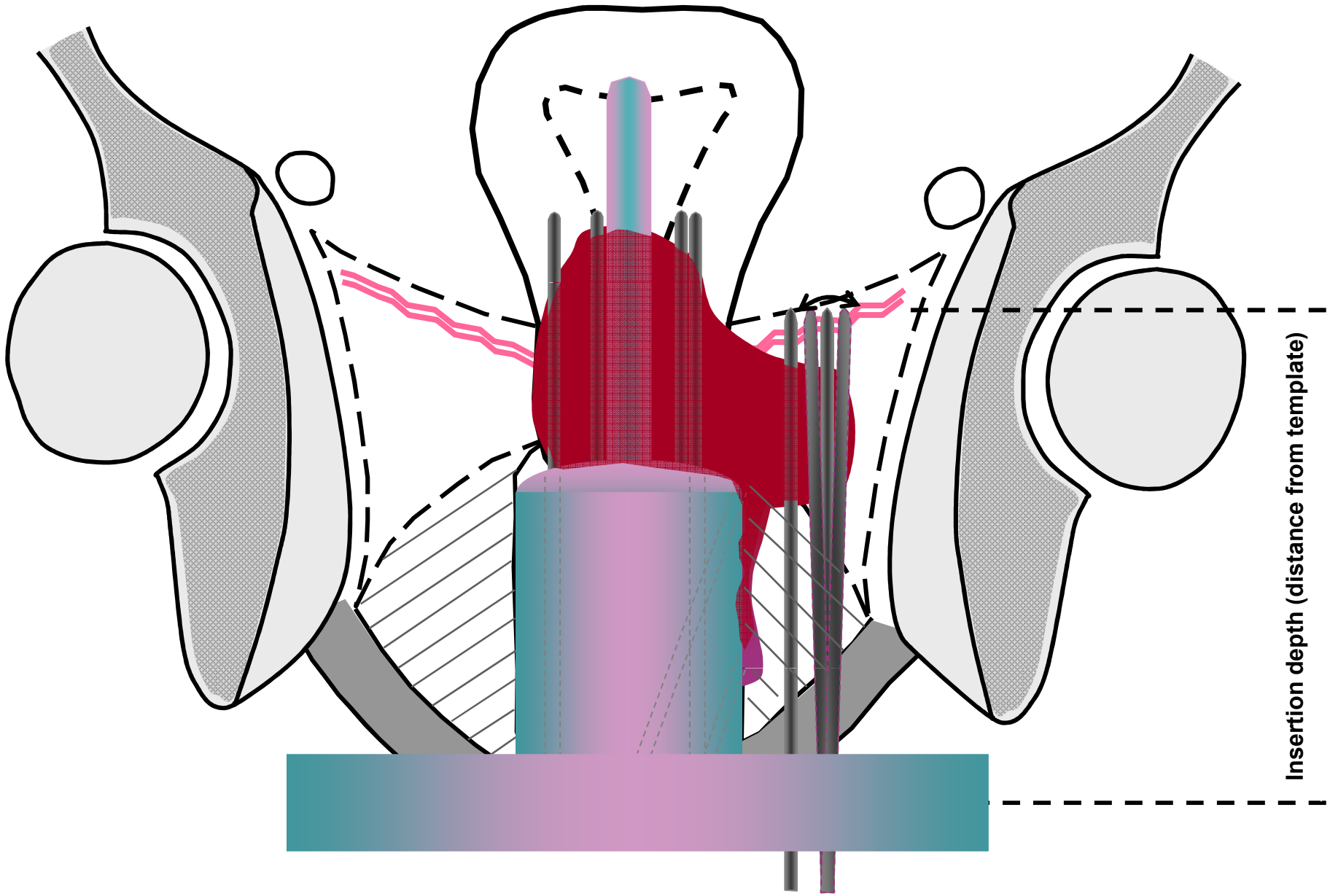
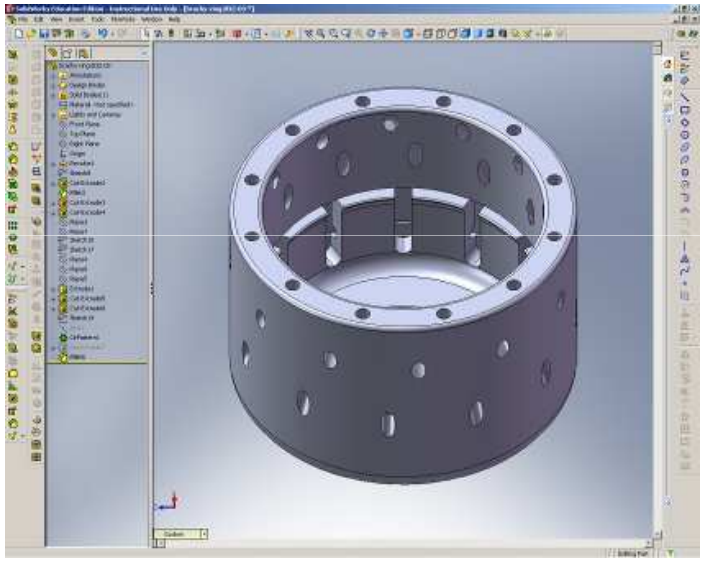
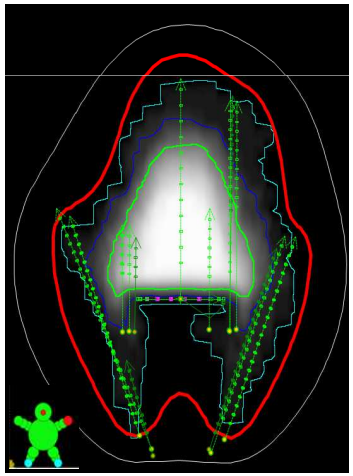

Insertion depth (distance from template)

Adaptive BT applicators

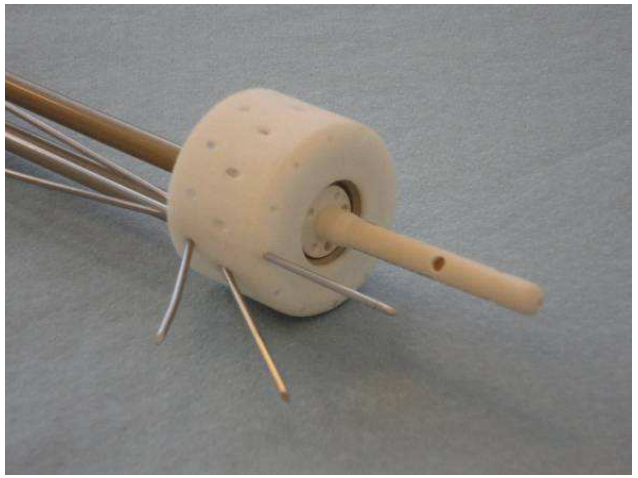
3D Printing

Virtual applicator





New applicator



Provided by Primoz Petric and Jacob Lindegaard Ljubljana/Aarhus

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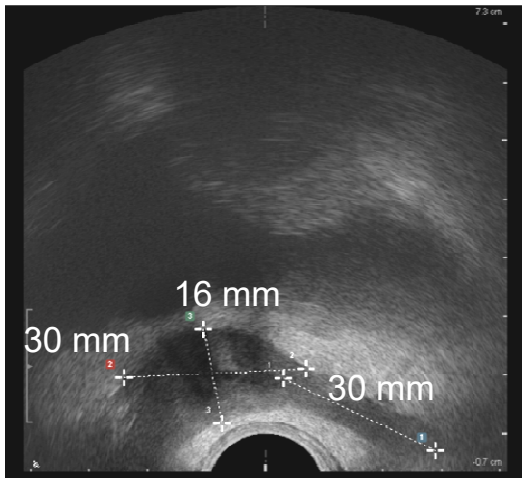
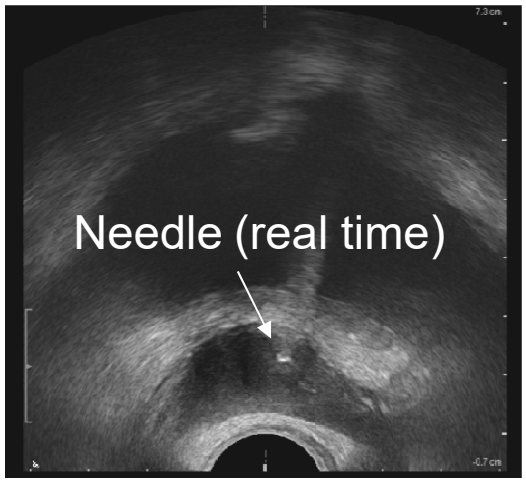
Ultrasound

Findings at Brachytherapy

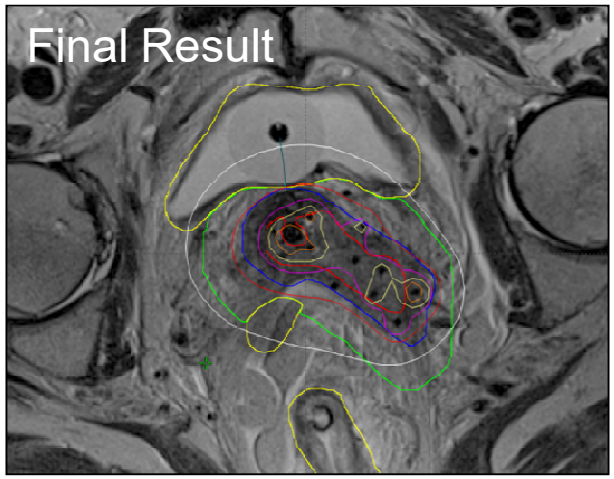
Cervix cancer

Assess Tumour size & Topography





Transrectal Ultrasound



T2W FSE MRI (same patient)

Decide on application technique, Guide insertion, Aid treatment planning

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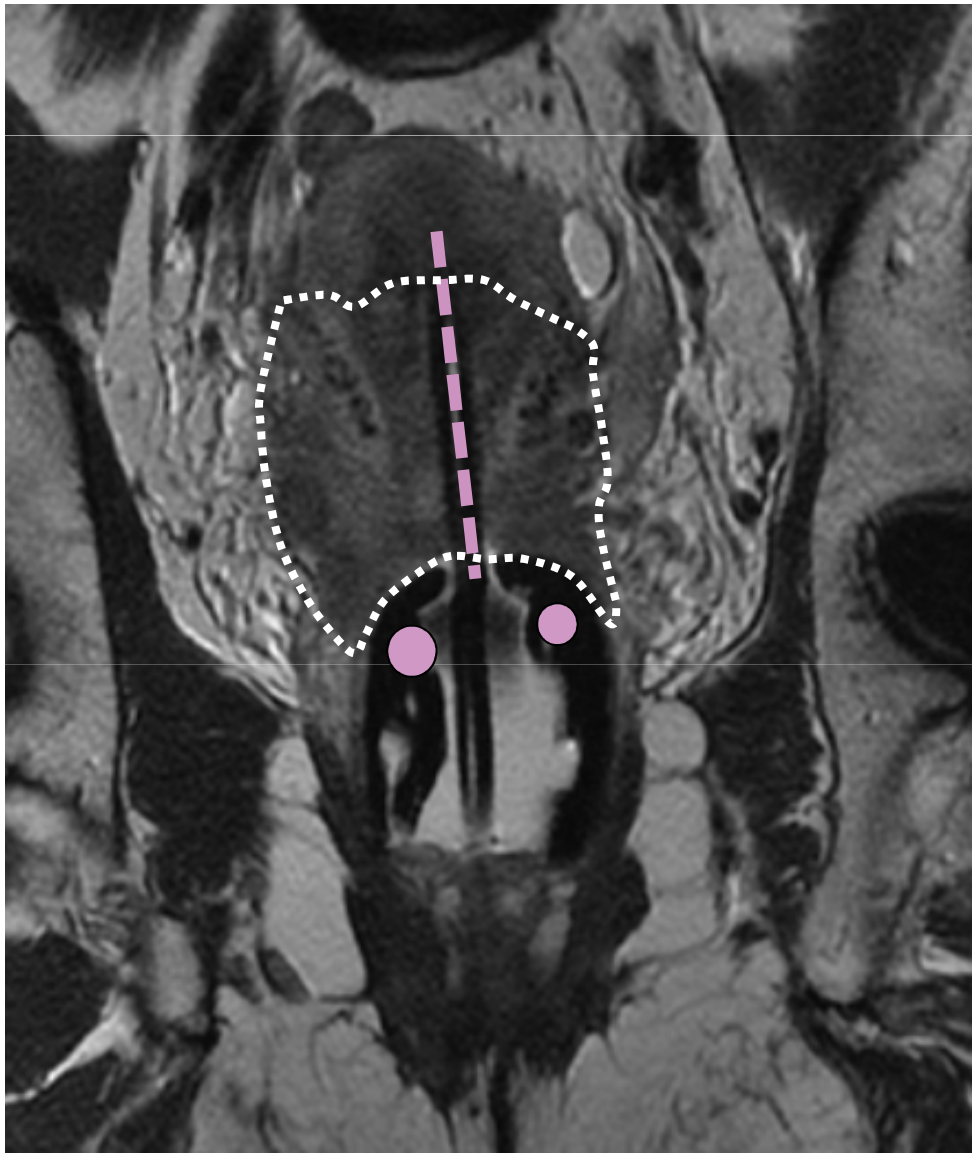
Example from real life / TIP and tricks



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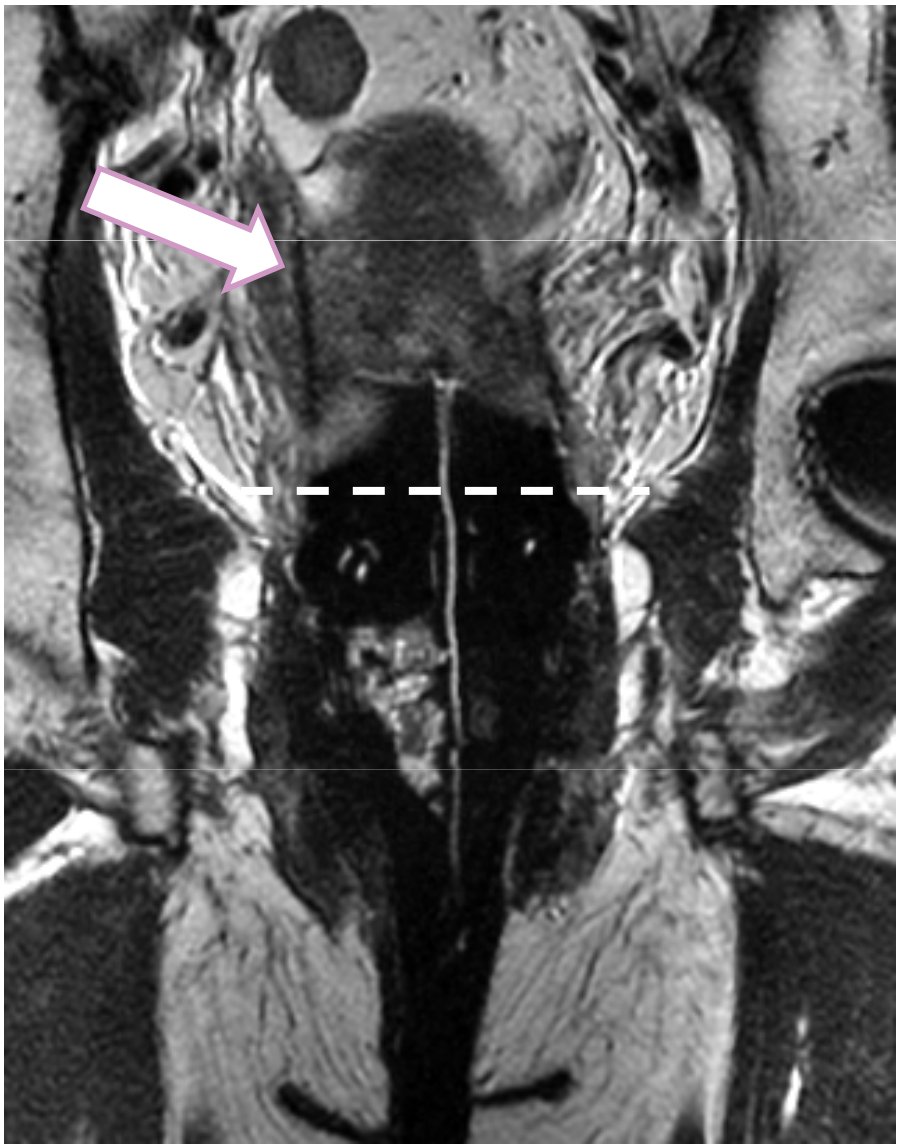
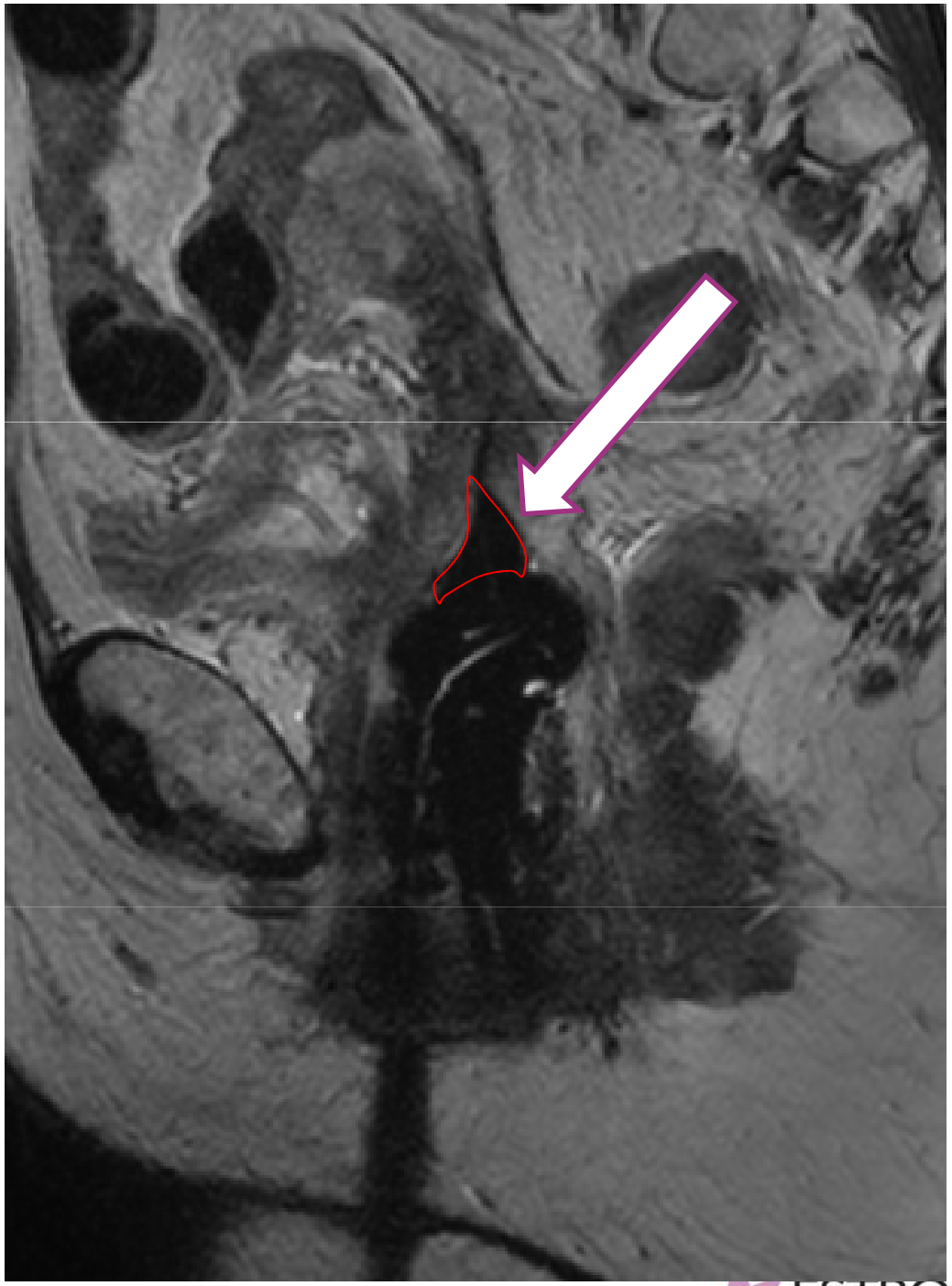
Tips and tricks





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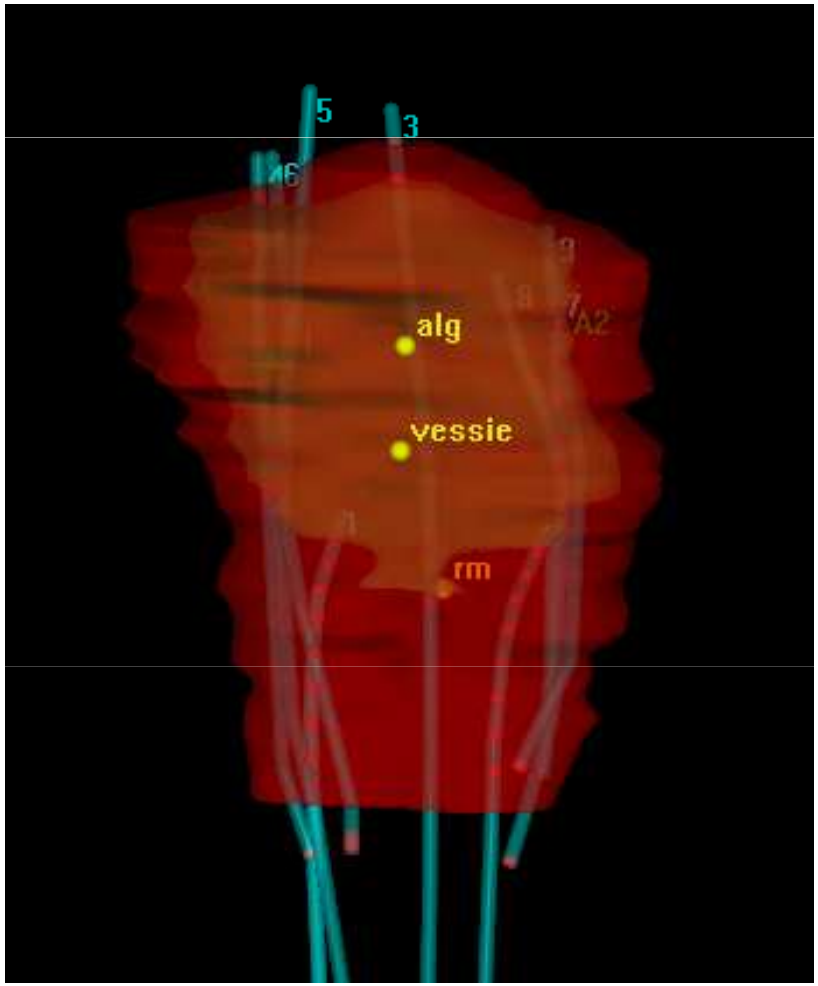
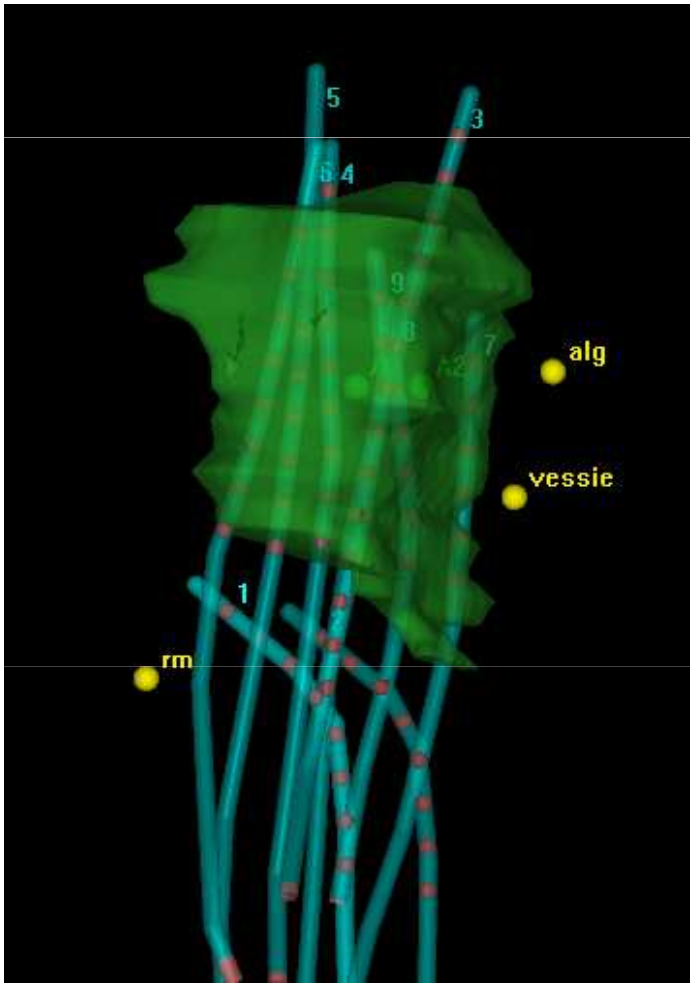
Tip and tricks





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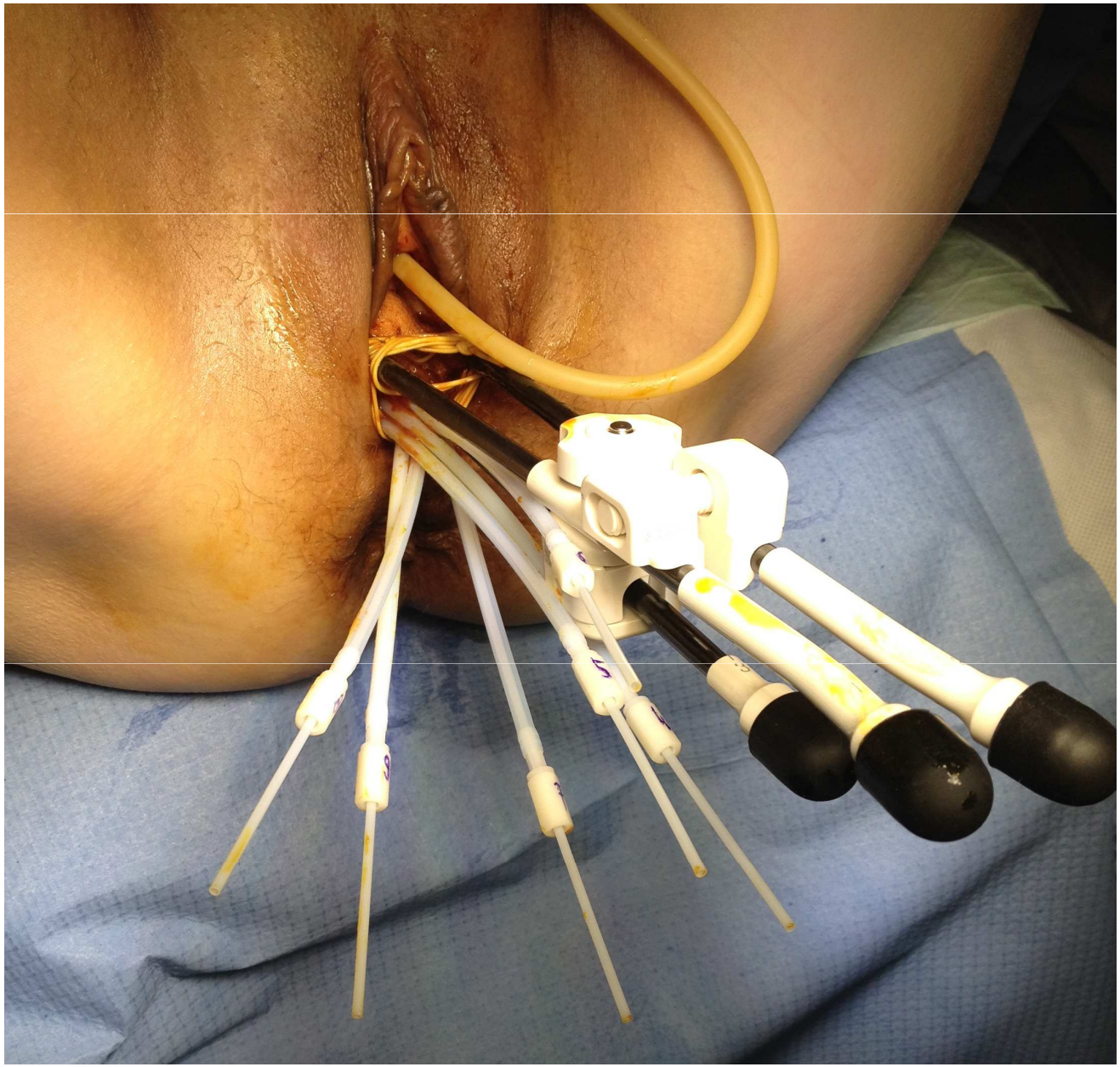
Identification of catheters



Tips and tricks

Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	1	-5.3	90.6	-53.8	1.00	0.00	15.27	
1	2	-6.1	87.8	-49.7	1.00	0.00	15.27	
1	3	-6.9	85.0	-45.7	1.00	0.00	15.27	
1	4	-7.2	81.4	-42.2	1.00	0.00	15.27	
1	5	-7.3	77.4	-39.4	1.00	0.00	15.27	
1	6	-7.3	72.5	-38.4	1.00	0.00	15.27	
1	7	-7.3	67.7	-37.4	1.00	0.00	15.27	
1	8	-7.0	62.7	-36.9	0.53	0.00	8.10	
2	1	22.4	90.6	-47.9	1.00	0.00	15.27	
2	2	21.2	87.9	-43.8	1.00	0.00	15.27	
2	3	20.1	85.2	-39.8	1.00	0.00	15.27	
2	4	19.3	81.5	-36.6	1.00	0.00	15.27	
2	5	18.6	77.2	-34.3	1.00	0.00	15.27	
2	6	18.3	72.3	-33.3	1.00	0.00	15.27	
2	7	17.9	67.5	-32.2	1.00	0.00	15.27	
2	8	17.9	62.5	-31.7	0.53	0.00		
3	1	2.6	147.6	-34.0	0.53			
3	2	3.1	142.7	-35.1				
3	3	3.6	137.9					
3	4	4.2						
3	5							
3	6							
3	7							
3	8							1.73
3	9							1.41
3	10							1.41
3	11							1.41
3	12							1.41
3	13							
3	14	8.						

Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
4	1	-16.2	138.6	-44.9	0.25	0.00	3.78	
4	2	-16.0	133.6	-44.7	0.25	0.00	3.78	
4	3	-15.9	128.6	-44.3	0.25	0.00	3.78	
4	4	-15.8	123.7	-43.6	0.25	0.00	3.78	
4	5	-15.5	118.8	-43.0	0.25	0.00	3.78	
4	6	-15.1	113.8	-42.4	0.25	0.00	3.78	
4	7	-14.7	108.9	-41.7	0.25	0.00	3.78	
4	8	-14.3	103.9	-41.9	0.25	0.00	3.78	
4	9	-14.0	98.9	-42.1	0.25		3.78	
5	6	-11.1	122.7	-47.1			3.78	
5	7	-11.6	117.7				3.78	
5	8							
5	9							
5								
							5.94	
						0.00	5.94	
					0.25	0.00	3.78	
				-51.5	0.25	0.00	3.78	
			104.2	-52.6	0.25	0.00	3.78	
			-12.4	99.3	-53.7	0.25	0.00	3.78
7	1	25.2	123.6	-33.8	0.25	0.00	3.78	
7	2	25.2	118.6	-33.5	0.25	0.00	3.78	
7	3	25.5	113.6	-33.5	0.25	0.00	3.78	
7	4	25.8	108.6	-33.5	0.25	0.00	3.78	
7	5	26.1	103.6	-33.5	0.25	0.00	3.78	
7	6	26.3	98.7	-33.5	0.25	0.00	3.78	
8	1	18.0	123.8	-42.1	0.25	0.00	3.78	
8	2	19.6	119.1	-41.3	0.25	0.00	3.78	
8	3	21.5	114.6	-40.7	0.25	0.00	3.78	
8	4	23.5	110.0	-40.0	0.25	0.00	3.78	
8	5	25.0	105.3	-39.4	0.25	0.00	3.78	
8	6	26.4	100.5	-39.4	0.25	0.00	3.78	
9	1	23.6	129.7	-45.1	0.25	0.00	3.78	
9	2	24.2	124.8	-44.3	0.25	0.00	3.78	
9	3	24.8	119.9	-43.7	0.25	0.00	3.78	
9	4	25.9	115.0	-44.3	0.25	0.00	3.78	
9	5	26.8	110.2	-44.9	0.25	0.00	3.78	

The intracavitary component should remain predominant!

20%

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Vaginal primaries and recurrences

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Interstitial Techniques Vagina
General Principles

- *Primary vaginal tumors = **rare cancers***
  2% of gynaecological malignancies
- *No prospective randomized trial assessing the role of concomitant chemoradiation*
- *No prospective randomized trial **comparing endocavitary and interstitial techniques***

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Interstitial techniques vaginal cancer

- **Usually combined with external irradiation (45 Gy)**
- **Tumor location and morphology**
- **Tumor extension:**
  - **–at the time of diagnosis**
  - **–at the time of brachytherapy**
- **Thickness**
- **Contra-indication : +/- rectovaginal septum extension**

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Interstitial Techniques Vagina

Importance of initial work-up

Assessment of initial tumor extension with vaginal impression

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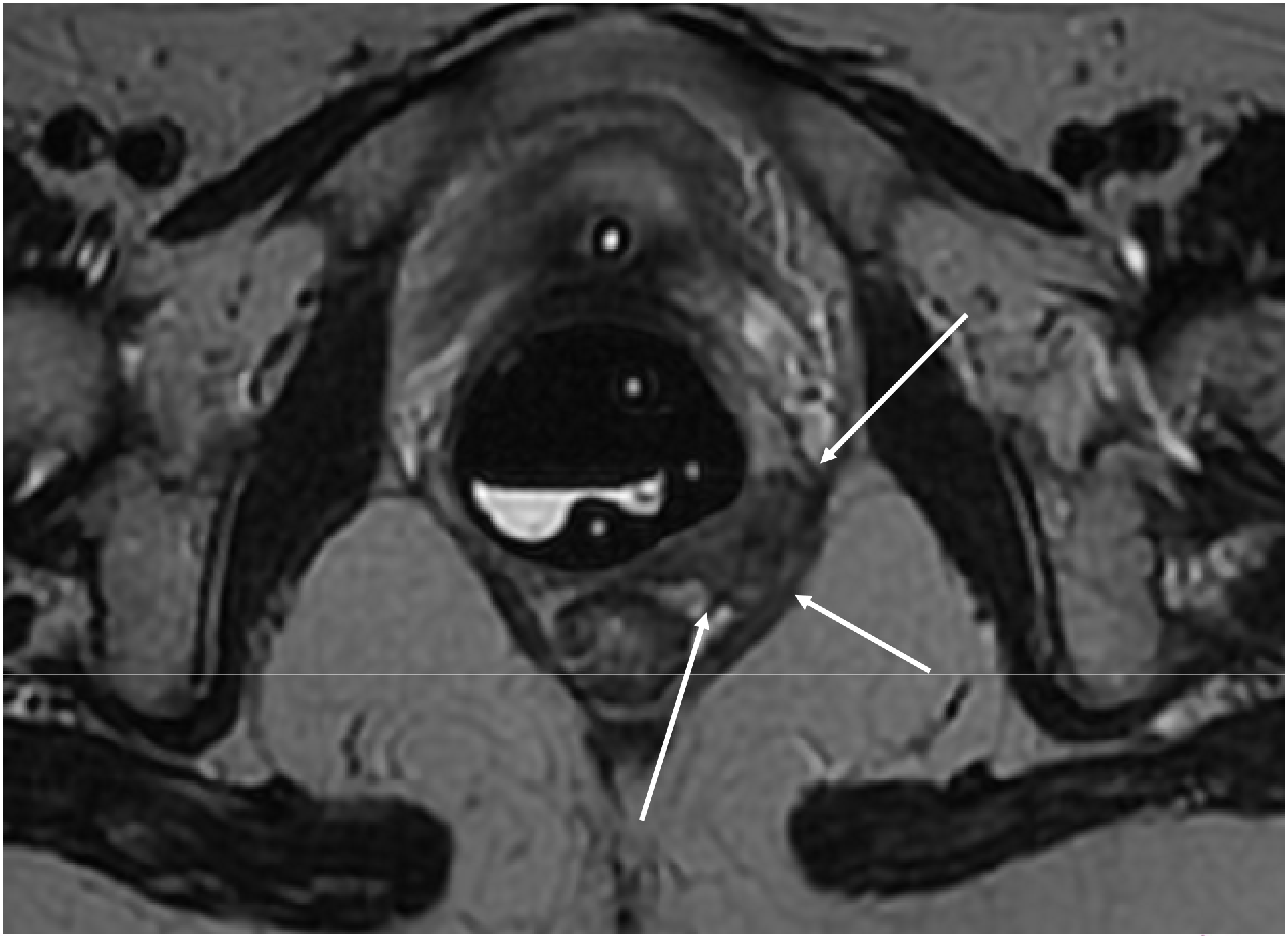

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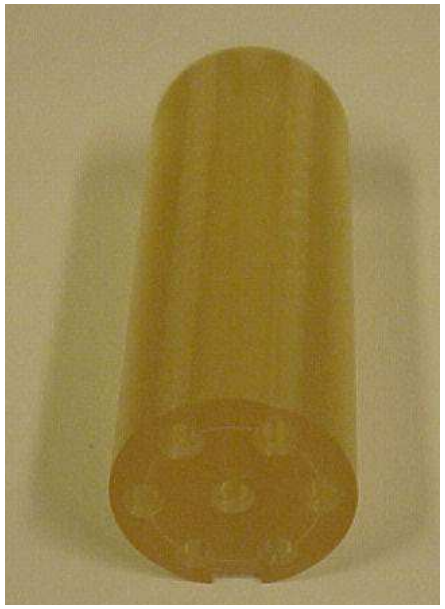
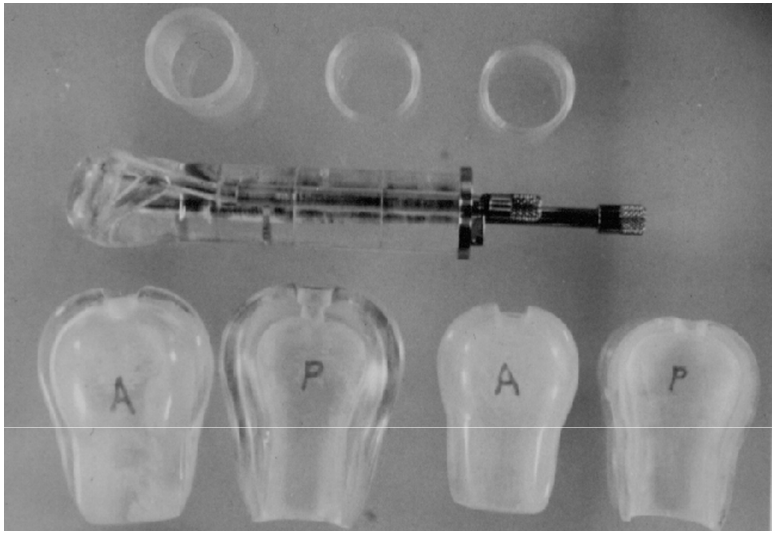
Interstitial Techniques Vagina

Intracavitary Techniques

Cylinder



Miralva applicator



Vaginal mould

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Interstitial Techniques Vagina

Limitations of pure intracavitary techniques

- *para-vaginal tumor growth*
- *para-metrial tumor growth*
- *middle/distal para-vaginal tumor extension*
- *unfavourable topography of organs at risk* ***(not predictable)***
- *patients with anatomy not allowing intracavitary brachytherapy with standard applicators*

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Interstitial Techniques Vagina

Indications

- *locally advanced disease*
  - *extensive vaginal disease*
  - *paravaginal invasion*
  - *parametrial invasion*
- *bad response after chemoradiation*
  Residual disease beyond 0.8 - 1 cm of the applicator surface
- *anatomy not allowing intracavitary BT with standard applicators*
- *vaginal recurrences: endometrium, cervix etc.*

Interstitial techniques vaginal cancer

- Transperineal templates :
  - Syed- Neblett applicator
  - MUPIT…
- Intra-vaginal templates
- Plastic tube
- Steel needles

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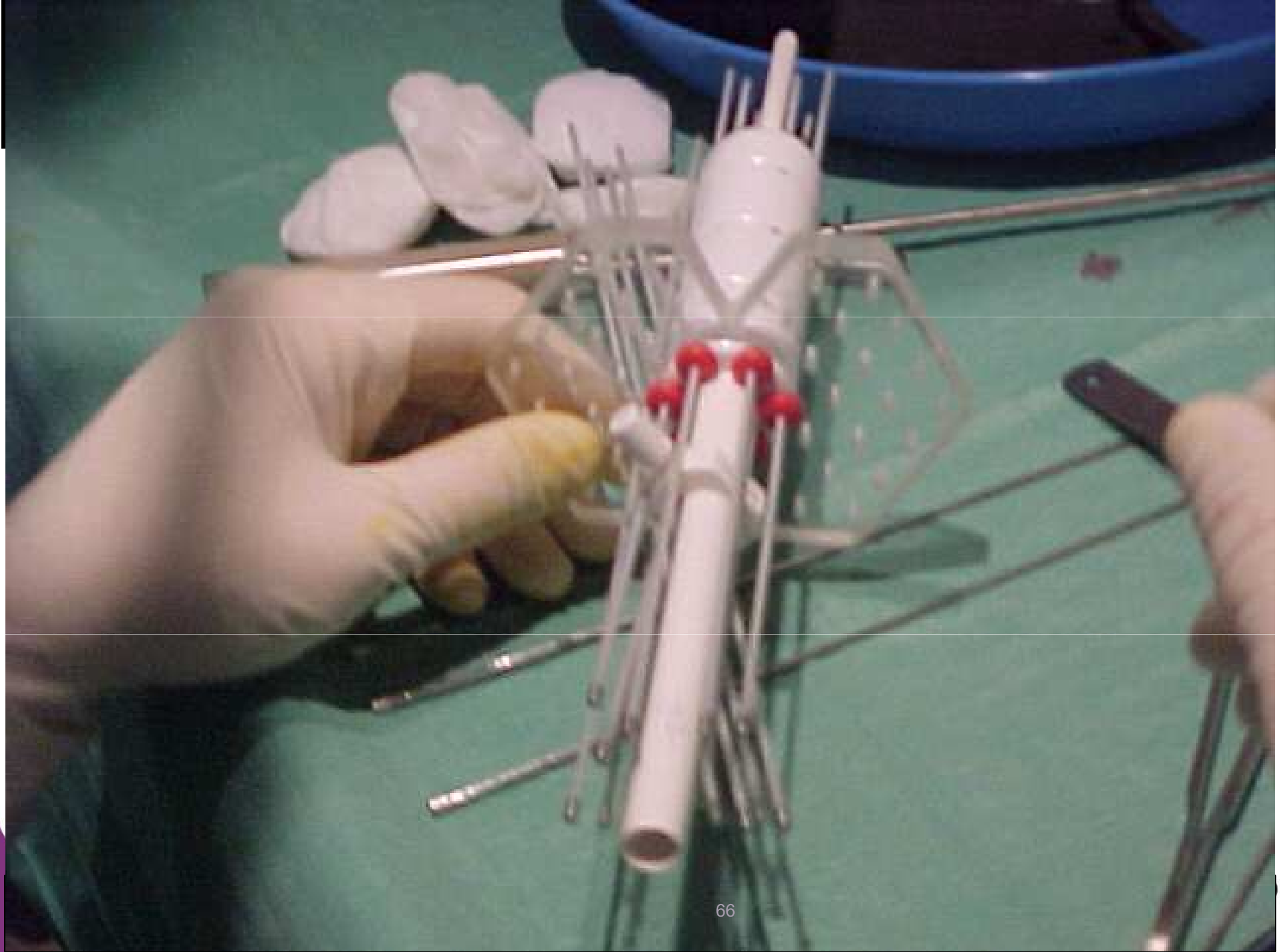
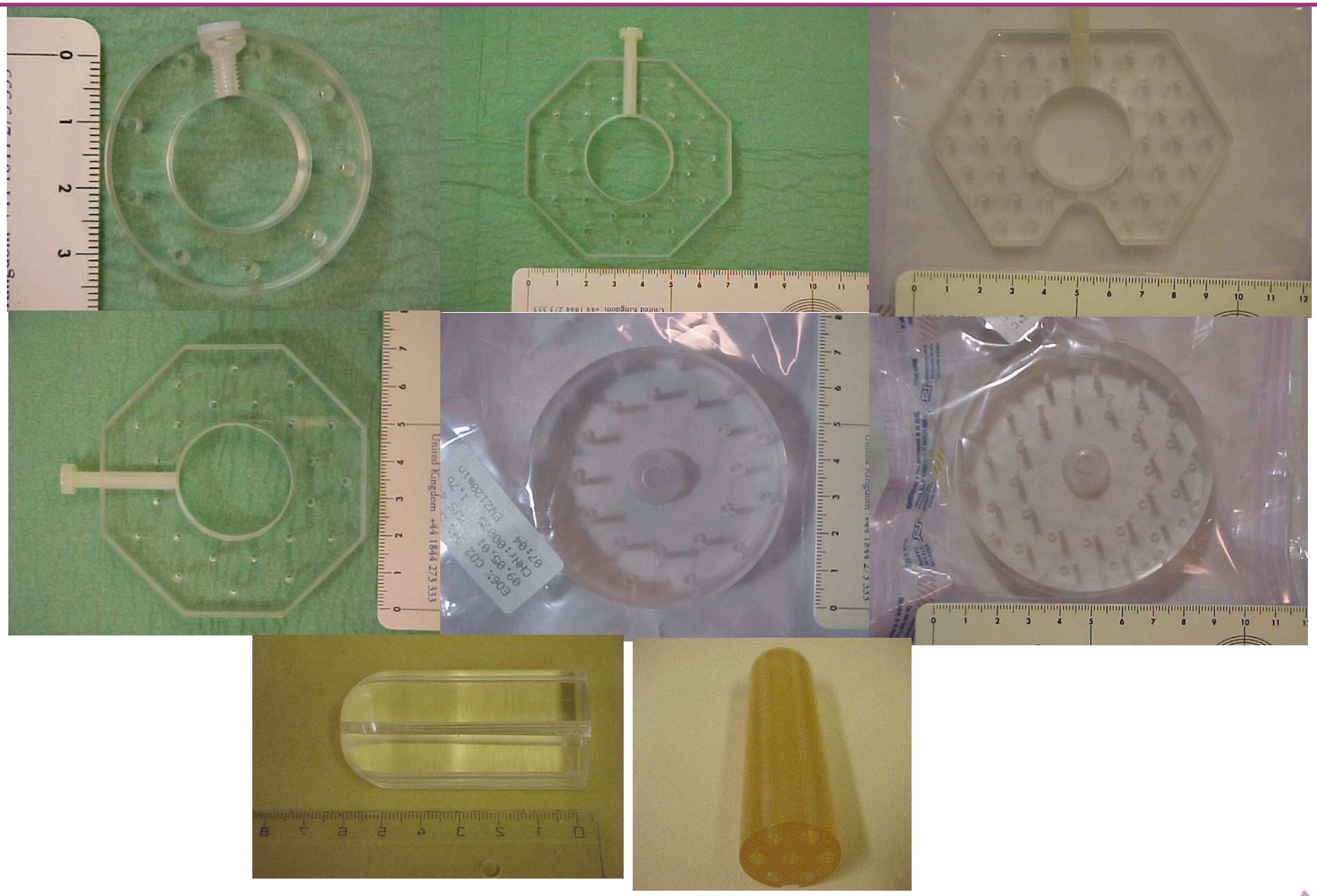


Interstitial Techniques Vagina

Techniques – Perineal templates



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Interstitial Techniques Vagina

Selection of application technique

Based on clinical examination and sectional imaging:

- *At the time of diagnosis*

  -initial tumor extension

- *During EBRT*

  -Quantitative and qualitative tumor regression

- *At the time of brachytherapy*

  -Topography of tumor in relation to the applicator

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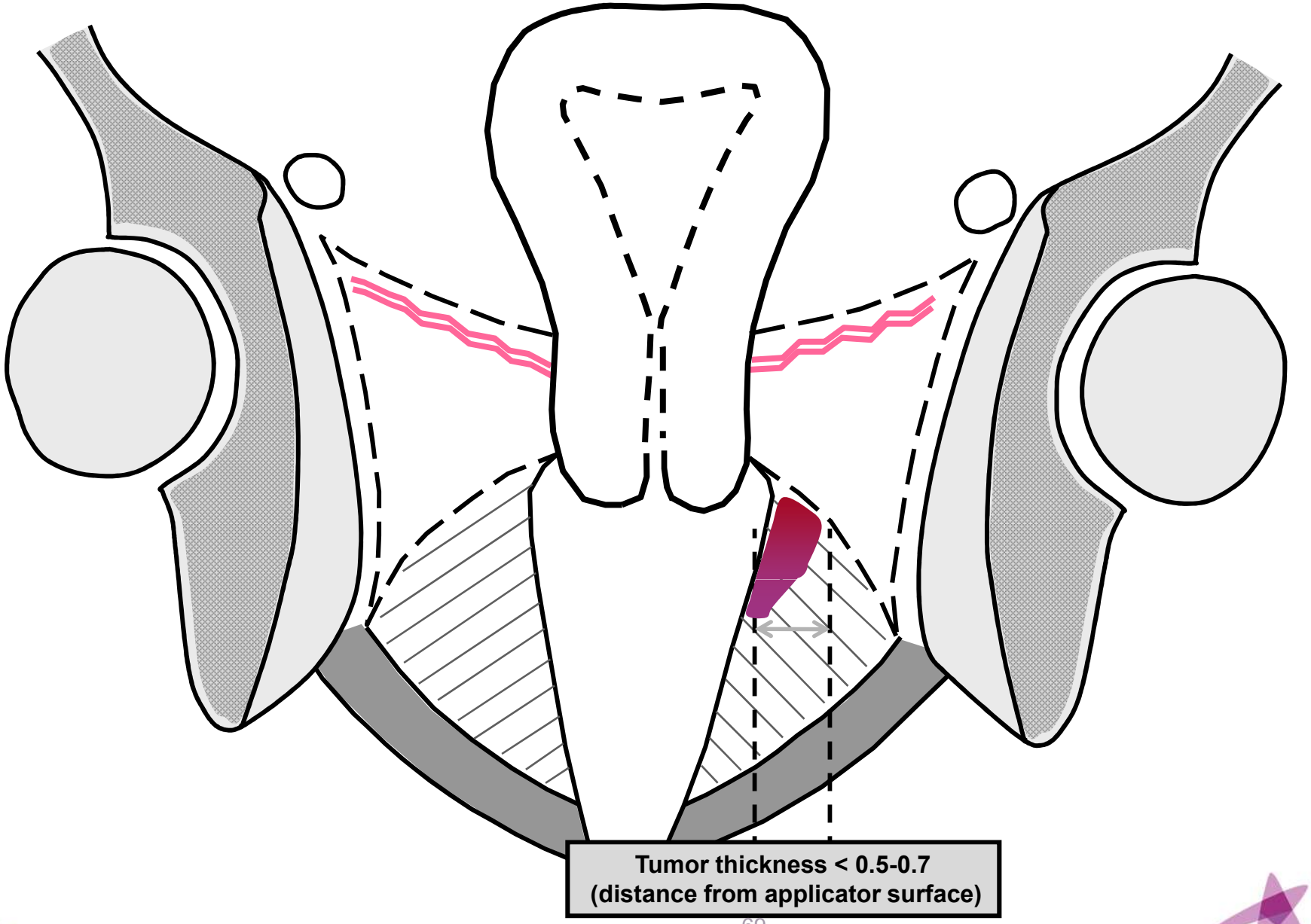
Interstitial Techniques Vagina

Pattern of tumor regression



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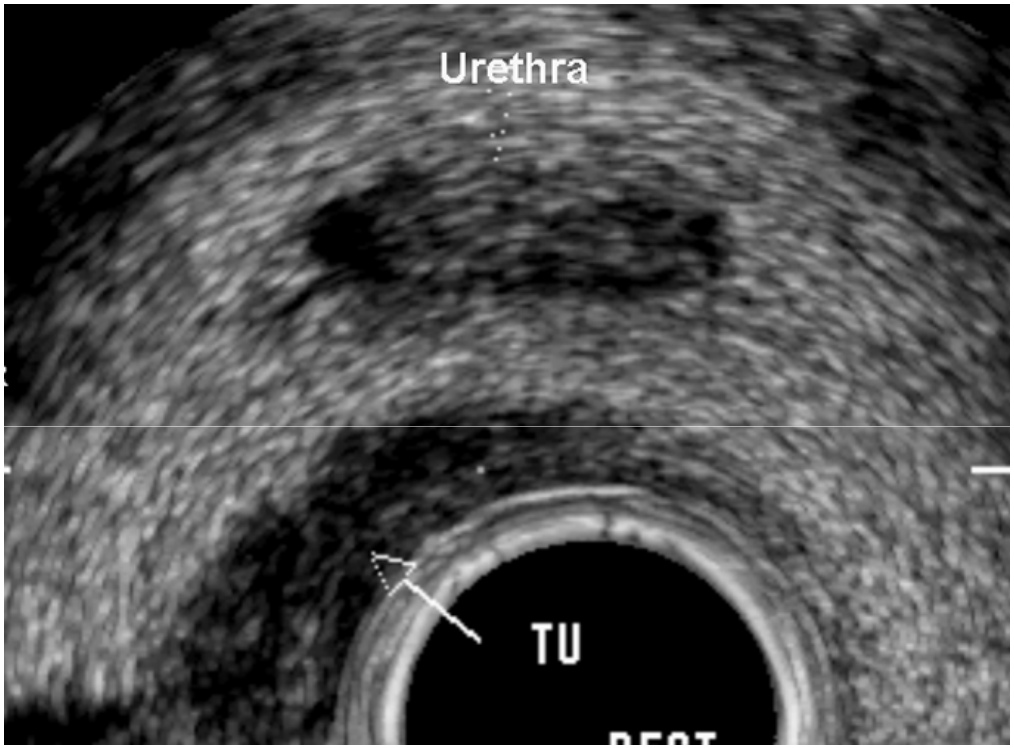
Importance of initial work-up

Assessment of tumor thickness with endosonography

decisive for selection of appropriate application technique



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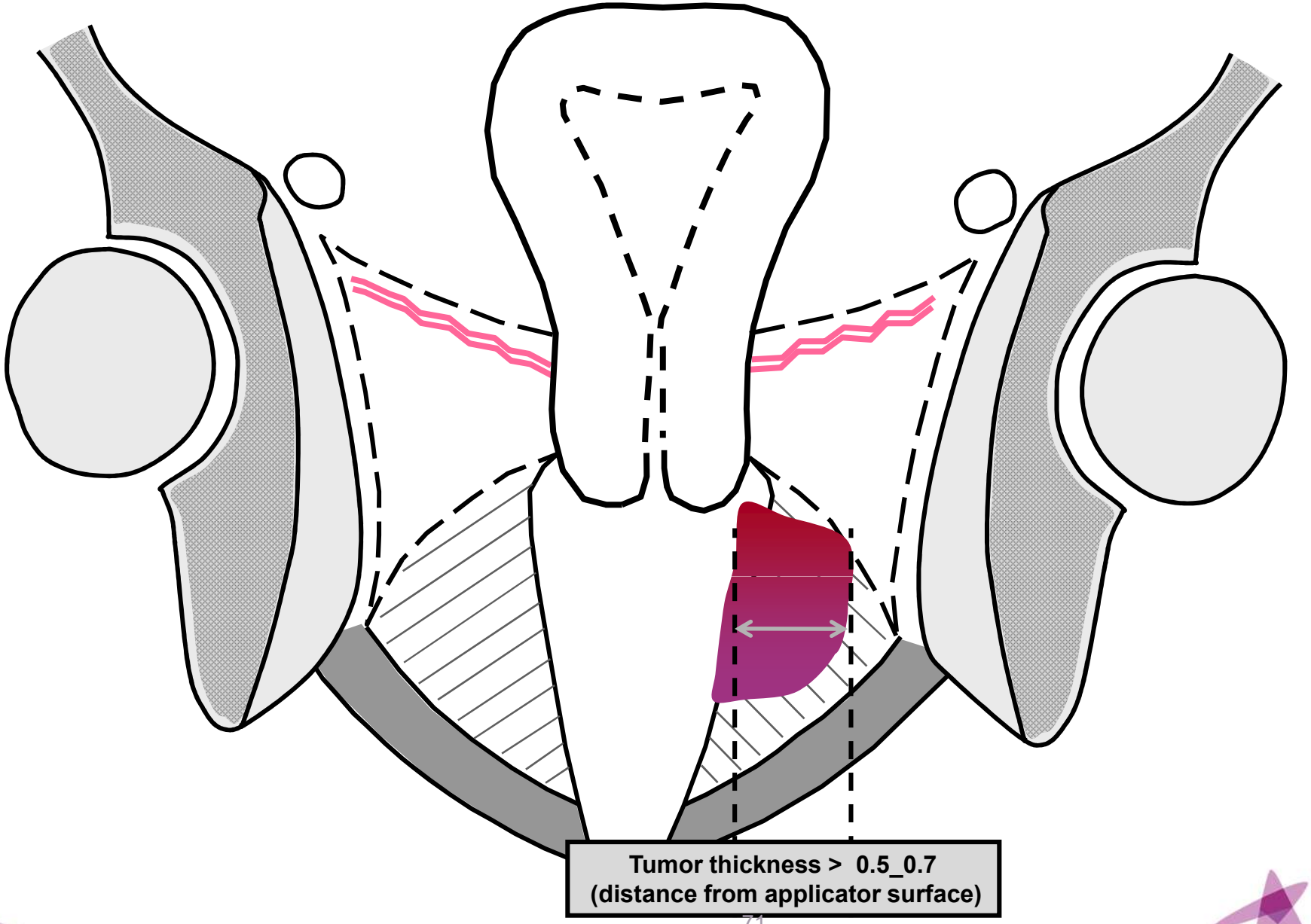
Interstitial Techniques Vagina

Pattern of tumor regression



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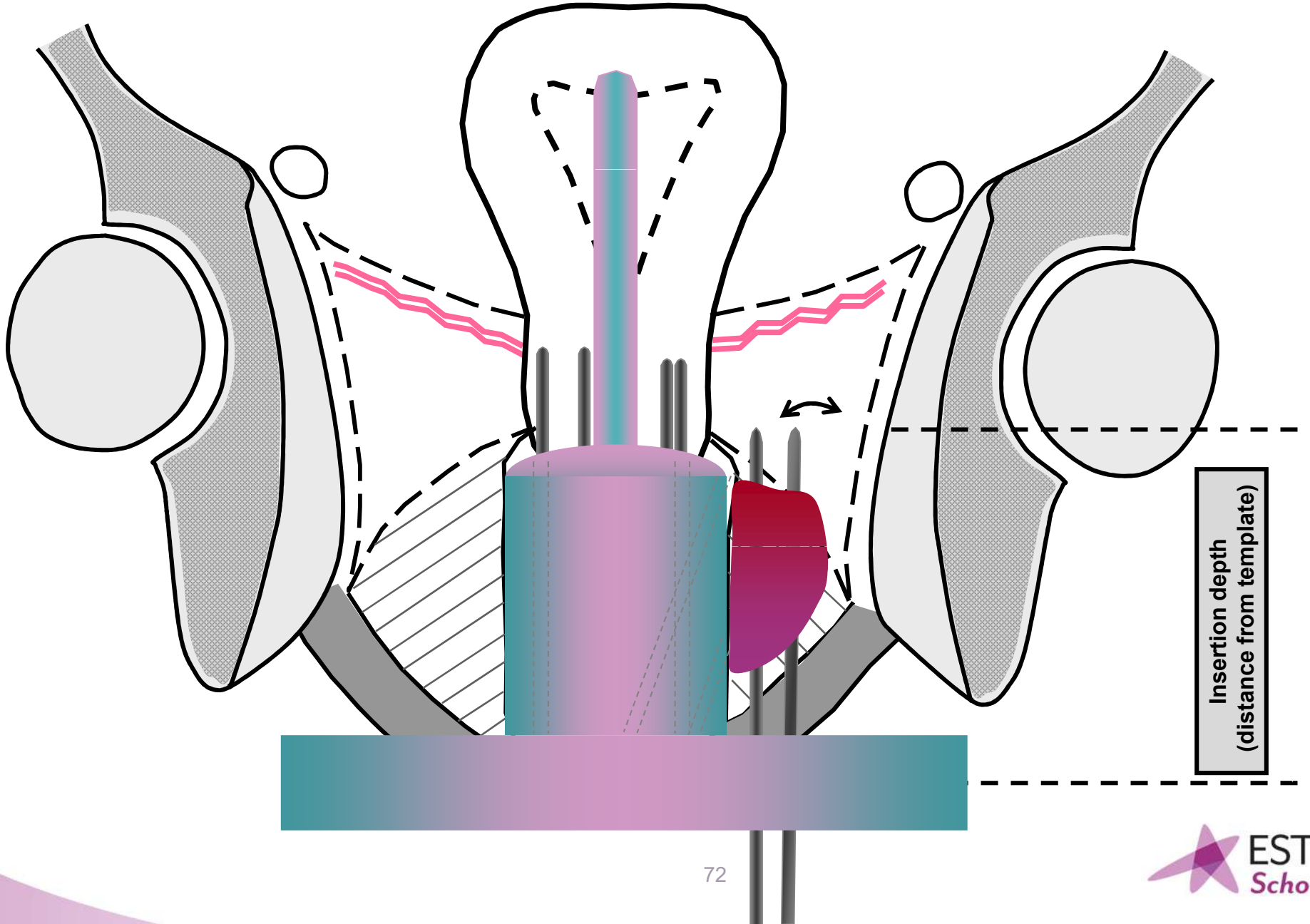
Interstitial Techniques Vagina

Pattern of tumor regression



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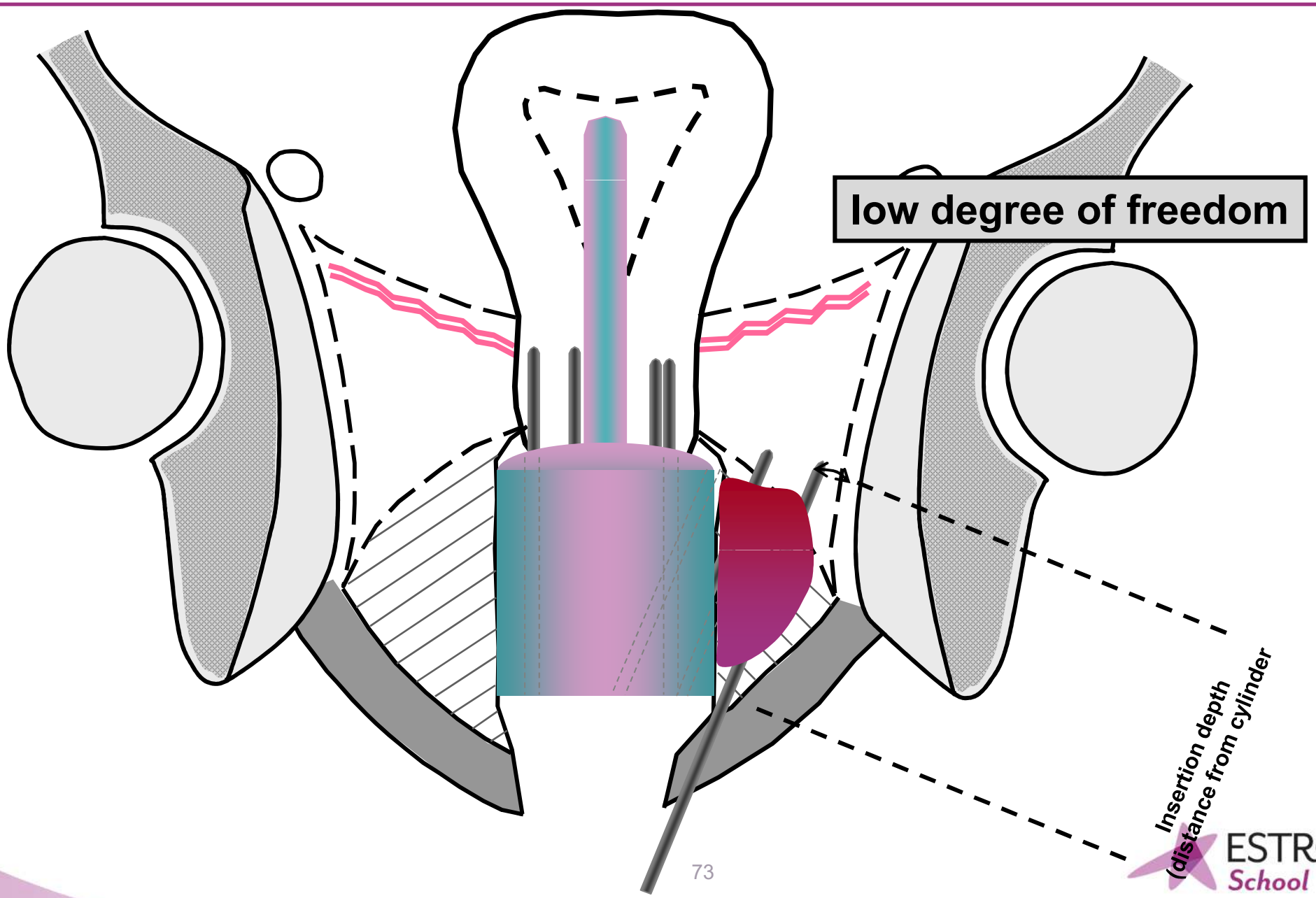
Interstitial Techniques Vagina

Pattern of tumor regression



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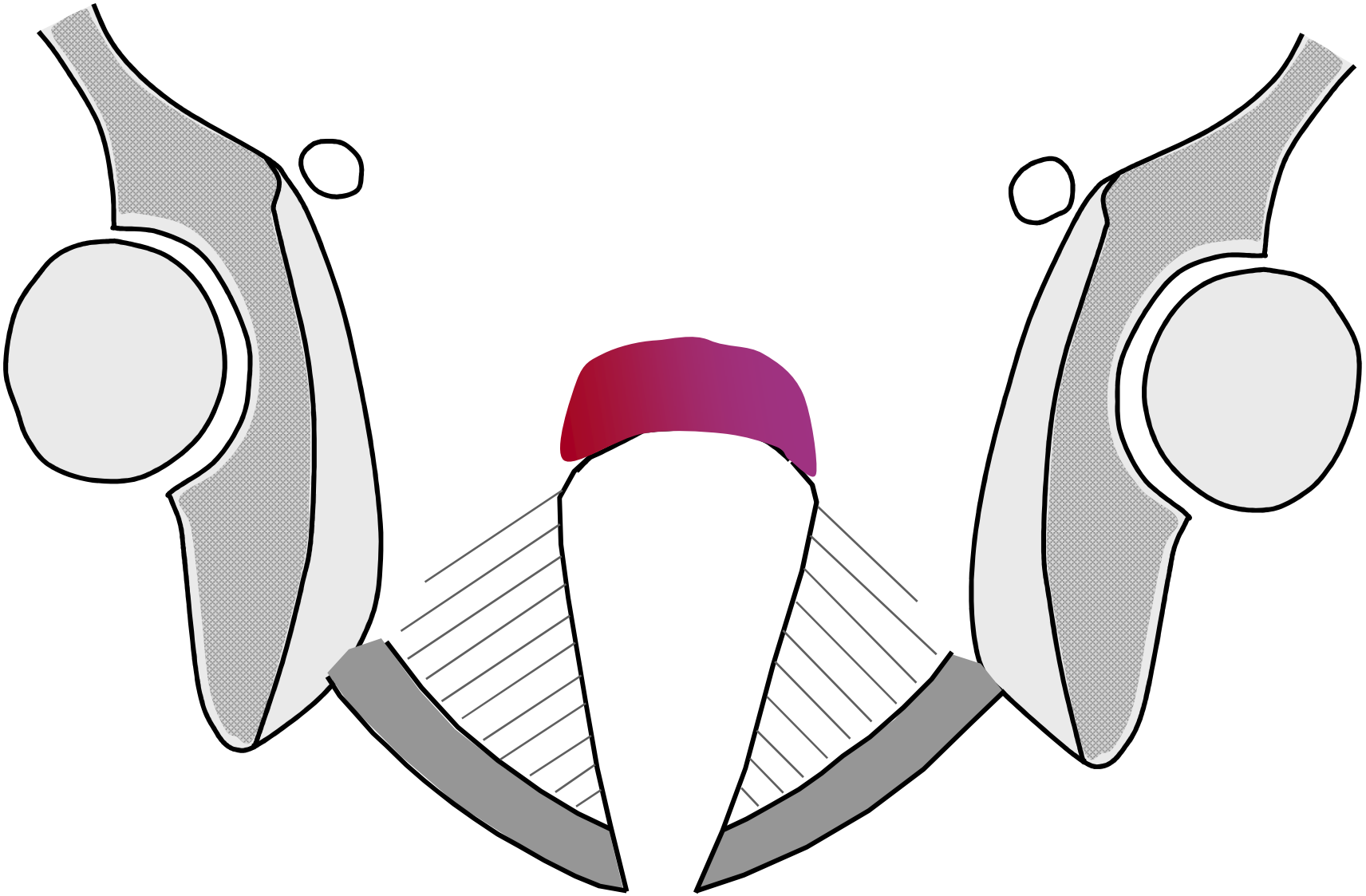
Interstitial Techniques Vagina

Vaginal Cuff



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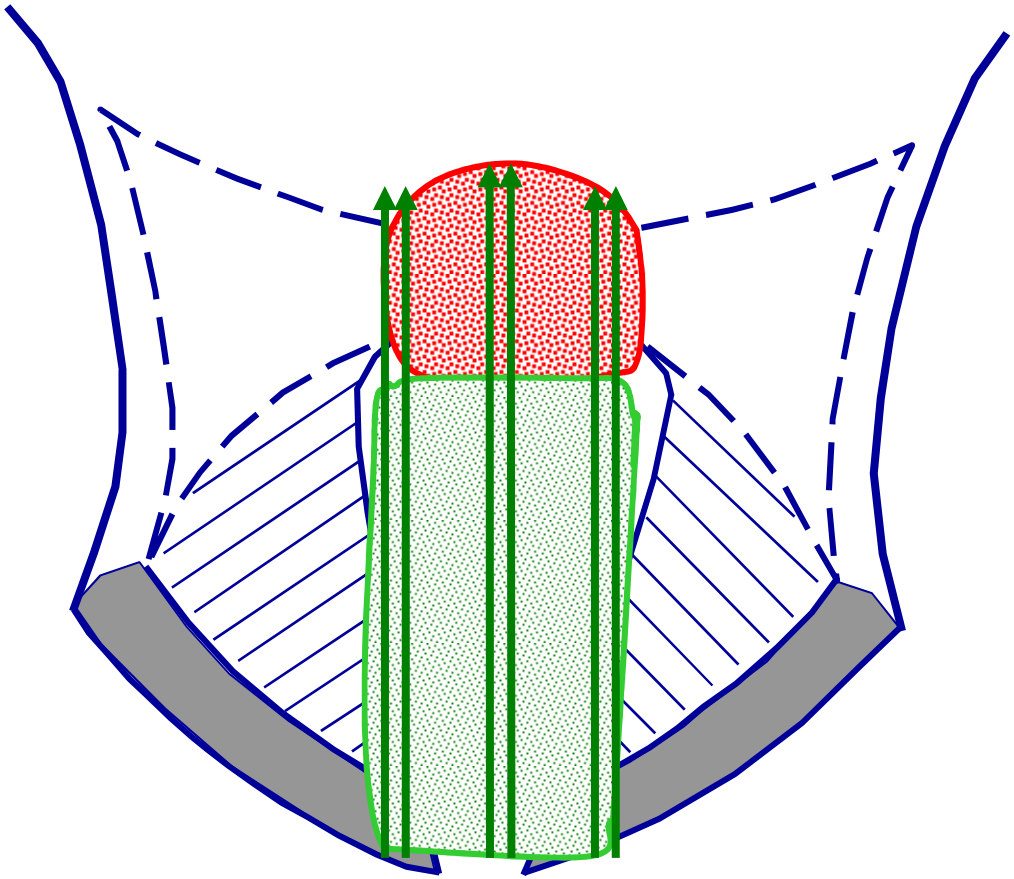
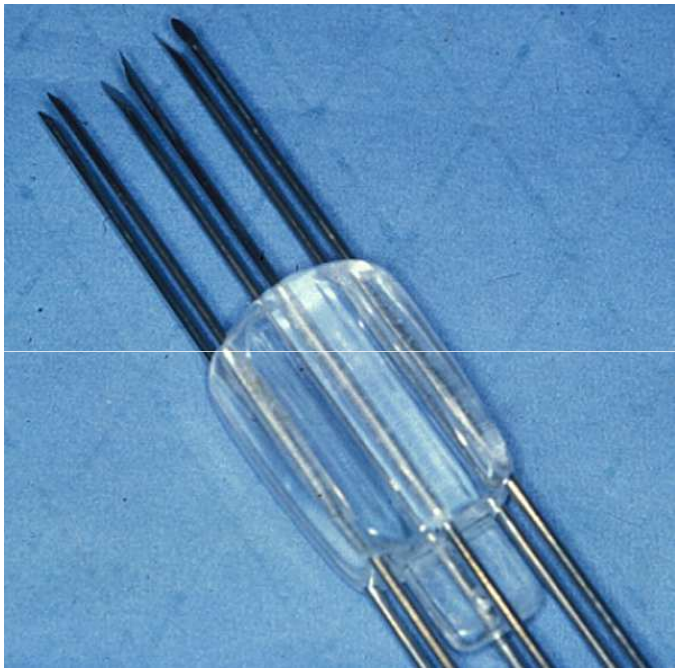
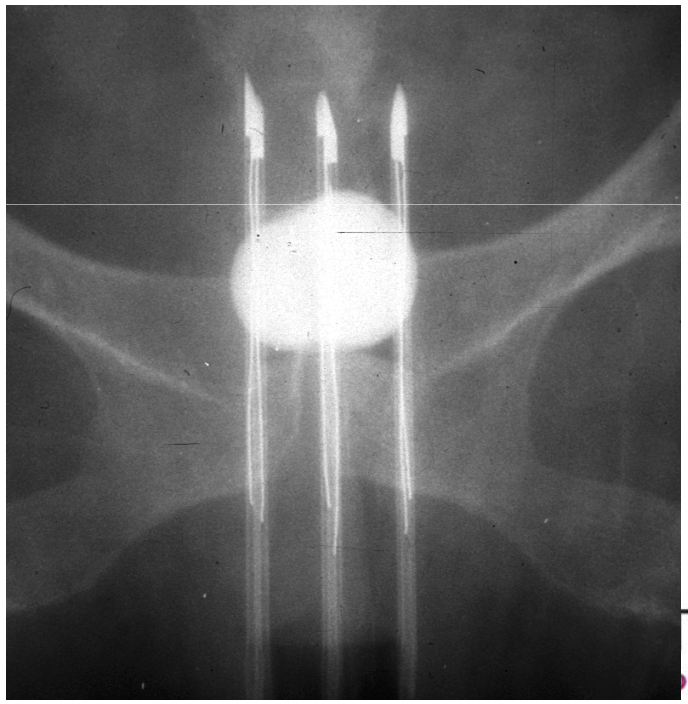
Apical tumors
> 10 mm thickness

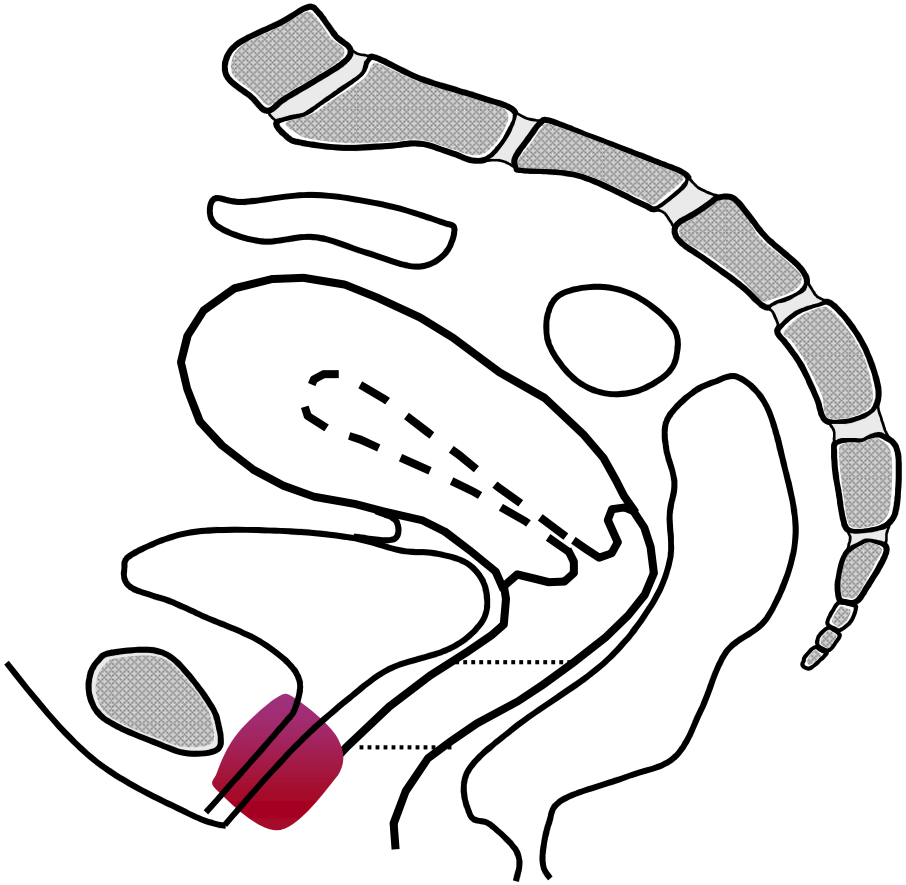




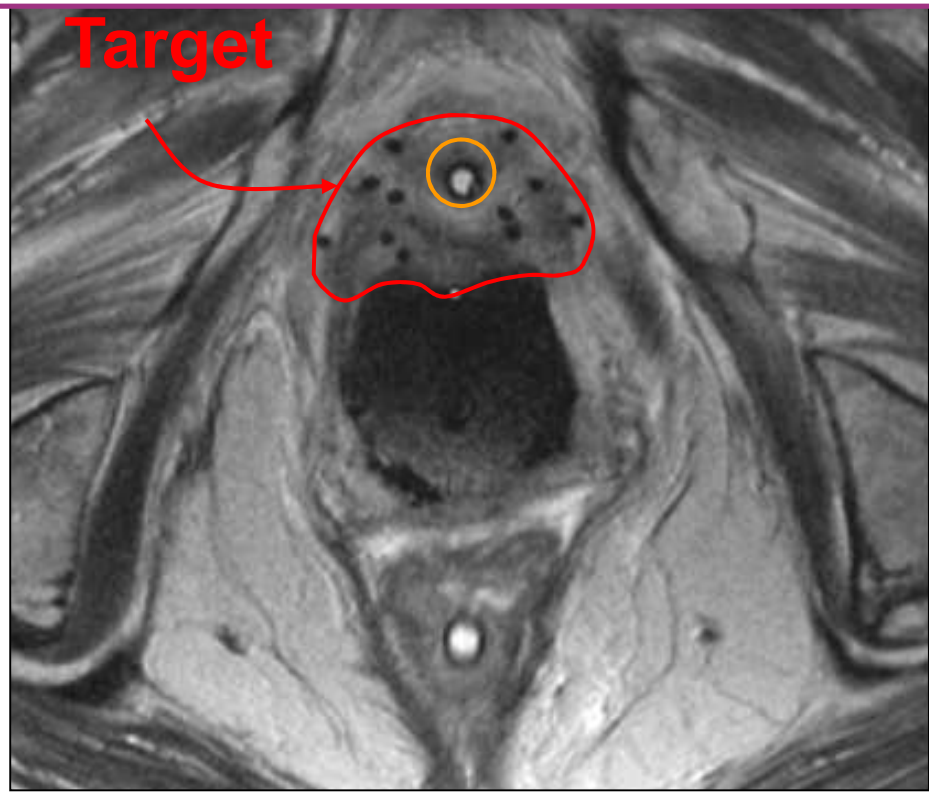


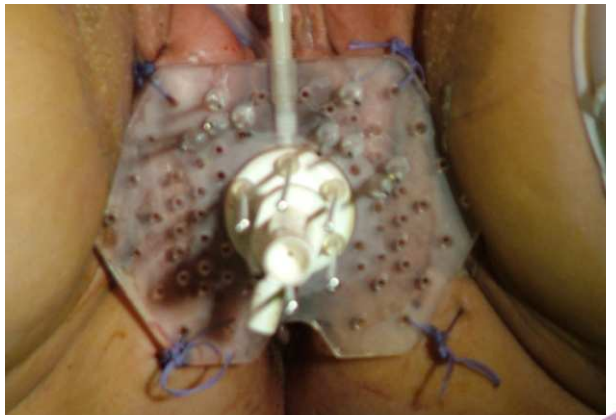
Interstitial Techniques Vagina

Pattern of tumor regression



Suburethral tumour





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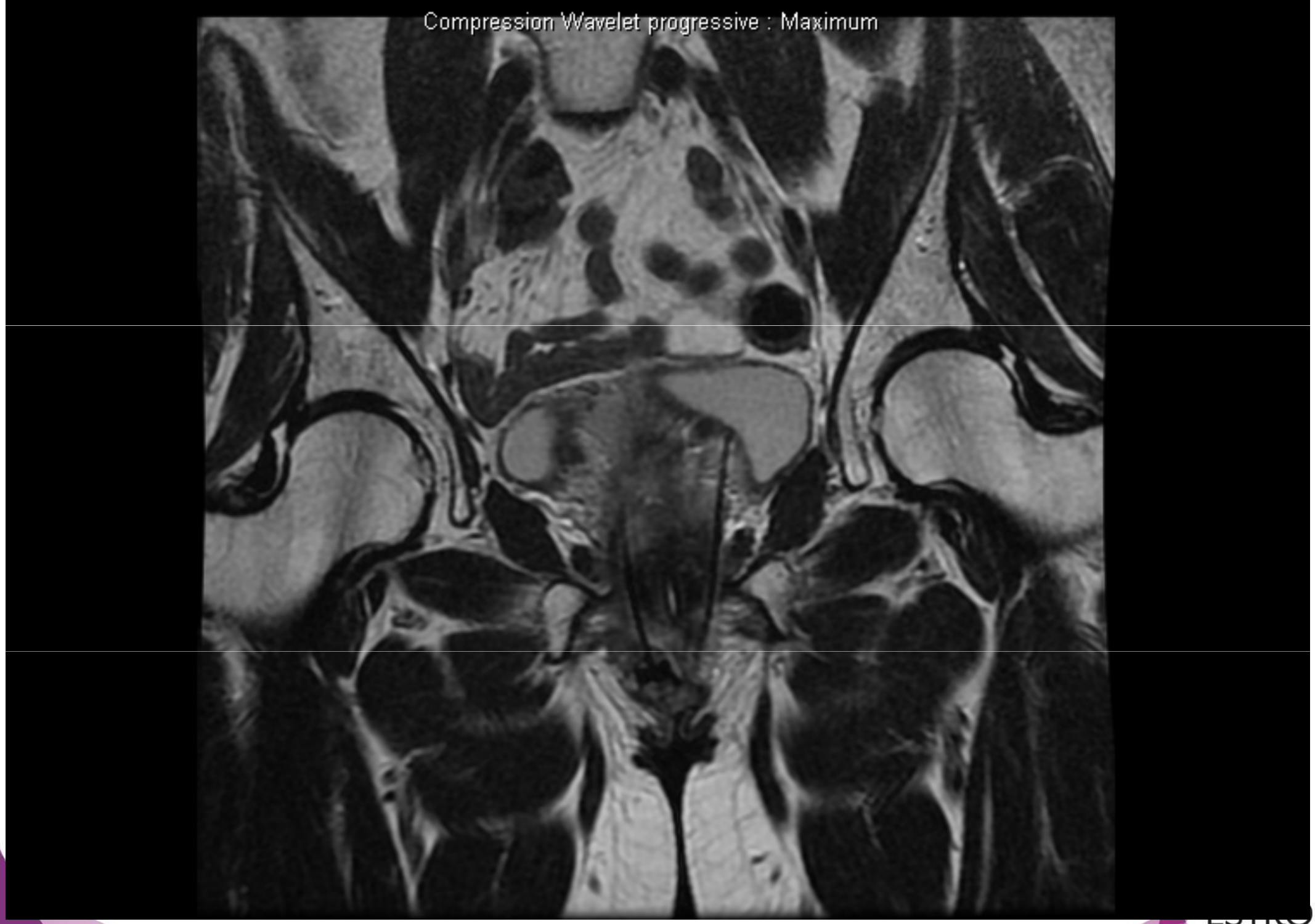
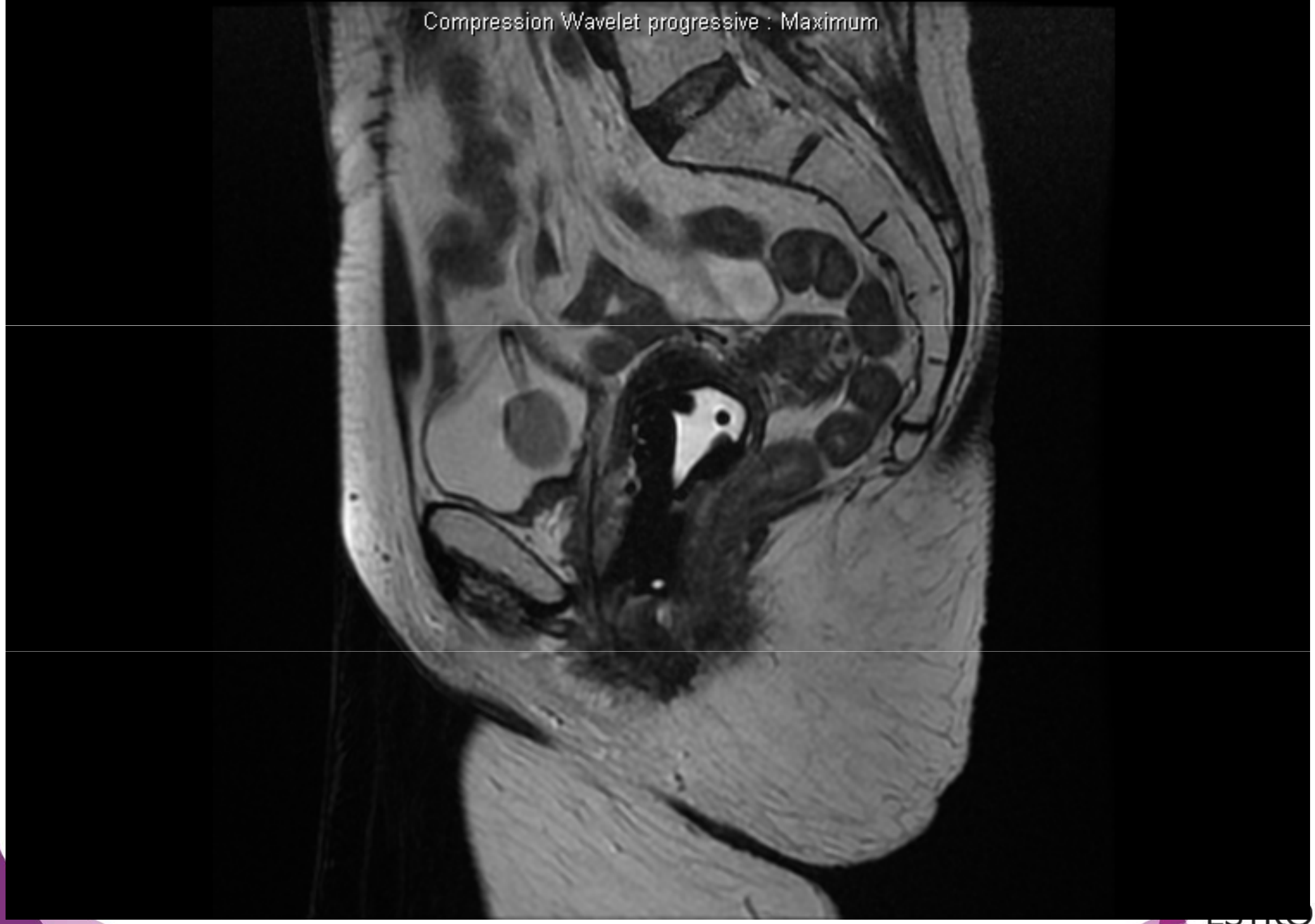
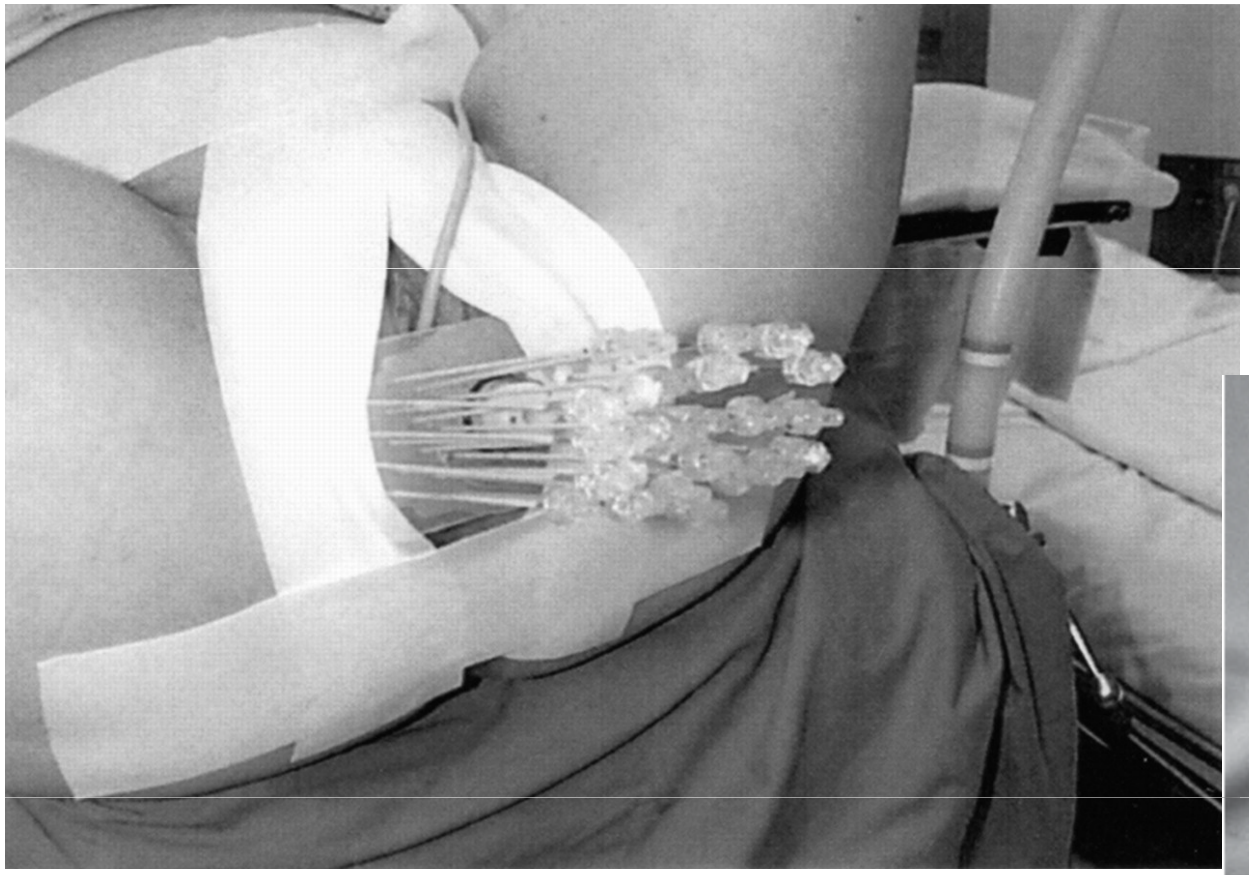

Compression Wavelet progressive : Maximum


Compression Wavelet progressive : Maximum

Interstitial techniques vaginal cancer



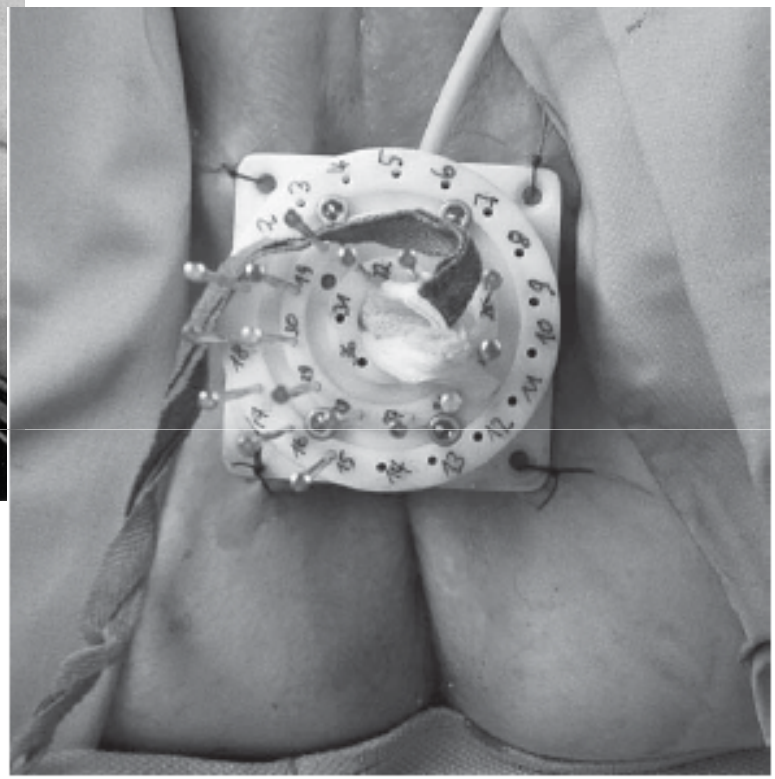
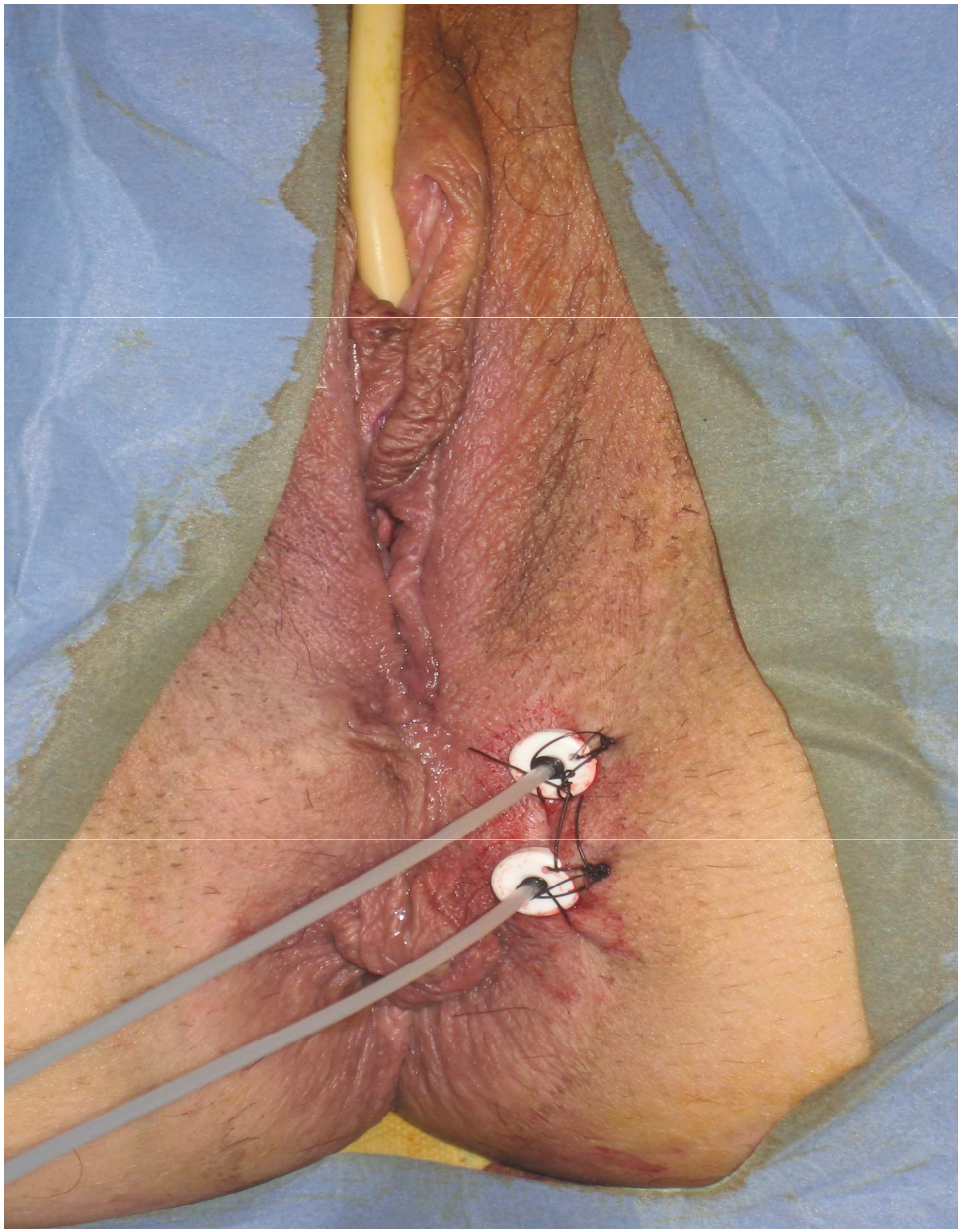


Figure 2. Interstitial brachytherapy of vaginal carcinoma using steel needles in two planes in right vaginal wall and one plane in left vaginal wall with template.

Transperineal template

Interstitial techniques vaginal cancer



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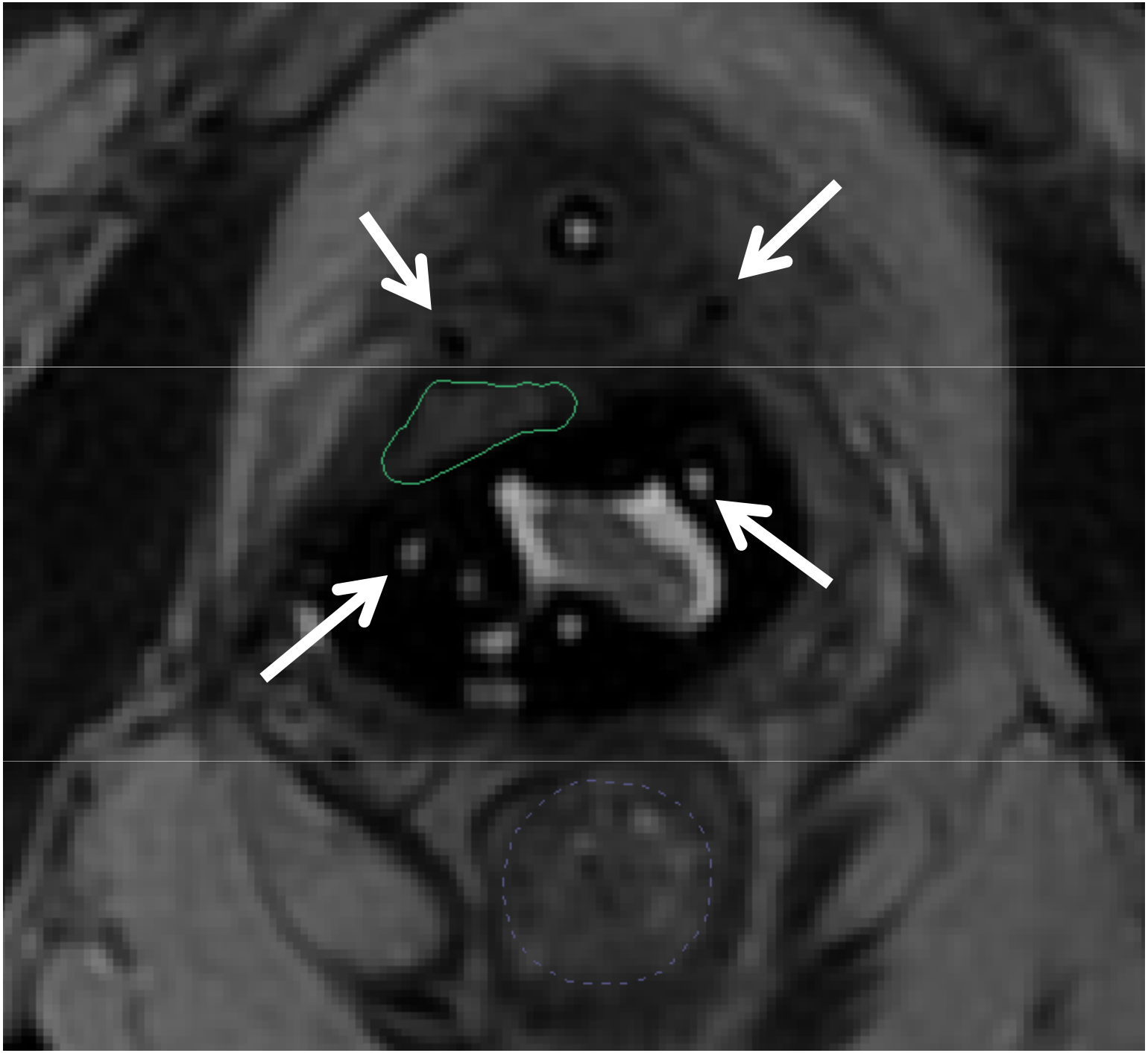

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Interstitial techniques vaginal cancer

- Brachytherapy usually combined with external irradiation
- Concomitant chemoradiation : 45 Gy
- 25-30 Gy to the CTV at the time of brachytherapy
- Taking into account doses to critical organs (rectum)

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Towards image-guided adaptive brachytherapy in vaginal cancer and vaginal relapses

« Work in progress »

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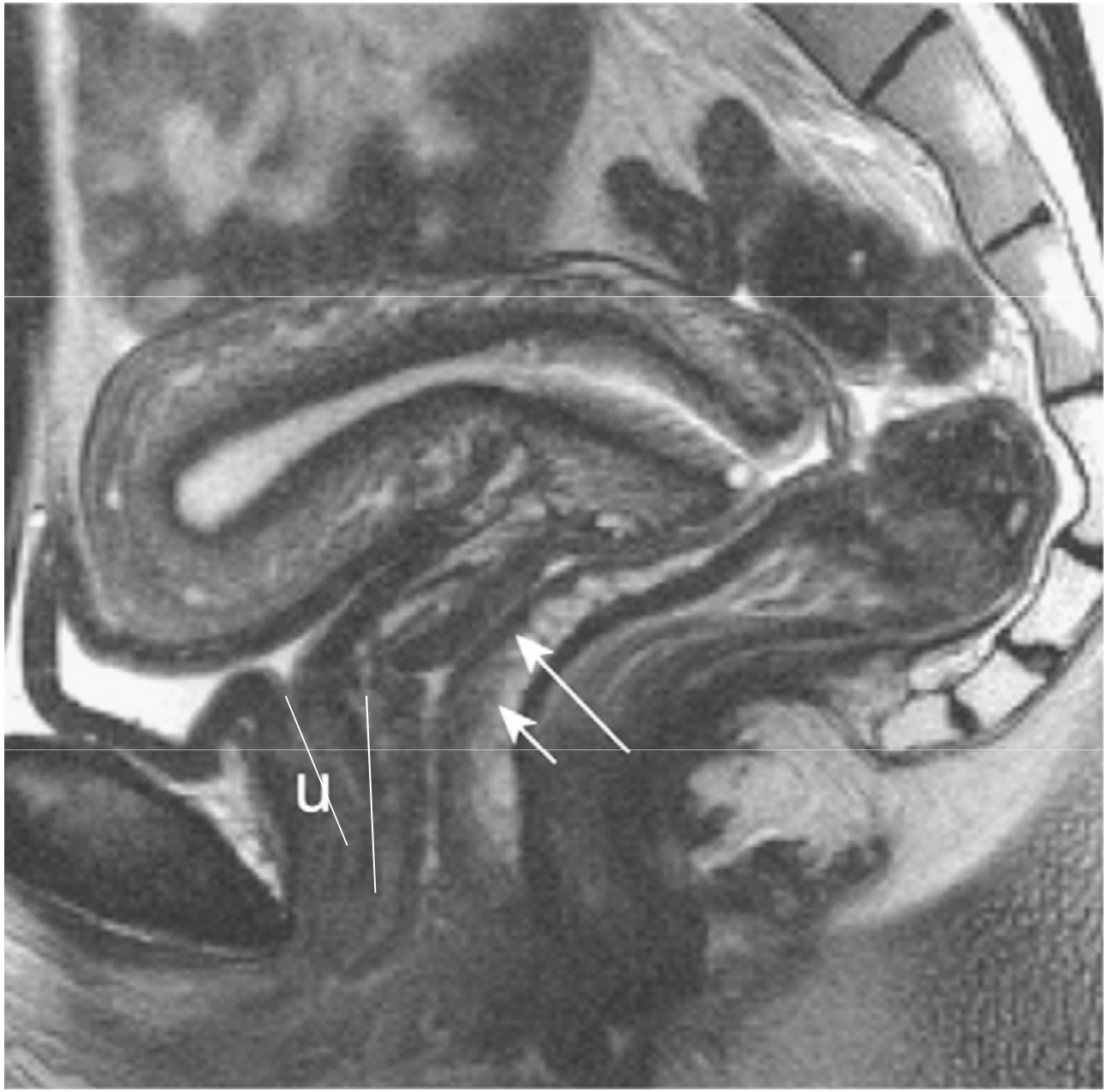
Vagina task force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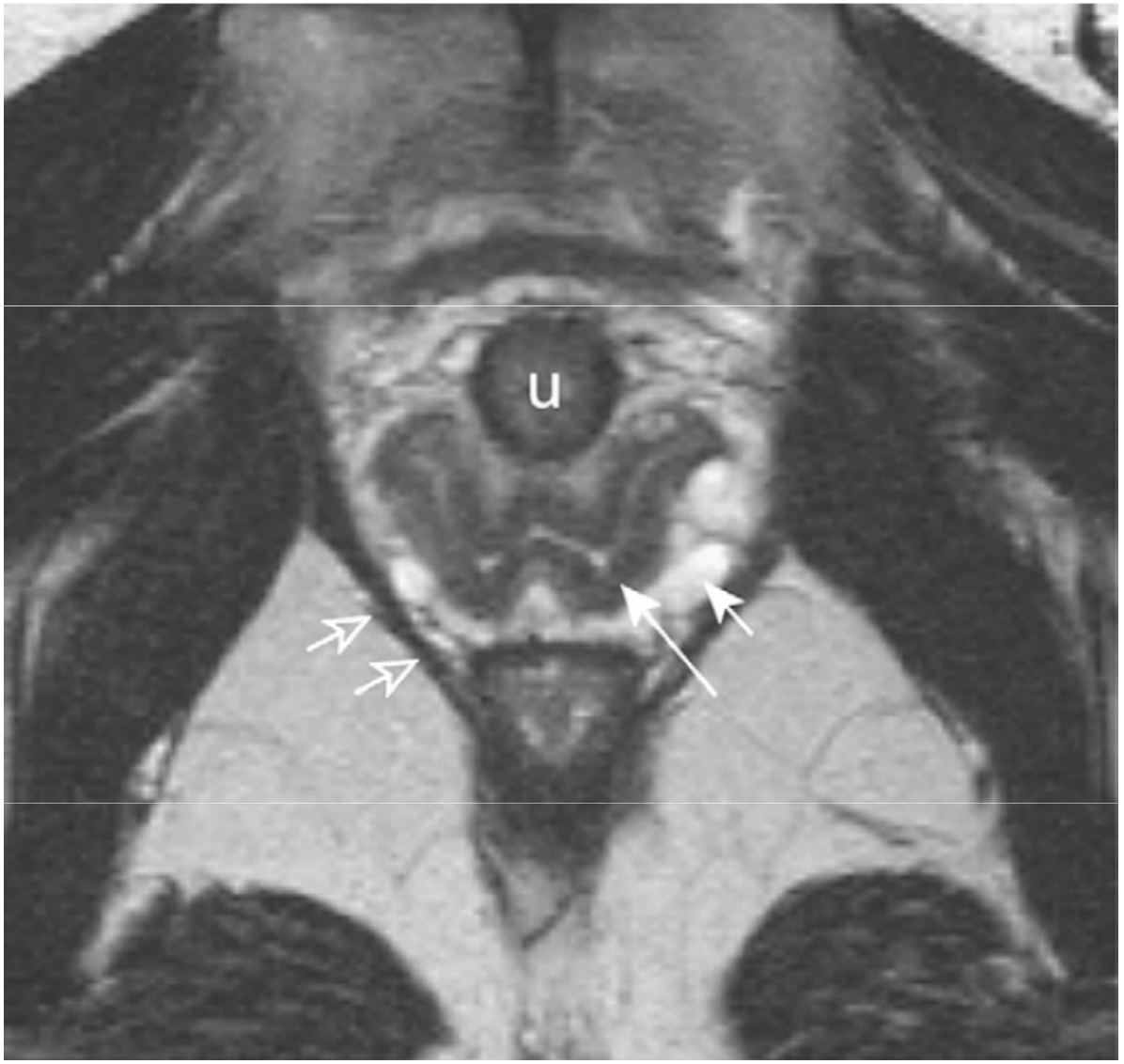
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Table 1 Clinical and magnetic resonance imaging (MRI) staging of primary vaginal carcinoma

Stage	FIGO clinical staging	MRI staging
I	Carcinoma limited to vagina	Tumour confined to the vaginal mucosa, or involves the muscle wall but does not extend into the paracolpol adventitia
II	Carcinoma involves the paravaginal tissues but does not extend to the pelvic wall	Tumour extends into the paracolpol adventitia
III	Carcinoma extends to the pelvic wall	Tumour is in continuity with the bony pelvis or the muscles of the pelvic sidewall
IVA	Carcinoma extends beyond the true pelvis or clinically involves the mucosa of the bladder or rectum	Tumour directly extends beyond the pelvis or involves the mucosa of the bladder or rectum
IVB	Distant metastases	Metastases outside the pelvis

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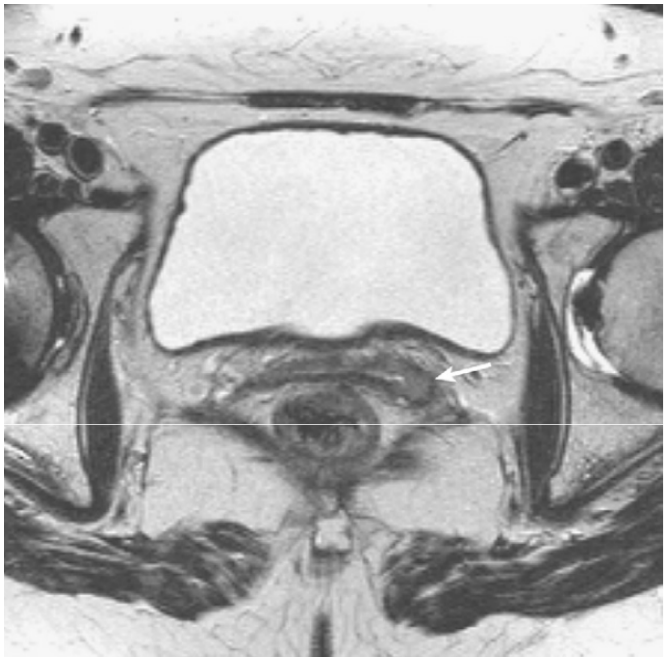

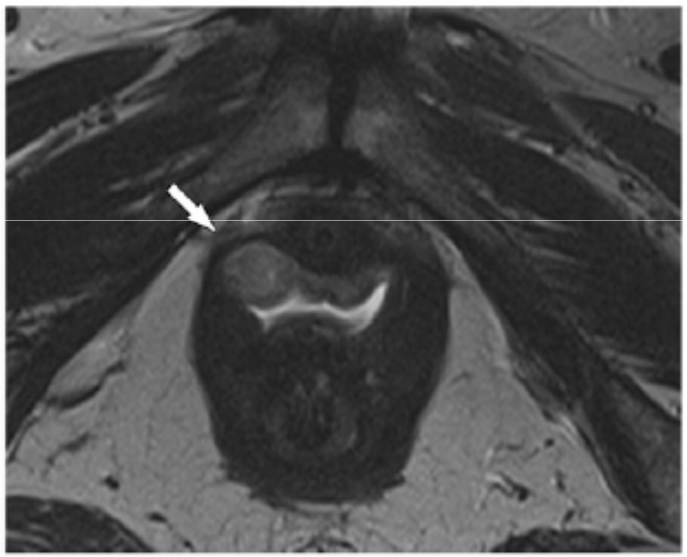

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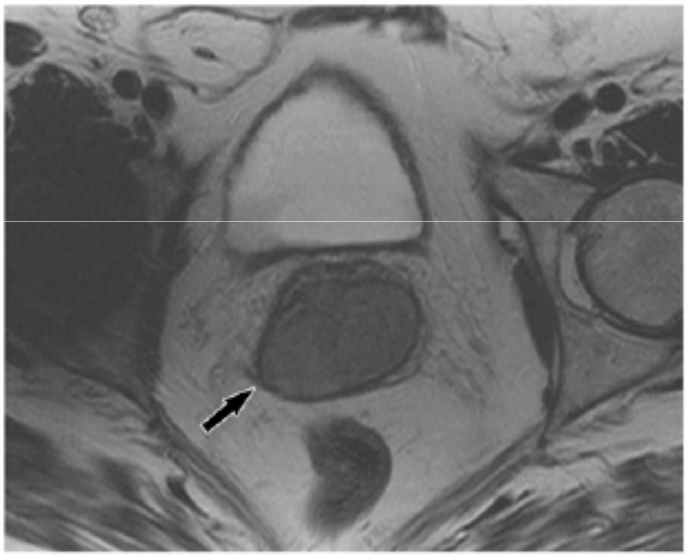

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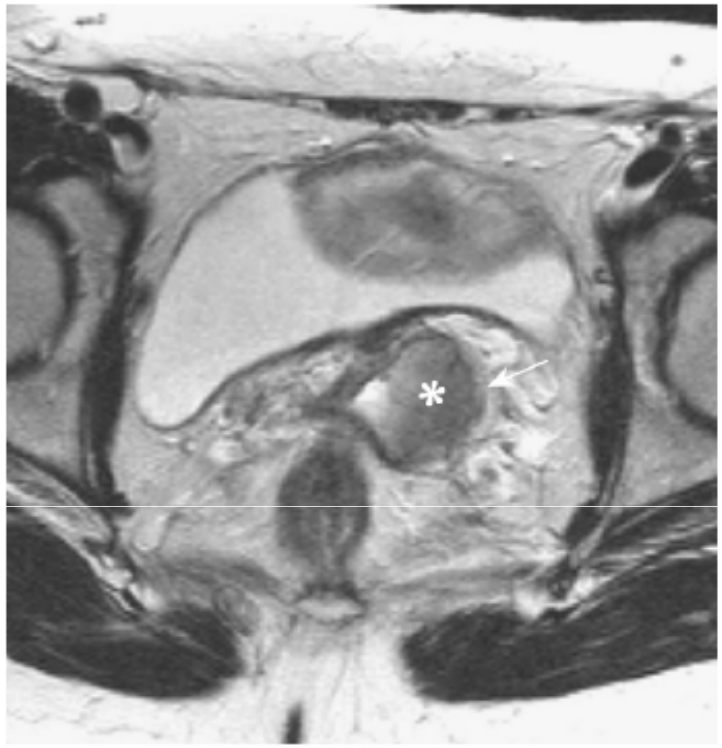
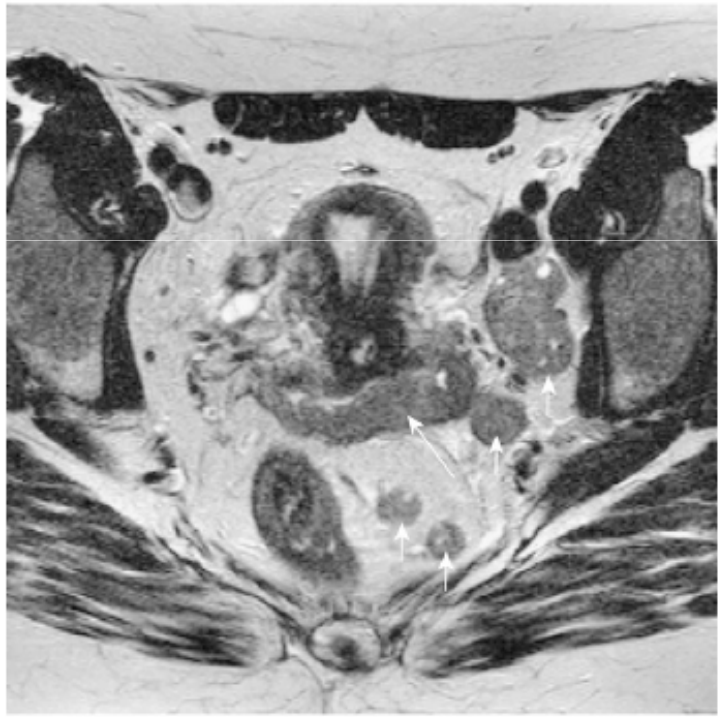
ESTRO School



(a)

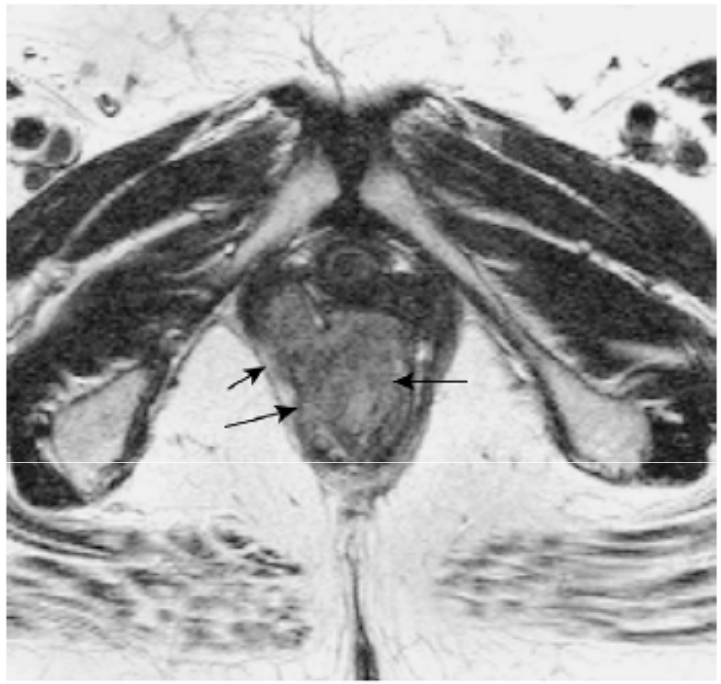


(b)

ESTRO School

(a)

(b)



(a)

(b)

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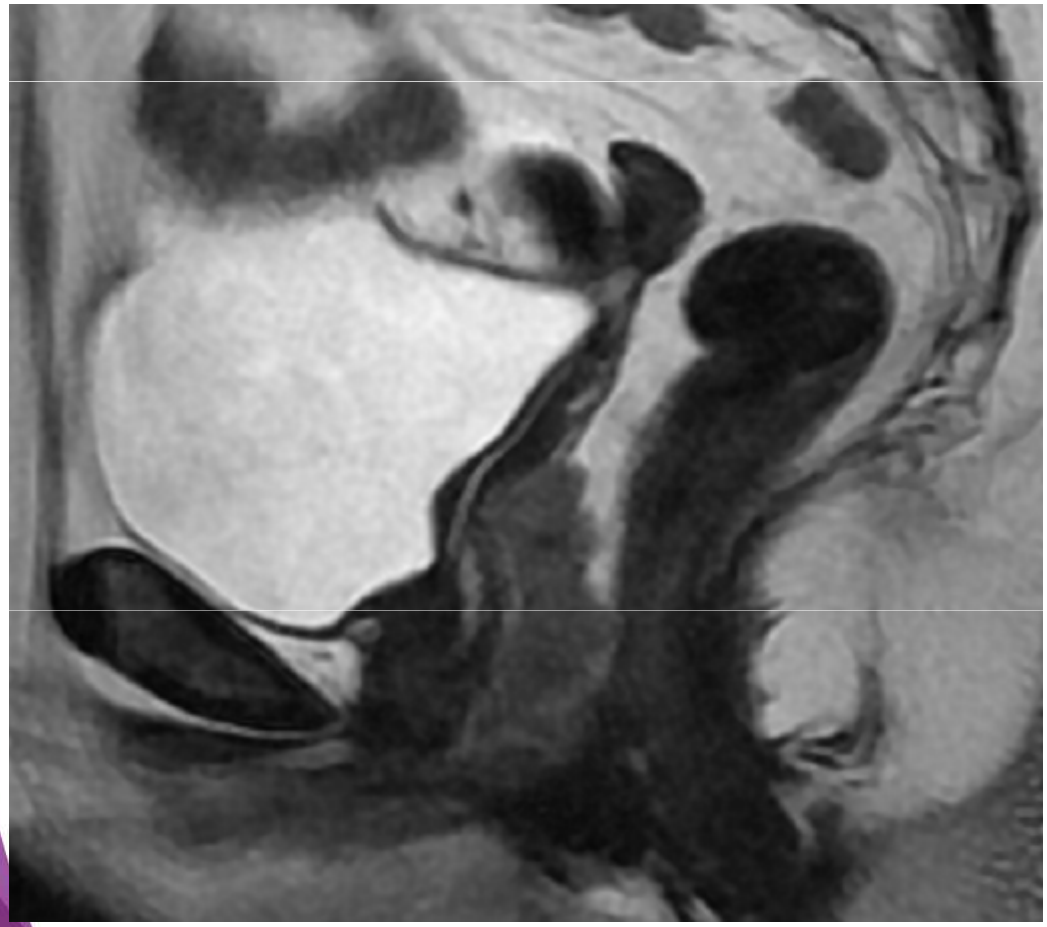
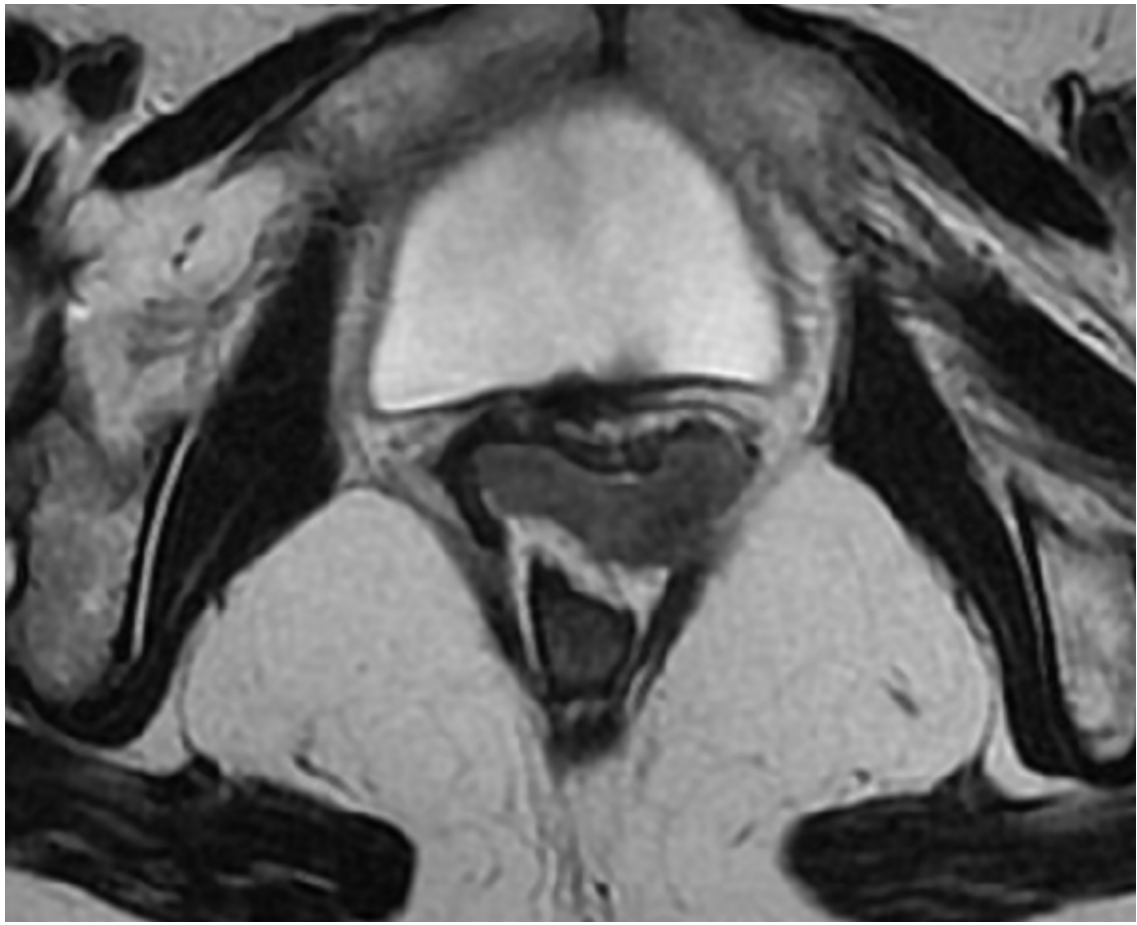
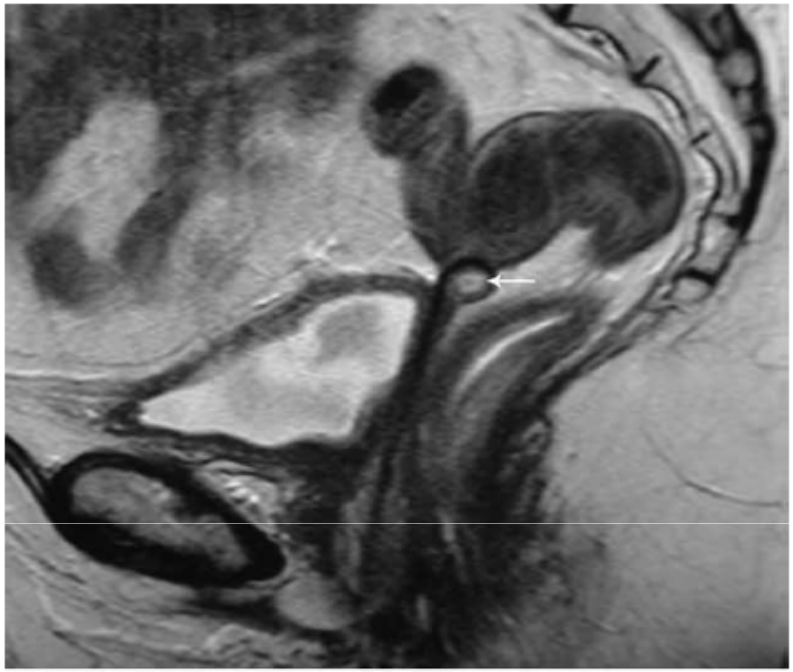
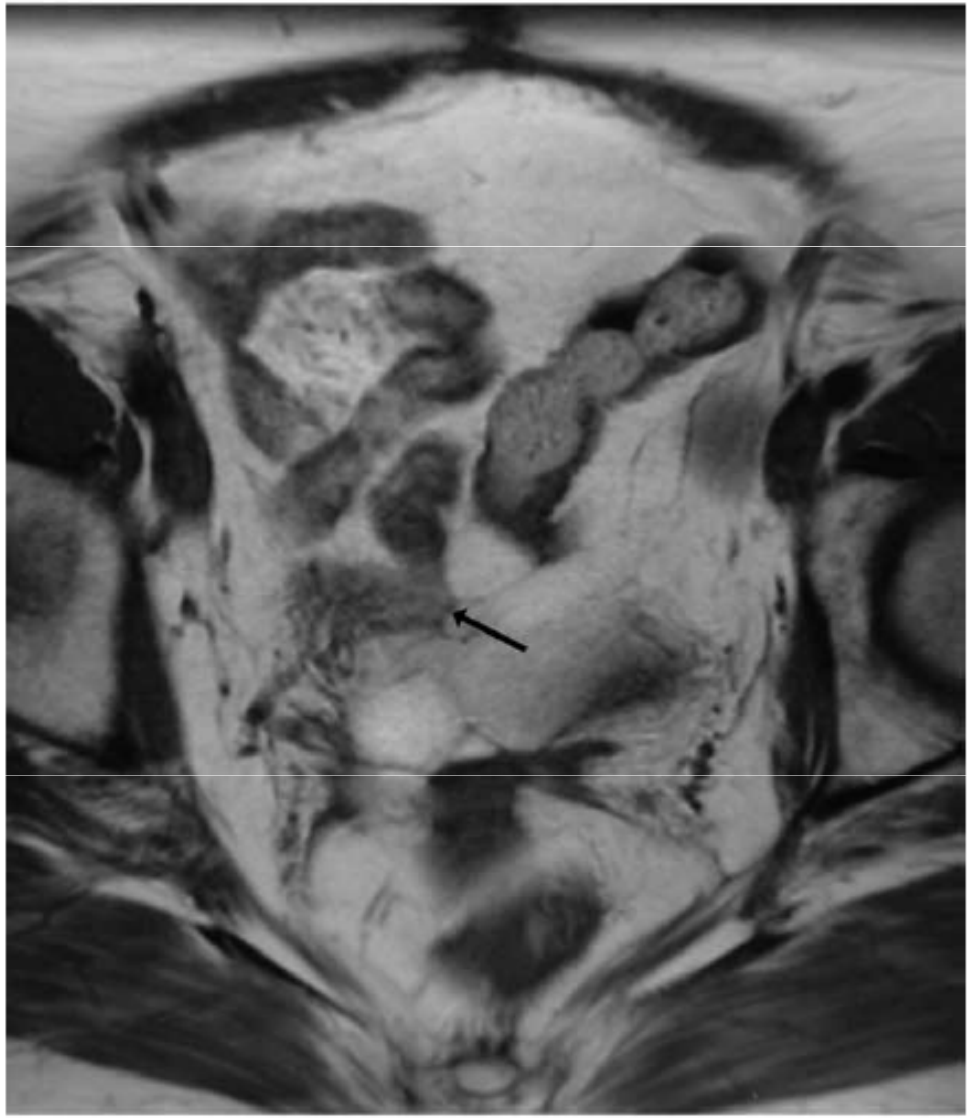
MRI-guided brachytherapy?





ESTRO School





5 cases / 1 per centre

- Similar management: concomitant chemo-RT and BT
- Adaptation of the GEC recommendations
  - Volumes: CTV
  - Several planning aims
- Similarities

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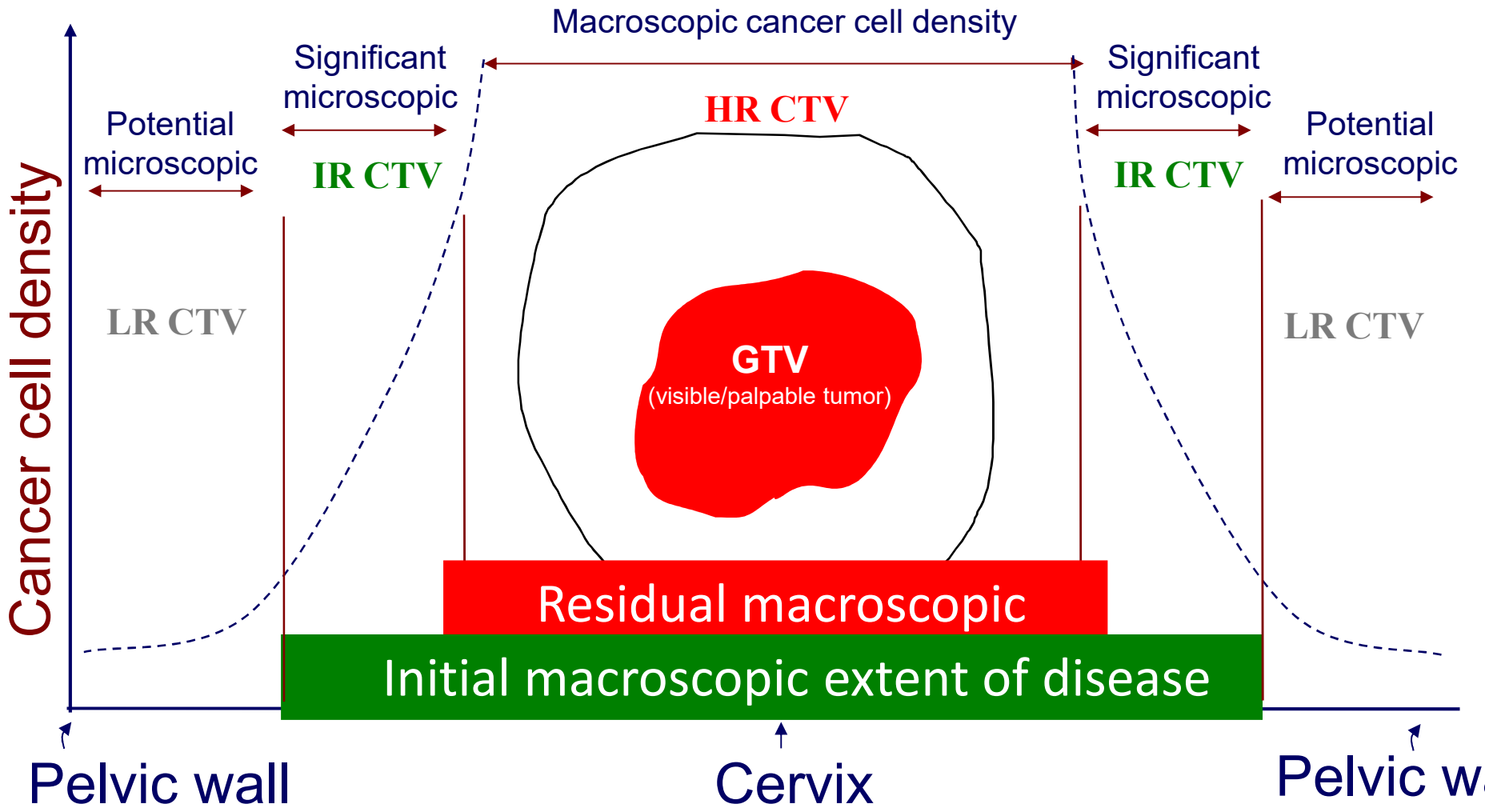
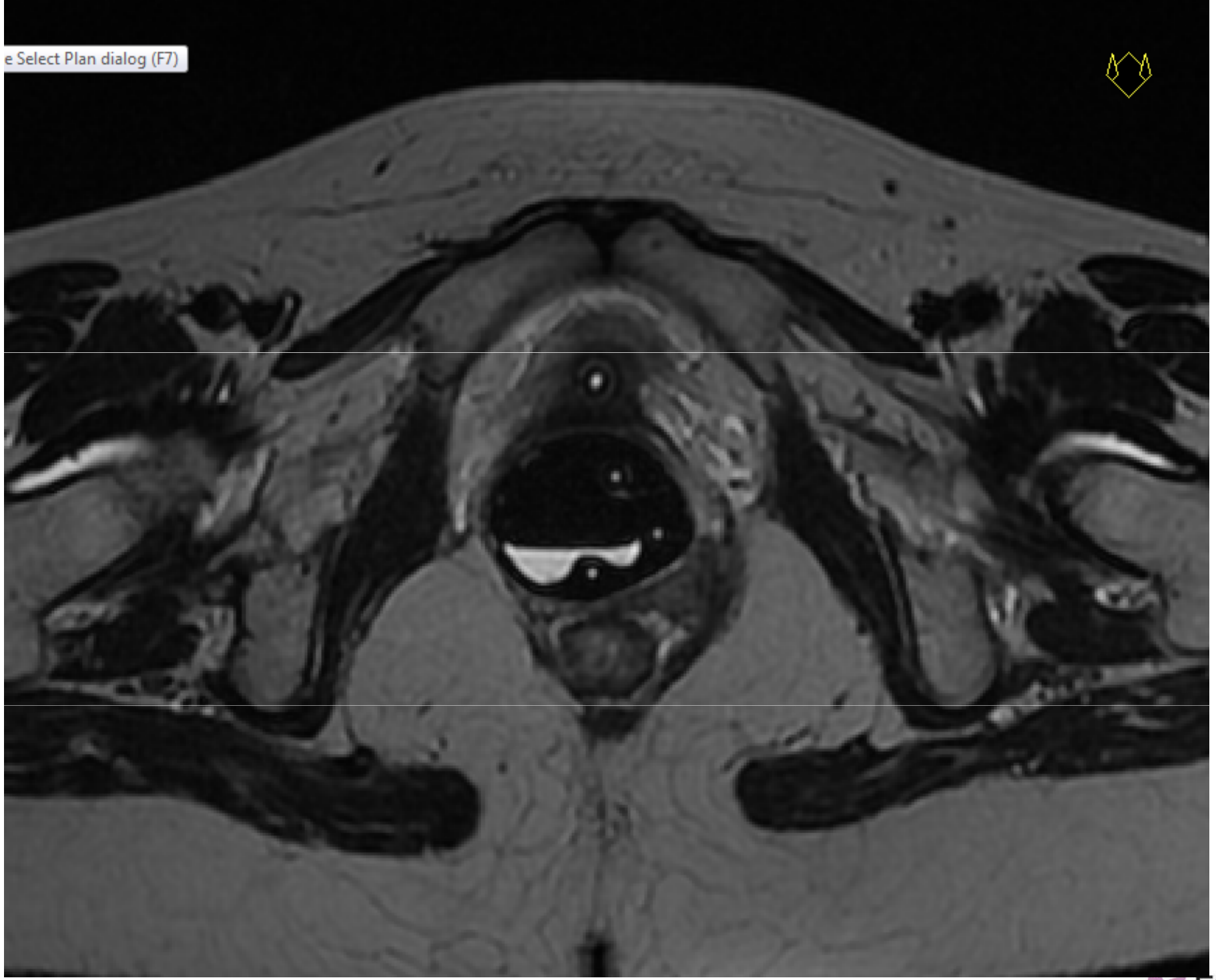
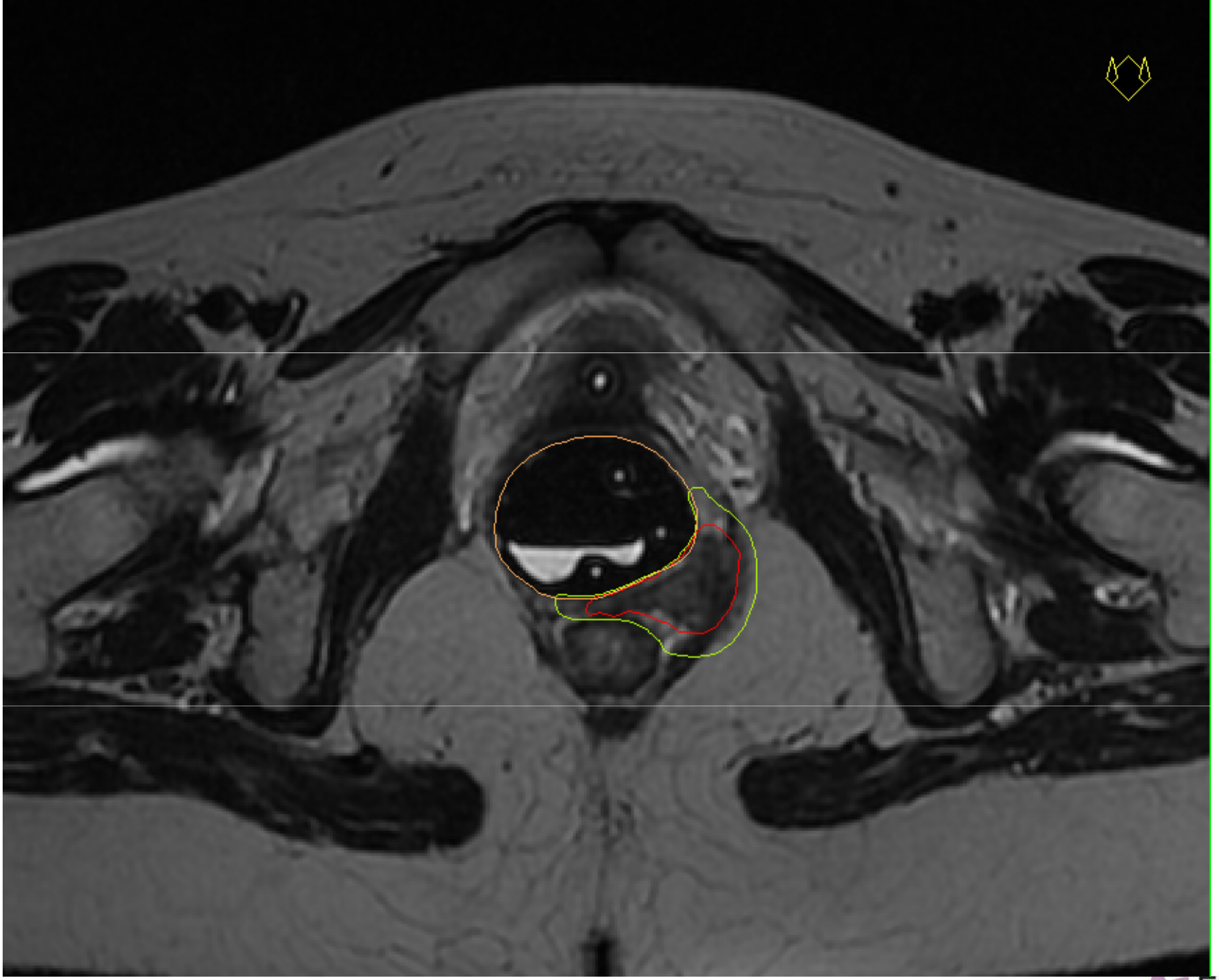
GEC-ESTRO target volume concept

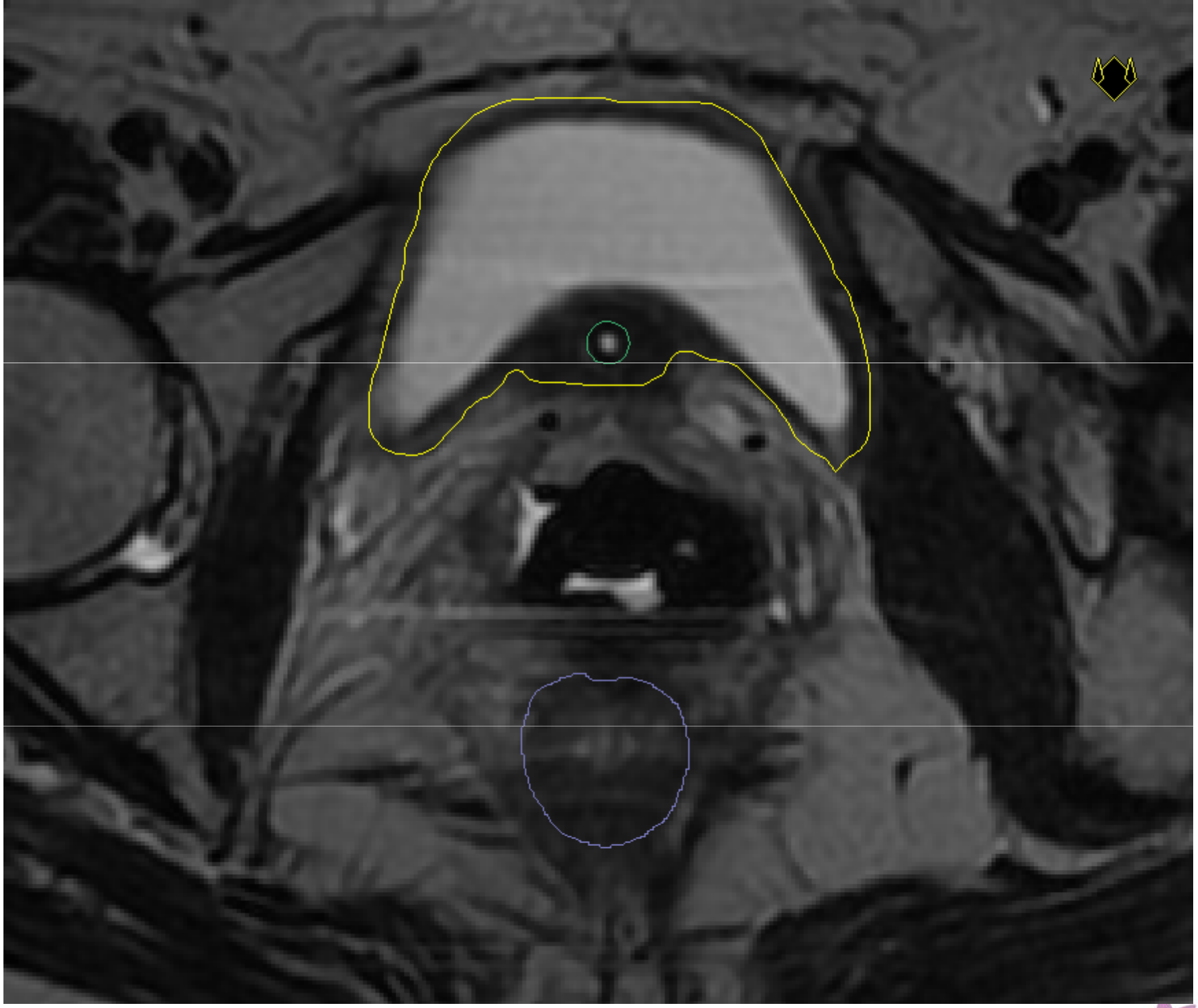
>80 Gy - >60 Gy - 45Gy

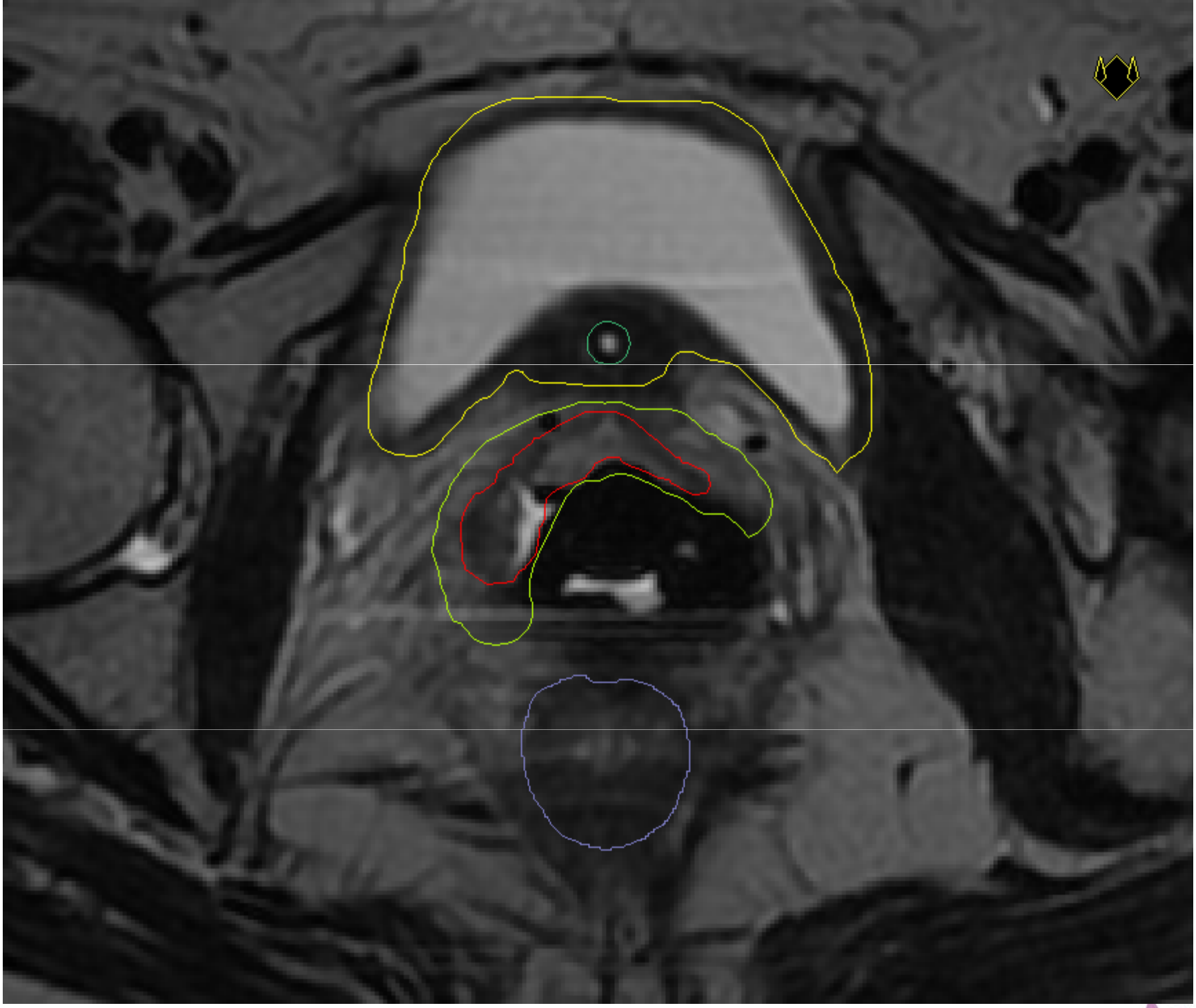


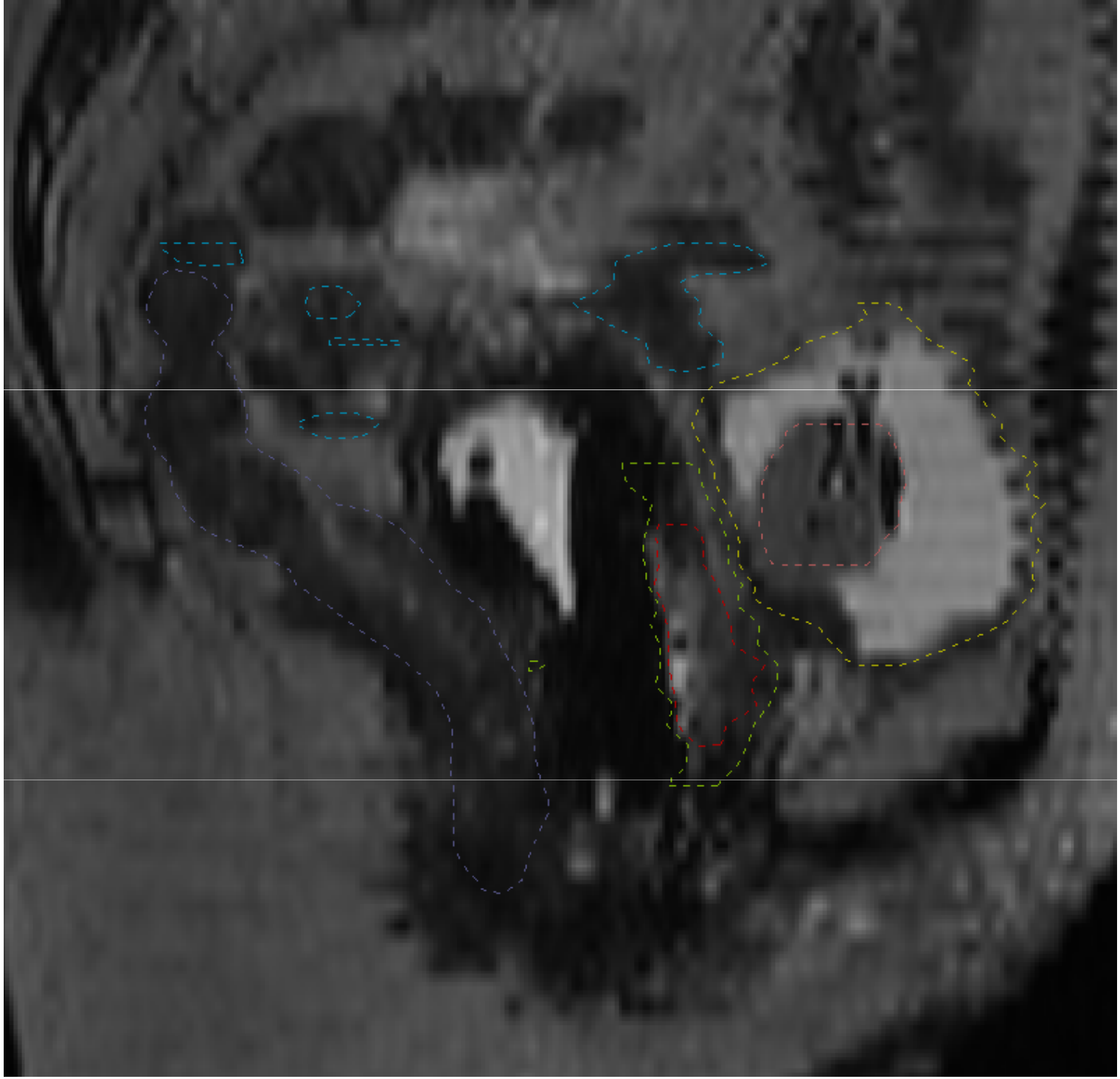
Radiother and Oncol 2005

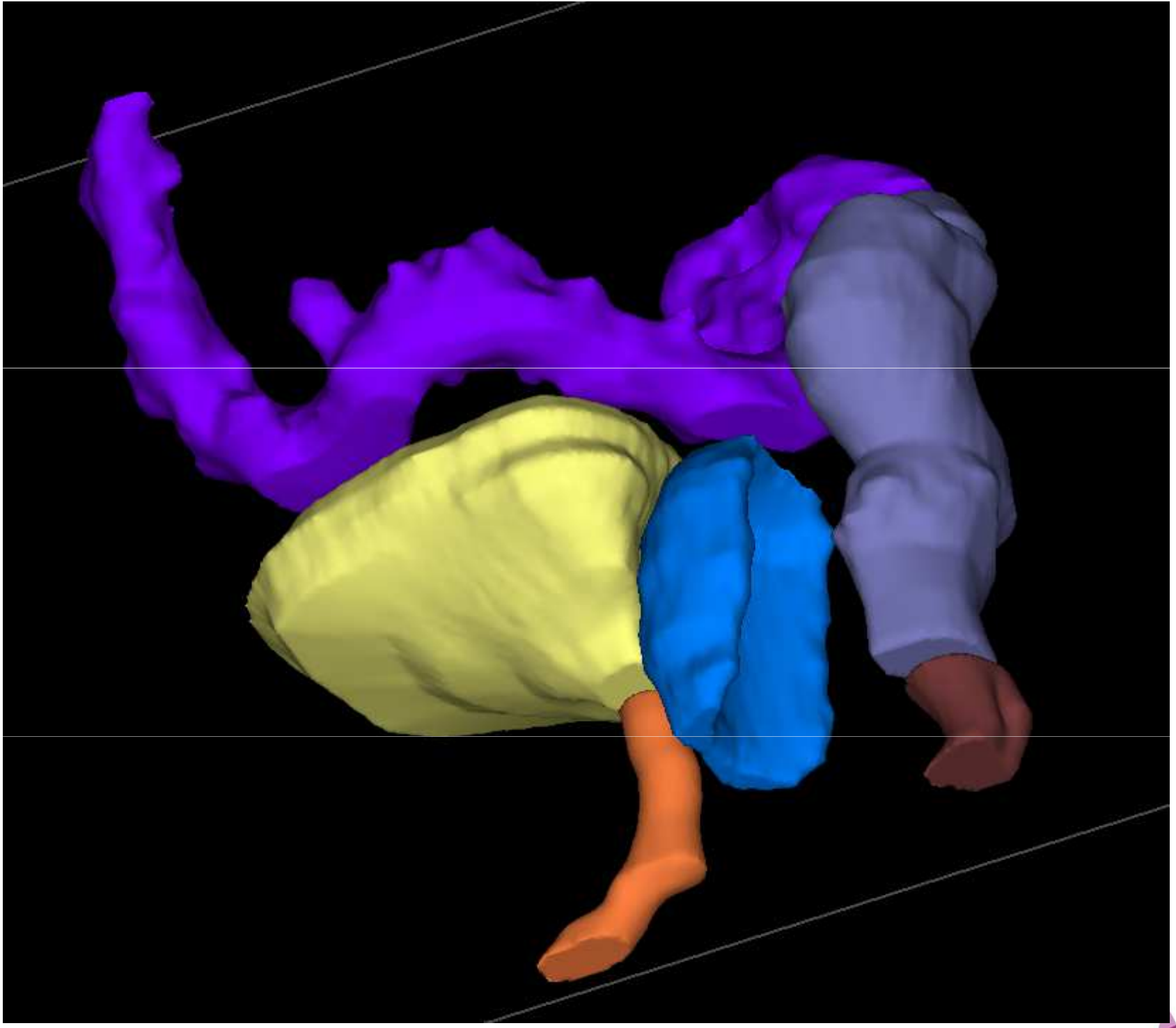

e Select Plan dialog (F7)

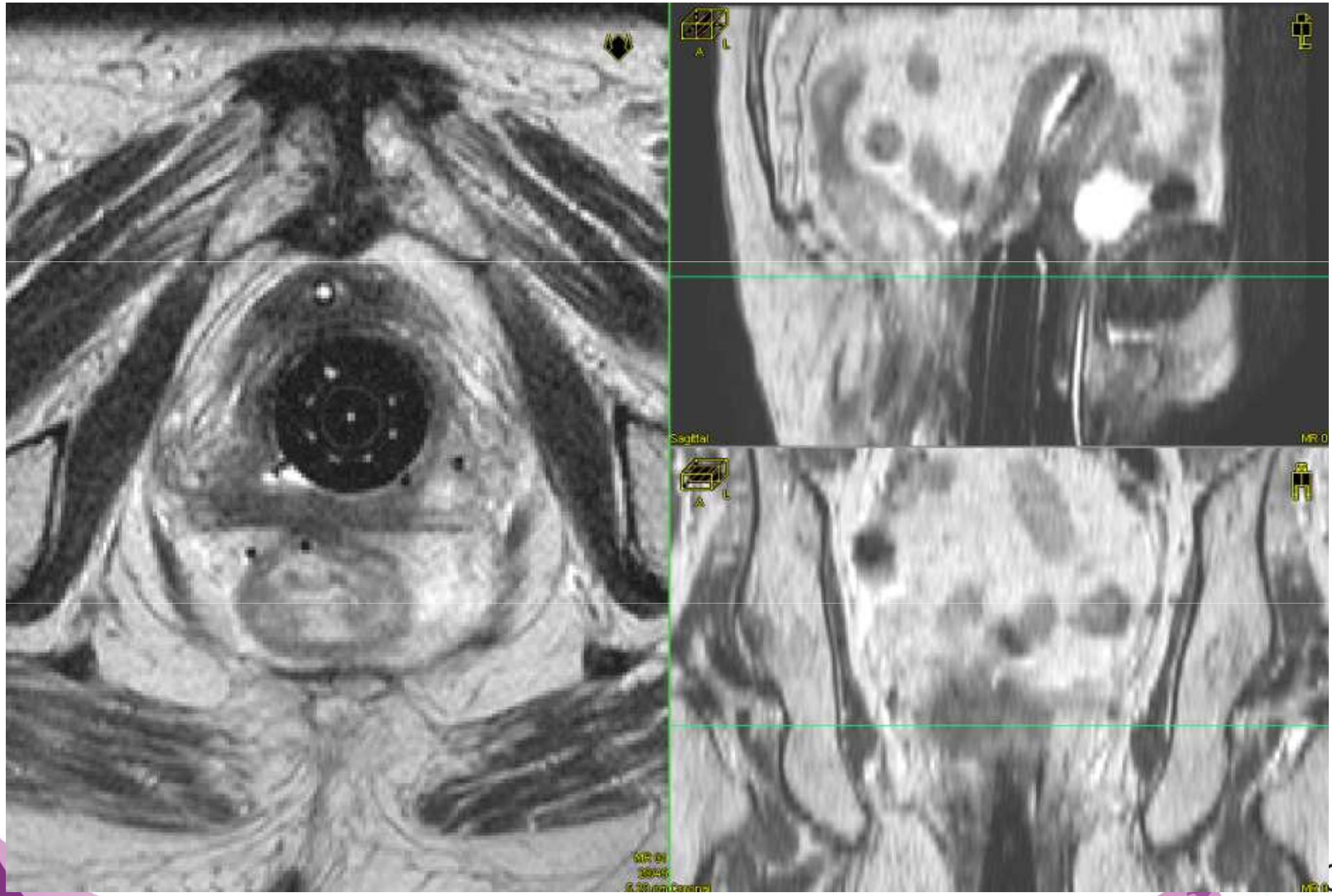


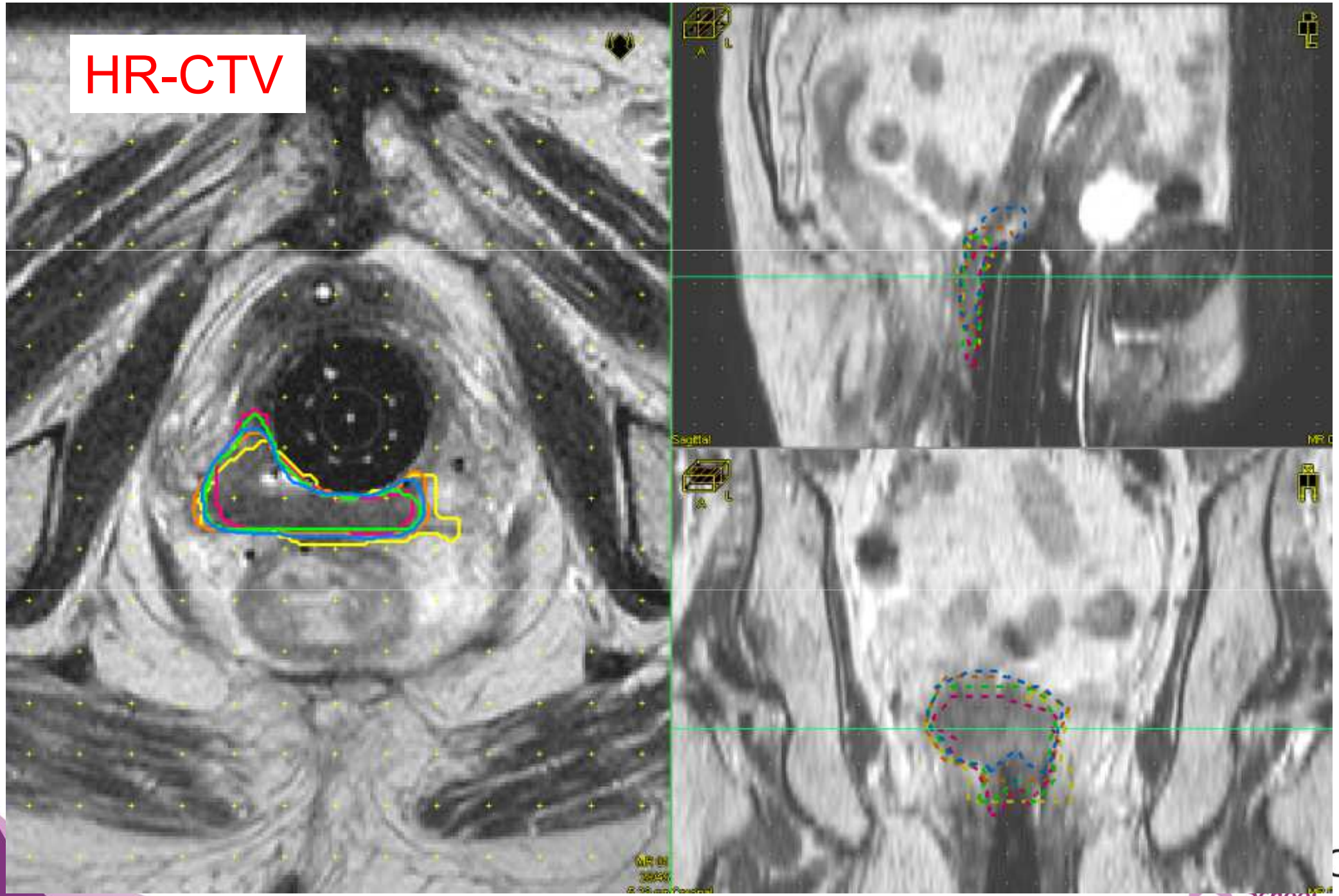


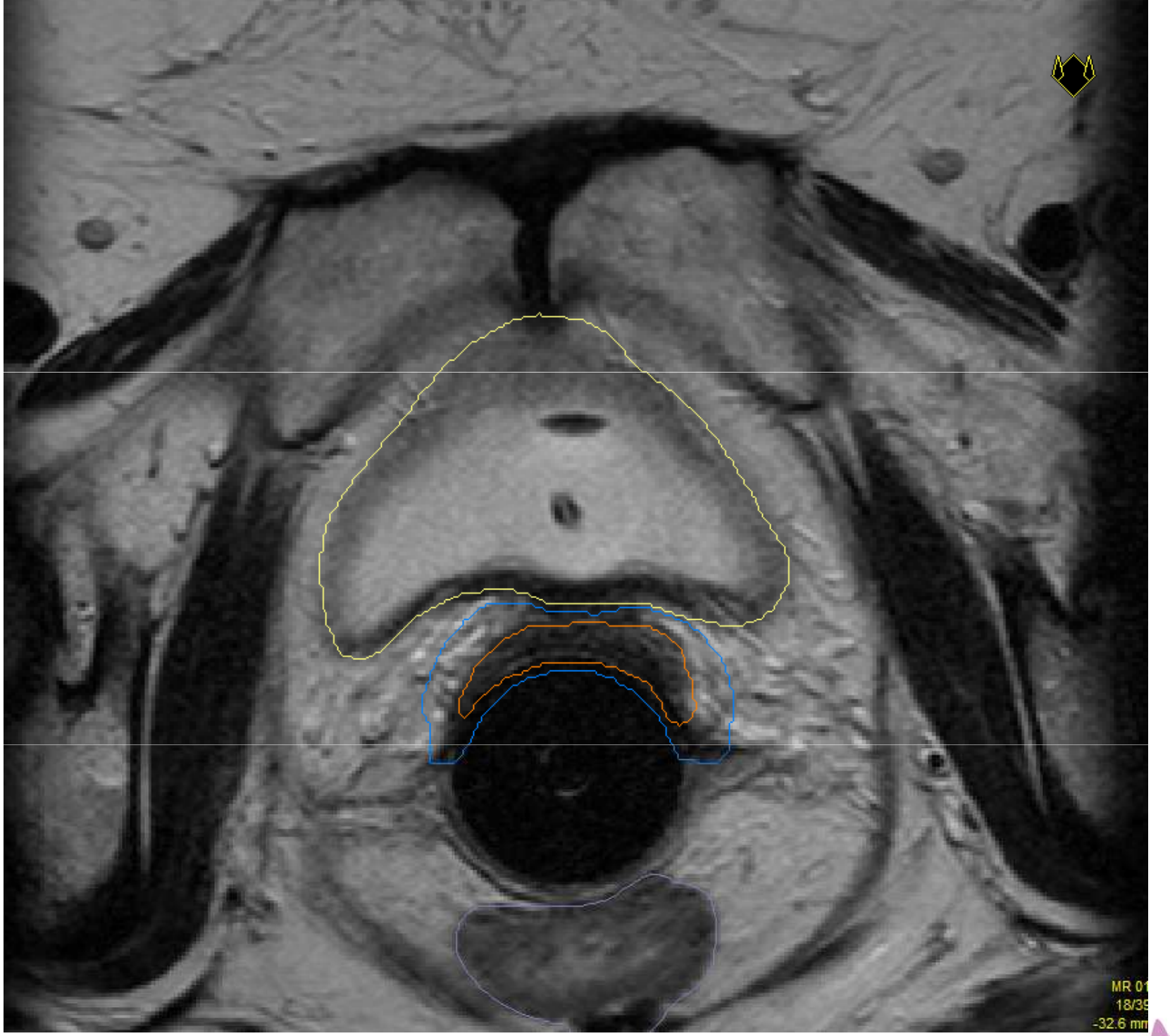


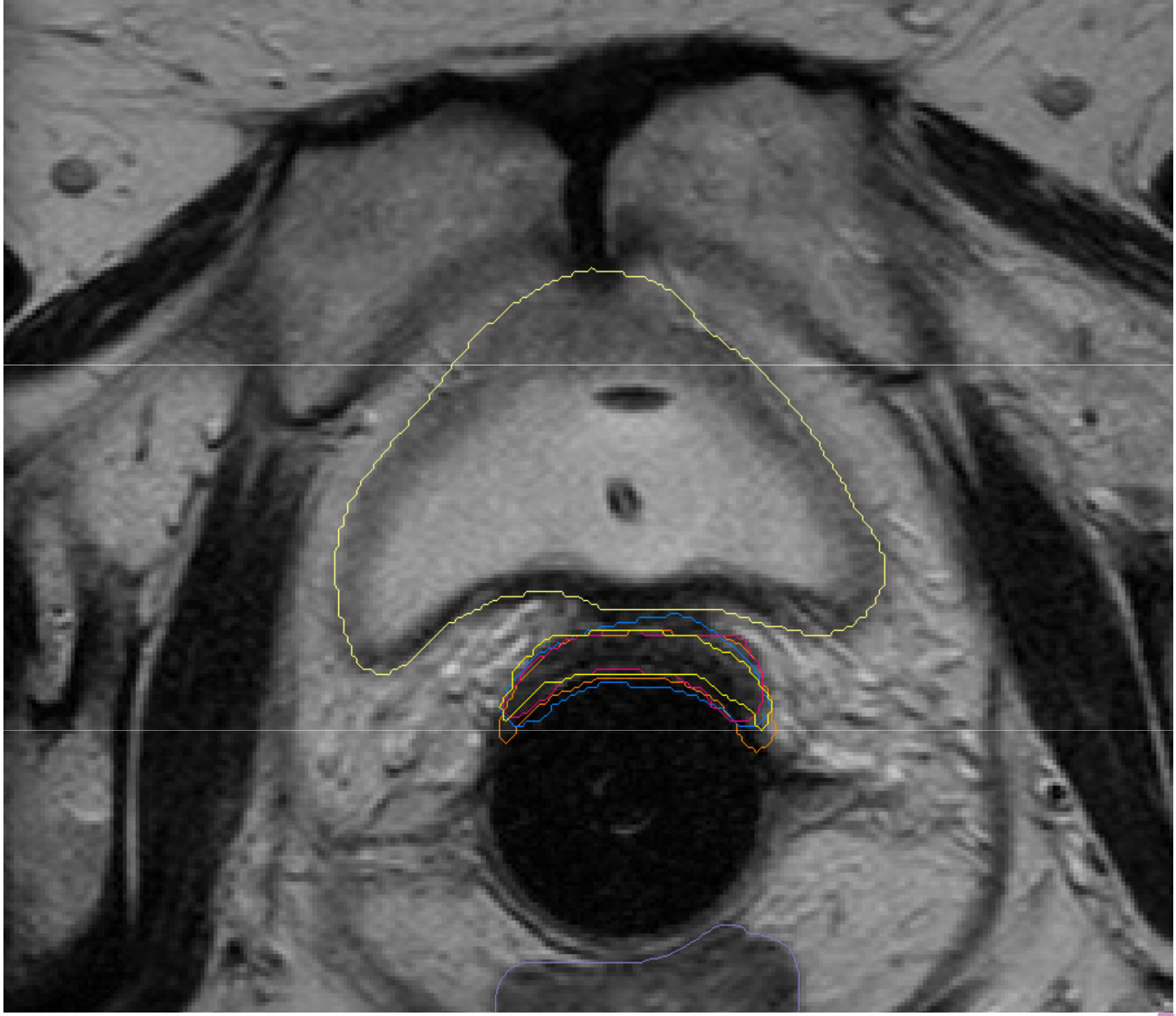





A
L
Sagittal
MR 0
A
L


HR-CTV
Sagittal


MR 01
18/39
-32.6 mm

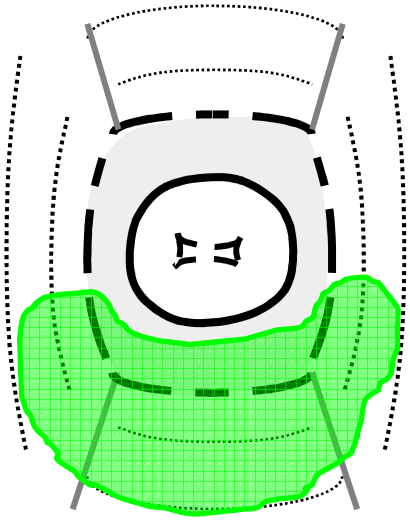


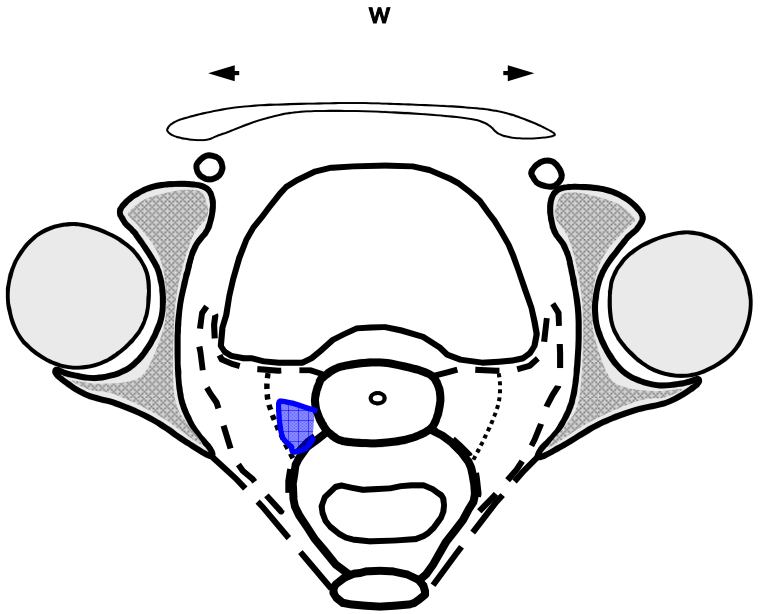
ESTRO School

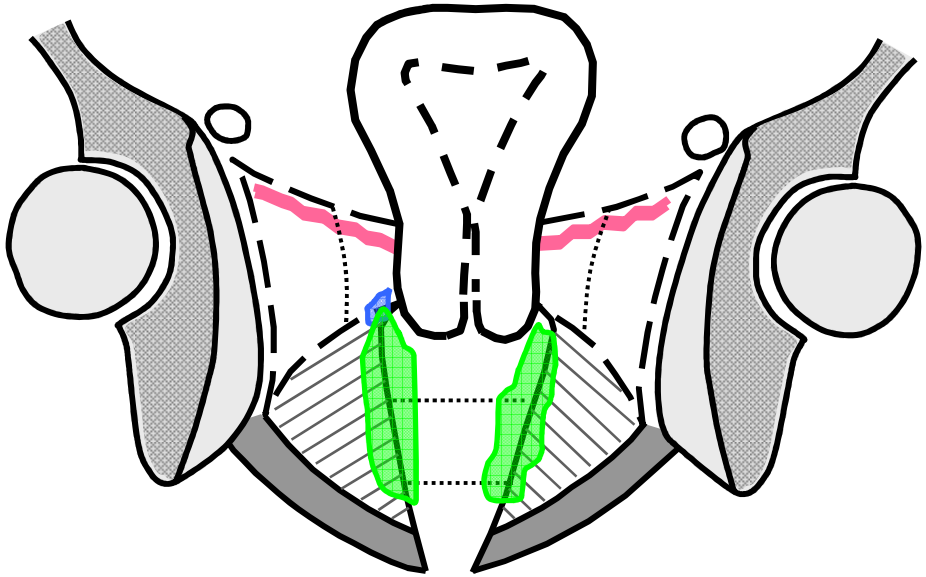
What we learned (so far…)

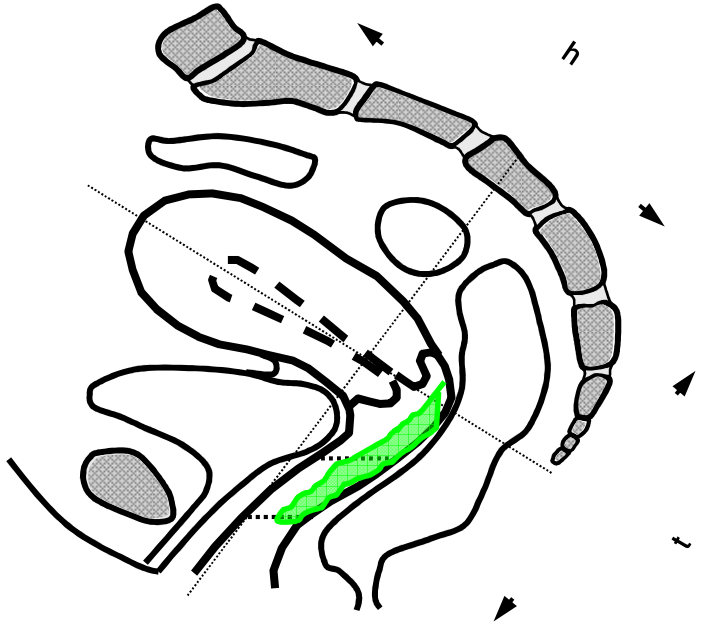
- MRI of the lesion at diagnosis
  - Is not performed with the applicator
  - Vaginal impression
  - MRI with gel
- Deformities of the vagina with application
  - Extension of the lesion and vaginal walls
  - Unconformities between clinical examination and MRI findings
- Accurate description of the lesion
  - Is crucial
  - Cartoons used for cervix are not adapted

w = 4.0 cm
h = 5.0 cm
t = 1.5 cm









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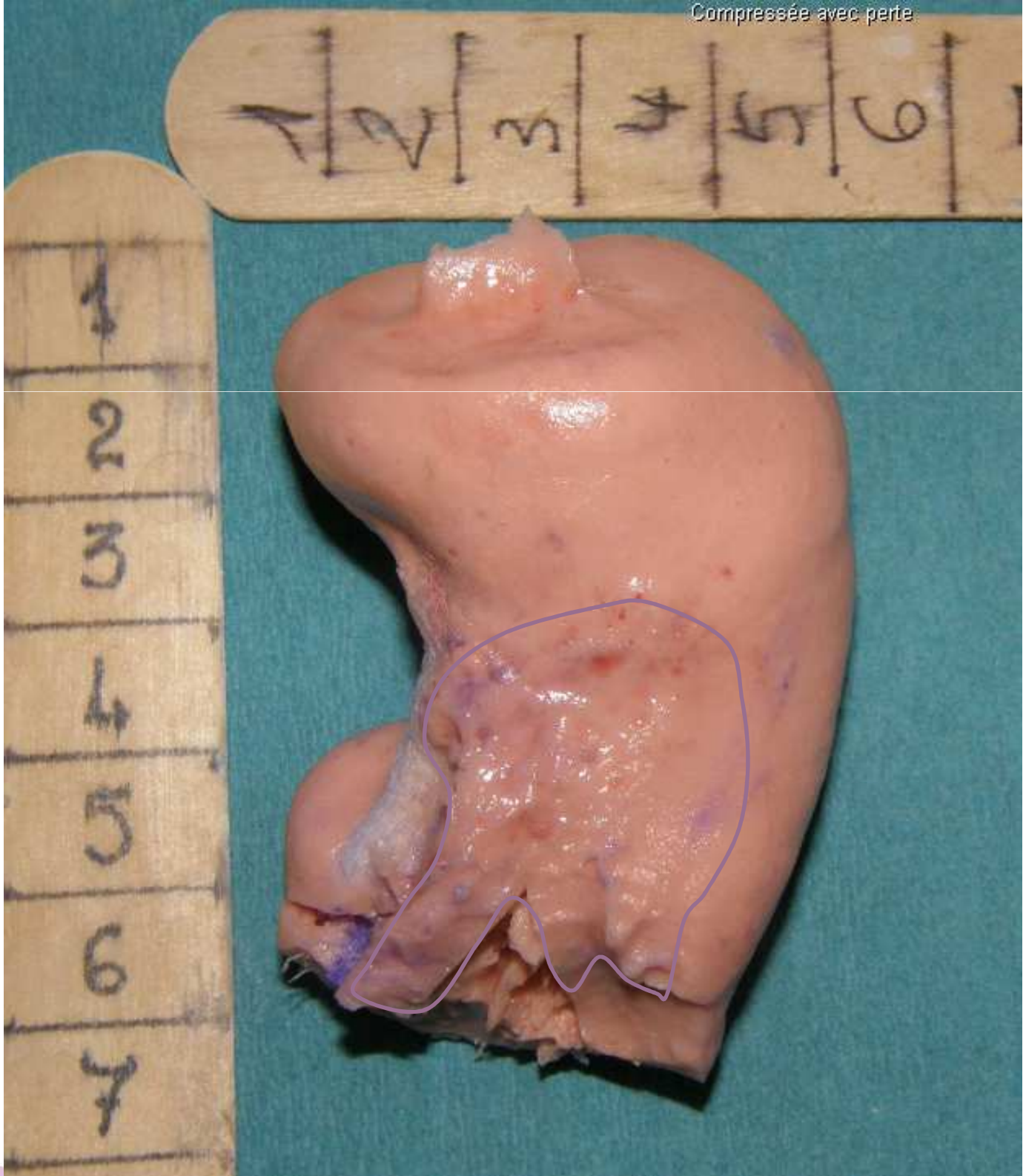
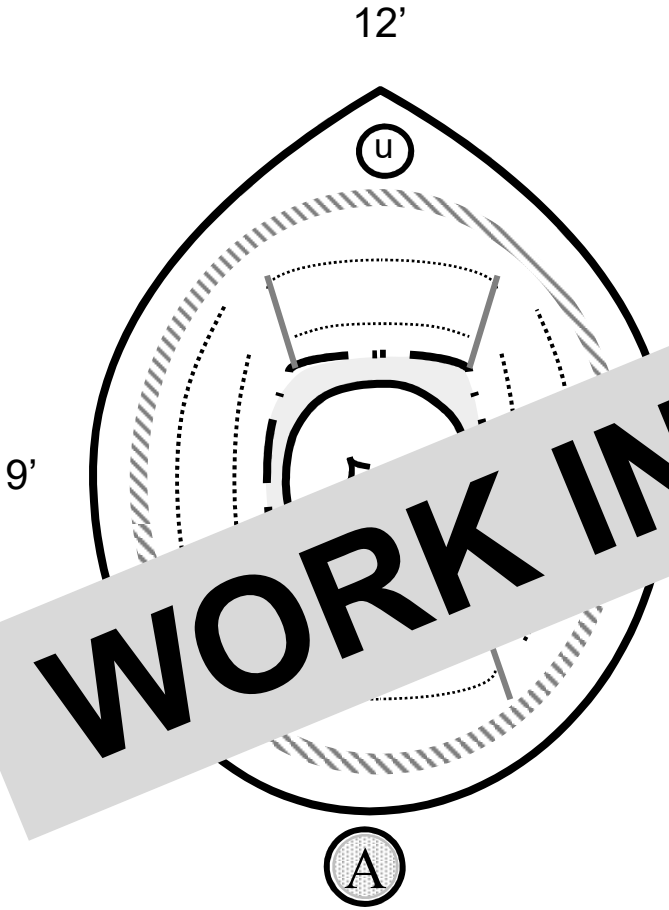
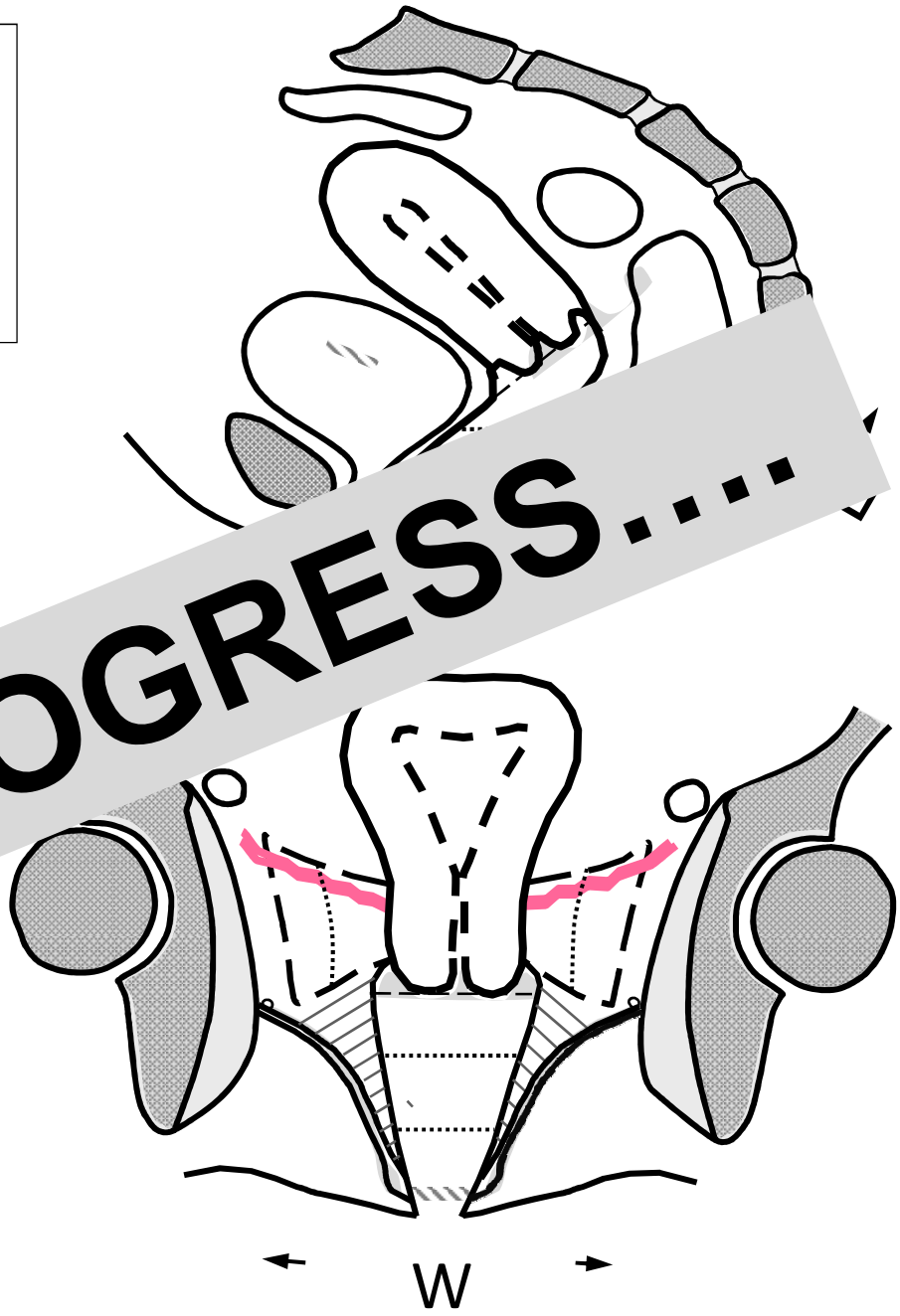

Compressée avec perte

At Diagnosis ☐ At Brachytherapy ☐ EBRT ____ Gy

Maximal tumour dimensions
Clockwise involvement ___ to ___ o'clock
Thickness =___ cm (perpendicular to vaginal axis)
Width = ___ cm (incl. paravaginal extension)
Length =___ cm (along vaginal axis)
Proximal tumour free distance (length) =___cm
Distal tumour free distance (length) =___ cm





WORK IN PROGRESS....

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Clinical Drawing: Vagina + intact uterus

Upper 1/

Middle 1/3 vagina

Lower 1/3 vagina

WORK IN PROGRESS....

Conclusion

- Interstitial techniques when inappropriate coverage (topographic and dosimetric) with pure intracavitary techniques
- Several approaches (applicators,guidance) available
- Adaptation of the application technique to the topography at the time of brachytherapy
- Balance between intracavitary and interstitial sources? **20%**
- Development of new applicators
- Recommendations for image guided BT? CTV?

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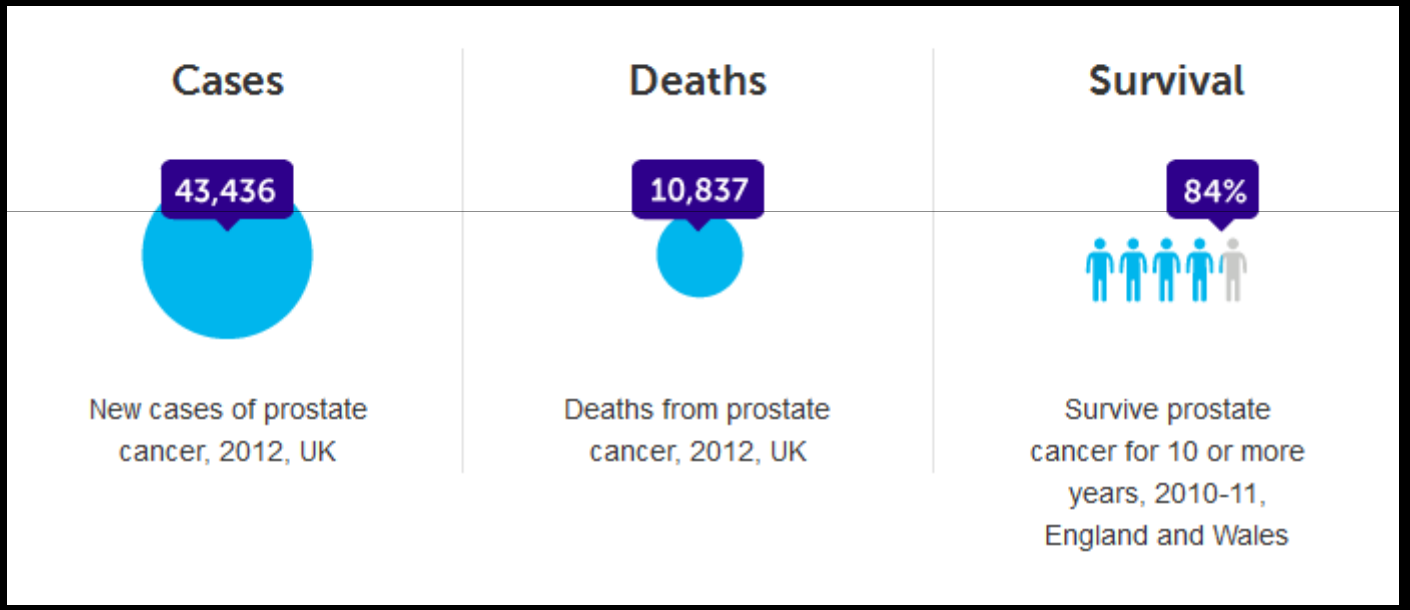
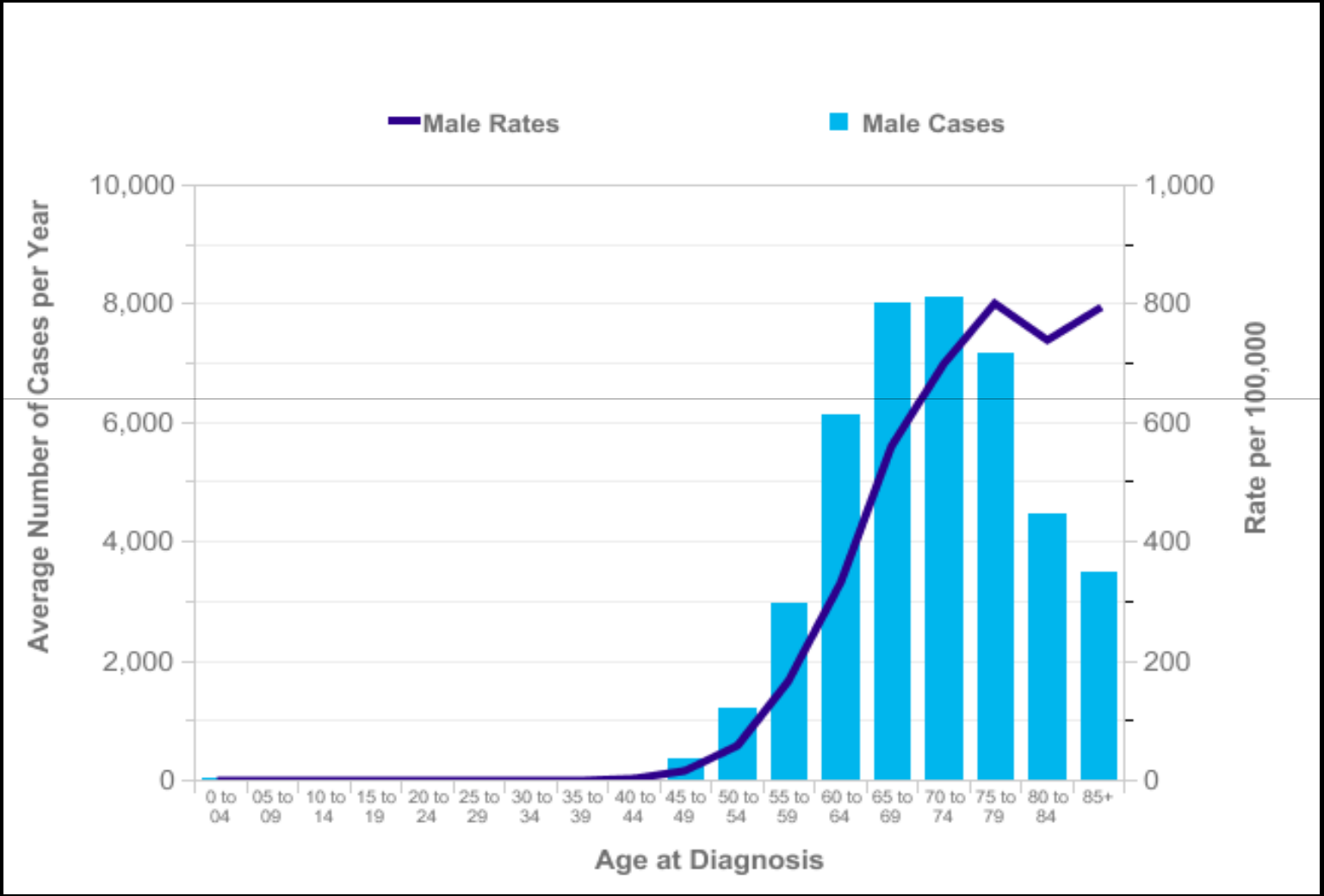
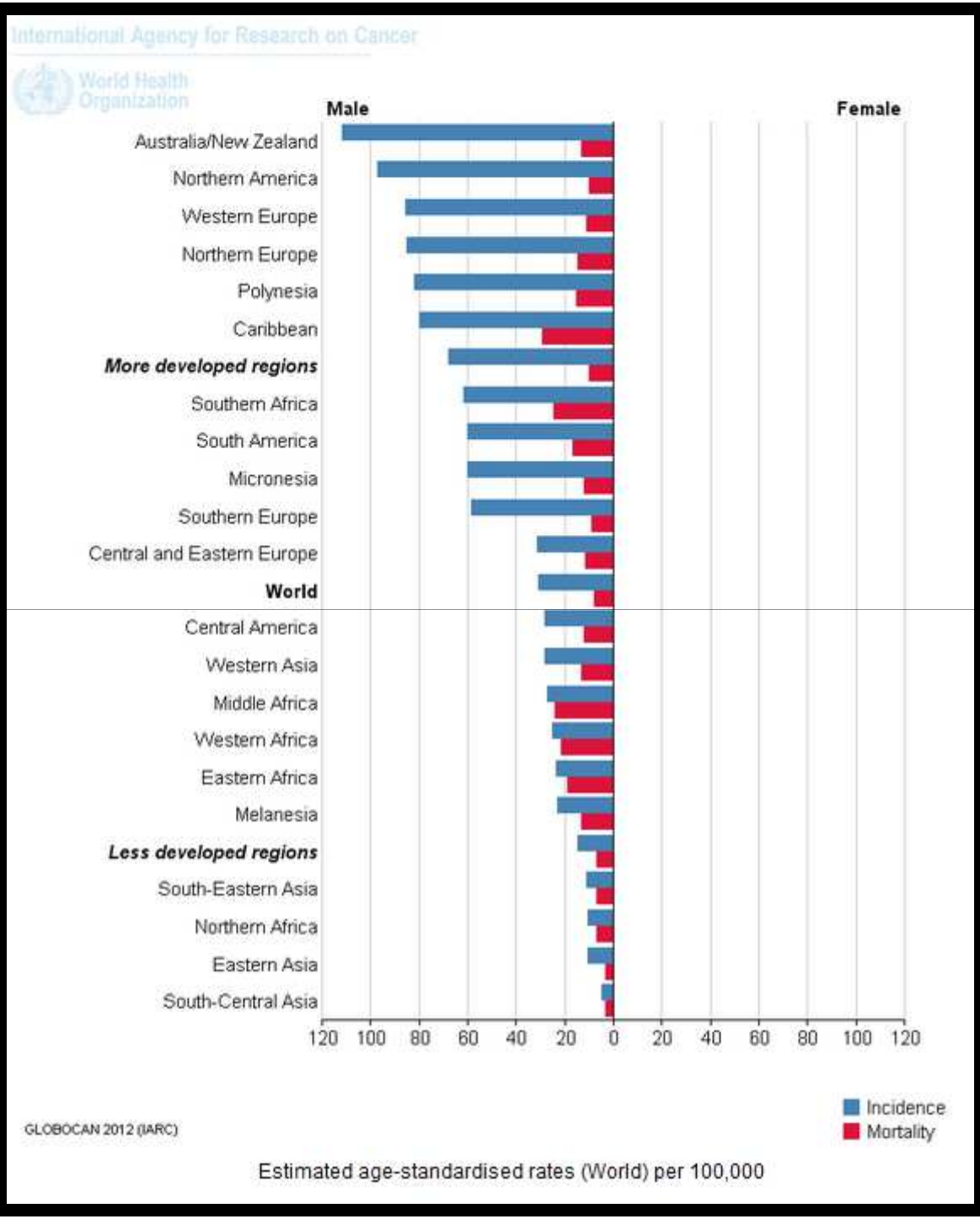
Brachytherapy for prostate cancer Introduction



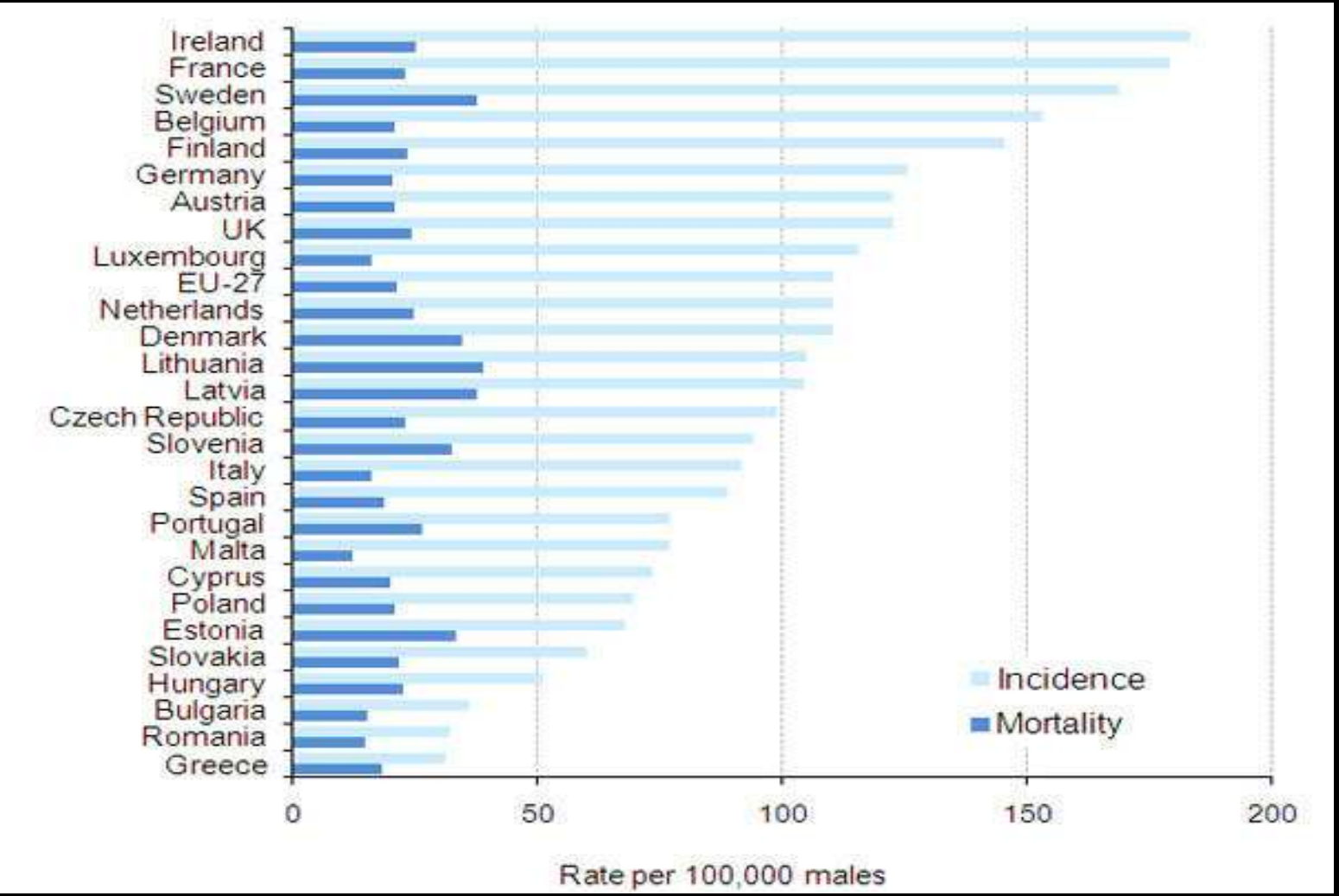
Peter Hoskin
Mount Vernon Cancer Centre

Age specific incidence rates UK 2009/11




International Agency for Research on Cancer
World Health Organization
Male
Female
Australia/New Zealand
Northern America
Western Europe
Northern Europe
Polynesia
Caribbean
More developed regions
Southern Africa
South America
Micronesia
Southern Europe
Central and Eastern Europe
World
Central America
Western Asia
Middle Africa
Western Africa
Eastern Africa
Melanesia
Less developed regions
South-Eastern Asia
Northern Africa
Eastern Asia
South-Central Asia
120 100 80 60 40 20 0 20 40 60 80 100 120
Incidence
Mortality
GLOBOCAN 2012 (IARC)
Estimated age-standardised rates (World) per 100,000

Age standardised incidence and mortality rates 2008 Europe



Prognosis of localised prostate cancer

- Presenting PSA
- Gleason score
- T stage

- Perineural invasion
- Length/% of biopsy core involved

- Age at presentation and comorbidity

- Size of dominant lesion on MRI

Risk stratification in prostate cancer

- LOW
  - PSA <10
  - Gleason 6 or less
  - T2a or less
- INTERMEDIATE
  - ONE of the above exceeded
- HIGH
  - TWO or more of the above exceeded

Selection for brachytherapy

Organ confined disease

BRACHYTHERAPY ALONE

Early periprostatic spread

Gross periprostatic spread

BRACHYTHERAPY + EBRT

Partin tables

Probability of organ confined disease in very early prostate cancer (based on the Partin tables) [55]

Gleason score	T1c	T2a	T2b	T2c
PSA 2.6–4.0				
2–4	92% (82–98)	85% (69–96)	80% (61–95)	78% (58–94)
5–6	84% (81–86)	71% (66–75)	63% (57–59)	61% (50–70)
PSA 4.1–6.0				
2–4	90% (78–98)	81% (63–95)	75% (55–93)	73% (52–93)
5–6	80% (78–83)	66% (62–70)	57% (52–63)	55% (44–64)
PSA 6.1–10.0				
2–4	87% (73–97)	76% (56–94)	69% (47–91)	67% (45–91)
5–6	75% (72–77)	58% (54–61)	49% (43–54)	46% (36–56)

Figure in brackets are 95% confidence intervals.

BJUI SUPPLEMENTS

Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group

Peter Grimm[1], Ignace Billiet[2], David Bostwick[3], Adam P. Dicker[4], Steven Frank[5], Jos Immerzeel[6], Mira Keyes[7], Patrick Kupelian[8], W. Robert Lee[9], Stefan Machtens[10], Jyoti Mayadev[11], Brian J. Moran[12], Gregory Merrick[13], Jeremy Millar[14], Mack Roach[15], Richard Stock[16], Katsuto Shinohara[15], Mark Scholz[17], Ed Weber[18], Anthony Zietman[19], Michael Zelefsky[20], Jason Wong[21], Stacy Wentworth[22], Robyn Vera[23] and Stephen Langley[24]

[1]Prostate Cancer Center of Seattle, WA, USA, [2]Urology Centre Kortrijk, Belgium, [3]Bostwick Laboratories, Glen Allen, VA, USA, [4]Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, USA, [5]MD Andersen Center, Houston, TX, USA, [6]The Prostate Clinic, Utrecht, The Netherlands, [7]BC Cancer Agency Vancouver Center, Vancouver, BC, Canada, [8]UCLA, Los Angeles, CA, USA, [9]Duke University Medical Center, Durham, NC, USA, [10]Department of Urology, Marien-Krankenhaus, Bergisch Gladbach, Germany, [11]University of California, Davis, CA, USA, [12]Chicago Prostate Center, Westmont, IL, USA, [13]Urologic Research Institute, Wheeling Jesuit University, WV, USA, [14]Alfred Health and Monash Univeristy, Melbourne, Australia, [15]University of California, San Francisco, CA, USA, [16]Mt Sinai Medical Center, New York, USA, [17]Prostate Cancer Research Institute, Los Angeles, CA, USA, [18]Prostate Cancer Center of Seattle, WA, USA, [19]Harvard Medical School, Boston, MA, USA, [20]Memorial Sloan Kettering Cancer Center, New York, USA, [21]University of California, Irvine, CA, USA, [22]Piedmont Radiation Oncology, Greensboro, NC, USA, [23]Virginia Commonwealth University, Richmond, VA, USA, and [24]Department of Urology, Royal Surrey County Hospital, Guildford, UK

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Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group

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	No. of patients (no. of studies)		
Treatment type	Low risk	Intermediate	High
RP	6447 (6)	3696 (4)	5149 (11)
Robotic RP	706 (1)	479 (1)	200 (1)
Seeds alone	8133 (17)	5808 (15)	295 (1)
Seeds + EBRT	726 (1)	1554 (6)	2864 (15)
EBRT + seeds + ADT	–	–	1231 (6)
HDR (seeds)	226 (2)	607 (4)	869 (5)
Protons	388 (2)	162 (1)	–
EBRT alone	4735 (9)	2969 (10)	3828 (11)
HIFU	227 (1)	–	–
Cryotherapy	–	175 (1)	357 (2)
Seeds + ADT	–	165 (1)	–

ADT, androgen deprivation therapy; HDR, high dose radiotherapy; HIFU, high intensity focused ultrasound; RP, radical prostatectomy; EBRT, external beam radiation.

CANCER CONTROL RATES: COMPARISON OF TREATMENT OPTIONS

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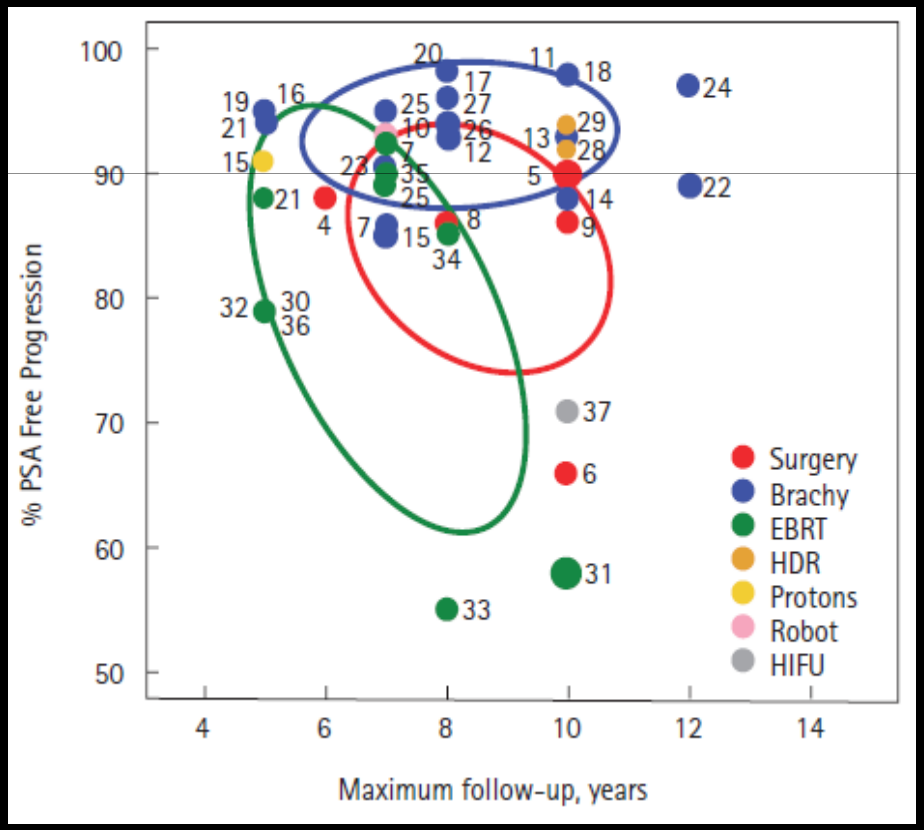
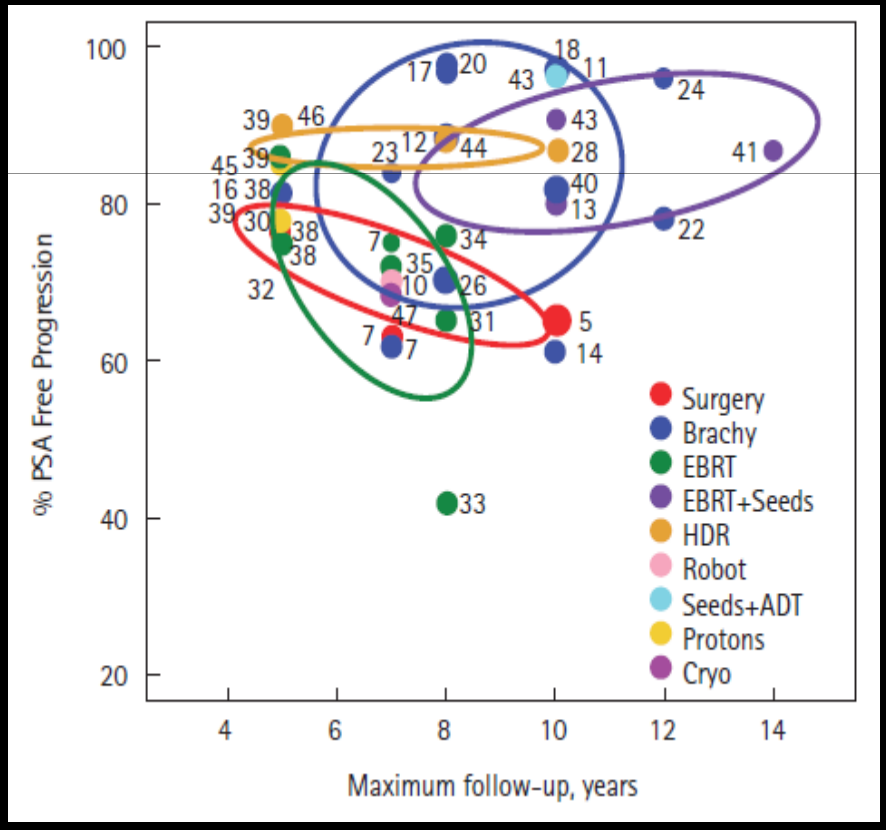
LOW risk



INTERrisk



CANCER CONTROL RATES: COMPARISON OF TREATMENT OPTIONS

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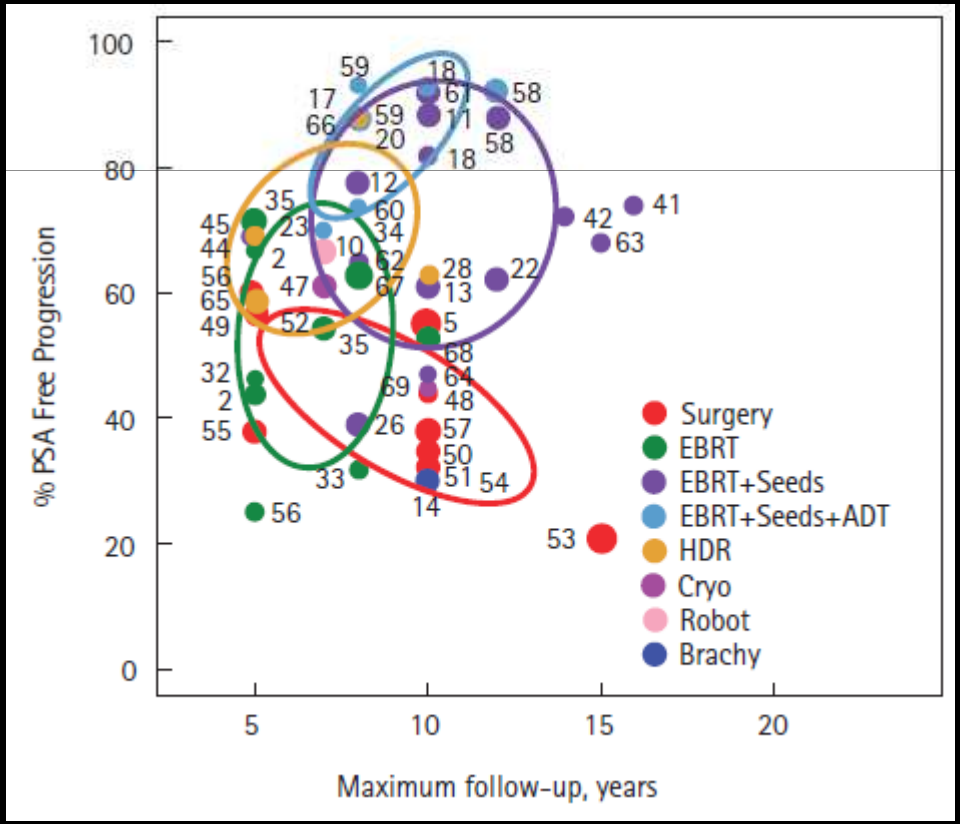
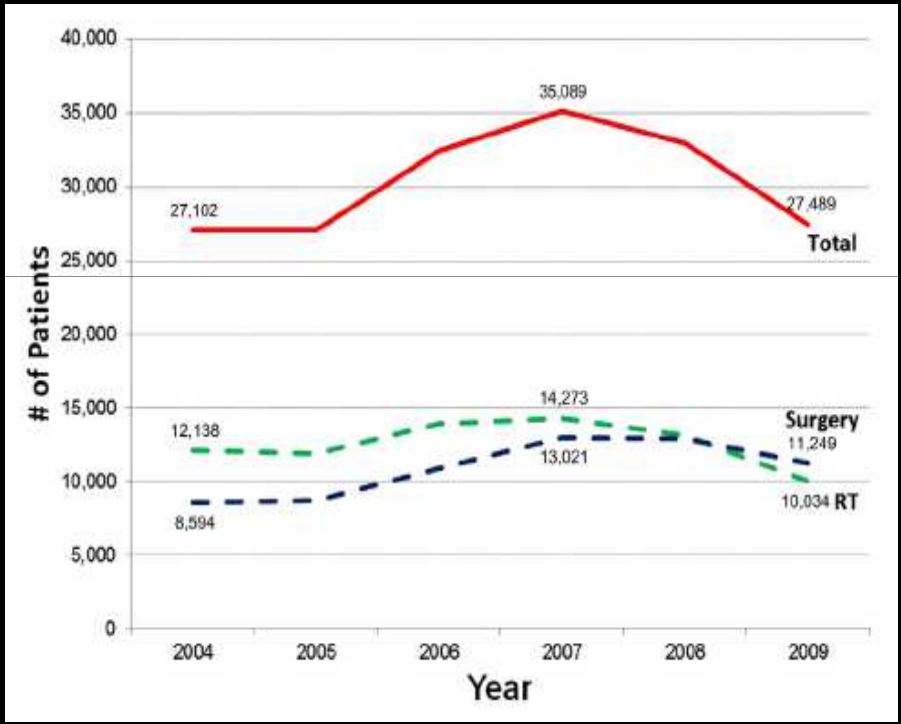
HIGH risk

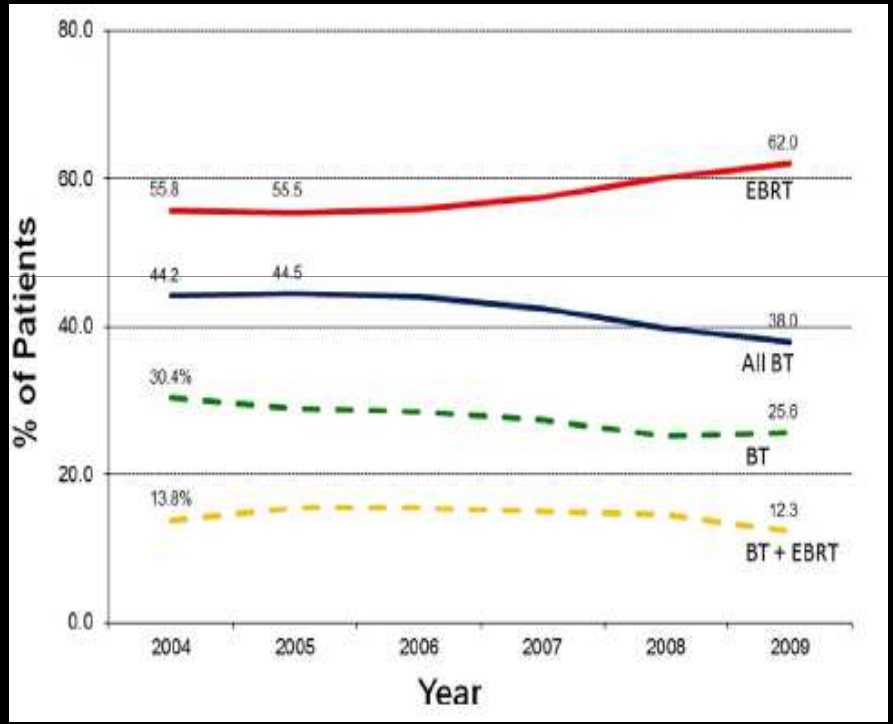


Declining use of brachytherapy for the treatment of prostate cancer

Usama Mahmood[1,*], Thomas Pugh[1], Steven Frank[1], Lawrence Levy[1], Gary Walker[1], Waqar Haque[1], Matthew Koshy[2], William Graber[3], David Swanson[3], Karen Hoffman[1], Deborah Kuban[1], Andrew Lee[1]

Brachytherapy 13 (2014) 157–162





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Permanent Prostate Implants

Permanent prostate implants
choice of isotopes

- Low energy photons
- High nominal specific activity

	I125	Pd103	Cs131
Half life (days)	59.4	17.0	9.7
Mean photon energy (keV)	28.4	20.7	30.3
HVL (mm)	0.025	0.0085	0.022
Nominal specific activity ($x10^5 TBqkg^{-1}$)	6.5	27	38

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Dose rate and clinical outcome

No difference in outcome demonstrated in clinical studies.

No preference of one isotope above the other

	I125	Pd103
Average dose rate (cGy/h)	7	19
Prescribed dose	144 Gy	115 Gy

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PATIENT SELECTION

Risk Stratification in Prostate Cancer

- Low
  - PSA < 10 ng/ml
  - Gleason score ≤ 6
  - ≤ T2a
- Intermediate
  - One risk factor

  High
  - Two risk factors

Risk Stratification in Prostate Cancer

- Low
  - PSA < 10 ng/ml
  - Gleason score ≤ 6
  - ≤ T2a
- Intermediate
  - One risk factor
- High
  - Two risk factors

Suitable for monotherapy

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Select on Urinary Complaints to prevent Bladder Retention

- Anamnestic no or limited urinary complaints
  - Urinary frequency, obstruction, incontinence
- IPSS
  - < 8-19
- Qmax
  - >10-15 ml/s
- PVR
  - < 150-200 ml

Prostate Volume and Pubic Arch

Large prostate volumes | > 50-60 ml

- Higher probability on acute bladder retention
- Higher probability on pubic arch interference
  - Leads to poor dosimetric outcome

Large volume prostate

Volume down sizing with:

- Antiandrogen: e.g. bicalutamide daily 100 mg
  - Breast irradiation or tamoxifen 10 mg to prevent gynaecomastia
- LHRH analogue
- Duration 3-6 months

Risk Stratification in Prostate Cancer

- Low
  - PSA < 10 ng/ml
  - Gleason score ≤ 6
  - ≤ T2a
- Intermediate
  - One risk factor
- High
  - Two risk factors

Suitable for combined therapy
- EBRT
- ADT

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TECHNIQUES

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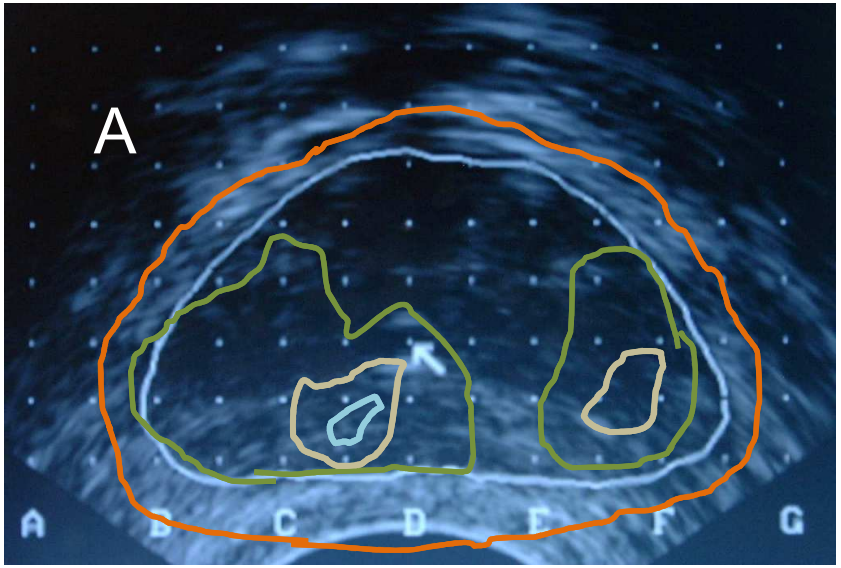
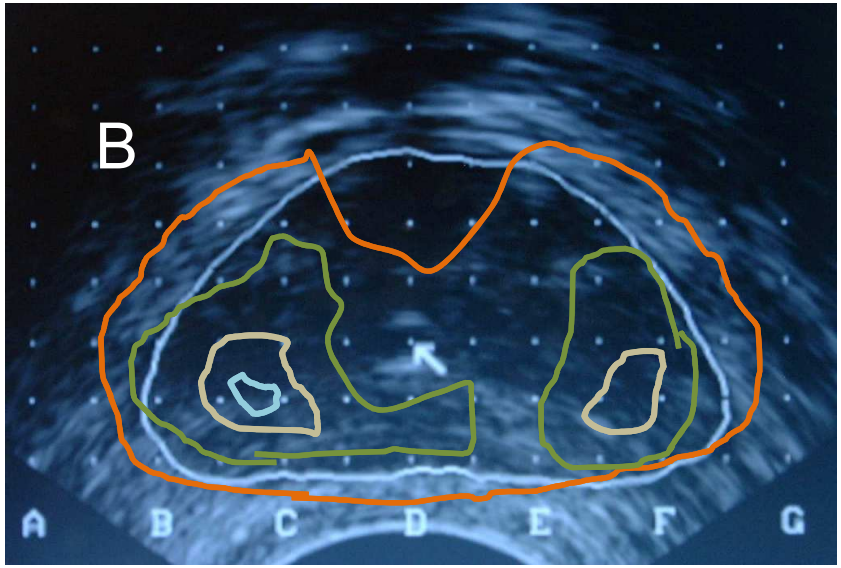
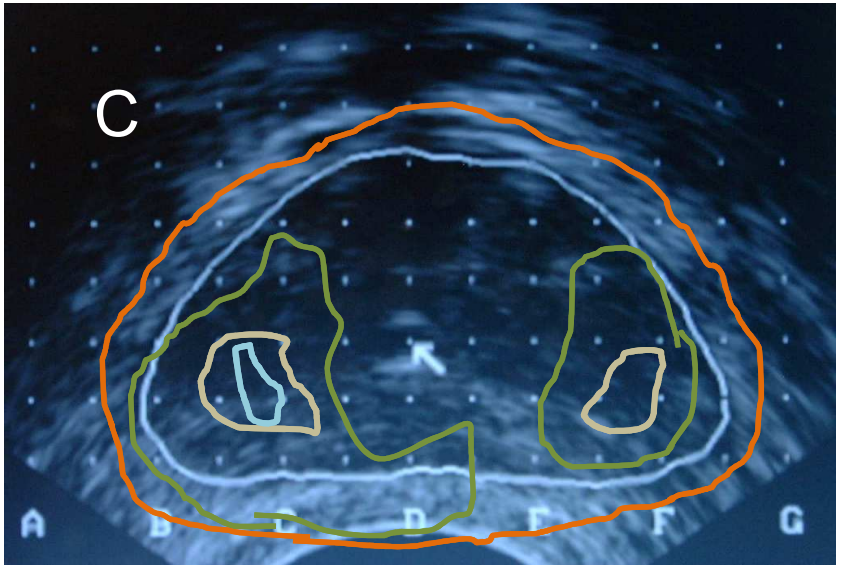
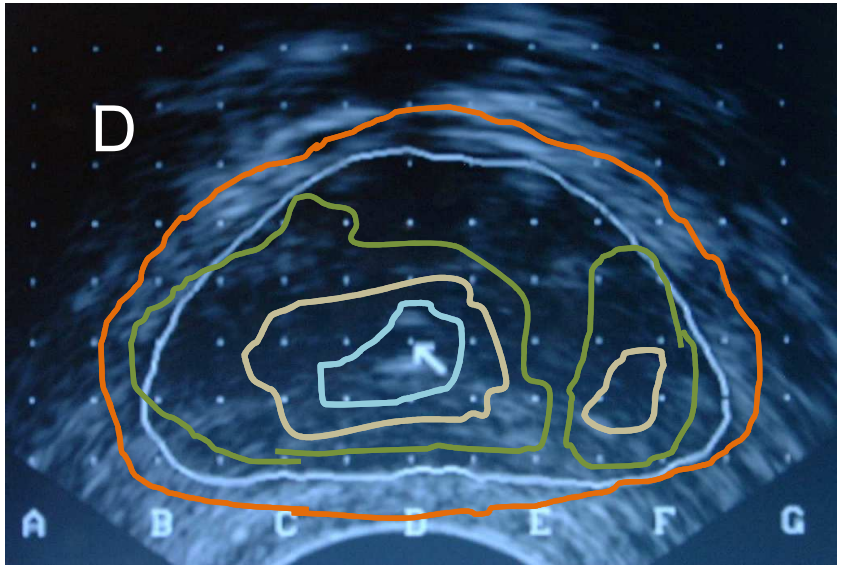
Which Isodose distribution would you prefer?





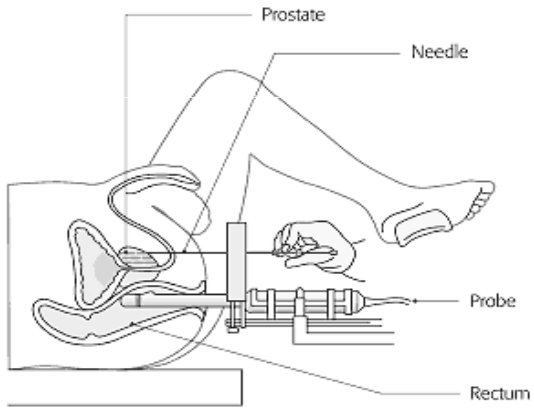
100 %
140%
150%
170%

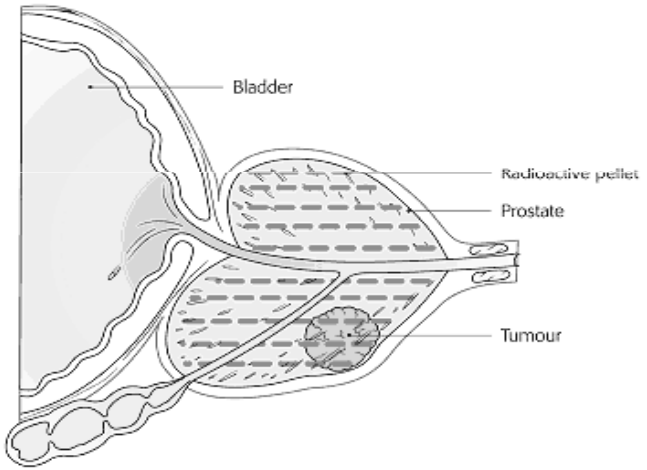




Perineal prostate implantation

- Perineal technique
- Ultrasound guided
- Ultrasound probe on immobilizer
- Template





Holm, J Urol 1983

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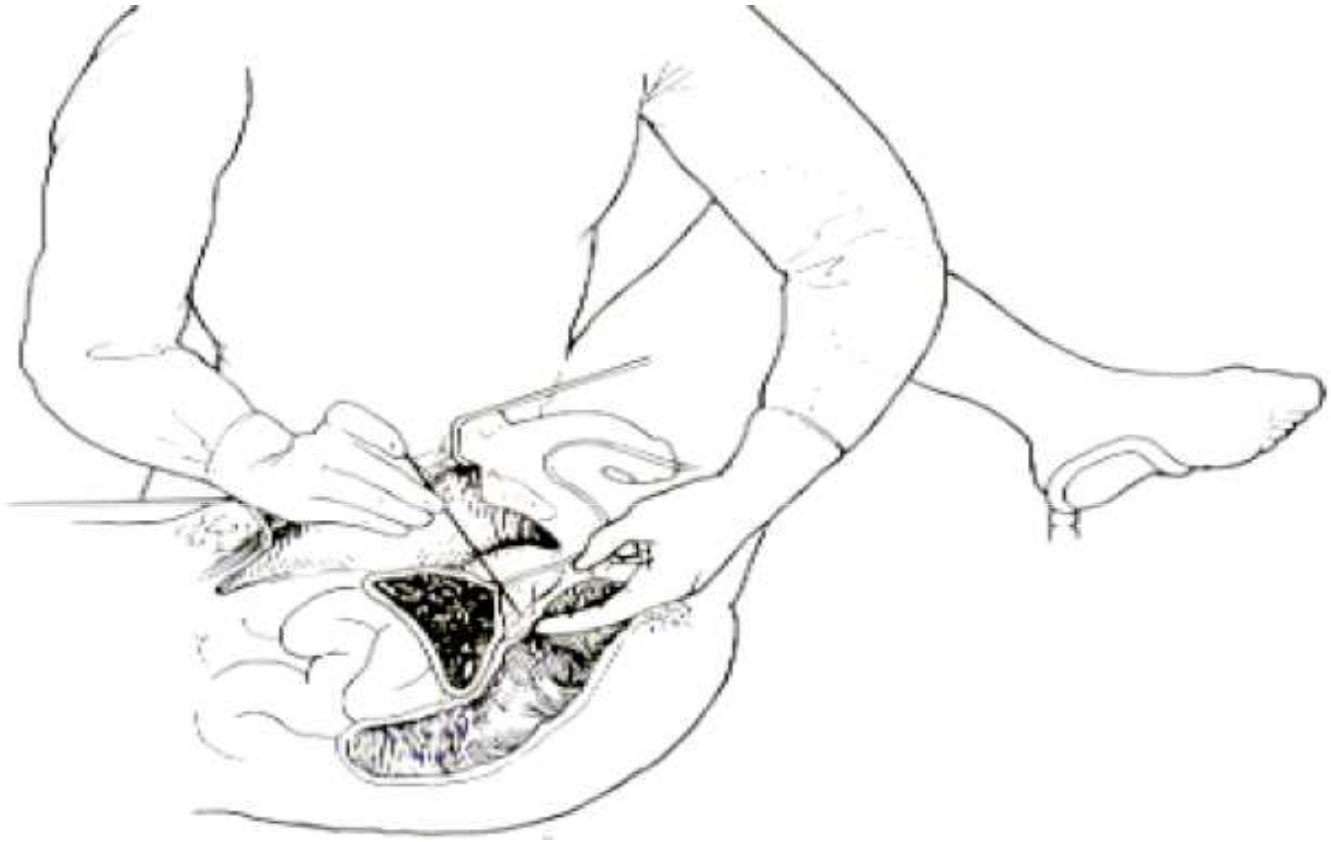
Retropubic Prostate Implant Technique



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Results Retropubic Technique

- MSKCC
  - Local failure 48%
- NKI
  - Local failure 52%
- Poor seed distribution. Quality of implant poor. Abandonment in early 80s

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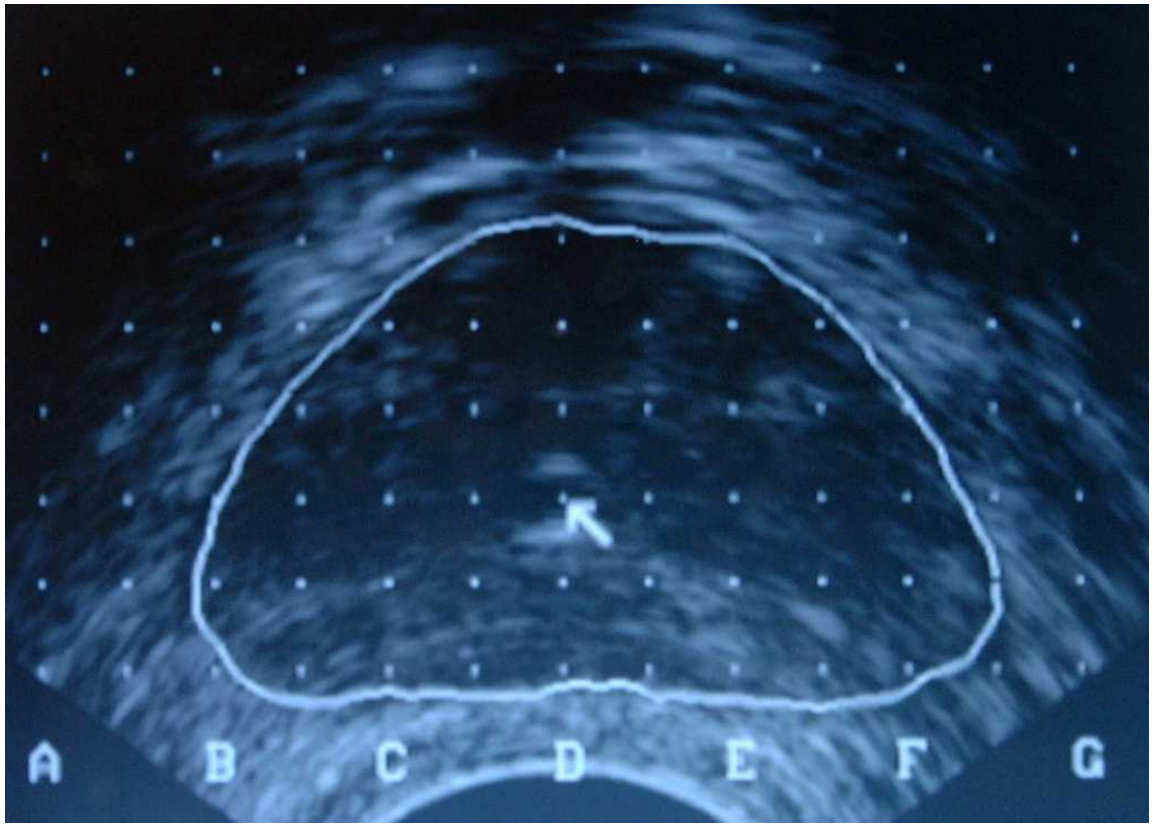
Procedure Seed Implantation

Volume study

# of seeds



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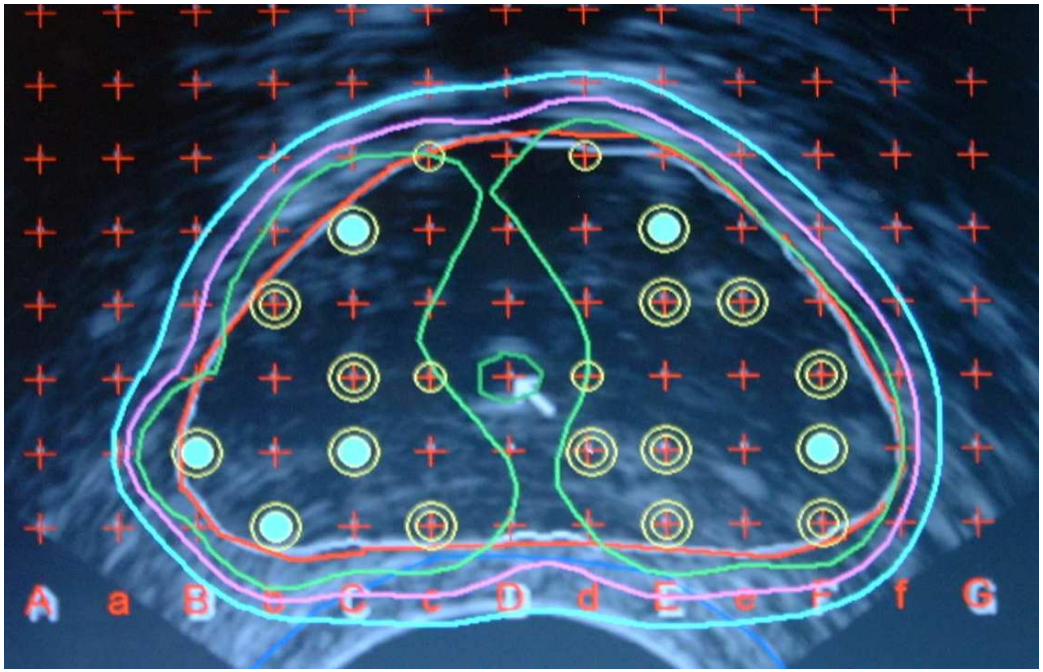
Preplan

Full coverage of prostate
- V100
- D90

Relative sparing of urethra and rectum



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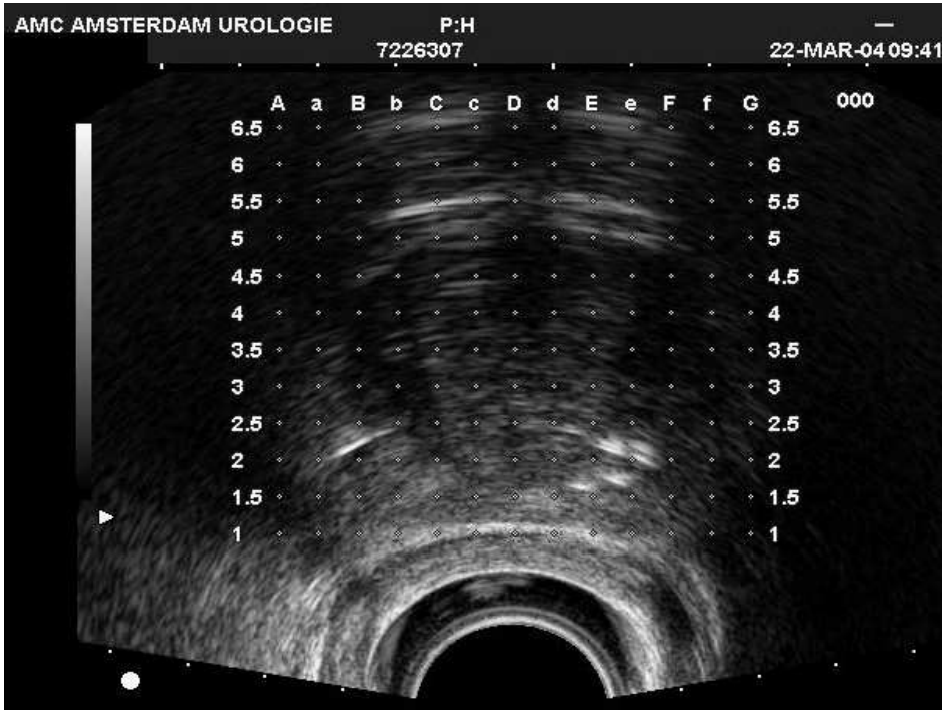
AMC AMSTERDAM UROLOGIE
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7226307
22-MAR-04 09:41
A a B b C c D d E e F f G
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6.5
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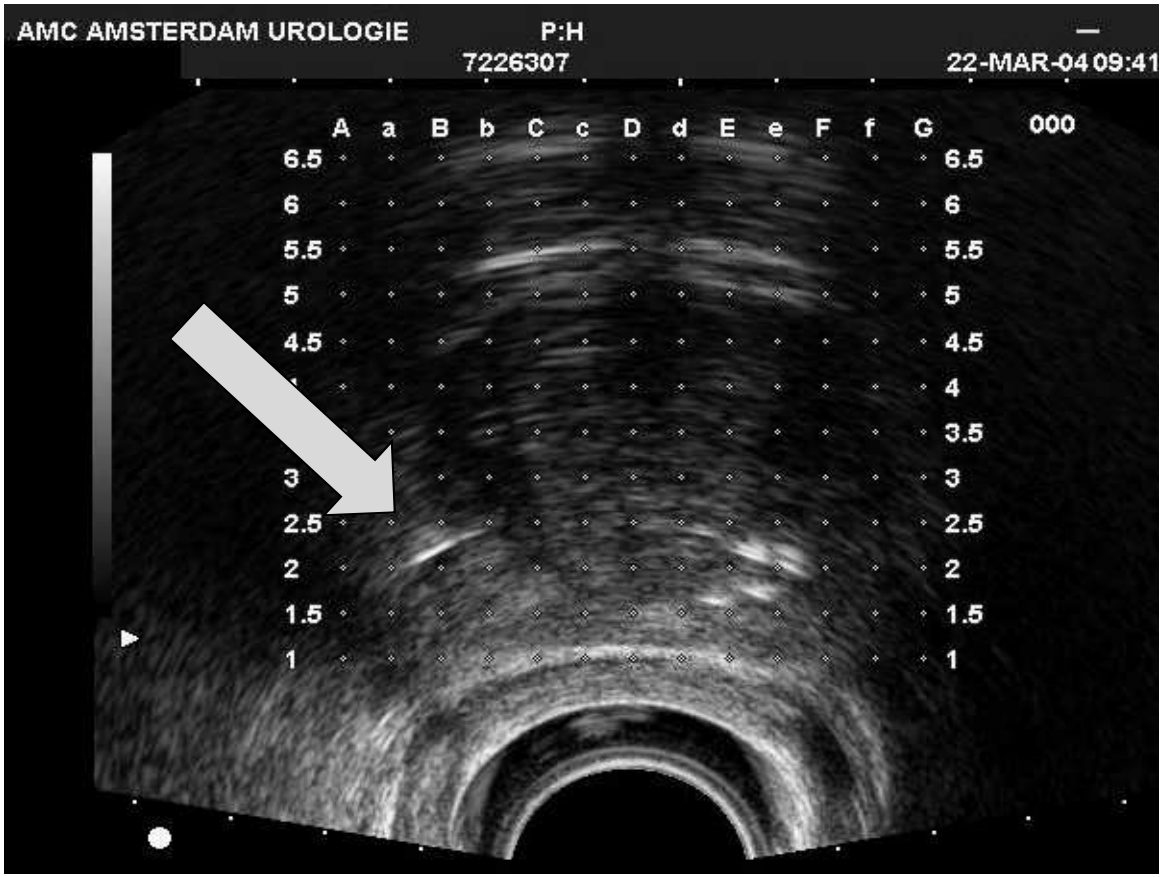
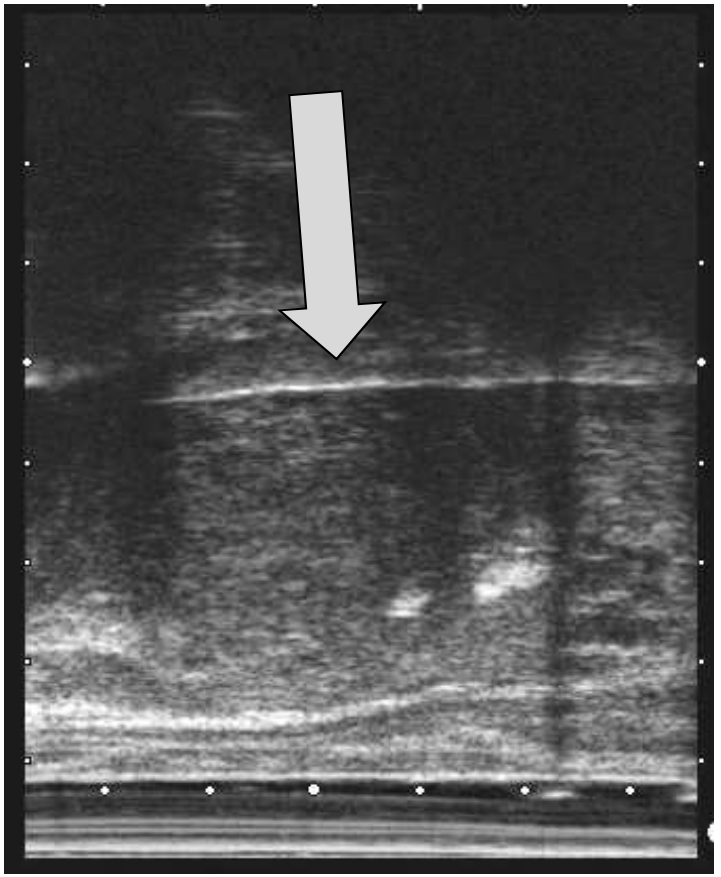
1

Implantation on Ultrasound

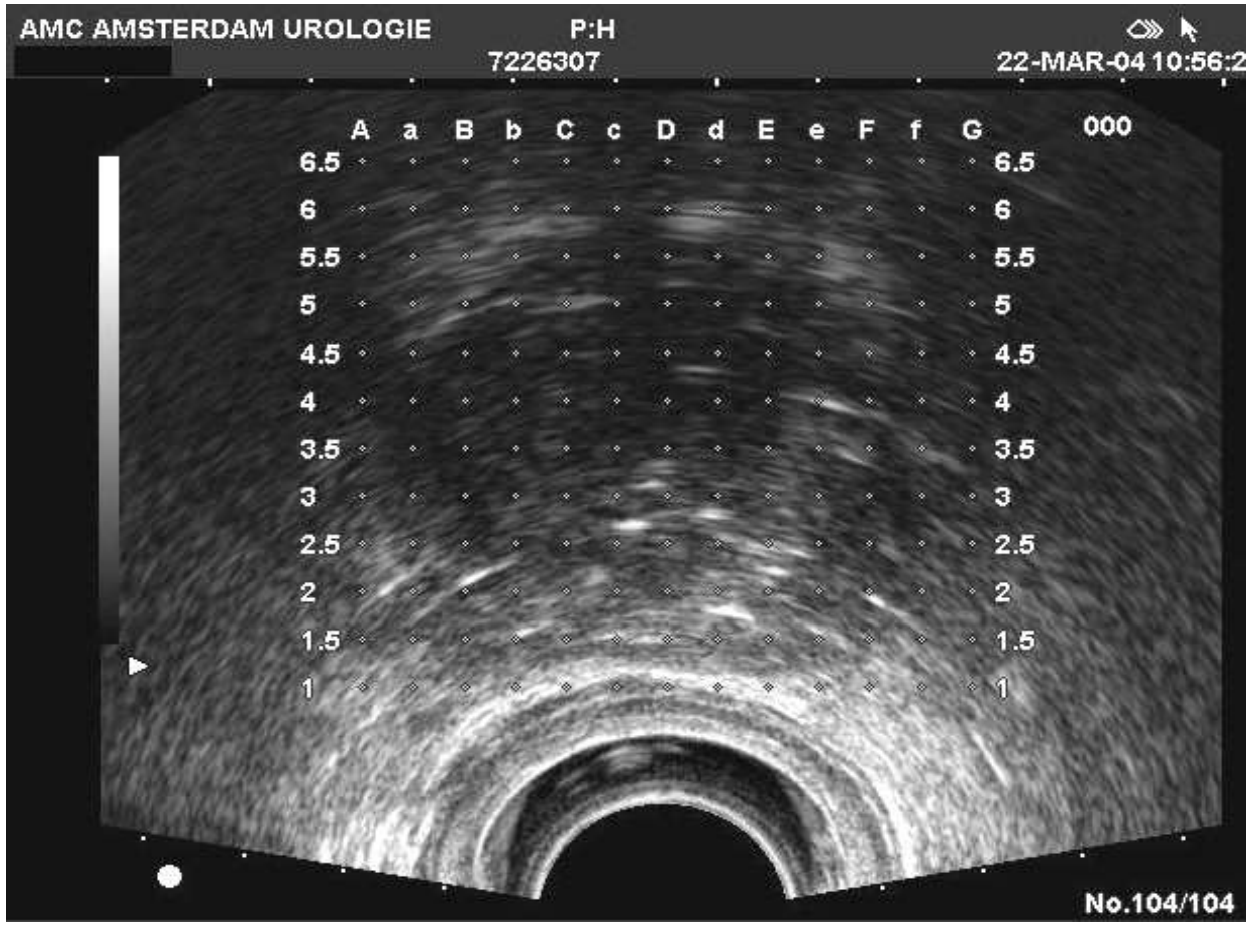


Transversal view

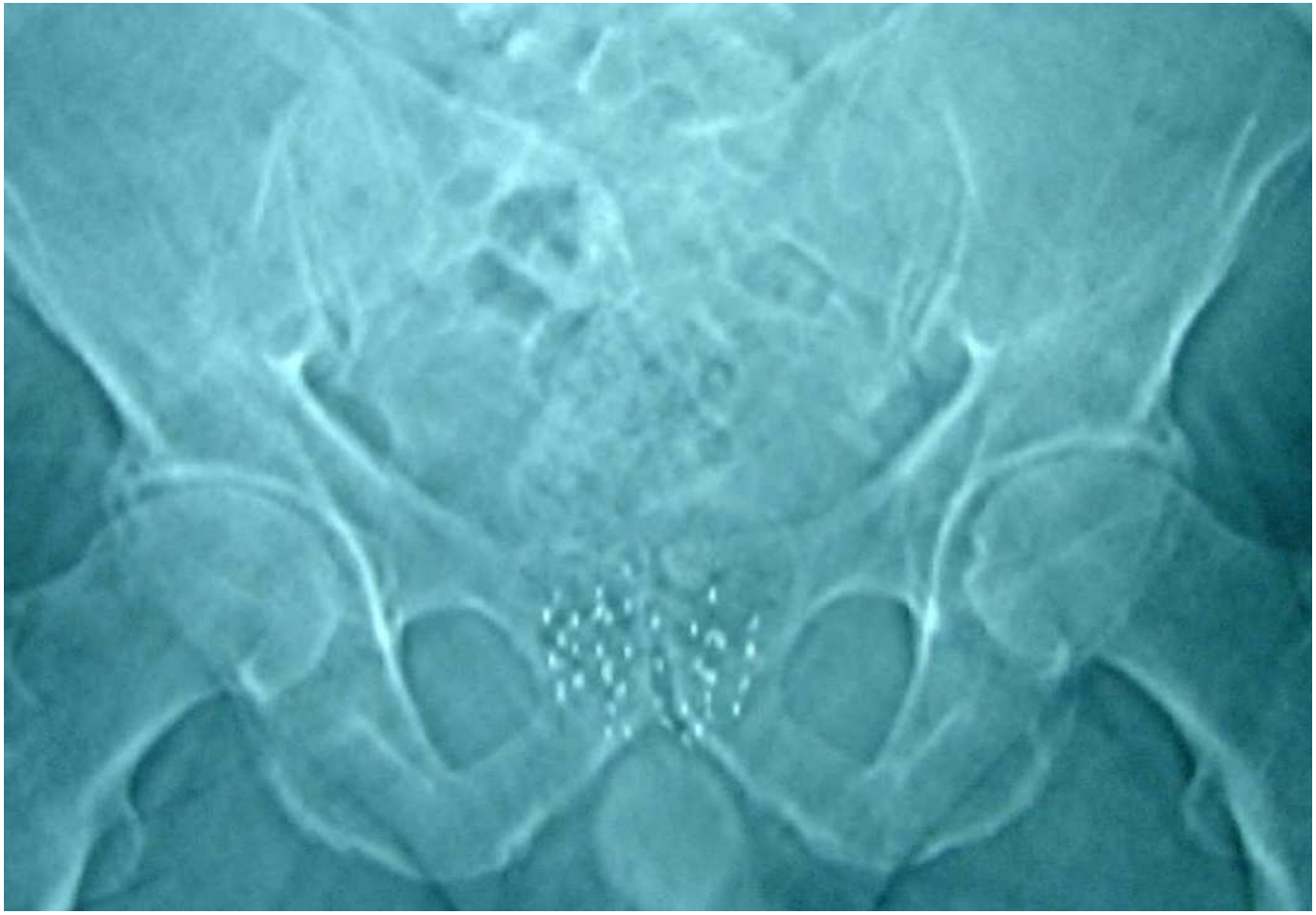


Longitudinal view

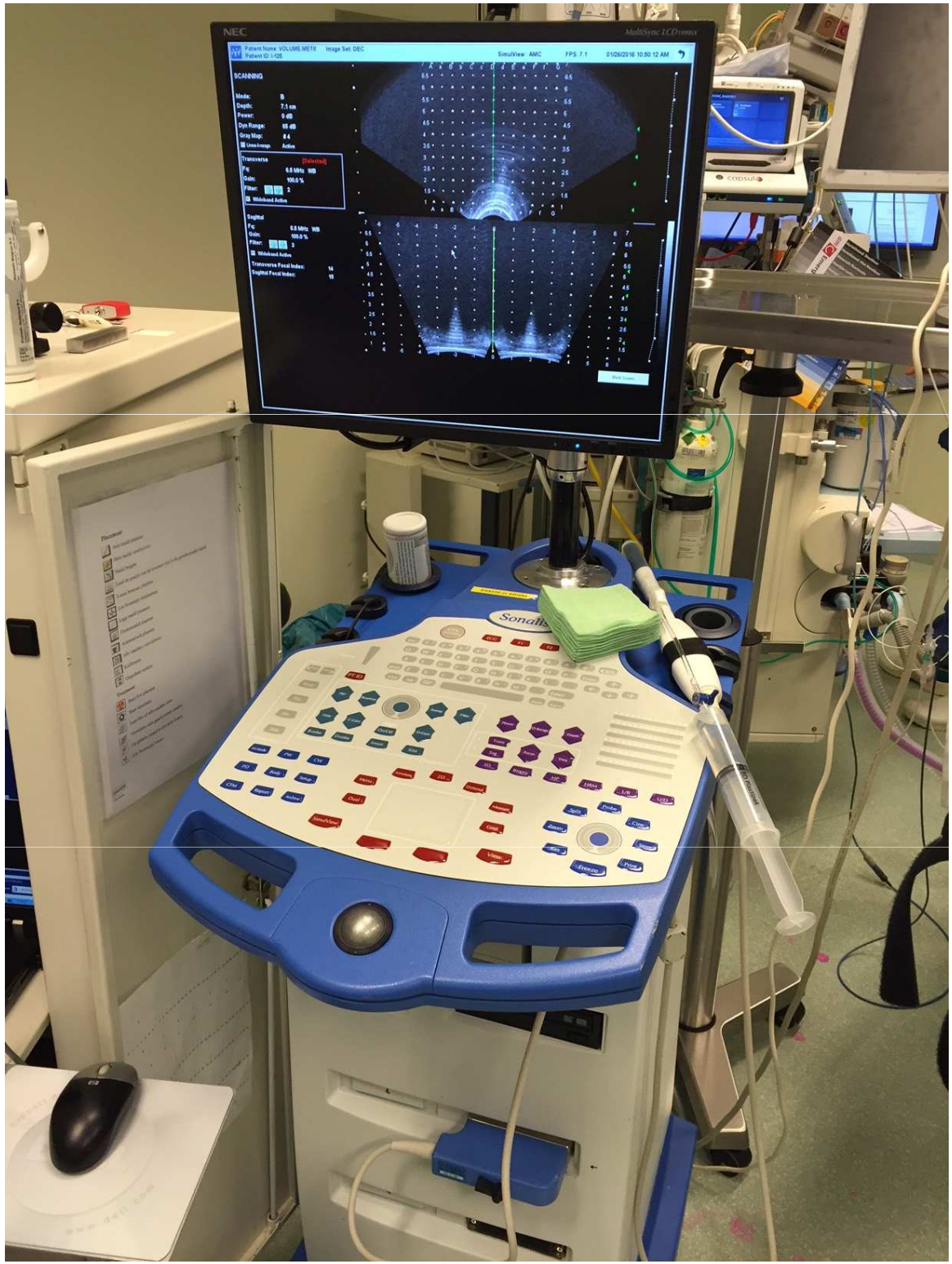
Distribution of Radioactive



Result



US machine



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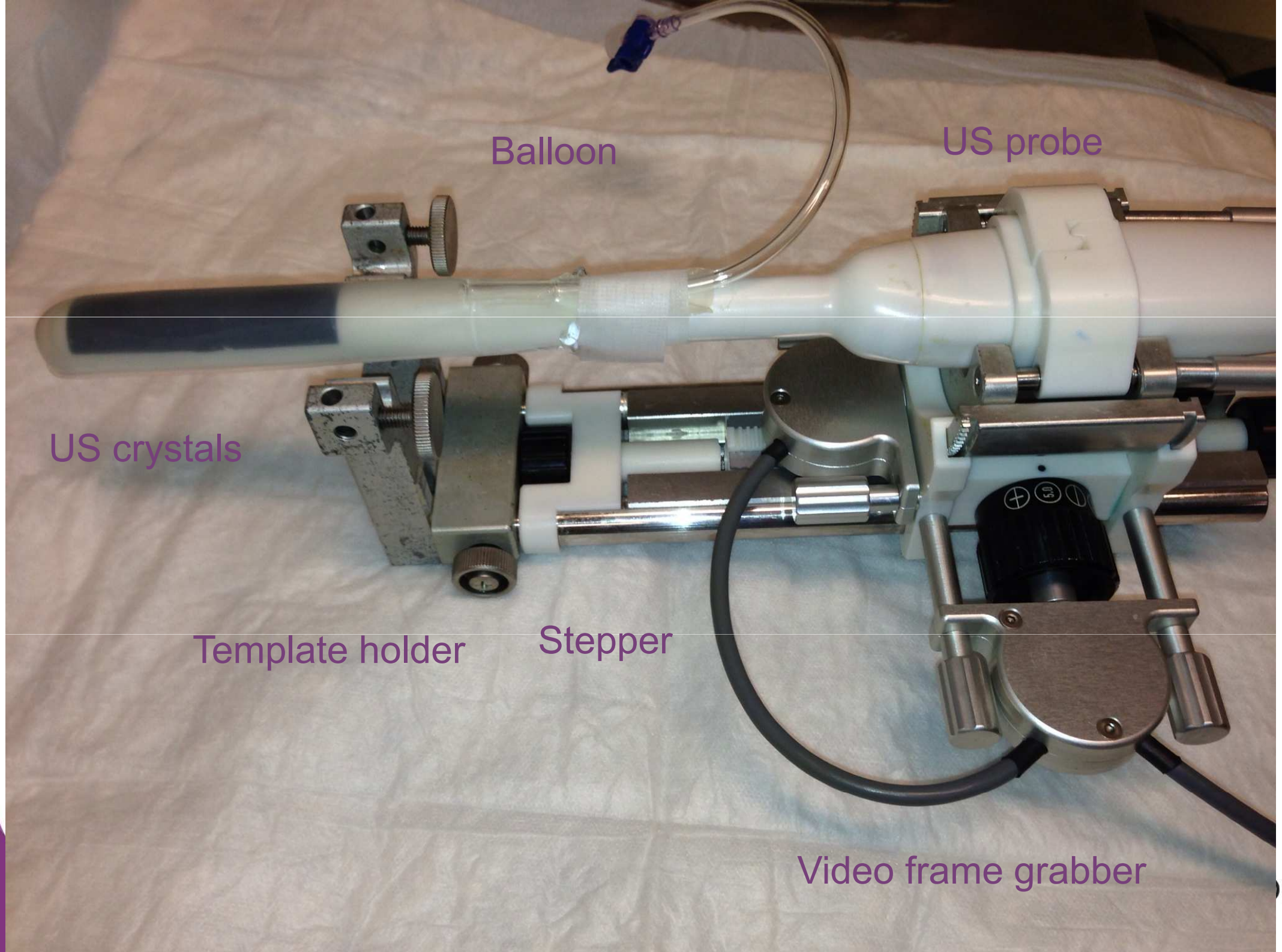
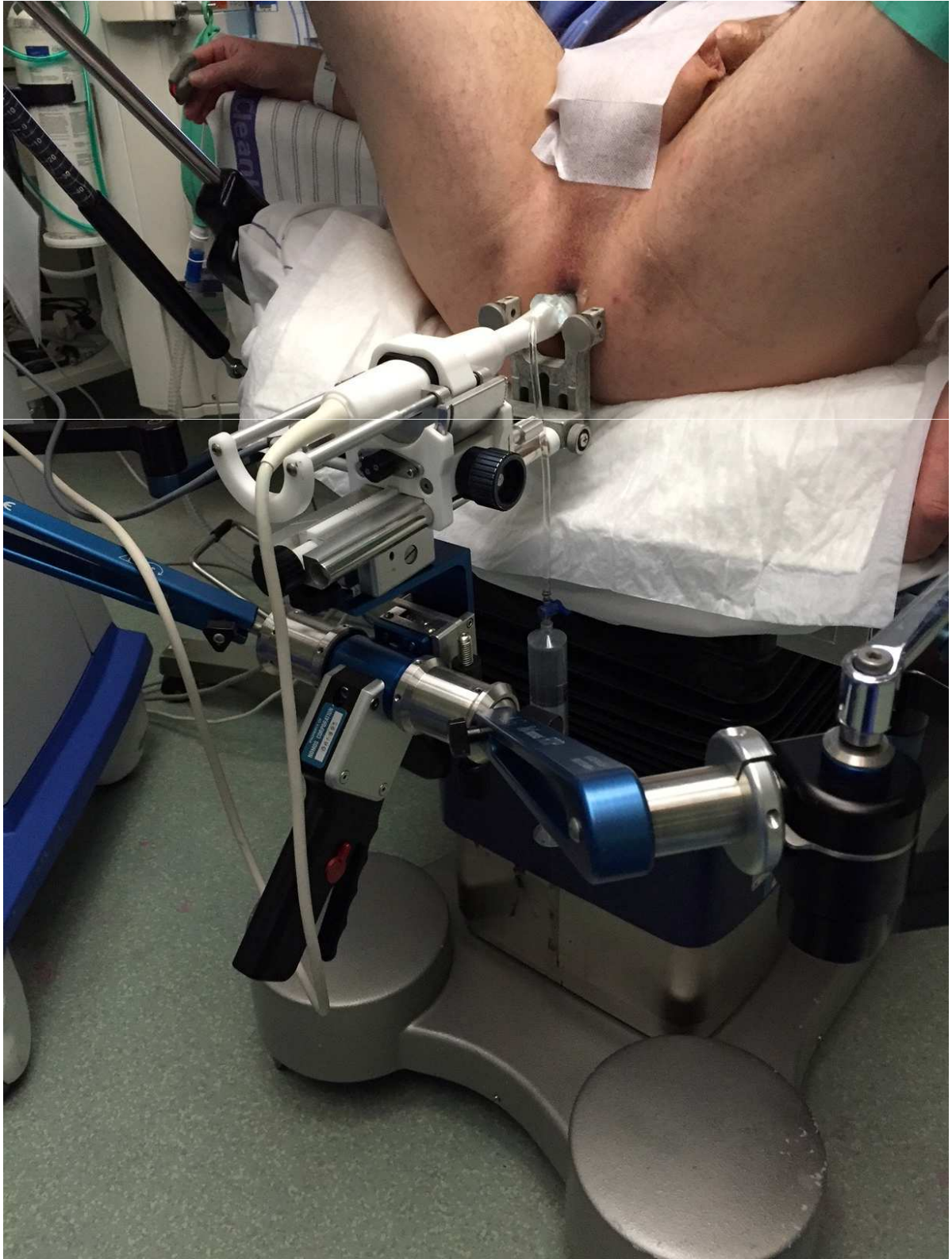
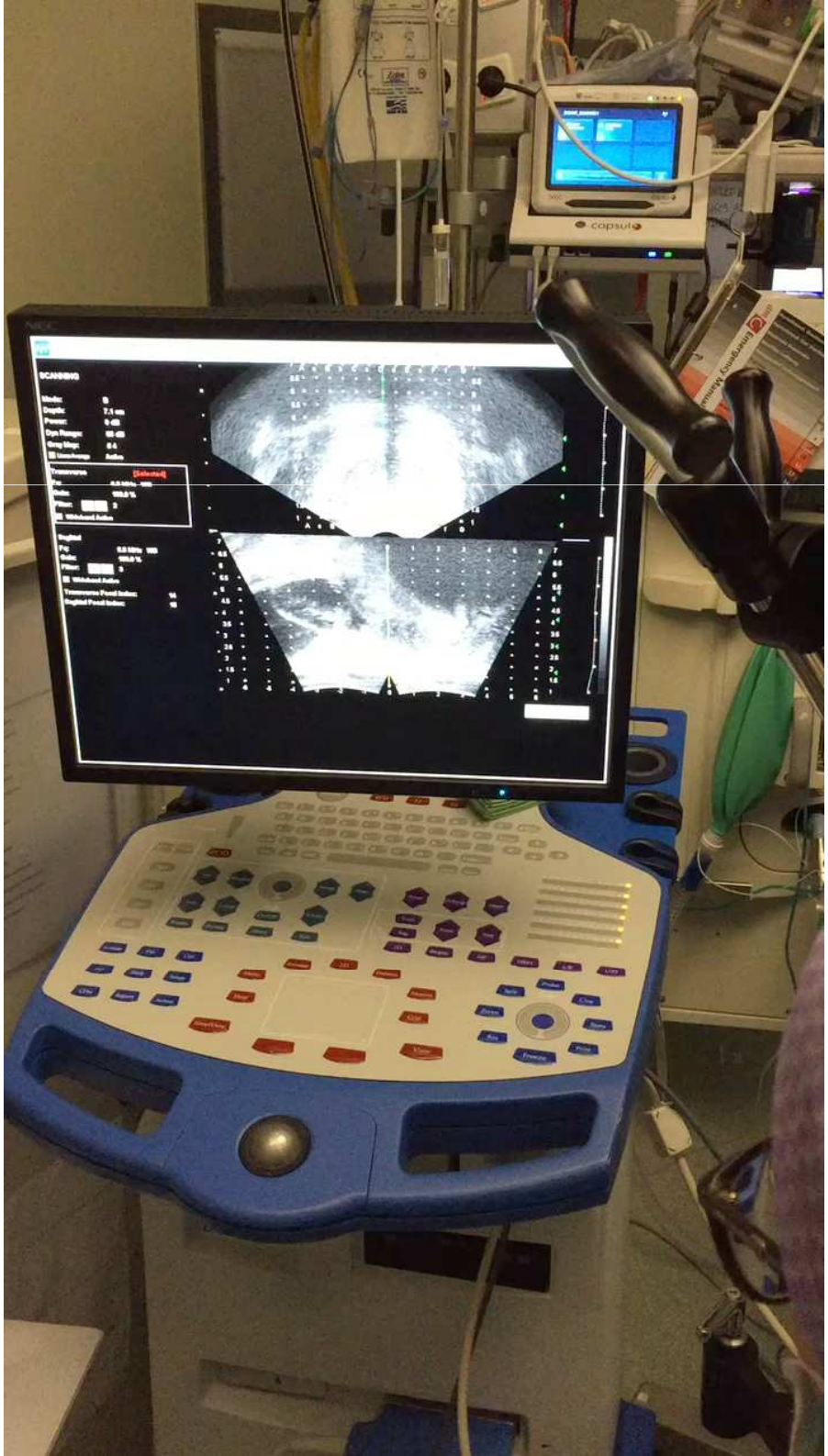

Balloon
US probe
US crystals
Template holder
Stepper
Video frame grabber

Balloon on top of US probe





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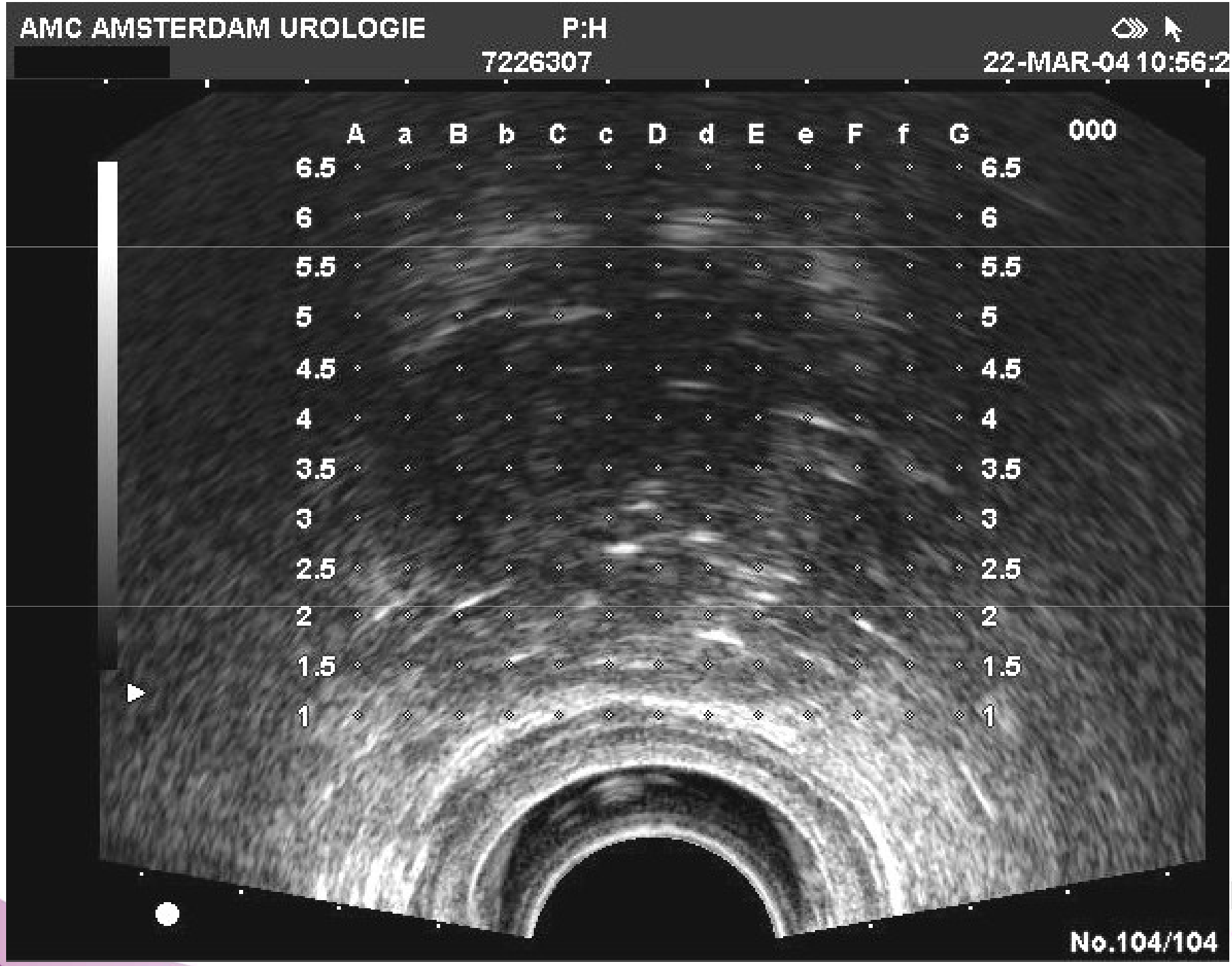
Positioning of the probe. Prostate symetrically within frame.



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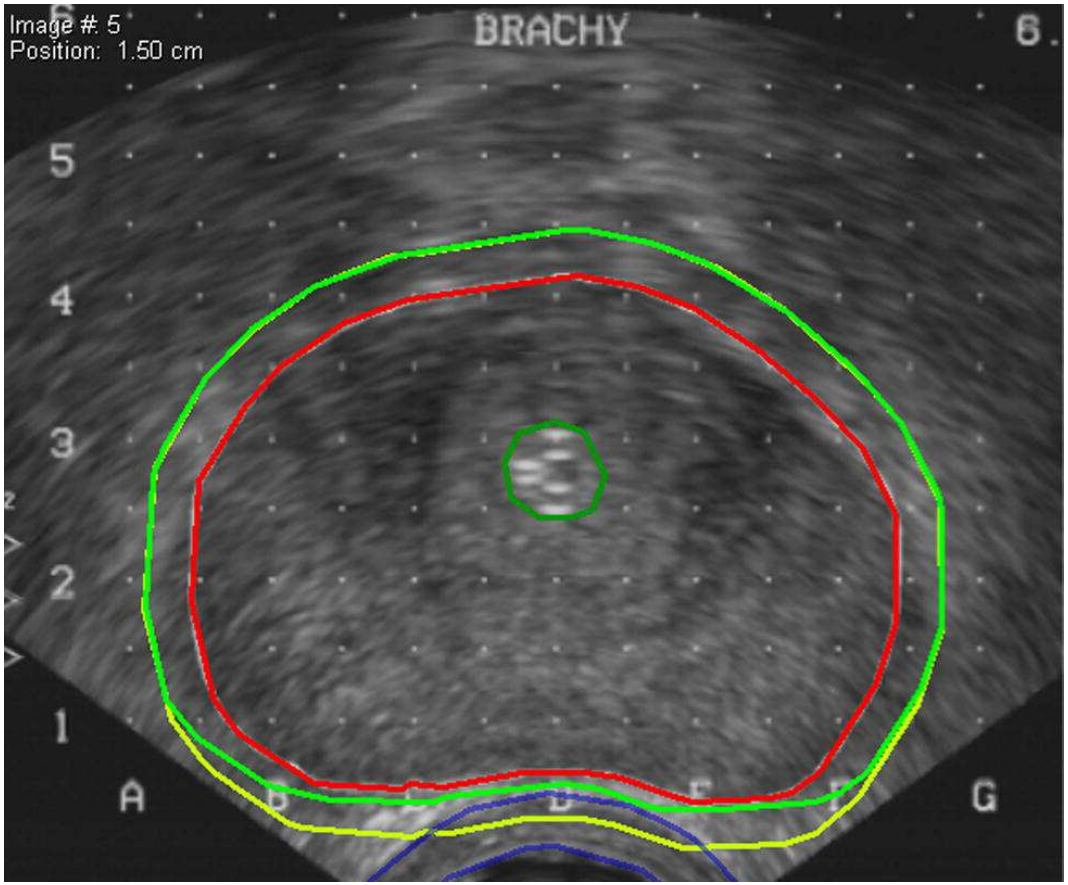
Prostate contouring



ESTRO definitions

Prostate gland

CTV = prostate gland + 3 mm

PTV = CTV

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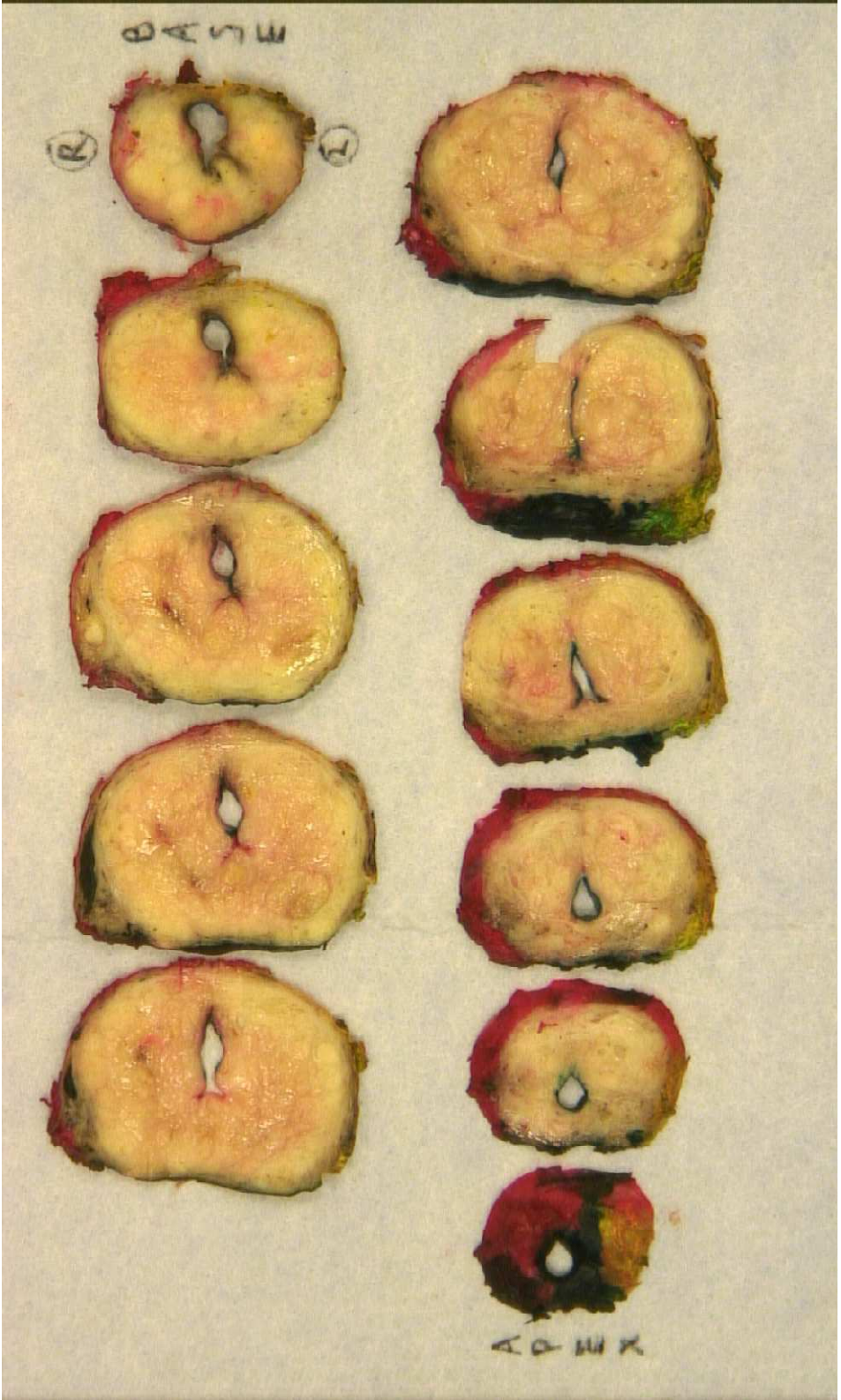

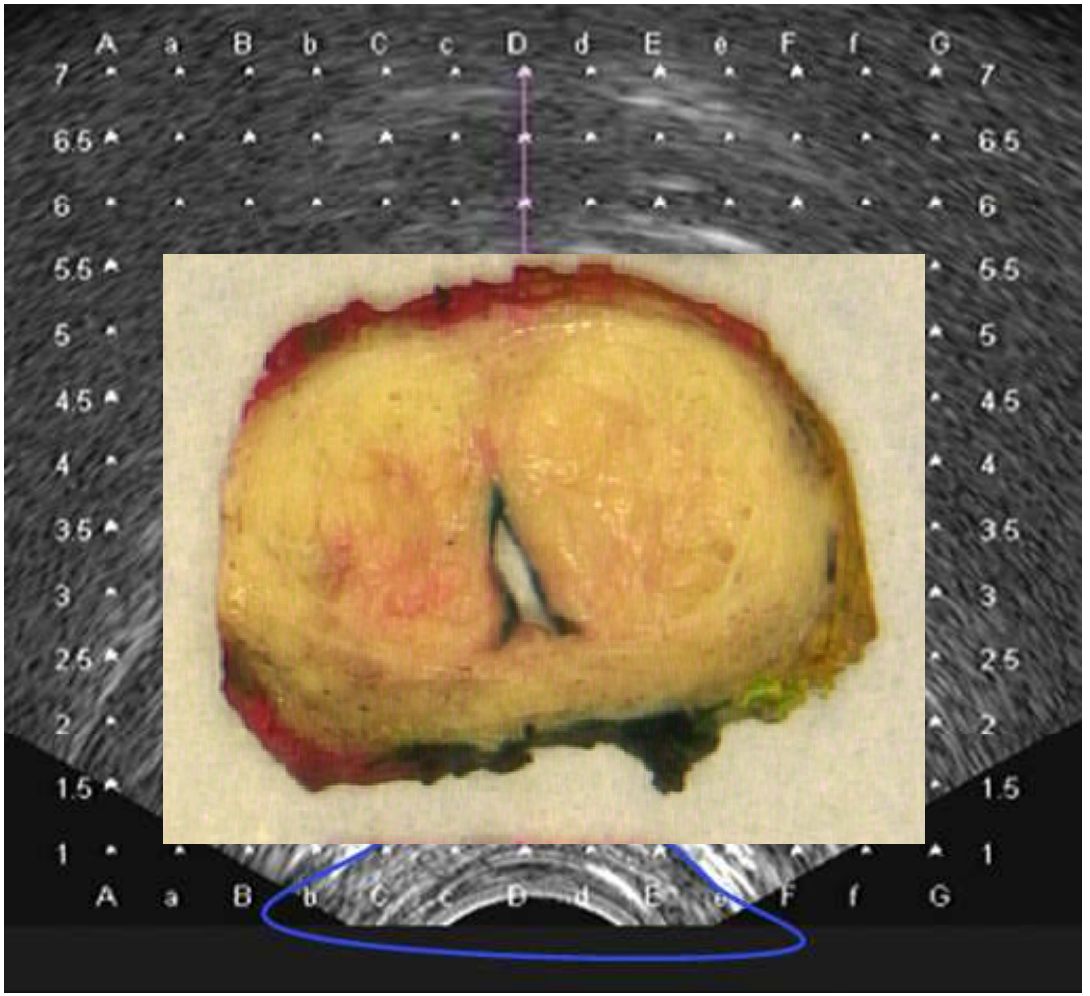
A a B b C c D d E e F f G
7
6.5
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2
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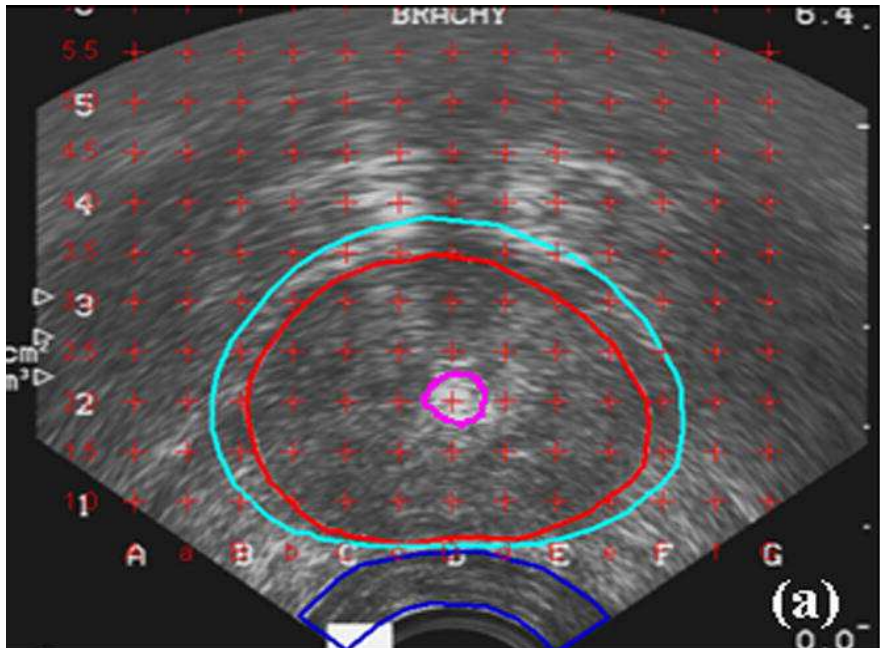
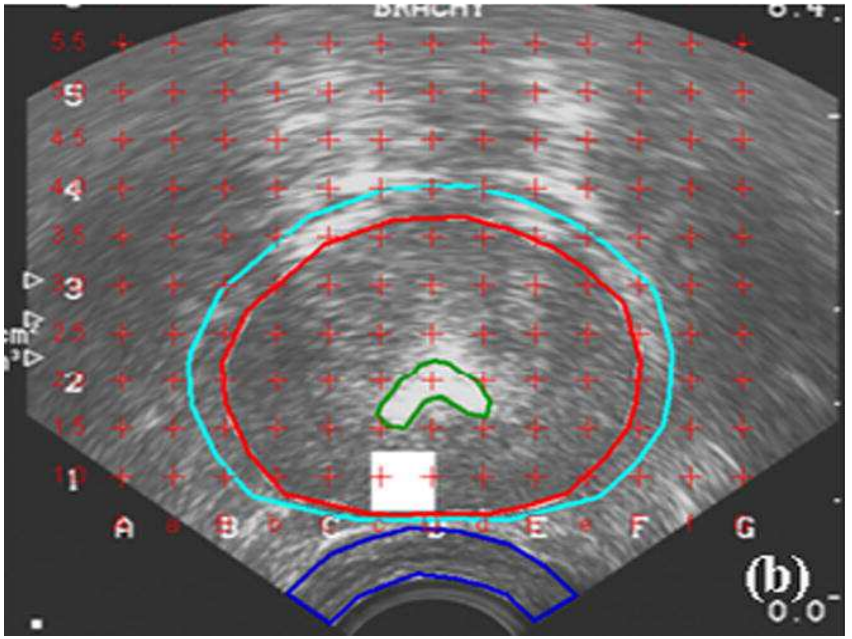
1

Contouring the urethra

Catheter



Aerated Gel



Prostate D90 183 Gy 187 Gy Δ 2%

Anderson et al.Radiother Oncol 2010

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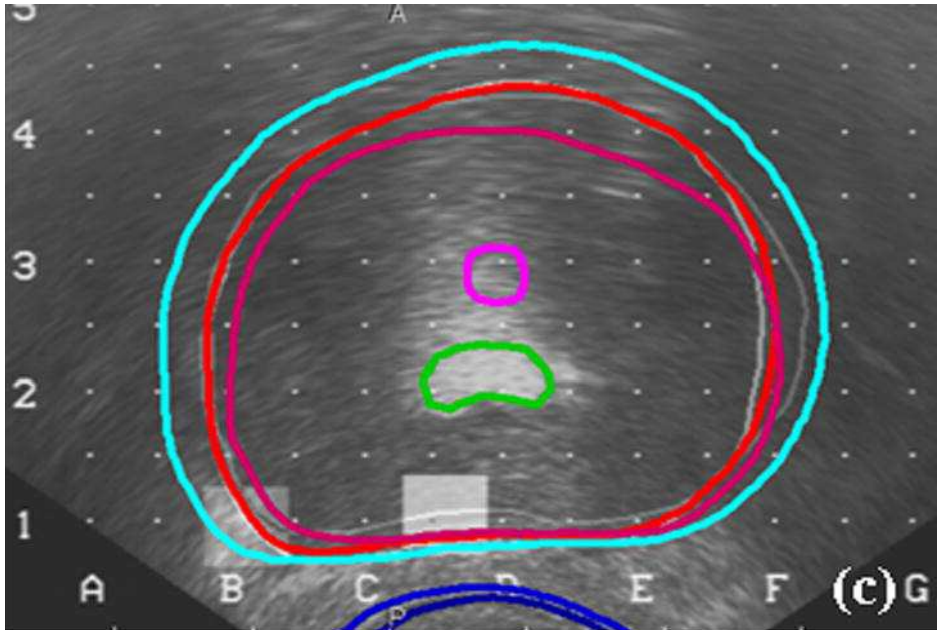

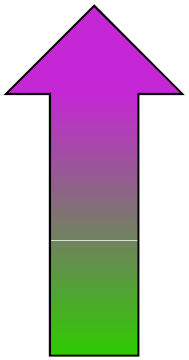

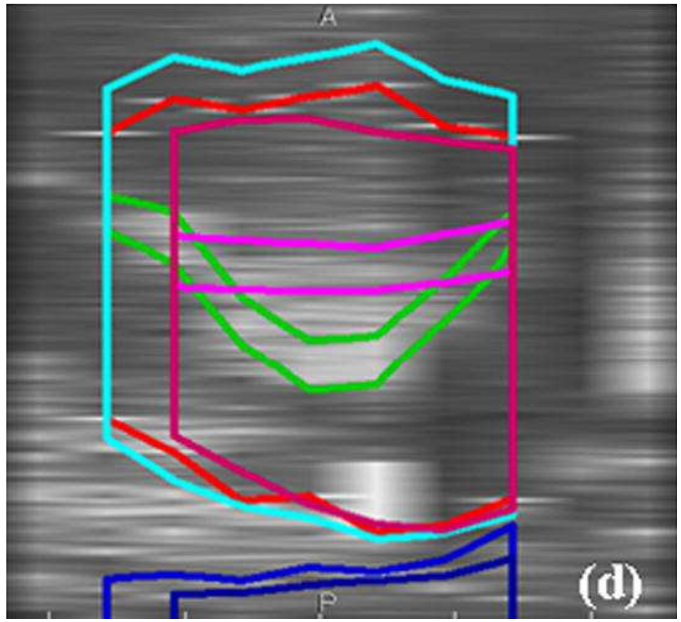

Gel plans

- **Less central dose**
- **Higher rectum dose**

Anderson et al.Radiother Oncol 2010

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Dosimetry (ESTRO recommendations)

Prostate	
V100	≥ 95%
D90	> 100% (144 Gy)
V150	≤ 50%
Rectum	
D2cm^3	< 100% (144 Gy)
D0.1cm^3	< 140% (200 Gy)
Urethra	
D10	< 150% (216 Gy)
D30	< 130% (187 Gy)

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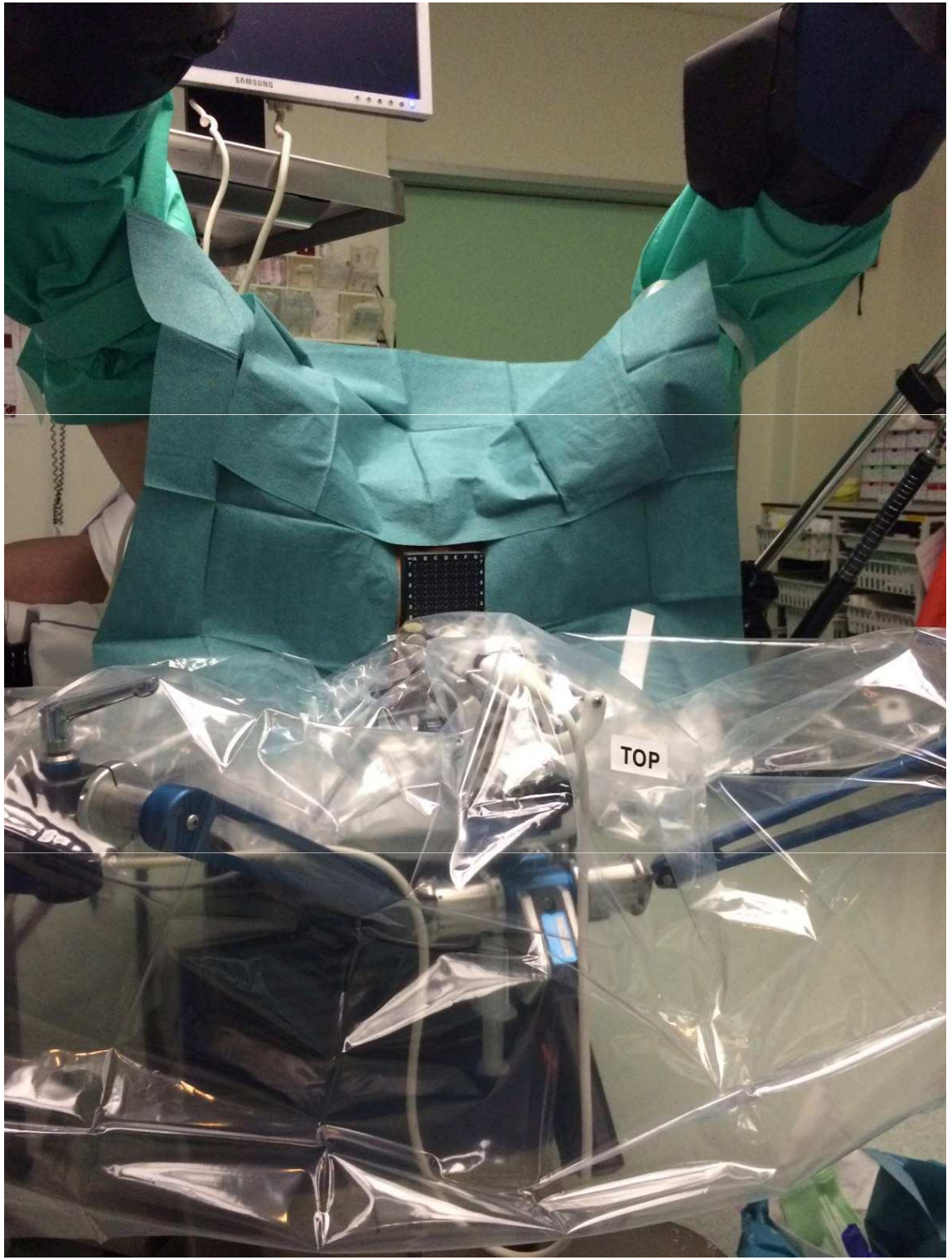
Litothomy position



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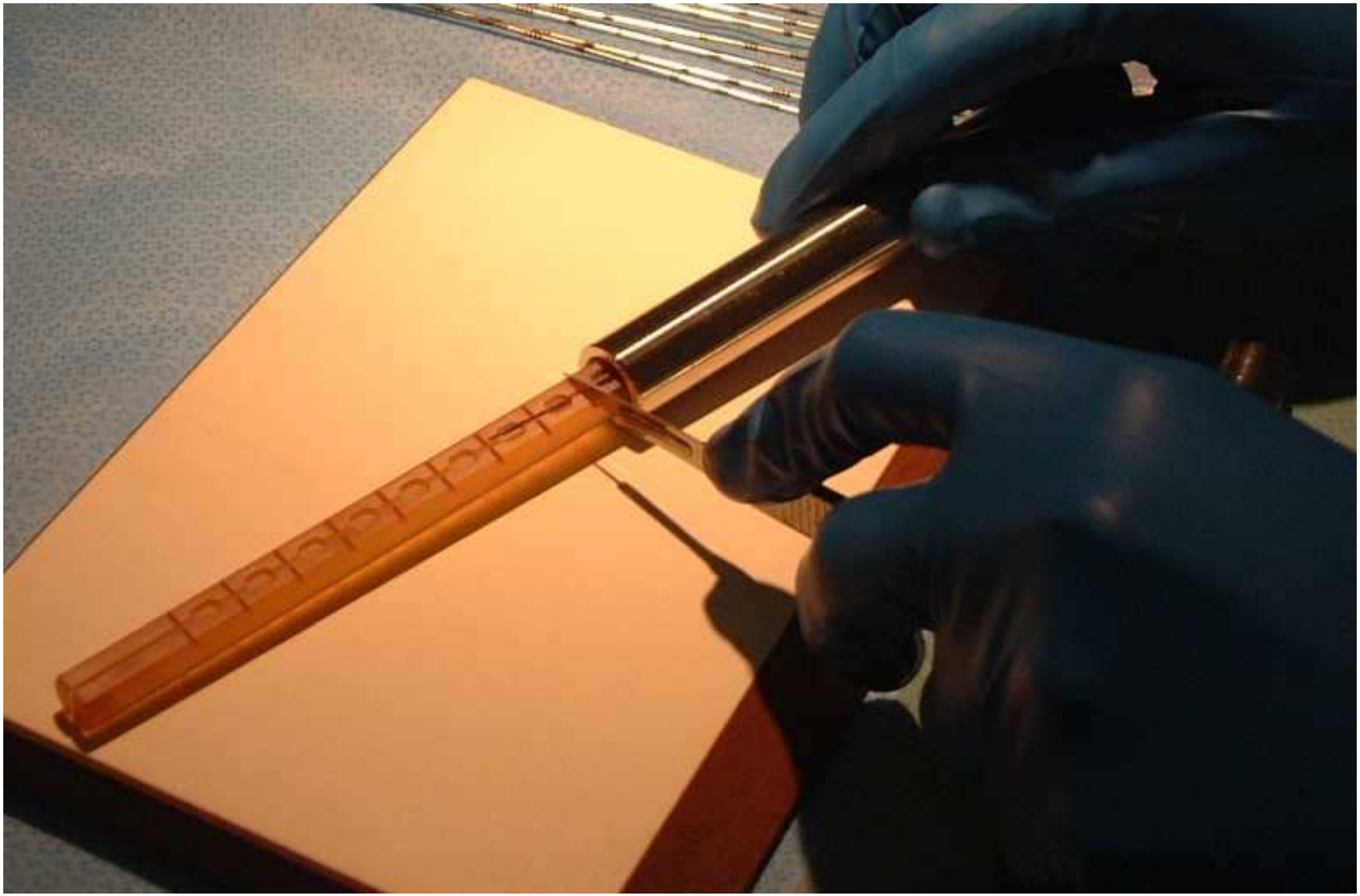
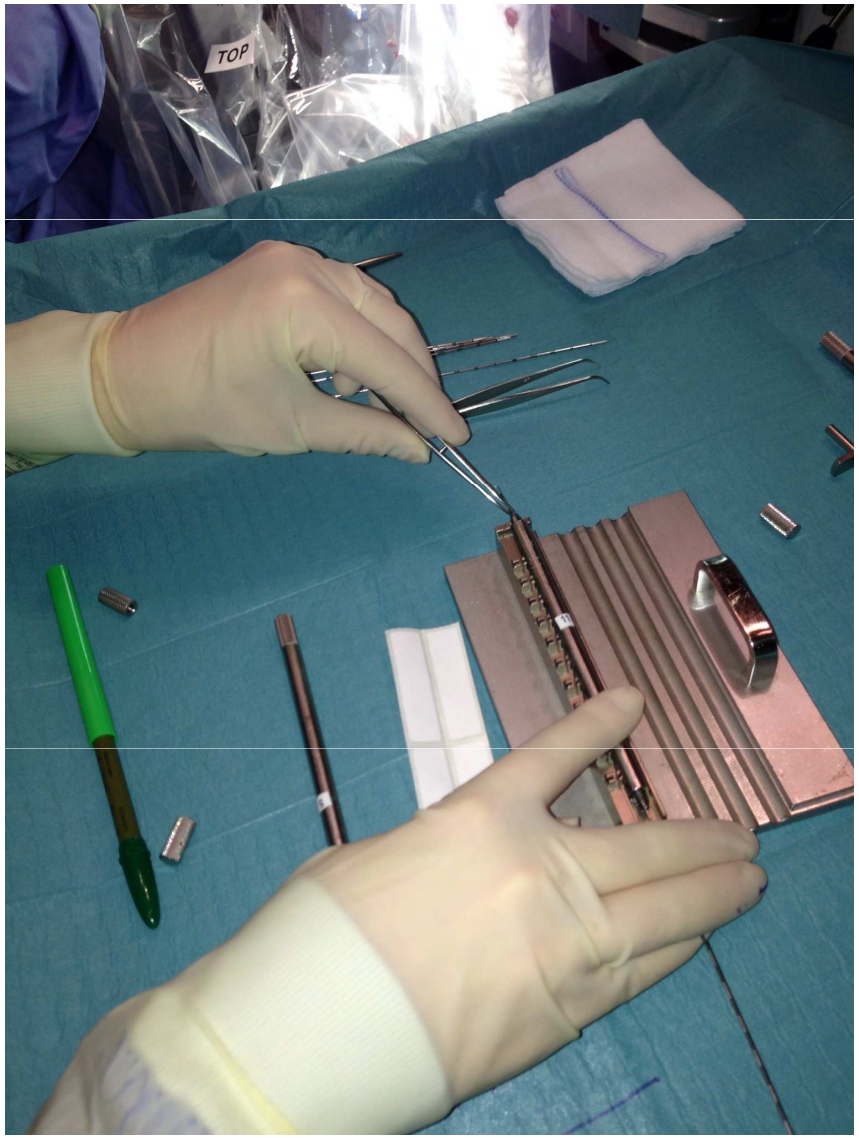
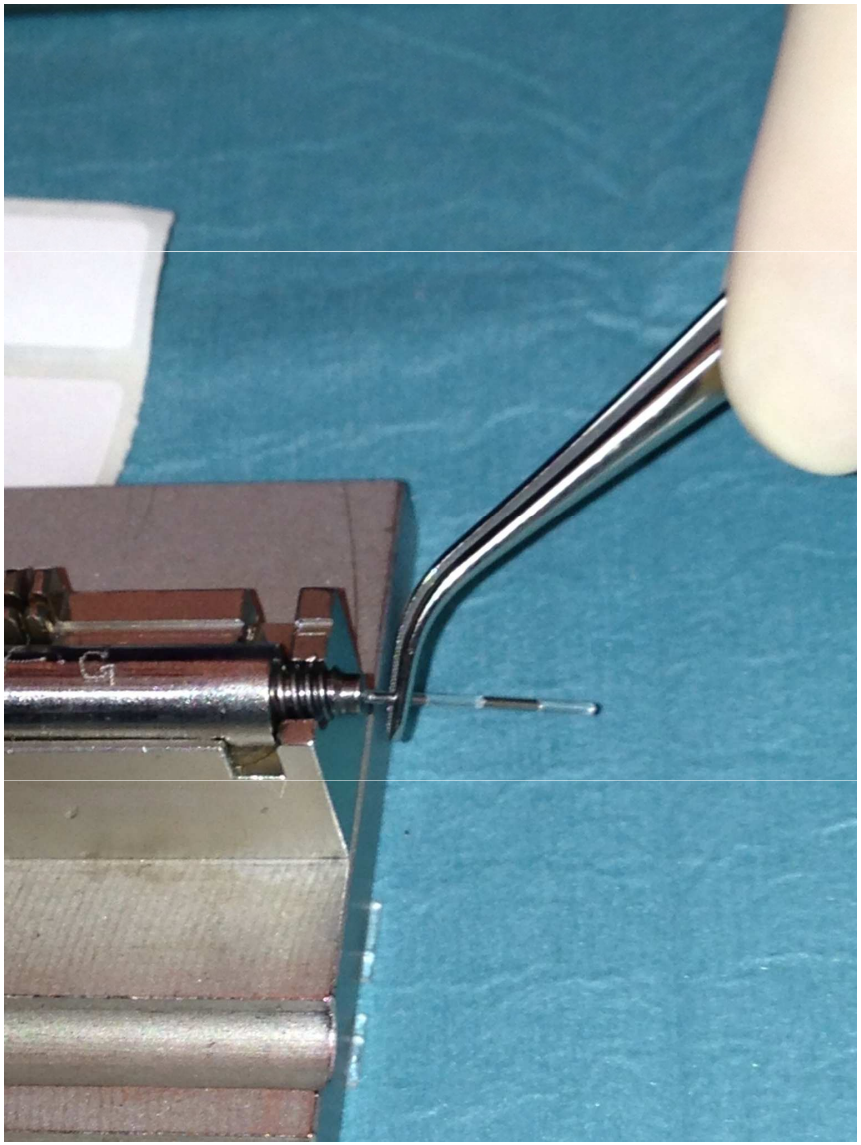
Cutting strands

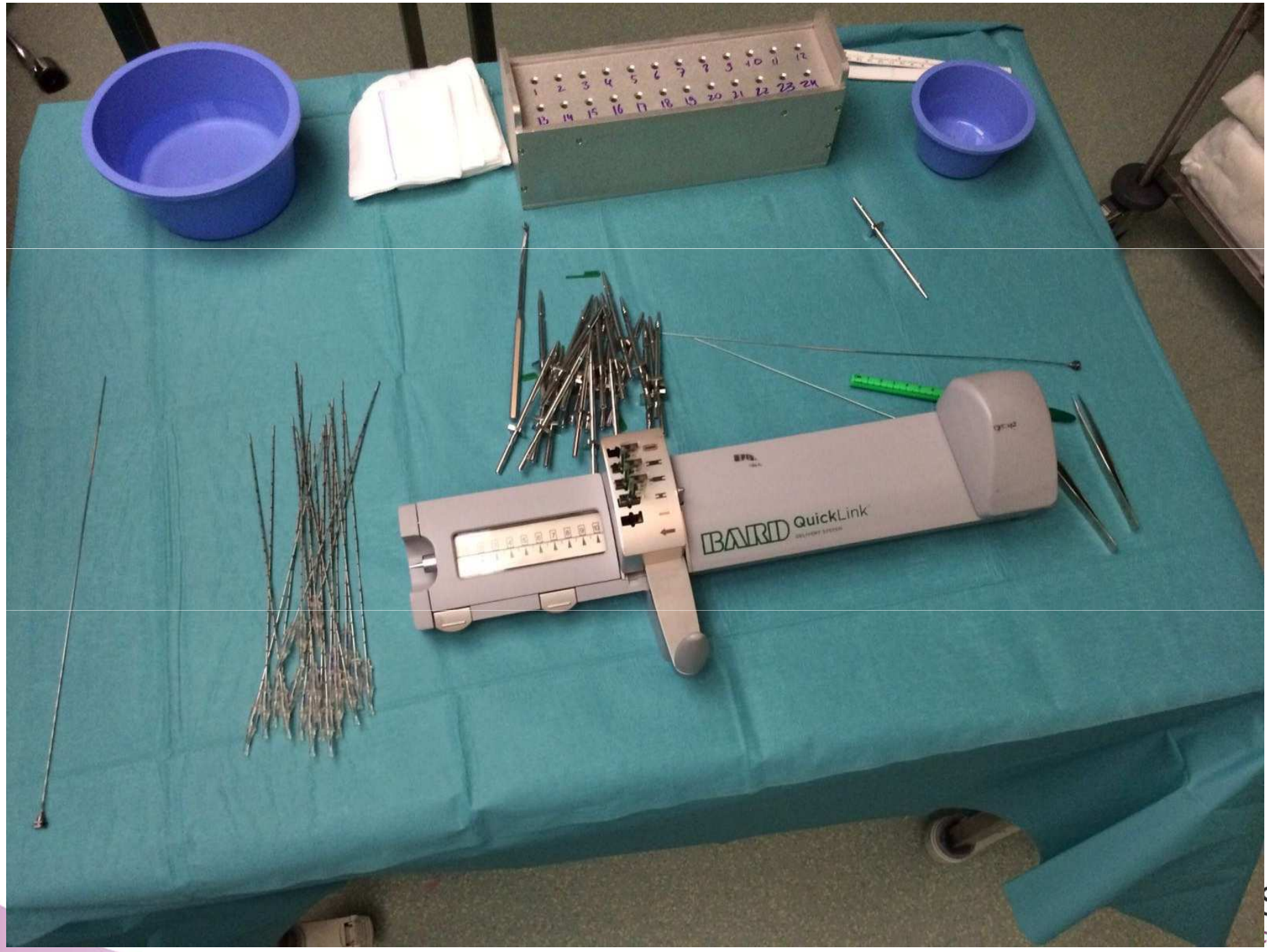


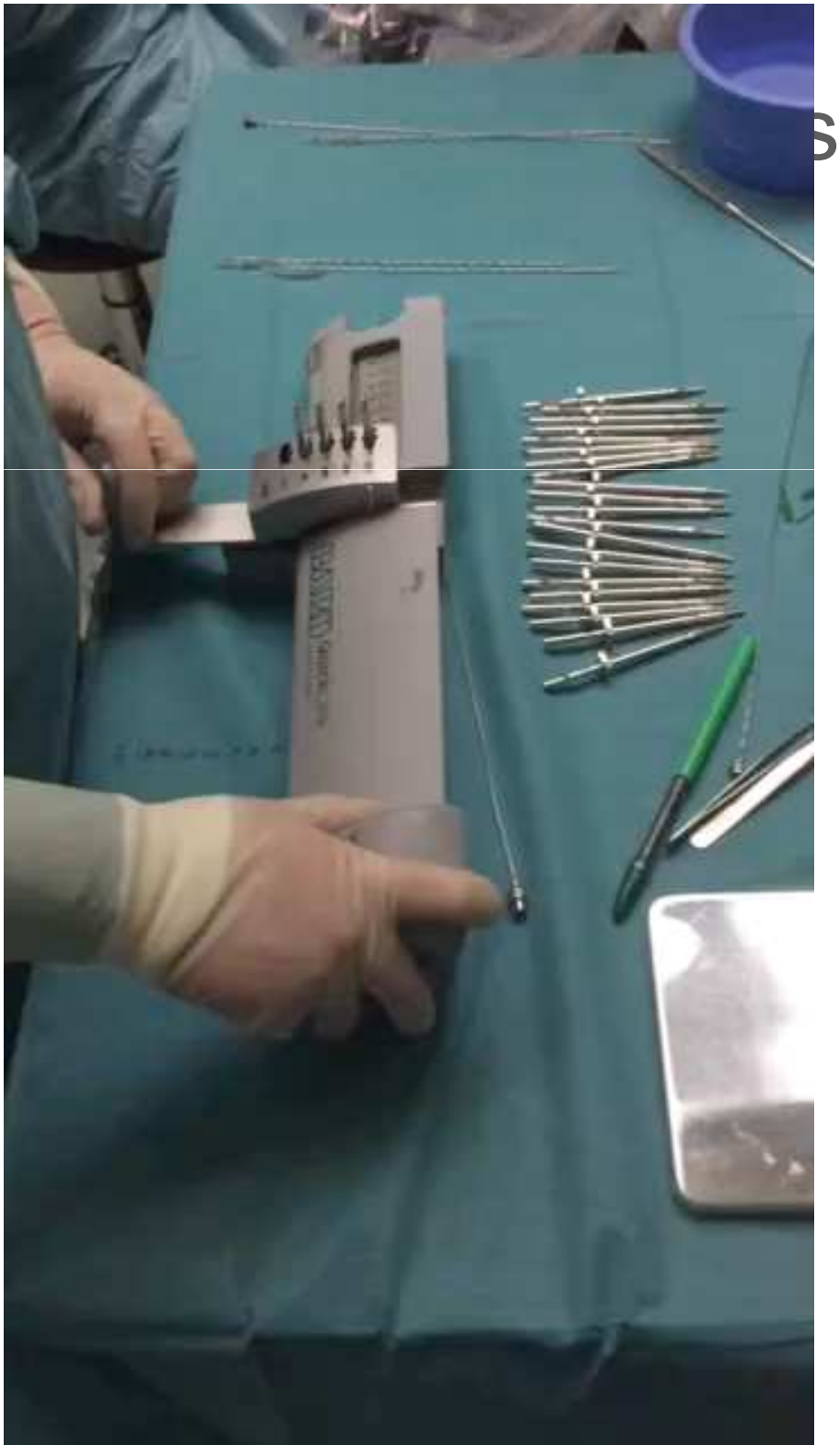
Cutting Strands



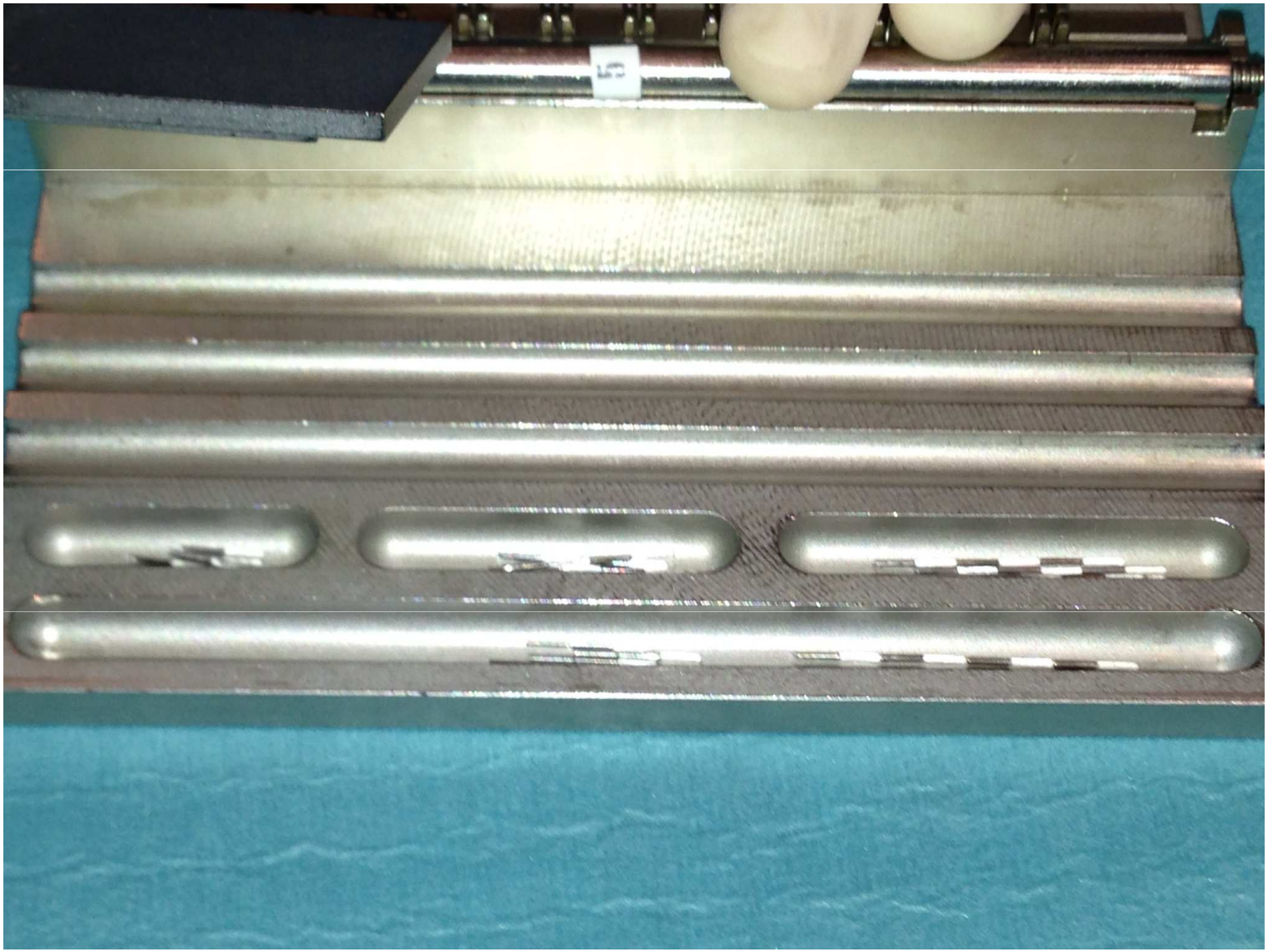


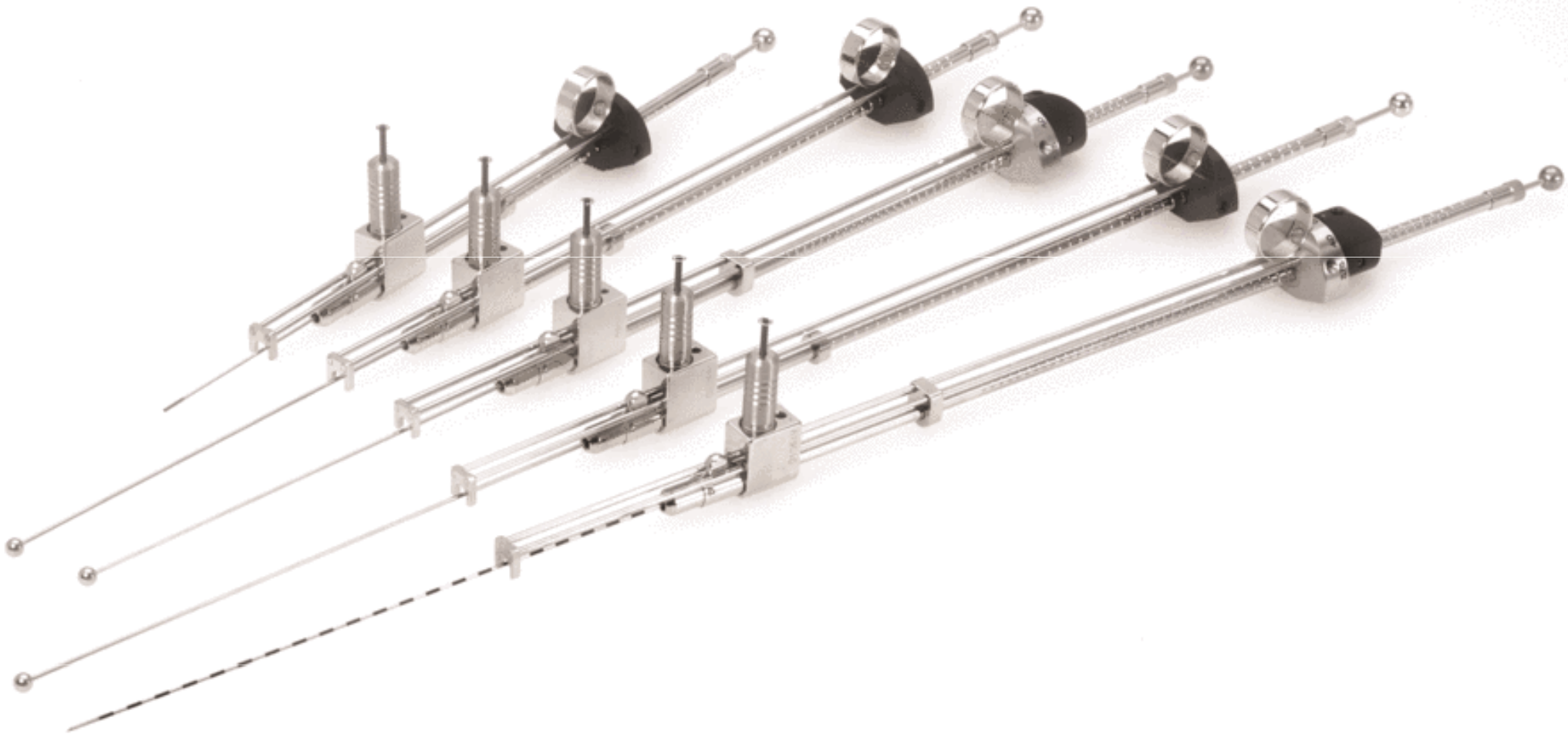
Composing Strands – Construction Devices





Storage of Sources





From: www.micknuclear.com

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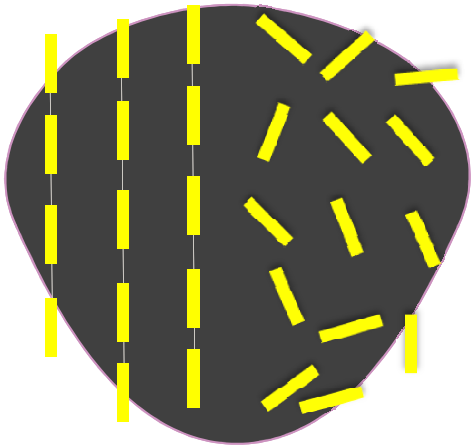
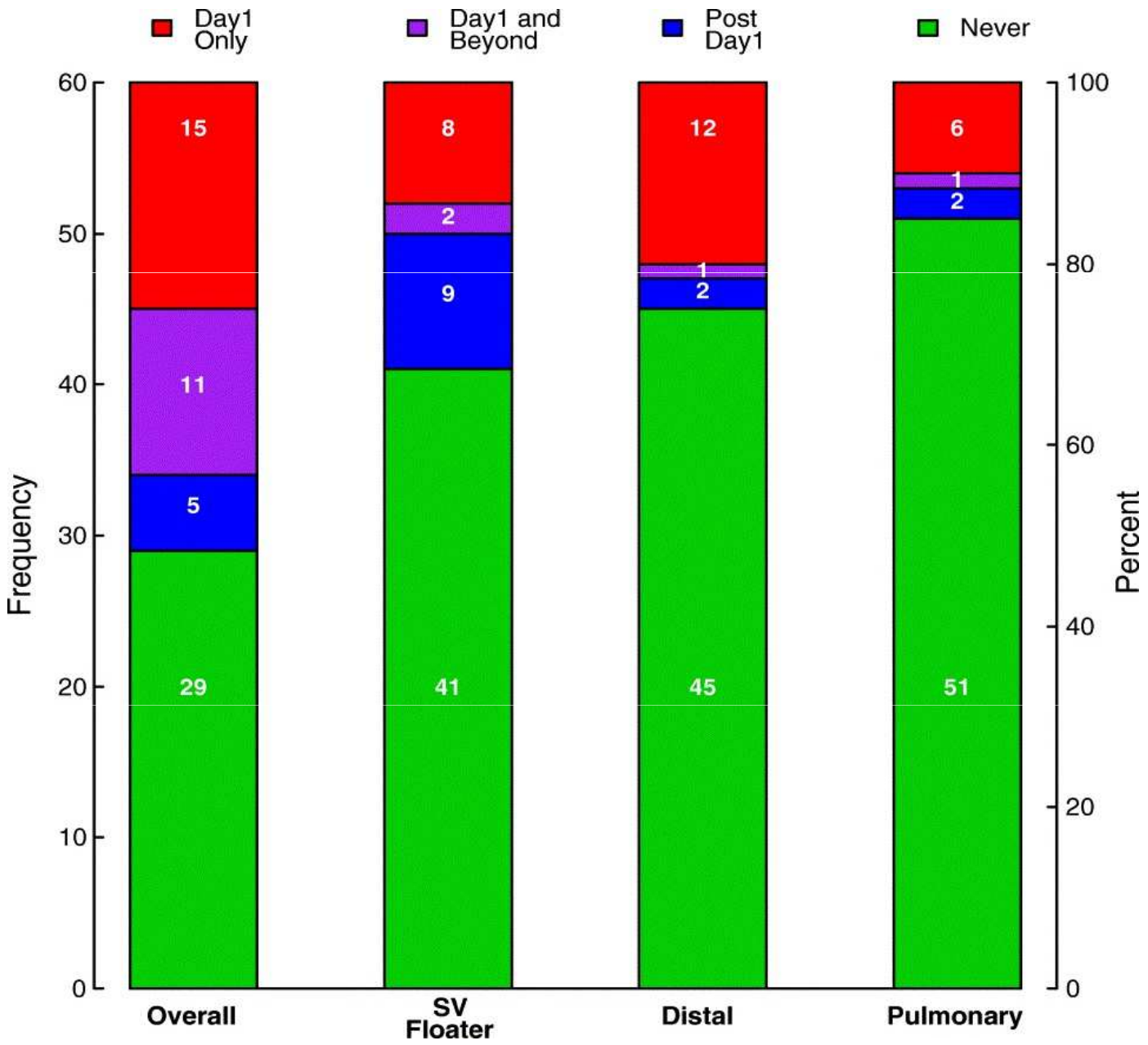
Prostate seed implants



Stranded Loose

Seed Migration



Fuller, Brachytherapy 2004

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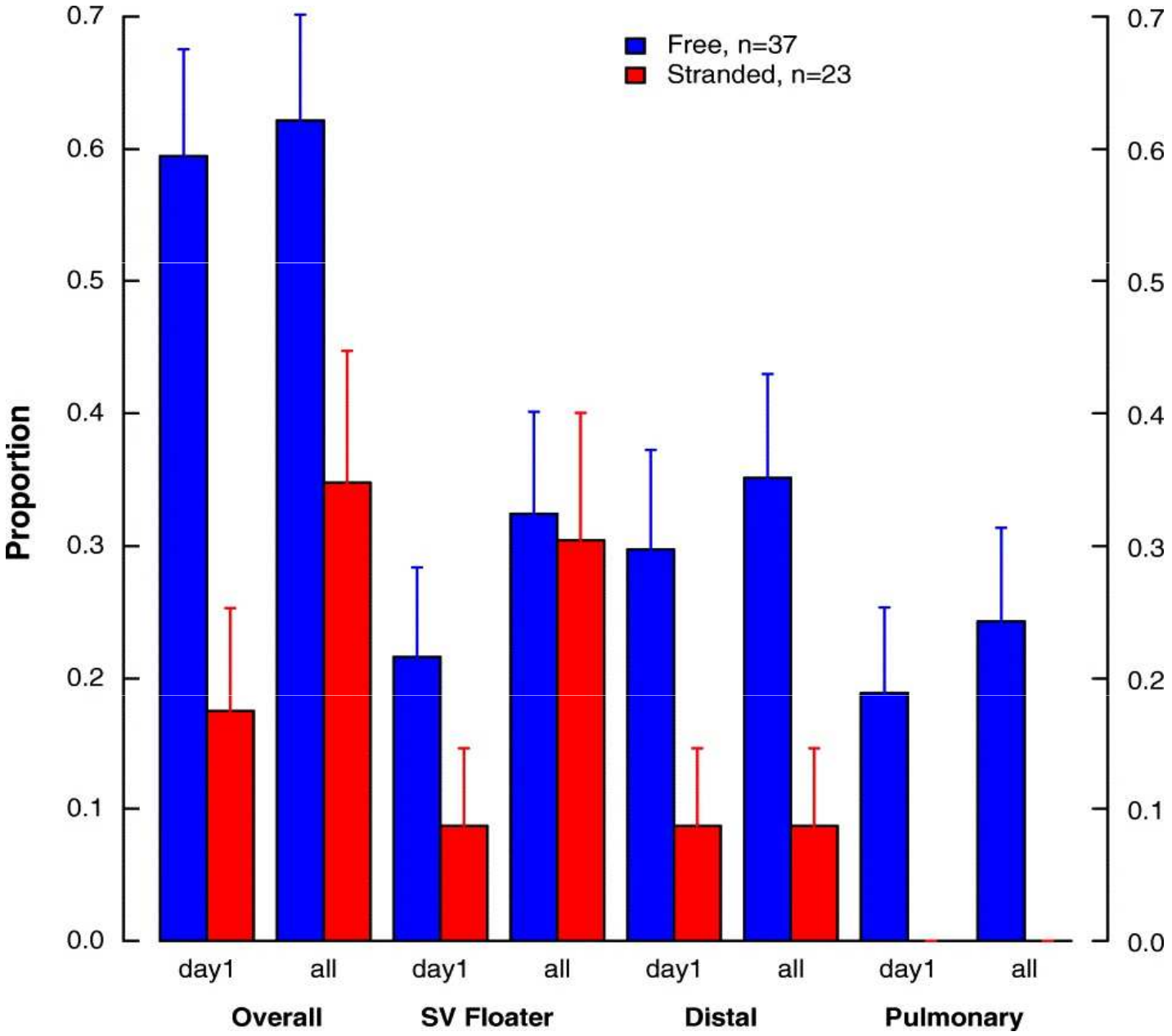
Seed Migration



Fuller, Brachytherapy 2004

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Seed Migration

	LS 20 patients 2160 seeds	SS 20 patients 2236 seeds
Bladder	1	1
Urine	1	22
Pelvis	0	1
Lung	5	0
Ejaculate	6	0
Total seeds	0.6%	1.1%
Total patients	5	6

SS: Stranded seeds
LS: Loose seeds

Saibishkumar, Int J Radiat Oncol Biol Phys 2009

Seed migration

- Negative pressure in needle track when withdrawing
- Contraction of perineal musculature
- Protruding into the bladder

Comparison Stranded vs Loose Seeds

	Prostate Dosimetry	OAR Dosimetry
Fagundes 2004	+	
Fuller 2004	+	
Heysek 2006	+	
Saibishkumar 2009	=	
Saibishkumar 2008		+
Moerland 2009	-	

+: Stranded better
-: Loose better
=: No difference

There is no preference of one system above the other

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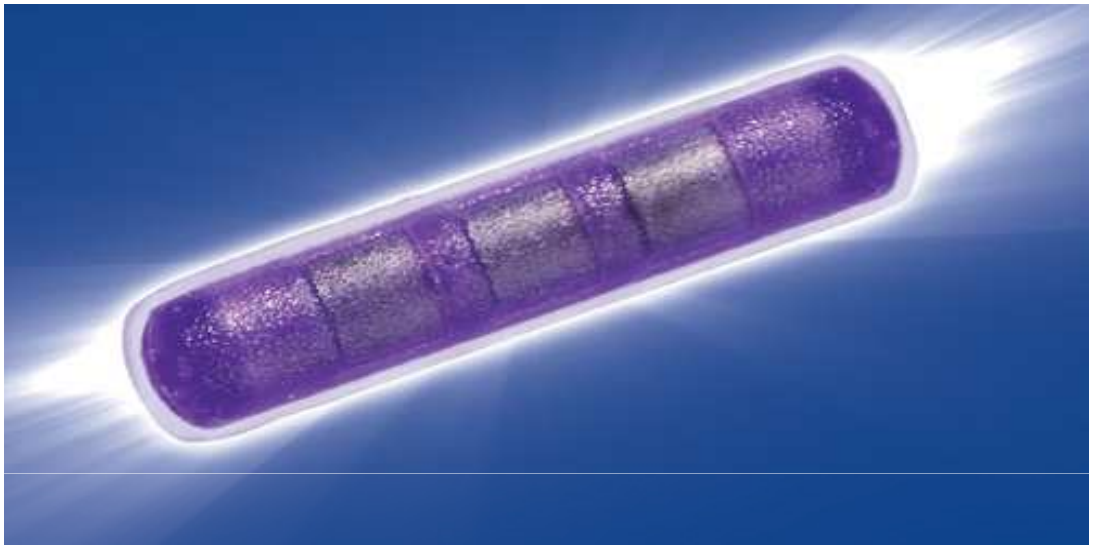
Coated Seeds

BRACHYSOURCE®
BARD Medical



AnchorSeed®
BrachySolutions

Coated vs Uncoated Seeds

		Displacement (mm)		RV100		D90	
		C	UC	C	UC	C	UC
Badwan 2010	Day 0	2.4	3.1	0.04	0.08	108.5	105.7
Bowes 2013		3.3	3.2	0.9	0.6	122.1	120.4

C: Coated seeds
UC: Uncoated seeds

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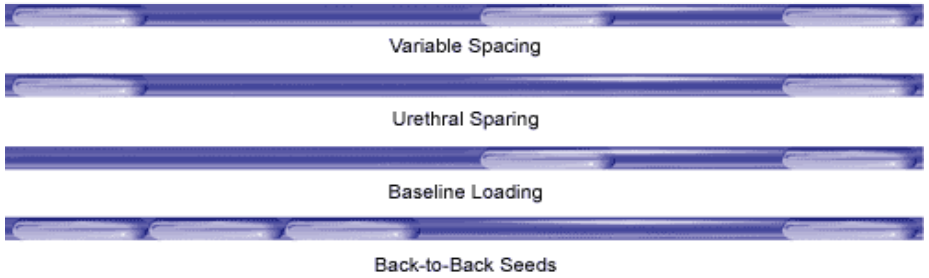
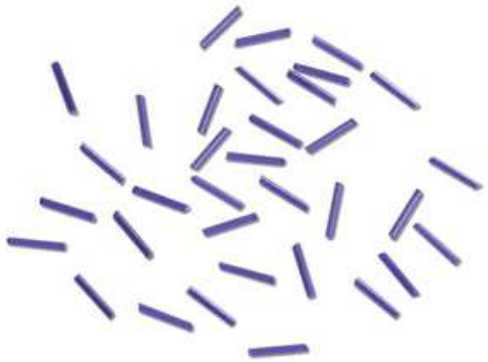
Source configuration

Stranded sources



Loose sources



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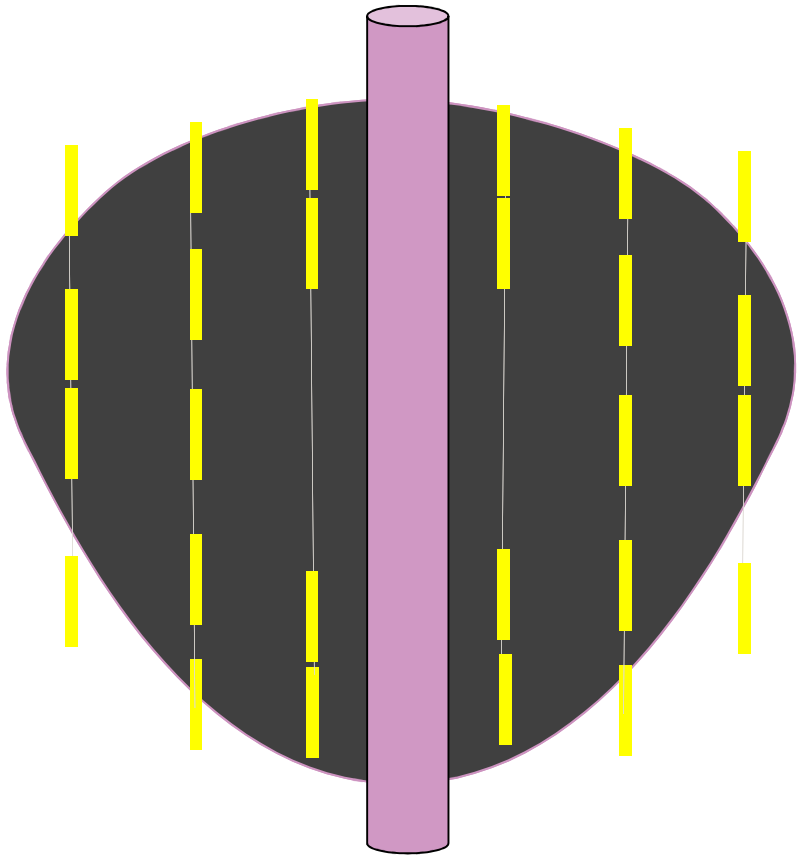
Source configuration



Planning

- Nomogram
- Preplan
- Intraoperative plan

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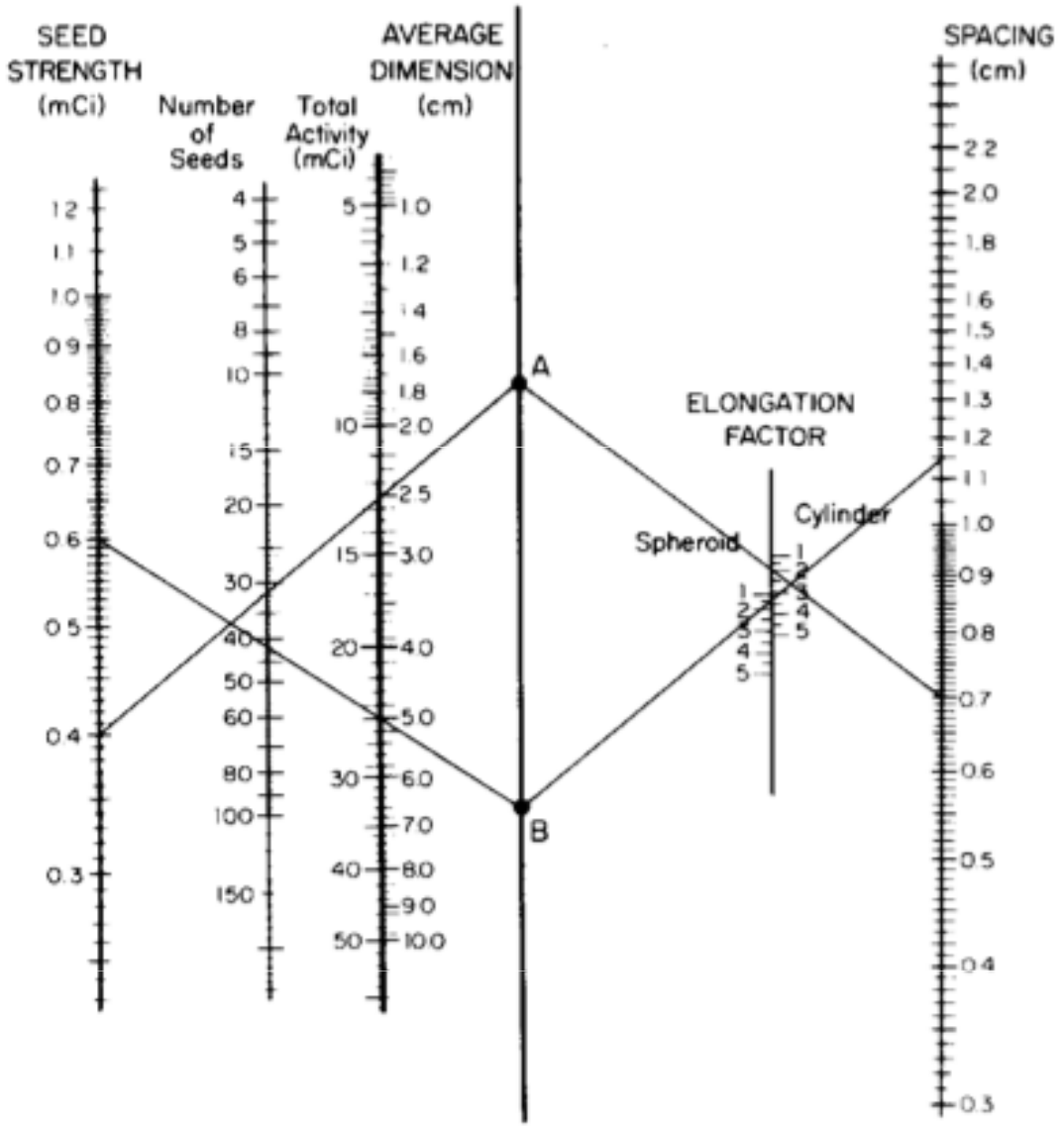

Anderson nomogram

Preplan v.s. Intraoperative plan

Preplan

Outpatient TRUS prior to implant

Positioning probe as outpatient situation

Less OR time used

No possibility for interactive planning

Edema effect not taken into account

No physicist/dosimetrist needed in OR

Number of seeds to order more accurate

Intraoperative plan

TRUS at time of implant

Probe stays in position during whole treatment

More OR time used

Interactive planning possible

Geometry changes are taken into account

Physicist/dosimetrist needed in OR

Risk of inappropriate seed ordering

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Preplan v.s. Intraoperative plan

Preplan

Outpatient TRUS prior to implant

Positioning probe as outpatient situation

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More OR time used

Interactive planning possible

Geometry changes are taken into account

Physicist/dosimetrist needed in OR

Risk of inappropriate seed ordering

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Preplan v.s. Intraoperative plan

Preplan	Intraoperative plan
Outpatient TRUS prior to implant	TRUS at time of implant
Positioning probe as outpatient situation	Probe stays in position during whole treatment
Less OR time used	More OR time used
No possibility for interactive planning	**Interactive planning possible**
Edema effect not taken into account	Geometry changes are taken into account
No physicist/dosimetrist needed in OR	Physicist/dosimetrist needed in OR
Number of seeds to order more accurate	Risk of inappropriate seed ordering

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Preplan v.s. Intraoperative plan

Preplan

Outpatient TRUS prior to implant

Positioning probe as outpatient situation

Less OR time used

No possibility for interactive planning

Edema effect not taken into account

No physicist/dosimetrist needed in OR

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Probe stays in position during whole treatment

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Interactive planning possible

Geometry changes are taken into account

Physicist/dosimetrist needed in OR

Risk of inappropriate seed ordering

ESTRO School

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Probe stays in position during whole treatment

More OR time used

Interactive planning possible

Geometry changes are taken into account

Physicist/dosimetrist needed in OR

Risk of inappropriate seed ordering

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Intraop Planning (ABS)

Planning modality	Description
Intraoperative pre-planning	Plan in OR Immediate execution of plan
Interactive planning	Refinement of plan with Dose calculation from needle position feedback
Dynamic dose calculation	Updating dose distribution Seed position feedback

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Comparison Planning Methods

Classic pre-planning vs. Intraoperative pre-planning

Author	D90	V100
Beyer; 2000	-	97% vs. 94%
Wilkinson; 2000	120 Gy vs. 136 Gy (P<0.001)	76% vs. 84% (P<0.001)
Gewanter; 2000	95% vs. 85% (P=0.08)	80% vs. 83% (P=0.48)
Matzkin; 2003	53% vs. 114% (P<0.001)	58% vs. 95% (P<0.001)
Shah; 2006	75% vs. 90%	-

Adapted from Polo et al; Radiother Oncol; 2010

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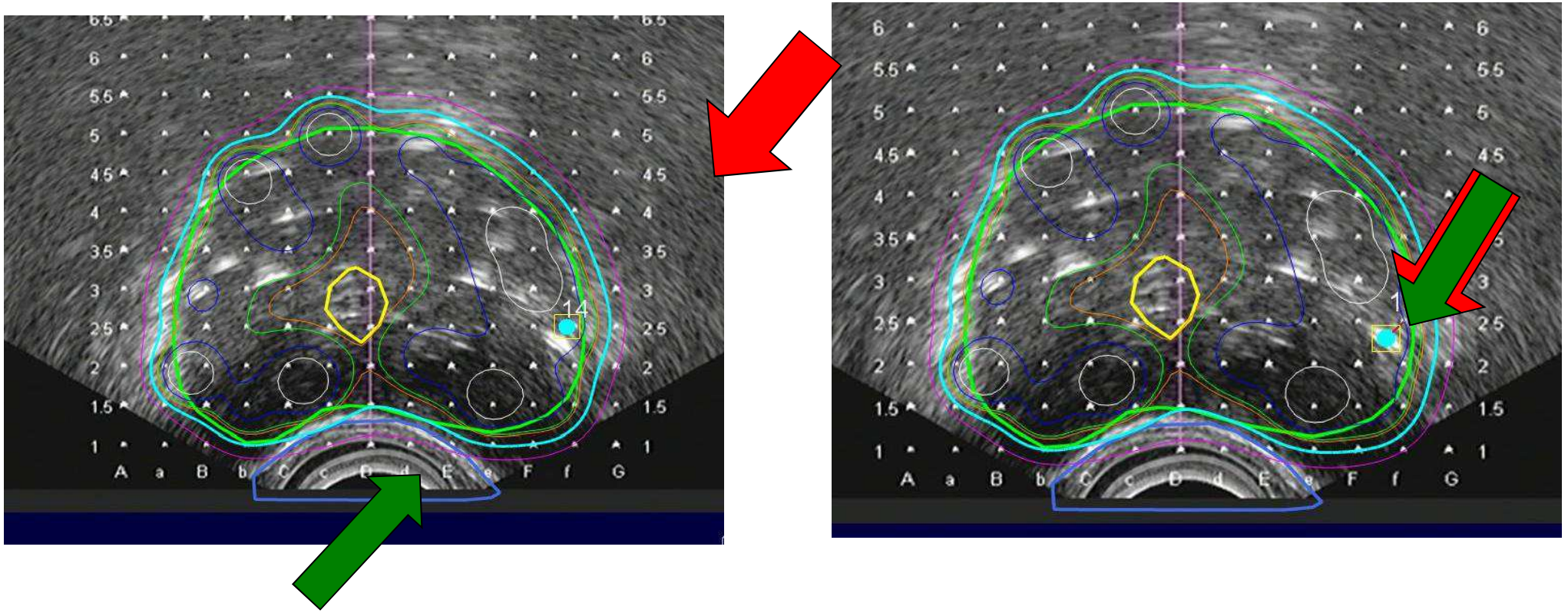
Dynamic Dose Planning



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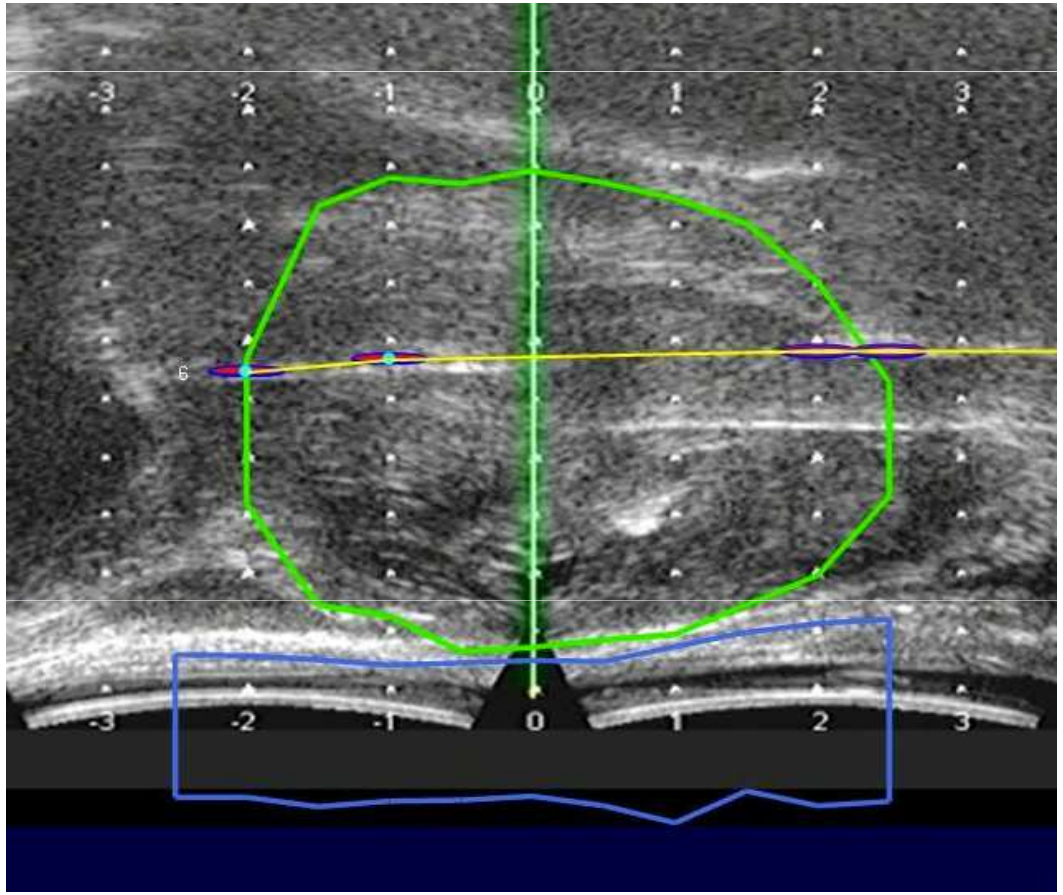
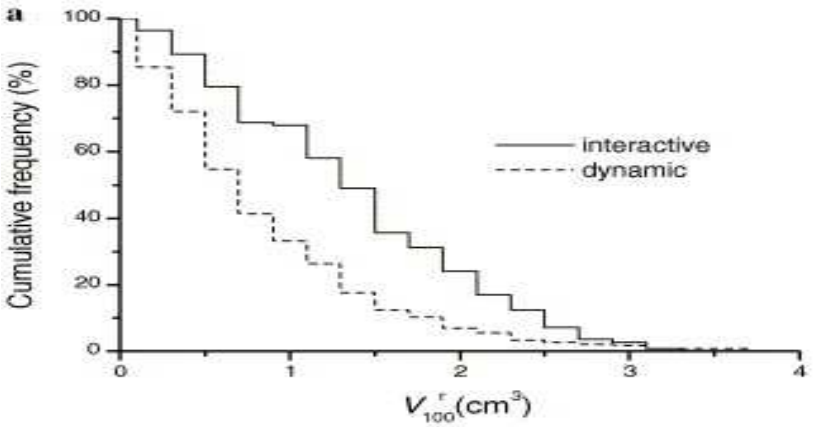
Dynamic Dose Planning



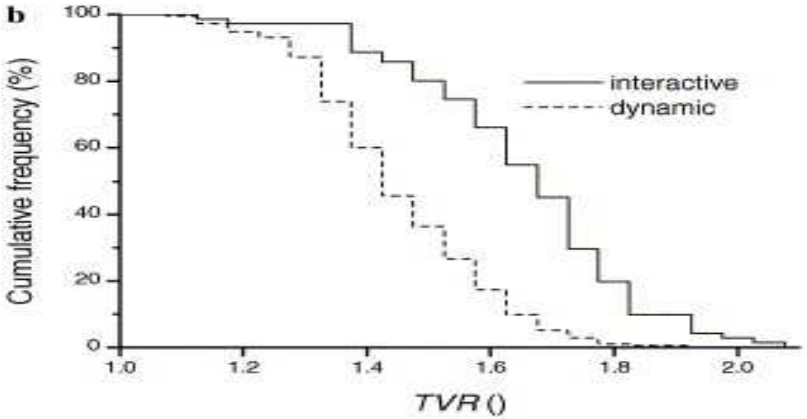
Academisch Medisch Centrum

Universiteit van Amsterdam

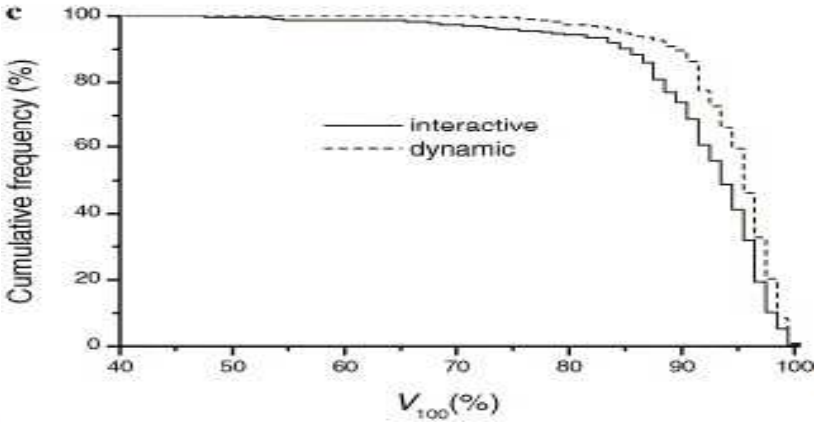
ESTRO School



Rectum dose



Dose outside target



V100prostate

Gert J. Meijer , Hetty A. van den Berg , Coen W. Hurkmans , Pascal E. Stijns , Jan H. Weterings

Dosimetric comparison of interactive planned and dynamic dose calculated prostate seed brachytherapy

Radiotherapy and Oncology Volume 80, Issue 3
2006 378 - 384

http://dx.doi.org/10.1016/j.radonc.2006.07.038

Documentation of procedure
Prostate volume
Number of seeds Number of needles used
Total acitivity implanted
Planned dose
D90 V100 V150

Minimal requirements

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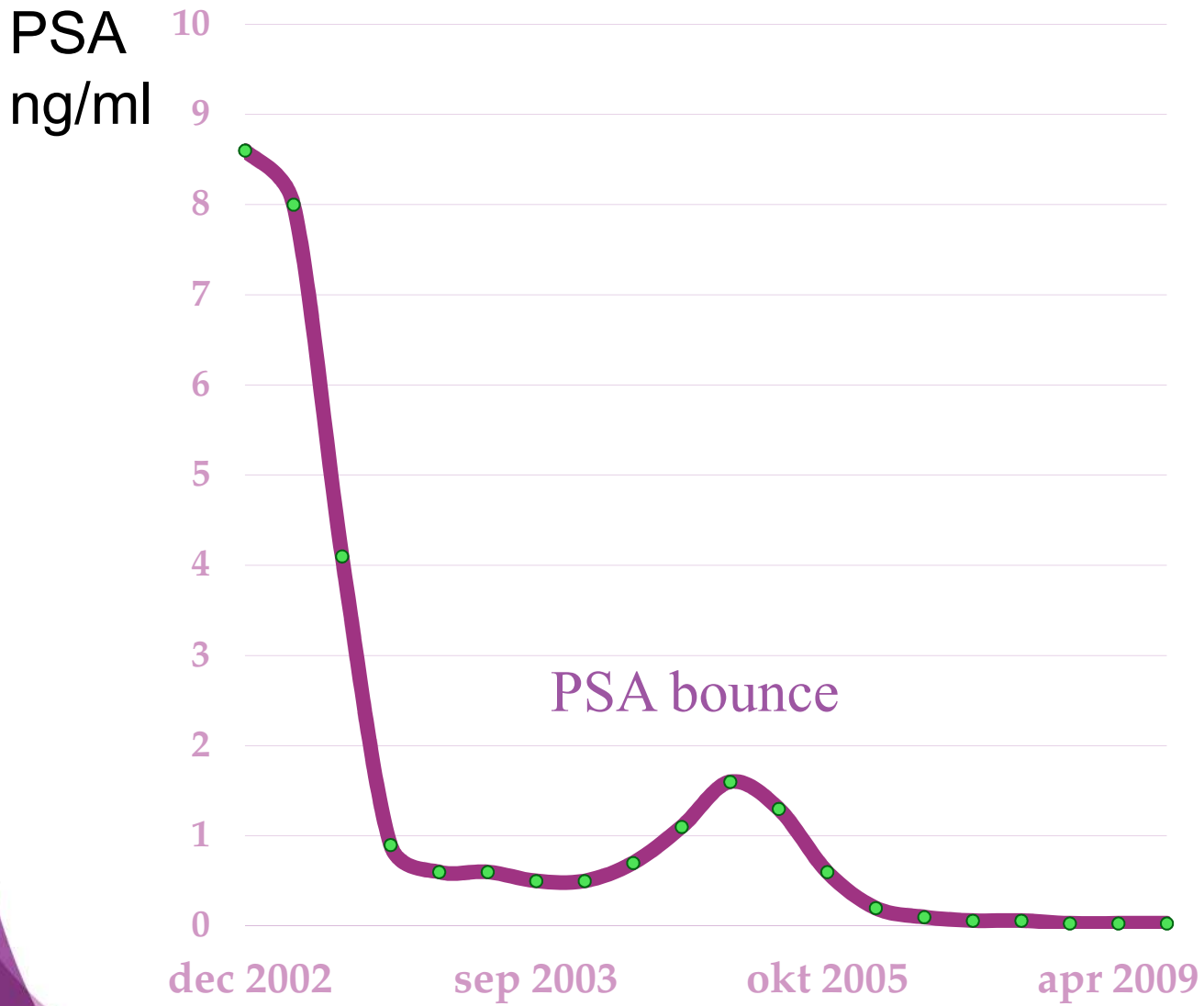
Follow-up with PSA



Criteria recurrence:

Nadir + 2 ng/ml

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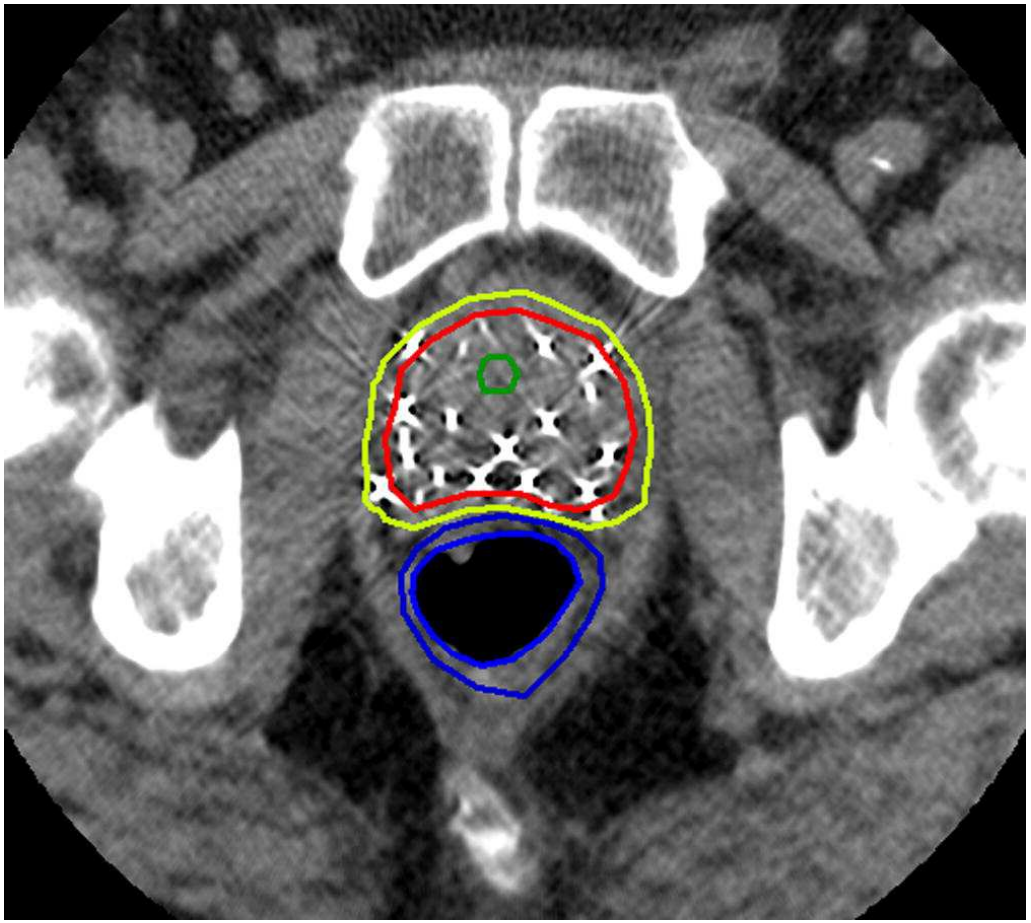
Postop contouring and dosimetry



CTV prostate

CTV prostate + margin

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Postop Parameters for Reporting

Prostate
D90
V100
V150
OAR
Primary parameters
D2cm^3_Rectum
D10_Urethra
Secondary parameters
D0.1cm^3_Rectum, V100_Rectum
D0.1cm^3_Urethra, D30_Urethra, D5_Urethra

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Outcome Permanent Implant

Kupelian et al. Int J Radiat Oncol Biol Phys 2004;58:25-33

950 patients

Median FU: 47 months (12-111)

T1-T2

Mean PSA 9,6 ng/ml

Gleason 6 (76%), 7 (21%), 8 (3%)

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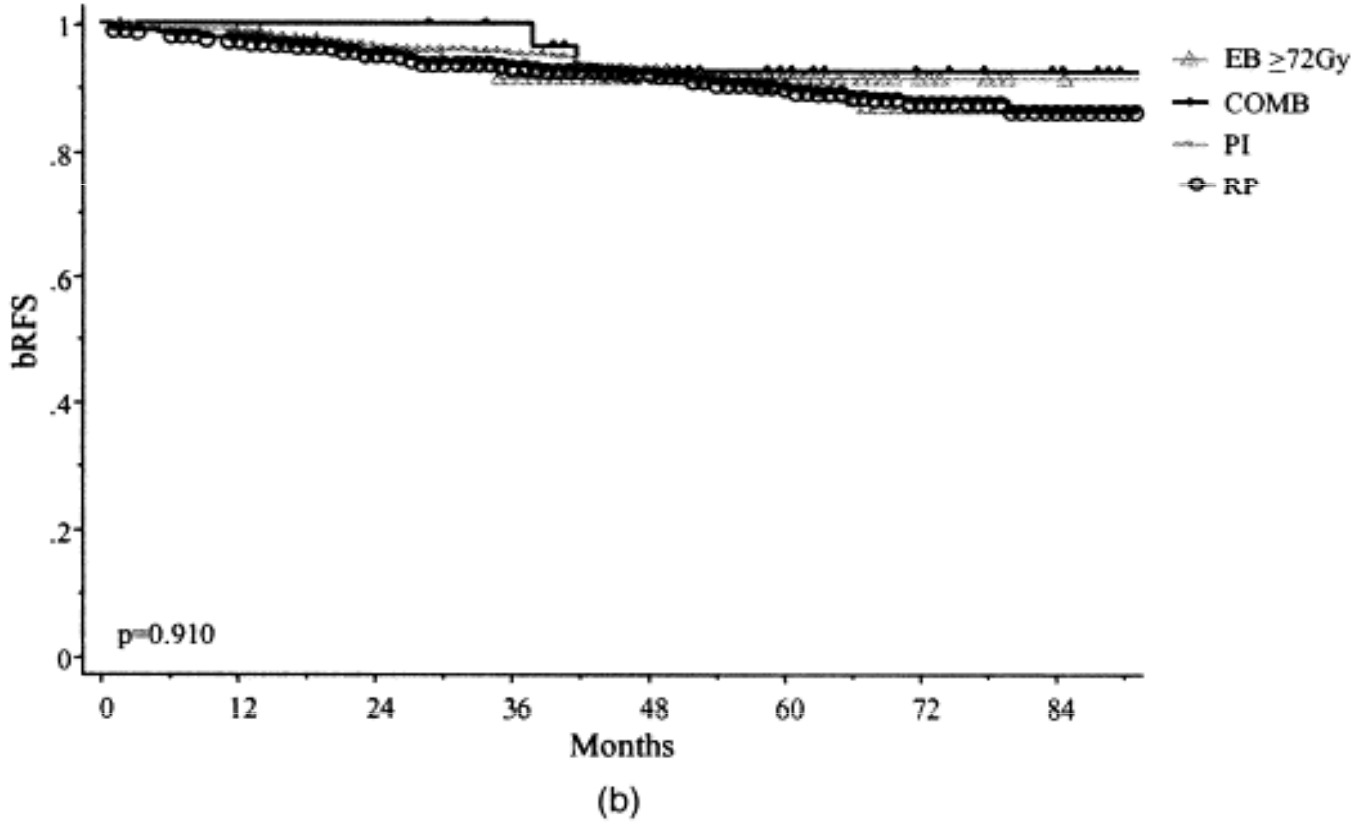


Fig. 3. Biochemical relapse-free results for favorable-risk (Stage T1-T2a, iPSA ≤10 ng/mL, and bGS ≤6) patients by treatment modality. (a) All favorable cases: RP, EBRT <72 Gy, EBRT ≥72 Gy, PI, or COMB. (b) Excludes EBRT <72. Abbreviations as in Fig. 2.

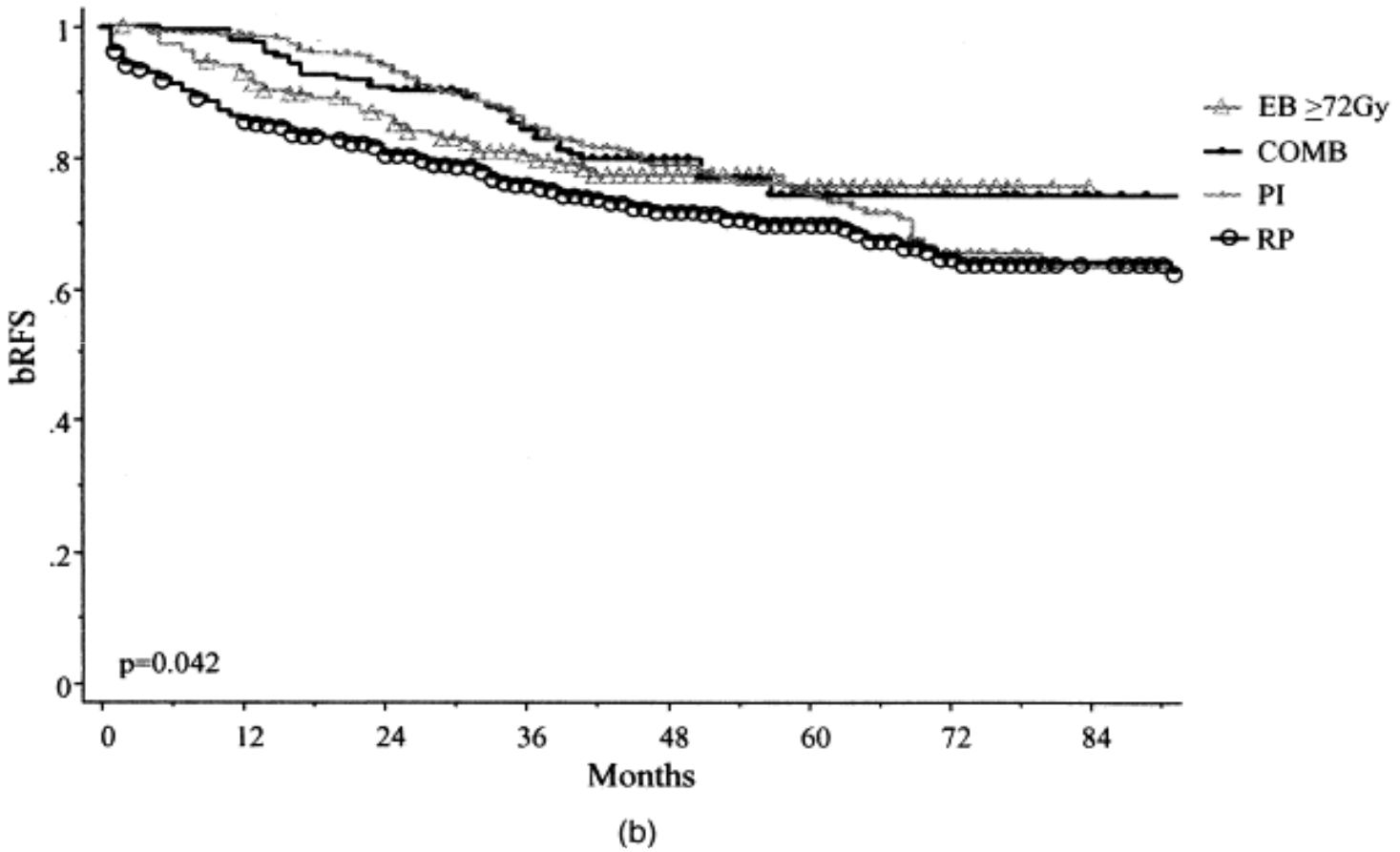
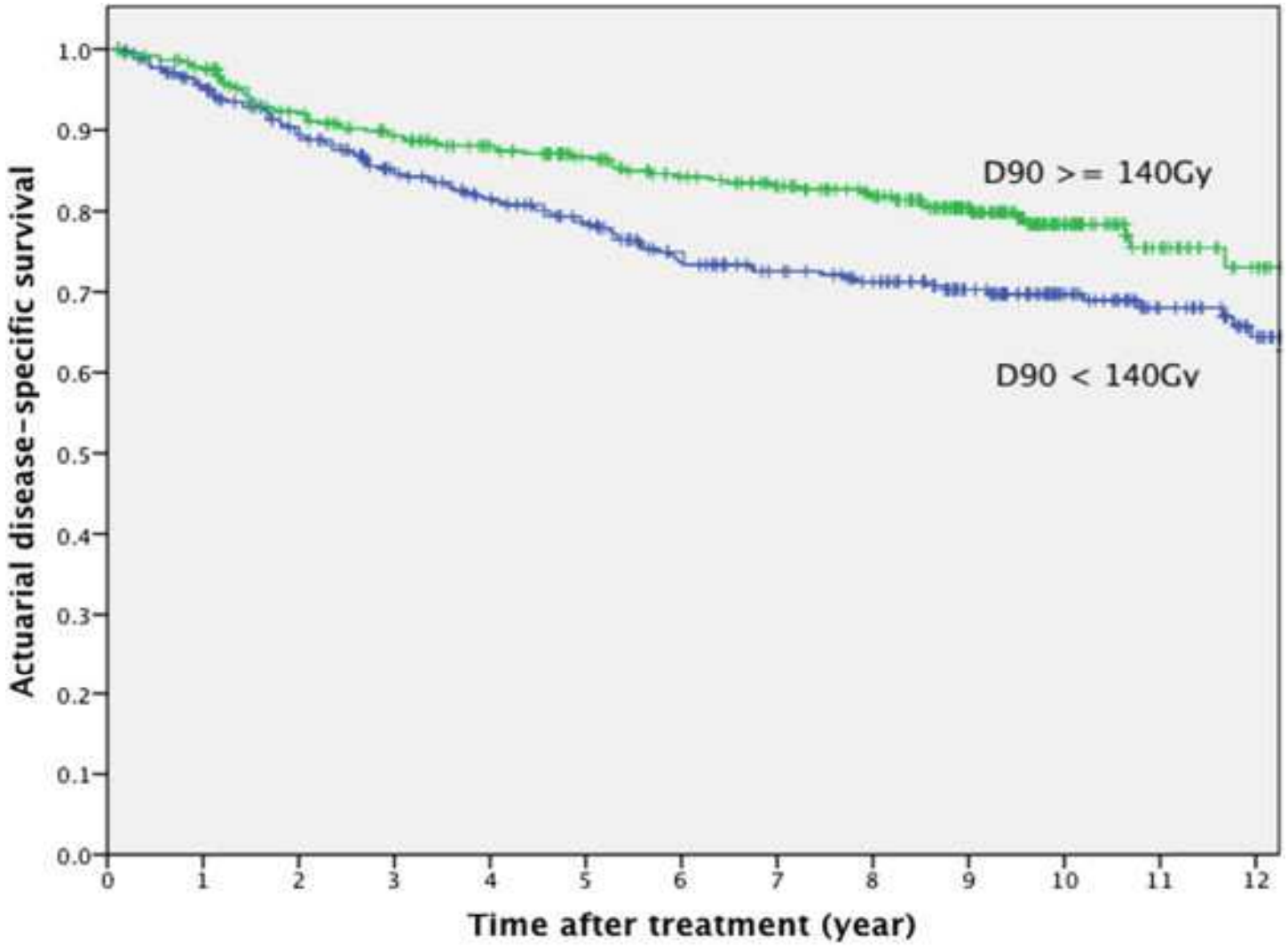


Fig. 4. Biochemical relapse-free results for unfavorable-risk (Stage T2b, iPSA >10 ng/mL, or bGS ≥7) patients by treatment modality. (a) All unfavorable cases: RP, EBRT <72 Gy, EBRT ≥72 Gy, PI, or COMB. (b) Excludes EBRT <72. Abbreviations as in Fig. ...



A Henry. Clin Oncol (R Coll Radiol) 2015; doi: 10.1016/j.clon.2015.03.004

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Outcome

Systematic Review
Peinemann et al. Eur Urol 2011;60:881-893

Most studies T1-T2
Majority Gleason <7 and PSA < 10 ng/ml
(20-30% PSA ≥10 ng/ml)

5 year OS: 71-96%

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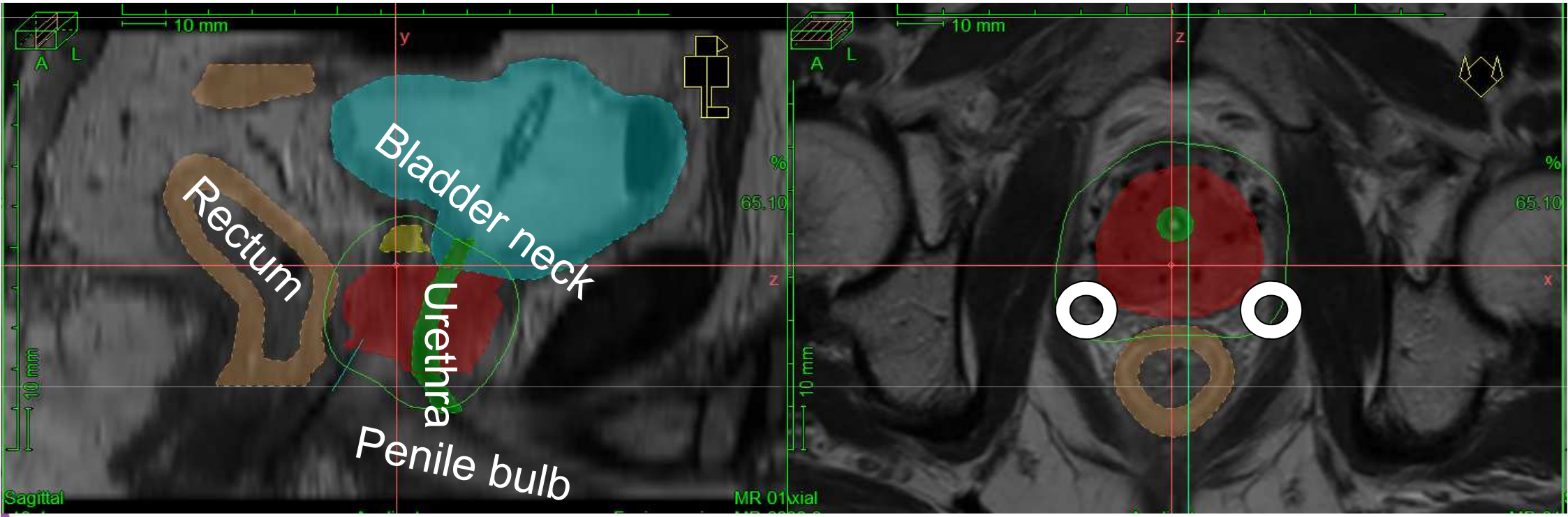
OAR



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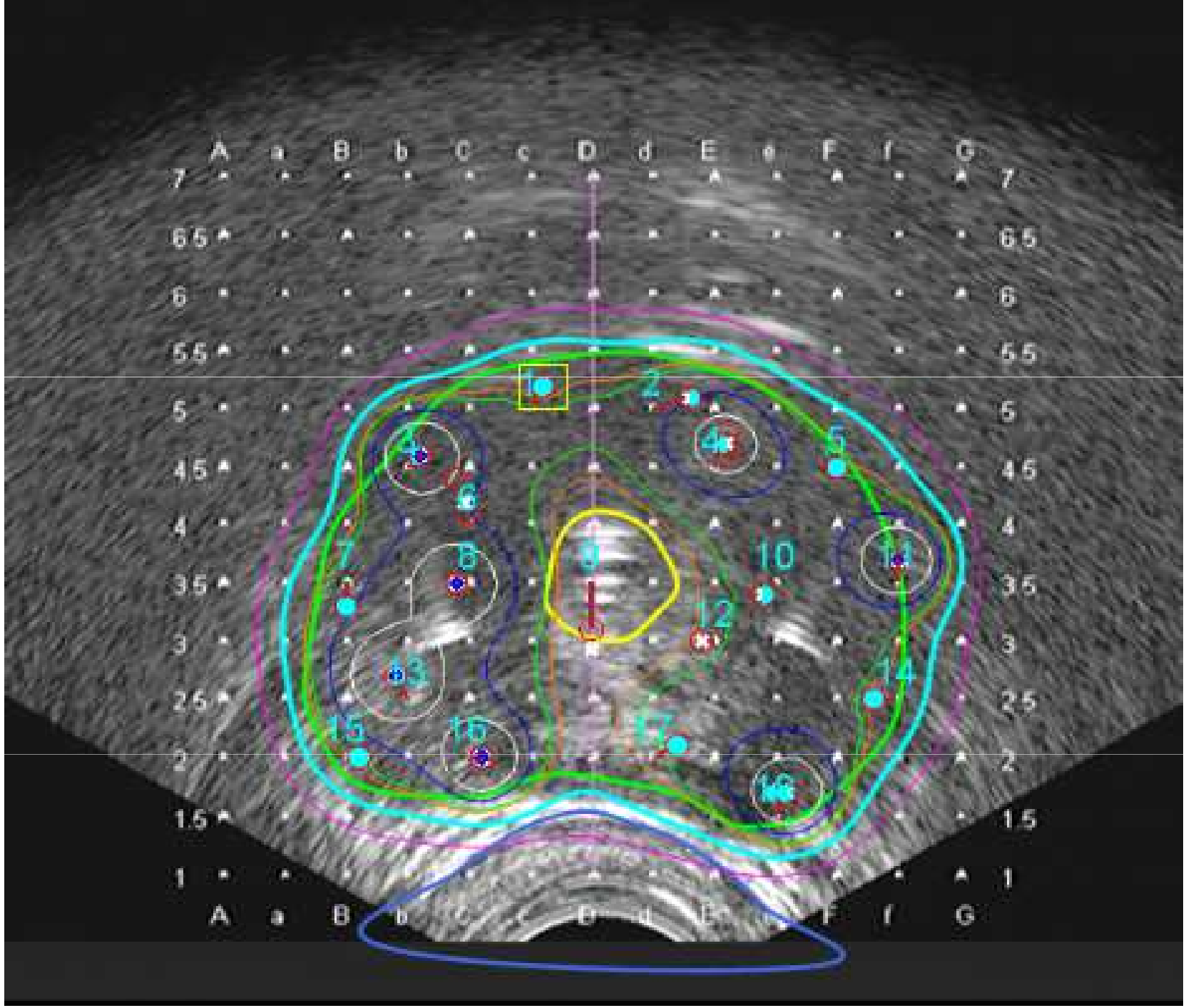
A a B b C c D d E e F f G
7
65
6
55
5
45
4
35
3
25
2
15
1
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14
15
16
17

GI Toxicity

Budäus et al. Eur Urol 2012;61:112-127

Author		G2	G3	
Gomez-Iturriaga Pina	I125	11.7	3.2	Urology 2010;75:1412–6
Gelblum	Pd103 I125	6.5	0.4	Int J Radiat Oncol Biol Phys 2000;48:119–24
Gelblum	PD103 /I125 + EBRT	7.1	0.7	Int J Radiat Oncol Biol Phys 2000;48:119–24
Lee	I125 + EBRT	4	0	Cancer 2007;109:1506–12
Zelefsky	I125	9	0.4	Int J Radiat Oncol Biol Phys 2000;47:1261–6.

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GU Toxicity

Budäus et al. Eur Urol 2012;61:112-127

Author		G2	G3	
Gomez-Iturriaga Pina	I125	1.1	0	Urology 2010;75:1412–6
Lee	I125 + EBRT	3	1	Cancer 2007;109:1506–12
Zelefsky	I125	55	3	Int J Radiat Oncol Biol Phys 2000;47:1261–6.
Ishiyama	HDR + EBRT	4	12	Int J Radiat Oncol Biol Phys 2009;75:23–8

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Erectile Dysfunction

Budäus et al. Eur Urol 2012;61:112-127

Author		Erectile function (%)	
Stone	I125	61	Urology 2007;69:338-342
Bottomley	I125	42	Radiother Oncol 2007;82:46-49
Cesaretti	I125, Pd103	32-68	BJUI Int 2007;100:362-67
Sanchez-Ortiz	I125, Pd103	49	Int J Impot Res 2000;12:S18-S24
Merrick	I125, Pd103	39	Int J Radiat Oncol Biol Phys 2002;52:893-902
Mabjeesh	I125	80	Int J Impot Res 2005;17:96-101
Merrick	I125, Pd103	59	Int J Cancer 2001;96:313-319
Taira	I125, Pd103	56	Int J Radiat Oncol Biol Phys 2009;75:639-648

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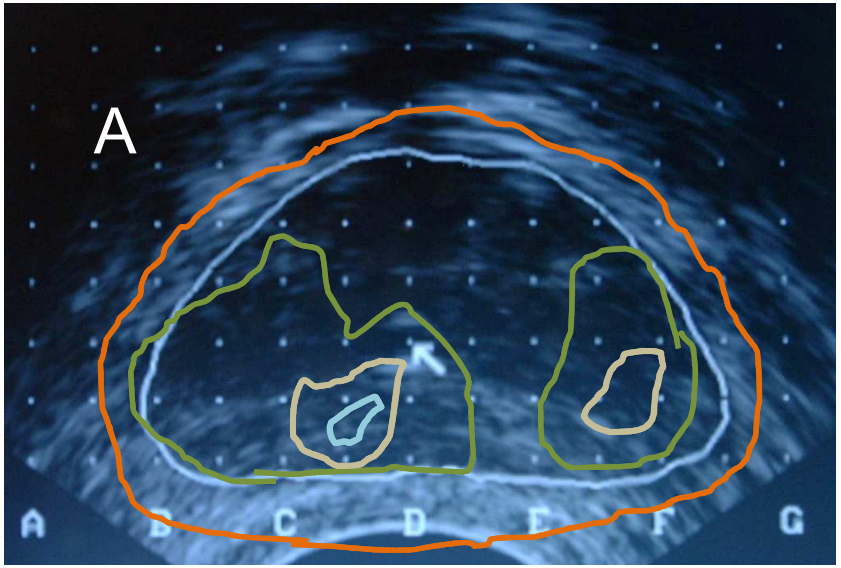
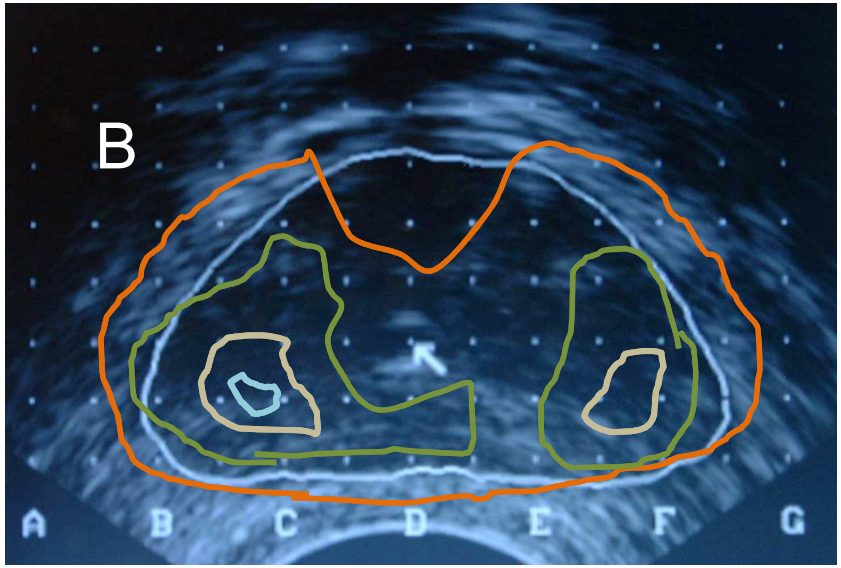
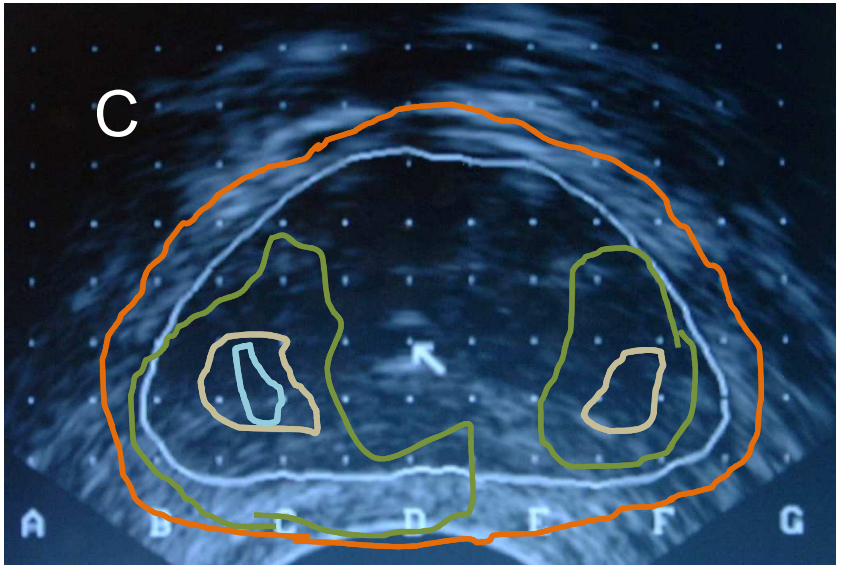
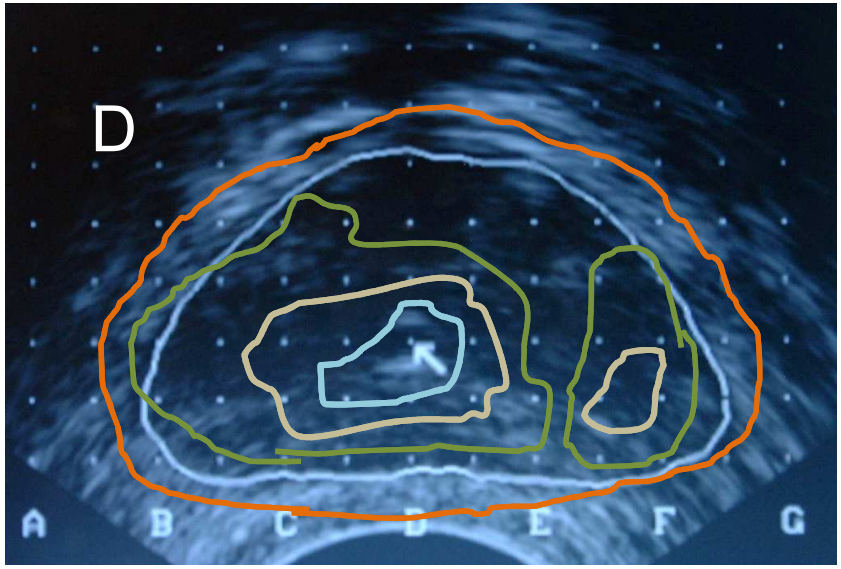
Which Isodose distribution would you prefer?





100 %
140%
150%
170%





High Dose Rate Prostate Brachytherapy

Peter Hoskin
Mount Vernon Cancer Centre

HDR Prostate Brachytherapy

Practical advantage

Physical advantage

Biological advantage

HDR implant: biological advantage 2Gy EQD

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam 74Gy/37f	74	74	74
• HDR Boost schedules after 45Gy/25f			
• Ext beam	42.4	43.3	44.2
16Gy/4f	67.5	65.1	62.8
16Gy/2f	85.8	76.8	68.4
23Gy/2f	127.8	106.1	85.4
• HDR Boost after 35.7Gy/13f			
• Ext beam	43.4	40.5	37.9
17Gy/2f	91.8	77.6	64.1

Indications for HDR prostate brachytherapy

- Boost with external beam
- Monotherapy

GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: An update

Peter J. Hoskin[a,*,1], Alessandro Colombo[b,1], Ann Henry[c,1], Peter Niehoff[d,1], Taran Paulsen Hellebust[e,1], Frank-Andre Siebert[f,1], Gyorgy Kovacs[g,1]

[a] Mount Vernon Cancer Centre, Northwood, UK; [b] Department of Radiotherapy, Manzoni Hospital, Lecco, Italy; [c] St. James Institute for Oncology, Leeds, UK; [d] Department of Radiotherapy, City Hospital Cologne, Germany; [e] DNR Norwegian Radium Hospital, Oslo, Norway; [f] Universitätsklinikum Schleswig-Holstein, Kiel; and [g] University Hospital Schleswig-Holstein Campus Lübeck, Germany

Radiotherapy and Oncology xxx (2013)

Inclusion criteria

- Stages T1b–T3b
- Any Gleason score
- Any PSA level

Exclusion criteria

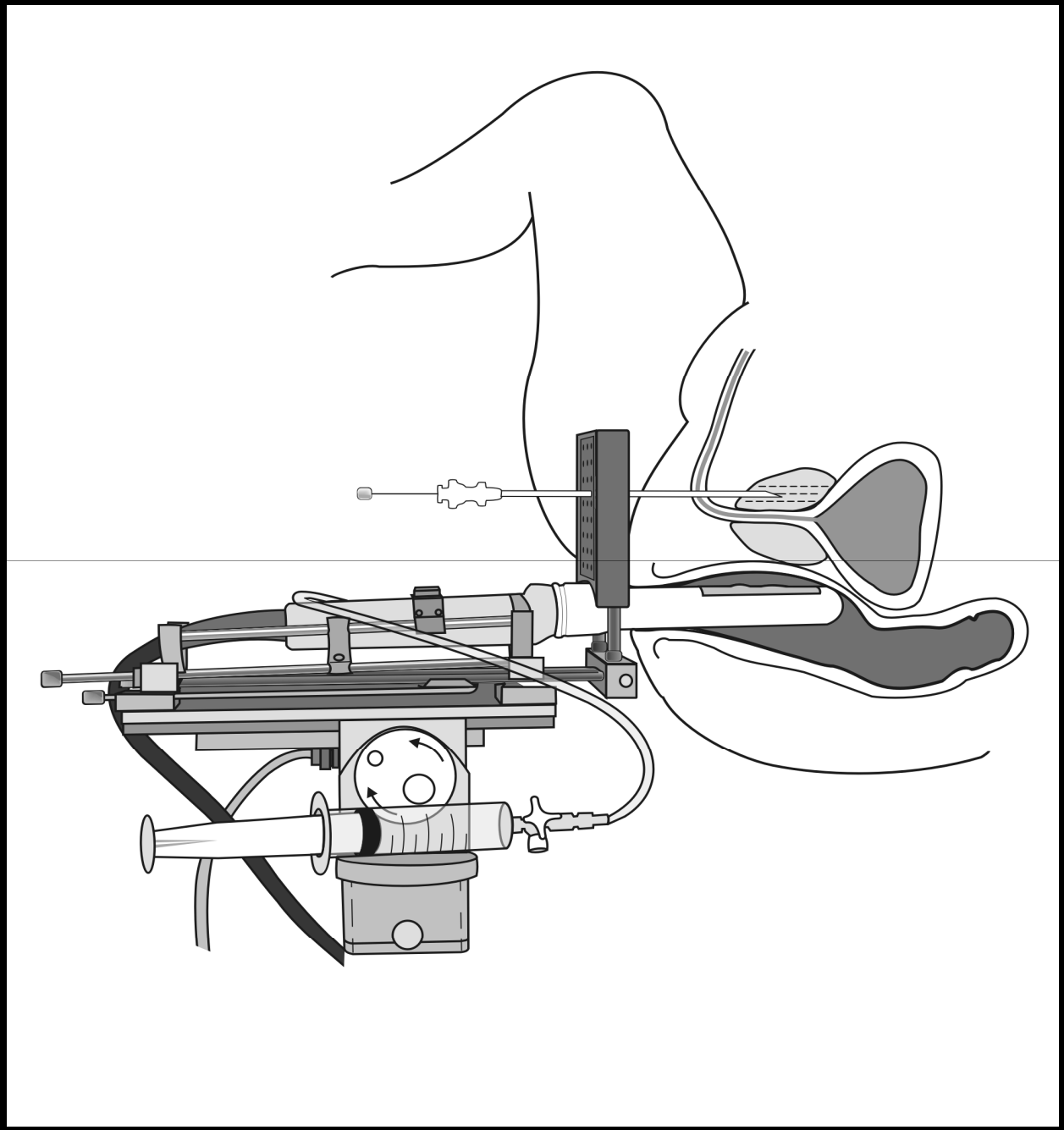
- TURP within 3–6 months
- Maximum urinary flow rate (Qmax) <10 ml/s
- IPSS > 20
- Pubic arch interference
- Lithotomy position or anaesthesia not possible
- Rectal fistula

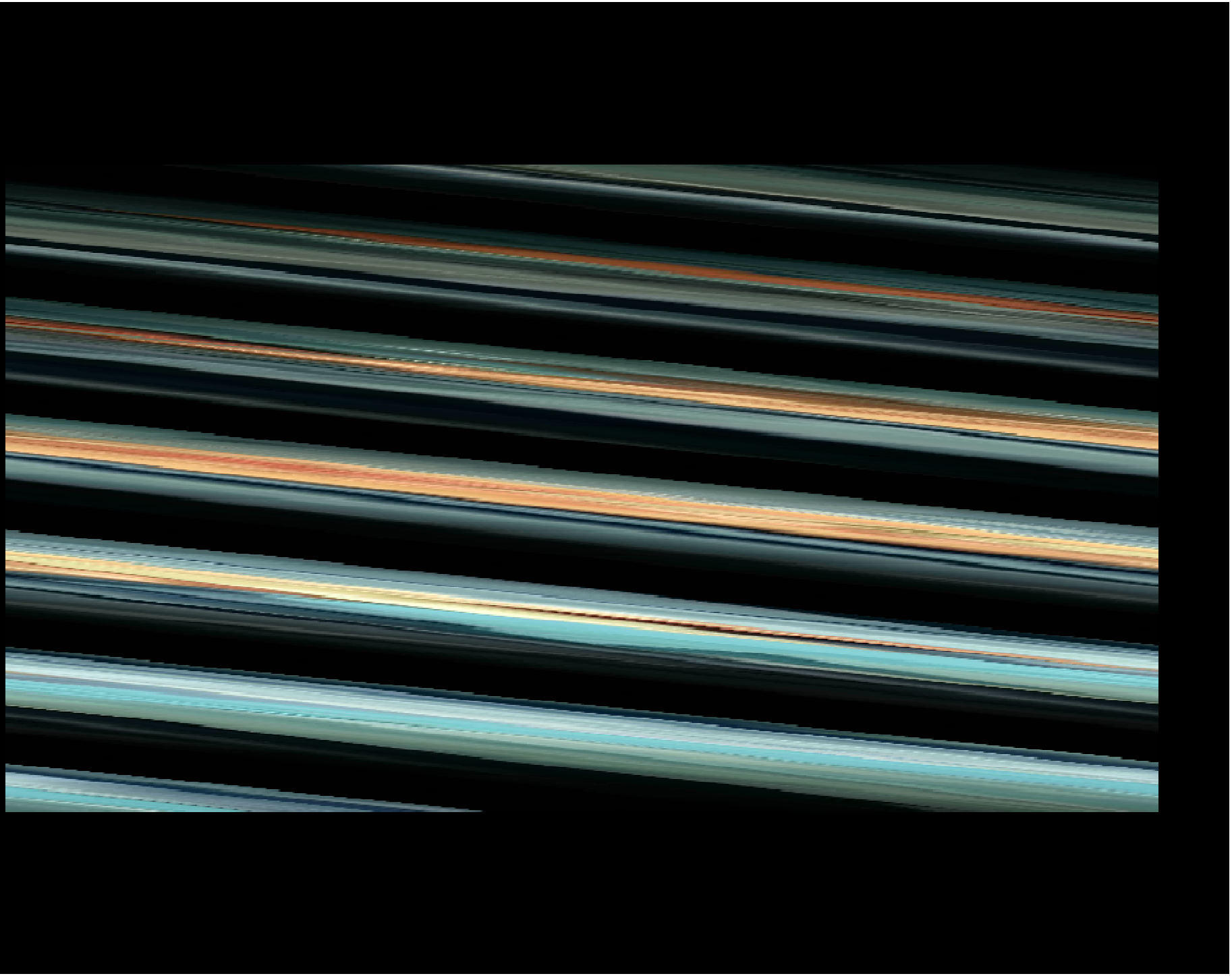
Contraindications to HDR brachytherapy are:

- Age >80yrs
- PSA>40ng/ml
- Clopidogrel
- T3B disease
- IPSS 18

HDR brachytherapy procedure

- Assessment
- Implantation
- Imaging
- Volume definition
- Dosimetry
- Verification and delivery
- Implant removal





HDR brachytherapy procedure

- Assessment
- Implantation
- Imaging
- Volume definition
- Dosimetry
- Verification and delivery
- Implant removal

HDR implant: imaging and volume definition

- Ultrasound
  - Real time (SWIFT and VITESSE)
  - Planned post implant without moving patient
- CT / MRI
  - Post implant after patient transfer

GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: An update

Peter J. Hoskin[a,*,1], Alessandro Colombo[b,1], Ann Henry[c,1], Peter Niehoff[d,1], Taran Paulsen Hellebust[e,1], Frank-Andre Siebert[f,1], Gyorgy Kovacs[g,1]

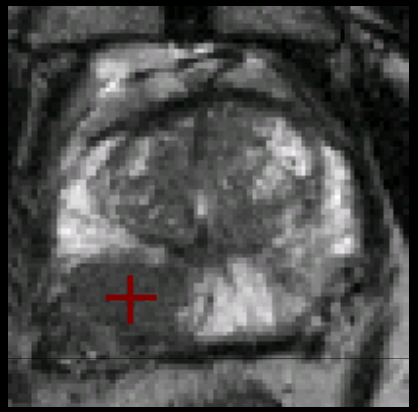
[a] Mount Vernon Cancer Centre, Northwood, UK; [b] Department of Radiotherapy, Manzoni Hospital, Lecco, Italy; [c] St. James Institute for Oncology, Leeds, UK; [d] Department of Radiotherapy, City Hospital Cologne, Germany; [e] DNR Norwegian Radium Hospital, Oslo, Norway; [f] Universitätsklinikum Schleswig-Holstein, Kiel; and [g] University Hospital Schleswig-Holstein Campus Lübeck, Germany

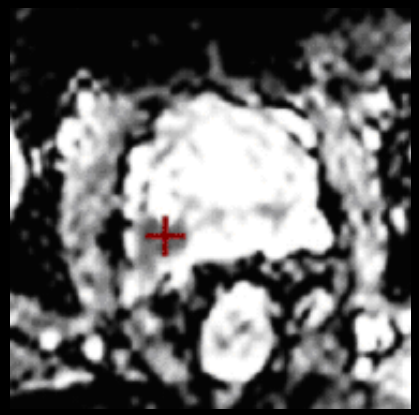
Radiotherapy and Oncology xxx (2013)

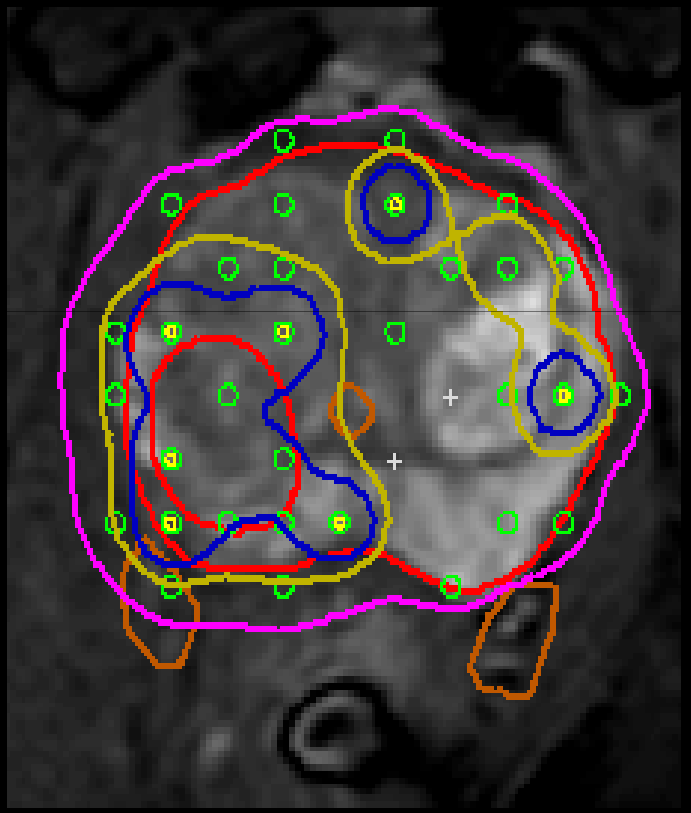
- Clinical target volume (CTV) is defined by:
  - the prostate capsule
  - plus any macroscopic extracapsular disease or seminal vesicle involvement identified on diagnostic images expanded by 3 mm to encompass potential microscopic disease. This is usually constrained posteriorly to the anterior rectal wall and superiorly to the bladder base.

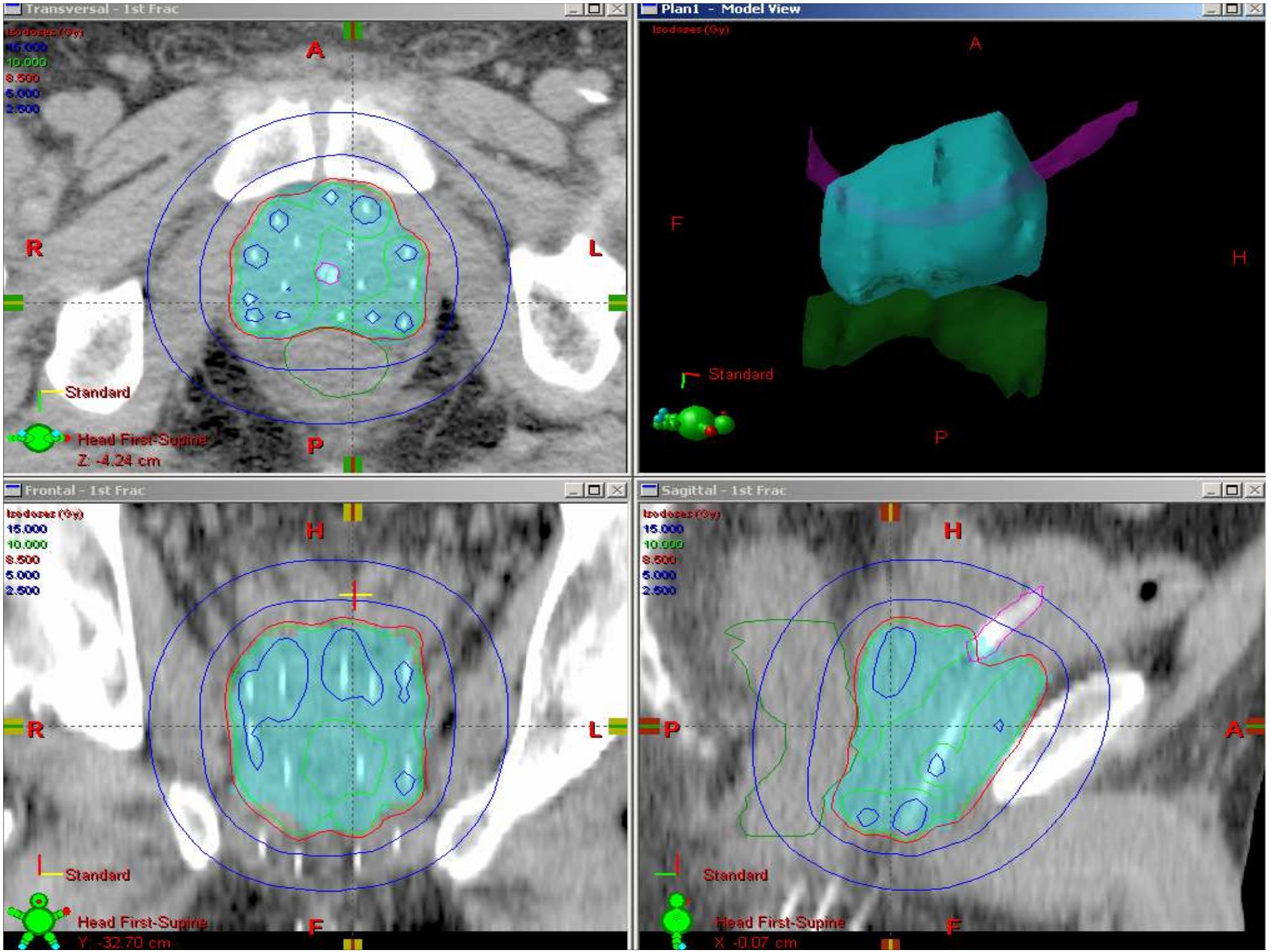
- CTV subvolumes. These may include boost volumes to the peripheral zones or other sites defined from imaging where it is considered there are significant tumour volumes. Each should be designated separately as CTV1, CTV2, CTV3 etc.

CTV subvolumes








Transversal - 1st Frac
Isodoses (Gy)
15.000
10.000
8.500
5.000
2.500
A
R
L
P
Standard
Head First-Supine
Z: -4.24 cm
Plan1 - Model View
Isodoses (Gy)
A
F
H
P
Standard
Frontal - 1st Frac
Isodoses (Gy)
15.000
10.000
8.500
5.000
2.500
H
R
L
F
Standard
Head First-Supine
Y: -32.70 cm
Sagittal - 1st Frac
Isodoses (Gy)
15.000
10.000
8.500
5.000
2.500
H
P
A
F
Standard
Head First-Supine
X: -0.07 cm

HDR brachytherapy boost: Planning aim

after

External beam

- 45 Gy in 25 fractions over 5 weeks.
- 46 Gy in 23 fractions over 4.5 weeks.
- 35.7 Gy in 13 fractions over 2.5 weeks.
- 37.5.Gy in 15 fractions over 3 weeks.

- 15 Gy in 3 fractions.
- 11–22 Gy in 2 fractions.
- 12–15 Gy in 1 fraction.

HDR schedules: normal tissue constraints

Organ	26 Gy	31.5 Gy	34 Gy	36 Gy
Urethra				
D_{30} (Gy)	13.75–14.75	10.76–11.79		
Volume (cc)	0–0.06 (V_{15Gy})	0–0.21 (V_{12Gy})	0.01–0.65 (V_{10Gy})	0–0.83 (V_{10Gy})
Rectum				
D_{2cc} (Gy)	5.8–10.3	5.51–8.78	5.14–7.36	5.01–7.45
Volume (cc)	0–0.25 ($V_{12.5Gy}$)	0–0.19 (V_{10Gy})	0–0.24 ($V_{8.5Gy}$)	0–0.29 ($V_{8.5Gy}$)

Rectum D2cc: EQD2 75Gy
Urethral D30: EQD2 130Gy
Urethral D10: EQD 2 110Gy

DOSE ESCALATION IMPROVES CANCER-RELATED EVENTS AT 10 YEARS FOR INTERMEDIATE- AND HIGH-RISK PROSTATE CANCER PATIENTS TREATED WITH HYPOFRACTIONATED HIGH-DOSE-RATE BOOST AND EXTERNAL BEAM RADIOTHERAPY

ALVARO A. MARTINEZ, M.D., F.A.C.R.,* JOSE GONZALEZ, M.D.,* HONG YE, M.S.,* MIHAI GHILEZAN, M.D., PH.D.,* SUGANDH SHETTY, M.D.,* KENNETH KERNEN, M.D.,† GARY GUSTAFSON, M.D.,* DANIEL KRAUSS, M.D.,* FRANK VICINI, M.D.,* AND LARRY KESTIN, M.D.*

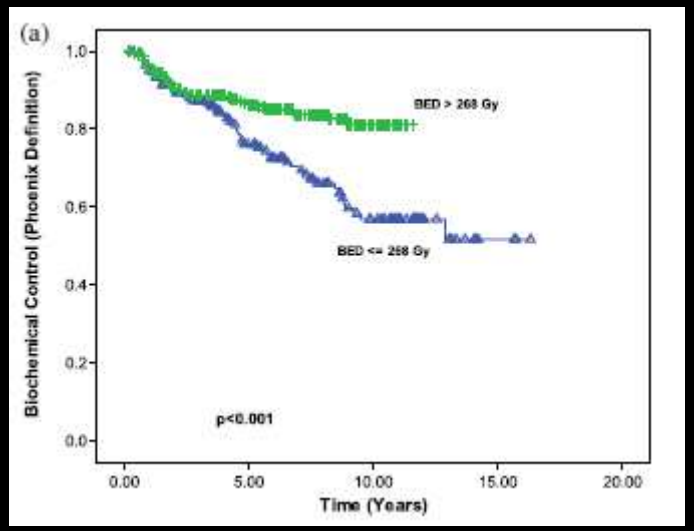
472 patients: 1992-2007: inter/high risk

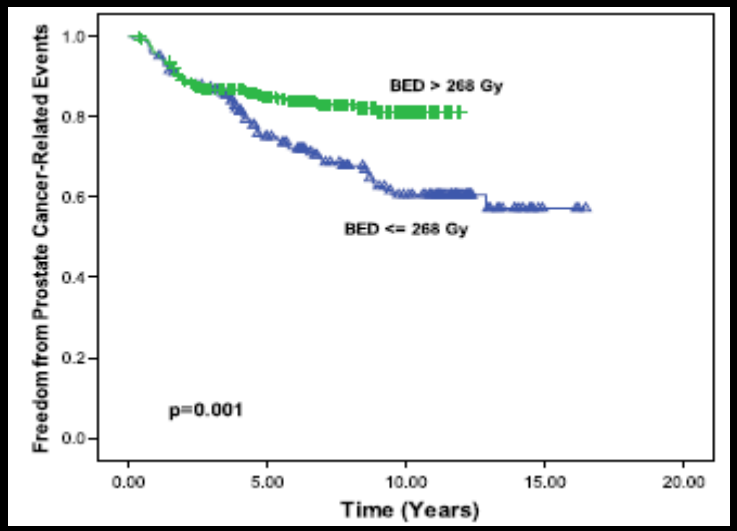
IJROB 2010

Age	
Median (range)	68 yrs (42–85)
T stage	
T1c	25.0% (118)
T2	63.3% (298)
T3	11.7% (55)
Pre-RT PSA	
< 4 ng/ml	6.6% (31)
4 to <10 ng/ml	51.6% (242)
10 to <20 ng/ml	28.6 % (134)
≥ 20 ng/ml	13.2% (62)
Gleason score	
≤ 6	35.0% (165)
7	44.2% (209)
8–10	20.8% (98)
Follow-up	
median (range)	8.2 (0.4–17.0)

Dose group	Group	No. of cases (n = 472)	Mean follow-up (years)	Median follow-up (years)	Range (years)	BED (α/β of 1.2) P-EBRT plus HDR
Low dose	5.5 Gy x 3 fractions	26	11.2	11.2	2.1–17.0	215 Gy
	6.0 Gy x 3 fractions	21	10.3	10.9	1.1–16.1	231 Gy
	6.5 Gy x 3 fractions	32	10.5	10.9	2.0–15.0	248 Gy
	8.25 Gy x 2 fractions	44	8.2	8.9	1.5–13.3	253 Gy
	8.75 Gy x 2 fractions	44	8.7	9.3	3.4–12.3	268 Gy
High dose	9.50 Gy x 2 fractions	111	8.3	9.7	1.2–11.9	292 Gy
	10.5 Gy x 2 fractions	125	6.2	7.0	0.4–11.0	327 Gy
	11.5 Gy x 2 fractions	69	6.0	6.2	0.4–9.3	366 Gy
All cases		471	7.8	8.2	0.4–17.0	

Dose group	No. of cases (n = 472)	BF (nadir +2)	BF(nadir +5 in 24 month, then nadir +2)	Locoregional failure	Distant metastasis failure	Clinical failure	Clinical DFS	Prostate cancer-related events
Low dose	167	43.1%	41.2%	14.3%	12.4%	23.4%	55.2%	39.4%
High dose	305	18.9%	15.5%	2.8%	5.7%	7.7%	71.9%	18.9%
p value		<0.001	<0.001	0.001	0.028	<0.001	0.014	0.001
All cases	472	29.4%	26.6%	7.8%	8.3%	14.3%	64.8%	27.5%

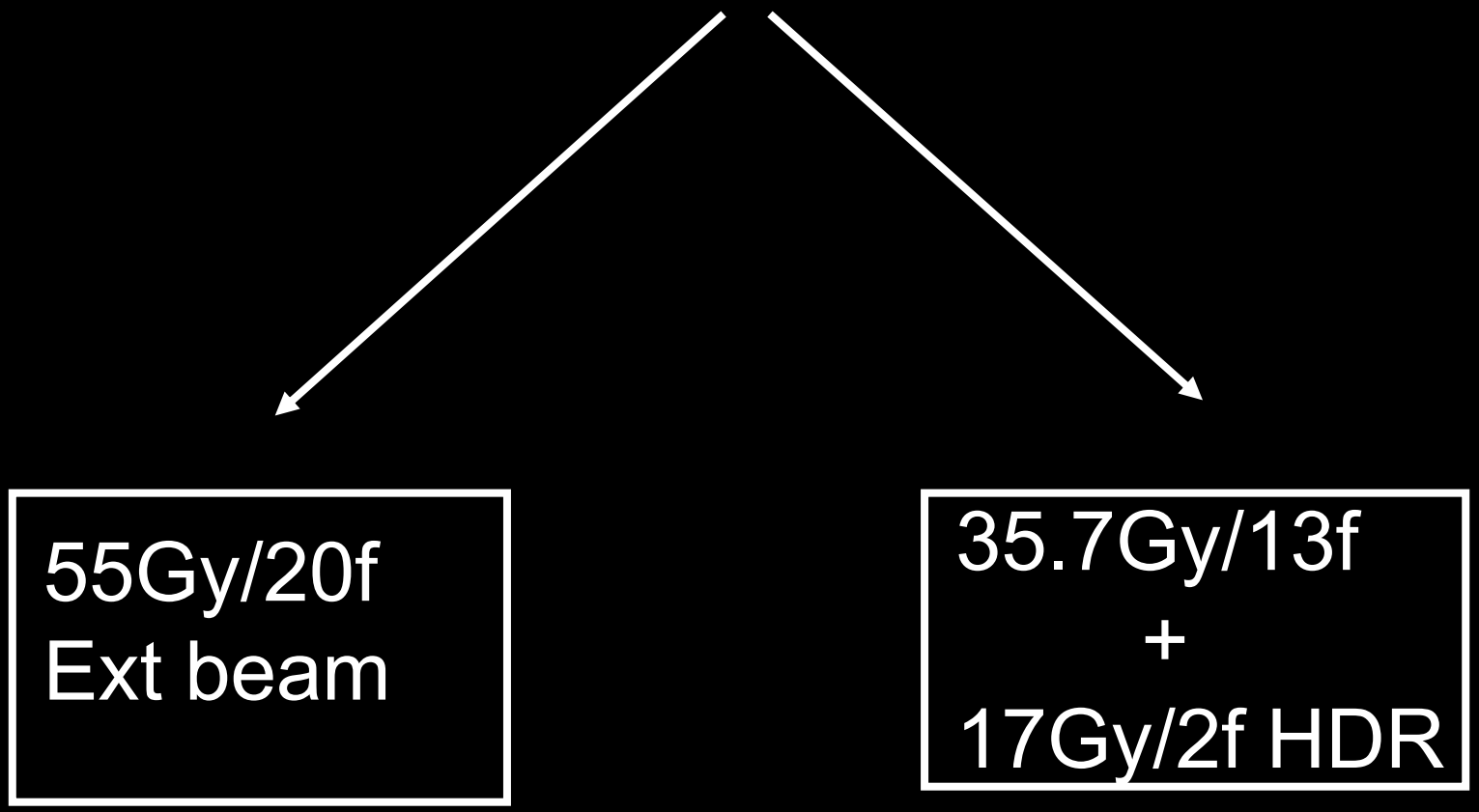




268Gy = 100.5Gy (αβ=1.2)

Martinez et al 2010

MVH RCT



Closed 08/05: 220 patients randomised

HDR implant: biological advantage in EQD2

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam 78Gy/39f	78.0	78.0	78.0
55Gy/20f	66.8	62.5	58.4
• HDR Boost after 35.7Gy/13f 17Gy/2f	91.9	77.7	64.2

Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Peter J. Hoskin [a], Ana M. Rojas [a,*], Peter J. Bownes [b], Gerry J. Lowe [a], Peter J. Ostler [a], Linda Bryant [a]

[a]Cancer Centre, Mount Vernon Hospital, Northwood, UK; [b]St. James's Institute of Oncology, St. James's University Hospital, Leeds, UK

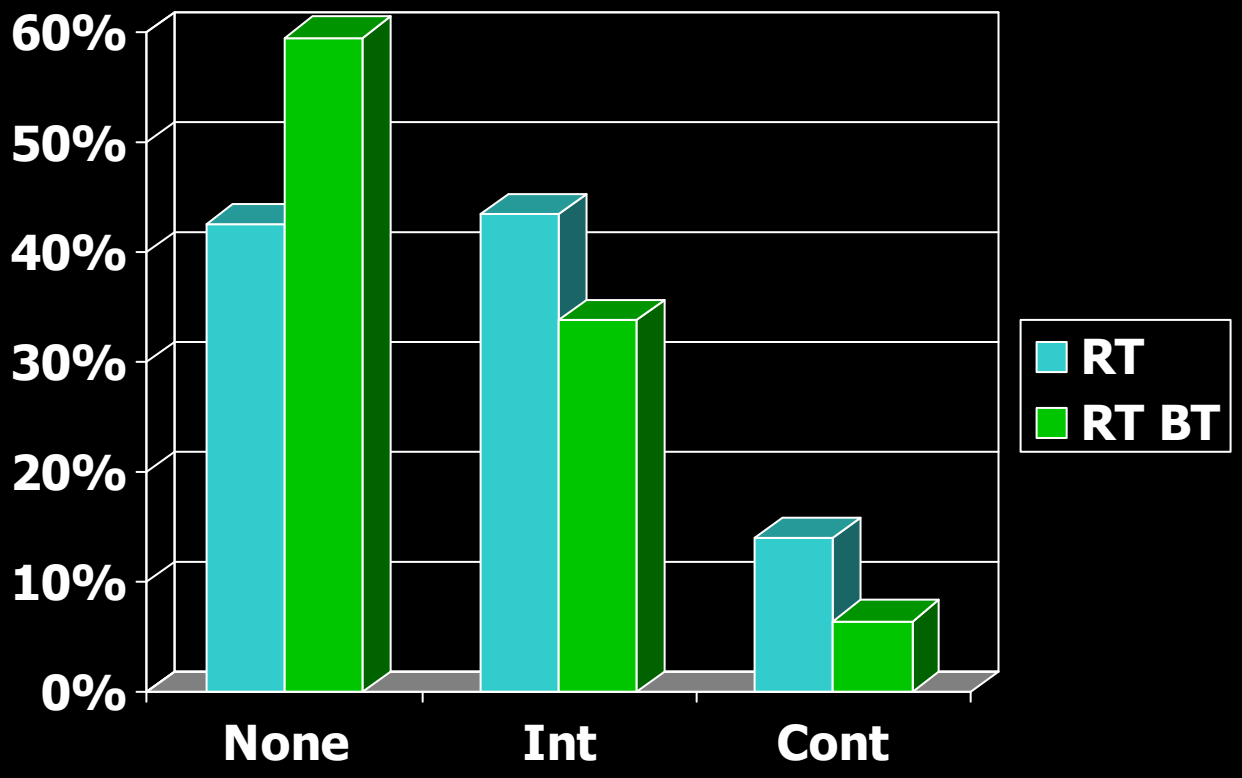
Radiotherapy and Oncology xxx (2012) xxx–xxx

Demographic details of patients given external beam radiotherapy alone (arm 1) or with a boost of high-dose-rate brachytherapy (arm 2).

Variable	Category	Arm 1 (n = 106) n (%)	Arm 2 (n = 110) n (%)
Age	Median	70	70
	Range	47–80	47–80
Follow-up time (months)	Median	85	85
	Mean	88	86
	Range	9–147	8–144
T stage	T_1	27 (25)	29 (26)
	T_2	55 (52)	47 (43)
	T_3	24 (23)	34 (31)
Gleason	<7	48 (45)	46 (42)
	7	40 (38)	44 (40)
	≥8	18 (17)	20 (18)
PSA (μg/l)	<10	36 (34)	35 (32)
	10–20	43 (41)	45 (41)
	>20	27 (25)	30 (27)
Risk Group[a]	Low	7 (7)	2 (2)
	Intermediate	43 (40)	48 (44)
	High	56 (53)	60 (54)
ADT	No	26 (25)	25 (23)
	Yes	80 (75)	85 (77)
ADT (duration)			
6 months	Low	2 (29)	1 (50)
6 months	Intermediate	26 (60)	29 (60)
≤3 years	High	52 (93)	55 (92)

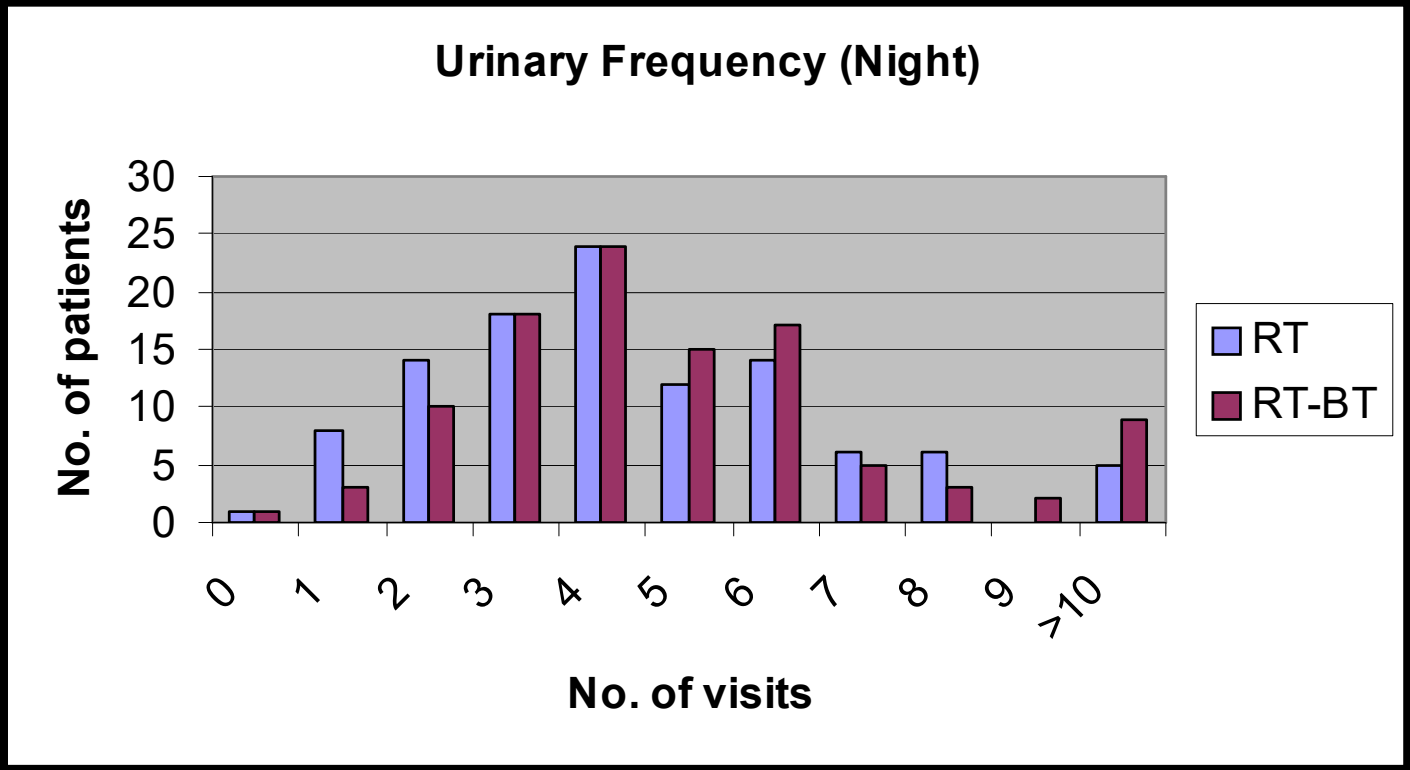
Median follow up 7 yrs

Acute toxicity: rectal discharge



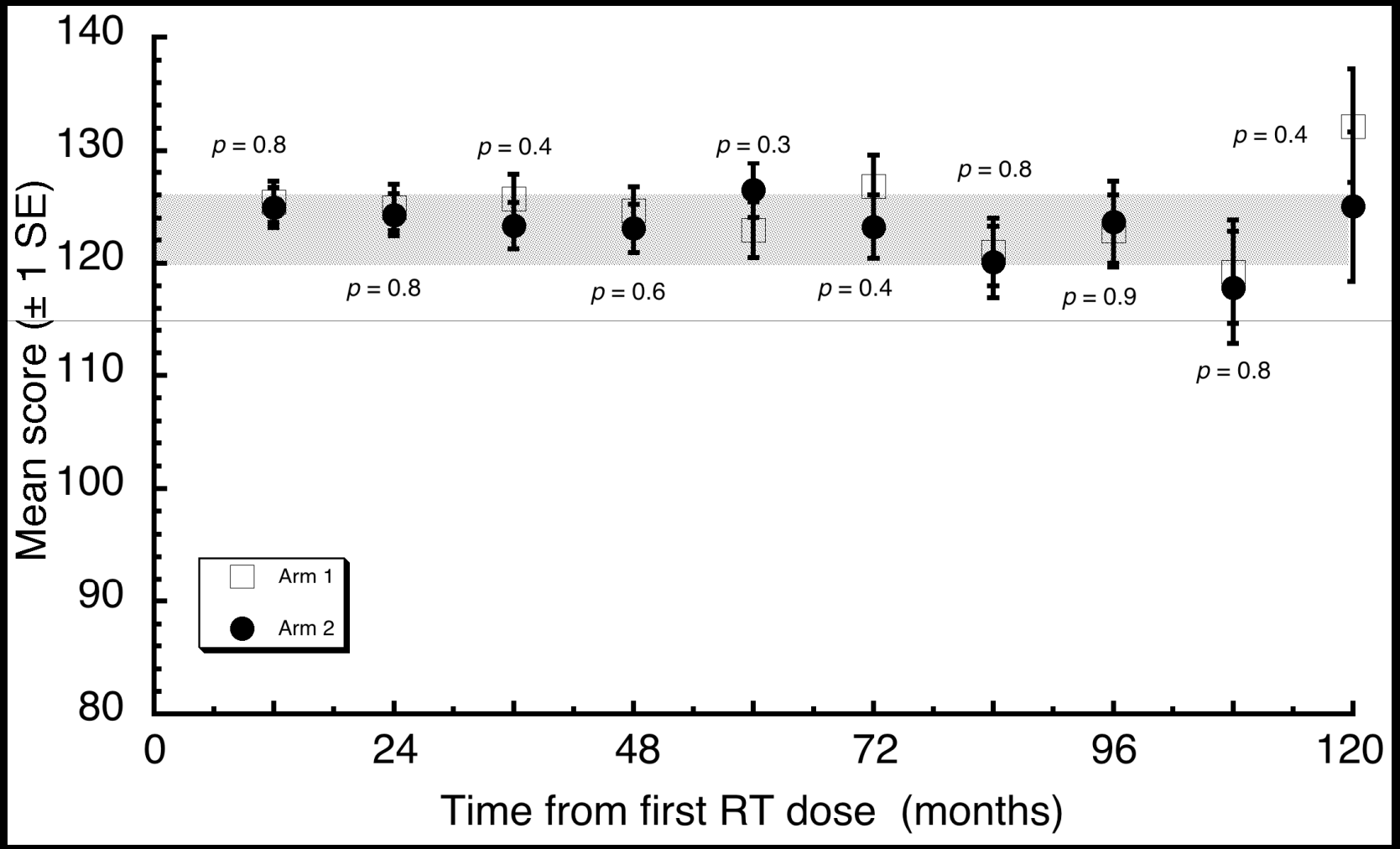
P=0.025

Acute toxicity: urinary frequency



P=0.136

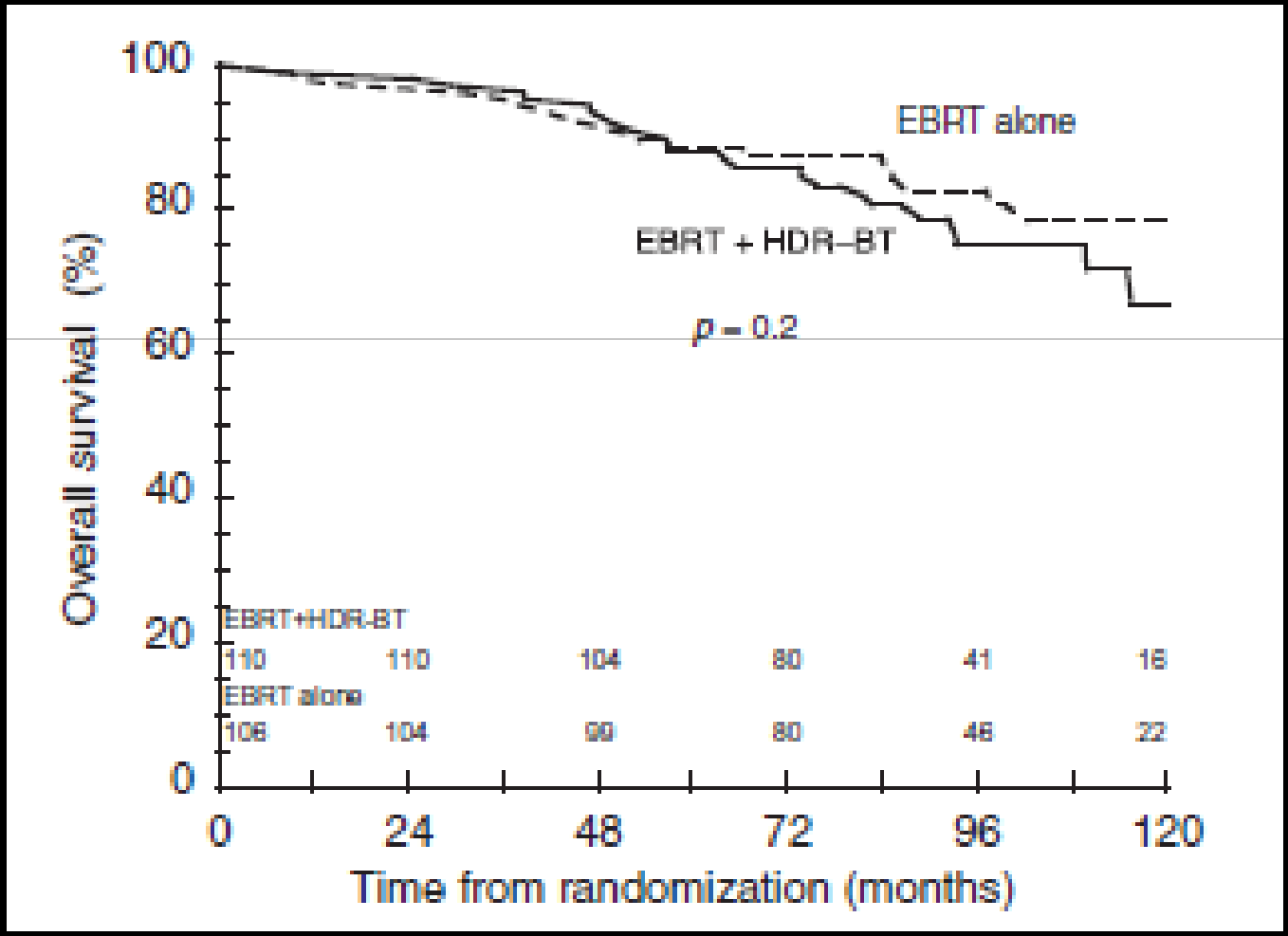
FACT-P total scores (range 0 to 152)



Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Radiotherapy and Oncology xxx (2012) xxx–xxx

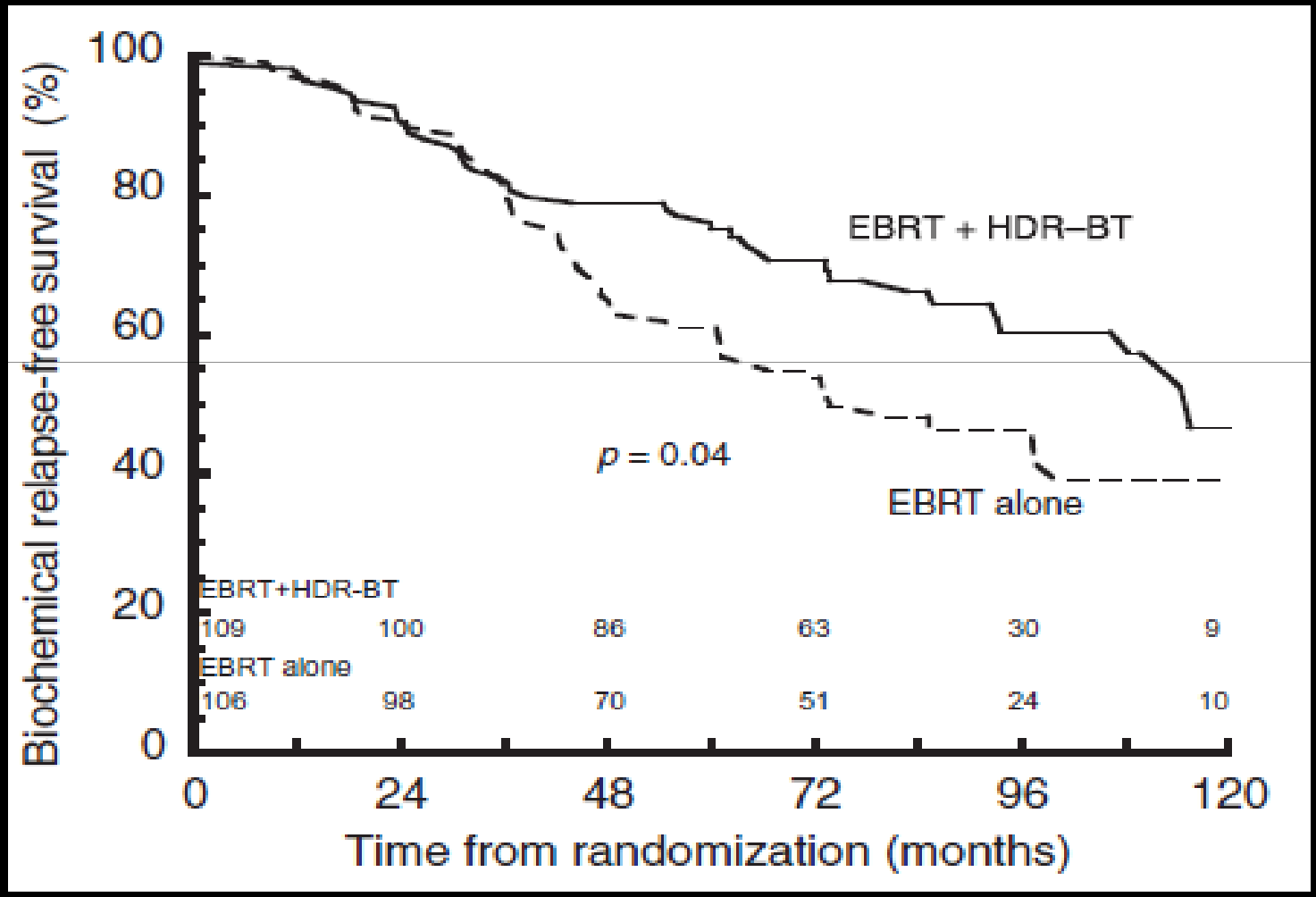
Overall survival



Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Radiotherapy and Oncology xxx (2012) xxx–xxx

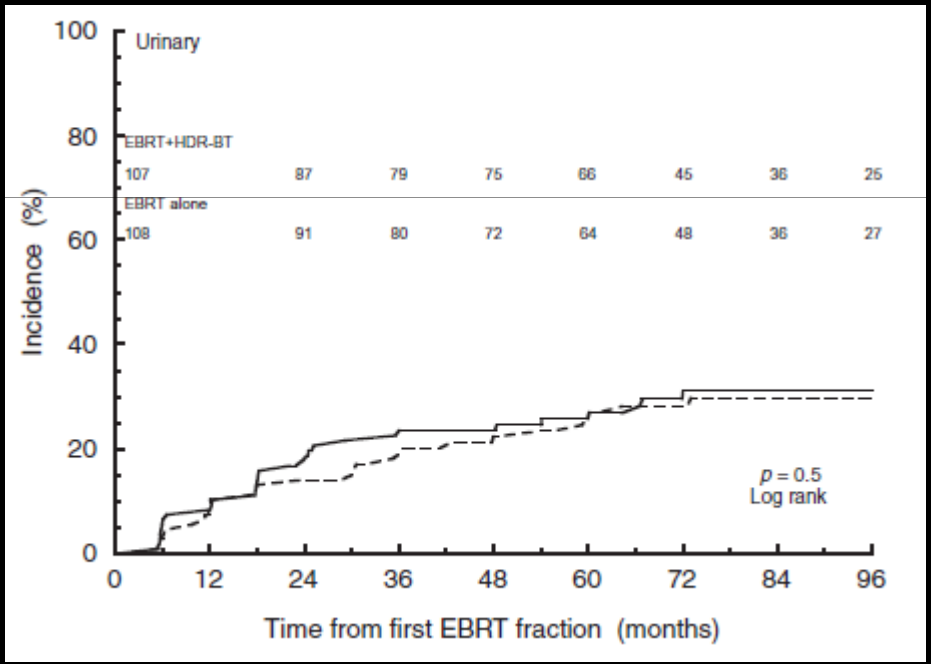
Biochemical relapse free survival

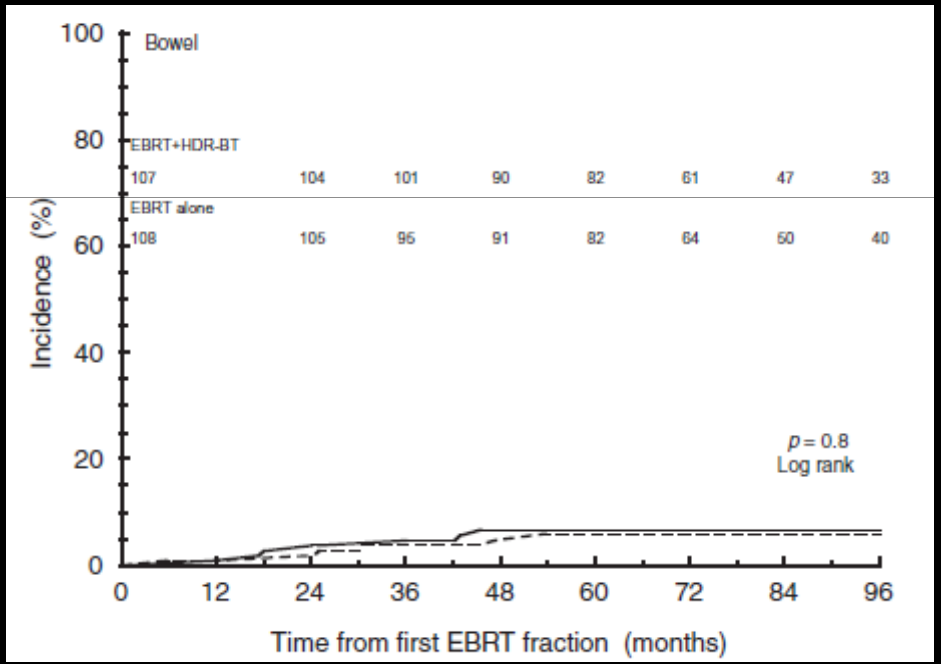


Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Radiotherapy and Oncology xxx (2012) xxx–xxx

Toxicity





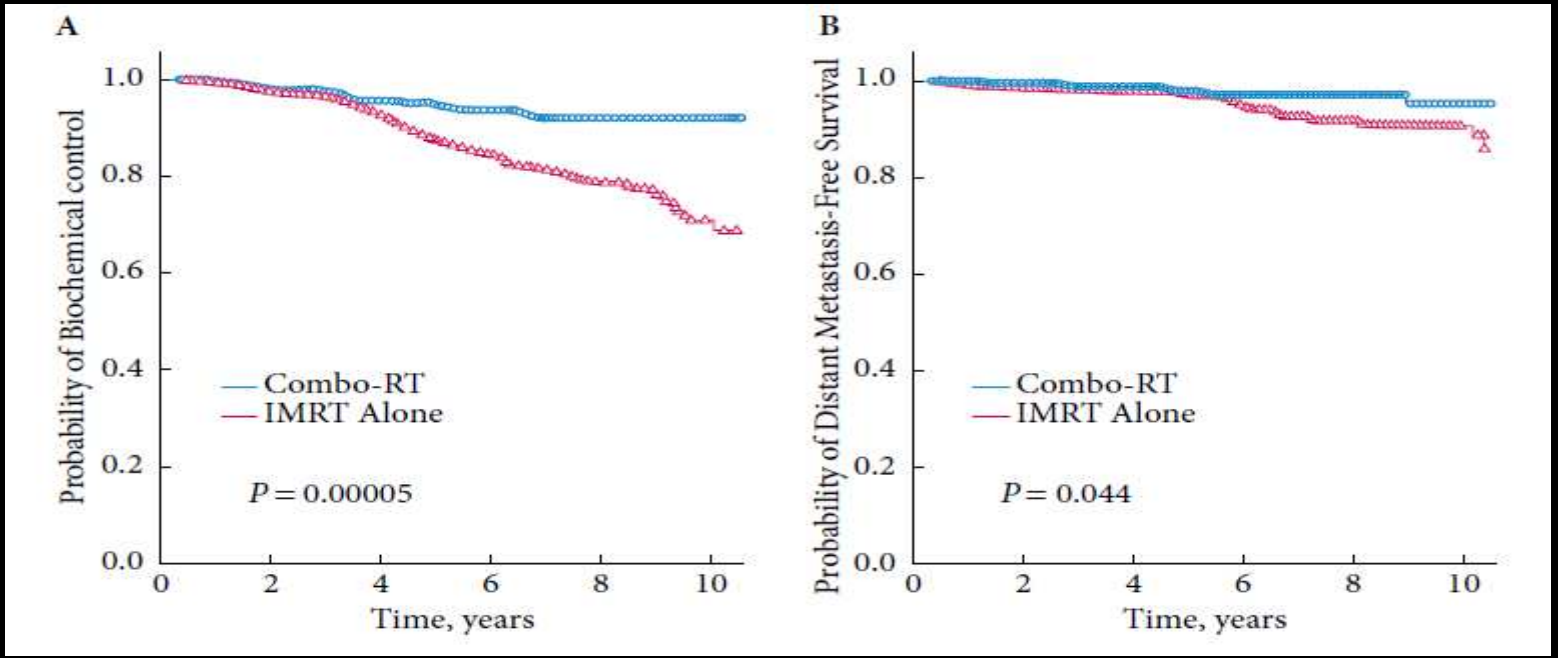
Comparison of high-dose (86.4 Gy) IMRT vs combined brachytherapy plus IMRT for intermediate-risk prostate cancer

Daniel E. Spratt, Zachary S. Zumsteg, Pirus Ghadjar, Marisa A. Kollmeier, Xin Pei, Gilad Cohen*, William Polkinghorn, Yoshiya Yamada and Michael J. Zelefsky

*Departments of Radiation Oncology and *Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY,*

BJU Int 2014; **114**: 360–367

IMRT 86.4Gy: 470
vs
IMRT 45-50.4+ BT : 400 (LDR 100-110Gy - 260, HDR 16.5-22.5 in 3f - 140)



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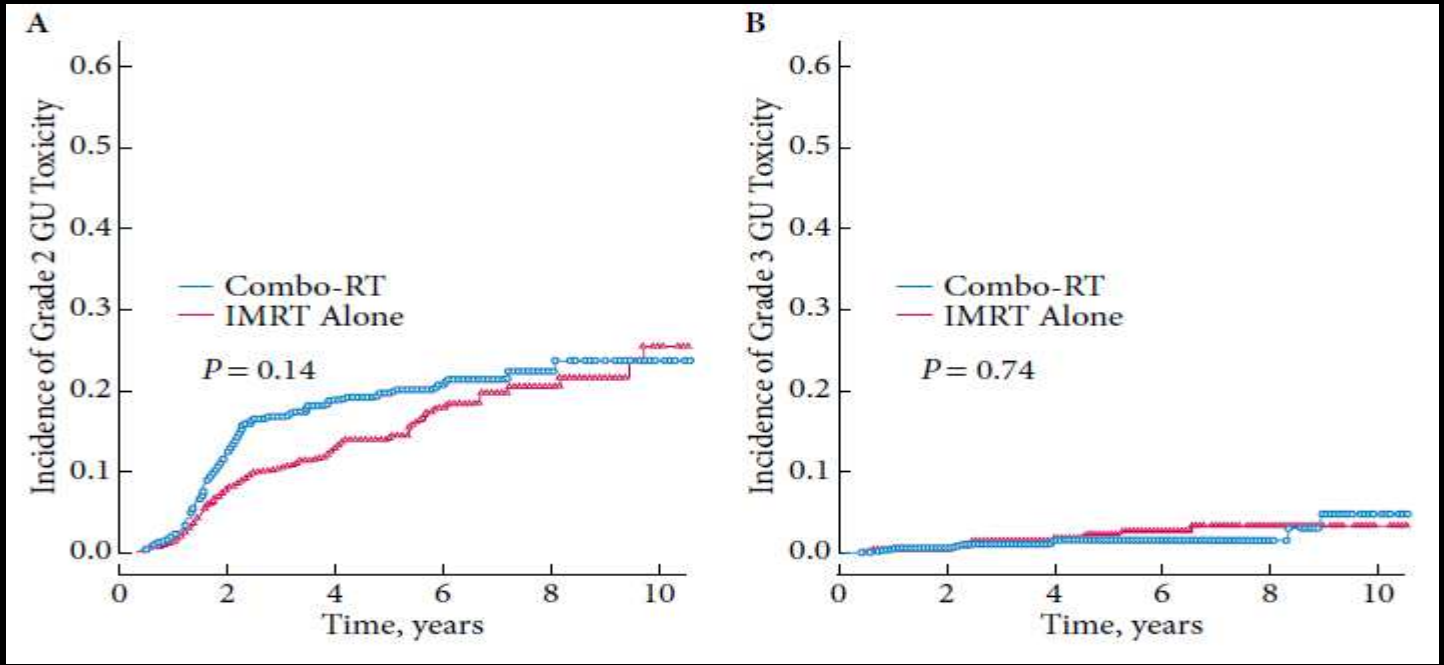


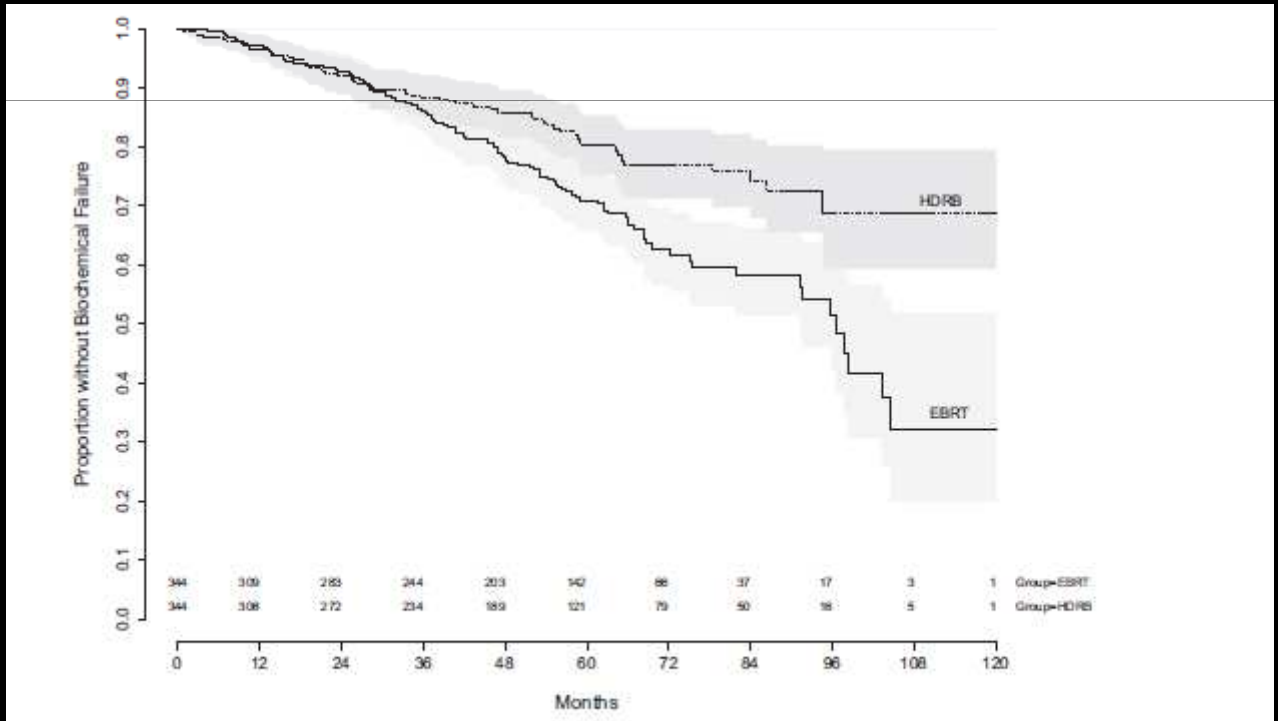
Direct 2-Arm Comparison Shows Benefit of High-Dose-Rate Brachytherapy Boost vs External Beam Radiation Therapy Alone for Prostate Cancer

Richard Khor, MBBS,* Gillian Duchesne, MD, FRANZCR,*,† Keen-Hun Tai, FRANZCR,* Farshad Foroudi, FRANZCR,* Sarat Chander, FRANZCR,* Sylvia Van Dyk, DipAppSc,* Margaret Garth, DipAppSc,* and Scott Williams, MD, FRANZCR*

*Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Centre, and University of Melbourne, Melbourne, Australia; and †Monash University, Melbourne, Australia

Int J Radiation Oncol Biol Phys, Vol. 85, No. 3, pp. 679–685, 2013

344 patients 46Gy/23f + 19.5GY/3f HDR vs 344 patients 3D CRT 74Gy/37f
Risk group: Intermediate 41%; High 59%



Actuarial FFbF plots of matched EBRT and HDRB treatment cohorts. Bands indicate 95% confidence intervals.

Brachytherapy Improves Biochemical Failure—Free Survival in Low- and Intermediate-Risk Prostate Cancer Compared With Conventionally Fractionated External Beam Radiation Therapy: A Propensity Score Matched Analysis

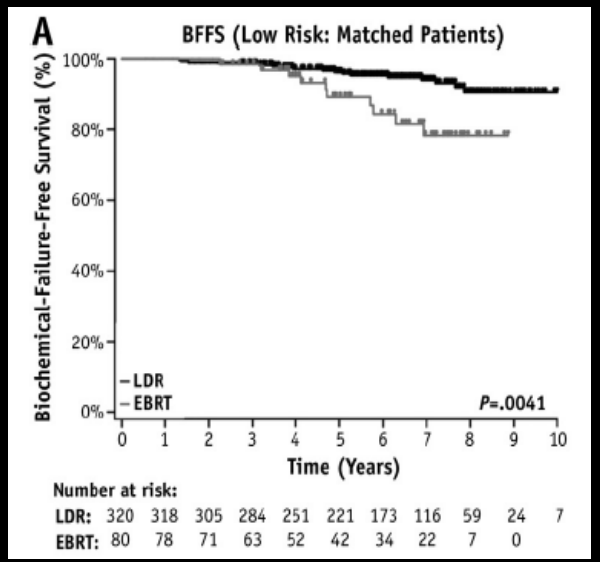
Graham D. Smith, MRT(T), MSc,* Tom Pickles, MD,† Juanita Crook, MD,‡ Andre-Guy Martin, MD,§ Eric Vigneault, MD,§ Fabio L. Cury, MD,‖ Jim Morris, MD,† Charles Catton, MD,¶ Himu Lukka, MD,# Andrew Warner, MSc,** Ying Yang, MSc,†† and George Rodrigues, MD, PhD*,**

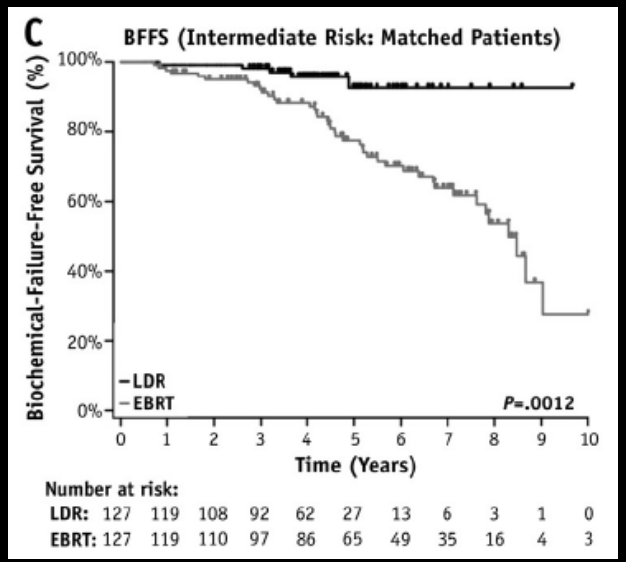
Int J Radiation Oncol Biol Phys, Vol. ■, No. ■, pp. 1–12, 2015

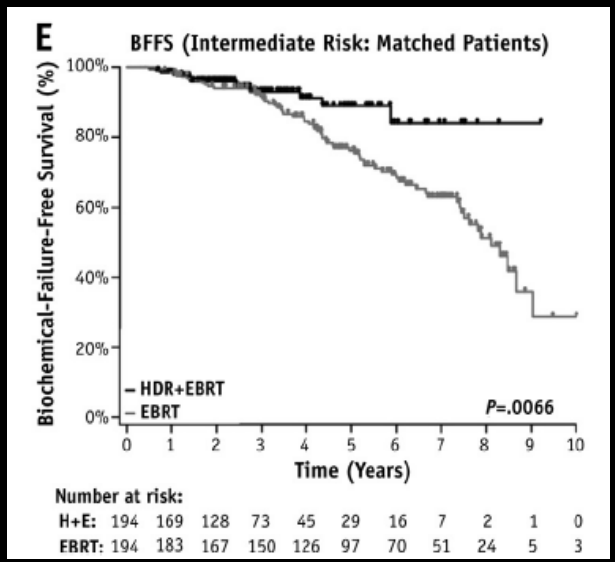
7974 PATIENTS FROM 4 Canadian centres:

Low risk EBRT vs LDR BT
Inter risk EBRT vs LDR BT
Inter risk EBRT vs EBRT +HDR BT

EBRT: 70-79.8Gy; LDR 144Gy; HDR 10-20Gy







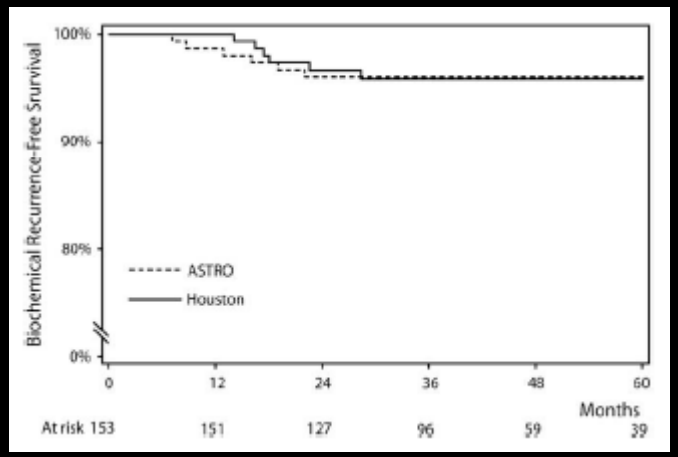
AN EIGHT-YEAR EXPERIENCE OF HDR BRACHYTHERAPY BOOST FOR LOCALIZED PROSTATE CANCER: BIOPSY AND PSA OUTCOME

FRANÇOIS BACHAND, M.D.,* ANDRÉ-GUY MARTIN, M.D., M.SC.,* LUC BEAULIEU, PH.D.,*†
FRANÇOIS HAREL, M.SC.,† AND ÉRIC VIGNEAULT, M.D., M.SC.*

*Département de Radio-oncologie, and †Centre de Recherche de L'Hôtel-Dieu de Québec, L'Hôtel-Dieu de Québec, Centre Hospitalier Universitaire de Québec (CHUQ), Centre de Recherche en Cancérologie de l'Université Laval, Québec, Canada

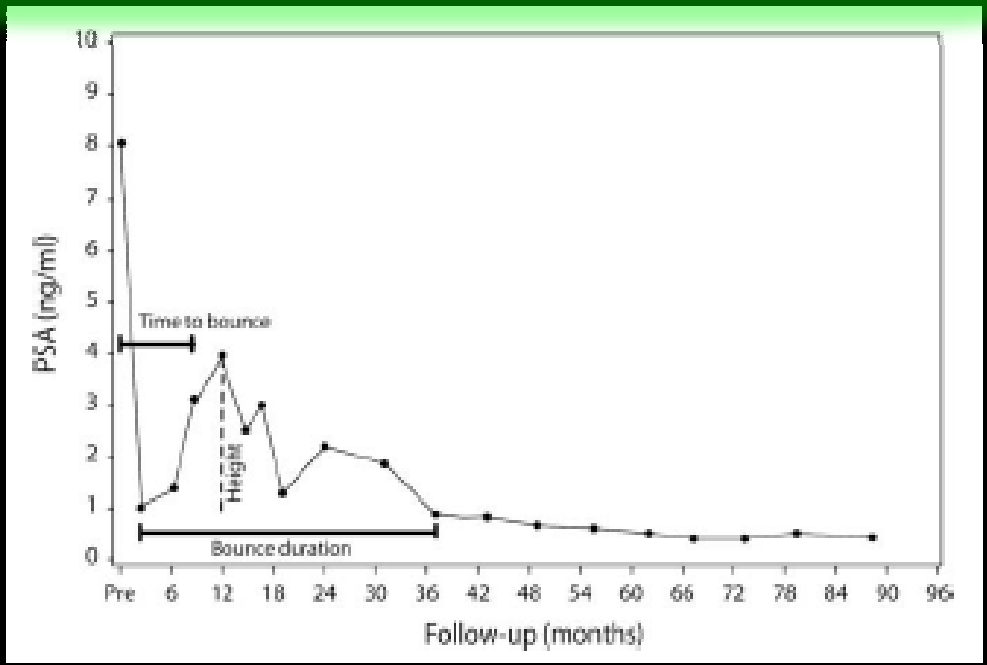
IJROB 2009

1996-2001: 40-44Gy + 18-20Gy/2f HDR
antiandrogens in 51%



n=153

Bounce (≥2 ng/ml above nadir) in 9.8%
Median time 15.2mo (IQR 11.1-17.7)
Median duration 18.7 (IQR 12.1-29)
Median height 3.24ng/ml (IQR 2.51-3.98)



HDR PROSTATE BRACHYTHERAPY

INDICATIONS

- Boost with external beam therapy
  - Intermediate/high risk disease
    - PSA10-20
    - Gleason 7+
    - T2c T3
- Monotherapy
  - Intermediate risk disease
  - ? Good risk disease vs seeds

HDR Monotherapy for Localised Prostate Cancer

- HDR brachytherapy is an established technique enabling high dose delivery to prostate gland
- HDR brachytherapy has potential advantages especially for more advanced prostate cancer
  - Physical implant flexibility
  - Biological advantage of large fractions

HDR brachytherapy monotherapy: Planning aim

34 Gy in 4 fractions.
36–38 Gy in 4 fractions.
31.5 Gy in 3 fractions.
26 Gy in 2 fractions.

MONOTHERAPEUTIC HIGH-DOSE-RATE BRACHYTHERAPY FOR PROSTATE CANCER: FIVE-YEAR RESULTS OF AN EXTREME HYPOFRACTIONATION REGIMEN WITH 54 GY IN NINE FRACTIONS

YASUO YOSHIOKA, M.D., PH.D.,* KOJI KONISHI, M.D.,* IORI SUMIDA, PH.D.,* YUTAKA TAKAHASHI, PH.D.,* FUMIAKI ISOHASHI, M.D.,* TOSHIYUKI OGATA, PH.D.,* MASAHIKO KOIZUMI, M.D., PH.D.,* HIDEYA YAMAZAKI, M.D., PH.D.,† NORIO NONOMURA, M.D., PH.D.,‡ AKIHIKO OKUYAMA, M.D., PH.D.,‡ AND TAKEHIRO INOUE, M.D., PH.D.*

*Department of Radiation Oncology, Osaka University Graduate School of Medicine, Osaka, Japan; †Department of Radiology, Kyoto Prefectural University of Medicine, Kyoto, Japan; ‡Department of Urology, Osaka University Graduate School of Medicine, Osaka, Japan

IJROB 2010

- 54Gy in 9 fractions
- 112 patients 1996-2005
  - 15 LOW RISK
  - 29 INTER RISK
  - 68 HIGH RISK

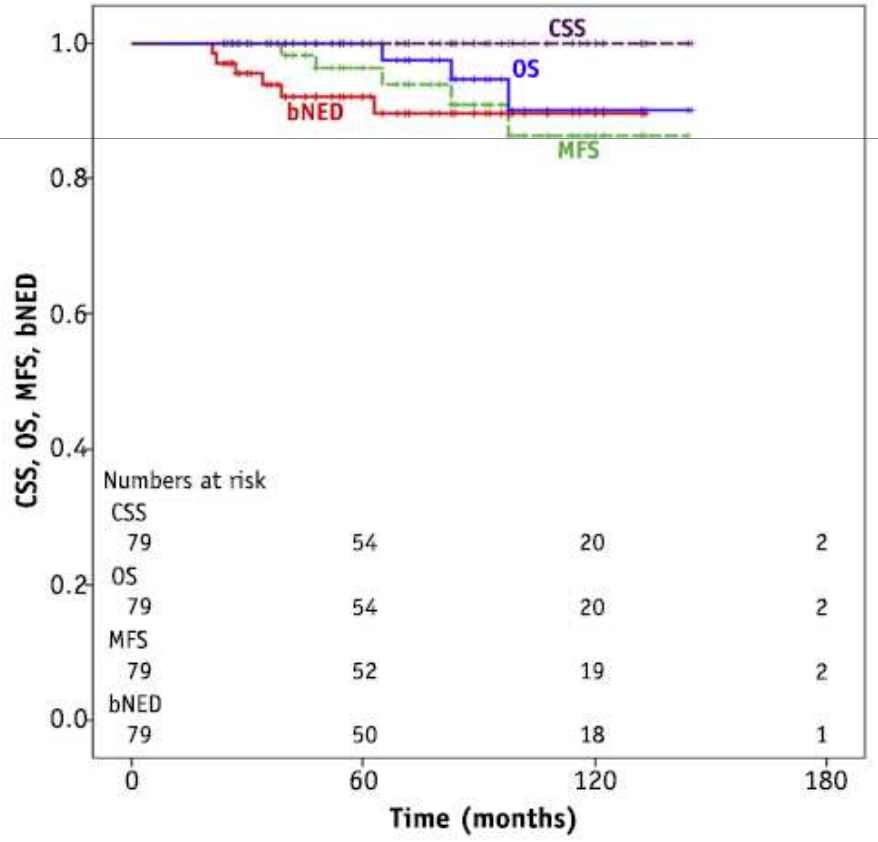
  - Neoadjuvant hormones in 94

High-Dose-Rate Brachytherapy as Monotherapy for Intermediate- and High-Risk Prostate Cancer: Clinical Results for a Median 8-Year Follow-Up

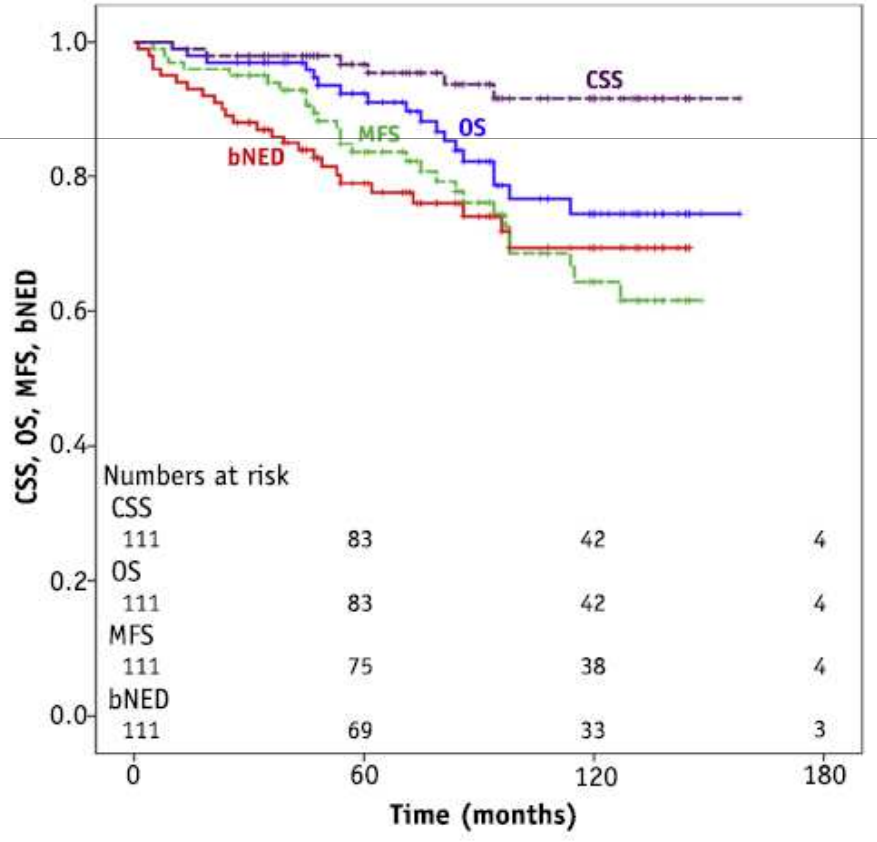
Int J Radiation Oncol Biol Phys, Vol. ■, No. ■, pp. 1–8, 2015

Yasuo Yoshioka, MD,* Osamu Suzuki, MD,* Fumiaki Isohashi, MD,* et al

Intermediate risk



High risk



Published HDR monotherapy studies

Author, y (ref.)	No. of patients	HDR dose			Median follow-up (y)	Biochemical control (risk group)
		Gy/fraction	Fractions (no. of implants)	Total		
Yoshioka et al, 2011 (14)	111	6	9 (1 implant)	54 Gy	5.4	85% low-risk at 5 y 93% intermediate-risk at 5 y 79% high-risk at 5 y
Hoskin et al, 2012 (15)	197	8.5-9	4 (1 implant)	34-36 Gy	4.5-5	95% intermediate-risk at 4 y
		10.5	3 (1 implant)	31.5 Gy	3	
		13	2 (1 implant)	26 Gy	0.5	87% high-risk at 4 y
Rogers et al, 2012 (19)	284	6	6 (2 implants)	36 Gy	3	94% intermediate-risk at 5 y
Mark et al, 2010 (13)	301	7.5	6 (2 implants)	45 Gy	8	88% all
Prada et al, 2012 (20)	40	19	1 (1 implant)	19 Gy	1.6	100% low-risk at 32 mo 88% intermediate-risk at 32 mo
Martinez et al, 2010 (12)	248	7	6 (2 implants)	42 Gy	4.8	91% low- and intermediate-risk at 5 y (WBH series)
		9.5	4 (1 implant)	38 Gy		87% low- and intermediate-risk at 5 y (CET series)
Demanes et al, 2011 (17)	298	7	6 (2 implants)	42 Gy	5.2	97% low- and intermediate-risk at 5 y
		9.5	4 (1 implant)	38 Gy		
Present study	718	9.5	4 (1 implant)	38 Gy	4.4	95% low-risk at 5 y
		9.5	4 (2 implants)	38 Gy		
		11.5	3 (3 implants)	34.5 Gy		93% intermediate-risk at 5 y 93% high-risk at 5 y

From Zamboglu et al IJROB 2013

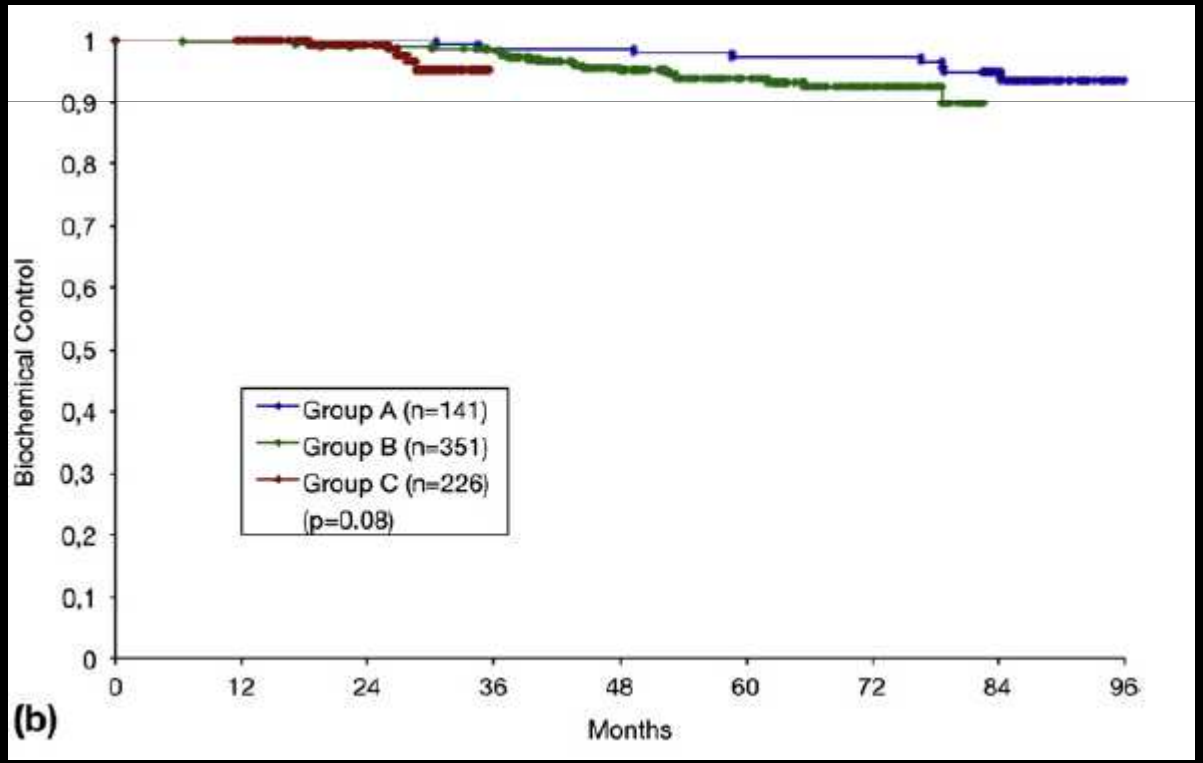
High-Dose-Rate Interstitial Brachytherapy as Monotherapy for Clinically Localized Prostate Cancer: Treatment Evolution and Mature Results

Nikolaos Zamboglou, MD, PhD,* Nikolaos Tselis, MD, PhD,* Dimos Baltas, PhD,† Thomas Buhleier, MD, PhD,* Thomas Martin, MD, PhD,‡ Natasa Milickovic, PhD,† Sokratis Papaioannou, MSc,† Hanns Ackermann, PhD,§ and Ulf W. Tunn, MD, PhD||

**Department of Radiation Oncology, Klinikum Offenbach, Offenbach, Germany; †Department of Medical Physics and Engineering, Klinikum Offenbach, Offenbach, Germany; ‡Department of Radiation Oncology, Klinikum Bremen-Mitte, Bremen, Germany; §Institute of Biostatistics, J.W. Goethe University of Frankfurt, Frankfurt, Germany; and ||Department of Urology, Klinikum Offenbach, Offenbach, Germany*

Int J Radiation Oncol Biol Phys, Vol. 85, No. 3, pp. 672–678, 2013

718 patients: 38Gy/4f/48hrs
38Gy/4f/15days
34.5Gy/3f/6weeks



High-Dose-Rate Interstitial Brachytherapy as Monotherapy for Clinically Localized Prostate Cancer: Treatment Evolution and Mature Results

Nikolaos Zamboglou, MD, PhD,* Nikolaos Tselis, MD, PhD,* Dimos Baltas, PhD,† et al

Acute toxicity

	No. of occurrences (%) in group A (n=141)		No. of occurrences (%) in group B (n=351)		No. of occurrences (%) in group C (n=226)	
Grade	Gastrointestinal	Genitourinary	Gastrointestinal	Genitourinary	Gastrointestinal	Genitourinary
Grade 5	0%	0%	0%	0%	0%	0%
Grade 4	0%	0%	0%	0%	0%	0%
Grade 3	1 (0.7%)	13 (9.2%)	0%	17 (4.8%)	0%	9 (3.9%)
Grade 2	0%	22 (15.6%)	6 (1.7%)	58 (16.5%)	8 (3.5%)	40 (17.6%)
Grade 1	26 (18.4%)	66 (46.8%)	55 (15.7%)	169 (48.1%)	28 (12.3%)	83 (36.7%)

Late toxicity

	No. of occurrences (%) in group A (n=141)				No. of occurrences (%) in group B (n=351)				No. of occurrences (%) in group C (n=225)			
	Grade				Grade				Grade			
Toxicity	1	2	3	4	1	2	3	4	1	2	3	4
Genitourinary												
Frequency/ urgency	48 (34.0%)	13 (9.2%)	3 (2.1%)	-	105 (29.9%)	17 (4.8%)	2 (0.6%)	-	61 (27.1%)	17 (7.5%)	0	-
Dysuria	9 (6.3%)	1 (0.7%)	1 (0.7%)	0	17 (4.8%)	4 (1.1%)	2 (0.6%)	0	18 (8.0%)	4 (1.7%)	1 (0.4%)	0
Incontinence	7 (4.9%)	11 (7.8%)	1 (0.7%)	1 (0.7%)	30 (8.6%)	18 (5.1%)	1 (0.3%)	0	26 (11.5%)	17 (7.5%)	1 (0.4%)	1 (0.4%)
Retention	22 (15.6%)	39 (6.3%)	4 (2.8%)	0	59 (16.8%)	19 (5.4%)	7 (2.0%)	0	26 (11.5%)	10 (4.4%)	2 (0.8%)	0
Erectile dysfunction	45 (31.9%)	30 (21.2%)	17 (12.0%)	-	85 (24.2%)	55 (15.7%)	58 (16.5%)	-	53 (23.5%)	41 (18.2%)	43 (19.1%)	-
Gastrointestinal (rectum)												
Pain	2 (1.4%)	1 (0.7%)	1 (0.7%)	0	7 (2.0%)	1 (0.3%)	1 (0.3%)	0	6 (2.6%)	0	0	0
Mucositis/ necrosis	0	1 (0.7%)	5 (3.5%)	0	0	3 (0.8%)	4 (1.2%)	0	0	1 (0.4%)	1 (0.4%)	0
Diarrhea	1 (0.7%)	0	0	0	0	0	0	0	1 (0.4%)	0	0	0

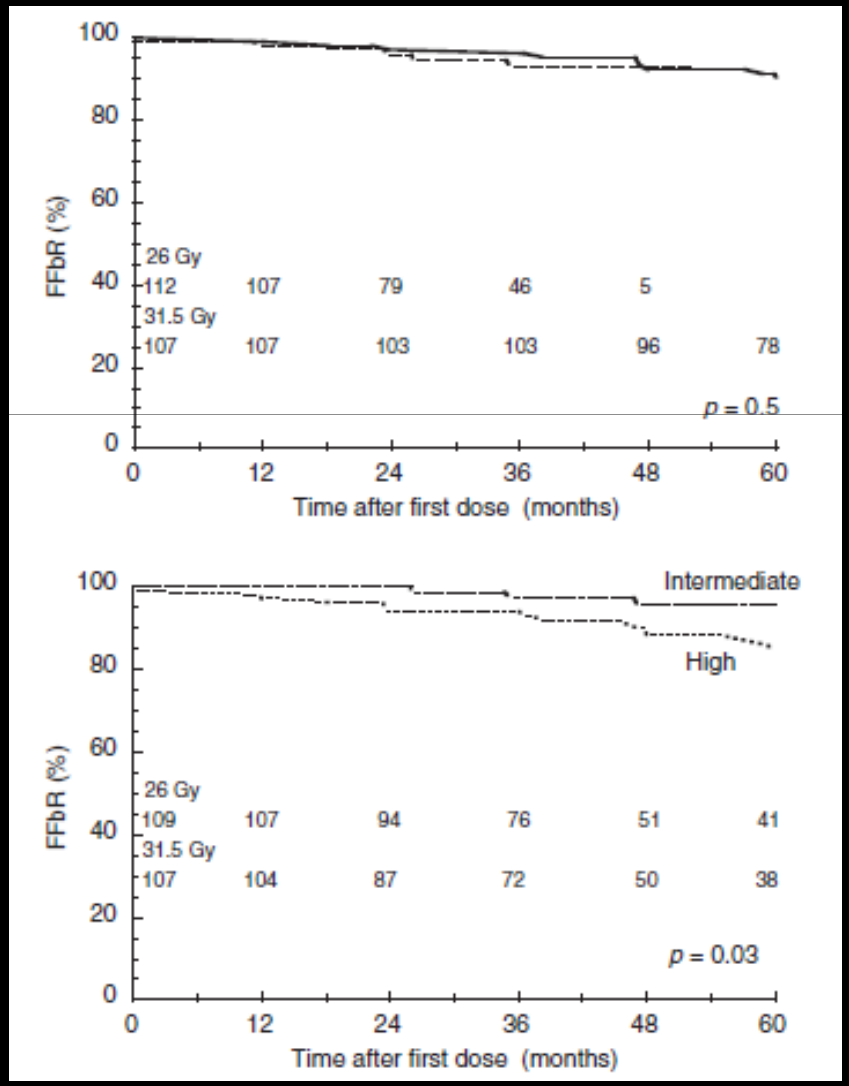
Int J Radiation Oncol Biol Phys, Vol. 85, No. 3, pp. 672–678, 2013

High-dose-rate brachytherapy with two or three fractions as monotherapy in the treatment of locally advanced prostate cancer

Peter Hoskin, Ana Rojas*, Peter Ostler, Robert Hughes, Roberto Alonzi, Gerry Lowe, Linda Bryant

Cancer Centre, Mount Vernon Hospital, Northwood, UK

Radiotherapy and Oncology 112 (2014) 63–67



High-dose-rate interstitial brachytherapy as monotherapy in one fraction and transperineal hyaluronic acid injection into the perirectal fat for the treatment of favorable stage prostate cancer: Treatment description and preliminary results

Pedro J. Prada[1,*], Isabel Jimenez[1], Herminio González-Suárez[1], José Fernández[2], Covadonga Cuervo-Arango[1], Lucia Mendez[1]

Brachytherapy 11 (2012) 105–110

40 patients: 19Gy
Low risk : 29
Inter risk: 11

32 month bRFS

Low risk: 100%
Inter risk: 88%

Toxicity	Grade	Pretreatment *n* (%)	1 wk[a] *n* (%)	3 mo[a] *n* (%)	6 mo[a] *n* (%)	Last toxicity[b] *n* (%)
Urinary tract pain (dysuria)	0	40 (100)	14 (35)	37 (92.5)	38 (95)	38 (95)
	1	0 (0.0)	26 (65)	3 (7.5)	2 (2)	2 (2)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urinary tract obstruction	0	10 (25)	9 (22.5)	24 (60)	29 (72.5)	29 (72.5)
	1	30 (75)	31 (77.5)	16 (40)	18 (27.5)	18 (27.5)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Incontinence	0	40 (100)	40 (100)	40 (100)	40 (100)	40 (100)
	1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Frequency/urgency	0	28 (70)	27 (67.5)	29 (72.5)	34 (85)	37 (92.5)
	1	12 (30)	13 (32.5)	11 (27.5)	6 (15)	3 (7.5)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Retention	0	40 (100)	39 (97.5)	40 (100)	40 (100)	40 (100)
	1	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

No Gi toxicity
Sexual preservation: 89%

HDR implant: biological advantage: 2Gy EQD

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam 74Gy/37f	78	78	78
• I125 seeds 145Gy	70	70	70
• HDR mono 36Gy/4f	108	81.8	57.0
31.5Gy/3f	108	80.2	53.8
26Gy/2f	108	78.0	49.8

HDR BOOST with EBRT

- Optimal means of dose escalation for intermediate/high risk patients
- Dose escalation results in better PSA RFS

- Acute toxicity equivalent or less than external beam
- Late toxicity equivalent to external beam

HDR Monotherapy

- HDR monotherapy is feasible using 2 to 4 fractions ……? 1 dose
- Acute toxicity is limited to transient urinary disturbance, returning to baseline at 12 weeks
- Biochemical results for advanced disease are encouraging.
- ?Further dose escalation is possible or necessary

Florence, March 13-16 2015

ESTRO School

Modern Brachytherapy Techniques

WWW.ESTRO.ORG/SCHOOL

Use of Dose Volume Histograms in Brachytherapy

ESTRO Teaching Course

Florence, 2016

Dimos Baltas

E-mail: dimos.baltas@uniklinik-freiburg.de

ESTRO School

Topics

- Introduction on Dose Optimization in Brachytherapy
- Forward Planning & Techniques
- Inverse Optimization and Planning
- **Dose Evaluation**
- Quality Parameters and Indices

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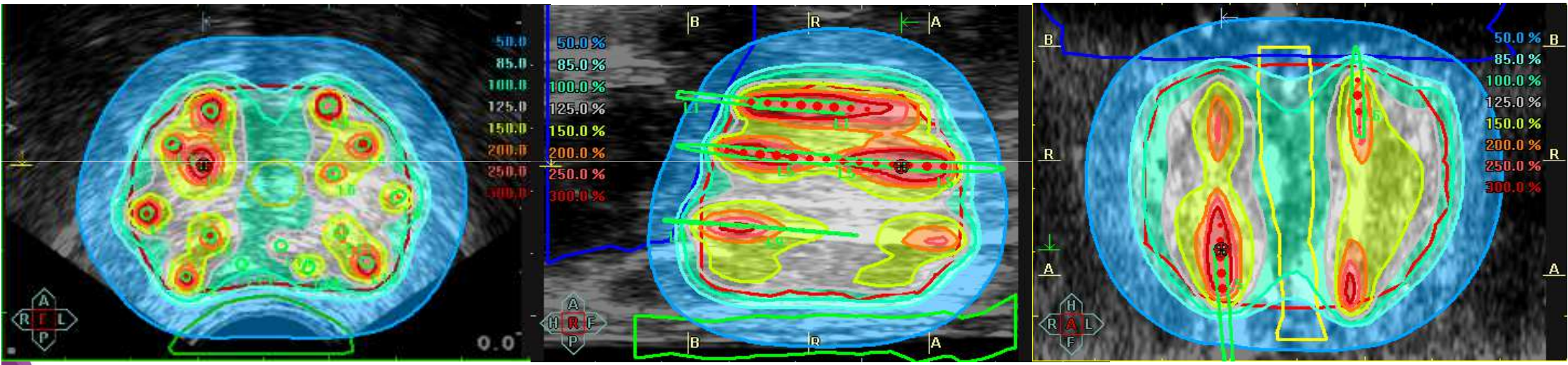
Dose Evaluation

- Visual Inspection of 2D and 3D Dose Distributions

2D Dose Distribution relative to Anatomy (Target, OARs)

Prostate



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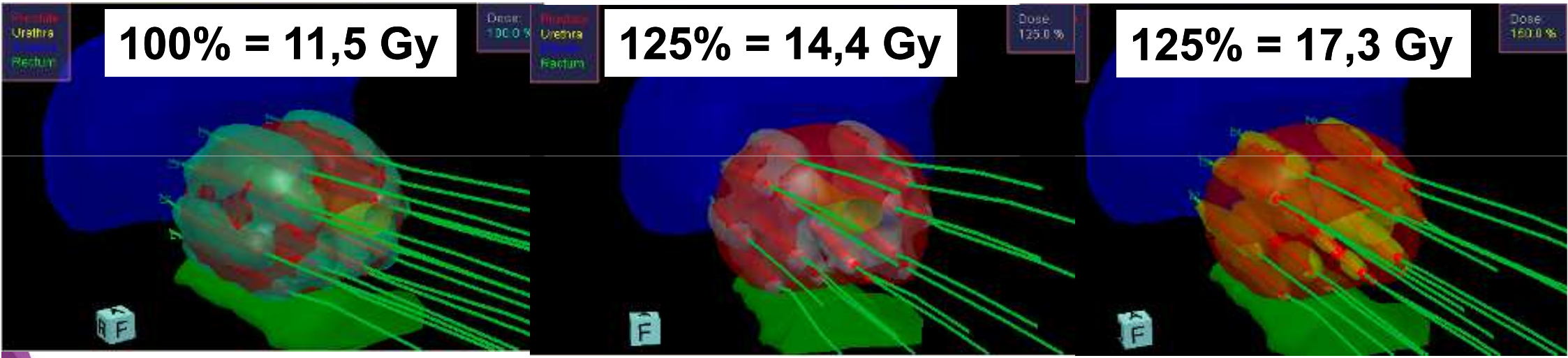
Dose Evaluation

- Visual Inspection of 2D and 3D Dose Distribution

3D Dose Distribution relative to Anatomy (Target, OARs)

Prostate



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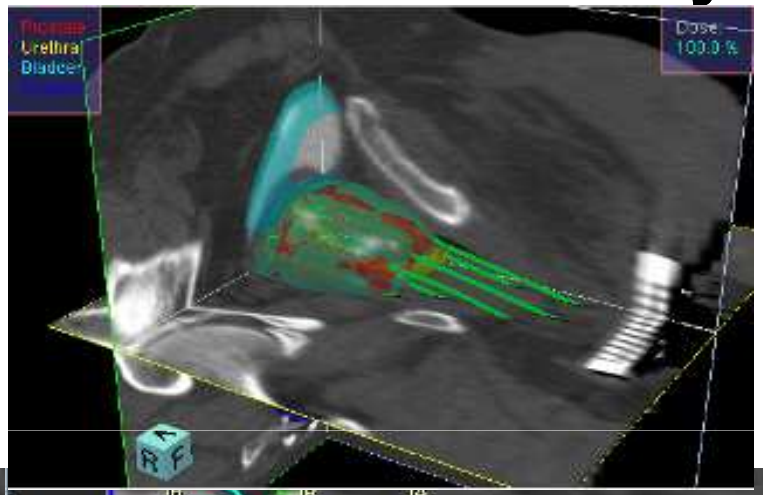
Dose Evaluation

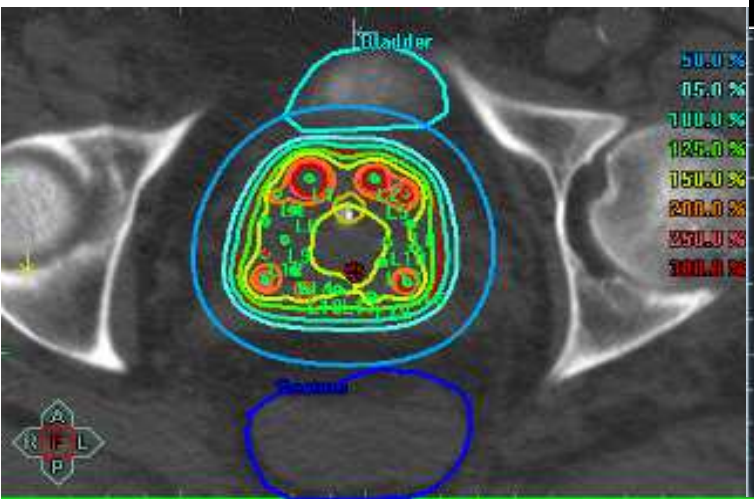
- Visual Inspection of 2D and 3D Dose Distributions

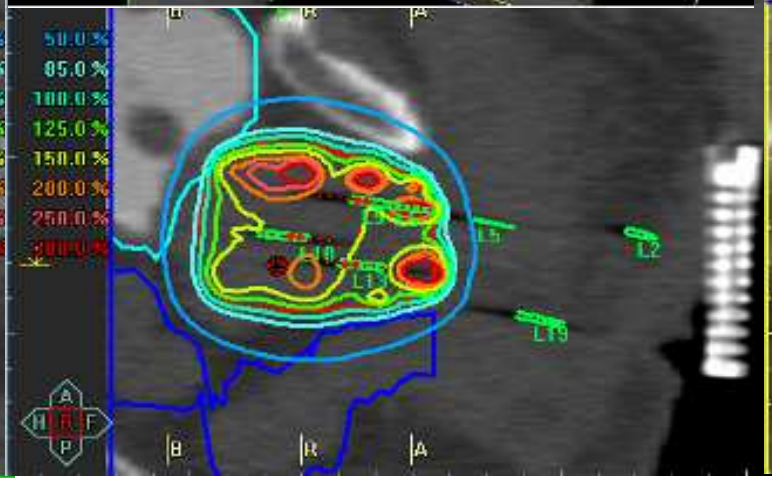
2D Dose Distribution relative to Anatomy (Target, OARs)

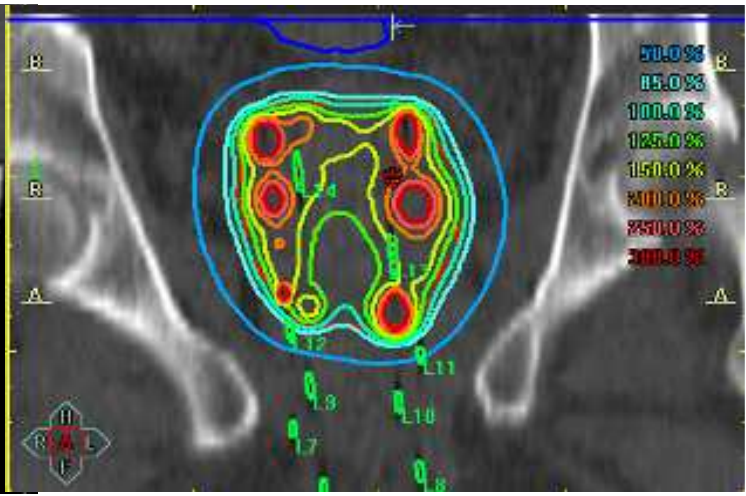


Cutting planes

Prostate



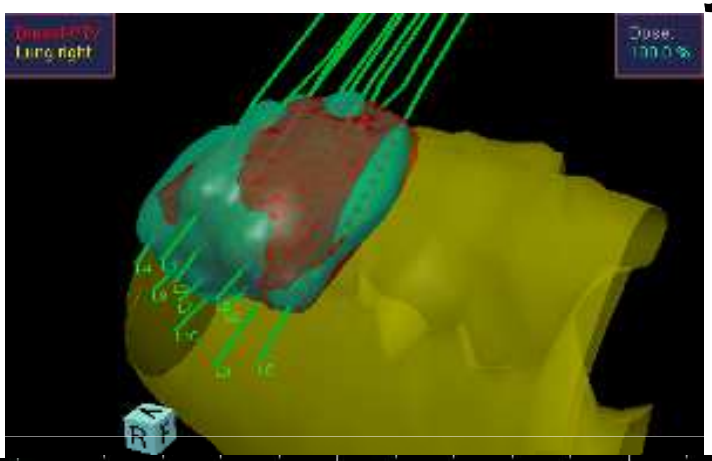




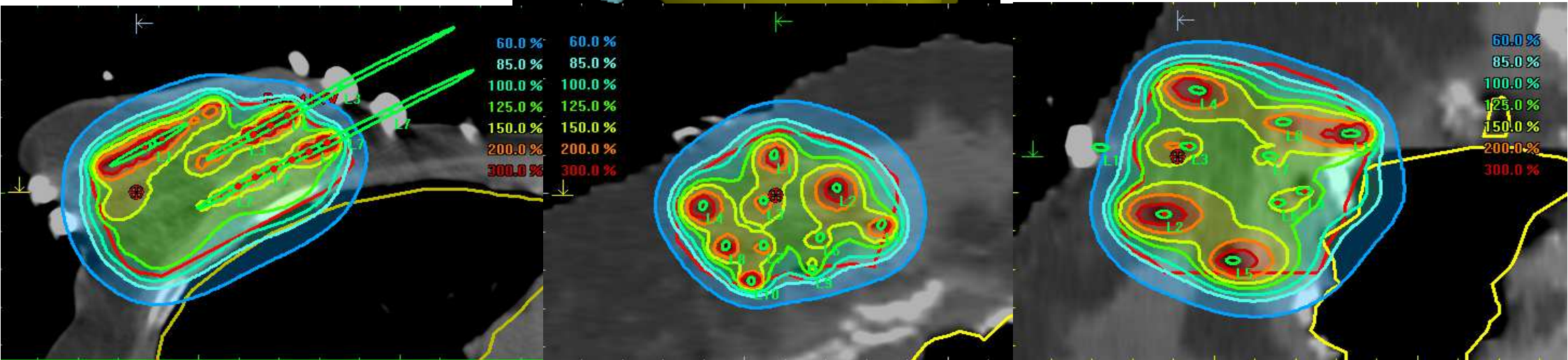
Dose Evaluation

- Visual Inspection of 2D and 3D Dose Distributions

2D Dose Distribution relative to Anatomy (Target, OARs)



Breast

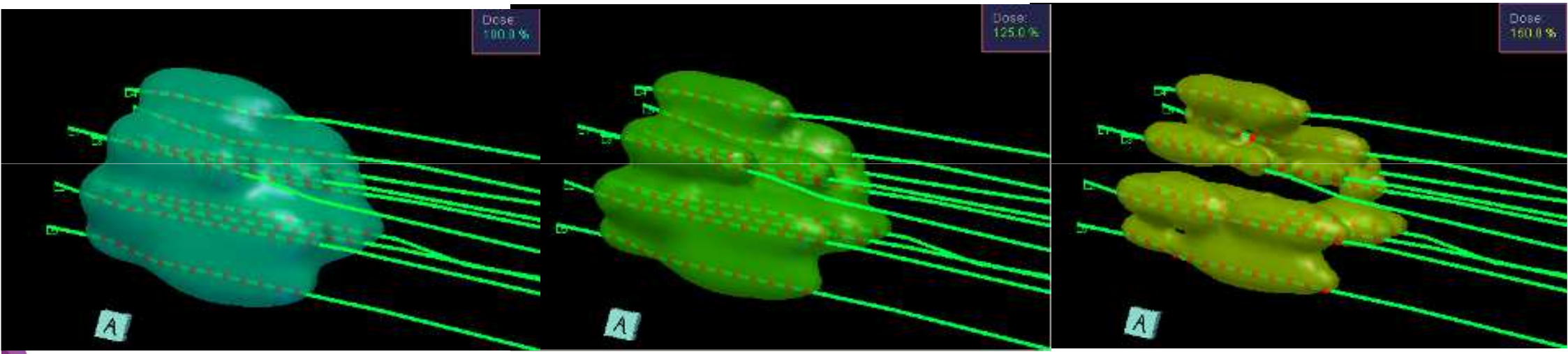


Dose Evaluation

- Visual Inspection of 2D and 3D Dose Distributions

3D Dose Distribution relative to Catheters (No Anatomy)

Breast



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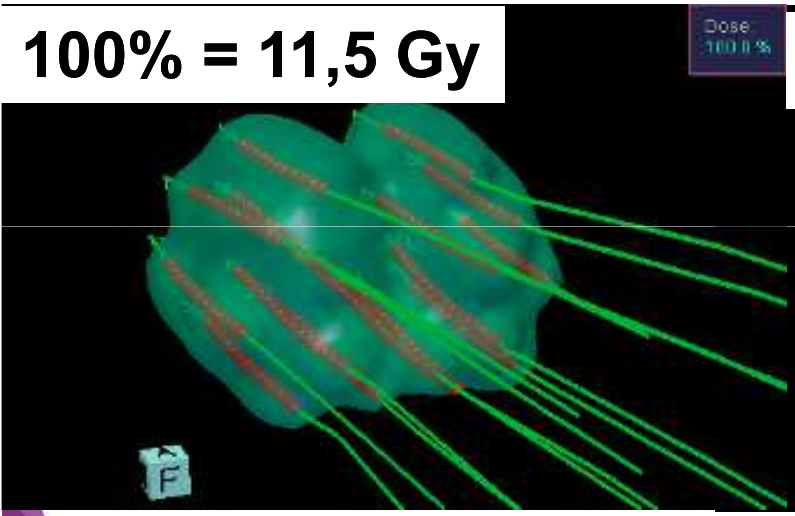
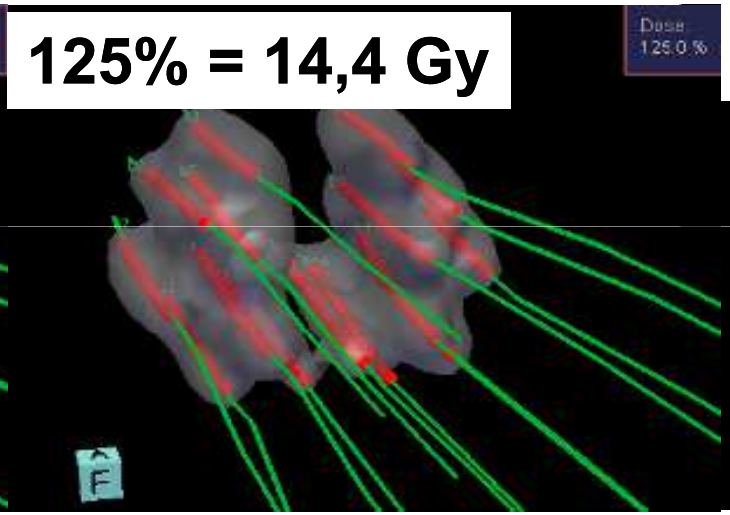
Dose Evaluation

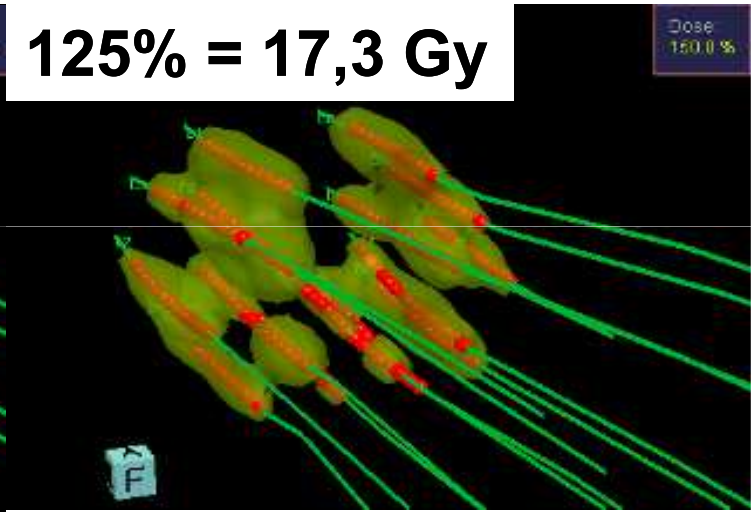
- Visual Inspection of 2D and 3D Dose Distributions

3D Dose Distribution relative to Catheters (No Anatomy)

Prostate







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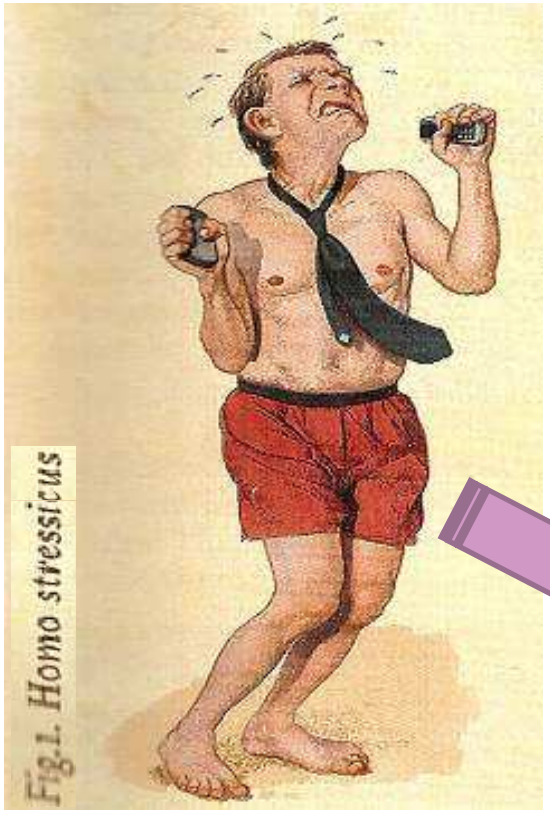
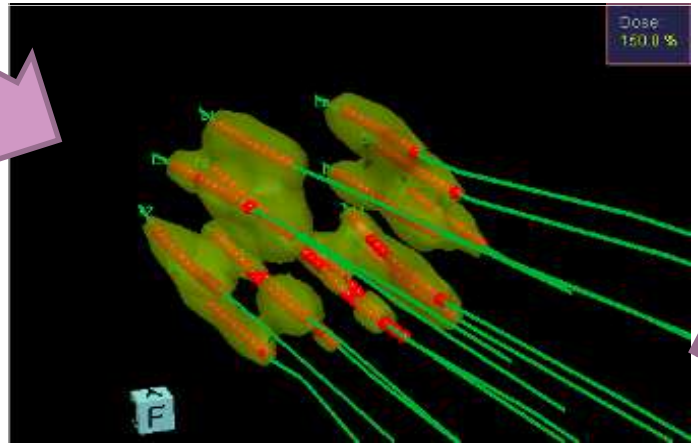


Fig.1. Homo stressicus


Dose
150.0 %

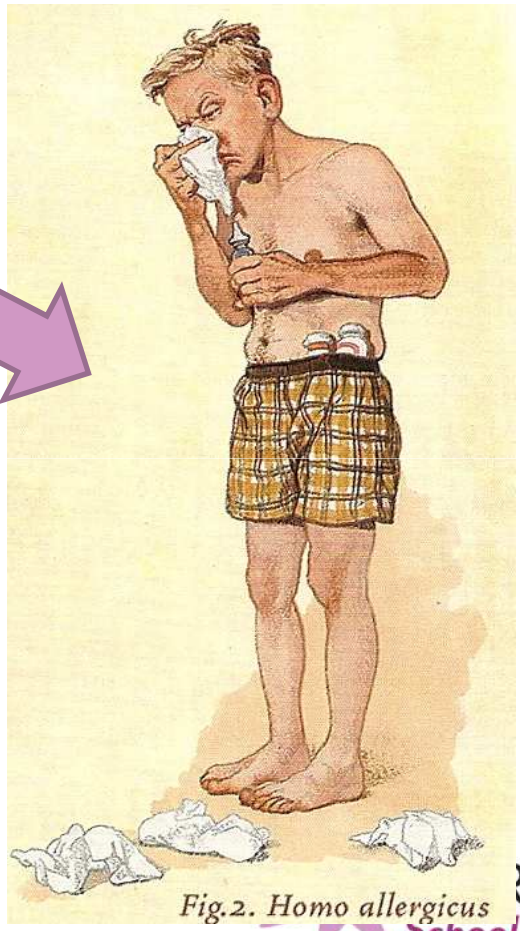


Fig.2. Homo allergicus

Dose Evaluation

- The Dose Volume Histogram (DVH)

Definition:

"A DVH of a dose distribution is represented as a graph with a series of dose intervals on its horizontal axis and on the vertical axis, for each dose interval, a volume related to that dose interval."

Dose Evaluation

- The Dose Volume Histogram (DVH)

  - For Anatomical Volumes of Interest (VOIs) (Target/PTV and OARs)

  This requires 3D Imaging (CT, MR, U/S)

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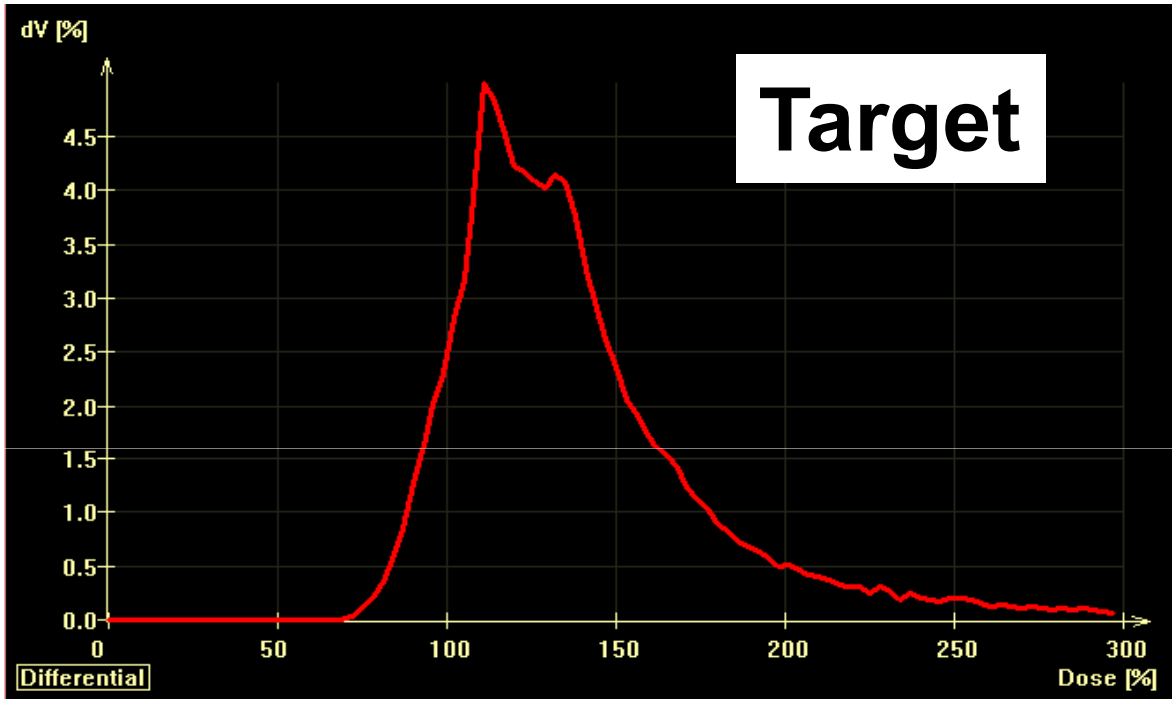
Quality Parameters and Indices

- The Dose Volume Histogram: The Differential DVH

It is the frequency distribution of dose in a VOI (Target or OAR)

For each bin e.g. [100, 103]% = [11,50 - 11,85] Gy it is the volume of the VOI (Target or OAR) in mm³ or cm³ or % of the VOI receiving a dose value within that bin



A narrow peak indicates homogeneity!

Dose Interval divided in "bins" in cGy or Gy or %

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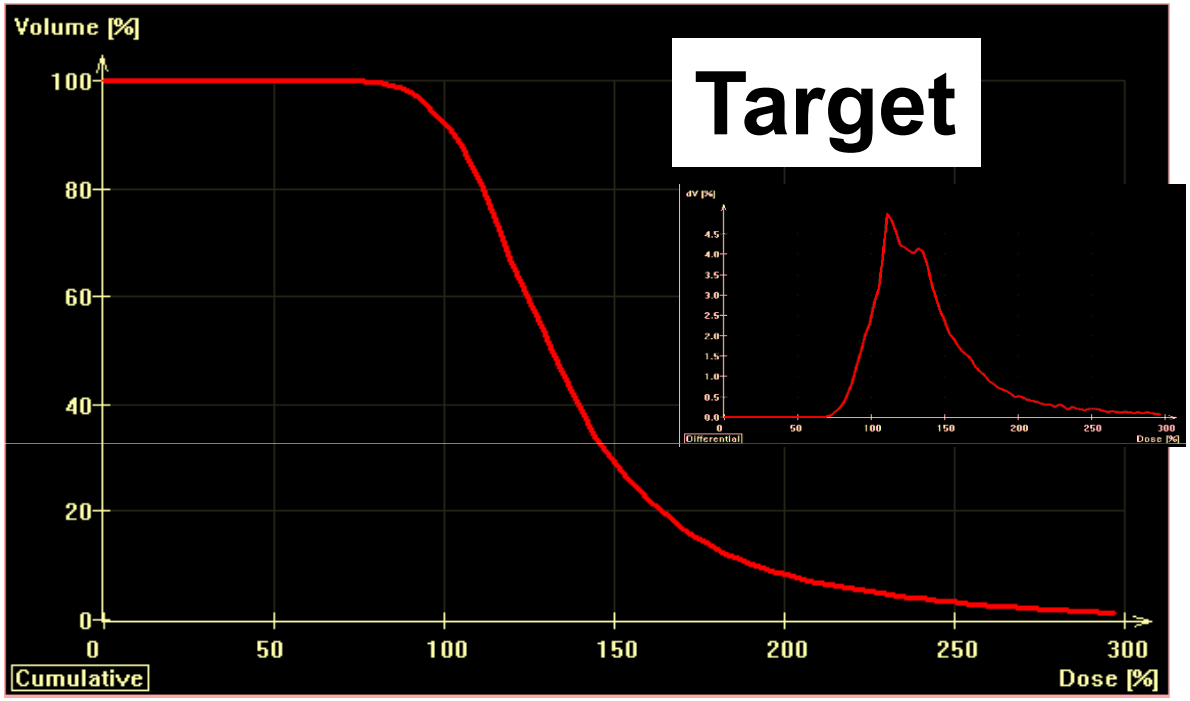
Quality Parameters and Indices

- The Dose Volume Histogram: The Cumulative DVH

It is:

1 – {the cumulative frequency distribution of dose in a VOI (Target or OAR)}

For each bin e.g. [100, 103]% = [11,50 - 11,85] Gy it is the volume of the VOI (Target or OAR) in mm³ or cm³ or % of the VOI receiving a dose value at least as high as the low bin limit, here 100%



The curve indicates how much of the volume is covered by the "required" dose value

Dose Interval divided in "bins" in cGy or Gy or %

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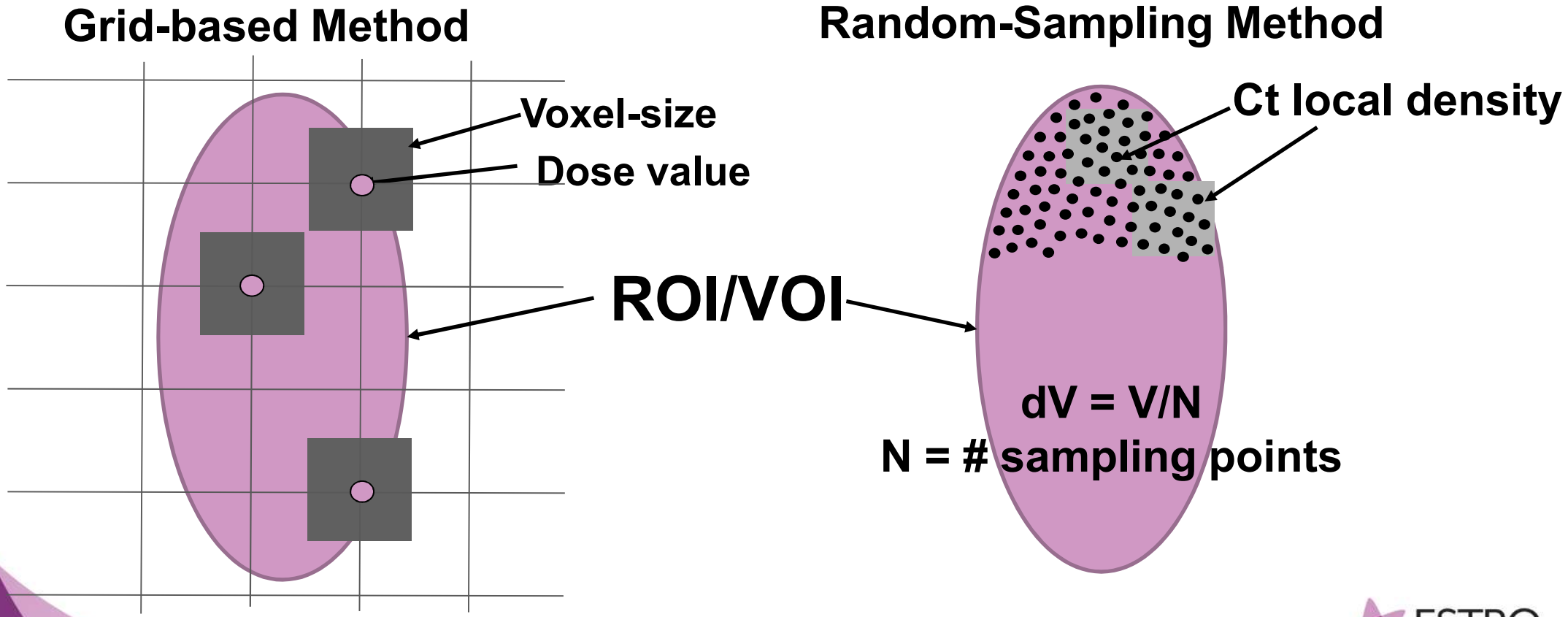
The Dose Volume Histogram:

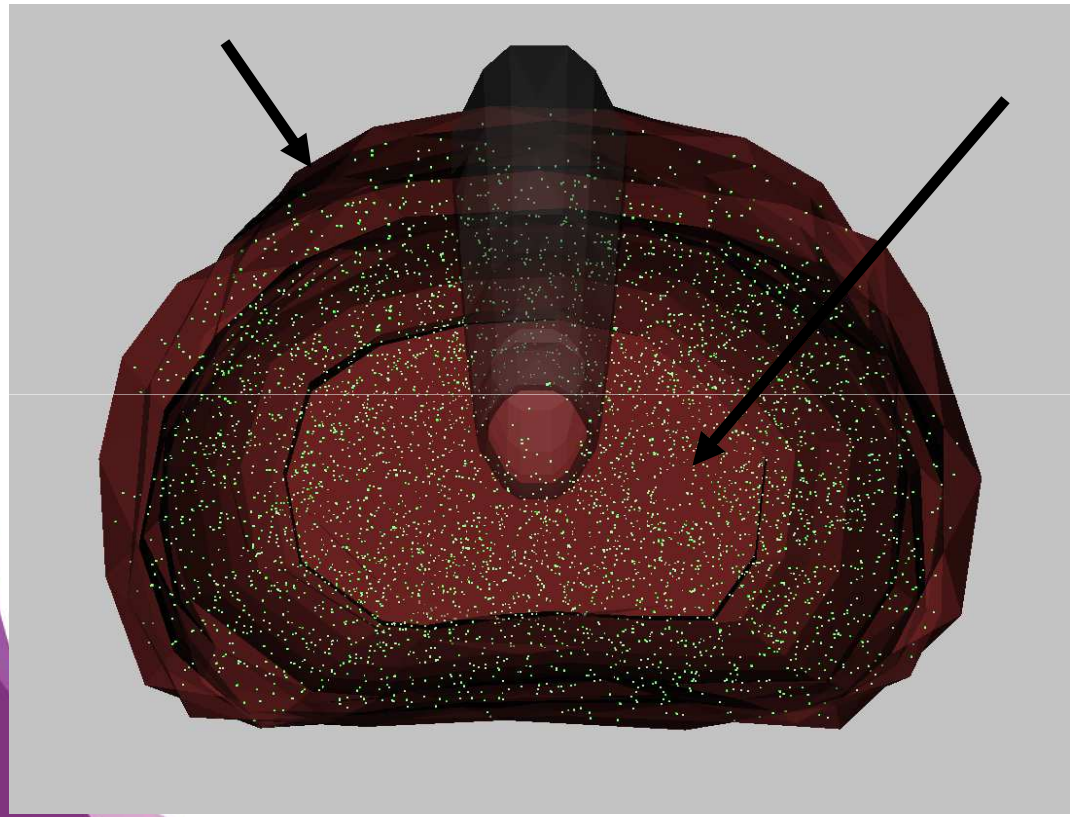
- Dependence on Methodology/Algorithm of RTP



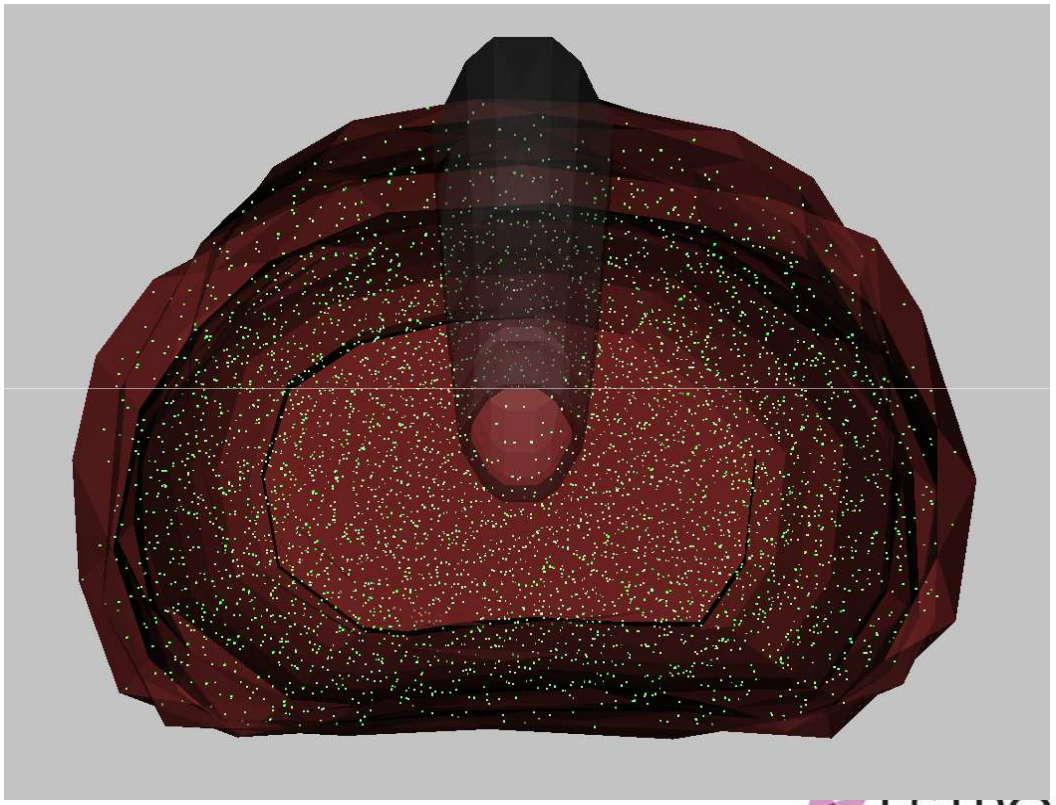
The Dose Volume Histogram:

- Dependence on Methodology/Algorithm of RTP

Random Sampling in 3D:5000 Points



Quasi-Random / Hamilton Sampling in 3D: 5000 Points

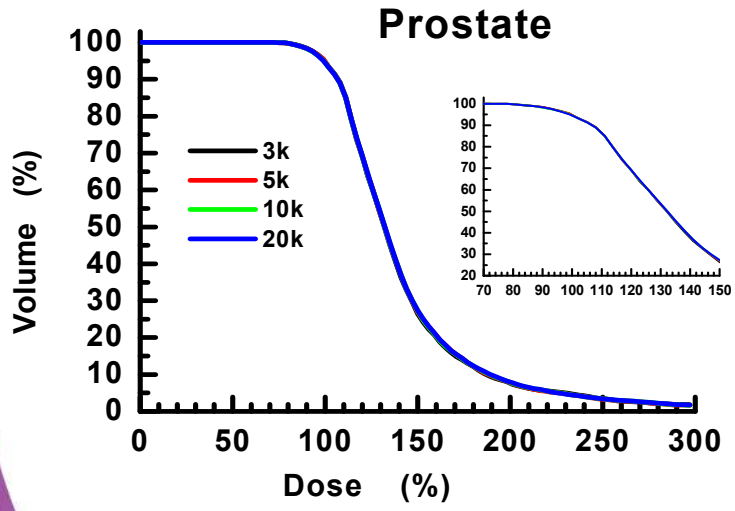


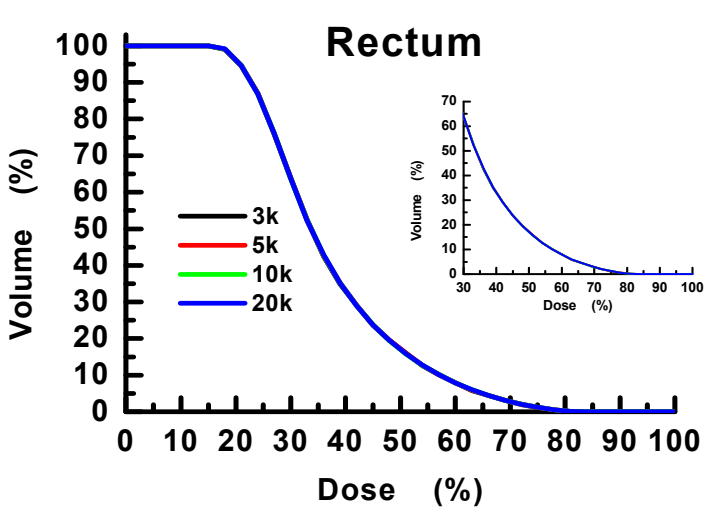
The Dose Volume Histogram:

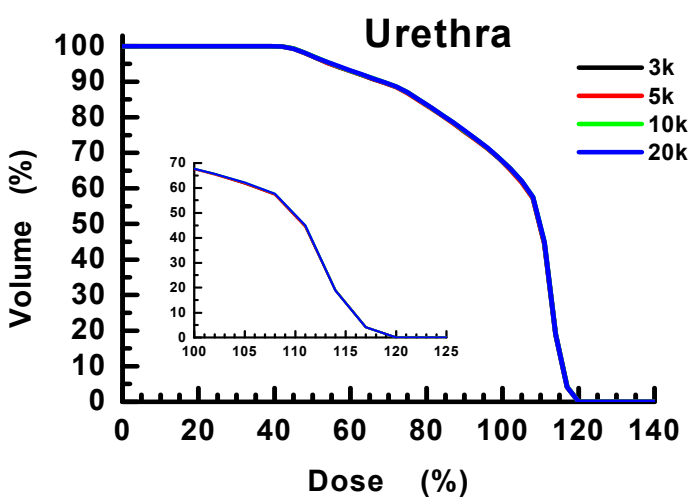
- Dependence on Methodology/Algorithm of RTP

Random Sampling in 3D:5k Points

Quasi-Random / Hamilton Sampling in 3D: 5k Points







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Dose Evaluation

- The Dose Volume Histogram (DVH)

  - For Catheter related Volume

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The Natural Dose Volume Histogram (NDVH)

Differential DVH of "ideal point source"

The values of the differential DVH for an ideal point source can be calculated directly because the isodose surfaces are spheres with the source as center, of which the volumes are easily calculated: $V = (4/3)\,\pi\, r^3$. For an ideal point source with $D = S / r^2$, V can be written as a function of D:

$$V = (4/3)\,\pi\, S^{3/2}\, D^{-3/2}$$

Then, analytically the differential DVH for an ideal point source with $D = S / r^2$ is given by:

$$dV / dD = -2\,\pi\, S^{3/2}\, D^{-5/2}$$

It is then clear that, as the dose decreases, dV / dD increases more than quadratically.

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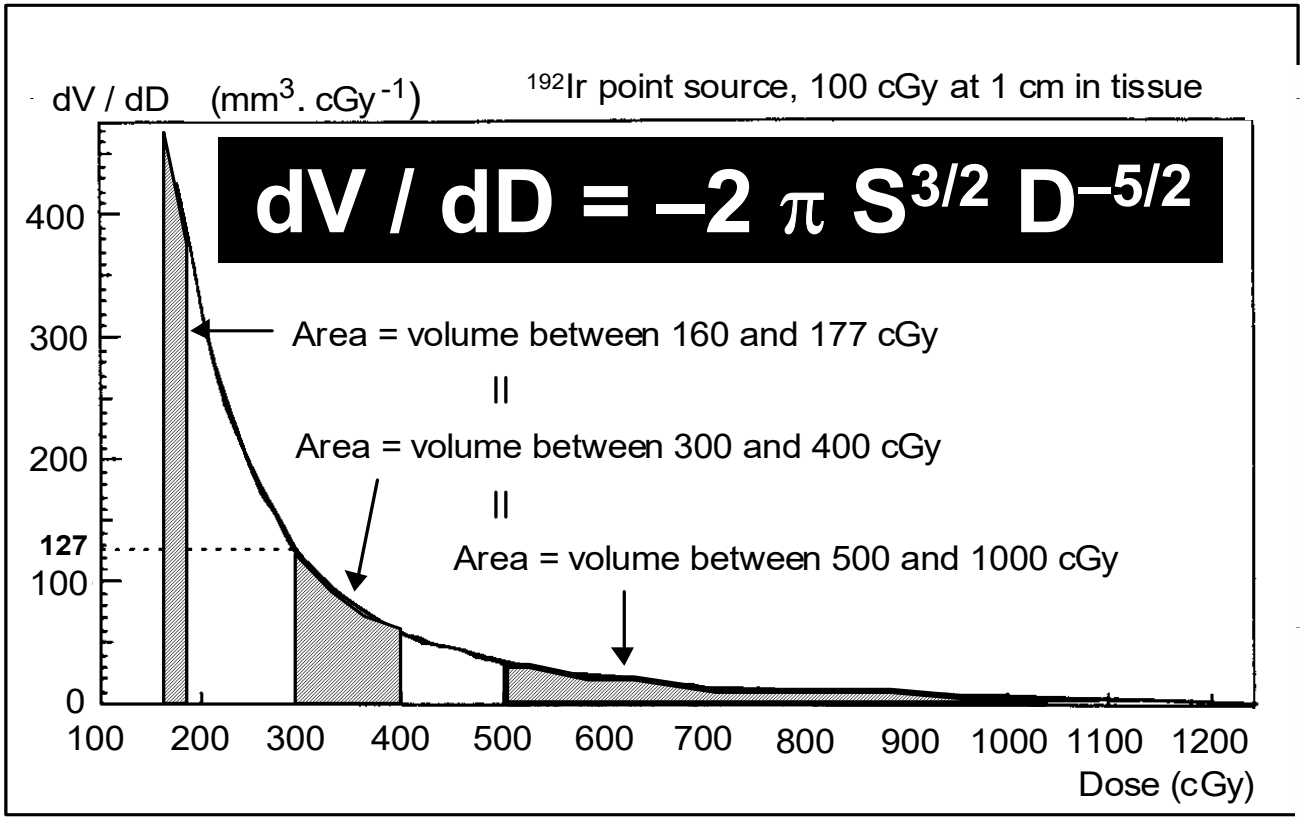
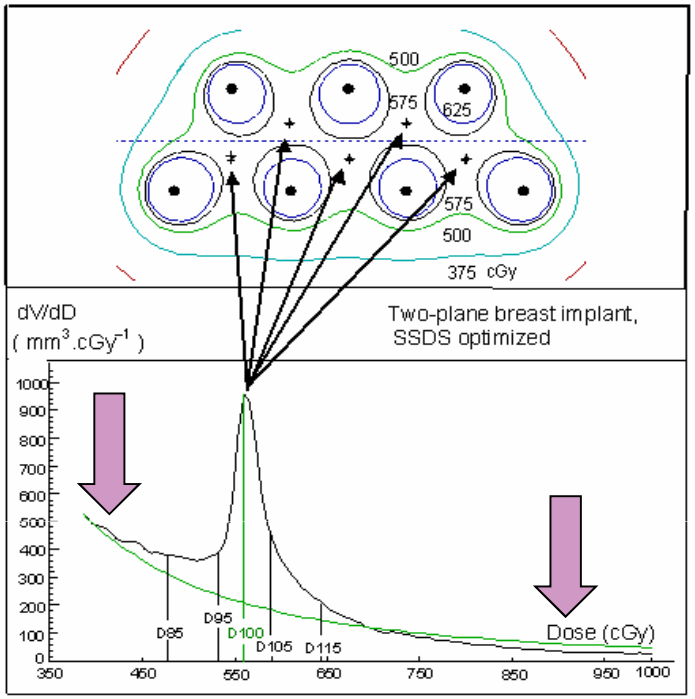
The Natural Dose Volume Histogram (NDVH)

A differential DVH of an ^{192}Ir point source





A differential DVH of a volume implant behaves *as a single point source* for very low doses and for very high doses (see figure at the right).

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The Natural Dose Volume Histogram (NDVH)

Differential DVH of "ideal point source"

The values of the differential DVH for an ideal point source can be calculated directly because the isodose surfaces are spheres with the source as center, of which the volumes are easily calculated: $V = (4/3)\,\pi\, r^3$. For an ideal point source with $D = S / r^2$, V can be written as a function of D:

$$V = (4/3)\,\pi\, S^{3/2}\, D^{-3/2}$$

But, if we define $u = D^{-3/2}$ we have:

$$dV / du = (4/3)\,\pi\, S^{3/2}$$

dV / du becomes a constant propotional to the source strength $S^{3/2}$.

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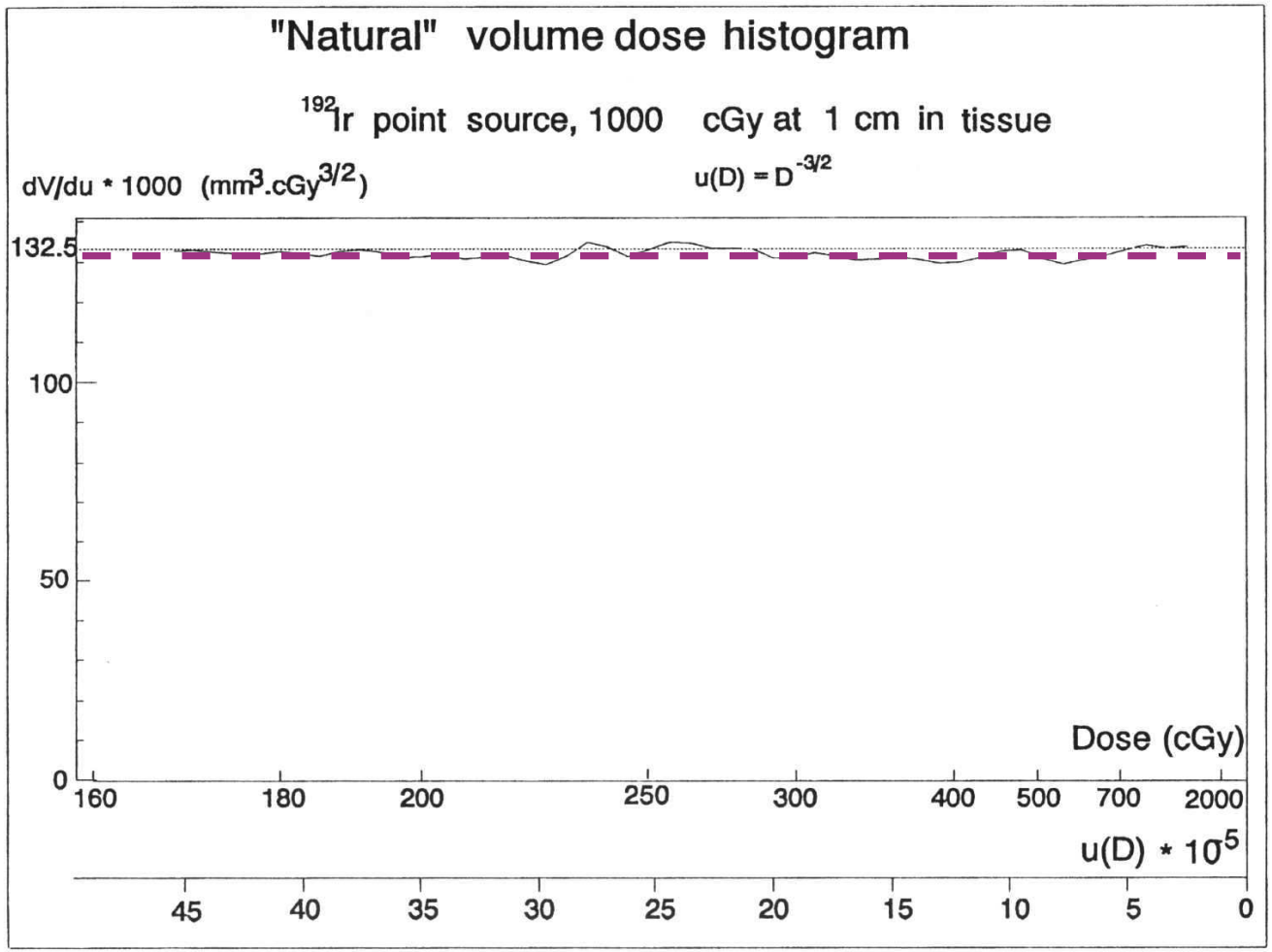
The Natural Dose Volume Histogram (NDVH)

A Natural Dose Volume Histogram

Example: for a point source



The mathematical trick **is to scale the axis in such a way that in a NDVH the curve for a point source geometry is "flat"**

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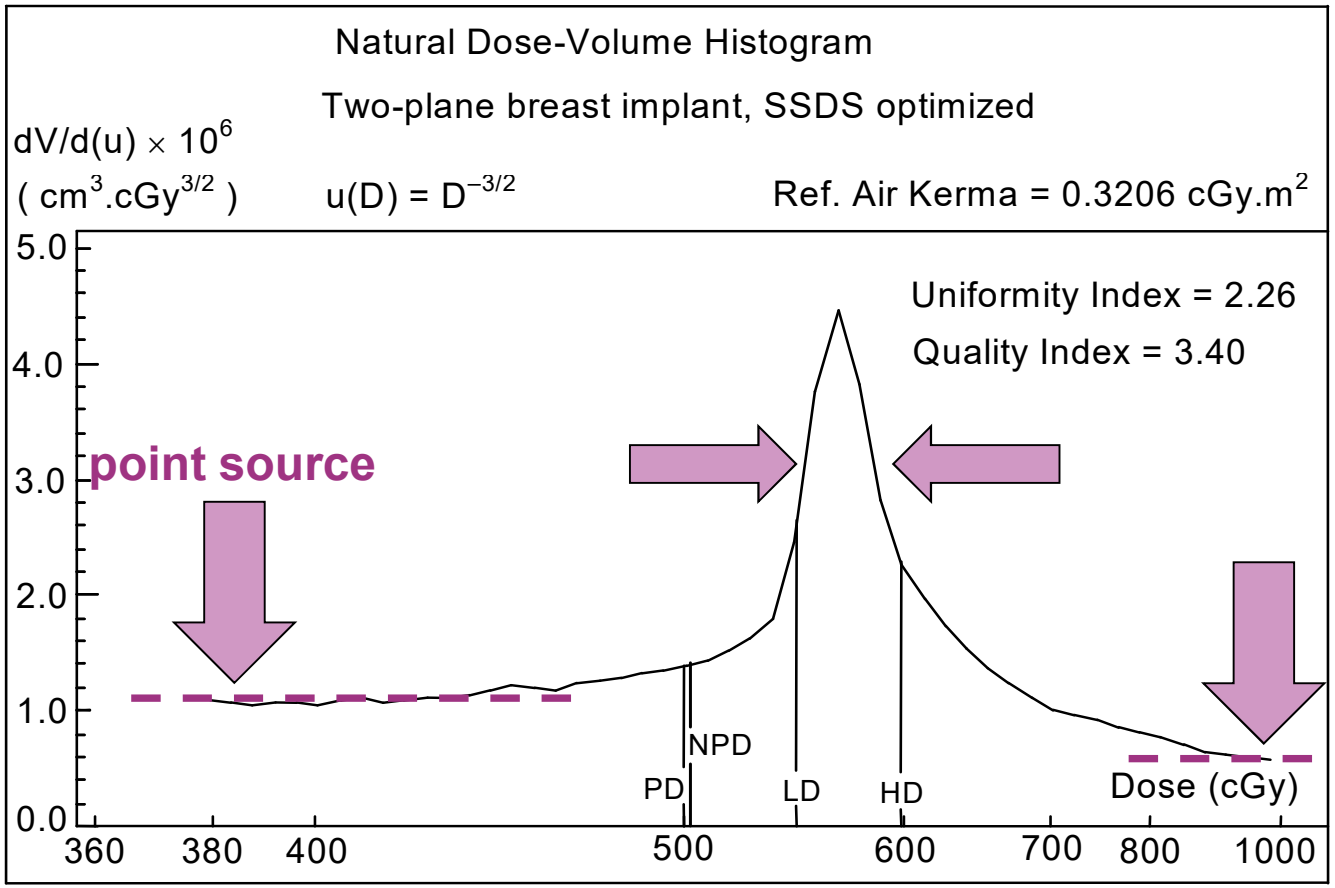
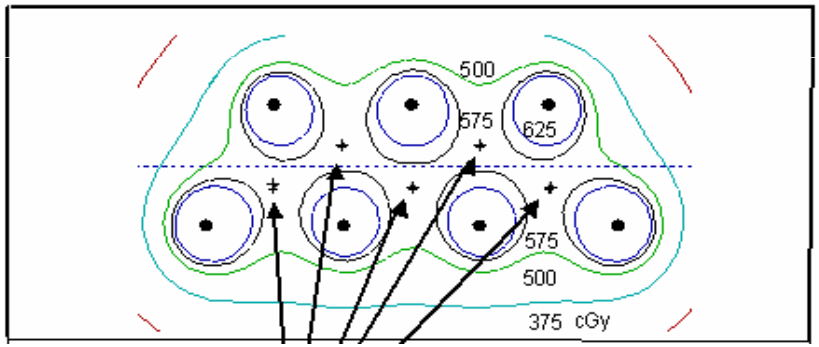
The Natural Dose Volume Histogram (NDVH)





Natural dose-volume histogram of an optimized two-plane breast implant. The prescription dose PD is defined as 90% of the mean dose in the basal dose points, i.e. 90% of the peak dose value. The prescription dose PD coincides with the natural prescription dose NPD which lies at the base of the peak at the Low Dose side.

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Topics

- Introduction on Dose Optimization in Brachytherapy
- Forward Planning & Techniques
- Inverse Optimization and Planning
- Dose Evaluation
- **Quality Parameters and Indices**

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Quality Parameters and Indices

- **Dose Volume Histogram (DVH) based (anatomy)**
  - Dose-Volume-Parameters for Target (V_{100}, D_{98}, D_{90}, ...)
  - Dose-Volume-Parameters for OARs (D_{10}, D_1, D_{2cm^3}, $D_{0.1cm^3}$ ...)
- **Conformity based**
  - Coverage Index CI for Target
  - Conformal Index COIN for Target and OARs
  - External Volume Index EI for normal tissue
- **Implant Volume based**
  - Natural Dose Volume Histogram
  - Uniformity Index UI
  - Quality Index QI
  - Natural Dose Ratio NDR

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Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)

ELSEVIER

Radiotherapy and Oncology 74 (2005) 137–148

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GEC/ESTRO-EAU recommendations on temporary brachytherapy using stepping sources for localised prostate cancer

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Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)

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GEC/ESTRO recommendations

GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: An update

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ABSTRACT

Background: HDR afterloading brachytherapy (HDRBT) for prostate cancer is now established as an effective technique to achieve dose escalation in the radical treatment of localized prostate cancer. The previous guidelines published in 2005 from GEC ESTRO and EAU have been updated to reflect the current and emerging roles for HDRBT in prostate cancer. *Patients and method:* The indications for HDRBT in dose escalation schedules with external beam are wide ranging with all patients having localized disease eligible for this technique. Exclusion criteria are few encompassing patients medically unfit for the procedure and those with significant urinary outflow symptoms. *Results:* Recommendations for patient selection, treatment facility, implant technique, dose prescription and dosimetry reporting are given. *Conclusions:* HDRBT in prostate cancer can be practiced effectively and safely within the context of these guidelines with the main indication being for dose escalation with external beam. HDRBT used alone is currently under evaluation and its role in focal treatment and recurrence will be areas of future development.

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- Dose Volume Histogram (DVH) based (anatomy)

Table 3
Reporting parameters for HDR prostate brachytherapy.

1. External beam dose
2. Implant technique; number of catheters;
3. Total reference air kerma (TRAK). Total source exposure
4. Pattern of dwell times for each applicator
5. CTV: D90, V100, V150, V200
6. PTV (if defined): D90, V100, V150, V200
7. Organs at risk:
   a. Rectum: D2 cc, D0.1 cc
   b. Urethra: D0.1 cc, D10, D30

Other volumes which may be recorded but are not considered mandatory: GTV, subvolumes within CTV/PTV and Penile bulb.

- planned vs. aimed D_{90}
- Conformal Index COIN
- Quality parameters – DNR …

Implant quality

Through optimisation, a balance will be reached between dose–volume constraints for OARs and for the target. The D90 will then become the prescription dose, individualised for each patient. The D90 should be higher than the planning aim, i.e. >100%. In addition, the PTV V100 should be at least 95% of the planning aim dose.

Various conformity indices have been described which evaluate the PTV coverage balanced by the OAR doses such as the COIN [48]. Within the implant the dose non-homogeneity ratio (DNR) should be documented from the ratio V150/V100.

Quality Parameters and Indices

- **Dose Volume Histogram (DVH) based (anatomy)**

Radiotherapy and Oncology 83 (2007) 3–10
www.thegreenjournal.com

Guidelines prostate brachytherapy

Tumour and target volumes in permanent prostate brachytherapy: A supplement to the ESTRO/EAU/EORTC recommendations on prostate brachytherapy

Carl Salembier[a], Pablo Lavagnini[b], Philippe Nickers[c], Paola Mangili[d], Alex Rijnders[a], Alfredo Polo[e], Jack Venselaar[f], Peter Hoskin[g,*], on behalf of the PROBATE group of GEC ESTRO

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Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)

Clinical target volume (equals planning target volume). Physical parameters correlating with a good pre-implantation dosimetry:

- The V_{100} (the percentage of the CTV that receives the prescribed dose) must be at least 95% ($V_{100} \geqslant 95\%$ of CTV).
- Therefore, the D_{90} (the dose that covers 90% volume of the CTV) will be larger than the prescription dose ($D_{90} > 100\%$ of prescription dose).
- The V_{150} (the percentage of the CTV that receives 150% of the prescription dose), should be equal to or less than 50% ($V_{150} \leqslant 50\%$ of CTV).

Table 2
Dosimetry parameters for organs at risk

Preplan	Postplan
Rectum	
D_{2cc}	D_{2cc}
$D_{0.1cc}(\sim D_{max})$	V_{100}
	V_{150}
Urethra	
D_{10}	D_{10}
D_{30}	D_{30}
	D_5

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Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)

Radiotherapy and Oncology 78 (2006) 67-77
www.thegreenjournal.com

ESTRO project

Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

Richard Pötter[a,*], Christine Haie-Meder[b], Erik Van Limbergen[c], Isabelle Barillot[d], Marisol De Brabandere[c], Johannes Dimopoulos[a], Isabelle Dumas[b], Beth Erickson[e], Stefan Lang[a], An Nulens[c], Peter Petrow[f], Jason Rownd[e], Christian Kirisits[a]

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- Dose Volume Histogram (DVH) based (anatomy)

Table 1
Recommendations for recording and reporting 3D gynaecological brachytherapy

Complete description of clinical situation including
anatomy and pathology and imaging examination
dimensions and volume of GTV at diagnosis and at time of brachytherapy
dimensions and volumes of HR CTV and IR CTV, respectively
Complete description of 3D sectional imaging technique and contouring procedure
Complete description of brachytherapy technique
radionuclide; source type (wire, stepping source); source strength; applicator type; type of afterloading (manual or remote); description of additional interstitial needles if any
Treatment prescription and treatment planning
applicator reconstruction technique, standard loading pattern, dose specification method; optimisation method, if applied
Prescribed dose
Total Reference Air Kerma (TRAK)
Dose at point A (right, left, mean)
D100, D90 for GTV and HR CTV and IR CTV, respectively
Dose to bladder and rectum for ICRU reference points
$D_{0.1cc}$, D_{1cc}, D_{2cc} for organs at risk (e.g. rectum, sigmoid, bladder) (vagina[a])
D_{5cc}, D_{10cc} for organs at risk if contouring of organ walls is performed
Complete description of time-dose pattern: physical and biologically weighted doses ($\alpha/\beta = 10$ Gy for GTV and CTV; $\alpha/\beta = 3$ Gy for OAR; $T_{1/2} = 1.5$ h for GTV, CTV and OAR)

[a] For vagina dose volume parameters still need to be defined.

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Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)

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0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.01.043

CLINICAL INVESTIGATION **Cervix**

THREE-DIMENSIONAL IMAGING IN GYNECOLOGIC BRACHYTHERAPY: A SURVEY OF THE AMERICAN BRACHYTHERAPY SOCIETY

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Purpose: To determine current practice patterns with regard to three-dimensional (3D) imaging for gynecologic brachytherapy among American Brachytherapy Society (ABS) members.
Methods and Materials: Registered physician members of the ABS received a 19-item survey by e-mail in August 2007. This report excludes physicians not performing brachytherapy for cervical cancer.
Results: Of the 256 surveys sent, we report results for 133 respondents who perform one or more implantations per year for locally advanced cervical cancer. Ultrasound aids 56% of physicians with applicator insertion. After insertion, 70% of physicians routinely obtain a computed tomography (CT) scan. The majority (55%) use CT rather than X-ray films (43%) or magnetic resonance imaging (MRI; 2%) for dose specification to the cervix. However, 76% prescribe to Point A alone instead of using a 3D-derived tumor volume (14%), both Point A and tumor volume (7%), or mg/h (3%). Those using 3D imaging routinely contour the bladder and rectum (94%), sigmoid (45%), small bowel (38%), and/or urethra (8%) and calculate normal tissue dose–volume histogram (DVH) analysis parameters including the D2cc (49%), D1cc (36%), D0.1cc (19%), and/or D5cc (19%). Respondents most commonly modify the treatment plan based on International Commission on Radiation Units bladder and/or rectal point dose values (53%) compared with DVH values (45%) or both (2%).
Conclusions: More ABS physician members use CT postimplantation imaging than plain films for visualizing the gynecologic brachytherapy apparatus. However, the majority prescribe to Point A rather than using 3D image based dosimetry. Use of 3D image–based treatment planning for gynecologic brachytherapy has the potential for significant growth in the United States. © 2010 Elsevier Inc.

3D image based brachytherapy, Cervical cancer, Survey.

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Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)
  - Dose-Volume-Parameters for Target (V_{100}, D_{90}, ...)

D_{100}: the dose that covers 100% of the target volume, what is equivalent the MTD proposed by ICRU report 58 (ICRU 1998); for the case we consider CTV.

D_{98}: the dose that covers 98% of the target volume.

D_{90}: the dose that covers 90% of the target volume.

V_{100}: the percentage of the target volume that receives at least the prescribed dose, which is set to 100%.

V_{150}: the percentage of the target volume, which receives at least 150% of the prescribed dose.

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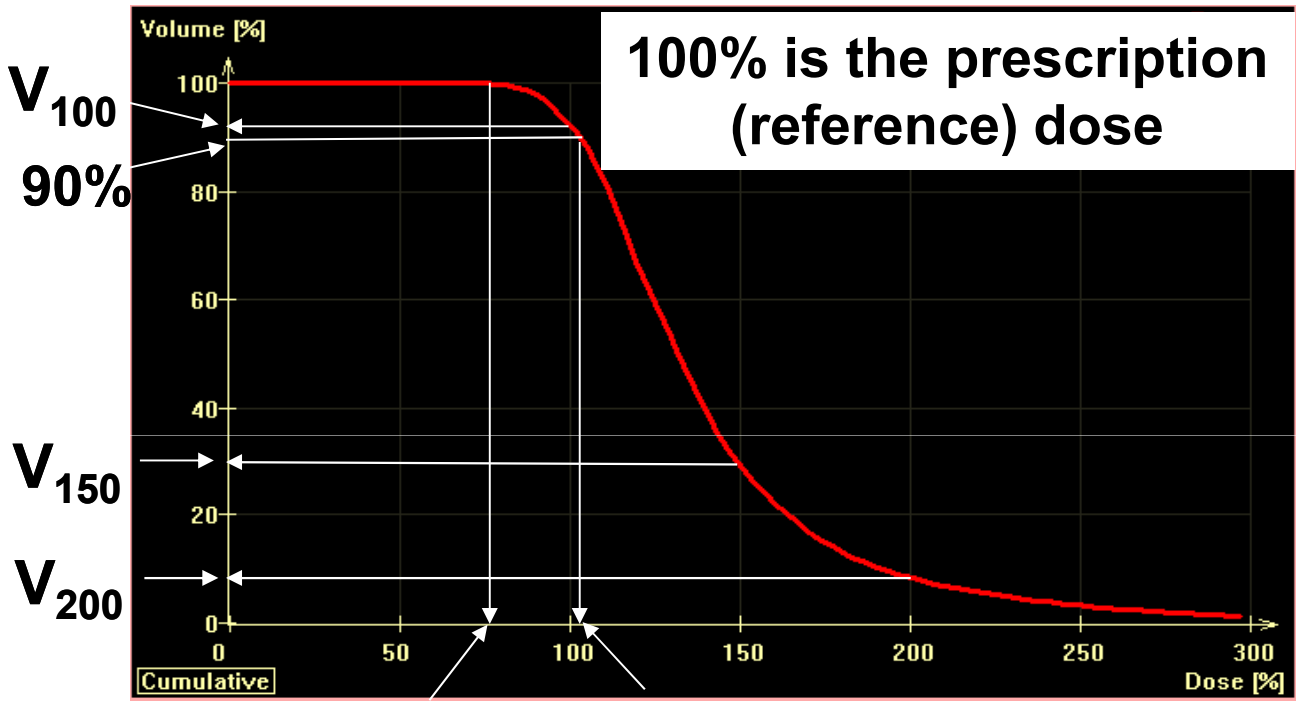
Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)
  - Dose-Volume-Parameters for Target (V_{100}, D_{98}, D_{90}, ...)

Cumulative DVH



V_{100}

90%

V_{150}

V_{200}

D_{100} or D_{min}

D_{90}

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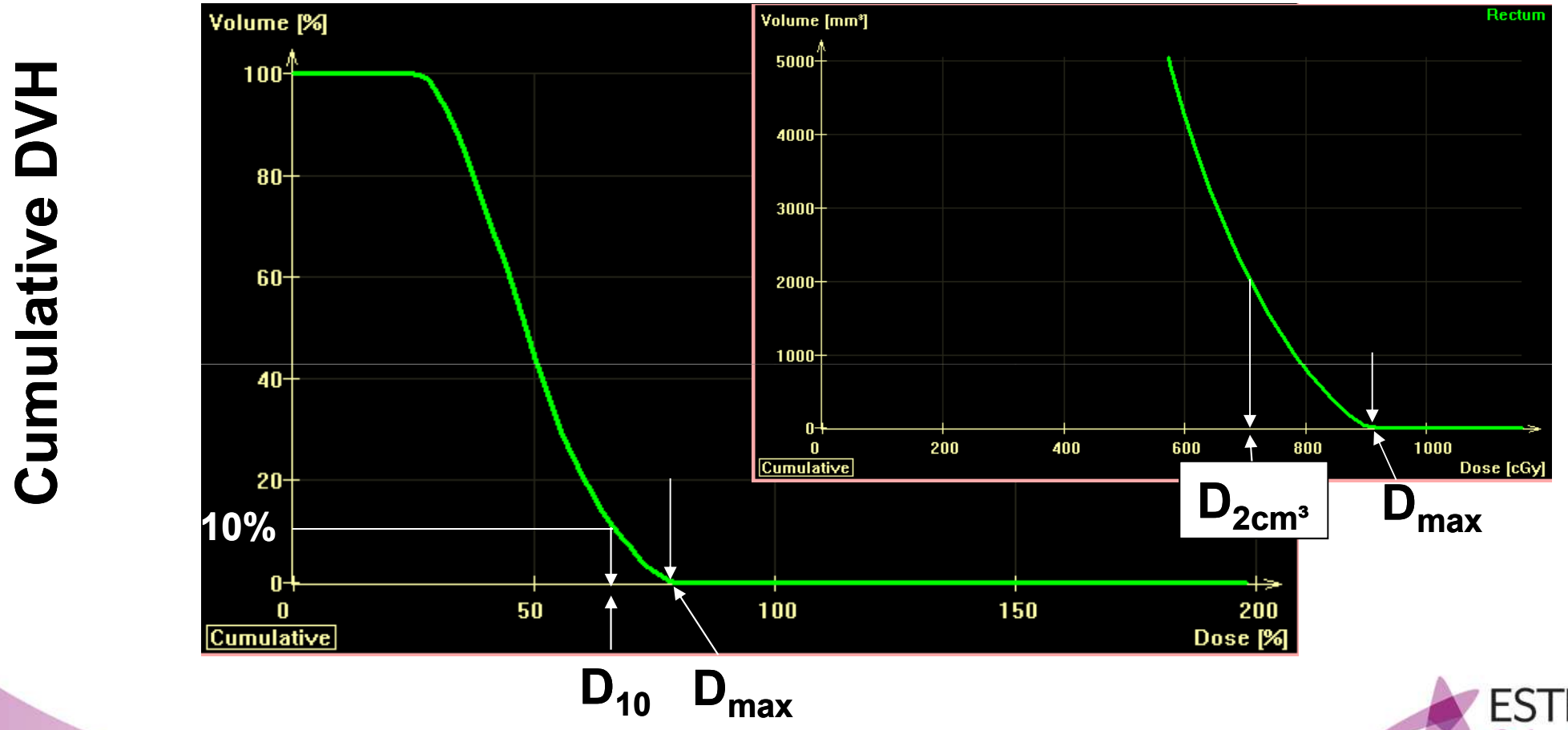
100% is the prescription
(reference) dose

Quality Parameters and Indices

- Dose Volume Histogram (DVH) based (anatomy)
  - Dose-Volume-Parameters for OARs (D_{10}, D_{2cm^3}, ...)



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The problematic Minimum Target Dose or Minimum Peripheral Dose:

In spite of the high sensitivity of the minimum dose MTD or minimum peripheral dose MPD in the planning target volume against delineation inaccuracies and the used resolution of the calculation grid or number of sample points, these values are still in the national, European, American and International Reports and Recommendations.

Due to the extended use of individual plan optimisation (prostate, Gyn, breast, ...) utilising modern inverse optimisation tools in RTPs, the dose prescription and distribution becomes individual and is now the best achievable compromise between PTV-related and OAR-related objectives. Thus we learned, that we have to distinguish between the "aimed" or "intended" prescription dose to the PTV (protocol) and the individually realised – "planned" prescription dose.

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“Aimed” versus “Planned”:

For the example of prostate and considering the published papers and recommendations, the majority of these refer as “planned” doses, individual prescription, the achieved D_{90} values for the PTV.

Those values are more stable regarding delineation inaccuracies and resolution of the calculation grid or number of sample points than the minimum dose values.

Thus we have in general the “aimed” D_{90} value for the PTV (institutional/study protocol value) and the “planned” D_{90} value, that is the value that is really achieved (and probably delivered) in the individual treatment planning process and becomes the individual dose prescription.

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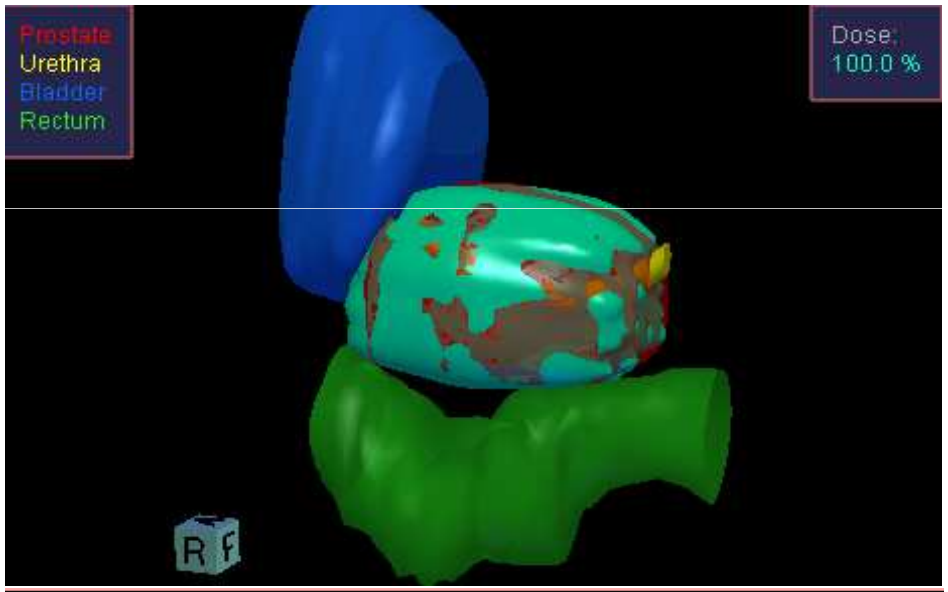
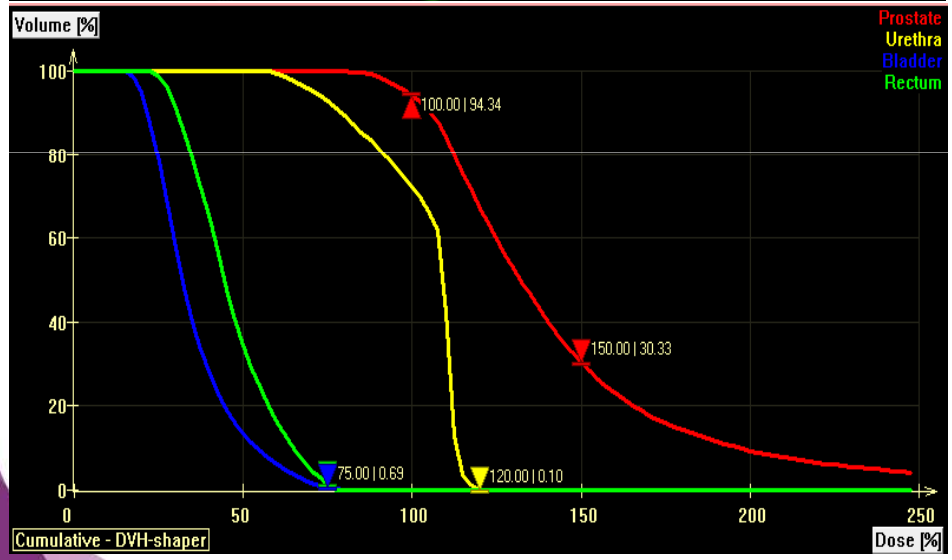
Dose Prescription: Aimed *versus* Planned

Prostate-Example



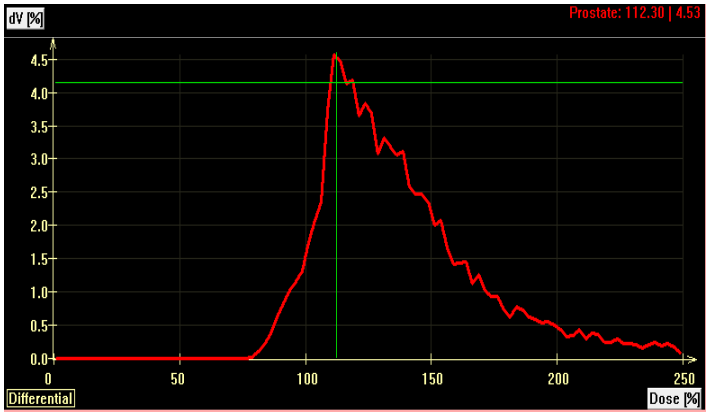


Aimed PD : 100% = 11,50Gy

D_{90} :	105,55%	=	12,14Gy
D_{95} :	98,75%	=	11,34Gy
D_{98} :	85,67%	=	9,85Gy
D_2 :	283,71%	=	32,63Gy
D_{mean}:	145,27%	=	16,71Gy
D_{50} :	123,28%	=	14,18Gy

≈ 18%
≈ 23-45%
to the aimed PD

Individually planned



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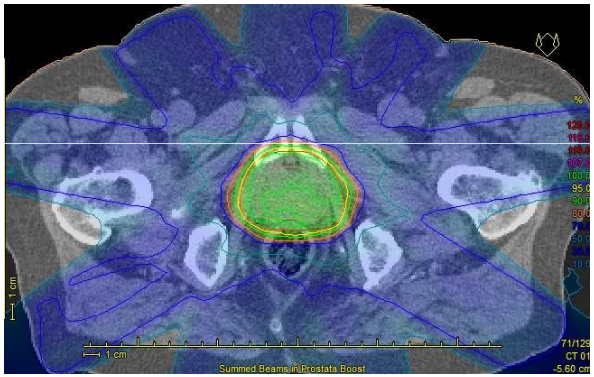
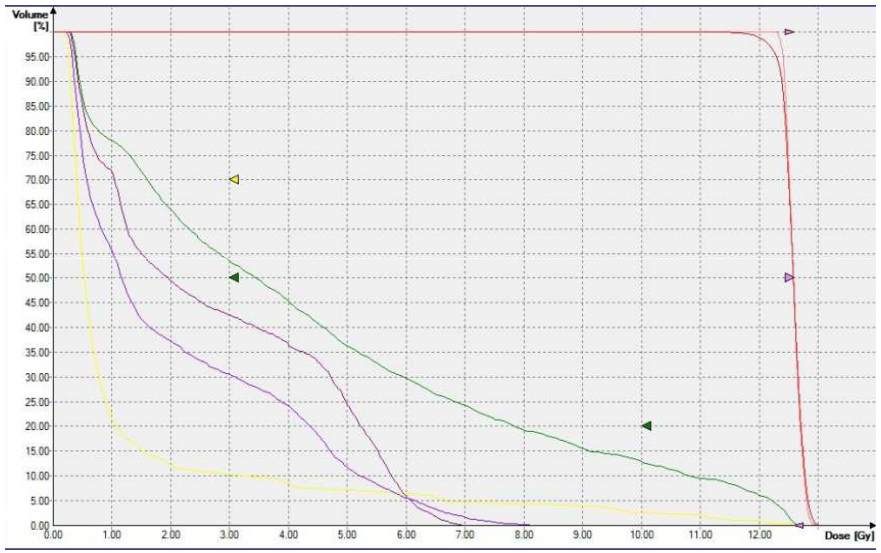
Dose Prescription: Aimed *versus* Planned

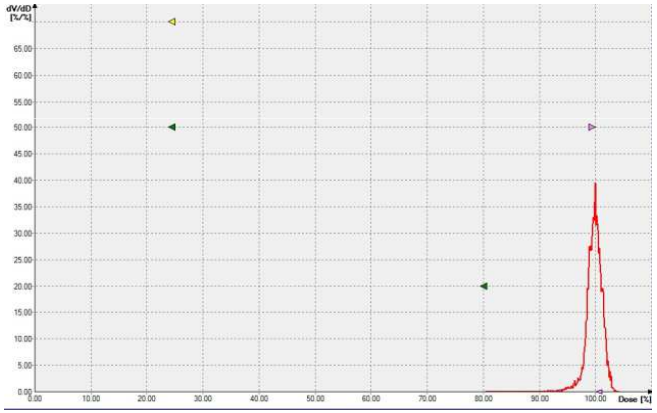
Prostate-Example





Aimed PD : 100% = 11,50Gy

D_{90} :	98,21%	=	11,29Gy
D_{95} :	97,57%	=	11,22Gy
D_{98} :	96,20%	=	11,06Gy
D_2 :	102,30%	=	11,77Gy
D_{mean}:	100,00%	=	11,50Gy
D_{50} :	100,00%	=	11,50Gy



Individually planned

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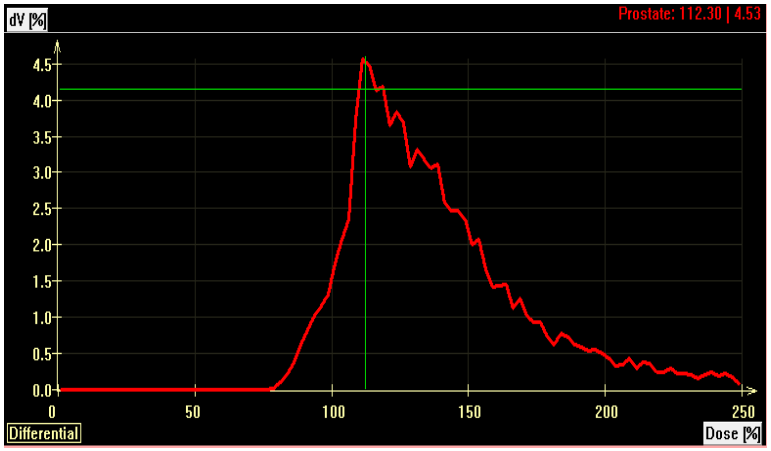
Dose Prescription: Aimed *versus* Planned

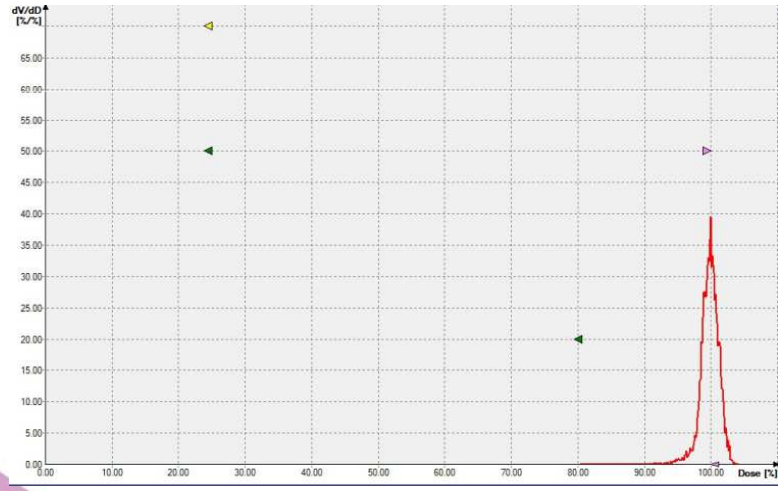
Prostate-Example

- Dose Prescription BRT vs. ERT?

BRT



ERT



Aimed PD : 100% = 11,50Gy

D_{90} :	105,55%	vs.	98,21%
D_{95} :	98,75%	vs.	97,57%
D_{98} :	85,67%	vs.	96,20%
D_2 :	283,71%	vs.	102,30%
D_{mean}:	145,27%	vs.	100,00%
D_{50} :	123,28%	vs.	100,00%

Individually planned

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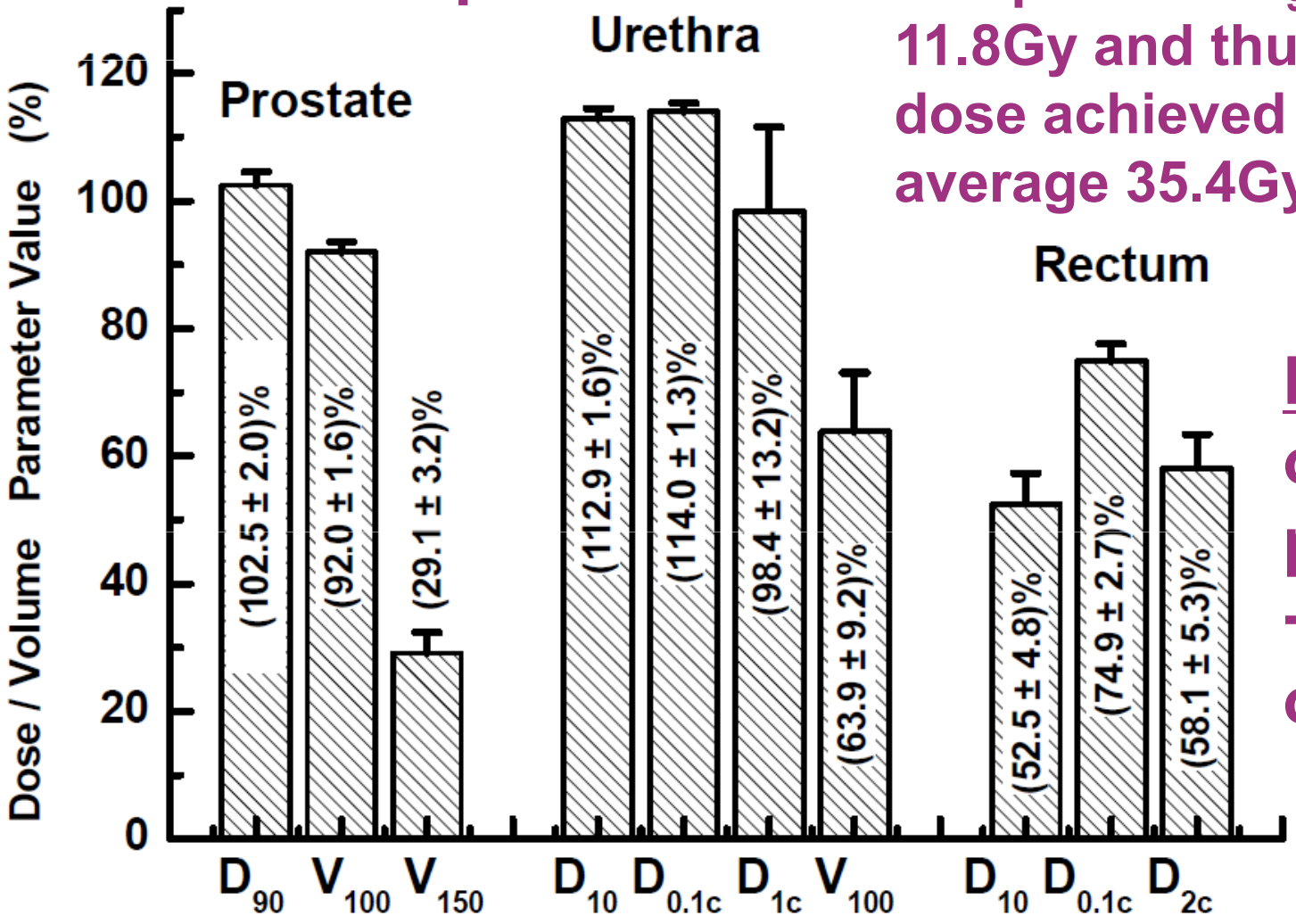
“Aimed” versus “Planned”: ATTENTION

Offenbach Protocol for Monotherapy: 3x11,5Gy = 34,5Gy

120 Implants



The planned D_{90} is on average 11.8Gy and thus the planned total dose achieved in 3 fractions is on average 35.4Gy !

For Offenbach:
on average planned D_{90} is +2,5% of the aimed D_{90}

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“Aimed” versus “Planned”: ATTENTION

International Journal of Radiation Oncology biology • physics

www.redjournal.org

104 consecutive patients and a total of 208 implants PCA

Physics Contribution

High-Dose-Rate Prostate Brachytherapy Consistently Results in High Quality Dosimetry

Evan C. White, MD, Mitchell R. Kamrava, MD, John Demarco, PhD, Sang-June Park, PhD, Pin-Chieh Wang, PhD, Oluwatosin Kayode, MS, Michael L. Steinberg, MD, and D. Jeffrey Demanes, MD

California Endocurietherapy at UCLA, Department of Radiation Oncology, David Geffen School of Medicine of the University of California at Los Angeles, Los Angeles, California

Received Jan 7, 2012. Accepted for publication Mar 20, 2012

Monotherapy protocol with “intended/aimed” 7.25Gy/fraction for 6 fractions and total of 43.5Gy

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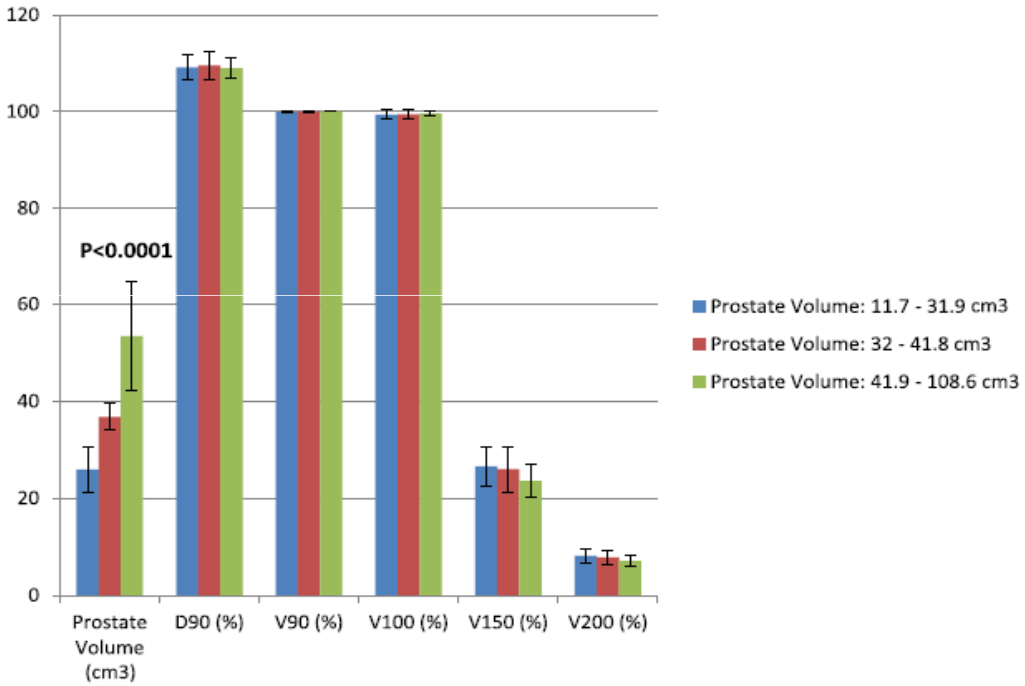
“Aimed” versus “Planned”: ATTENTION



On average “planned” D_{90} of 7.9Gy per fraction and the total “planned” dose achieved in 6 fractions is 47.4Gy
versus
“intended/aimed” 7.25Gy and 43.5Gy accordingly.

Table 2 Target (CTV) and OAR dosimetry

CTV	Mean	SD	Minimum	Maximum
D90	109.2	2.6	102.3	118.4
V90	100.0	0.1	99.6	100.0
V100	99.5	0.8	93.7	100.0
V150	25.4	4.2	15.5	42.2
V200	7.8	1.4	4.7	13.2
Prostate volume (cm^3)	38.7	13.4	11.7	108.6
CTV volume (cm^3)	75.1	20.6	33.4	156.5

For UCLA:

on average planned D_{90} is +9,2% of the aimed D_{90}

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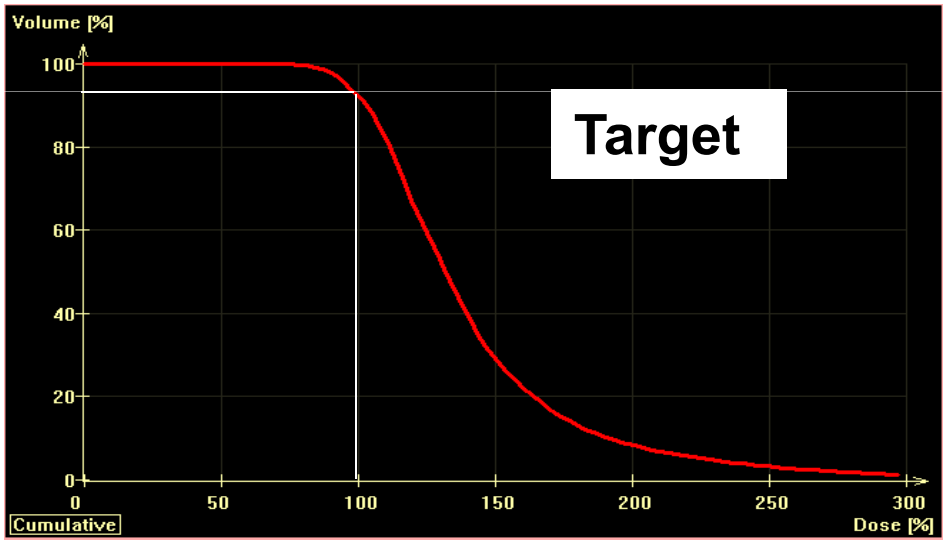
Quality Parameters and Indices

- Conformity based
  - Coverage Index CI for Target

“Fraction of the target volume receiving a dose equal or greater than the reference dose (100%)”

$$CI = V_{100} / 100$$



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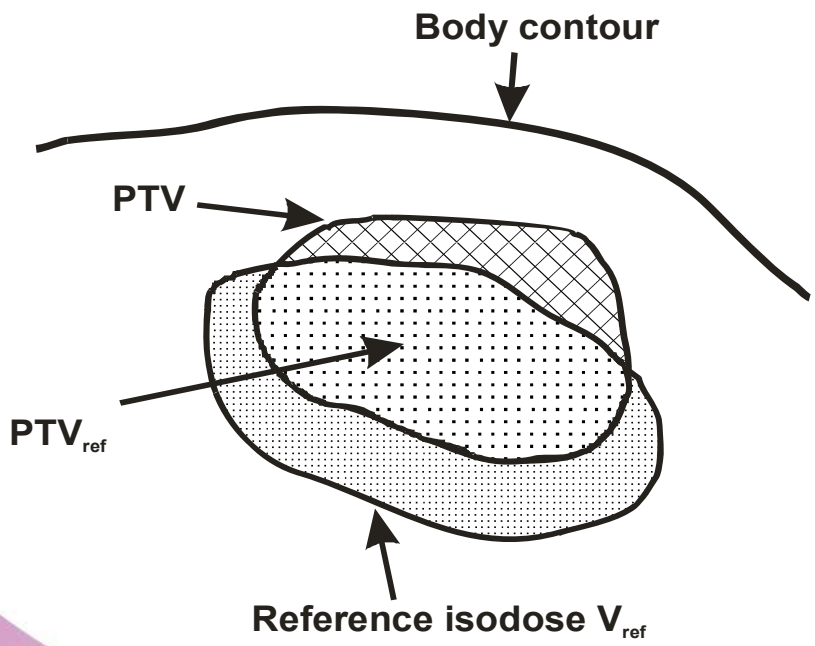
Quality Parameters and Indices

- **Conformity based**
  - **Conformal Index COIN without OARs**

How well fits the 3D shape of D_{ref} the target volume PTV



$$\mathbf{COIN = c_1 \times c_2}$$

$$c_1 = \frac{PTV_{ref}}{PTV} \qquad c_2 = \frac{PTV_{ref}}{V_{ref}}$$

Reference isodose = D_{ref} = 100 %

Baltas D, Kolotas C et al.
Int J Rad Oncol Biol Phys 40, 512-524, 1998

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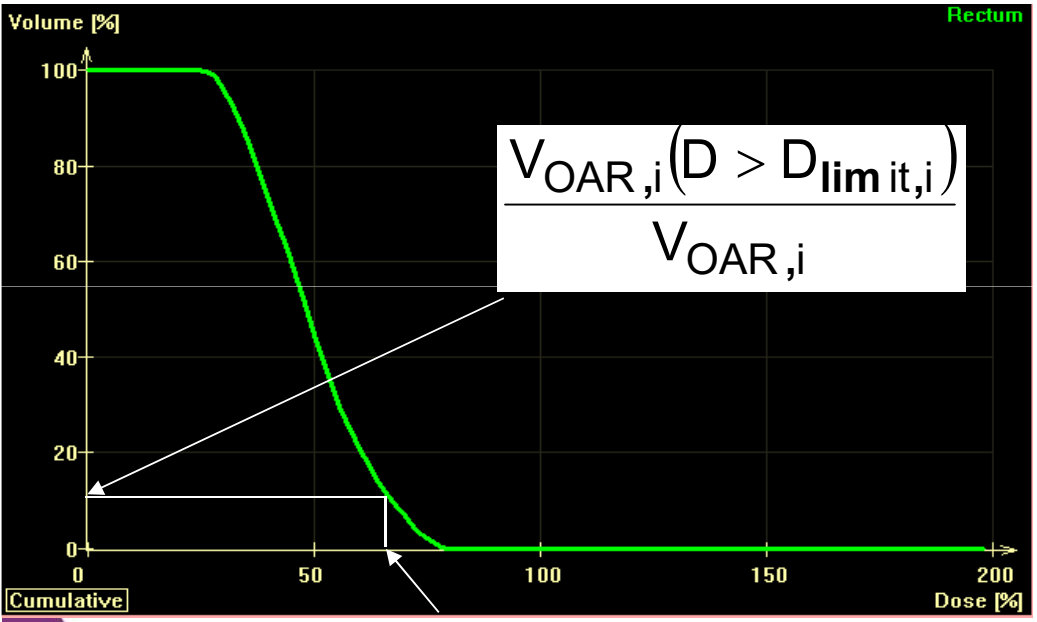
Quality Parameters and Indices

- Conformity based
  - Conformal Index COIN including OARs

$$COIN = c_1 \times c_2 \times c_3$$



$$c_3 = \prod_{i=1}^{N_{OARs}} \left[1 - \frac{V_{OAR,i}(D > D_{limit,i})}{V_{OAR,i}} \right]$$

$D_{limit,i}$ is the dose limit for the ith OAR.
N_{OARs} is the total number of OARs.

Milickovic N, Lahanas M et al.
Phys Med Biol 47, 2263-2280, 2002

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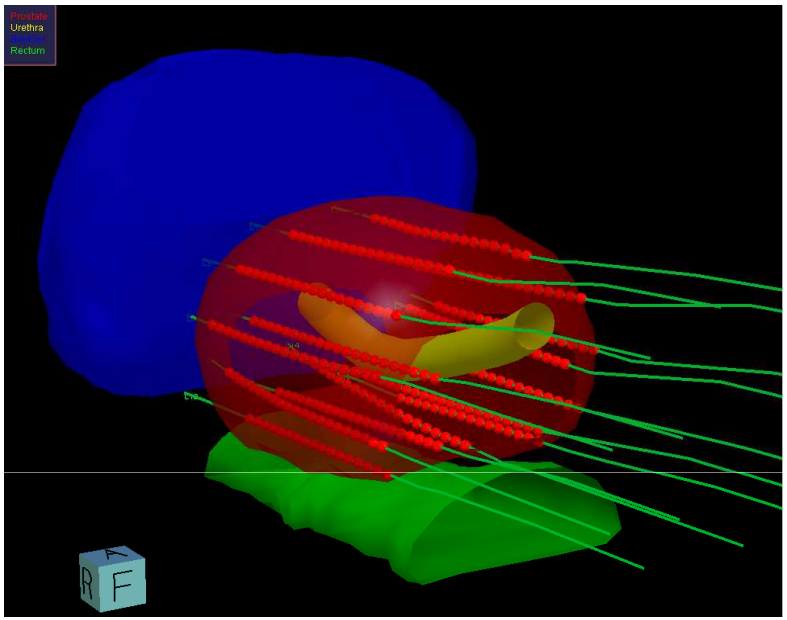
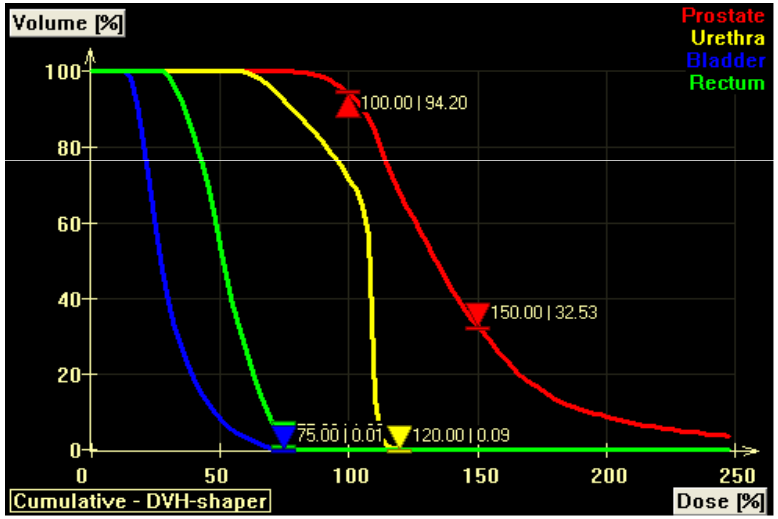
Quality Parameters and Indices: Conformal Index COIN

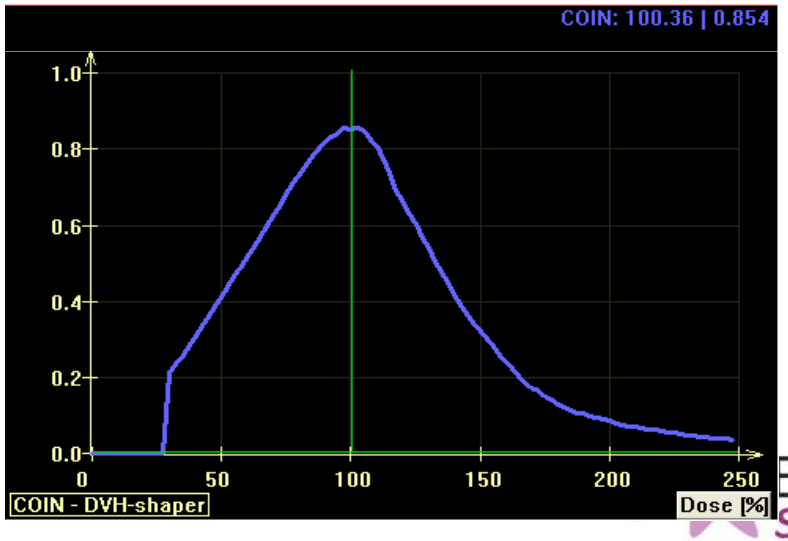
Implant



DVHs



COIN-Distribution



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Quality Parameters and Indices

- **Conformity based**
  - **External Volume Index EI**

How much is the extension of D_{ref} outside the target volume

$$EI = \frac{V_{tissue,ref}}{PTV} x100 = \left[\frac{c_1}{c_2} - c_1 \right] x100$$

$V_{tissue,ref}$ is the normal tissue volume covered by D_{ref}
PTV is the target volume
c_1 and c_2 are the two coefficients of COIN

Meertens H, Borger J et al.
***Nucletron International*; 300–306 1994.**

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Quality Parameters and Indices

- Implant Volume based
  - Natural Dose Volume Histogram based Indices
    - Uniformity Index UI
    - Quality Index QI
    - Natural Dose Ratio NDR

“Natural” Dose Volume Histograms are calculated by most TPSs

Histograms can be inspected for their appearance

Indices are derived and shown based on these NDVHs

Anderson LL
Med Phys 13 (6); 898-903, 1986
Van der Laarse R, Prins TPE
***Nucletron International*; 352–372, 1994.**

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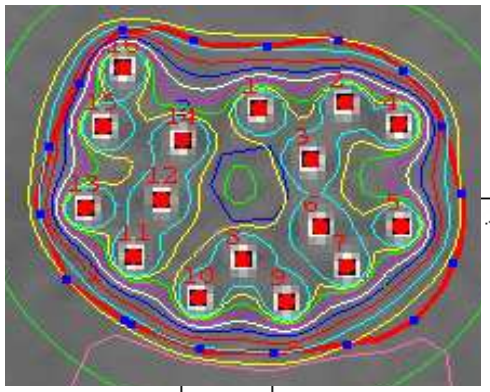
Natural Dose Ratio (NDR)



Prescription dose: 500 cGy
Peak dose: 756 cGy
Low dose: 677 cGy
High dose: 864 cGy

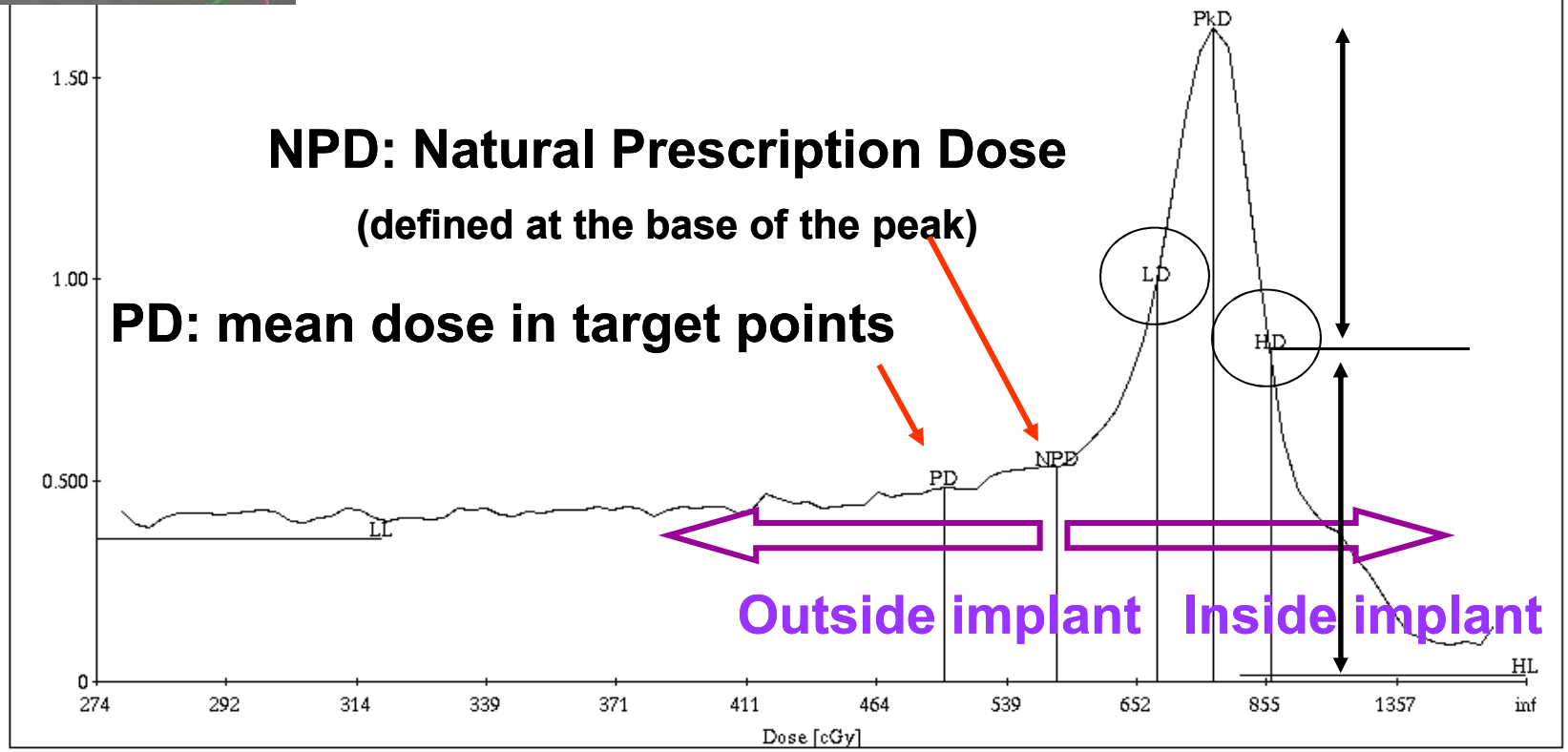
Nat. prescr. dose (Manual): 576 cGy
Quality index: 2.33
Uniformity index: 1.47
Nat. dose ratio (Manual): 1.15

Natural Dose Ratio NDR = NPD / PD = 1.15

NPD: Natural Prescription Dose

(defined at the base of the peak)

PD: mean dose in target points



DVH_0 : Natural DVH on implant. State : Consistent.

Classical Geometric Optimization on Volume

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Uniformity Index UI

The Uniformity Index UI which can be extracted from the natural volume dose histogram (Anderson 1986), is defined as:

$$UI = \frac{V(PD - HD)}{V(PD)} * \frac{u(PD)}{u(PD) - u(HD)}$$

With PD the prescription dose, HD the dose at half maximum of the peak at the high dose side, V(PD-HD) the volume receiving a dose between PD and HD, V(PD) the volume receiving at least the prescription dose PD and $u(D)= D^{-3/2}$.

This uniformity index, thus, depends not only on the uniformity of the dose distribution but also on the choice of the reference isodose. It expresses the amount of the treatment volume which is concentrated between the prescription dose, PD, and the high dose side of the peak, HD.

Quality Index QI

The Quality Index QI is defined to suppress the influence of the chosen reference dose:

$$QI = \frac{V(LD - HD)}{V(LD)} * \frac{u(LD)}{u(LD) - u(HD)}$$

With LD the dose at half maximum of the peak at the low dose side, V(LD-HD) the volume receiving a dose between LD and HD and V(LD) the volume receiving at least dose LD.

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Other techniques are under development/investigation

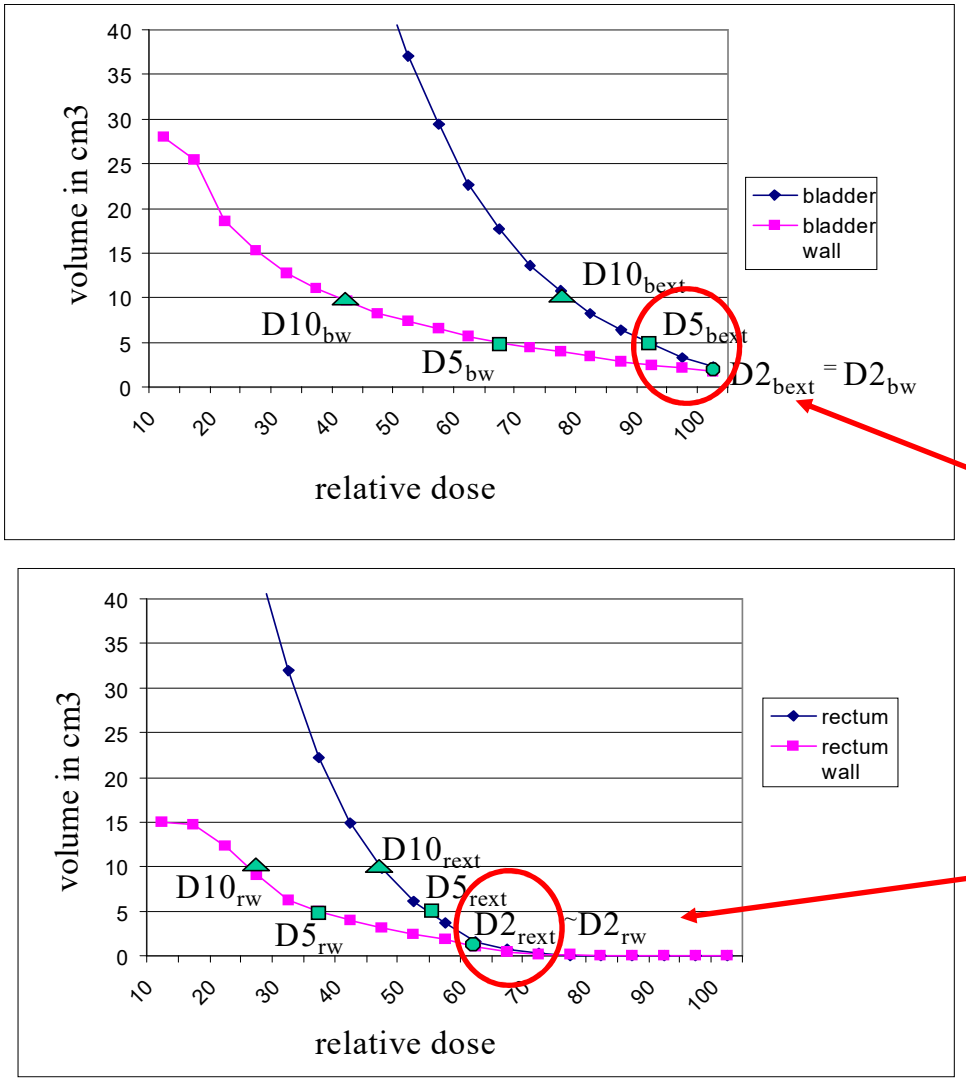
Dose Volume Histograms

Dose "Wall" Histograms

Dose "Surface" Histograms

- ***Needs careful 3-D imaging consideration***
- ***Recommended in some international reports***
- ***(and what about inter-observer variation….?)***

On the usefulness of organ or organ-wall contouring, DHVs: in the small-volume-part of the graphs, the curves tend to come very close together



Pat #5

Cut off -volume 2-3 ccm

Fig.1

(from: Wachter-Gerstner et al. R&O 2003)

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Take home messages:

- DVHs are useful to help you plan the patient treatment (Plan optimization and comparison of different plans)
- DVHs are useful to evaluate your prescription or to prescribe (dose to a volume)
- Volume-Dose (V, D_V or D,V_D) parameters and “Quality” parameters can be derived from DVHs
- Attention: Aimed versus planned prescription (e.g. D_{90})
- Predictive value of such (quality) parameters still has to be proven for general use !

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Radiobiology of permanent implants and HDR BT for prostate cancer

Erik Van Limbergen MD, PhD

University Hospital Gasthuisberg
Leuven, Belgium

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^{125}I seeds

- Introduction in clinical practice since 1965
- Different seeds with different emission

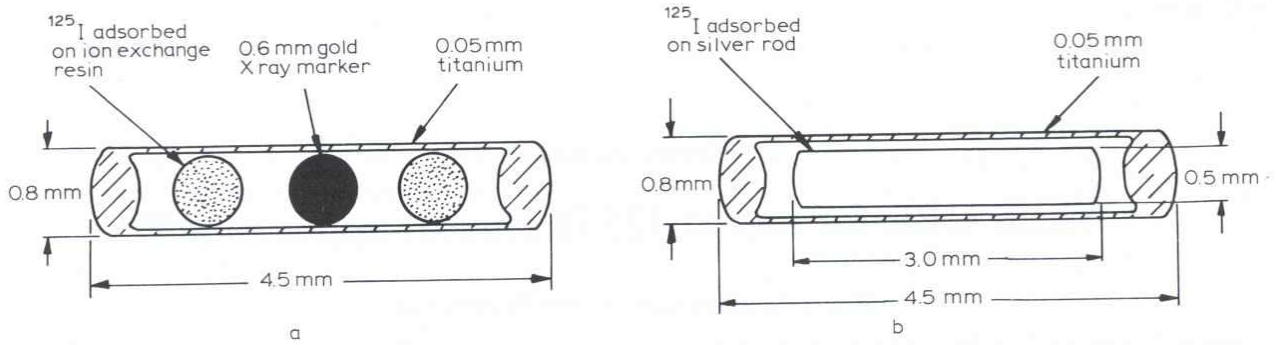

Fig. 1. Diagram of a ^{125}I seed and encapsulation design. (a) Old type of seed, model 6701; (b) new type of seed, model 6711 [27].

- Application in : Prostate PI

  CNS, Lung, Pancreas ,

  H&N,Breast PI

  Eye melanoma

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^{125}I and ^{103}Pd

Low Energy

- Major advantage for radioprotection
- High RBE

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RBE ^{125}I and ^{103}Pd

	mean energy	half life	RBE
• ^{125}I	28 keV X rays	60 d	1- 2.4*
• ^{103}Pd	21 keV X rays	17 d	1.9**

- * overview litterature 1968-2000
- ** C. Ling et al 2000

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RBE ^{125}I and ^{103}Pd

- LET of radiation
- Dose rate

- Biological system, end points,
- Tissue involved
  - repair capacity α/β ratio
  - repair kinetics $T^{1/2}$
  - repopulation kinetics T^{pot}
- Reference beam

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LET ^{125}I and ^{103}Pd

- Low energy γ emission
  - ^{125}I 28 keV X rays
  - ^{103}Pd 21 keV X rays
- = high LET radiation

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Lineal Energy Spectra diff. nucleides

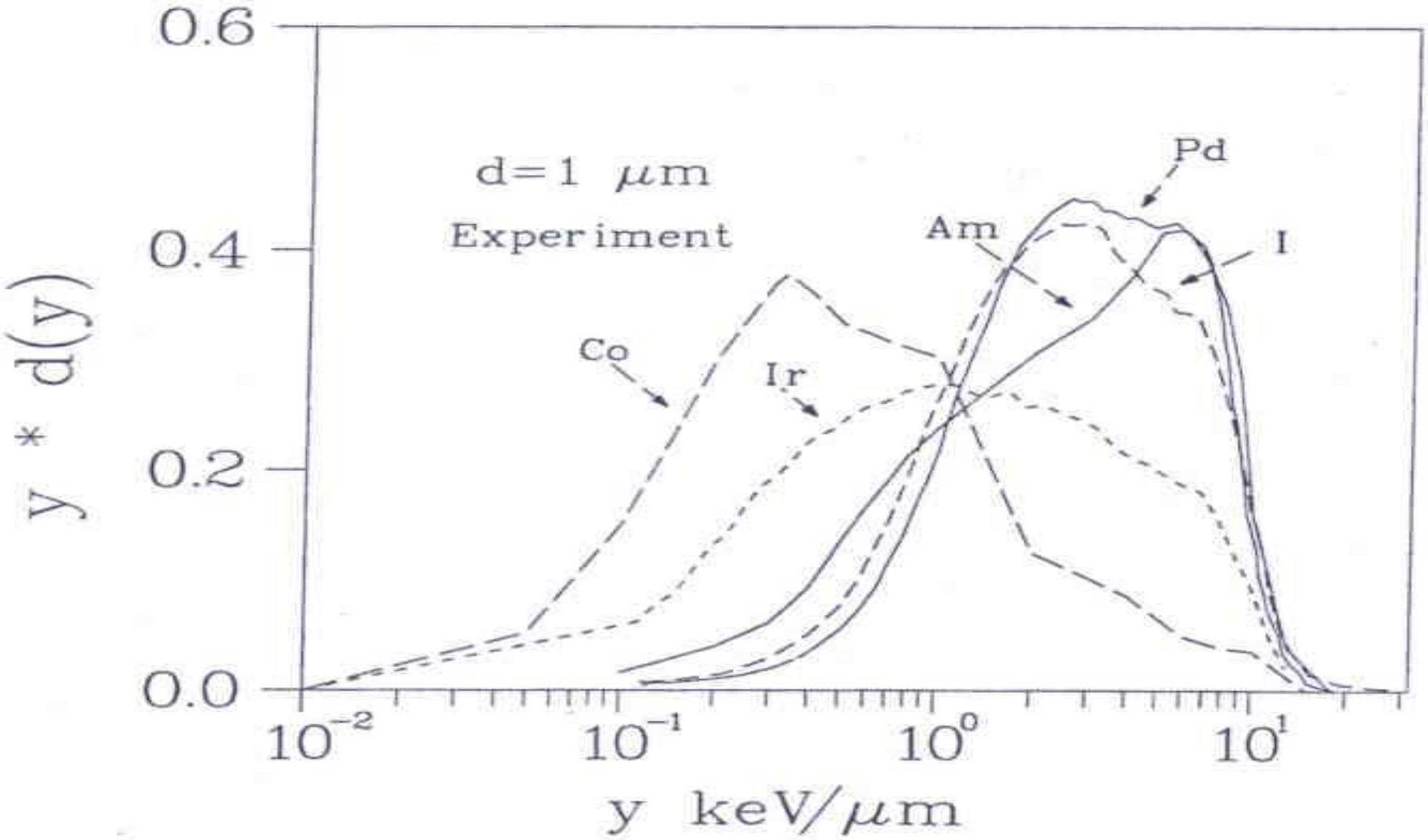

Fig. 8. Measured lineal energy spectra for different brachytherapy sources.

RBE ^{125}I and ^{103}Pd

- LET of radiation
- Dose rate

- Biological system, end points,
- Tissue involved
  - repair capacity α/β ratio
  - repair kinetics $T^{1/2}$
  - repopulation kinetics T^{pot}
- Reference beam

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RBE ^{125}I and ^{103}Pd

- Dose rates
  - ^{125}I 7 cGy/h IDR 144 Gy in 10 months
  - ^{103}Pd shorter half life 21 cGy/h IDR 125 Gy in 3 months

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Dose rate effects

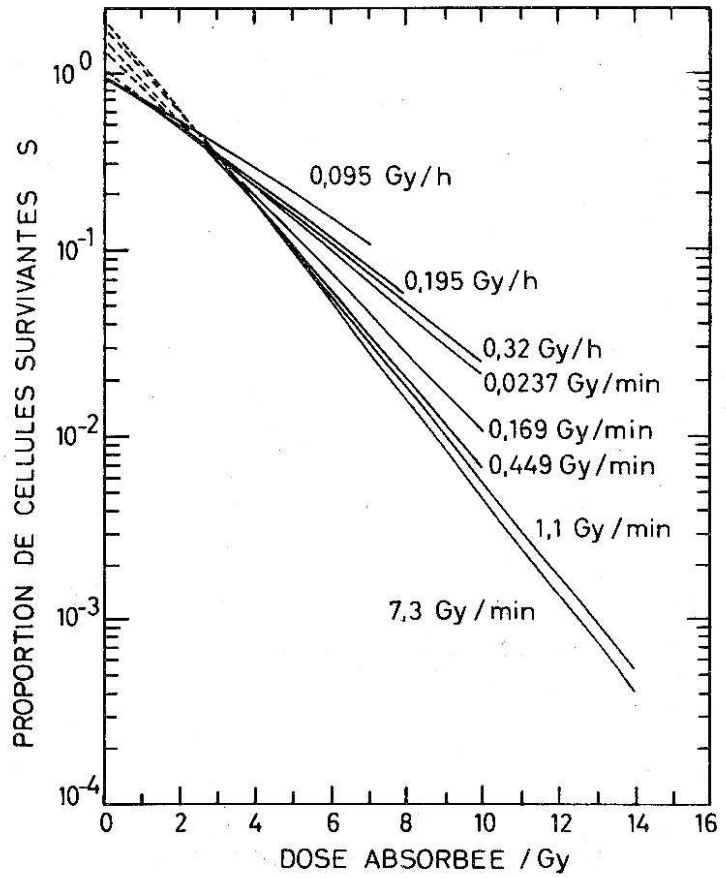
$$E = \alpha D + g \beta D^2$$

$$g = \frac{2\,(r\,t - 1 + e^{(-r\,t)})}{(r\,t)^2}$$

$$r = 0.693 / T½$$

Higher DR (TI) RBE 1.15 -1.2

Lower DR (PI) RBE 2 - 2.2



RBE and Dose rates ^{125}I

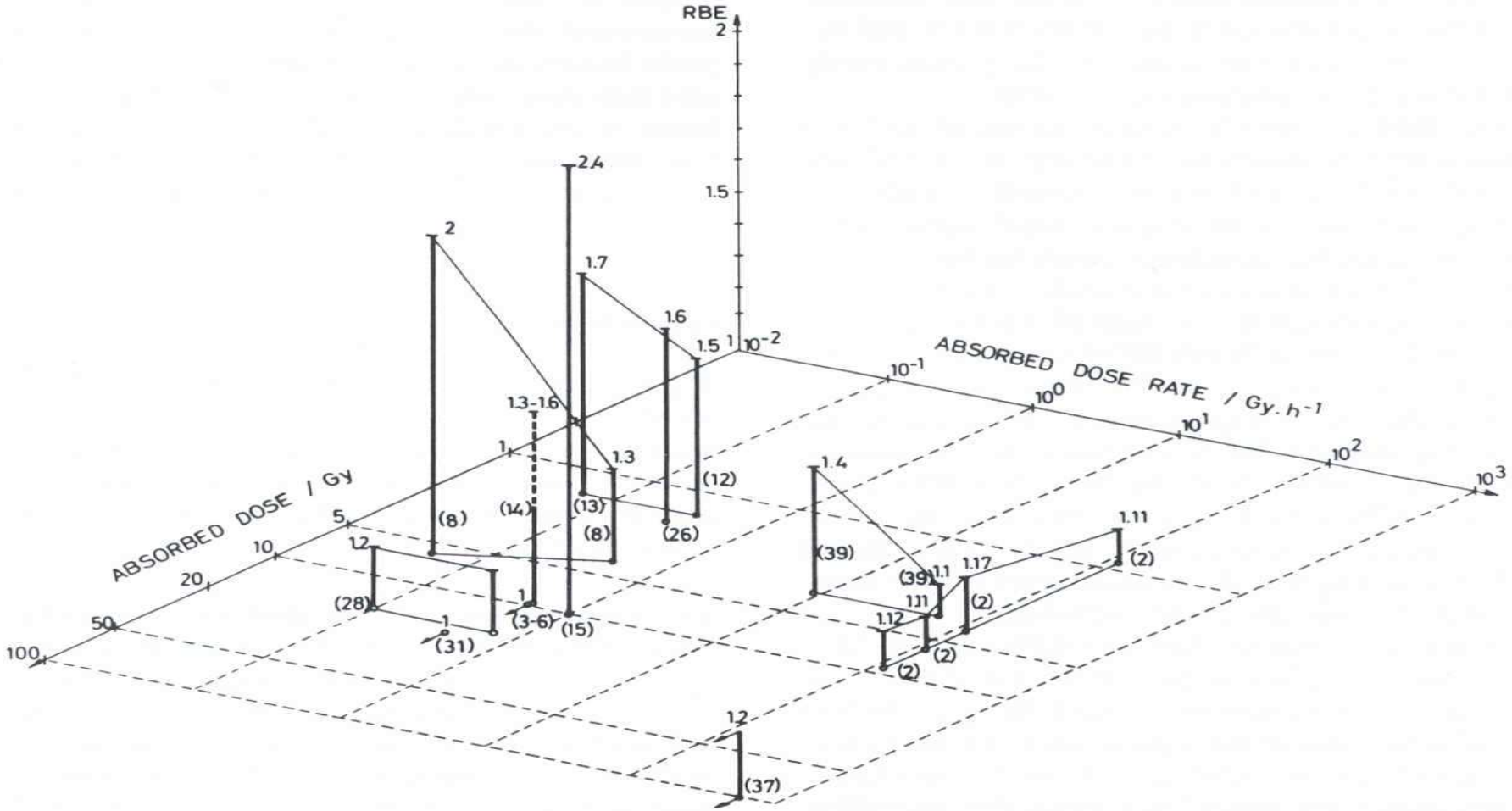


Fig. 4. Summary of the published radiobiological data on RBE of ^{125}I and low energy X-rays (reference radiation ^{60}Co). The observed RBE values are represented by the height of the vertical bars (a zero height corresponds to RBE = 1). RBE is expressed as a function of absorbed dose of the reference beam (left abscissa) and absorbed dose rate of the reference beam (right abscissa). For each value, the exact RBE is indicated (upper number), together with the literature reference (number between brackets). When several values have been obtained by the same author and with the same biological system (differing from dose or dose rate), they are connected

RBE and Dose rates ^{125}I

		RBE *	
Permanent implants			
Low dose rates	^{125}I	(0.08 Gy/h)	
1.6 - 2.4			
			^{103}Pd
(0.14 Gy/h)		1.9	
Eye melanoma			
High dose rates	^{125}I		
1.1 - 1.2			

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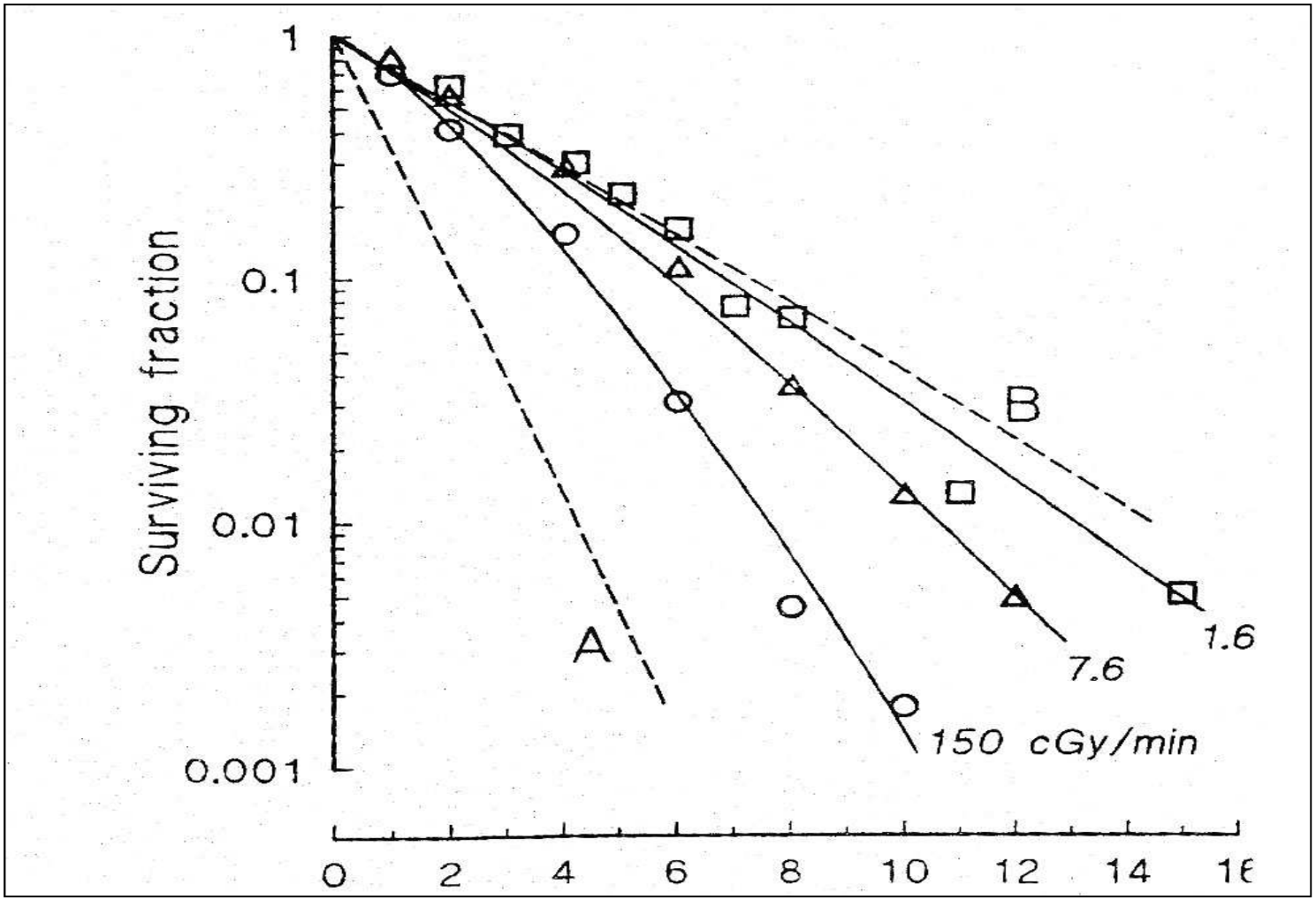
Very Low Dose Rate



Dose M to compensate for repopulation

	Time				
Tpot	5 d	10 d	20 d	30 d	40 d
2 d	5 Gy	10 Gy	20 Gy	30 Gy	40 Gy
5 d	2 Gy	4 Gy	8 Gy	12 Gy	16 Gy
10 d	1 Gy	2 Gy	4 Gy	6 Gy	8 Gy

With M = 2 Gy.T/Tpot

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Very Low Dose Rate

- Example PCa with ^{125}I implant:
- 150 Gy with initial dose rate of 7 cGy/h
- If Tpot = 6 days (better 25days?):
  - Critical dose =120 Gy reached after 140 days (23.5 times Tpot) when Dose Rate is 1.4 cGy/h
  - Compensation dose to overcome repopulation

    M = 47 Gy (2 Gy.t/Tpot)
  - Effective dose is 120 - 47= 73 Gy not taking into account variations in RBE due to DRE

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^{125}I versus ^{103}Pd

- Radiobiological modeling :
  - low α/β (3 Gy)
  - and $T^{1/2}$ = 1h

^{103}Pd is more cytotoxic

if T^{pot} is < 25 d (King)

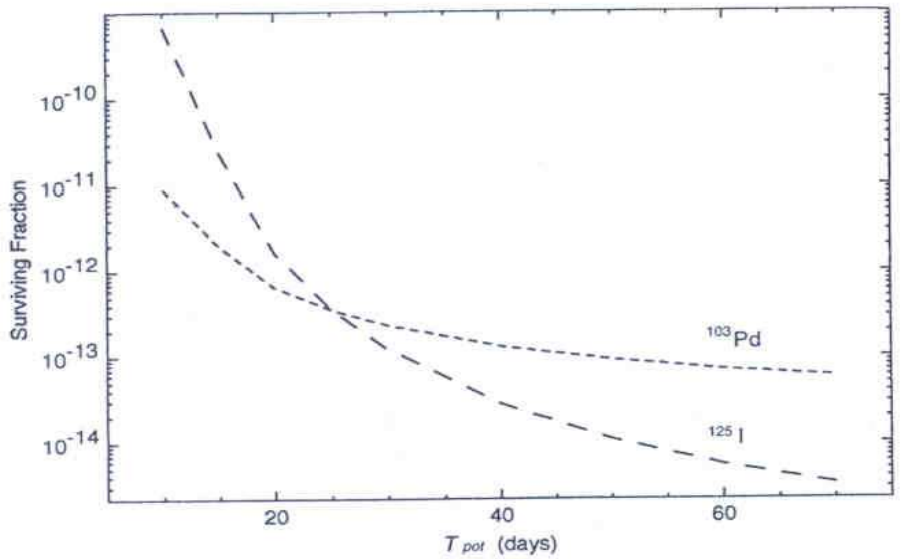

Fig. 1. Cell survival (on logarithmic scale) as a function of T_{pot} for ^{125}I and ^{103}Pd. This radiobiologic model assumes $\alpha/\beta = 3$, $\alpha = 0.3$, and a sublethal damage repair half-life of 1 h. For very short T_{pot}, the models predict more cell kill with ^{103}Pd, but for longer times ^{125}I is predicted to achieve more cell kill. Equivalent cell kill (i.e., crossover point) occurs when T_{pot} is about 25 days in this model.

- In high risk PCa with short T^{pot} , ^{103}Pd could be advantageous

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^{125}I versus ^{103}Pd

- Clinical outcome:
  - Matched pair study (Cha et al. 1999):
  - ^{125}I and ^{103}Pd have equivalent clinical outcome
    - regardless for Gleason score and initial PSA
    - 5 y NED survival is identical

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^{125}I versus ^{103}Pd

- Clinical outcome:

  Phase III Trial (Herstein et.al 2005)

  More proctitis with Palladium
  More Urethritis with Iodine
  At 12 months same IPSS score

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What is the true α/β ratio for prostate cancer?

Brenner & Hall 1999:

Ext beam vs I-125 implant

α/β = 1.5 (95% CI 0.8 - 2.2)

Fowler et al 2001:

Ext beam vs I-125 or Pd-103 implant

α/β = 1.49 (95% CI 1.25 - 1.76)

What is the true α/β ratio for prostate cancer?

Calculated α/β ratios for prostate carcinoma and late rectal toxicity, respectively.

α/β (Gy) Prostate carcinoma	α/β (Gy) Late rectal toxicity	References
1.5 (assumed)	2.3	Marzi et al. (2009) [40]
–	5.4	Brenner (2004) [41]
3.1 (1.7–4.5)	–	Wang et al. (2003) [42]
1.2	–	Brenner et al. (2002) [43]
1.49 (1.25–1.76)	–	Fowler et al. (2001) [33]
1.5 (1.4–1.7)	–	Brenner and Hall (1999) [32]
–	3.87	Deore et al. (1993) [44]

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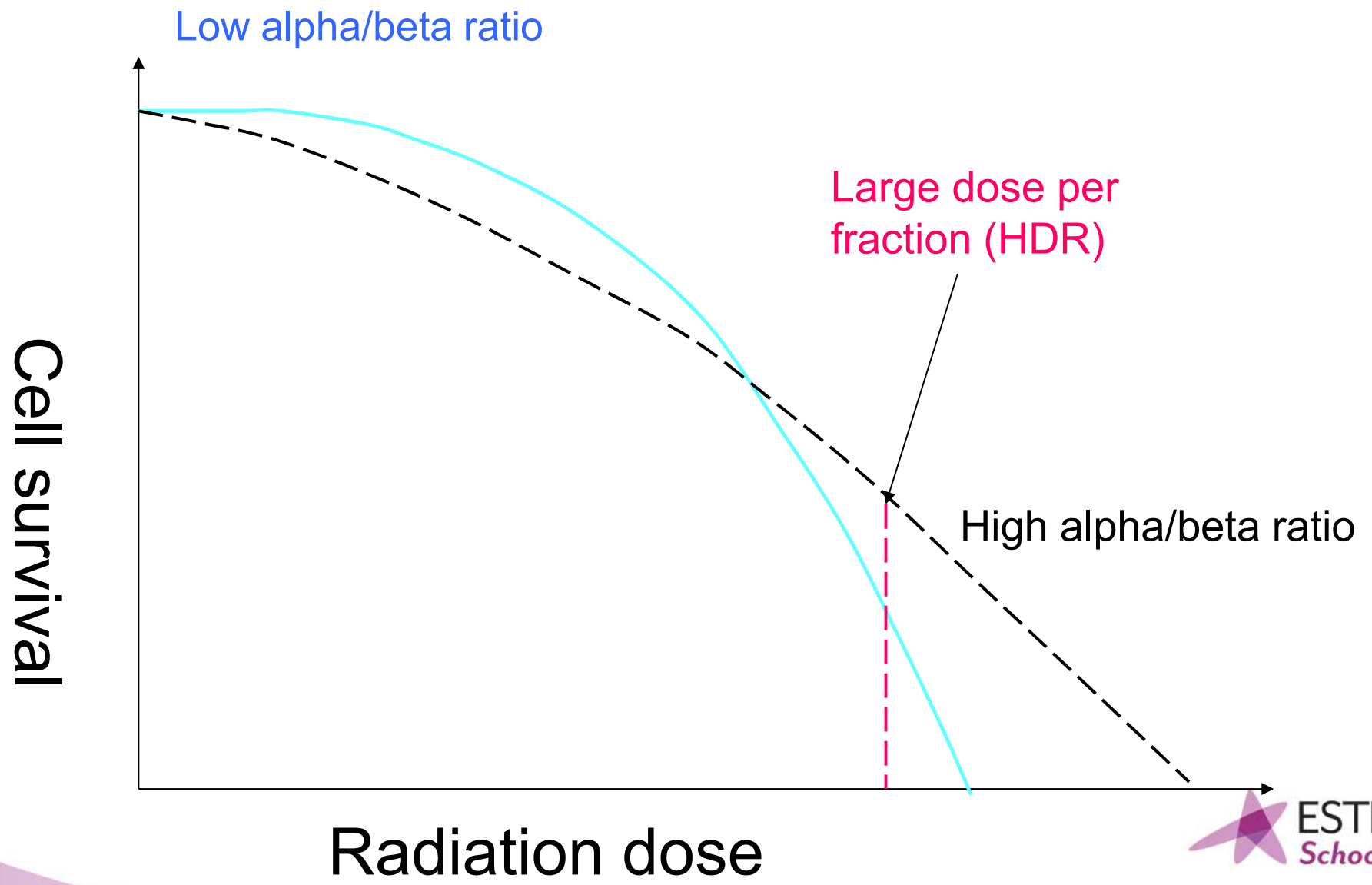
Idealised cell survival curve



HDR implant boost: biological advantage in EQD2

	α/β 1.5	α/β 3.5	α/β 10
Ext beam			
74Gy/37f	74	74	74
HDR **Boost** schedules after 45Gy/25f			
Ext beam	42.4	43.3	44.2
16Gy/4f	67.5	65.1	62.8
16Gy/2f	85.8	76.8	68.4
23Gy/2f	127.8	106.1	85.4
HDR **Boost** after 35.7Gy/13f			
Ext beam	43.4	40.5	37.9
17Gy/2f	91.8	77.6	64.1

HDR-mono implant: biological advantage in EQD2

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam 74Gy/37f	74	74	74
• HDR mono 34Gy/4f	96.9	74.2	52.4
36Gy/4f	108	81.8	57.0
31.5Gy/3f	108	80.2	53.8

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Brachytherapy for Bronchus ca

Erik Van Limbergen MD, PhD
University Hospital Gasthuisberg
3000 Leuven

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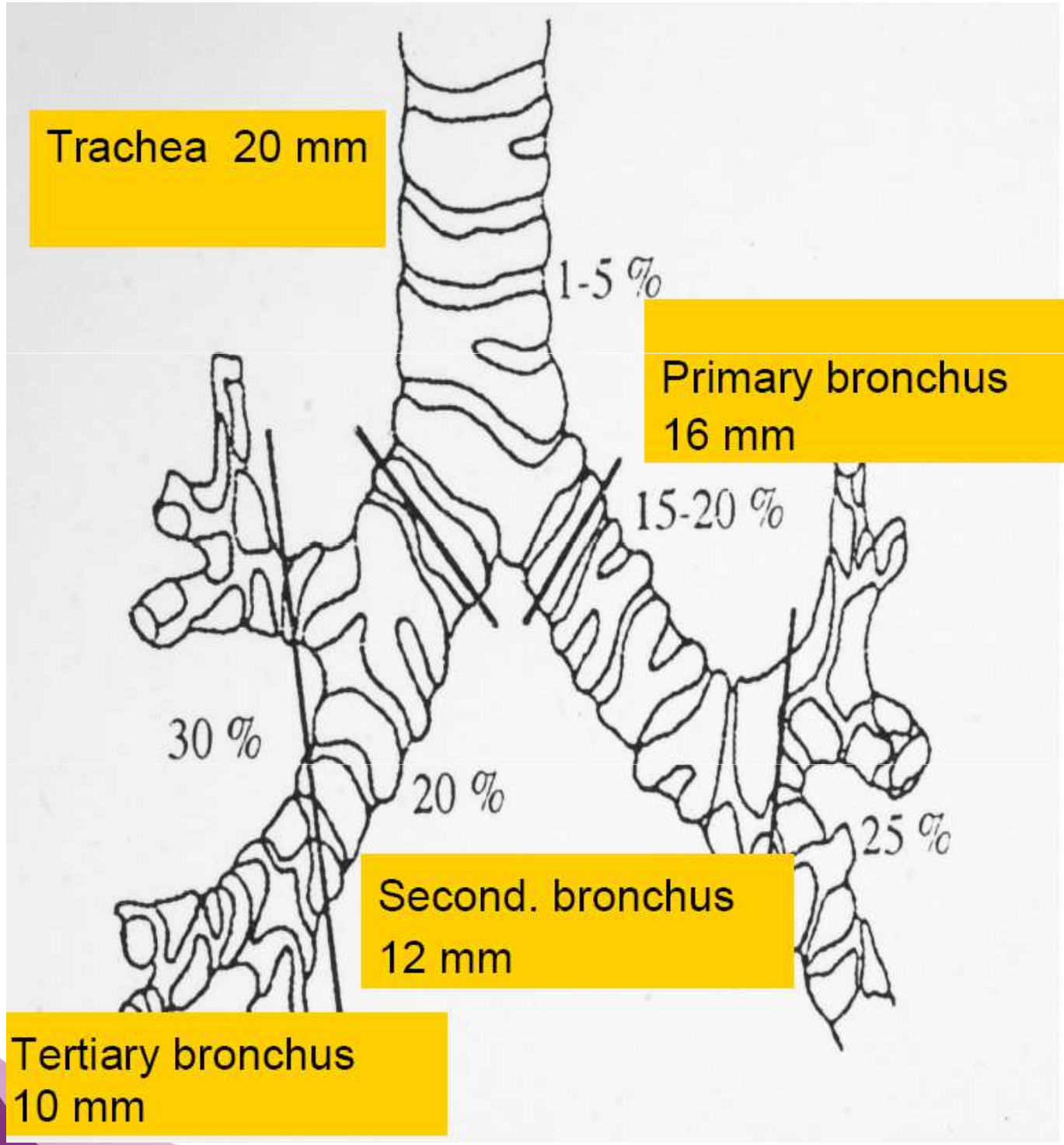


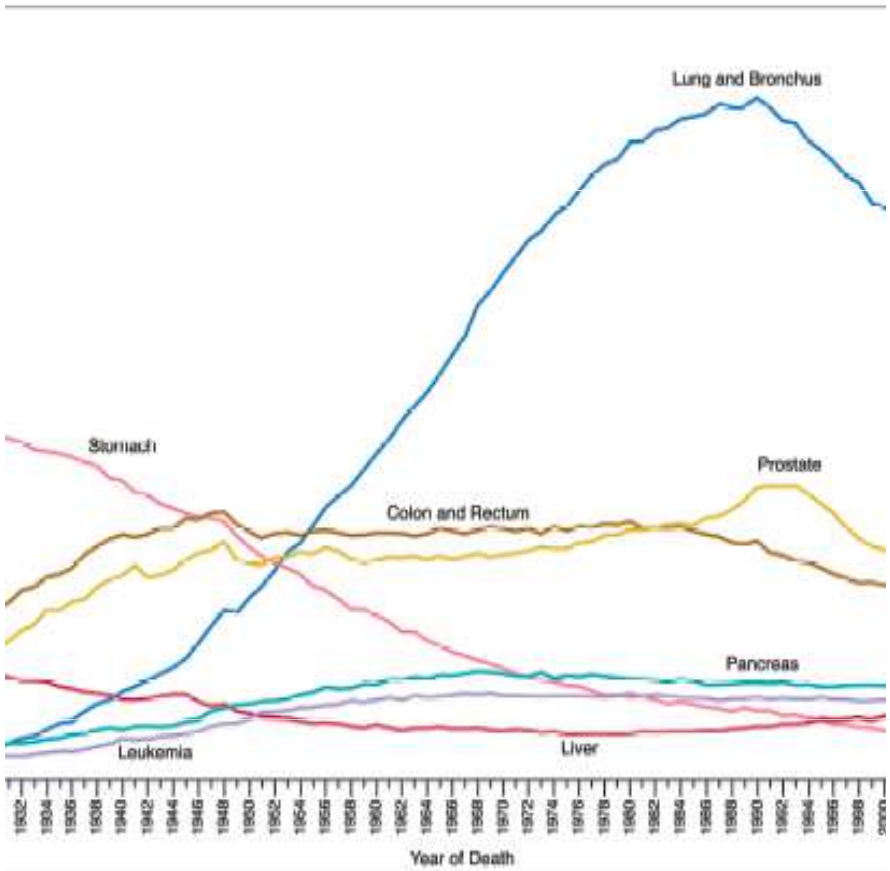
Diameters

Lumina 90%

Walls 5%

Lung and bronchus Ca. death

CA Cancer J Clin 2005;5[illegible] Cancer Statistics, 2005



al Age-adjusted Cancer Death Rates* Among Males for Selected Cancer Types, US, 1930 to 2001.
ated to the 2000 US standard population.
es in ICD coding, numerator information has changed over time. Rates for cancers of the lung and bronchus, colon and rectum, and
these changes.
y Public Use Data Tapes, 1960 to 2001, US Mortality Volumes, 1930 to 1959, National Center for Health Statistics, Centers for Disea
tion.

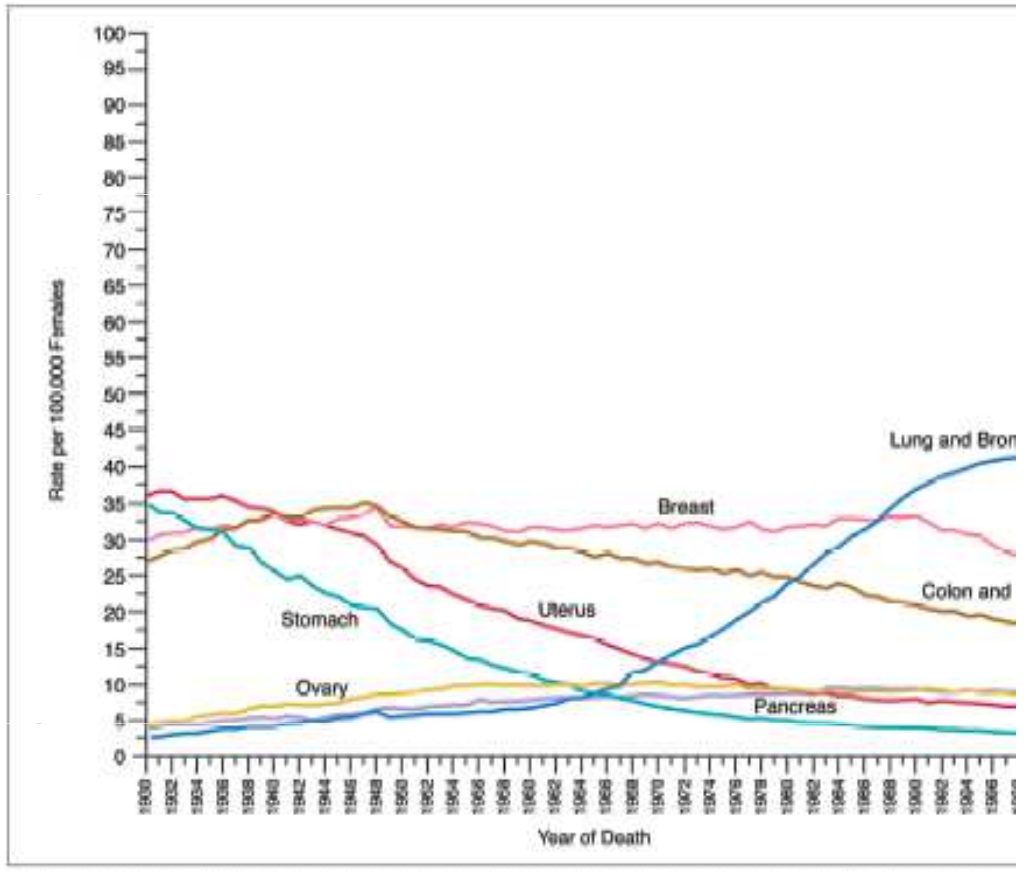


FIGURE 8 Annual Age-adjusted Cancer Death Rates* Among Females for Selected Cancer Types, US, 1930 to 2001.
*Rates are age-adjusted to the 2000 US standard population.
Note: Due to ICD coding, numerator information has changed over time. Rates for cancers of the uterus, ovary, lung and bronchus, and colo
affected by these changes. Uterus cancers are for uterine cervix and uterine corpus combined.
Source: US Mortality Public Use Data Tapes, 1960 to 2001, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Cente
Control and Prevention.

NDINGS

[illegible] cancers of the skin. More than 1 million cases

more than 56% of all newly diagnosed cancers.

estimated cancer cases in women

Surgery

- Surgery is the gold standard for NSC stage I:
  - Survival @ 5 y = 45 - 65%
  - Local relapses = 5 - 20%
  - Seconds primaries = 15 - 20%
- Only 20-25% of the patients are operated
  - Respiratory Insuff
  - Performance status
  - Pulmonary history (surgery, irradiation)

Lung Cancer
failures after irradiation

EBRT 50-70Gy:

– 60% local recurrences

60% die from airway obstruction

–respiratory failure

–obstructive pneumonia

–Sepsis

–Couching

– Haemophtysis

Symptoms of obstruction

Couching	45-75%
Haemophtysis	25-35%
Dyspnea due to atelectasis	40-60%
Retro obstructrive pneumonia	25%

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Indications for BT in Bronchus cancer

- Palliative airway obstruction
- Curative for ROC Bronchus ca

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Indications BT in lung ca (1)

- **1-PALLIATIVE TREATMENT**
- endobronchial tumor growth
- often in combination with endobronchial laser or stenting in selected cases
- endobronchial recurrence in RT-field

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Work Up

- Bronchoscopy — BIOPSY
  LOCATION
  MEASUREMENT of LENGTH
  AMOUNT of OBSTRUCTION
- Chest X Ray
- CT - SCAN — EXTENT OF LOCAL DISEASE
- PET - SCAN
- **Pneumonologist, Radiation Oncologist**

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Contra indications BT in lung ca

- Obstruction by extrabronchial compression
- Peripheral lesions not accessible by bronchoscopy

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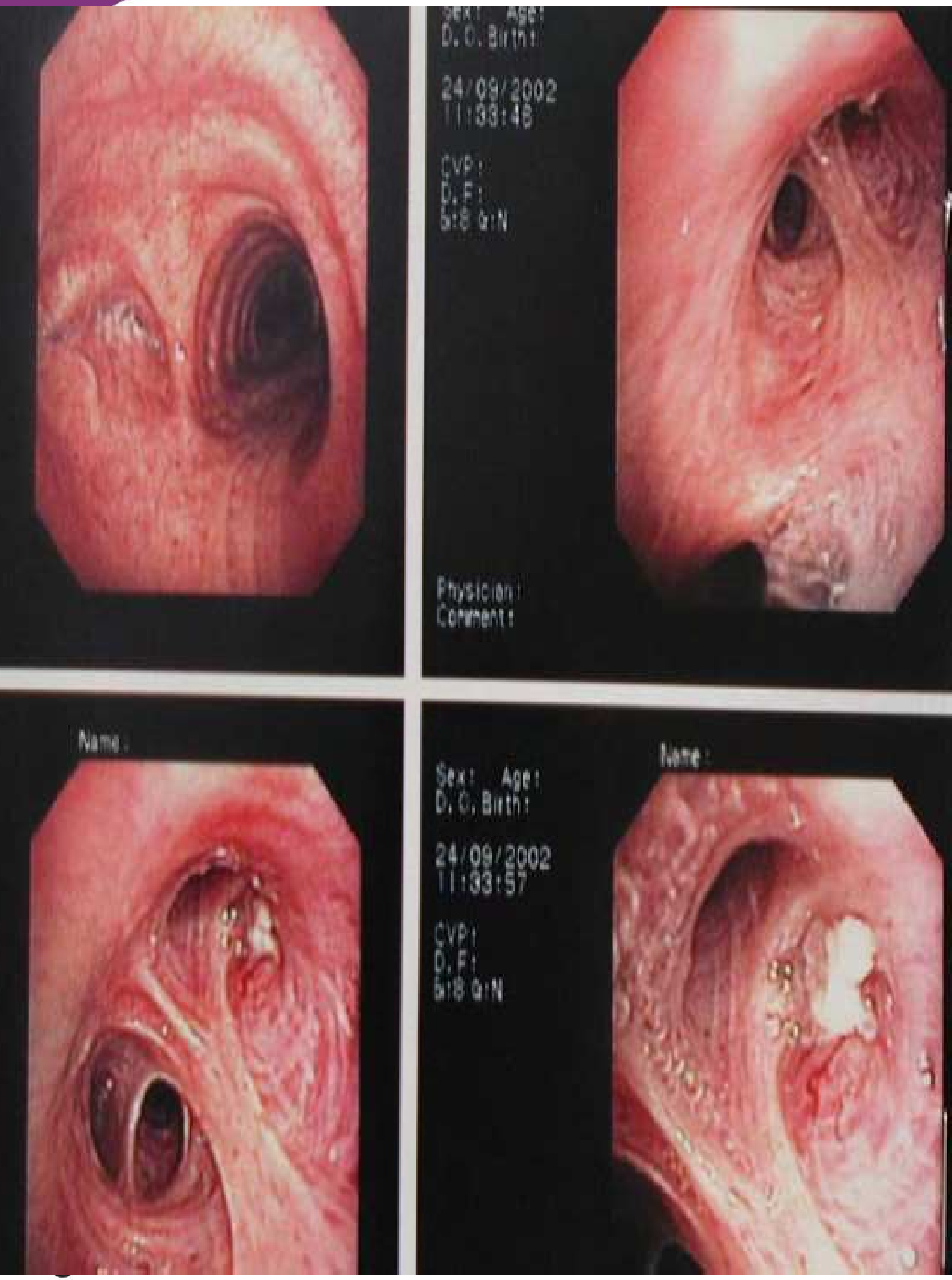
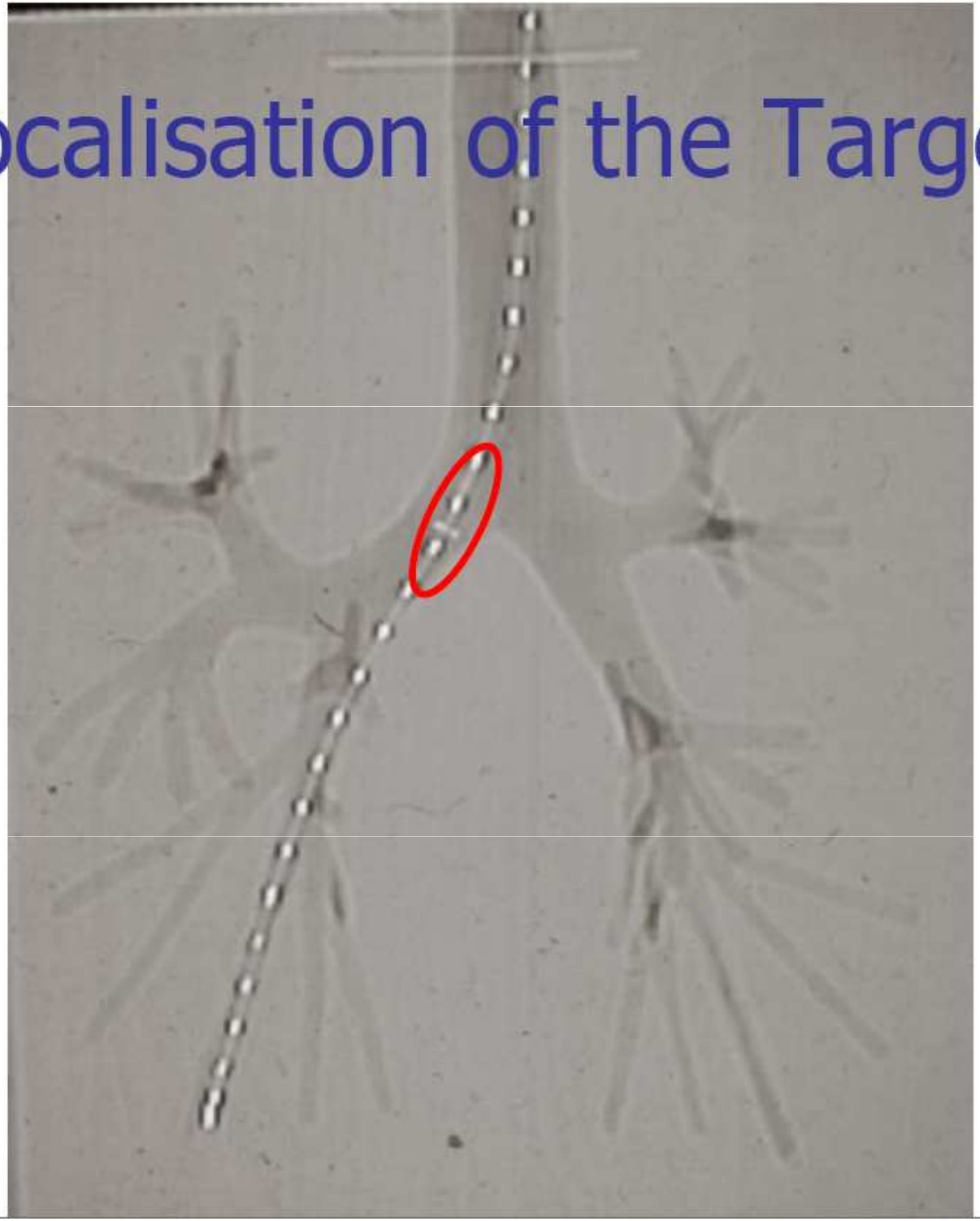
Local Anesthesia


Sex: Age:
D.O.Birth:
24/09/2002
11:33:48
CVP:
D.F:
B:8 G:N
Physician:
Comment:
Name:
Name:
Sex: Age:
D.O.Birth:
24/09/2002
11:33:57
CVP:
D.F:
B:8 G:N

Localisation of the Target



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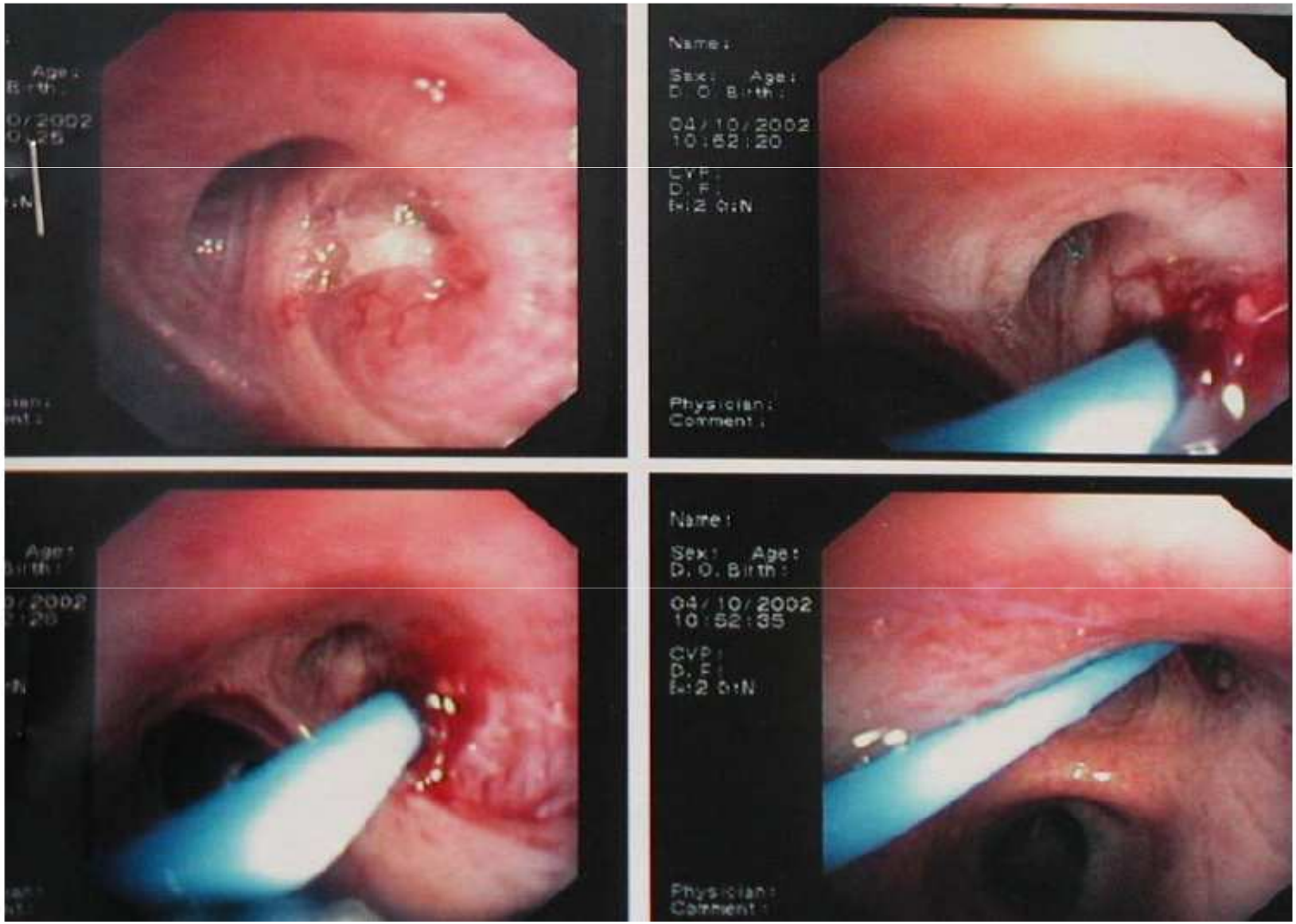
Positioning of the catheter



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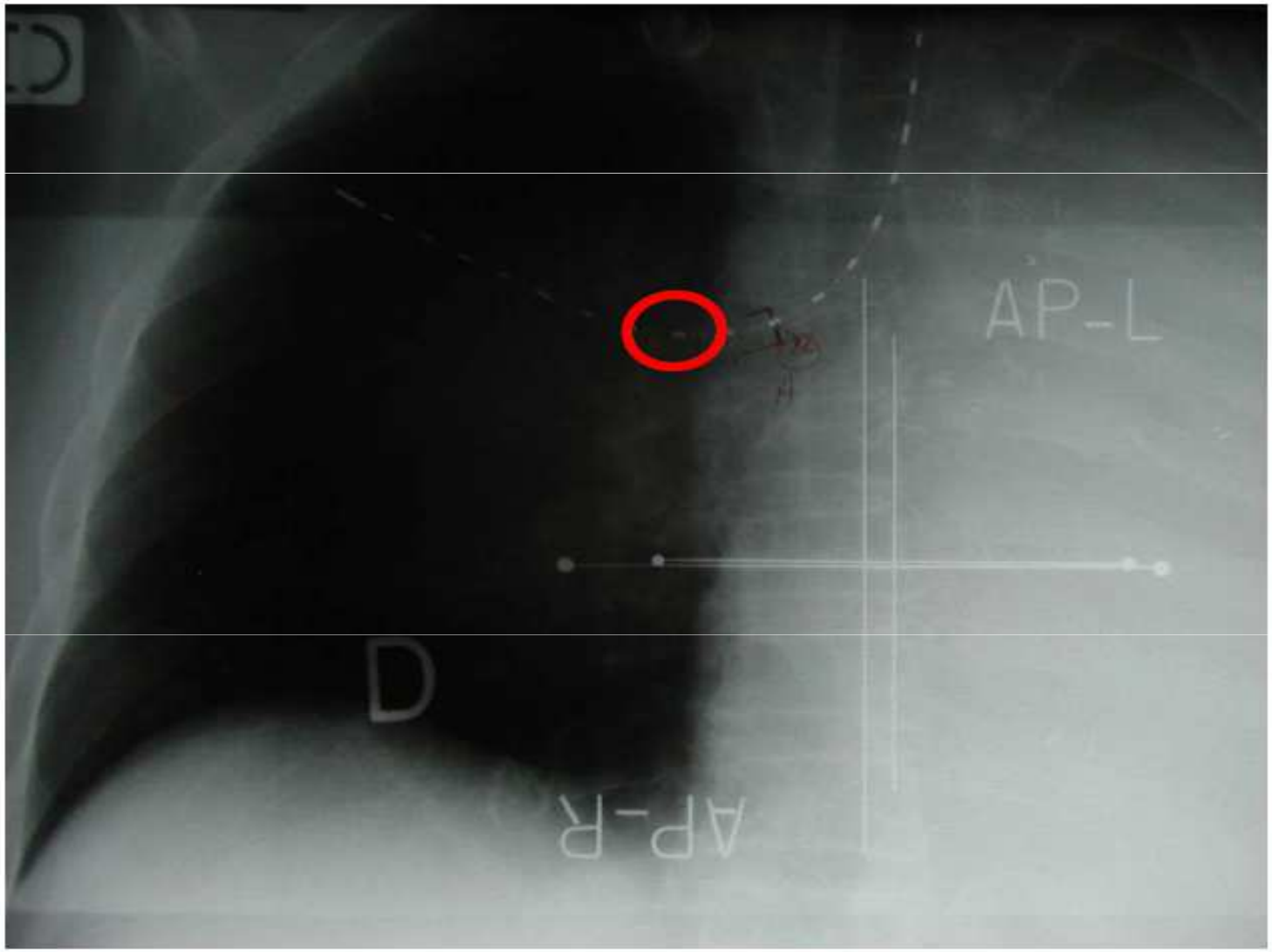
Localisation of the target

Catheter
+
X Rays



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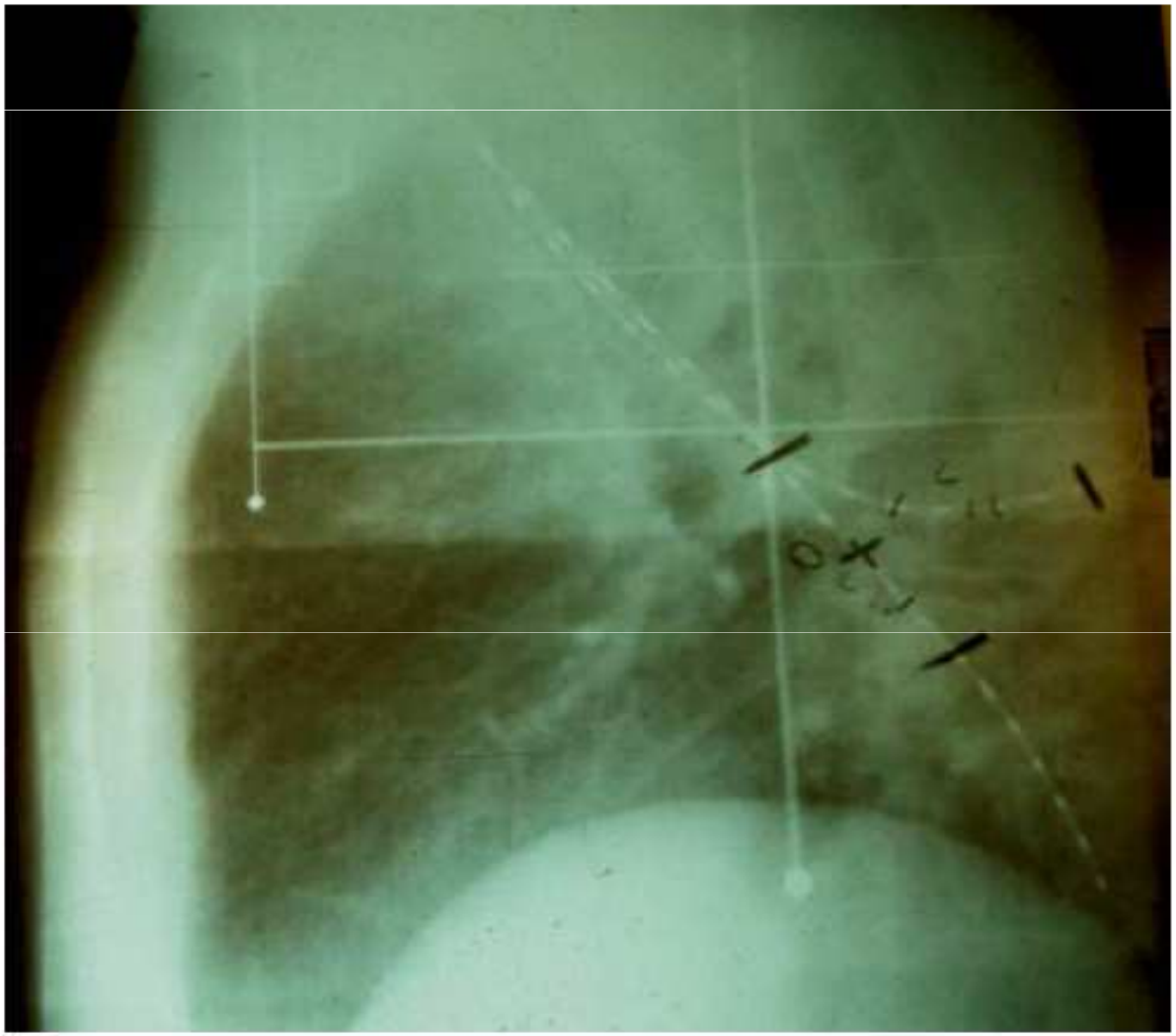
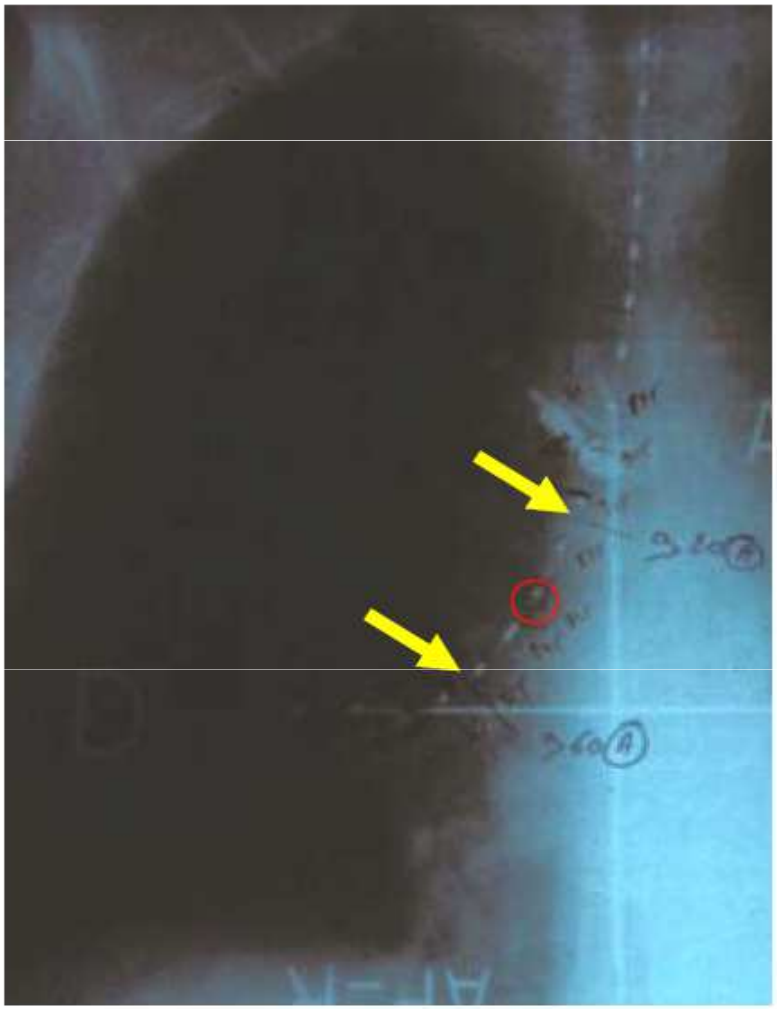
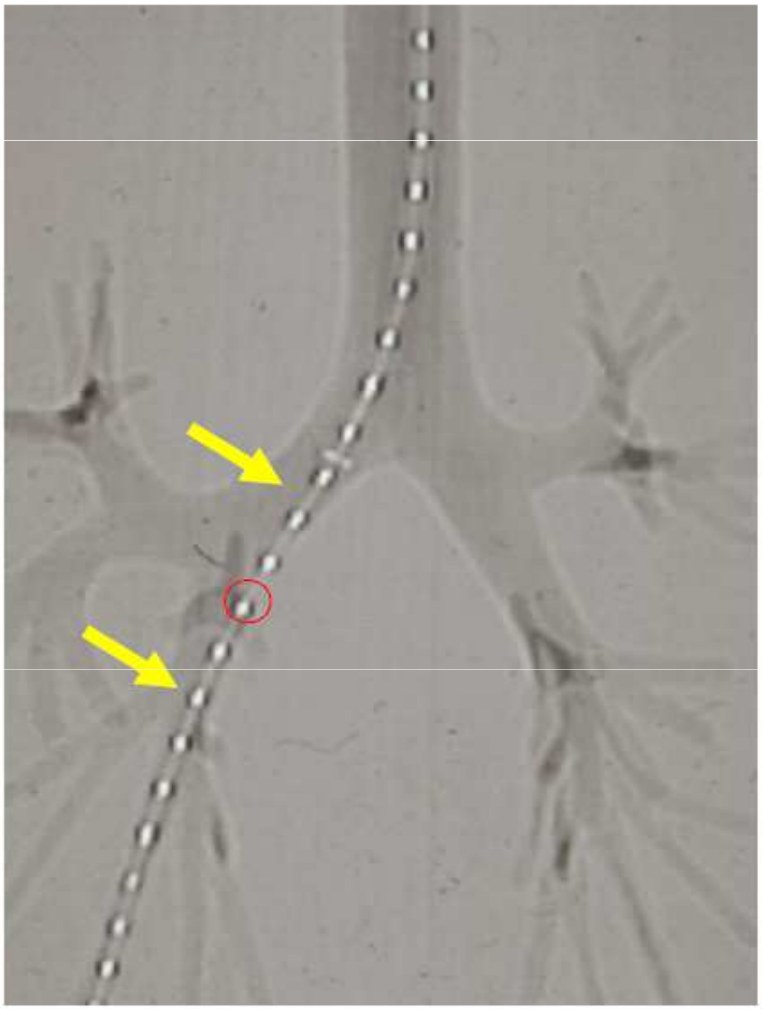
Lateral



Target PTV = GTV + 2 cm





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Treatment Planning, Dose Calculation

- **Determination of the Target length** on radiograph (e.g. 2 cm beyond GTV)
- **Dose prescription** at a certain depth (1 cm or >)
- **Dose recording**
  - Dose at 5 mm from applicator surface
  - Dose at applicator surface

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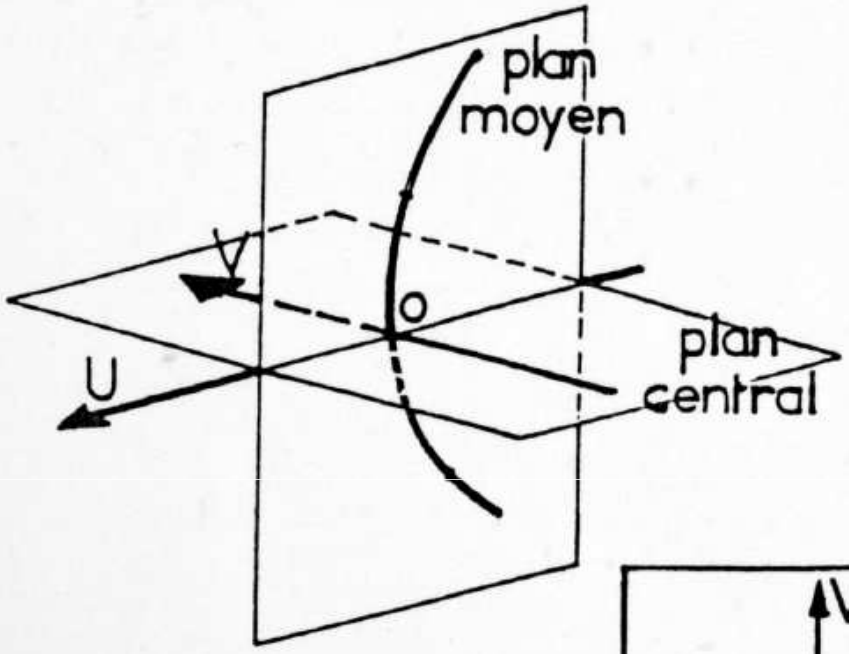
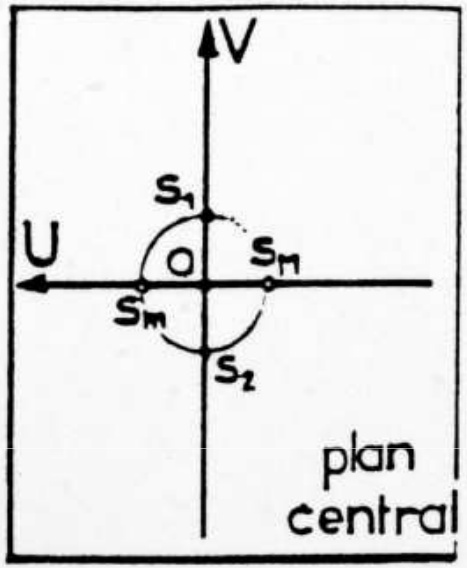
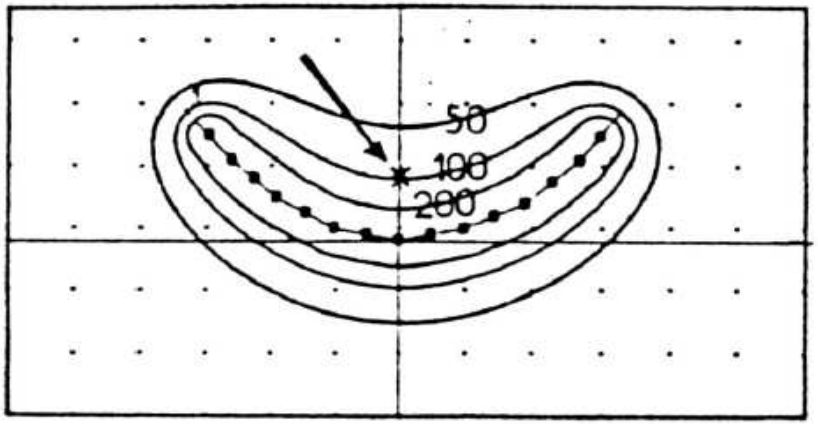




$$D_S = \frac{D_{S1} + D_{S2}}{2}$$

D_{SM} :

D_{Sm} :

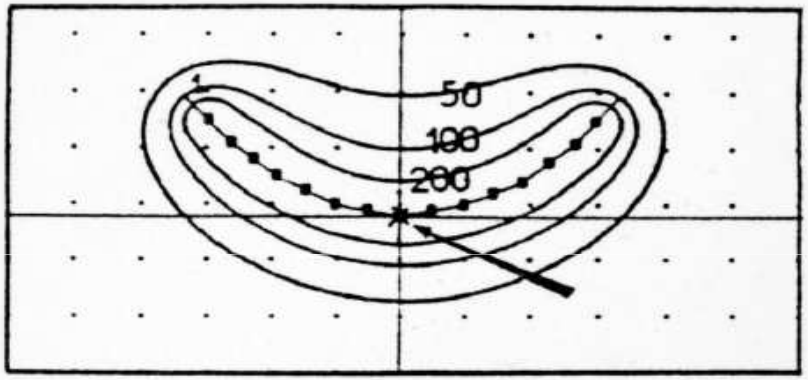


0.22884 cGy*m^-2
on: 5.0 mm

D_S = 82

V_{D_S} : 16,8
V_{20_3} : 5,0

D_{SM} :100 D_{Sm} :70,5
optimisation non
oui
standard
autre



0.25257 cGy*m^-2
on: 5.0 mm

D_S = 100

V_{D_S} : 20,0
V_{20_3} : 5,9

D_{SM} :122 D_{Sm} :86
optimisation non
oui
standard
autre

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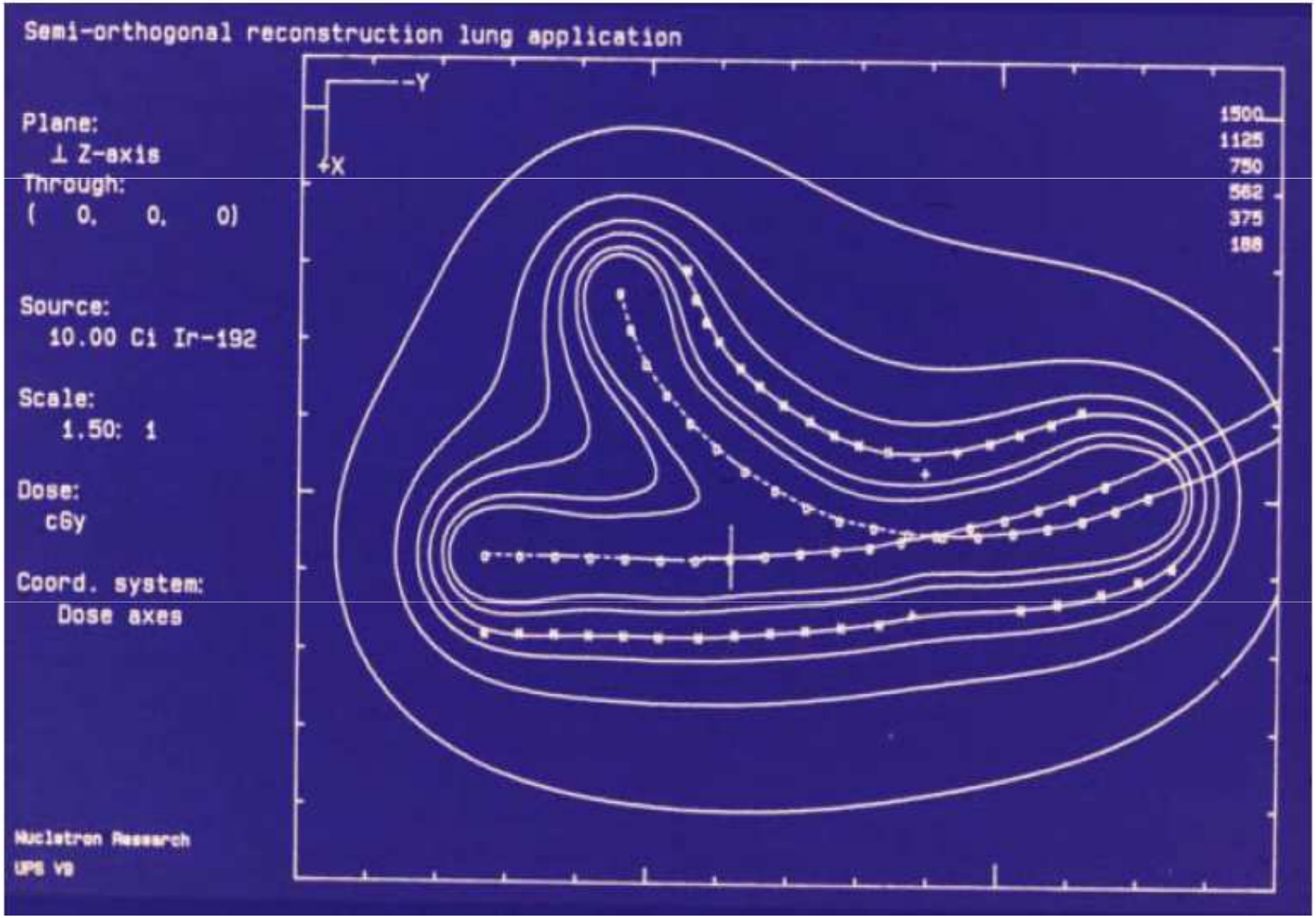
Dose prescription at 1 cm :
= dose at 1.5 cm from the forque



Marinello et al

ESTRO School

Dose and Fractionation

- HDR prefered because of patient´s comfort (coughing)
- Dose per fraction 5-10 Gy at 10 mm
- Total dose of BT dependent on treatment protocol
  - Palliative Brachytherapy alone: 2 to 4 fractions
  - BT after EBT ~ 2 fractions at 5-7 Gy

ESTRO School

Acute Side effects

- Coughing : +++
- Cardiac arrythmia, hypotension (cardiac arrest)
- Bronchospasm
- Pneumothorax : +++ chest X-Rays control
- Massive Bleeding

ESTRO School

Respons to Treatment

- Partial Remission 101/188 (54%)
- Minor Response 25/188 (13%)
- No change 29/188 (16%)

Macha et al. 1990

ESTRO School

Symptoms improvement

Manchester Christie Hospital

(Stout 1998)

- Dyspnea: 52-61%
- Cough 55-63%
- Pulmonary collapse 43-69%
- Haemoptysis 87-96%

Overall Symptom improvement in 60-70%

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Late Side Effects (Treatment/Tumour related)

- Radiation Bronchitis (5-10%)
- Bronchial Stenosis (<5%)
- Haemoptysis (up to 20%)
- Fistula (arteries, oesophagus) ~ 5%

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Late side effects Palliative

	Sutejda	Zajac	Gollins
Treatment	1-3 X 10Gy	1-5 X 5-10Gy	1 X 15-20Gy
Intention	Palliat	Palliat	Palliat
Bleeding	32.3%	1.2%	7.9%
PNO			
Stenosis			
Fistula		2.4%	0
Infections / Abcedation			

Fatal bleeding

Related to

tumor progression

Length of treated area

Not to fraction size or EBRT

Hennequin et al 1998

Related to total dose

- **60 Gy EBRT + 2*4.8 Gy HDR : 18.9%**
- **60 Gy EBRT : 14.2%(p= 0.53)**

Huber et al 1997

ESTRO School

Indications BT in lung ca (2)

2-CURATIVE INTENT

- EBRT and BT boost
- bronchial stump recurrences
- positive resection margins

BT alone for small Tumours

- T1(-T2) or *in-situ*
- N0
- Deep infiltration < 1 cm

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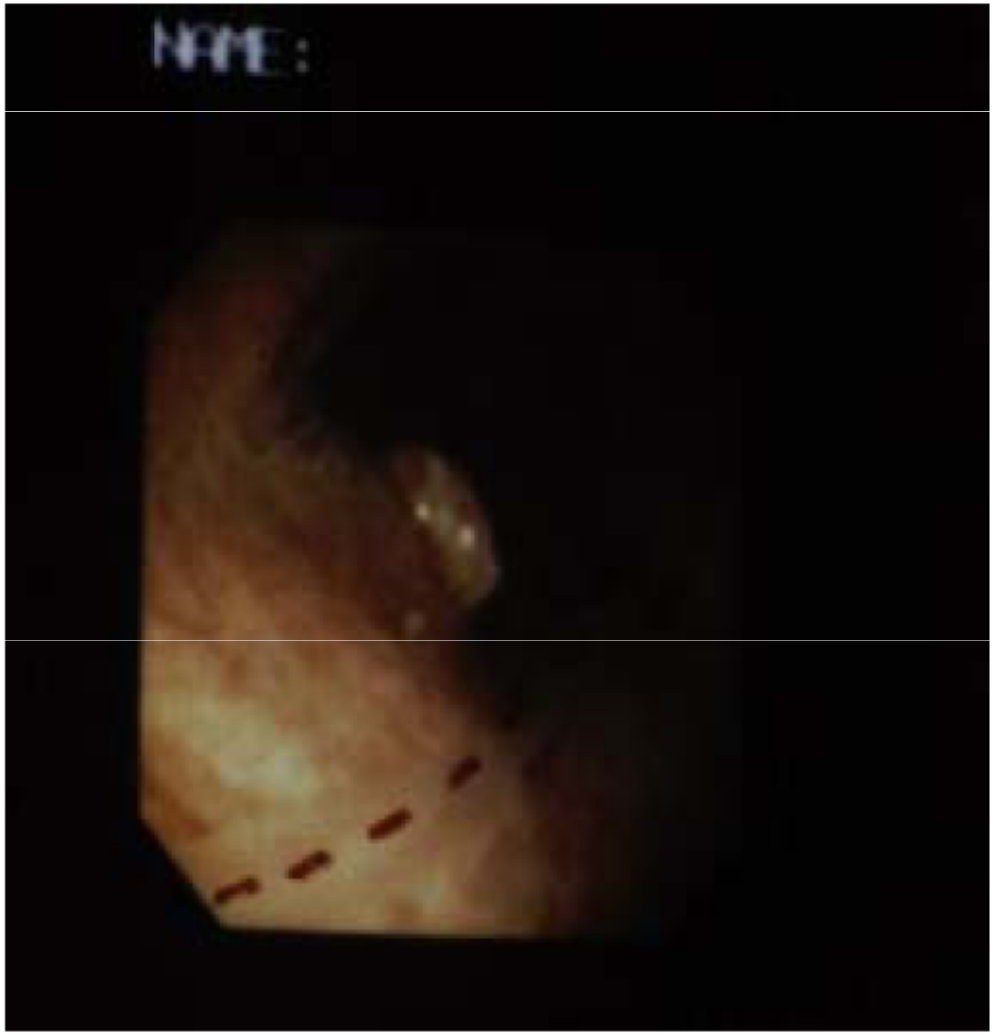
Benefits of brachytherapy

- High dose
- Small volume
- Conformal treatment
- Sparing the normal lung tissue
- Mobile with breathing
- Minimises functional consequences

ESTRO School

Small tumors



Curative intent results

	#pts	Dose/fr	local Control	Survival @ years
Speiser	151	3 x 7.5Gy / 5-10mm	80%	
Trédaniel	29	6 x 7Gy / 10mm	72%	55% @ 2
Hennequin	69	6 x7Gy / 10mm	78%	51% @ 3
Taulelle	22	3-4 x 8-10Gy / 10mm	95.5%	71% @ 1
Pérol	19	3-5 x 7Gy / 10mm	83%	58% @ 2
Marsiglia	34	6 x 5Gy / 10mm	94%	78% @ 2
Peiffert	35	6x 5Gy / 10mm	94.3%	54% @ 2

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Late side effects Curative BT

	Trédaniel	Taulelle	Pérol	Marsiglia	Peiffert
Treatment	6 X 7Gy	3-4 X 8-10Gy	3-5 X 7Gy	6 X 5Gy	6 X 5Gy
Intention	Curative	Curative	Curative	Curative	Curative
Bleeding	3.5%	6.9%	10.5%	2.9%	0
PNO	0	0.5%	5.3%	2.9%	3%
Stenosis		6.3%	66.6%		36.6%
Fistula		1.6%			
Infections / Abcedation	4.3%				18.3%

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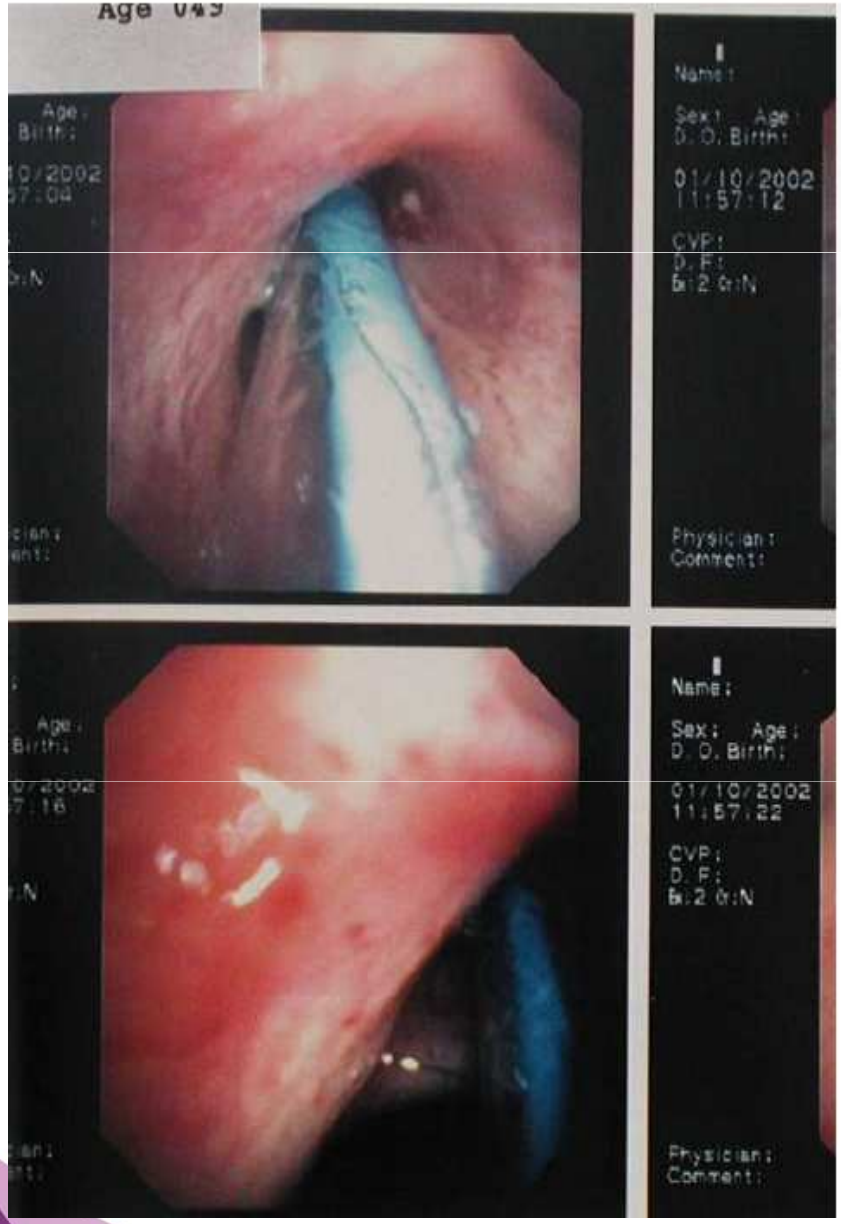
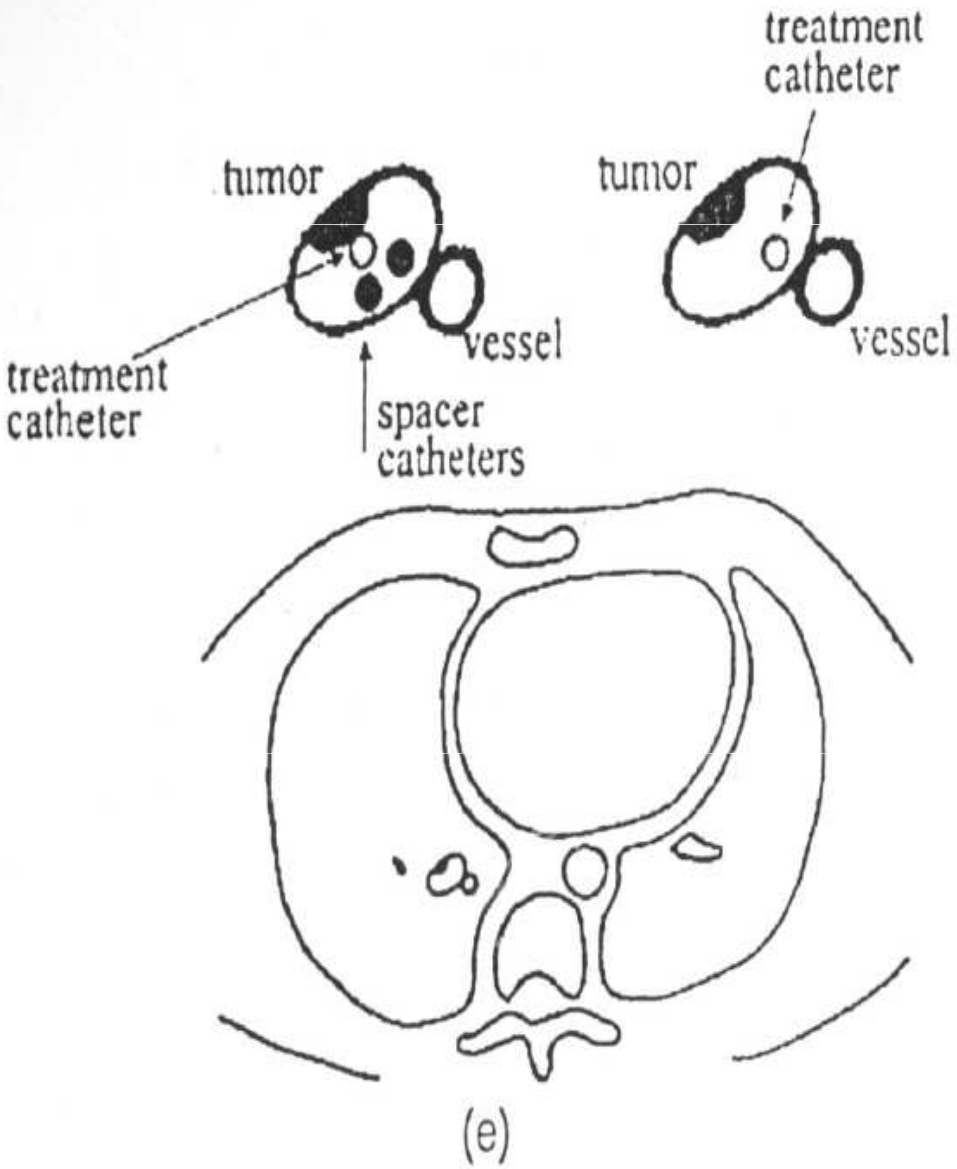
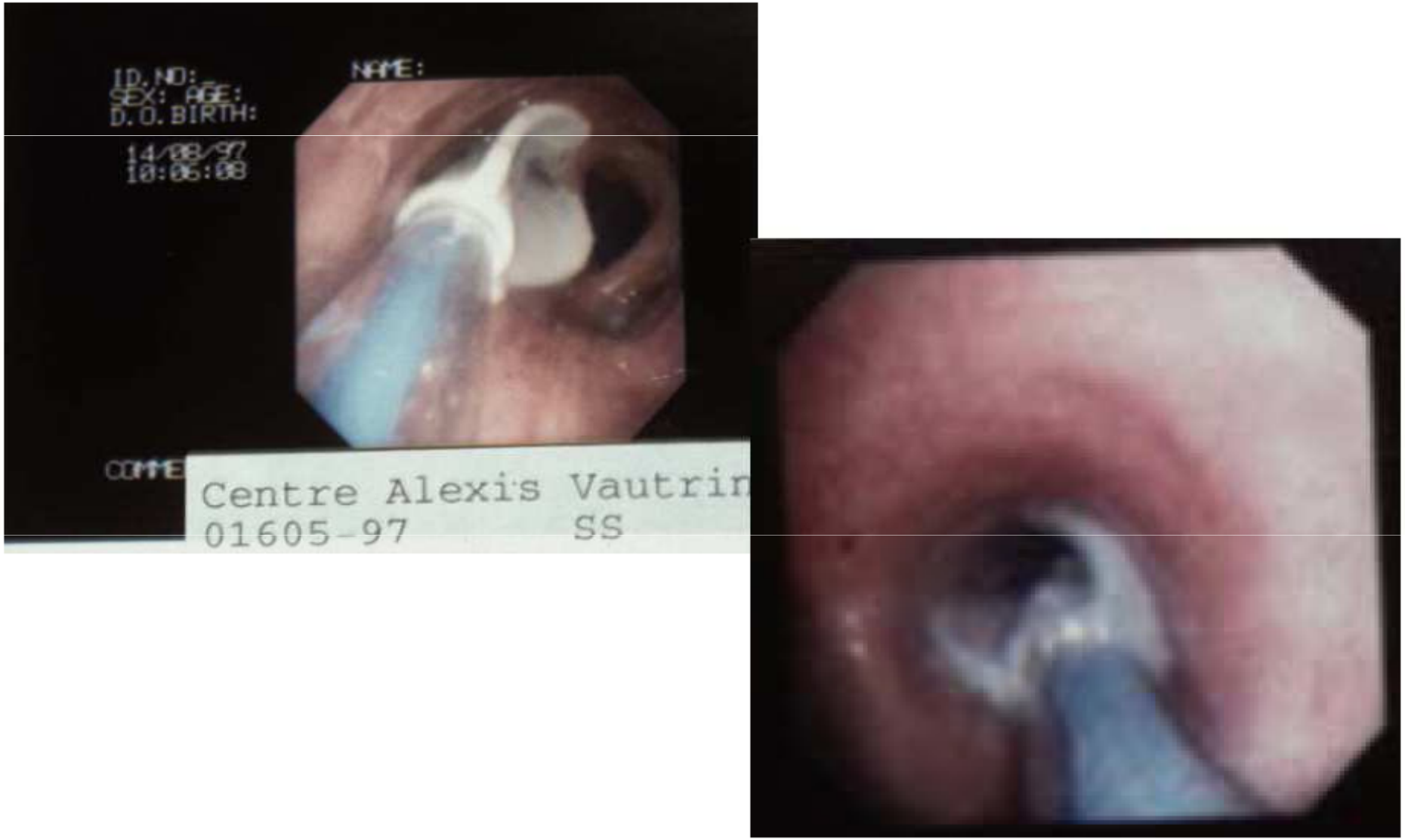
Description / spacer

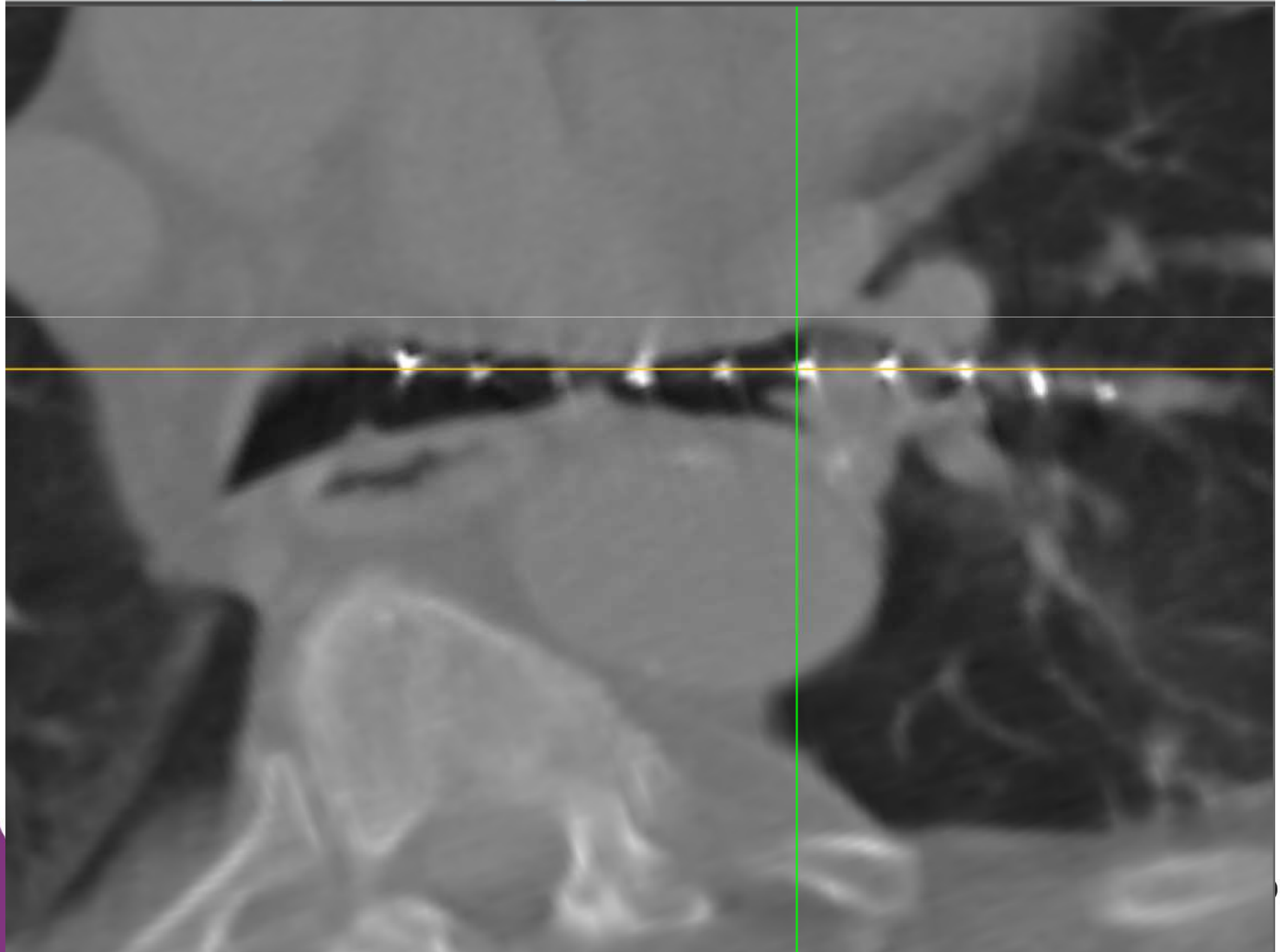


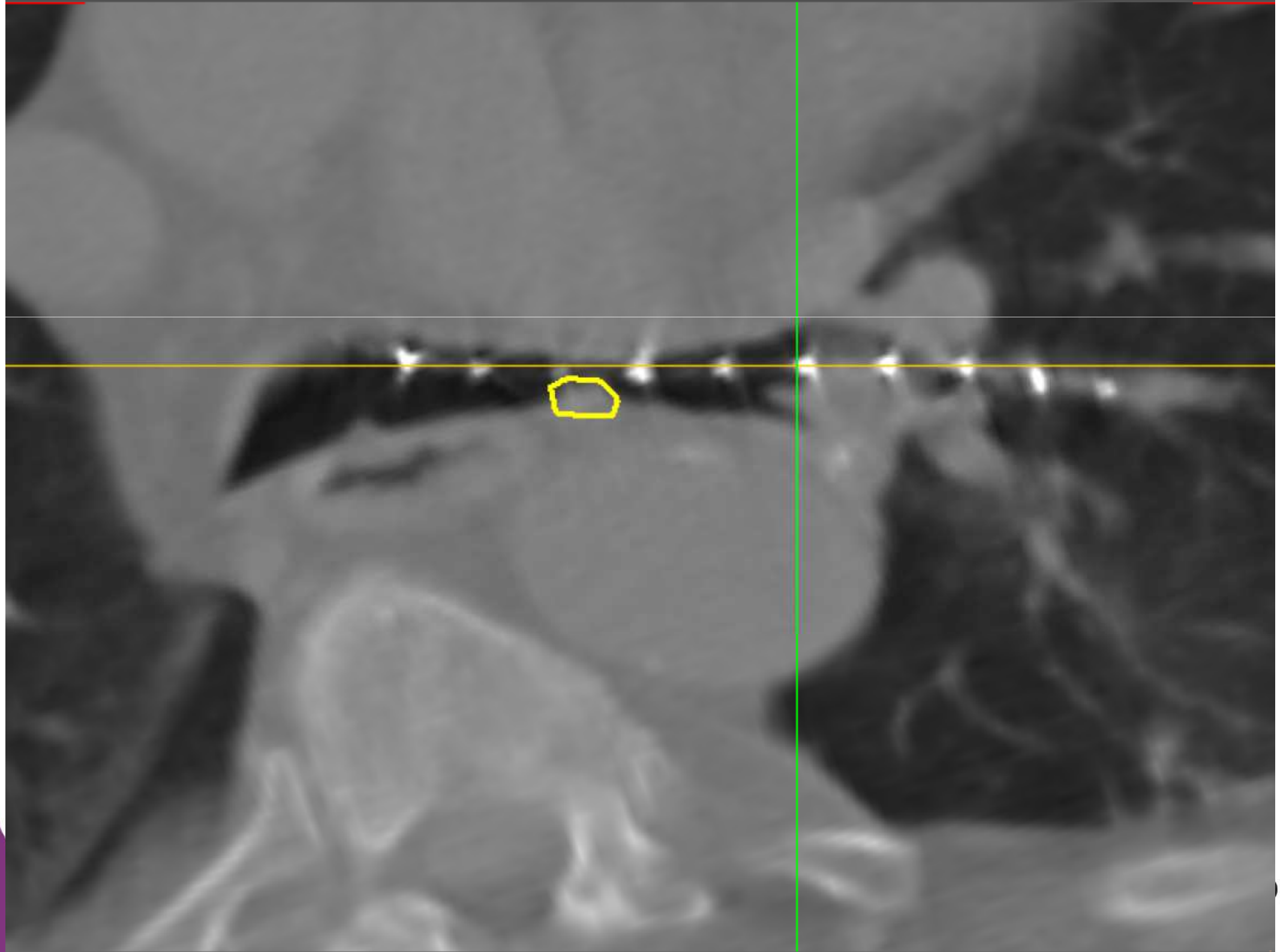


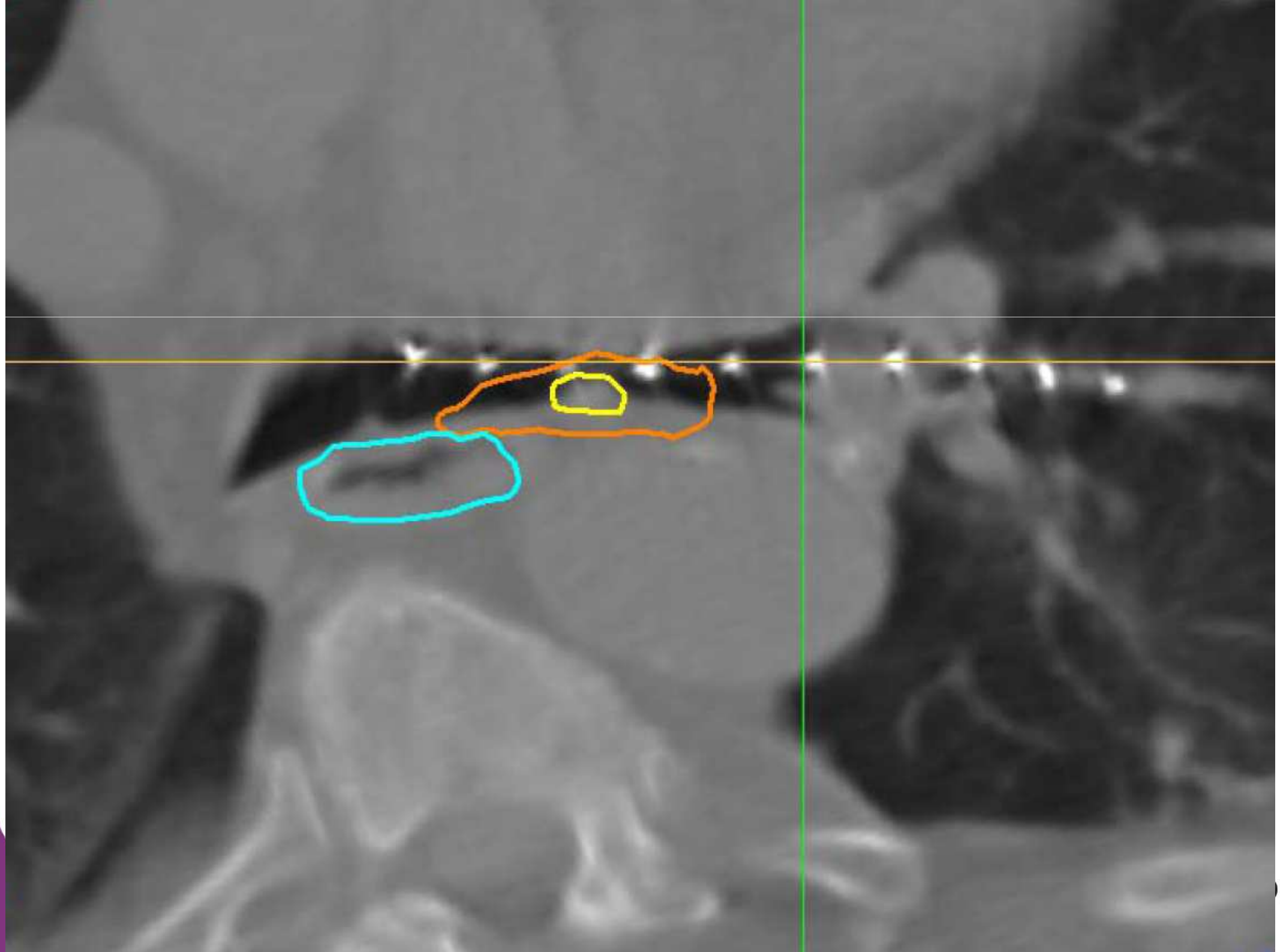
Technique

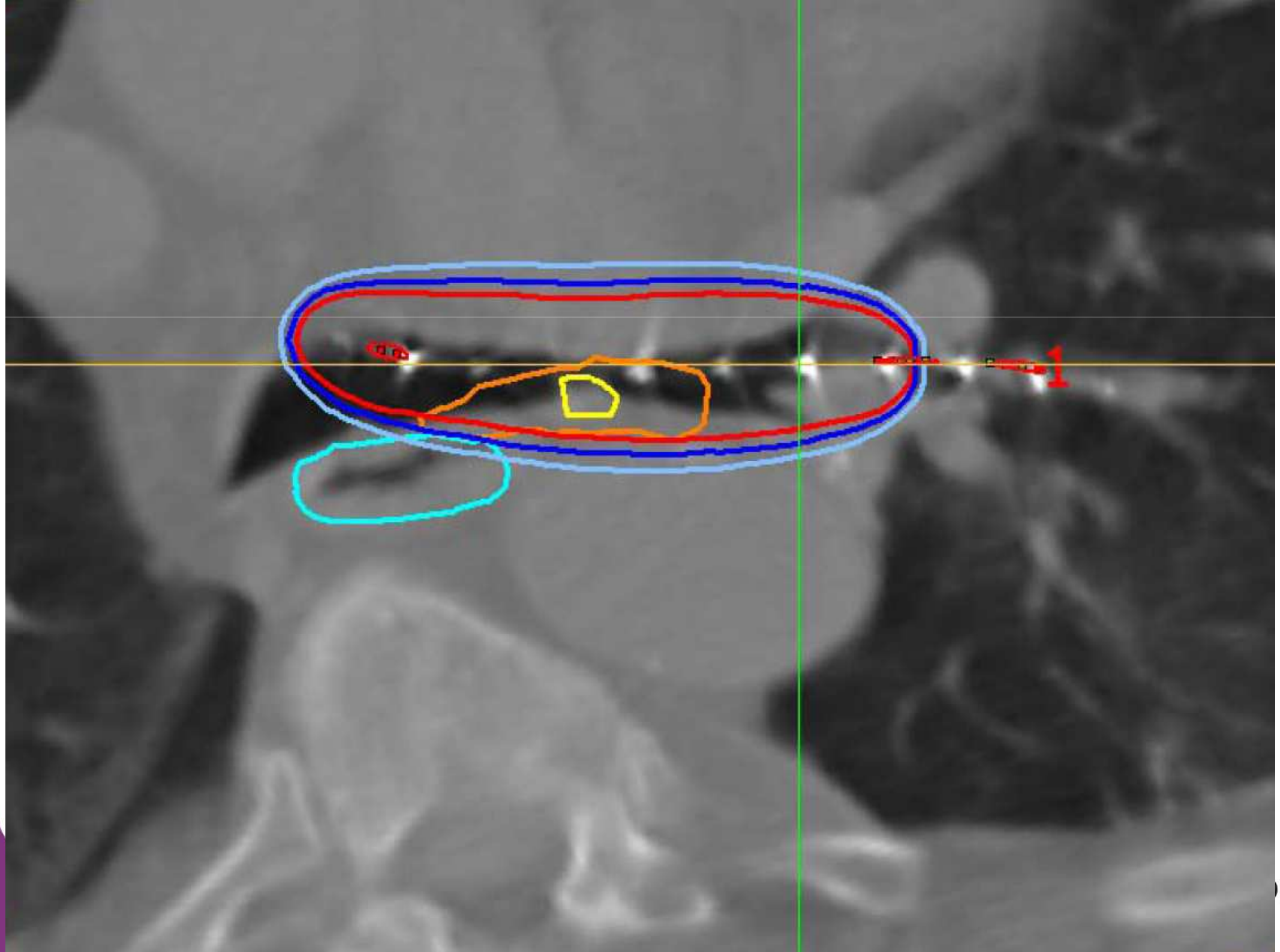
Centering system



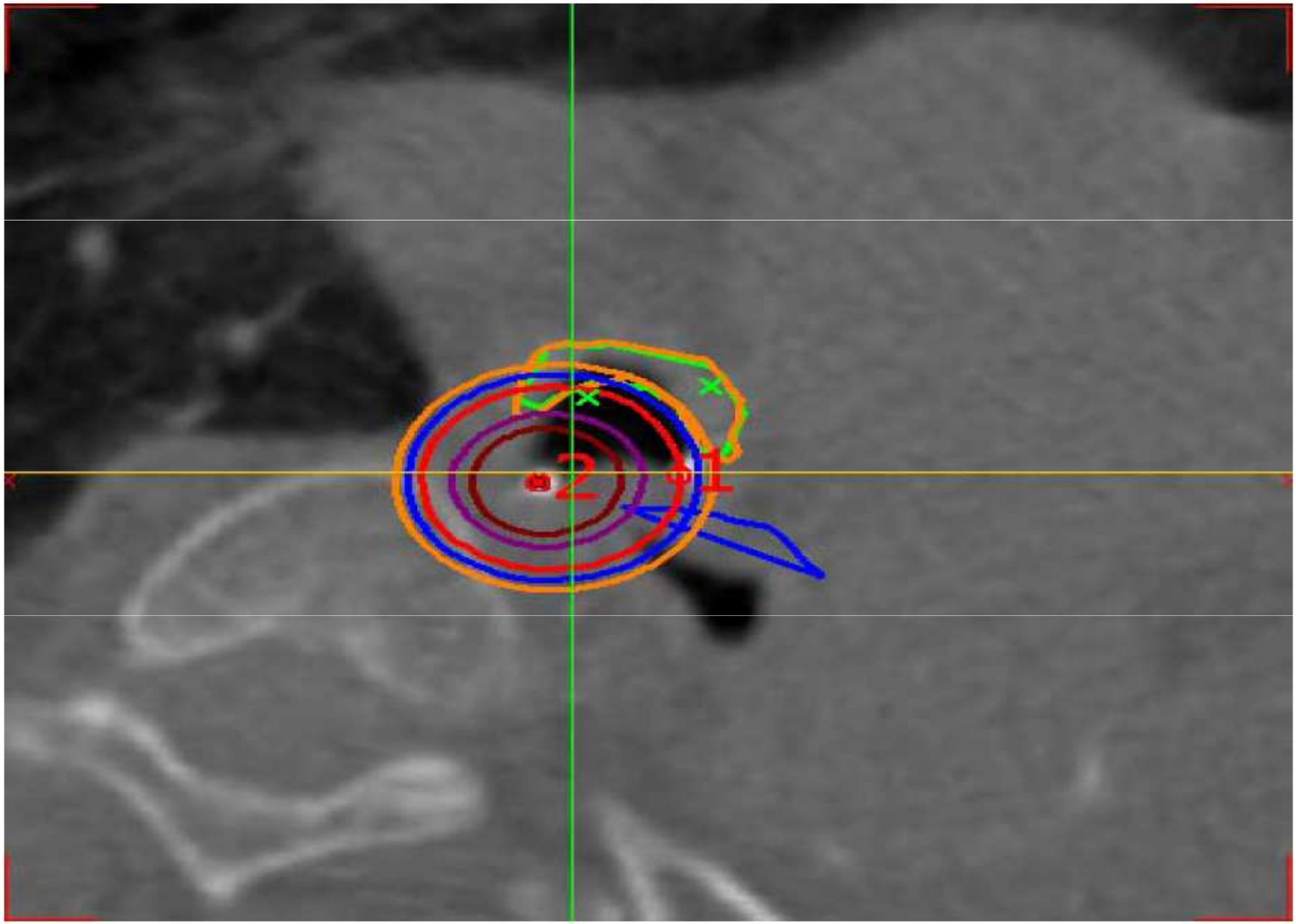







1

Een catheter 6 Gy op 1 cm



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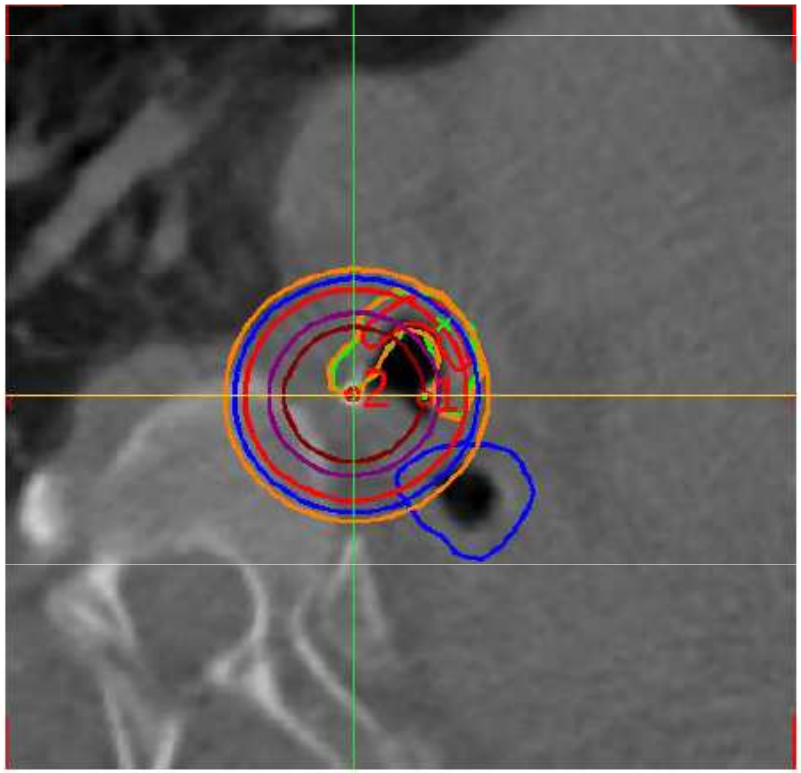
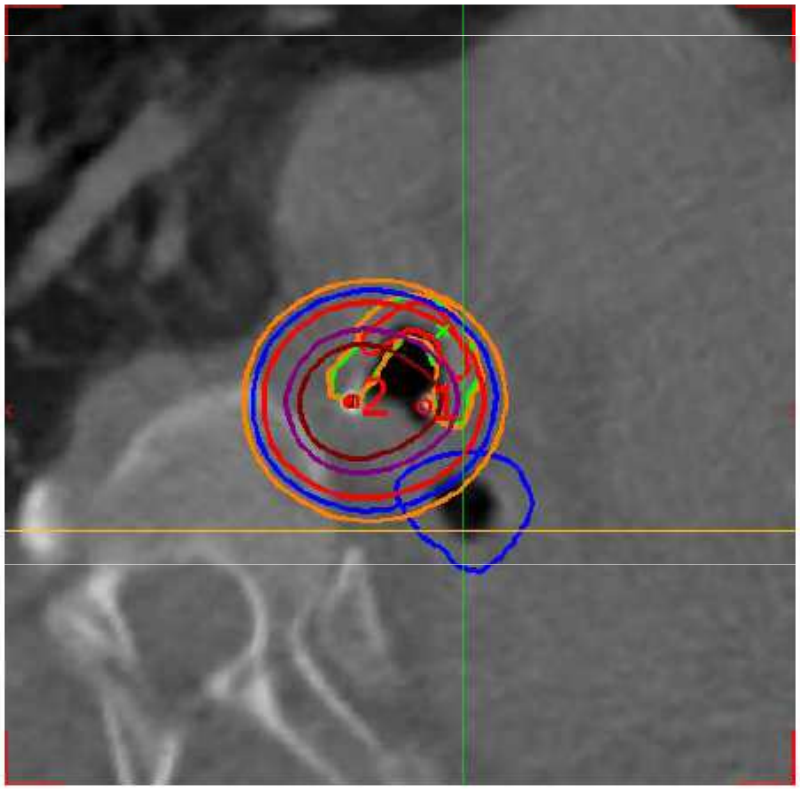
10 Gy GTV

1 catheter 8 Gy CTV 2 catheters

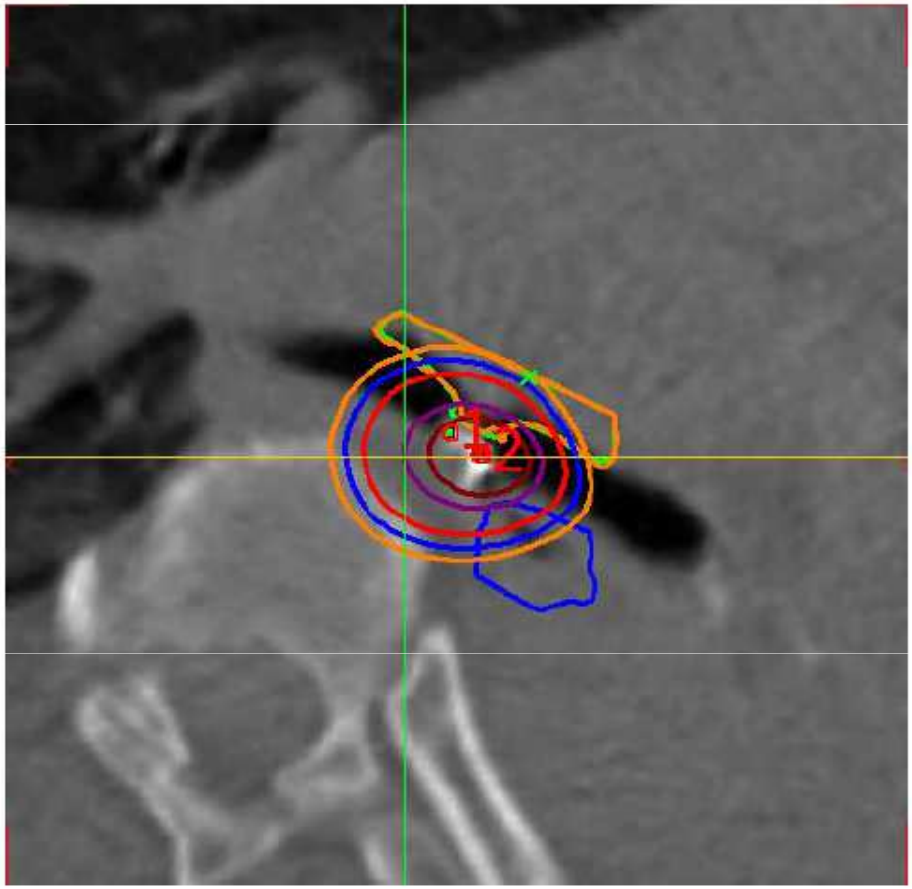


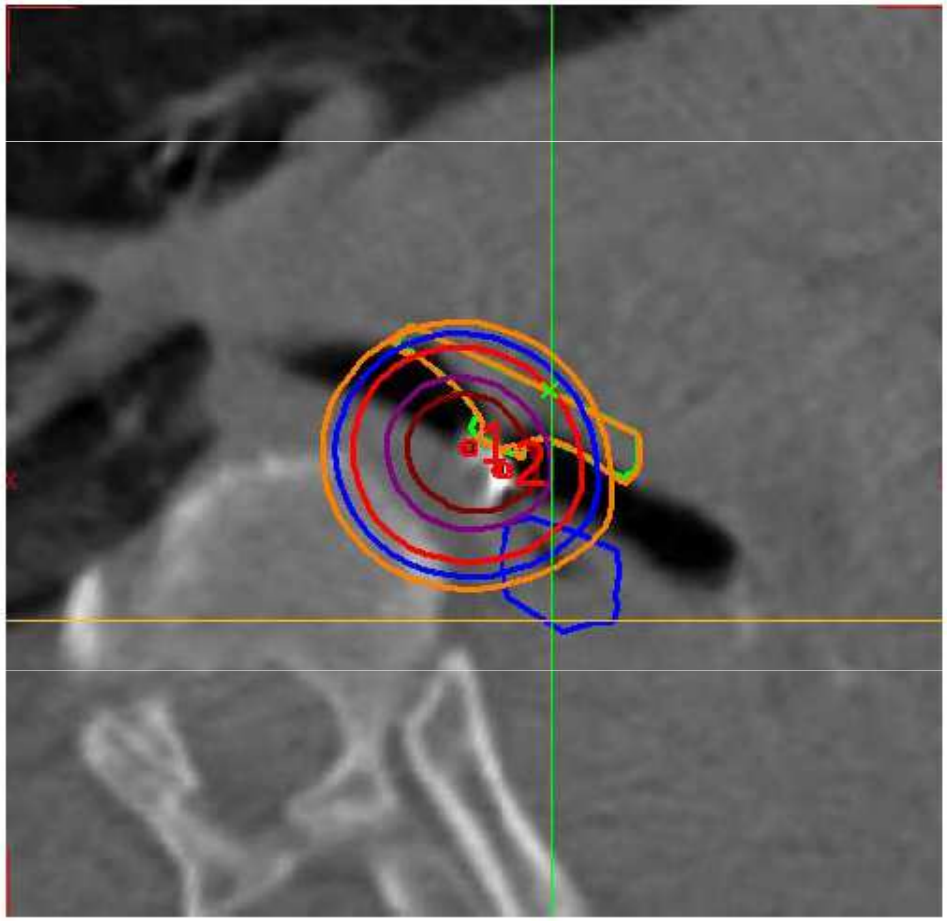


Slokdarm 2cc < 6,5 Gy

10 Gy GTV

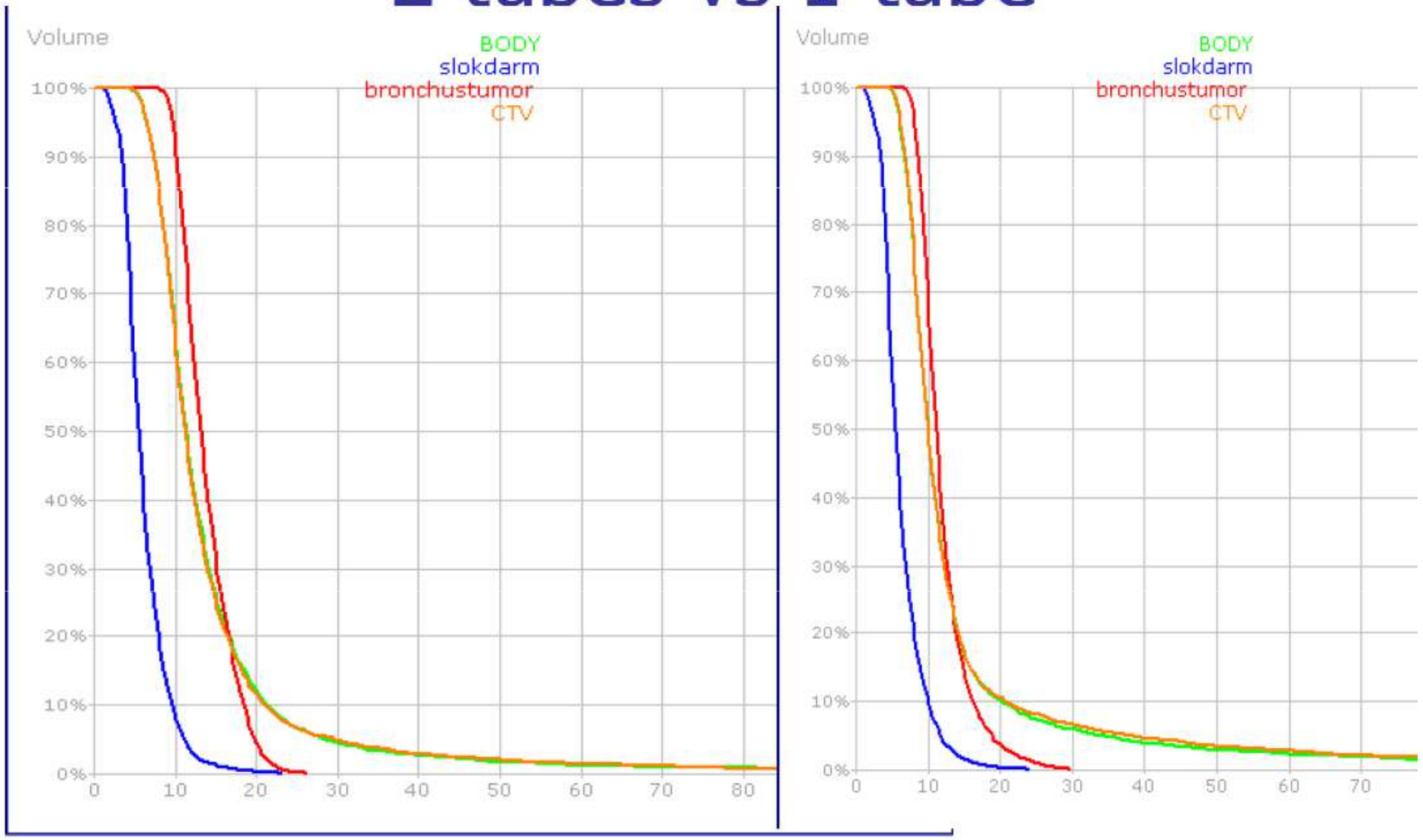
1 catheter 8 Gy CTV 2 catheters





2cc Slokdarm < 6.5 Gy

3D conformal
2 tubes vs 1 tube



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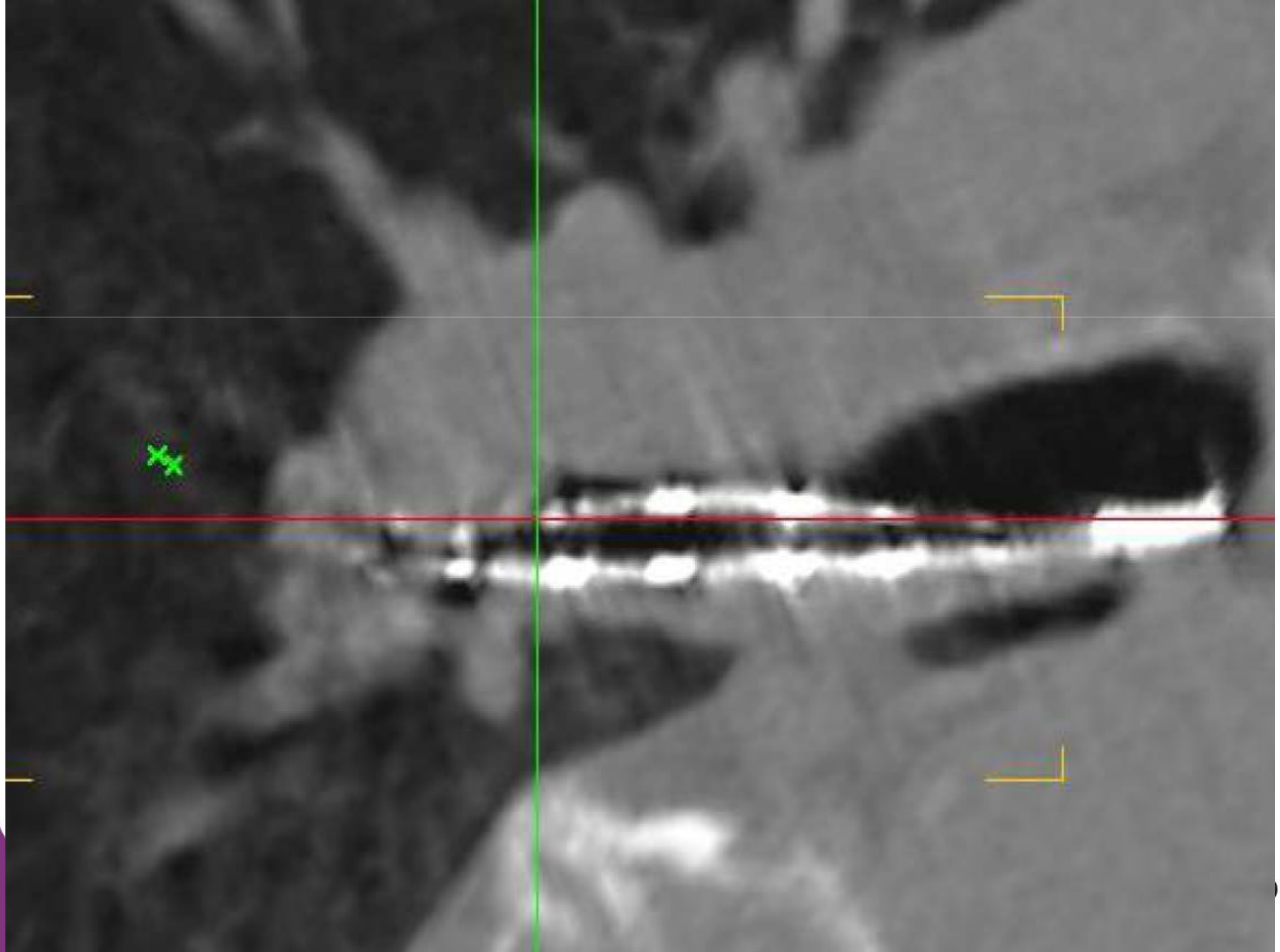

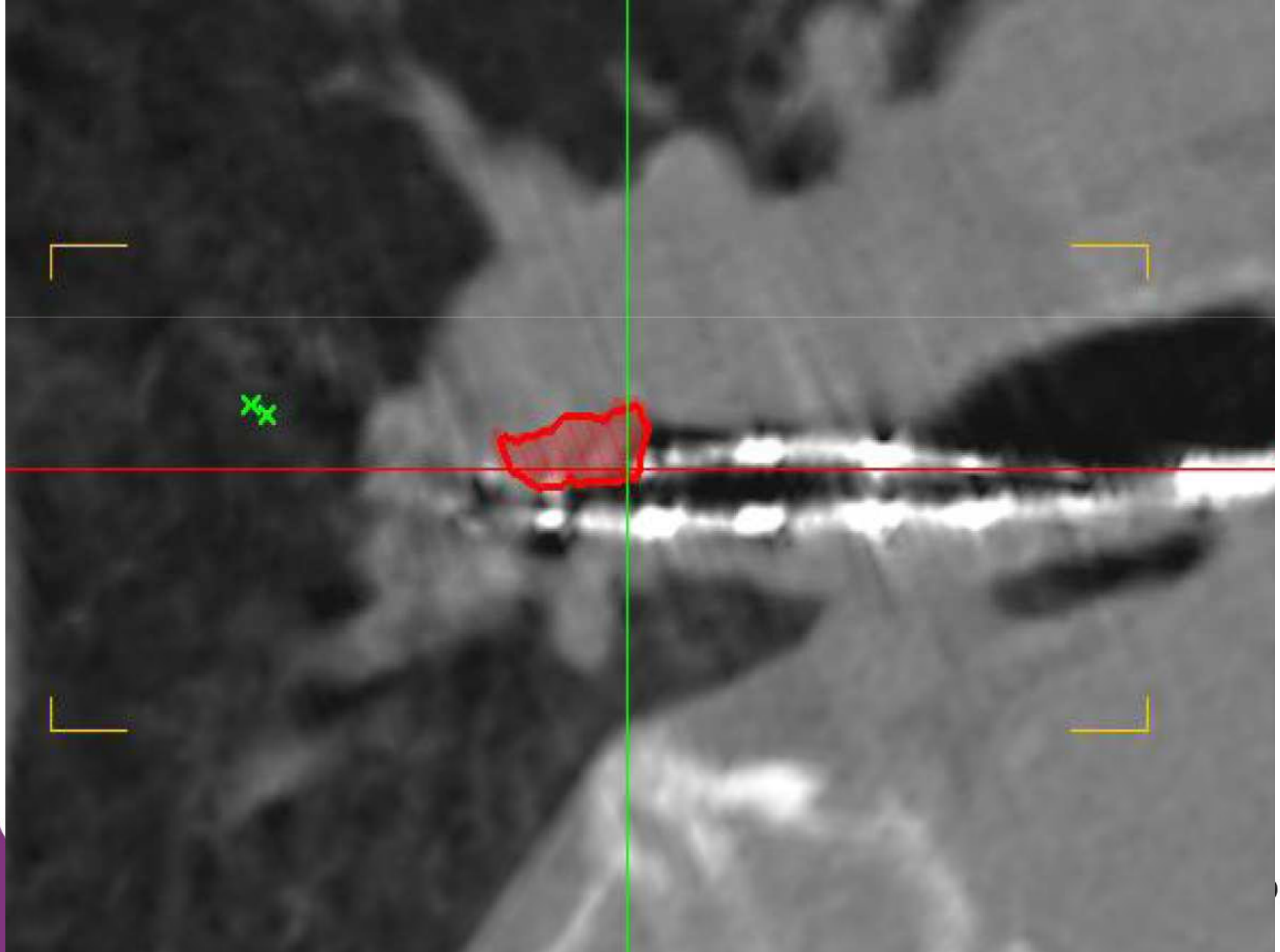

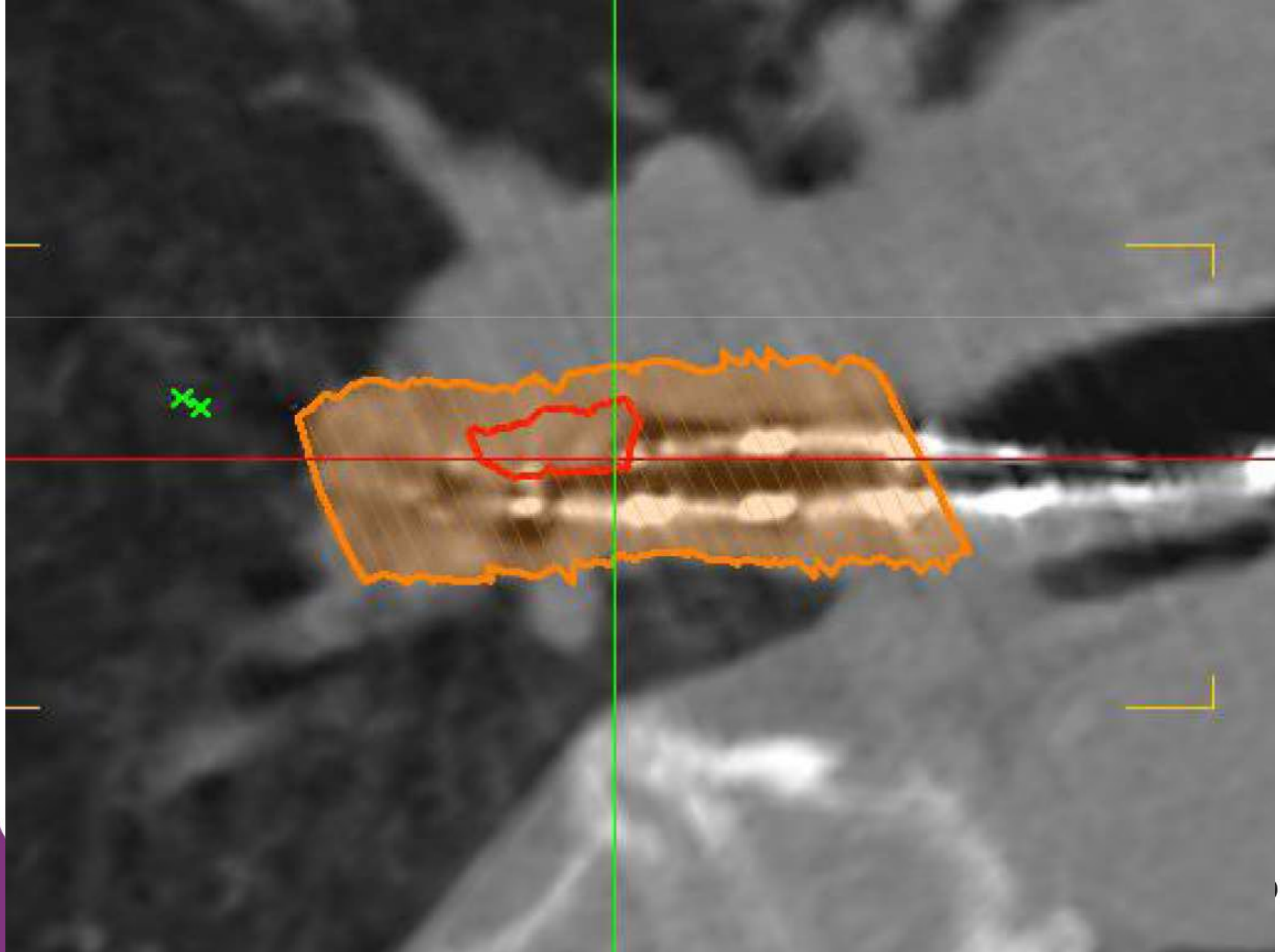

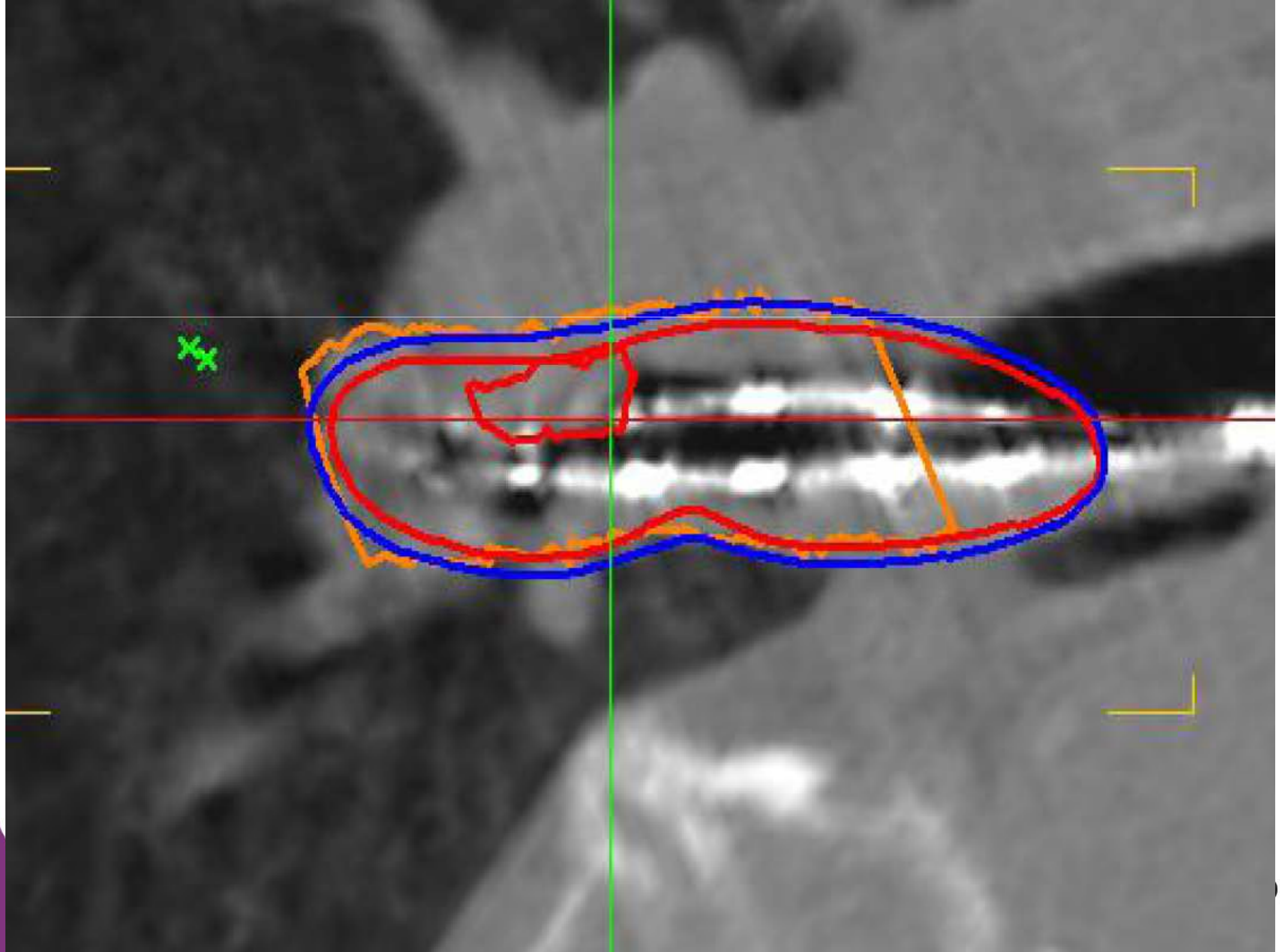

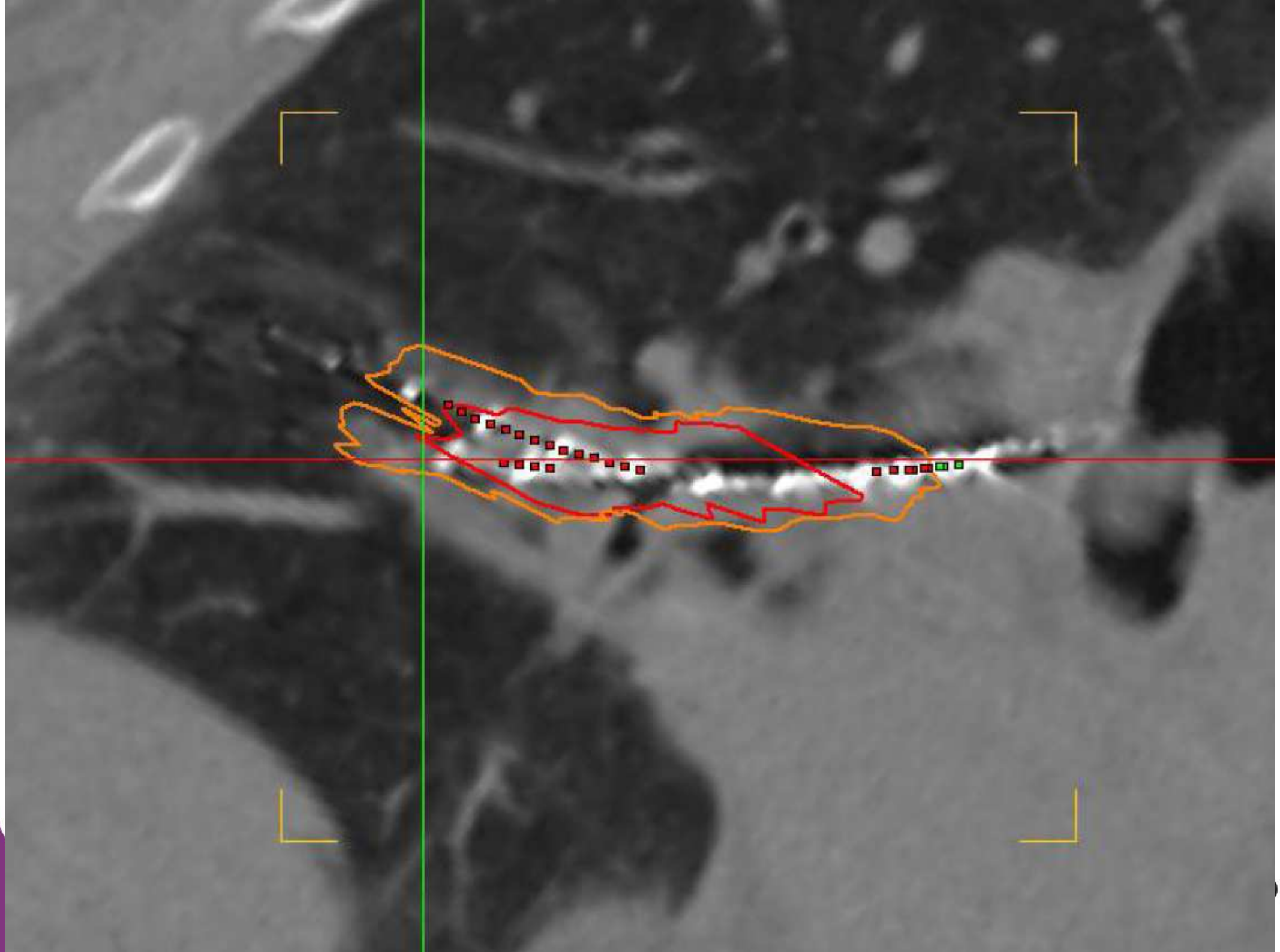

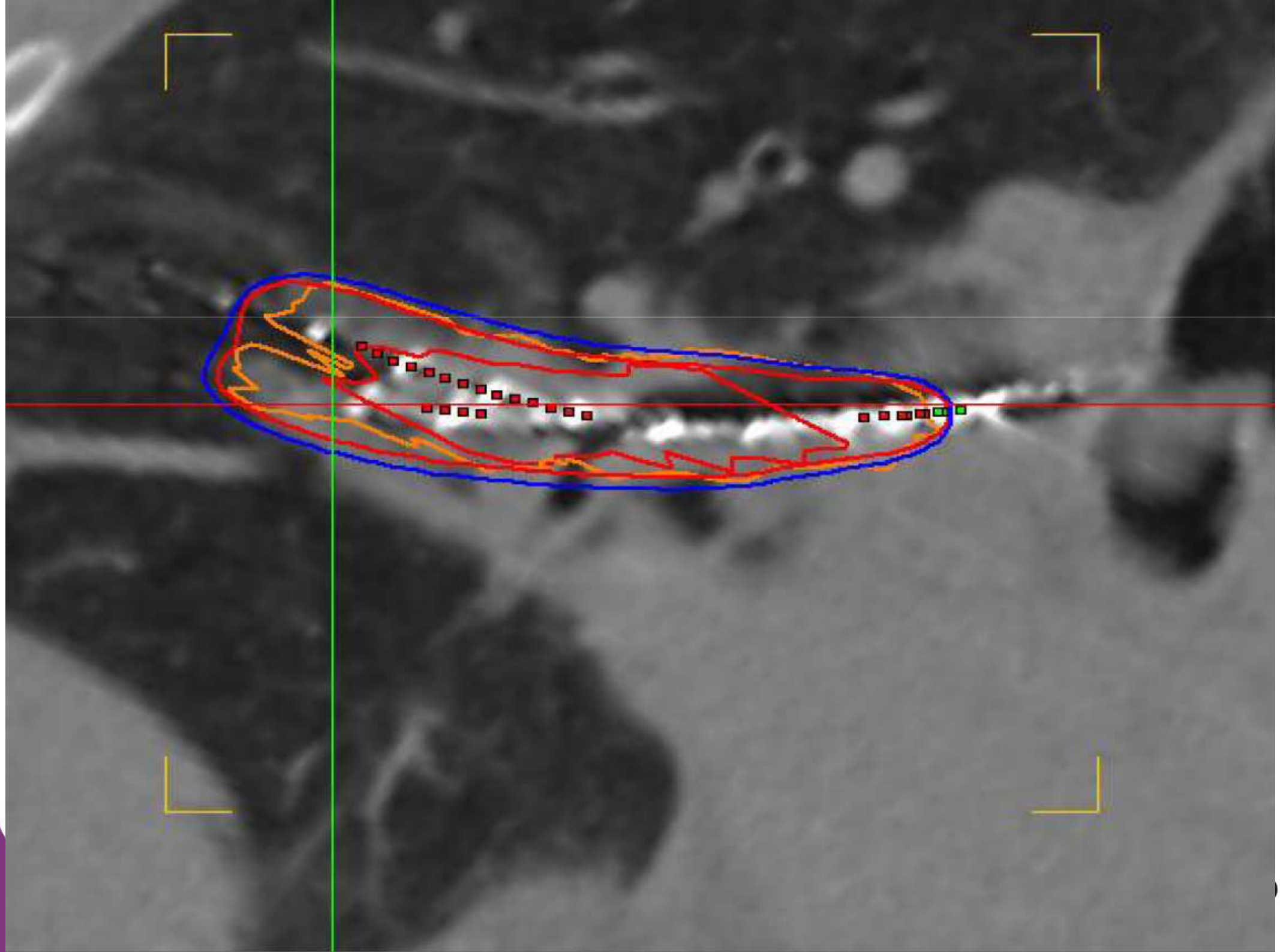

UZL series Bronchusca
3 D Image Guided BT

PT	n F	tubes	Dose@1cm	D90 GTV	D90 CTV	D 2cc EF
NC	5	1	6	14,5 (9.5-19,5)	6,7(6,1-7,4)	4,5(4,1-5)
VW	5	1	7,1 (6-8)	13,4 (10,2-17,4)	8,3 (5,9-11,4)	5,'4 (4,15,9)
WH	5	2	6,6 (6-7,7)	13,8 (10,5-15)	8,6 (8-10,3)	2,5 (2,1-3)
KD	2 (B)	2	12,4 (10-13,9)	8,7 (7,3-10,2)	6,4 (5,4-7,3)	6,8 (6,6-7)
BJ	5	2	6,1 (6-6,6)	12,4 (8,2-15,6)	8,3 (7,2-8,9)	0,5(0,4-0,6)

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CONCLUSIONS BRONCHUS BT

- Palliative AND curative
- Good tolerance of the procedure
- Stenosis, bleeding(technical improvements)
- Probably better dose distribution with 3D and double loaded catheters

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Brachytherapy for Esophageal Cancer

ESTRO School

B Pieters
Academic Medical Center / University of Amsterdam

INTRALUMINAL BRACHYTHERAPY IN ESOPHAGEAL CANCER

Early Disease: Neoadjuvant chemoradiation + Surgery or mucosal resection

alternative treatment: EBRT + brachytherapy

Advanced Disease: palliative (chemo-)radiation as EBRT +/- BT or EBRT + BT

Advanced or recurrent disease with luminal obstruction:

Brachytherapy alone

aim: rapid and lasting relief of symptoms from dysphagia

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ESOPHAGEAL ANATOMY

elastic tube: about 25 cm long

transversal section: thumb-like shape
- about 2 cm laterolateral
- about 1 cm ventrodorsal

inner surface „star like“ (irregular)
- folded mucosa
- loose submucosa
- (up to some mm thick)

thin muscle layers

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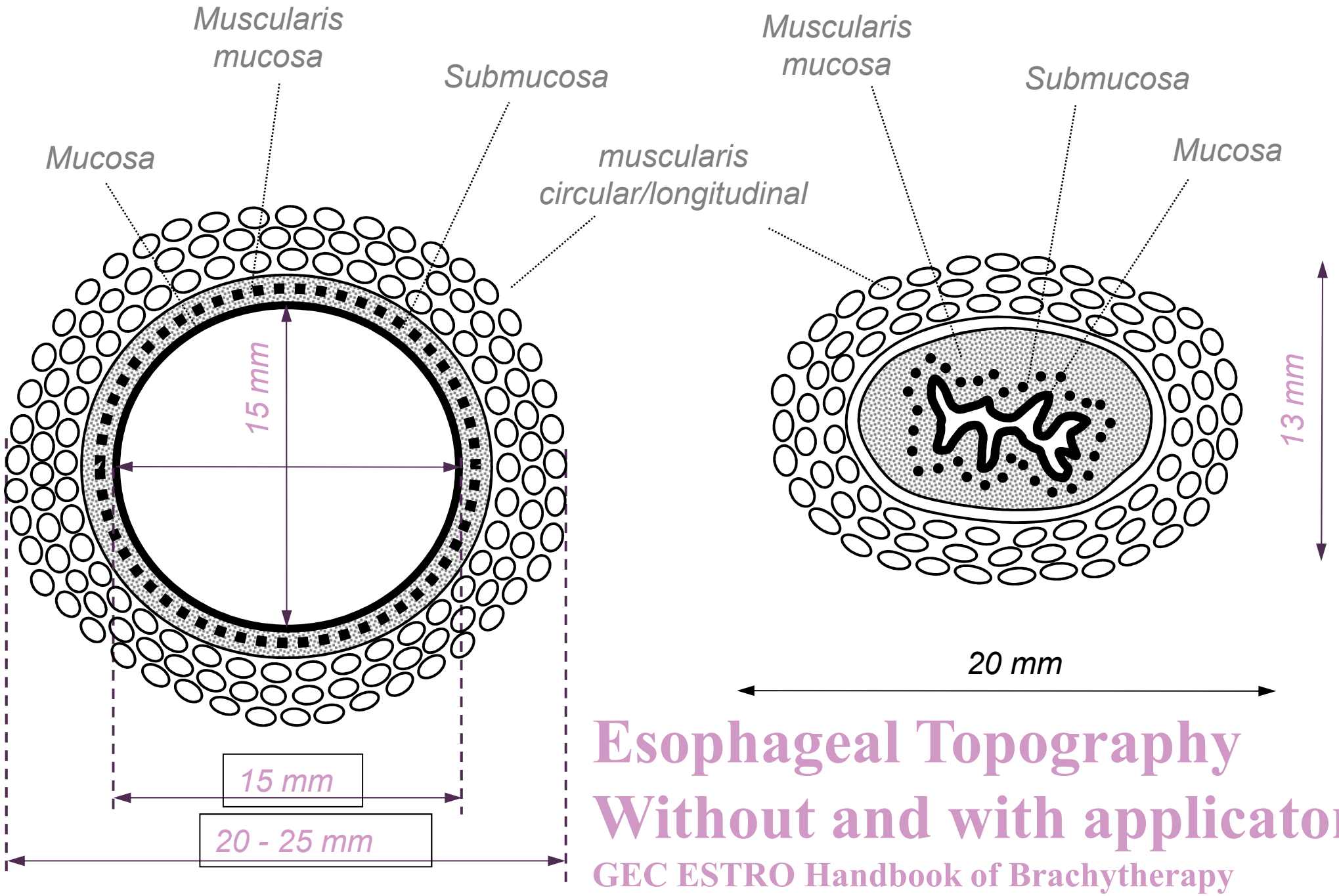

Esophageal Topography Without and with applicator

GEC ESTRO Handbook of Brachytherapy

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Work up

general performance

nutritional status / weight loss

symptoms from dysphagia or pain

physical examination

(chest X-ray)

endoscopy

computed tomography

Endosonography

Ultrasound neck

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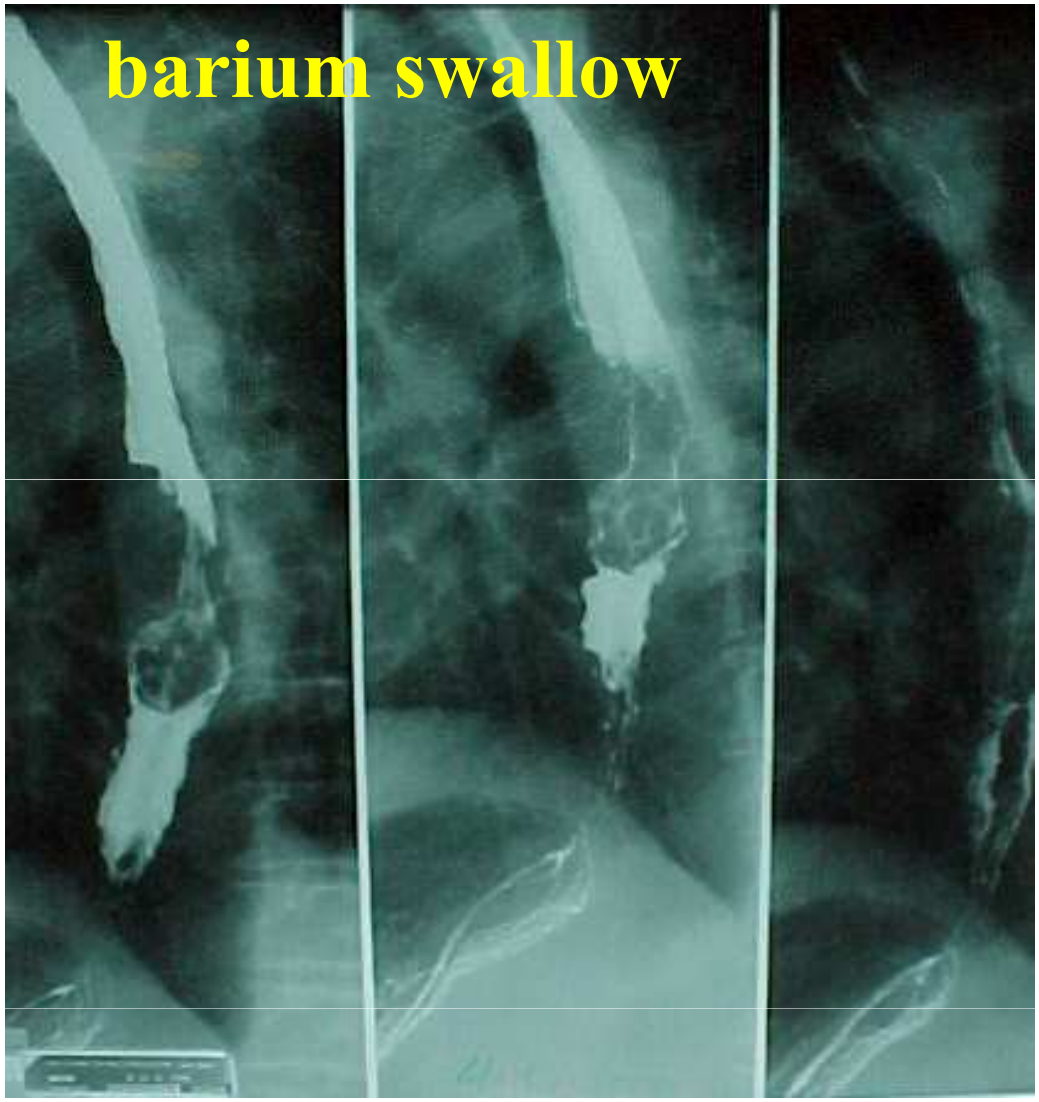

barium swallow

esophagoscopy

endosonography
AMC AMSTERDAM
GE DEPARTMENT
DIST. +1.03cm
ROB G80 C4
1:ENDO

ESTRO School

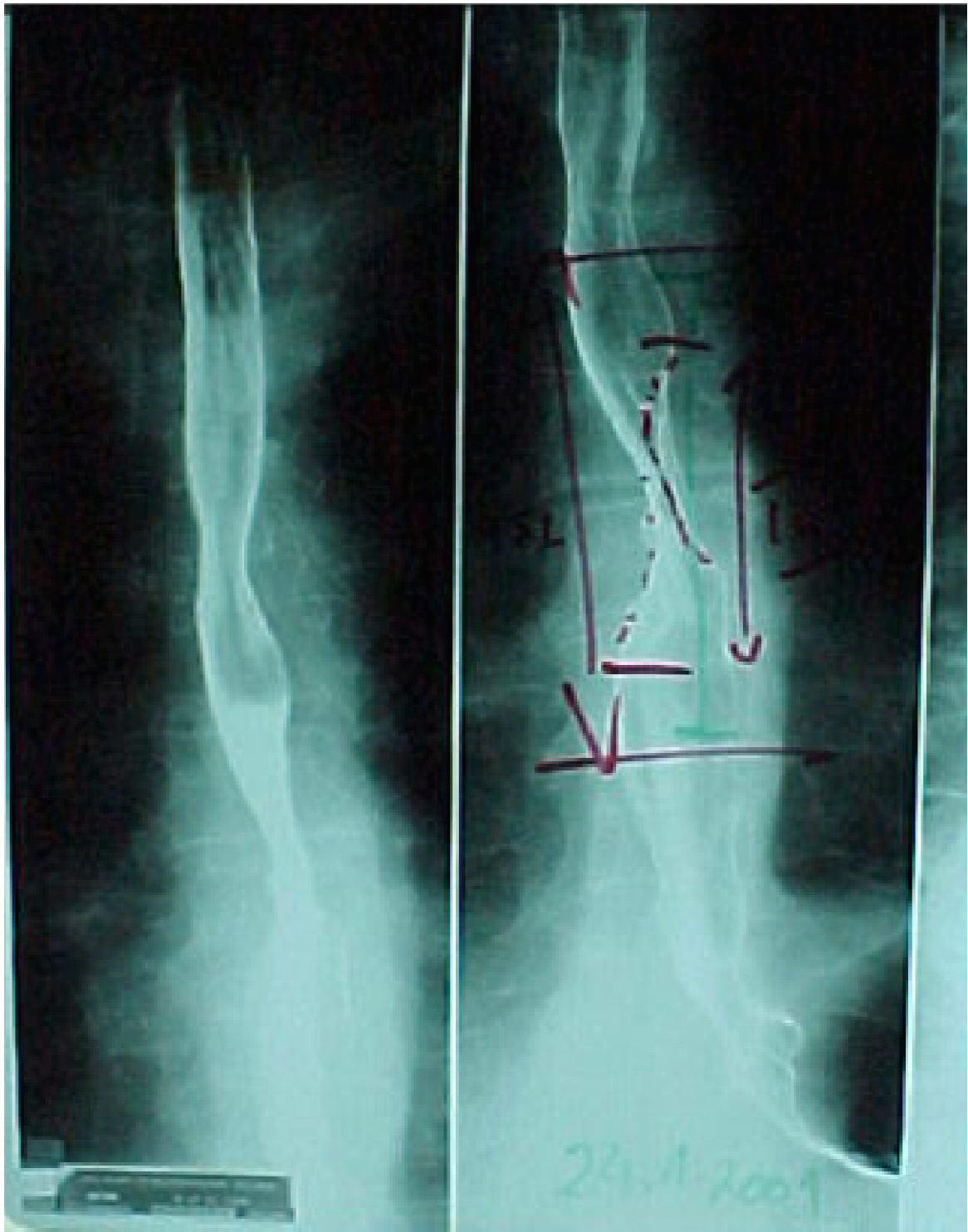
Double Contrast

barium swallow

Length of GTV

„GTL“

Related to carina



INDICATIONS: ESOPHAGEAL BRACHYTHERAPY

ADVANCED DISEASE

(DYSPHAGIA BY TUMOR OBSTRUCTION)

- Primary treatment/treatment for recurrence -

BRACHYTHERAPY ALONE

combined with: dilatation

laser resection

BOOST TREATMENT AFTER TUMOUR REMISSION by EBT

(most often palliative setting)

SUPERFICIAL TUMORS/EARLY DISEASE

(BRACHYTHERAPY ALONE)

BOOST TREATMENT AFTER EBT

(most often curative intent)

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CONTRA-INDICATION ESOPHAGEAL BRACHYTHERAPY

FISTULA

(Infiltration of the Trachea (pars membranacea))

Indication directly after stent placement is questionable (Dutch STEBRA study)

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TARGET DEFINITION

Findings from esophagoscopy, barium swallow
computed tomography

Documentation (radiograph) of tumour extension during application with anatomical landmarks

GTV: Depth: tumor thickness
thickness of esophageal wall
Length: Tumor length

CTV: safety margin for subclinical disease: CTL
PTV: safety margin for uncertainties: PTL

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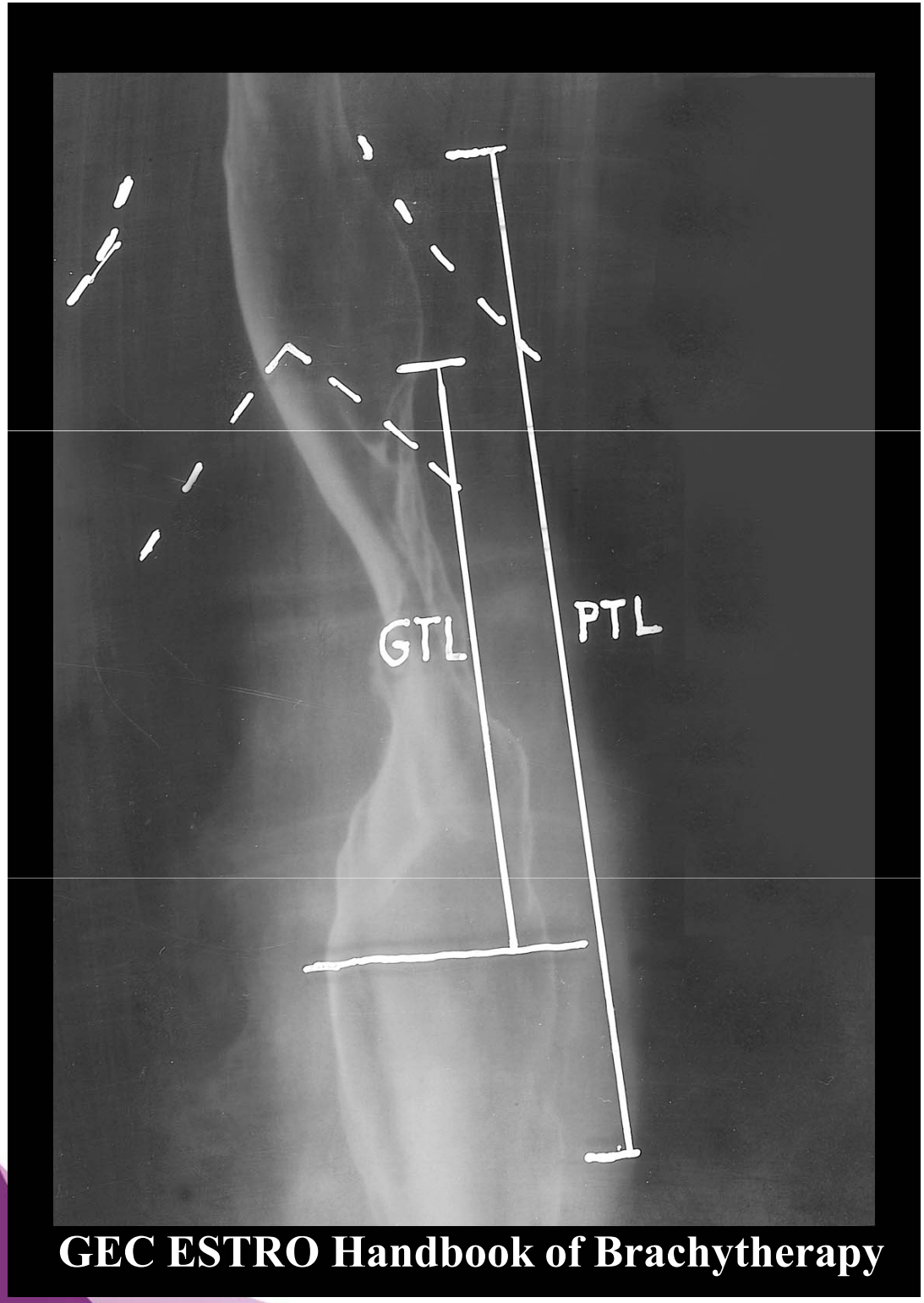

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Double Contrast barium swallow

Length of GTV „GTL“

Length of PTV „PTL“

Related to carina

ESTRO School

TECHNIQUE OF APPLICATION

Single catheter technique

Radiography assisted application
Fluoroscopy assisted application
Endoscopy assisted application

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VARIATIONS IN APPLICATOR DESIGN
- according to different pathology -

Diameter: 1.7 to 16 mm
scaling system

tubes of different diameters
tube-in-tube technique

solid tubes (large diameter)
bougie-applicators
balloon applicators

all with a channel for a small diameter catheter carrying the source (Ir 192)

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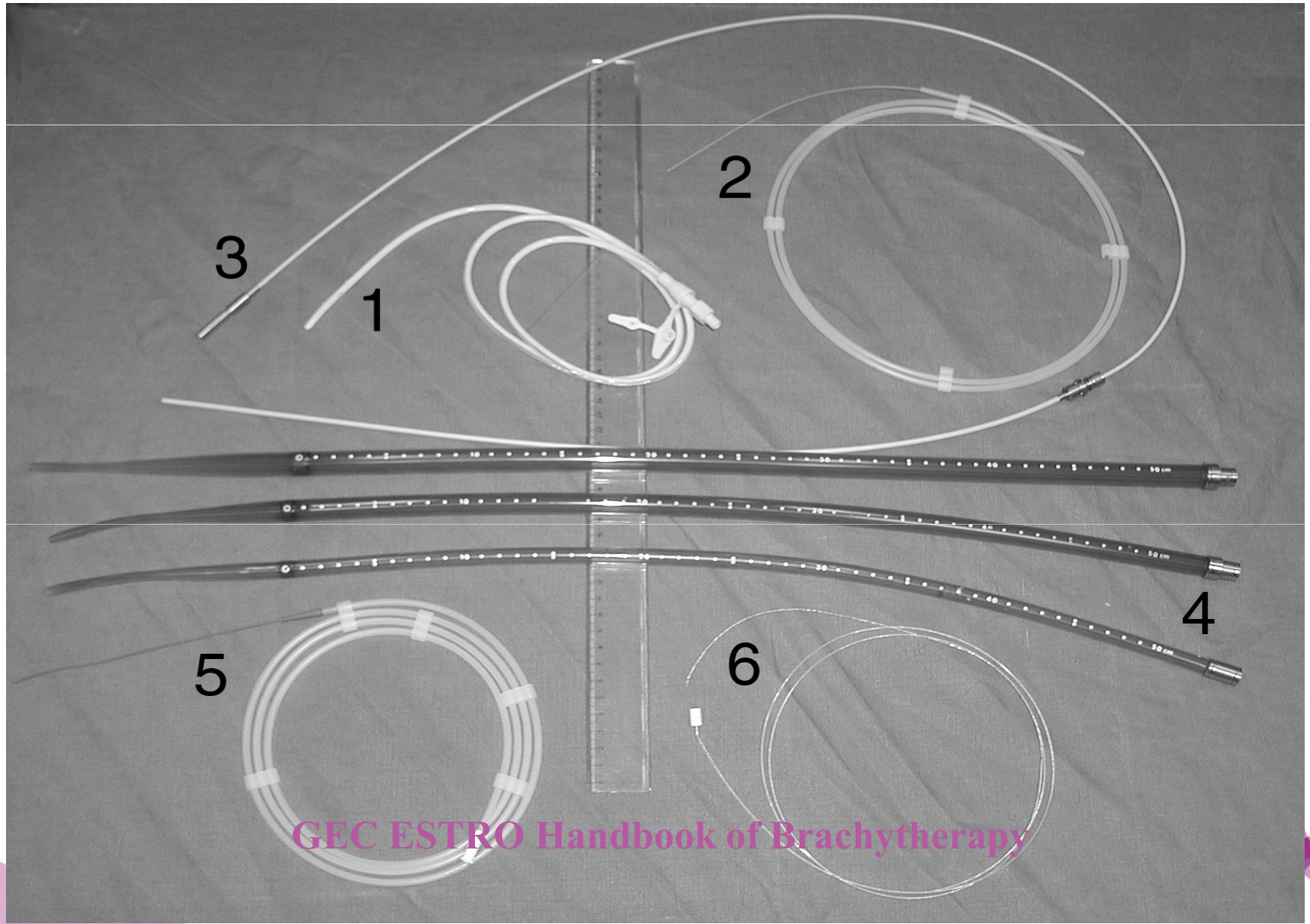
VARIATIONS IN APPLICATOR DESIGN
- according to different pathology -



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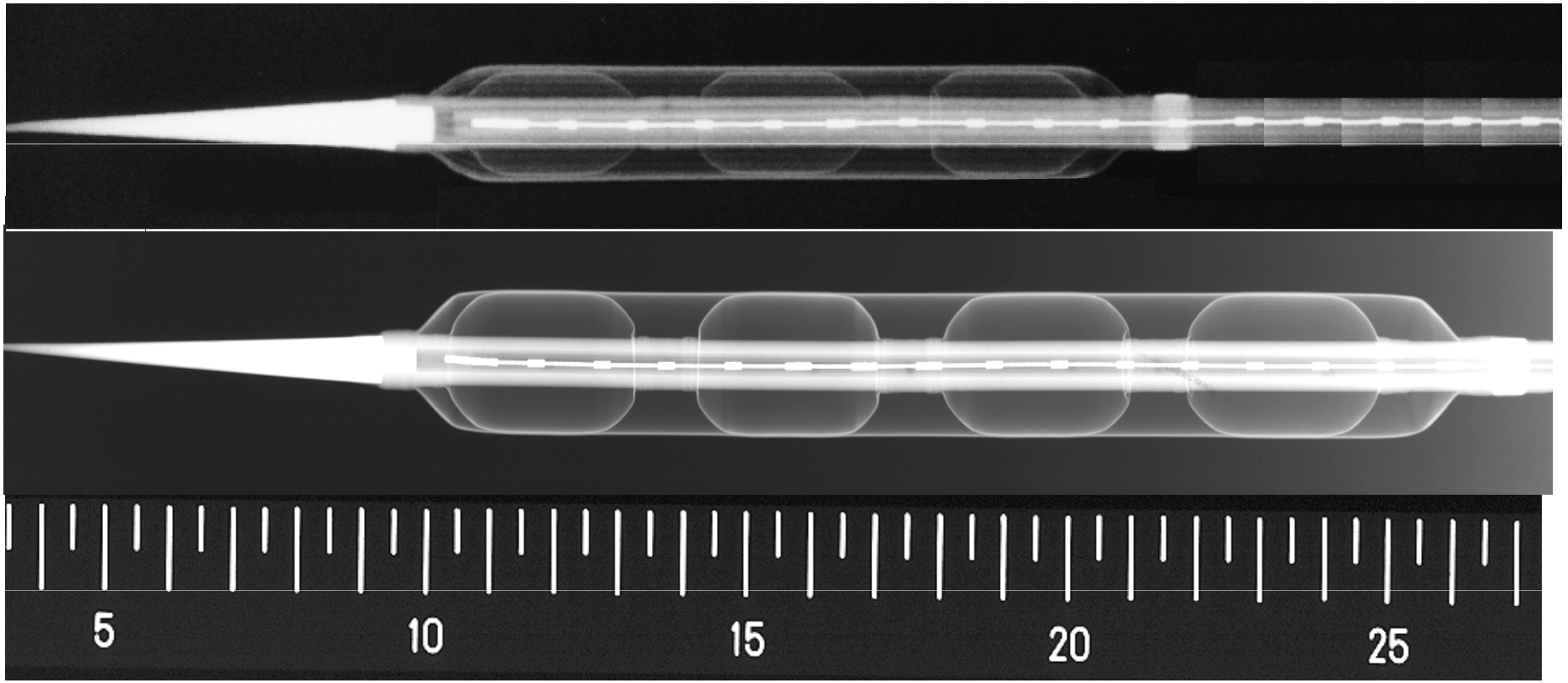
Japanese Balloon Applicators



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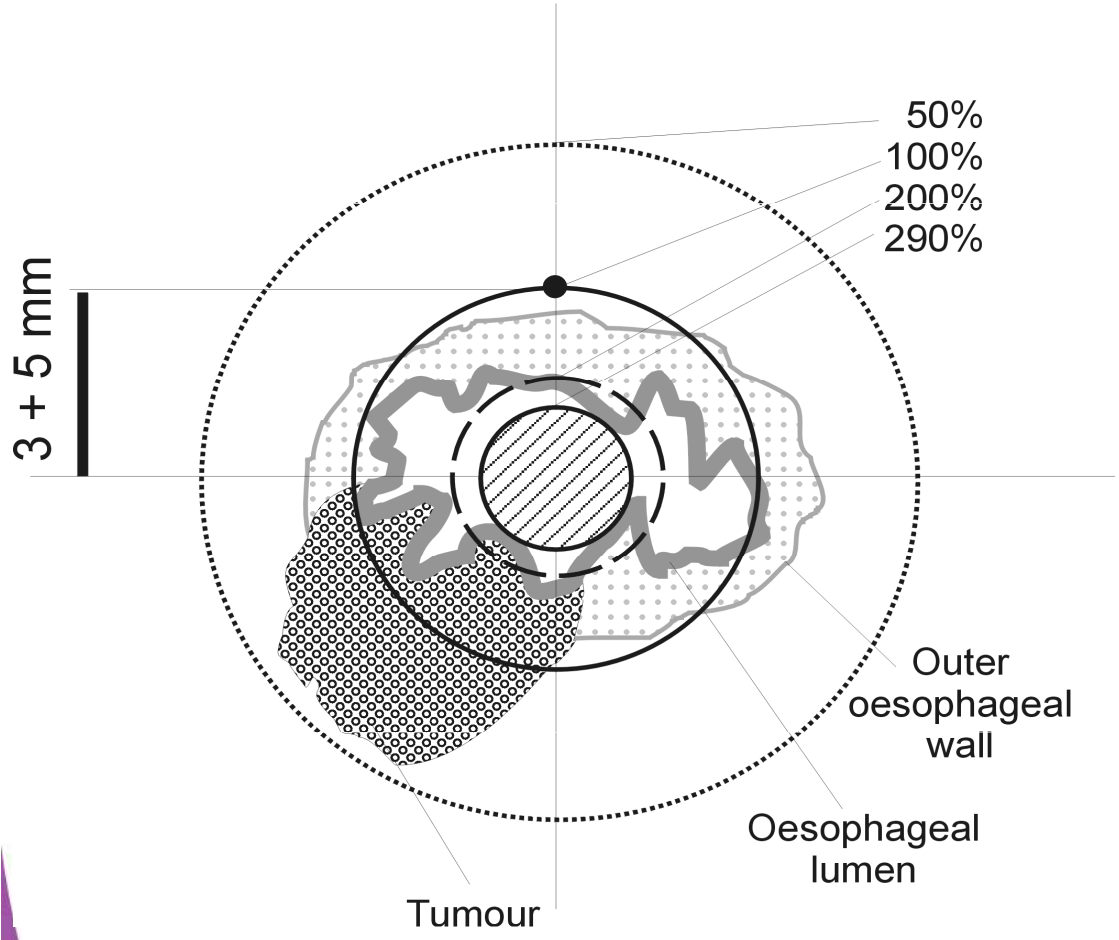
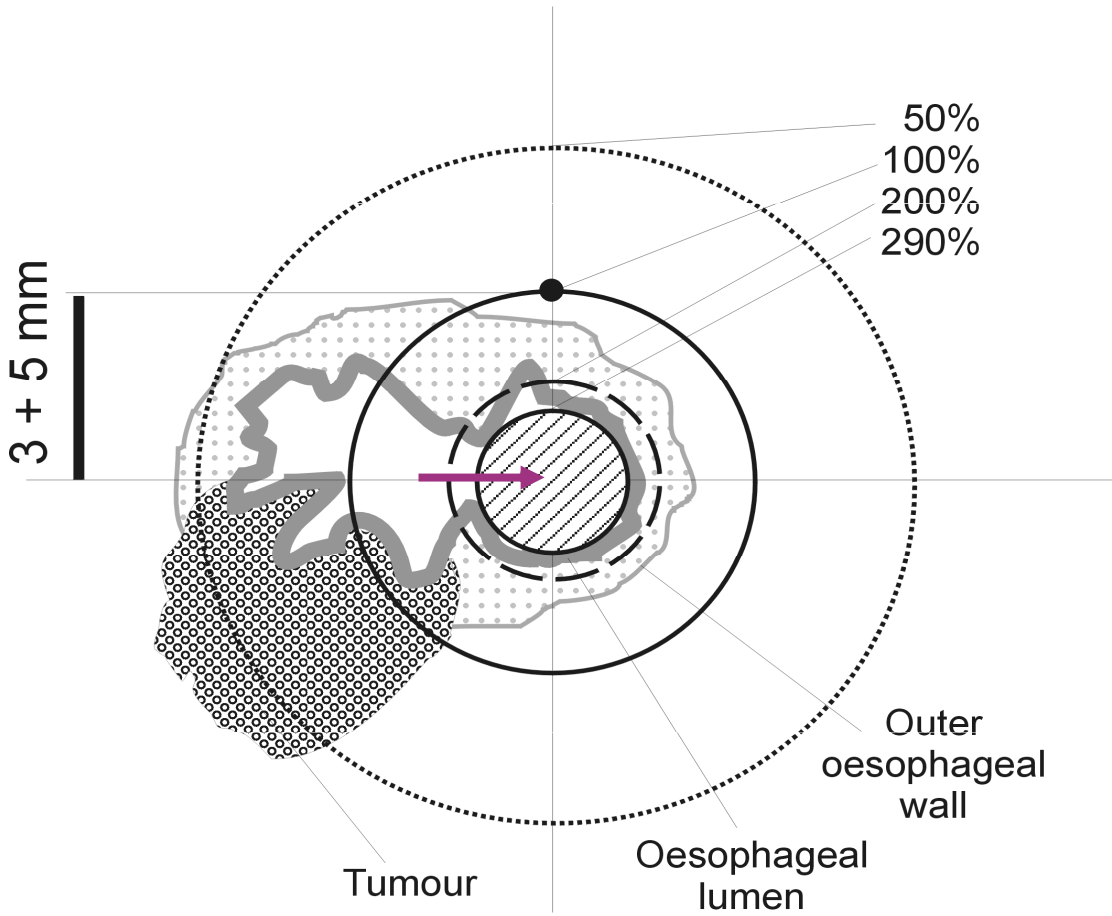
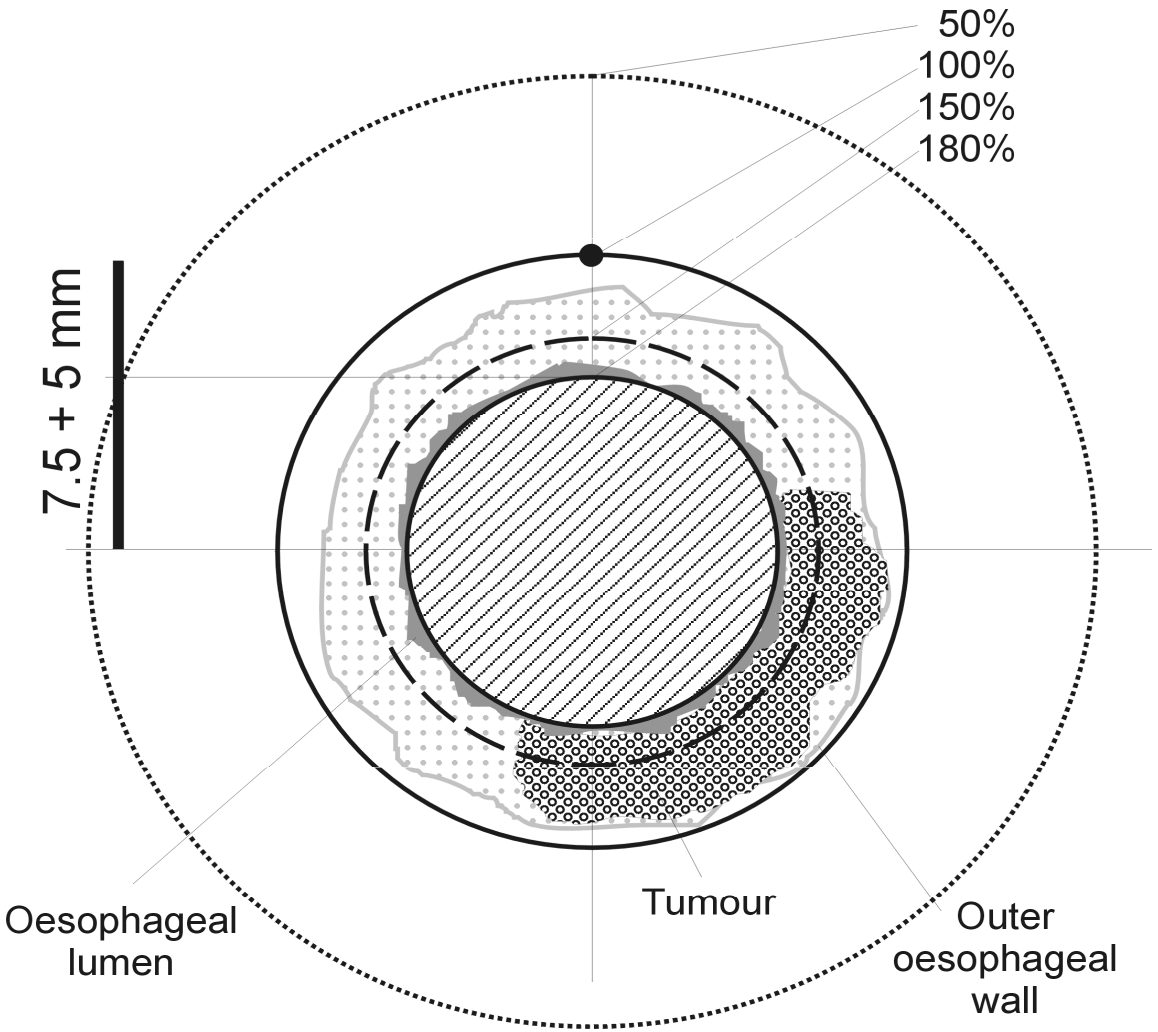
Small diameter appl. in a wide oesophageal lumen
Centered / Non-centered position





Inappropriate Technique !

Appropriate technique in wide oesophageal lumen



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Recording and reporting at 5 mm from the applicator surface

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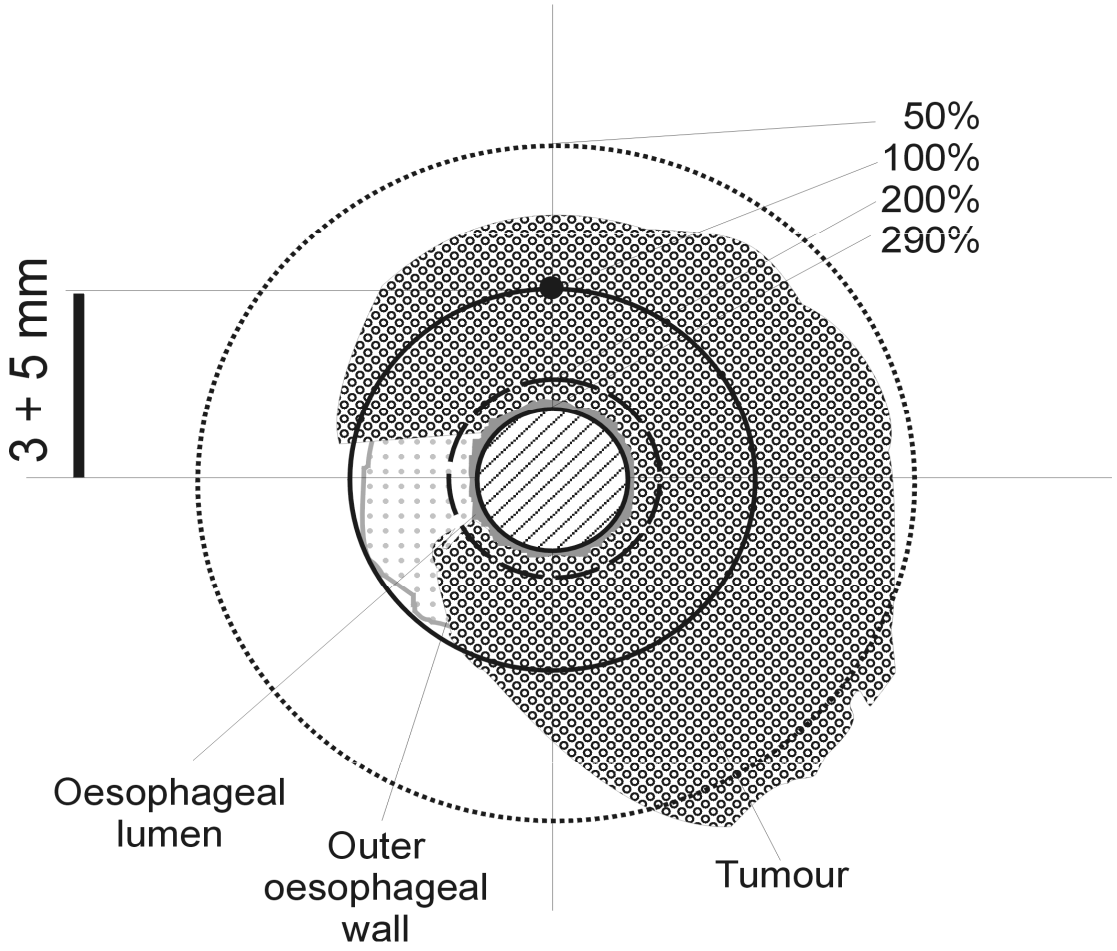
Appropriate technique in narrow oesophageal lumen



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Recording and reporting at 5 mm from the applicator surface

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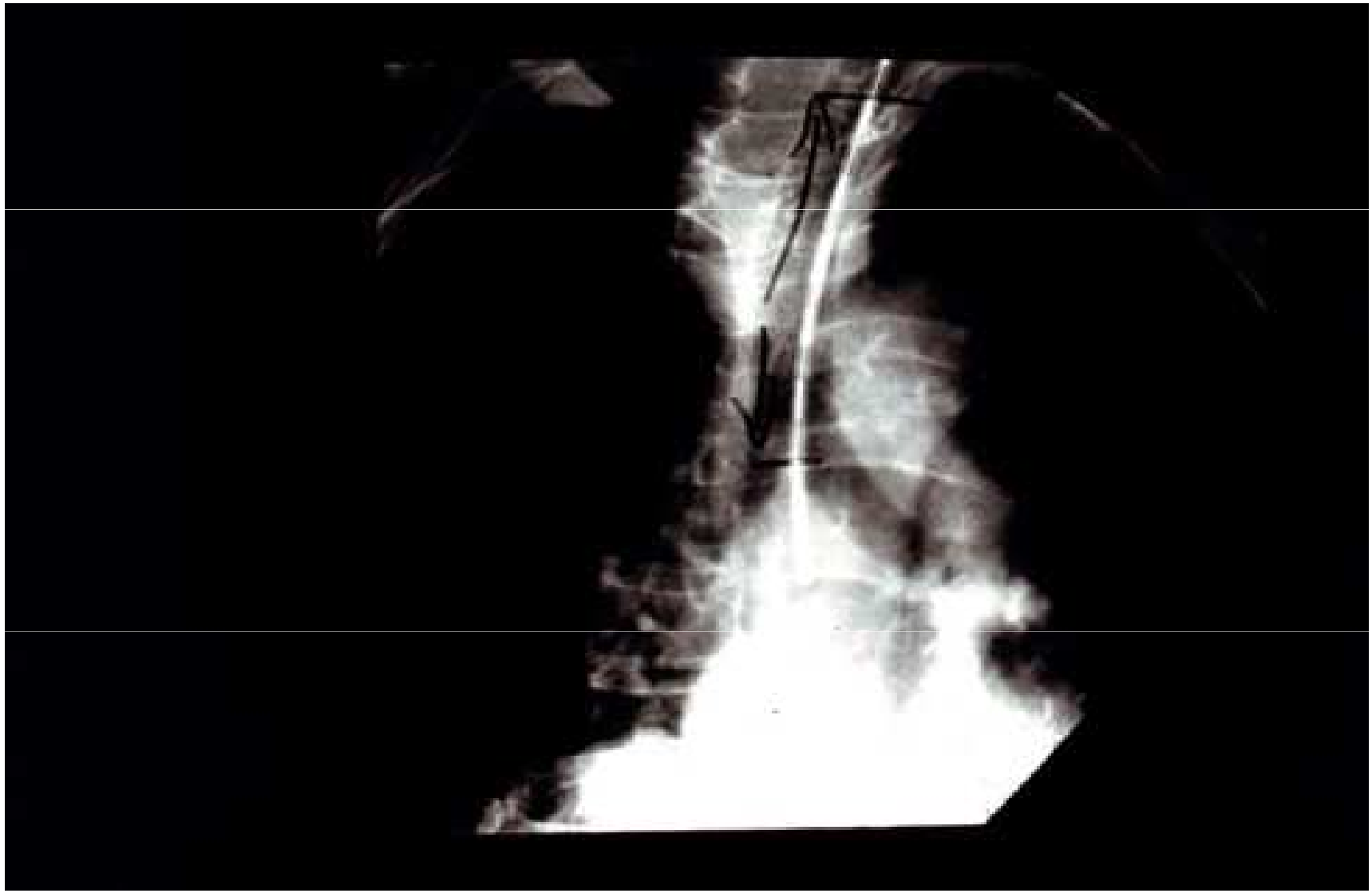
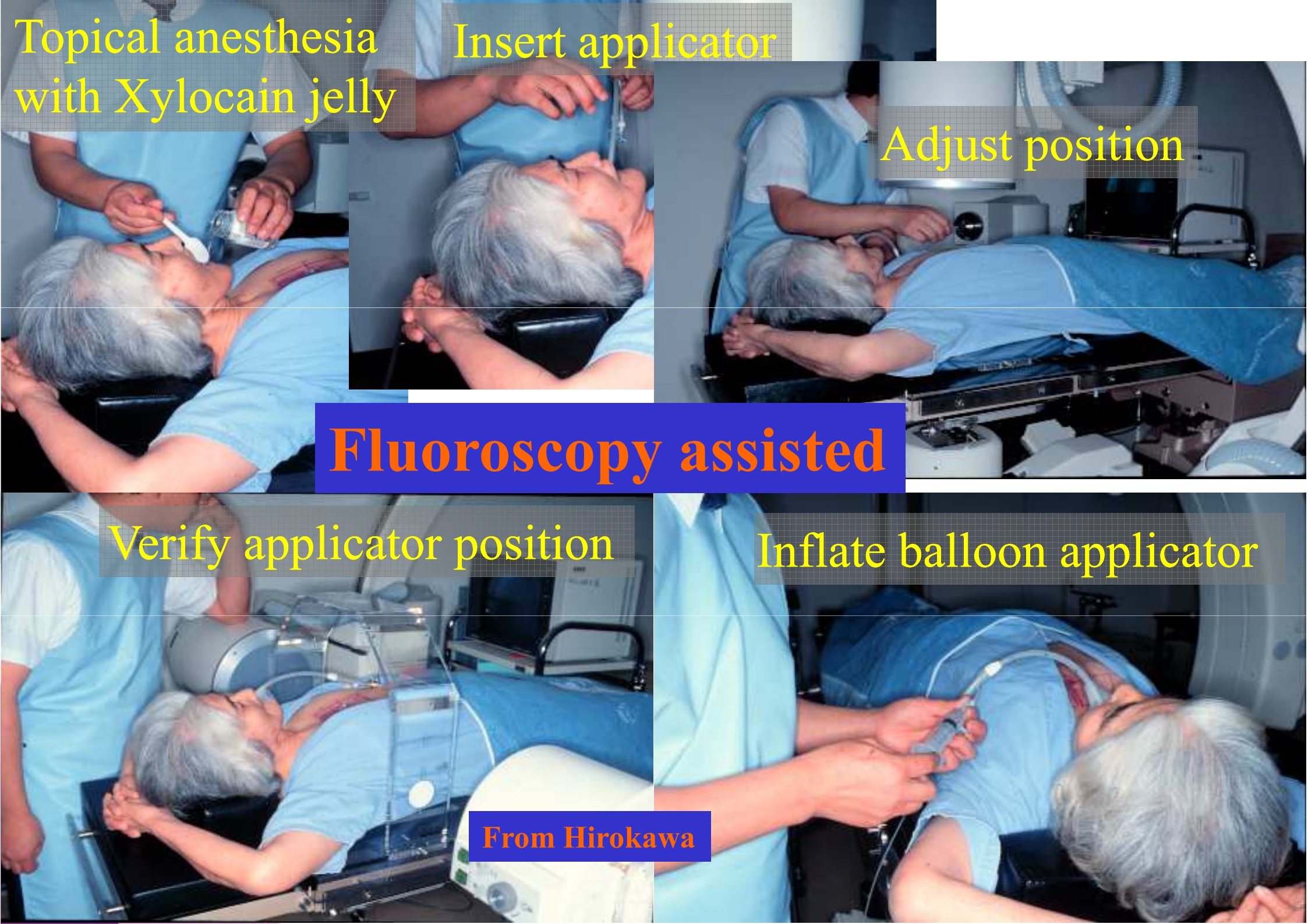
Radiography
assisted

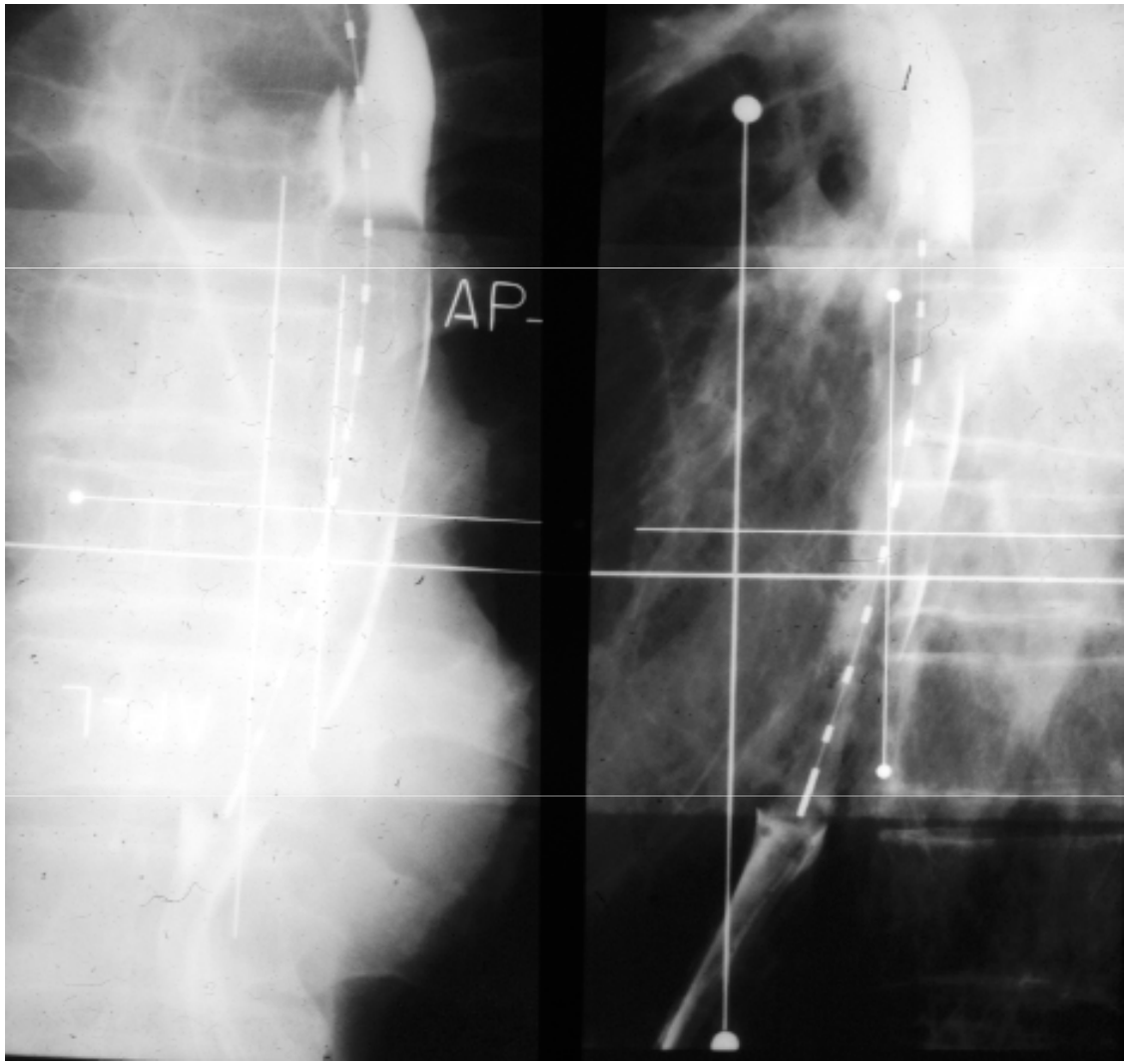
Clinical application
Remission
after EBT

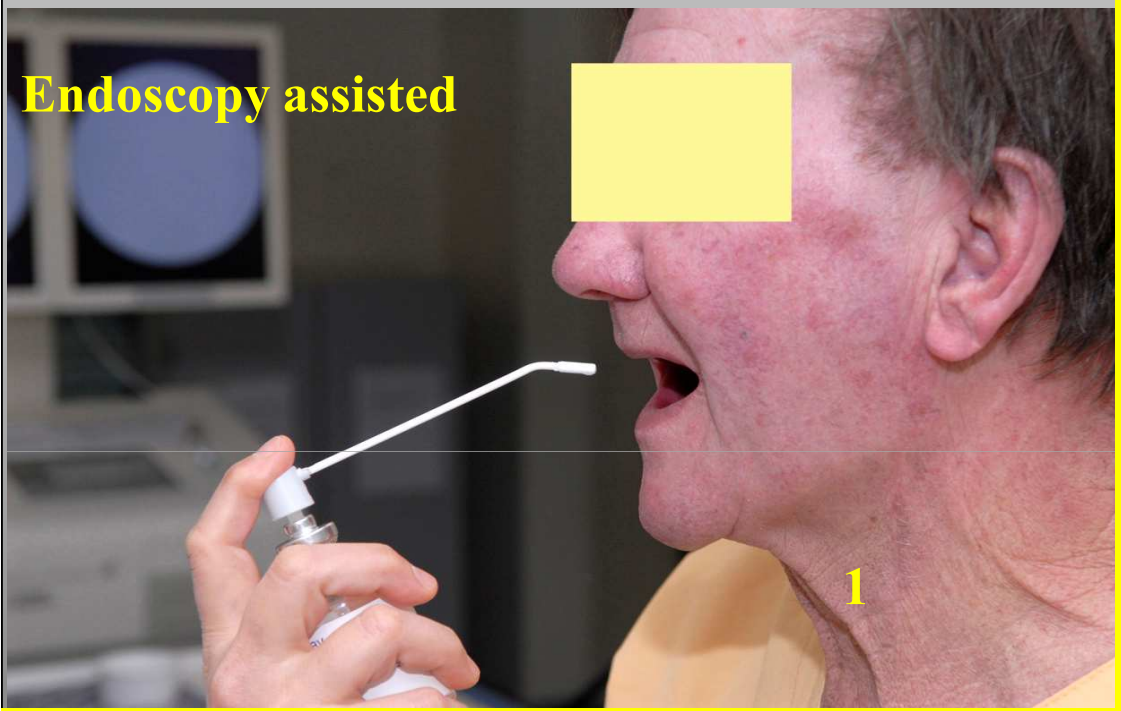
Localisation Radiograph with applicator and carina

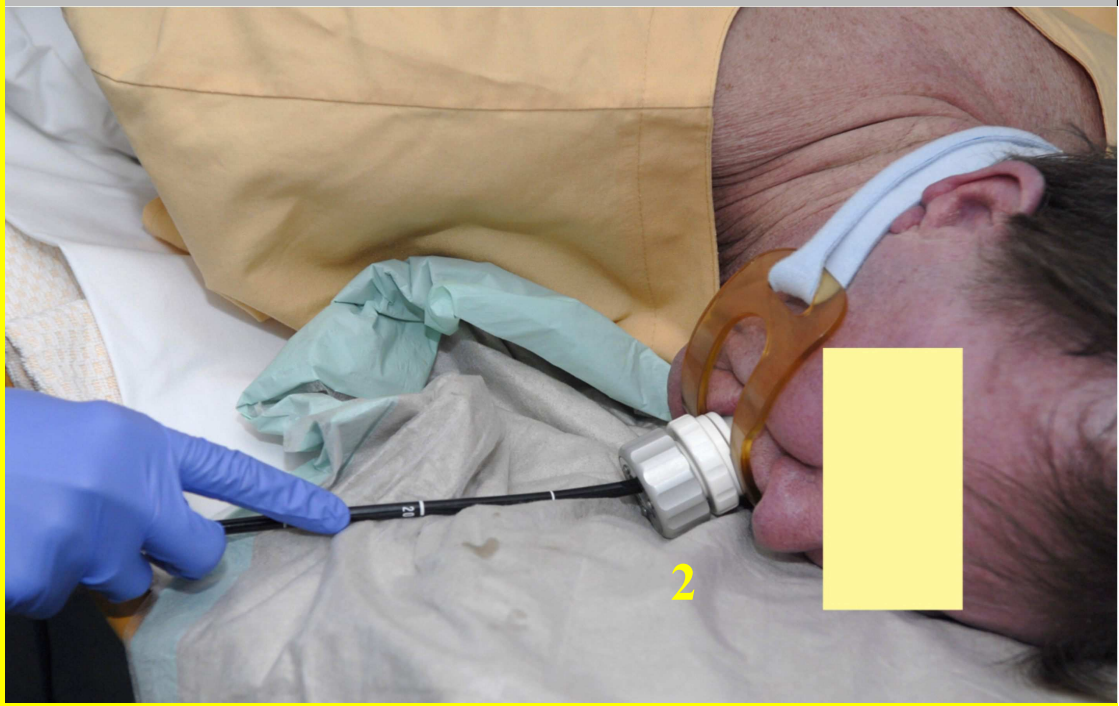



Topical anesthesia with Xylocain jelly
Insert applicator
Adjust position
Fluoroscopy assisted
Verify applicator position
Inflate balloon applicator
From Hirokawa

Example with balloon catheter




Endoscopy assisted
1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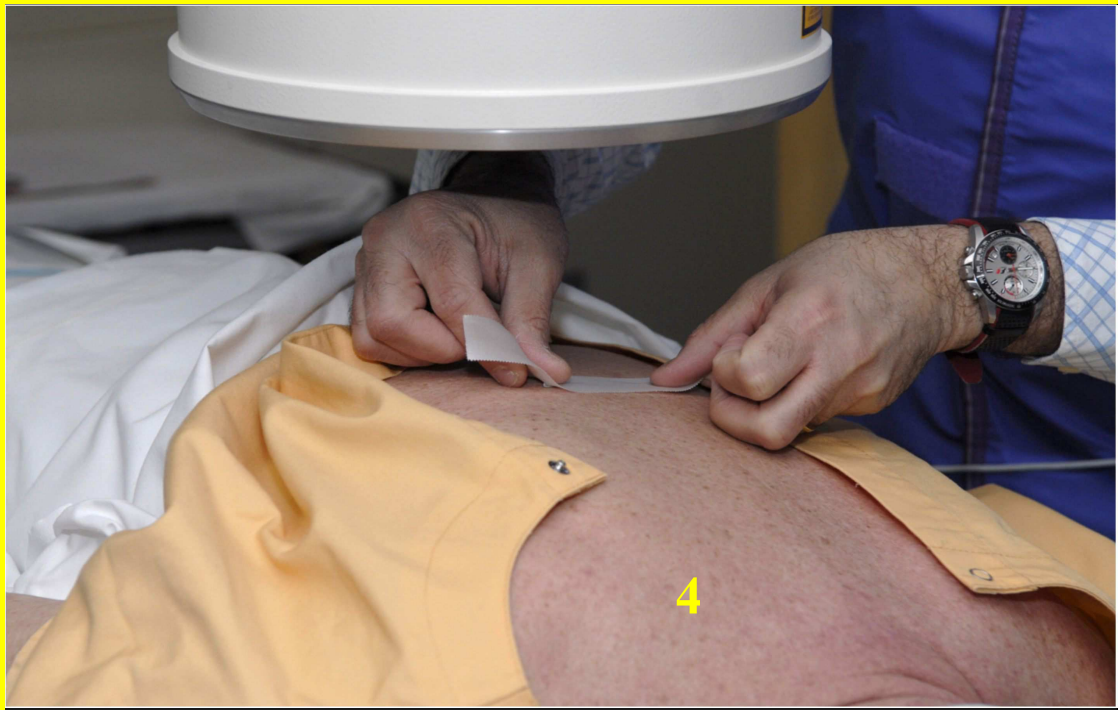
3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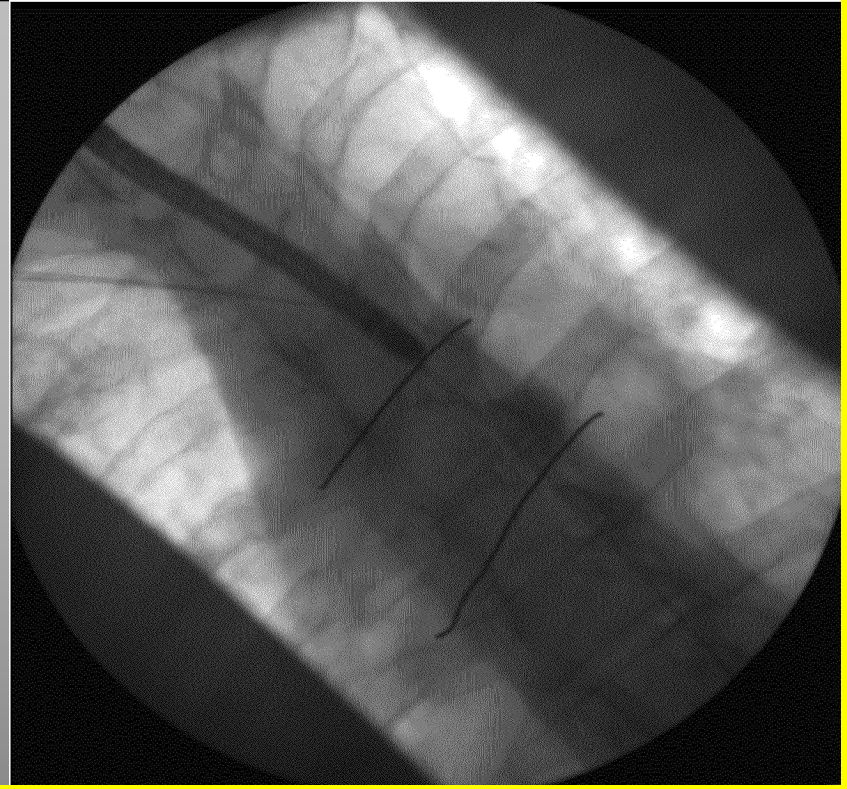

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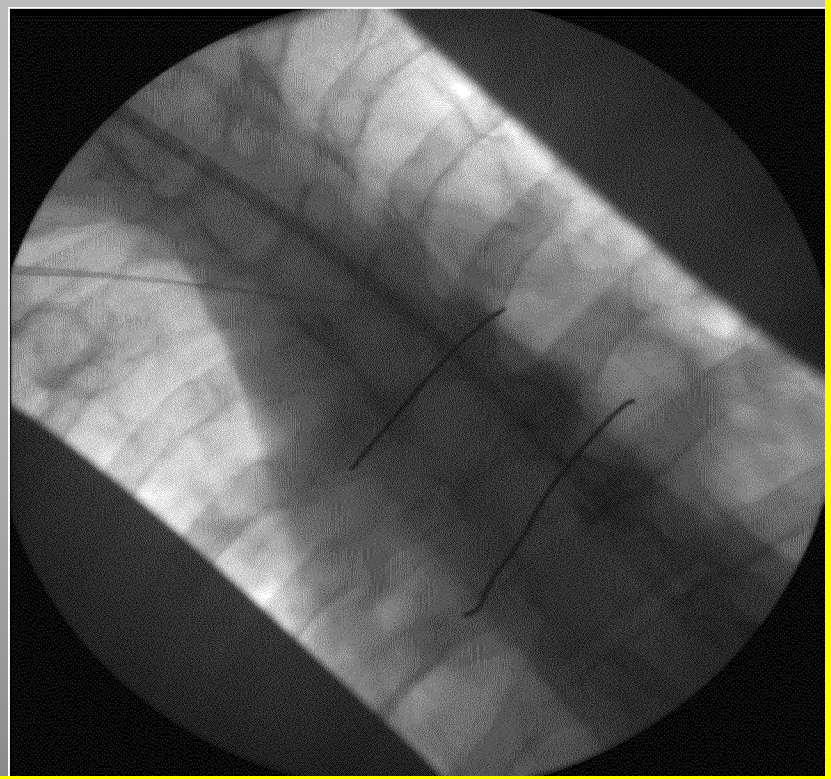
6

7

8



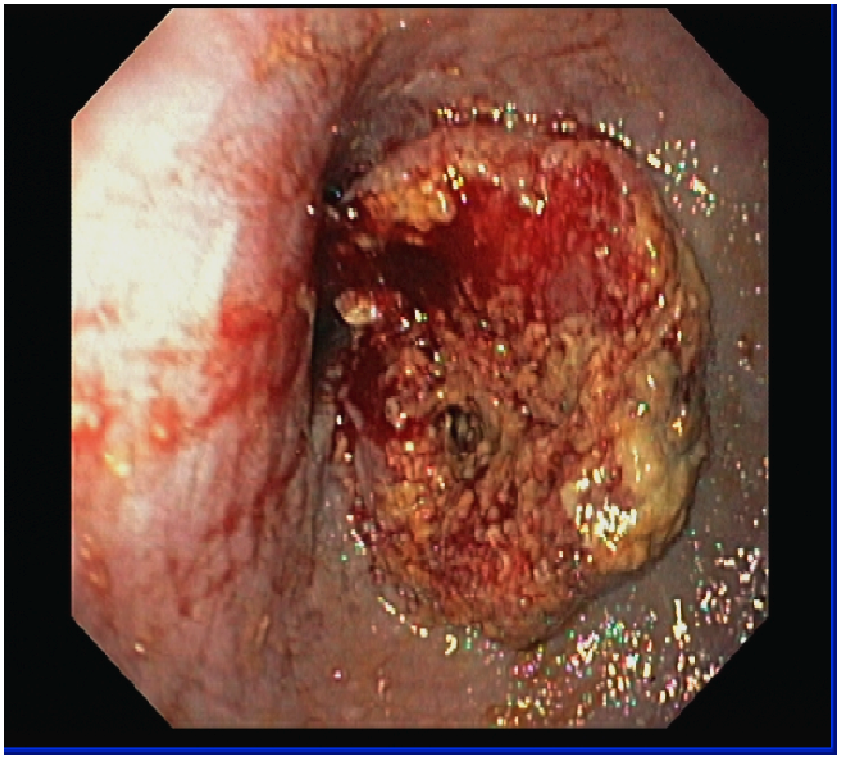
9

10

11

12

Brachytherapy in Esophageal Cancer
Endoscopy assisted application with guide wire in advanced obstructive disease



From R. Sur

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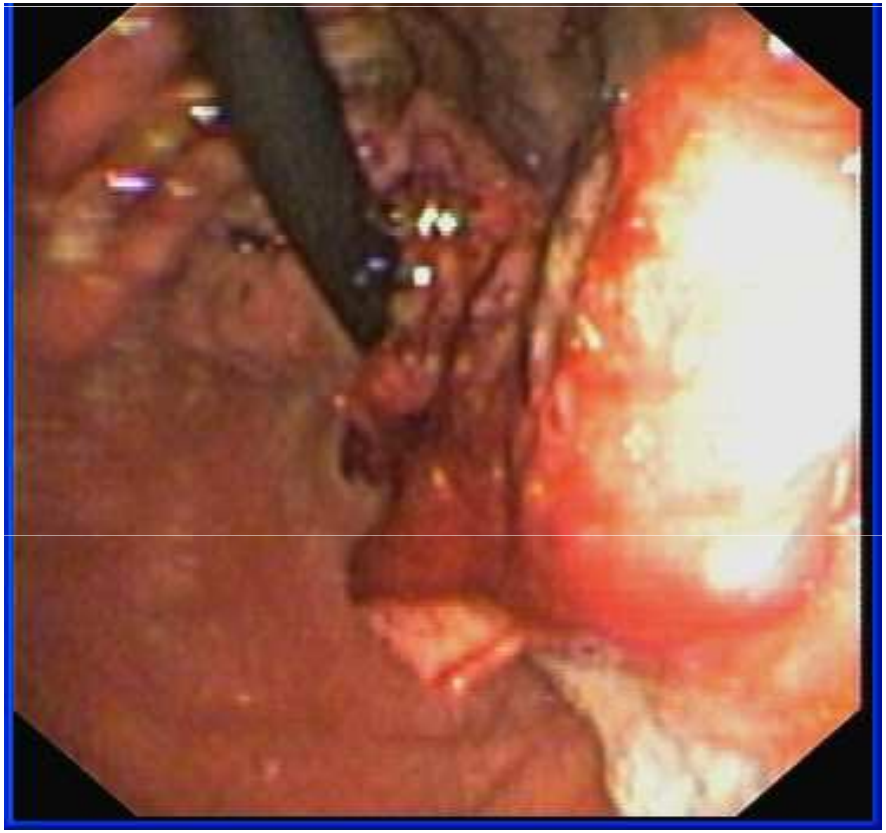
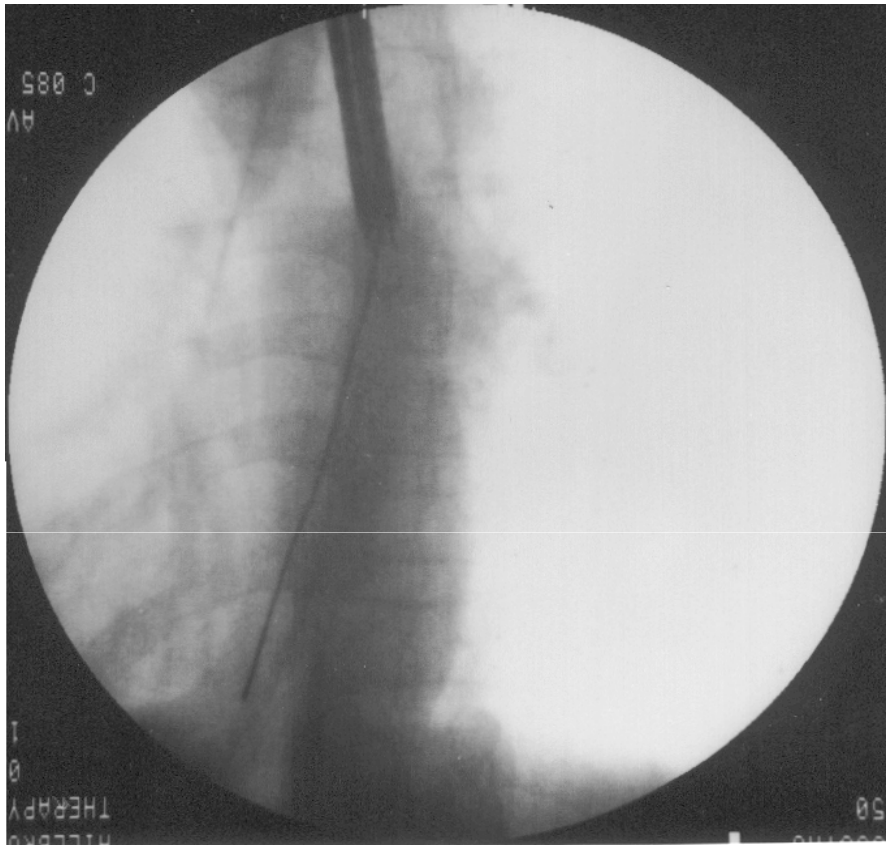
Brachytherapy in Esophageal Cancer
Endoscopy assisted application with guide wire in advanced obstructive disease





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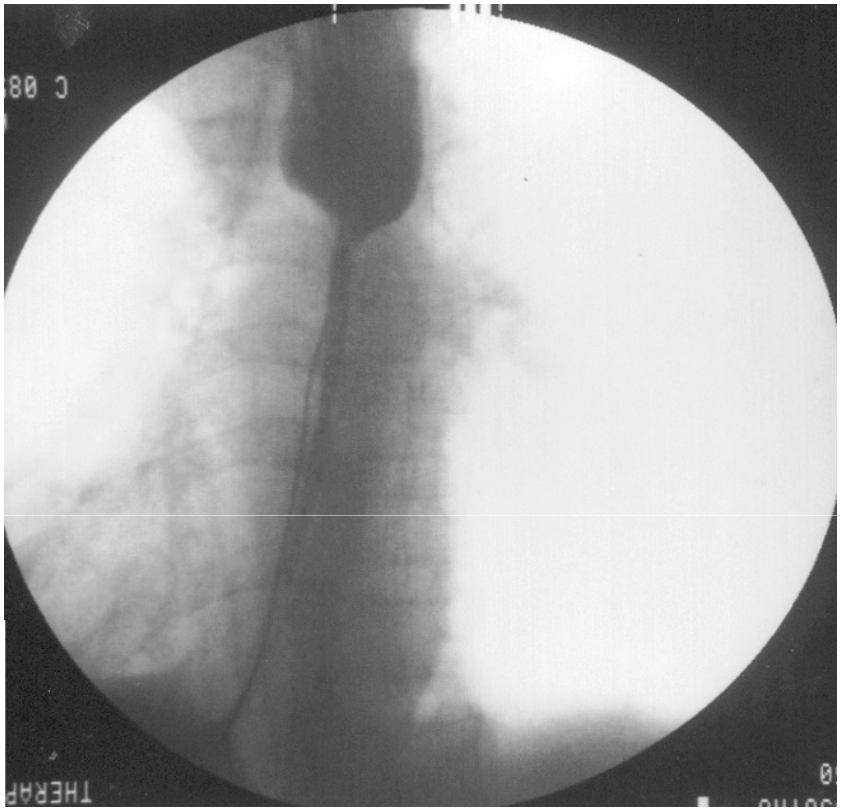
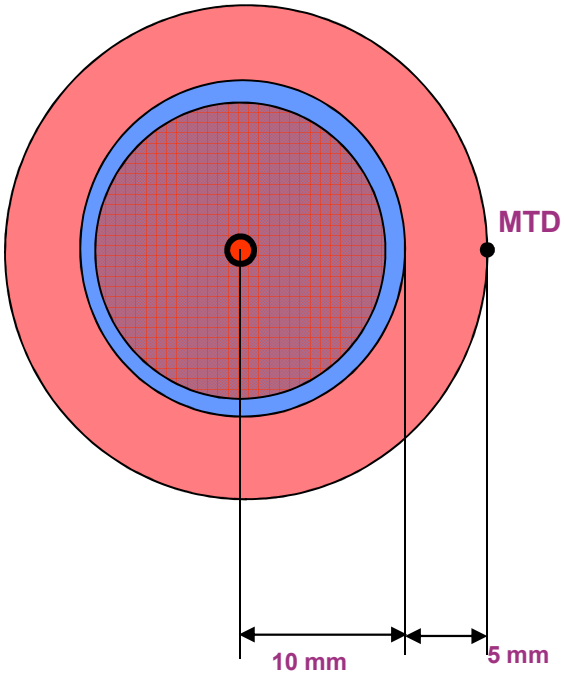
Brachytherapy in Esophageal Cancer
Endoscopy assisted application with guide wire in advanced obstructive disease



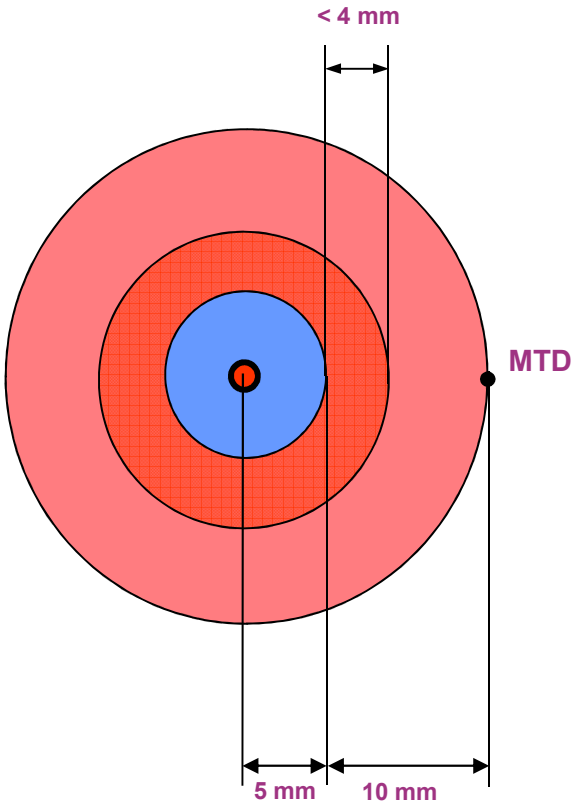
Diameter applicator:

20 mm



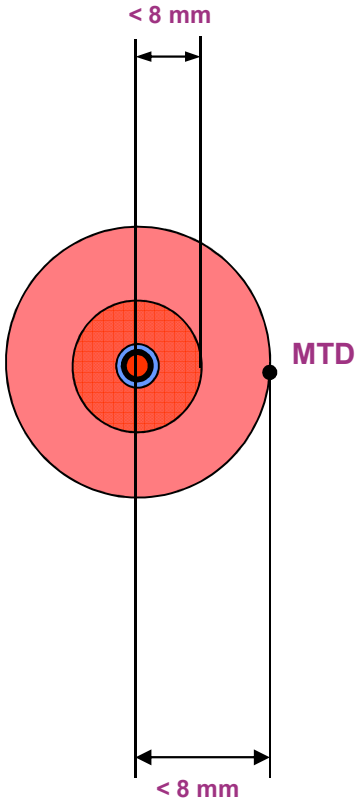
Diameter applicator:

10 mm



Diameter applicator:

2 mm



The hyperdose sleeve can be within the catheter, but in many cases high doses are present in the treated volume

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Individual Prescribing at x mm

Systematic Recording and Reporting

Length of the Planning Target Volume (PTL)
Length of the Reference Volume (RVL)
    at 5 mm from the applicator surface

Reference Dose
    at 5 mm from the applicator surface
    at the applicator surface

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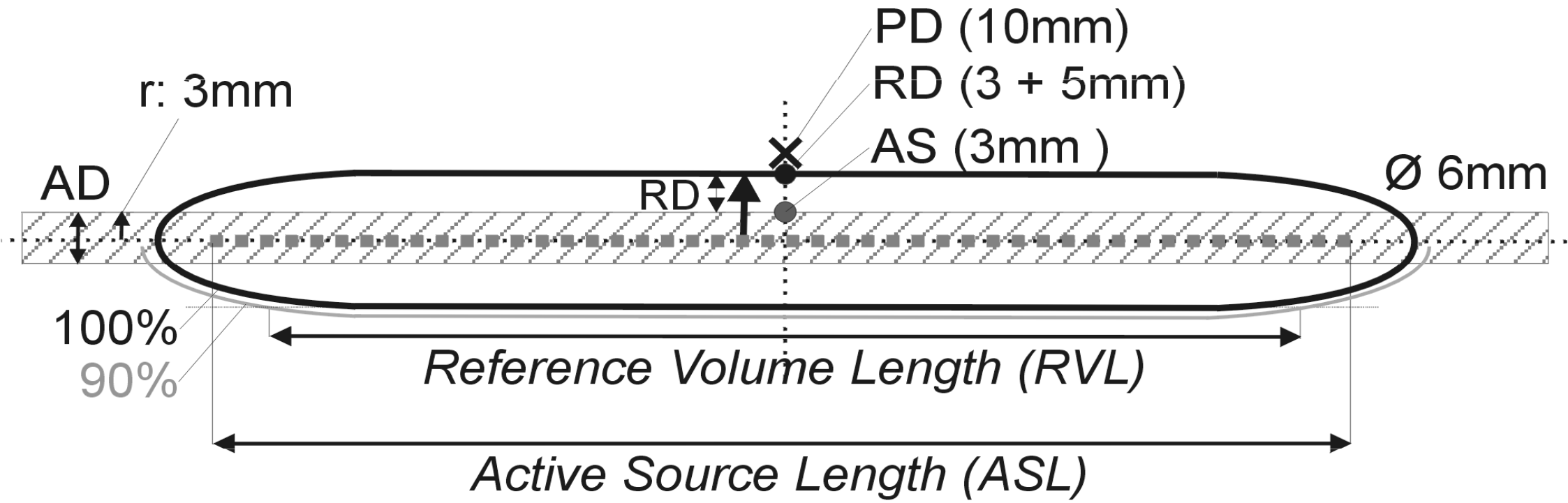
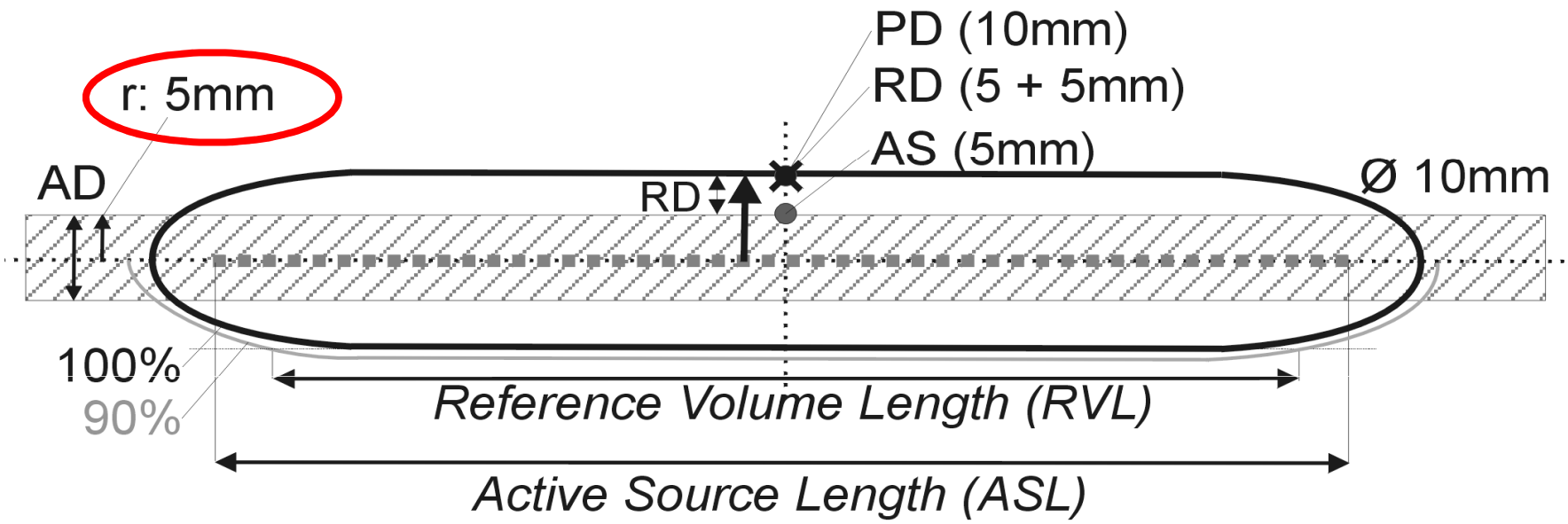
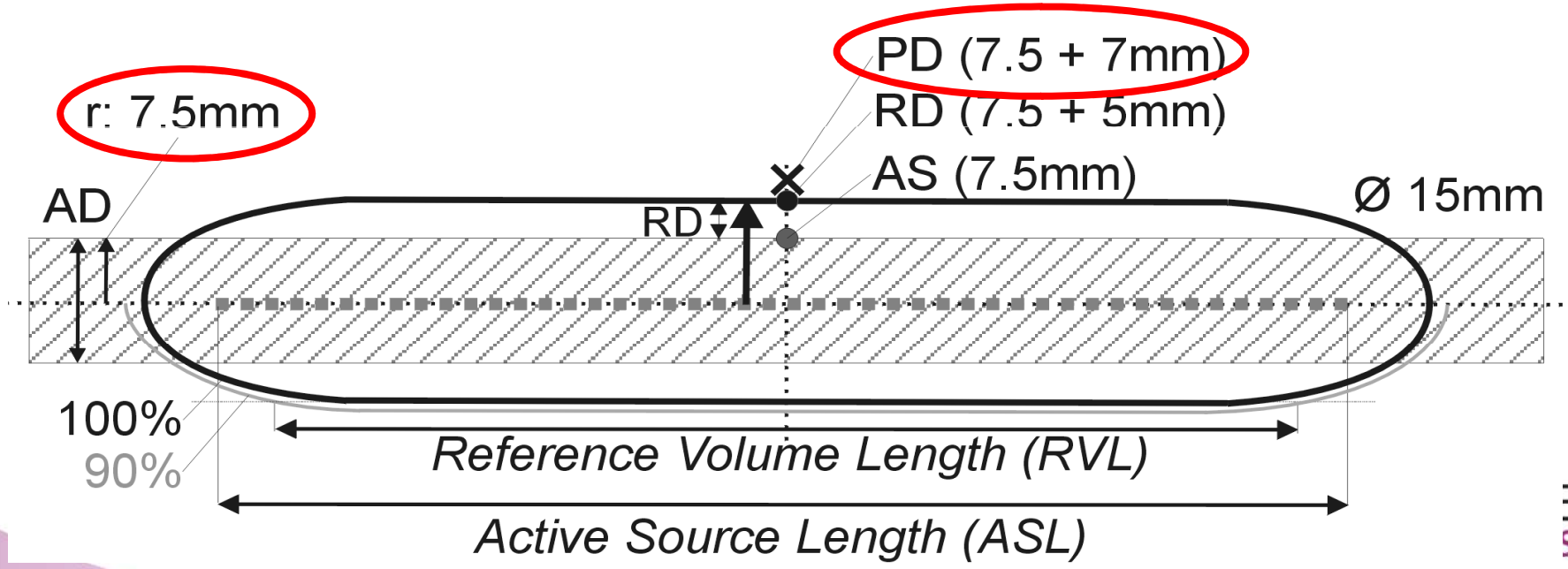
Prescribing, Recording and Reporting oesophageal treatment





GEC ESTRO Handbook of Brachytherapy



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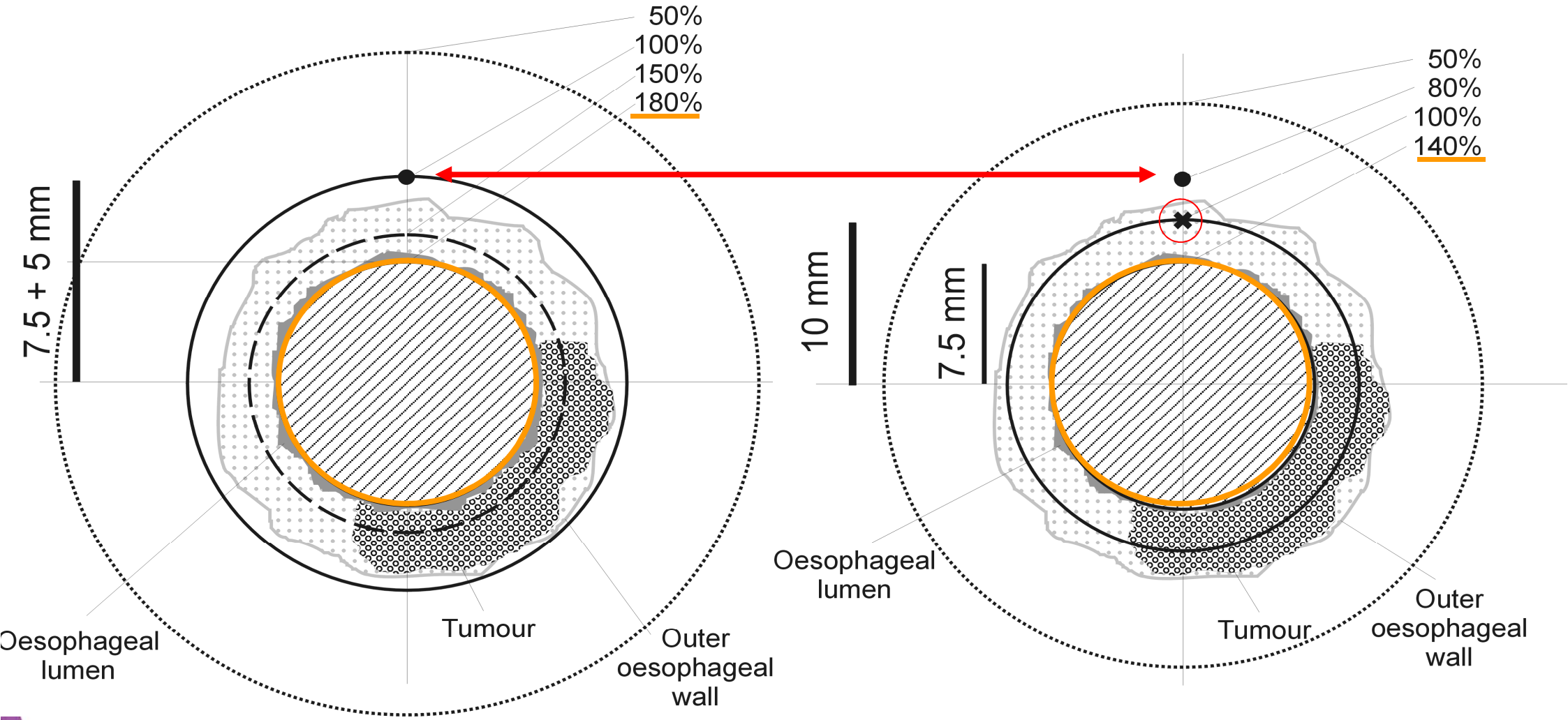
Different prescription technique

GEC ESTRO Handbook of Brachytherapy



Recording and reporting at 5 mm from the applicator surface

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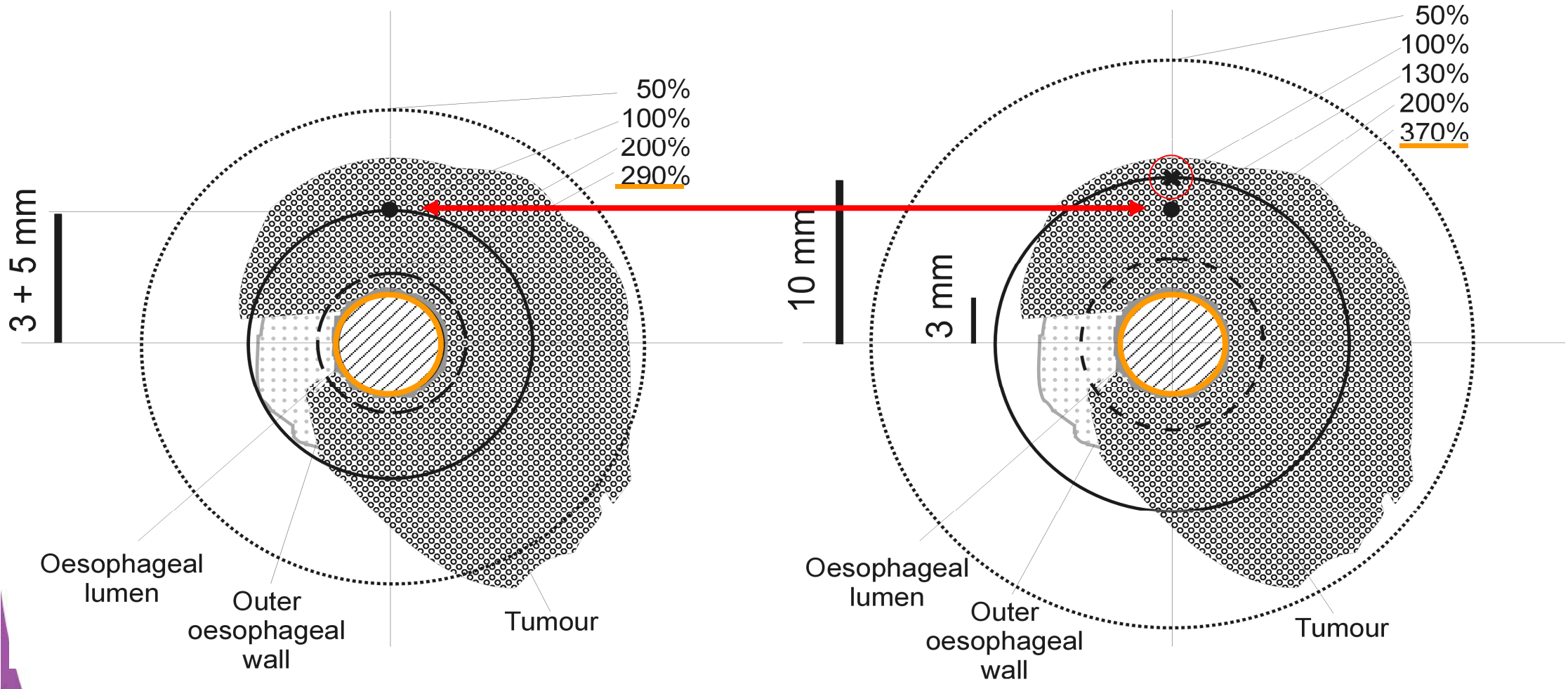
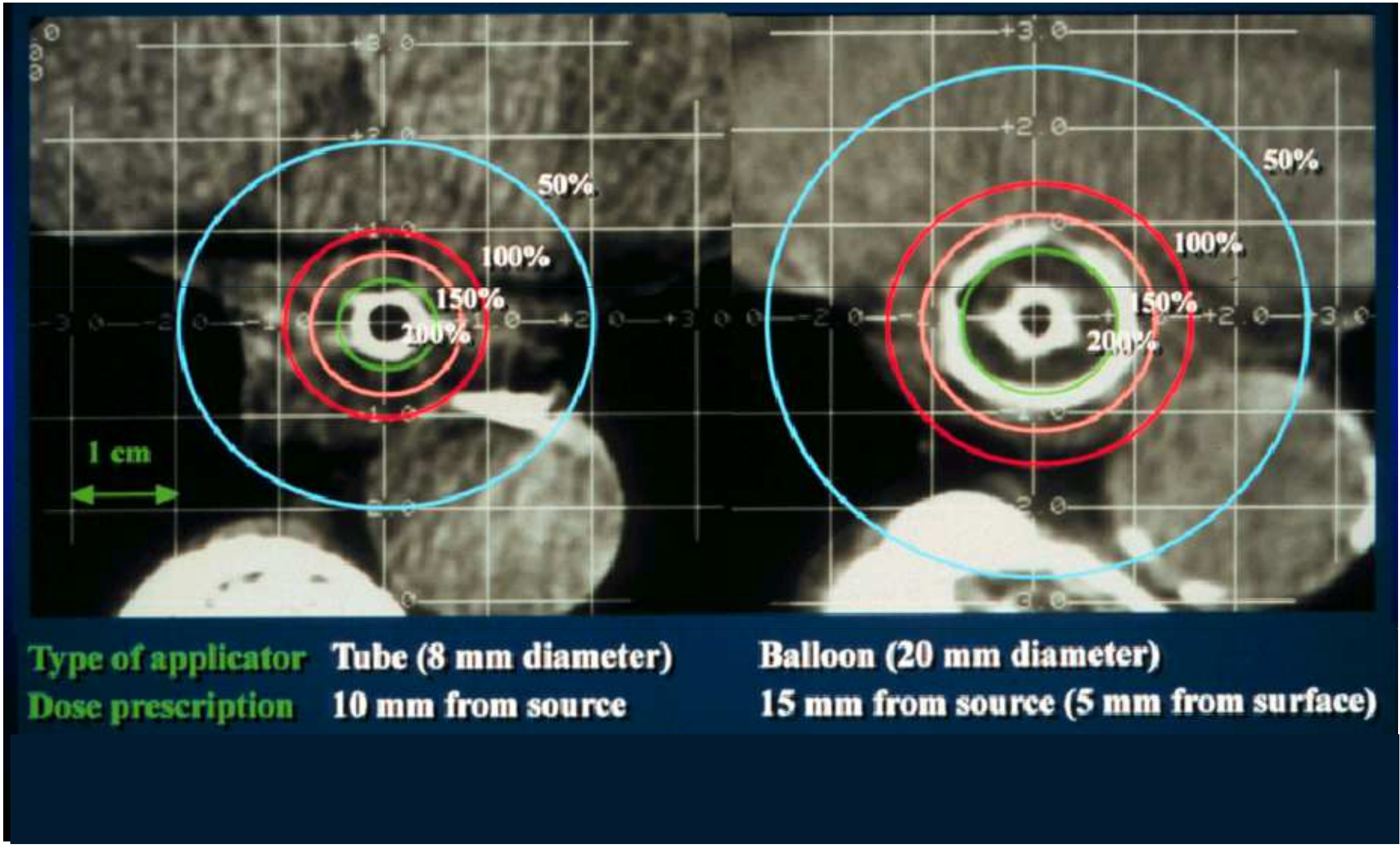
Different prescription technique

GEC ESTRO Handbook of Brachytherapy



Recording and reporting at 5 mm from the applicator surface

ESTRO School



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DOSE AND FRACTIONATION
- combination treatment EBT and BT -

palliative approach
EBT: 45-46 Gy with 1.8-2 Gy per fraction
30 Gy with 3 Gy per fraction
BT: 10-16 Gy in 2 fractions
10 Gy in 1 fraction

curative approach
EBT: 55-60 Gy with 2 Gy per fraction
BT: 10-15 Gy at 5 mm in 2-3 fractions

time interval
EBT-BT: 1-2 weeks
BT: 1-2 weeks

Fast symptom relief
BT1-EBT-BT2

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PDR Treatment

Perform treatment in several runs (e.g. 4 runs)

If treatment is interrupted target volume will be more homogeneously treated

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RESULTS

overall symptom relief

e.g. from dysphagea (mean 4 – 10 mths)
about two thirds of patients

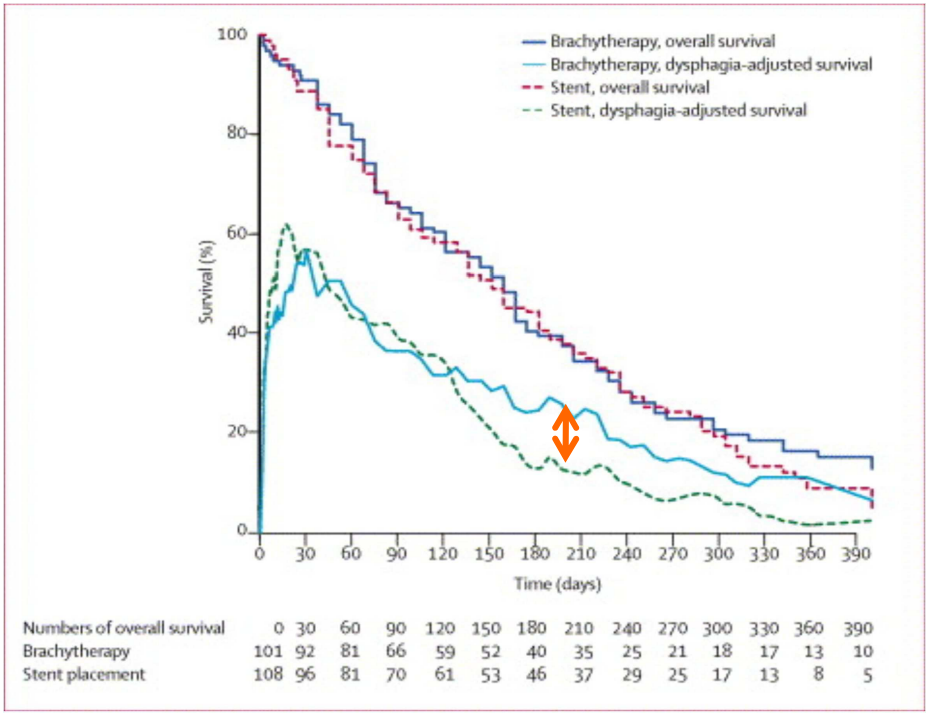
overall improvement in general performance, weight

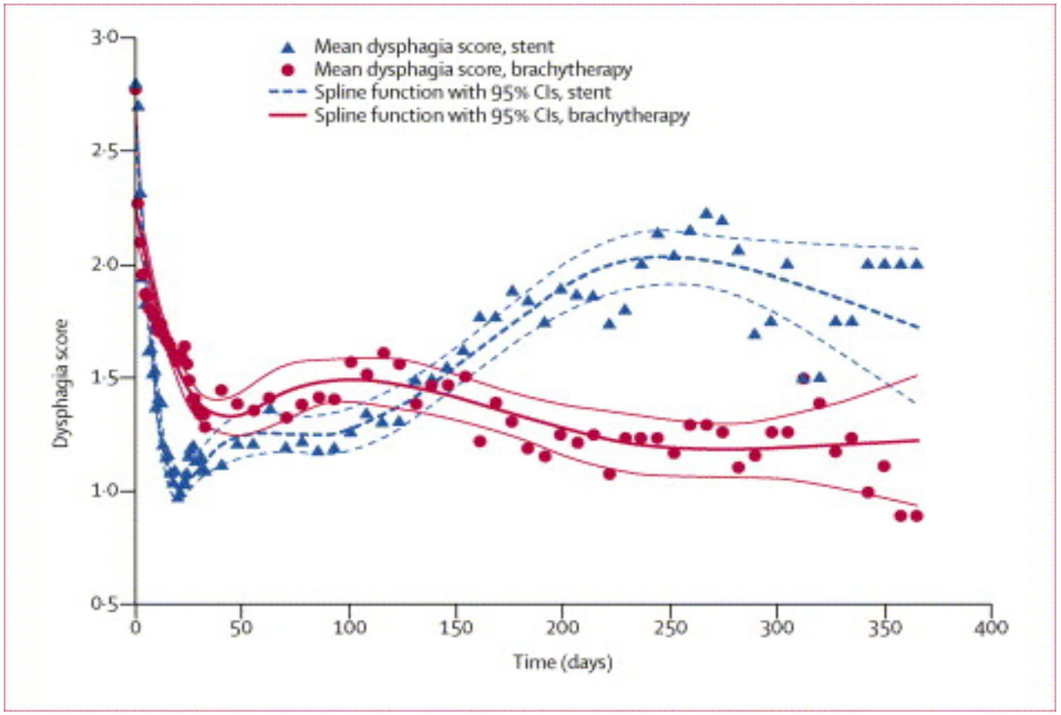
about two thirds of patients

partial remission:	**70 %**
complete response:	**20 %**
local tumor control:	**49-71 % (one year)**
survival (stage I/II):	**37 % (2 years)**
survival (stage III/IV):	**7 % (2 years)**

Ask et al, Acta Oncol 2003;42:462
Mujis et al, Radiother Oncol 2012;102:303
Sharma et al. Int J Radiat Oncol Biol Phys 2002;52:340

Palliative Treatment Stent vs Single Dose Brachytherapy





	Brachy	Stent	P
Total compl	21%	33%	0.02
Major compl	13%	25%	0.02

Homs et al., Lancet, 2004;364:1497

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Combination Stent and Brachytherapy

Day 1: Brachytherapy 12 Gy
Day 2: Biodegradable stent

47 % intervention-related major complications

Retrosternal pain
Vomiting
Dysphagia
Hematemesis

Hirdes, Gastroint Endoscopy,2012;76:267-274

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SIDE EFFECTS

acute effects

oesophagitis (up to 80 %)
fistula (up to 5 %)

subacute, late effects

chronic oesophagitis, ulceration (up to 30 %)
stricture (10-30 %)
fistula (5-10 %)

Hishikawa et al., Radiother Oncol 1991;21:107,
Sharma et al. Int J Radiat Oncol Biol Phys 2002;52:310

Chemoradiation + Brachy

RTOG 92-07

50 Gy EBT + 3 x 5 Gy HDR

4 x 5FU / CDDP

Applicator diameter 4-6 mm, prescrption 10 mm

CR 73%

G3 acute Tox 58%, G4 late Tox 8%

Gaspar et al., Int. J. Radiat. Oncol. Biol. Phys. 37; 593-599, 1997

60 Gy EBT + 2 x 5 Gy HDR

3 x 5FU / CDDP / MMC

Applicator diameter 10-14 mm, prescription @ 5mm

3 + 5 y Survival: 27% and 18%

G3-4 late Tox 11%

Calais et al., Int. J. Radiat. Oncol. Biol. Phys. 38; 769-775, 1997

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Improvement in Chemoradiation Without Brachytherapy

366 resectable tumors (T2-3N0-1M0)

Randomization RT vs. CRT followed by resection

41.4 Gy (1.8) + paclitaxel 50 mg/m2

+ carboplatin AUC = 2 mg/ml/min

92% R0 resections

Pathologic CR 29%

Median Survival: RT 24 mths vs. CRT 49.4 mths.

3 y OS: RT 44% vs. CRT 58%

Van Hagen, New Engl J Med 2012;366:2074-2084

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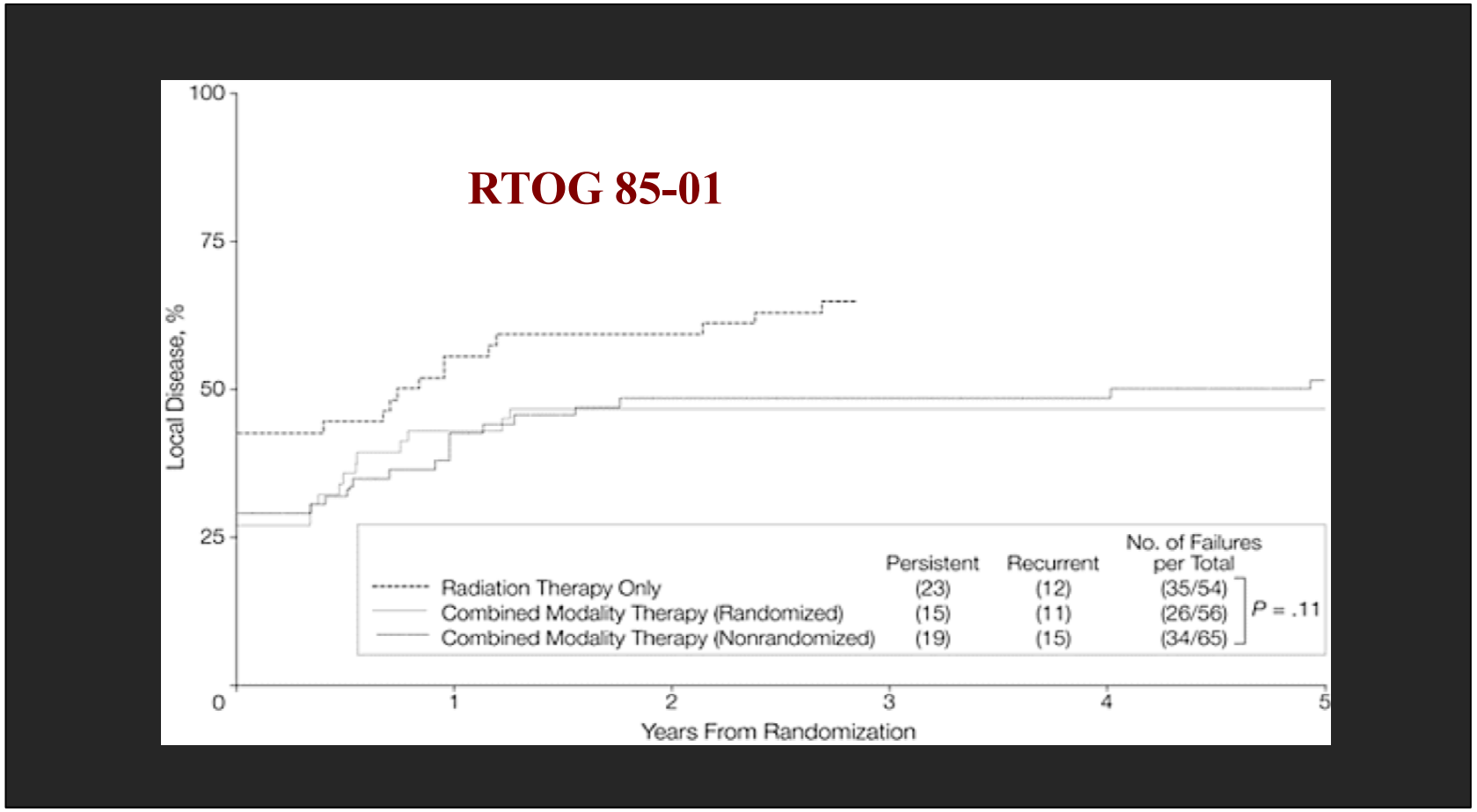
Improvement in Chemoradiation Without Brachytherapy



5 y OS: 26% vs 0%

CRT with Cisplatin + 5FU

Cooper, JAMA 1999: 281:1623-1627

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Improvement in Chemoradiation Without Brachytherapy

127 inoperable or irresectable tumors (T4N0-1 M0/M1a)

Median Follw-up: 44.5 mths

50.4 Gy (1.8) + paclitaxel 50 mg/m2
+ carboplatin AUC = 2 mg/ml/min

Local recurrence: 42 %

Median OS: 17 months

Mohammad, BMC Cancer 2014;56

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Policy

- Curative treatment
  - Chemoradiation seems superior to EBRT + Brachy
  - If chemotherapy is not possible EBRT + Brachy is an option
- Palliative treatment
  - Brachytherapy ± EBRT

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