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GEC-ESTRO

Comprehensive and Practical Brachytherapy

Budapest 5– 8 March 2017

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Budapest 2017

Welcome to the

30th

GEC-ESTRO Brachytherapy Course

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Renaud Mazeron
1977-2016

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GEC-ESTRO-BT Teaching Course
Budapest 2017

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Lectures

Day 1
Radioactivity
Isotope
Dose calculation
Implantation systems

Radiobiology

Intraluminal
Skin

Applicator localization and Basic planning

Day 2
Dose distribution
Dose optimization

Prostate
Breast
Anal canal

Day 3
DVH
Safety and Protection

Gynecology

Day 4
Uncertainties

Head & neck
Endometrial
Bladder
Pediatrics

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Contouring

Day 2
Result
Prostate
contouring

Correction
Prostate
contouring

Day 3
Result correction
prostate
contouring

Result cervix
contouring

Correction cervix
contouring

Day 4
Result correction
cervix
contouring

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Practical sessions

Day 1	Day 2	Day 3
Applicators Intraluminal Skin Applicator localization Dose Normalization	Applicators Prostate Breast Prostate planning	Applicators Gynecology Cervix planning

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Companies:

- Eckert & Ziegler BEBIG
- Elekta
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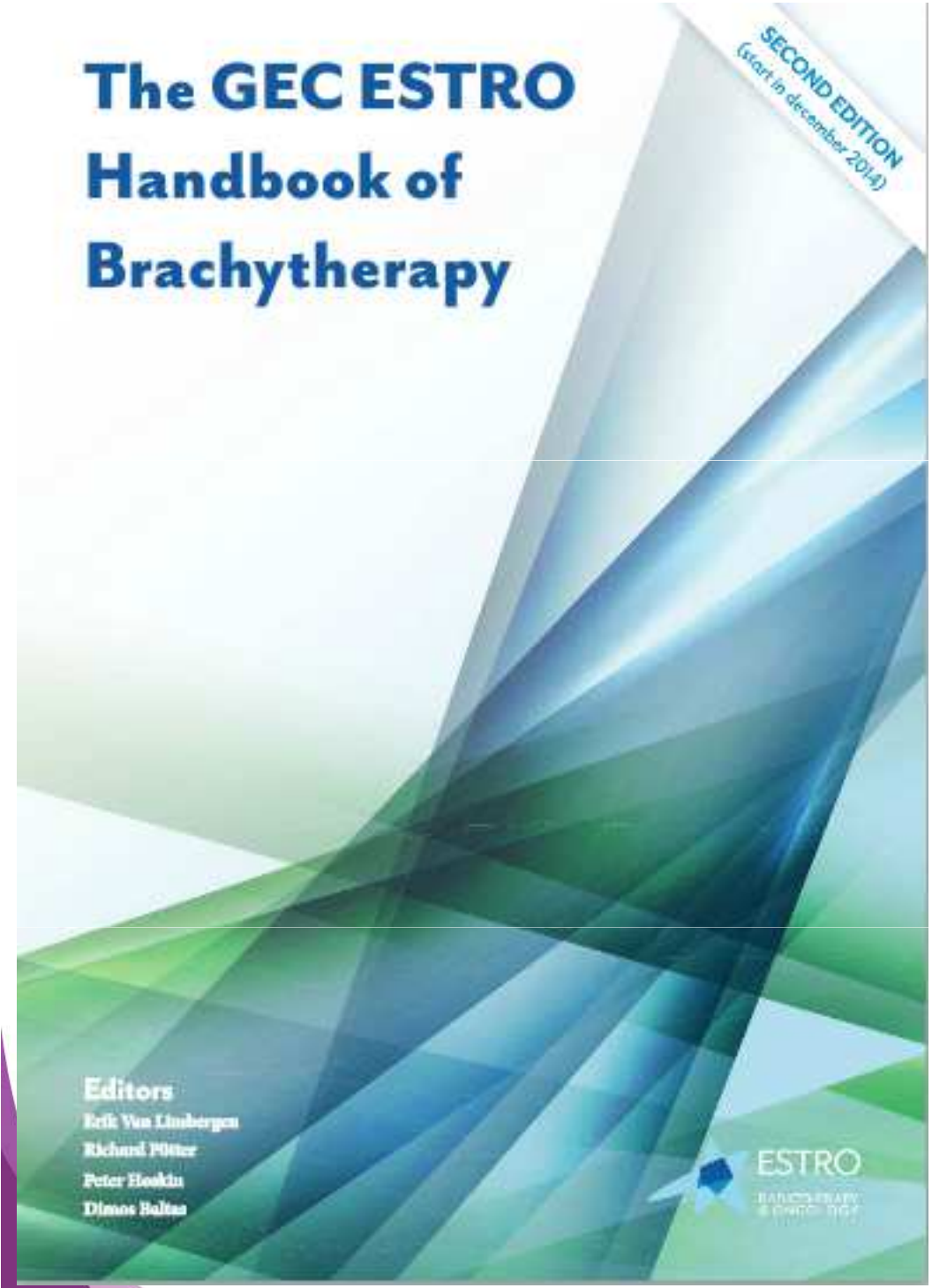

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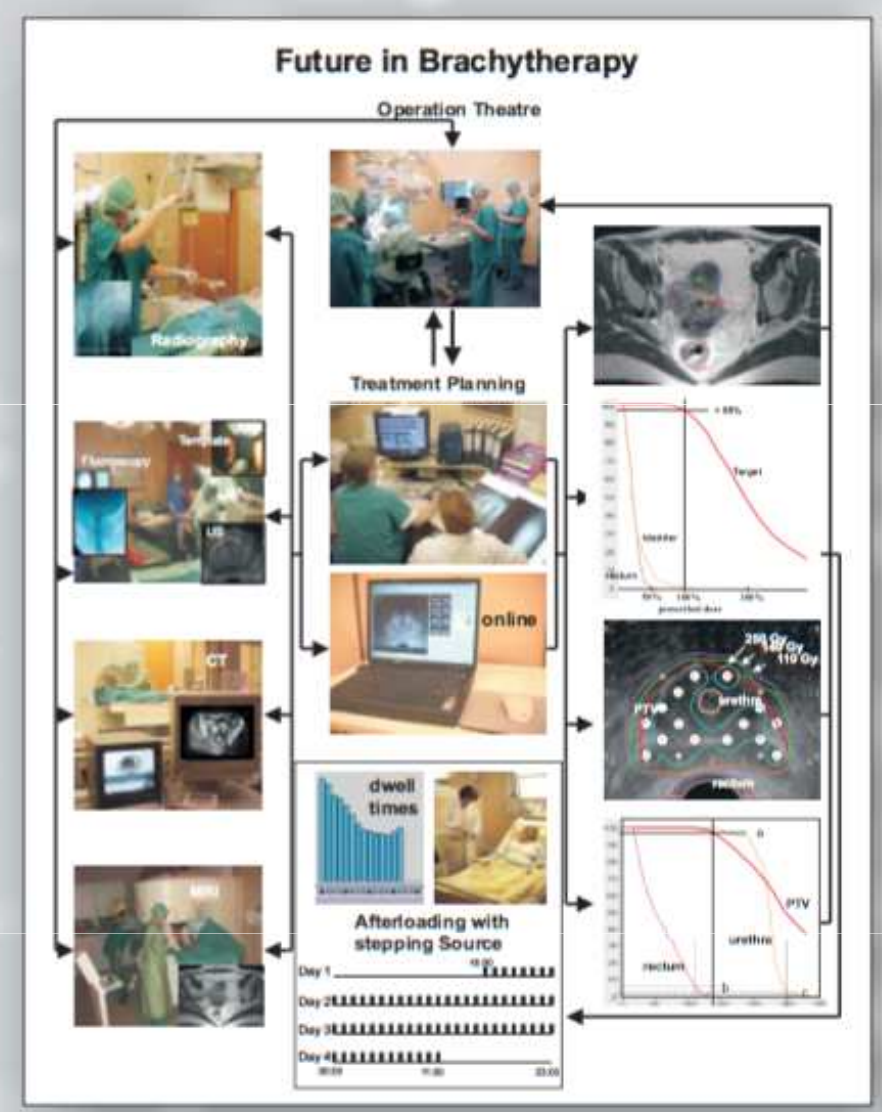


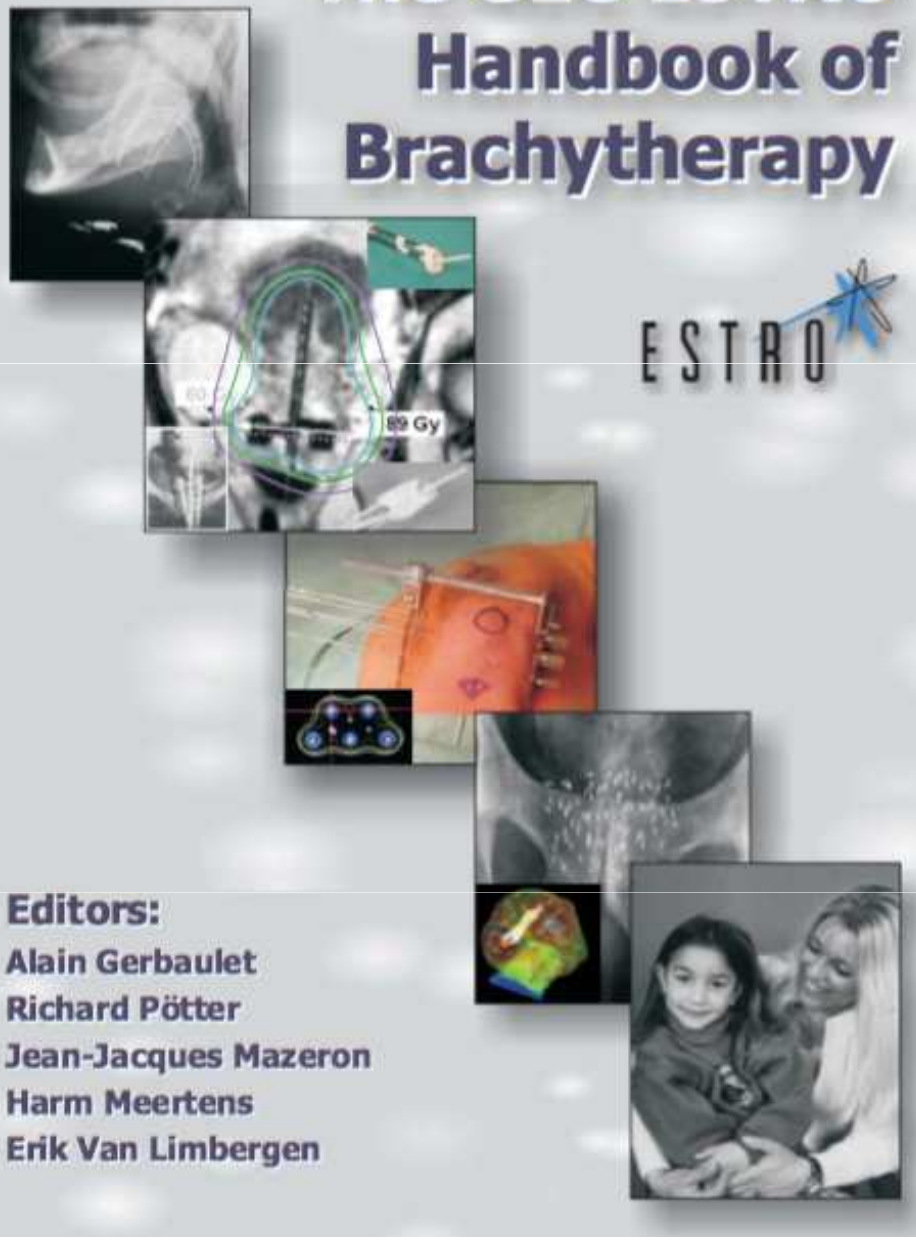
Integration of Clinical Skill and Experience, Modern Imaging (MRI, CT, US), Computer Assisted Treatment Planning with DVH Analysis and Dose Optimisation by Stepping Source Technology.

ISBN 90-804532-6

The GEC ESTRO Handbook of Brachytherapy

A. Gerbaulet, R. Pötter, J.-J. Mazeron, H. Meertens, E. Van Limbergen

The GEC ESTRO Handbook of Brachytherapy



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Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group: considerations and pitfalls in commissioning and applicator reconstruction in 3D image-based treatment planning of cervix cancer brachytherapy.

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.

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.

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Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC- ESTRO) breast cancer working group based on clinical evidence (2009).

GEC-ESTRO recommendations for brachytherapy for head and neck squamous cell carcinomas.

GEC/ESTRO-EAU recommendations on temporary brachytherapy using stepping sources for localised prostate cancer.

Inter-observer comparison of target delineation for MRI-assisted cervical cancer brachytherapy: application of the GYN GEC-ESTRO recommendations.

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

Tumour and target volumes in permanent prostate brachytherapy: a supplement to the ESTRO/EAU/EORTC recommendations on prostate brachytherapy.

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Radioactivity: What we need to know

ESTRO Teaching Course

Budapest, 2017

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Topics

- **Some History**
- Atoms
- Radioactive Decay
- Summary

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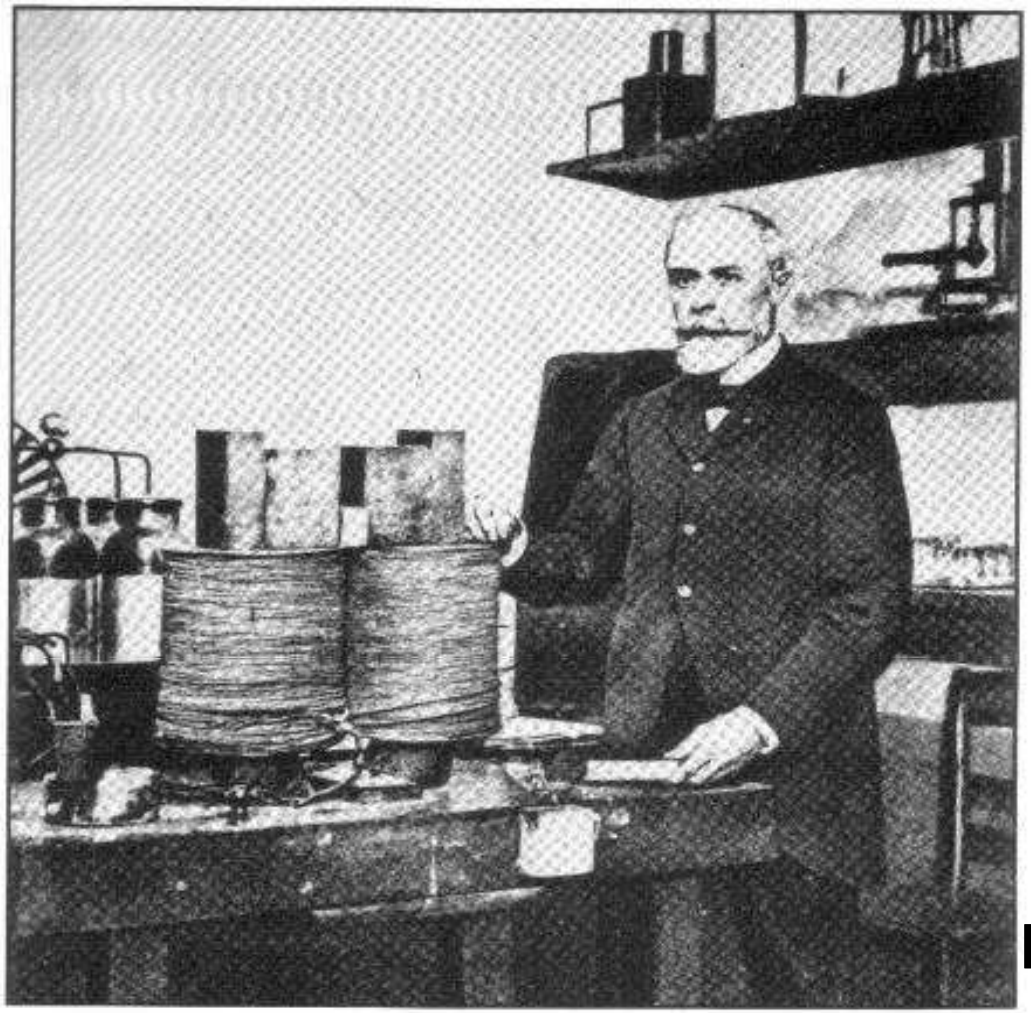
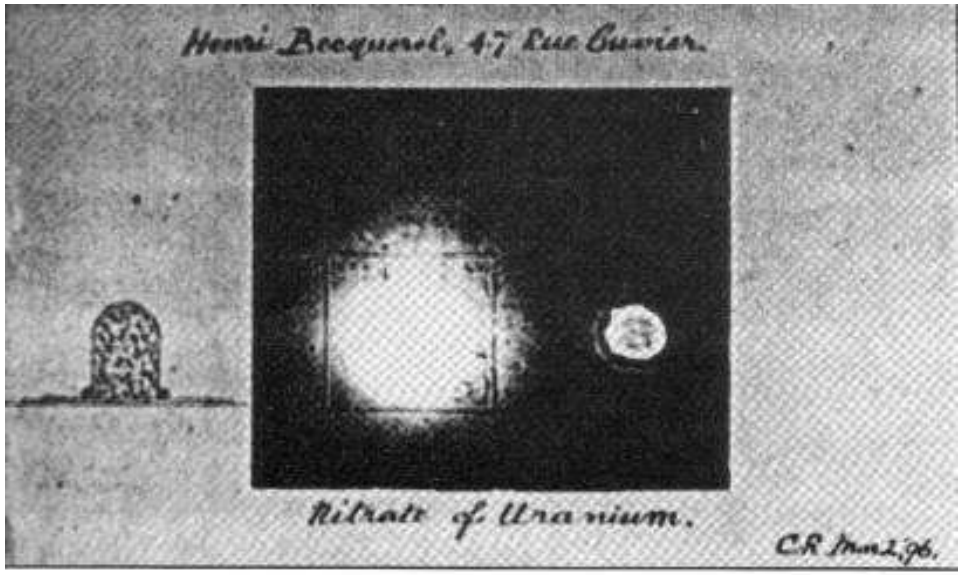
History: Radioactivity & Radium

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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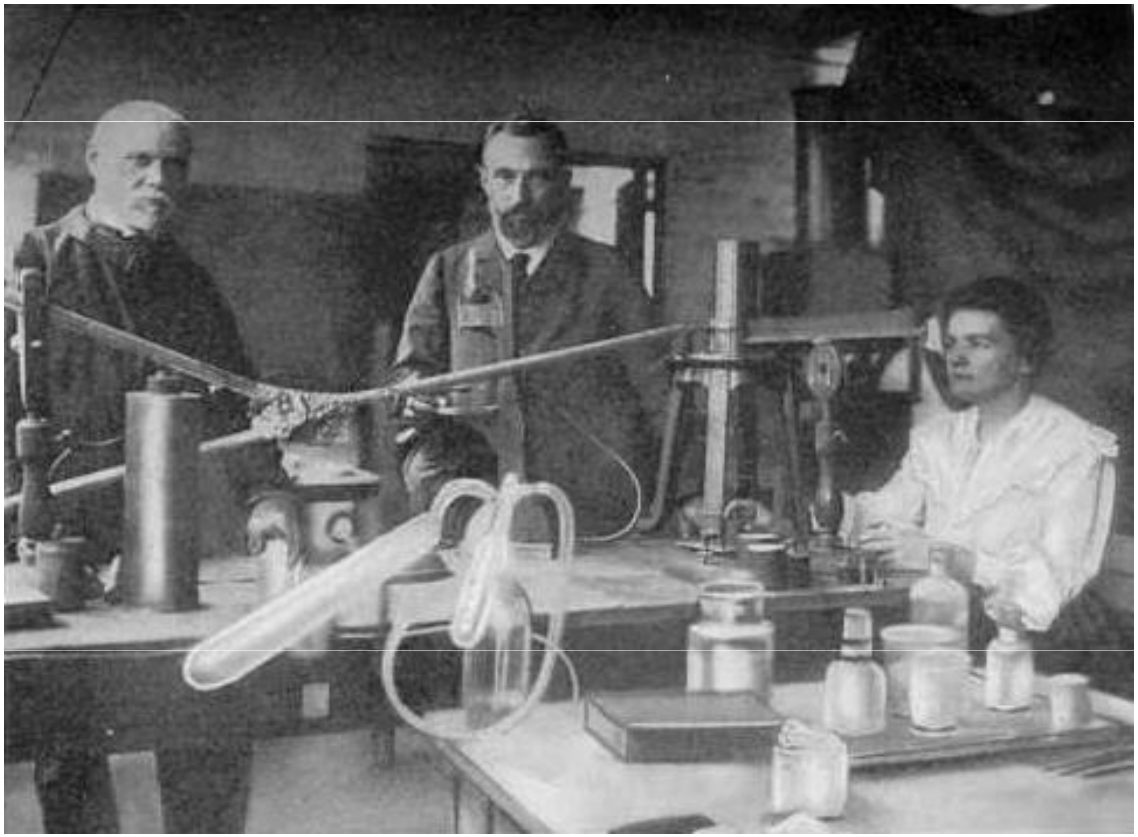
History: Radioactivity & Radium



Curies in their Laboratory where Radium was discovered

Discovery of Radium
December 1898

Pierre and Marie Curie

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Topics

- Some History
- **Atoms**
- Radioactive Decay
- Summary

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Atoms

In ancient Greek philosophy the term *atom* (the indivisible) was used to describe the small indivisible pieces, of which matter consists. Father of the so-called *Atomism* theory was the Thracian philosopher Leucippus (in Greek Leucippos, 450-370 BC), a student of the philosopher Zenon from Helea. According to Leucippus and to his student the Thracian philosopher Democritus (in Greek Democritos - Δημόκριτος, 460-370 BC) matter is built of identical, invisible and indivisible particles, the atoms (in Greek atoma). Atoms are continuously moving in the infinite empty space. This infinite empty space exists without itself being made of atoms. Atoms show variations in their form and size and they tend to be bound with other atoms. This behaviour of the atoms results in the building of the material world. According to Democritus, the origin of the universe was the result of the incessant movement of atoms in space.

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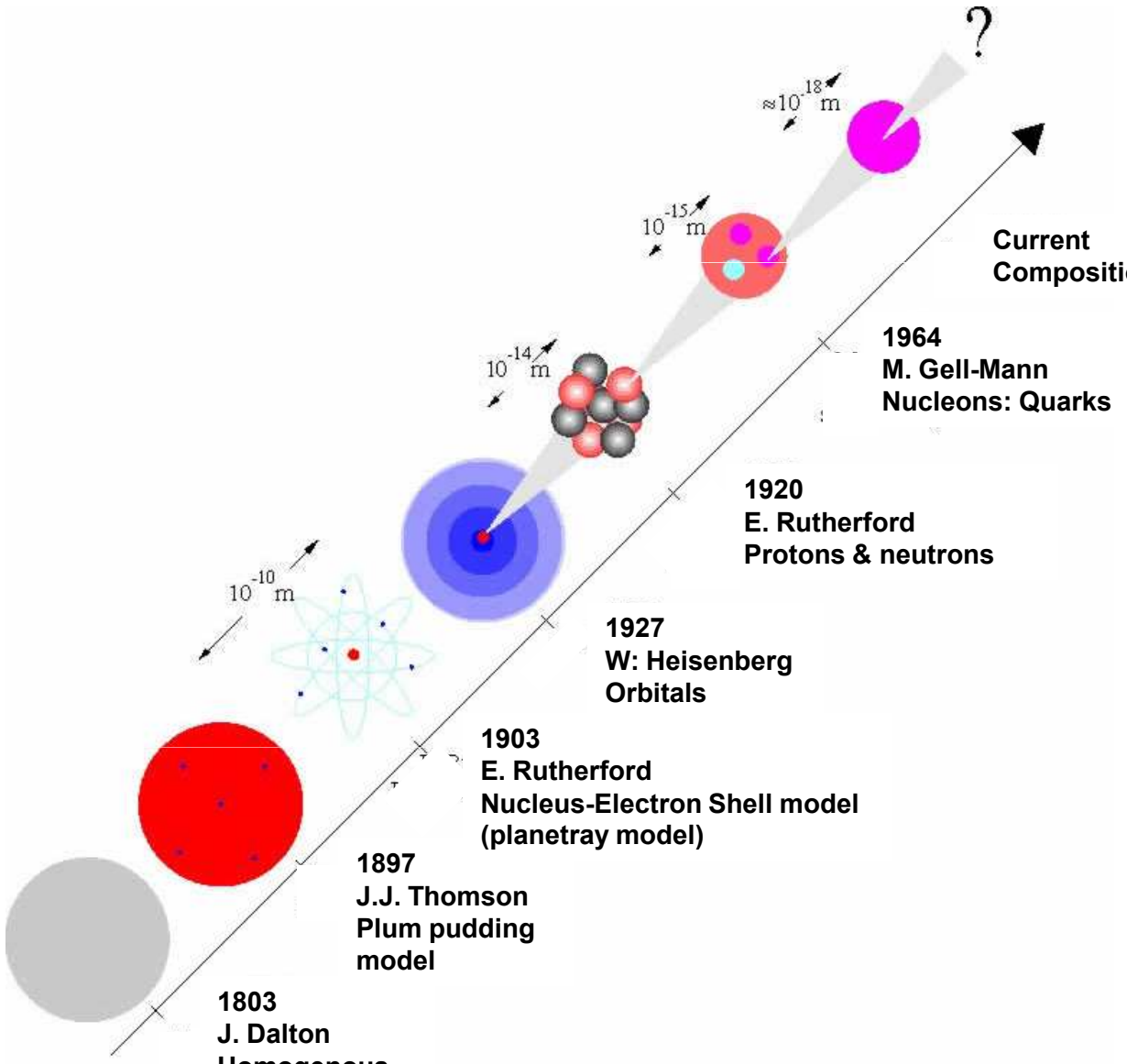
Atoms: History of Model Development



Democritus
460-370 BC

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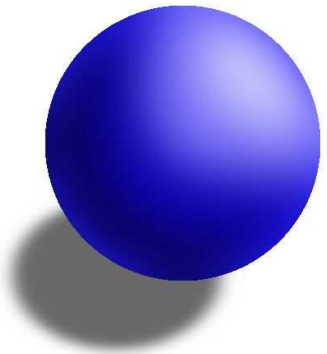
Atoms: Dalton´s Theory

In this sense atoms were the elementary particles of nature. It was in 1803, more than 2000 years later, when John Dalton (1766-1844) first provided evidence of the existence of atoms by applying chemical methods. In his theory, Dalton supported the concept that matter is built of indivisible atoms of different weights.

All atoms of a specific chemical element are in respect of their mass (weight) and their chemical behaviour identical.

Furthermore, according to Dalton's theory, atoms have a spherical shape, are filled homogeneously with matter and follow strictly the laws of classical mechanics.

Atoms are able to build compounds keeping their proportion to each other in the form of simple integers. If these compounds decompose the atoms involved emerge unchanged from this reaction.



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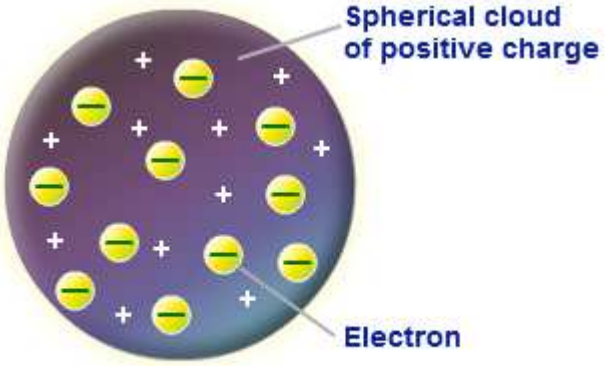
Atoms: Thomson´s discovery of Electrons

In 1897 Sir Joseph John Thomson (1856-1940) performed his famous experiment with cathode rays, where he proved that cathode radiation can be deflected by electric and magnetic fields and thus consisted of charged particles, the electrons.
In the following years several experiments where the scattering of electron beams was studied showed that the largest portion of the space occupied by the atoms is empty.
Based on these results Thomson proposed in 1904 that atoms consist of a spherical positive electrical charge distribution, like a liquid, in which the negative charged electrons are moving: the Thomson's compact atom model.

Thomson´s atom model



Thomson's Plum pudding model

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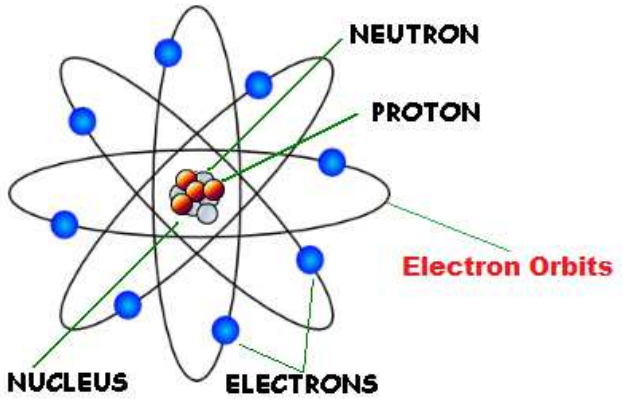
Atoms: Rutherford´s Atom Model

Ernest Rutherford (1871-1937) and his group in 1911 disproved the Thomson's atom model in a series of scatter experiments using alpha particles and gold foils. He was surprised to discover that the largest portion of the incident alpha particles was able to penetrate the foil having been only slightly deflected. Only a small portion were scattered at large angles.

According to these results, Rutherford suggested that the positive atomic charge and almost all the atomic mass is concentrated in a very small central body with a diameter of some *femtometers* (1 fm = 10^{-15}m) instead of being distributed over the whole volume of the atom with a diameter of about 0.1nm. Originally Rutherford ignored the sign of the charge of the nucleus, since as he pointed out, the angular distribution of the scattered alpha particles is independent of the sign of the nuclear charge.



Atoms: Rutherford´s Atom Model

It was van den Broek who first in 1913 suggested that the charge in the atomic nucleus expressed in elementary charge units (e) is equal to the atomic number Z. The atomic number Z was originally introduced as a serial increasing number assigned to the known elements when these are sorted according to increasing atomic weight (the periodic table of elements proposed by Dmitrij Iwanowitsch Mendelejew (1834-1907) in 1869).

The definitive interpretation of Z was achieved by Henry Moseley (1887-1915).

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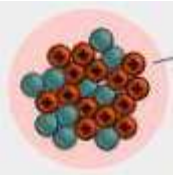
Atomic Nucleus

Until 1932 physicists assumed that atomic nuclei are constructed of protons, alpha-particles and electrons.

In 1932 Sir James Chadwick (1891-1974) identified the neutron by interpreting correctly the results of the experiments carried out mainly by Jean Frédéric (1897-1958) and Irène Joliot-Curie (1900-1956): neutrons, uncharged particles were ejected out of beryllium nuclei after their bombardment with alpha-particles. Chadwick considered neutrons to be an electron-proton compound and added it to the nuclear mix.

In July 1932 Heisenberg published his neutron-proton nuclear model by assuming that neutrons and protons to be the constituents of the nucleus. His nucleus also contained electrons, nuclear electrons, bound and unbound ones.

The assumption of the existence of nuclear electrons was completely rejected in the late 1930's after the introduction of the neutrino by Pauli in 1931 and the establishment of Enrico Fermi's (1901-1954) theory of beta-decay published in 1933.



Nomenclature of Nuclei

It was Truman P. Kohman in 1947, first proposed that individual atomic species should be called nuclides. In this way a nuclide is completely defined by the two numbers, atomic number Z and neutron number N, whereas an element or chemical element is characterised by its atomic number Z. Kohman's set of definitions have been generally adopted and are summarised in following Table:

Nomenclature of nuclei according to Kohman	
Term	**Description**
Nuclides	Z, A
Isotopes	Common Z
Isotones	common N = A - Z
Isobars	common A
Isodiapheres	common (N – Z)
Isomers	common Z and A

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Nomenclature of Nuclei

A nuclide X with atomic number Z and mass number A is then schematically represented by:

$$ {}^{A}_{Z}X $$

Examples

$$ {}^{12}_{6}C, \qquad {}^{16}_{8}O, \qquad {}^{40}_{20}Ca $$

If it is needed the neutron number N is also given:

$$ {}^{A}_{Z}X_{N} $$

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Topics

- Some History
- Atoms
- **Radioactive Decay**
- Summary

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Radioactive Decay

Nuclear transformation processes

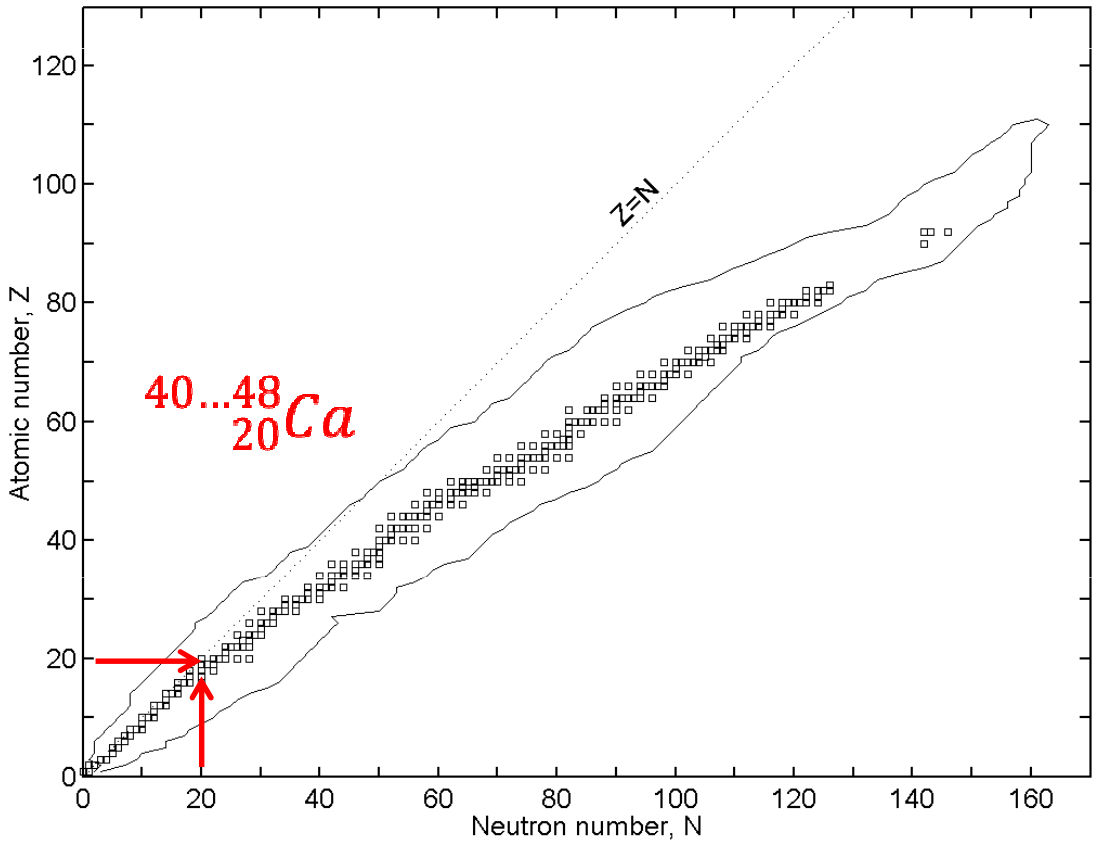
Nuclear transformation processes are those inducing transitions from one nuclear state to another. They can fall into two categories:

- those which occur ***spontaneously***, referred to as ***decays*** and
- those which are initiated by ***bombardment*** with a particle from outside, called ***reactions***.

When a process occurs spontaneously conservation of energy requires that the final state be of lower energy than the initial state and the difference in these energies is liberated as kinetic energy of energetic particles being emitted.

Radioactive Decay

There exist only 274 stable nuclides (forming the stability valley in figure) and ~2800 unstable nuclides (radionuclides).



Baltas D, Sakelliou L, Zamboglou N: The Physics of Modern Brachytherapy for Oncology, Taylor & Francis, 2007

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Radioactive Decay

All unstable nuclei spontaneously transform into other nuclear species by means of different decay processes that change the Z and N numbers of nucleus, until stability is reached.
Such spontaneous nuclear processes are called ***radioactive decays***.

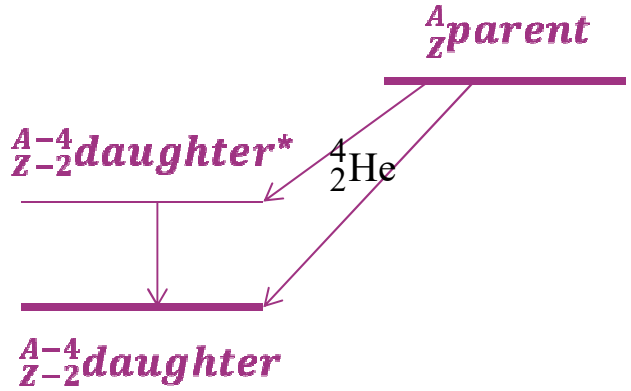
Among well-known radioactive decays are:

- alpha decay
- beta decay (incl. electron capture)
- spontaneous fission of heavy nuclei

Excited states of nuclei are also unstable (usually when a nucleus decays by alpha- or beta-emission it is left in an excited state) and eventually decay to the ground state by emission of gamma-radiation (no change of Z or N occurs).

Radioactivity is thus a property of the nucleus, according to which the nucleus decays to a more stable state.

Radioactive Decay



- **Alpha decay**

This occurs in very heavy nuclei, with very high atomic number, Z > 82. All nuclides with atomic number higher than 82 are unstable and the majority follow the alpha decay scheme. This is shown in the following equation:

$$^{A}_{Z}\text{parent} \Rightarrow {}^{A-4}_{Z-2}\text{daughter} + {}^{4}_{2}\text{He} + Q_{\alpha}$$

Q_{α} is the disintegration energy which is distributed between the kinetic energy of the emitted α-particle (this represents the majority) and the recoil energy of the daughter nucleus.
This means that the emitted α-particles have *discrete energy values* (hence a discrete energy spectrum) that are lower than the disintegration energy Q_{α}.

$$^{226}_{88}\text{Ra} \Rightarrow {}^{222}_{86}\text{Rn} + {}^{4}_{2}\text{He} + 4.8706\ \text{MeV}$$

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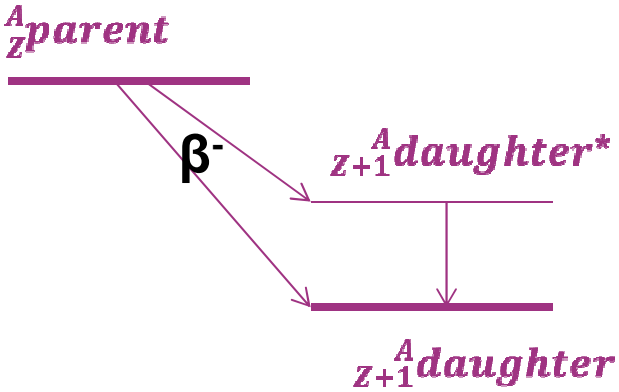
Radioactive Decay



- **β^- decay**

Unstable nuclides having an excessive number of neutrons in comparison to protons tend to reduce their number of neutrons by undergoing β- decay where the basic transformation process is:

$$^{1}_{0}n \Rightarrow {}^{1}_{+1}p + {}^{0}_{-1}\beta + {}^{0}_{0}\overline{\nu}_{e}$$

According to this in the β- decay the atomic number of the nucleus is increased by 1 and the number of neutrons in the nucleus is decreased by 1, where the mass number remains unchanged. Thus β- decay is in contrast to alpha decay an *isobaric nuclei transformation*. The β- general disintegration scheme is shown in the following equation:

$$^{A}_{Z}\text{parent} \Rightarrow {}^{A}_{Z+1}\text{daughter} + {}^{0}_{-1}\beta + {}^{0}_{0}\overline{\nu}_{e} + Q_{\beta^-}$$

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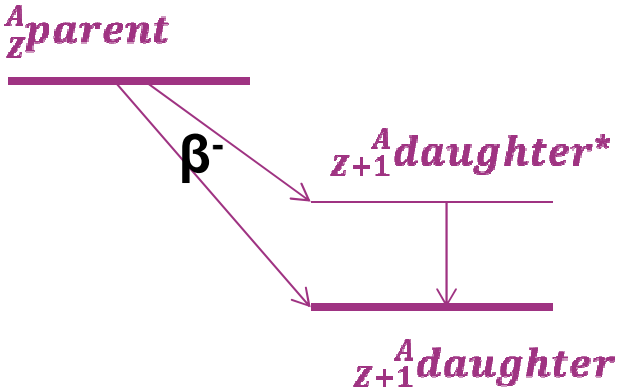
Radioactive Decay



- β^- decay

The β^--particle and the antineutrino share the disintegration energy $Q_{\beta-}$.
The emitted β^--particle can *have any kinetic energy* up to the maximum possible, $T_{\beta-,max}$, as can be derived from:

$$E_{\beta-,max} = Q_{\beta-}$$

and

$$\overline{E}_{\beta^-} \approx \frac{E_{\beta^-,max}}{3}$$

$$^{137}_{55}\mathrm{Cs} \Rightarrow {}^{137}_{56}\mathrm{Ba} + {}^{0}_{-1}\beta + {}^{0}_{0}\overline{\nu}_{e} + 1.1756\ \mathrm{MeV}$$

$E_{\beta-,max}$ = 0.514 MeV or 1.1756 MeV

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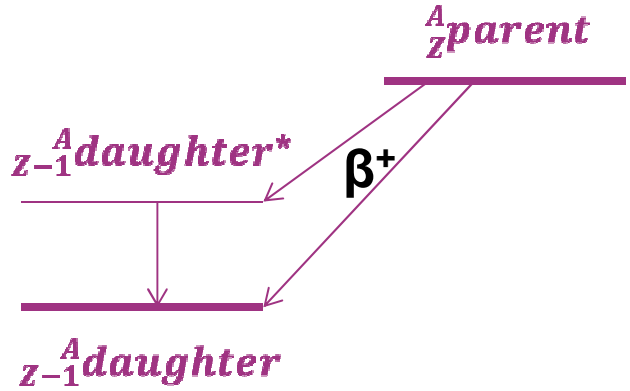
Radioactive Decay



- **β^+ decay**

Unstable nuclides having an excessive number of protons in comparison to neutrons tend to reduce their number of protons by undergoing β^+ decay where the basic transformation process is

$$^{1}_{+1}p \Rightarrow {}^{1}_{0}n + {}^{0}_{+1}\beta^{+} + {}^{0}_{0}\nu_e$$

The neutrino (electron-neutrino), ν_e , is like antineutrino a neutral particle (lepton) with practically 0 rest mass (< 18 eV). According to this in the β^+ decay the atomic number of the nucleus is decreased by 1 and the number of neutrons is increased by 1 where the mass number remains unchanged. β^+ decay like β^- decay is an isobaric nuclei transformation.

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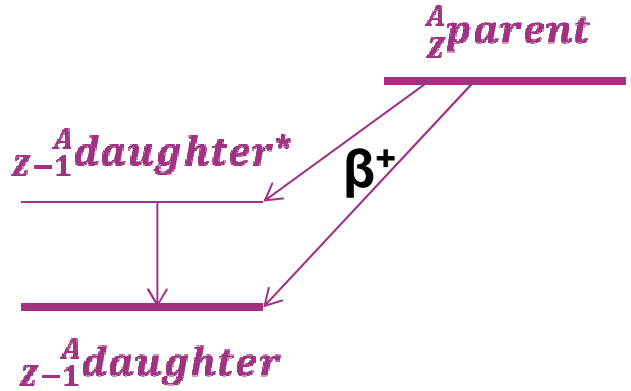
Radioactive Decay



- **β^+ decay**

The β^+ general disintegration scheme is shown in the following equation

$$^{A}_{Z}\text{parent} \Rightarrow {}^{A}_{Z-1}\text{daughter} + {}^{0}_{+1}\beta^{+} + {}^{0}_{0}\nu_e + Q_{\beta^+}$$

The β^+-particle and the neutrino share the disintegration energy $Q_{\beta+}$.
The emitted β^+-particle can *have any kinetic energy* up to the maximum possible, $T_{\beta+,max}$, as can be derived from:

$$E_{\beta+,max} = Q_{\beta+}$$

and

$$\overline{E}_{\beta^+} \approx \frac{E_{\beta^+,max}}{3}$$

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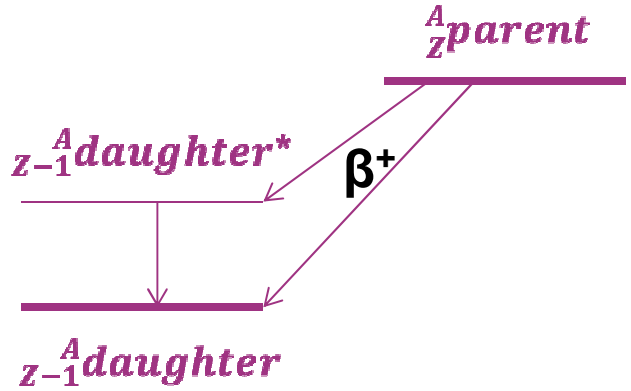
Radioactive Decay



- β^+ decay

$$^{22}_{11}\mathrm{Na} \Rightarrow {}^{22}_{10}\mathrm{Ne} + {}^{0}_{+1}\beta^{+} + {}^{0}_{0}\nu_{e} + 2.8422\ \mathrm{MeV}$$

The β^+-particle and the neutrino share the disintegration energy $Q_{\beta+}$.
The emitted β^+-particle can *have any kinetic energy* up to the maximum possible, $T_{\beta+,max}$, as can be derived from:

$$E_{\beta+,max} = Q_{\beta+} - 1.2745\ \mathrm{MeV} = 1.5677\ \mathrm{MeV}$$

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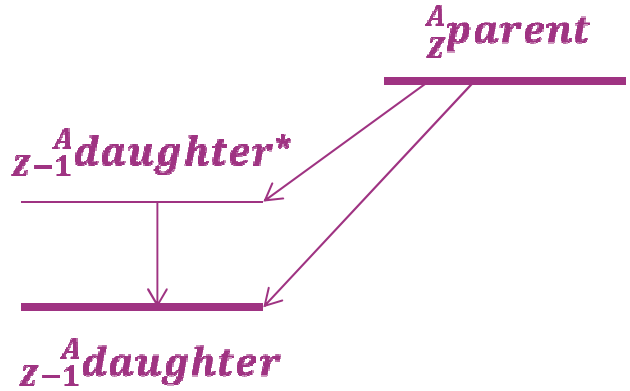
Radioactive Decay



- **Electron Capture (EC)**

A second possibility for unstable nuclides having an excessive number of protons in comparison to neutrons to be transformed to stable nuclides is the *electron capture* (EC). Electron capture is an alternative decay scheme for such nuclides to the β^+ decay which requires that the parent atom has an excess energy (mass) of at least 1.022 MeV in order to be able to undergo such a β^+ decay scheme. The basic transformation process behind the electron capture is

$$^{1}_{+1}p + {}^{0}_{-1}e \Rightarrow {}^{1}_{0}n + {}^{0}_{0}\nu_e$$

An orbital electron of the parent atom is captured by the nucleus. Candidates for the electron capture process are orbit electrons from any of the orbit shells K, L, M, etc. Practically electrons from the K shell are mostly involved due to their close neighbourhood to nucleus. In dependence on the origin of the involved electron the electron capture process is called K capture, L capture, etc.

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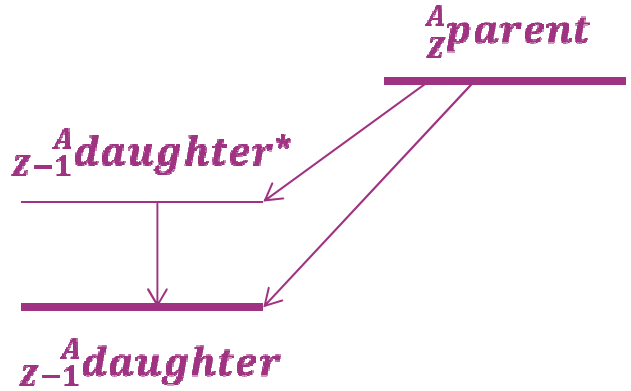
Radioactive Decay



- **Electron Capture (EC)**

Similar to the competitive β^+ decay, electron capture is an isobaric nuclei transformation (the mass number A remains unchanged).
The EC general disintegration scheme is shown in the following equation

$$^{A}_{Z}\text{parent} + {}^{0}_{-1}\text{e} \Rightarrow {}^{A}_{Z-1}\text{daughter} + {}^{0}_{0}\nu_e + Q_{EC}$$

$$^{22}_{11}\text{Na} \Rightarrow {}^{22}_{10}\text{Ne} + {}^{0}_{0}\nu_e + 2.8422\ \text{MeV}$$

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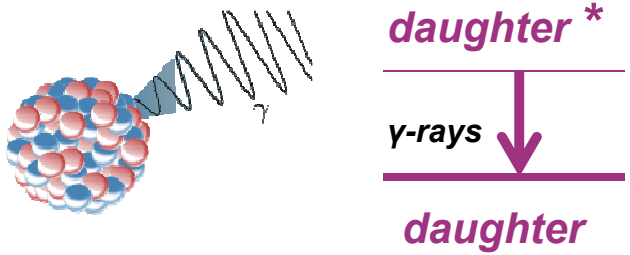
Radioactive Decay



- **Gamma Decay and Internal Conversion (IC)**

For all the decay schemes, the daughter nucleus is in most of the cases in an excited energetic state. Its energy excess is usually emitted as γ-rays: these are photons, having their origin in nucleus and showing *a line energy spectrum (photons emitted at discrete energies)*. This process of emitting *γ-rays* is called *gamma decay*.

In addition to the γ-ray emission, there is another mechanism by which the daughter nucleus can loss its energy excess. This is by transferring its energy excess directly to an inner orbital electron, which then escapes the atom with a kinetic energy equal to the difference of the nucleus excess energy and the binding energy of the involved electron. This process is called *internal conversion (IC)* and the involved electron is called *internal conversion electron (CE)*.
In both gamma decay and internal conversion process, the atomic number Z, the mass number A as well as the number of neutrons N in the nucleus remain unchanged.

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Radioactive Decay

- **Gamma Decay and Internal Conversion (IC)**

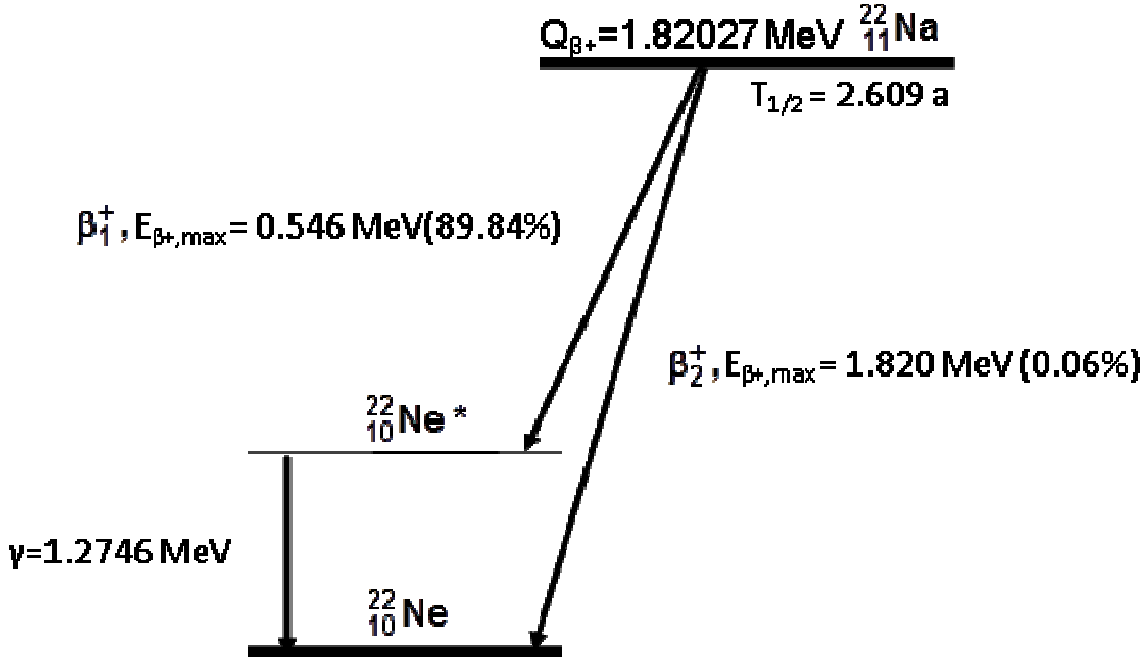
  The internal conversion process occurs mainly in nuclei with a high nuclear charge (high atomic number Z), where due to the strong electromagnetic attractive forces the atomic electrons at the inner orbits have a finite probability of staying in nucleus of that atom. In these atoms, the inner orbits are at very close distances to the nucleus. Thus an electron from such an orbit can directly take over the energy excess of the nucleus.

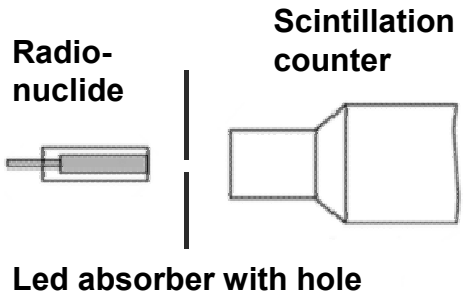
  The energy distribution of the conversion electrons show *a line spectrum*, that is, as also for the case of γ-rays, characteristic for each nucleus.

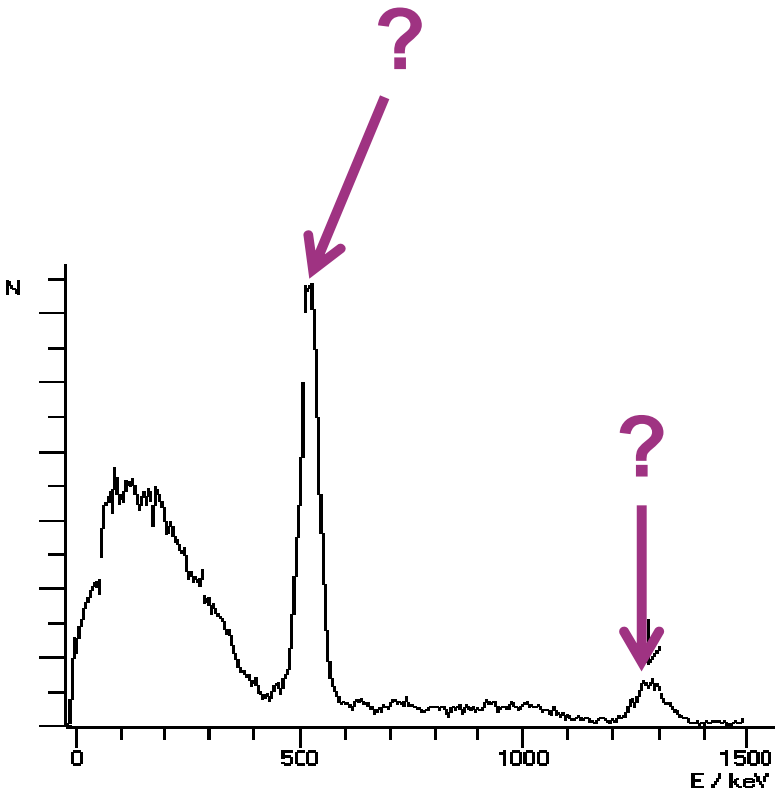
  In internal conversion, there will be a missing electron (hole) at the involved electron orbit. This will be then filled by another electron of a higher orbit, where characteristic *X-rays or Auger electrons* production will be the result.

Radioactive Decay: Example

- β^+ decay of ^{22}Na

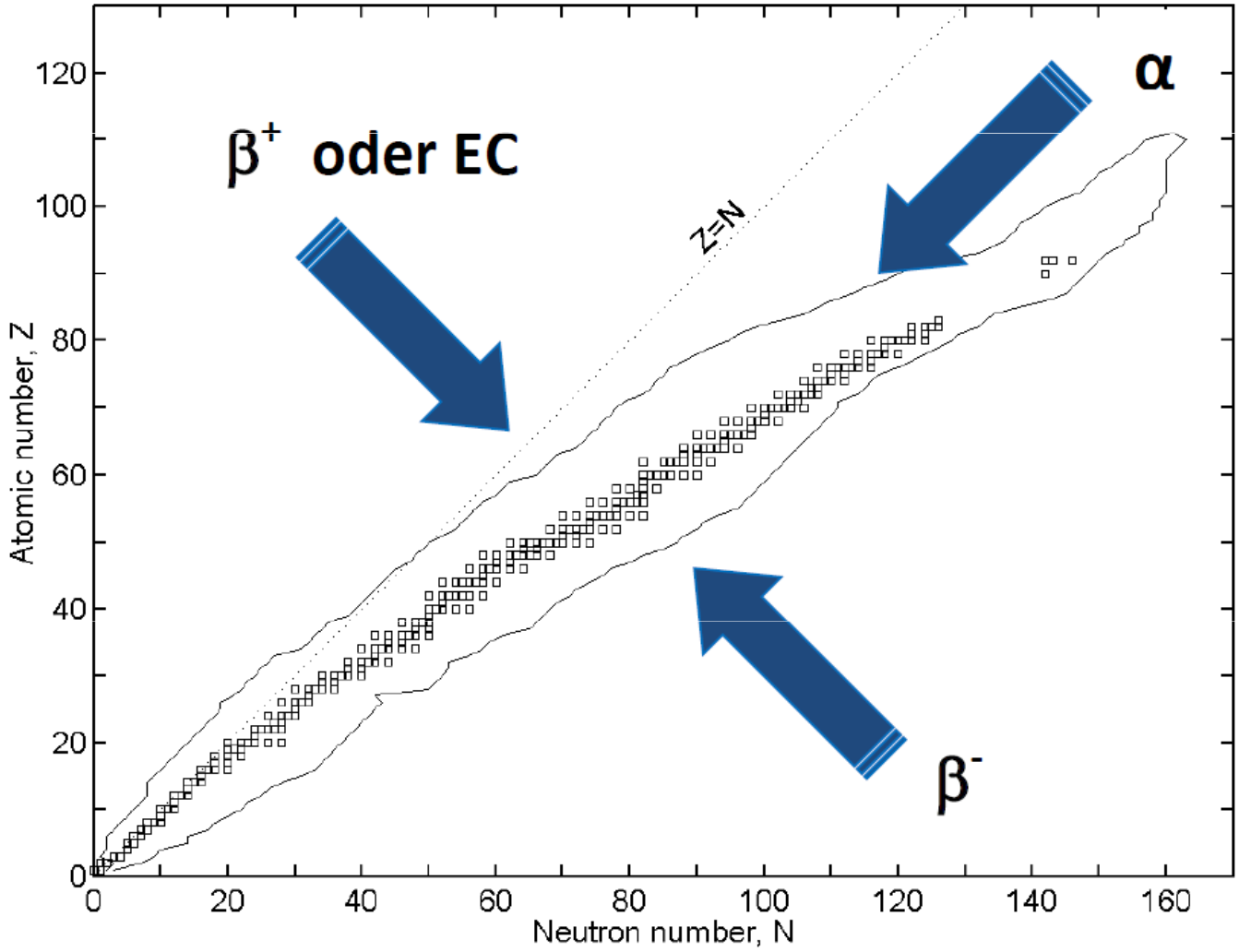






γ-Spectrum of the decay

Radioactive Decay: Summary



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Radioactive Decay: Activity A

The probability for a radioactive decay per unit time for a specific nuclide is constant and called the ***decay constant, λ***.

Since radioactive decay is a stochastic, spontaneous process it is not possible to identify which particular atoms out of an amount of a specific radionuclide will undergo such decay at a specific time. It is only possible to predict the mean number of disintegrated nuclei at a specific time, i.e. the ***activity A(t)*** defined as:

$$A(t) = -\frac{dN(t)}{dt}$$

where dN(t) is the number of decays observed during the time interval dt:
the minus sign is included since dN(t)/dt is negative due to the decrease of N(t) with time while activity, A(t), is a positive number.

The SI unit of activity is the ***becquerel*** (Bq, named after the discoverer of radioactivity):
1 Bq=1 disintegration per second =$1s^{-1}$.
Activity was traditionally measured in units of ***curies (Ci):*** 1 Ci = 3.7 10^{10} Bq.
Definition of 1 Ci: Activity contained in 1g ^{226}Ra

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Radioactive Decay: Activity A

Experimentally, it is found that the activity, A(t), at any instant of time t is directly proportional to the number, N(t), of the radioactive parent nuclei present at that time:

$$A(t) = \lambda N(t)$$

where λ is the decay constant. Combining the two equations:

$$A(t) = -\frac{dN(t)}{dt} \quad \text{and} \quad A(t) = \lambda N(t) \quad \text{we have} \quad -\frac{dN(t)}{dt} = \lambda N(t)$$

Integrating this differential equation results to:

$$N(t) = N_0 \exp(-\lambda t)$$

where N_0 is the (initial) number of radioactive nuclei at t=0, i.e. N_0=N(0).

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Radioactive Decay: Exponential Law

Multiplying both sides of the equation by the decay constant λ and considering equation, results to the following equation for the activity

$$N(t) = N_0 \exp(-\lambda t) \quad \Rightarrow \quad \lambda N(t) = \lambda N_0 \exp(-\lambda t)$$

Considering $A(t) = \lambda N(t)$ the following equation for the activity results:

$$A(t) = A_0 \exp(-\lambda t)$$

$$N(t) = N_0 \exp(-\lambda t)$$

Both these equations present the ***exponential law of radioactive decay***, which states that the number of nuclei that have not decayed in the sample as well as the activity of the sample, both ***decrease exponentially with time***.

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Radioactive Decay: Half Life $T_{1/2}$

The time needed ***for half of the radionuclides to decay***, or equivalently the activity of a sample to be reduced to half its initial value, is called ***half life, $T_{1/2}$*** :

$$\frac{N_0}{2} = N_0 \exp(-\lambda T_{1/2}) \quad \Rightarrow \quad T_{1/2} = \frac{\ln 2}{\lambda}$$

or equivalently

$$A(T_{1/2}) = \frac{A_0}{2} = A_0 \exp(-\lambda T_{1/2})$$

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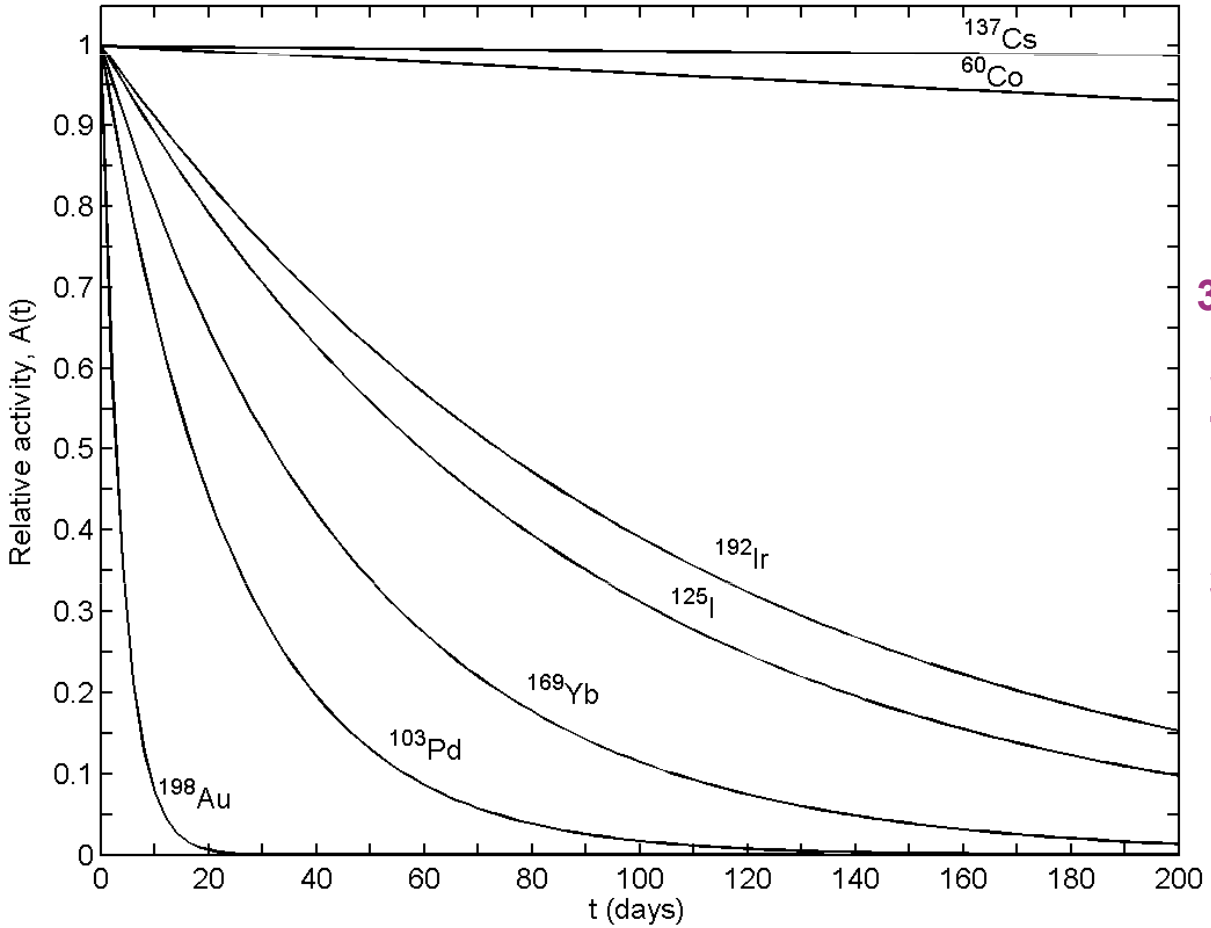
Radioactive Decay

Exponential decrease of unit activity with time for various radionuclides used in brachytherapy which are characterized by half lives spanning from a couple of days to thirty years.

$$\frac{A(t)}{A_0} = \exp(-\lambda t)$$

$$= \exp\left(-\frac{\ln 2}{T_{1/2}} t\right)$$



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Radioactive Decay: Mean Lifetime τ

The ***mean lifetime τ***, i.e. the average lifetime of a given radioactive nucleus is the average value of t calculated as:

$$\tau = \langle t \rangle = \frac{\int_0^\infty t\,dN(t)}{\int_0^\infty dN(t)} = \frac{N_0 \int_0^\infty \lambda\, t \exp(-\lambda t)\, dt}{N_0} = \frac{1}{\lambda}$$

The mean lifetime τ, is the reciprocal of the decay constant λ, and this result comes natural since the decay constant has the physical meaning of the disintegration probability, i.e. the fraction of decays taking place per unit time. **Apparently, within time τ the initial number of nuclei decreases by a factor of e (e ≈ 2.7183):**

$$\tau = \frac{1}{\lambda} = \frac{T_{1/2}}{\ln 2} = \frac{T_{1/2}}{0.69315} = 1.4427\, T_{1/2}$$

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Radioactive Decay: Specific Activity $A_{specific}$

The ***specific activity*** $A_{specific}$ (Bq.kg^{-1}) of a radioactive source of mass m containing a single radionuclide of activity A is given by:

$$A_{specific} = \frac{A}{m}$$

Using the decay constant λ, the specific activity $A_{specific}$ for a pure radionuclide can be calculated by:

$$A_{specific} = \lambda \frac{N_A}{M} = \frac{\ln 2}{T_{1/2}} \frac{N_A}{M}$$

where N_A is the Avogadro constant and M is the molar mass of the radionuclide:

N_A = 6.0221367 10^{23} mol^{-1}

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Radioactive Decay: Specific Activity $A_{specific}$

$$A_{specific} = \lambda \frac{N_A}{M} = \frac{\ln 2}{T_{1/2}} \frac{N_A}{M}$$

- **Molar mass of ^{226}Ra is 226.02 g/mol**
- **$T_{1/2}$ of decay for ^{226}Ra is 1600 a**
- **Thus considering 1a = 365x24x60x60 s ➔ $T_{1/2}$ = 5.0458 x 10^{10} s**
- **and N_A = 6.02214 x10^{23} mol^{-1} (Avogadro-Number)**
- **A_{spec} for ^{226}Ra is 3.7x10^{10} Bq/g = 37 GBq/g =1 Ci/g**

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Topics

- Some History
- Atoms
- Radioactive Decay
- **Summary**

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Radiobiology of LDR-PDR-HDR Brachytherapy

Erik Van Limbergen MD PhD

Department of Radiation Oncology
University Hospital Gasthuisberg
Leuven Belgium

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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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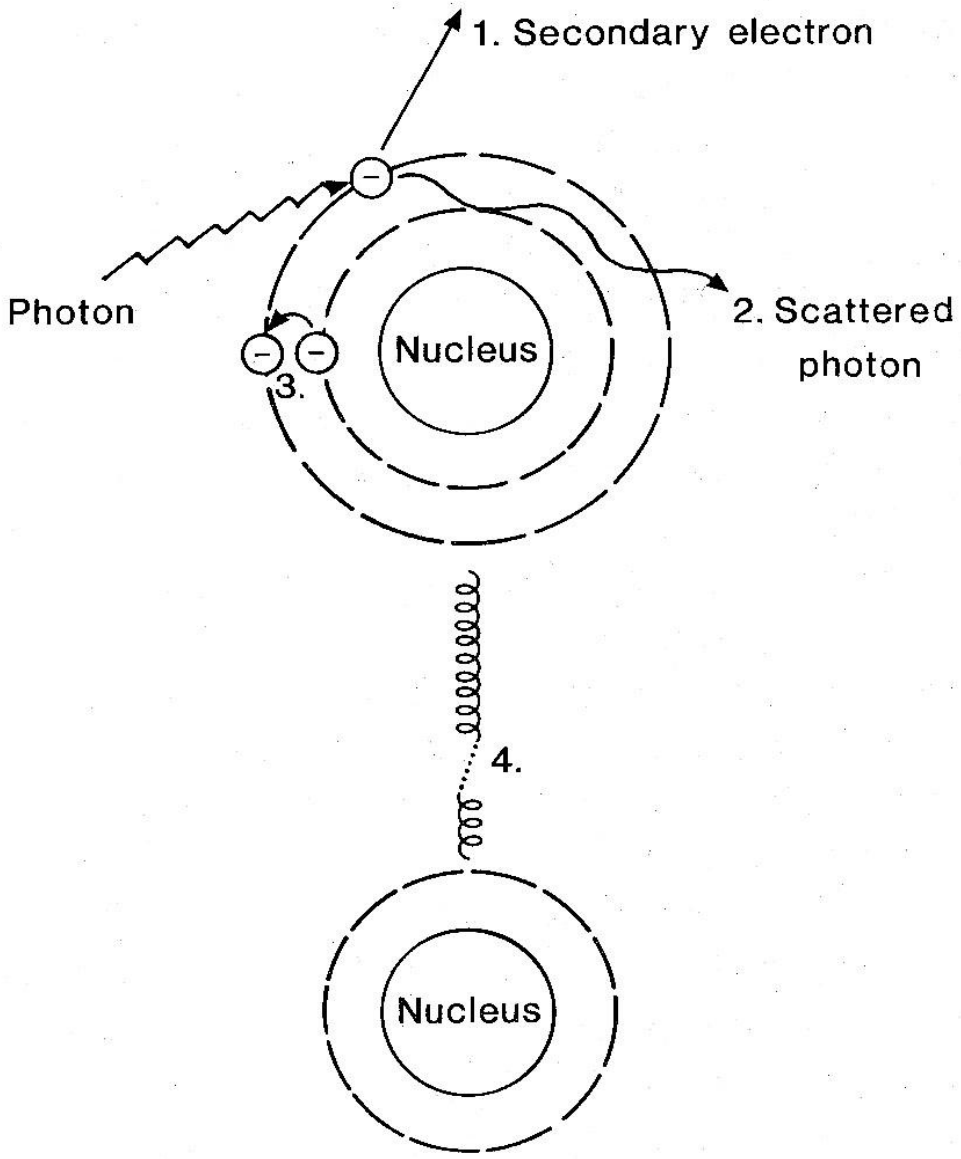
DNA Damage by ionising irradiation

Physical phase

excitation

ionisation

- Photoelectric absorbtion
- Compton effect
- Pair formation



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DNA Damage by

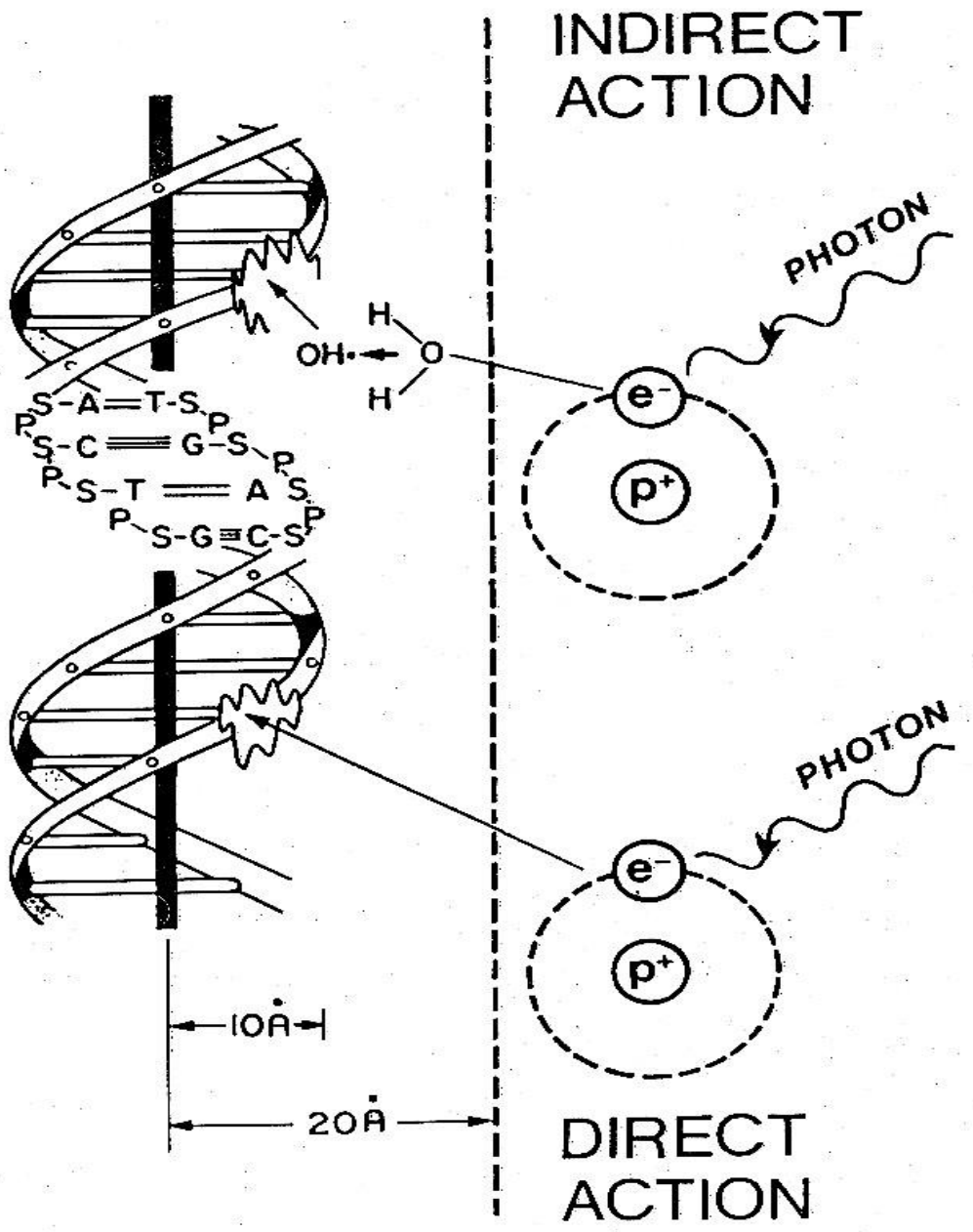
ionising irradiation

Chemical phase

direct and indirect action

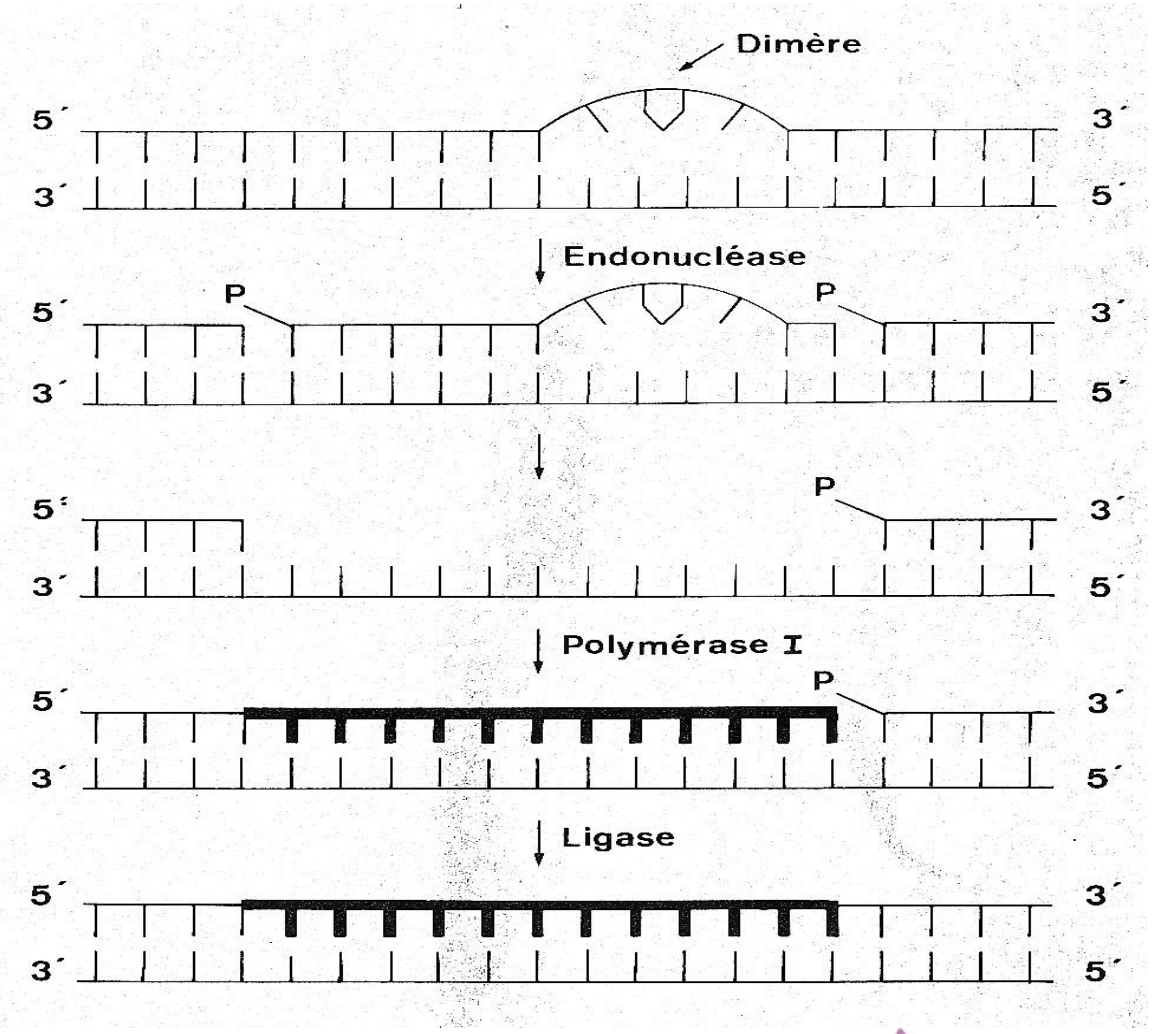
free radicals

damage fixation



Check and REPAIR Enzymes

- Exonucleases
- Endonucleases
- Transscriptases
- Polymerases
- Ligases



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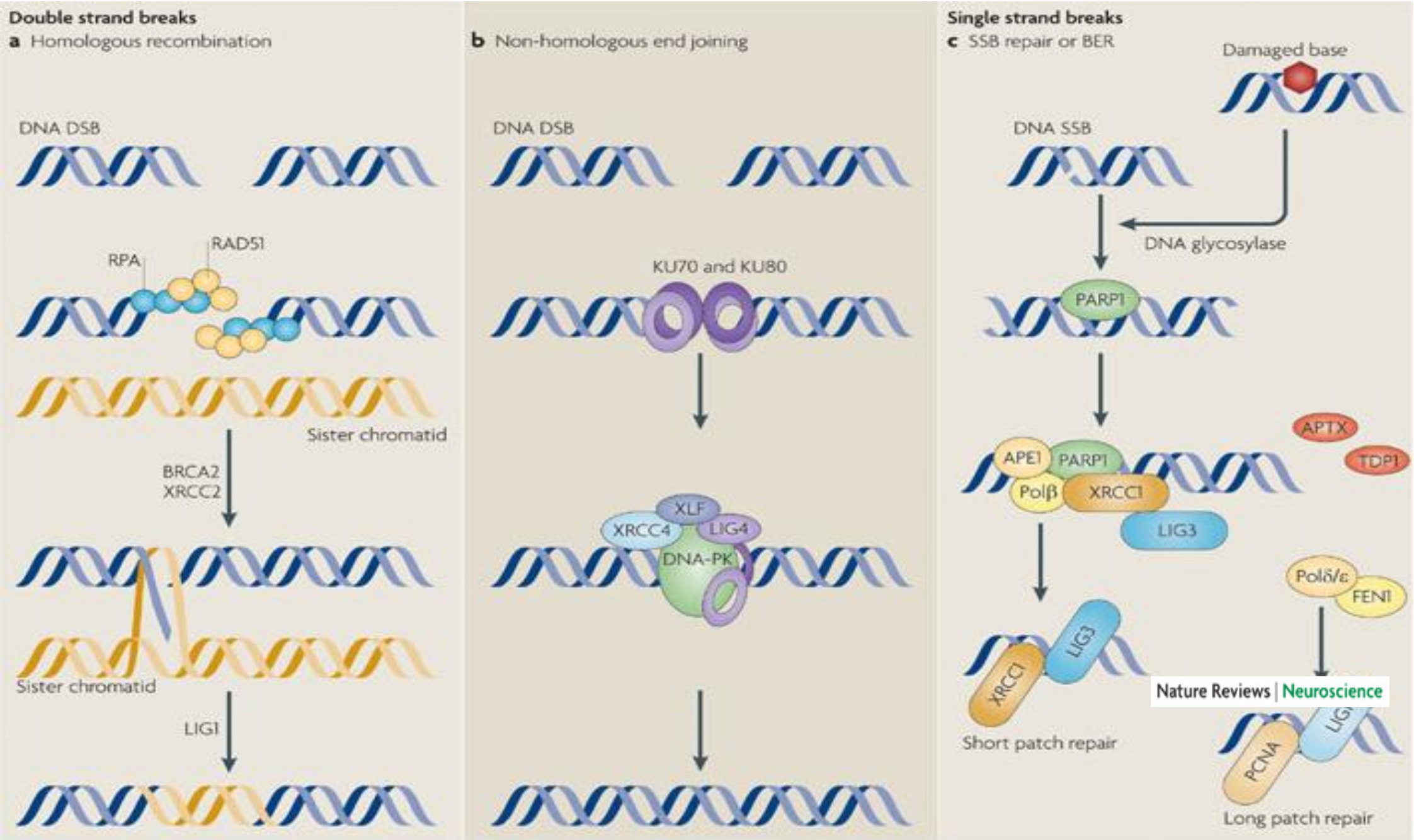
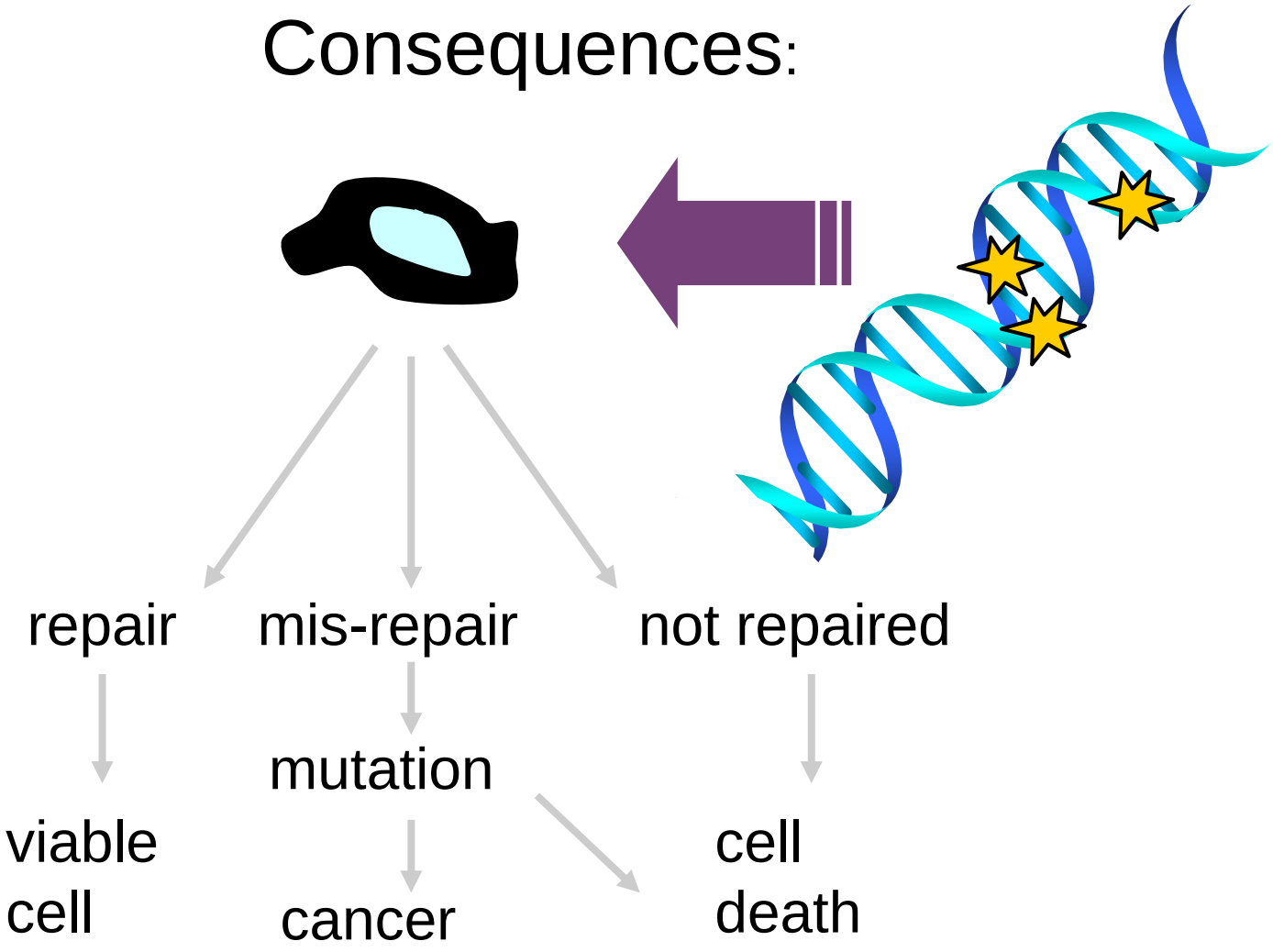
Enzymatic repair processes



Radiation damage to a cell



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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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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

- RBE
- Treated Volumes
- Dose inhomogeneities

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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

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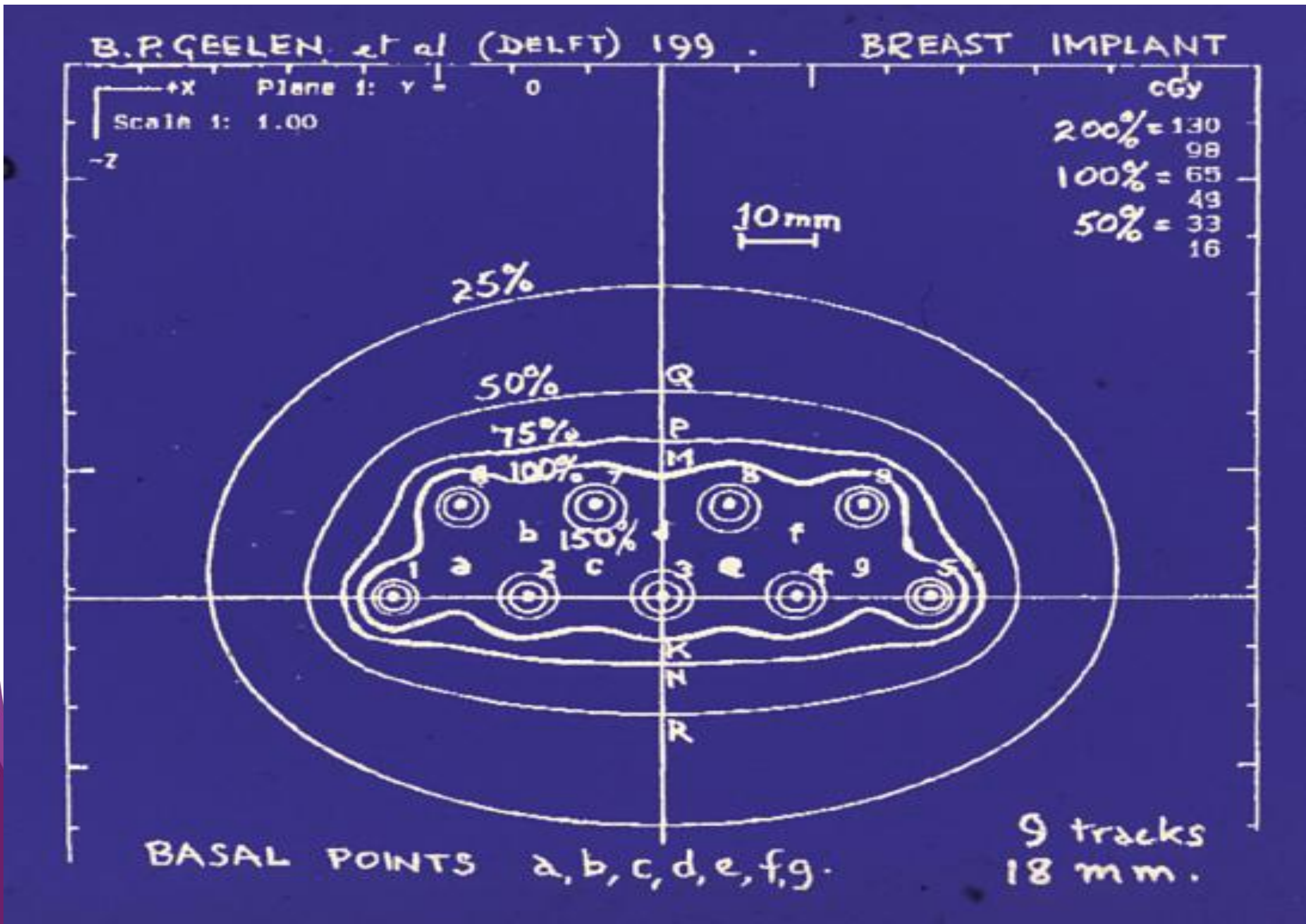
B.P.GEELEN et al (DELFT) 199 . BREAST IMPLANT
+X Plane 1: Y = 0
Scale 1: 1.00
-Z
cGy
200% = 130
98
100% = 65
49
50% = 33
16
10mm
25%
50%
75%
100%
150%
Q
P
M
K
N
R
1
2
3
4
5
6
7
8
9
a
b
c
d
e
f
g
BASAL POINTS a, b, c, d, e, f, g.
9 tracks
18 mm.

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 with complete repair

- Over a short treatment time (a few days)

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Dose Rate Effects

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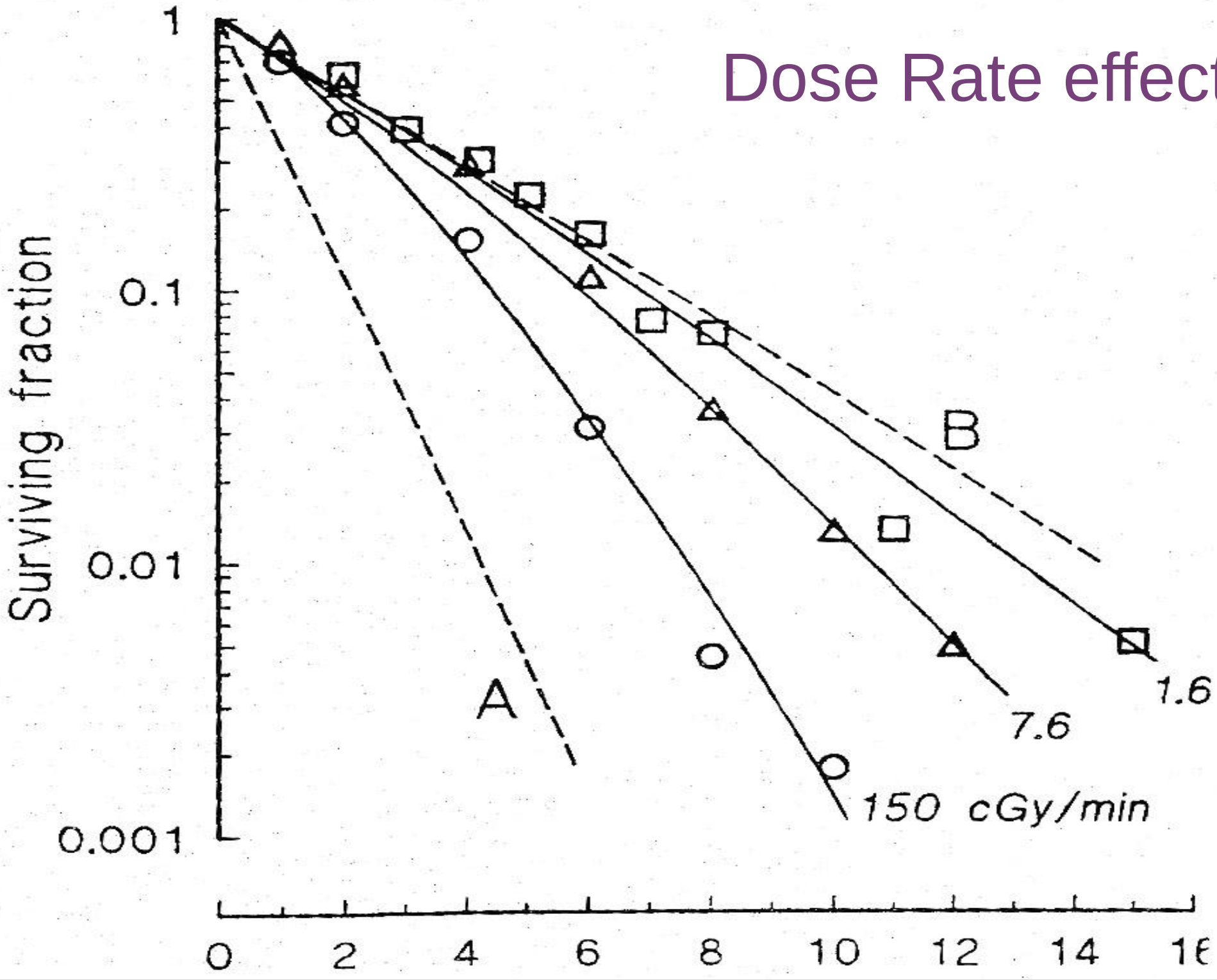
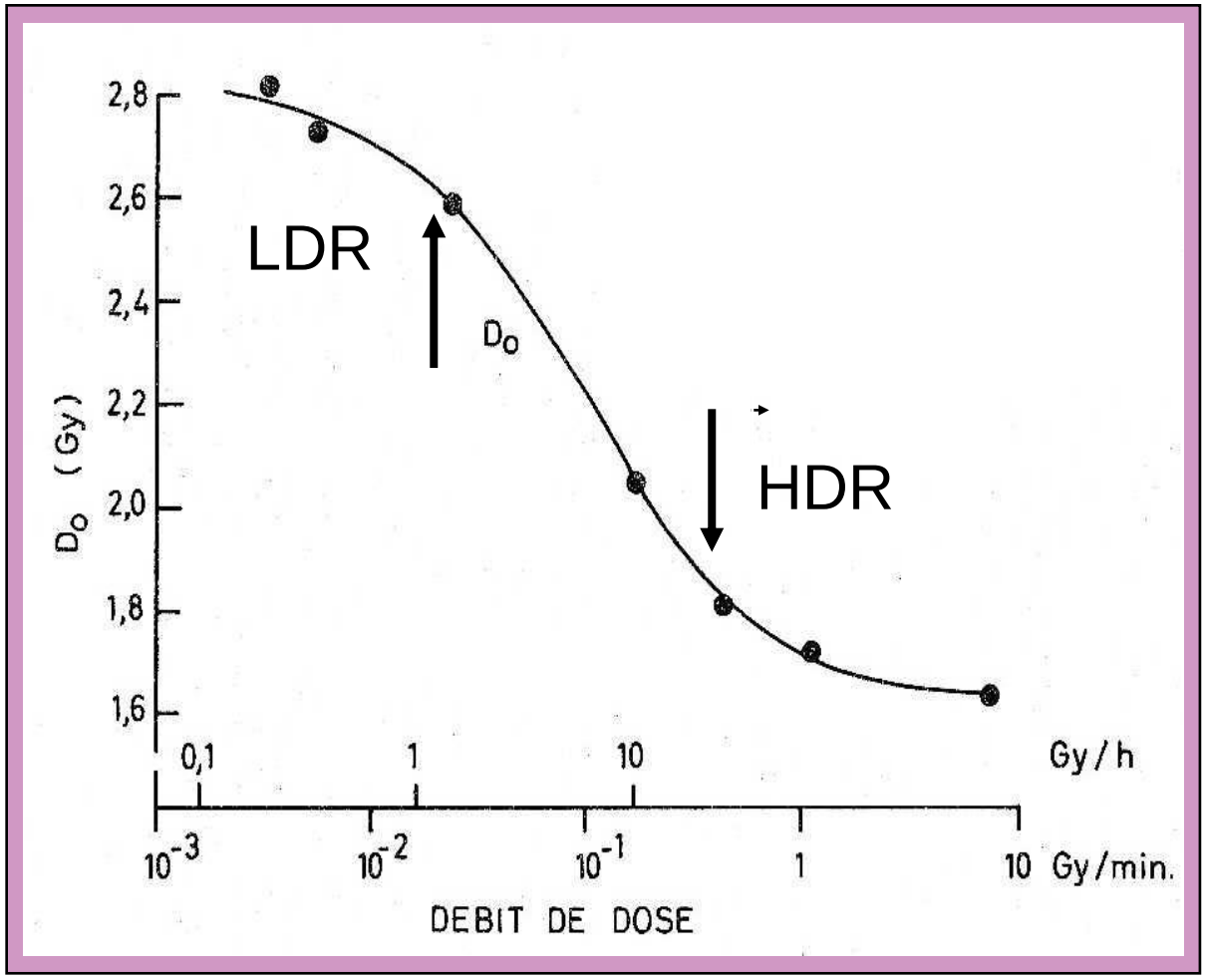
Dose Rate effect



Dose Rate Effect



ICRU 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

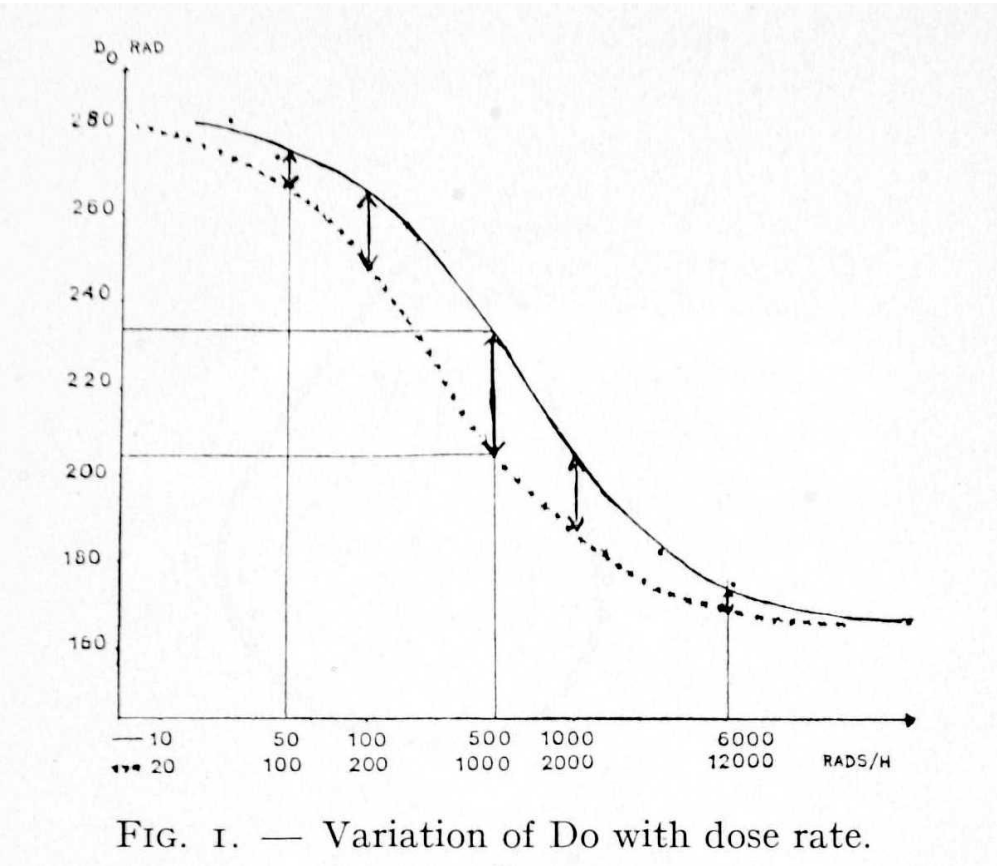
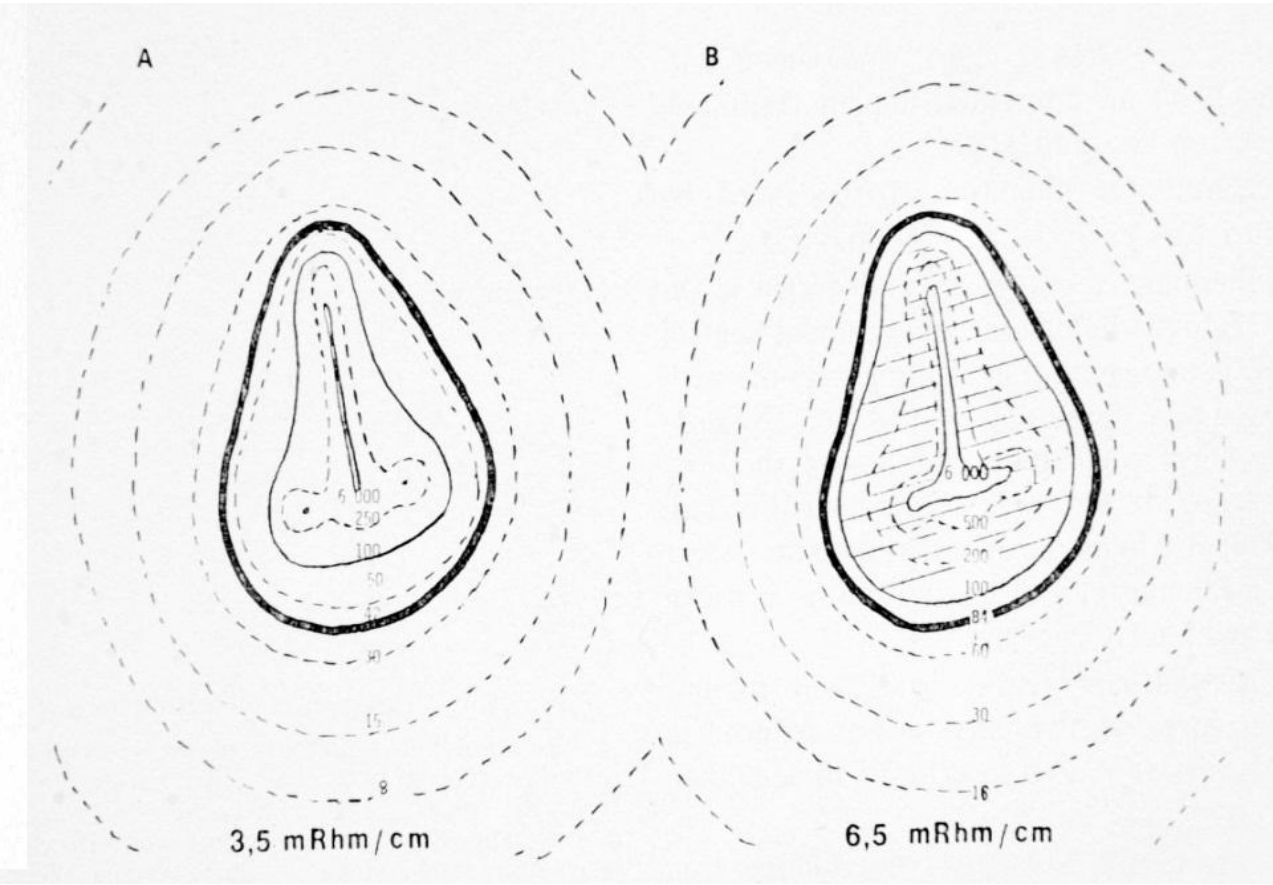


FIG. 1. — Variation of Do with dose rate.



Different spatial effect of changing DR in ICBT

Van Limbergen ea 1985

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Dose rates used in BT

- Low Dose Rate: continuous.
- Medium Dose Rate: fractionated.
- High Dose Rate: fractionated.
- Pulsed Dose Rate: hyperfractionated.

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HDR

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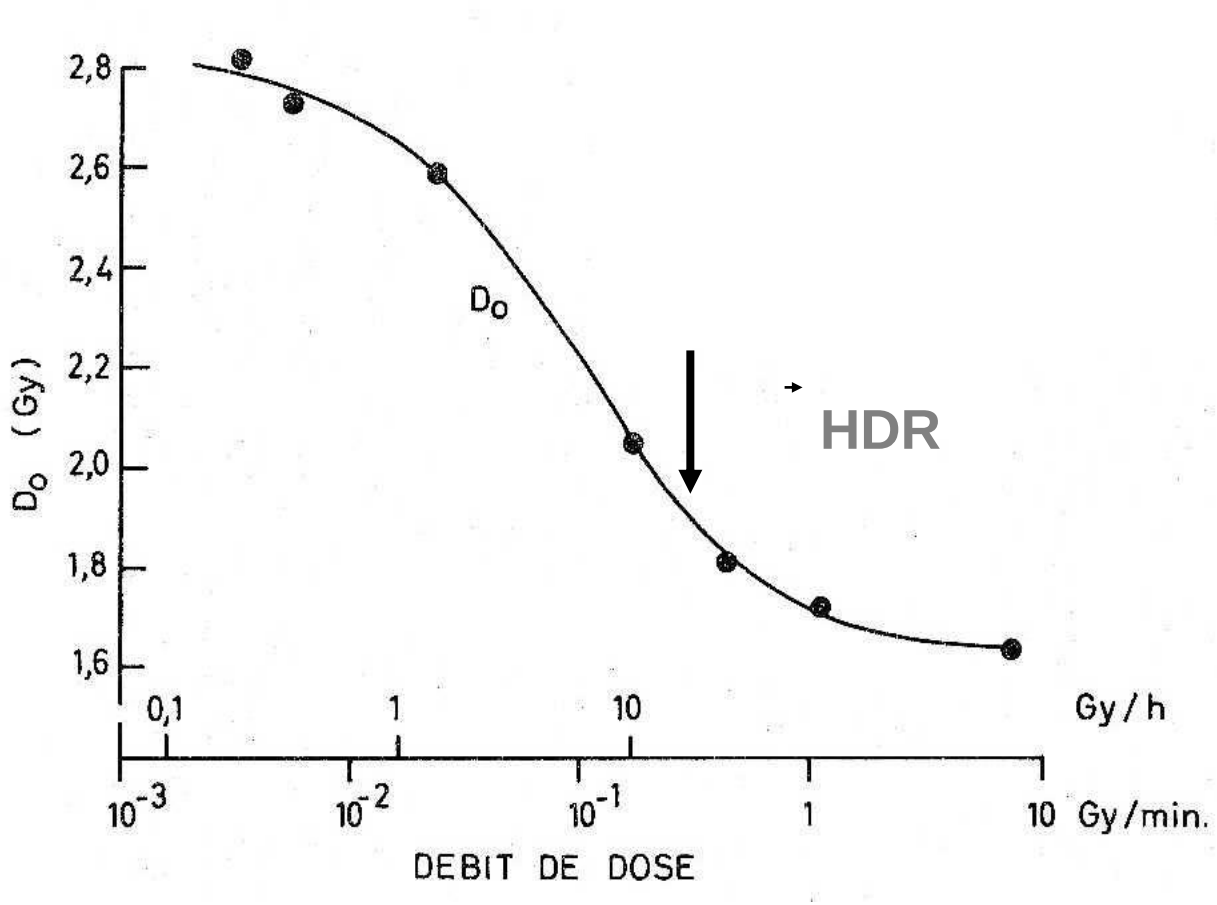
Dose Rate Effect



HDR

≥ 12 Gy/h

(≥ 0.2Gy/min)

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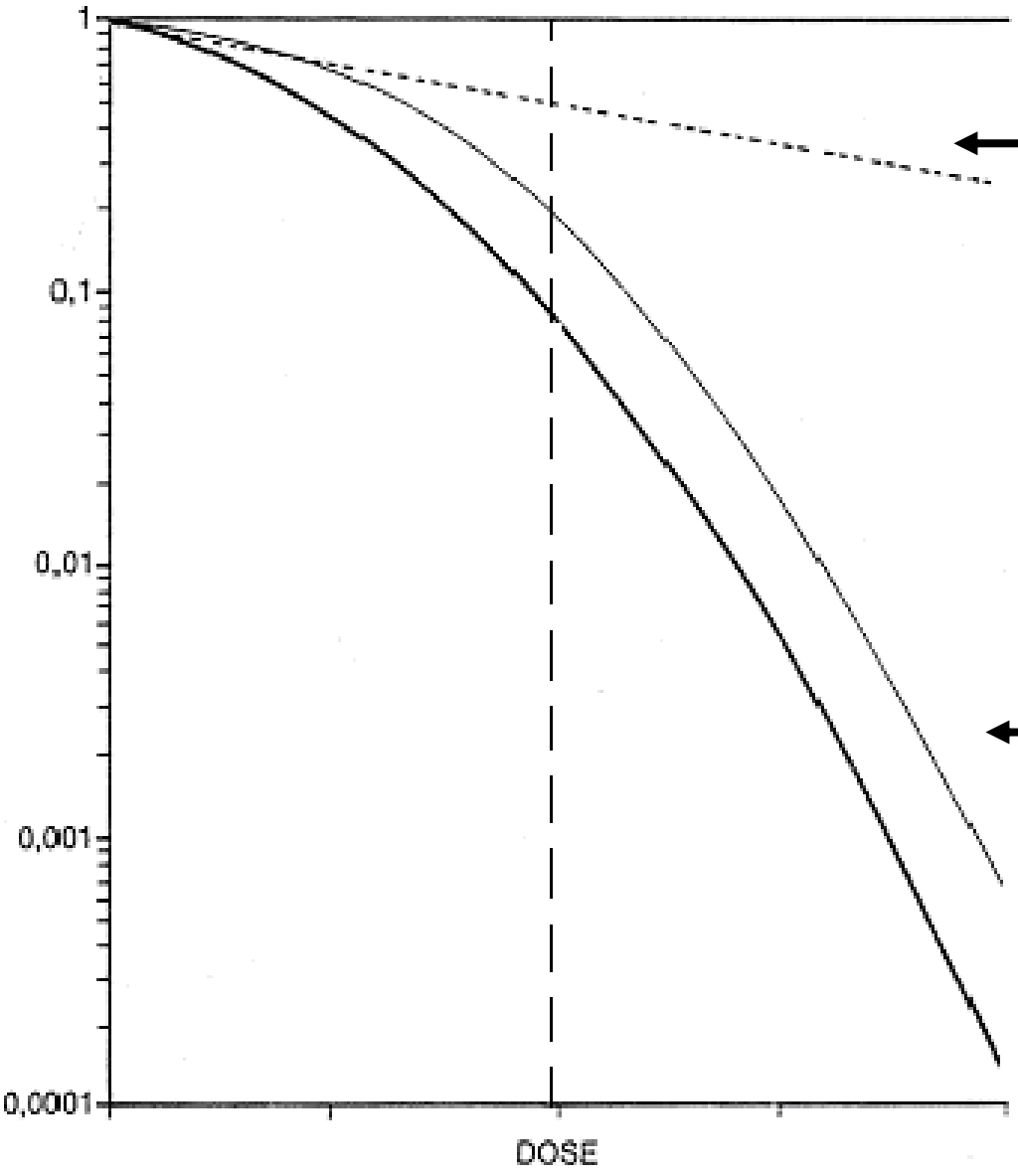
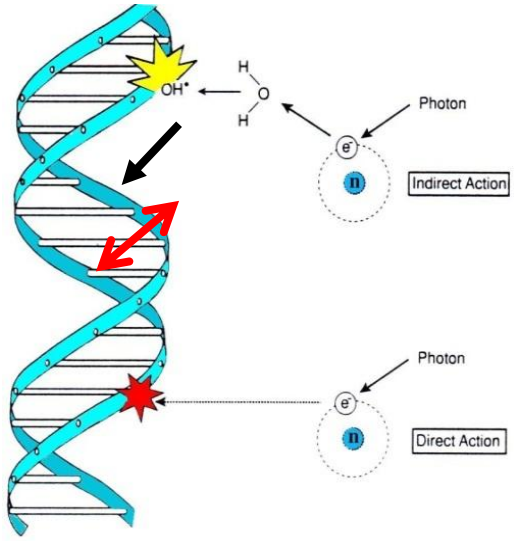
Survival fraction Linear Quadratic Model



Linear component



Quadratic component

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Linear quadratic model

$E = \alpha D$ lethal non repairable

linear term

$E = \beta D^2$ sublethal repairable

quadratic term

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

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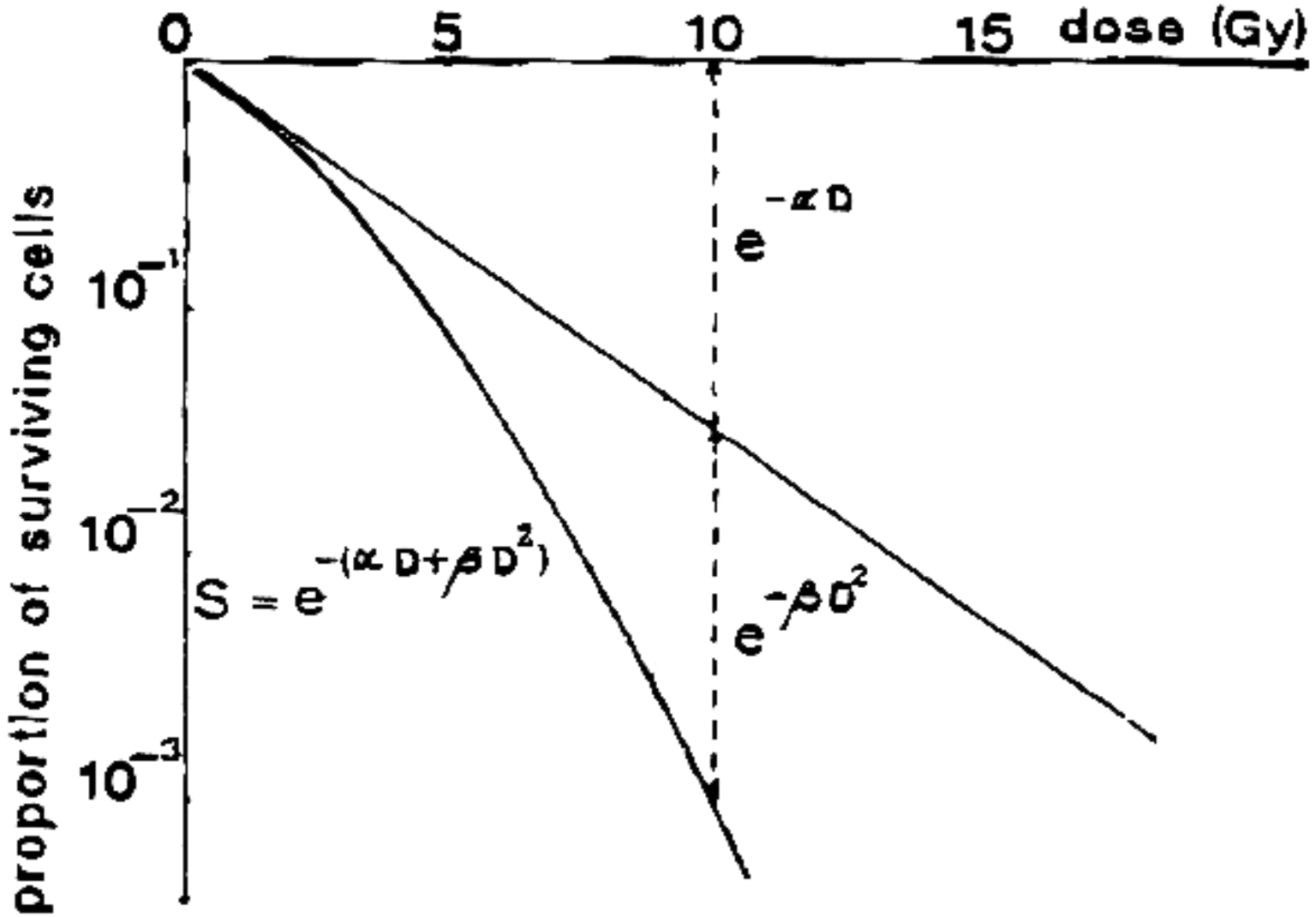
Repair capacity: the α/β ratio



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The α/β ratio

- 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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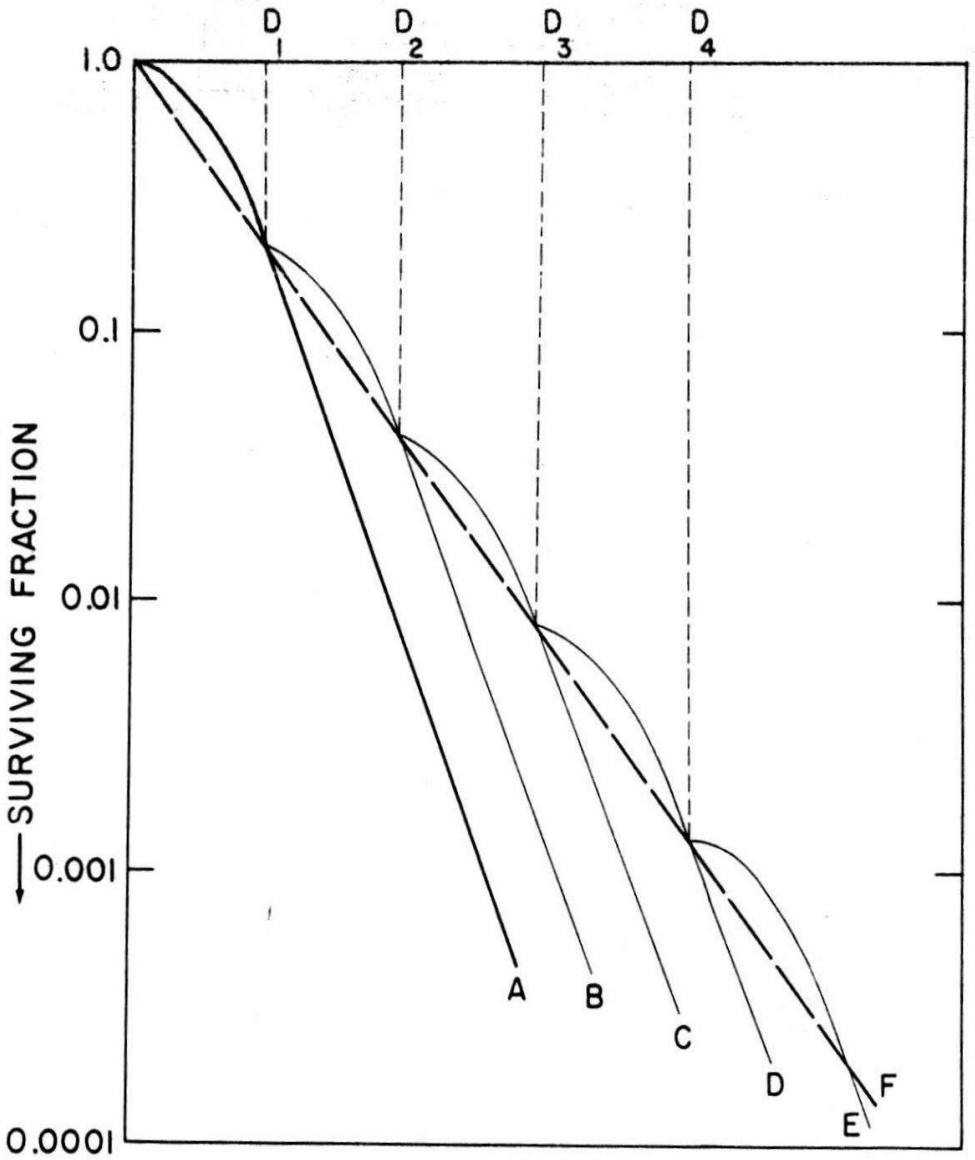
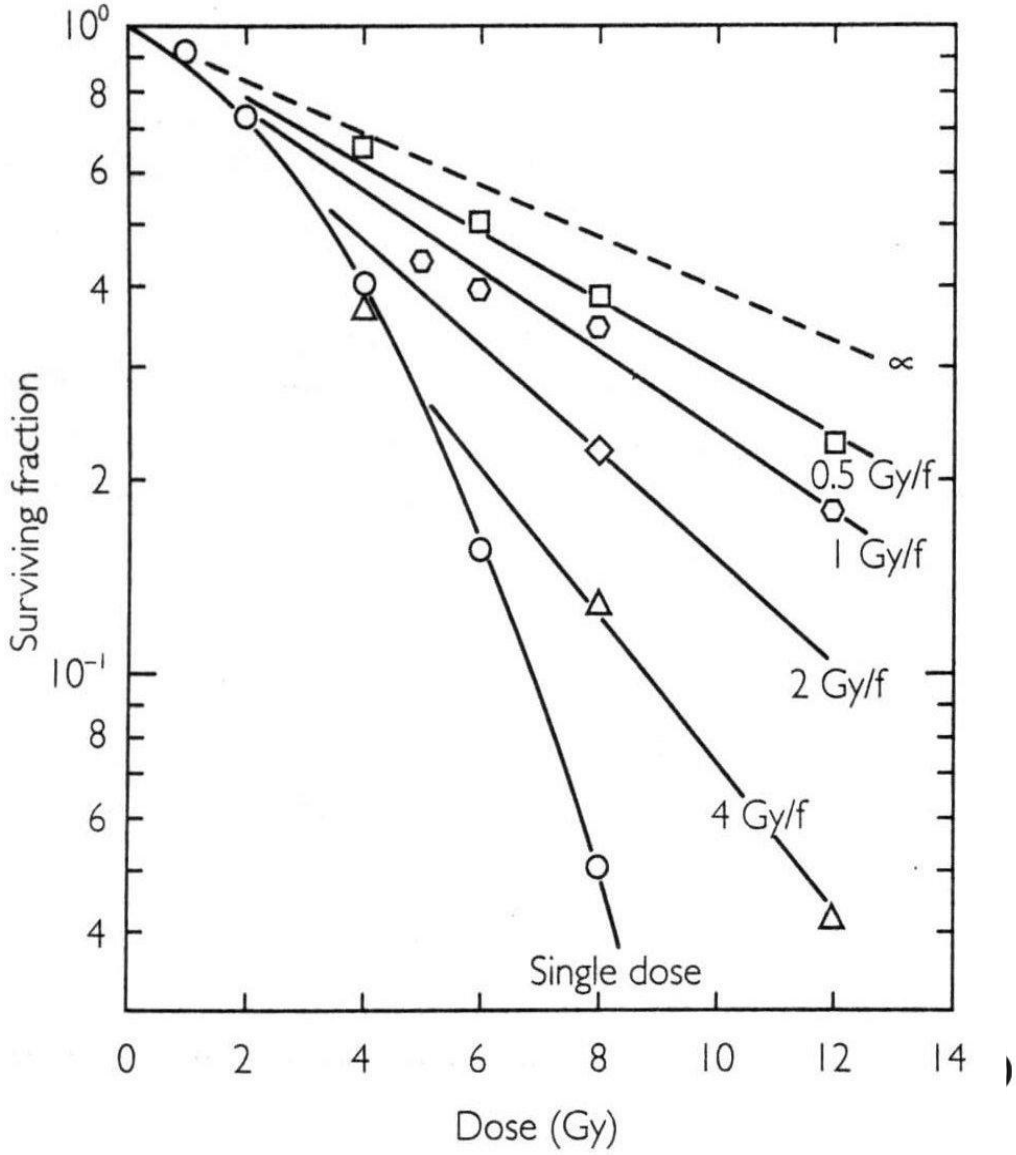
HDR brachytherapy effect of fraction size





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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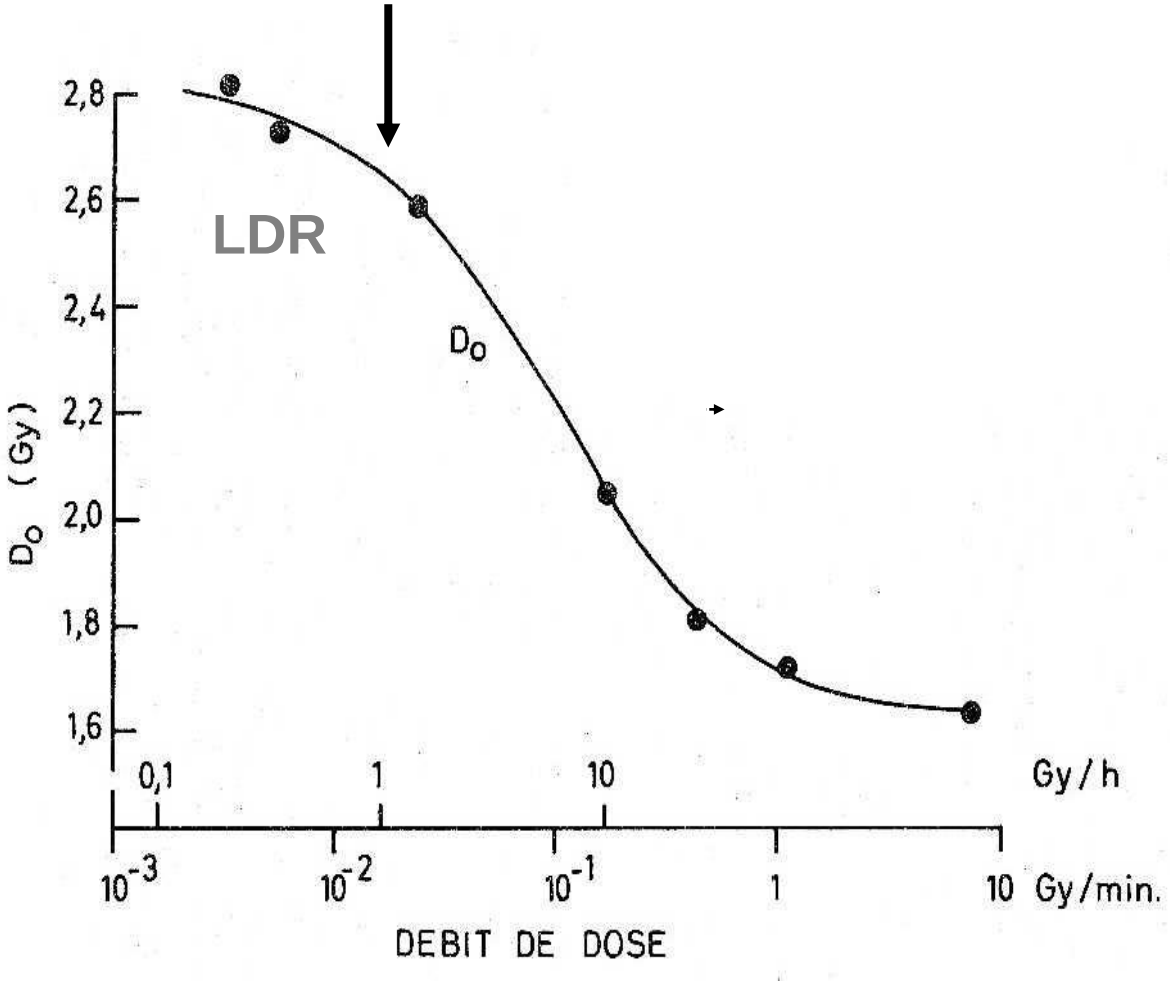
Dose Rate Effect



LDR

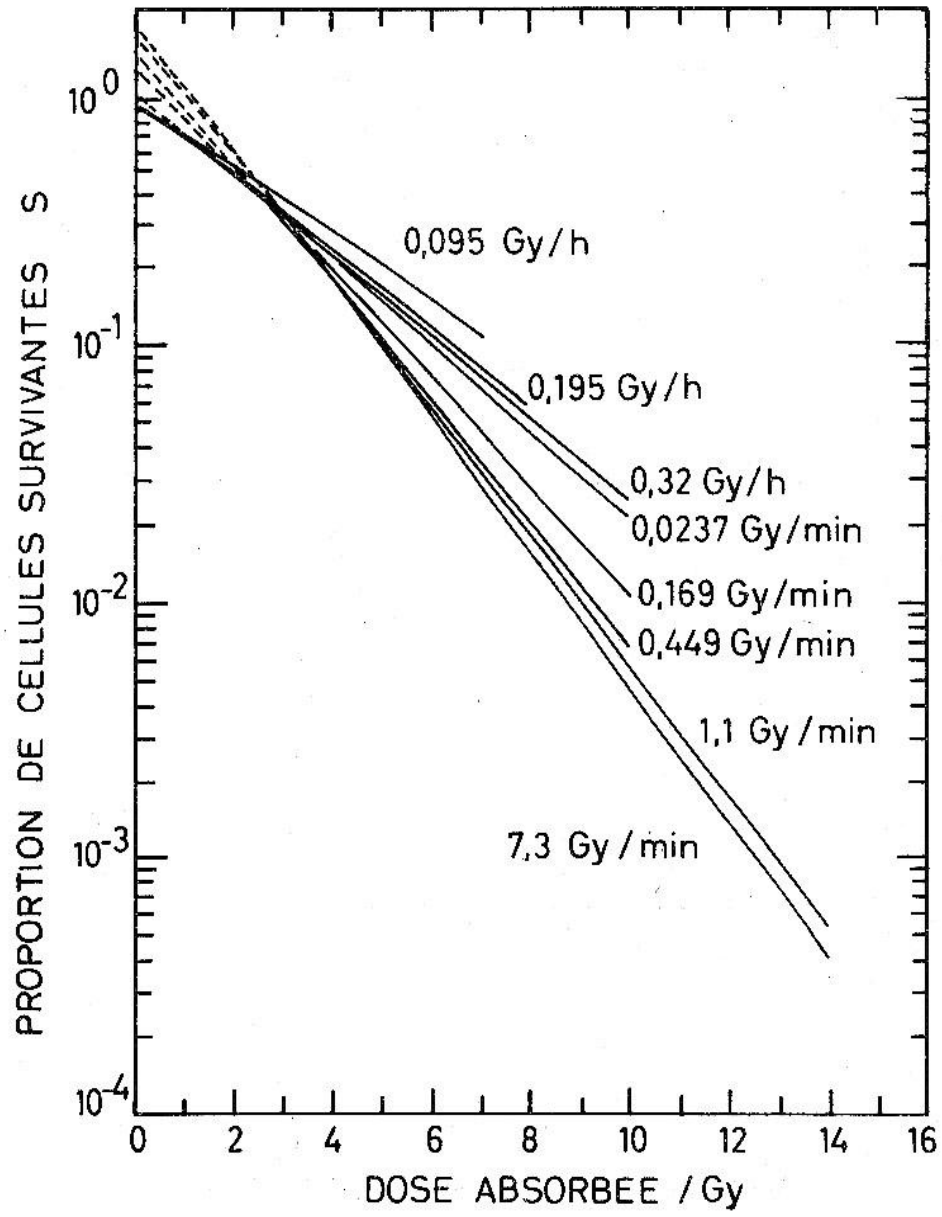
0.4 - 1 Gy/h

LDR Linear quadratic model

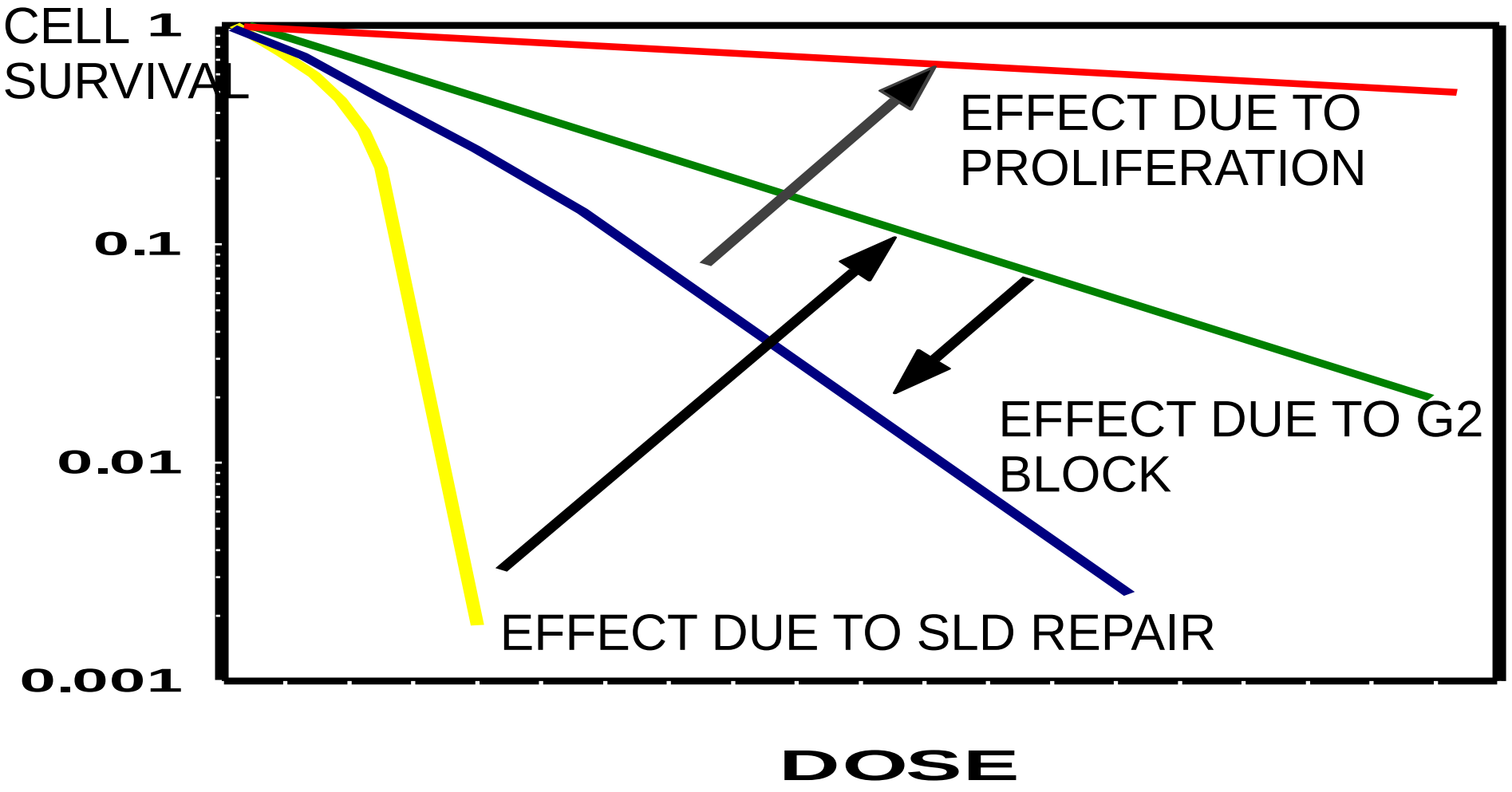
$$E = \alpha D + g \beta D^2$$

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

$$\mu = 0.693 / T^{1/2}$$



Low dose rate RT



French Cooperative GYNE-BT 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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LDR BT phase III Dose rate trial at IGR

- 204 stage Ib or II cervical carcinomas
- 60 Gy uterovaginal ^{137}Cs irradiation followed by surgery
- Randomisation between two dose rates:

  0.38 or 0.73 Gy/h

Haie e.a. Int. J. Radiat. Oncol. Biol. Phys. 25, 405-412, 1993.

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IGR phase III trial

- No significant differences in local control and survival
- Overall complications and side effects observed after 6 months significantly more frequent ($p < 0.01$) in the higher dose rate group

Haie e.a. Int. J. Radiat. Oncol. Biol. Phys. 29, 953-960, 1994.

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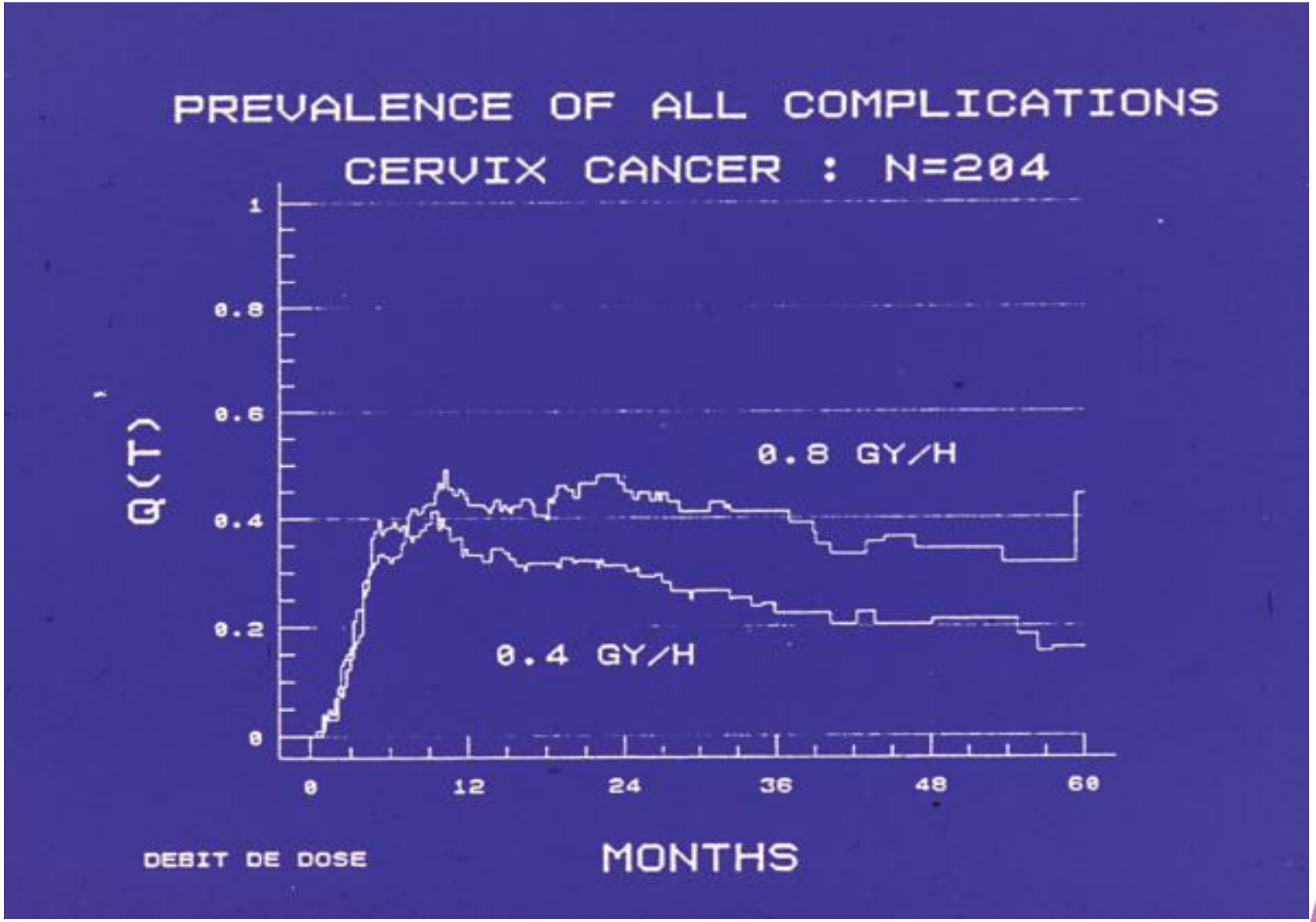
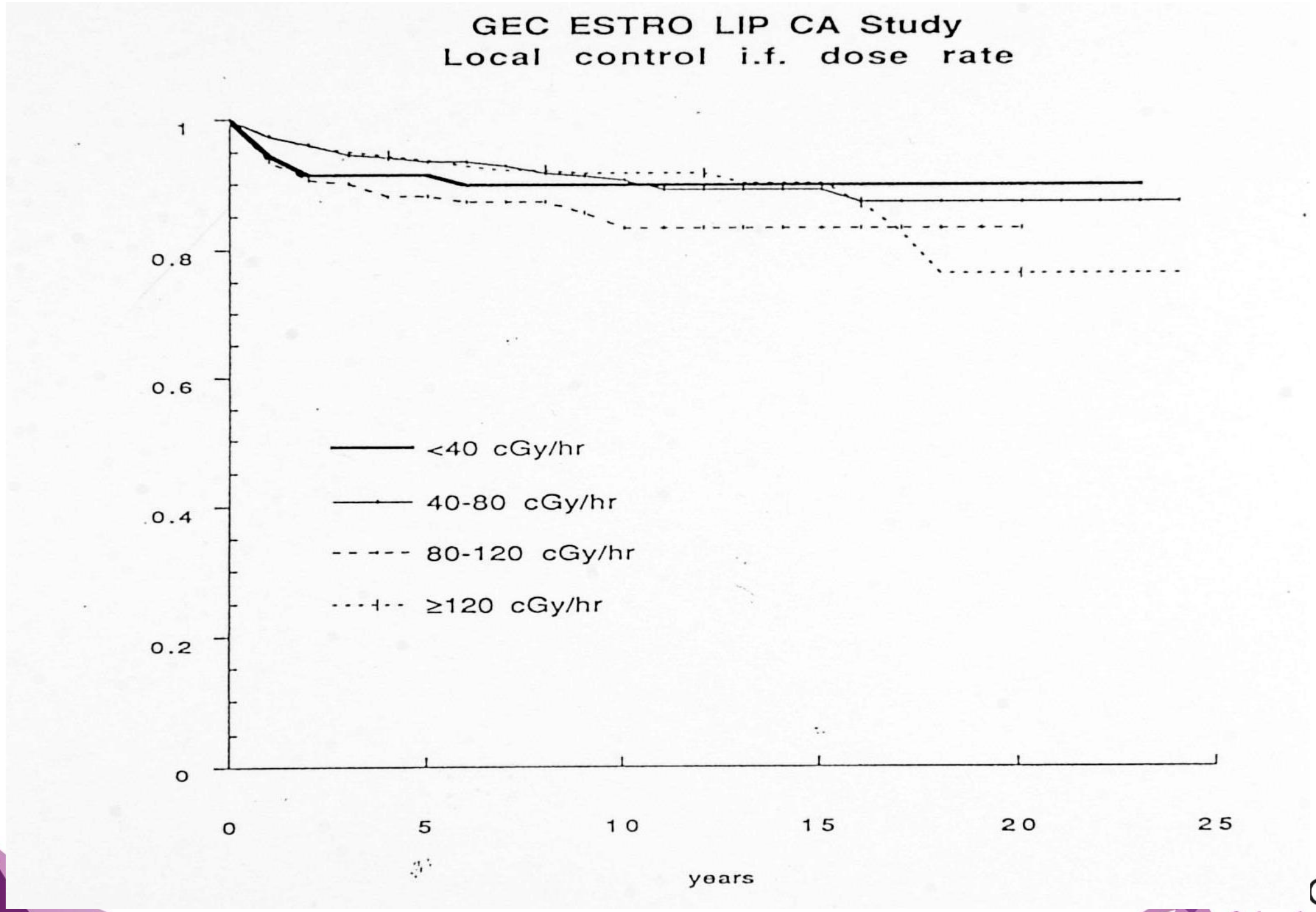
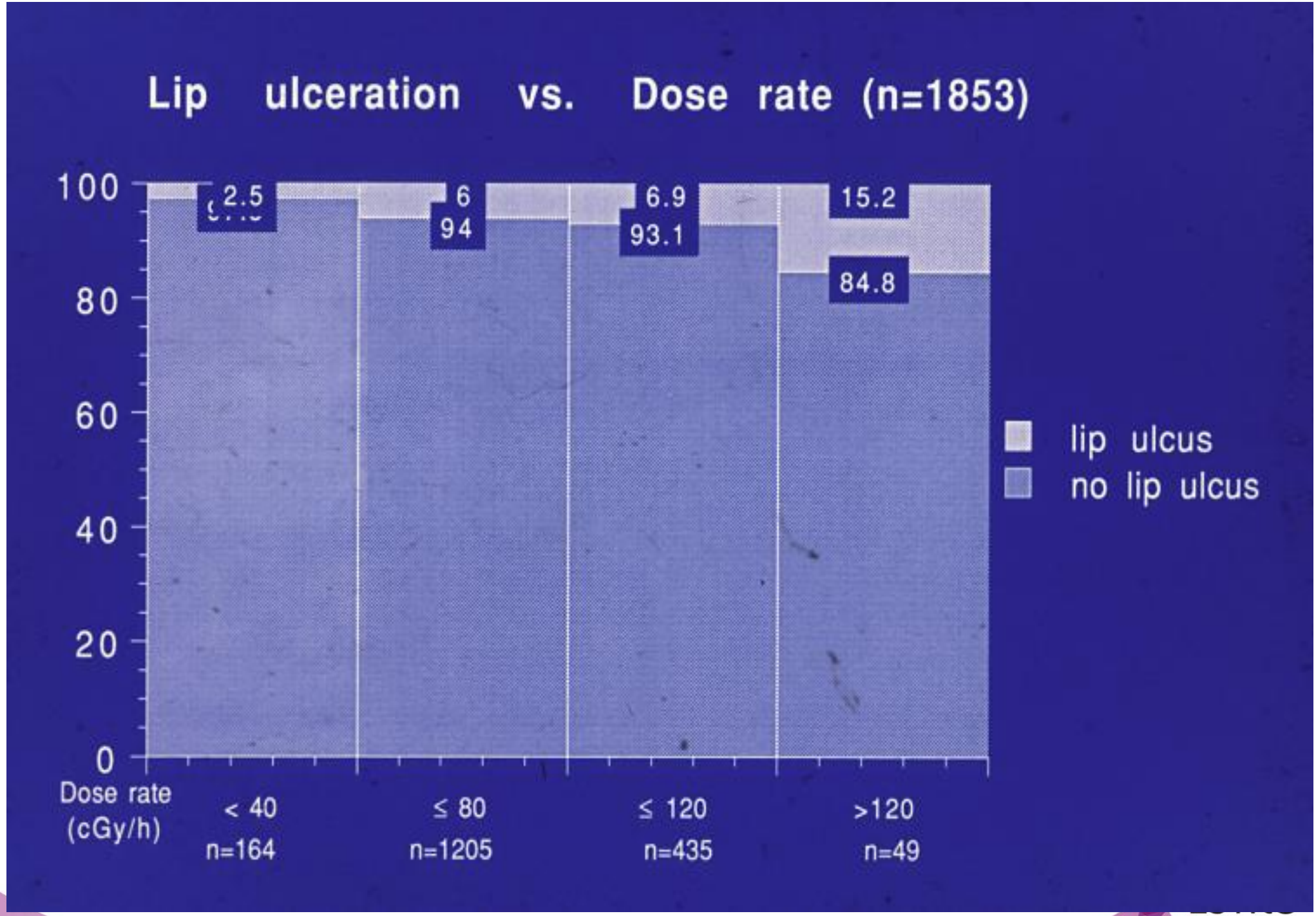
IGR phase III trial




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
0
5
10
15
20
25
years


Lip ulceration vs. Dose rate (n=1853)
100
80
60
40
20
0
2.5
6
94
6.9
93.1
15.2
84.8
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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LDR brachytherapy

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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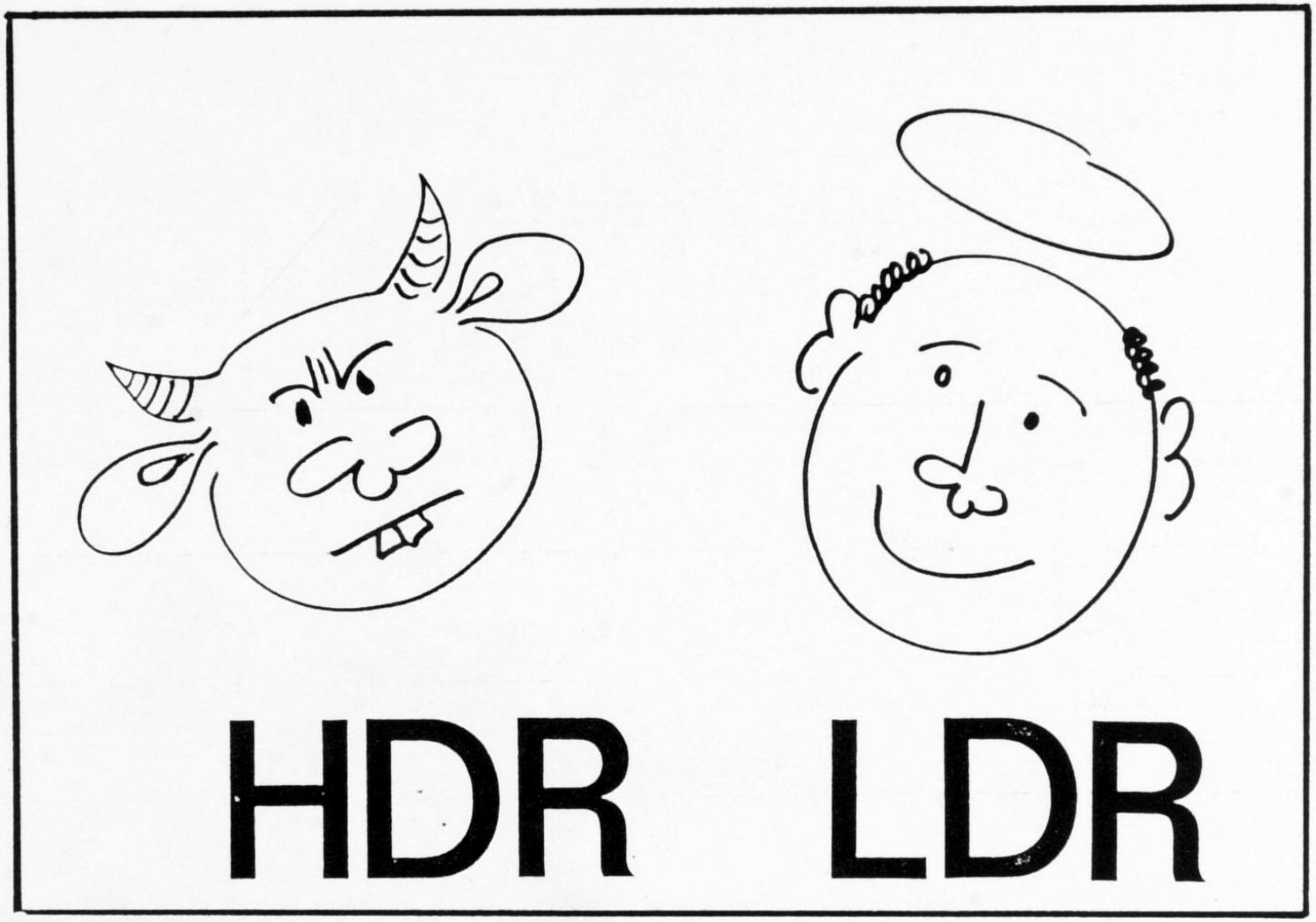

HAS LOW DOSE RATE VIRTUES BY ITSELF ?

HDR- ICBT: late complications

Clinical Data		HDR vs LDR		
➢ Review literature *				
(Fu and Phillips 1990)	G2-4	12.0%	18.0%	
➢ 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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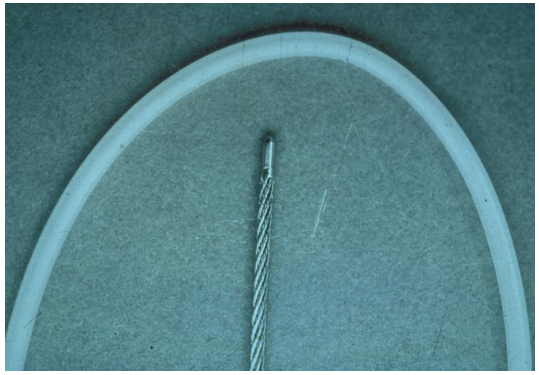
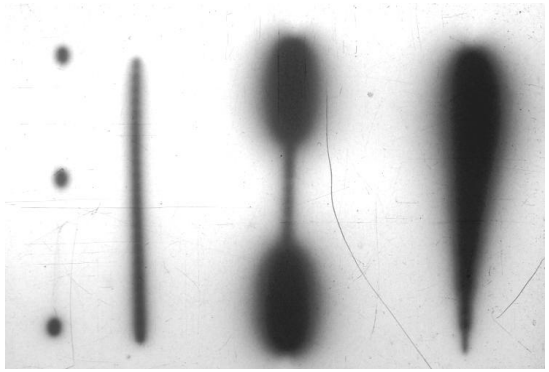
PDR

PULSED DOSE RATE ……..

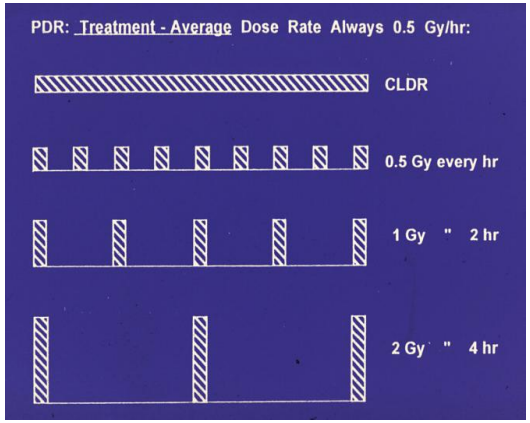
THE BEST OF BOTH WORLDS .

- **HDR stepping source technology**





- **Mimicking LDR radiobiology**



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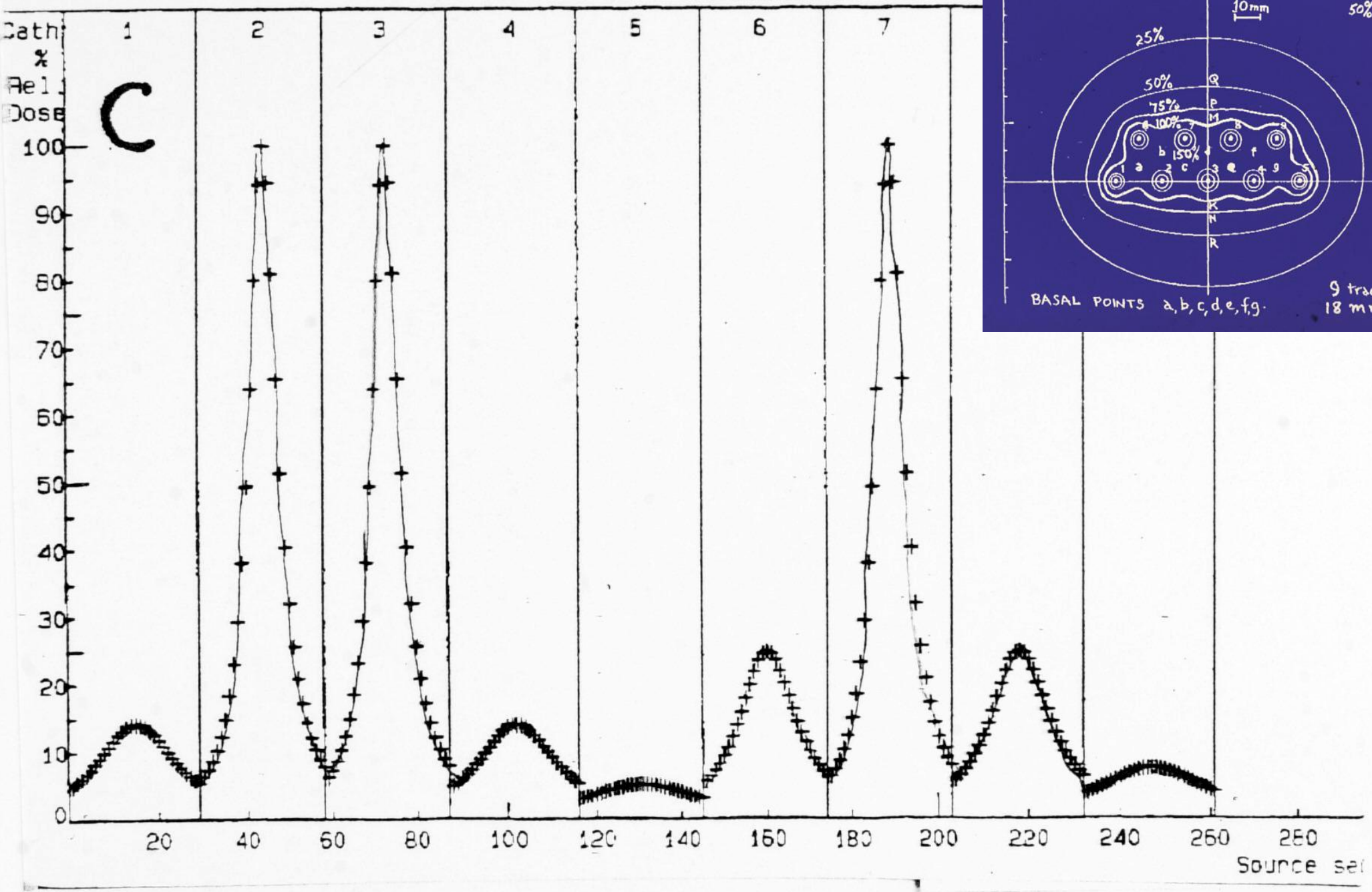
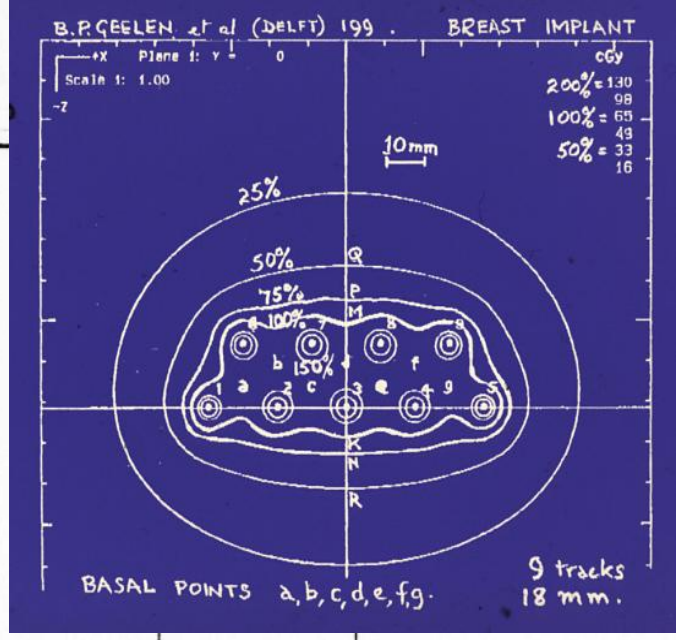
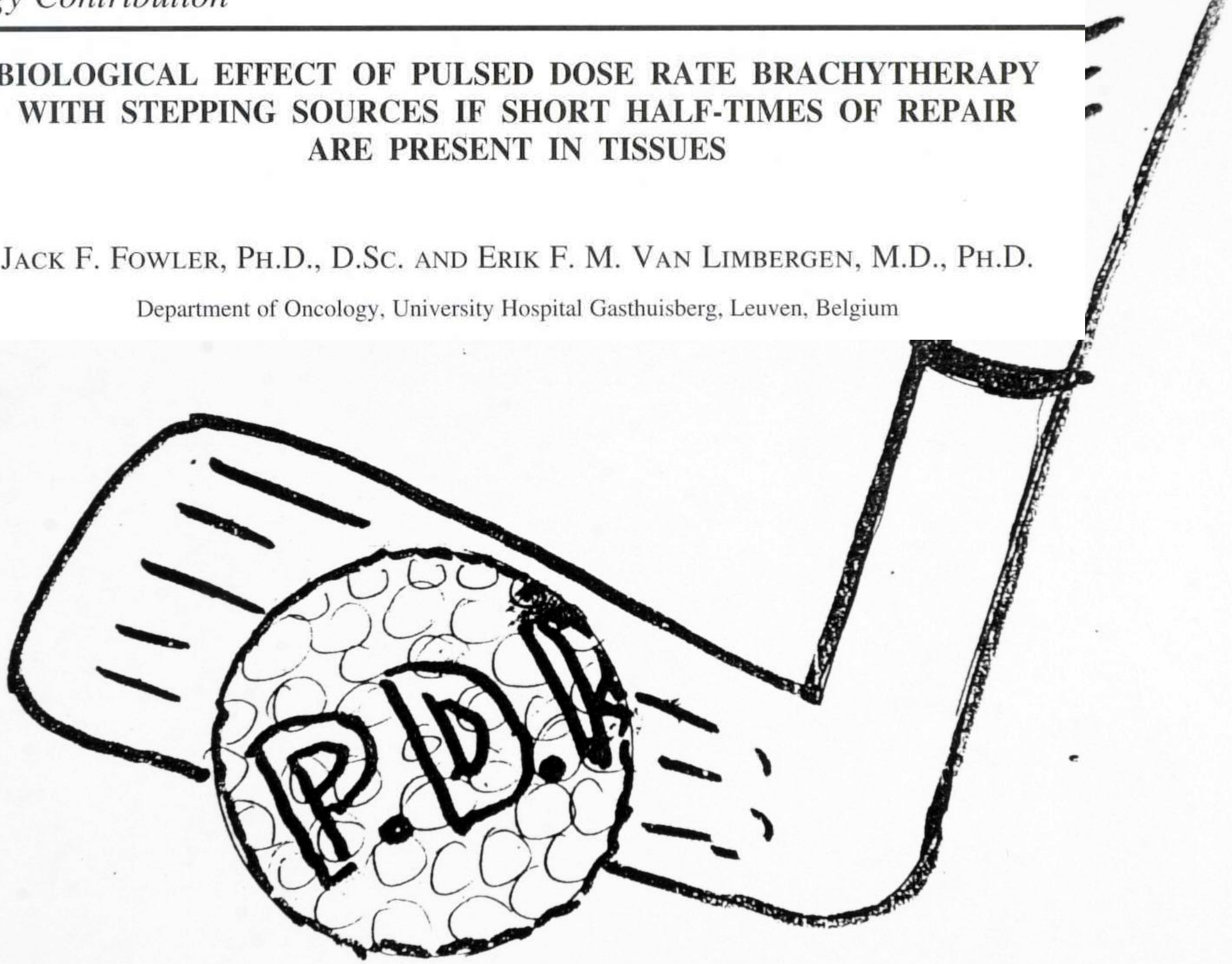

Cath
%
Rel
Dose
1
2
3
4
5
6
7
C
100
90
80
70
60
50
40
30
20
10
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
Source


B.P.GEELEN et al (DELFT) 199 . BREAST IMPLANT
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.

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



INSTANTANEOUS DOSE RATES IN PDR INTERSTITIAL IMPLANTS

Distance from the source	370GBq	185GBq
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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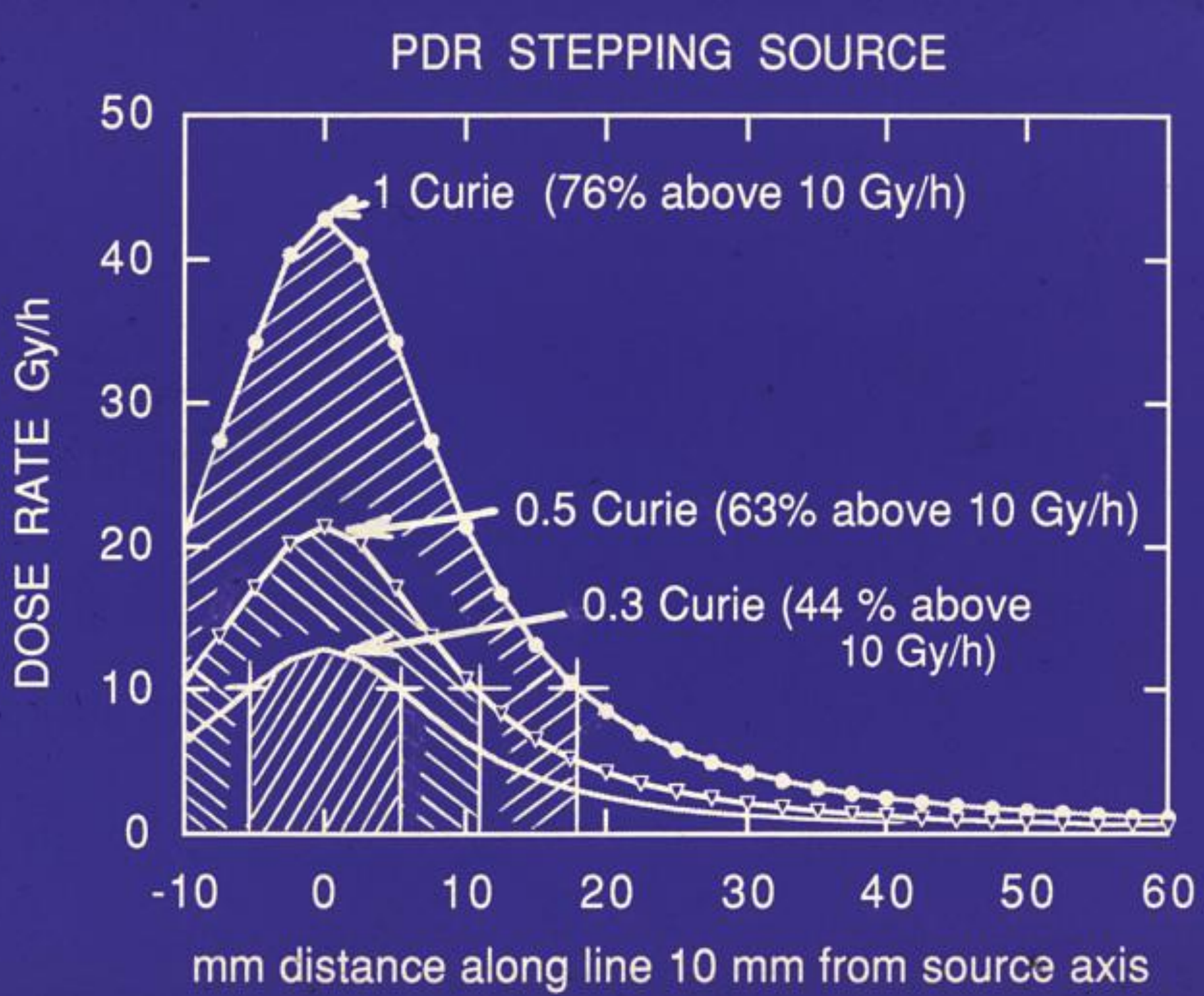
PDR STEPPING SOURCE
DOSE RATE Gy/h
50
40
30
20
10
0
1 Curie (76% above 10 Gy/h)
0.5 Curie (63% above 10 Gy/h)
0.3 Curie (44 % above
10 Gy/h)
-10
0
10
20
30
40
50
60
mm distance along line 10 mm from source axis

PDR 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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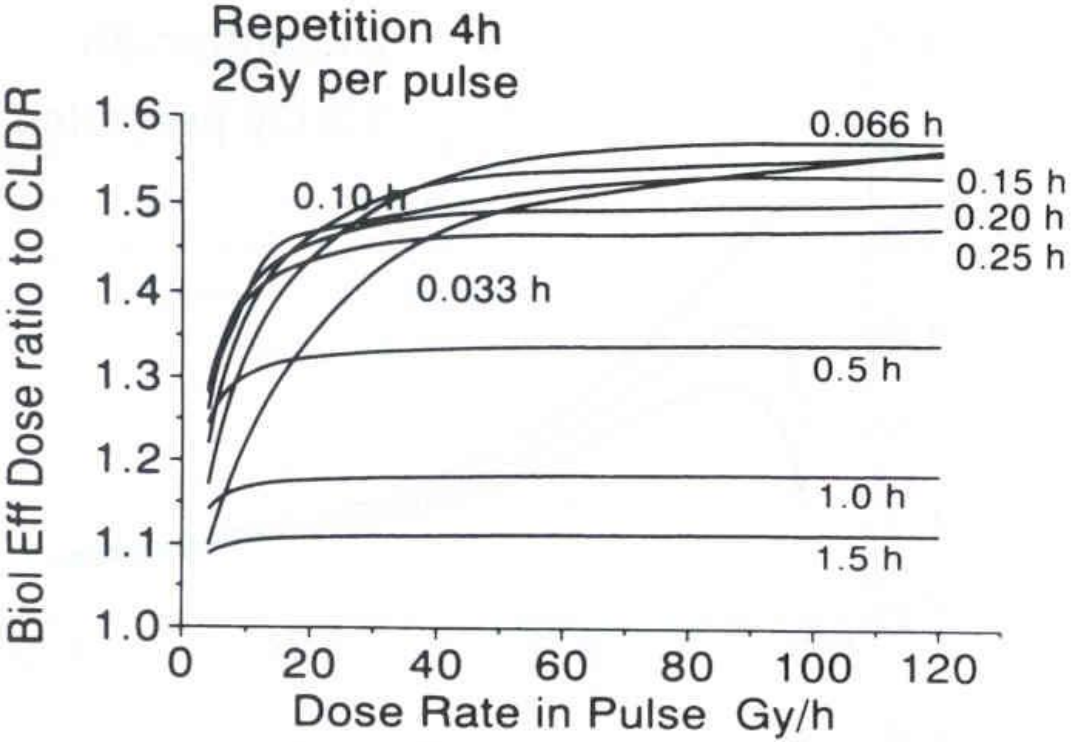
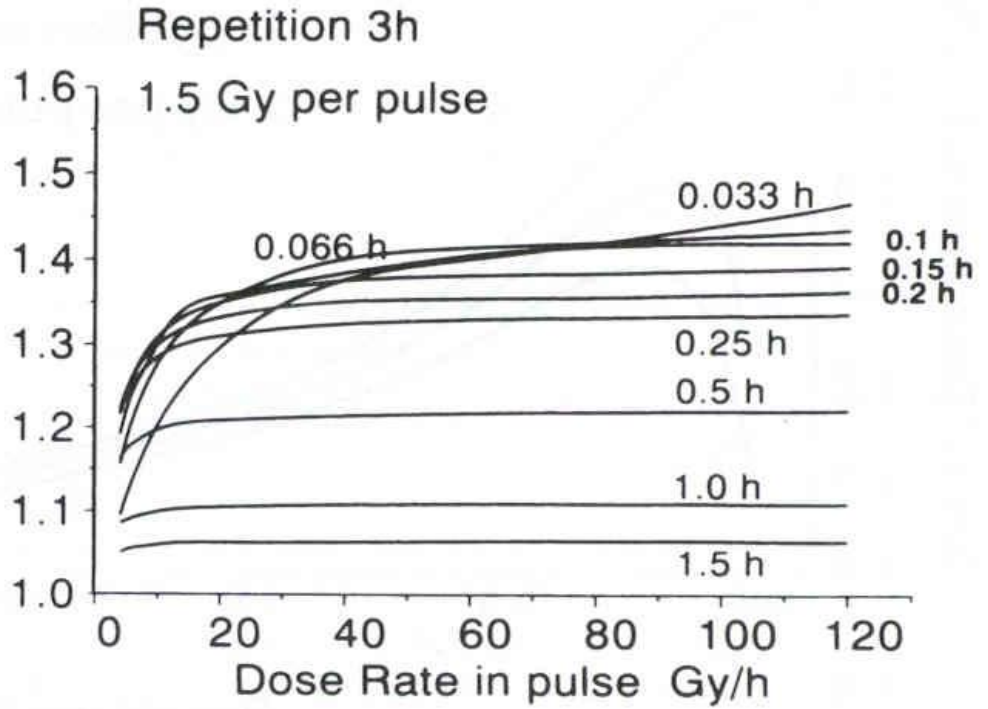
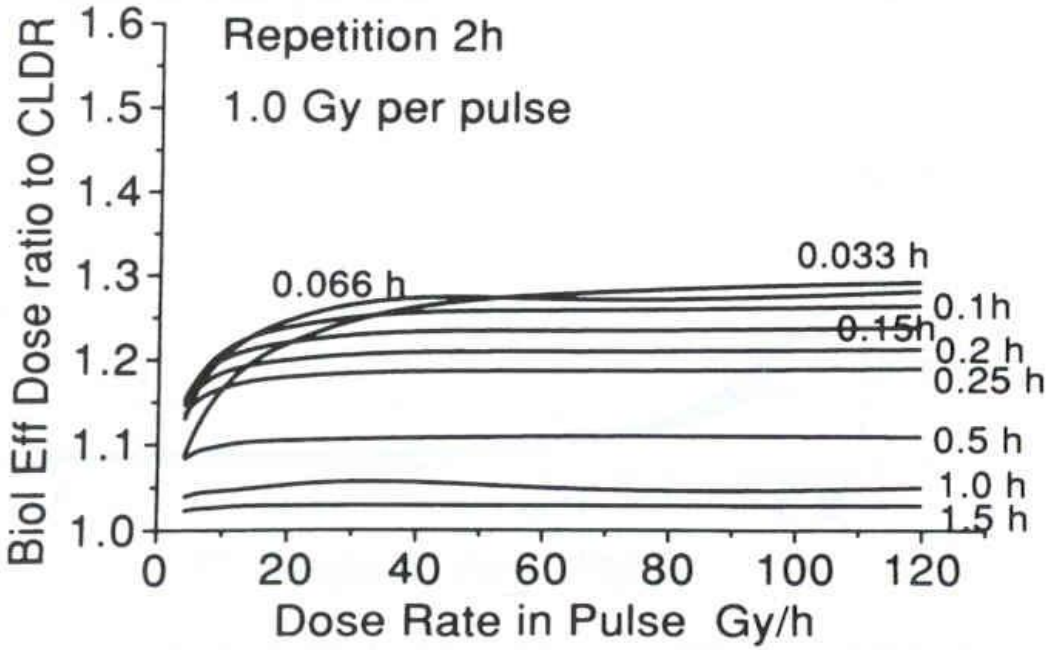
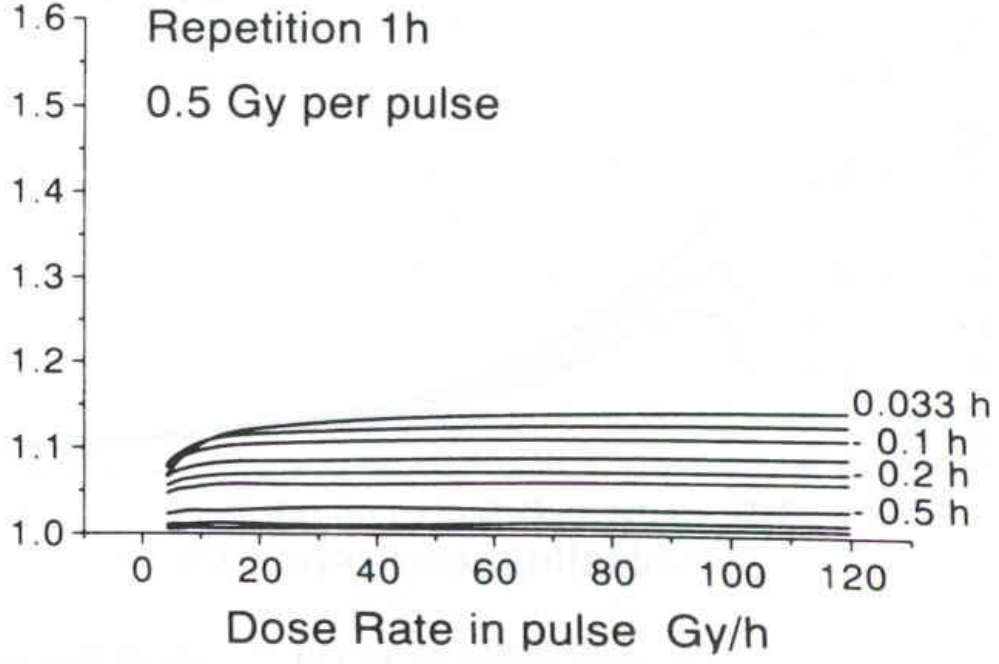

Repetition 4h
2Gy per pulse
Biol Eff Dose ratio to CLDR
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.066 h
0.10 h
0.15 h
0.20 h
0.25 h
0.033 h
0.5 h
1.0 h
1.5 h
0
20
40
60
80
100
120
Dose Rate in Pulse Gy/h


Repetition 3h
1.5 Gy per pulse
1.6
1.5
1.4
1.3
1.2
1.1
1.0
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
0
20
40
60
80
100
120
Dose Rate in pulse Gy/h


Repetition 2h
1.0 Gy per pulse
Biol Eff Dose ratio to CLDR
1.6
1.5
1.4
1.3
1.2
1.1
1.0
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
0
20
40
60
80
100
120
Dose Rate in Pulse Gy/h


Repetition 1h
0.5 Gy per pulse
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.033 h
0.1 h
0.2 h
0.5 h
0
20
40
60
80
100
120
Dose Rate in pulse Gy/h

Conclusion PDR (1)

- More than 40 - 75 % of the time, and much more of the dose is delivered

  at > 10 Gy/hr HDR

Conclusion PDR (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 PDR (3)

- The enhanced effects are especially seen in cells

  - with small α/β
  - fast T 1/2 (<0.5hr)

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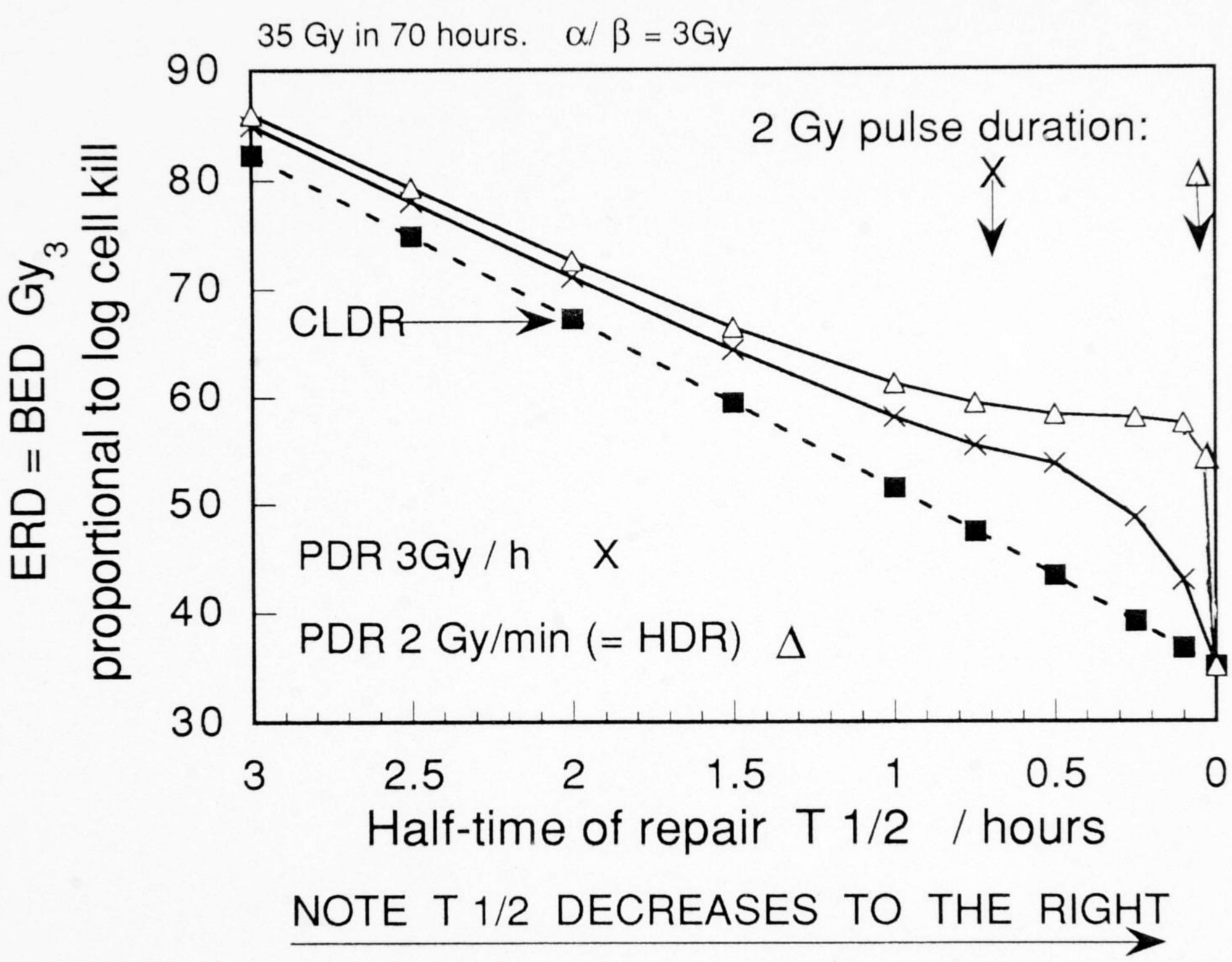
35 Gy in 70 hours. α/ β = 3Gy
90
80
70
60
50
40
30
ERD = BED Gy3
proportional to log cell kill
2 Gy pulse duration:
X
CLDR
PDR 3Gy / h X
PDR 2 Gy/min (= HDR) Δ
3
2.5
2
1.5
1
0.5
0
Half-time of repair T 1/2 / hours
NOTE T 1/2 DECREASES TO THE RIGHT

EQD_2

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Conclusion HDR

- Main factors are
  - TOTAL DOSE
  - FRACTION SIZE

- $TE = (d + \alpha/\beta) D$

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comparing 2 HDR schedules

- **$D' (\alpha/\beta + d') = D (\alpha/\beta + d)$**
- With:

  D and D’ = total dose

  d and d’ = dose per fraction

  Early reacting tissues: α/β = 10 Gy

  Late reacting tissues: α/β = 3 Gy

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Conclusion LDR

- Main factors are
  - TOTAL DOSE
  - DOSE RATE

- $TE = (\alpha/\beta + 2.9.T½.DR)D$

Conclusion PDR

- Main factors are
  - TOTAL DOSE
  - PULSE SIZE

- $TE = (\alpha/\beta + (1+Hm)d)D$

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Common Language EQ D2

TE LDR =
TE PDR=
TE HDR=

} TE of $(\alpha/\beta + 2)$ D

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

* Corrected for Dose Rate and T1/2 in LDR ,
for Pulse Size , IT and T1/2 in PDR

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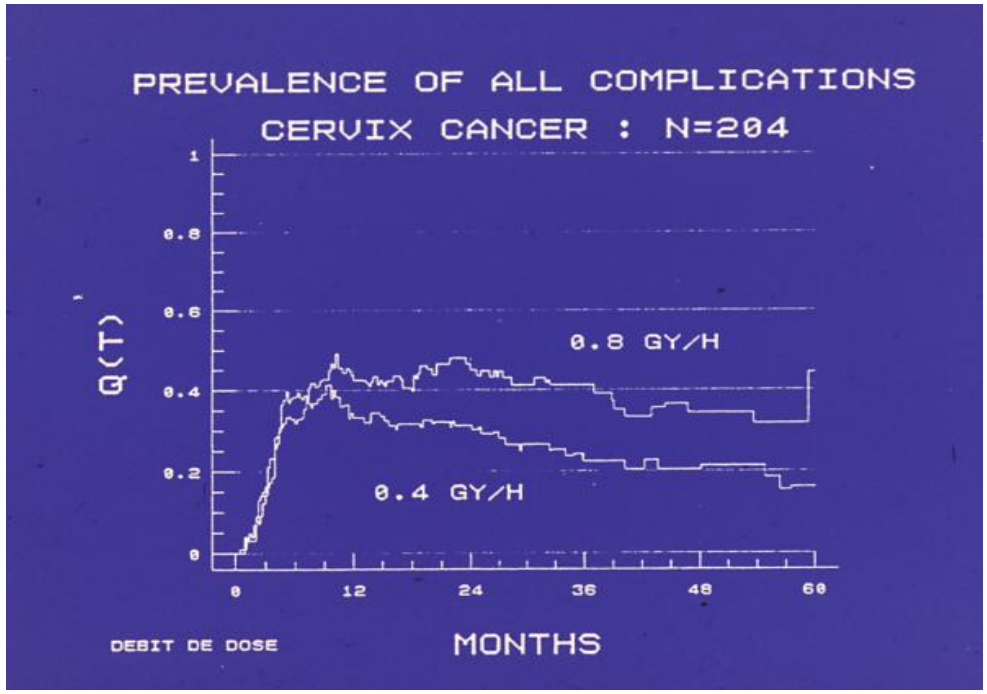

IGR phase III

	EQD2	
	CA	LE
LDR - 60 Gy - 0,38 Gy/hr	55 Gy	56 Gy
LDR - 60 Gy - 0.73 Gy/hr	60.5 Gy	74 Gy

early: α/β **= 10 Gy - T1/2 = 1 hr**
late: α/β **= 3 Gy - T1/2 = 1.5 hr**

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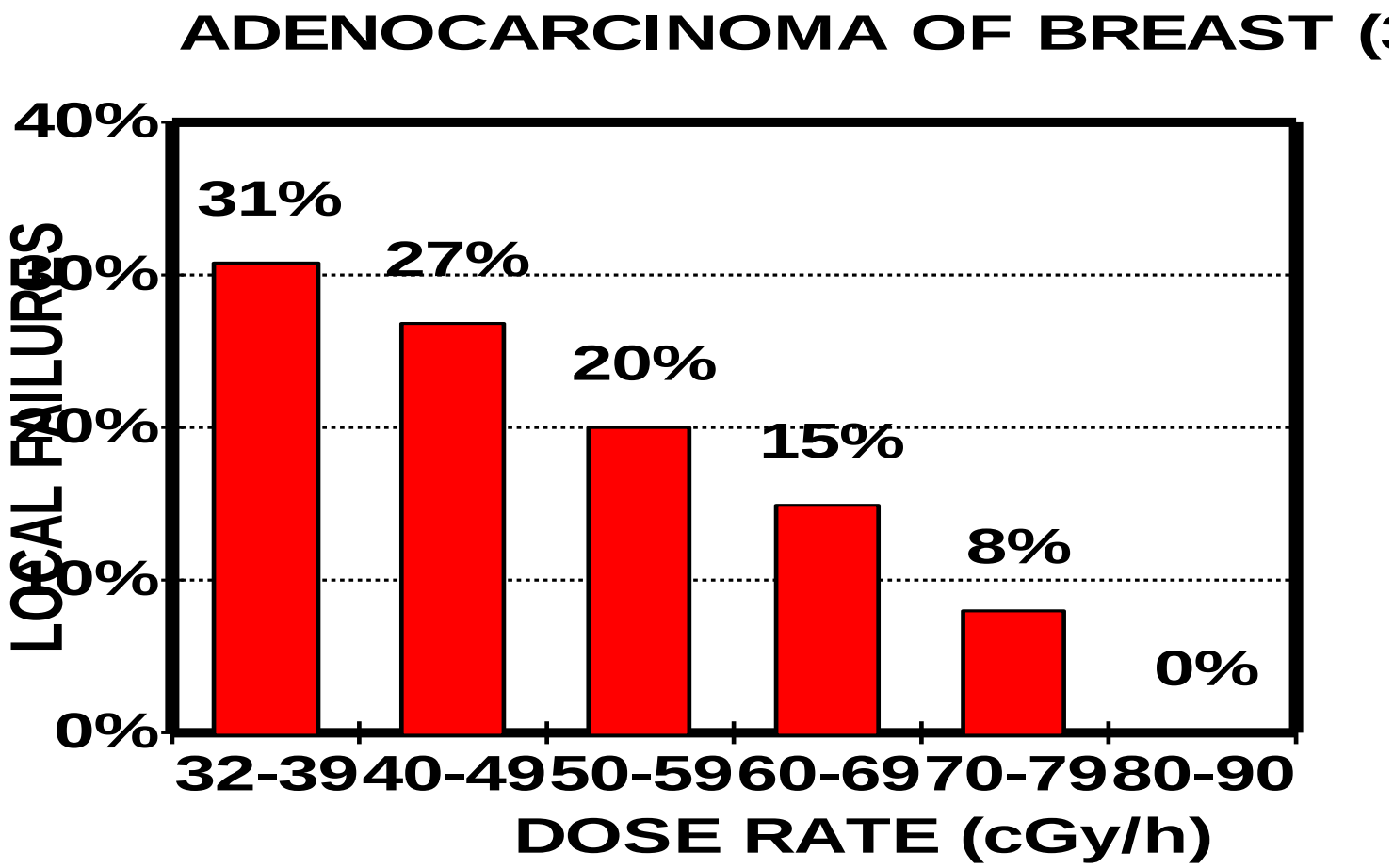
Influence of dose rate on local control of breast carcinoma treated by external beam irradiation + 37 Gy iridium 192 implant

Mazeron et al IJROB1991



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Mazeron IRBT breast data

Mazeron et al IJROB1991

Equiv. dose of 37 Gy LDR (α/β = 5 Gy , $T_{1/2}$ = 1 hr)

- 31 Gy at 0,3 Gy/ hr
- 36 Gy at 0,6 Gy/hr
- 41 Gy at 0,9 Gy/ hr

$$\mathbf{D.(\alpha/\beta + 2.9.T_{½}.DR)}$$

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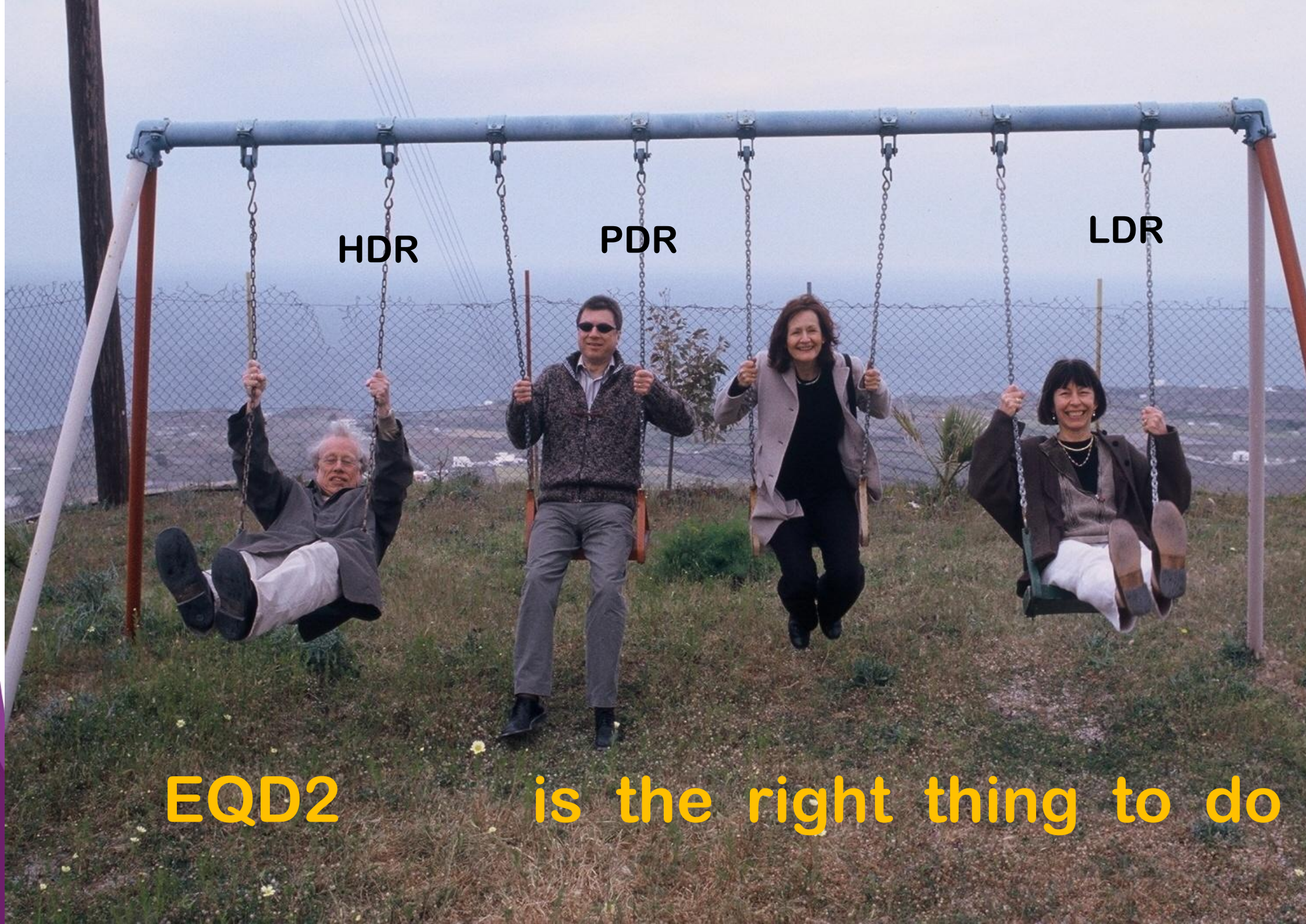
HDR
PDR
LDR
EQD2 is the right thing
to do


HDR
PDR
LDR
EQD2
is the right thing to do

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WWW.ESTRO.ORG/SCHOOL

Radioisotopes
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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Topics

- **Particles Emitted and Particles used**
- Mean & Effective Energy
- Half Value Layer (HVL)
- Radioisotope Characteristics
- Radioisotopes
- Summary

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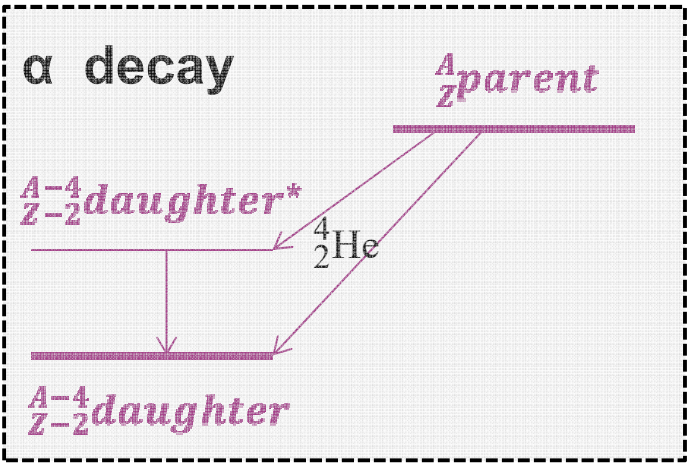
Particles – Irradiation emitted

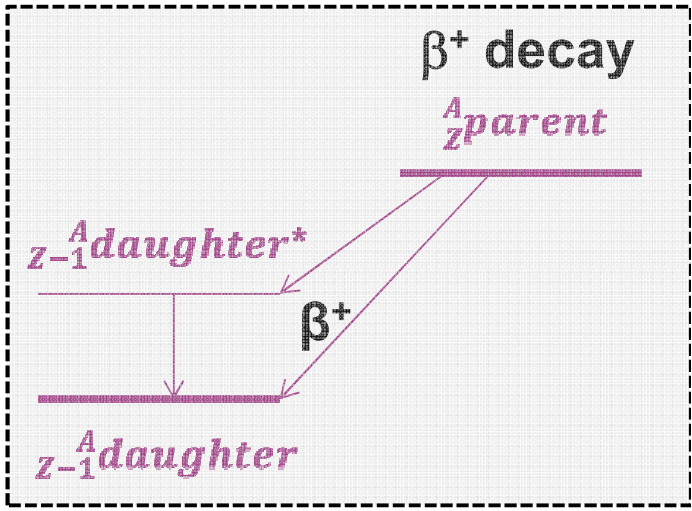


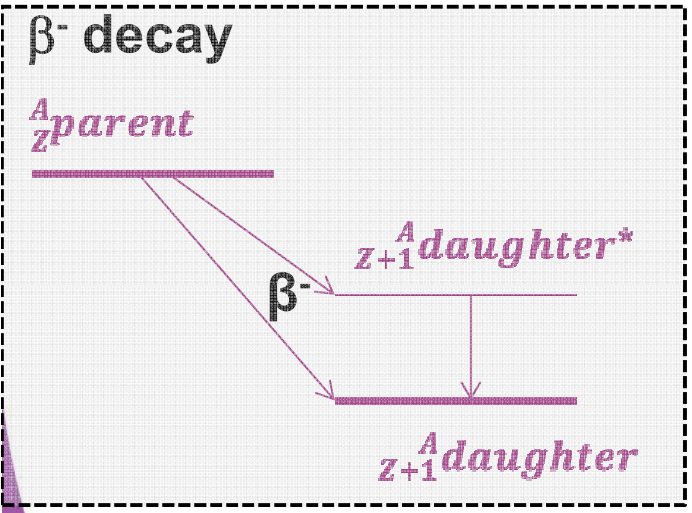
α-particles
e⁻ (Auger, CE)

γ-rays
XR-Characteristic

β⁺-particles
e⁻ (Auger, CE)

γ-rays
XR-Characteristic



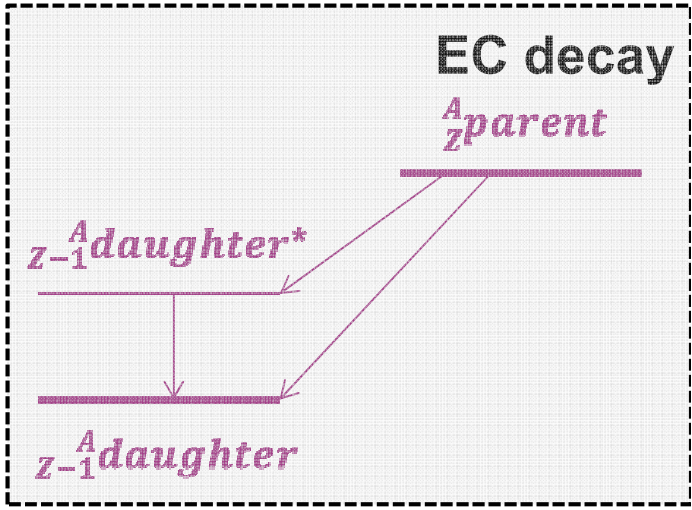


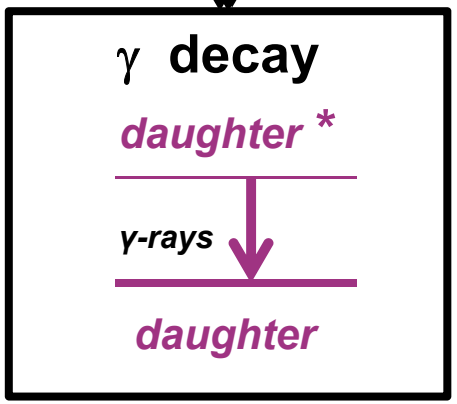
β⁻-particles
e⁻ (Auger, CE)

γ-rays
XR-Characteristic

e⁻ (Auger, CE)

γ-rays
XR-Characteristic





γ-rays & XR-Characteristic: discrete energies – line spectrum

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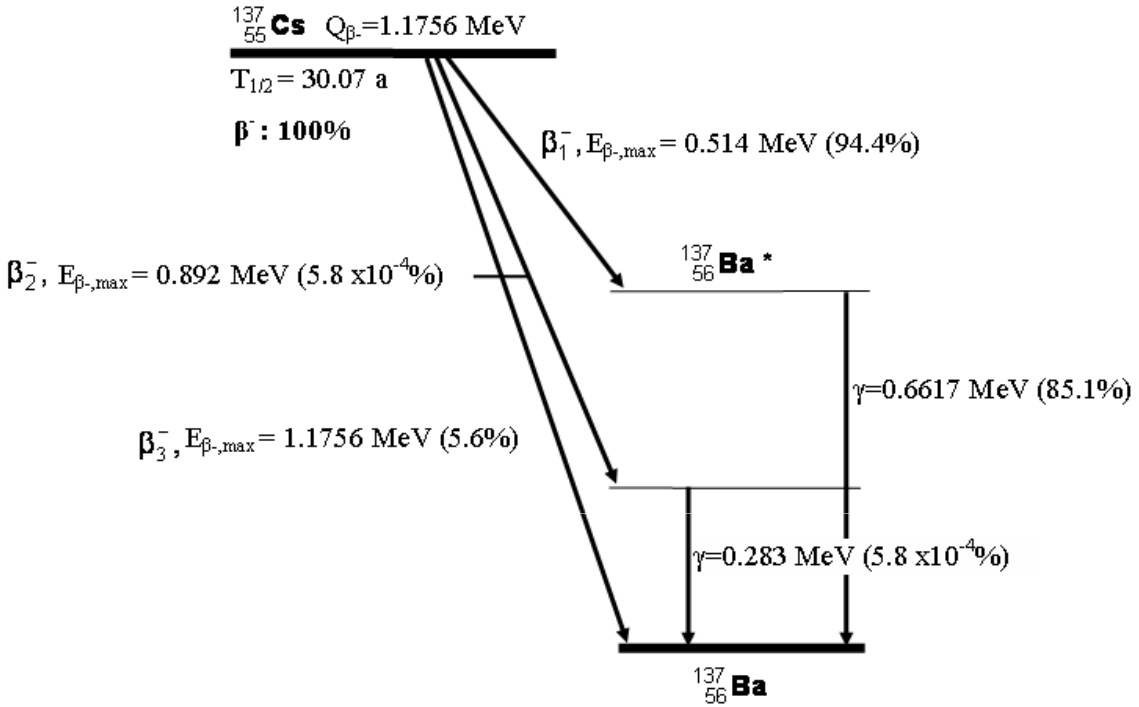
Particles – Irradiation emitted

Example: β^- decay of ^{137}Cs ➔ β^- particles



Beta-:

Energy (keV)	End-point energy (keV)	Intensity (%)
174.32 *6*	513.97 *17*	94.70 % *20*
334.65 *8*	892.13 *20*	5.8E-4 % *8*
416.26 *8*	1175.63 *17*	5.30 % *20*

$$\overline{E}_{\beta^-} \approx \frac{E_{\beta^-,max}}{3}$$

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Particles – Irradiation emitted

Example: β^- decay of ^{137}Cs ➔ Electrons (Auger, CE)

	Energy (keV)	Intensity (%)
Auger L	3.67	7.40 % *10*
Auger K	26.4	0.78 % *3*
CE K	624.216 *3*	7.79 % *11*
CE L	655.668 *3*	1.402 % *20*
CE M	660.364 *3*	0.300 % *4*
CE N	661.404 *3*	0.0646 % *9*
CE O	661.637 *3*	0.00965 % *14*

661.657 keV (γ-rays)
–
binding E of electron

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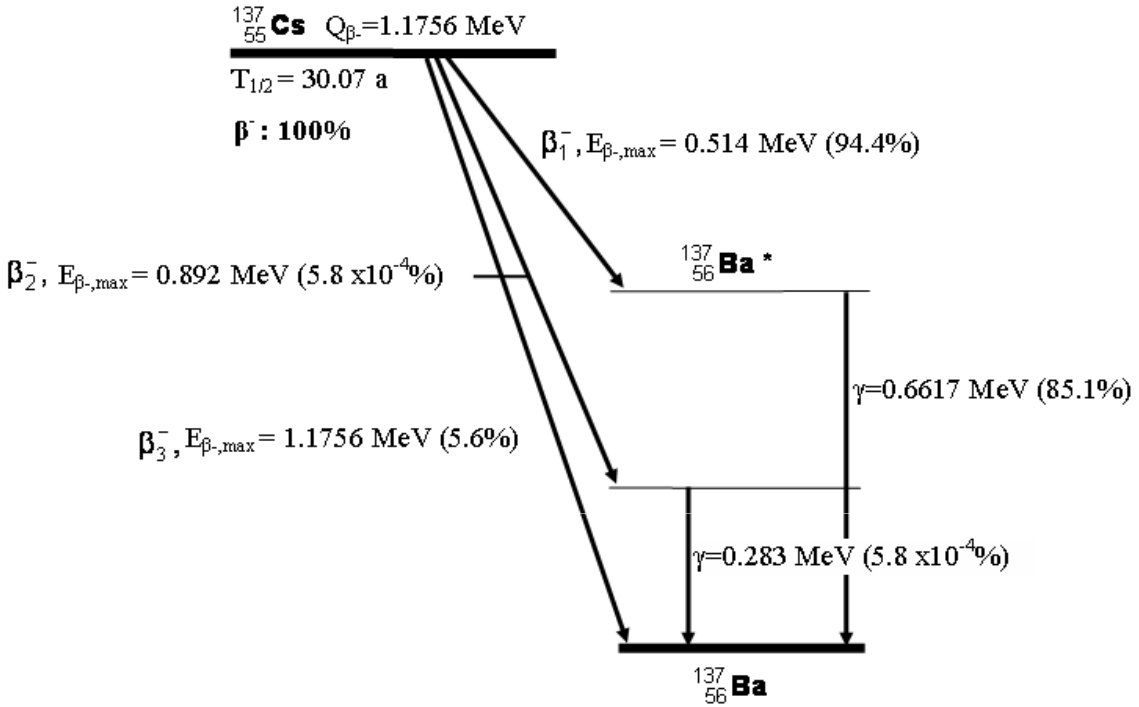
Particles – Irradiation emitted

Example: β^- decay of ^{137}Cs ➔ Photons



Characteristic γ-rays

Energy (keV)	Intensity (%)
XR 1 4.47	0.91 % *4*
XR kα2 31.817	1.99 % *5*
XR kα1 32.194	3.64 % *10*
XR kβ3 36.304	0.348 % *9*
XR kβ1 36.378	0.672 % *18*
XR kβ2 37.255	0.213 % *6*
283.5 *1*	5.8E-4 % *8*
661.657 *3*	85.10 % *20*

Particles – Irradiation used

Example: β^- decay of ^{137}Cs ➔ β^- electrons

Beta-:

Energy (keV)	End-point energy (keV)	Intensity (%)
174.32 *6*	513.97 *17*	94.70 % *20*
334.65 *8*	892.13 *20*	5.8E-4 % *8*
416.26 *8*	1175.63 *17*	5.30 % *20*

low particle energies are completely filtered by the source material itself and its encapsulation

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Particles – Irradiation used

Example: β^- decay of ^{137}Cs ➔ Electrons (Auger, CE)

	Energy (keV)	Intensity (%)
Auger L	3.67	7.40 % *10*
Auger K	26.4	0.78 % *3*
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CE L	655.668 *3*	1.402 % *20*
CE M	660.364 *3*	0.300 % *4*
CE N	661.404 *3*	0.0646 % *9*
CE O	661.637 *3*	0.00965 % *14*

low particle energies are completely filtered by the source material itself and its encapsulation

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Particles – Irradiation used

Example: β^- decay of ^{137}Cs ➔ Photons

		Energy (keV)	Intensity (%)
Characteristic	XR 1	4.47	0.91 % *4*
	XR kα2	31.817	1.99 % *5*
	XR kα1	32.194	3.64 % *10*
	XR kβ3	36.304	0.348 % *9*
	XR kβ1	36.378	0.672 % *18*
	XR kβ2	37.255	0.213 % *6*
γ-rays		283.5 *1*	5.8E-4 % *8*
		661.657 *3*	85.10 % *20*

Very low photon energy lines are filtered by the source material itself and its encapsulation and applicator/catheters material

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Topics

- Particles Emitted and Particles used
- **Mean & Effective Energy**
- Half Value Layer (HVL)
- Radioisotope Characteristics
- Radioisotopes
- Summary

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Particles – Mean Energy

Example: β^- decay of ^{137}Cs ➔ Photons

The emission weighted mean energy E_{mean} is defined as:

	Energy (keV)	Intensity (%)
Characteristic	XR 1	4.47	0.91 % *4*
	XR kα2	31.817	1.99 % *5*
	XR kα1	32.194	3.64 % *10*
	XR kβ3	36.304	0.348 % *9*
	XR kβ1	36.378	0.672 % *18*
	XR kβ2	37.255	0.213 % *6*
γ-rays		283.5 *1*	5.8E-4 % *8*
		661.657 *3*	85.10 % *20*
		E_i	f_i

$$E_{mean} = \frac{\sum_i f_i \cdot E_i}{\sum_i f_i} = 615.4\,keV$$

f_i is the intensity (or emission frequency) of the specific energy line E_i and the sum is taken over all photon ray energies E_i of the radionuclide spectrum.

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Particles – Effective Energy

Example: β^- decay of ^{137}Cs ➔ Photons

For dosimetric purposes it is more appropriate to consider the effective energy E_{eff} defined as the air-kerma weighted mean energy. This is given by:

	Energy (keV)	Intensity (%)
Characteristic	XR 1	4.47	0.91 % *4*
	XR kα2	31.817	1.99 % *5*
	XR kα1	32.194	3.64 % *10*
	XR kβ3	36.304	0.348 % *9*
	XR kβ1	36.378	0.672 % *18*
	XR kβ2	37.255	0.213 % *6*
γ-rays		283.5 *1*	5.8E-4 % *8*
		661.657 *3*	85.10 % *20*

$$E_{eff} = \frac{\sum_i f_i \cdot E^2{}_i \cdot \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i}}{\sum_i f_i \cdot E_i \cdot \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i}} = 651.8 keV$$

E_i f_i

$\left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i}$ **is the mass energy transfer coefficient for photons of energy E_i in air.**

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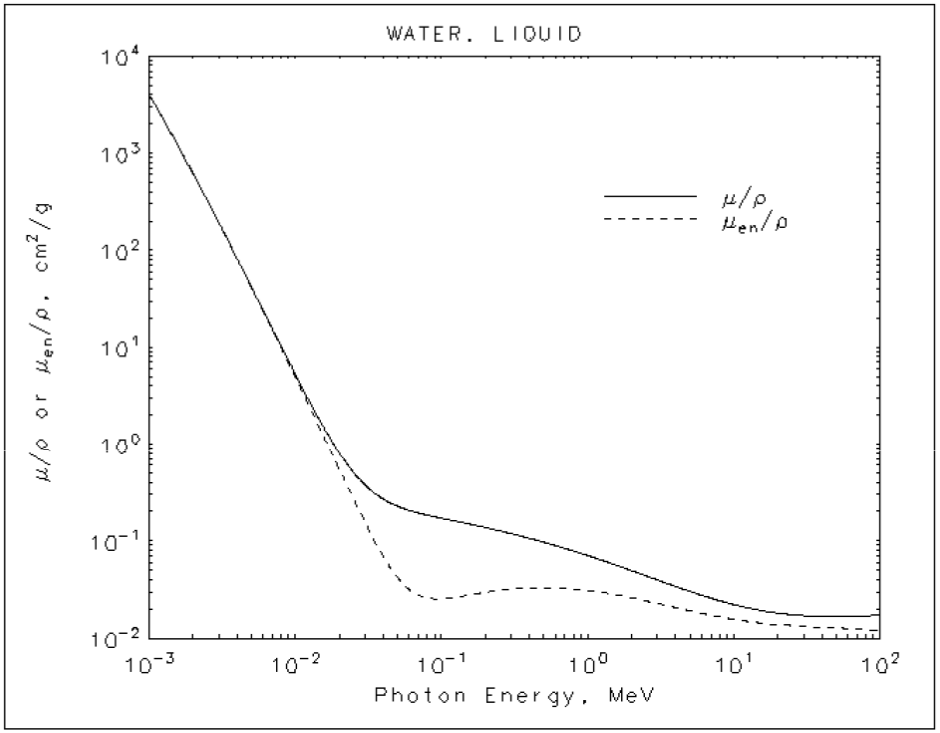
Particles – Effective Energy

Mass energy transfer coefficient $\left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i}$

NIST ➔ http://physics.nist.gov/PhysRefData/XrayMassCoef/tab4.html



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Particles – Effective Energy

Mass energy transfer coefficient $\left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i}$

NIST ➔ http://physics.nist.gov/PhysRefData/XrayMassCoef/tab4.html

X-Ray Mass Attenuation Coefficients

Table 3. Values of the mass attenuation coefficient, μ/ρ, and the mass energy-absorption coefficient, μ_{en}/ρ, as a function of photon energy, for elemental media. Atomic absorption edges are indicated by the shell designation.

Z	Element	Z	Element	Z	Element	Z	Element
1	H Hydrogen	24	Cr Chromium	47	Ag Silver	70	Yb Ytterbium
2	He Helium	25	Mn Manganese	48	Cd Cadmium	71	Lu Lutetium
3	Li Lithium	26	Fe Iron	49	In Indium	72	Hf Hafnium
4	Be Beryllium	27	Co Cobalt	50	Sn Tin	73	Ta Tantalum
5	B Boron	28	Ni Nickel	51	Sb Antimony	74	W Tungsten
6	C Carbon, Graphite	29	Cu Copper	52	Te Tellurium	75	Re Rhenium
7	N Nitrogen	30	Zn Zinc	53	I Iodine	76	Os Osmium
8	O Oxygen	31	Ga Gallium	54	Xe Xenon	77	Ir Iridium
9	F Fluorine	32	Ge Germanium	55	Cs Cesium	78	Pt Platinum
10	Ne Neon	33	As Arsenic	56	Ba Barium	79	Au Gold
11	Na Sodium	34	Se Selenium	57	La Lanthanum	80	Hg Mercury
12	Mg Magnesium	35	Br Bromine	58	Ce Cerium	81	Tl Thallium
13	Al Aluminum	36	Kr Krypton	59	Pr Praseodymium	82	Pb Lead
14	Si Silicon	37	Rb Rubidium	60	Nd Neodymium	83	Bi Bismuth
15	P Phosphorus	38	Sr Strontium	61	Pm Promethium	84	Po Polonium
16	S Sulfur	39	Y Yttrium	62	Sm Samarium	85	At Astatine
17	Cl Chlorine	40	Zr Zirconium	63	Eu Europium	86	Rn Radon
18	Ar Argon	41	Nb Niobium	64	Gd Gadolinium	87	Fr Francium
19	K Potassium	42	Mo Molybdenum	65	Tb Terbium	88	Ra Radium
20	Ca Calcium	43	Tc Technetium	66	Dy Dysprosium	89	Ac Actinium
21	Sc Scandium	44	Ru Ruthenium	67	Ho Holmium	90	Th Thorium
22	Ti Titanium	45	Rh Rhodium	68	Er Erbium	91	Pa Protactinium
23	V Vanadium	46	Pd Palladium	69	Tm Thulium	92	U Uranium

Abstract | Introduction | Mass Atten. Coef. | Mass Energy-Absorp. Coef. | Summary | References

Particles – Effective Energy

Mass energy transfer coefficient $\left(\frac{\mu_{tr}}{\rho}\right)_{\alpha, E_i}$

NIST ➔ http://physics.nist.gov/PhysRefData/XrayMassCoef/tab4.html

X-Ray Mass Attenuation Coefficients

Table 4. Values of the mass attenuation coefficient, μ/ρ, and the mass energy-absorption coefficient, μ_{en}/ρ, as a function of photon energy, for compounds and mixtures. The compositions of various human tissues were taken from ICRU Report 44 (1989). Absorption edges for the constituent atoms are indicated by the atomic number and shell designation.

Material	Material
A-150 Tissue-Equivalent Plastic	Glass, Lead
Adipose Tissue (ICRU-44)	Lithium Fluoride
Air, Dry (near sea level)	Lithium Tetraborate
Alanine	Lung Tissue (ICRU-44)
Bakelite	Magnesium Tetraborate
Blood, Whole (ICRU-44)	Mercuric Iodide
Bone, Cortical (ICRU-44)	Muscle, Skeletal (ICRU-44)
B-100 Bone-Equivalent Plastic	Ovary (ICRU-44)
Brain, Grey/White Matter (ICRU-44)	Photographic Emulsion, Kodak Type AA
Breast Tissue (ICRU-44)	Photographic Emulsion, Standard Nuclear
C-552 Air-equivalent Plastic	Plastic Scintillator, Vinyltoluene
Cadmium Telluride	Polyethylene
Calcium Fluoride	Polyethylene Terephthalate, "Mylar"
Calcium Sulfate	Polymethyl Methacrylate
15 mmol L^{-1} Ceric Ammonium Sulfate Solution	Polystyrene
Cesium Iodide	Polytetrafluoroethylene, "Teflon"
Concrete, Ordinary	Polyvinyl Chloride
Concrete, Barite (Type BA)	Radiochromic Dye Film, Nylon Base
Eye Lens (ICRU-44)	Testis (ICRU-44)
Ferrous Sulfate, Standard Fricke	Tissue, Soft (ICRU-44)
Gadolinium Oxysulfide	Tissue, Soft (ICRU Four-Component)
Gafchromic Sensor	Tissue-Equivalent Gas, Methane Based
Gallium Arsenide	Tissue-Equivalent Gas, Propane Based
Glass, Borosilicate "Pyrex"	Water, Liquid

Abstract | Introduction | Mass Atten. Coef. | Mass Energy-Absorp. Coef. | Summary | References

Topics

- Particles Emitted and Particles used
- Mean & Effective Energy
- **Half Value Layer (HVL)**
- Radioisotope Characteristics
- Radioisotopes
- Summary

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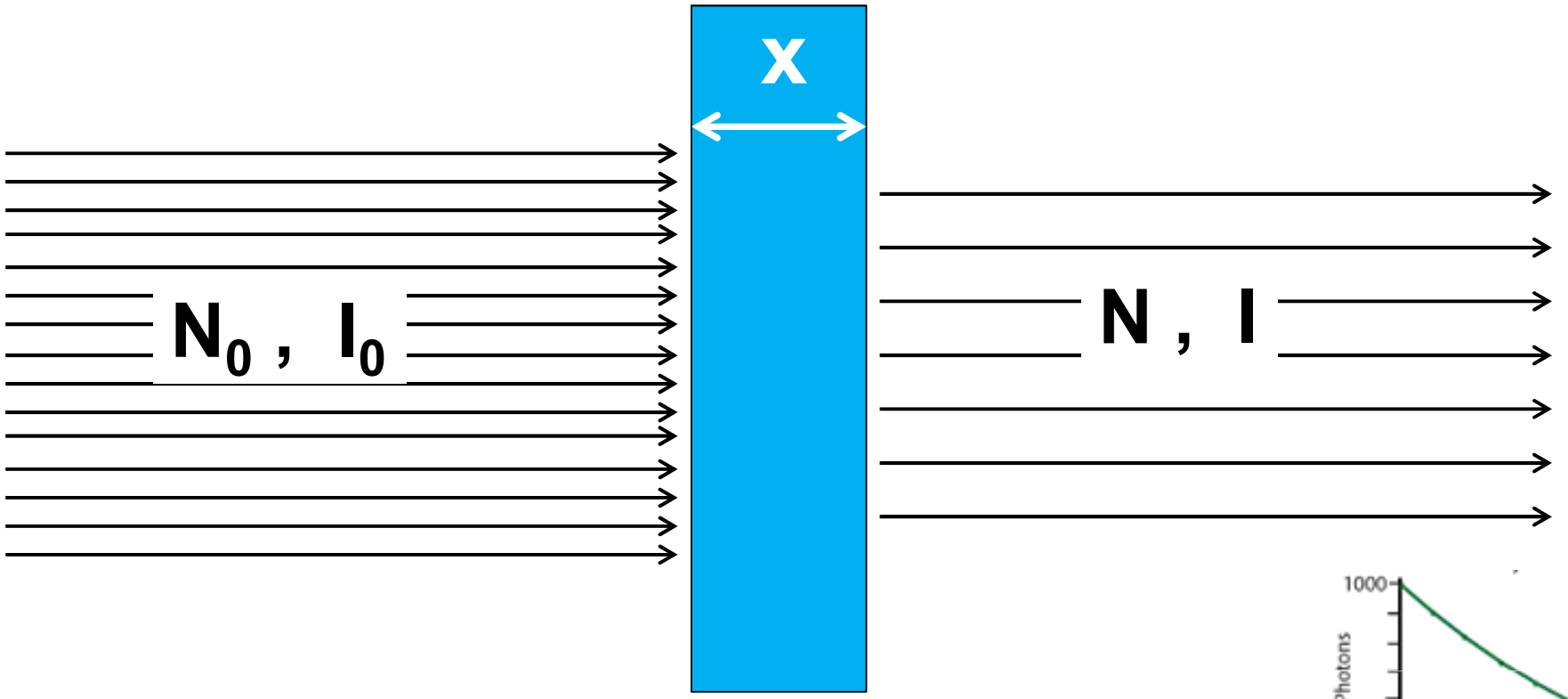
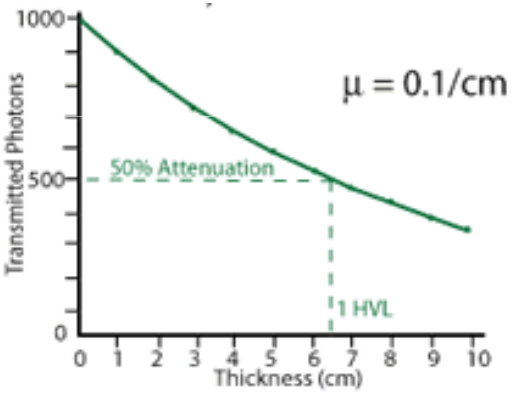
Photon Radiation – Attenuation



$$N = N_0 e^{-\mu x} \quad \text{or} \quad I = I_0 e^{-\mu x}$$



μ: the attenuation coefficient (cm^{-1}).
Its value depends on both material and Energy of photons

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Photon Radiation – Attenuation Coefficients

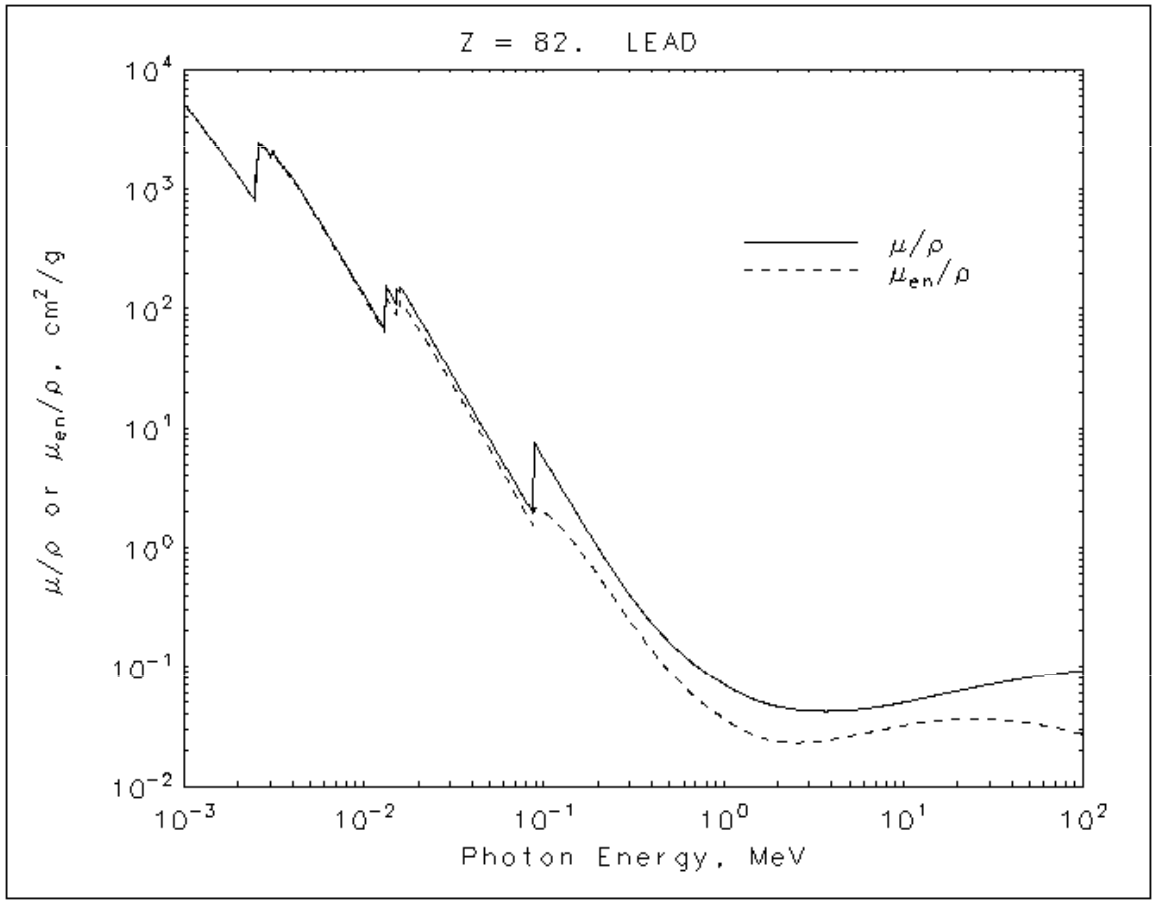
$$N = N_0 e^{-\mu x}$$

or

$$\mathrm{I} = I_0 e^{-\mu x}$$

$\mu = (\mu/\rho).\rho$

$\rho_{lead} = 11.35\ g\ cm^{-3}$



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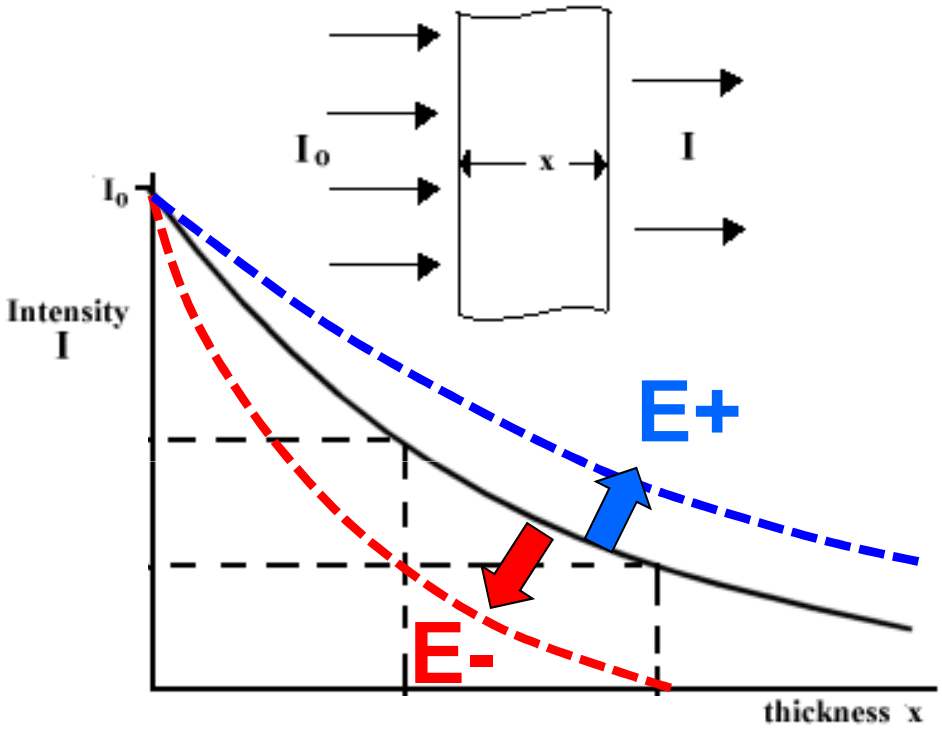
Photon Radiation – Attenuation Coefficients

$$N = N_0 e^{-\mu x} \quad \text{or} \quad I = I_0 e^{-\mu x}$$

Linear Attenuation Coefficients (in cm^{-1}) for a range of materials at gamma-ray energies of 100, 200 and 500 keV.

Absorber	100 keV	200 keV	500 keV
Air	0.000195	0.000159	0.000112
Water	0.167	0.136	0.097
Carbon	0.335	0.274	0.196
Aluminium	0.435	0.324	0.227
Iron	2.72	1.09	0.655
Copper	3.8	1.309	0.73
Lead	59.7	10.15	1.64



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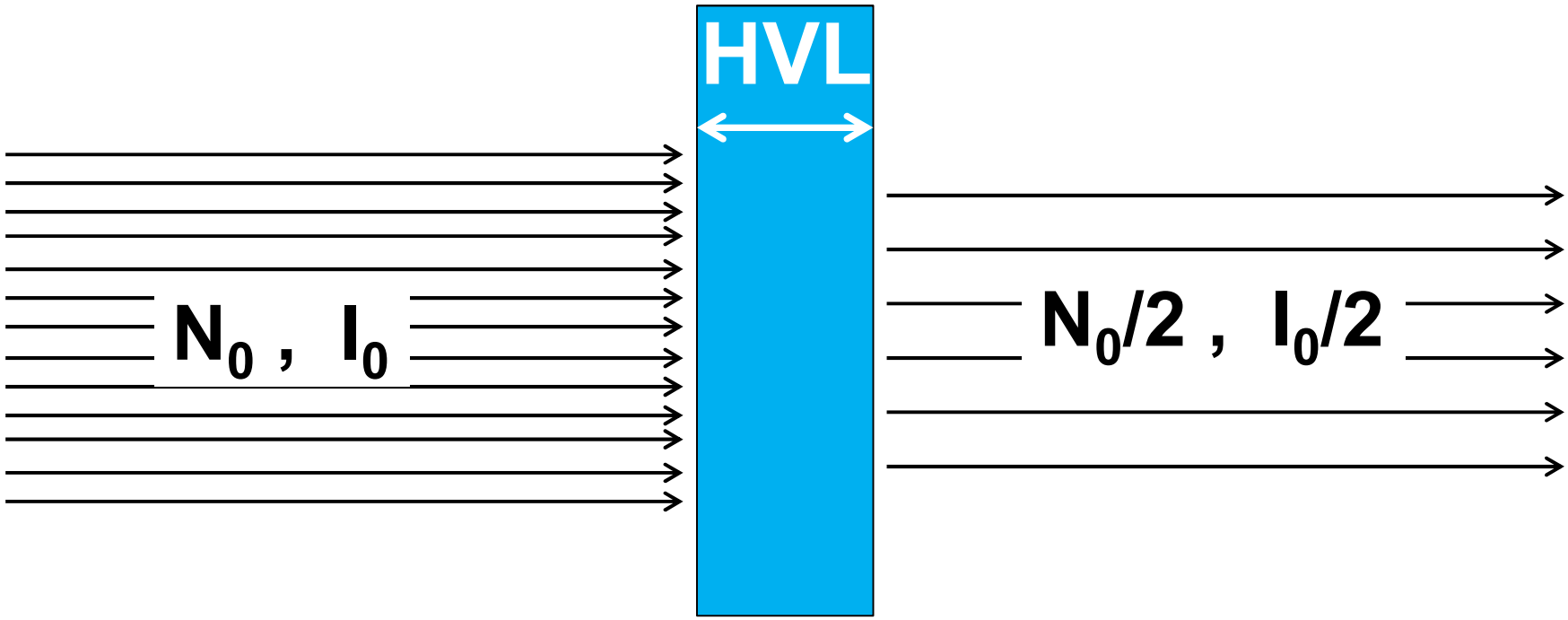
Photon Radiation – Attenuation - HVL



$$N = N_0 e^{-\mu x} \quad \text{or} \quad I = I_0 e^{-\mu x} \quad \text{and thus} \quad HVL = \frac{ln2}{\mu}$$

μ: the attenuation coefficient (cm^{-1}).
Its value depends on both *Material* and *Energy* of photons

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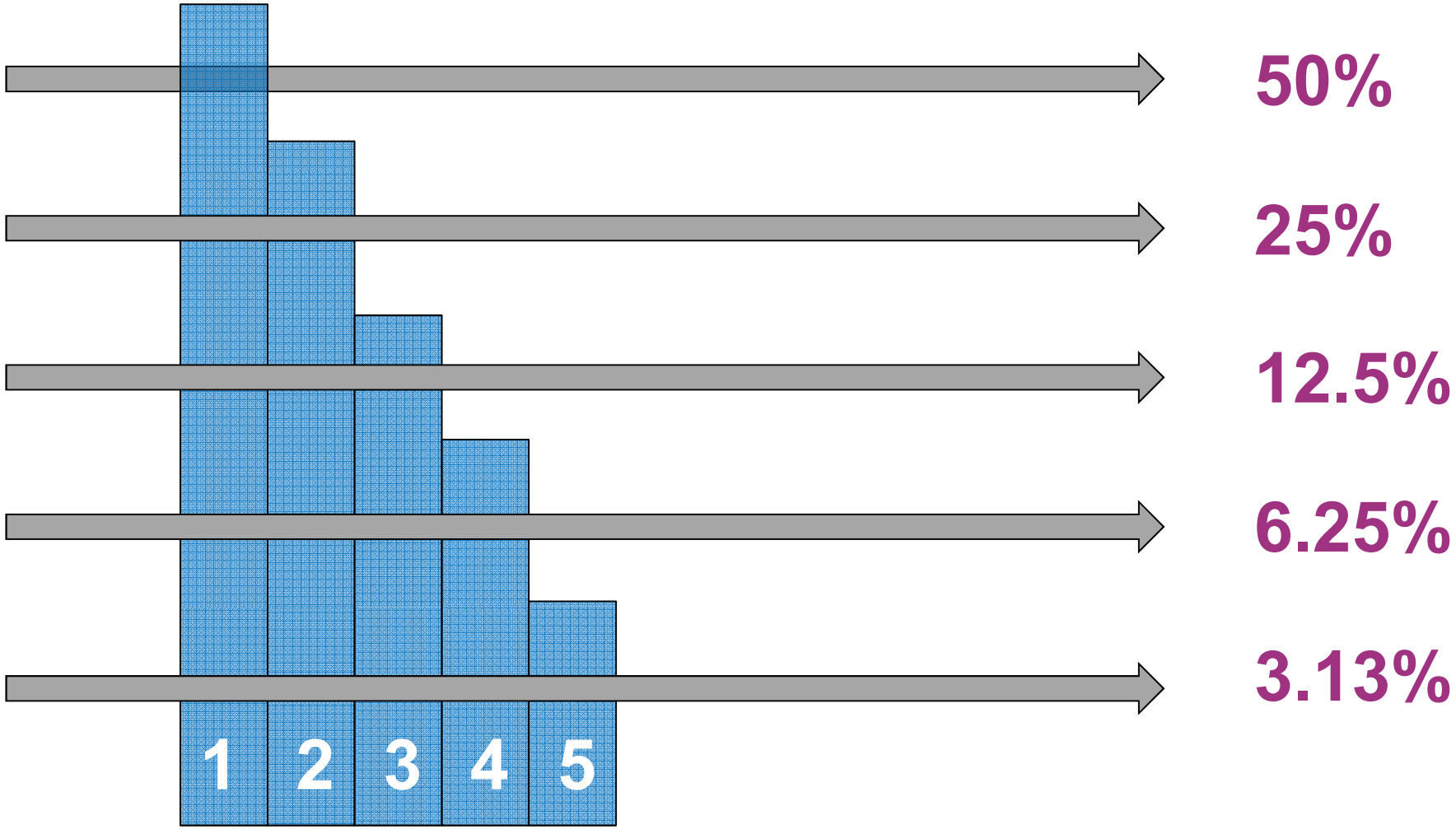
Photon Radiation – Attenuation - HVL



Half Value Layer – HVL ➔ **%**

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Photon Radiation – Attenuation - HVL

Half Value Layers (in cm) for a range of materials at gamma-ray energies of 100, 200 and 500 keV.

Absorber	100 keV	200 keV	500 keV
Air	3555	4359	6189
Water	4.15	5.1	7.15
Carbon	2.07	2.53	3.54
Aluminium	1.59	2.14	3.05
Iron	0.26	0.64	1.06
Copper	0.18	0.53	0.95
Lead	0.012	0.068	0.42

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Photon Radiation – Attenuation - HVL

$$N = N_0 e^{-\mu x} \quad \text{or} \quad I = I_0 e^{-\mu x} \quad \text{and} \quad HVL = \frac{ln2}{\mu}$$

Attention:

- Indicative
- Valid only for “narrow” beams
- Valid when no beam hardening occurs
- Overestimates attenuation

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Topics

- Particles Emitted and Particles used
- Mean & Effective Energy
- Half Value Layer (HVL)
- **Radioisotope Characteristics**
- Radioisotopes
- Summary

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Radioisotope Characteristics

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

Radioisotope Characteristics

Radionuclides: the different “Characters”

A Radionuclide of a very short half life is most probably candidate for:

a) **pulse dose rate (PDR) brachytherapy**

b) **permanent implants**

c) **HDR afterloader-based brachytherapy**

Radioisotope Characteristics

Radionuclides: the different “Characters”

A Radionuclide with low specific activity is most probably candidate for:

a) **low dose rate brachytherapy**

b) **permanent implants**

c) **constructing very small sources of very high activity**

Topics

- Particles Emitted and Particles used
- Mean & Effective Energy
- Half Value Layer (HVL)
- Radioisotope Characteristics
- **Radioisotopes**
- Summary

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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.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[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]

Radionuclides: ^{60}Co

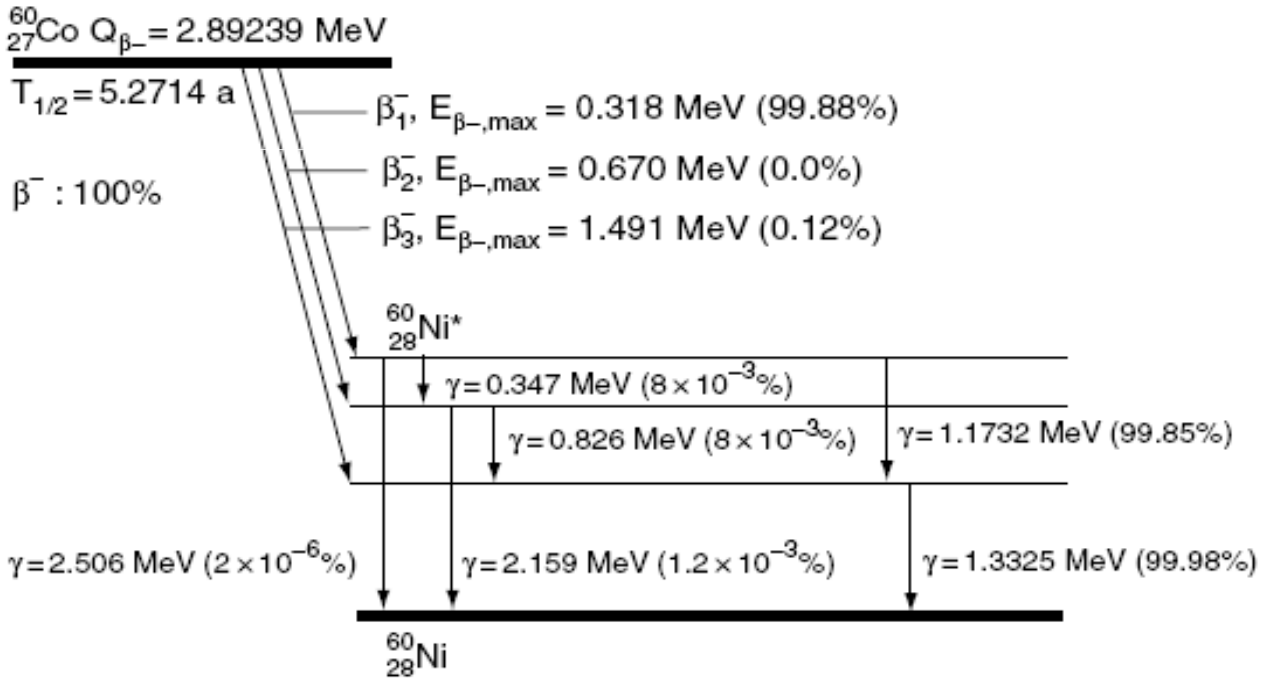

FIGURE 5.3
Schematic representation of β^- decay of $^{60}_{27}$Co which decays almost totally (99.92%) to the third excited state of $^{60}_{28}$Ni. The disintegration energy for the decay is $Q_{\beta^-} = 2.8239$ MeV. The two main γ-rays are 1.1732 and 1.3325 MeV, both with an intensity of approximately 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]

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Radionuclides: ^{137}Cs

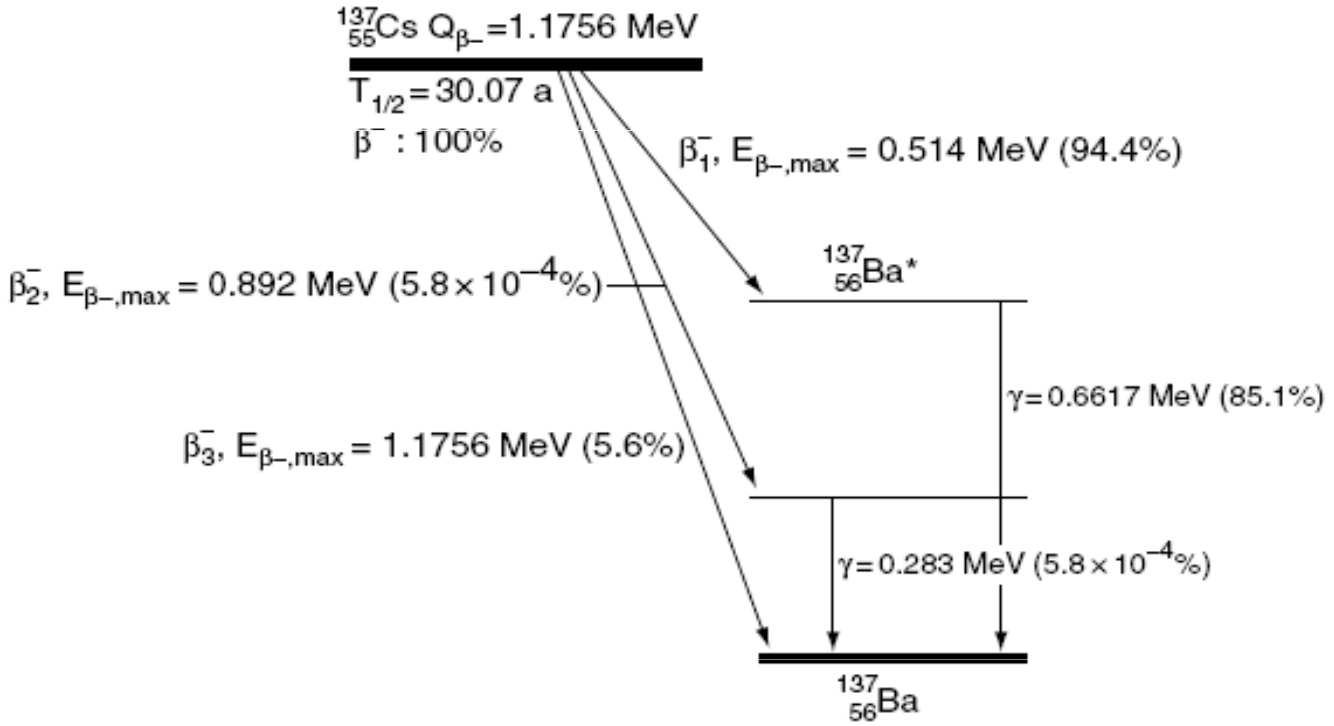

FIGURE 5.4
Schematic representation of β^- decay of $^{137}_{55}Cs$ which decays mainly (94.4%) to the second excited state of $^{137}_{56}Ba$. The disintegration energy for the decay is $Q_{\beta^-} = 1.1756$ MeV. There is practically a single γ-ray emitted of 0.6617 MeV with an absolute intensity of 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: ^{198}Au

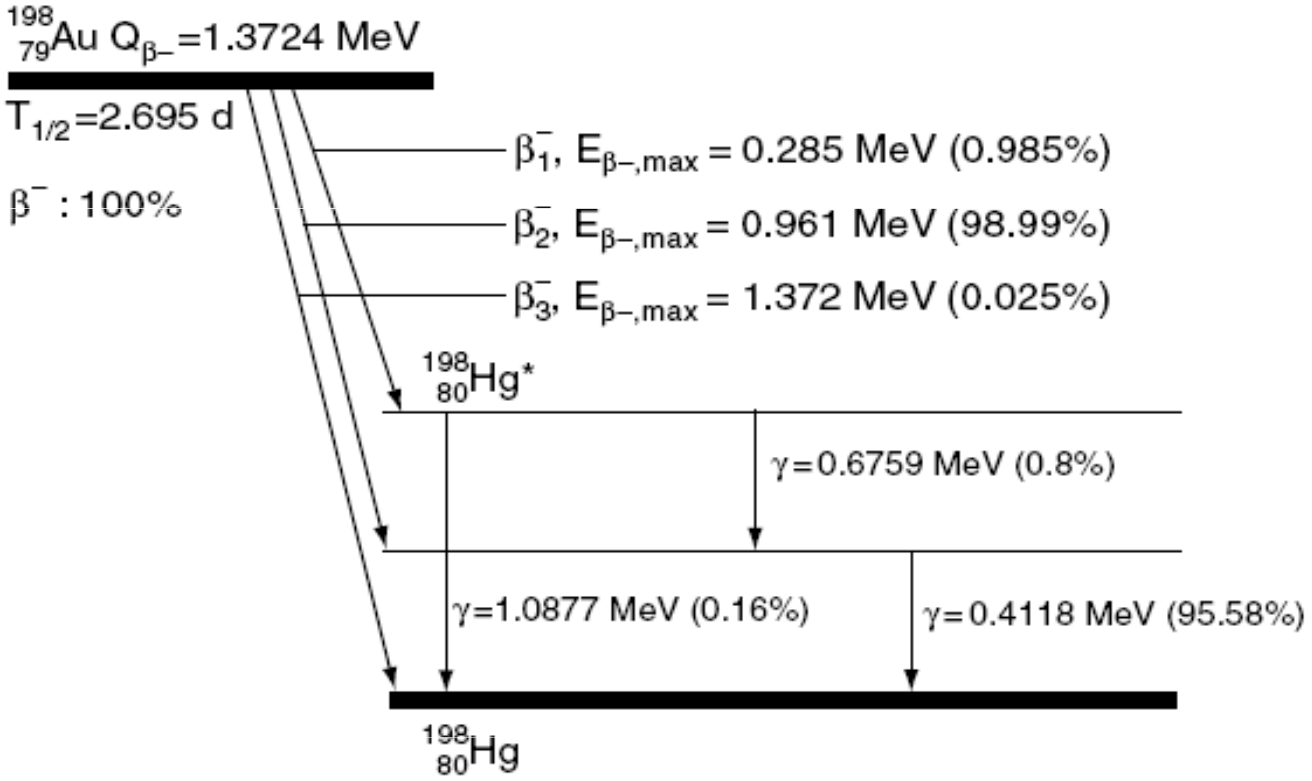

FIGURE 5.5
Schematic representation of β^- decay of $^{198}_{79}$Au which decays mainly (98.99%) to the second excited state of $^{198}_{80}$Hg. The disintegration energy for the decay is $Q_{\beta^-} = 1.3724$ MeV. There is mainly a γ-ray emitted of 0.412 MeV with an intensity of 95.58%.[3] On average, 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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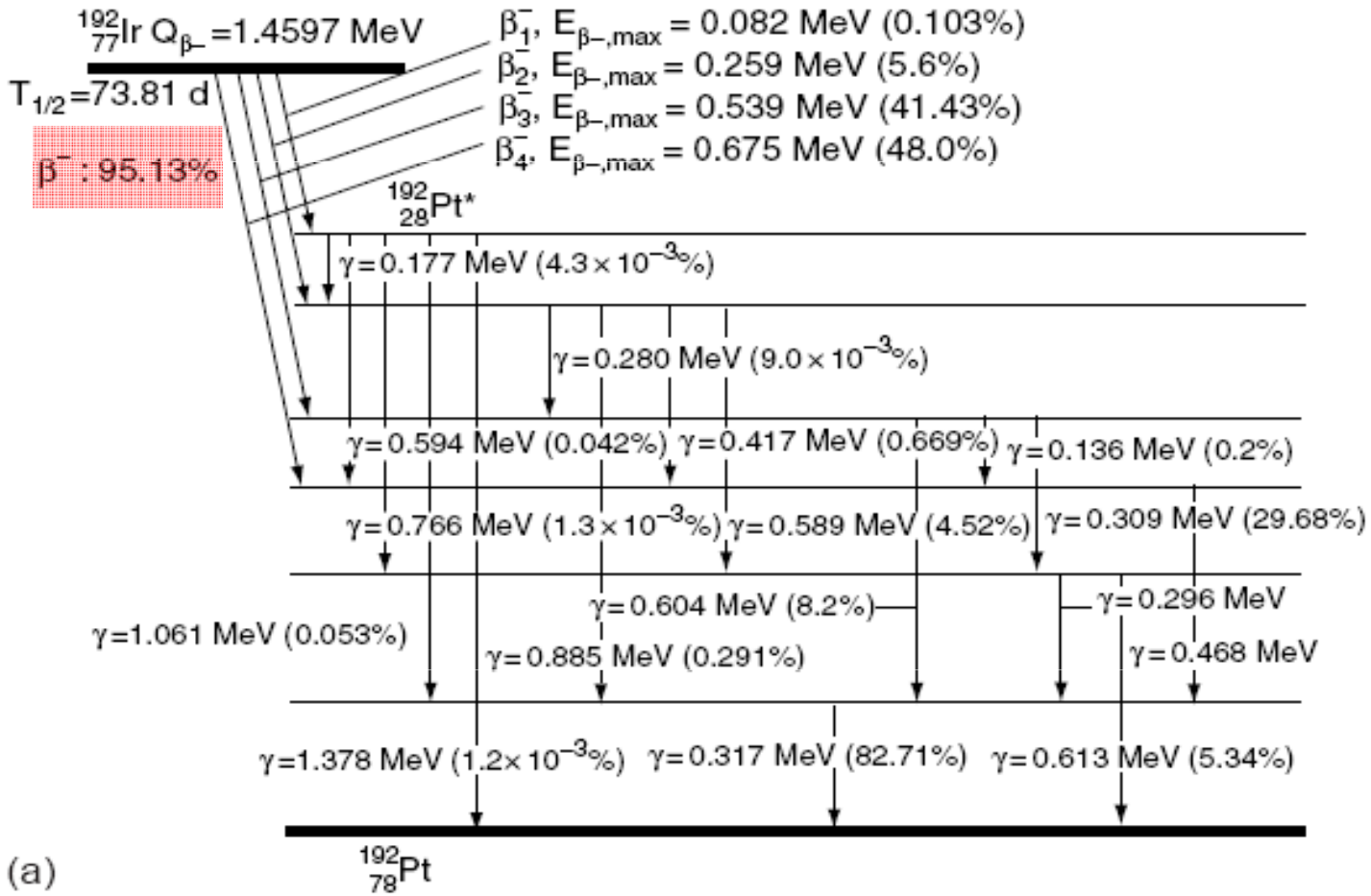
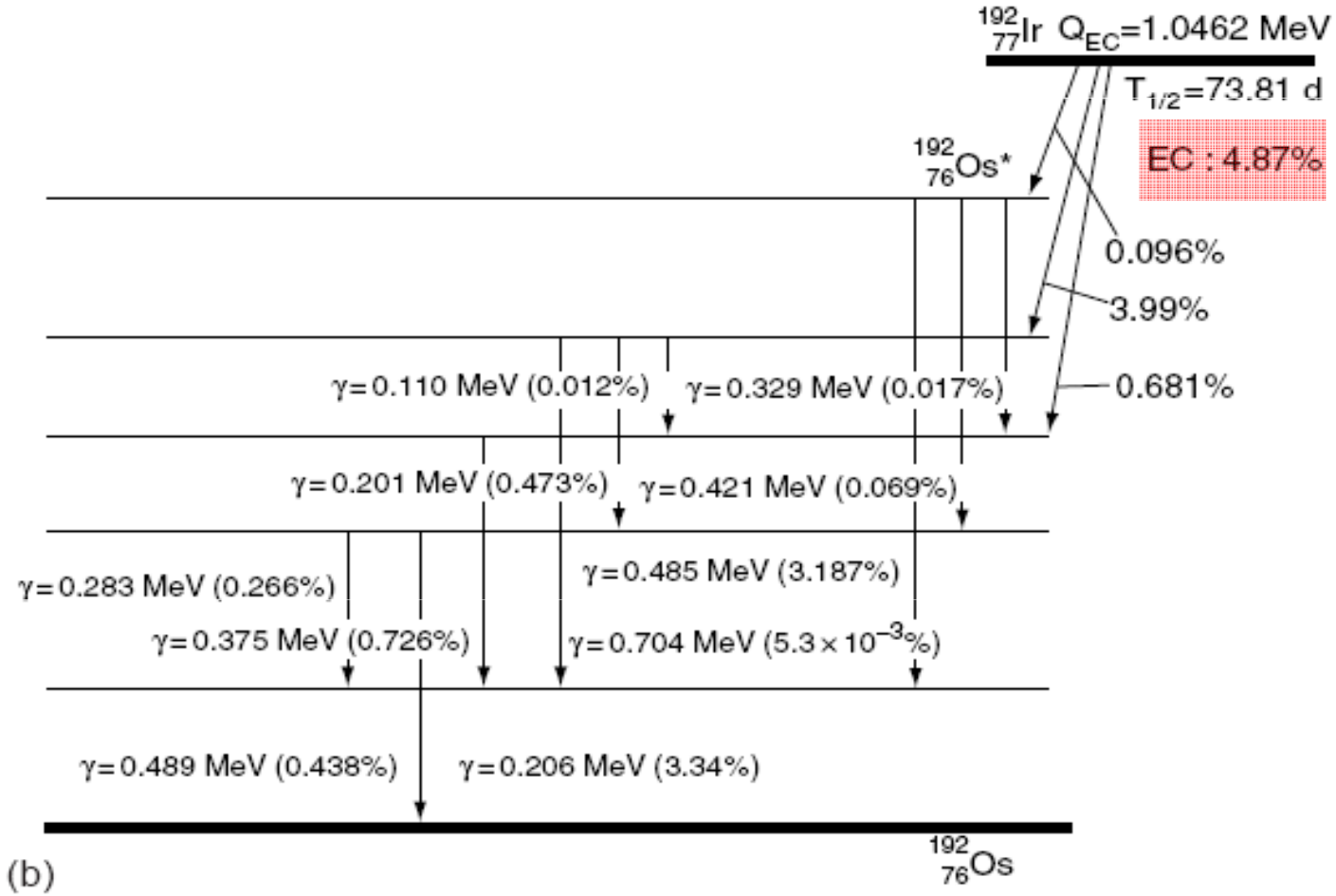
Radionuclides: ^{192}Ir - β^- Decay



Radionuclides: ^{192}Ir - EC Decay



Radionuclides: ^{125}I

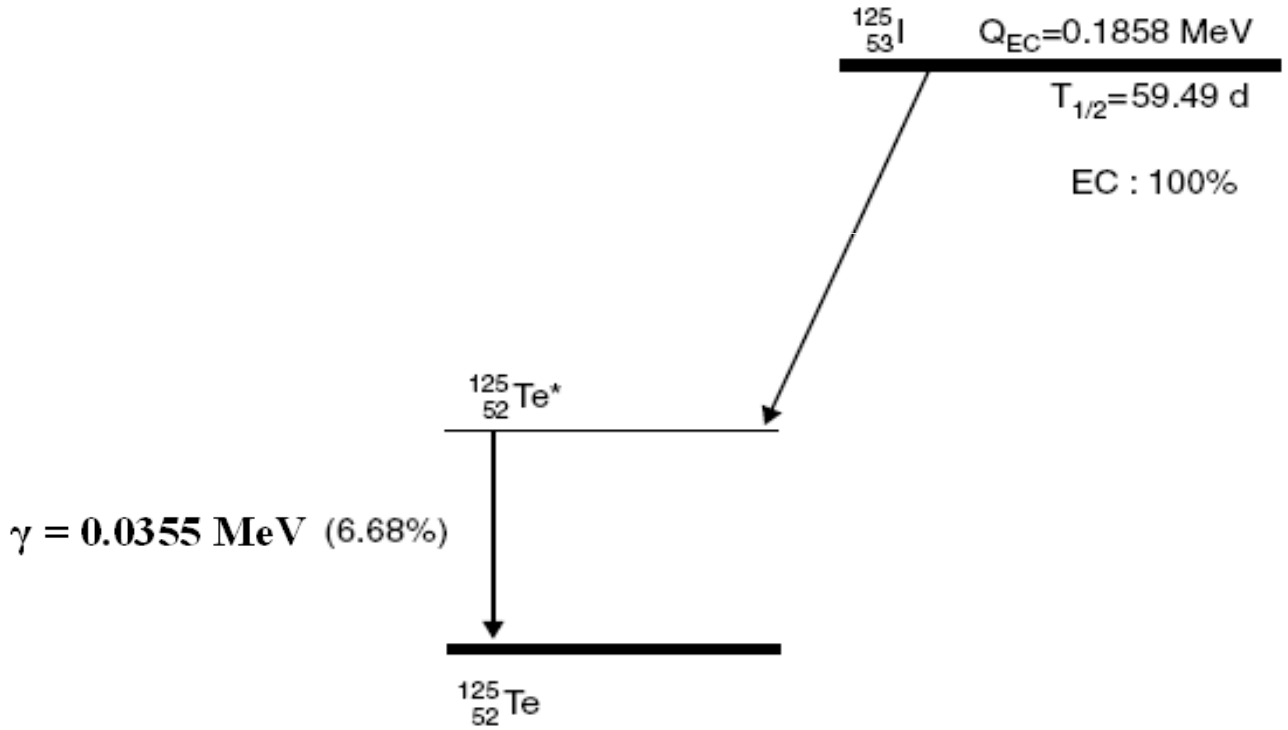


FIGURE 5.7
Schematic representation of EC decay of $^{125}_{53}$I to the first excited state of $^{125}_{52}$Te. The disintegration energy for the decay is $Q_{EC} = 0.1858$ MeV. There is a single γ-ray of 0.035 MeV with an intensity of 6.68% emitted, whereas there are several characteristic x-rays emitted 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]

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Radionuclides: ^{103}Pd

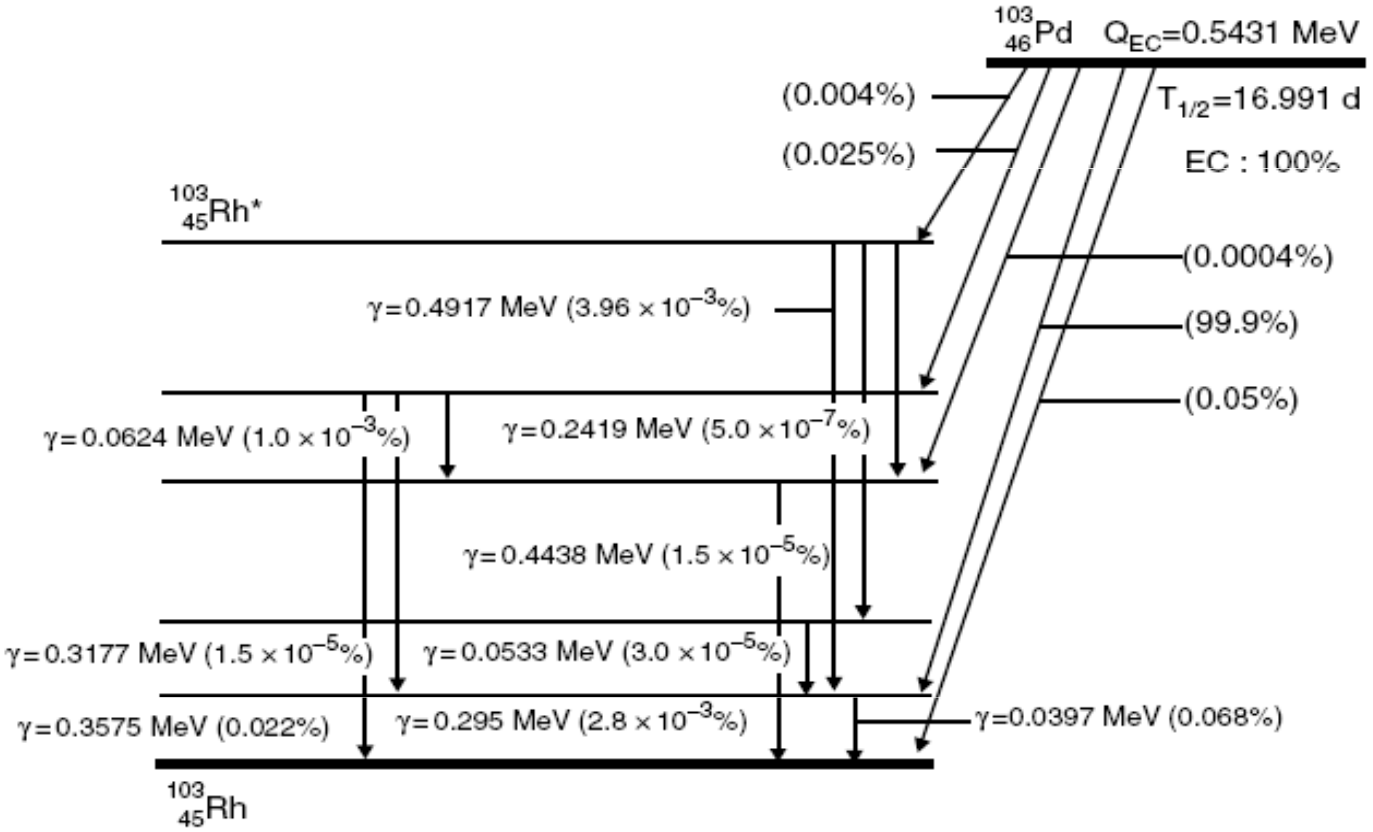

FIGURE 5.8
Schematic representation of EC decay of $^{103}_{46}$Pd to the different excited states and the ground state of $^{103}_{45}$Rh. The disintegration energy for the decay is $Q_{EC} = 0.5431$ MeV. The γ-rays emitted have very low, almost negligible intensities. There are several characteristic 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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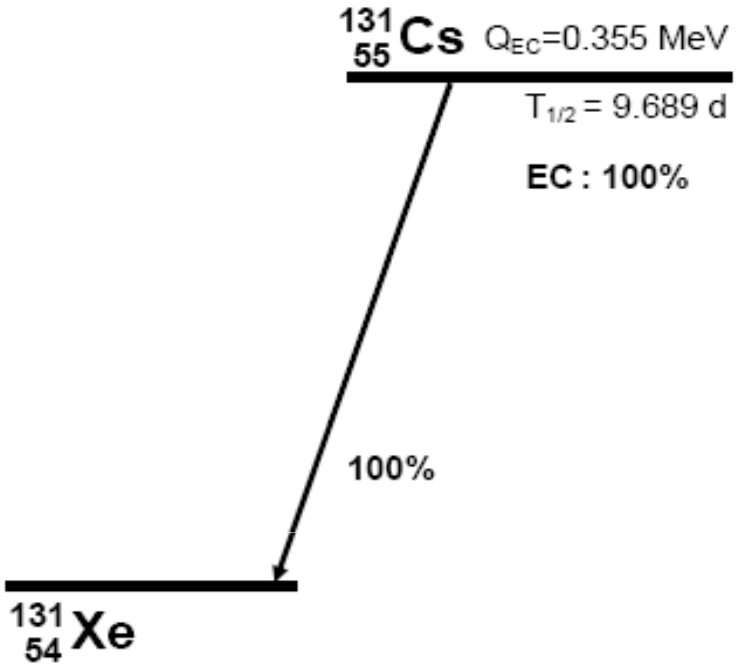
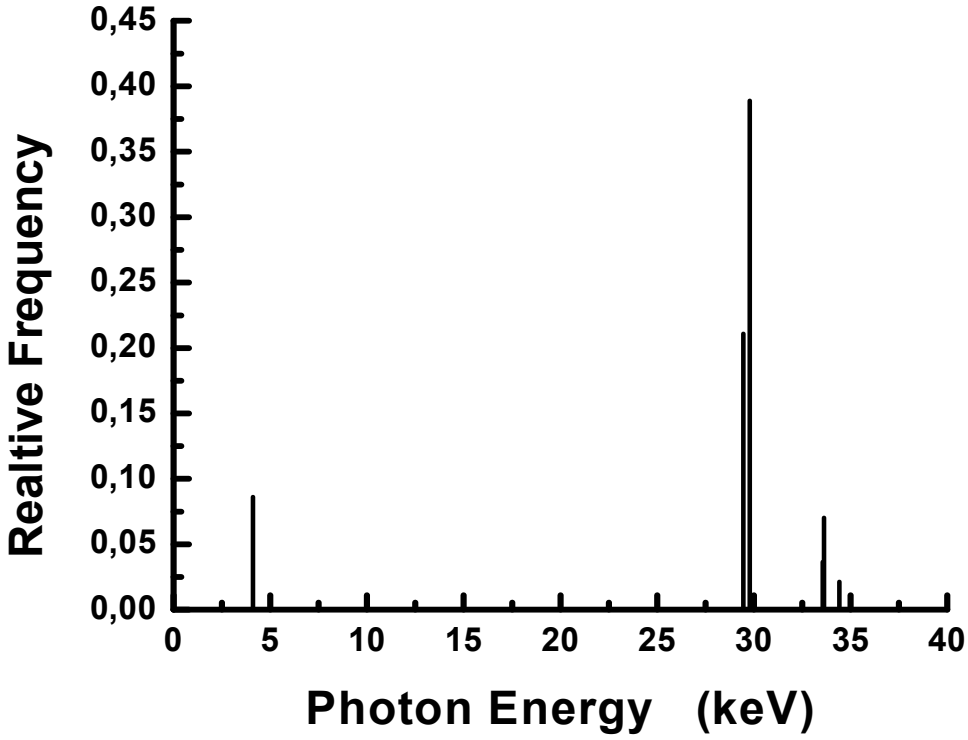
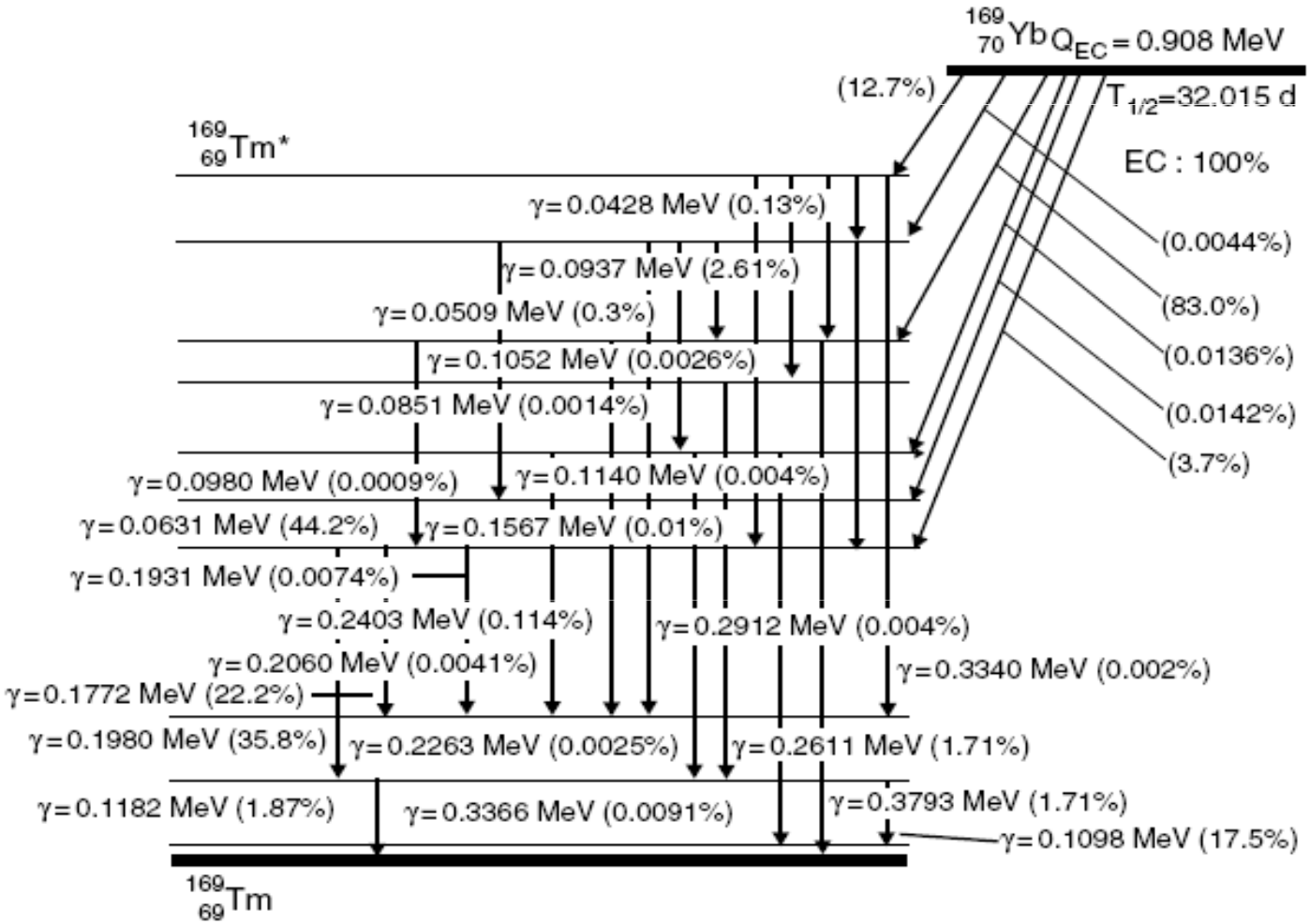
Radionuclides: ^{131}Cs





Radionuclides: ^{169}Yb



Radionuclides: Shielding

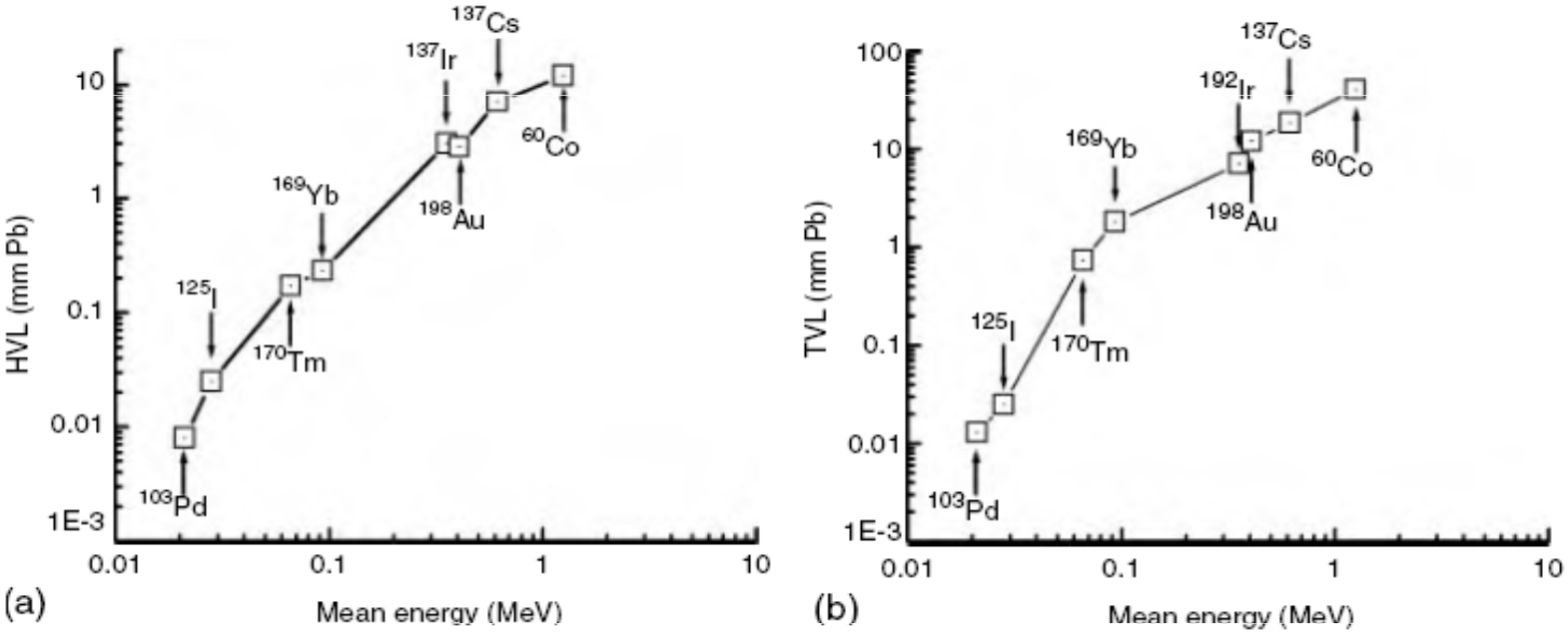


FIGURE 5.2

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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Topics

- Particles Emitted and Particles used
- Mean & Effective Energy
- Half Value Layer (HVL)
- Radioisotope Characteristics
- Radioisotopes
- **Summary**

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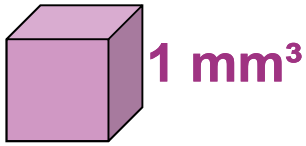
Radionuclides: Summary

The Role of Specific *Activity* and *Density* ρ

Maximal A in 1 mm³ of Radionuclide Material

- ^{192}Ir → 2 1,0 (7,7 TBq)
- ^{137}Cs → 7 8×10^{-4}
- ^{60}Co → 5 5×10^{-2}
- ^{198}Au → 1 23 x
- ^{170}Tm → 4 0,3 x
- ^{169}Yb → 3 0,8 x
- ^{204}Tl → 6 3×10^{-2}



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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	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 PARIS SYSTEM

Previsional implantation rules for

Interstitial brachytherapy

Erik Van Limbergen

University Hospital Leuven

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Paris System

- Dedicated to interstitial brachytherapy
- Developped in the 1960s / complete system
- Created for I^{192} wires
- Set of rules tacking into account
  - The geometry and method of application
  - In order to get a suitable dose distribution

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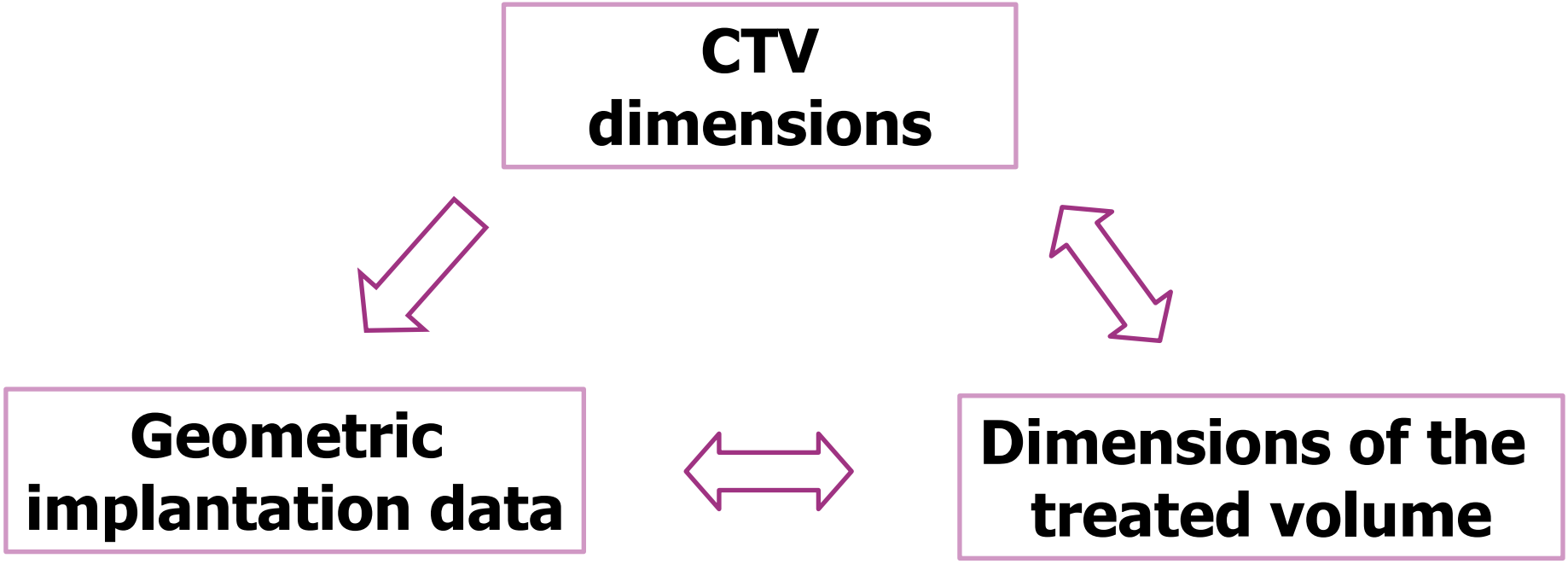
Predictive implant system



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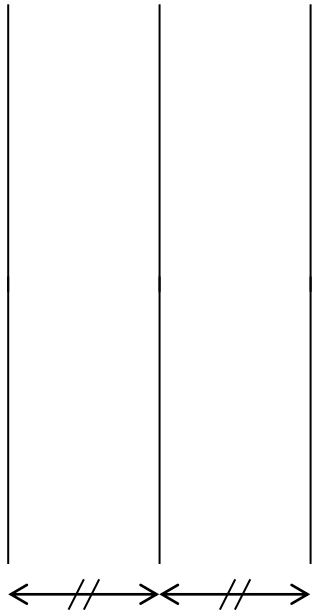
Paris system: Basic principles (1)

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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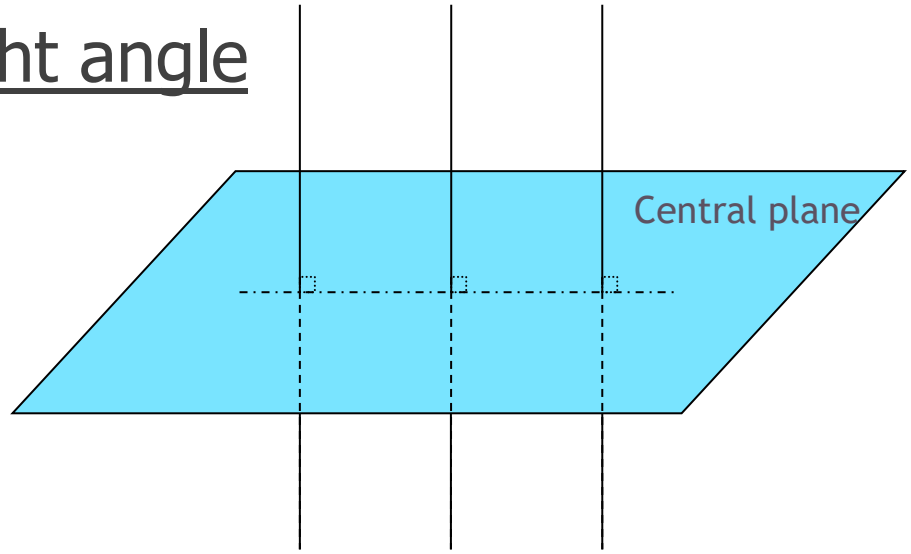
Paris system: Basic principles (2)

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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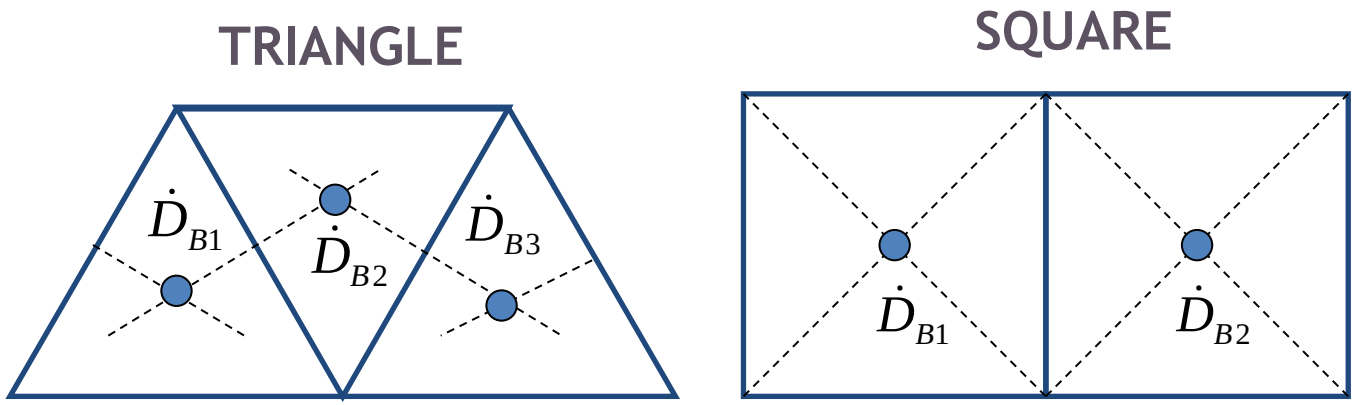
Paris system: Dosimetry

- 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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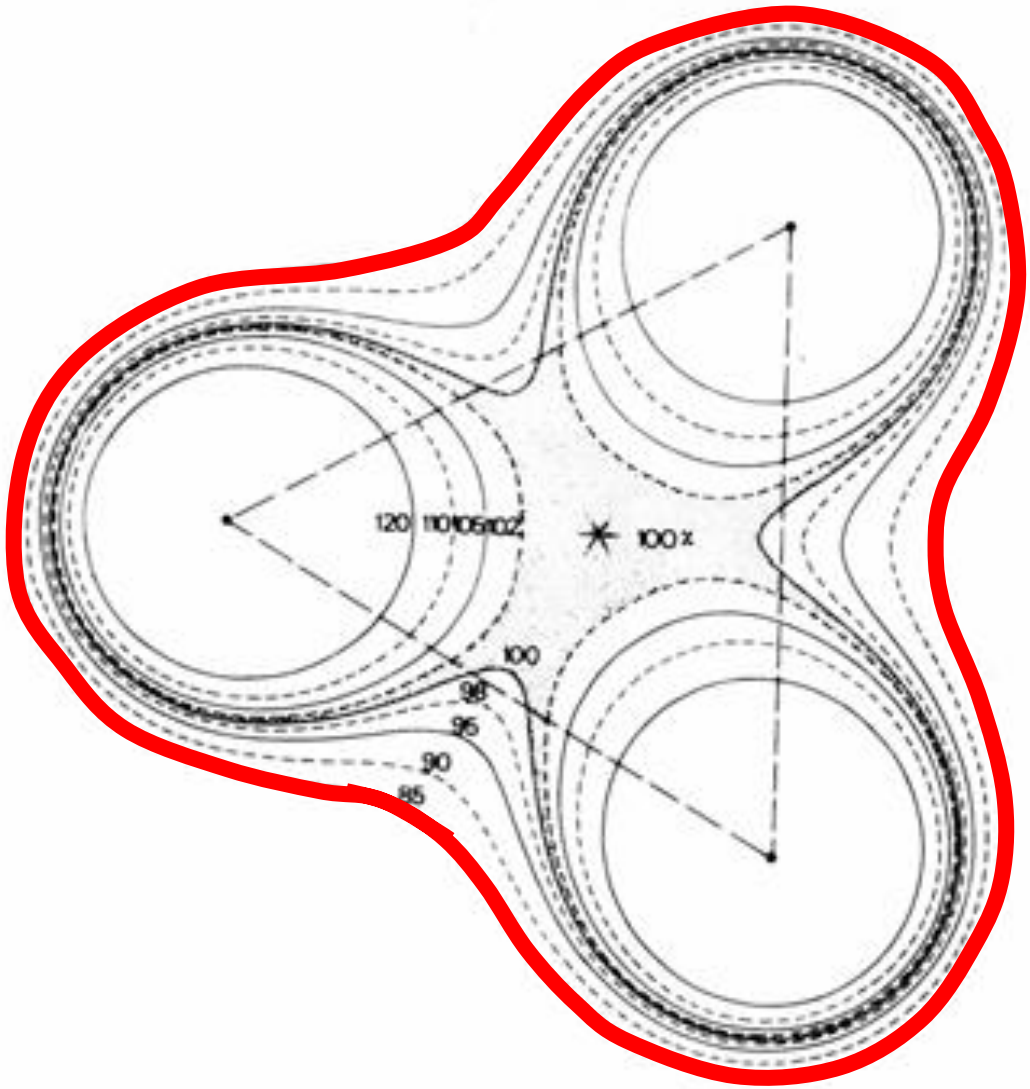
D_{Ref} = 0.85 x BD



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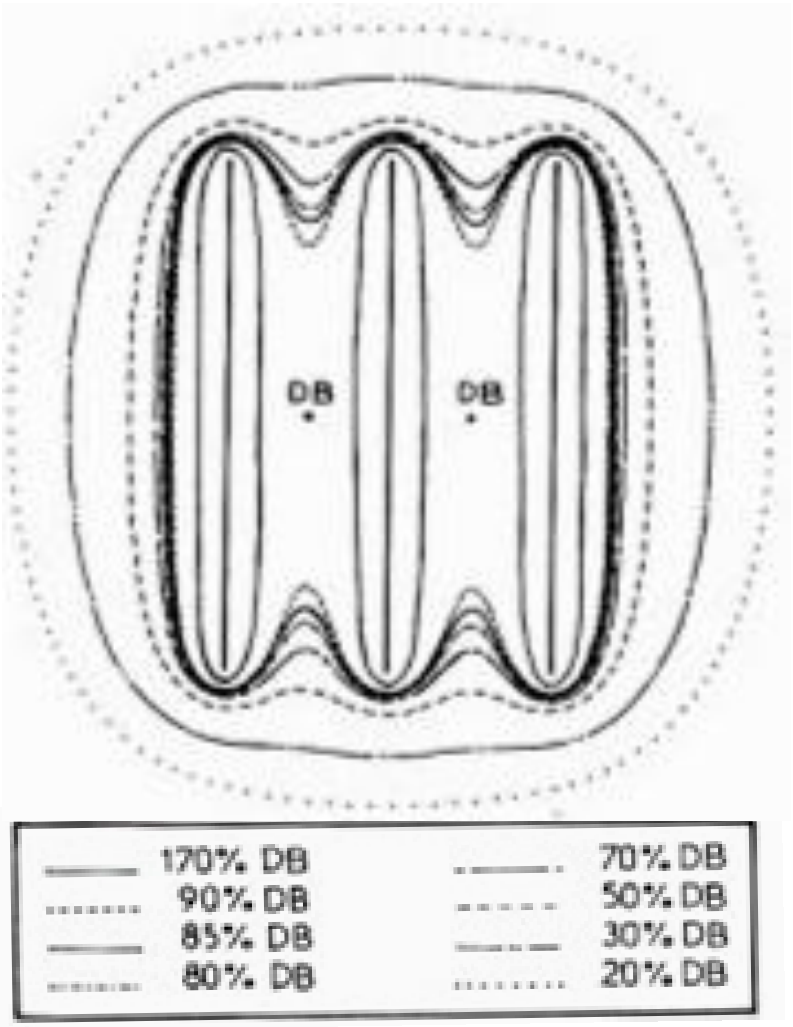
Why 85%?

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



- Based on clinical experience + compromise!
  - High isodose

➔ **Good homogeneity**

  - Low isodose

➔ **Shape / coverage**

➔ **Measurements on real cases**

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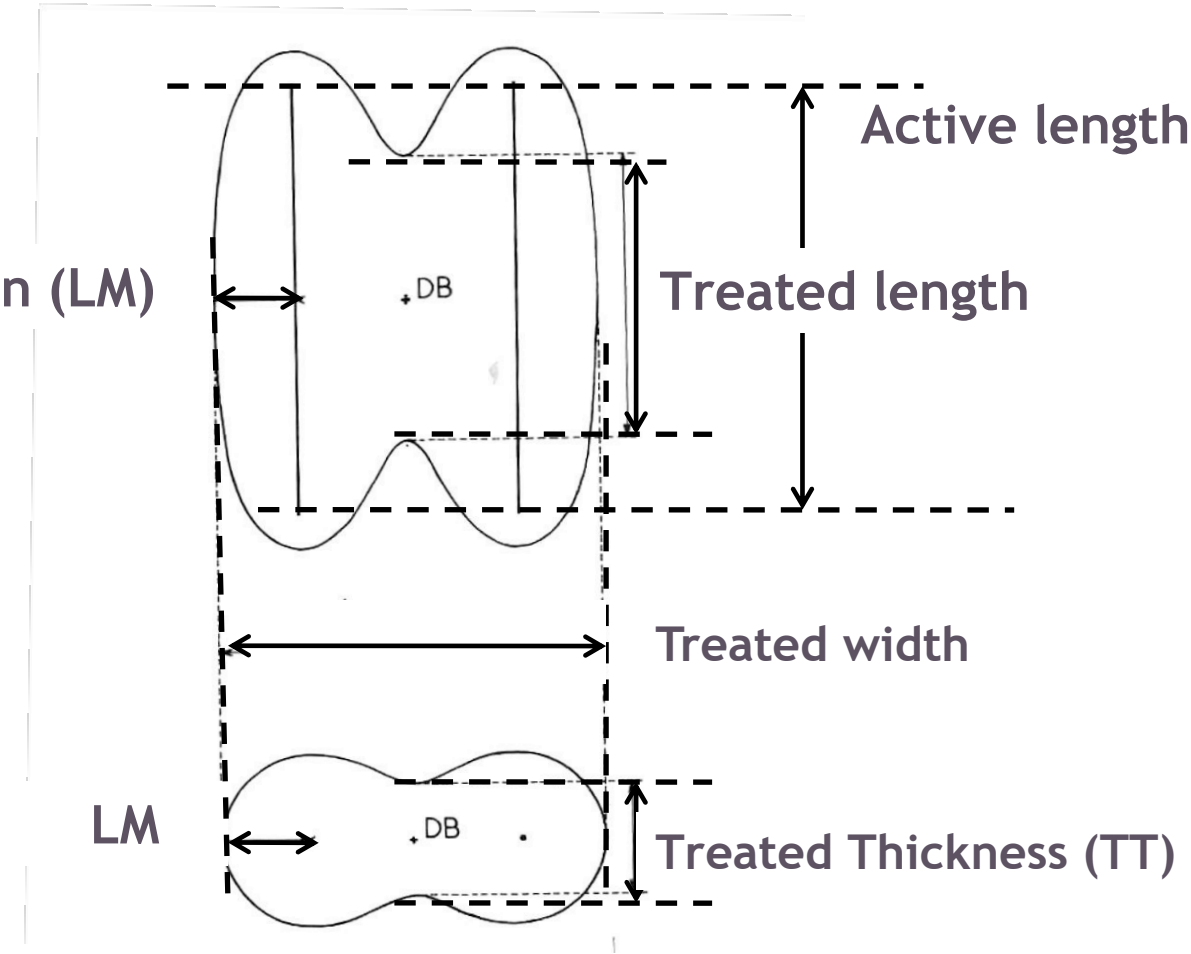
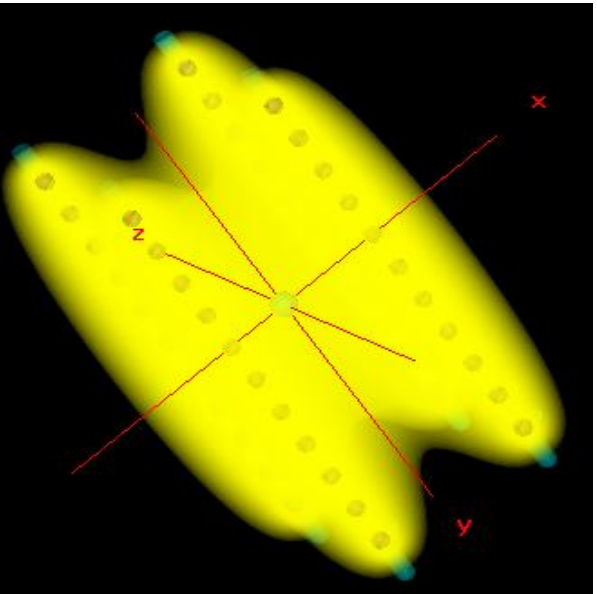
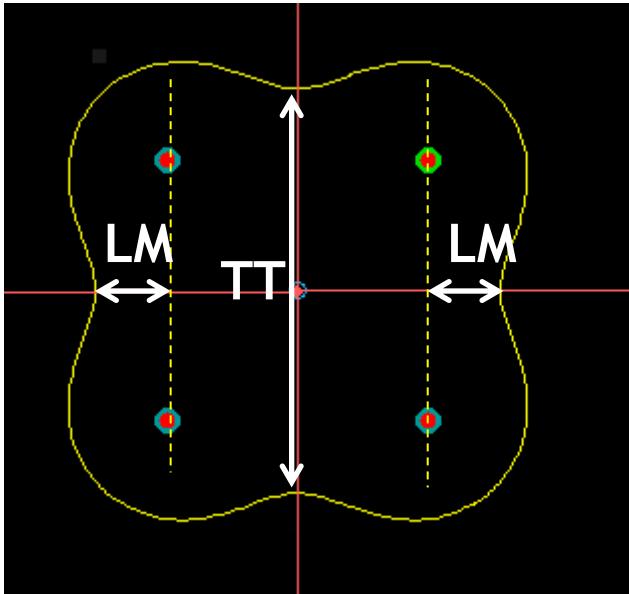

Active length
Lateral margin (LM)
DB
Treated length
Treated width
LM
DB
Treated Thickness (TT)


x
z
y


LM
TT
LM

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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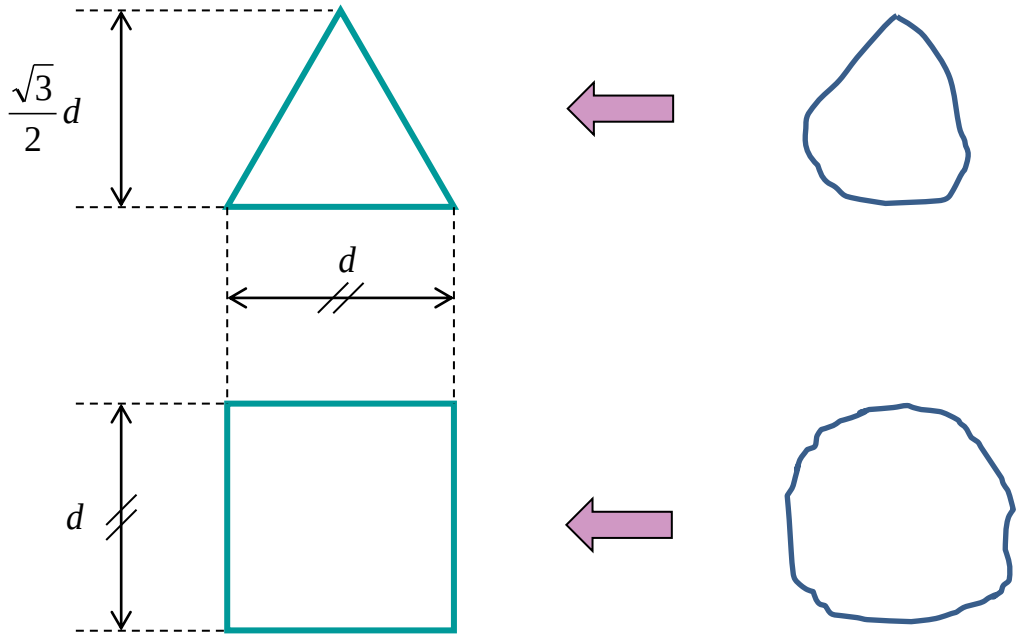
Paris system: Predictive dosimetry

- 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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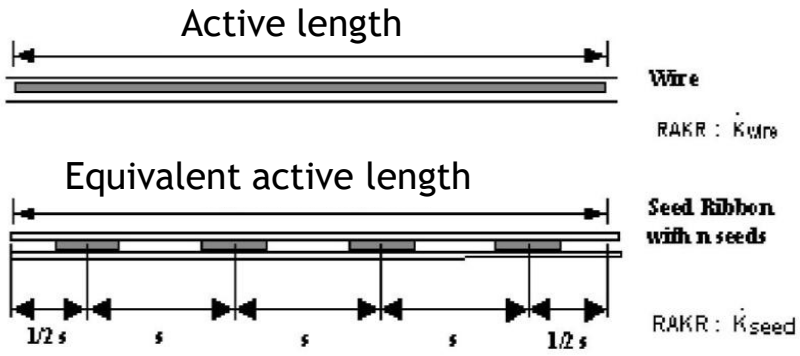
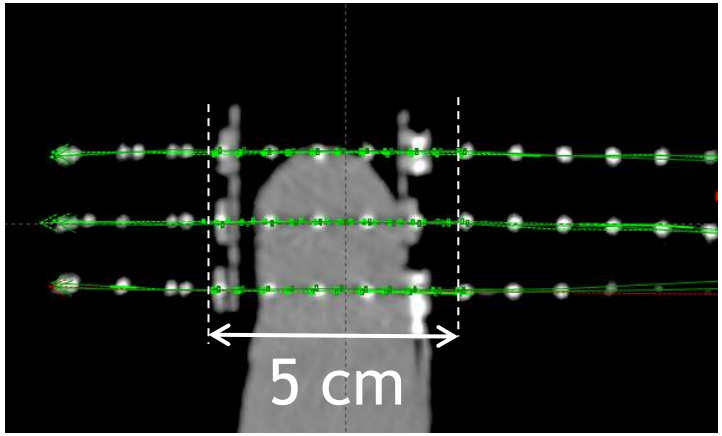
Validity limits for the Paris system

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?

Equivalent active length



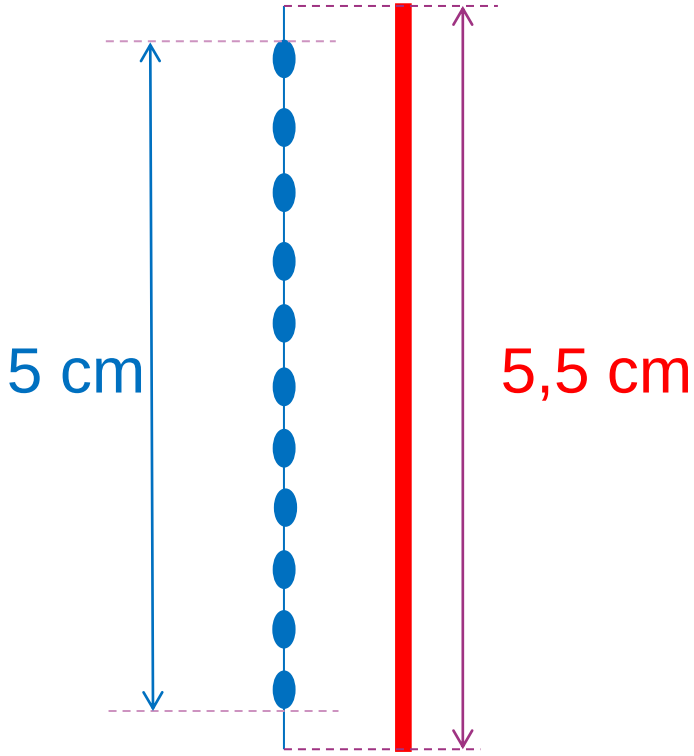


$$AL = EAL = n \times s$$

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 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

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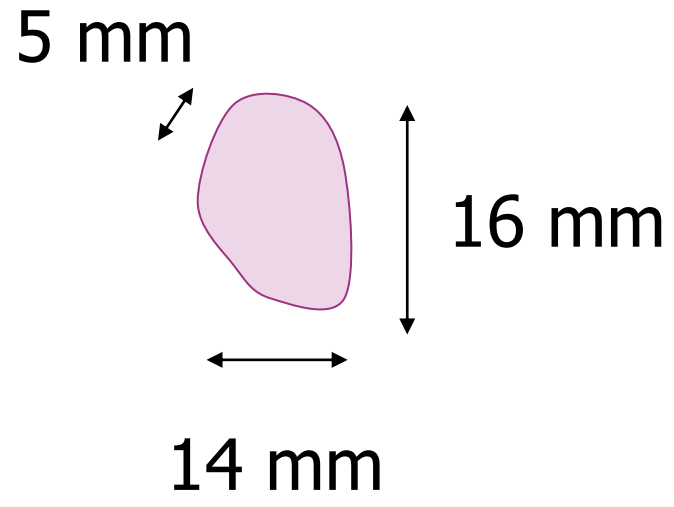
Paris system

Practical example

Basal cell carcinoma

CTV : 16 mm x 14 mm x 5 mm

L x W x T



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1st Step: number of planes

CTV thickness determination

CTV : 16 mm x 14 mm x 5 mm

L x W x T

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1st Step

CTV 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

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1st Step

One plane is enough

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

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2nd Step: spacing

Source spacing selection as a function of CTV 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

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2nd Step: spacing

Source spacing selection as a function of CTV 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)

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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

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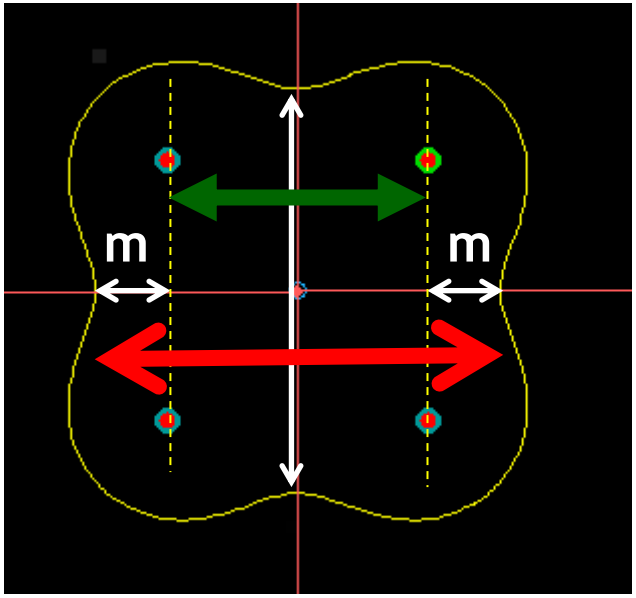
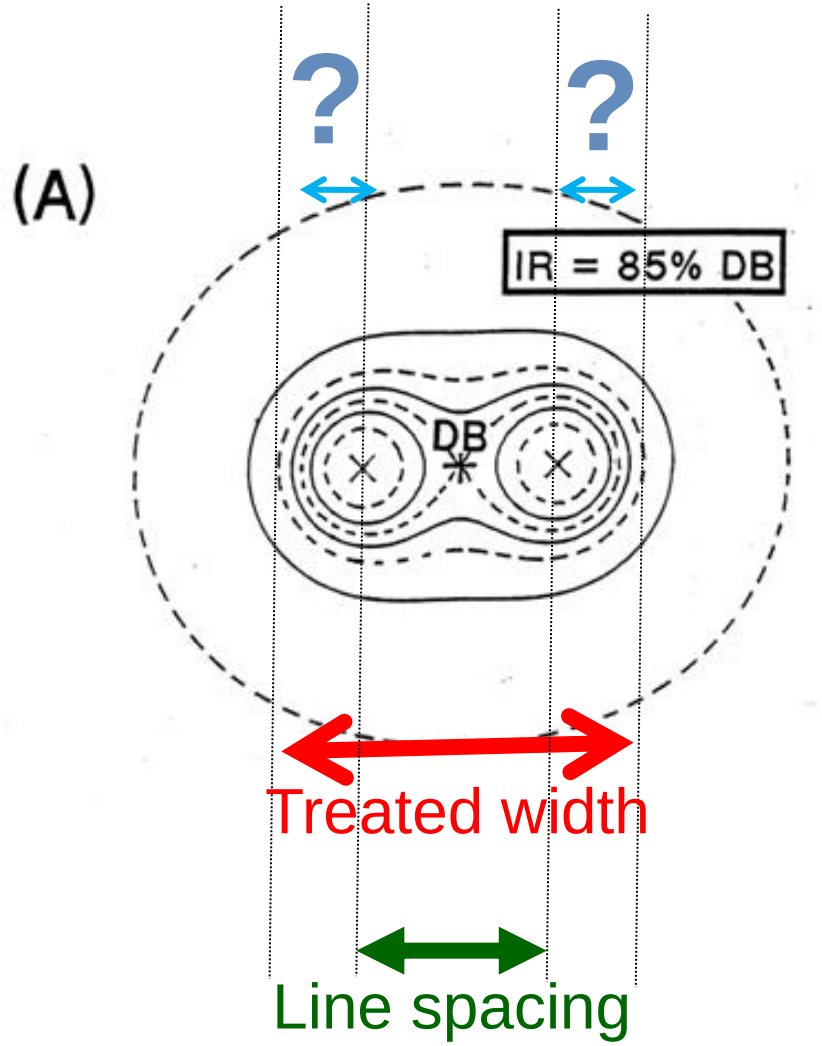
Lateral Margins





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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/spacing = 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

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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

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Paris system

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

2 lines :
10 mm apart
20 mm long

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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

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

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1st Step

CTV 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

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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

CTV 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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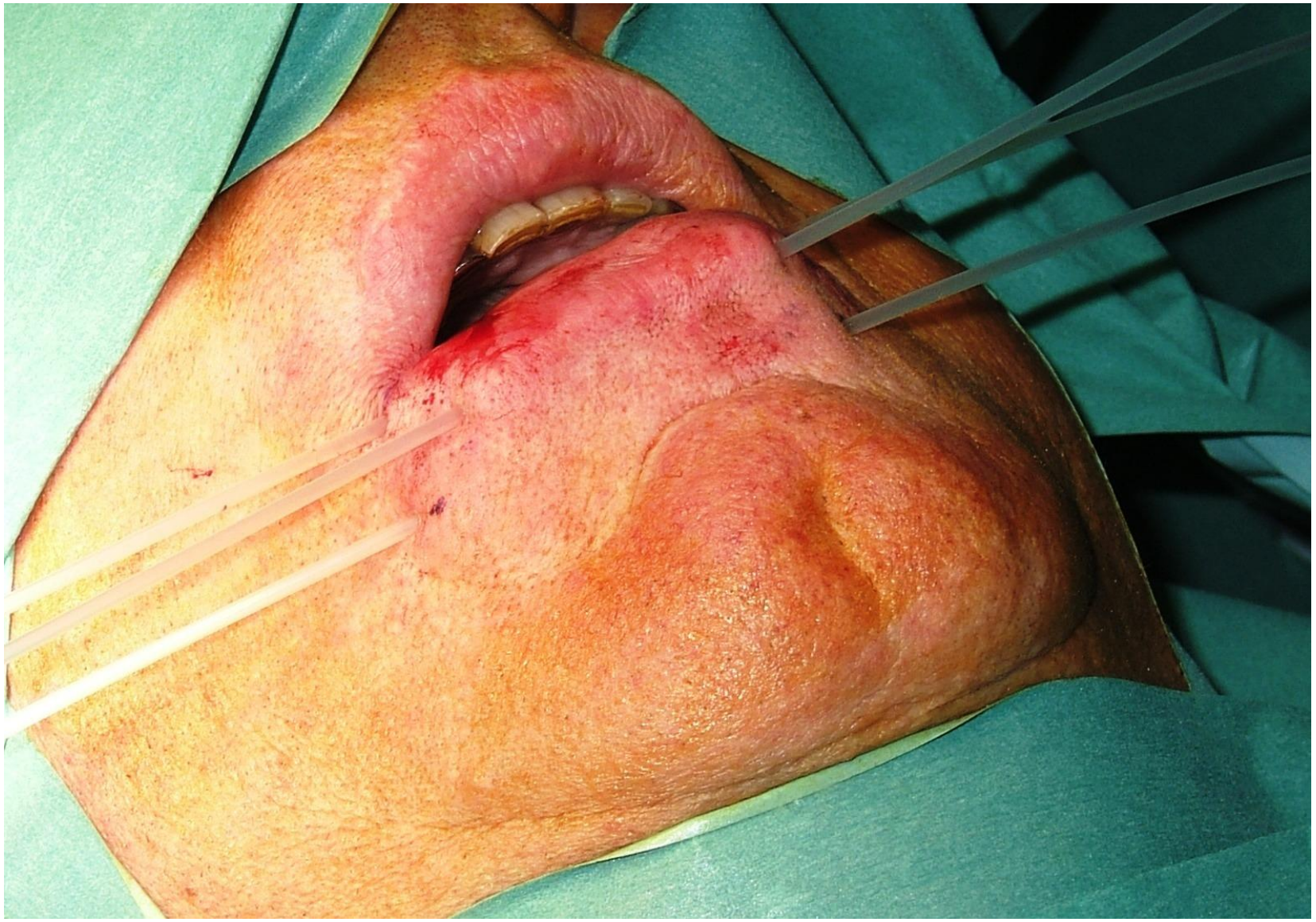
Geometry = shape



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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 CTV 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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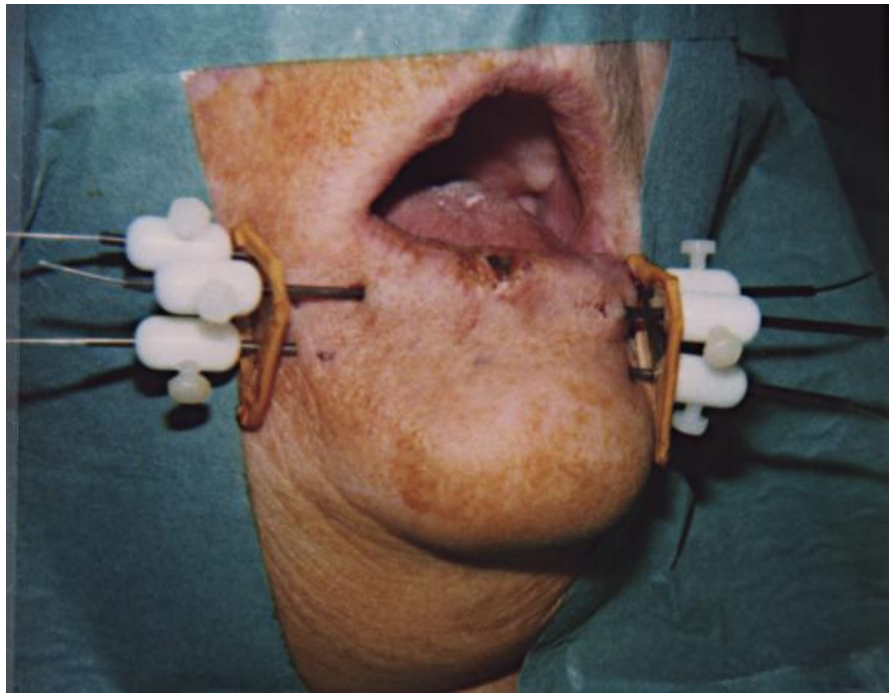

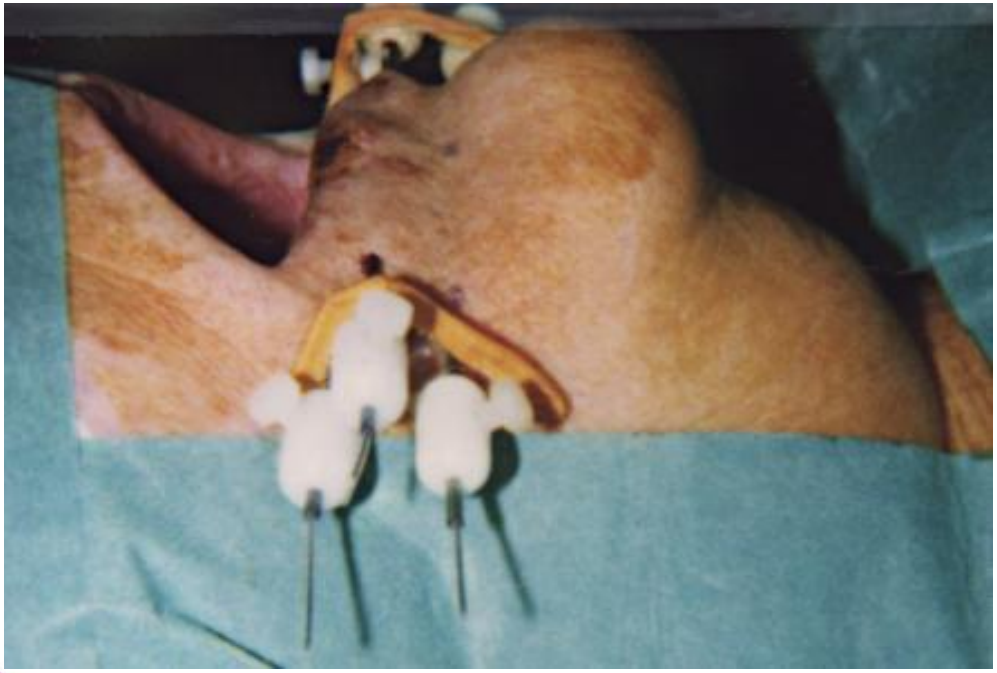

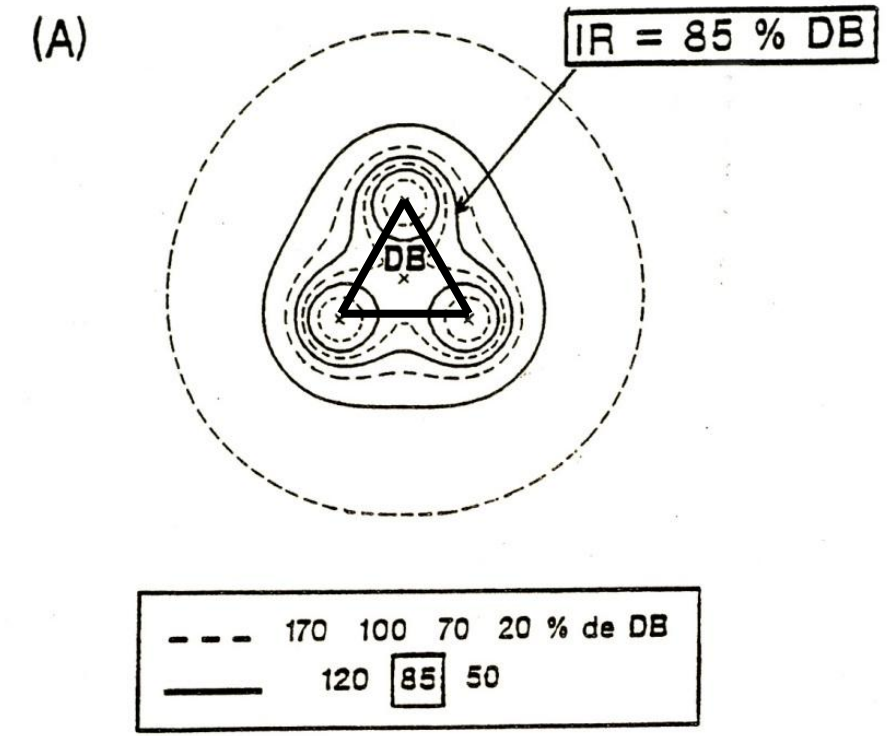

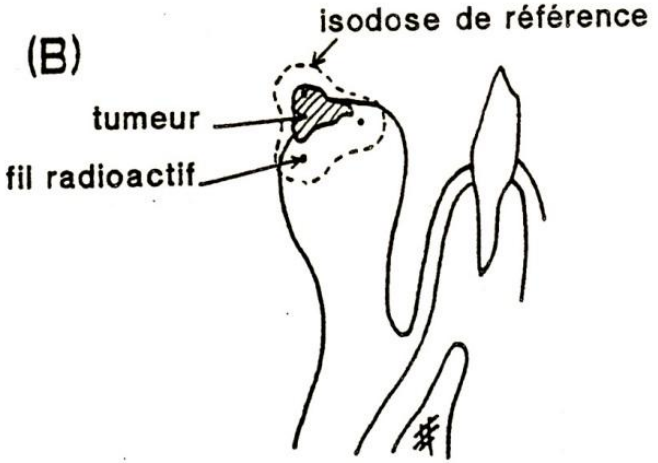

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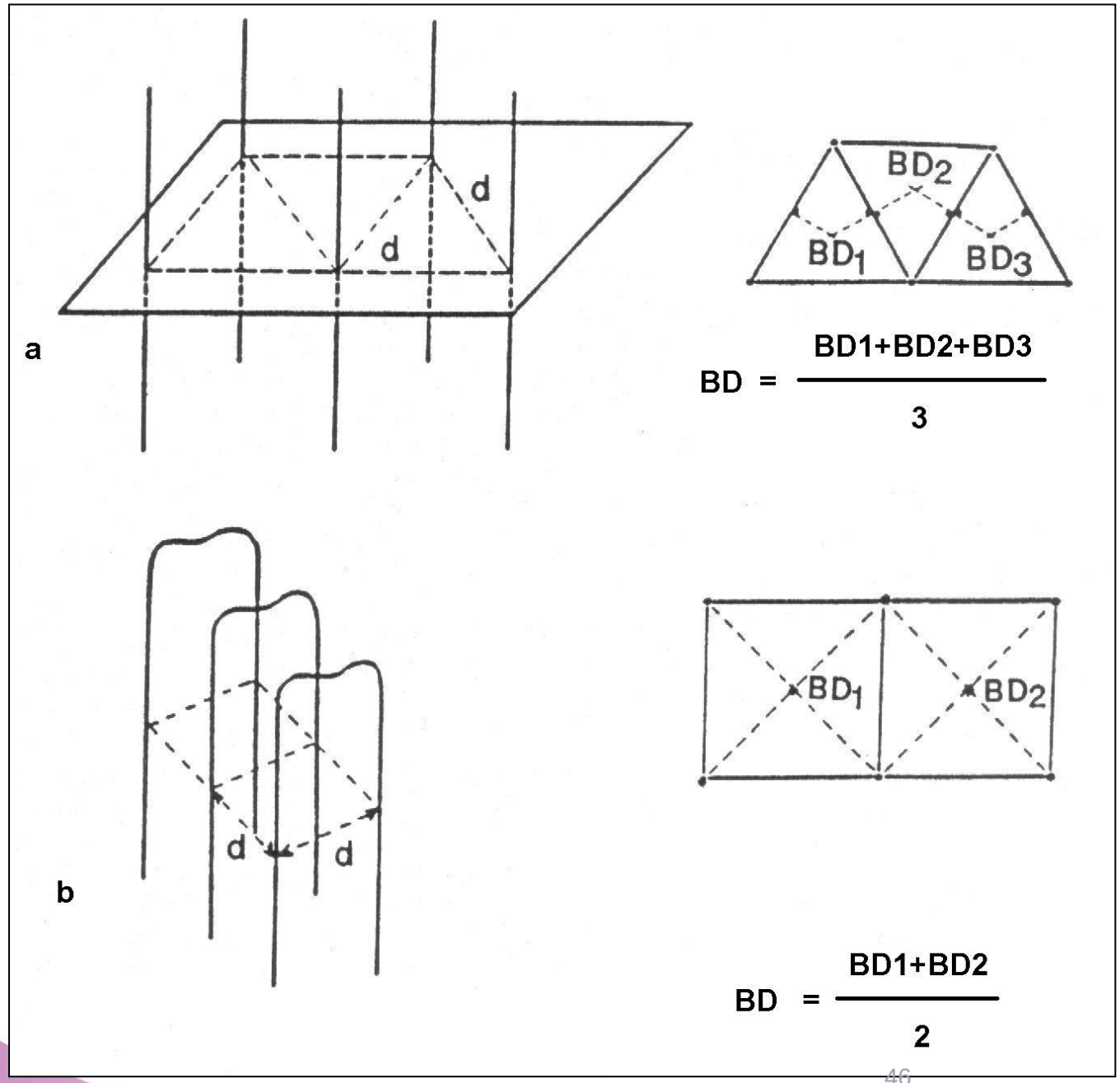
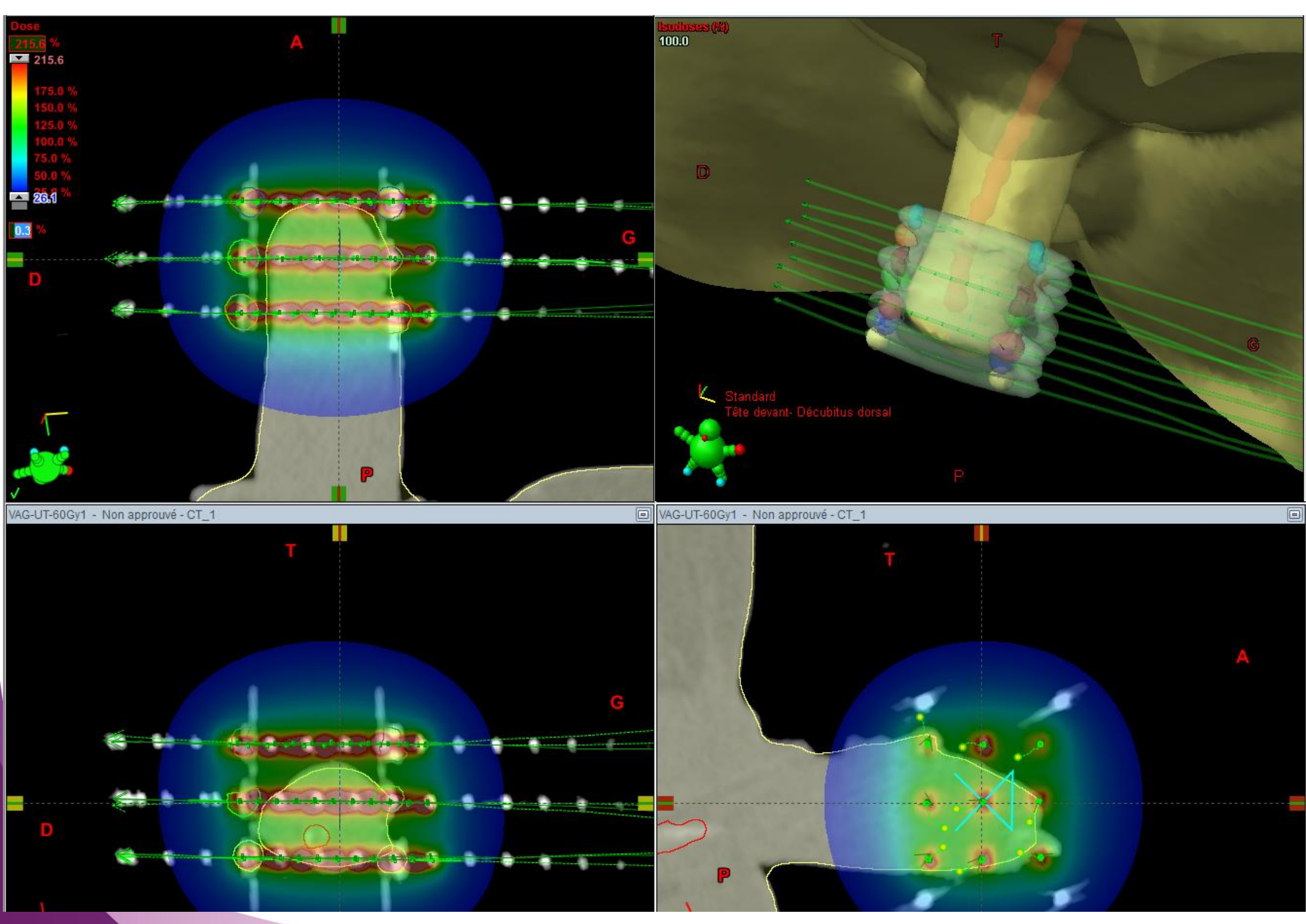
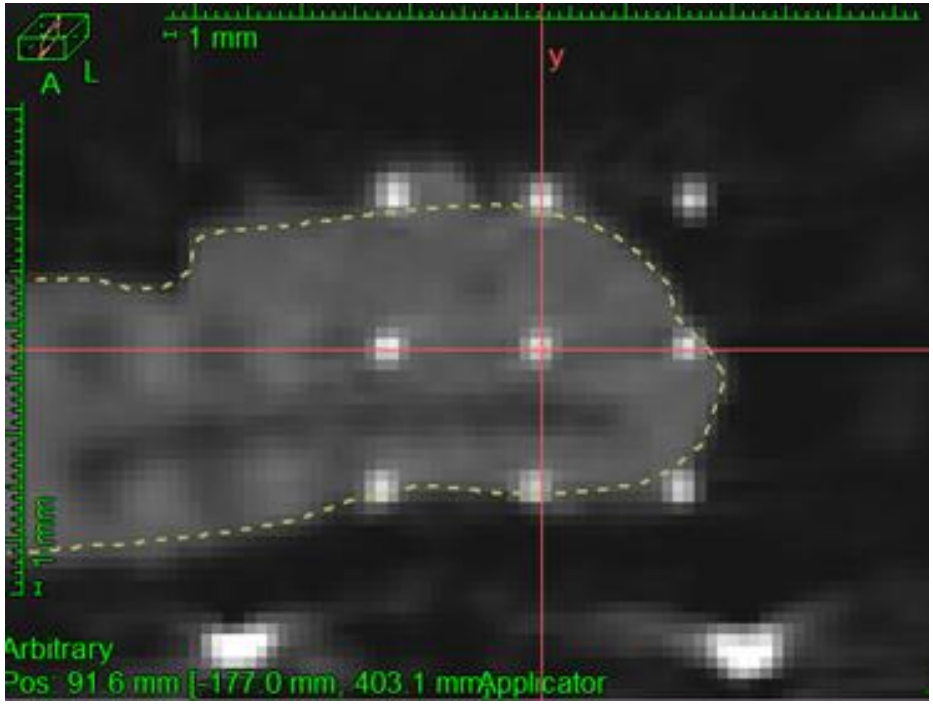
Multiple squares / triangles

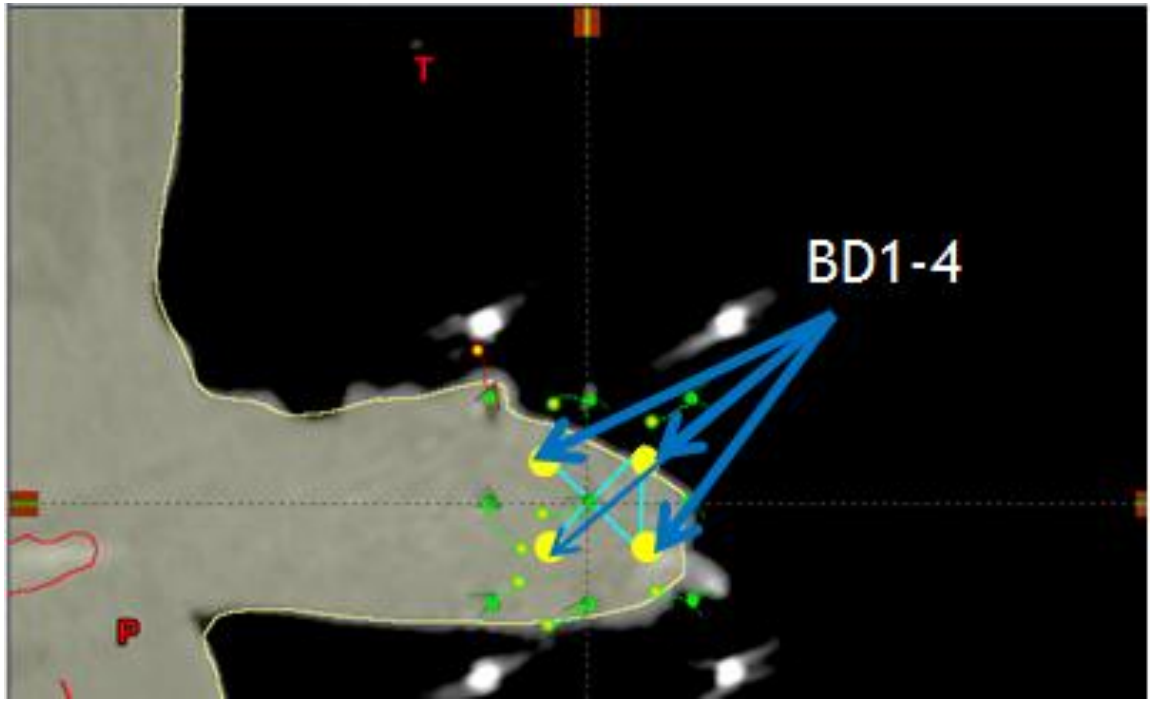


a : triangles
b : squares

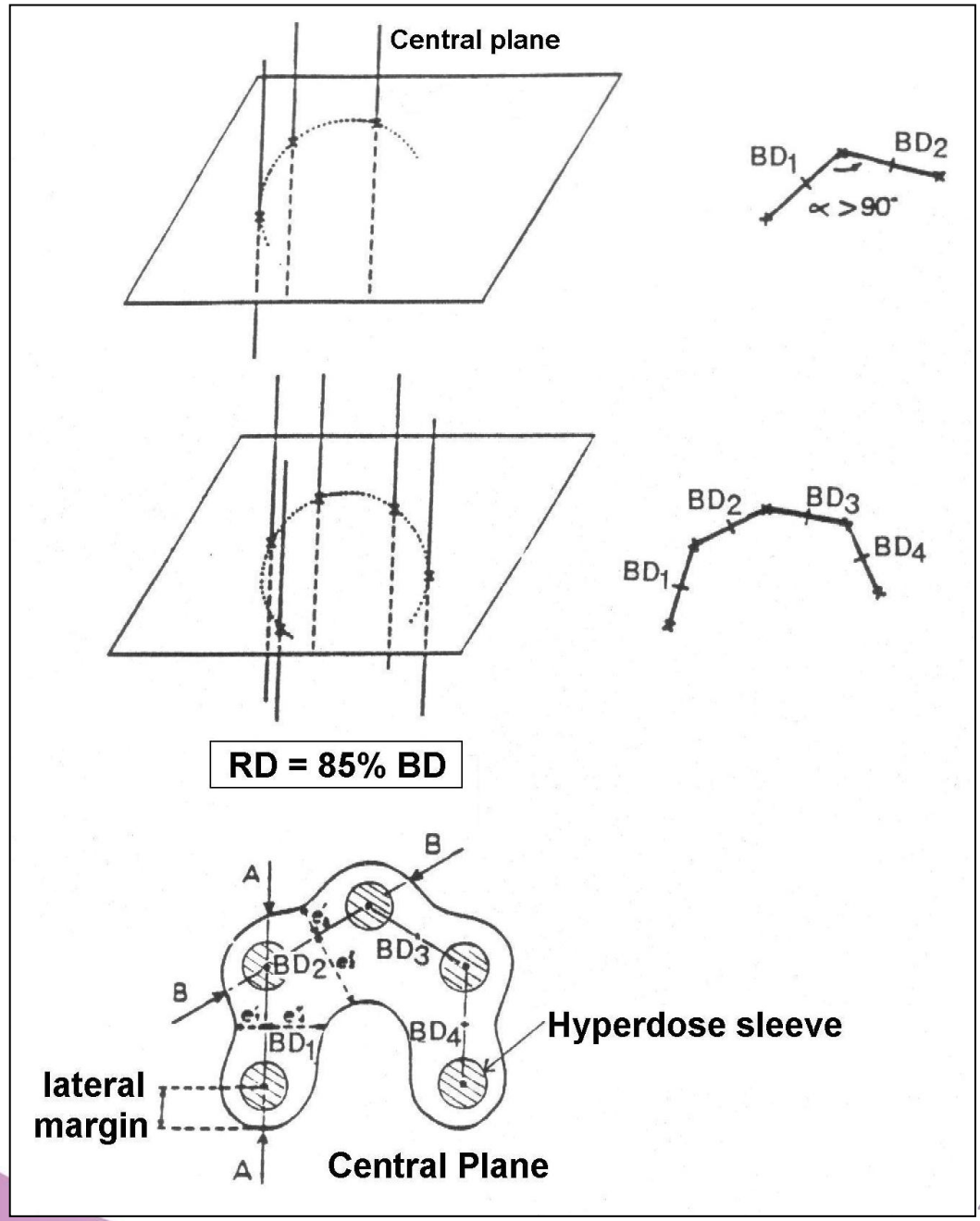

Dose
215.6 %
215.6
175.0 %
150.0 %
125.0 %
100.0 %
75.0 %
50.0 %
26.1
0.3 %
A
D
G
P
Isodoses (%)
100.0
T
D
G
P
Standard
Tête devant- Décubitus dorsal
VAG-UT-60Gy1 - Non approuvé - CT_1
T
G
D
VAG-UT-60Gy1 - Non approuvé - CT_1
T
A
P

BD points definitions





Basal/reference dose rate calculation



Example with curved plane line arrangement

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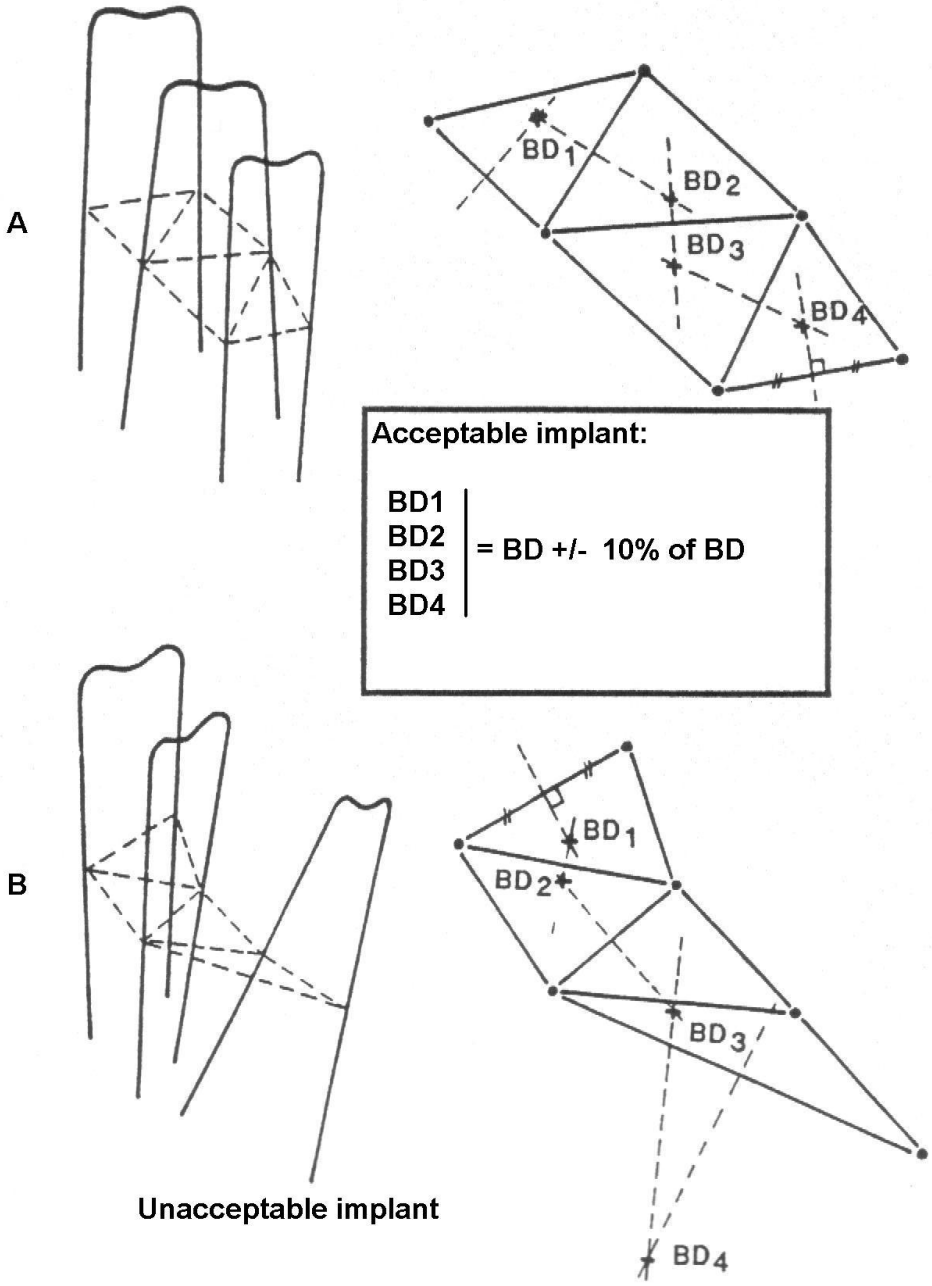
Basal dose rate calculation



implants with imperfect geometry

Acceptable if
0.9 BD<BDi<1.10 BD

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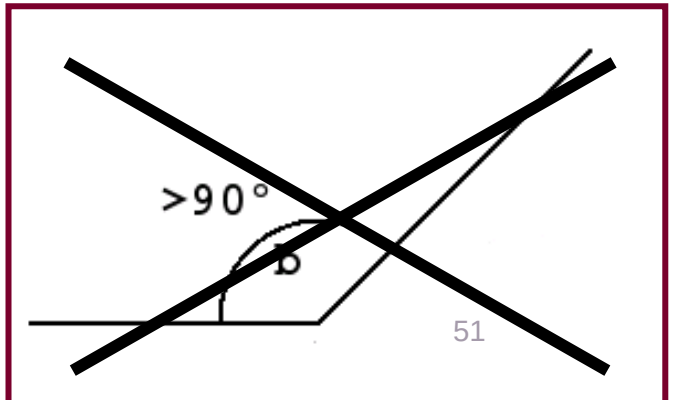
Paris system

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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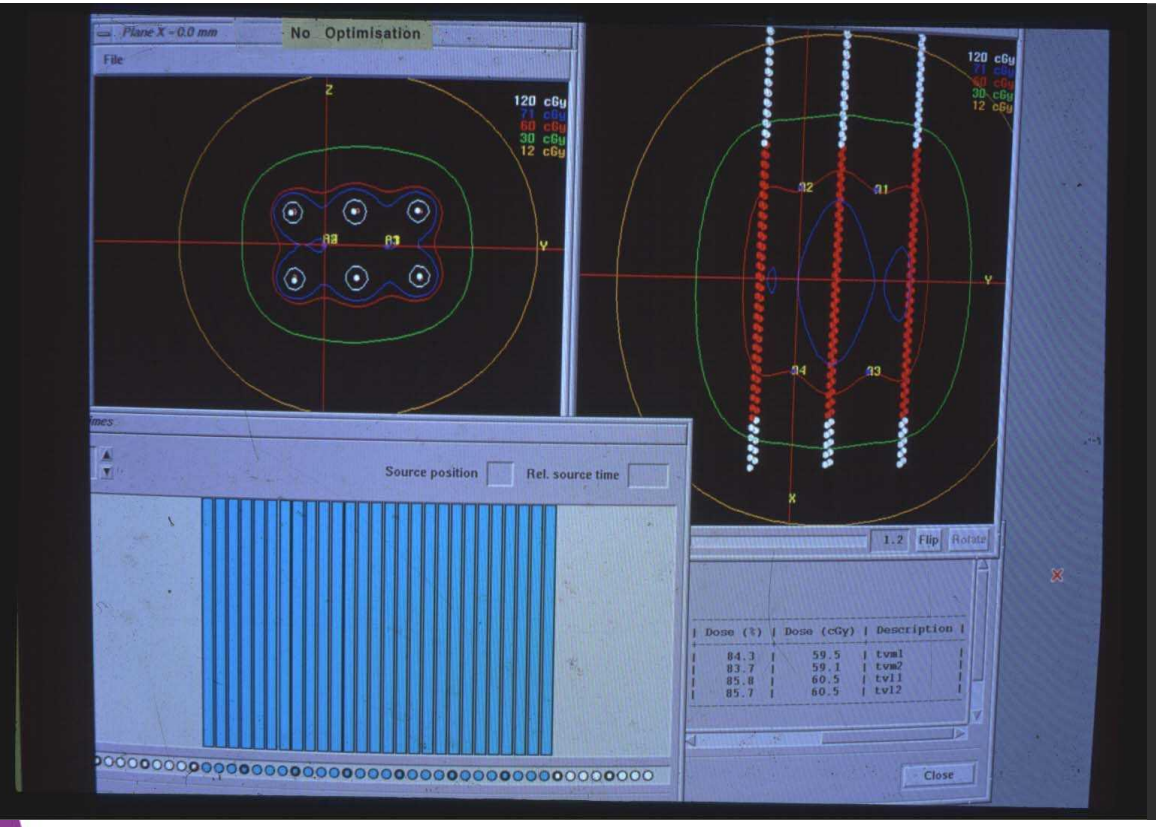
Is optimization required?

- 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)

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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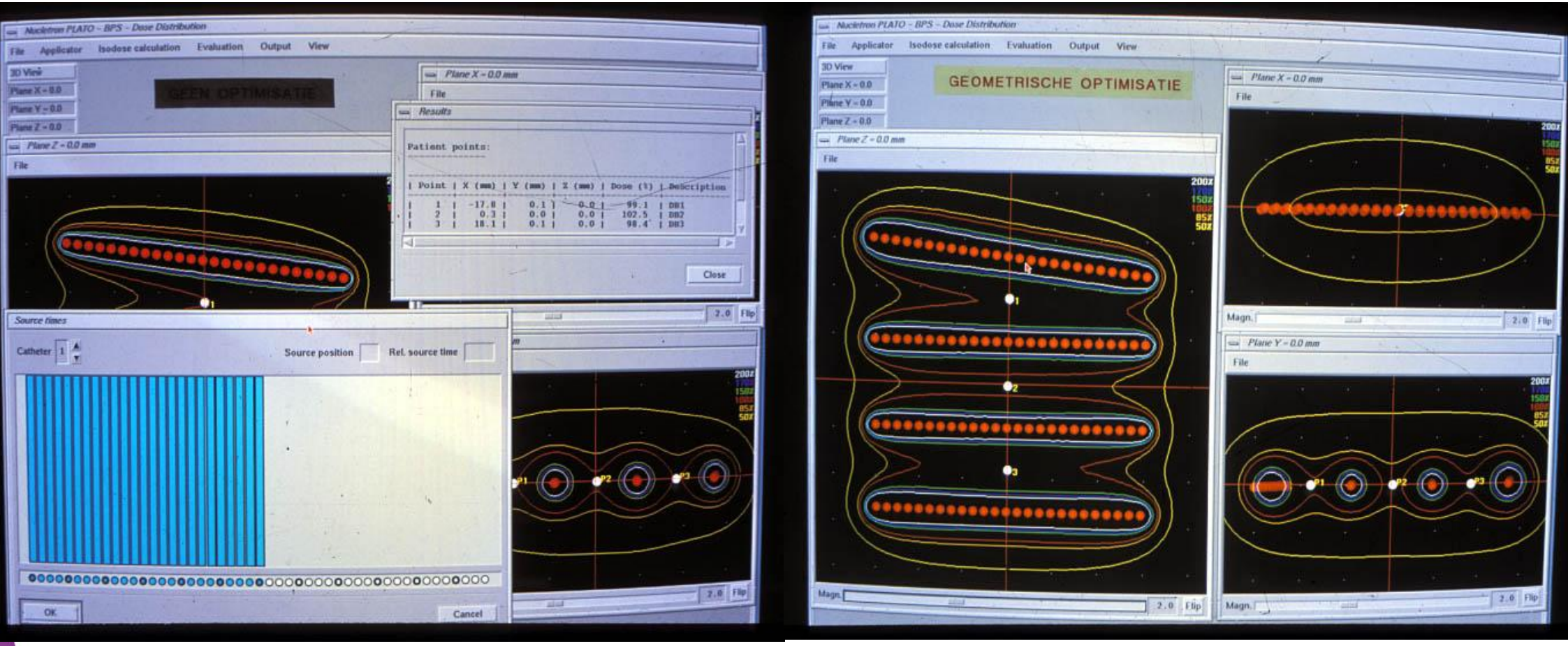
Correction of slight deviations



Slight divergence of source carriers

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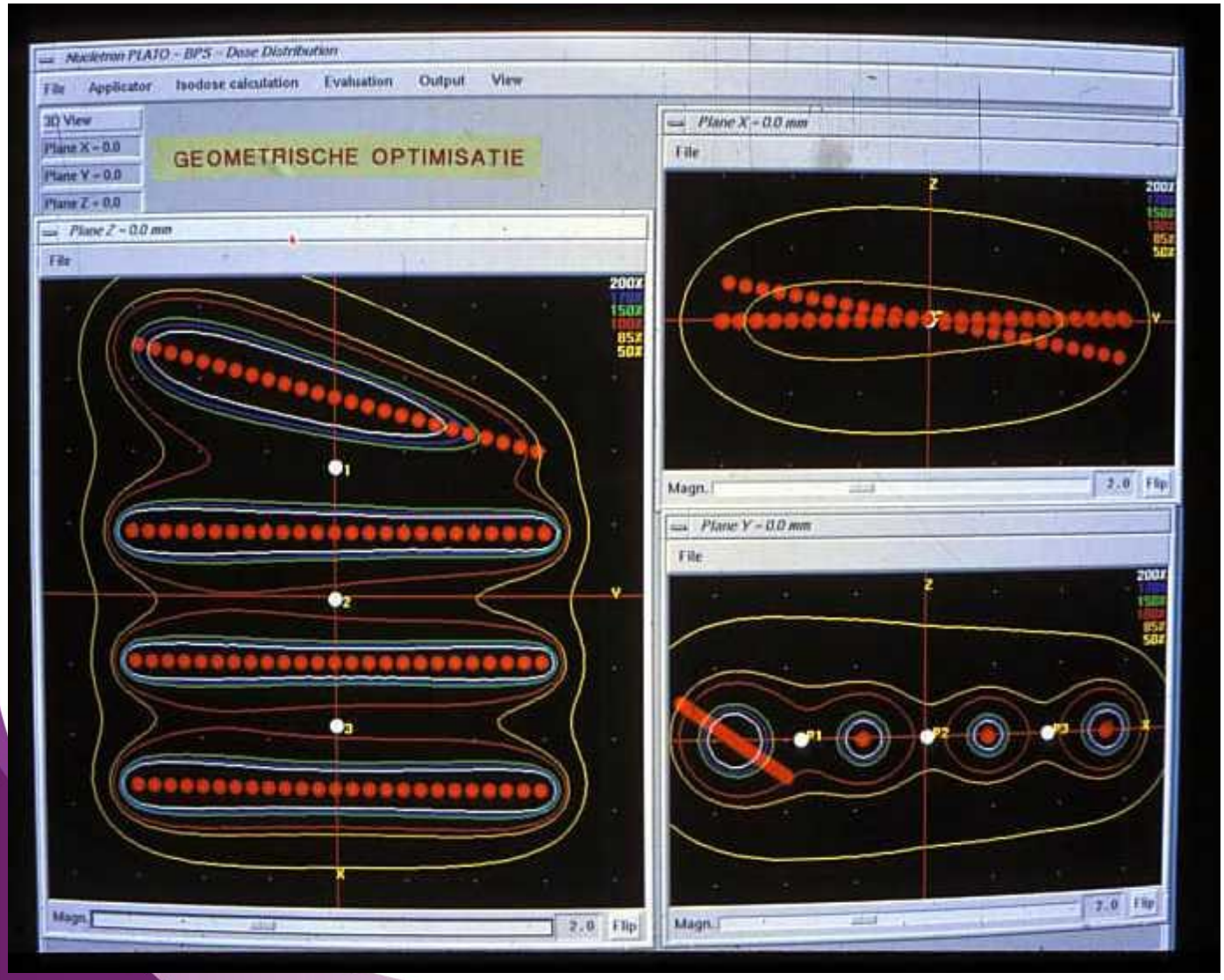
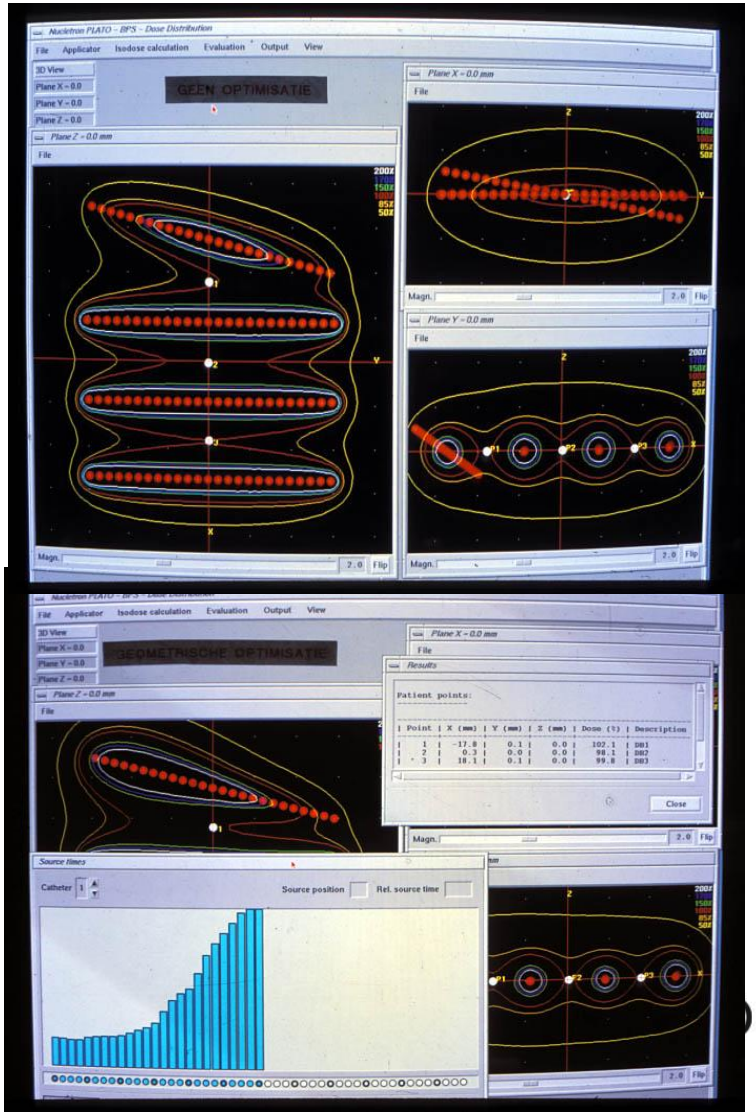
Dwell time optimization can never make a bad implant good





Always start with a good implant!

And then

IMPROVE IT

with optimization!!!

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Creating a common language

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

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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 dos = Mean Central Dose

Prescription dose = Minimum Target Dose

Always report the Prescription Dose

And its relation to the MCD in %

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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]

[a]*Department of Radiotherapy and Radiobiology, Vienna University, Medical School, General Hospital of Vienna, Währinger Gürtel 18–22, A-1090 Vienna, Austria*
[b]*Department of Radiation Oncology, University of Leuven, Leuven, Belgium*
[c]*Department of Surgery, Vienna University, Medical School, General Hospital of Vienna, Vienna, Austria*
[d]*Department of Gynaecology, Vienna University, Medical School, General Hospital of Vienna, Vienna, Austria*
[e]*Institute of Medical Statistics, Vienna University, Medical School, General Hospital of Vienna, Vienna, Austria*

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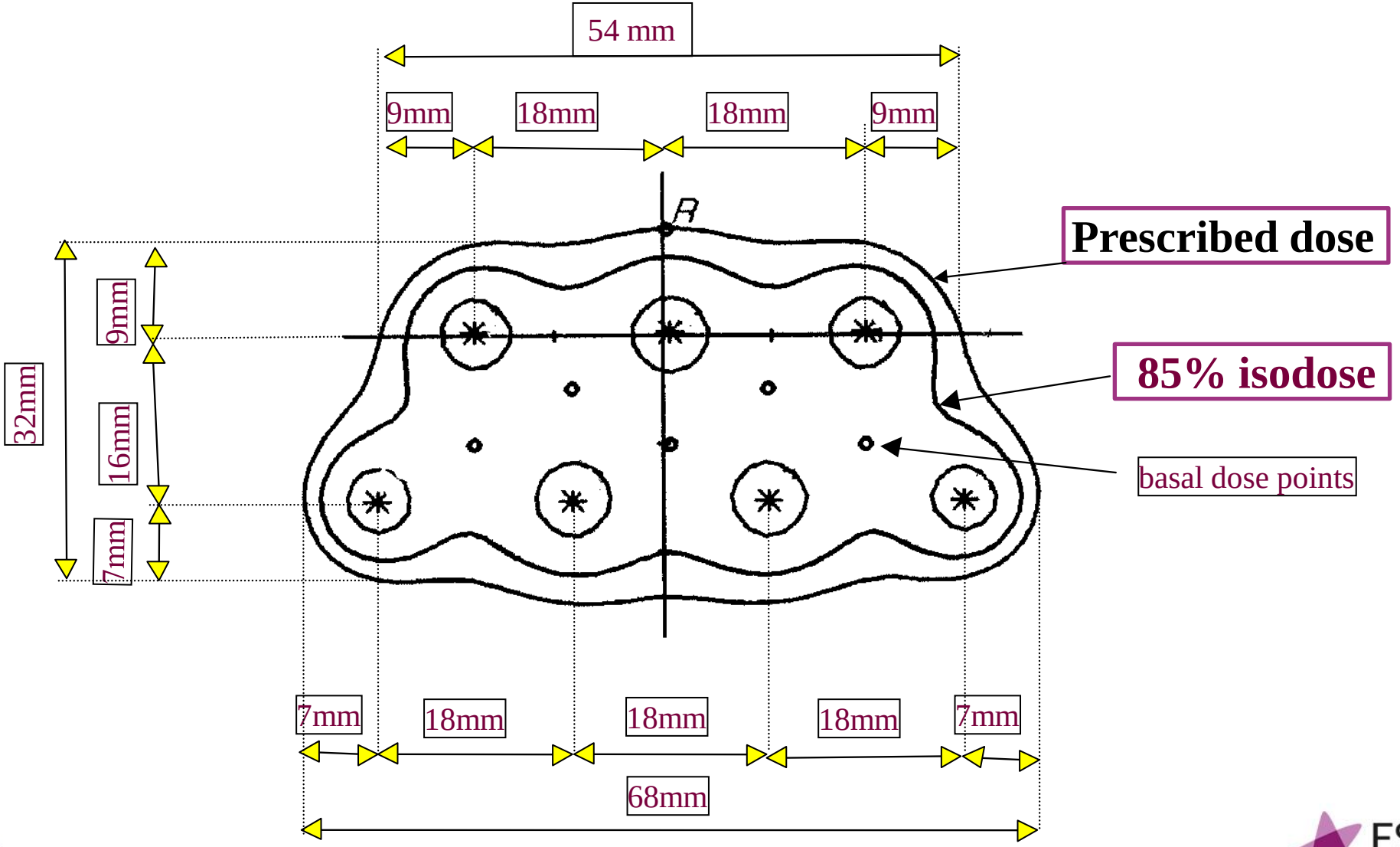
Interstitial breast brachytherapy central plane dose recording*- implant with 7 needles -



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

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

20 Gy was prescribed on the **71,3 %** and not on the 85% of the MCD

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Brachytherapy for Esophageal Cancer

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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**

Locally advanced Disease:

- **Palliative (chemo-)radiation +/- BT**
- **EBRT + BT**

Advanced/metastasized or relapse with luminal obstruction:

- **Brachytherapy alone**
  - **Aim: rapid and lasting relief of symptoms from dysphagia**

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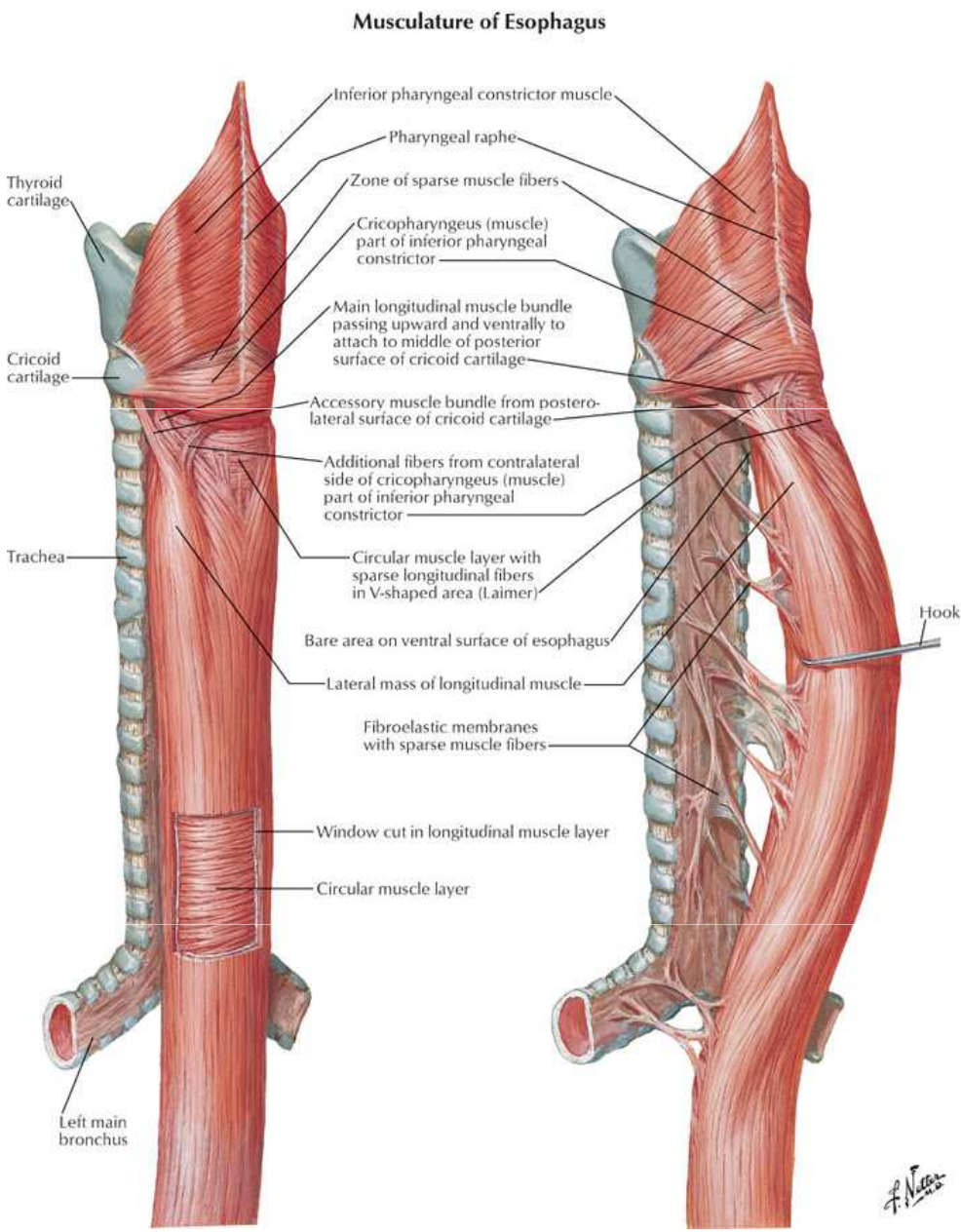
ESOPHAGEAL ANATOMY

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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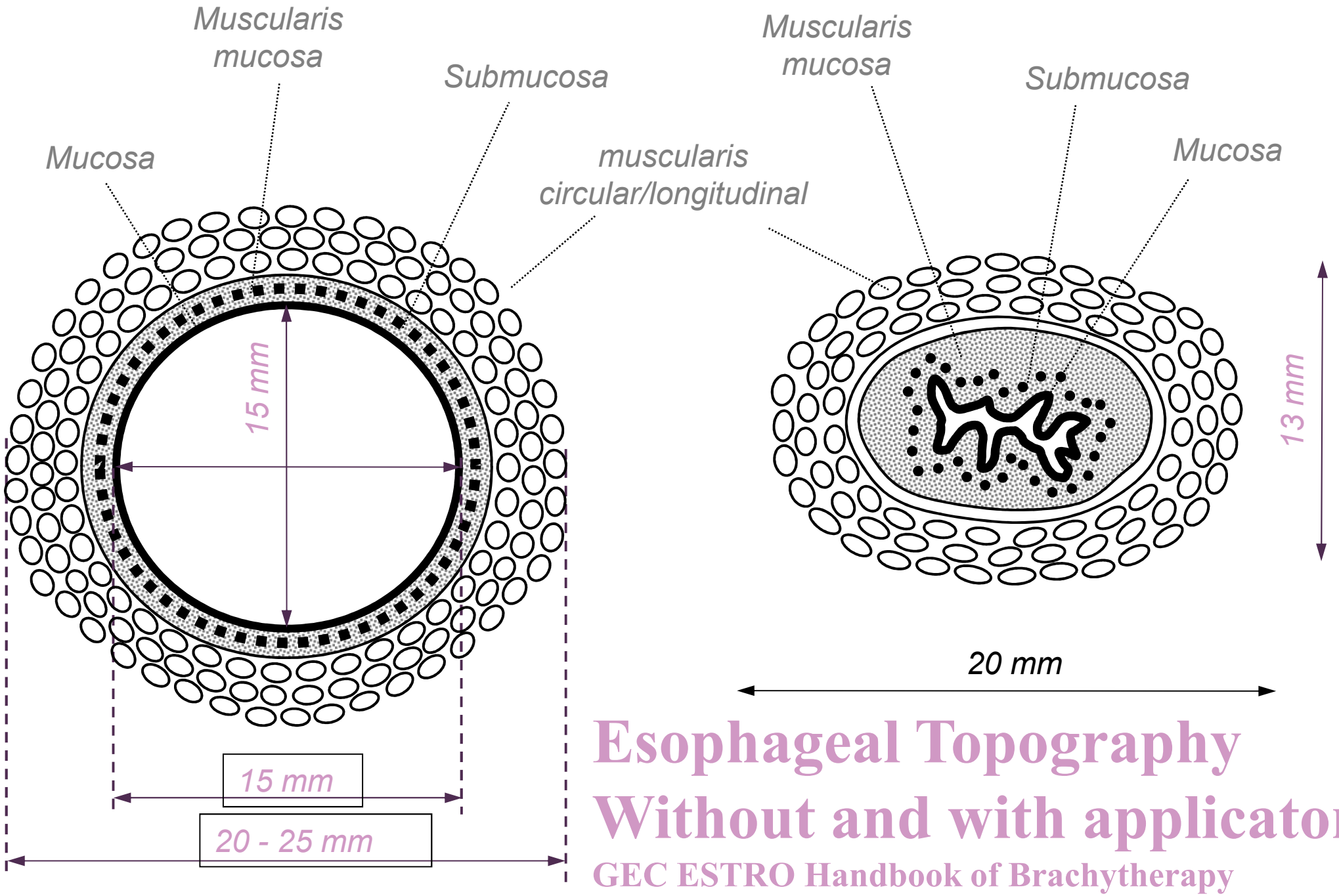

Esophageal Topography Without and with applicator

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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

FDG-PET

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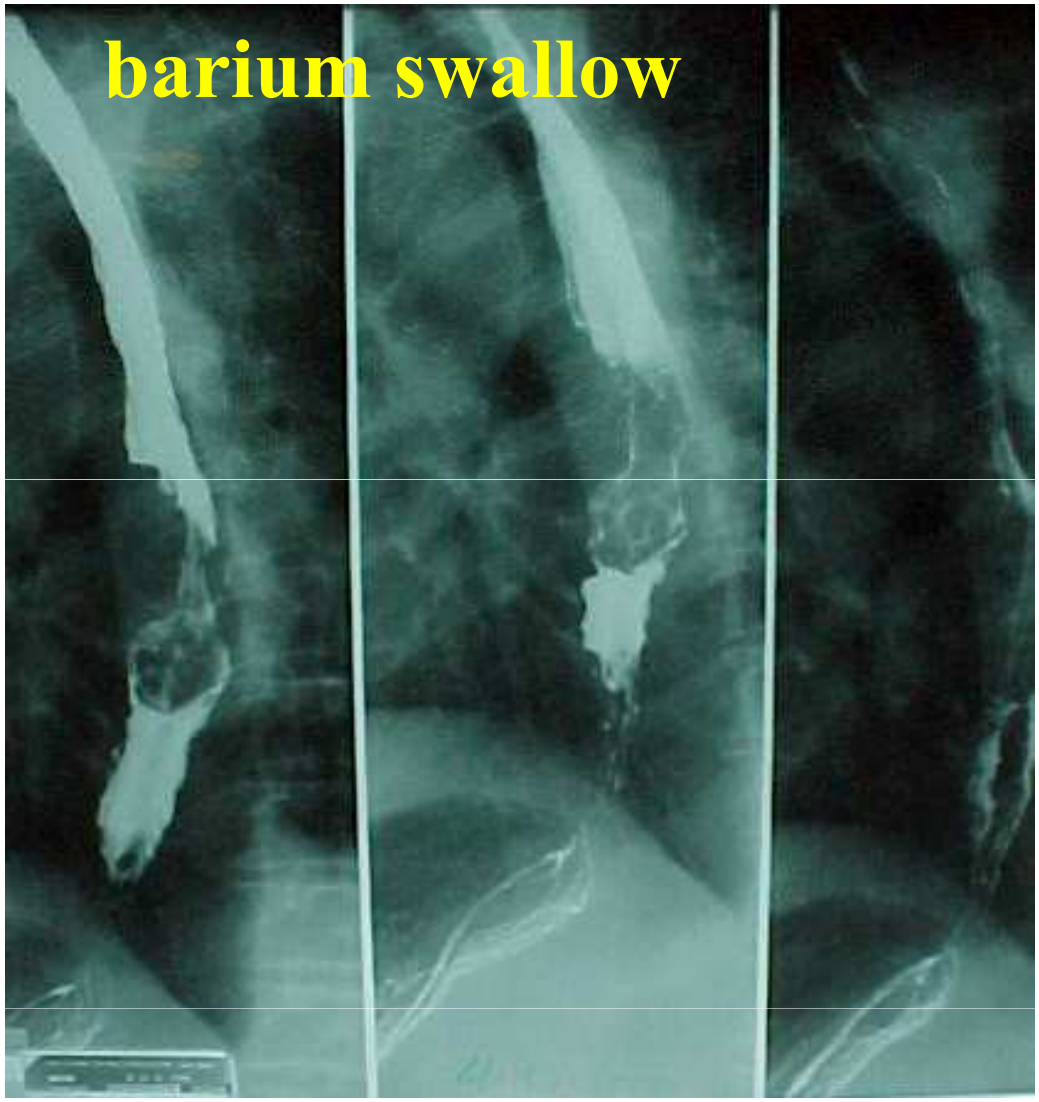
barium swallow

esophagoscopy

endosonography
AMC AMSTERDAM
GE DEPARTMENT
DIST. +1.03cm
ROB G80 C4
1:ENDO

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INDICATIONS: ESOPHAGEAL BRACHYTHERAPY

(LOCALLY) ADVANCED/METASTASIZED DISEASE

- Primary treatment/treatment for recurrence -

BRACHYTHERAPY ALONE
combined with: dilatation
laser resection

BOOST TREATMENT AFTER TUMOUR REMISSION by EBRT
(most often palliative setting)

SUPERFICIAL TUMORS/EARLY DISEASE

(BRACHYTHERAPY ALONE)
BOOST TREATMENT AFTER EBT
(most often curative intent)

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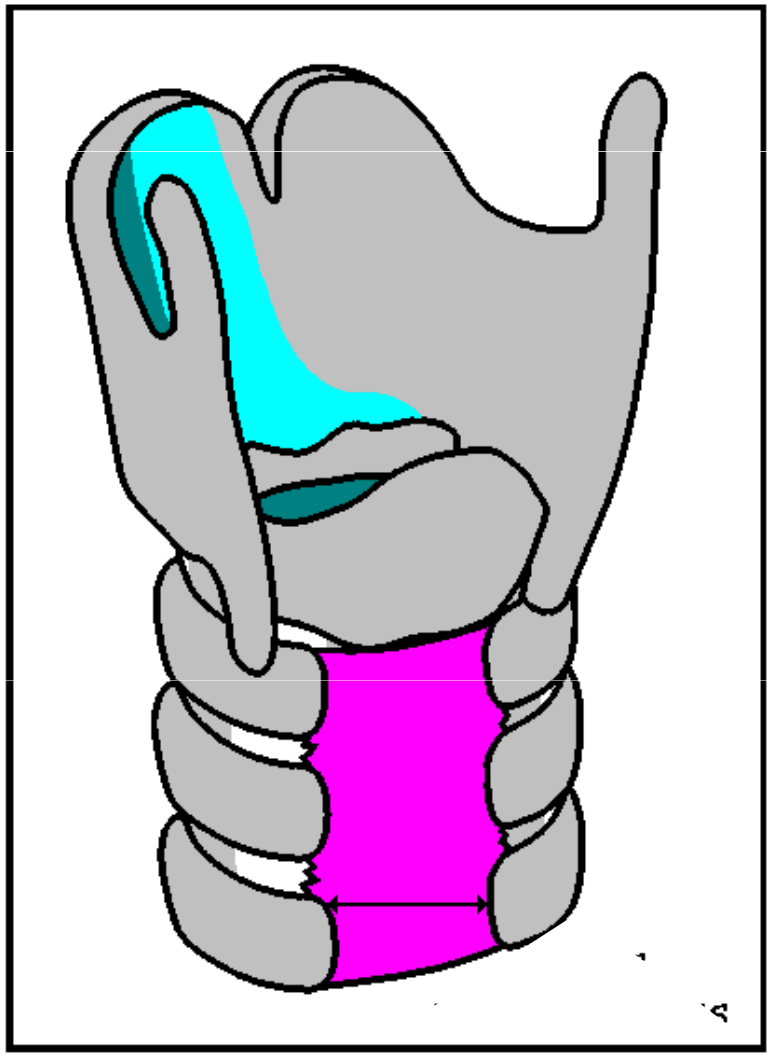
CONTRA-INDICATION ESOPHAGEAL BRACHYTHERAPY

FISTULA

(Infiltration of the Trachea (pars membranacea))



Indication directly after stent placement is questionable (Dutch STEBRA study)

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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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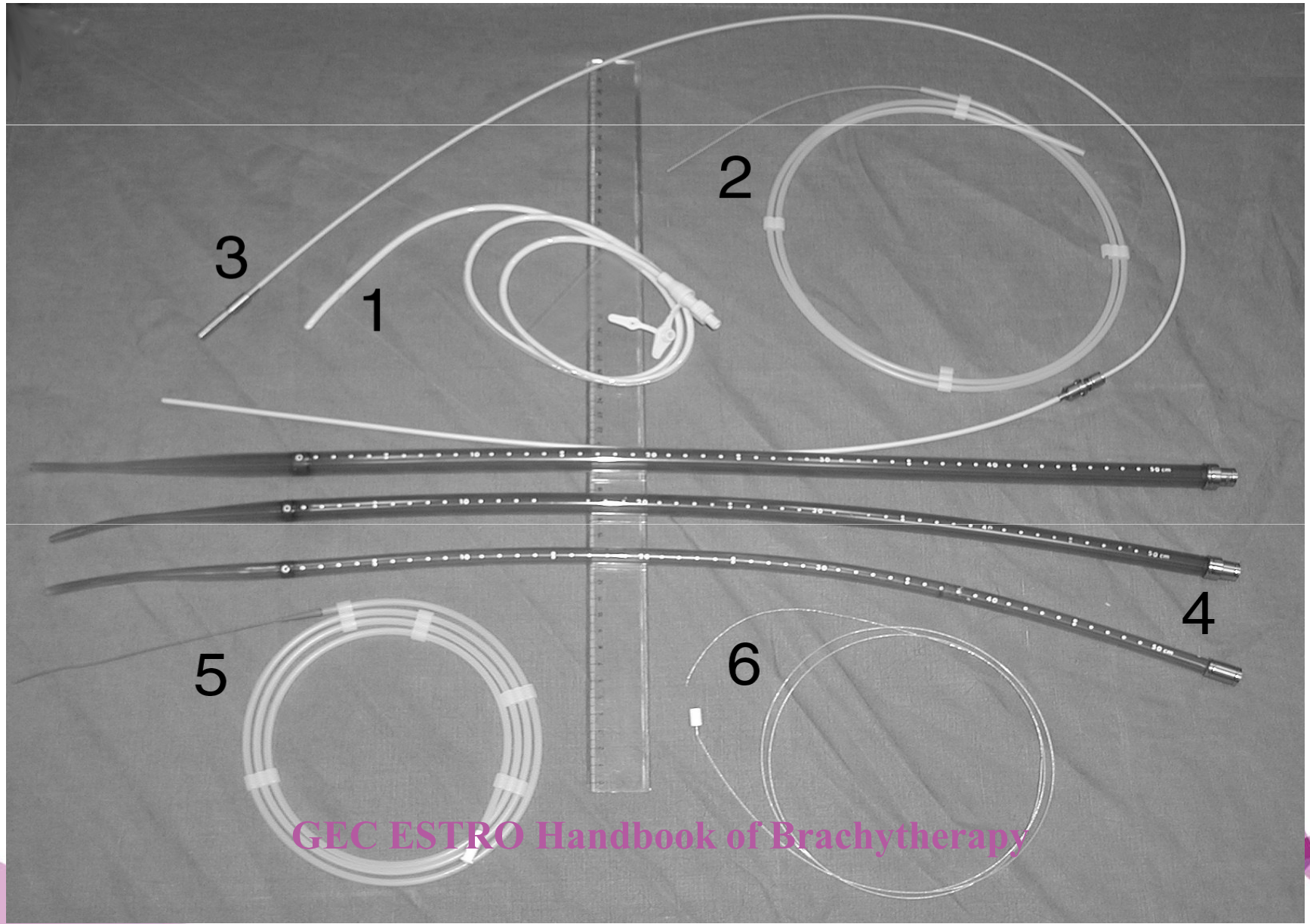
VARIATIONS IN APPLICATOR DESIGN
- according to different pathology -



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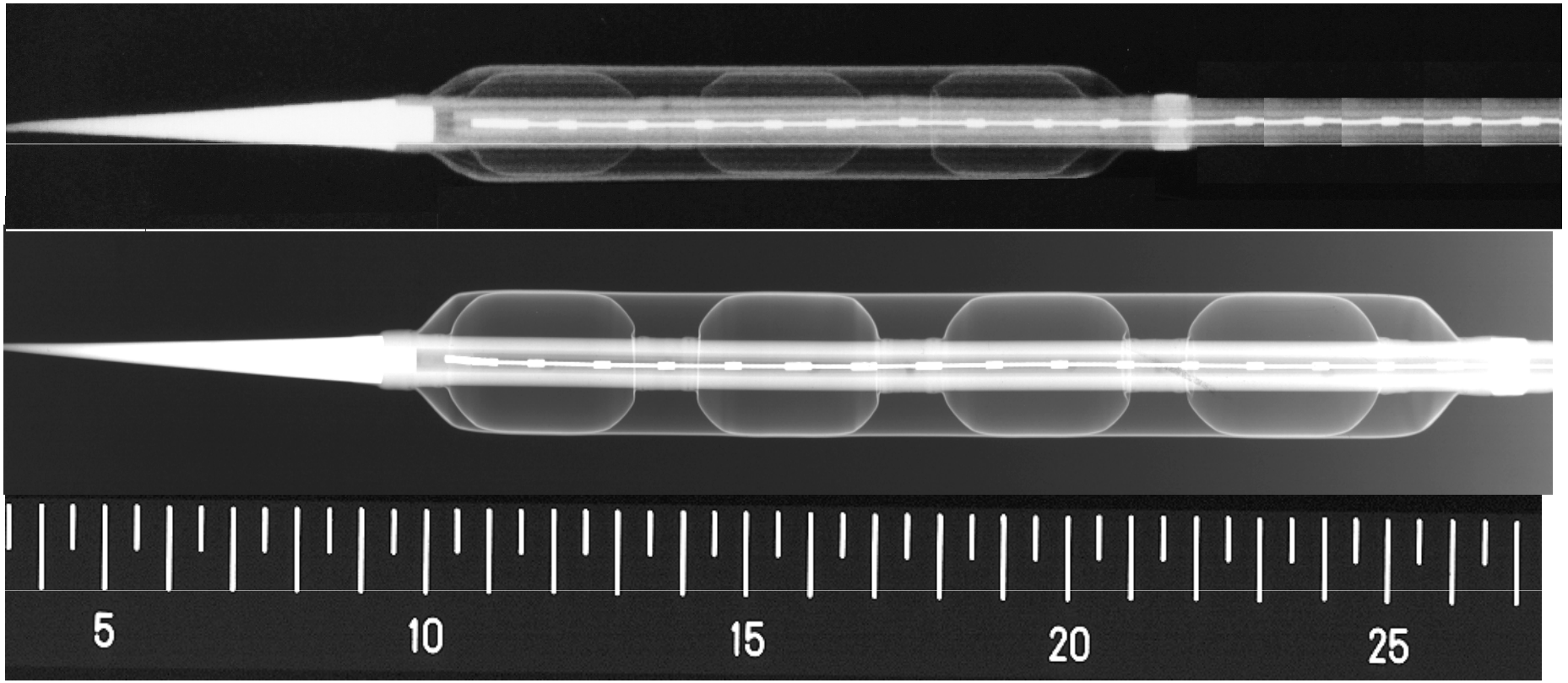
Japanese Balloon Applicators



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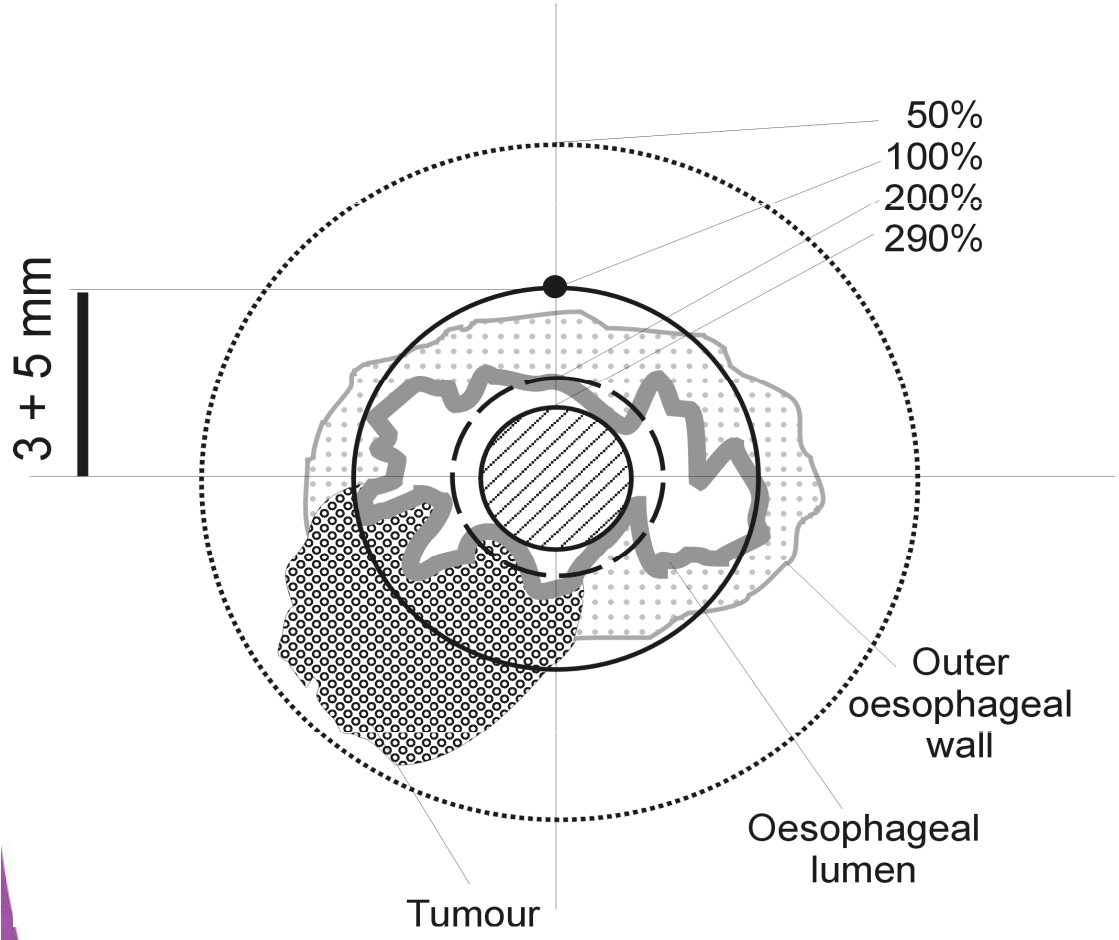
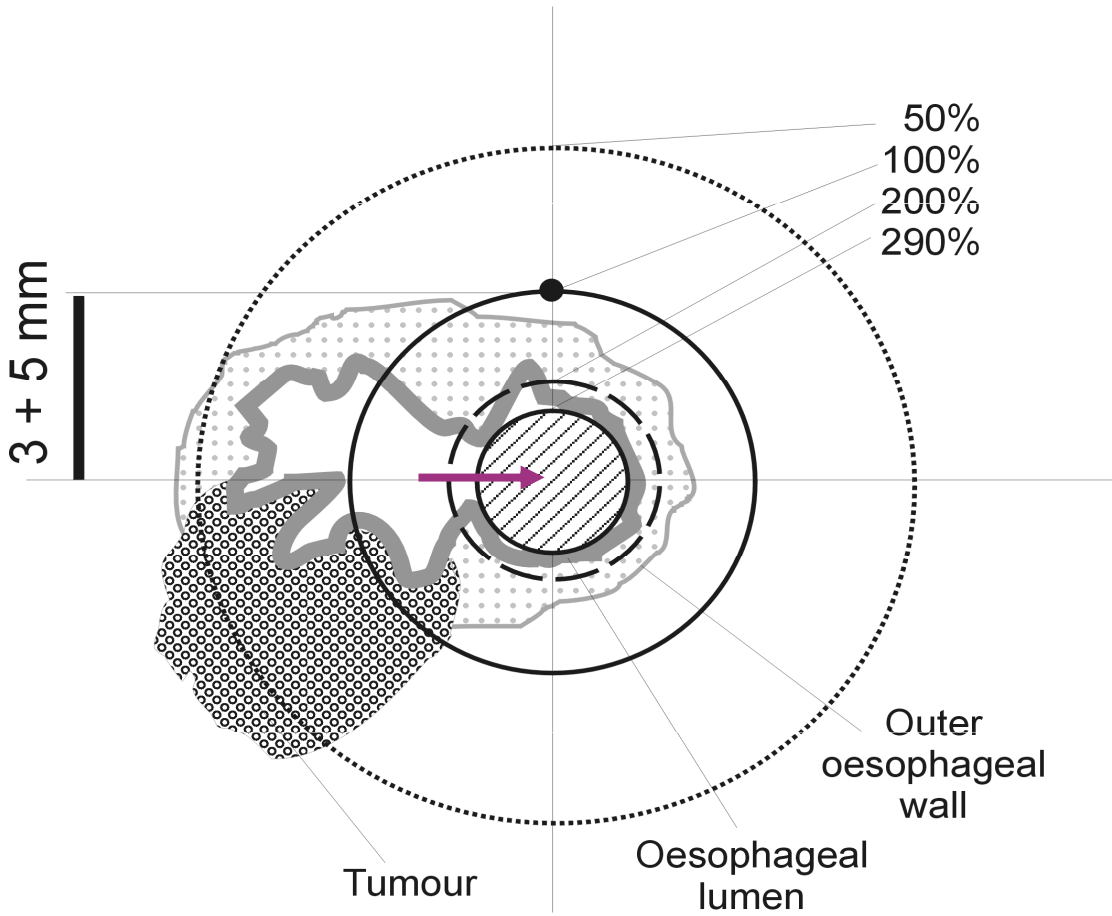
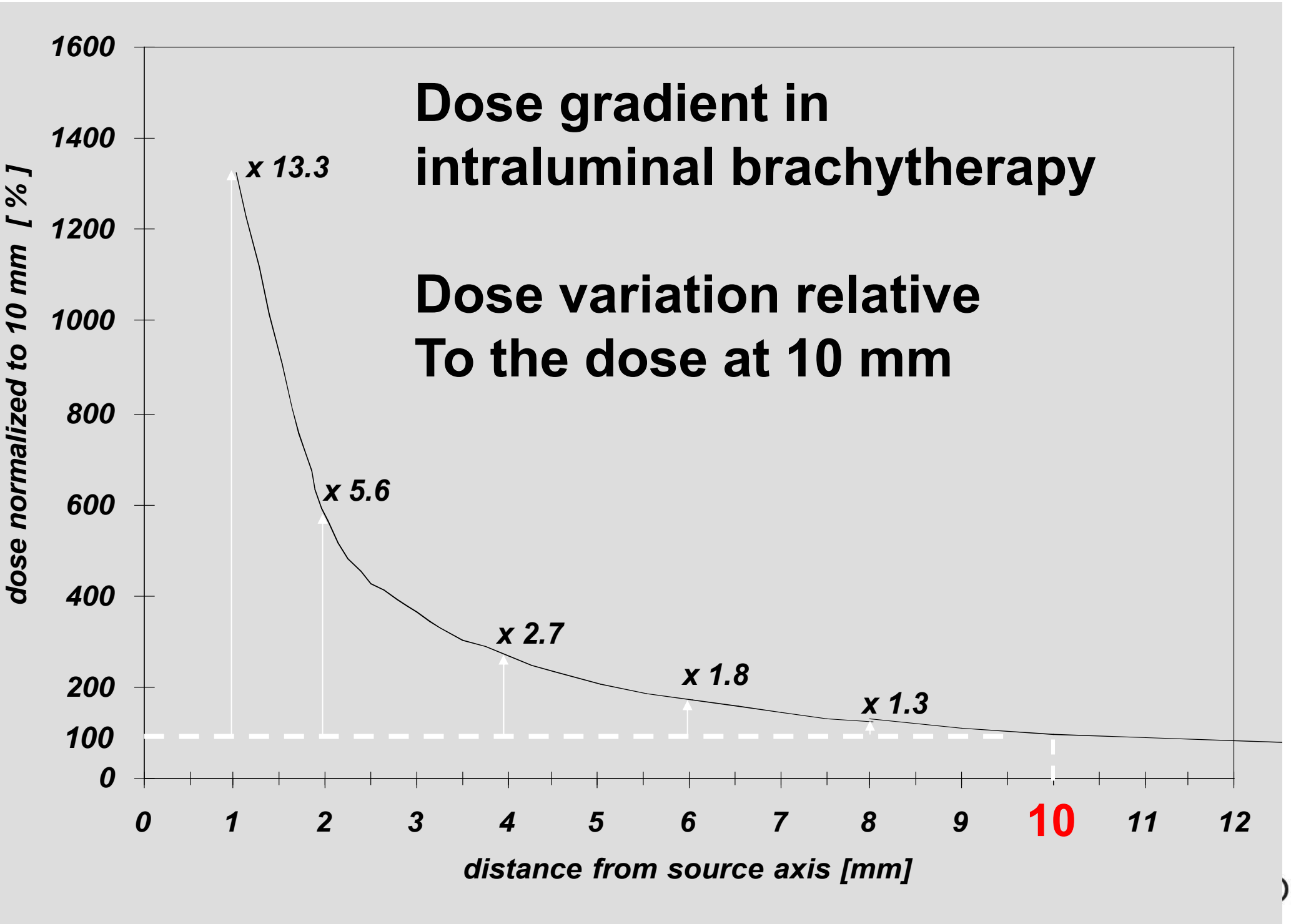
Small diameter appl. in a wide oesophageal lumen
Centered / Non-centered position

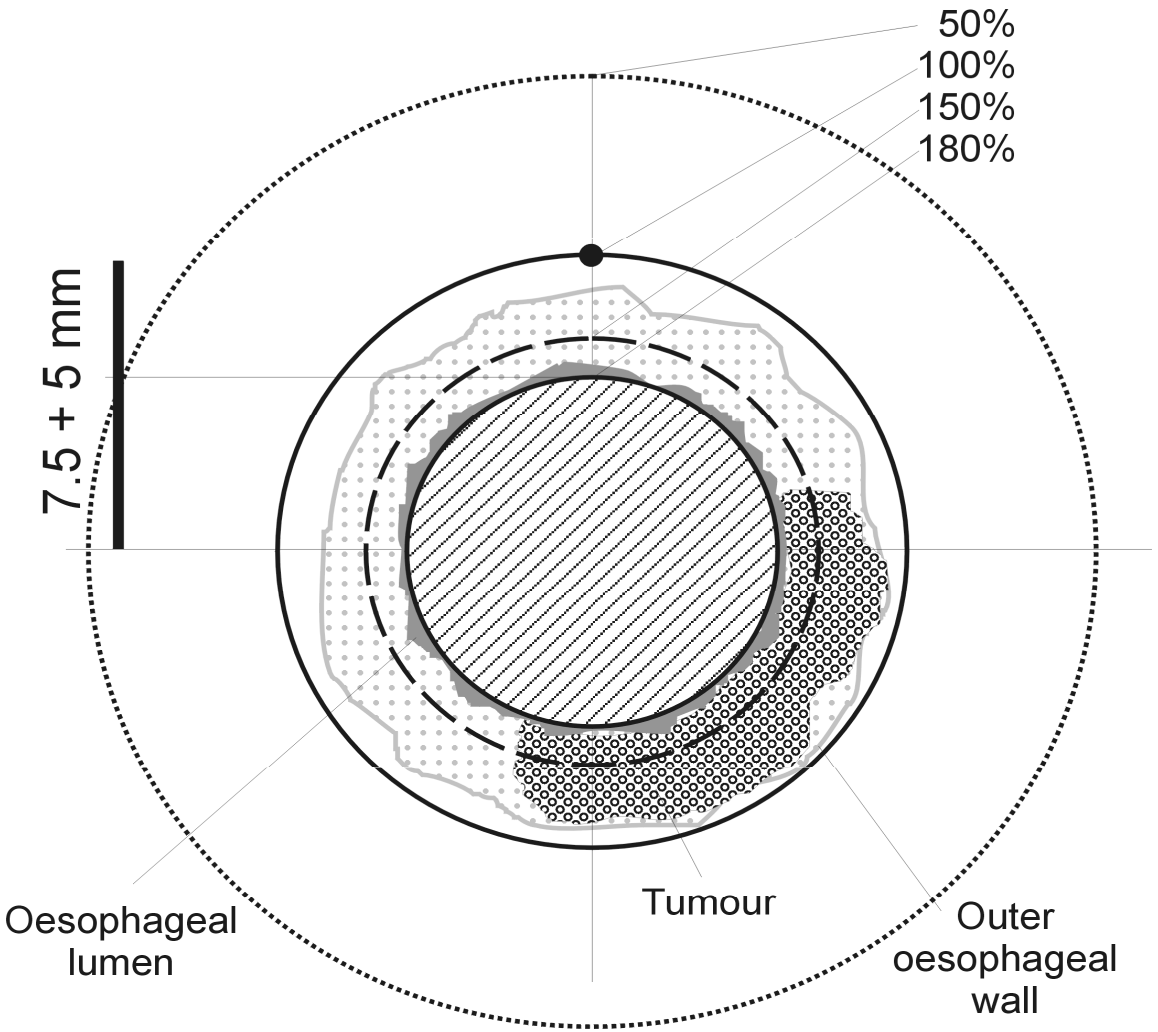




Inappropriate Technique !


Dose gradient in intraluminal brachytherapy
Dose variation relative To the dose at 10 mm
dose normalized to 10 mm [%]
1600
1400
1200
1000
800
600
400
200
100
0
x 13.3
x 5.6
x 2.7
x 1.8
x 1.3
0
1
2
3
4
5
6
7
8
9
10
11
12
distance from source axis [mm]

Appropriate technique in wide oesophageal lumen



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Recording and reporting at 5 mm from the applicator surface

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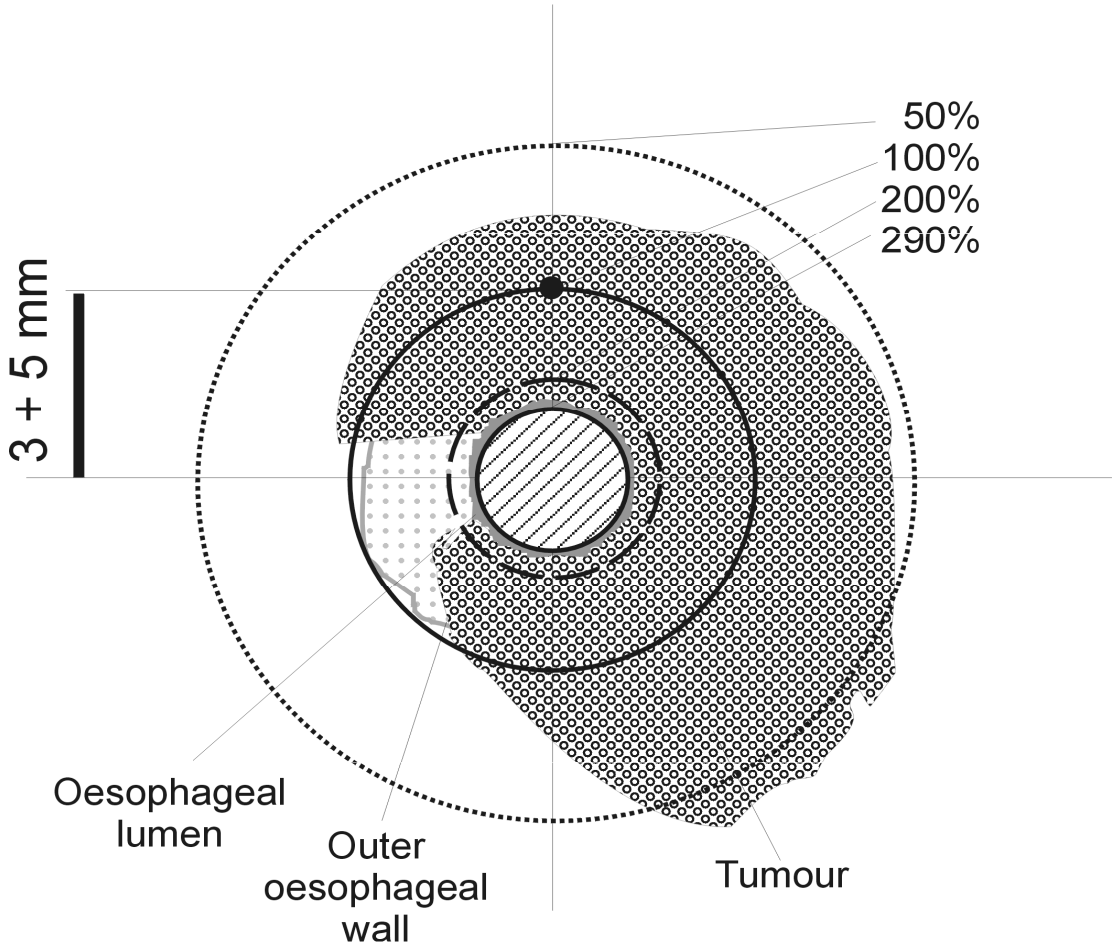
Appropriate technique in narrow oesophageal lumen



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Recording and reporting at 5 mm from the applicator surface

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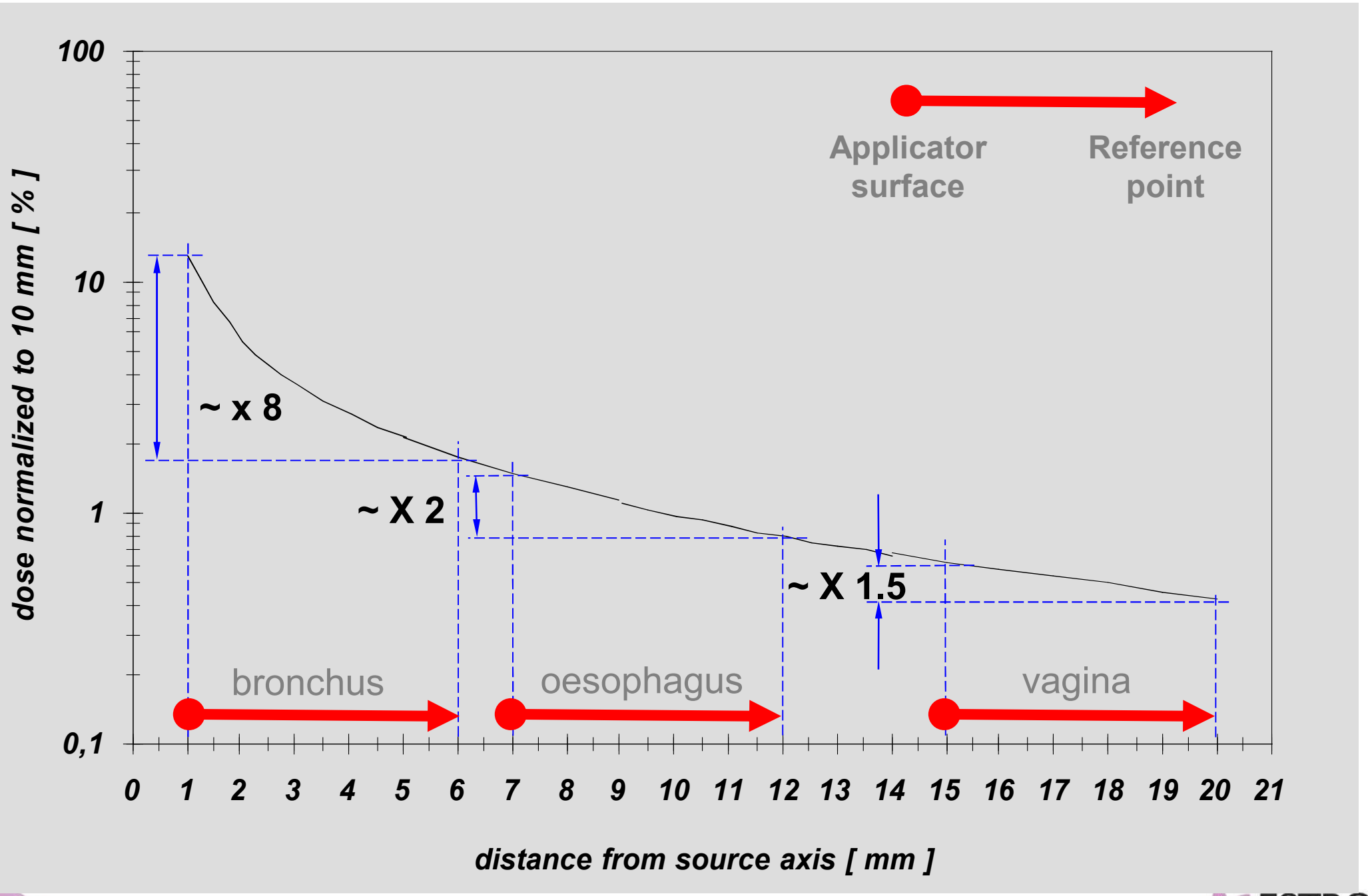
Dose gradient in intraluminal brachytherapy



Dose variation: applic. surface and 5 mm tissue depth

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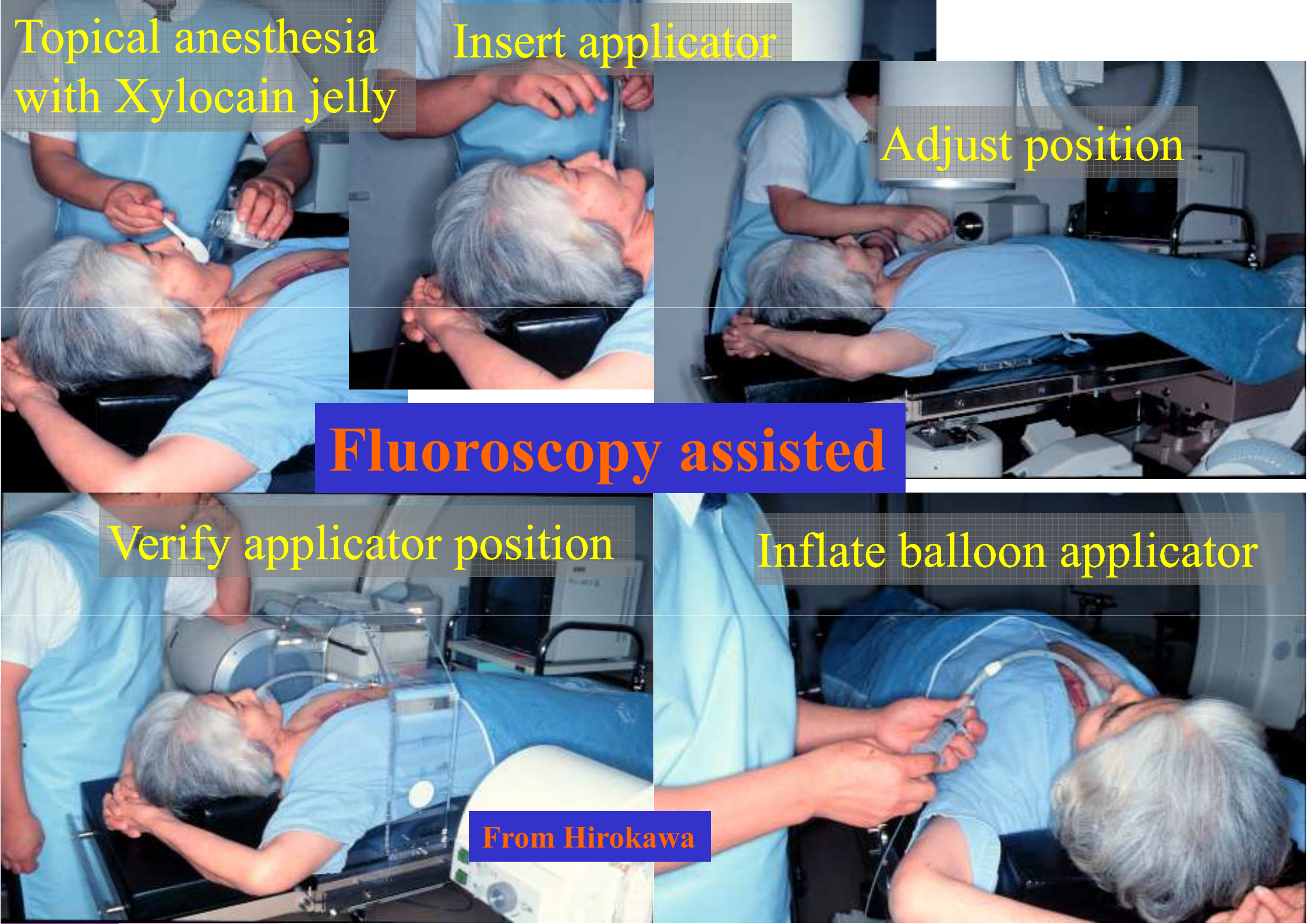
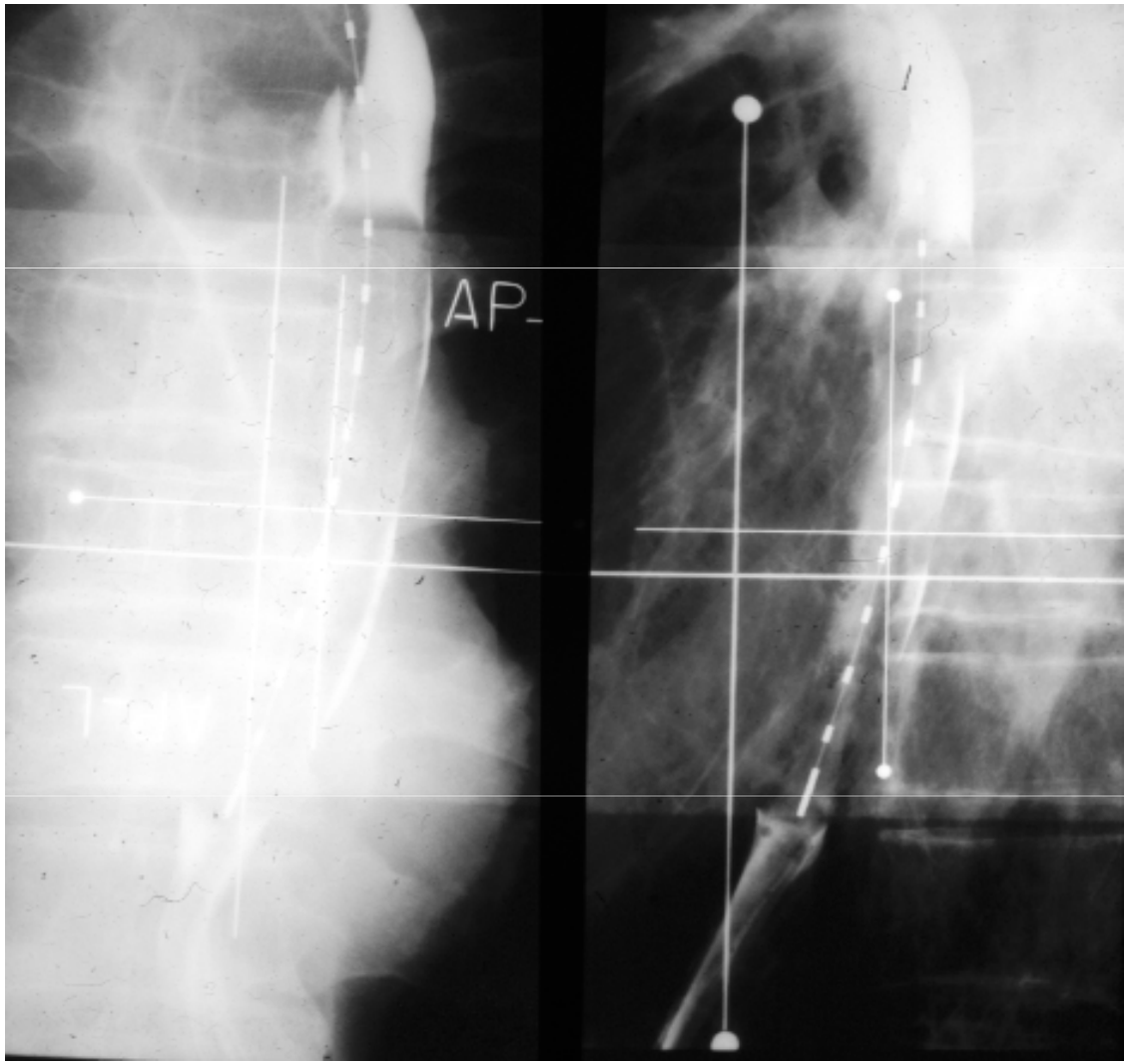

Topical anesthesia with Xylocain jelly
Insert applicator
Adjust position
Fluoroscopy assisted
Verify applicator position
Inflate balloon applicator
From Hirokawa

Example with balloon catheter



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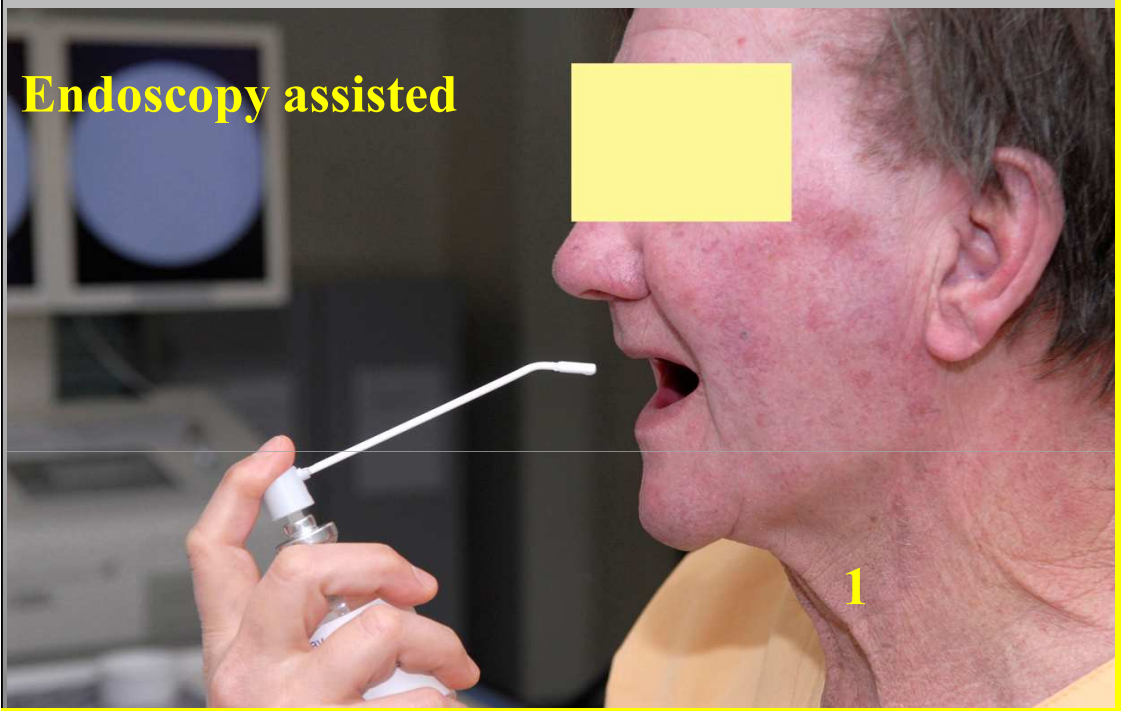
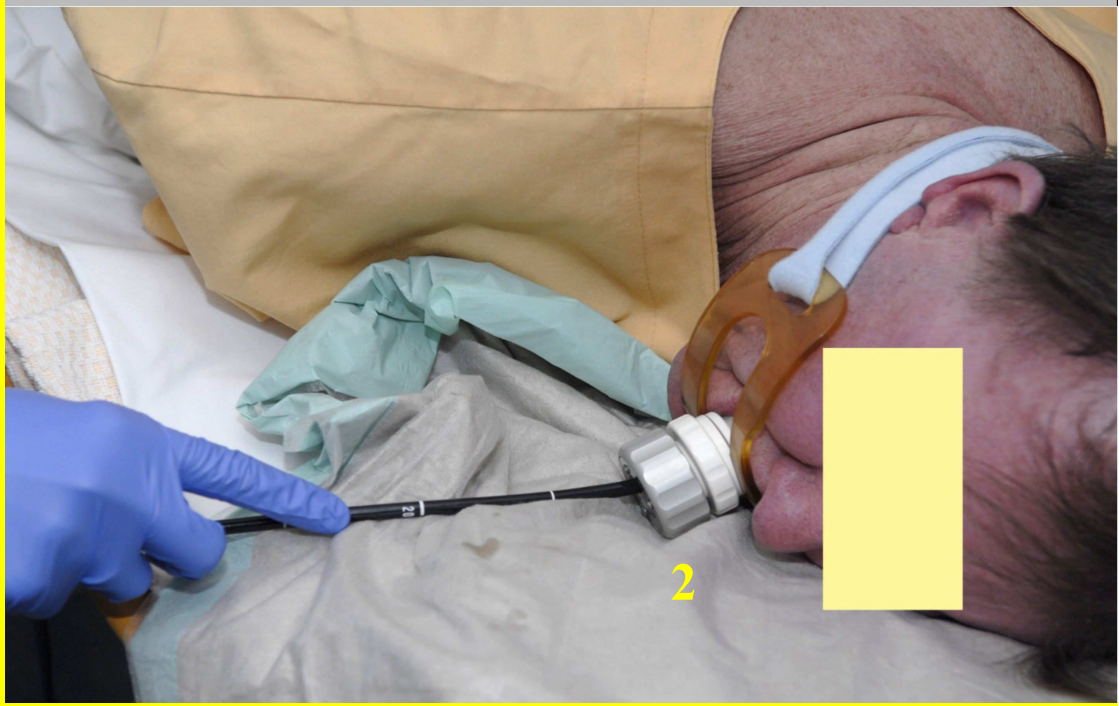
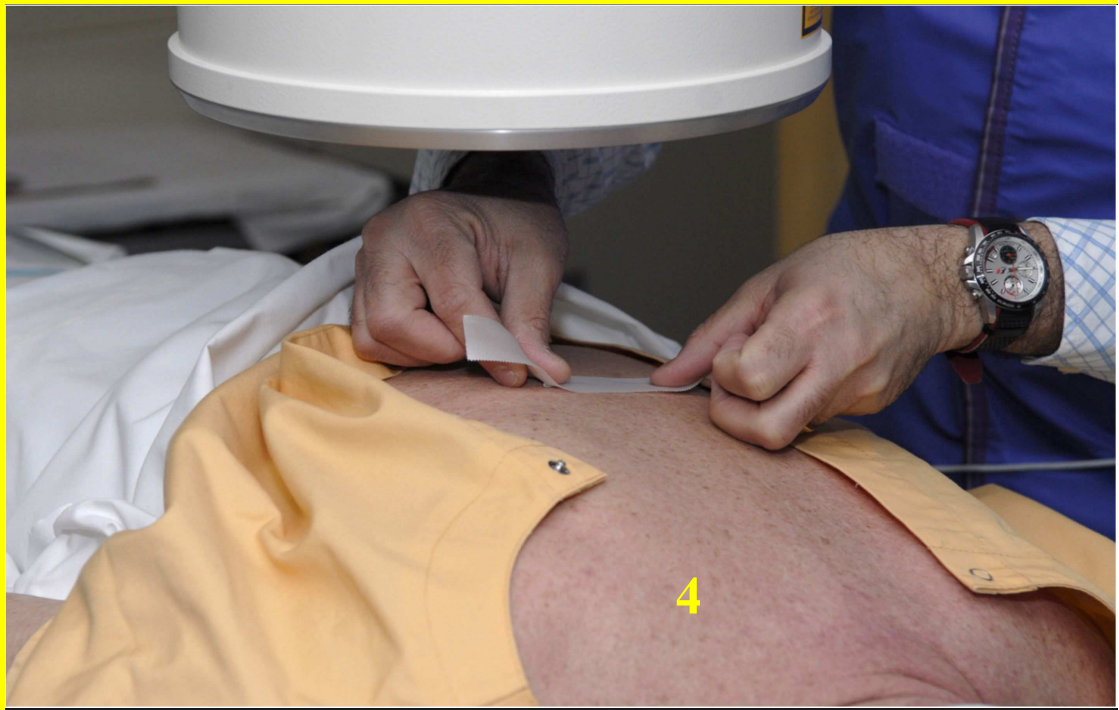

Endoscopy assisted
1


2

3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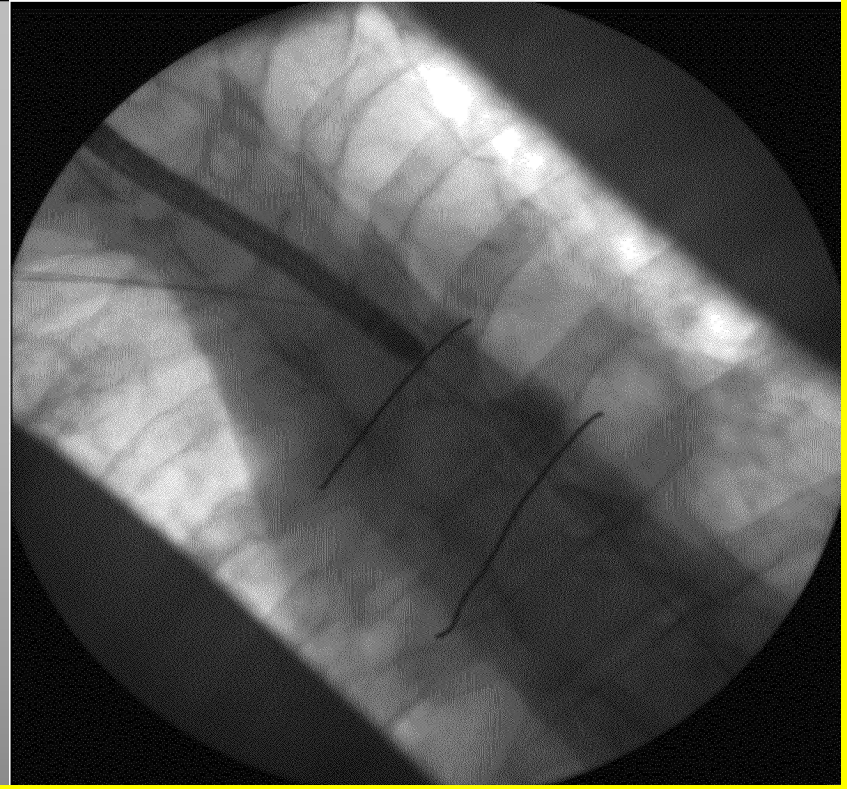
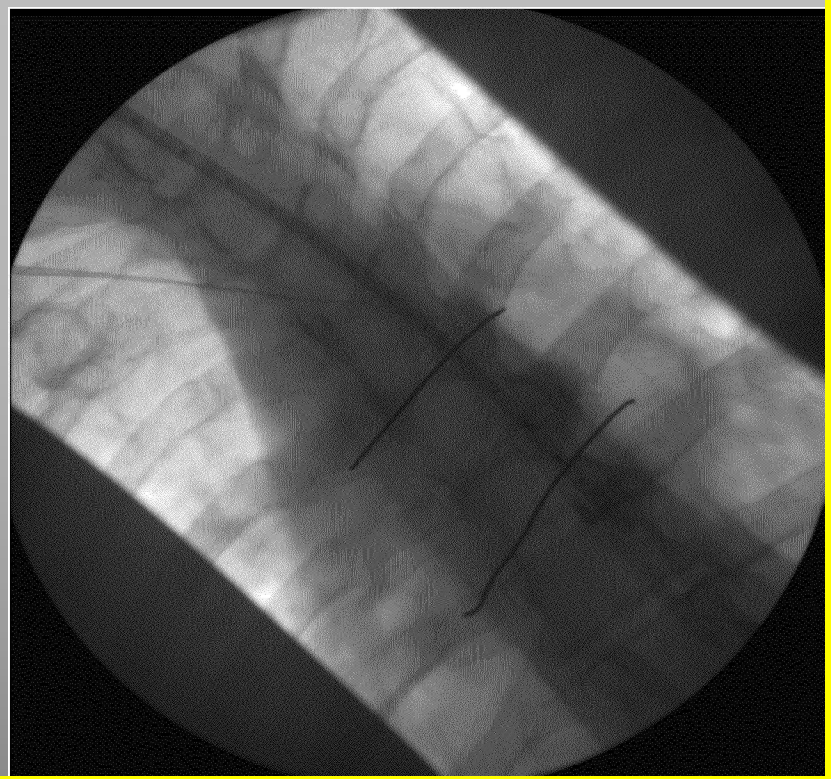


5

6

7

8



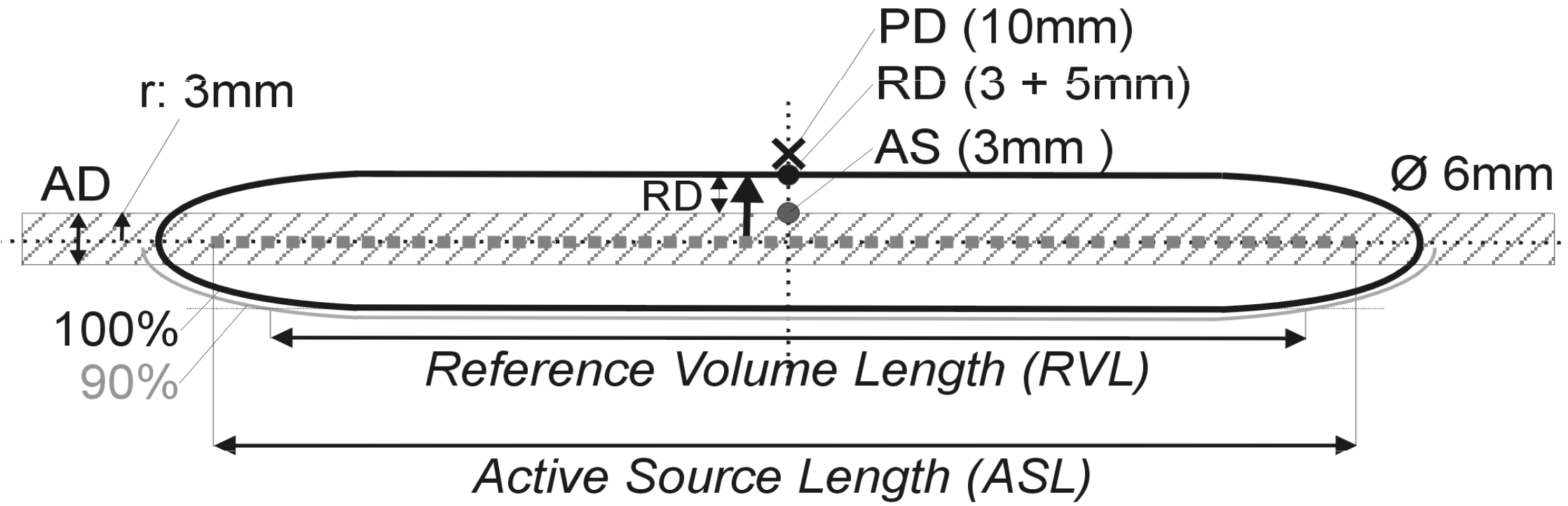
9

10

11

12

Prescribing, Recording and Reporting oesophageal treatment



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1st edition

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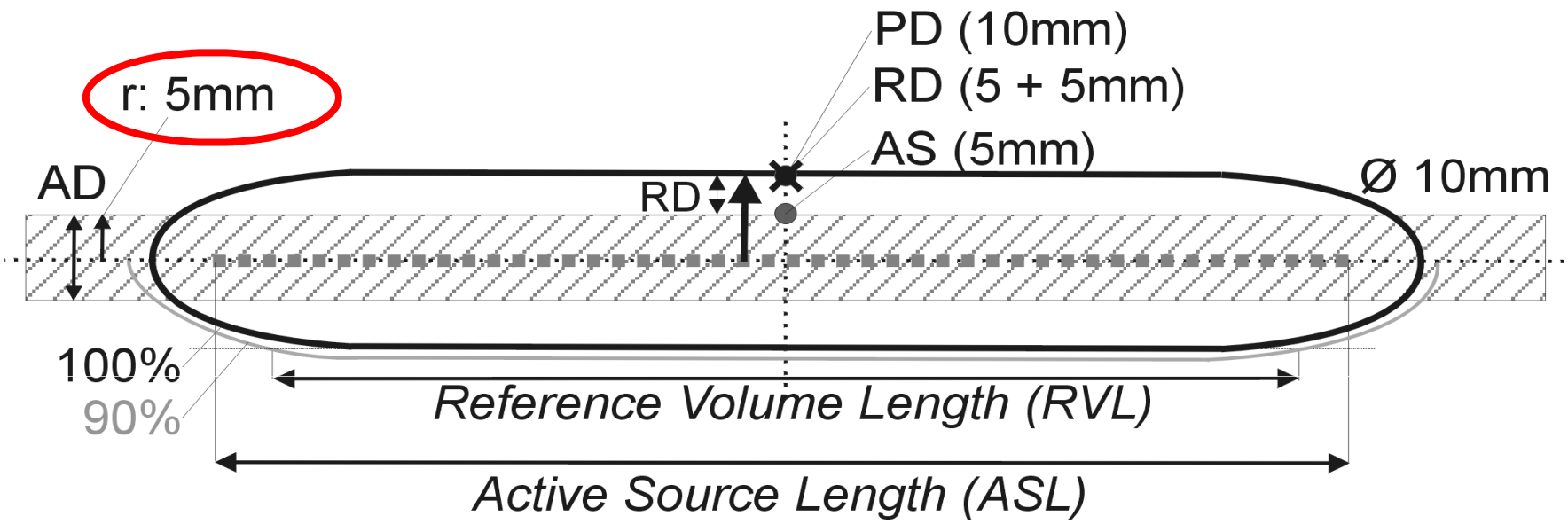

GEC ESTRO Handbook of Brachytherapy
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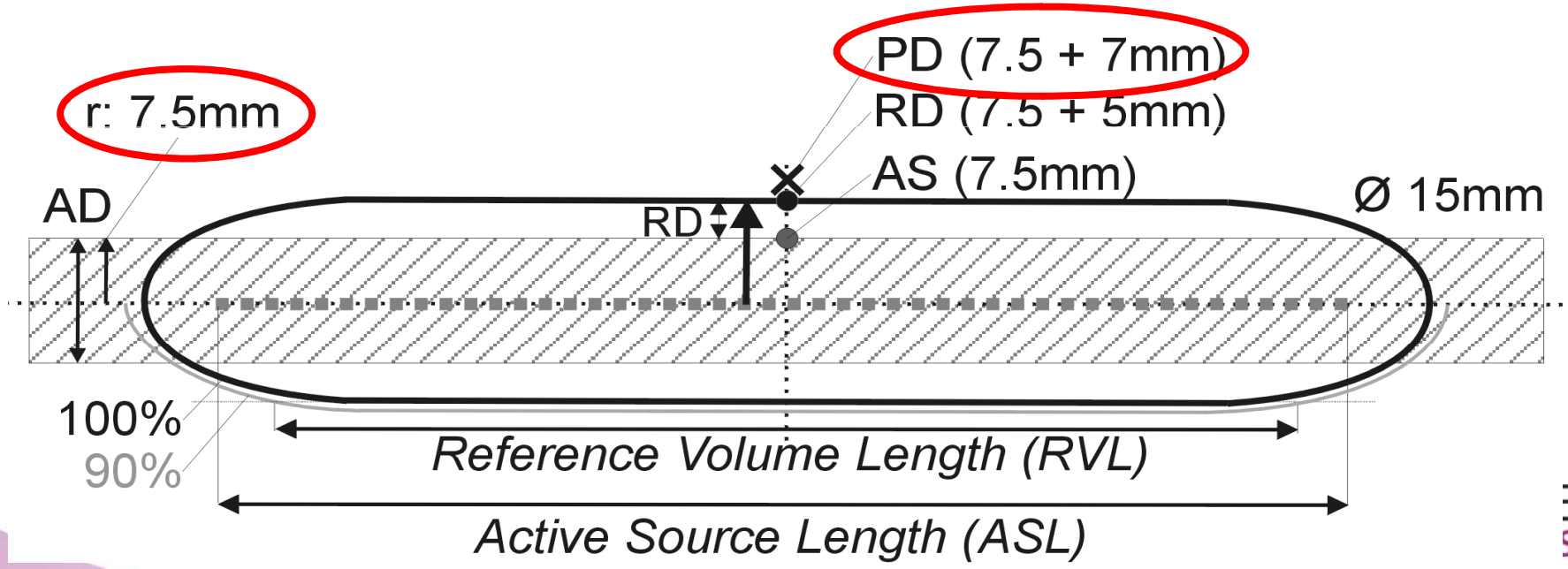

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Different prescription technique

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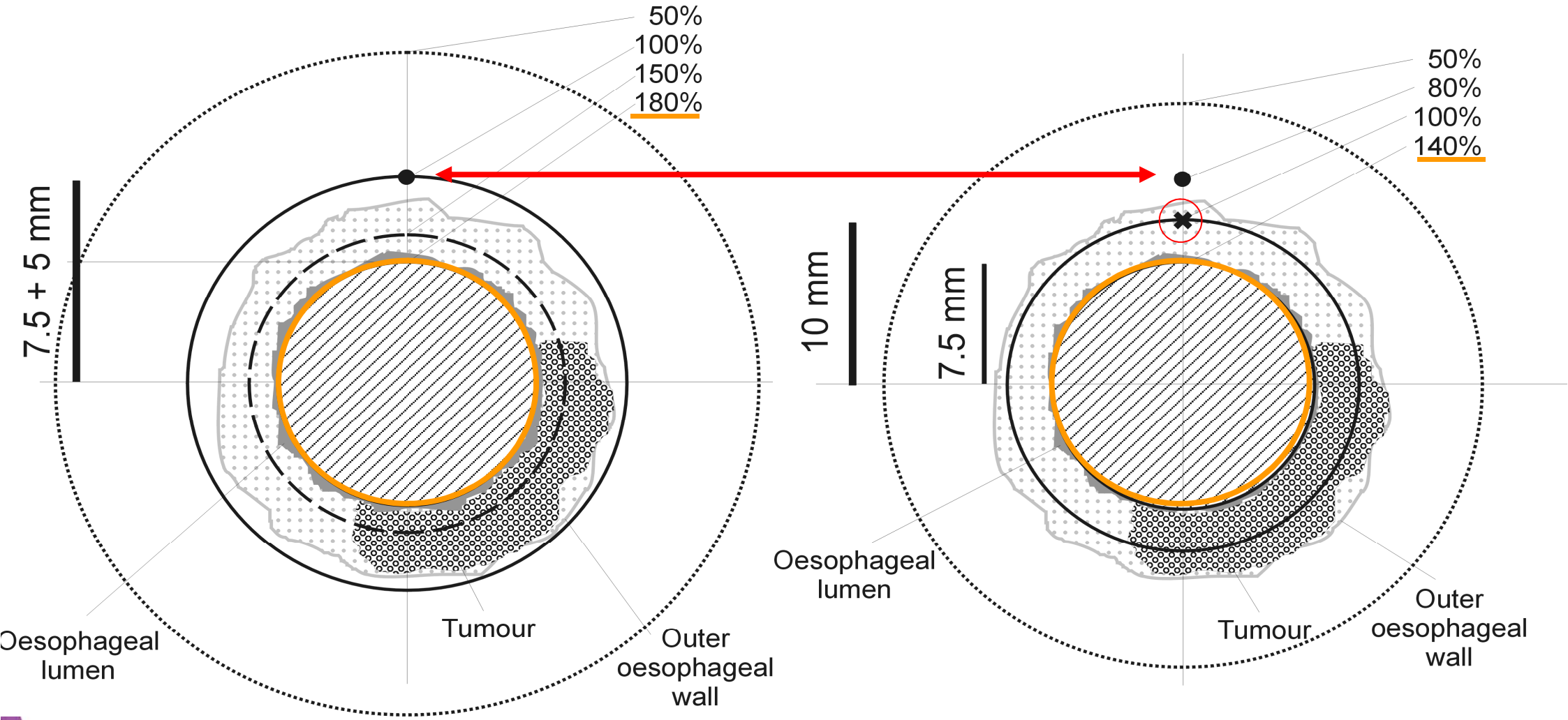

Recording and reporting at 5 mm from the applicator surface

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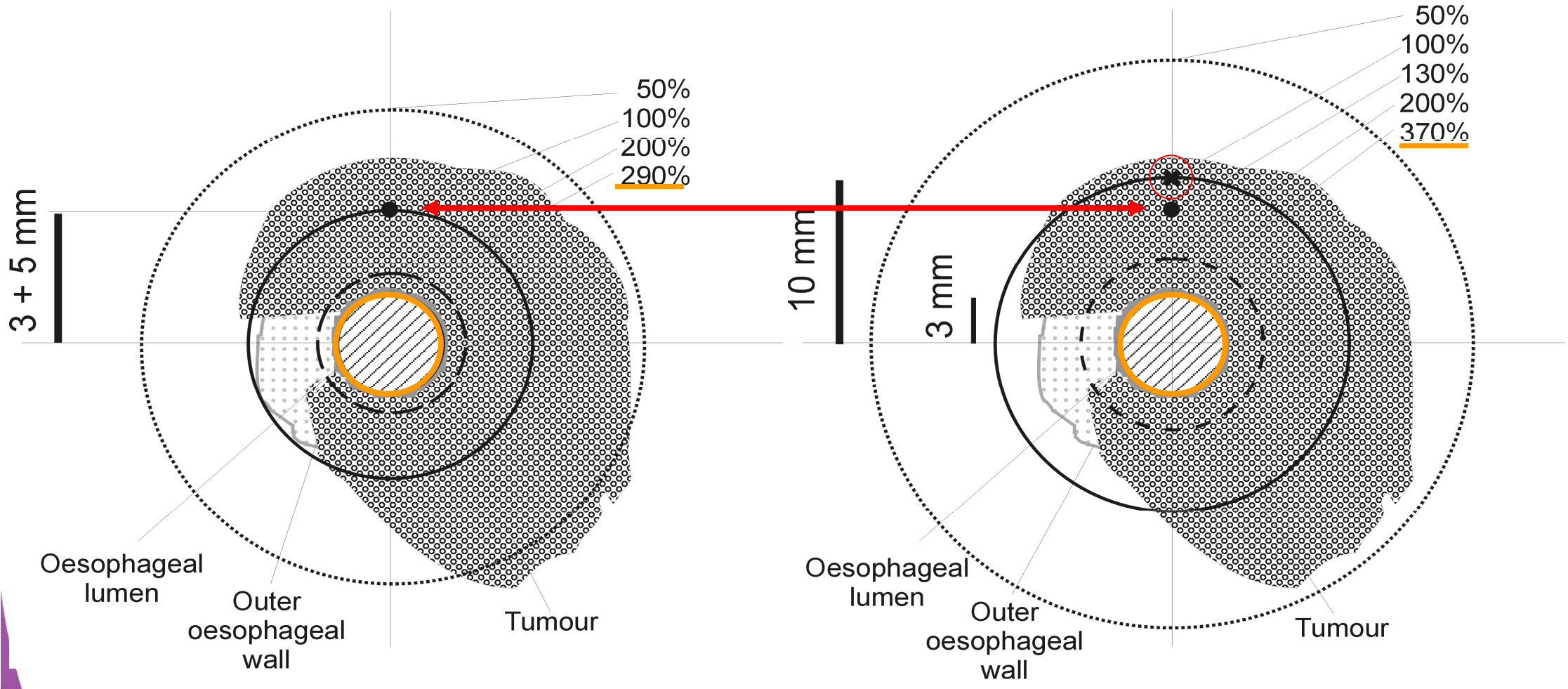
Different prescription technique

GEC ESTRO Handbook of Brachytherapy



Recording and reporting at 5 mm from the applicator surface

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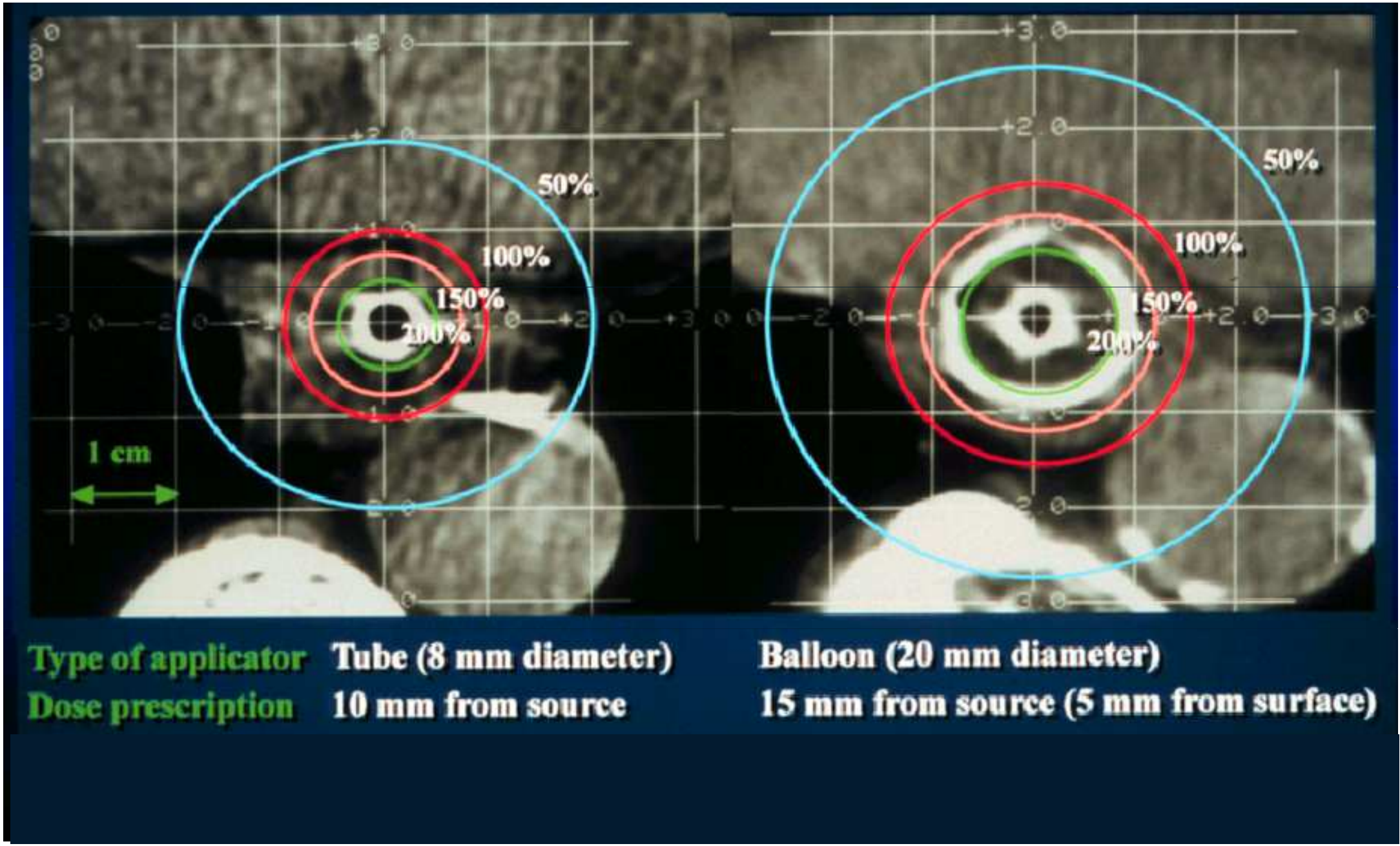

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DOSE AND FRACTIONATION
- combination treatment EBT and BT -

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 dose

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

Quick symptom relief
BT1-EBT-BT2

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RESULTS

overall symptom relief

e.g. from dysphagea (mean 4 – 10 mths)
about two thirds of patients

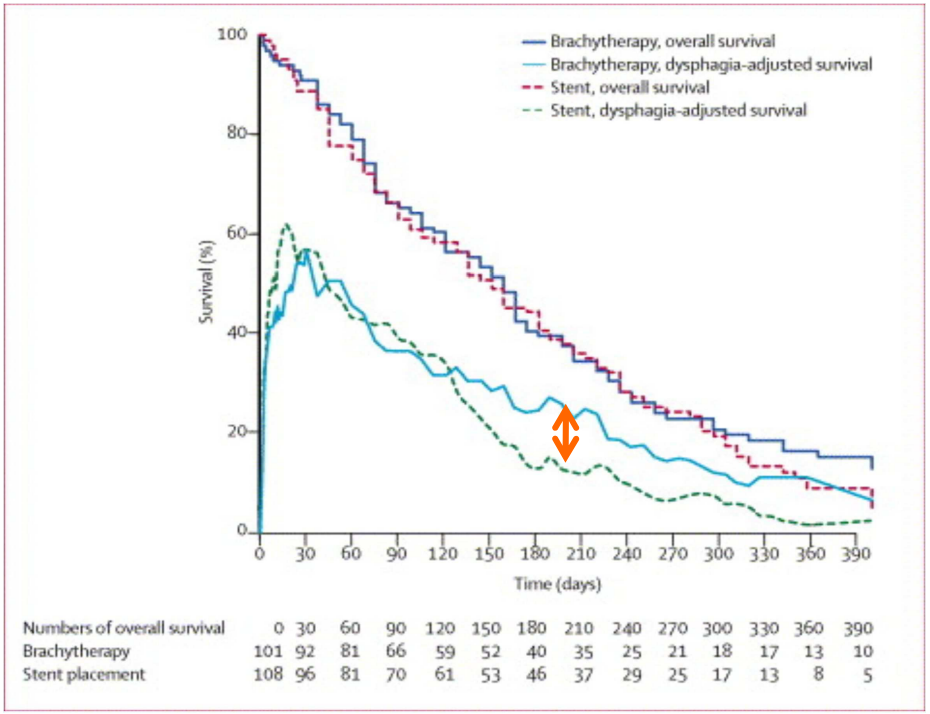
overall improvement in general performance, weight

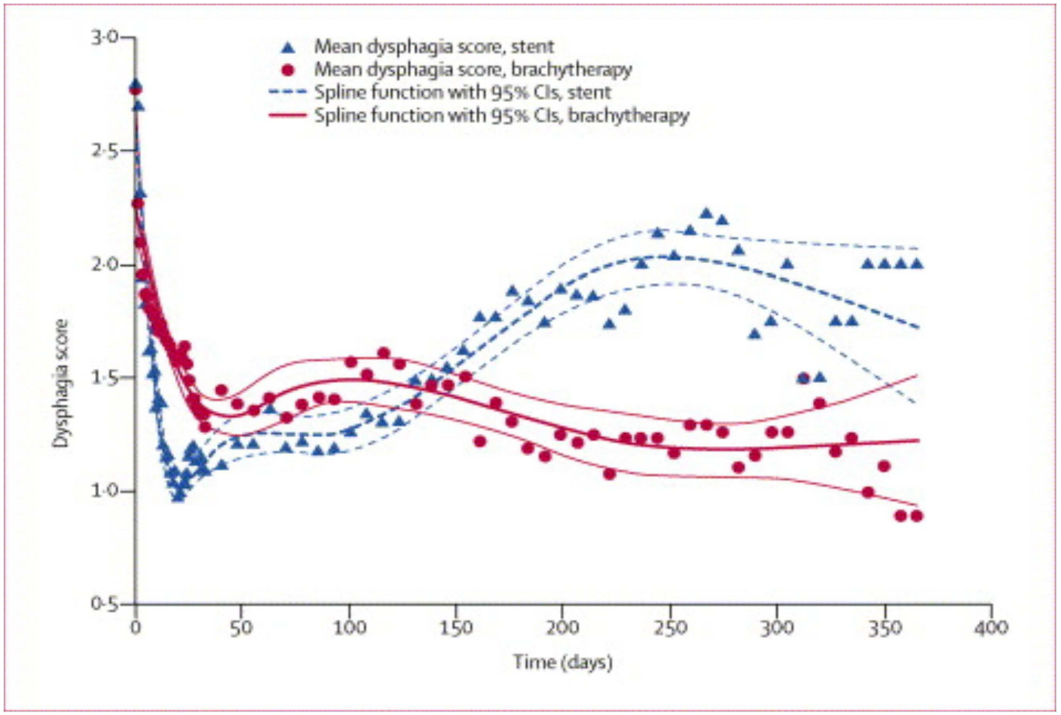
about two thirds of patients

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
Muijs et al, Radiother Oncol 2012;102:303
Sharma et al. Int J Radiat Oncol Biol Phys 2002;52:310

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

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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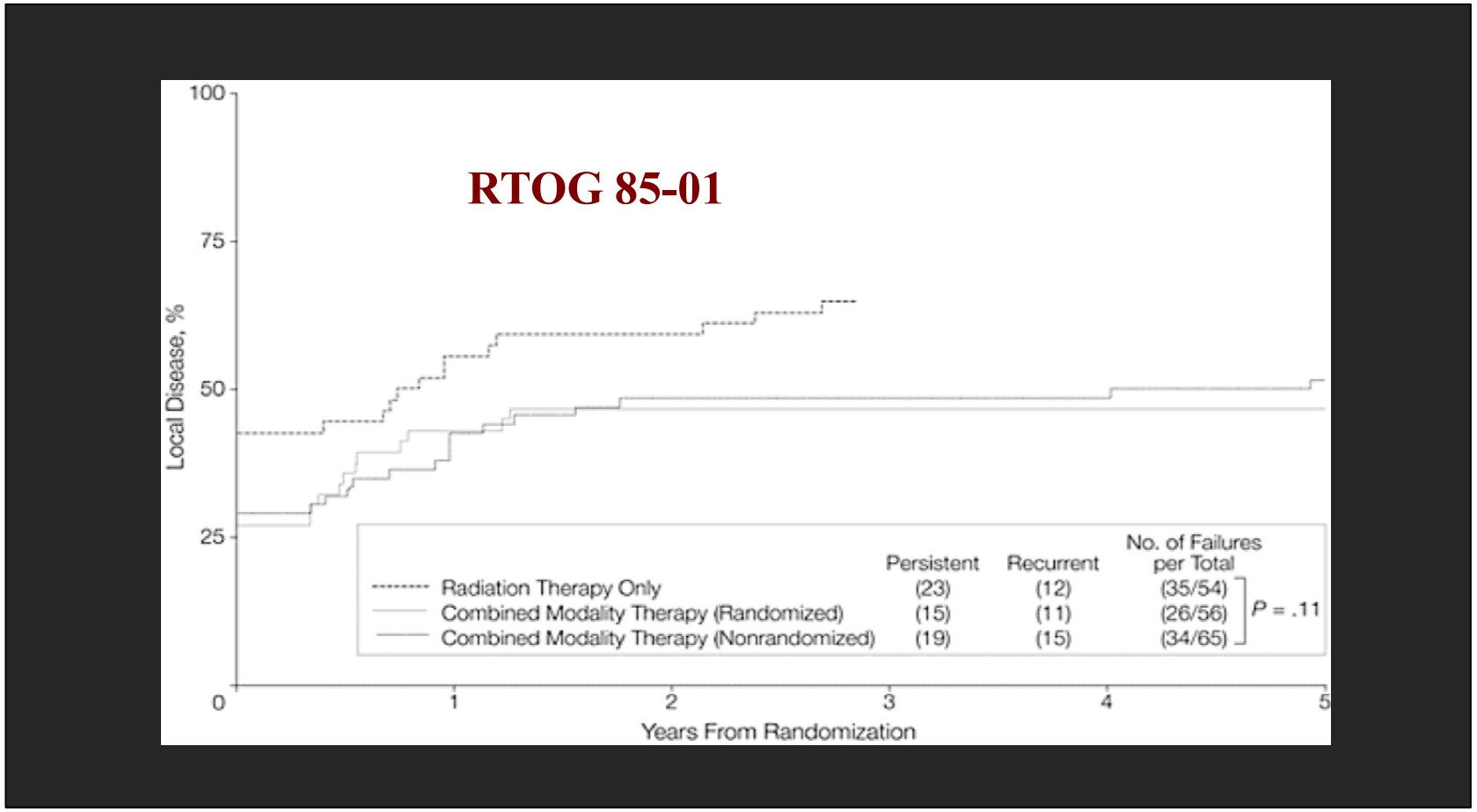
Improvement in Chemoradiation Without Brachytherapy



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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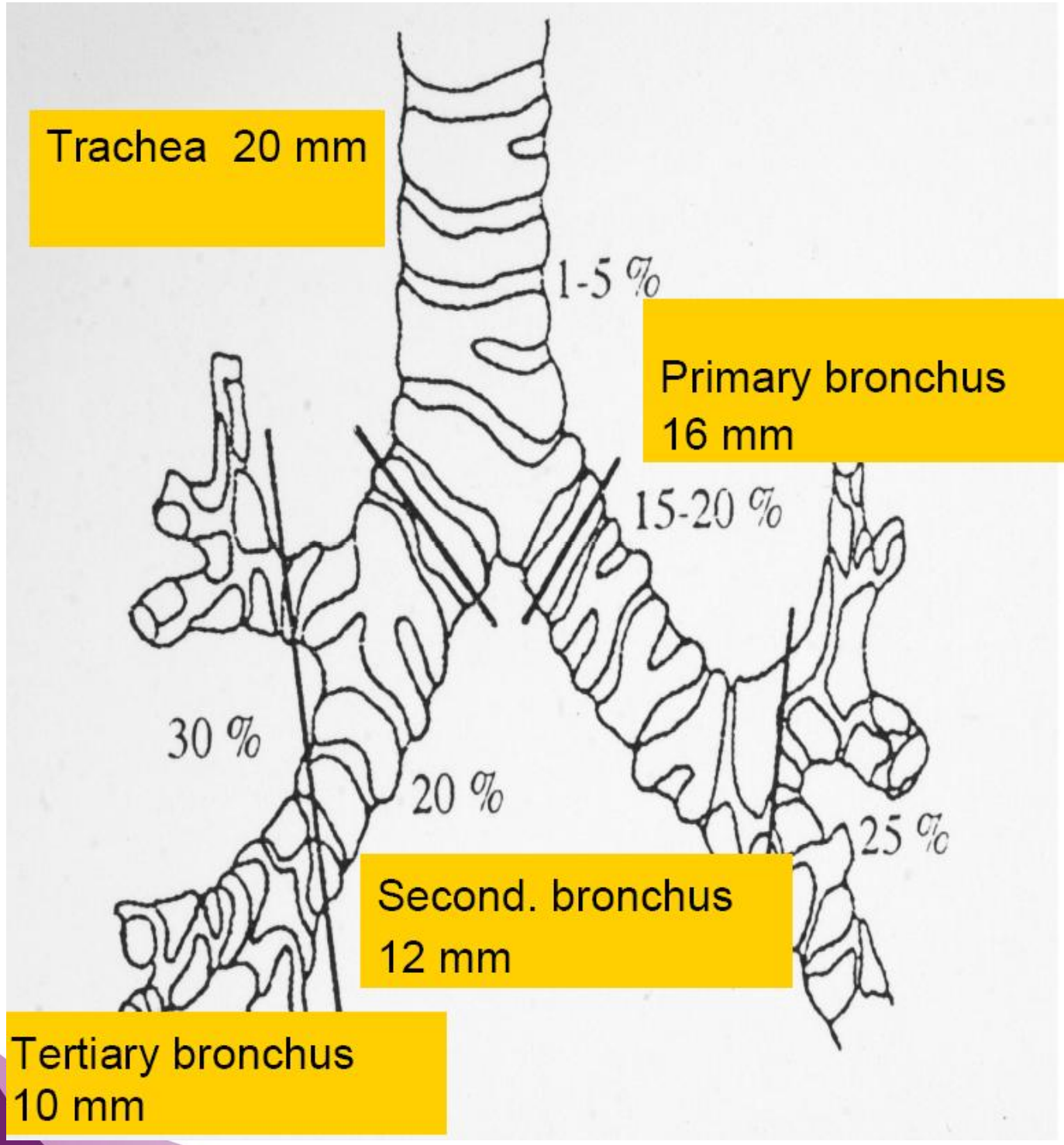
WWW.ESTRO.ORG/SCHOOL

Brachytherapy for Bronchus ca

Erik Van Limbergen MD, PhD
University Hospital Gasthuisberg
3000 Leuven

ESTRO School



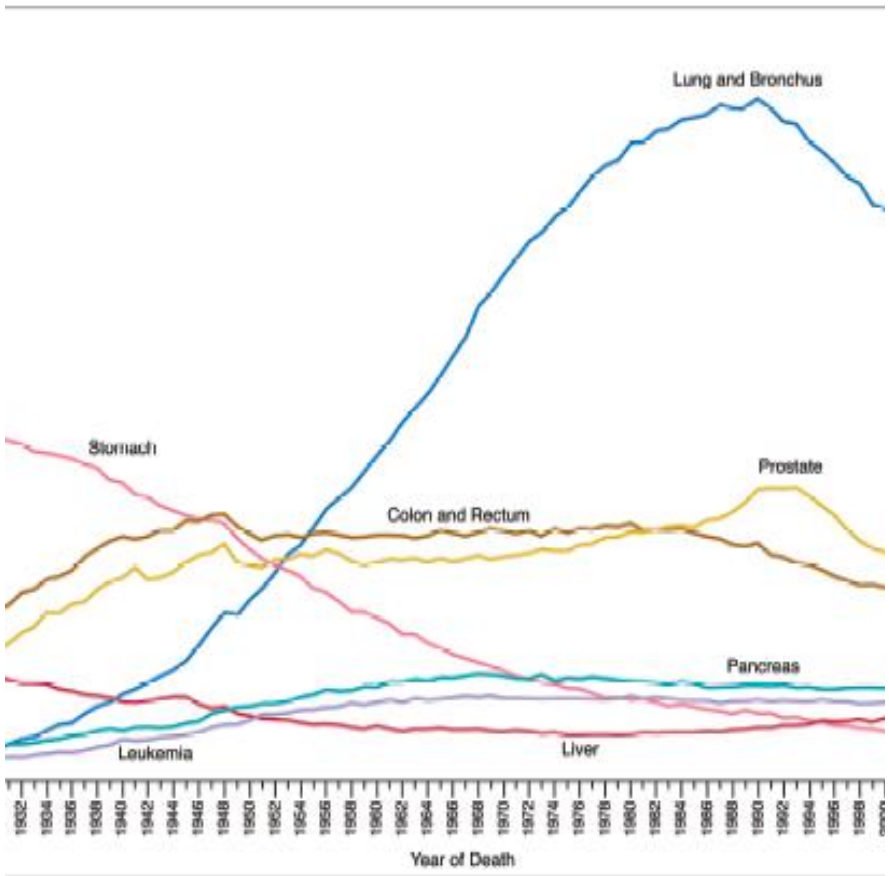
Diameters

Lumina 90%

Walls 5%

Lung and bronchus Ca. death

CA Cancer J Clin 2005;6 Cancer Statistics, 2005



al Age-adjusted Cancer Death Rates* Among Males for Selected Cancer Types, US, 1930 to 2001.
sted 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 Dise
tion.

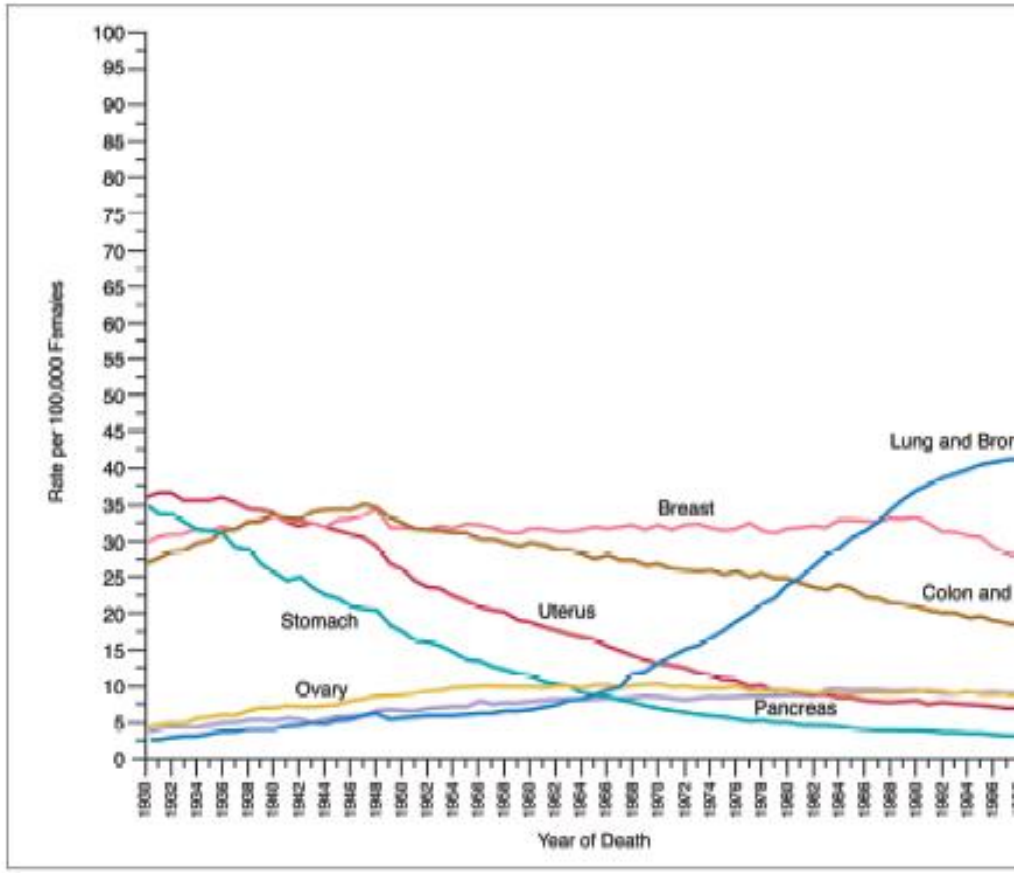


FIGURE 5 Annual Age-adjusted Cancer Death Rates* Among Females for Selected Cancer Types, US, 1930 to 2001.
*Rates are age-adjusted to the 2000 US standard population.
Note: Due to ICD coding, numerator information has changed over time. Rates for cancers of the uterus, ovary, lung and bronchus, and 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.

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 +/- CT:

- 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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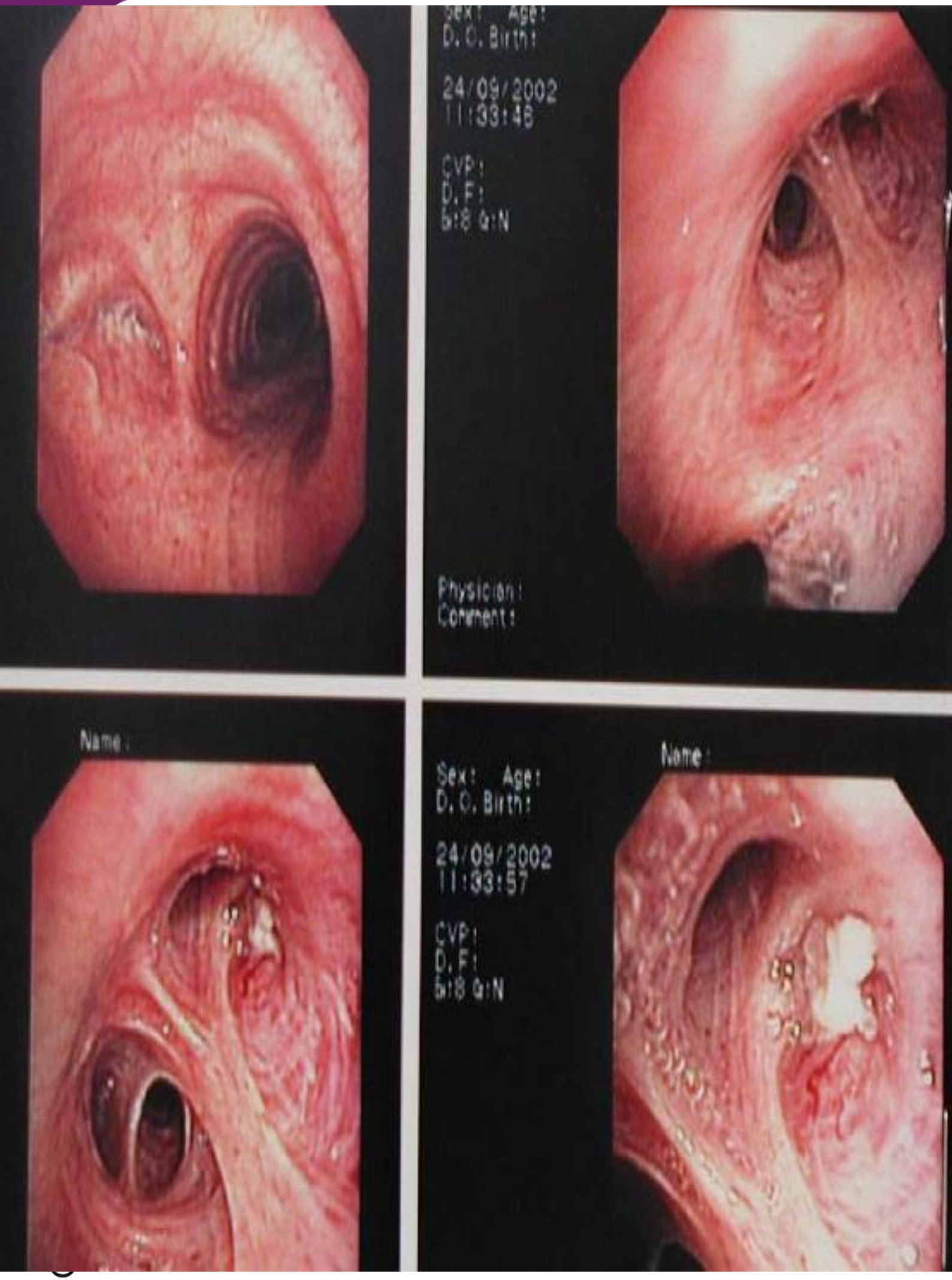
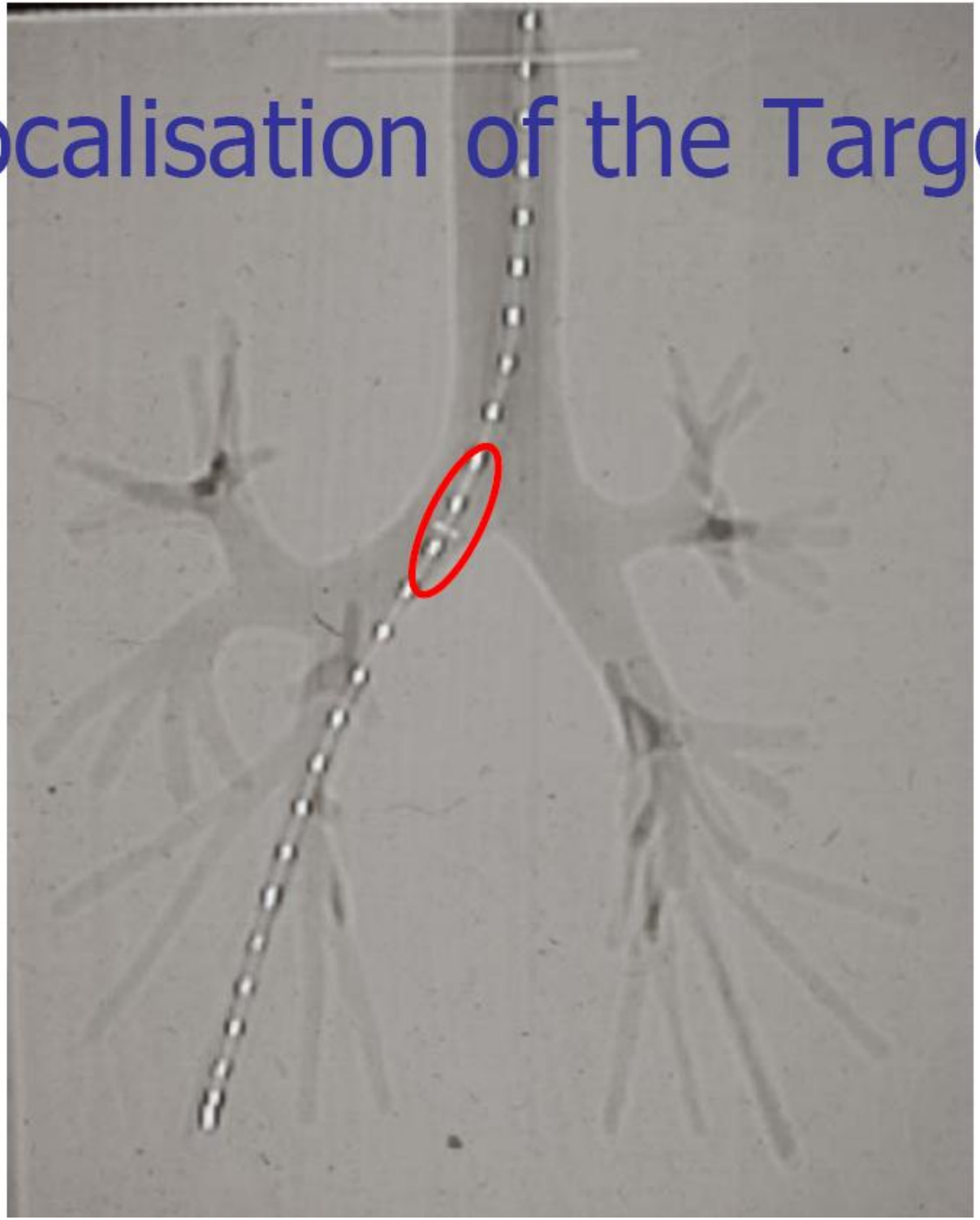
Local Anesthesia


Sex: Age:
D.O.Birth:
24/09/2002
11:33:46
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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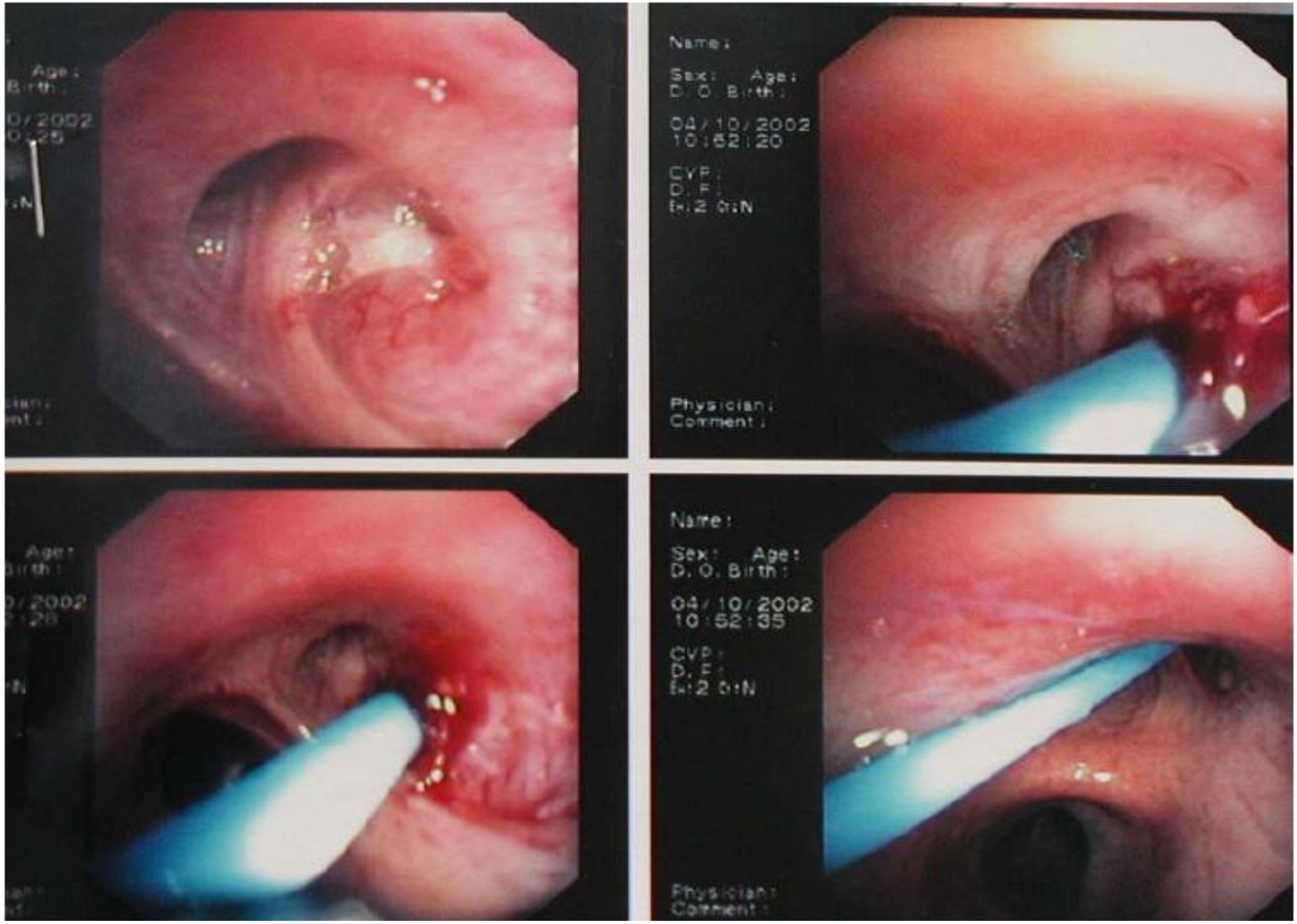
Positioning of the catheter



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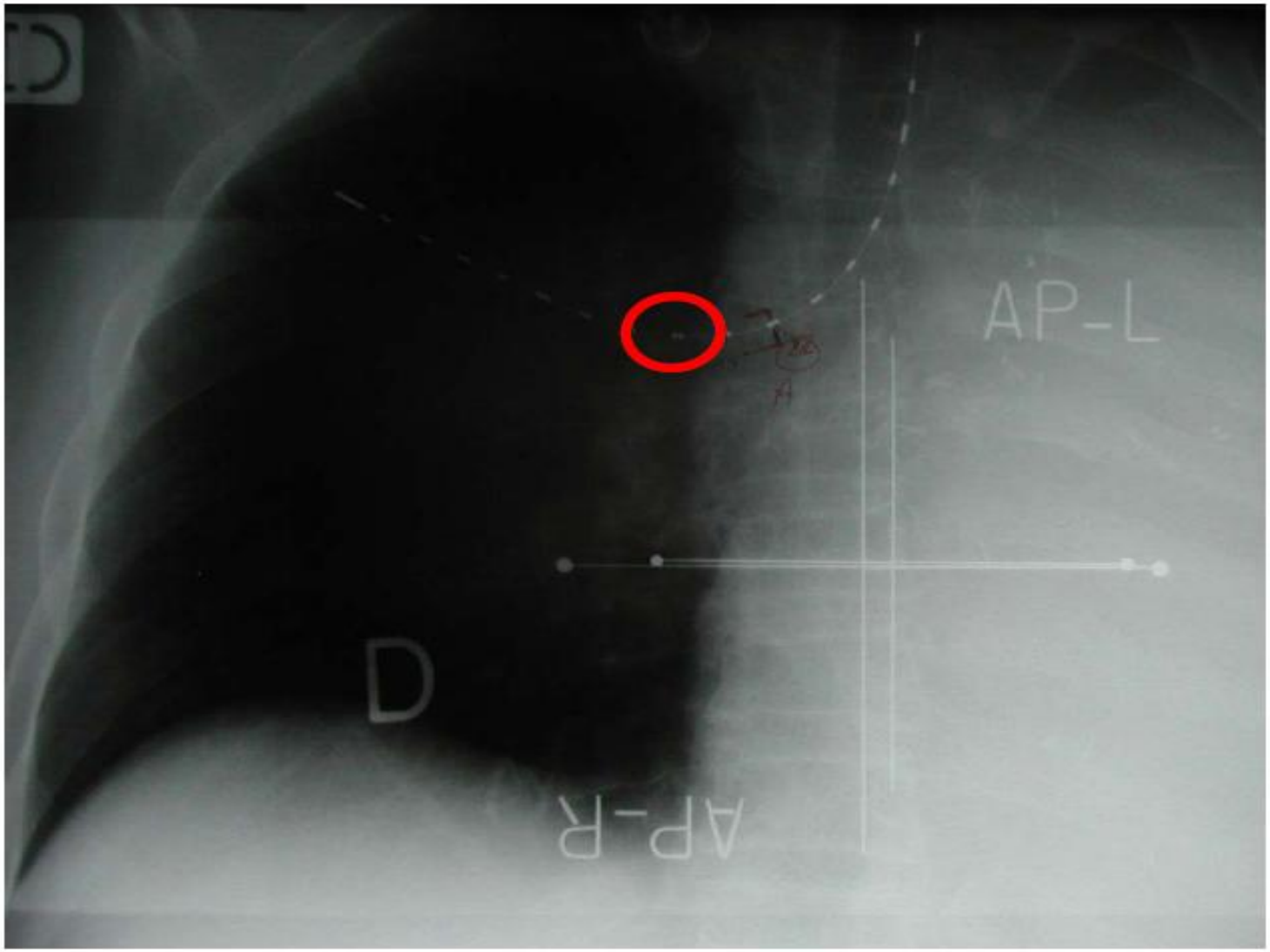
Localisation of the target

Catheter
+
X Rays



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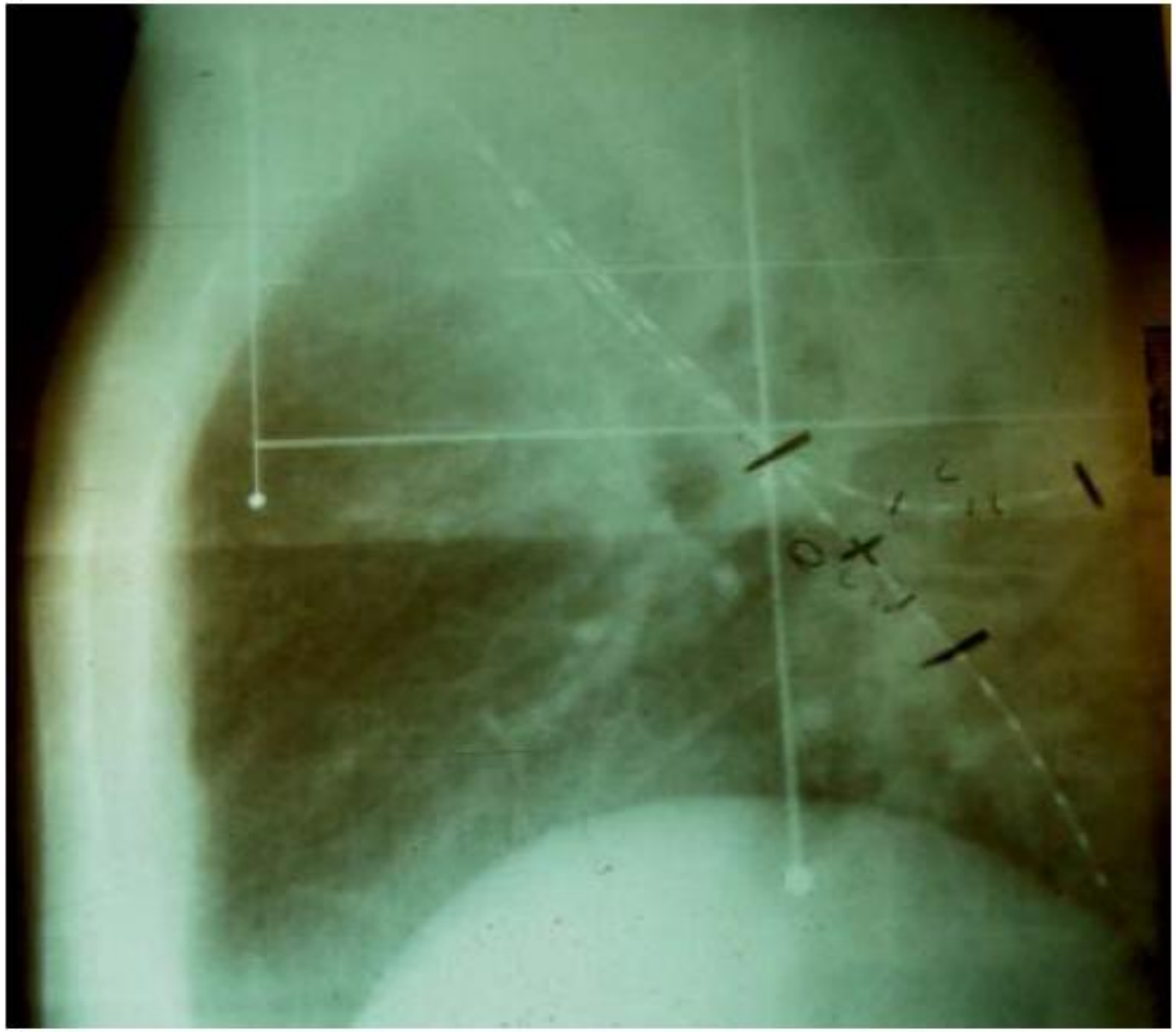
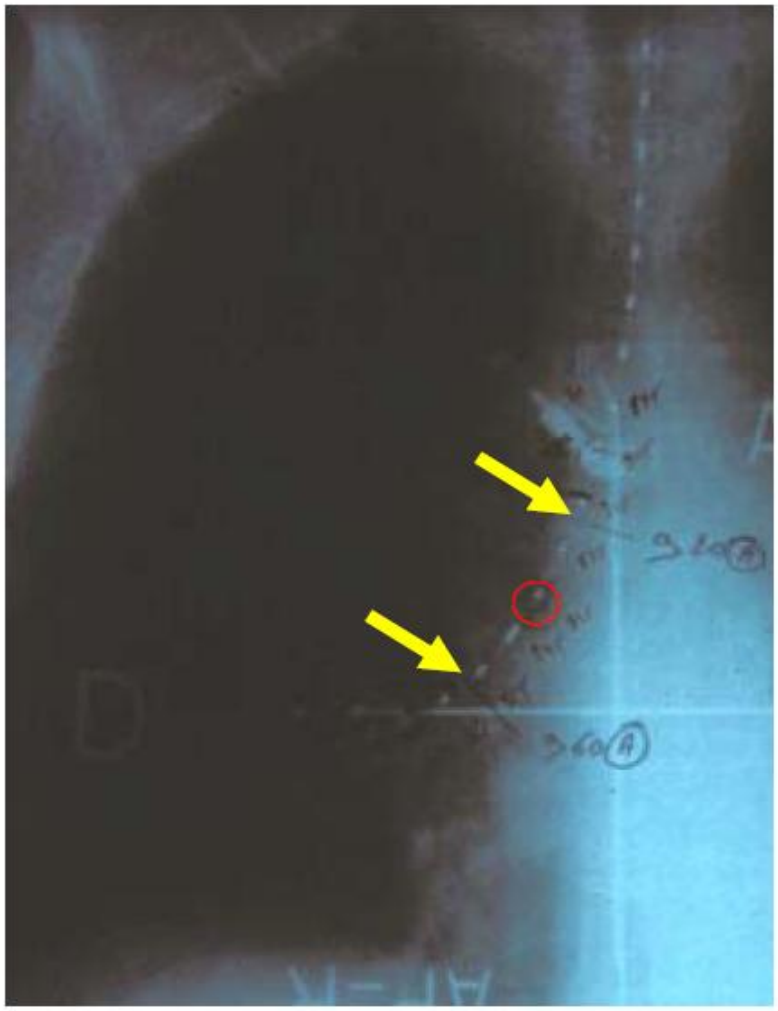
Lateral



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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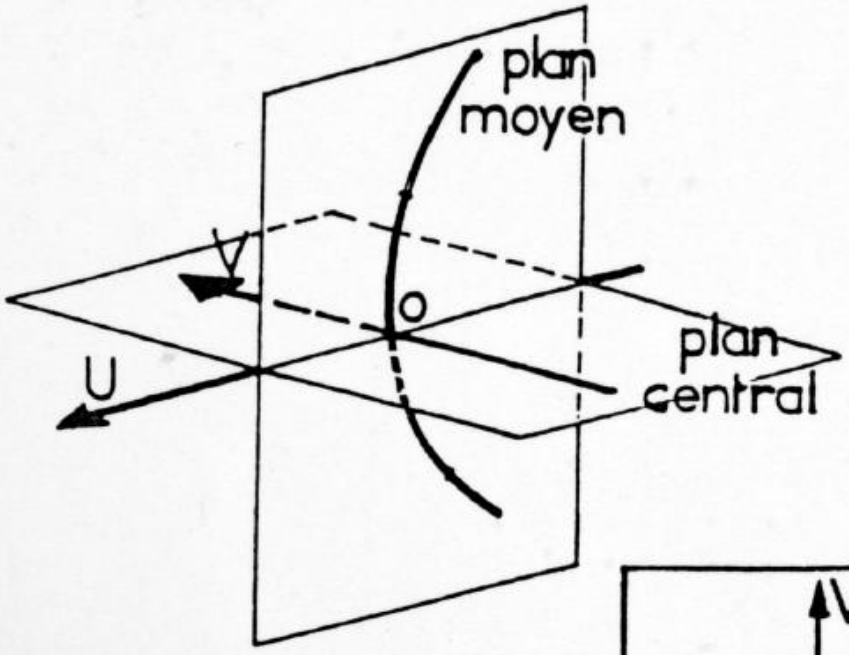
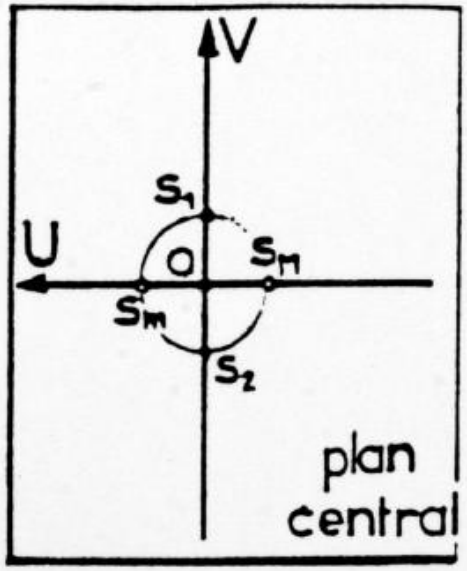
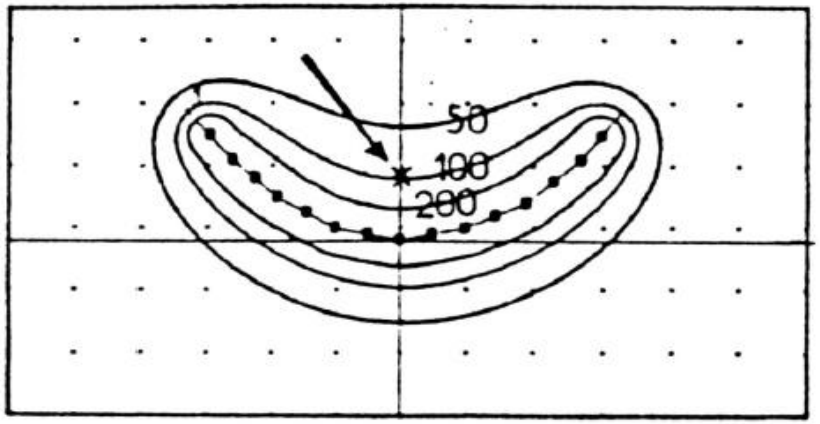




$$D_S = \frac{D_{S1} + D_{S2}}{2}$$

D_{SM} :

D_{Sm} :

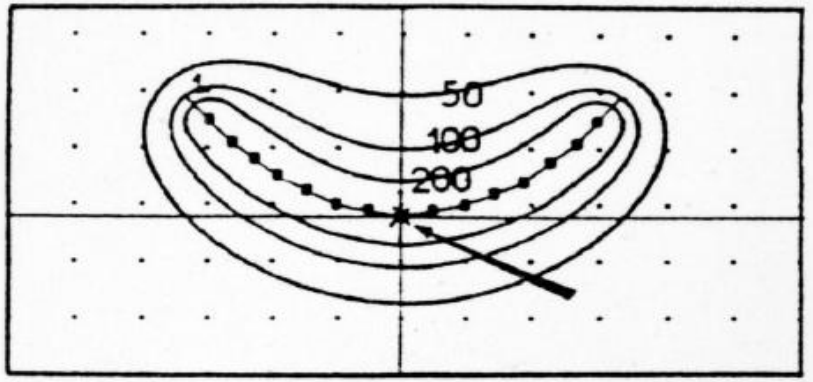


0.22884 cGy*m^-2
on: 5.0 mm

D_S = 82

V_{D_S} : 16,8
V_{20} : 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} : 5,9

D_{SM} :122 D_{Sm} :86
optimisation non
oui standard ☐
autre ☐

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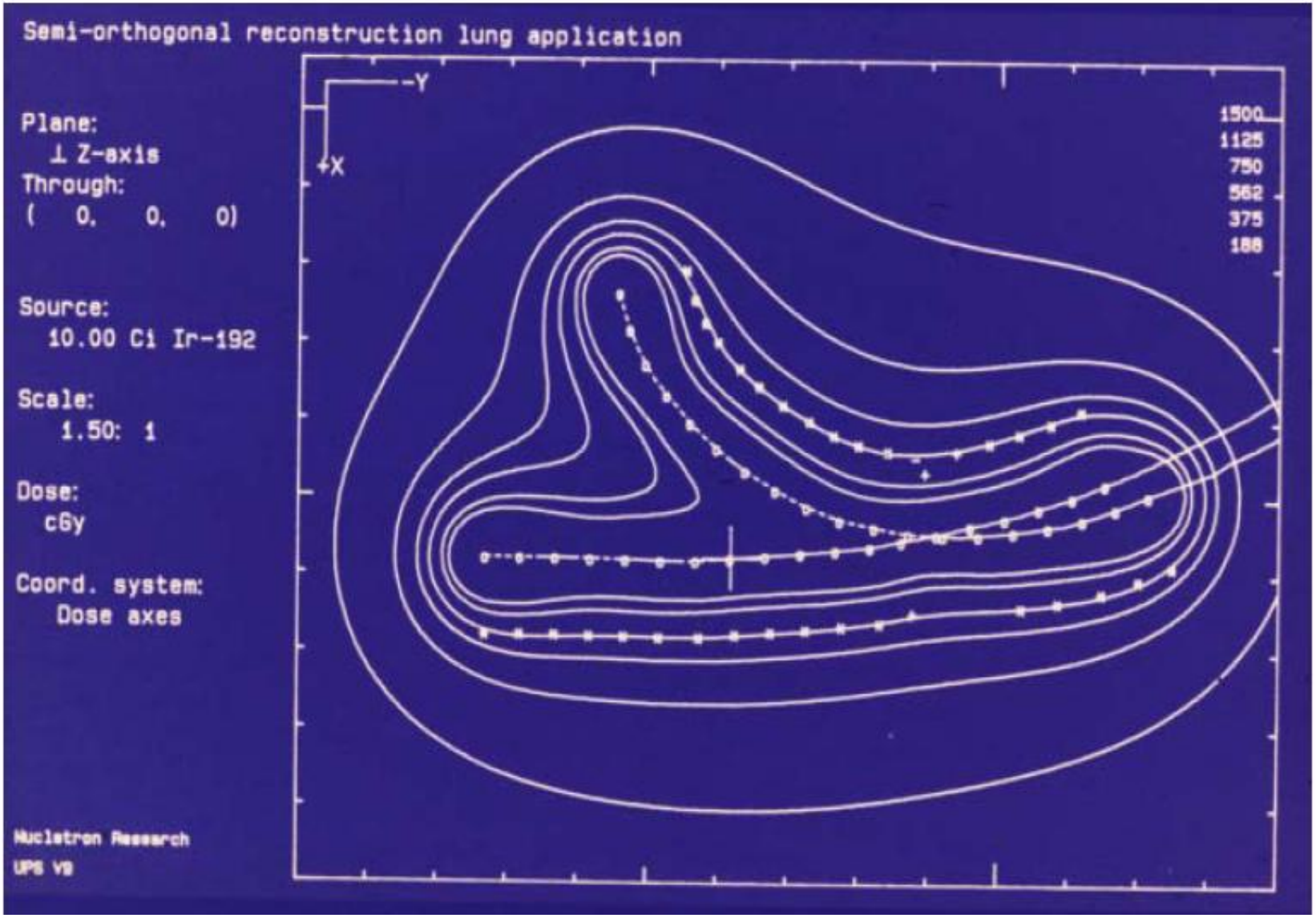
Dose prescription at 1 cm :
= dose at 1.5 cm from the forque



Marinello et al

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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

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Acute Side effects

- Coughing : +++
- Cardiac arrythmia, hypotension (cardiac arrest)
- Bronchospasm
- Pneumothorax : +++ chest X-Rays control
- Massive Bleeding

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Respons to Treatment

- Partial Remission 101/188 (54%)
- Minor Response 25/188 (13%)
- No change 29/188 (16%)

Macha et al. 1990

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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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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

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

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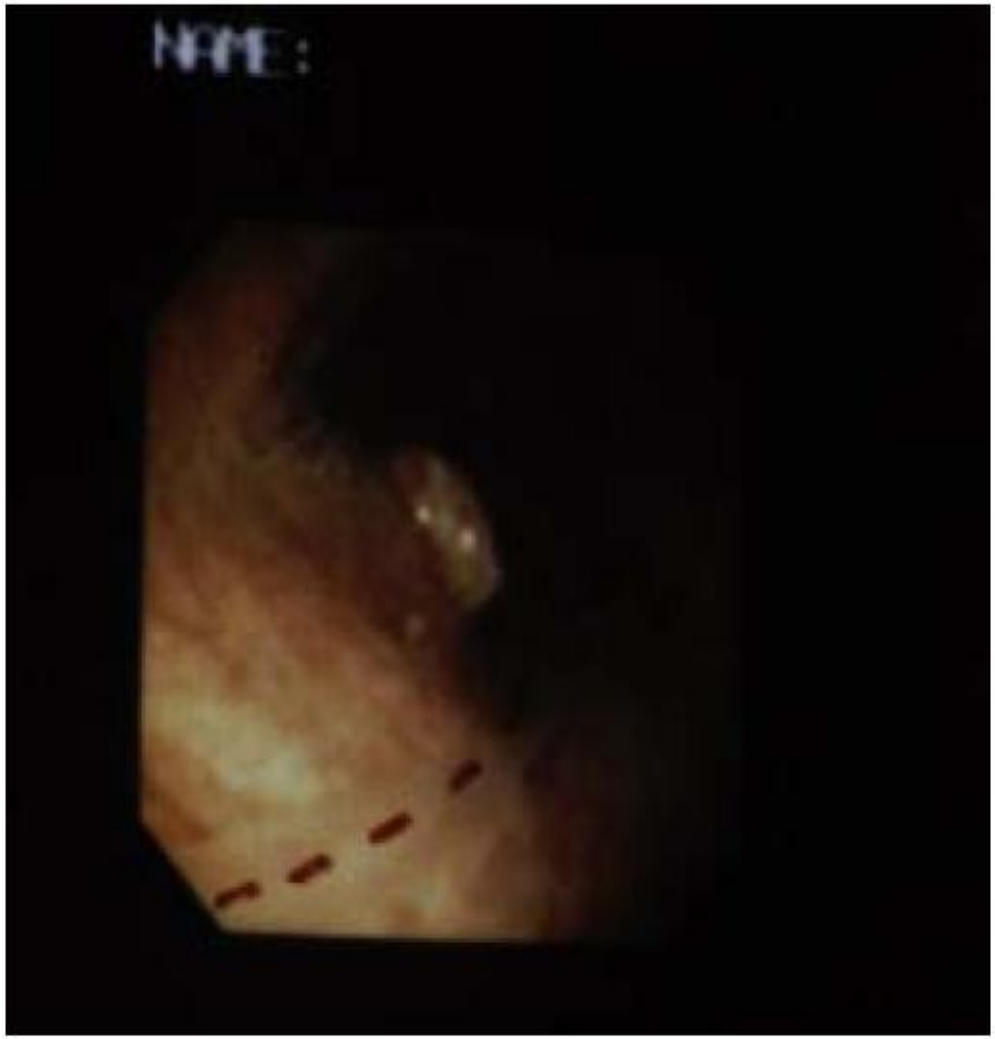
Small tumors



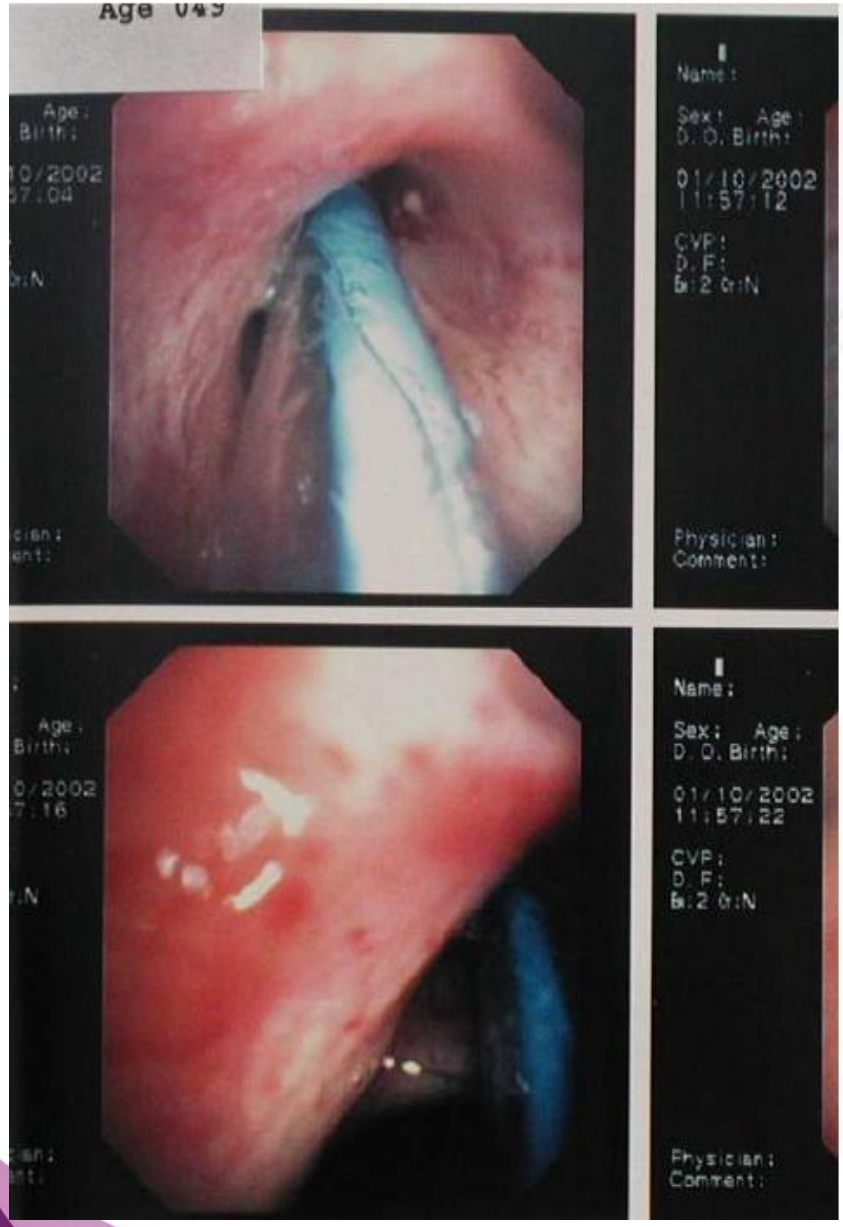
Curative intent results

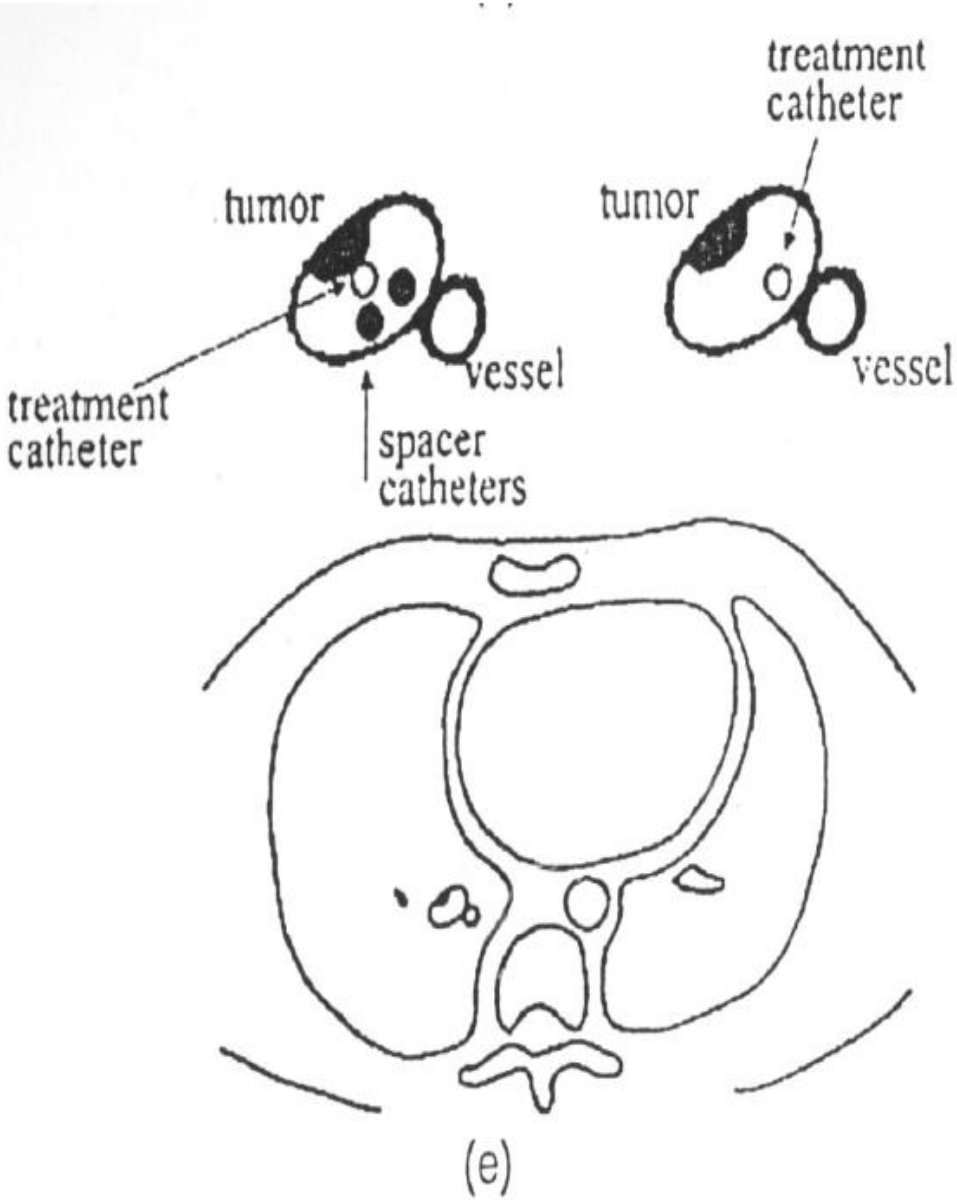
	#pts	Dose/fr	local Control	Survival @ years
Speiser	151	3 x 7.5Gy / 5-10mm	80%	
Trédaniel	29	6 x 7Gy / 10mm	72%	55% @ 2
Hennequin	69	6 x7Gy / 10mm	78%	51% @ 3
Taulelle	22	3-4 x 8-10Gy / 10mm	95.5%	71% @ 1
Pérol	19	3-5 x 7Gy / 10mm	83%	58% @ 2
Marsiglia	34	6 x 5Gy / 10mm	94%	78% @ 2
Peiffert	35	6x 5Gy / 10mm	94.3%	54% @ 2

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%

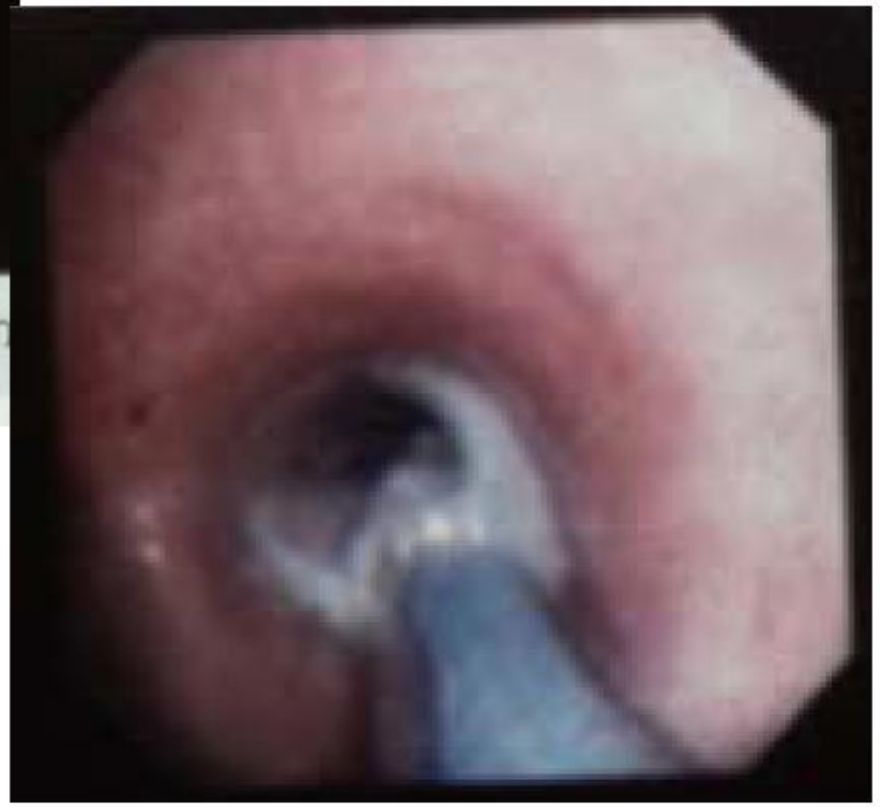
Description / spacer

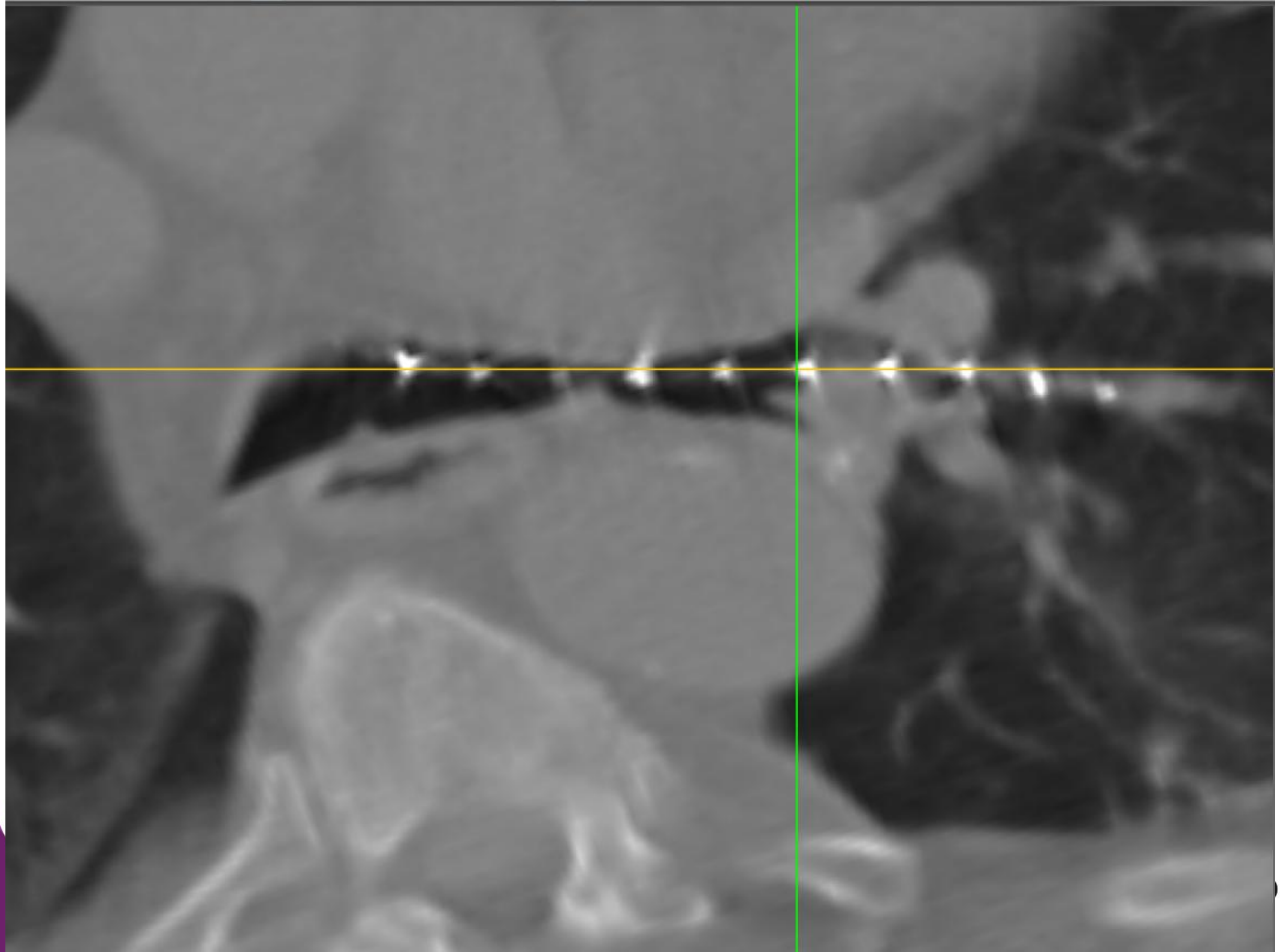


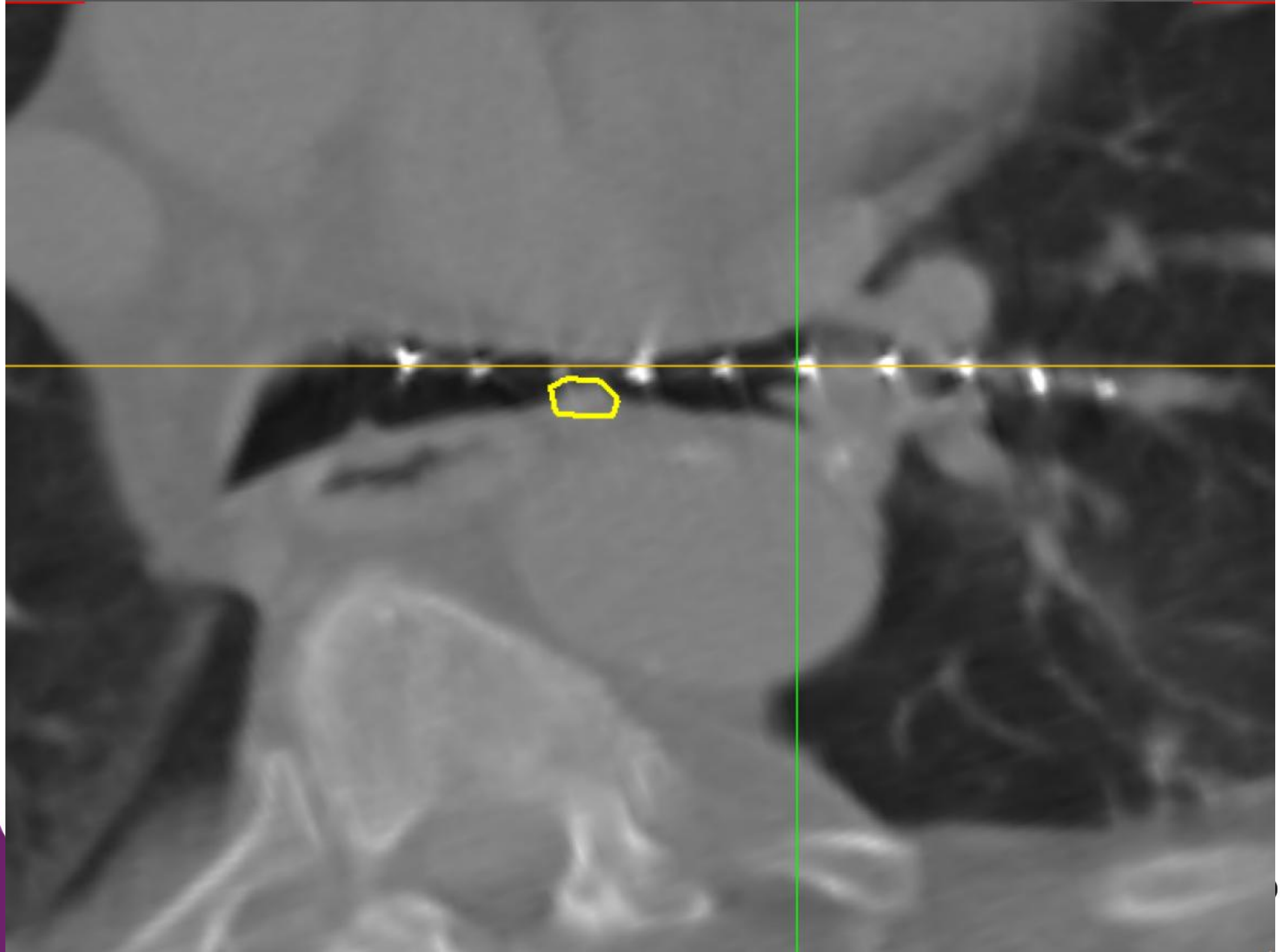


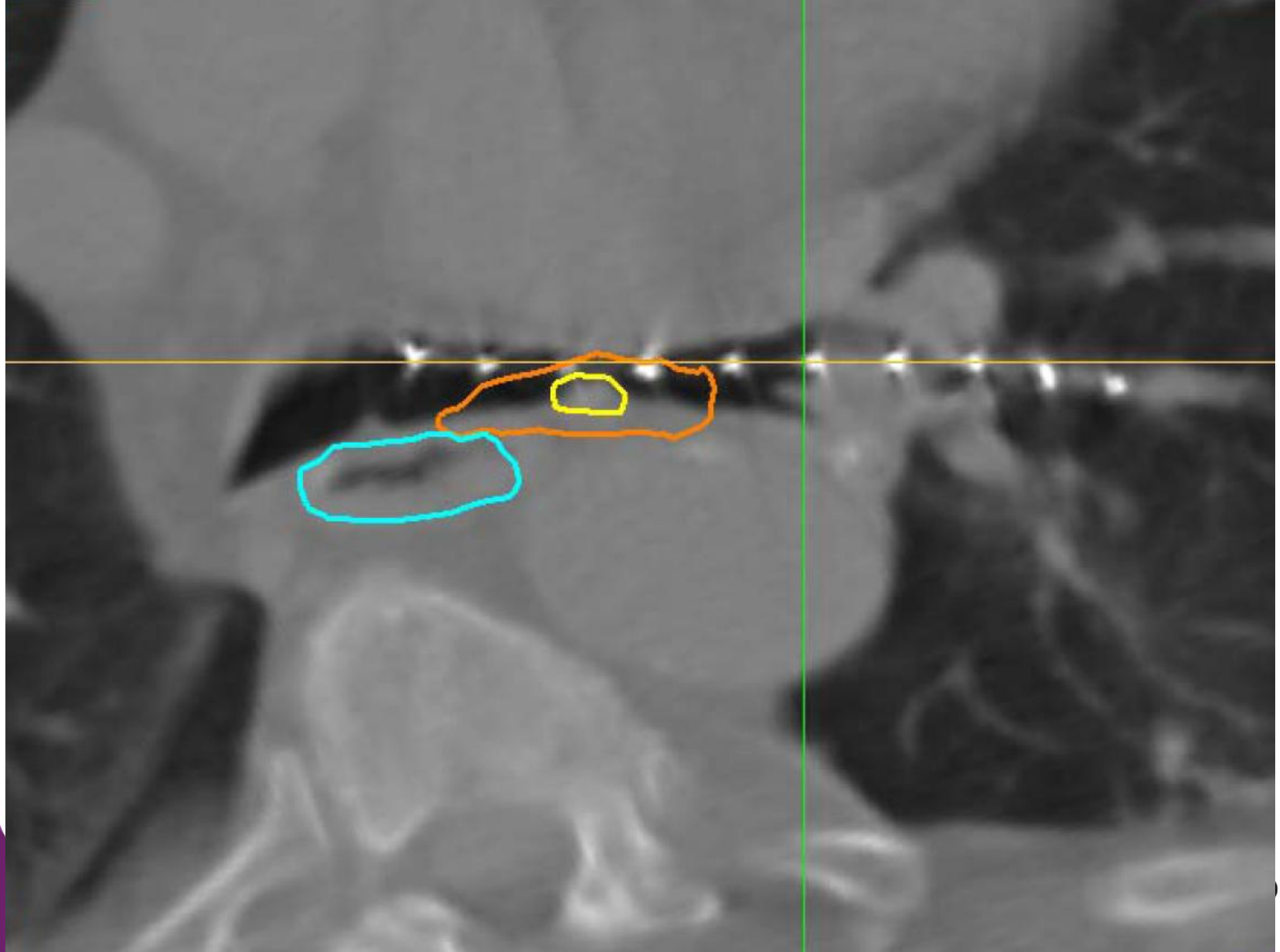
Technique

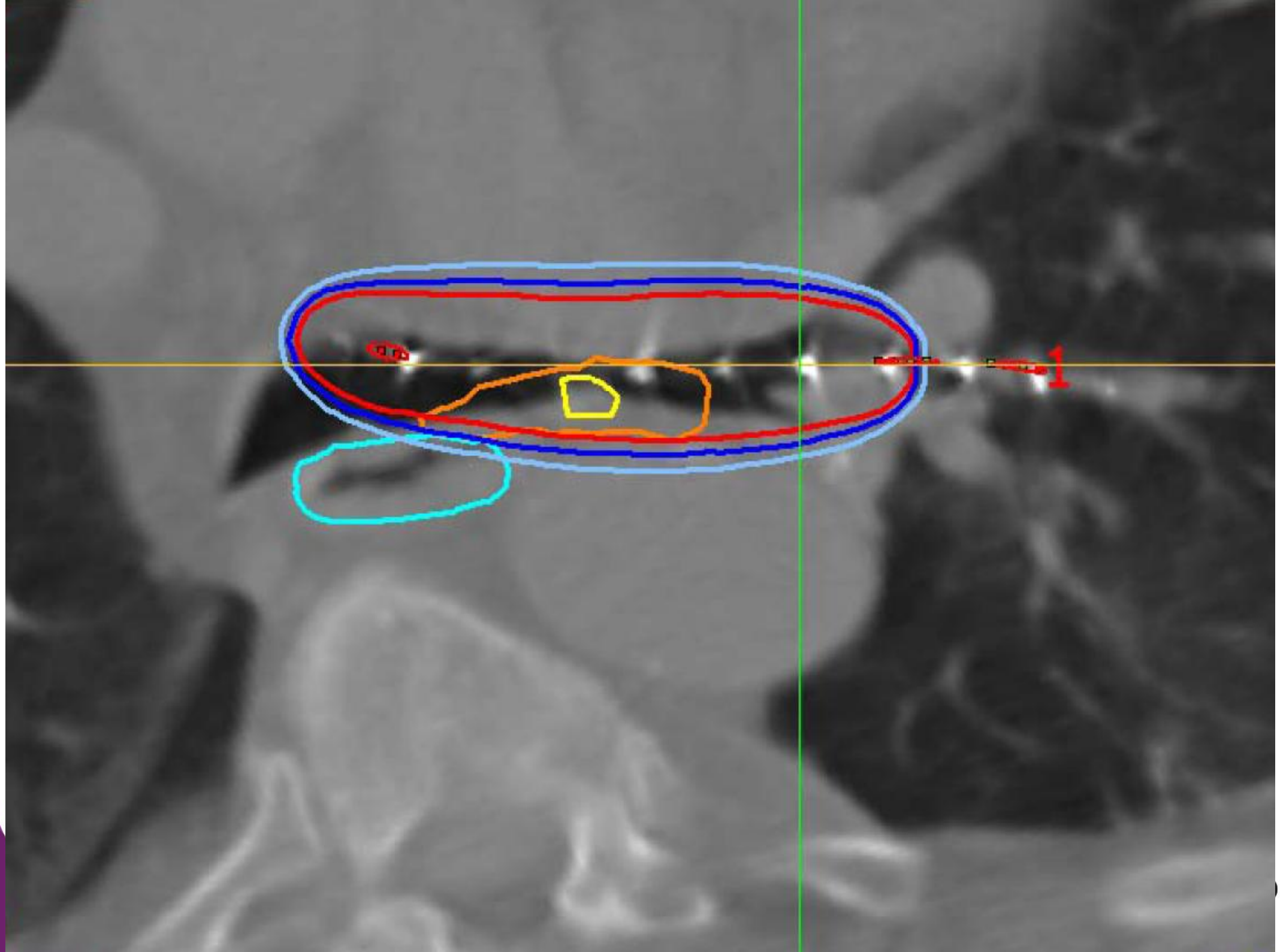
Centering system



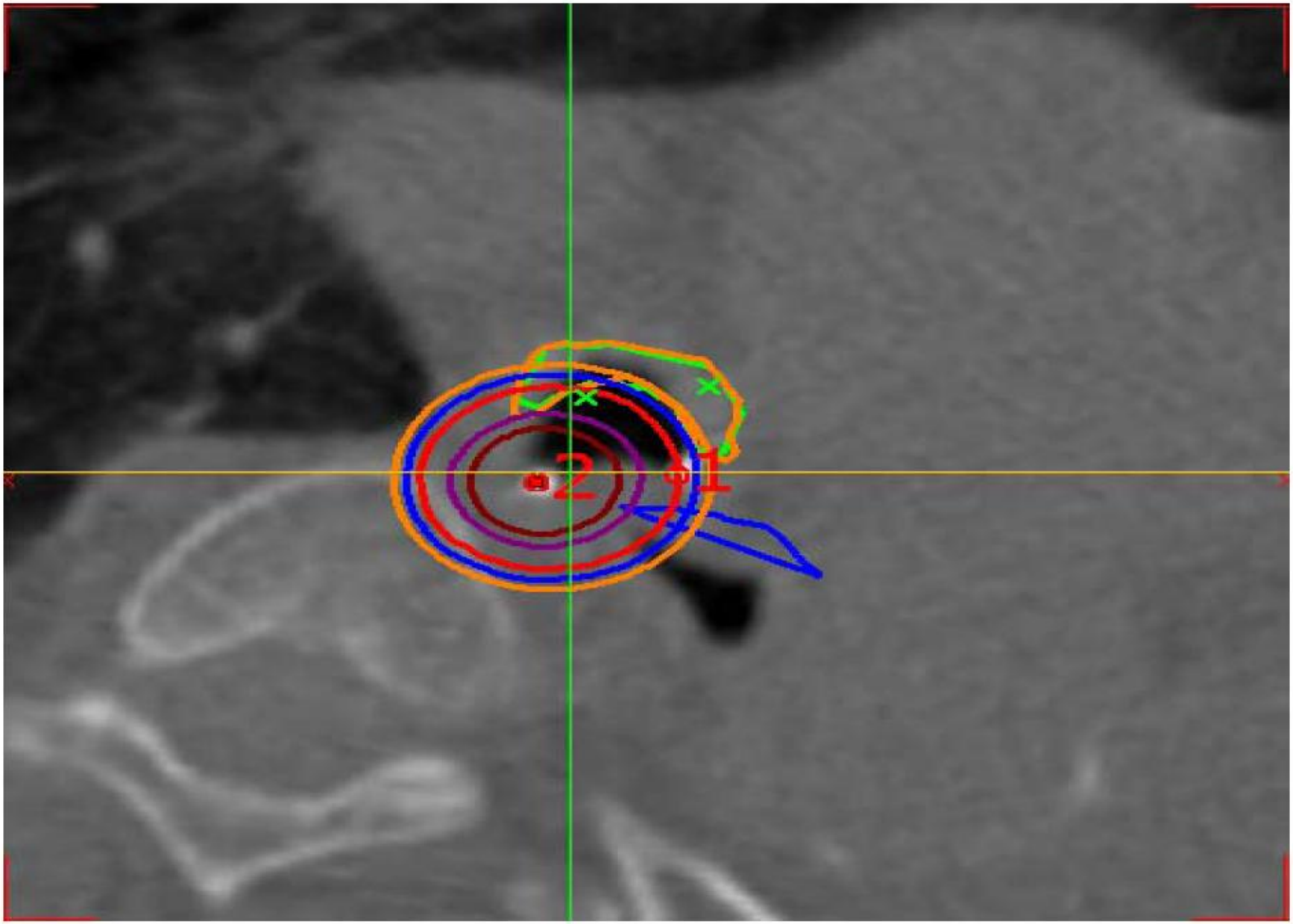







1

Een catheter 6 Gy op 1 cm



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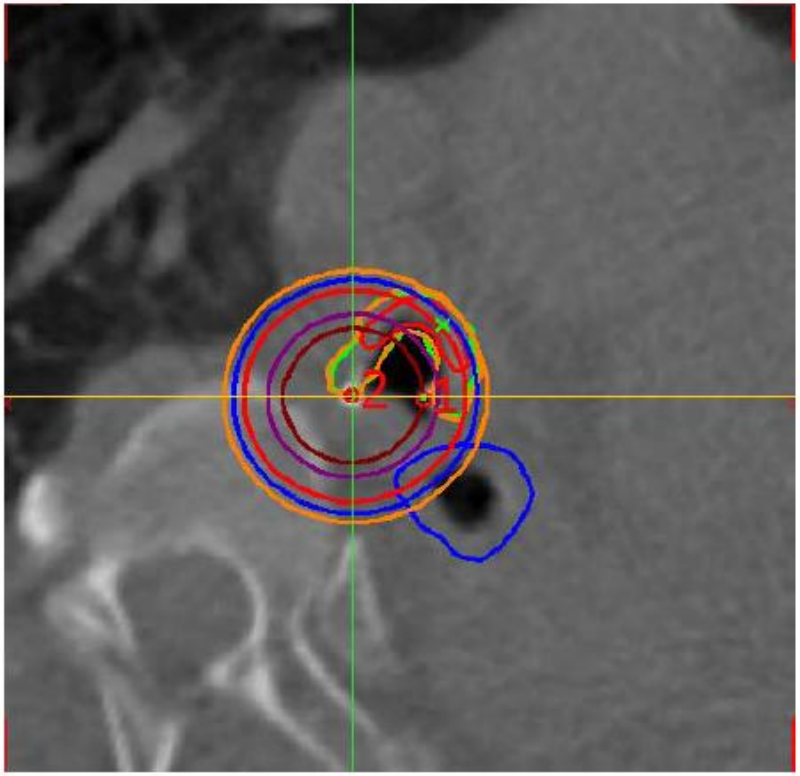
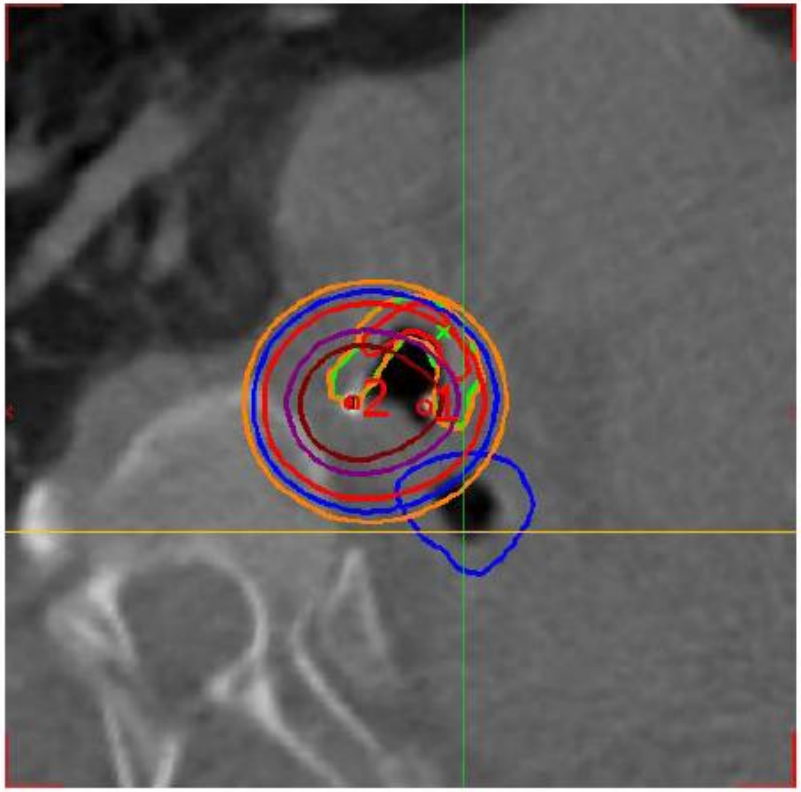
10 Gy GTV

1 catheter 8 Gy CTV 2 catheters





Slokdarm 2cc < 6,5 Gy

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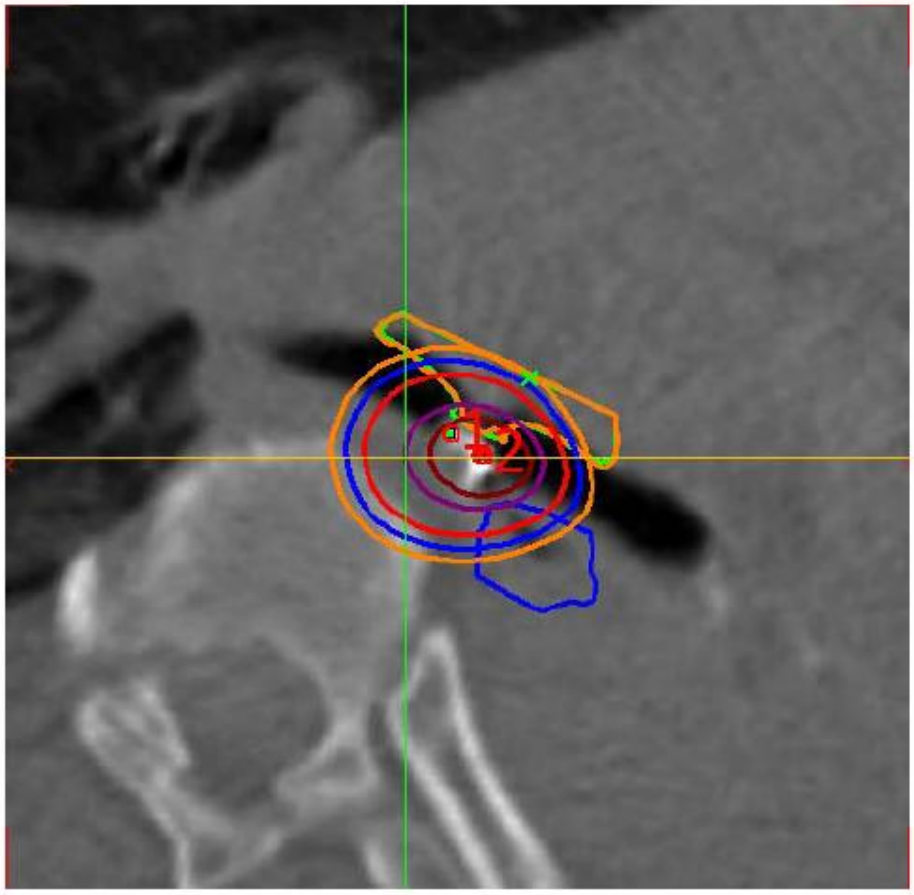
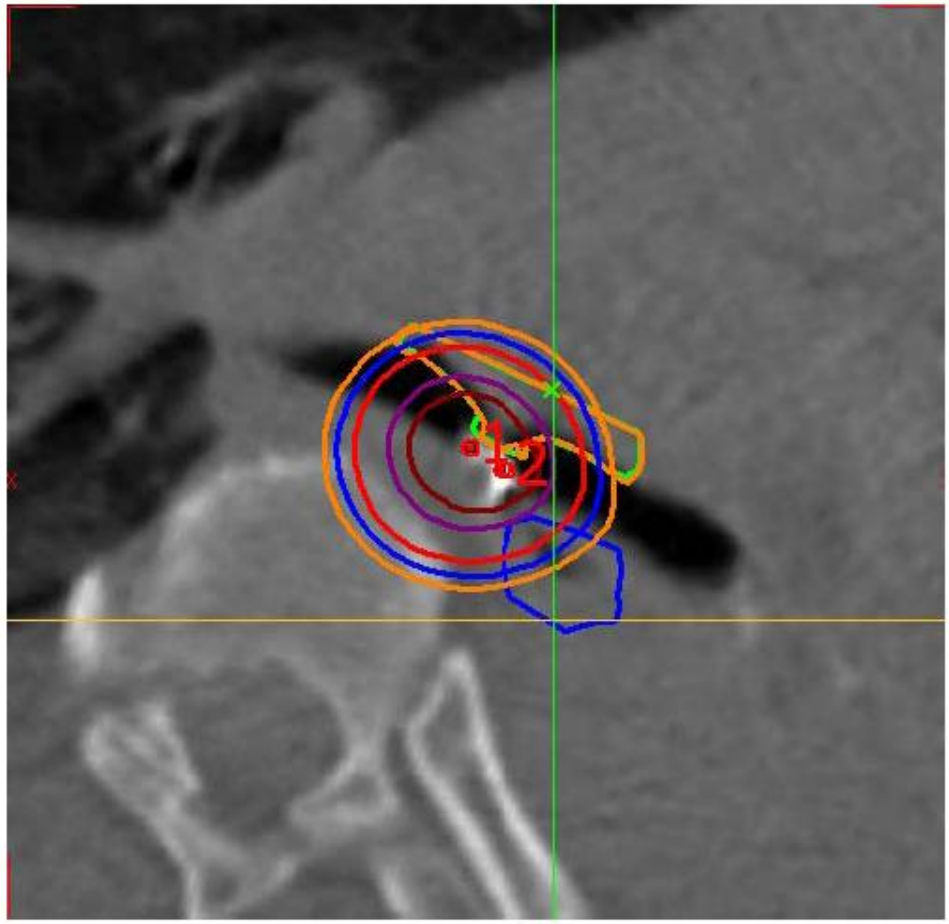
10 Gy GTV

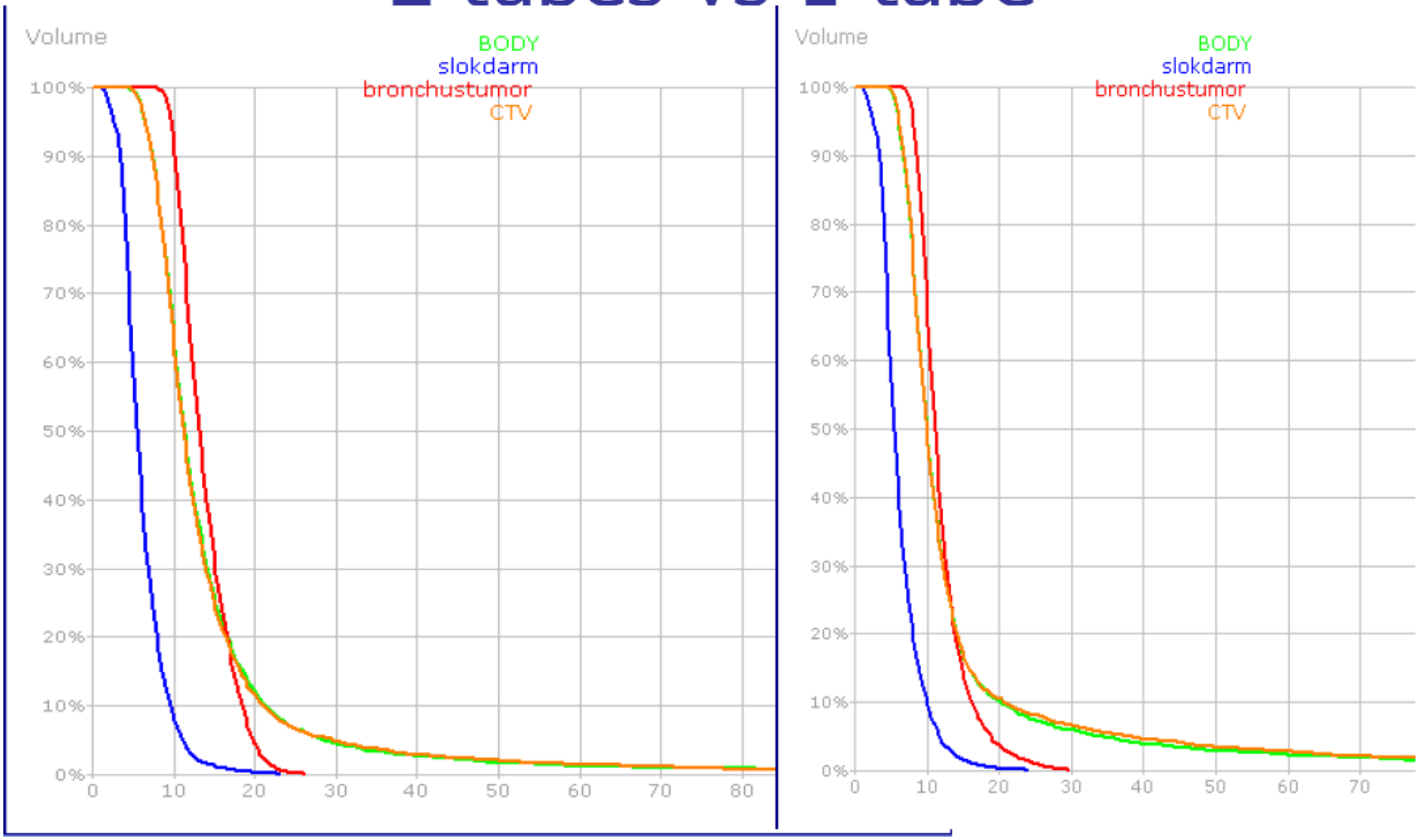
1 catheter 8 Gy CTV 2 catheters





2cc Slokdarm < 6.5 Gy

3D conformal
2 tubes vs 1 tube



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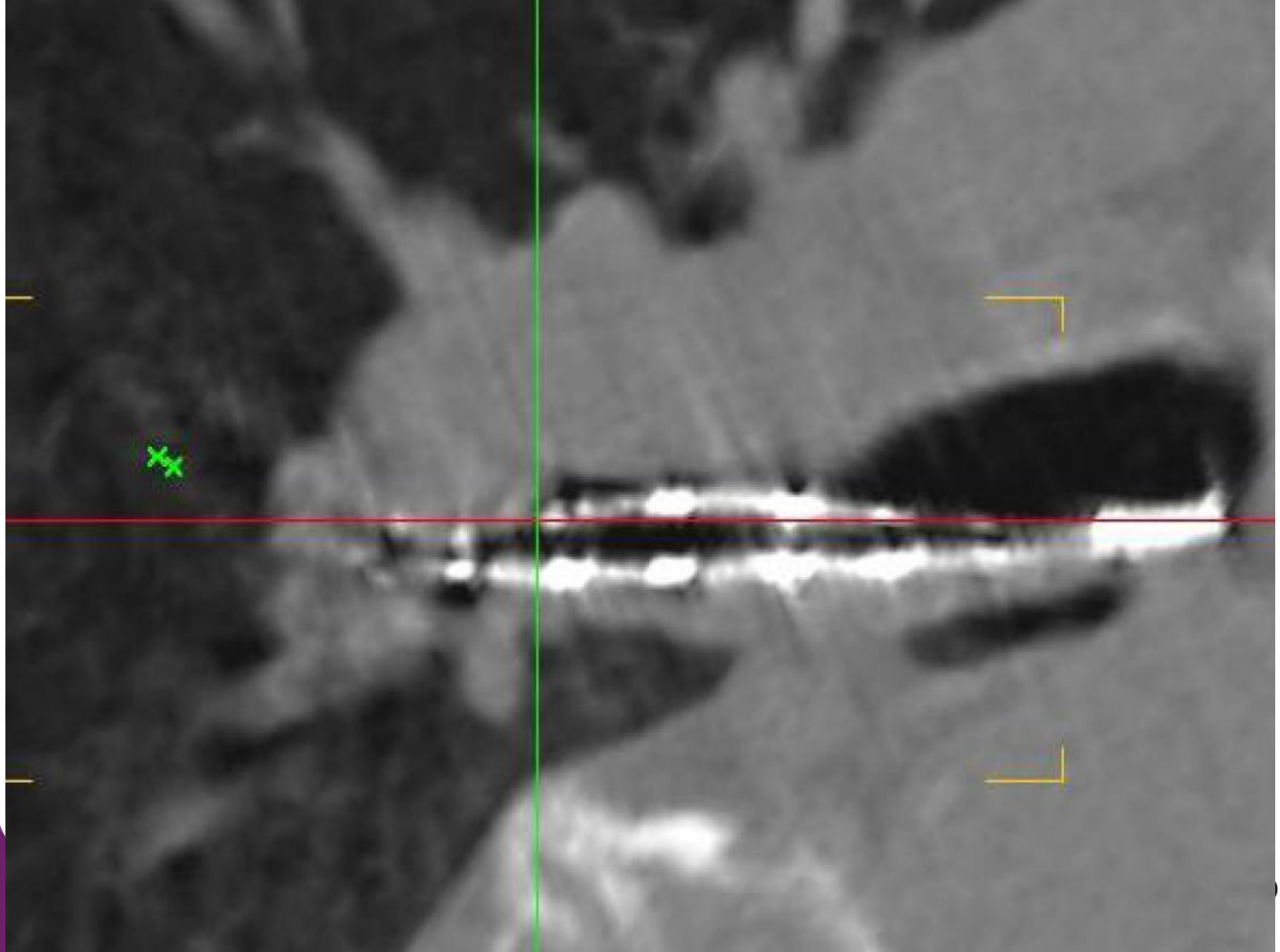

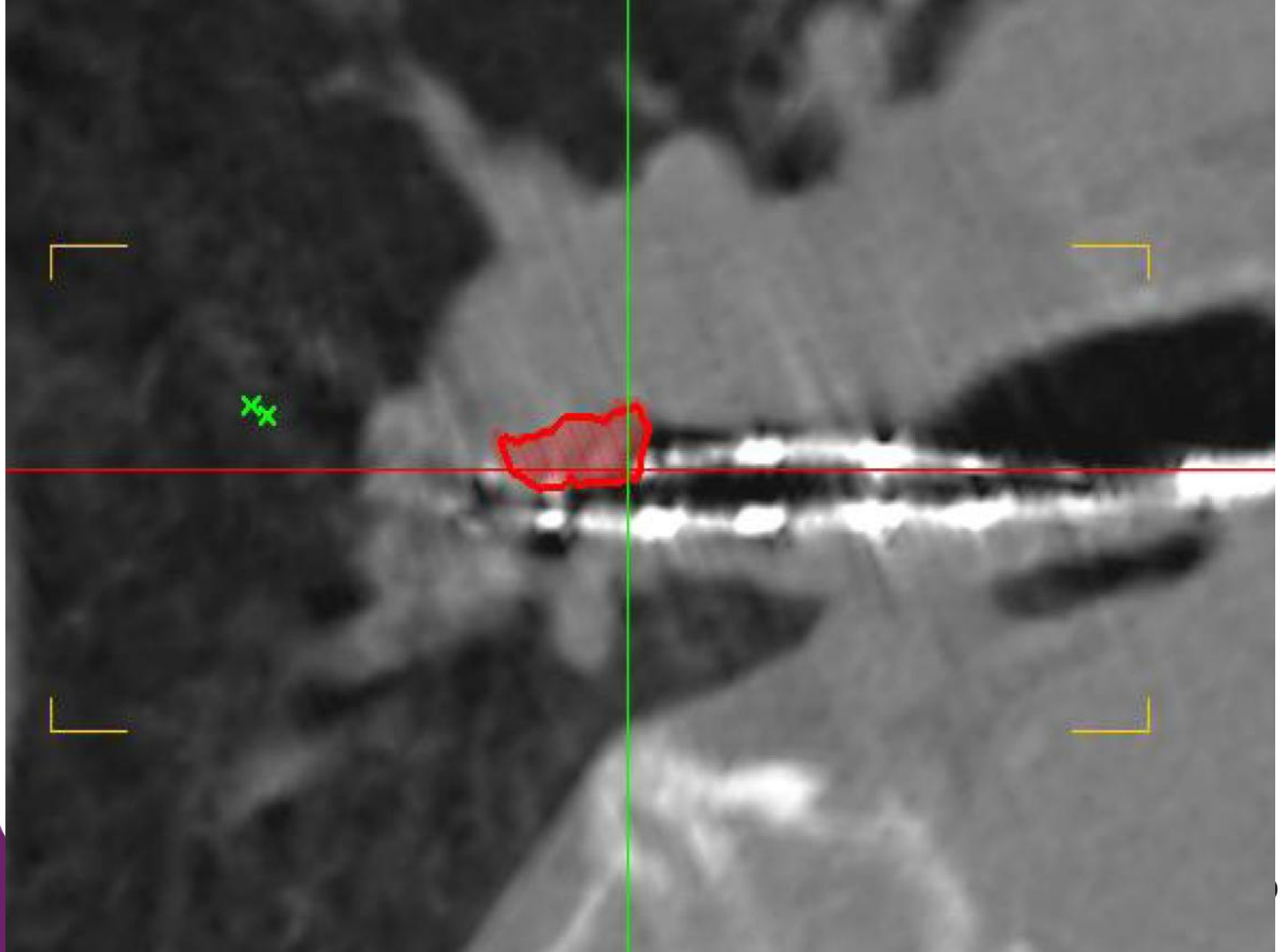

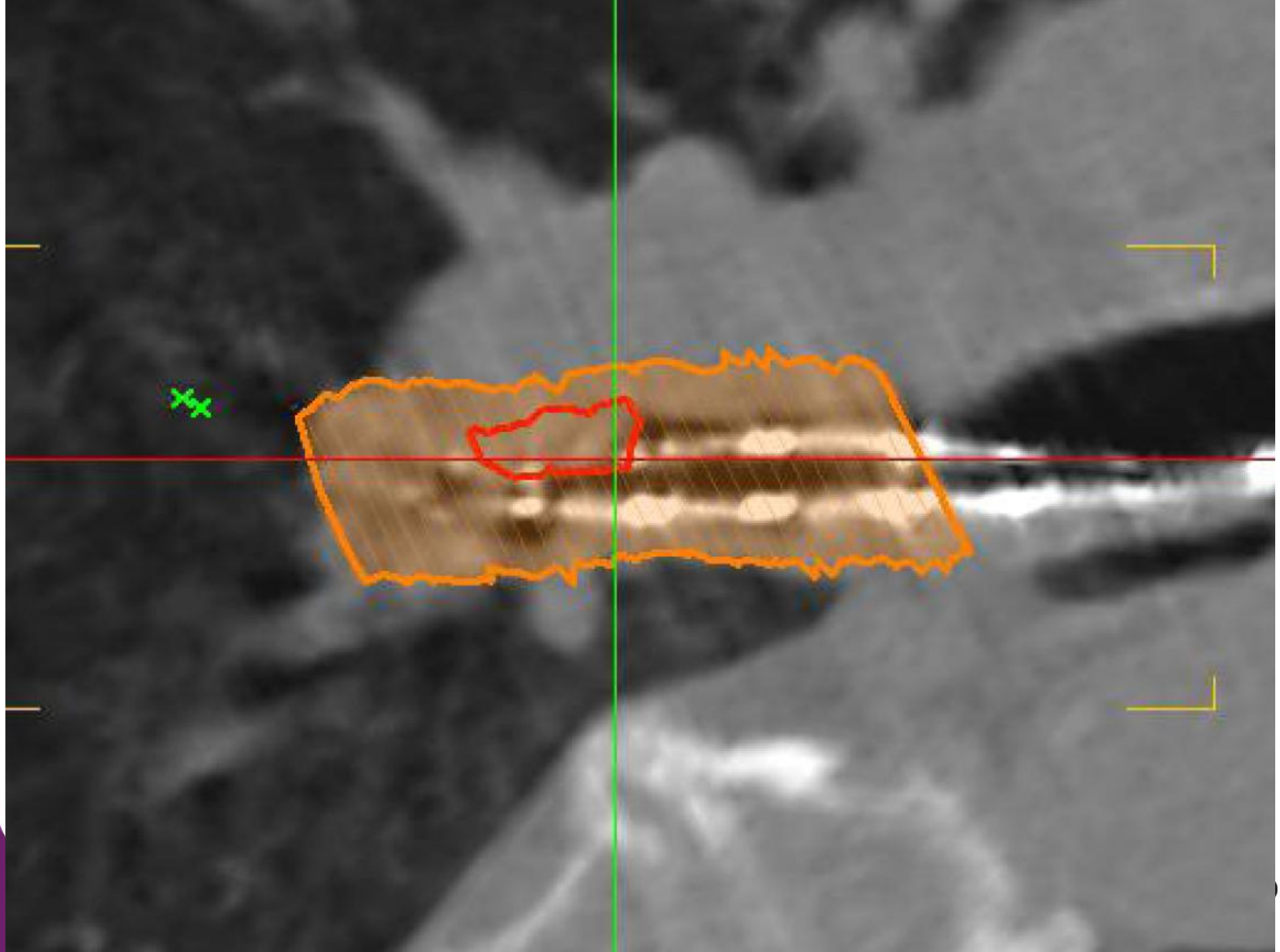

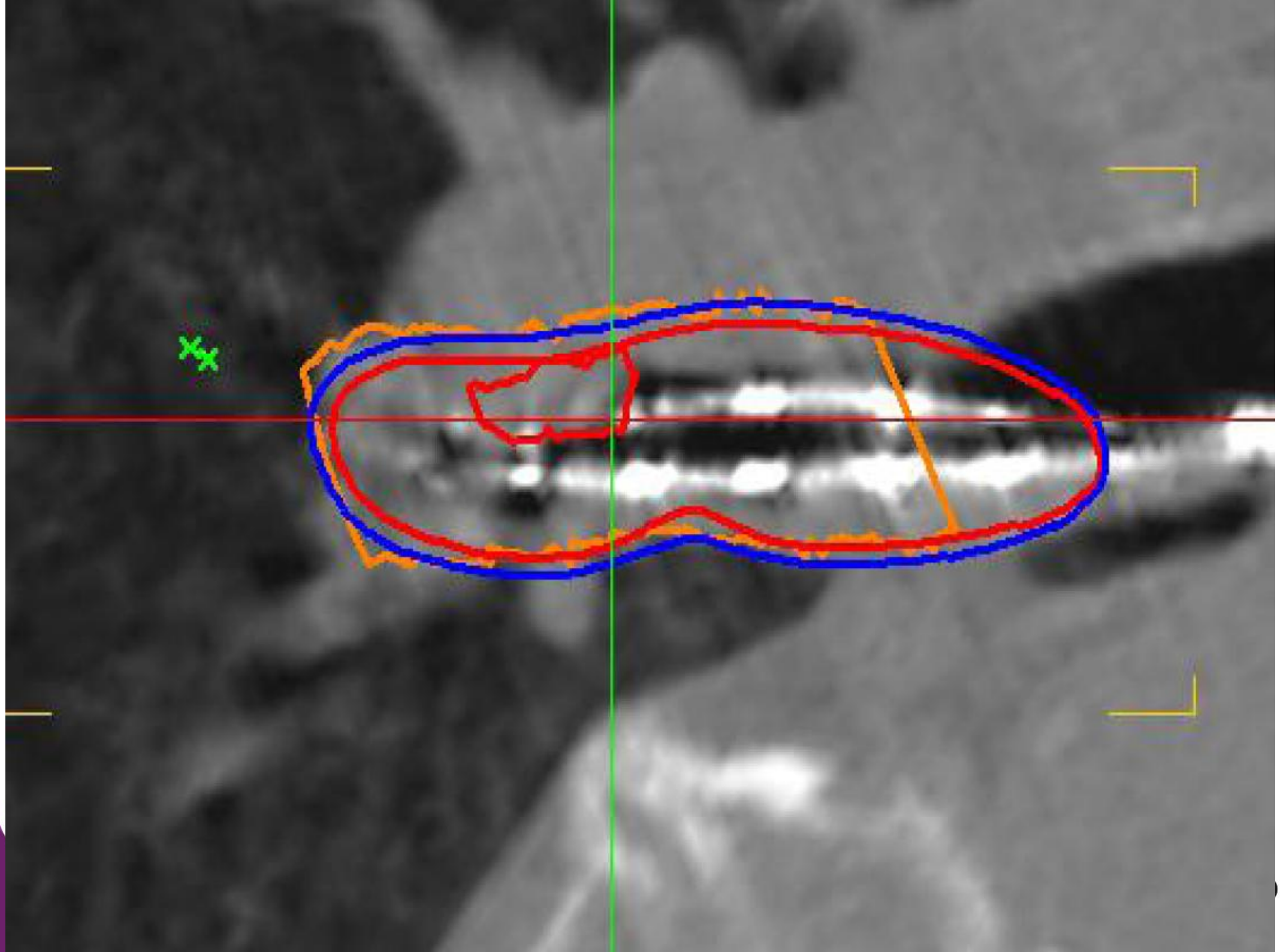

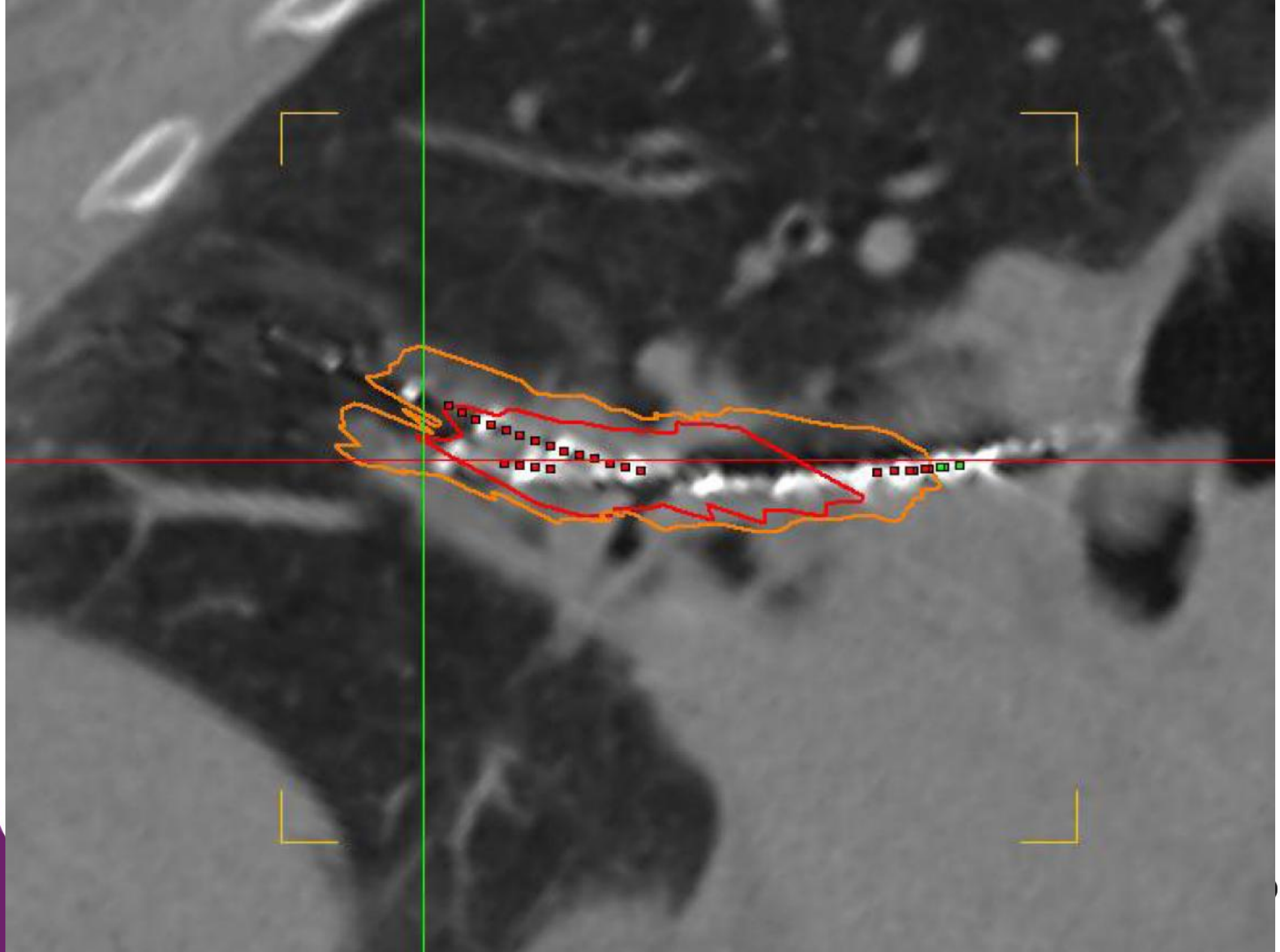

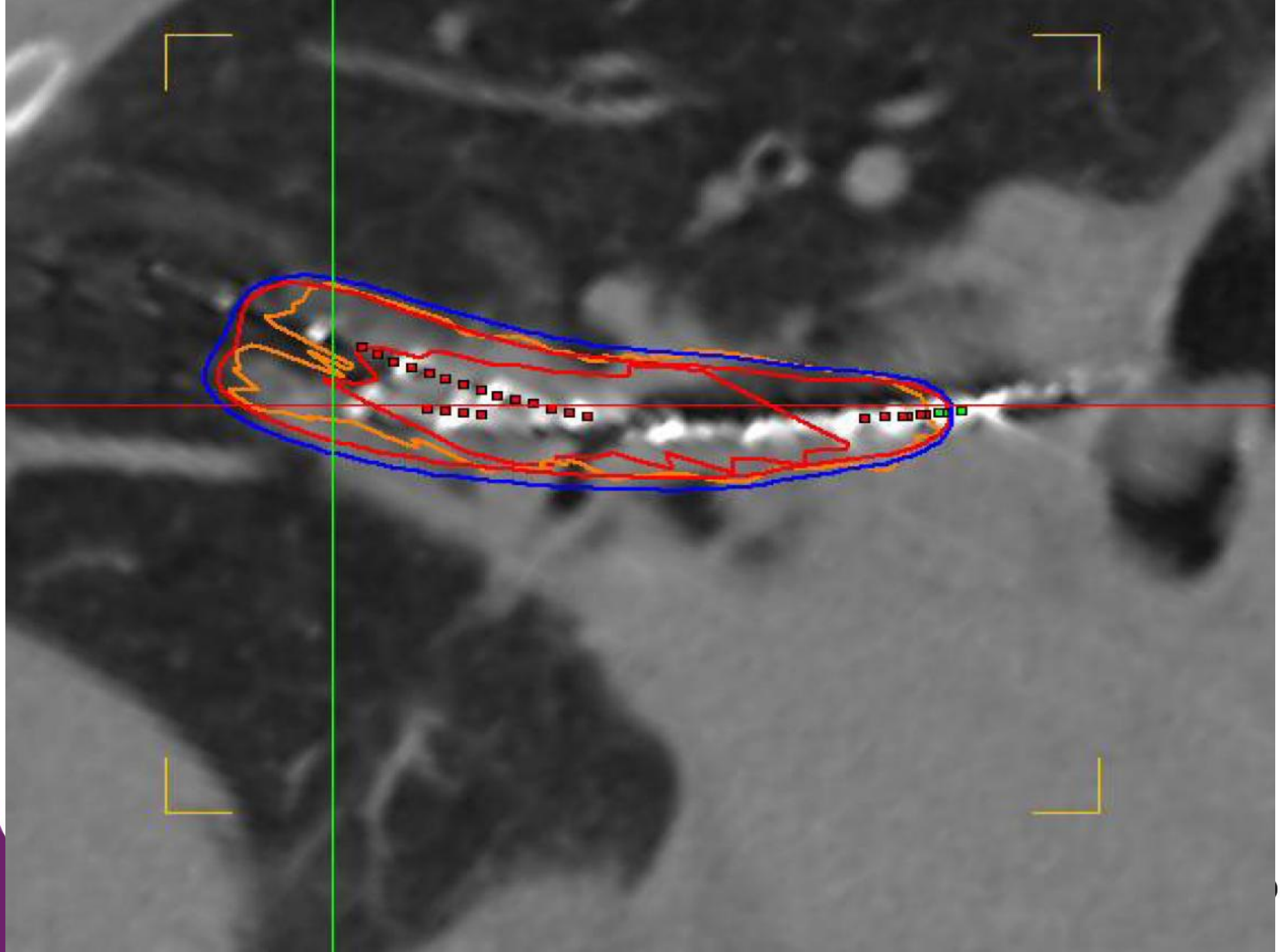

UZL series Bronchusca
3 D Image Guided BT

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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WWW.ESTRO.ORG/SCHOOL

Dose Calculation
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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Topics

- **Exposure, Kerma**
- Air Kerma-rate constant
- Reference Air Kerma-rate/Source Strength
- Dose Calculation

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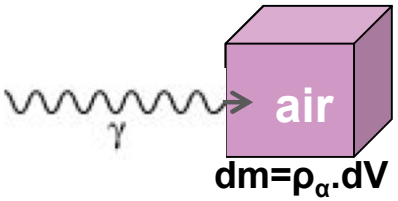
Exposure X

Let us consider a volume element dV filled by air of mass dm at a point in a photon radiation field. If dQ is the absolute value of the total charge of the ions of one sign produced in air when all the electrons and positrons liberated or created by photons in the air filled volume element dV are completed stopped in this volume, then the *exposure* X (C.kg^{-1}) is defined as



$$X = \frac{dQ}{dm} = \frac{1}{\rho_a} \cdot \frac{dQ}{dV}$$

where ρ_α is the density of air in volume dV. It has to be mentioned that according to this definition ionisation produced by Auger electrons are included in dQ where ionisation produced by radiative processes such as bremsstrahlung and fluorescence photons is not included in dQ.
The SI unit of Exposure is 1 C.kg^{-1}.

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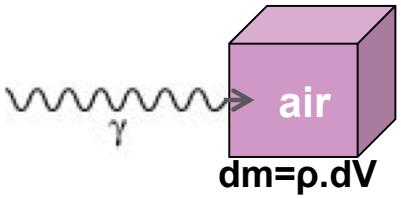
Kerma K

Let us consider a volume element dV filled by a material of mass dm at a point in photon radiation field. The quantity *kerma* refers to the kinetic energy of charged particles such as electrons and positrons that have been liberated by uncharged particles (photons). Kerma does not include the energy that has been expended against the binding energies of these charged particles even if this is usually a relatively small component. The name kerma for this quantity is derived from the Kinetic Energy Released per unit Mass.

If dE_{tr} is the sum of the initial kinetic energies of all charged particles liberated by uncharged particles within a volume element dV of a material containing a mass dm=ρ.dV of that material, then the *kerma* K (J.kg^{-1}) is given by



$$K = \frac{dE_{tr}}{dm} = \frac{1}{\rho} \cdot \frac{dE_{tr}}{dV}$$

The name of the SI unit for kerma is gray (Gy): 1 Gy = 1 J.kg^{-1}. Considering dE_{tr} it has to be mentioned that this includes also the kinetic energy of Auger electrons.

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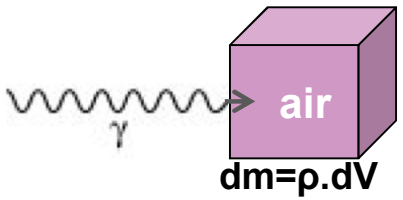
Kerma K

Considering now uncharged particles (photons) of a given energy distribution, then the kerma K is given according to



$$K = \int_E \Phi_E . E . \left(\frac{\mu_{tr}}{\rho} \right)_E . dE = \int_E \Psi_E . \left(\frac{\mu_{tr}}{\rho} \right)_E . dE$$

$$K = \frac{dE_{tr}}{dm} = \frac{1}{\rho} . \frac{dE_{tr}}{dV}$$

where Φ_E and Ψ_E are the energy distribution of fluence and energy fluence of the photons respectively.

$(\mu_{tr}/\rho)_E$ is the mass energy transfer coefficient of the material under consideration for photons of energy E.

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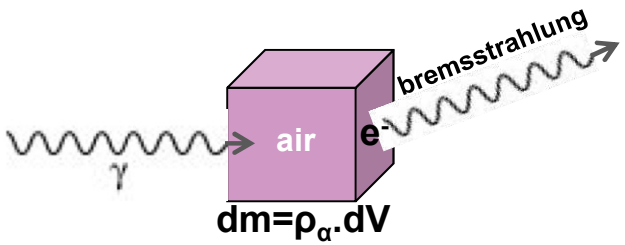
Exposure X and Air Kerma K_α

When the volume element dV in the radiation field is filled by air then we have the air kerma, K_α.

Then the following relationship between exposure X and air kerma K_α exists



$$X = K_a$$

$$X = \frac{dQ}{dm}$$

$$K = \frac{dE_{tr}}{dm}$$

e is the elementary charge and W is the mean energy expended in air per ion pair formed, W/e = 33.97 $J.C^{-1}$.

$\bar{g}_a$ **Is the mean value of g_α, the fraction of the energy of the electrons liberated by photons in air that lost to radiative processes (bremsstrahlung and fluorescence, g_α < 0.3% for E ≤ 1MeV).**

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Topics

- Exposure, Kerma
- **Air Kerma-rate constant**
- Reference Air Kerma-rate/Source Strength
- Dose Calculation

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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 a 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, then the *air kerma-rate constant* Γ_δ of that radionuclide is defined as:

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

If the unit gray (Gy) for the kerma and becquerel (Bq) for the activity are used, then the unit of the air kerma-rate constant is $Gy.s^{-1}.Bq^{-1}.m^2$.

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Air Kerma-rate constant Γ_δ

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

Photons are here considered to be gamma rays, characteristic x rays and internal bremsstrahlung.

The air kerma-rate constant is defined for an ideal point source and is characteristic for each radionuclide.

Considering a real source of finite size, attenuation and scattering in the source itself occur and annihilation radiation and external bremsstrahlung may be produced.

Considering the energy cut-off δ its value depends on the specific application. For simplification and standardisation it is recommended that δ is expressed in keV. The notation Γ_{10} for the air kerma-rate constant means that a value of 10 keV for the energy cut-off δ is used.

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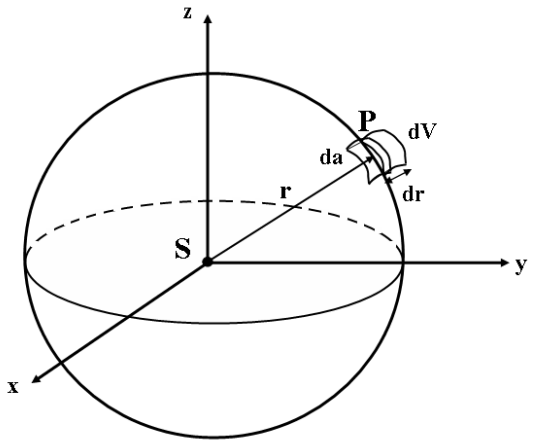
Air Kerma-rate constant Γ_δ

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



Ideal point source S of a specific radionuclide positioned at a given position in free space with activity A

Air-filled volume element dV at the point P in a radial distance r from the point source

The source is emitting a single photon of energy E per disintegration (E > δ)

The energy fluence rate of photons at P is given by:

$$\dot{\Psi} = \underbrace{\left(\frac{da}{4\pi \cdot r^2}\right)}_{\text{isotropic emission}} \cdot \left(\frac{1}{da}\right) \cdot A \cdot E = \left(\frac{1}{4\pi \cdot r^2}\right) \cdot A \cdot E$$

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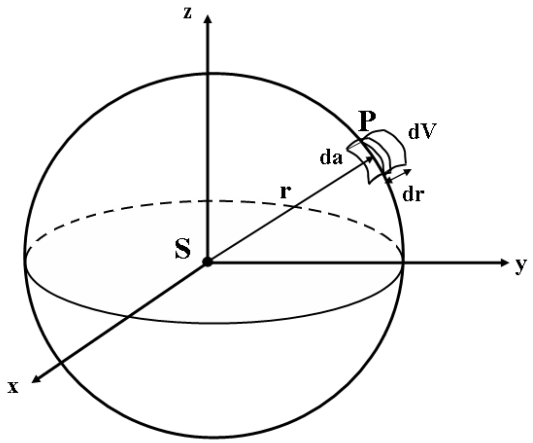
Air Kerma-rate constant Γ_δ

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



Consequently, and according to definition of air kerma rate at point P, is:

$$\dot{K}_\delta = \dot{\Psi} \cdot \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha,E} = \left(\frac{1}{4\pi \cdot r^2}\right) \cdot A \cdot E \cdot \left(\frac{\mu_{tr}}{\rho}\right)_{\alpha,E}$$

with

$$\dot{\Psi} = \left(\frac{da}{4\pi \cdot r^2}\right) \cdot \left(\frac{1}{da}\right) \cdot A \cdot E = \left(\frac{1}{4\pi \cdot r^2}\right) \cdot A \cdot E$$

Combining above equations, the air kerma-rate *constant* Γ_δ for the mono-energetic point source is given by (multiplication by r² and division by A)**:**

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

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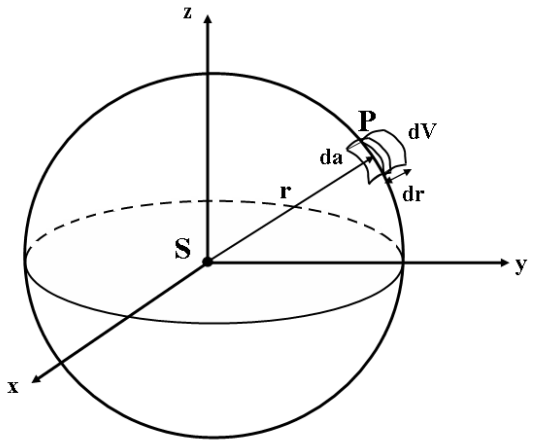
Air Kerma-rate constant Γ_δ

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



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

For the case of a point source with a known photon spectrum the above expression takes the following form:

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

where n_i is the number of photons emitted with energy E_i per disintegration and $(\mu_{tr}/\rho)_{\alpha,Ei}$ is the mass energy transfer coefficient of air for the photon energy E_i.
i is the index over all emitted photon energies E_i with $E_i > \delta$.

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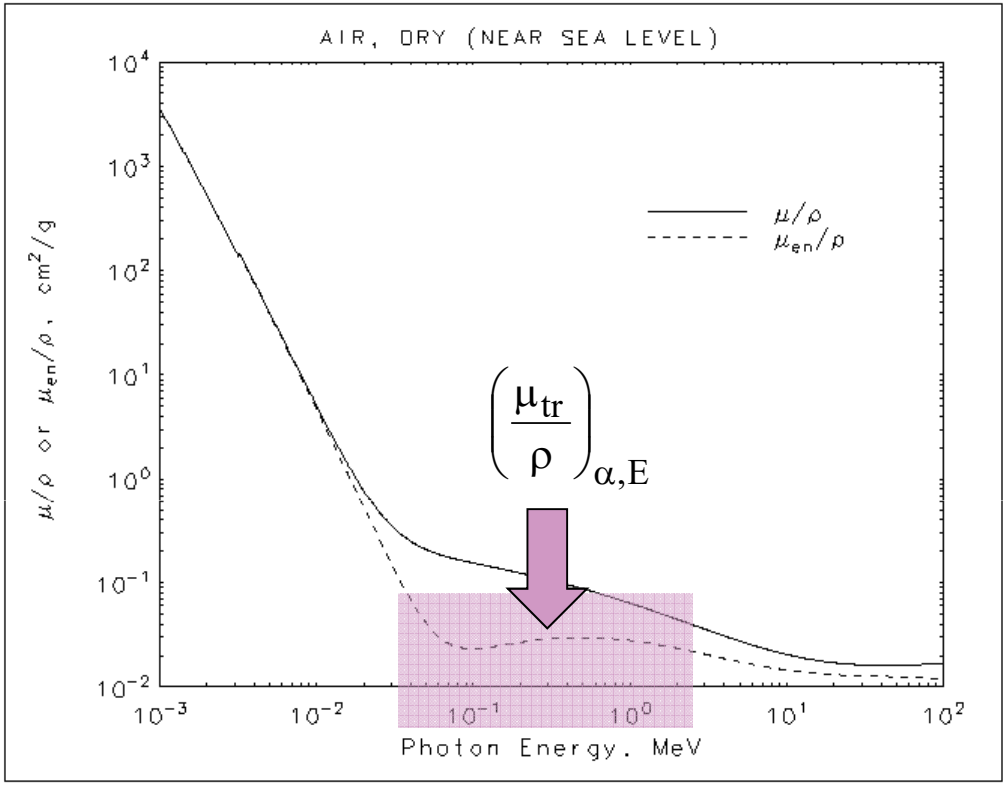
Air Kerma-rate constant Γ_δ

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

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



Γ_δ for ^{137}Cs = 0.0771 µGy h^{-1} MBq^{-1} m^2

Γ_δ for ^{60}Co = 0.3059 µGy h^{-1} MBq^{-1} m^2

Γ_δ for ^{60}Co is ≈ 4x of that of ^{137}Cs

E for ^{60}Co is ca. double of that of ^{137}Cs ?

^{60}Co: 2.0 photons per decay/disintegration
^{137}Cs: 0.9 photons per decay/disintegration

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Air Kerma-rate constant Γ_δ

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

Table 5.12 Physical characteristics of radionuclides used in brachytherapy. Photon energy ranges, mean and effective photon energies are accord… 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 radionuclid… urces 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 **0.73**	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 **0.9**	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 **2.0**	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 **1.0**	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 **1.4**	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 **2.3**	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 **0.8**	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 **0.06**	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 **3.3**	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]

X.X average number of photons emitted per decay with E > 10keV

Topics

- Exposure, Kerma
- Air Kerma-rate constant
- **Reference Air Kerma-rate/Source Strength**
- Dose Calculation

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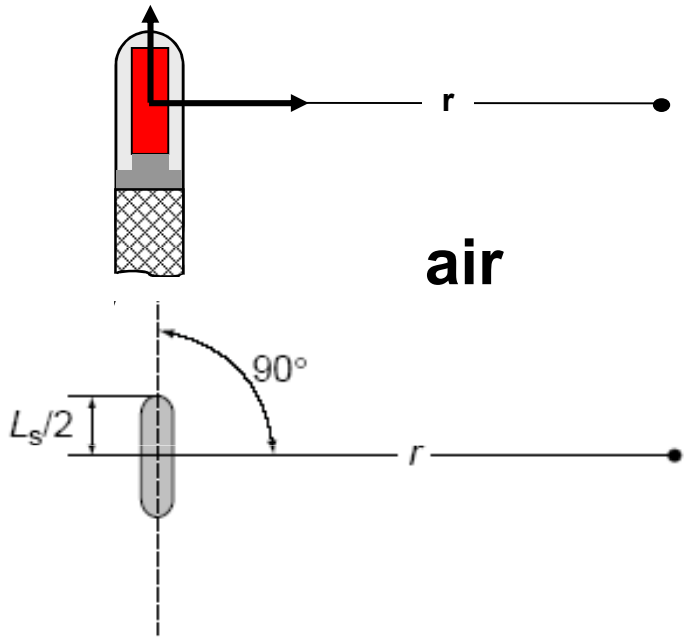
Reference Air Kerma Rate / Source Strength

In our days the strength of the source is defined in terms of energy deposition per unit time at a specific distance in air:

Air Kerma Rate (in air) in μGy . h^{-1} at 1 m



For linear sources this can be expressed in Air Kerma Rate units per unit of length

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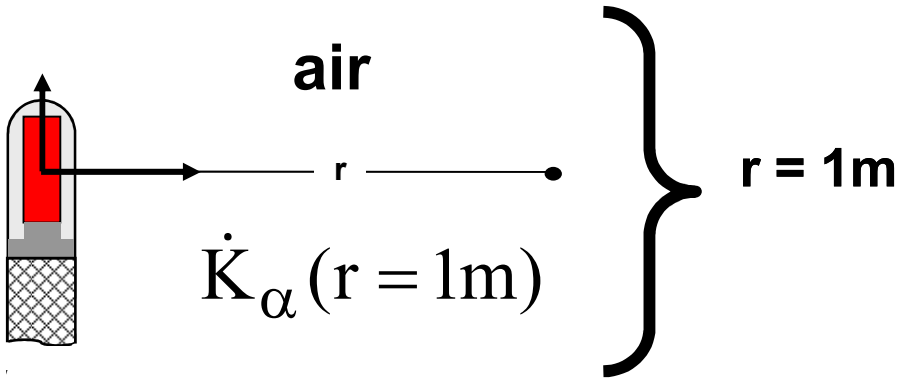
Reference Air Kerma Rate / Source Strength

Reference Air Kerma Rate $K_R = K_{\alpha,\alpha}(r=1m)$ in $\mu Gy \cdot h^{-1}$ at 1 m



The reference air kerma rate of a source is defined as the air kerma rate in air at a reference distance of one metre from the centre 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 centre to the reference point at one metre has to be at right angles to the long axis of the source.

In 1985, the ICRU Report 38[5] defined as an emission specification quantity for γ-rays emitting brachytherapy sources the *reference air kerma rate*.

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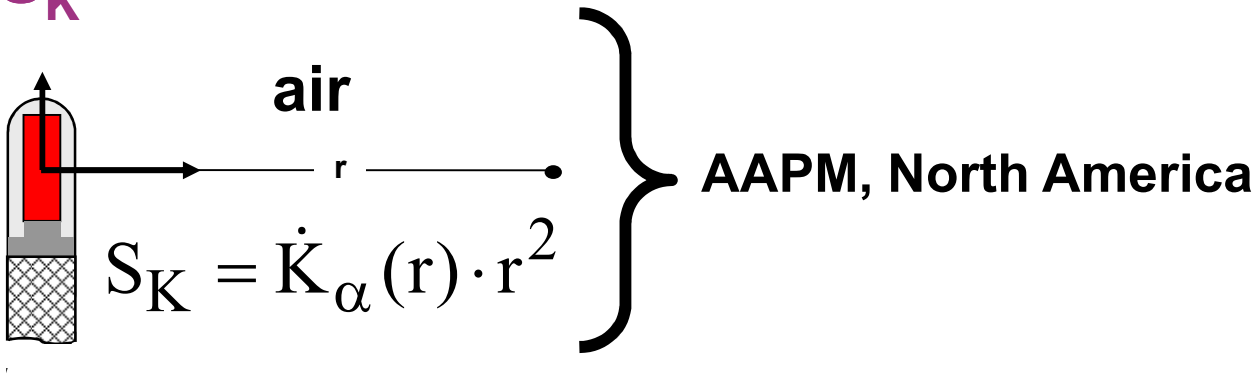
Reference Air Kerma Rate / Source Strength

Air Kerma Strength S_K



The American Association of Physicists in Medicine in their Report No. 21 by the AAPM Task Group No 32 introduced in 1987 the idea for the specification of brachytherapy sources in terms of strength. 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 centre along the perpendicular bisector and the square of the distance r.

The distance r must be chosen to be large enough so that the source can be treated ***as a point source*** and so that the ***finite*** **dimensions of the detector** used for the measurement have no influence on the result!

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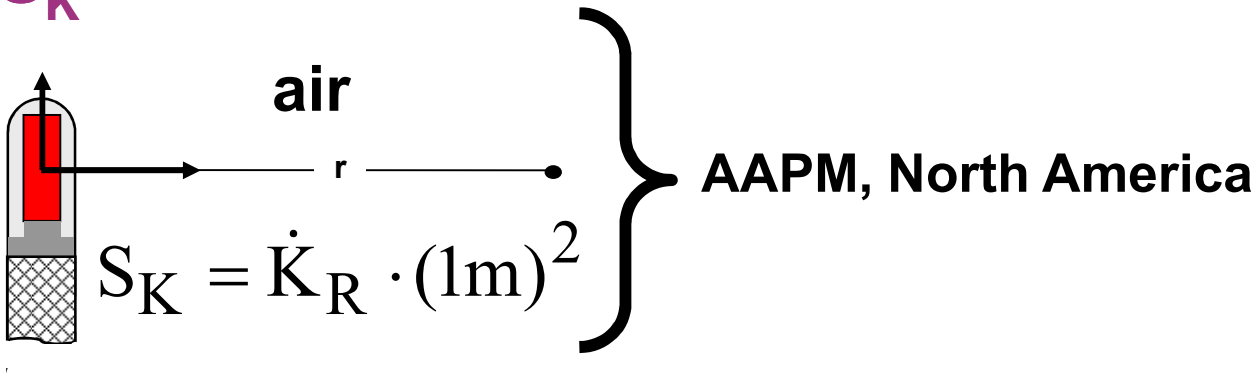
Reference Air Kerma Rate / Source Strength

Air Kerma Strength S_K



The recommended unit for air kerma strength is μGy.m².h^{-1} and has been denoted by the symbol U:

$$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$$

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Reference Air Kerma Rate / Source Strength

The air kerma rate based source strength specifications, reference air rate kerma K_R and air kerma strength S_K, are a measure of the radiation field intensity in free space around brachytherapy sources, considering *a priori* the effects of:

(a) source and

(b) source encapsulation

and making no use of intermediate constants.

TABLE 7.1

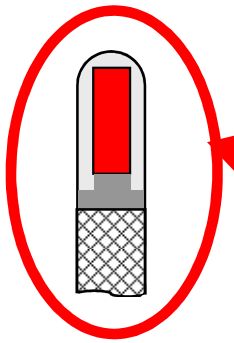
Units and Unit Conversion Factors for Reference Air Kerma Rate and Air Kerma Strength

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 $Gy\ s^{-1}\ Bq^{-1}\ m^2$	$\mu Gy\ h^{-1}\ MBq^{-1}\ m^2$	$(1/3600) \times 10^{-12}\ Gy\ s^{-1}\ Bq^{-1}\ m^2 = 2.778 \times 10^{-16}\ Gy\ s^{-1}\ Bq^{-1}\ m^2$
			$\mu Gy\ h^{-1}\ MBq^{-1}\ m^2$	$1.0\ U\ MBq^{-1}$

The "Strength" of a Source

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

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.

For example for HDR ^{192}Ir sources: 10Ci = 370 GBq ➔ ≈ 41 kU

41000 μGy.m².h^{-1}

41000 cGy.cm².h^{-1}

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Topics

- Exposure, Kerma
- Air Kerma-rate constant
- Reference Air Kerma-rate/Source Strength
- **Dose Calculation**

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Dose Calculation: The TG-43 Protocol

- **Dose Rate from a single Source**
- Dose from Dose Rate
- Many Sources
- Limitations

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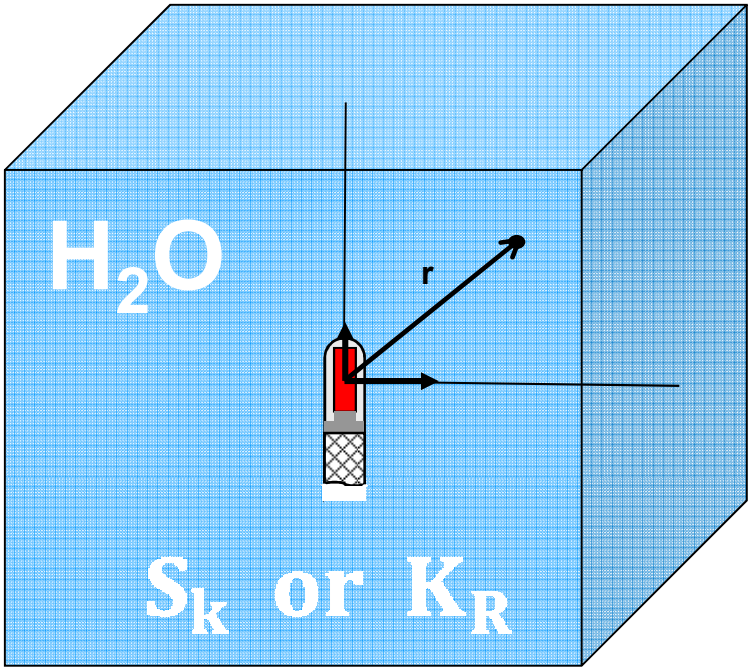
Dose Calculation

How can we calculate the dose rate or dose resulted from a single source at a point in space (dose to water in water)?



$$\dot{D} = \dot{D}(\vec{r}) = \ ?$$

^{137}Cs, ^{60}Co, ^{192}Ir, ^{125}I, ^{103}Pd,….

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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, HEBD 2012)

➔ *Why this formalism???*

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

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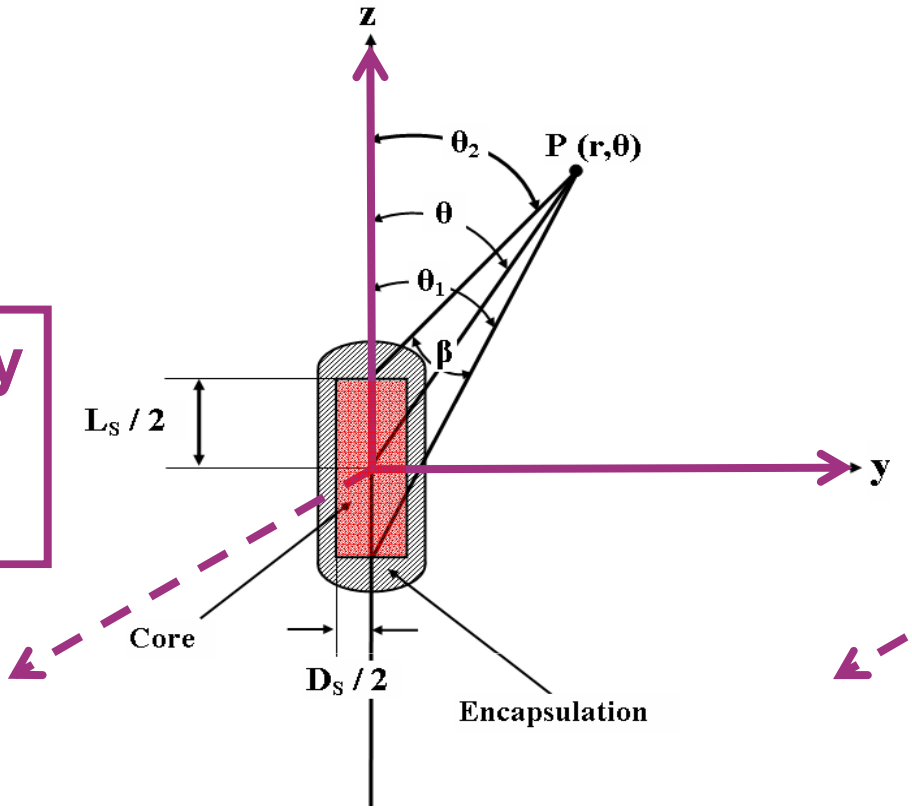
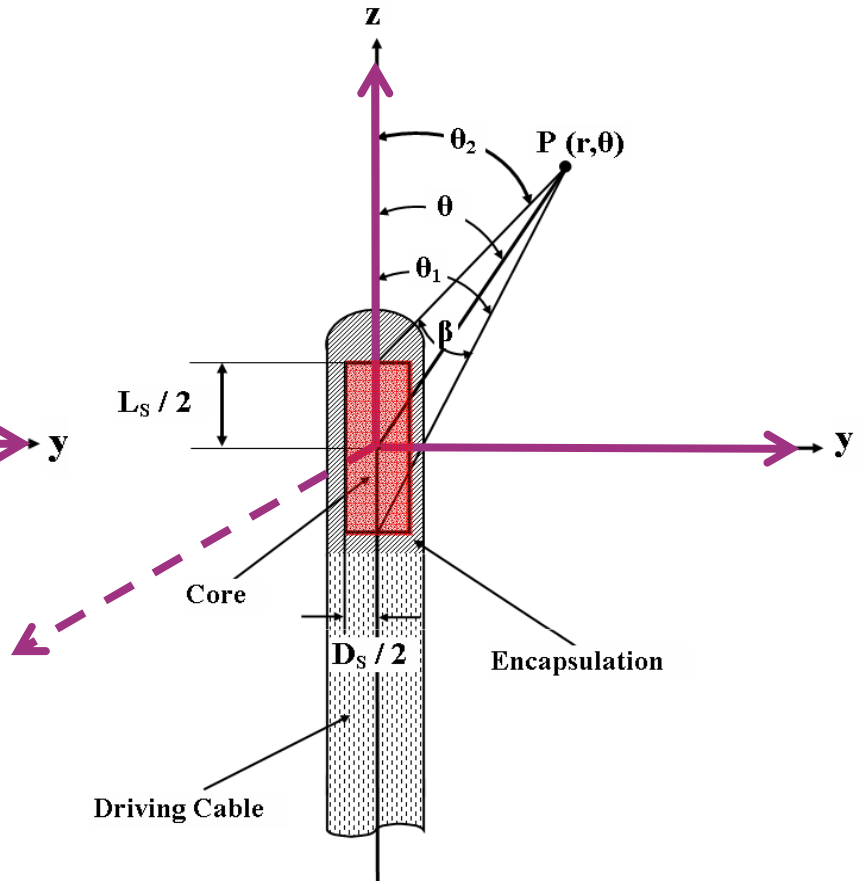
Dose calculation – AAPM-TG43: The Coordinate System

$$\dot{D}(P) = \dot{D}(\vec{r}) = \dot{D}(r,\theta)$$

Cylindrically Symmetric Source





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Active core of the source (radioactive material)

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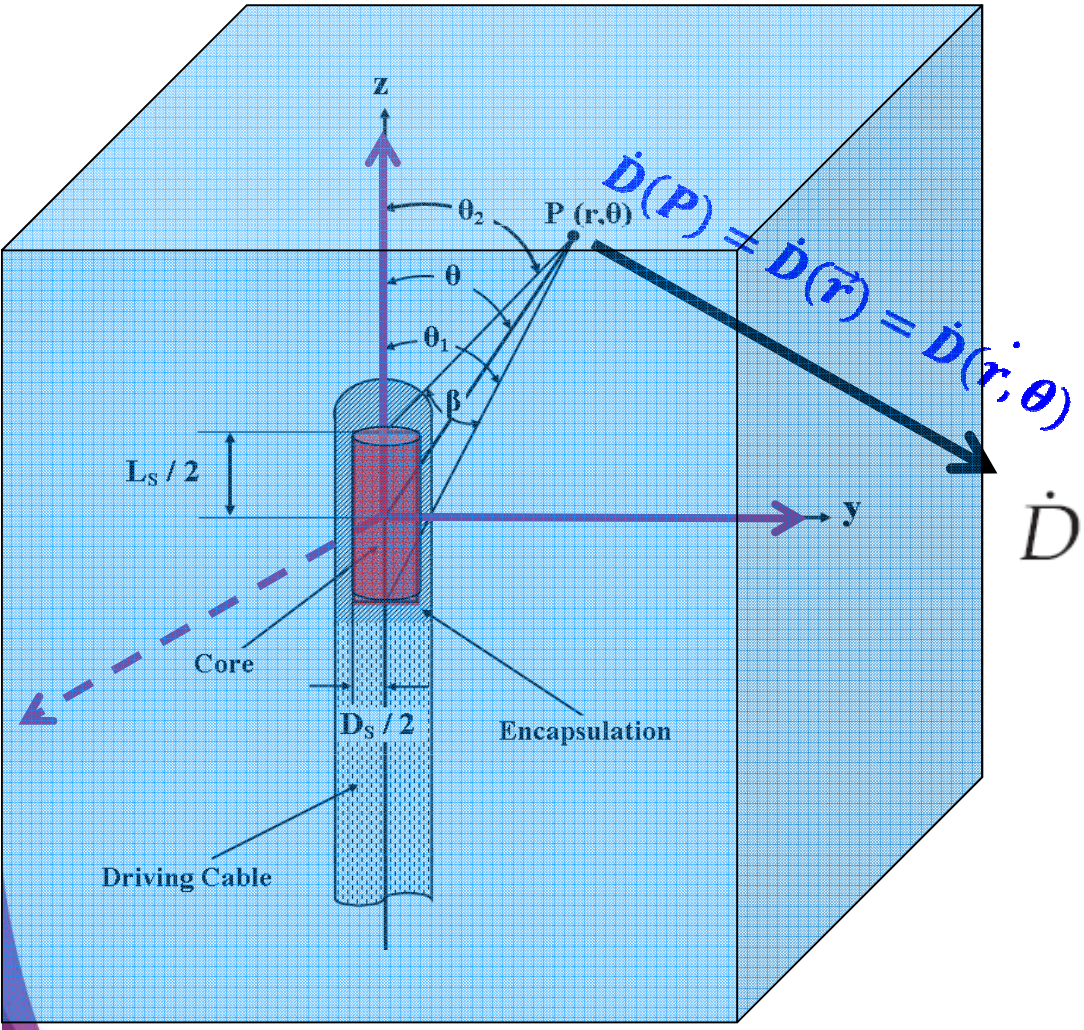
Dose calculation – AAPM-TG43: The formalism



Dose rate from a single source at a point in water-filled space (in Gy min^{-1} or cGy min^{-1} or cGy h^{-1}):
dose to water in water

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

5 x Multiplications
1 x Division

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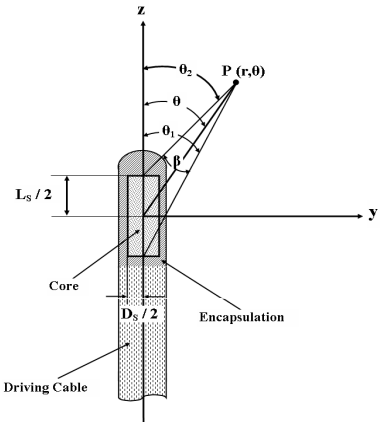
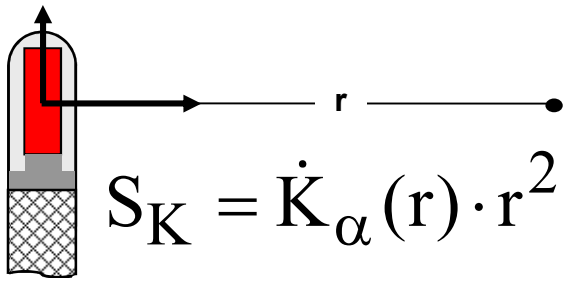
Dose calculation – AAPM-TG43: The Source Strength

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



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.
This is the actual strength of the specific source we consider.



The recommended unit for air kerma strength S_K is $\mu Gy.m^2.h^{-1}$ and has been denoted by the symbol U:

$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$

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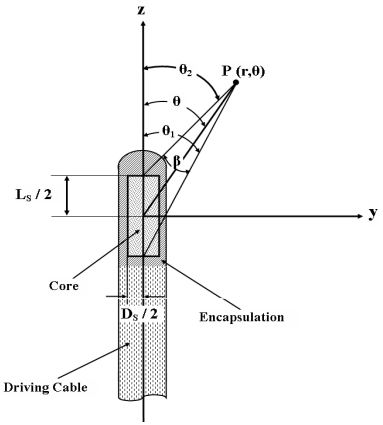
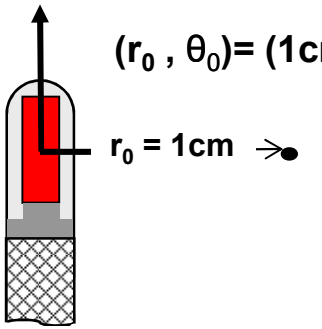
Dose calculation – AAPM-TG43: The Dose Rate Constant Λ

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



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 ($\theta_0 = 90^0$), per unit air kerma strength, S_K:



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

Λ is expressed in units of $cGy.h^{-1}.U^{-1}$ and
$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$

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Dose calculation – AAPM-TG43: The Dose Rate Constant Λ

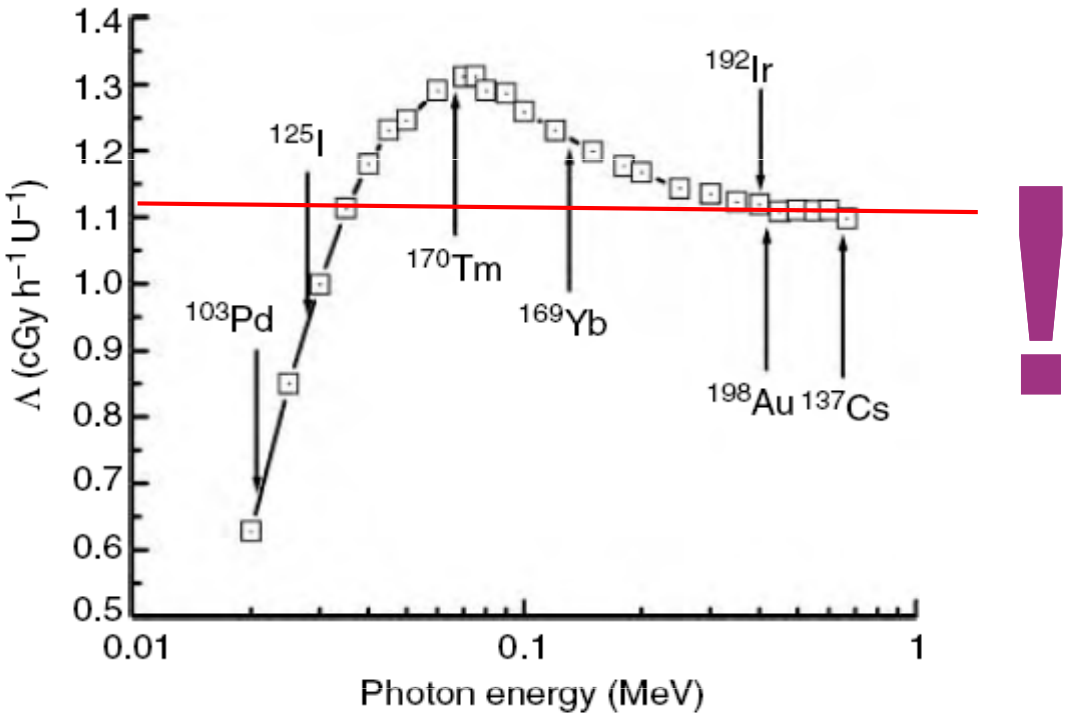

FIGURE 8.7
Energy dependence of the dose rate constant Λ expressed in cGy h^{-1} U^{-1} for monoenergetic point sources in the energy range of 0.020 to 0.700 MeV. The Λ values for the effective energies E_{eff}, see Equation 5.2, of the brachytherapy relevant radionuclides listed in Table 5.2 are indicated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

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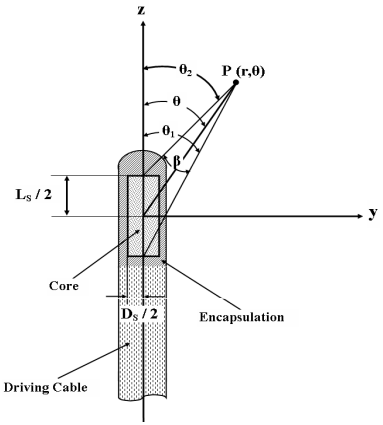
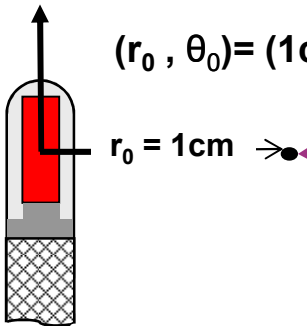
Dose calculation – AAPM-TG43: S_K and Λ

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



The product of the actual source strength S_K and the dose rate constant Λ of the source and radionuclide considered is the actual dose rate at 1 cm radial distance at $\theta = \theta_0 = 90^0$.



$$\Lambda = \frac{\dot{D}(r_0,\theta_0)}{S_K} \quad \text{and thus} \quad \dot{D}(r_0,\theta_0) = S_K \cdot \Lambda$$

Λ is expressed in units of $cGy.h^{-1}.U^{-1}$ and

$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$

Dose rate is in $cGy.h^{-1}$

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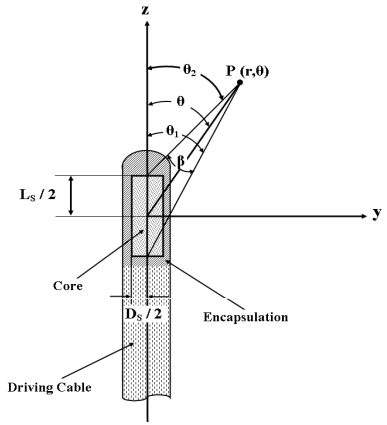
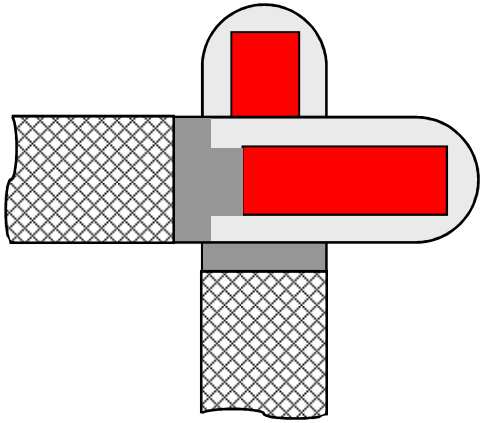
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

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





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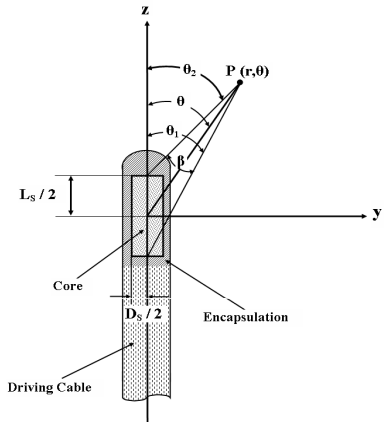
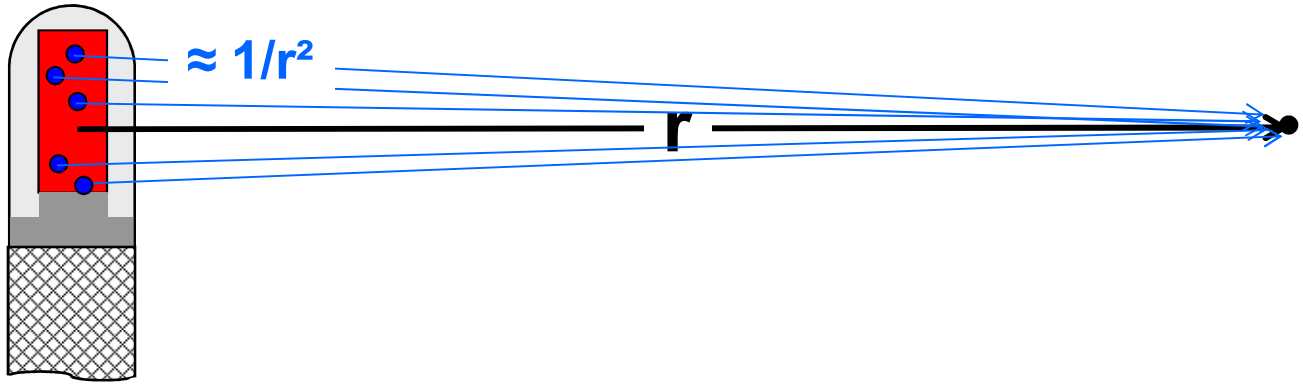
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

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



Source, S — **r** — **Dose Point, P**

$\approx 1/r^2$



$\neq 1/r^2$

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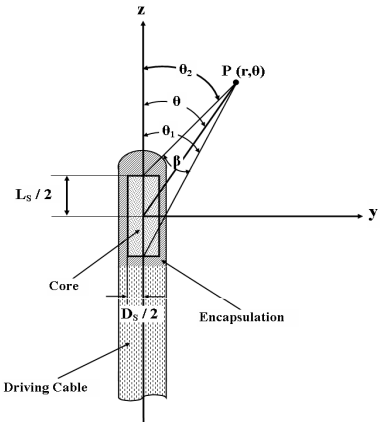
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

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



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 does not consider scatter and attenuation!**

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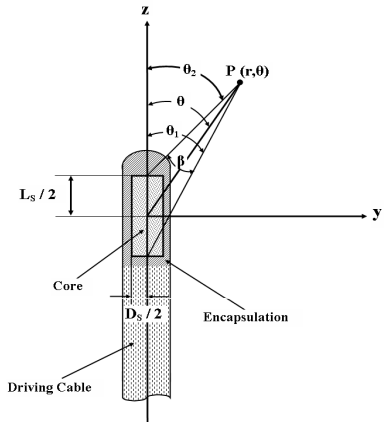
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):



I. Point Source Approximation $G_P(r,\theta)$

Source, S ⟶ **r** ⟶ **Dose Point, P**

$\approx 1/r^2$

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

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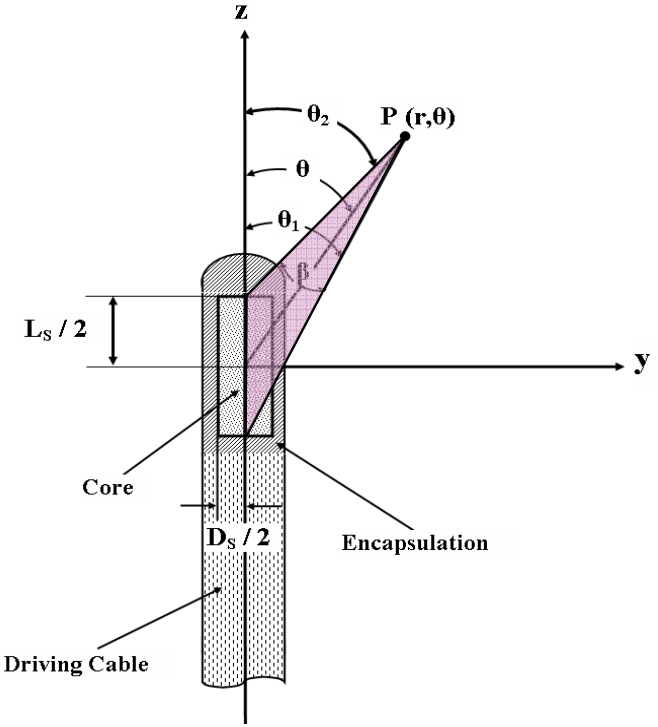
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

II. Line Source Approximation $G_L(r,\theta)$

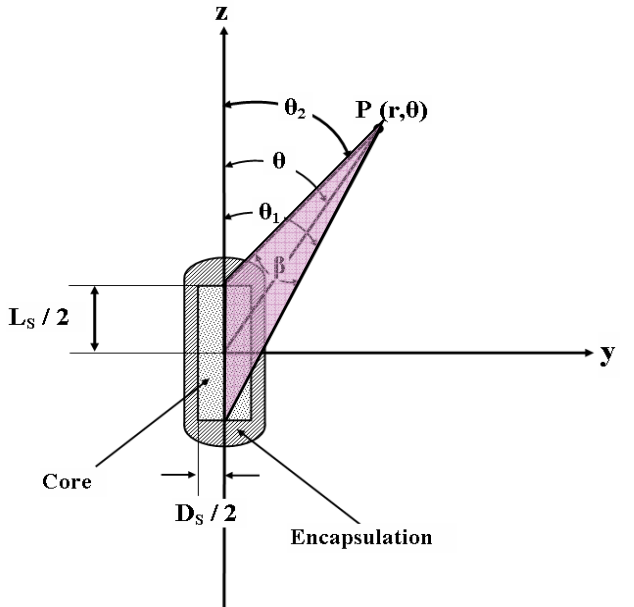
With $\beta = \theta_2 - \theta_1$

$$G_L(r,\theta) = \frac{\beta}{L_S\, r\, sin\theta}$$

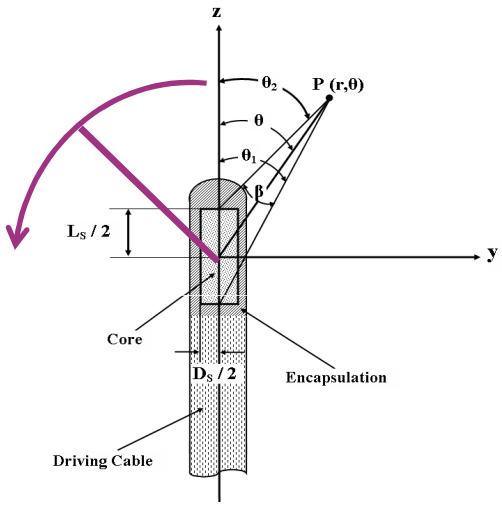


Where for $\theta = 0^\circ$ or 180°

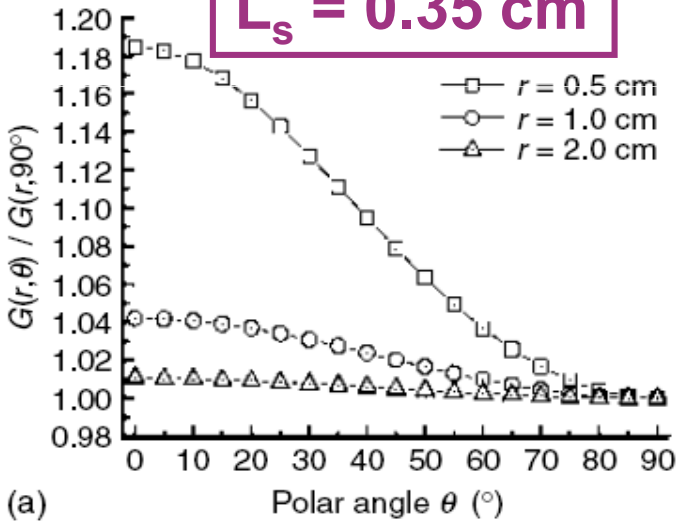
$$G_L(r,\theta) = \frac{1}{r^2 - \frac{L_S^2}{4}}$$



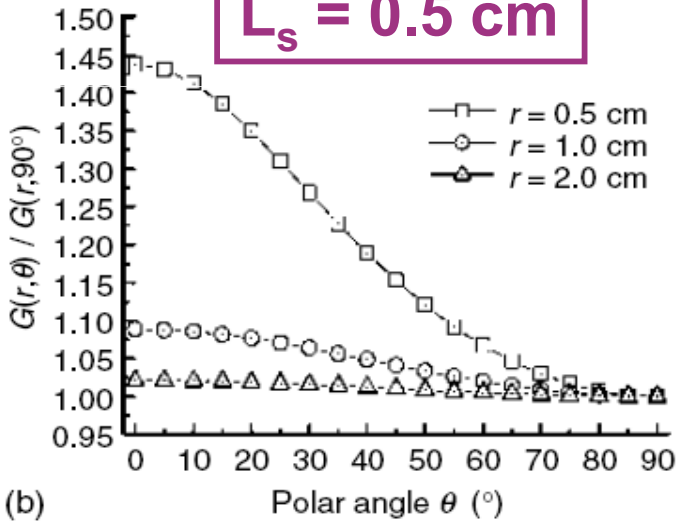
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):



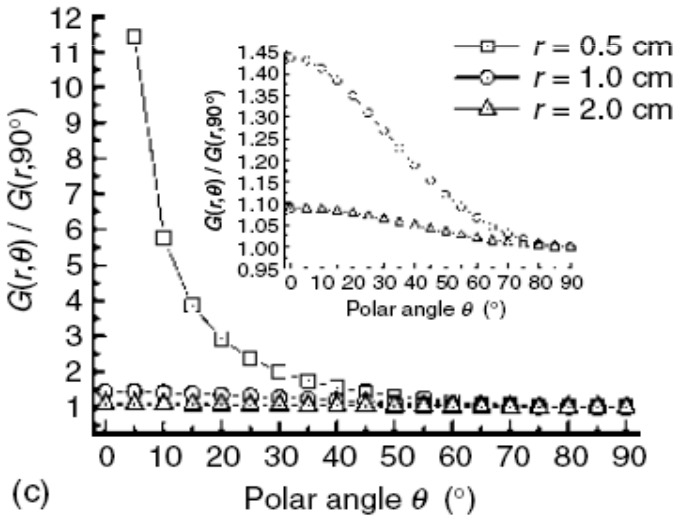
L_s = 0.35 cm



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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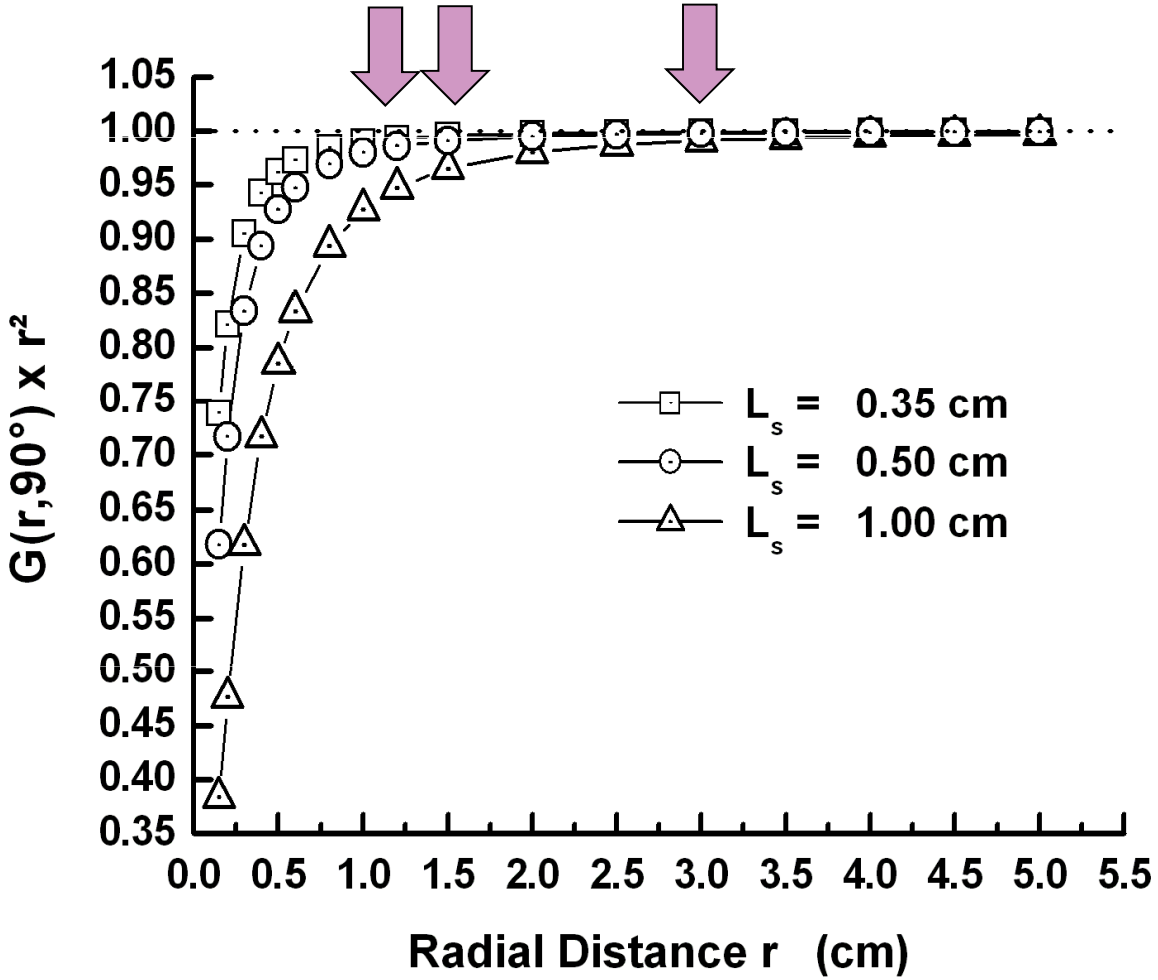
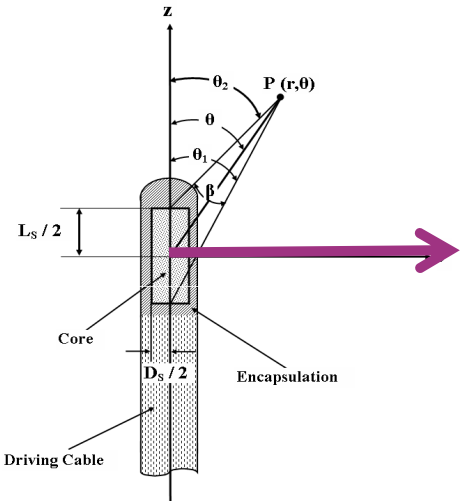
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):





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

!

Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

General calculation of the geometry function $G_L(r,\theta)$

HEBD > 50keV, 2012

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

Dose calculation for photon-emitting brachytherapy sources with average energy higher than 50 keV: Report of the AAPM and ESTRO, *Medical Physics 39 (5), 2904-2029, 2012.*

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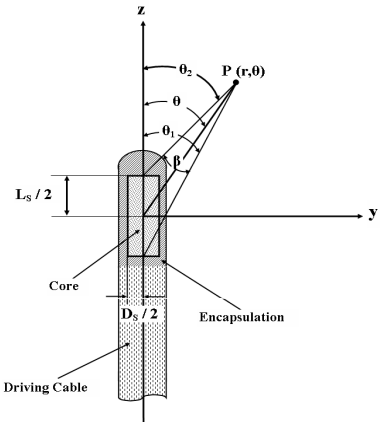
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

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



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 = 90⁰**.

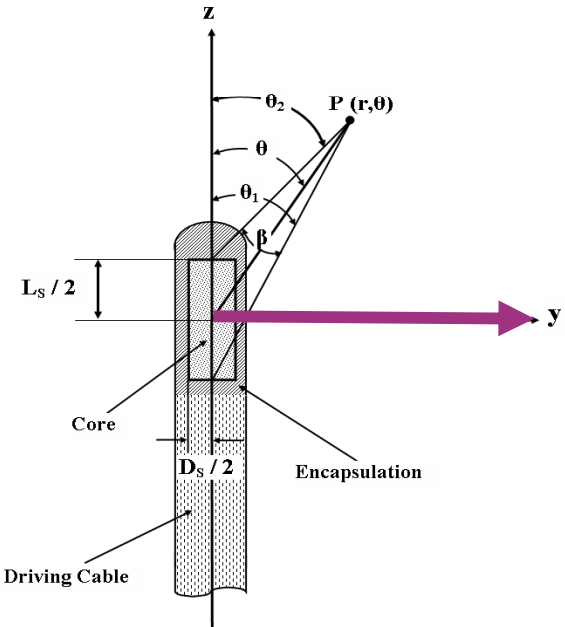
g(r) is a dimensionless quantity.

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

!

g(r) depends in general on source design and radionuclide.

The "Inverse-Square-Law" is filtered out !!!



g(r)

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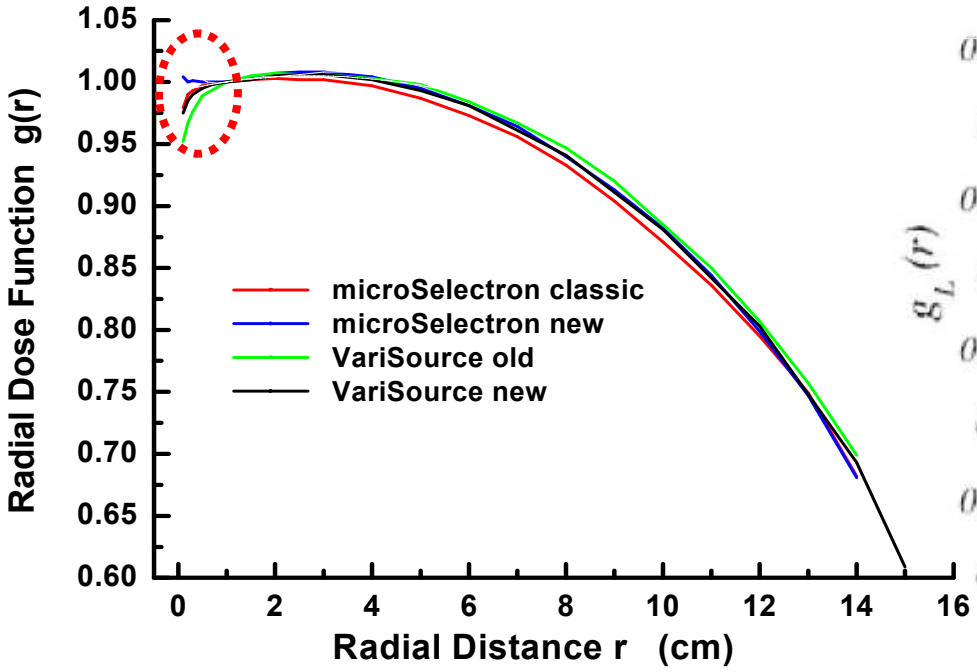
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{192}Ir – HDR Sources



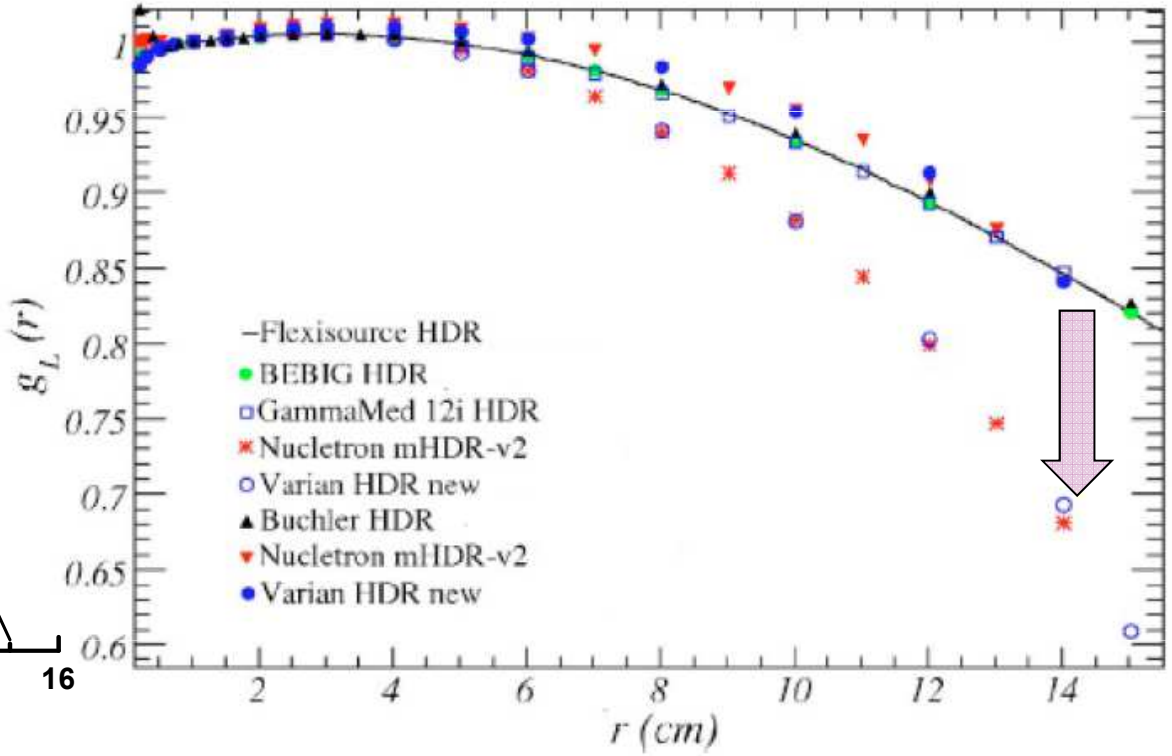


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Figure 7. Comparison of the radial dose functions for various 192Ir HDR sources.

Dosimetric characterization of a high dose rate ^{192}I source for brachytherapy application using Monte Carlo simulation and benchmarking with thermoluminescent dosimetry.
Bidmeshki et al., *Int. J. Radiat. Res., Vol. 12 No. 3, July 2014*

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Dose Calculation: The TG-43 Protocol

- **Dose Rate from a single Source**
- Dose from Dose Rate
- Many Sources
- Limitations

To be Continued ….. Monday 09:15 !

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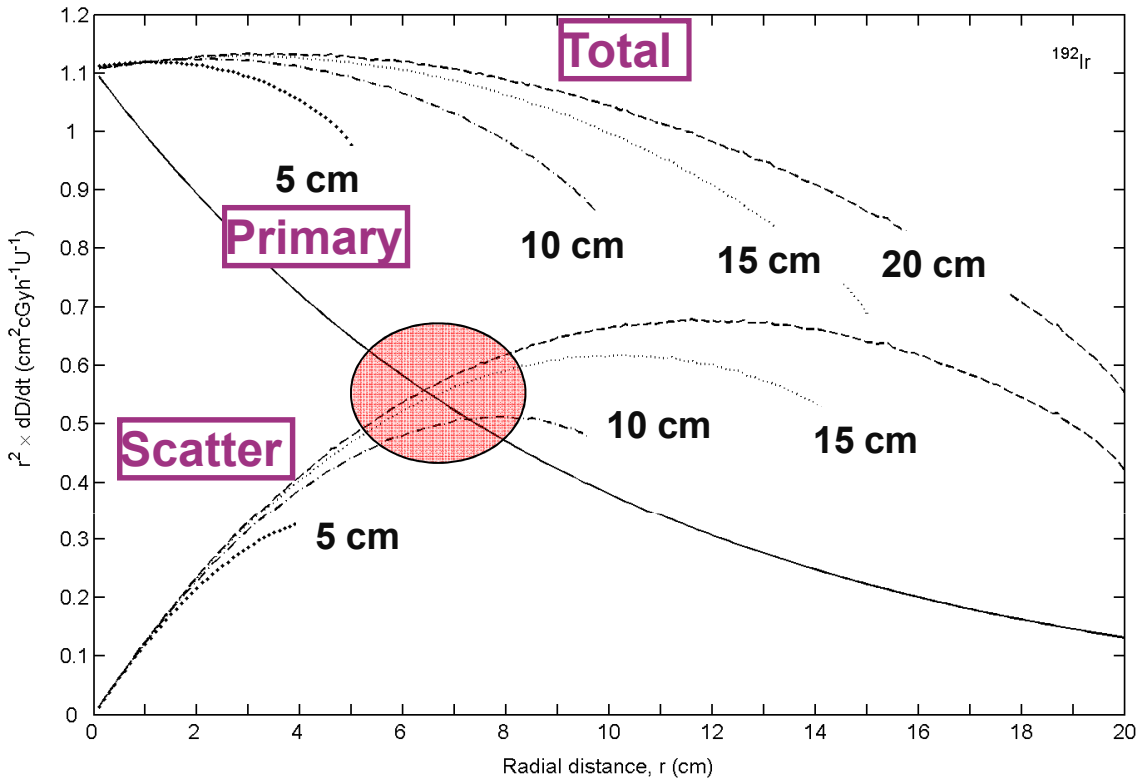
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

Attention which data sets to consider: full scatter conditions

Ideal point sources of ^{192}Ir



R= 5 cm, 10 cm, 15 cm and 20 cm radius.

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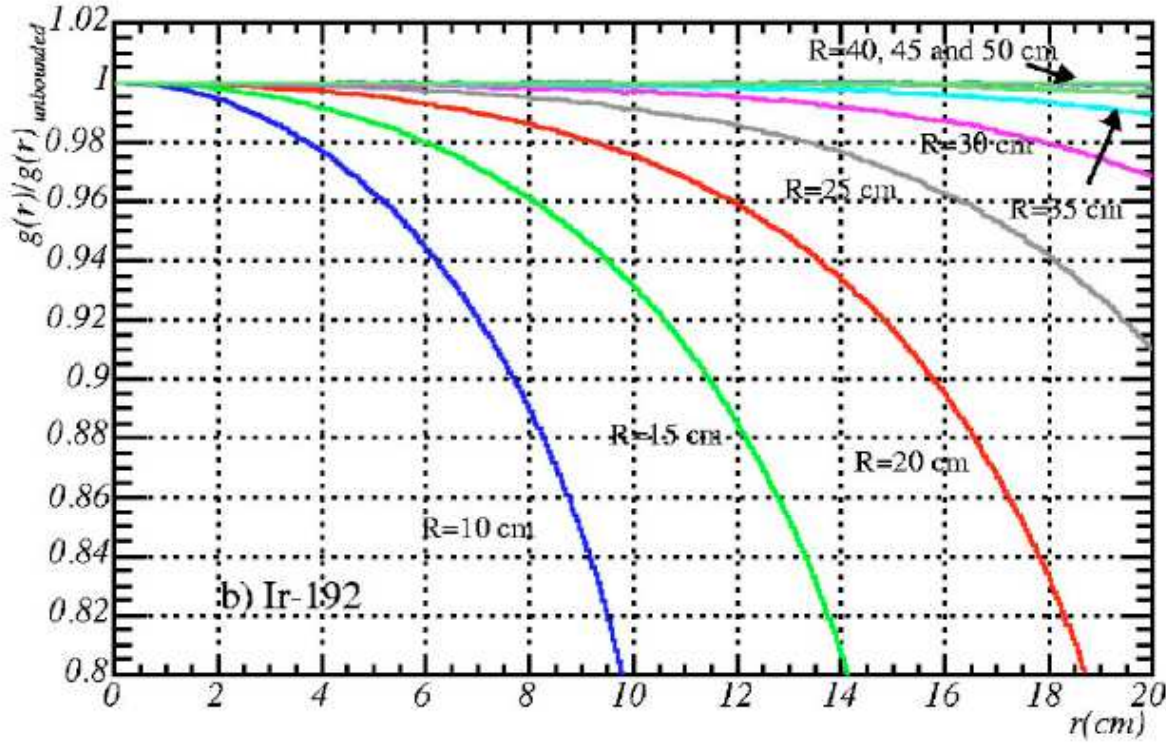
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

Attention which data sets to consider: full scatter conditions

Ideal point sources of ^{192}Ir



Ratio between g(r) for spherical phantom of size R and for an unbounded phantom.

Calatayud, Granero & Ballester, Med Phys 31 (7), 2004

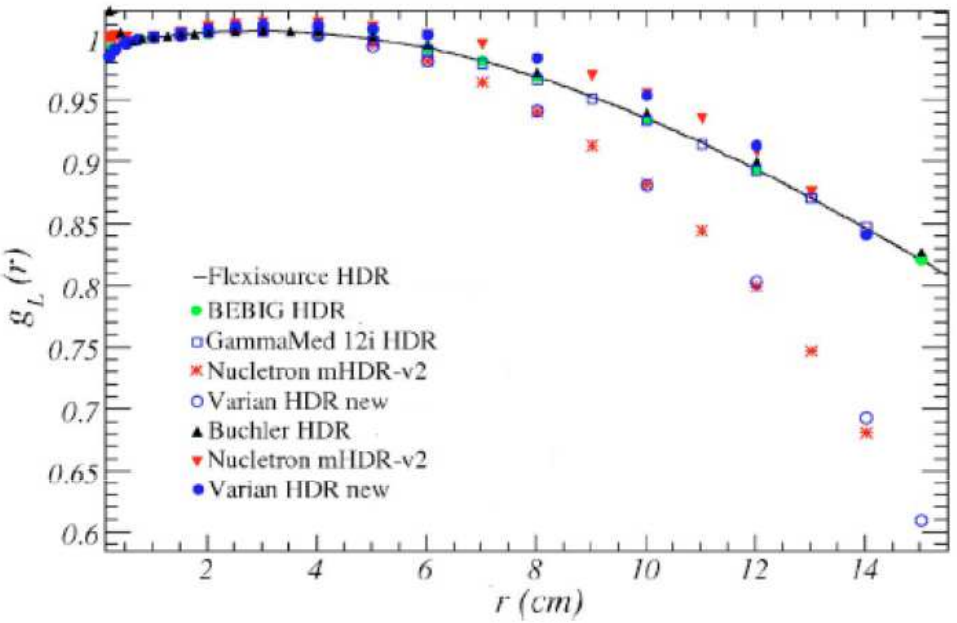


Figure 7. Comparison of the radial dose functions for various 192Ir HDR sources.

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Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{192}Ir vs ^{60}Co HDR Sources

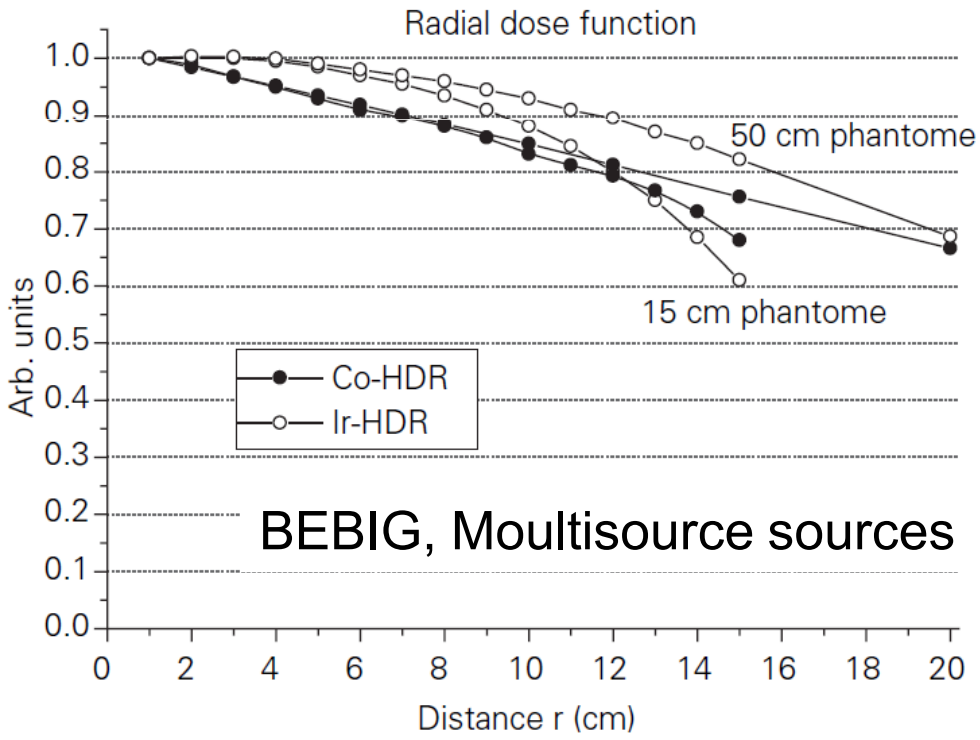

Figure 5. Influence of the phantom size on the radial dose function.

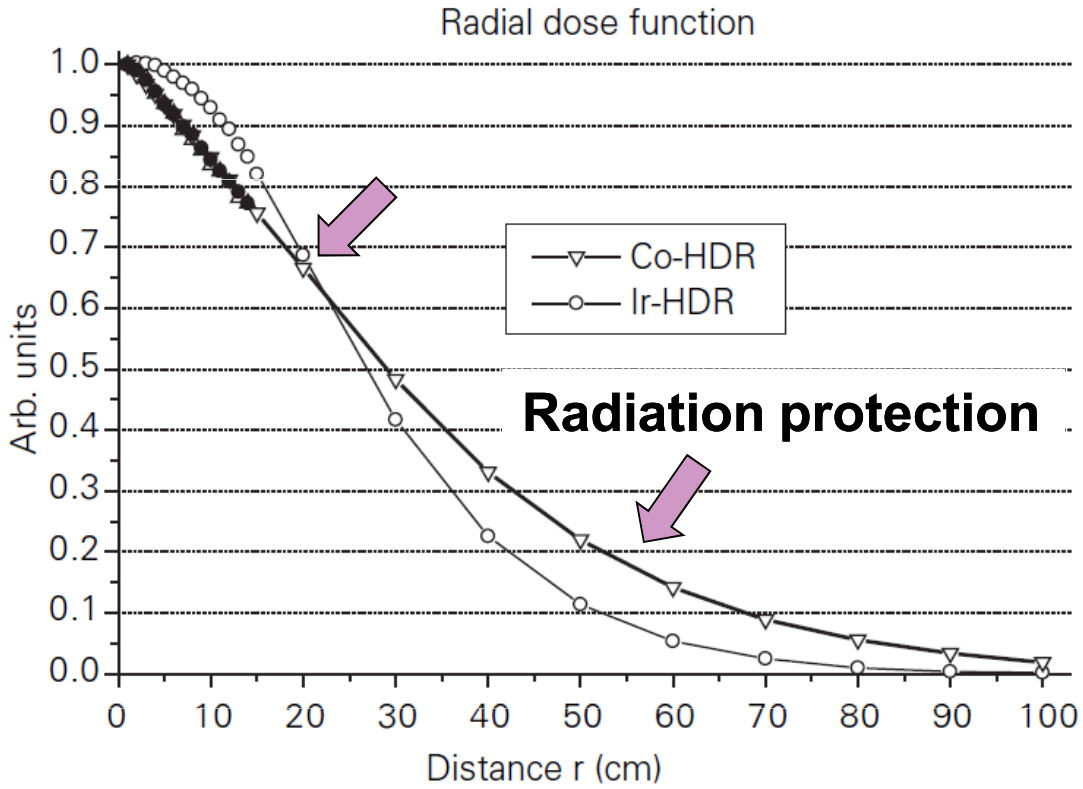

Figure 4. Radial dose function for greater distances from the source.

Comparison of ^{60}Co and ^{192}Ir sources in High Dose Rate Afterloading Brachytherapy, Richter J., Baier K., Flentje M., Strahlenther Onkol, No. 4, 2008

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Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{192}Ir vs ^{60}Co HDR Sources

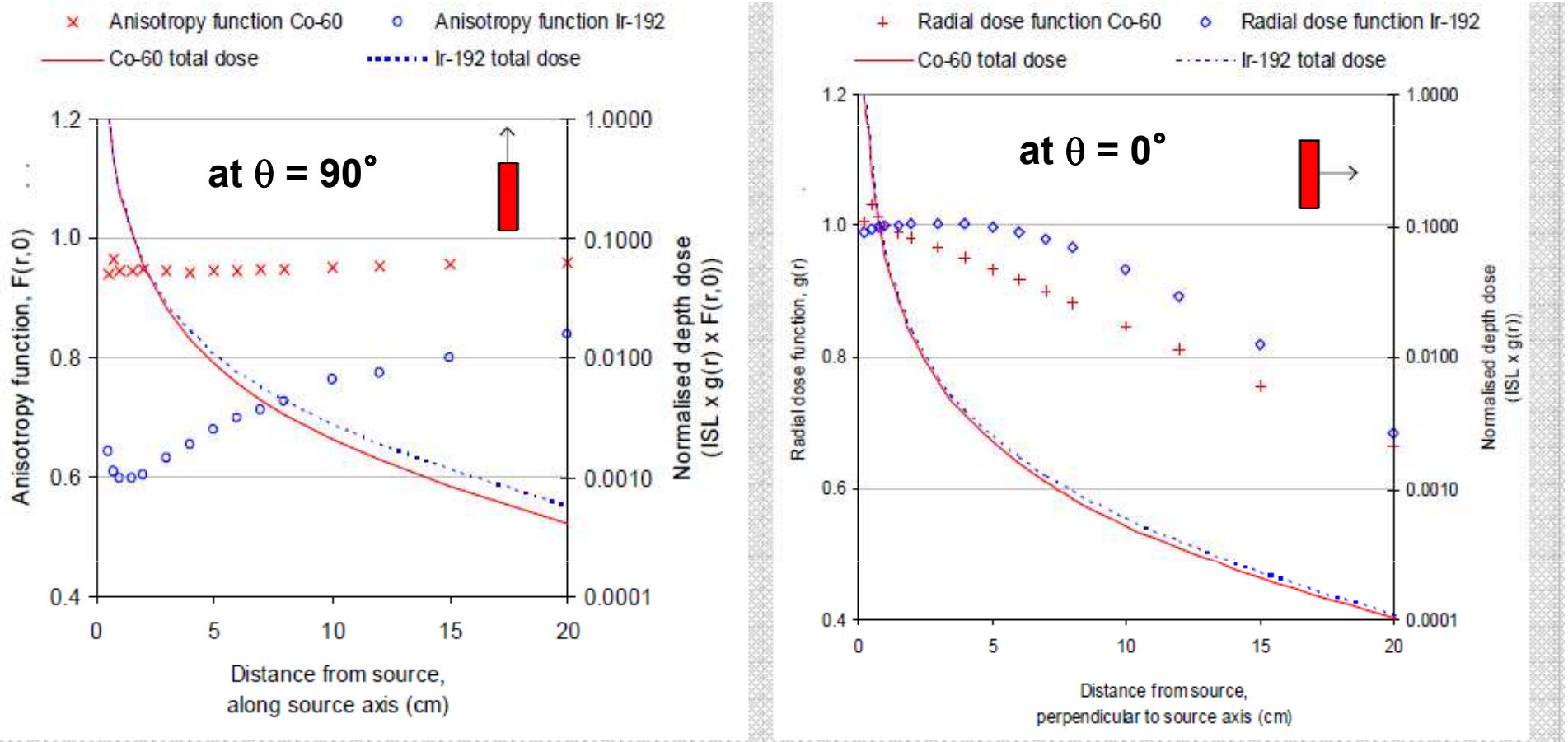

Fig 2. Effect of radial dose function and anisotropy on dose curves in (left) direction perpendicular to source axis and (right) distance along source axis

Palmer A. et al., Co-60 or Ir-192 for HDR Brachytherapy? Evaluating Source Parameters, CTV & OAR Doses, Portsmouth Hospitals, antony.palmer@porthosp.nhs.uk.

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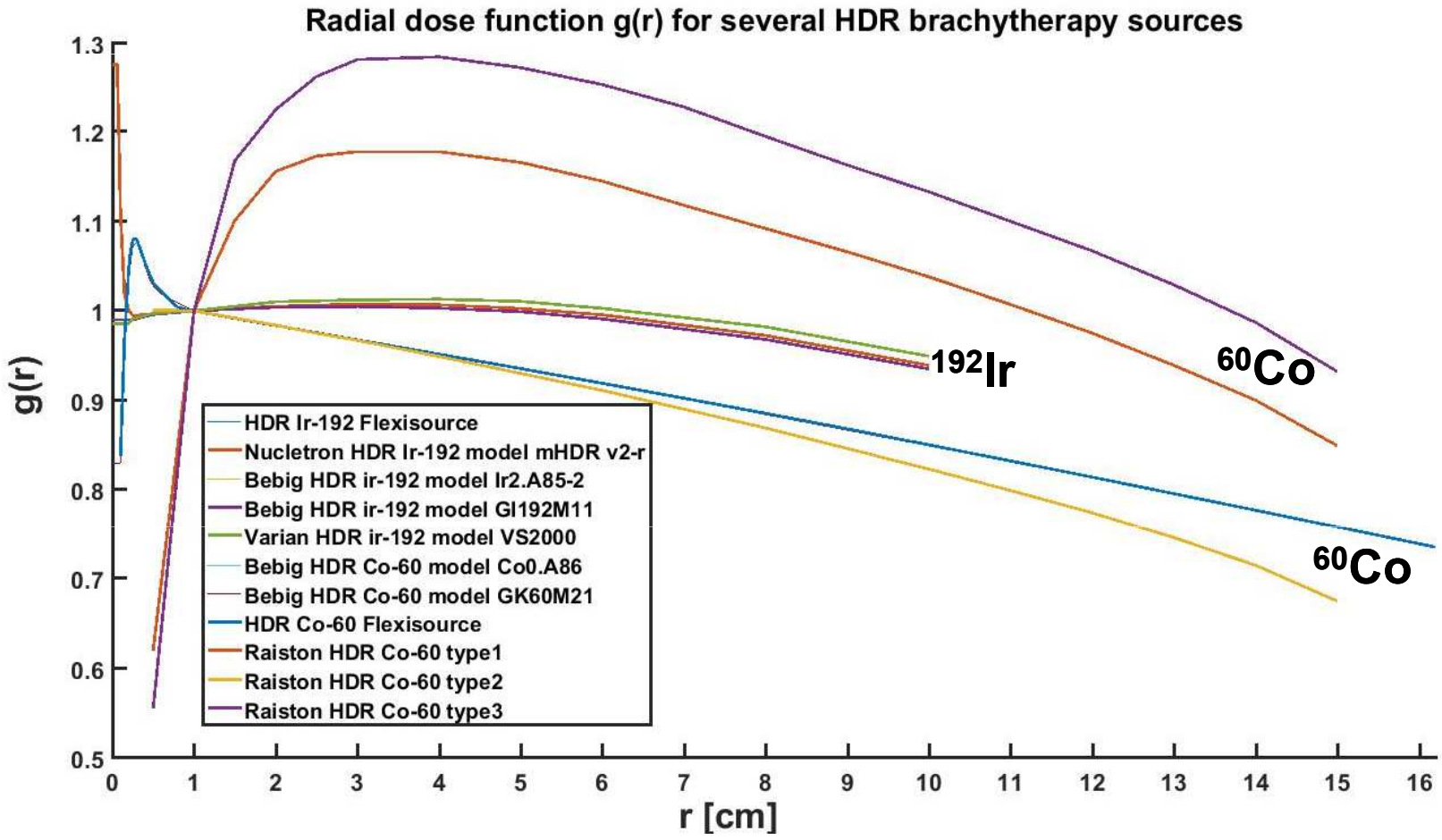
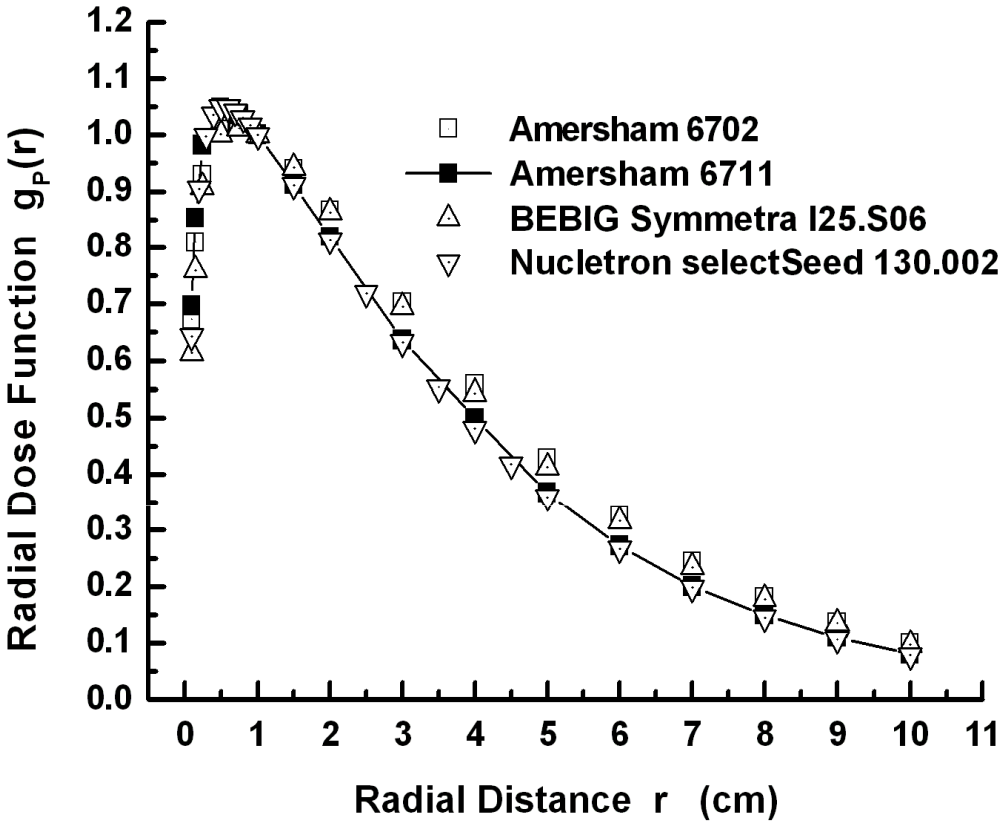
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{192}Ir vs ^{60}Co HDR Sources



Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{125}I seeds



Different Sources

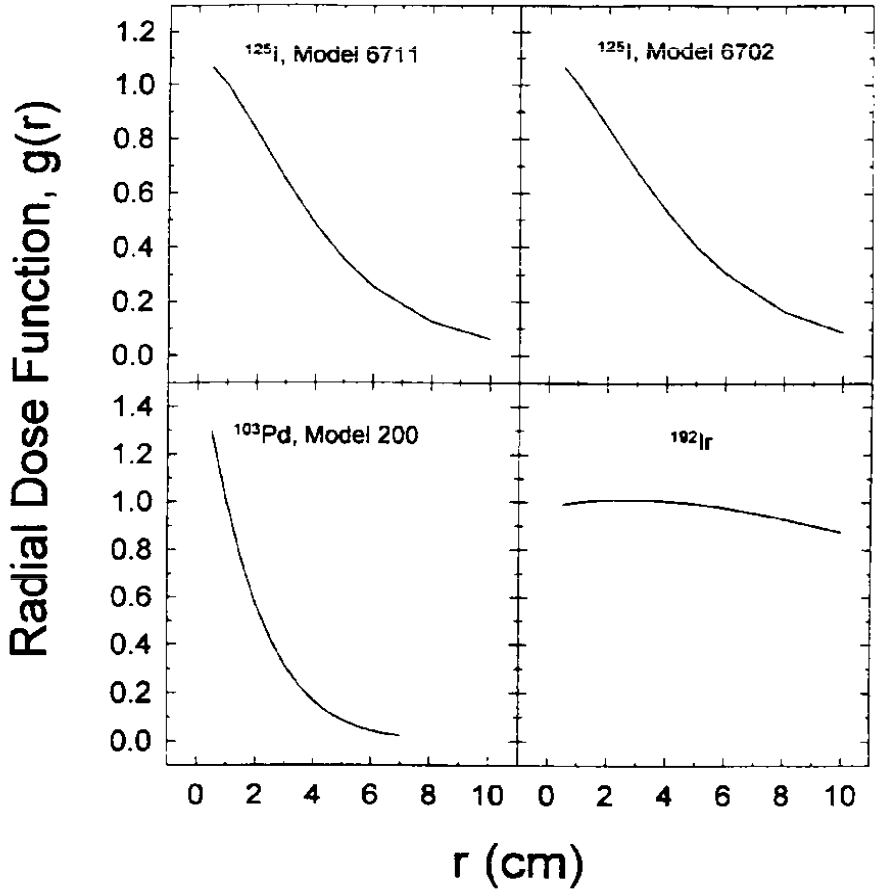


FIG. 2. Radial dose functions in a Solid Water medium for ^{103}Pd, ^{125}I, and ^{192}Ir sources.

Dose calculation – AAPM-TG43: The Anisotropy Function F(r, θ):

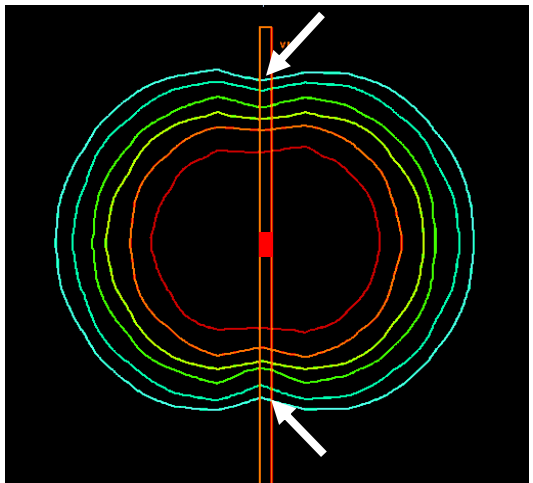
$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

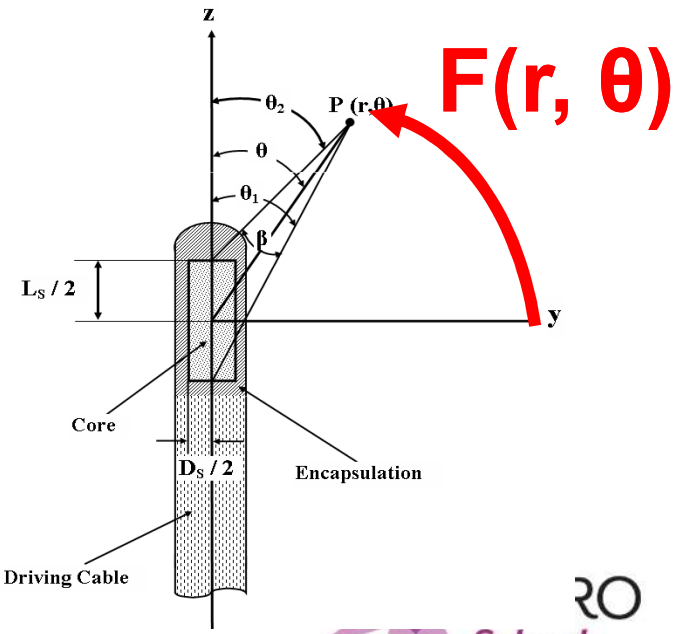
F(r, θ): The anisotropy function that considers the effect of absorption and scatter of the photons within the source active core and encapsulation material as well as part of the driving cable if any.

F(r, θ) is a dimensionless quantity.

It is always F(r, θ=90⁰) = 1.00

F(r, θ) depends in general on source design and radionuclide.



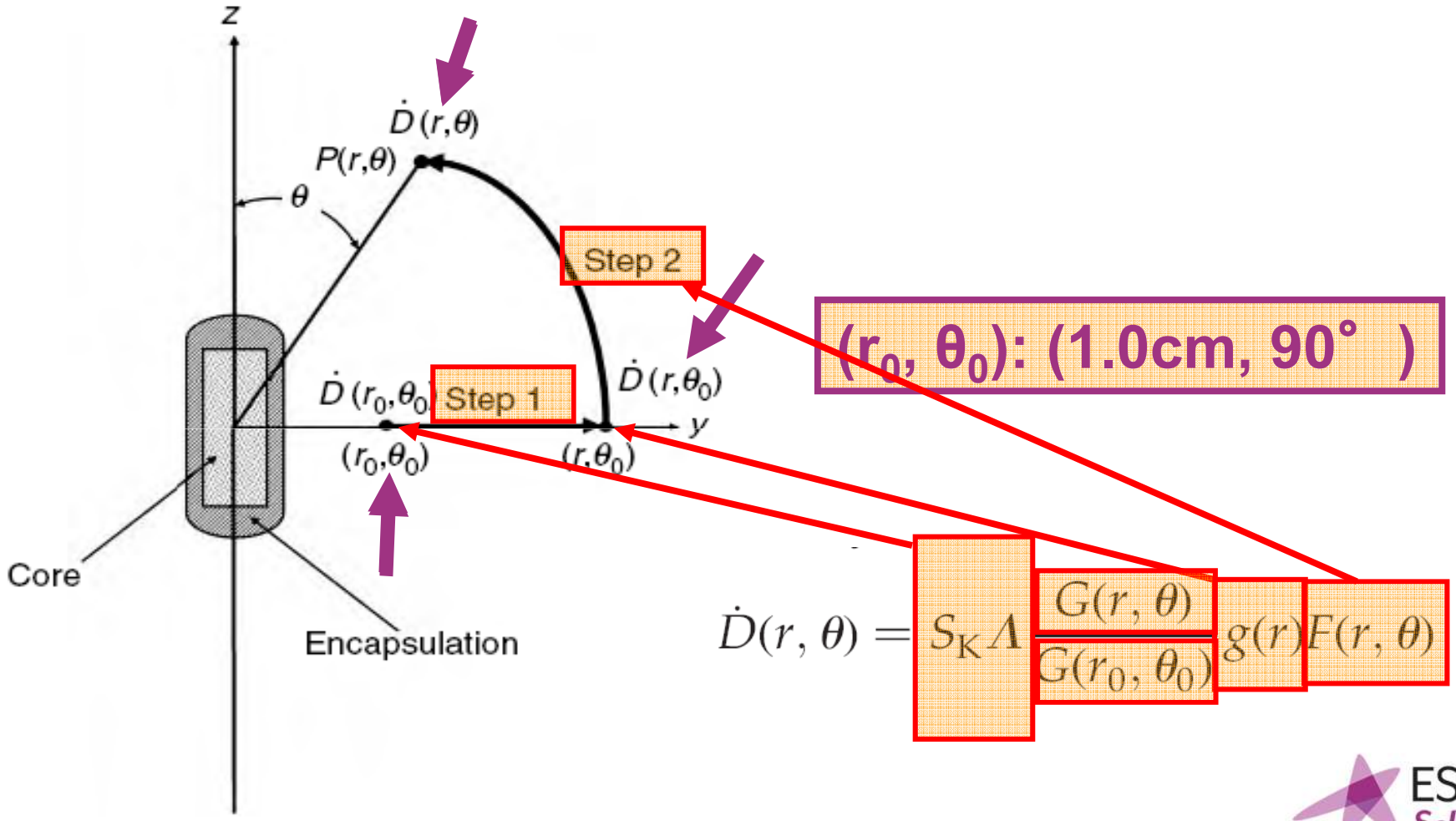


F(r, θ)

Dose calculation – AAPM-TG43

Summary:

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



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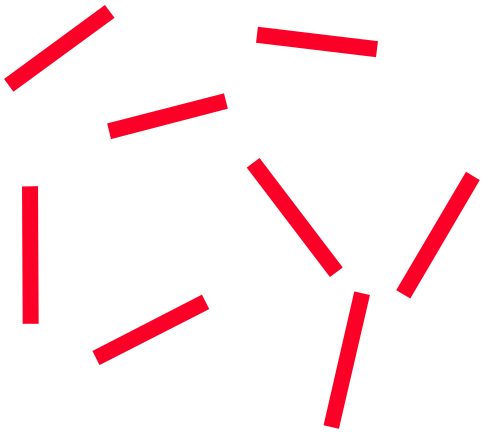
Dose calculation – AAPM-TG43

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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(Received 22 August 2003; revised 11 December 2003; accepted for publicatio
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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(Received 3 January 2007; revised 19 March 2007; accepted for publicatio
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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(Received 18 March 2010; accepted for publication 22 March 2010; published 29 April 2010)
[DOI: 10.1118/1.3388848]

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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(Received 11 November 2011; revised 30 March 2012; accepted for publication 30 March 2012; published online 3 May 2012)

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Dose calculation – AAPM-TG43

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

Parameter	$r < r_{min}$ Extrapolation	$r_{min} < r \leq r_{max}$ Interpolation	$r > r_{max}$ Extrapolation
$g_L(r)$	Nearest neighbor or zeroth-order extrapolation *(Ditto)*	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 *(Ditto)*	Bilinear (*bilinear*) interpolation method for $F(r, \theta)$ *(Ditto)*	Nearest neighbor or zeroth-order *r*-extrapolation *(Ditto)*

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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 (e.g., ^{137}Cs Selectron from Nucletron) where a 2D model cannot 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 $G_L(r,\theta)$:

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

Dose calculation – AAPM-TG43

Reference TG43 source data

http://www.estro.org/about/governance-organisation/committees-activities/tg43

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IR-192 HDR SOURCES

Manufacturer	Source	Model	Origin	Status
Varian Medical Systems Inc. USA	GammaMed HDR	12i	HEBD	consensus
Nucletron, an Elekta company	Flexisource Ir-192	Flexisource	HEBD	consensus
Oncology Systems Inc.	M-19	M-19	HEBD	consensus
Buchler facts	Buchler HDR	G0814	HEBD	consensus
Eckert & Ziegler BEBIG GmbH, Germany	BEBIG HDR Ir-192	Ir2.A85-2	HEBD	consensus
Nucletron, an Elekta company	Nucletron mHDR	mHDR-v1 (classic)	HEBD	consensus
Nucletron, an Elekta company	Nucletron mHDR	mHDR-v2	HEBD	consensus
Varian Medical Systems Inc. USA	GammaMed HDR	Plus	HEBD	consensus
Varian Medical Systems Inc. USA	New VariSource HDR	VS2000	HEBD	consensus
Eckert & Ziegler BEBIG GmbH, Germany	BEBIG HDR Ir-192	GI192M11	HEBD	consensus
Varian Medical Systems Inc. USA	VariSource HDR	Varian(classic)	HEBD	recommended
None (generic virtual source). Visit IROC/Houston Registry	MBDCA	Generic	MBDCA-WG	

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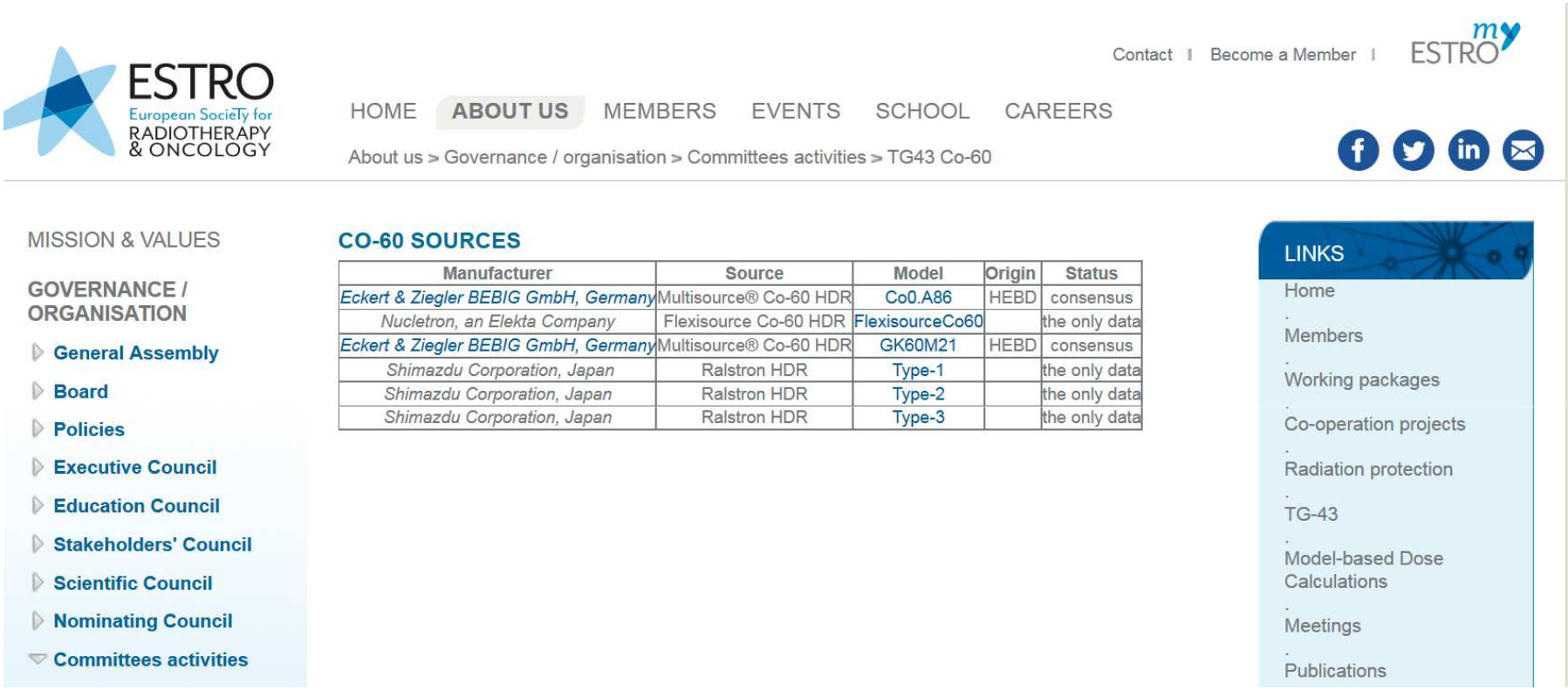
Dose calculation – AAPM-TG43

Reference TG43 source data

http://www.estro.org/about/governance-organisation/committees-activities/tg43



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CO-60 SOURCES

Manufacturer	Source	Model	Origin	Status
Eckert & Ziegler BEBIG GmbH, Germany	Multisource® Co-60 HDR	Co0.A86	HEBD	consensus
Nucletron, an Elekta Company	Flexisource Co-60 HDR	FlexisourceCo60		the only data
Eckert & Ziegler BEBIG GmbH, Germany	Multisource® Co-60 HDR	GK60M21	HEBD	consensus
Shimazdu Corporation, Japan	Ralstron HDR	Type-1		the only data
Shimazdu Corporation, Japan	Ralstron HDR	Type-2		the only data
Shimazdu Corporation, Japan	Ralstron HDR	Type-3		the only data

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Dose Calculation: The TG-43 Protocol

- Dose Rate from a single Source
- **Dose from Dose Rate**
- Many Sources
- Limitations

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Dose from Dose-Rate

TG-43 derives the Initial Dose Rate

$$D(r,\theta) = \int_{t=t_0=0}^{t=T} \dot{D}(r,\theta,t_0) \cdot e^{-\lambda\cdot(t-t_0)} \cdot dt = \dot{D}(r,\theta,t_0) \cdot \left(\frac{1}{\lambda}\right) \cdot \left(1 - e^{-\lambda\cdot T}\right) = \dot{D}(r,\theta,t_0) \cdot \tau \cdot \left(1 - e^{-\frac{T}{\tau}}\right)$$

t_0: is the time of the begin of the treatment

τ **= $T_{1/2}$ / ln2** , the mean lifetime of the Radionuclide, λ **= 1 /** τ

$T_{1/2}$: is 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 Initial Dose Rate: T << τ

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

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

$$\tau = \frac{1}{\lambda} = \frac{T_{1/2}}{\ln 2} = 1.4427\, T_{1/2}$$

TG-43 derives the Initial Dose Rate: T >> τ

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

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.

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

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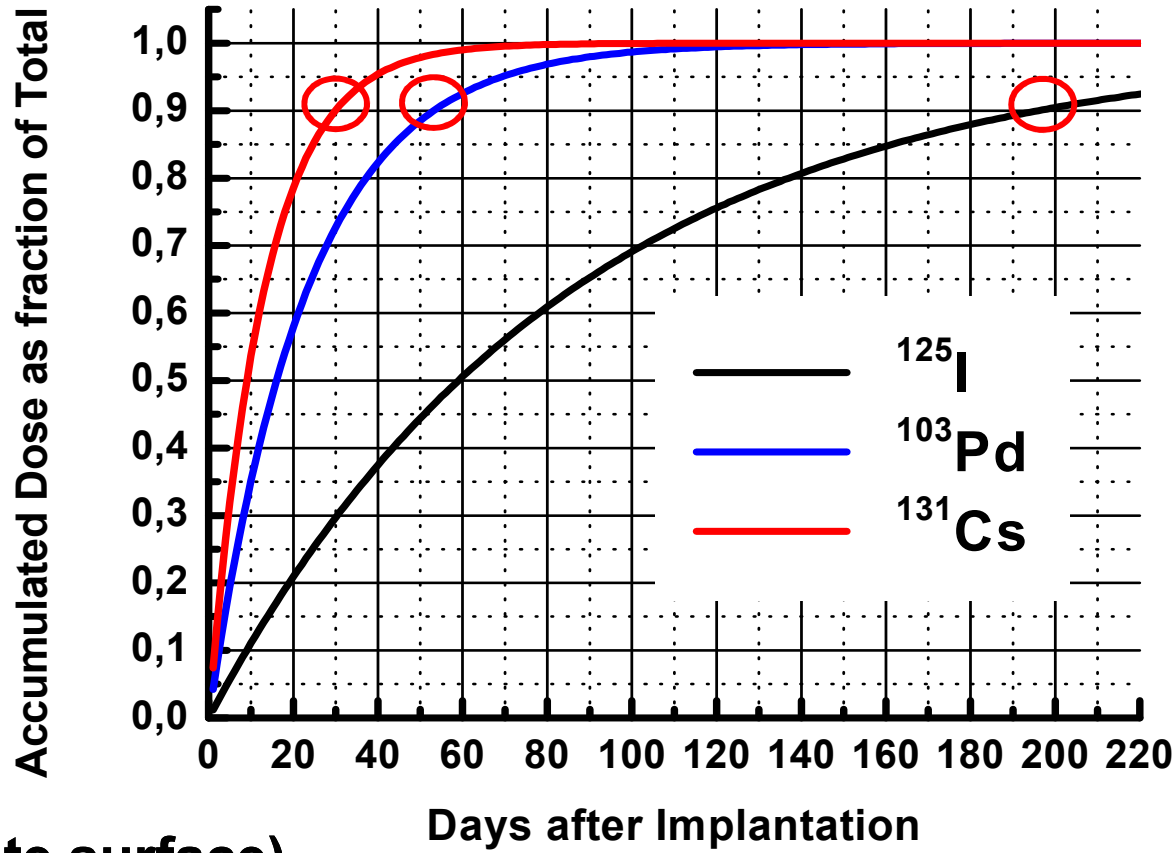
Dose from Dose-Rate: Dose Accumulation over Time

Total Dose (100% = 1.0)

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



- **Initial Dose Rate (at the prostate surface)**
  30 cGy.h^{-1} for ^{131}Cs
  versus
  7 cGy.h^{-1} for ^{125}I and 20 cGy.h^{-1} for ^{103}Pd

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Dose from Dose-Rate: Units Conversion Factor

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

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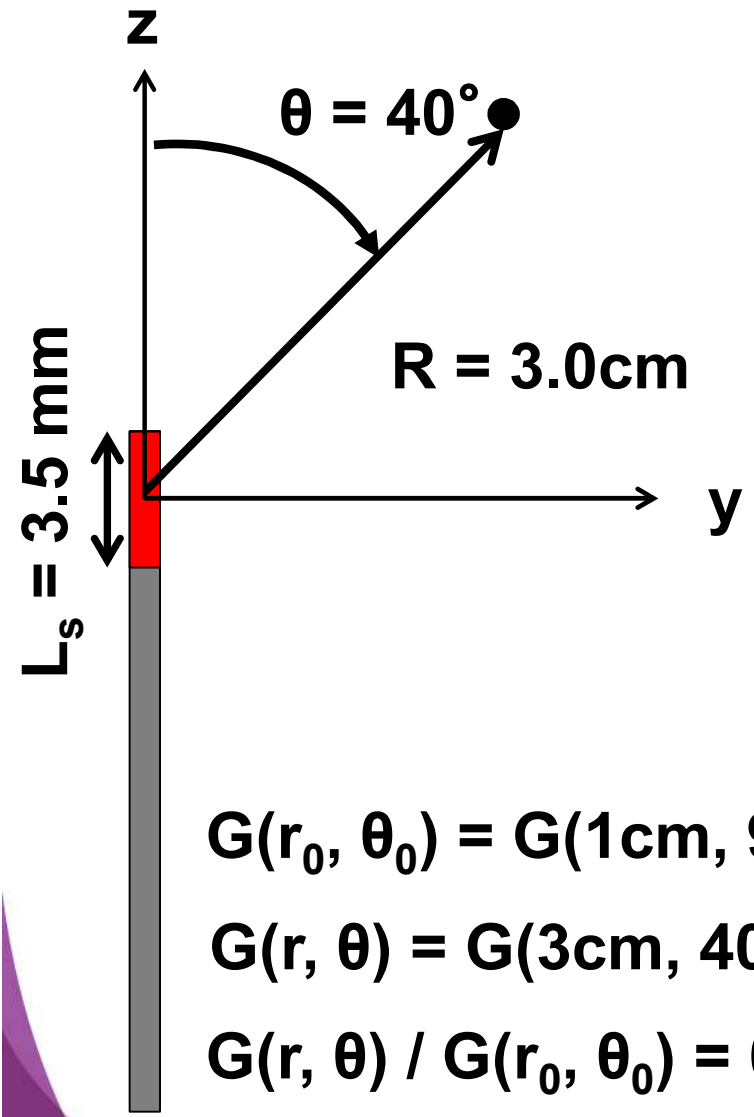
Practical Example: Bebig ^{192}Ir-HDR Source



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

S_K = 40.000 U

Λ = 1,108 cGy/(hU)

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

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

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

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

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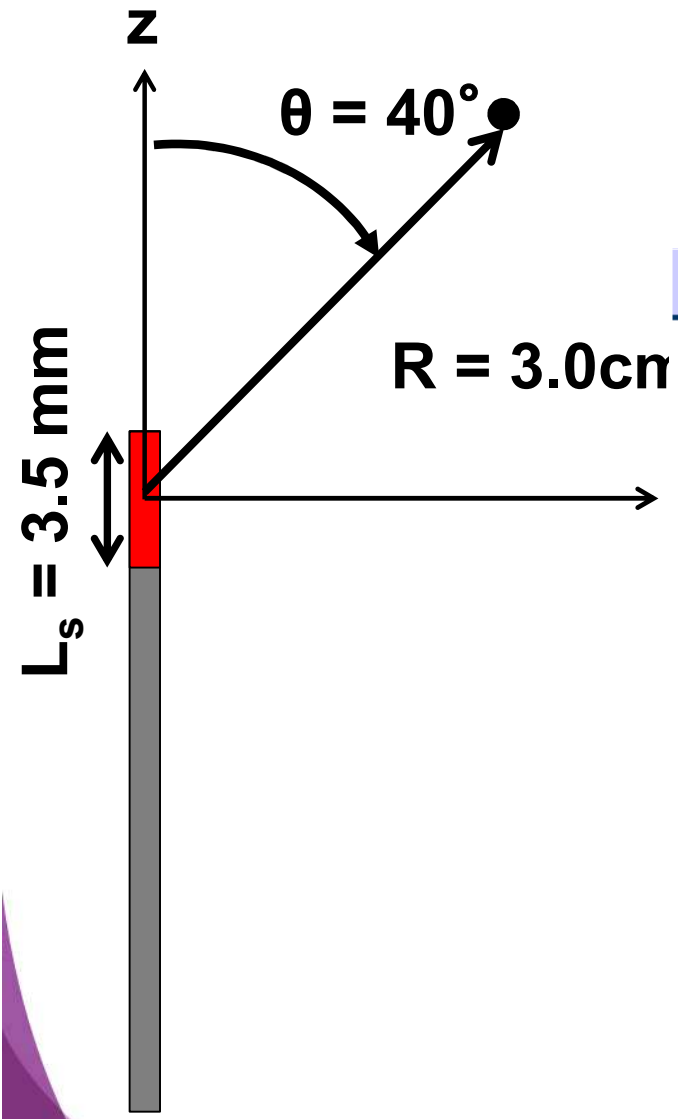
Practical Example: Bebig ^{192}Ir-HDR Source



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

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

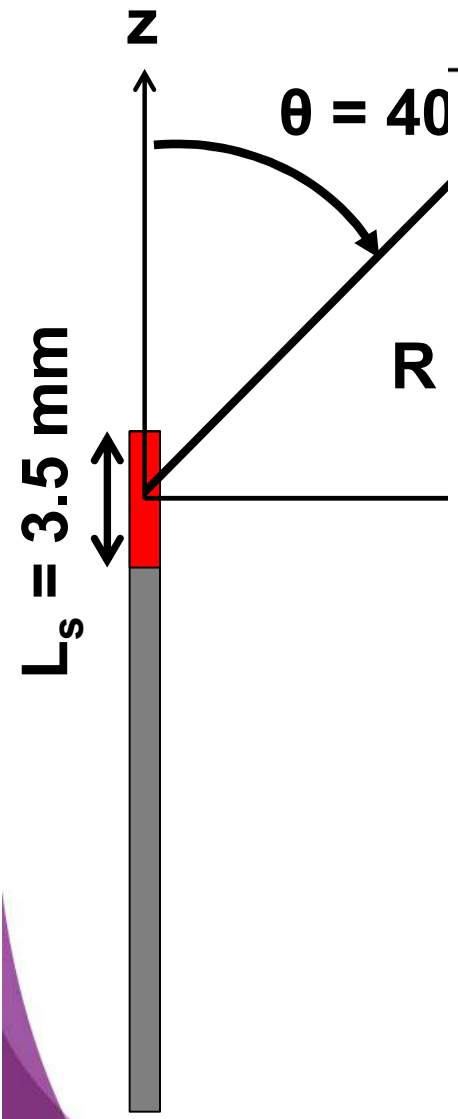
Fitted to: $g(r) = a_0 + a_1 r + a_2 r^2 + a_3 r^3 + a_4 r^4 + a_5 r^5$

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	0.995	0.995	0.994	0.995	0.996	0.995
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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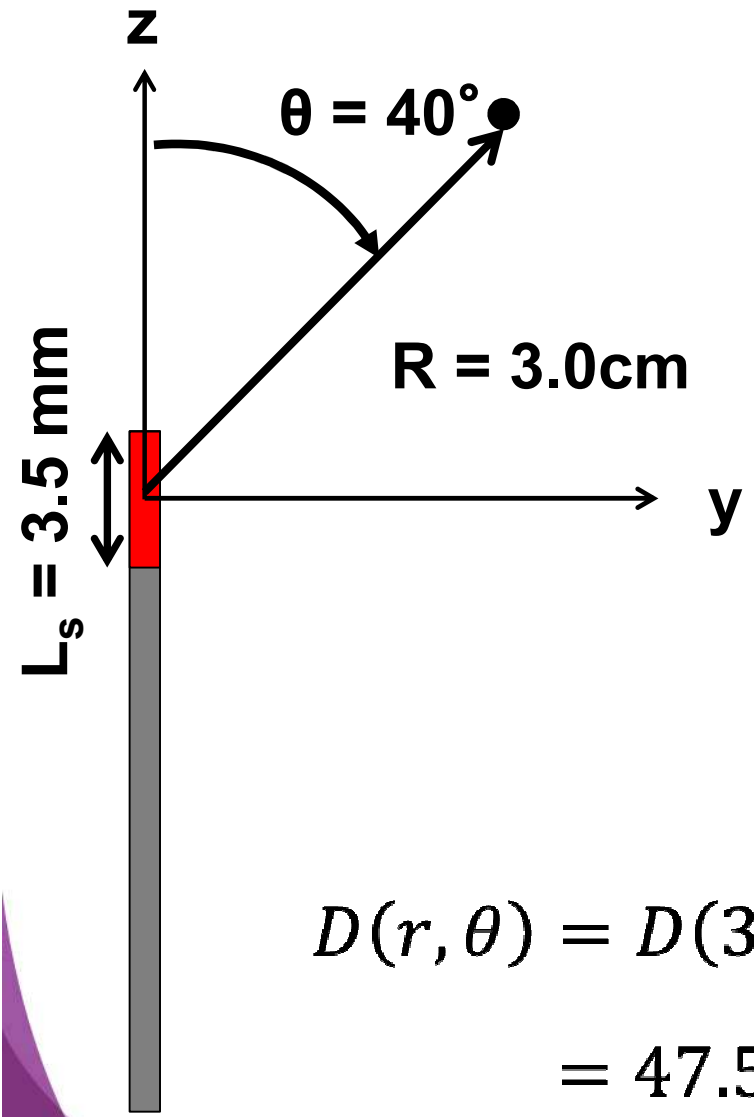
Practical Example: Bebig ^{192}Ir-HDR Source



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

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

$$D(r,\theta) = D(3cm, 40^0) = 4{,}755.05 \frac{cGy}{h}$$

$$= 47.551 \frac{Gy}{h} = 0.793 \frac{Gy}{min}$$

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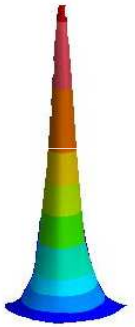
Some Thoughts …

without formulas …

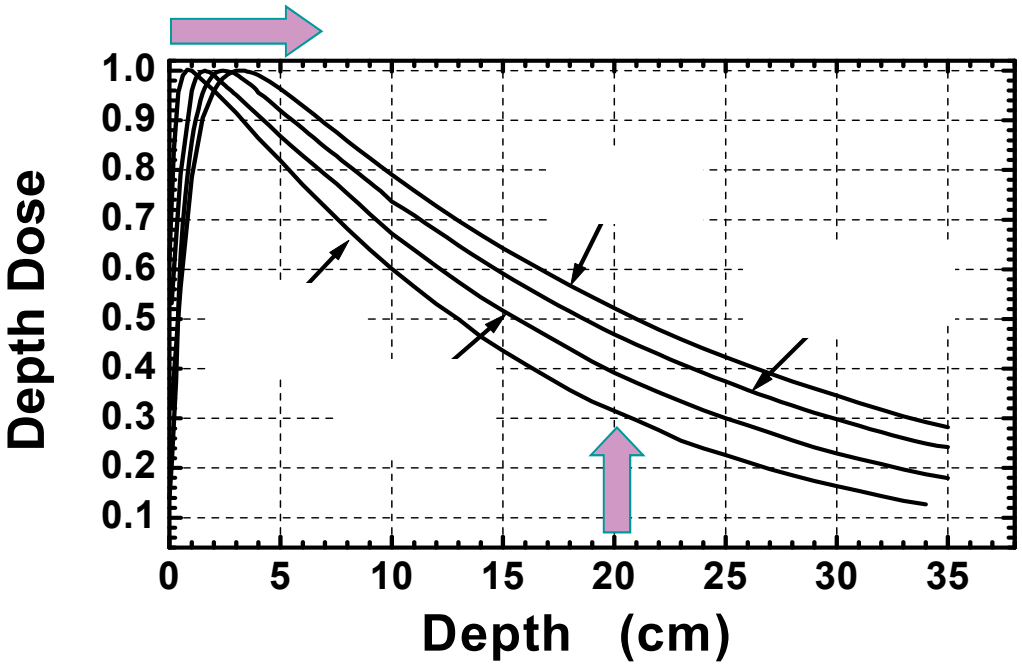
Depth Dose Curve: BRT *versus* EBRT

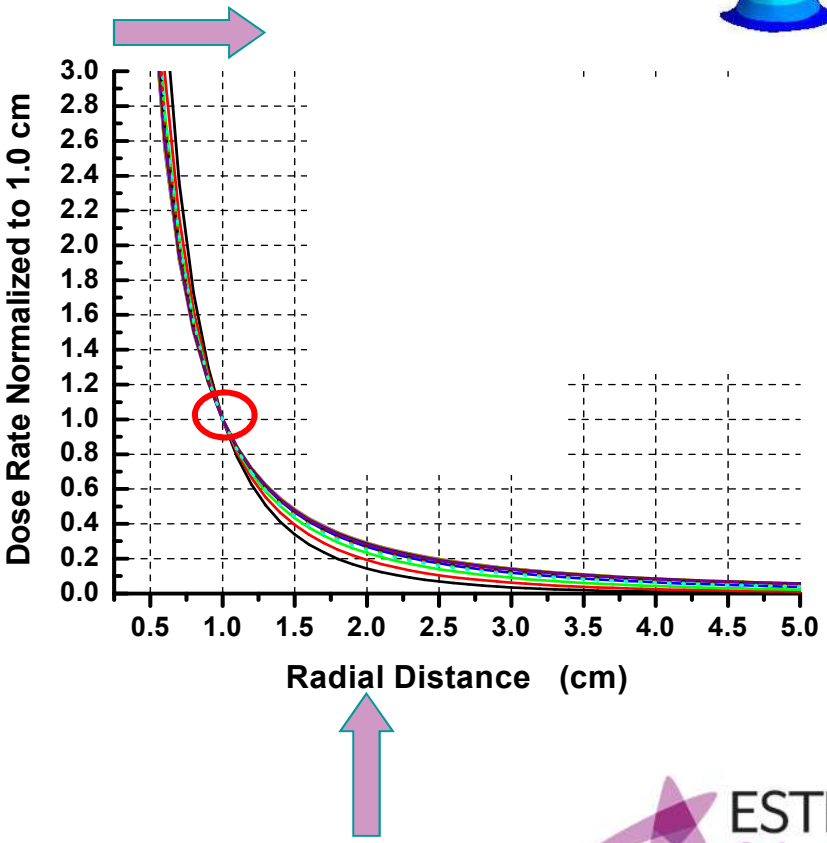
EBRT: Photonen 4, 6, 10 & 18MV ???

BRT: Photonen 20, 30, 40, 60, … 600keV ???



ERT **10 : 1** **BRT**





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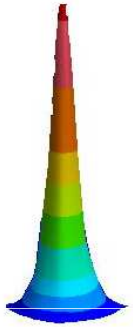
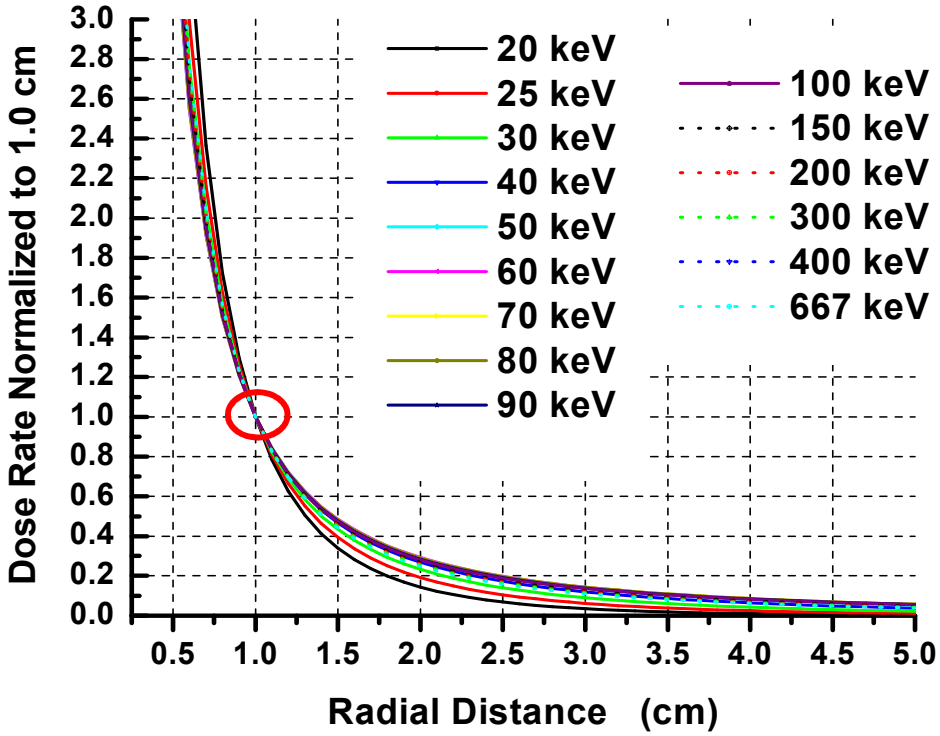
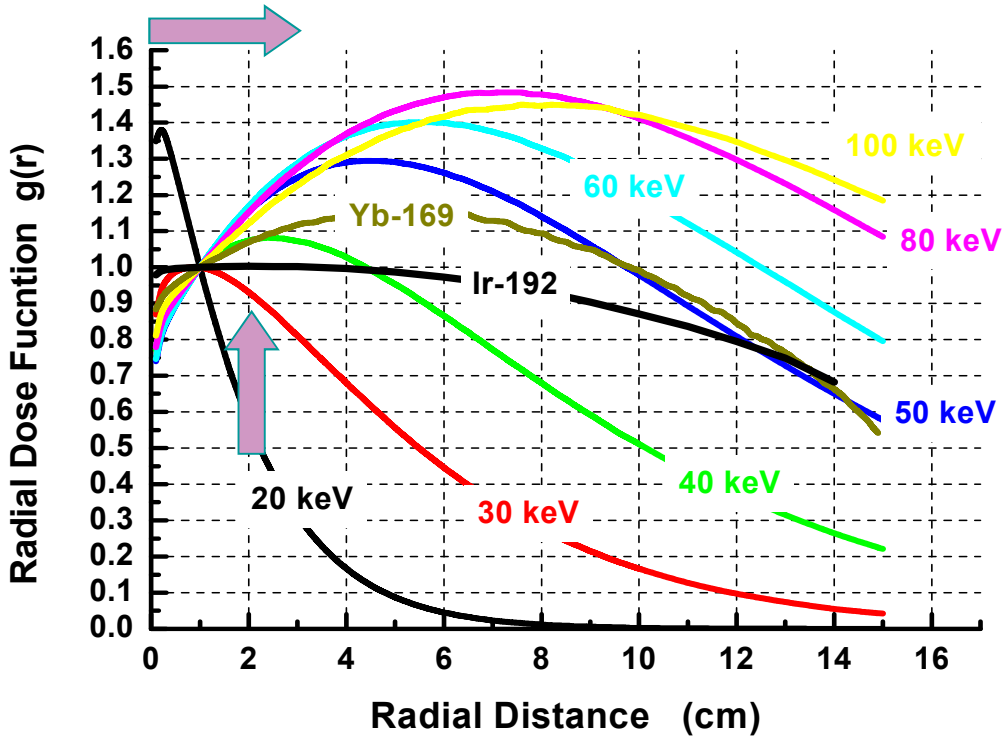
Depth Dose Curve: BRT *versus* EBRT

BRT



BRT: Physics Scatter / absorption





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Dose Calculation: The TG-43 Protocol

- Dose Rate from a single Source
- Dose from Dose Rate
- **Many Sources**
- Limitations

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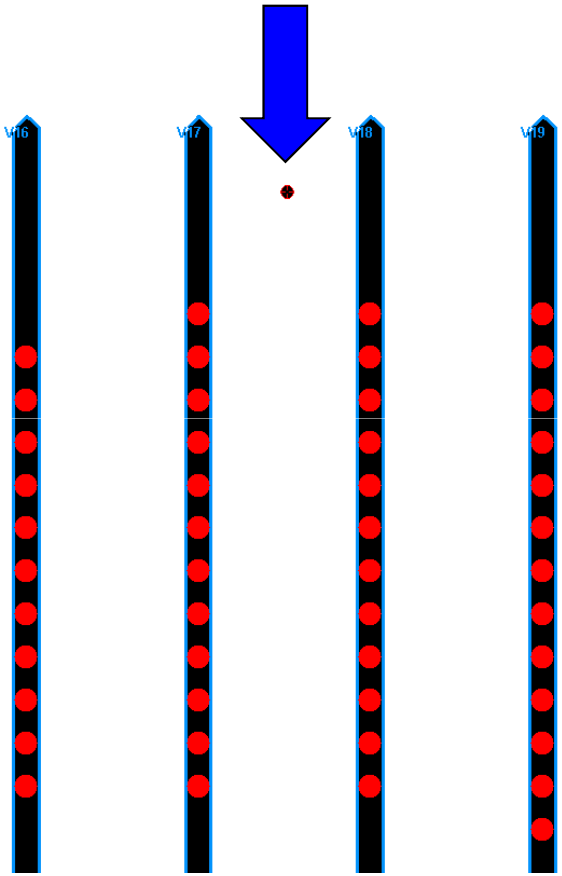
Complexity …..

Many Catheters/Needles, Many Sources …

$$D(P) = D(\vec{r}) = ?$$



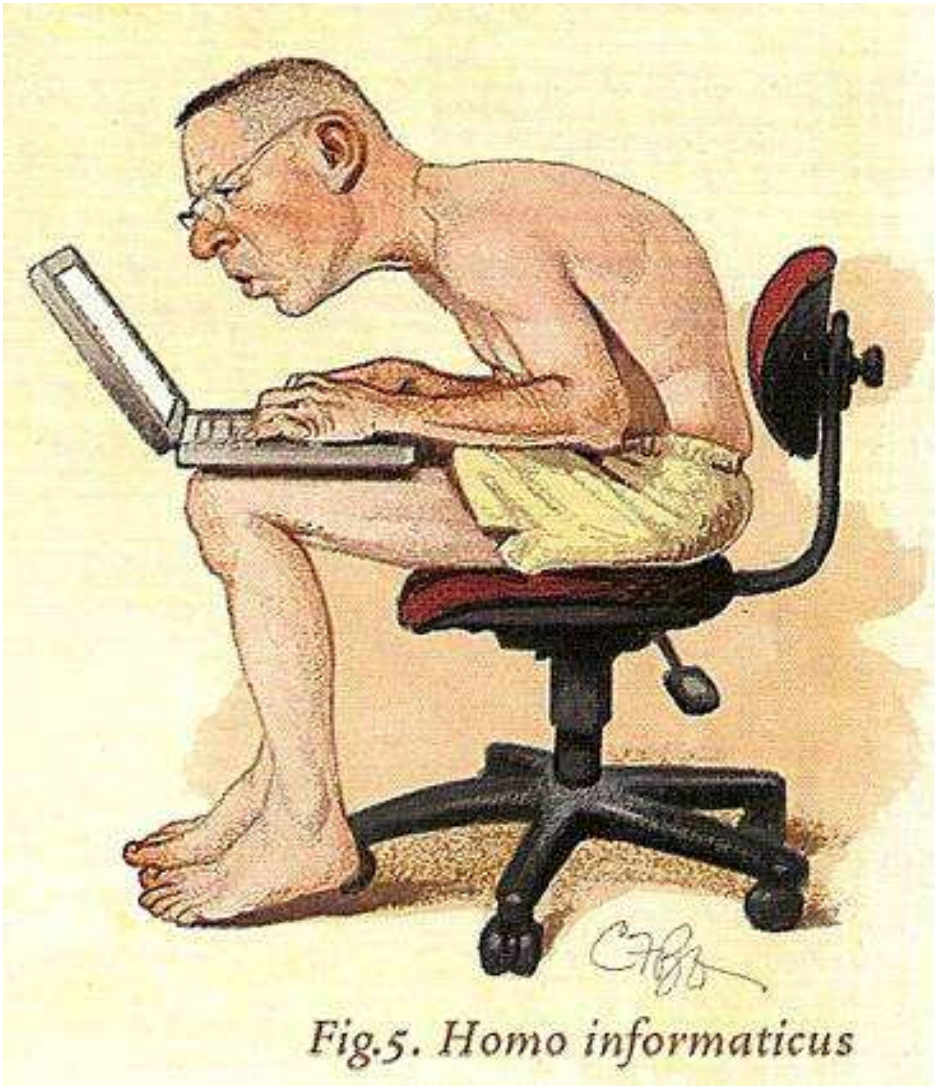
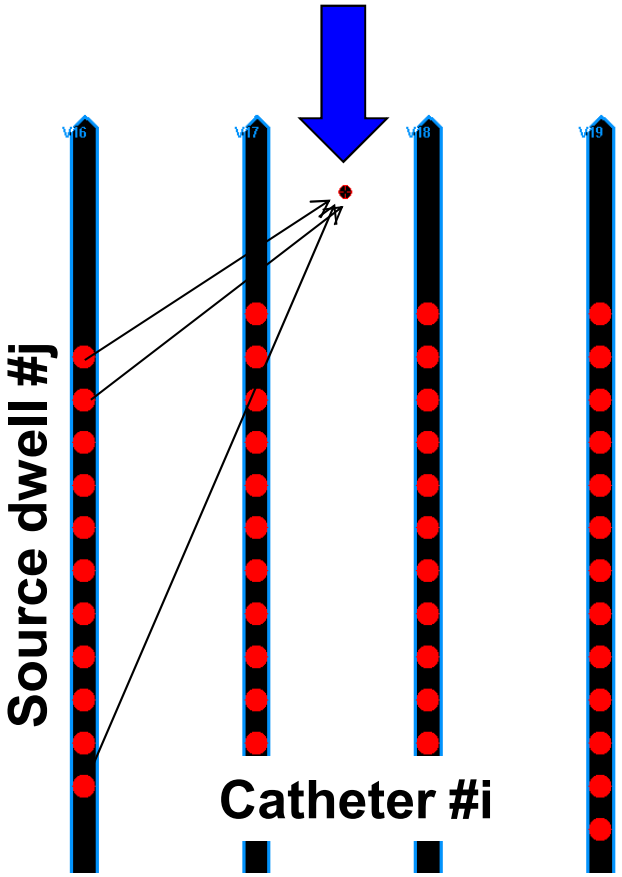


Fig.5. Homo informaticus

Complexity …..

Many Catheters/Needles, Many Sources …

$$D(P) = D(\vec{r}) = ?$$



$$D(P) = \sum_{i=1}^{N_{catheters}} \sum_{j=1}^{M_{sources,i}} t_{i,j} \dot{D}_{i,j}(P)$$

$$with\ \dot{D}_{i,j}(P) = \left\{ S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta) \right\}_{P,i,j}$$

Superposition method

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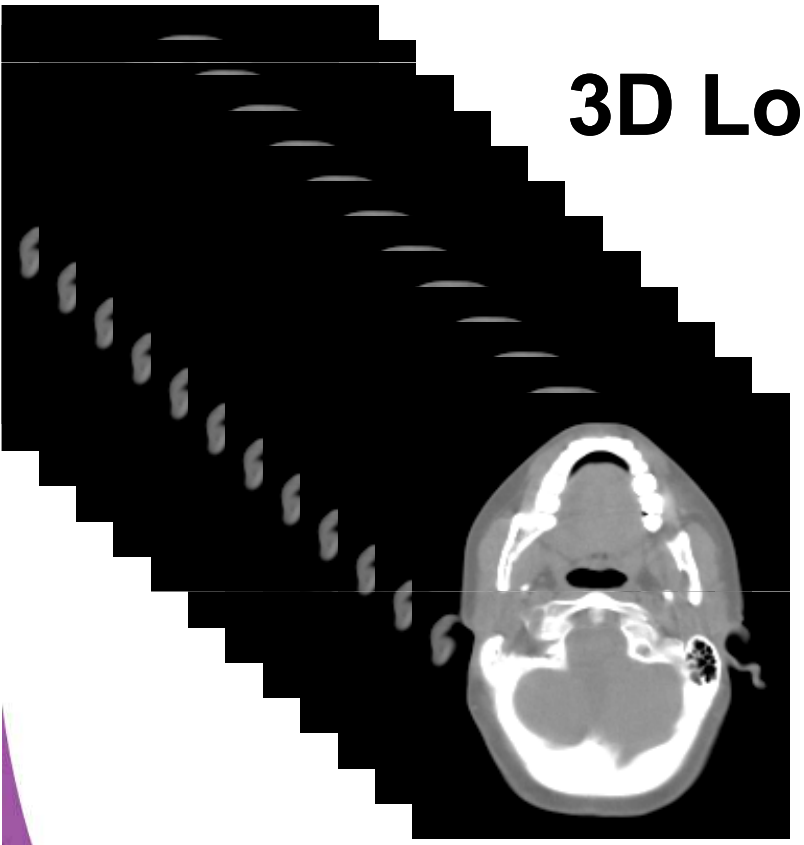
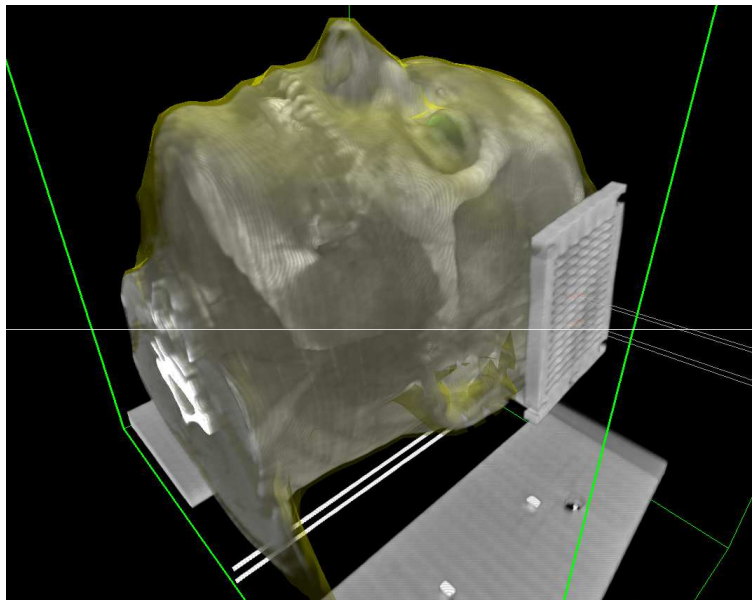
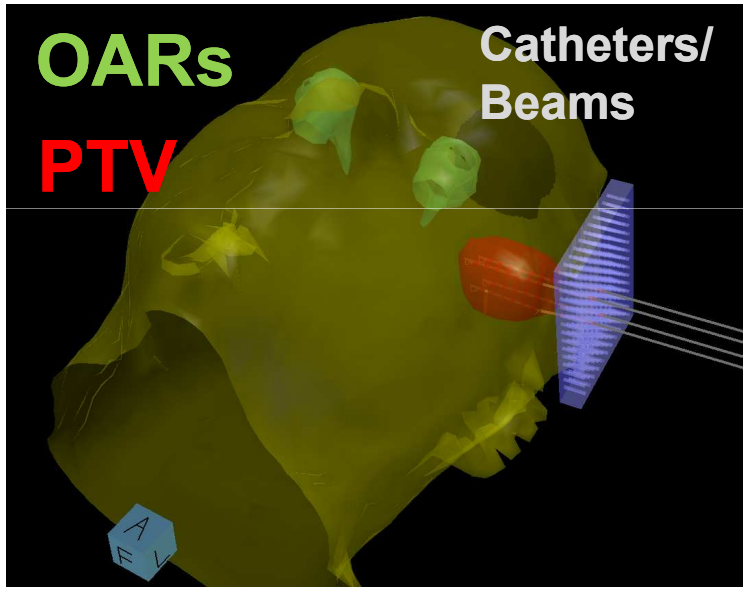
We have to identify/localize the catheters (our fields) and the related Anatomy ….



3D Localization →





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Dose / Dose Rate Calculation at a Point

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

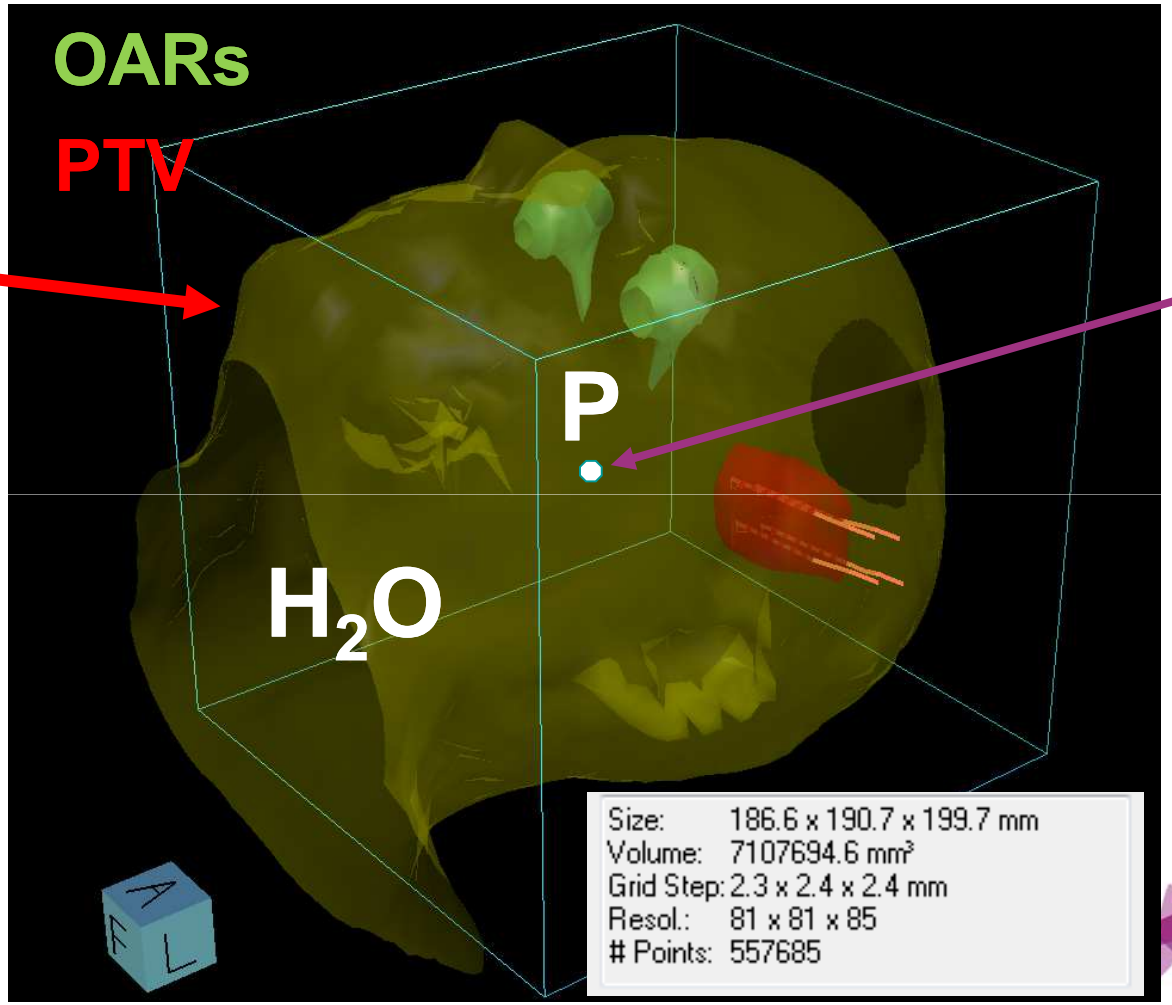
Superposition

^{192}Ir

^{60}Co

^{169}Yb

…



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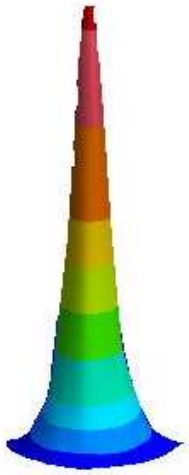
2D Dose Distribution

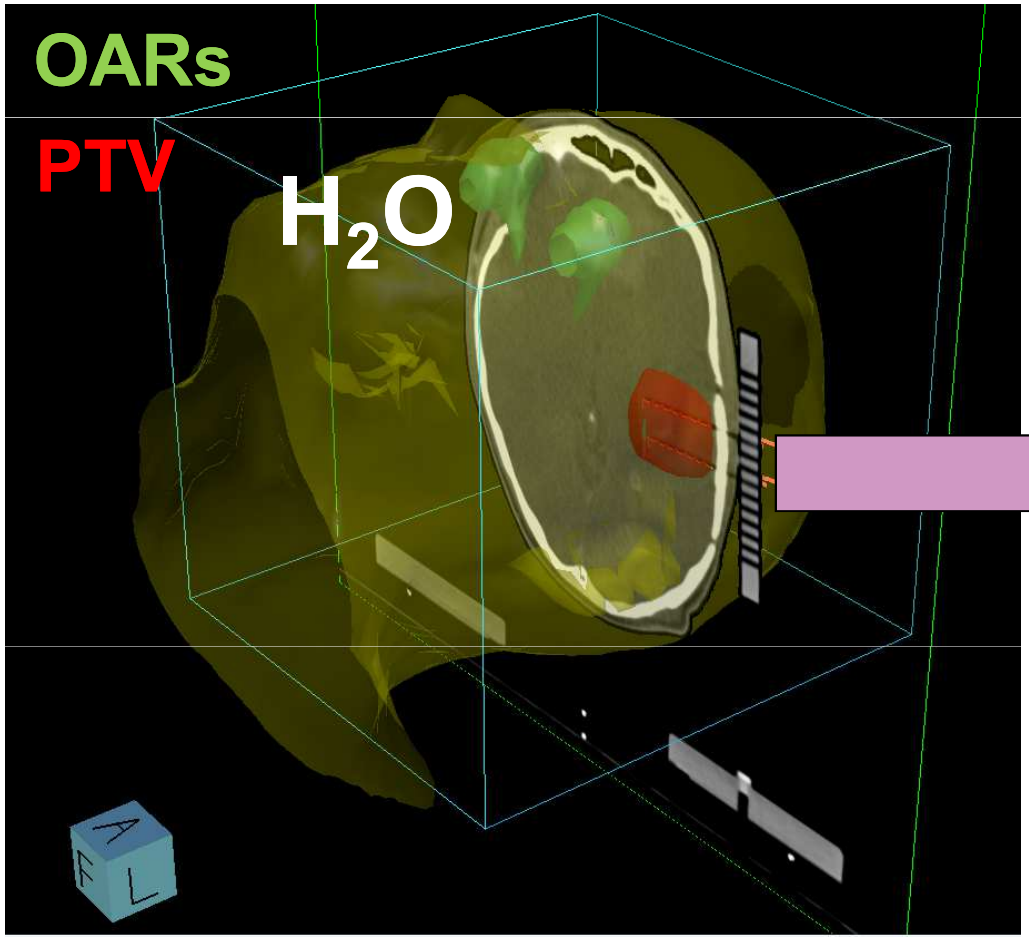


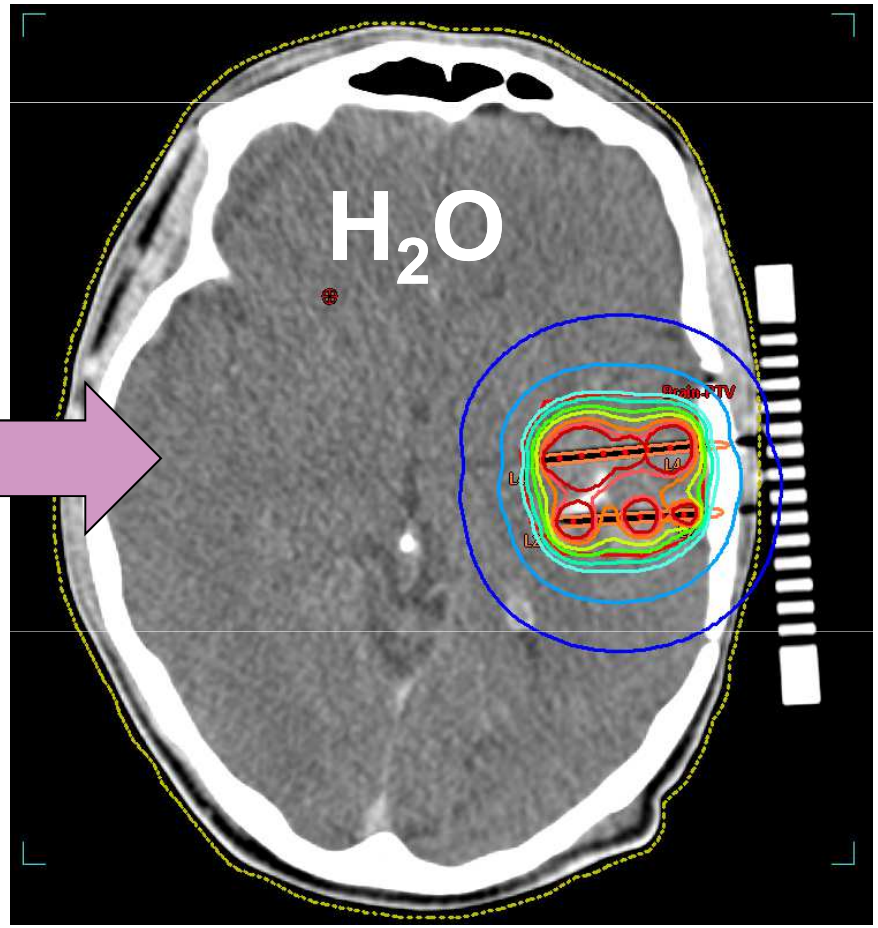
^{192}Ir

^{60}Co

^{169}Yb

...





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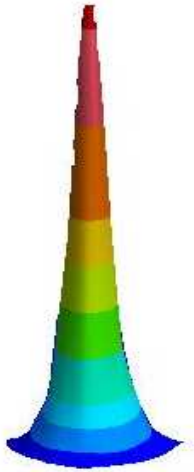
3D Dose Distribution

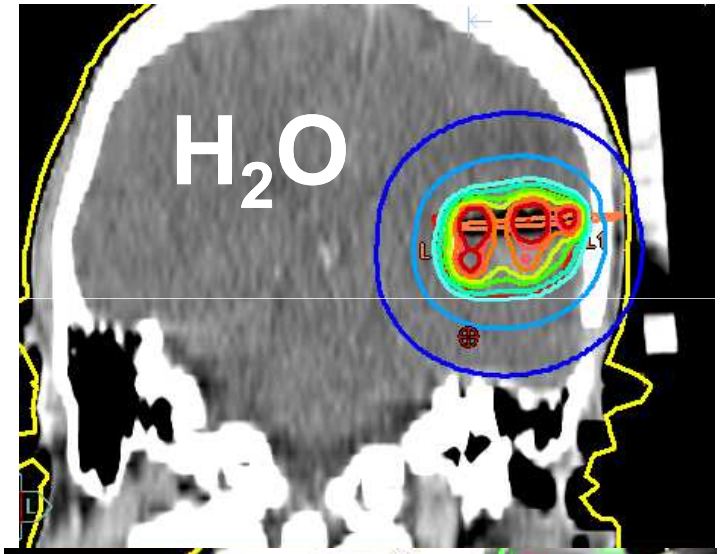


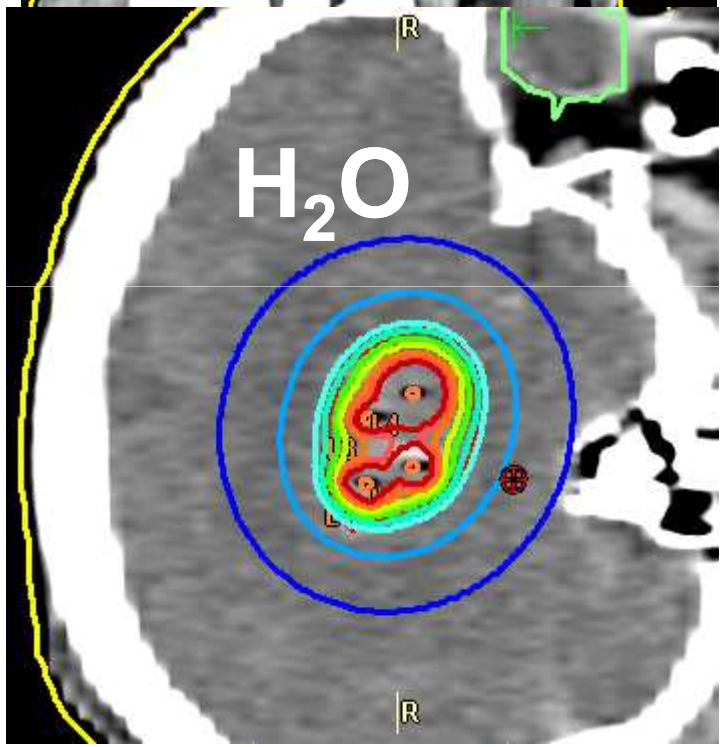
^{192}Ir

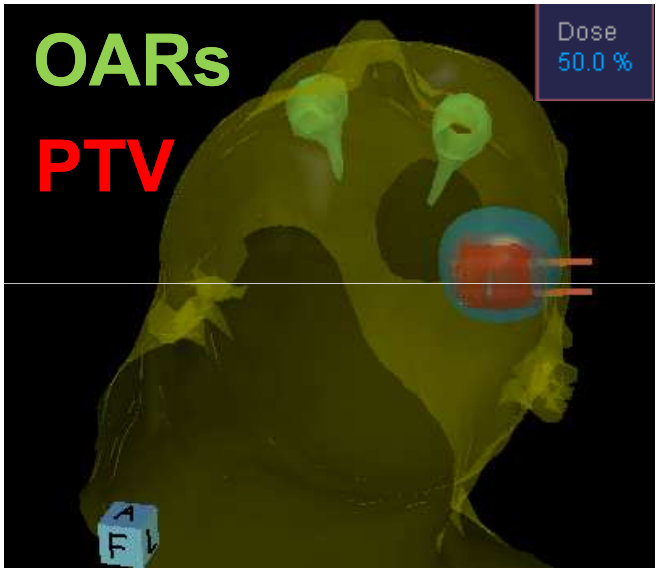
^{60}Co

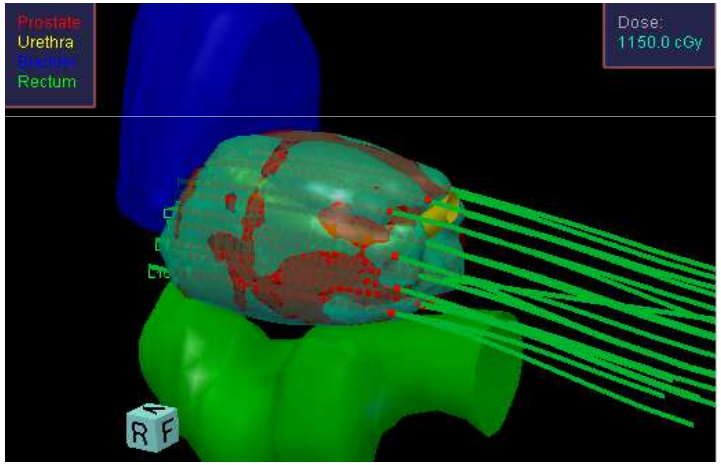
^{169}Yb

...









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Dose Calculation: The TG-43 Protocol

- Dose Rate from a single Source
- Dose from Dose Rate
- Many Sources
- **Limitations**

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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

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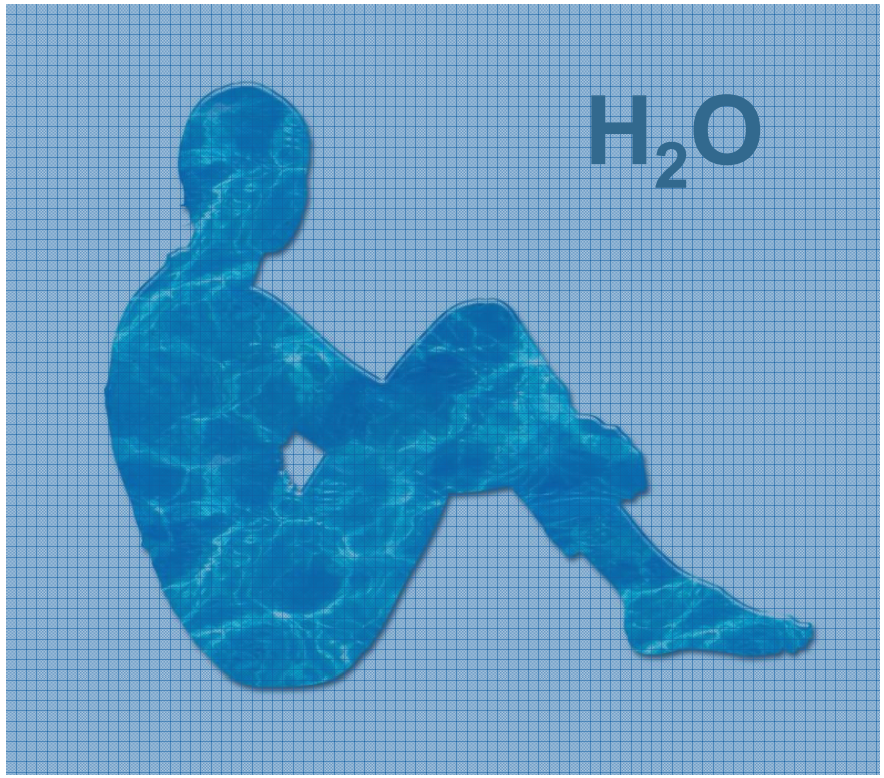
Limitations of TG-43 based Dose Calculation

Assumptions !!!



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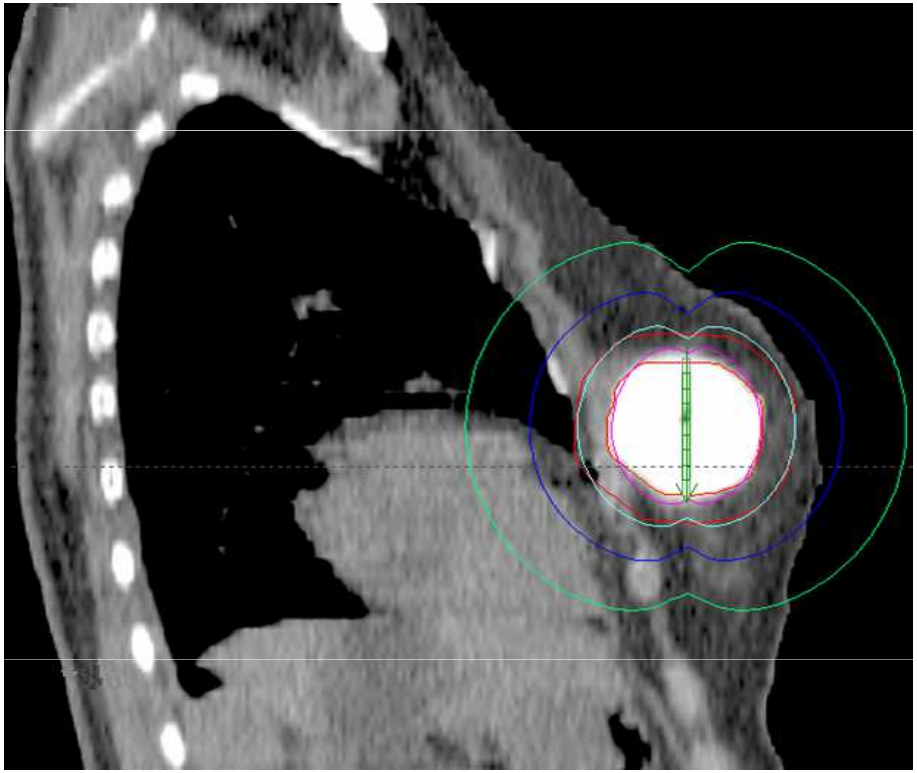

Homogeneous water medium ?

Full scatter conditions ?

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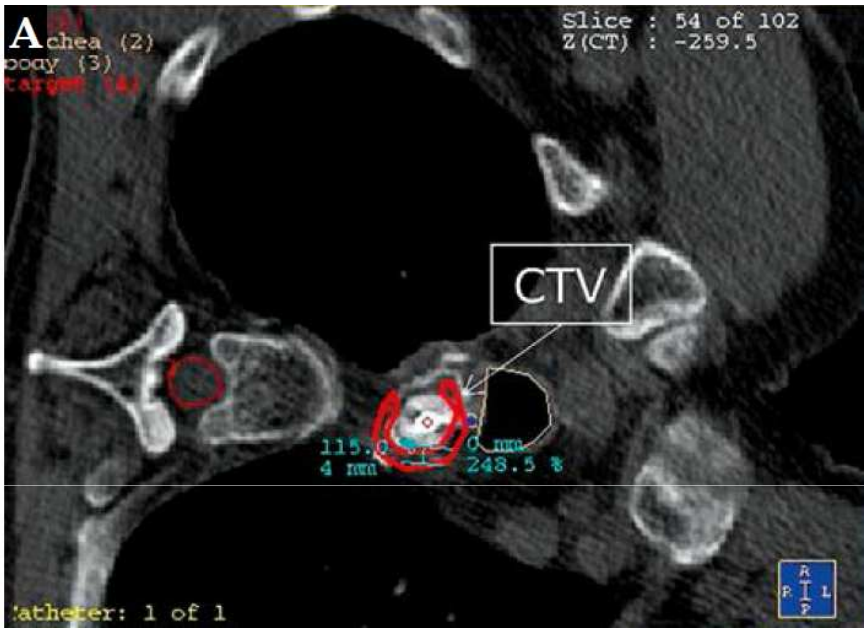
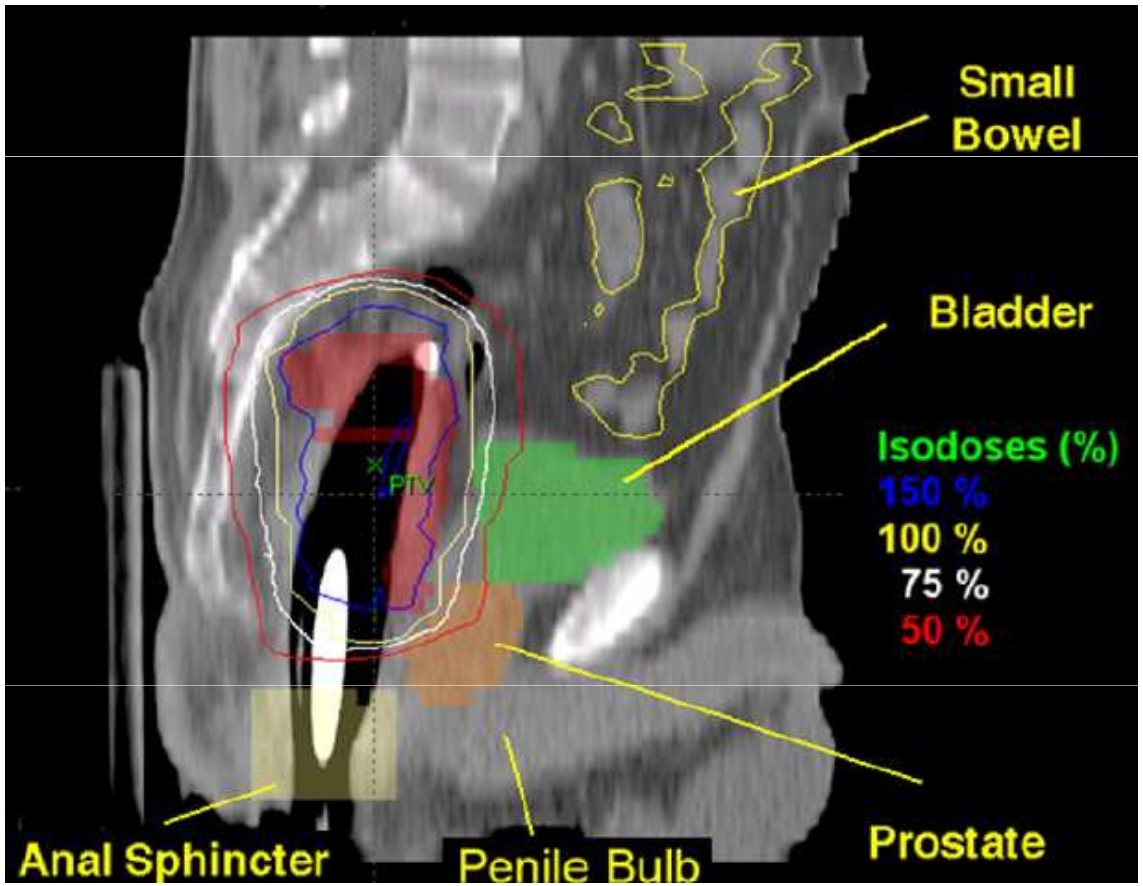
Limitations of TG-43 based Dose Calculation Assumptions !!!

Homogeneous water medium ?



Lettmaier & Strnad. J Contemp Brachytherapy 2014; 6, 2: 236–241, DOI: 10.5114/jcb.2014.43780



Vuong et al. Seminars in Colon & Rectal Surgery, doi:10.1053/j.scrs.2010.01.009, 2010

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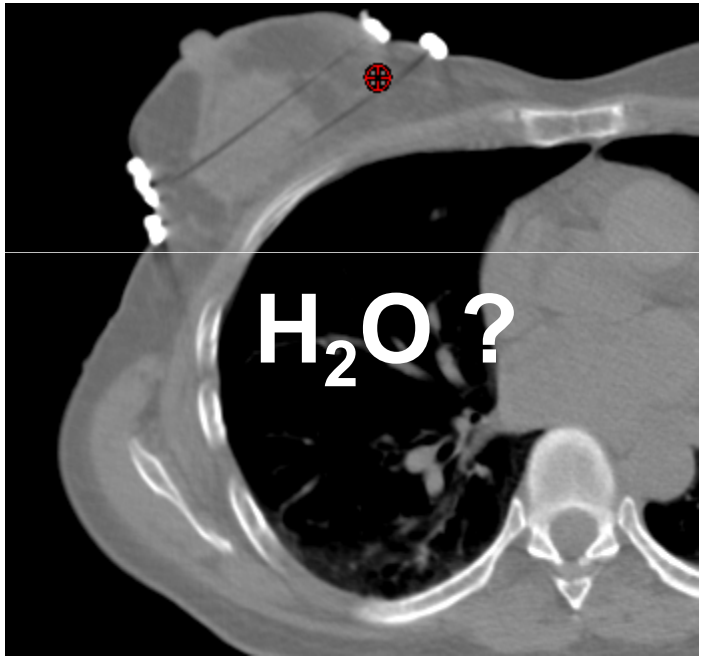
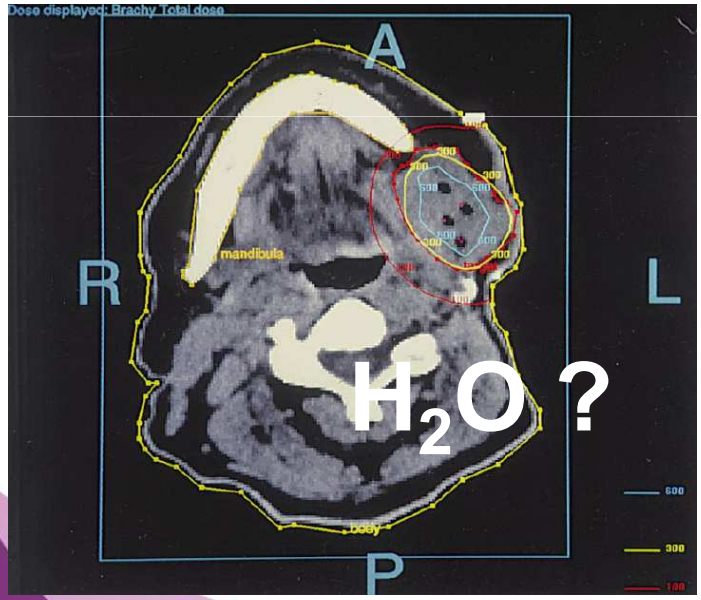
Limitations of TG-43 based Dose Calculation Assumptions: Full scatter Conditions?





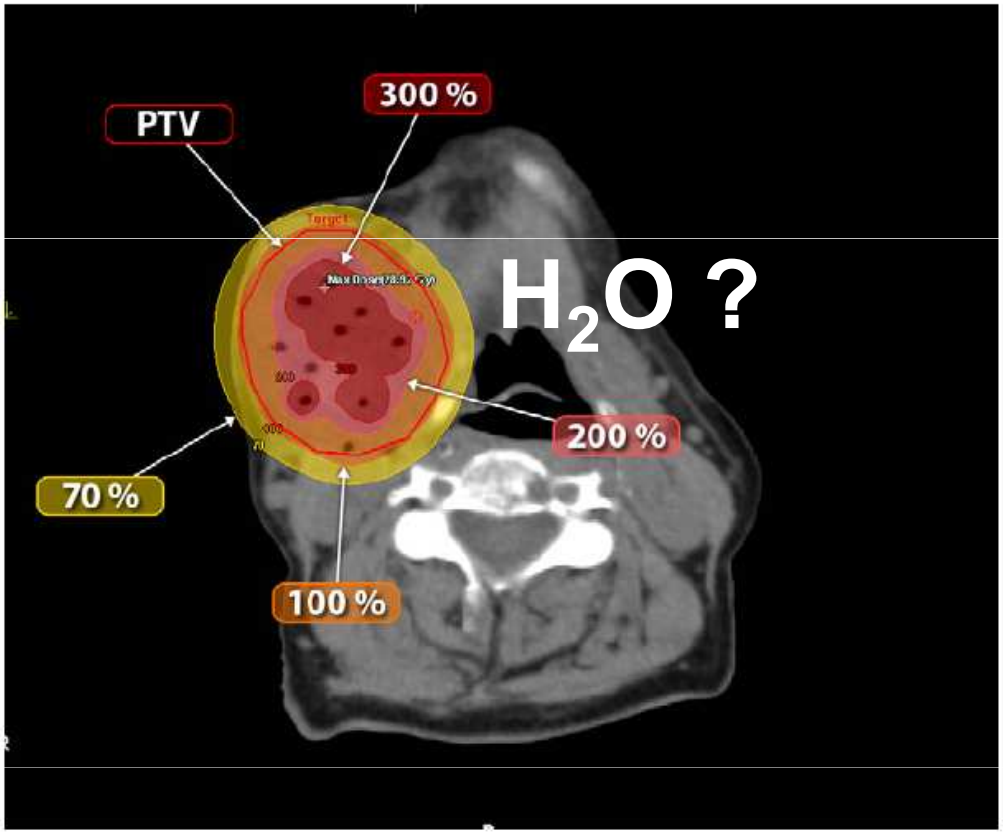


Fig. 1. Axial CT-image showing a right-sided submandibular lymph node recurrence with 2D-isodose distribution after CT-based treatment planning for a plane lying centrally to the target extension. The color gradation represents: red = 300% isodose = 9.0 Gy, pink = 200% isodose = 6.0 Gy, orange = 100% isodose = 3.0 Gy and yellow = 70% isodose = 2.1 Gy. The target volume is denoted as red delineated PTV and the interstitial catheters identifiable as dark dots inside it. The PTV measures 132.5 cm^2.

Tselis N et al. Radiotherapy & Oncology 98, 2011
doi:10.1016/j.radonc.2010.10.025

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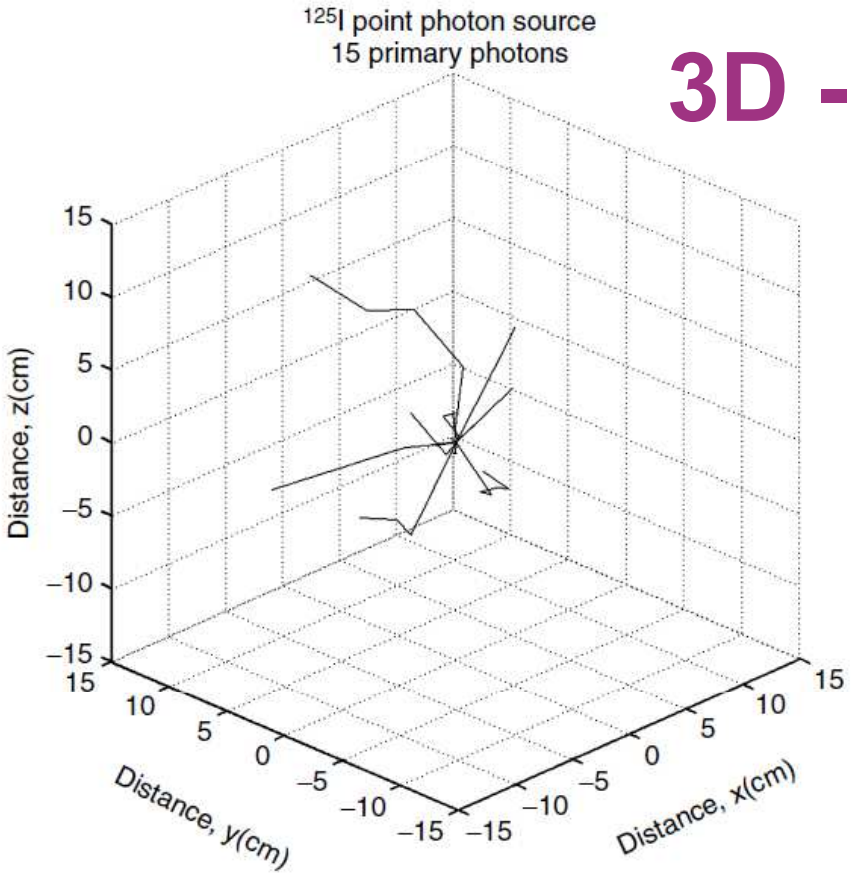
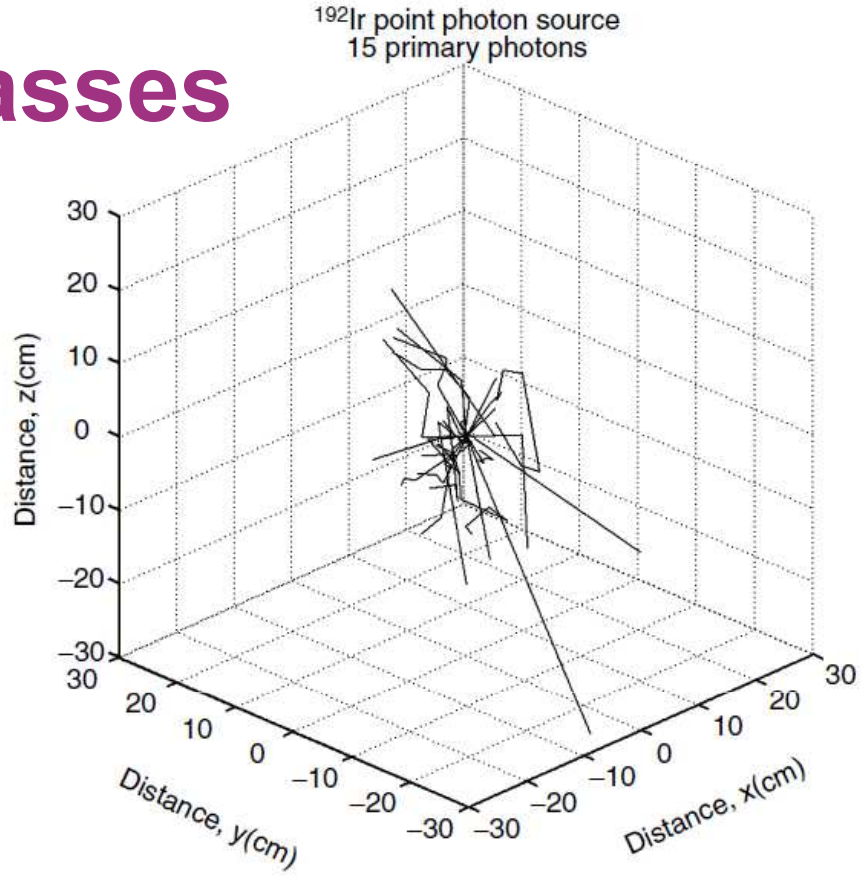
Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

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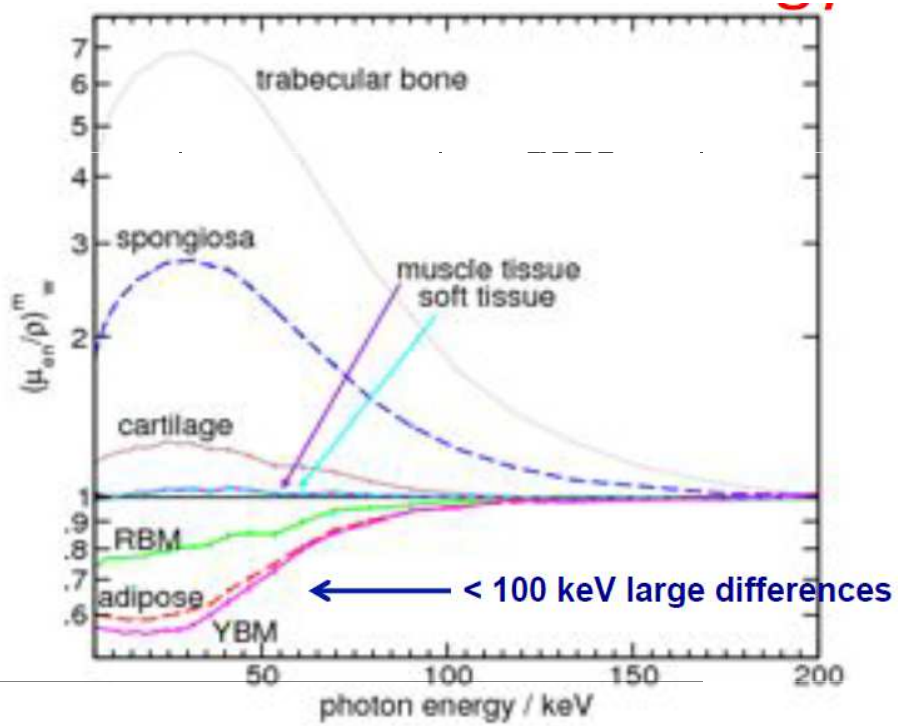
Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

Sensitivity of Anatomic Sites to Dosimetric Limitations of Current Planning Systems

anatomic site	photon energy	absorbed dose	attenuation	s		
prostate	high					
	low	XXX	XXX			
breast	High					
	low	XXX	XXX			
GYN	high					
	low	XXX	XXX			
skin	high					
	low	XXX				
lung	high					
	low	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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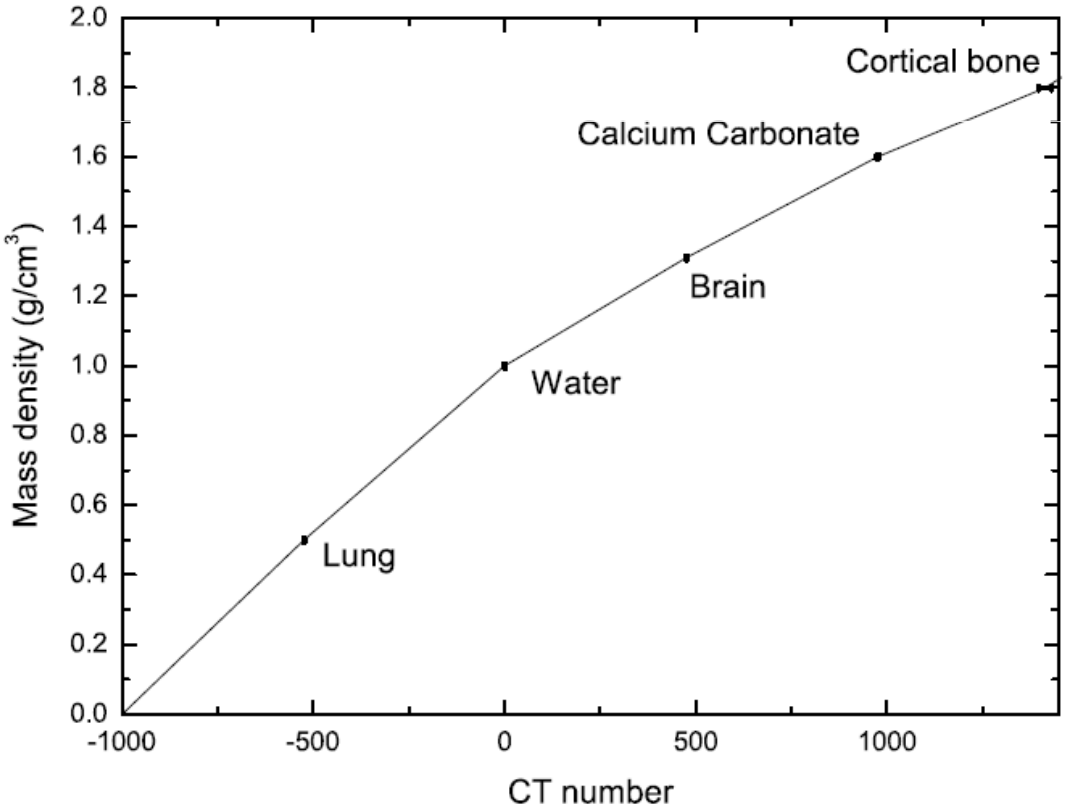
Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation



$$HU_{tissue} = \left\{ \frac{\mu_{tissue} - \mu_{water}}{\mu_{water}} \right\} \cdot 1000$$

CT: Calibration curve Hus vs. ρ or ρ_e

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

BJR
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Received: 24 February 2014 | Revised: 10 July 2014 | Accepted: 14 July 2014
doi: 10.1259/bjr.20140163

Cite this article as:
Papagiannis P, Pantelis E, Karaiskos P. Current state of the art brachytherapy treatment planning dosimetry algorithms. Br J Radiol 2014;87: 20140163.

BRACHYTHERAPY DOSIMETRY SPECIAL FEATURE: REVIEW ARTICLE

Current state of the art brachytherapy treatment planning dosimetry algorithms

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Medical Physics Laboratory, Medical School, National and Kapodistrian University of Athens, Athens, Greece

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E-mail: *ppapagi@med.uoa.gr*

ABSTRACT

Following literature contributions delineating the deficiencies introduced by the approximations of conventional brachytherapy dosimetry, different model-based dosimetry algorithms have been incorporated into commercial systems for ^{192}Ir brachytherapy treatment planning. The calculation settings of these algorithms are pre-configured according to criteria established by their developers for optimizing computation speed *vs* accuracy. Their clinical use is hence straightforward. A basic understanding of these algorithms and their limitations is essential, however, for commissioning; detecting differences from conventional algorithms; explaining their origin; assessing their impact; and maintaining global uniformity of clinical practice.

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Thank you very much for your Attention

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Budapest, March 5-8 2017

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Modern Brachytherapy Techniques

ESTRO TEACHING COURSE

Budapest 2017

BRACHYTHERAPY IN KELOIDS

Jose Luis Guinot

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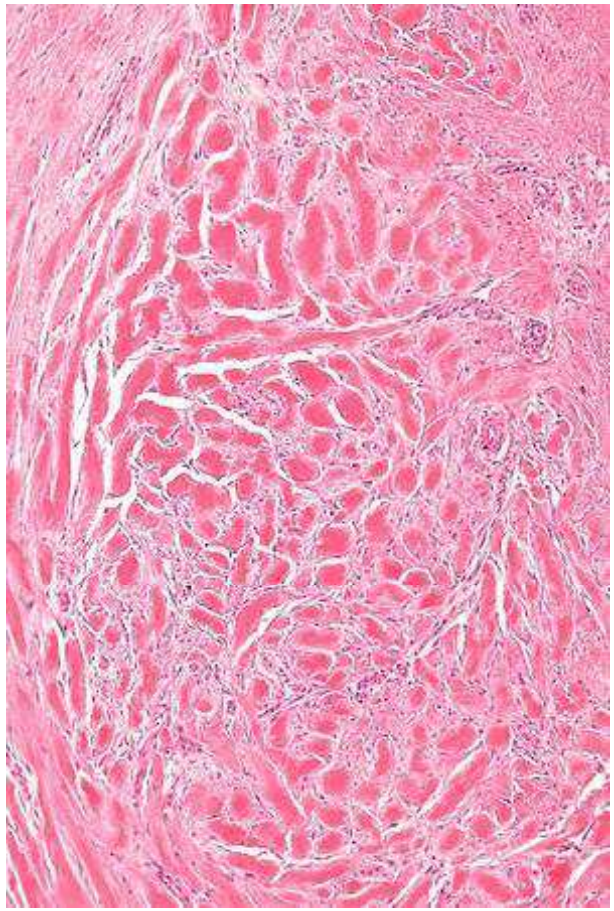
INTRODUCTION

- A keloid is an abnormal proliferation of scar tissue that forms at the site of cutaneous injury (surgical incision or trauma); it does not regress and grows beyond the original margins of the scar.
- Keloids are benign dermal fibroproliferative tumors with no malignant potential.
- The production of extracellular matrix proteins, collagen, elastin, and proteoglycans presumably is due to a prolonged inflammatory process in the wound.



https://librepathology.org/wiki/Keloid

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EPIDEMIOLOGY

- Keloids are found only in humans
- In 5-15% of wounds.
- Both sexes equally,
- Higher incidence of women presenting with keloids, possibly secondary to the cosmetic implications.
- In persons with highly pigmented skin is 15 times higher
- Average age at onset is 10-30 years.
- Persons at the extremes of age rarely develop keloids.

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EPIDEMIOLOGY

- Keloid formation can occur within a year after injury
- The most frequently involved sites are areas that are constantly subjected to high skin tension.
- Wounds on the anterior chest, shoulders, flexor surfaces of the extremities (eg, deltoid region), and anterior neck and wounds that cross skin tension lines.
- a wound healing by secondary intention >3 weeks.
- Wounds with chronic inflammation, (earring) or repeated trauma.

INDICATIONS TO TREAT

- Most patients are concerned about cosmesis, or present with complaints of pruritic pain or a burning sensation around the scar.
- Symptomatic keloids not responding to topic treatment
- Local disturbances
- Functional compromise
- Emotional or cosmetic alteration

- AVOID: keloids on burned areas, pregnancy, age<18

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TREATMENT

- Recurrence rates with surgery alone range from 45-100%.
- corticosteroid injection,
- steroid injection with pressure dressing,
- Cryotherapy
- Interferon intralesional
- x-ray therapy, 5 Gy x 3 days
- Brachytherapy LDR or HDR
- HDR with surgical excision → good to excellent cosmetic results with 80-94% no recurrence. hyperpigmentation (5%) telangiectasia (7%)

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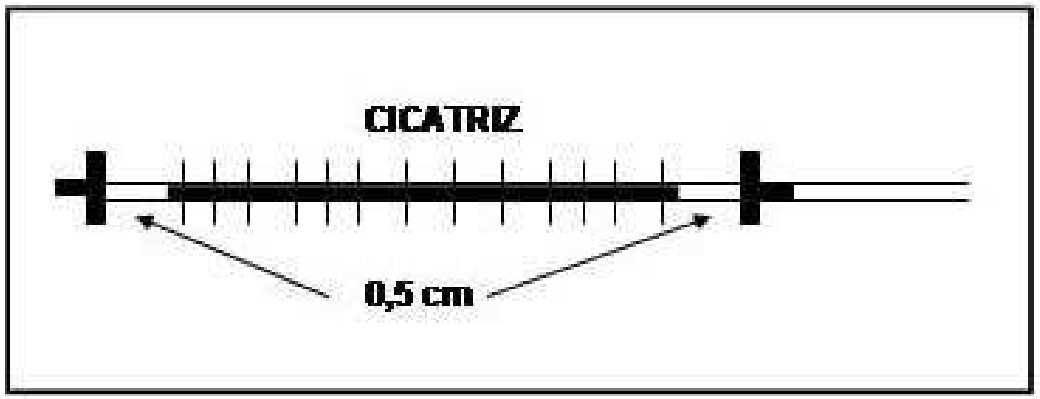
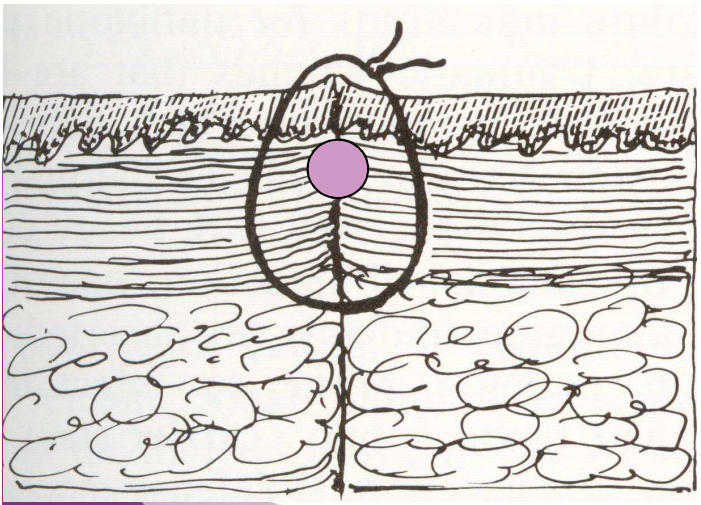

CICATRIZ
0,5 cm



IVO. Valencia
3 x 5 Gy

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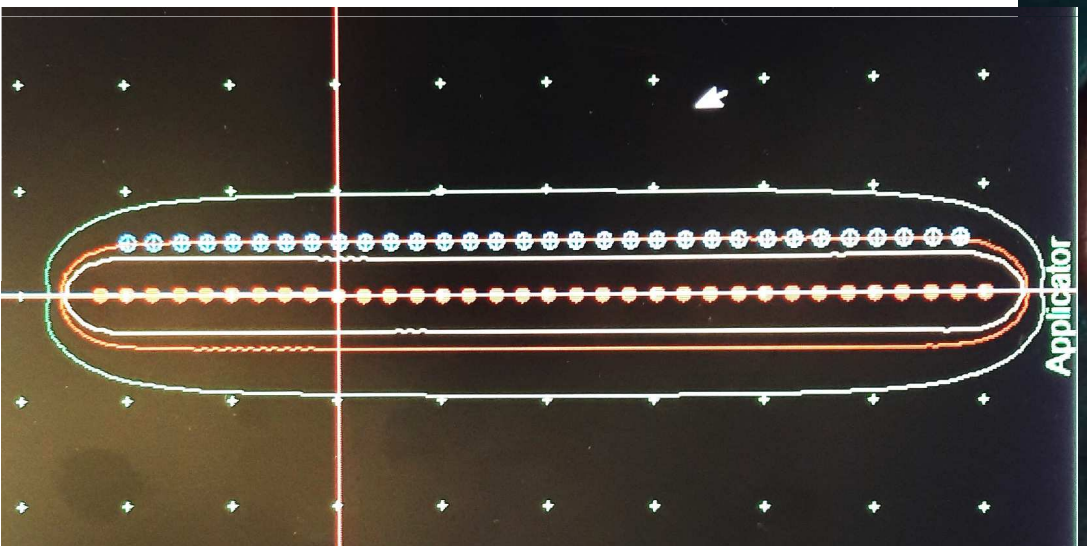
Prescription: 5mm



First session before 6 hours
Two sessions the next day

IVO: 3 x 5 Gy HDR
at 5mm from the axis

TREATMENT: LDR vs HDR

- I.E.O. Milan. **LDR 16 Gy, HDR 12 Gy**
- recurrence rates were similar
  - 46 keloids with LDR: **30.4%**
  - 50 keloids with HDR: **38%**
- Recurrence rate was higher in males, <44 years, for arms, neck, and chest wall anatomic sites and for symptomatic keloids
- pain, itching, or stress, present at diagnosis in 64 keloids, were relieved in 92% with HDR but in 68% with LDR.

↑ recurrences
→ Low doses

De Cicco L, Vischioni B, Vavassori A, et al. Postoperative management of keloids: Low-dose rate and high-dose-rate brachytherapy. Brachytherapy; 2014; 13:508-513.

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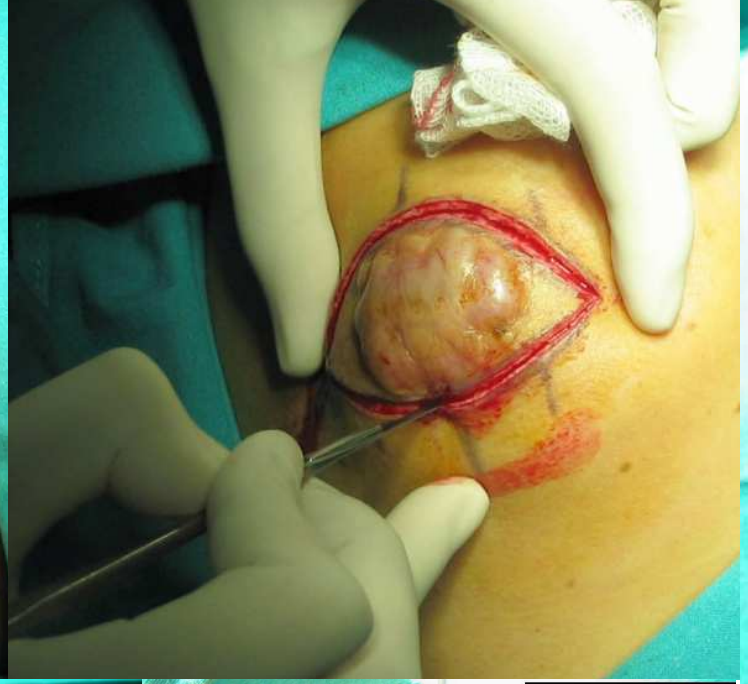

Alvarez A, Garcia T, Herranz R. Queloides. BT con LDR. Guia de braquiterapia. SEOR 2007.

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TREATMENT: RECALCITRANT KELOIDS

- 43 patients with 67 keloids in total.
- After extralesional excision, HDR **2 × 6 Gy** the first **within 4 hours** after surgery and the second within 24 hours.
- Recurrence rate: **3.1%** mean FU 33.6 months.
- Complaints of pain and pruritus decreased by 82.9 and 87.2 percent,
- Pigmentation problems were seen in 21.4%

Are 2 fractions enough?

Van Leeuwen MC, Stokmans SC, Bulstra AE et at. High-dose-rate brachytherapy for the treatment of recalcitrant keloids: a unique, effective treatment protocol. Plast Reconstr Surg. 2014;134:527-34

TREATMENT: RECURRENT KELOIDS

- 24 patients with 32 recurrent keloids with two or more failed treatment modalities, 3 patients had been previously treated with EBRT
- with perioperative HDR; **3 x 6 Gy to 5 mm** total dose of 18 Gy within 36 hours after the resection.
- Disappearance of pain and pruritus was noticed in all patients (19).
- FU 29.4 m, 2 keloid recurrences and 2 mildly hypertrophied scars. Local control: **94%.**
- Pigmentary abnormalities in 3 patients,
- mild delay in the wound-healing process, 6 pat.

Jiang P, Baumann R, Dunst J et al. Perioperative Interstitial High-Dose-Rate Brachytherapy for the Treatment of Recurrent Keloids: Feasibility and Early Results.IJROBP 2016; 94:532-6.

TREATMENT: DOSES

- 35 Pat with 54 keloids, HDR within 6 hours
- 1 x 4 Gy + 2 x 3 Gy. 4 recurrences/9
- 1 x 6 Gy + 2 x 4 Gy 1 recurrence /38
- **3 x 6 Gy** 0 recurrences /7
- Better cosmetic results were found at the higher-dose schemes.

Better higher doses

Veen RE, Kal HB. Postoperative high-dose-rate brachytherapy in the prevention of keloids. Int J Radiat Oncol Biol Phys. 2007 Nov 15;69(4):1205-8.

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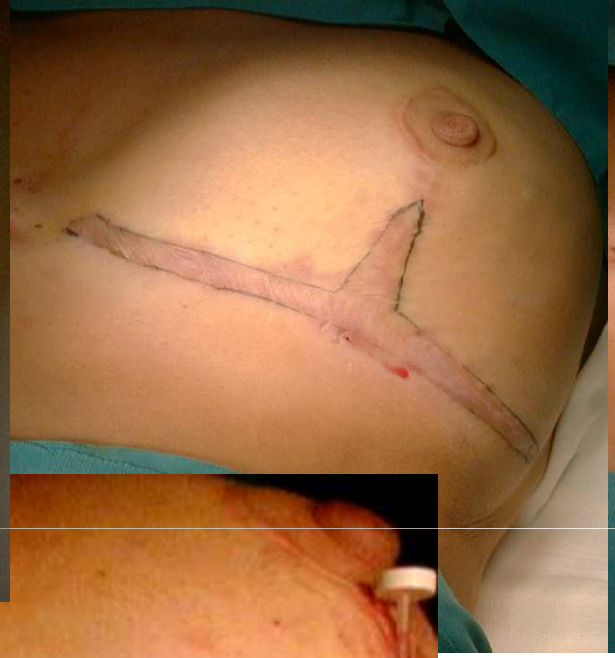
TREATMENT

- 169 keloids treated with HDR (1991-1998).
- 147 surgery + HDR **4 x 3 Gy in 24 h** (9am, 15pm, 21pm, and 9 am next day).
- 22 definitive HDR 18 Gy in **6 x 3 Gy in one ½ days**
- HDR within 30-60 min of surgery **at 1 cm** from the center of the catheter
- 7 years FU recurrences 4.7%

  prior surgery **3.4%**, HDR alone: **13.6%.**
- Cosmetic results good or excellent in 130/147 patients
- Skin pigmentation changes: 10 telangiectasias: 12

Guix B, Henríquez I, Andrés A, Finestres F, Tello JI, Martínez A. Treatment of keloids by high-dose-rate brachytherapy: A seven-year study. IJROBP 2001; 50:167-72.

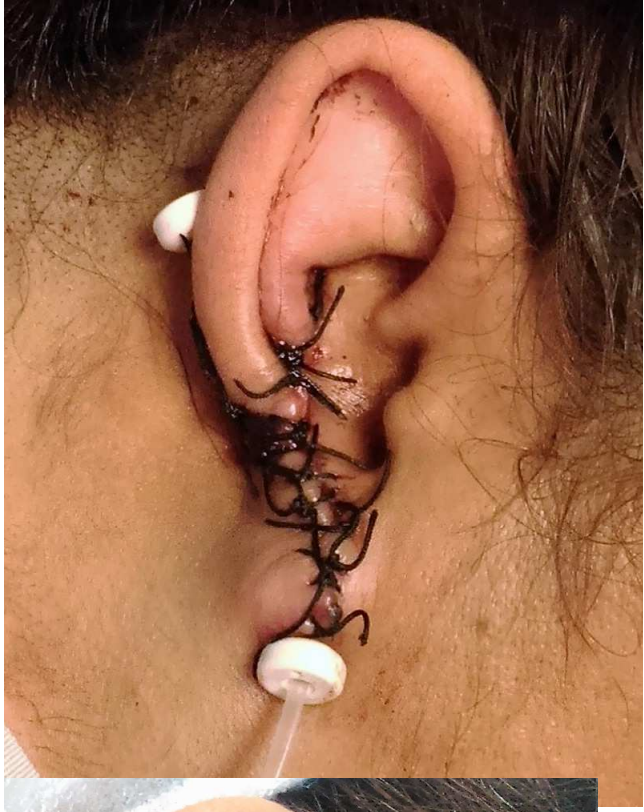


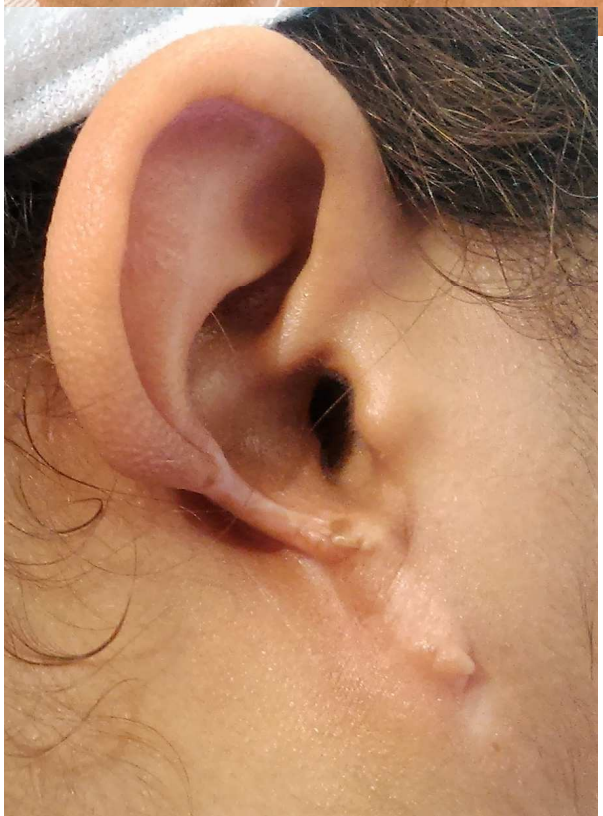
Guix B, Henriquez I, Tello JI, Caravante MD. Queloides. BT con HDR. Guia de braquiterapia. SEOR 2007.

TREATMENT: EARLOBES KELOIDS

- 145 pat/174 lesions, 86% primary,
  14% recurrent.
- Recurrence rates: 4.7% and 0%
- Overall recurrence rate **4%**
- No complications during the 18-month FU
- The groups treated with 15 Gy (3 x 5 Gy) and 10 Gy (2 x 5 Gy) postsurgical radiotherapy did not differ significantly in terms of recurrence rate ($p>0.05$).

Ogawa R, Huang C, Akaishi S, et al. Analysis of surgical treatments for earlobe keloids: analysis of 174 lesions in 145 patients. Plast Reconstr Surg. 2013 Nov;132(5):818-825





TREATMENT: SURGERY vs EBRT vs HDR

- 125 pat with 264 keloids (Los Angeles CA)
  - excision alone (n = 28),
  - post-excision EBRT (n = 197),
  - post-excision HDR brachytherapy (n = 39).

EBRT better

- **54%** recurred after surgical excision alone (9m FU)
- **19%** recurred with post-excision EBRT (42m FU)
- **23%** recurred with post-excision HDR (12m FU).

  (P < .01).
- EBRT significantly delayed the time of keloid recurrence over brachytherapy by a mean difference of 2.5 years (P < .01).

Hoang D, Reznik R, Orgel M, Li Q, Mirhadi A, Kulber DA. Surgical excision and adjuvant brachytherapy vs external beam radiation for the effective treatment of keloids: 10-Year Institutional Retrospective Analysis. Aesthet Surg J. 2017 Feb;37(2):212-225.

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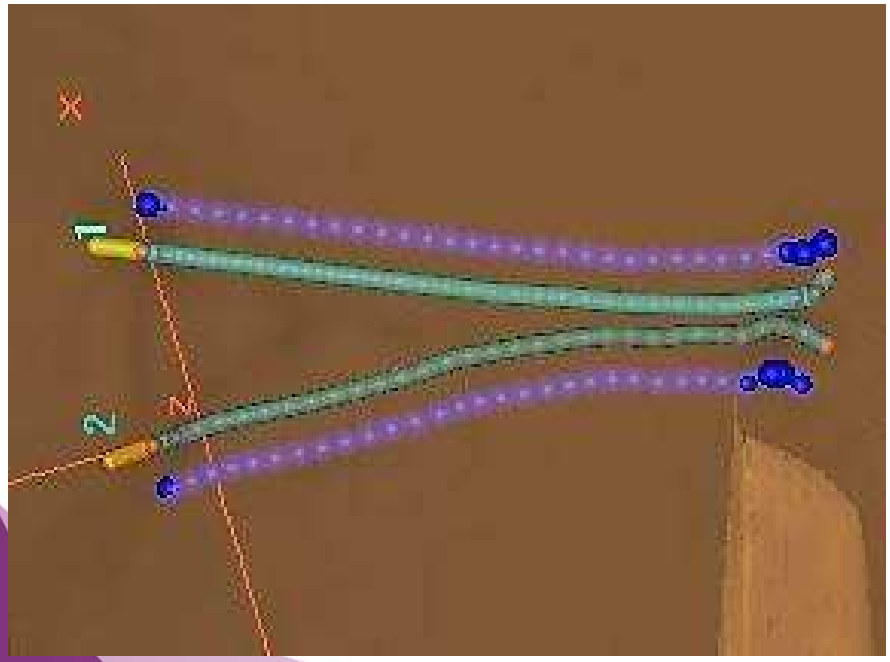
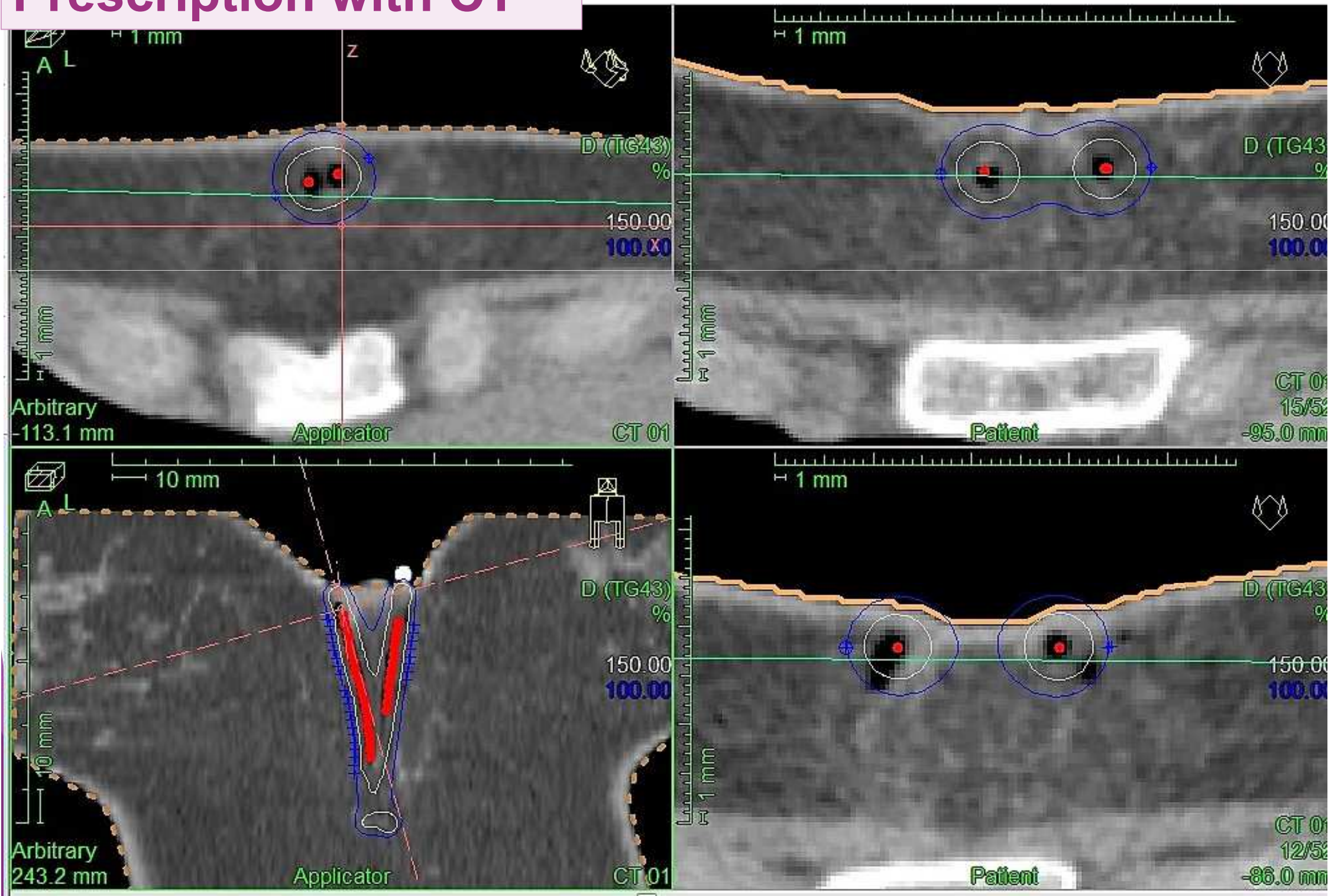
Prescription with CT

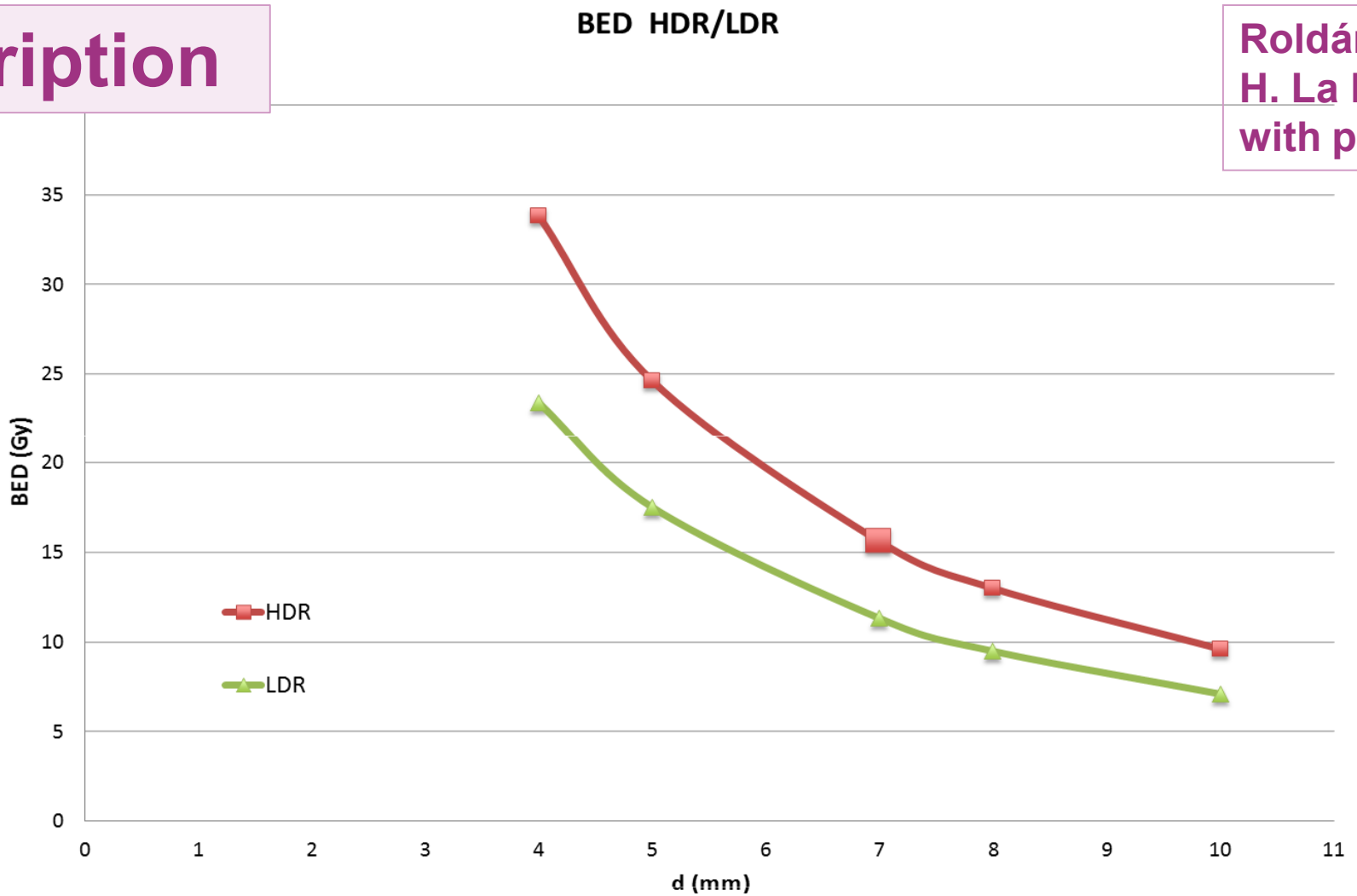


Prescription with CT



Prescription

Roldán S, Tormo A
H. La Fe. Valencia.
with permission



Distance			5mm	7mm	10mm
HDR 2002	4 x 3 Gy to 7mm	BED	24.6 Gy	15.6 Gy	9.6 Gy
		EQD2	20.5 Gy	13 Gy	8 Gy
LDR 1998	15 Gy to 5mm	BED	17.5 Gy	11.3 Gy	7.1 Gy
		EQD2	14.6 Gy	9.4 Gy	5.9 Gy

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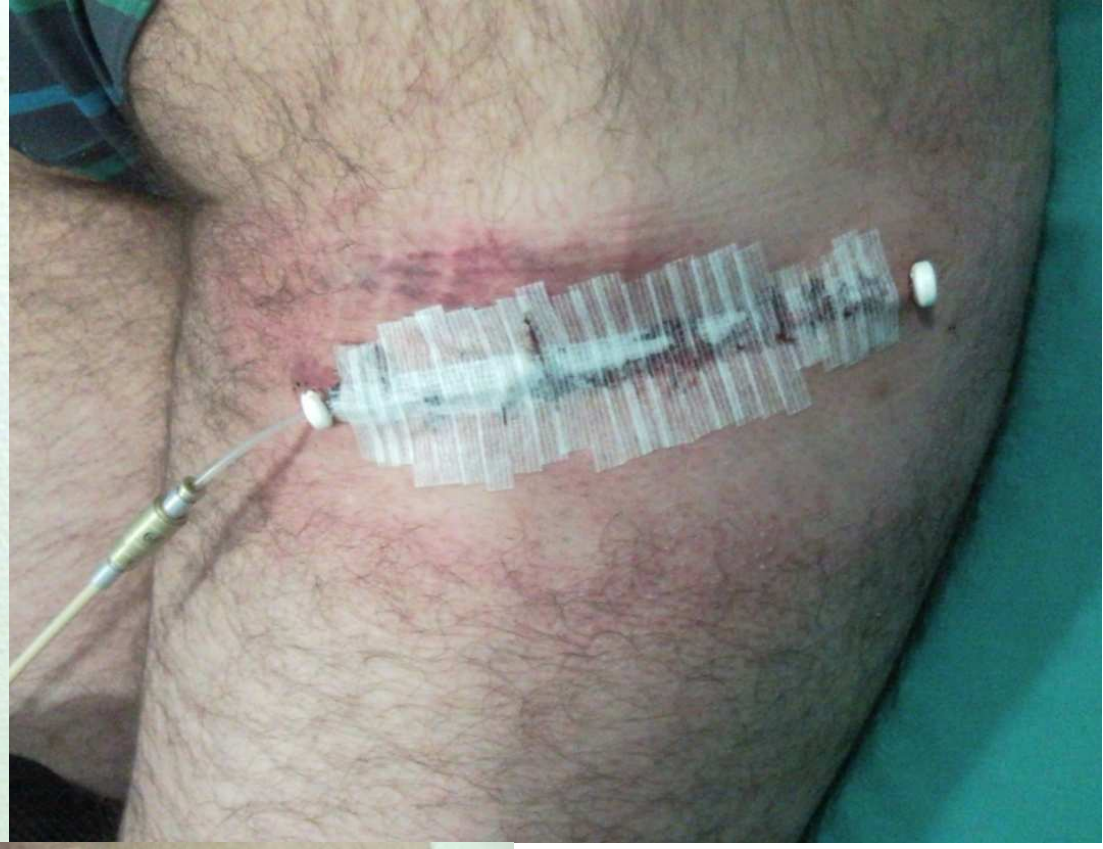
TOXICITY

- Excellent cosmetic outcome in 75-85%
- Pigmentation
- Cutaneous fibrosis
- Telangiectasia
- Second induced tumours:

5 cases out of 6741 patients trested with EBRT or Brachy (1/1348 pat) no clearly related.

Ragoowansi R, Cornes PG, Moss AL, Glees JP. Treatment of keloids by surgical excision and immediate postoperative single-fraction radiotherapy. Plast Reconstr Surg. 2003 May;111(6):1853-9.



IVO. Valencia
4 x 5 Gy, results at 9 months.

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Reirradiation is posible

IVO. Valencia
3 x 5 Gy, partial recurrence → re-radiation

TAKE HOME MESSAGES:

- **Perioperative brachytherapy is an optimal option to prevent recurrences after surgery of keloids**
- **LDR and HDR offer similar results, maybe better with HDR**
- **First session must start before 6 hours after surgery**
- **Total doses are low**
  - **3 Gy x 4 at 7-10mm total: 12Gy**
  - **5 Gy x 3-4 at 5mm 15-20 Gy**
  - **6 Gy x 2-3 at 5mm 12-18 Gy**
- **Earlobe keloids have more recurrences (not easily covered?)**
- **Recurrences can be radiated again.**

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WWW.ESTRO.ORG/SCHOOL

BASIC PLANNING

CATHETER RECONSTRUCTION, DOSE POINTS AND PLANNING BASICS

COMPREHENSIVE AND PRACTICAL BRACHYTHERAPY

ESTRO Teaching Course, Budapest 2017

Emmie Kaljouw
emmiekaljouw@amc.uva.nl

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Basic planning

- Single catheter or single plane implant
- Catheter reconstruction without a scan
- Catheter identification
- Imaging, slice spacing and thickness
- Digitising catheters in TPS
- Multiple catheters
- Normalisation points
- Catheter reconstruction
- Dwell position activation
- Treatment planning: target points
- Treatment planning: margin around the target
- Optimisation

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Single catheter or single plane implant

- Limited tumour volume
  - Tumour of tractus digistive or respiratory tract
  - Keloid
  - Bladder

- Imaging dependent on location of implant
  - Superficial catheter: usually no imaging
  - Deep implant, no tumour left, only organ at risk: CT

- Dose prescription
  - Based on clinical grounds
  - Standard planning with dose points

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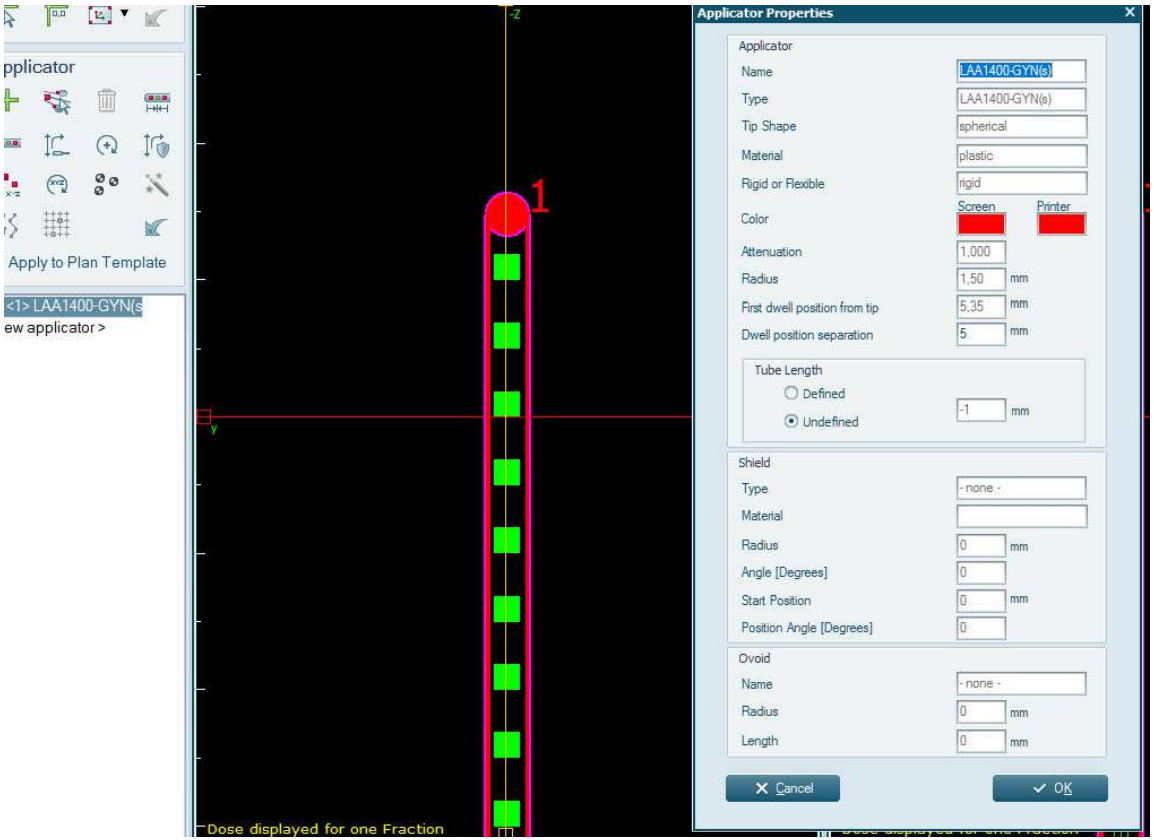
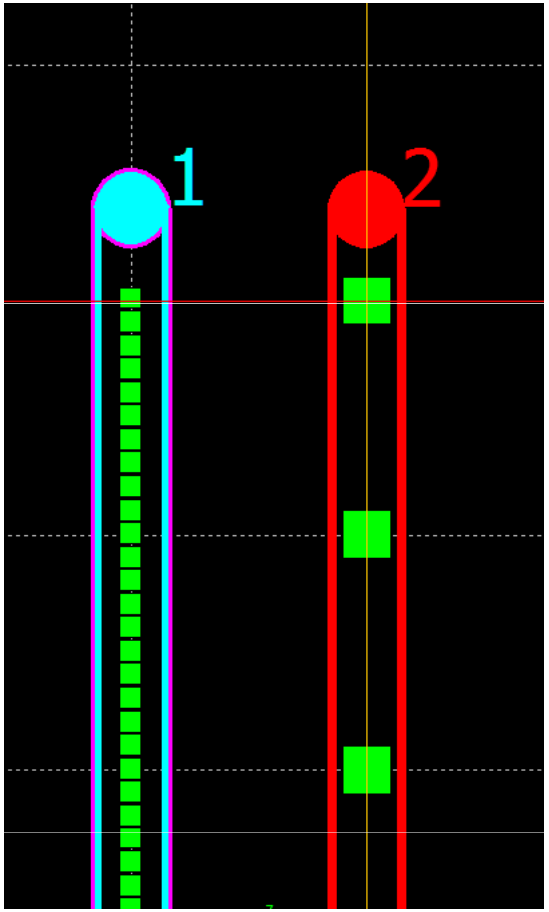
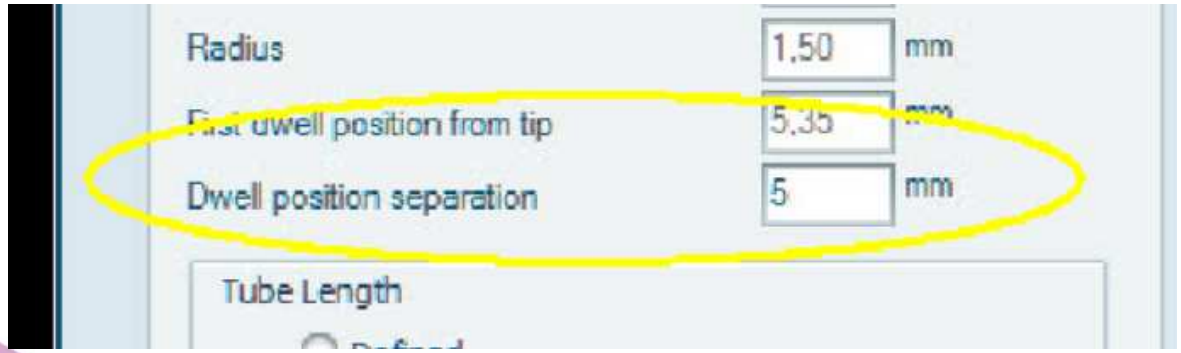
Catheter reconstruction without a scan







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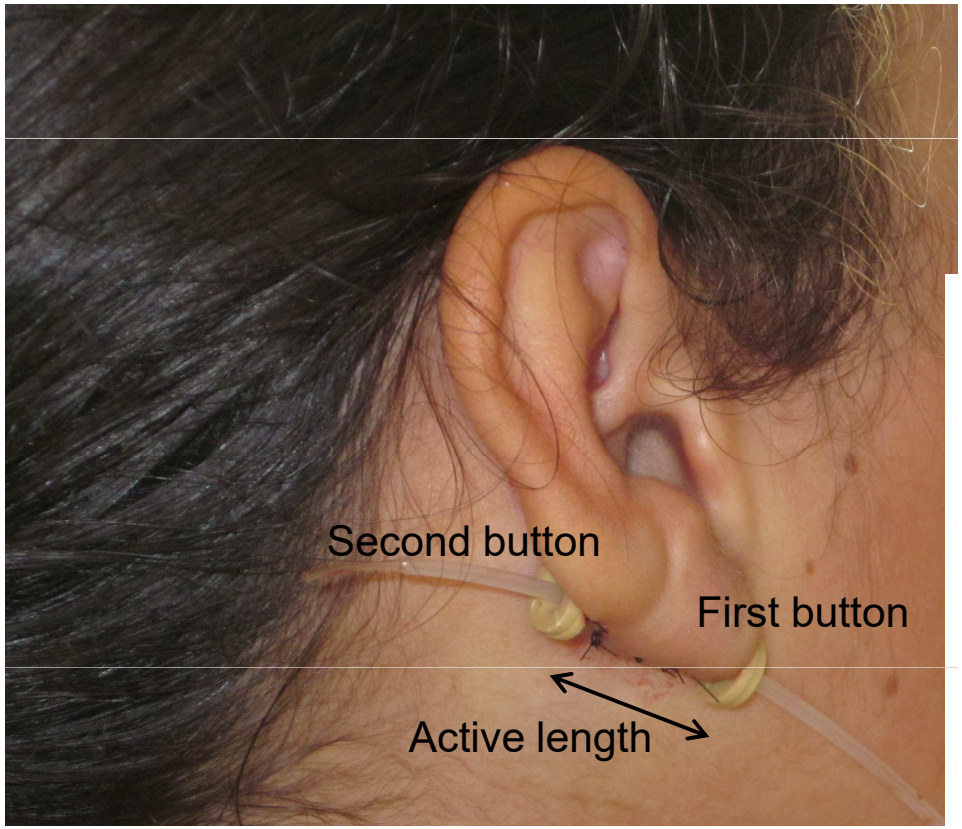
Catheter reconstruction without a scan



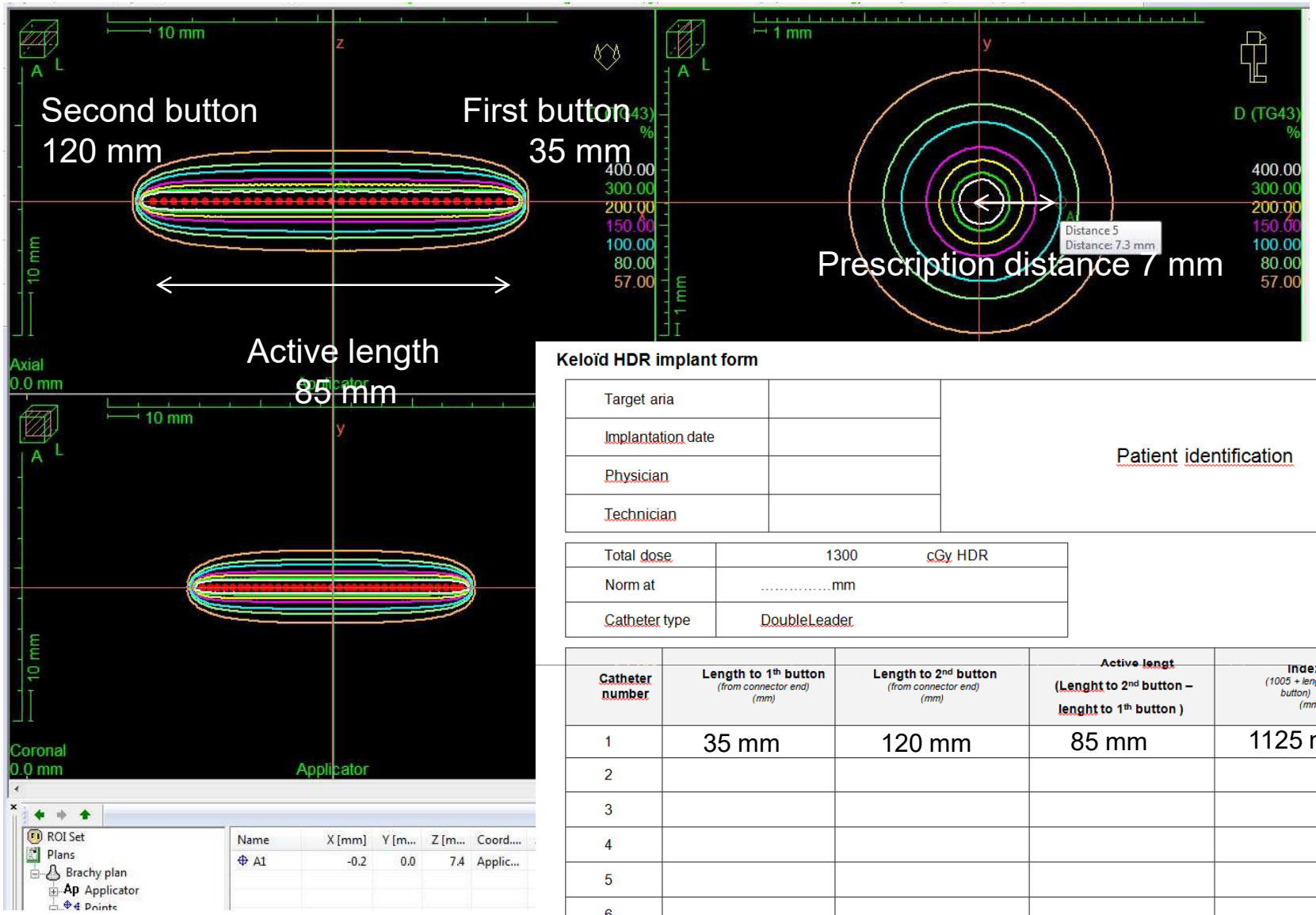
Keloïd HDR implant form

Target aria		Patient identification
Implantation date		
Physician		
Technician		

Total dose	1300 cGy HDR
Norm at	.....mm
Catheter type	DoubleLeader

Catheter number	Length to 1th button (from connector end) (mm)	Length to 2nd button (from connector end) (mm)	Active lengt (Lenght to 2nd button – lenght to 1th button)	Indexer (1005 + length to 2nd button) (mm)	Transfer tubes	Offset (mm)
1					Straight 6F	0
2					Straight 6F	0
3					Straight 6F	0
4					Straight 6F	0
5					Straight 6F	0
6					Straight 6F	0
7					Straight 6F	0

Catheter reconstruction without a scan



Keloïd HDR implant form

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1	35 mm	120 mm	85 mm	1125 mm	Straight 6F	0
2					Straight 6F	0
3					Straight 6F	0
4					Straight 6F	0
5					Straight 6F	0
6					Straight 6F	0
7					Straight 6F	0

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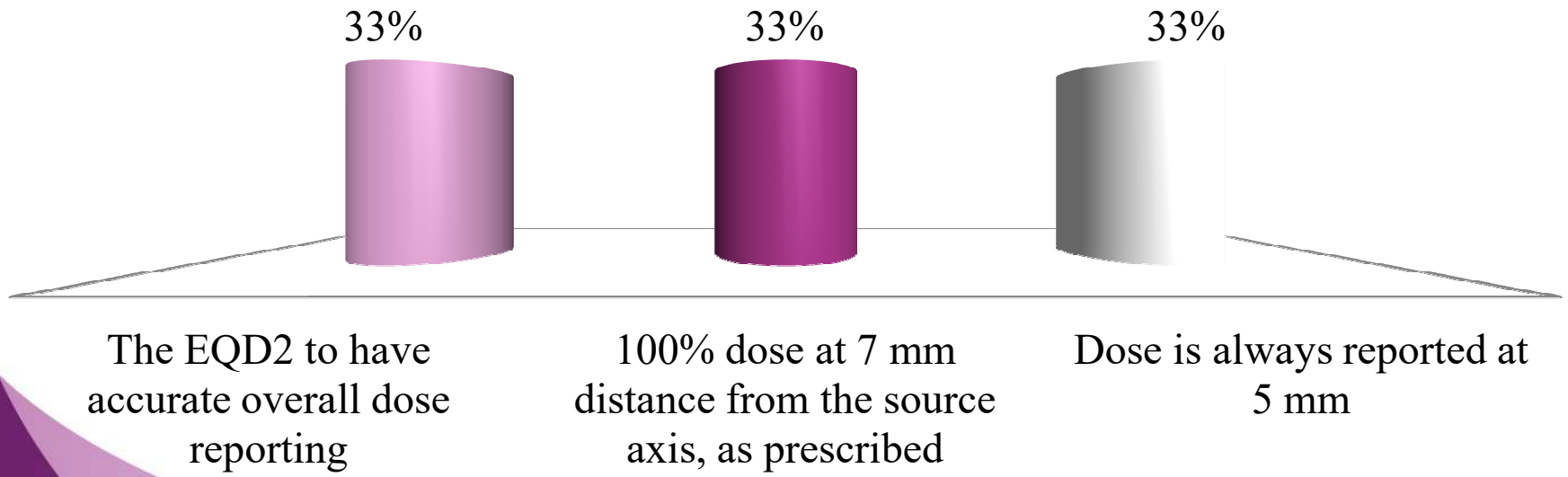
What prescribed dose should be reported in this case?

A. The EQD2 to have accurate overall dose reporting
B. 100% dose at 7 mm distance from the source axis, as prescribed
C. Dose is always reported at 5 mm



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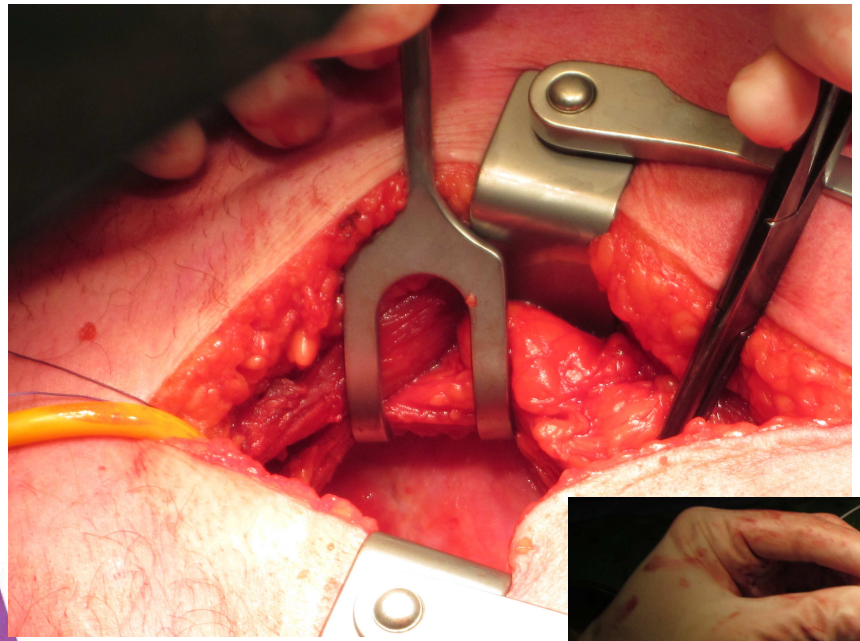
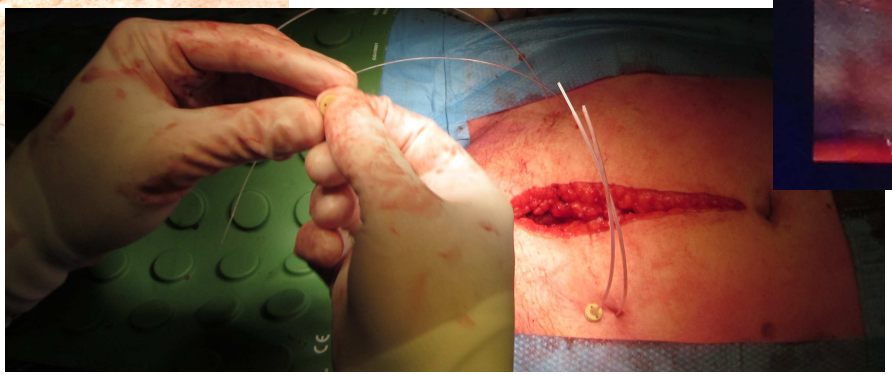
Catheter identification

- Catheter identification
  - Documentation of the catheters used
  - Number/ colour catheters
  - Documentation of catheter order
  - Documentation of position of catheters in relation to implant





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Catheter identification

Implantation form multiple catheters

Date:
Physician:
Technician:

Patient name:
Patient number:
Date of birth:

Total dose	cGy	
Dose per puls	cGy	
Number of pulses		
Period time	.....uur .....min.	
Stepsize	□ 2,5mm □ 5mm	
PDR	□ Bleu	□ Green
Transfertubes	Straight	

Template design:

Catheter / Channel number	Catheter Length (mm)	Transfer tubes	Indexer (mm)	Offset (mm)
1		Straight		-5
2		Straight		-5
3		Straight		-5
4		Straight		-5
5		Straight		-5
6		Straight		-5
7		Straight		-5
8		Straight		-5
9		Straight		-5
10		Straight		-5

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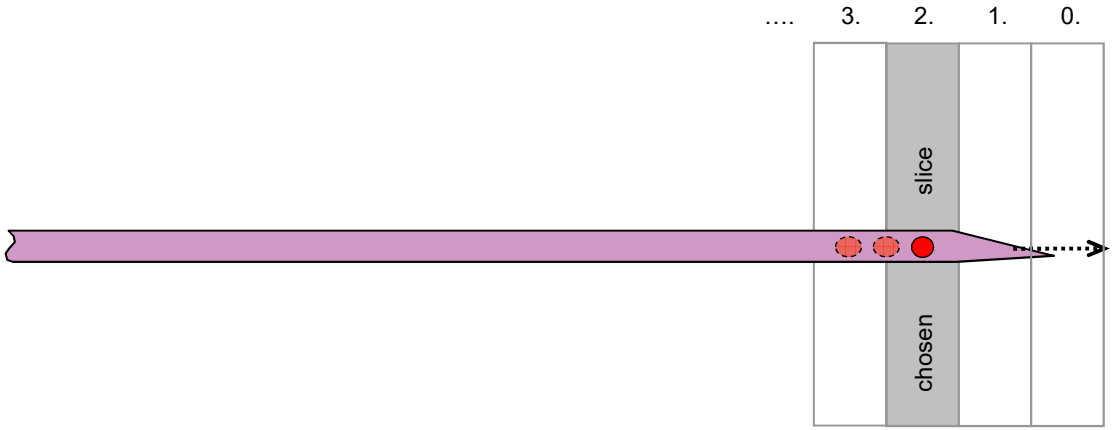
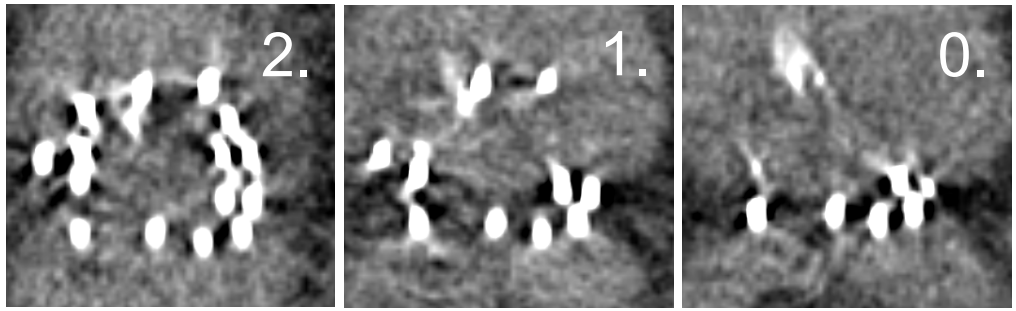
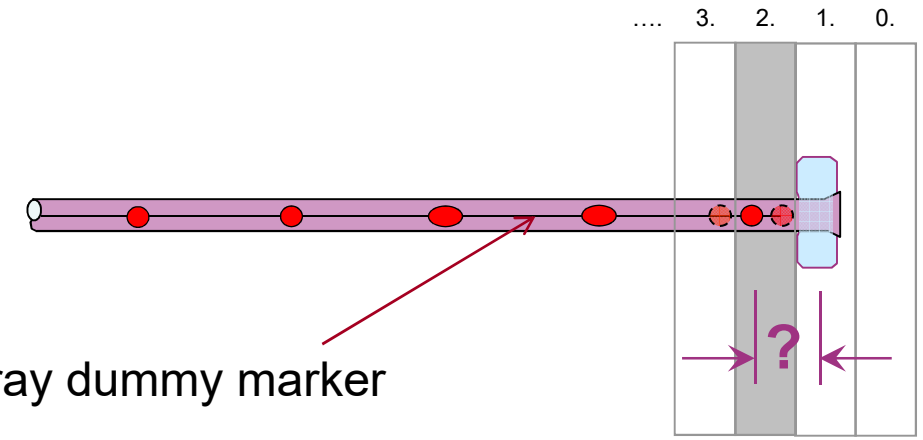
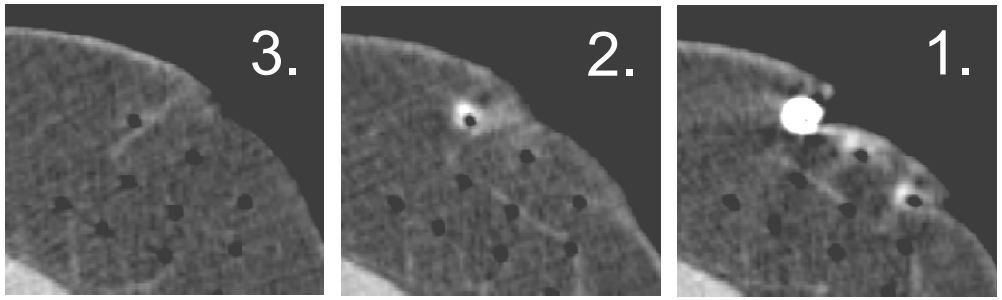
Imaging, Slice spacing and thickness









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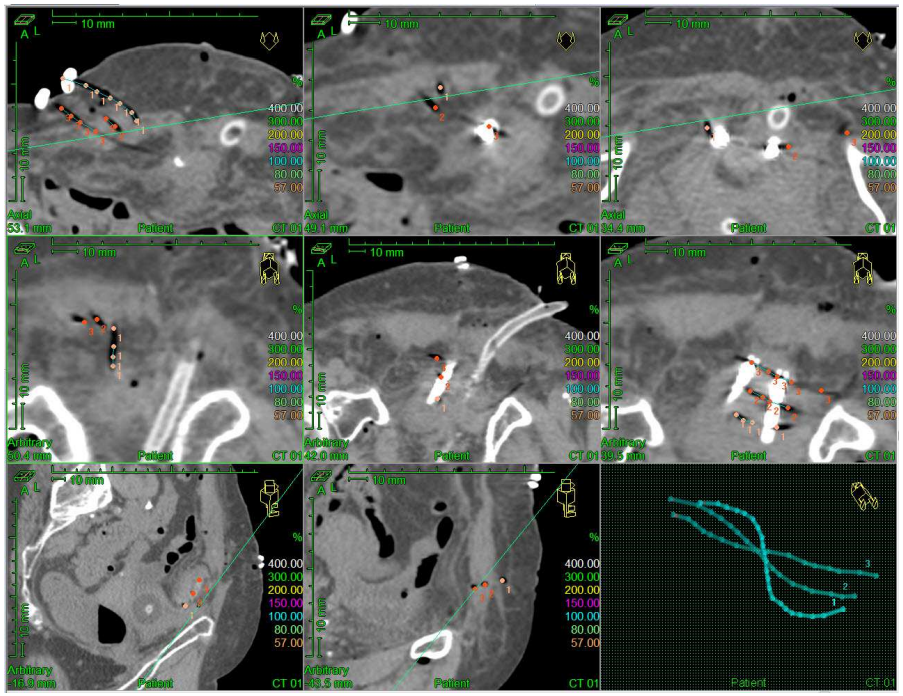
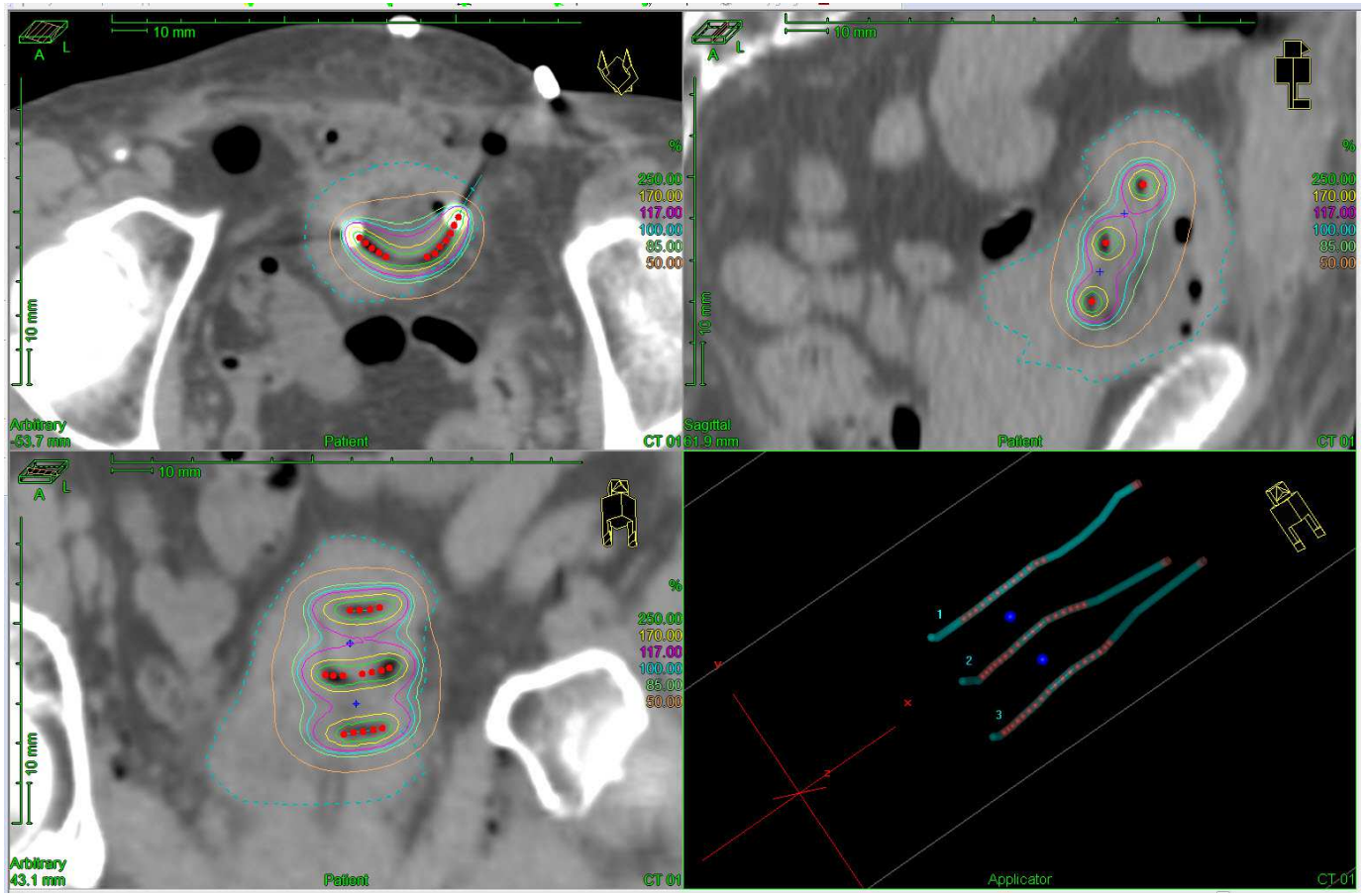
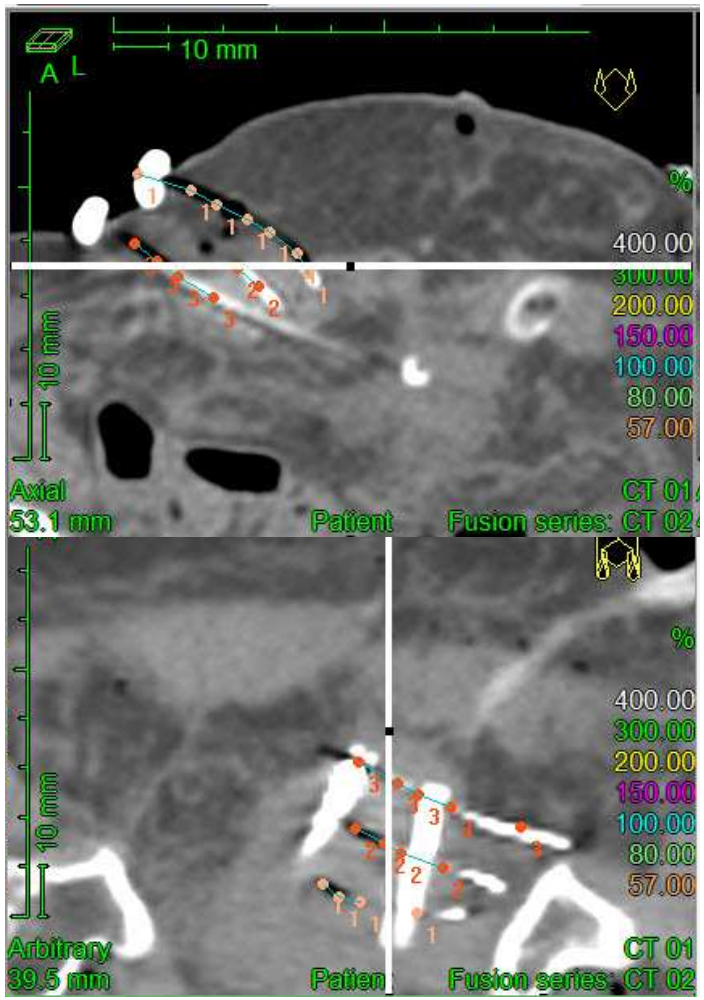
Digitising catheter in TPS

- Import images in treatment planning system
- Find tip or connecting end of the catheter
- Digitise the catheters in the right order
- Enter the right catheter length in the TPS
- Enter the distance from catheter tip to first dwell position in the TPS



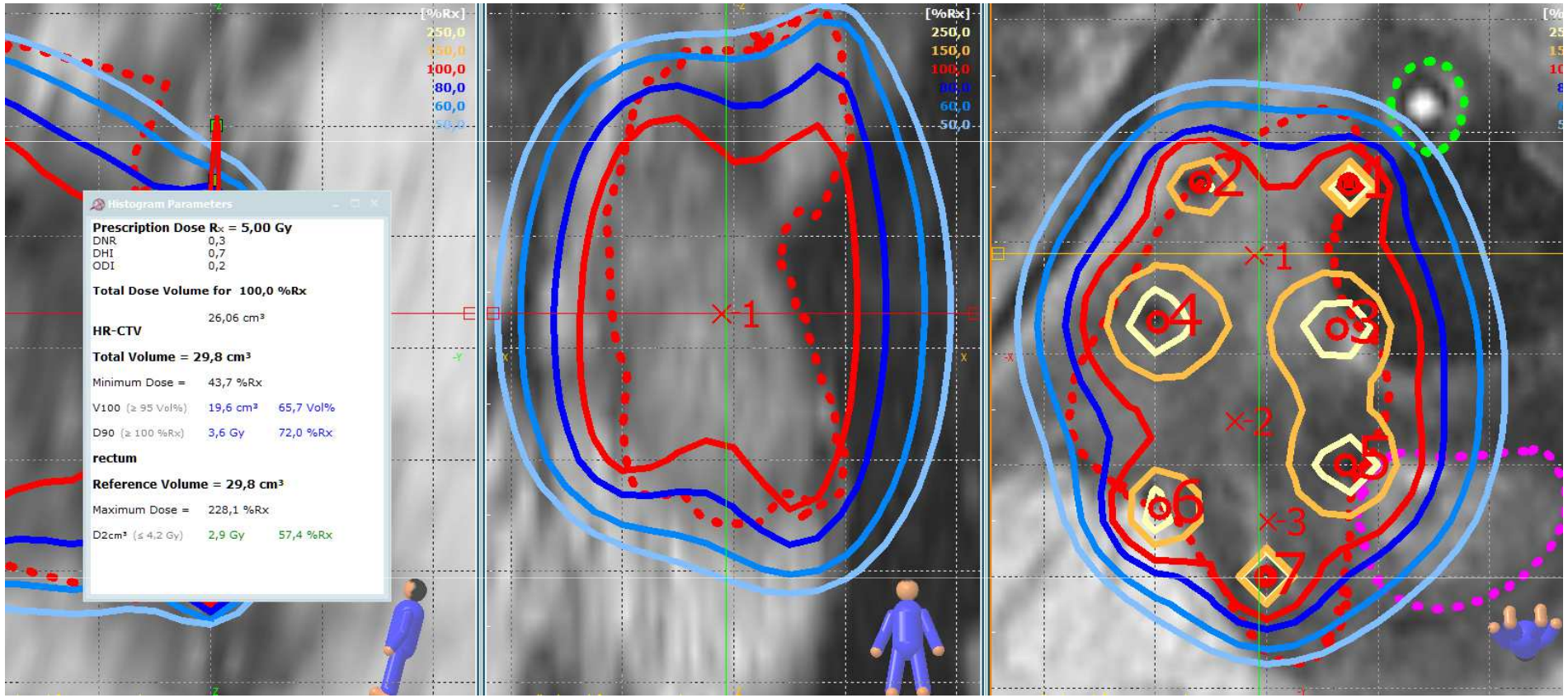
Multiple catheters, single plane



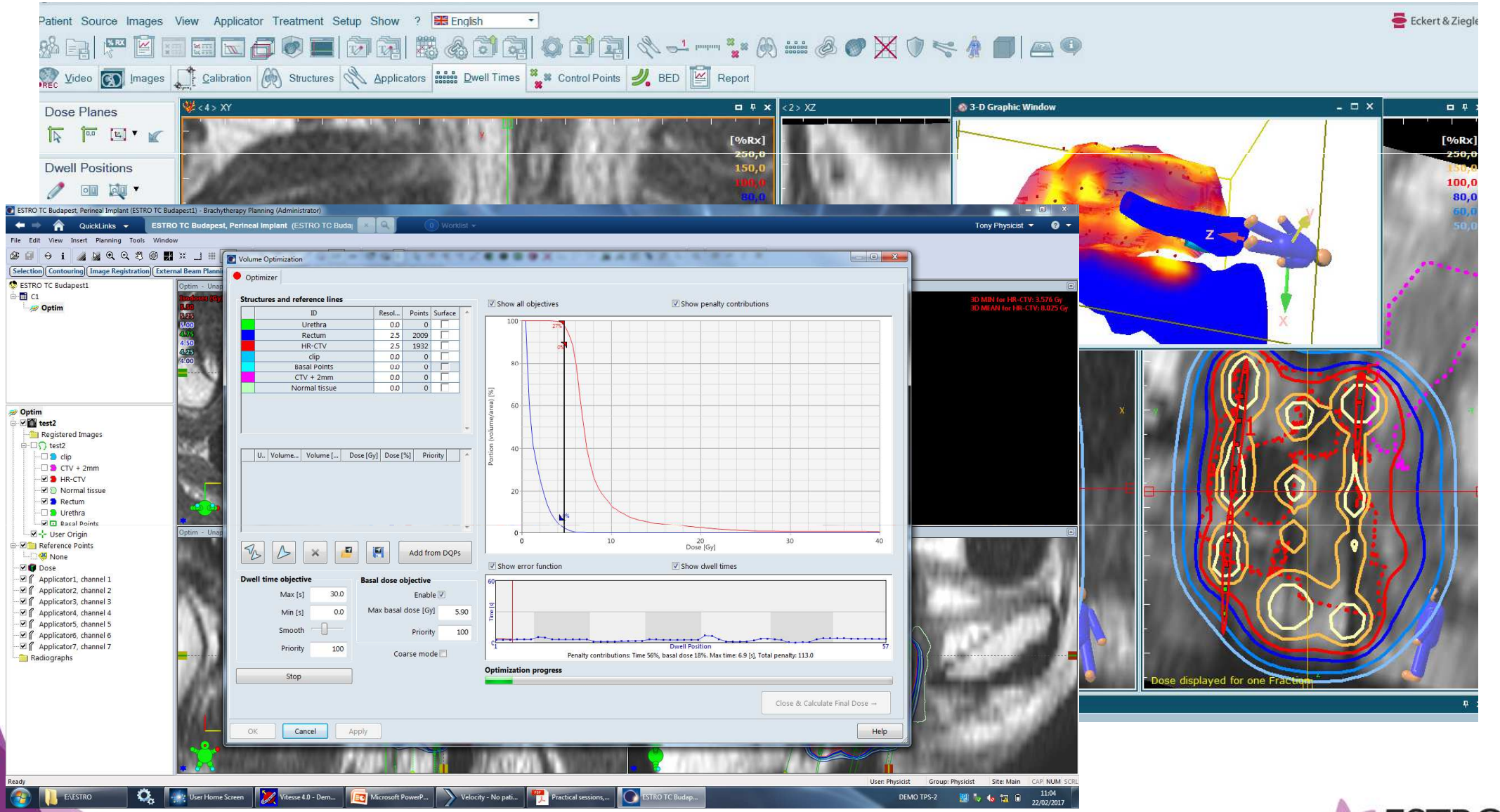


Synthetic catheter reconstruction with and without line marker

Multiple catheters, multiple planes



Multiple catheters, multiple planes



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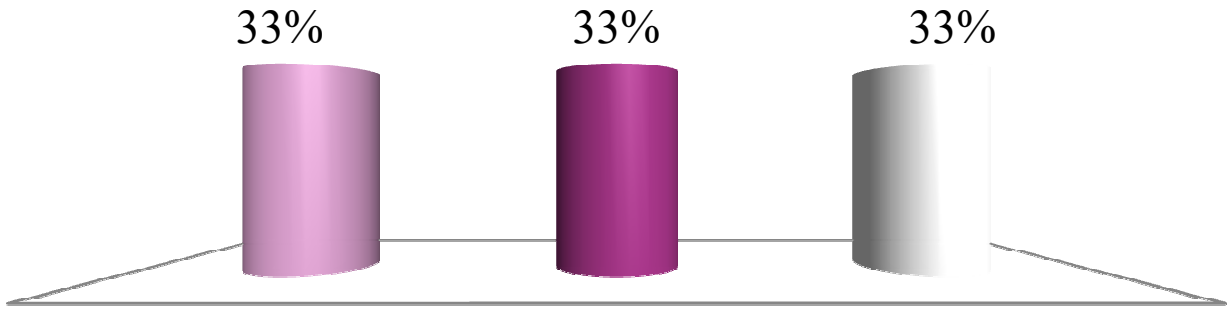
How could a vaginal wall tumour like this (2x3x3 cm at time of BT) best be treated?

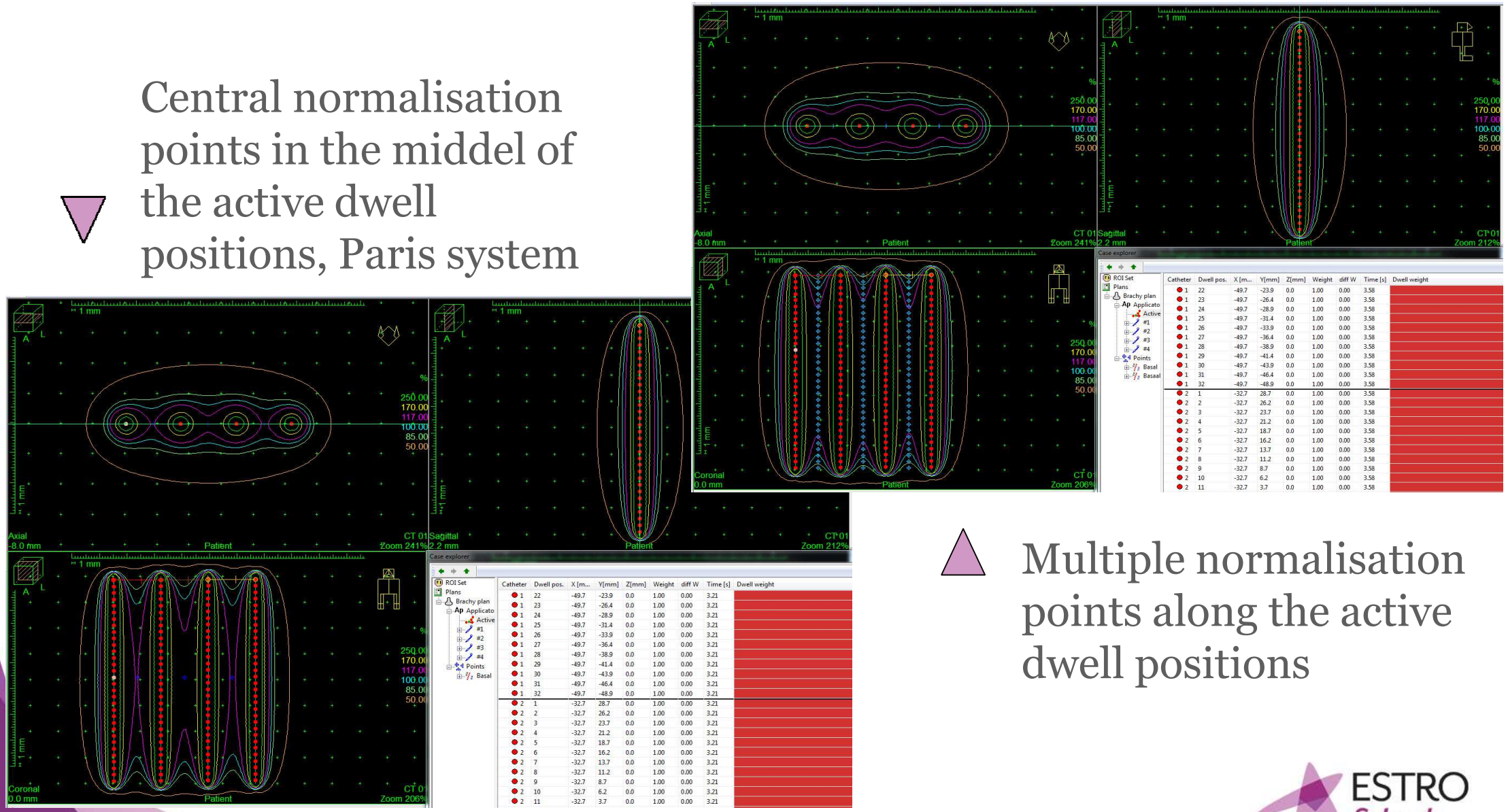
A. Multichannel applicator, because the needle configuration will always be the same
B. Tumour growth exceeding 10 mm from the vaginal wall requires a template
C. Template with individual needle configuration, allows for best target coverage



nel applicator, Tumour growth exceeding 10 mm from the vaginal wall requires a template for best target cov

Normalisation points

Central normalisation points in the middel of the active dwell positions, Paris system



Multiple normalisation points along the active dwell positions

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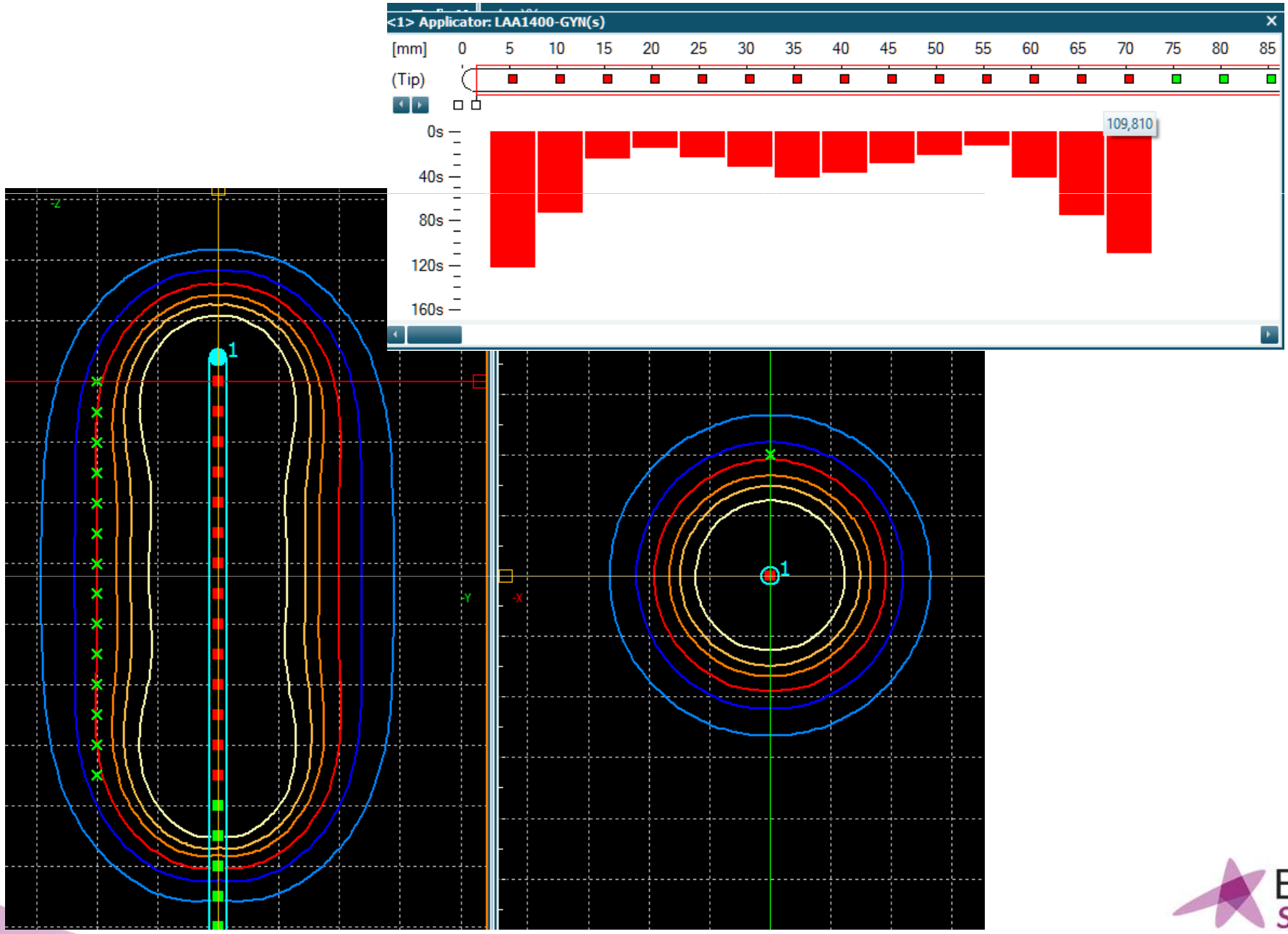
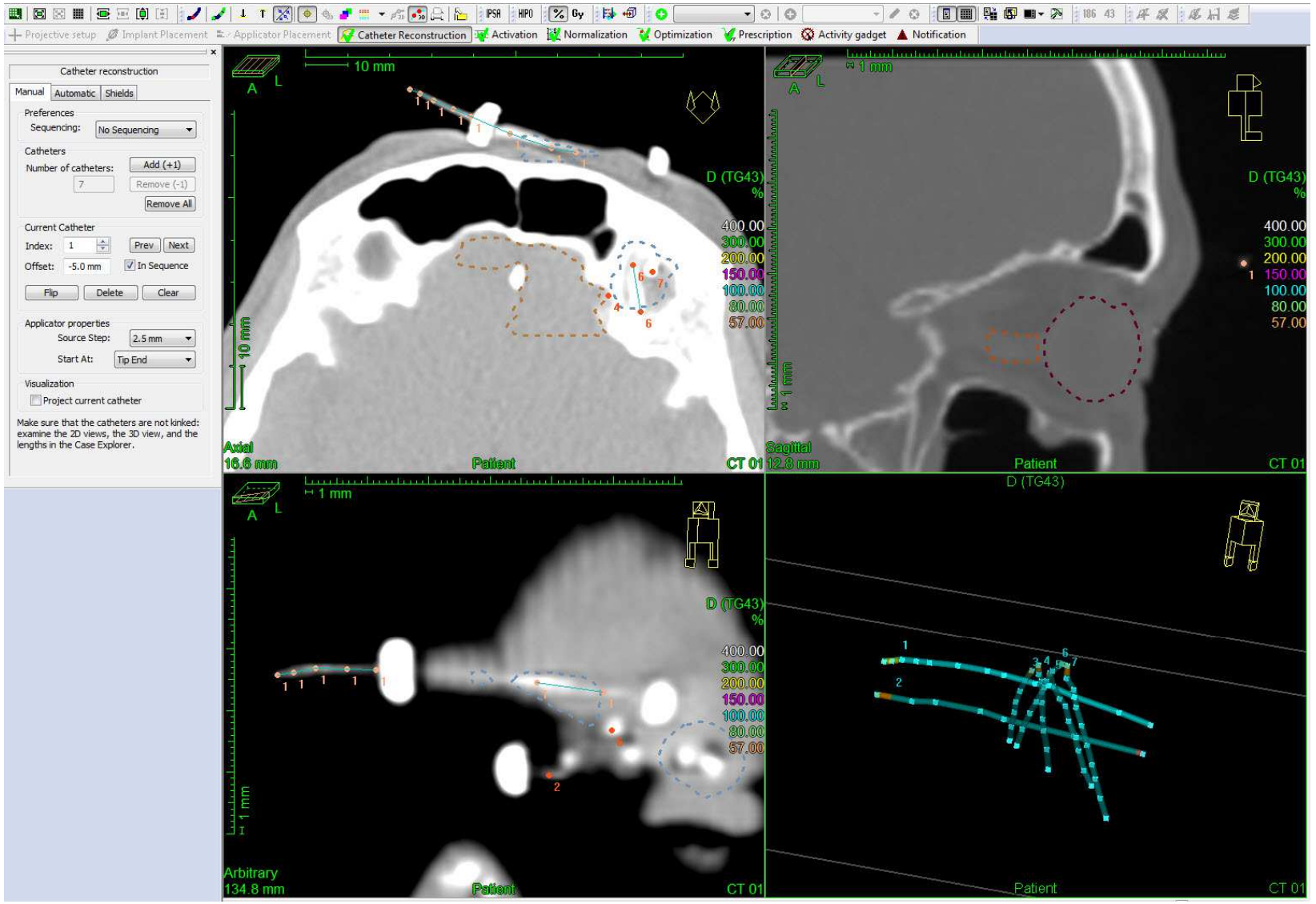
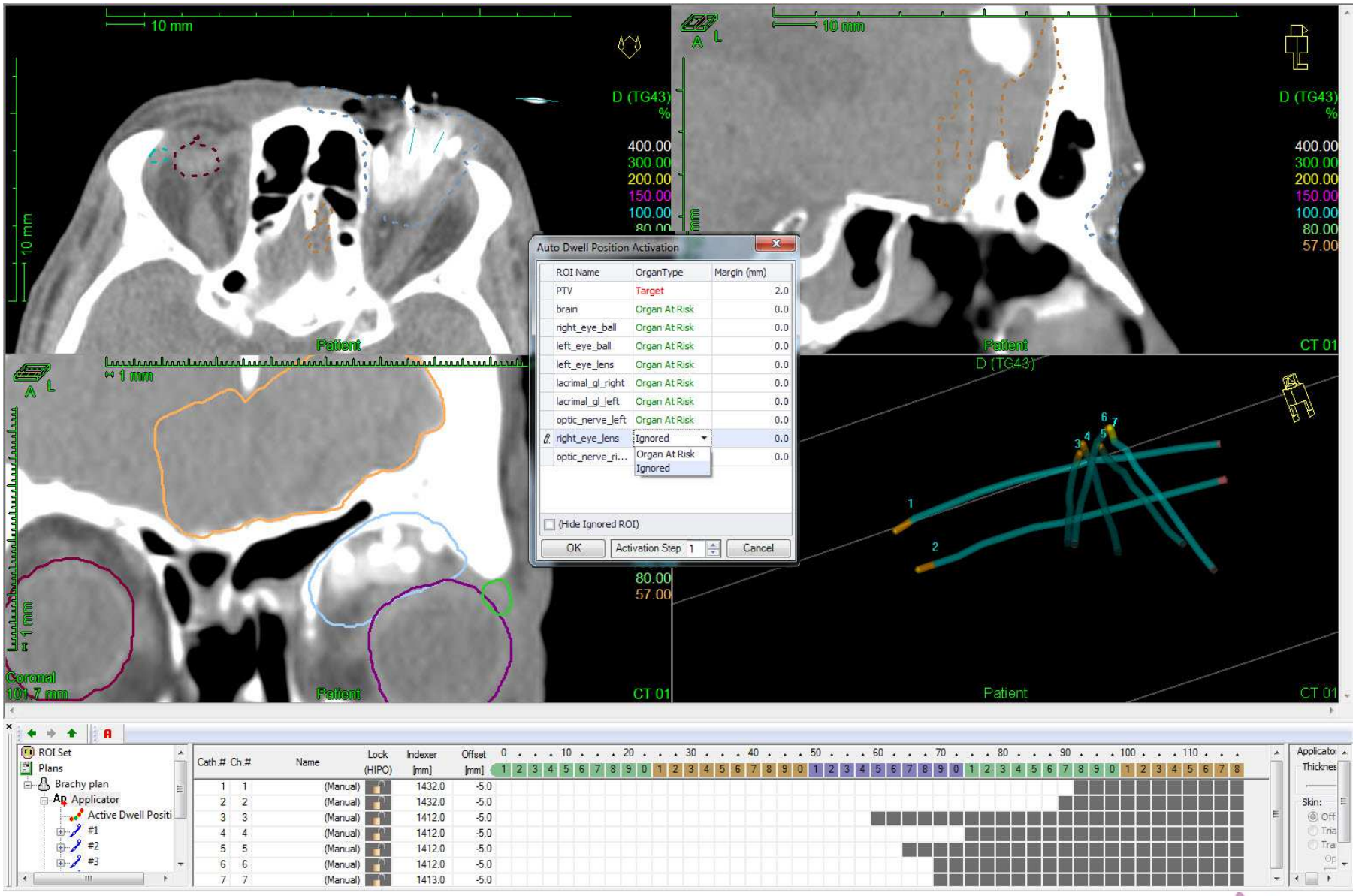
Normalisation points



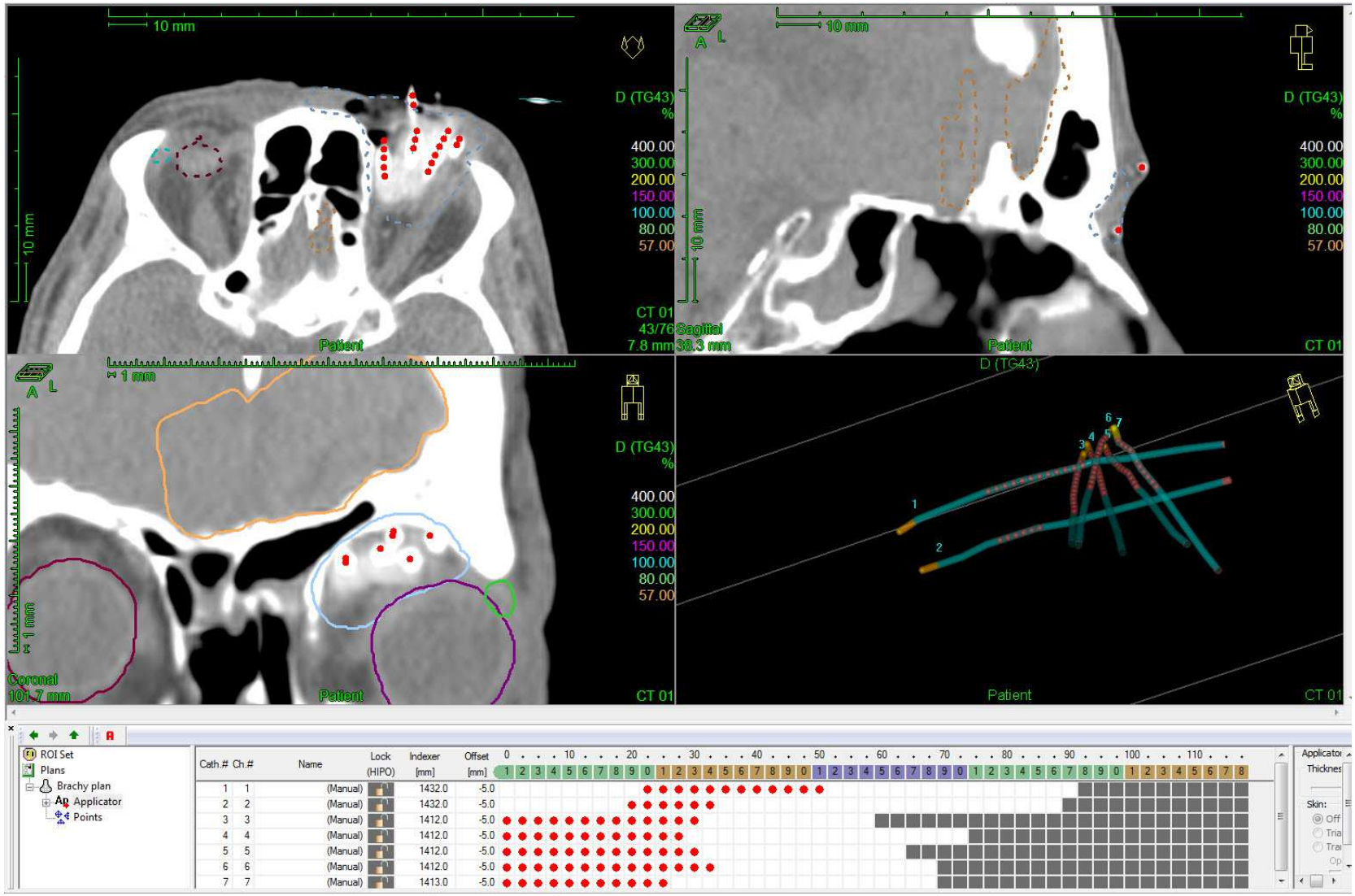
Catheter reconstruction



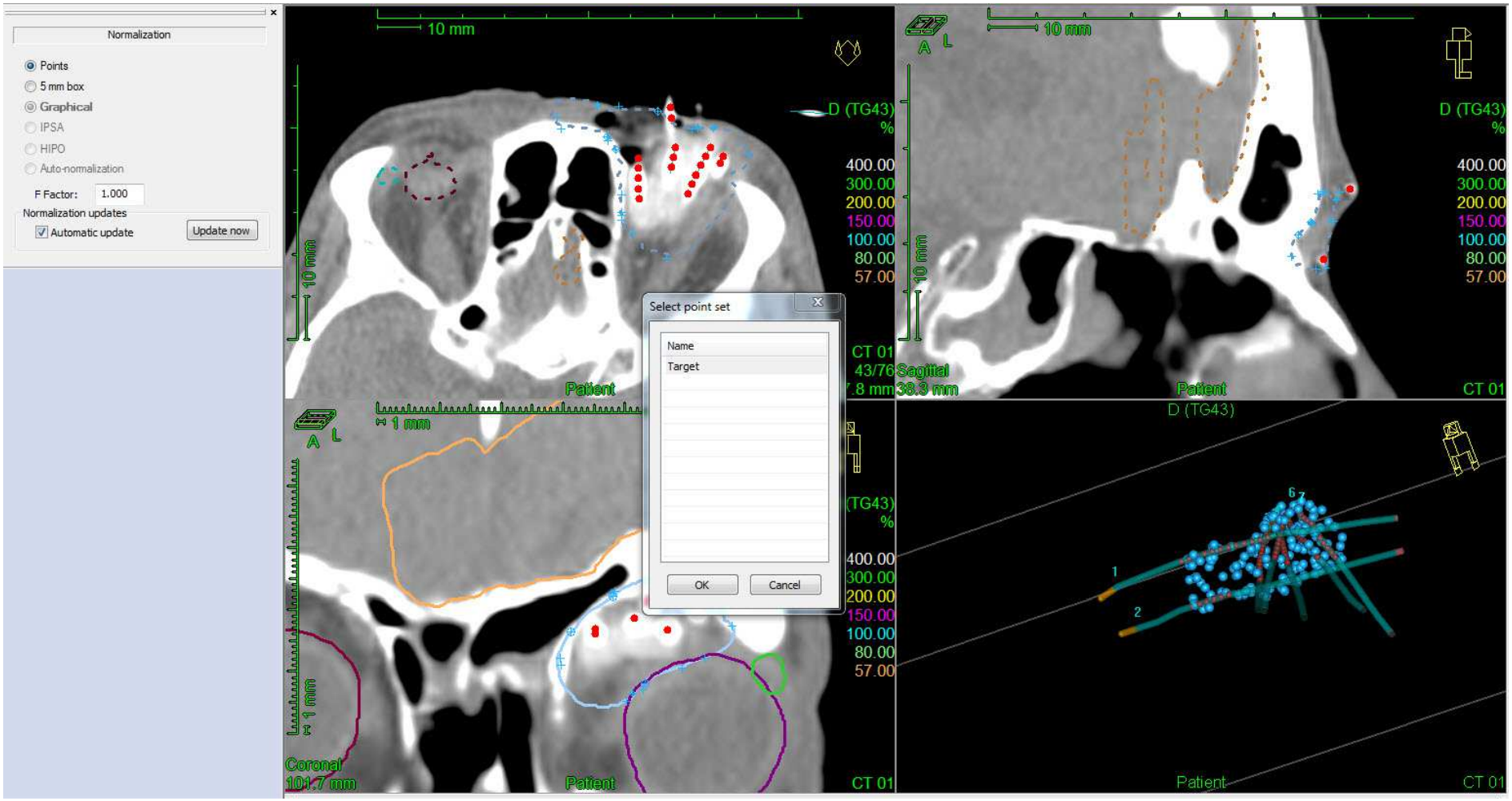
Dwell position activation



Dwell position activation



Treatment planning: target points



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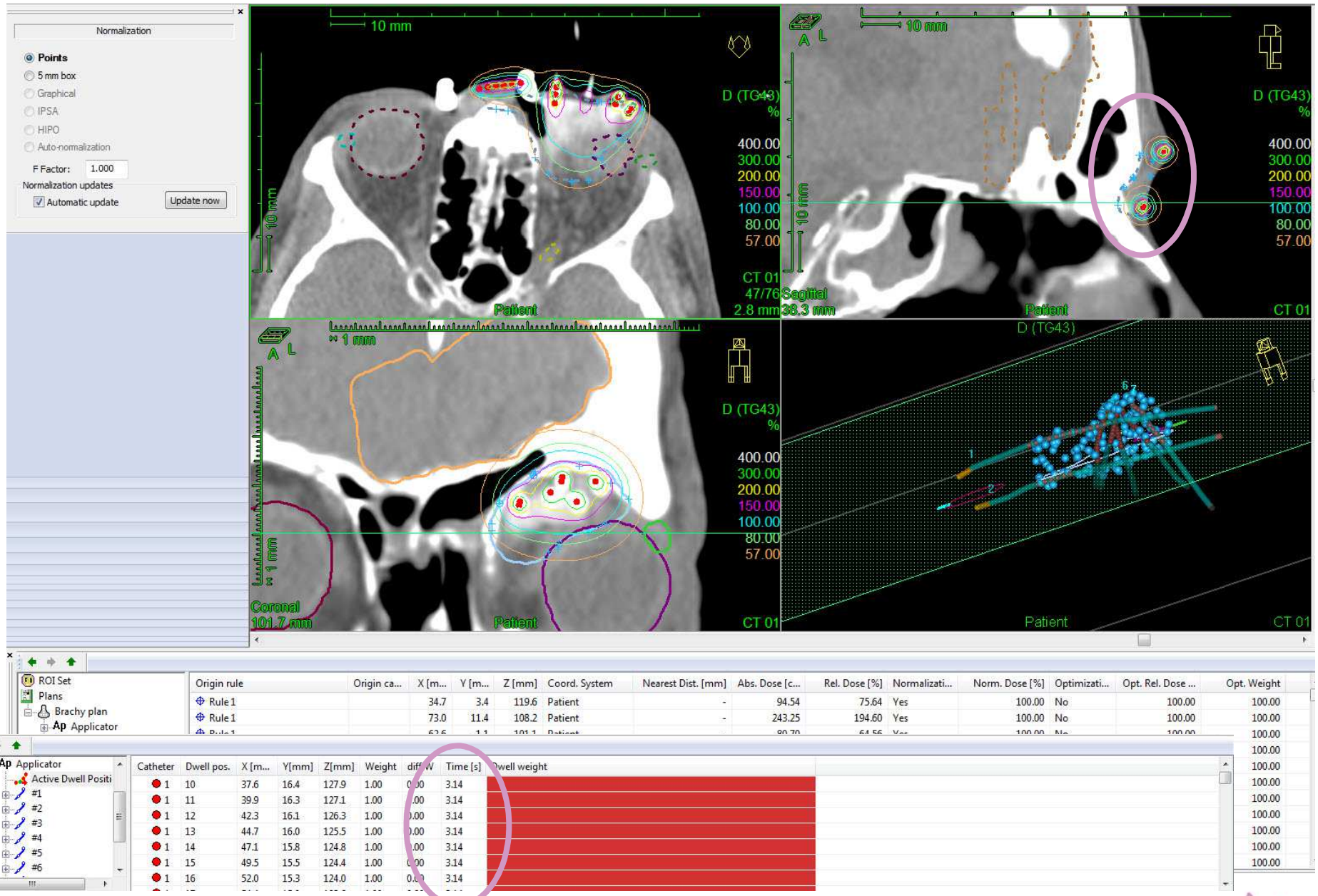
Treatment planning: target points



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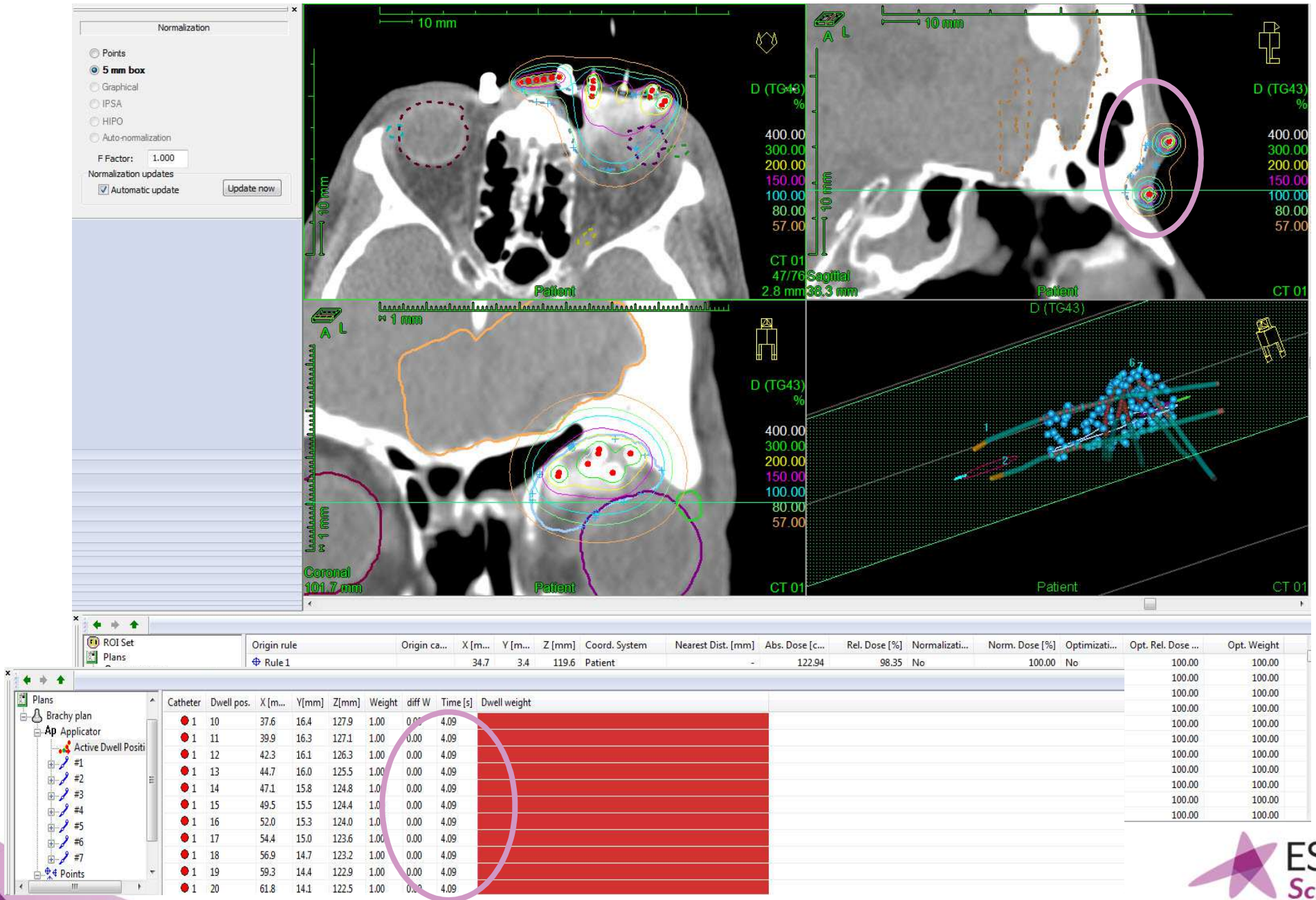
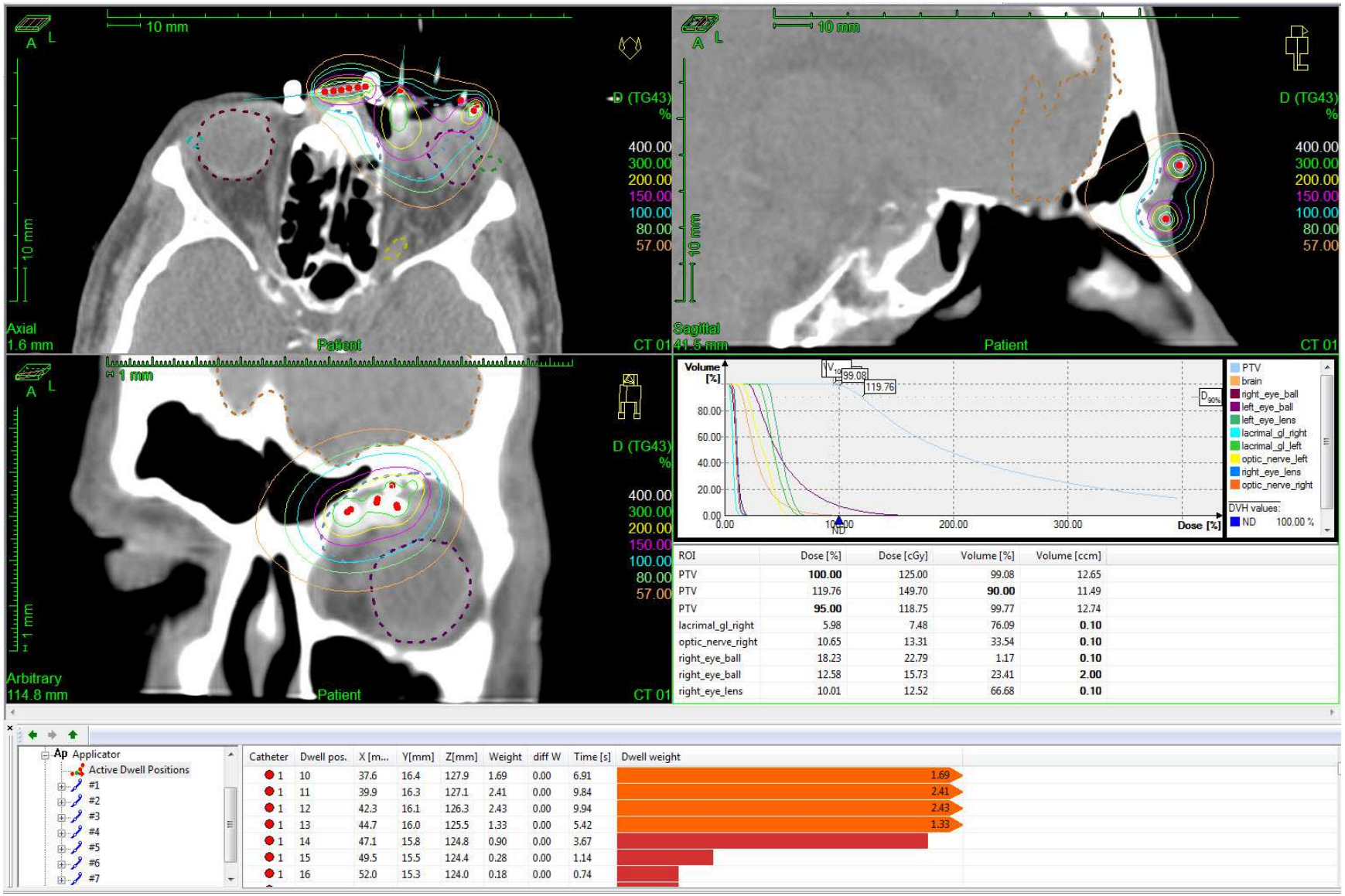
Treatment planning: margin around the target



Optimisation



ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
PTV	**100.00**	125.00	99.08	12.65
PTV	119.76	149.70	**90.00**	11.49
PTV	**95.00**	118.75	99.77	12.74
lacrimal_gl_right	5.98	7.48	76.09	**0.10**
optic_nerve_right	10.65	13.31	33.54	**0.10**
right_eye_ball	18.23	22.79	1.17	**0.10**
right_eye_ball	12.58	15.73	23.41	**2.00**
right_eye_lens	10.01	12.52	66.68	**0.10**

Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	10	37.6	16.4	127.9	1.69	0.00	6.91	1.69
1	11	39.9	16.3	127.1	2.41	0.00	9.84	2.41
1	12	42.3	16.1	126.3	2.43	0.00	9.94	2.43
1	13	44.7	16.0	125.5	1.33	0.00	5.42	1.33
1	14	47.1	15.8	124.8	0.90	0.00	3.67	
1	15	49.5	15.5	124.4	0.28	0.00	1.14	
1	16	52.0	15.3	124.0	0.18	0.00	0.74	

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Thank you for you attention

- In the afternoon practical sessions, you have the opportunity to practice the catheter reconstruction and Paris system yourself

Budapest, March 5-8 2017

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Comprehensive and Practical Brachytherapy

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ESTRO TEACHING COURSE

Comprehensive and Practical Brachytherapy

Budapest 2017

BRACHYTHERAPY IN SKIN CANCER

Dr. José Luis Guinot

Fundación Instituto Valenciano de Oncología (I.V.O.). Valencia.

E-mail: jguinot@fivo.org

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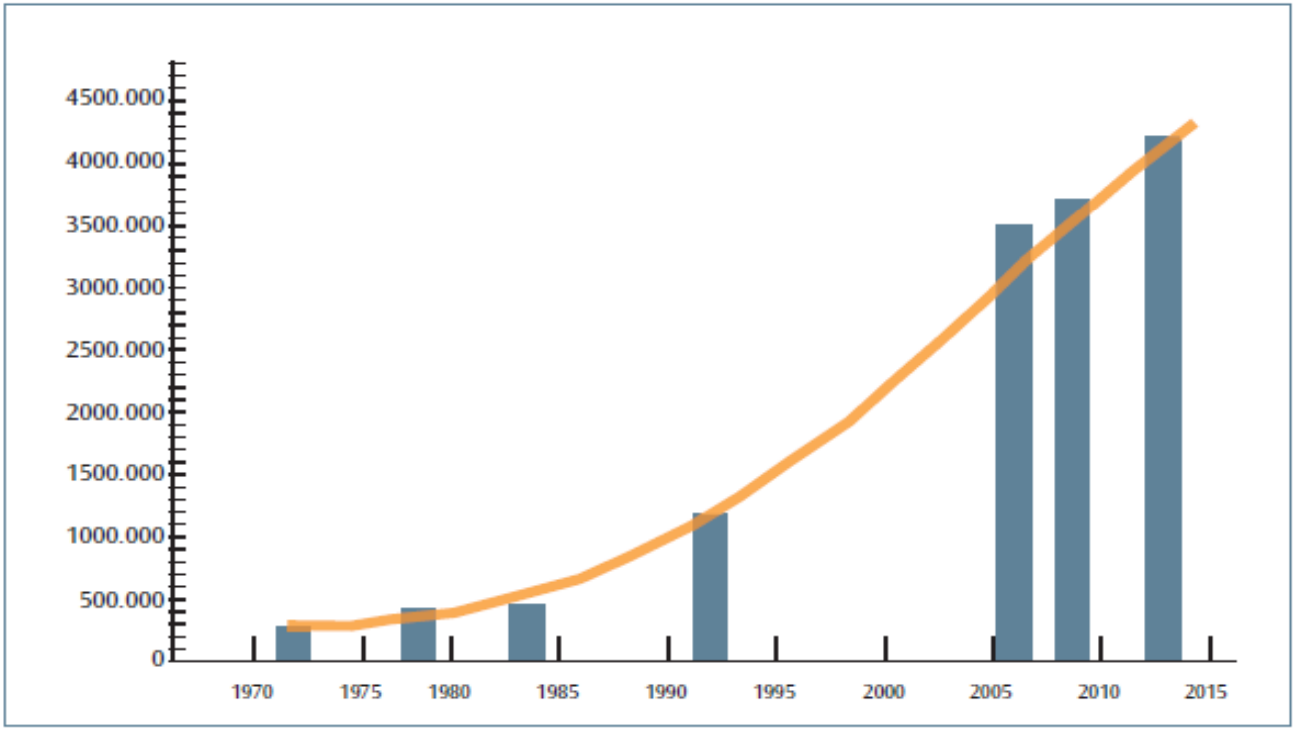
Incidence of non-melanoma skin cancer

- An estimated 4 million new lesions arise every year in the USA
- It is a disease of the elderly, more than half of new patients are 65 years or older
- Nearly 30% of Caucasians living in areas of exposure to high ultraviolet radiation will develop a NMSC in their lifetime
- The incidence rate is increasing 3-6% per year and continues to rise as the population ages



H. W. Rogers, et al, "Incidence Estimate of Nonmelanoma Skin Cancer in the United States, 2006," *Arch Dermatol, vol. 146, no. 3, pp. 283-287, 2010.*

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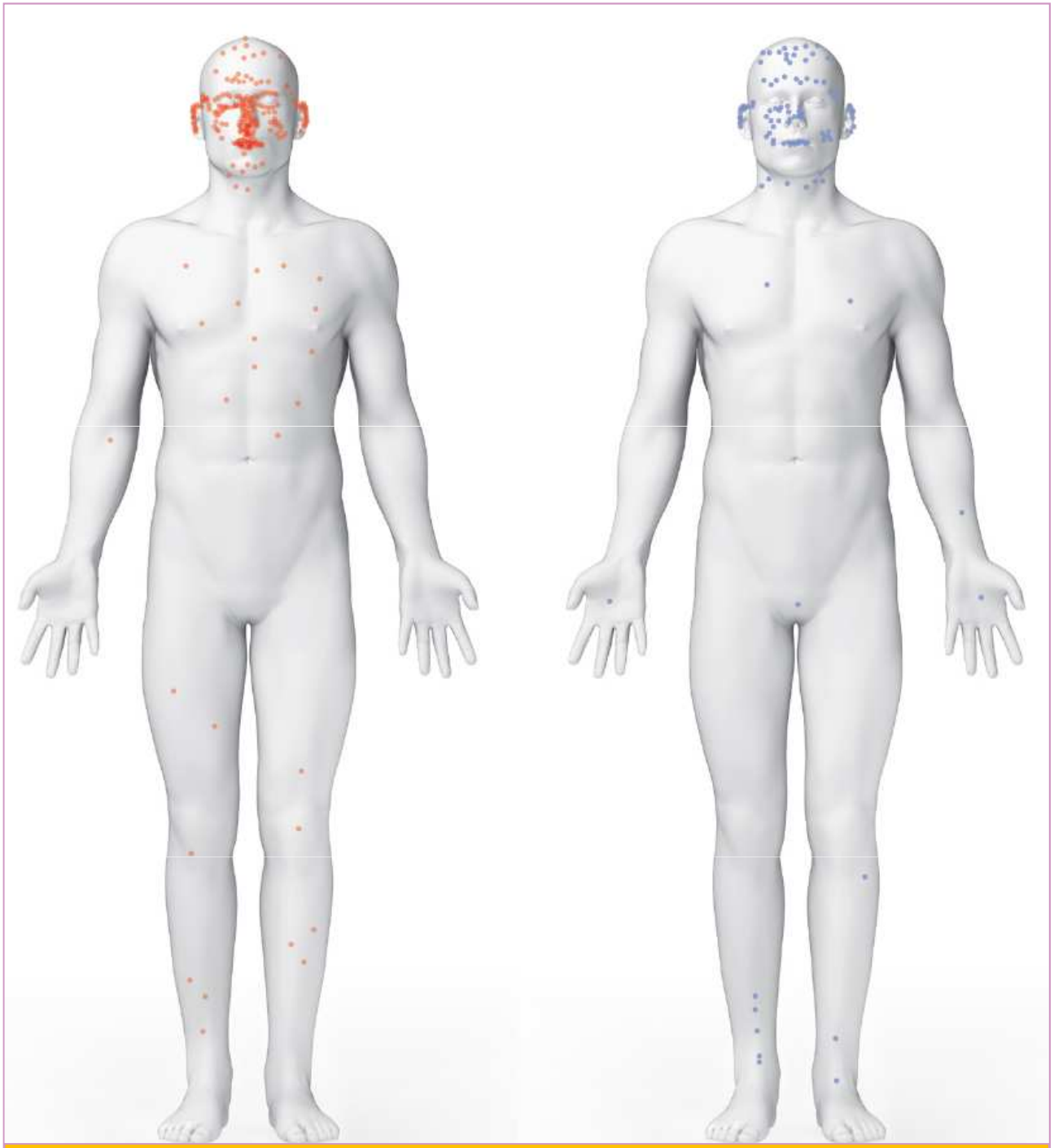
- About half of the skin cancer patients will develop a new unrelated primary lesion within 5 years after the initial diagnosis
- Over 80% occur in the head and neck region
- Lesions mainly affect cosmetically sensitive areas: face, nose (30%), eyelids, ears, scalp, lips
- 90% of lesions are small, <20mm and thickness is confined to a few mm.



Anatomical distribution

Basal cell ca (red) and Squamous cell ca (blue)

J. Locke, et al "Radiotherapy for epithelial skin cancer," *Int. J. Radiation Oncology Bio. Phys., vol. 51, no. 3, pp. 748-755, 2001.*

Treatment of choice

- Surgery and radiotherapy appear to be the most effective treatments with surgery showing the lowest failure rates

- Topical therapies should be reserved for those patients where surgery or radiation therapy is contraindicated or impractical

- Only one randomized trial of surgery versus radiotherapy in basal cell carcinoma of the face showed at four years significantly more persistent tumours and recurrences in the radiotherapy group as compared to the surgery group

Bath-Hextall FJ1, et al. Interventions for basal cell carcinoma of the skin. Cochrane Database Syst Rev. 2007; Jan24:(1):C D003412.

Avril M-F, et al. Basal cell carcinoma of the face: surgery or radiotherapy? Results of a randomized study. Br J Cancer 1997; 76: 100-6.

Reasons to select Radiation instead of surgery

Patient related	Tumor related
Elder and debilitated patients	Multiple and diffuse lesions (scalp)
Use of blood thinners	Recurrent tumors
Chronic diseases with high risk of postoperative wound complications	Advanced lesions requiring complex surgery (grafts os flaps)
Prone to keloid formation	Location in areas cosmetically or functionally sensitive
Refusal of surgery	lips, nose, ears, eyelids

Modified from Patel R and Loonstra AK

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Indications of skin brachytherapy

- Exclusive brachytherapy:

  in epidermal skin cancers T1 - T2 N0 on the face for which curative surgery with adequate margins cannot be offered without mutilation or without the need for extensive reconstructive surgery under general anaesthesia.

- Brachytherapy as a boost:

  in larger T2 - T3 or in N+ cases after EBRT to the primary tumour and lymph nodes.

- Postoperative Brachytherapy:

  when close or positive margins, or in some cases of nerve involvement.

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Contraindications of skin brachytherapy

- Malignant melanoma of the skin
- Skin cancers invading bony structures.
- Upper eyelid lesions
- Where the anatomical situation makes the source positioning needed to provide adequate covering of the target volume impossible (Pinna tumour involving both the concha and the external auditory canal, ear conduct…)

- RELATIVE???

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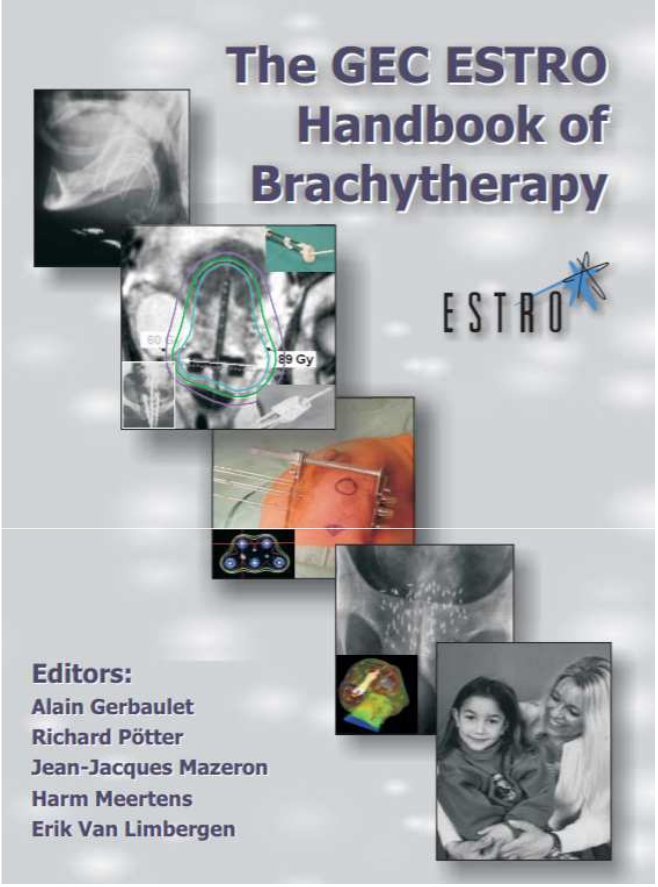
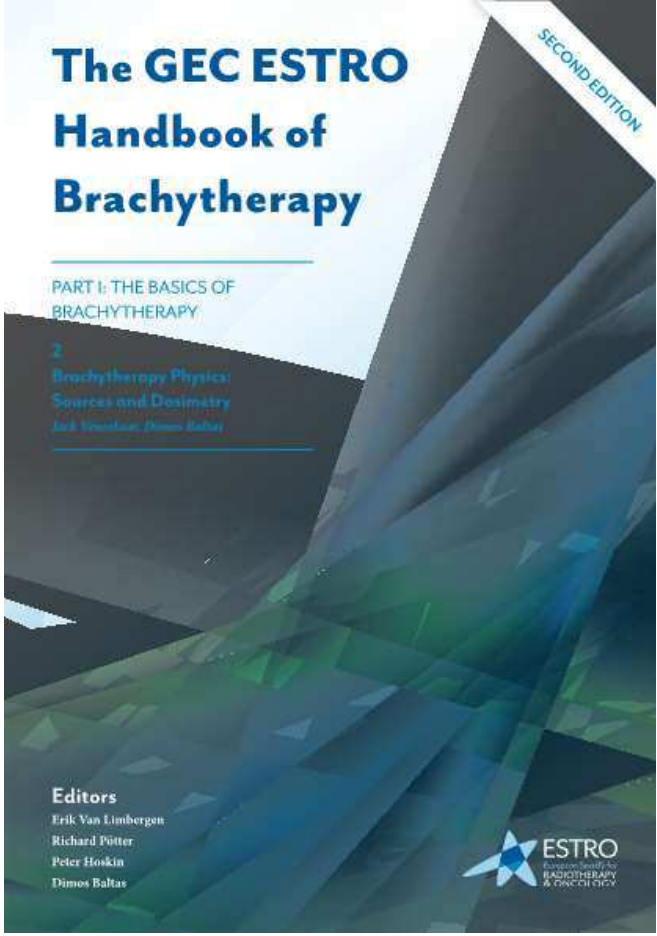


GEC-ESTRO
HANDBOOK
2002



Brachytherapy in Skin Cancer

- Jose Luis Guinot M.D.,
- Jose Pérez-Calatayud Ph. D.,
- Erik Van Limbergen M.D.,Ph.D

(updated March 2017)

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ELSEVIER

BRACHYTHERAPY

Brachytherapy ■ (2015) ■

Review Article

Aspects of dosimetry and clinical practice of skin brachytherapy: The American Brachytherapy Society working group report

Zoubir Ouhib[1,*], Michael Kasper[1], Jose Perez Calatayud[2,3], Silvia Rodriguez[3], Ajay Bhatnagar[4], Sujatha Pai[5], John Strasswimmer[6,7]

Ouhib Z, Kasper M, Perez Calatayud J, et al. Aspects of dosimetry and clinical practice of skin brachytherapy: The American Brachytherapy Society working group report. J. Brachytherapy. 2015 Nov-Dec;14(6):840-58.

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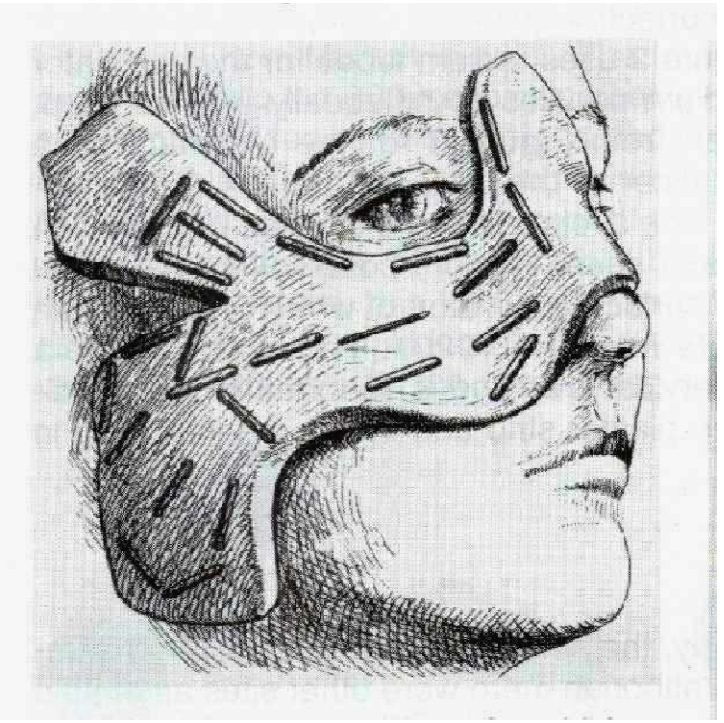
HDR CONTACT BRACHYTHERAPY IN SKIN CARCINOMAS (PLESIOTHERAPY)

- FLAPS
- MOULDS
- SURFACE APPLICATORS



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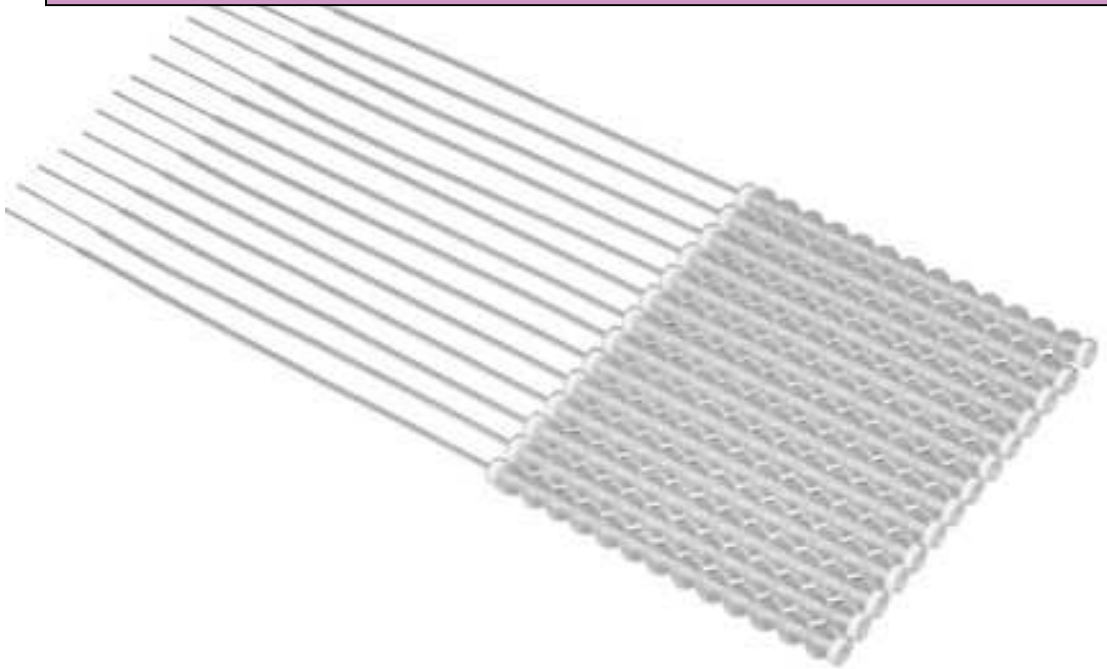
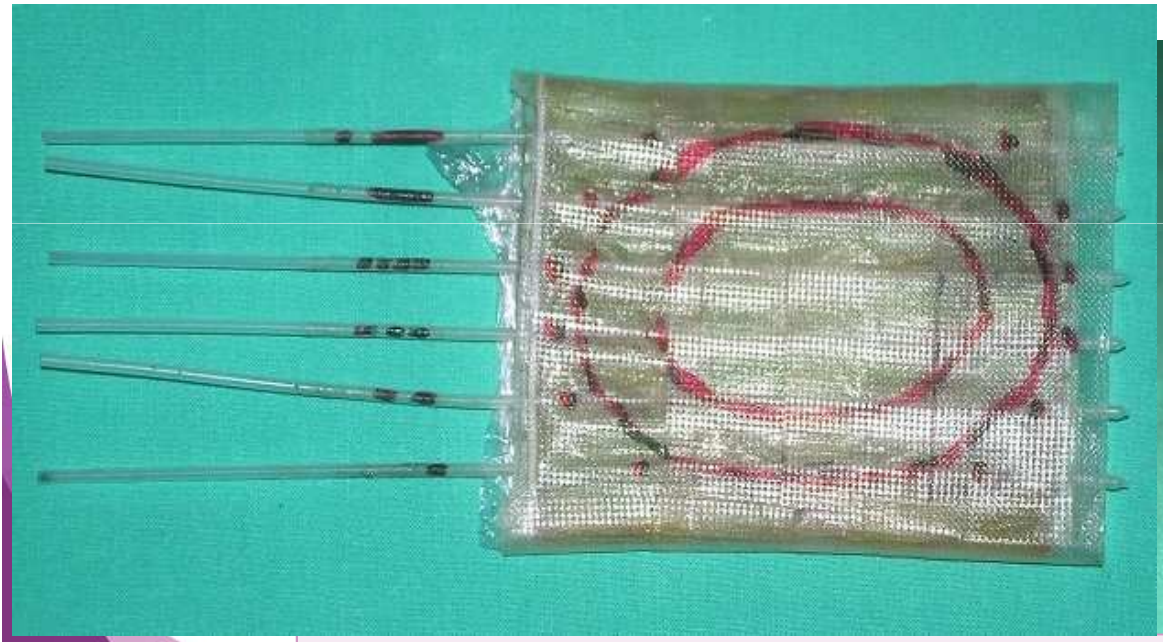
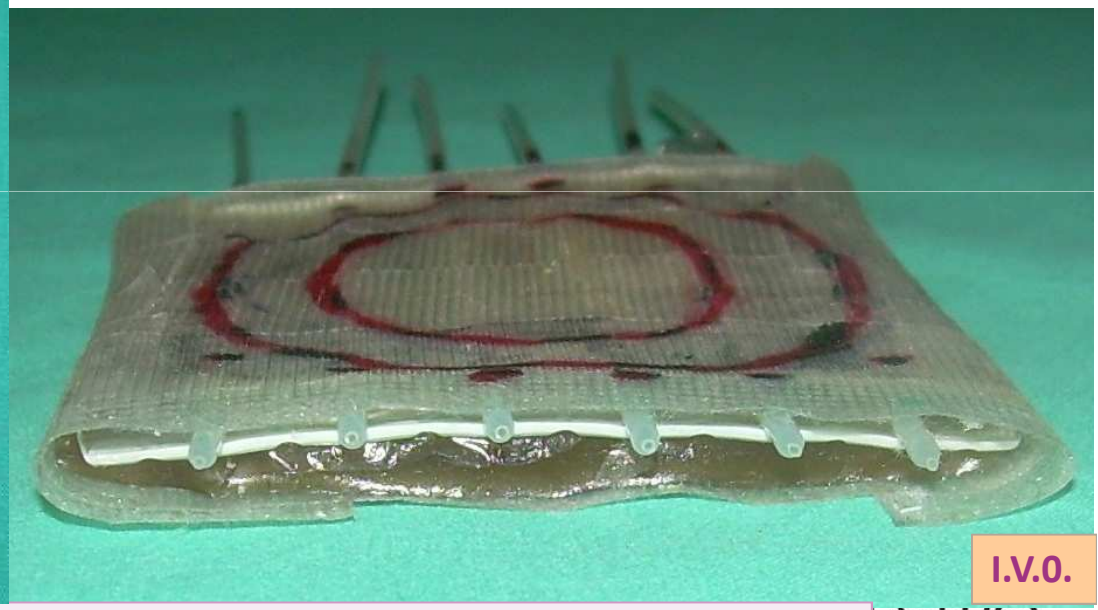
Freiburg Flap applicator



Hand-made flaps





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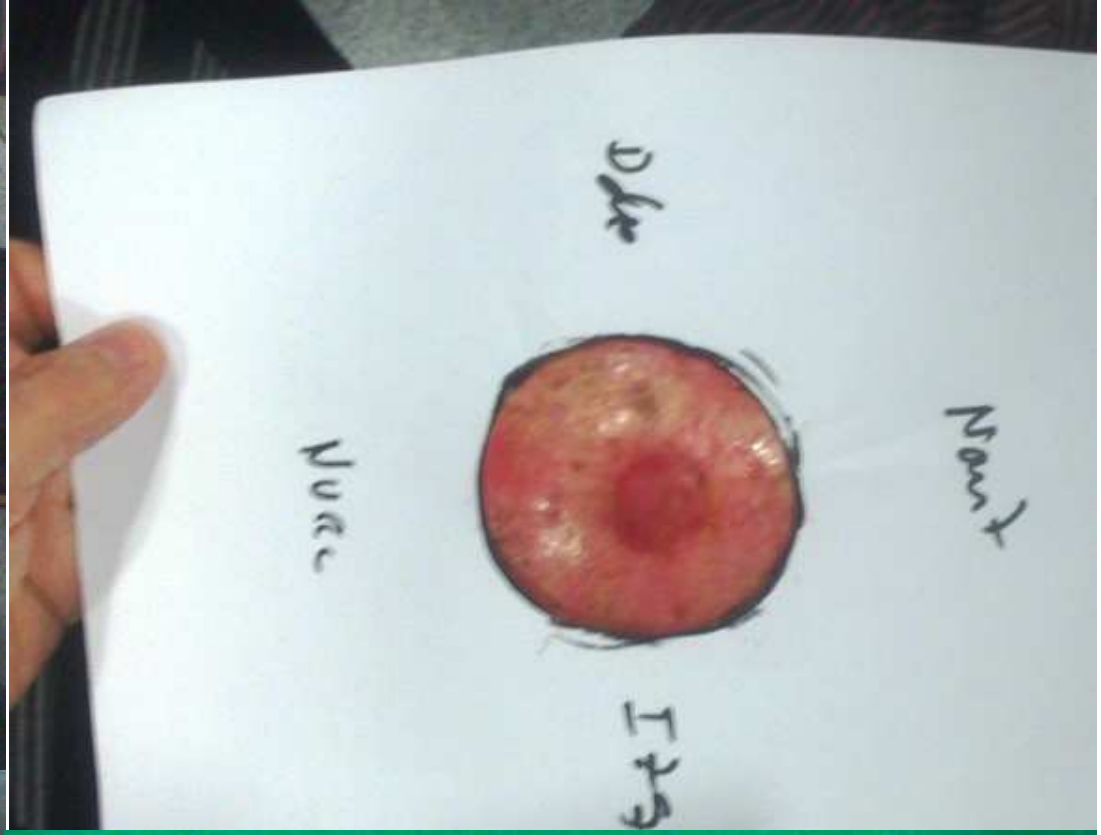
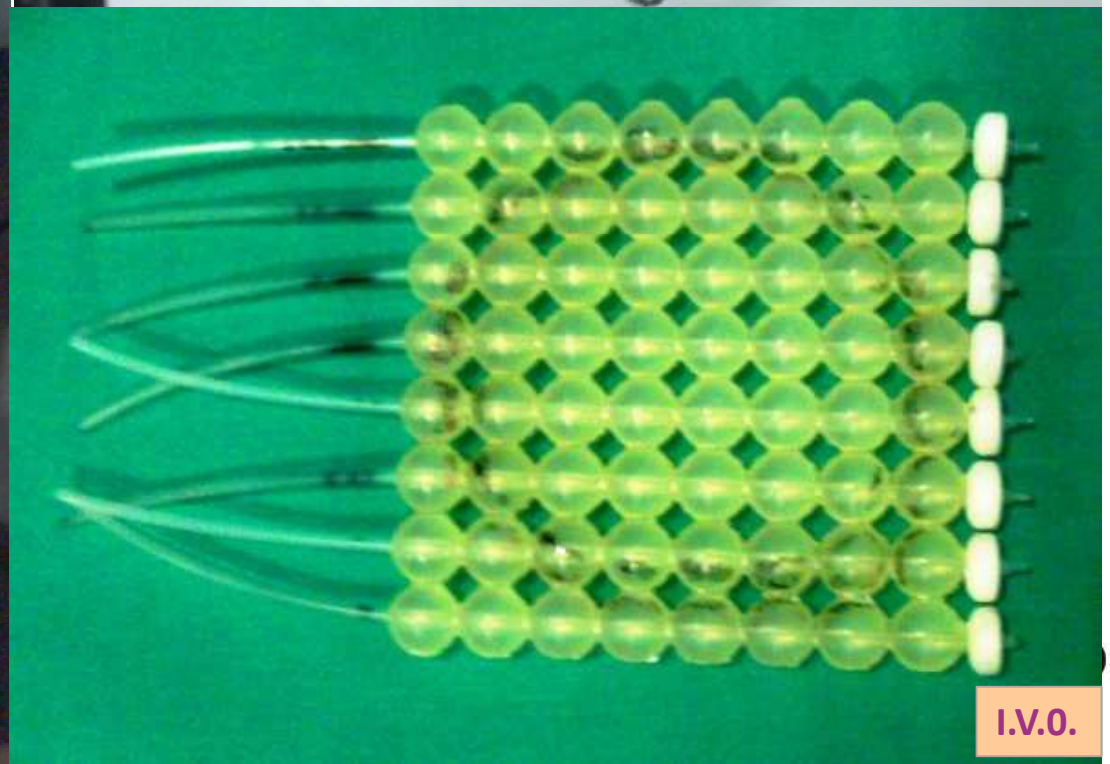
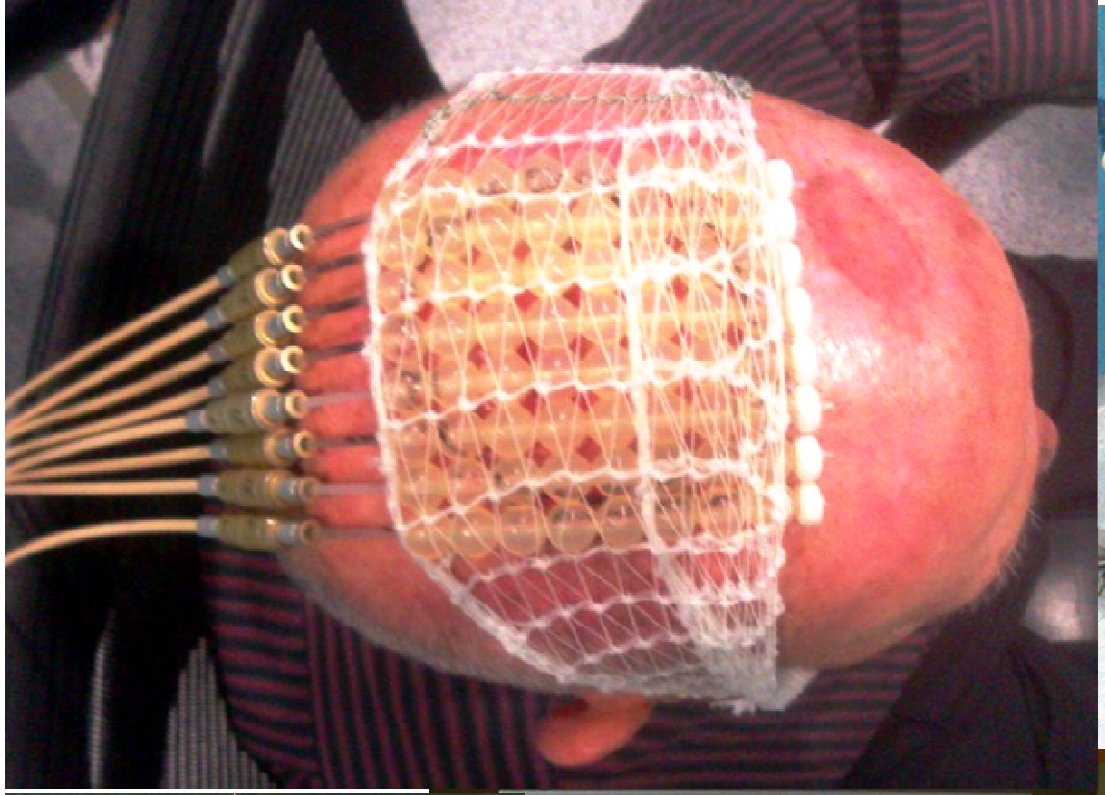
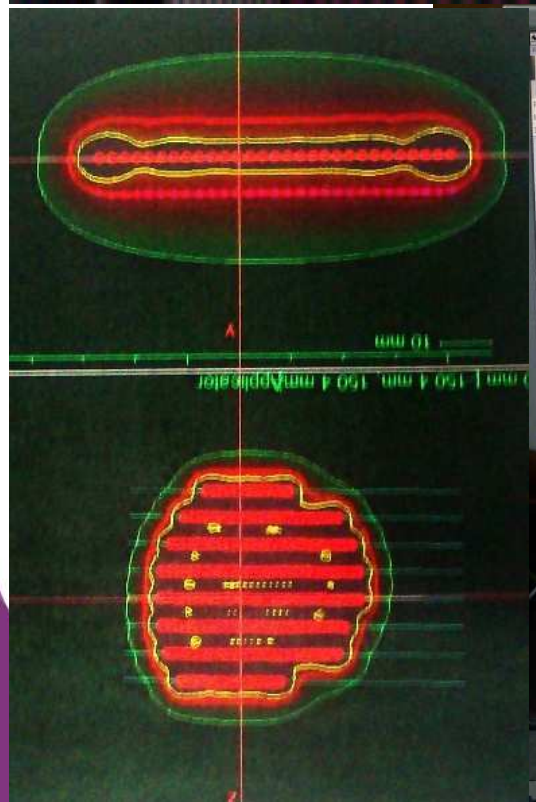
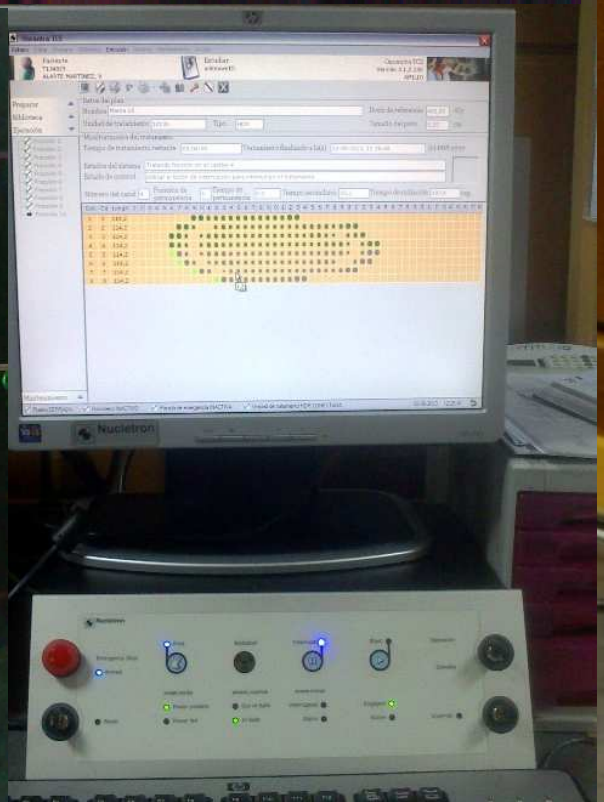
Maroñas M, Guinot JL, Arribas L, et al. Treatment of facial cutaneous carcinoma with high-dose rate contact brachytherapy with customized molds. Brachytherapy 2011;10(3):221-7.




I.V.0.







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SCC. Nerve involvement. Free margin

I.V.0.

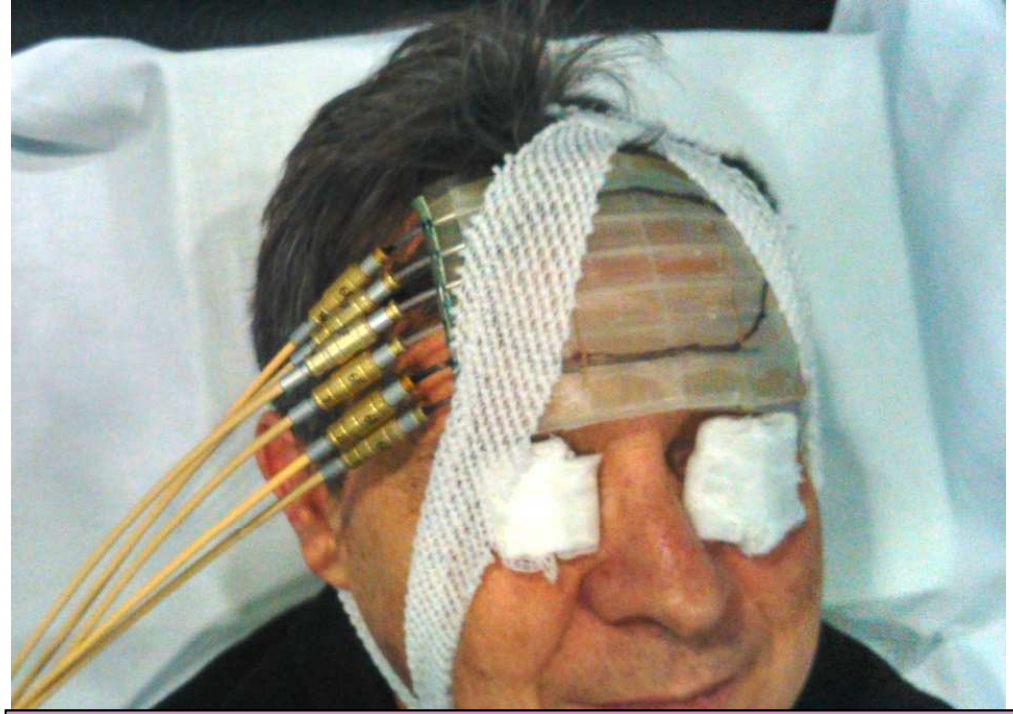
13 x 4 Gy
3/week
To 3mm
under skin

Last week

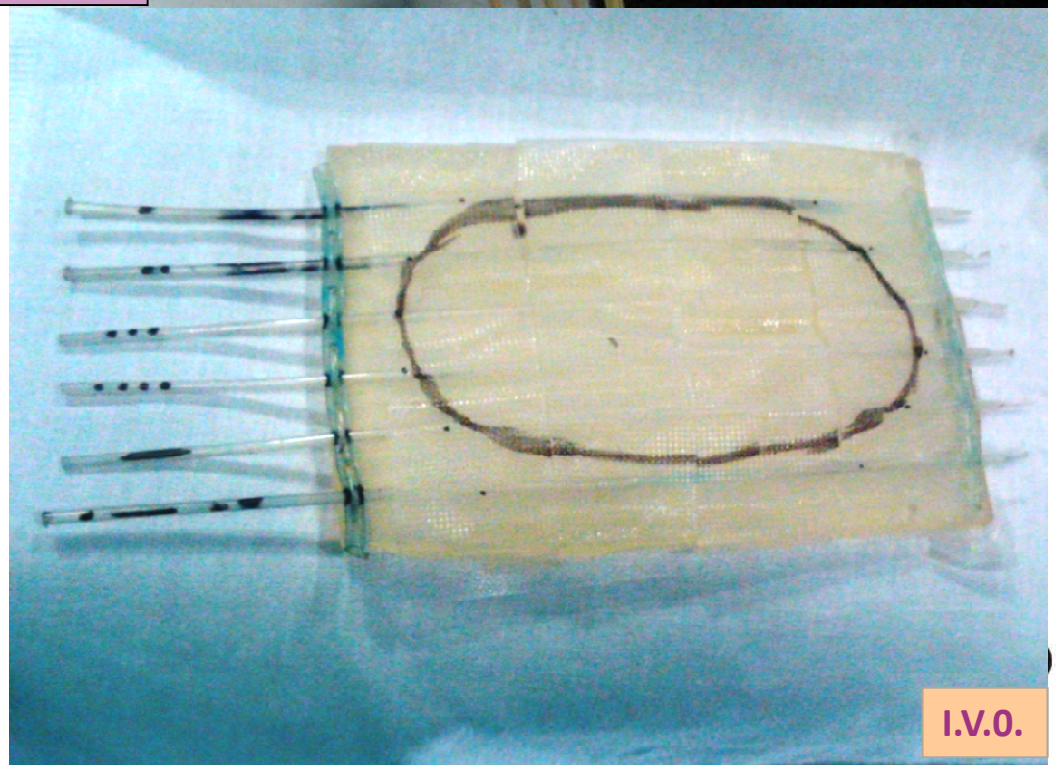
15 months later

30 months later

I.V.0.



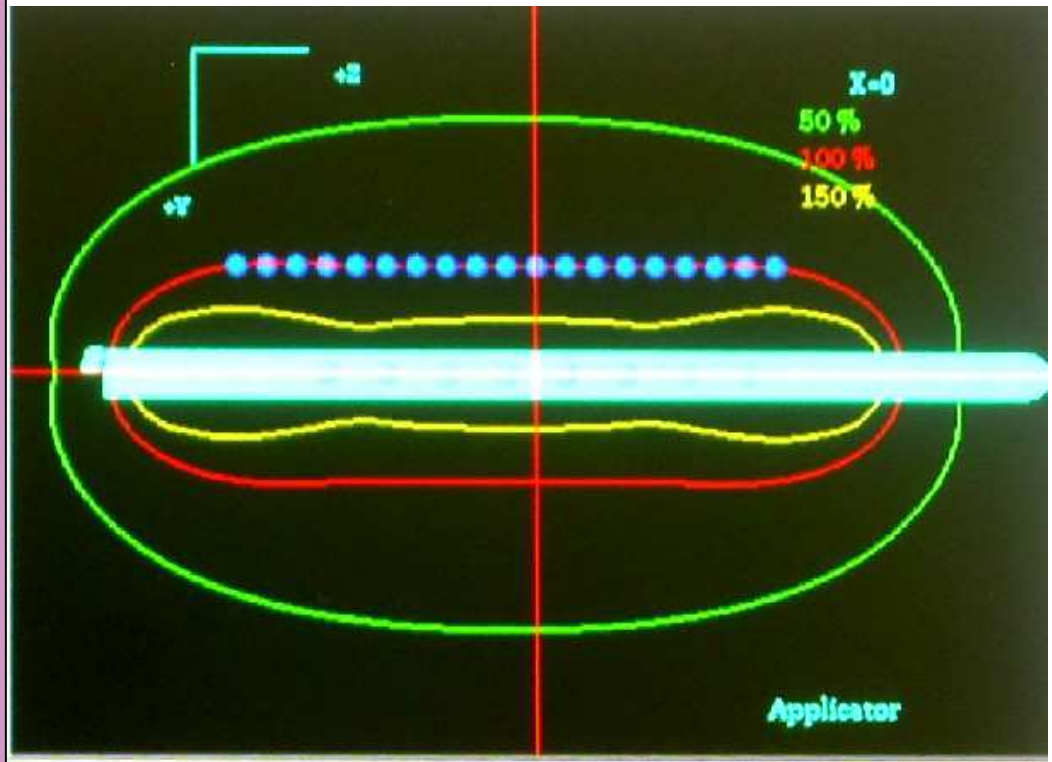
SCC. Forefront. Positive margin

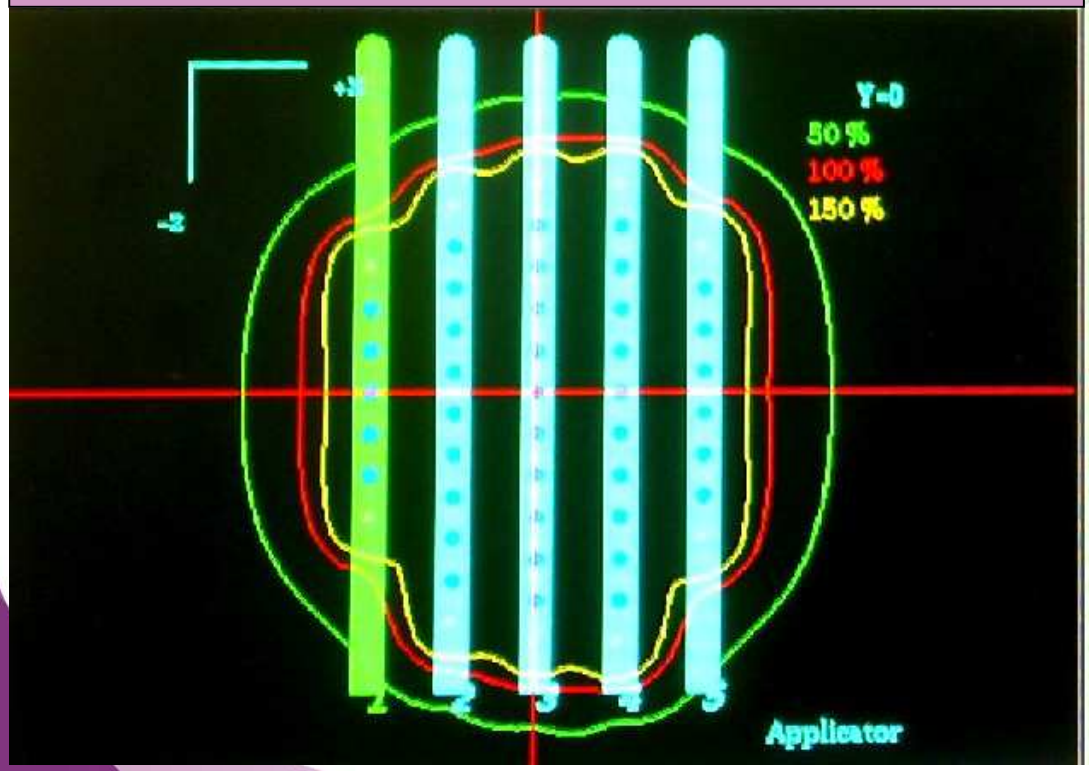


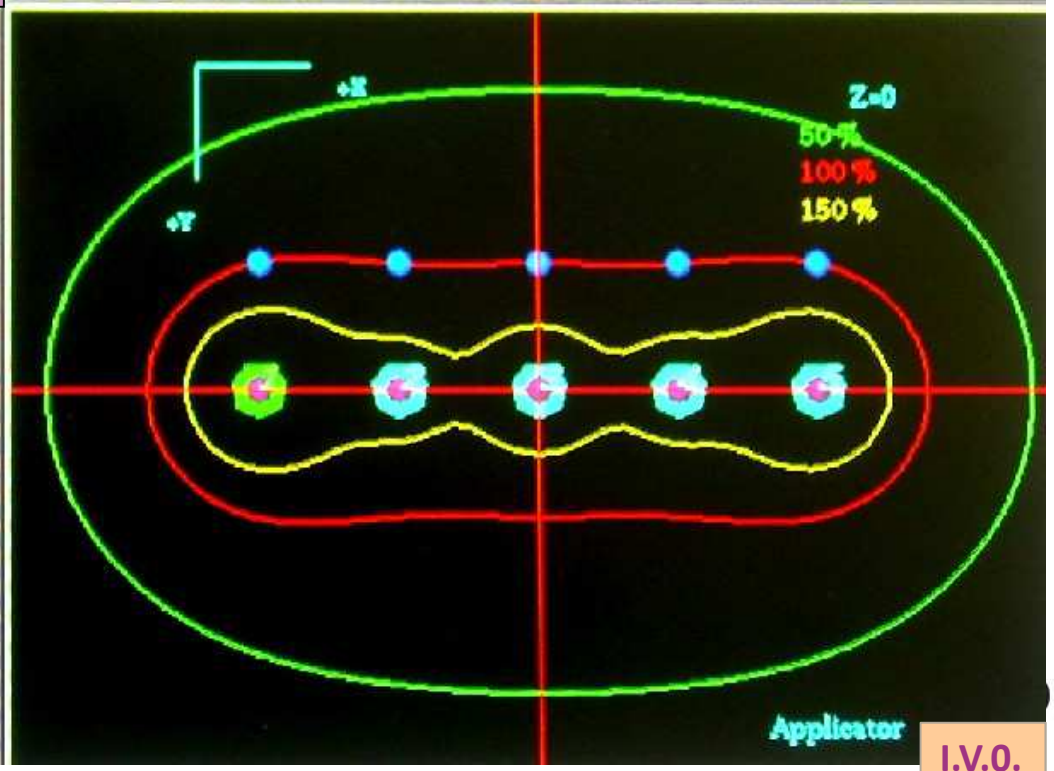
I.V.0.

Prescription at 3mm under the skin

3 Gy x 17-18 frac. 3/week
4 Gy x 12-13 frac. 2-3/week
7 Gy x 5-6 frac. Once a week







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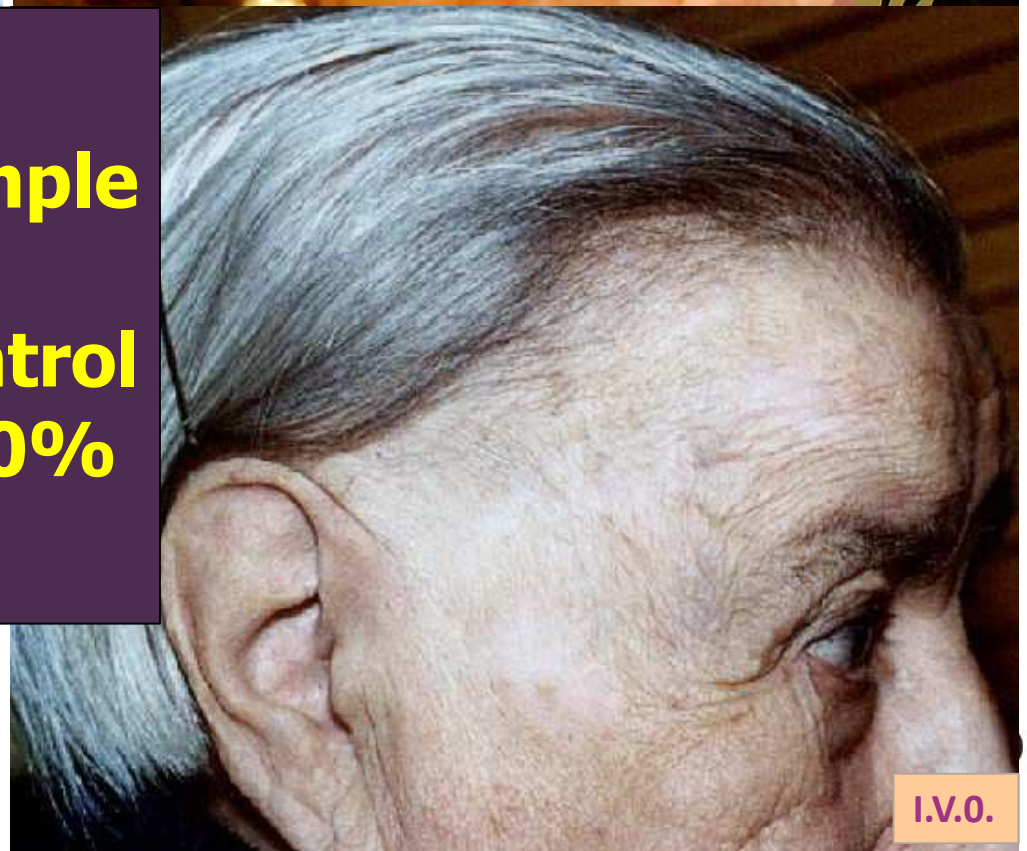
Temple

Control 100%



I.V.0.

12 x 4 Gy
2 year later

I.V.0.

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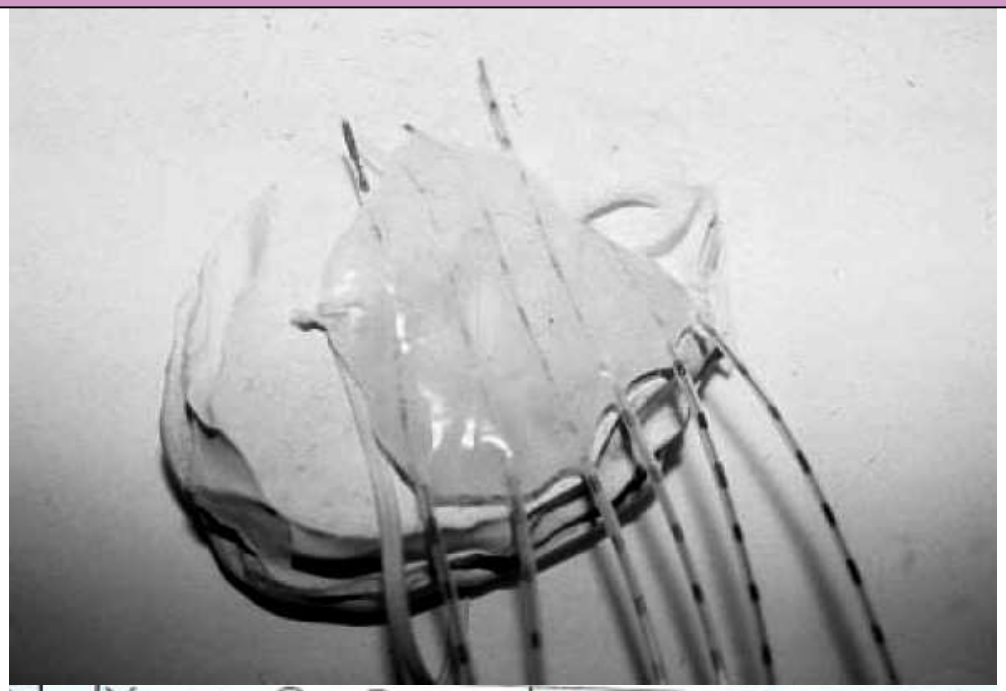
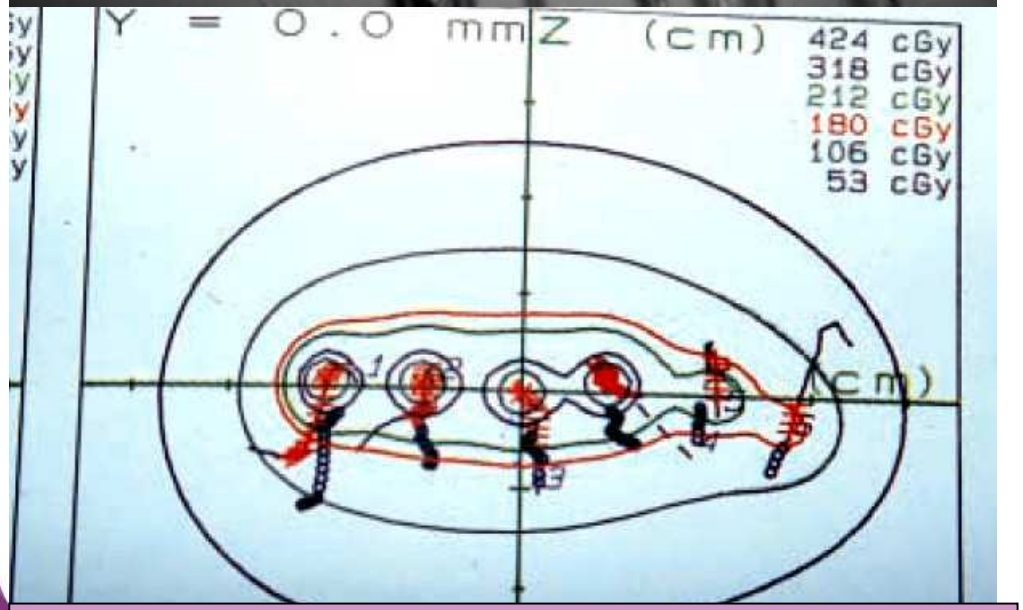
Moulds. Foundation IMOR. Barcelona

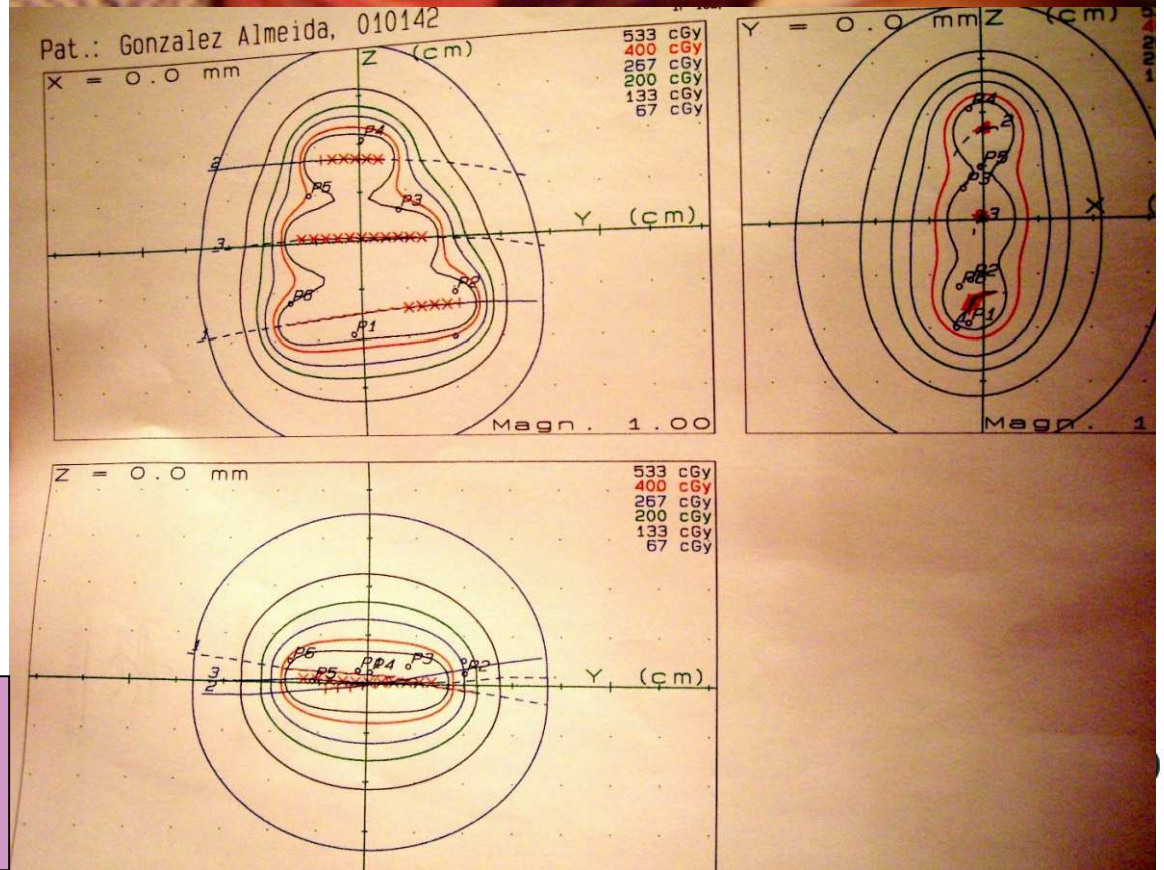




33-36 x 1’8 Gy. Split 3weeks
Tu> 4 cm + 10 x 1’8 Gy

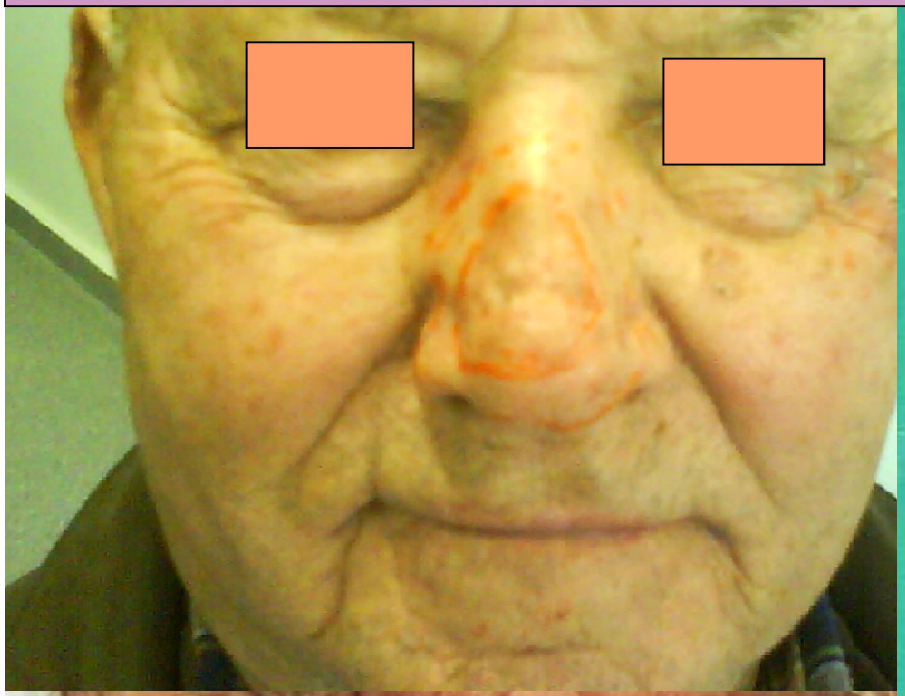
Guix B, Finestres F, Tello JI, et al. Treatment of skin carcinomas of the face by high-dose-rate brachytherapy and custom-made surface molds. Int J Radiat Oncol Biol Phys 2000; 47: 95-102.

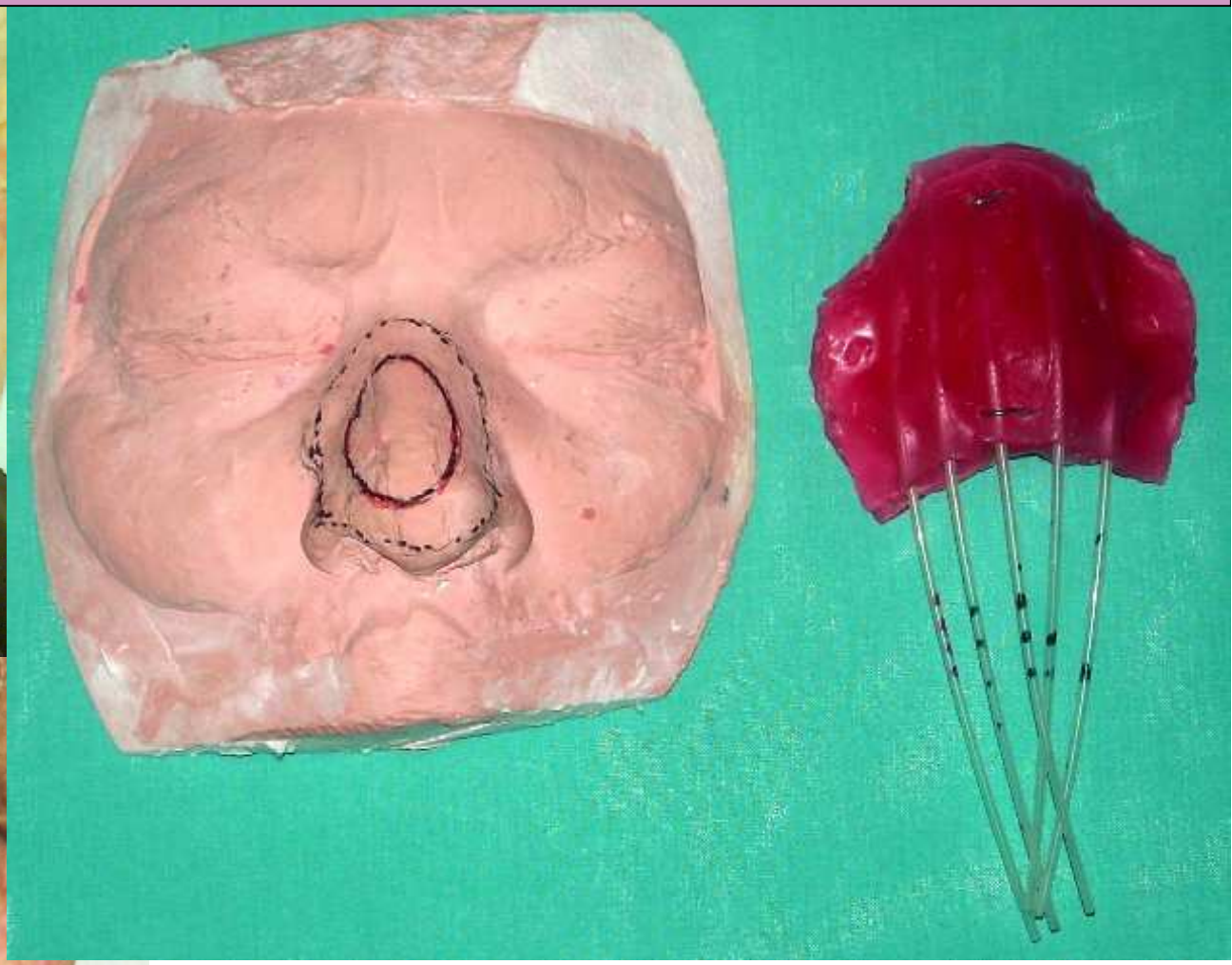
Moulds. Las Palmas



Young: 33-35 f. x 2 Gy
Elder: 9-10 f. x 5 Gy

Wax moulds for nose or curved areas. IVO VALENCIA





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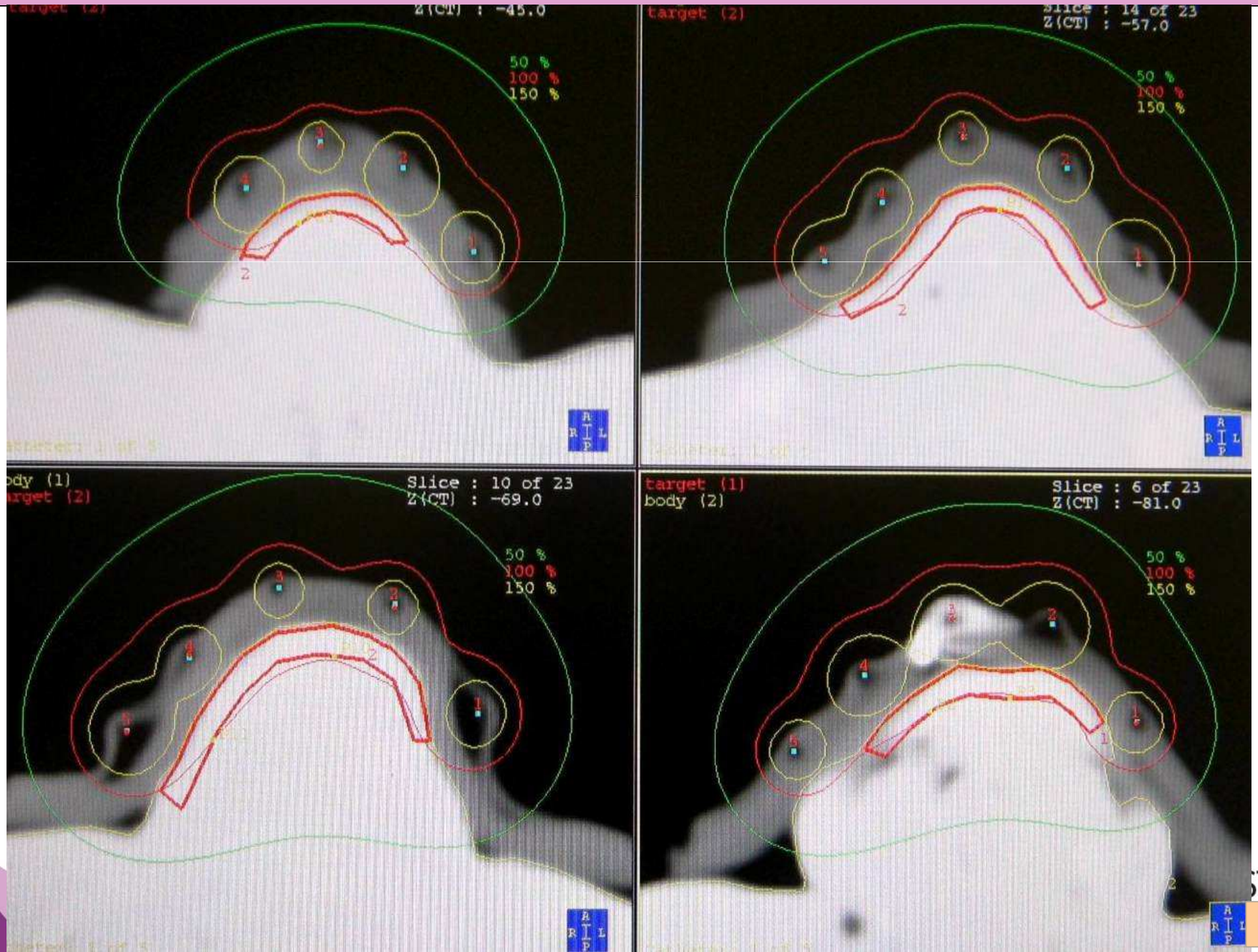
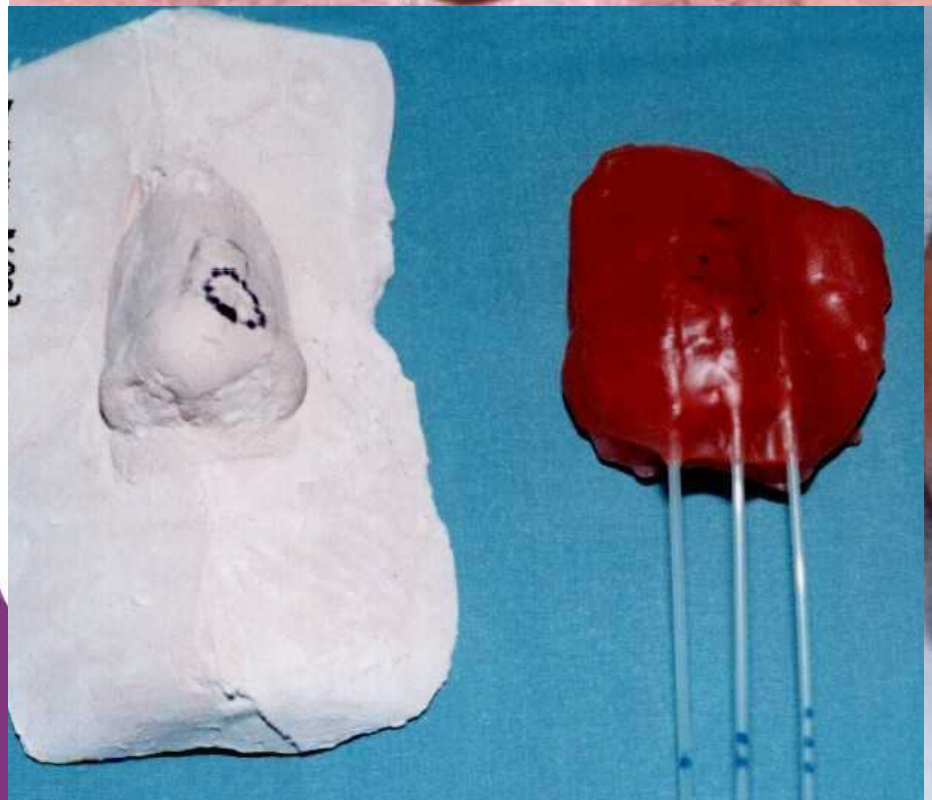
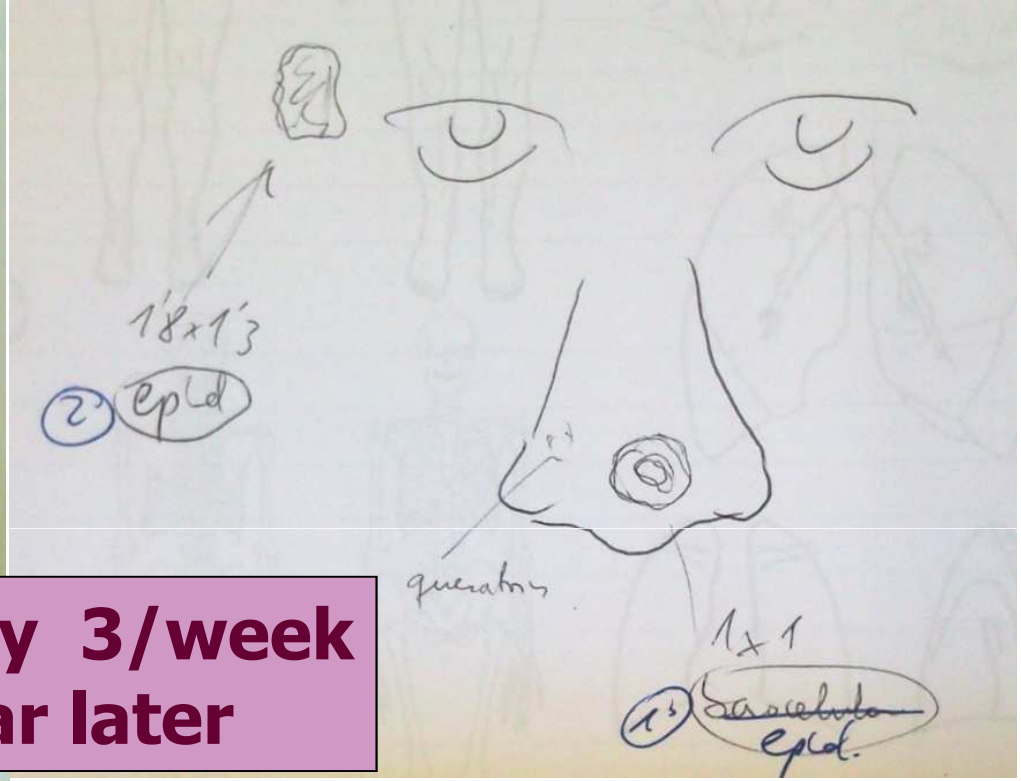
3-4 Gy at 3 mm from skin surface, 3 times per week



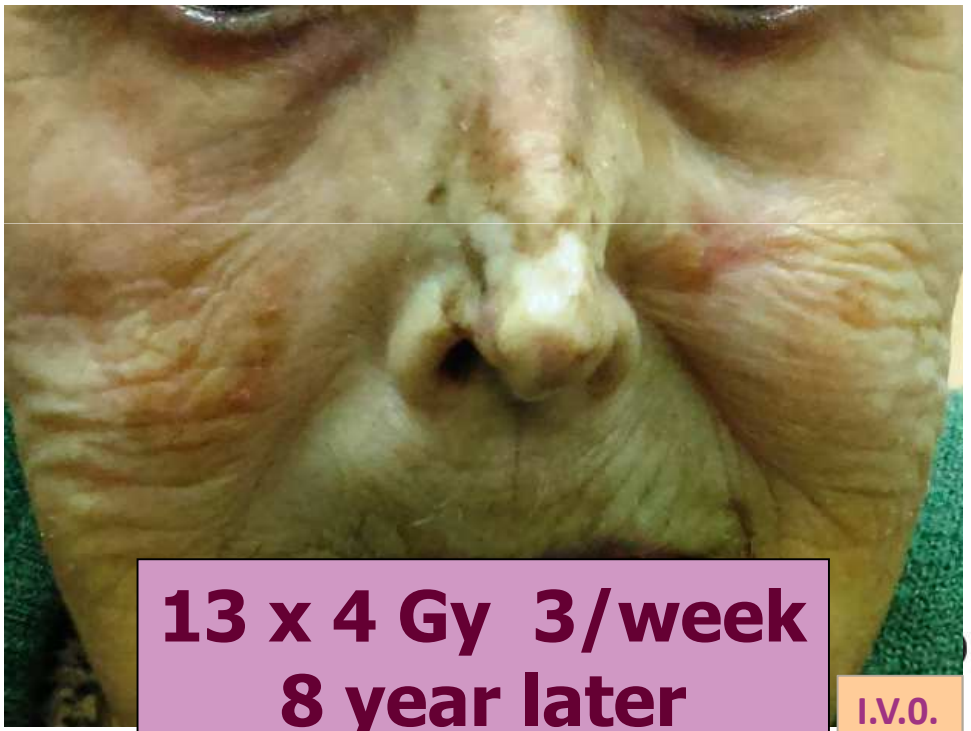
Local control 83% + salvage 100%



I.V.O.



13 x 4 Gy 3/week
3 year later



13 x 4 Gy 3/week
8 year later

I.V.0.

Fig. 1. Images of customized mold (wax and plastic mold).

results of hypofractionated high-dose-rate plesiotherapy on basal cell carcinoma. Initial lesion and 2 years

3Gy x 15-16
Basal ca
3Gy x 18 SCC
3/week
to 5mm from skin

Arenas M, Arguis M, Diez-Presa L, et al. Hypofractionated high-dose-rate plesiotherapy in nonmelanoma skin cancer treatment. Brachytherapy 2015;14:859-865.

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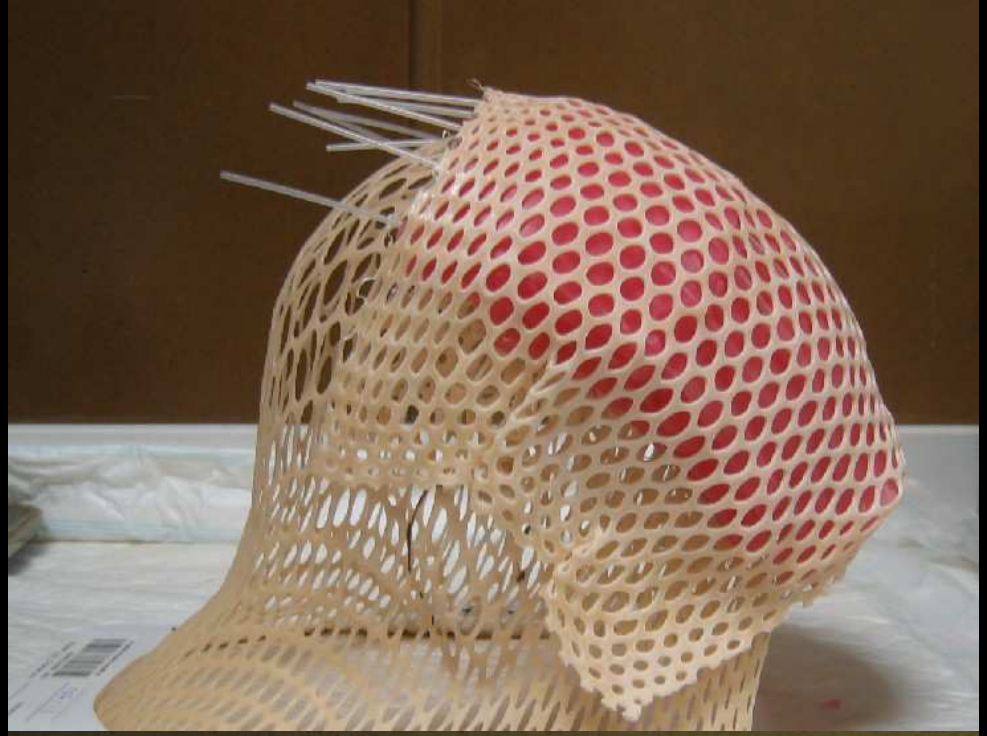
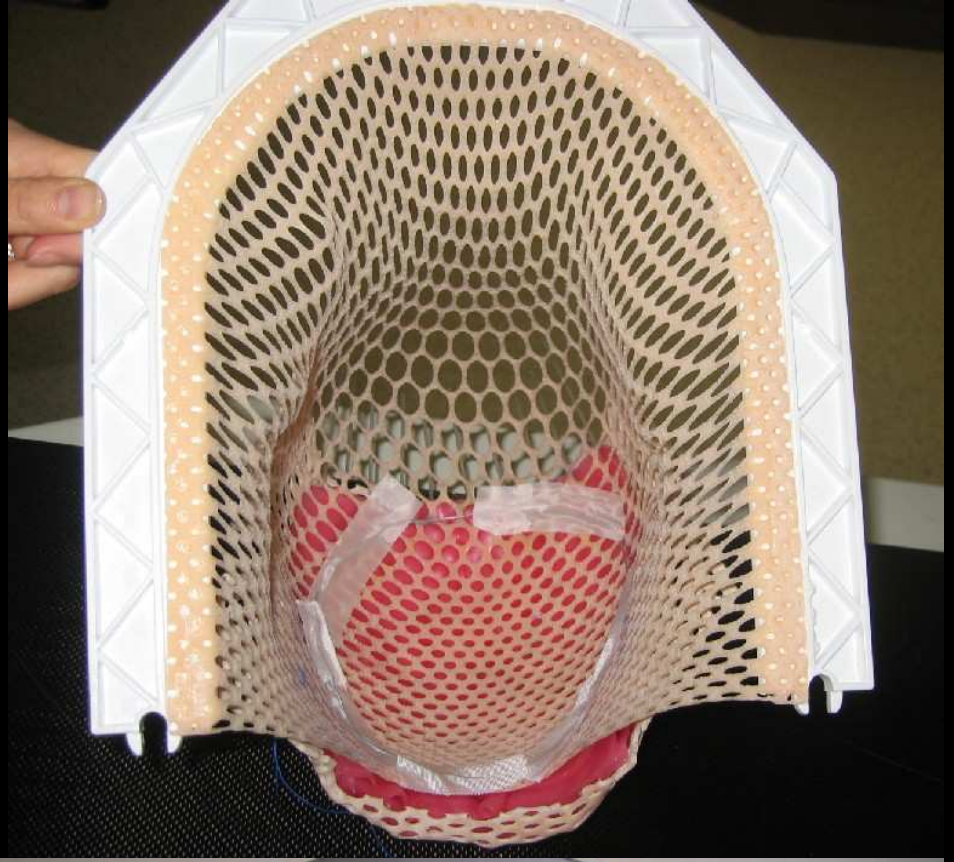
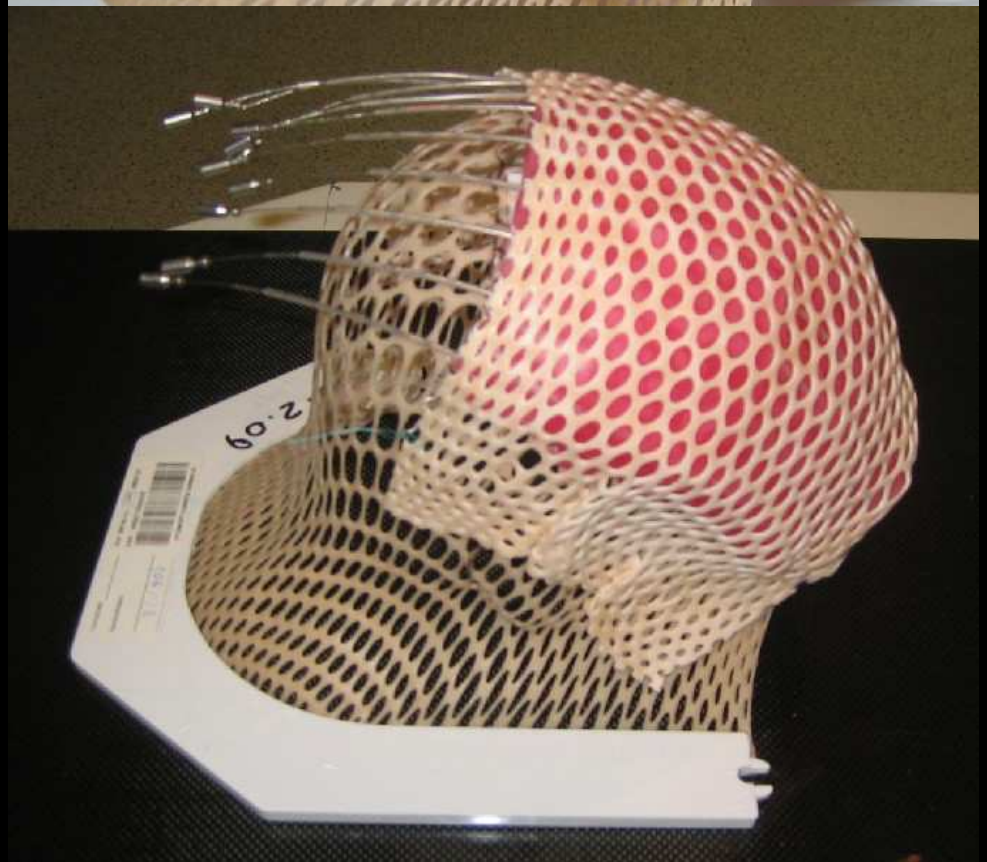
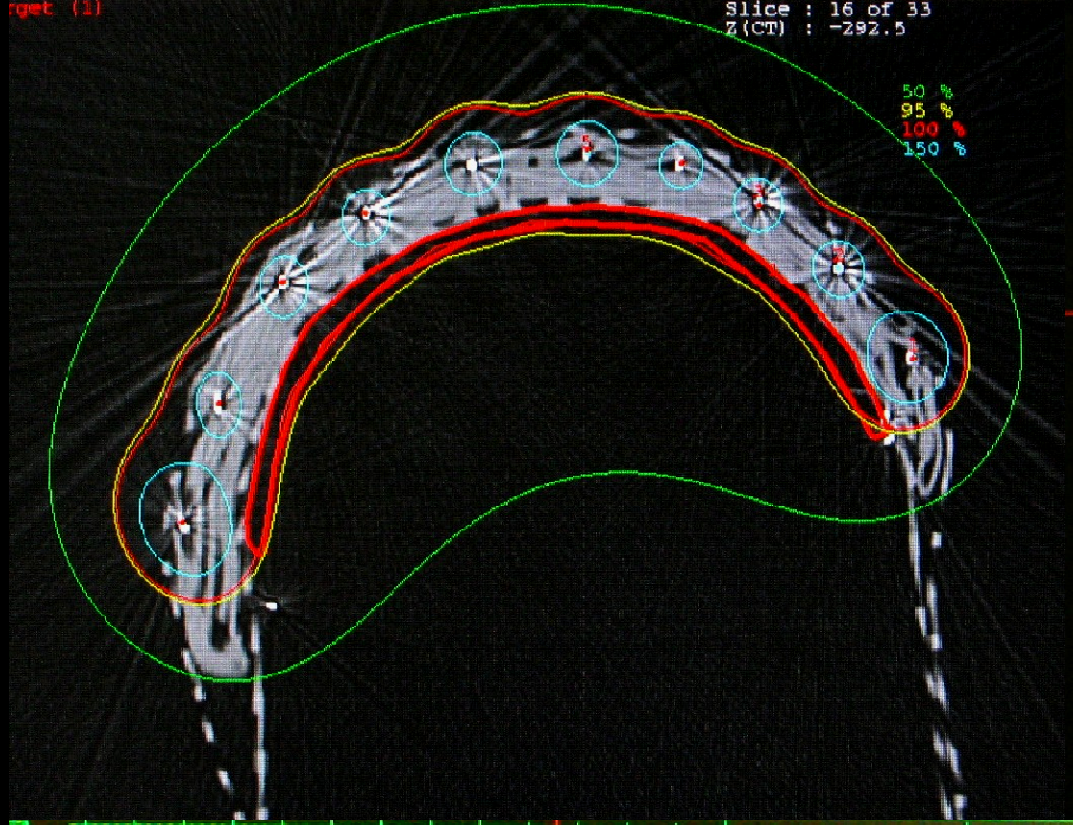
Wax moulds for scalp. IVO VALENCIA

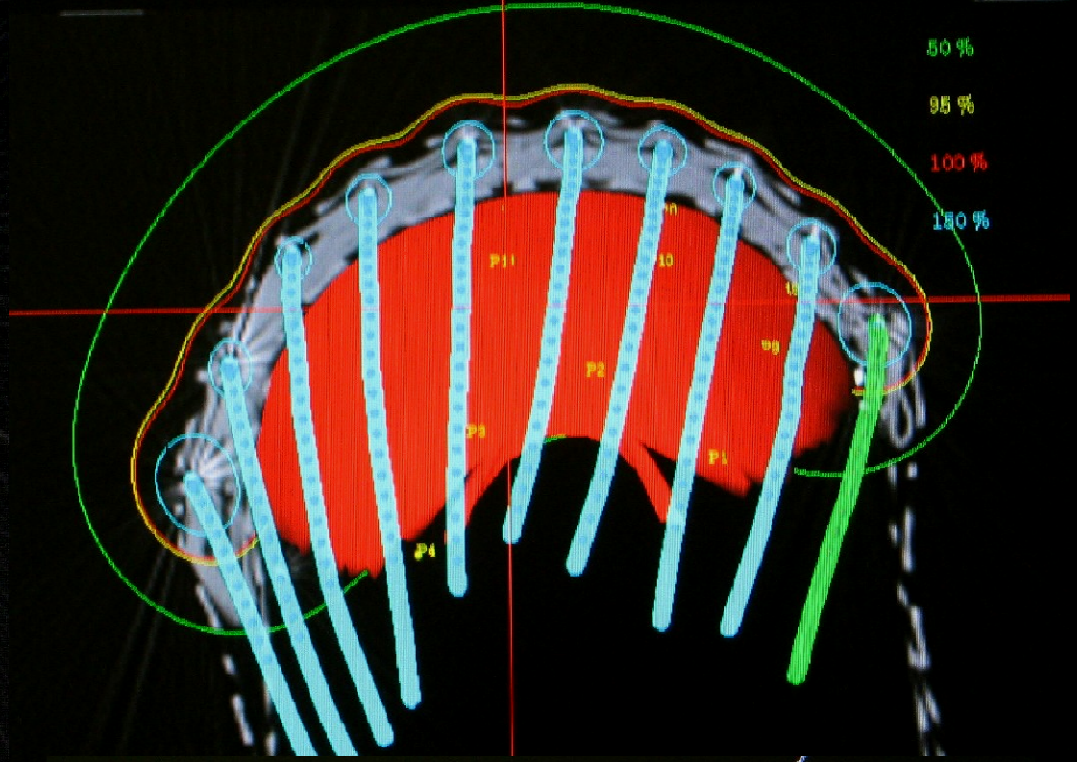


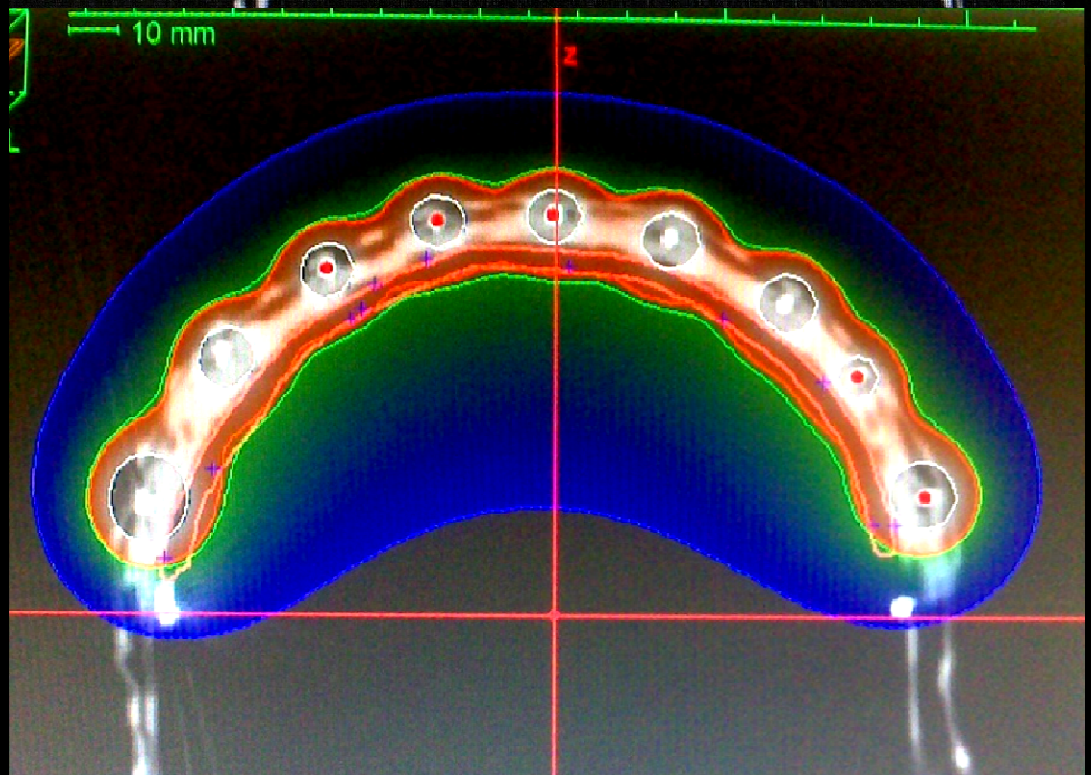


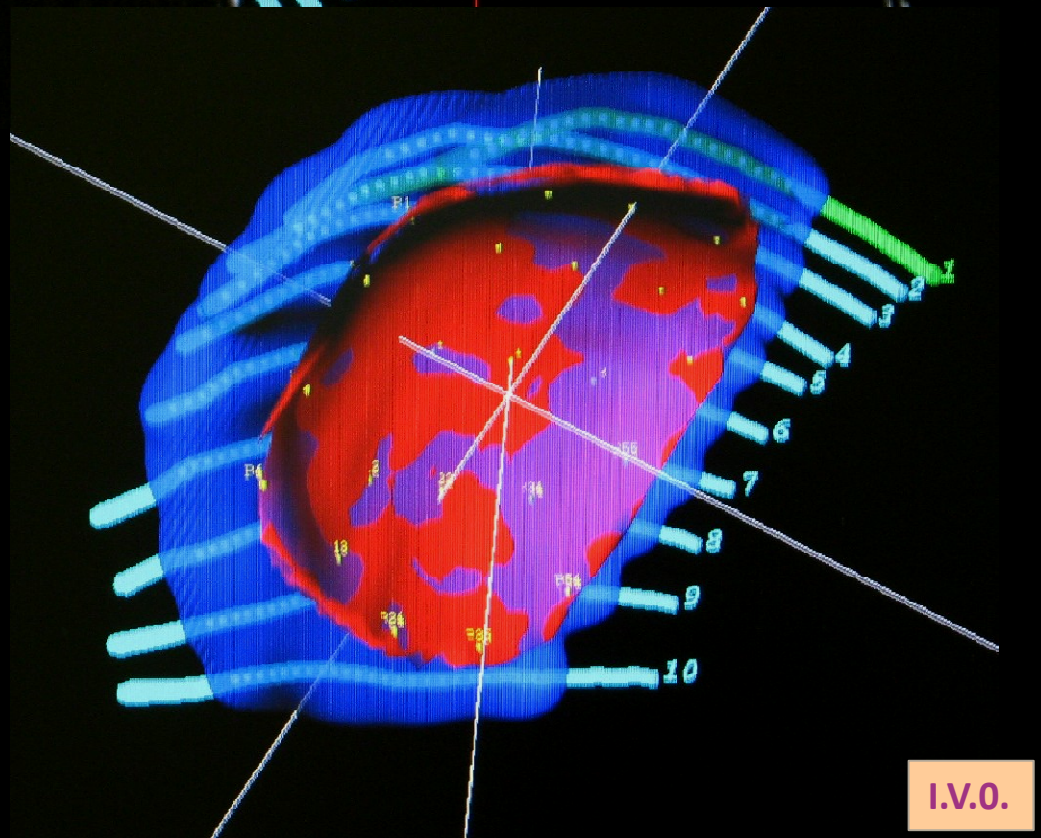


I.V.0.

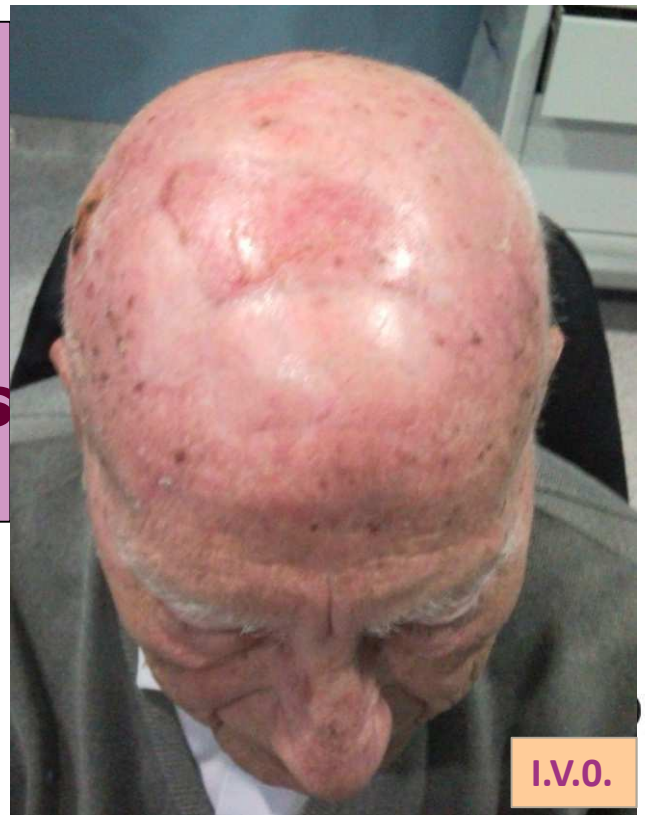

Slice : 16 of 33
Z(CT) : -292.5
50 %
95 %
100 %
150 %


50 %
95 %
100 %
150 %


10 mm


I.V.0.

2 Gy/day
x 5/week
30-33 frac.
6-6,5 weeks



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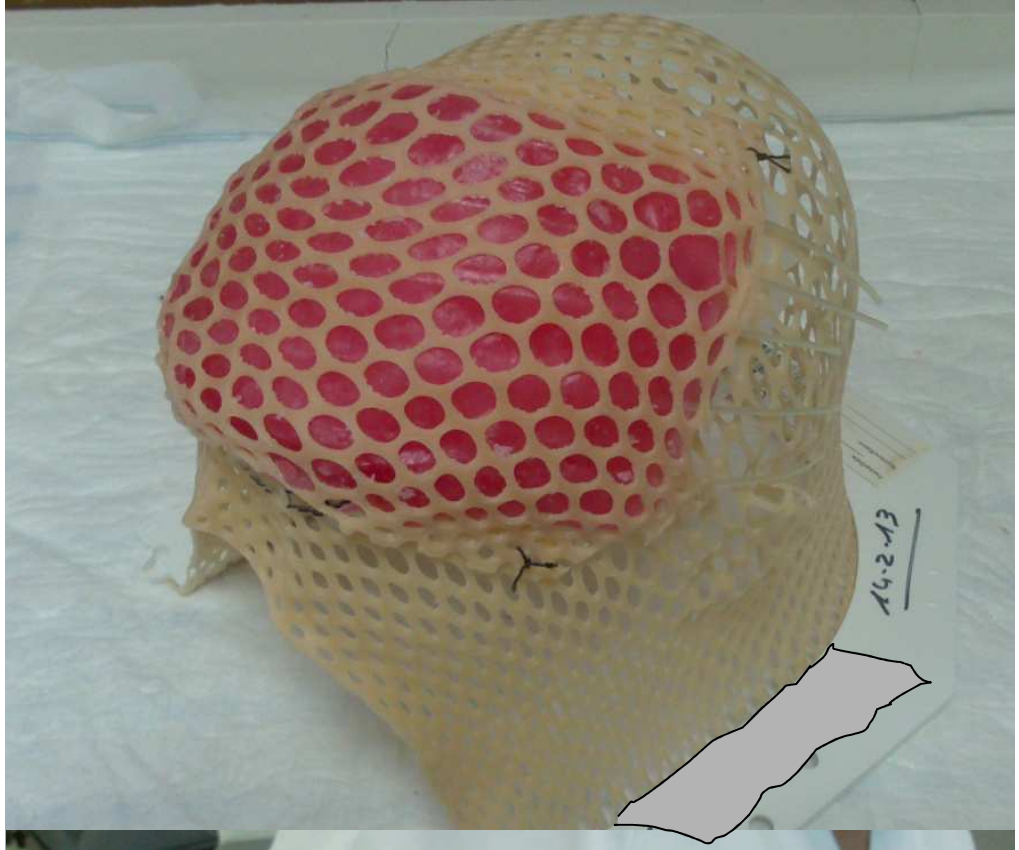

I.V.0.

custom mold applicator (scar shown in red)

Freiburg flap on a shin lesion with mask/flap mounted

Ouhib Z, Kasper M, Perez Calatayud J, et al. Aspects of dosimetry and clinical practice of skin brachytherapy: The American Brachytherapy Society working group report. J. Brachytherapy. 2015 Nov-Dec;14(6):840-58.

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Courtesy of Agata Rembielak. Christie's Hospital. Manchester

1 month FU

2 month FU

4 month FU

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SURFACE APPLICATORS IN SKIN CARCINOMAS

In small tumors (PTV<3cm), depth <3-4mm
- HDR (Leipzig / Valencia)
- Electronic BT (Xoft / Esteya)

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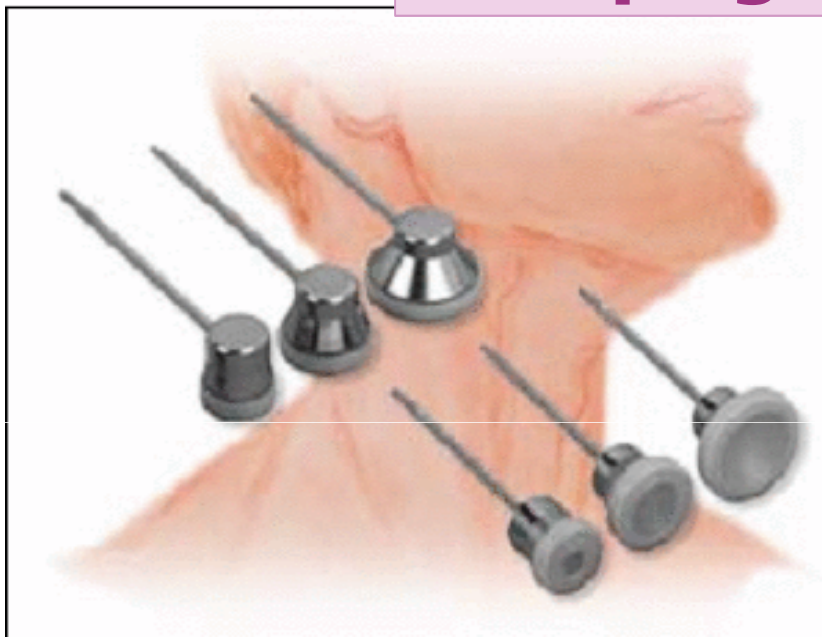
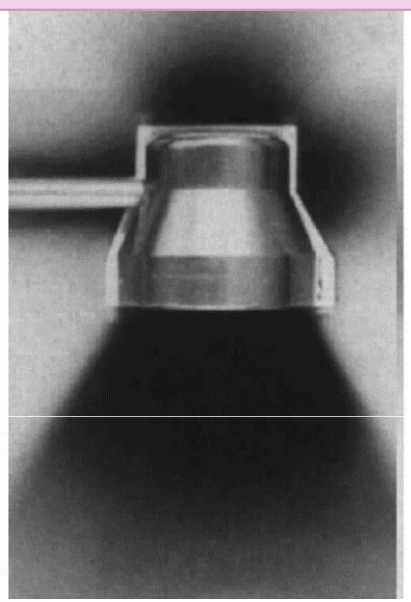
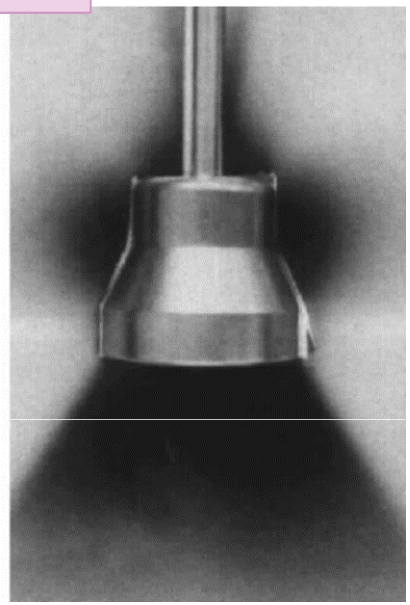
Leipzig applicator



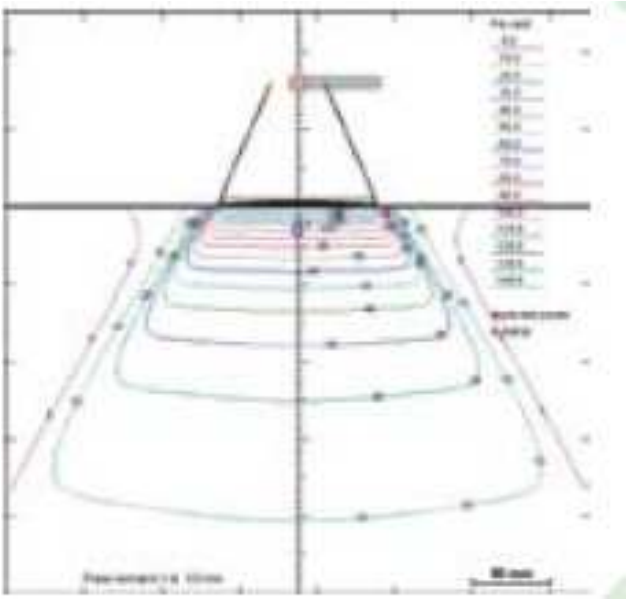


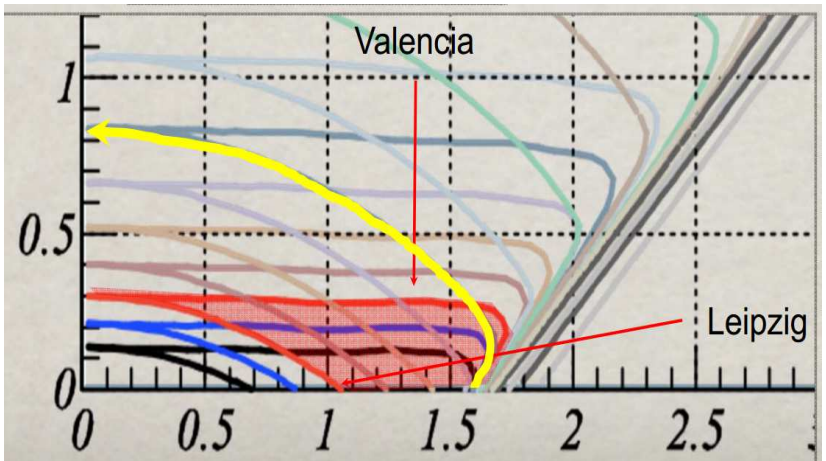


5-10Gy
30-40Gy
1-2 /week
To different depths

Kohler-Brock A, Prager W, Pohlmann S, et al. (The indications for and results of HDR afterloading therapy in diseases of the skin and mucosa with standardized surface applicators (the Leipzig applicator)). Strahlenther Onkol 1999;175:170-174.

Valencia applicator





Electronic surface applicators

Designed to obtain dose distributions similar to Leipzig/ Valencia app with low energy Xray (50-69.7kV)

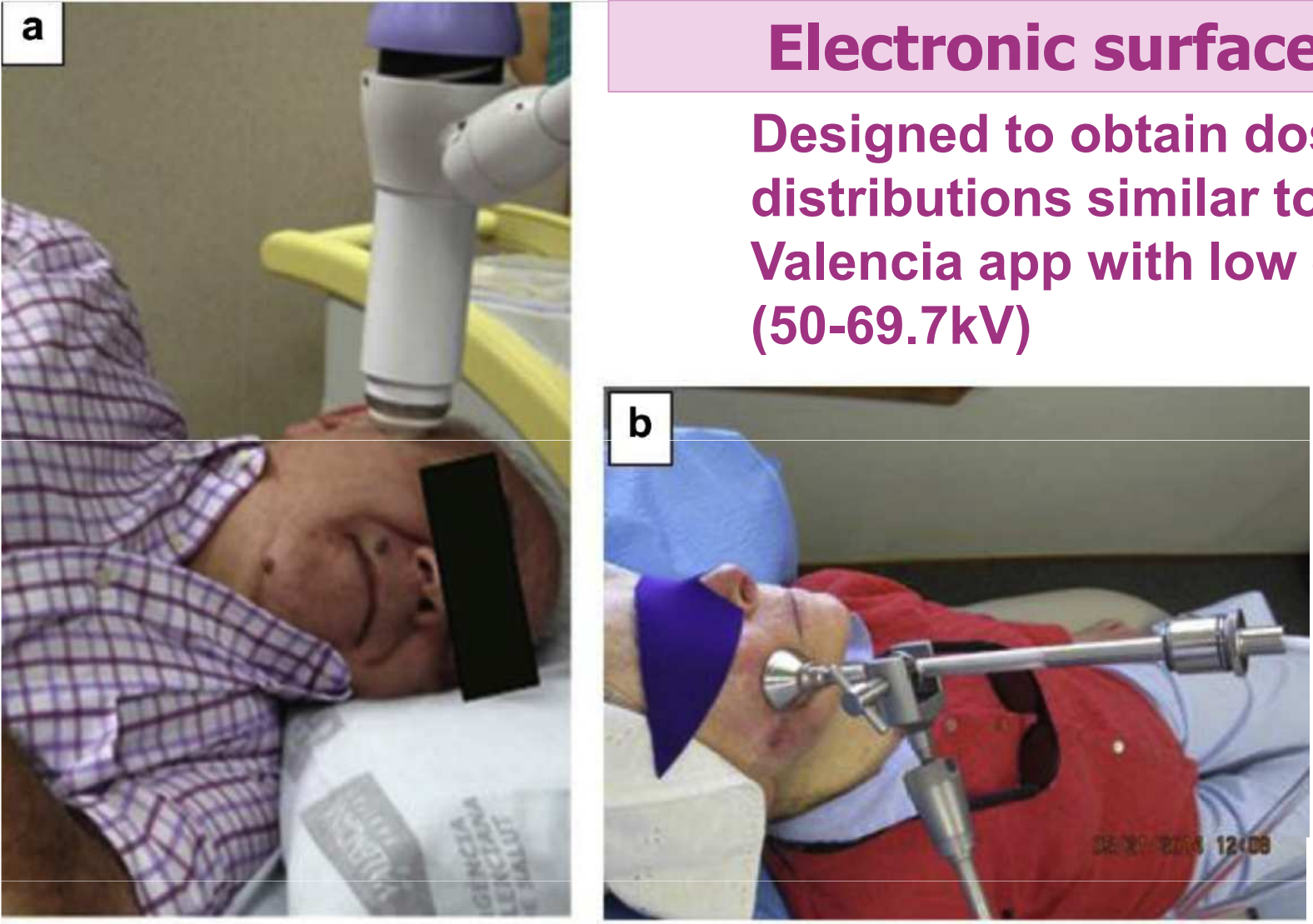
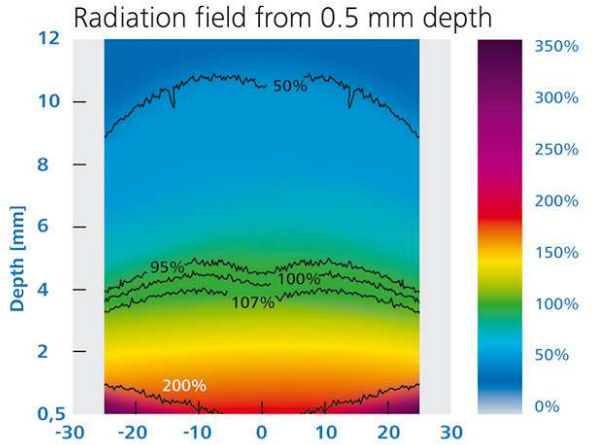


Fig. 7. Electronic brachytherapy: (a) Esteya patient setup. (b) Xoft patient setup.

Esteya

Xoft

Intrabeam Surface applicator



Ouhib Z, Kasper M, Perez Calatayud J, et al. Aspects of dosimetry and clinical practice of skin brachytherapy: The American Brachytherapy Society working group report. J. Brachytherapy. 2015 Nov-Dec;14(6):840-58.

Valencia applicator

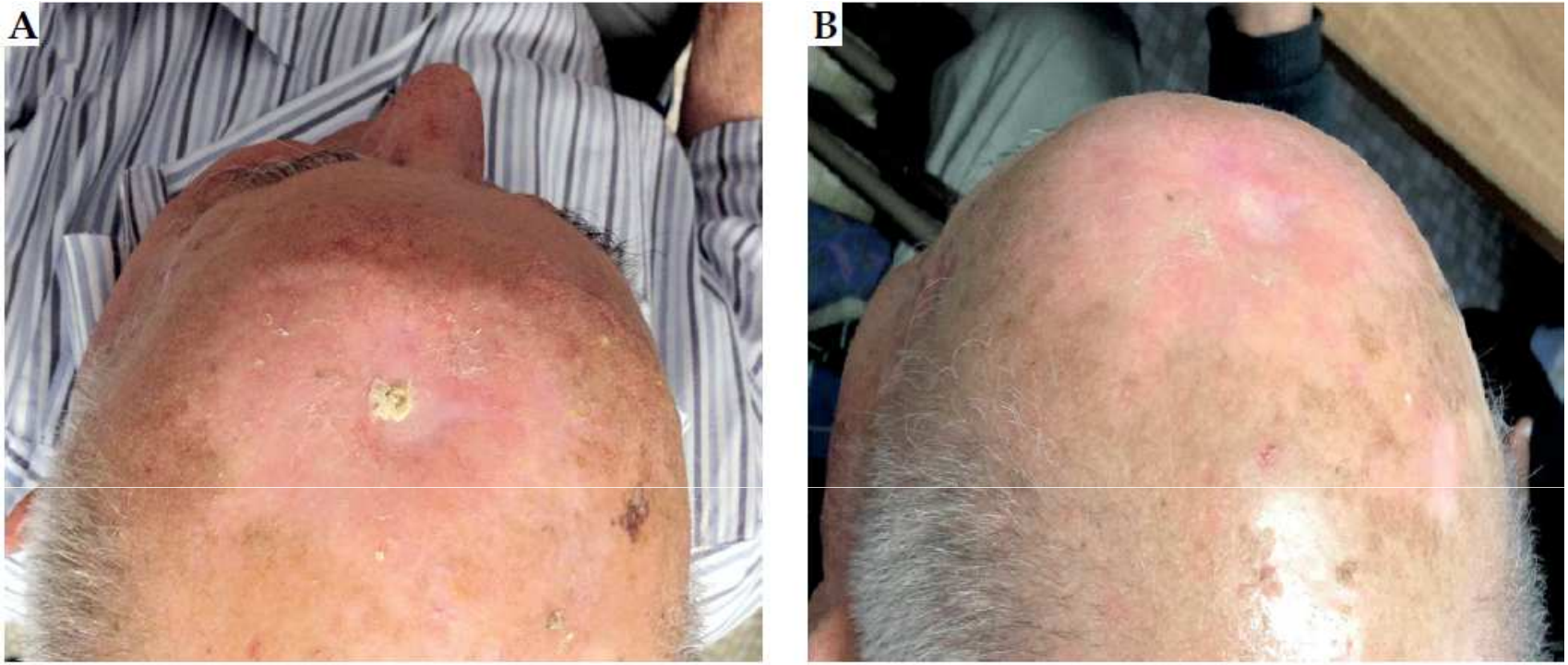


Fig. 2. An example of complete response (B) after nine months of treatment of NMSC with HDR-BT using a Valencia applicator

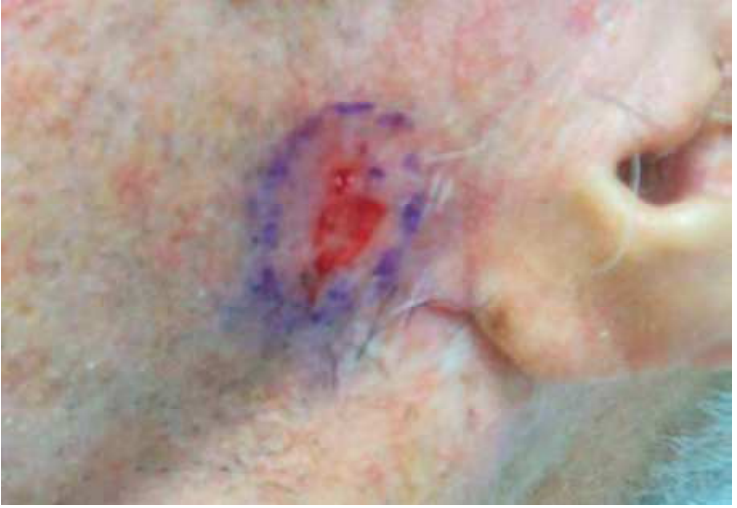
5Gy x 8 (BED α/β:10) 60 Gy
5Gy x 10 (BED α/β:10) 75 Gy
2-3 /week
to max 4mm

Delishaj D., Laliscia C, Manfredi B et al. Non-melanoma skin cancer treated with high dose rate brachytherapy and Valencia applicator in elderly patients: a retrospective case series. J Contemp Brachytherapy; 2015; 7: 362-444.

7Gy x 6
6Gy x 7 (BED α/β:10) 70 Gy
2 /week
to max 4mm

Tormo A, Celada F, Rodriguez S, et al. Non-melanoma skin cancer treated with HDR Valencia applicator: clinical outcomes J. Contemp Brachyther 2014; 6(2) 167-172.

ESTRO School



Valencia applicator: results

Tormo A, Celada F, Rodriguez S, et al. Non-melanoma skin cancer treated with HDR Valencia applicator: clinical outcomes J. Contemp Brachyther 2014; 6(2) 167-172.

ESTRO School

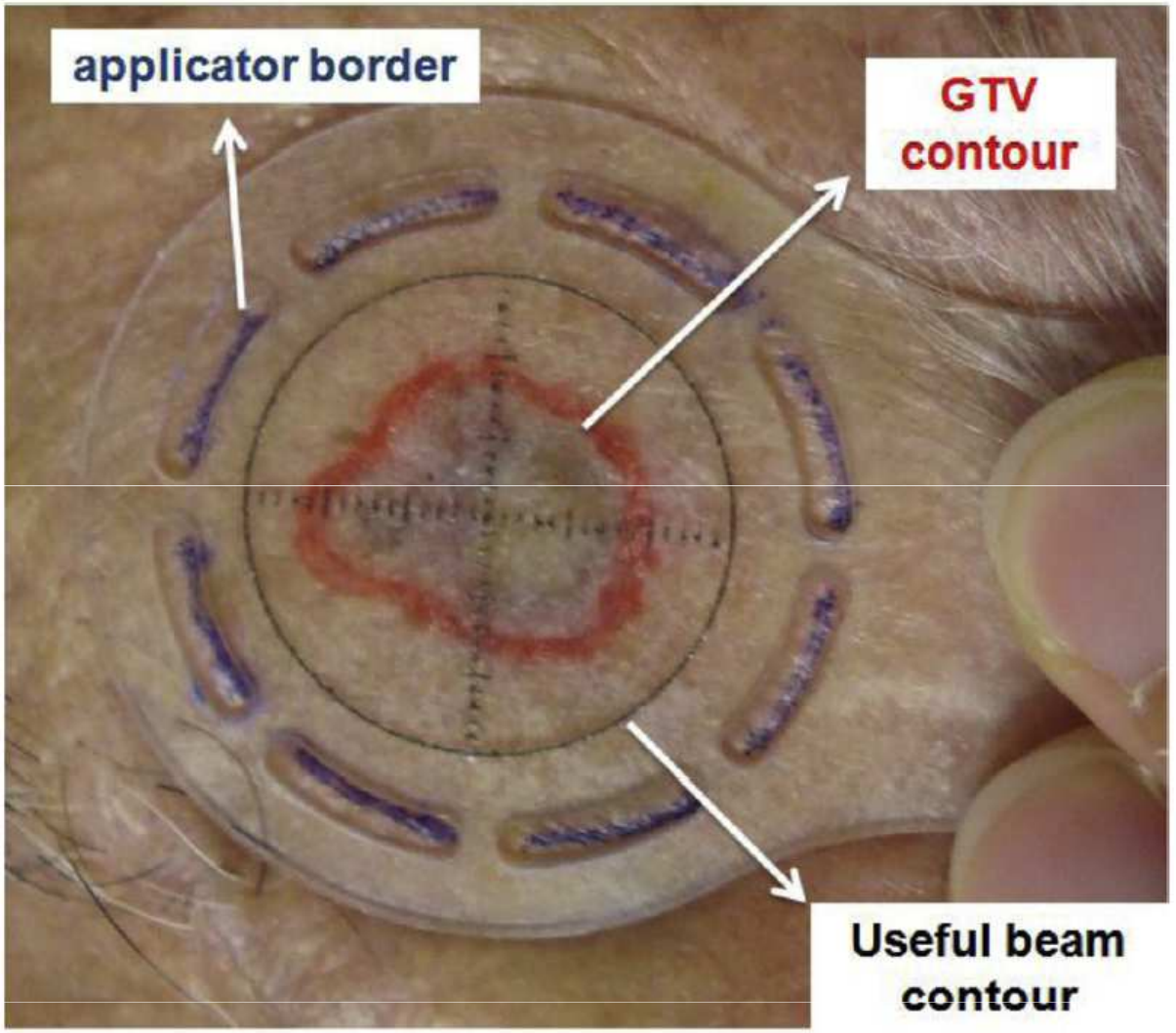


Fig. 11. Patient planning and simulation using La Fe template from Pons-Llanas *et al.* (94). The template includes graduated rulers. GTV = gross target volume.

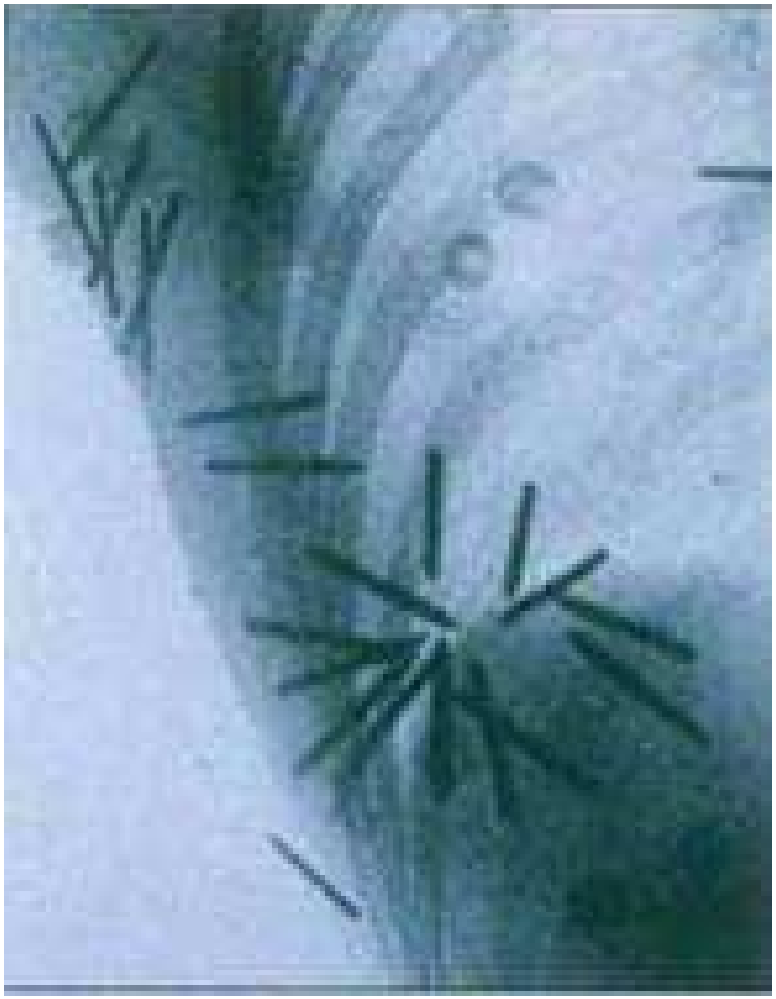
Courtesy of J. Pérez-Calatayud

Pons-Llanas O, Ballester-Sanchez R, Celada-Alvarez FJ, et al. Clinical implementation of a new electronic brachytherapy system for skin brachytherapy. J Contemp Brachytherapy 2014;6:417-423.

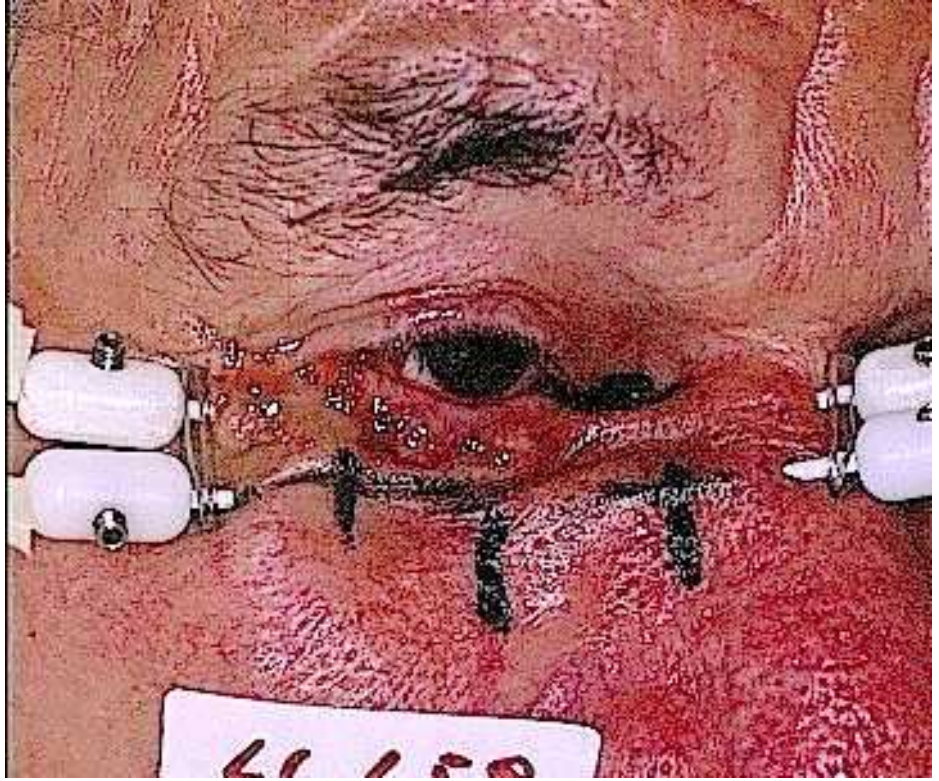
ESTRO School

INTERSTITIAL BRACHYTHERAPY IN SKIN CARCINOMAS

- Plastic tubes
- Rigid needles



ESTRO School



Ir-192 LDR plastic tubes. 60 Gy. Inner cantus. Eyelid

I.V.O.

Courtesy of Bengt Johannson. Orebro. Sweden

HDR interstitial or surface. SCC Ear.

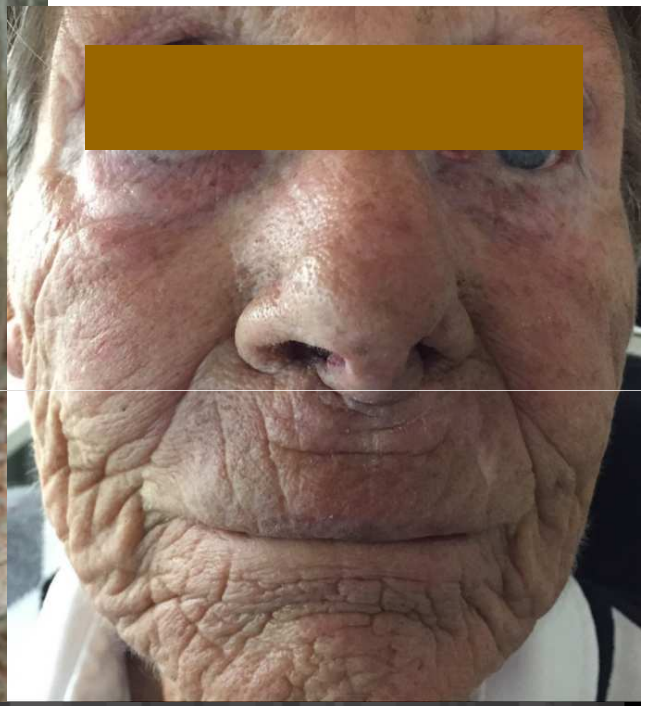
Courtesy of Silvia Rodriguez. Clinica Benidorm. Alicante. Spain

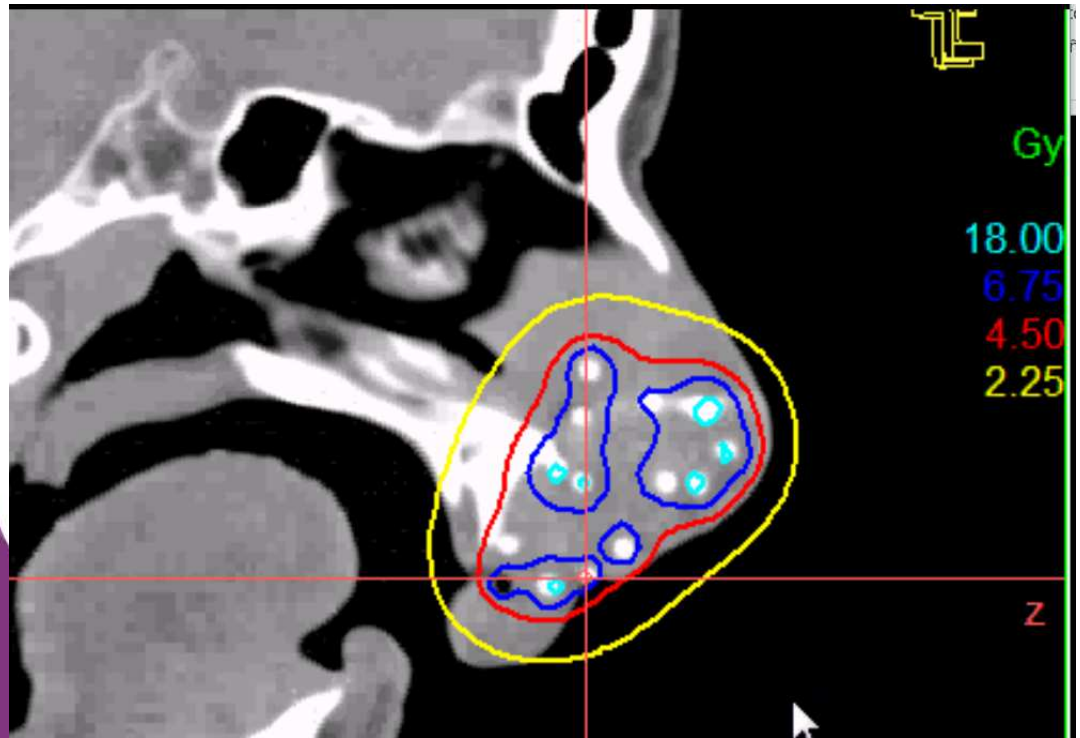
HDR plastic tubes

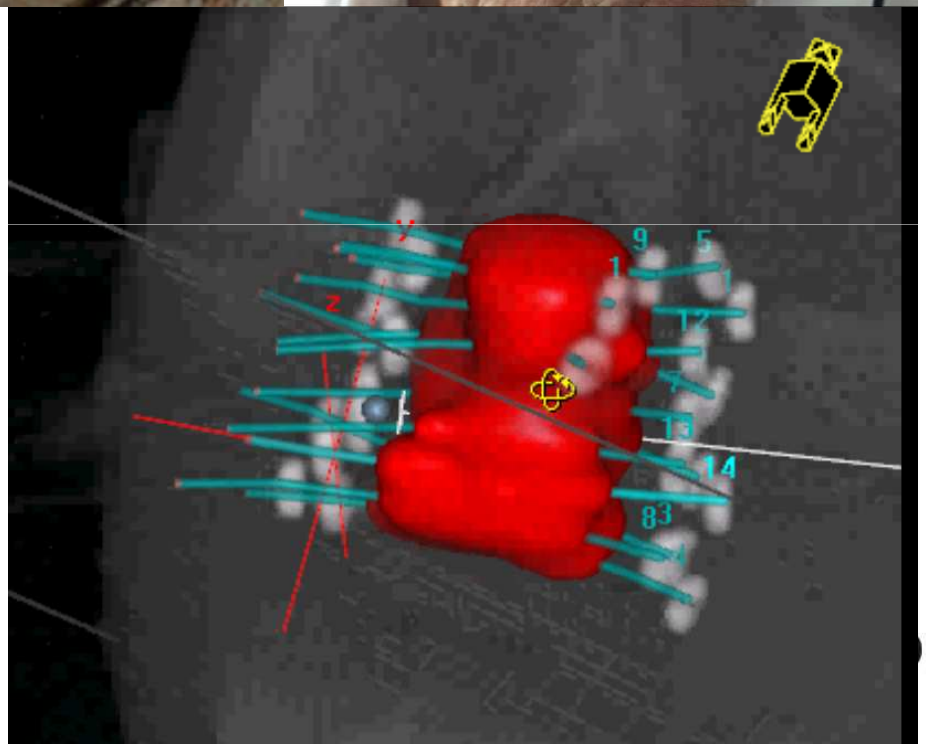
Twice a day

Cinica Benidorm

Courtesy of Gyoergy Kovacs. Lubeck







Adnexal skin carcinoma close margin

3 plastic tubes

HDR 4.5 Gy x 9 twice a day

x five days

Result at 32 months

I.V.0.

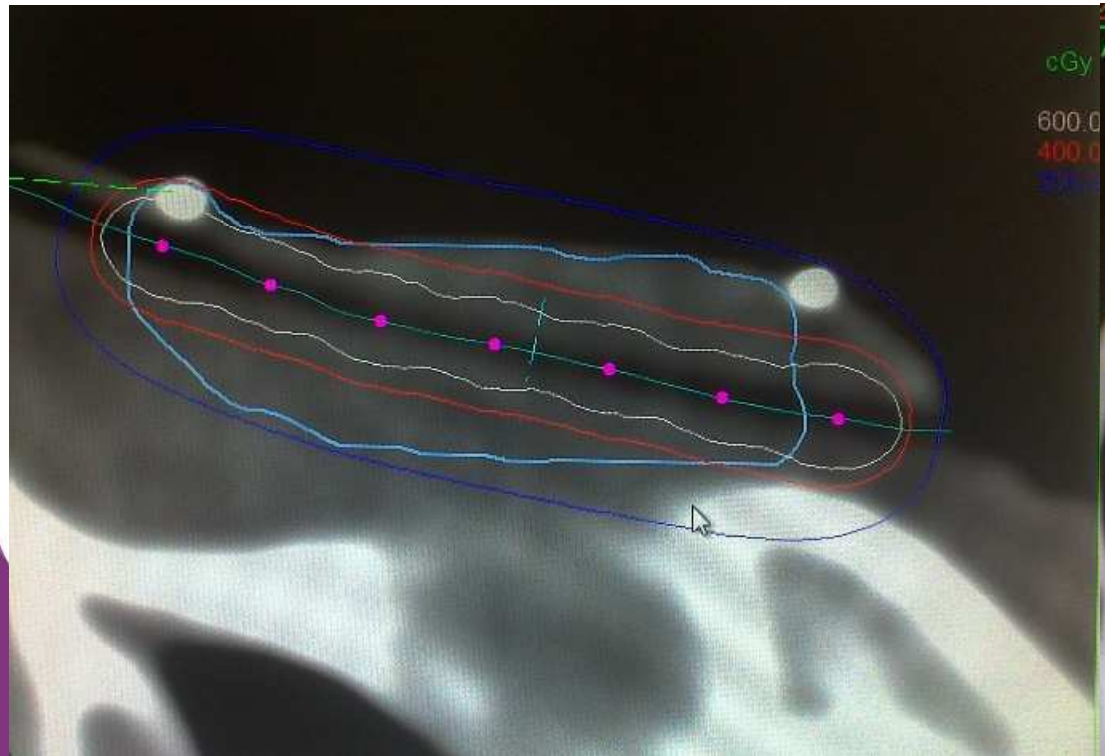
Eyelid close margin

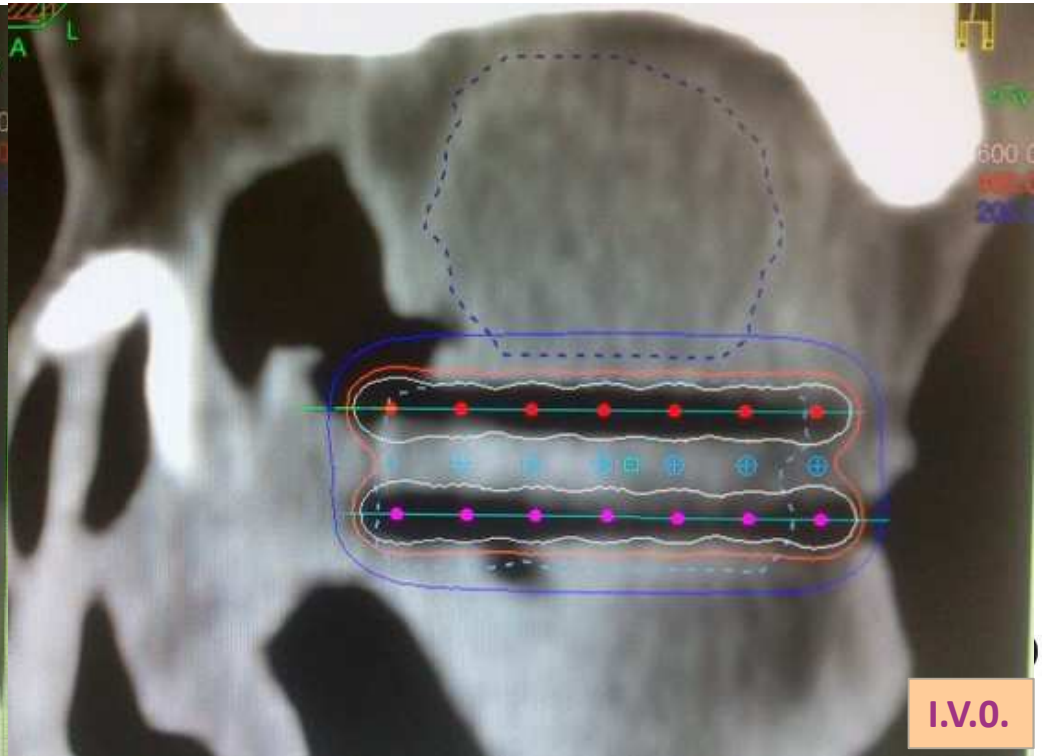
HDR

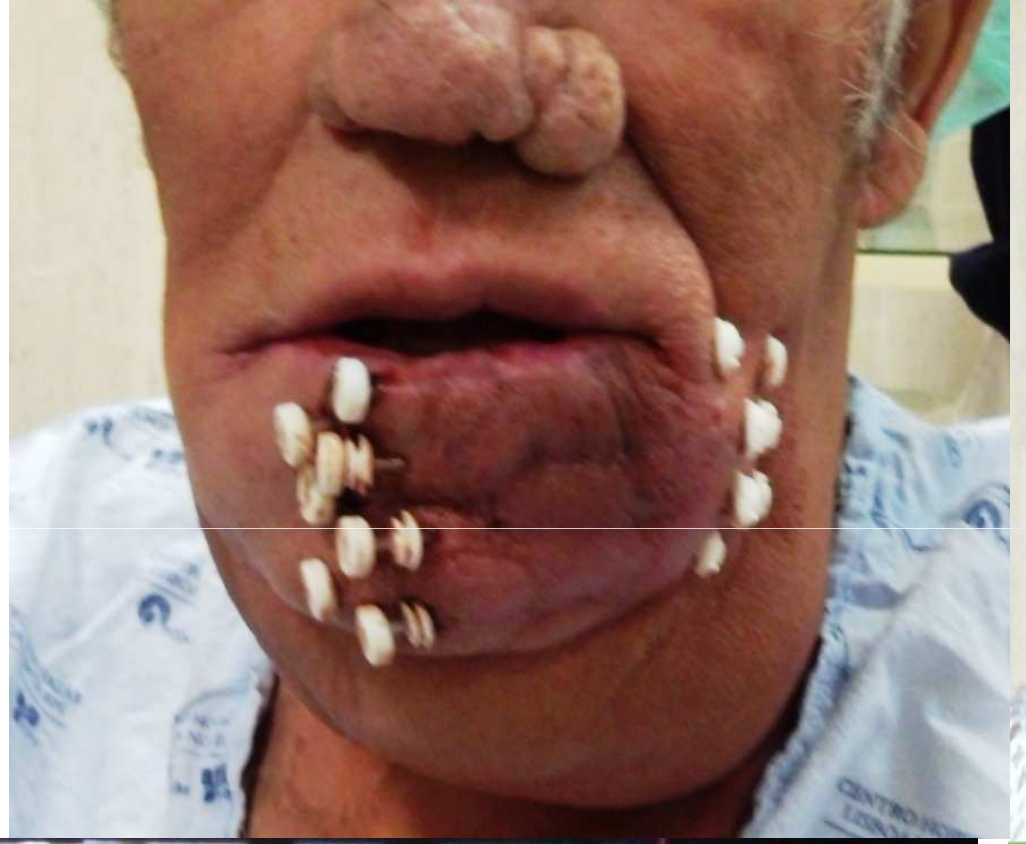
9-10 frac.

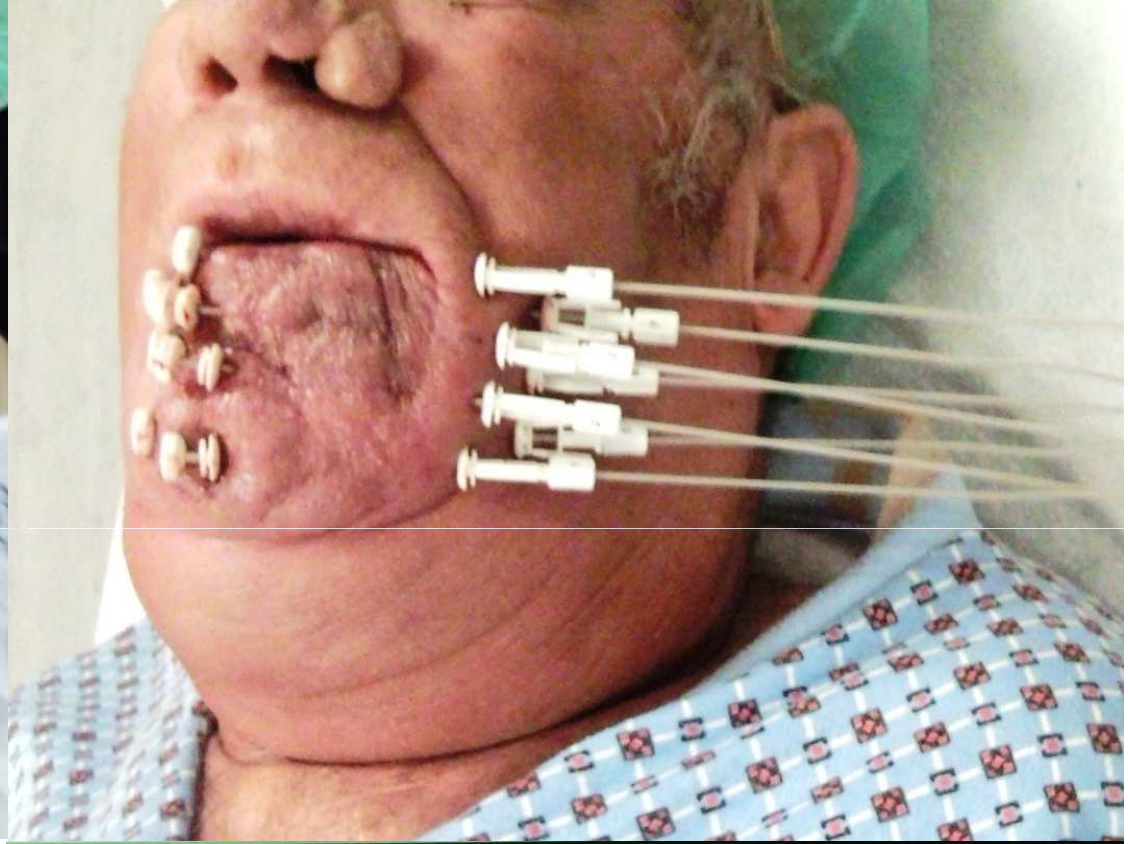
4Gy B.I.D.

5 days









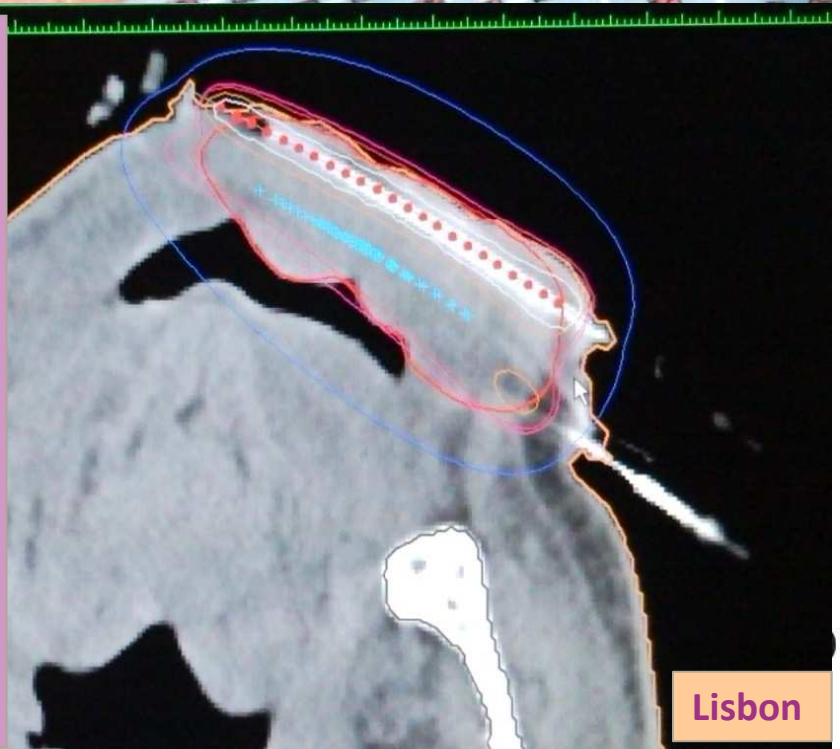
SCC lip, skin involvement

HDR plastic tubes

EBRT 50 Gy + 5 x 4Gy

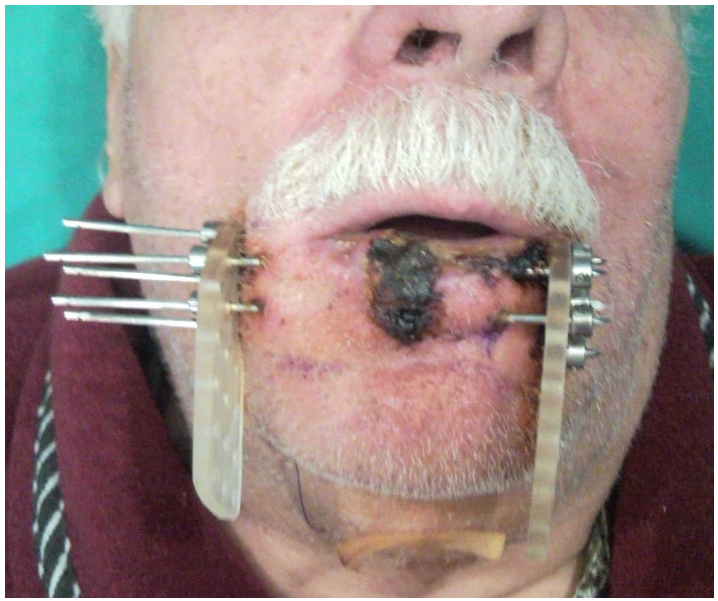
B.I.D.

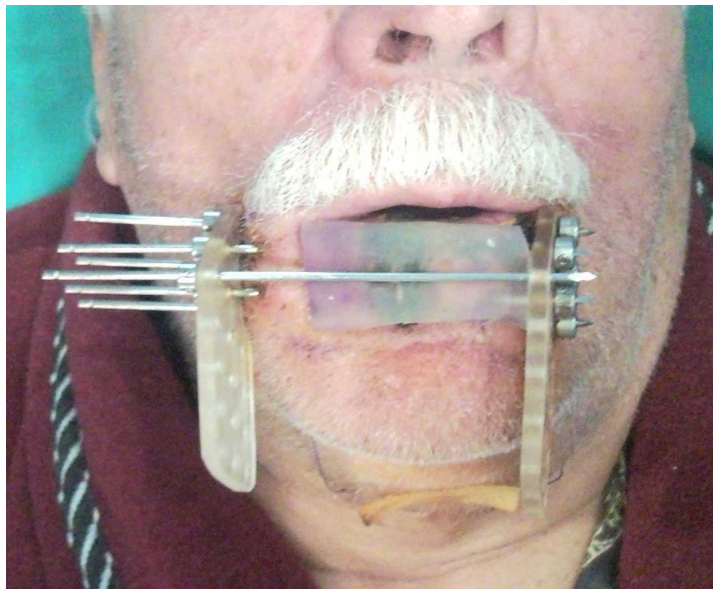
3 days

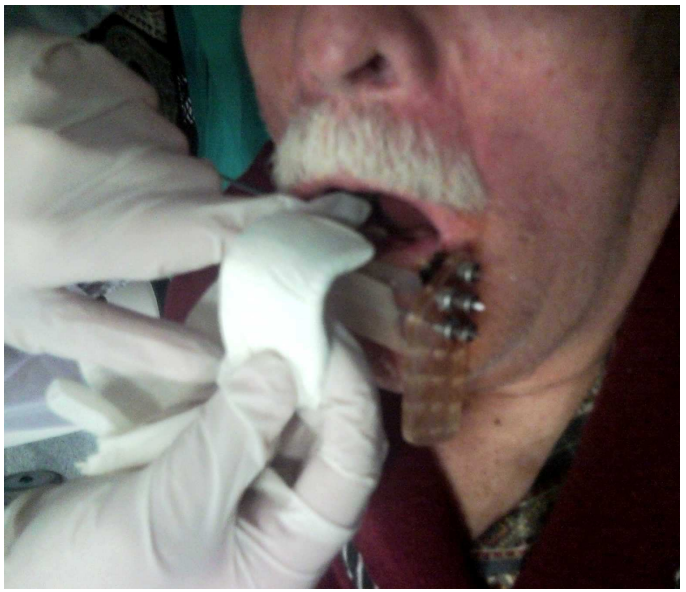


HDR BRACHYTHERAPY OF LIP CARCINOMAS WITH RIGID NEEDLES IN FIVE DAYS (I.V.O.)

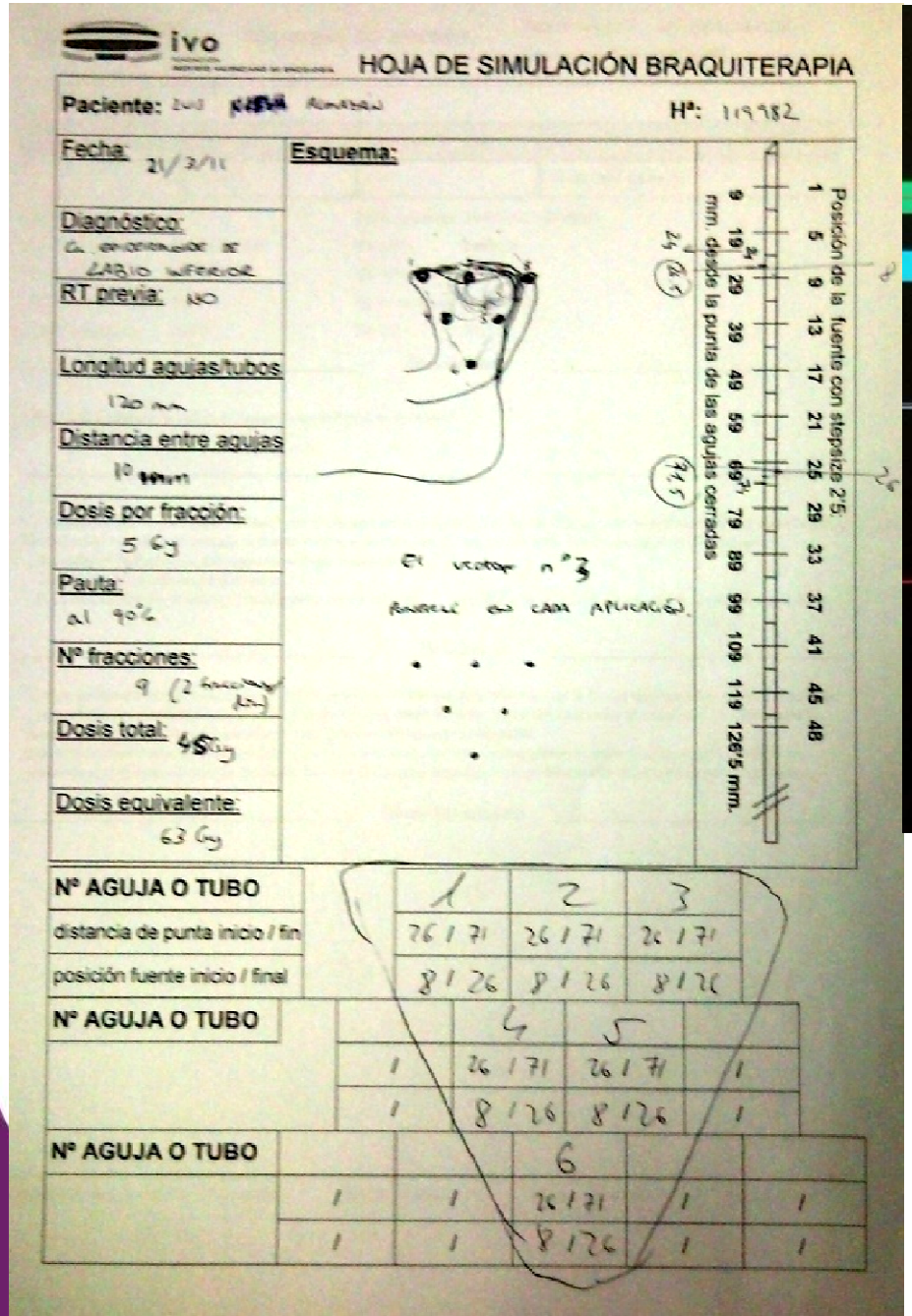
Guinot JL, Arribas L, Tortajada MI, et al. From low dose rate to high dose rate brachytherapy in lip carcinoma: equivalent results with fewer complications Brachytherapy. 2013;12(6):528-34.







HDR BRACHYTHERAPY OF LIP CARCINOMAS WITH RIGID NEEDLES IN FIVE DAYS


ivo

HOJA DE SIMULACIÓN BRAQUITERAPIA

Paciente: [illegible] Hª: 119982

Fecha: 21/3/11

Esquema:

Posición de la fuente con stepsize 2'5:
1 5 9 13 17 21 25 29 33 37 41 45 48
9 19 29 39 49 59 69 79 89 99 109 119 126'5 mm.
mm. desde la punta de las agujas cerradas

Diagnóstico: [illegible]

RT previa: NO

Longitud agujas/tubos: 130 mm

Distancia entre agujas: 10 mm

Dosis por fracción: 5 Gy

Pauta: al 90%

Nº fracciones: 9 (2 [illegible])

Dosis total: 45 Gy

Dosis equivalente: 63 Gy

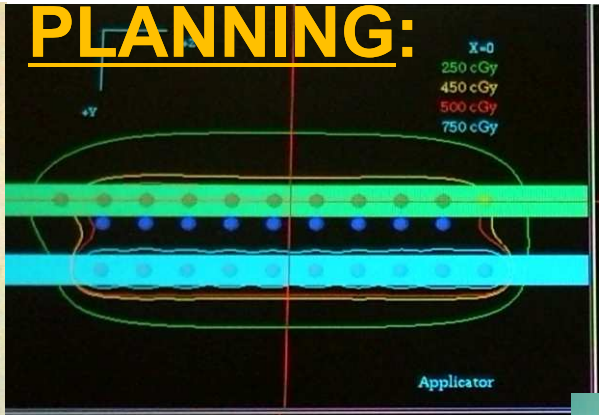
El vector nº 3 [illegible] en cada aplicación.

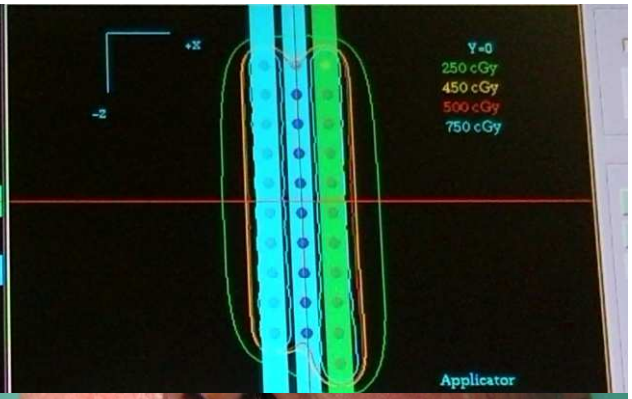
Nº AGUJA O TUBO	1	2	3
distancia de punta inicio / fin	26 / 71	26 / 71	26 / 71
posición fuente inicio / final	8 / 26	8 / 26	8 / 26

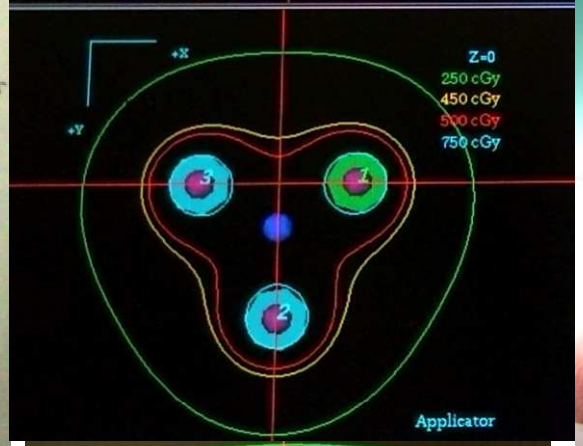
Nº AGUJA O TUBO	4	5	
1	26 / 71	26 / 71	1
1	8 / 26	8 / 26	1

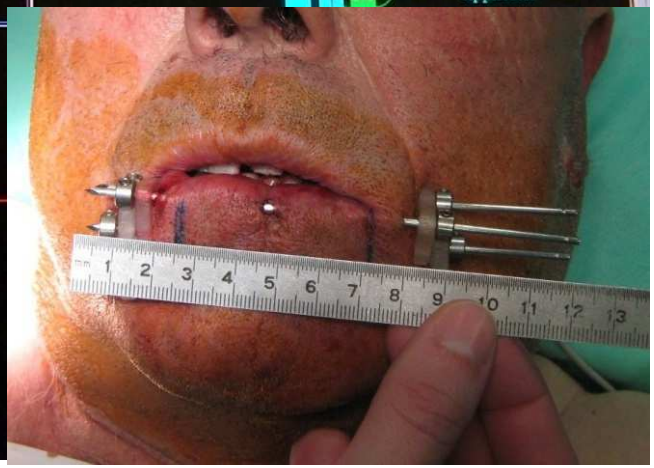
Nº AGUJA O TUBO	6		
1	1	26 / 71	1 1
1	1	8 / 26	1 1

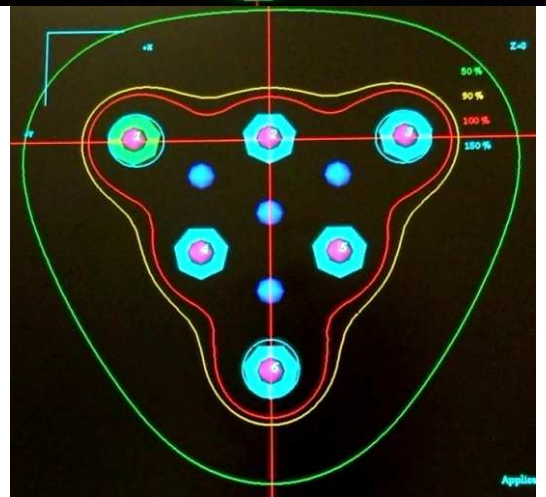
PLANNING:







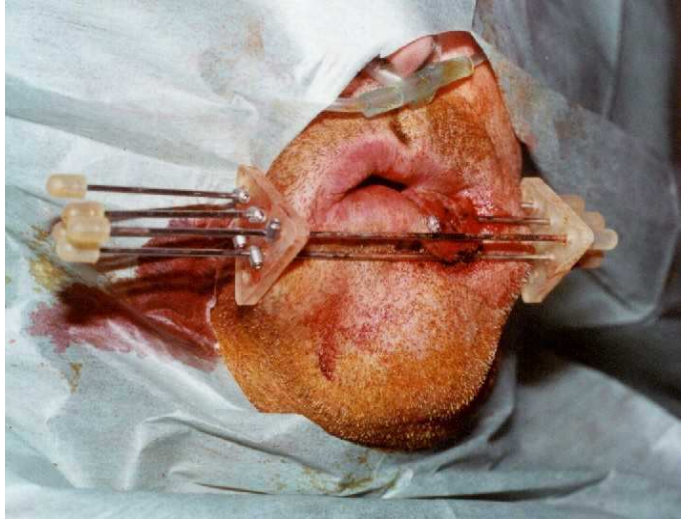


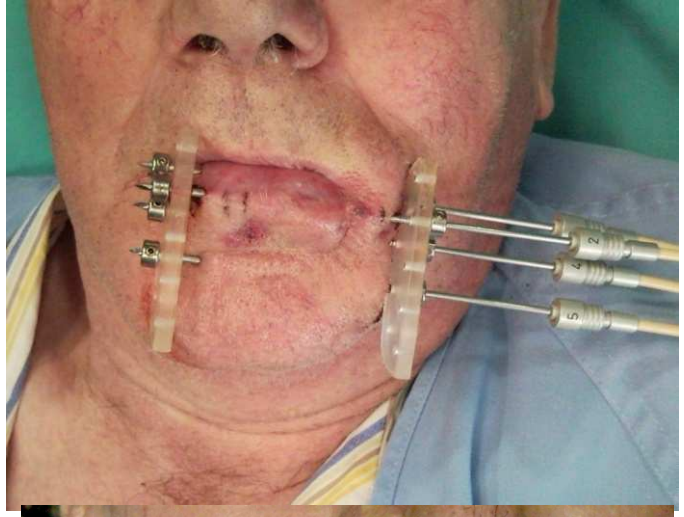


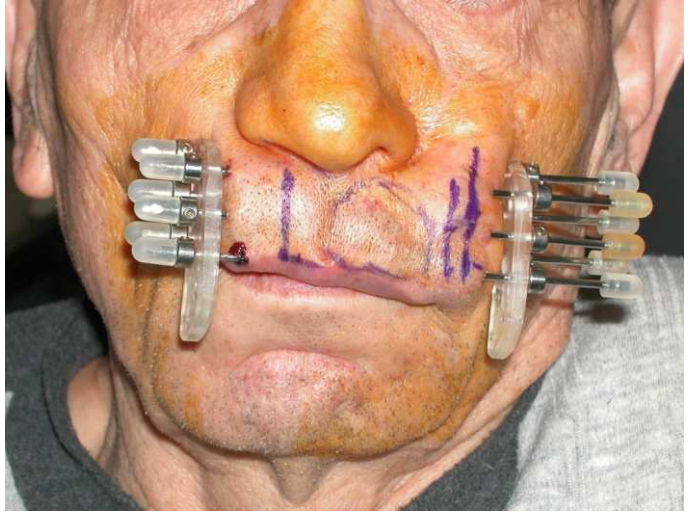
DOSIMETRY:

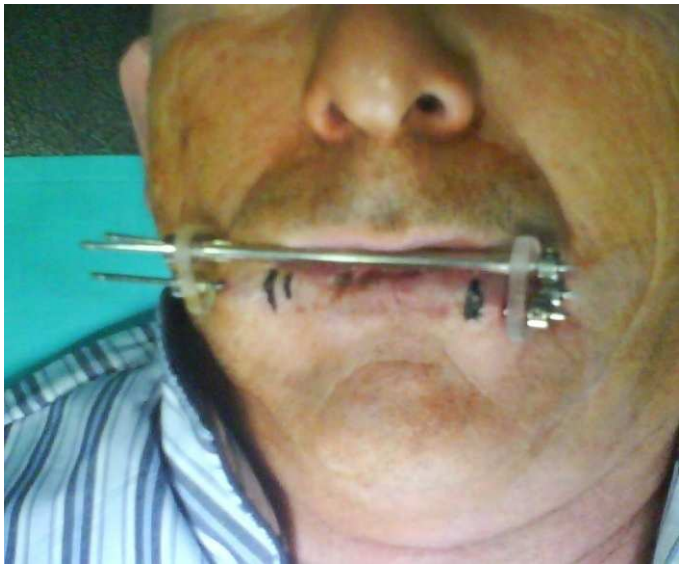
High homogeneity
4,5 Gy x 9 = 40.5 Gy
5 Gy x 9 = 45 Gy
B.I.D. 5 days

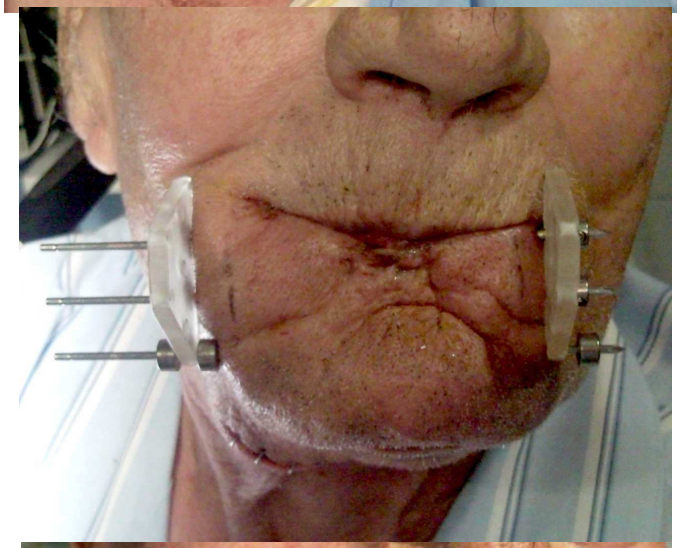
I.V.O.

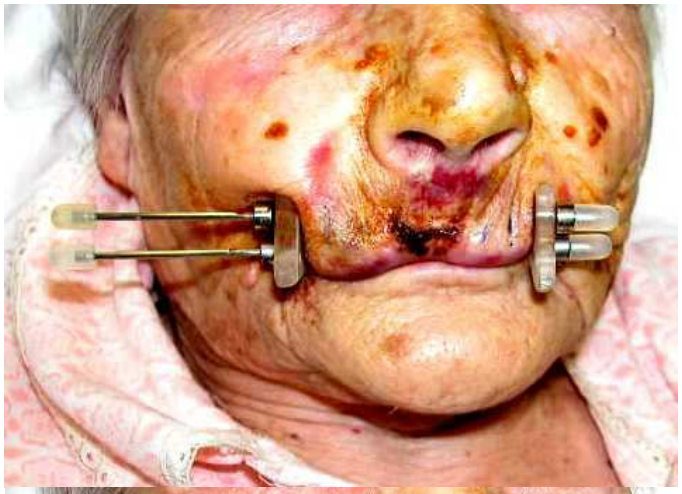


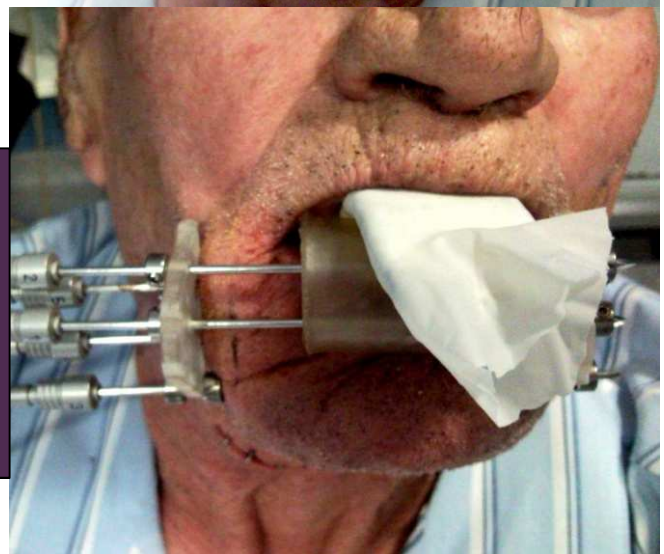


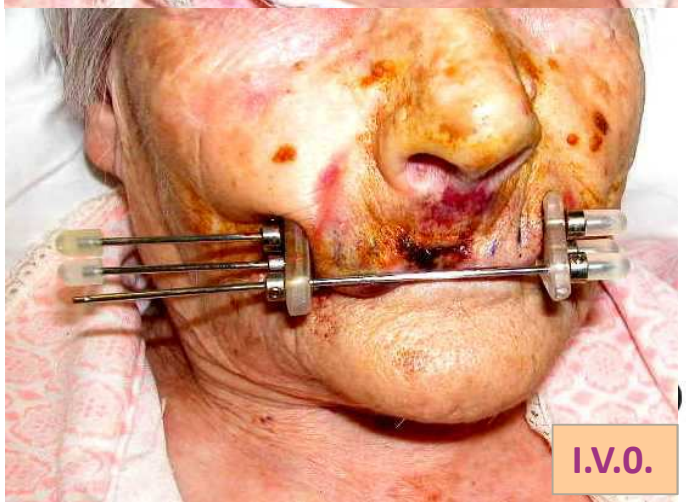






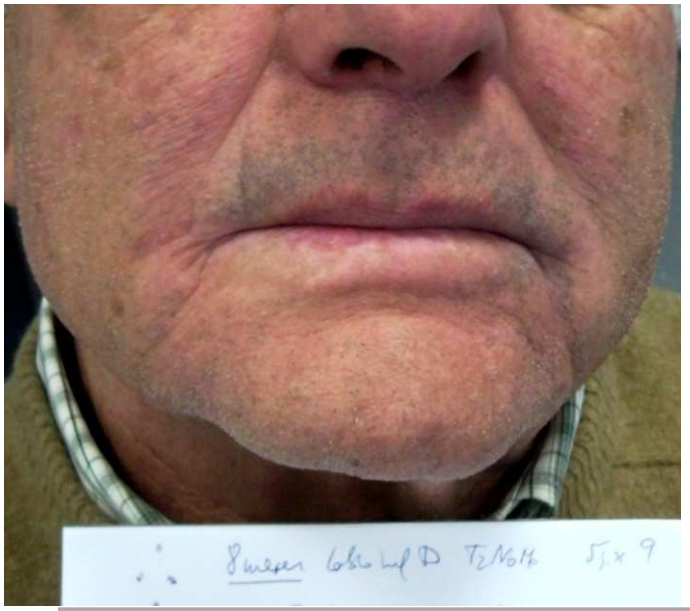
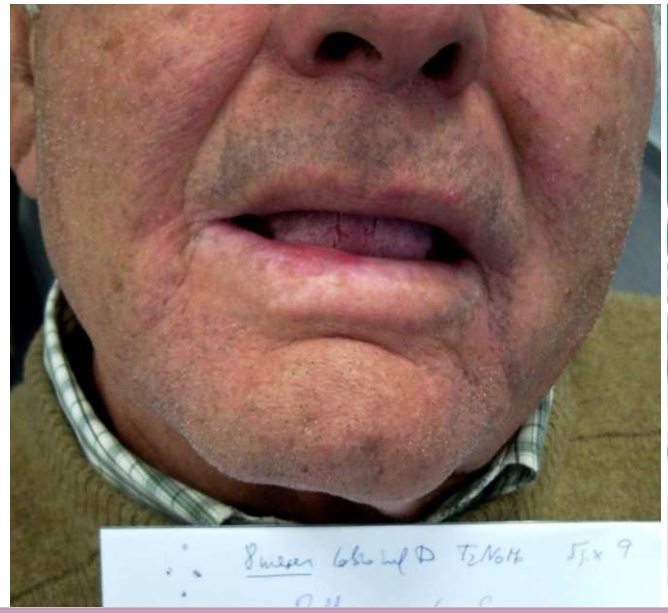
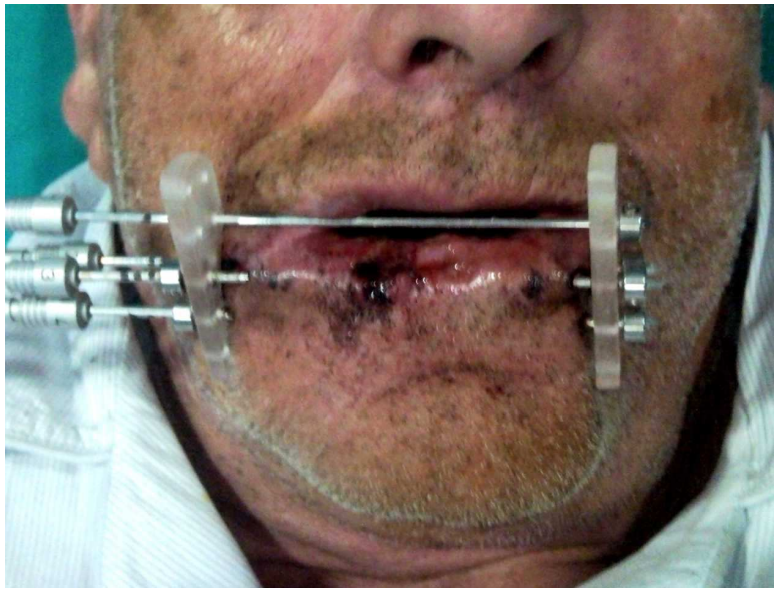




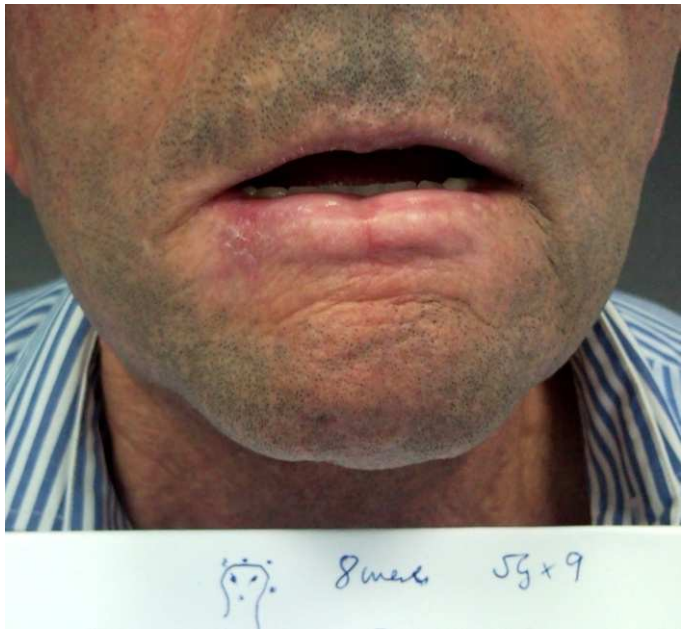


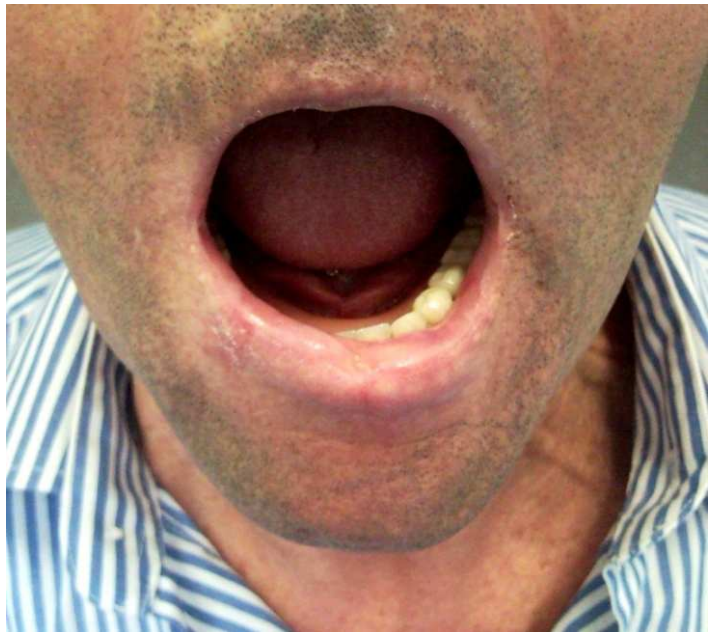
Local control with HDR
T1-T4: 94.8%
T1: 100%
T2: 97%

I.V.0.

T2N0 SCC. HDR 5Gy x9. Four needles in diamond shape. Results at nine months





T2N0 SCC plus sentinel node. 60 years old HDR 5Gy x9. Four needles in diamond shape. Results at eight months

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I.V.O.

T2N0 SCC. HDR 5Gy x9. 96 years old. Functional results at nine months

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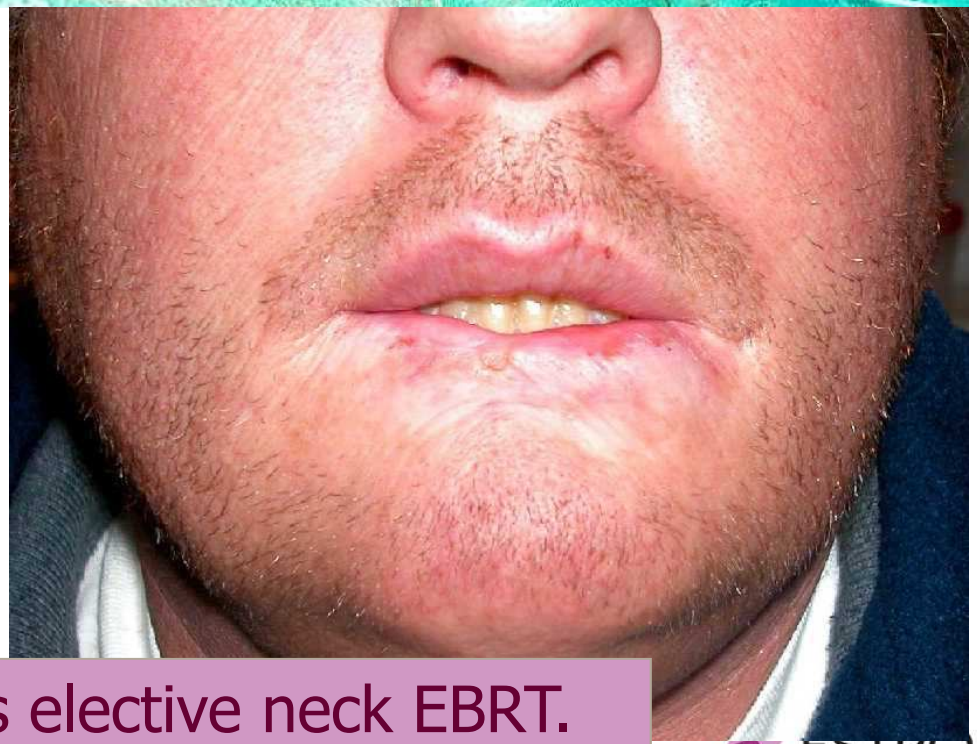
I.V.O.



T4N0 SCC. 36 y.o. HDR 5.3 Gy x9 plus elective neck EBRT.
Eight needles. Results at 24 months

Target volume

The clinical target volume for well-delineated squamous cell or basal cell carcinomas is the palpable or visible tumour with a safety margin

- 3-5 mm for skin cancers
- 5 mm for lip cancers
- 7-10 mm for bad-defined lesions (such as morphea-like basal cell carcinomas)

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Dosimetry

- In **interstitial implants**, CT scan slices with dummy sources and radio-opaque markers in the edges of the CTV .
- optimized dosimetry adjusting isodose curves to the CTV
- Avoid hot spots (Keep the Dose-nonuniformity-ratio DNR <0.35)
- With parallel tubes or needles the modified Paris System (SSDS van der Laarse) is used and the prescription is to 90% isodose.

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Dosimetry

- In contact brachytherapy (**plesiotherapy)**, the prescription is at distance, 3-4 mm (5mm ABS) under the skin surface. If we need to treat a deeper tumor, an interstitial procedure is advisable
- A PTV must be added due to small changes in positioning every day.
- The skin surface is receiving more than the prescribed dose (120-140%).
- Leipzig and Valencia applicators have a gradient of 10%/mm and Esteya 7%/mm .

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Dose and fractionation

- With HDR BT, **interstitial implants**,
- twice a day 6 hours apart, 3-5 Gy, to finish the treatment in a similar time to the LDR techniques, in 4-5 days.
- **Plesiotherapy:**
- In small tumors, 5-10 Gy per fraction 2-3 days per week.
- In large areas (scalp), 2-3 Gy per day is preferable.
- intermediate 3-5 Gy per fraction x three days per week
- Total dose:
  - 51-54 Gy (3Gy x 17-18 fractions),
  - 44-48 Gy (4 Gy x 11-12 fractions),
  - 40-42 Gy (5Gy x 8, 6Gy x 7, 7Gy x 6),
  - 35 Gy (7 Gy x 5 fractions).

Maroñas M, Guinot JL, et al. Treatment of facial cutaneous carcinoma with high-dose rate contact brachytherapy with customized molds. Brachytherapy 2011;10(3):221-7.

Montero A, et al. HDR plesiotherapy with custom-made moulds for the treatment of non-melanoma skin cancer. Clin Transl Oncol 2009; 11:760-4

Alam M, et al. The use of brachytherapy in the treatment of nonmelanoma skin cancer: a review. J Am Acad Dermatol. 2011; 65(2):377-88.

Advantages of HDR BT - I

- Radioprotection is complete; isolation is not required
- The moulds and surface applicators are easy to place and patients do not report discomfort and the treatment is administered on an outpatient basis, unlike interstitial implant patients.
- The dose distribution on the skin surface with contact HDR-BT shows a sharp gradient, similar to the conventional low-energy X-ray, in contrast to the electron dose distribution. This gradient allows a higher dose to the first mm and lower dosis to the deeper tissues.

Alam M, et al. The use of brachytherapy in the treatment of nonmelanoma skin cancer: a review. J Am Acad Dermatol. 2011; 65(2):377-88.

Sabbas AM, et al. HDR Brachytherapy with surface applicators: Technical considerations and dosimetry. Technol Cancer Res Treat 2004;3:259-267

Advantages of HDR BT - II

- The multicatheter applicator on moulds allows to conform the isodose to irregular surfaces, not possible with orthovoltage photons or electrons .
- Full-scalp irradiation results in lower risk of excessive brain irradiation compared with external beam irradiation
- The optimization techniques result in superior dose uniformity at the prescription depth with HDR surface applicators
- The occupation time of the accelerators can be decreased.

Alam M, et al. The use of brachytherapy in the treatment of nonmelanoma skin cancer: a review. J Am Acad Dermatol. 2011; 65(2):377-88.

Sabbas AM, et al. HDR Brachytherapy with surface applicators: Technical considerations and dosimetry. Technol Cancer Res Treat 2004;3:259-267

Radiation therapies are underused

- Currently primary radiotherapy is being underutilized; less than 2% of skin cancer patients in the USA and 1-8% in Europe

- When multidisciplinary teams include radiation oncologists in addition to dermatologists in the treatment of non-melanoma skin cancer (NMSC) patients, radiotherapy is recommended in approximately 20% of cases

Bath-Hextall FJ1, Perkins W, Bong J, Williams HC. Interventions for basal cell carcinoma of the skin. Cochrane Database Syst Rev. 2007; Jan24:(1):CD003412.

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CONCLUSIONS

- HDR Brachytherapy is safe and effective in skin tumors
- It is very useful to preserve the organ and the function
- Acute reactions are well tolerated
- Late effects are hypopigmentation and atrophy
- BT is an alternative to surgery and should be offered and considered in skin tumors committees.

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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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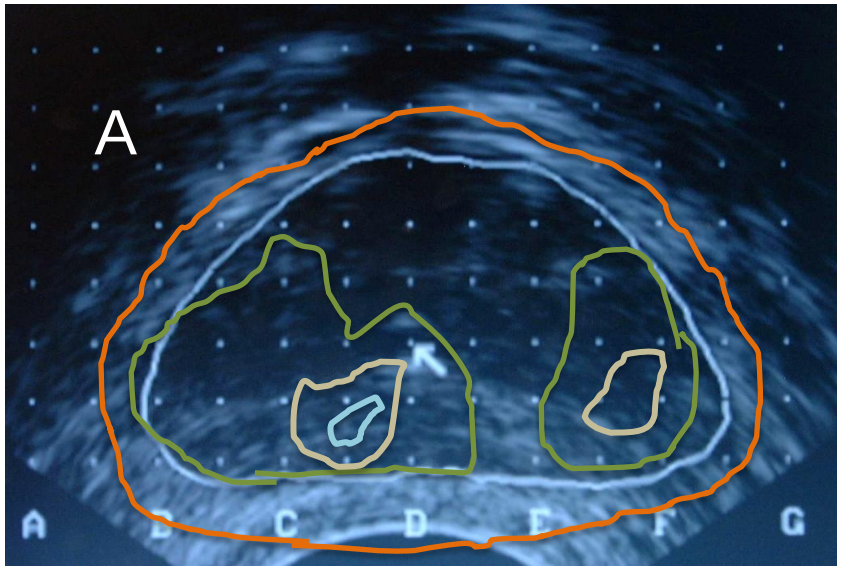
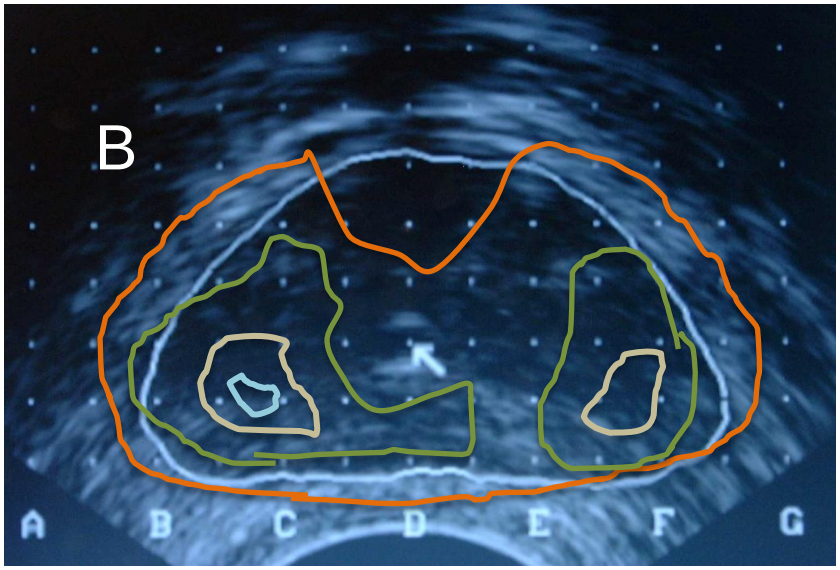
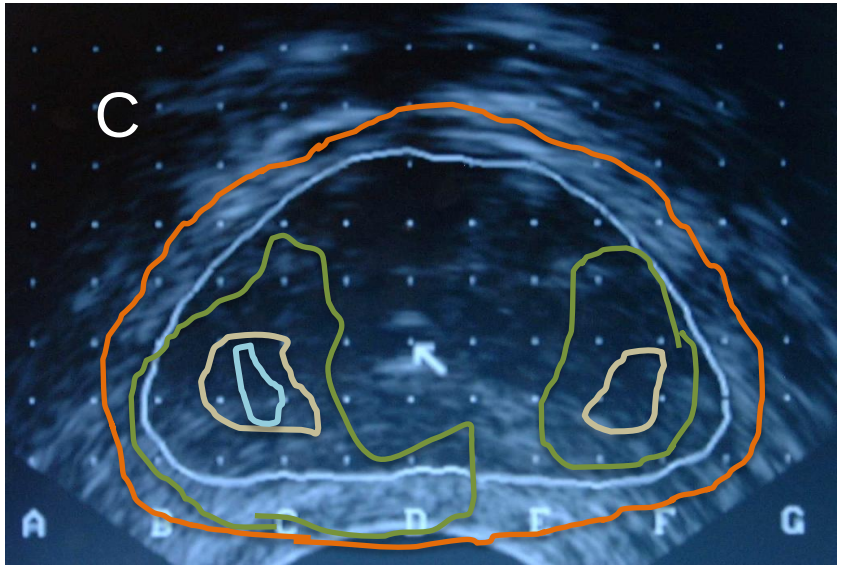
TECHNIQUES

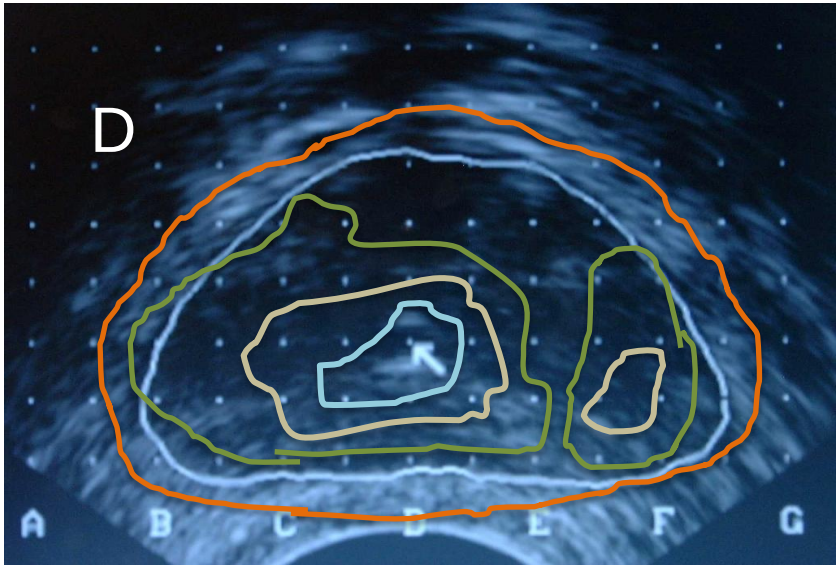
Which Isodose distribution would you prefer?





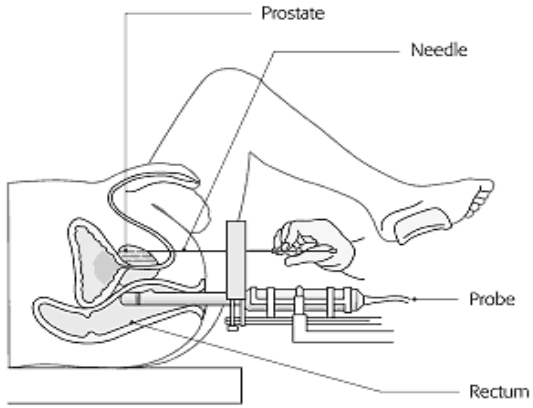
100 %
140%
150%
170%

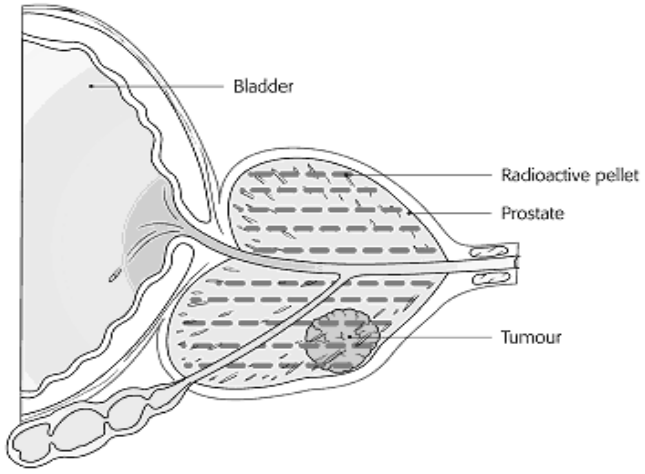




Perineal prostate implantation

- Perineal technique
- Ultrasound guided
- Ultrasound probe on immobilizer
- Template





Holm, J Urol 1983

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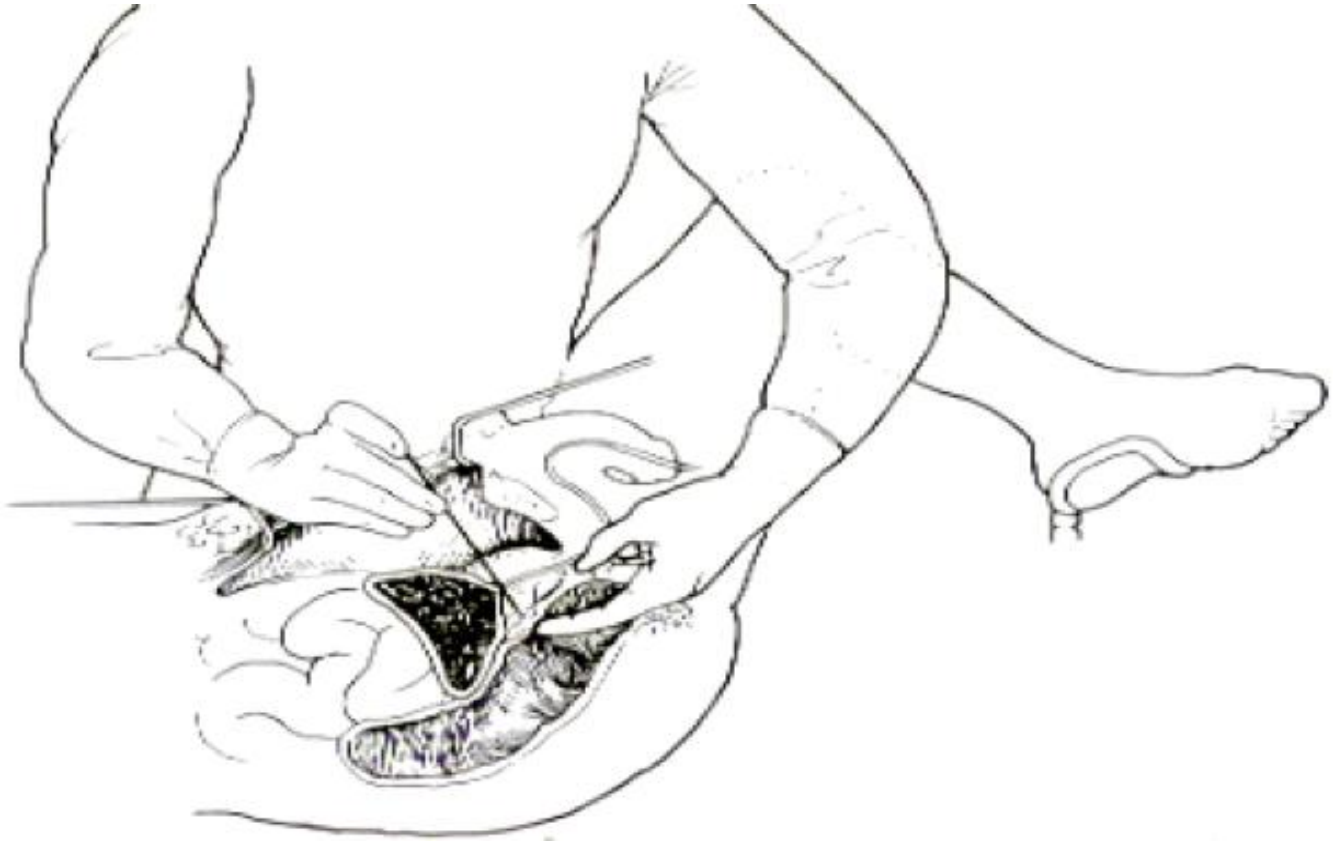
Retropubic Prostate Implant Technique



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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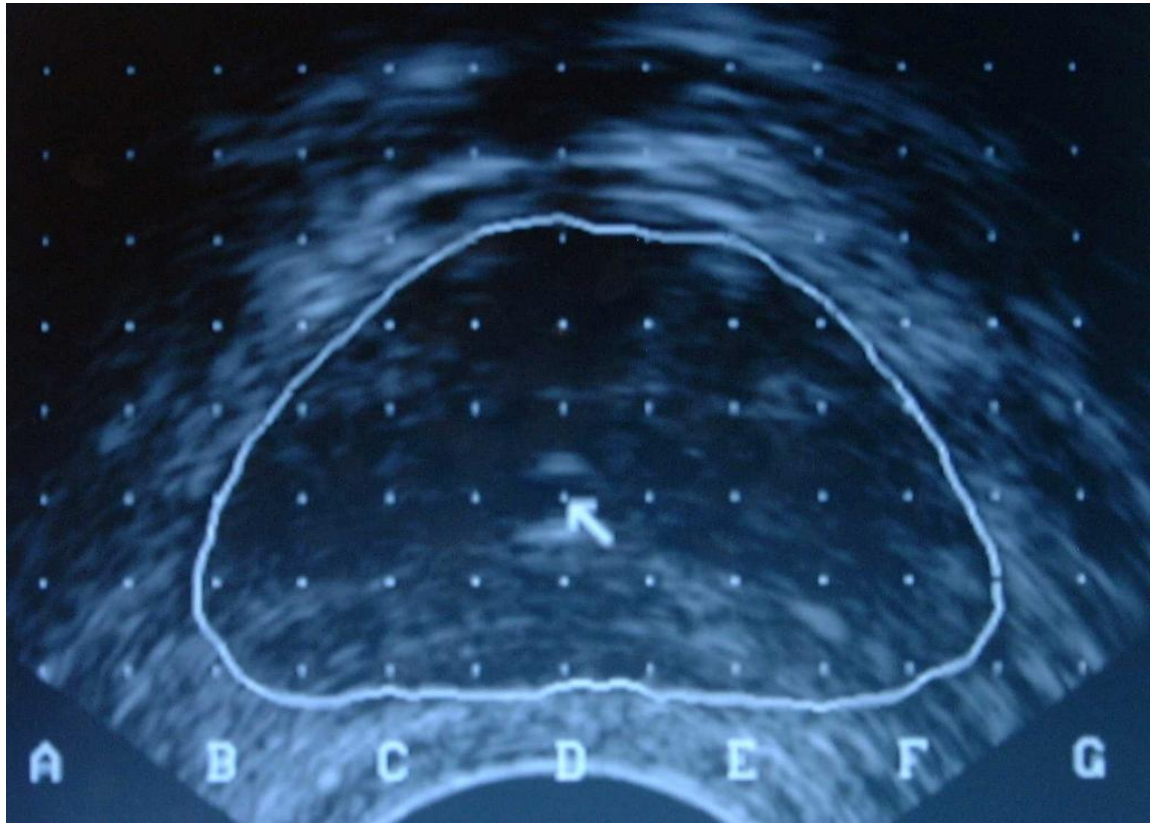
Procedure Seed Implantation

Volume study

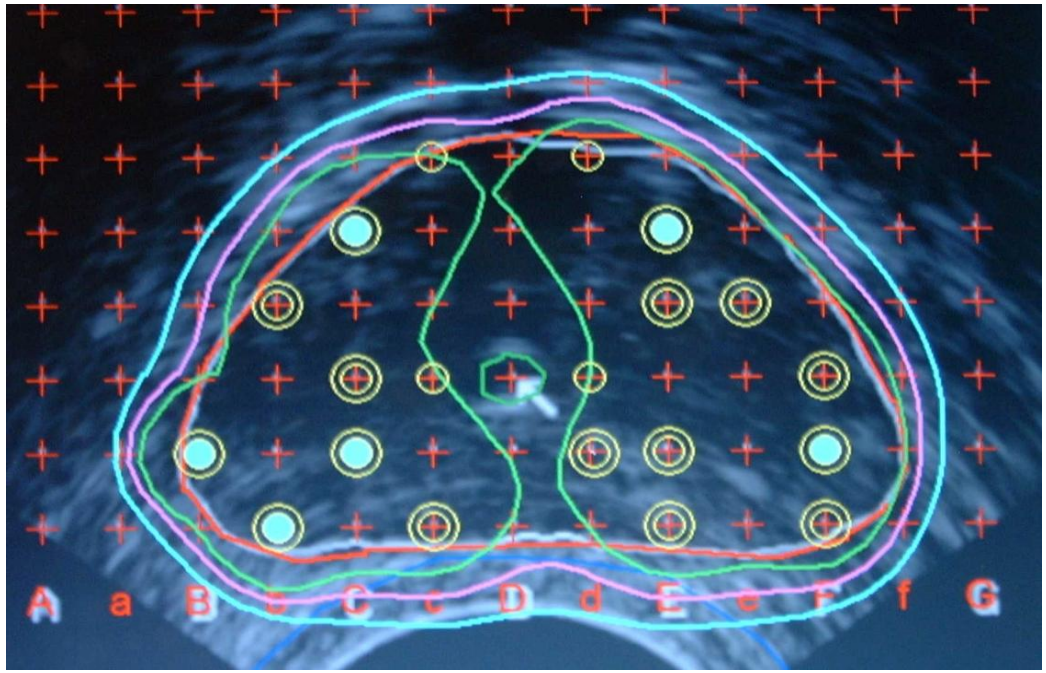
# of seeds



Preplan

Full coverage of prostate
- V100
- D90

Relative sparing of urethra and rectum



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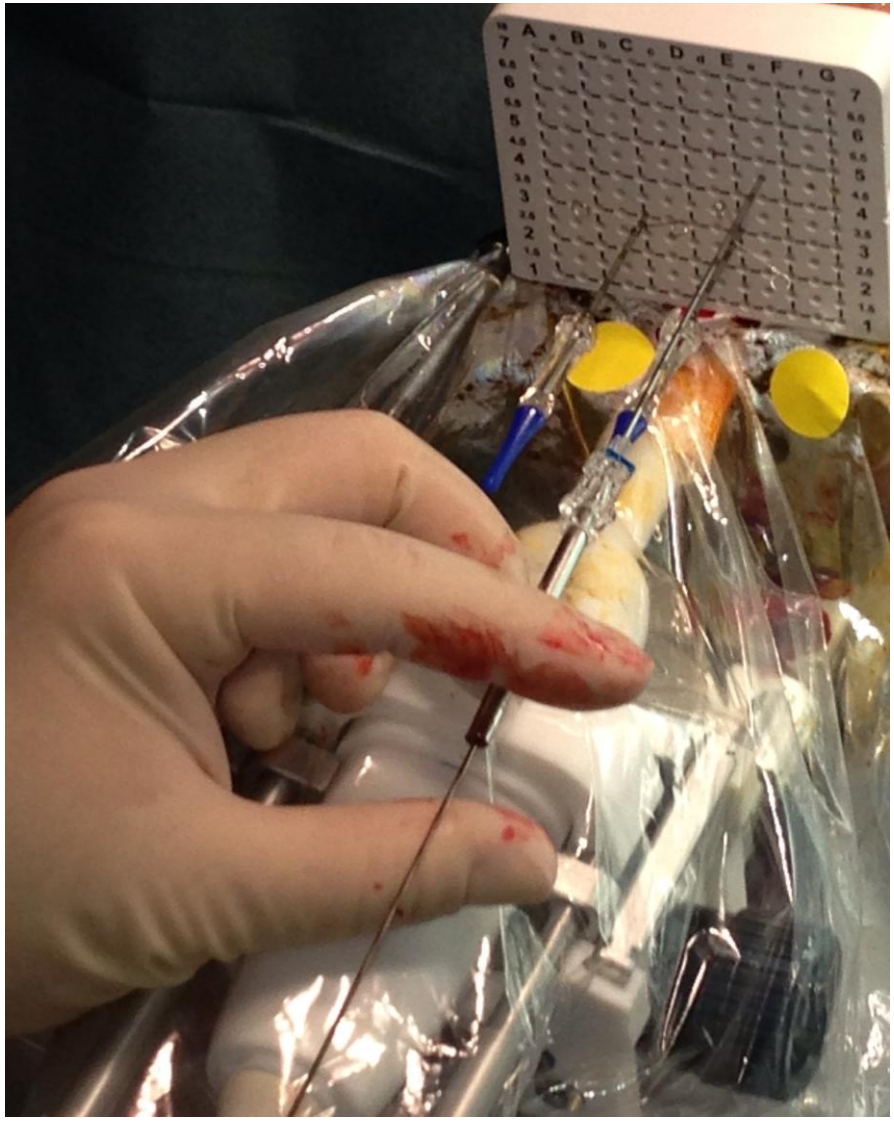

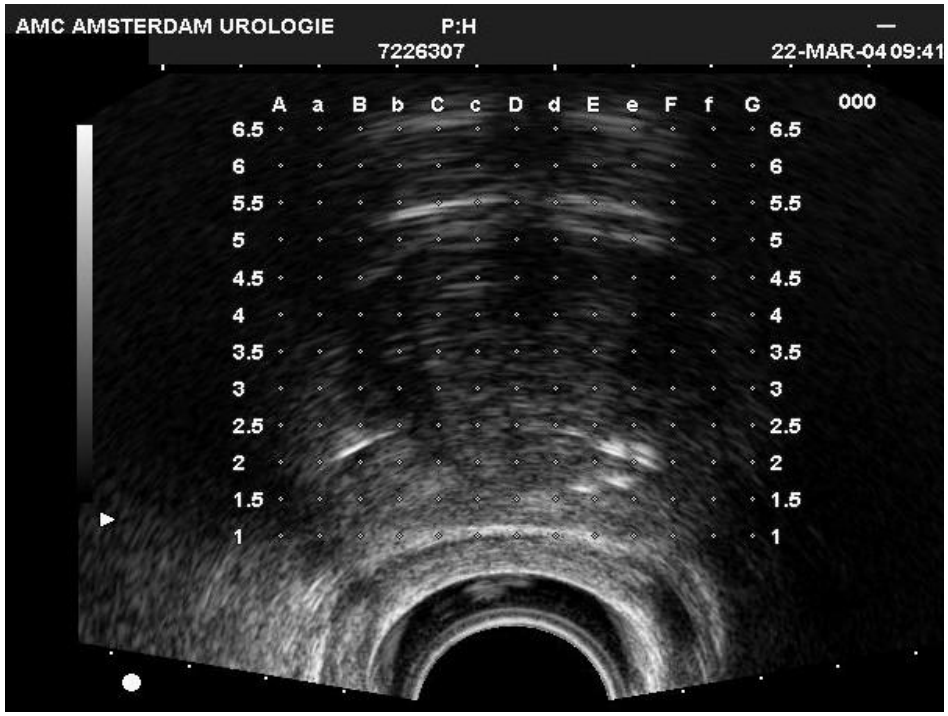

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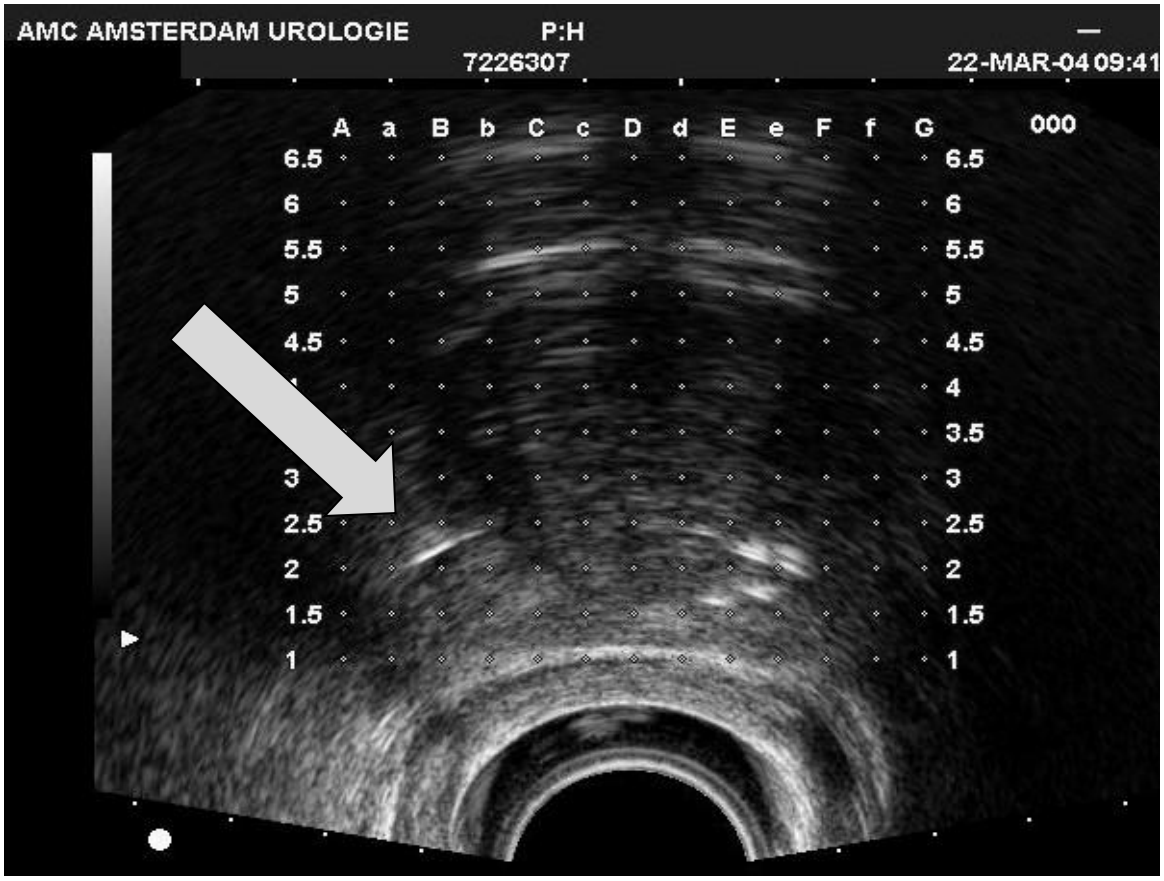
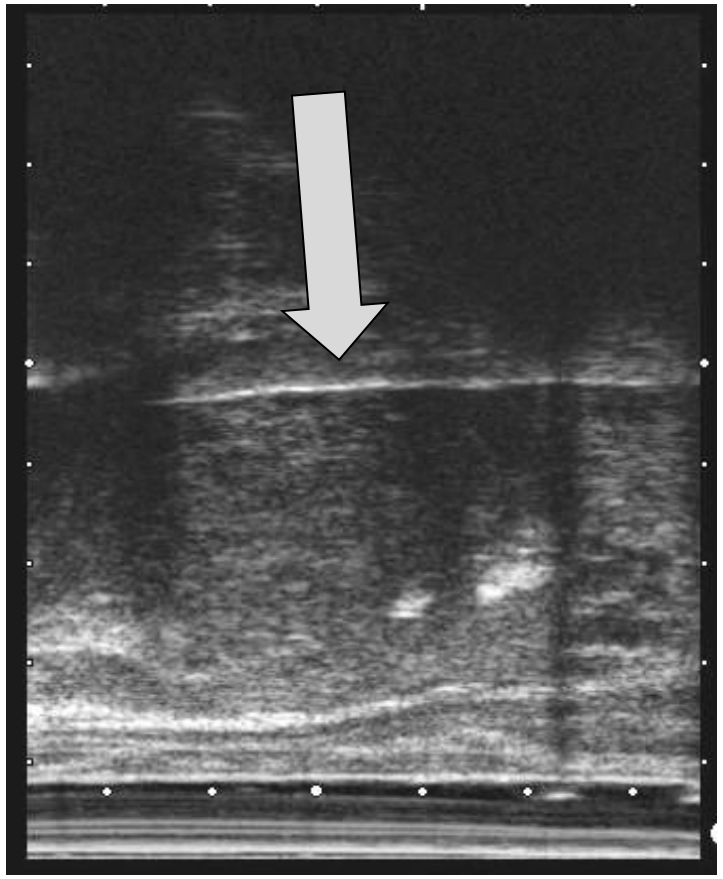
Implantation on Ultrasound

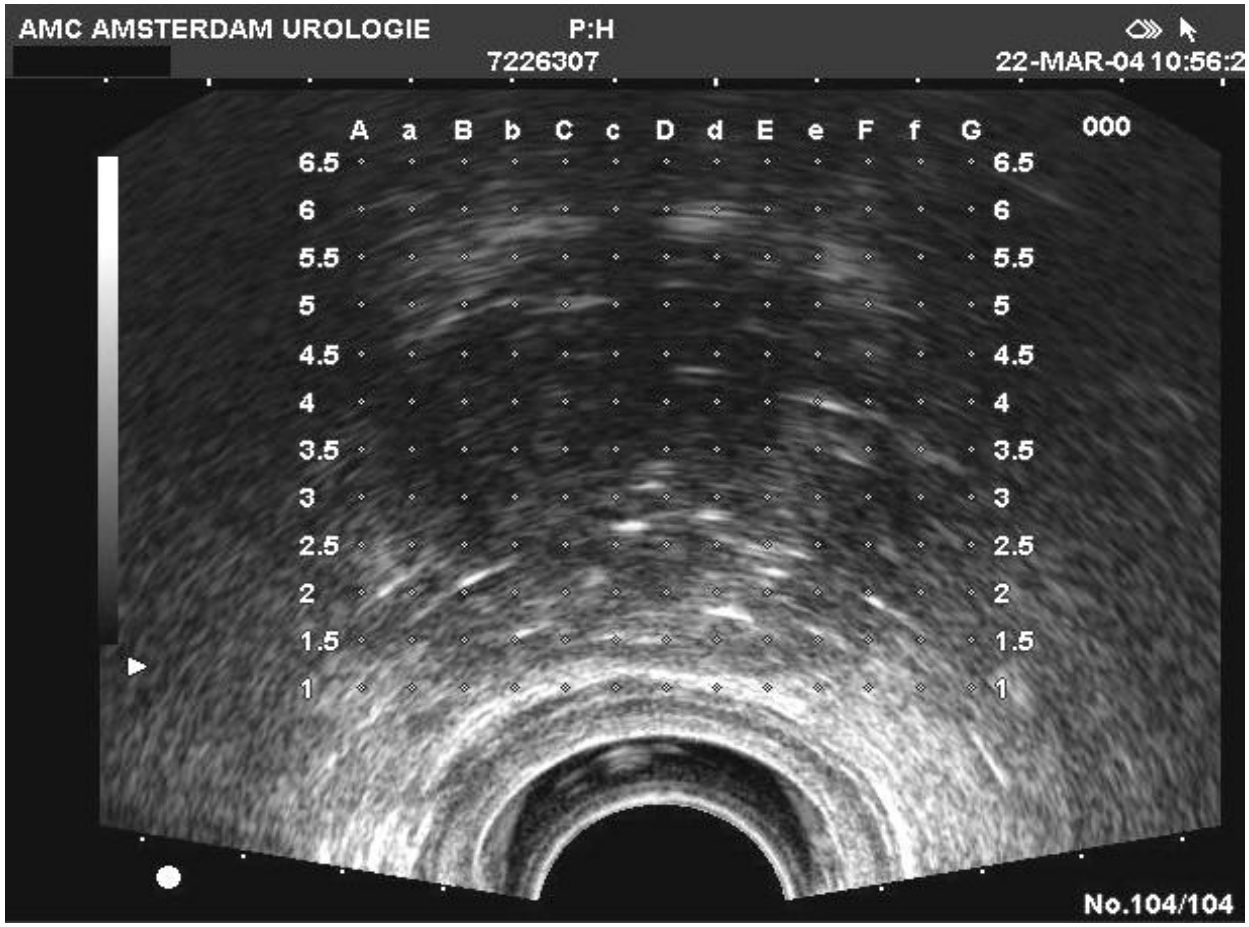


Transversal view

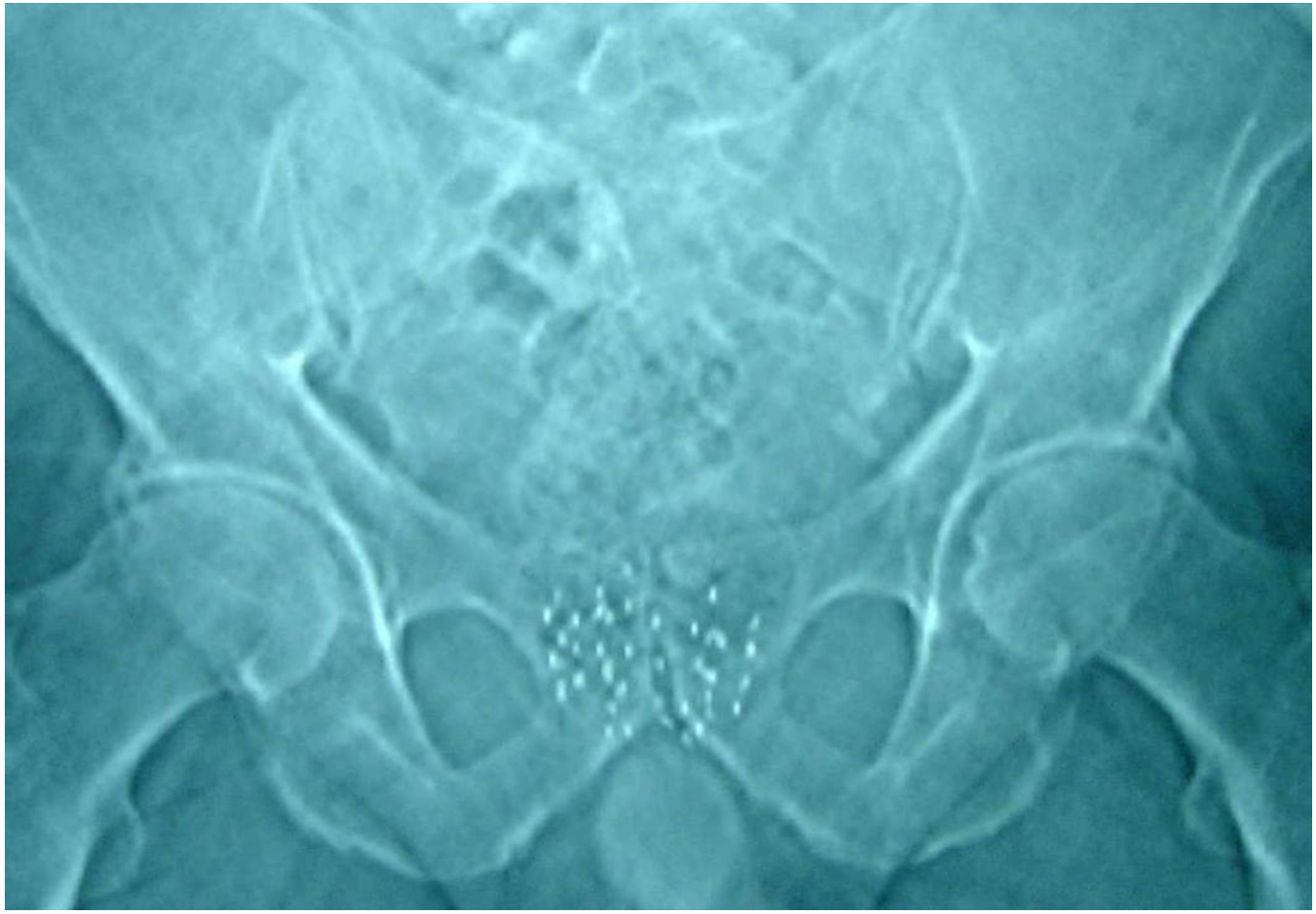


Longitudinal view

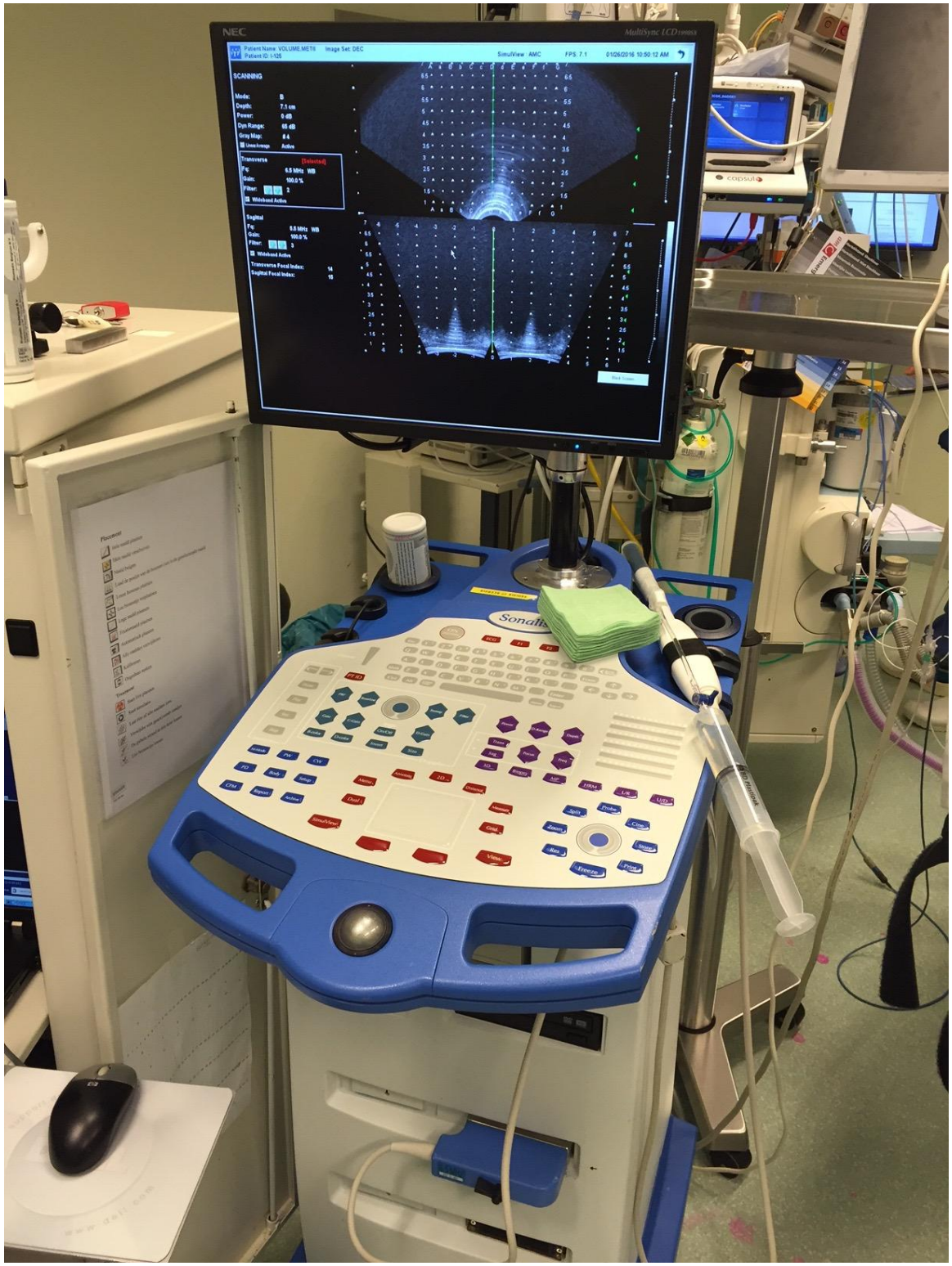
Distribution of Radioactive



Result



US machine



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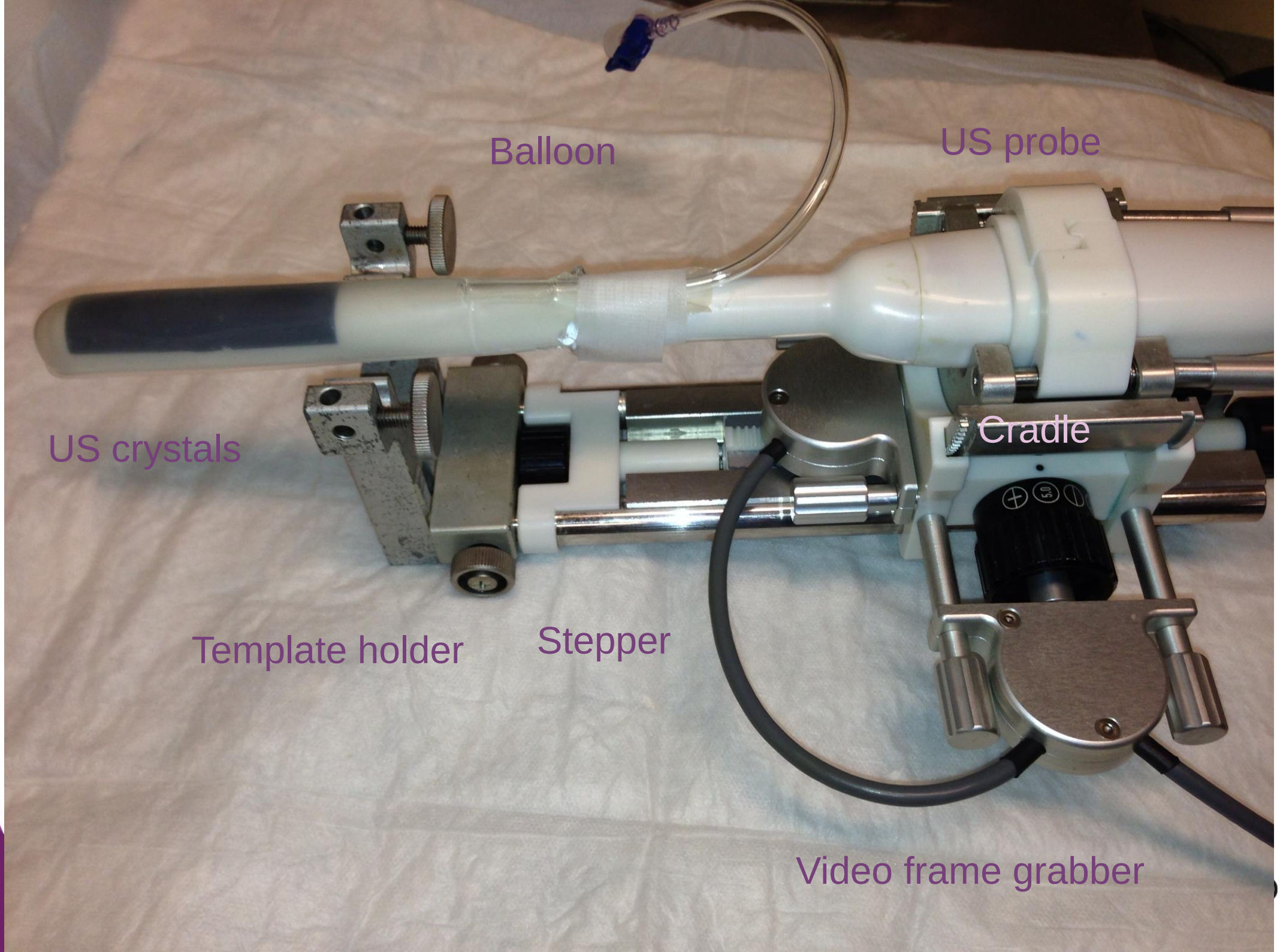
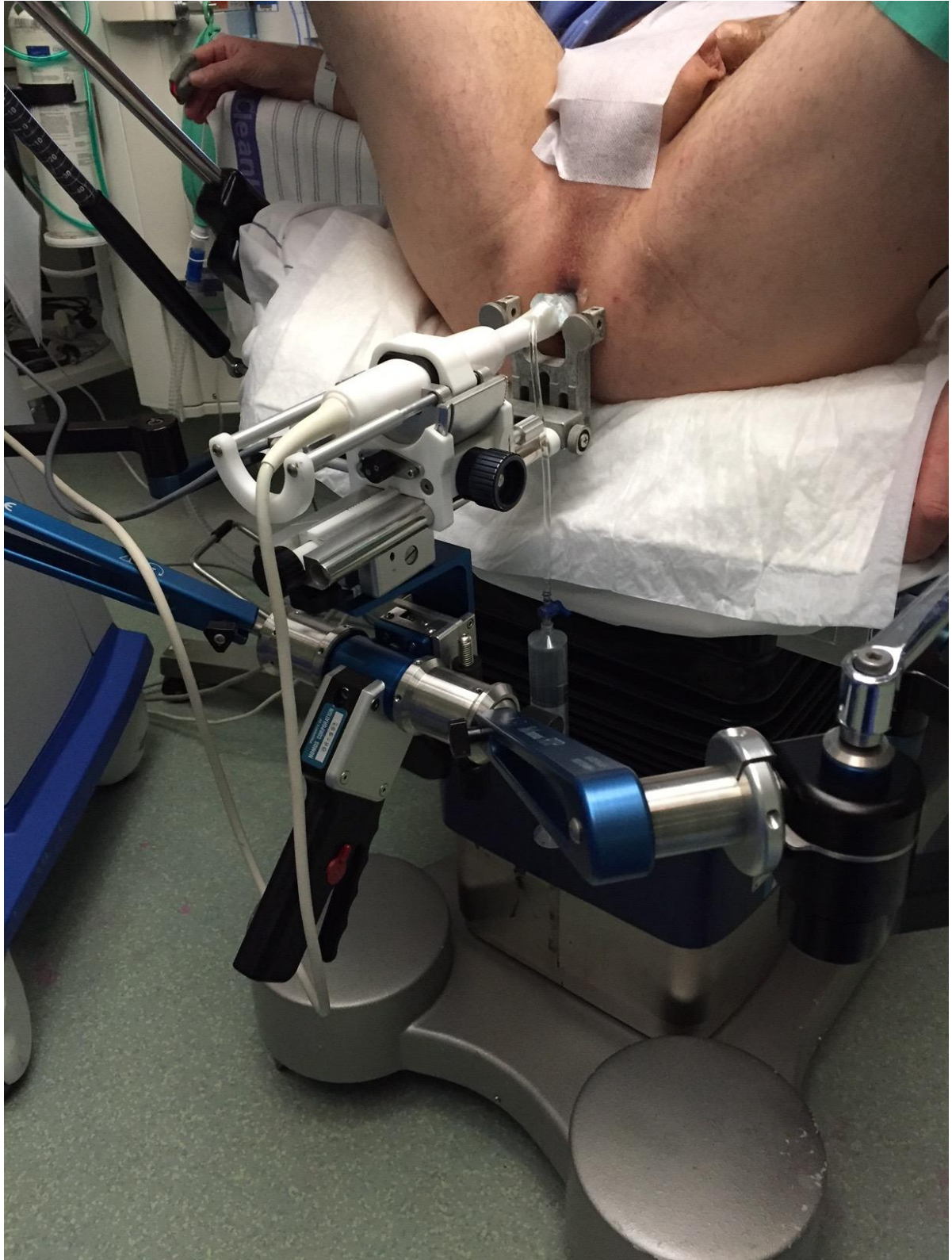
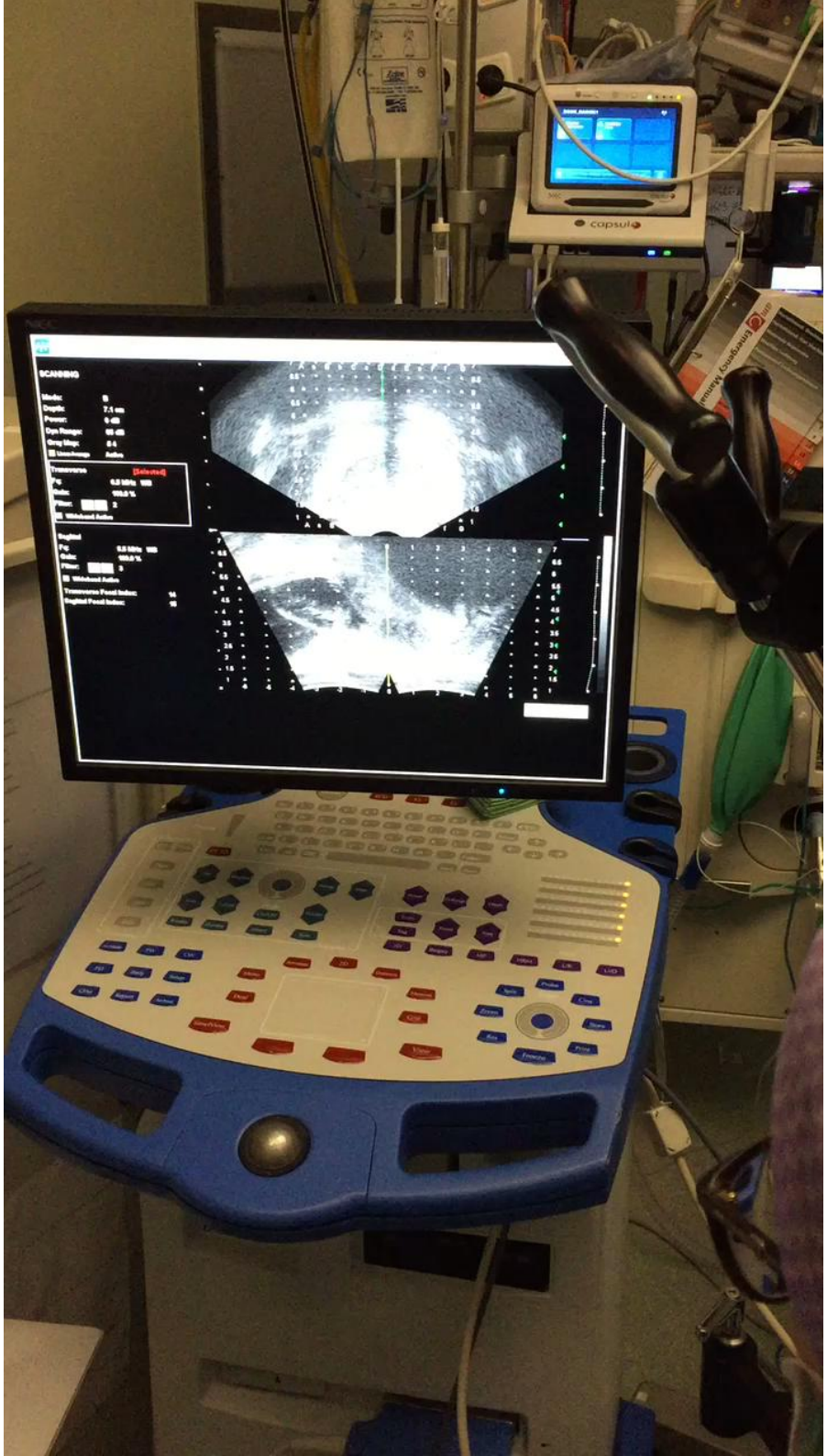

Balloon
US probe
US crystals
Cradle
Template holder
Stepper
Video frame grabber

Balloon on top of US probe





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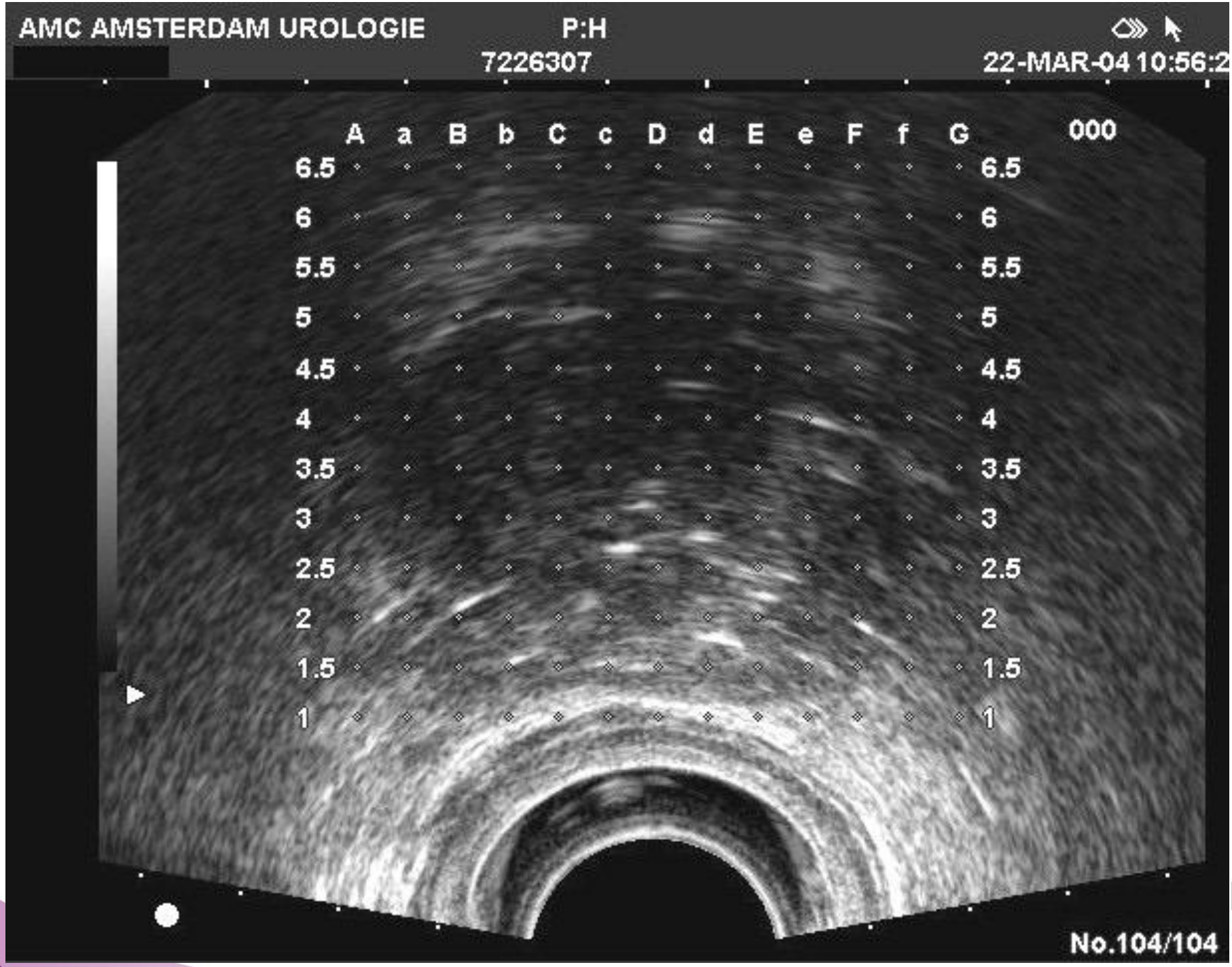
Positioning of the probe. Prostate symetrically within frame.



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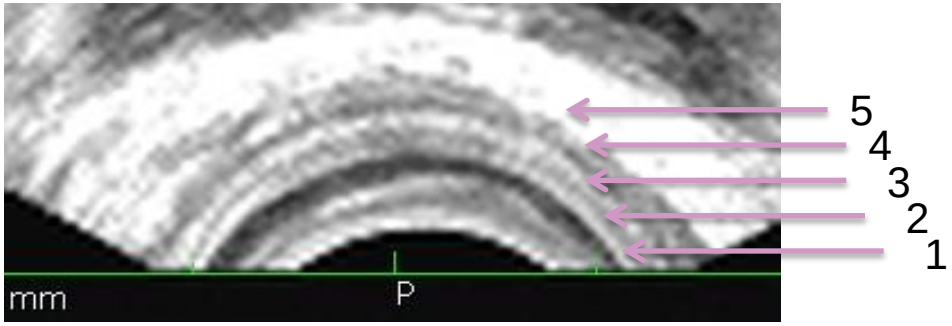
Ultrasound - Prostate

Hypoechoic signal

Ultrasound - Rectum

- 5 Layers
  - Interface balloon and mucosa: Hyperechoic
  - Mucosa and muscularis mucosae: Hypoechoic
  - Submucosa: Hyperechoic
  - Muscularis propria: Hypoechoic
  - Perirectal fat: Hyperechoic



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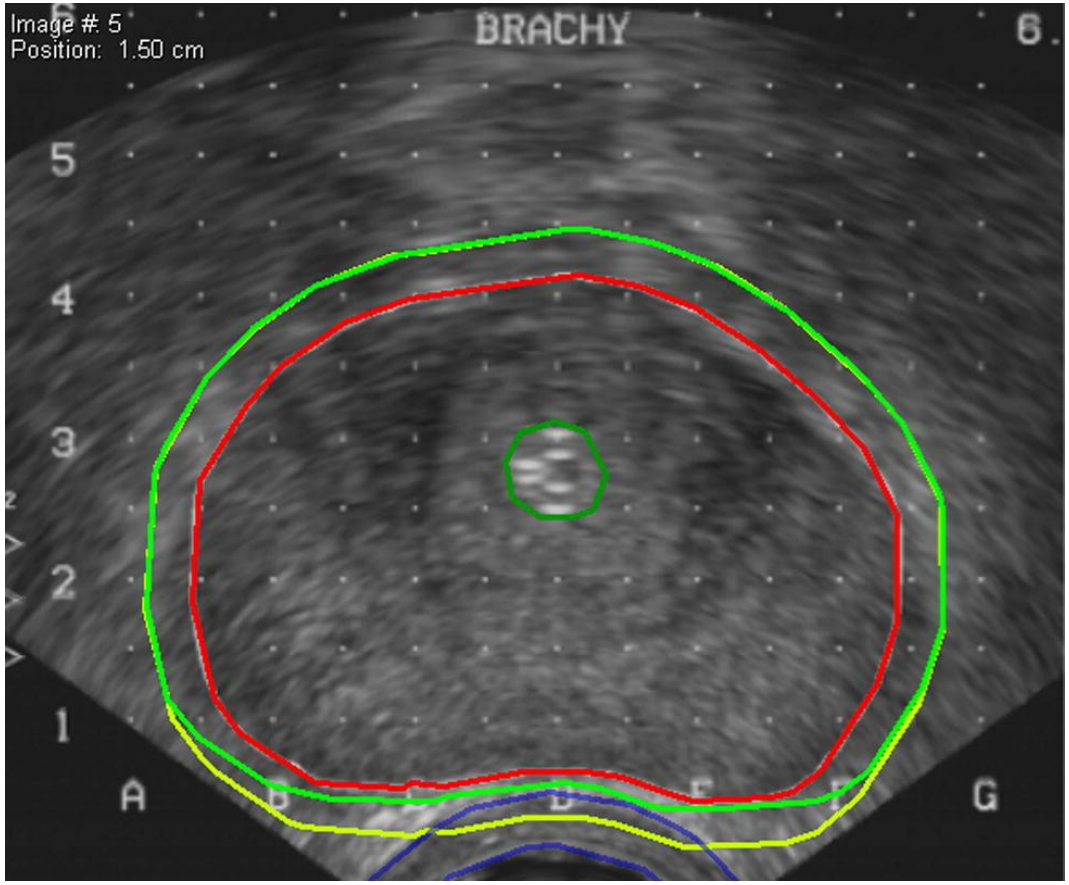
Ultrasound - Rectum

Ultrasound – Seminal vesicle

Prostate contouring



ESTRO definitions

Prostate gland

CTV = prostate gland + 3 mm

PTV = CTV

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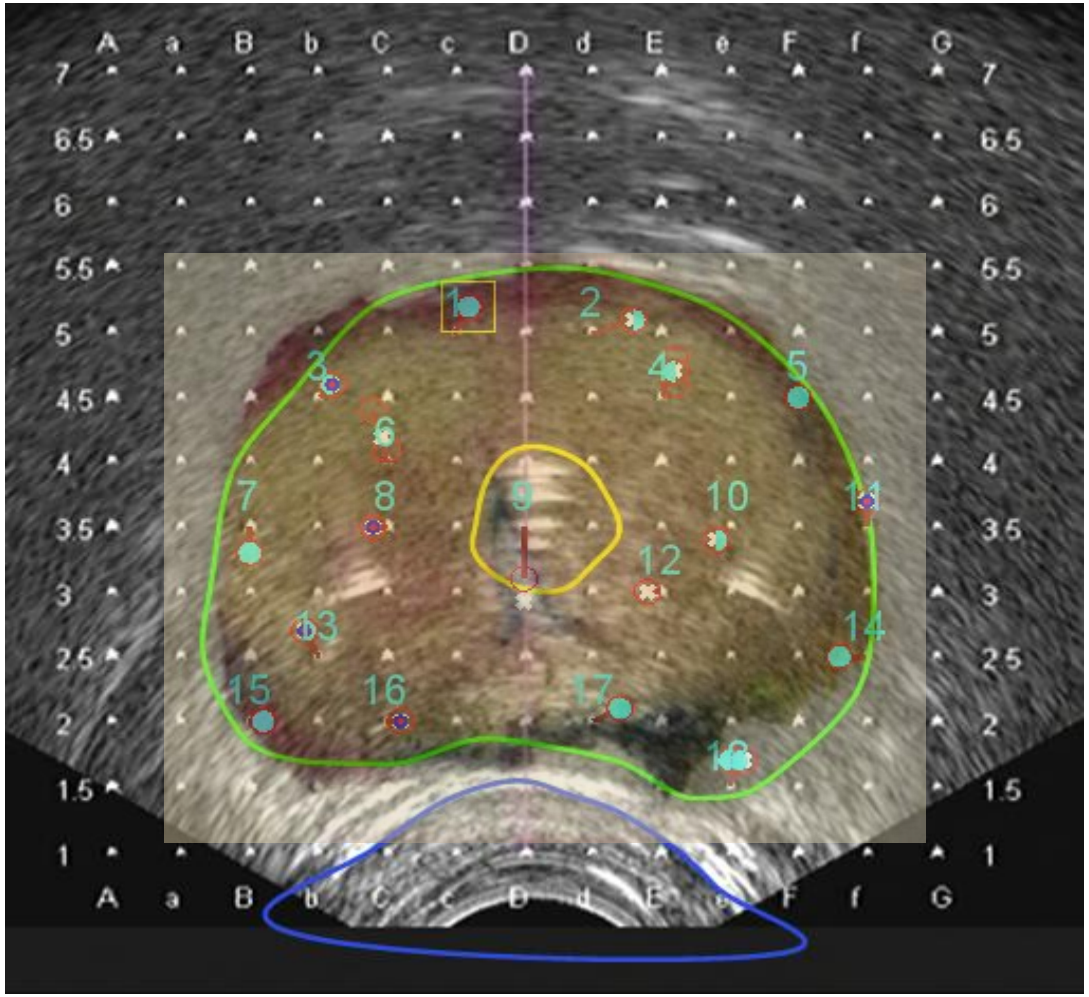
A a B b C c D d E e F f G
7
6.5
6
5.5
5
4.5
4
3.5
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1
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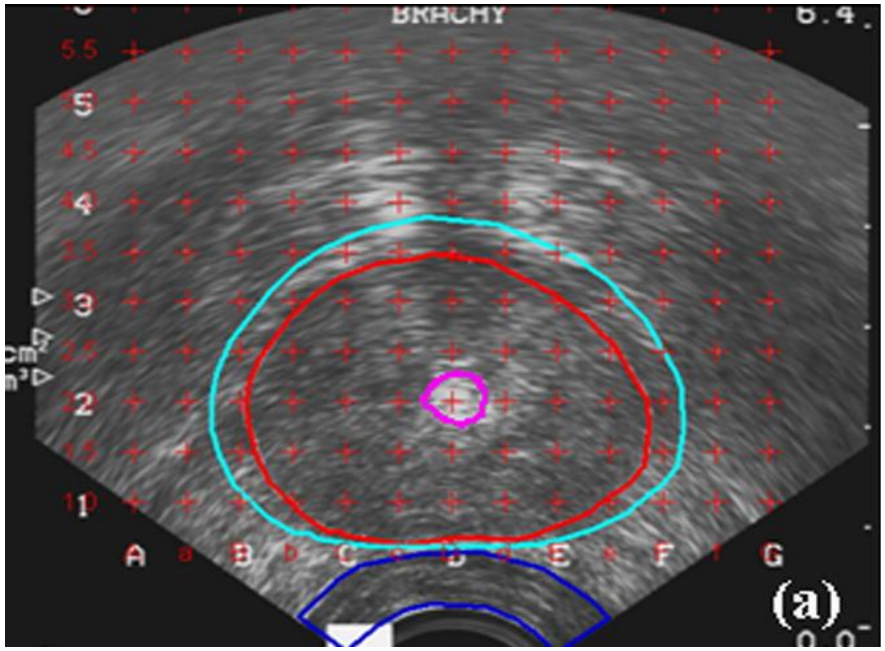
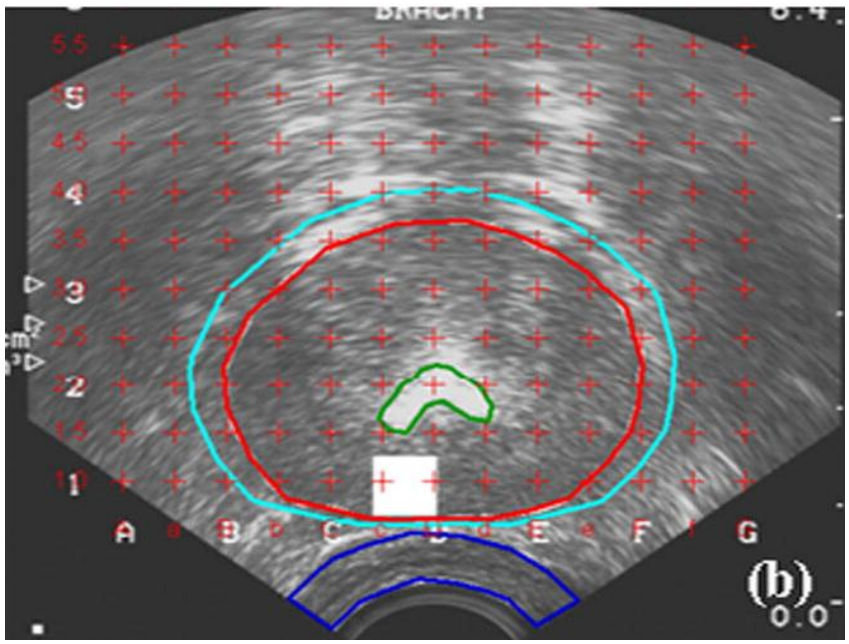
Contouring the urethra

Catheter



Aerated Gel



Prostate D90 183 Gy 187 Gy Δ 2%

Anderson et al.Radiother Oncol 2010

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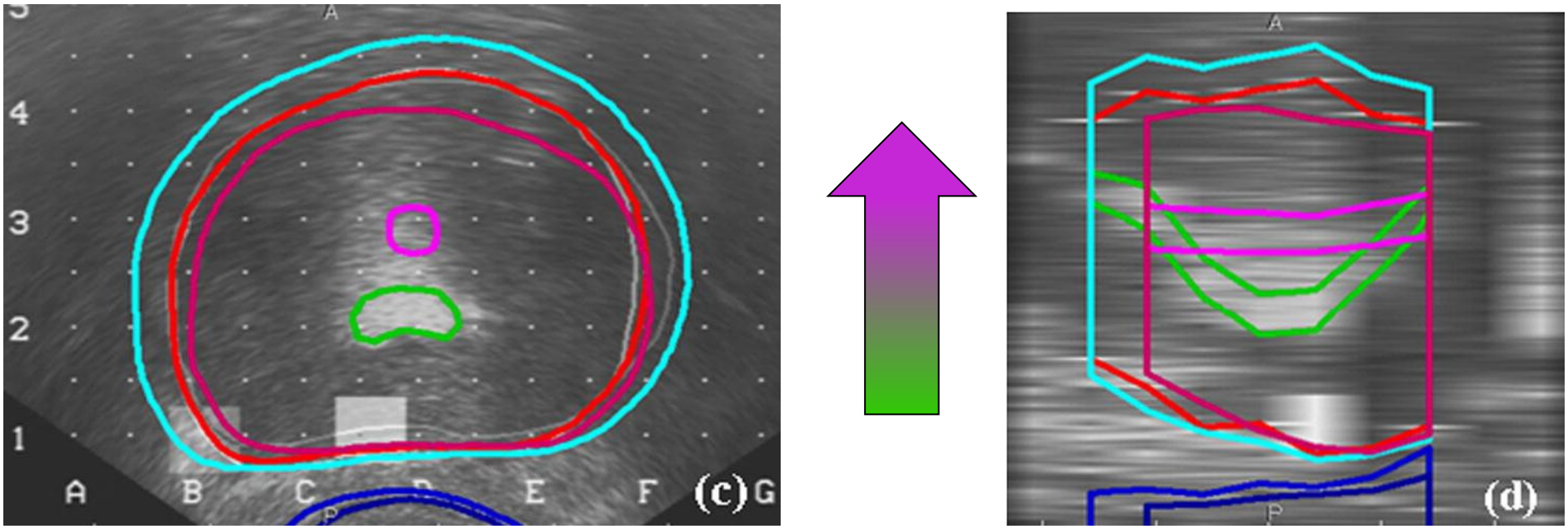

Gel plans

- **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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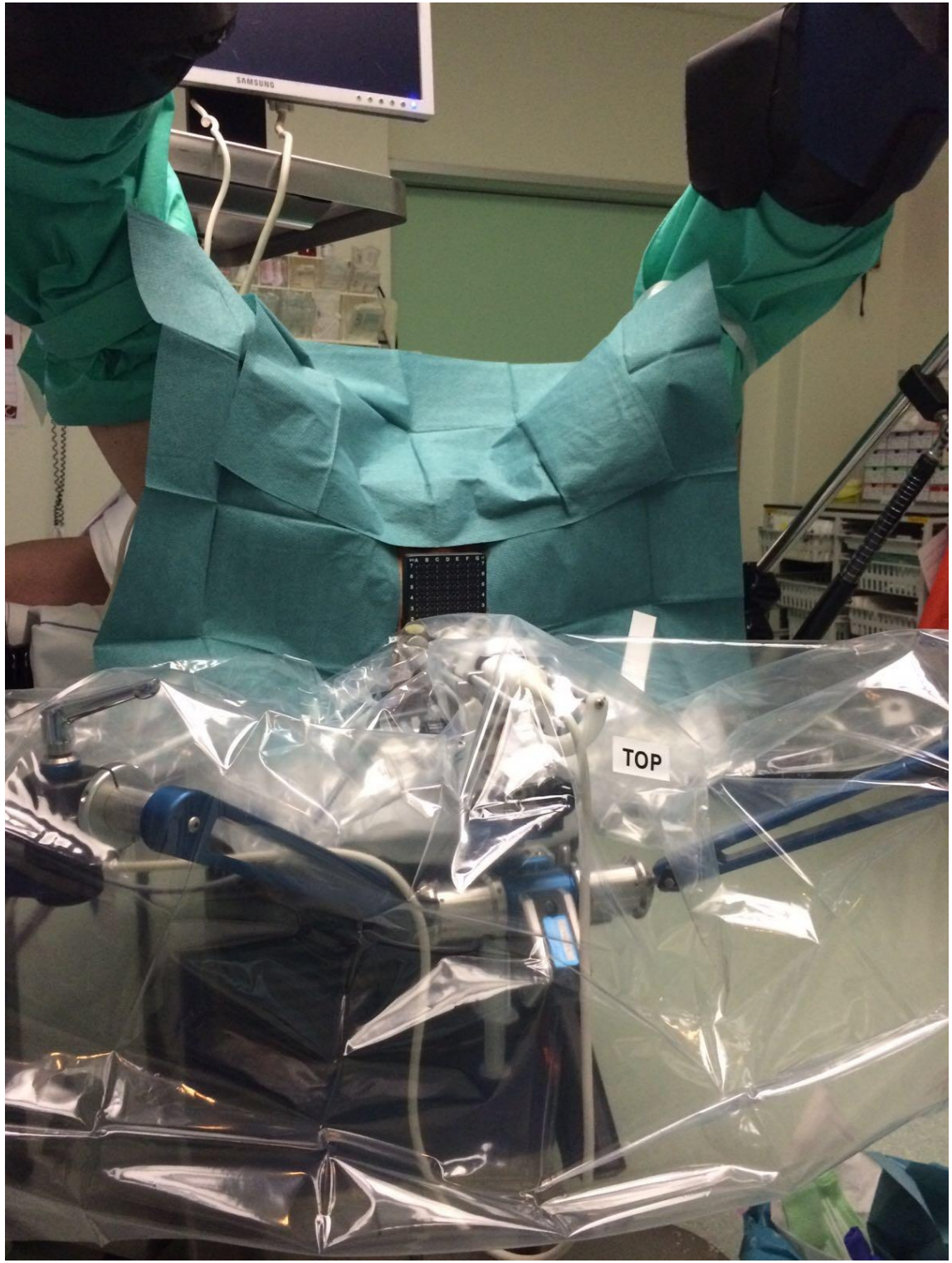
Litothomy position



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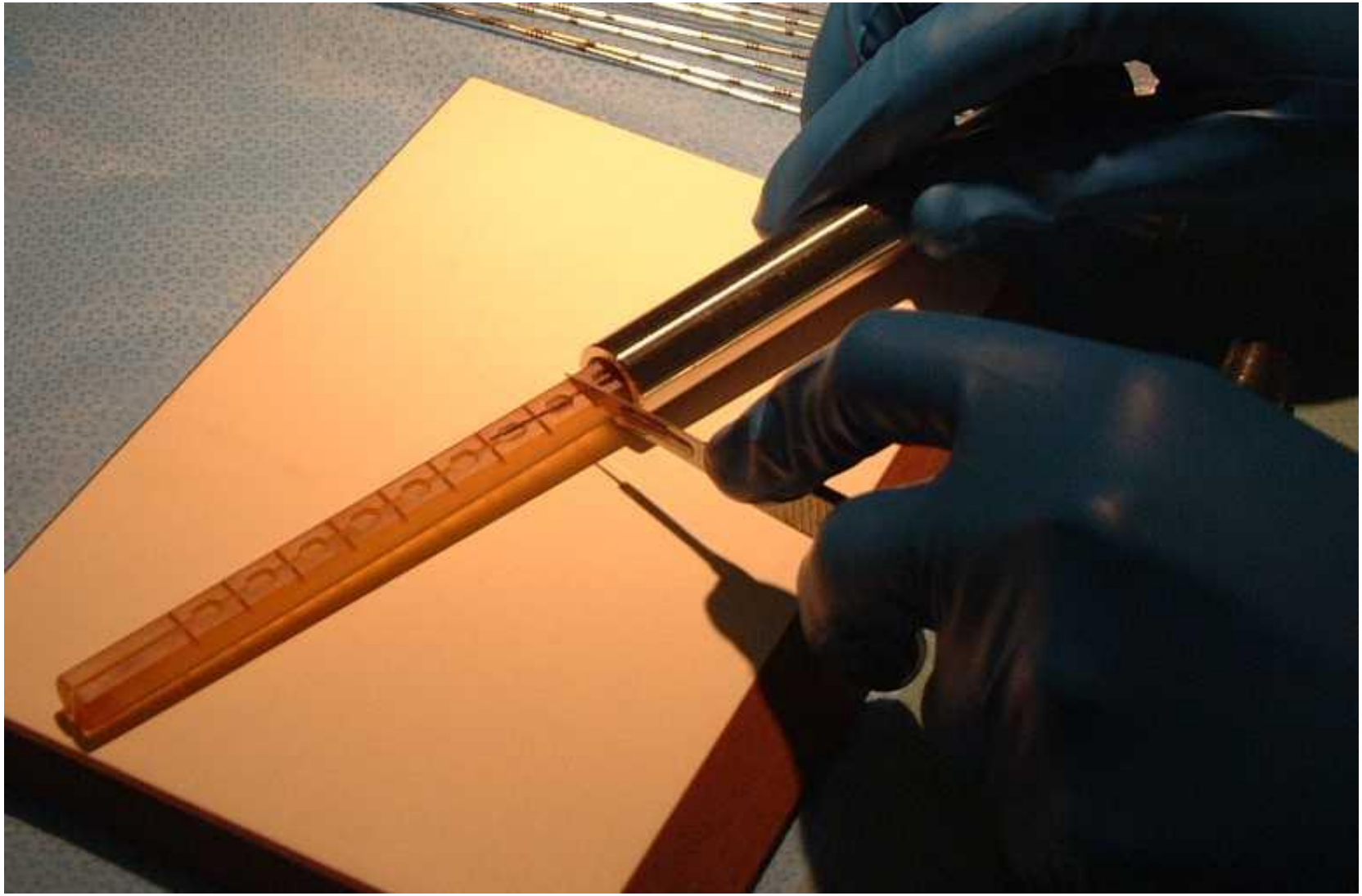
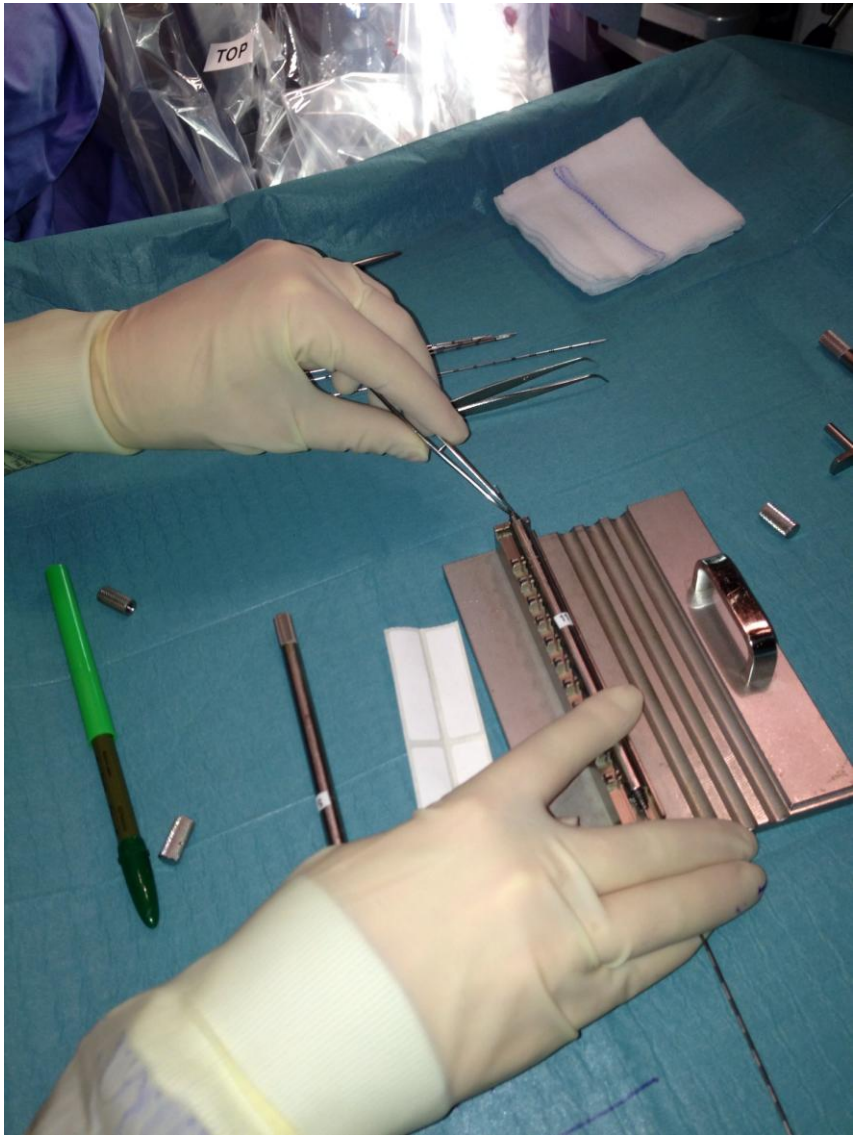
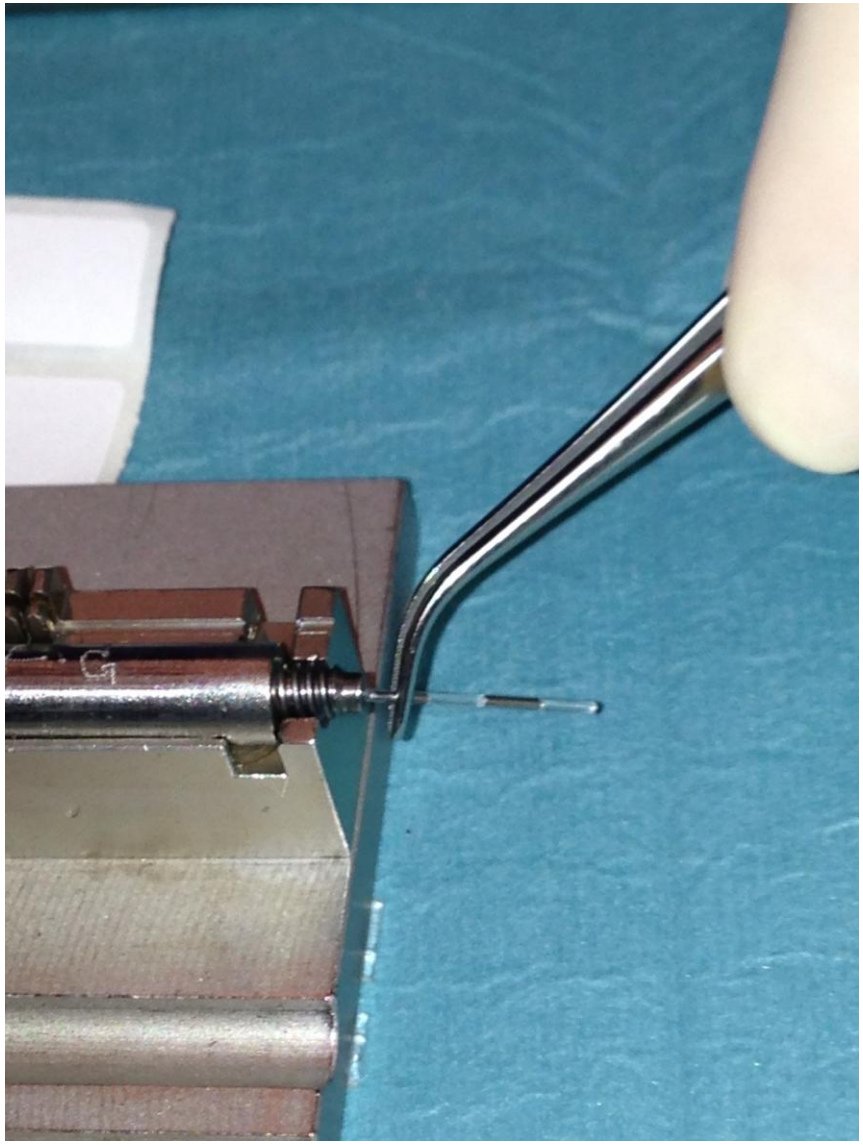
Cutting strands



Cutting Strands





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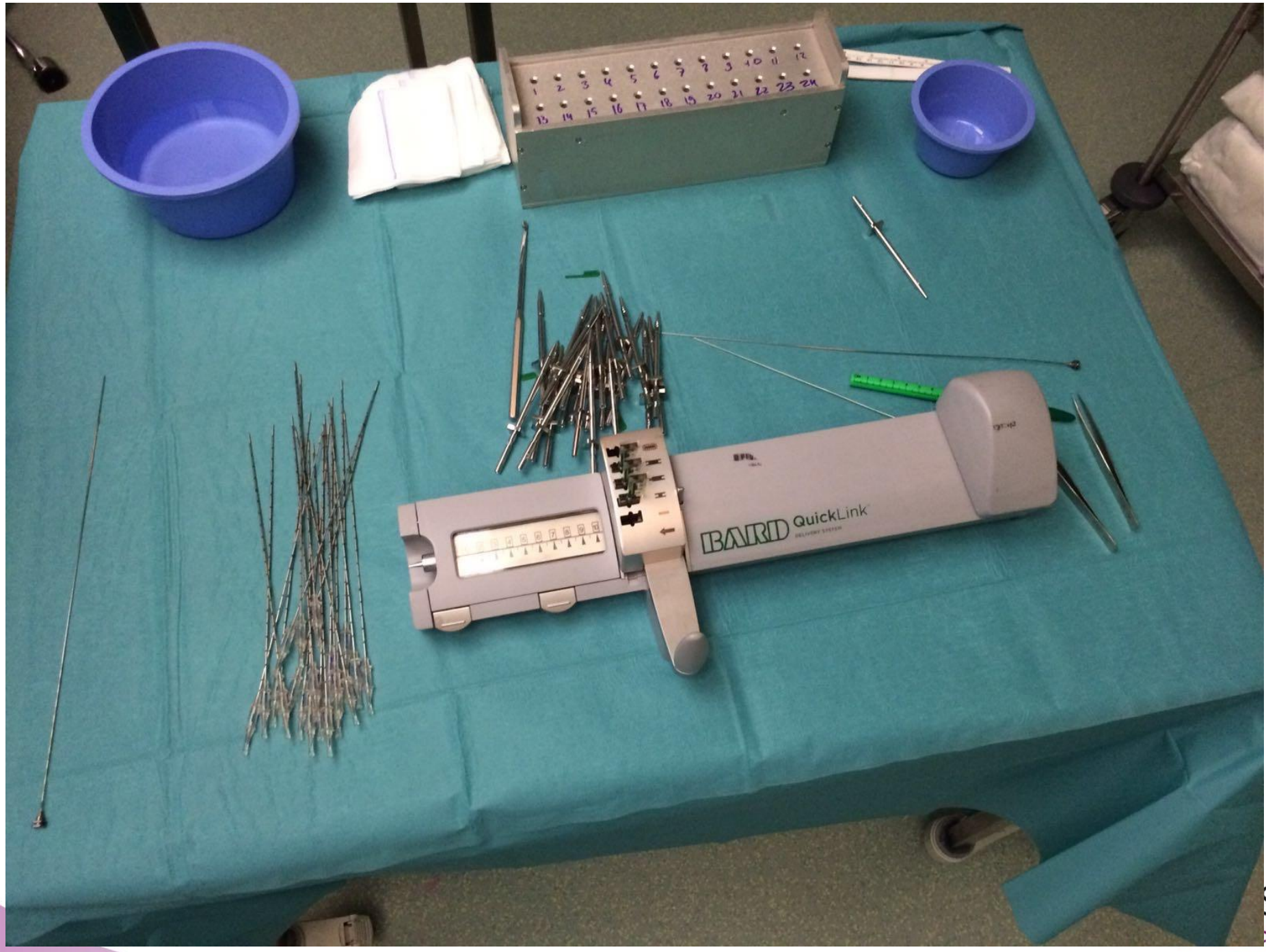
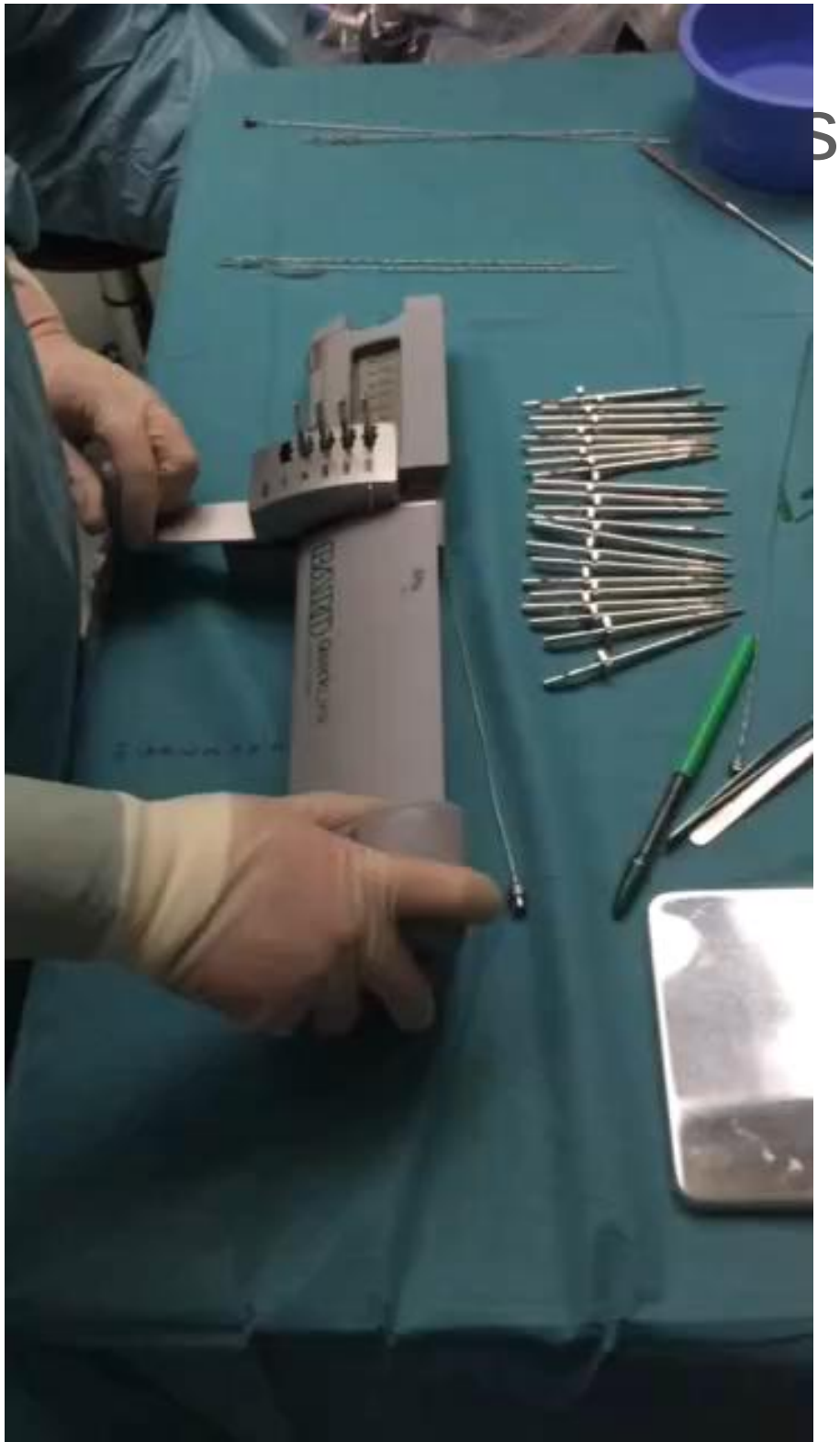
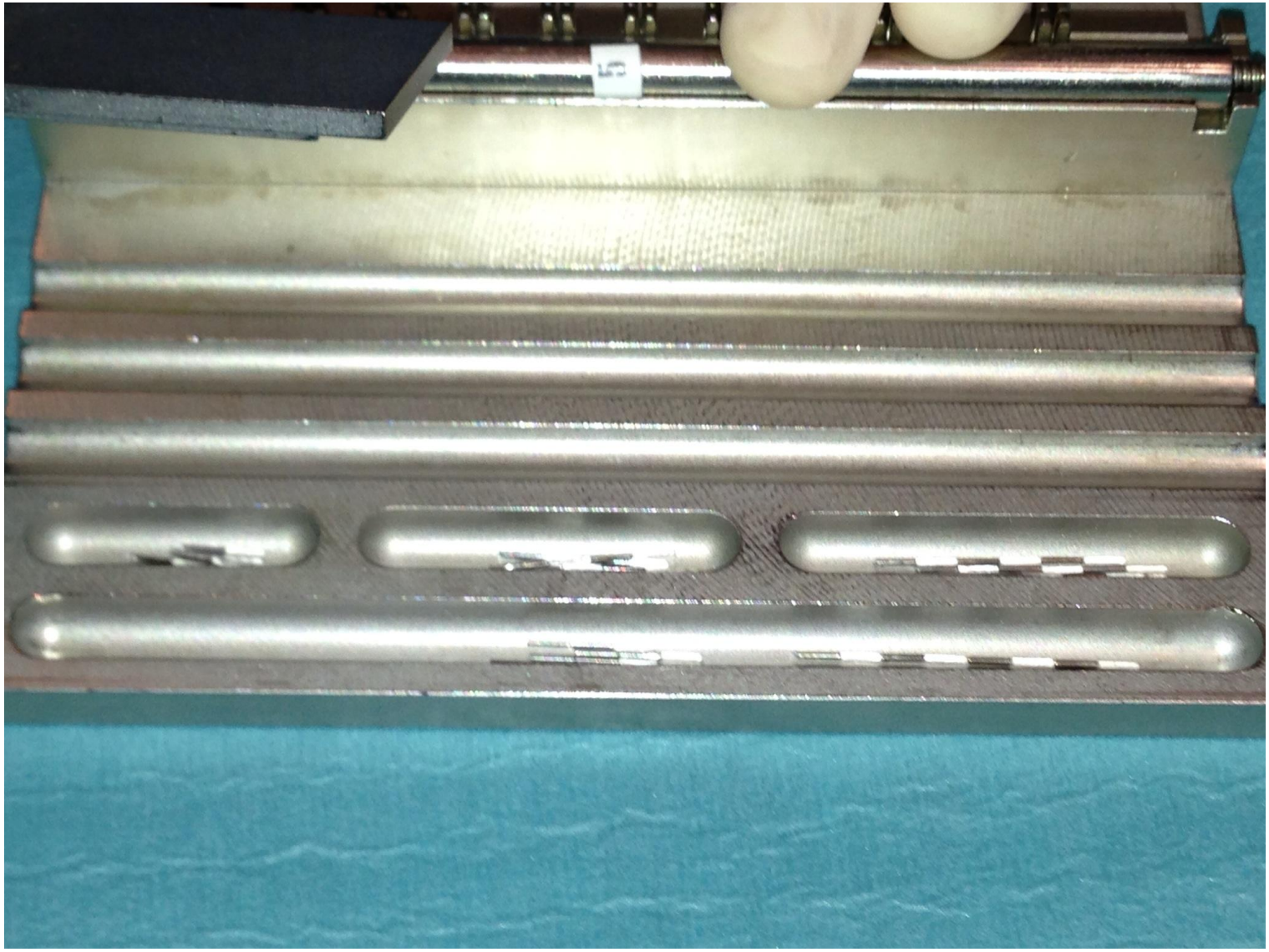
Composing Strands – Construction Devices



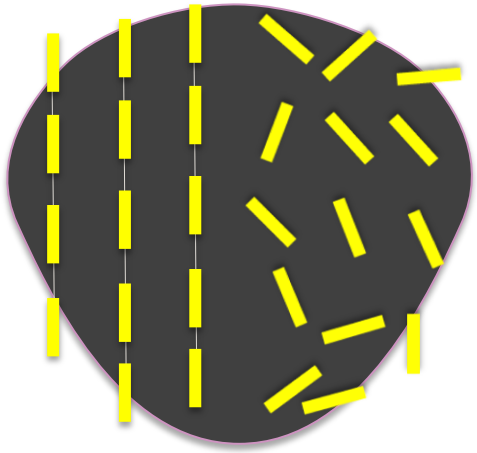


Storage of Sources



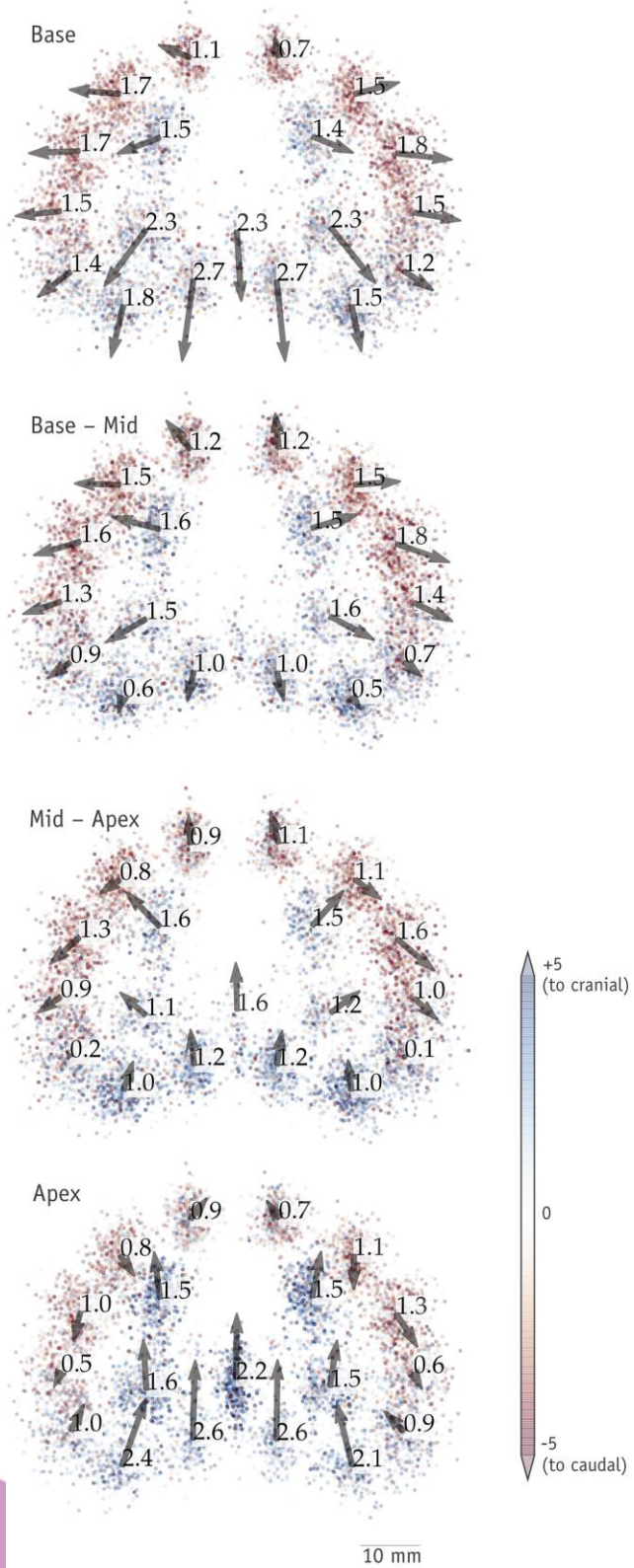
From: www.micknuclear.com

Prostate seed implants



Stranded Loose

Seed Displacement between TRUS and CBCT



R. Westendorp et al. 2016, Int. Radiat. Oncol. Biol. Phys;96:197-205

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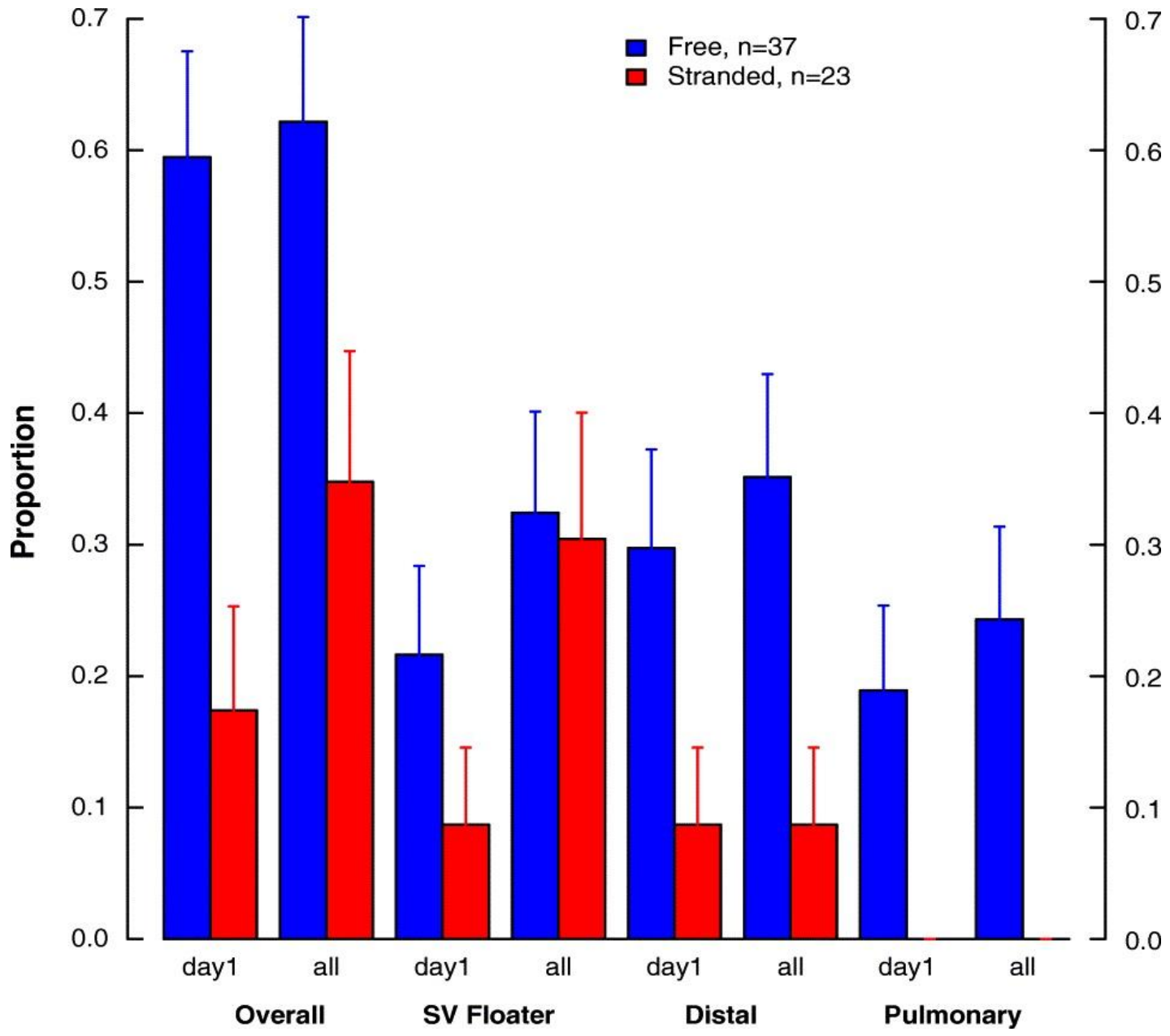
Seed Migration



Fuller, Brachytherapy 2004

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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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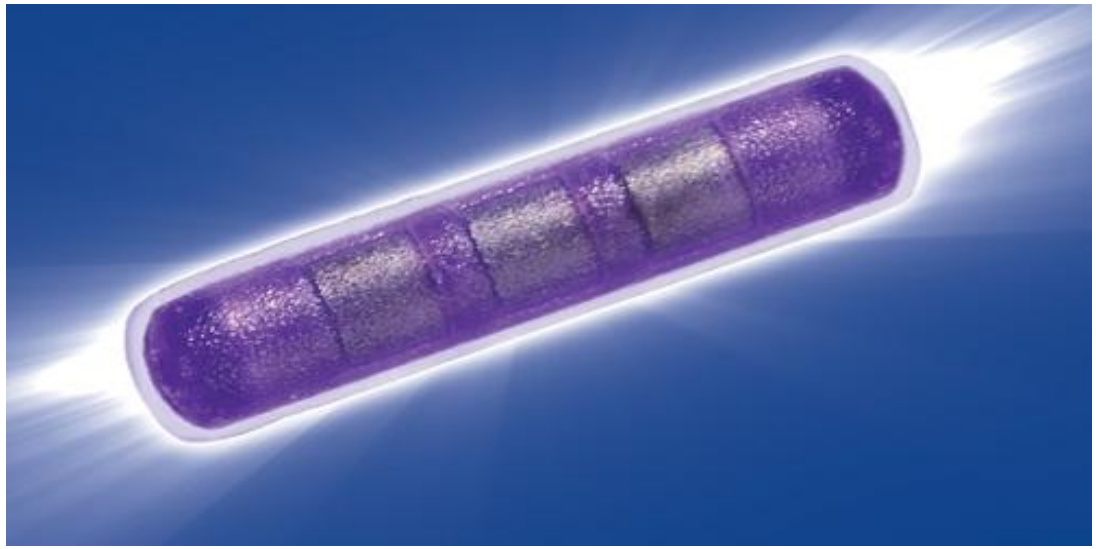
Coated Seeds

BRACHYSOURCE®
BARD Medical



AnchorSeed®
BrachySolutions

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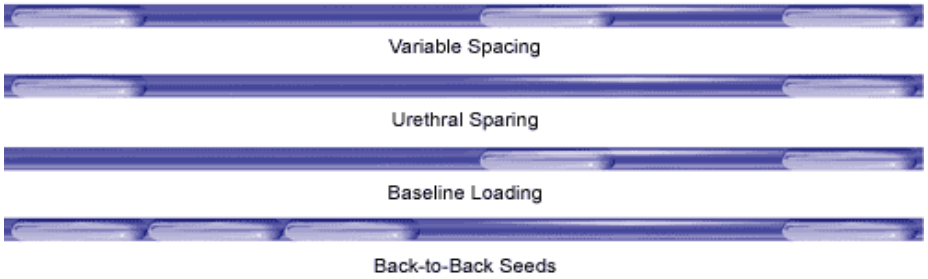
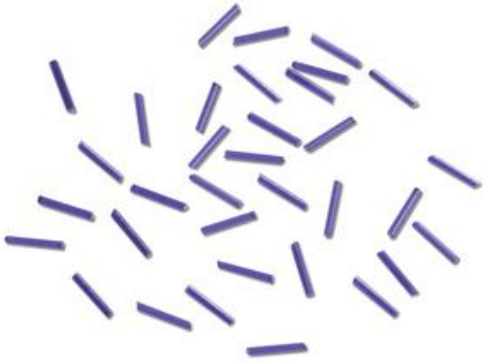
Source configuration

Stranded sources



Loose sources



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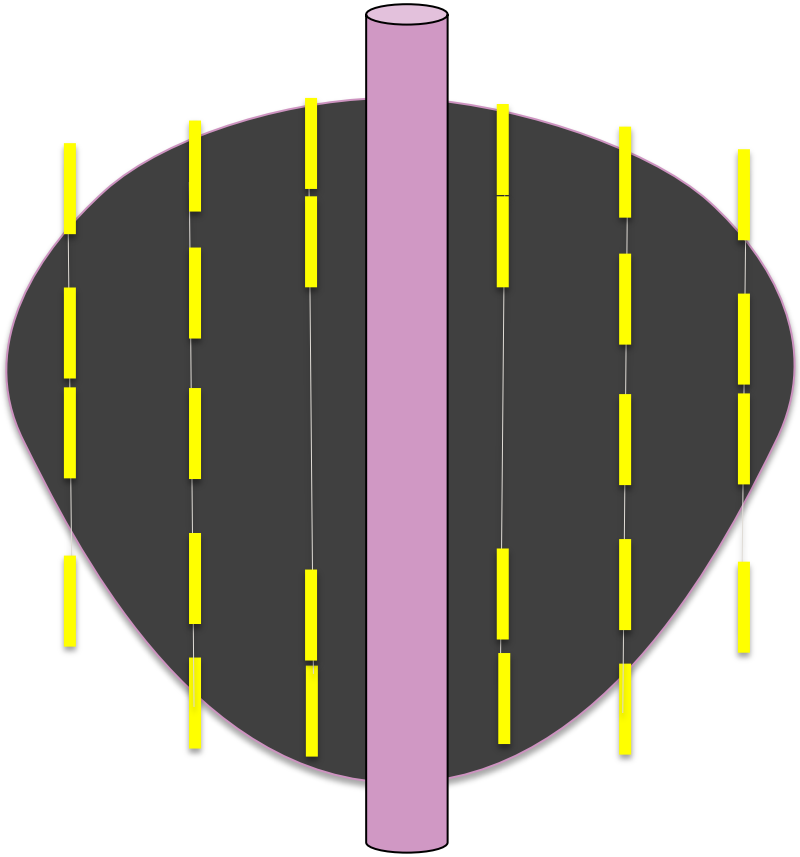
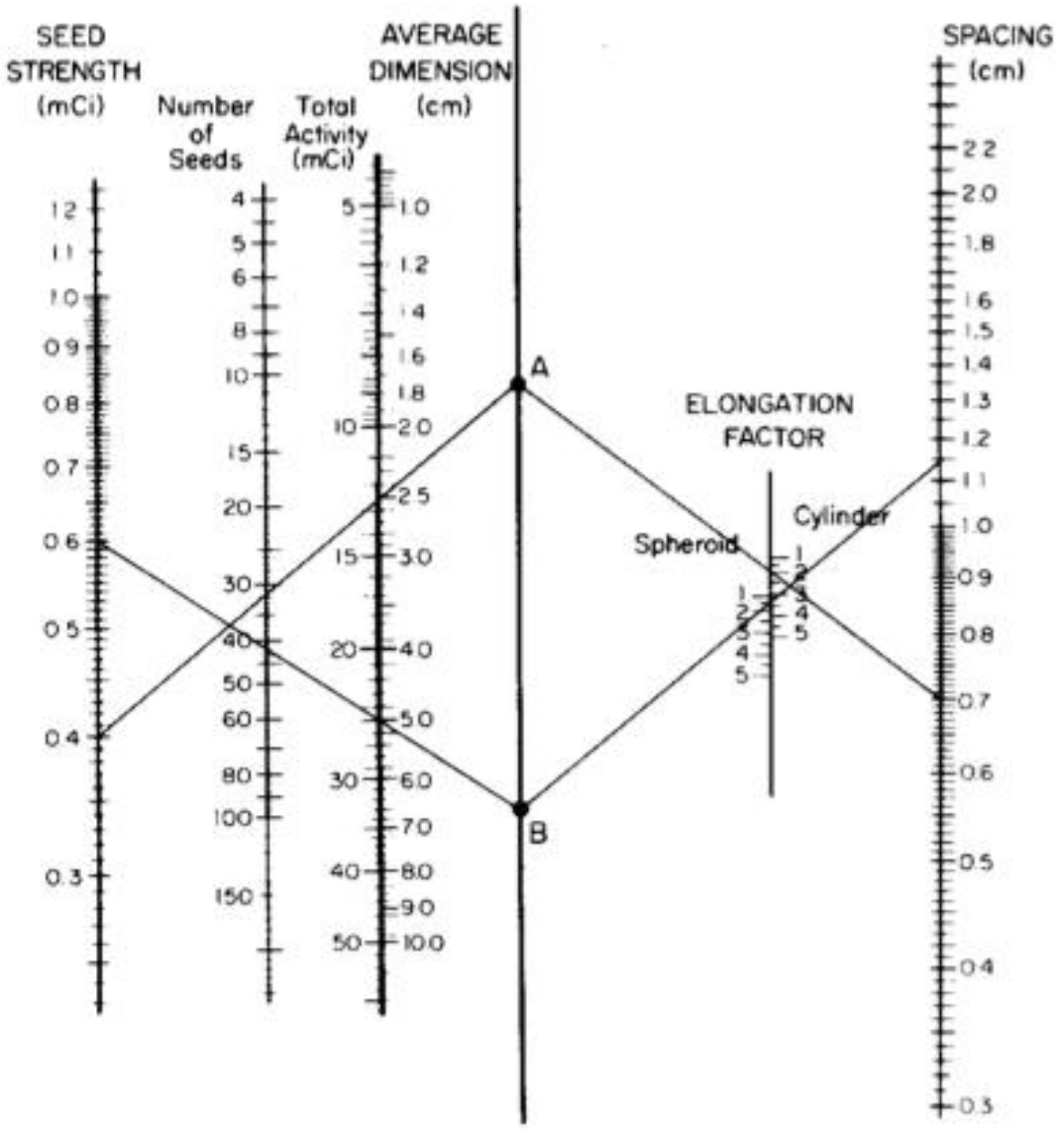
Source configuration



Planning

- Nomogram
- Preplan
- Intraoperative plan



Anderson nomogram

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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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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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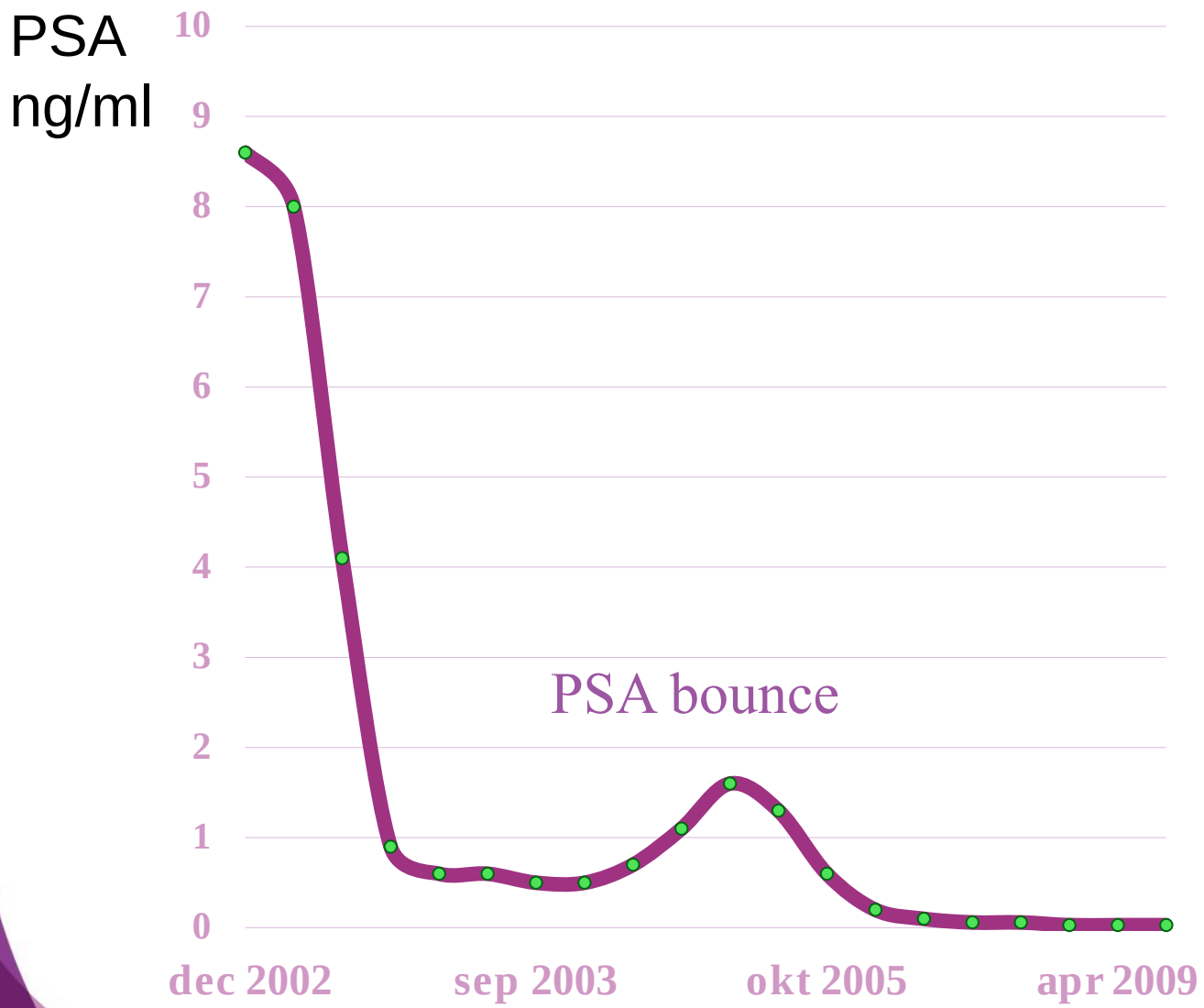
Follow-up with PSA



Criteria recurrence:

Nadir + 2 ng/ml

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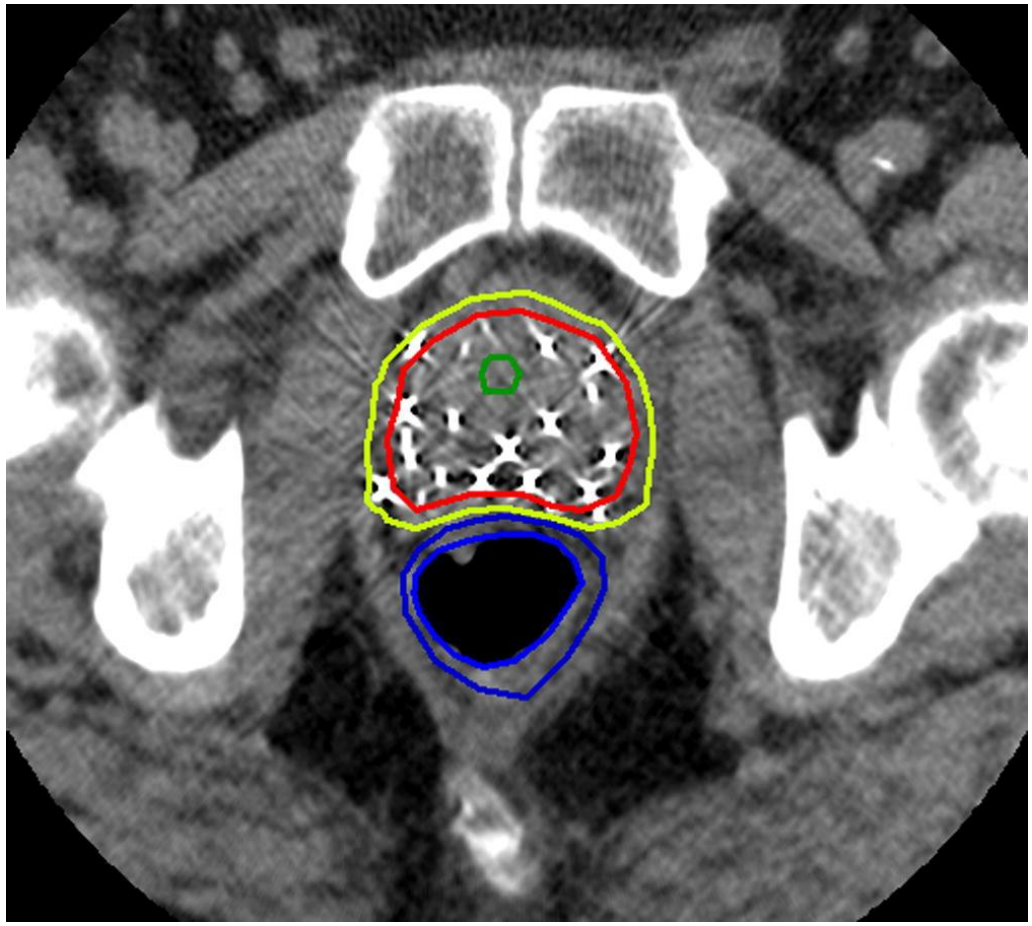
Postop contouring and dosimetry



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%)

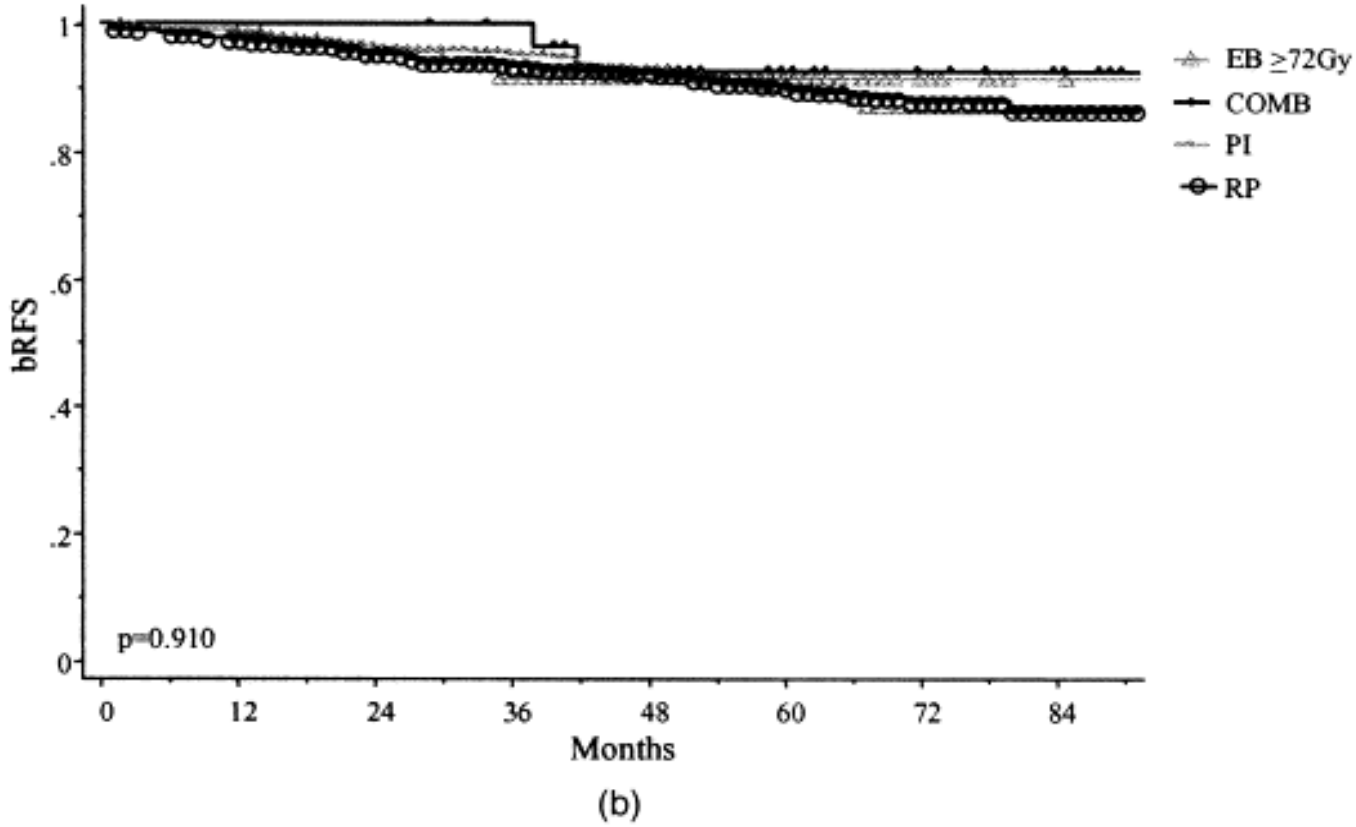


Fig. 3. Biochemical relapse-free results for favorable-risk (Stage T1-T2a, iPSA ≤10 ng/mL, and bGS ≤6) patients by treatment modality. (a) All favorable cases: RP, EBRT <72 Gy, EBRT ≥72 Gy, PI, or COMB. (b) Excludes EBRT <72. Abbreviations as in Fig. 2.

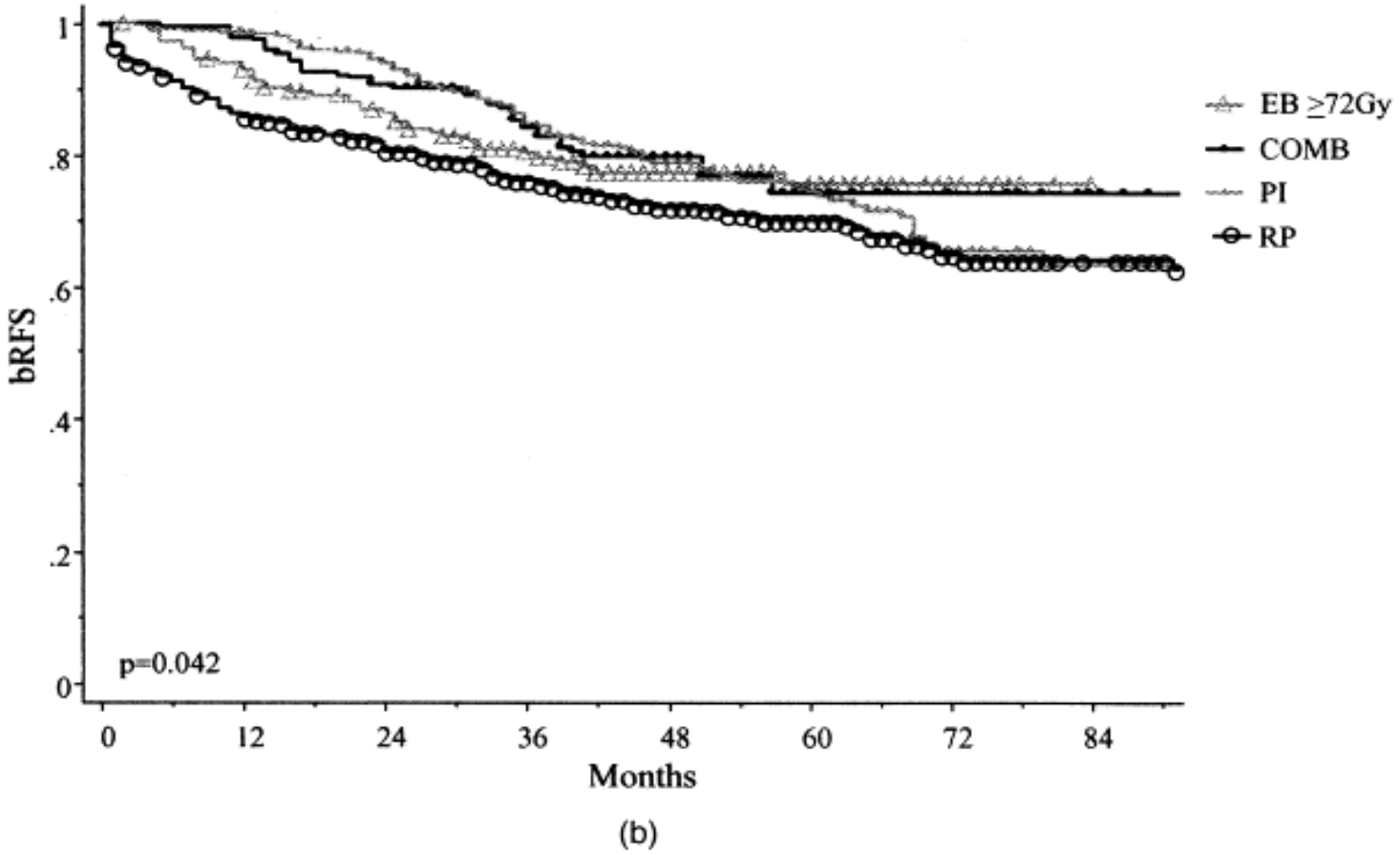
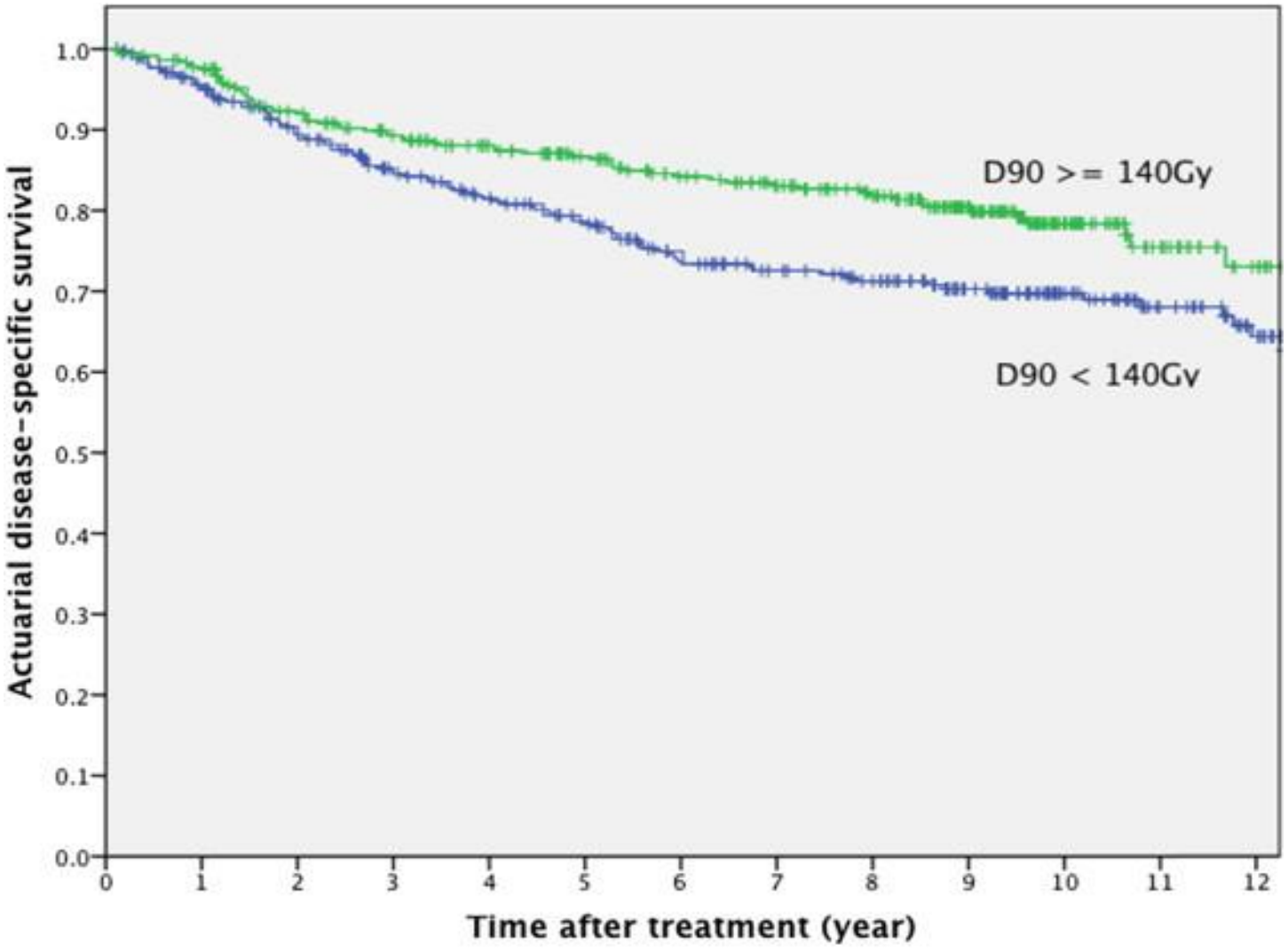


Fig. 4. Biochemical relapse-free results for unfavorable-risk (Stage T2b, iPSA >10 ng/mL, or bGS ≥7) patients by treatment modality. (a) All unfavorable cases: RP, EBRT <72 Gy, EBRT ≥72 Gy, PI, or COMB. (b) Excludes EBRT <72. Abbreviations as in Fig. ...



A Henry. Clin Oncol (R Coll Radiol) 2015;27:382-386
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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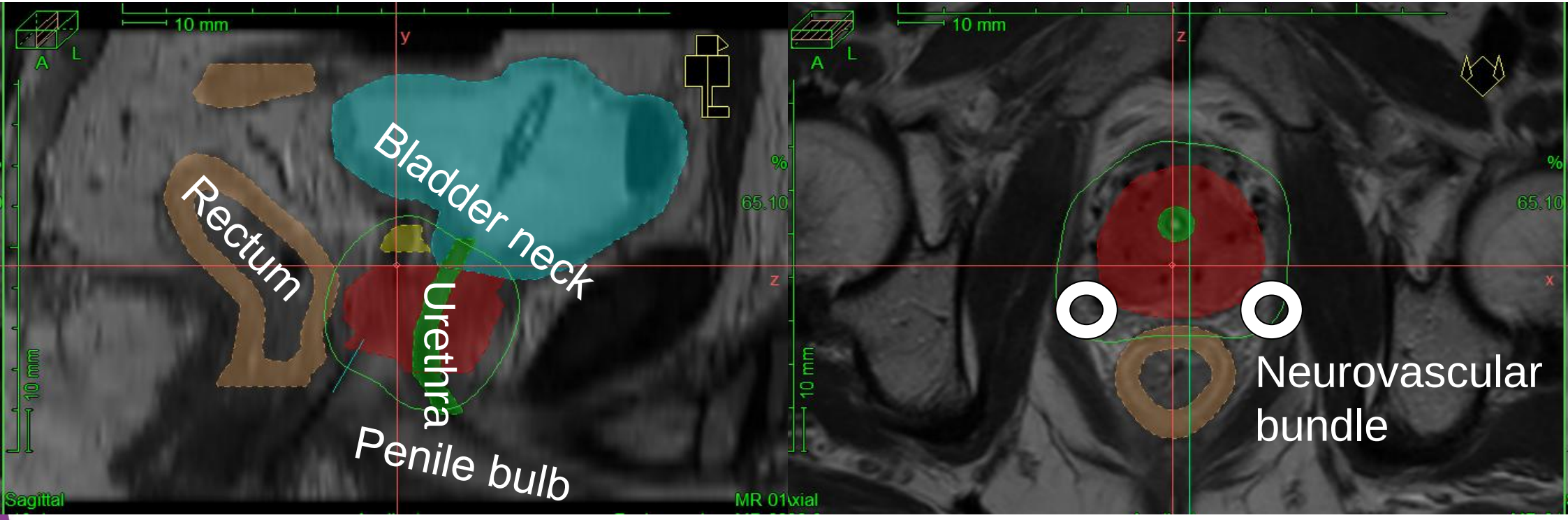
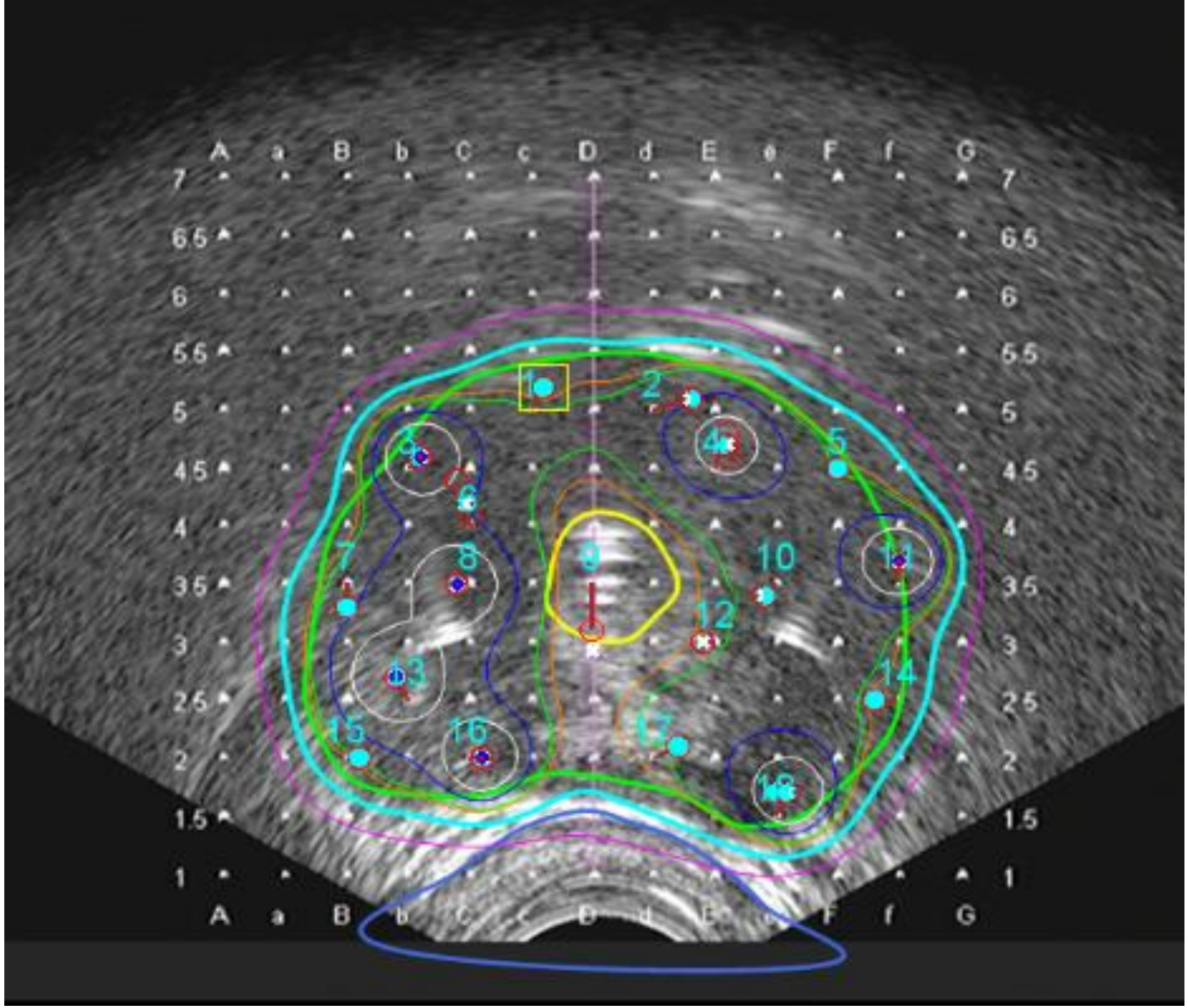
OAR


10 mm
A
L
y
%
65.10
z
10 mm
Rectum
Bladder neck
Urethra
Penile bulb
Sagittal
10 mm
A
L
z
%
65.10
x
10 mm
Neurovascular bundle
MR 01\xial


A a B b C c D d E e F f G
7
6.5
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1
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18

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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WWW.ESTRO.ORG/SCHOOL

Dose Calculation
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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Topics

- **Exposure, Kerma**
- Air Kerma-rate constant
- Reference Air Kerma-rate/Source Strength
- Dose Calculation

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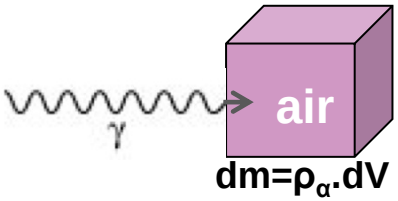
Exposure X

Let us consider a volume element dV filled by air of mass dm at a point in a photon radiation field. If dQ is the absolute value of the total charge of the ions of one sign produced in air when all the electrons and positrons liberated or created by photons in the air filled volume element dV are completed stopped in this volume, then the *exposure* X (C.kg^{-1}) is defined as



$$X = \frac{dQ}{dm} = \frac{1}{\rho_a} \cdot \frac{dQ}{dV}$$

where ρ_α is the density of air in volume dV. It has to be mentioned that according to this definition ionisation produced by Auger electrons are included in dQ where ionisation produced by radiative processes such as bremsstrahlung and fluorescence photons is not included in dQ.
The SI unit of Exposure is 1 C.kg^{-1}.

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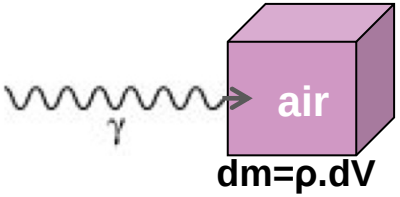
Kerma K

Let us consider a volume element dV filled by a material of mass dm at a point in photon radiation field. The quantity *kerma* refers to the kinetic energy of charged particles such as electrons and positrons that have been liberated by uncharged particles (photons). Kerma does not include the energy that has been expended against the binding energies of these charged particles even if this is usually a relatively small component. The name kerma for this quantity is derived from the Kinetic Energy Released per unit Mass.

If dE_{tr} is the sum of the initial kinetic energies of all charged particles liberated by uncharged particles within a volume element dV of a material containing a mass dm=ρ.dV of that material, then the *kerma* K (J.kg^{-1}) is given by



$$K = \frac{dE_{tr}}{dm} = \frac{1}{\rho} \cdot \frac{dE_{tr}}{dV}$$

The name of the SI unit for kerma is gray (Gy): 1 Gy = 1 J.kg^{-1}. Considering dE_{tr} it has to be mentioned that this includes also the kinetic energy of Auger electrons.

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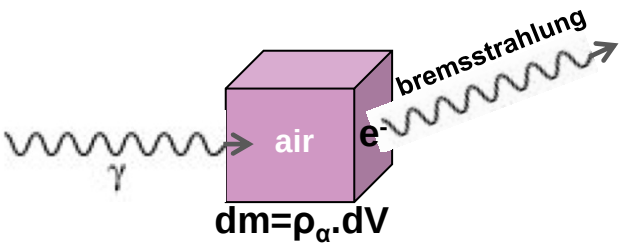
Exposure X and Air Kerma K_α

When the volume element dV in the radiation field is filled by air then we have the air kerma, K_α.

Then the following relationship between exposure X and air kerma K_α exists



$$X = K_a$$

$$X = \frac{dQ}{dm}$$

$$K = \frac{dE_{tr}}{dm}$$

e is the elementary charge and W is the mean energy expended in air per ion pair formed, W/e = 33.97 J.C^{-1}.

$\bar{g}_a$ **Is the mean value of g_α, the fraction of the energy of the electrons liberated by photons in air that lost to radiative processes (bremsstrahlung and fluorescence, g_α < 0.3% for E ≤ 1MeV).**

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Topics

- Exposure, Kerma
- **Air Kerma-rate constant**
- Reference Air Kerma-rate/Source Strength
- Dose Calculation

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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 a 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, then the *air kerma-rate constant* Γ_δ of that radionuclide is defined as:

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

If the unit gray (Gy) for the kerma and becquerel (Bq) for the activity are used, then the unit of the air kerma-rate constant is $Gy.s^{-1}.Bq^{-1}.m^2$.

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Air Kerma-rate constant Γ_δ

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

Photons are here considered to be gamma rays, characteristic x rays and internal bremsstrahlung.

The air kerma-rate constant is defined for an ideal point source and is characteristic for each radionuclide.

Considering a real source of finite size, attenuation and scattering in the source itself occur and annihilation radiation and external bremsstrahlung may be produced.

Considering the energy cut-off δ its value depends on the specific application. For simplification and standardisation it is recommended that δ is expressed in keV. The notation Γ_{10} for the air kerma-rate constant means that a value of 10 keV for the energy cut-off δ is used.

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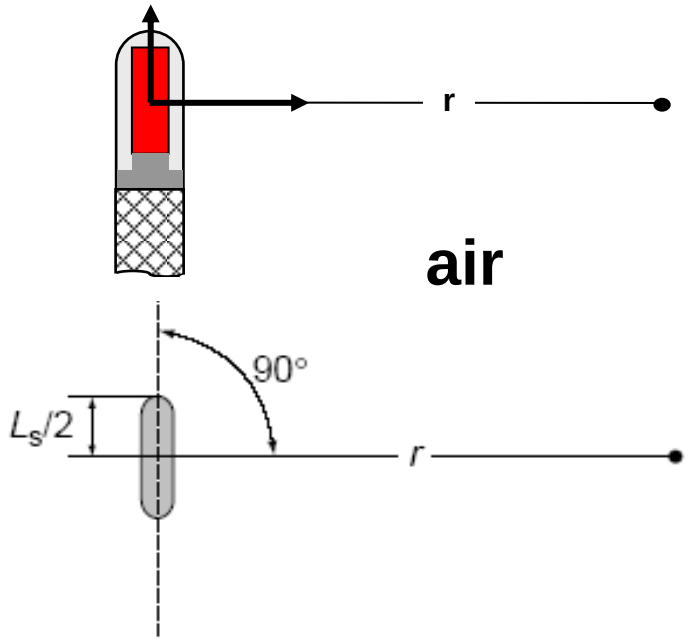
Topics

- Exposure, Kerma
- Air Kerma-rate constant
- **Reference Air Kerma-rate/Source Strength**
- Dose Calculation

Reference Air Kerma Rate / Source Strength

In our days the strength of the source is defined in terms of energy deposition per unit time at a specific distance in air:

Air Kerma Rate (in air) in μGy . h^{-1} at 1 m



For linear sources this can be expressed in Air Kerma Rate units per unit of length

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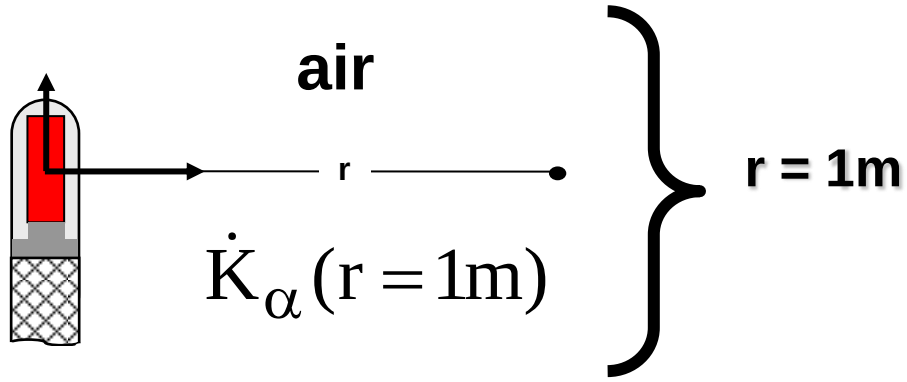
Reference Air Kerma Rate / Source Strength

Reference Air Kerma Rate $K_R = K_{\alpha,\alpha}(r=1m)$ in $\mu Gy \cdot h^{-1}$ at 1 m



The reference air kerma rate of a source is defined as the air kerma rate in air at a reference distance of one metre from the centre 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 centre to the reference point at one metre has to be at right angles to the long axis of the source.

In 1985, the ICRU Report 38[5] defined as an emission specification quantity for γ-rays emitting brachytherapy sources the *reference air kerma rate*.

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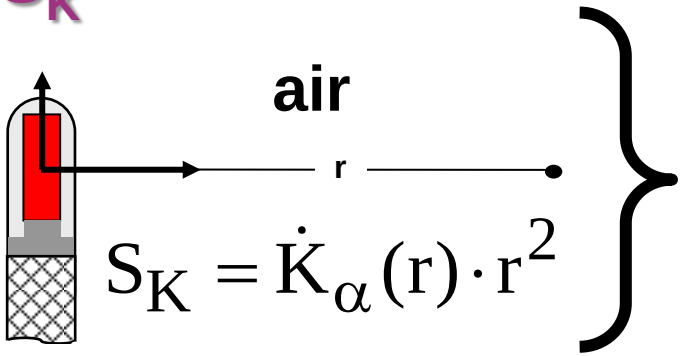
Reference Air Kerma Rate / Source Strength

Air Kerma Strength S_K



AAPM, North America

The American Association of Physicists in Medicine in their Report No. 21 by the AAPM Task Group No 32 introduced in 1987 the idea for the specification of brachytherapy sources in terms of strength. 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 centre along the perpendicular bisector and the square of the distance r.

The distance r must be chosen to be large enough so that the source can be treated ***as a point source*** and so that the ***finite*** **dimensions of the detector** used for the measurement have no influence on the result!

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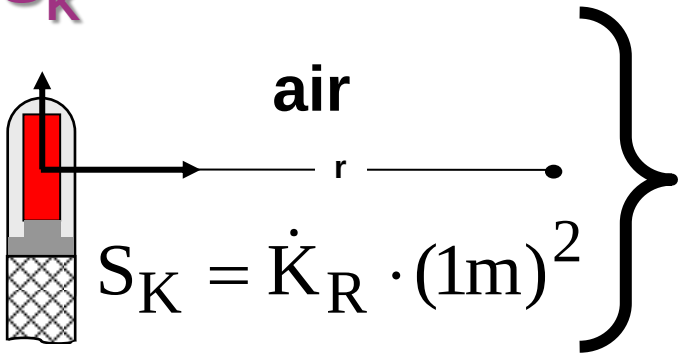
Reference Air Kerma Rate / Source Strength

Air Kerma Strength S_K



AAPM, North America

The recommended unit for air kerma strength is μGy.m².h^{-1} and has been denoted by the symbol U:

$$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$$

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Reference Air Kerma Rate / Source Strength

The air kerma rate based source strength specifications, reference air rate kerma K_R and air kerma strength S_K, are a measure of the radiation field intensity in free space around brachytherapy sources, considering *a priori* the effects of:

(a) source and

(b) source encapsulation

and making no use of intermediate constants.

TABLE 7.1

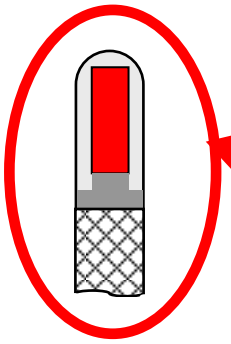
Units and Unit Conversion Factors for Reference Air Kerma Rate and Air Kerma Strength

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 $Gy\ s^{-1}\ Bq^{-1}\ m^2$	$\mu Gy\ h^{-1}\ MBq^{-1}\ m^2$	$(1/3600) \times 10^{-12}\ Gy\ s^{-1}\ Bq^{-1}\ m^2 = 2.778 \times 10^{-16}\ Gy\ s^{-1}\ Bq^{-1}\ m^2$
			$\mu Gy\ h^{-1}\ MBq^{-1}\ m^2$	$1.0\ U\ MBq^{-1}$

The "Strength" of a Source

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

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.

For example for HDR ^{192}Ir sources: 10Ci = 370 GBq ➔ ≈ 41 kU

41000 μGy.m².h^{-1}

41000 cGy.cm².h^{-1}

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Topics

- Exposure, Kerma
- Air Kerma-rate constant
- Reference Air Kerma-rate/Source Strength
- **Dose Calculation**

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Dose Calculation: The TG-43 Protocol

- **Dose Rate from a single Source**
- Dose from Dose Rate
- Many Sources
- Limitations

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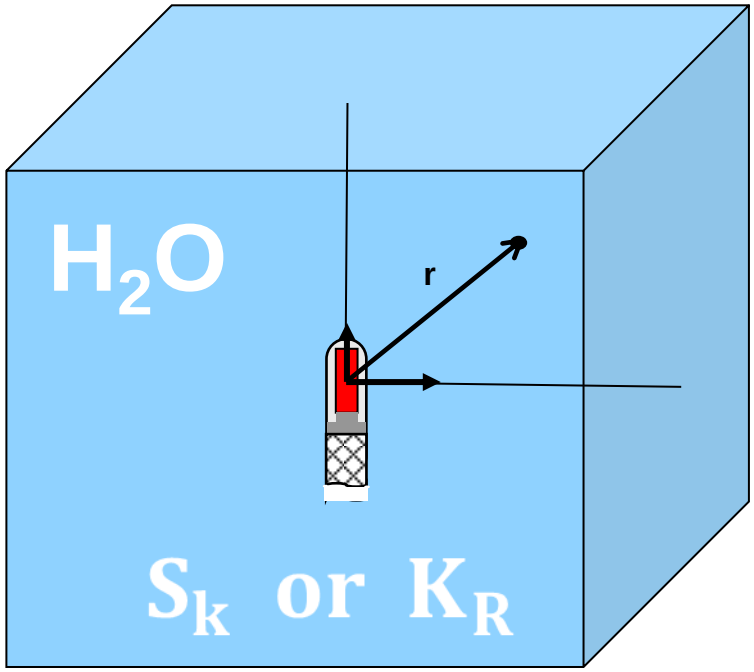
Dose Calculation

How can we calculate the dose rate or dose resulted from a single source at a point in space (dose to water in water)?



$$\dot{D} = \dot{D}(\vec{r}) = \ ?$$

^{137}Cs, ^{60}Co, ^{192}Ir, ^{125}I, ^{103}Pd,….

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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, HEBD 2012)

➔ ***Why this formalism???***

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

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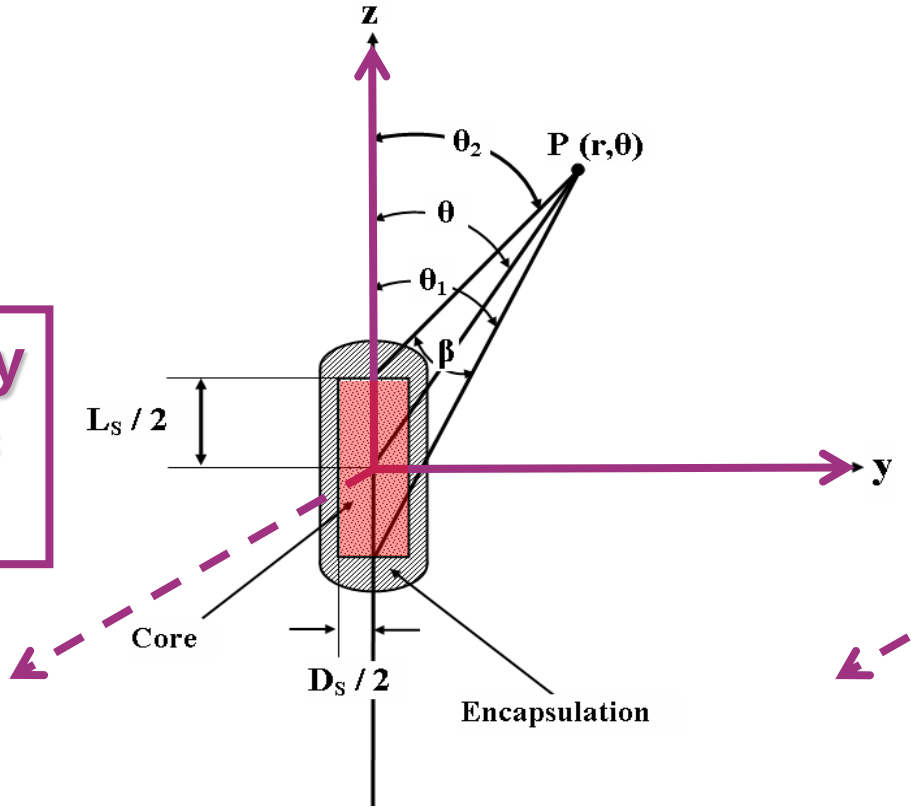
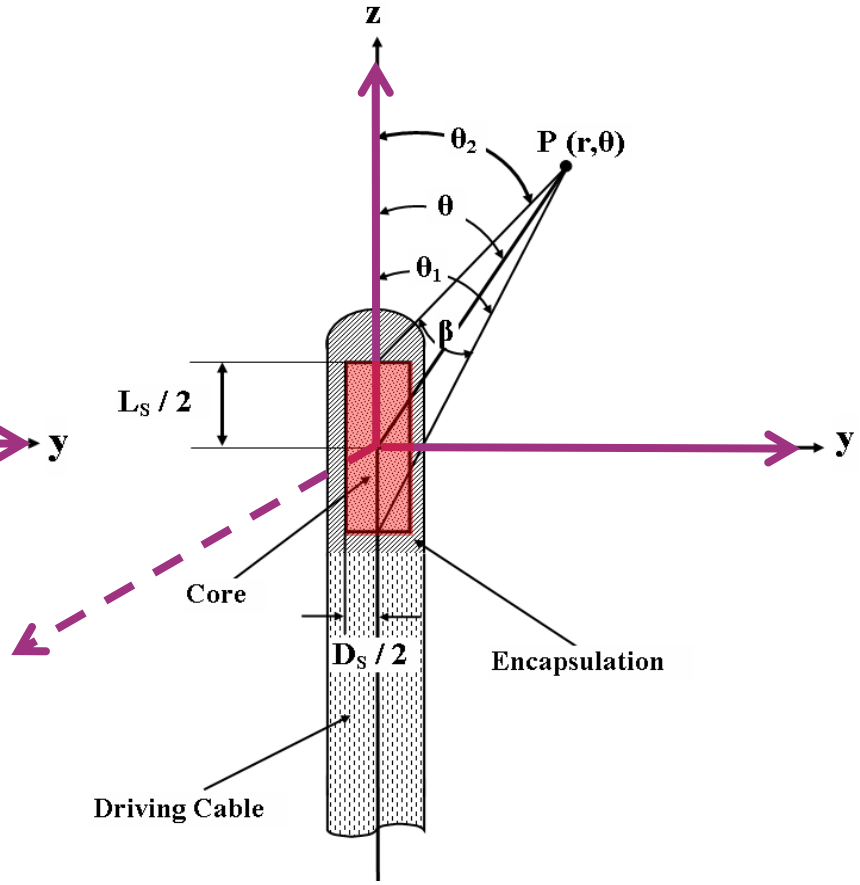
Dose calculation – AAPM-TG43: The Coordinate System

$$\dot{D}(P) = \dot{D}(\vec{r}) = \dot{D}(r, \theta)$$

Cylindrically Symmetric Source





!

Active core of the source (radioactive material)

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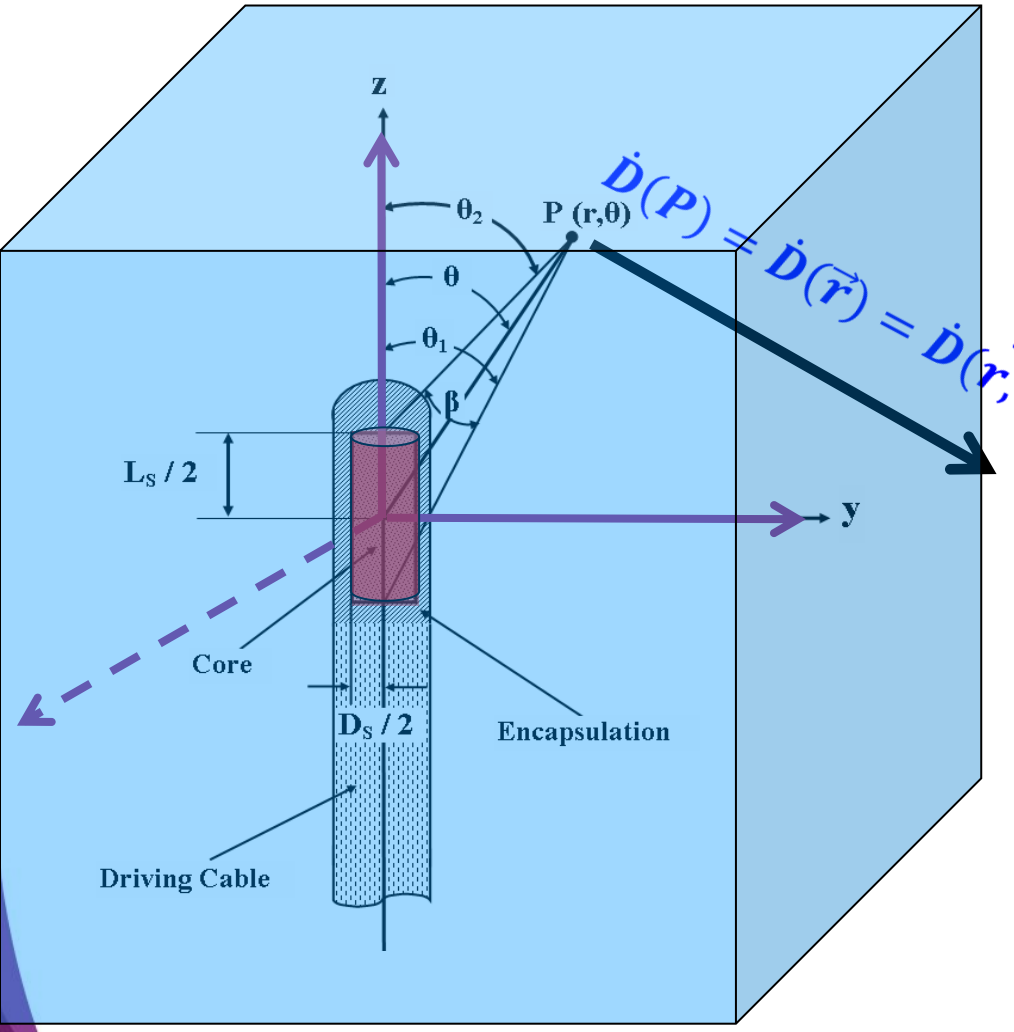
Dose calculation – AAPM-TG43: The formalism



Dose rate from a single source at a point in water-filled space (in Gy min^{-1} or cGy min^{-1} or cGy h^{-1}):
dose to water in water

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

5 x Multiplications
1 x Division

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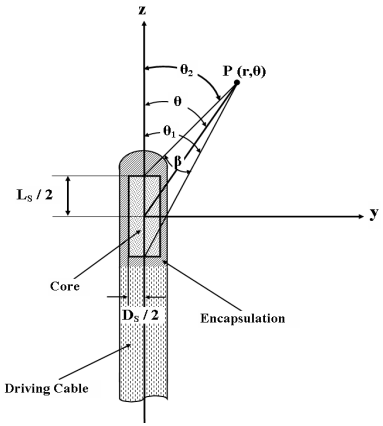
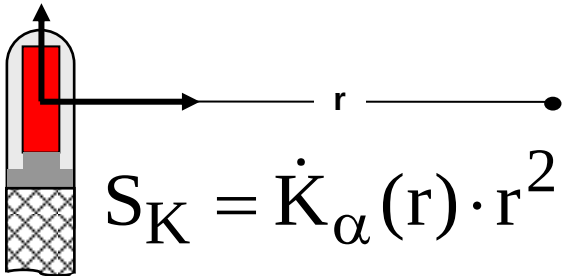
Dose calculation – AAPM-TG43: The Source Strength

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



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.
This is the actual strength of the specific source we consider.



The recommended unit for air kerma strength S_K is μGy.m².h^{-1} and has been denoted by the symbol U:

1U = 1 μGy.m².h^{-1} = 1 cGy.cm².h^{-1}

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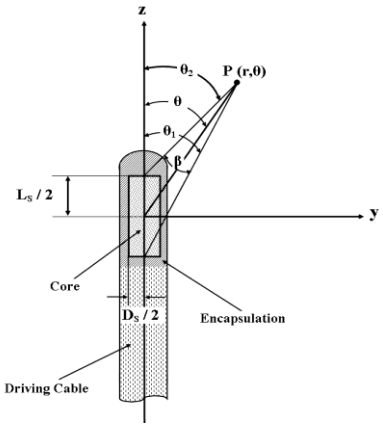
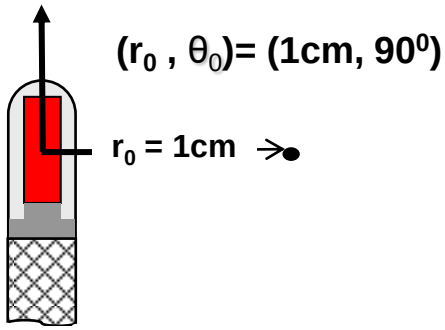
Dose calculation – AAPM-TG43: The Dose Rate Constant Λ

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



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 ($\theta_0 = 90^0$), per unit air kerma strength, S_K:



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

Λ is expressed in units of $cGy.h^{-1}.U^{-1}$ and

$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$

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Dose calculation – AAPM-TG43: The Dose Rate Constant Λ

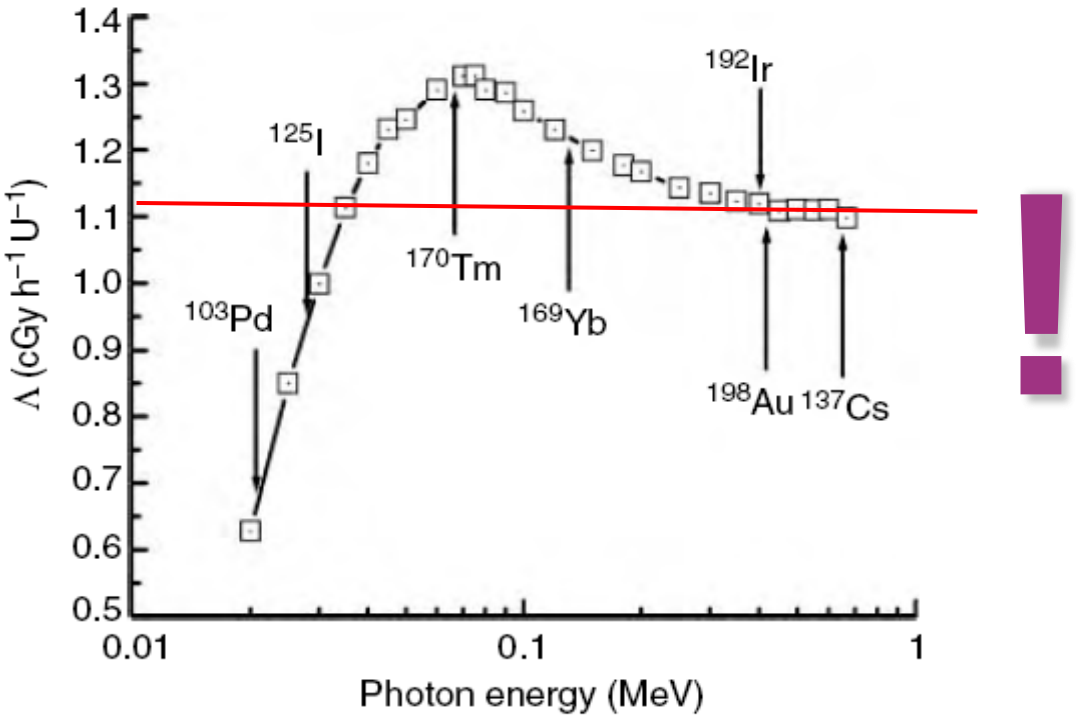

FIGURE 8.7
Energy dependence of the dose rate constant Λ expressed in cGy h^{-1} U^{-1} for monoenergetic point sources in the energy range of 0.020 to 0.700 MeV. The Λ values for the effective energies E_{eff}, see Equation 5.2, of the brachytherapy relevant radionuclides listed in Table 5.2 are indicated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

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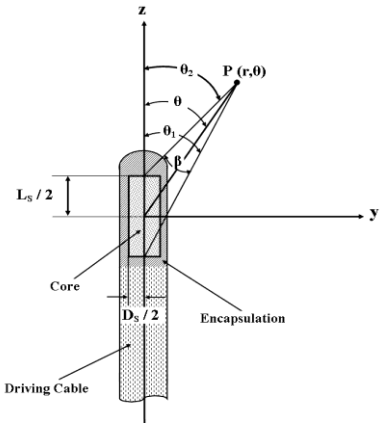
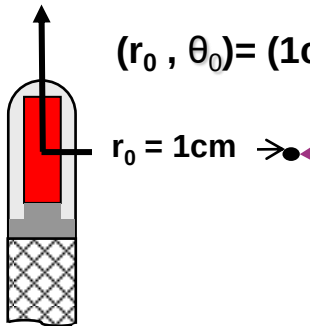
Dose calculation – AAPM-TG43: S_K and Λ

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



The product of the actual source strength S_K and the dose rate constant Λ of the source and radionuclide considered is the actual dose rate at 1 cm radial distance at $\theta = \theta_0 = 90^0$.



$$\Lambda = \frac{\dot{D}(r_0,\theta_0)}{S_K} \quad \text{and thus} \quad \dot{D}(r_0,\theta_0) = S_K . \Lambda$$

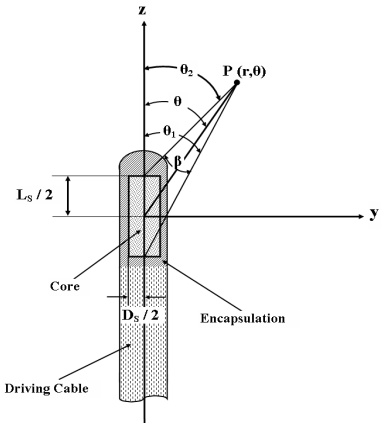
Λ is expressed in units of $cGy.h^{-1}.U^{-1}$ and

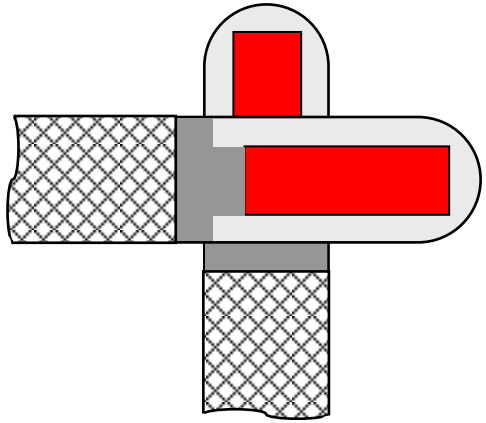
$1U = 1\ \mu Gy.m^2.h^{-1} = 1\ cGy.cm^2.h^{-1}$

Dose rate is in $cGy.h^{-1}$

Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

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





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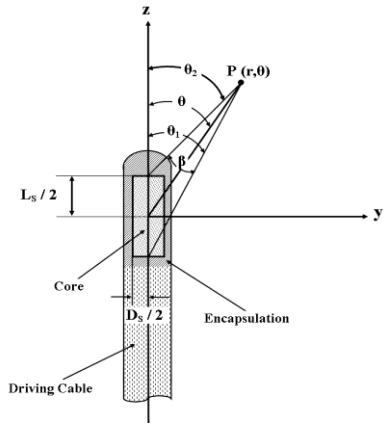
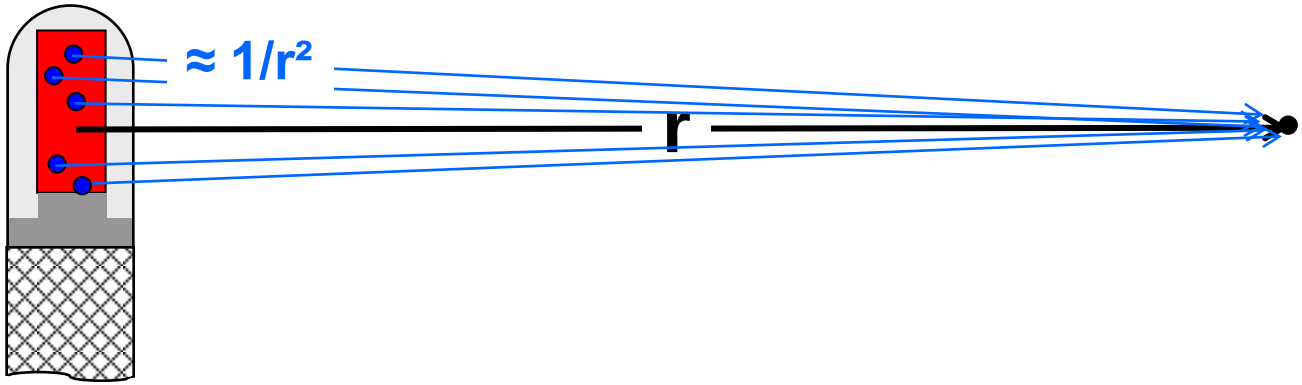
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

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



Source, S → **r** → **Dose Point, P**

≈ 1/r²



≠ 1/r²

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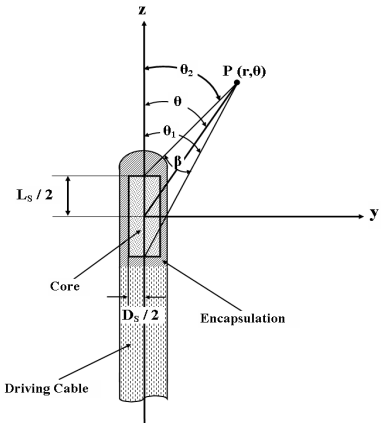
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

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



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 does not consider scatter and attenuation!**

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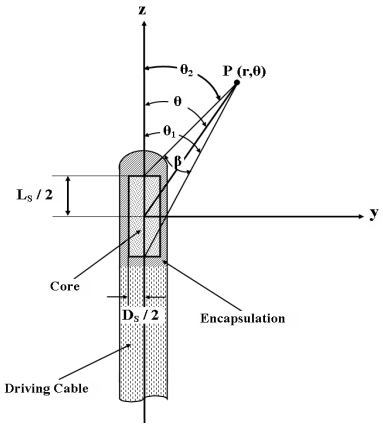
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):



I. Point Source Approximation $G_P(r,\theta)$

Source, S ⟶ **r** ⟶ **Dose Point, P**

$\approx 1/r^2$

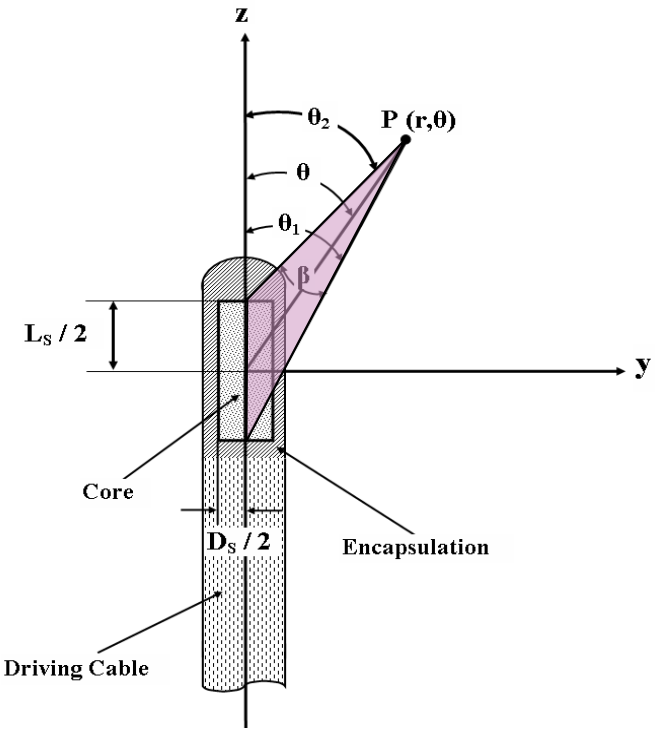
$$G_P(r,\theta) = G_P(r) = \frac{1}{r^2}$$

Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):

II. Line Source Approximation $G_L(r,\theta)$

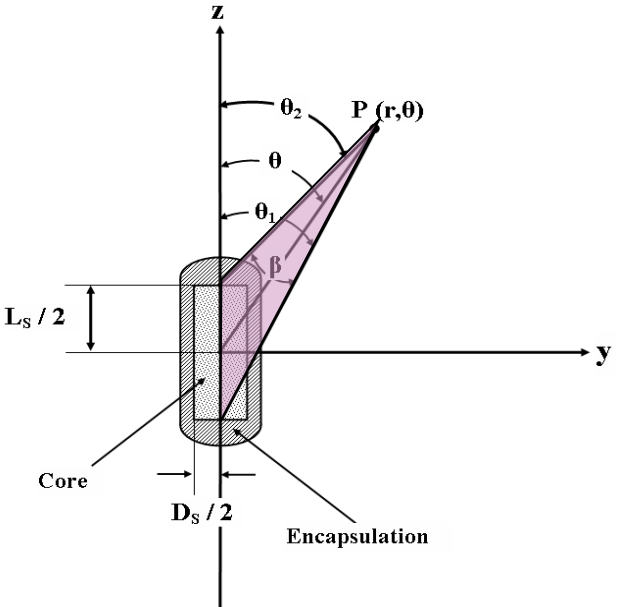
With $\beta = \theta_2 - \theta_1$

$$G_L(r,\theta) = \frac{\beta}{L_S\, r\, sin\theta}$$

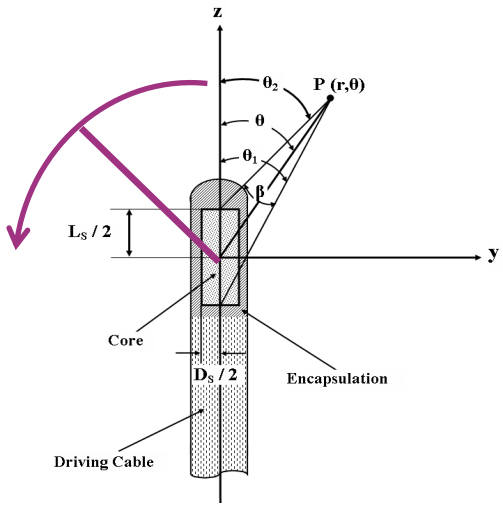


Where for $\theta = 0^\circ$ or 180°

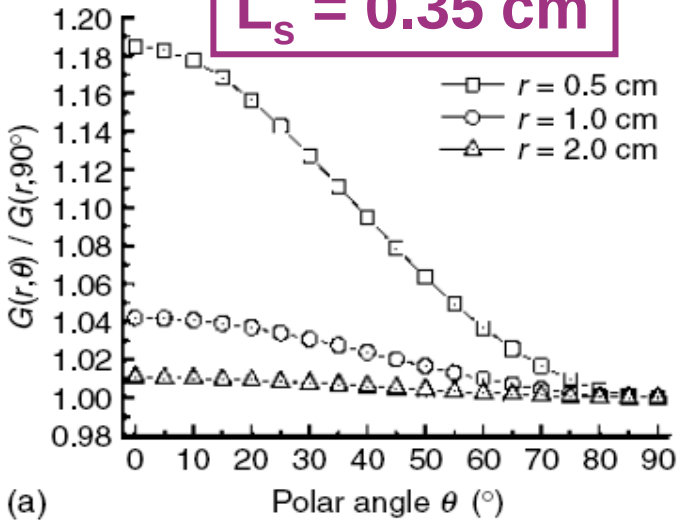
$$G_L(r,\theta) = \frac{1}{r^2 - \frac{L_s^2}{4}}$$



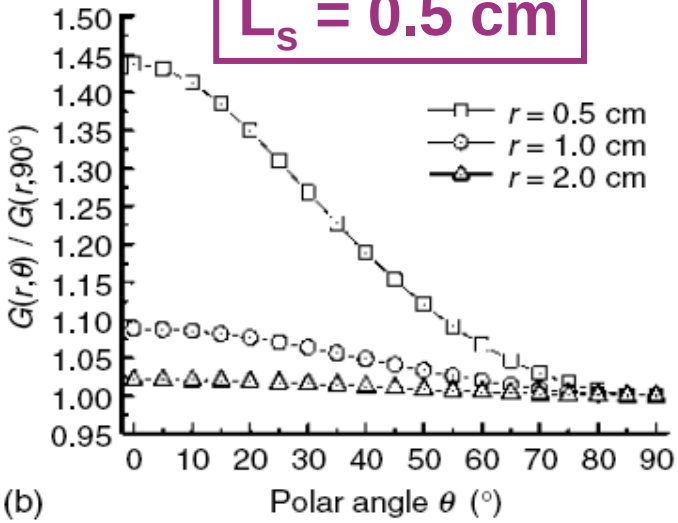
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):



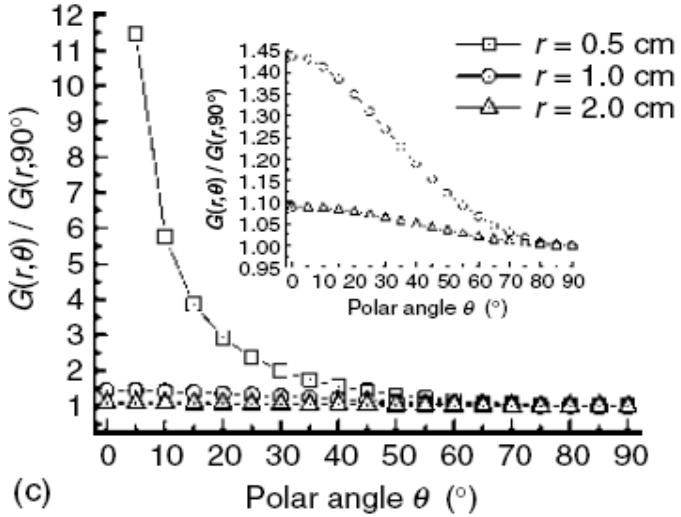
L_s = 0.35 cm



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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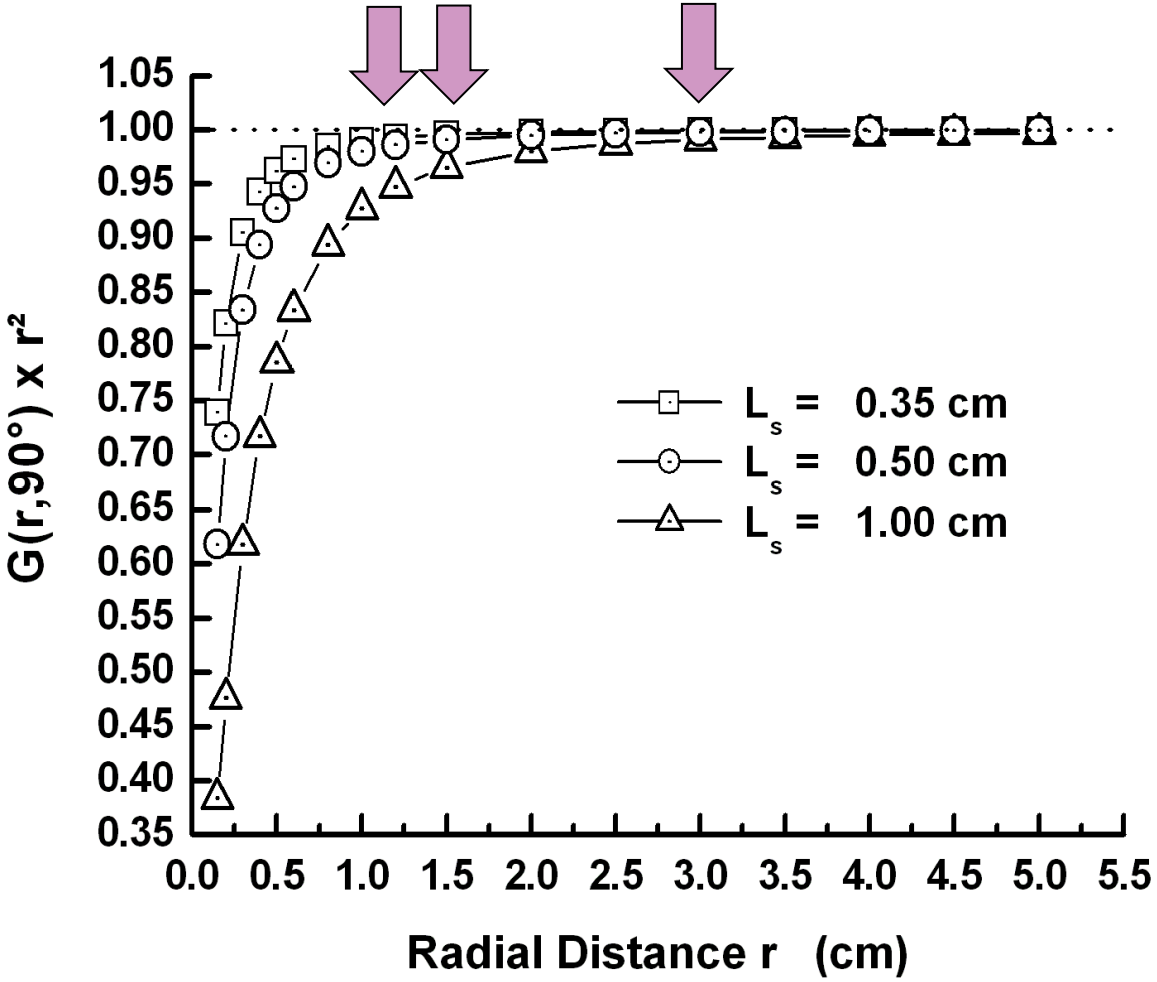
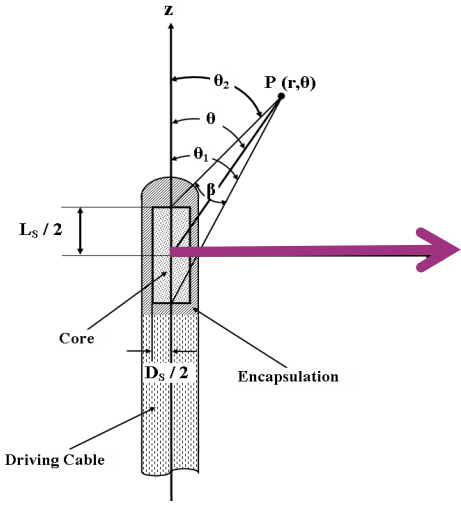
Dose calculation – AAPM-TG43: The Geometry Function G(r,θ):



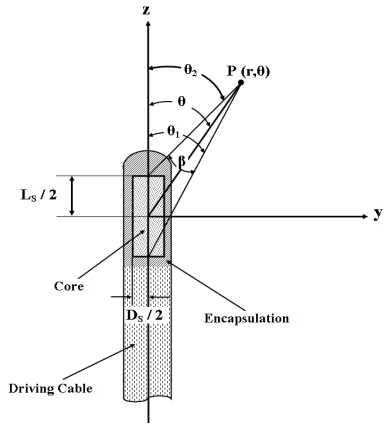


$$G(r,\theta)r^2 \approx 1.0 \;\forall_r > 3L_s$$

!

Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

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



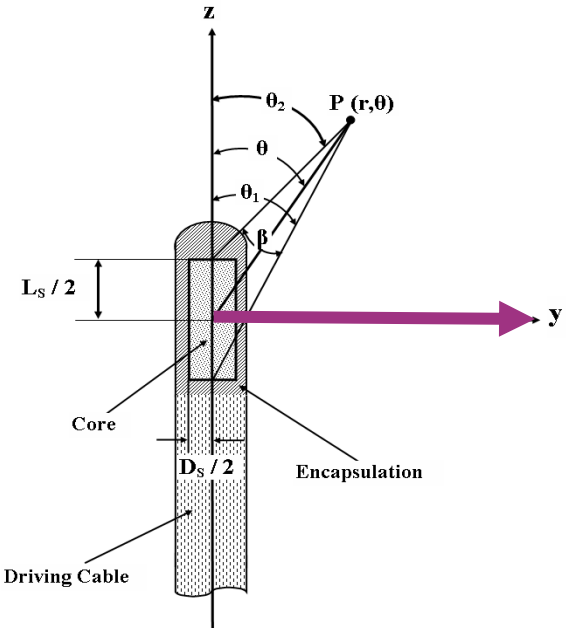
g(r): The radial dose function that considers the distance dependence of absorption and scatter of the photon rays in the water medium along the transversal axis, that is the y-axis or equivalently for **θ = 90⁰**.

g(r) is a dimensionless quantity.

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

g(r) depends in general on source design and radionuclide.

The "Inverse-Square-Law" is filtered out !!!



g(r)

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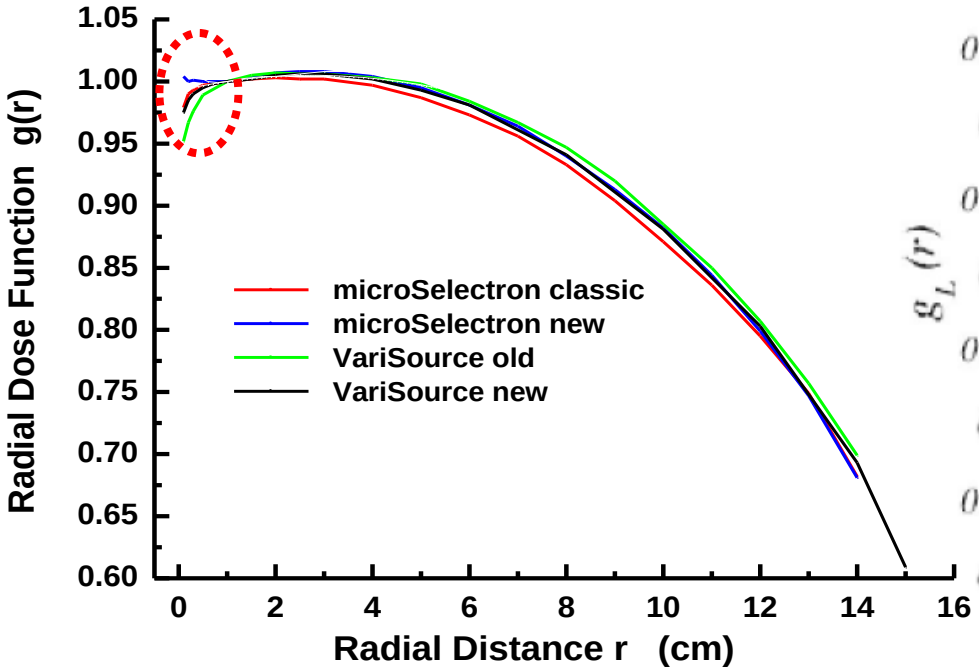
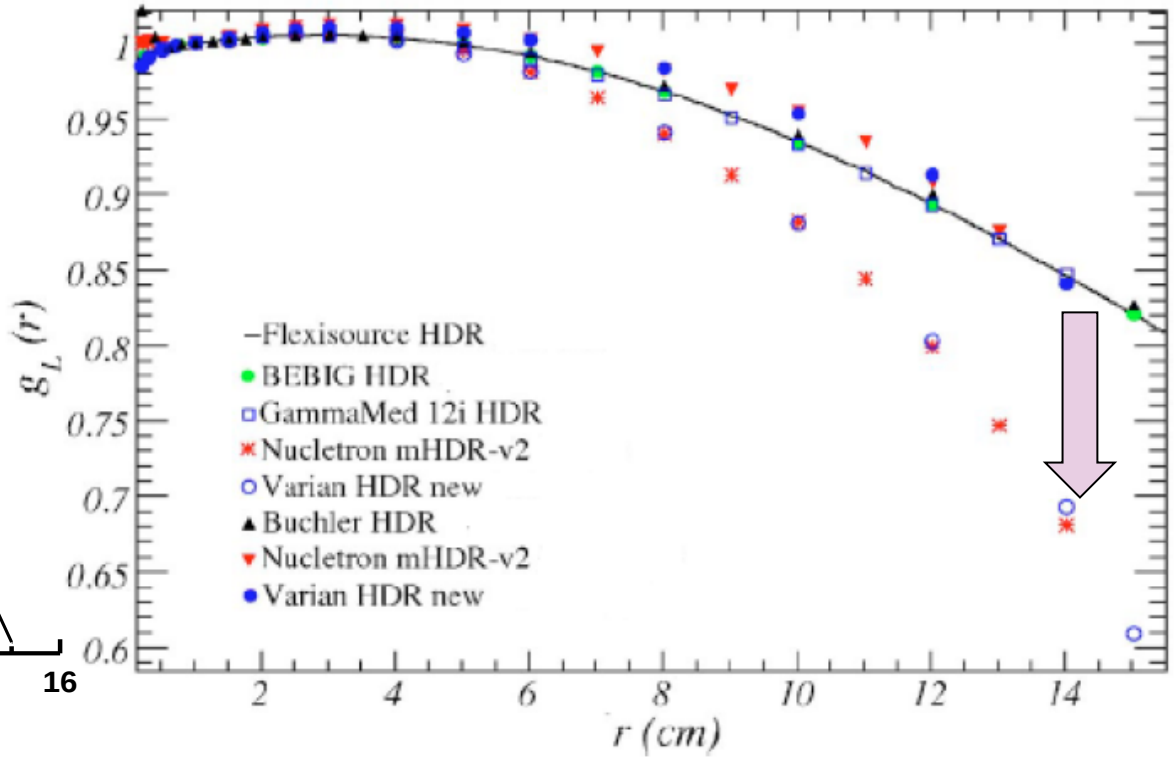
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{192}Ir – HDR Sources





?

Figure 7. Comparison of the radial dose functions for various 192Ir HDR sources.

Dosimetric characterization of a high dose rate ^{192}I source for brachytherapy application using Monte Carlo simulation and benchmarking with thermoluminescent dosimetry.
Bidmeshki et al., *Int. J. Radiat. Res., Vol. 12 No. 3, July 2014*

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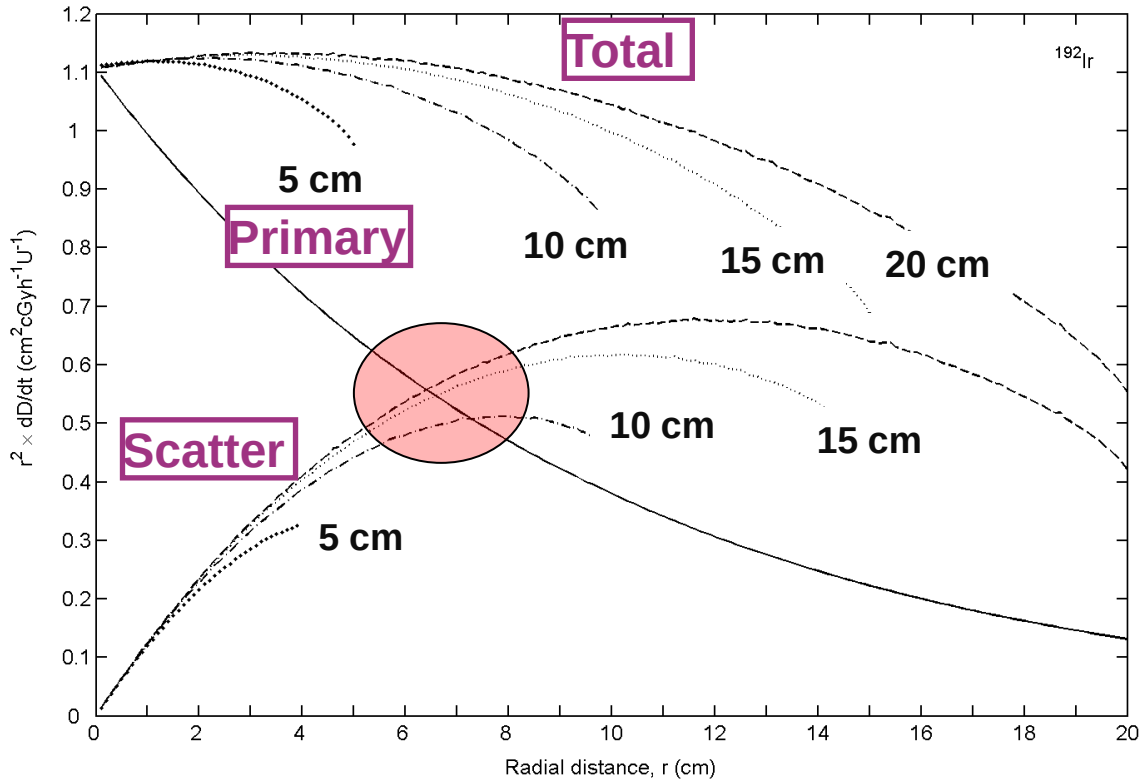
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

Attention which data sets to consider: full scatter conditions

Ideal point sources of ^{192}Ir



R= 5 cm, 10 cm, 15 cm and 20 cm radius.

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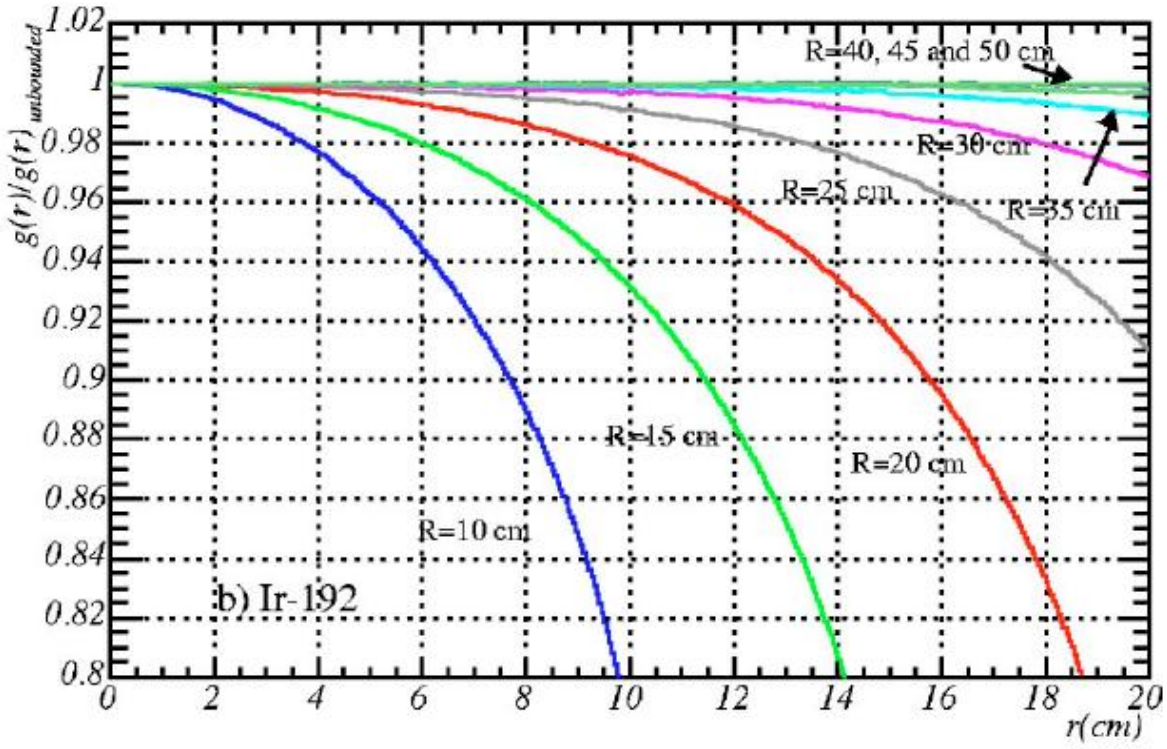
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

Attention which data sets to consider: full scatter conditions

Ideal point sources of ^{192}Ir



Ratio between g(r) for spherical phantom of size R and for an unbounded phantom.

Calatayud, Granero & Ballester, Med Phys 31 (7), 2004

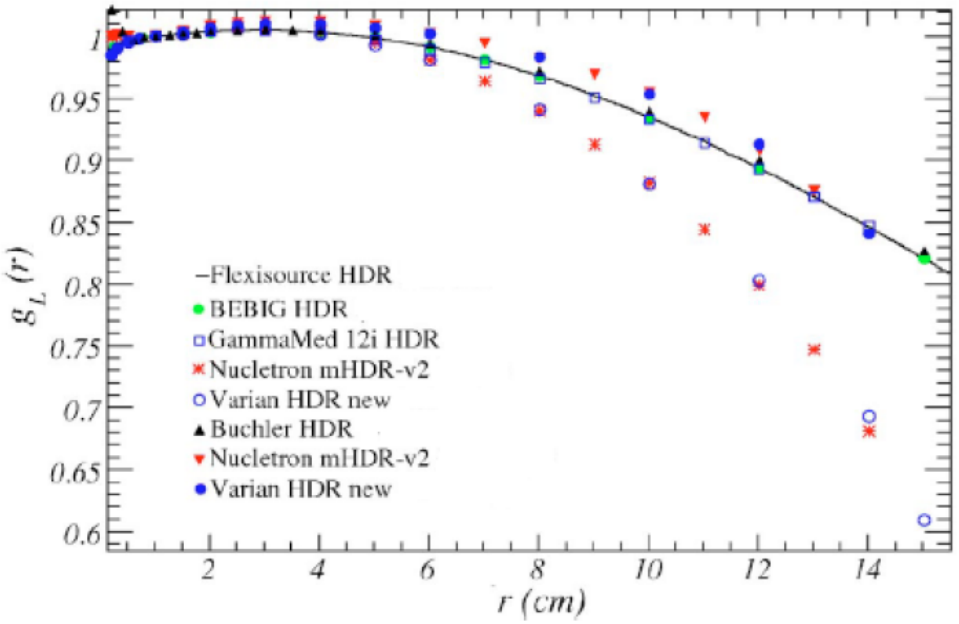


Figure 7. Comparison of the radial dose functions for various 192Ir HDR sources.

Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{192}Ir vs ^{60}Co HDR Sources

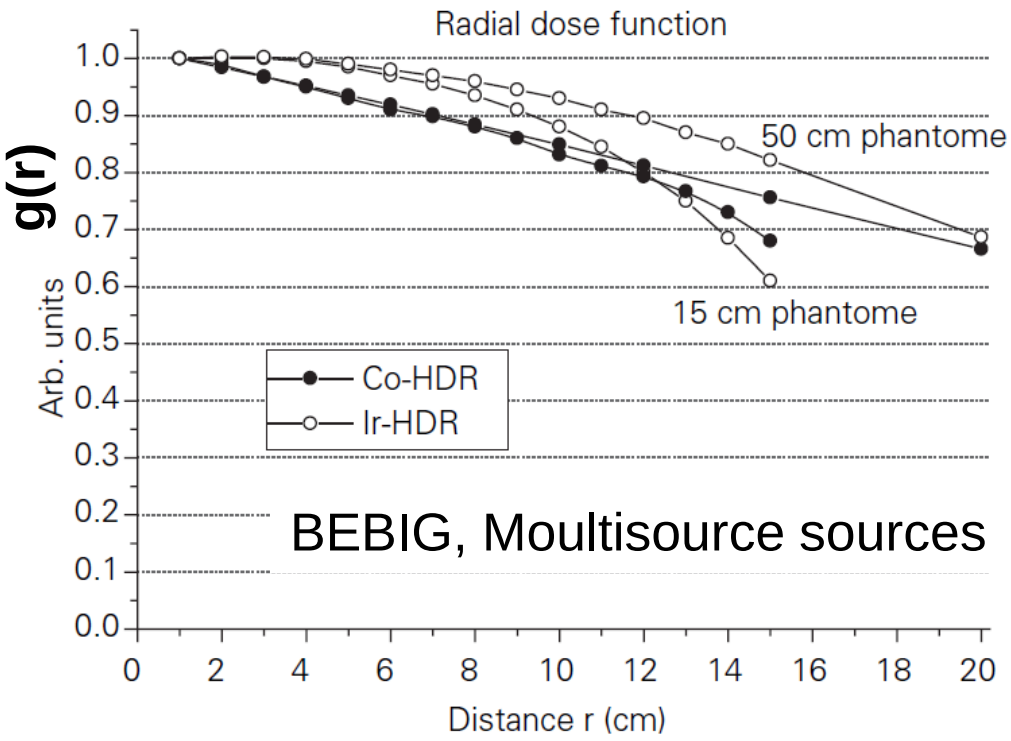


Figure 5. Influence of the phantom size on the radial dose function.

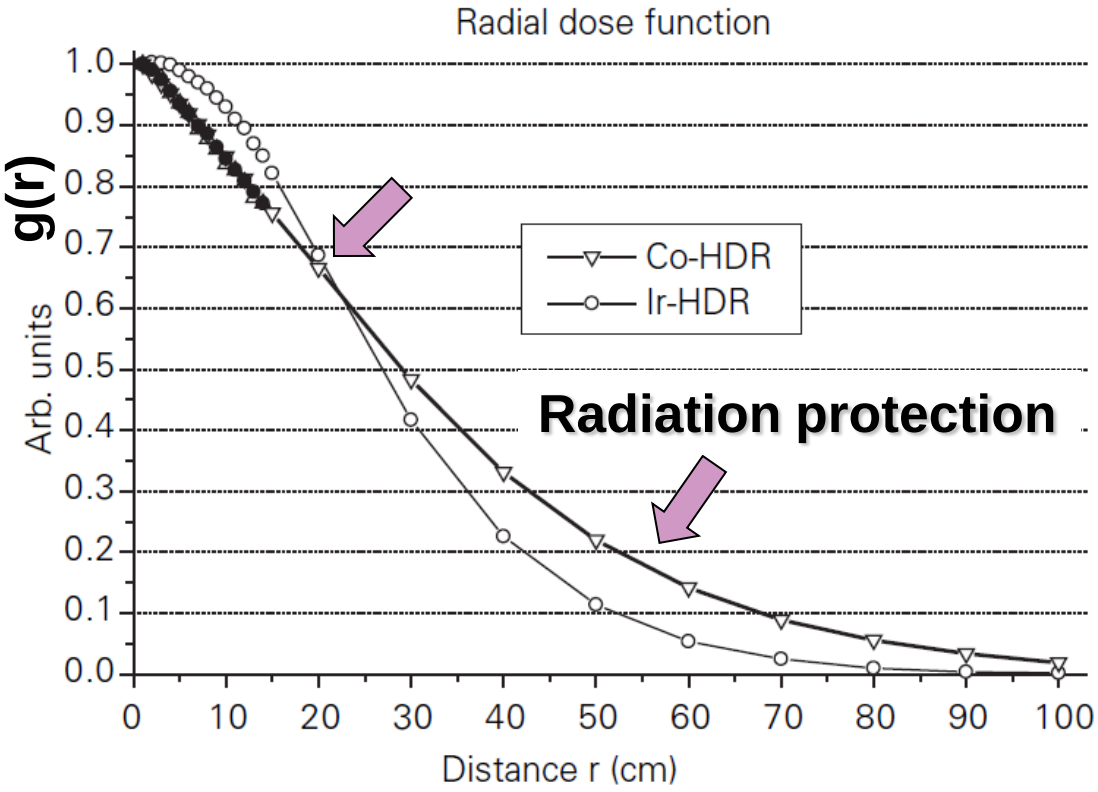


Figure 4. Radial dose function for greater distances from the source.

Comparison of ^{60}Co and ^{192}Ir sources in High Dose Rate Afterloading Brachytherapy, Richter J., Baier K., Flentje M., Strahlenther Onkol, No. 4, 2008

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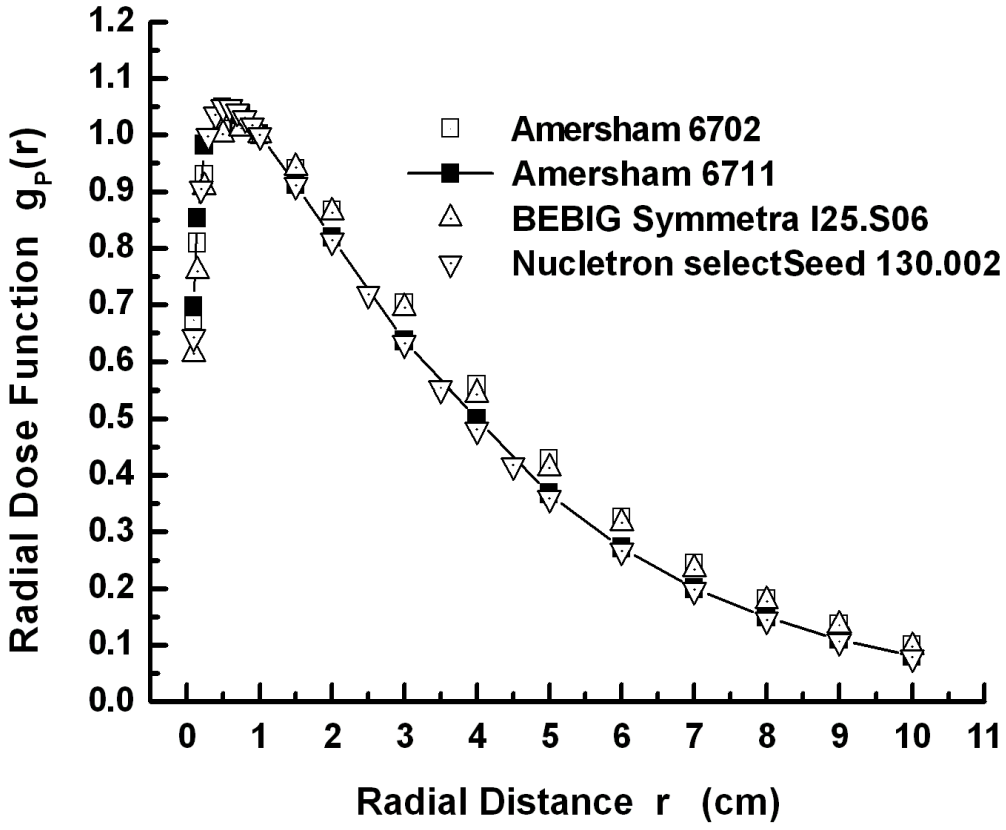
Dose calculation – AAPM-TG43: The Radial Dose Function g(r):

^{125}I seeds



Different Sources

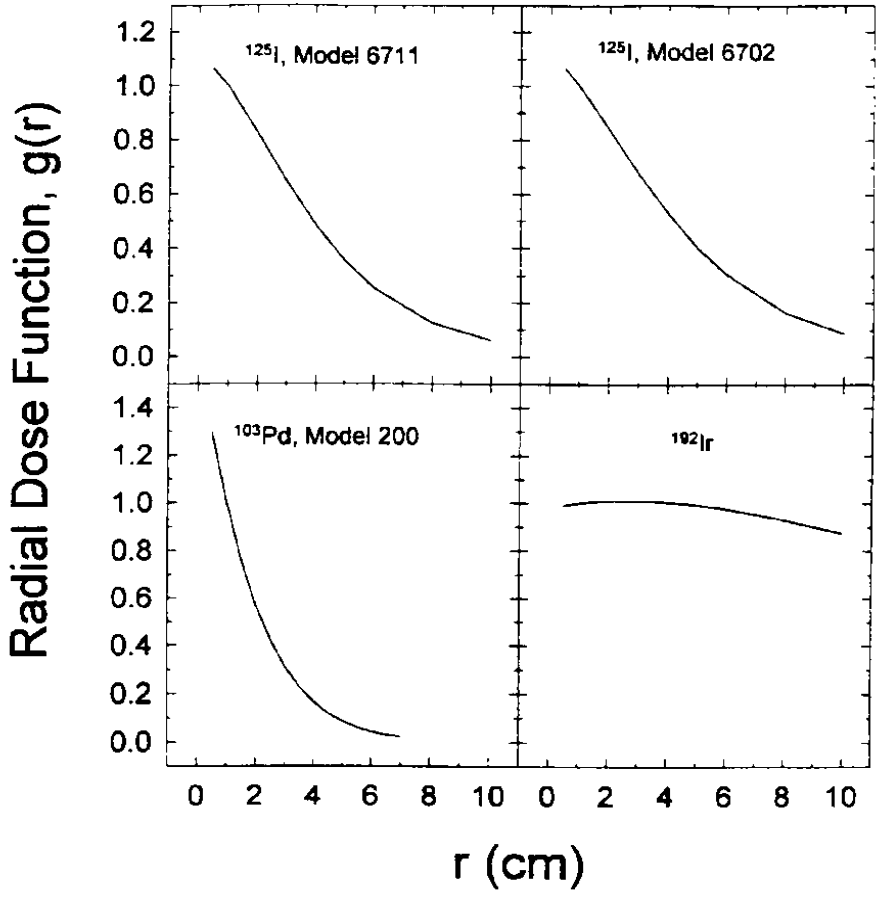


FIG. 2. Radial dose functions in a Solid Water medium for ^{103}Pd, ^{125}I, and ^{192}Ir sources.

Dose calculation – AAPM-TG43: The Anisotropy Function F(r, θ):

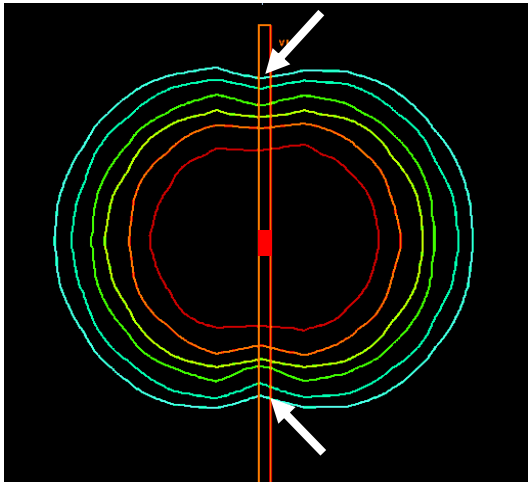
$$\dot{D}(r,\theta) = S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta)$$

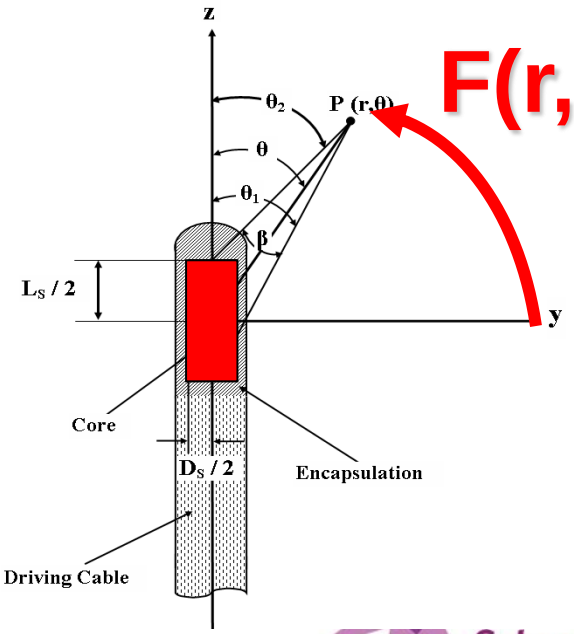
F(r, θ): The anisotropy function that considers the effect of absorption and scatter of the photons within the source active core and encapsulation material as well as part of the driving cable if any.

F(r, θ) is a dimensionless quantity.

It is always F(r, θ=90⁰) = 1.00

F(r, θ) depends in general on source design and radionuclide.





F(r, θ)

Dose calculation – AAPM-TG43: Dose, g(r) and F(r, θ):

^{192}Ir vs ^{60}Co HDR Sources

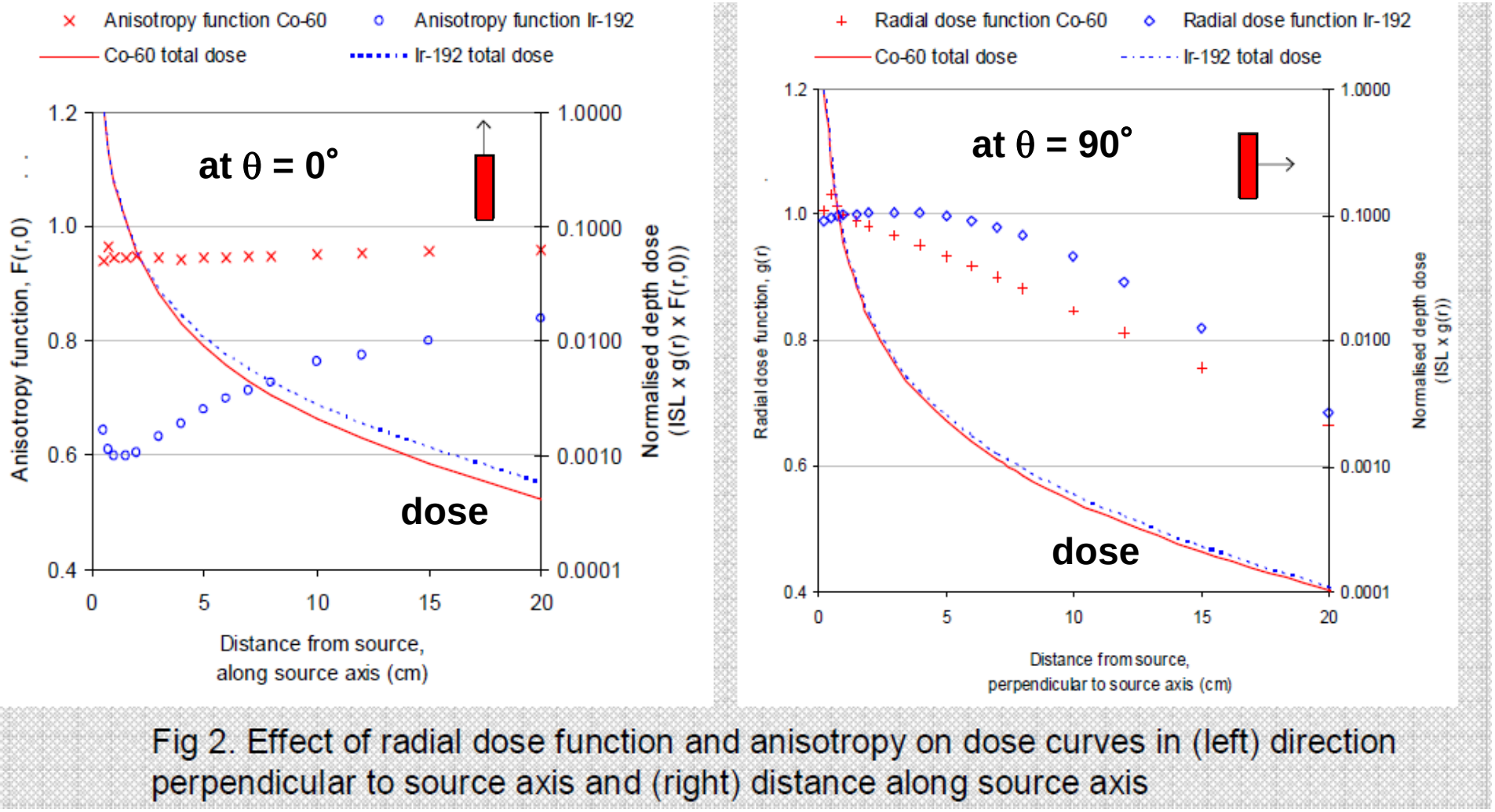


Fig 2. Effect of radial dose function and anisotropy on dose curves in (left) direction perpendicular to source axis and (right) distance along source axis

Palmer A. et al., Co-60 or Ir-192 for HDR Brachytherapy? Evaluating Source Parameters, CTV & OAR Doses, Portsmouth Hospitals, antony.palmer@porthosp.nhs.uk.

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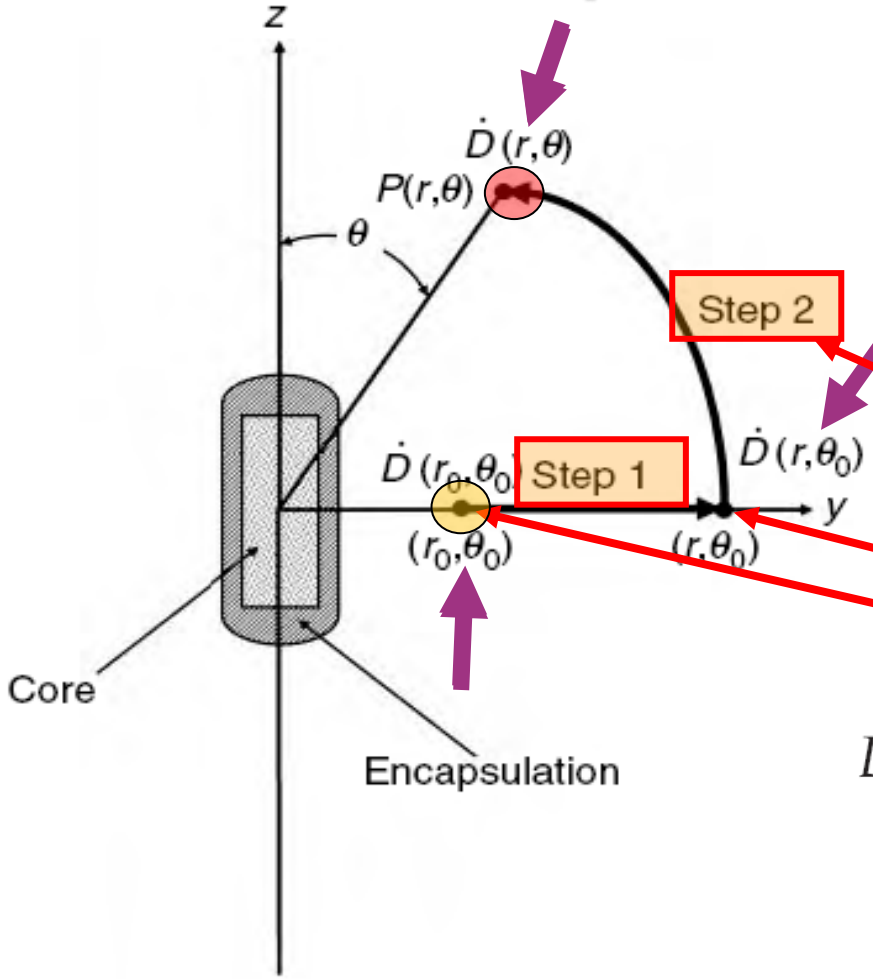
Dose calculation – AAPM-TG43

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

Reference TG43 source data

http://www.estro.org/about/governance-organisation/committees-activities/tg43

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IR-192 HDR SOURCES

Manufacturer	Source	Model	Origin	Status
Varian Medical Systems Inc. USA	GammaMed HDR	12i	HEBD	consensus
Nucletron, an Elekta company	Flexisource Ir-192	Flexisource	HEBD	consensus
Oncology Systems Inc.	M-19	M-19	HEBD	consensus
Buchler facts	Buchler HDR	G0814	HEBD	consensus
Eckert & Ziegler BEBIG GmbH, Germany	BEBIG HDR Ir-192	Ir2.A85-2	HEBD	consensus
Nucletron, an Elekta company	Nucletron mHDR	mHDR-v1 (classic)	HEBD	consensus
Nucletron, an Elekta company	Nucletron mHDR	mHDR-v2	HEBD	consensus
Varian Medical Systems Inc. USA	GammaMed HDR	Plus	HEBD	consensus
Varian Medical Systems Inc. USA	New VariSource HDR	VS2000	HEBD	consensus
Eckert & Ziegler BEBIG GmbH, Germany	BEBIG HDR Ir-192	GI192M11	HEBD	consensus
Varian Medical Systems Inc. USA	VariSource HDR	Varian(classic)	HEBD	recommended
None (generic virtual source). Visit IROC/Houston Registry	MBDCA	Generic	MBDCA-WG	

LINKS

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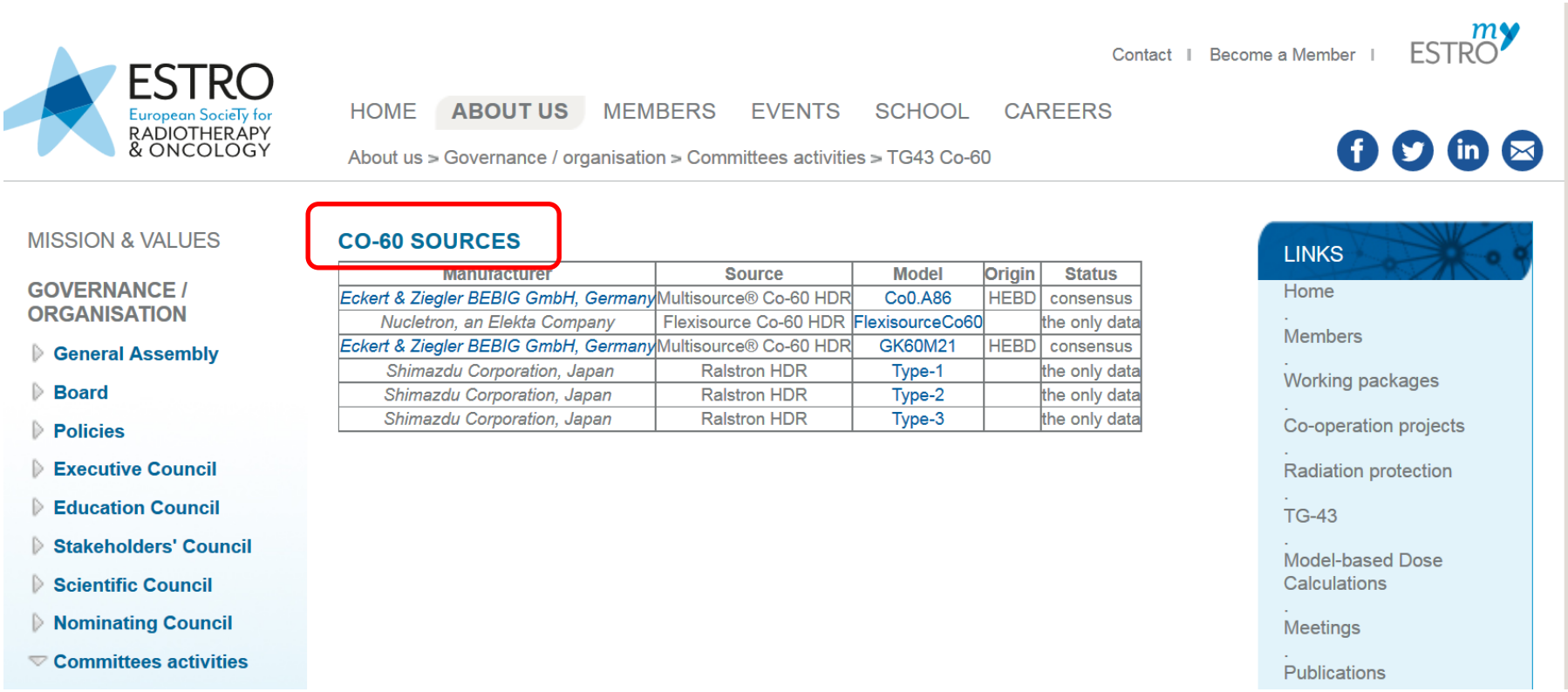
Dose calculation – AAPM-TG43

Reference TG43 source data

http://www.estro.org/about/governance-organisation/committees-activities/tg43



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- Nominating Council
- Committees activities

CO-60 SOURCES

Manufacturer	Source	Model	Origin	Status
Eckert & Ziegler BEBIG GmbH, Germany	Multisource® Co-60 HDR	Co0.A86	HEBD	consensus
Nucletron, an Elekta Company	Flexisource Co-60 HDR	FlexisourceCo60		the only data
Eckert & Ziegler BEBIG GmbH, Germany	Multisource® Co-60 HDR	GK60M21	HEBD	consensus
Shimazdu Corporation, Japan	Ralstron HDR	Type-1		the only data
Shimazdu Corporation, Japan	Ralstron HDR	Type-2		the only data
Shimazdu Corporation, Japan	Ralstron HDR	Type-3		the only data

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Dose Calculation: The TG-43 Protocol

- Dose Rate from a single Source
- **Dose from Dose Rate**
- Many Sources
- Limitations

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Dose from Dose-Rate

TG-43 derives the Initial Dose Rate

$$D(r,\theta) = \int_{t=t_0=0}^{t=T} \dot{D}(r,\theta,t_0) \cdot e^{-\lambda\cdot(t-t_0)} \cdot dt = \dot{D}(r,\theta,t_0) \cdot \left(\frac{1}{\lambda}\right) \cdot \left(1 - e^{-\lambda\cdot T}\right) = \dot{D}(r,\theta,t_0) \cdot \tau \cdot \left(1 - e^{-\frac{T}{\tau}}\right)$$

t_0: is the time of the begin of the treatment

$\tau = T_{1/2} / \ln 2$, the mean lifetime of the Radionuclide, **$\lambda = 1 / \tau$**

$T_{1/2}$: is 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 Initial Dose Rate: $T \ll \tau$

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

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 ➔ T = dwell time

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Dose from Dose-Rate

$$\tau = \frac{1}{\lambda} = \frac{T_{1/2}}{\ln 2} = 1.4427\, T_{1/2}$$

TG-43 derives the Initial Dose Rate: T >> τ

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

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.

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

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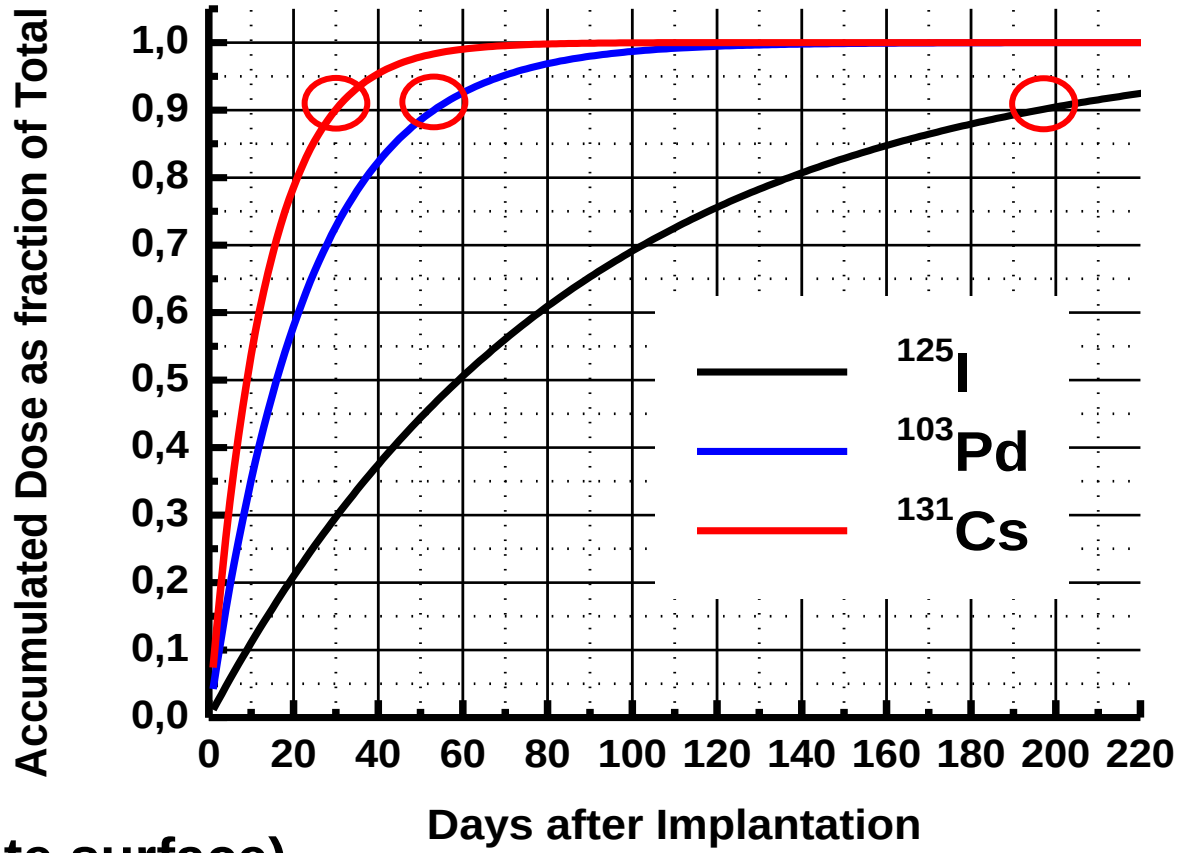
Dose from Dose-Rate: Dose Accumulation over Time

Total Dose (100% = 1.0)

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



- **Initial Dose Rate (at the prostate surface)**
  30 cGy.h^{-1} for ^{131}Cs
  versus
  7 cGy.h^{-1} for ^{125}I and 20 cGy.h^{-1} for ^{103}Pd

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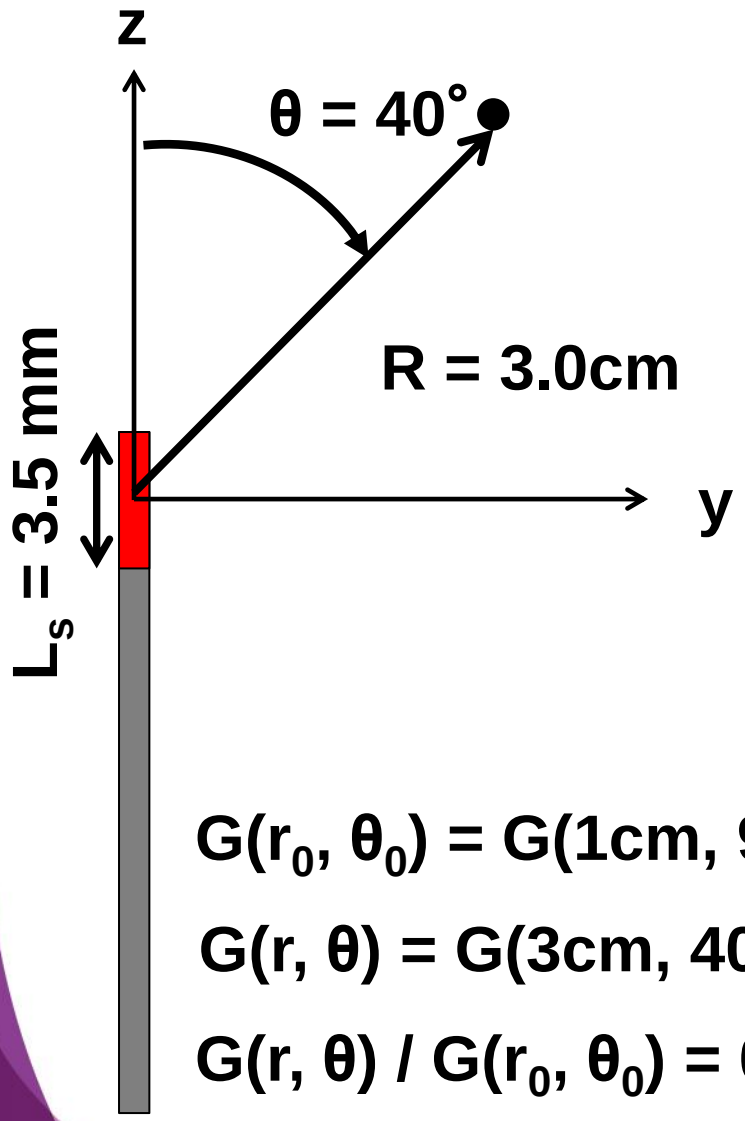
Practical Example: Bebig ^{192}Ir-HDR Source



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

S_K = 40.000 U

Λ = 1,108 cGy/(hU)

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

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

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

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

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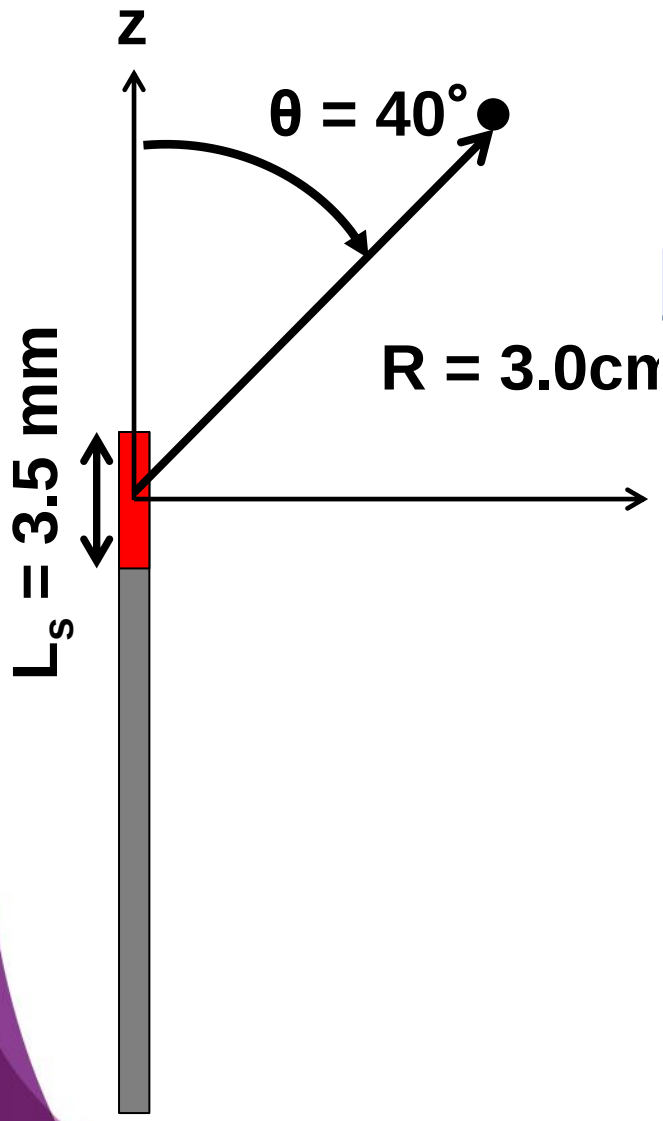
Practical Example: Bebig ^{192}Ir-HDR Source



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

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

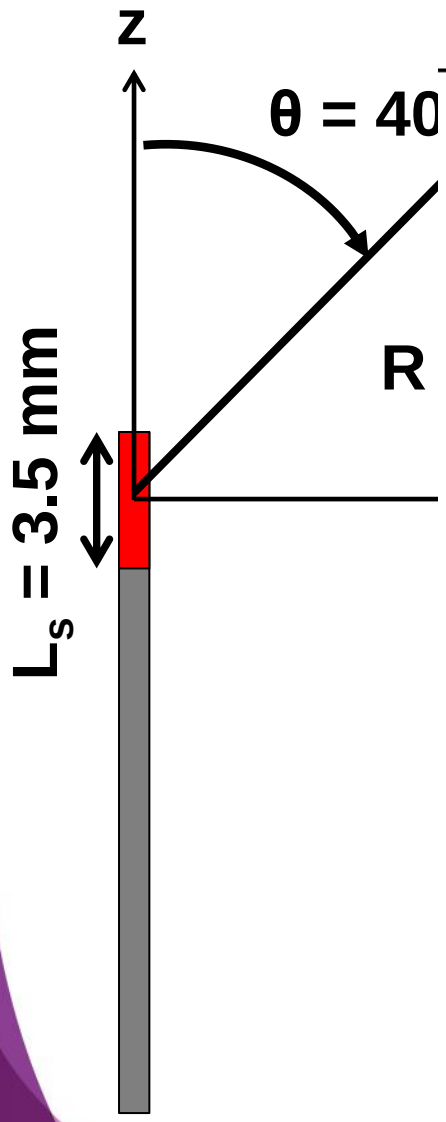
Range: 0.25 to 20 cm

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	0.995	0.995	0.994	0.995	0.996	0.995
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, 40º) = 0.951

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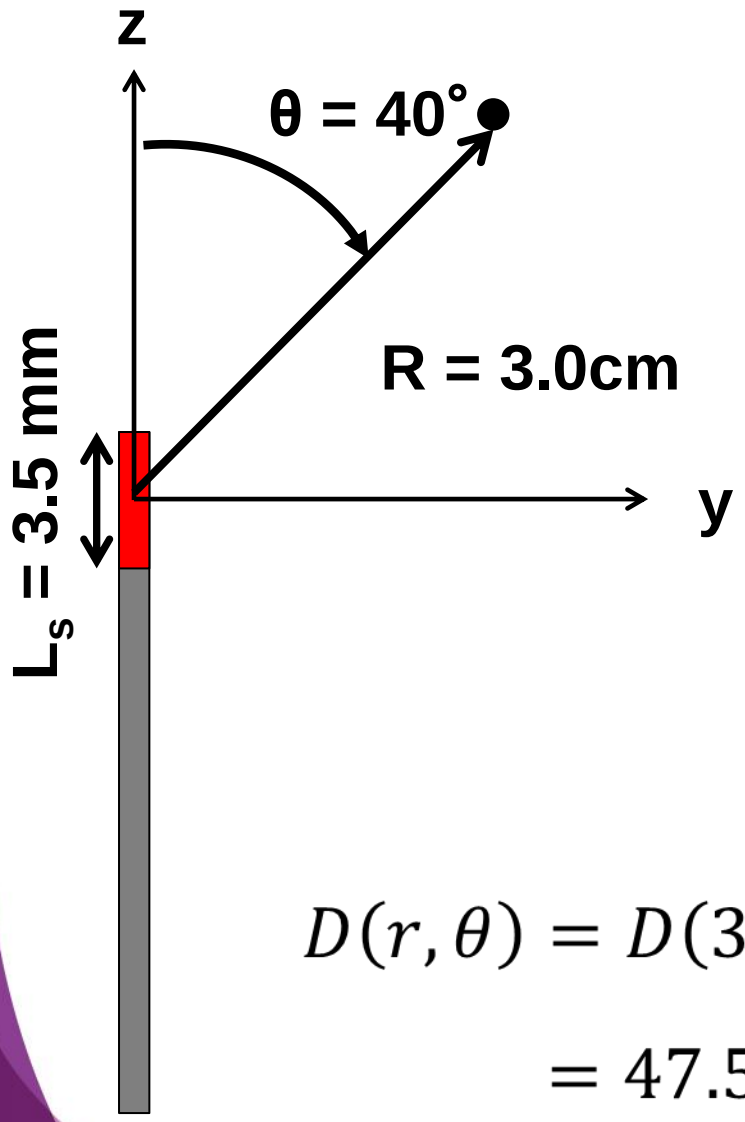
Practical Example: Bebig ^{192}Ir-HDR Source



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

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

$$D(r,\theta) = D(3cm, 40^0) = 4{,}755.05 \frac{cGy}{h}$$

$$= 47.551 \frac{Gy}{h} = 0.793 \frac{Gy}{min}$$

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Some Thoughts …

- Dose Rate from a single Source
- Dose from Dose Rate
- Many Sources
- Limitations

without formulas …

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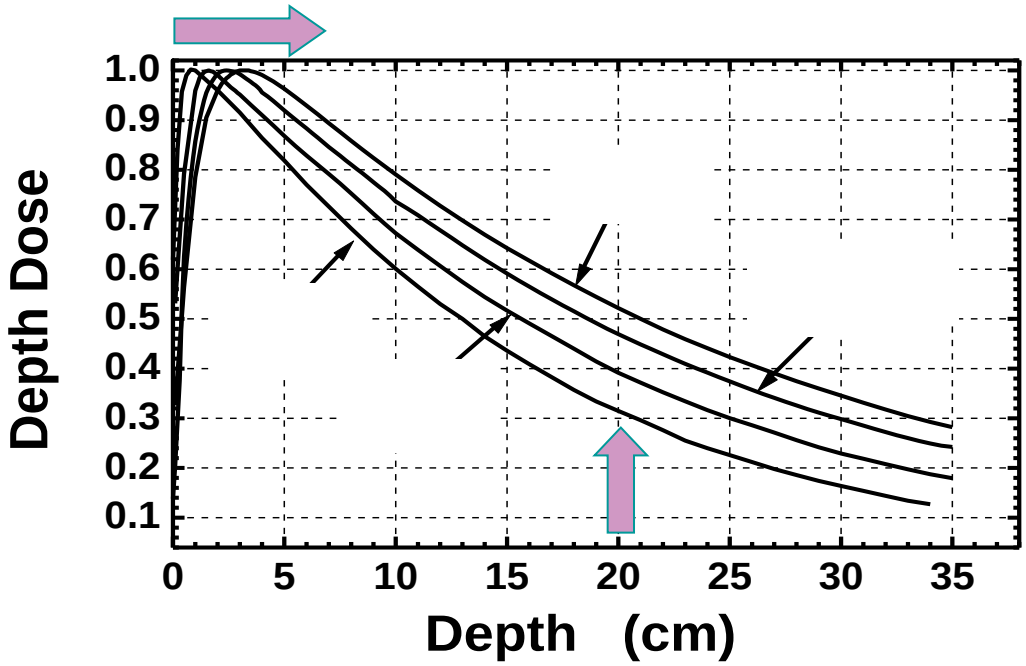
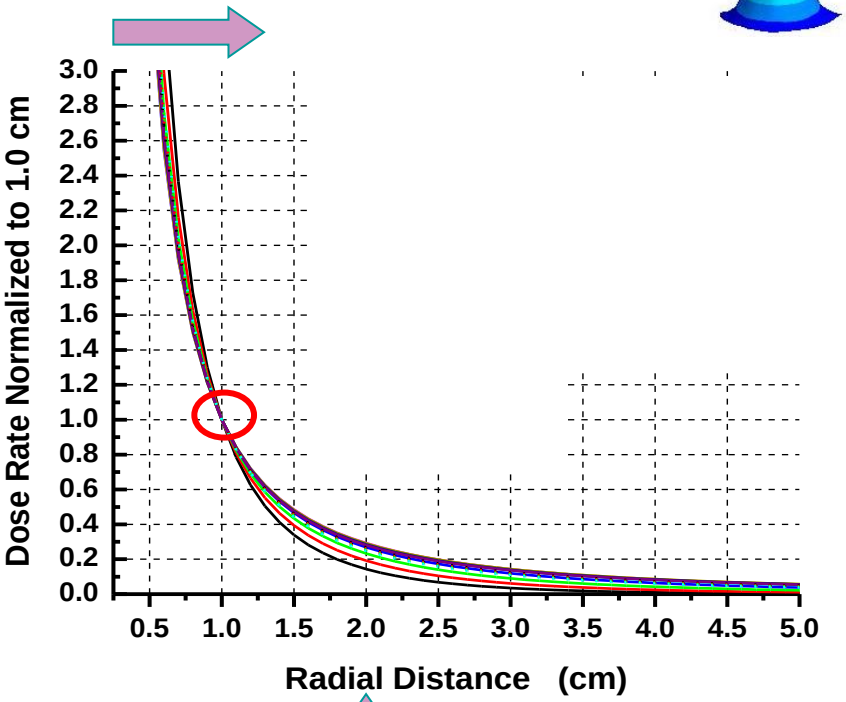
Depth Dose Curve: BRT *versus* EBRT

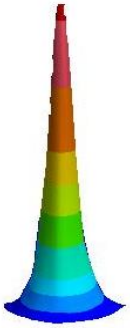
EBRT: Photonen 4, 6, 10 & 18MV ???

BRT: Photonen 20, 30, 40, 60, … 600keV ???

ERT **10 : 1** **BRT**

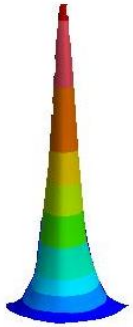




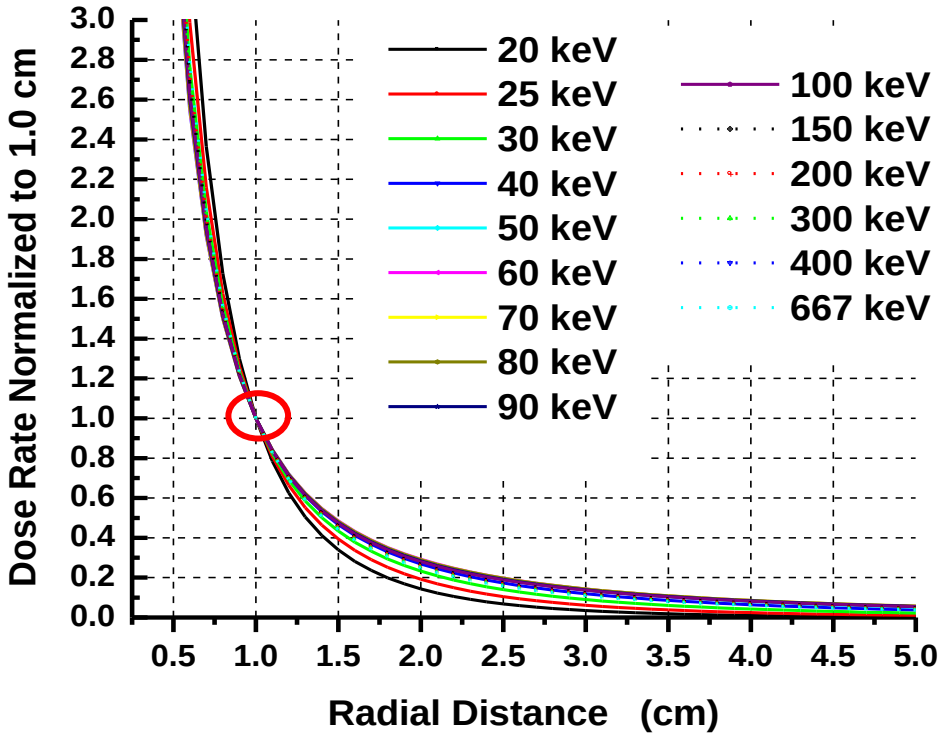


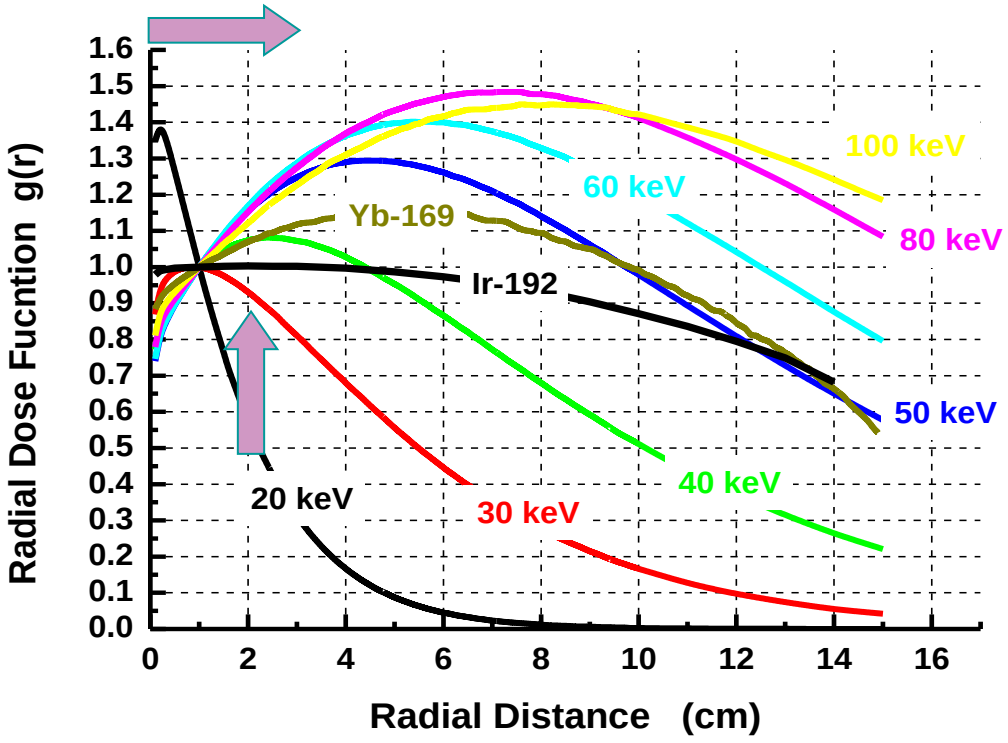
Depth Dose Curve: BRT *versus* EBRT

BRT



BRT: Physics Scatter / absorption





Dose Calculation: The TG-43 Protocol

- Dose Rate from a single Source
- Dose from Dose Rate
- **Many Sources**
- Limitations

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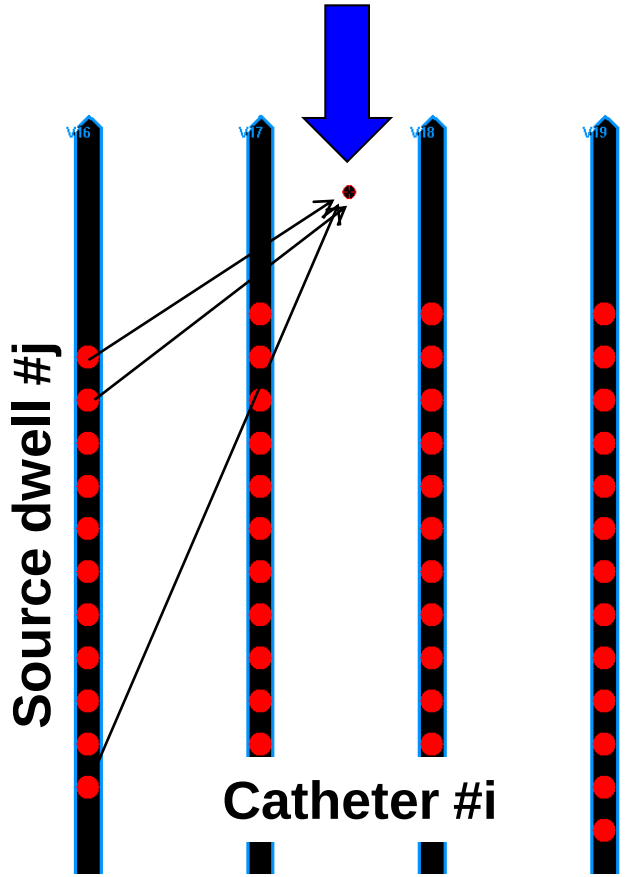
Complexity …..

Many Catheters/Needles, Many Sources …

$$\boldsymbol{D(P) = D(\vec{r}) = ?}$$



$$D(P) = \sum_{i=1}^{N_{catheters}} \sum_{j=1}^{M_{sources,i}} t_{i,j}\dot{D}_{i,j}(P)$$

$$with\ \dot{D}_{i,j}(P) = \left\{ S_K \Lambda \frac{G(r,\theta)}{G(r_0,\theta_0)} g(r) F(r,\theta) \right\}_{P,i,j}$$

Superposition method

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Dose / Dose Rate Calculation at a Point

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

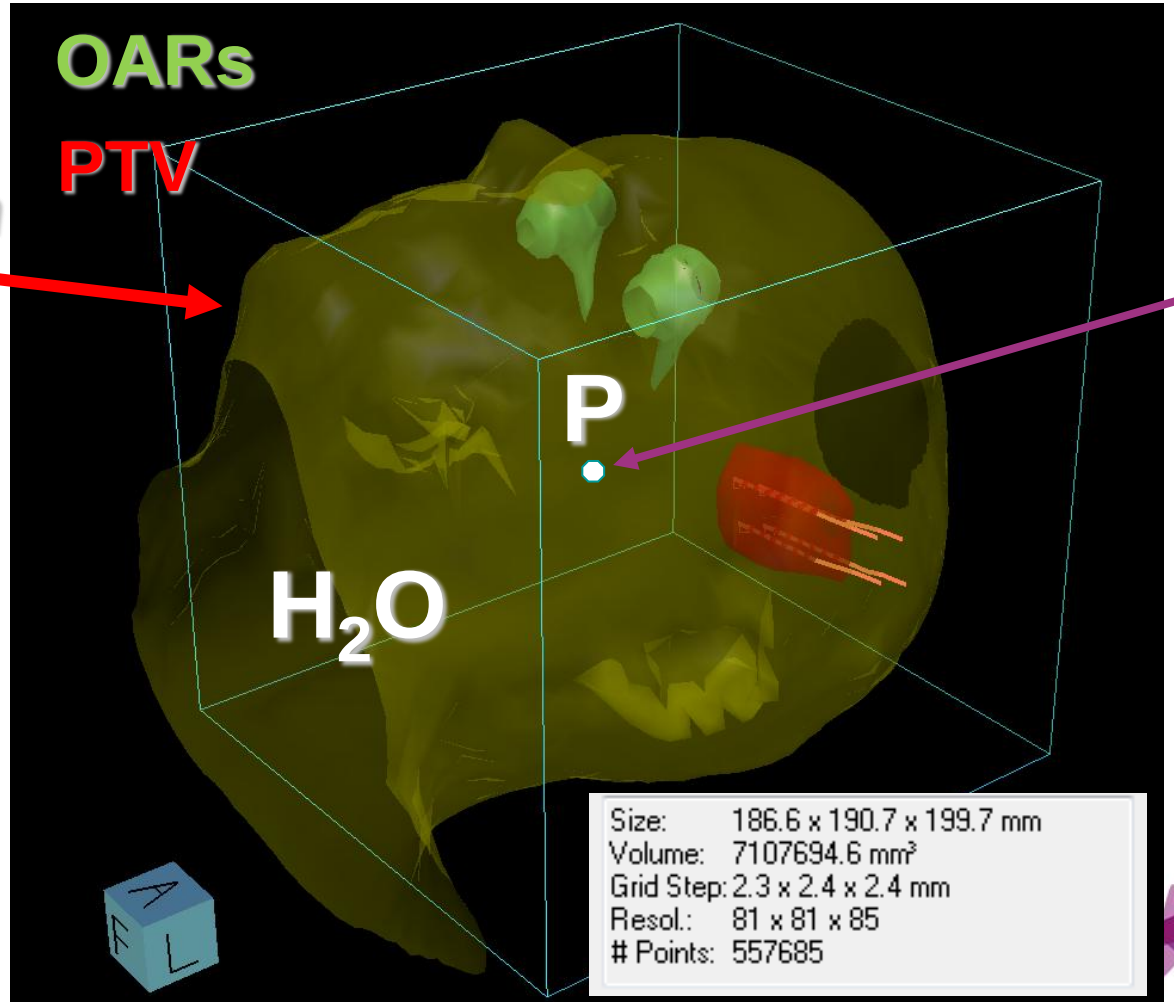
Superposition

^{192}Ir

^{60}Co

^{169}Yb

…



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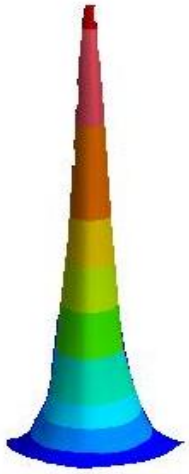
2D Dose Distribution

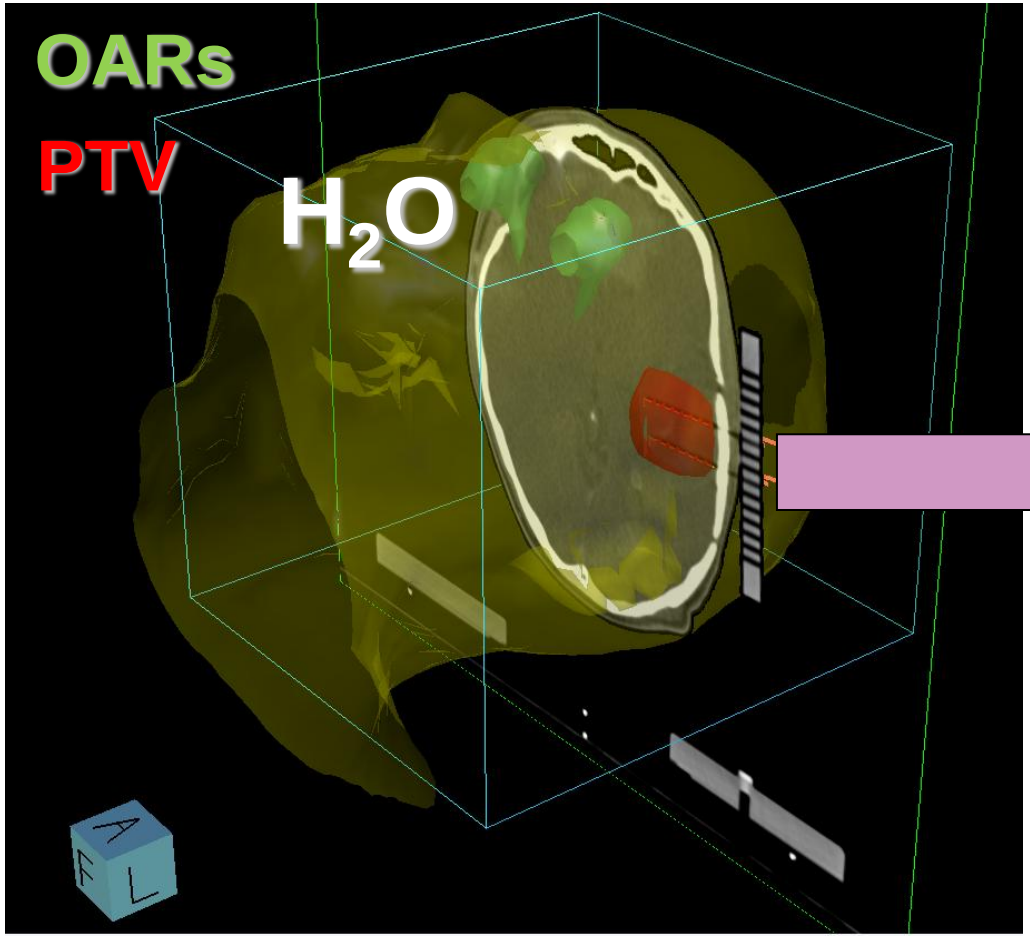


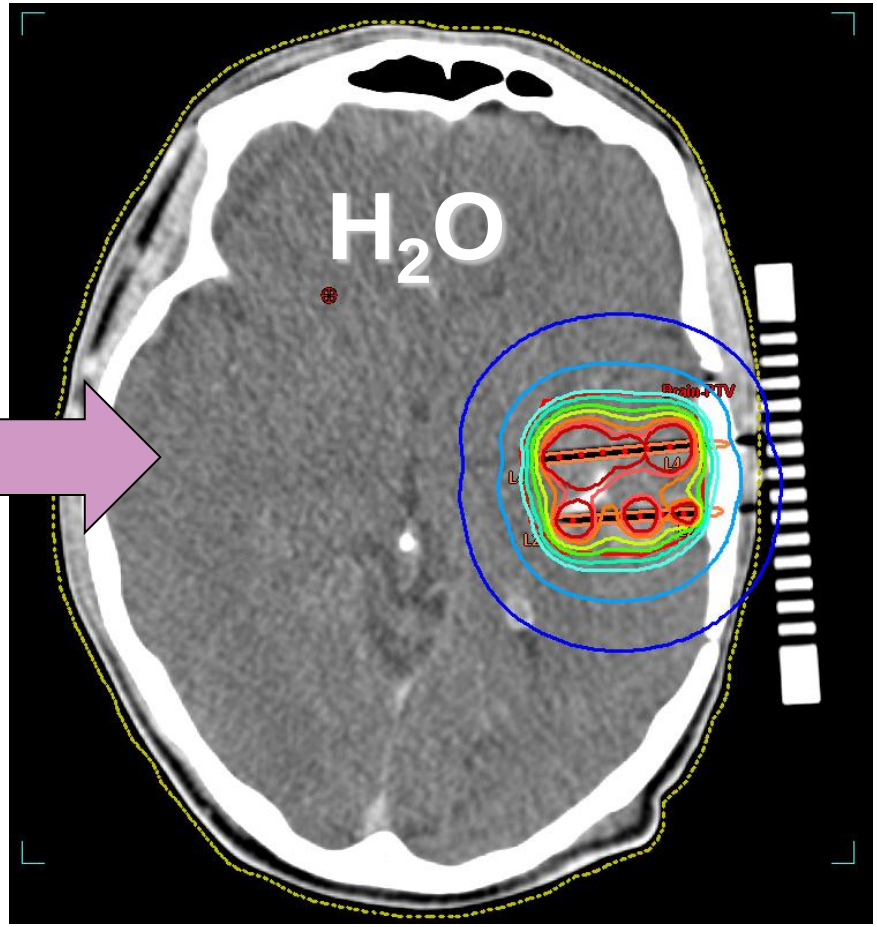
^{192}Ir

^{60}Co

^{169}Yb

...





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Dose Calculation: The TG-43 Protocol

- Dose Rate from a single Source
- Dose from Dose Rate
- Many Sources
- **Limitations**

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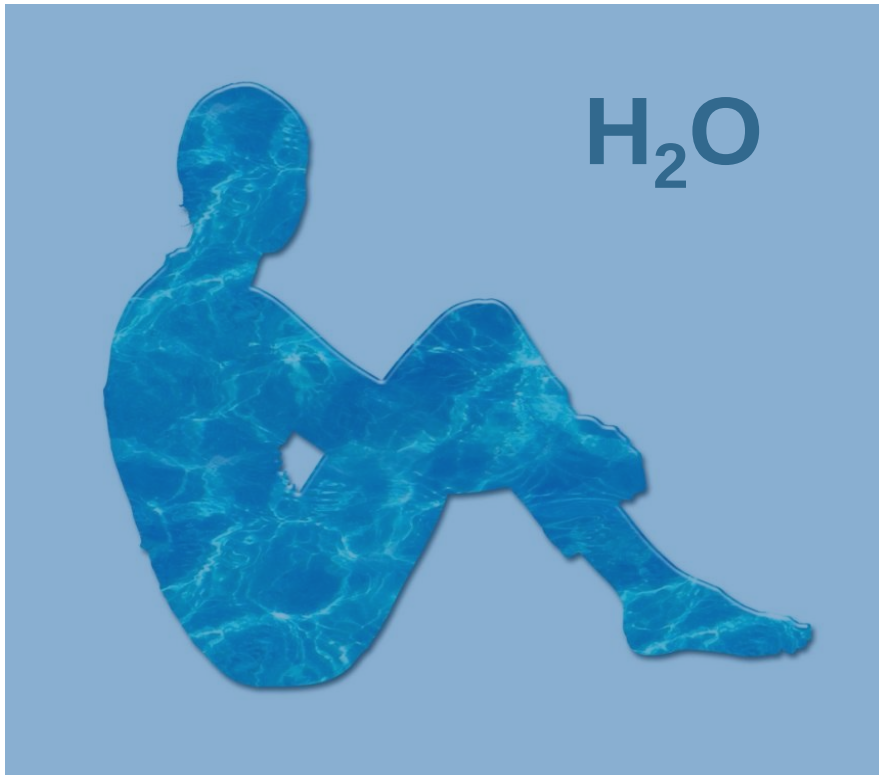
Limitations of TG-43 based Dose Calculation

Assumptions !!!



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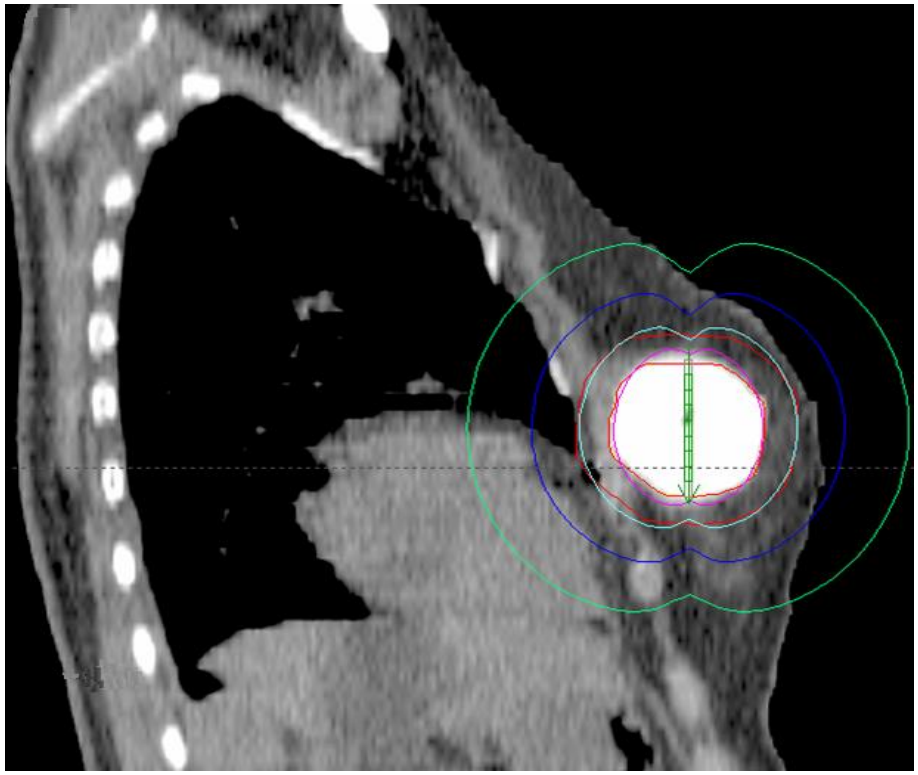

Homogeneous water medium !

Full scatter conditions !

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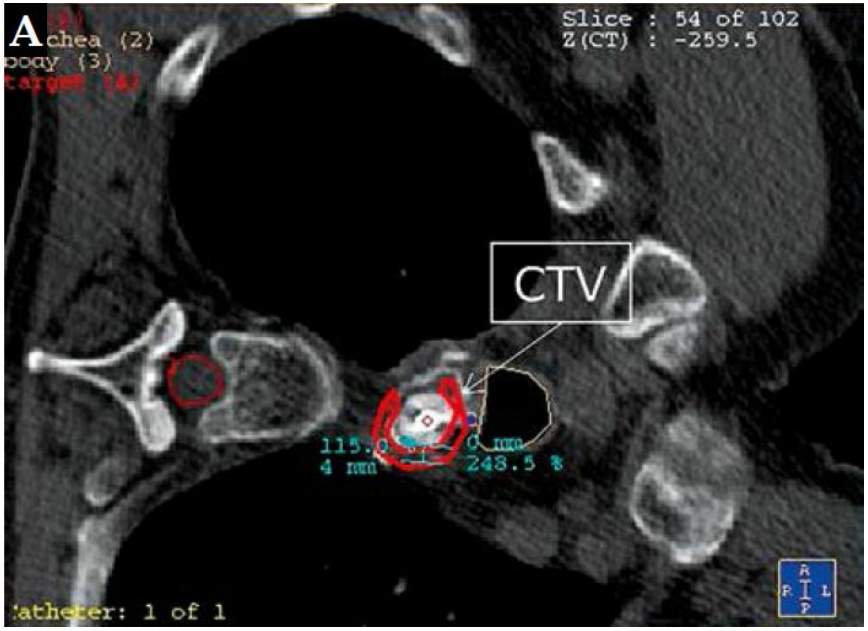
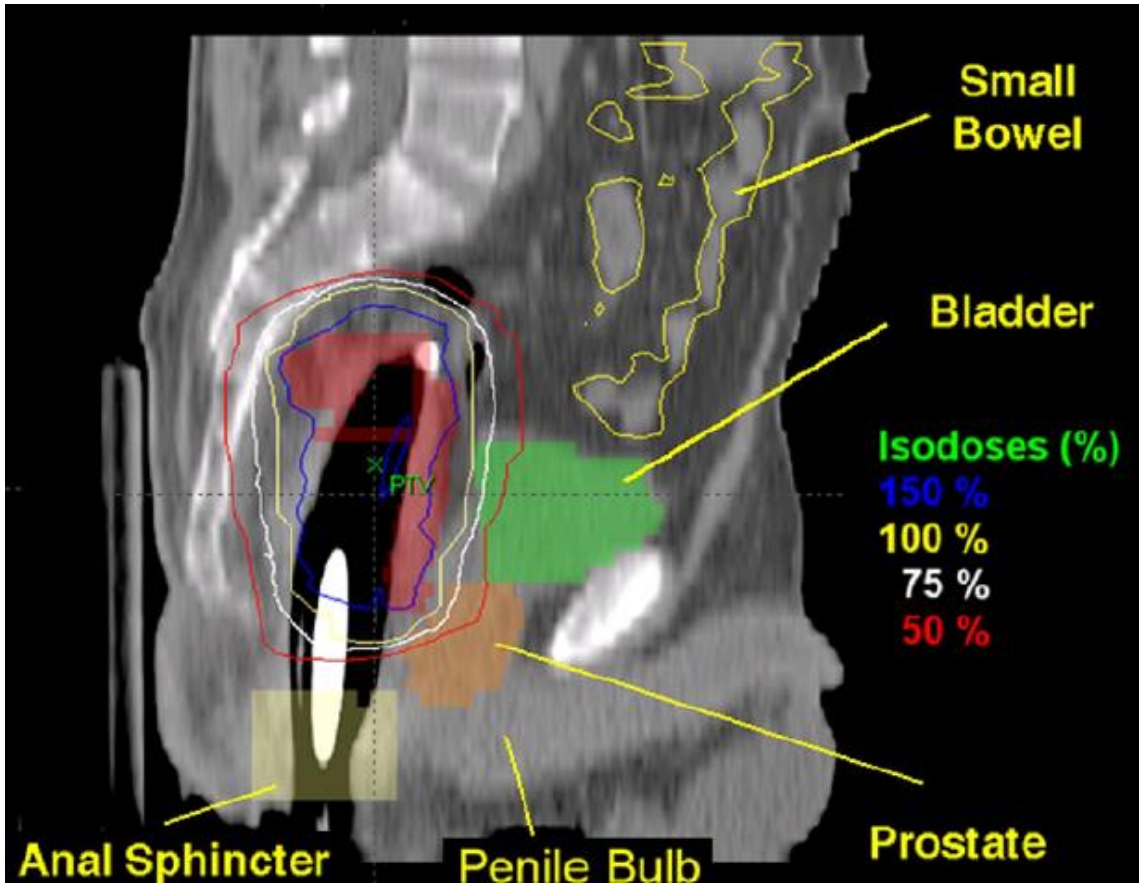
Limitations of TG-43 based Dose Calculation Assumptions !!!

Homogeneous water medium ?





Lettmaier & Strnad. J Contemp Brachytherapy 2014; 6, 2: 236–241, DOI: 10.5114/jcb.2014.43780

Vuong et al. Seminars in Colon & Rectal Surgery, doi:10.1053/j.scrs.2010.01.009, 2010

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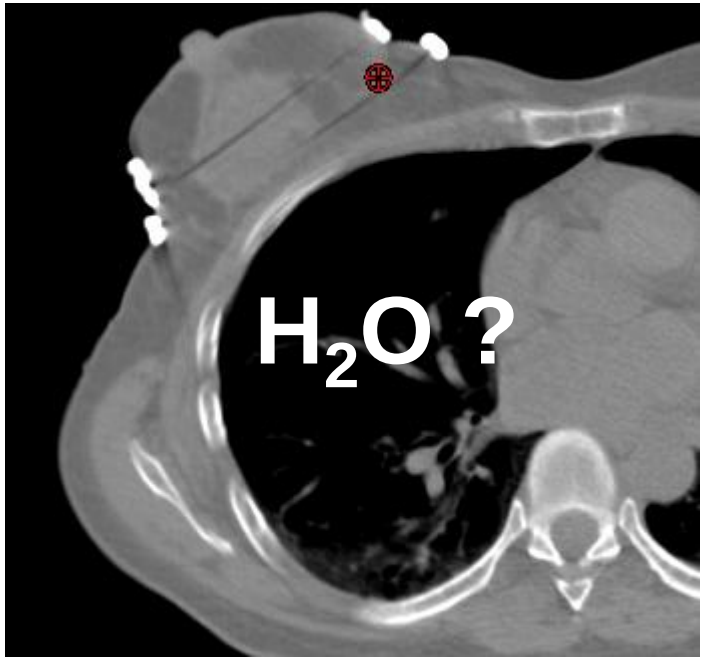
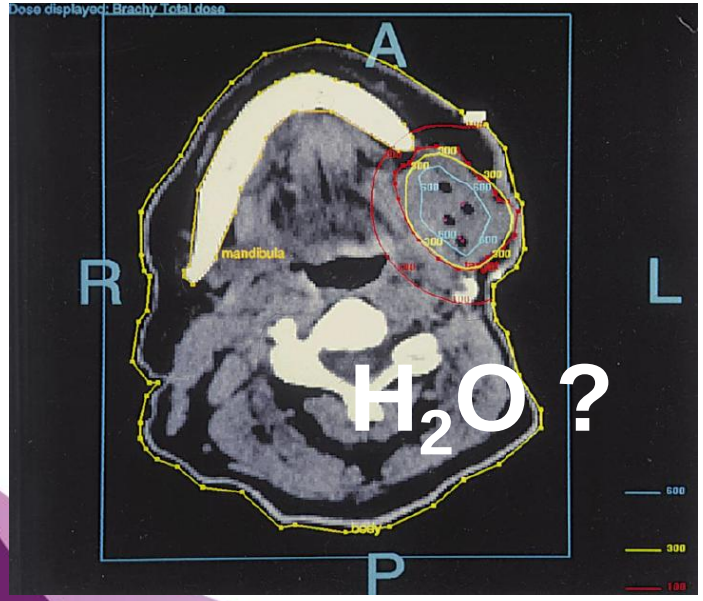
Limitations of TG-43 based Dose Calculation Assumptions: Full scatter Conditions?





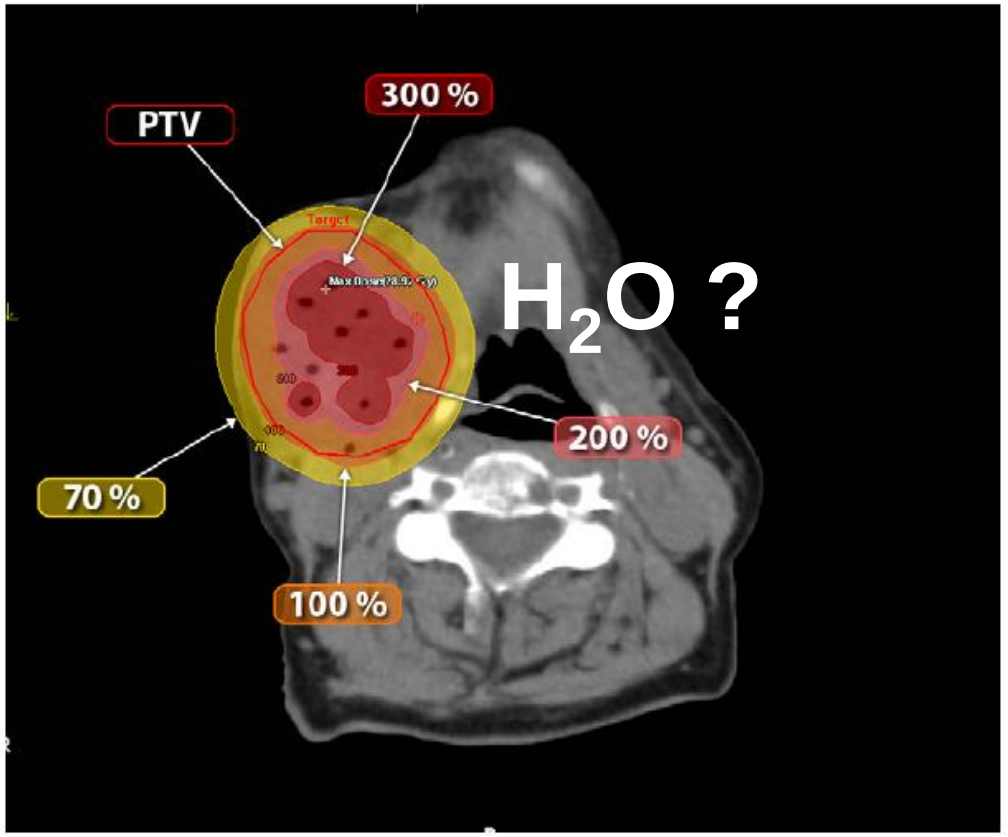


Fig. 1. Axial CT-image showing a right-sided submandibular lymph node recurrence with 2D-isodose distribution after CT-based treatment planning for a plane lying centrally to the target extension. The color gradation represents: red = 300% isodose = 9.0 Gy, pink = 200% isodose = 6.0 Gy, orange = 100% isodose = 3.0 Gy and yellow = 70% isodose = 2.1 Gy. The target volume is denoted as red delineated PTV and the interstitial catheters identifiable as dark dots inside it. The PTV measures 132.5 cm^2.

Tselis N et al. Radiotherapy & Oncology 98, 2011
doi:10.1016/j.radonc.2010.10.025

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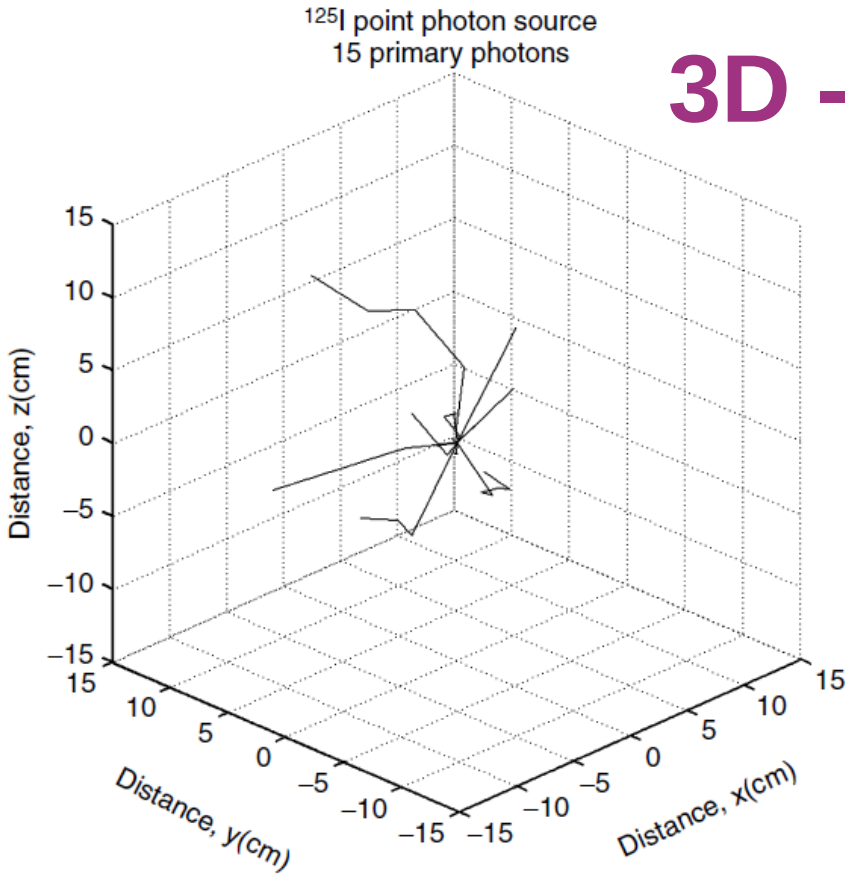
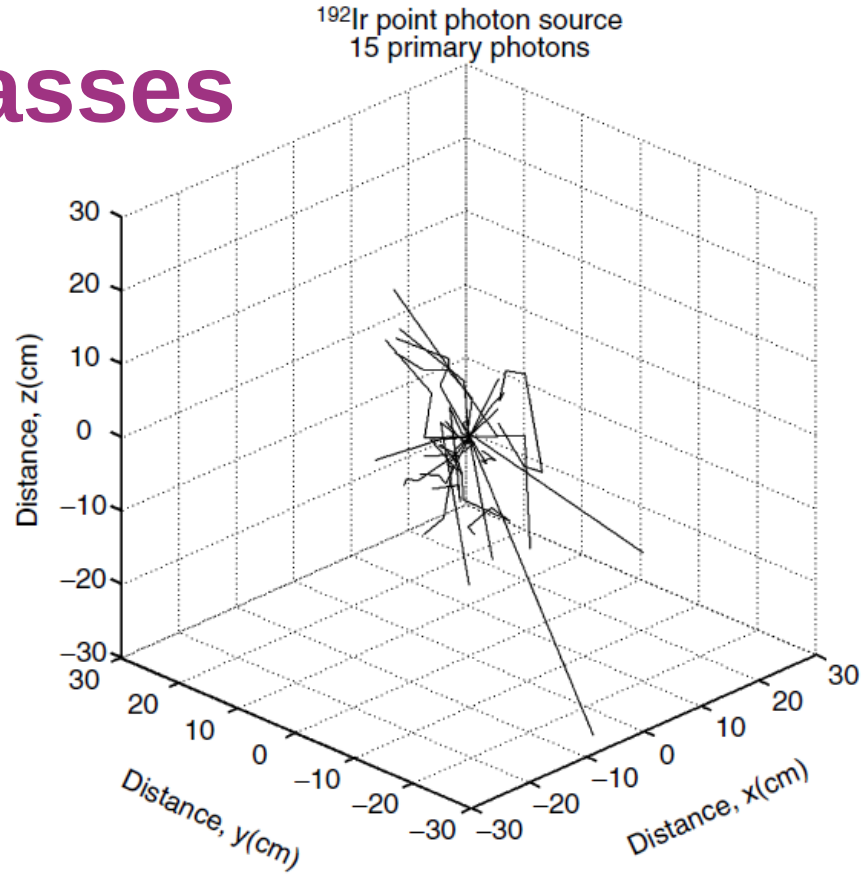
Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

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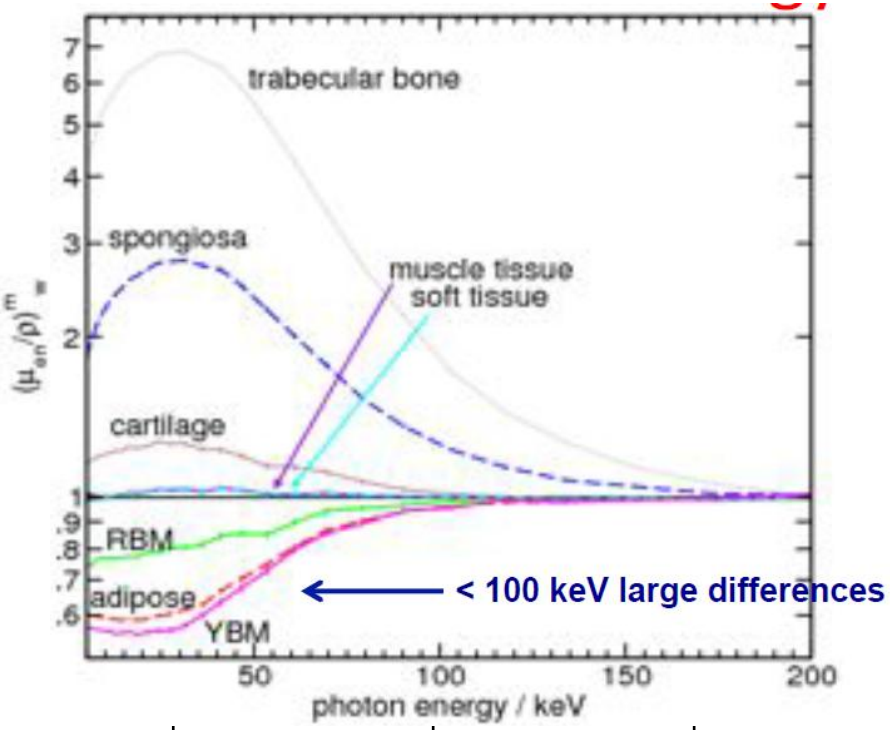
Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation

Sensitivity of Anatomic Sites to Dosimetric Limitations of Current Planning Systems

anatomic site	photon energy	absorbed dose	attenuation	s		
prostate	high					
	low	XXX	XXX			
breast	High					
	low	XXX	XXX			
GYN	high					
	low	XXX	XXX			
skin	high					
	low	XXX				
lung	high					
	low	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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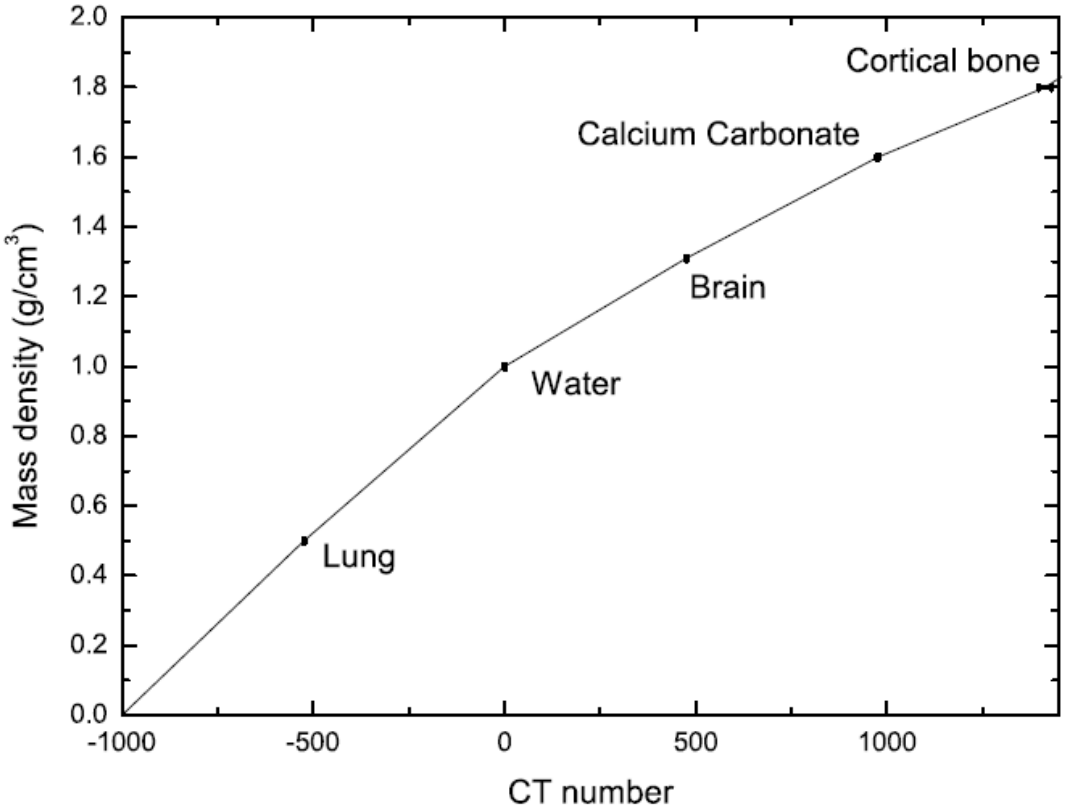
Limitations of TG-43 based Dose Calculation or 2D versus 3D Dose Calculation



$$HU_{tissue} = \left\{\frac{\mu_{tissue} - \mu_{water}}{\mu_{water}}\right\} \cdot 1000$$

CT: Calibration curve Hus vs. ρ or ρ_e

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

BJR
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Received: 24 February 2014 | Revised: 10 July 2014 | Accepted: 14 July 2014
doi: 10.1259/bjr.20140163

Cite this article as:
Papagiannis P, Pantelis E, Karaiskos P. Current state of the art brachytherapy treatment planning dosimetry algorithms. Br J Radiol 2014;87: 20140163.

BRACHYTHERAPY DOSIMETRY SPECIAL FEATURE: REVIEW ARTICLE

Current state of the art brachytherapy treatment planning dosimetry algorithms

P PAPAGIANNIS, PhD, E PANTELIS, PhD and P KARAISKOS, PhD

Medical Physics Laboratory, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Address correspondence to: Mr Panagiotis Papagiannis
E-mail: *ppapagi@med.uoa.gr*

ABSTRACT

Following literature contributions delineating the deficiencies introduced by the approximations of conventional brachytherapy dosimetry, different model-based dosimetry algorithms have been incorporated into commercial systems for ^{192}Ir brachytherapy treatment planning. The calculation settings of these algorithms are pre-configured according to criteria established by their developers for optimizing computation speed *vs* accuracy. Their clinical use is hence straightforward. A basic understanding of these algorithms and their limitations is essential, however, for commissioning; detecting differences from conventional algorithms; explaining their origin; assessing their impact; and maintaining global uniformity of clinical practice.

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Thank you very much for your Attention

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Dose Calculation: The TG-43 Protocol

- **Dose Rate from a single Source**
- Dose from Dose Rate
- Many Sources
- Limitations

To be Continued ….. Monday 09:15 !

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High dose rate brachytherapy in prostate cancer

Peter Hoskin
Mount Vernon Cancer Centre

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Indications for HDR prostate brachytherapy

- Boost with external beam
- Monotherapy

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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

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HDR brachytherapy procedure

- Assessment
- Implantation
- Imaging
- Volume definition
- Dosimetry
- Verification and delivery
- Implant removal

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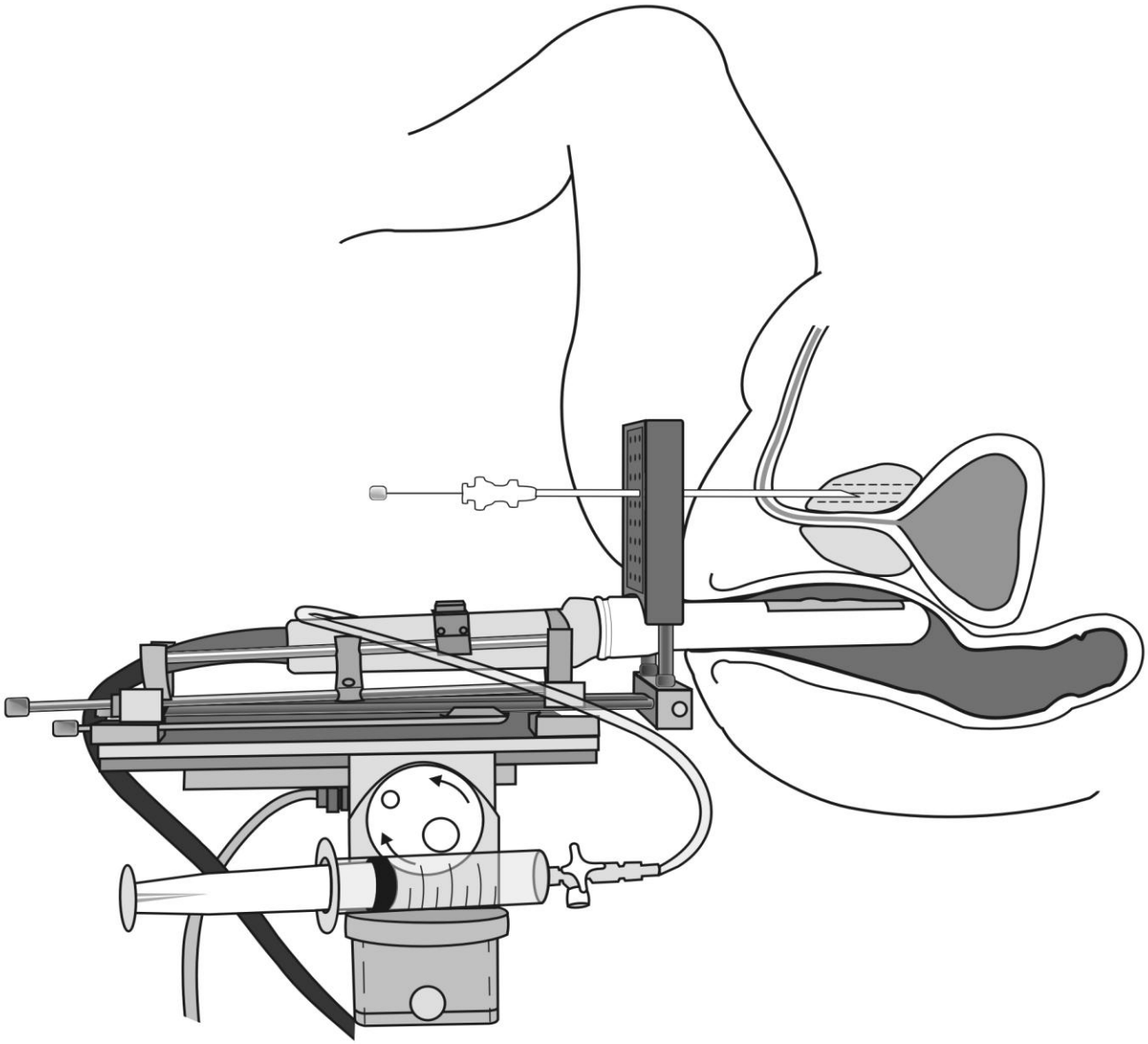

HDR implant: imaging and volume definition

- 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

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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.

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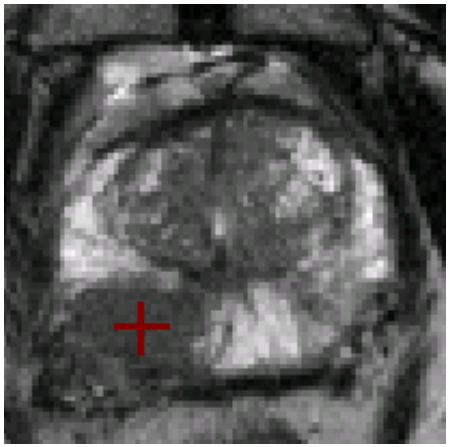
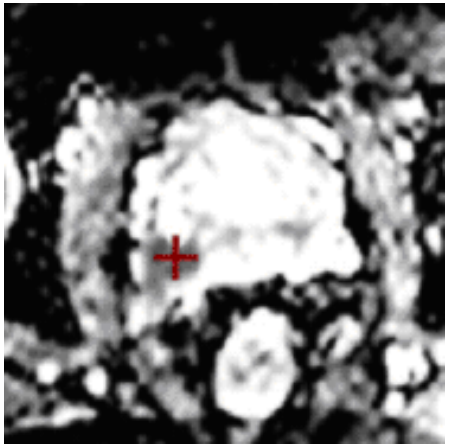
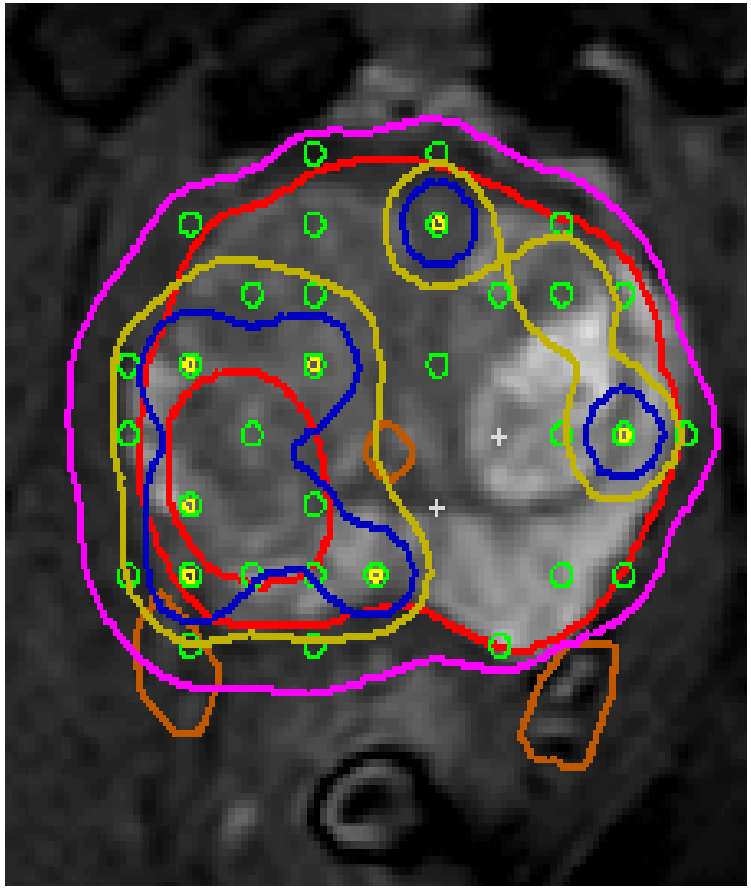
CTV subvolumes







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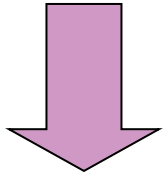
HDR brachytherapy boost: Planning aim

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.

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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

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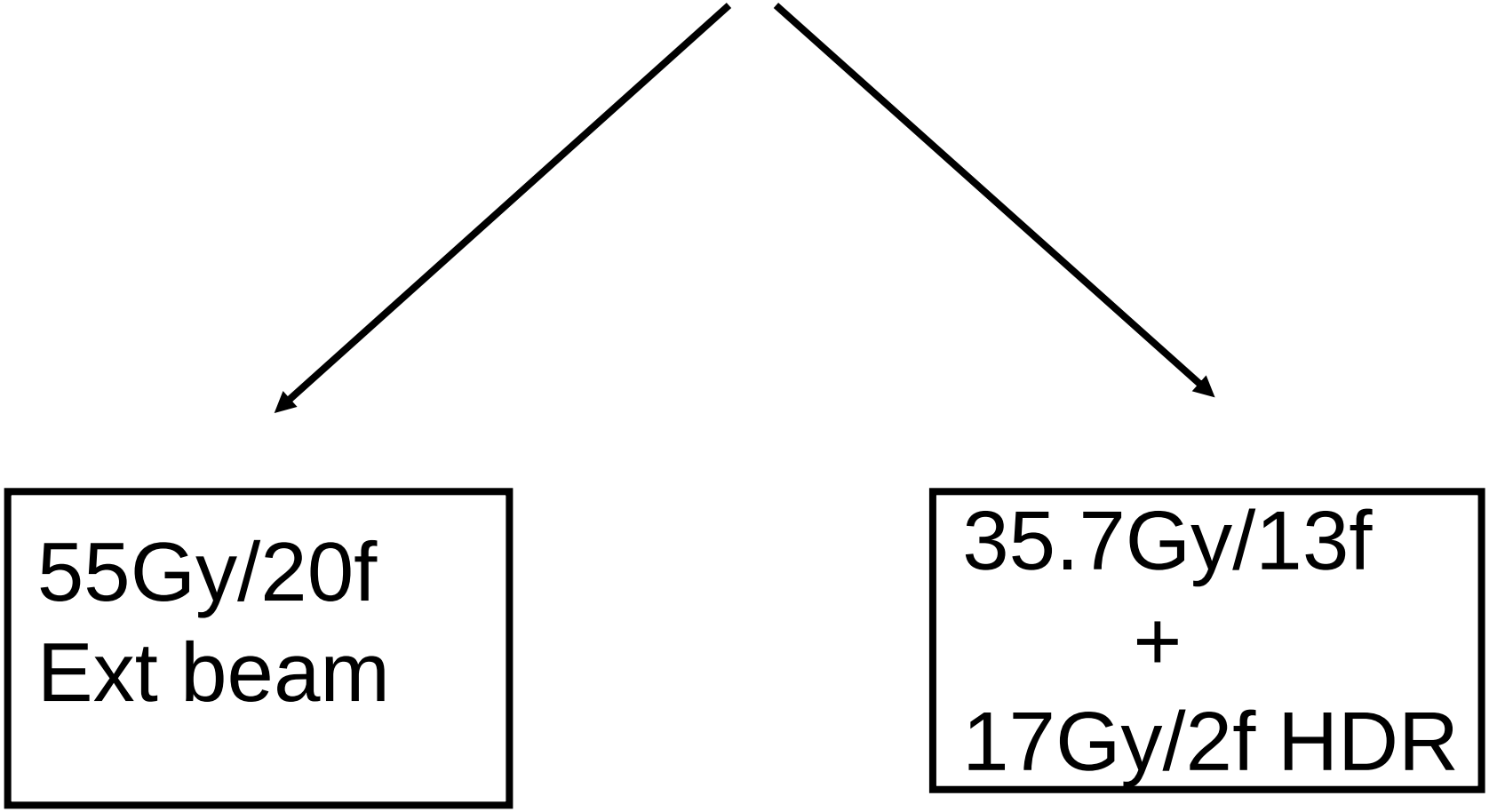
MVH RCT



Closed 08/05: 220 patients randomised

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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

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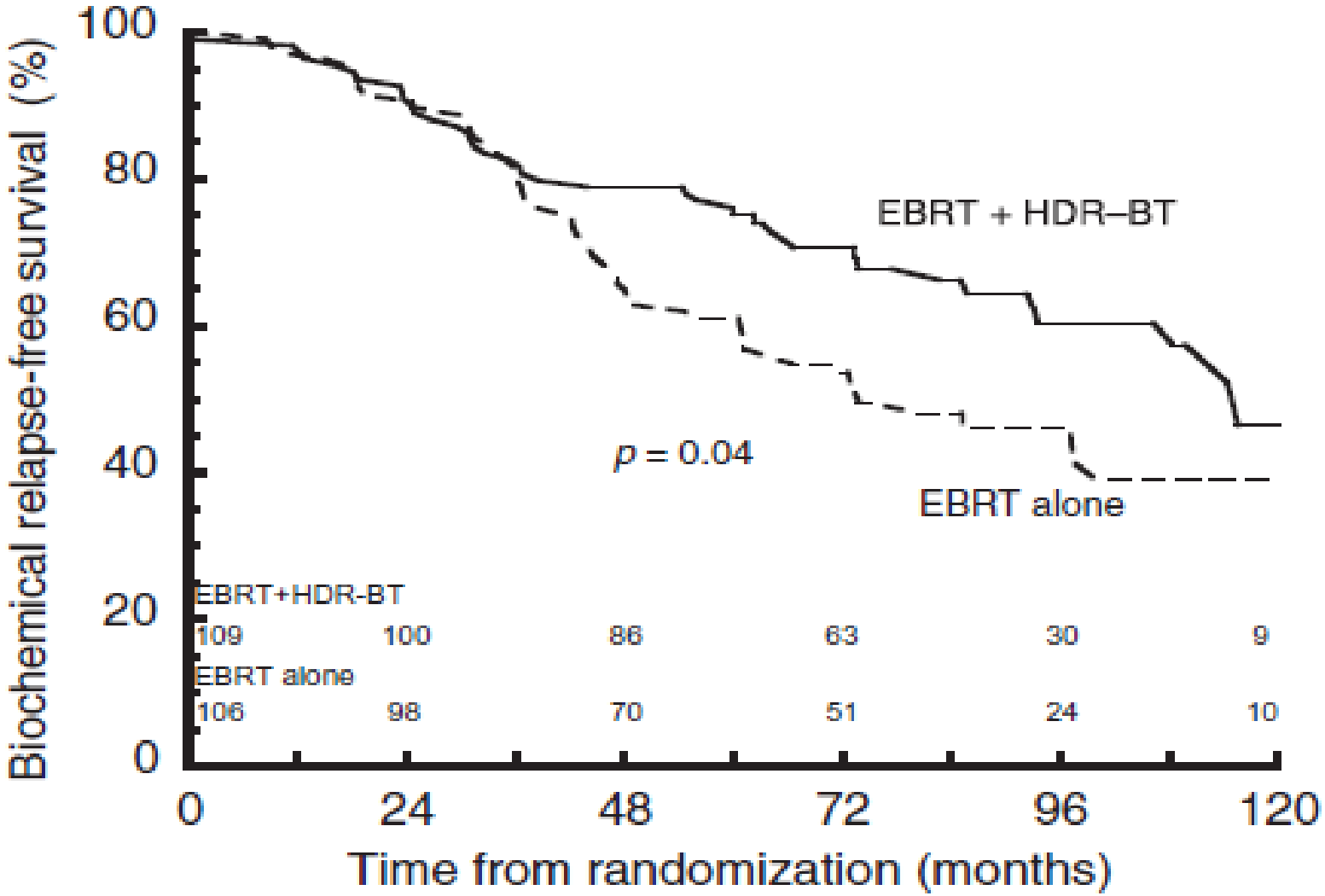
Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Radiotherapy and Oncology xxx (2012) xxx–xxx

Biochemical relapse free survival



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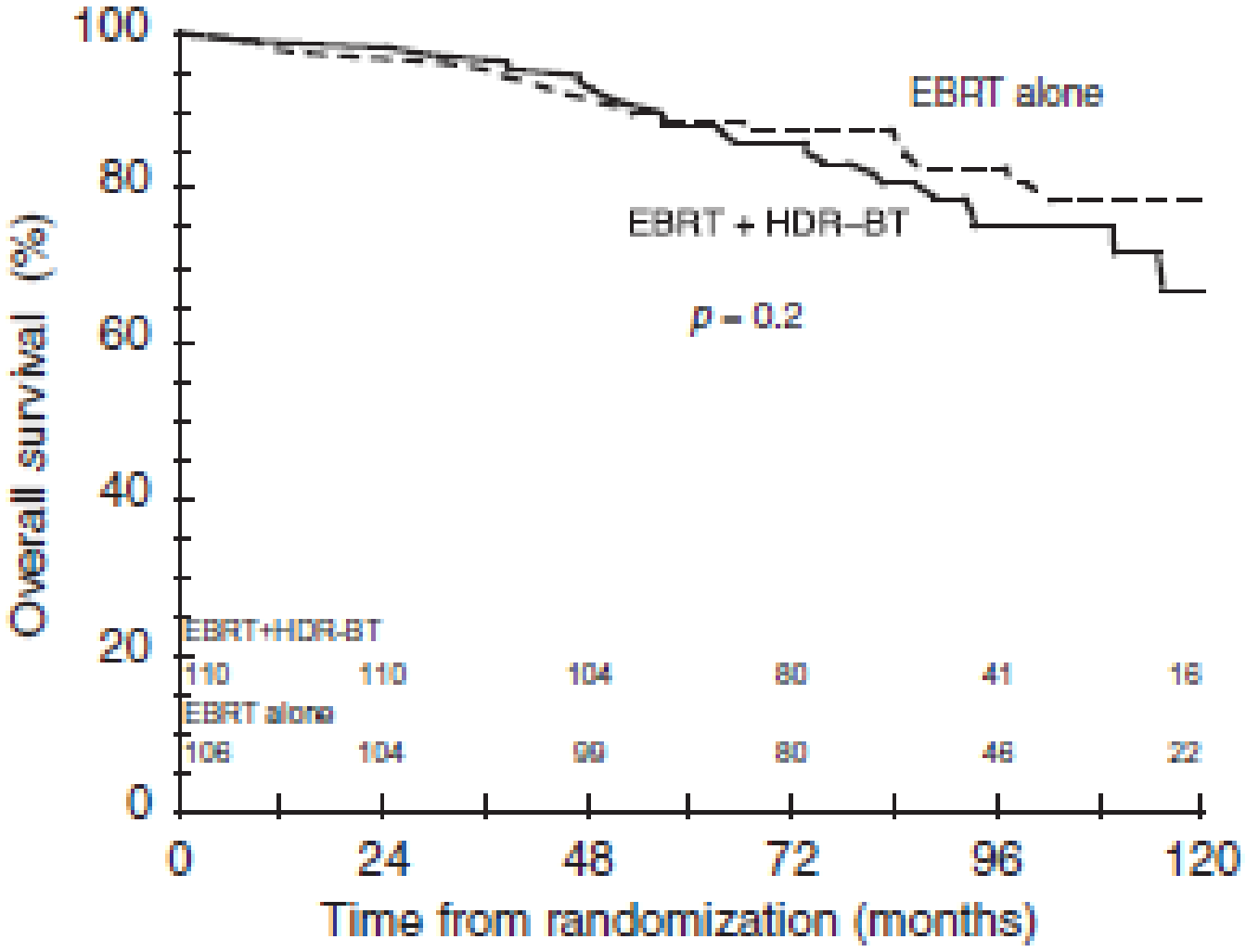
Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Radiotherapy and Oncology xxx (2012) xxx–xxx

Overall survival



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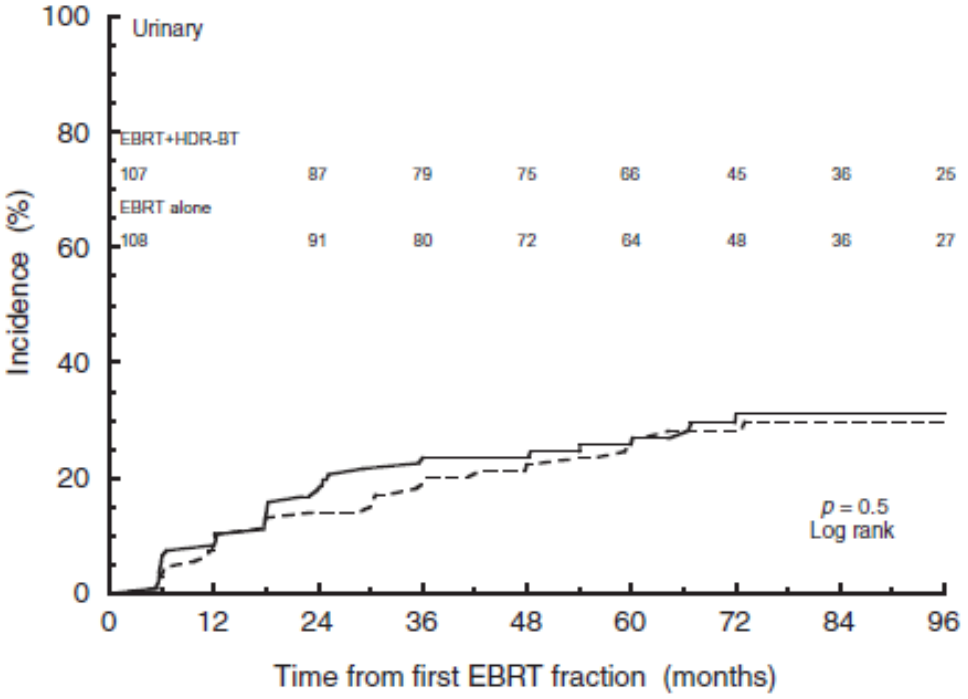
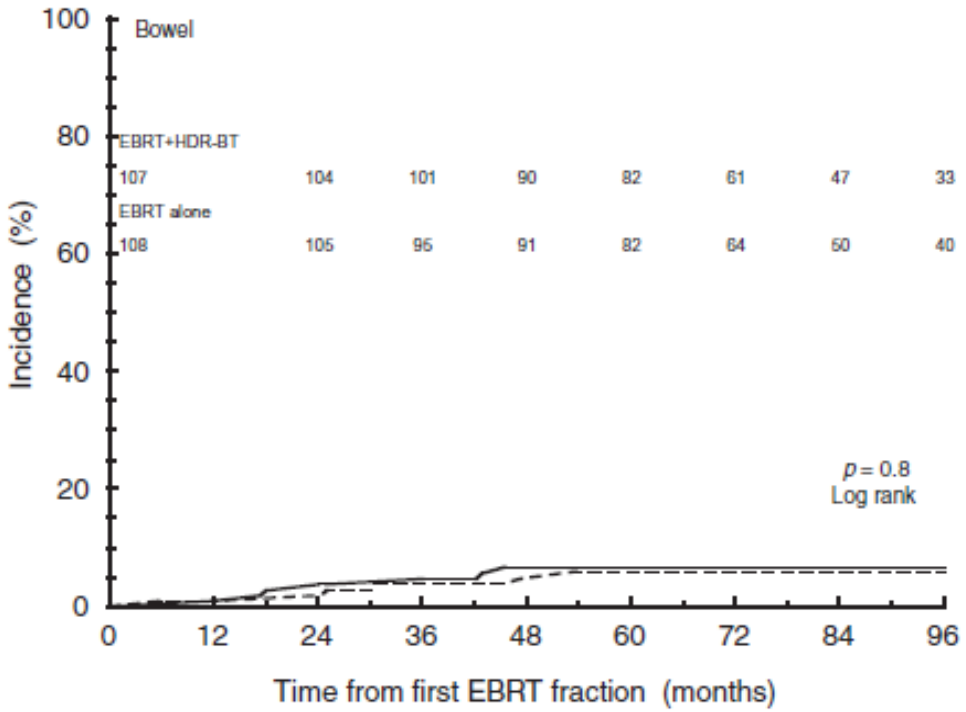
Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Radiotherapy and Oncology xxx (2012) xxx–xxx

Toxicity





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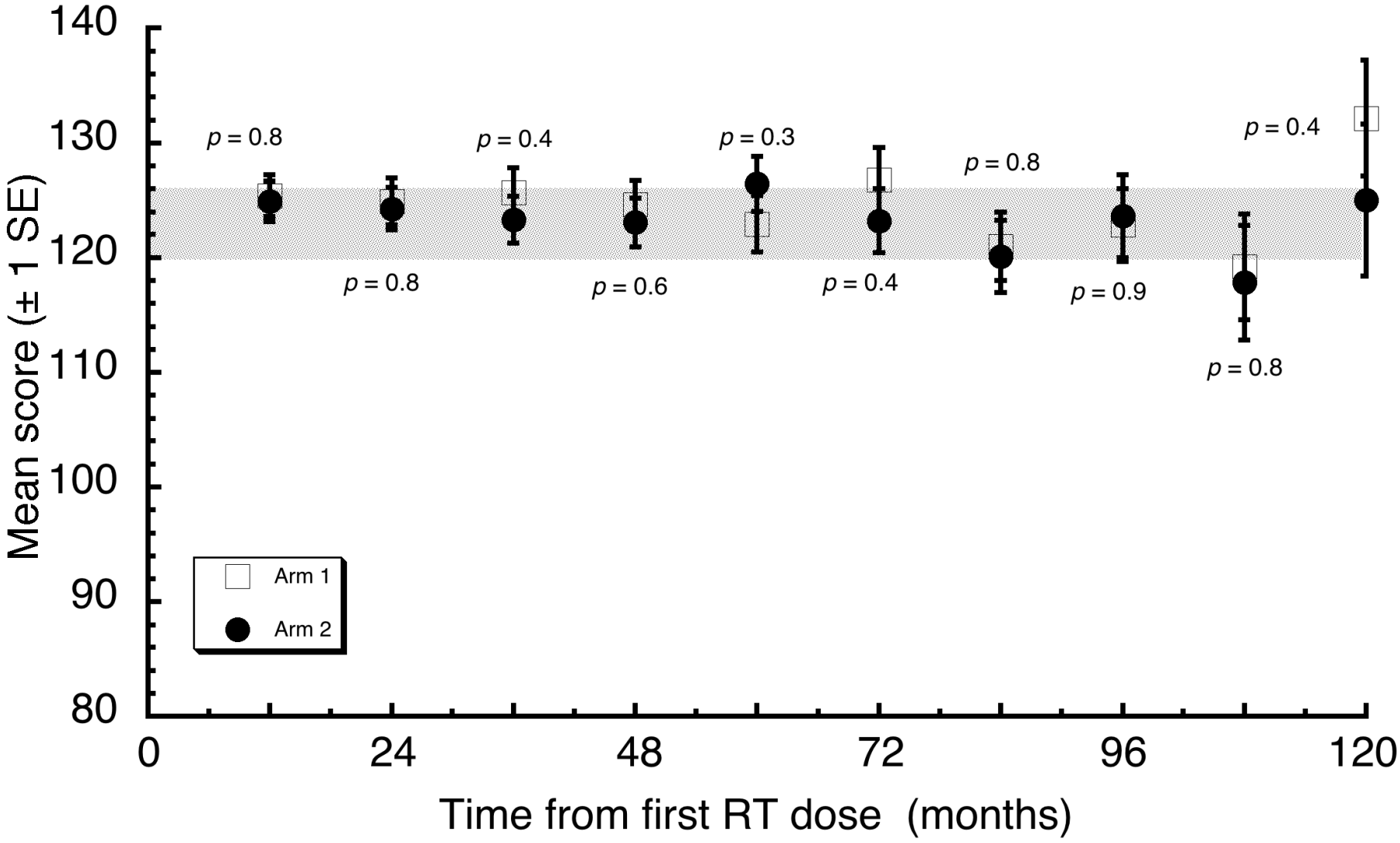
FACT-P total scores (range 0 to 152)



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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

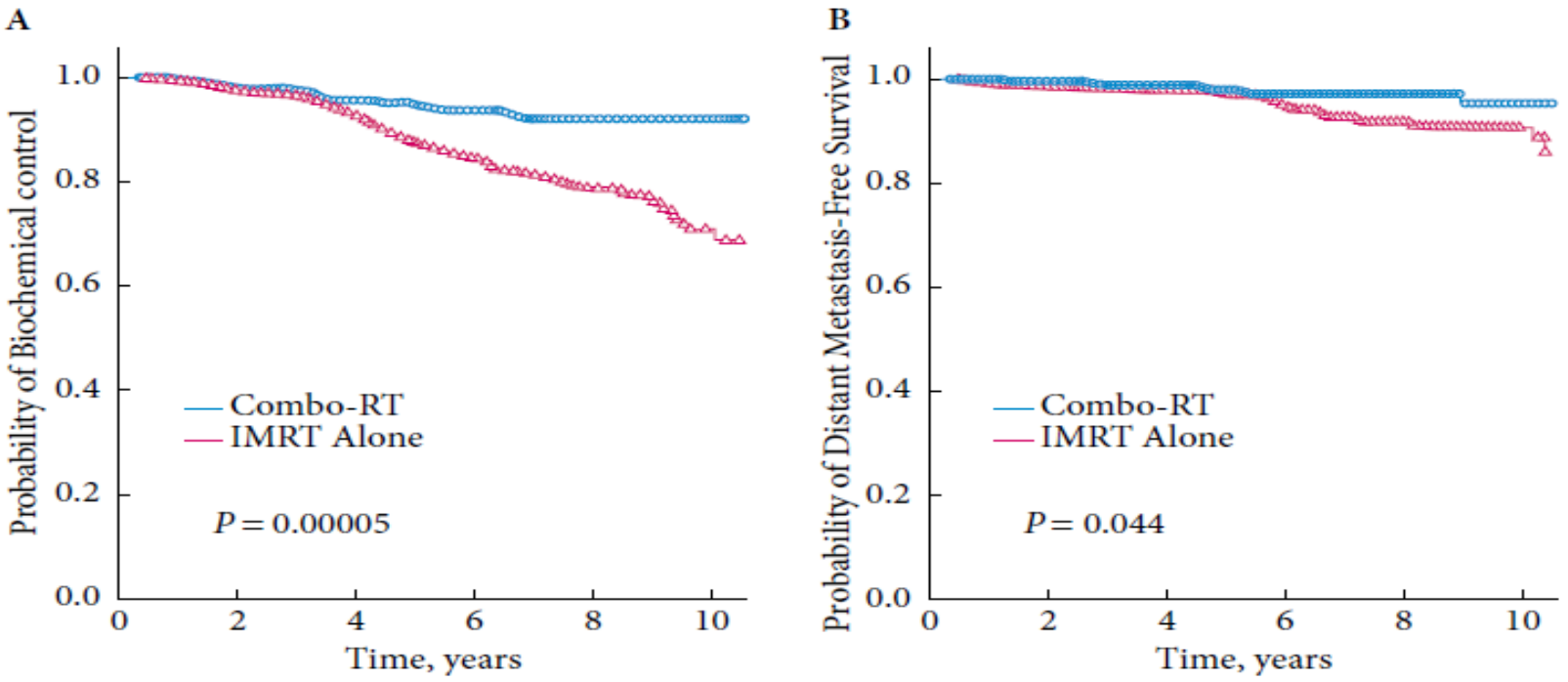
*Departments of Radiation Oncology and *Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY,*

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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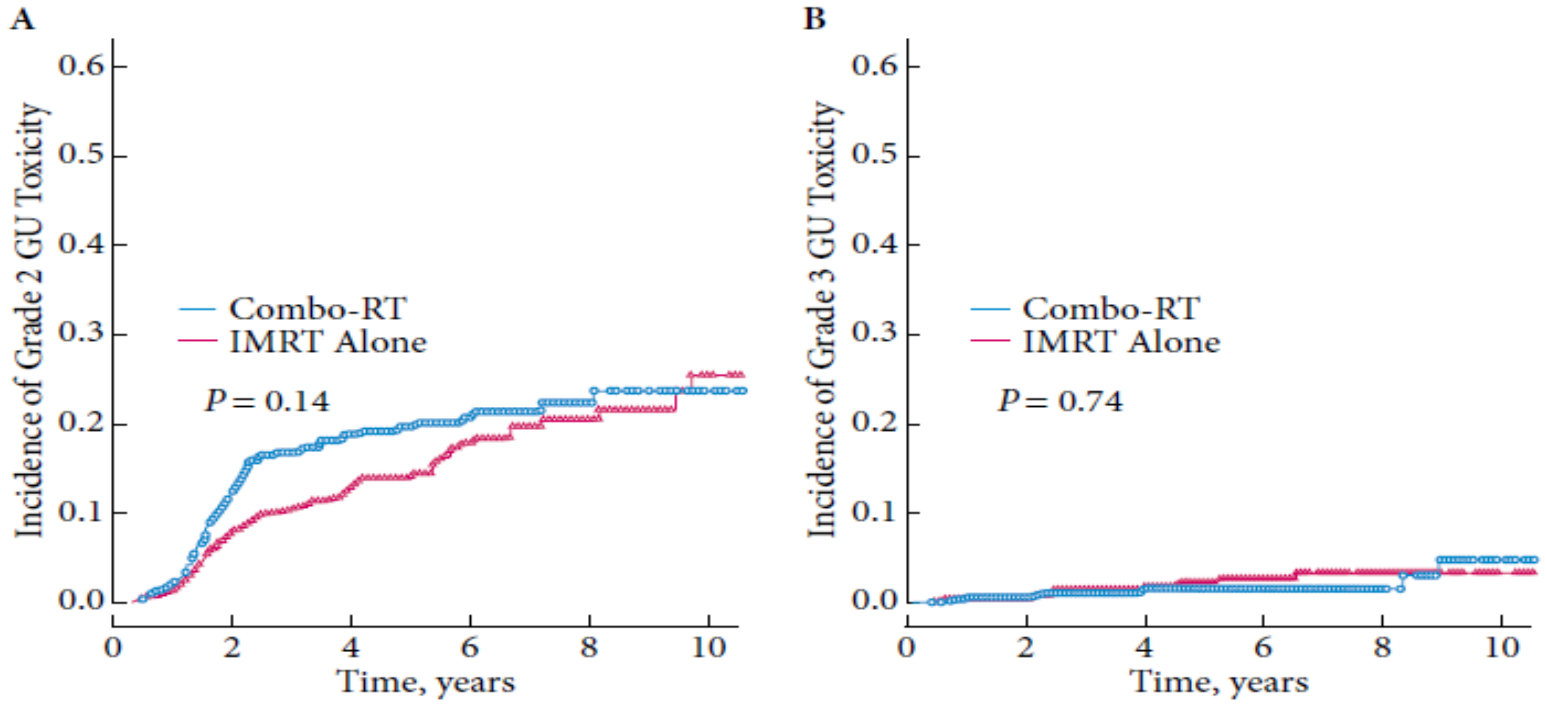


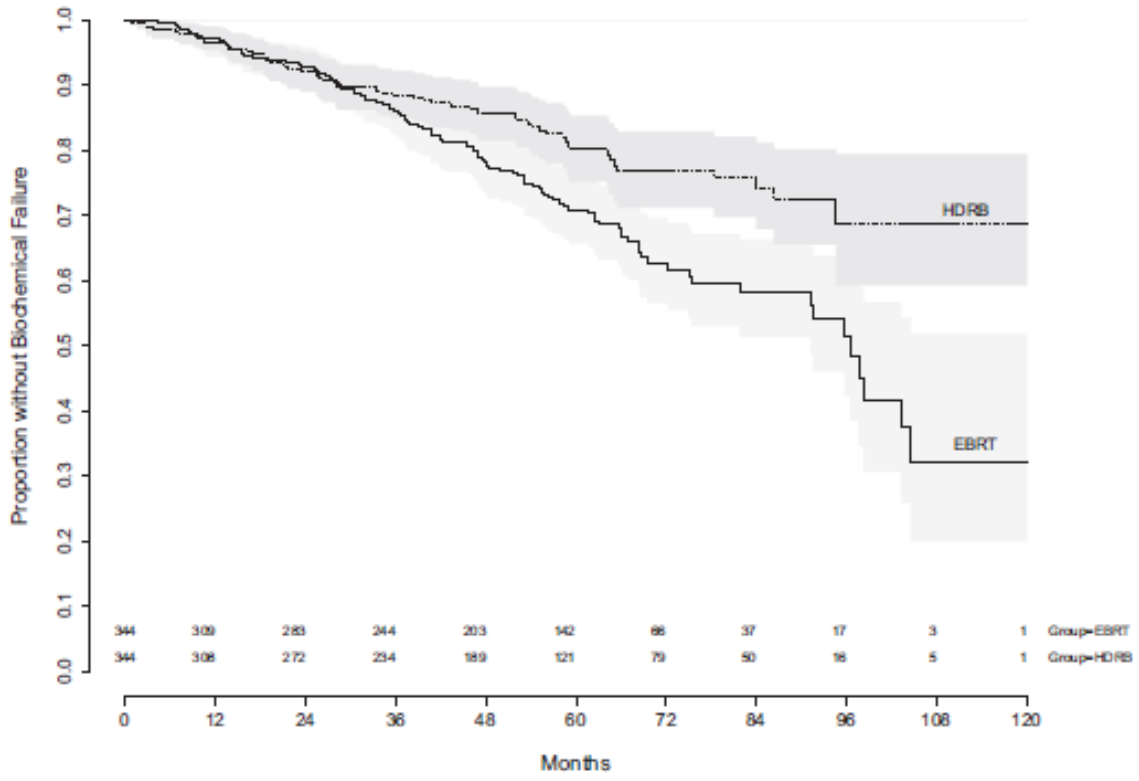
Direct 2-Arm Comparison Shows Benefit of High-Dose-Rate Brachytherapy Boost vs External Beam Radiation Therapy Alone for Prostate Cancer

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.

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Toxicity of HDR BT in prostate cancer

Acute

- Urinary
  - Frequency urgency dysuria
    increases to week 4-6
    resolves by week 12-16
  - Retention: rare
- Rectal
  - Frequency and urgency
    rare
- Erectile function
  - Little data in acute period

Late

- Urinary
  - Stricture: 6-8%
  - Incontinence: 1-2%
- Rectal
  - Rectal bleeding: 2%
- Erectile function
  - Retained in 60-70%

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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

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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.

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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

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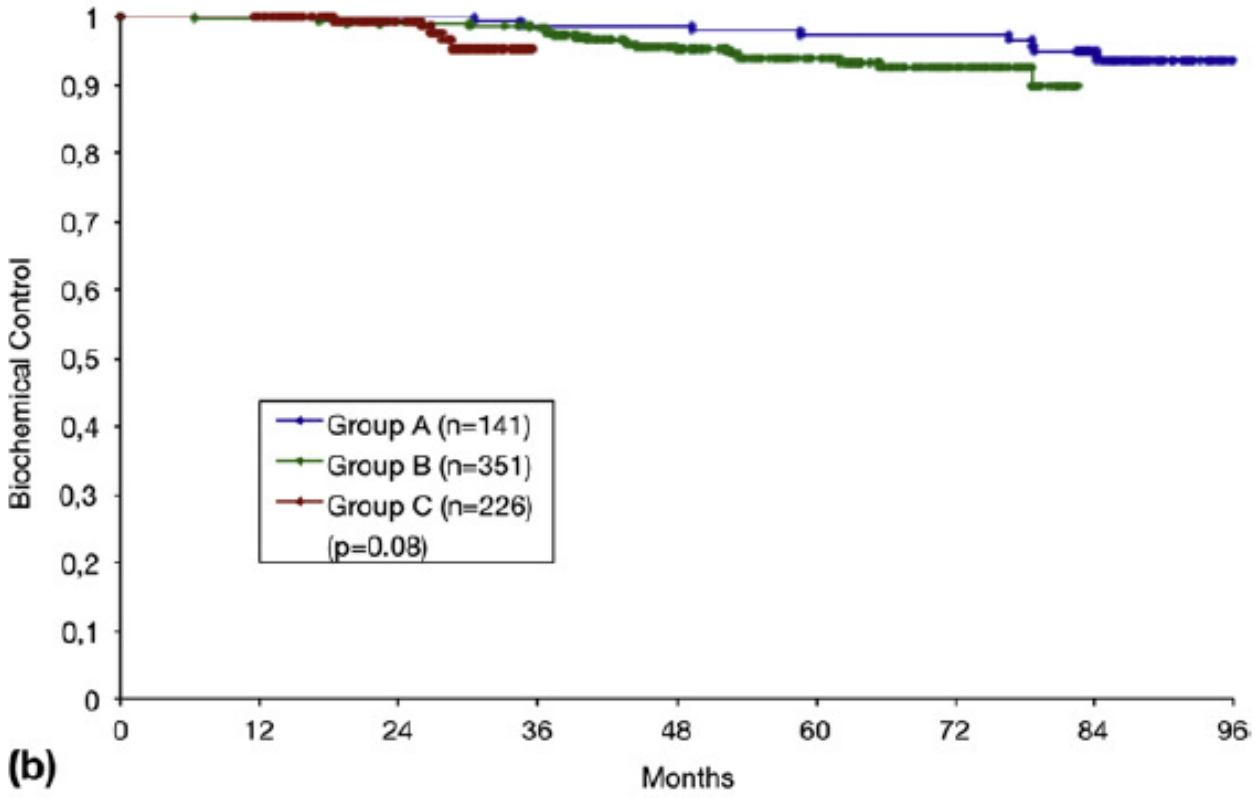
High-Dose-Rate Interstitial Brachytherapy as Monotherapy for Clinically Localized Prostate Cancer: Treatment Evolution and Mature Results

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



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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

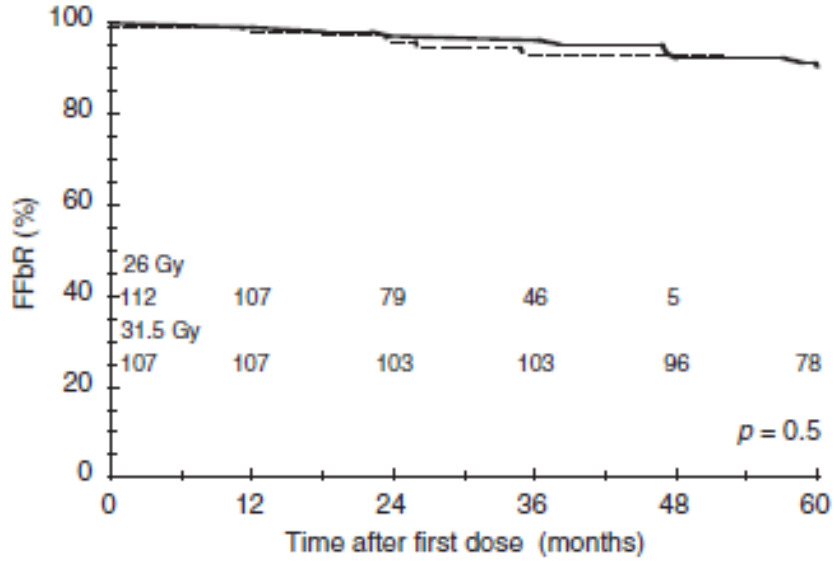
Int J Radiation Oncol Biol Phys, Vol. 85, No. 3, pp. 672–678, 2013

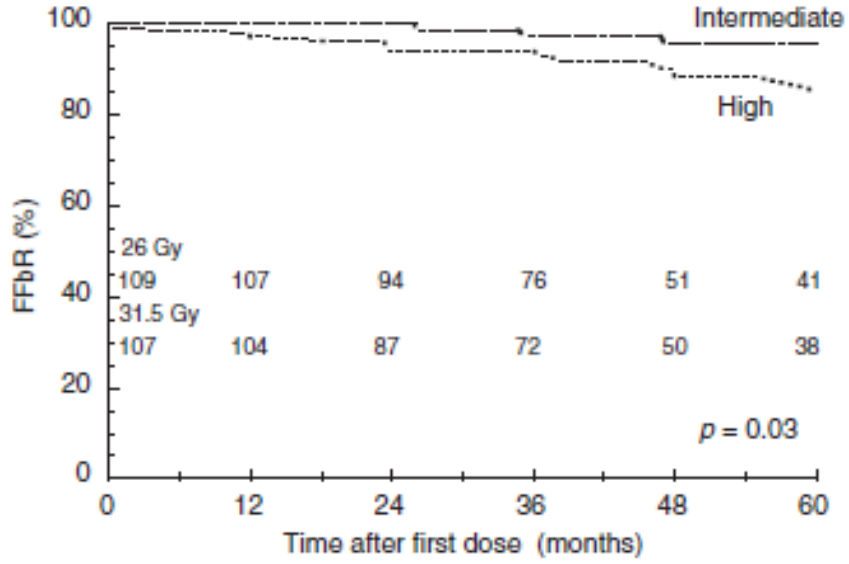
High-dose-rate brachytherapy with two or three fractions as monotherapy in the treatment of locally advanced prostate cancer

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





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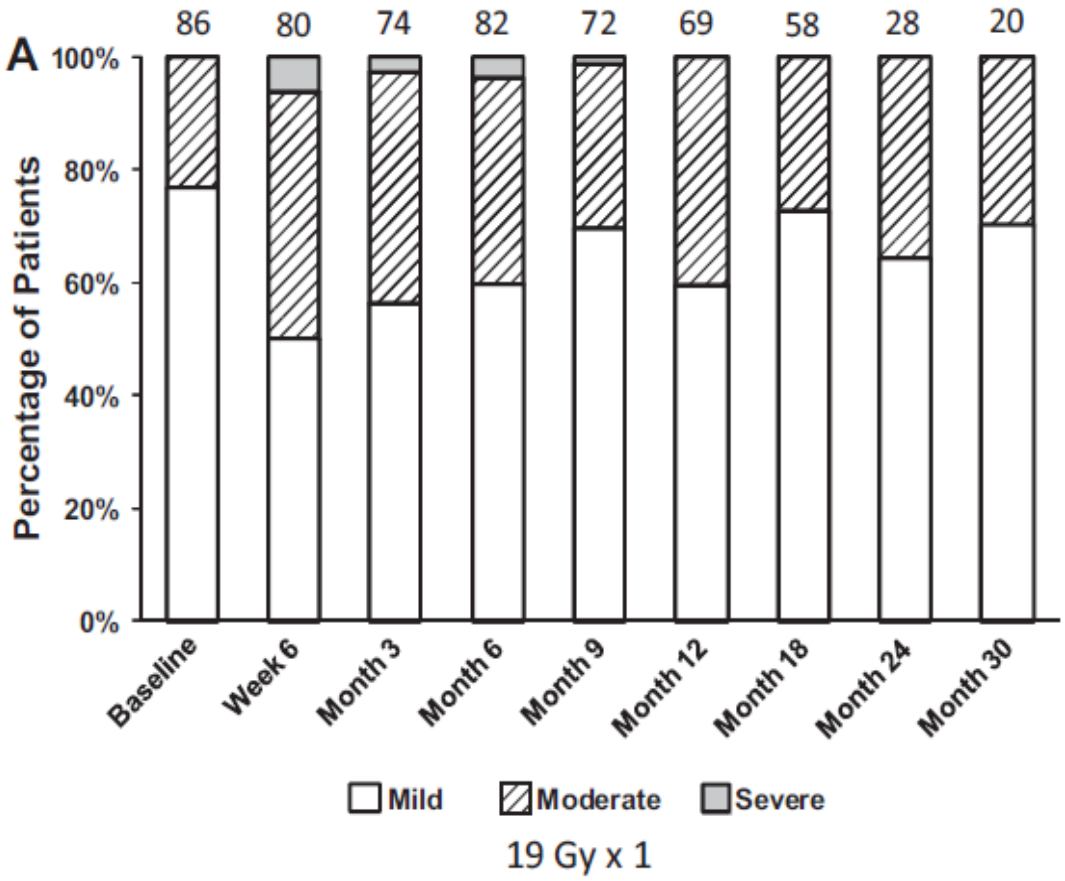
Prostate high dose-rate brachytherapy as monotherapy for low and intermediate risk prostate cancer: Early toxicity and quality-of life results from a randomized phase II clinical trial of one fraction of 19 Gy or two fractions of 13.5 Gy

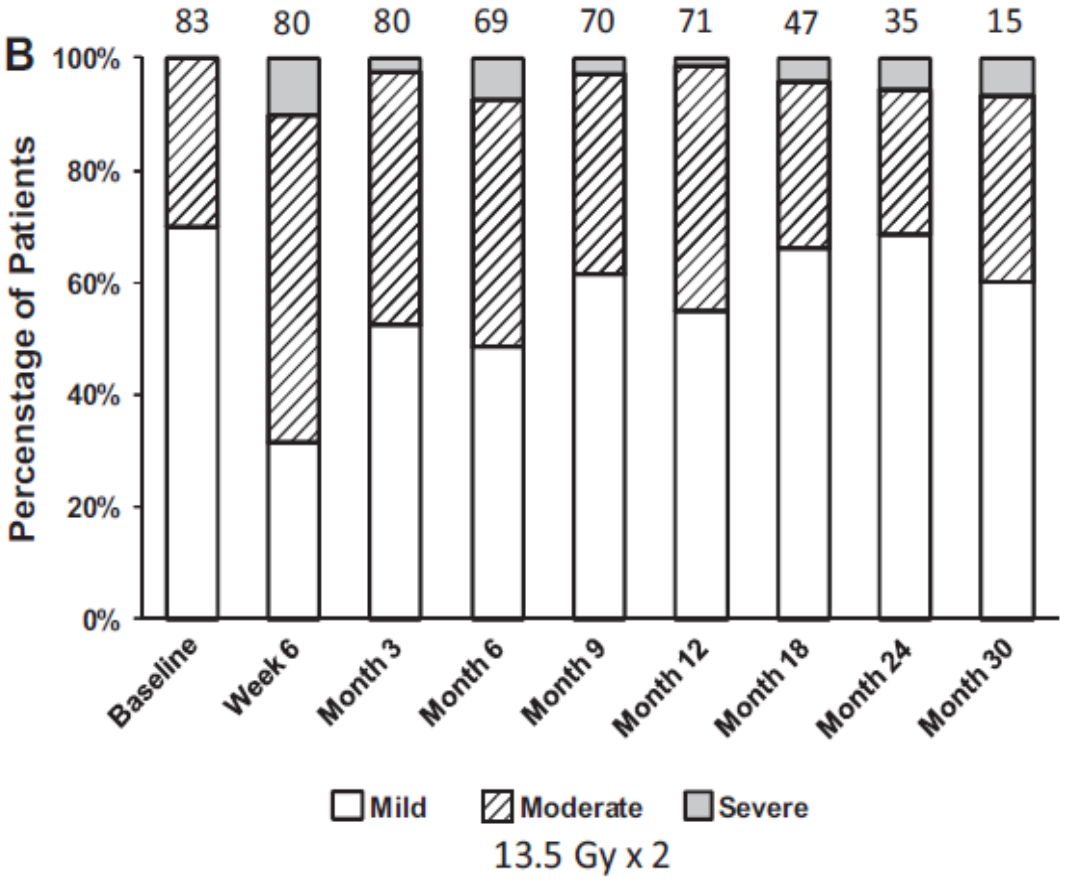
Radiotherapy and Oncology xxx (2016)

Gerard Morton*, Hans T. Chung, Merrylee McGuffin, Joelle Helou, Laura D'Alimonte, Ananth Ravi, Patrick Cheung, Ewa Szumacher, Stanley Liu, Motasem Al-Hanaqta, Liying Zhang, Alexandre Mamedov, Andrew Loblaw

Categorical IPSS scores

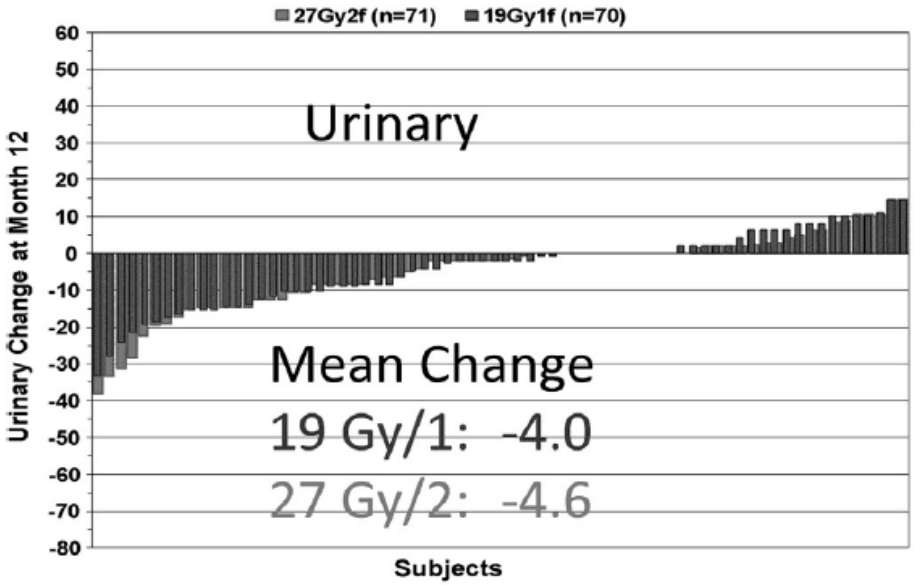


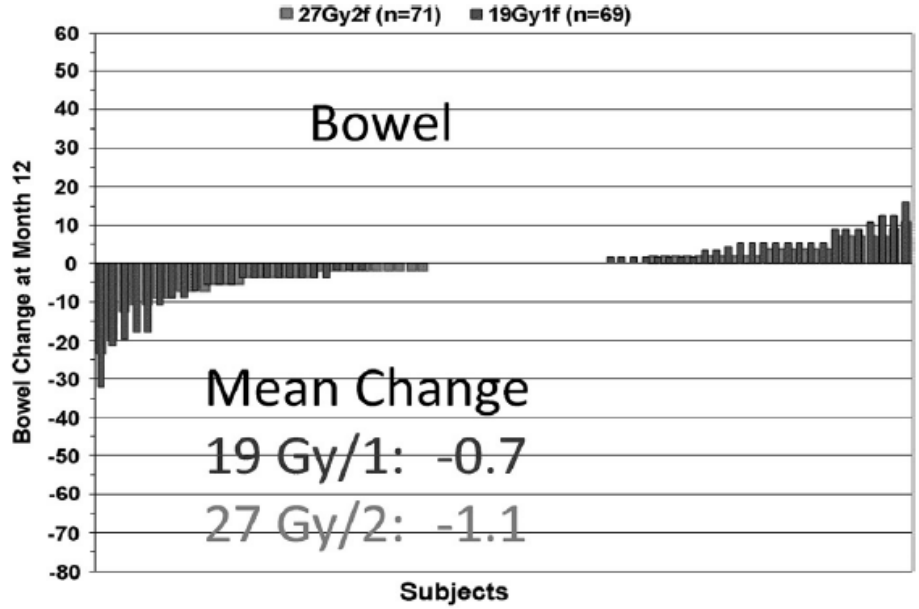
19 Gy x 1

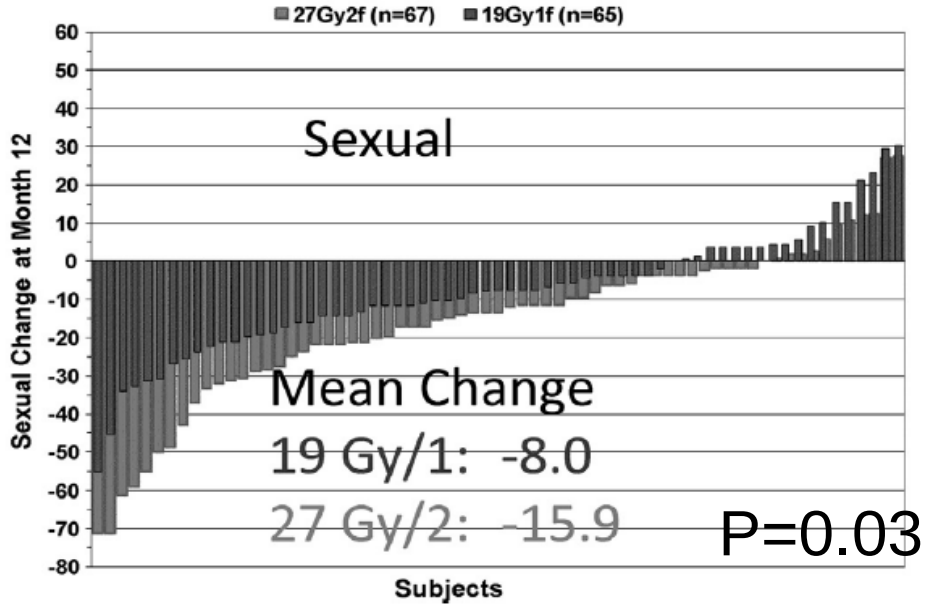


13.5 Gy x 2

EPIC Domain scores







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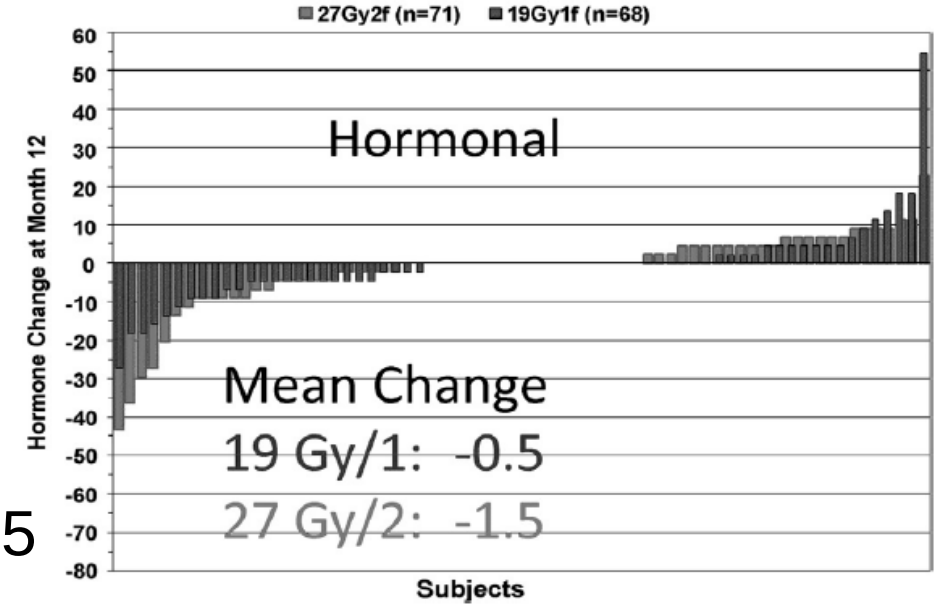

Morton et al 2016

HDR implant: biological advantage: 2Gy EQD

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam 78Gy/39f	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

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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

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NICE National Institute for Health and Care Excellence

Prostate cancer: diagnosis and treatment

Issued: January 2014

Consider high-dose rate brachytherapy in combination with external beam radiotherapy for men with intermediate- and high-risk localised prostate cancer. **[new 2014]**

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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

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WWW.ESTRO.ORG/SCHOOL

Dose Optimization
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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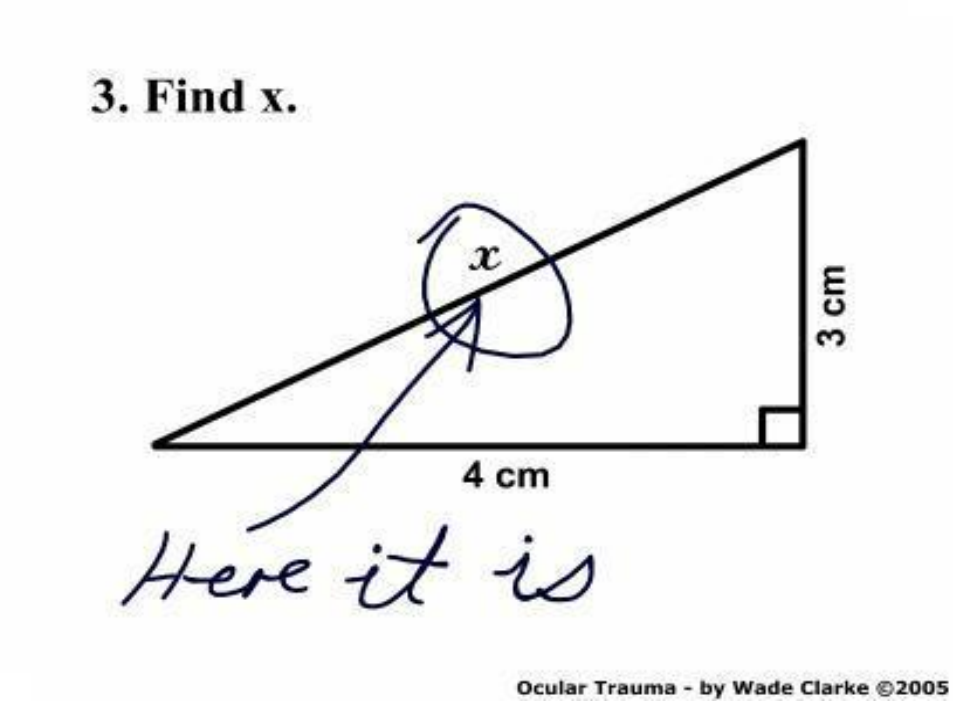
Introduction on Dose Optimization

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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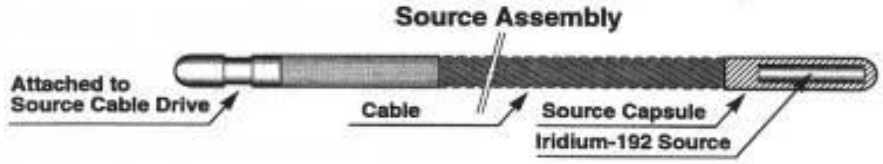
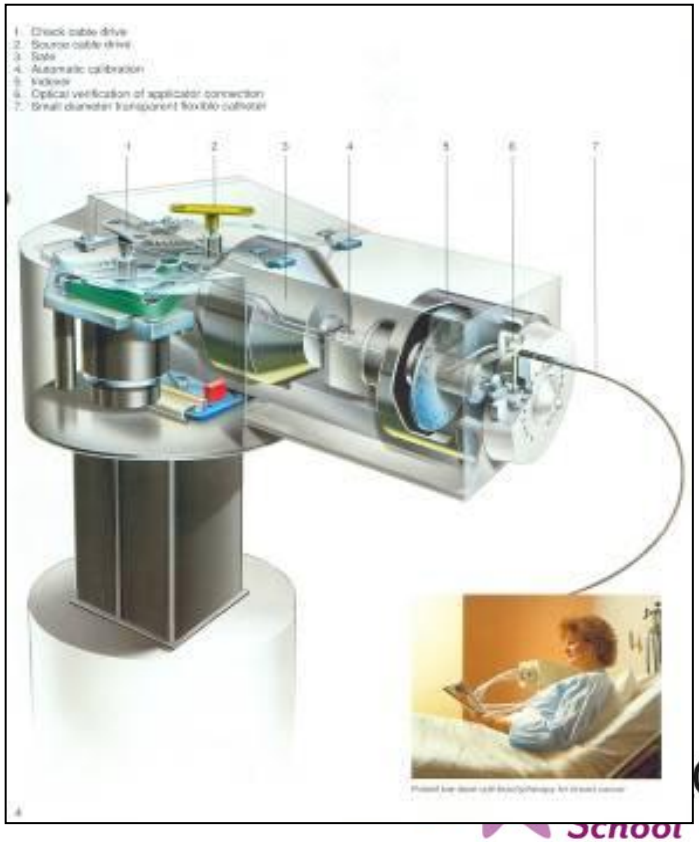
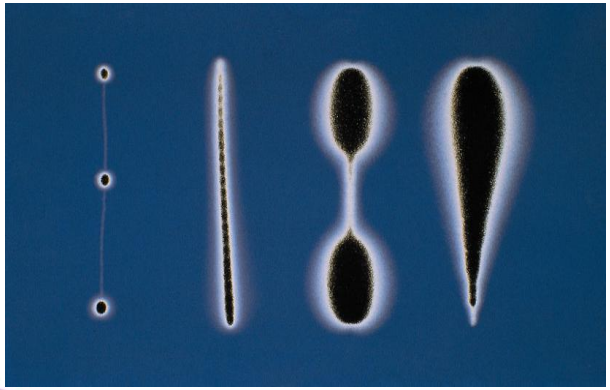
Optimization in interstitial Brachytherapy

- **Temporary interstitial brachytherapy**
- **HDR and PDR afterloading techniques**
- **Single stepping Iridium-192 source (^{60}Co, ^{169}Yb, …):**
  - **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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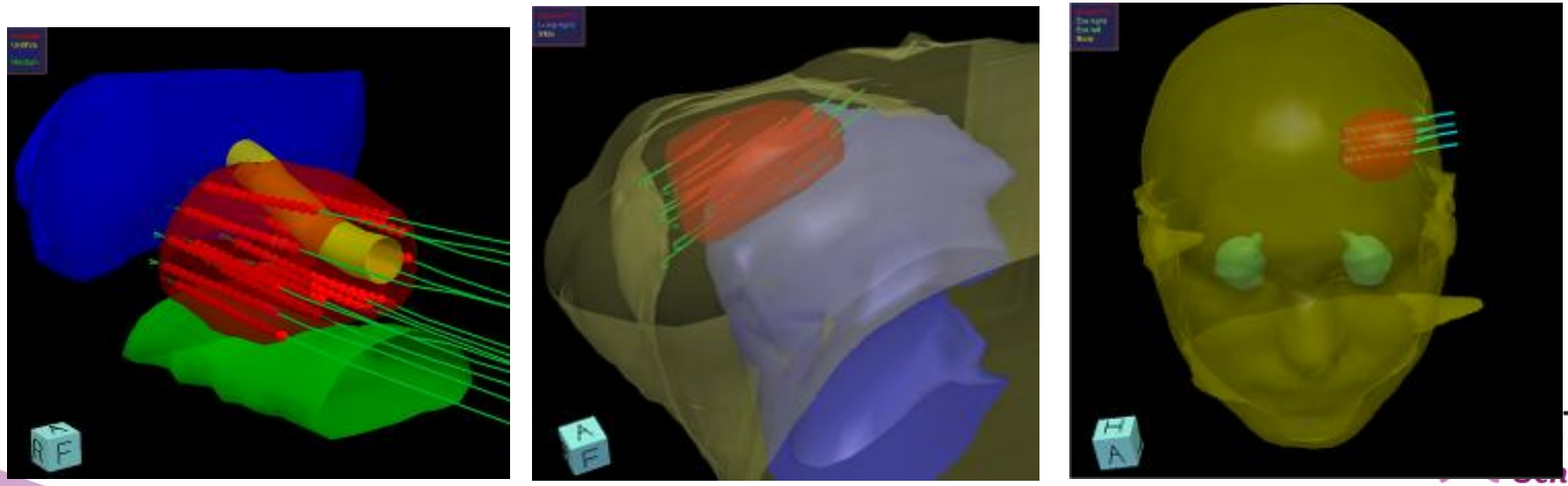
Introduction on Dose Optimization

Our “System” in Brachytherapy

Anatomy

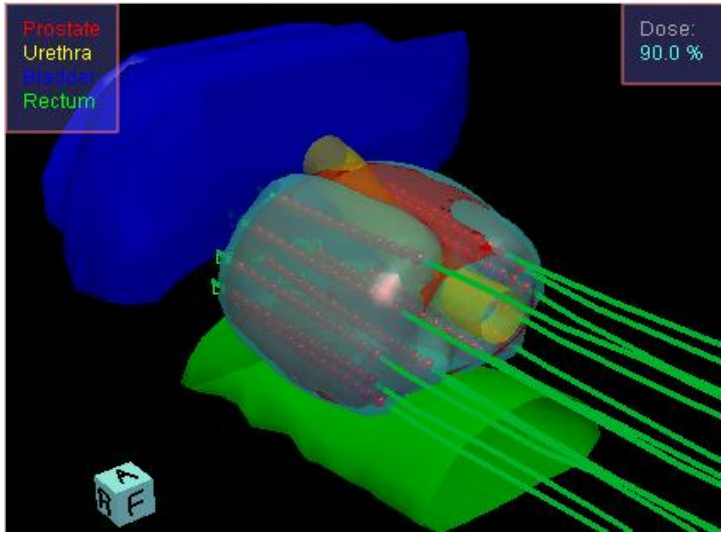
Catheters & Source Dwell Positions

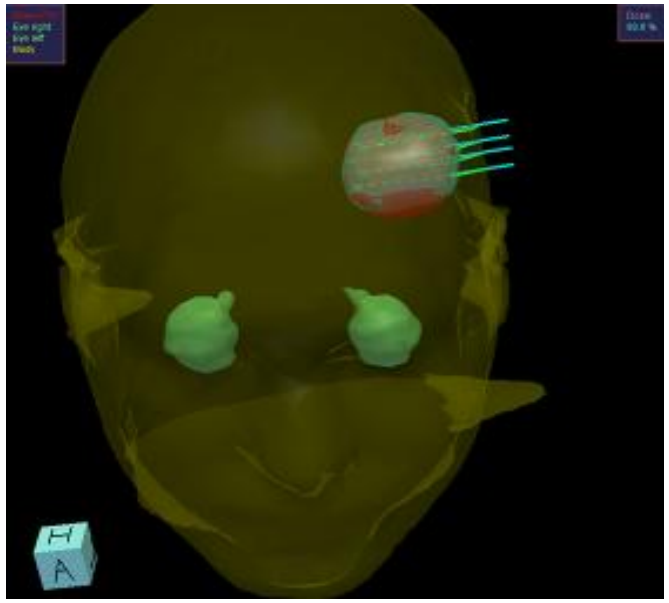


Introduction on Dose Optimization

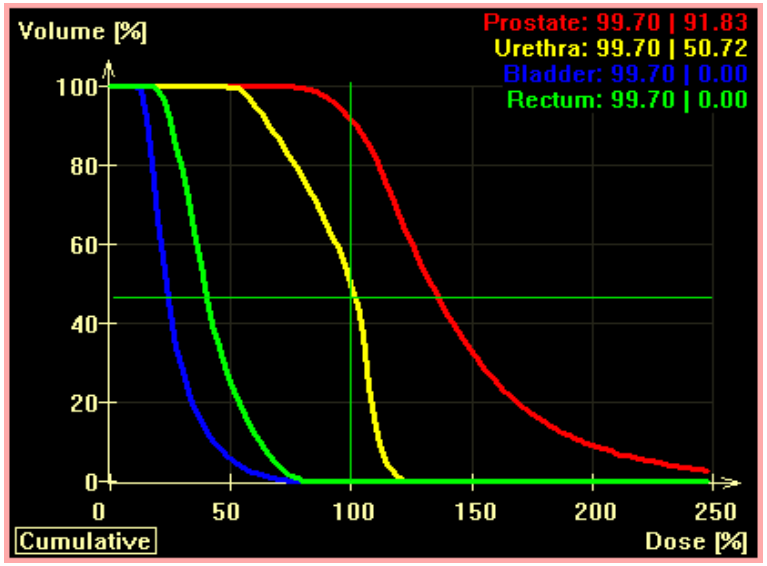
Our “Result” in Brachytherapy

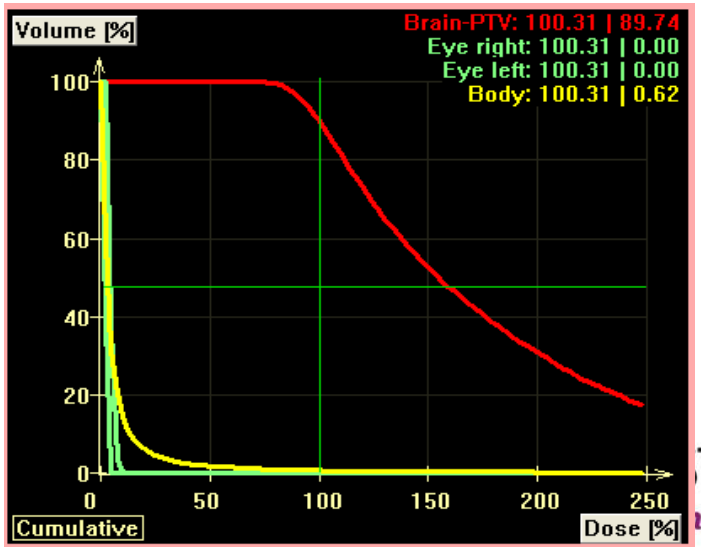
Spatial Dose Distribution 2D & 3D





Anatomy based Dose Evaluation DVHs





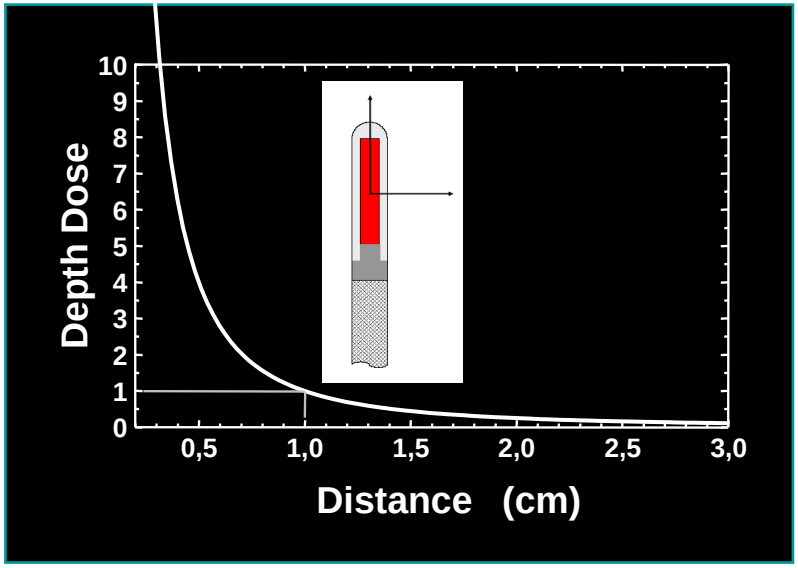
Introduction on Dose Optimization

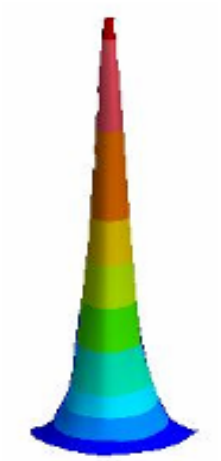
The “System-Law” in Brachytherapy: the Dosimetric Kernel

^{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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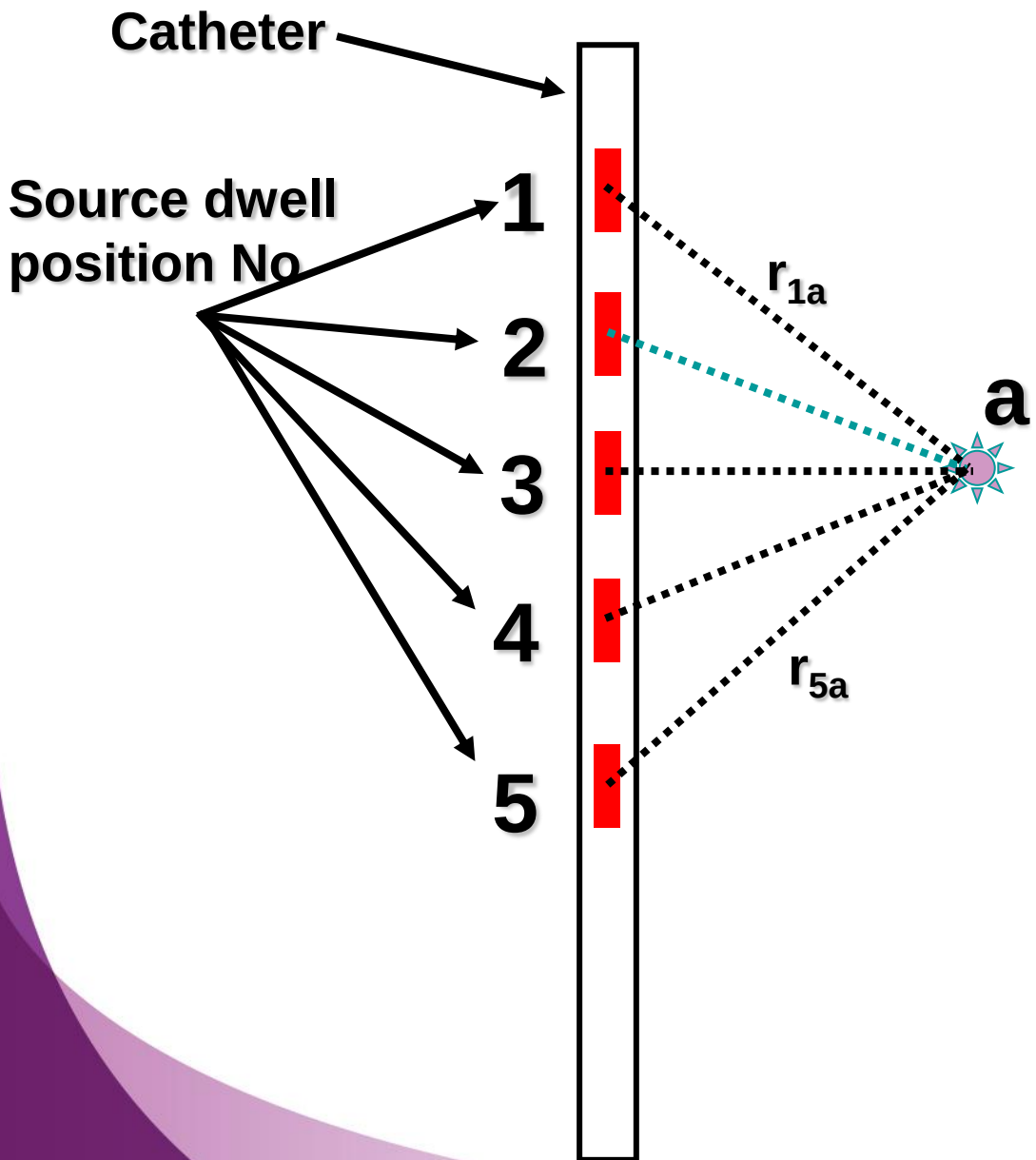
Introduction on Dose Optimization



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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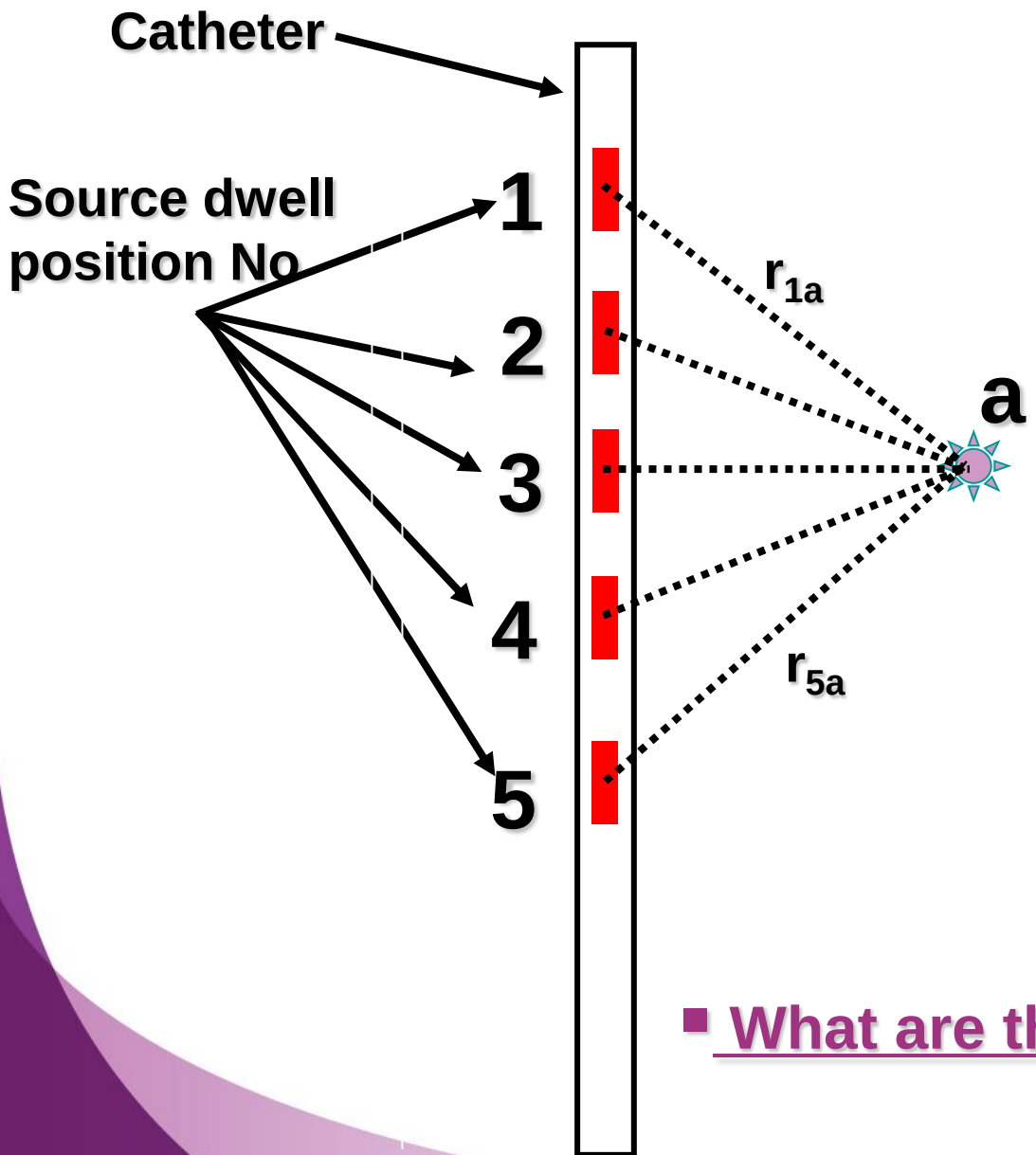
Introduction on Dose Optimization



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

- 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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Topics

- Introduction on Dose Optimization in Brachytherapy
- **Forward Planning & Techniques**
- Inverse Optimization and Planning
- Dose Evaluation
- Quality Parameters and Indices

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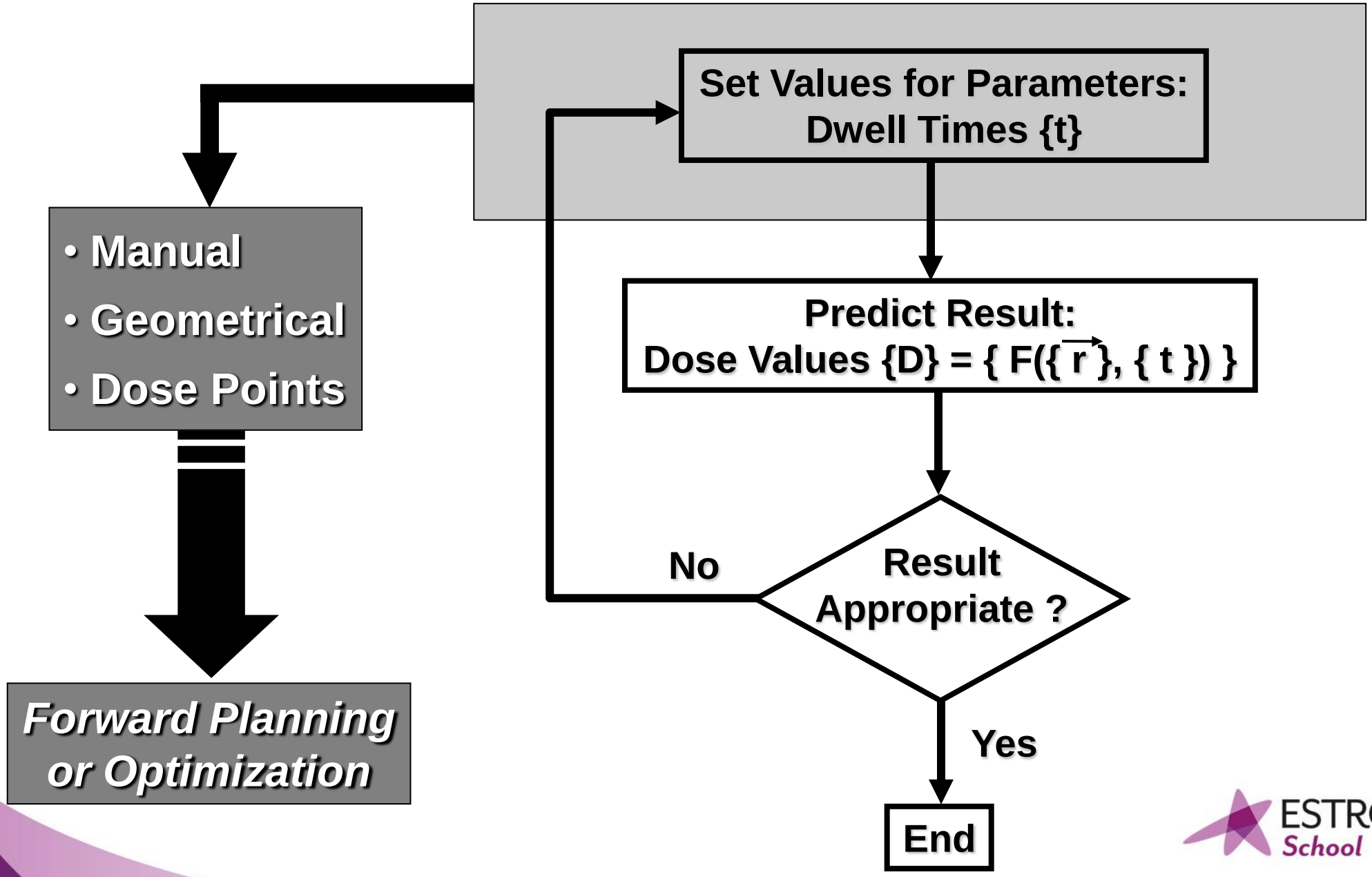
Our “Forward Problem” in Brachytherapy



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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
- **Automatic Selection / Adjustment of Dwell Times T_i**

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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 neighbouring SDPs (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**

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

$$D_b \approx \left(T_1 \cdot \frac{1}{r_{1b}^2}\right) + \left(T_2 \cdot \frac{1}{r_{2b}^2}\right) + \left(T_3 \cdot \frac{1}{r_{3b}^2}\right) \ldots$$

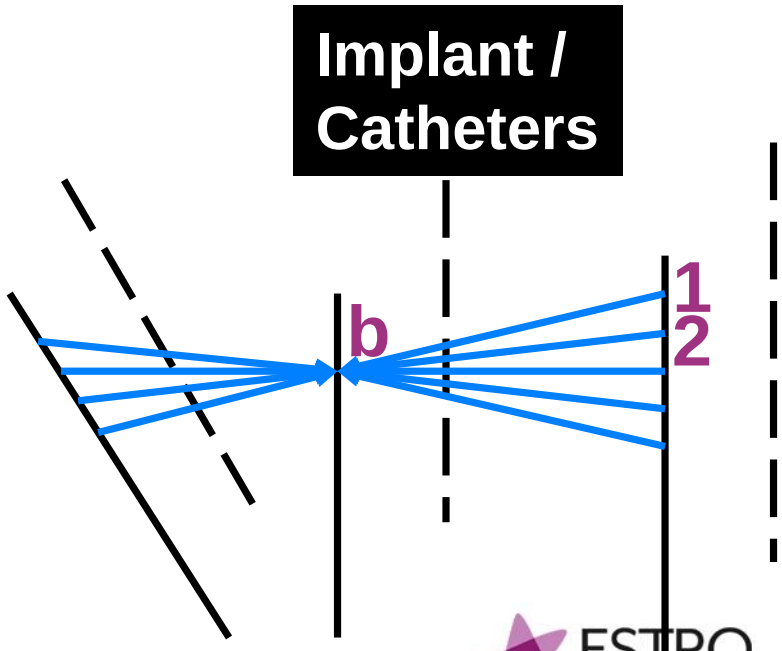
2

$$T_b := \left(\frac{1}{D_b}\right)$$

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.**

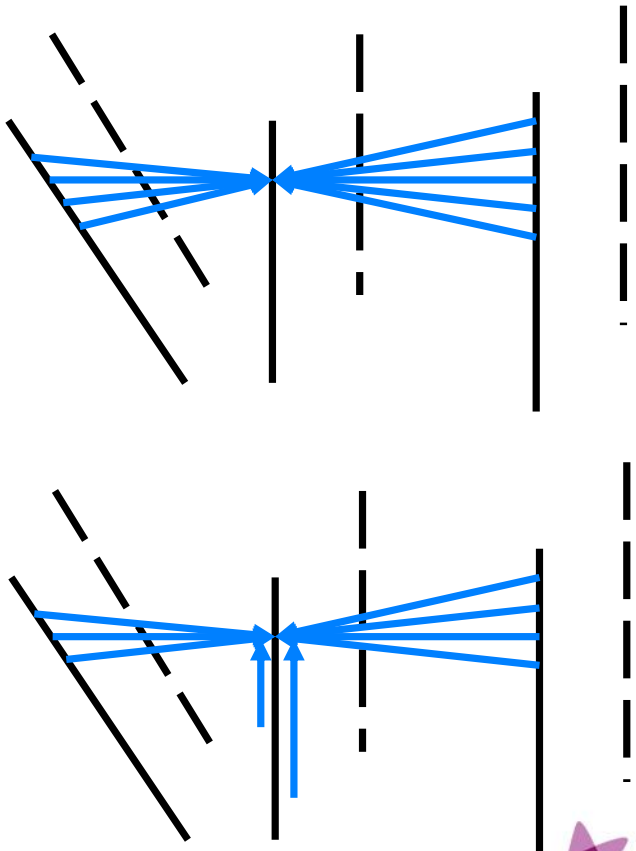
- **Volume:**

  only SDPs in others catheters are taken into account

- **Distance:**

  all other SDPs

  are taken into account



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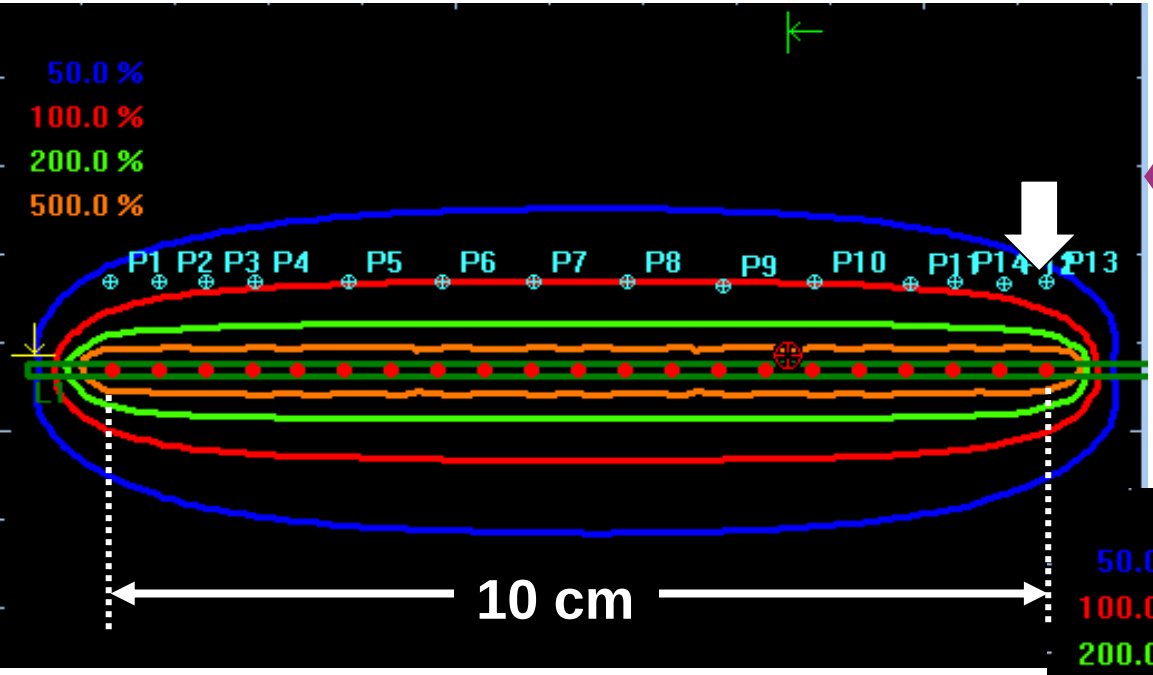
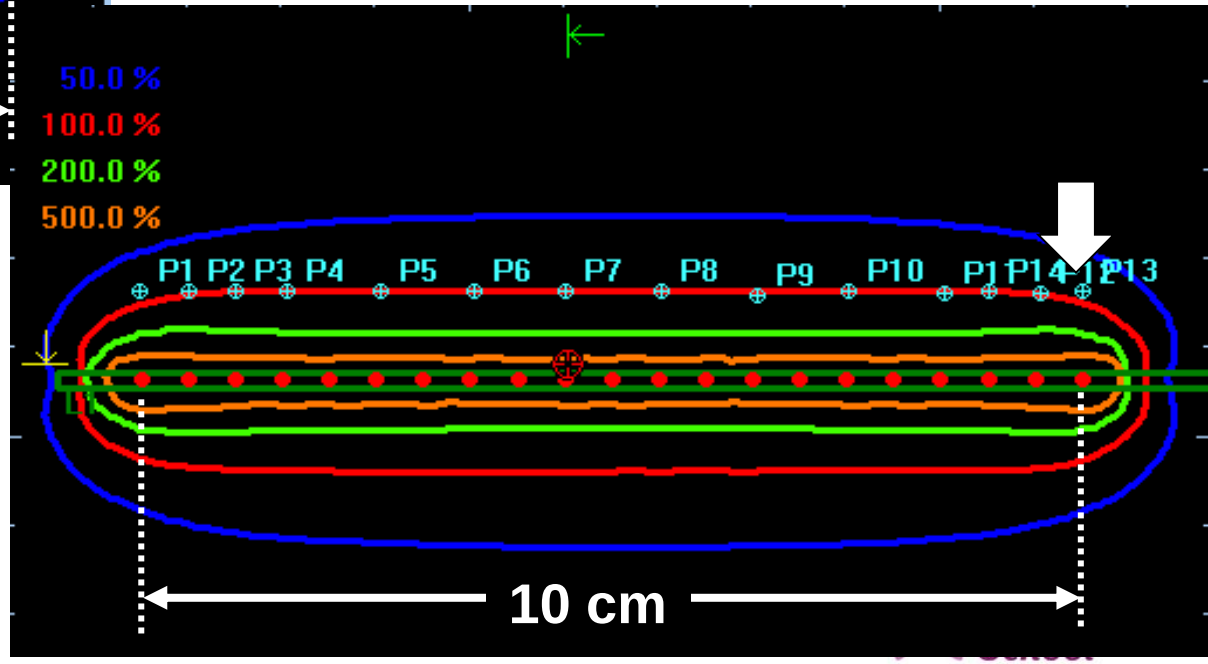
Forward Planning / Optimization

Geometrical "*Optimisation*", GO



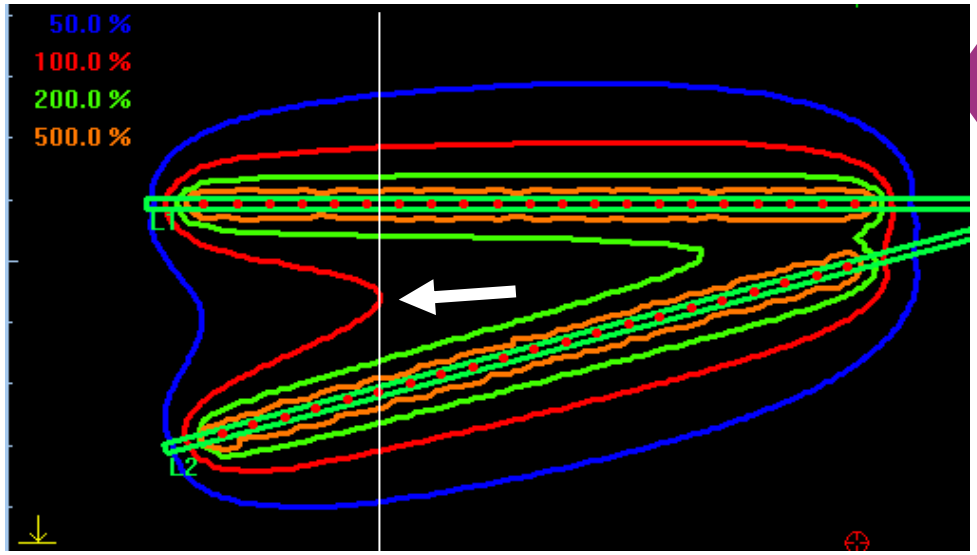
Equal Dwell Times

GO - Distance



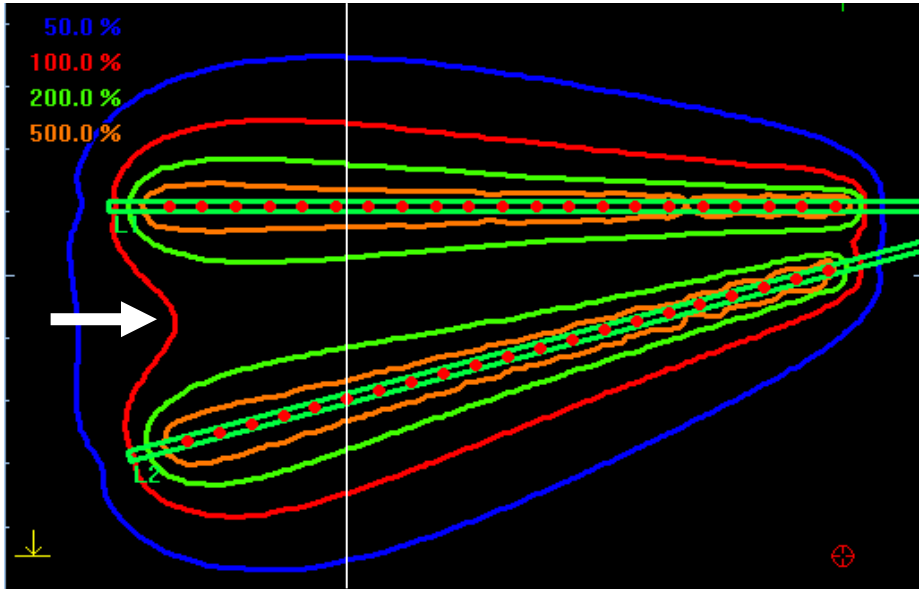
Forward Planning / Optimization

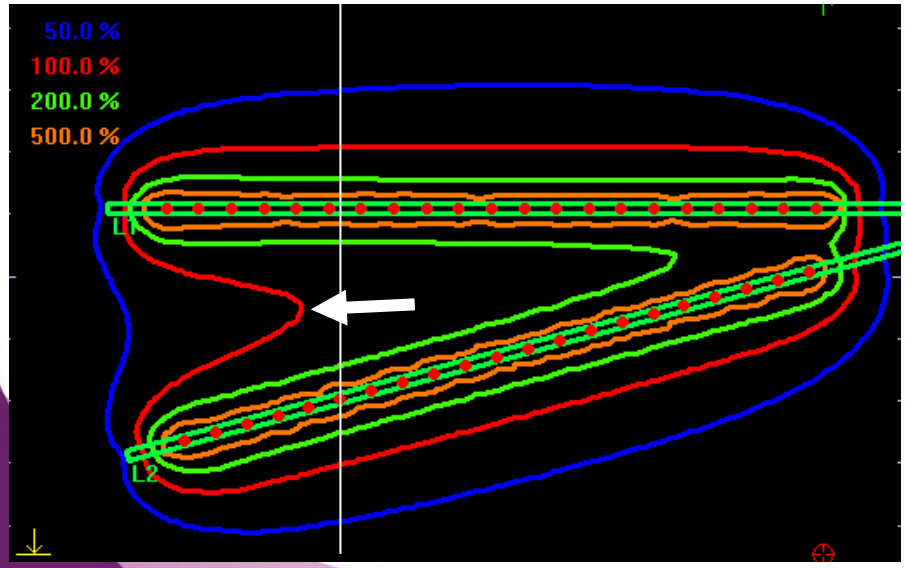
Geometrical "*Optimisation*", GO



Equal Dwell Times

GO - Volume





GO - Distance

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Forward Planning / Optimization

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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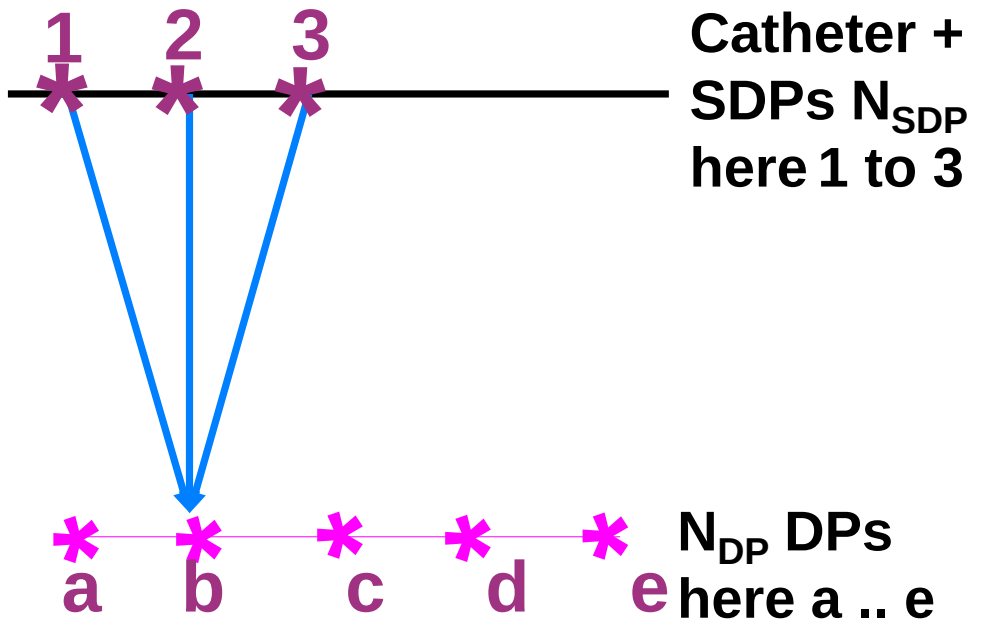
Forward Planning / Optimization

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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Forward Planning / Optimization

Dose Points-based Adjustment of Dwell Times T_i (DPO)

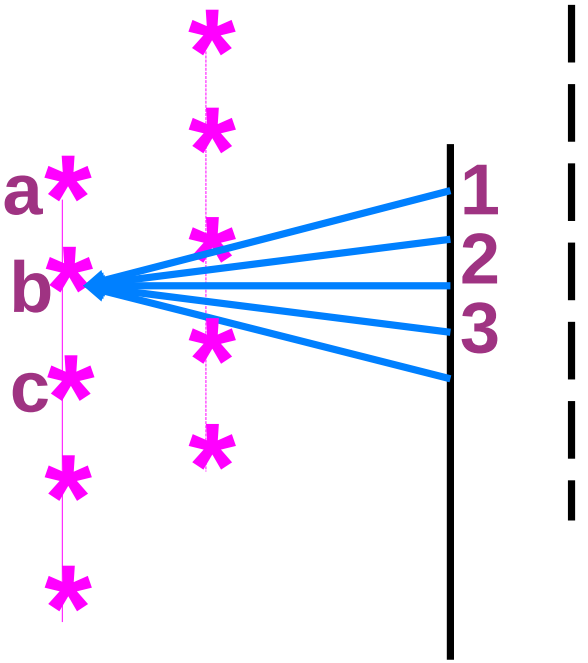
$$D_b \approx \left(T_1 \cdot \frac{1}{r_{1b}^2}\right) + \left(T_2 \cdot \frac{1}{r_{2b}^2}\right) + \left(T_3 \cdot \frac{1}{r_{3b}^2}\right) \ldots = 10\,\text{Gy}$$

$$D_a \approx \left(T_1 \cdot \frac{1}{r_{1a}^2}\right) + \ldots = 10\text{Gy}$$

$$D_c \approx \left(T_1 \cdot \frac{1}{r_{1c}^2}\right) + \ldots = 10\text{Gy}$$

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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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 (D-V)**
- **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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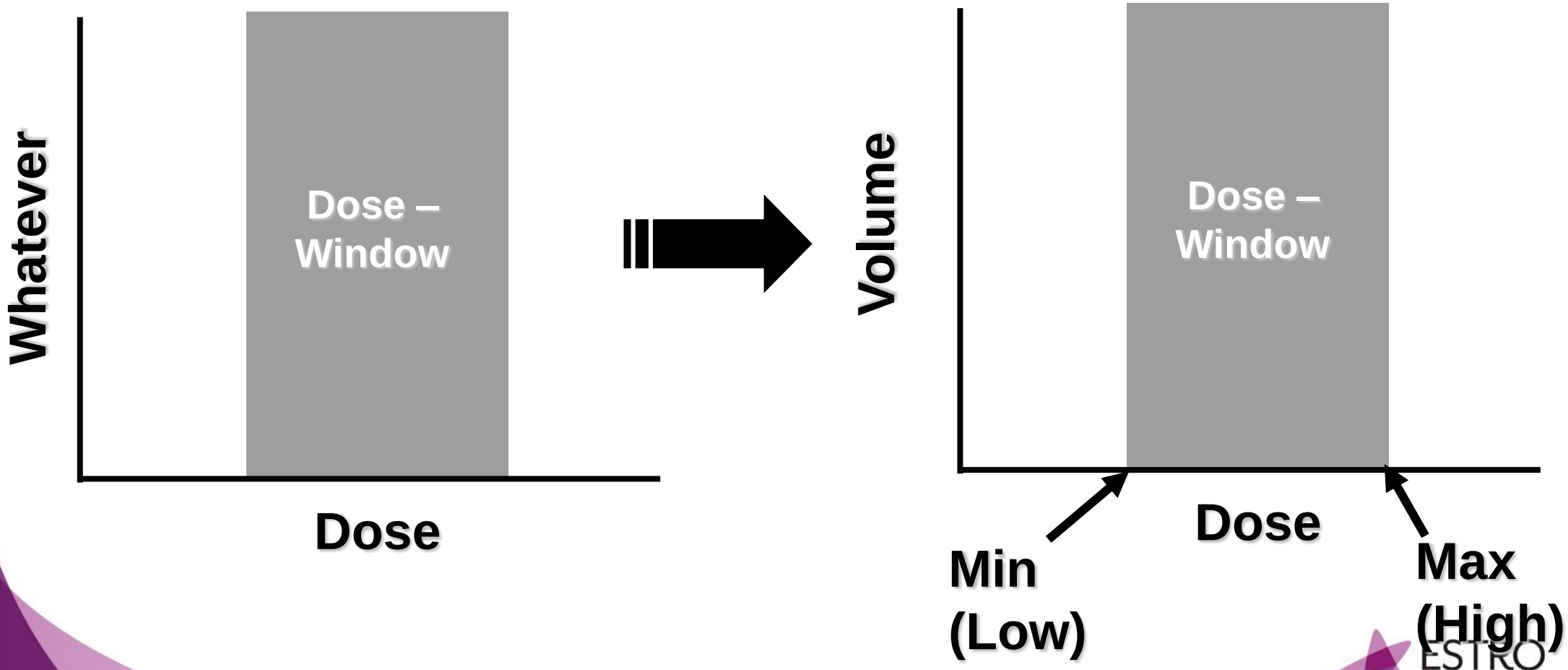
Inverse Optimization and Planning

Our Wishes: “ideal” Dose Distribution



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Inverse Optimisation and Planning: Objectives

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_j is the dose at the jth-sampling point for the ith-objective function:

$$d_j^i(\mathrm{x}) = \sum_{k=1}^{N_{cath}}\sum_{l=1}^{N_{ASDP}^k} x_{lk}^2\,\tilde{d}^{\,i}_{jkl}$$

- k: **Catheters/ Needles/ Applicators**
- l: **Active SDPs**
- x_{lk}^2: **Dwell time t_{lk}**

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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 $V_{0\%}$

$$f_i = \frac{1}{N_i}\sum_{j=1}^{N_i}\left[\left[d_j^i(\mathbf{x}) - D_H^i\right]^p\right] \quad \forall \; d_j^i(\mathbf{x}) > D_H^i$$

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 relative 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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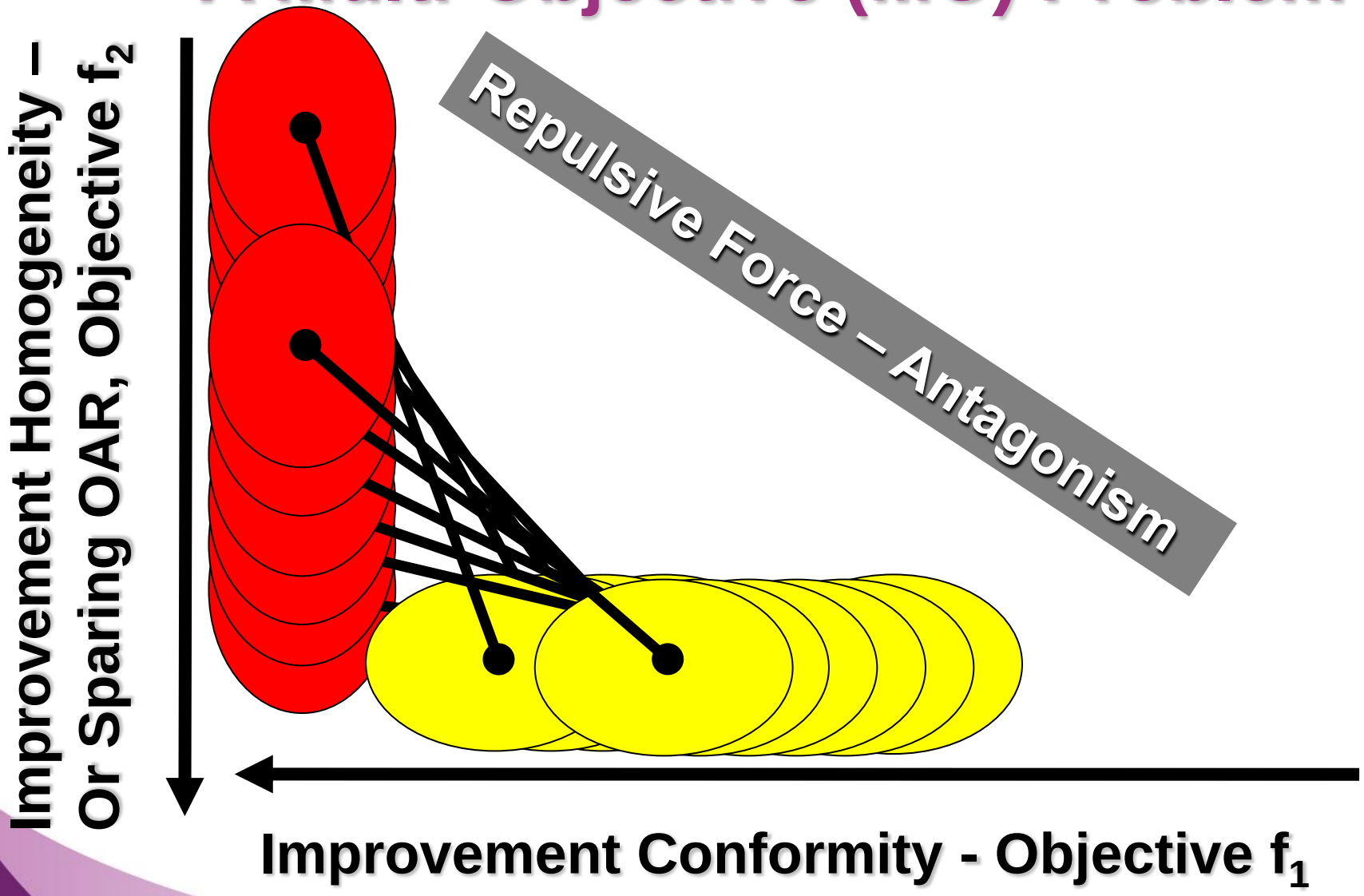
Inverse Optimization and Planning

A Multi-Objective (MO) Problem



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Inverse Optimization and Planning

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!

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VOLUME IMPLANT OF THE PROSTATE

COMPREHENSIVE AND PRACTICAL BRACHYTHERAPY

ESTRO Teaching Course, Budapest 2017

Emmie Kaljouw
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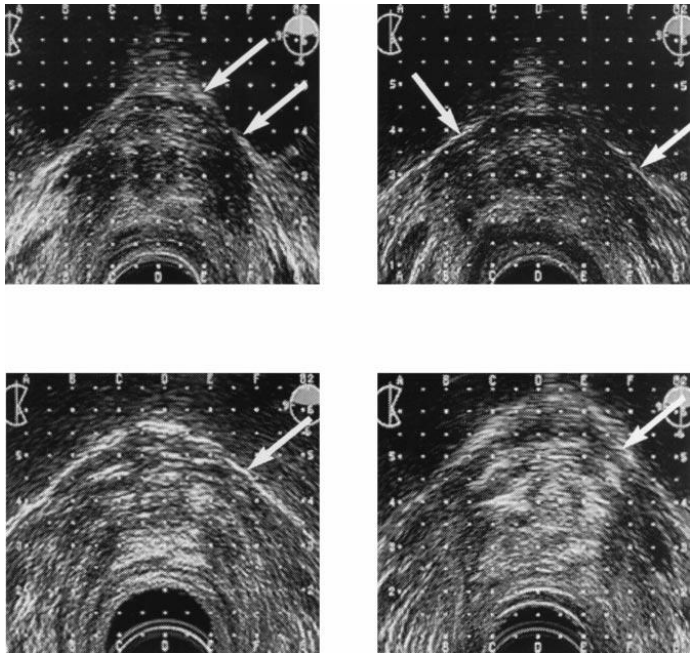
Volume implant of the prostate

- Pre-treatment activities
- Performing an ultrasound
- Registration of TRUS and MRI
- Source activity
- Pre-plan versus intra-operative plan
- Real time planning in the OR, LDR
- Catheter identification
- Registration of CT and MRI
- Catheter reconstruction based on MRI
- Activation of dwell positions
- Post-planning, HDR
- Treatment plan optimisation

Pre-treatment activities

- Measure prostate volume in advance
  - Preferably under same conditions as in OR
  - Evaluate the position of the prostate and pubic arch



Wallner et al, **Use of TRUS to predict pubic arch interference of prostate brachytherapy**, Int J Radiat Oncol Biol Phys, 43, 1999, pp 583-585

- When TRUS is the primary image set on the OR, fusion with pre-operative MRI might be desirable

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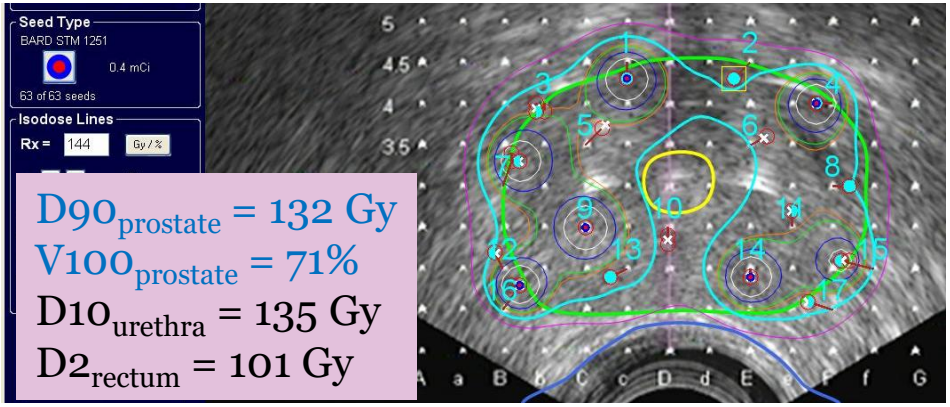
Performing an Ultrasound

- Fixation of the probe to the table top
  - For reliable reconstruction
- Guidance of catheter/ applicator placement
  - Real-time information
- Connection to a treatment planning system
  - Performing pre-planning (and post-planning)

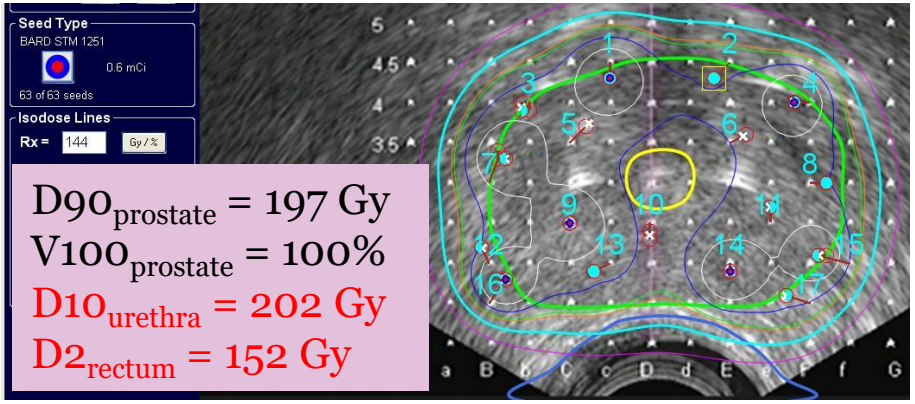
- Real time reconstruction of the catheters/ applicator
  - Good visibility of the tip of the catheter/ applicator
- Deformation of the tissue due to ultrasound probe
  - Treatment in same position as imaging

Source activity

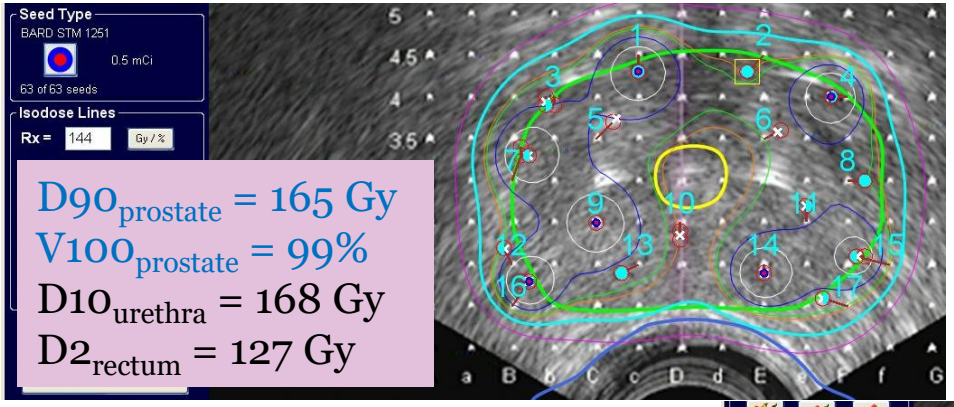
- Determine which activity works best for your practice
- Important to enter the right activity in the treatment planning system



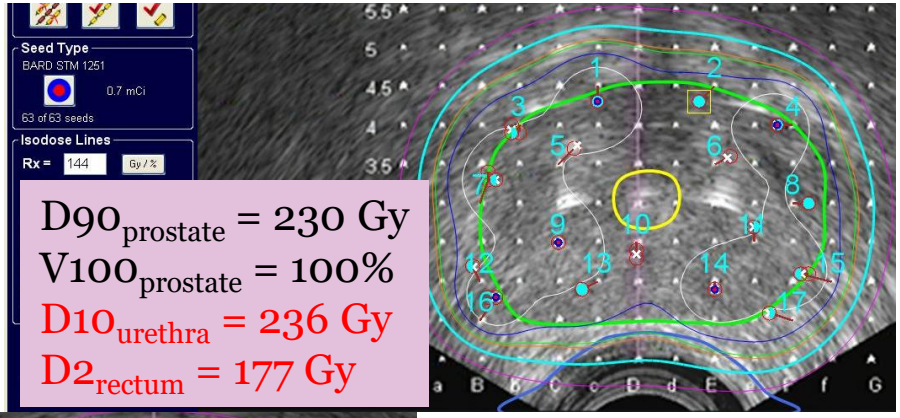
$D90_{prostate}$ = 132 Gy
$V100_{prostate}$ = 71%
$D10_{urethra}$ = 135 Gy
$D2_{rectum}$ = 101 Gy



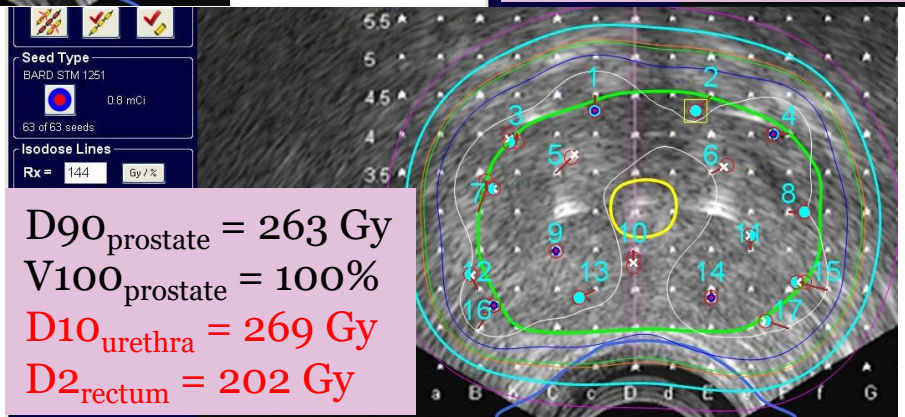
$D90_{prostate}$ = 197 Gy
$V100_{prostate}$ = 100%
$D10_{urethra}$ = 202 Gy
$D2_{rectum}$ = 152 Gy



$D90_{prostate}$ = 165 Gy
$V100_{prostate}$ = 99%
$D10_{urethra}$ = 168 Gy
$D2_{rectum}$ = 127 Gy



$D90_{prostate}$ = 230 Gy
$V100_{prostate}$ = 100%
$D10_{urethra}$ = 236 Gy
$D2_{rectum}$ = 177 Gy



$D90_{prostate}$ = 263 Gy
$V100_{prostate}$ = 100%
$D10_{urethra}$ = 269 Gy
$D2_{rectum}$ = 202 Gy

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Pre-plan versus intra-operative plan

Pre-planning

- Outpatient TRUS prior to implant
- Positioning probe as outpatient situation
- Less OR time needed
- No possibility for interactive planning
- Oedema effect not taken into account
- No physicist/dosimetrist needed in OR
- Number of seeds to order more accurate

Intra-operative plan

- TRUS at time of implant
- Probe stays in position during whole treatment
- More OR time needed
- Interactive planning possible
- Geometry changes are taken into account
- Physicist/dosimetrist needed in OR
- Risk of inappropriate seed ordering

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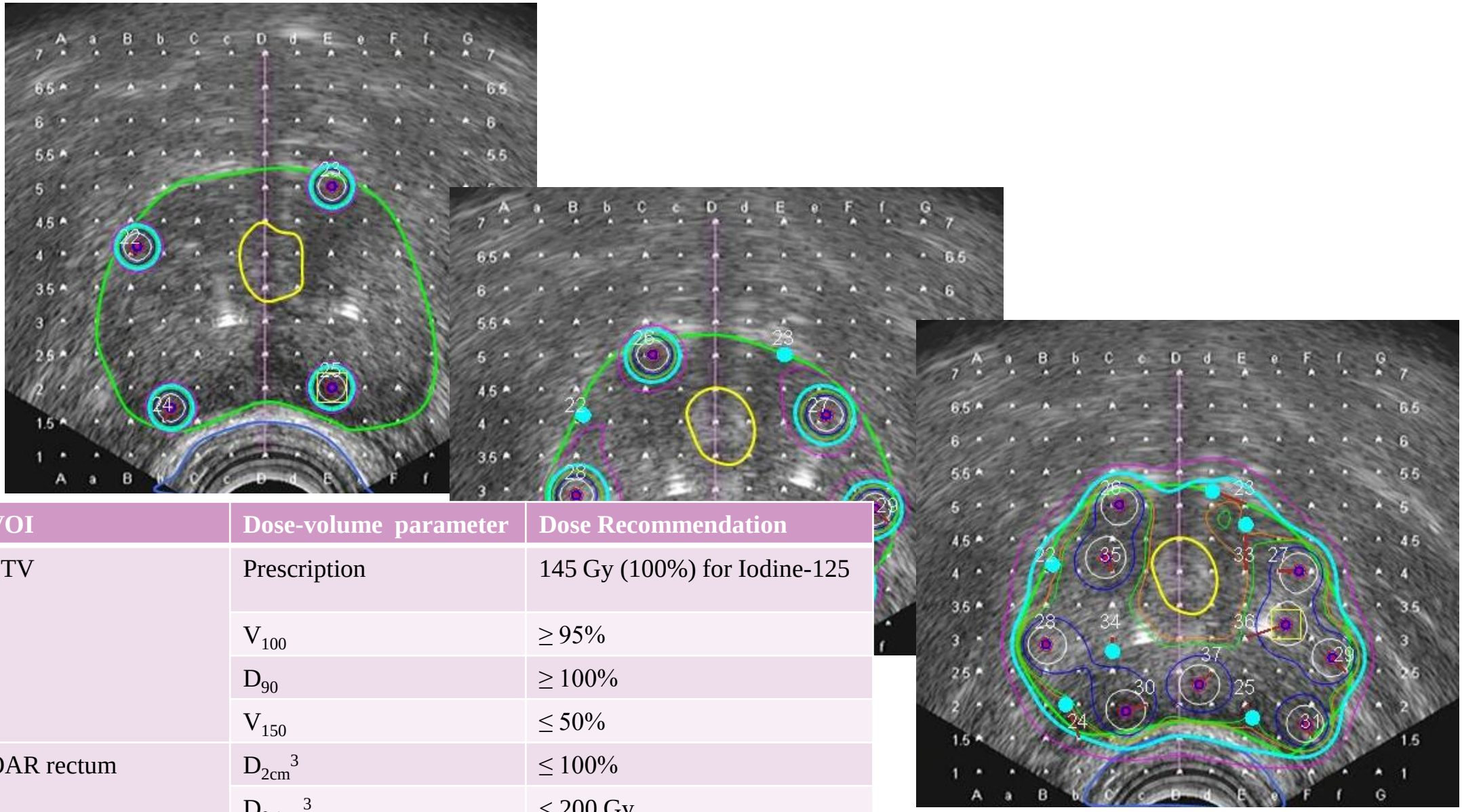
Real time planning in the OR, LDR



VOI	Dose-volume parameter	Dose Recommendation
PTV	Prescription	145 Gy (100%) for Iodine-125
	V_{100}	≥ 95%
	D_{90}	≥ 100%
	V_{150}	≤ 50%
OAR rectum	D_{2cm^3}	≤ 100%
	$D_{0.1cm^3}$	< 200 Gy
OAR prostatic urethra	D_{10}	< 150%
	D_{30}	< 130%

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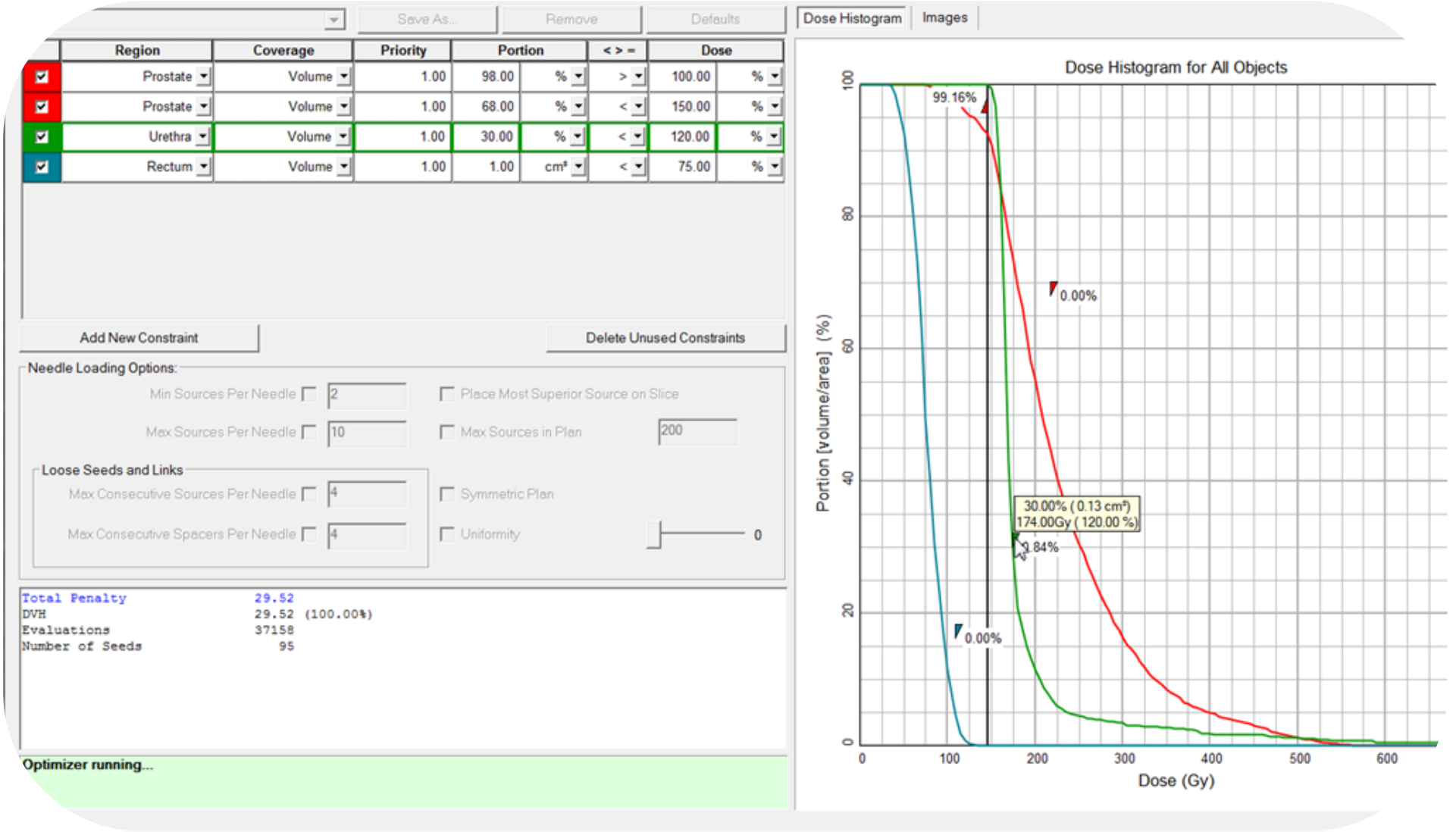
Real time planning in the OR, LDR



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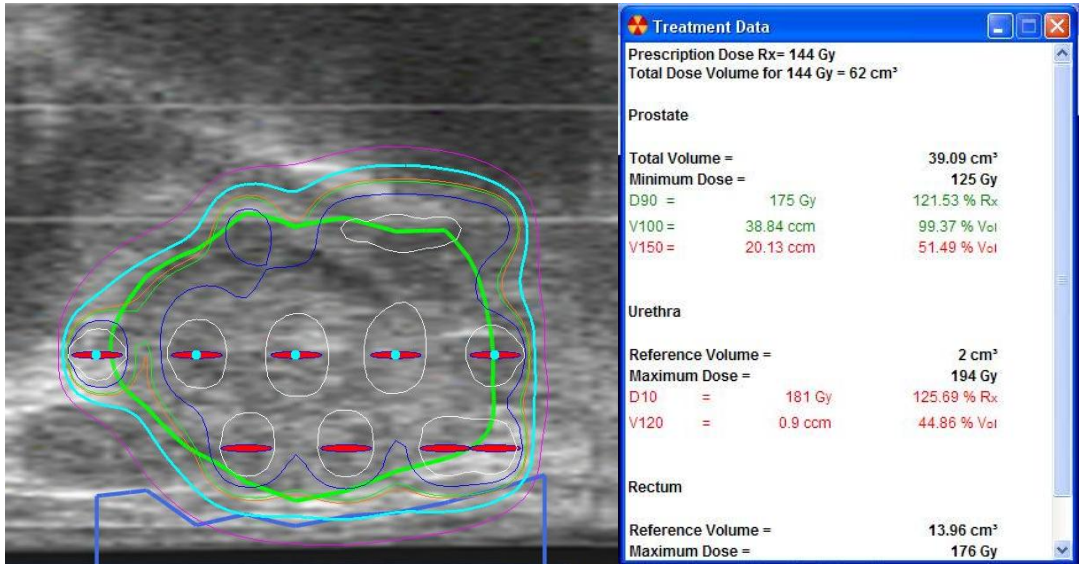
Real time planning in the OR, LDR



Treatment Data

Prescription Dose Rx= 144 Gy
Total Dose Volume for 144 Gy = 62 cm³

Prostate

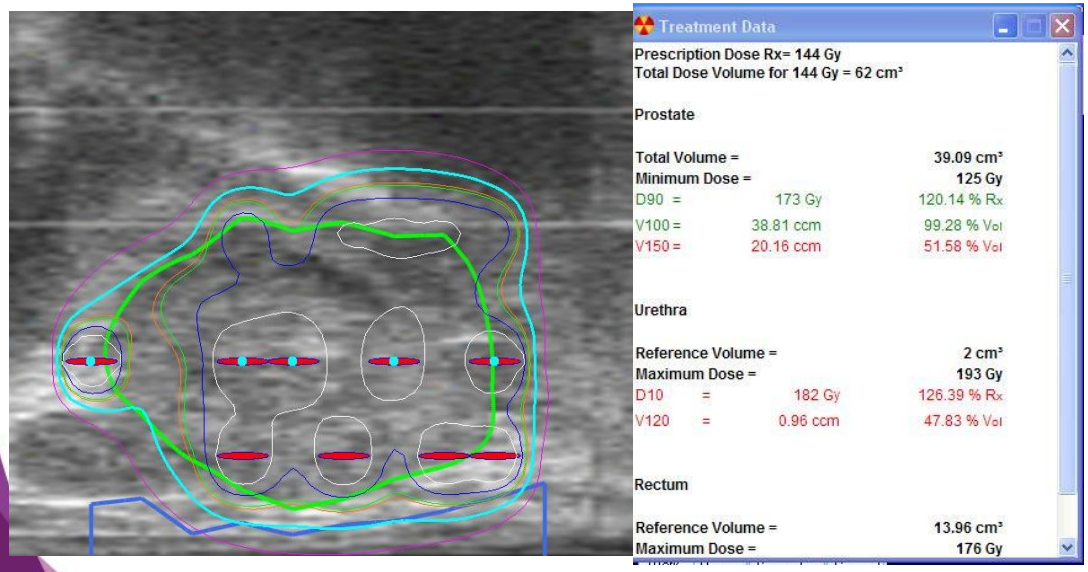
Total Volume =		39.09 cm³
Minimum Dose =		125 Gy
D90 =	175 Gy	121.53 % Rx
V100 =	38.84 ccm	99.37 % Vol
V150 =	20.13 ccm	51.49 % Vol

Urethra

Reference Volume =		2 cm³
Maximum Dose =		194 Gy
D10 =	181 Gy	125.69 % Rx
V120 =	0.9 ccm	44.86 % Vol

Rectum

Reference Volume =	13.96 cm³
Maximum Dose =	176 Gy



Treatment Data

Prescription Dose Rx= 144 Gy
Total Dose Volume for 144 Gy = 62 cm³

Prostate

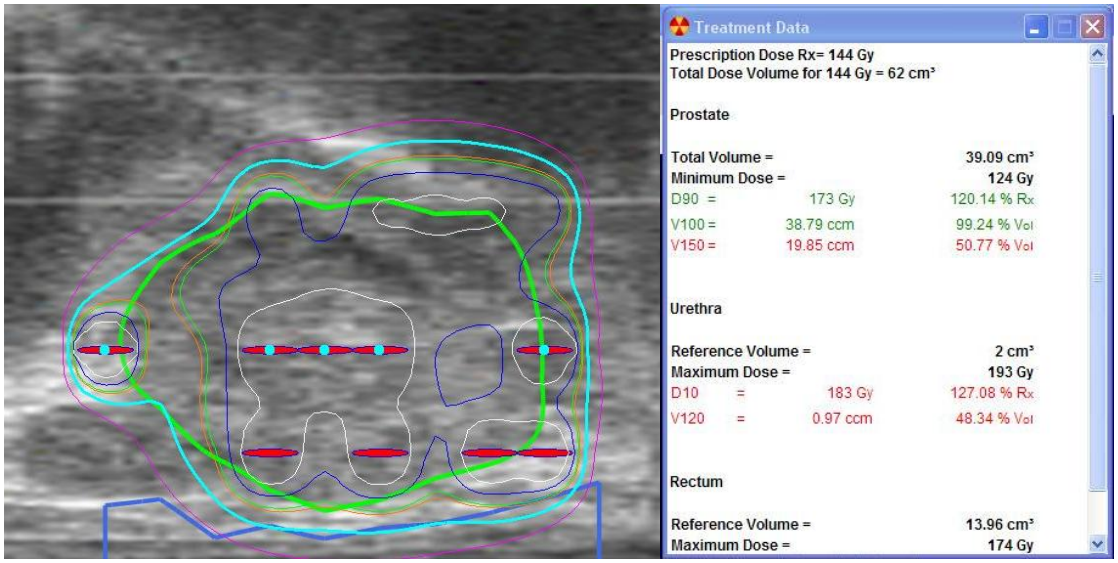
Total Volume =		39.09 cm³
Minimum Dose =		125 Gy
D90 =	173 Gy	120.14 % Rx
V100 =	38.81 ccm	99.28 % Vol
V150 =	20.16 ccm	51.58 % Vol

Urethra

Reference Volume =		2 cm³
Maximum Dose =		193 Gy
D10 =	182 Gy	126.39 % Rx
V120 =	0.96 ccm	47.83 % Vol

Rectum

Reference Volume =	13.96 cm³
Maximum Dose =	176 Gy



Treatment Data

Prescription Dose Rx= 144 Gy
Total Dose Volume for 144 Gy = 62 cm³

Prostate

Total Volume =		39.09 cm³
Minimum Dose =		124 Gy
D90 =	173 Gy	120.14 % Rx
V100 =	38.79 ccm	99.24 % Vol
V150 =	19.85 ccm	50.77 % Vol

Urethra

Reference Volume =		2 cm³
Maximum Dose =		193 Gy
D10 =	183 Gy	127.08 % Rx
V120 =	0.97 ccm	48.34 % Vol

Rectum

Reference Volume =	13.96 cm³
Maximum Dose =	174 Gy

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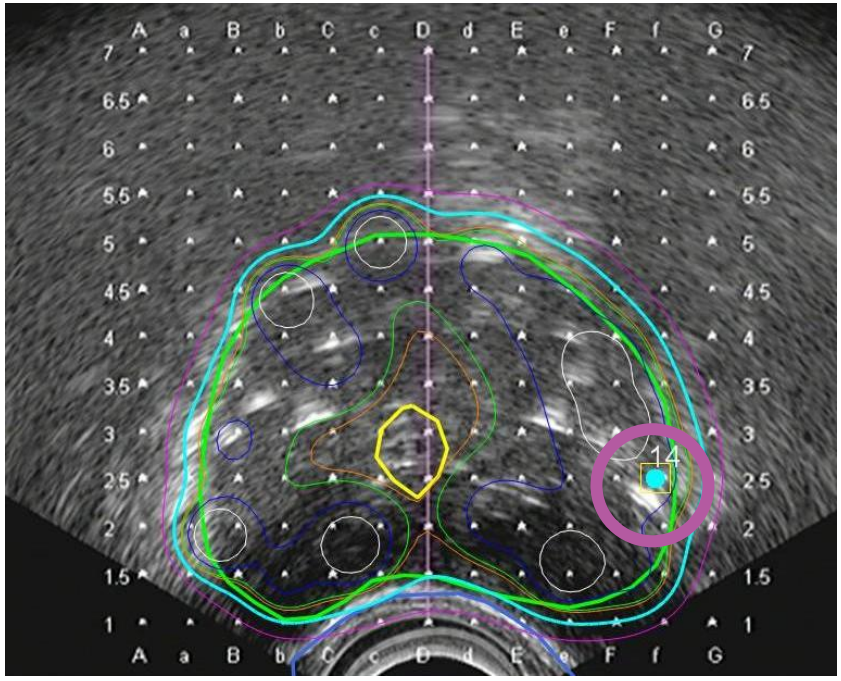
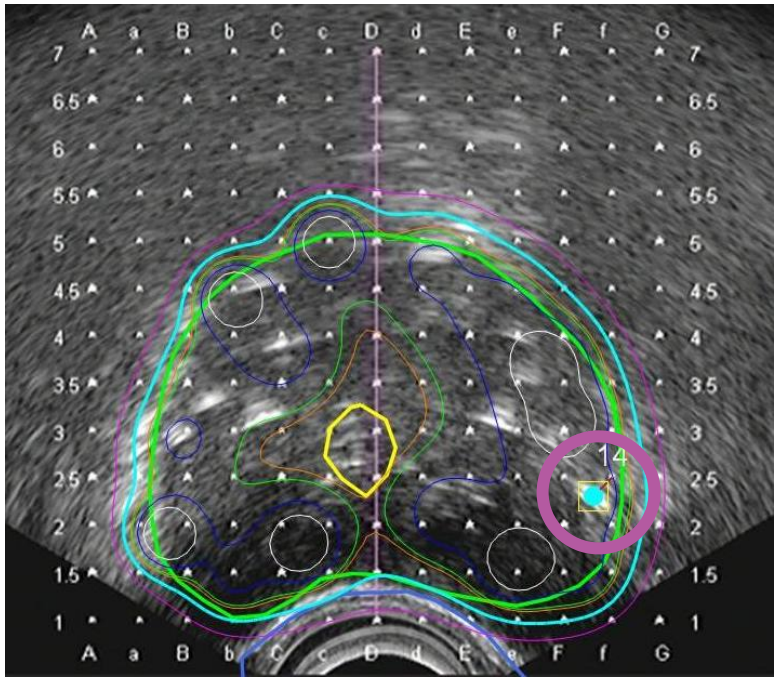
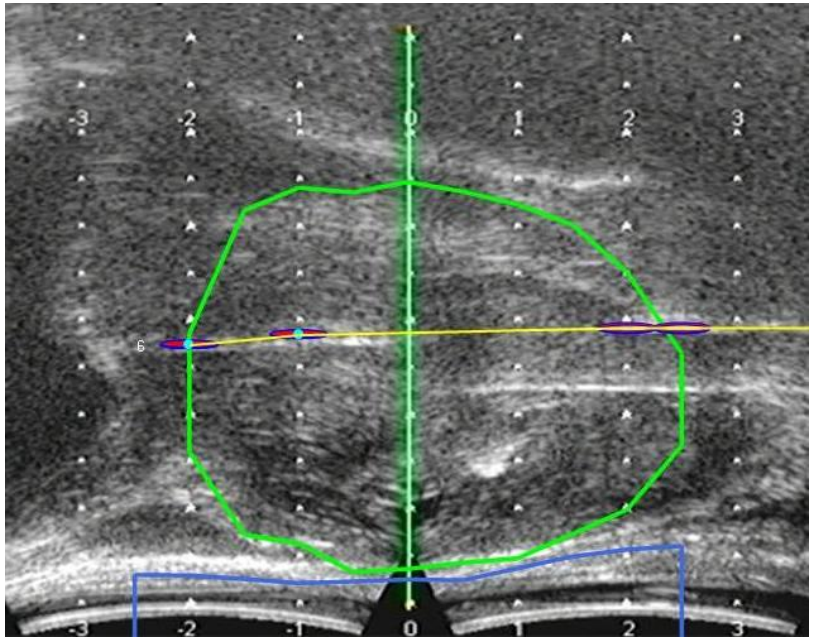
Real time planning in the OR, LDR



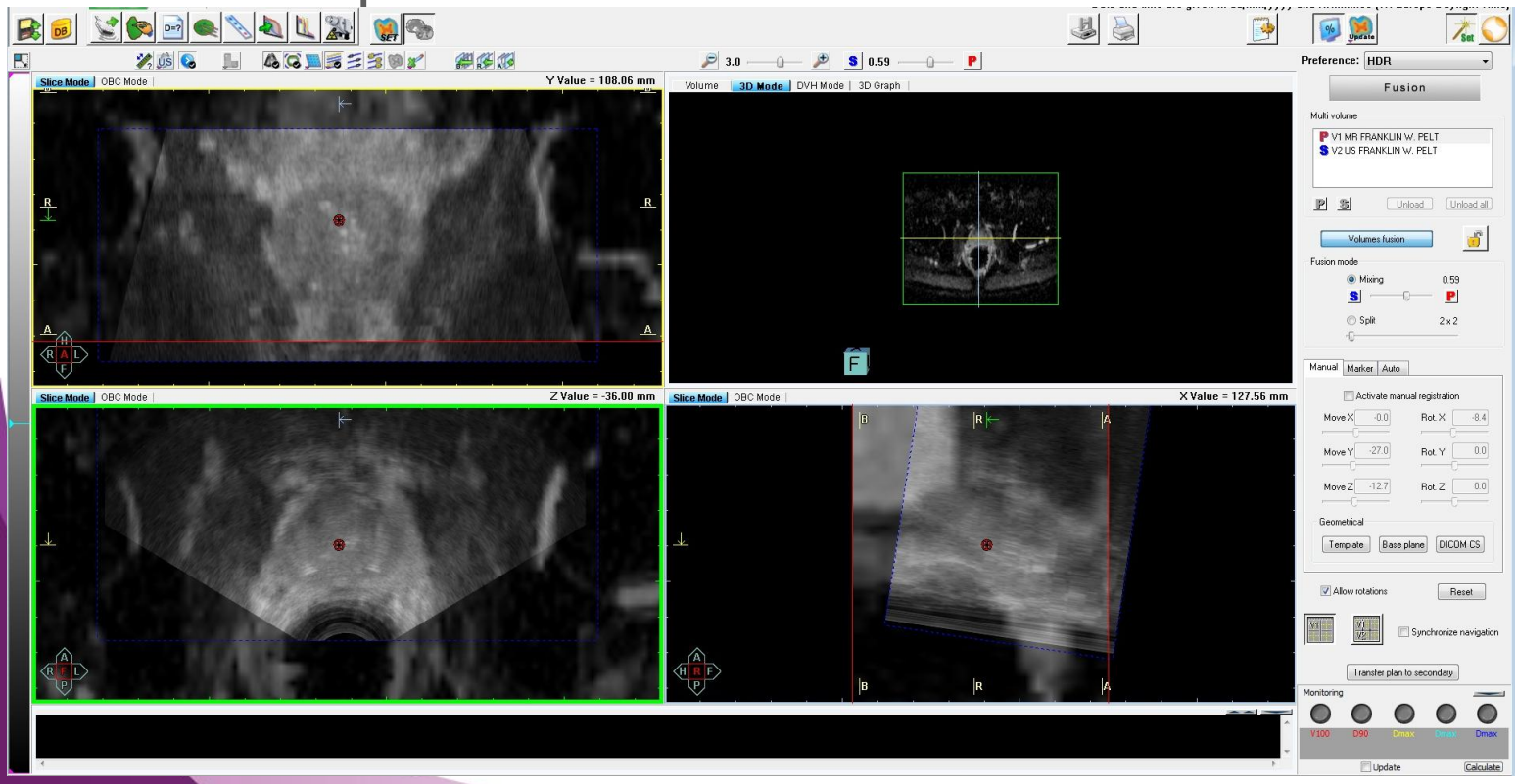
Adjust planned position to real position





Registration TRUS and MRI

- Pre-operative MR images, even with contour
- Real time TRUS images
- Registration to get more detailed information about the position of the tumour site



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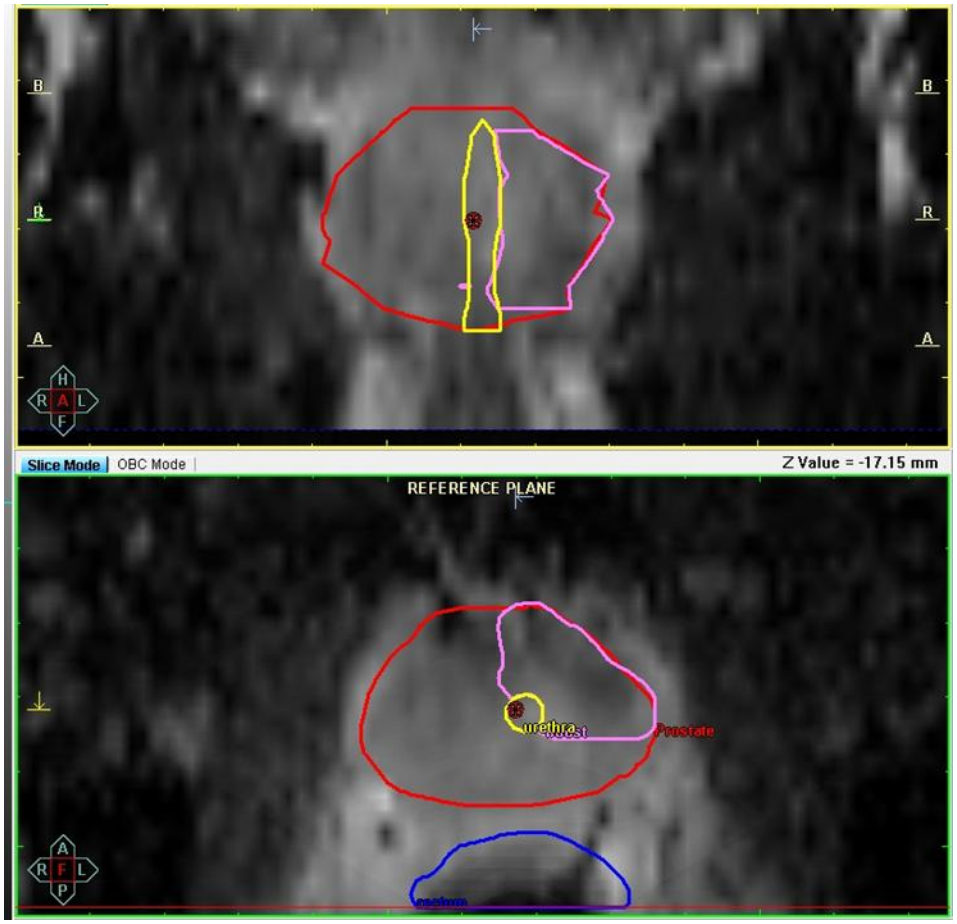
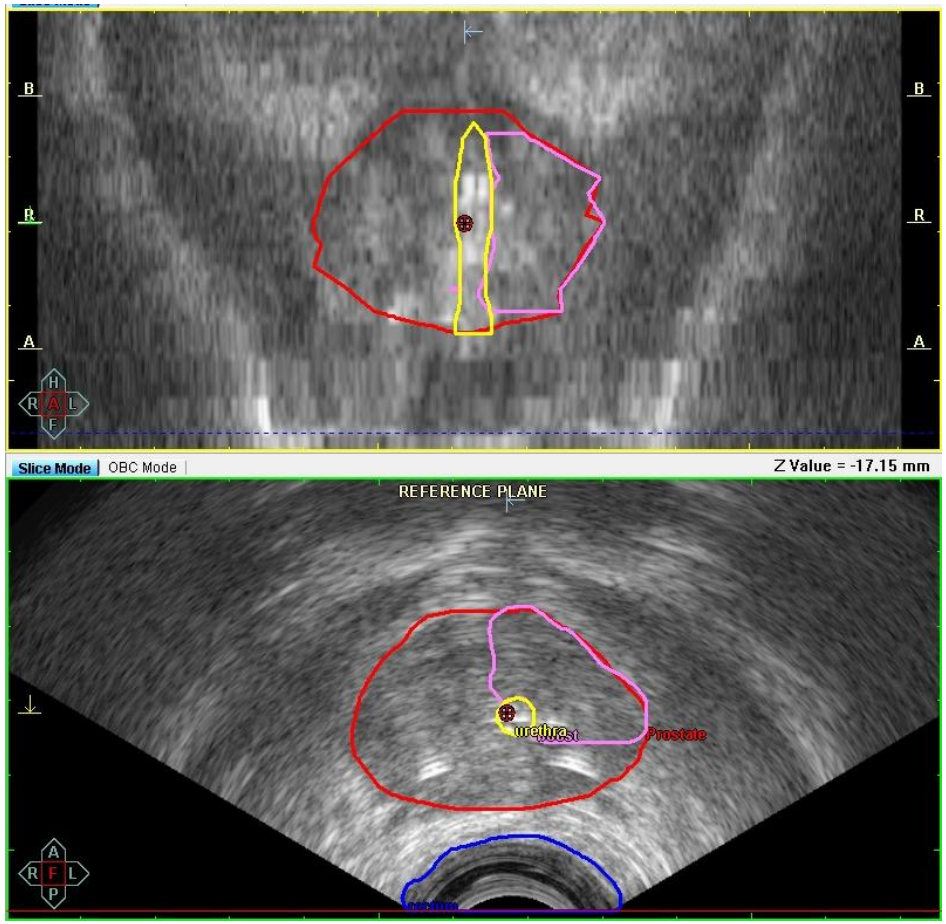
Registration TRUS and MRI

- Pre-operative MRI



- Real-time TRUS



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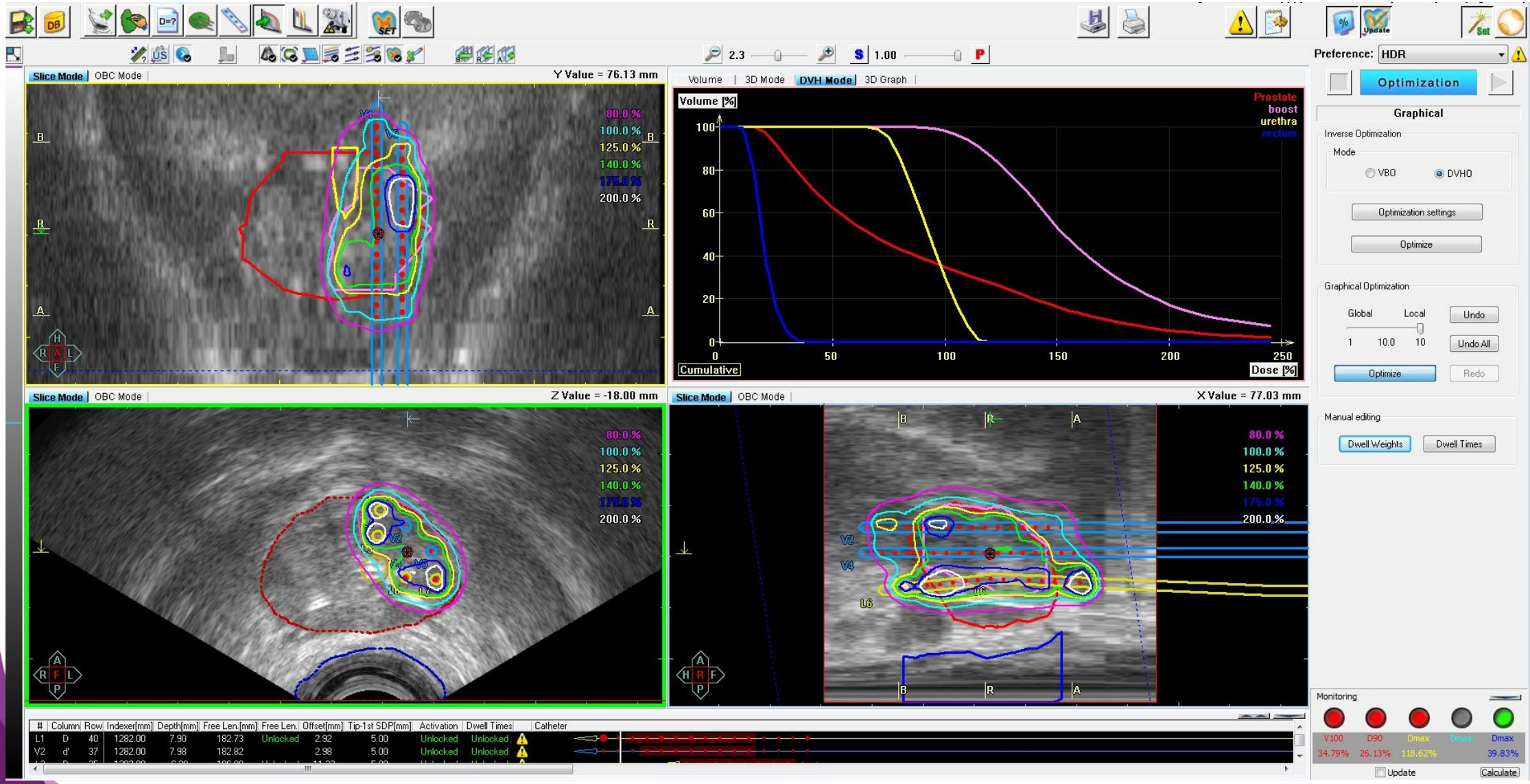
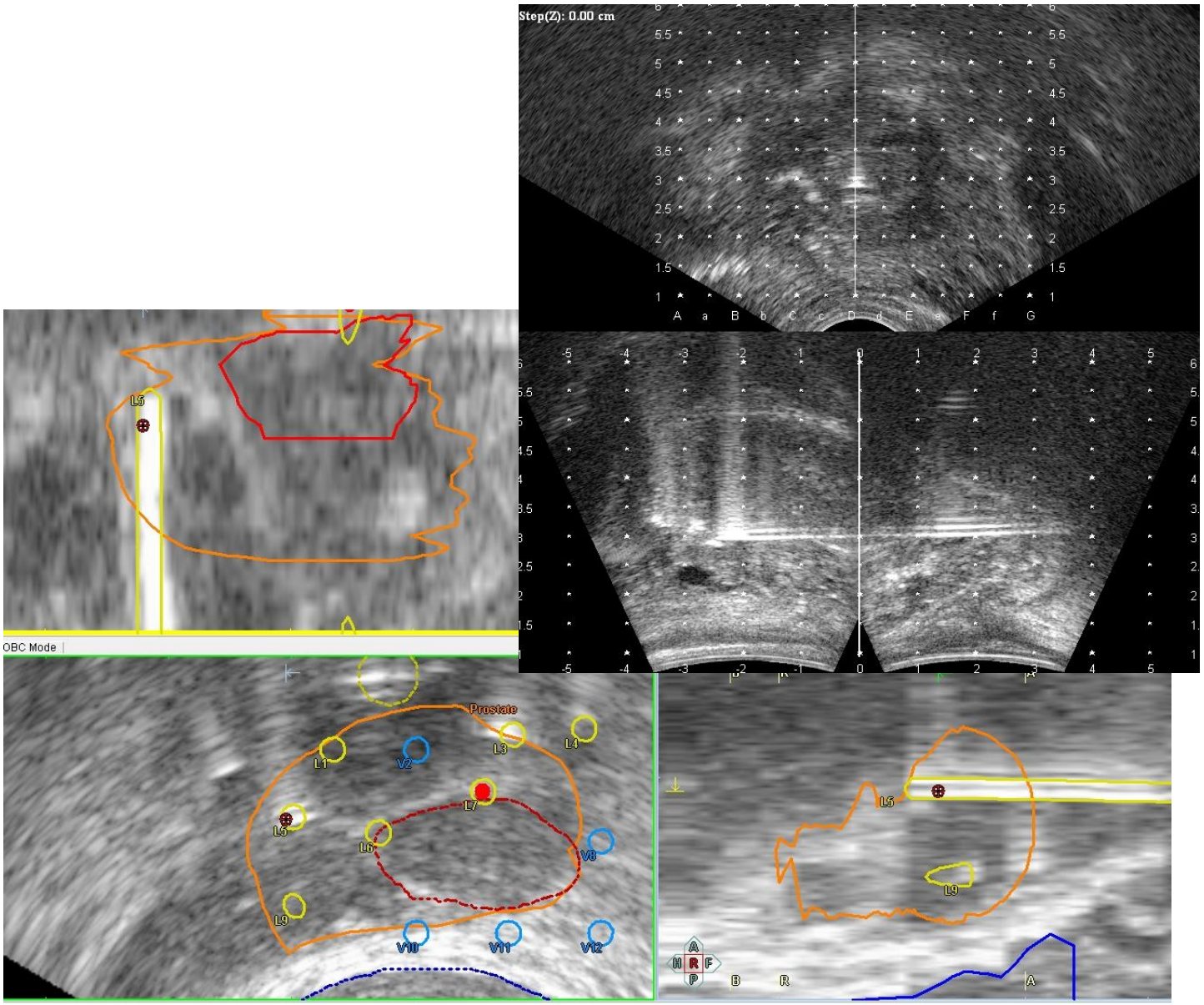
Registration TRUS and MRI



Real time planning in the OR



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Catheter identification

- Catheter identification
  - Documentation of catheter used
  - Number/ colour catheters
  - Documentation of catheter order
  - Documentation of position of catheters in relation to implant

Prostate HDR Implantform □ 1x13Gy □ 3 x 10Gy □ … x … Gy

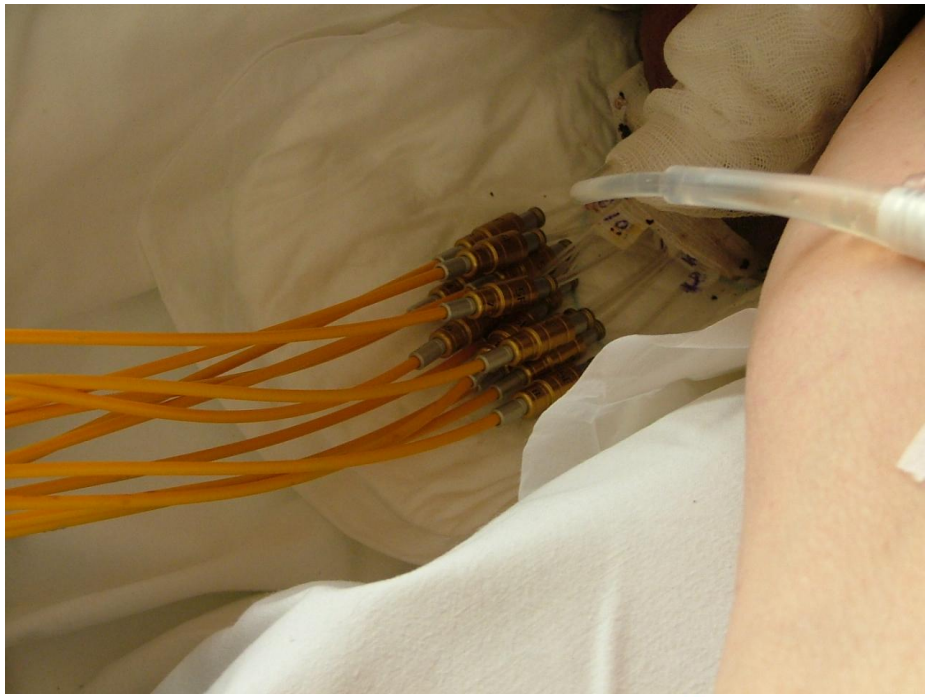
Date:
Physician:
Technician:

Patient name:
Patient number:
Date of birth:

Total dose	cGy	
Dose per fraction	cGy	
Number of fractions		
Stepsize	□ 2,5mm	□ 5mm
Transfertubes catheters		

Catheters: BCH Ella 009-01

Catheter (= channel number)	Catheter Length (mm)	Transfertube	Indexer (mm)	Offset (mm)
1	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
2	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
3	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
4	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
5	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
6	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
7	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
8	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
9	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
10	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5
11	282	Rechtstreeks	1282 (1005 + 282 - 5)	-5



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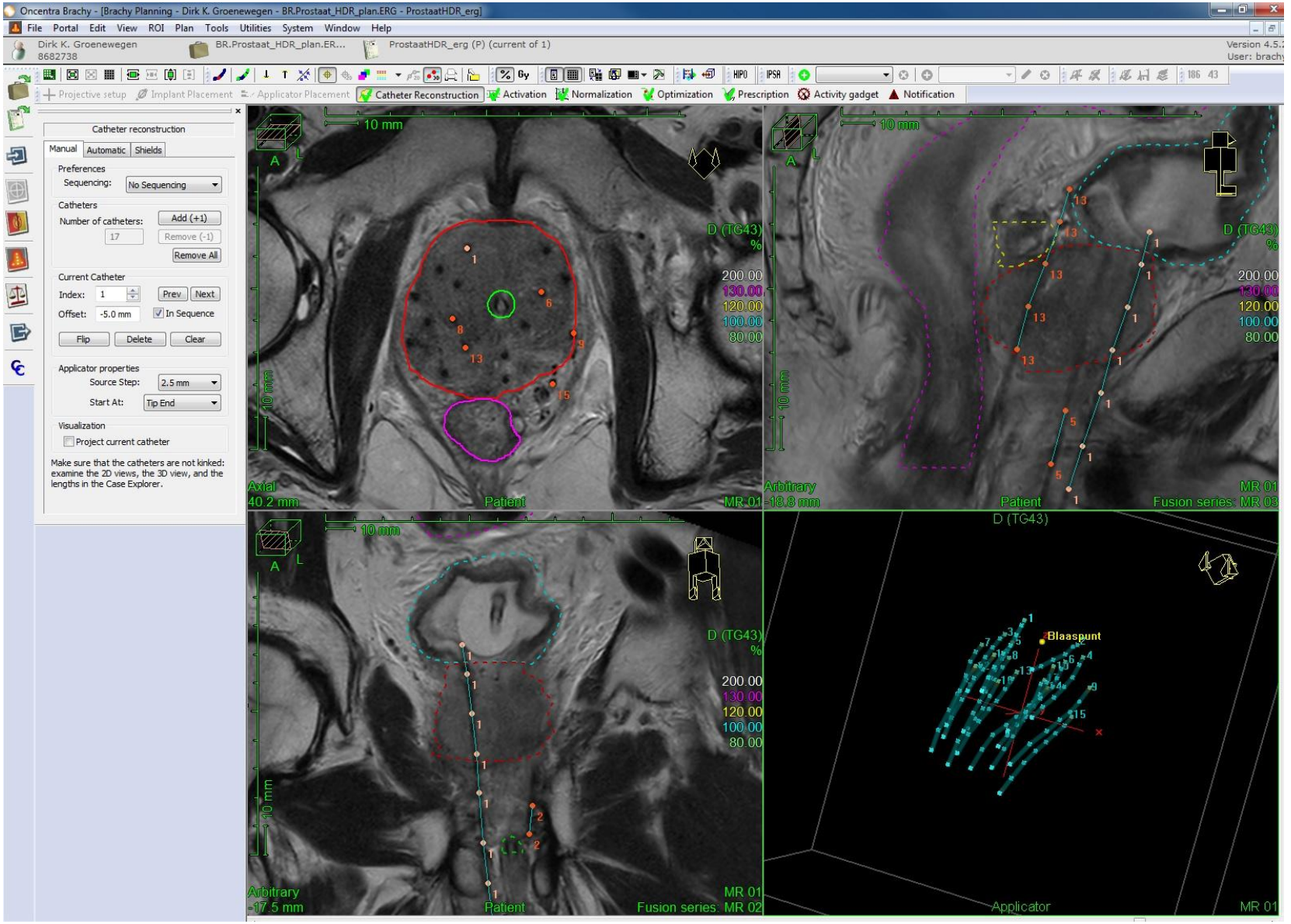
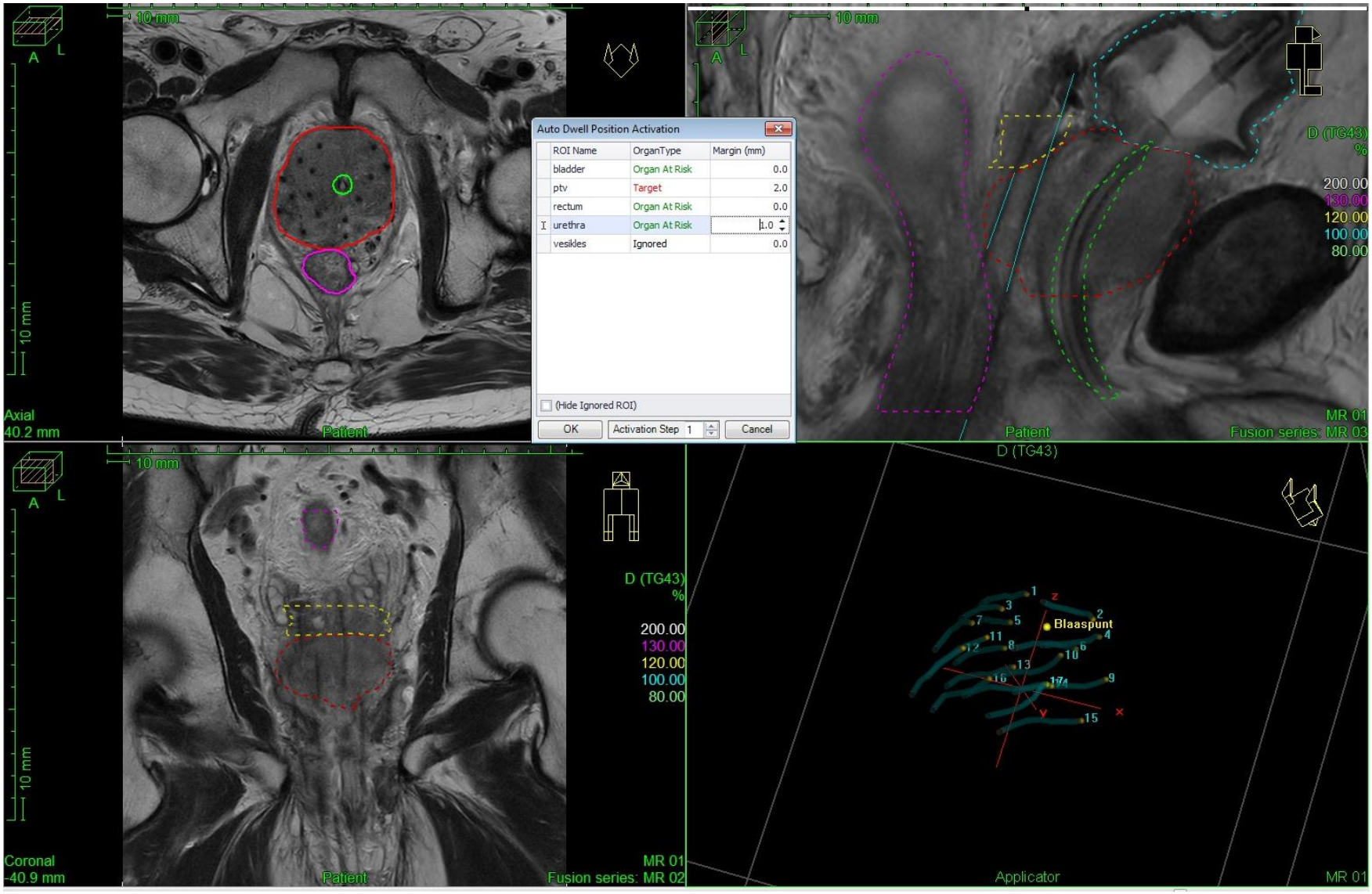
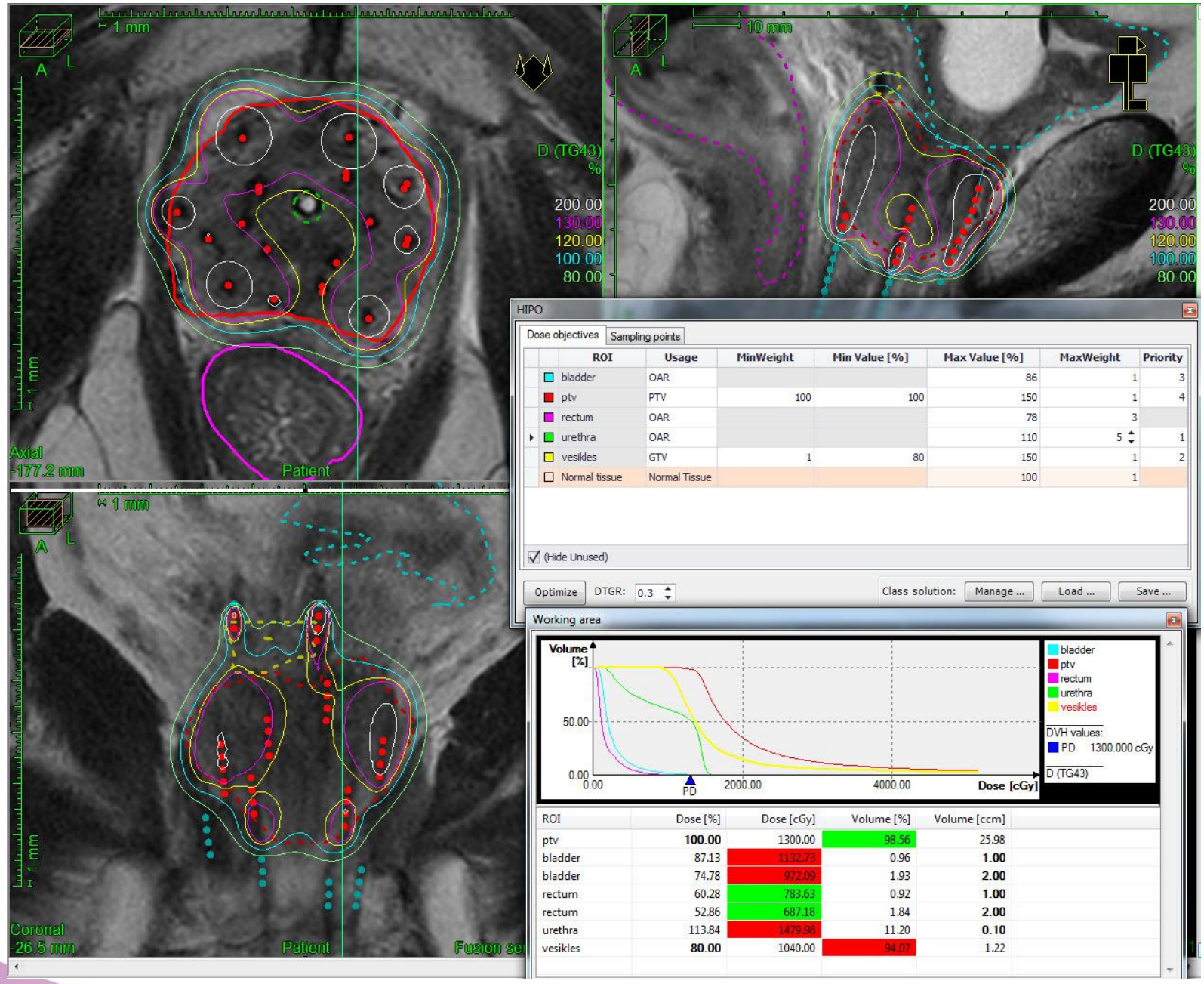
Catheter reconstruction based on MRI



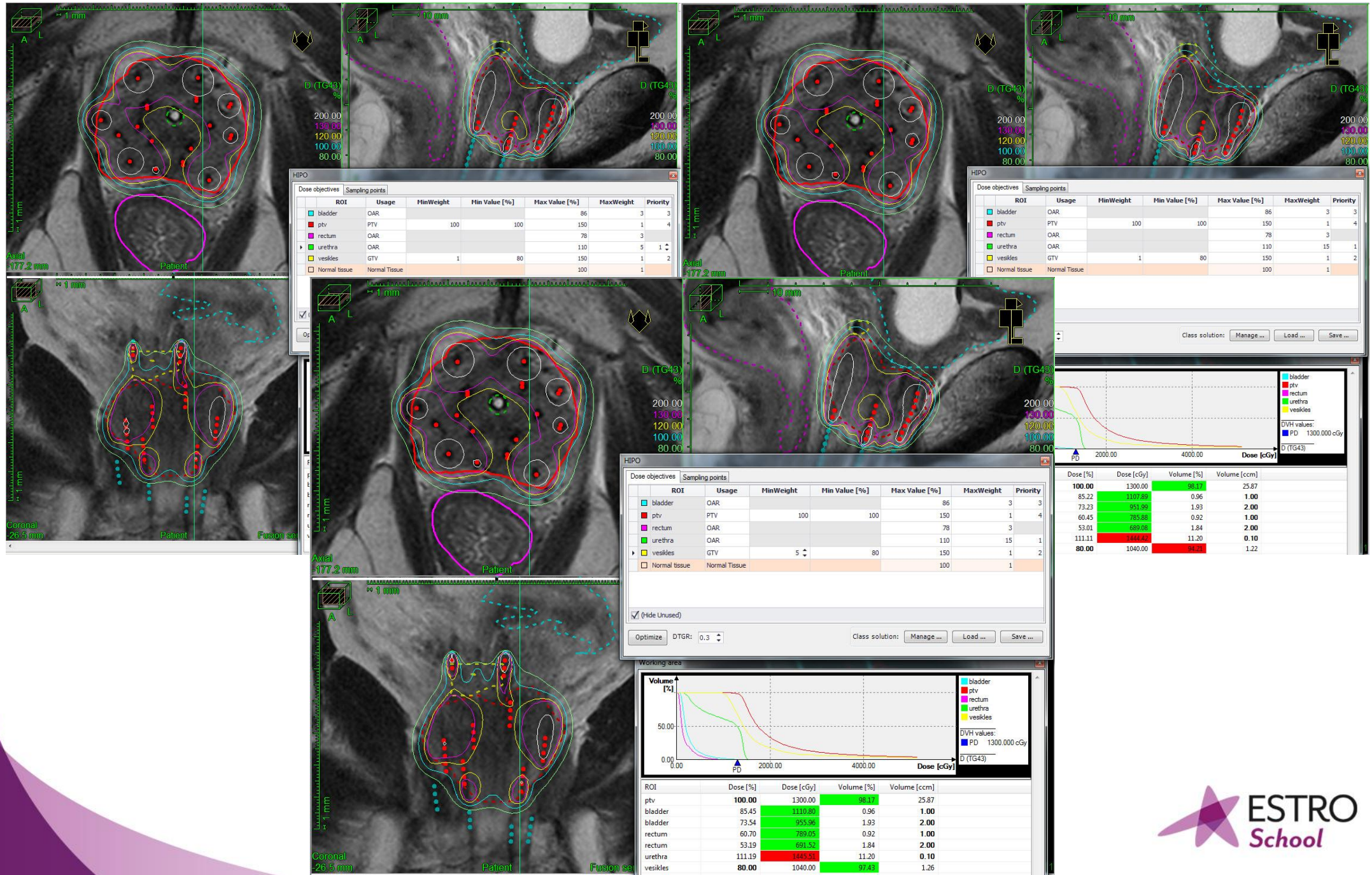
Dwell position activation



Post-planning, HDR

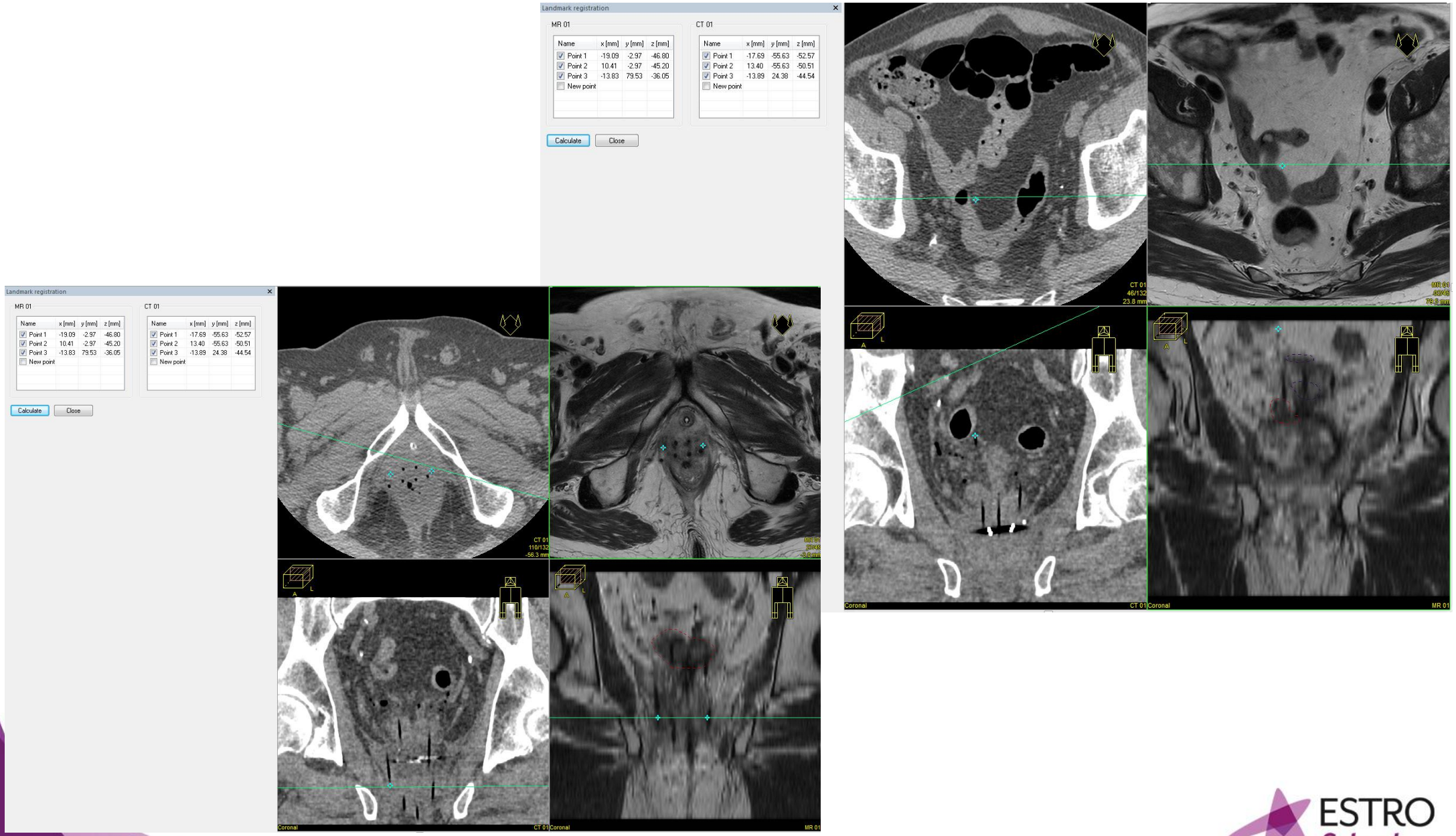


Treatment plan optimisation



Treatment plan optimisation

Registration of CT and MRI



Thank you for your attention

- Now you've seen some possibilities
- This afternoon you have the opportunity to work with the treatment planning systems yourself

ESTRO School

Budapest, March 5-8 2017

ESTRO School

Comprehensive and Practical Brachytherapy

WWW.ESTRO.ORG/SCHOOL

BREAST BRACHYTHERAPY

ESTRO TEACHING COURSE

Comprehensive and Practical Brachytherapy

Budapest 2017

Dr. José Luis Guinot

Fundación Instituto Valenciano de Oncología (I.V.O.). Valencia.

E-mail: jguinot@fivo.org

ESTRO School

Boost after breast conserving surgery and EBRT

Why a boost?

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The goal of the radiation after breast conserving surgery (BCS) is to avoid local recurrence

But…

Every four local recurrences avoided, one dead by breast cancer is avoided at 15 years

Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*

Lancet 2005; 366:2087-2106

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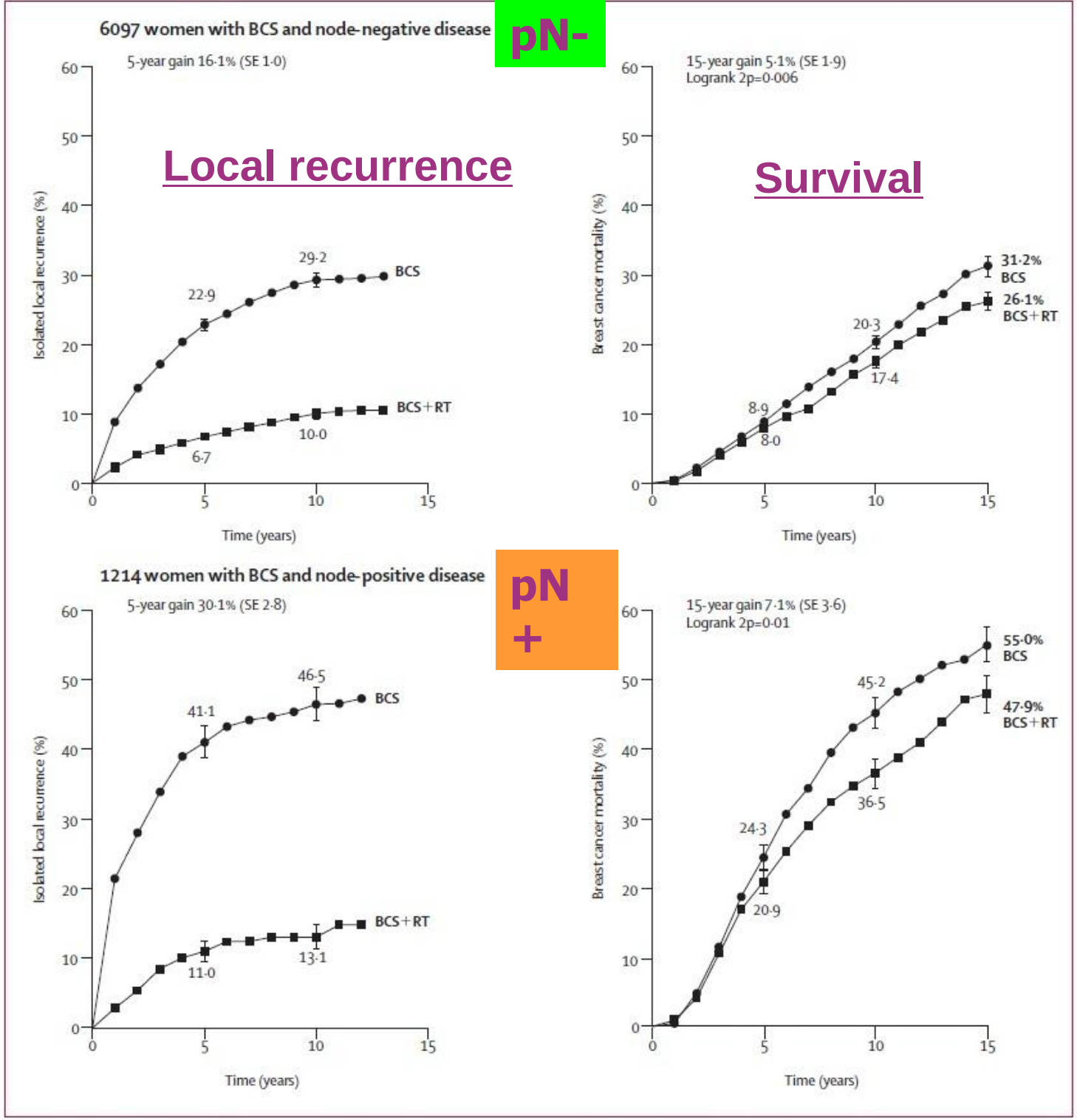


Figure 2: **Effect of radiotherapy (RT) after BCS on local recurrence and on breast cancer mortality—15-year probabilities**
Data from 10 trials. Vertical lines indicate 1 SE above or below the 5, 10, and 15 year percentages.

Benefit of radiation after BCS

Benefit in local control:

In N0 16% (5y)
In N+ 30% (5y)

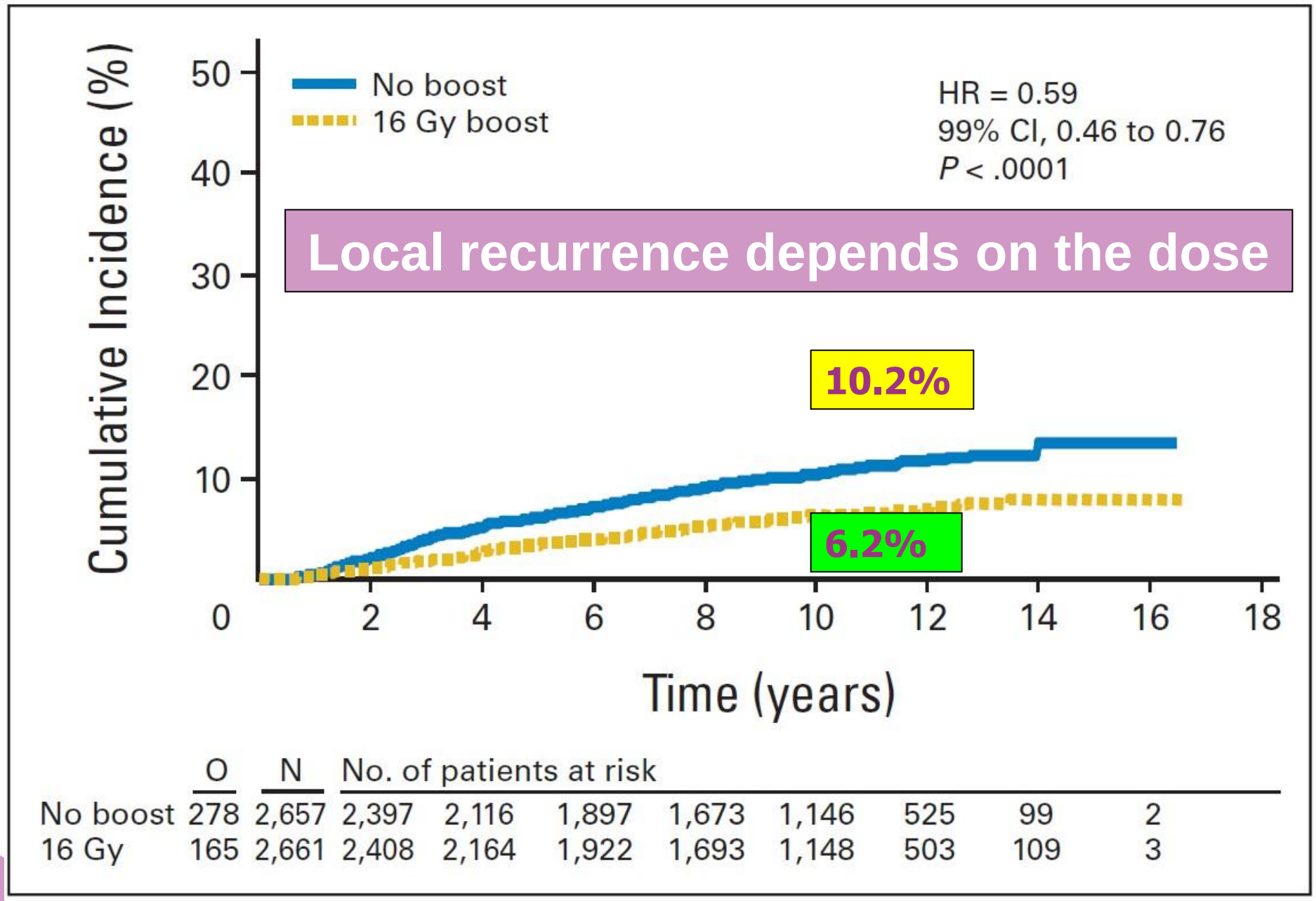
Benefit in survival:

In N0 5% (15y)
In N+ 7% (15y)

Lancet 2005

10-Year Results of the Randomized Boost Versus No Boost EORTC 22881-10882 Trial

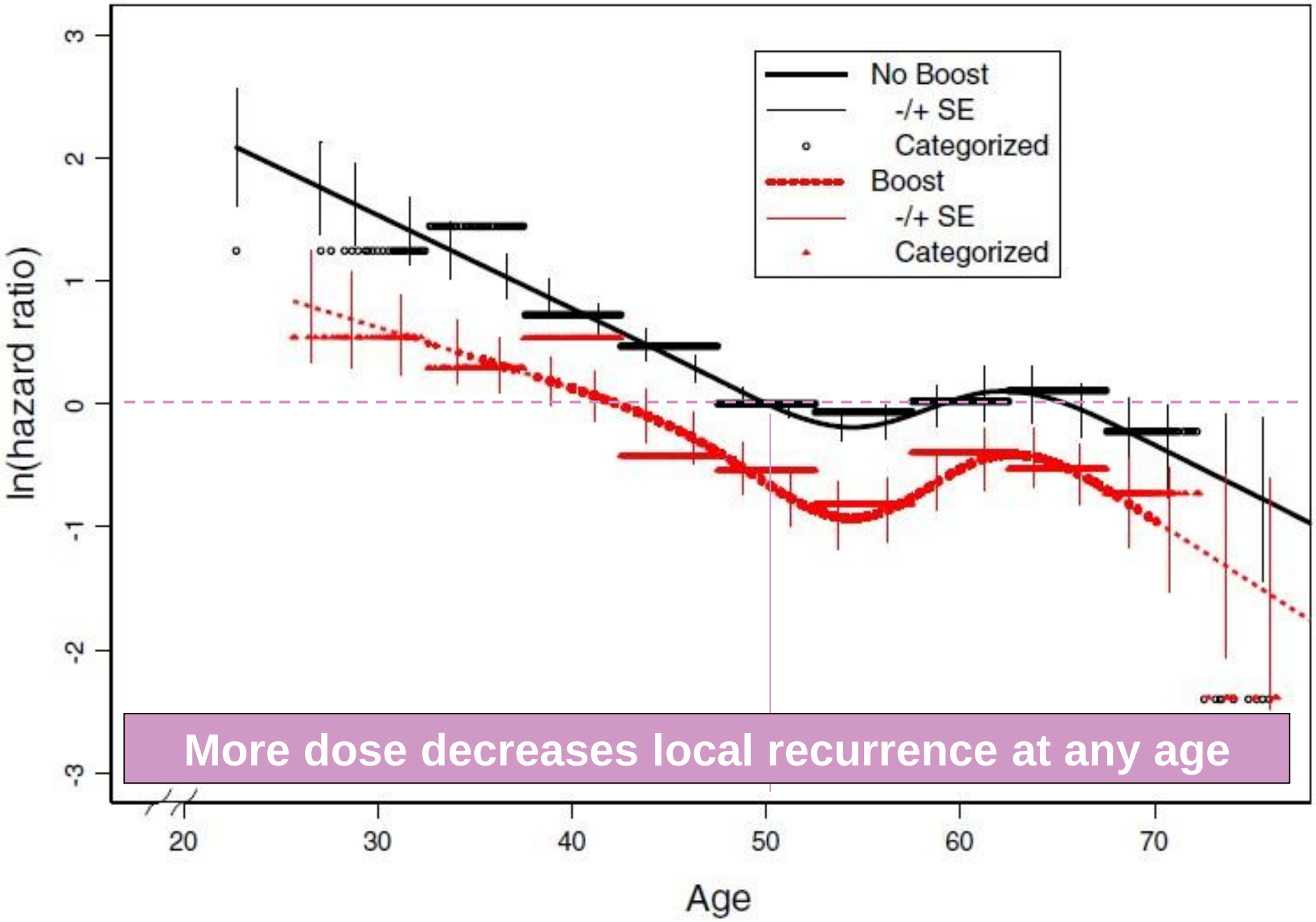
5318 patients T1-2 free margins. **Bartelink H et al. J Clin Oncol 2007;25:3259-65**



Local recurrence risk depending on age and dose

Age and radiation dose in breast cancer

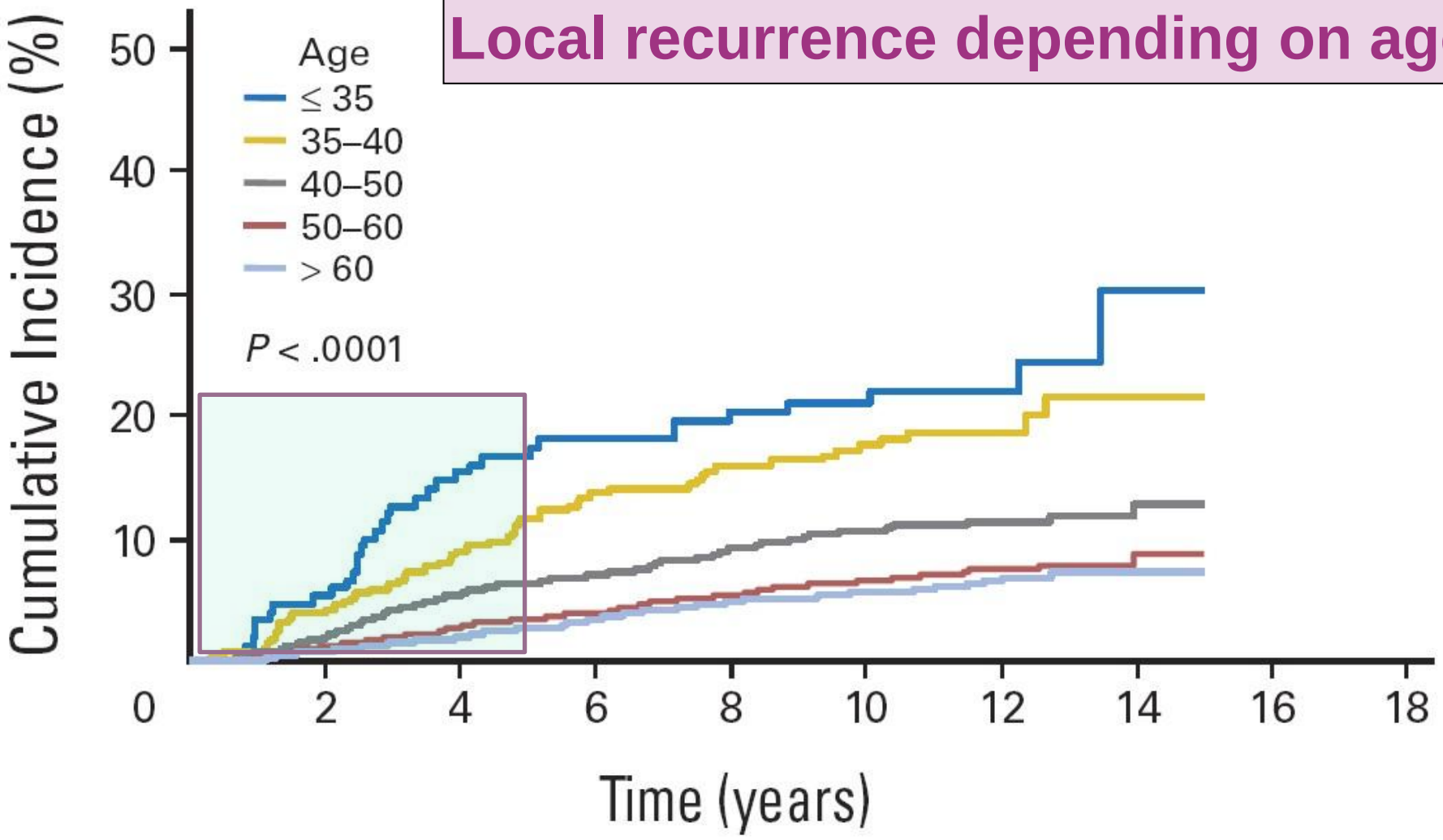
Antonini N, et al. Radiat Oncol 82 (2007) 265-271



More dose decreases local recurrence at any age

Bartelink H et al J Clin Oncol 2007;25:3259-65

Local recurrence depending on age



Age	O	N	No. of patients at risk						
≤ 35	34	154	127	101	88	75	56	25	6
35–40	53	295	252	221	189	167	127	56	13
40–50	140	1,334	1,201	1,058	936	840	574	271	62
50–60	119	1,803	1,646	1,496	1,347	1,191	798	351	64
> 60	97	1,732	1,579	1,404	1,259	1,093	739	324	63

Local recurrence depending on age and boost to the tumor bed

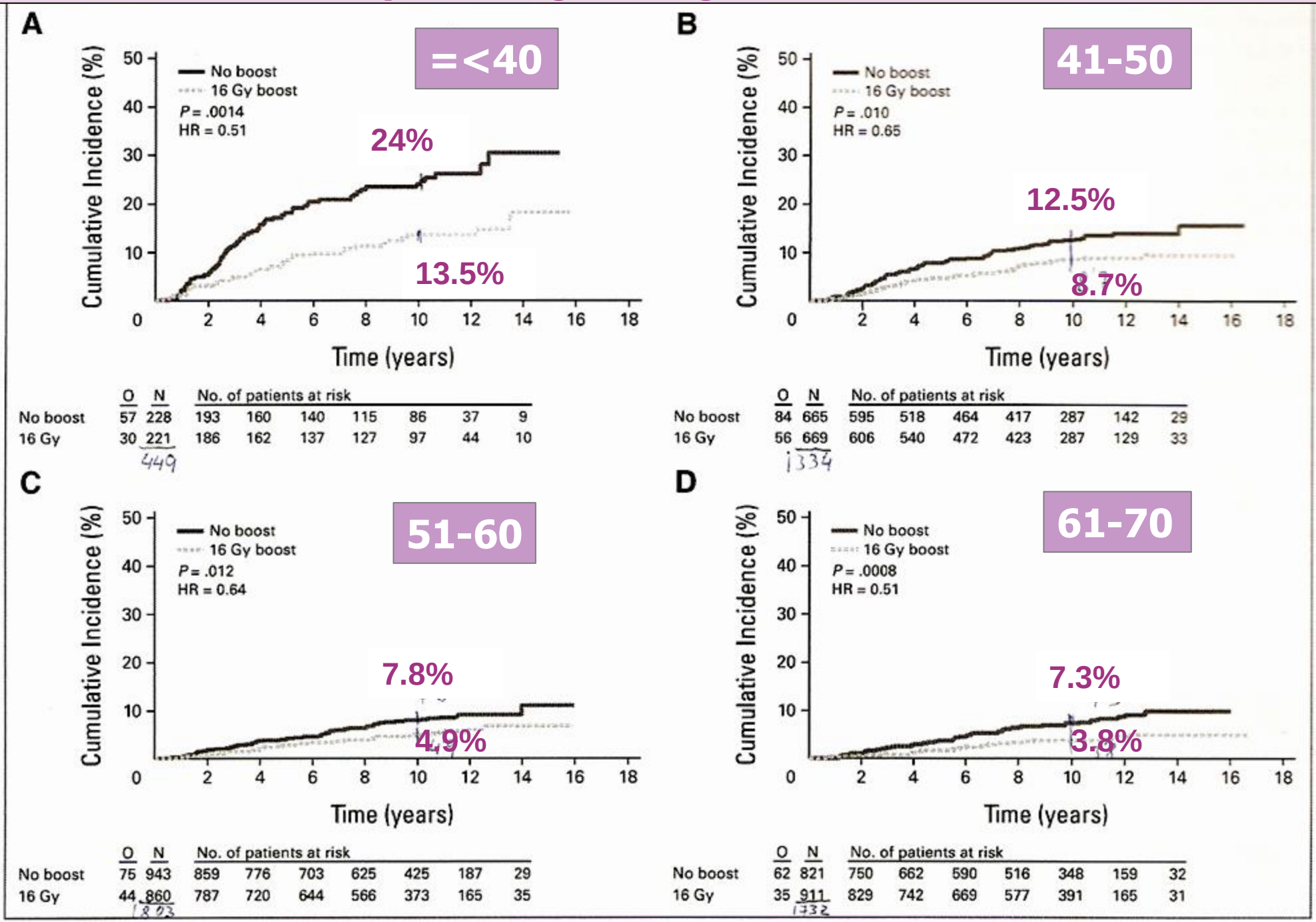


Fig 3. Cumulative incidence of ipsilateral breast cancer recurrence according to age. Age (A) ≤ 40, (B) 41 to 50, (C) 51 to 60, and (D) > 60 years. HR, hazard ratio; O, occurrences; N, number of patients at risk.

Groups of risk

Low

< 7.5%

Median

7.5-12.5%

High

12.5-20%

Very high

>20%

	Number of patients	RT 50 Gy	RT 66 Gy
Bartelink 2007			
total	2657 p	10'2	
	2661 p		6'2
>60-70	821	7'3	
	911		3'8
51-60	943	7'8	
	860		4'9
41-50	665	12'5	
	669		8'7
=<40	228	24	
	221		13'5
Jones 2009	1616		
=>51	464	~8	
	449		~5
=<50	294	19'4	
	287		11'4
G1-2	588	~9'5	
	589		~6
G3	174	18'9	
	188		8'6
Bartelink 2011			
>50 y G3		10'8	
			4
=<50 G1-2		19'2	
			5'7
=<50 y G3		28'5	
			13,5

Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial

Harry Bartelink, Philippe Maingon, Philip Poortmans, Caroline Weltens, Alain Fourquet, Jos Jager, Dominic Schinagl, Bing Oei, Carla Rodenhuis, Jean-Claude Horiot, Henk Struikmans, Erik Van Limbergen, Youlia Kirova, Paula Elkhuizen, Rudolf Bongartz, Raymond Miralbell, David Morgan, Jean-Bernard Dubois, Vincent Remouchamps, René-Olivier Mirimanoff, Sandra Collette, Laurence Collette; on behalf of the European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups

Boost vs No Boost
EORTC 22881-10882 Trial
1989-1996
5318 T1-2
Free margins

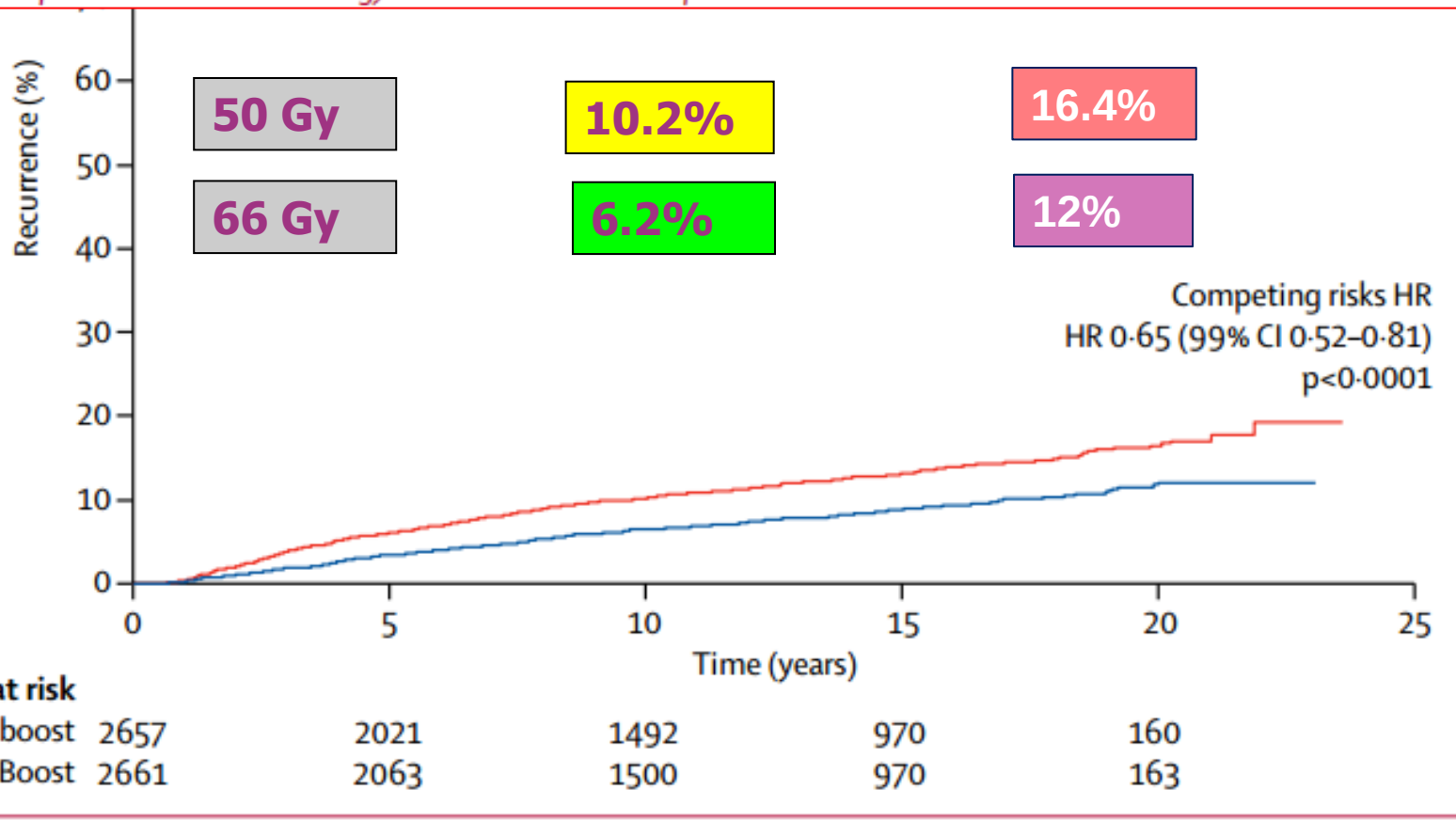
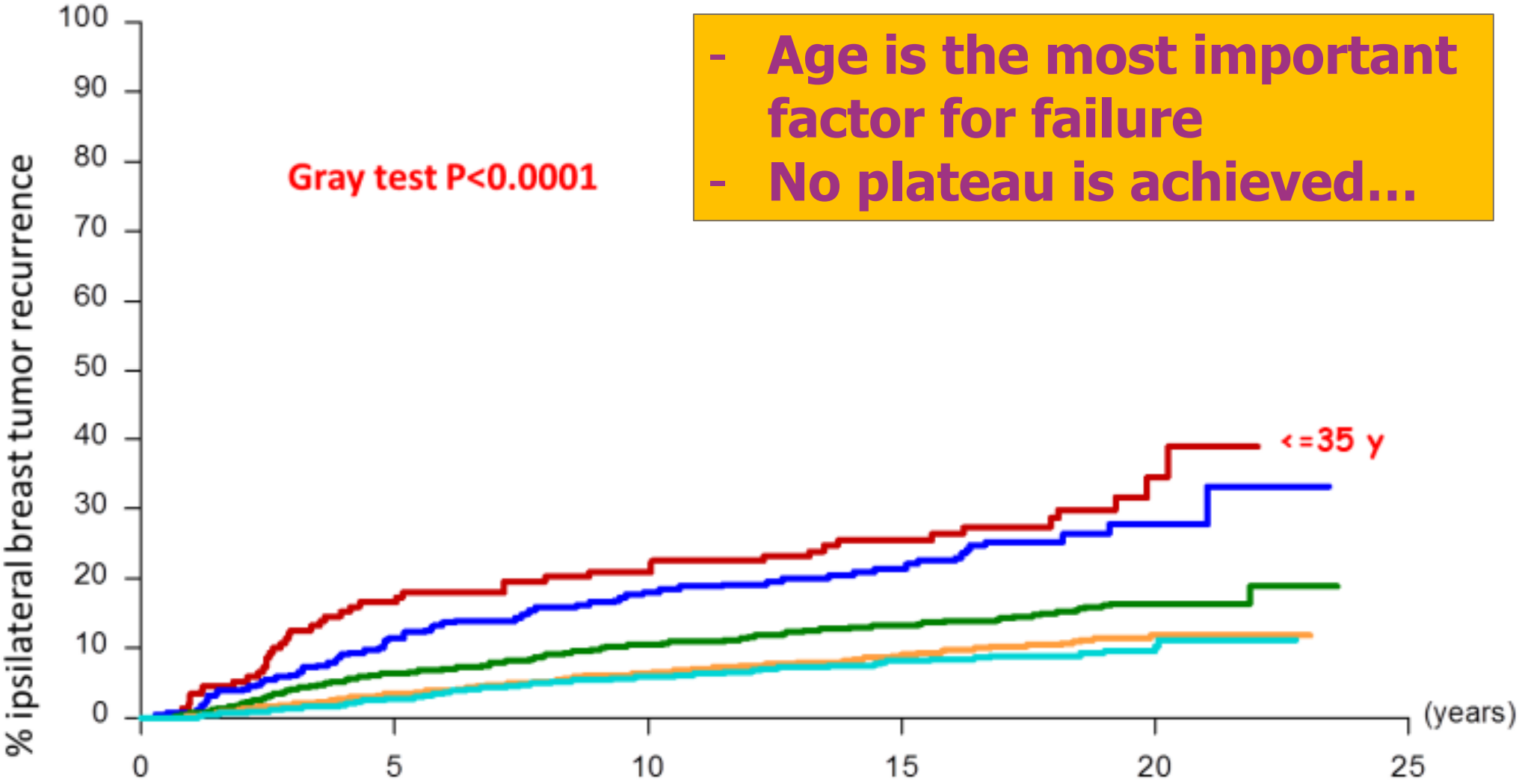


Figure 3: Ipsilateral breast tumour recurrence

Bartelink H. Lancet Oncol. 2015 Jan; 16(1):47-56

Breast failure depends on the dose

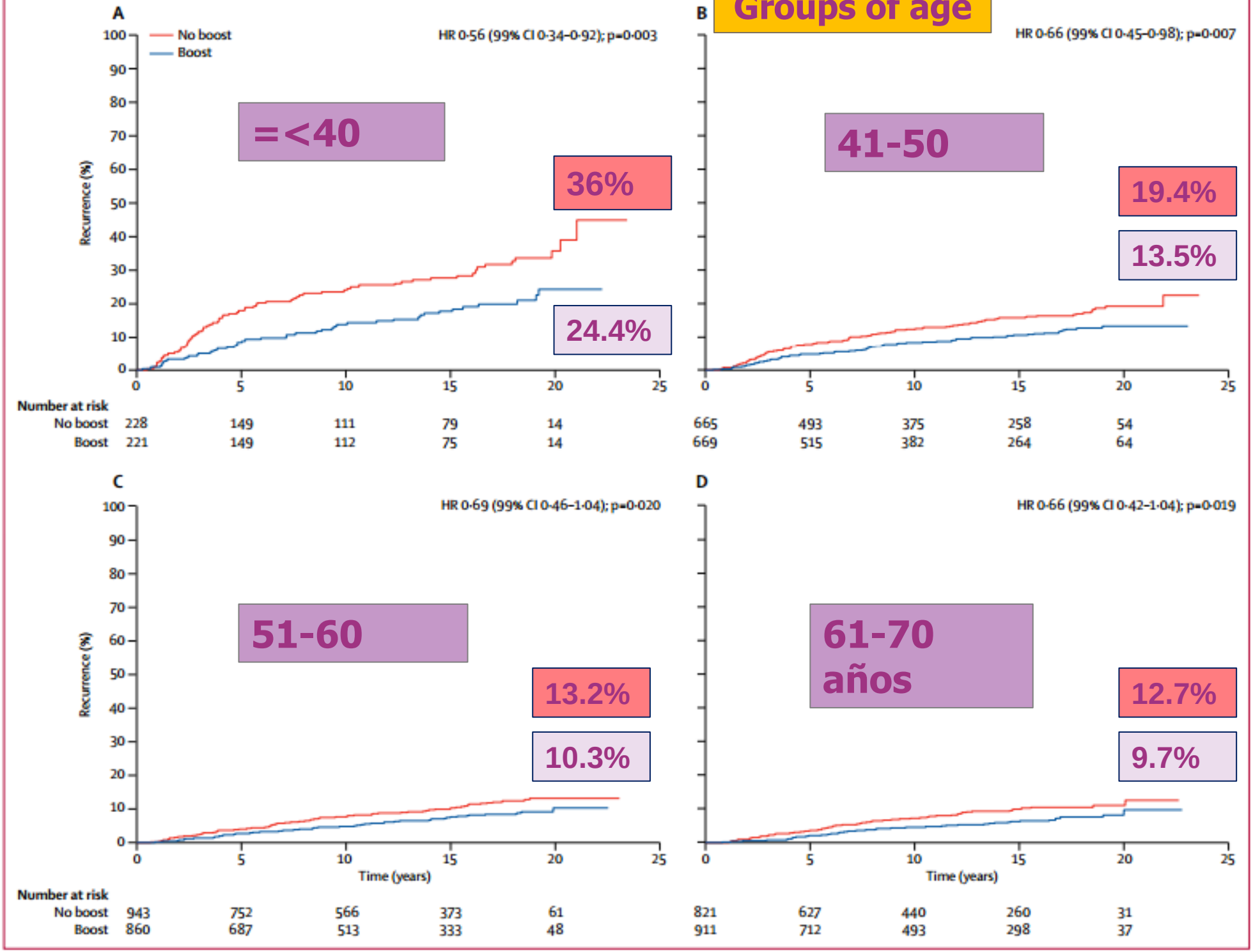
- **Age is the most important factor for failure**
- **No plateau is achieved…**



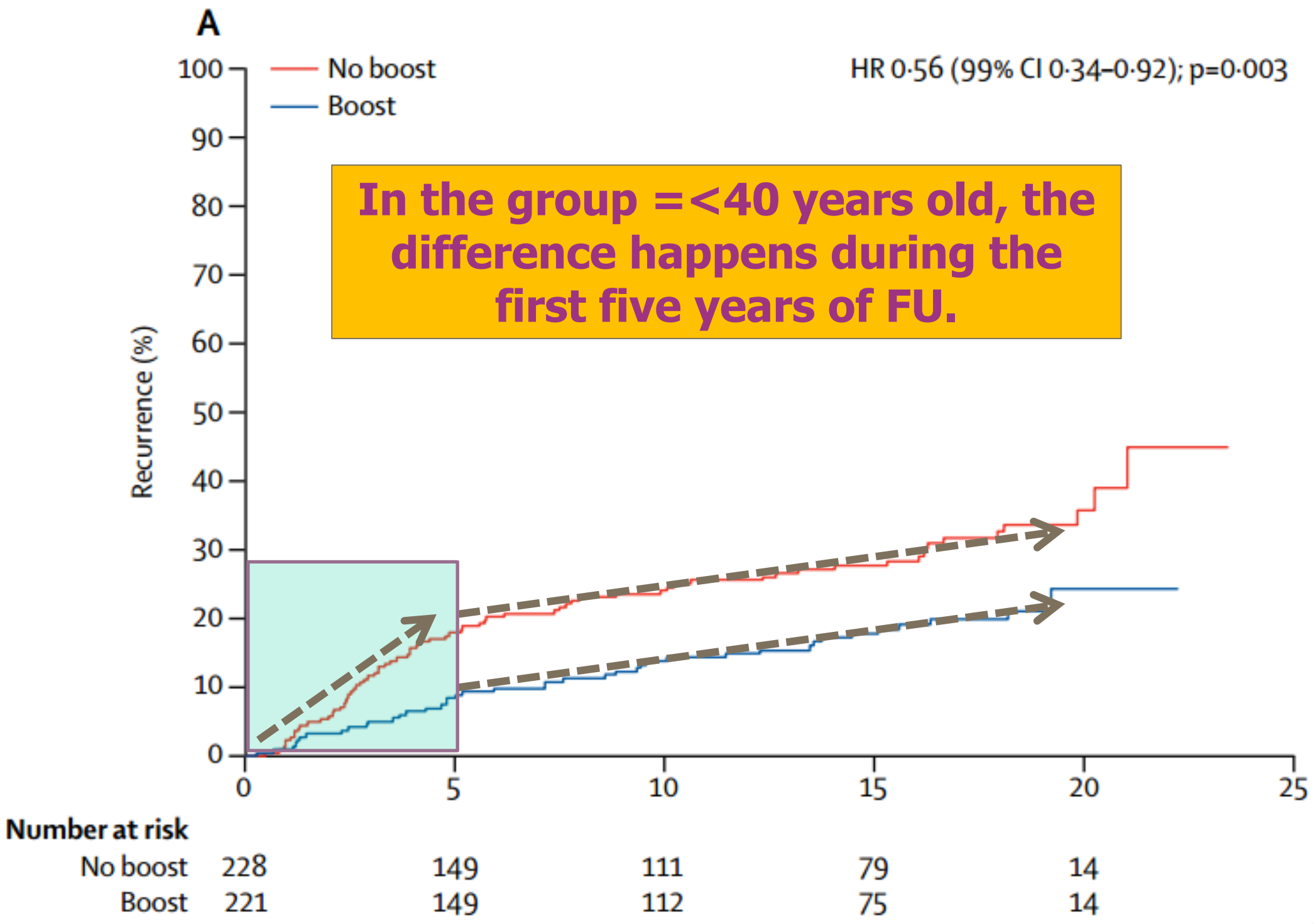
O	N	Number of patients at risk :				Age (years)
44	154	93	69	53	9	<=35 y
69	295	205	154	101	19	35 - 40
182	1334	1008	757	522	118	40 - 50
164	1803	1439	1079	706	109	50 - 60
132	1732	1339	933	558	68	>60

Bartelink H. Lancet Oncol. 2015 Jan; 16(1):47-56

Groups of age

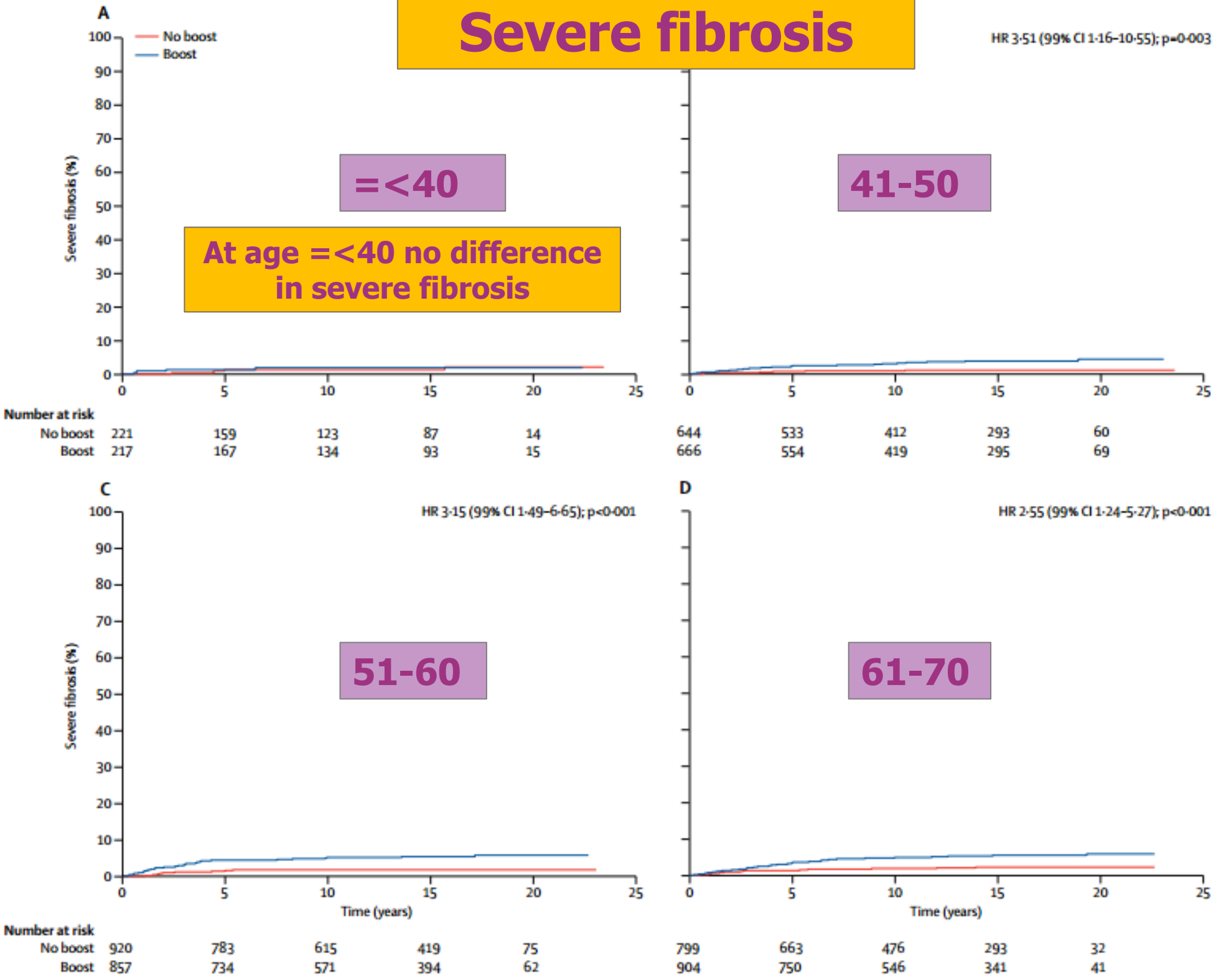


Bartelink H. Lancet Oncol. 2015 Jan; 16(1):47-56



Bartelink H. Lancet Oncol. 2015 Jan; 16(1):47-56

Severe fibrosis



Boost after breast conserving surgery and EBRT

How to boost?

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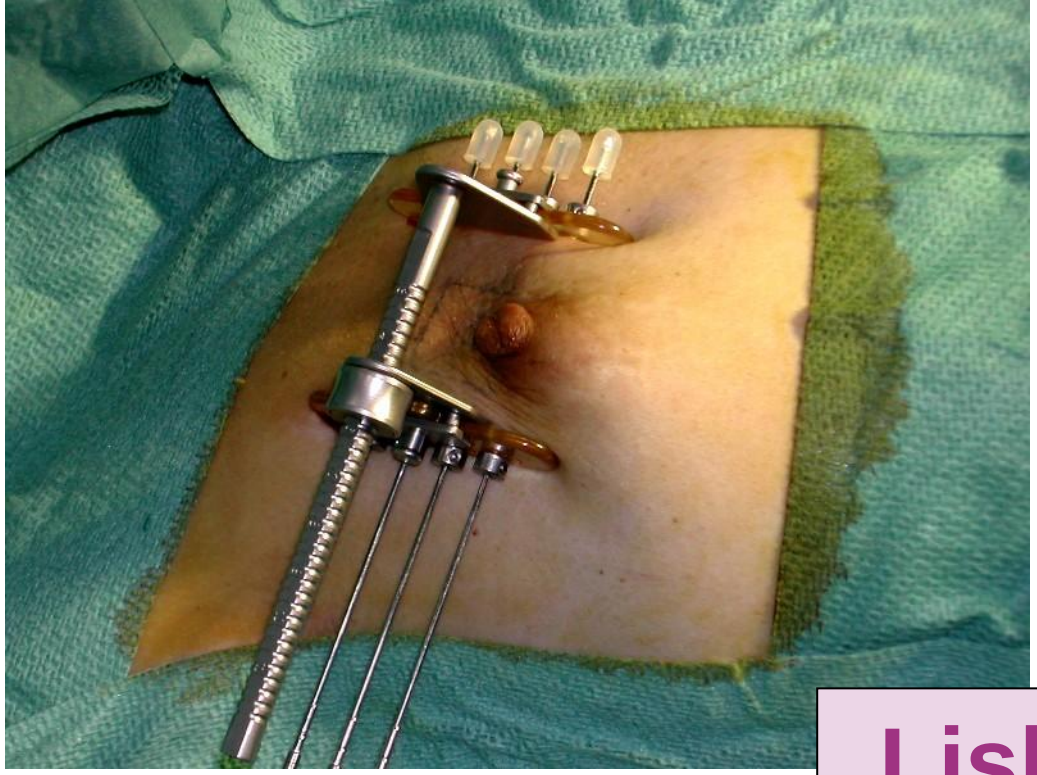
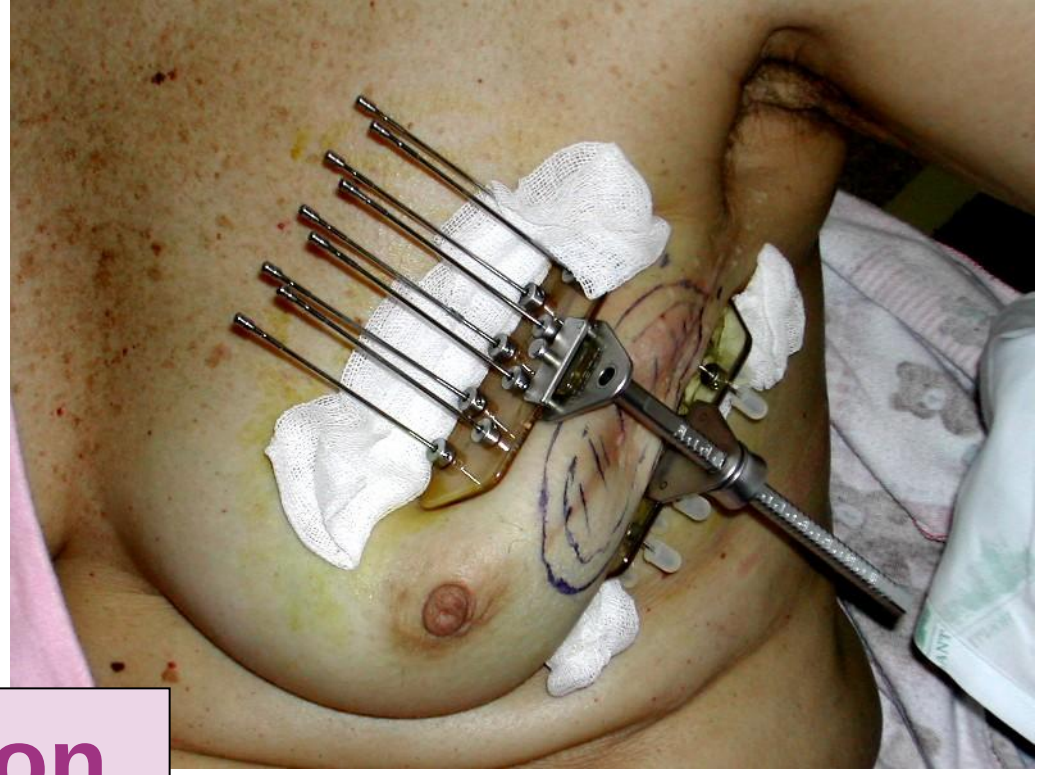
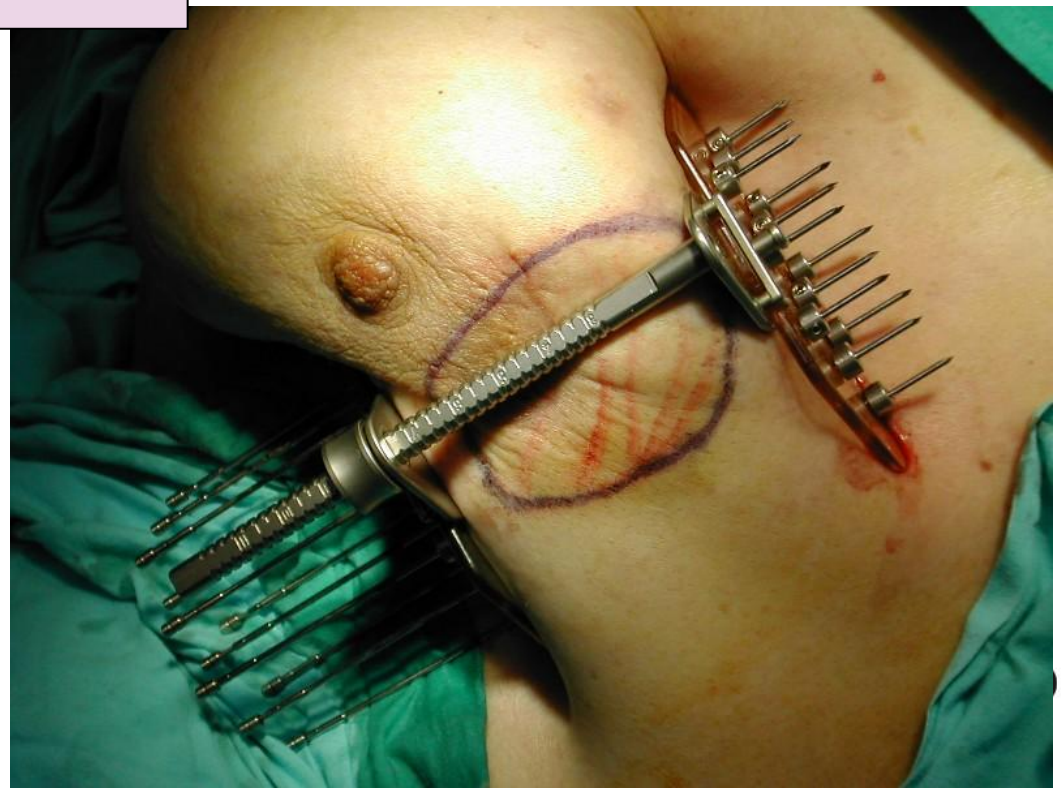
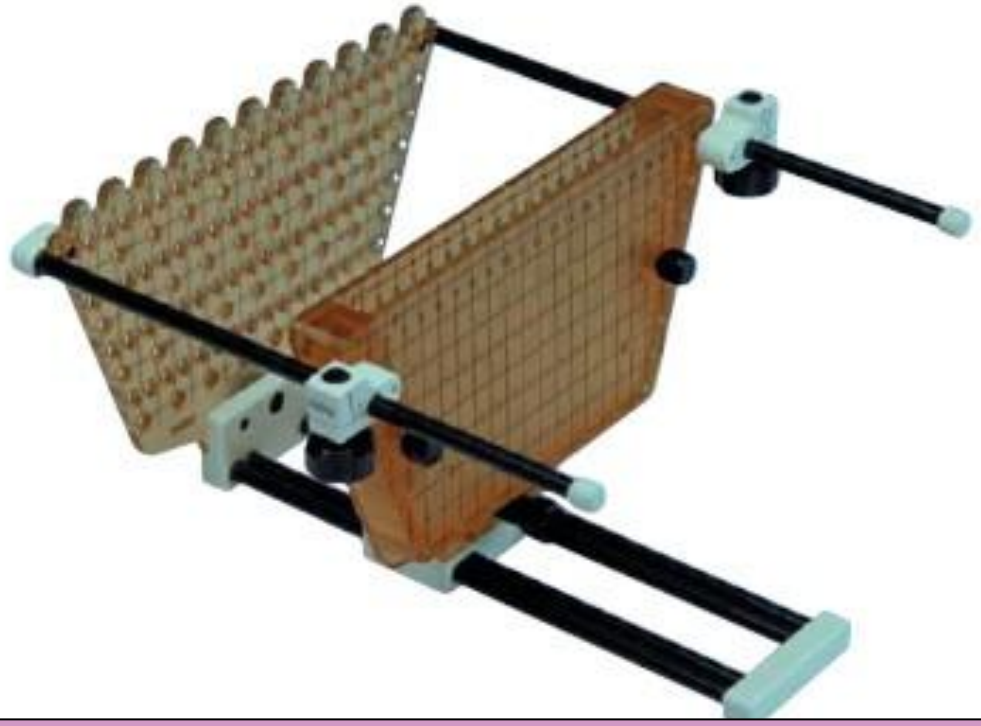
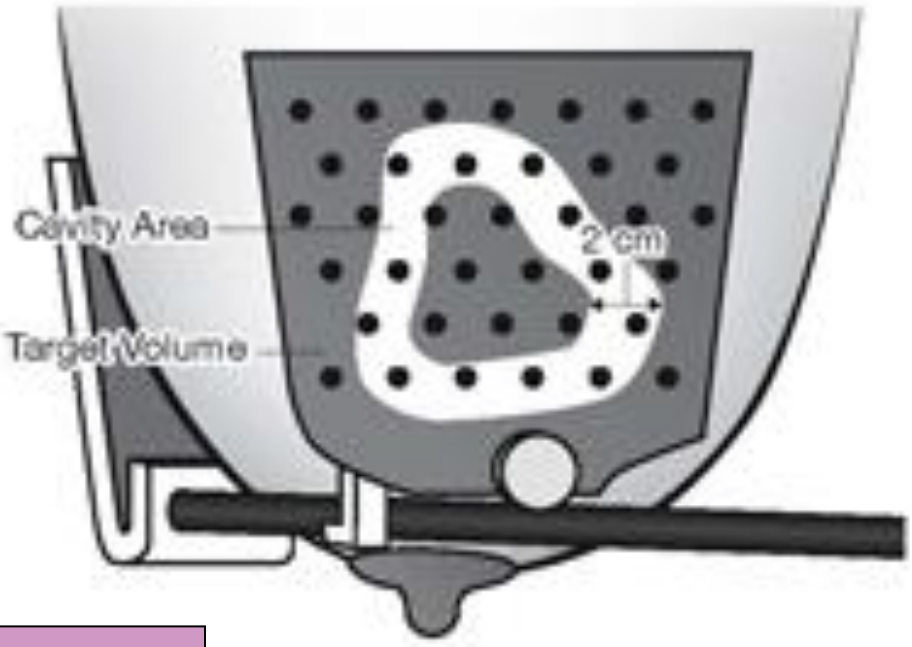




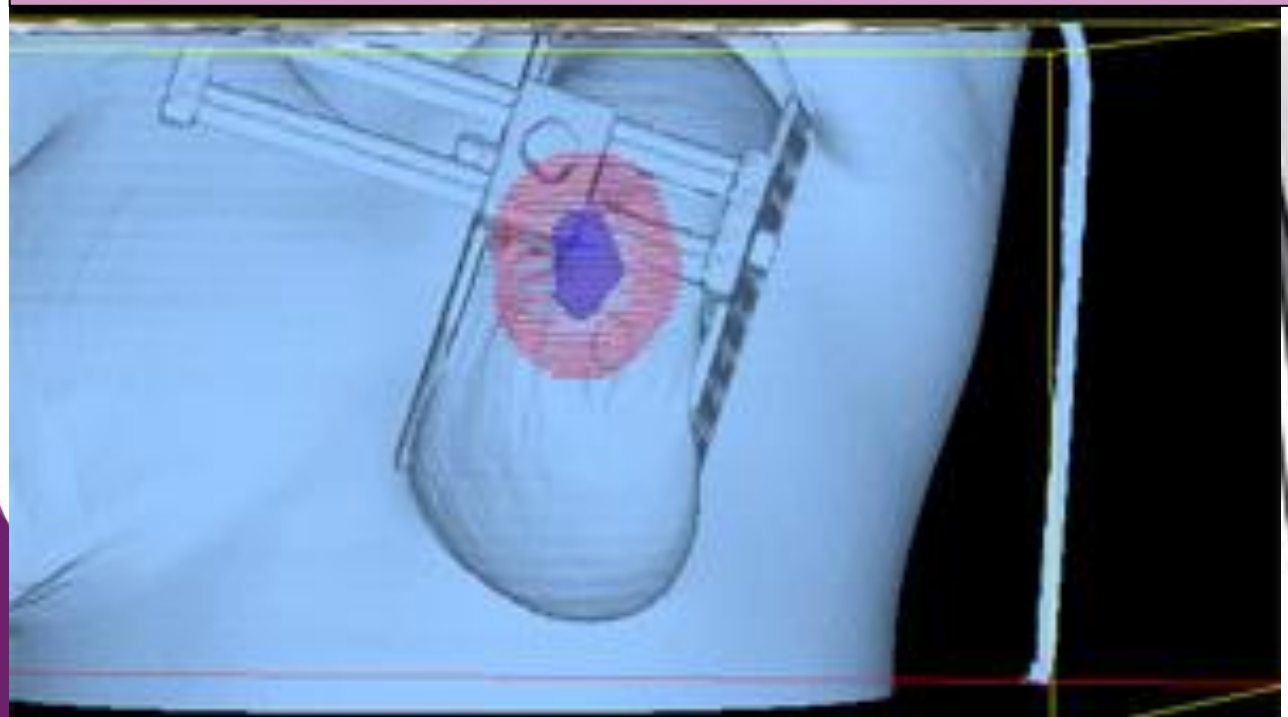
Lisbon

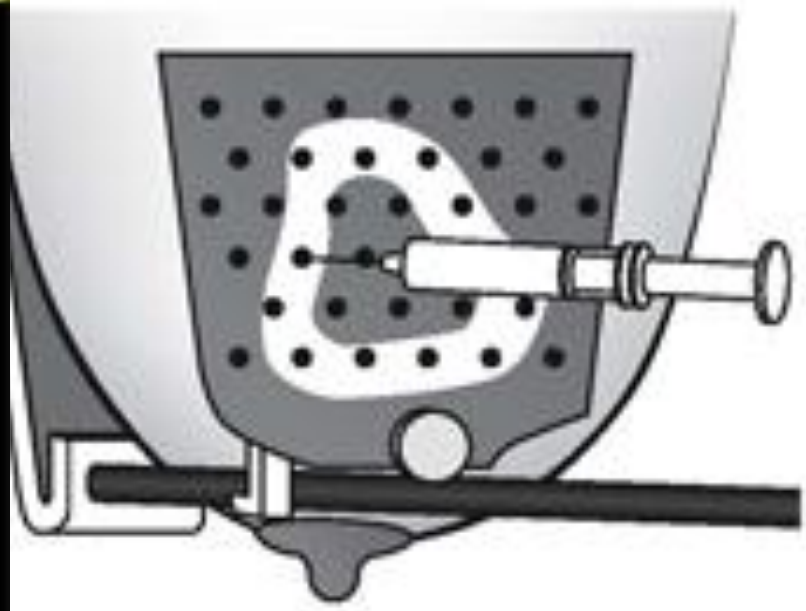




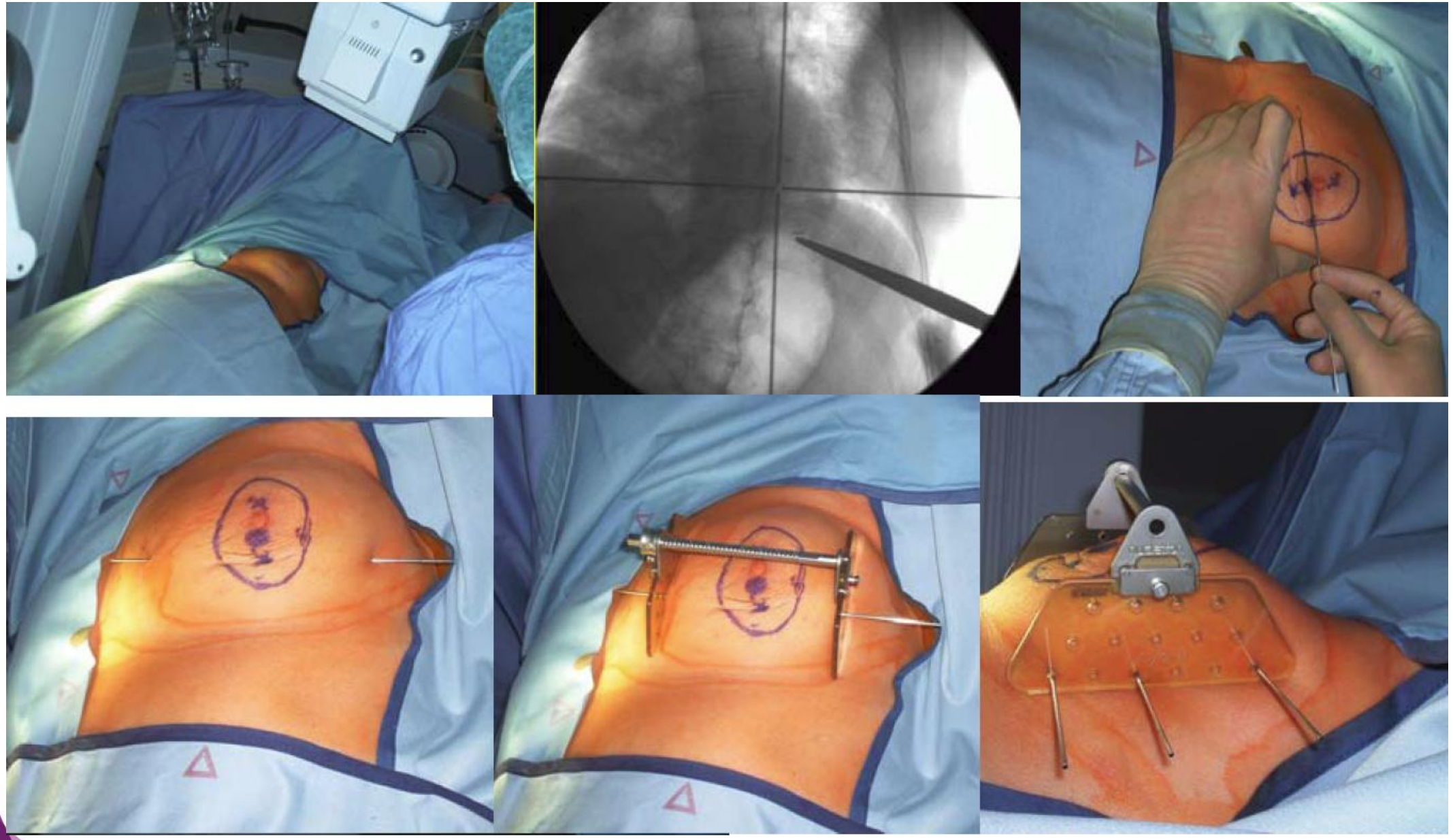


Prone position: Kuske applicator

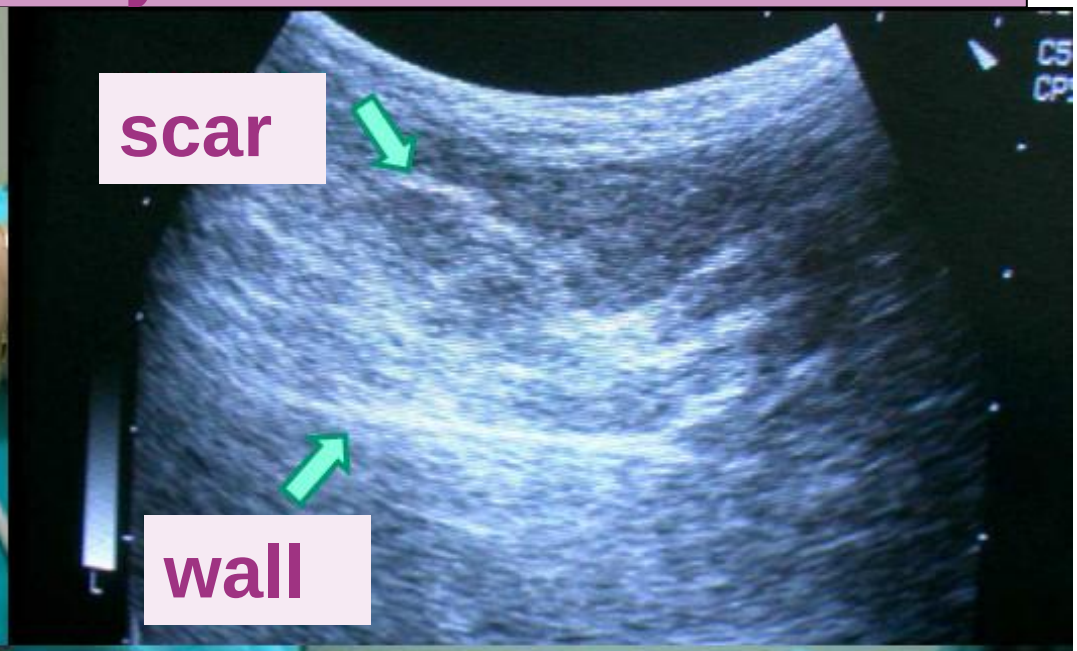




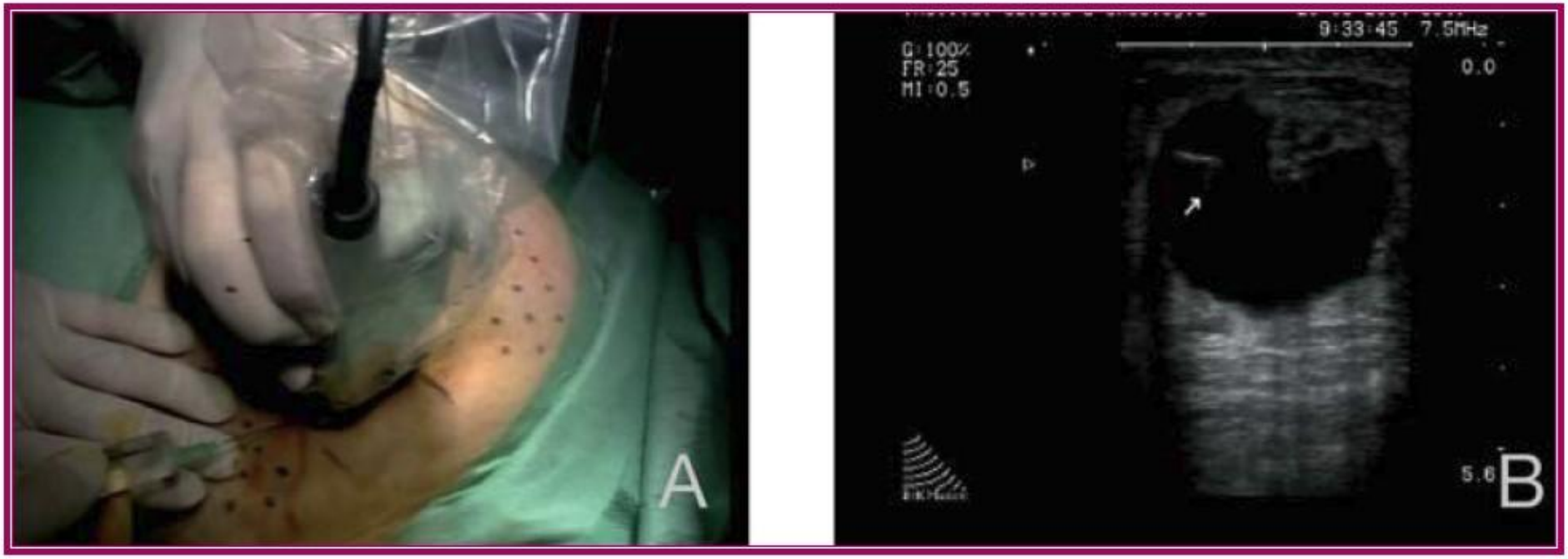
clips and X-Ray. Erlangen. Germany



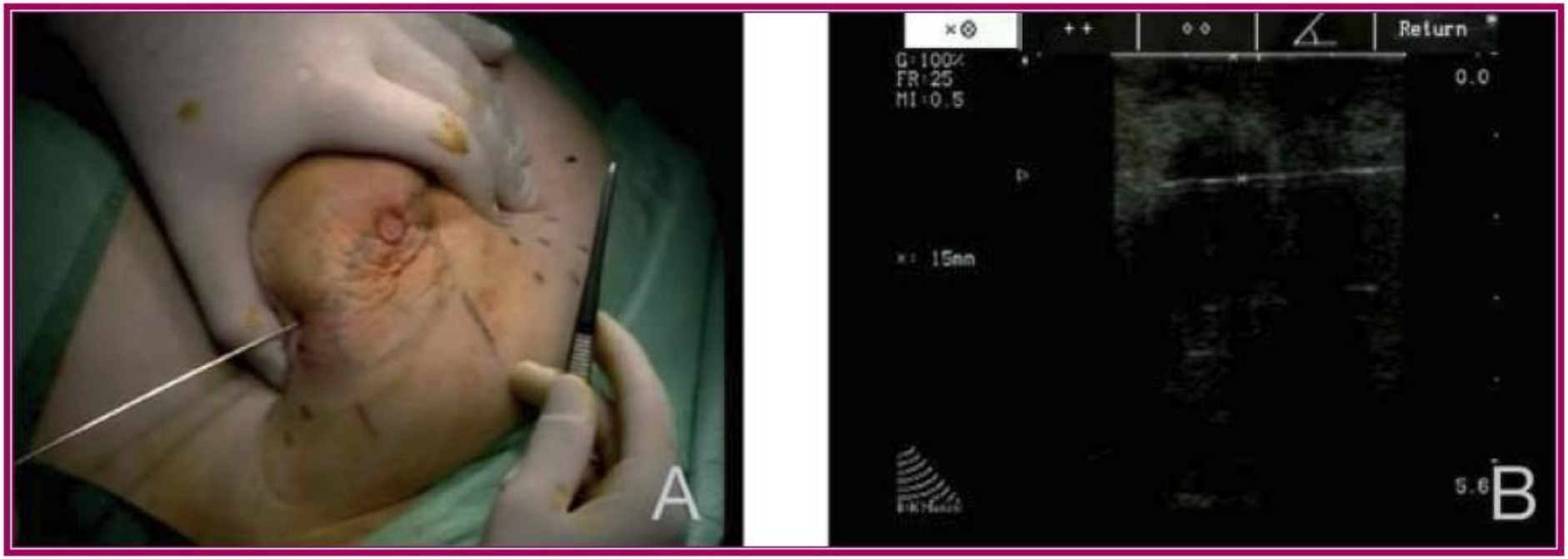
Definition of tumor bed by ultrasound
Closed cavity. IVO.

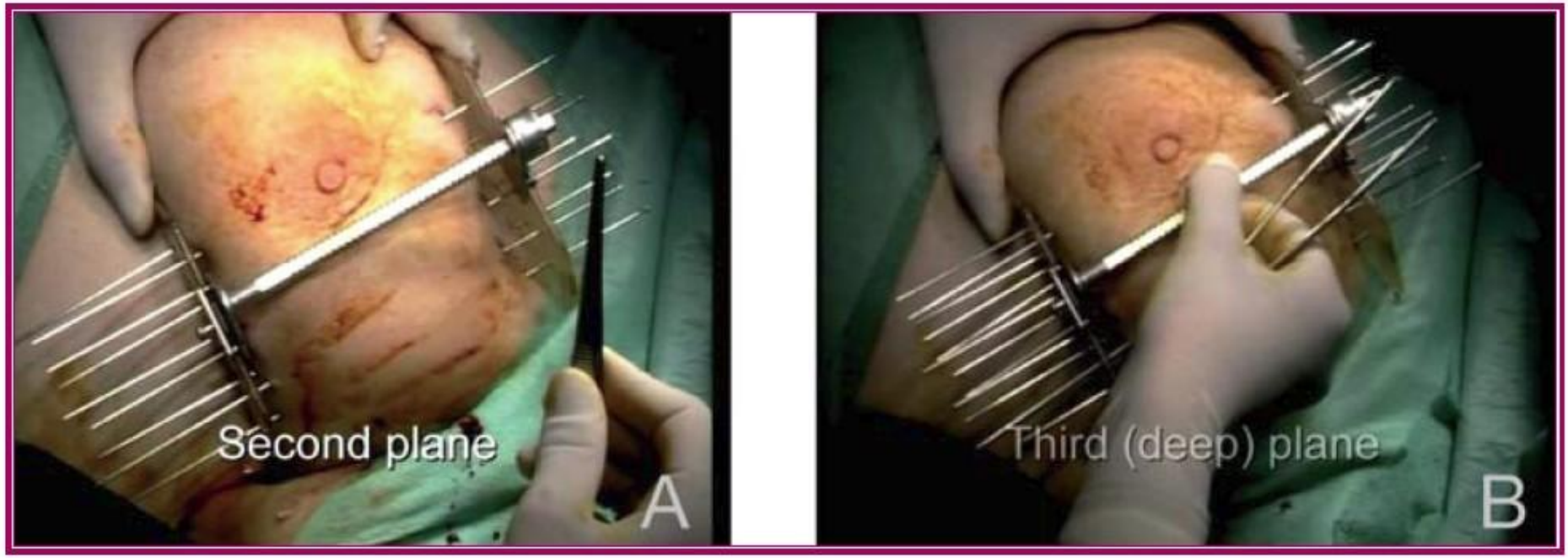


Imaging guided BT (IGBT) by ultrasound
Closed cavity. IVO.

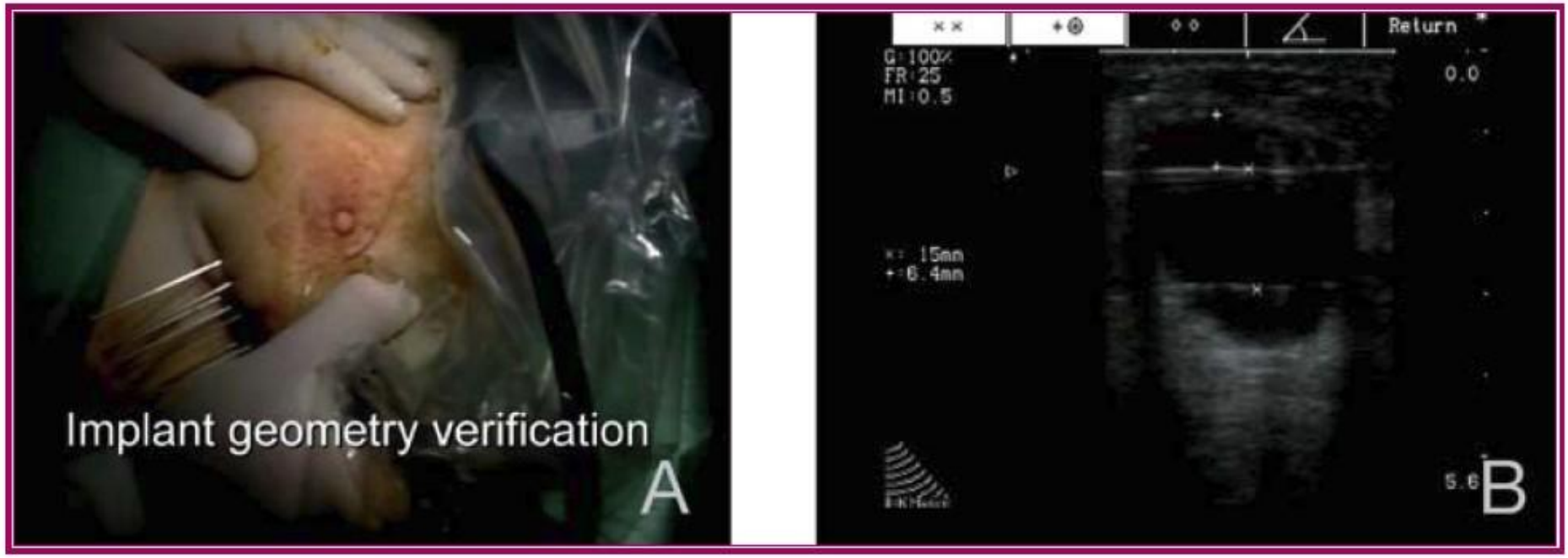


Visualization by ultrasound. Opened cavity. ICO. Barcelona





Visualization by ultrasound. Opened cavity. ICO. Barcelona



Boost after breast conserving surgery and EBRT

Needles or plastic tubes?
Fast-boost

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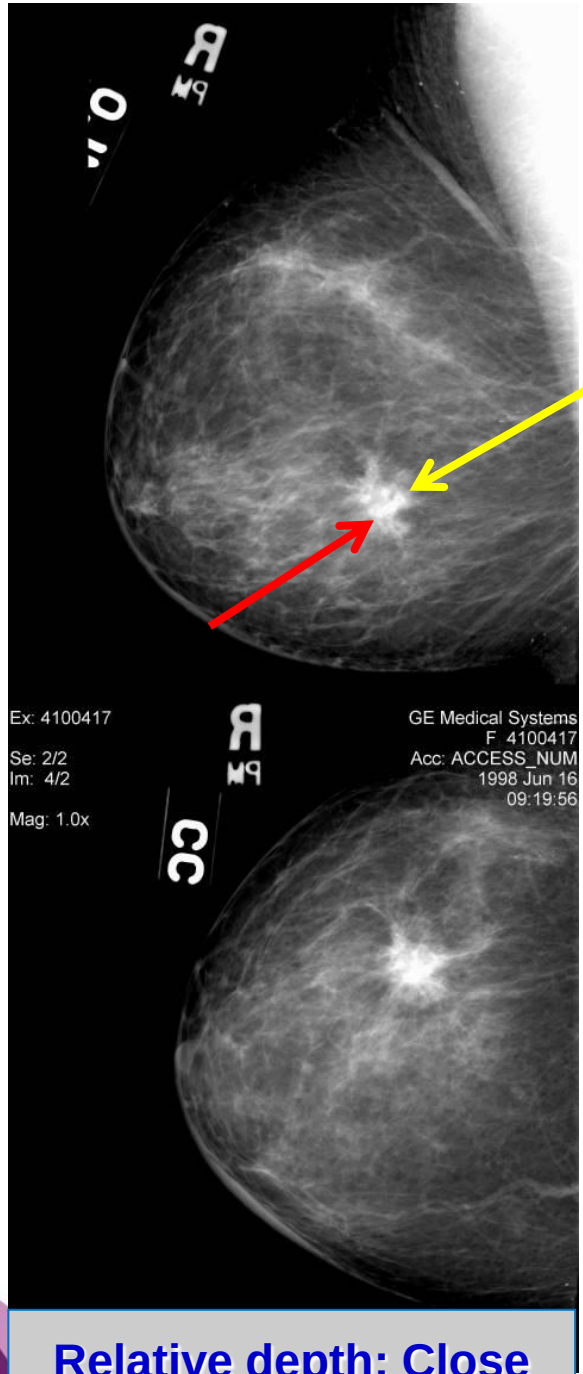
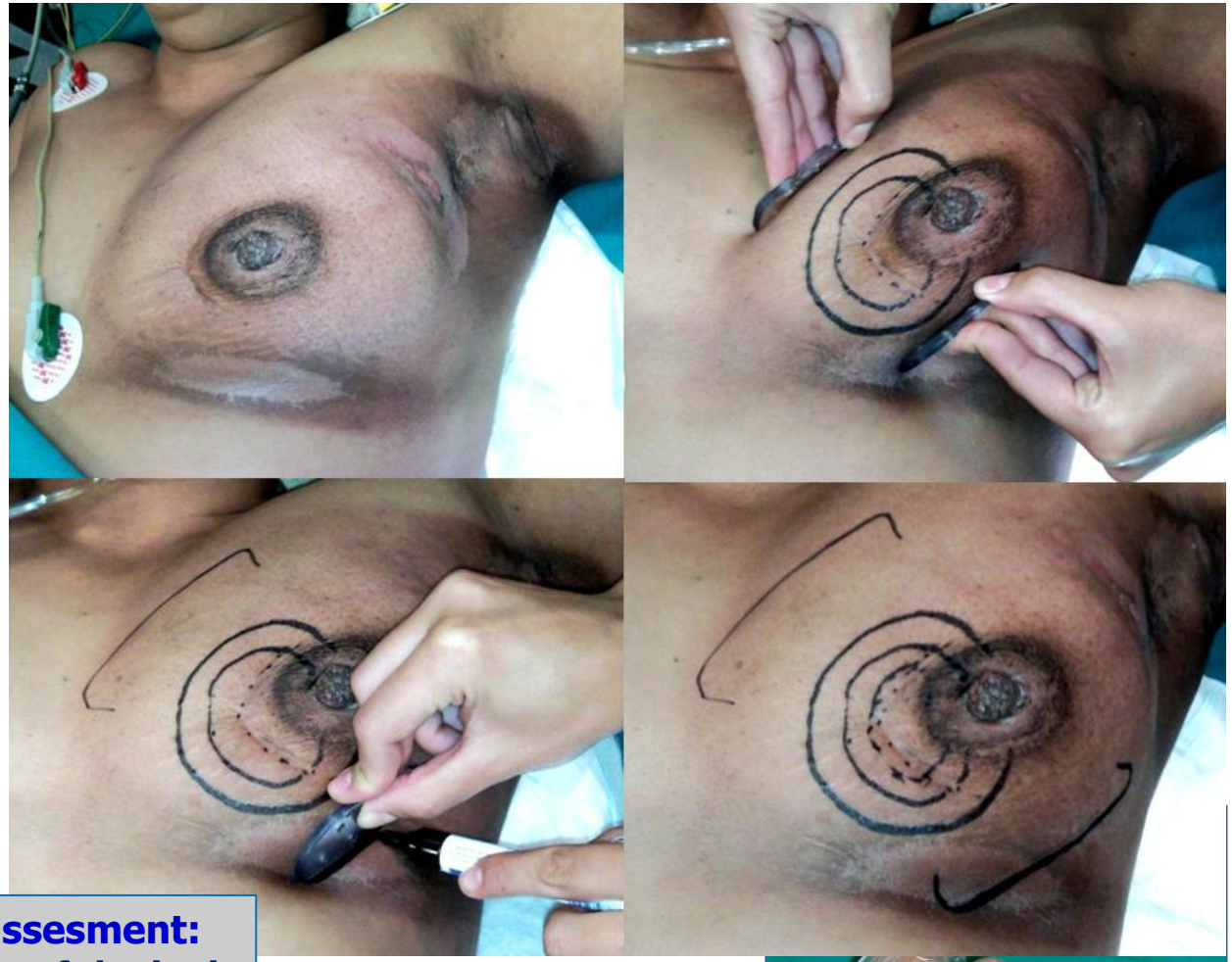
FAST-BOOST TECHNIQUE. IVO. VALENCIA



Relative depth: Close to skin or chest wall



- **Clinical assesment:**

Localization of the bed tumour by Mamograms/MRI images

- **Surgeon description**
- **Patient description**
- **Surgical bed palpation**
- **Scar only when the tumour was palpable**
- **no clips**

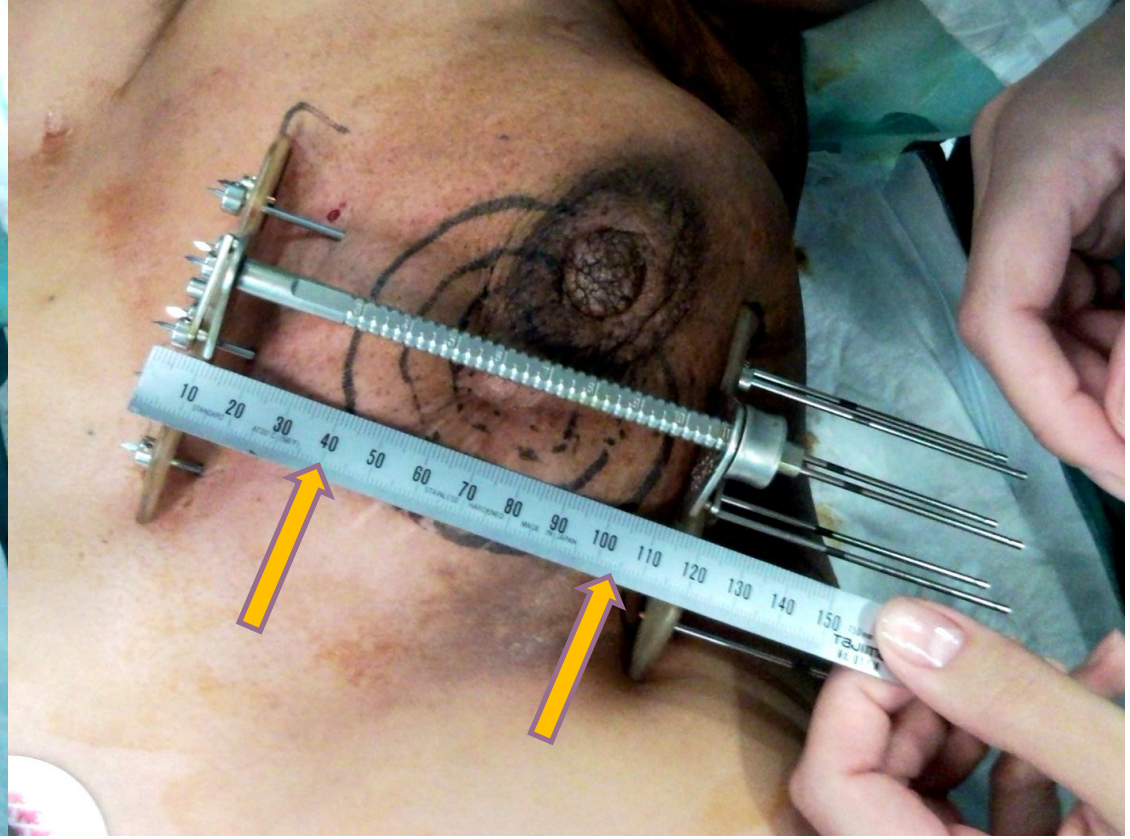
-Sedation and local anaesthesia

x3: one night with the needles

x1: outpatient

Deformation of bed tumor to our convenience

IVO



- the dwell position number 1 is placed at 9 mm from the tip of the closed needle
- the first and last dwell positions are registered
- No simulation or CT scan is performed.

Target definition:

- Surgical bed +2 cm margin
- More margin towards nipple
- At least one cm out of entrance and exit points.

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ivo

HOJA DE SIMULACIÓN BRAQUITERAPIA

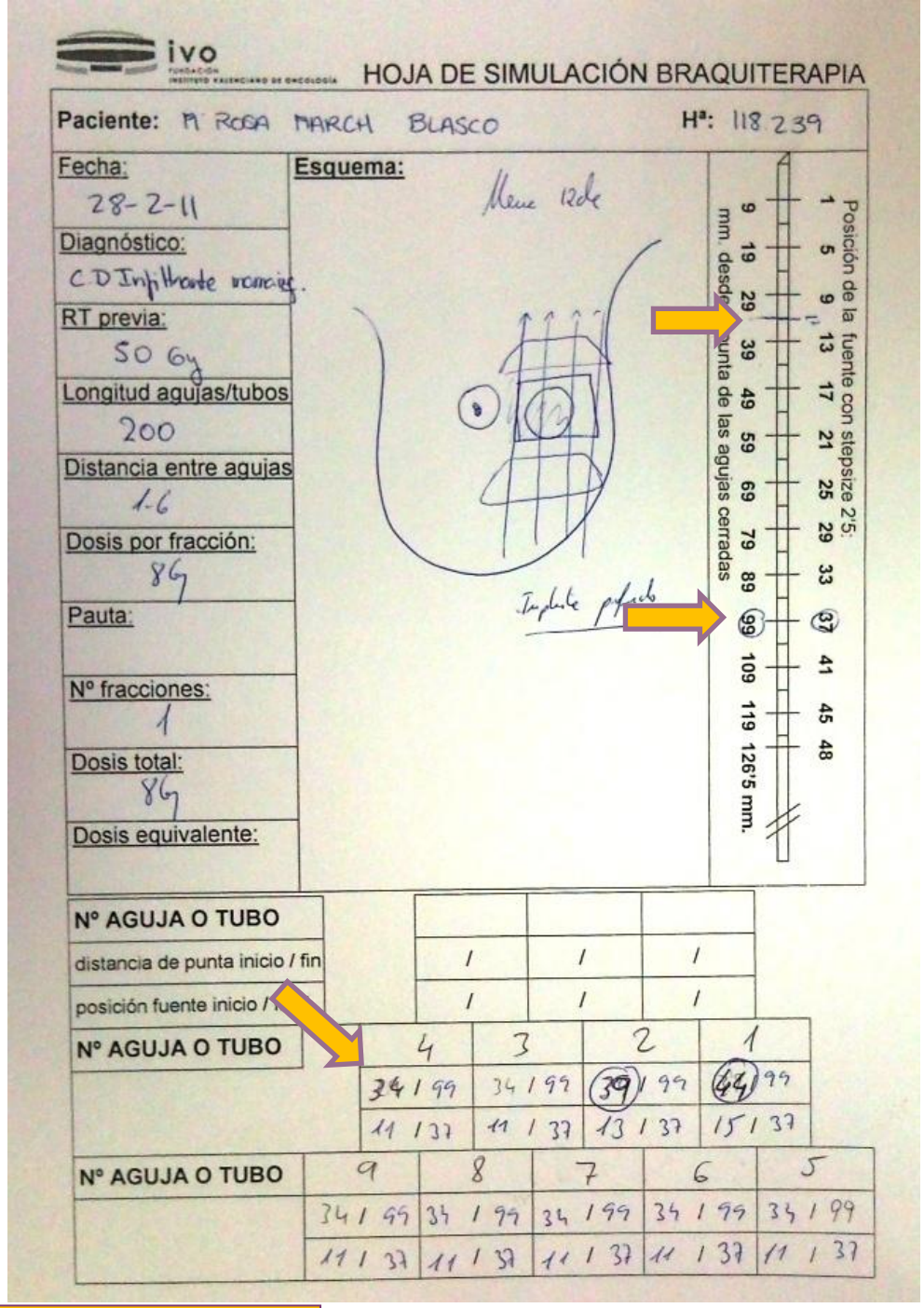
Paciente:	Hª:
Fecha:	Esquema:
Diagnóstico:	
RT previa:	
Longitud agujas/tubos	
Distancia entre agujas	
Dosis por fracción:	
Pauta:	
Nº fracciones:	
Dosis total:	
Dosis equivalente:	

Posición de la fuente con stepsize 2'5:
1 5 9 13 17 21 25 29 33 37 41 45 48
mm. desde la punta de las agujas cerradas
9 19 29 39 49 59 69 79 89 99 109 119 126'5 mm.

Nº AGUJA O TUBO			
distancia de punta inicio / fin	/	/	/
posición fuente inicio / final	/	/	/

Nº AGUJA O TUBO				
	/	/	/	/
	/	/	/	/

Nº AGUJA O TUBO					
	/	/	/	/	/
	/	/	/	/	/



Theoretical calculation 4.4 Gy
To the 85 % isodose
optimization in volume

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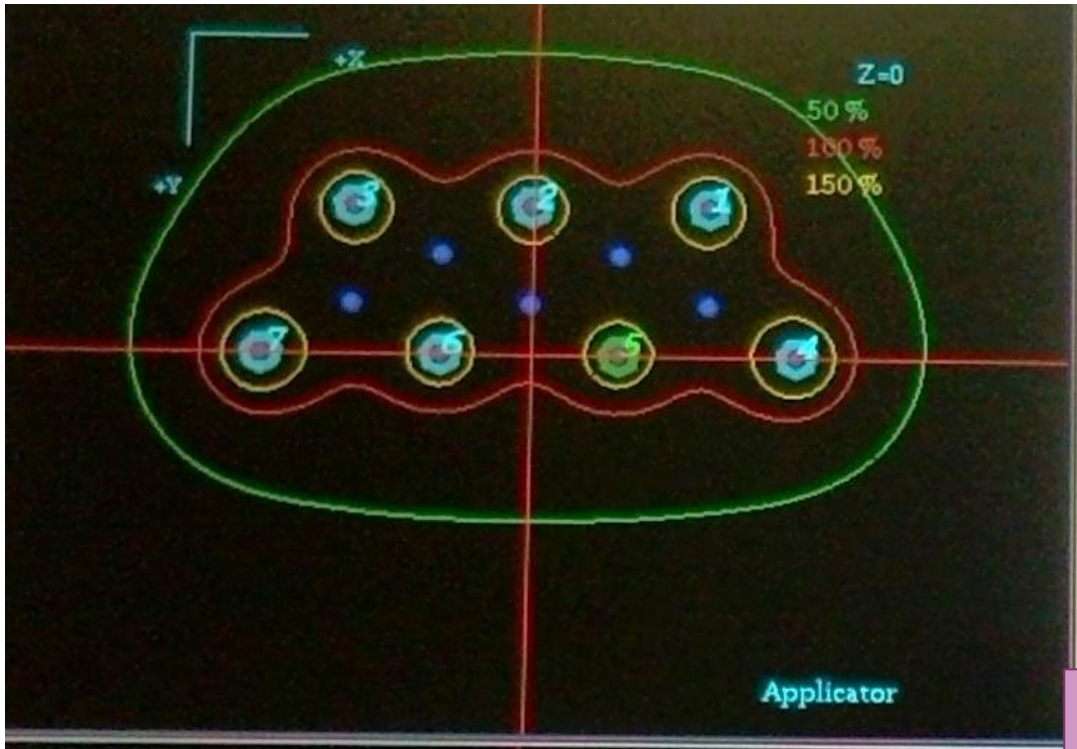
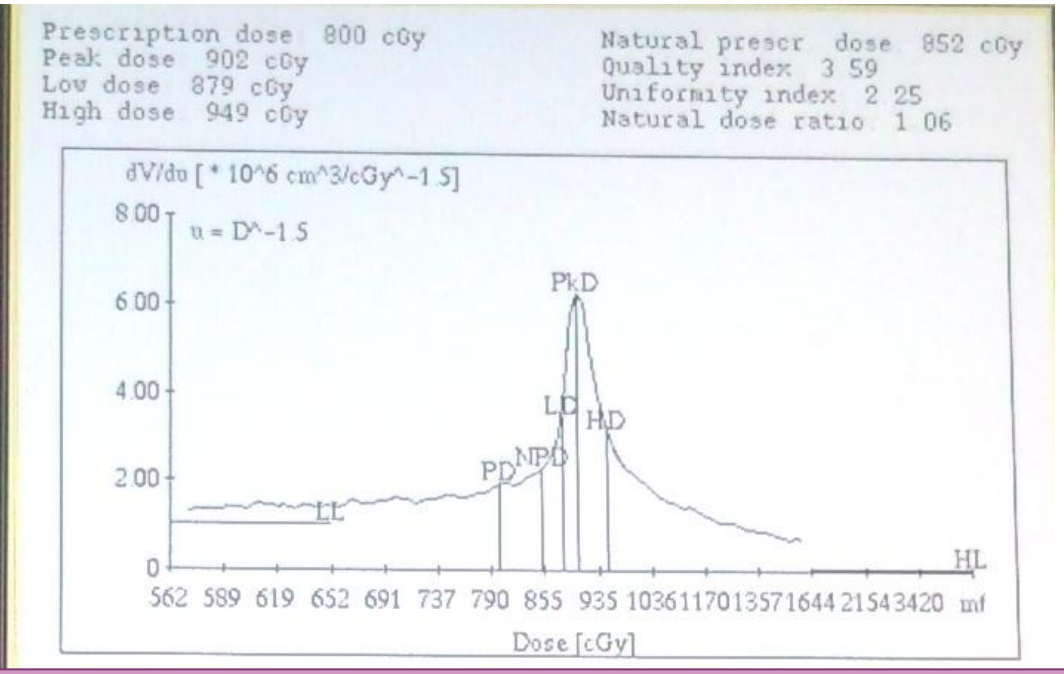
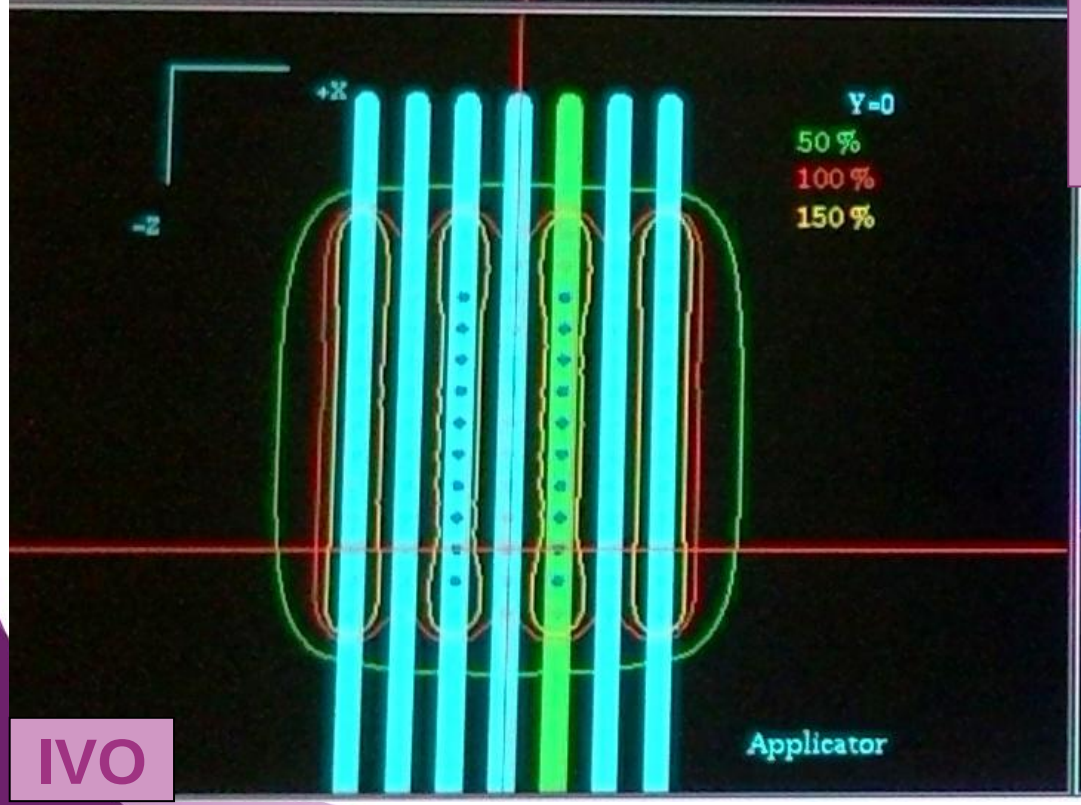
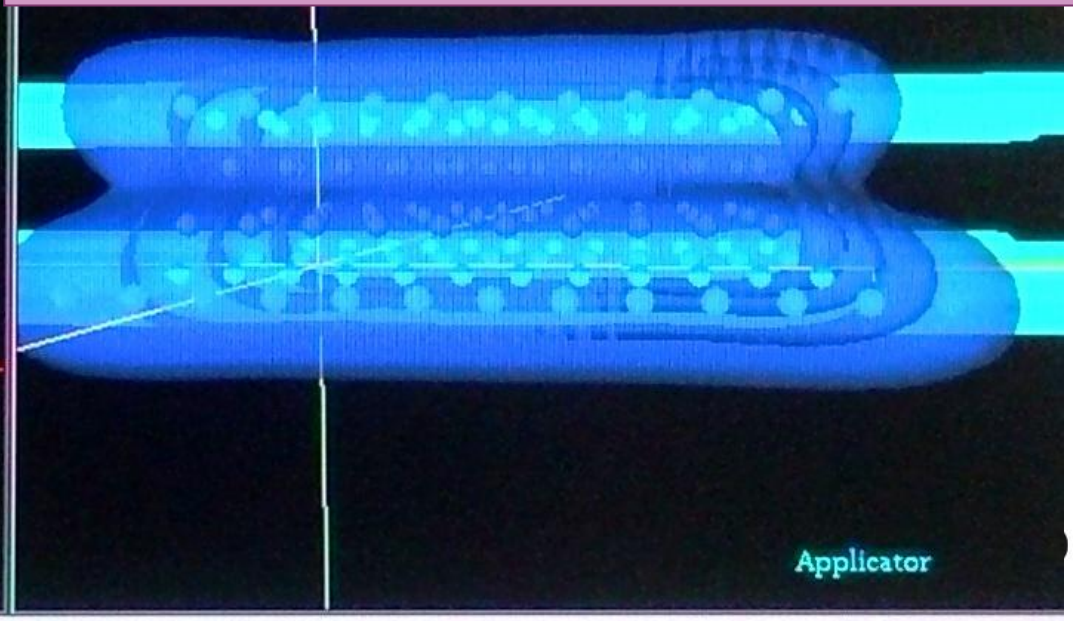






Theoretical calculation 7-8 Gy
To the 90 % isodose
optimization in volume



IVO

FAST-BOOST TECHNIQUE

- Fast target definition by clinical assesment: 15′
- Fast implant with parallel needles: 30′
- Fast dosimetric calculation: 15′
- Fast treatment duration: 10-15′
- Fast needles withdrawal: 10-15′

Patient discharged 2-3 hours after arriving to the hospital

IVO

Boost after breast conserving surgery and EBRT

How much dose?

Free margins

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How much dose?

SINGLE FRACTION HDR BOOST							
			N. patients	Gy per fraction	Local failure	Follow -up y.	% good Cosmesis
Resch	2002	Viena	274	7-12	3.9%	10	38
Neumanova	2008	Brno	215	8-12	1.5%	5	86
Hammer	1994	Linz	212	10	4.6%	5	78
Knauerhase	2008	Rostock	75	8-12	5.9%	10	78
Budrukkar	2007	Bombay	153	10	8%	10	83
Lopez	2009	Madrid	210	7	6%	10	86-96
Guinot. IVO	2012	Valencia	84	7	4.4%	10	92.5
BARTELINK	2007		2661	16Gy	6.2%	10	

Be careful with cosmesis

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Importance of the prescription: Boost HDR to 10mm

Resch A. 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. Radiother Oncol 2002;63:47-58

410 patients (Viena)

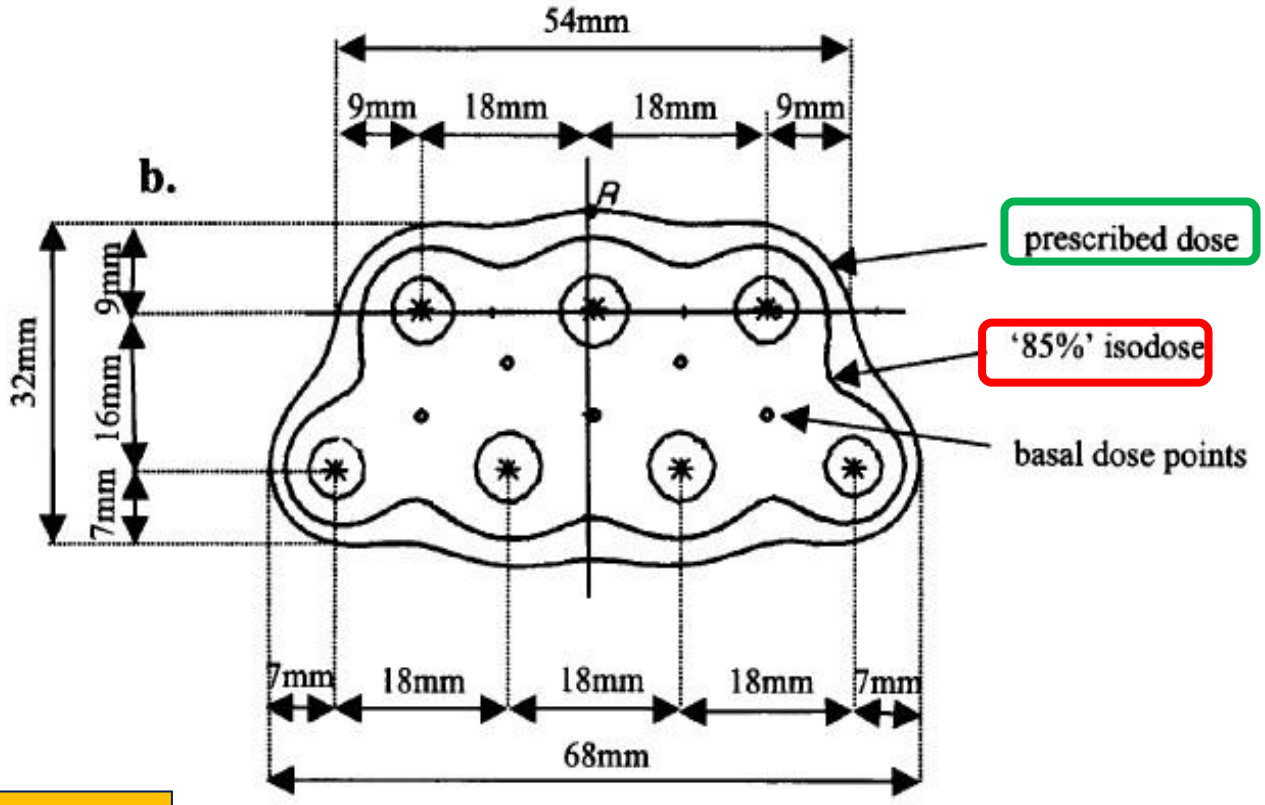
Local relapse 3.9%

Cosmesis

Excellent-good 38%

Moderate 55%

Bad 7%



↑25%

↑31%

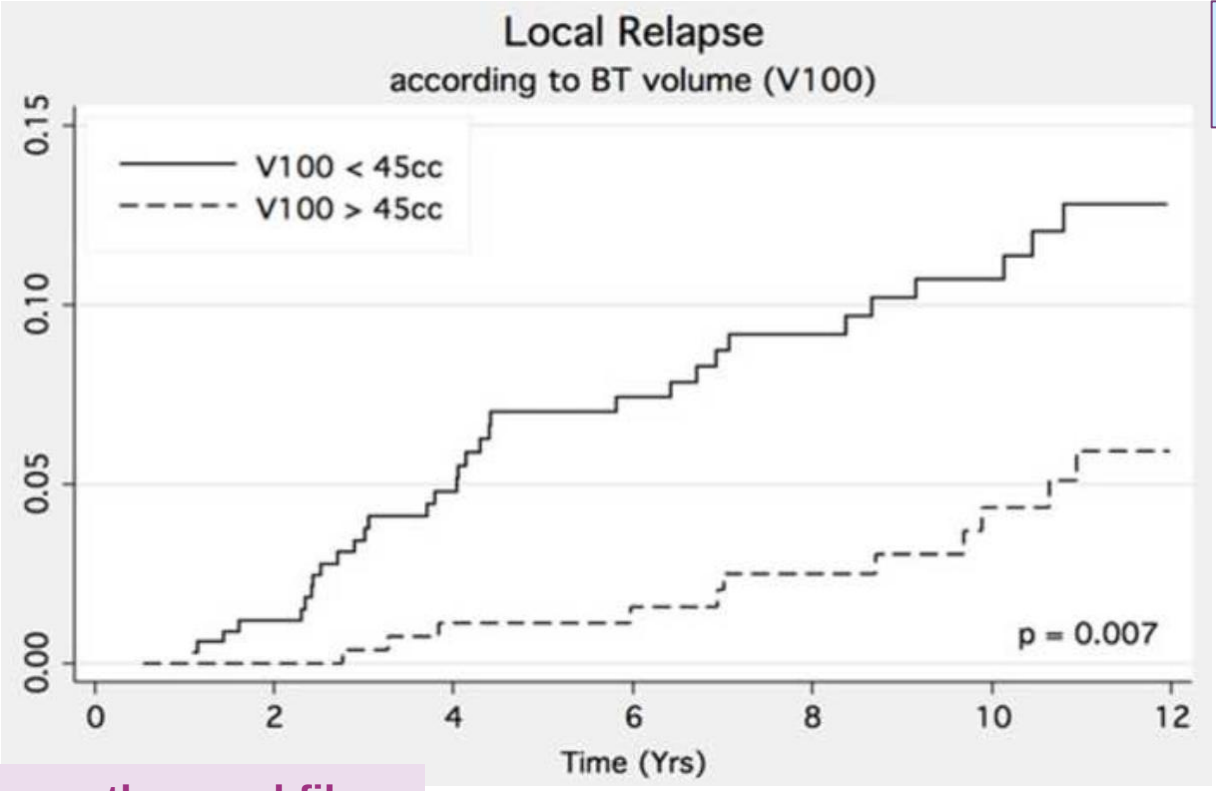
LDR: 20 Gy (9.9 - 27 Gy)

LDR, 6 cm active length	Five needles		Seven needles		Nine needles	
	Dose (Gy)	Volume (ccm)	Dose (Gy)	Volume (ccm)	Dose (Gy)	Volume (ccm)
'Prescribed isodose'	20	87	20	105	20	133
'Mean central dose' (MCD)	33		29		28	
'85% isodose'	28	50	25	71	24	96
'High dose-isodose'	50	8	43	11	43	13

HDR: 9.7 Gy (7 – 12 Gy)

'Prescribed dose'	9.7 ± 1.1
'Mean central dose'	15.0 ± 2.0
'85% of mean central dose'	12.7 ± 1.7
'Prescribed dose'	83 ± 31
'85% of mean central dose'	52 ± 22
'High dose volume' (150% of MCD)	8 ± 3
'Low dose volume' (90% of MTD)	96 ± 36
'Homogeneity index'	0.65 ± 0.06

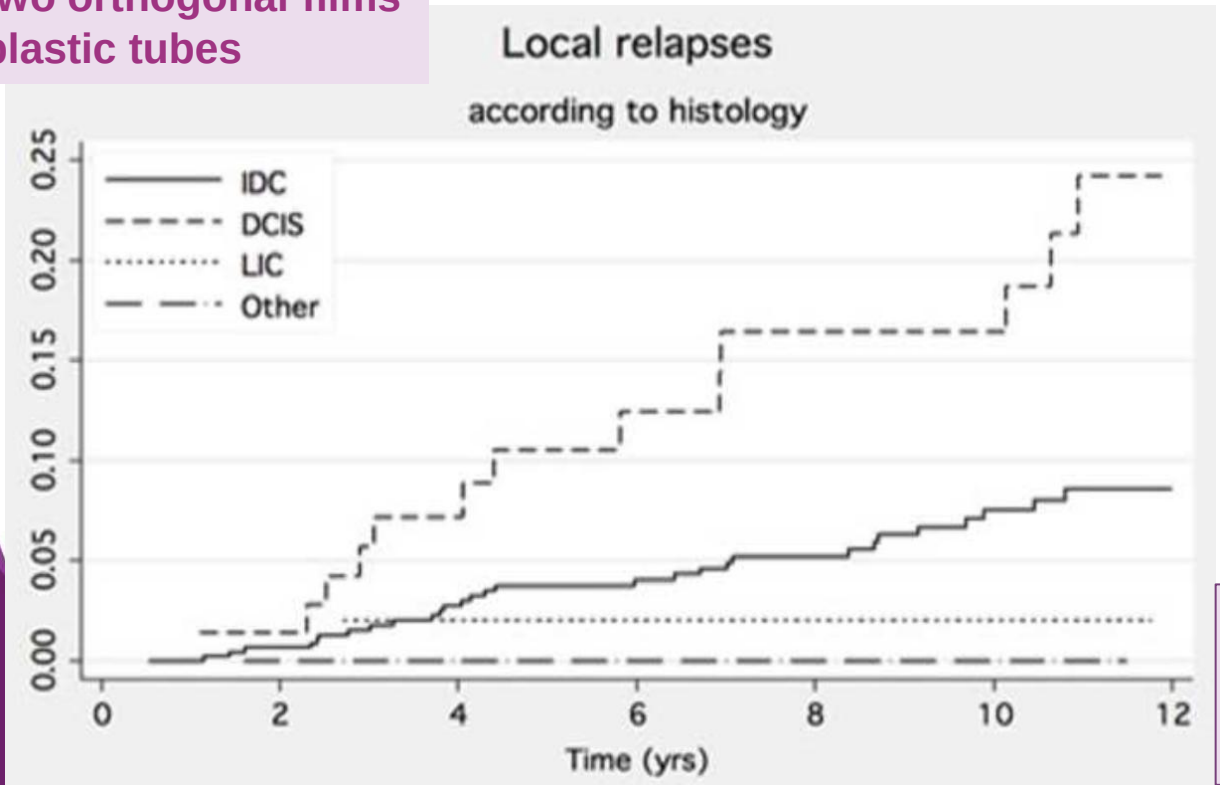
Boost 2 x 5Gy



- 621 patients T1–T2, N0-1 lumpectomy + EBRT (44 Gy in 5 weeks), + 2 x 5 Gy HDR.
- **One plane 89%, 3 lines 84%**
- FU 10.3years,
- 10-year local relapse: **7.4%**

- Cosmetic results: excellent 22% good 58%, fair 15%, and poor 5%

two orthogonal films
plastic tubes



- **Small-volume implantation (V100<45cc) and DCIS correlated with local relapse.**

- **When surgical bed could not be accurately localized, the boost volume should be large to avoid local recurrence.**

Quéro L, Guillerm S, Taright N, 10-Year follow-up of 621 patients treated using high-dose rate brachytherapy as ambulatory boost technique in conservative breast cancer treatment. Radiother Oncol. 2017;122(1):11-16

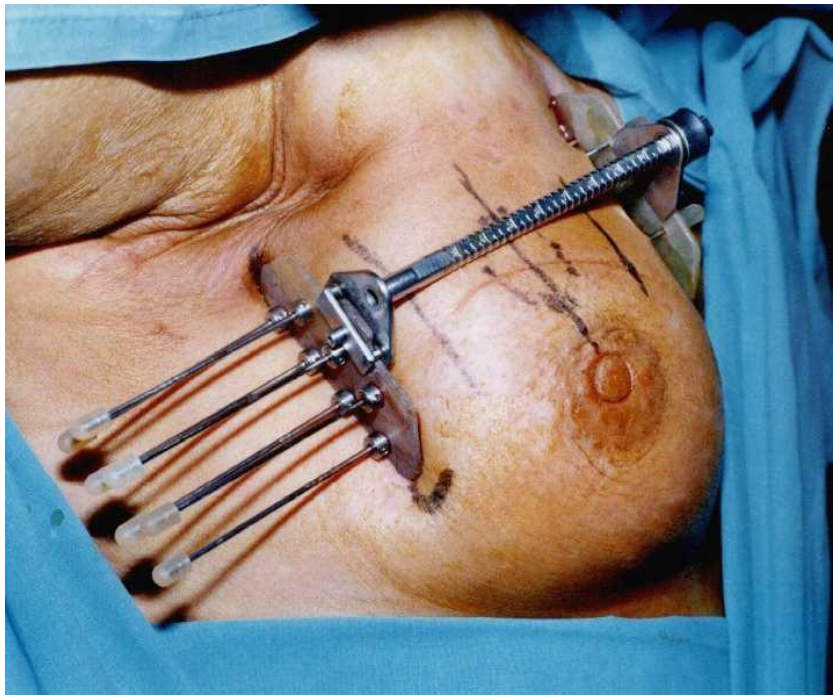
Ten-year results of a phase II study with a single fraction of high-dose-rate brachytherapy (FAST-boost) after whole breast irradiation in invasive breast carcinoma

2012

José Luis Guinot · M. Isabel Tortajada · María Carrascosa · Vicente Crispín · Ana Otero · Belén Ríos · Eleonor Rivin · Miguel Santos · Pablo Soler · Leoncio Arribas

84 consecutive patients (1999-2000)

- **F.U. 10 years**
- **Invasive breast carcinoma**
- **Conservative surgery with free margins >4mm**
- **Whole breast EBRT 46-50 Gy**
- **Single dose HDR boost brachytherapy 7 Gy**
- **Local failure 4.4%**



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Guinot JL et al. Clin Transl Oncol 2012; 14:109-115

LATE COMPLICATIONS

- Cosmetic results good or excellent in 92.5%
- 3 fibrosis (3.6%)
- 0 telangiectasia

the low rate of complications can be related with the high homogeneity

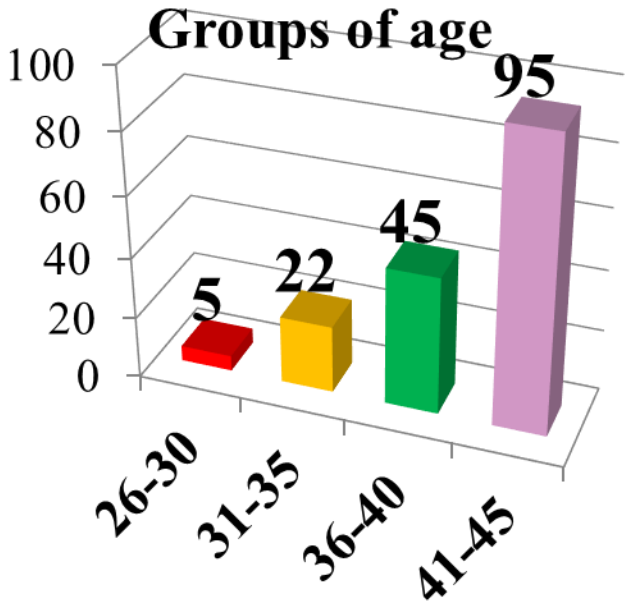
- Mean irradiation volume 82 cc (60-147)
- Median DNR: 0.21
- Uniformity index: 1.95 (1.66 – 2.13)

Young women

2015

High-Dose-Rate Brachytherapy Boost Effect on Local Tumor Control in Young Women With Breast Cancer

Jose-Luis Guinot, MD,* Cristobal Baixauli-Perez, PhysD,†
Pablo Soler, MD,* Maria Isabel Tortajada, MD,* Araceli Moreno, MD,*
Miguel Angel Santos, MD,* Alejandro Mut, MD,*
Francisco Gozalbo, MD,‡ and Leoncio Arribas, MD*



- 167 consecutive patients (1999 to 2008)
- 26-45 years old
- Invasive breast ca.
- free margins >4mm
- Whole breast EBRT 50 Gy
- Single HDR brachytherapy 7 Gy
- Chemotherapy: 86%,
- hormonal treat: 77%

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Guinot JL et al. Int J Radiat Oncol Biol Phys 2015 Jan 1;91(1):165-71

Young women

Breast failure at 10 years: 4,4%

LATE COMPLICATIONS

- 5 (3%) fibrosis
- 0 telangiectasia

COSMETIC RESULTS

- good or excellent 97%

Guinot JL et al. Int J Radiat Oncol Biol Phys 2015 Jan 1;91(1):165-71

Young women

COMPARISON WITH PUBLISHED

Breast failure in women ≤ 40 years old

	N.	age	%	F.U.	Treat.
Bartelink EORTC 22811-10882	221	≤40	13.5%	10	RT50+ 16Gy
	228	≤40	23.9%	10	RT50
Van der Leest (Maastrich)	758	≤40	17.9%	10	
Bollet (Paris)	209	<40	38%	10	
Oh (Houston)	196	35-40	8.3%	5	
		<35	12.1%	5	
IVO (Valencia)	72	≤40	5.6%	10	RT50+ ATD7Gy

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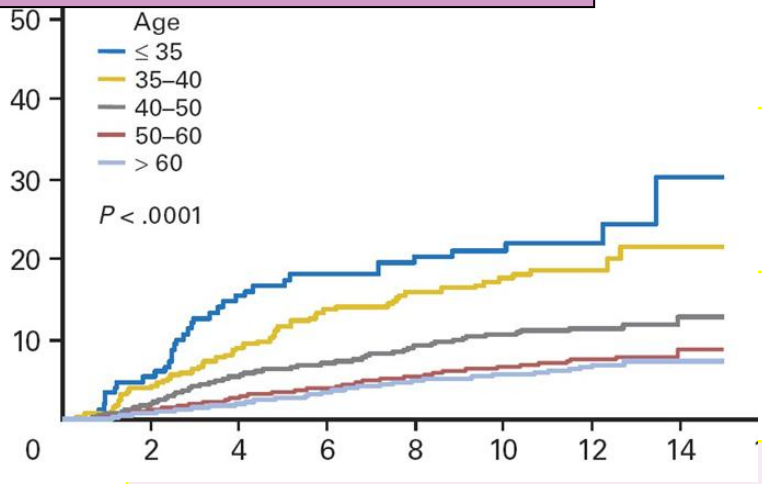
Young women



Comparison with EORTC 22811-10882

Breast failure at 10 years

	RT 50	RT50 +16Gy	RT+ 7Gy HDR
41-50 years old	12.5%	8.7%	4.3%
≤40 years old	23.9%	13.5%	5.6%
≤50 years old	19.4%	11.4%	4.9%
≤50 years old G1-2	19.2%	5.7%	2.5%
≤50 years old G3	28.5%	13.5%	8.9%

Breast failure rate halves with a single fraction of 7 Gy

Boost after breast conserving surgery and EBRT

How much dose?

Close or involved margins

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SURGICAL MARGINS INVOLVED

Society of Surgical Oncology/ ASTRO Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer

- 33 studies including 28,162 patients
- Positive margins (ink on invasive carcinoma or ductal carcinoma in situ) are associated with a **2-fold increase** in the risk of IBTR compared with negative margins.
- This increased risk is not mitigated by favorable biology, endocrine therapy, or a radiation boost.
- More widely clear margins than no ink on tumor do not significantly decrease the rate of IBTR compared with no ink on tumor.

Moran MS et al. Society of Surgical Oncology/American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer. Int J Radiation Oncol Biol Phys, Vol. 88, No. 3, pp. 553-564, 2014

SURGICAL MARGINS INVOLVED

Society of Surgical Oncology–ASTRO–ASCO Consensus Guideline on Margins for Breast-Conserving Surgery with Whole breast irradiation in Ductal Carcinoma In Situ

- 20 studies including 7,883 patients
- Negative margins halve the risk of IBTR compared

with positive margins (ink on DCIS).

- A 2-mm margin minimizes the risk of IBTR
- More widely clear margins do not significantly decrease IBTR compared with 2-mm margins.
- Negative margins narrower than 2 mm alone are not an indication for mastectomy, and factors known to affect rates of IBTR should be considered for re-excision.

Morrow M et al. Society of Surgical Oncology–American Society for Radiation Oncology–American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with WholeBreast Irradiation in Ductal Carcinoma In Situ. Ann Surg Oncol (2016) 23:3801–3810

Local recurrence with close or positive margins

Table 2. Local recurrence rates in breast cancer with negative, close (<2 mm), or positive margins

Study (reference)	Parameter	Negative (%)		Close (%)		Positive (%)	
		5 y	10 y	5 y	10 y	5 y	10 y
Freedman *et al.* 1999 (32)		4	7	7	14	5	12
Freedman *et al.* 2002 (38)	Age ≤35 y						34
Leong *et al.* 2004 (10)		4	8			12	25
Gage *et al.* 1996 (23)		2				16	
						Focal: 9	
						Gross: 28	
Schnitt *et al.* 1994 (22)	>60 Gy	0		4		Focal: 6	
						Gross: 21	
DiBiase *et al.* 2002 (31)	65 Gy	6	12			15	33
Anscher *et al.* 1993 (40)		2				10	
Kunos *et al.* 2006 (17)		2.1		8.9			
Karasawa *et al.* 2005 (16)	<5 mm				<2 mm: 9		14.1
					<5 mm: 13		
Jobsen *et al.* 2003 (39)		3.1	6.9			5.6	12.2
Jobsen *et al.* 2003 (39)	Age ≤40 y	8.4				36.9	
	Age >40 y	2.6				2.2	
Smitt *et al.* 1995 (12)			2				Close/+: 18
Park *et al.* 2000 (21)	8-y FU, >60 Gy		7		7		Focal: 14
							Gross: 27
Cowen *et al.* 2000 (11)	N0 (no CT)					20	29
Neuschatz *et al.* 2003 (34)	12-y FU		0		<2 mm: 9		17
					<5 mm: 5		
Peterson *et al.* 1999 (13)	8-y FU		8		17		10
Obedian *et al.* 2000 (14)	64 Gy		2		2		17
Vicini *et al.* 2004 (20)	12-y FU		9				30

Guinot JL, Roldan S, Maronas M et al. Breast-conservative surgery with close or positive margins: can the breast be preserved with high-dose-rate brachytherapy boost? Int J Radiat Oncol Biol Phys. 2007;68:1381-1387

10 Gy vs 26 Gy boost with positive margins

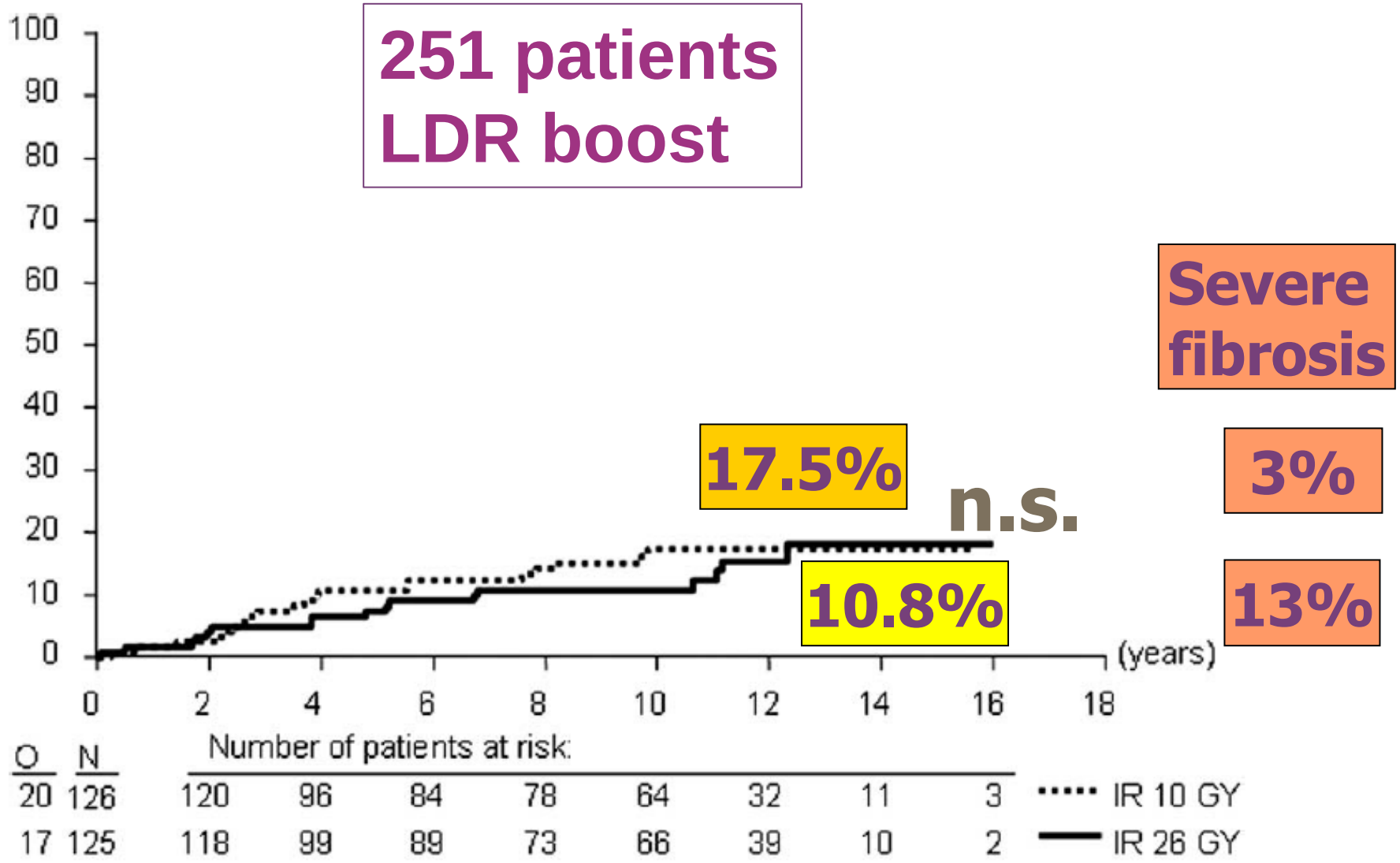


Fig. 1. Cumulative incidence of local failure (as first event).

Poortmans PM et al. Impact of the boost dose of 10 Gy versus 26 Gy in patients with early stage breast cancer after a microscopically incomplete lumpectomy: 10-year results of the randomised EORTC boost trial. Radiother Oncol. 2009 Jan;90(1):80-5.

HDR boost with close and positive margins

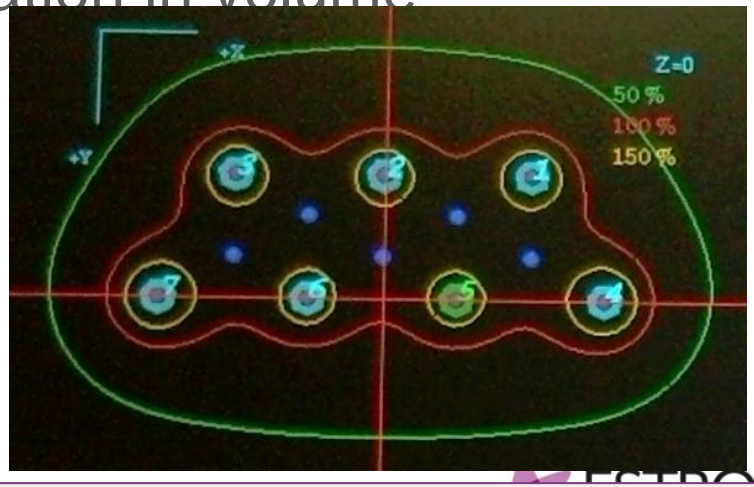
HDR boost with close and positive margins

BREAST-CONSERVATIVE SURGERY WITH CLOSE OR POSITIVE MARGINS: CAN THE BREAST BE PRESERVED WITH HIGH-DOSE-RATE BRACHYTHERAPY BOOST?

JOSE LUIS GUINOT, M.D.,

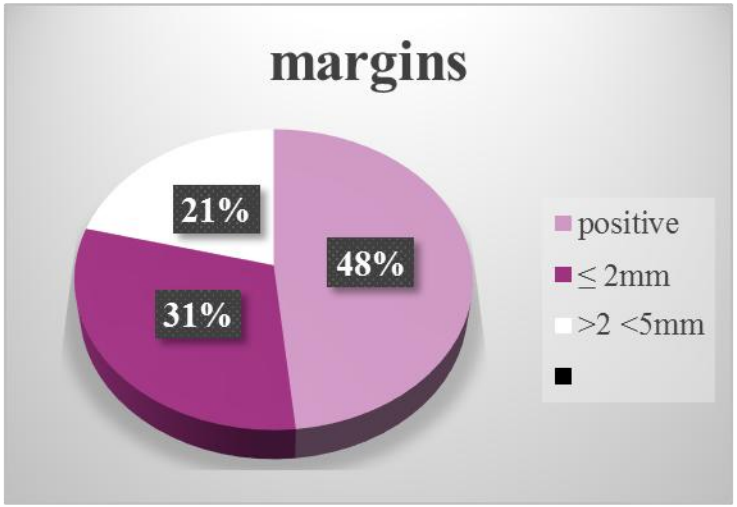
Guinot JL et al. Int J Radiat Oncol B P 2007; 68:1381-7

- 248 patients 1996-2011
- BCS, EBRT + HDR 3x4.4Gy
- Whole breast RT (50 Gy)
- metallic needles
- HDR three fractions of 4.4Gy with optimization in volume prescribed to the 85% isodose
- 3 x 4.7Gy to 90% isodose
- Two days at the hospital
- one night with the implant



Guinot JL, Tortajada MI, Santos MA et al. HDR boost decreases the risk of breast failure in invasive breast carcinoma with close or involved margins. Presented at ESTRO 2017

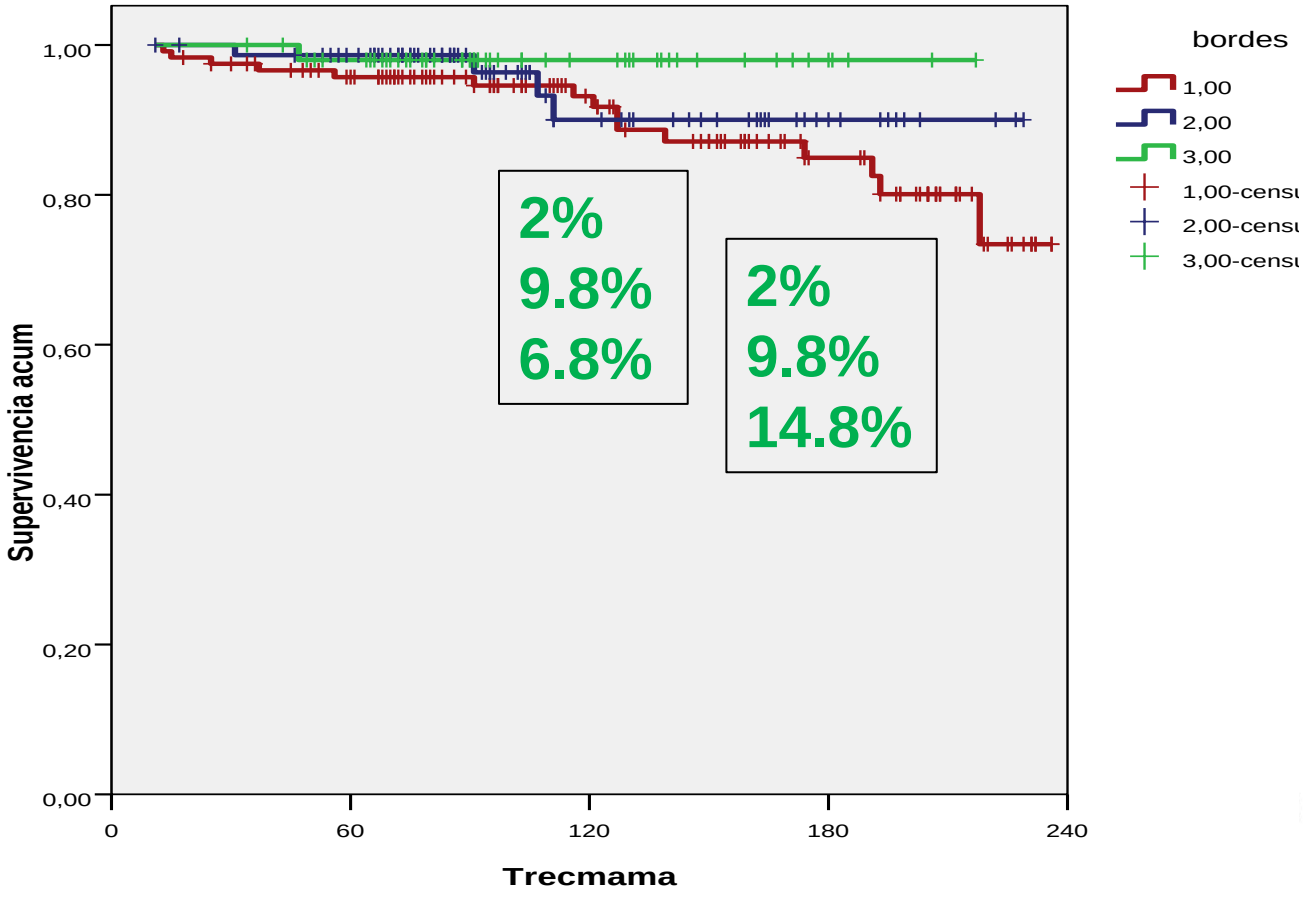
RESULTS: Local control by margin



	10 years	15 y.
15 / 120 margin +	93.2%	85.2%
4 / 76 margin ≤ 2mm	90.2%	90.2%
1 / 52 margin >2- <5mm	98%	98%

Mean follow-up 127 months

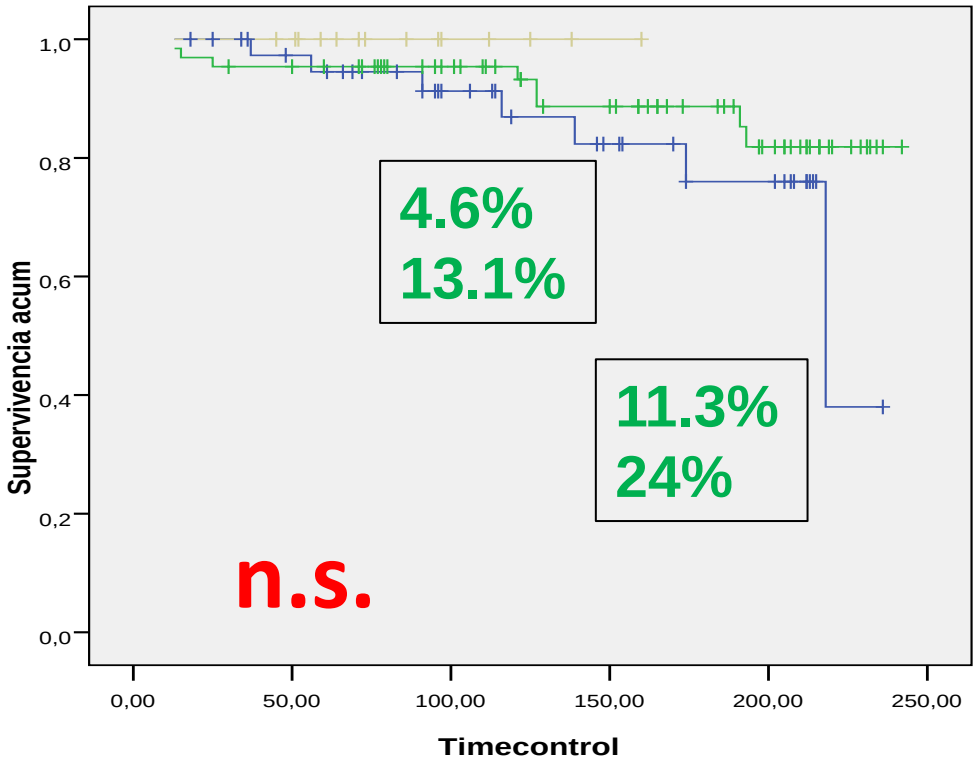
No difference if margin is by DCI or DCIS



RESULTS: Local control by age

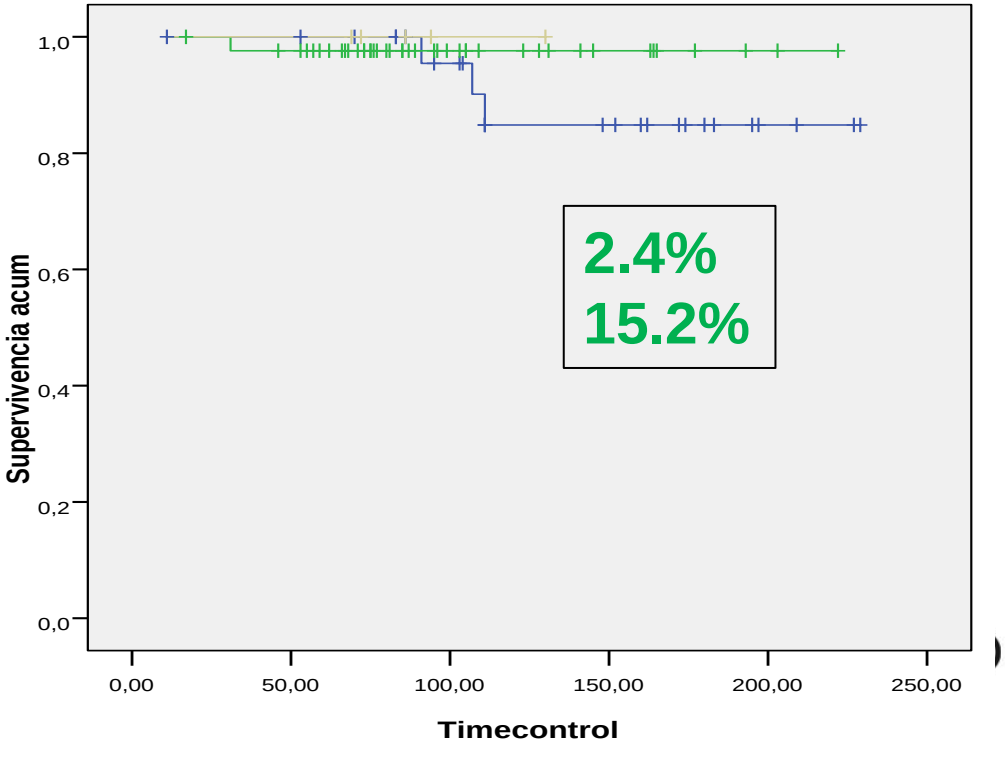
Positive margin

AGE		10 years	15 years
<=50	7/41	86.9%	76%
51-70	8/65	95.4%	88.7%
> 70	0/14	100%	100%



Close ≤2mm margin

AGE		10 years	15 years
<=50	3/28	84.8%	84.8%
51-70	1/43	97.6%	97.6%
> 70	0/5	100%	100%



RESULTS: Local control

No differences

- Hormonal receptors
- Hormonal treatment
- Chemotherapy
- Neoadjuvant chemotherapy

- T
- Number of borders
- Border with IDC or DCIS
- Second surgery (6/60)
- Surgery +-shaving

- Triple negative (1/12)
- Subtipe HER+ (1/9)
- G3 (5/56)
- Associated DCIS (12/148)
- EIC (3/59)
- Hystology ILC (0/9)

- Single plane (2/12)

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COSMESIS

Good or excellent: 85.8%

Fair or bad: 14.2%

DCI T2N0 Two positive margins by DCIS
Outer lower quadrant left breast
50Gy + 3 x 4.4Gy
At 16 years

LATE EFFECTS

(232 patients)

- **Fibrosis/induration 62 (26.7%)**
- **Volume reduction 15 (6.5%)**
- **Breast edema 15 (6.5%)**
- **Telangiectasia 8 (3.4%)**
- **Pigmentation 5 (2.1%)**
- **Infection 2 (0.9%)**

COMPARISON WITH BOOST TRIAL

Local recurrence depending on age and boost to the tumor bed

Bartelink H et al J Clin Oncol 2007;25:3259-65

Current study close + margins boost HDR

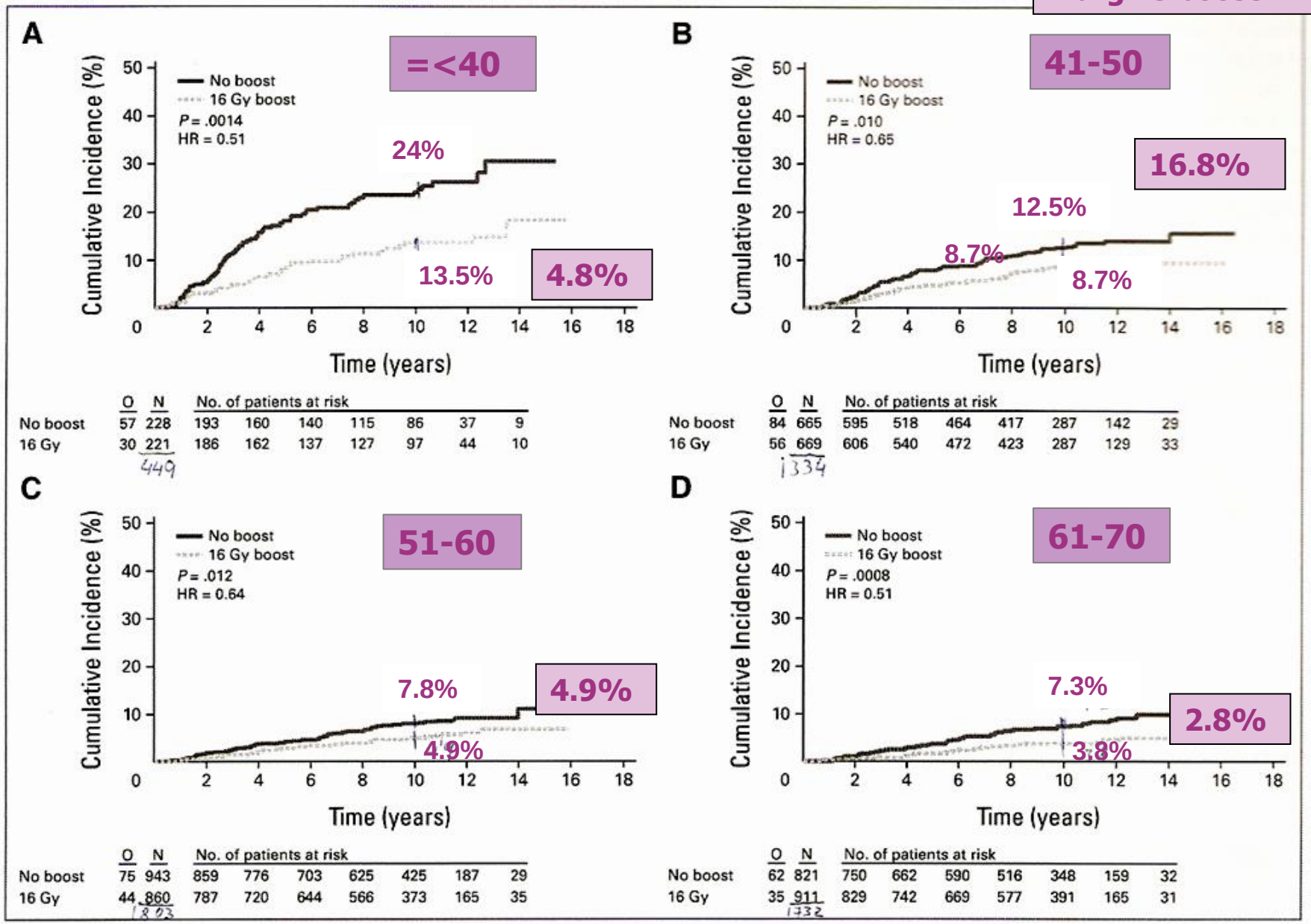

Fig 3. Cumulative incidence of ipsilateral breast cancer recurrence according to age. Age (A) ≤ 40, (B) 41 to 50, (C) 51 to 60, and (D) > 60 years. HR, hazard ratio; O, occurrences; N, number of patients at risk.

COMPARISON WITH BOOST TRIAL

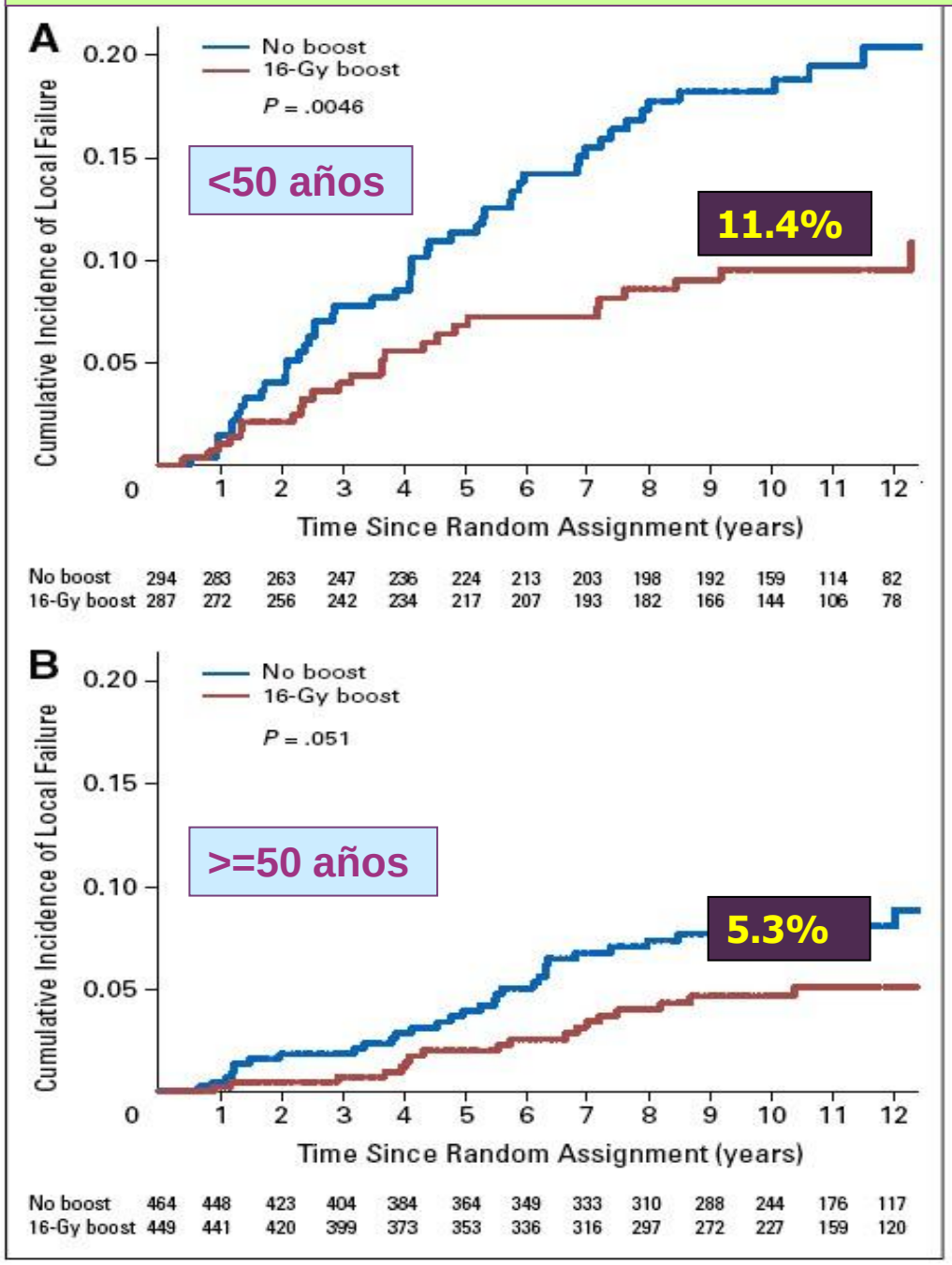

Fig 2. Cumulative incidence of local failure by boost group and age. (A) Patients younger than 51 years (P = .0046). (B) Patients older than 50 years (P = .051).

Age and dose

13.1%

11.9%

≤ 50 years old

Positive margin

Current study close + margins boost HDR

4.6%

3.2%

> 50 years old

Jones HA et al J Clin Oncol 2009;27:4939-47

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Boost after breast conserving surgery and EBRT

Is interstitial BT better?

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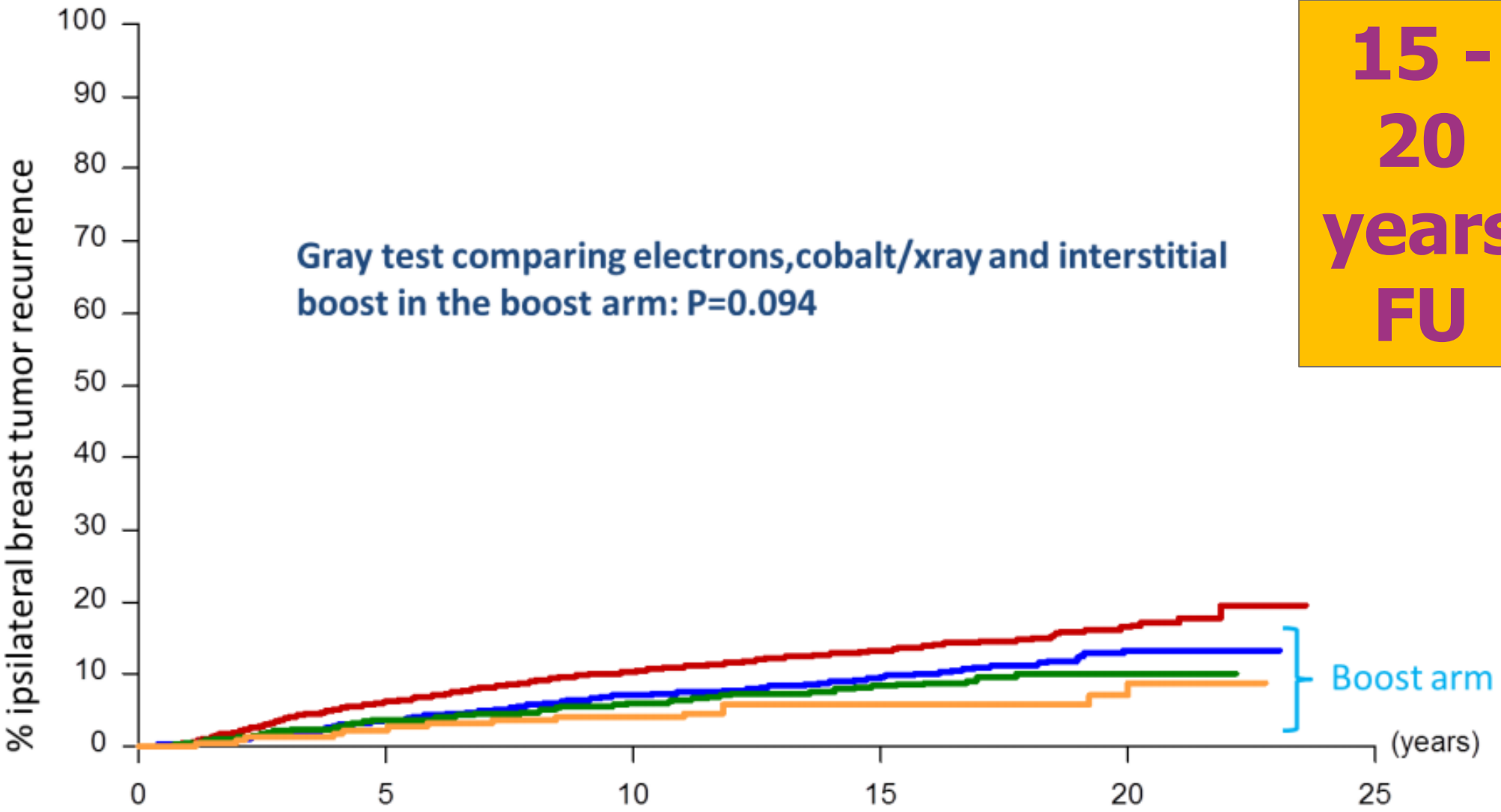
15 - 20 years FU



Gray test comparing electrons,cobalt/xray and interstitial boost in the boost arm: P=0.094

O	N	Number of patients at risk :				Type of boost
349	2610	1992	1467	949	153	No boost
162	1640	1295	941	611	81	Electrons
59	753	561	395	254	45	Co/X-ray
14	225	181	144	91	32	Interstitial

Poortmans et al R&O 2004, actualized 2014

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EORTC 22881/10882 “boost”

Poortmans et al (actualized 2008) median FU 10.8y

	Electrons	Photons	Interstitial	
Number with boost	1635 (63%)	753 (28%)	225 (9%)	Total 2661
Median boost dose	16 Gy	16 Gy	15 Gy	
Median boosted cc	144cc	288cc	60cc	
10 y. Local recurrence	**6.3%**	**5.3%**	**3.7%**	No boost 9.8%
Severe fibrosis	3.8%	5.3%	5.3%	No boost 1.6%

Boost after breast conserving surgery and EBRT

Is HDR BT better than LDR BT?

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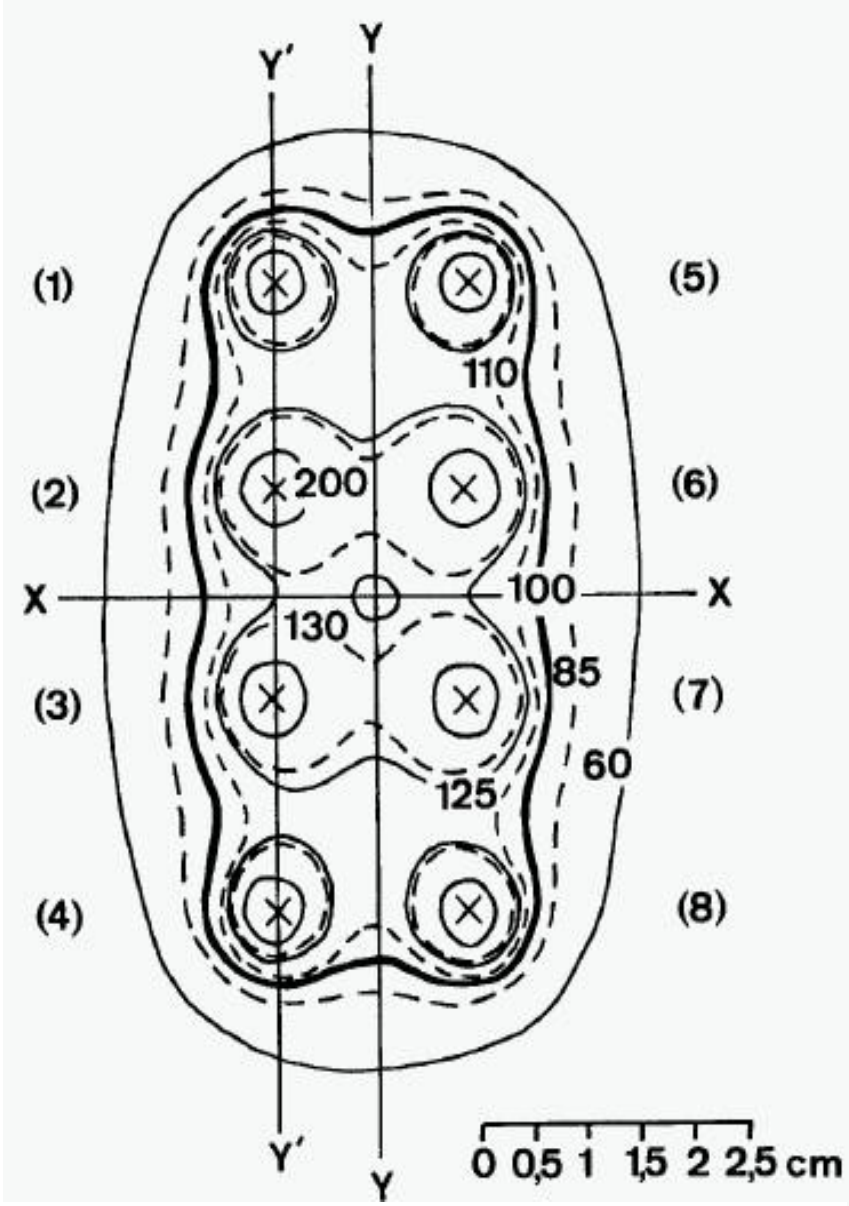
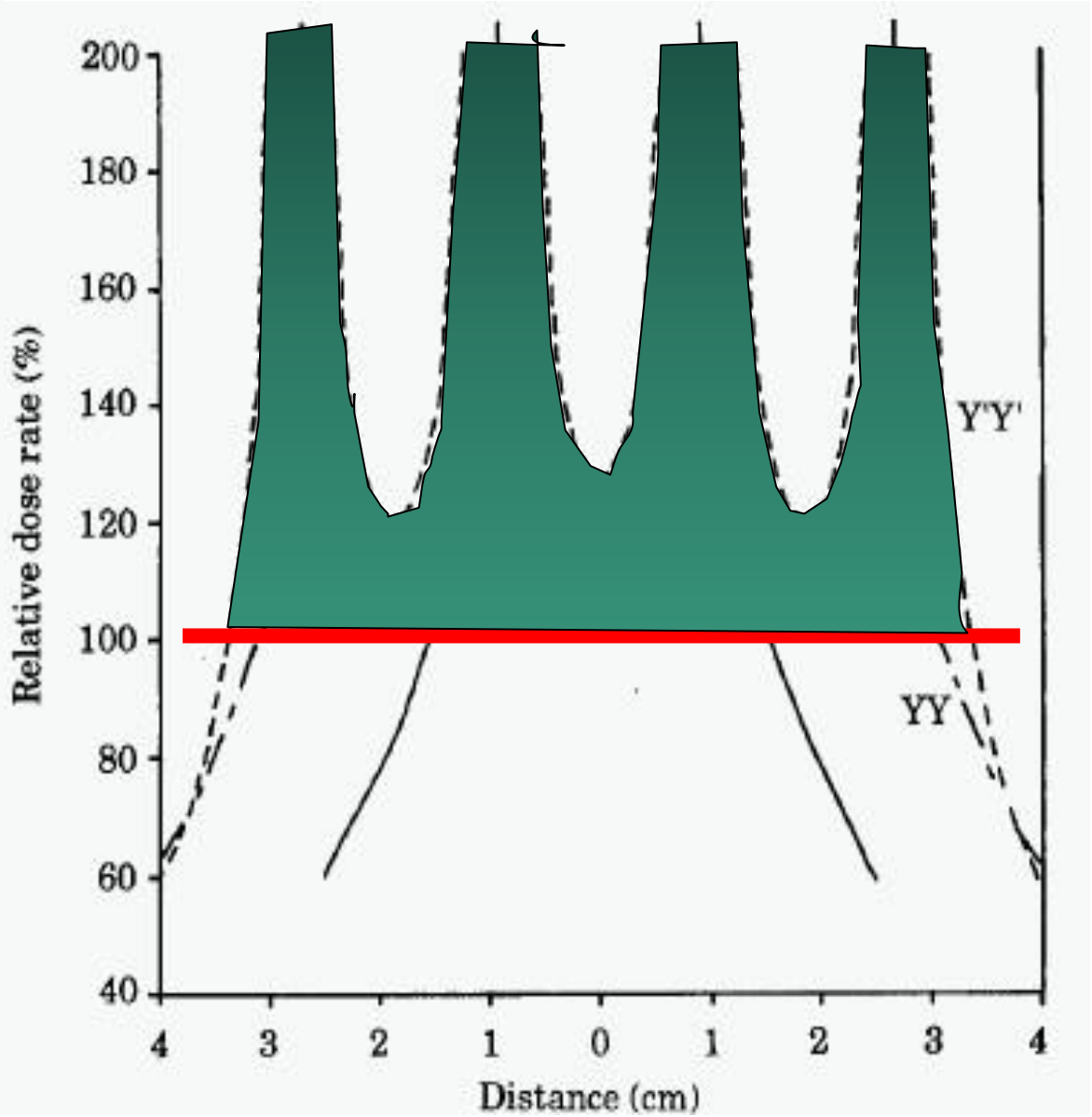
IN BRACHYTHERAPY THE DOSE INSIDE THE TREATED VOLUME IS FAR HIGHER THAN THE PRESCRIBED DOSE





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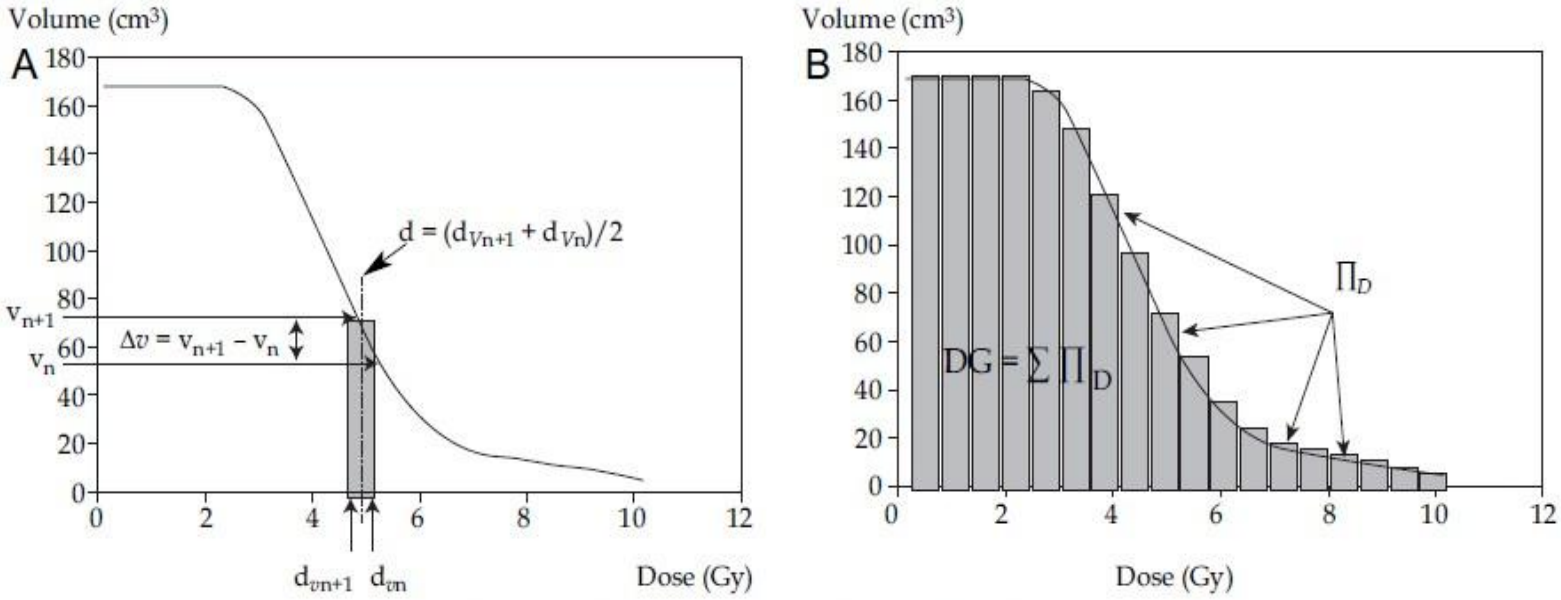


Fig. 3. DVH segmentation method for the calculation of elementary doses d ($d = (d_{Vn+1} + d_{Vn})/2$) delivered per fraction to elementary volumes Δv ($\Delta v = v_{n+1} - v_n$) (A) and calculation of the total dose delivered to the whole CTV taking into account the dose gradient DG ($DG = \Sigma \prod_D$) (B)

Dose gradient impact on equivalent dose at 2 Gy for high dose rate interstitial brachytherapy

Jean-Michel Hannoun-Levi, MD, PhD, Marie-Eve Chand-Fouche, MD, Catherine Dejean, PhD, Adel Courdi, MD

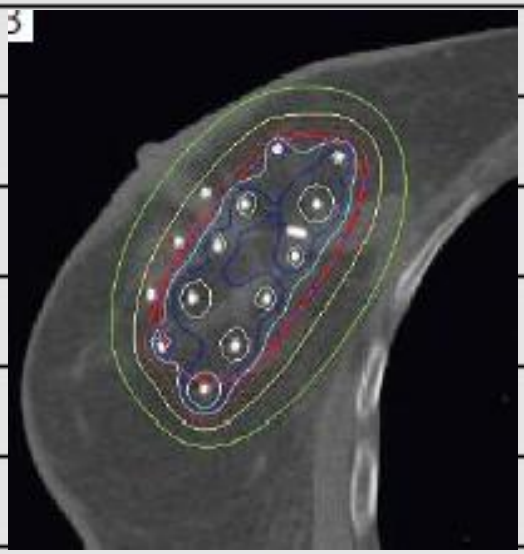
Department of Radiation Therapy, Antoine Lacassagne Cancer Center, Nice, France

J Contemp Brachyther 2012; 4,1:12-20

The inevitable dose gradient in BT ensures non-uniform dosage within the target volume and this extra-dose has its own biological effect

Table 2. Equivalent dose at 2 Gy of the physical prescribed dose taking into account or not the dose gradient for $\alpha/\beta = 1.5$, $\alpha/\beta = 3$, $\alpha/\beta = 4$ and $\alpha/\beta = 5$ in breast and prostate implants

	Breast implant **10 x 3.4 Gy**	
	Median (Gy)	Min/Max
DG not considered		
PPD	34	
EQD2		
$\alpha/\beta = 1.5$	–	
$\alpha/\beta = 3$	44	
$\alpha/\beta = 4$	42	
$\alpha/\beta = 5$	41	–
DG considered		
PPD	48	44-51
EQD2		
$\alpha/\beta = 1.5$	–	–
$\alpha/\beta = 3$	81	71-91
$\alpha/\beta = 4$	76	66-85
$\alpha/\beta = 5$	72	63-80



Single fraction 8 Gy

α/β 10: 13.5 Gy

α/β 4: 17 Gy

Taking into account the dose gradient

α/β 4: 20-25 Gy

Boost after breast conserving surgery and EBRT

CONCLUSIONS

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RISK GROUPS FOR BOOST

LOW RISK	INTERMEDIATE RISK	HIGH RISK
MEET ALL CRITERIA	MEET ANY CRITERIA	MEET ANY CRITERIA
Age >50	Age > 50 and one factor:	Positive margins
Size ≤ 3cm	- Size > 3cm	Age ≤ 40 and one factor
No triple negative	- Triple negative	- triple negative
Clear margins ≥ 2mm	- close margins <2mm	- close margins <2mm
EIC -	- EIC+	- EIC +
LVI -	- LVI +	
pN 0 (sentinel orALND)	- positive axilary nodes *	
Unicentric and unifocal	- Multicentric/multifocal	
	- after neoadjuvant therapy with residual tu	
	Age >40 < 50	
	Age ≤ 40 without major risk criteria	
BOOST NOT NEEDED	**BOOST 10-16Gy**	**BOOST ≥ 16 Gy**

* In case of pN+ with ≤3 positive nodes, age >60 and no other risk factors to omit the boost is justifiable.

TAKE HOME MESSAGES

- Every four local failures avoided, one death avoided at 15 years.
- Local recurrence is related to dose and young age.
- In young age, even with a boost, local recurrence goes up with F.U.
- If bed tumor is bad defined, larger volumes are required.
- Doses between 7-10 Gy HDR in a single dose are useful.
- In women aged ≤ 45 HDR boost improves local control.
- With positive/close margins, a high dose boost reduces local failure.
- A higher biological effect of HDR can explain this improved result.
- The boost dose has to be tailored to the risk factors
  - low risk..... no boost is mandatory (APBI)
  - medium risk..... 10-16 Gy or 1 x 7-8Gy (Fast-boost)
  - high risk..... ≥16Gy or 1 x 8-10Gy or 3 x 4.7Gy

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ESTRO TEACHING COURSE

Comprehensive and Practical Brachytherapy

Budapest 2017

Dr. José Luis Guinot

Fundación Instituto Valenciano de Oncología (I.V.O.). Valencia.

E-mail: jguinot@fivo.org

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ACELERATED PARTIAL BREAST IRRADIATION

Indications
Techniques
Results
Definition of CTV
Procedures: postop, periop
APBI as salvage

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INDICATIONS FOR APBI

GEC-ESTRO 2010

Table 8. GEC-ESTRO recommendations on patient selection for accelarated 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*)	pN1mi, pN1a (by ALND*)	pNx; ≥pN2a (4 or more positive nodes)
Neoadjuvant chemotherapy	Not allowed	Not allowed	If used

APBI = accelerated partial breast irradiation; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; LCIS = lobular carcinoma in situ; DCIS = ductal carcinoma in situ; HG = histologic grade; EIC = extensive intraductal component; LVI = lympho-vascular invasion; ER = estrogen receptor; PR = progesterone receptor; SLNB = sentinel lymph node biopsy; *ALND = axillary lymph node dissection (at least 6 nodes pathologically examined).

>60 y.o.

<2cm

Multifocal <2cm

ER+

APBI CONSENSUS RTOG 2009

RTOG 2009

Suitable

Cautionary

Unsuitable

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INDICATIONS FOR APBI

RTOG 2009. GEC-ESTRO 2010

Low-risk: good candidates
Intermediate-risk: optional
High-risk: contraindication for APBI

Polgar C et al. Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009) Radiother Oncol. 2010 Mar;94(3):264-73

American Brachytherapy Society acceptable criteria for accelerated partial breast irradiation

A.B.S. 2013

2016

Criteria	
Age	≥50 y old
Size	≤3 cm
Histology	All invasive subtypes and DCIS
Estrogen receptor	Positive/negative
Surgical margins	Negative
Lymphovascular space invasion	Not present
Nodal status	Negative

DCIS = ductal carcinoma *in situ*.

After European APBI trial,

- **Extensive intraductal carcinoma EIC+ is not aceptable**
- **Margin 2mm free**
- **Low risk pure DCIS is not clear**

Shah C, Vicini F, Wazer DE, Arthur D, Patel RR. The American Brachytherapy Society consensus statement for accelerated partial breast irradiation. Brachytherapy 2013; 12:267-277

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DIFFERENT TECHNIQUES
DIFFERENT RESULTS
Intraoperative
Intracavitary
Interstitial

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INTRAOPERATIVE IORT

- Electrons (ELIOT)
- X Ray 50 kV (TARGIT)
- Electronic BT: Xoft Axxent

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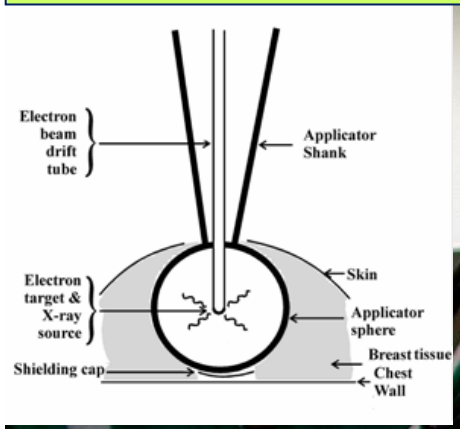
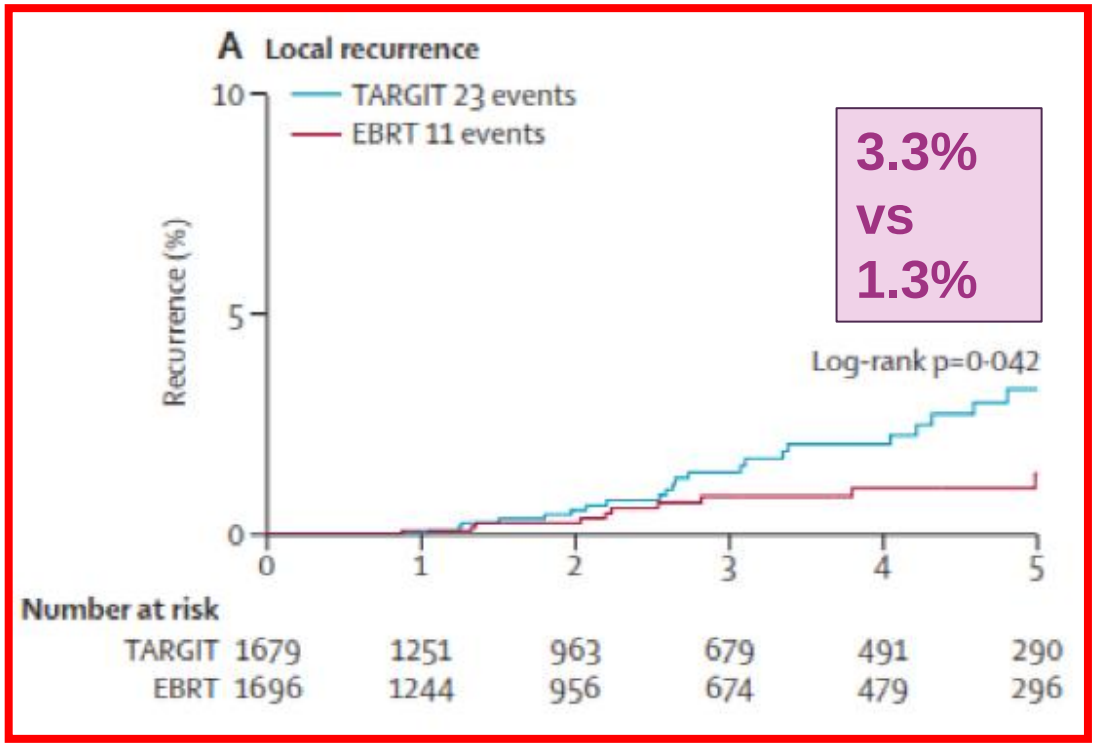
Intraoperative APBI IORT with 50 kV X-Rays. TARGIT



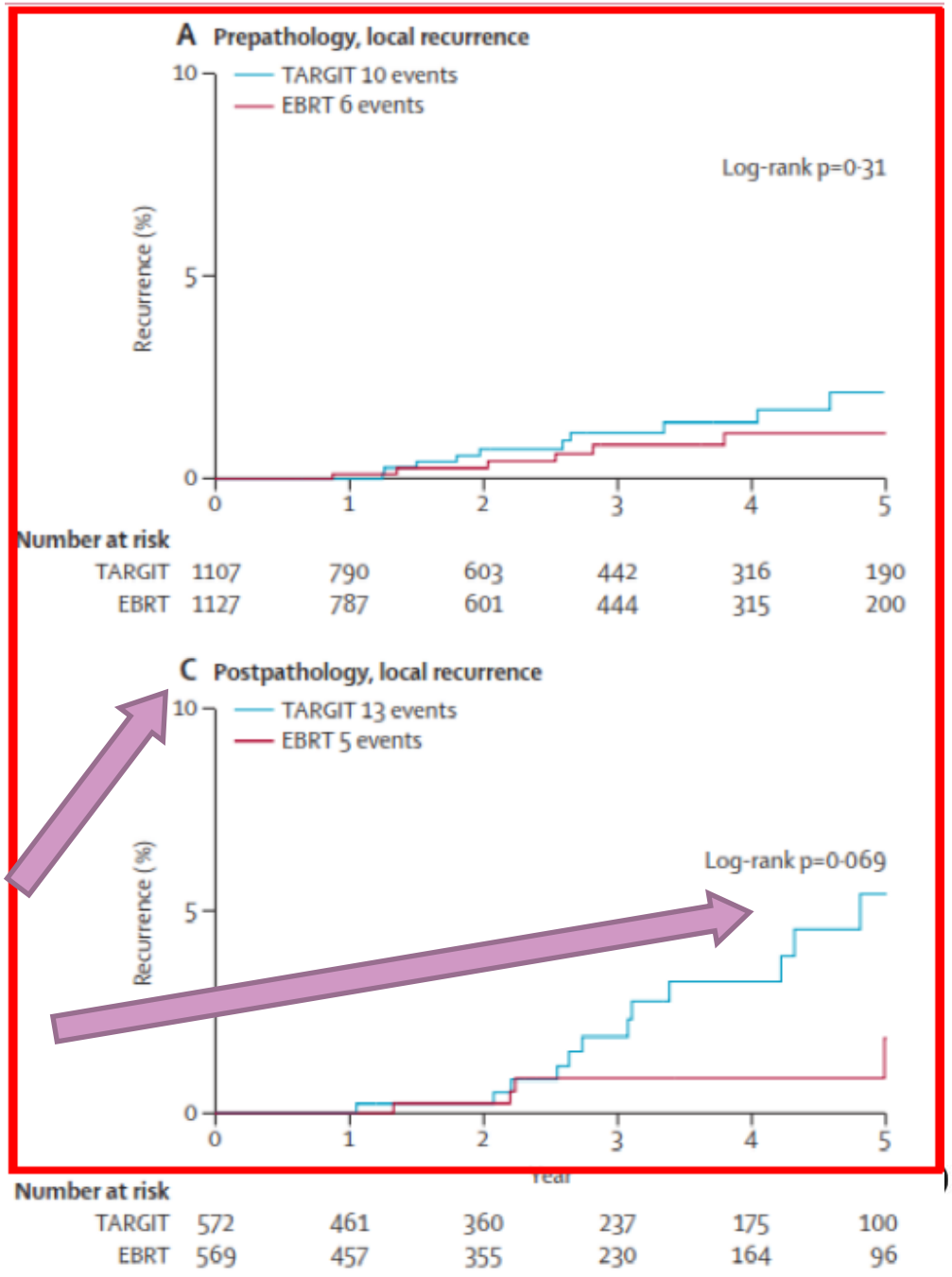
single dose of 14.7 –20 Gy
50 kV X-rays at the applicator surface
5 Gy at 1 cm over a 30-min period

Results APBI with intrabeam 2014



1721 TARGIT (15% of TARGIT received WBI)
1730 WBI

Bad results are related to unadequate localization of tumor bed



Vaidya JS et al. Risk adapted targeted intra-operative radiotherapy vs WBRT 5-year local control and OS from the TARGIT-A randomised trial. Lancet 2014; 383:603-13

INTRACAVITARY BRACHYTHERAPY

-MammoSite
- Contura
- SAVI

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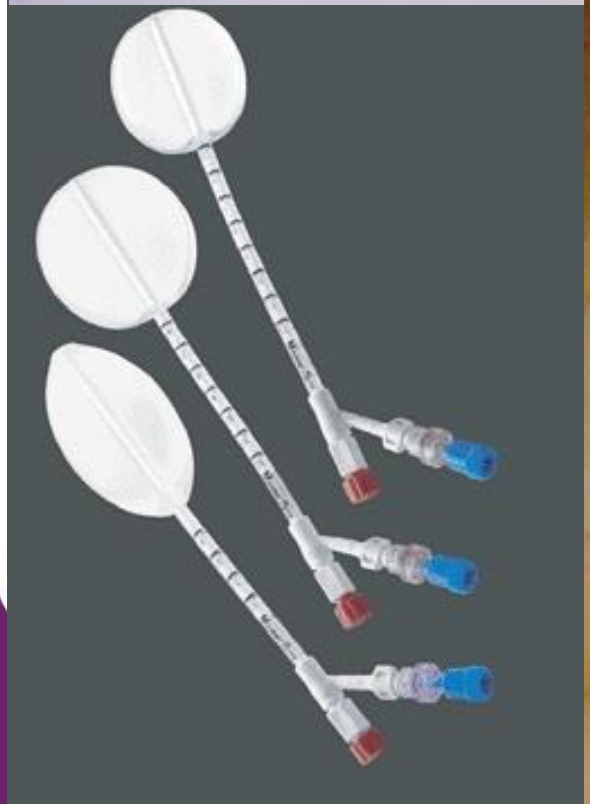
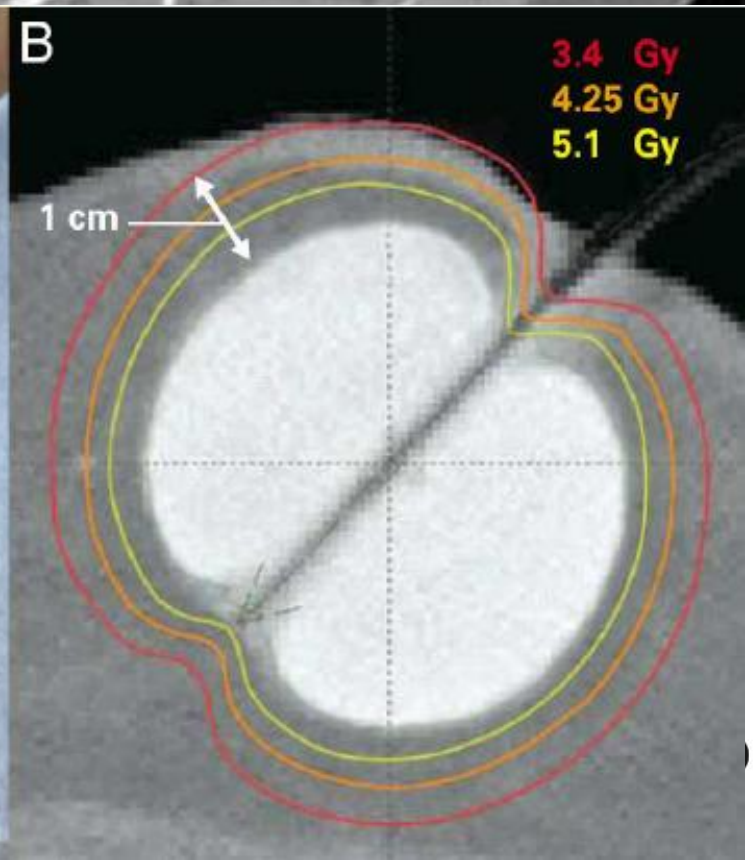
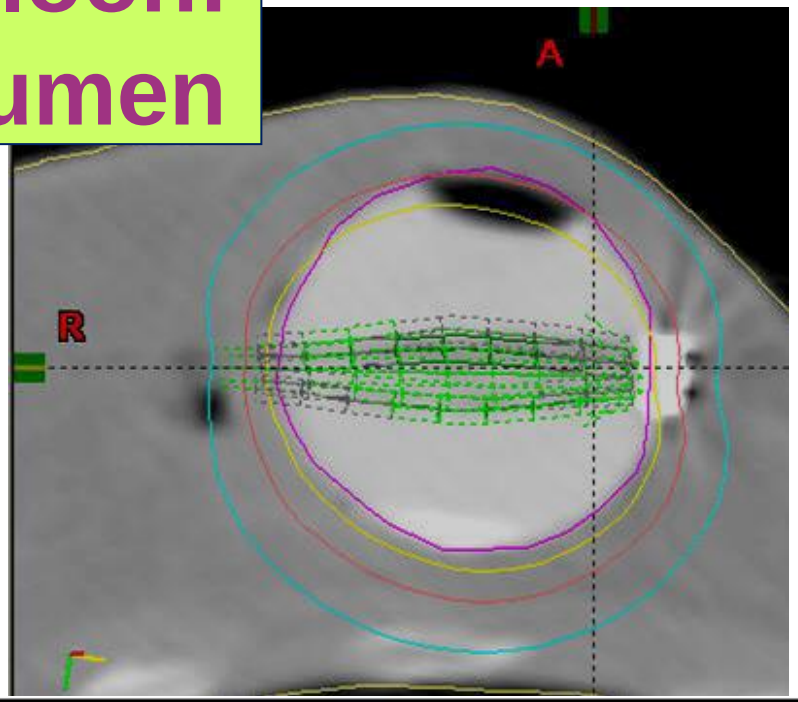
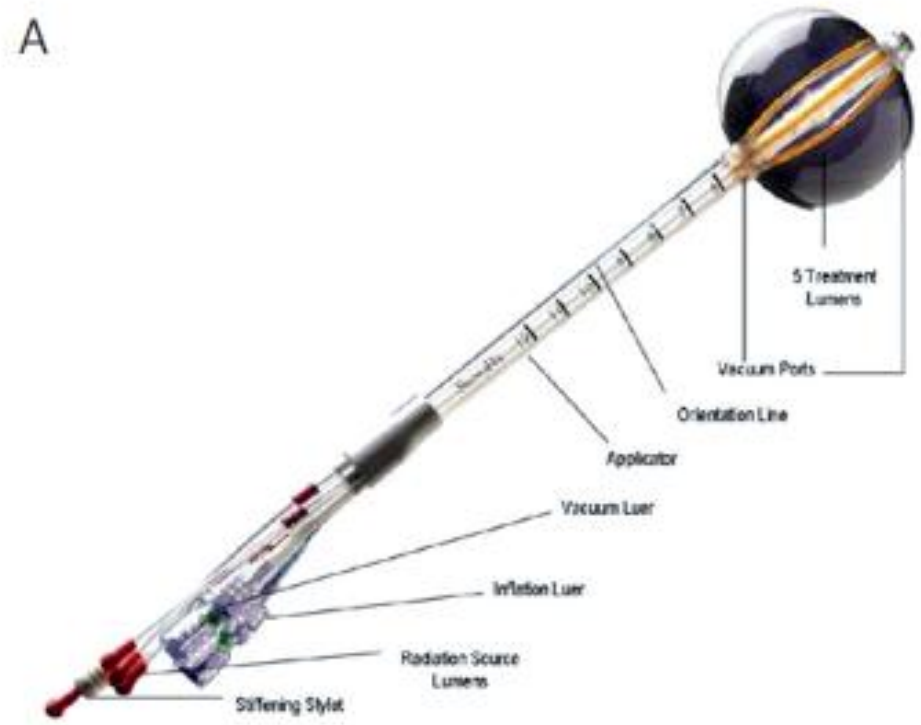
Intracavitary single-lumen catheter balloon: Mammosite





Intracavitary multilumen balloon: Contura; MammoSite multilumen





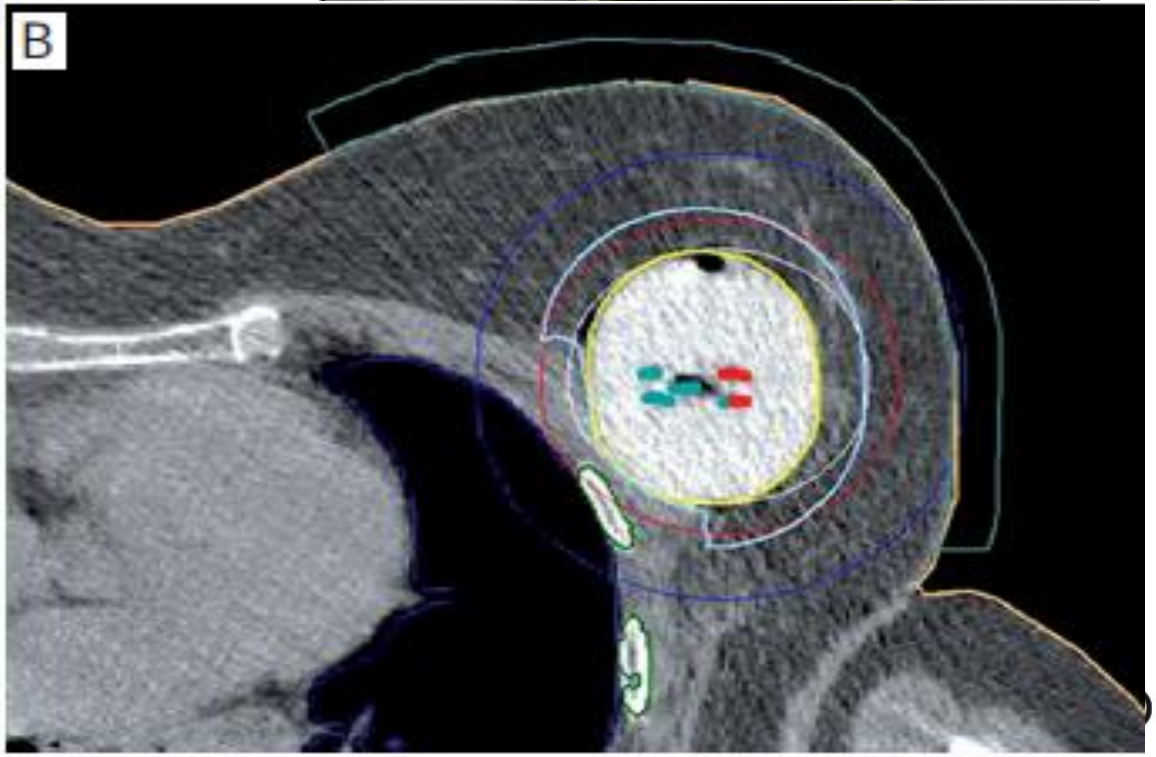
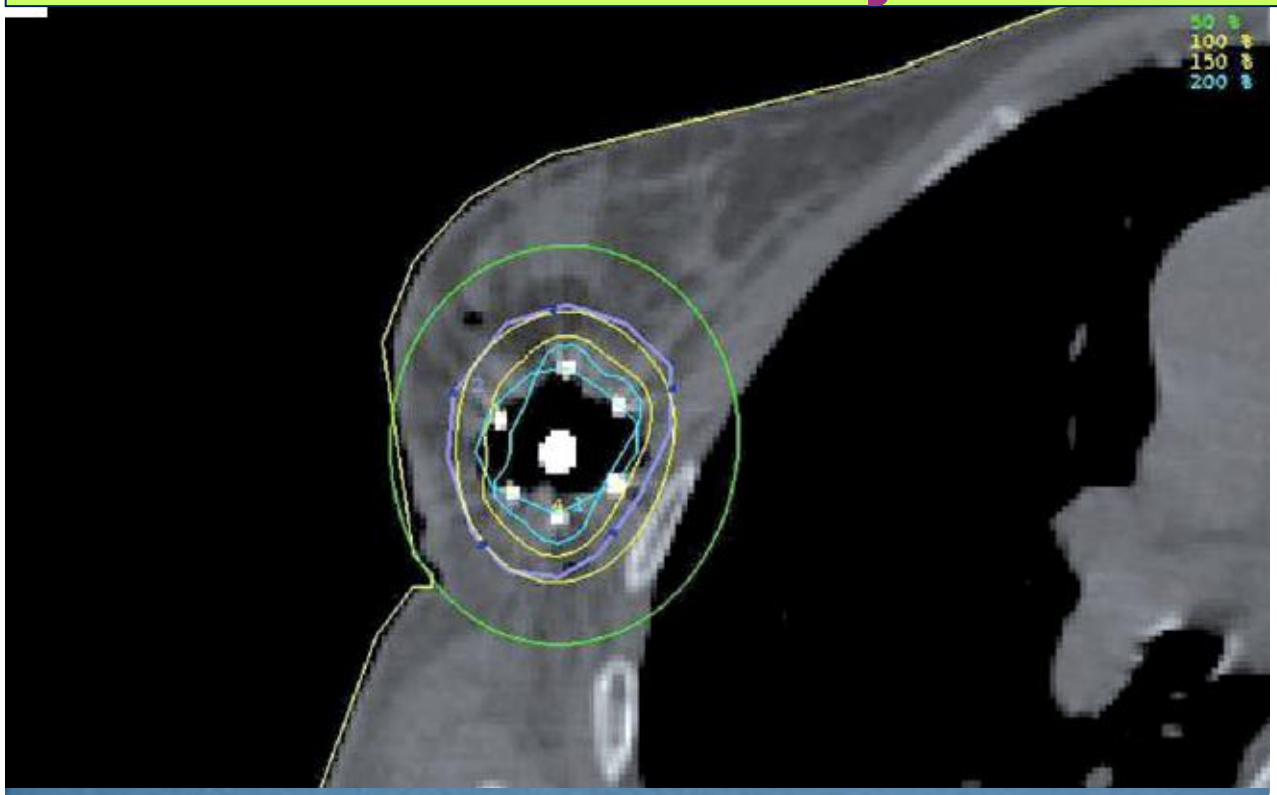
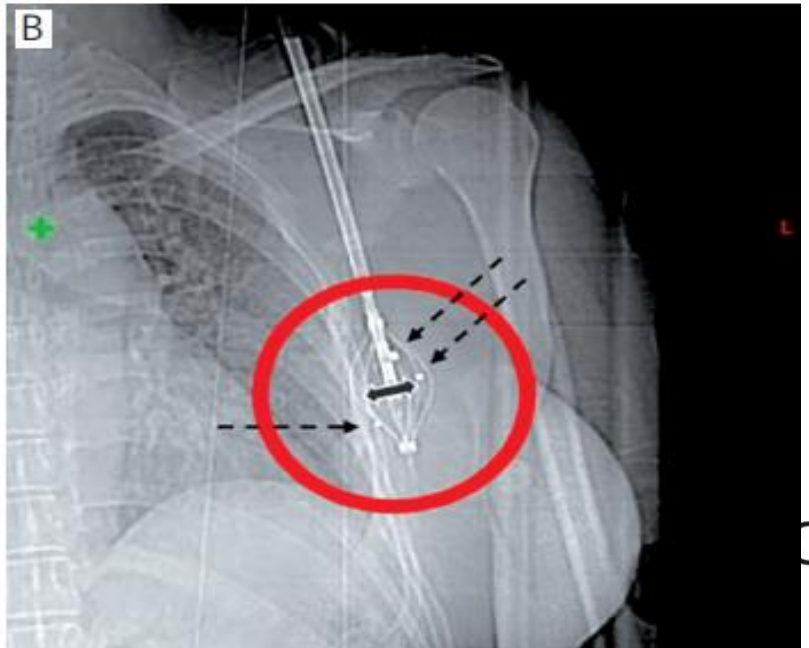


Fig. 7. A) Contura balloon applicator (SenoRx®) [30]. B) Con-

Intracavitary multilumen cage-like: Clear-Path SAVI Strut Adjusted Volume Implant





Results APBI with MammoSite

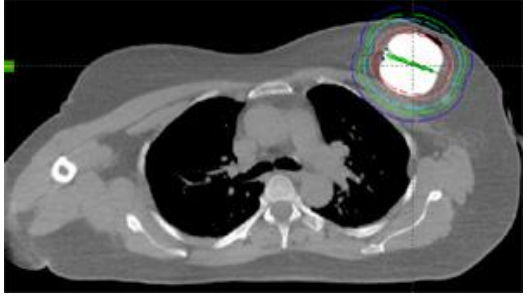
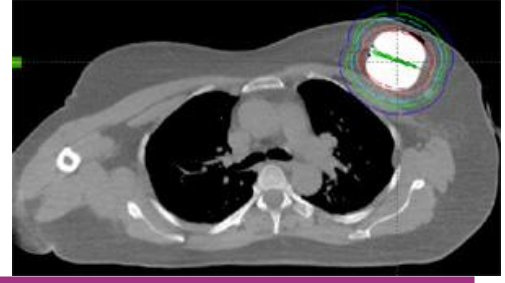


Table 8. Local recurrences after MammoSite [31]

Trial	No. of cases	Follow-up (months)	Local recurrences rate (%)
ASBS TRIAL [75]	1440	30	1.04
Tufts/Medical College Virginia/Rhode Island [71]	28	19	0
St. Vincent Cancer Center [66]	31	11	0
Rush University Medical Center [76]	70	26	5.7
Kaiser Permanente [49]	40	13	0
Medical University South Carolina [74]	90	24	2.2
ASBS DCIS TRIAL [77]	191	7	0
Wiliam Beaumont [68]	80	22	2.5
European TRIAL [73]	44	14	0
International TRIAL [78]	23	20	0
Western Pensylwania Hospital [79]	55	24	3.6
Oscar Lambret Center [69]	25	13	0

Short follow-up: 0-5,7% recurrences

Results APBI with MammoSite 2012



2127 patients (follow-up 5 years)

- ❖American Society of Breast Surgeons MammoSite Registry 1449
- ❖ 678 William Beaumont Hospital (Michigan): interstitial 221
  balloon 225
  3D-EBRT 206

No significant differences

ASTRO CONSENSUS	Suitable	Cautionary	Unsuitable
Patients	661	850	302
5-year local rec	2,5%	3,3%	4,6%

Wilkinson JB. Int J Radiat Oncol Biol Phys 2012 Nov

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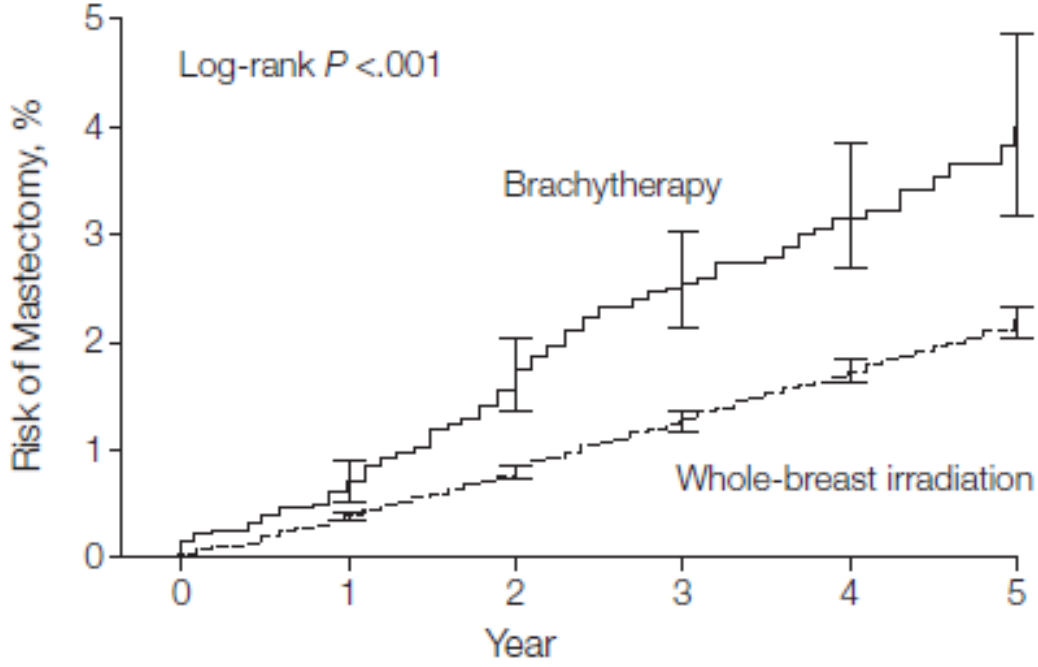
Results APBI with Mammosite vs WBI

Association Between Treatment With Brachytherapy vs Whole-Breast Irradiation and Subsequent Mastectomy, Complications, and Survival Among Older Women With Invasive Breast Cancer

2012

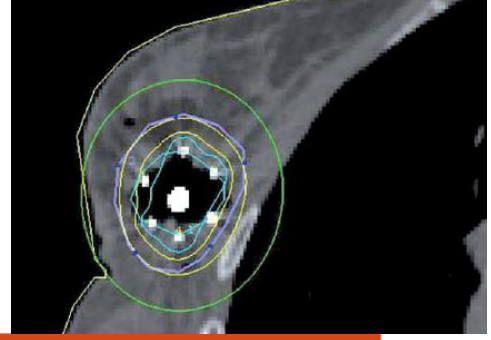
- **Retrospective study**
- **APBI Balloon technique vs WBI**
- **hazard ratio 2.2 of mastectomy**



No. of patients at risk						
Brachytherapy	6952	6746	4287	2419	1176	442
Whole-breast irradiation	85783	81651	62268	43704	26991	11735

Smith GI, Xu Y, Buchholz TA, et al. JAMA 2012;307:1827-37

Results APBI with SAVI 2013



	SAVI 4.5 yr ASTRO 2013 [1]	ASBS MammoSite Registry 5 yr Ann Surg Oncol 2013 [2]
# of Pts/Follow-up	101 pts/54 mo	1449 pts/63 mo
Telangiectasia	2.0%	Not reported
Seroma	2.0%	13.4%
Fat necrosis	0.0%	2.5%
Recurrence	2.0%	2.8%

[1] Yashar C, et al. Outcomes for APBI with Strut-based Brachytherapy: 101 Patients at 4.5 Years Median Follow Up. Poster presentation at the 55th Annual Meeting of the American Society for *Radiation Oncology, September 22–25, 2013.*

[2] Shah C, et al. Treatment Efficacy with Accelerated Partial Breast Irradiation (APBI): Final Analysis of the American Society of Breast Surgeons MammoSite(®) Breast Brachytherapy Registry Trial. *Ann Surg Oncol. 2013 Oct; 20(10): 3279-85.*

INTERSTITIAL MULTICATHETER BRACHYTHERAPY

Plastic tubes

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Results APBI with interstitial BT

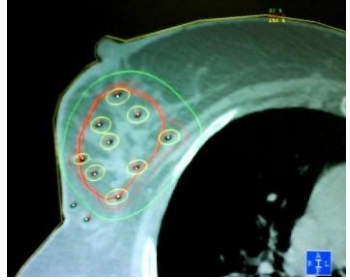

Table 6. Results of recent clinical experience with interstitial brachytherapy with more than 5 years follow-up [30]

Author	No of cases	Follow up interval (years)	Technique	Scheme	Total dose (Gy)	5-year LR (%)	Good/Excellent cosmesis
Strnad *et al.* [51]	274	5.25	PDR/HDR	PDR – 0.6 Gy/h HDR – 4 Gy × 8 fr.	PDR = 50 Gy HDR = 32 Gy	2.9%	90%
Antonucci *et al.* [52]	199	9.6	LDR/HDR	LDR – 0.52 Gy/h × 96 h HDR – 4 Gy × 8 fr. HDR – 3.4 Gy × 10 fr.	LDR = 50 Gy HDR = 32 Gy HDR = 34 Gy	5%	99%
Johansson *et al.* [53]	50	7.2	PDR	HDR – 50 Gy/5 d	50 Gy	4%	56%
Arthur *et al.* [54]	99	7	LDR/HDR	LDR – 3.5 Gy/5 d HDR – 3.4 Gy × 10 fr.	45 Gy (LDR) 34 Gy (HDR)	4%	n/a
Polgar *et al.* [55]	128	6.8	HDR	HDR – 5.2 Gy × 7 fr.	36.4 Gy	4.7%	77%
King *et al.* [56]	51	6.25	LDR/HDR	LDR – 4 d HDR – 4 Gy × 8 fr.	45 Gy (LDR) 32 Gy (HDR)	3.9%	75%
Otto *et al.* [57]	274	5.25	PDR/HDR	PDR – 5 d, 0.6 Gy/h HDR – 4 Gy × 8 fr.	49.8 Gy (PDR) 32 Gy (HDR)	2.9%	92%
Polgar *et al.* [58]	45	11.1	HDR	HDR – 4.33 Gy × 7 fr. HDR – 5.2 Gy × 7 fr.	30.3 Gy 36.4 Gy	4.4%	78%

LR – local recurrence; HDR – high dose rate; LDR – low dose rate; PDR – pulsed dose rate; n/a – data not available; h – hours, d – days; fr. – fractions

5-year follow-up : 2,9 - 5% recurrences. Good cosmesis.

Budapest phase III APBI 2007

National Institute of Oncology Budapest (1998-2004)

- 258 pat. T1 No-1_{mic} G1-2, no lobular, EIC-, margins-,
- FU 66m.
  - 130 WBI 50 Gy
  - 128 APBI
    - 88 BT HDR 36.4 Gy (5.2 Gyx7)
    - 40 electrons 50 Gy
- Cosmesis good/excellent **63% vs 77%** (p=0.009)

(**81% HDR vs 70% e-**)

Update at 7 years .

- **Local failures:** **3,3% vs 5,1%** (p=0,53)
- Regional failure: 1,7% vs 1,6% (p= 0,99)
- CSS 93,9% vs 96,2% (p=0,45)
- OS 89,4% vs 91,7% (p=0,44)

Same control, better cosmesis

Polgár C, Fodor J, Major T, Breast-conserving treatment with partial or whole breast irradiation for low-risk invasive breast carcinoma--5-year results of a randomized trial.Int J Radiat Oncol Biol Phys. **2007** Nov 1;69(3):694-702.

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12-year Matched-pair analysis

Matched pair analysis according to tumoral size, age, nodal status, hormonal receptors and treatment

12-year actuarial results	Interst. APBI	WBI	p
Number of patients	199	199	0,5
Breast failures	5%	3,8%	0,4
Failure in other quadrante	2%	1,9%	0,6
Local failure	3%	1,9%	0,2
Contralateral breast tumor	6%	8%	0,3
Regional failure	1,1%	0%	0,15
Metastasis	4,5%	10,1%	0,05
CSS	95%	93%	0,28
OS	71%	78%	0,06
Cosmesis good/excellent	99%	96%	0,1

WBH. William Beaumont Hospital. Michigan
Antonucci JV. Int J Radiat Oncol Biol Phys. 2009; 74(2):447-52.
Shah C. Radiother Oncol. 2011; 100:210-4

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What do we need to know?

GEC-ESTRO Breast Brachy Working Group

- WBI 50 Gy + e-10 Gy **(6 weeks)**
- interstitial multicatheter brachytherapy **(5 days)**
  - HDR 8 x 4 Gy (32 Gy) or 7 x 4.3 Gy (30.1 Gy)
  - PDR: 50 Gy 0.60 – 0.80 Gy/hora (1 pulse/hour, 24 hours/day)

Is APBI equivalent to Whole Breast Irradiation?

NSABP B-39/RTOG 0413 trial

- **WBI 50 Gy + 10-16 Gy (6-7weeks)**
- **BT interstitial multicatheter 3,4 Gy x 10 frac (5 days)**
- **BT intracavitary balloon 3,4 Gy x 10 frac (5 days)**
- **3D EBRT 3,85 Gy x 10 frac (2 weeks)**

Which is the optimal technique?

Not yet

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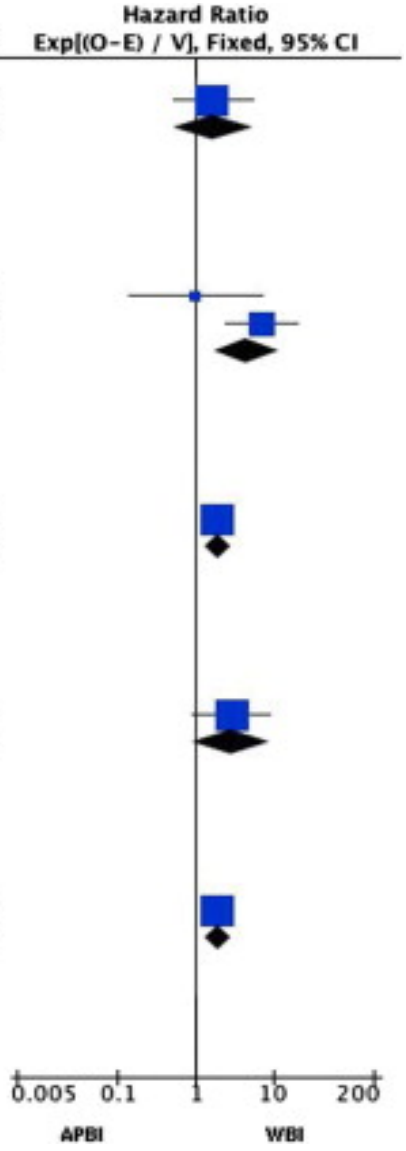
Meta-analysis of APBI

2015

Study or Subgroup	APBI Events	APBI Total	WBI Events	WBI Total	O−E	Variance	Weight	Hazard Ratio Exp[(O−E) / V], Fixed, 95% CI
1.1.1 Four years								
Vaidya 2010	6	1113	5	1119	1.365	2.727	100.0%	1.65 [0.50, 5.41]
Subtotal (95% CI)		**1113**		**1119**			**100.0%**	**1.65 [0.50, 5.41]**
Total events	6		5					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.83 (P = 0.41)								
1.1.2 Five years								
Rodriguez 2013	0	51	0	51	0	1	22.9%	1.00 [0.14, 7.10]
Veronesi 2013	21	651	4	654	6.598	3.36	77.1%	7.13 [2.45, 20.76]
Subtotal (95% CI)		**702**		**705**			**100.0%**	**4.54 [1.78, 11.61]**
Total events	21		4					
Heterogeneity: Chi^2 = 2.97, df = 1 (P = 0.08); I^2 = 66%								
Test for overall effect: Z = 3.16 (P = 0.002)								
1.1.3 Seven years								
Ribeiro 1993	69	353	39	355	16.672	24.916	100.0%	1.95 [1.32, 2.89]
Subtotal (95% CI)		**353**		**355**			**100.0%**	**1.95 [1.32, 2.89]**
Total events	69		39					
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.34 (P = 0.0008)								
1.1.4 Eight years								
Dodwell 2005	10	84	4	90	3.03	2.857	100.0%	2.89 [0.91, 9.21]
Subtotal (95% CI)		**84**		**90**			**100.0%**	**2.89 [0.91, 9.21]**
Total events	10		4					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.79 (P = 0.07)								
1.1.5 Ten years								
Polgar 2013	69	353	39	355	16.672	24.916	100.0%	1.95 [1.32, 2.89]
Subtotal (95% CI)		**353**		**355**			**100.0%**	**1.95 [1.32, 2.89]**
Total events	69		39					
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.34 (P = 0.0008)								



TARGIT

ELIOT

EBRT1993

Variety of techniques

EB / HDR

The technique is important for APBI

APBI is associated with higher local recurrence compared to WBI

Marta GN. Accelerated partial irradiation for breast cancer: Systematic review and meta-analysis of 8653 women in eight randomized trials. Radiat oncol 2015;114:42-49

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Interstitial multicatheter APBI Phase III GEC-ESTRO

2016

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

Vratislav Strnad, Oliver J Ott, Guido Hildebrandt, Daniela Kauer-Dorner, Hellen Knauerhase, Tibor Major, Jaroslaw Lyczek, Jose Luis Guinot, Jürgen Dunst, Cristina Gutierrez Miguelez, Pavel Slampa, Michael Allgäuer, Kristina Lössl, Bülent Polat, György Kovács, Arnt-René Fischedick, Thomas G Wendt, Rainer Fietkau, Marion Hindemith, Alexandra Resch, Anna Kulik, Leo Arribas, Peter Niehoff, Fernando Guedea, Annika Schlamann, Richard Pötter, Christine Gall, Martina Malzer, Wolfgang Uter, Csaba Polgár, on behalf of the Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO)

April 2004- July 2009 1184 low-risk patients

- **551 WBI 50Gy + boost 10Gy**
- **633 APBI interstitial multicatheter brachytherapy**

87% hormonal treatment, 11% chemotherapy

Strnad V et al.Lancet. 2016 Jan 16;387(10015):229-38

	APBI group (n=633)	WBI group (n=551)
Age (years)		
Median (IQR)	62 (54–67)	62 (54–68)
>40–50	91 (14%)	91 (17%)
>50–60	192 (30%)	162 (29%)
>60–70	256 (40%)	202 (37%)
>70	94 (15%)	96 (17%)
Menopausal status		
Premenopausal	108 (17%)	92 (17%)
Postmenopausal	525 (83%)	459 (83%)
Performance status		
0	604 (95%)	520 (94%)
1–2	26 (4%)	30 (5%)
Unknown	3 (<1%)	1 (<1%)
Tumour size and resection margins		
Tumour diameter (mm)	12 (9–17)	12 (9–17)
Surgical free margins (mm, range)	8 (2–40)	7 (2–25)
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%)
N stage		
pN0	127 (20%)	118 (21%)
pN0 sn	470 (74%)	408 (74%)
pN1 mi	5 (1%)	5 (1%)
No data	31 (5%)	20 (4%)
Grading		
1	248 (39%)	217 (39%)
2	319 (50%)	288 (52%)
3	57 (9%)	42 (8%)
No data	9 (1%)	4 (1%)

	APBI group (n=633)	WBI group (n=551)
Histological subtype		
Ductal	453 (72%)	424 (77%)
Lobular	85 (13%)	49 (9%)
Tubular	38 (6%)	36 (7%)
Mucinous	14 (2%)	13 (2%)
Papillary	5 (1%)	4 (1%)
Medullary	2 (<1%)	1 (<1%)
Unknown	36 (6%)	24 (4%)
Hormone receptor status		
ER+/PR+	510 (81%)	447 (81%)
ER−/PR+	5 (1%)	6 (1%)
ER+/PR−	69 (11%)	56 (10%)
ER−/PR−	34 (5%)	29 (5%)
Unknown	15 (2%)	13 (2%)
Systemic treatment		
Yes	572 (90%)	505 (92%)
No	59 (9%)	46 (8%)
No data	2 (<1%)	0
Antihormonal treatment		
Yes	549 (87%)	482 (87%)
No	82 (13%)	69 (13%)
No data	2 (<1%)	0
Chemotherapy		
Yes	63 (10%)	65 (12%)
No	568 (90%)	486 (88%)
No data	2 (<1%)	0

Similar characteristics in both groups

Local recurrence

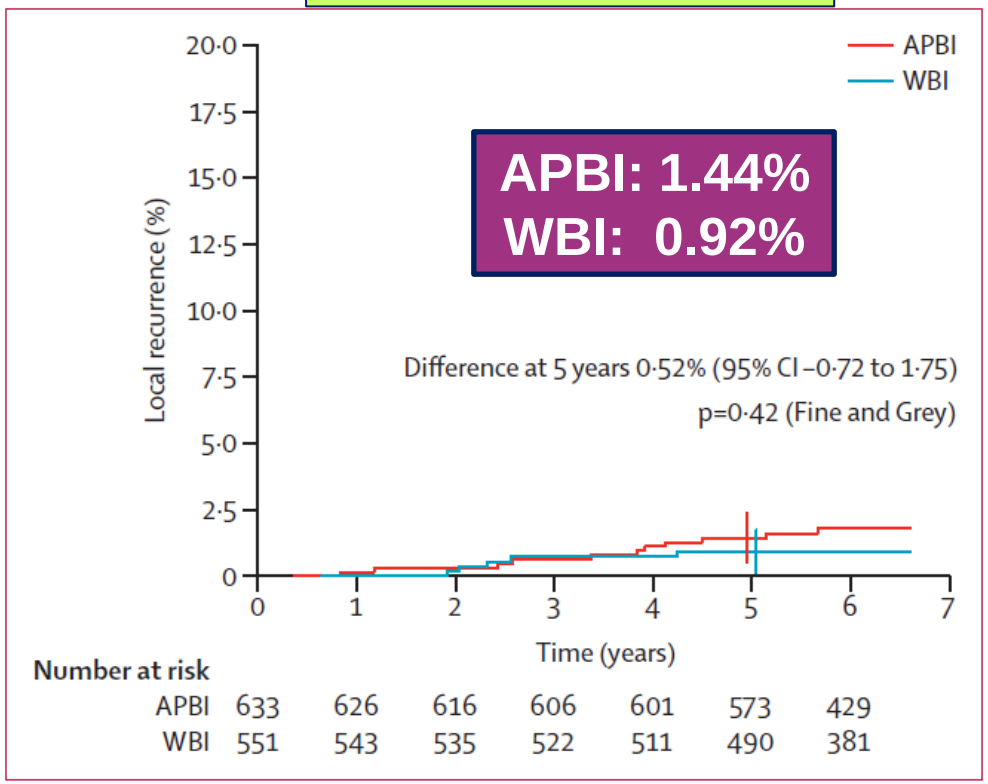


Figure 2: Ipsilateral breast tumour recurrence
APBI=accelerated partial breast irradiation. WBI=whole-breast irradiation.

Overall survival

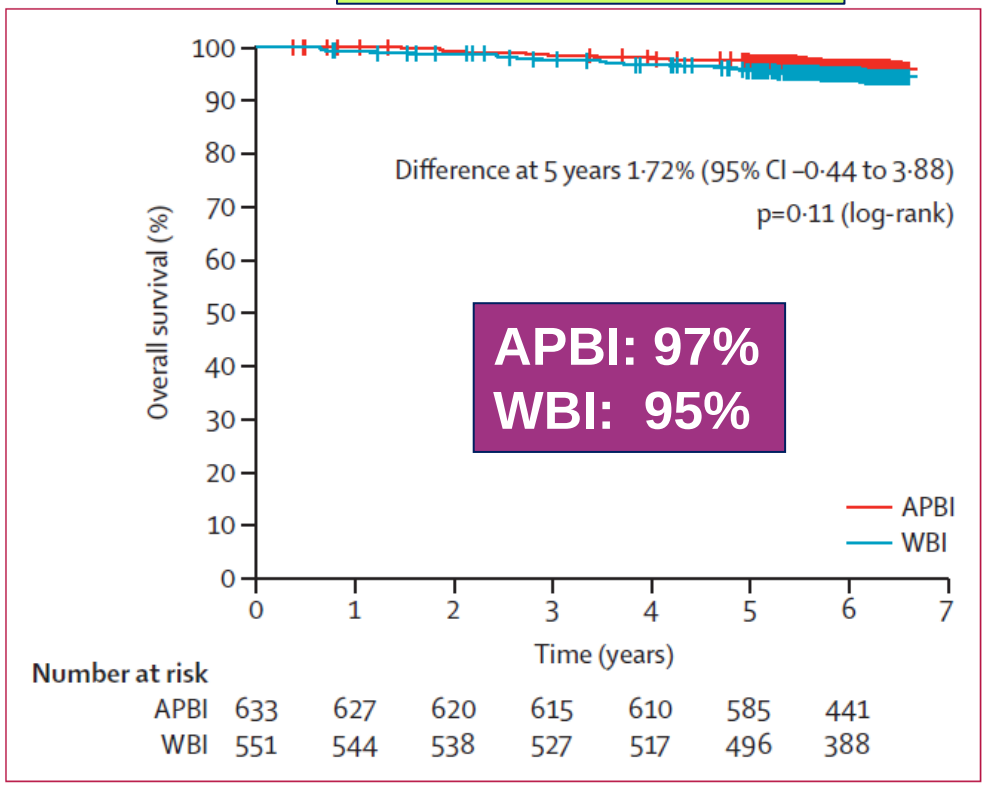


Figure 4: Overall survival
APBI=accelerated partial breast irradiation. WBI=whole-breast irradiation.

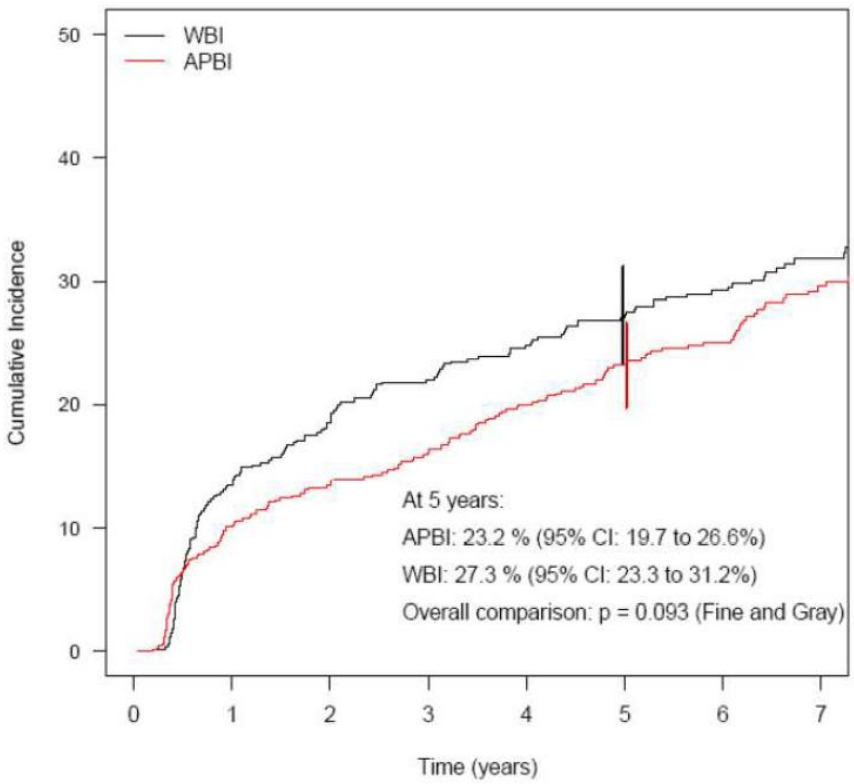
	APBI	WBI
No grade 4 late side-effects.		
5-year risk G2-3 late side-effects to the skin:	3.2%	5.7% (p=0.08)
5-year risk of G2–3 late subcutaneous tissue :	7.6%	6.3% (p=0.53)
Severe (G3) fibrosis at 5 years:	0	0.2% (p=0.46)

APBI using multicatheter brachytherapy can be regarded as a valid alternative treatment option after breast-conserving surgery and can be offered for all low-risk breast cancer patients in clinical routine.

Strnad V et al.Lancet. 2016 Jan 16;387(10015):229-38

School

Figure 3: **First occurrence of any late side-effects grade ≥ 2**



LATE SIDE EFFECTS

Polgár C, Ott OJ, Hildebrandt G et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. Lancet Oncol. 2017 Feb;18(2):259-268

Figure 4: **First occurrence of late skin toxicity grade ≥ 2**

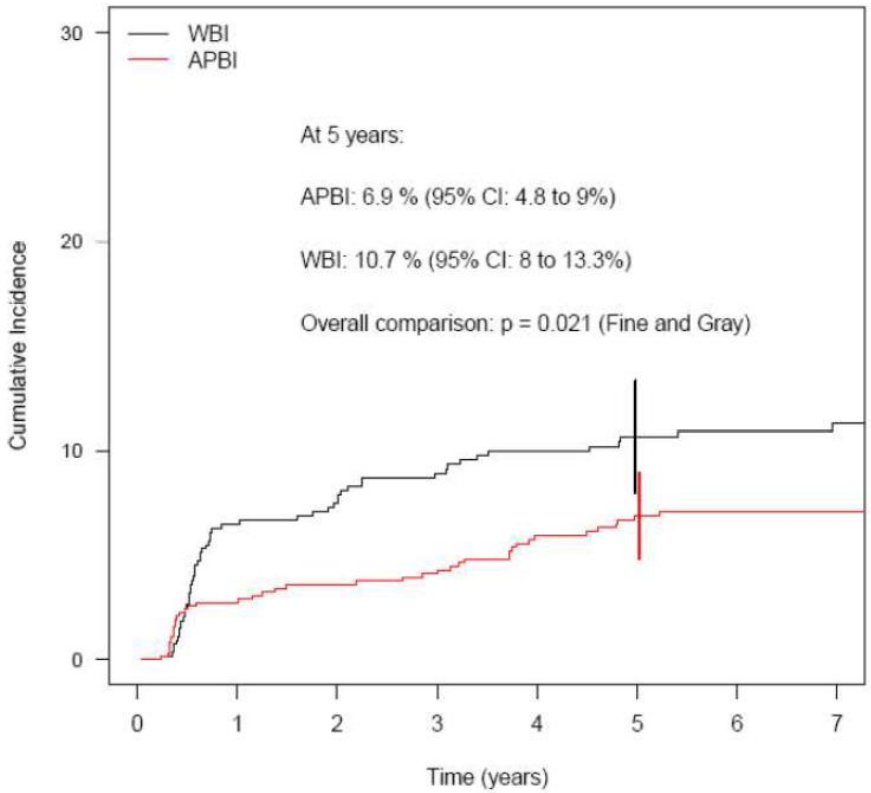
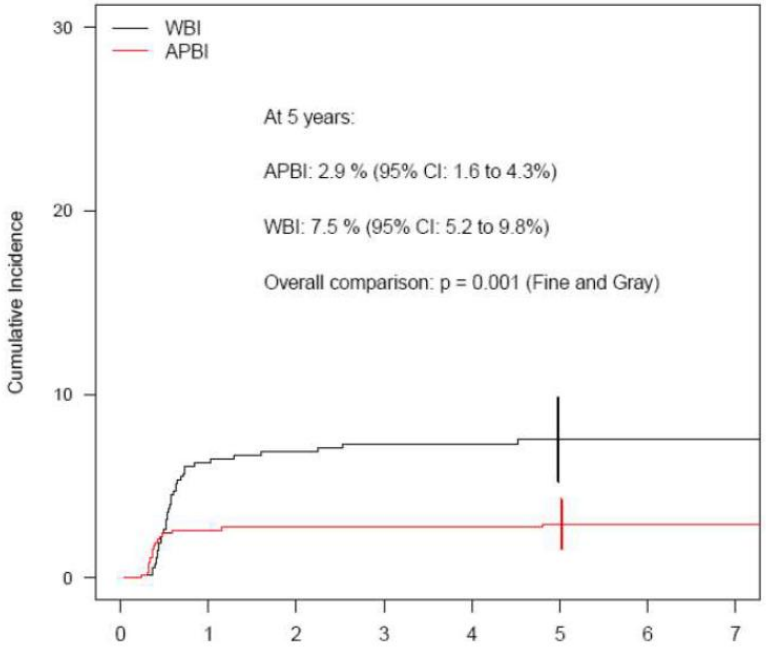


Figure 5: **First occurrence of late skin hyper-pigmentation grade ≥ 2**



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APBI: A NEW PARADIGM

633 cases treated in the APBI arm:

- 41-50 y.o. : 91
- Invasive lobular ca: 85
- pT2 <3cm: 67
- Grade 3: 57
- Pure low risk DCIS: 36
- Hormonal receptors -: 34
- pN1 mic: 5

APBI using multicatheter brachytherapy SHOULD be offered for all low-risk breast cancer patients with

- Invasive ductal carcinoma
- Age over 50
- pT1 and pT2 <3cm
- Hormonal receptors +
- pN0

This is a new paradigm: Low-risk cases do not need WBI (and we should avoid to radiate unnecessary tissue and OAR)

Strnad V et al.Lancet. 2016 Jan 16;387(10015):229-38

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LIMITATIONS TO DEFINE CTV

SURGICAL BED IS NOT EQUAL TO TUMOUR BED

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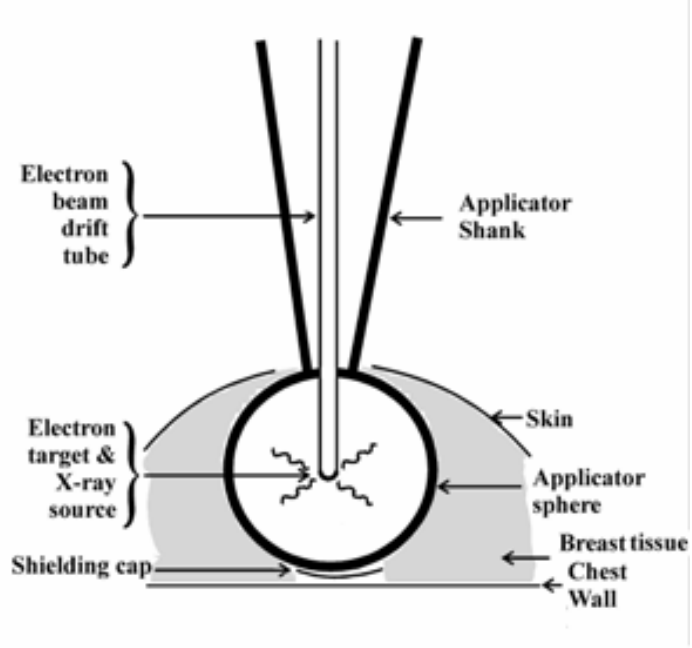
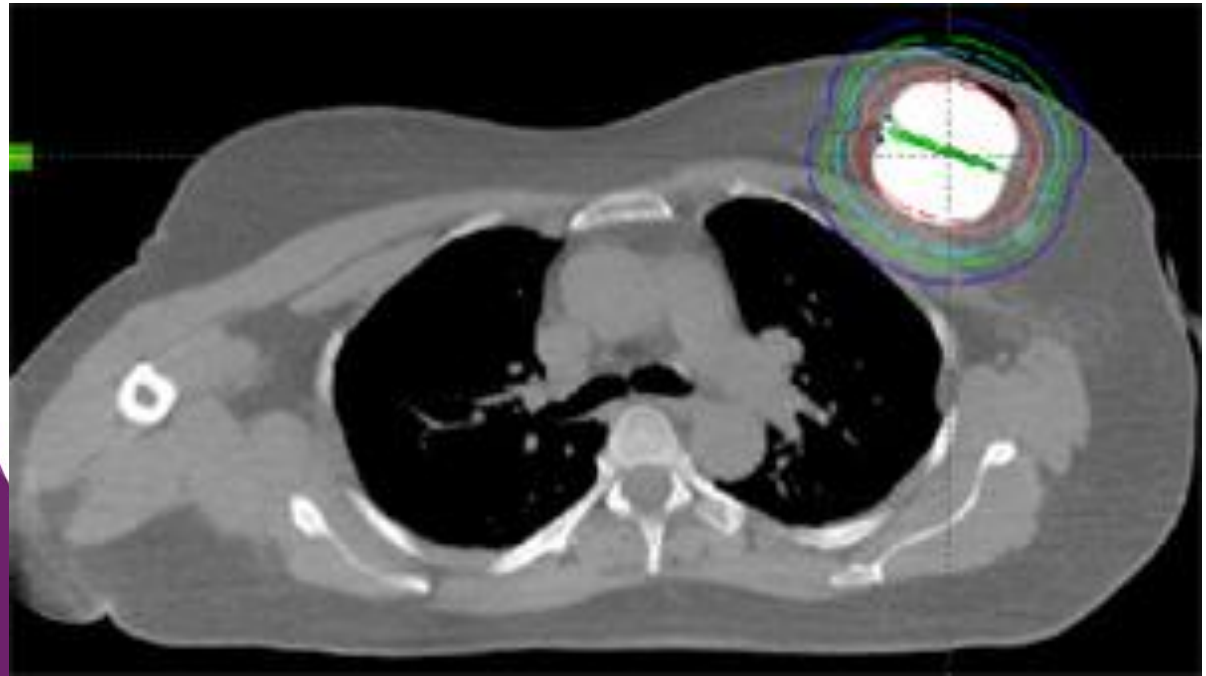
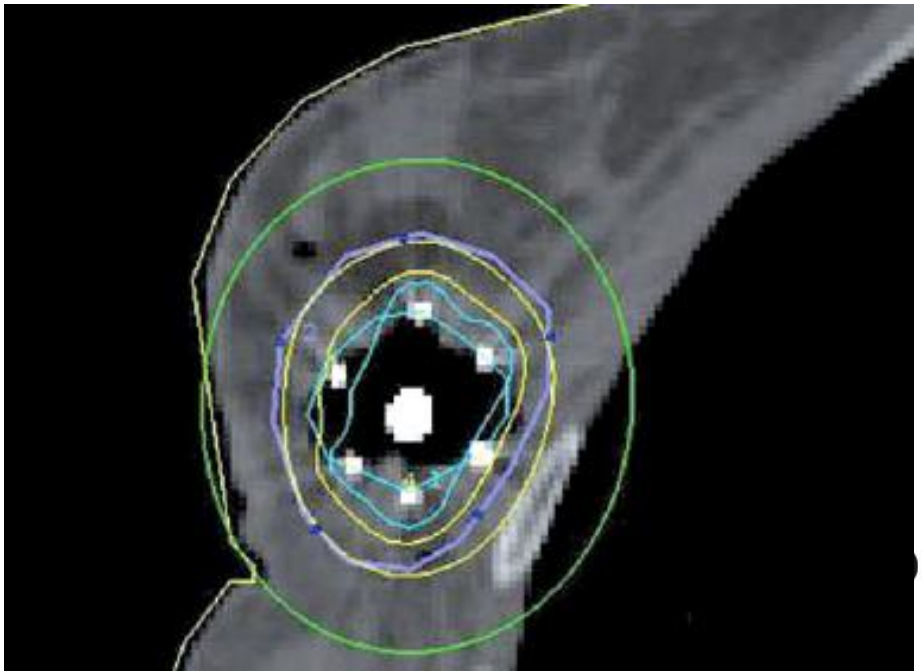
Limitations of endocavitary radiation

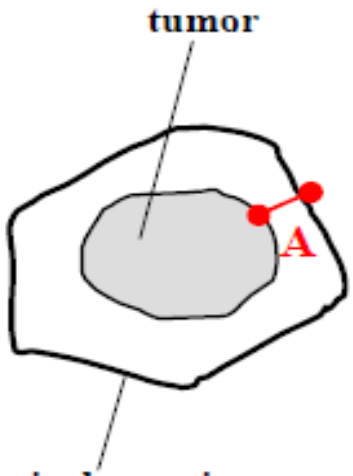
- Radiation is only given to the cavity
- No margin can be added
- The cavity is modified by the surgeon to create an sphere
- Skin and chest wall can receive a high dose
- Moreover, intraoperative irradiation misses information about margins





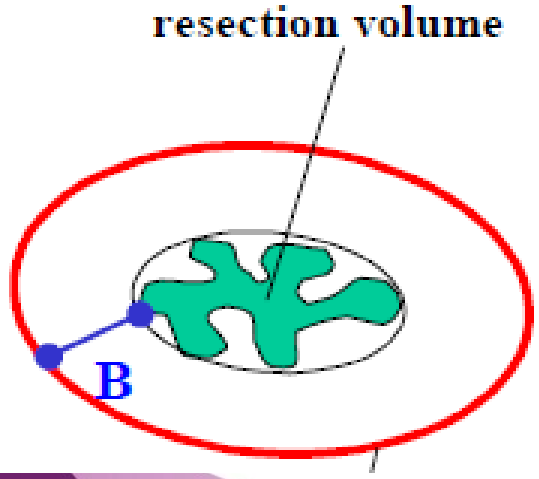


Definition of CTV and missed CTV



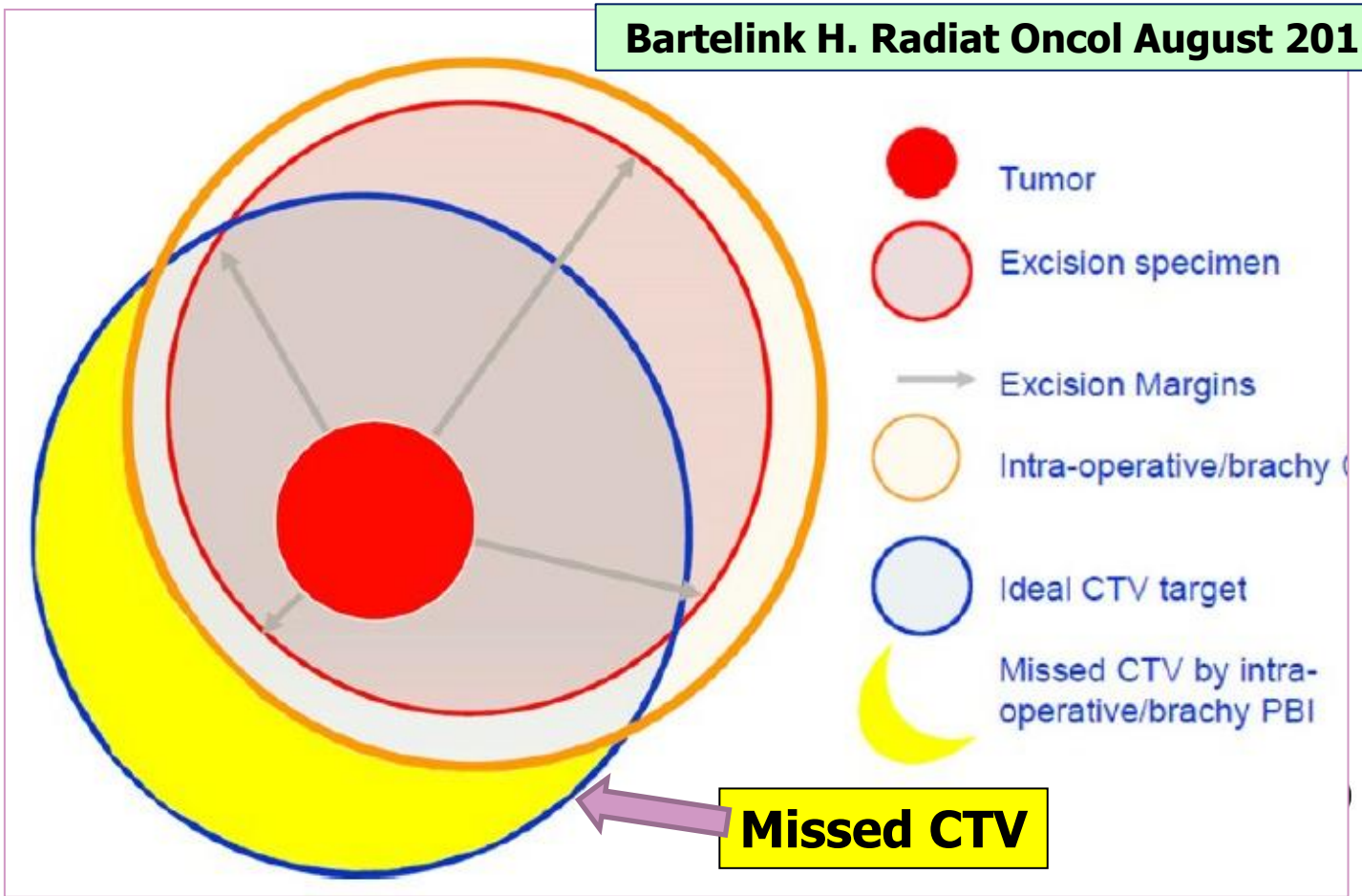
A = minimal resection margin
B = safety margin

B = >20 mm minus A



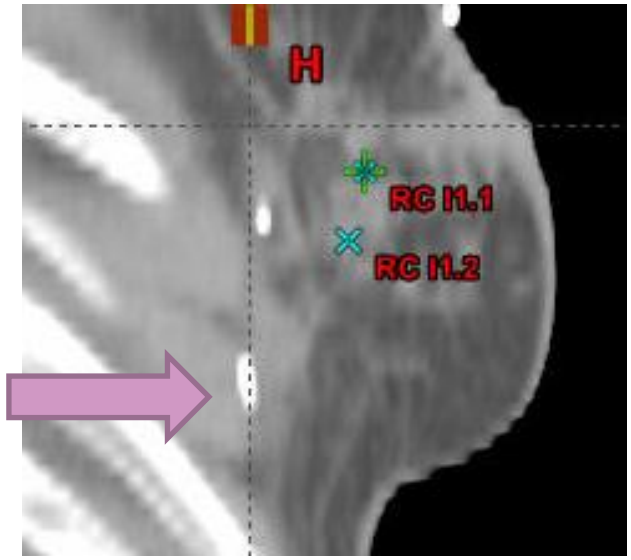
- **CTV requires 15-20mm free from the tumour border.**
- **The ideal situation is a tumour in the centre of the lumpectomy but that does not usually happen.**
- **A safety margin is required, not only to the cavity, but adding surgical margins and clinical assessment.**
- **The cavity is <u>a reference</u> to draw the CTV, <u>not the CTV</u>.**

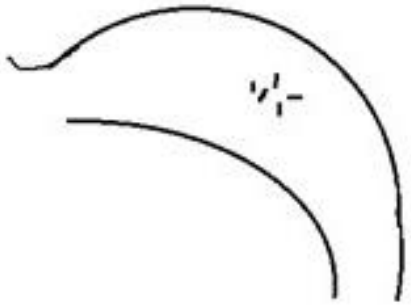
Bartelink H. Radiat Oncol August 2012



Limitations of CLIPS

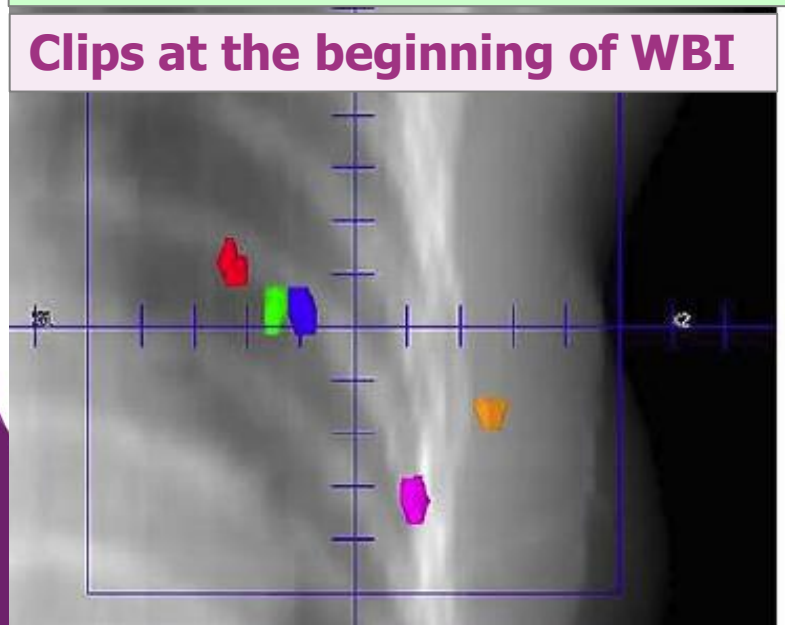
- Clips are useful to know where the surgeon arrived, but they have no a clear correlation with the tumour margins
- There are "irrelevant clips"
- Displacement of the clips along time



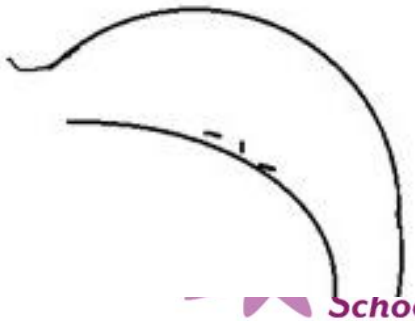


Decrease in tumor bed volume as defined by clips. Hepel JT et al

Clips at the beginning of WBI



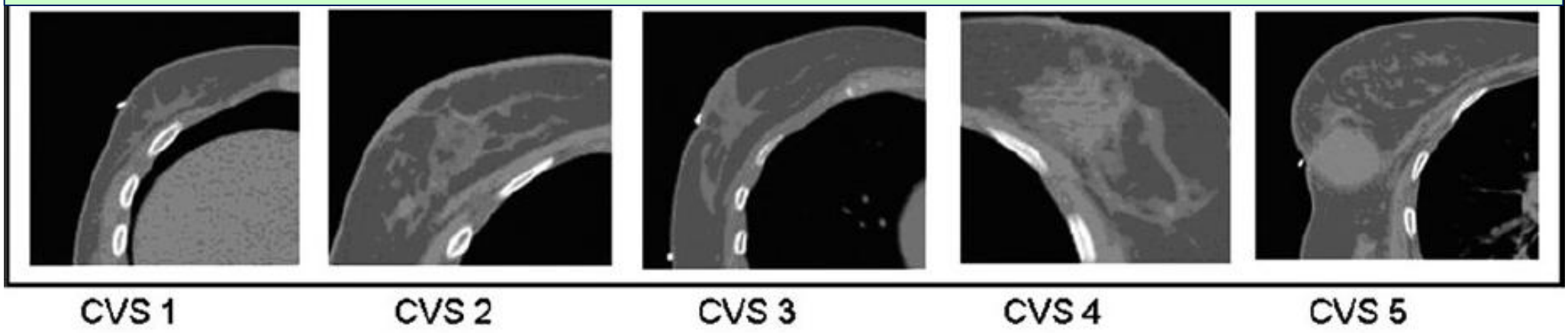
Clips after WBI, for the boost

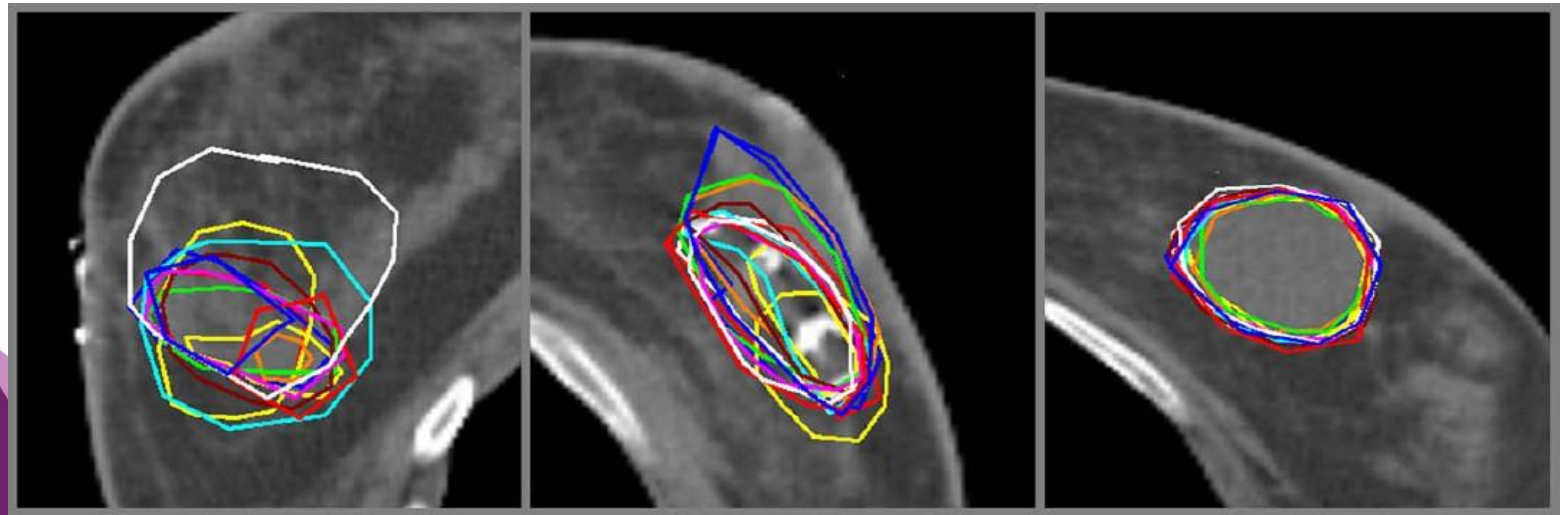


Limitations of CT images

- The main problem is to use an image technique (CT) to look for a tumour bed to be irradiated, <u>when no GTV can be seen</u>
- There will always be differences between observers!!!
- <u>Surgical scar</u> is useful but what we see is only the manipulated area, not the tumour bed !!!!!

CAVITY VISUALIZATION SCORE (CVS) Landis et al. IJRadiat Oncol Biol Phys 2007. 67:5





Van Mourik AM et al. Multiinstitutional study on target volume delineation variation in breast radiotherapy in the presence of guidelines. Radiother Oncol 2010; 94:286–291

DEFINITION OF CTV 2016

Guidelines for target definition after breast conserving open cavity surgery

Radiotherapy and Oncology 118 (2016) 199–204

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

GEC ESTRO breast cancer recommendations

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

Tibor Major [a,*], Cristina Gutiérrez [b], Benjamin Guix [c], Erik van Limbergen [d], Vratislav Strnad [e], Csaba Polgár [a], On behalf of Breast Cancer Working Group of GEC-ESTRO

[a] *Radiotherapy Centre, National Institute of Oncology, Budapest, Hungary;* [b] *Department of Radiation Oncology, Catalan Institute of Oncology;* [c] *Radiation Oncology, Institute IMOR, Barcelona, Spain;* [d] *Department of Radiotherapy, University Hospital Gasthuisberg, Leuven, Belgium; and* [e] *Department of Radiation Oncology, University Hospital Erlangen, Germany*

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GEC-ESTRO Recommendations for APBI PTV Definition After Open Cavity Surgery

1. Cavity visualization score ≥3 to minimize the interobserver variations.
2. Delineate only the homogeneous part of the postoperative seroma; exclude protrusions or sharp irregularities.
3. Surgical clips have to be surrounded by the contour with close contact (no margin)
4. CTV is created from the outlined surgical cavity with a safety margin taking into account the size of the free resection margin.
5. The total size of safety margin is always 20 mm which is the sum of the surgical and added safety margins.
6. CTV is limited to chest wall/pectoral muscles and 5 mm below the skin surface.

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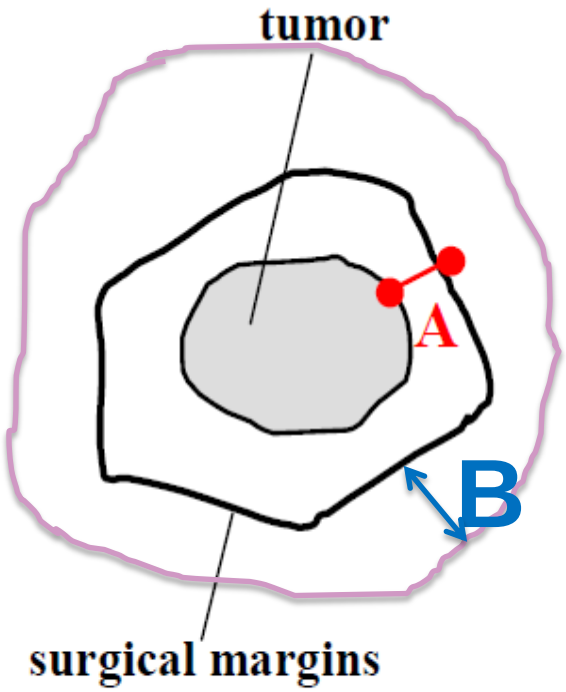
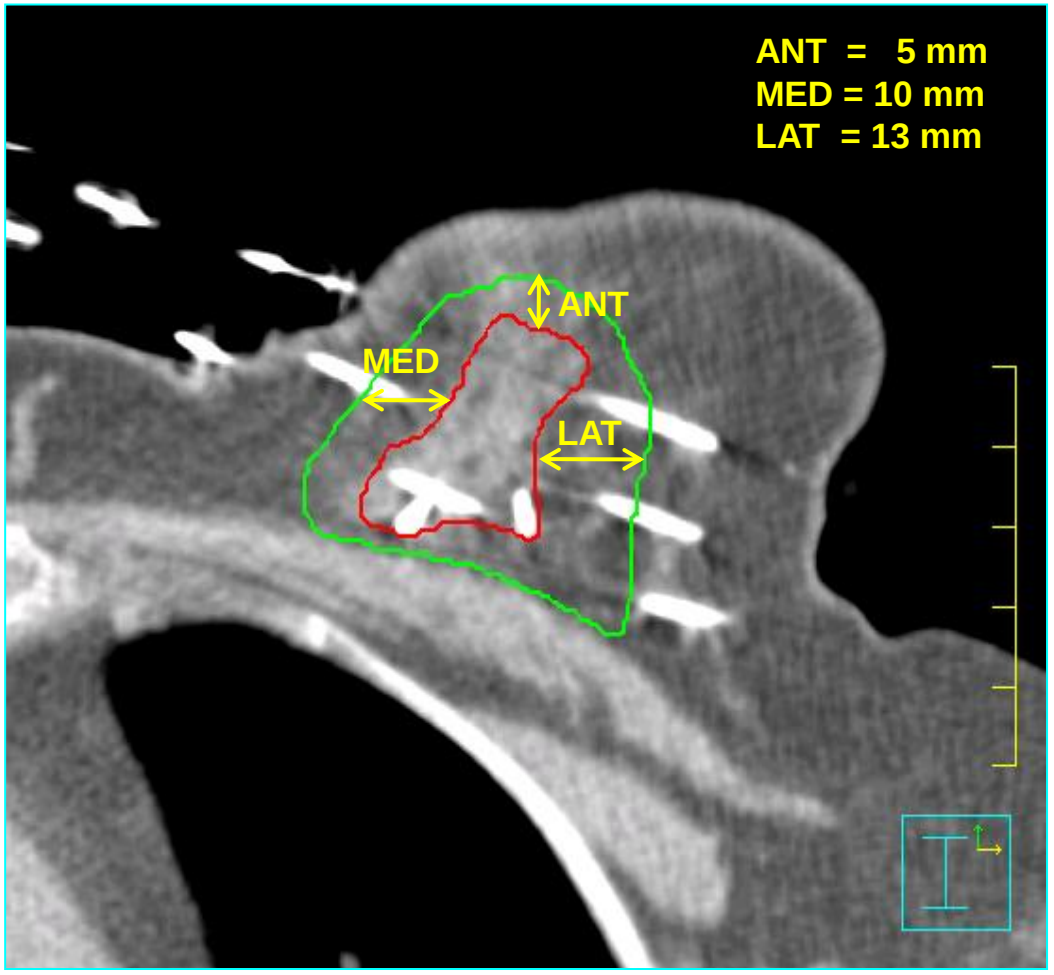
GEC-ESTRO Recommendations for APBI PTV Definition After Open Cavity Surgery



A = minimal resection margin

B = radiation margin

B = 20 mm - A



CTV (=PTV) definition from the cavity

Csaba Polgár & Tibor Major. National Institute of Oncology, Budapest, Hungary

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DEFINITION OF CTV 2015

Guidelines for target delineation after breast conserving closed cavity surgery

Radiotherapy and Oncology 115 (2015) 342–348

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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

[a] *Department of Radiation Oncology, University Hospital Erlangen, Germany;* [b] *Department of Radiation Oncology, Centre Antoine Lacassagne, Nice, France;* [c] *Department of Radiation Oncology, Fundación Instituto Valenciano de Oncología, Valencia, Spain;* [d] *Department of Radiation Oncology, Inselspital, University of Bern, Switzerland;* [e] *Department of Radiotherapy and Radiobiology, University Hospital Vienna, Austria;* [f] *Interdisciplinary Brachytherapy Unit, University of Lübeck, Germany;* [g] *Department of Radiation Oncology, National Institute of Oncology, Budapest, Hungary; and* [h] *Department of Radiotherapy, University Hospital Gasthuisberg, Leuven, Belgium*

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GEC-ESTRO Recommendations for APBI PTV Definition After Closed Cavity Surgery

Seven steps for target delineation after closed cavity surgery:

1. CT with radiopaque markers in the **skin scar** and **areola**
2. Delineation of **clips** (relevant and irrelevant)
3. Delineation of surgical bed – **whole surgical scar (WS)** inside breast if visible.
4. Delineation of **ImTV (Imaging correlated Target Volume)** regarding distance from skin and chest.
5. Delineation of **ETB (Estimated Tumour Bed)**
6. Delineation of **CTV** (Clinical Target Volume) ETB+ margin, excluding 5-10mm from skin and chest wall. CTV must include relevant clips, relevant WS, and ImTV.

7. Delineation of **PTV** (Planning Target Volume) if needed in big breasts or bad defined ETB

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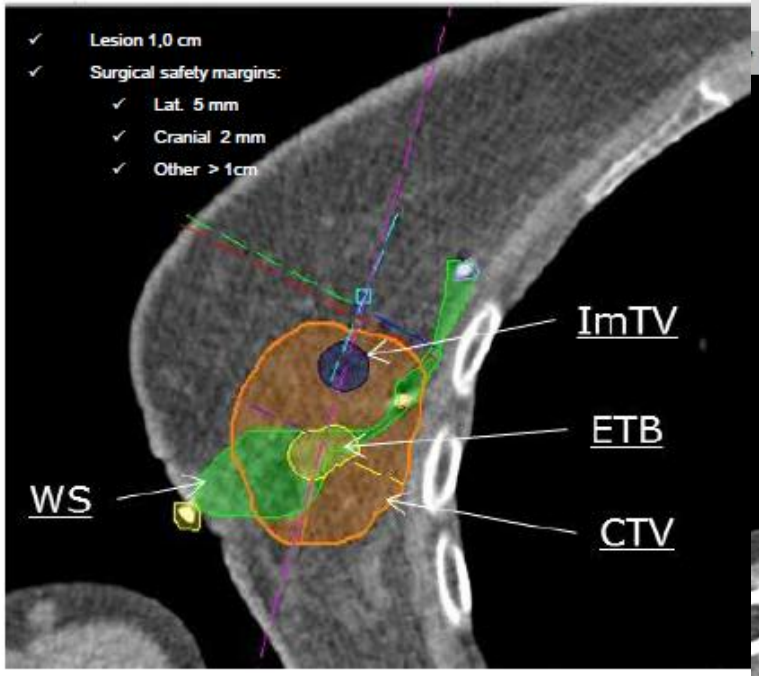
Guidelines for target delineation after breast conserving closed cavity surgery

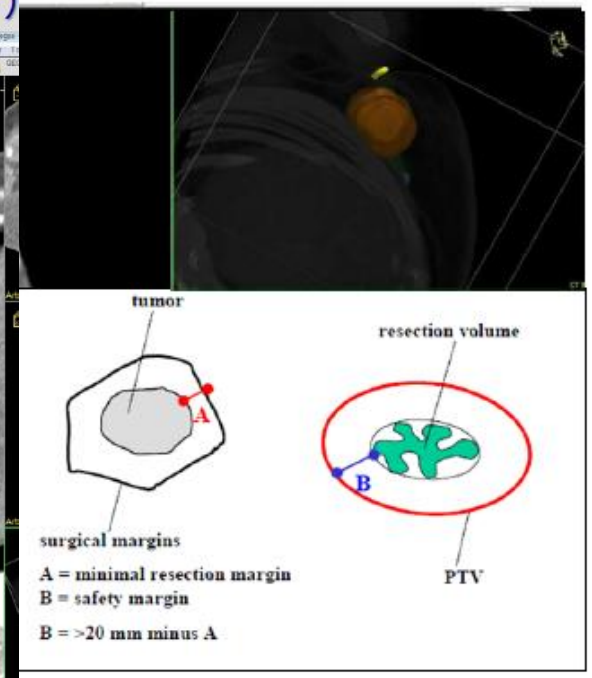
5. Definition and delineation of **CTV (Clinical Target Volume)**

ETB: Estimated tumour bed

- ✓ **CTV = ETB plus adapted safety margins**: 20 mm minus surgical margin, but at least 10 mm (a surgical margin of 3 mm requires a safety margin of 17mm).
- ✓ Thoracic wall and skin (thickness 5 mm) are not the part of CTV.



PTV(Brachy) vs. PTV(EBRT)



CTV <50 cc only in small breasts
CTV >200 cc not recommended

Clip 2	CT ...	0.08
Clip 3	CT ...	0.19
Clip 4	CT ...	0.19
CTV	CT ...	35.50
ETB	CT ...	1.41
ImTV	CT ...	1.22
PTV (EBRT)	CT ...	197.47
PTV_Brachytherapy	CT ...	58.99

For EBRT APBI PTV margin increases 3-4 fold the volume

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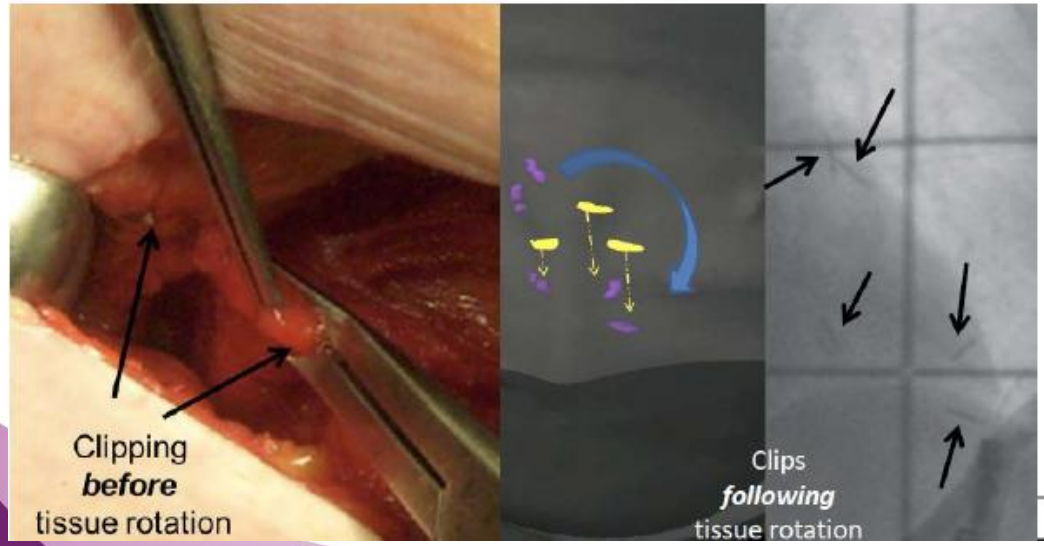
GEC-ESTRO Recommendations for APBI PTV Definition After Oncoplastic Surgery

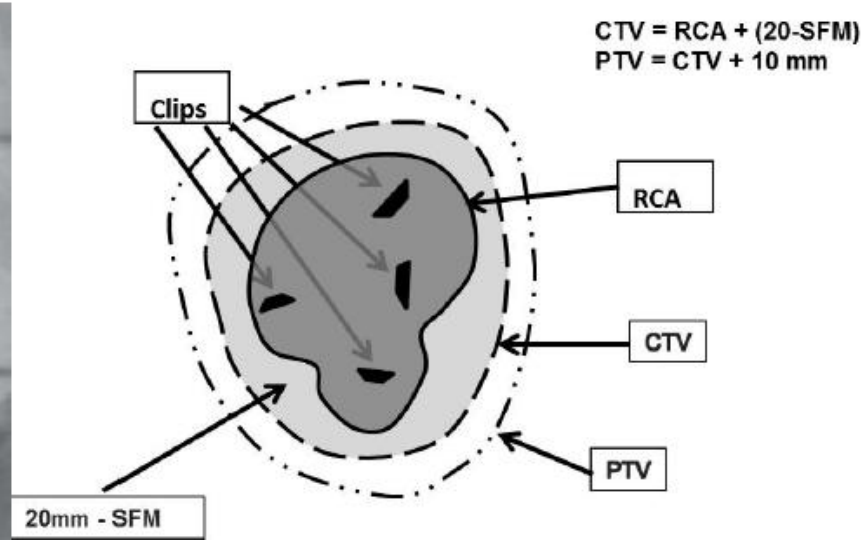
Guidelines

Special case of closed cavity – ONCOPLASTIC SURGERY

1. **CTV** is defined as the **sum of the relevant clipped area (RCA) and the distance of 20 mm** minus the smallest surgical free margin (SFM) defined by the pathologist (CTV= RCA + (20- SFM).

2. **PTV is defined as the CTV + 10 mm.**
   The additional distance of 10 mm resulting from the interobserver delineation variability is not influenced by setting clip markers.





TRO ool

PROCEDURE OF POSTOPERATIVE BRACHYTHERAPY

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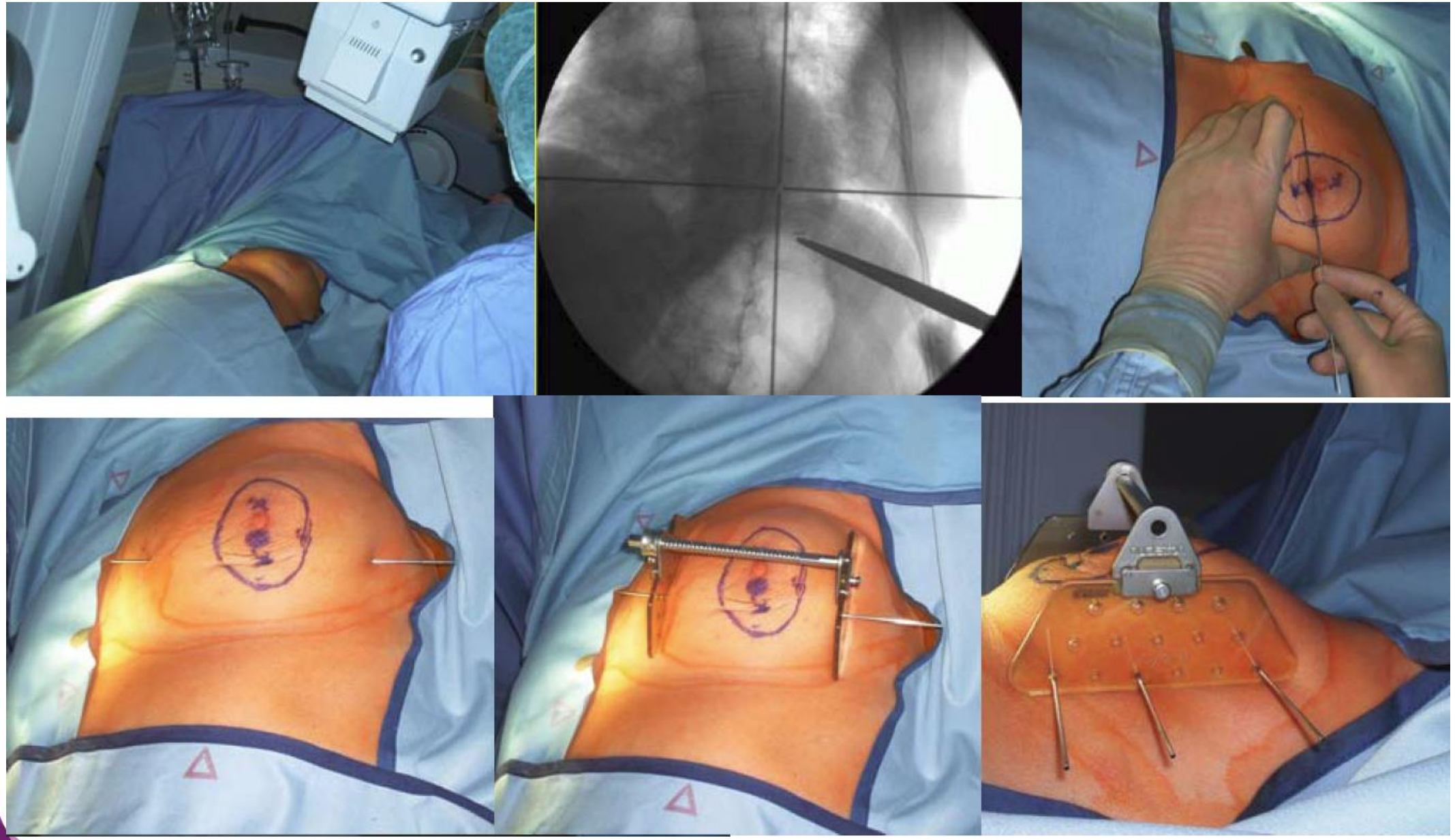
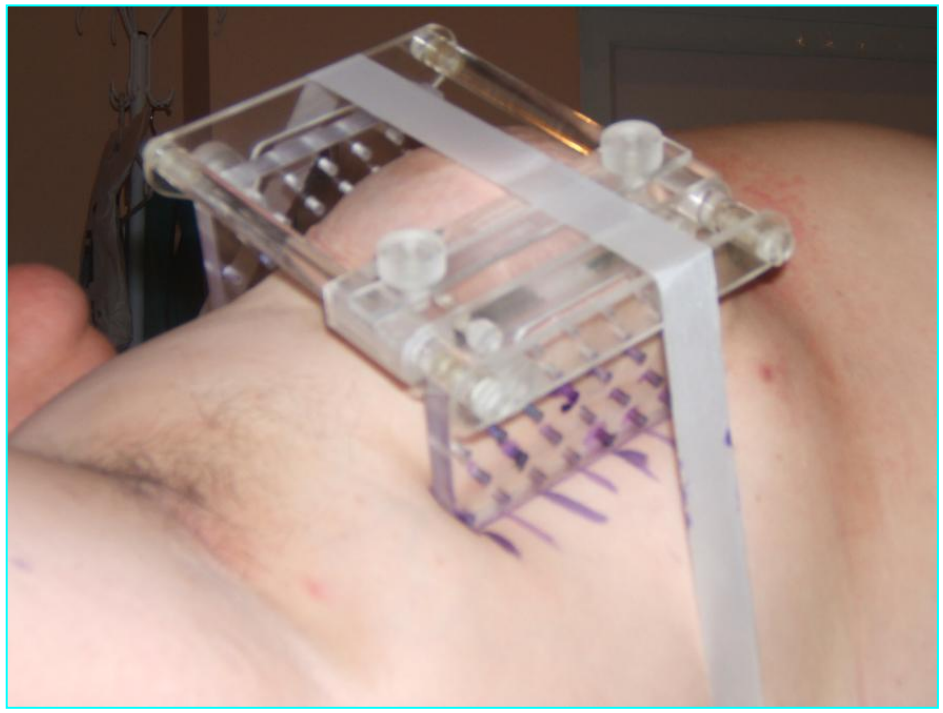
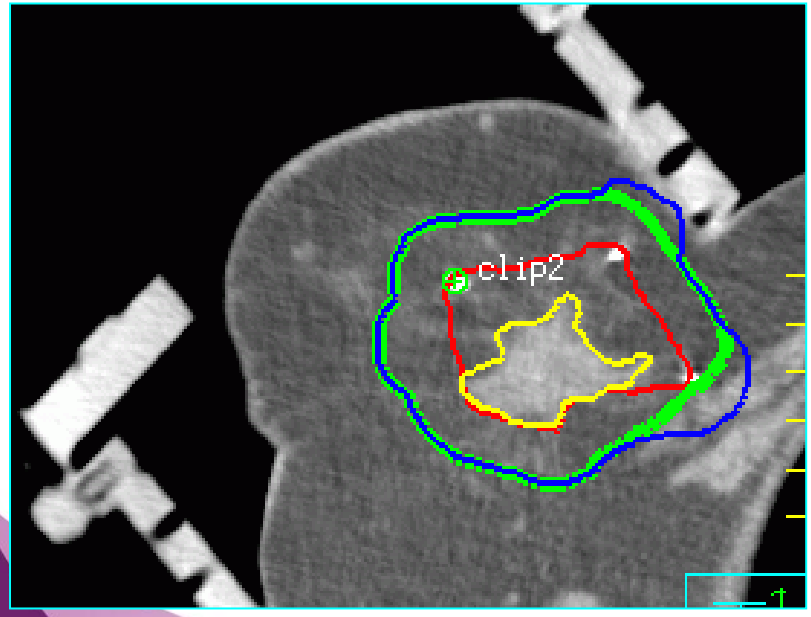
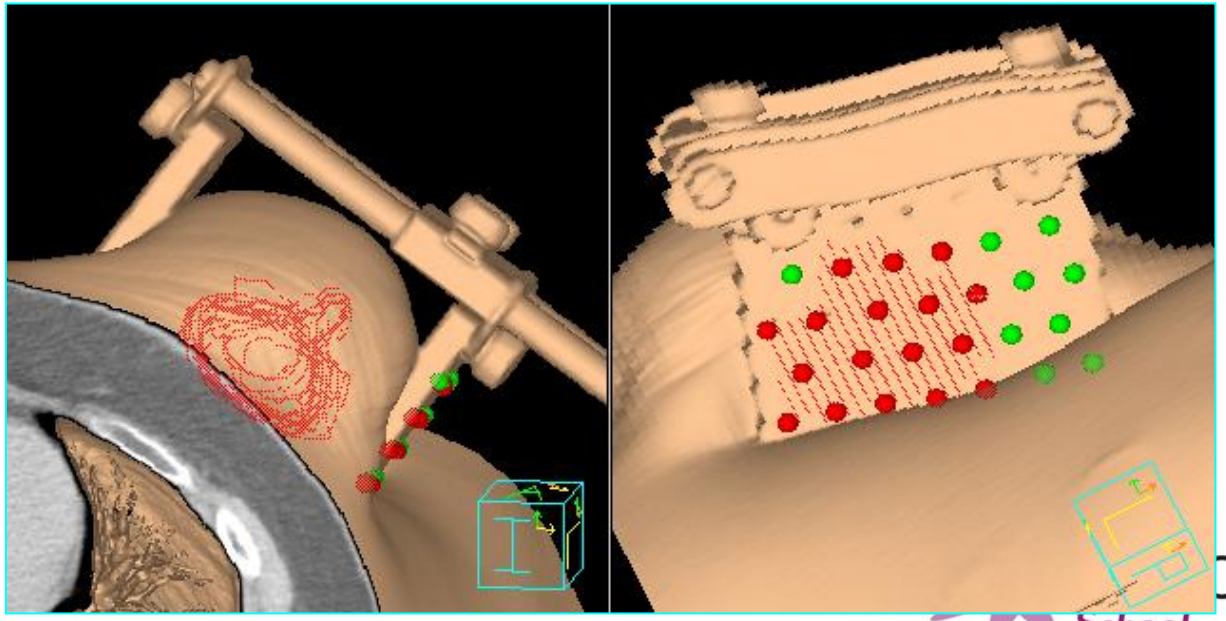
Technique Erlangen: X-Rays clips-guided implant. Closed cavity



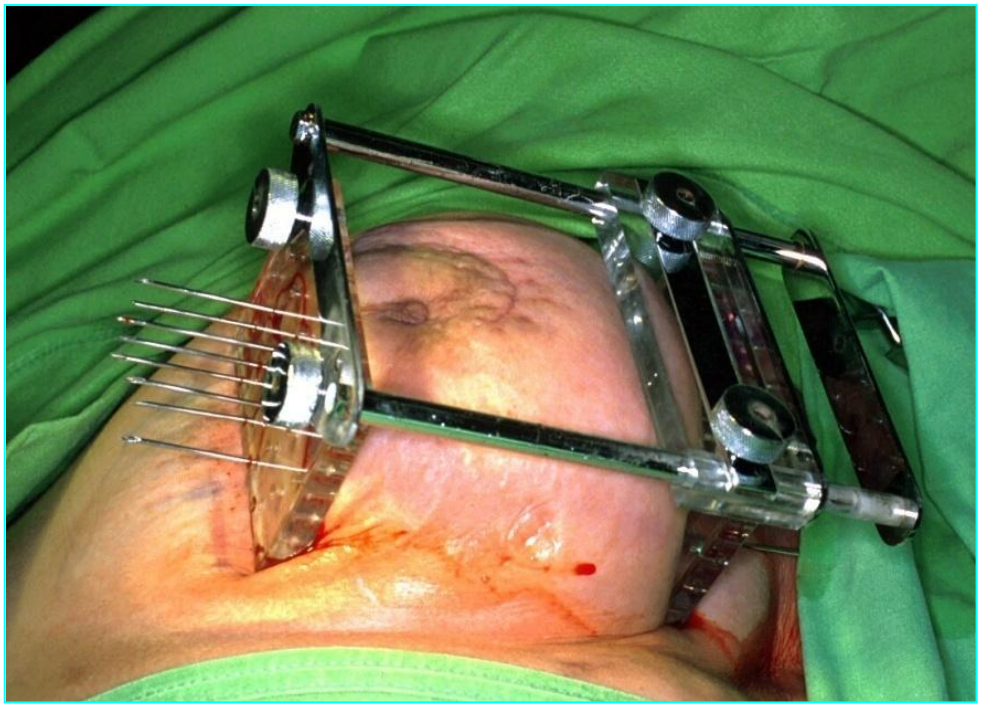
Technique Budapest: CT guided implant. Open cavity

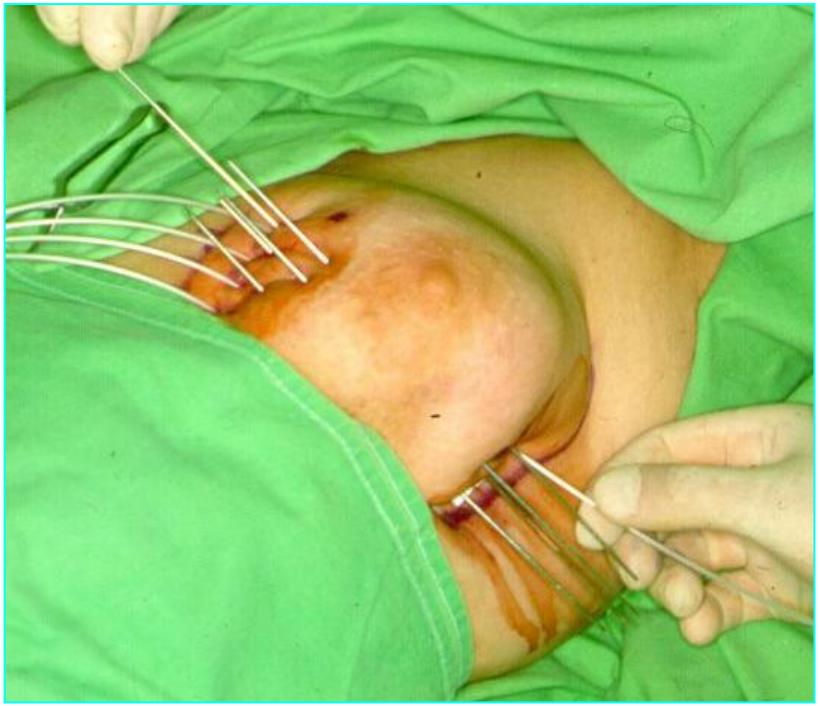


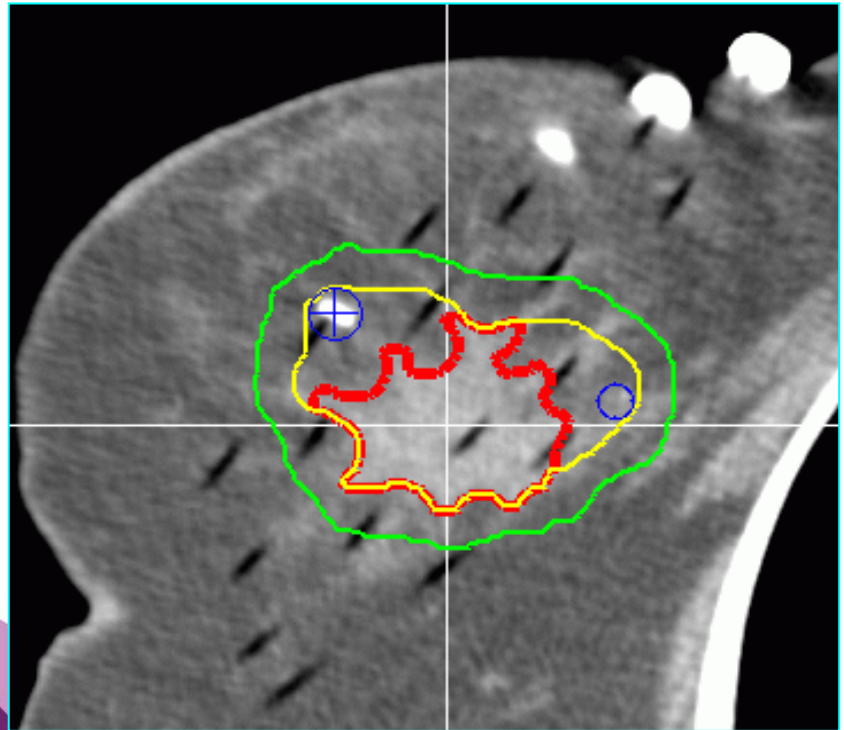


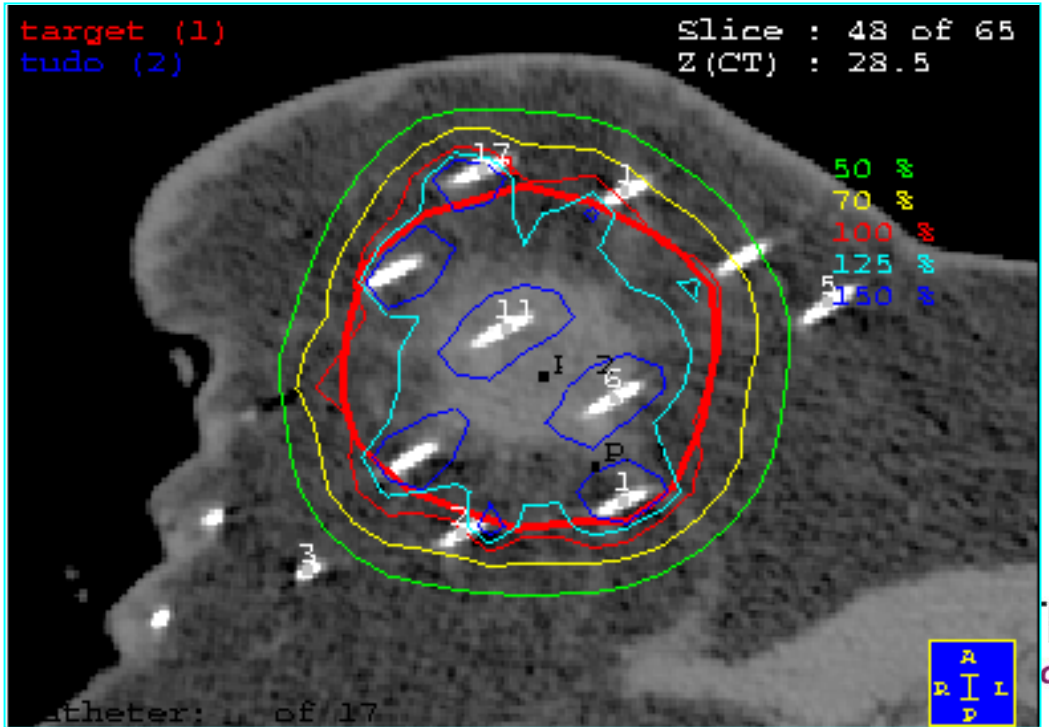


Technique Budapest: CT guided implant. Open cavity

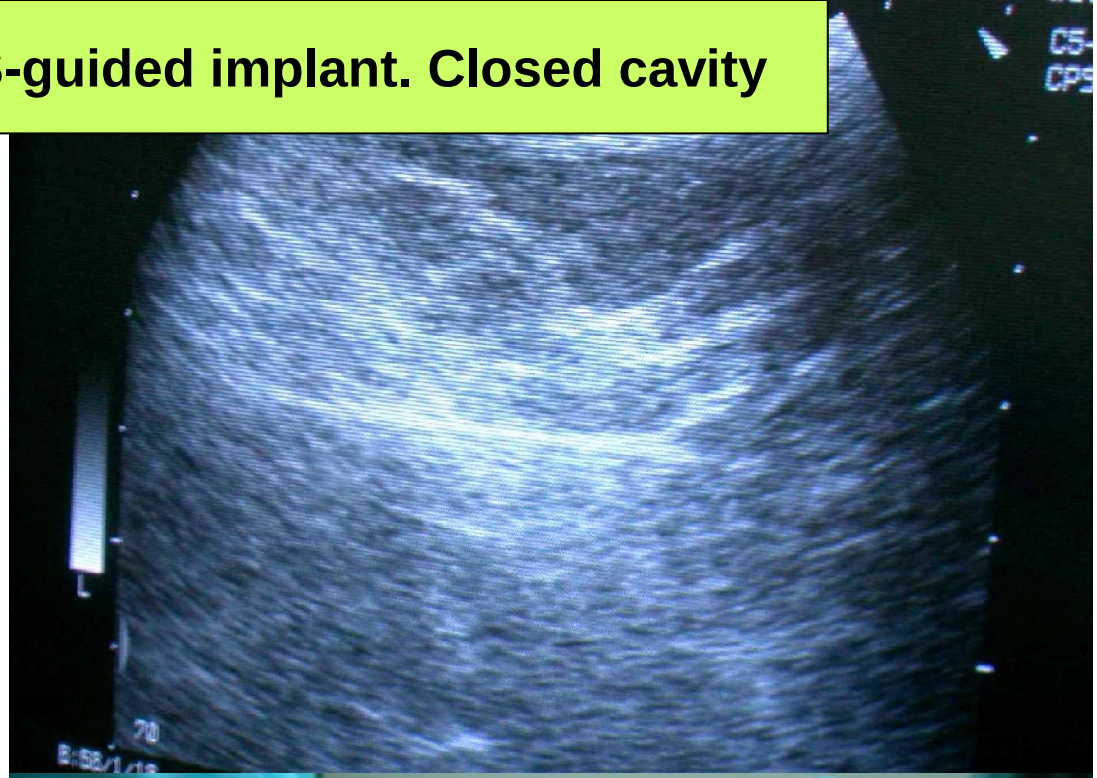


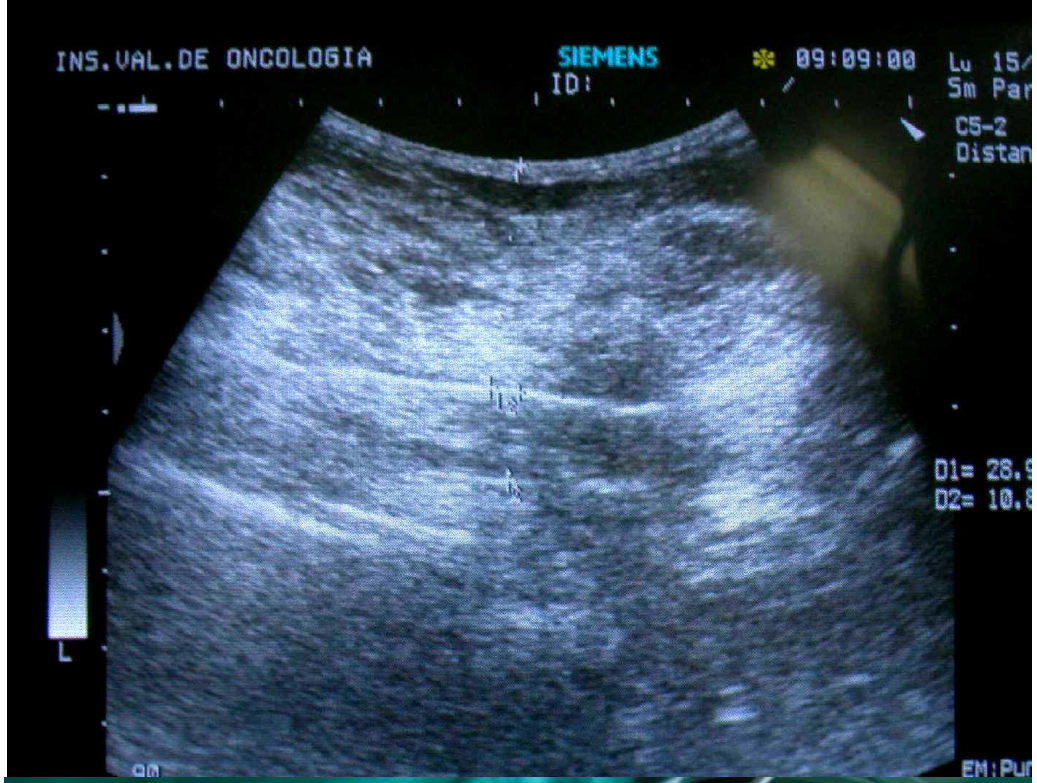






Technique IVO Valencia: US-guided implant. Closed cavity

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SIEMENS
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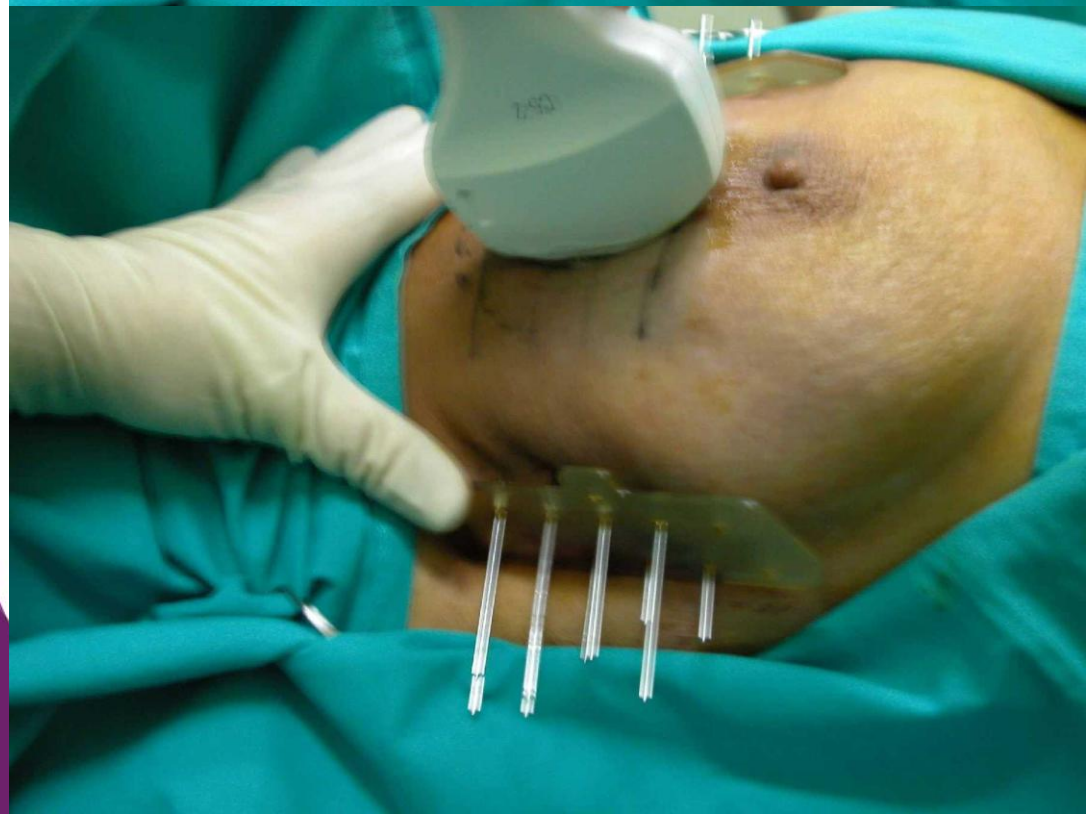
C5-2



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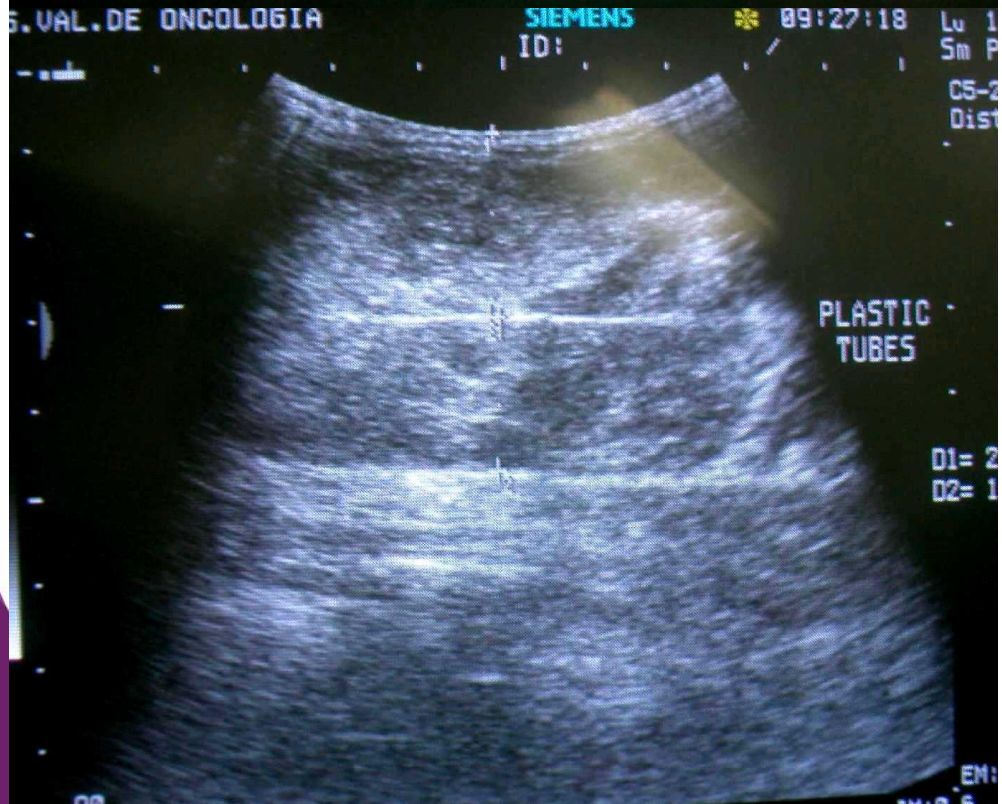
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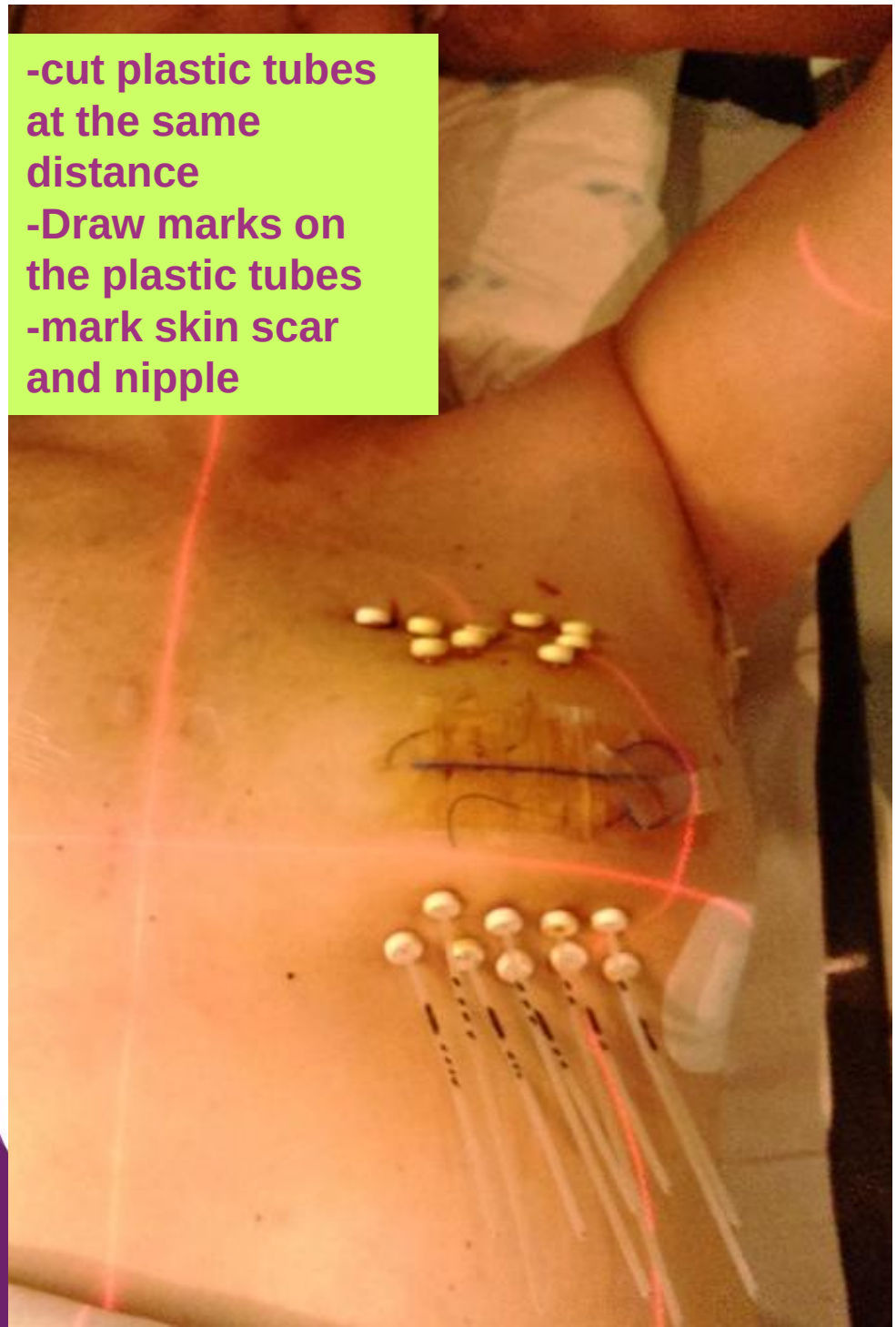
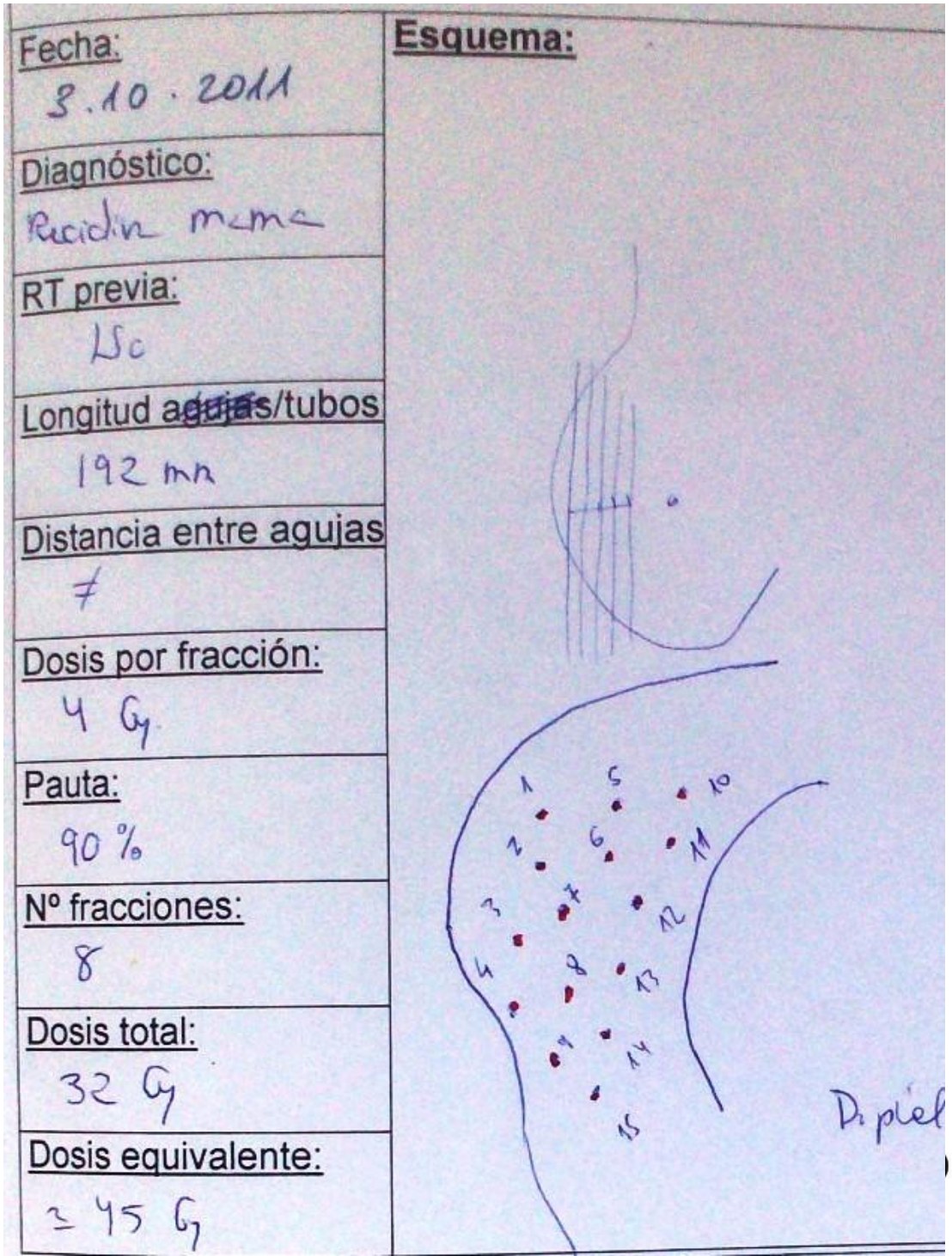
Planning CT scan 1-2 days later

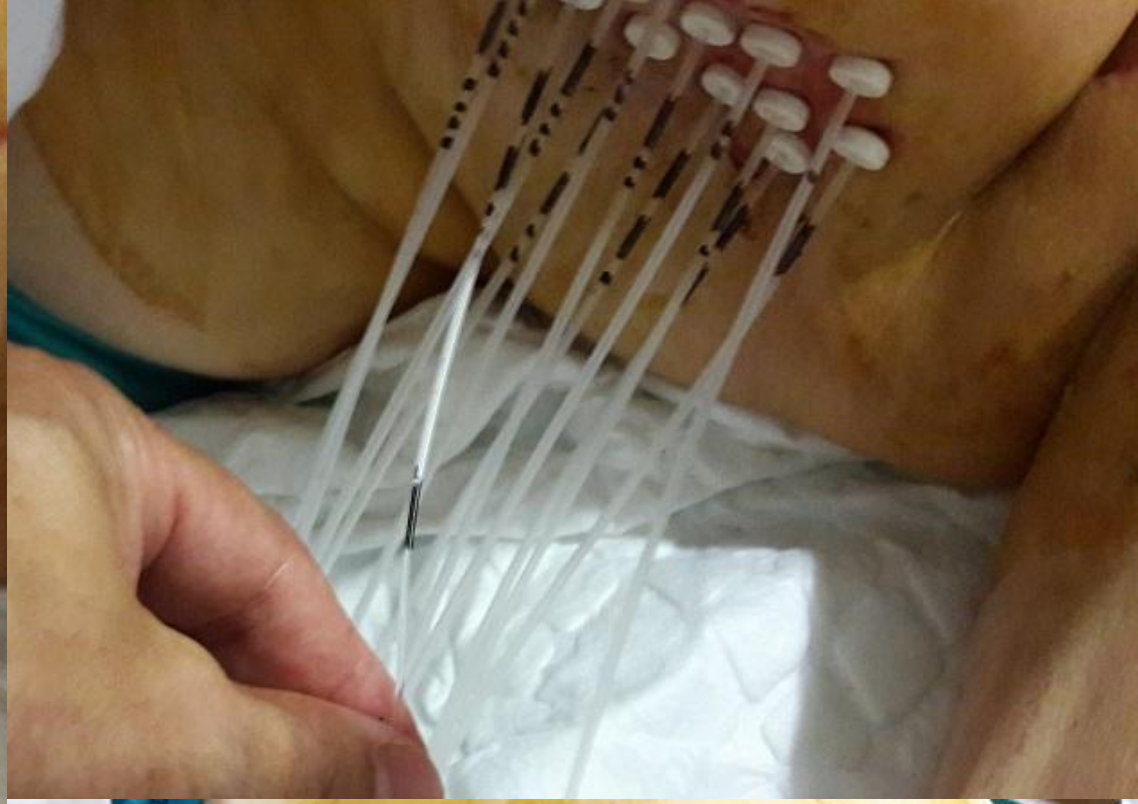


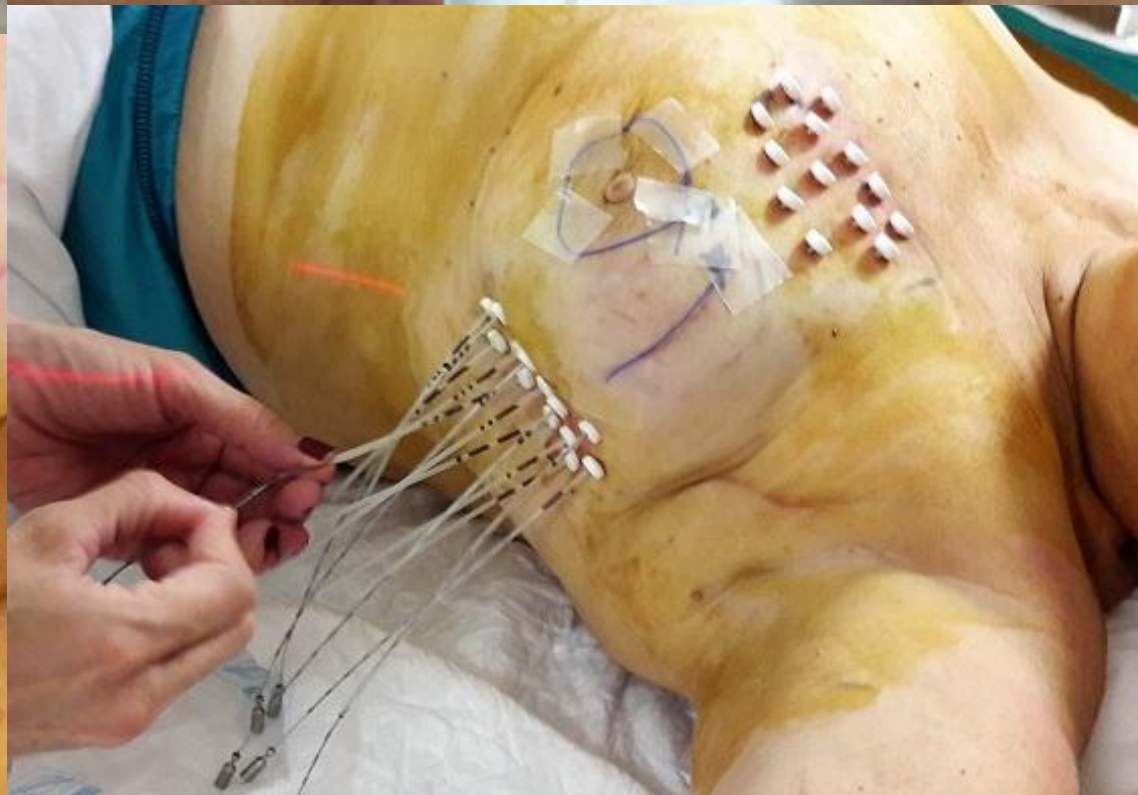
-cut plastic tubes at the same distance
-Draw marks on the plastic tubes
-mark skin scar and nipple

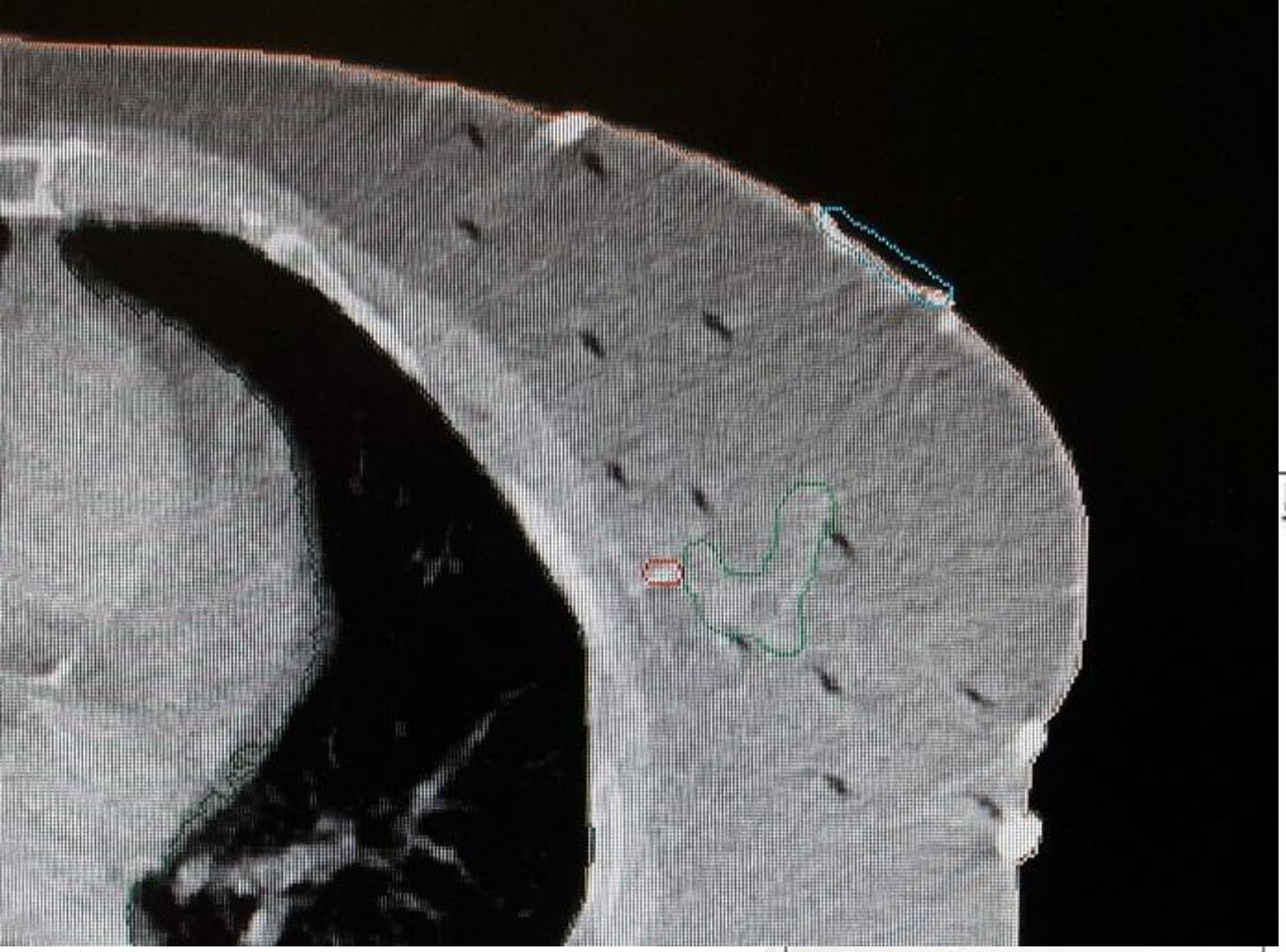
Planning sheet

Fecha: 3.10.2011	Esquema:
Diagnóstico: Recidiva mama	
RT previa: Qc	
Longitud agujas/tubos 192 mm	
Distancia entre agujas ≠	
Dosis por fracción: 4 Gy	
Pauta: 90 %	
Nº fracciones: 8	
Dosis total: 32 Gy	
Dosis equivalente: ≥ 45 Gy	









2.57 mm

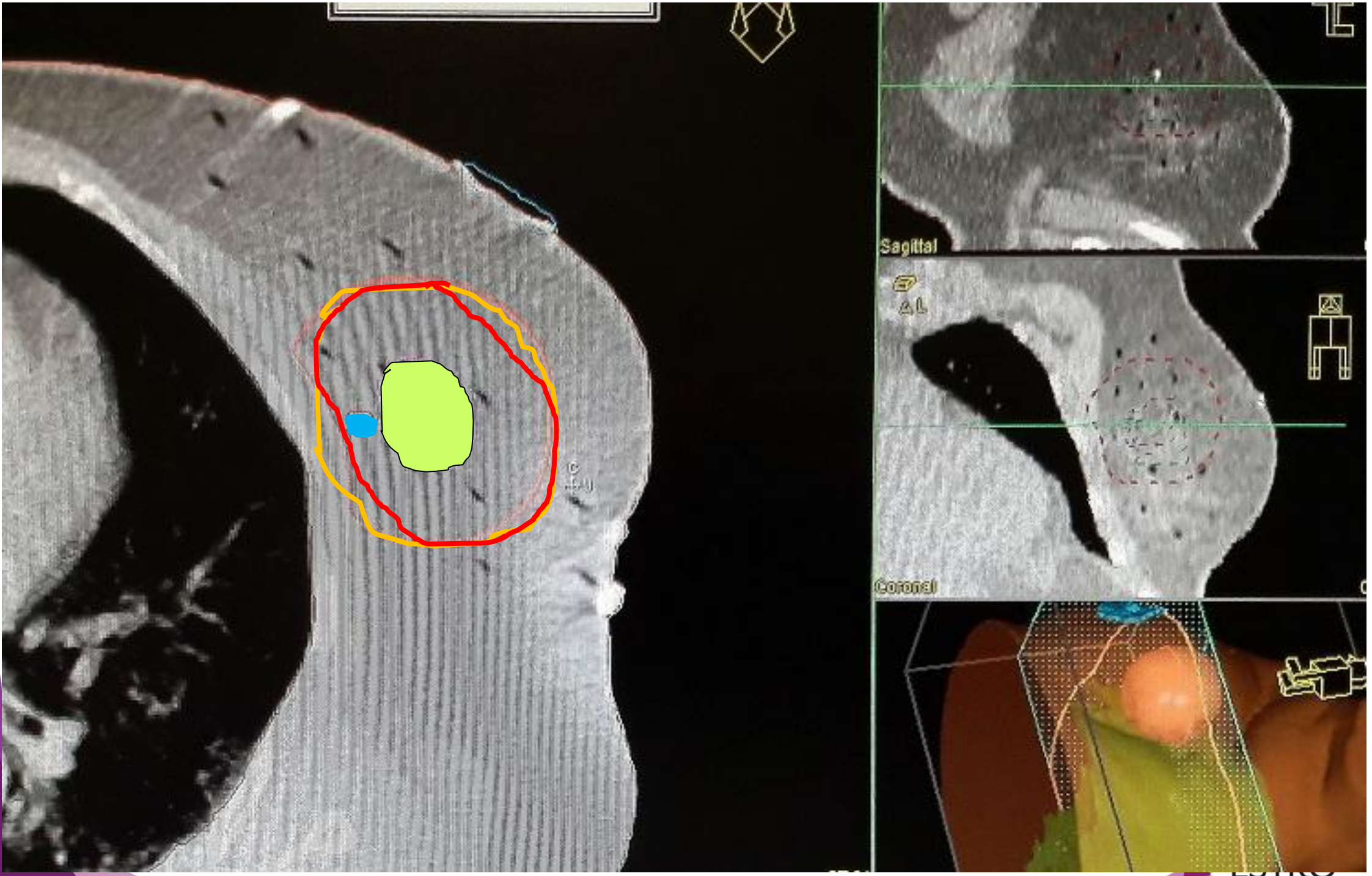
Distancia entre agujas

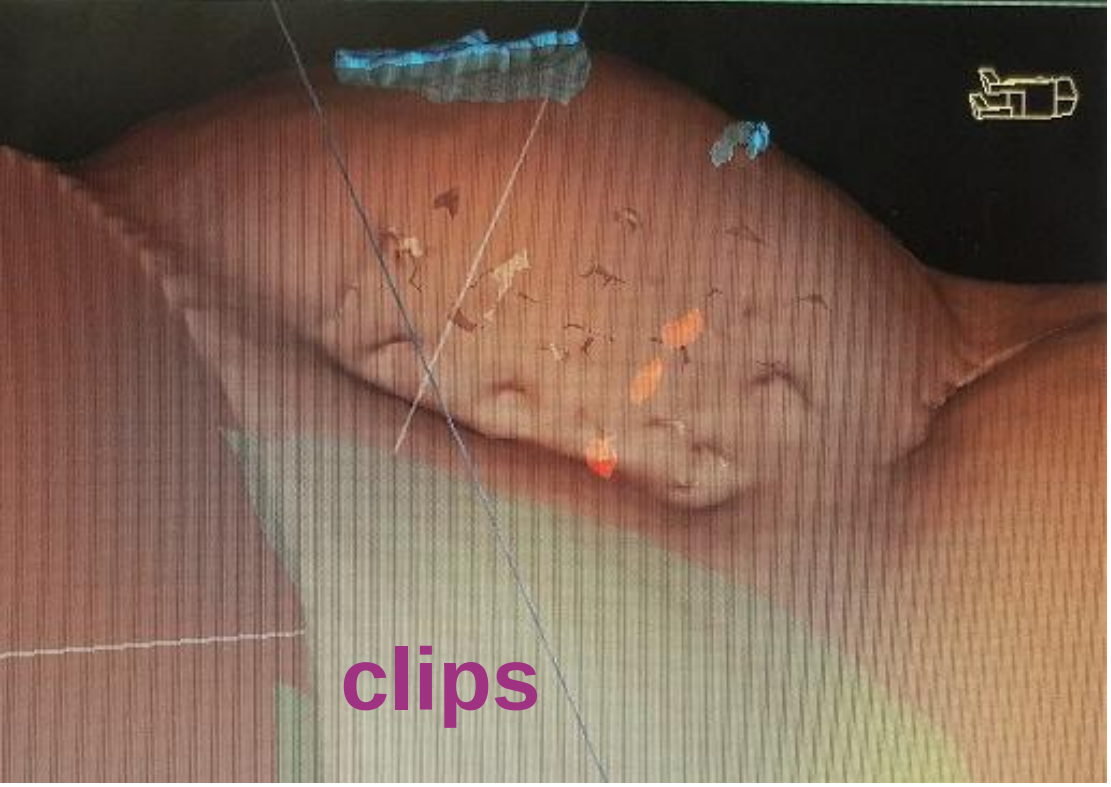
Dosis por fracción:

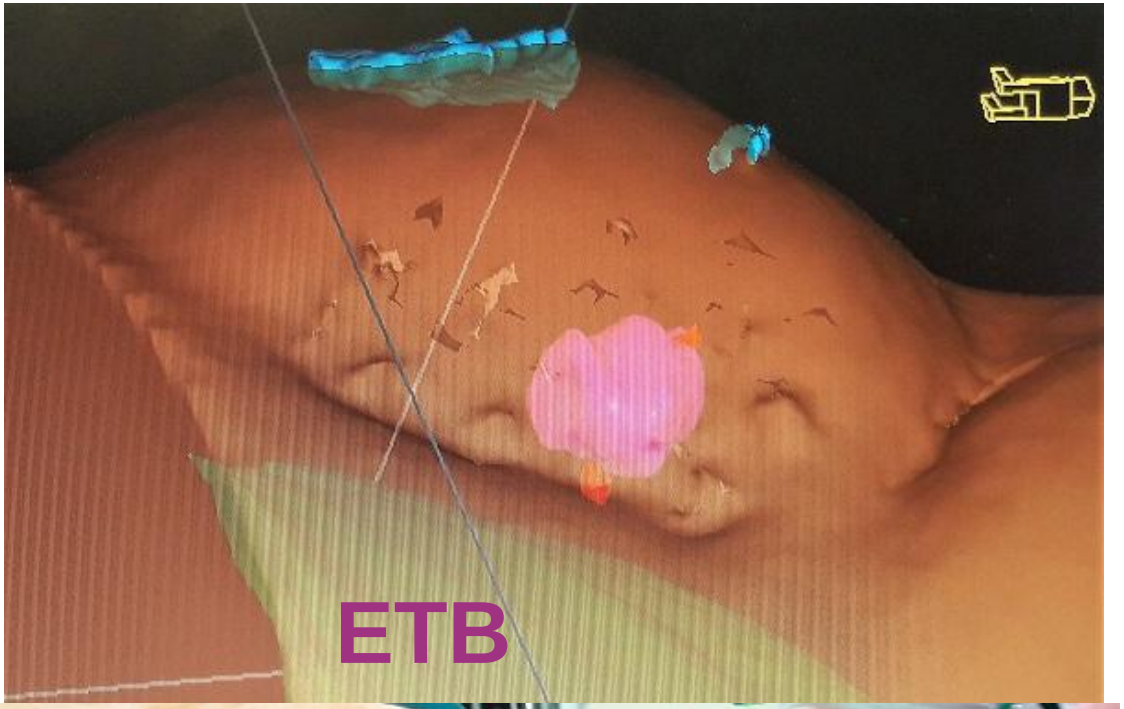
4.30 cGy

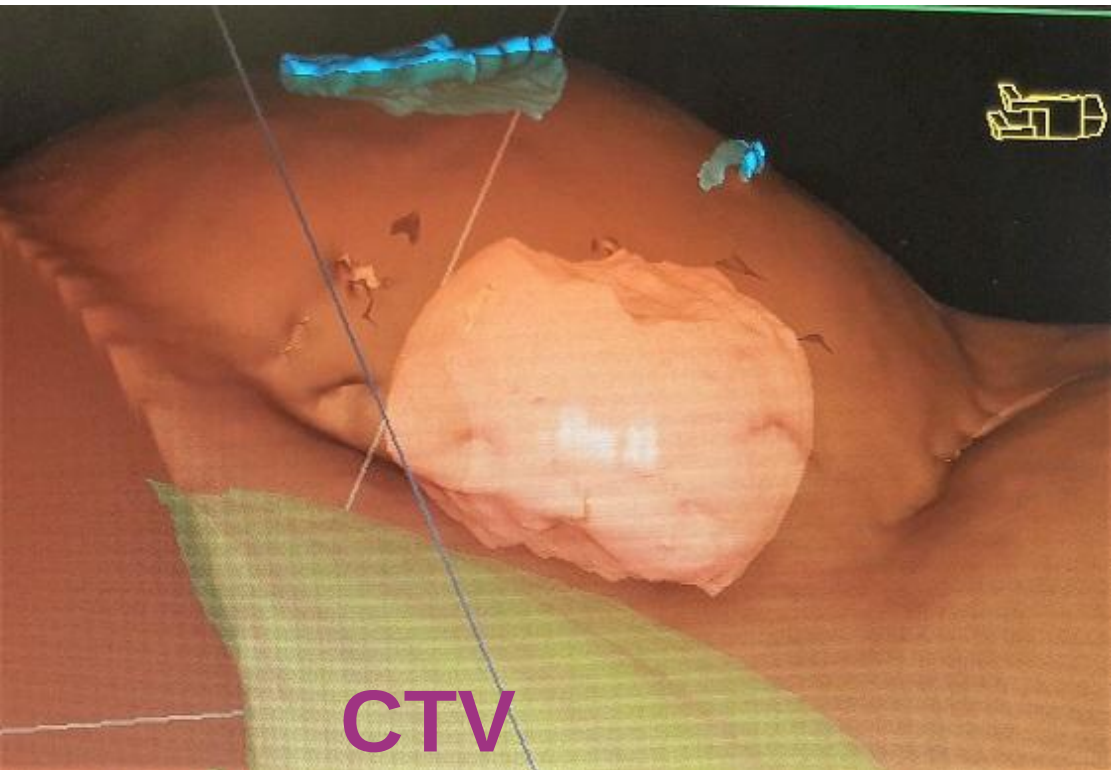
Pauta: volumen

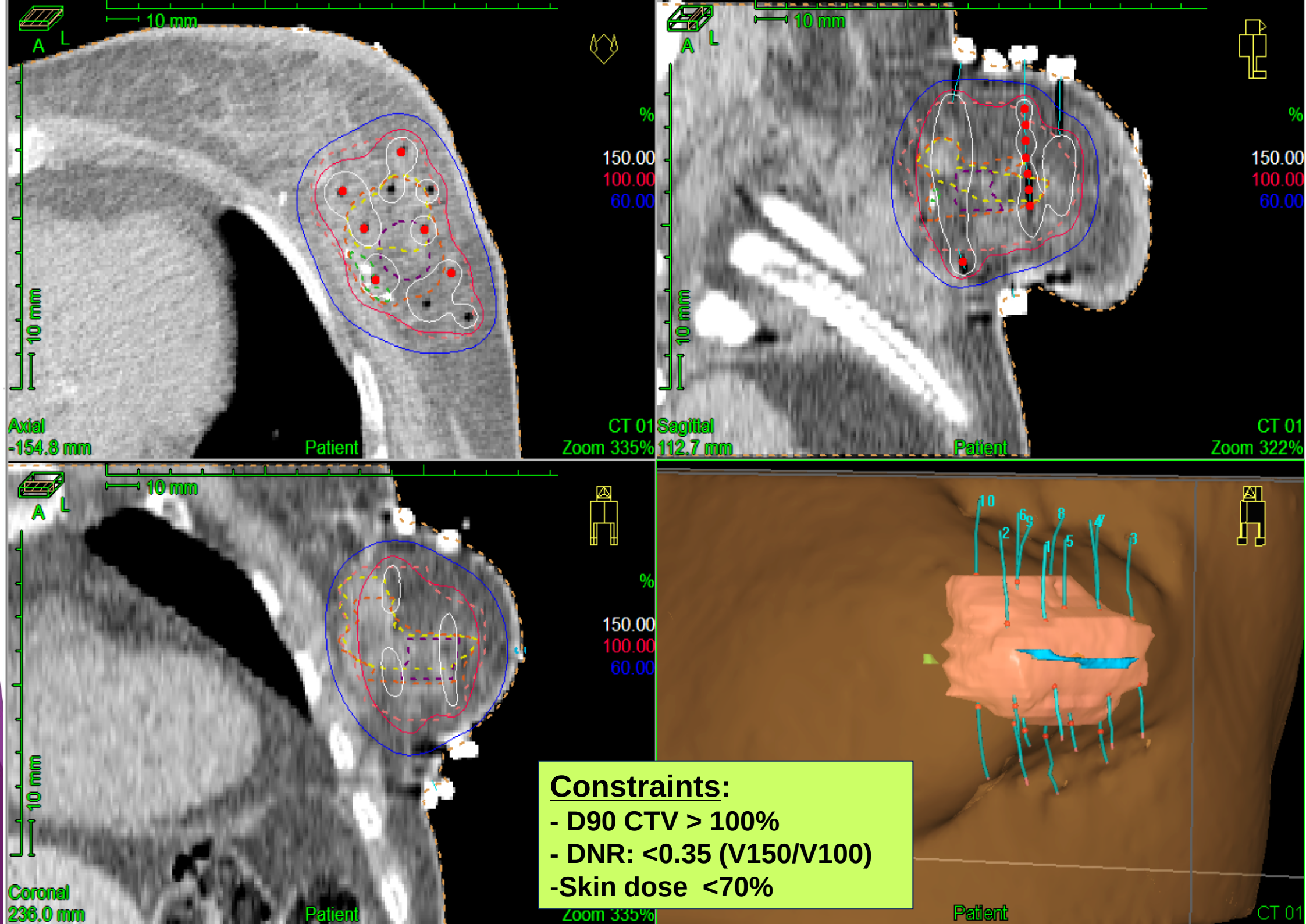
Esquema:

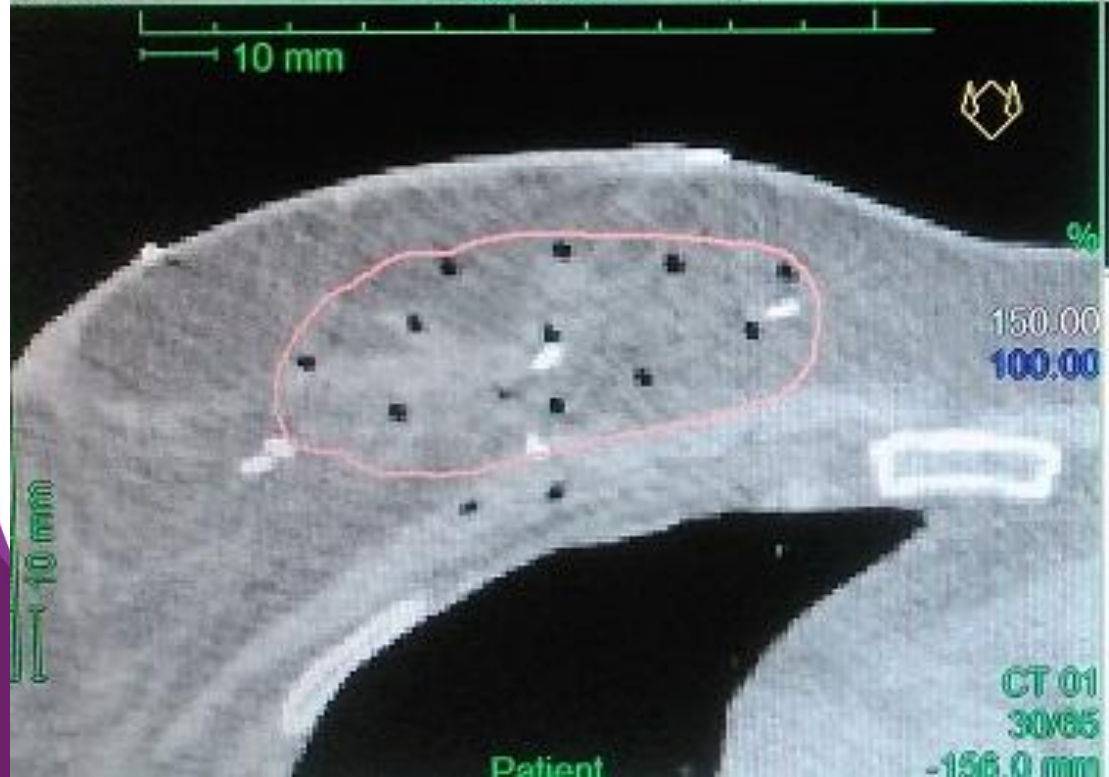

Sagittal
Coronal

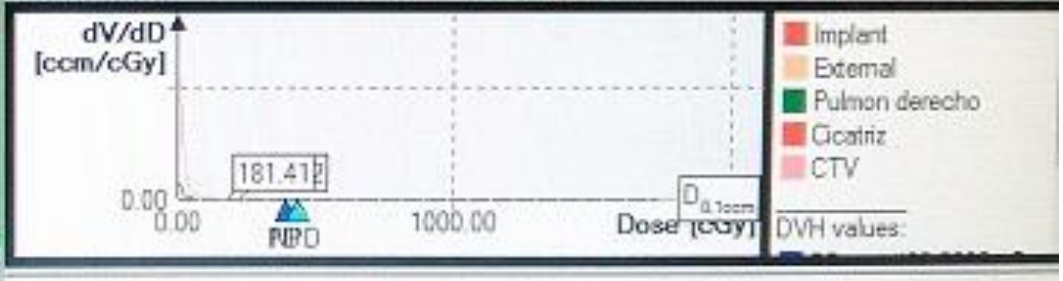

clips


ETB

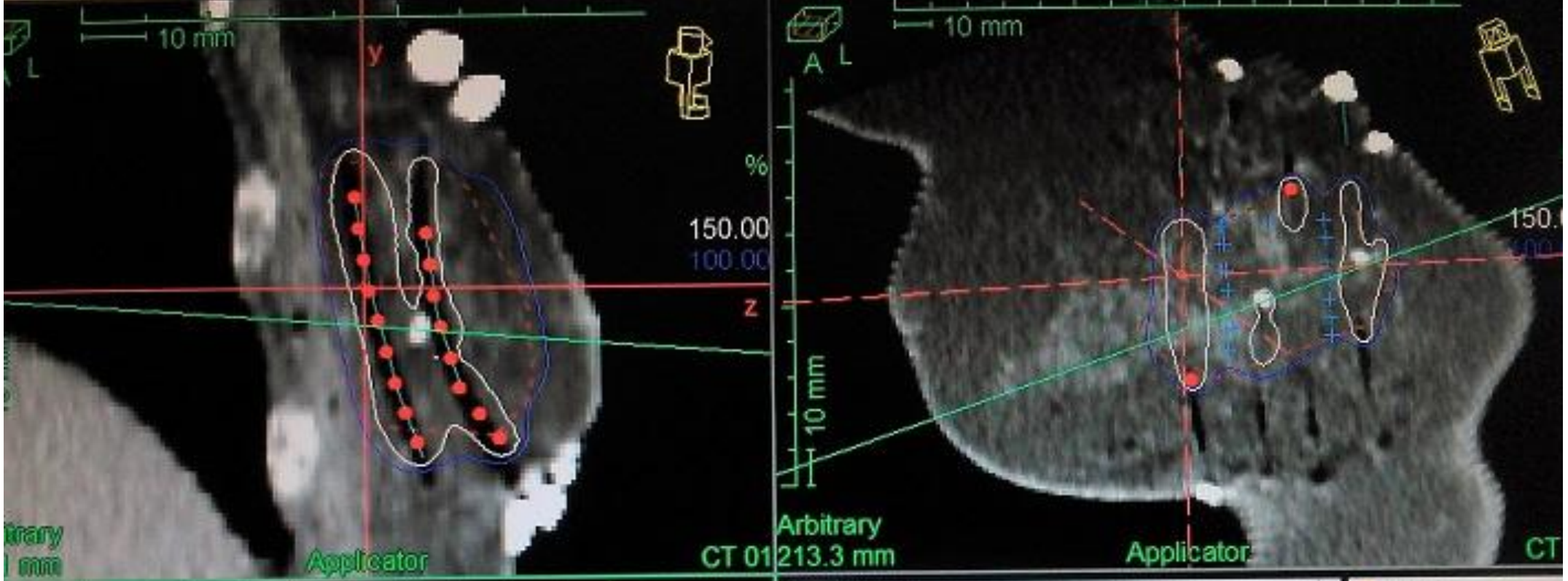

CTV


10 mm
A L
%
150.00
100.00
60.00
Axial
-154.8 mm
Patient
CT 01
Zoom 335%
Sagittal
112.7 mm
Zoom 322%
Coronal
236.0 mm
Constraints:
- D90 CTV > 100%
- DNR: <0.35 (V150/V100)
-Skin dose <70%





ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
CTV				
CTV	105.16	420.66	**90.00**	48.31
Cicatriz				
Cicatriz	56.48	225.92	6.06	**0.10**
External				
External	**100.00**	400.00	0.52	67.65
External	**150.00**	600.00	0.15	20.07
Pulmon derecho				
Pulmon dere...	45.35	181.41	0.01	**0.10**



D90: 105%

DNR: 0.29

ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
CTV				
CTV	105.16	420.66	**90.00**	48.31
Cicatriz				
Cicatriz	56.48	225.92	6.06	**0.10**
External				
External	**100.00**	400.00	0.52	67.65
External	**150.00**	600.00	0.15	20.07
Pulmon derecho				
Pulmon dere...	45.35	181.41	0.01	**0.10**

Results

PROCEDURE OF PERIOPERATIVE BRACHYTHERAPY

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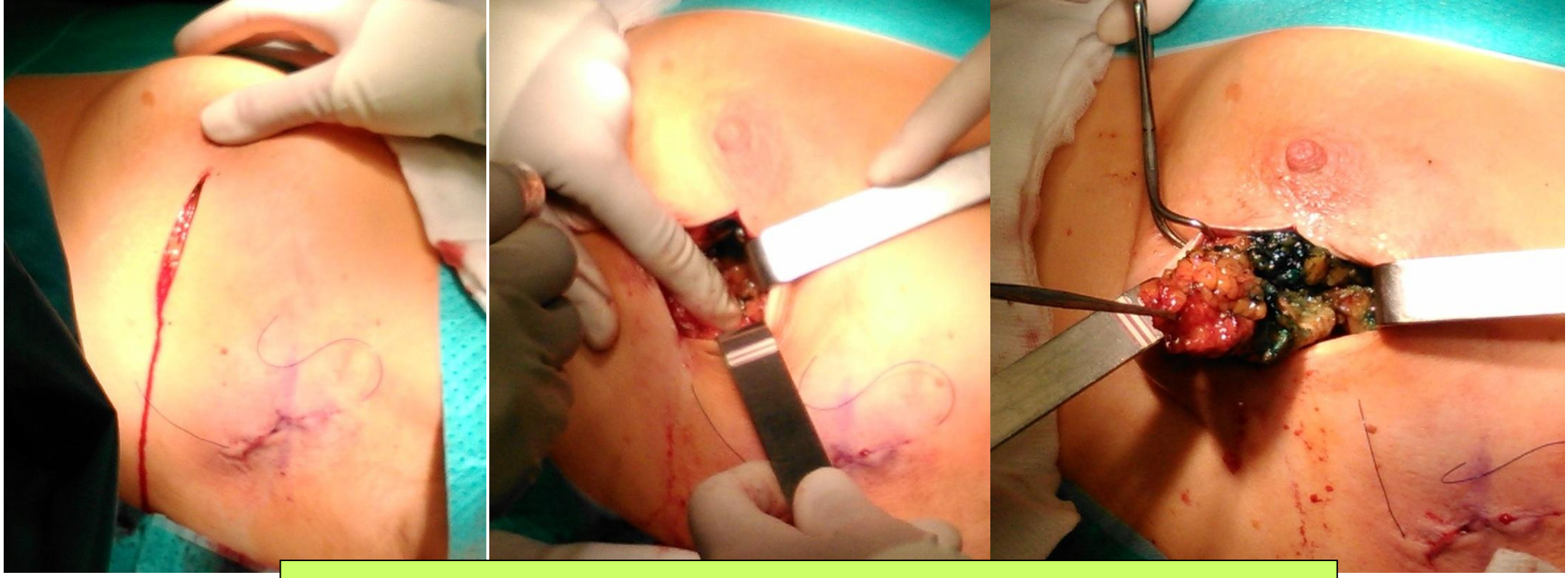
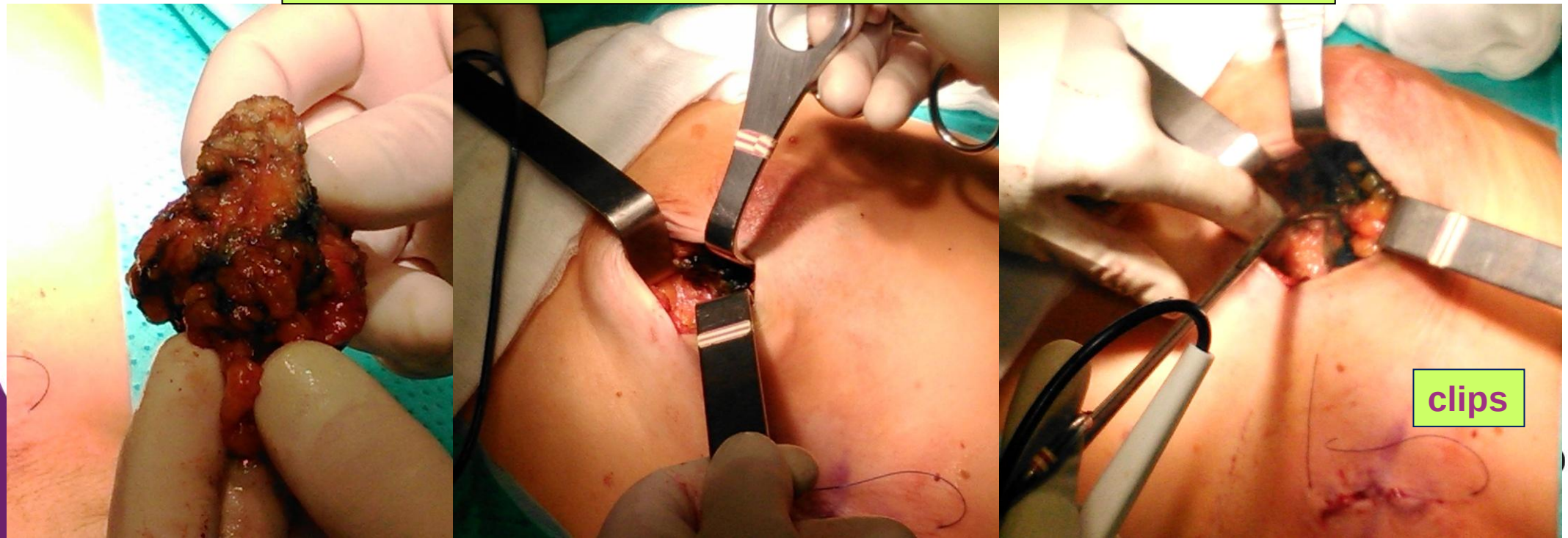
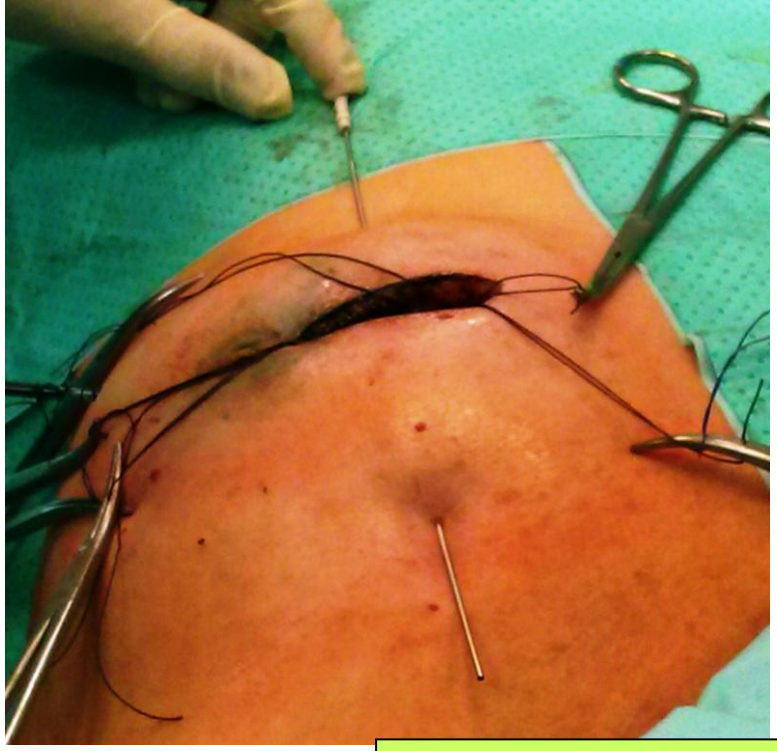
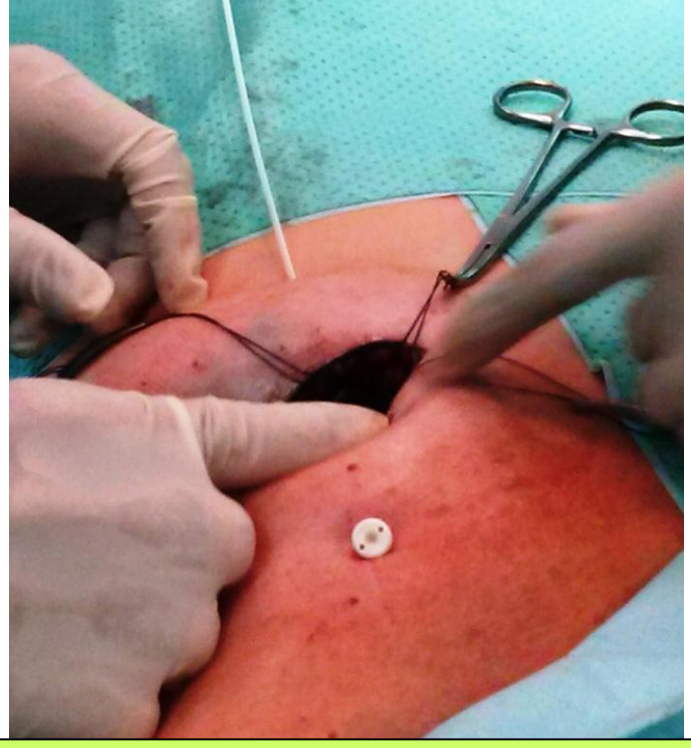
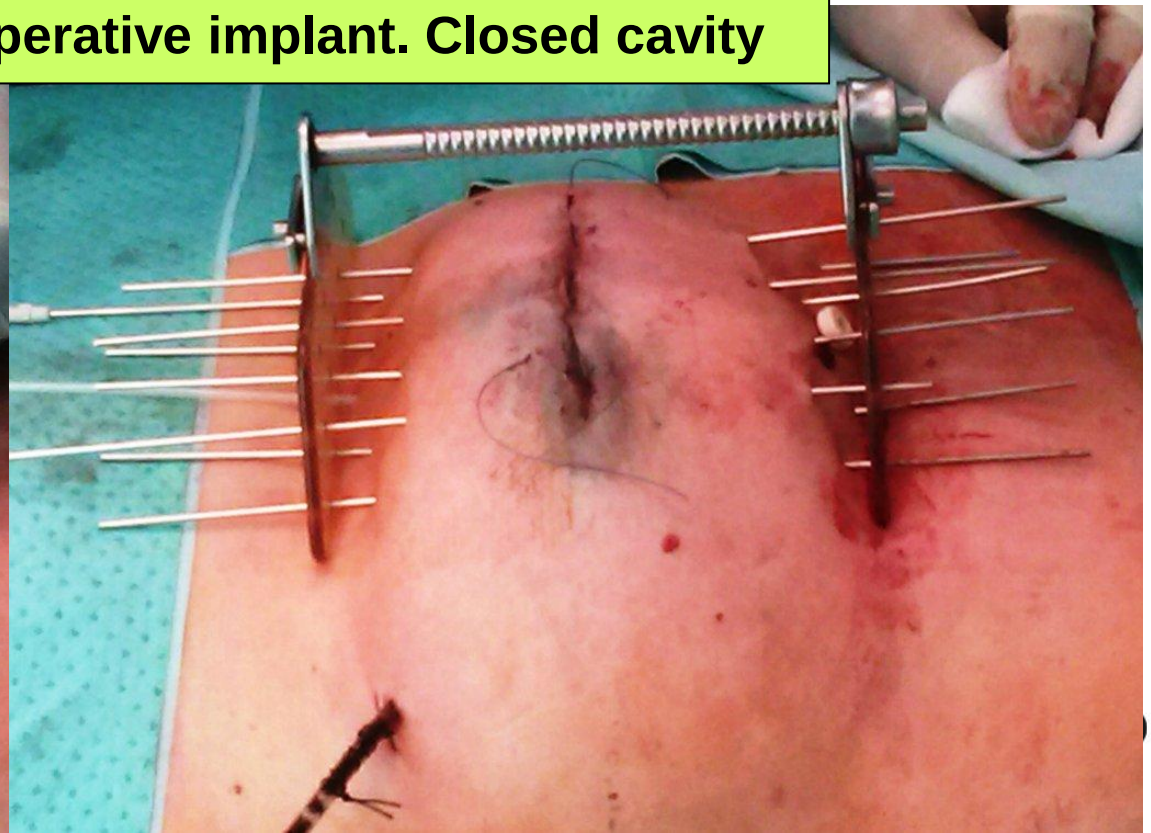


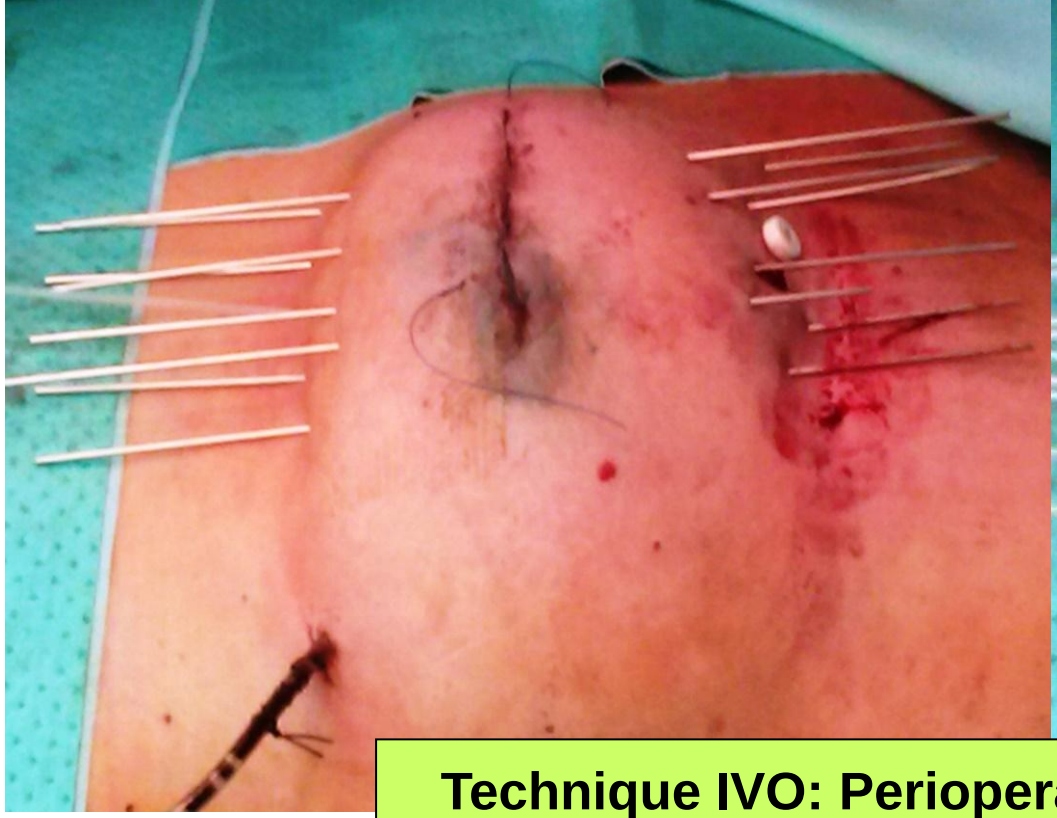
Technique IVO: Perioperative implant. Closed cavity

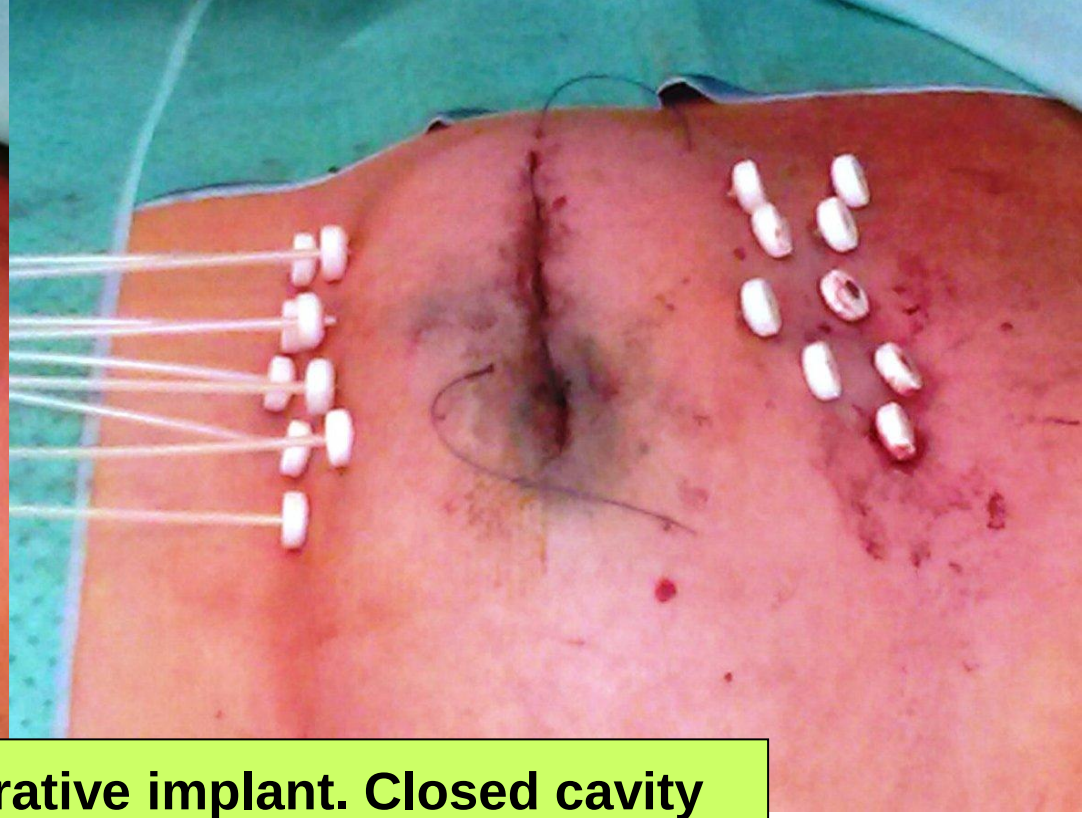


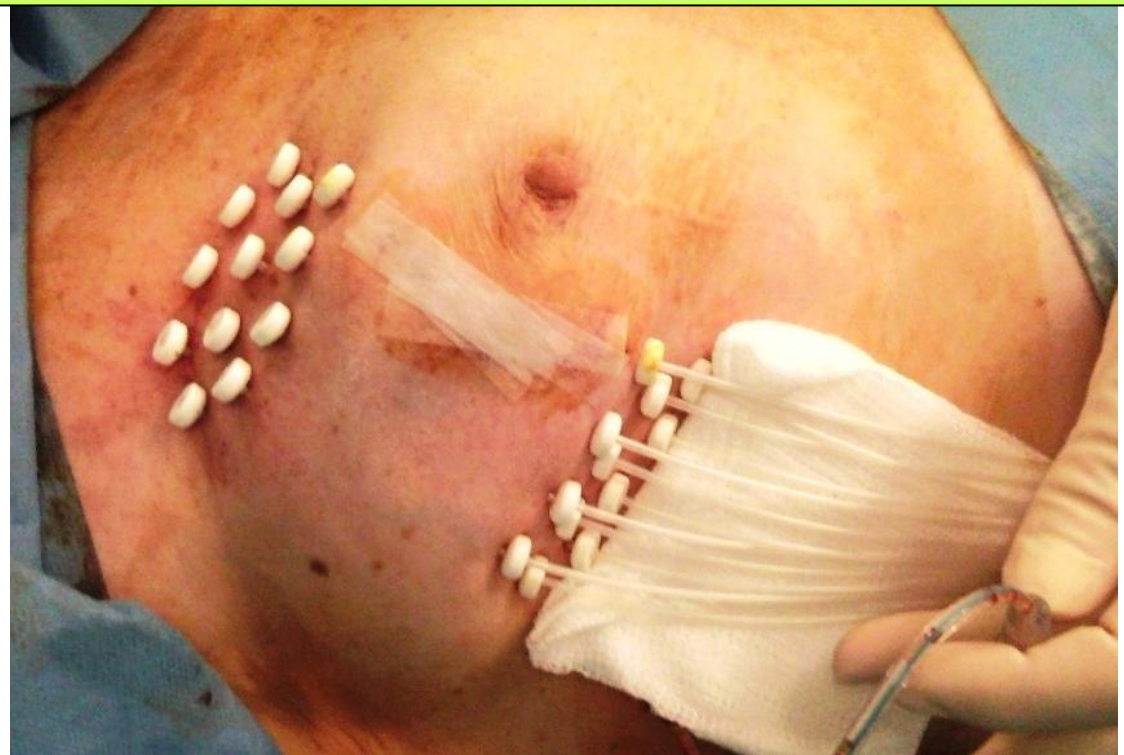
Technique IVO: Perioperative implant. Closed cavity







Technique IVO: Perioperative implant. Closed cavity



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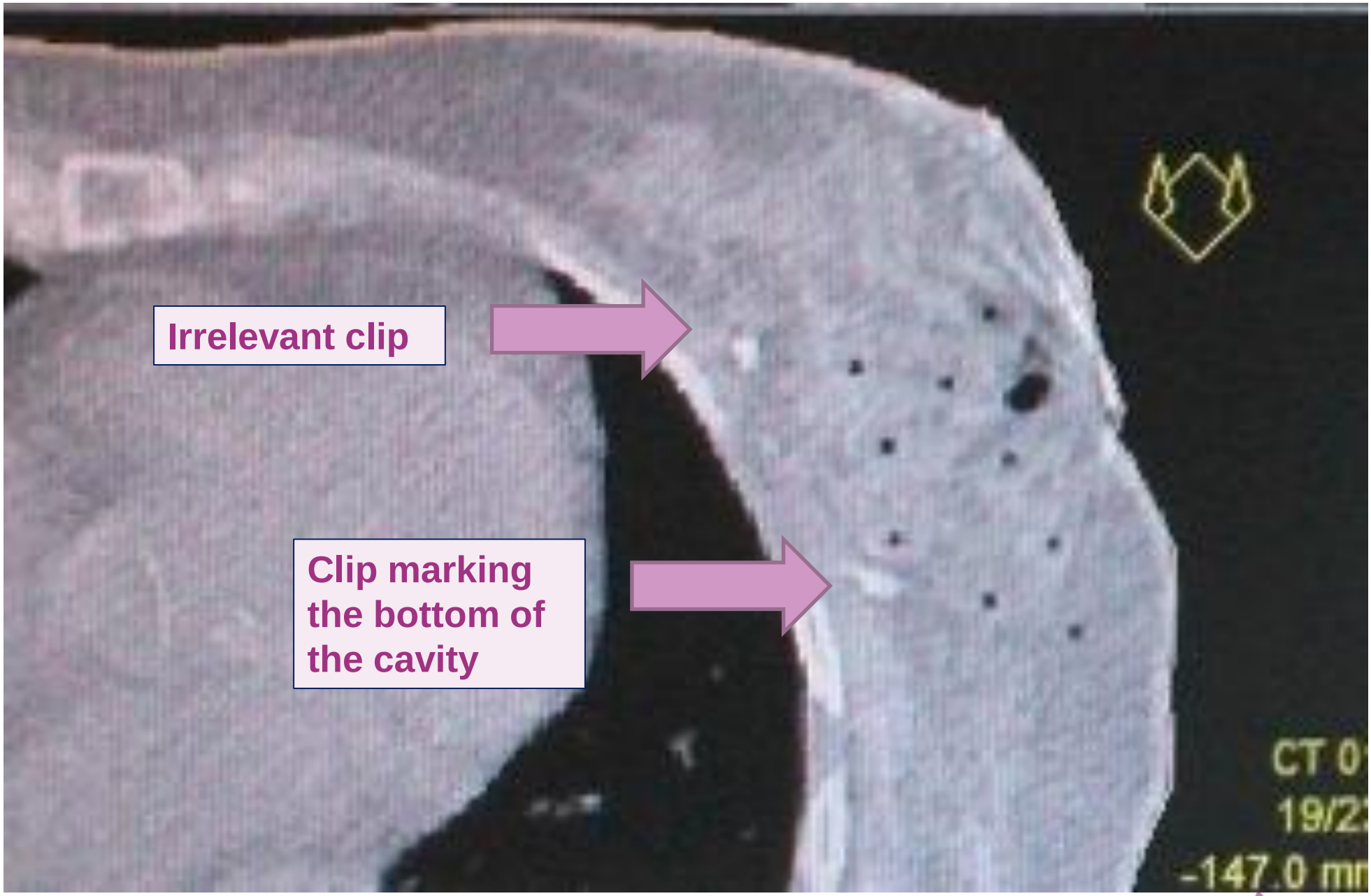

Relevance of clips placement

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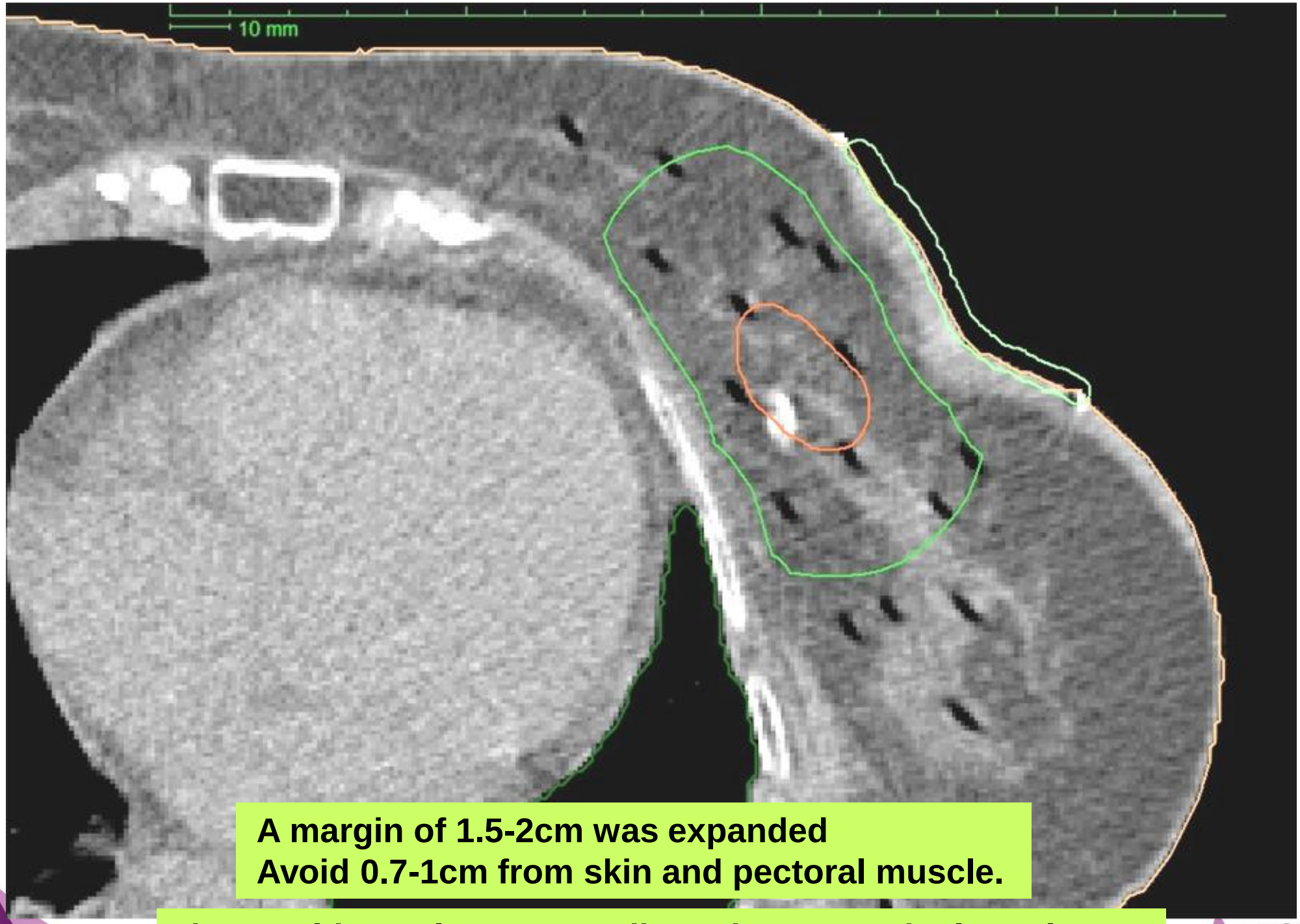
ETB: Estimated tumour bed. A small area above the guide-tube was drawn with central clips if present.



A margin of 1.5-2cm was expanded
Avoid 0.7-1cm from skin and pectoral muscle.

The resulting volume was adjusted to cover the lateral plastic tubes with a margin of a few mm to obtain the CTV.

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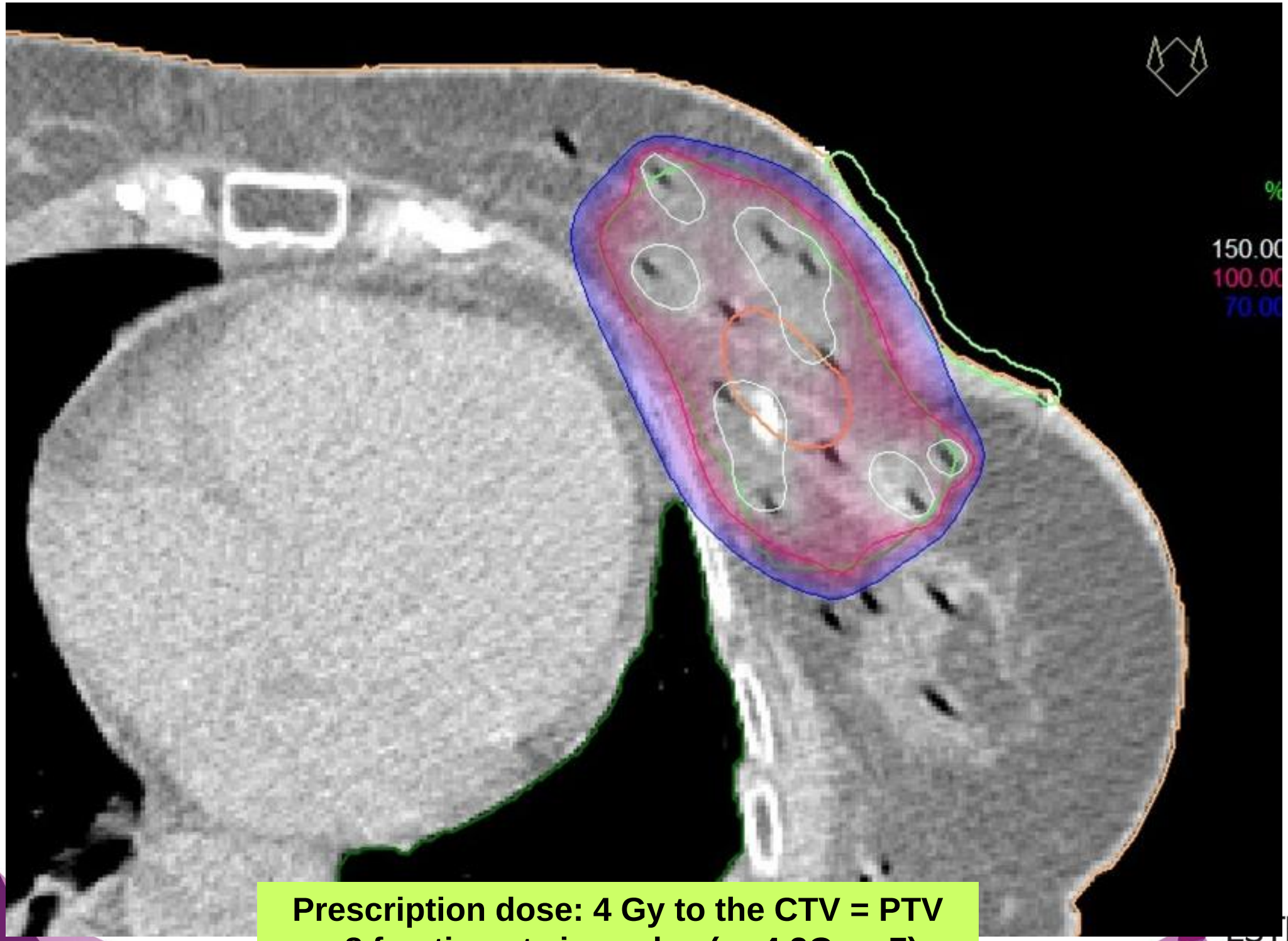


Prescription dose: 4 Gy to the CTV = PTV x 8 fractions twice a day (or 4.3Gy x 7)

Minimally Invasive Intraoperative Multicatheter Breast Implant (MIOMBI) in breast conservative surgery

2014

- **Clinica Universitaria de Navarra (CUN) . Pamplona. Spain**
  - 101 perioperative implants
  - procedure 25 minutes
  - number of catheters: 9 (4-14).
  - When pathologic report arrives, APBI 3.4Gy x 10 fractions
  - If some risk factor is present, 3.4 Gy x 4 in 2 days as a boost + EBRT hypofractionated 39.9 Gy in 15 fractions.

- No recurrences at 43 months

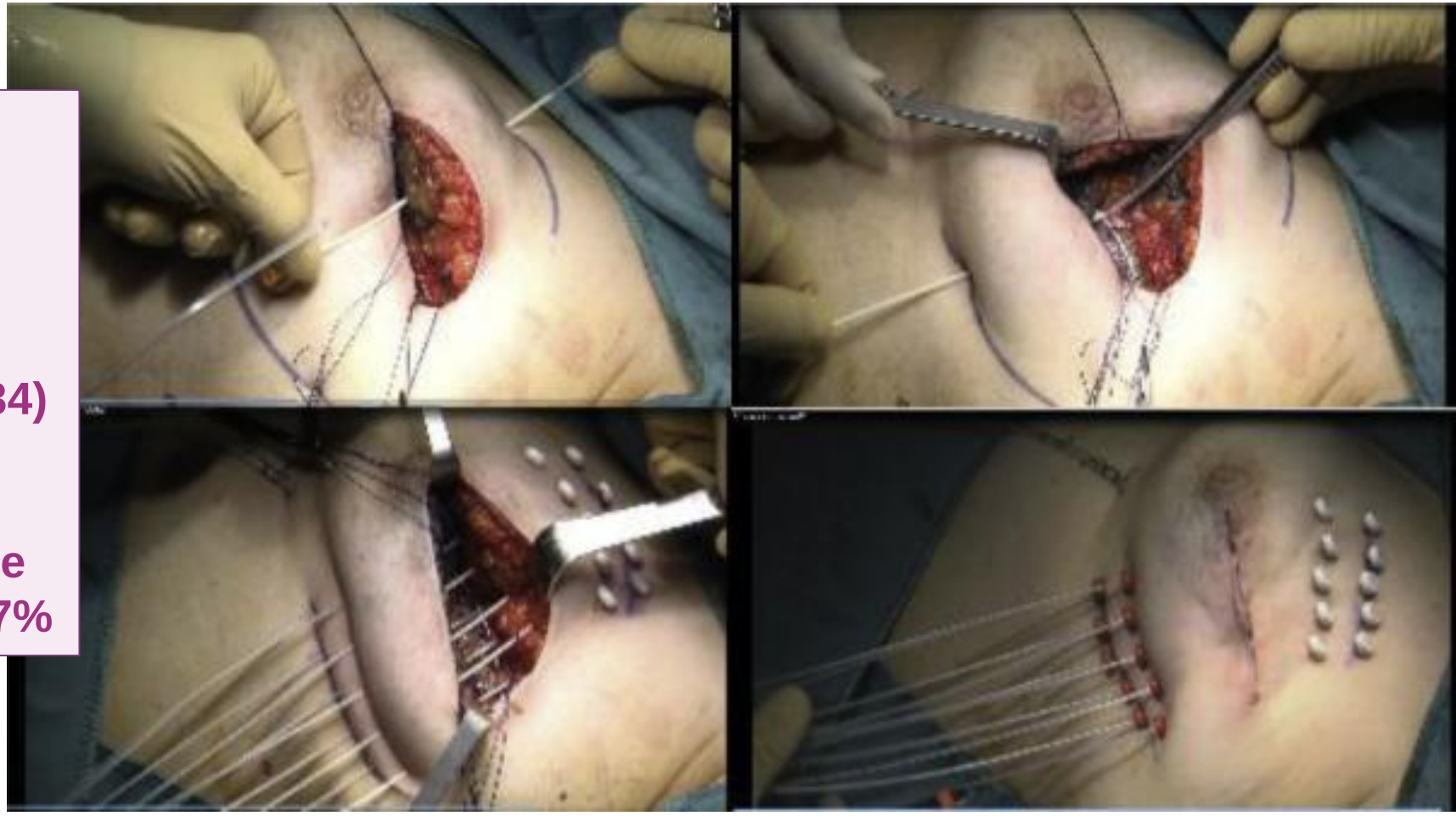
Cambeiro M, Aristu JJ, Moreno M. et al. Presented in ESTRO Viena 2014

C.U.N. NAVARRA Technique: Perioperative implant.

2016

Multicatheter breast implant during breast conservative surgery: Novel approach to deliver accelerated partial breast irradiation

Mauricio Cambeiro[1,*], Fernando Martinez-Regueira[2], Natalia Rodriguez-Spiteri[2],



2007-2014
122 cases,
perioperative
8 catheters (4-14)
3.4 Gy x 10 (88)
boost 3.4Gy x 4 (34)
Median FU 38 m
no local failure
Cosmetic outcome
excellent/good 87%

Closed cavity

Cambeiro M et al. Brachytherapy. 2016 Jul-Aug;15(4):485-94

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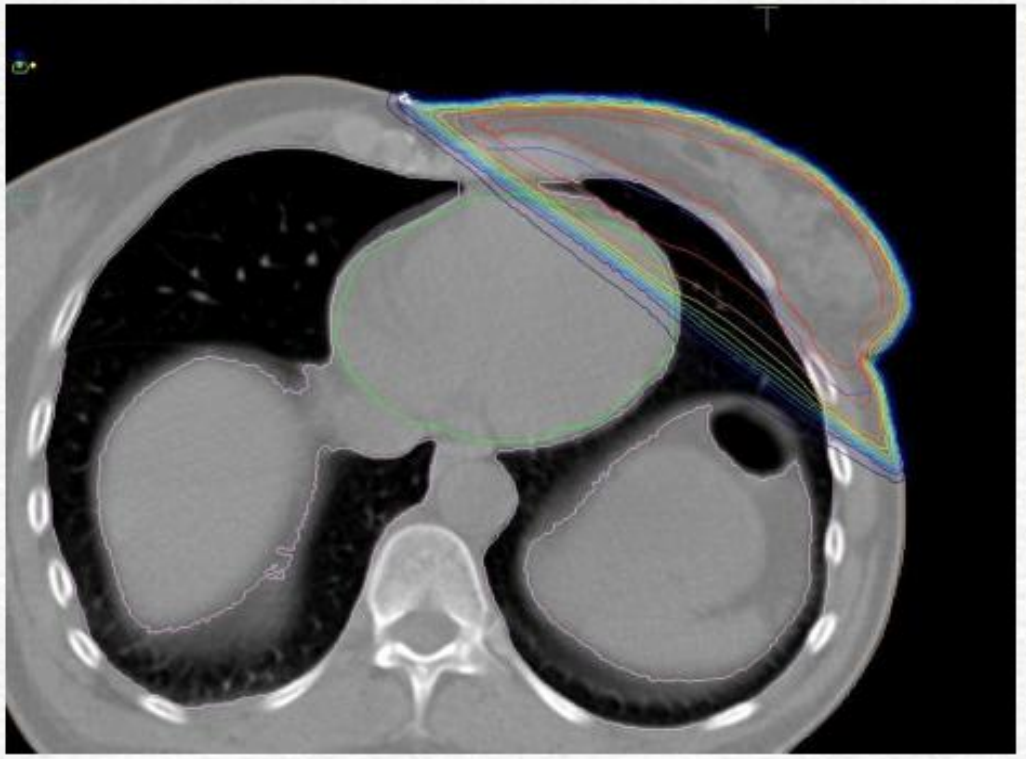

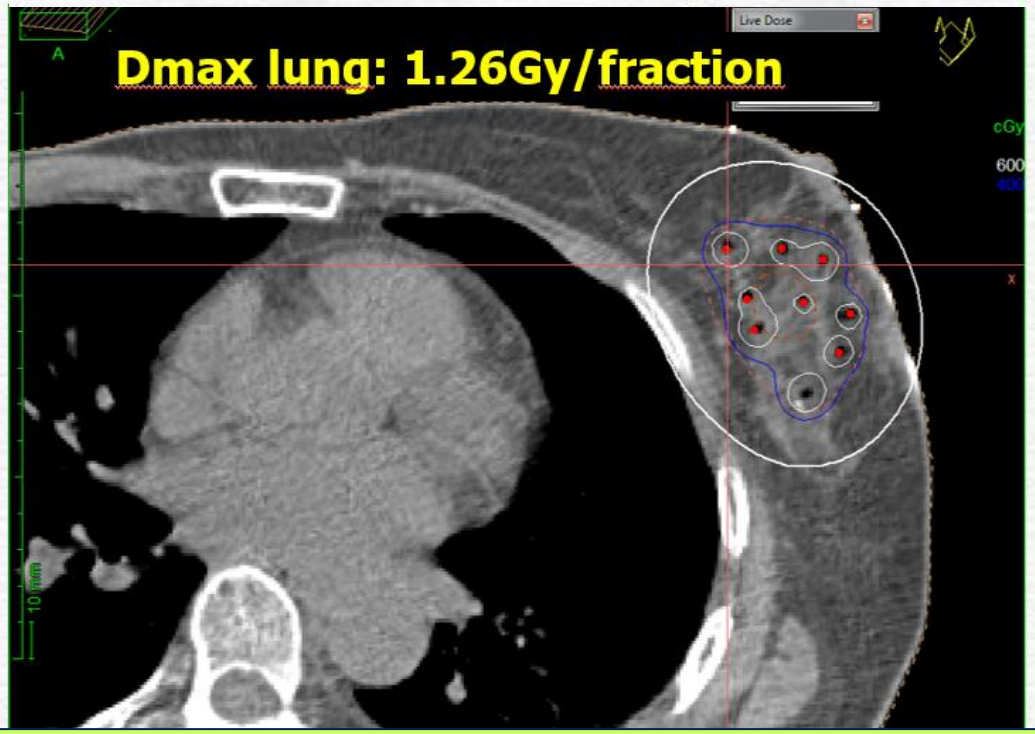

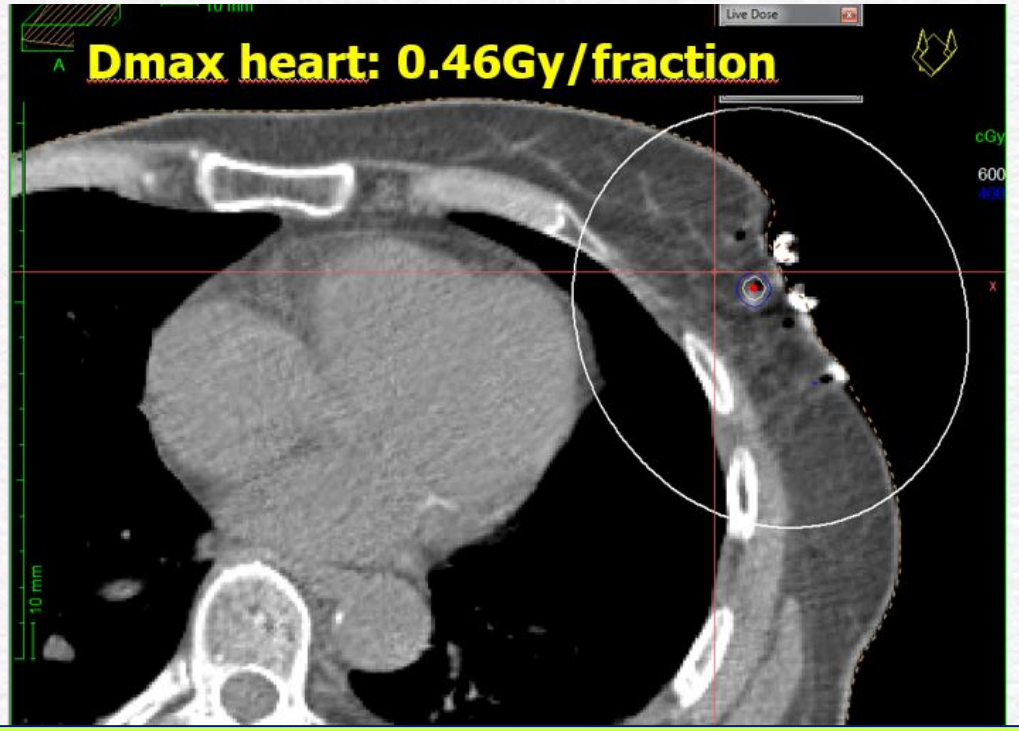

Dose to lung and heart with standard tangential beams and with interstitial BT.

Dose to OAR. Comparison of techniques

	Dose per fraction	Number of fractions	Total time days	Mean dose to lung	Maximum dose to lung	Maximum dose to heart
Standard EBRT	2Gy	25	33-35	11.4Gy	51.75 Gy	49.75 Gy
Hypofrac-tionated EBRT	2.67Gy	16	22	6.41Gy	43.7Gy	42Gy
POBT APBI	4Gy	8	4-5	1.2Gy	14Gy	8Gy

Guinot JL, Samper J, Santamaria P, et al. Doses to organs-at-risk decrease dramatically with multicatheter breast brachytherapy. Clin Transl Oncol 2015 suppl June.

APBI
BRACHYTHERAPY
AS SALVAGE

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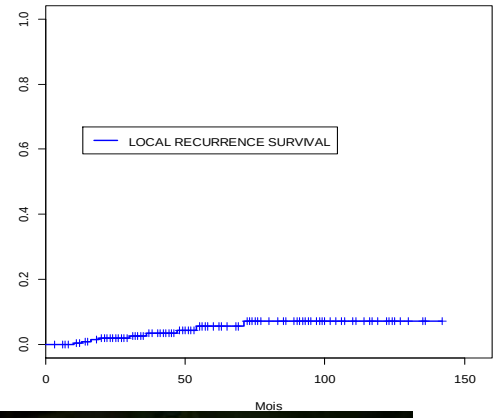
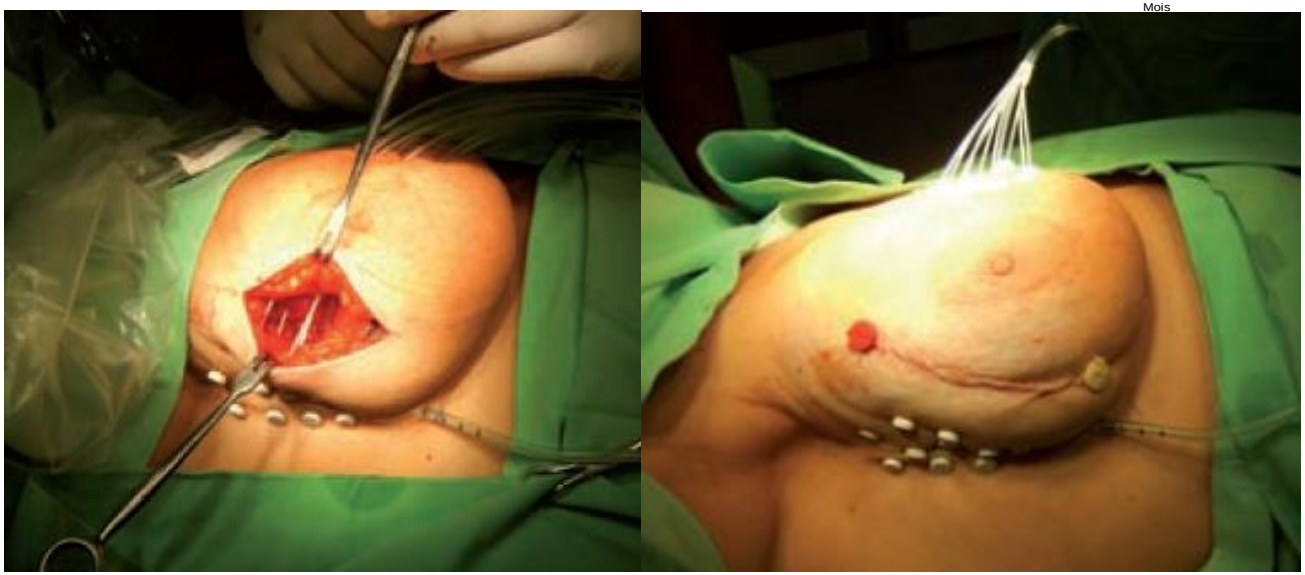
Second Conservative Treatment for Ipsilateral Breast Cancer Recurrence (IBCR): GEC-ESTRO Breast Cancer WG study

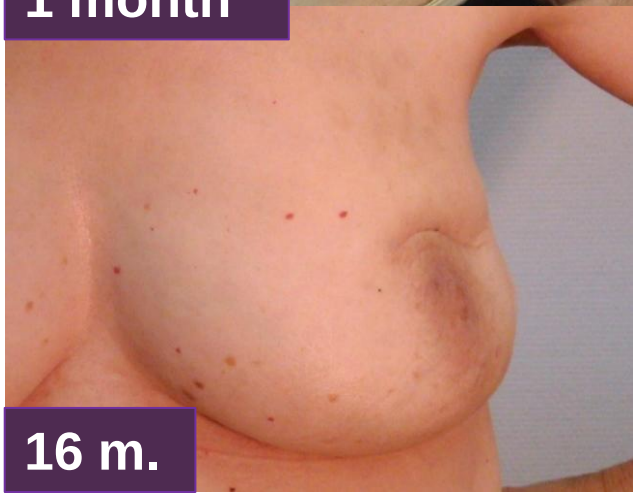
2013

Retrospective study
217 patients 2000-2010
5-year control 94,4%
10-year control 92,8%





1 month



16 m.

The breast can be preserved in more than 90%

Hannoun-Levi JM, et al. Accelerated partial breast irradiation with interstitial brachytherapy as second conservative treatment for ipsilateral breast tumour recurrence: multicentric study of the GEC-ESTRO Breast Cancer WorkingGroup. Radiother Oncol. 2013;108(2):226-31.

CONCLUSIONS

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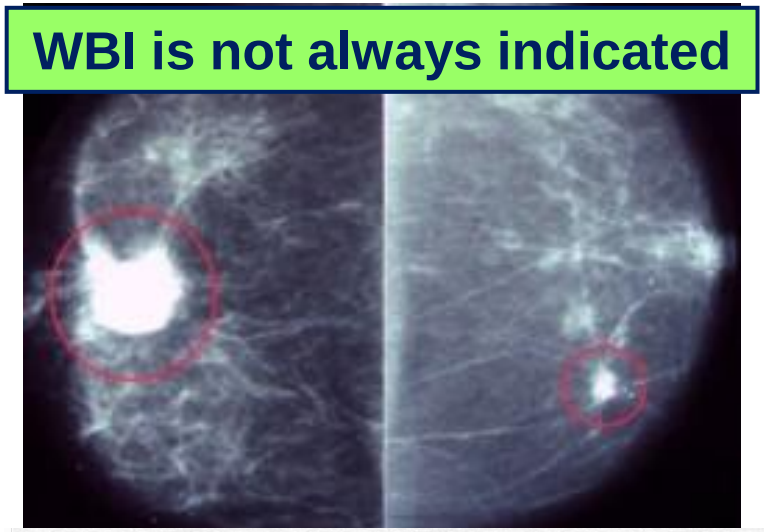
APBI: A new paradigm in low-risk early breast carcinoma

WBI is not always indicated

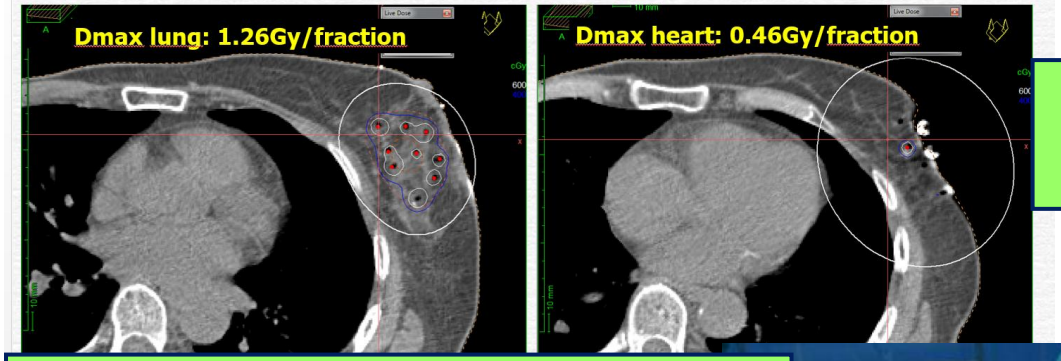


Multicatheter APBI is effective

Less time of treatment

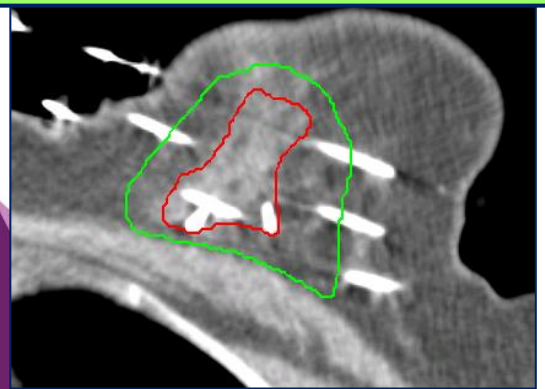
Less late effects

Right breast asimetry by EBRT



Less dose to OAR

Definition of CTV is required



Upper left breast implant APBI

Perioperative APBI is promising

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Accelerated partial breast irradiation: the new standard?

2016

In the near future, the challenge will be to select the most appropriate treatment for the individual patient, and personalise radiation therapy on the basis of tumour biology, tumour size and anatomy, breast anatomy, and individual patient requirements, wishes, and views.

ESTRO

Coles CE,Yarnold JR. Accelerated partial breast irradiation: the new standard? Lancet 2016; 387:201-2

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WWW.ESTRO.ORG/SCHOOL

Image Guided (CT/MR) Adaptive Brachytherapy for Anal Cancer

Erik Van Limbergen MD, PhD.
Dep. Radiation Oncology
University Hospital Gasthuisberg
Leuven/ Belgium

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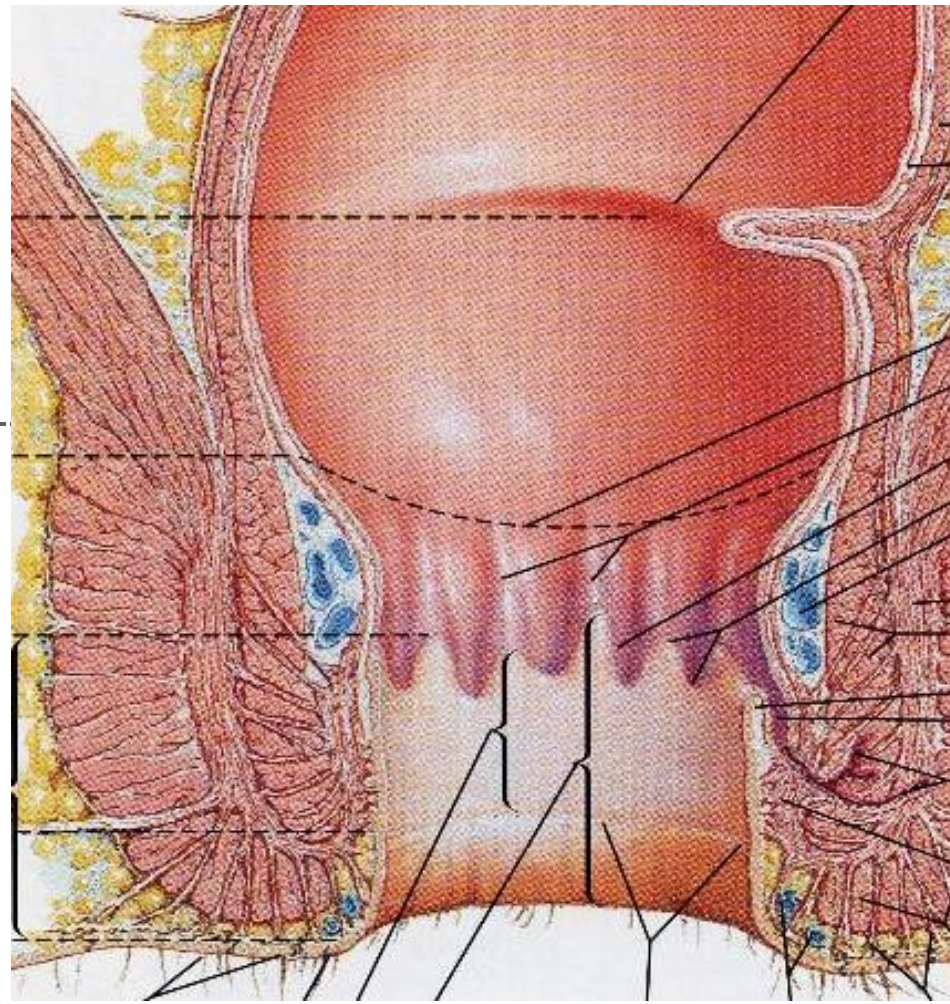
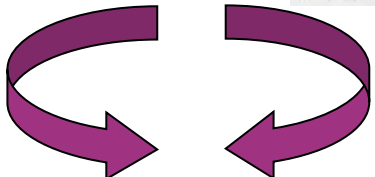
Anatomical Definitions

- **ANAL CANAL** :
  - 3 - 4 cm long
  - from the anorectal junction
  - to the peri-anal skin

  pectinate (dentate) line is at mid-canal



- **ANAL MARGIN** :
  - From the canal –margin junction
  - To the skin (5 cm diameter)



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Which patients benefit from irradiation and concomitant chemotherapy?

		Local Control	Surv. w/o colostomy	Disease spec. Survival	Survival
EORTC	RT only	55 % p = 0,02	40 % p = 0,002		55 % NS
	Radio-chemo	68 %	72 %		57 %
UKCCCR	RT only	39 % p <0,0001		61 % p = 0,02	58 % p = 0,25
	Radio-chemo	61 %		72 %	65 %

Ref. : Bartelink : J Clin Oncol 1997;5:2040-2049
: UKCCCR : Lancet 1996;348:1049-1054

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Decision to boost

- **Yes** if exclusive irradiation

- If Radio-Chemotherapy
  - Early stages: NO/YES
  - Large tumors or poor responders:YES

Radiotherapy and Oncology 87 (2008) 367–375
www.thegreenjournal.com

Anal cancer

Radiation dose associated with local control in advanced anal cancer: Retrospective analysis of 129 patients

Joachim Widder[a,b,*], Reinhard Kastenberger[a], Elisabeth Fercher[a], Rainer Schmid[a], Johannes A. Langendijk[b], Werner Dobrowsky[c], Richard Pötter[a]

[a]*Department of Radiotherapy, Medical University of Vienna, Austria,* [b]*Department of Radiotherapy, University Medical Centre Groningen, Groningen, The Netherlands,* [c]*Northern Centre of Cancer Treatment, Newcastle, UK*

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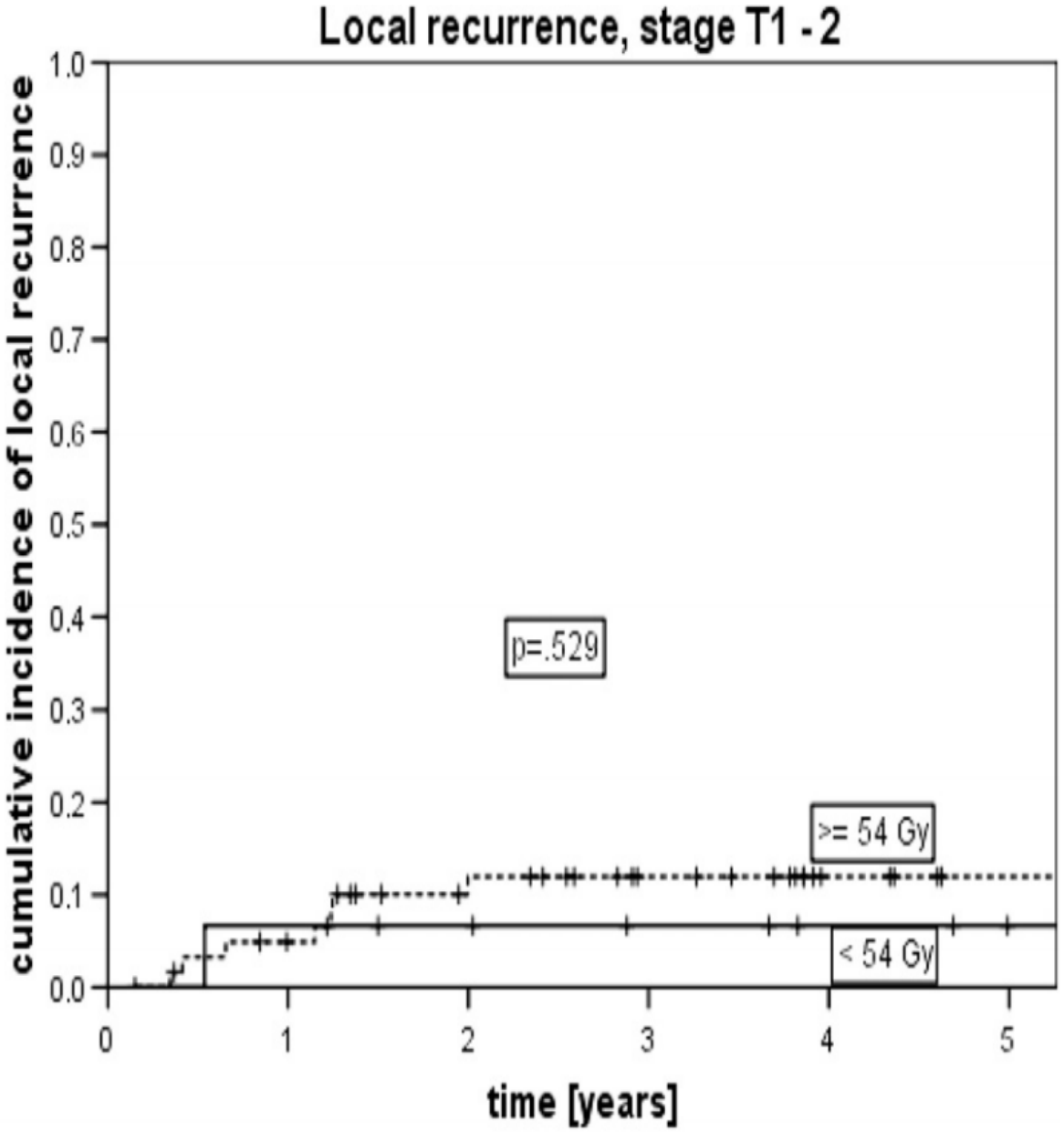
Widder 2008 LC ifo Dose



at risk, >= 54 Gy:	62	56	46	39	30	26
at risk, < 54 Gy:	16	14	13	11	9	7

Fig. 1. Local recurrence, stage T1–2.

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Widder 2008 LC ifo Dose

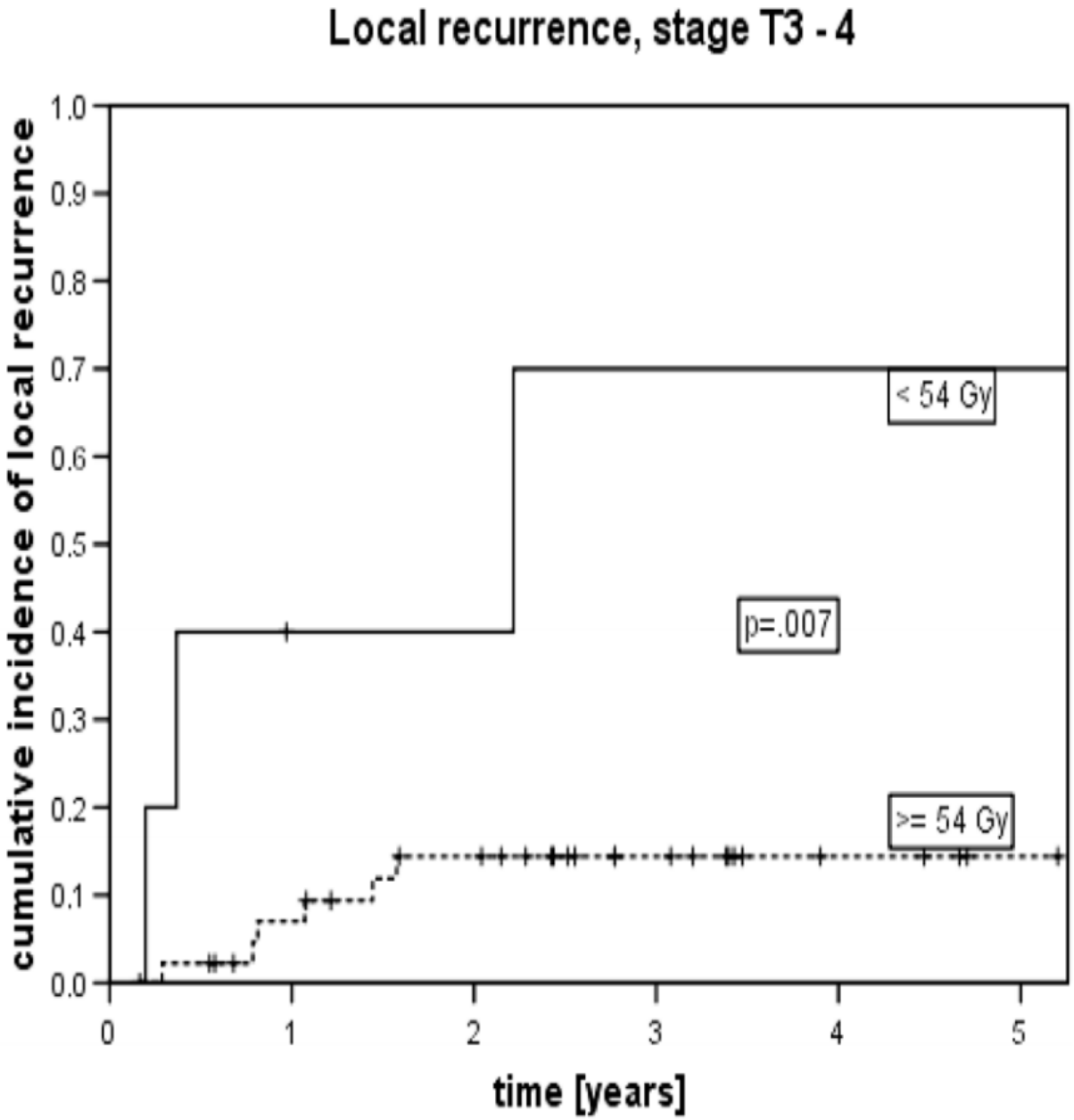

Fig. 2. Local recurrence, stage T3–4.

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UNICANCER
ACCORD 03 Trial

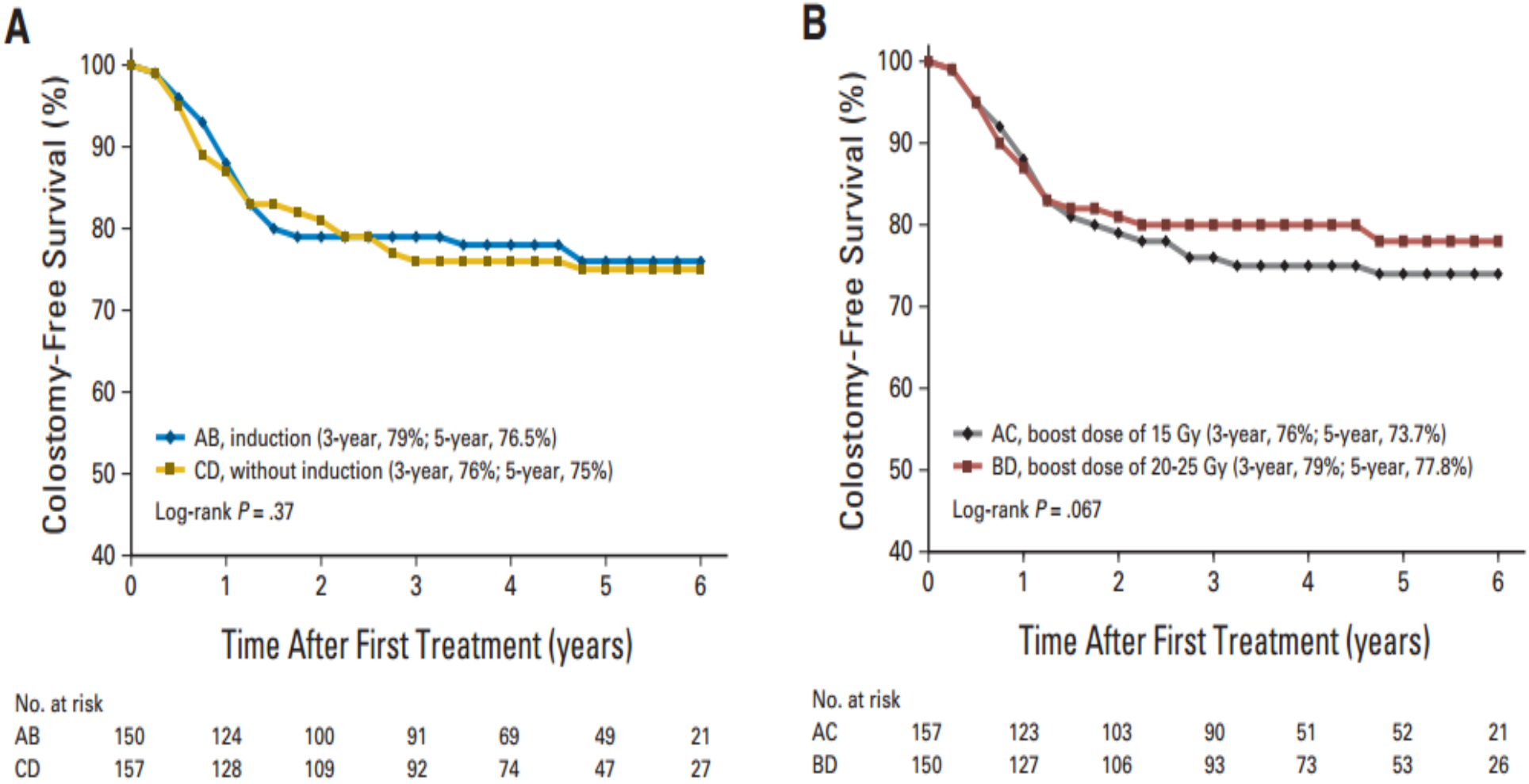

Fig 3. Actuarial colostomy-free survival. (A) Groups A+B versus groups C+D and (B) groups A+C versus groups B+D.

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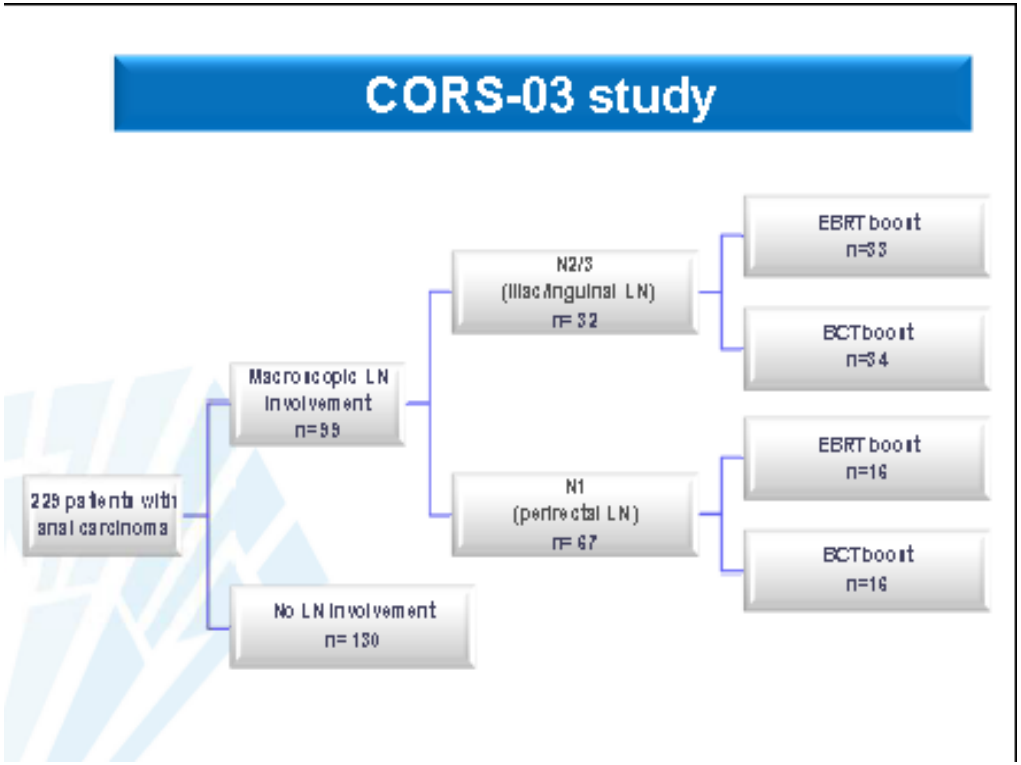
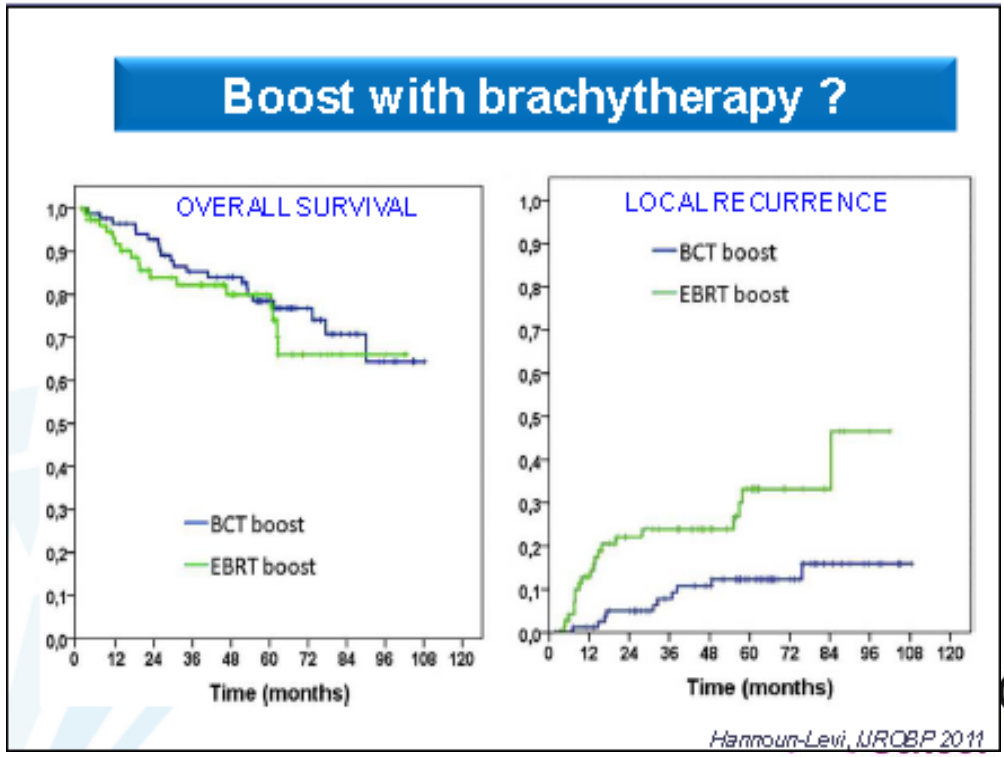
Boost: External RT or brachytherapy?





Impact of brachy

Local reccurence

I. J. Radiation Oncology ● Biology ● Physics Volume 80, Number 3, 2011

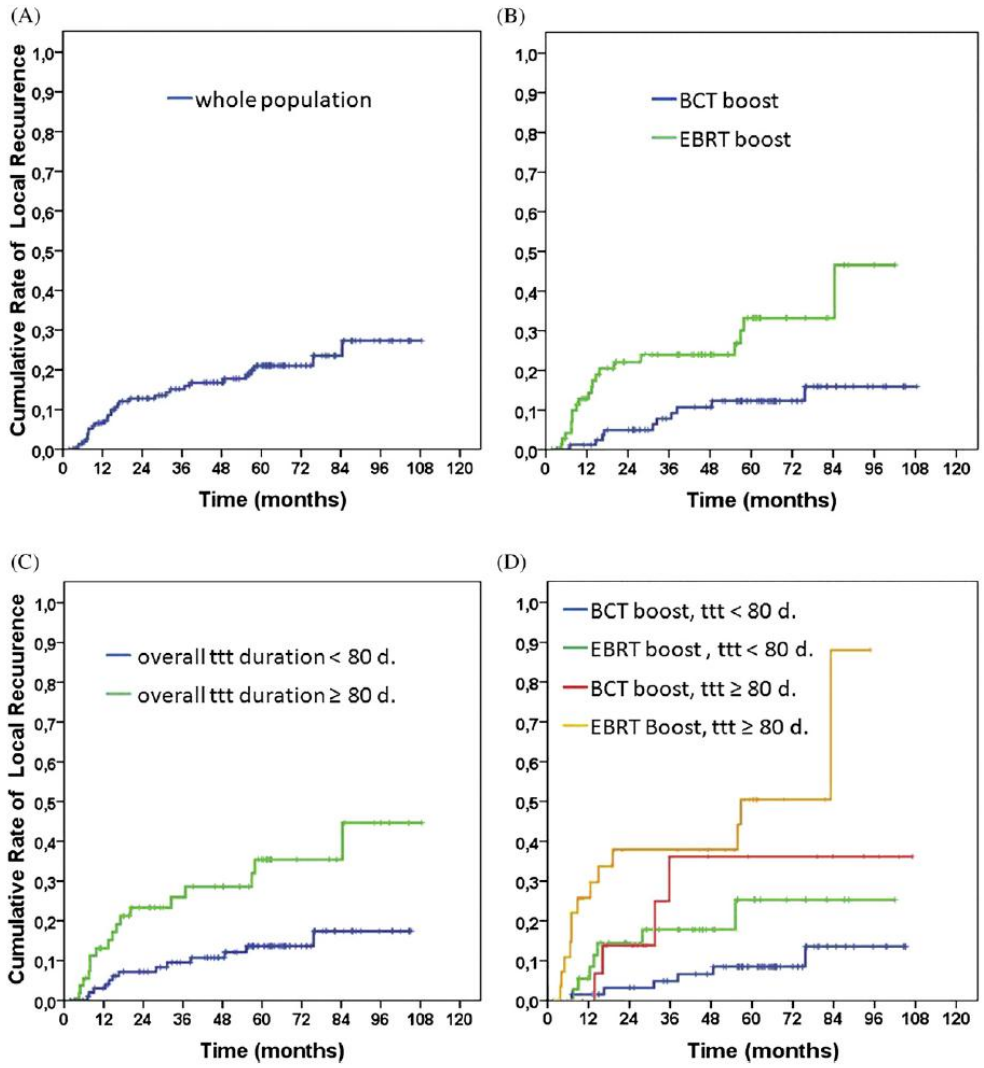


Fig. 3. Cumulative rate of local recurrence for the whole population (A), regarding the boost technique: brachytherapy (BCT) vs. external-beam radiotherapy (EBRT) (B), regarding the overall treatment time (<80 days vs. ≥80 days) (C), and combining boost technique and overall treatment time (D).

survival

I. J. Radiation Oncology ● Biology ● Physics Volume 80, Number 3, 2011

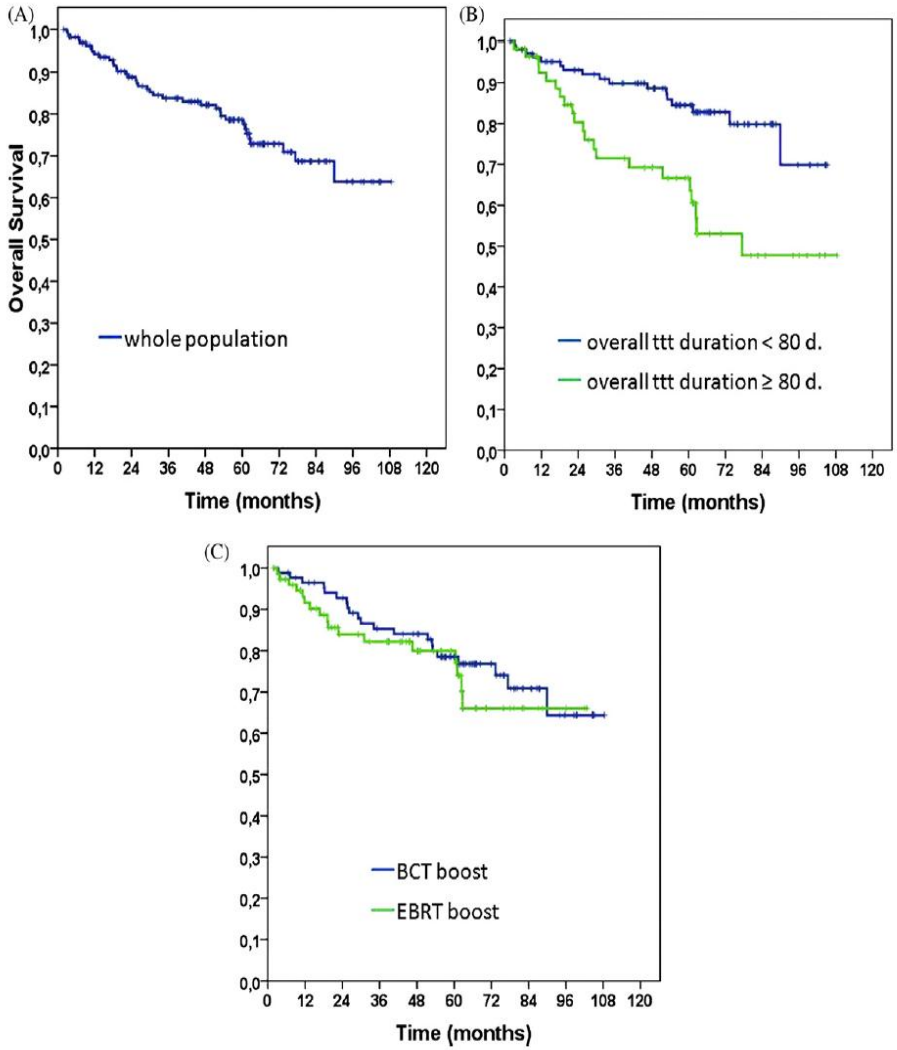


Fig. 2. Overall survival for the whole population (A), regarding the overall treatment time < 80 days vs. ≥80 days (B), according to the boost technique: brachytherapy (BCT) vs. external-beam radiotherapy (EBRT) (C).

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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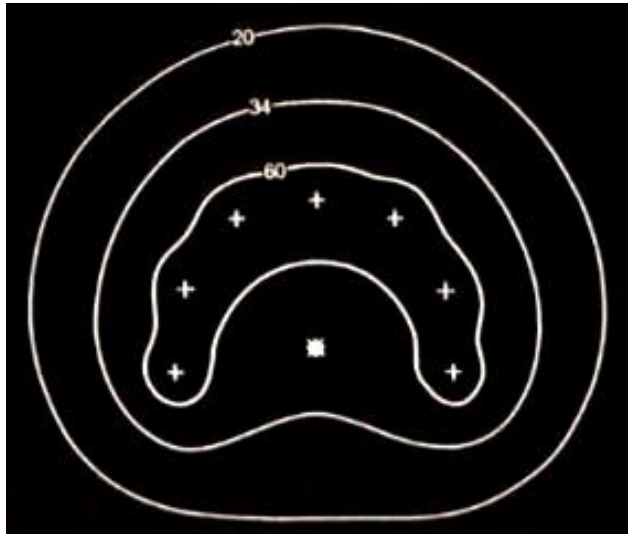
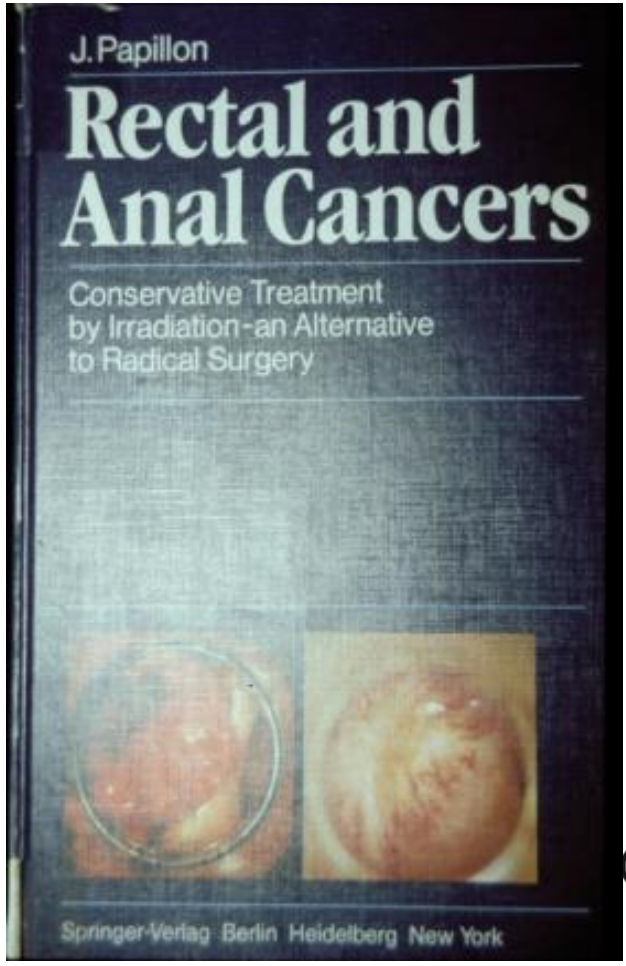
Goals of brachy in Anal Ca



- Reduce overall treatment time
- Increase the dose to improve local control
- On a small volume`
  - To reduce the risk of necrosis and stenosis
- Spare the controlateral sphincter
  - To increase the functional results



Indications of Brachytherapy

- 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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Classical treatment strategy of Anal Ca at UZLeuven

FUMIRT 45 Gy followed by BT boost

15 Gy PDR when CR

20 Gy PDR when PR

Surgery when SD or PD

BT CTV delineated by clips and Tattoos to reduce the treated volume at BT

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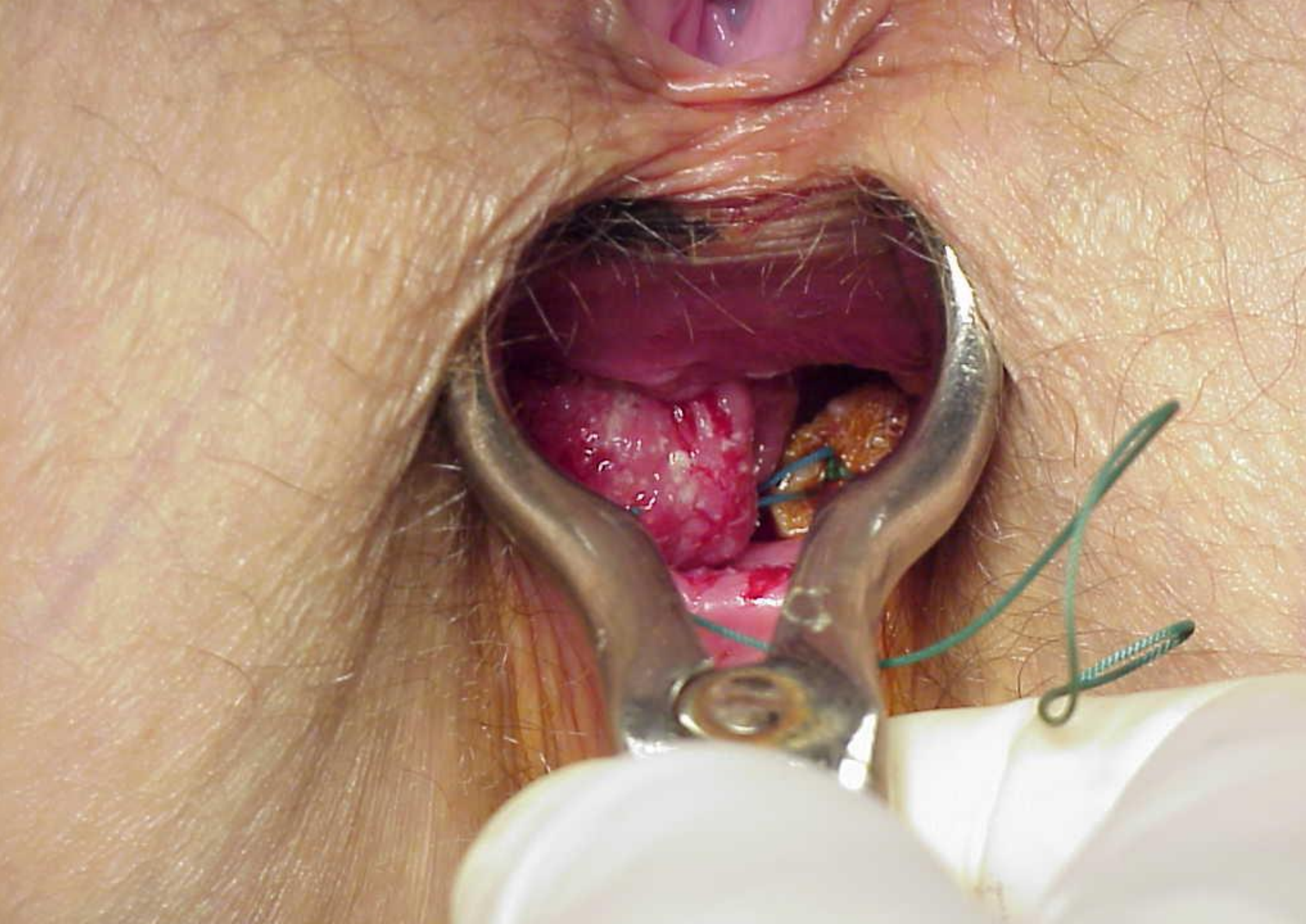
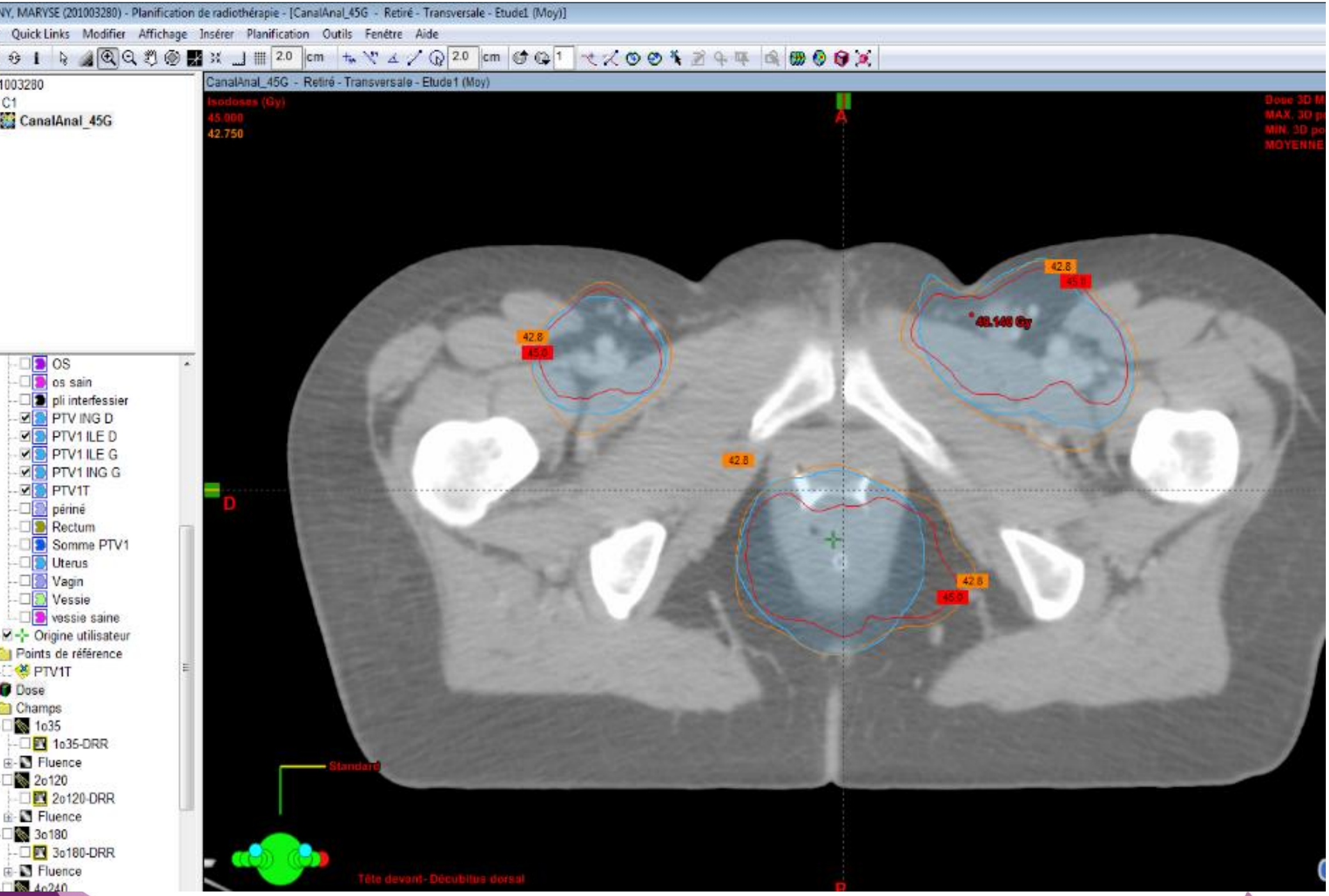
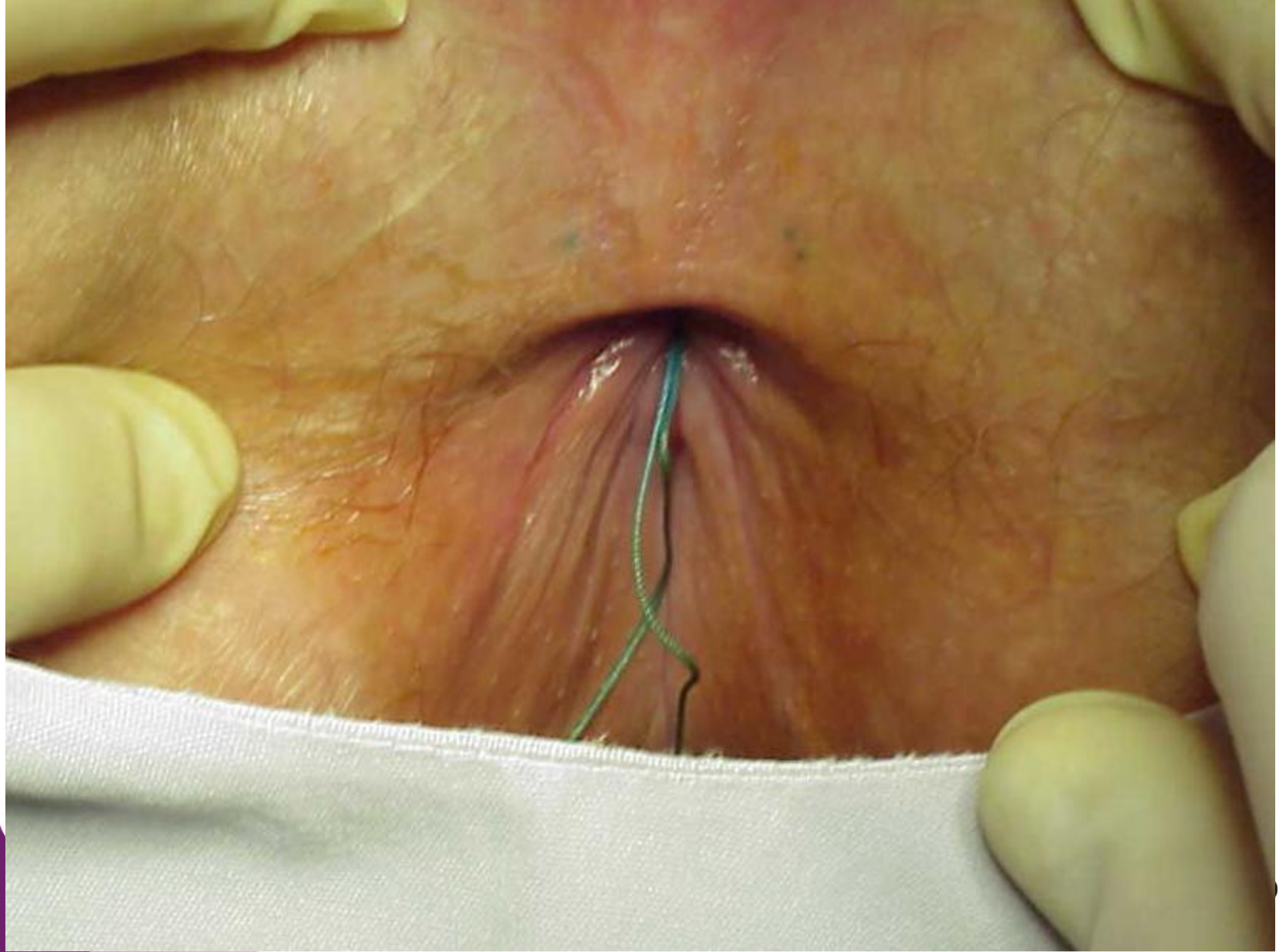
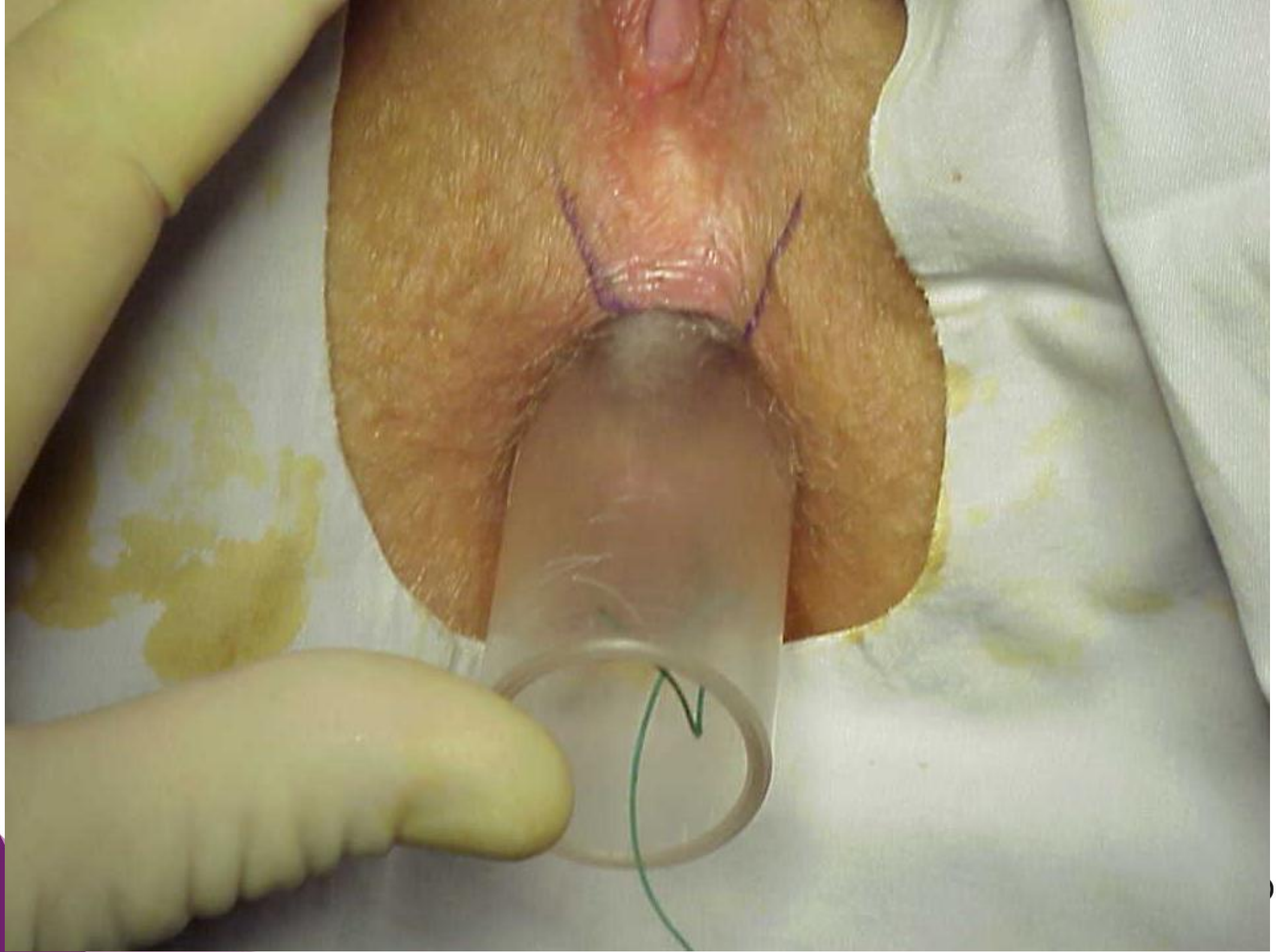
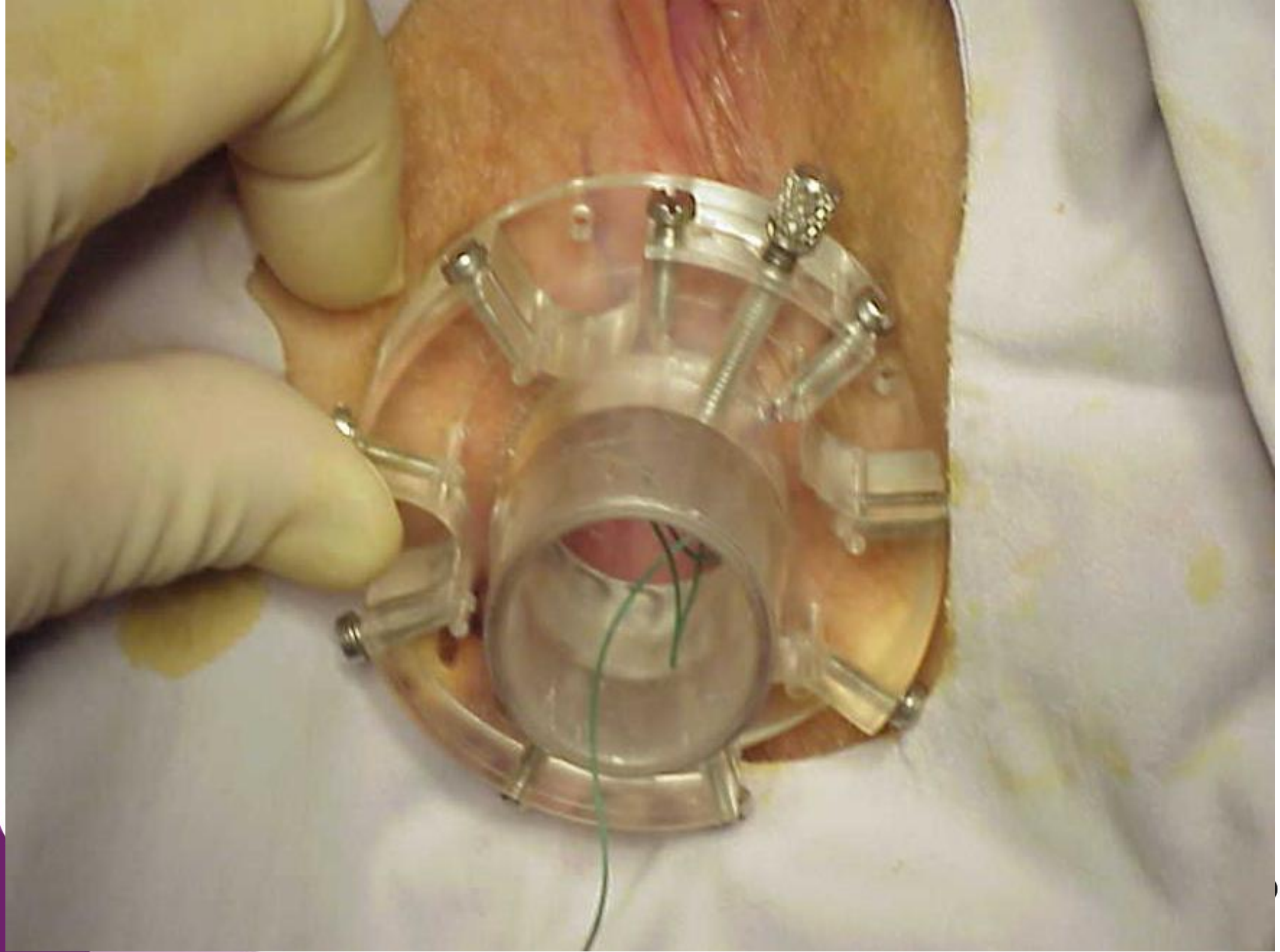
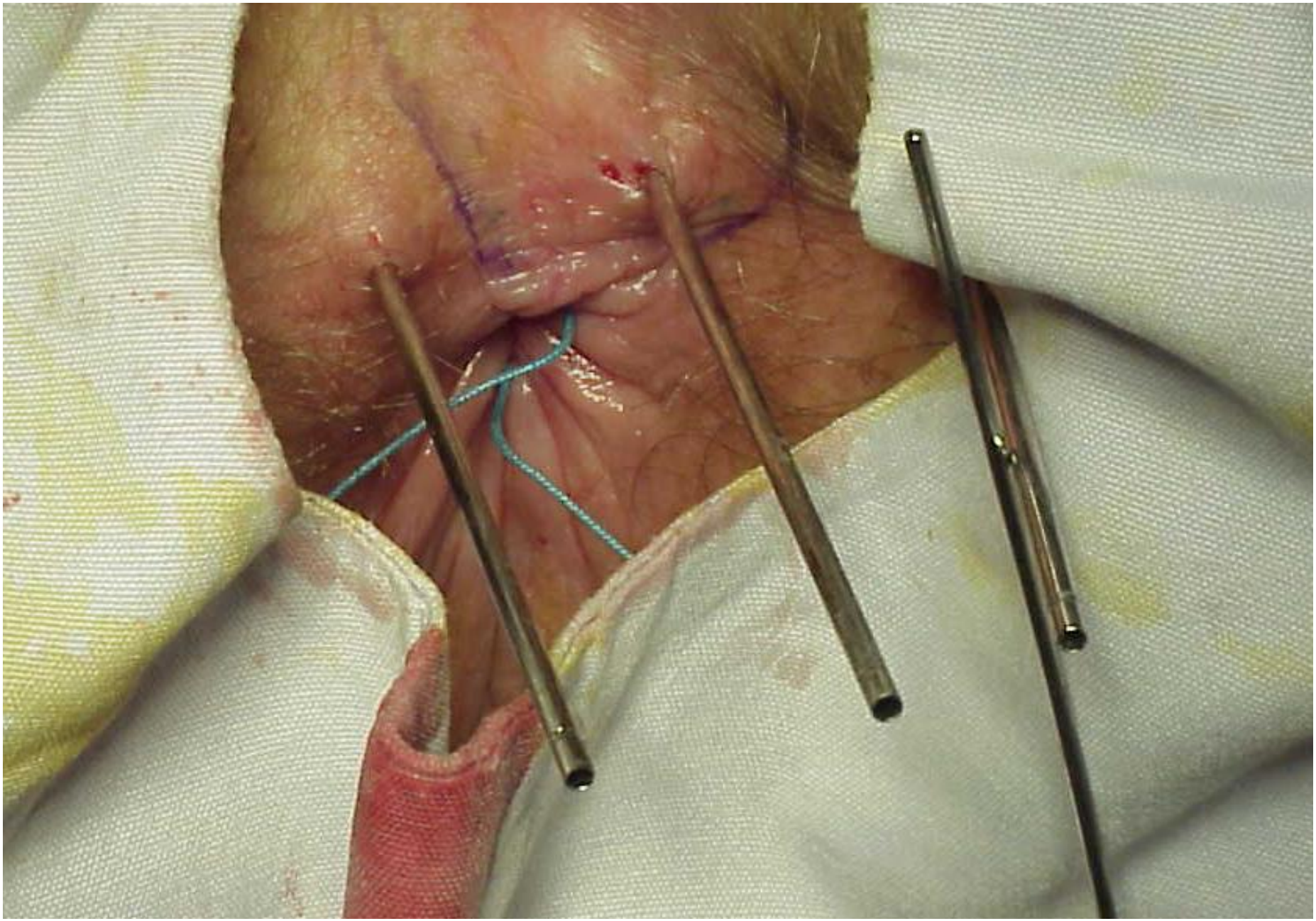


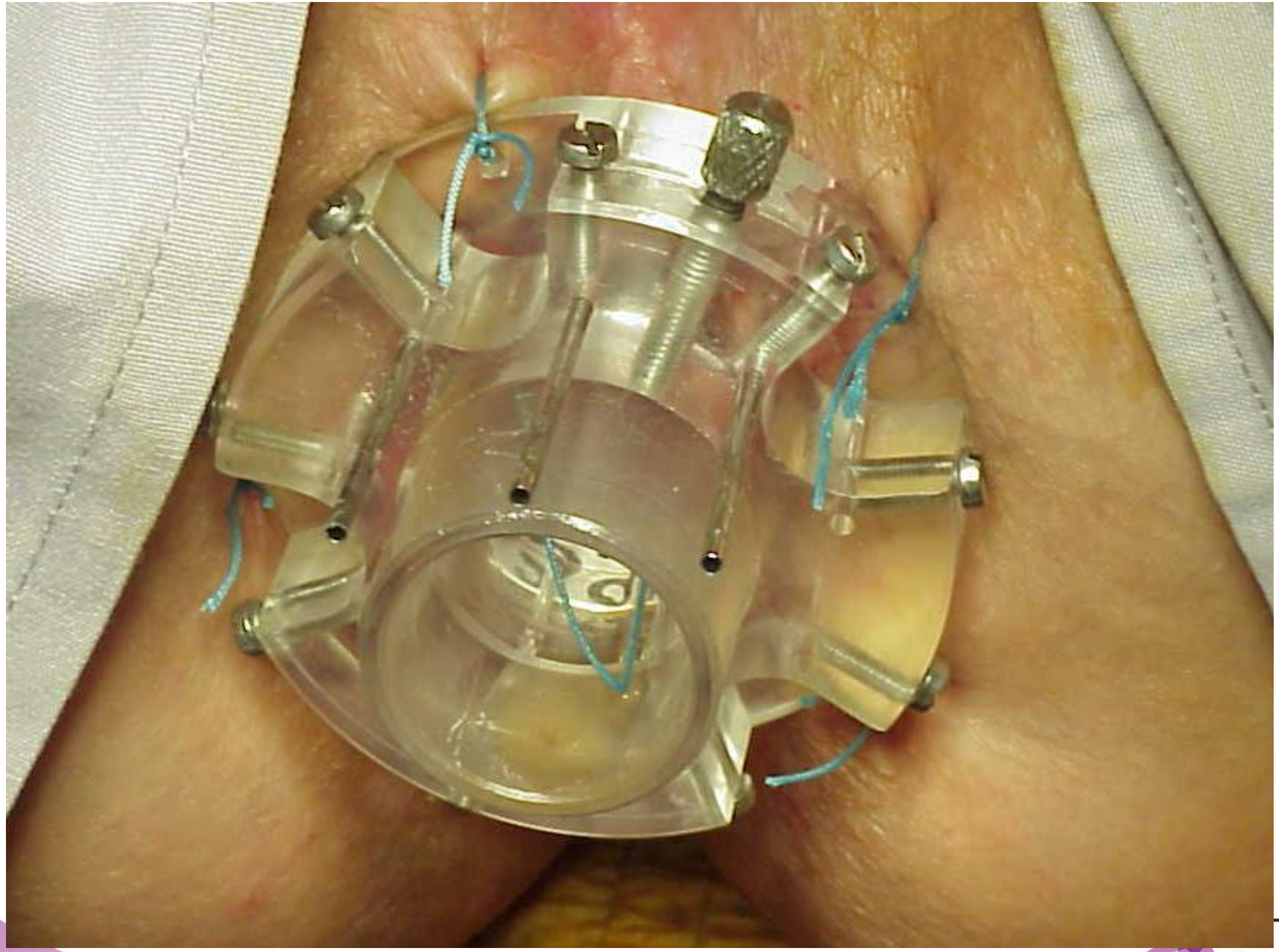

NY, MARYSE (201003280) - Planification de radiothérapie - [CanalAnal_45G - Retiré - Transversale - Etude1 (Moy)]
Quick Links Modifier Affichage Insérer Planification Outils Fenêtre Aide
CanalAnal_45G - Retiré - Transversale - Etude1 (Moy)
Isodoses (Gy)
45.000
42.750
CanalAnal_45G
OS
os sain
pli interfessier
PTV ING D
PTV1 ILE D
PTV1 ILE G
PTV1 ING G
PTV1T
périné
Rectum
Somme PTV1
Uterus
Vagin
Vessie
vessie saine
Origine utilisateur
Points de référence
PTV1T
Dose
Champs
1o35
1o35-DRR
Fluence
2o120
2o120-DRR
Fluence
3o180
3o180-DRR
Fluence
4o240
42.8
45.0
42.8
45.0
42.8
42.8
45.0
Standard
Tête devant - Décubitus dorsal

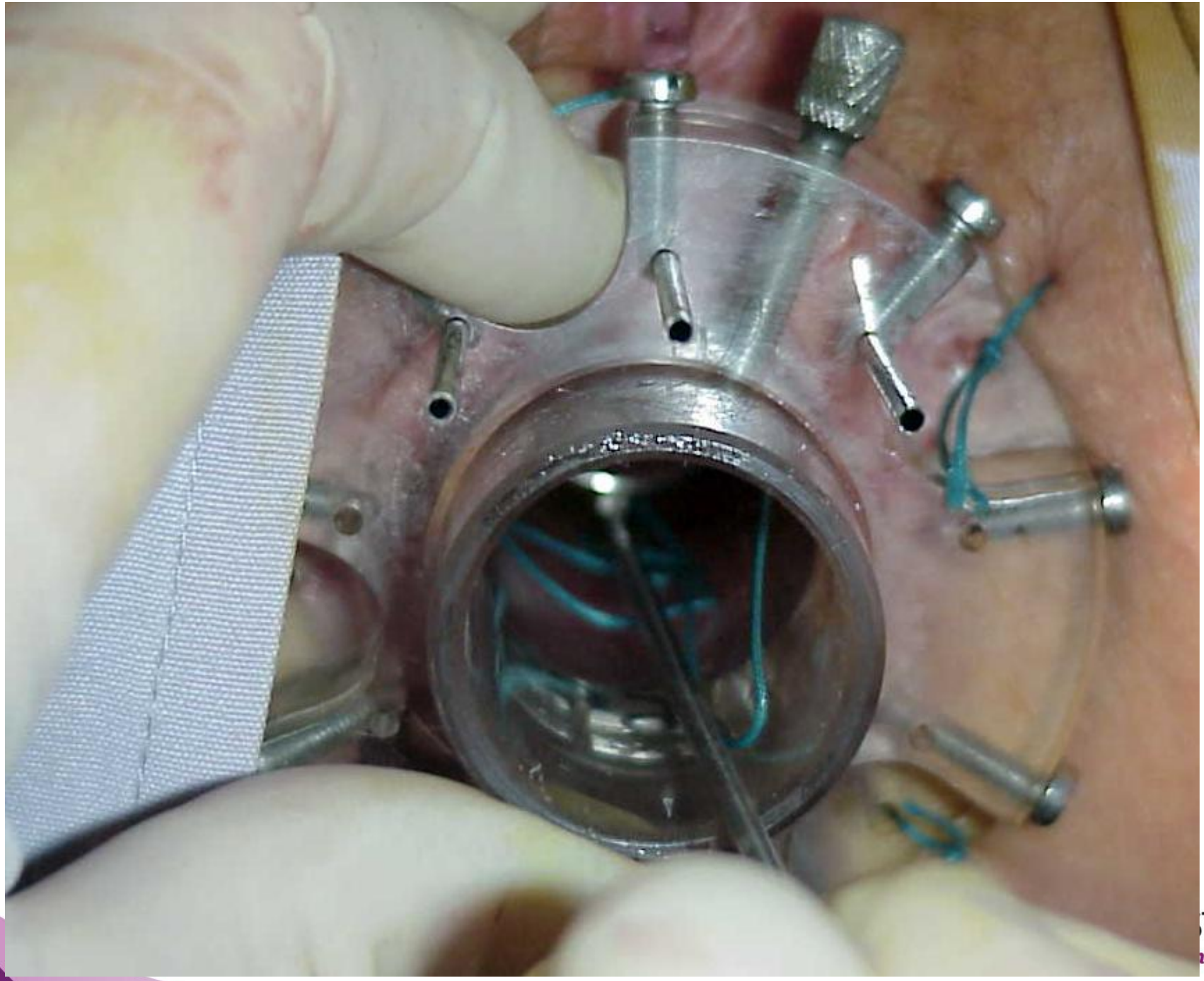












Anal Canal SCC UZL 1986-2001

- 48 pts T1-3 SCC UZLeuven 1986-2001

Pattern of failure SPINO	Local failure	Locoreg. failure	Distant failure	OS	Colostomy	Colostomy free survival
RT	7/17 (41%)	7/17 (41%)	5/17 (29%)	9/17 (53%)	3/17 (17%)	10/17 (59%)
RT + chemo	4/31 (13%)	8/31 (26%)	5/31 (16%)	22/31 (71%)	1/31 (3%)	26/31 (84%)
p-value	**0.02**	0.1	0.2	0.1		**0.04**

Geboers et al 2003

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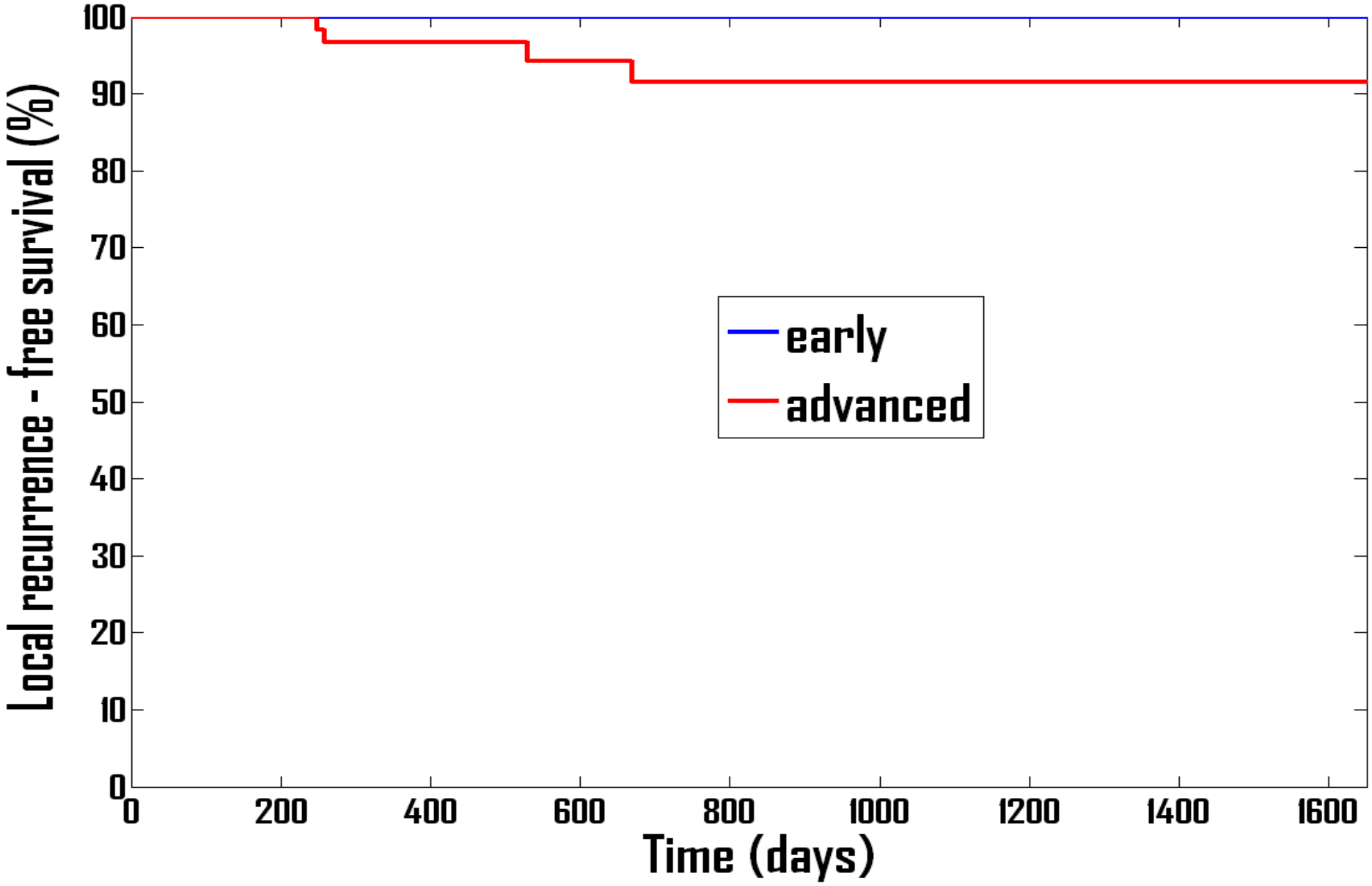
UZ Leuven 1986-2001 complications in 86 Anal SCC and Adenoca

- 10 /86 incontinence (G1,G2)
- 13 Flatulence
  - 9 mild (Gr 1)
  - 4 moderate (Gr 2)
- 34 Proctitis
  - 29 Gr 1 (not requiring medication)
  - 4 Gr 2 (requiring medication)
  - 1 Gr 3 (requiring transfusion) / BRT + CT

UZLeuven PDR series:83 pts



Van Brussel S, Janssen H , Van Limbergen E 2011

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Drawbacks of the Technique

- Tattoos very helpfull but may disappear
- Clips not always easily to position in the rigth place
- Clips may disappear or migrate to unrelevant positions
- CT not helpfull for delineating the GTV/CTV

Extremely good experiences with MRI Guided Adaptive BT for Cervixcancer stage I to IVa :

(96,4% local control at 10 y)

(Ribeiro et all RT&O 2016)

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MRI guided BT protocol

- Started in 2007
- MRI , PETCT at diagnosis
- Examination under general anesthesia , tattooing and placing of minimum 4clips
- CLINICAL Drawing
  - Clockwise location of tumorboarders
  - Measuring distances +/- from anal margin

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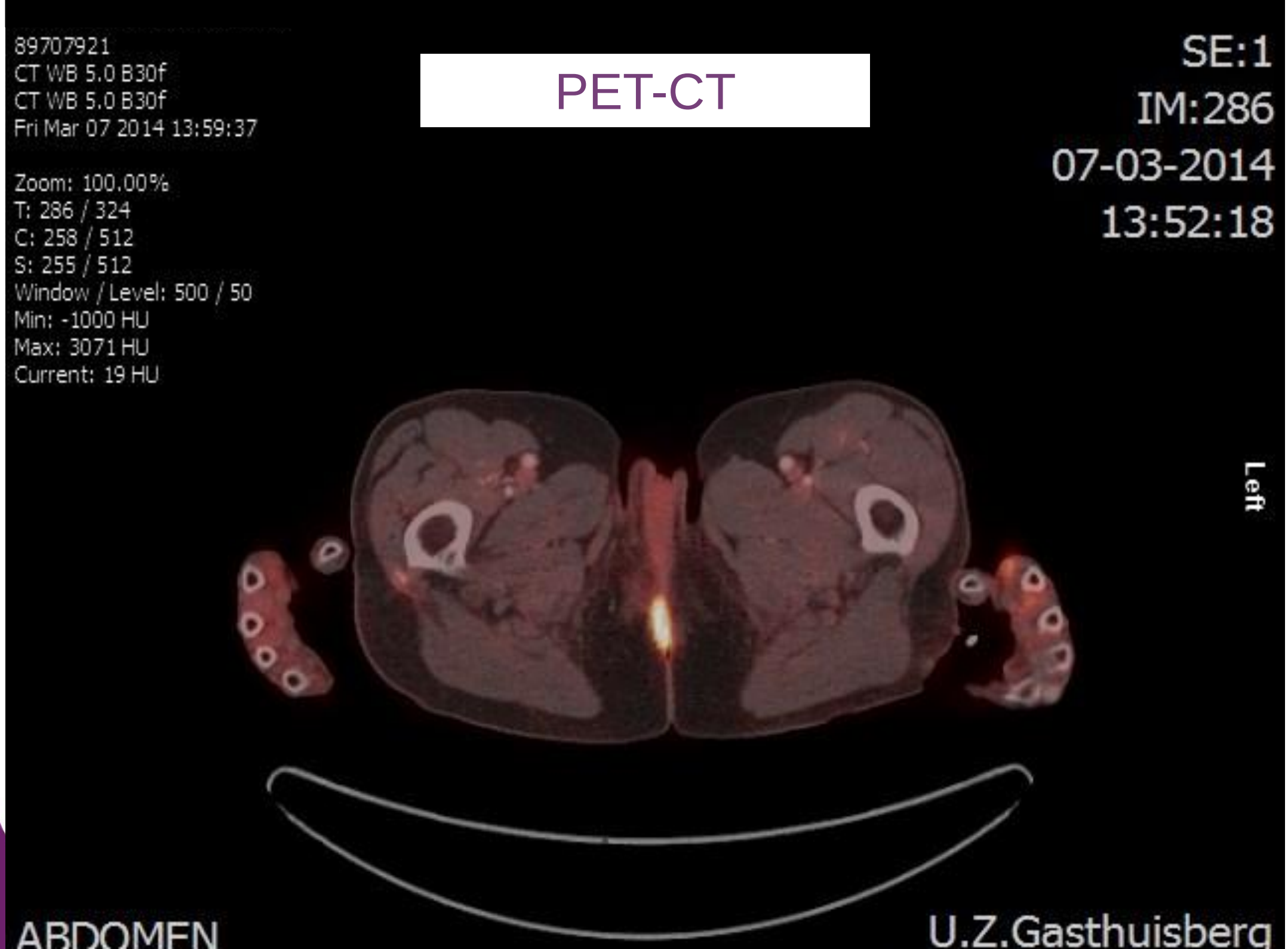
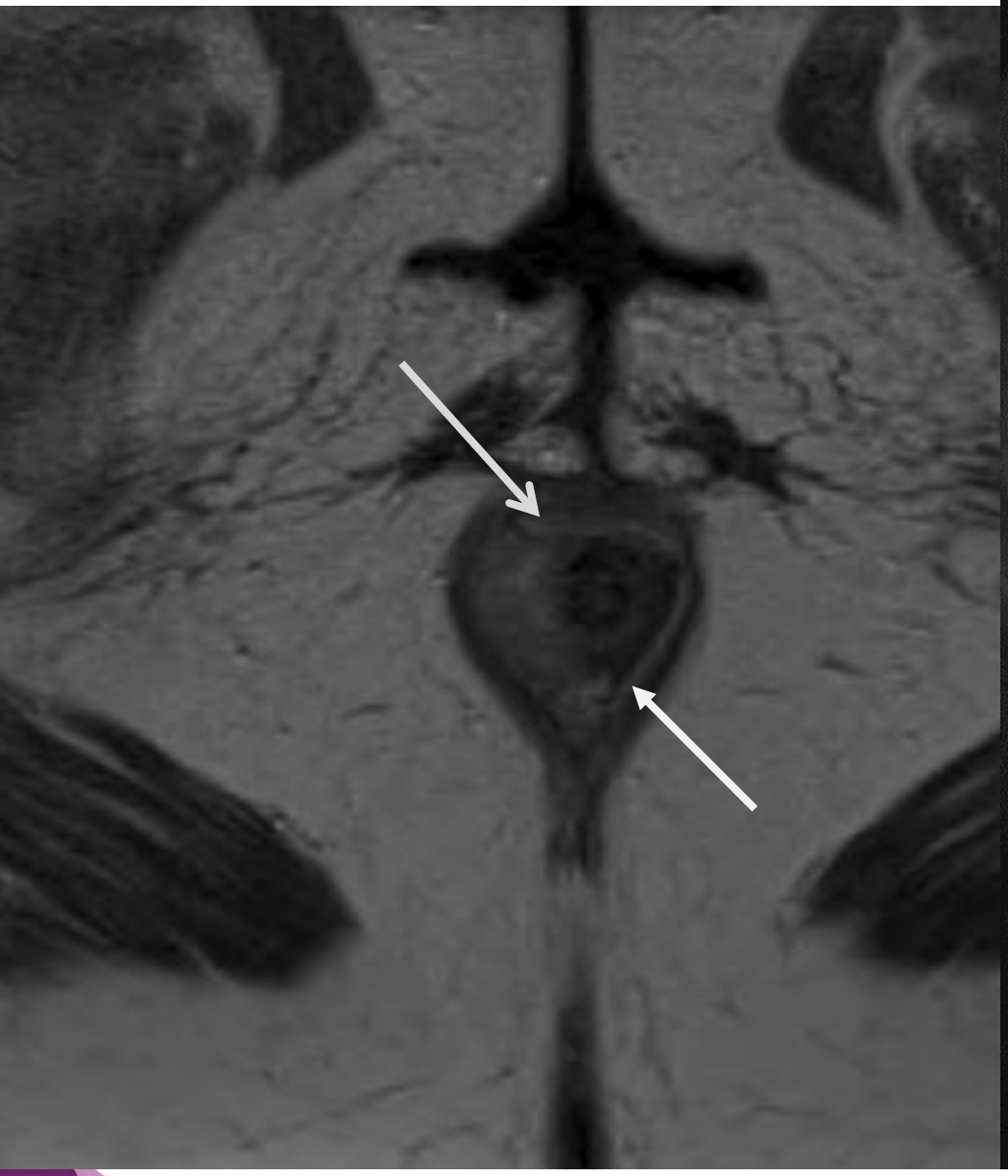
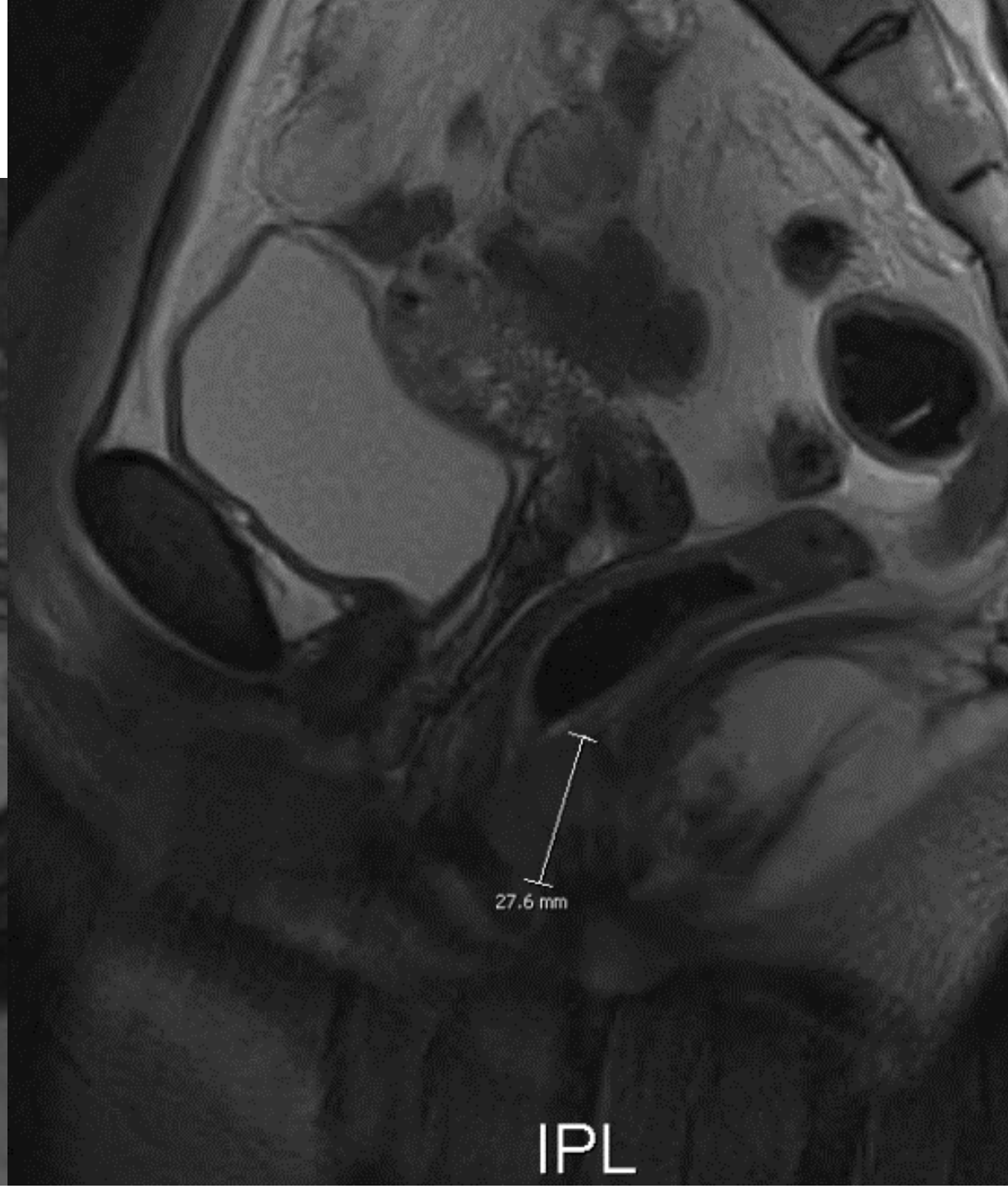
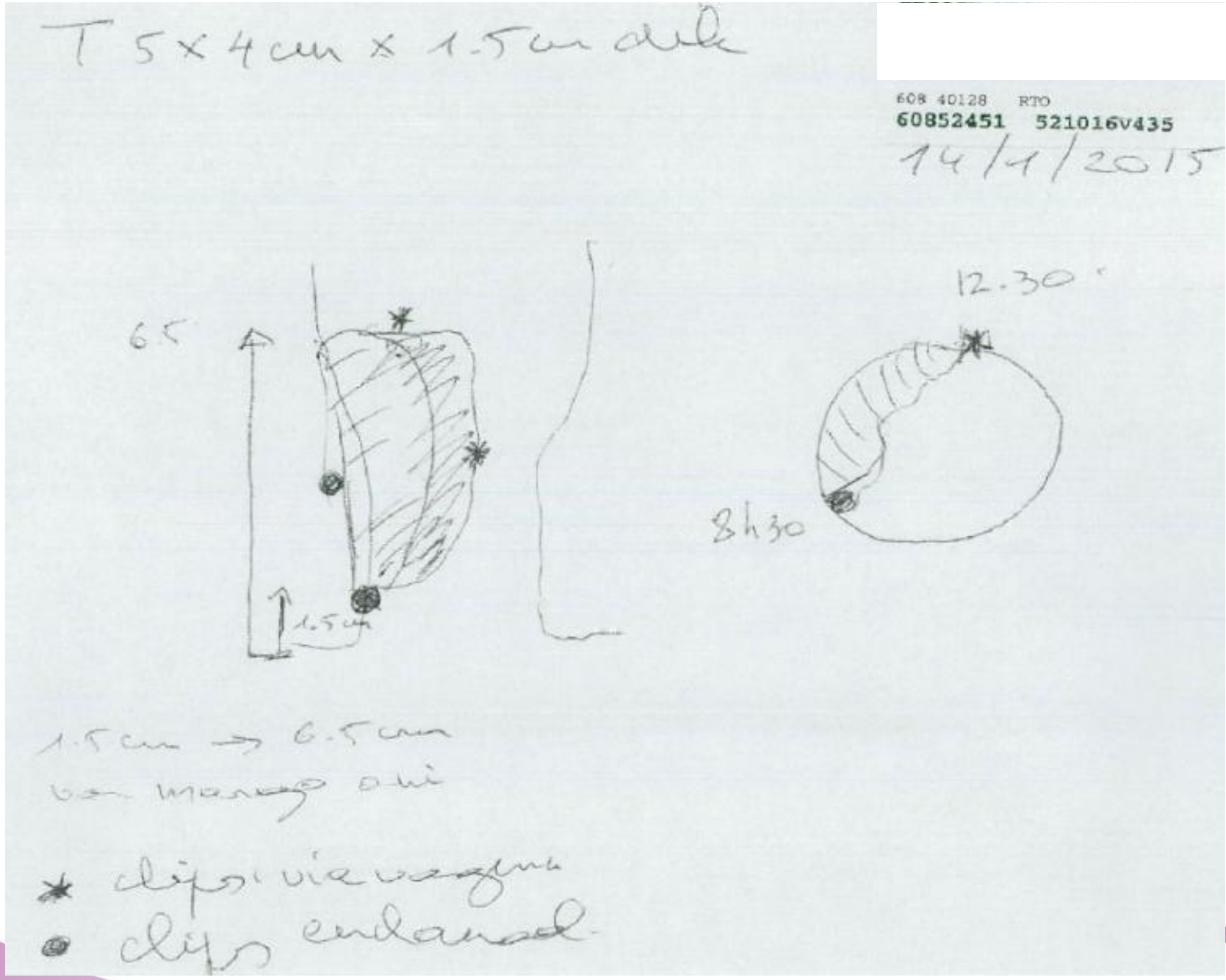

89707921
CT WB 5.0 B30f
CT WB 5.0 B30f
Fri Mar 07 2014 13:59:37
Zoom: 100.00%
T: 286 / 324
C: 258 / 512
S: 255 / 512
Window / Level: 500 / 50
Min: -1000 HU
Max: 3071 HU
Current: 19 HU
PET-CT
SE:1
IM:286
07-03-2014
13:52:18
Left
ABDOMEN
U.Z.Gasthuisberg

MRI PRE RCT





Examination under General Anesthesia



Delineation GTV / High Risk CTV

Dose Planning

HR-CTV

15 Gy

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ESMO / ESSO/ESTRO guidelines 2014

Brachytherapy

Brachytherapy is a highly conformal treatment which is able to deliver a high dose to the primary tumour, sparing surrounding normal tissues and the contralateral mucosa and sphincter. Expertise for iridium-192 interstitial implantation is limited to a few European institutions. Low-dose rate, high dose rate (HDR) and pulsed dose rate brachytherapy have been tested in clinical practice. There are currently limited data on the use of HDR brachytherapy in anal cancer and lack of consensus on the optimal fractionation schedule. Curative brachytherapy as a single modality is not recommended, but may be applicable as a boost following response to CRT. Double-plane, or volume implants may be necessary, depending on the extent of the tumour, but risk late necrosis and radiation proctitis. Computerised 3-dimensional image-based treatment planning should allow optimal dose distribution.

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Conclusion BT Anal Ca

- Highly conformal technique to boost
- Small volumes
- Able to spare most of the non uninvolved anus
- Precision depending on (combination of) technique(s)
- LDR / PDR proven efficacy
  HDR under investigation

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Cervix

Indication, tools and requirements, techniques, performing application

Peter Hoskin

Mount Vernon Cancer Centre

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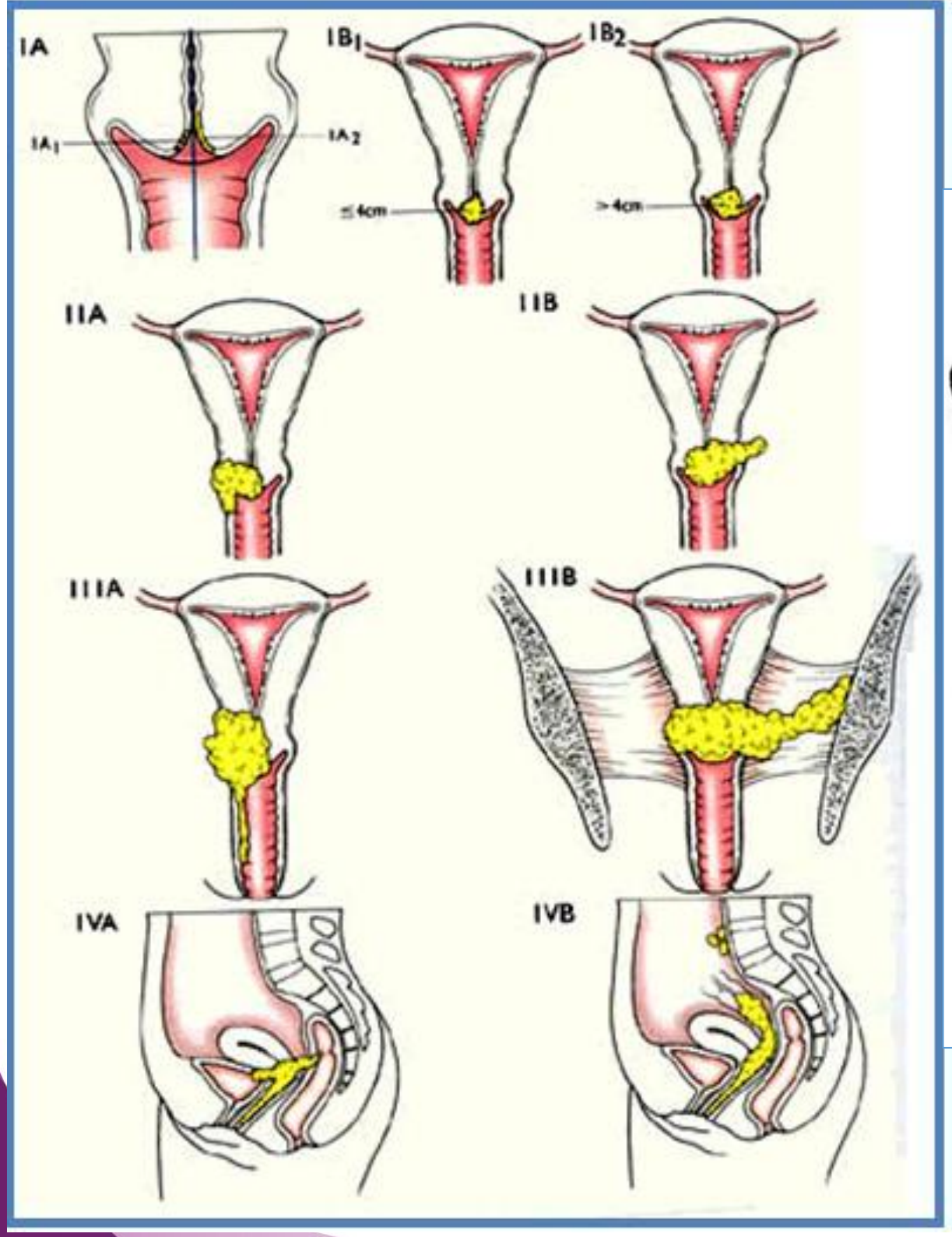
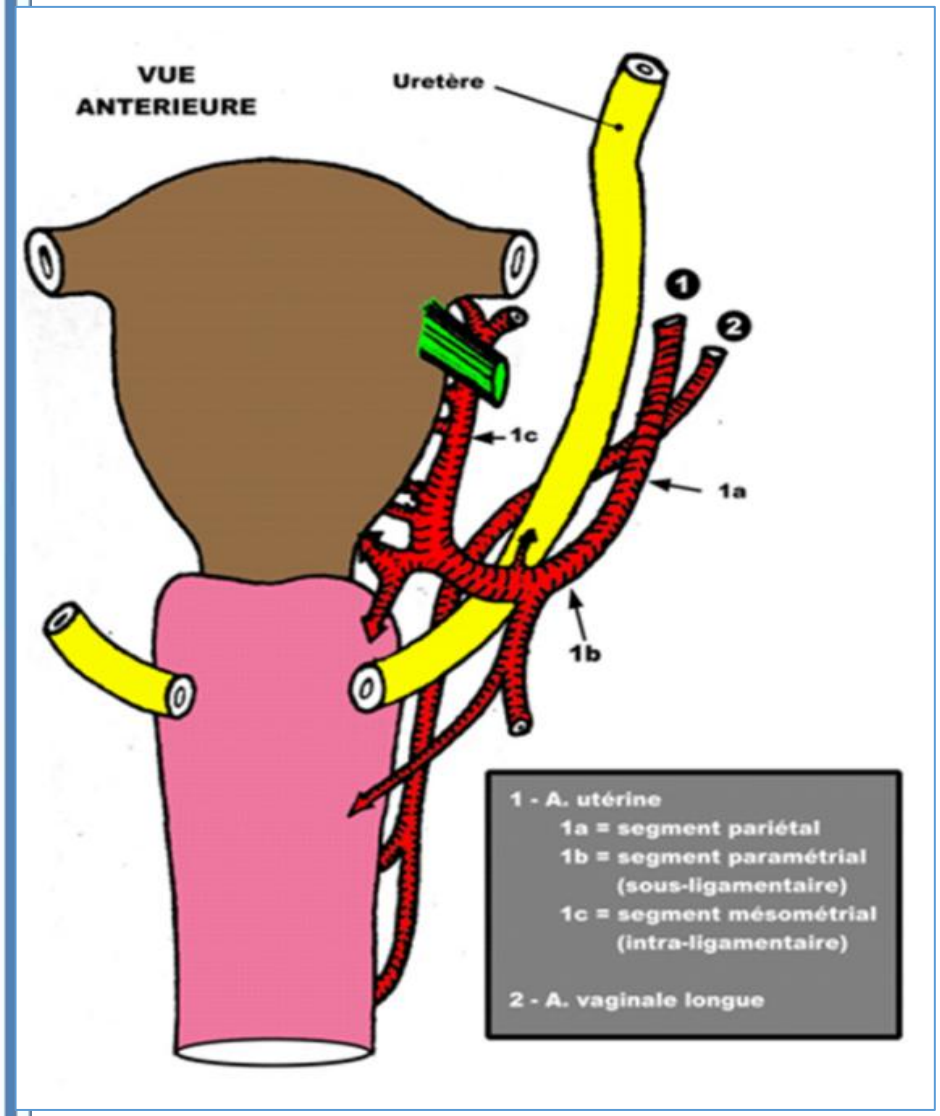
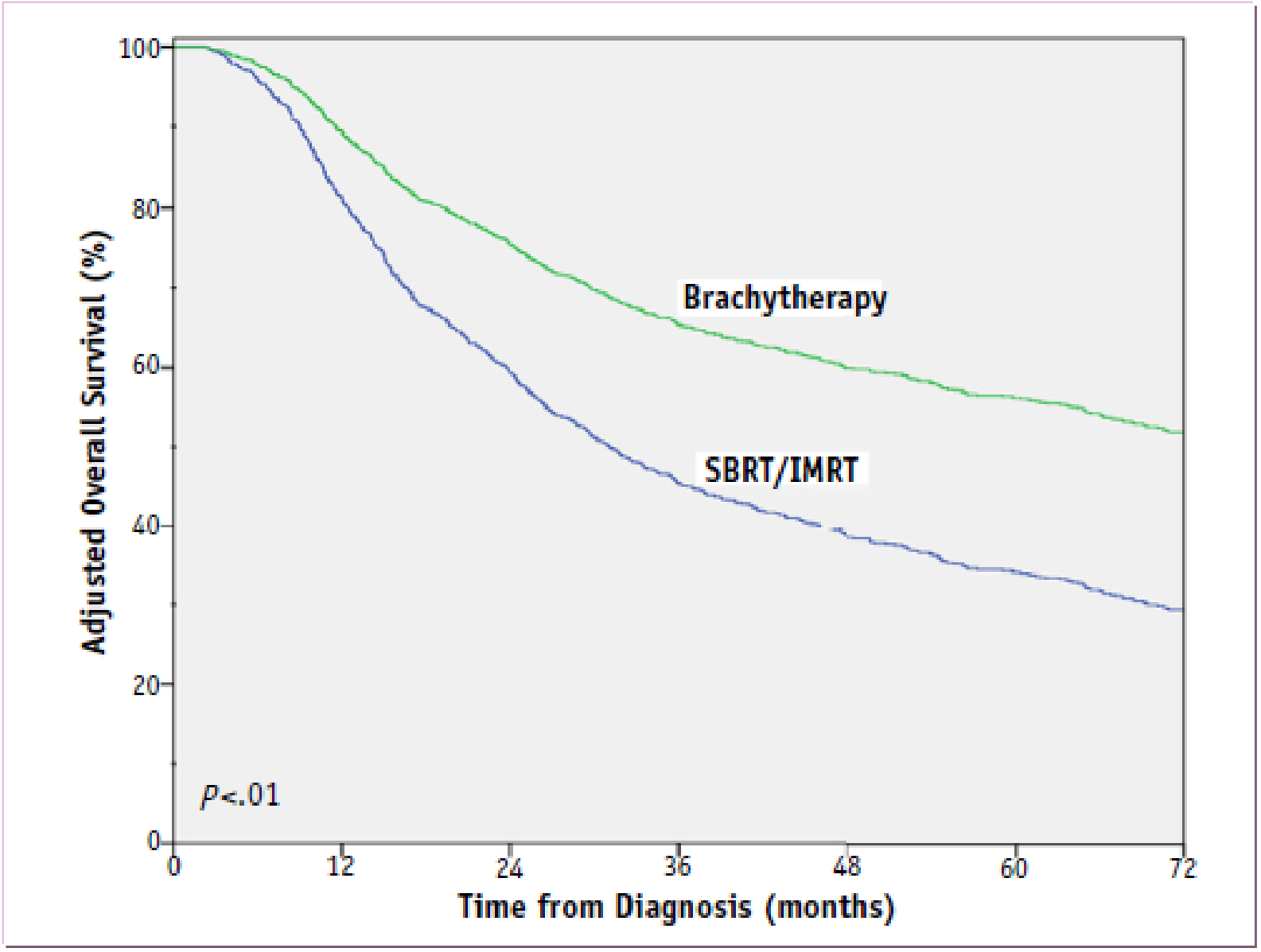

IA
IA1
IA2
IB1
≤4cm
IB2
>4cm
IIA
IIB
IIIA
IIIB
IVA
IVB


VUE
ANTERIEURE
Uretère
1
2
1c
1a
1b
1 - A. utérine
1a = segment pariétal
1b = segment paramétrial
(sous-ligamentaire)
1c = segment mésométrial
(intra-ligamentaire)
2 - A. vaginale longue

Brachytherapy is an essential component of chemoradiation Gill IJROBP 2014



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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

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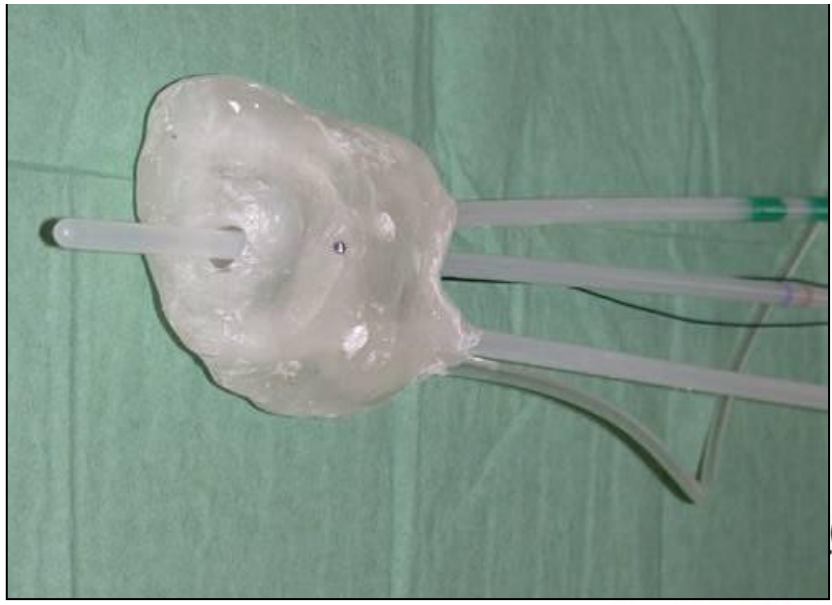
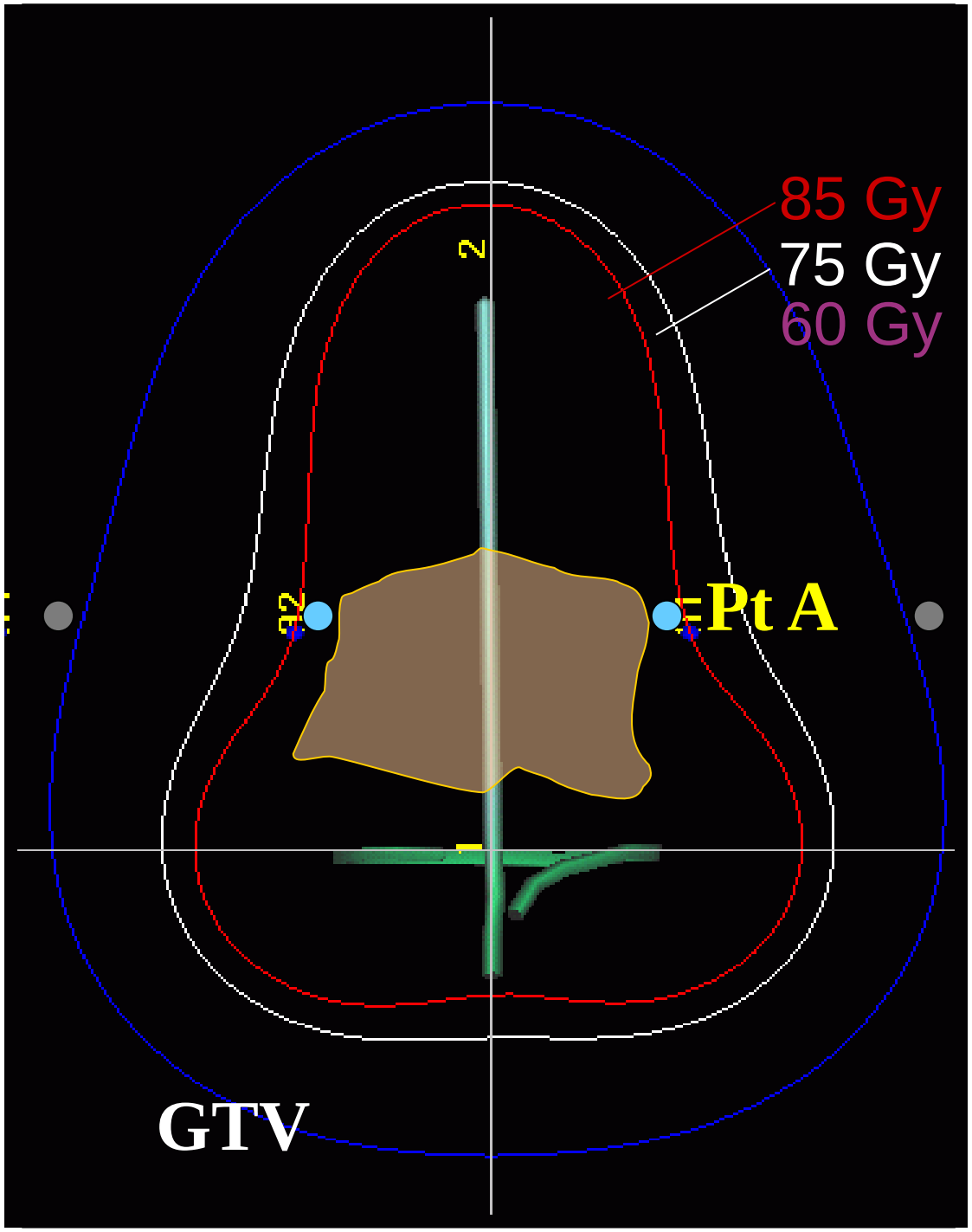
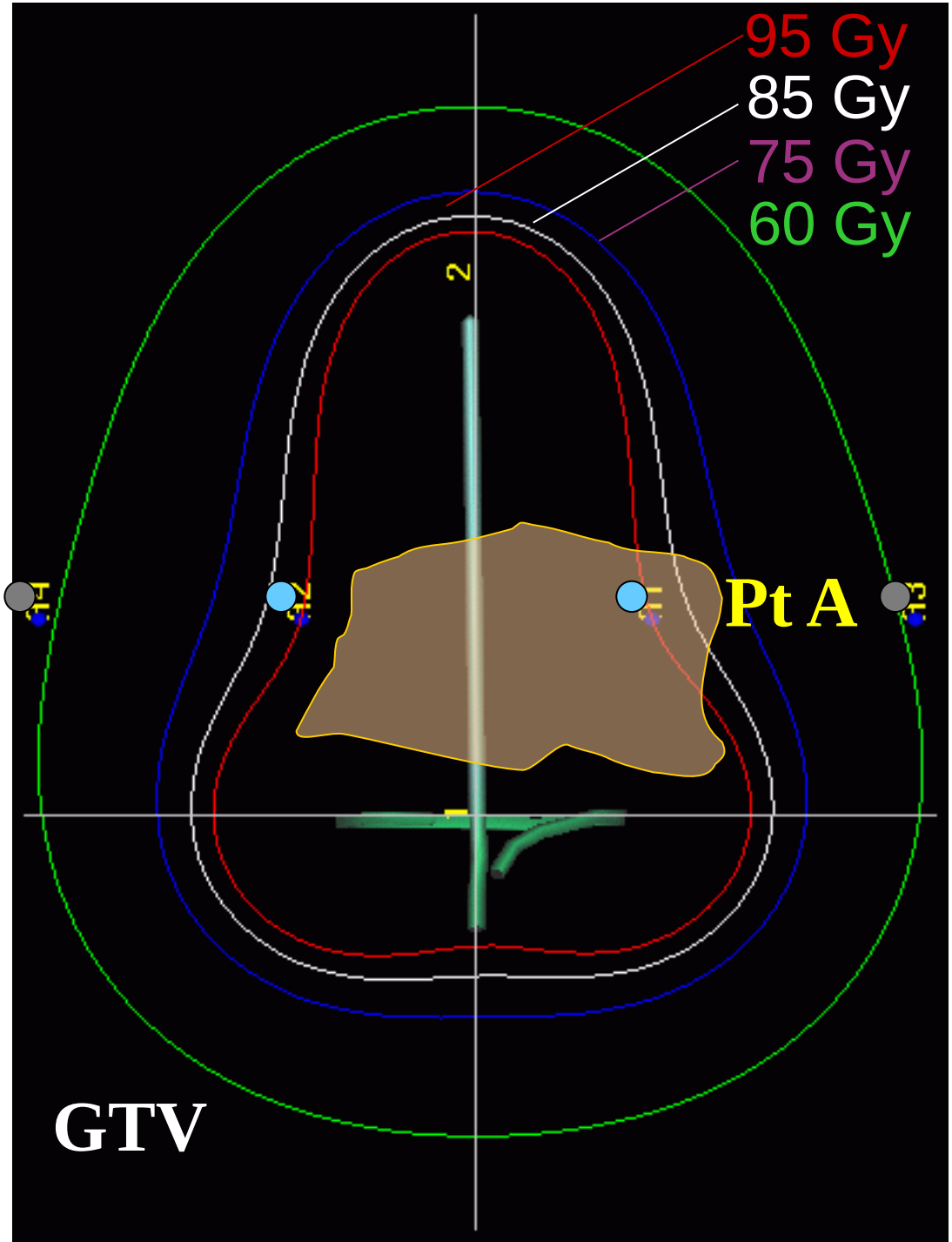
Applicators

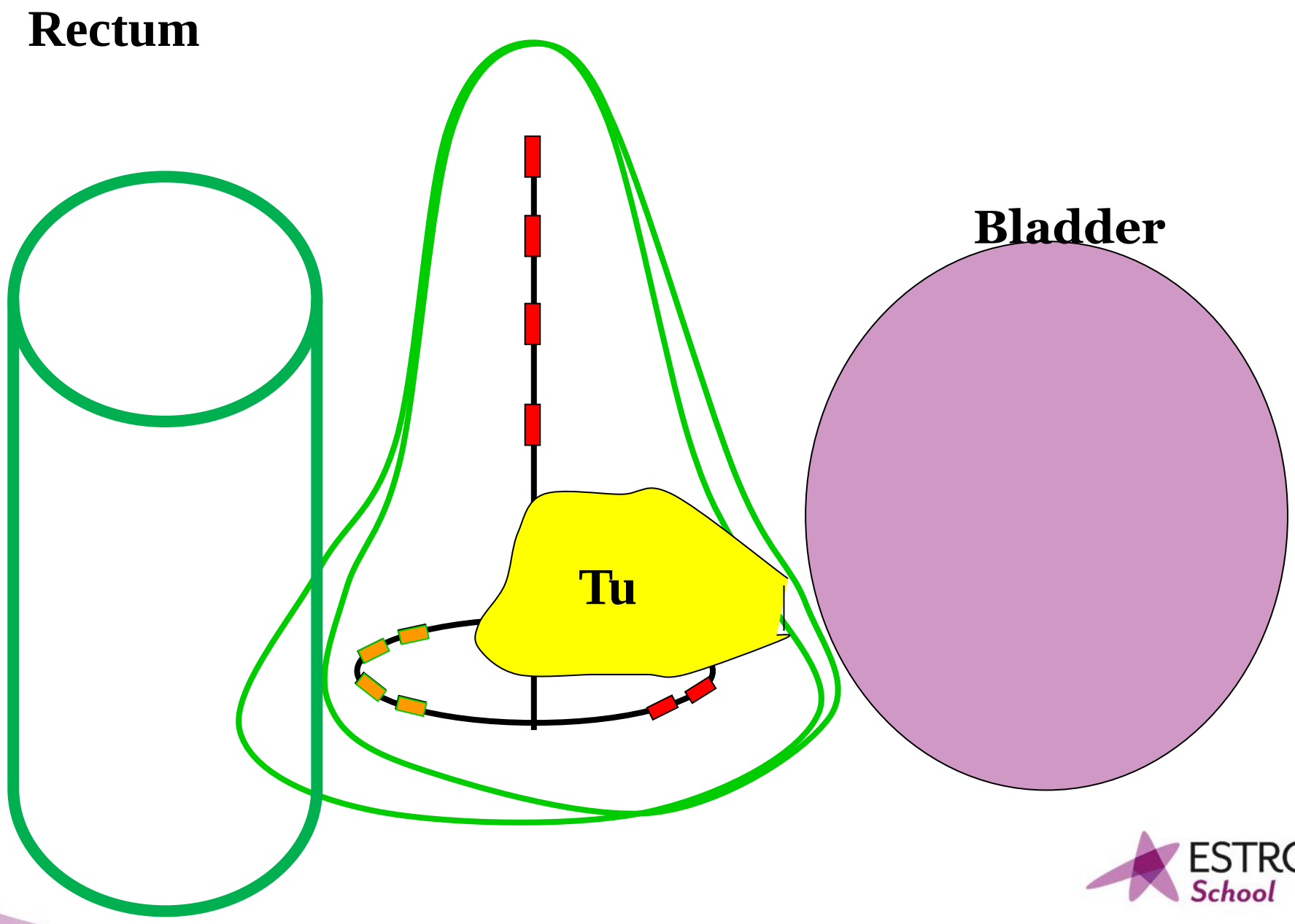


- Modern brachytherapy for cervical cancer is adaptive image guided prescribed to a CTV defined from cross sectional imaging .....preferably MR


85 Gy
75 Gy
60 Gy
Pt A
GTV


95 Gy
85 Gy
75 Gy
60 Gy
Pt A
GTV

Individual Adaptation to Tumour and OARs



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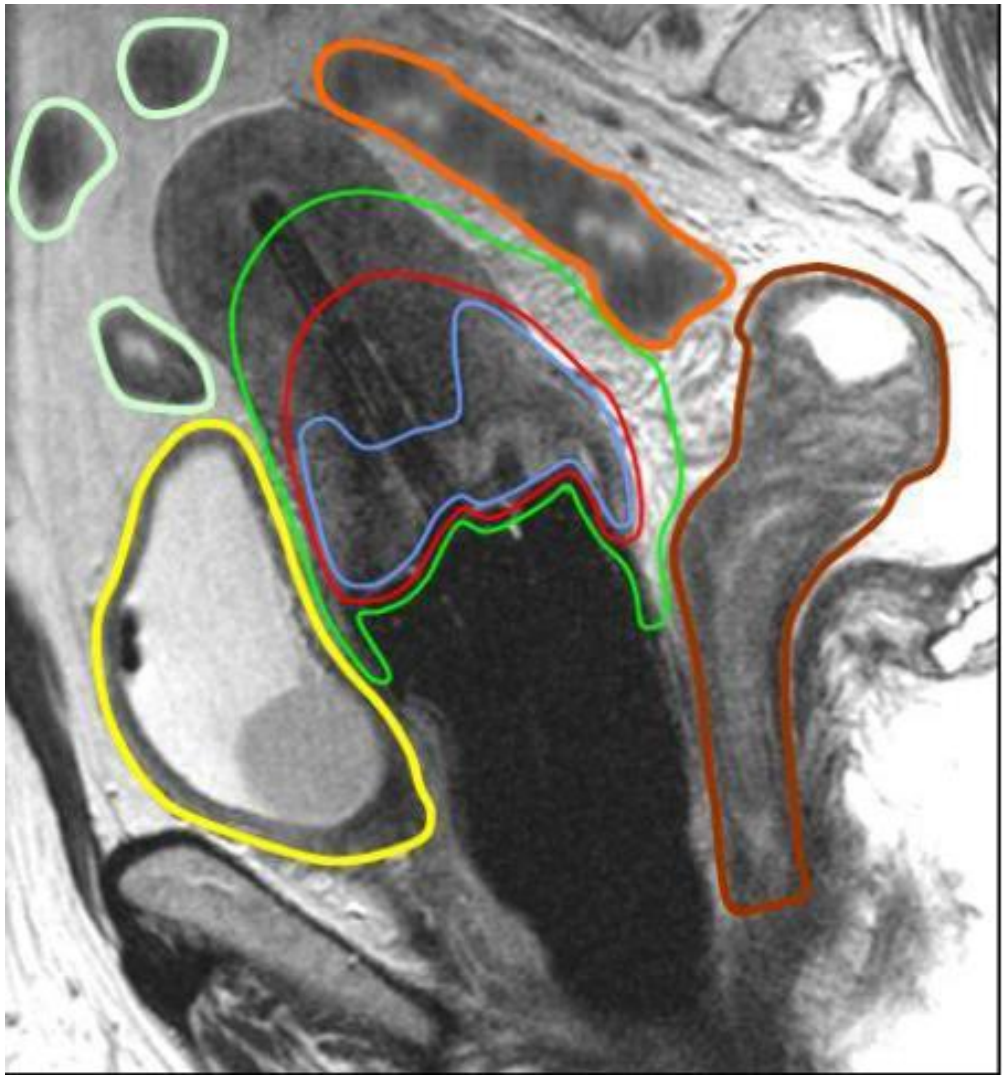
GTV
HR CTV
IR CTV



Bladder
Rectum
Sigmoid

Petric P. in Viswanathan et al. 2011

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Techniques and application

- Spinal or general anaesthesia
- Careful examination under anaesthetic
- Identify cervix and cervical canal
- If necessary dilate cervix and endometrial cavity
- Measure uterine cavity
- Select IU tube of appropriate angle and length
- Select vaginal sources
- Consider need for interstitial needles

- Insert applicators
- ? Rectal spatula
- Vaginal pack
- Stabilisation

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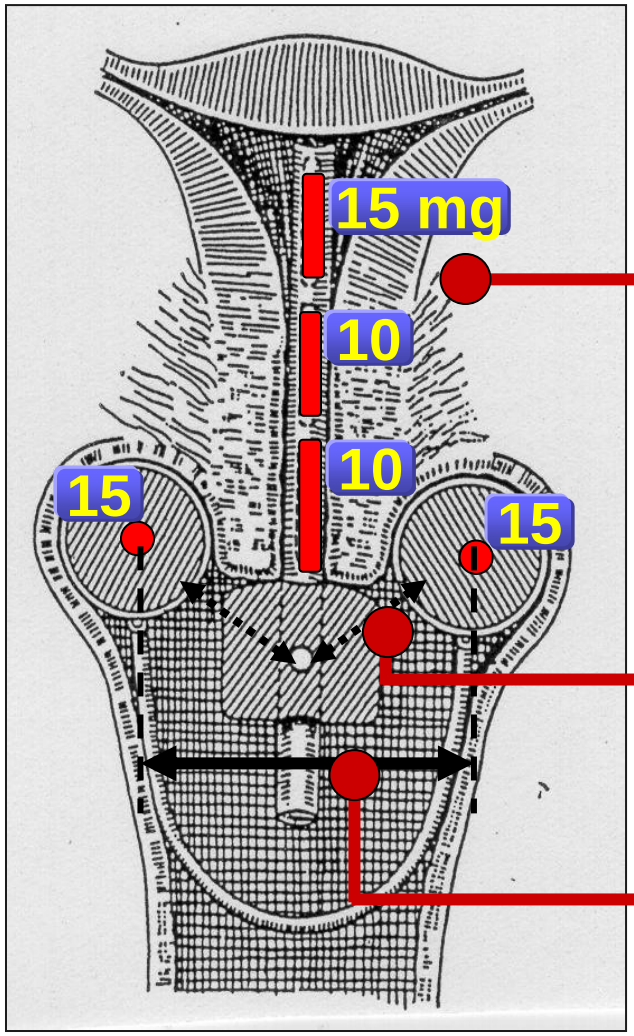
HISTORICAL PARIS TECHNIQUE

^{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

Tandem/ovoids manual preloading: ^{226}Ra

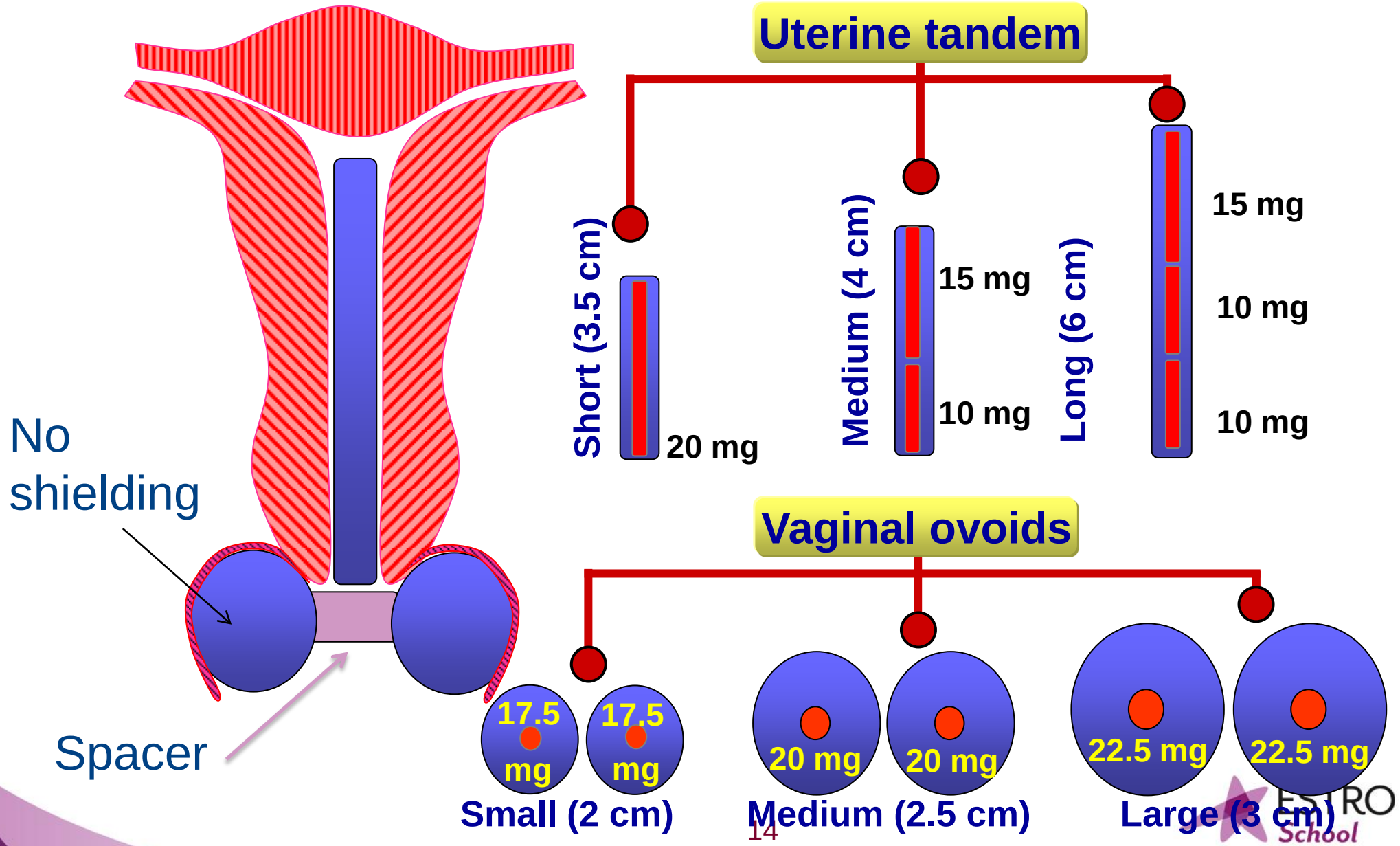
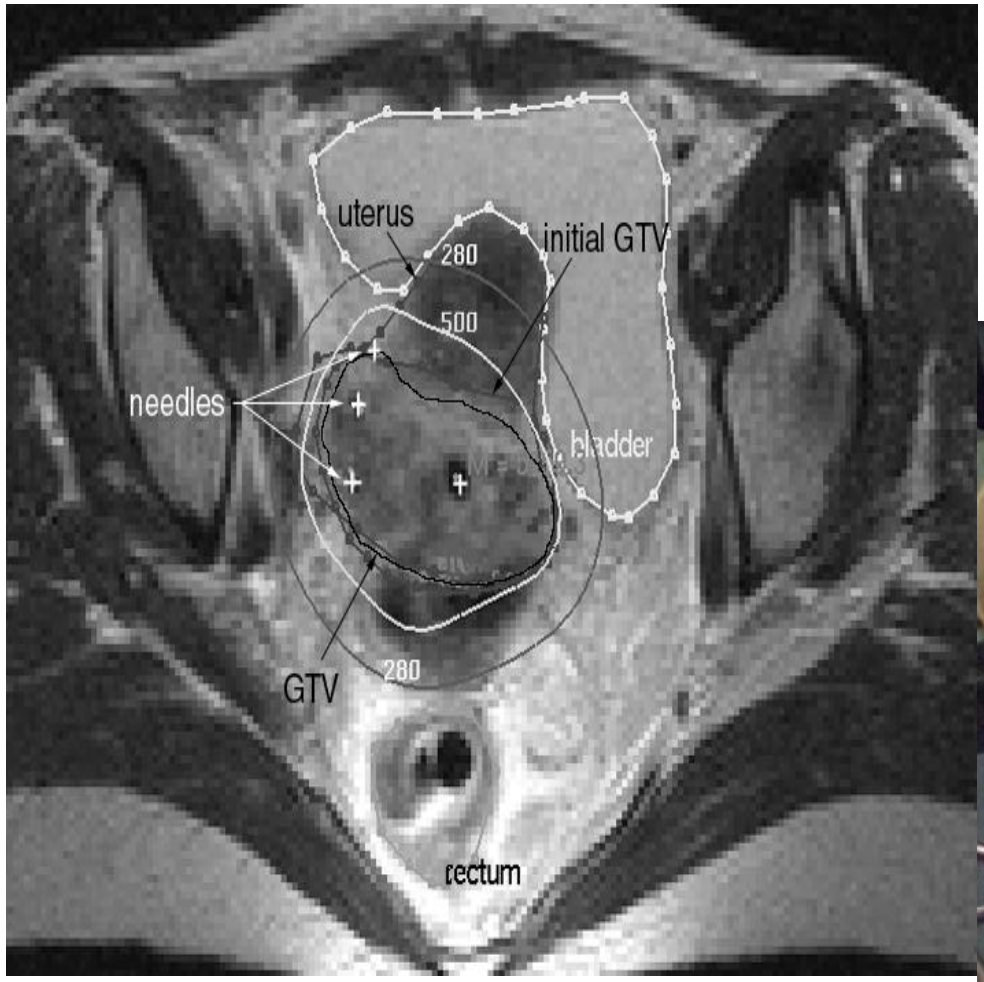
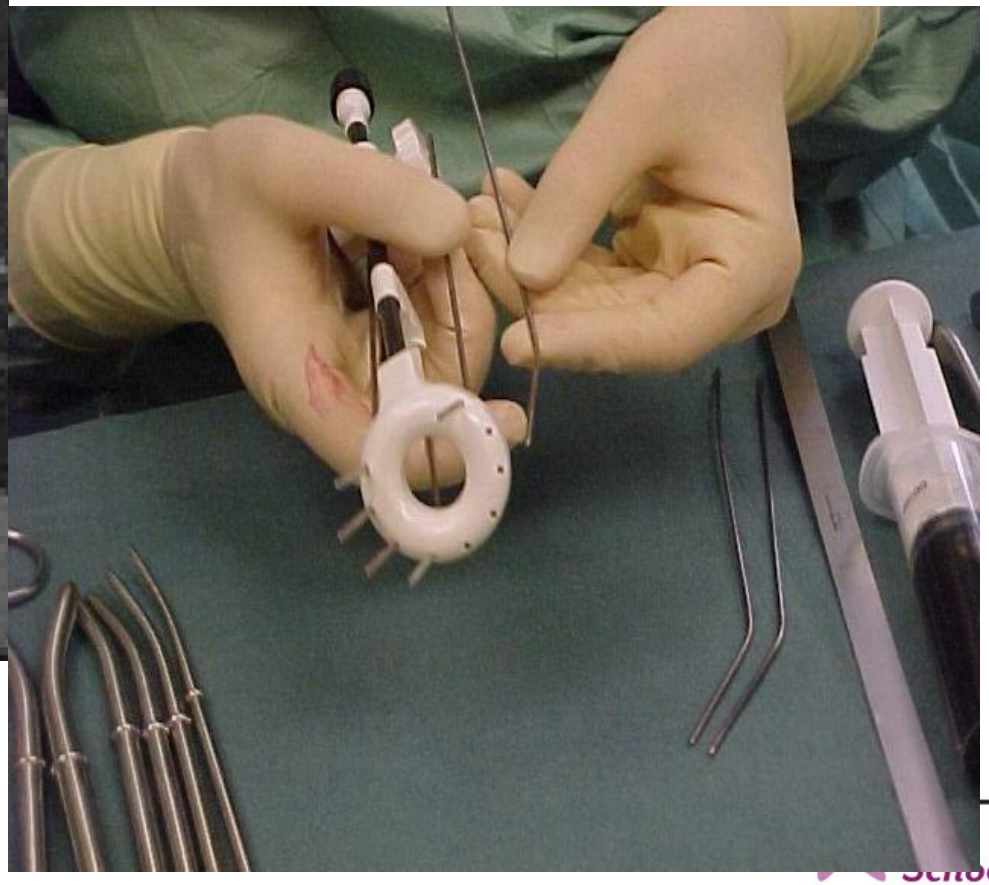
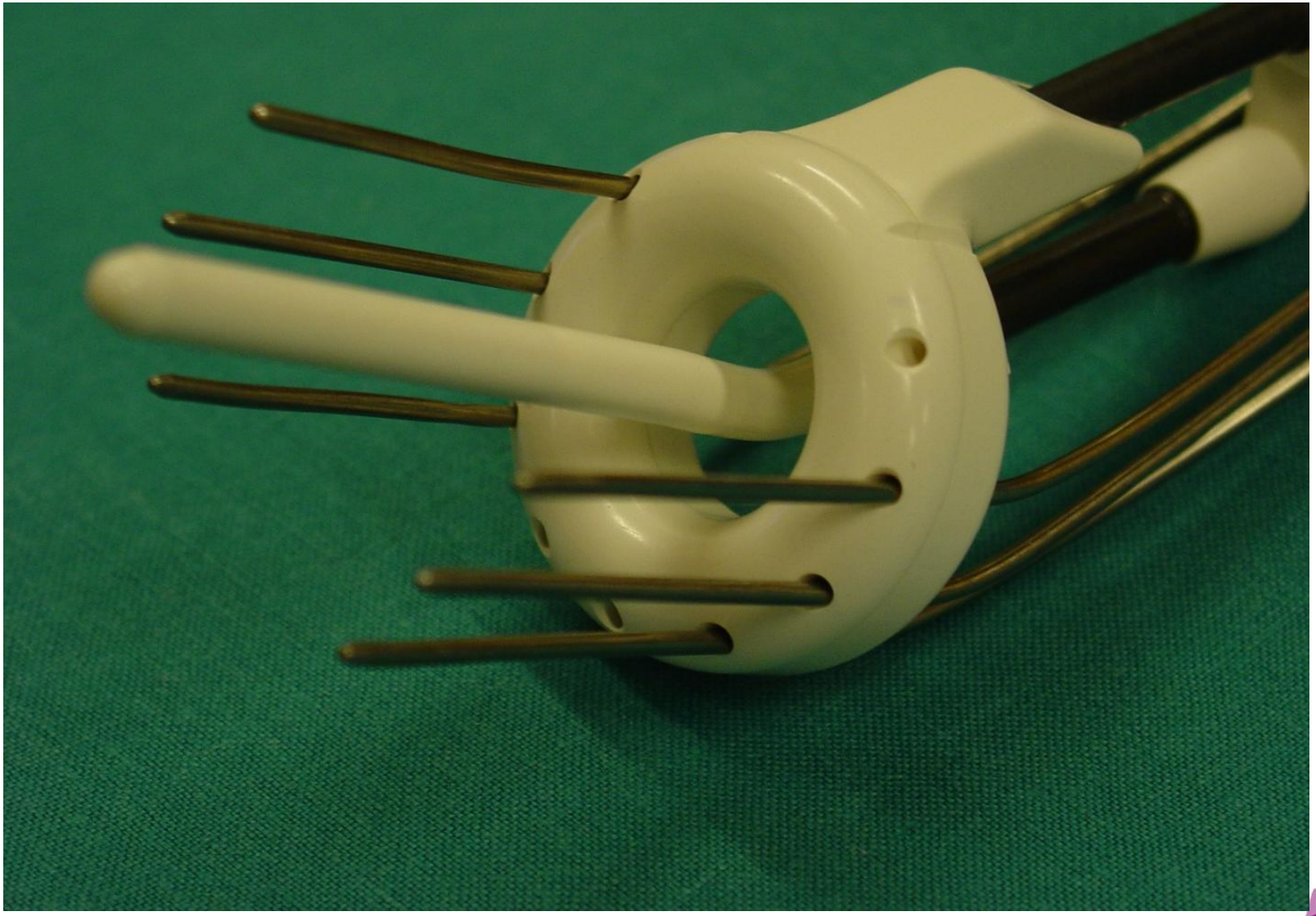


Image guided endocavitary and interstitital BT





Vienna applicator



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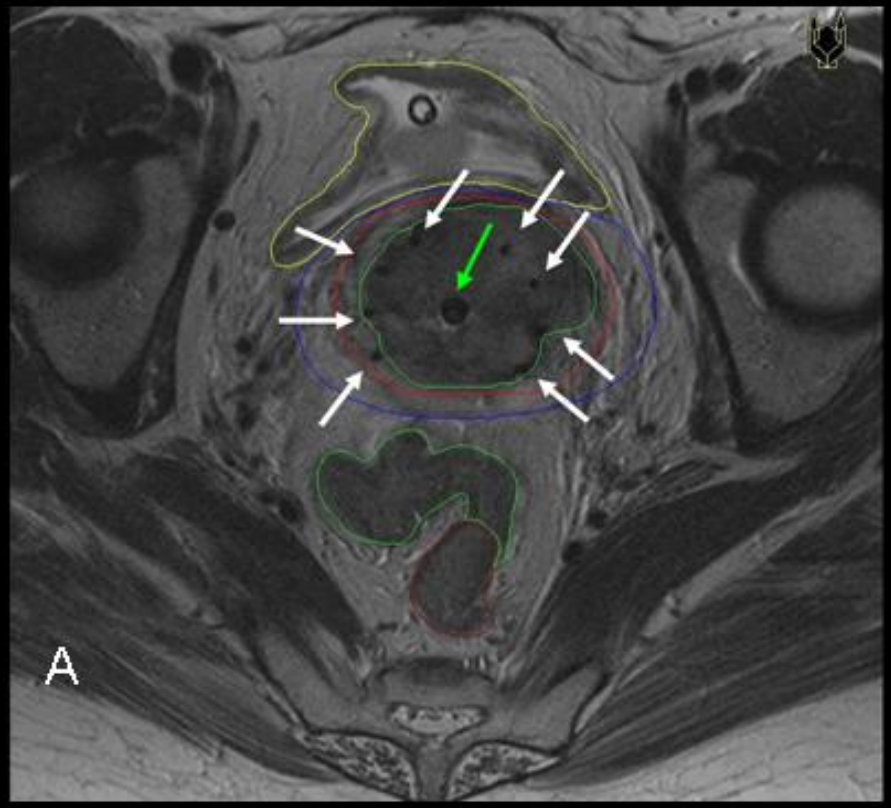
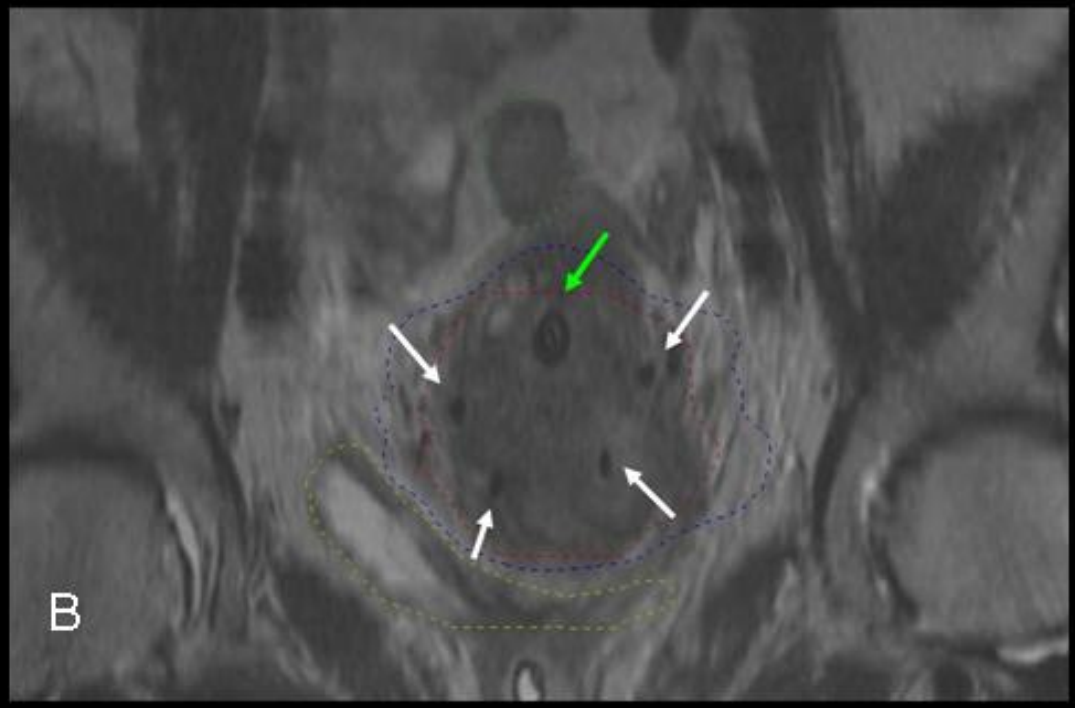
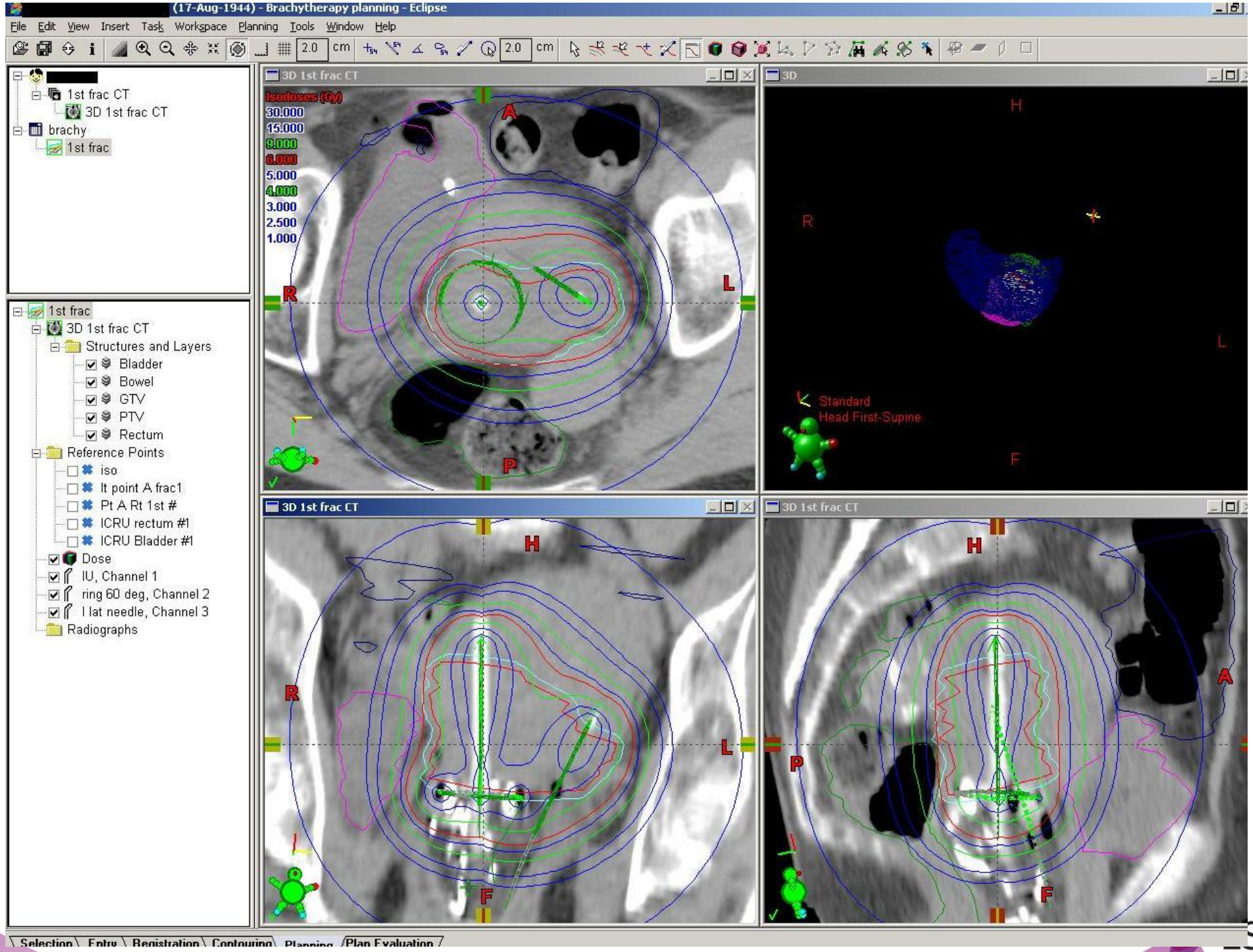

A


B



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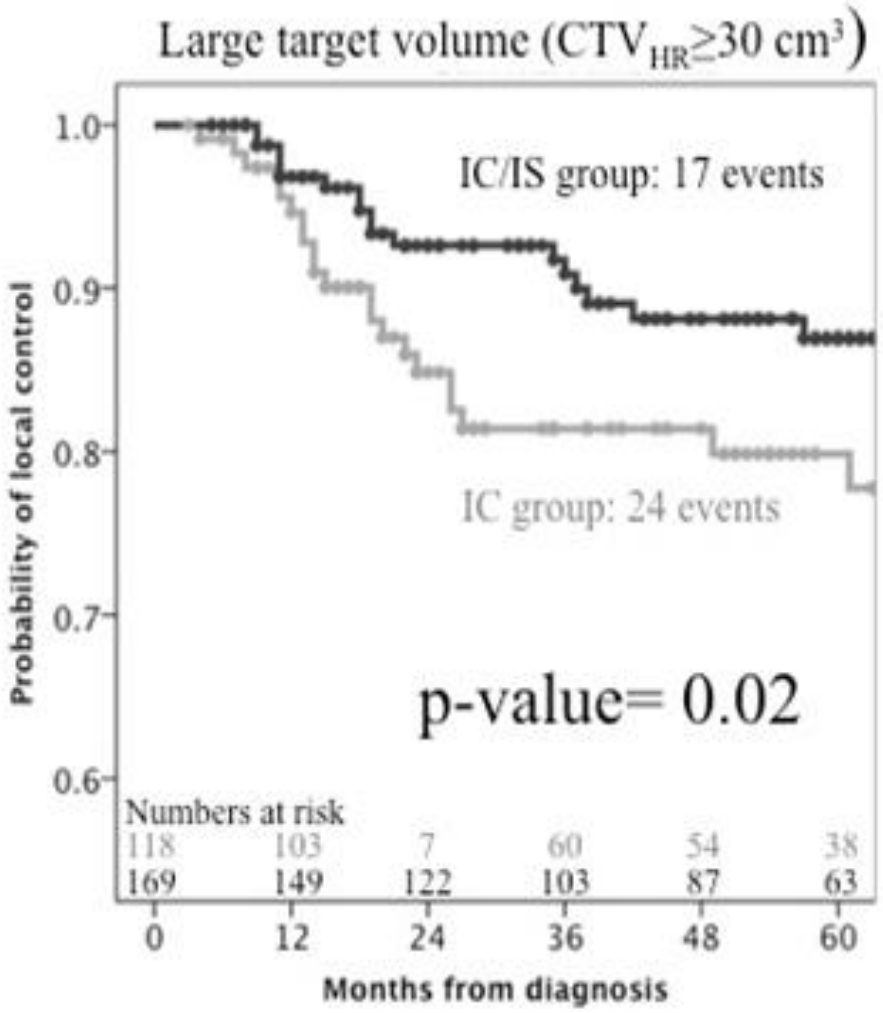
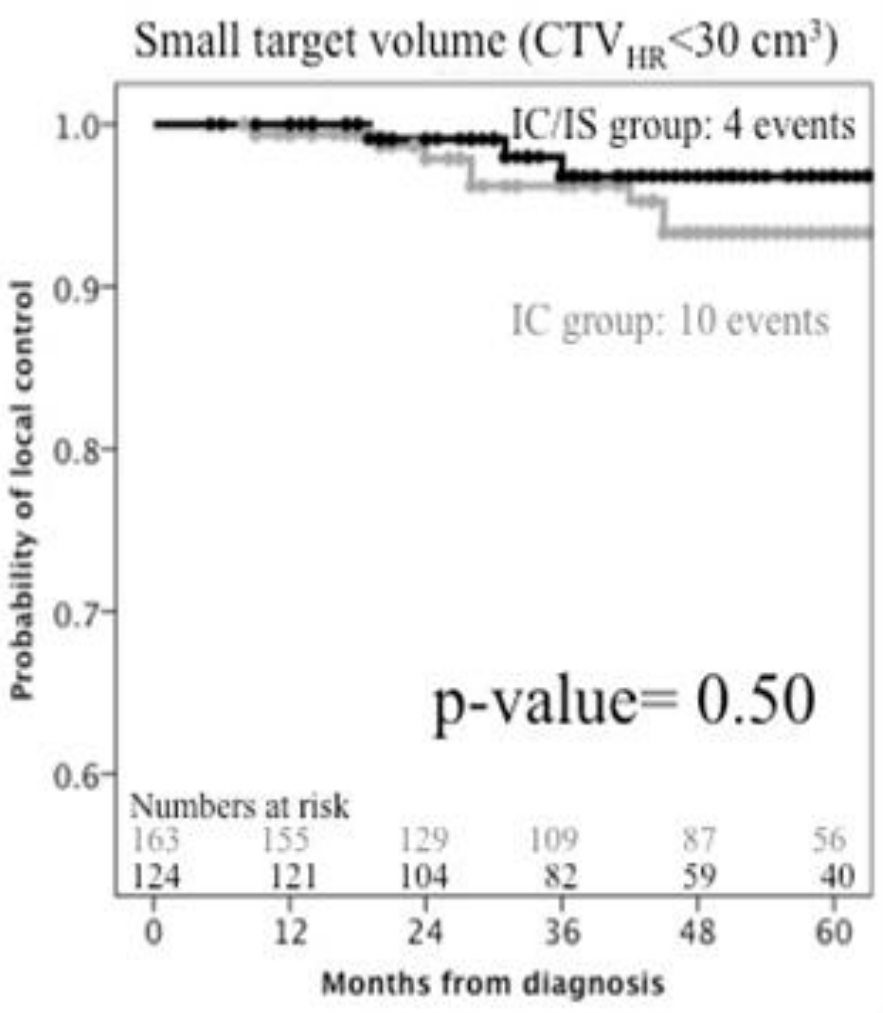
The impact of interstitial BT





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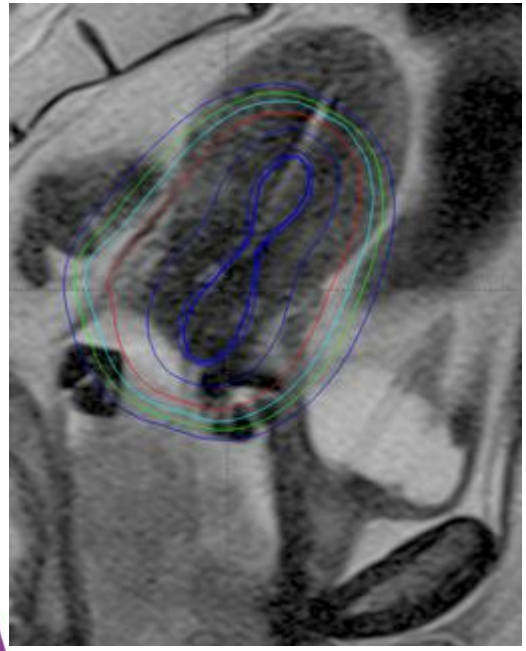
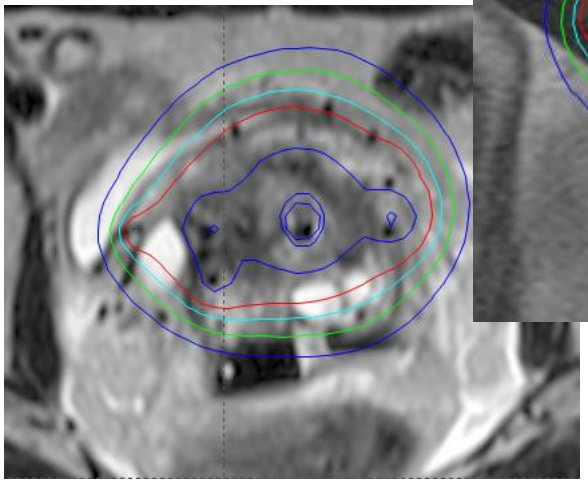
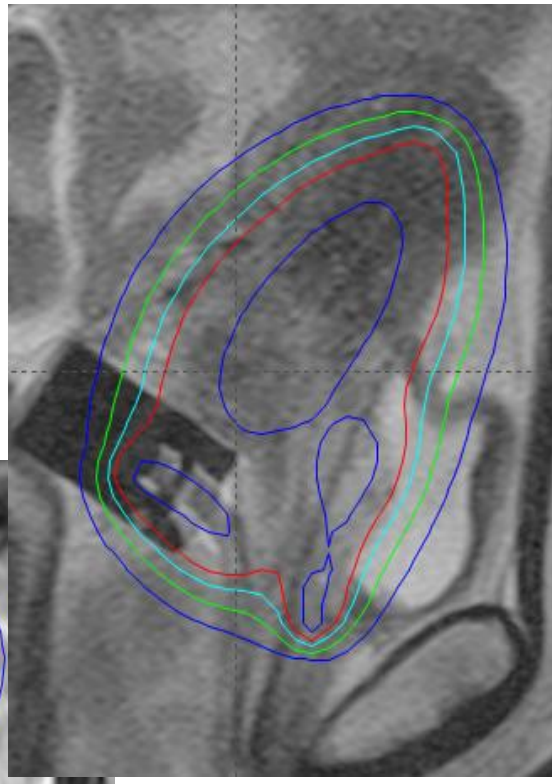
What about stage IIA and IIIA disease

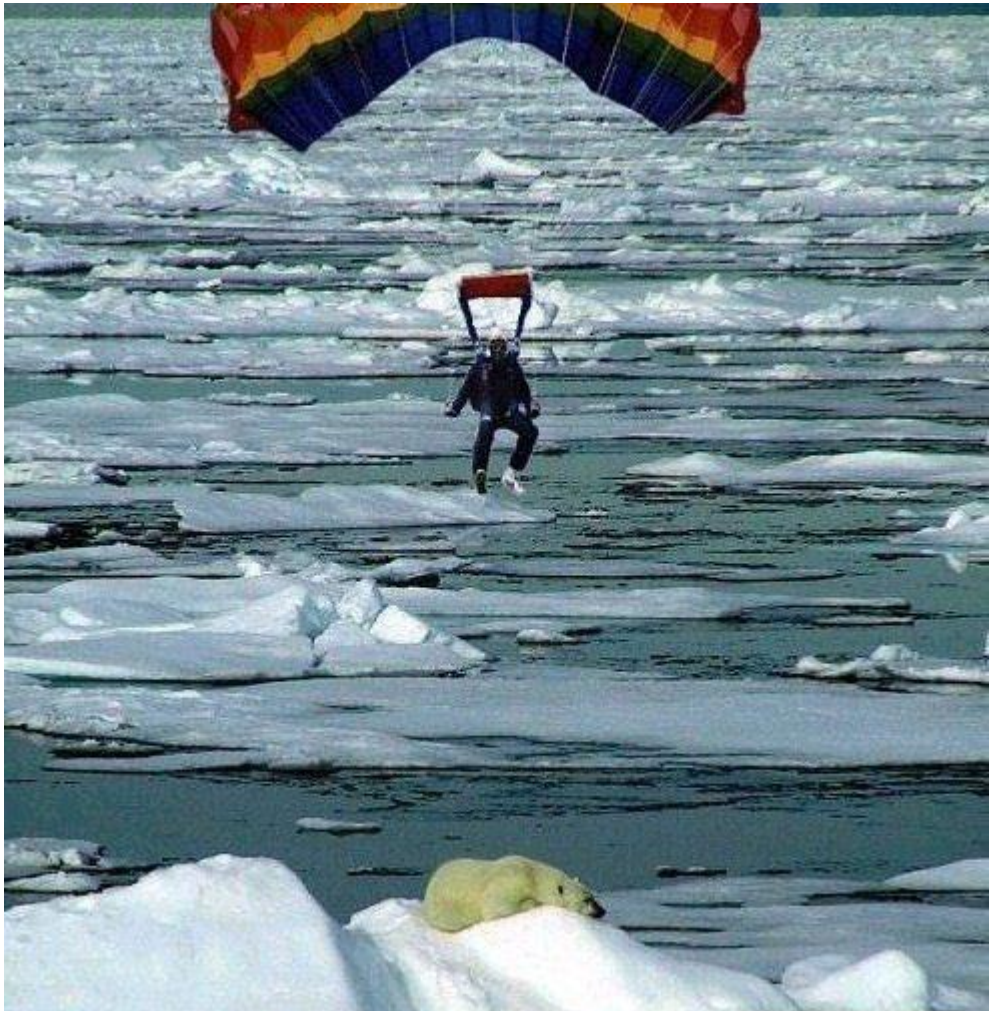
- Upper vaginal disease may be covered by dose envelope from ovoids or ring
- Separate or contiguous vaginal implant may be needed
- Integral applicators with multicatheter vaginal tube

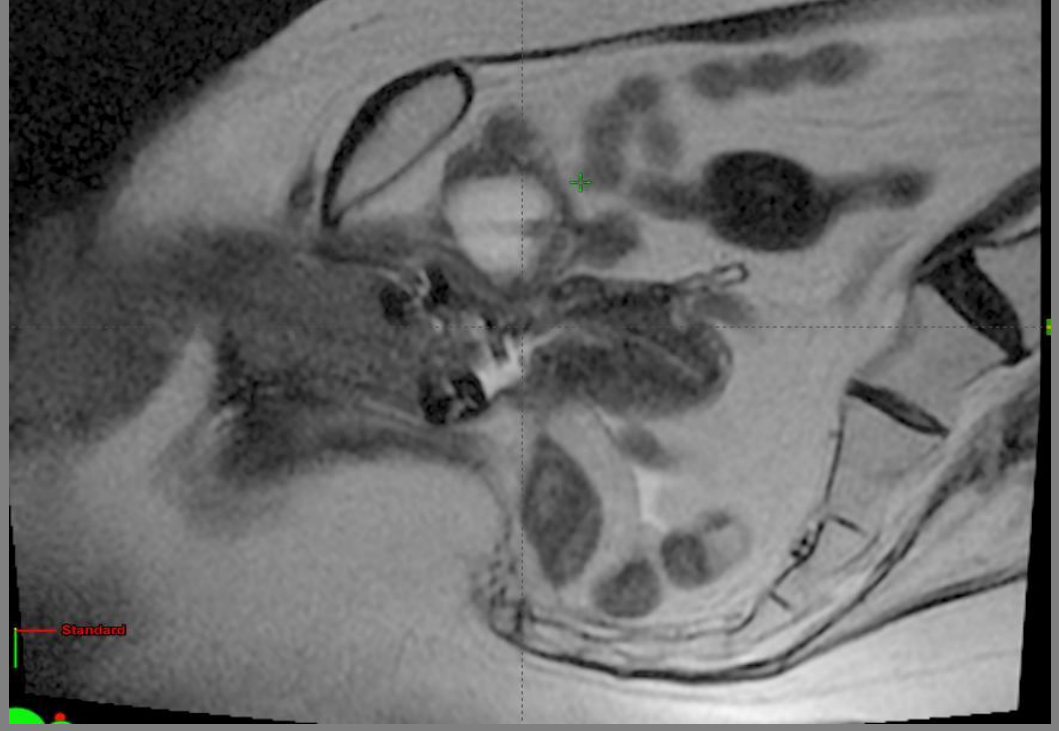






What to watch out for!

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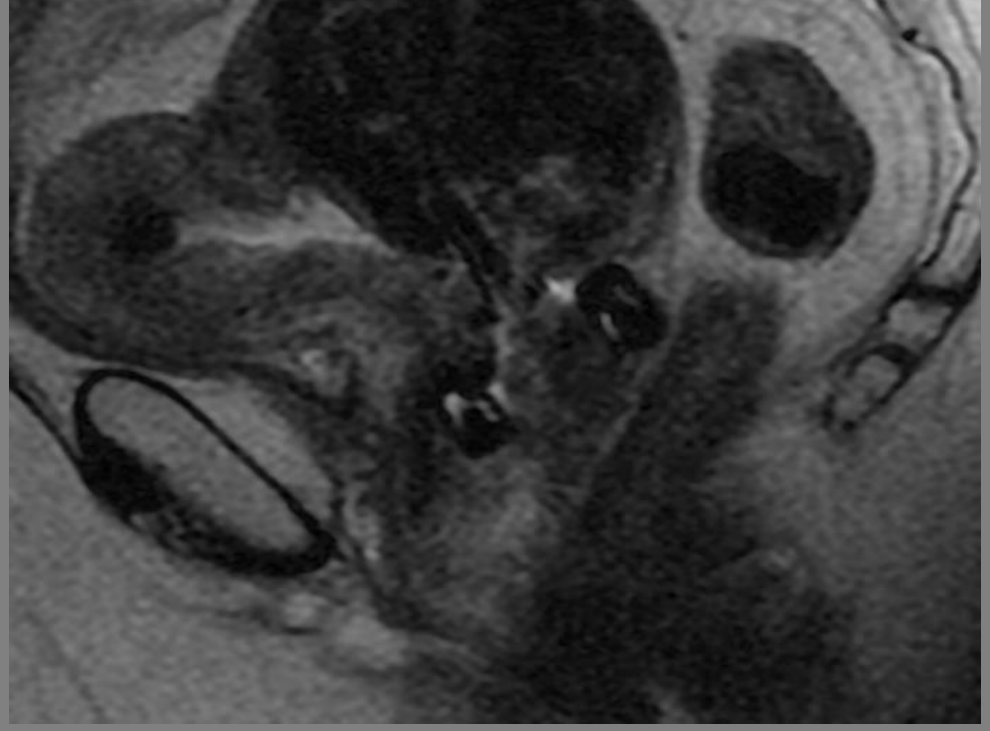

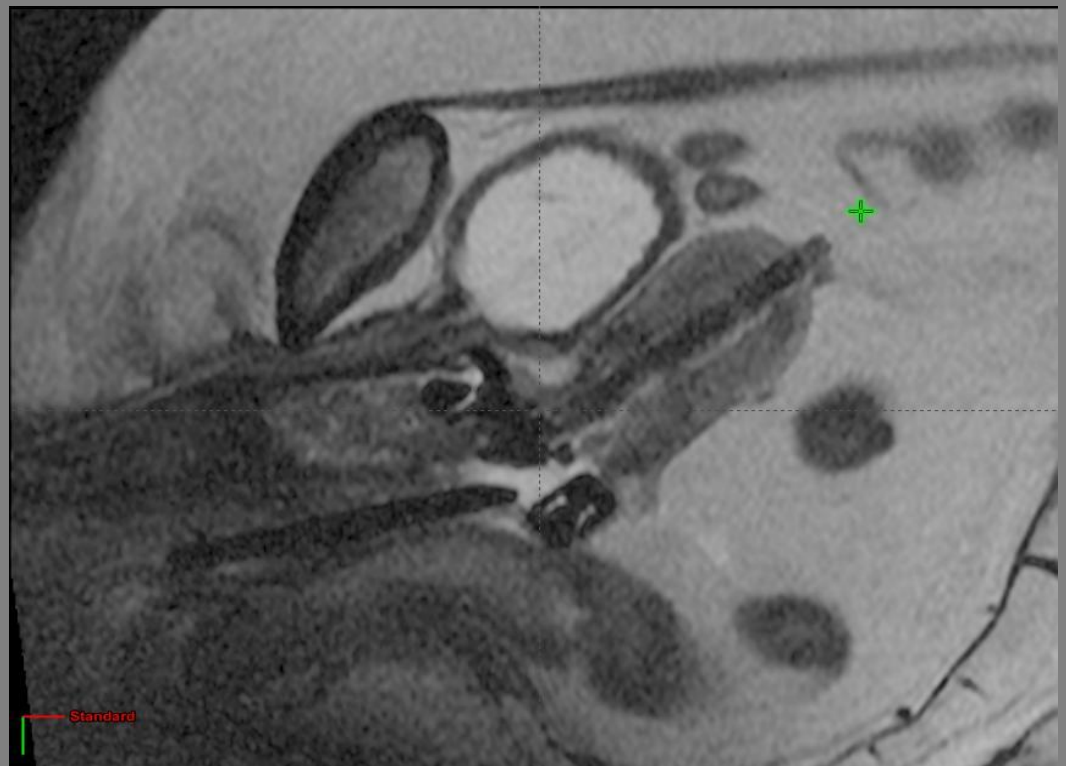
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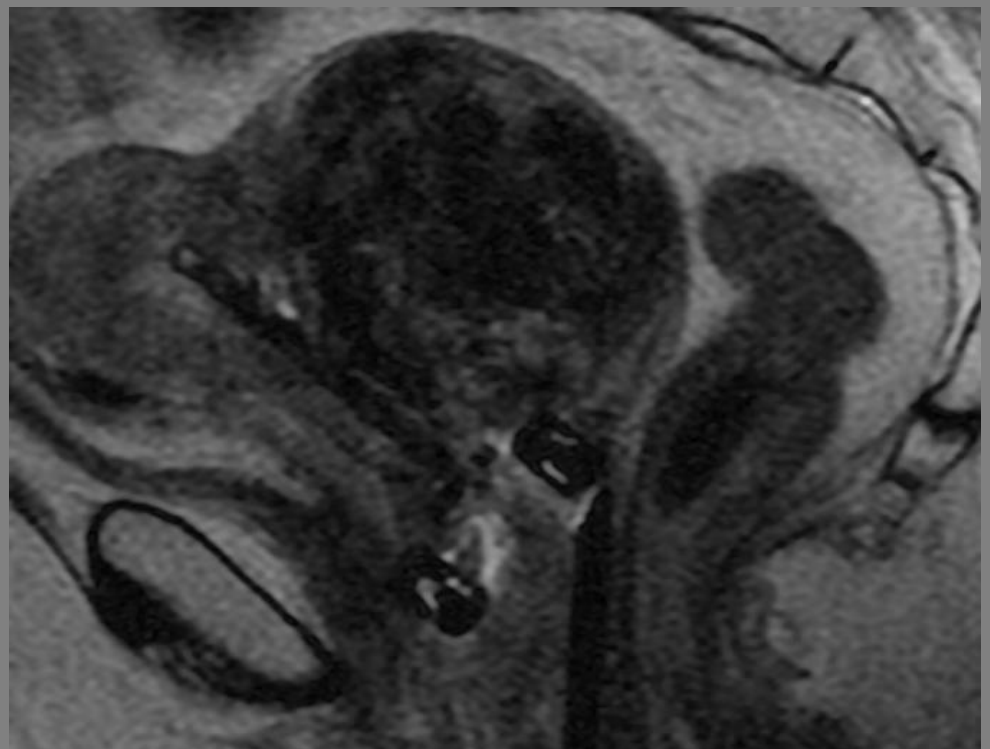
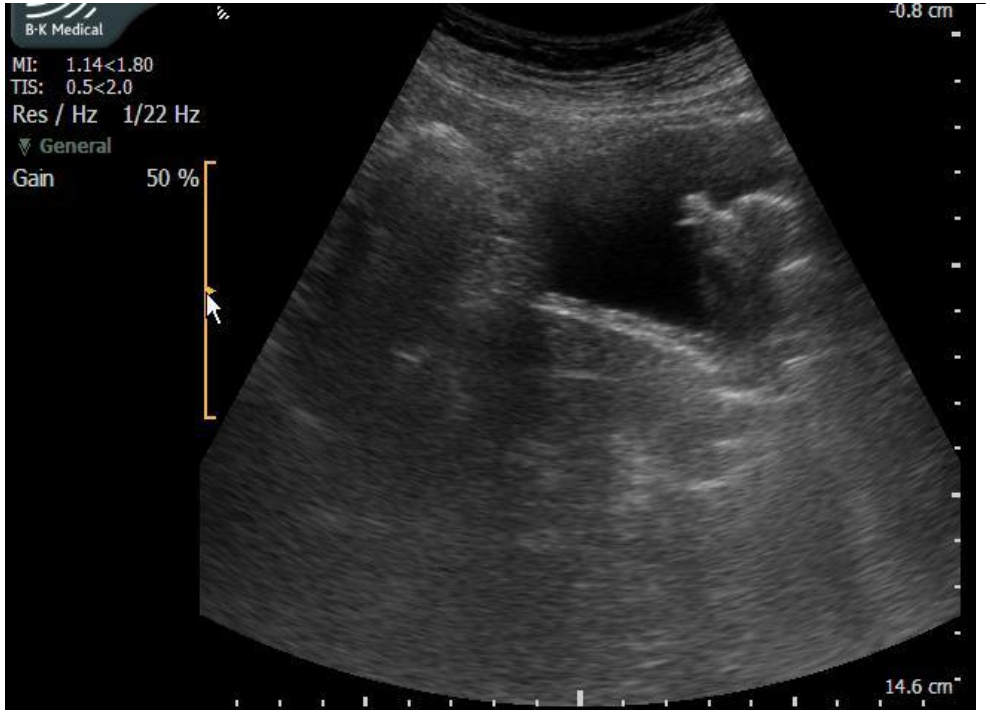
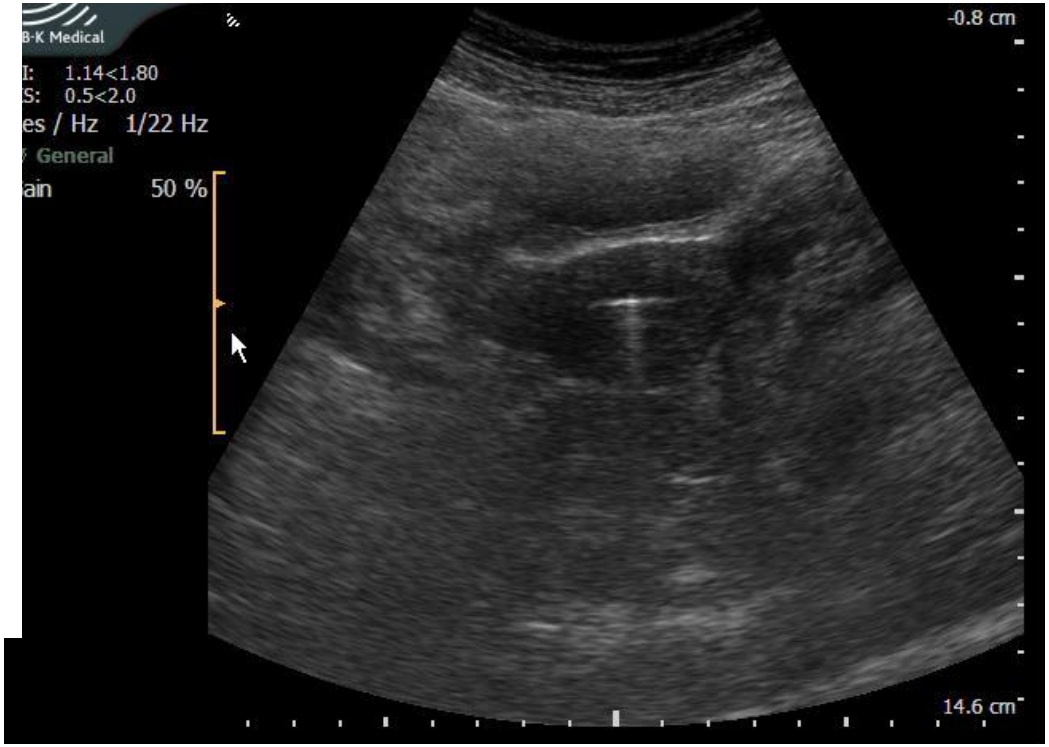


B-K Medical
MI: 1.01<1.80
TIS: 0.5<2.0
Res / Hz 1/28 Hz
General
Gain 50 %
-0.8 cm
10.9 cm


B-K Medical
MI: 1.14<1.80
TIS: 0.5<2.0
Res / Hz 1/22 Hz
General
Gain 50 %
-0.8 cm
14.6 cm


B-K Medical
I: 1.14<1.80
S: 0.5<2.0
es / Hz 1/22 Hz
General
ain 50 %
-0.8 cm
14.6 cm

Vaginal stenosis

- Check smallest vaginal applicators
- Ovoids are more flexible than the ring

- Interstitial applicators can provide vaginal source positions …. but will be free hand if no ring or ovoid

- If all else fails ….use single line source

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3D image acquisition

- MRI
  - T2 Sequences: axial, sagittal, frontal
  - Dummy sources
    - Water + iodo povidone (bubbles)
    - Facilitate the applicator reconstruction
    - Localize accurately the tip dwell position

- CT
  - Axial slice
  - Contrast enhancement

A
B
C

Dosimetry

- Dose may be defined at HR-CTV or IR-CTV
- Conventional loading patterns for tandem and vaginal source are the basis for initial dwell times
- Interstitial applicators should account for 10-15% of the total
- OAR tolerances should be defined and respected…..but clinical compromise often required

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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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WWW.ESTRO.ORG/SCHOOL

Cervix:
Hazards, results,complications

Peter Hoskin

Mount Vernon Cancer Centre

ESTRO School

Results and complications of 3D brachytherapy for cervical cancer

- Dosimetric
- Tumour control
- Complications

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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$_3$**

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RT&O 2008

Tumour dose

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 [$Gy_{\alpha\beta10}$]	80 ± 6	79 ± 5
GTV (volume = 6 ± 7 cc)		
D100 [$Gy_{\alpha\beta10}$]	94 ± 31	89 ± 19
D90 [$Gy_{\alpha\beta10}$]	118 ± 43	103 ± 24
D50 [$Gy_{\alpha\beta10}$]	191 ± 95	138 ± 36
HR-CTV (volume = 48 ± 19 cc)		
D100 [$Gy_{\alpha\beta10}$]	61 ± 6	64 ± 6
D90 [$Gy_{\alpha\beta10}$]	76 ± 9	79 ± 7
D50 [$Gy_{\alpha\beta10}$]	108 ± 18	105 ± 10
V(85 $Gy_{\alpha\beta10}$) [%]	74 ± 16	79 ± 13
V(80 $Gy_{\alpha\beta10}$) [%]	81 ± 15	86 ± 11
IR-CTV (volume = 112 ± 44 cc)		
D100 [$Gy_{\alpha\beta10}$]	55 ± 3	58 ± 3
D90 [$Gy_{\alpha\beta10}$]	65 ± 5	69 ± 4
D50 [$Gy_{\alpha\beta10}$]	89 ± 11	92 ± 7
V(60 $Gy_{\alpha\beta10}$) [%]	96 ± 5	99 ± 2
Reference volumes		
V_{ref}(100 $Gy_{\alpha\beta10}$) [cc]	67 ± 15	73 ± 13
V_{ref}(85 $Gy_{\alpha\beta10}$) [cc]	101 ± 21	112 ± 18
V_{ref}(60 $Gy_{\alpha\beta10}$) [cc]	339 ± 106	410 ± 95

HR CTV D90 <85Gy_{10}

X-ray: 13/16

Optimised: 11/16

Mean dose increase 3Gy optimised

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Potential of dose optimisation in MRI-based PDR brachytherapy of cervix carcinoma

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[a]Department of Radiation Oncology, University Hospital Leuven, Belgium, [b]Radiation Therapy Department, National Cancer Institute, Cairo University, Egypt

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

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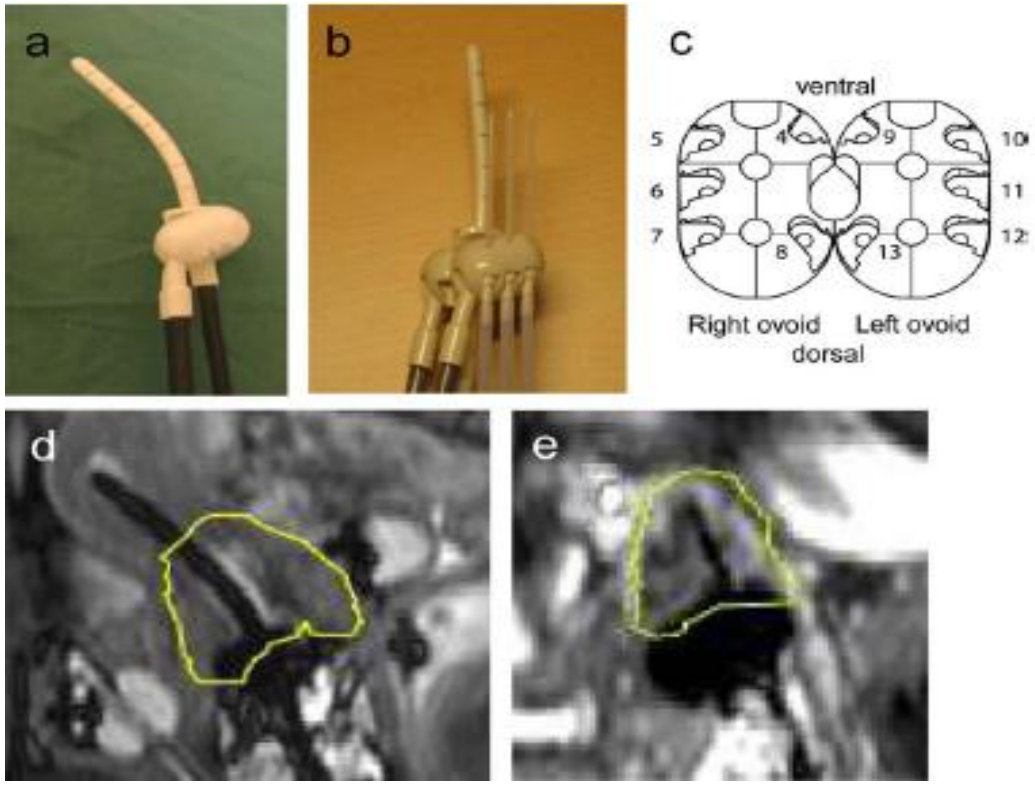
MRI-guided treatment-planning optimisation in intracavitary or combined intracavitary/interstitial PDR brachytherapy using tandem ovoid applicators in locally advanced cervical cancer

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



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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 $4.8 \pm 3.1\ Gy_{\alpha\beta 10}$ ($p = 0.07$).

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Results and complications of 3D brachytherapy for cervical cancer

- Dosimetric
- Tumour control
- Complications

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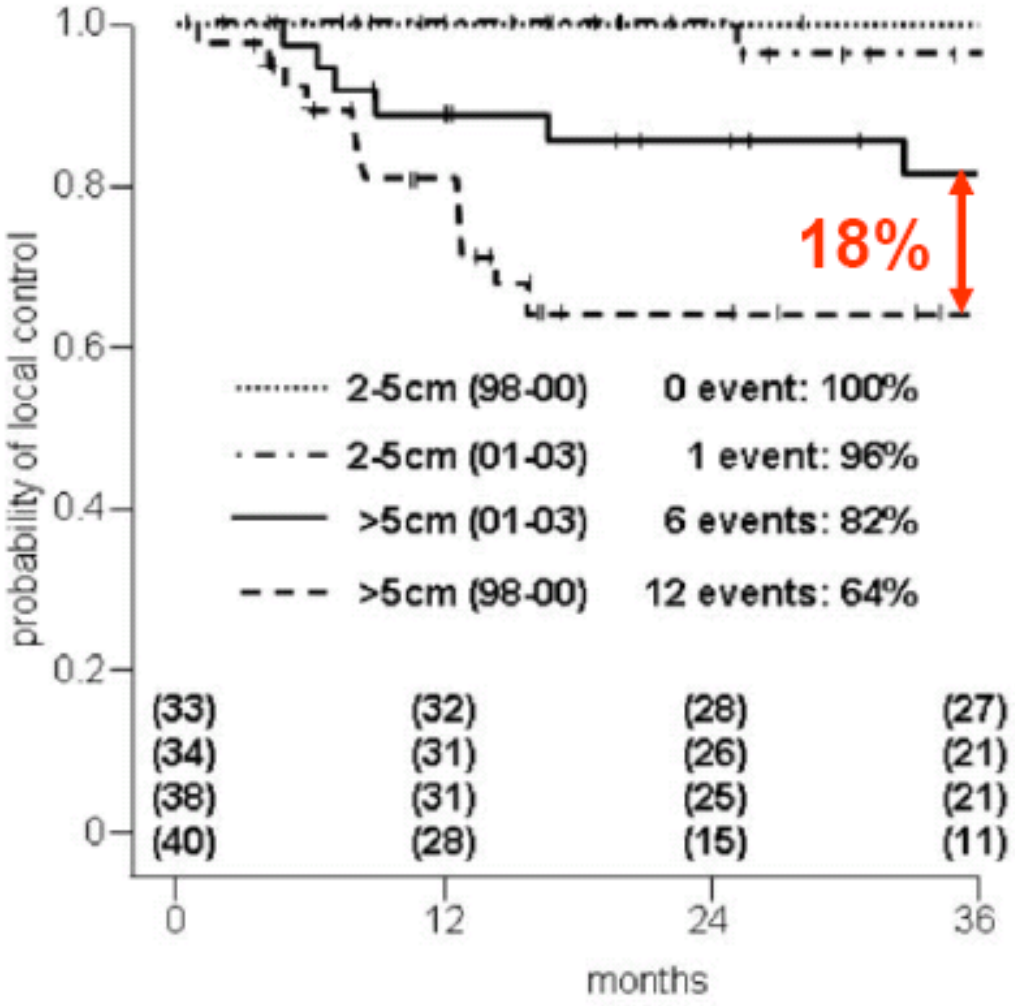
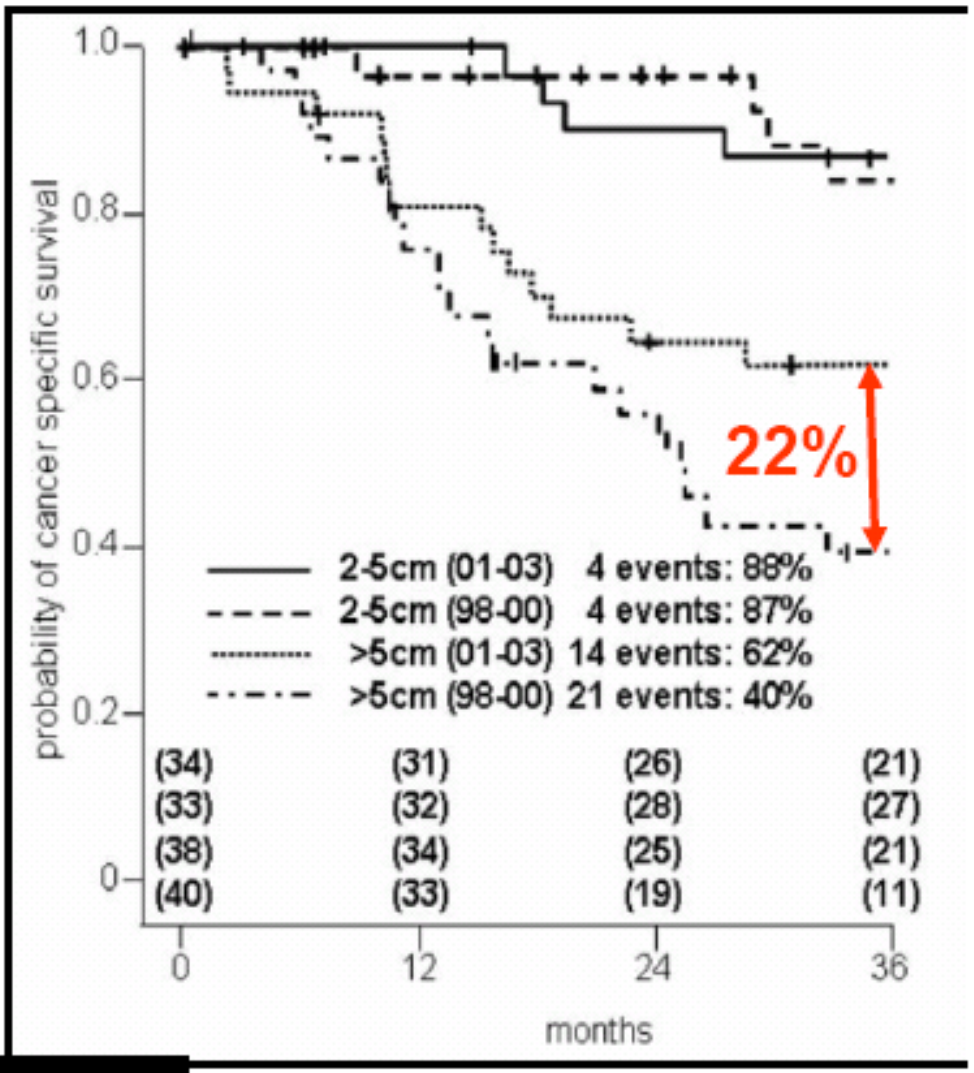
Image guided adpative brachytherapy (IGBT) cervix cancer local control and cancer specific survival (1998-2003) TREATMENT PERIOD (-/+ IGABT) AND TUMOUR SIZE





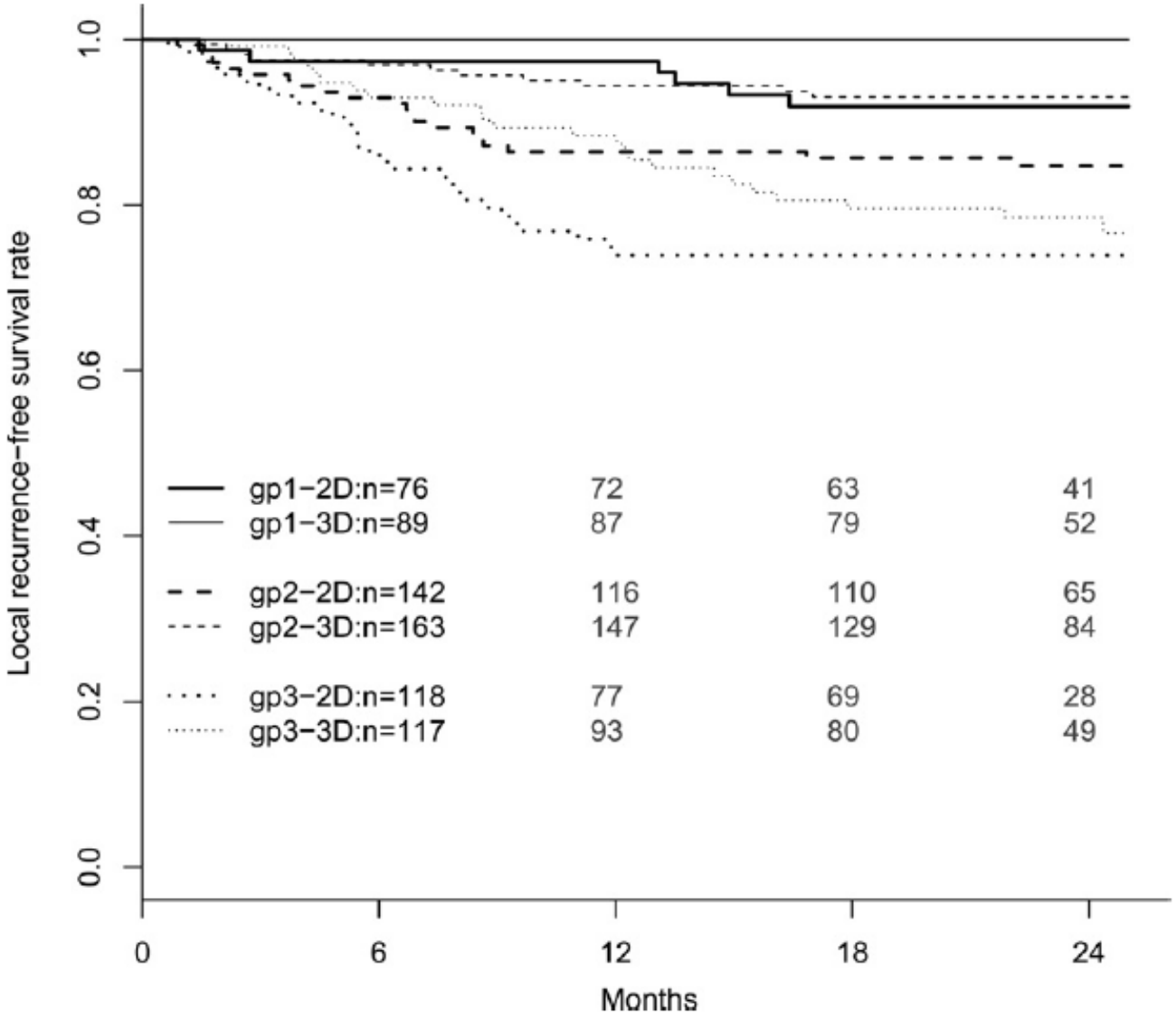
mean 81 Gy vs. 90 Gy in HR CTV

Pötter R. et al Radiother Oncol 2007

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



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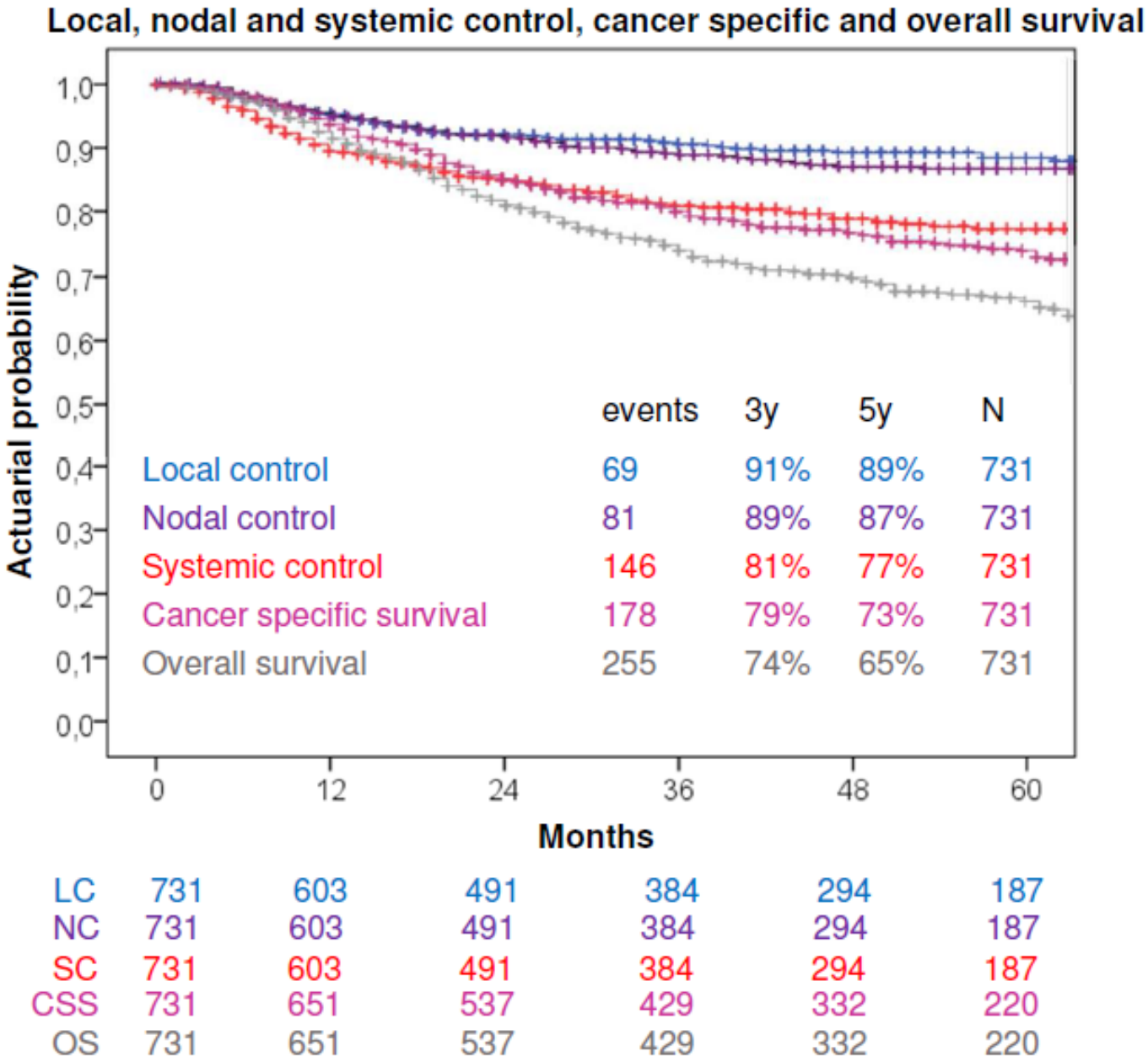
RetroEMBRACE



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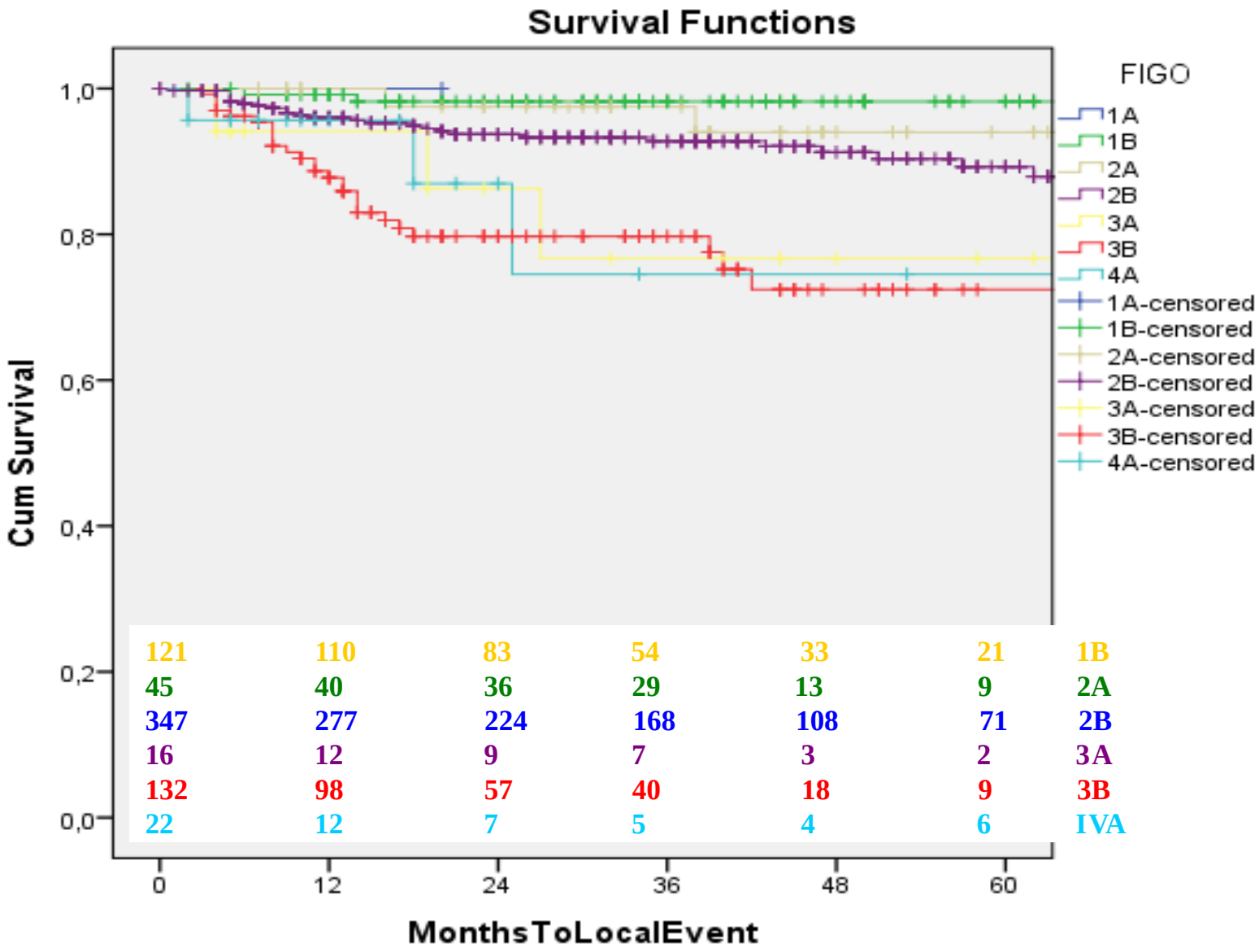
Stage related local control



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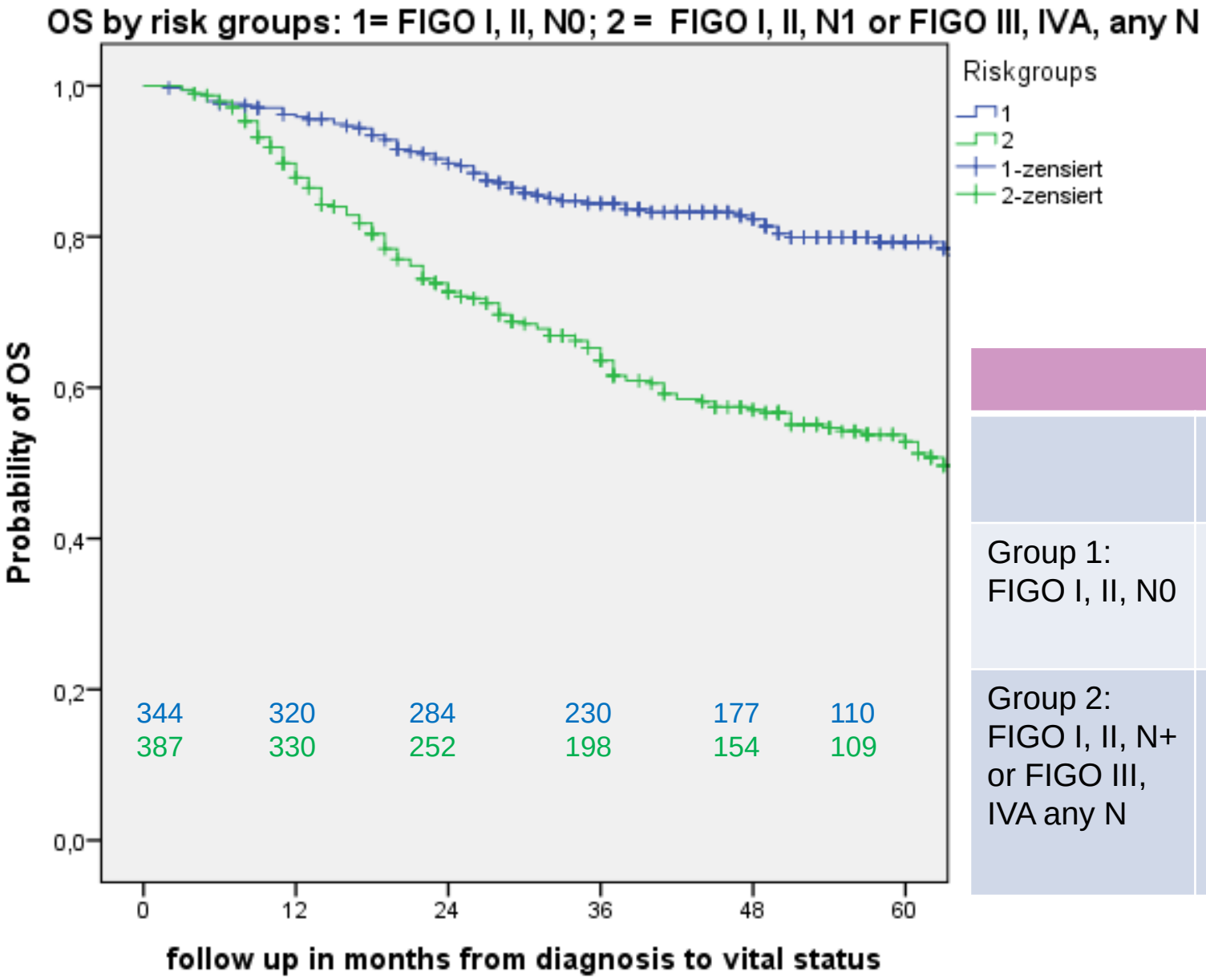
OS based on risk groups



Actuarial OS		
	at 3 years	at 5 years
Group 1: FIGO I, II, N0	84.4%	79.3%
Group 2: FIGO I, II, N+ or FIGO III, IVA any N	65.2%	52.8%

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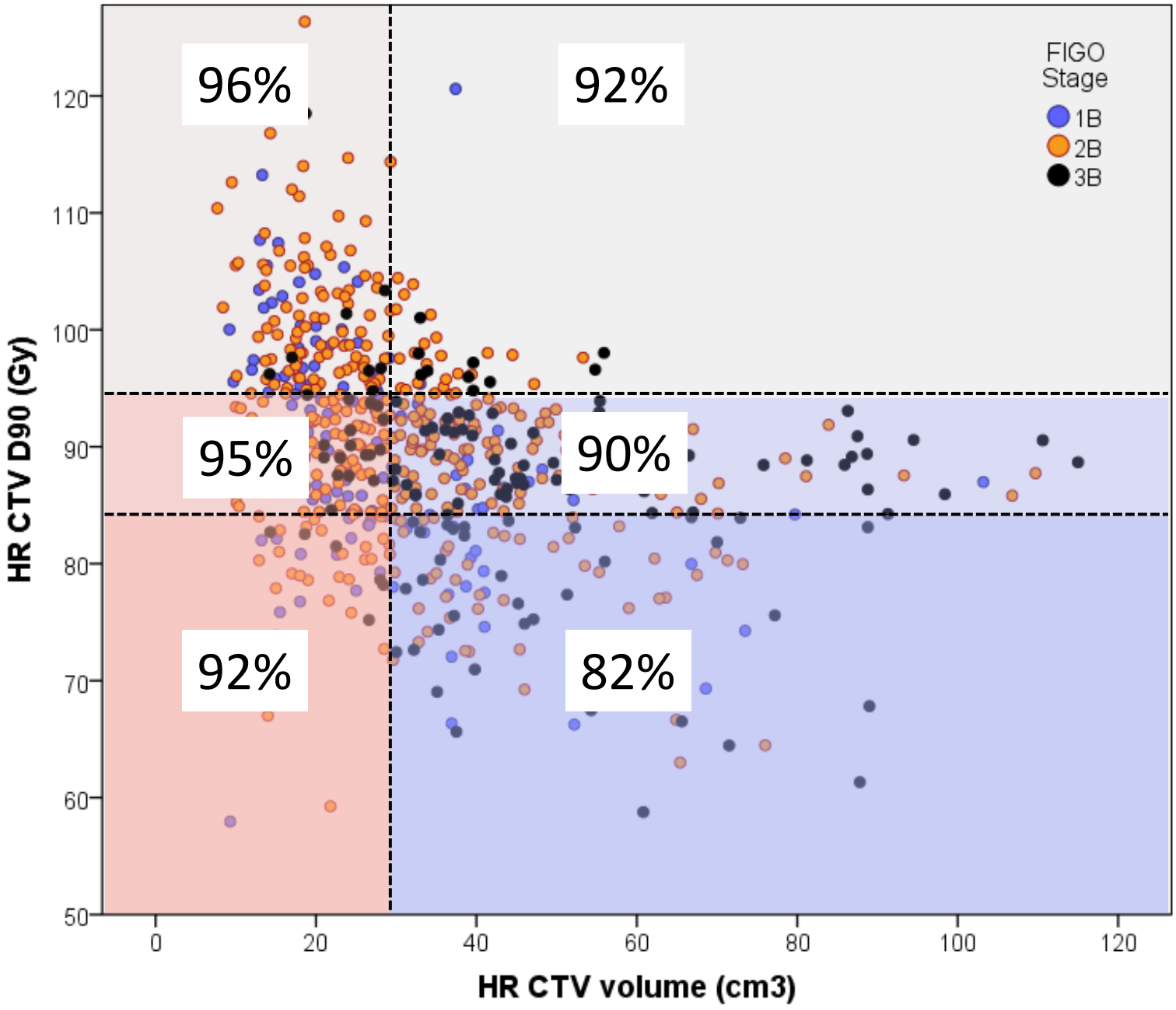
Local control according to dose and volume



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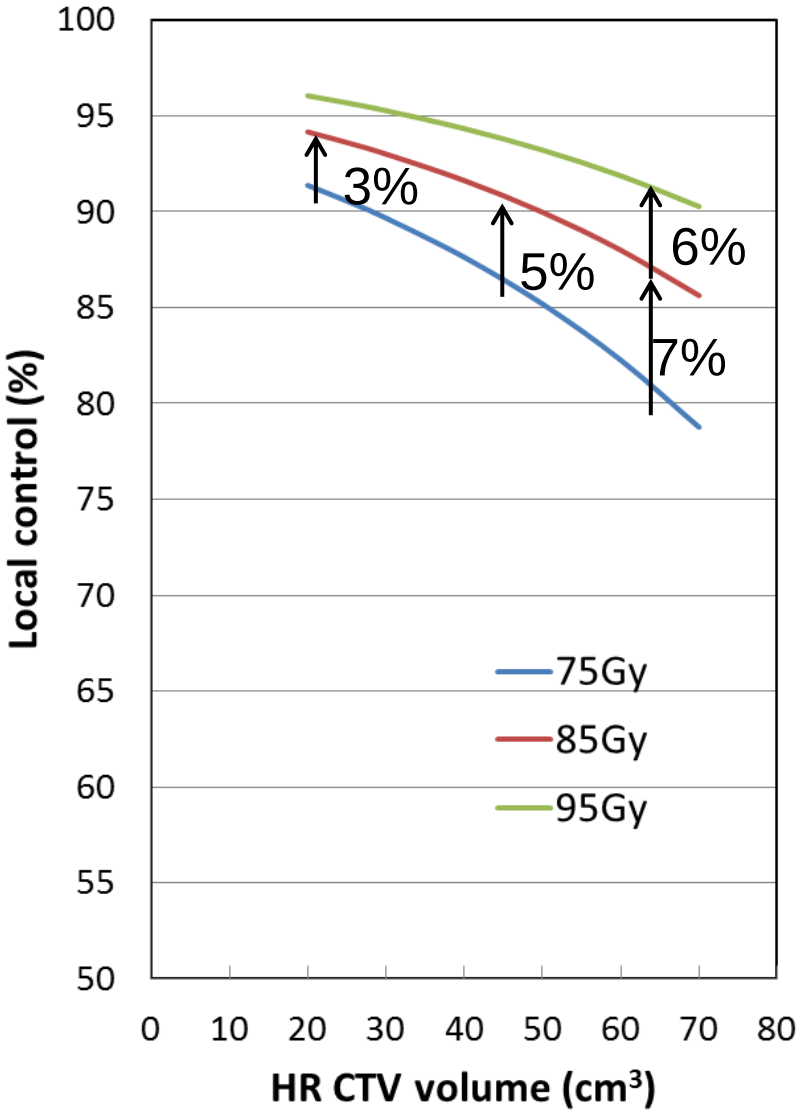
Dose volume response

- Cox regression
- Dose and volume continous co-variates
- Significance:
  - p=0.07 for CTV_{HR} D90
  - p=0.01 for CTV_{HR} volume
- Hazard ratios:
  - 0.962 for CTV_{HR} D90 (per Gy)
  - 1.018 for CTV_{HR} volume (per cc)

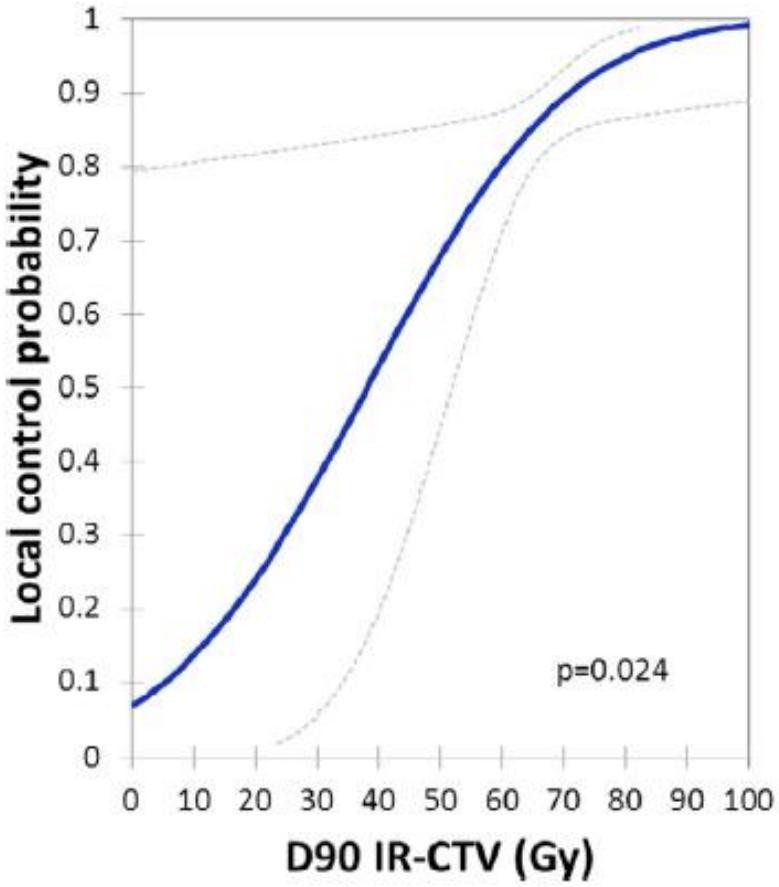
Local control at 3 years

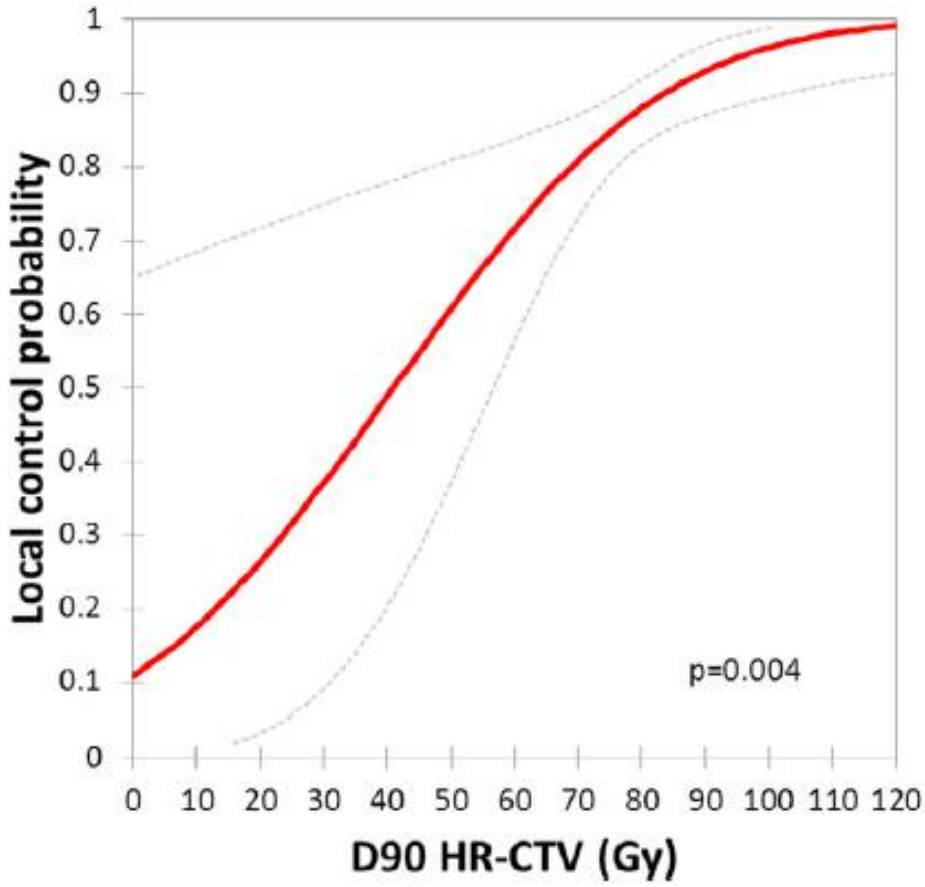


Impact of treatment time and dose escalation on local control in locally advanced cervical cancer treated by chemoradiation and image-guided pulsed-dose rate adaptive brachytherapy

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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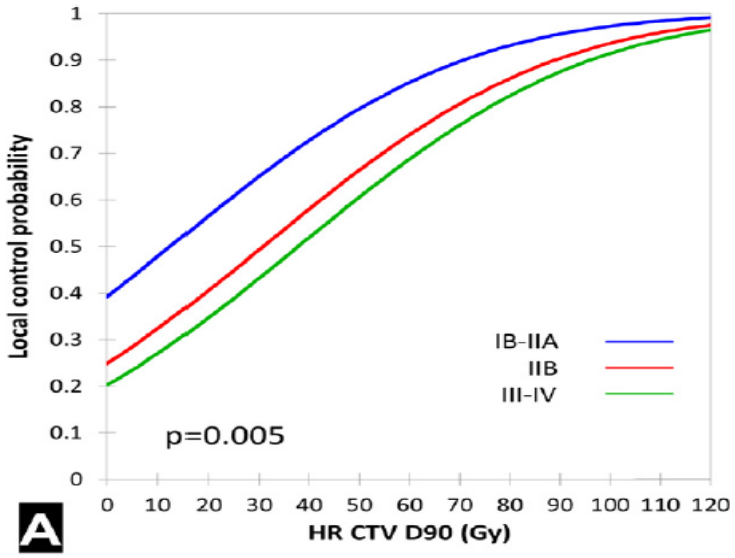

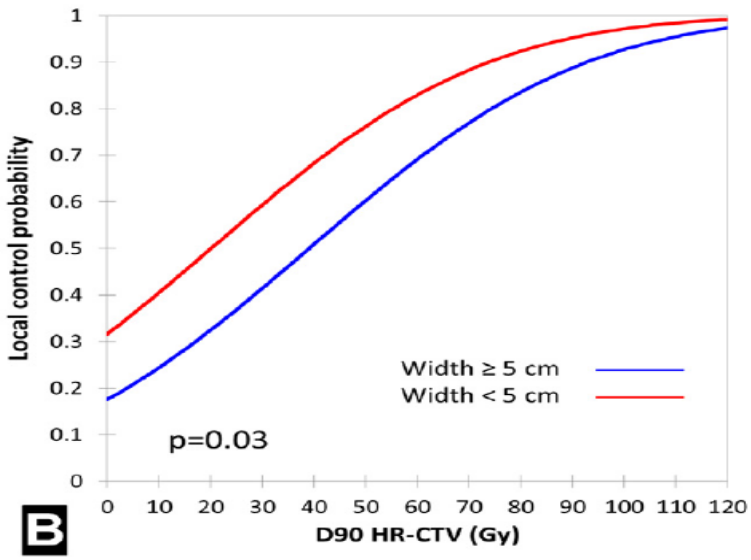

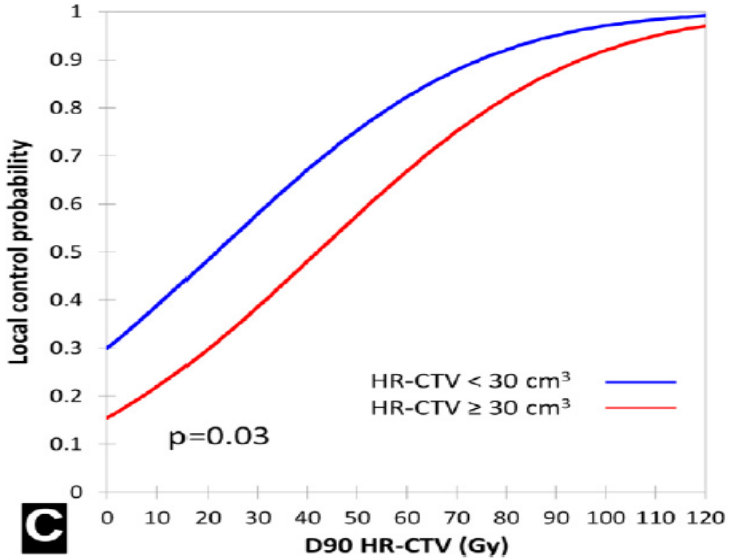

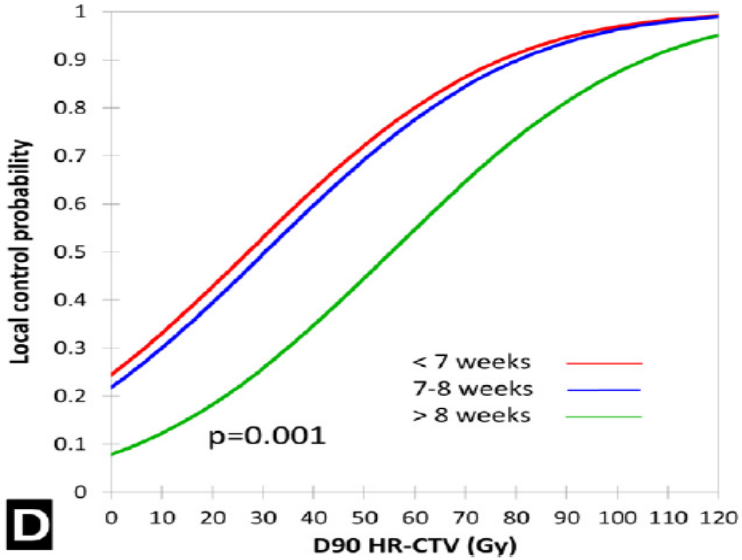

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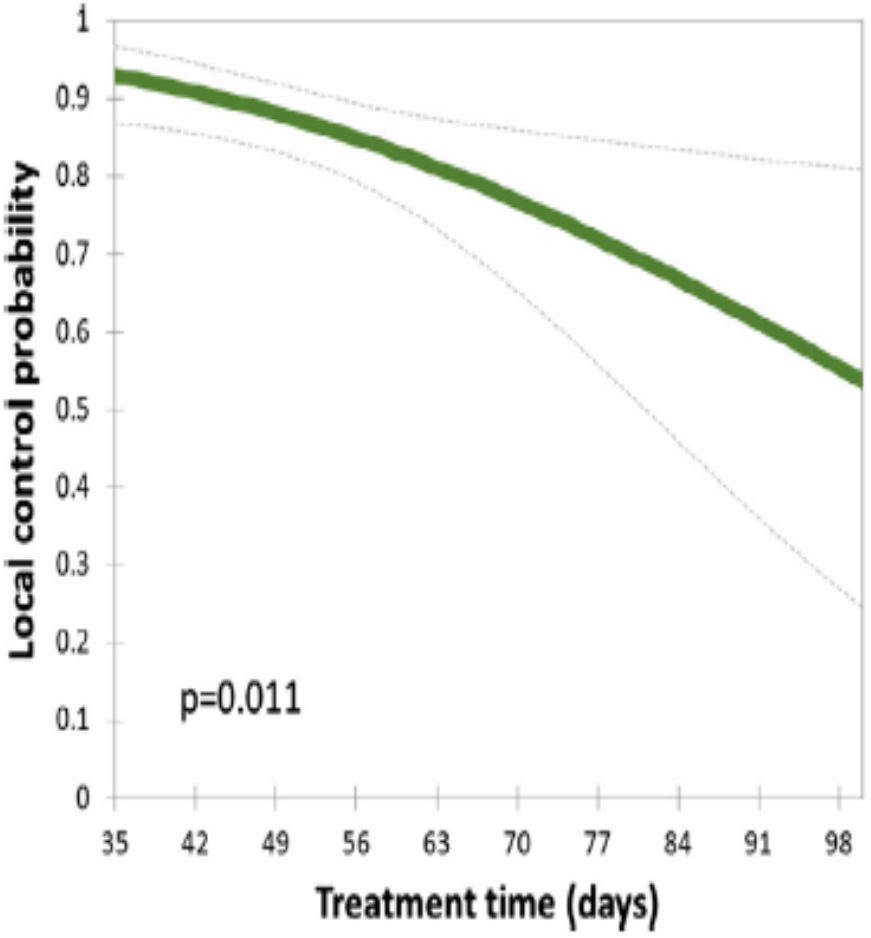
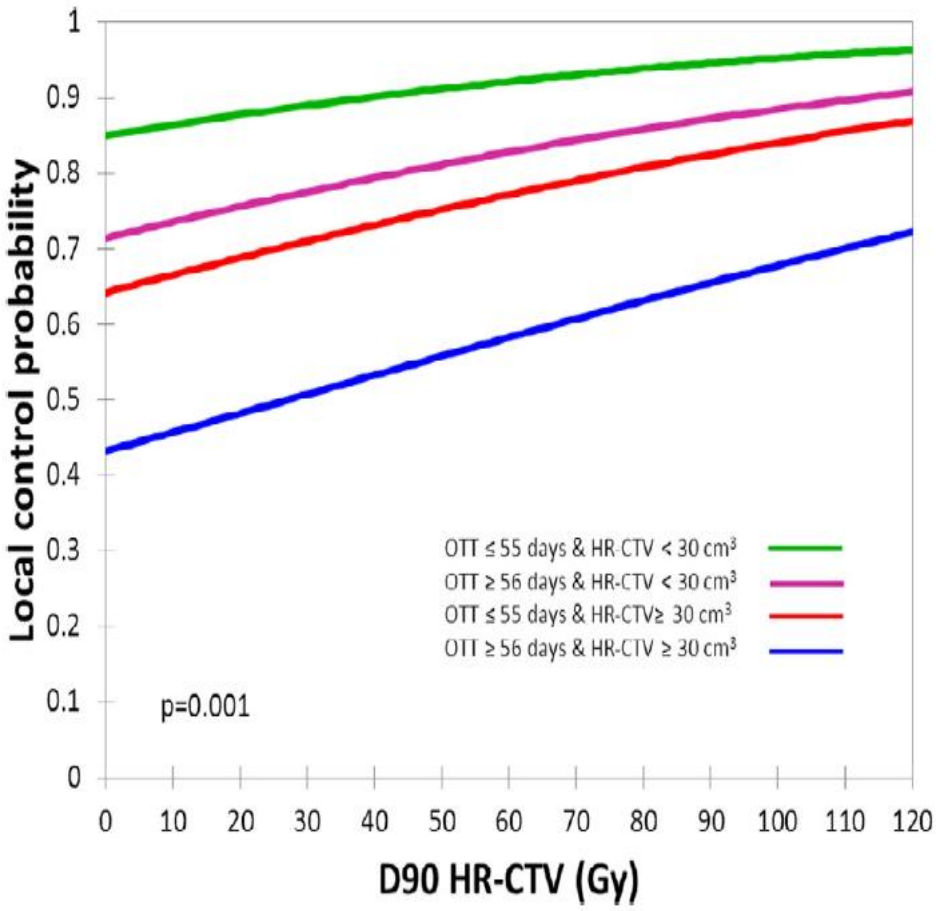
Radiotherapy and Oncology xxx (2014) xxx–xxx

225 patients: 25% IB2, 50% IIB, 10% IIIB





Results and complications of 3D brachytherapy for cervical cancer

- Dosimetric
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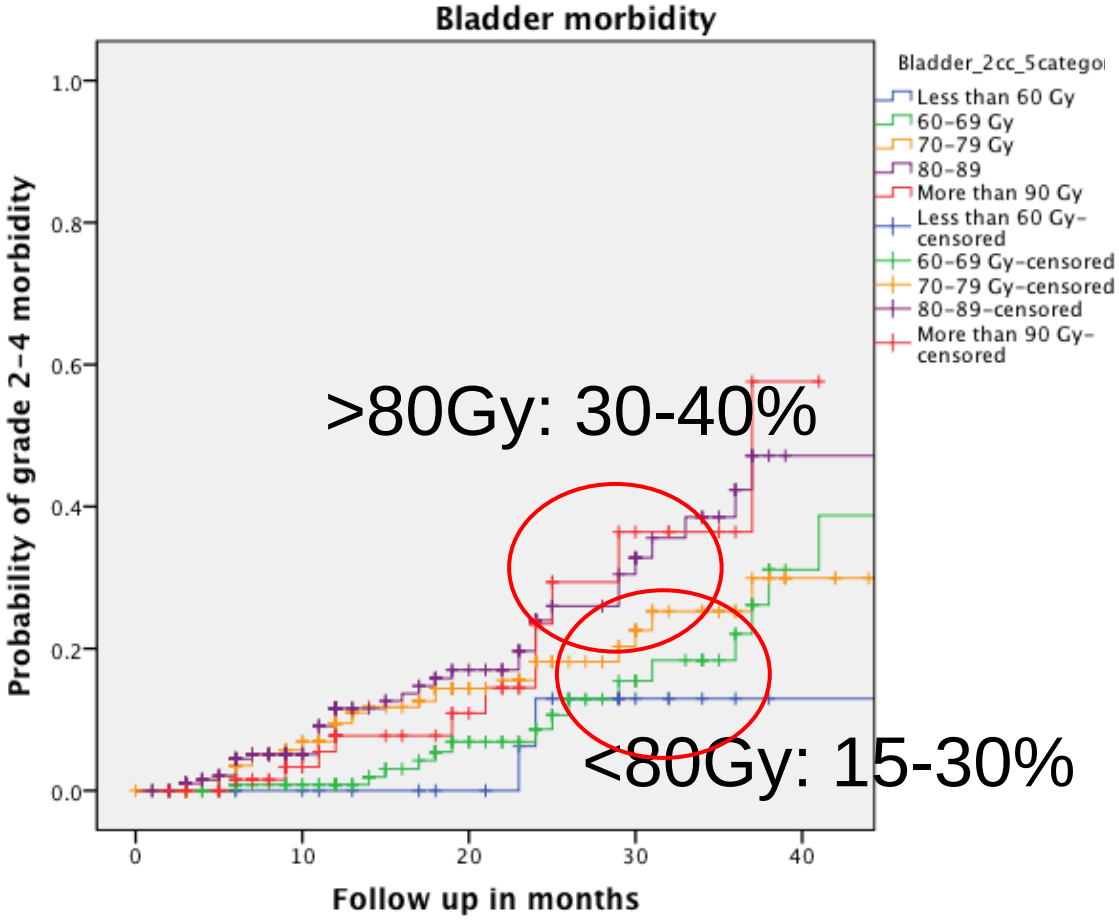
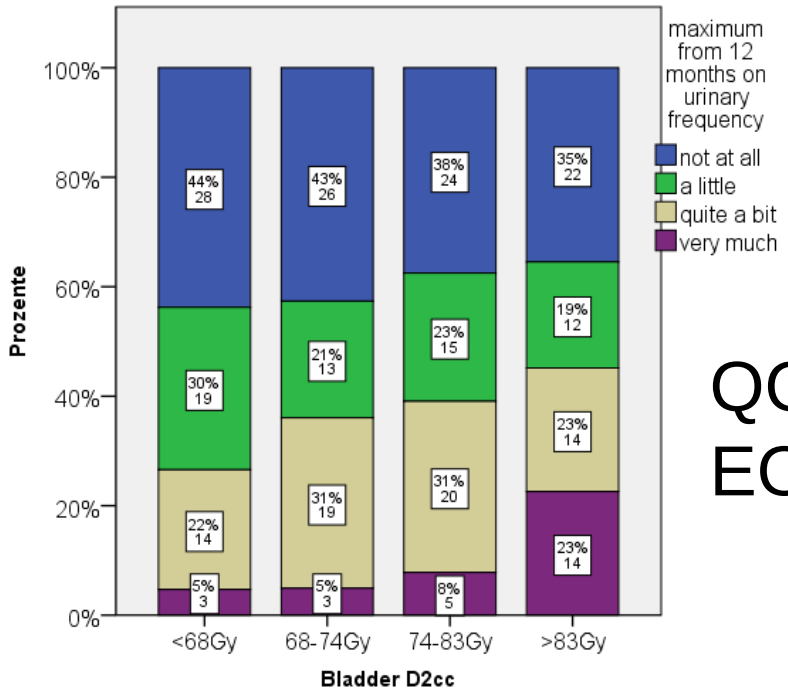
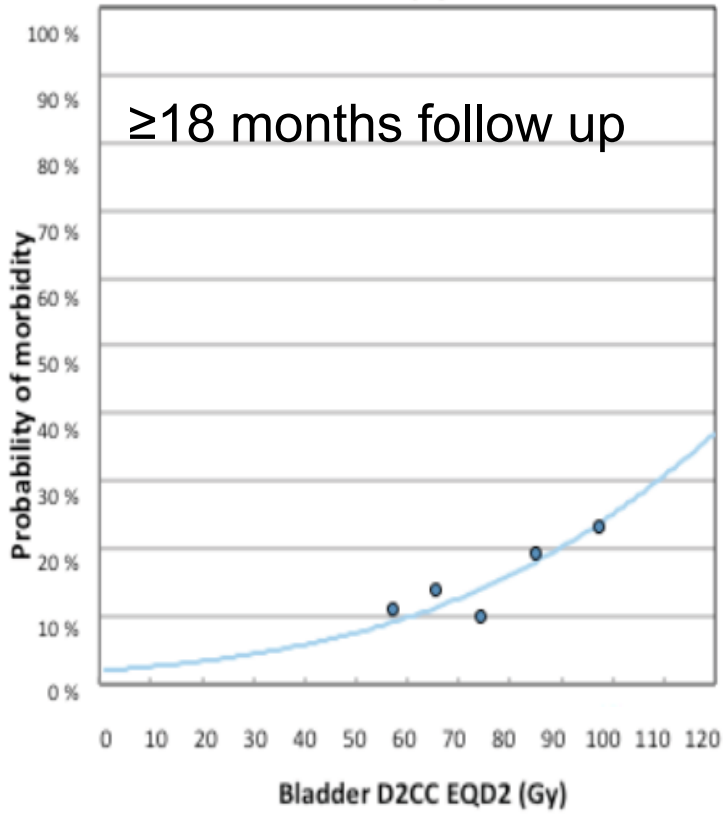
Bladder D2cc

- EMBRACE CTCAE
- All endpoints except ureter stenosis G≥2



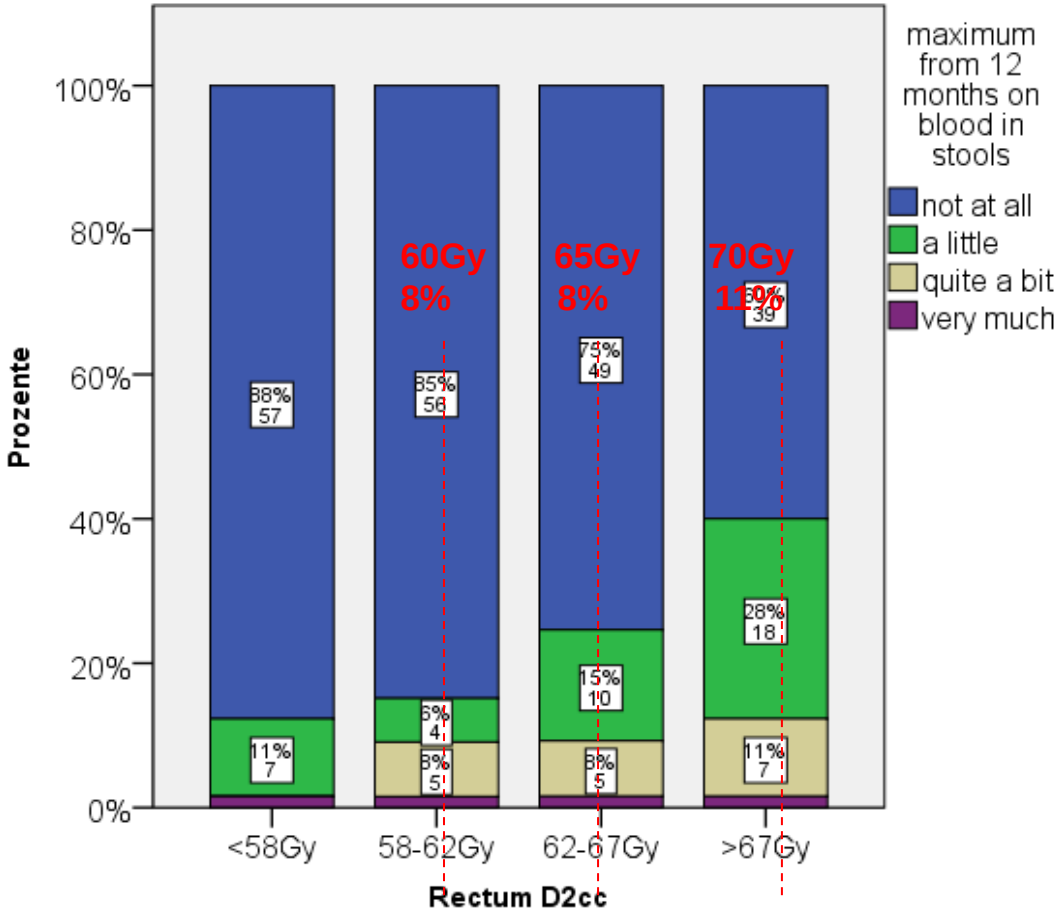


QOL EORTC

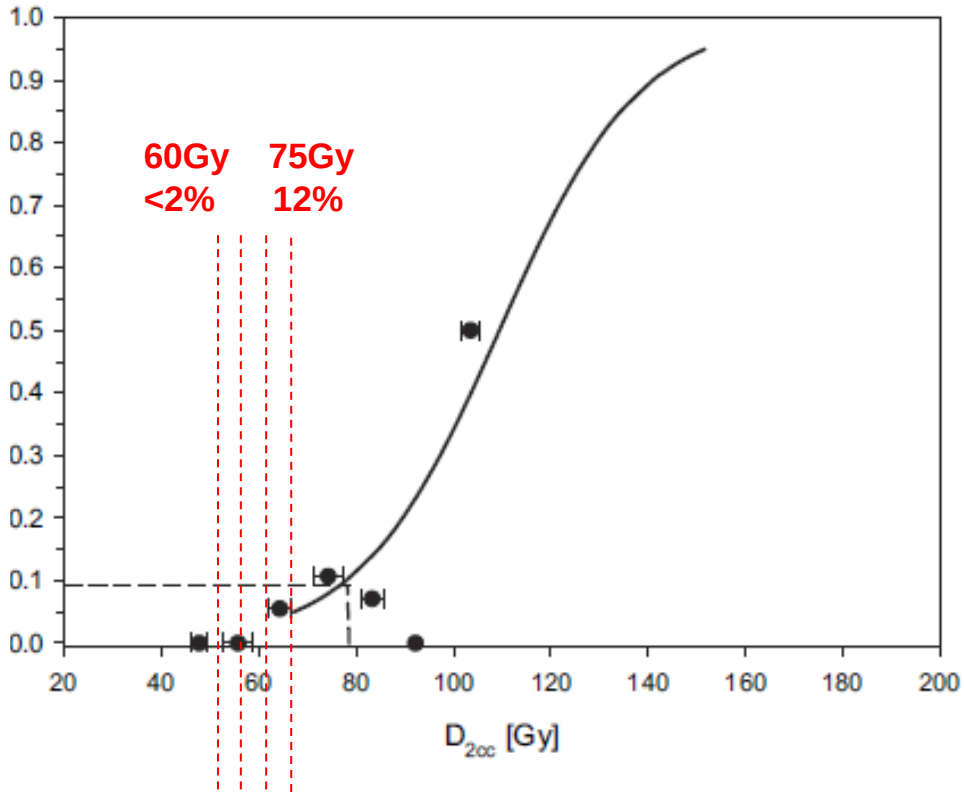


Rectum D2cc

EMBRACE data extraction
Oct 2012
Patient reported (≥12m FU)

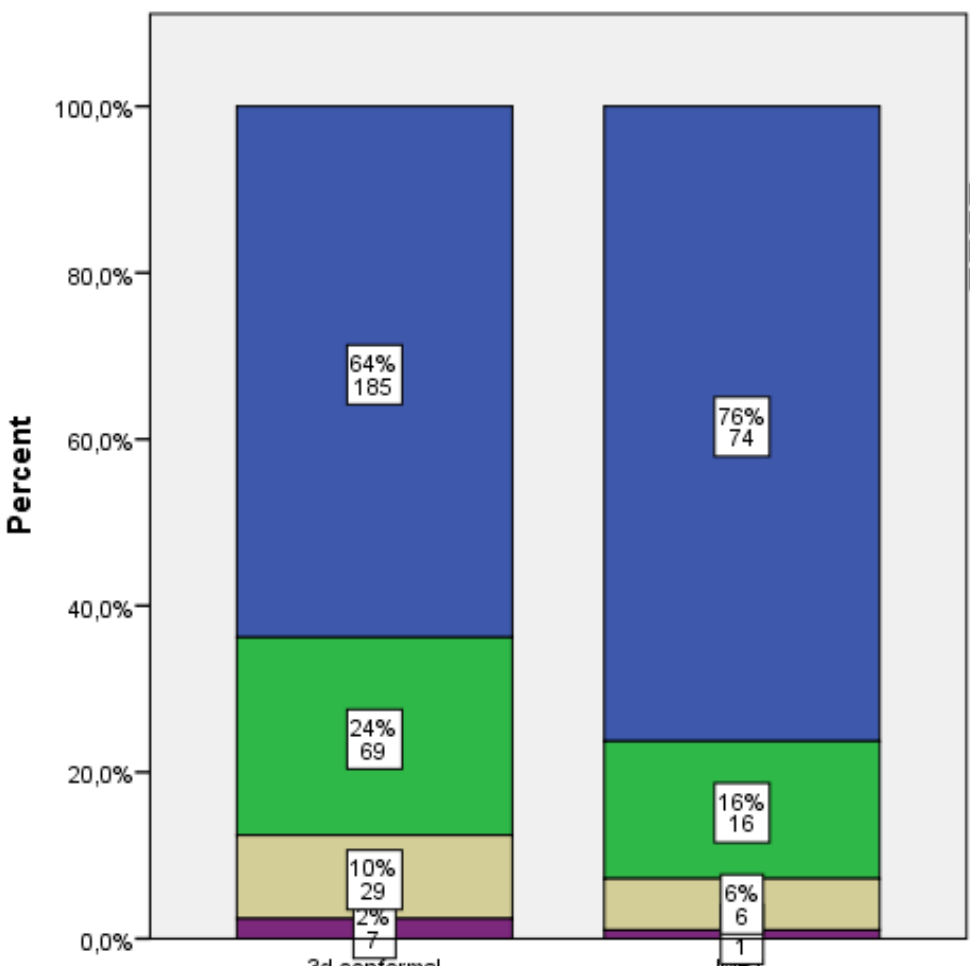


Georg et al 2011, 141 pts
≥G2 (mainly rectal bleeding)

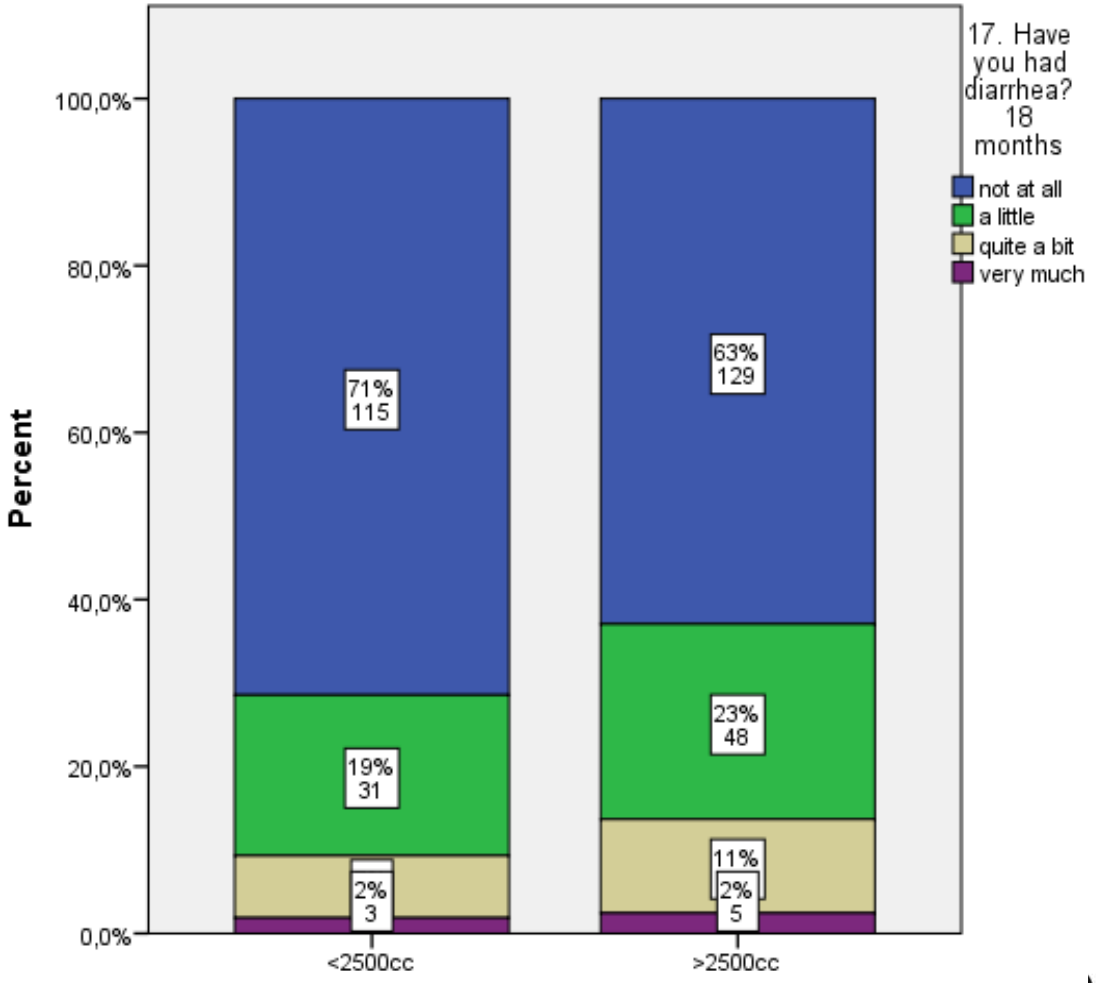


. Relationship between D_{2cc} and late side effects in the rec-

EBRT dose and Diarrhea
Patient reported prevalence at 18M, 390 patients

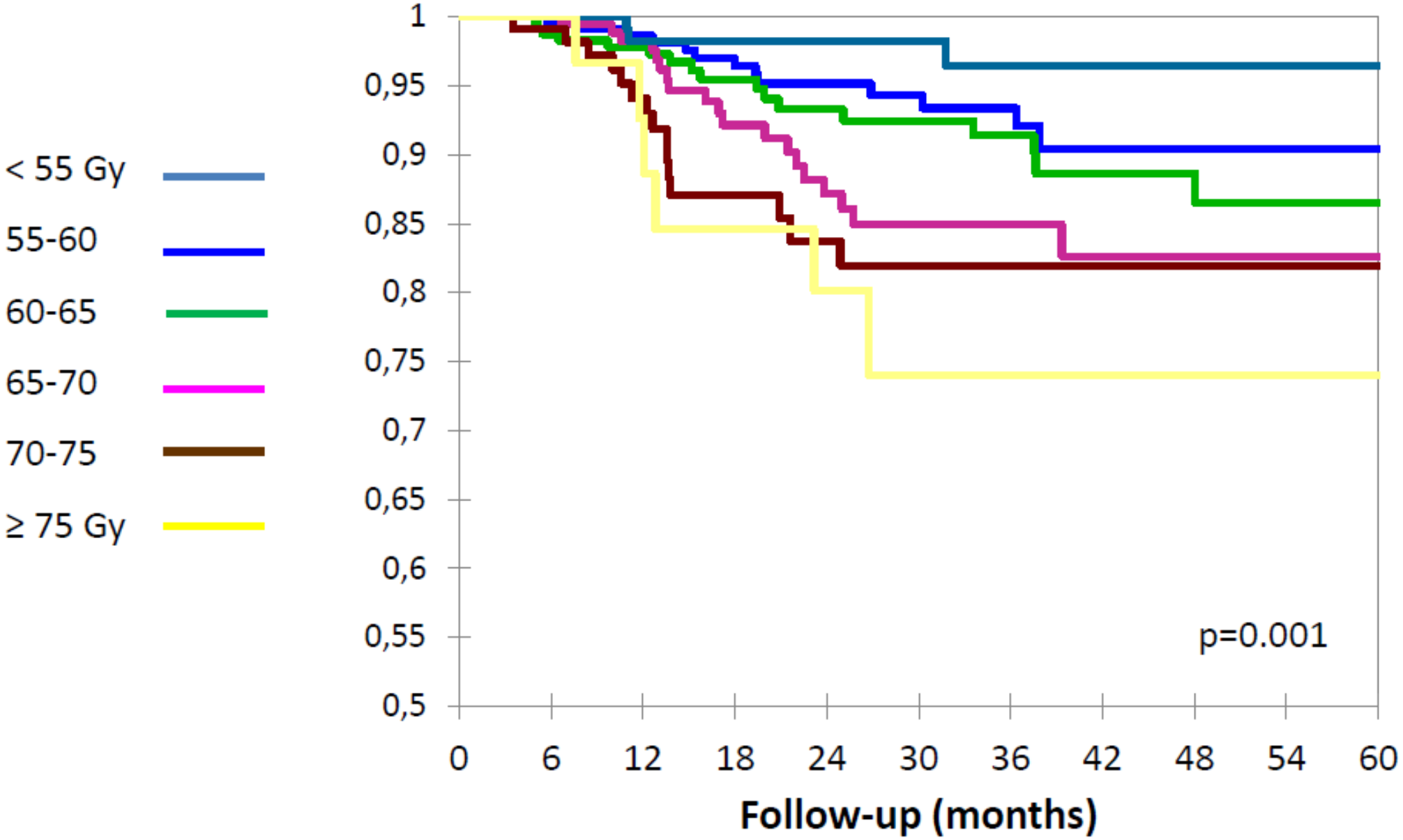


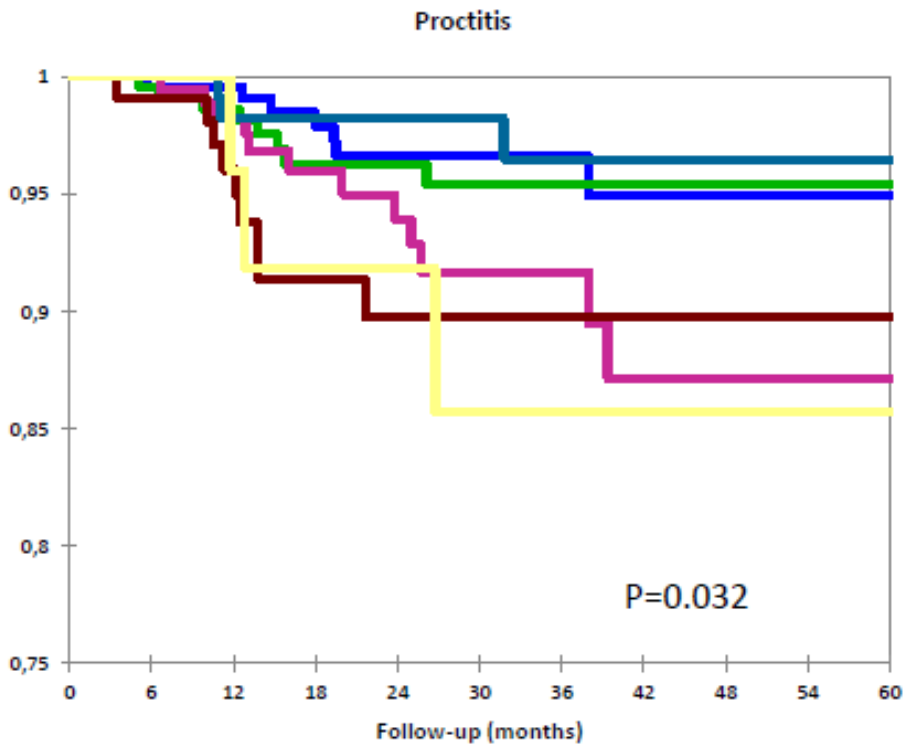
CRT IMRT

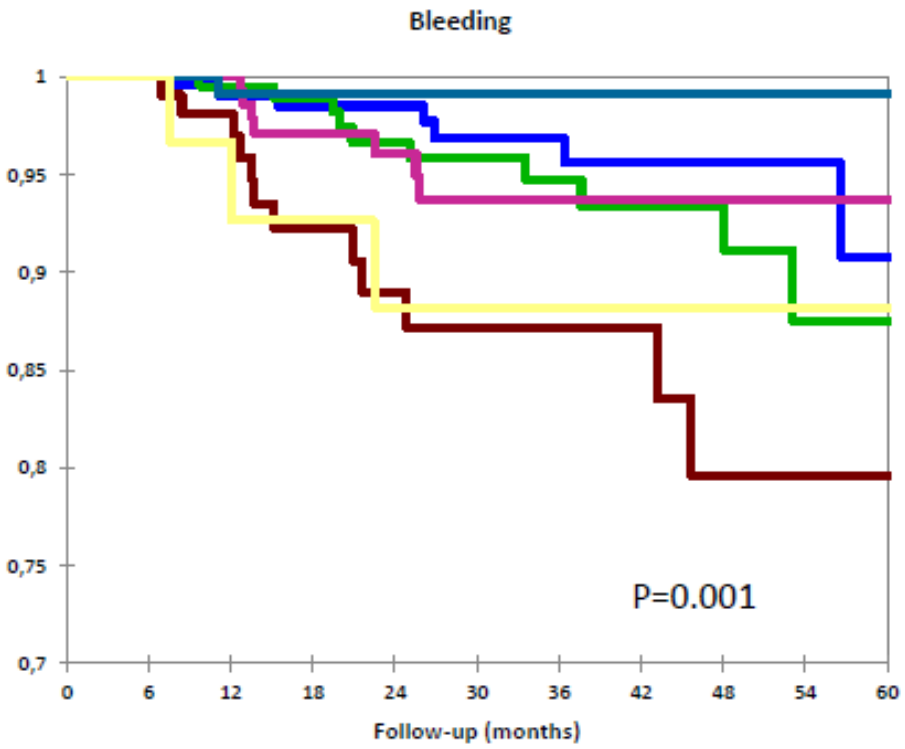


Volume irradiated to 43Gy

Grade 2-4 rectal morbidity







< 55 Gy

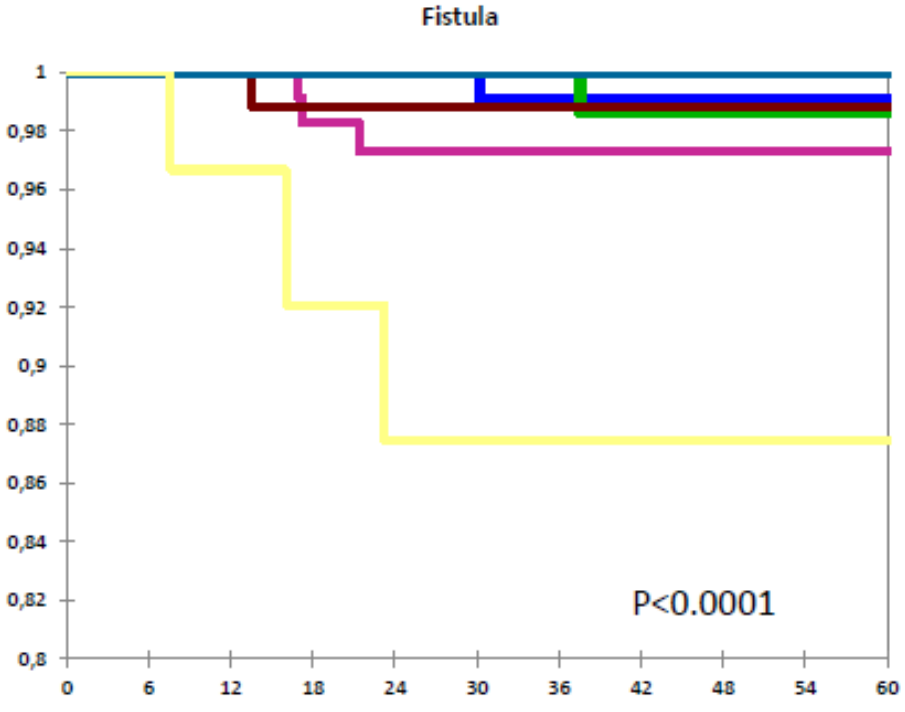
55-60

60-65

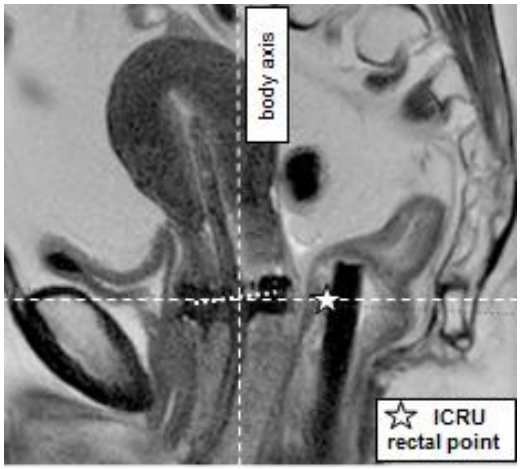
65-70

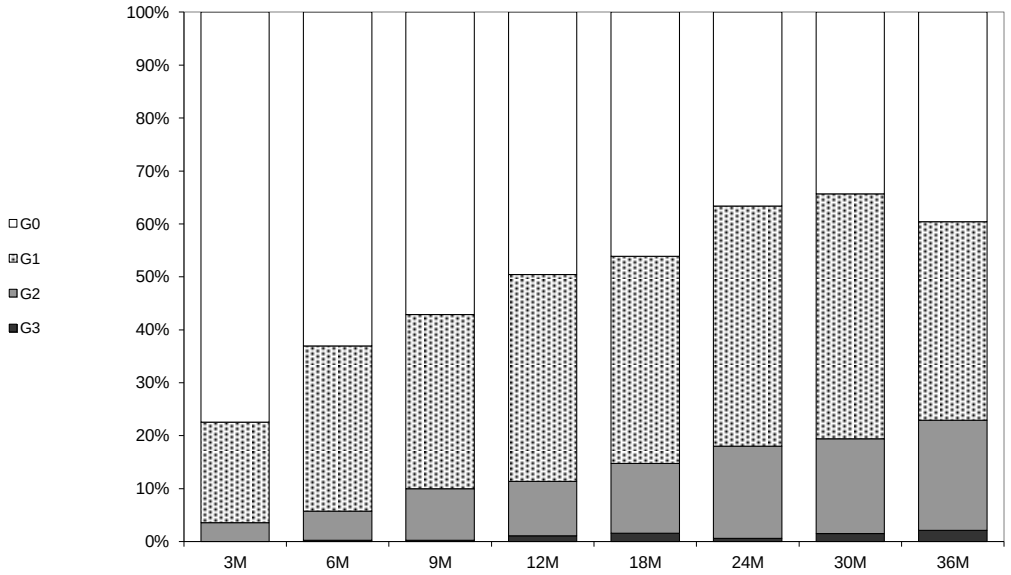
70-75

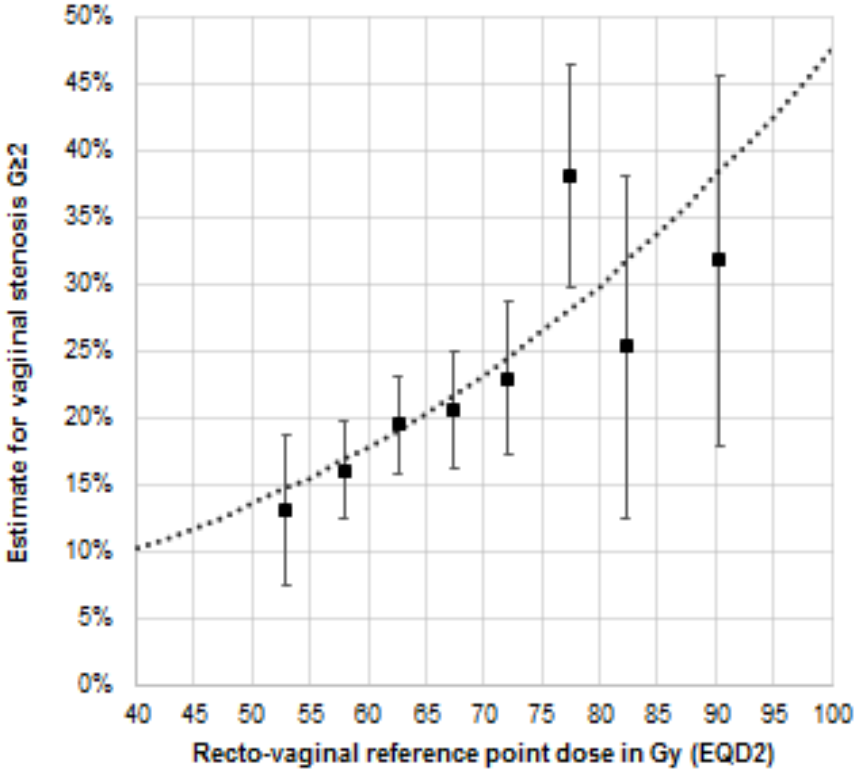
≥ 75 Gy

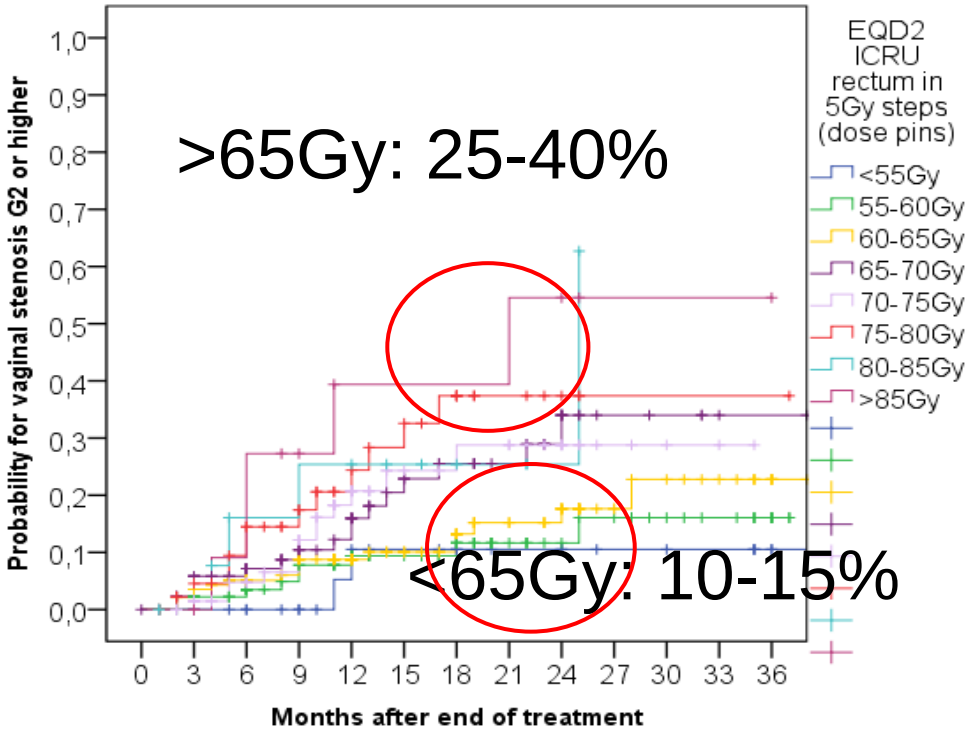


Vagina
ICRU rectal point



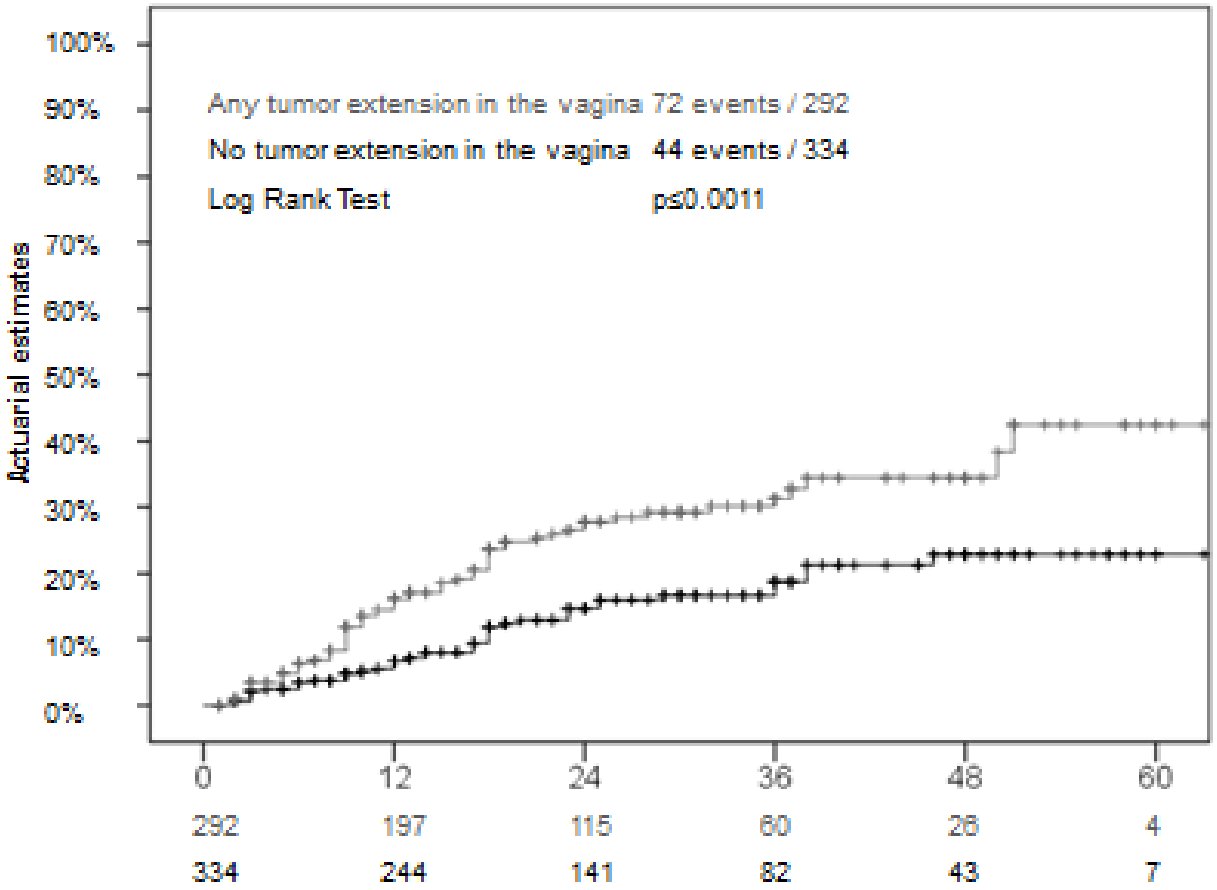






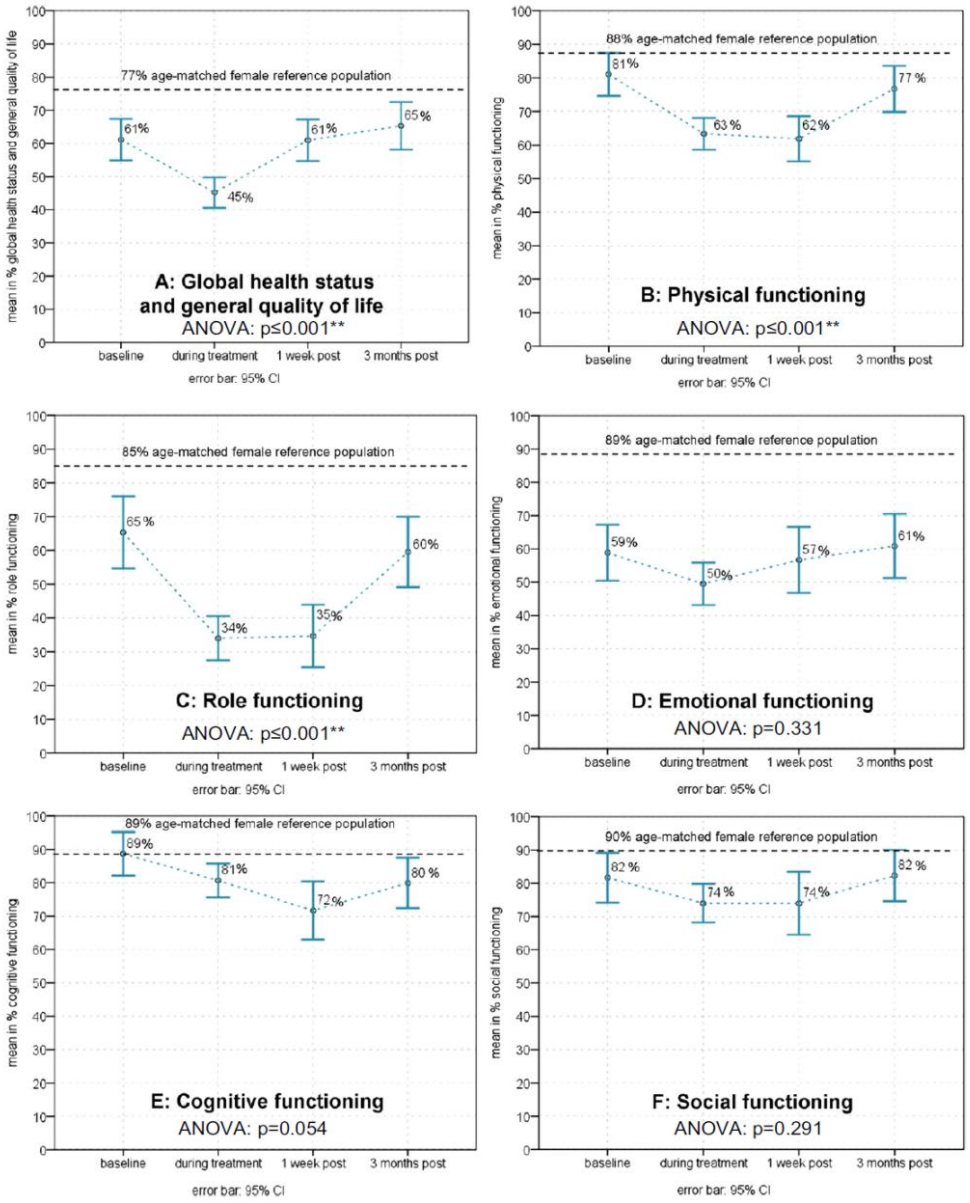
Vaginal morbidity in EMBRACE:

…….vaginal tumour involvement



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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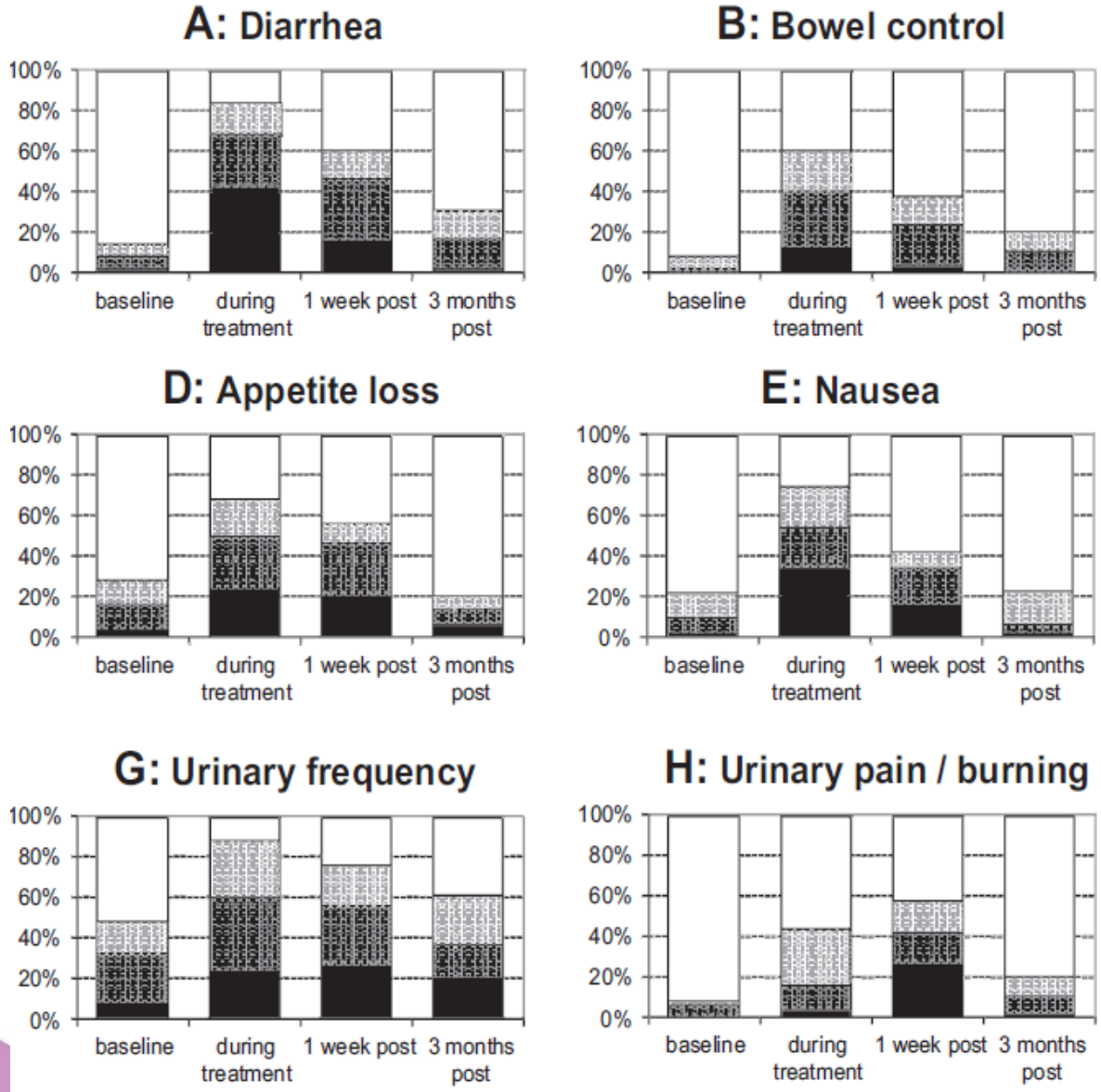

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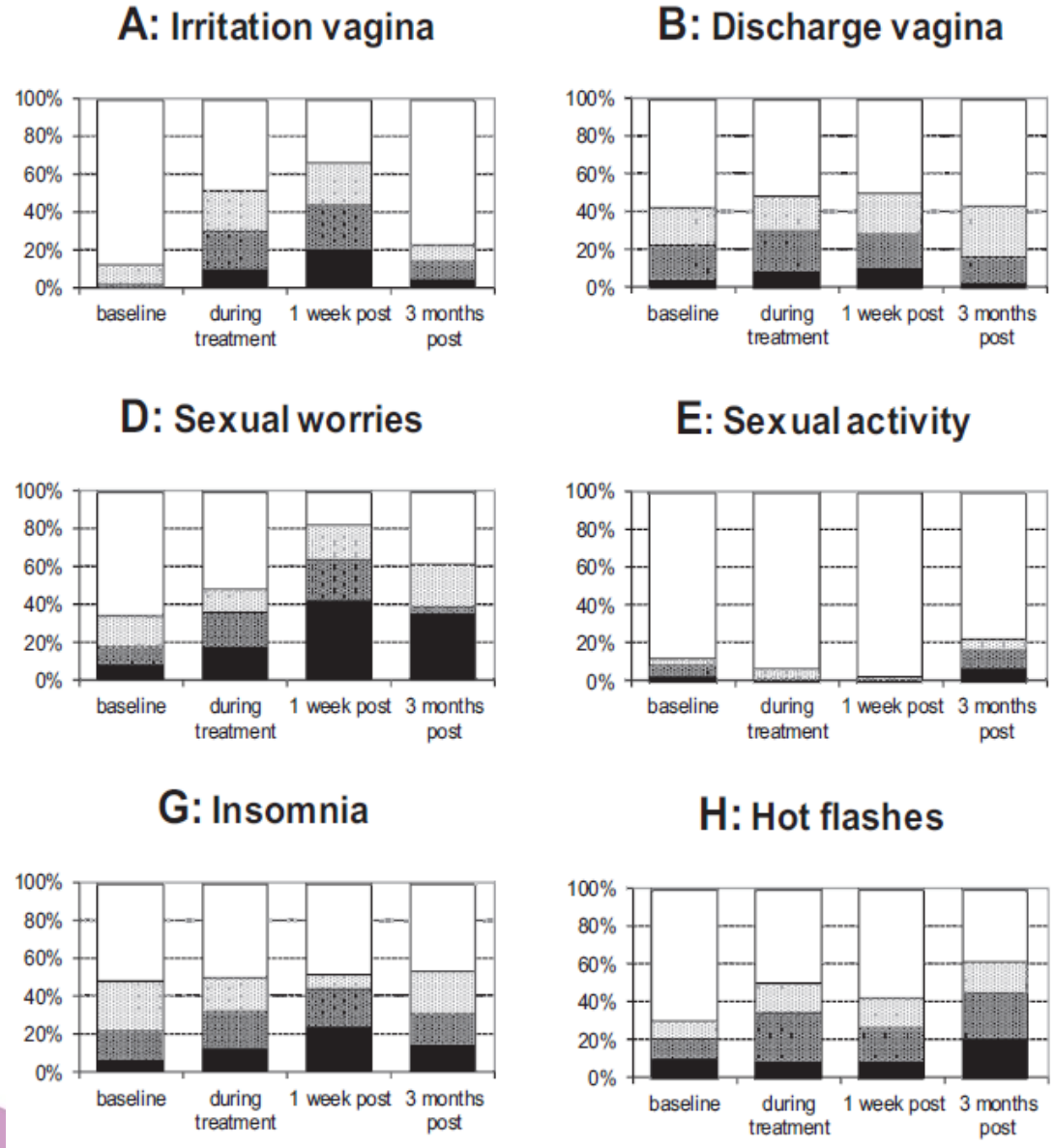
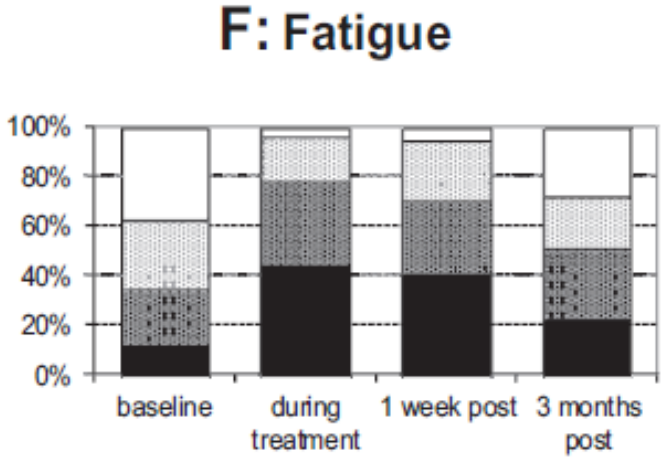


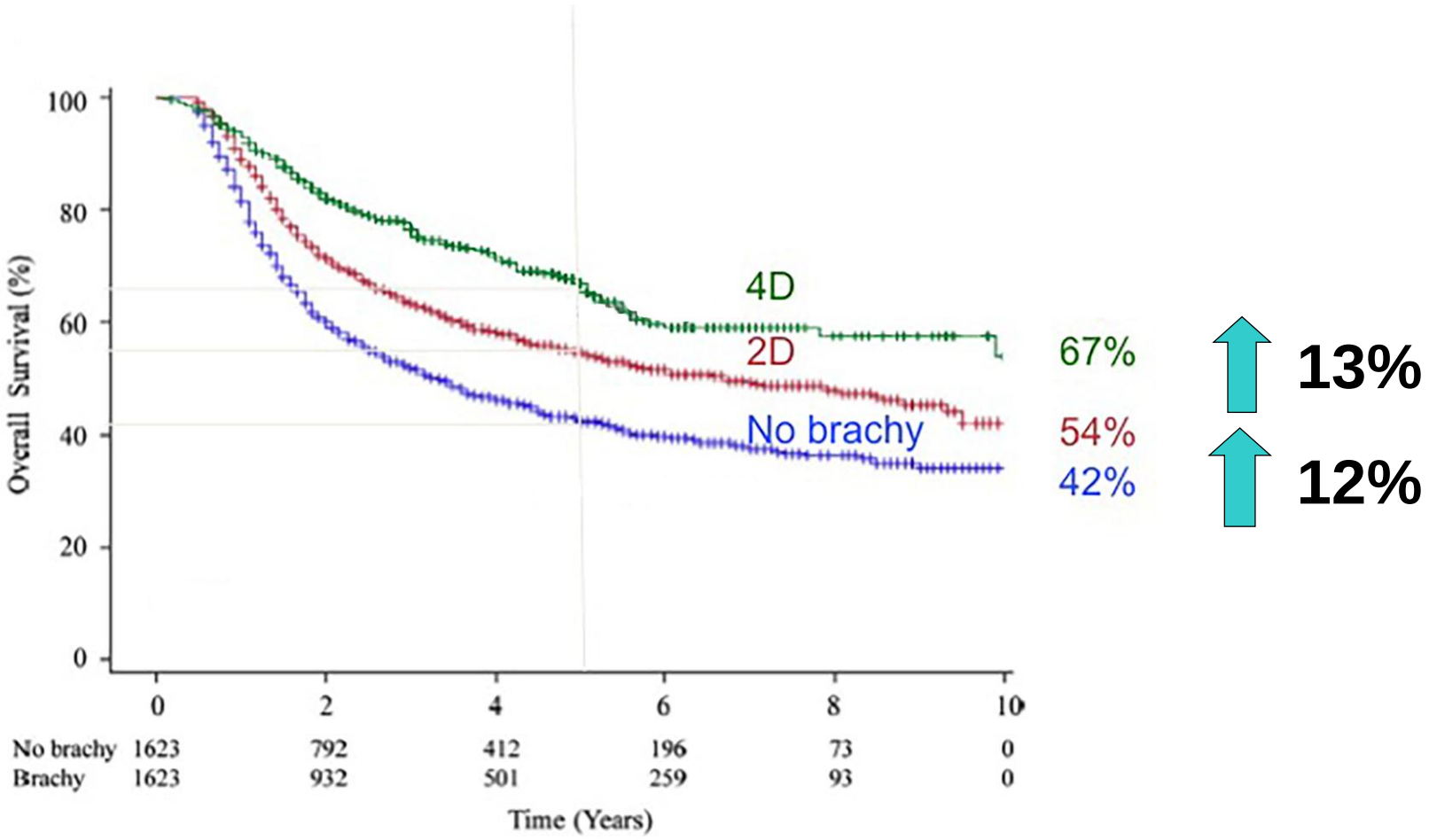


N=50
EORTC QLQ C30
EORTC QLQ Cx24

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

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WWW.ESTRO.ORG/SCHOOL

Concept of IR CTV and HR CTV, ICRU 89 report

Peter Hoskin
Mount Vernon Cancer Centre

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Dose Specification in Cervix Ca Brachytherapy

THEN…….Point A

NOW: Based on 3 D imaging

- GTV, CTV, PTV
- Organs at Risk, OARs

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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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ICRU/GEC ESTRO Report 89

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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Target Definitions

GTV	**:**	**Macroscopic Tumor at BT**
HIGH Risk CTV **HR-CTV**	**:**	**Residual tumour at BT +** **'grey zones' which may be areas of incomplete tumour regression**
INTERMED. Risk CTV : **IR-CTV**		**Macroscopic tumour-bearing regions at time of diagnosis (includes microscopic disease)**
LOW Risk CTV	**:**	**Includes potential microscopic tumour spread at time of diagnosis**

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Target Definitions

GTV	**:**	**Macroscopic Tumor at BT defined clinically and on MR**
HIGH Risk CTV **HR-CTV**	**:**	**Includes entire cervix and any extension into parametria, vagina or uterine cavity + 'grey zones'**
INTERMED. Risk CTV : **IR-CTV**		**HR=CTV expanded by 10-15mm *and* extended to include addition areas of known involvement at diagnosis eg lower vagina, upper uterine cavity.** **Constrained to OARs**

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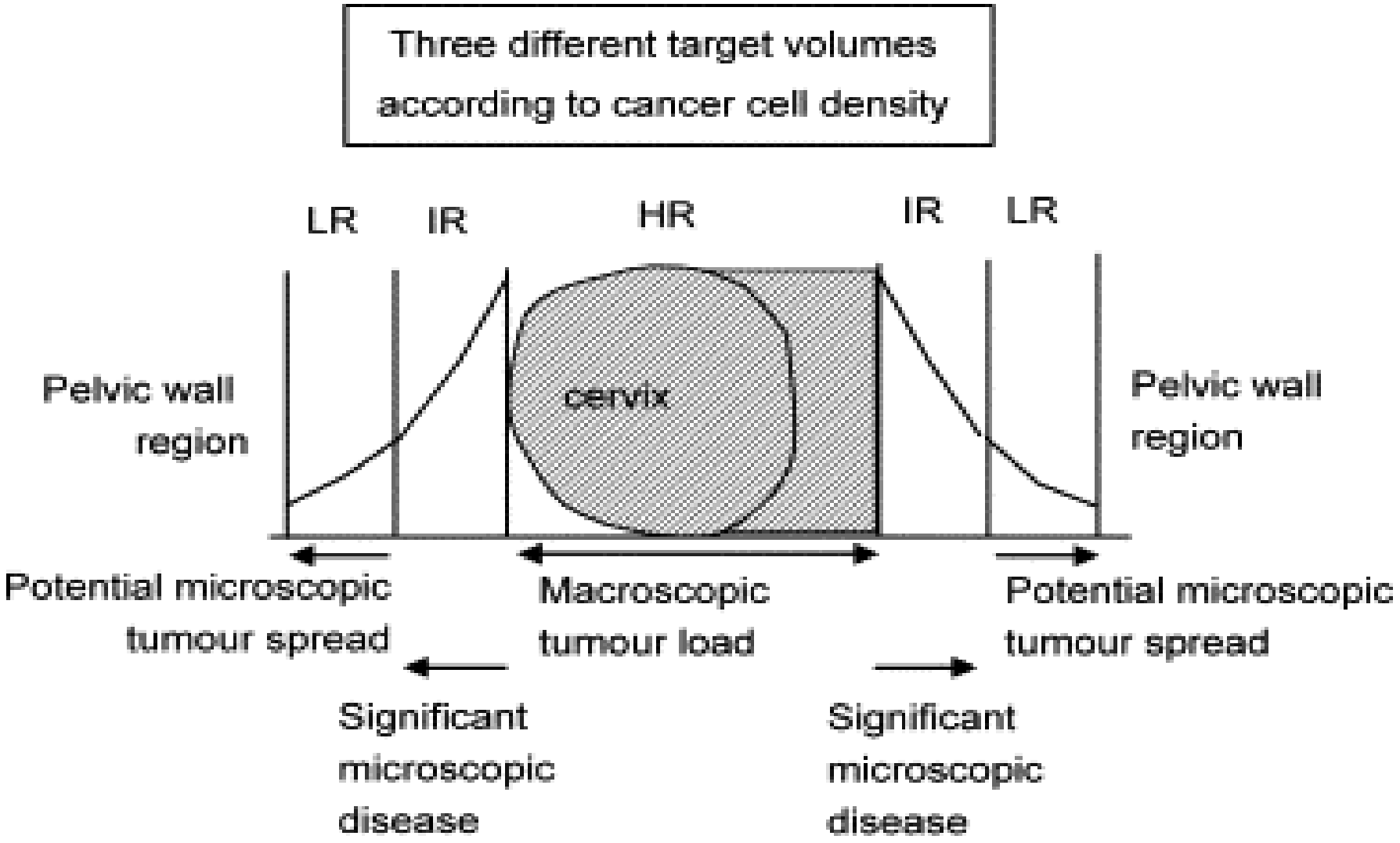
GEC ESTRO guidelines for gynae brachytherapy



Potter et al RT&O2005

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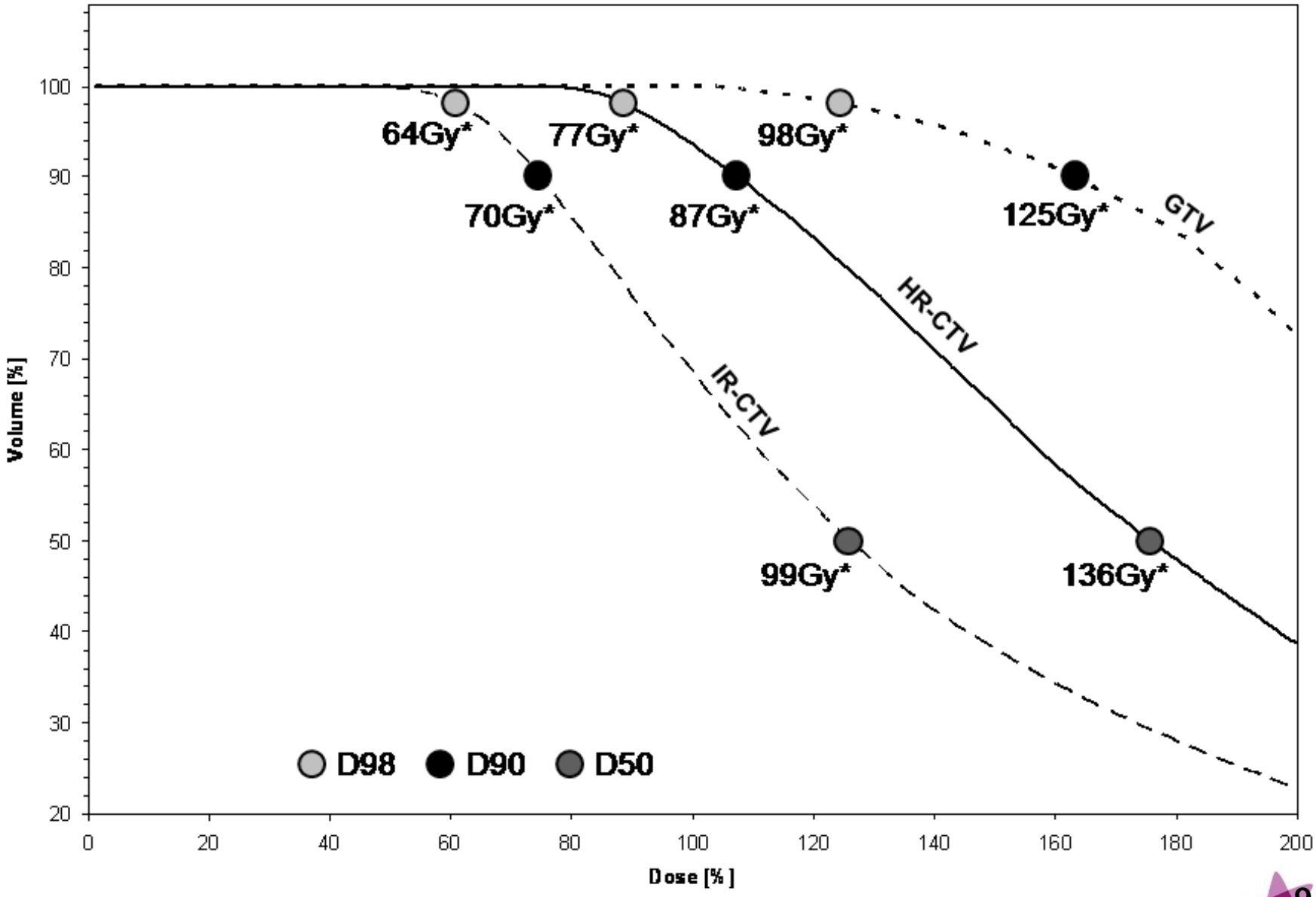
DVH for target volumes



How do we see the tumour?

- At diagnosis
  - EUA
  - MRI
  - ?CT PET
- At end of chemoradiation
  - Week 5 MRI
- At BT
  - EUA
  - MRI

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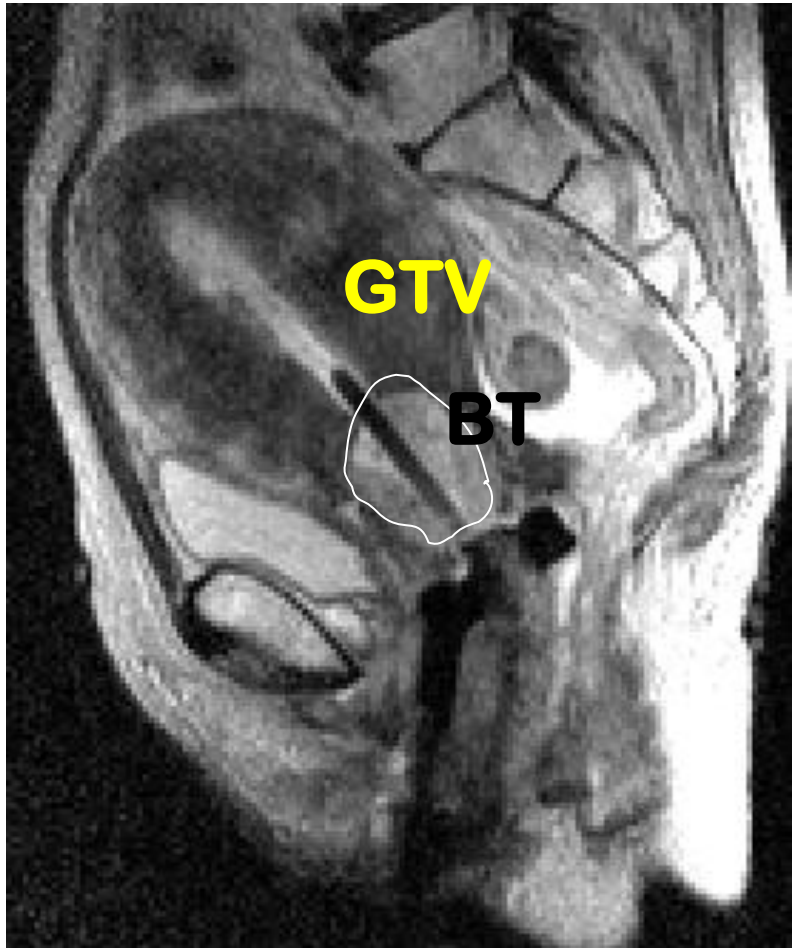
Cervix Cancer FIGO IB2
significant remission after EBRT



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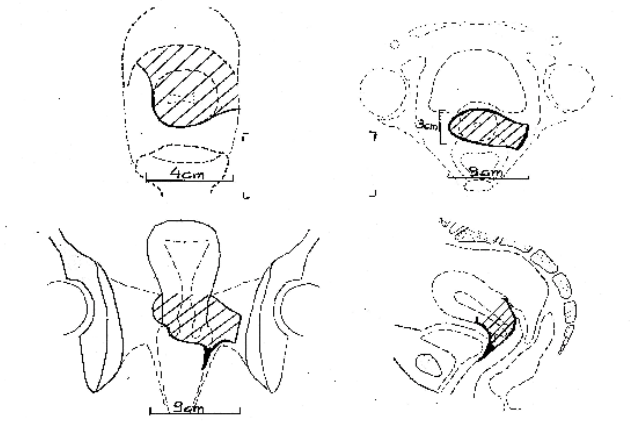
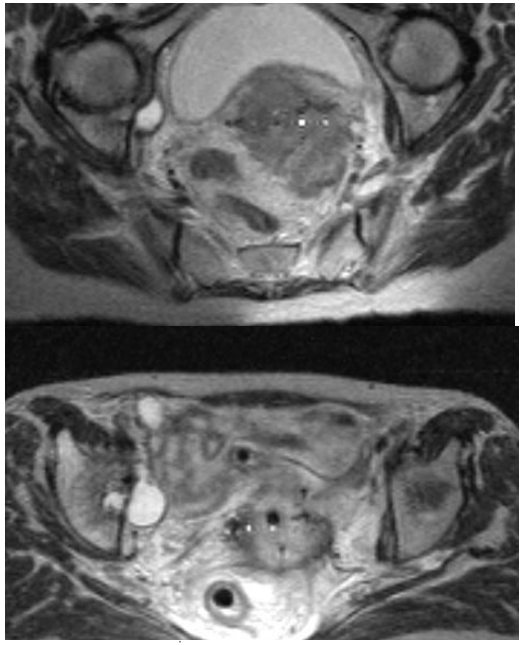
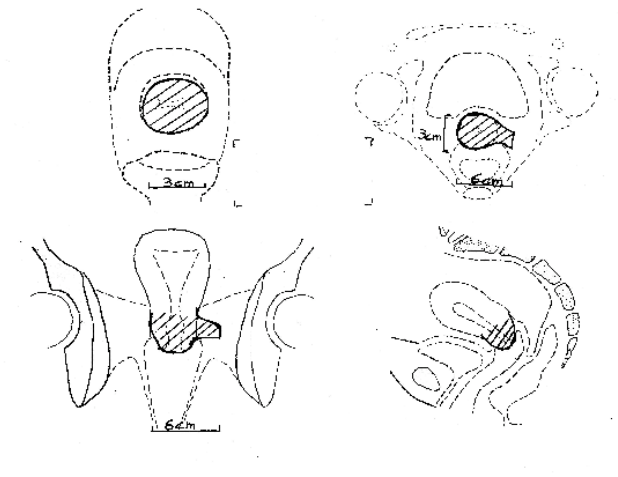
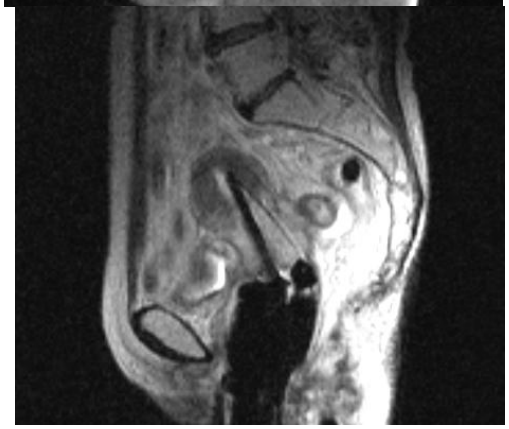
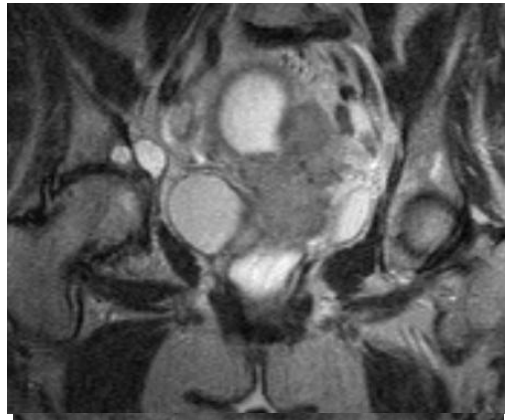


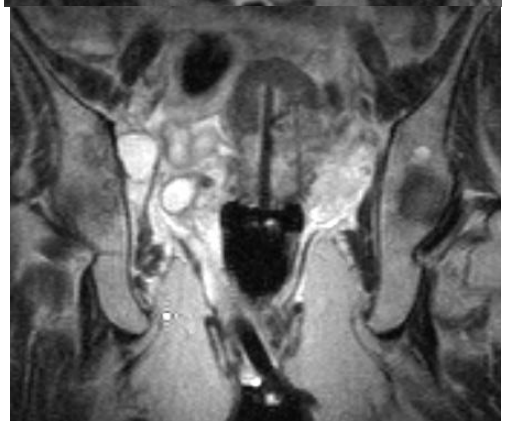




At diagnosis







At time of Brachytherapy

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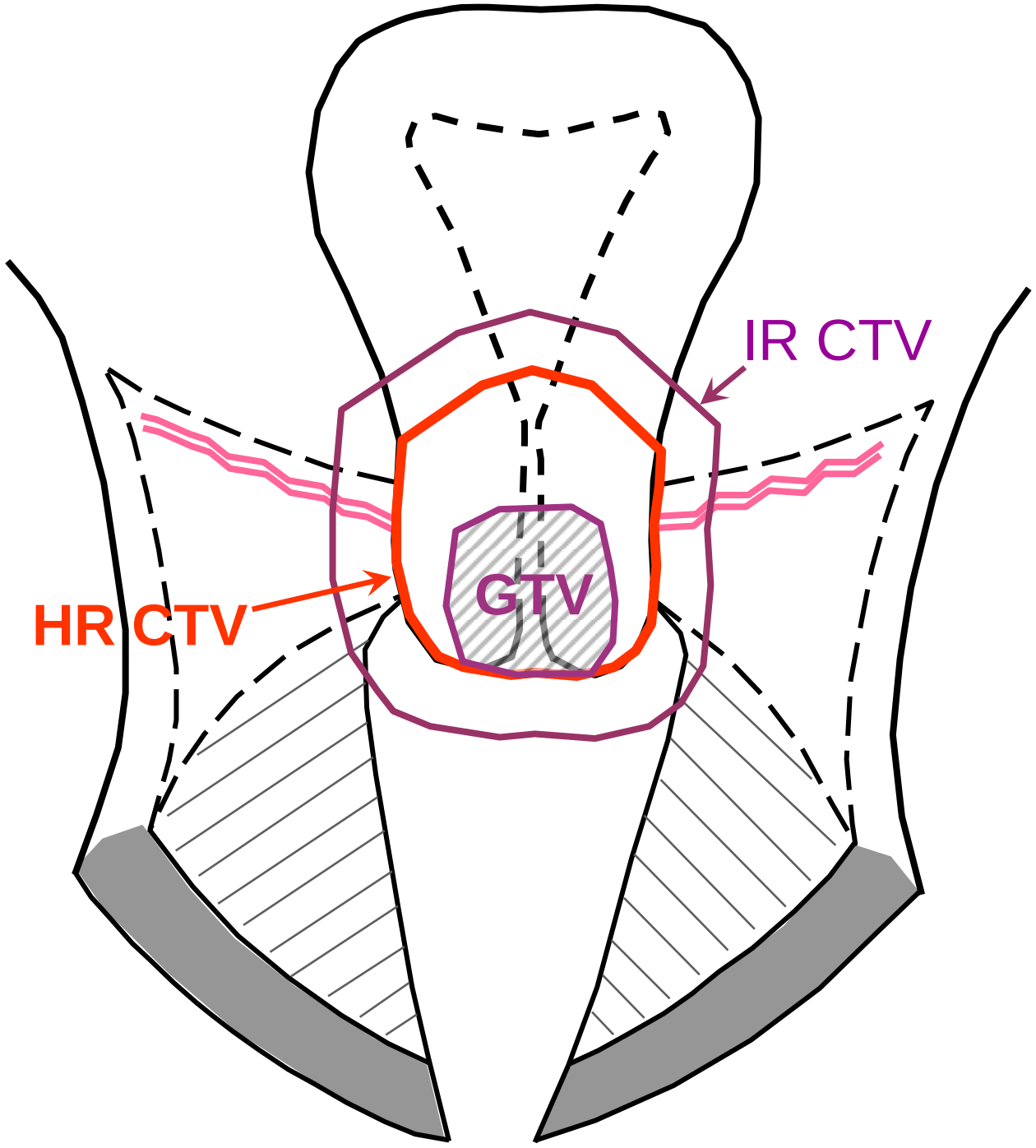
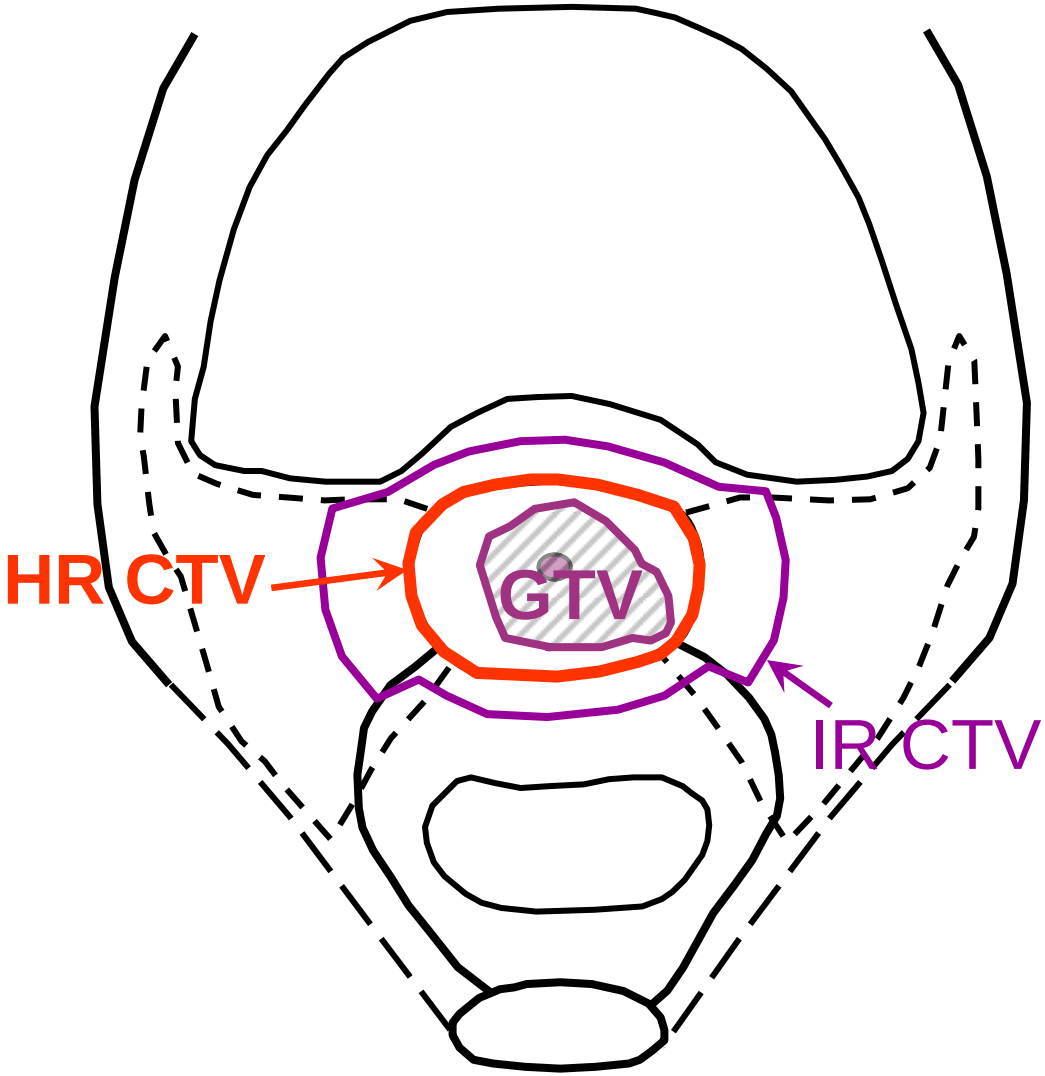
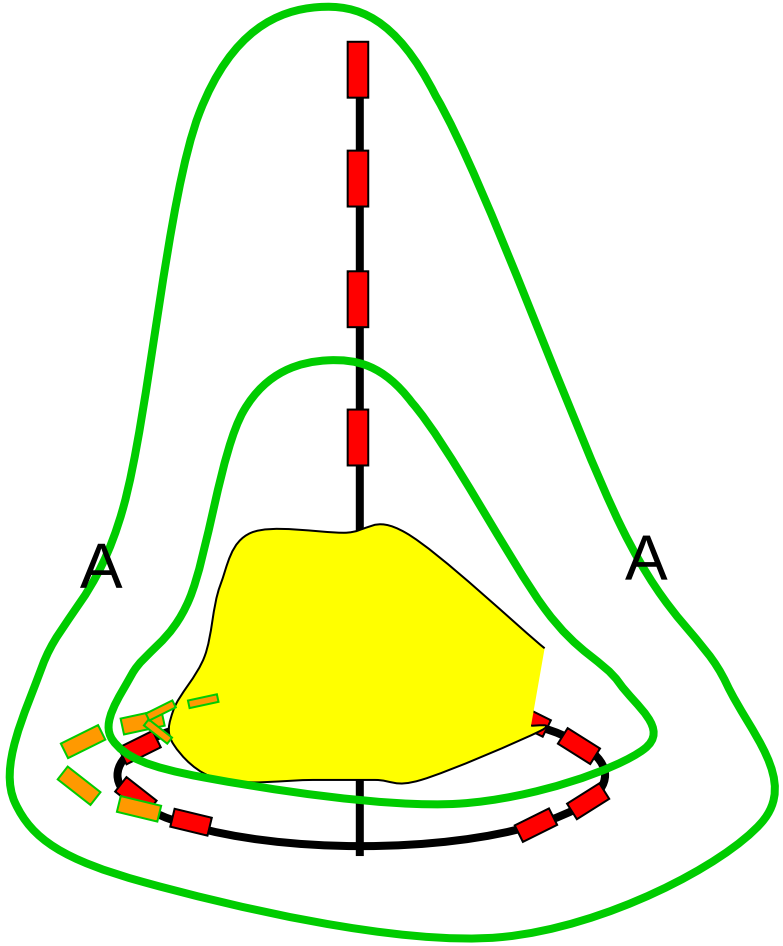
Stage IB



Stage IB



The paradox of HR-CTV in a small primary tumour



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Stage IIA-IV A

High Risk CTV:

- always whole cervix

  plus 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)

.....including any regions originally involved

.....constrained to OARs

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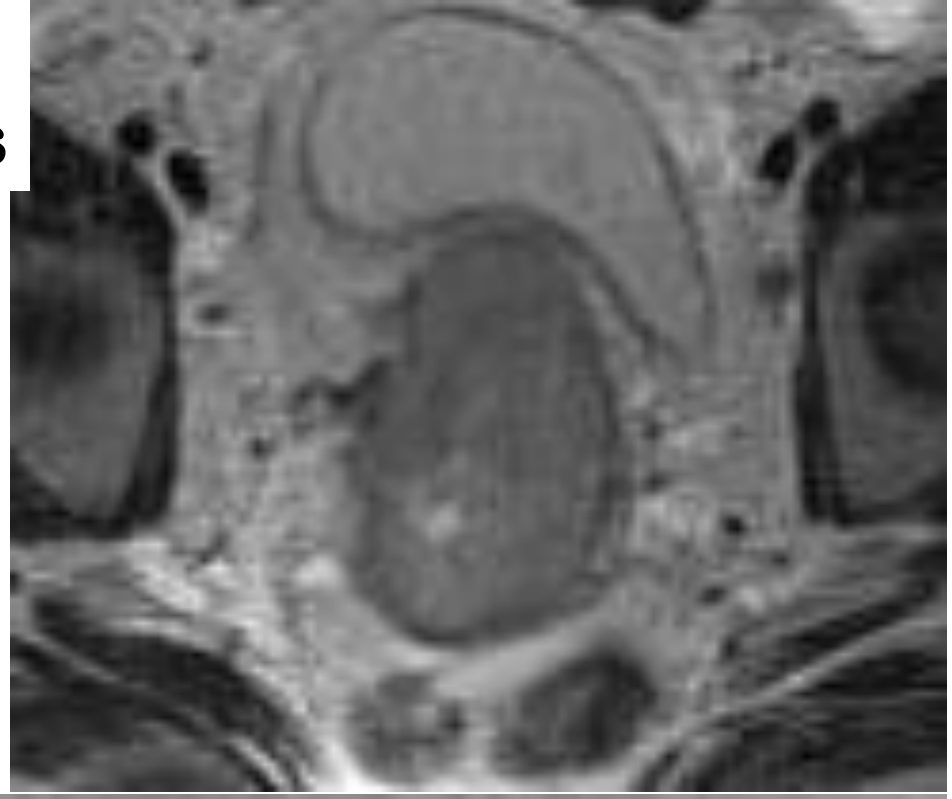
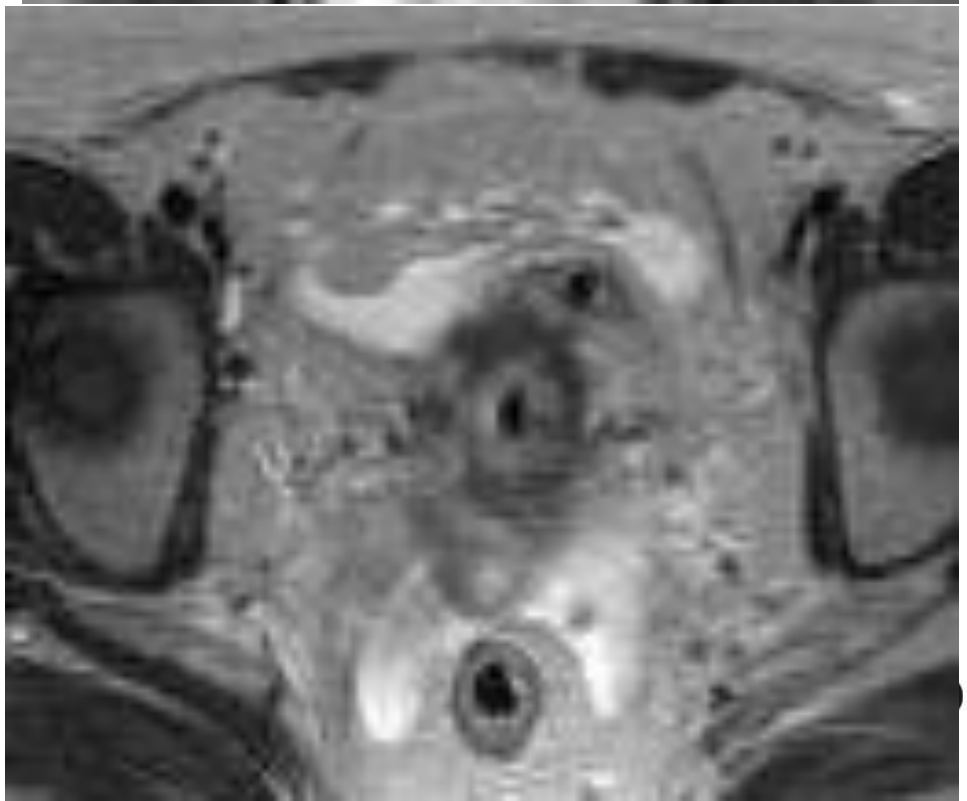
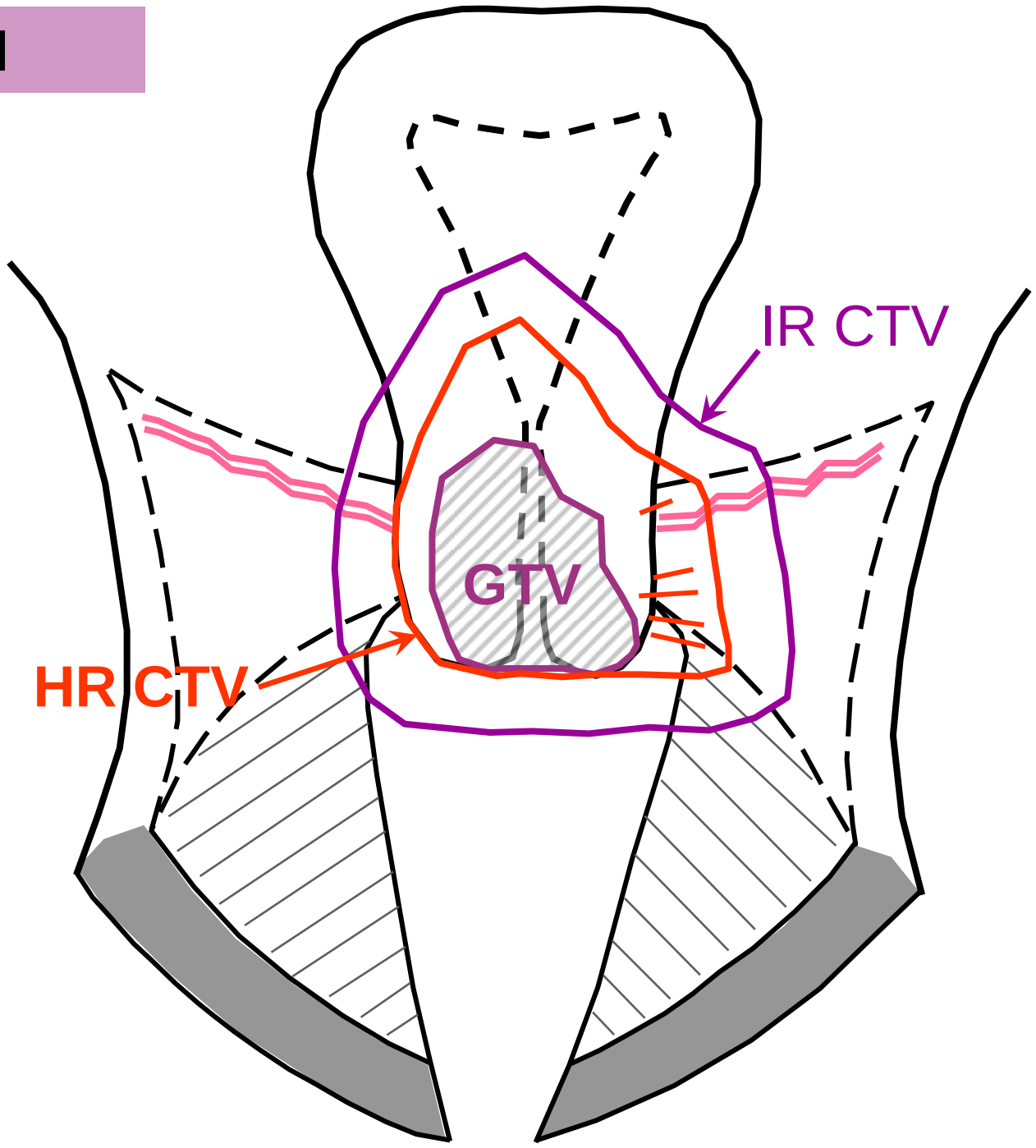
At diagnosis

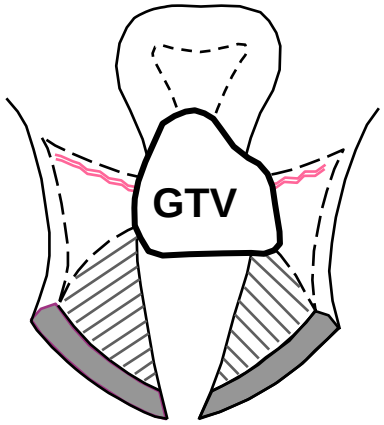


At Brachy therapy



STAGE II





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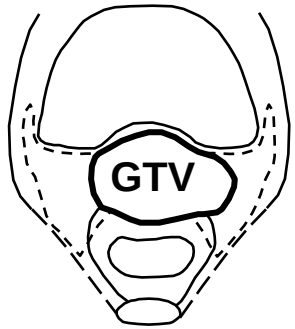
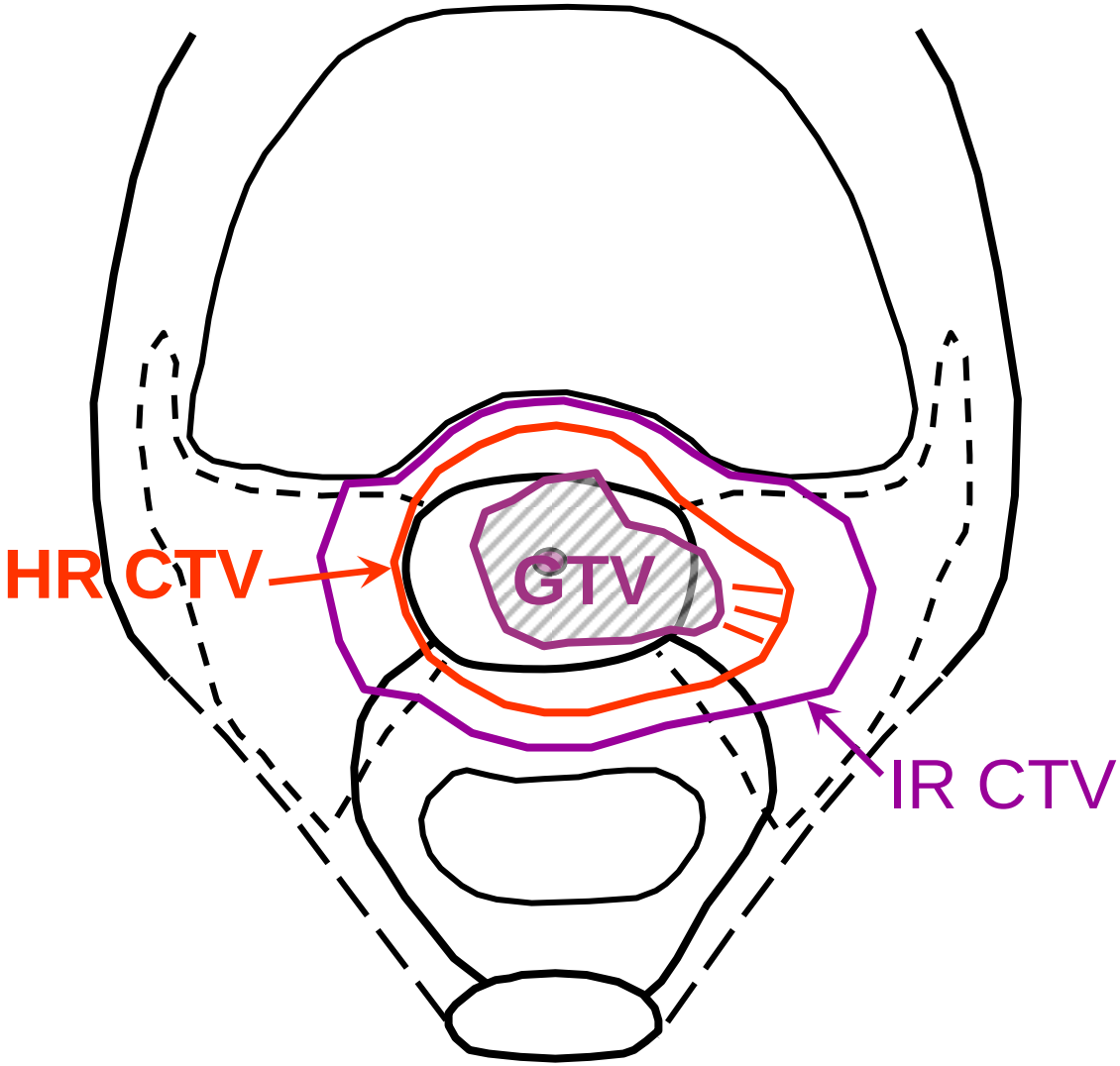
Stage II





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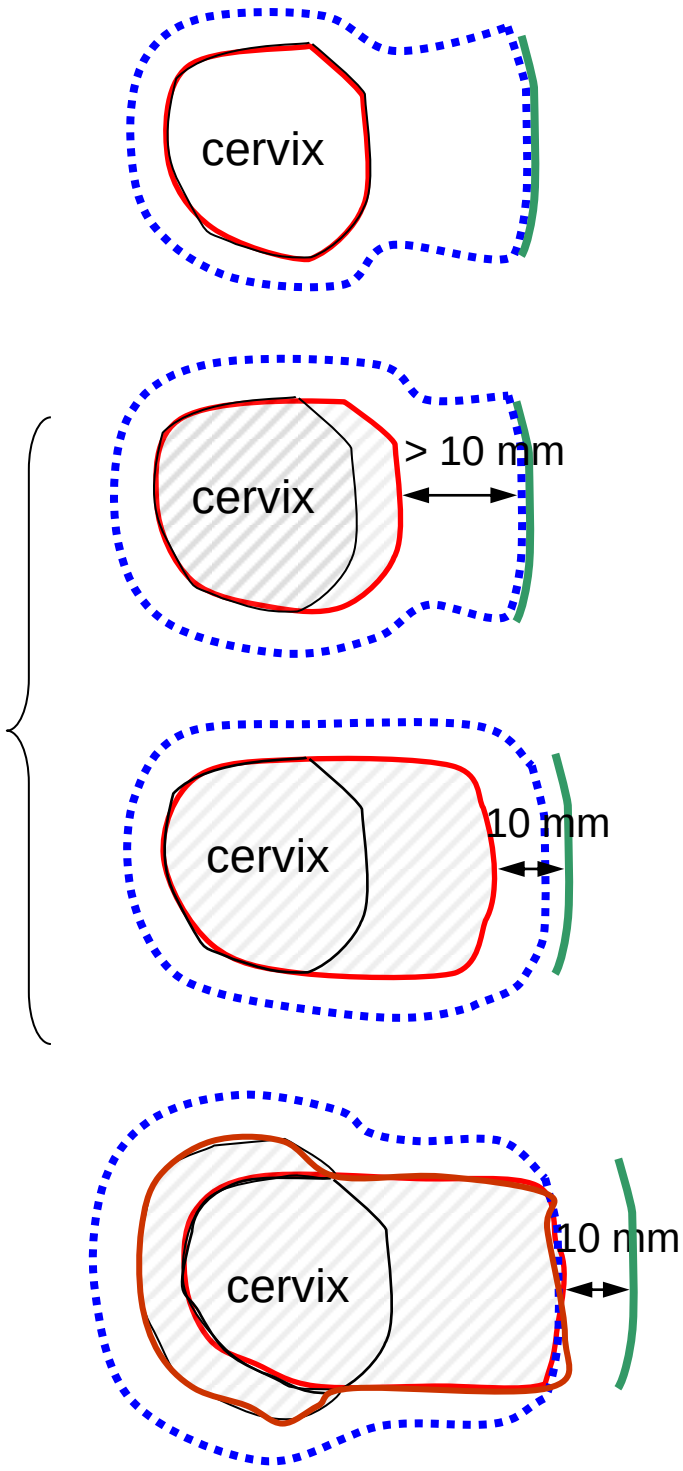
CTV BT

Extensive Disease

Complete remission

Partial remission

Stable disease



Legend

HR-CTV

IR-CTV

Initial tumour extension (at diagnosis)

Residual disease

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……..but I haven't got MRI access

.....so use what you have.....

- EUA
- CT
- CT PET
- Ultrasound

- Image registration

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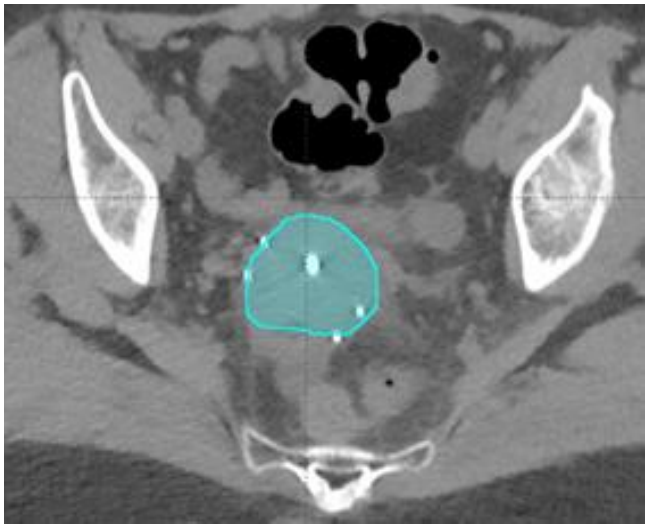
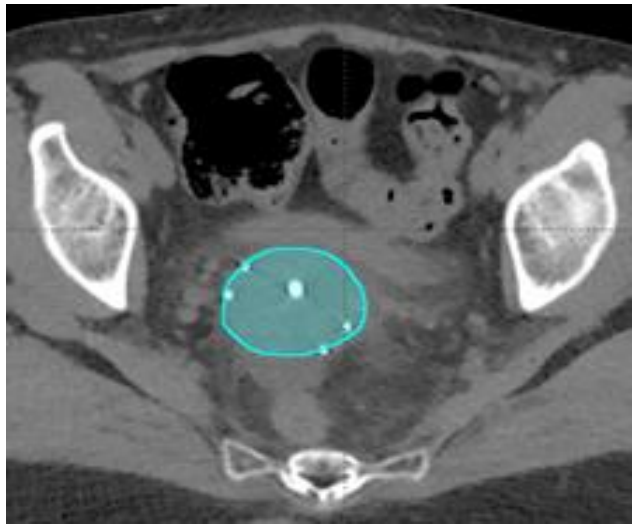
…what about fraction 2….and 3….and 4

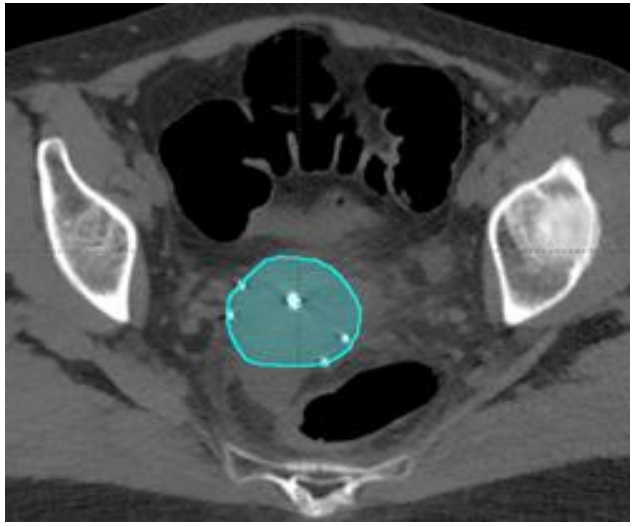
- If treating BT weekly…..
  - imaging before each fraction ……. essential
- If delivering all BT through 1 implant at end of CT-EBRT
  - imaging before each fraction ……. ? essential
  - Does it have to be MR?



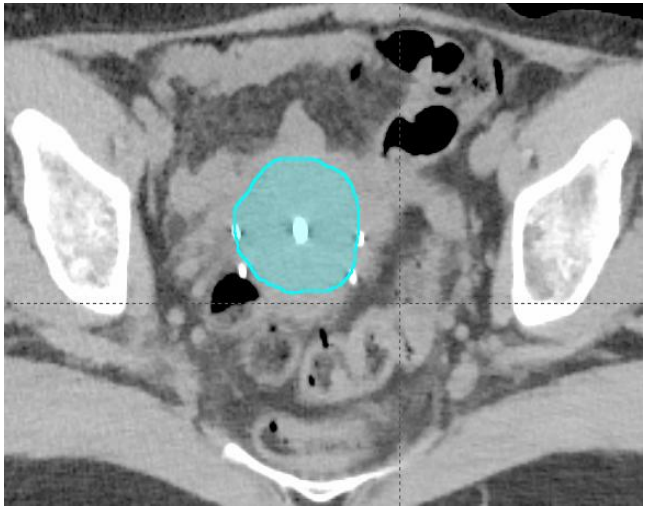
Day 1

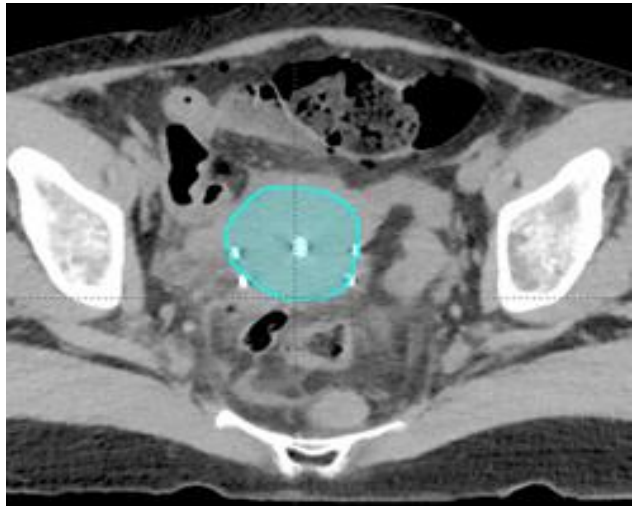


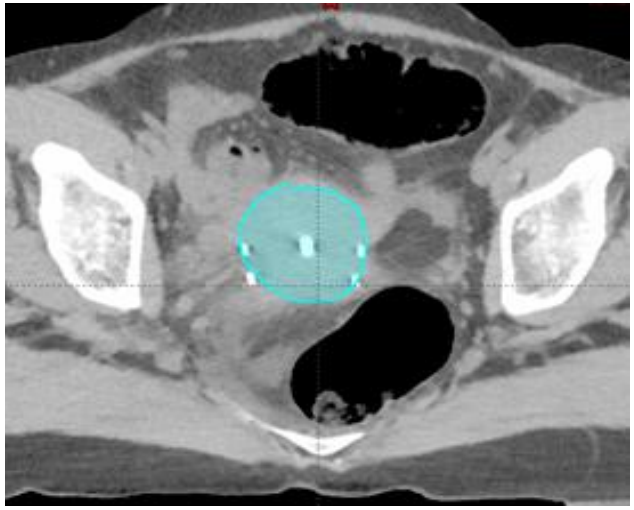
Day 2



Day 3







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Dogma in Brachytherapy
CTV = PTV

Assumption: no uncertainties

- Most likely true for HDR Brachytherapy

- ? LDR/PDR and fractionated HDR

  * Target
  * Different OAR: Rectum, Sigmoid, Bladder

Very few data!

Prospective 3D Image based evaluation needed

ESTRO TEACHING COURSE

Budapest 2017

How to use Dose Volume Histograms in Brachytherapy: cumulative DVH, differential DVH, natural DVH, D98, D90, V100, D2cc

Jose Luis Guinot

E-mail: jguinot@fivo.org

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DECISIONS IN RADIATION THERAPY

- Radiation therapy involves:

Giving a radiation dose → **Dosimetry**
in a certain time → **Calculation**
to a defined space → **PRESCRIPTION**
to have a therapeutic effect → **Biological effect**
with minimal complications.

PRESCRIPTION Where?

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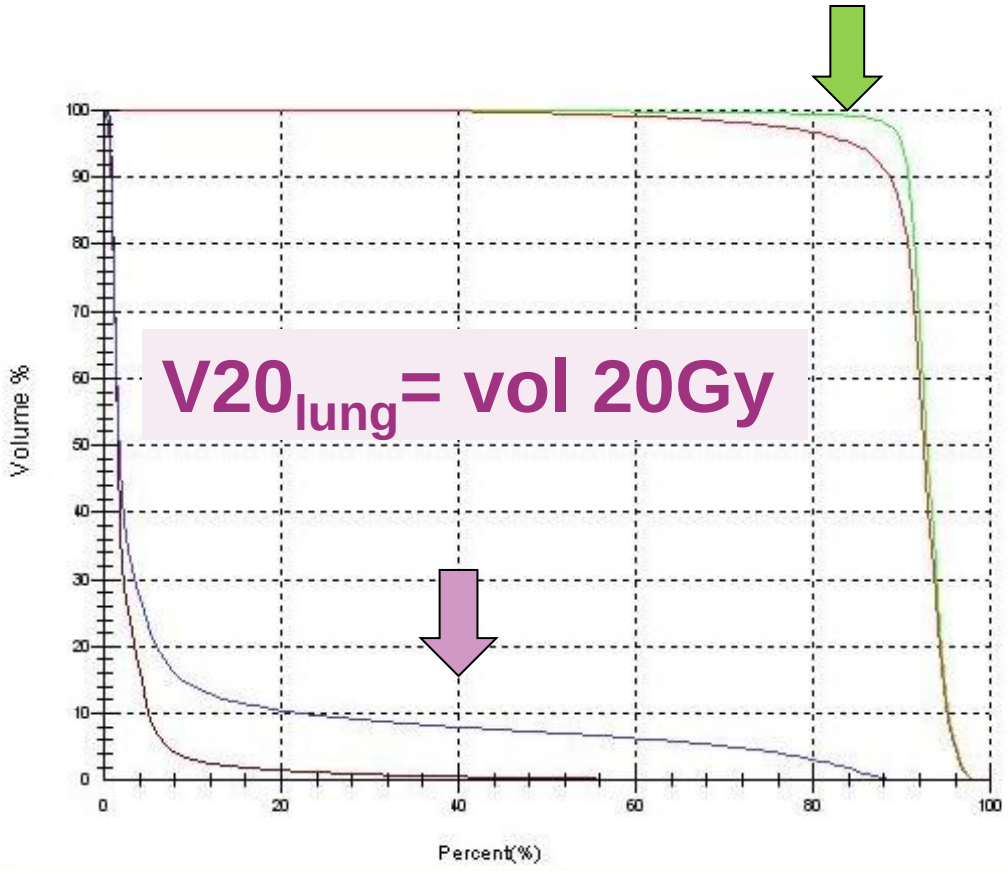
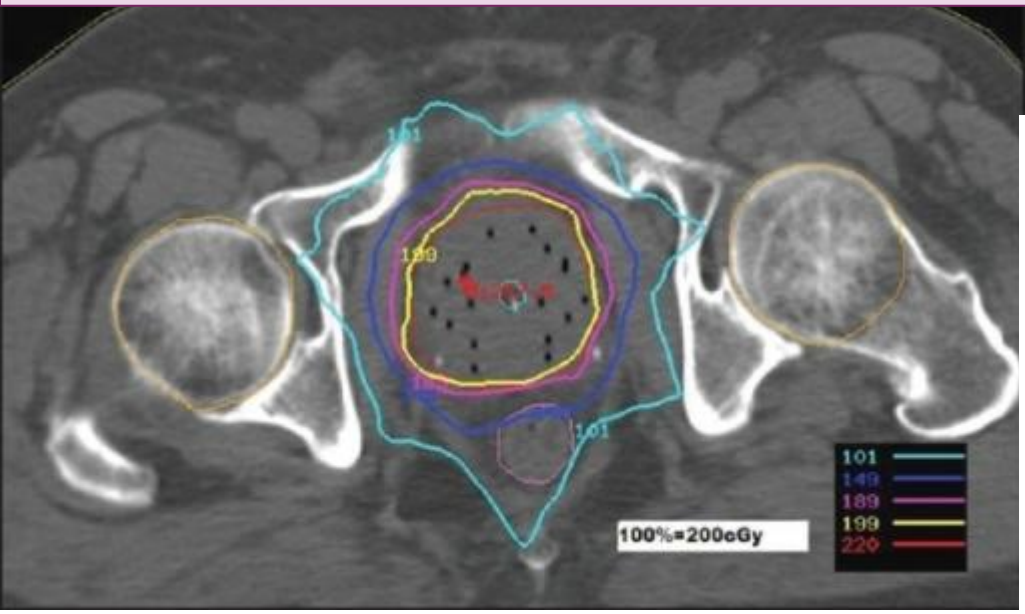
Dose Volume Histogram (DVH) in EBRT

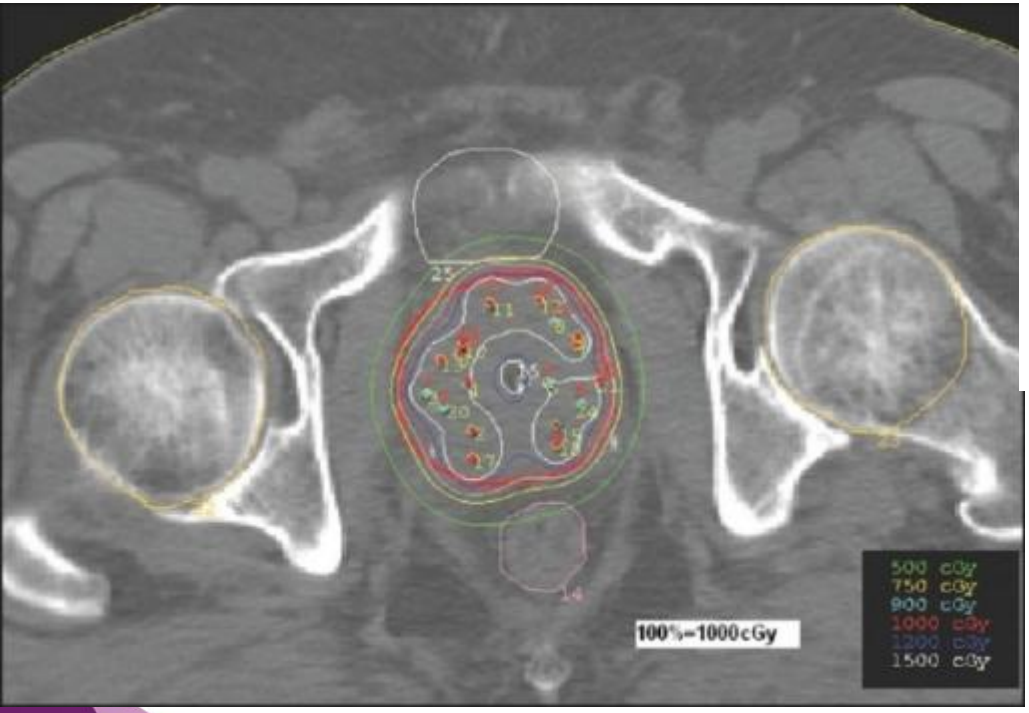
EBRT looks for an homogeneous distribution of dose

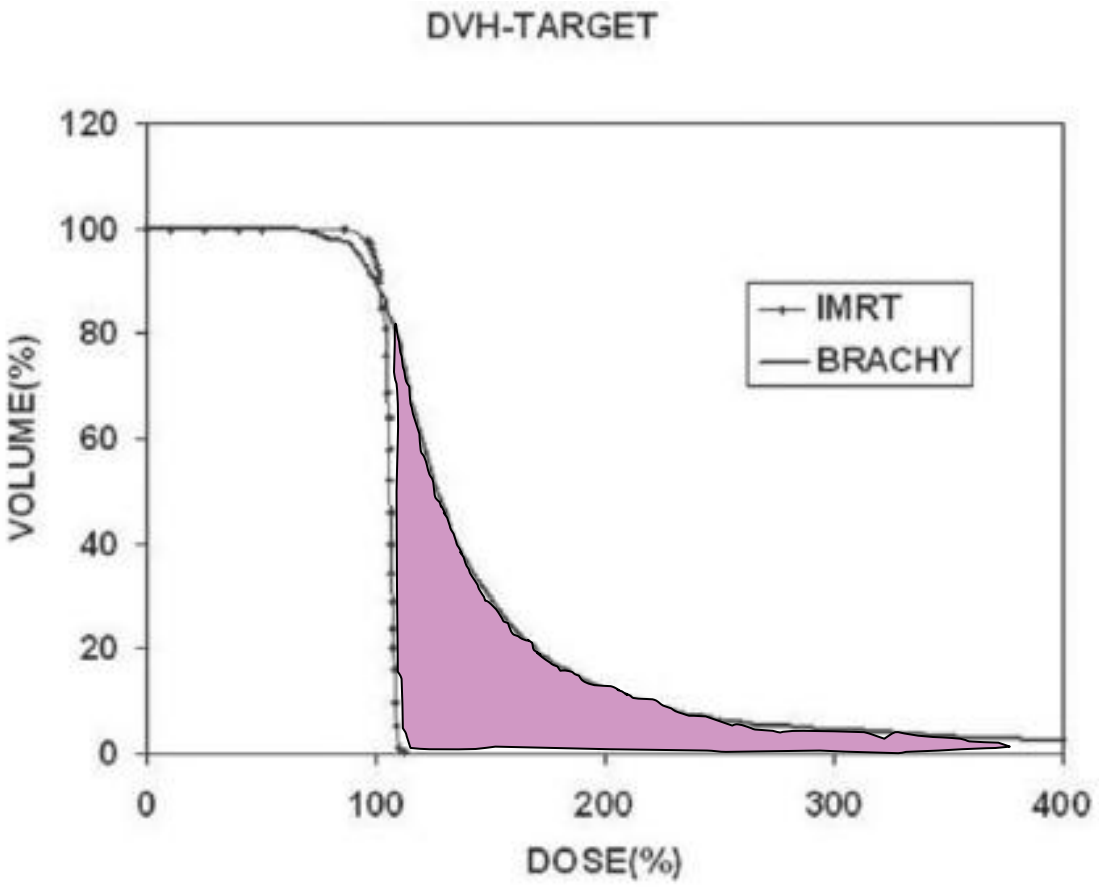
In external beam radiation therapy, DVH shows most of the CTV volume covered with the 95% of the prescribed dose



Comparison of DVH between EBRT and brachy







HDR brachytherapy delivers a much higher dose to the target, compared to the IMRT.

Murali V, Kurup PG, Mahadev P, Mahalakshmi S. Dosimetric analysis and comparison of IMRT and HDR brachytherapy in treatment of localized prostate cancer. J Med Phys (2010)

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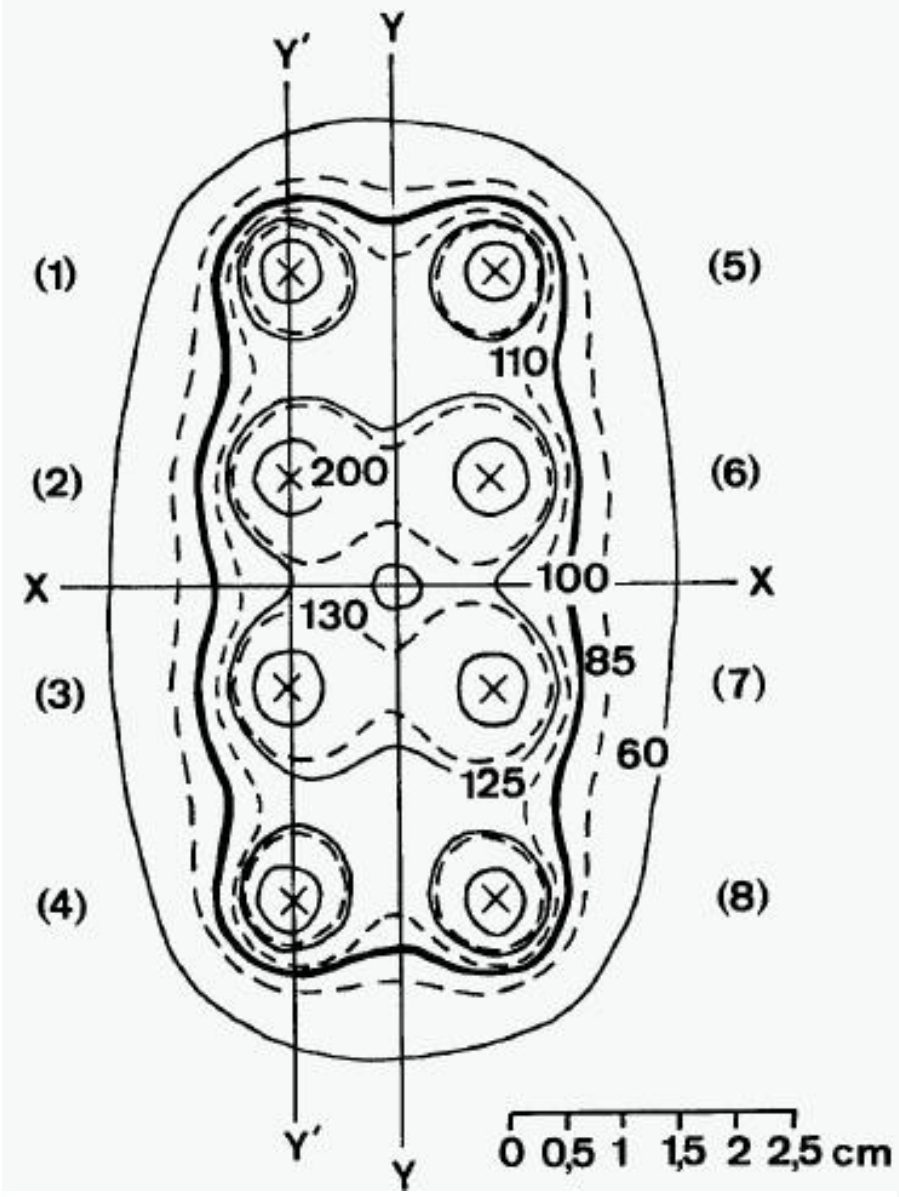
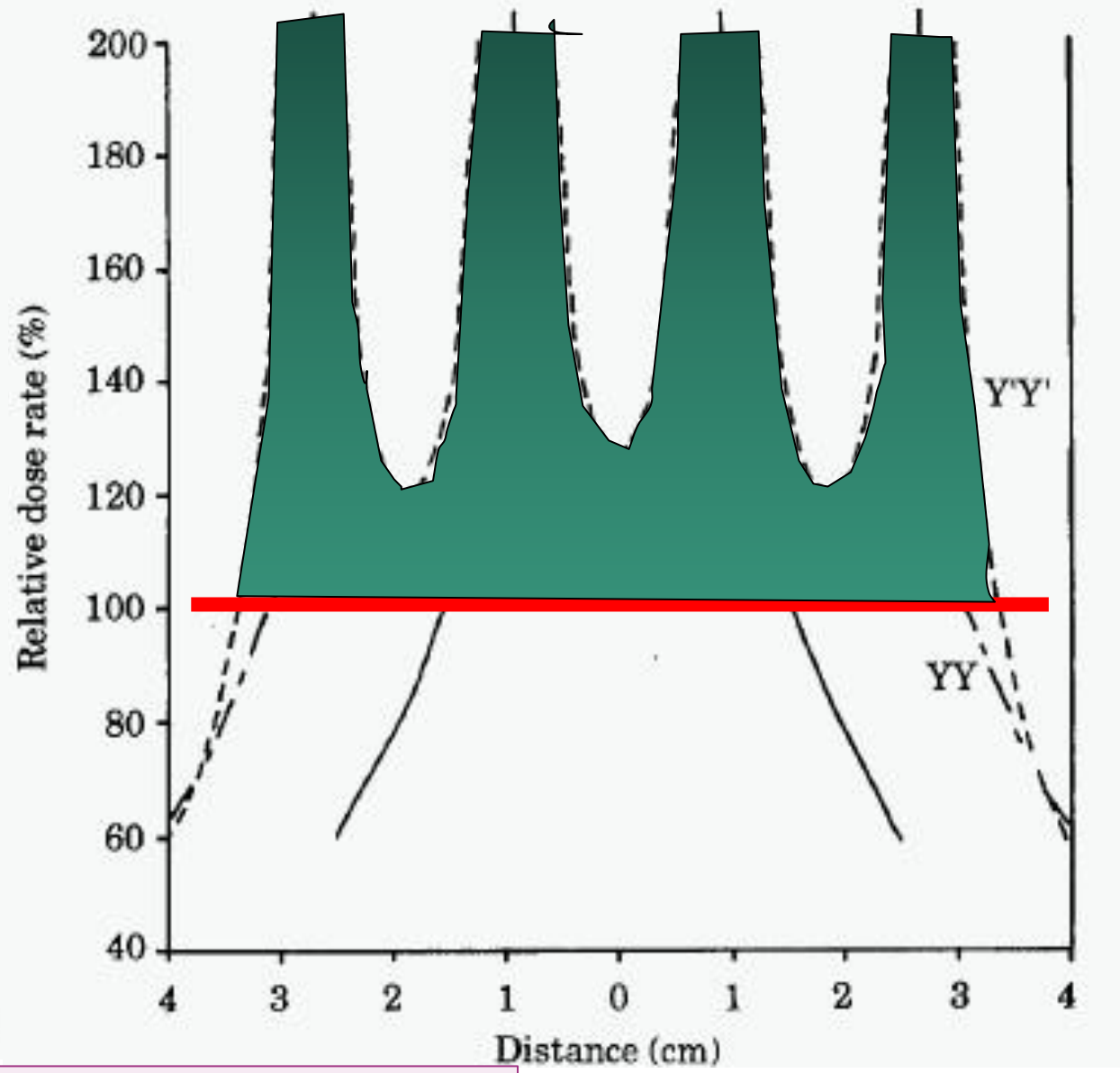
Brachytherapy delivers a very high dose inside the volume





The prescription dose is the peripheral dose.
How can we know the real dose inside?

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The high doses have a biological effect

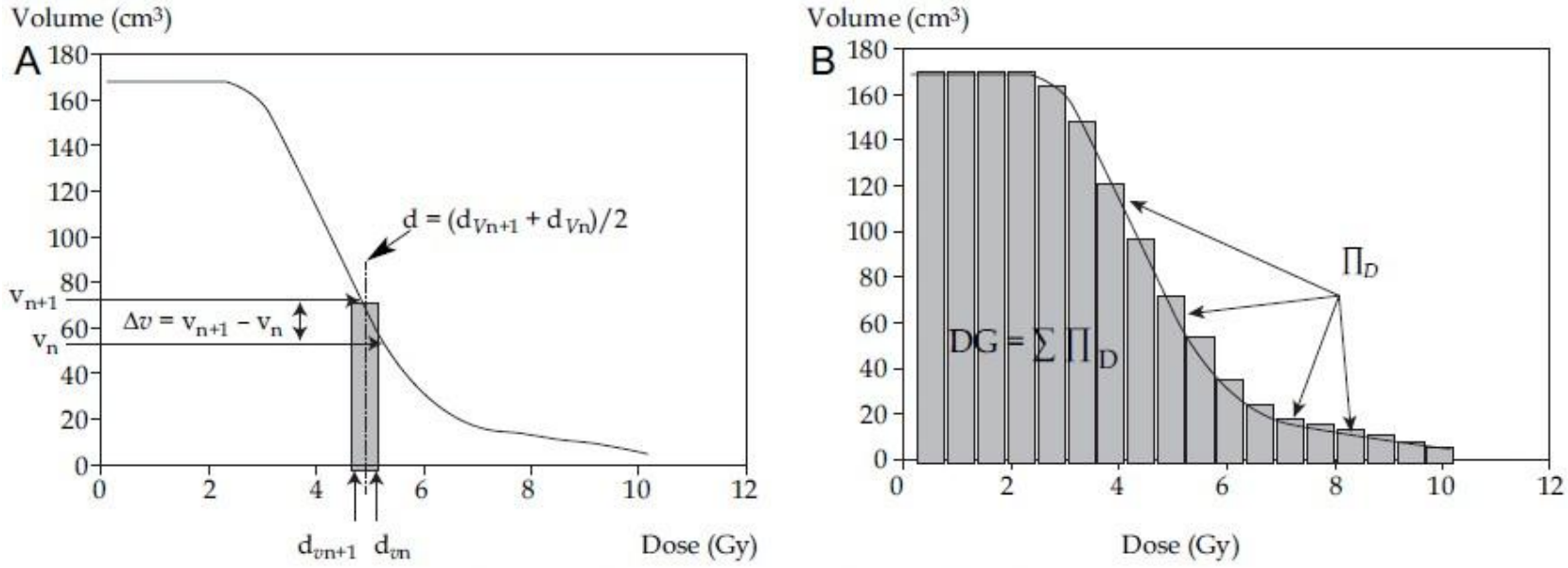

Fig. 3. DVH segmentation method for the calculation of elementary doses d ($d = (d_{Vn+1} + d_{Vn})/2$) delivered per fraction to elementary volumes Δv ($\Delta v = v_{n+1} - v_n$) (A) and calculation of the total dose delivered to the whole CTV taking into account the dose gradient DG ($DG = \Sigma\prod_D$) (B)

The inevitable dose gradient in BT ensures non-uniform dosage within the target volume and has its own biological effect

Dose gradient impact on equivalent dose at 2 Gy for high dose rate interstitial brachytherapy

Jean-Michel Hannoun-Levi, MD, PhD, Marie-Eve Chand-Fouche, MD, Catherine Dejean, PhD, Adel Courdi, MD
Department of Radiation Therapy, Antoine Lacassagne Cancer Center, Nice, France

J Contemp Brachyther 2012; 4,1:12-20

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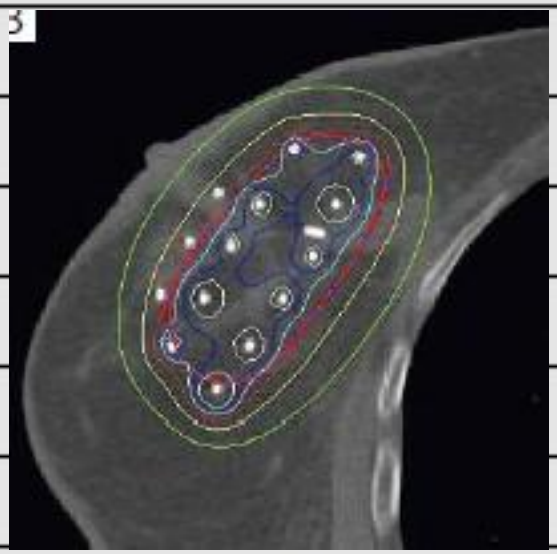
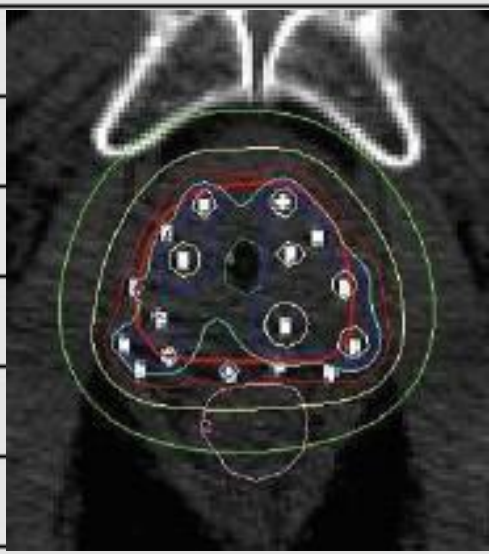
Table 2. Equivalent dose at 2 Gy of the physical prescribed dose taking into account or not the dose gradient for $\alpha/\beta = 1.5$, $\alpha/\beta = 3$, $\alpha/\beta = 4$ and $\alpha/\beta = 5$ in breast and prostate implants

	Breast implant **10 x 3.4 Gy**		Prostate implant **3 x 6 Gy**	
	Median (Gy)	Min/Max	Median (Gy)	Min/Max
DG not considered				
PPD	34		18	
EQD2				
$\alpha/\beta = 1.5$	–		39	
$\alpha/\beta = 3$	44		32	
$\alpha/\beta = 4$	42		–	
$\alpha/\beta = 5$	41	–	28	–
DG considered				
PPD	48	44-51	28	27-29
EQD2				
$\alpha/\beta = 1.5$	–	–	98	90-103
$\alpha/\beta = 3$	81	71-91	76	71-80
$\alpha/\beta = 4$	76	66-85	–	–
$\alpha/\beta = 5$	72	63-80	63	59-66





Dose Volume Histograms in Brachytherapy:

Based on the catheters (IMPLANT)

- Cumulative DVH
- Differential DVH
- Natural DVH

Based on the anatomy (TARGET/CTV/OAR)

(Requires 3d imaging CT/MR/US)

- Cumulative DVH in CTV
- Cumulative DVH in OAR

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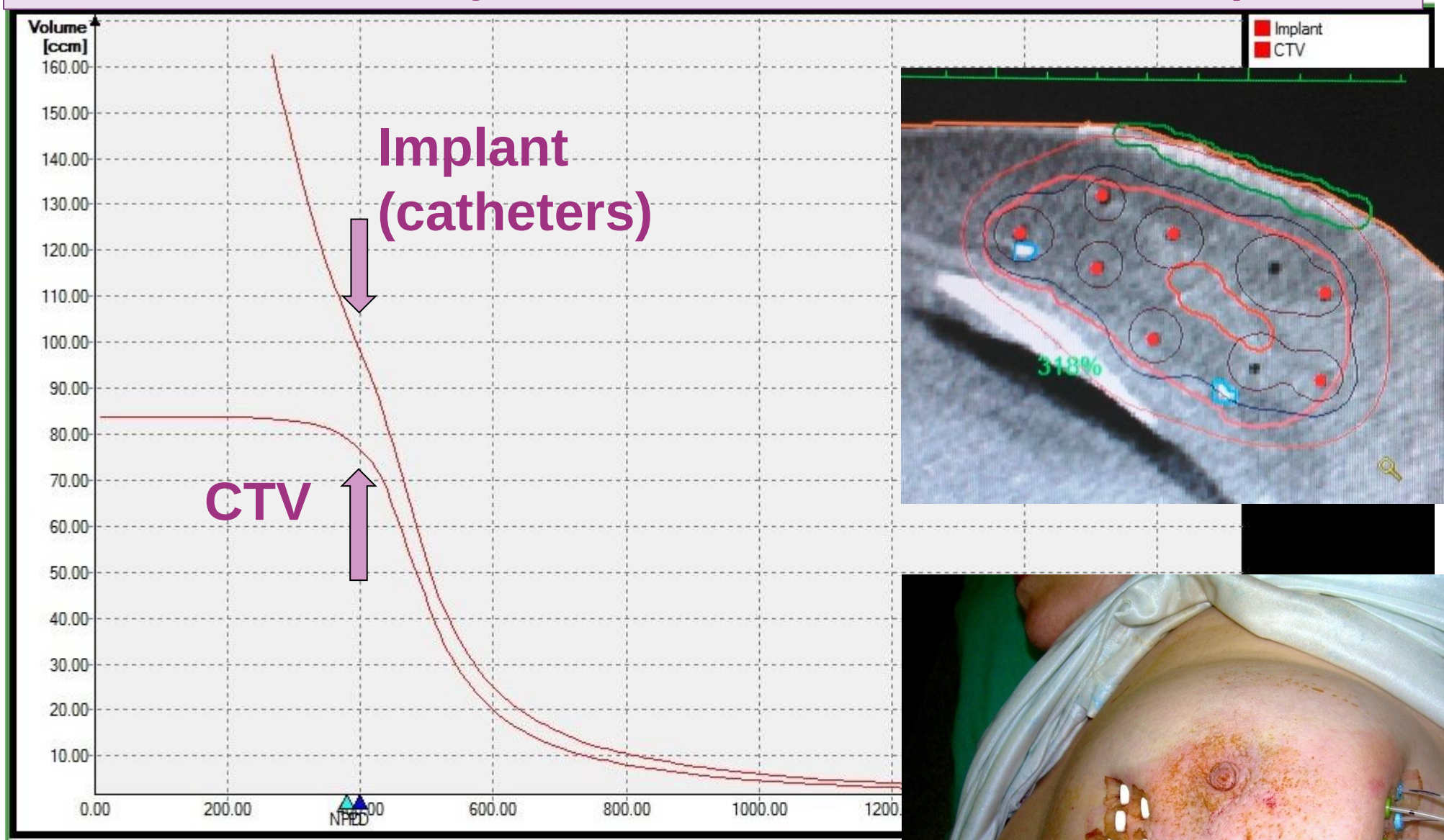
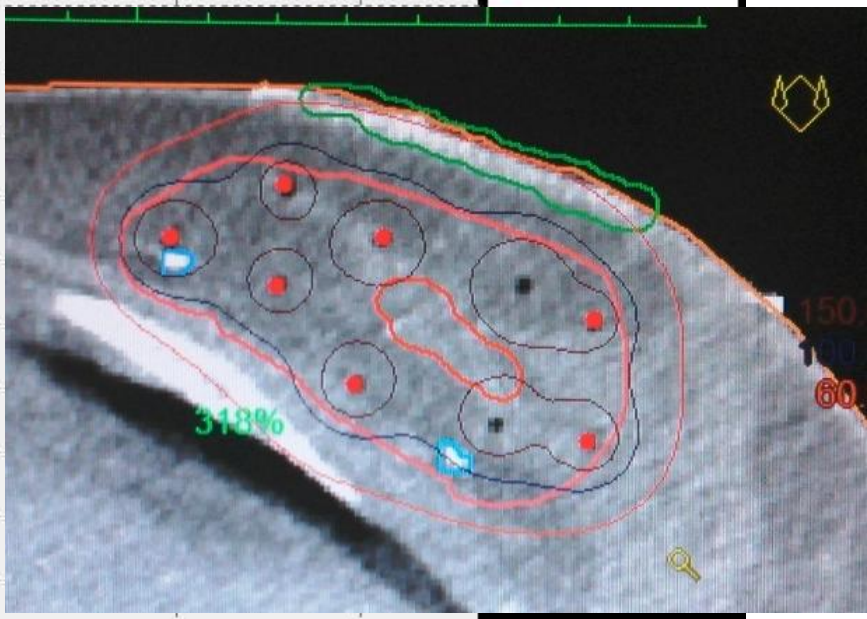
Breast A.P.B.I. 4Gy: cumulative DVH CTV and implant





ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
CTV	56.93	227.73	**100.00**	83.64
CTV	102.25	409.02	**90.00**	75.28
CTV	84.12	336.48	**98.00**	81.97
Implant	**100.00**	400.00	-	97.72
Implant	**150.00**	600.00	-	25.02
Implant	**200.00**	800.00	-	10.50

Dose Volume Histograms in Brachytherapy:

Based on the catheters (IMPLANT)

- **Cumulative DVH**
- **Differential DVH**
- **Natural DVH**

(no image is required)

Based on the anatomy (TARGET/CTV/OAR)

(Requires 3d imaging CT/MR/US)

- Cumulative DVH in CTV
- Cumulative DVH in OAR

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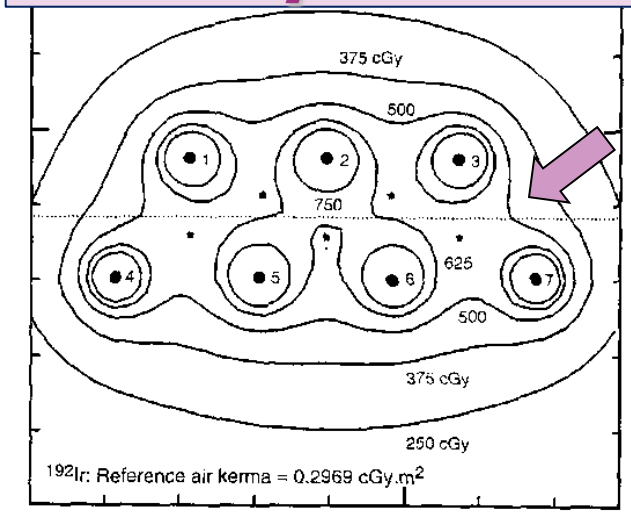
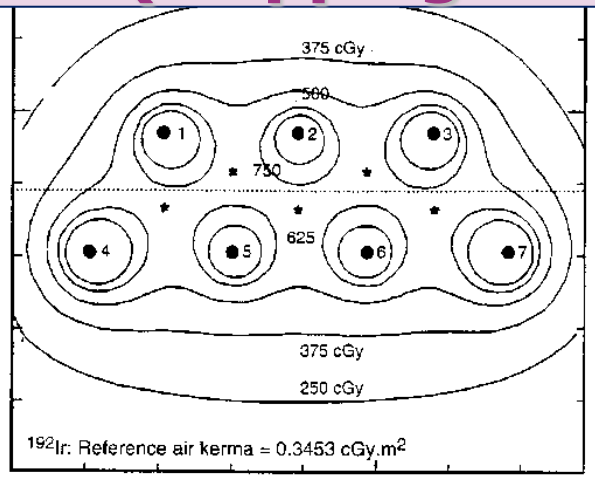
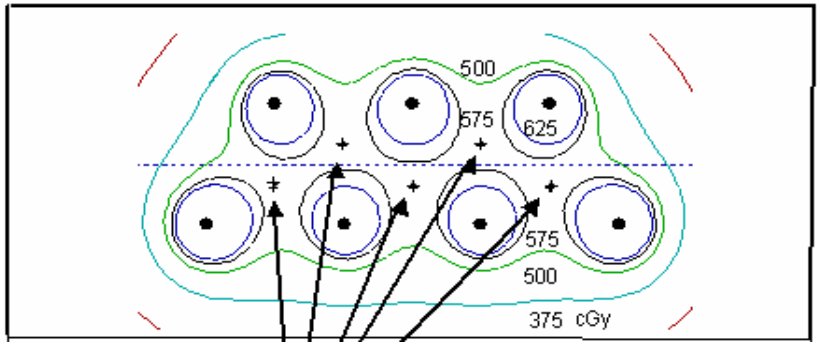
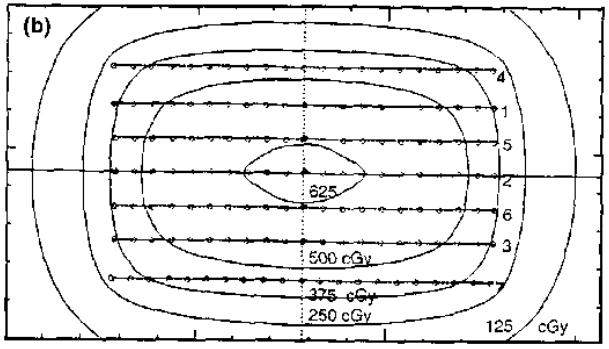
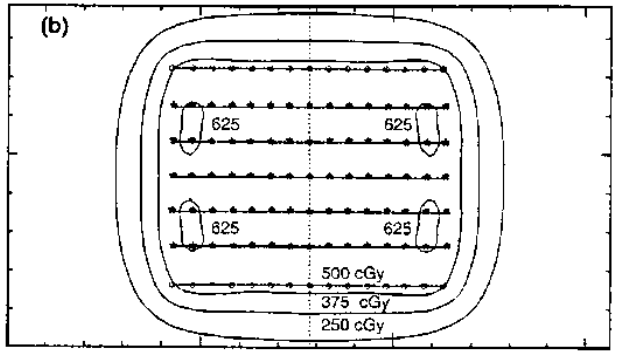
Paris System vs SSDS (stepping source) with optimization

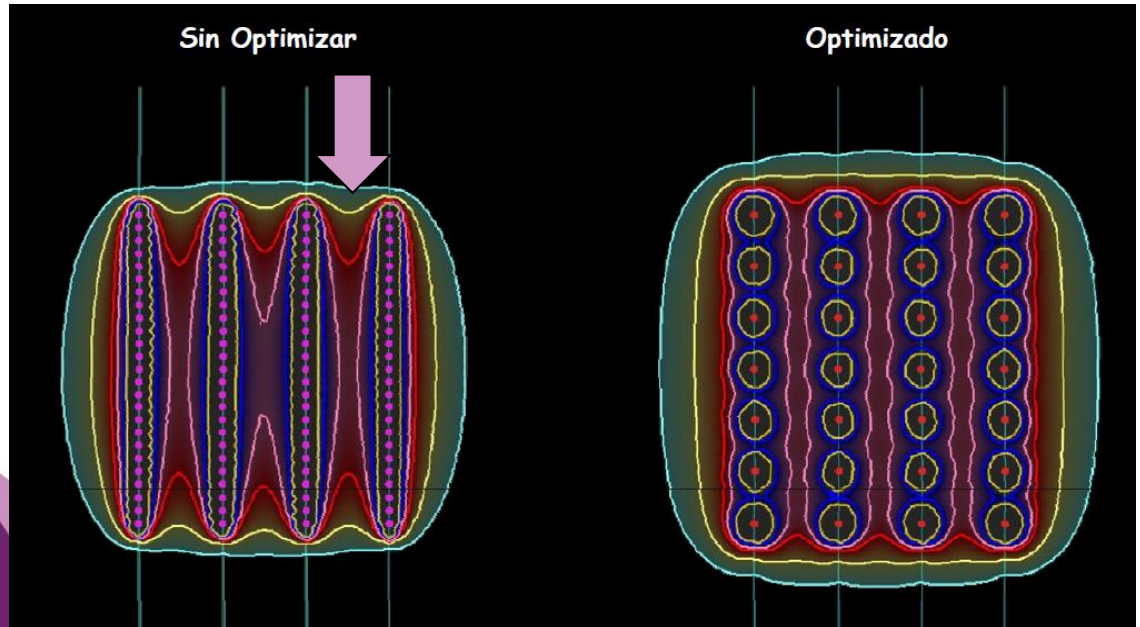












Media of basal points = 100% (normalization)

We cannot use 100% as the prescription isodose

Prescription is to an outer isodose

- **With LDR 85%**
- **With HDR 90% (optimization)**

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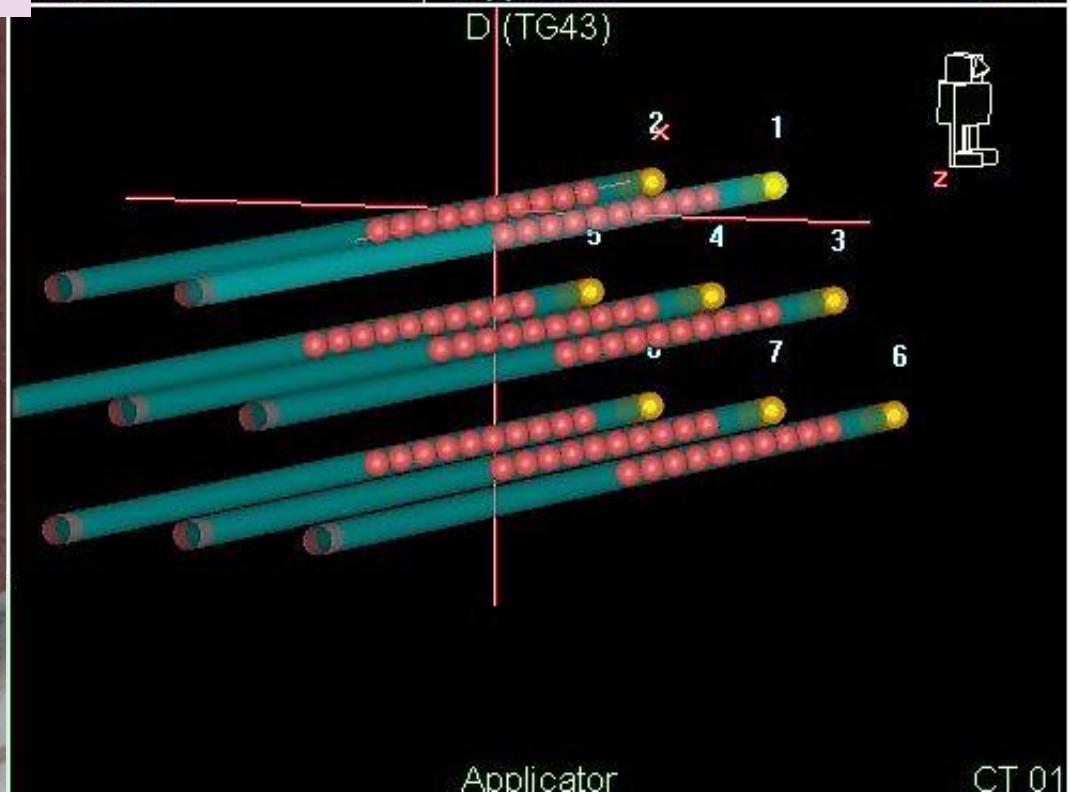
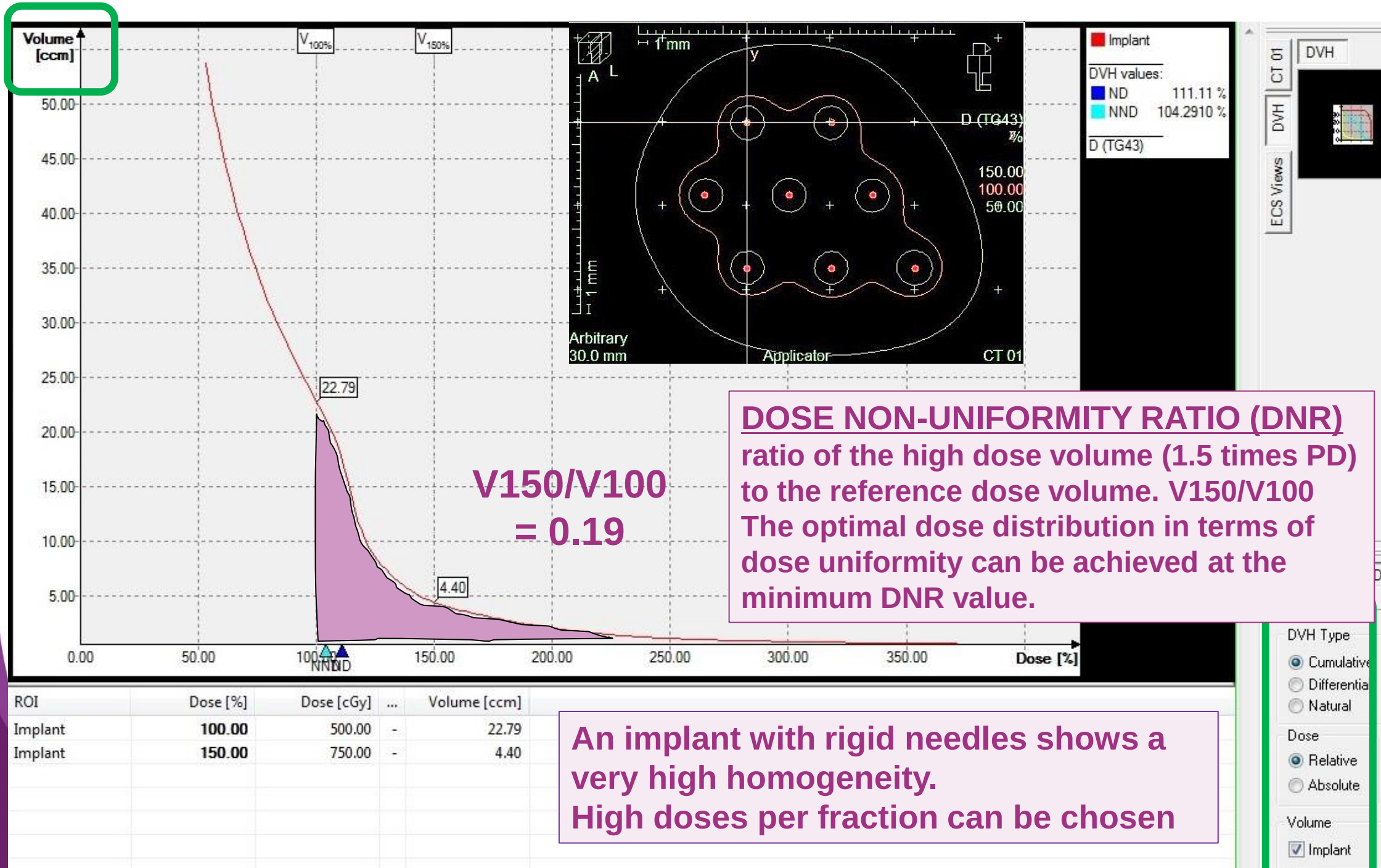
Lip cancer 8 rigid needles
HDR: 5Gy at 90% isodose



The Cumulative Dose Volume Histogram (CDVH): implant



V150/V100 = 0.19

DOSE NON-UNIFORMITY RATIO (DNR)

ratio of the high dose volume (1.5 times PD) to the reference dose volume. V150/V100 The optimal dose distribution in terms of dose uniformity can be achieved at the minimum DNR value.

ROI	Dose [%]	Dose [cGy]	...	Volume [ccm]
Implant	**100.00**	500.00	-	22.79
Implant	**150.00**	750.00	-	4.40

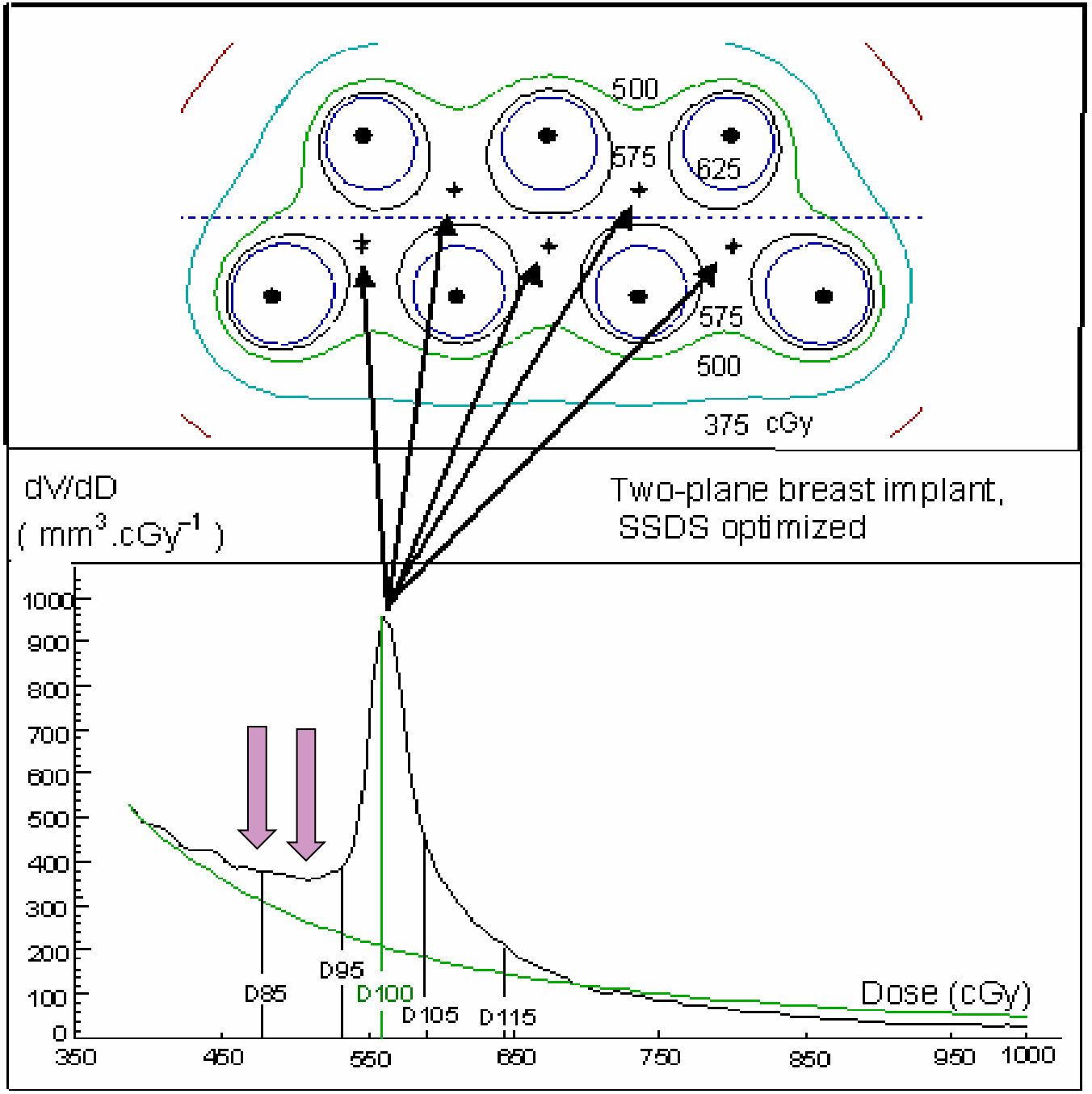
An implant with rigid needles shows a very high homogeneity.
High doses per fraction can be chosen

The Differential Dose Volume Histogram (DDVH)

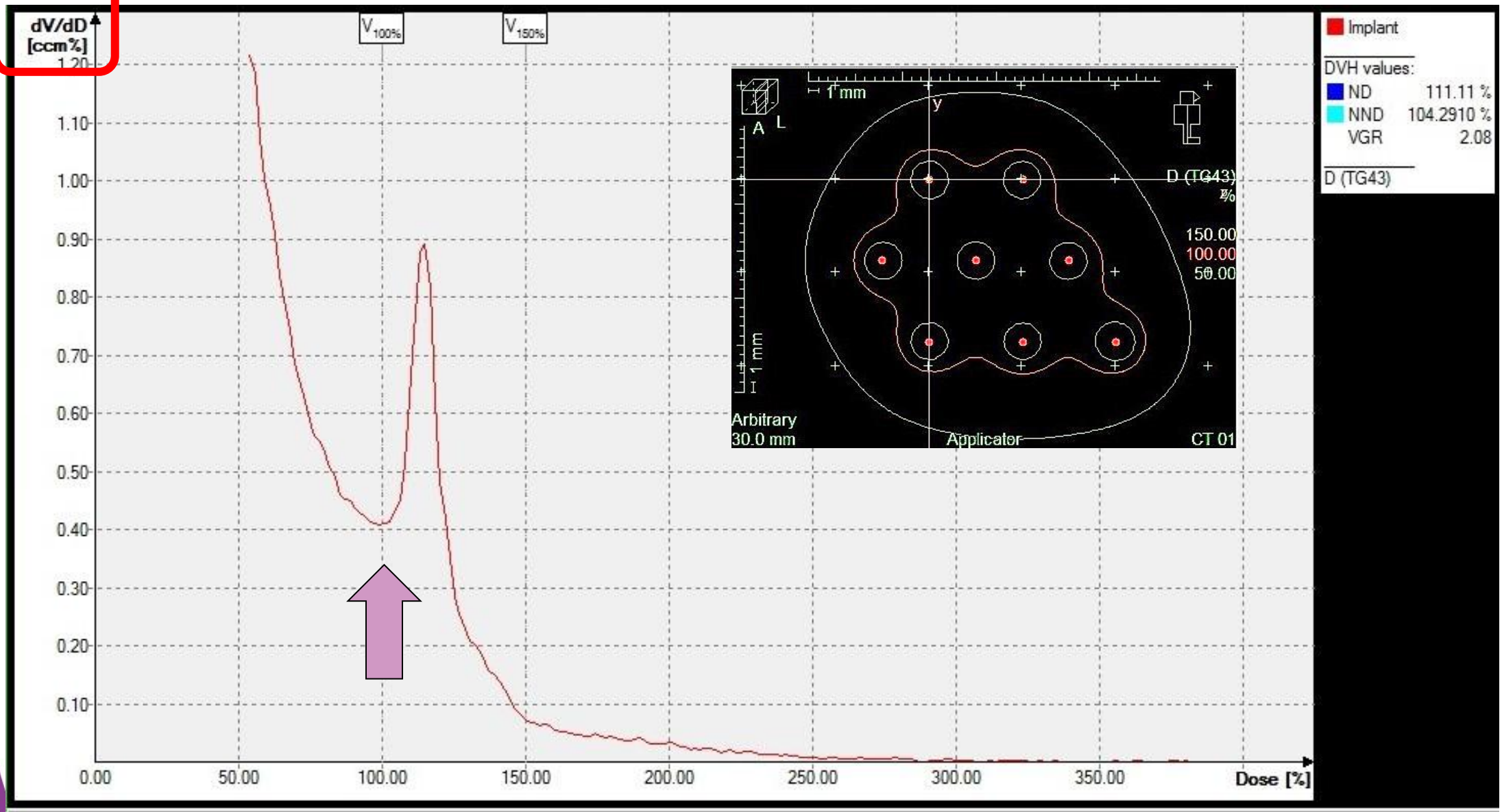
How can we choose the right isodose curve?

Differential DVH dV/ dD

A narrow peak indicates homogeneity!

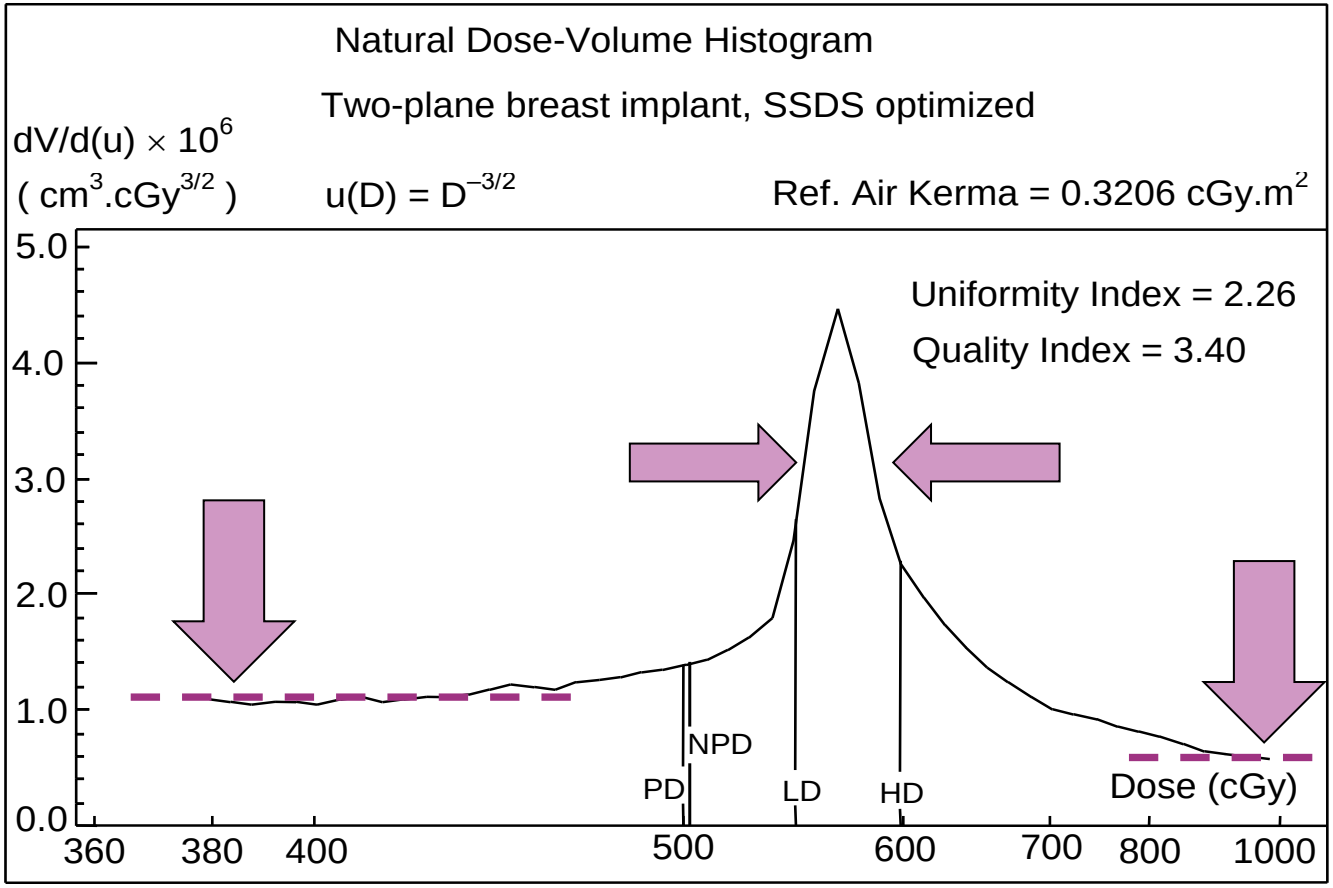


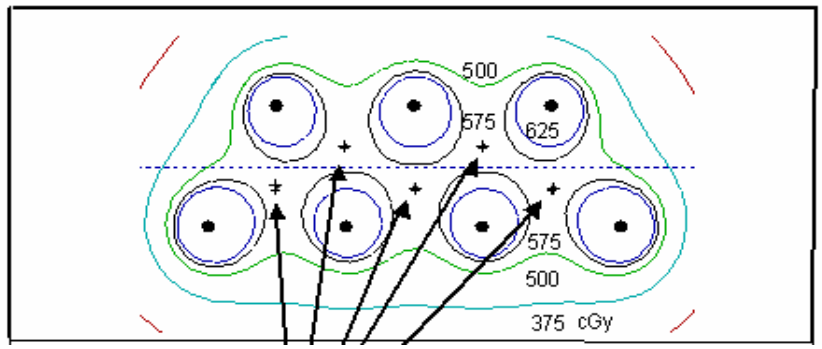
The Differential Dose Volume Histogram (DDVH)



ROI	Dose [%]	Dose [cGy]	...	Volume [ccm]
Implant	**100.00**	500.00	-	22.79
Implant	**150.00**	750.00	-	4.40

The Natural Dose Volume Histogram (NDVH)





- **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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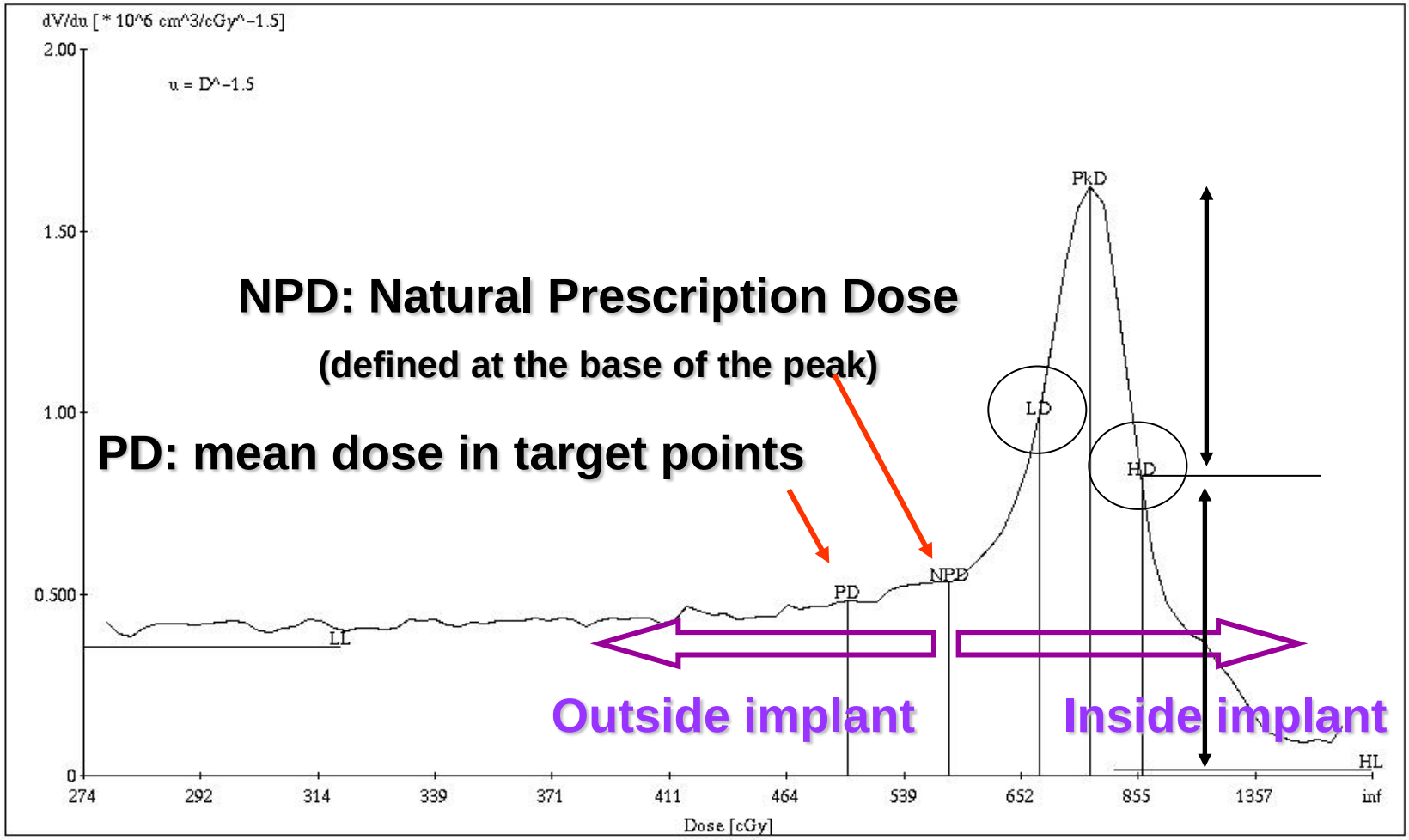
Courtesy of Dimos Baltas

Natural Dose Ratio (NDR)

Natural Prescription Dose NPD / Prescription Dose PD = 1.15

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



DVH_0 : Natural DVH on implant. State : Consistent. **Classical Geometric Optimization on Volume**

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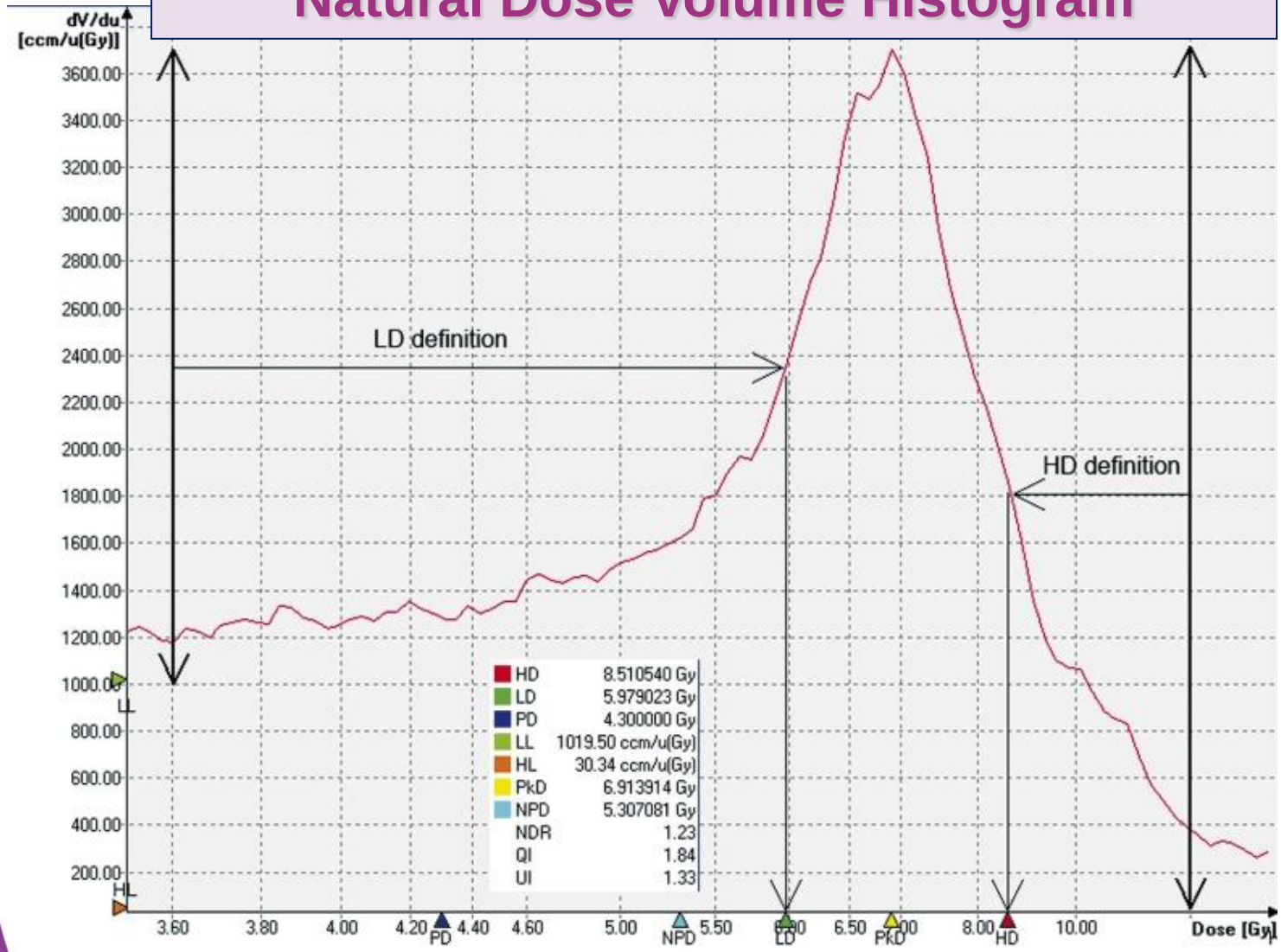
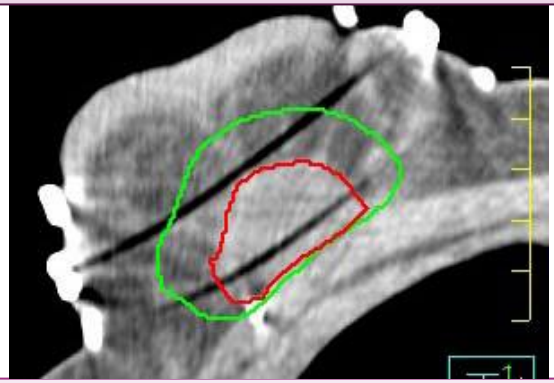
Courtesy of Dimos Baltas

VOLUMETRIC HOMOGENEITY PARAMETERS

Natural Dose Volume Histogram



The arrows shows the low dose LD and high dose HD
The LD and HD is used to define the QI and UI, respectively



UNIFORMITY INDEX (UI)

The narrower the peak, the more uniform the dose distribution is.

The UI depends on the prescribed dose and high dose HD, it can be used to compare implants with the same dose prescription only.

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.

Major T, Fröhlich G, Polgar C. Assessment of dose homogeneity in conformal interstitial breast brachytherapy with special respect to ICRU recommendations. J Contemp Brachytherapy. 2011; 3(3):150–5.

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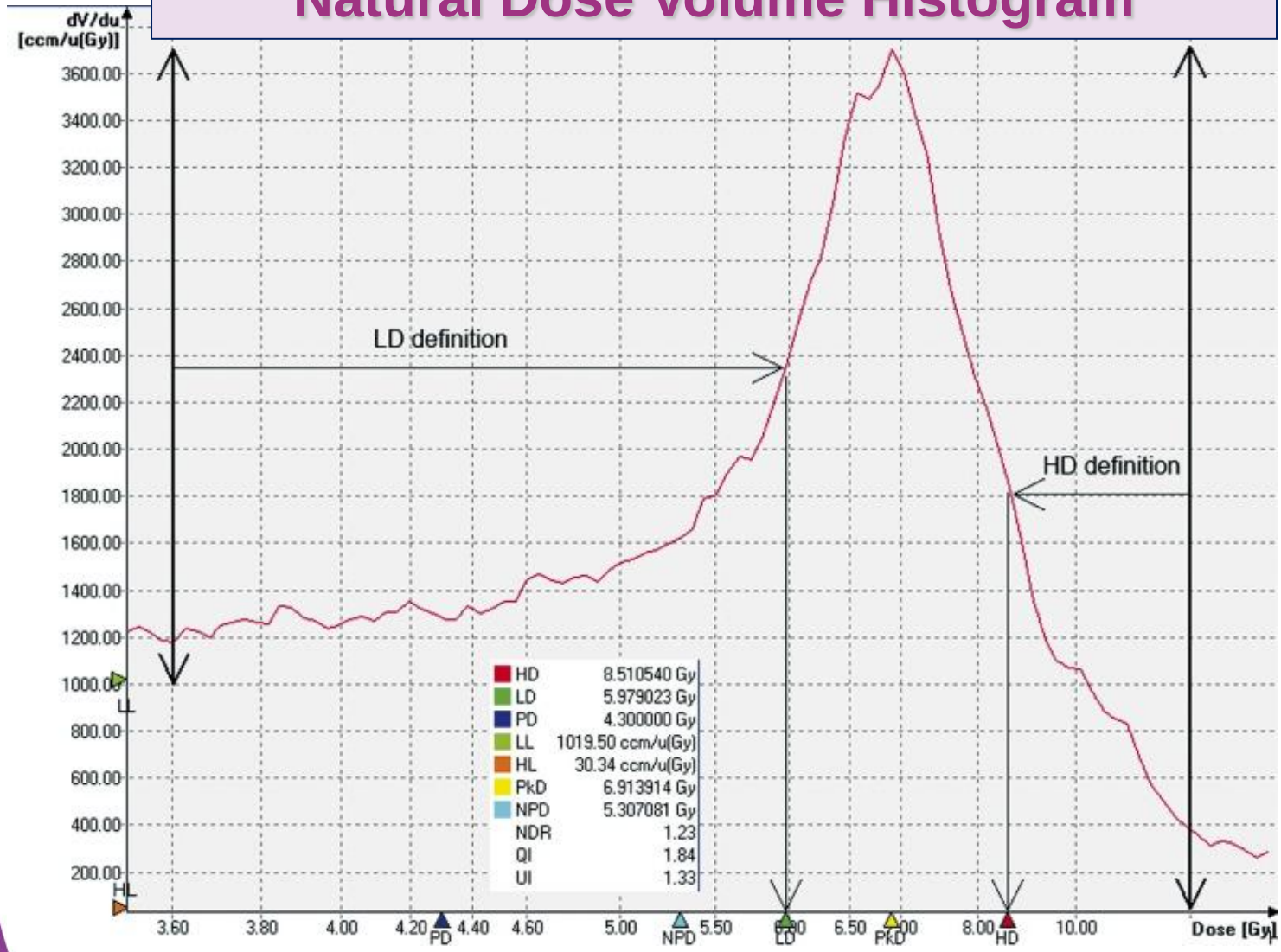
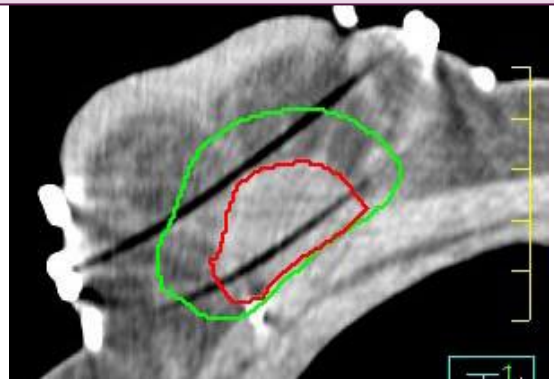
VOLUMETRIC HOMOGENEITY PARAMETERS

Natural Dose Volume Histogram





QUALITY INDEX (QI)

QI is similar to UI, but instead of the treatment dose (TD) the low dose (LD) is used.
It is independent on the prescribed dose

The Quality Index QI is defined to suppress the influence of the chosen reference dose

The arrows shows the low dose LD and high dose HD
The LD and HD is used to define the QI and UI, respectively

Major T, Fröhlich G, Polgar C. Assessment of dose homogeneity in conformal interstitial breast brachytherapy with special respect to ICRU recommendations. J Contemp Brachytherapy. 2011; 3(3):150–5.

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VOLUMETRIC HOMOGENEITY PARAMETERS

Volumetric homogeneity parameters for 49 HDR breast implants

Characteristics	Mean	Range
V_{PTV}	66.4 cm^3	15.5-176.0 cm^3
V_{ref}	78.8 cm^3	23.2-209.5 cm^3
DNR	0.32	0.25-0.41
DHI	0.66	0.50-0.76
UI	1.49	1.18-1.62
QI	1.94	1.22-3.07

DOSE NON-UNIFORMITY RATIO (DNR)

V150 /V100 <0.35

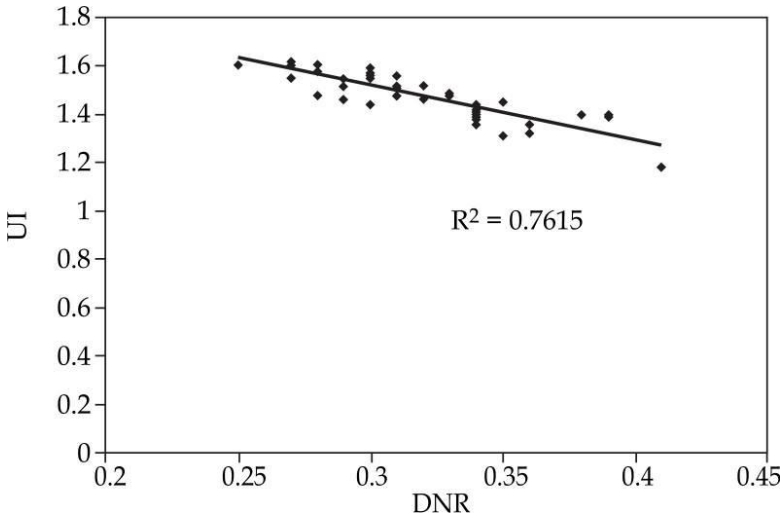
DOSE HOMOGENEITY INDEX (DHI)

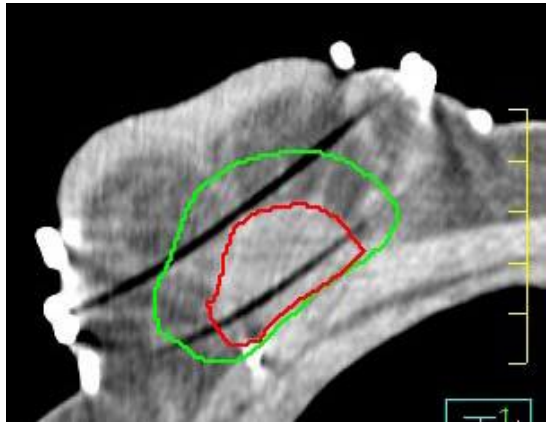
It can be calculated only for the implant geometry

DHI = 1 – DNR

and can also be related to the volume of the PTV. relative homogeneity index (HI).

DHI=(V100 – V150)/V100.





Major T, Fröhlich G, Polgar C. Assessment of dose homogeneity in conformal interstitial breast brachytherapy with special respect to ICRU recommendations. J Contemp Brachytherapy. 2011; 3(3):150–5.

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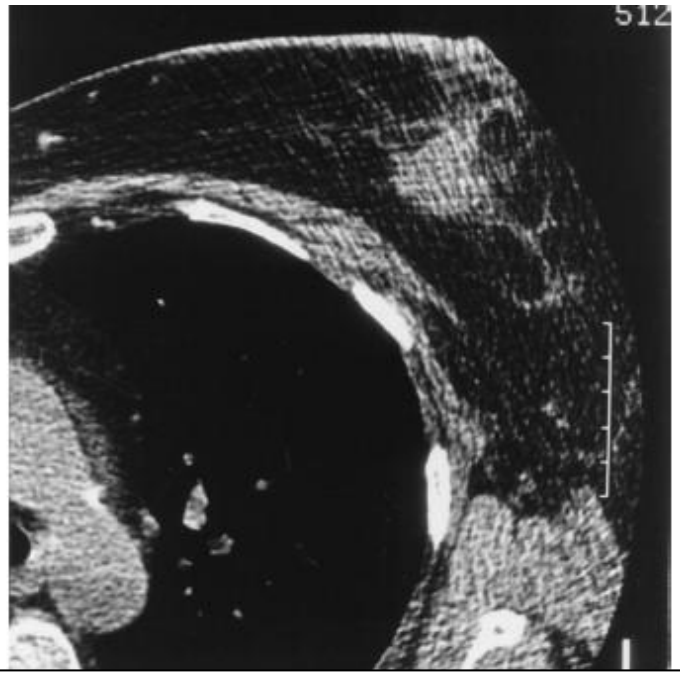
Breast cancer CT (closed cavity): 3.4 Gy to volume



Wazer DE, et al. Clinically evident fat necrosis in women treated with HDR brachytherapy alone for early-stage breast cancer. Int J Radiat Oncol Biol Phys 2001, 50:107–111

34 Gy in 10 fractions was prescribed as <u>the minimum dose anywhere within the prescription volume</u>

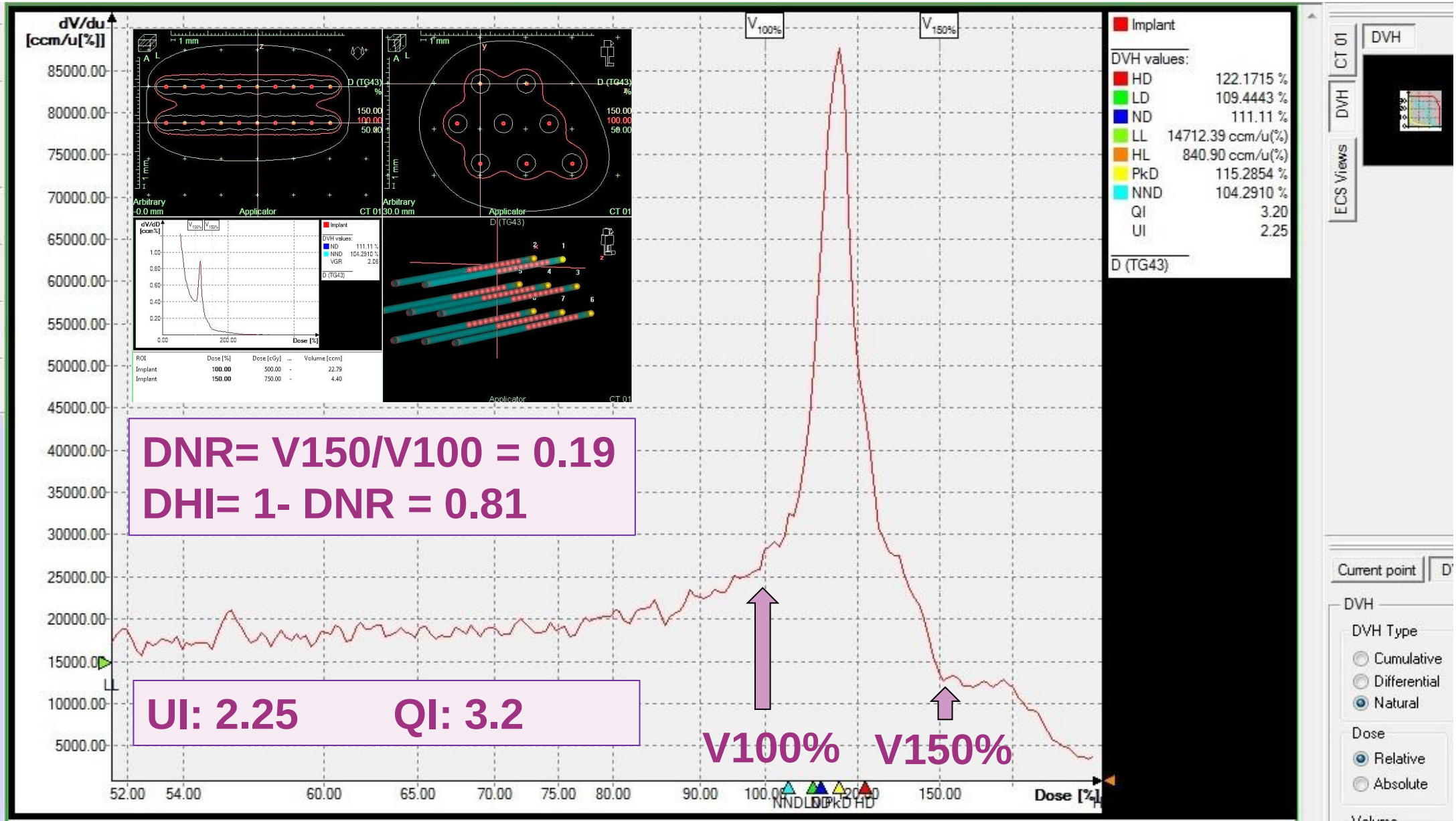
27% developed clinically evident fat necrosis

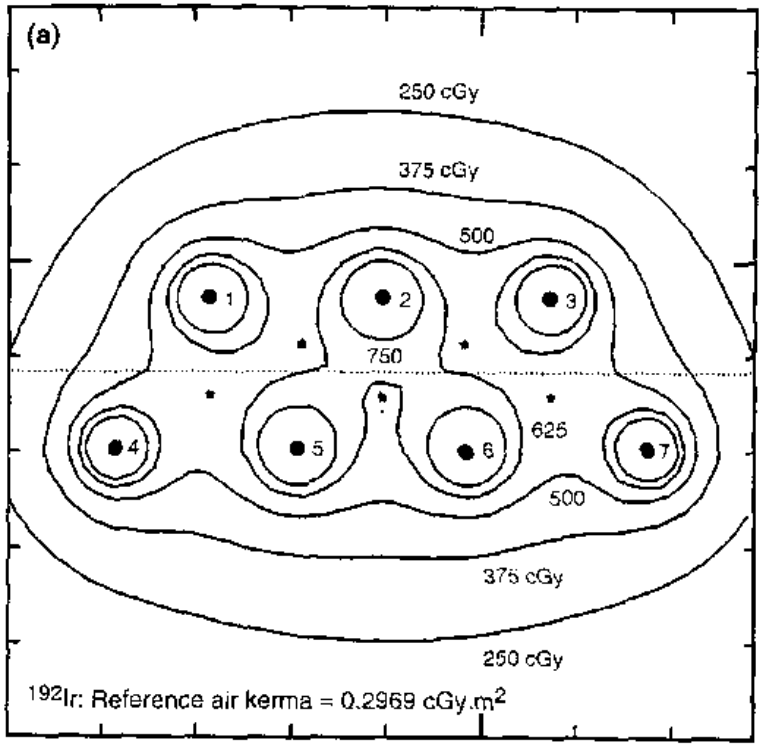
	fat necrosis	no fat necrosis	Baglan WBH	Budrakkar Mumbai (85%)
V100	234.4 cc	147.7 cc (p<0.03)	216 cc	124cc
V150	69.0 cc	36.2 cc (p<0.01)	26 cc	30cc
				18% fat necrosis
DHI	0.82	0.85	0.87	0.74

The volume of the implant, the volume of dose "hotspots" V150 and V200, and the dose homogeneity of the implant DHI were strongly correlated with adverse outcome.

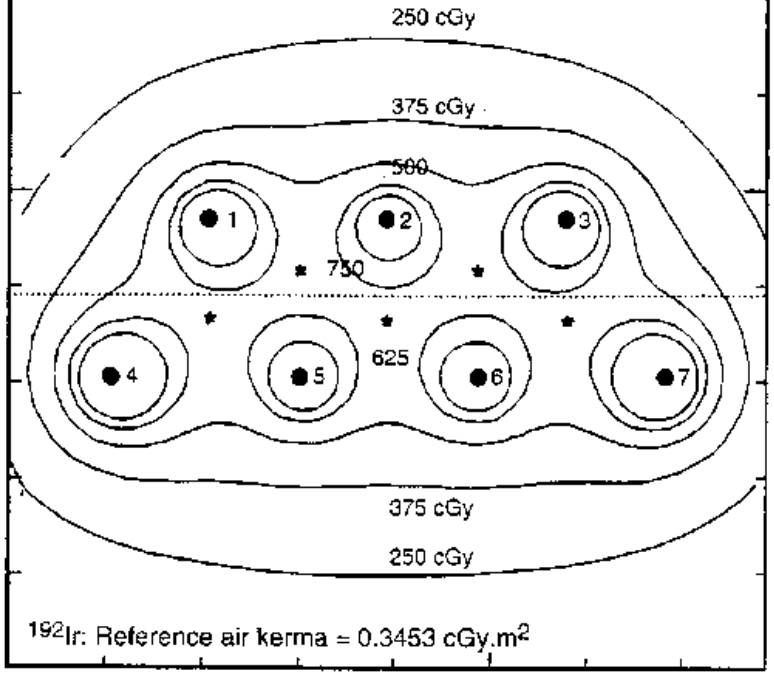
Wazer DE et al. APBI: An analysis of variables associated with late toxicity and long-term cosmetic outcome after HDR interstitial brachytherapy. Int J Radiat Oncol Biol Phys 2006; 64:489–495

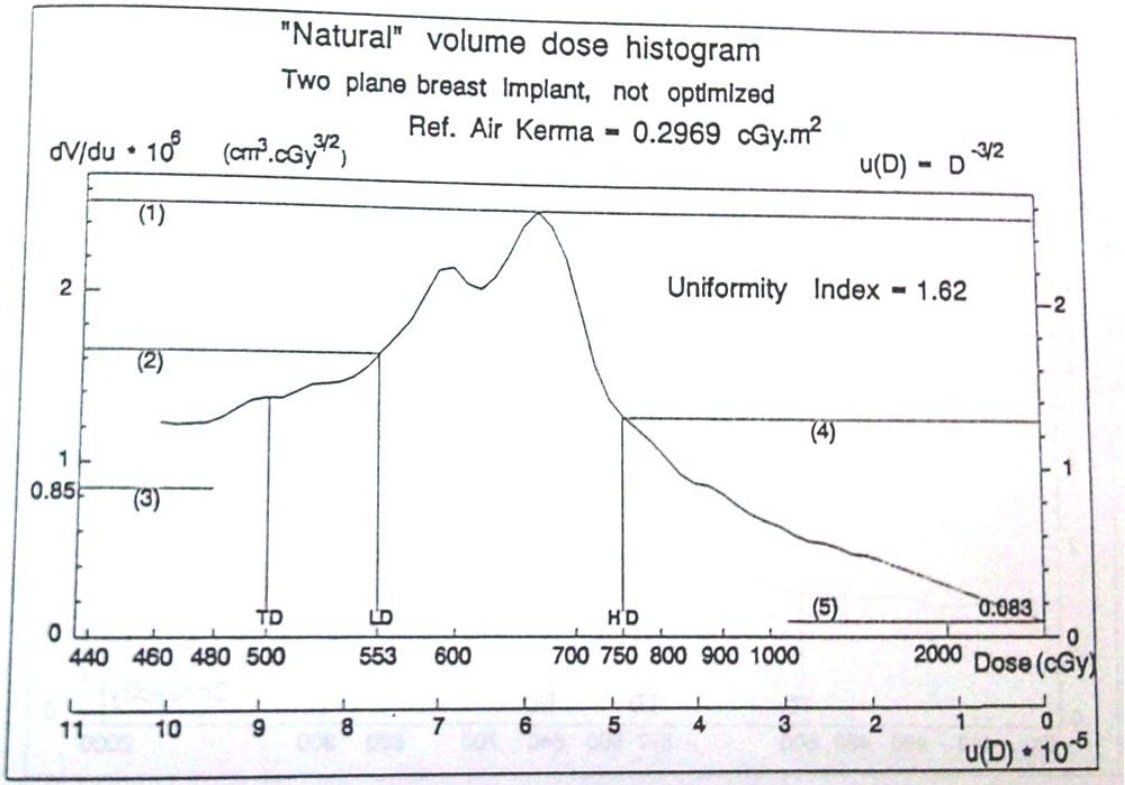
The Natural Dose Volume Histogram (NDVH)

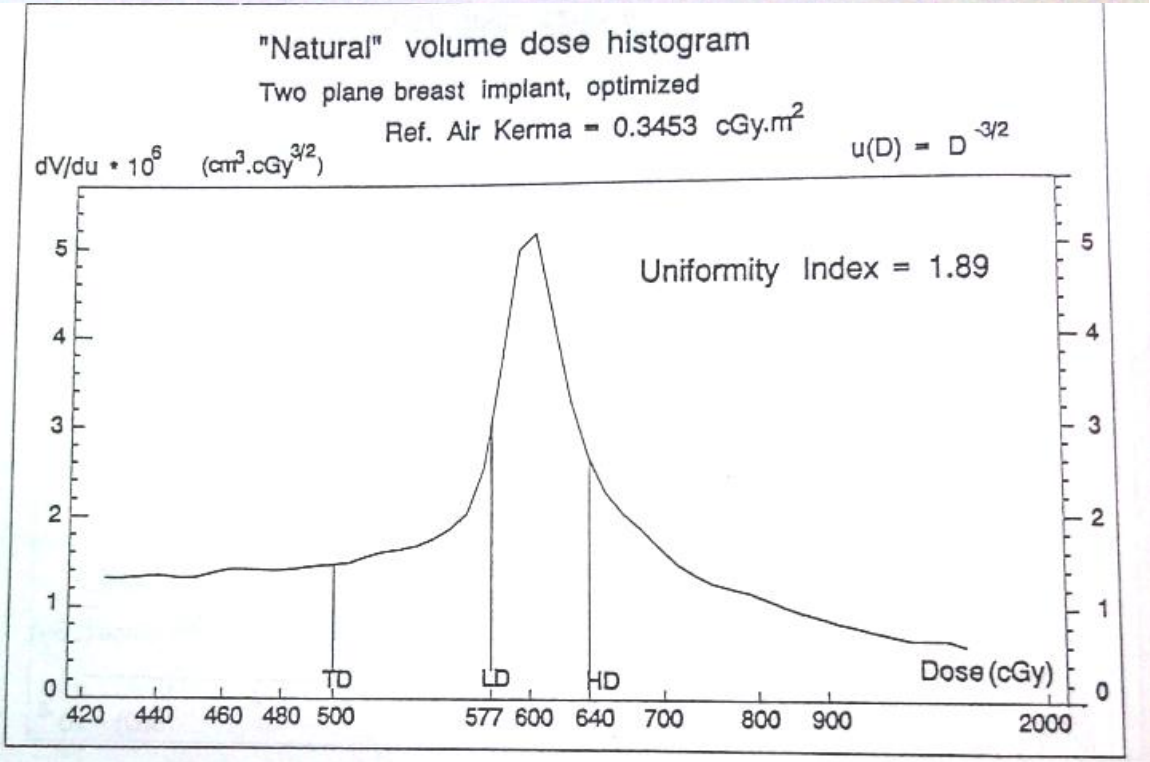




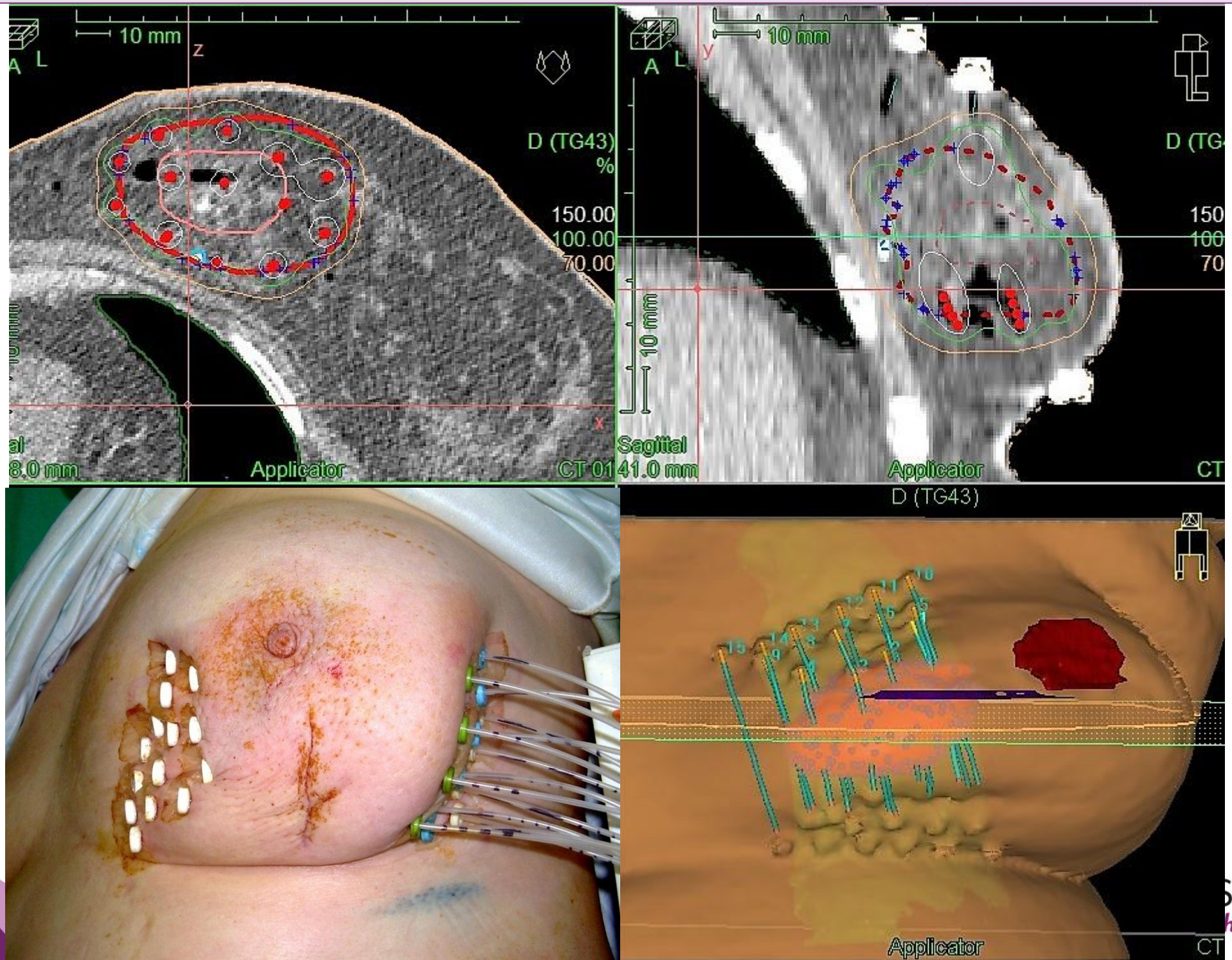
Optimization



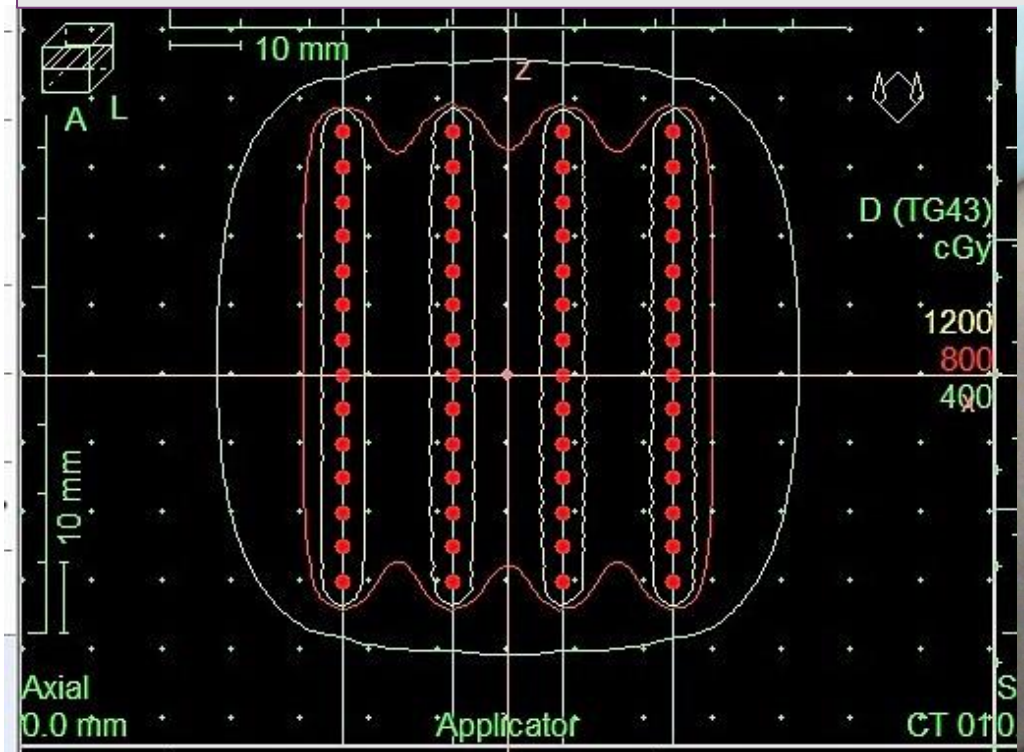


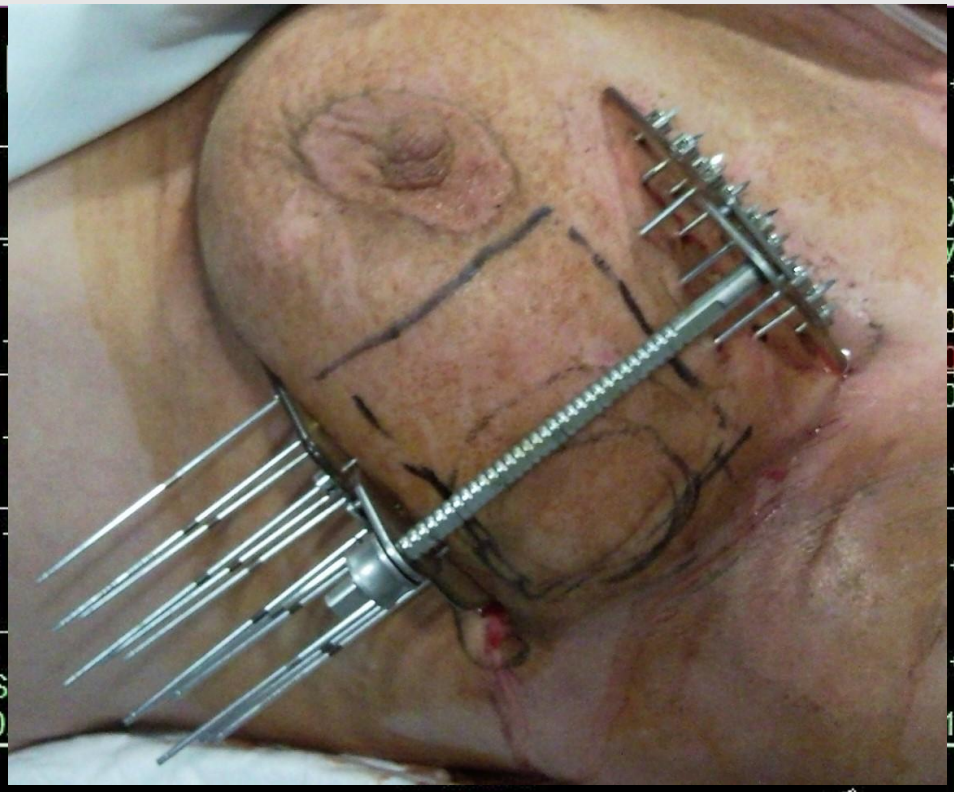


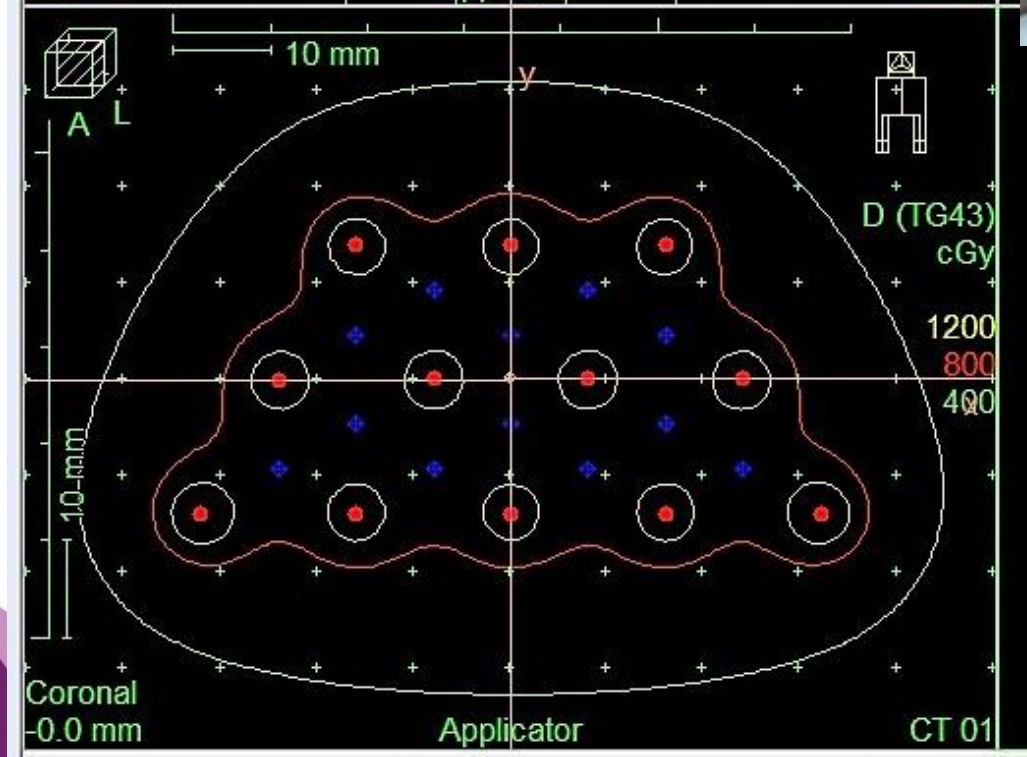
Breast A.P.B.I. 4Gy: isodoses

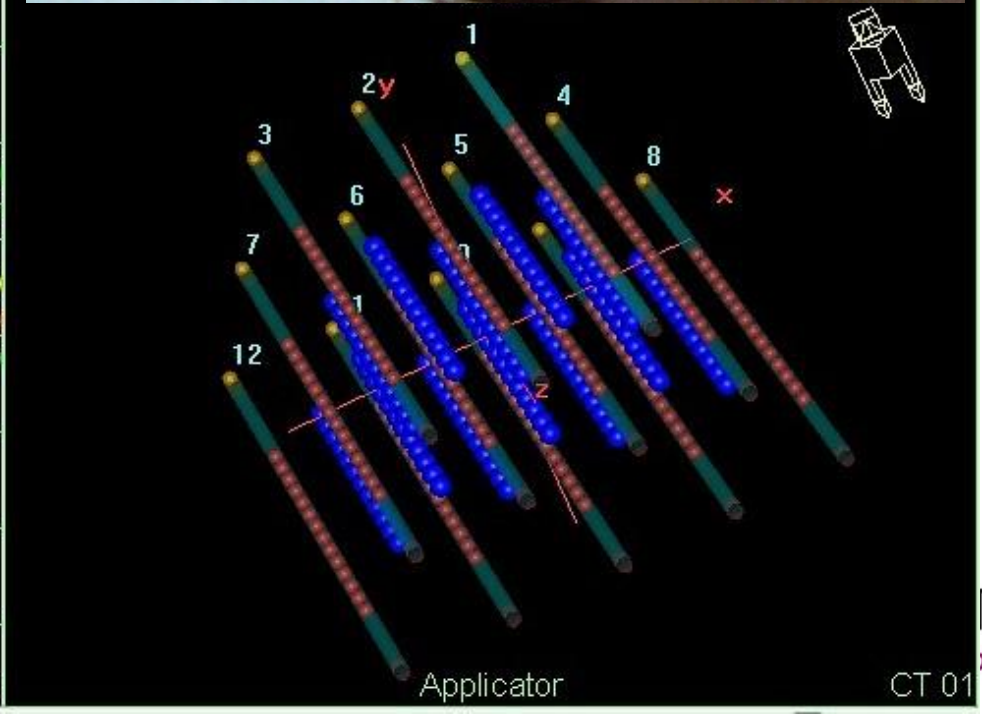


Breast postoperative boost 8Gy: isodoses

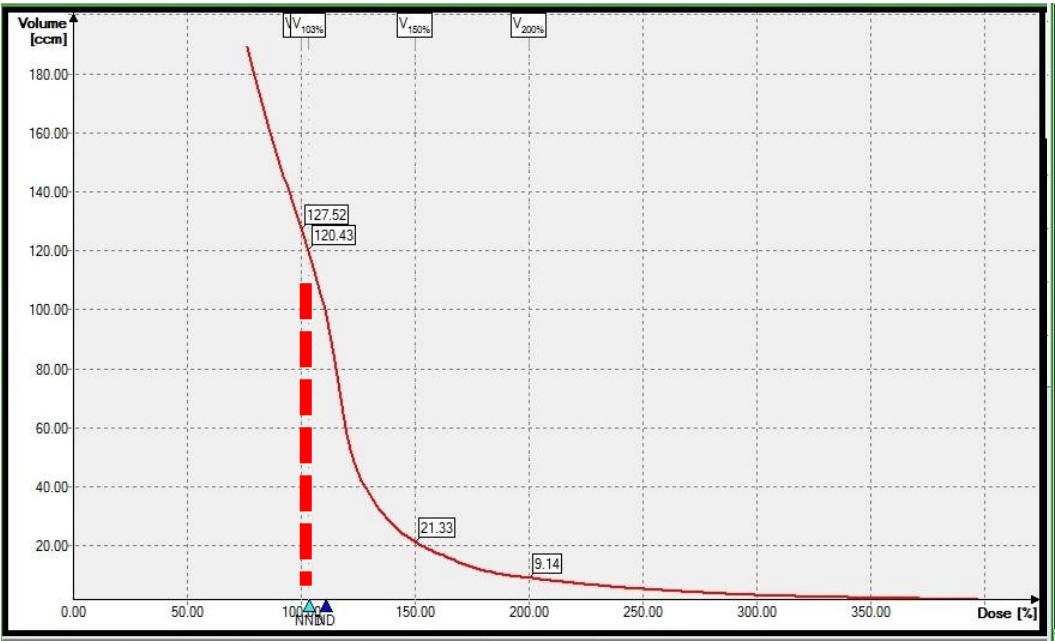




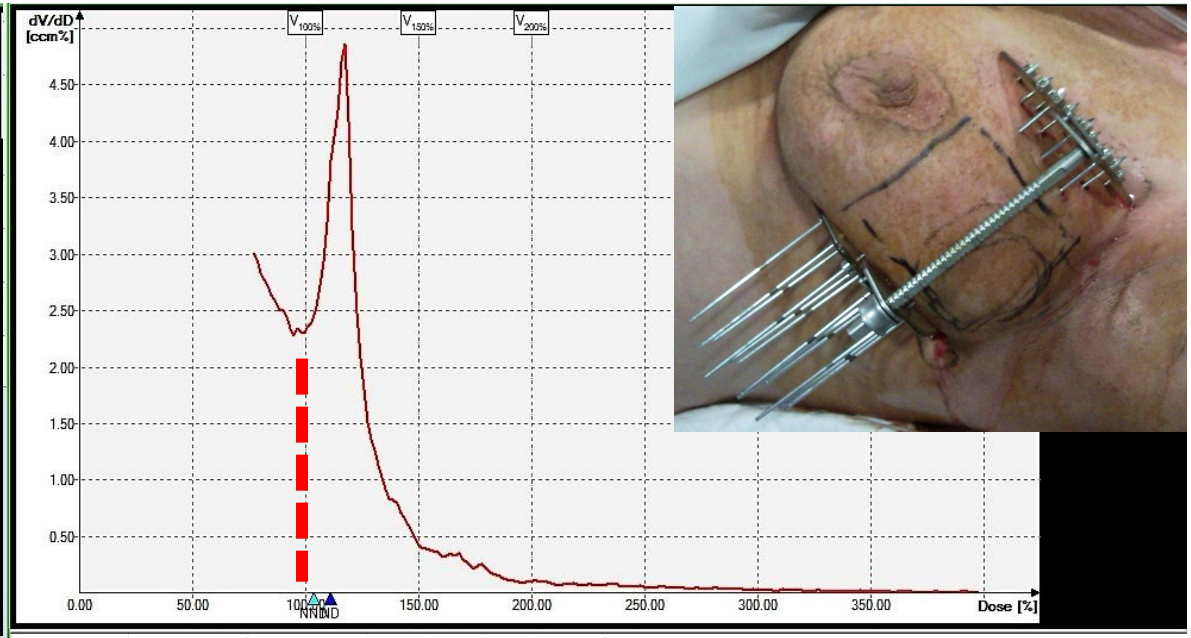




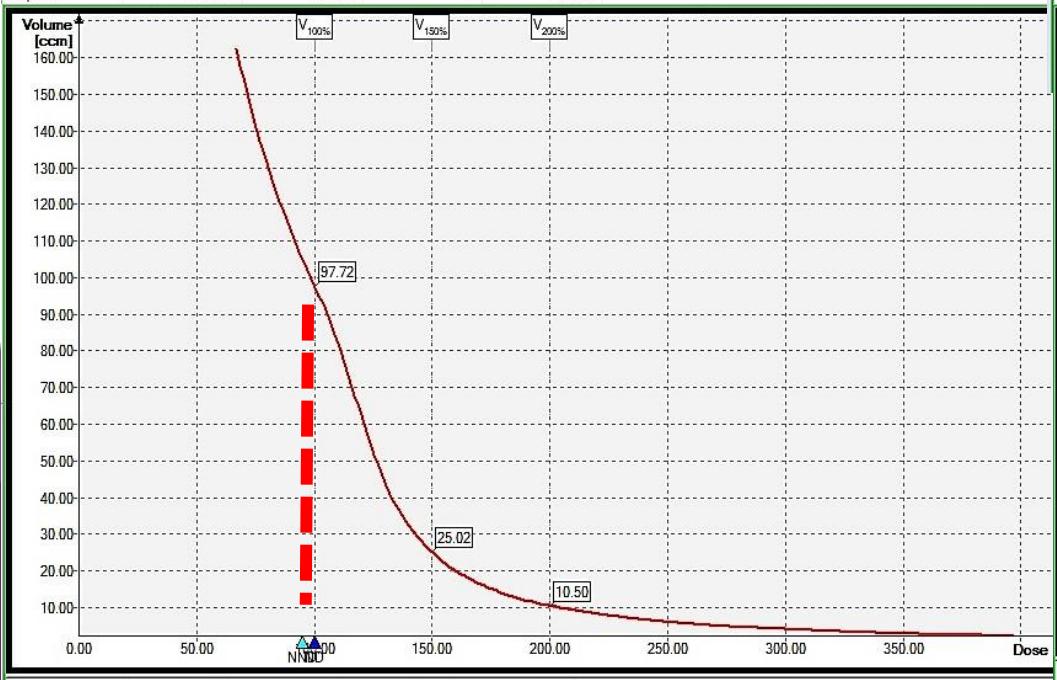
Comparison of cumulative and diferential DVH implant



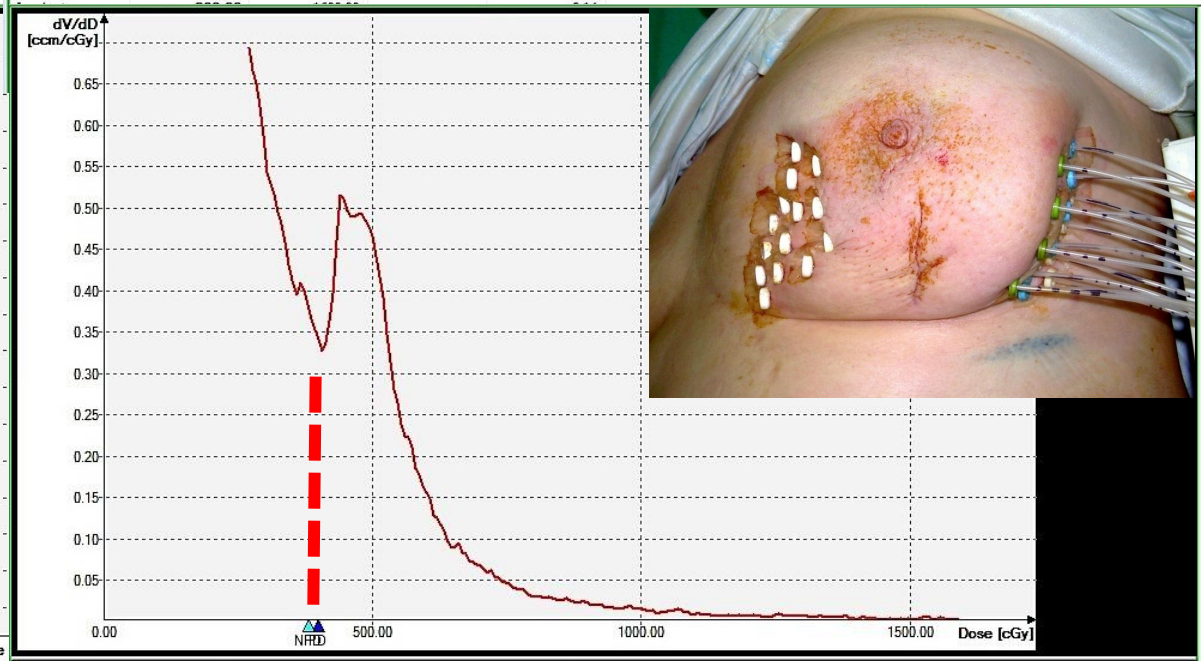
ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
Implant	**100.00**	800.00	-	127.52
Implant	**103.00**	824.00	-	120.43



ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
Implant	**100.00**	800.00	-	127.52
Implant	**150.00**	1200.00	-	21.33



ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
Implant	**100.00**	400.00	-	97.72
Implant	**150.00**	600.00	-	25.02

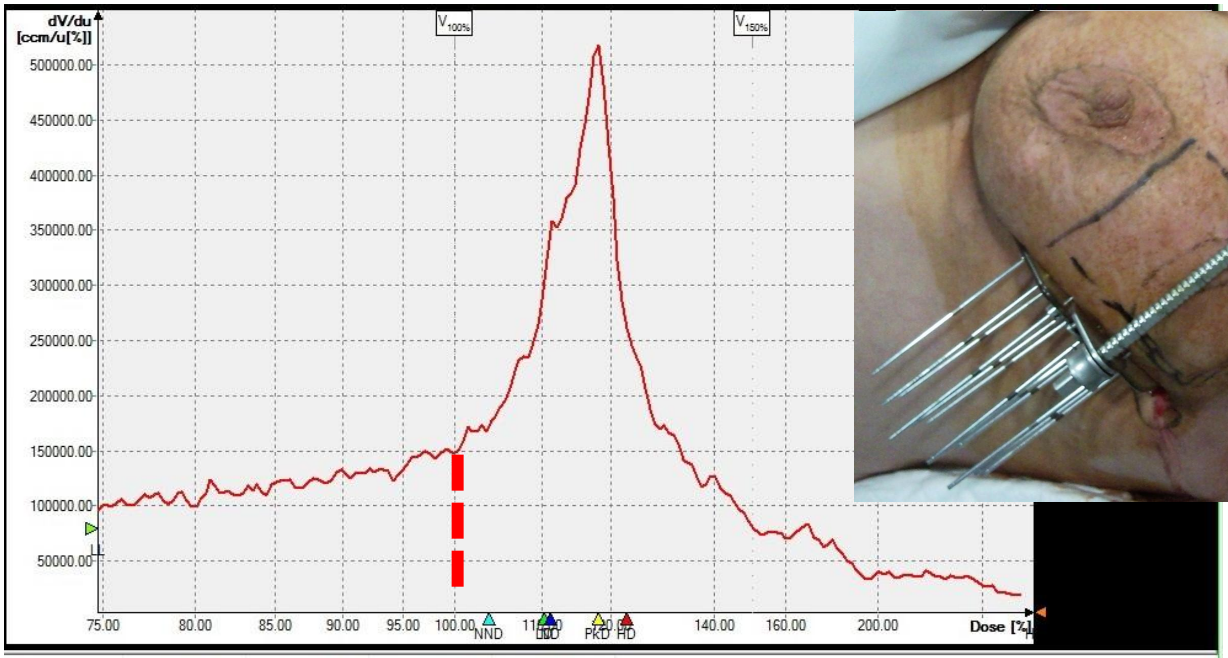


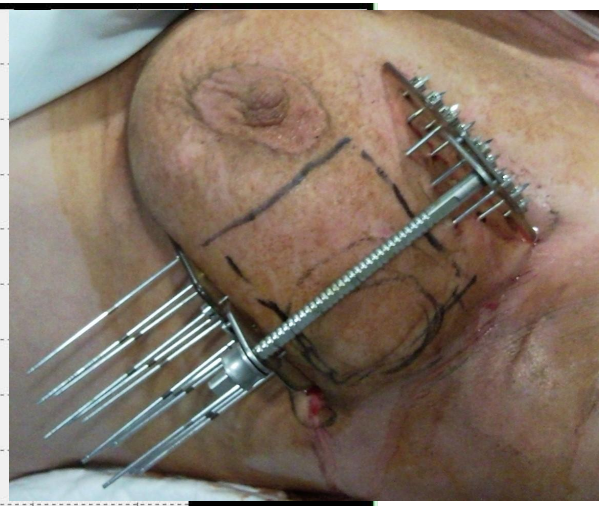
ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
Implant	**100.00**	400.00	-	97.72
Implant	**150.00**	600.00	-	25.02
Implant	**200.00**	800.00	-	10.50

Comparison of natural DVH implant

Breast postoperative boost 8Gy 12 rigid needles

DNR= 0.16
QI= 3.40
UI= 2.31

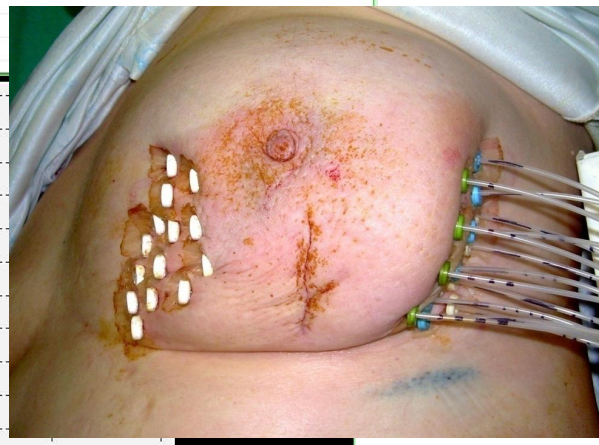




ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
Implant	**100.00**	800.00	-	127.52
Implant	**150.00**	1200.00	-	21.33
Implant	**200.00**	1600.00	-	9.14

Breast A.P.B.I. 4Gy 15 plastic tubes

DNR= 0.25
QI= 1.80
UI= 1.63



ESTRO School

Dose Volume Histograms in Brachytherapy:

Based on the catheters (IMPLANT)

- Cumulative DVH
- Differential DVH
- Natural DVH

Based on the anatomy (TARGET/CTV/OAR)

(Requires 3d imaging CT/MR/US)

- **Cumulative DVH in CTV**
- Cumulative DVH in OAR

ESTRO School

Dose Volume Histograms in Brachytherapy:

- **Dose Volume Histogram (DVH) based on 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 Minimum Target Dose 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.

V: volume that receives % doses
D: Doses that receives % volume

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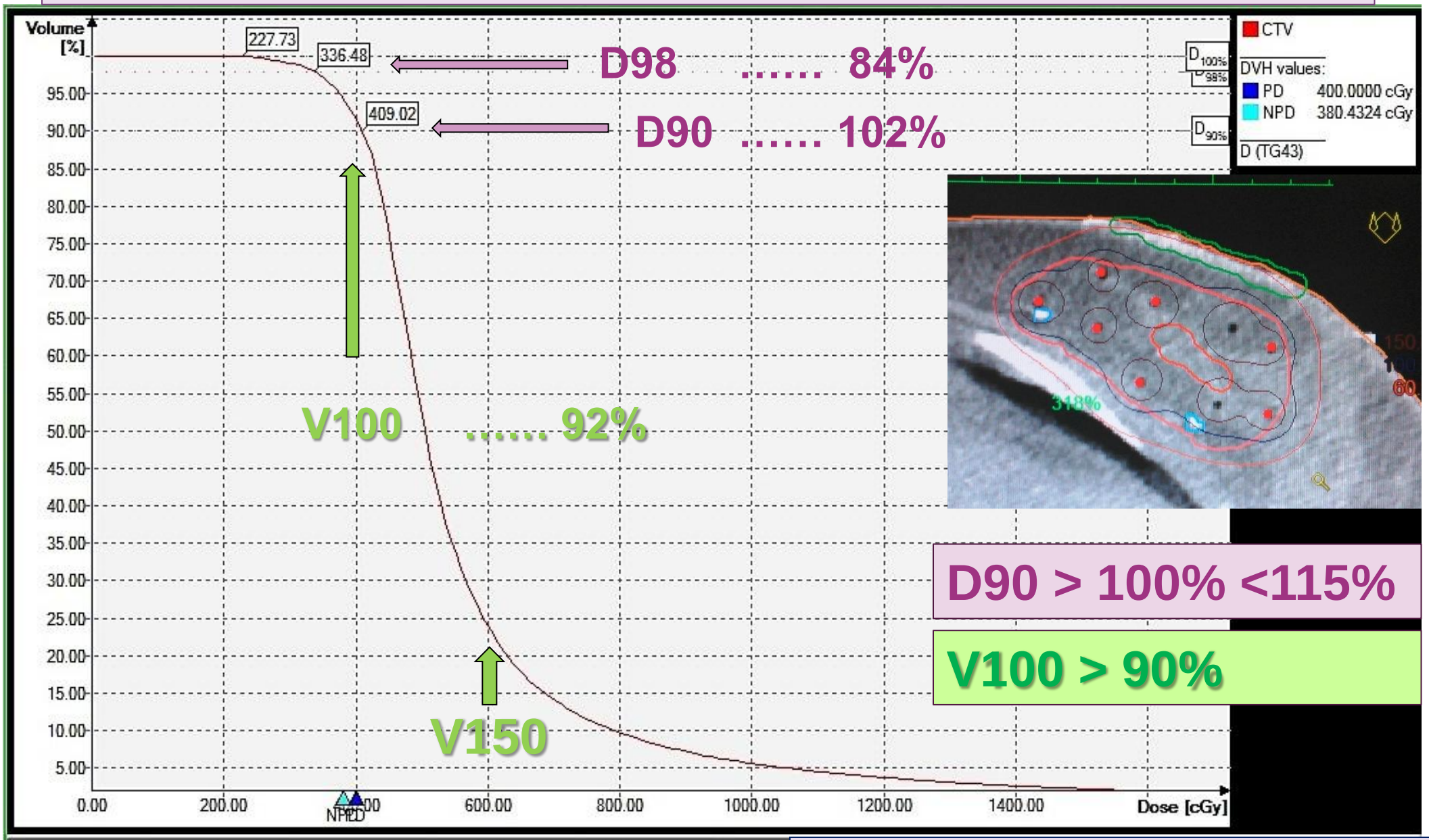
Breast A.P.B.I. 4Gy: cumulative DVH CTV



D90 > 100% <115%

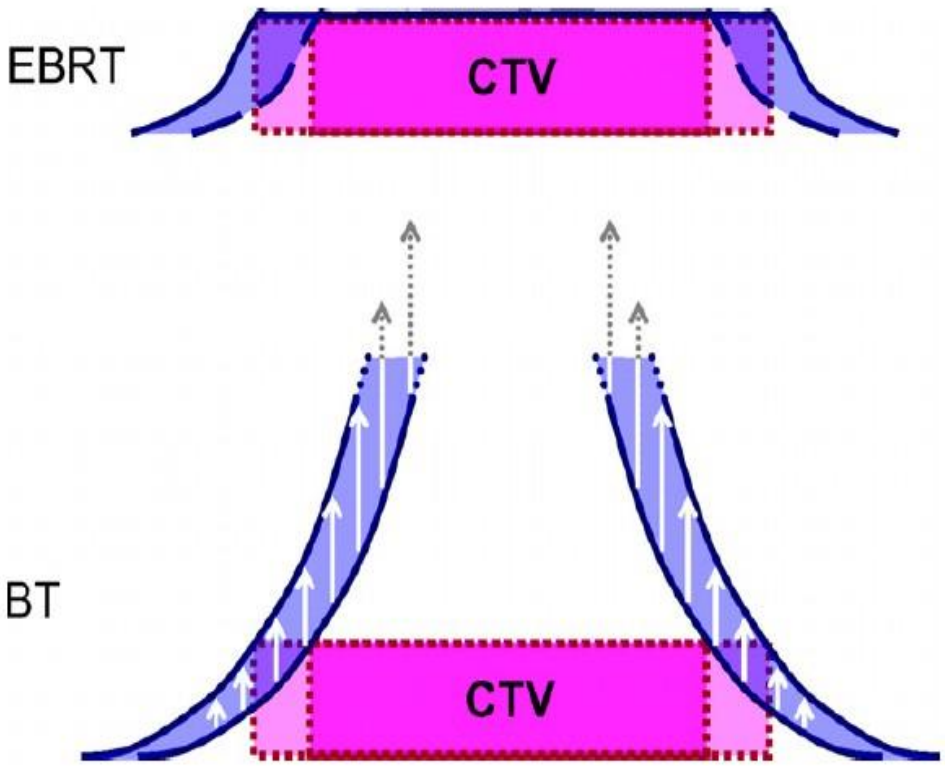
V100 > 90%

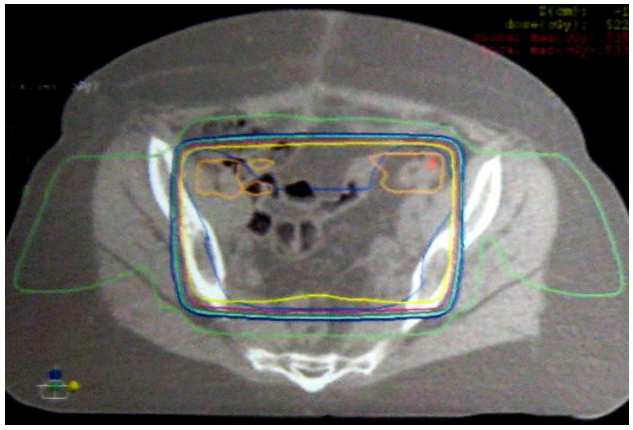
ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
CTV	56.93	227.73	**100.00**	83.64
CTV	102.25	409.02	**90.00**	75.28
CTV	84.12	336.48	**98.00**	81.97

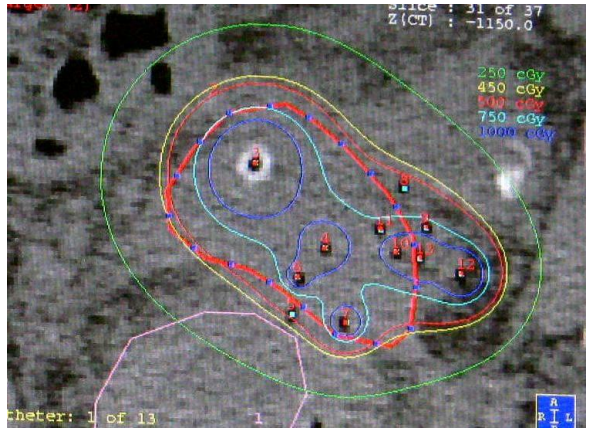
The curve indicates how much of the volume is covered by the "required" dose value

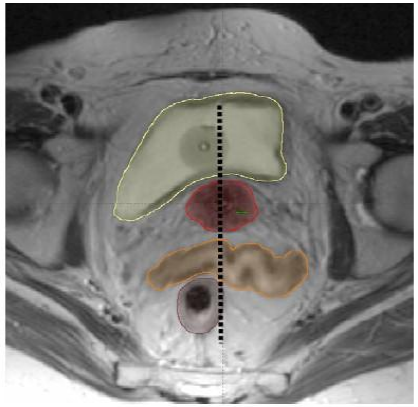
WHY TO USE D90 INSTEAD OF D98 OR D100: MARGINS

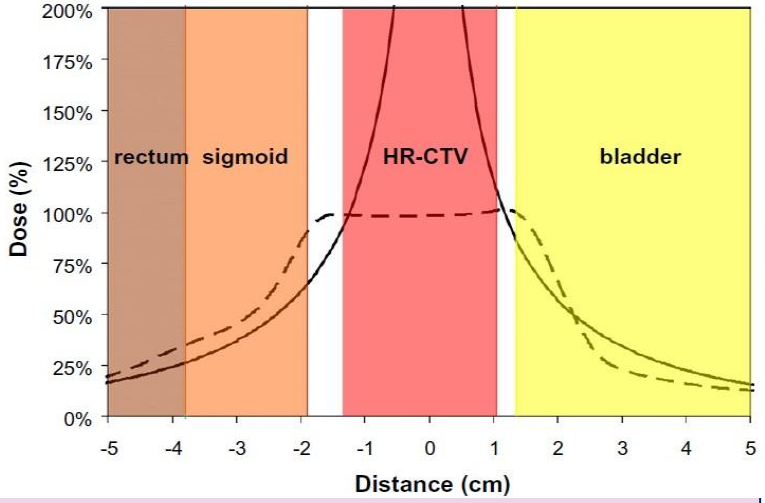
In EBRT a PTV margin will result in an increase of the volume irradiated to a high dose. The dose plateau becomes larger in size, but the CTV dose remains unchanged.







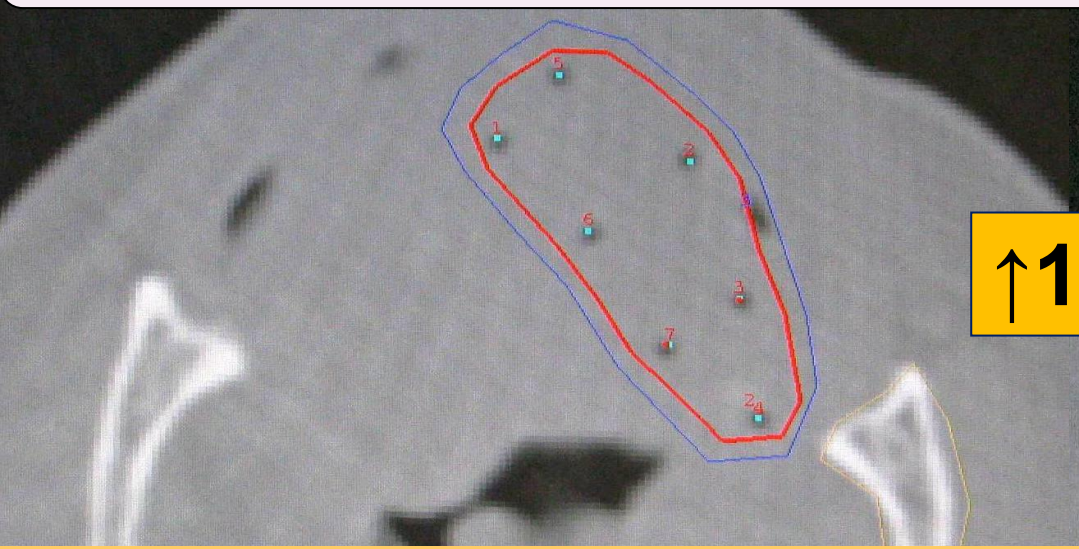




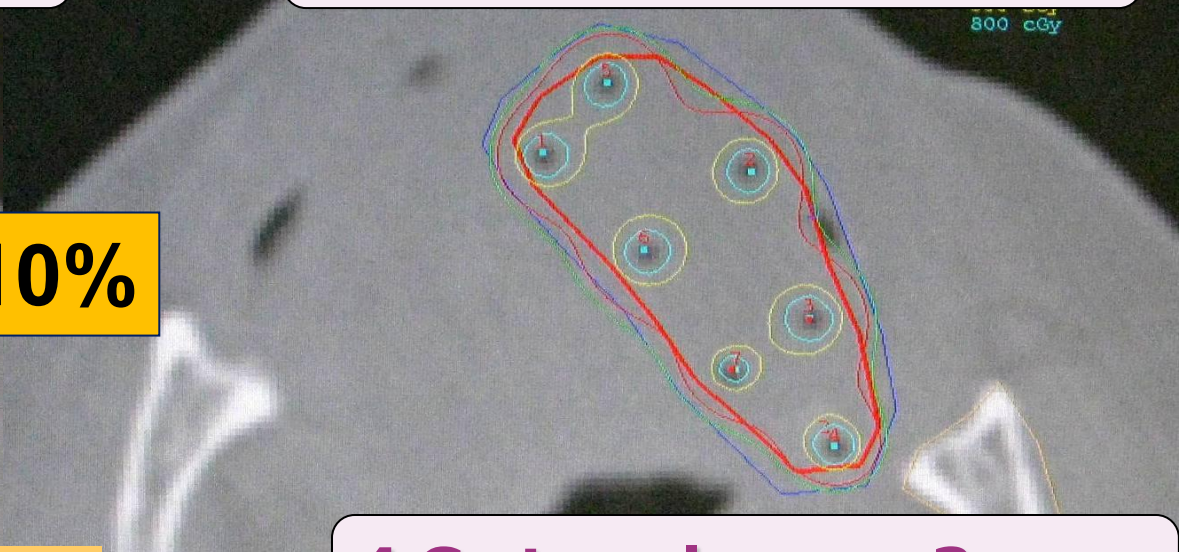
In BT a PTV margin into the lateral and antero-posterior direction and a renormalisation of dose according to the PTV will result in a general dose escalation. Application of PTV margins is strongly discouraged

Tanderup K. PTV margins should not be used to compensate for uncertainties in 3D image guided intracavitary BT. Radiother Oncol 2010; 97:495-500

Removed tongue cancer CT



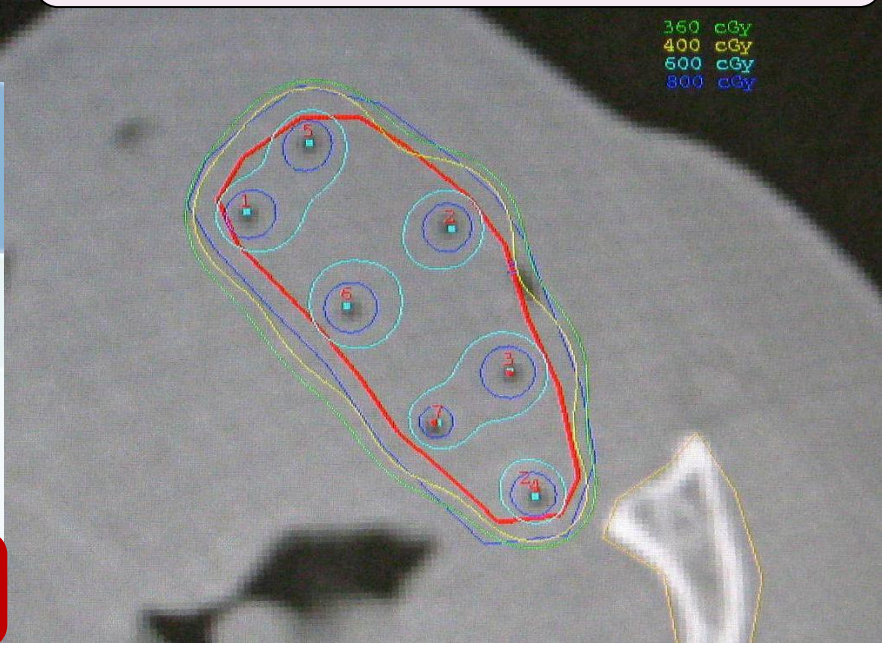
4 Gy to 90% isodose



↑10%

Without GTV, CTV is related to the applicator… Subjetive drawn

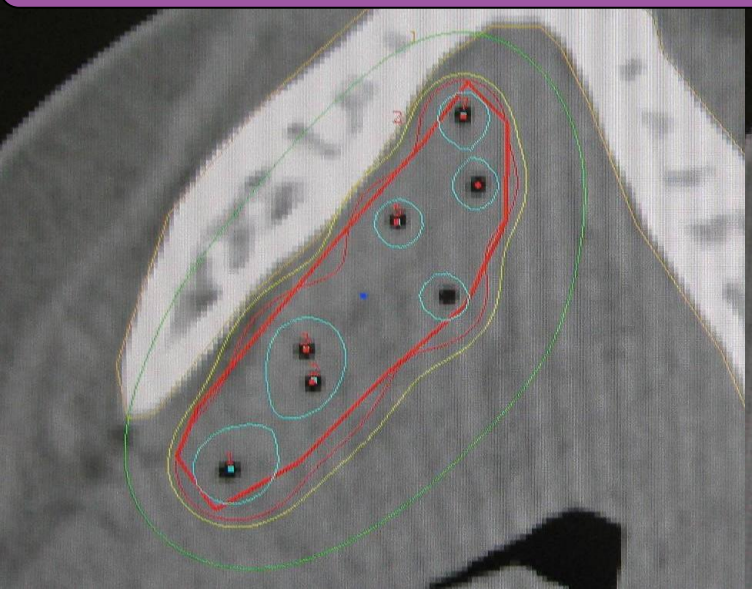
4 Gy to volume + 3mm

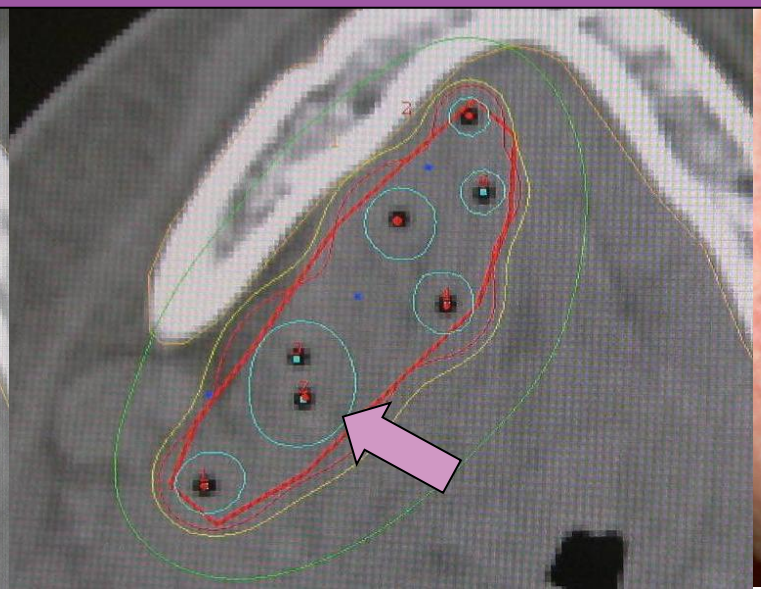


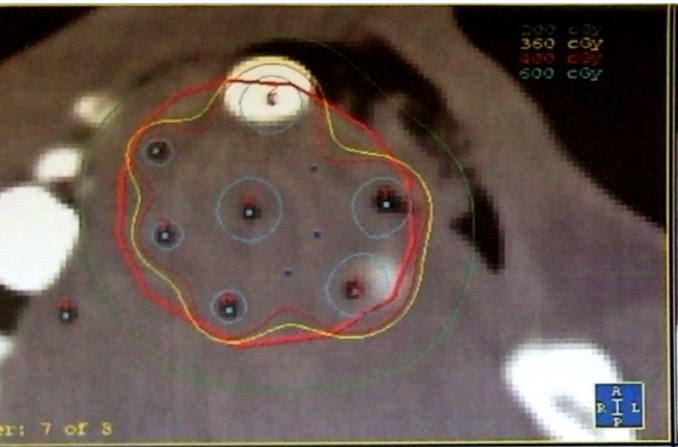
	Volume 400cGy	Volume 600cGy	D90 target	DNR
target	24.6 cc	7.52 cc	401cGy	0,30
Target + 3mm	40.5 cc	13.58cc	441cGy	0,33
	164%	180%	+10%	+ 10%

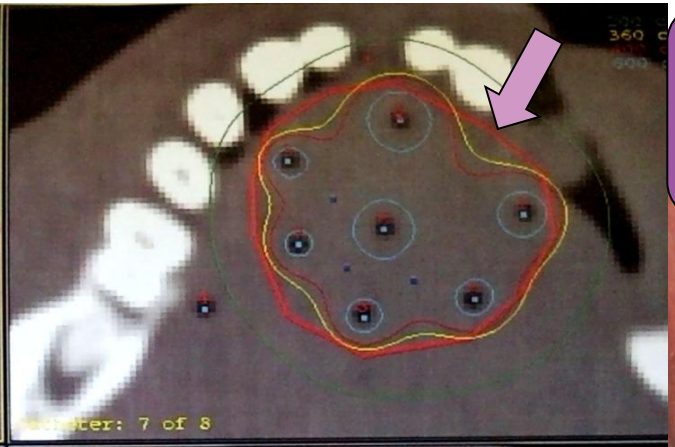
With 12 fractions, the $EQD2_{10}$ is 71 Gy instead of 63 Gy

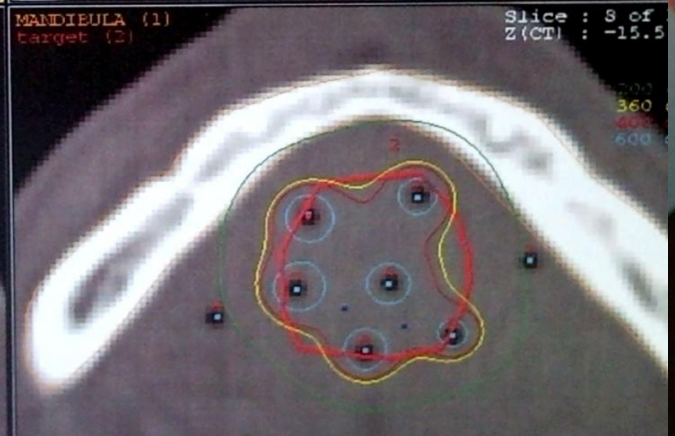
Tongue cancer CT: Hot spots result in soft tissue necrosis



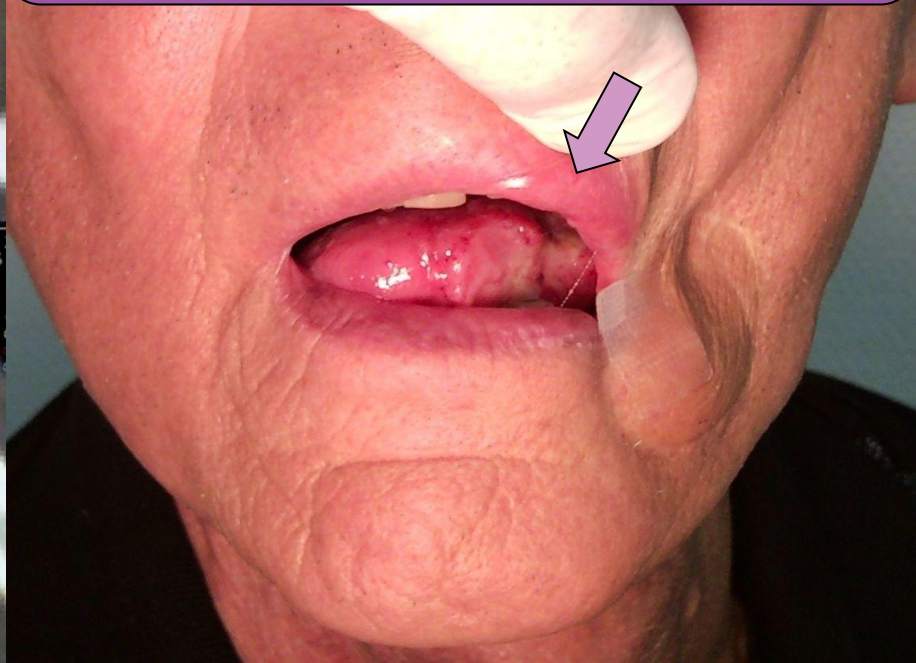




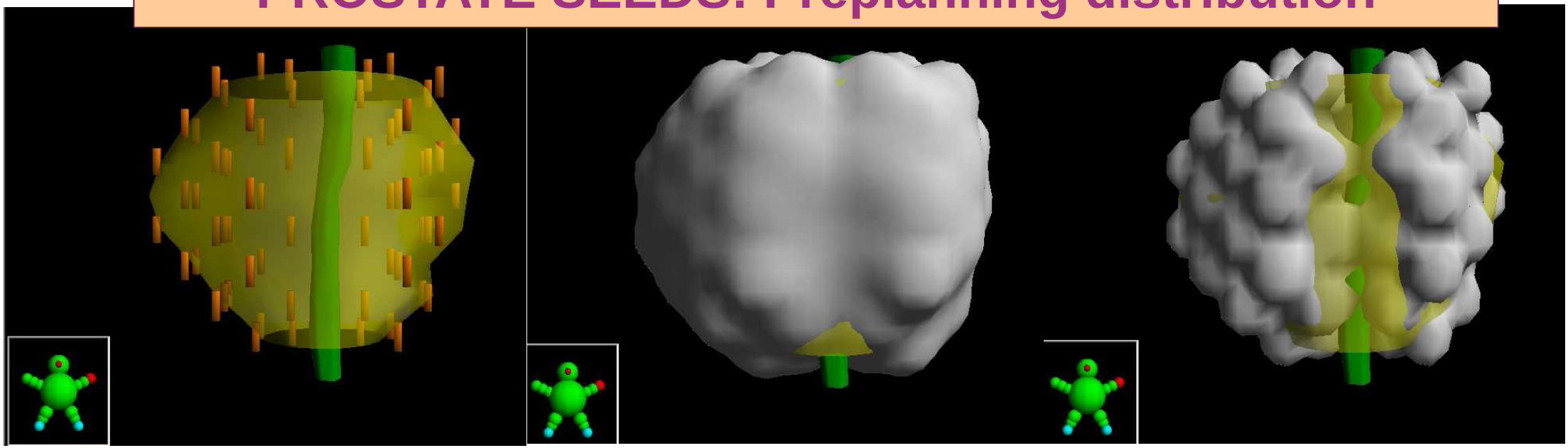


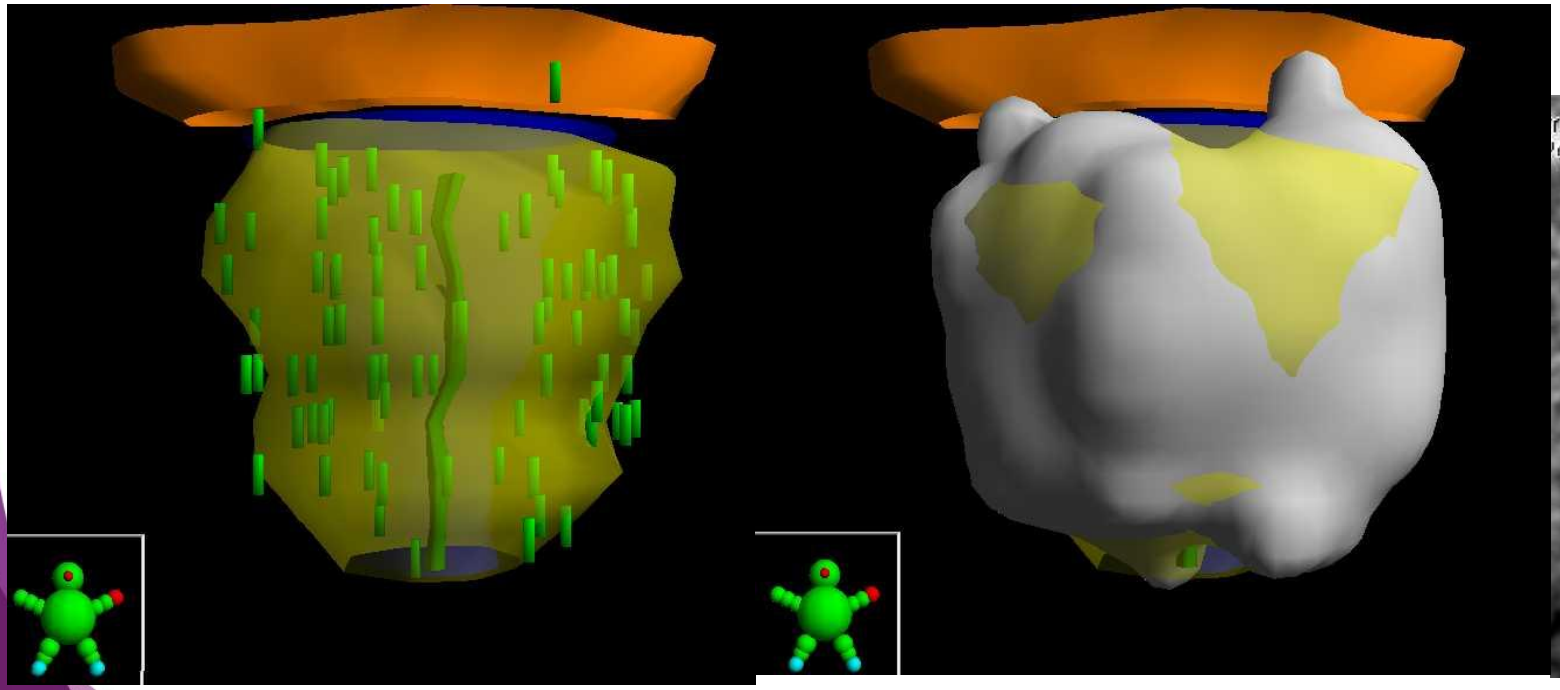


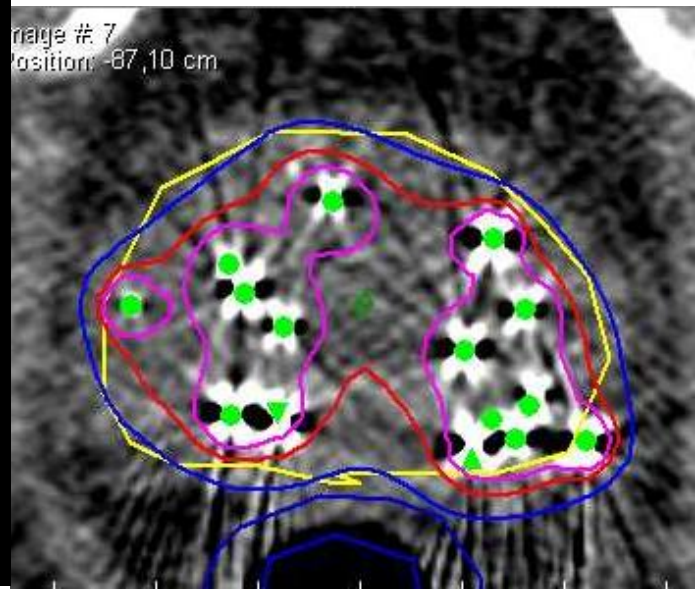
D90 is not enough if cold spots are present



PROSTATE SEEDS: Preplanning distribution

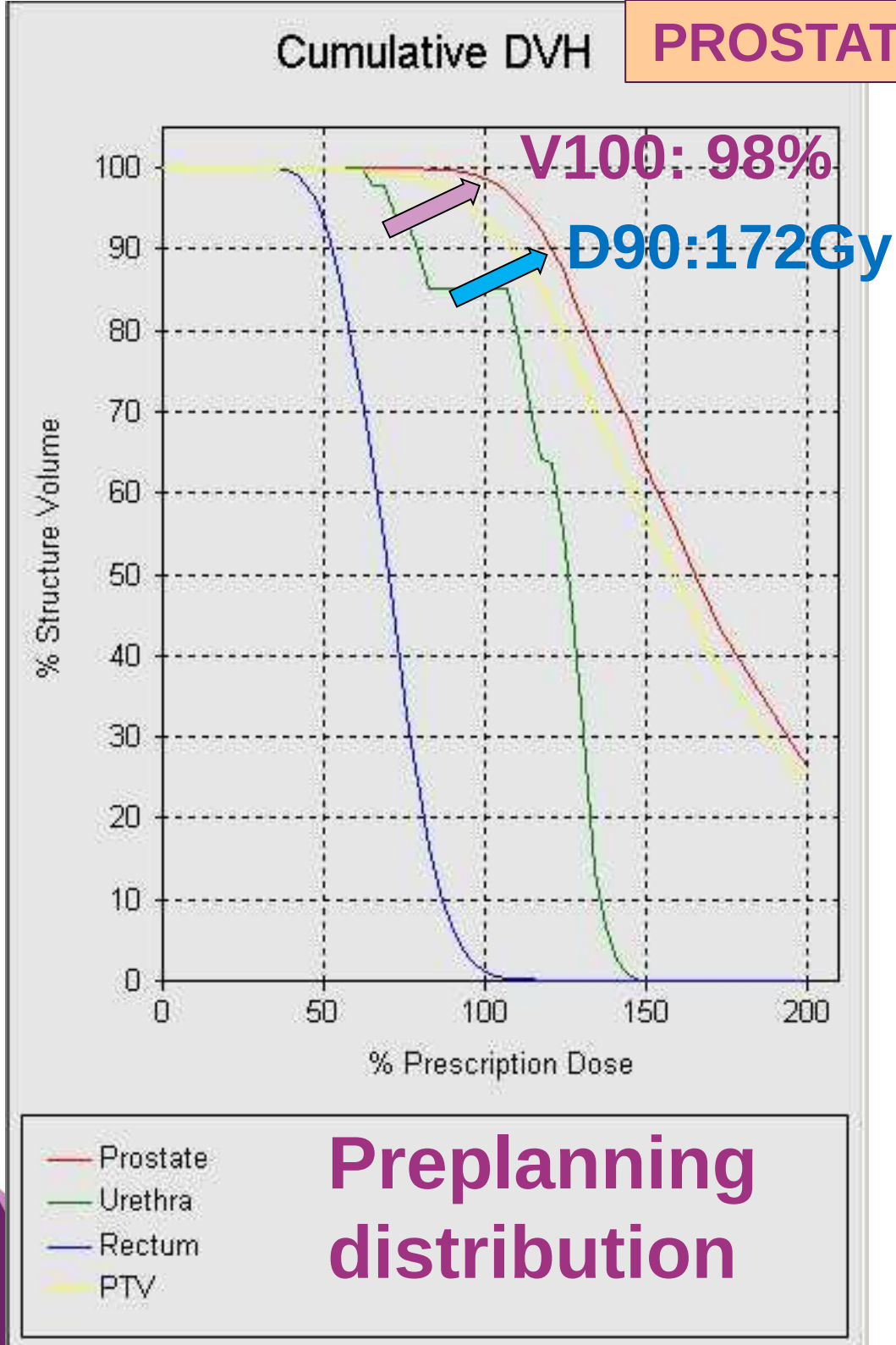


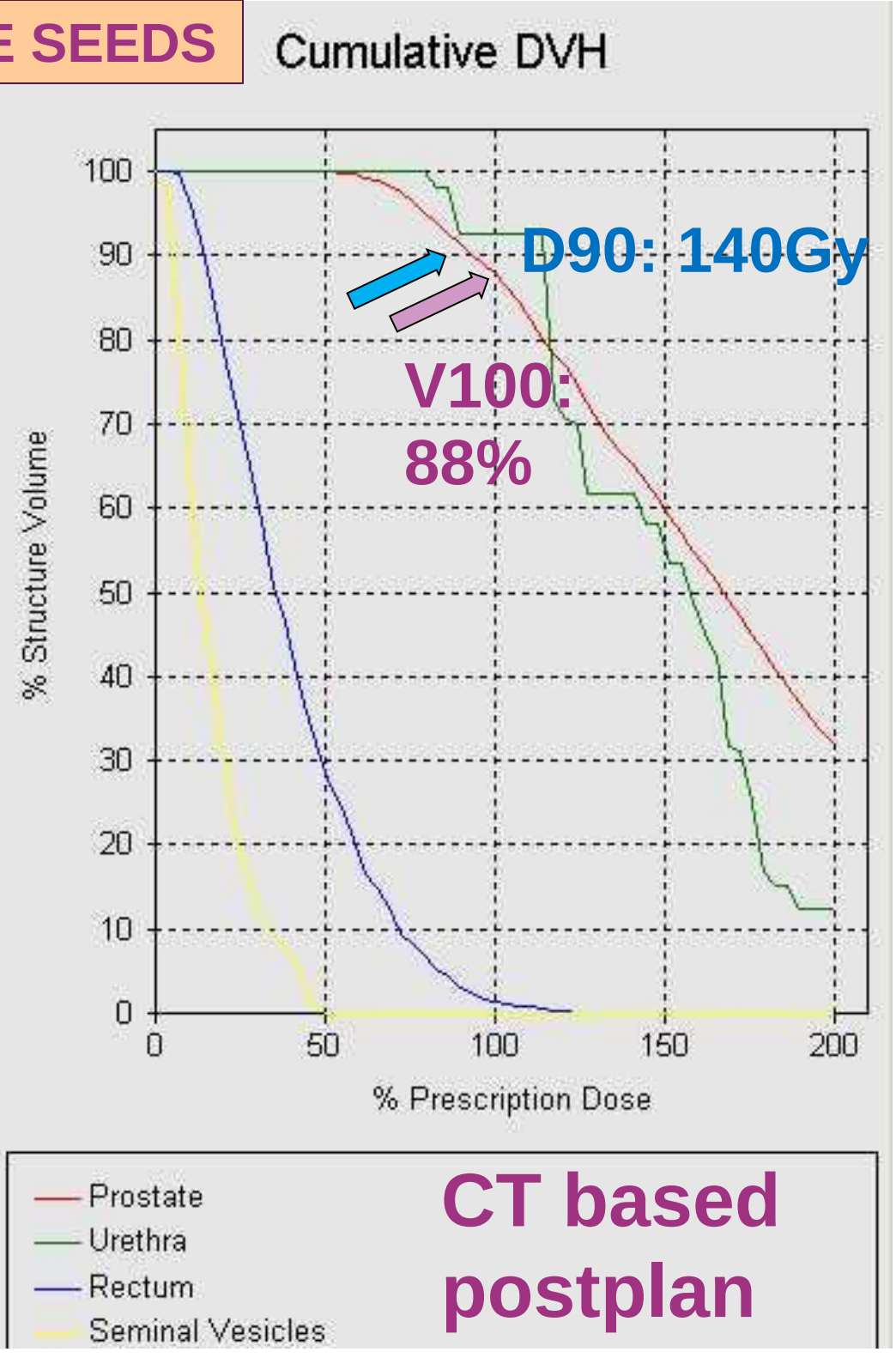




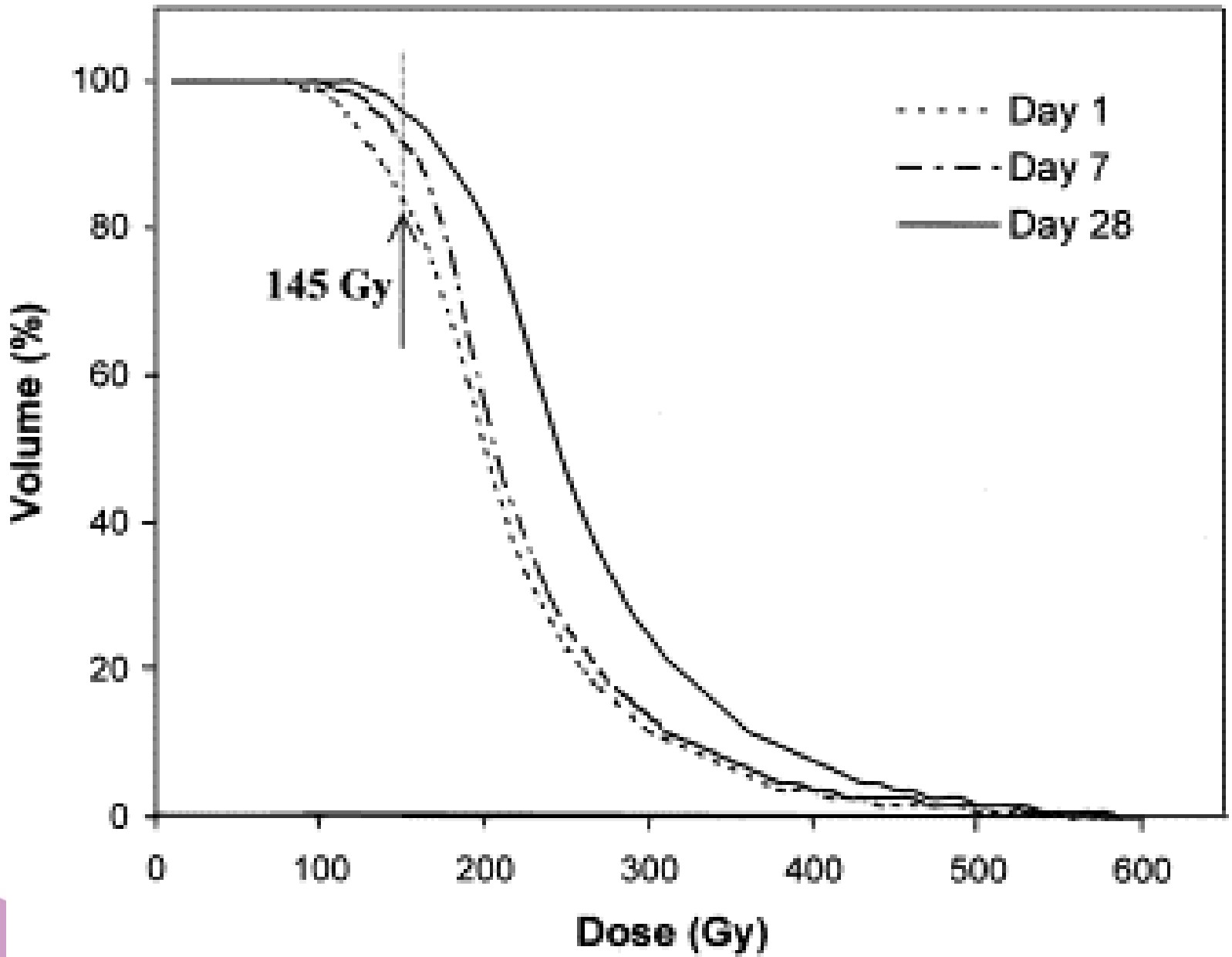
PROSTATE SEEDS: CT based postplan

PROSTATE SEEDS





PROSTATE SEEDS: CT based postplan
CHANGE OF VOLUME ALONG TIME



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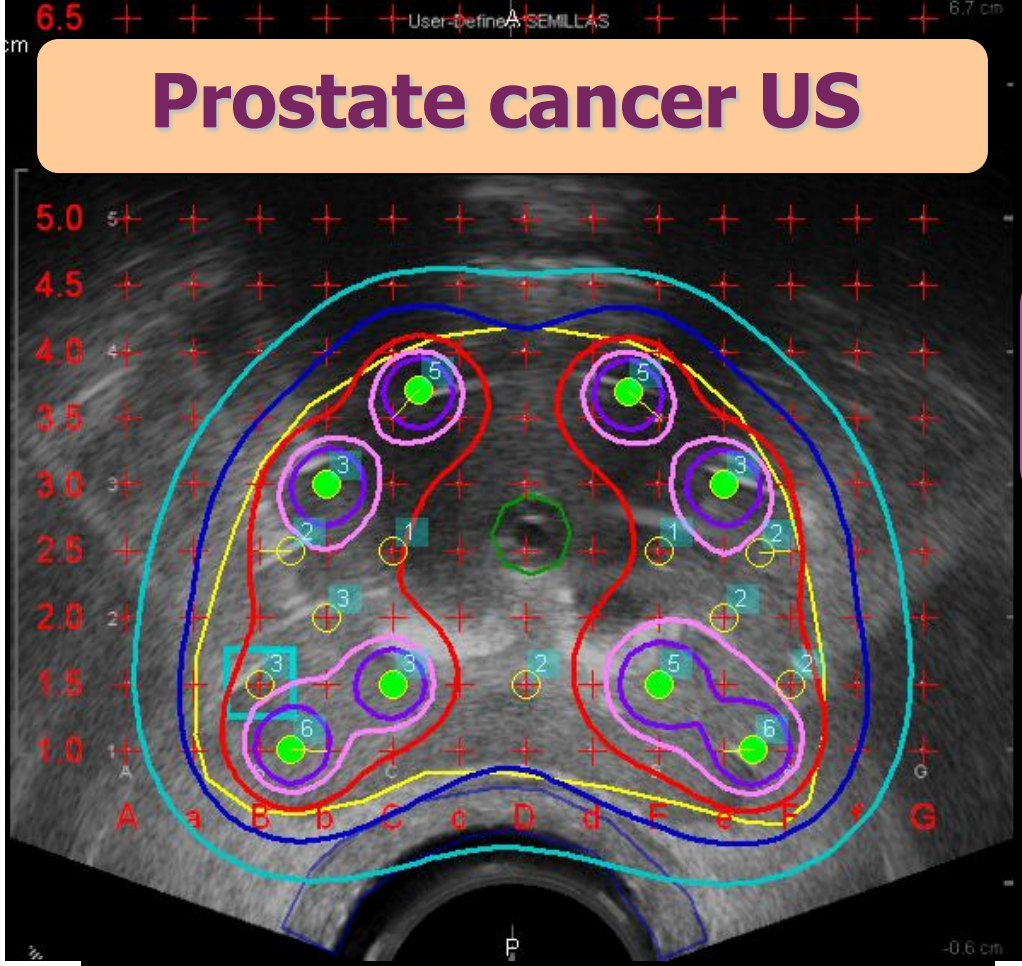
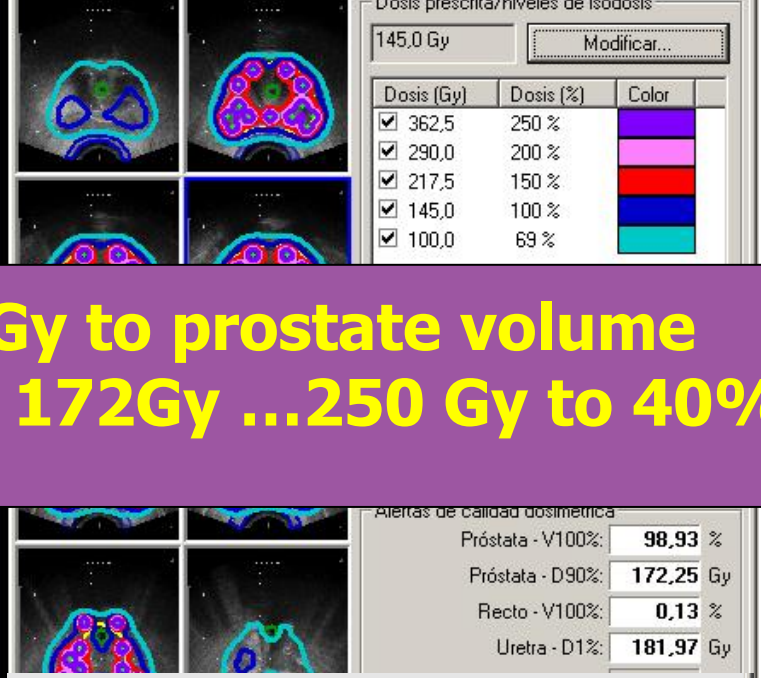
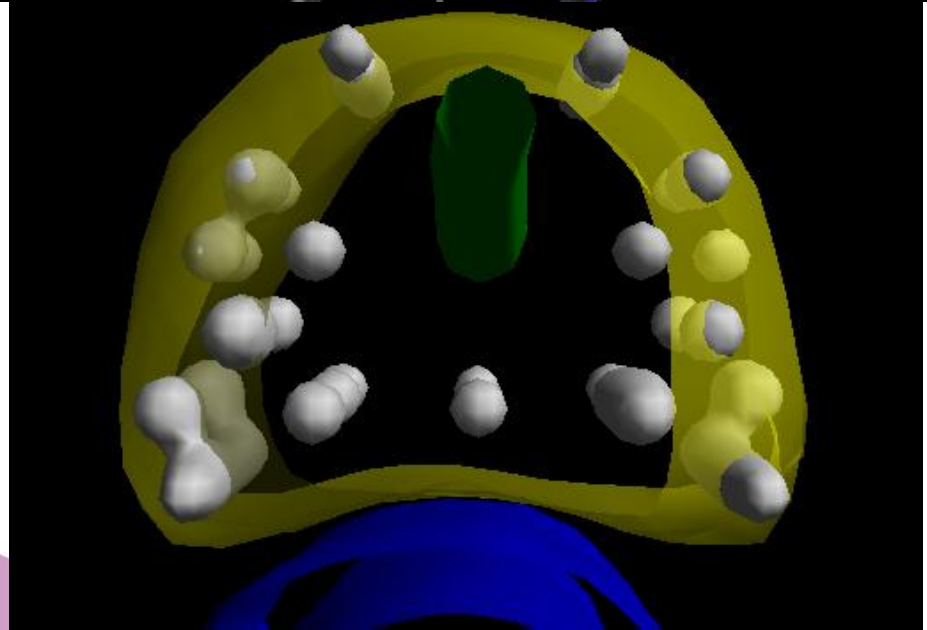
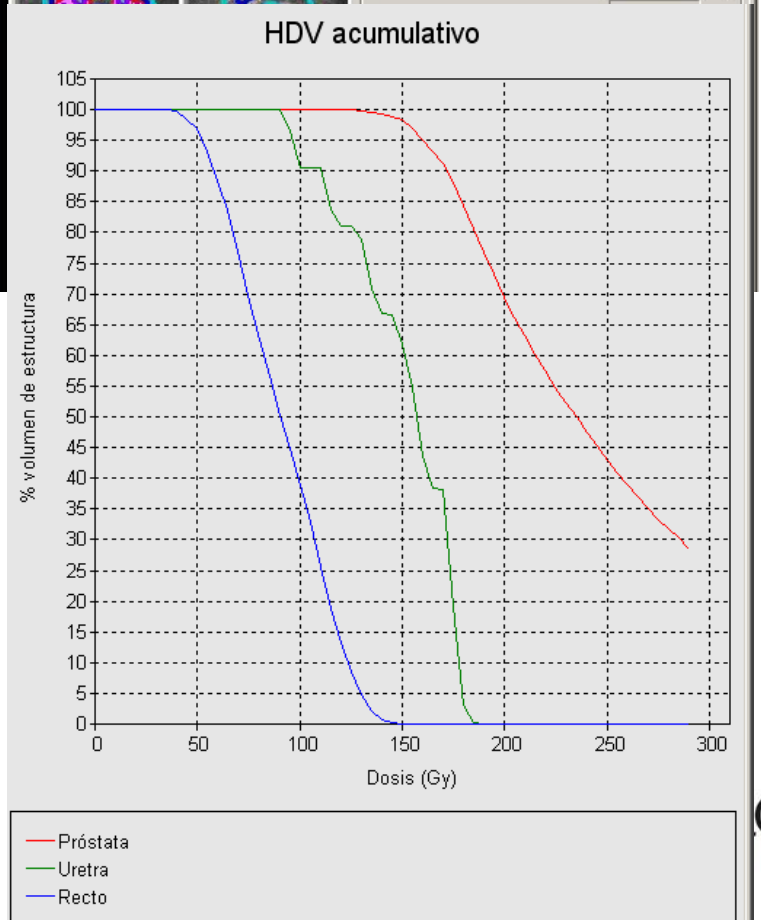
Prostate cancer US



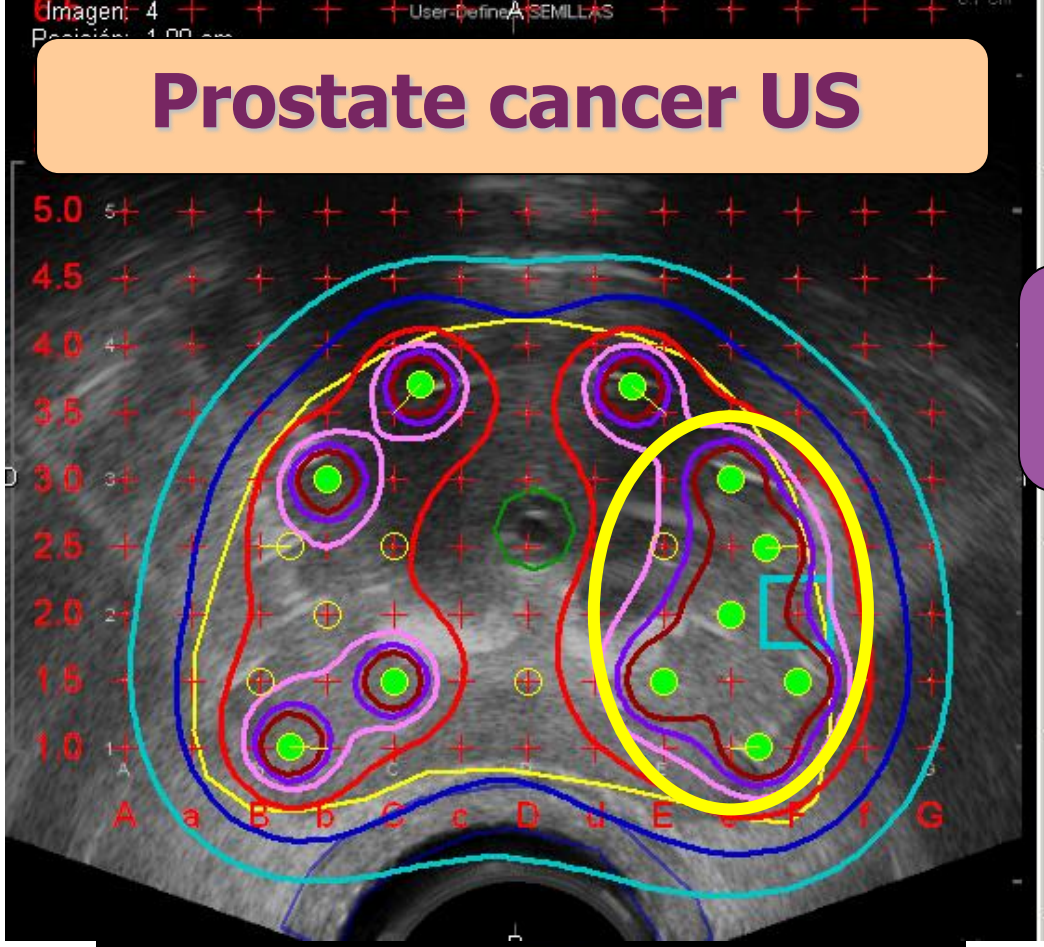


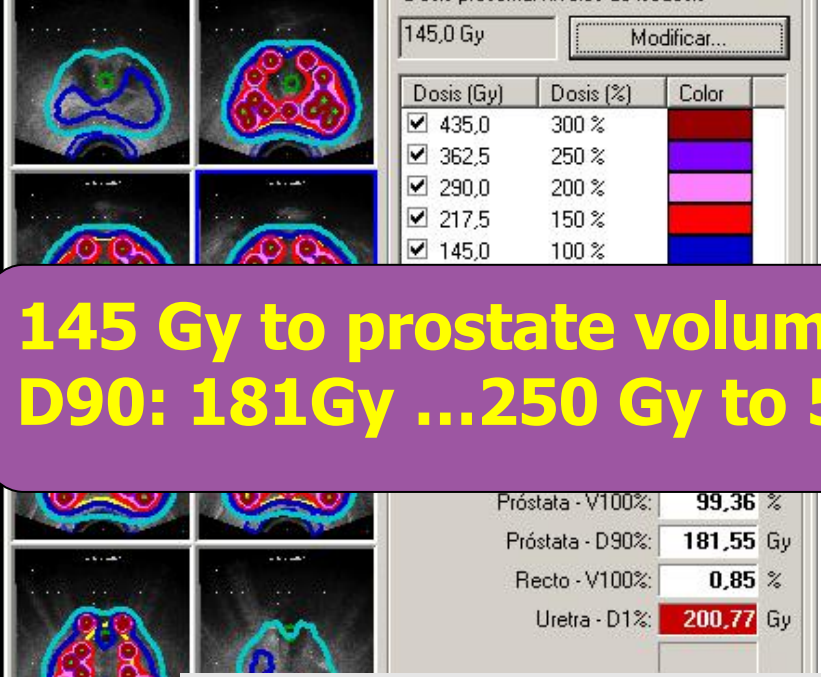
145 Gy to prostate volume
D90: 172Gy ...250 Gy to 40%



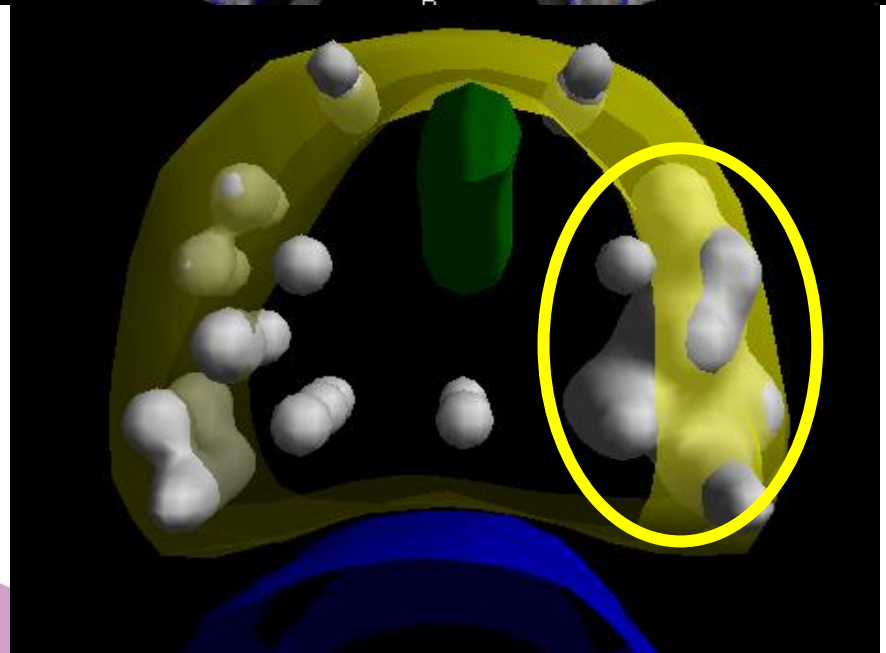


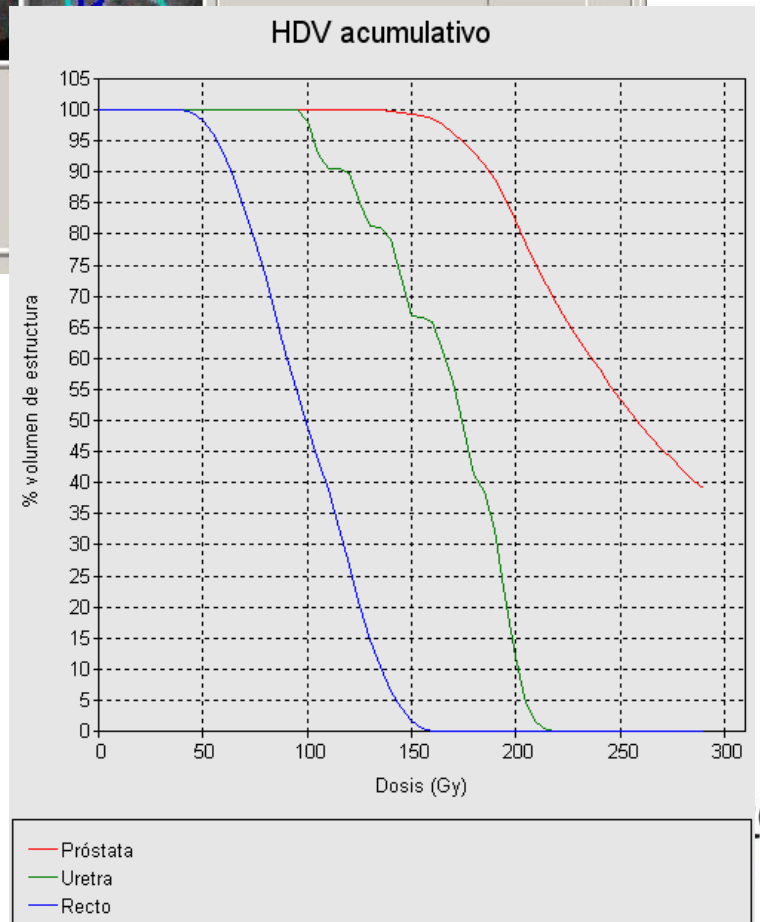
Prostate cancer US





145 Gy to prostate volume
D90: 181Gy ...250 Gy to 55%

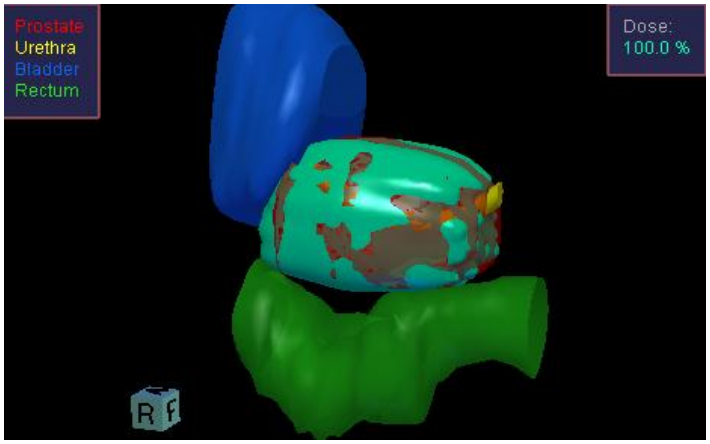




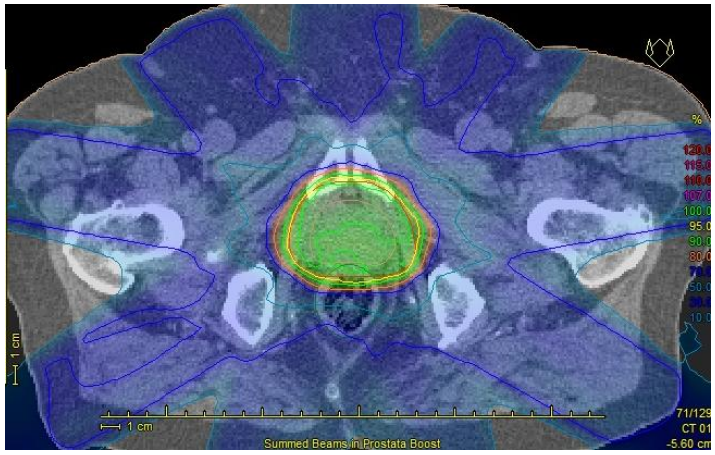
Dose Prescription: Aimed *vs* Planned or Given Dose

Prostate brachytherapy delivers a very high dose

BRT



EBRT



Aimed PD : 100% = 11,50Gy

	Brachytherapy		EBRT
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

Courtesy of Dimos Baltas

ESTRO School

Reporting Parameters for prostate brachy

- CTV: D90, V100, V150, V200
- OAR: Rectum D2cc, D0.1cc
- OAR: Urethra D0.1cc, D10, D30

- Implant quality
- D90 >100%
- V100 CTV >95% of the planning aim dose
- V150 ≤ 50% of the CTV

Radiotherapy and Oncology 107 (2013) 325–332

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journal homepage: www.thegreenjournal.com

GEC/ESTRO recommendations

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]

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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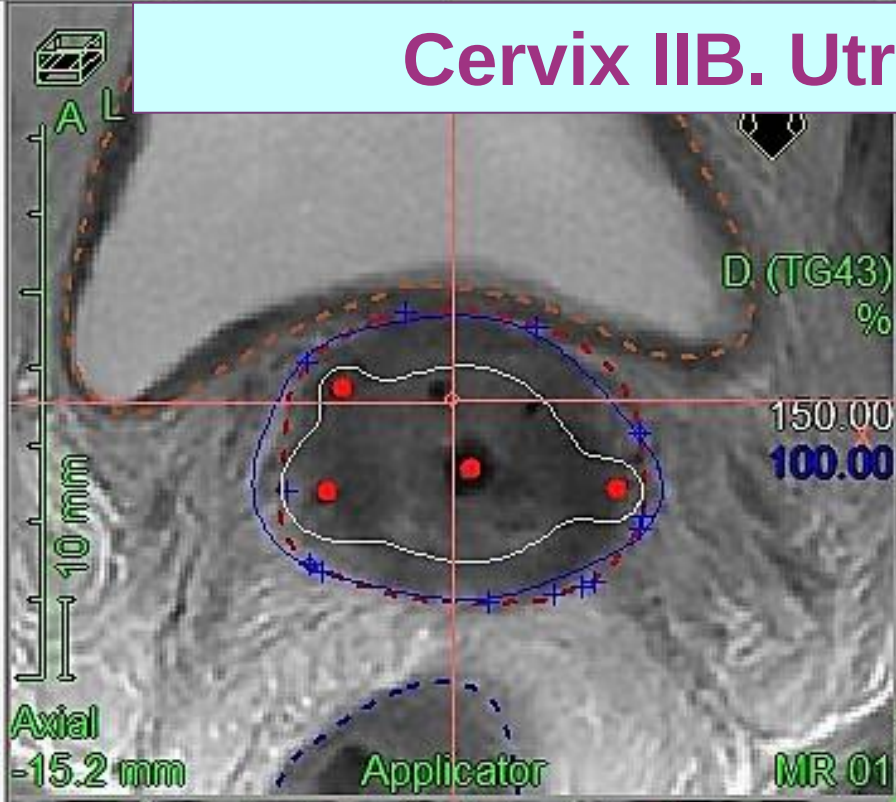
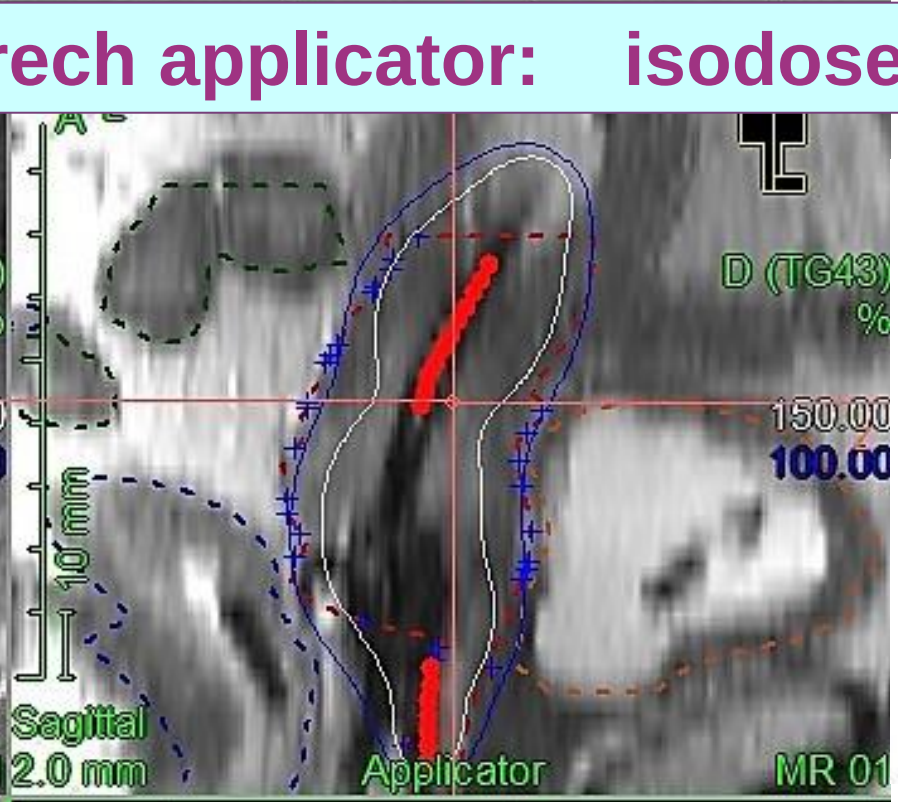
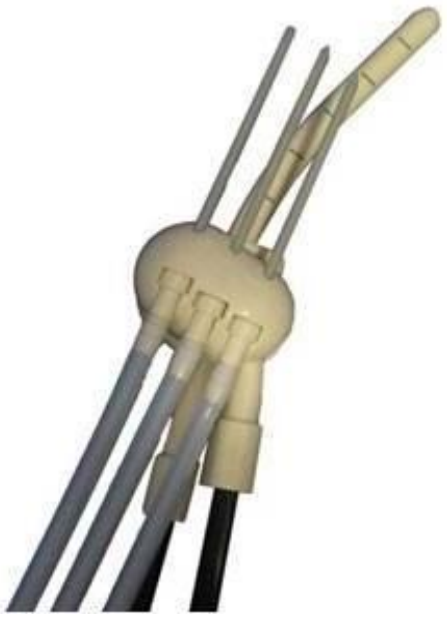
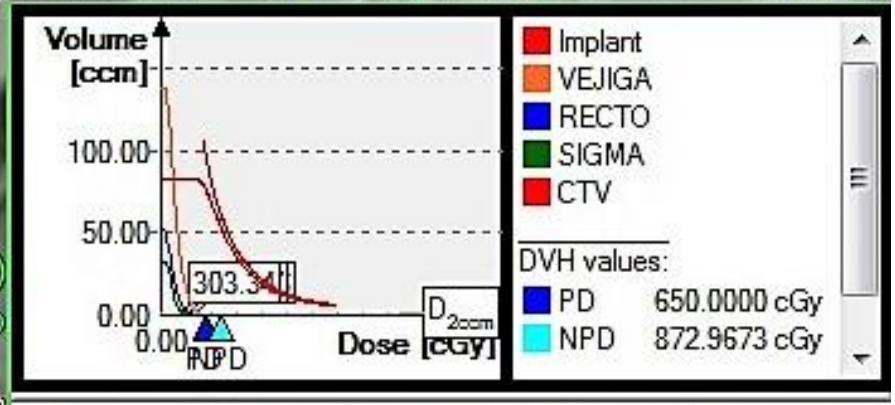
Cervix IIB. Utrech applicator: isodoses









ROI	Dose [%]	Dose [cGy]	Volume...	Volume [...
CTV	104.02	676.13	**90.00**	74.07
Implant	**100.00**	650.00	-	97.53
Implant	**150.00**	975.00	-	50.29
RECTO	59.61	387.47	3.87	**2.00**
SIGMA	46.67	303.34	6.29	**2.00**
VEJIGA	79.44	516.36	1.45	**2.00**

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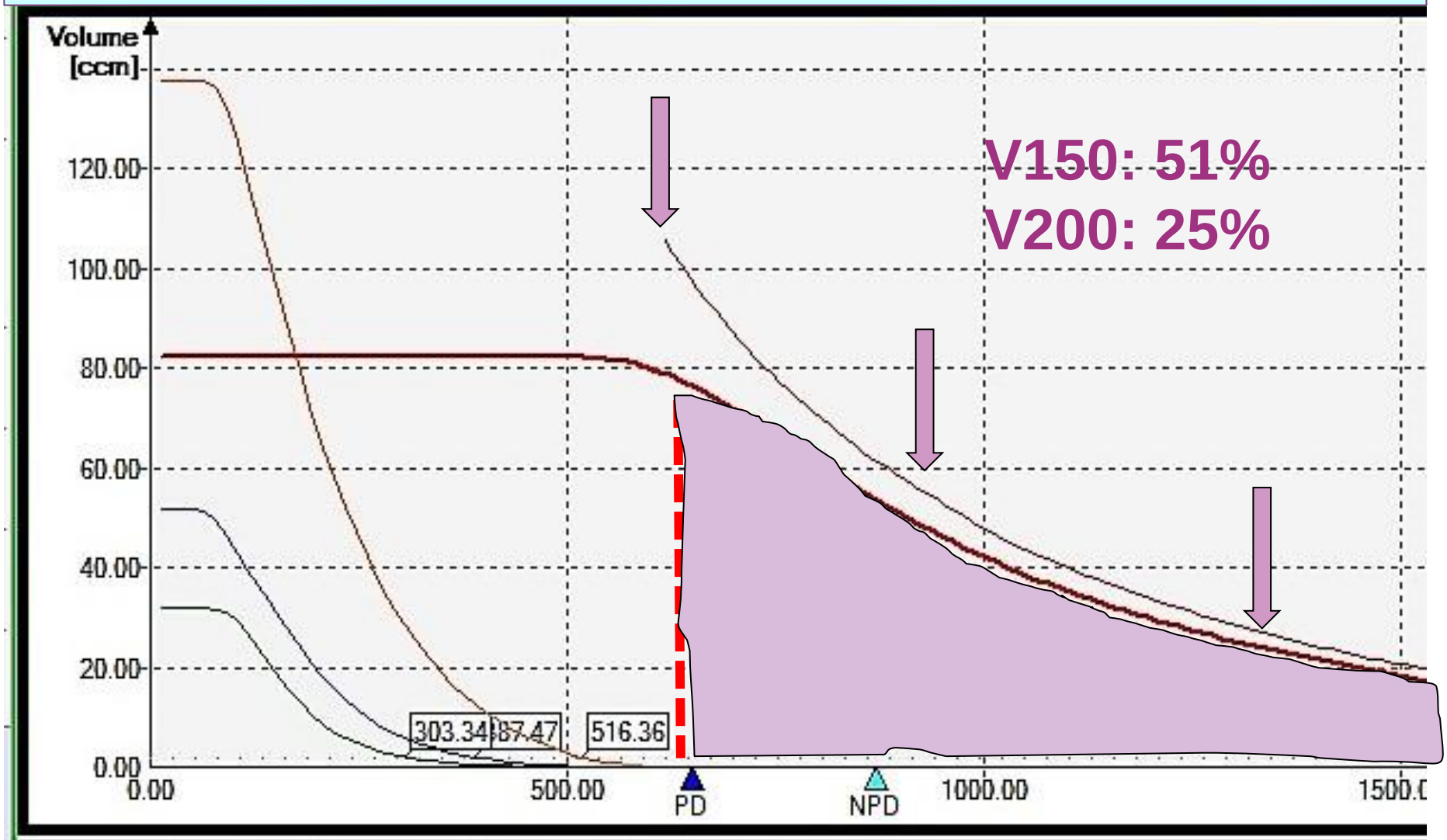
Cervix IIB. Utrech applicator: cumulative DVH



ROI	Dose [%]	Dose [cGy]	Volume...	Volume [...
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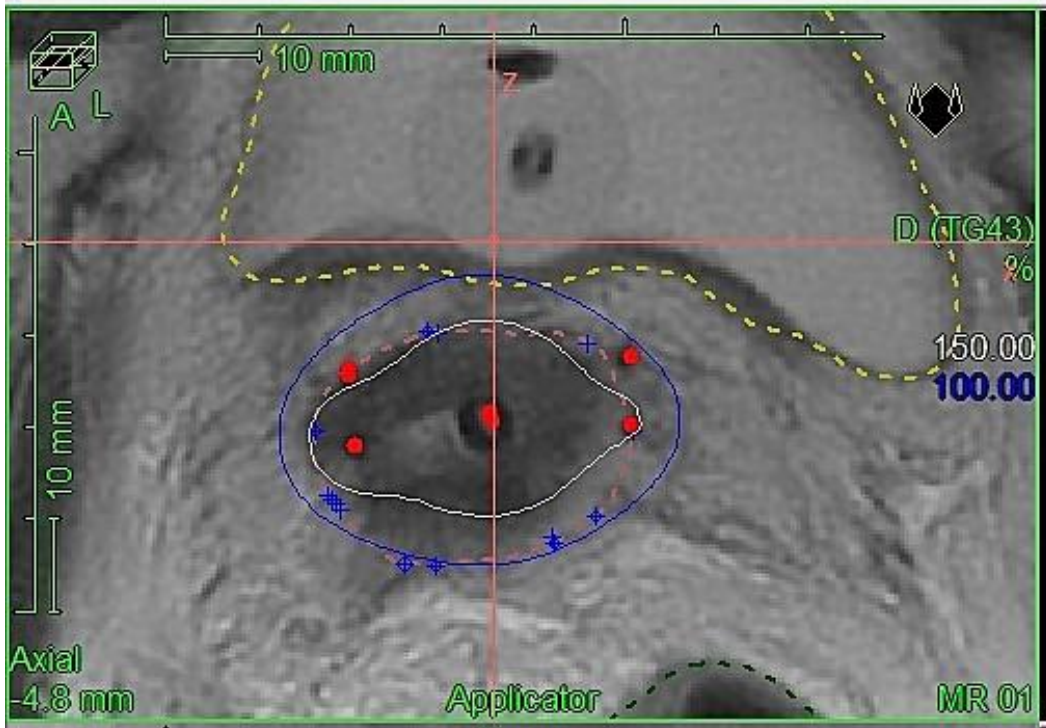
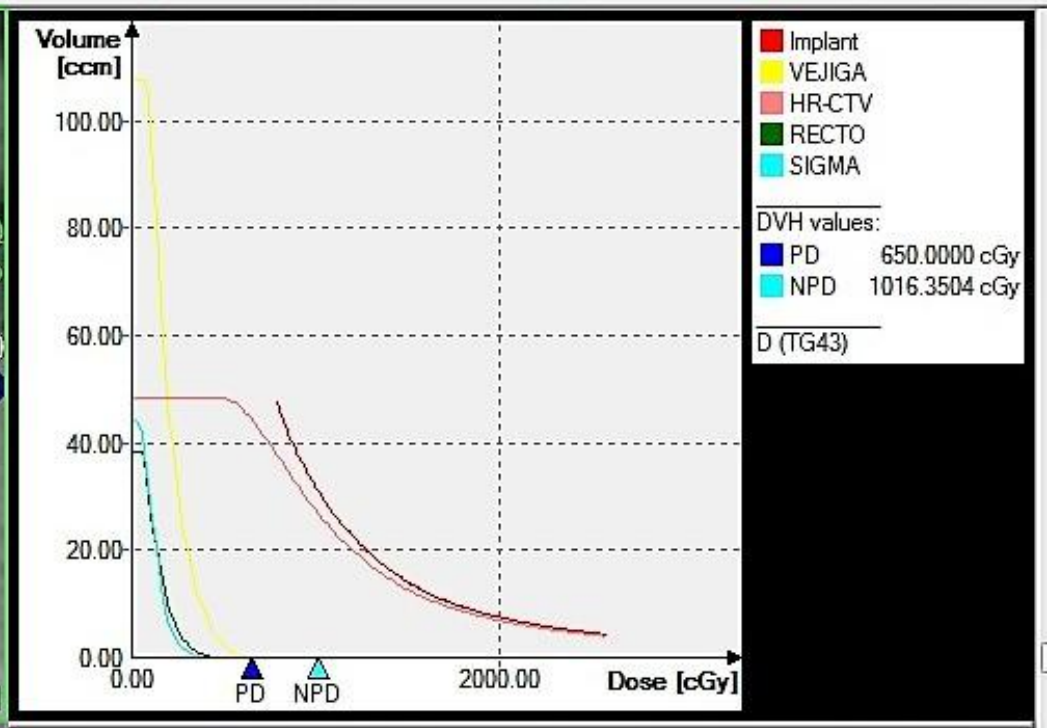
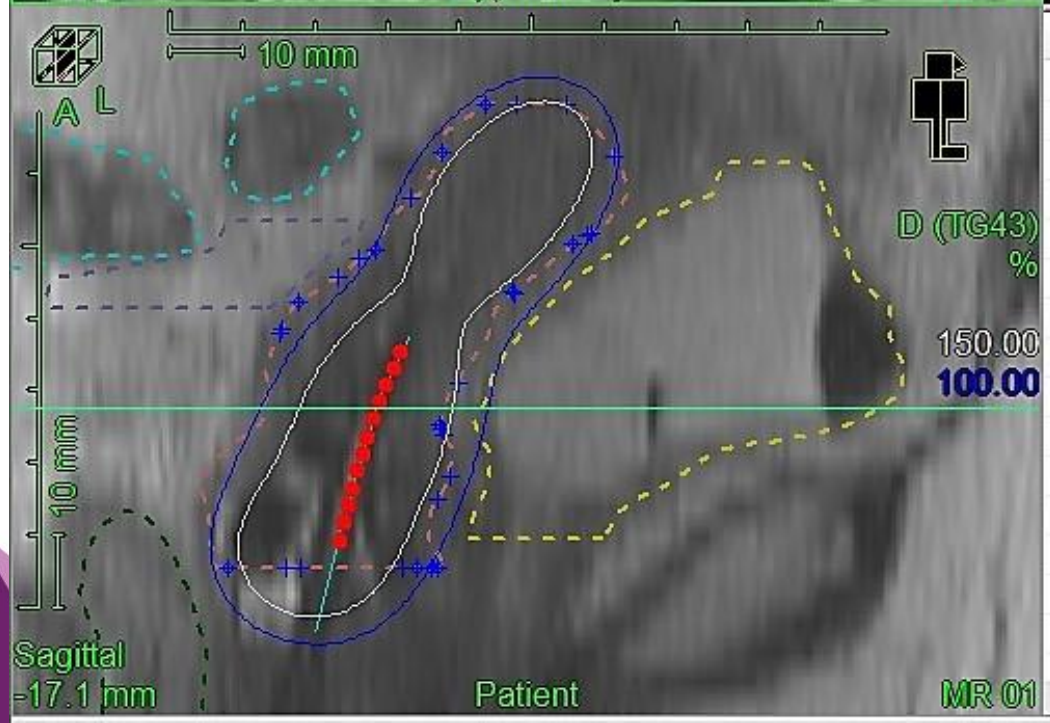
SIGMA	46.67	303.34	6.29	**2.00**
VEJIGA	79.44	516.36	1.45	**2.00**

V150= 9.75 x 4= EQD2 65Gy
V200= 13Gy x4= EQD2 100 Gy

Cervix IIB. Utrech applicator: D90 D98





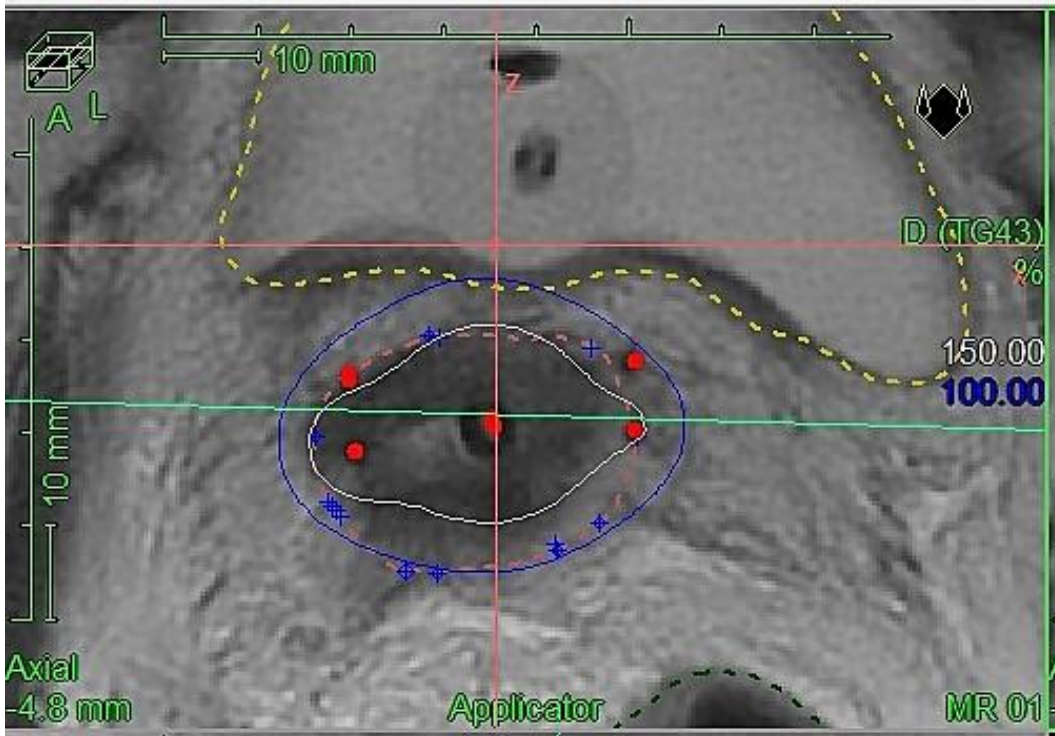


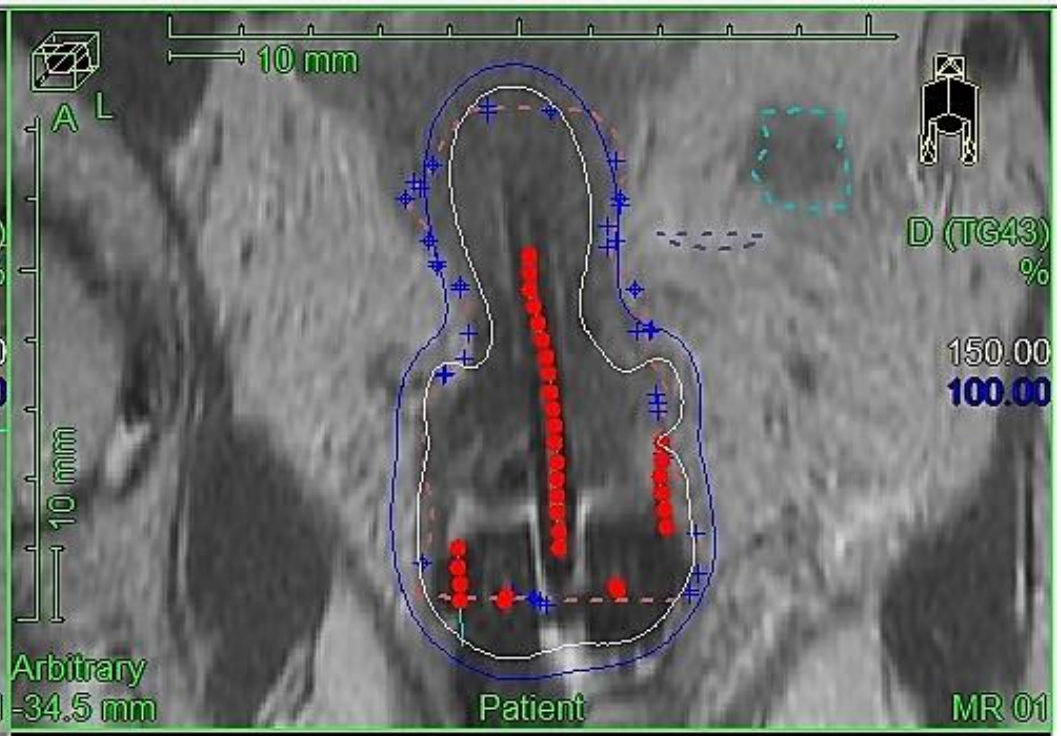
ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
HR-CTV	102.61	666.99	**90.00**	43.70
HR-CTV	85.16	553.54	**98.00**	47.58
RECTO	56.71	368.63	**2.00**	0.77
SIGMA	47.75	310.40	**2.00**	0.88
VEJIGA	77.45	503.45	**2.00**	2.15

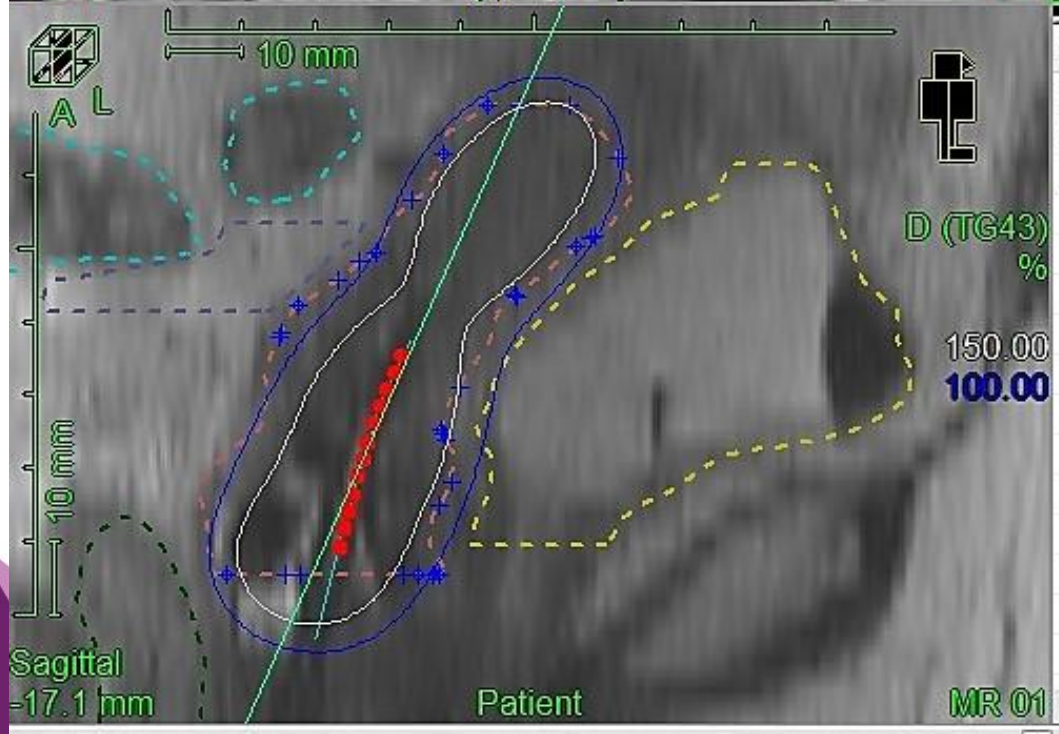
D90: 102%

D98: 85%

Cervix IIB. Utrech applicator: isodoses







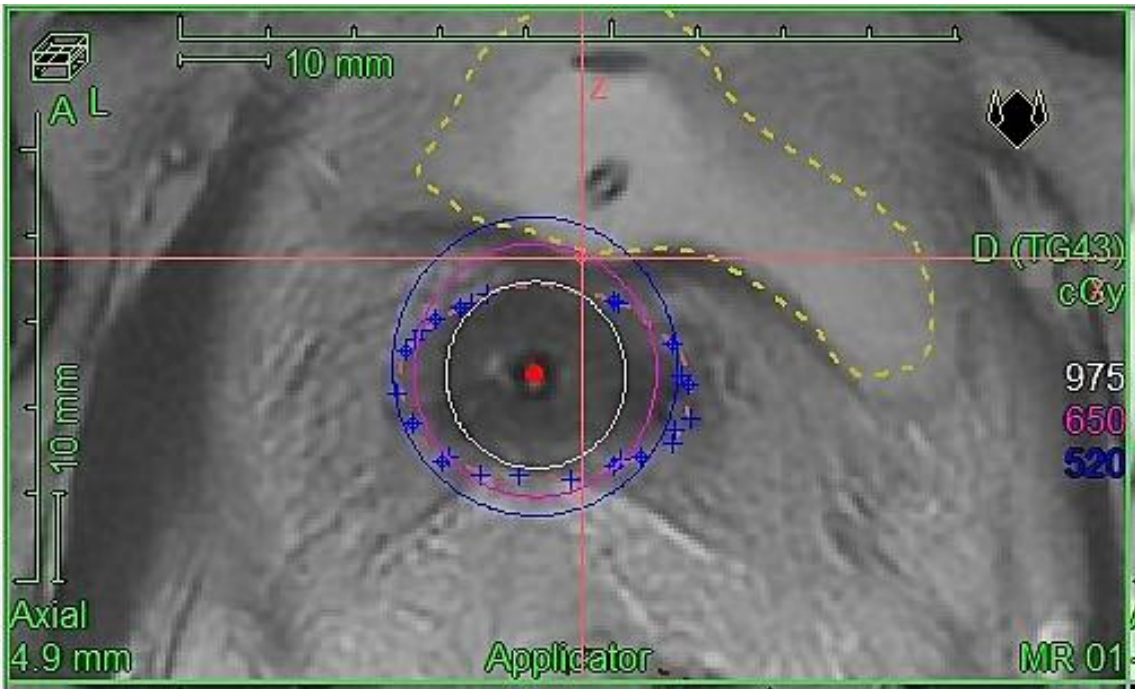
ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
External	**100.00**	650.00	1.08	65.09
External	**150.00**	975.00	0.56	33.88
External	**200.00**	1300.00	0.32	19.54

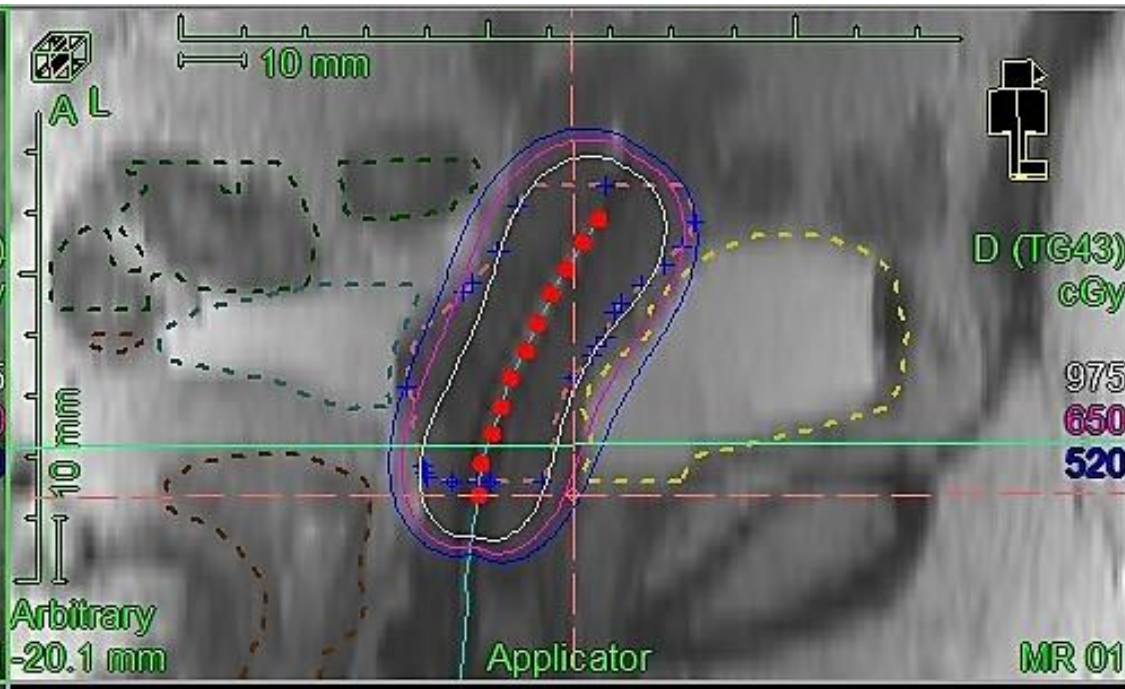
DNR= 0.52

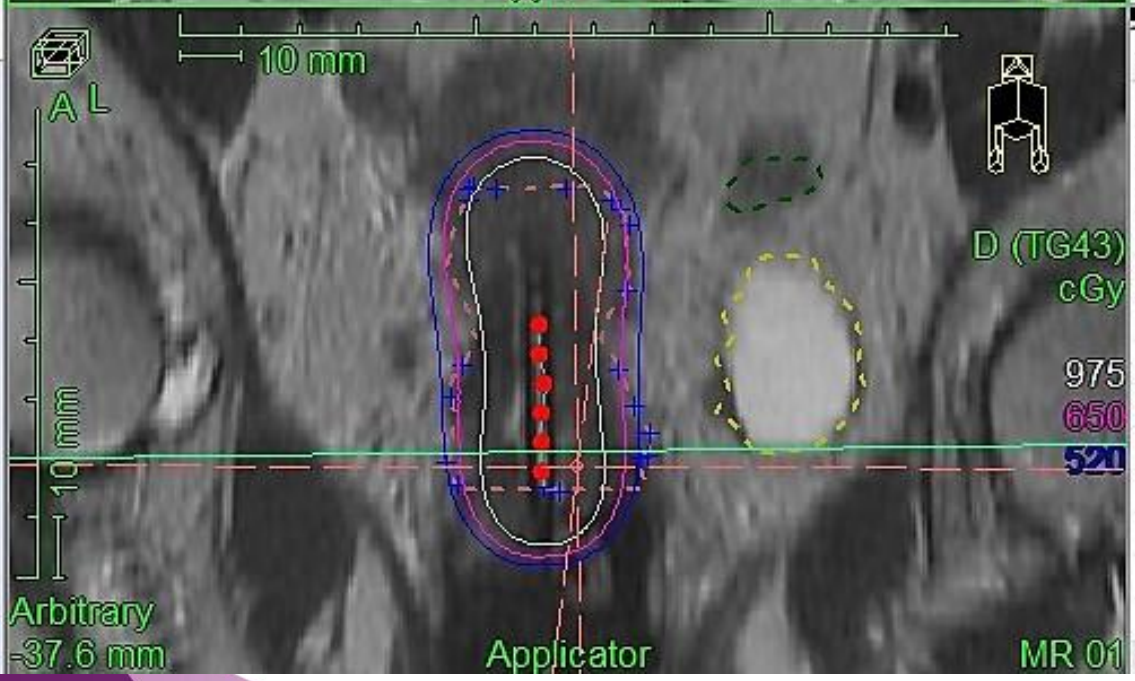
V150= 52%

V200= 30%

Cervix IIB. TANDEM applicator: isodoses







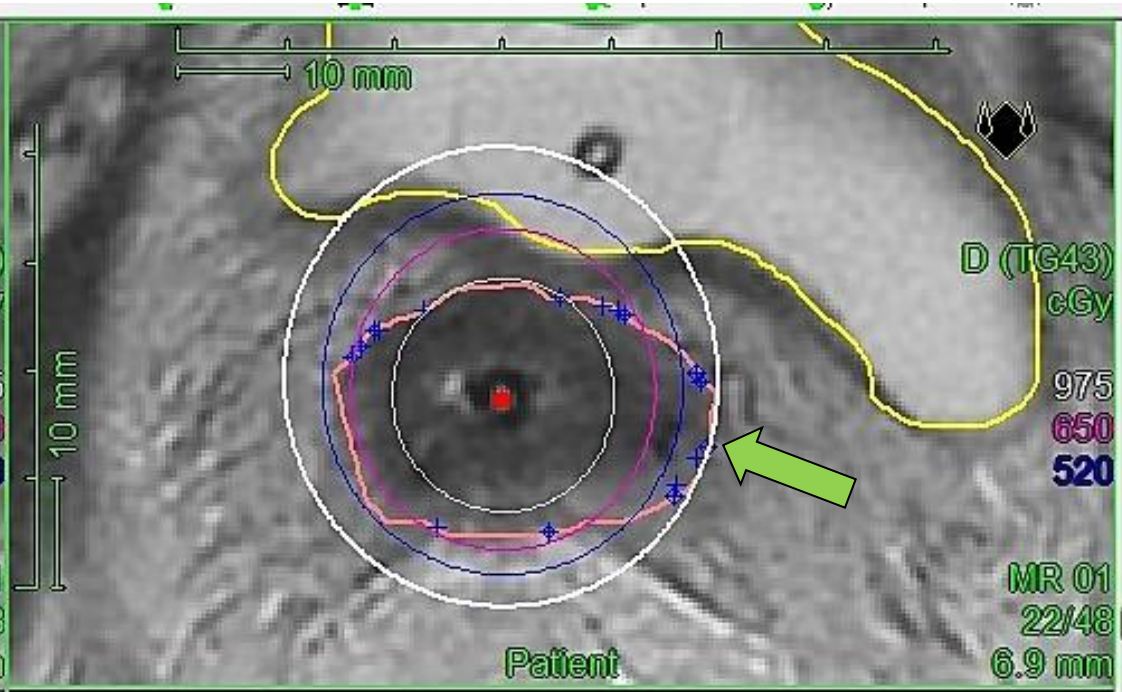
ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
External	**100.00**	650.00	0.48	43.98
External	**150.00**	975.00	0.27	24.31
External	**200.00**	1300.00	0.17	15.57

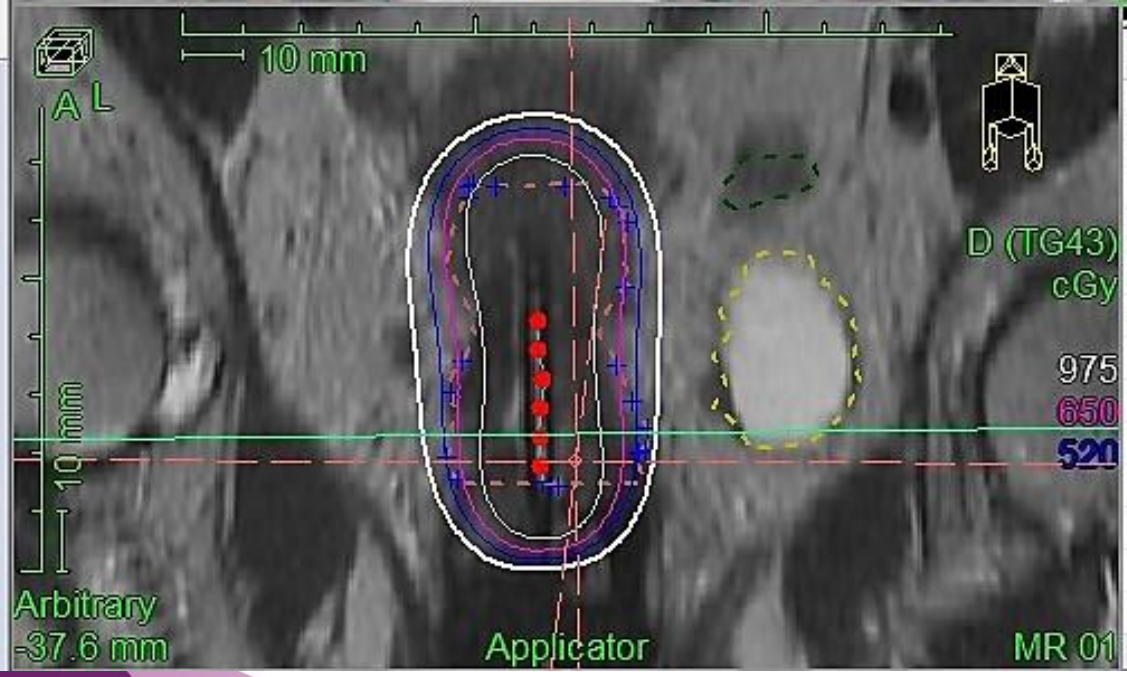
DNR= 0.55

V150 = 55%

V200 = 35%

Cervix IIB. TANDEM applicator: isodoses





ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
HR-CTV	66.65	433.24	**100.00**	29.99
HR-CTV	97.57	634.22	**90.00**	26.99
HR-CTV	79.46	516.47	**98.00**	29.39
RECTO	36.90	239.84	**2.00**	0.66
SIGMA	46.41	301.64	**2.00**	0.65
VEJIGA	81.63	530.60	**2.00**	2.07

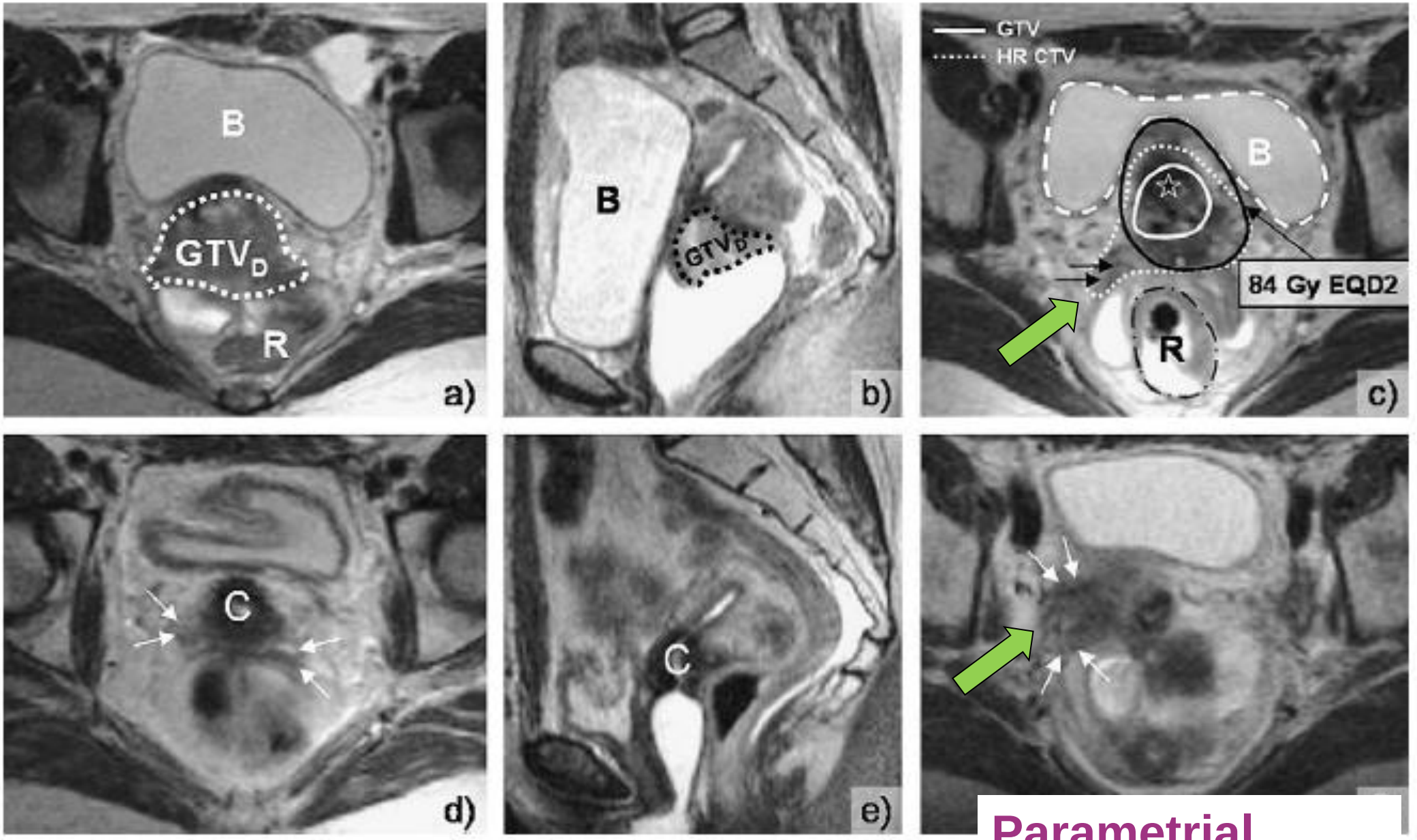
D90: 97.5%

D98: 79.5%

4Gy x 4 = EQD2 18.7Gy

initial tumour GTV

isodoses



complete response at 6 months

Parametrial recurrence at 9m

Dimopoulos J, et al

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 1, pp. 56–63, 2009

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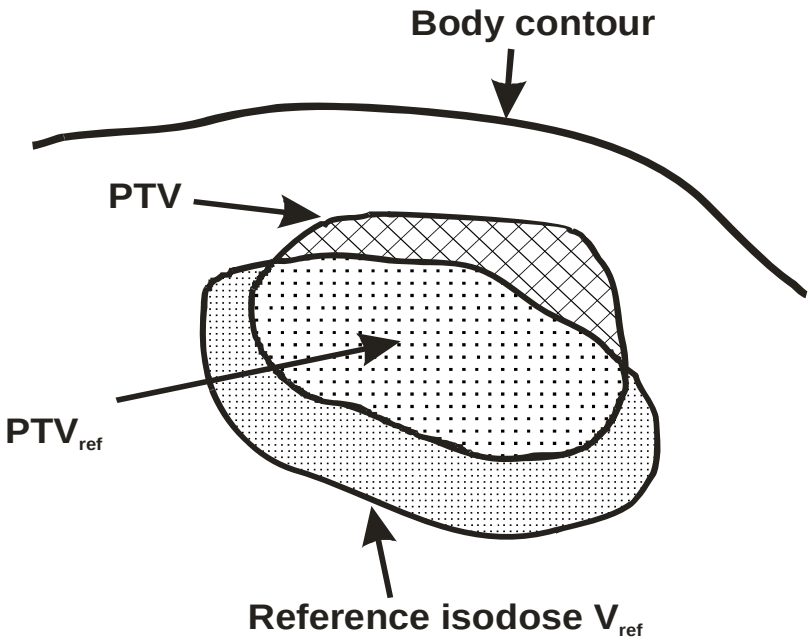
CONFORMITY PARAMETERS

- Conformal Index COIN

How well fits the 3D shape of D_{ref} the target volume PTV



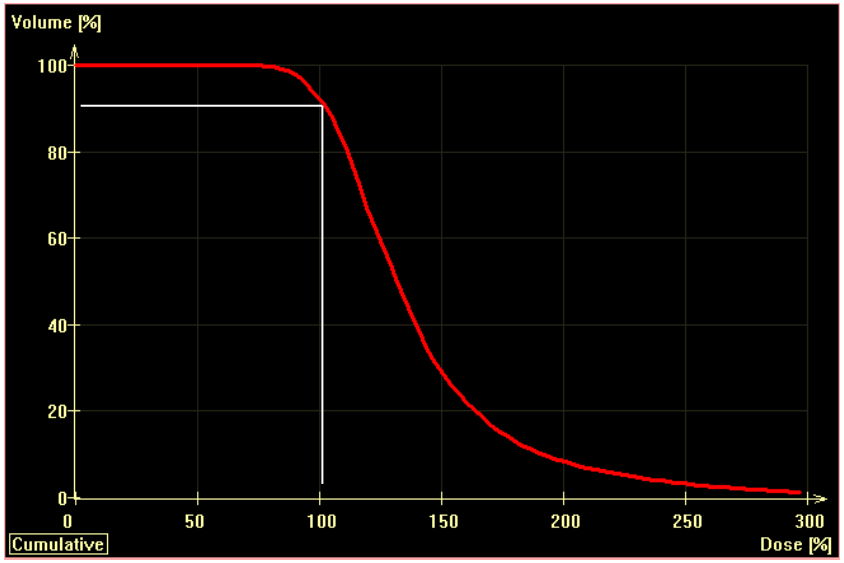
COIN = c_1 x c_2

$$c_1 = \frac{PTV_{ref}}{PTV} \qquad c_2 = \frac{PTV_{ref}}{V_{ref}}$$

- Coverage Index CI

Fraction of the target volume receiving a dose equal or greater than the reference dose (100%)

$CI = V_{100} /100$



It is variable, depending on the shape of the target / PTV

Courtesy of Dimos Baltas

Baltas D, Kolotas C et al. *Int J Rad Oncol Biol Phys* 40, 512-524, 1998

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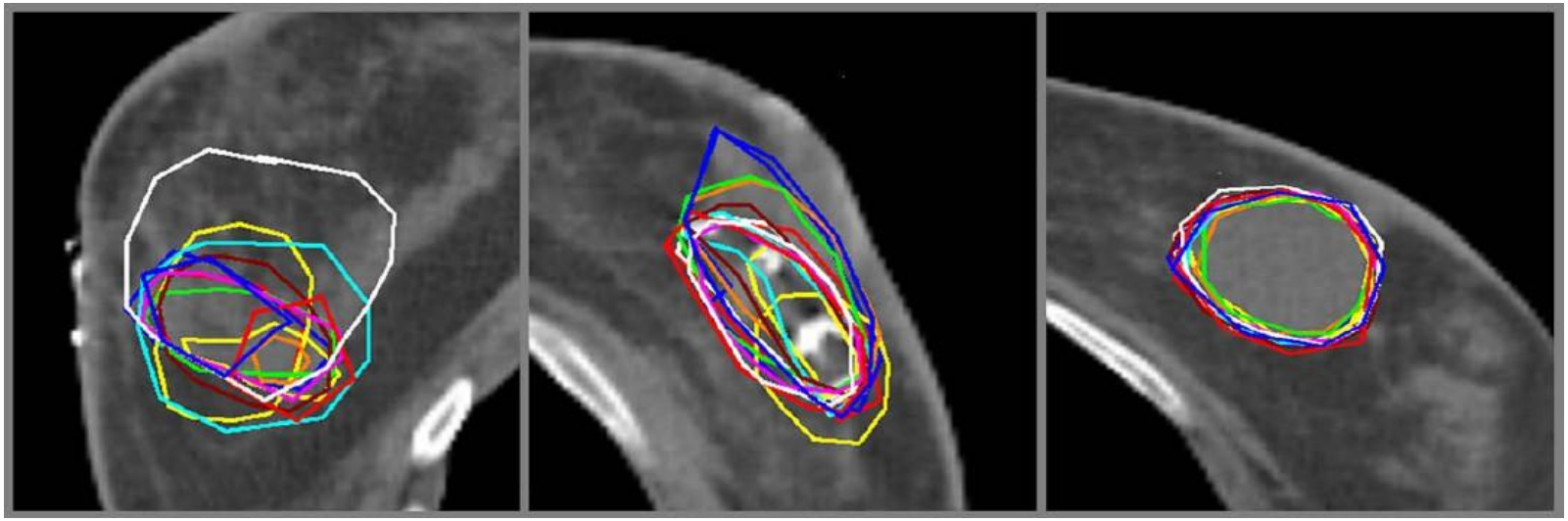
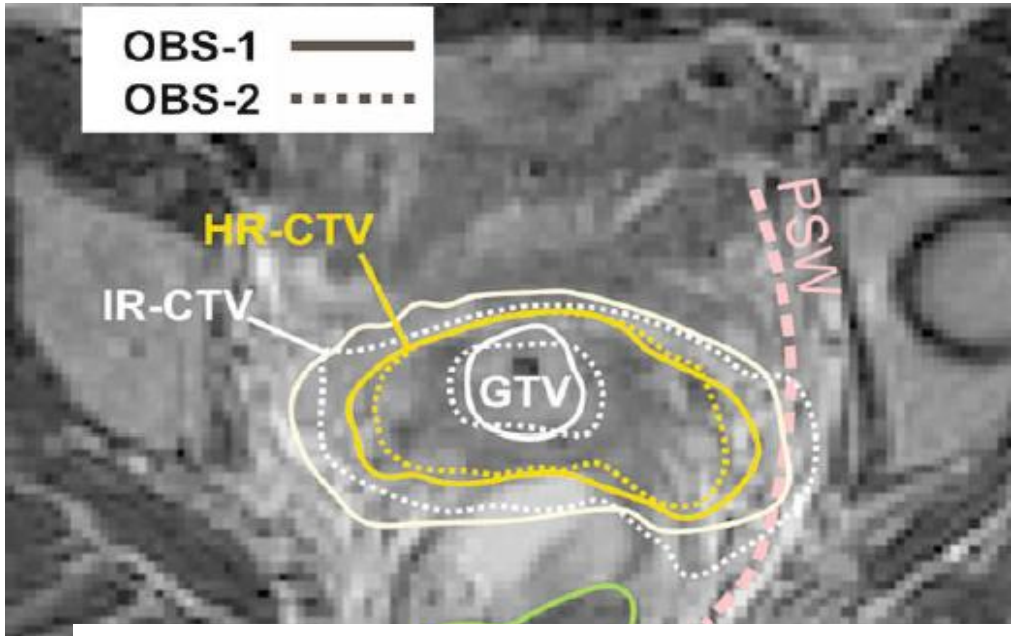
CAN WE PROPERLY DRAW THE RIGHT VOLUME FOR DOSE PRESCRIPTION?



Van Mourik AM et al. Multiinstitutional study on target volume delineation variation in breast radiotherapy in the presence of guidelines. Radiother Oncol 2010; 94:286–291

Inter-observer comparison of target delineation

Parameters based on the CTV are always subjective. Parameters based on the catheters are independent of the observer.



Dimopoulos J, et al Radiotherapy and Oncology 91 (2009) 166–172

Dose Volume Histograms in Brachytherapy:

Based on the catheters (IMPLANT)

- Cumulative DVH
- Differential DVH
- Natural DVH

Based on the anatomy (TARGET/CTV/OAR)

(Requires 3d imaging CT/MR/US)

- Cumulative DVH in CTV
- **Cumulative DVH in OAR**

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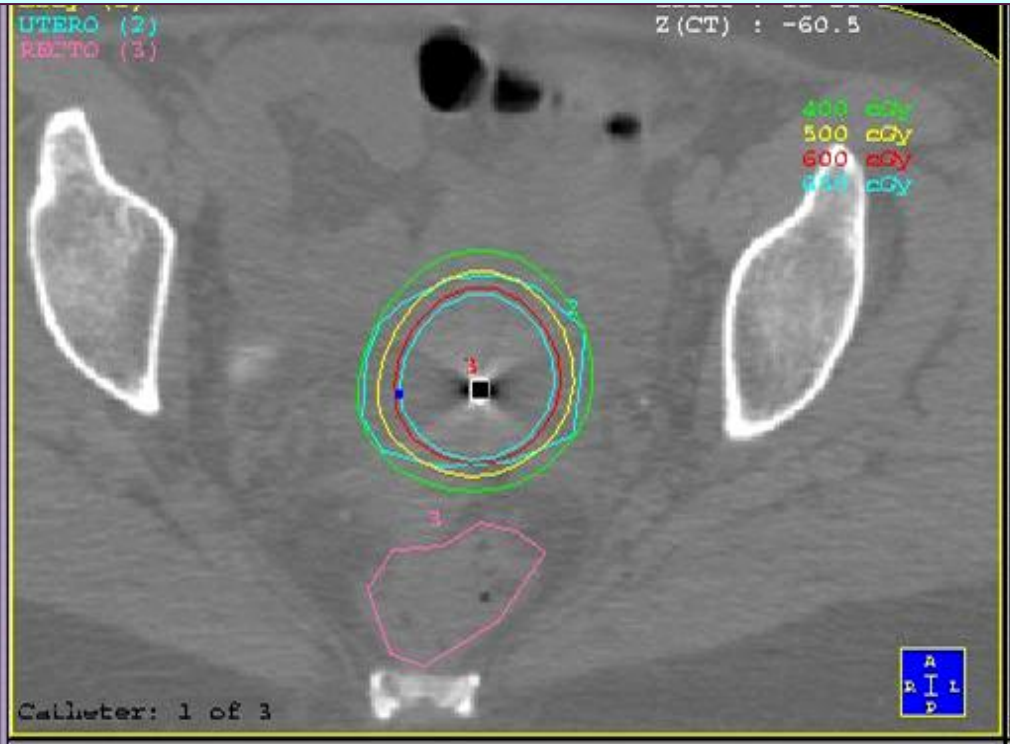
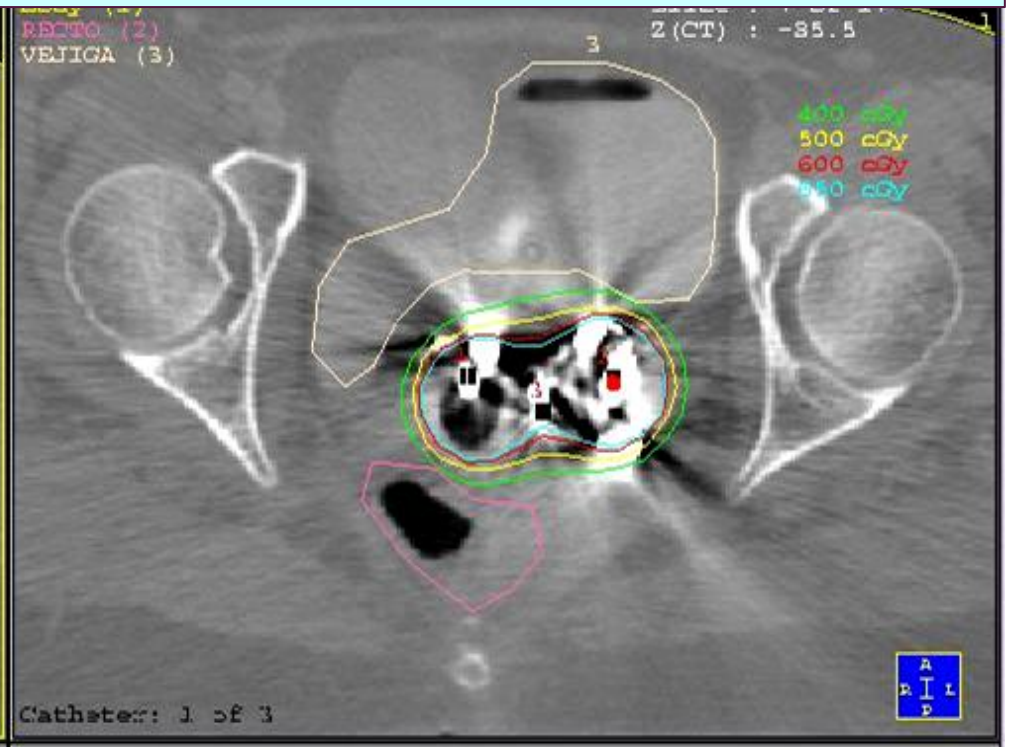
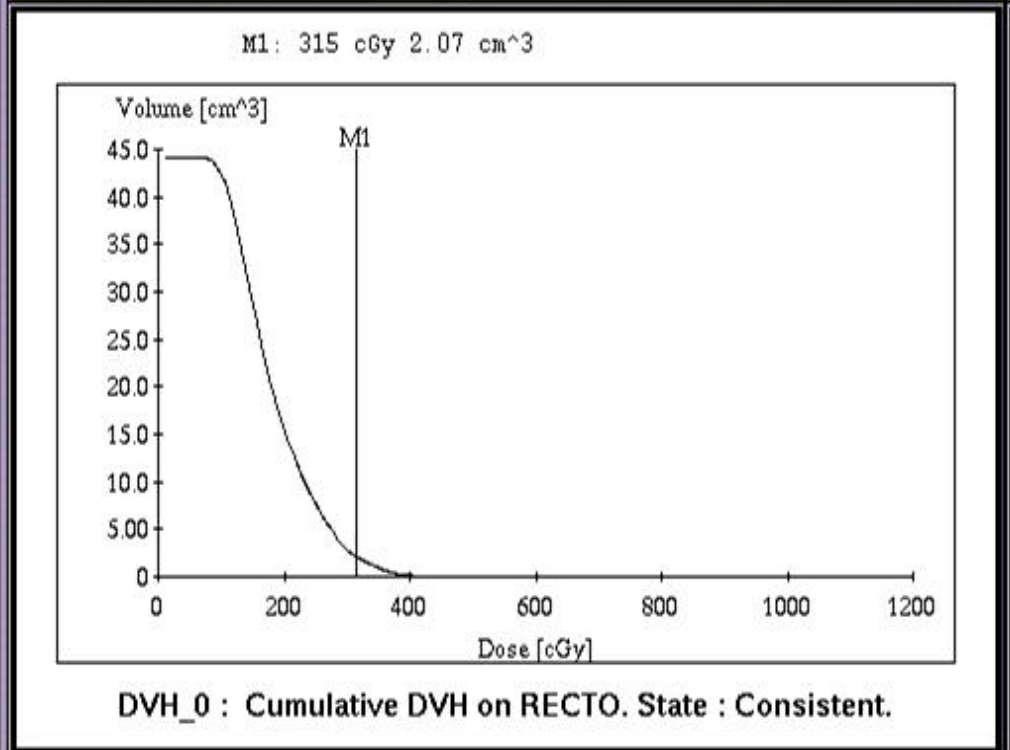
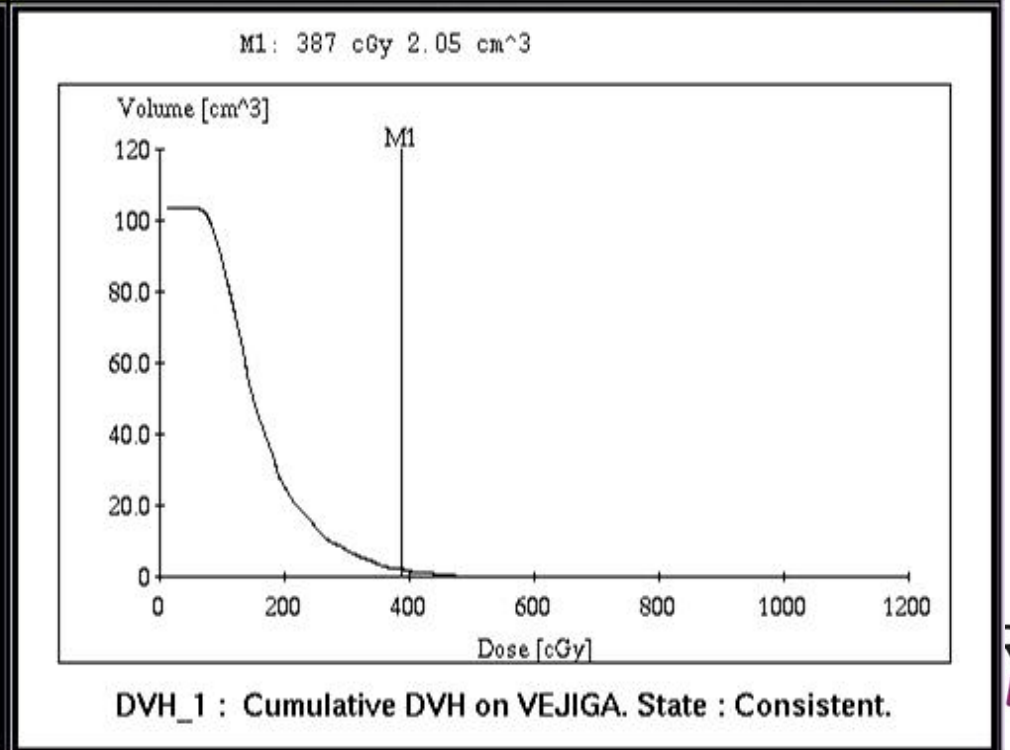
CUMULATIVE DVH FOR ORGANS AT RISK IN CERVIX







DVH_0 : Cumulative DVH on RECTO. State : Consistent.



DVH_1 : Cumulative DVH on VEJIGA. State : Consistent.

ORGANS AT RISK IN CERVIX

O.A.R. Alfa/beta 2.5-3

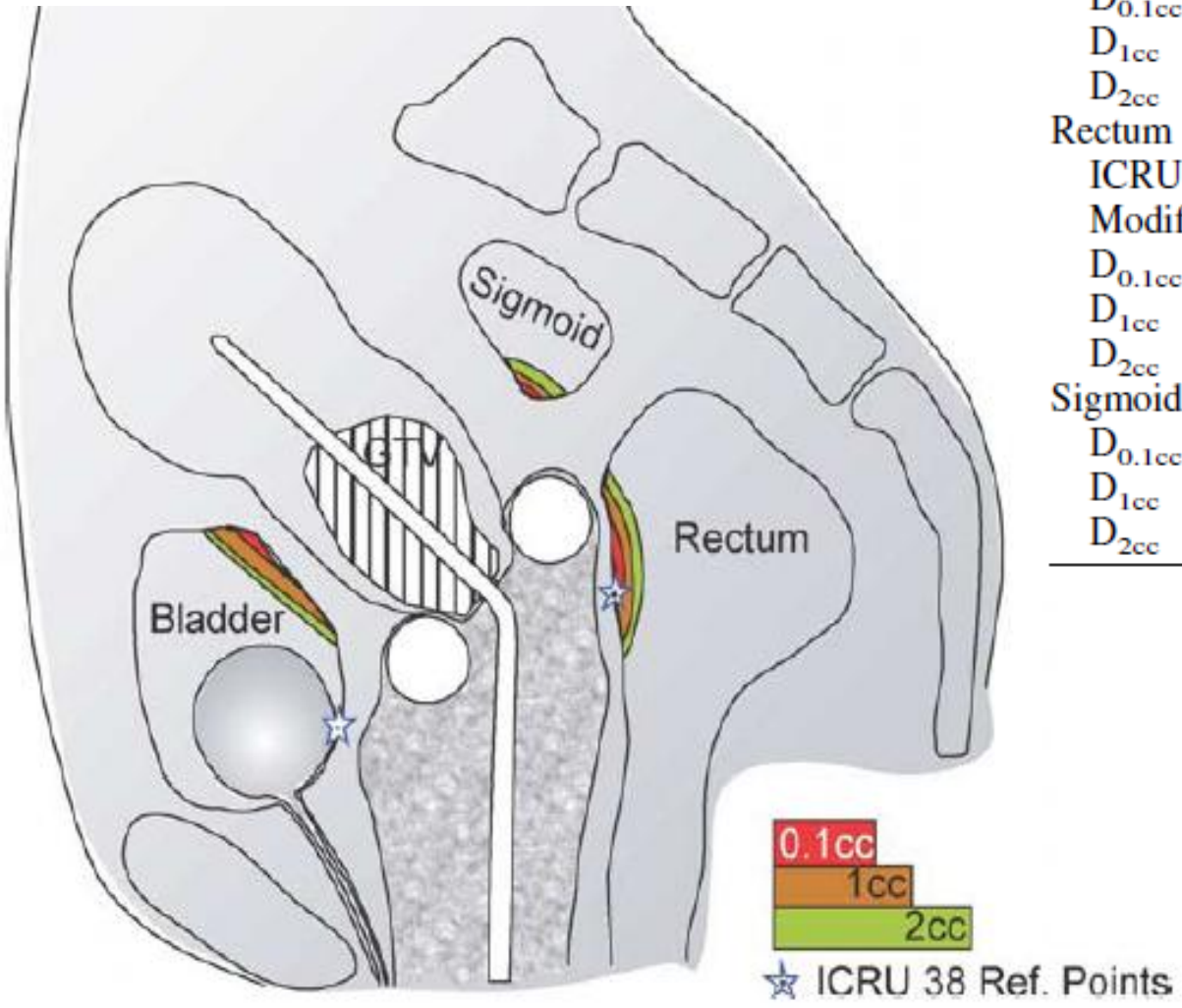


Table 2. Results for organs at risk

Parameter	Mean value ± 1 SD
Bladder	
ICRU point	73 ± 19 $Gy_{\alpha\beta3}$
1.5 cm cranially to ICRU point	92 ± 47 $Gy_{\alpha\beta3}$
$D_{0.1cc}$	113 ± 30 $Gy_{\alpha\beta3}$
D_{1cc}	90 ± 16 $Gy_{\alpha\beta3}$
D_{2cc}	83 ± 14 $Gy_{\alpha\beta3}$
Rectum	
ICRU point	71 ± 13 $Gy_{\alpha\beta3}$
Modified ICRU point shifted to probe	63 ± 9 $Gy_{\alpha\beta3}$
$D_{0.1cc}$	77 ± 9 $Gy_{\alpha\beta3}$
D_{1cc}	69 ± 6 $Gy_{\alpha\beta3}$
D_{2cc}	66 ± 6 $Gy_{\alpha\beta3}$
Sigmoid	
$D_{0.1cc}$	85 ± 14 $Gy_{\alpha\beta3}$
D_{1cc}	71 ± 8 $Gy_{\alpha\beta3}$
D_{2cc}	67 ± 7 $Gy_{\alpha\beta3}$

- **Doses in EQD2 to 2cc of organs at risk:**
- **Bladder: 85- 90 Gy**
- **Rectum 75 Gy**
- **Sigmoid 75 Gy**

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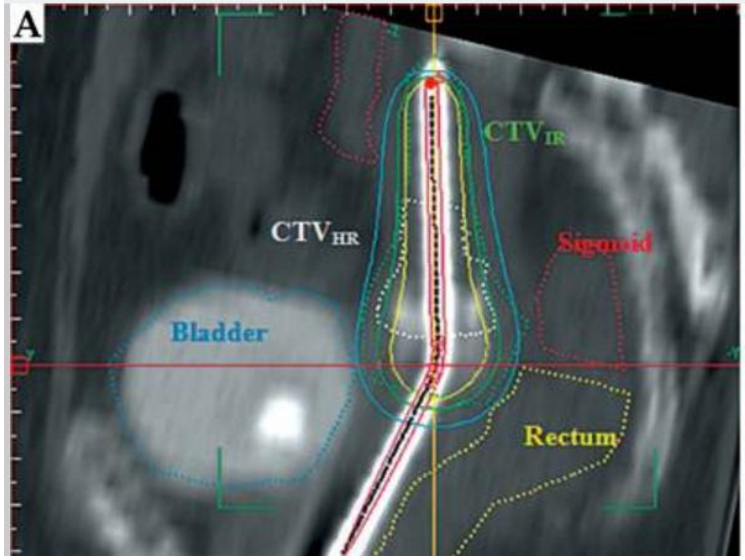
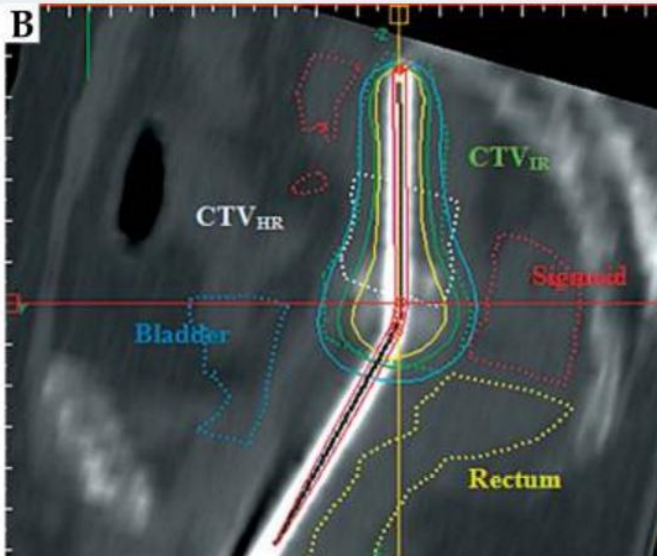
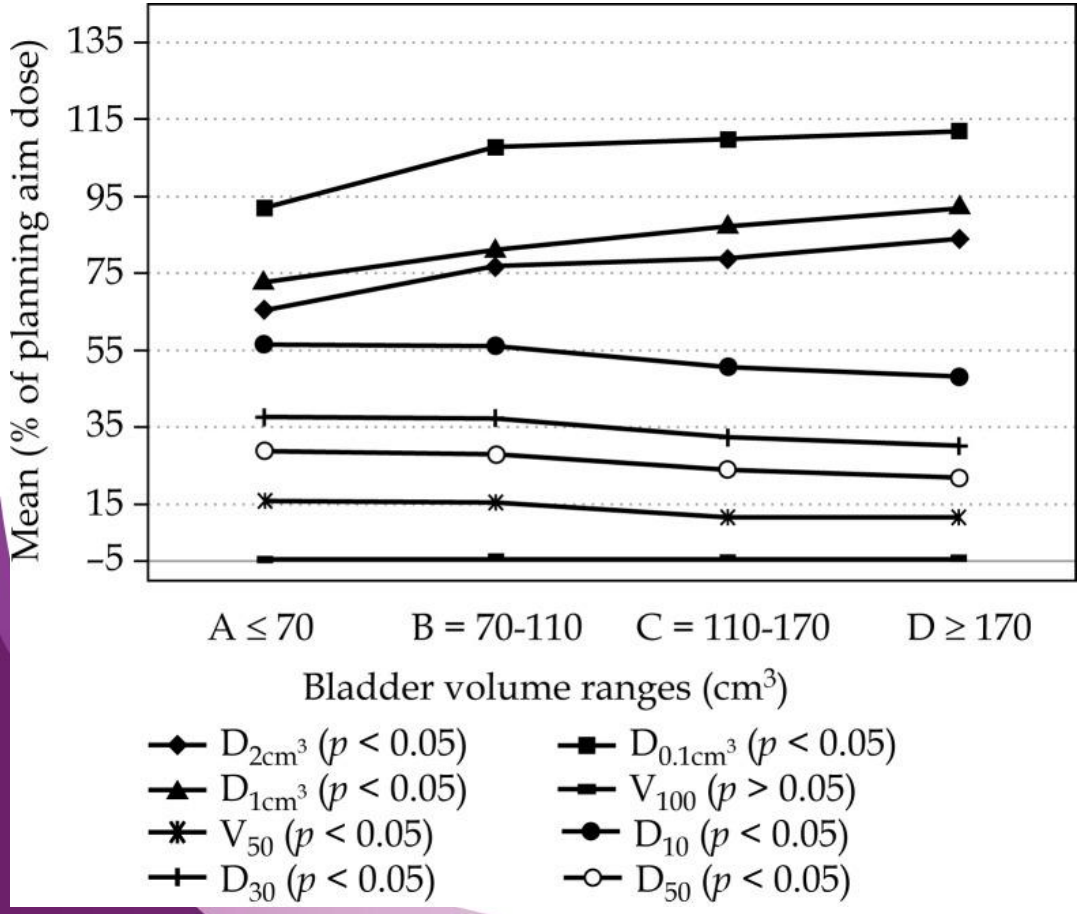
CUMULATIVE DVH FOR BLADDER IN CERVIX BRACHY







There is a relationship between the volumes of OARs and their received doses.
Selecting a bladder with a volume of about 70 cm3 or less proved to be better with regards to the dose to the bladder, rectum, and sigmoid.

Siavashpour Z, Aghamiri MR, Jaberi R et al. Optimum organ volume ranges for organs at risk dose in cervical cancer intracavitary brachytherapy. J Contemp Brachytherapy. 2016 Apr; 8(2): 135–142.

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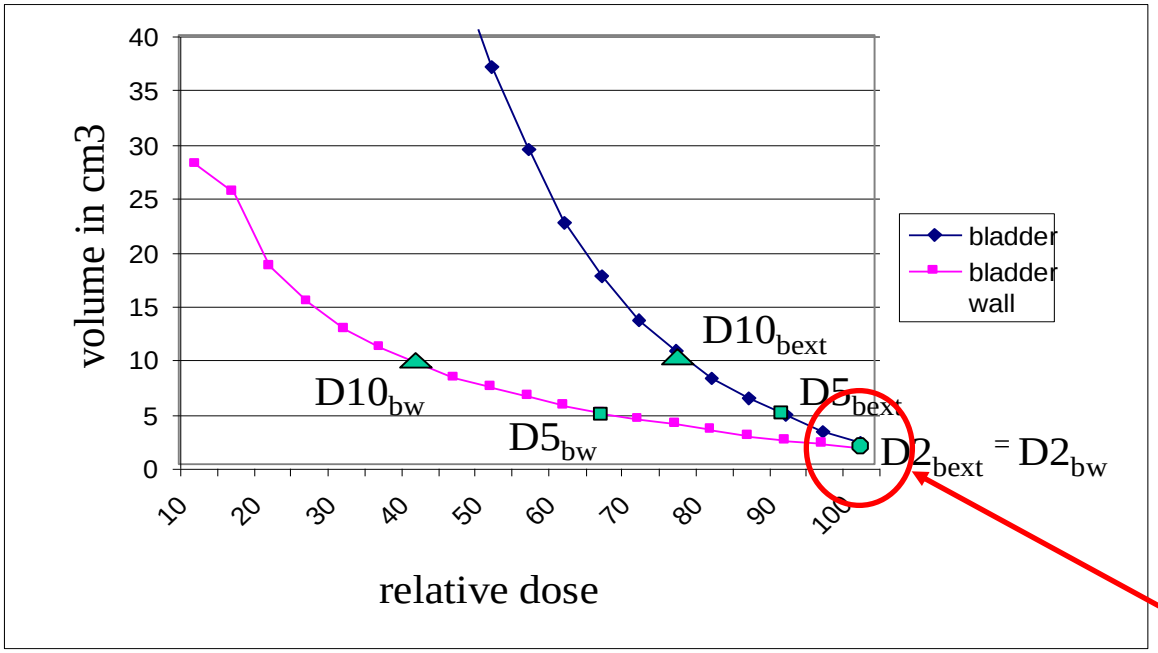
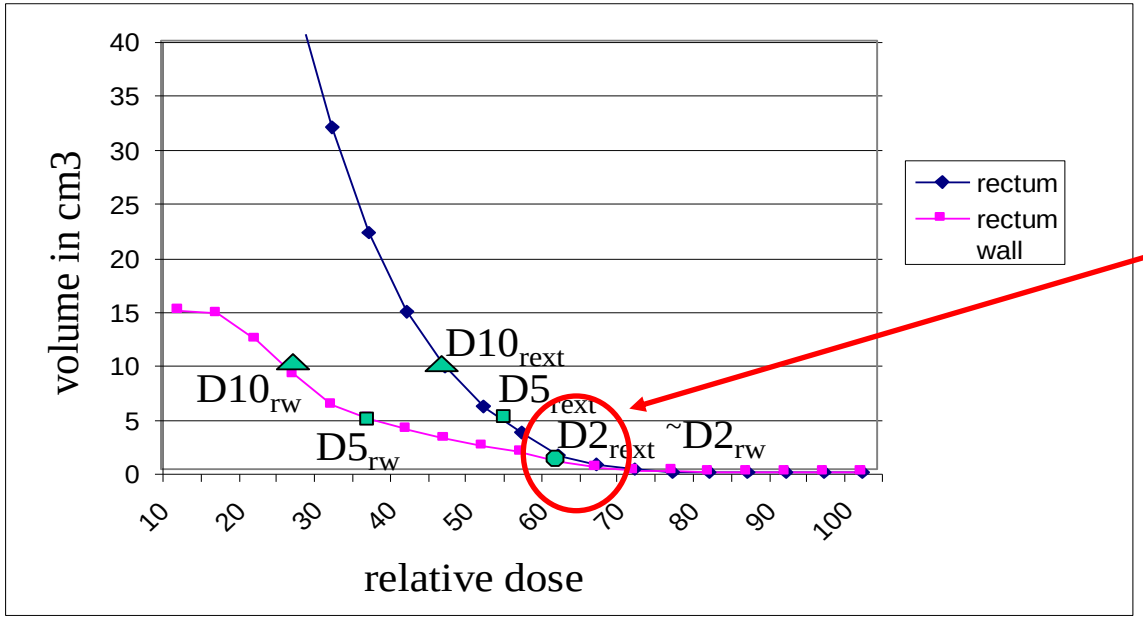
CUMULATIVE DVH FOR O.A.R. IN CERVIX BRACHY

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





Cut off -volume 2-3 ccm

Fig.1

Courtesy of Dimos Baltas

Wachter-Gerstner et al. R&O 2003)

School

Reporting Parameters for HDR cervix brachy

- Dose at point A
- CTV: D100, D90, for GTV, HR-CTV, IR-CTV
- OAR: D2cc, D1cc, D0.1cc
- OAR: Rectum, sigmoid, bladder

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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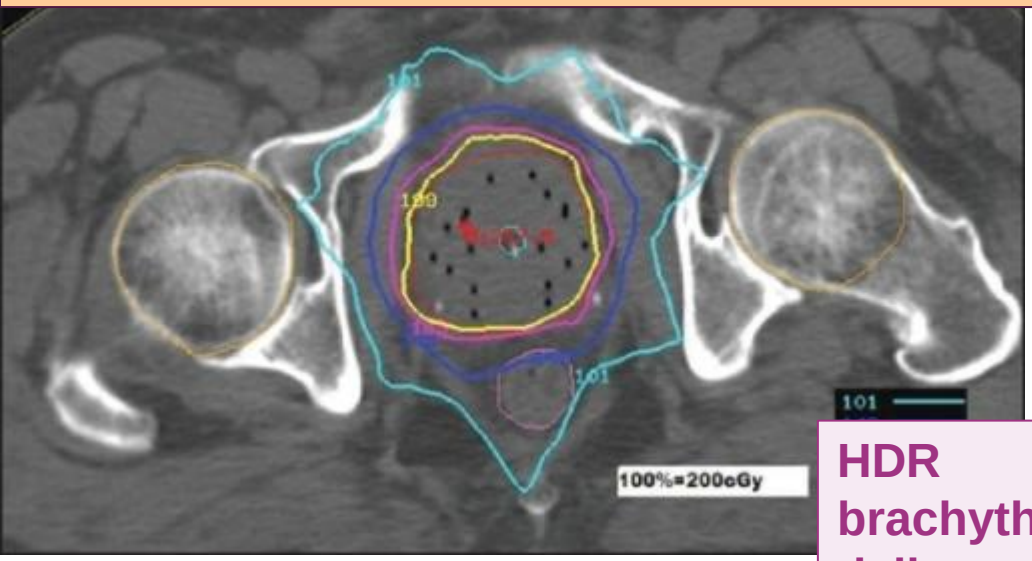
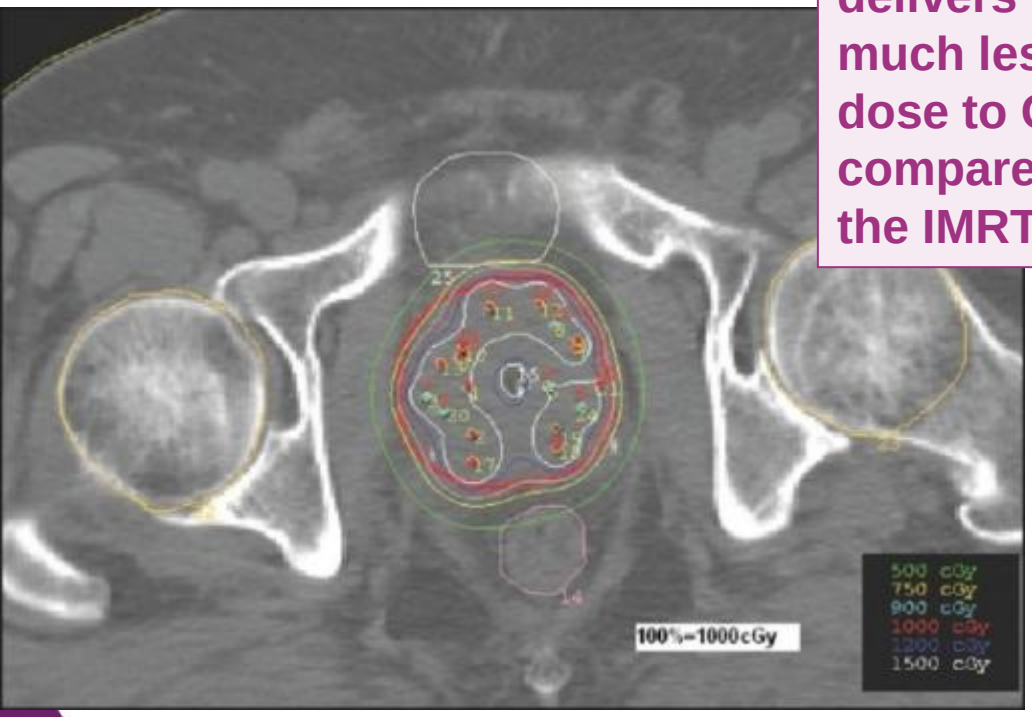
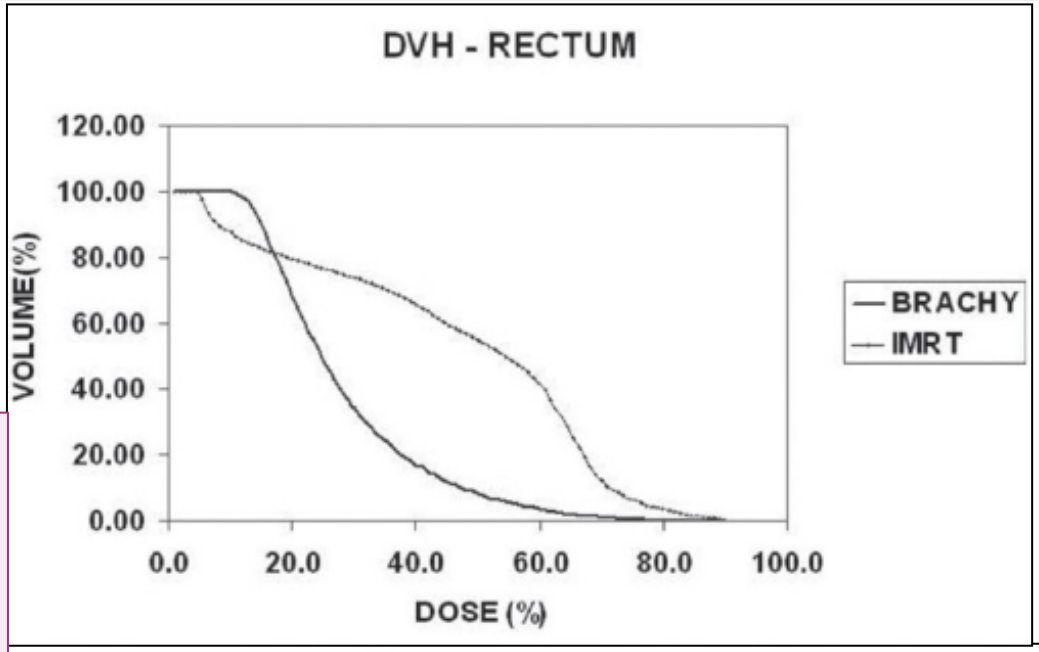
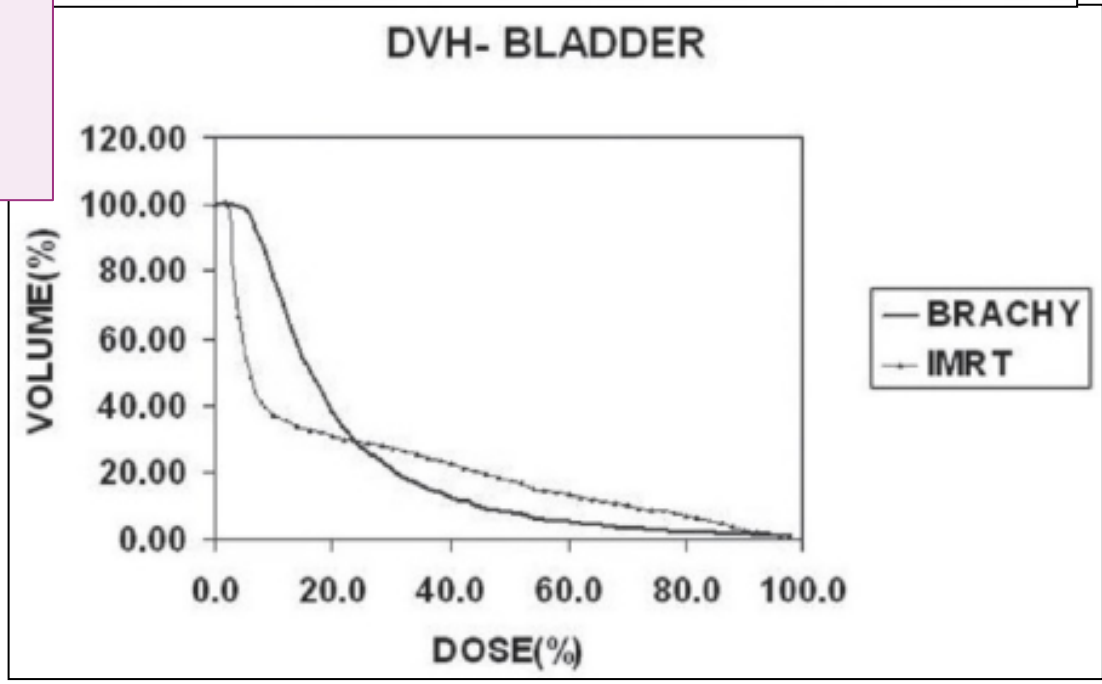
CUMULATIVE DVH FOR ORGANS AT RISK IN PROSTATE





HDR brachytherapy delivers a much lesser dose to OAR, compared to the IMRT.





Murali V, Kurup PG, Mahadev P, Mahalakshmi S. Dosimetric analysis and comparison of IMRT and HDR brachytherapy in treatment of localized prostate cancer. J Med Phys (2010)

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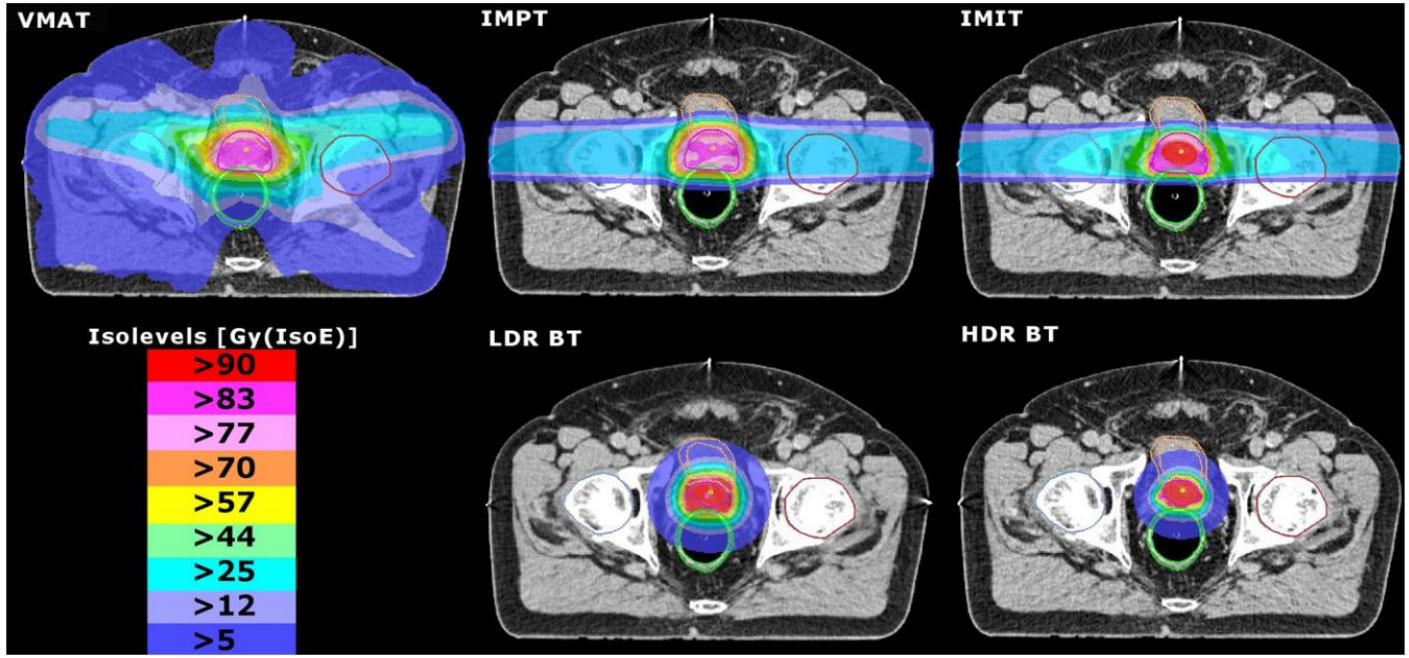
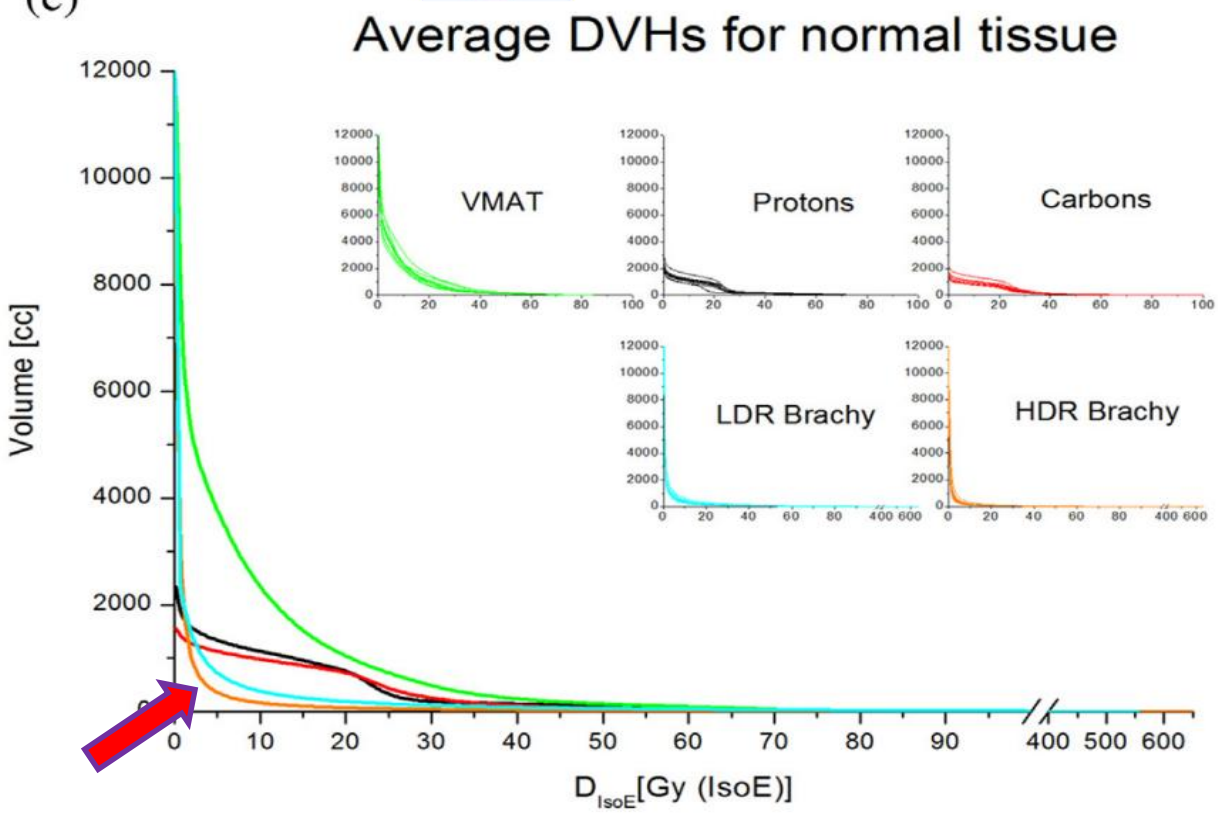
Dosimetric advantages of brachytherapy IN PROSTATE



(c)



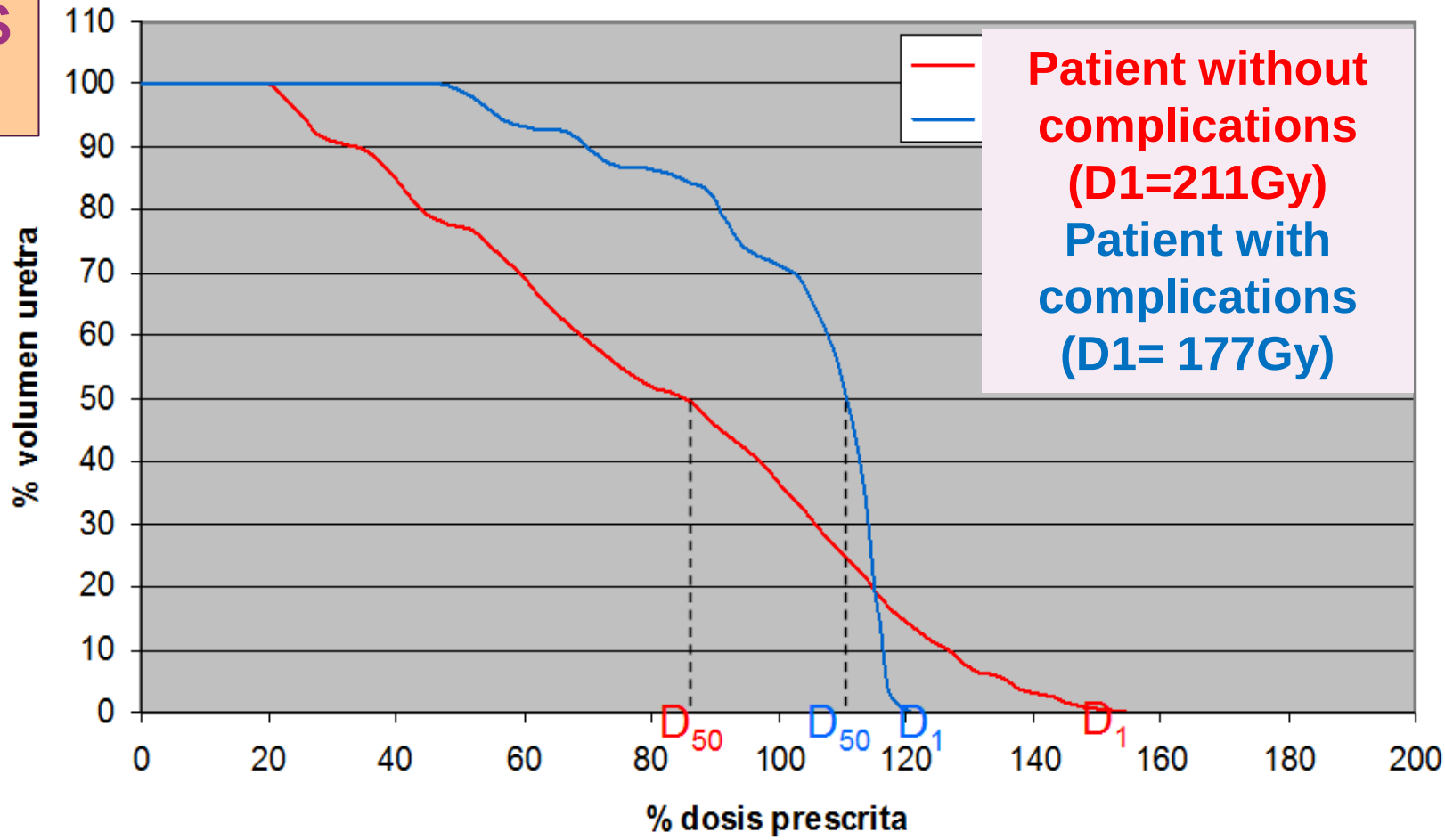
Brachytherapy offers the best DVH and the lowest volume

Georg D et al. Dosimetric considerations to determine the Optimal Technique for Localized Prostate Cancer Among External Photon, Proton, or Carbon-Ion Therapy and High-Dose-Rate or Low-Dose-Rate Brachytherapy. Int J Radiation Oncol Biol Phys, Vol. 88, No. 3, pp. 715-722, 2014

PROSTATE SEEDS IMPLANT 145 Gy

- 88 patients without any urinary complication
- 26 bladder catheter over 2 weeks (13) or trans-urethral resection procedure (TURP) (13),

DVH: urethral D1 (Dose to 1%), D10, D30, D50, prostate V100 and V150, and mean urethral dose



The difference between urethral D1 and D50 "index C_{1-50}", is lower in cases with complications (p= 0.009)
With values over 37.5Gy, only 2 cases developed complications out of 28 (7.1%).
With differences <20.7Gy, 10 / 18 (55.6%) required long-time bladder catheter or TURP.

An index C_{1-50} <20.7Gy is correlated with urethral complications. During the real-time procedure, a higher difference between D1 and D50 can decrease the risk of urethral complications during the follow-up.

Oliver L, Guinot JL, González-Perez V, Campo V, Bosó C, Cano A, Guardino C, De los Dolores V, Crispín V. INFLUENCE OF DVH IN URINARY COMPLICATIONS IN PROSTATE LDR BRACHYTHERAPY

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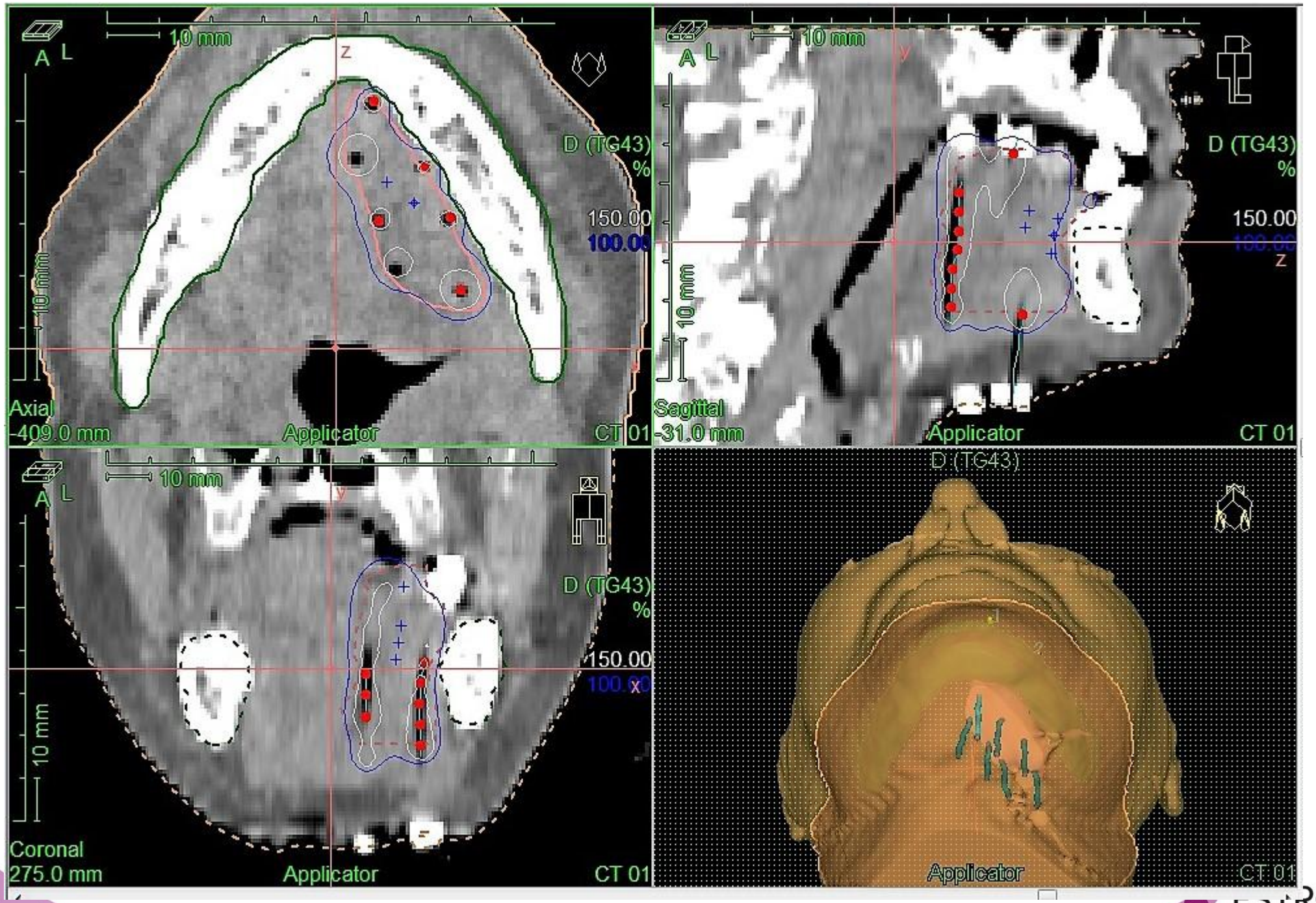
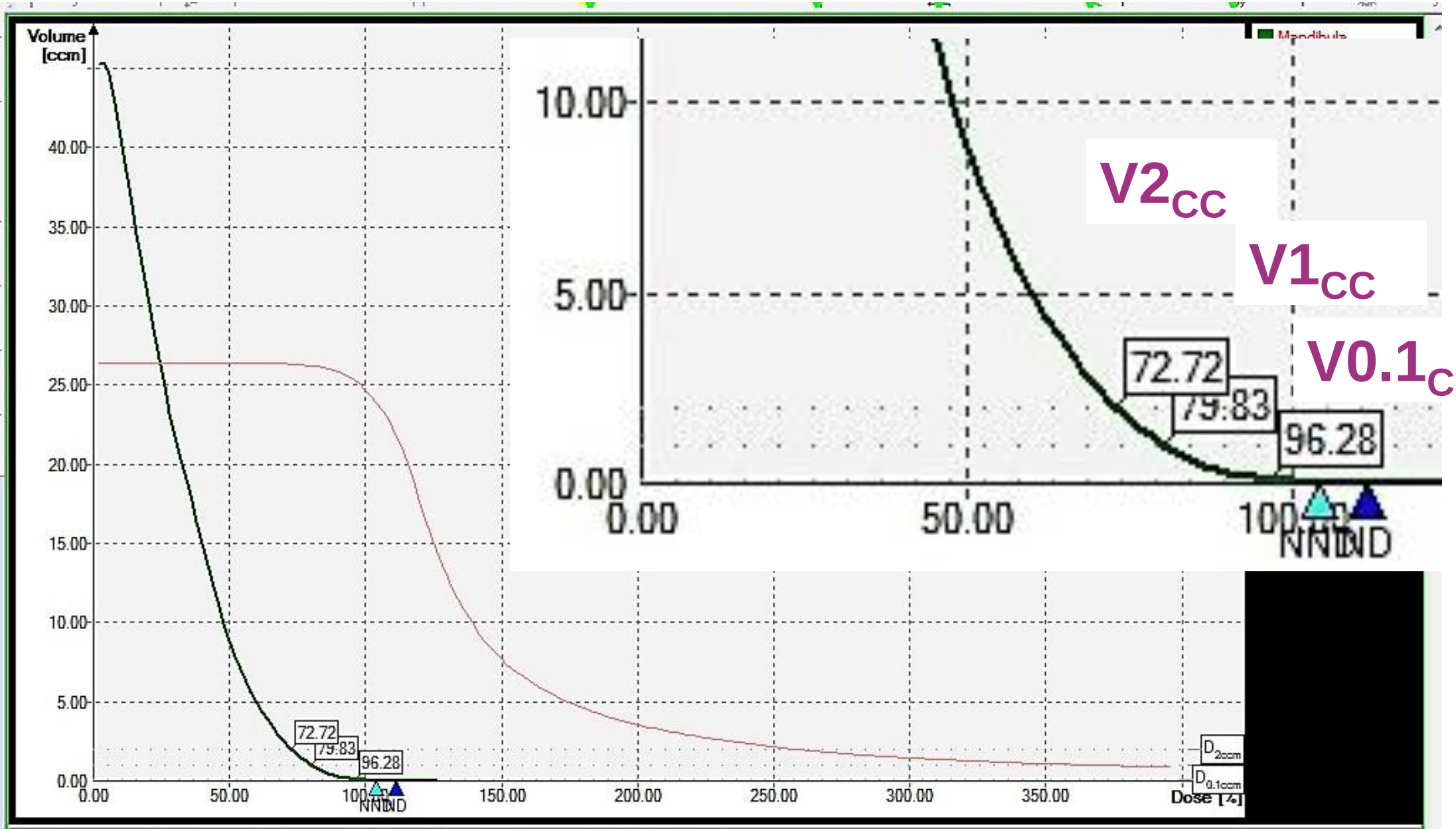
Tongue postoperative brachytherapy: isodoses



Tongue postoperative brachytherapy: cumulative DVH CTV

ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
CTV	66.05	198.14	**100.00**	26.39
CTV	104.63	313.89	**90.00**	23.75
CTV	89.69	269.06	**98.00**	25.86
Mandibula	96.28	288.85	0.22	**0.10**
Mandibula	79.83	239.49	2.21	**1.00**
Mandibula	72.72	218.15	4.42	**2.00**

Tongue postoperative brachytherapy: cumulative DVH bone



$V2_{cc}$

$V1_{cc}$

$V0.1_{cc}$

ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
CTV	104.63	313.89	**90.00**	23.75
Mandibula	96.28	288.85	0.22	**0.10**
Mandibula	79.83	239.49	2.21	**1.00**
Mandibula	72.72	218.15	4.42	**2.00**

Mandible
V 0.1cc < prescription dose

Modified prescription in Brachytherapy

Prescription to volume (3D)

- DVH to target and OAR
- Cervix, prostate,

Prescription to isodose (2D)

- Parallel and fixed catheters
- Breast, lip, interstitial skin

Prescription to distance mm (1D)

- Single line
- Bronchus, esophagus, vaginal cylinder

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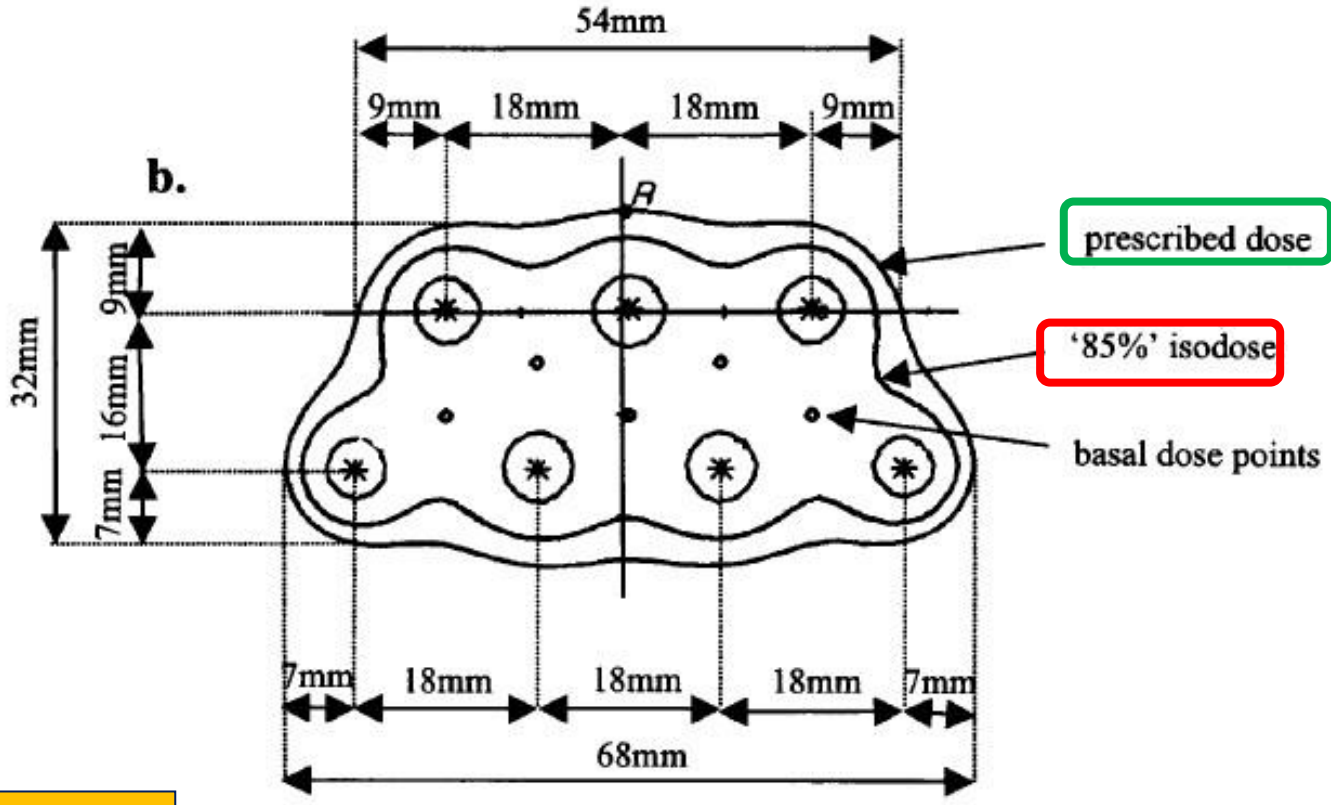
Breast cancer with needles: Boost 9-10 Gy HDR to 10mm

Resch A. 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. Radiother Oncol 2002;63:47-58

410 patients (Viena)

Local relapse 3.9%

Cosmesis
Excellent-good 38%
Moderate 55%
Bad 7%



LDR: 20 Gy (9.9 - 27 Gy)

↑25%

LDR, 6 cm active length	Five needles		Seven needles		Nine needles	
	Dose (Gy)	Volume (ccm)	Dose (Gy)	Volume (ccm)	Dose (Gy)	Volume (ccm)
'Prescribed isodose'	20	87	20	105	20	133
'Mean central dose' (MCD)	33		29		28	
'85% isodose'	28	50	25	71	24	96
'High dose-isodose'	50	8	43	11	43	13

↑31%

HDR: 9.7 Gy (7 – 12 Gy)

'Prescribed dose'	9.7 ± 1.1
'Mean central dose'	15.0 ± 2.0
'85% of mean central dose'	12.7 ± 1.7
'Prescribed dose'	83 ± 31
'85% of mean central dose'	52 ± 22
'High dose volume' (150% of MCD)	8 ± 3
'Low dose volume' (90% of MTD)	96 ± 36
'Homogeneity index'	0.65 ± 0.06

Clin Transl Oncol (2012) 14:109-115
DOI 10.1007/s12094-012-0769-3

Breast cancer with needles: 7 Gy to 90% isodose

RESEARCH ARTICLES

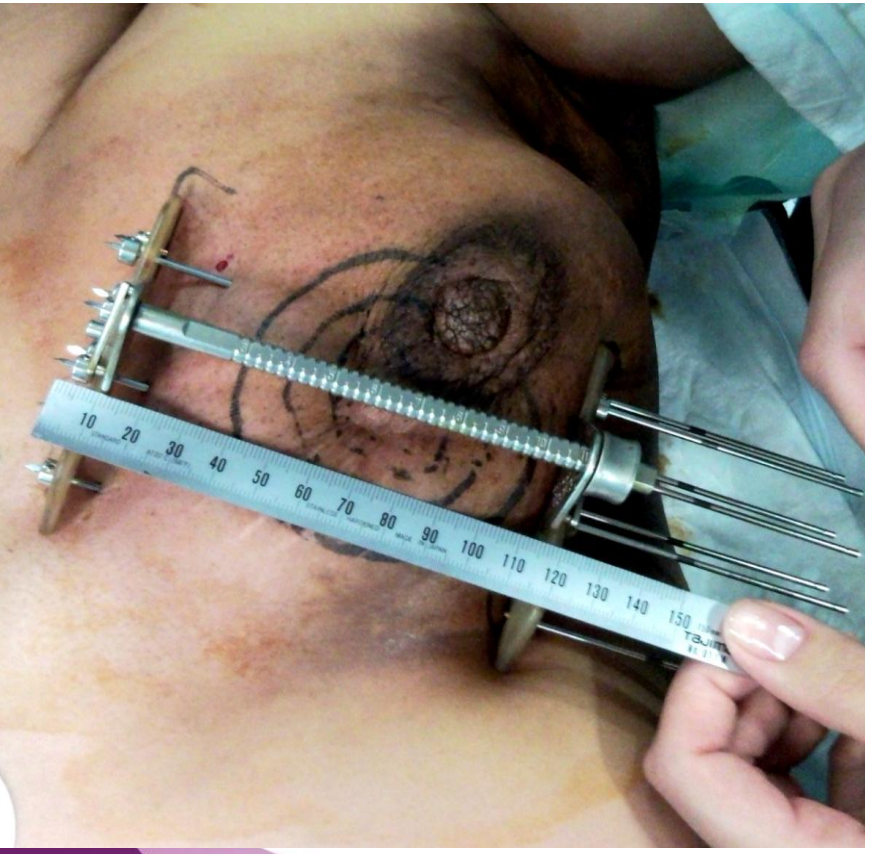
Ten-year results of a phase II study with a single fraction of high-dose-rate brachytherapy (FAST-boost) after whole breast irradiation in invasive breast carcinoma

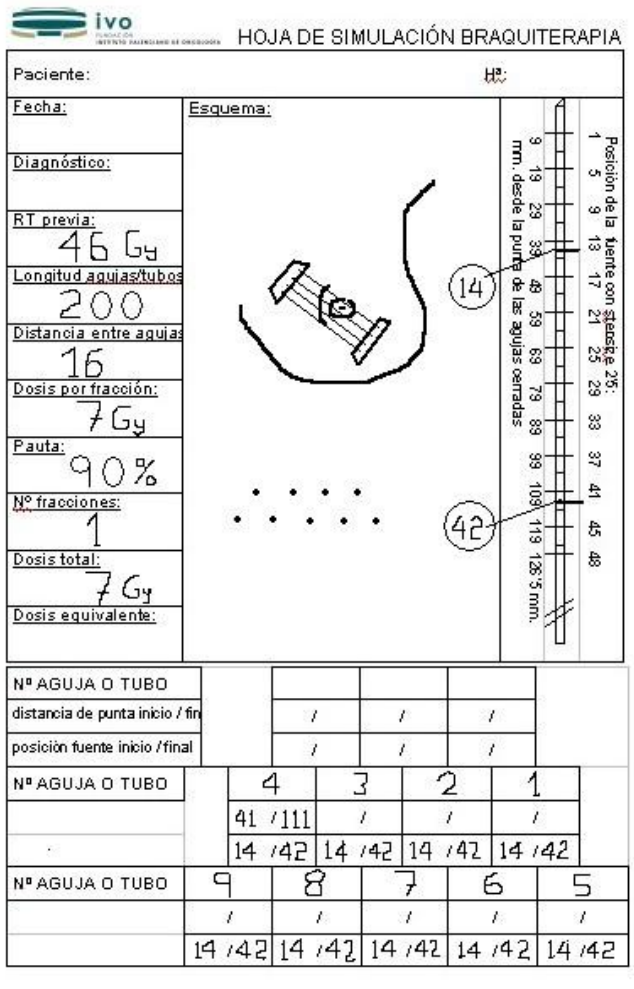
José Luis Guinot · M. Isabel Tortajada · María Carrascosa · Vicente Crispín · Ana Otero · Belén Ríos · Eleonor Rivin · Miguel Santos · Pablo Soler · Leoncio Arribas

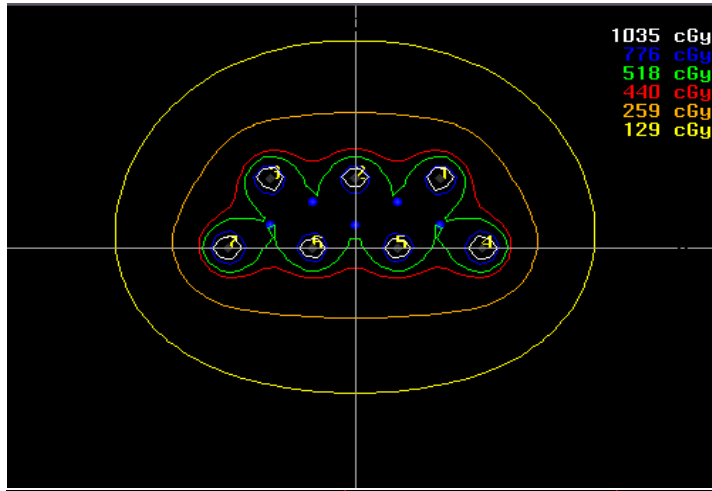
Local relapse 4.4% (10 y)

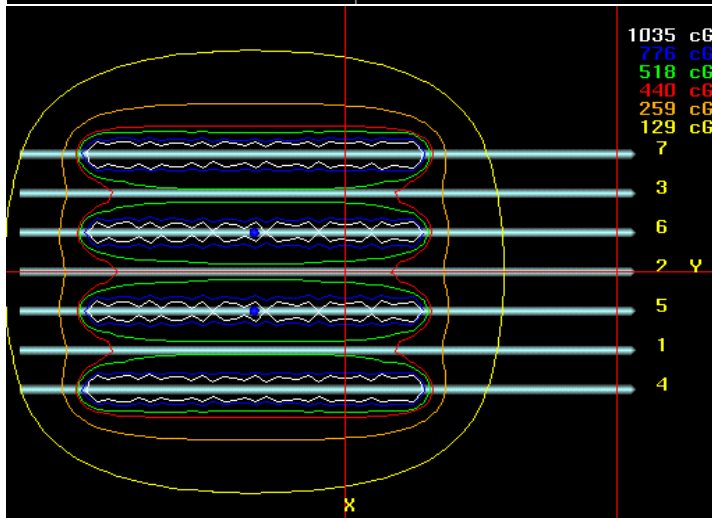
Cosmesis

Excellent-good : 92.5%

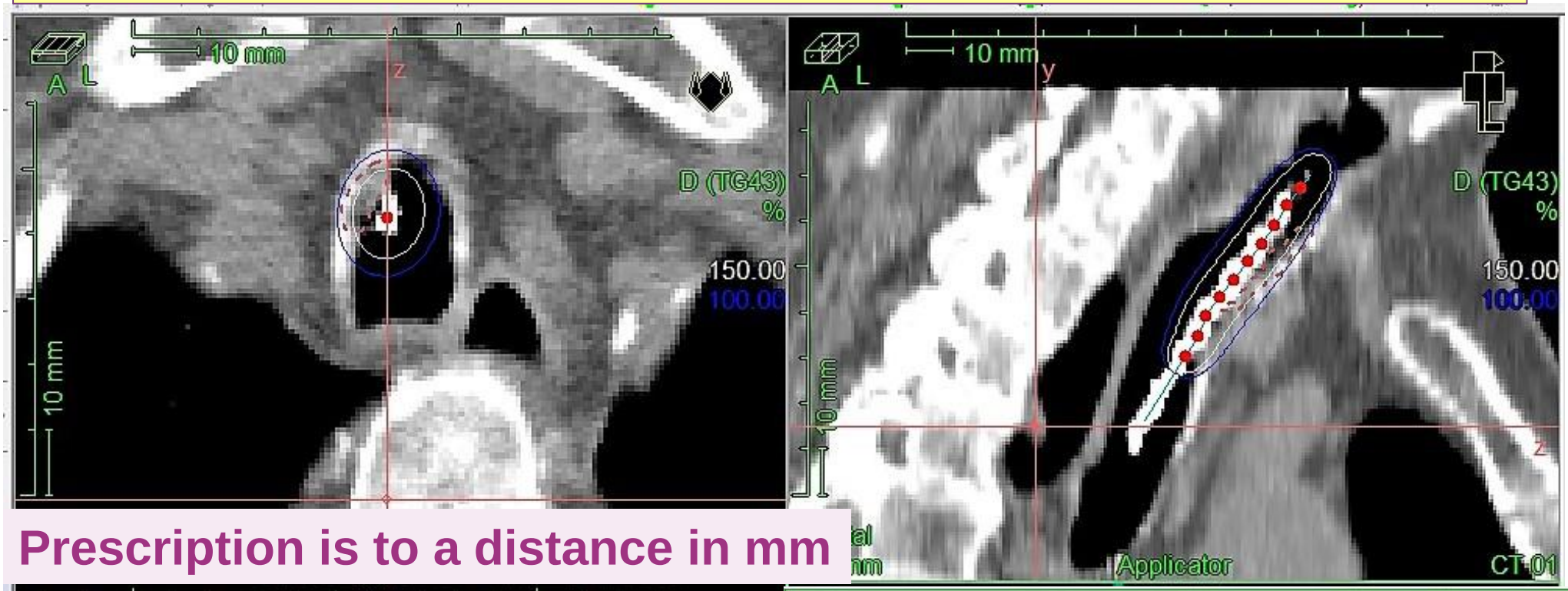




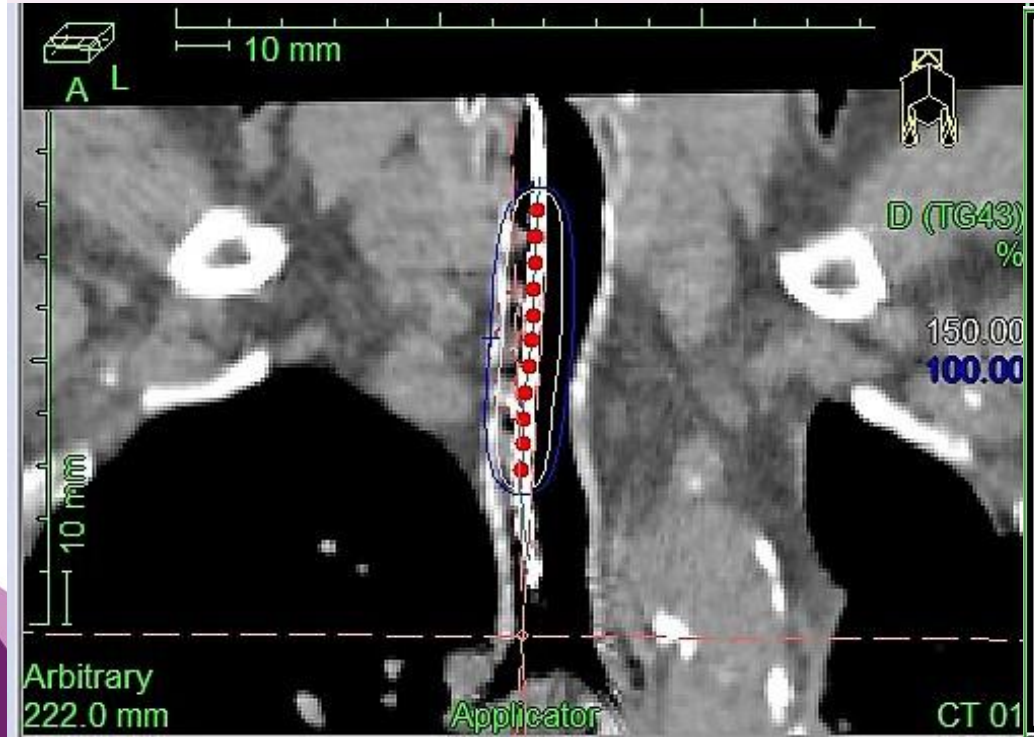


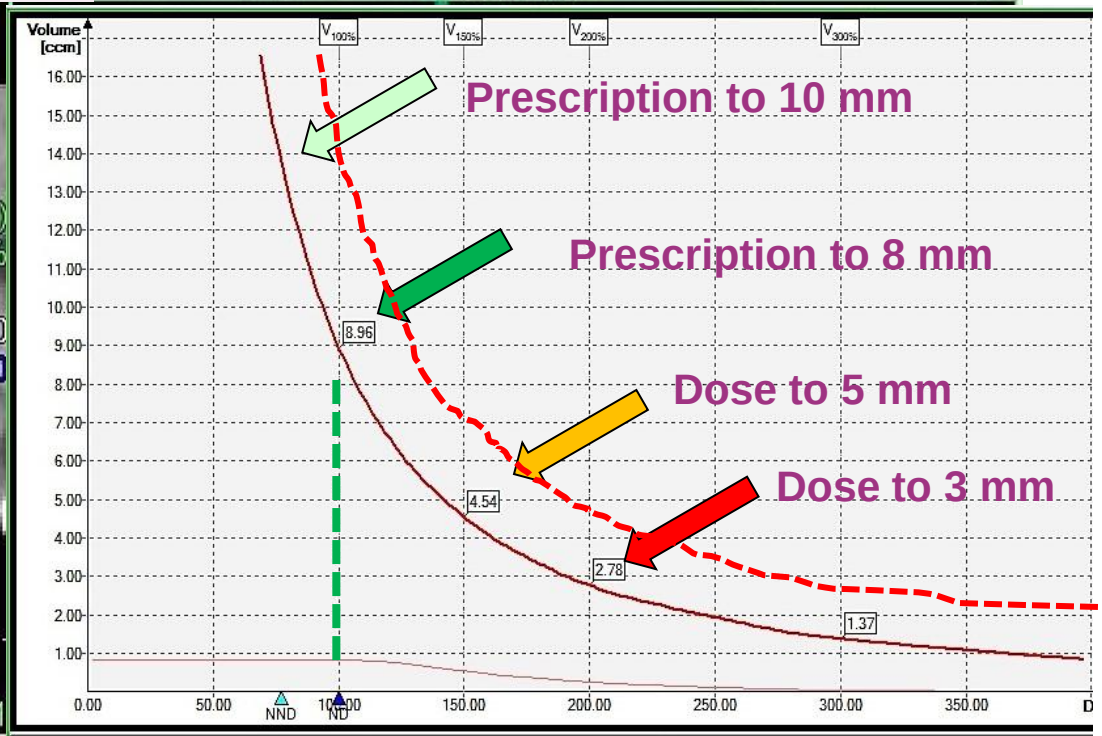


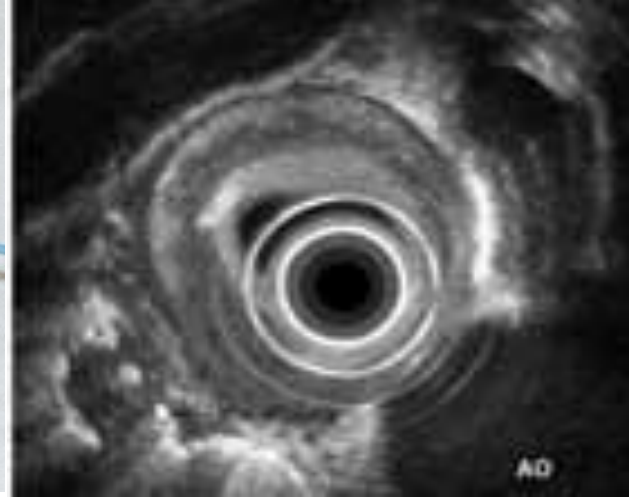
Tracheal endoluminal brachytherapy 5Gy at 8mm from axis



Prescription is to a distance in mm

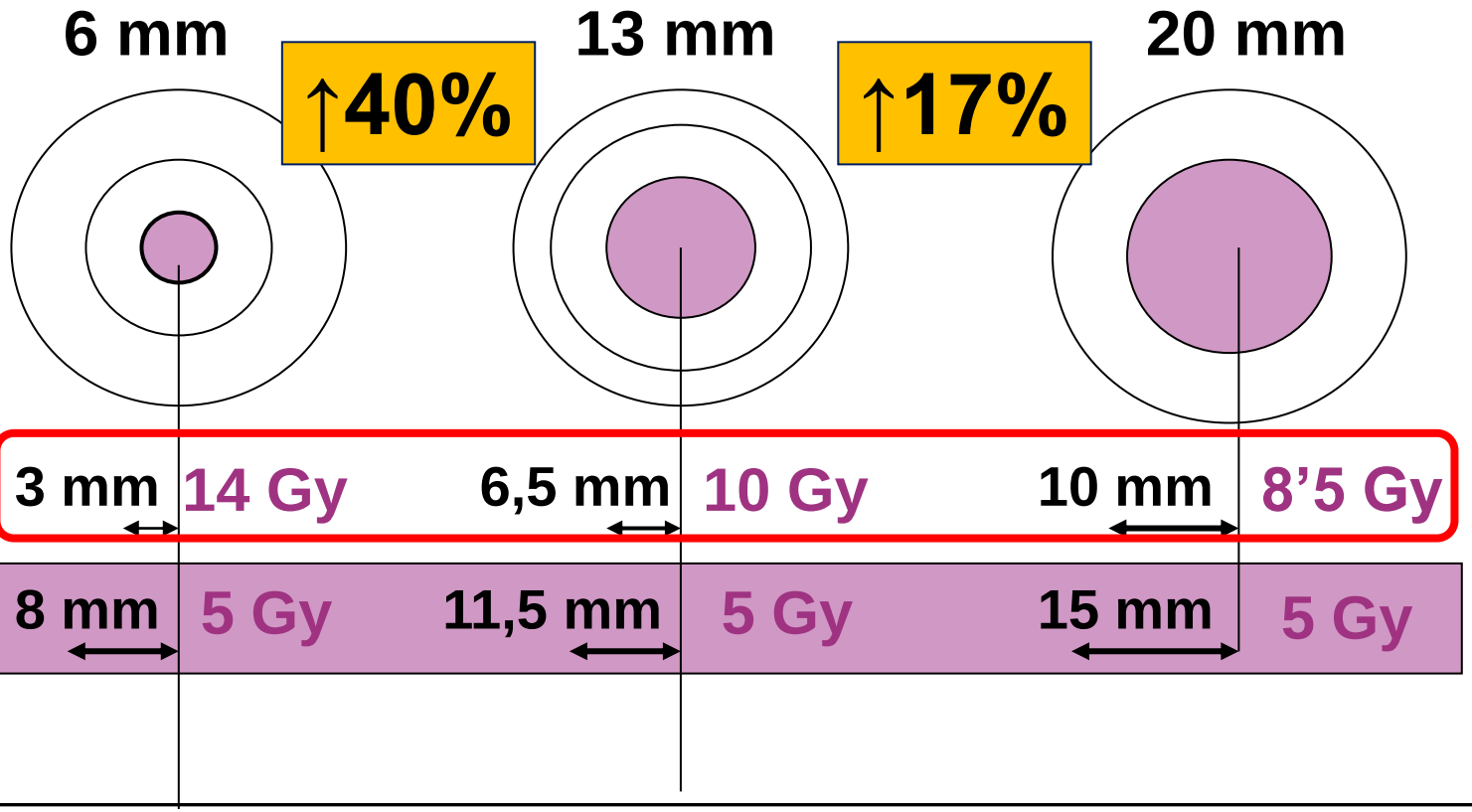






Esophagus:

Prescription 5 Gy to 5mm from app surface



Gaspar LE
RTOG 9207
EBRT + BT + concurrent CT localized ca. of esophagus
-12% fistulas
- **2-4 mm applicators**

Equivalent dose	~ 30 Gy	~ 18 Gy	~ 14,5 Gy on mucose
Complications	~45 Gy	~ 27 Gy	~ 18 Gy

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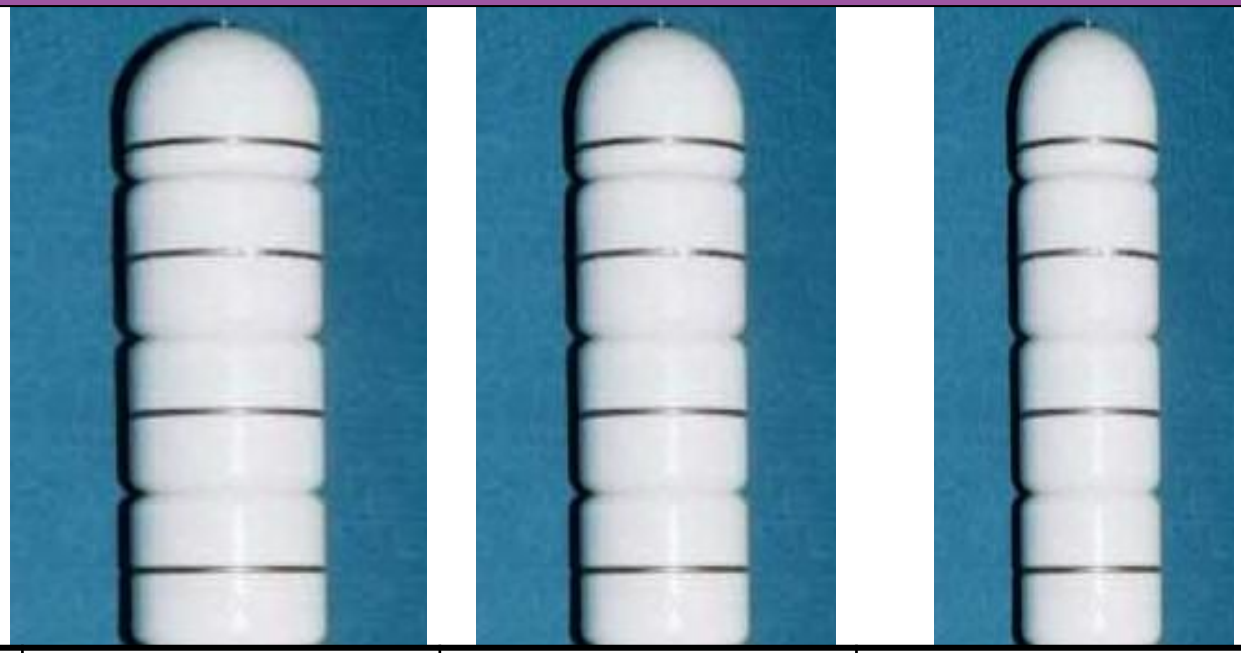
Vaginal BT (Dome): 4.5 Gy to 5mm from vaginal surface

VAGINAL CYLINDER: (DOME)
Variation of prescription doses depending on the diameter



Cilinder diameter	**3cm**	2.5cm	2cm
Prescription to 0.5 cm	**4.5 Gy**	4.5 Gy	4.5 Gy
Dose to surface	**7-7.5 Gy**	8-9 Gy	>10 Gy
Eq. Dose to surface	**11-12 Gy**	13-15 Gy	16-18 Gy
Modified prescription to 0.5 cm	**4.5 Gy**	**4 Gy**	**3.5 Gy**

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Take home messages:

- DVHs are mandatory in brachytherapy due to the gradient of dose and the high dose inside the implant
- Margin to the CTV is not convenient, therefore D90 > PD and V100 > 90% are useful.
- V150 should not be over 1/3 of the implant (DNR or DHI)
- In prostate and cervix, DNR of 0.5 is allowed because they are no functional organs.
- Natural DVH and quality parameters QI, UI, are useful for comparison of different plans
- DVHs are needed to prescribe dose to a volume and to evaluate the prescription to the CTV and OAR
- Take into account “aimed vs planned” prescription
- Without CTV, prescription is to an isodose. Select properly
- With a single line, prescription is to distance in mm.
- Follow the guidelines

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Image Guided Brachytherapy

Bradley Pieters

Academic Medical Center / University of Amsterdam

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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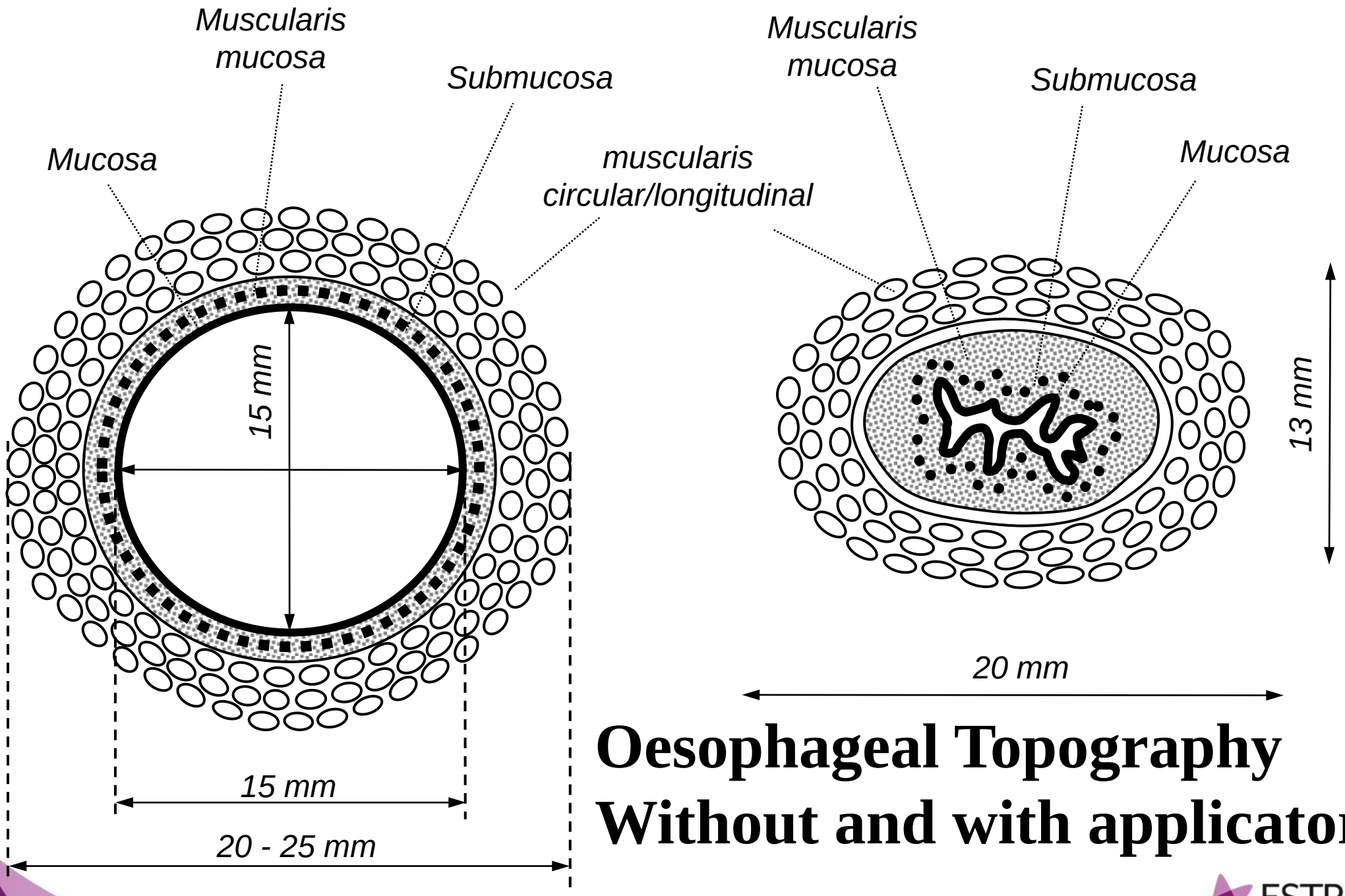

Oesophageal Topography Without and with applicator

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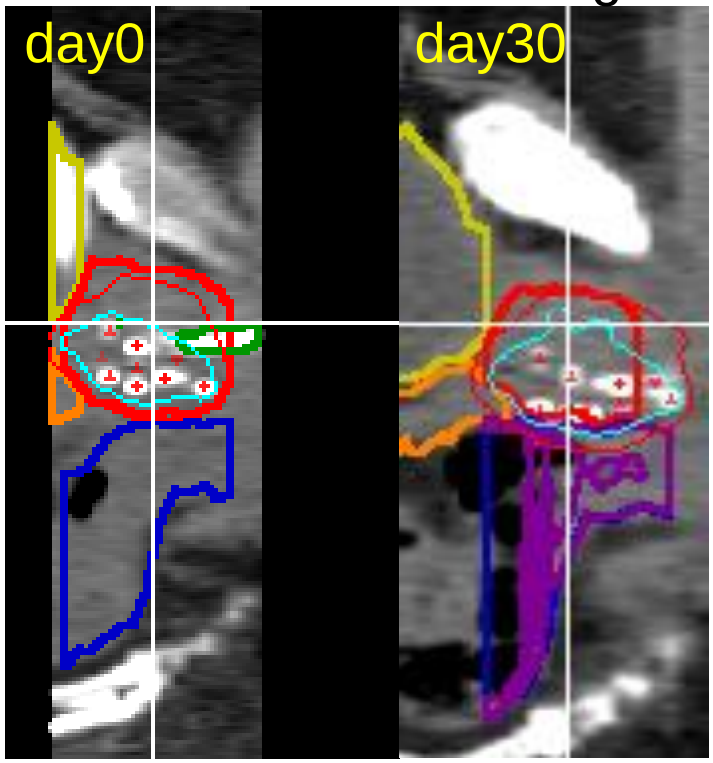
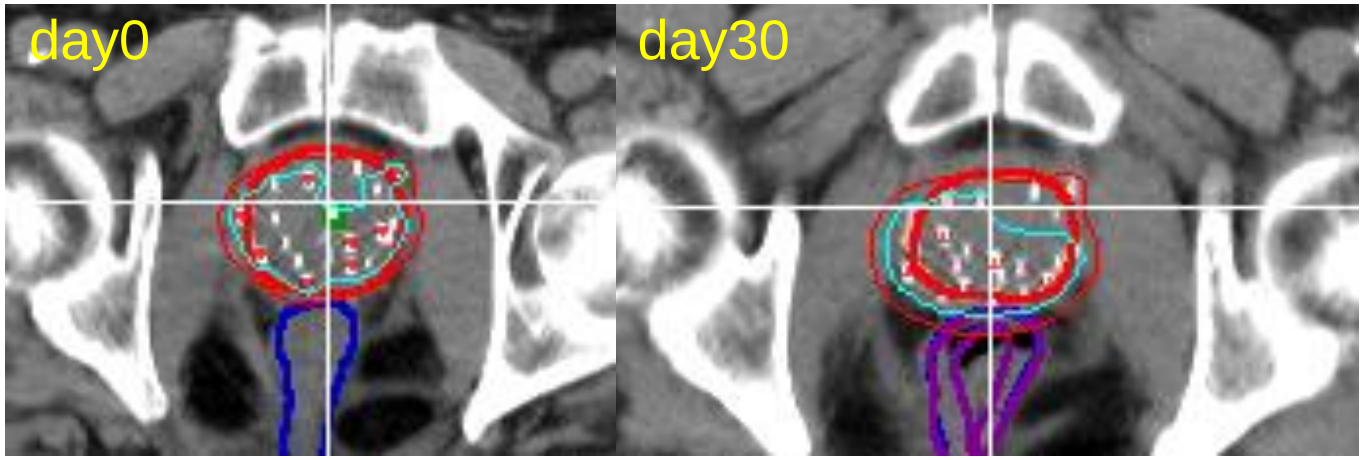
Decongest prostate edema: decreasing the volume

sagittal

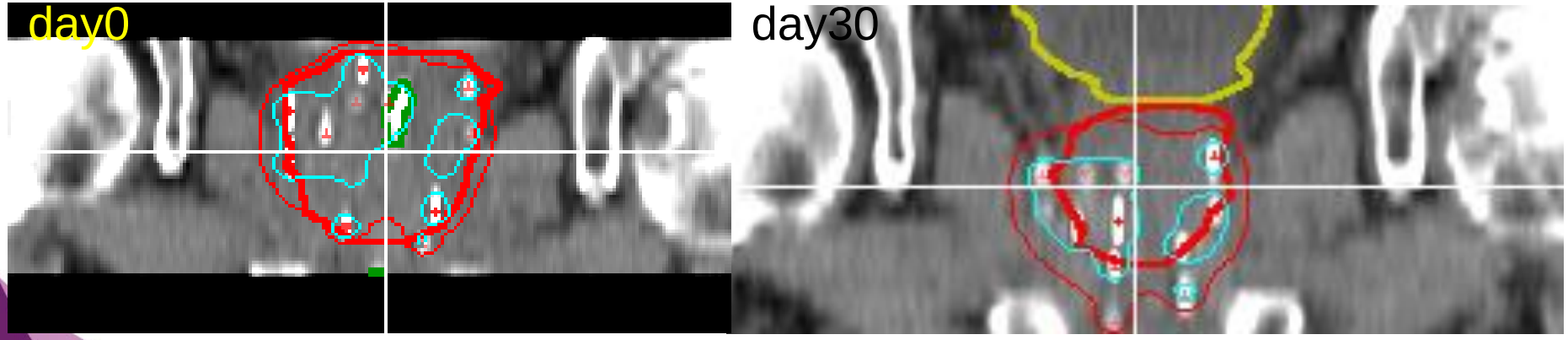


transverse



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

coronal



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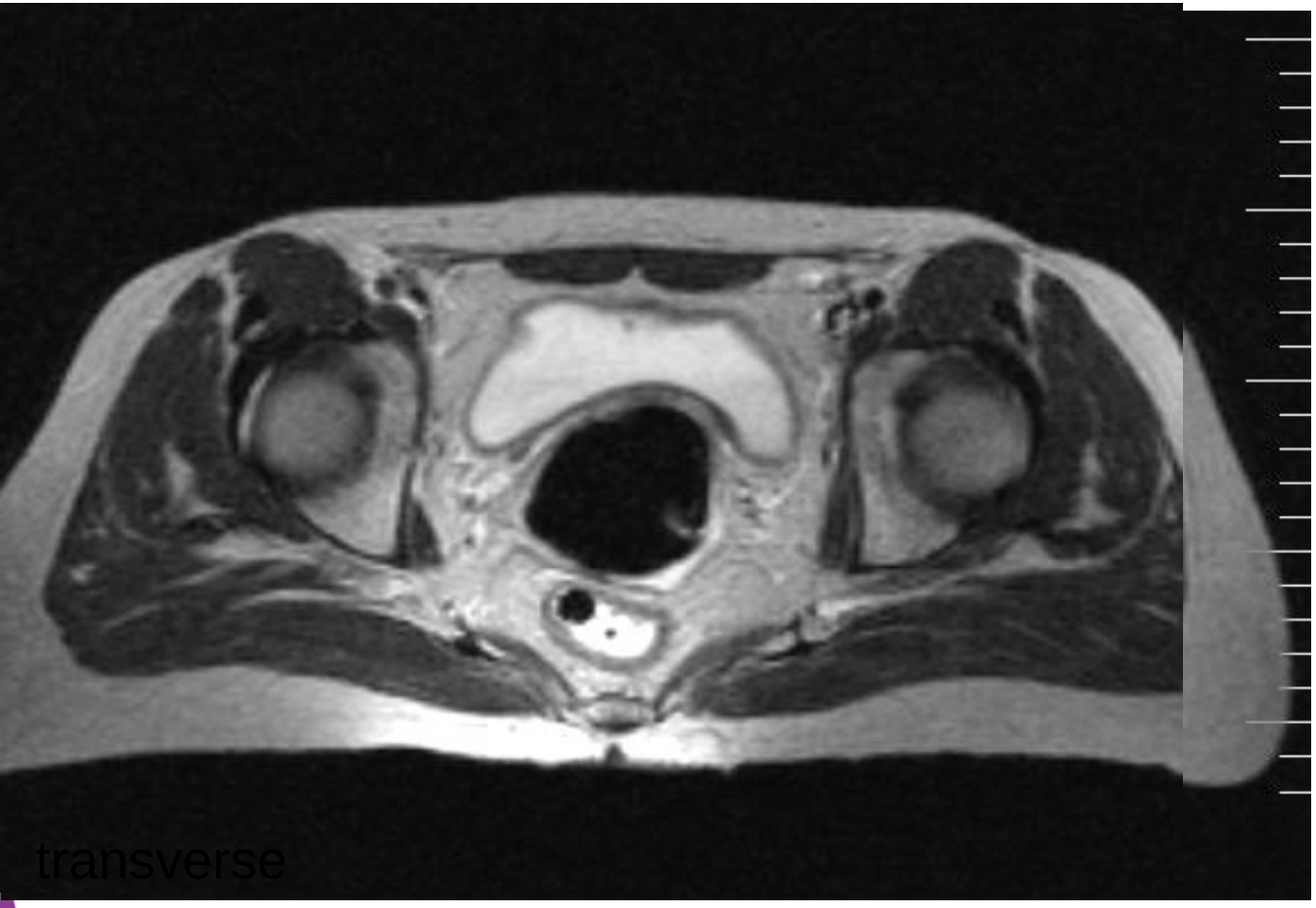
Impact of insertion of a Tandem-Ring Applicator on topography

before brachytherapy



without/with applicator

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Applicator Impact on Imaging in brachytherapy (II)

Interdependence between

Applicator and Imaging System:

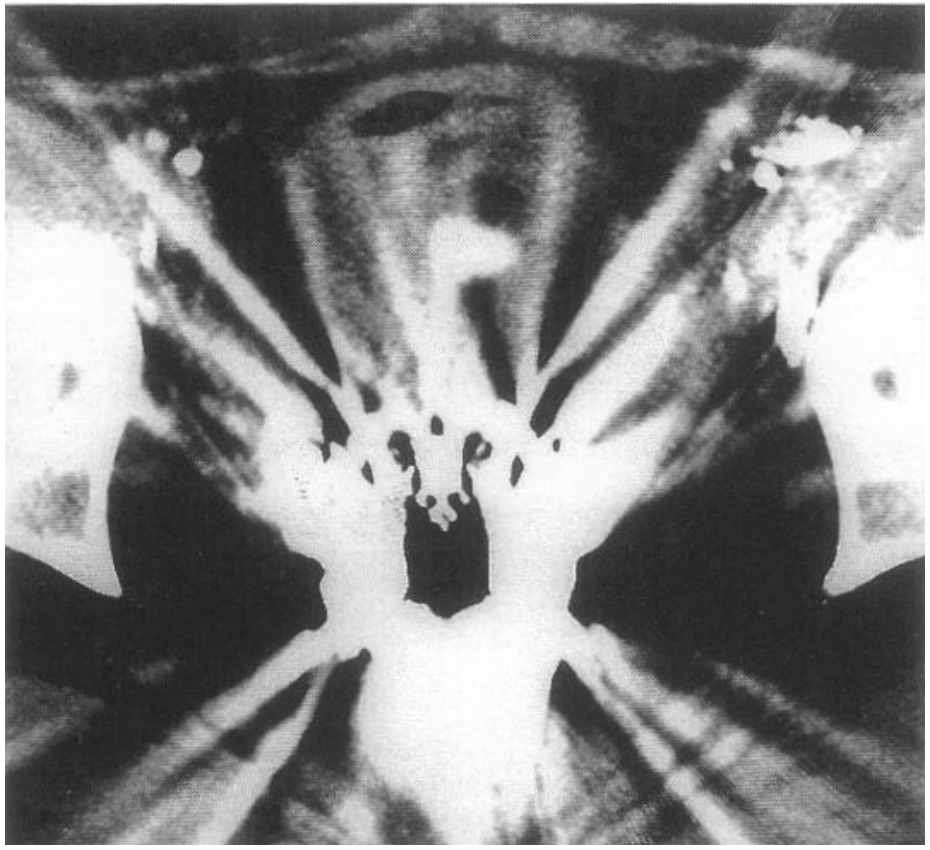
X-ray, CT, MRI, US, ...

feasibility of imaging (e.g. metallic tubes)

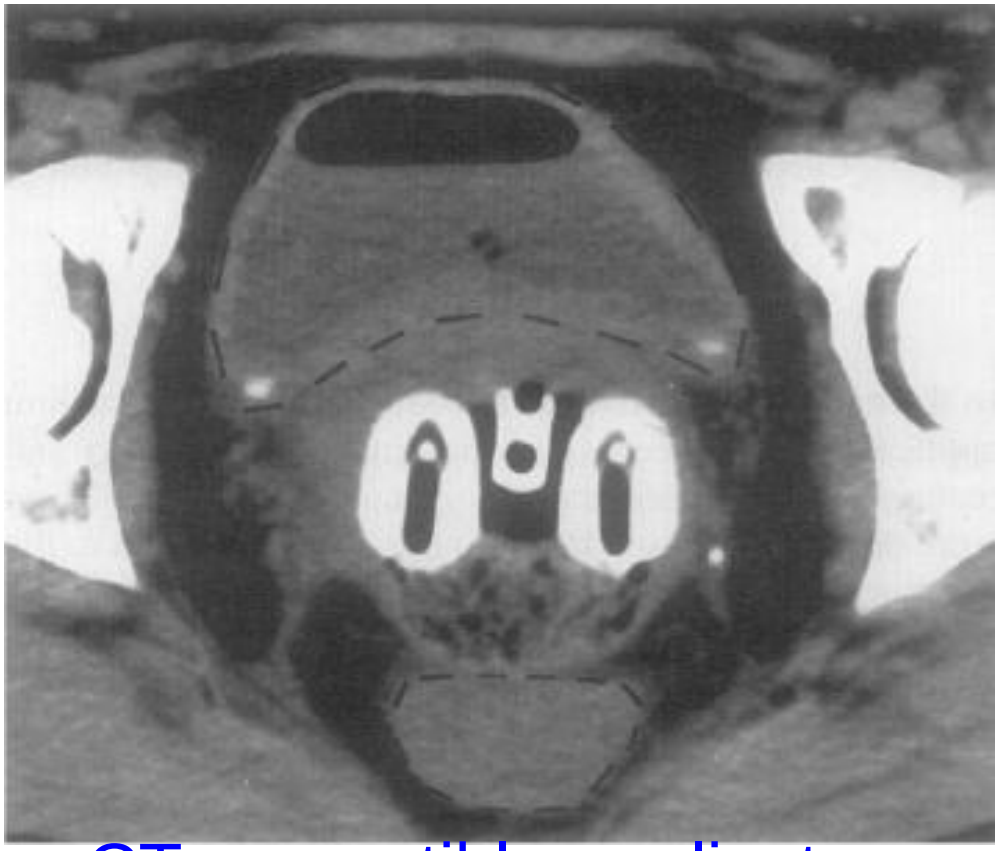
visibility (dependent on image system)

validity

Computed tomography
Applicator depiction



Metallic Applicator Artefacts



CT-compatible applicator
optimal depiction quality

Steggerda et al. J. Brachytherapy Int. 1998

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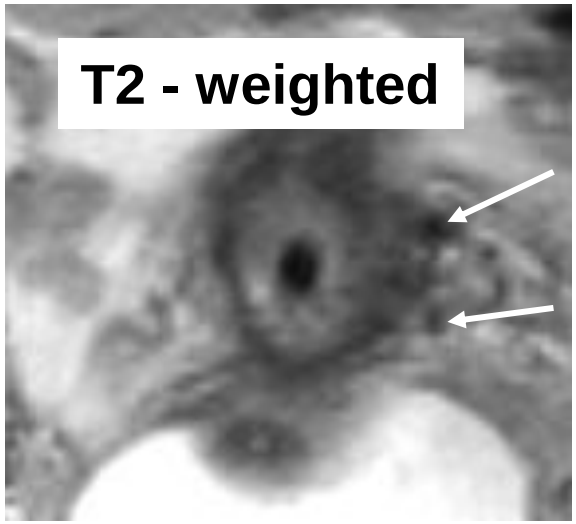
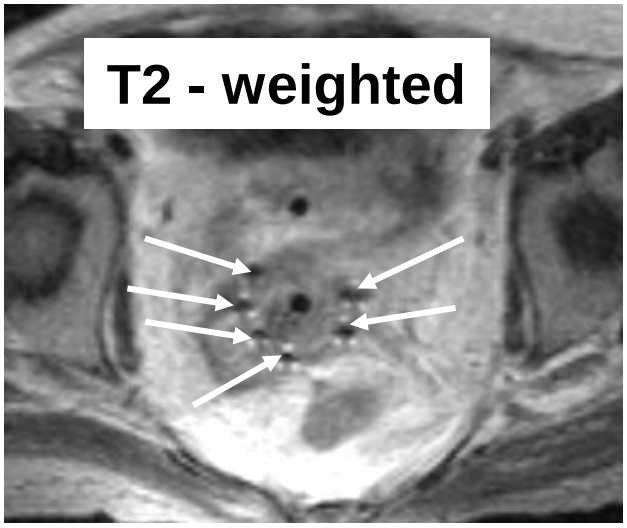
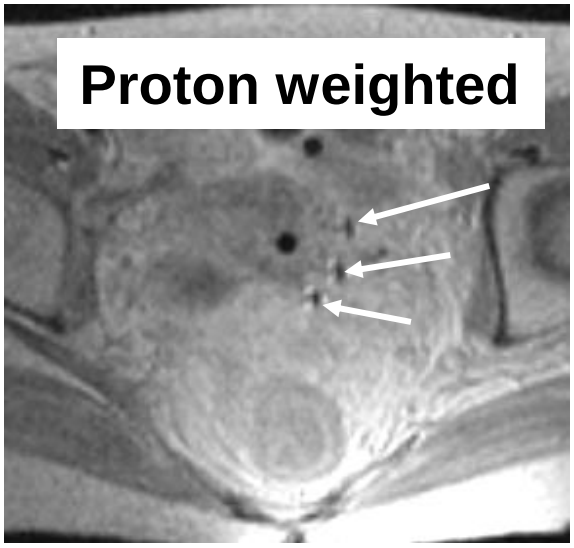
Needle Depiction

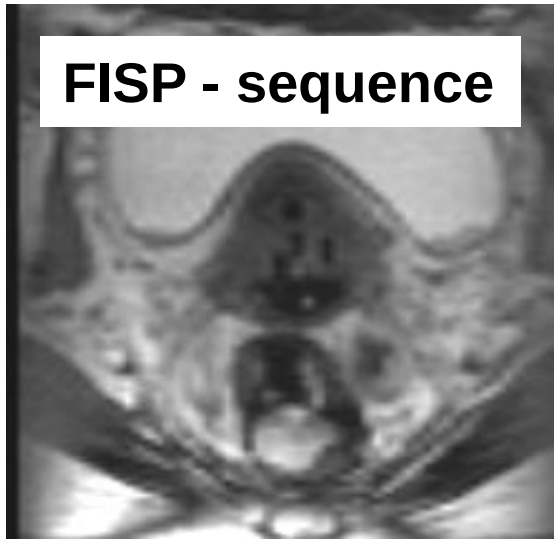


poor quality



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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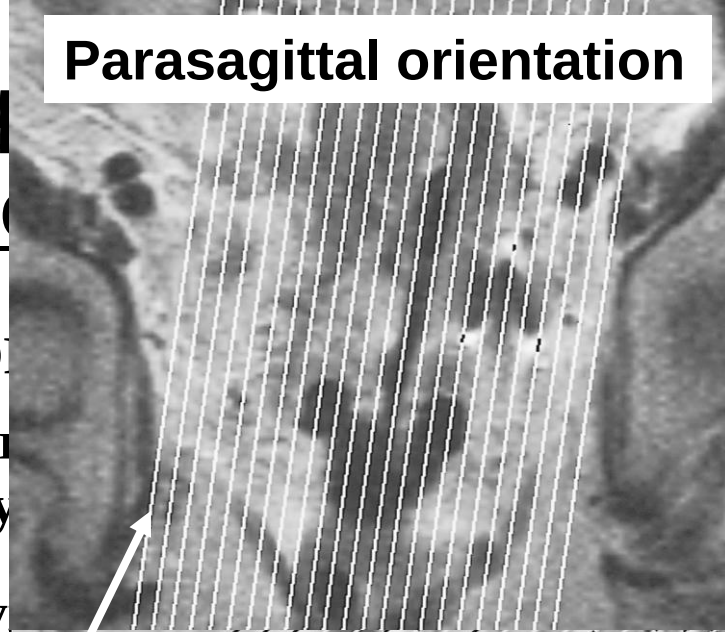
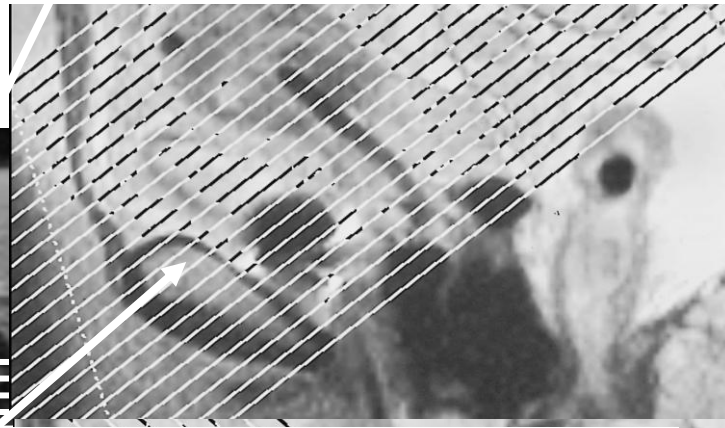
3D-MRI assisted image acq
Multiplanar capability-specifi

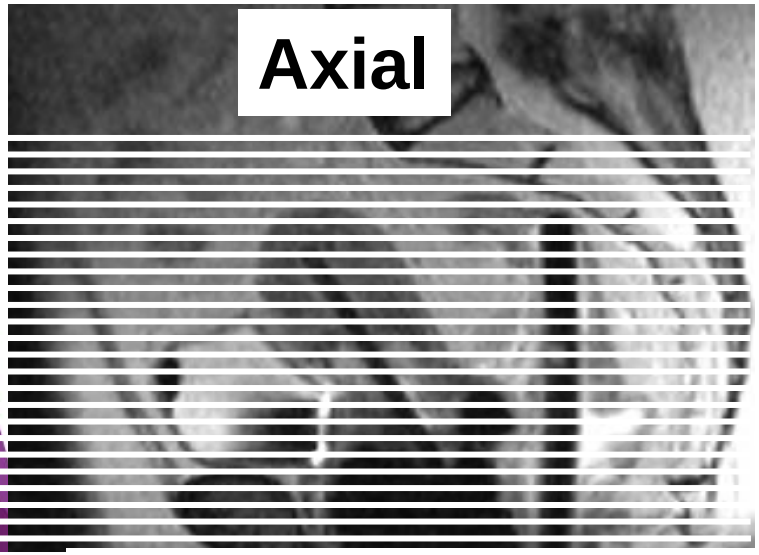
PLANE	COVERAGE-BO
T2 axial	discus L5
T2 sagittal	pelvic wall (obturator muscle)
T2 frontal or frontal oblique	entire uterus - cervix - vagina - tumor

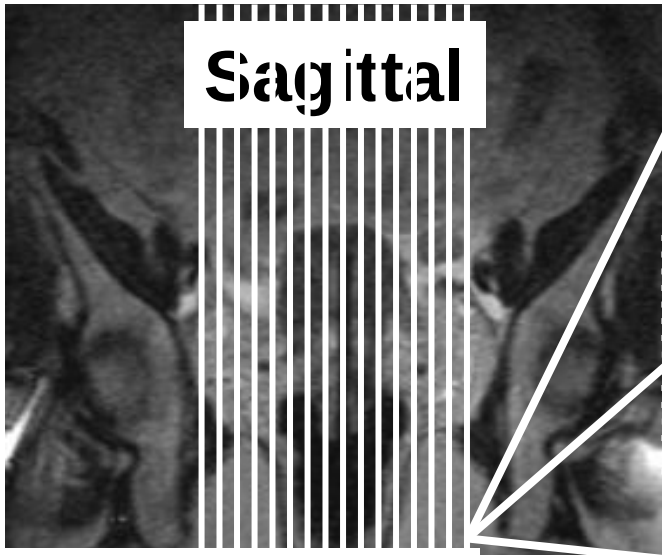
infer
of sy
pelv



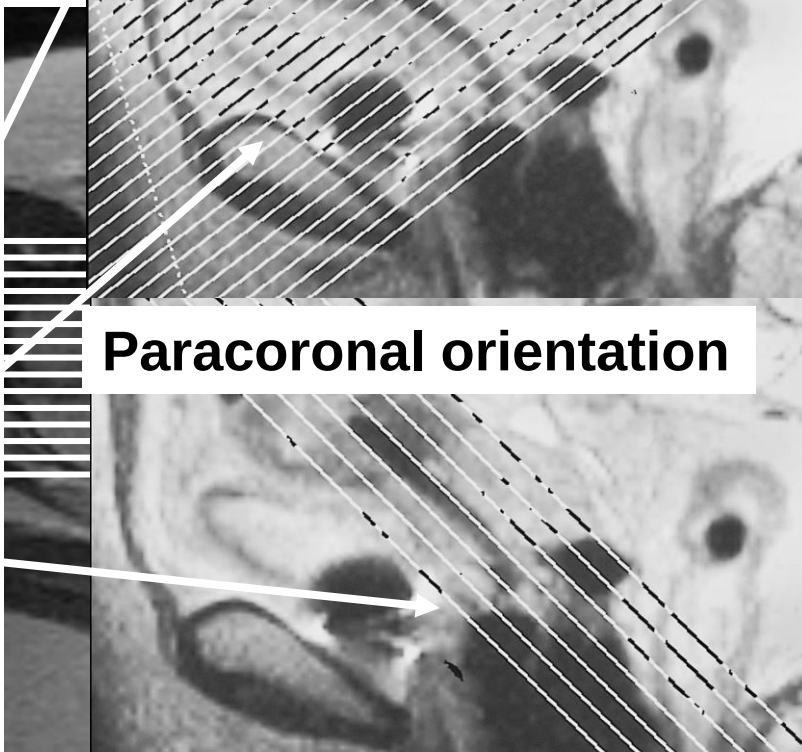
Paratransverse orientation



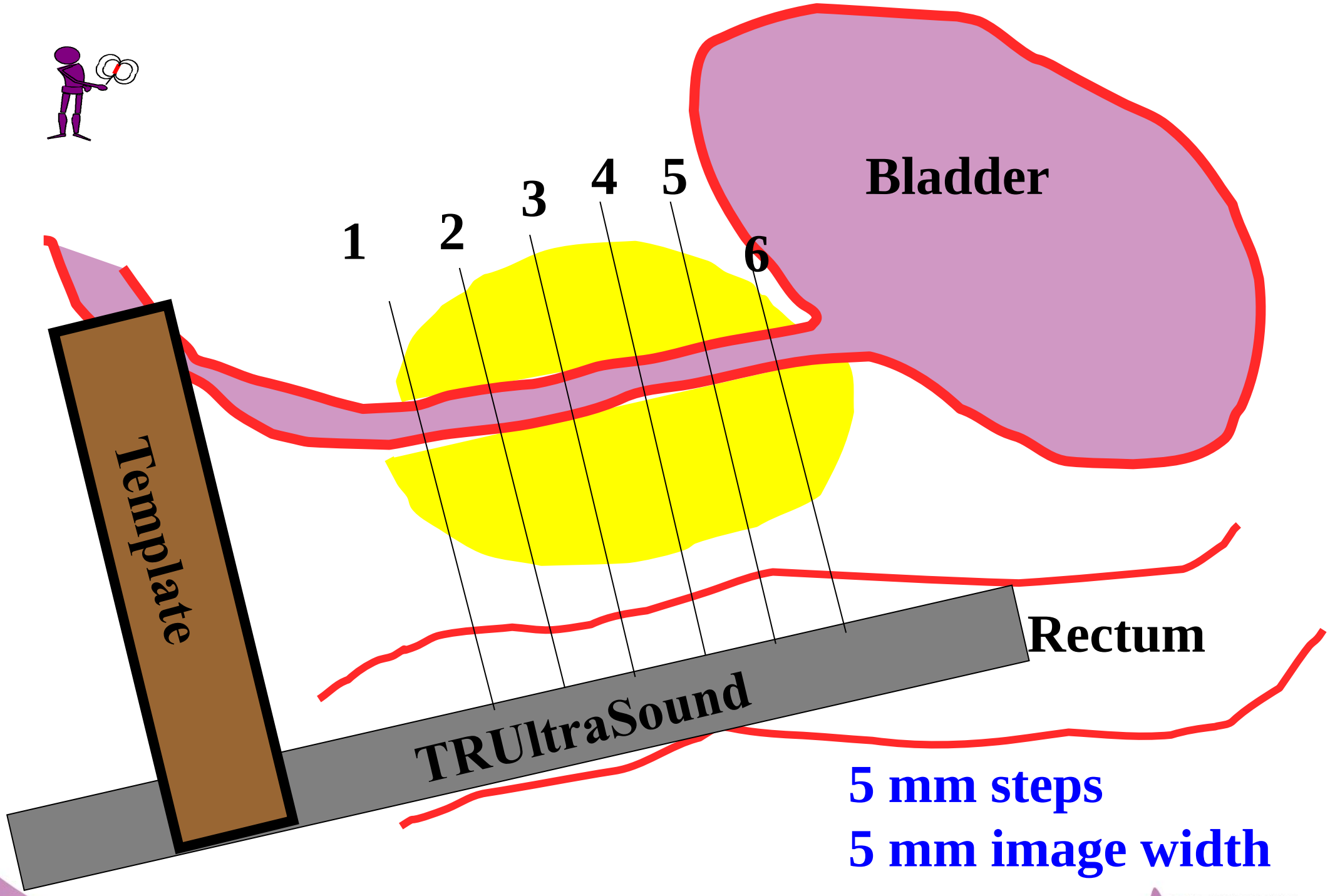




Paracoronal orientation



Slice orientation parallel/orthogonal to applicator axis


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

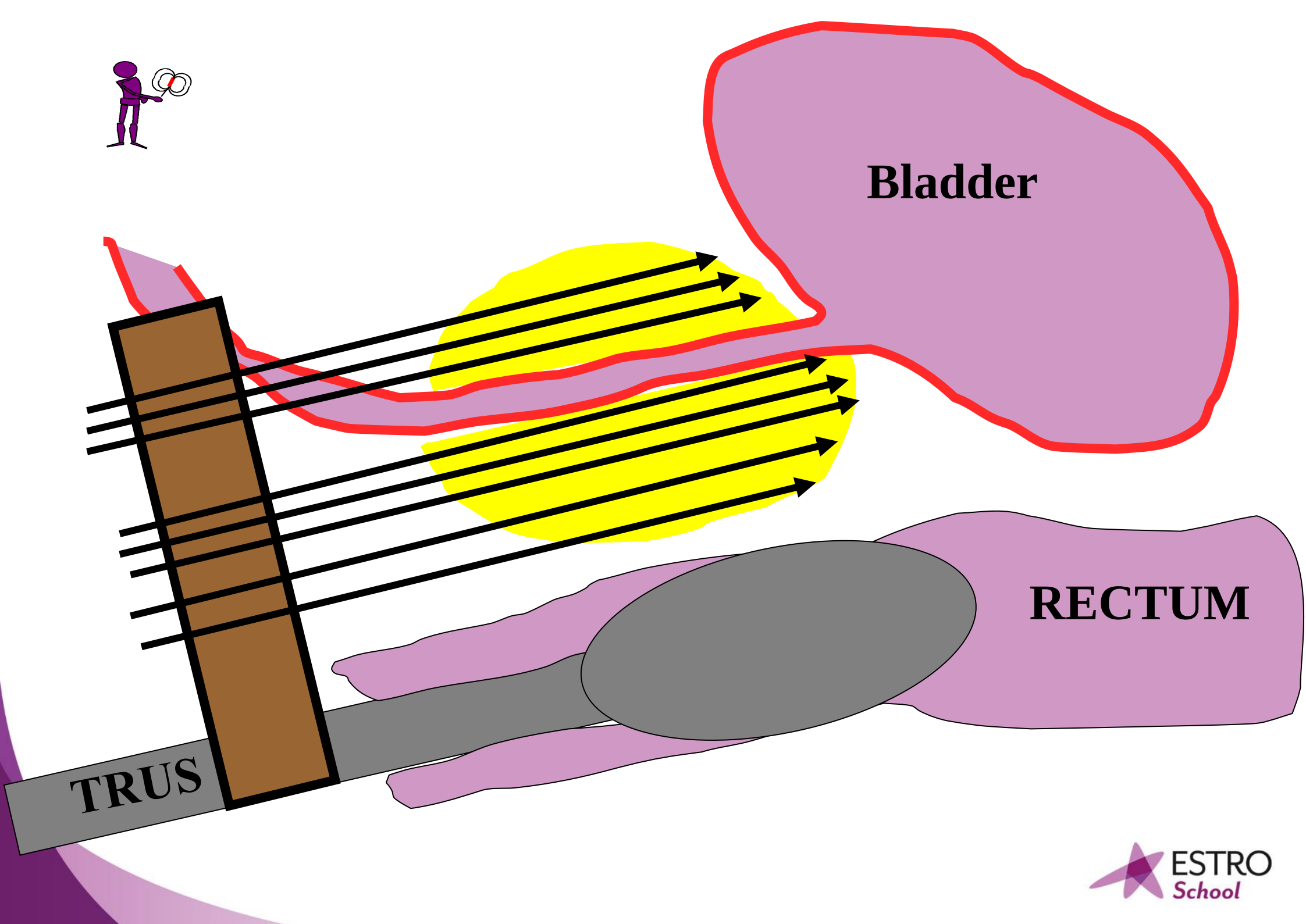
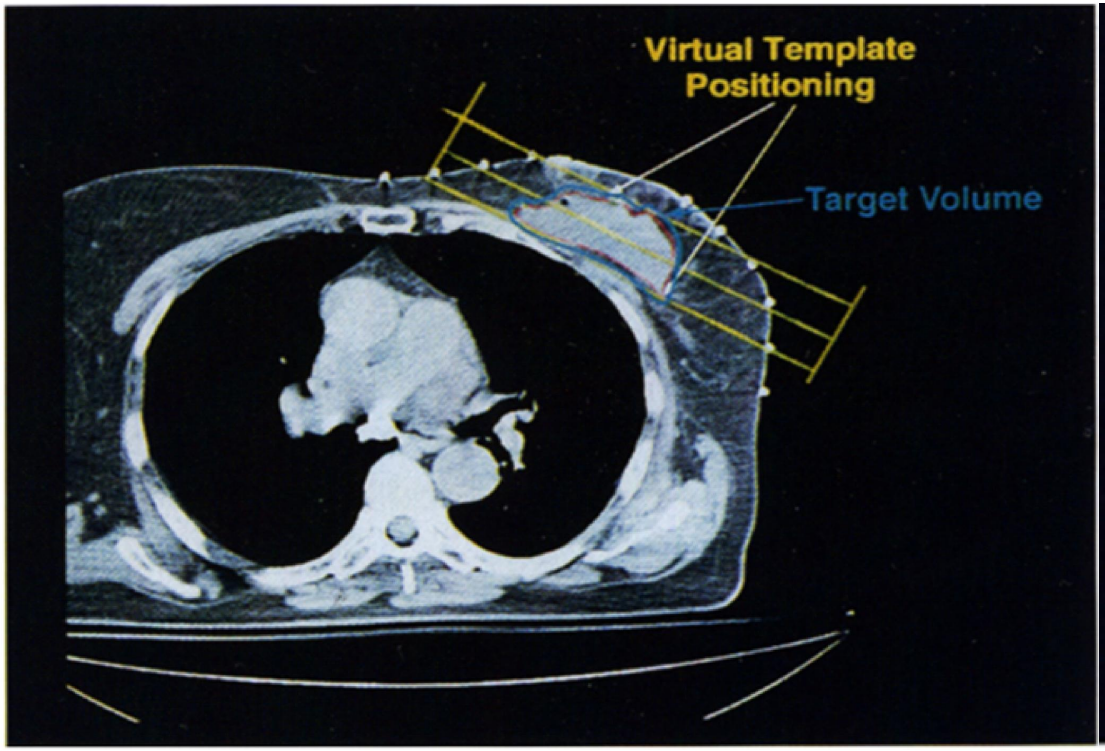
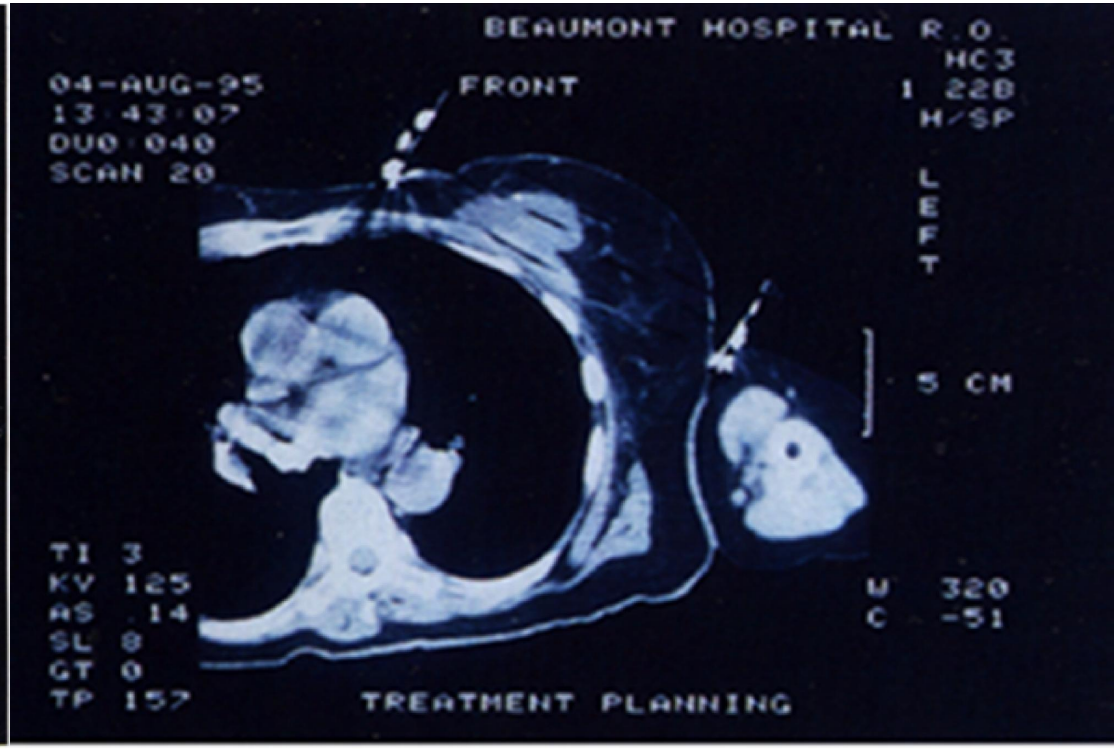

Bladder
RECTUM
TRUS

Image Guidance





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

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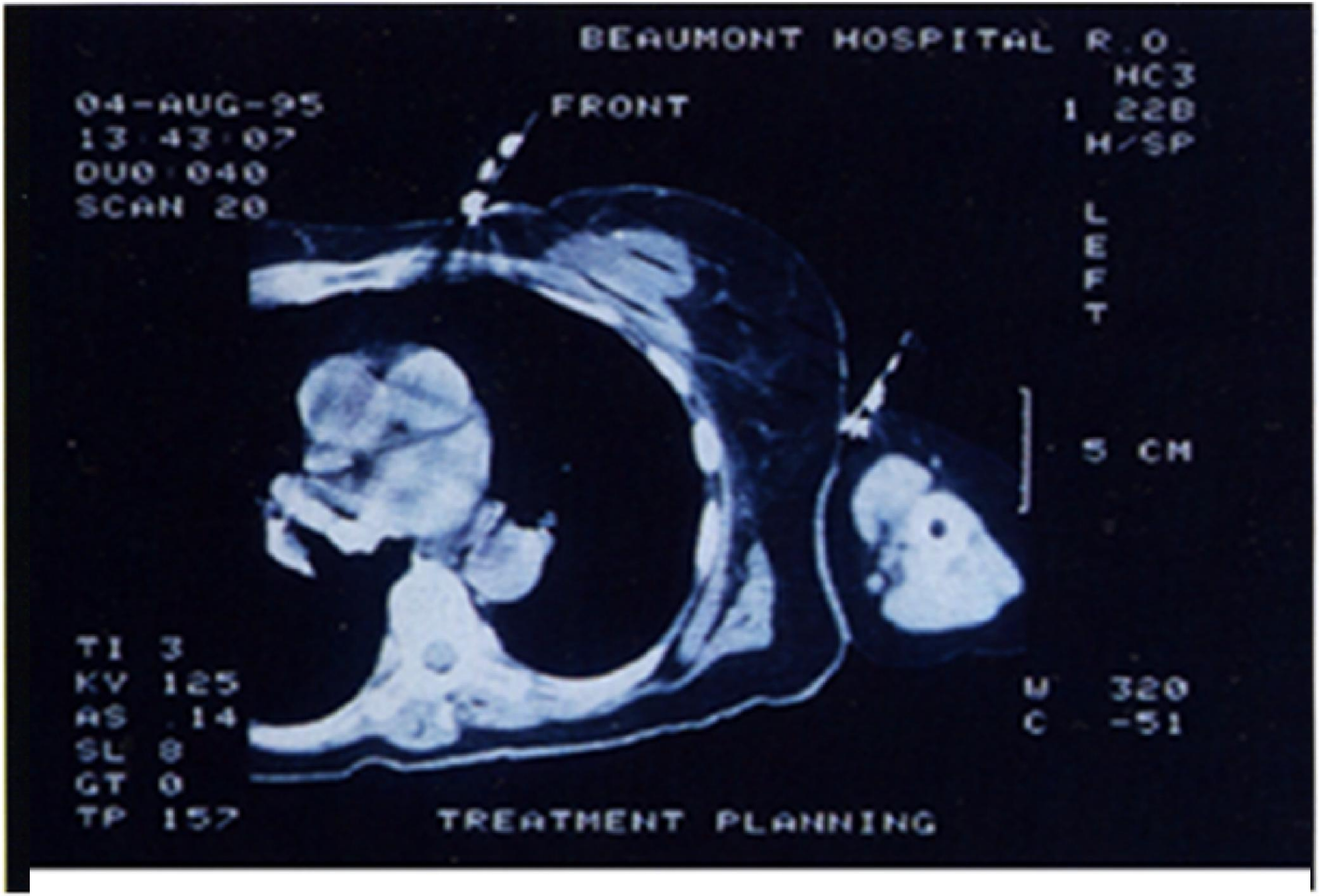
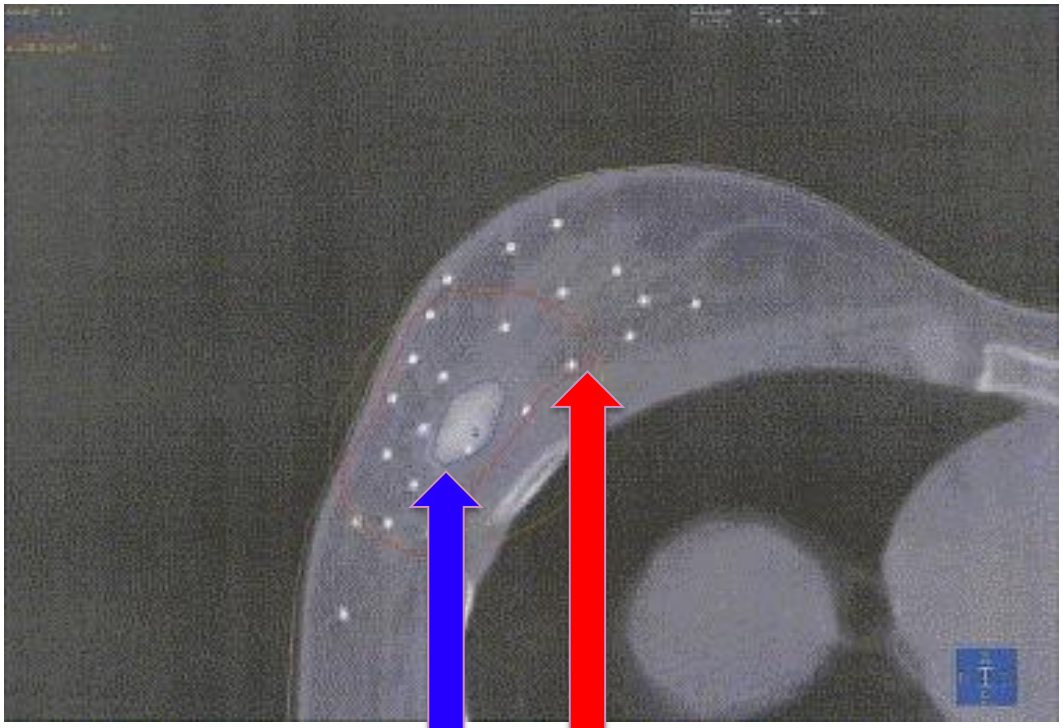
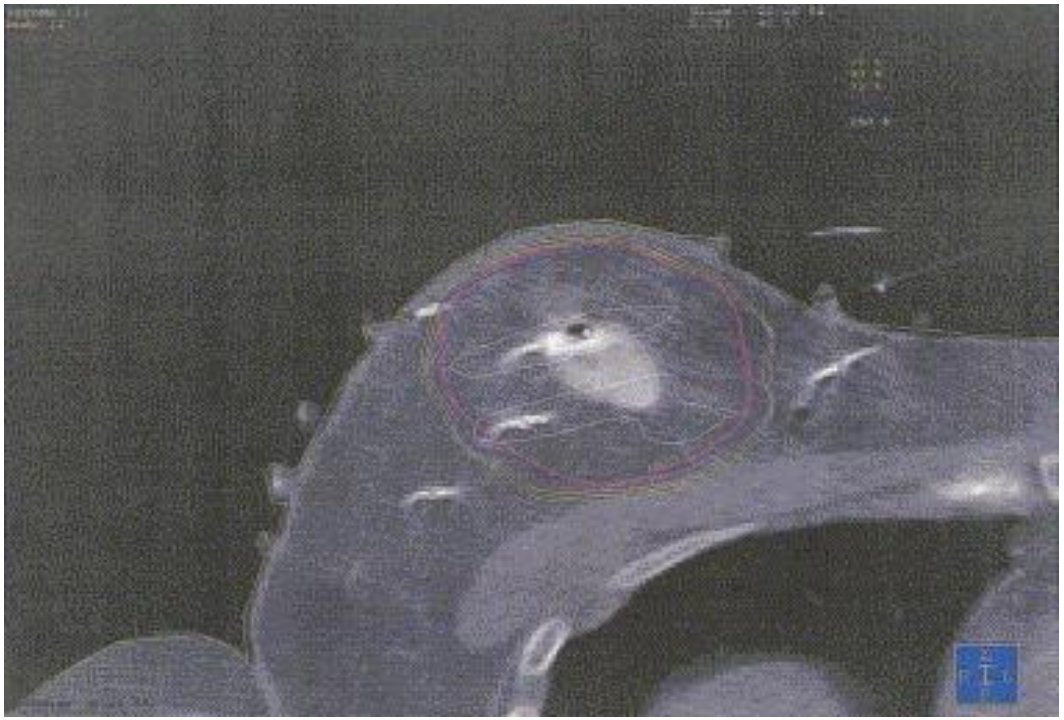

BEAUMONT HOSPITAL R.O.
MC3
1 22B
H/SP
04-AUG-95
13:43:07
DUO:040
SCAN 20
FRONT
LEFT
5 CM
TI 3
KV 125
AS 14
SL 8
GT 0
TP 157
W 320
C -51
TREATMENT PLANNING

CT-guided implantation

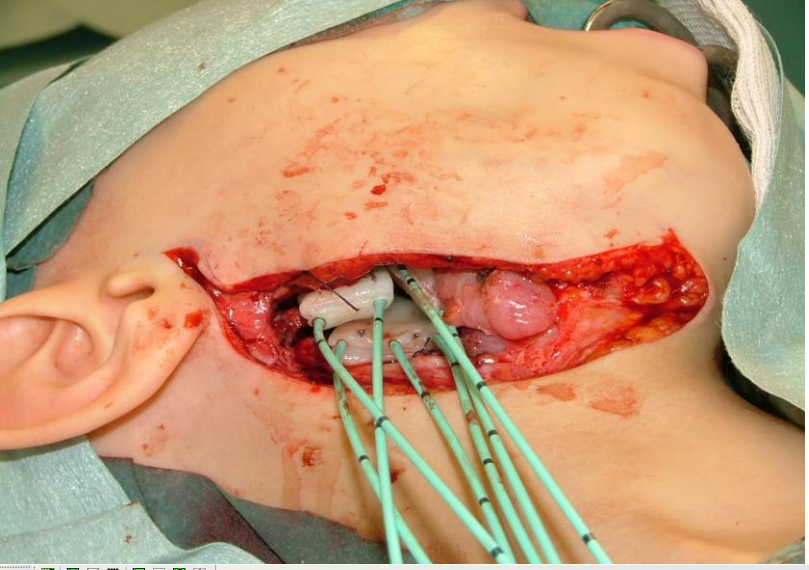




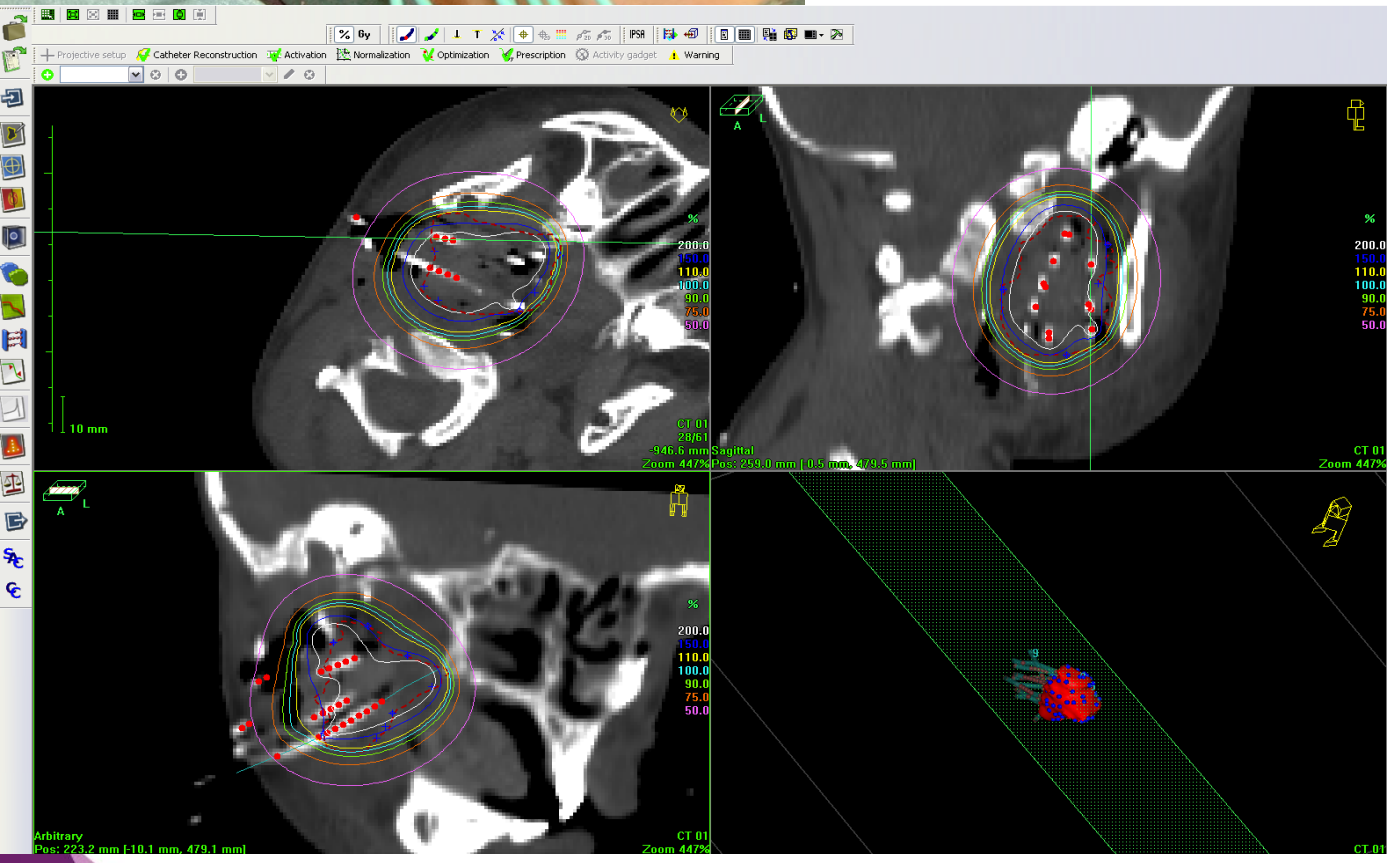
Lumpectomy cavity

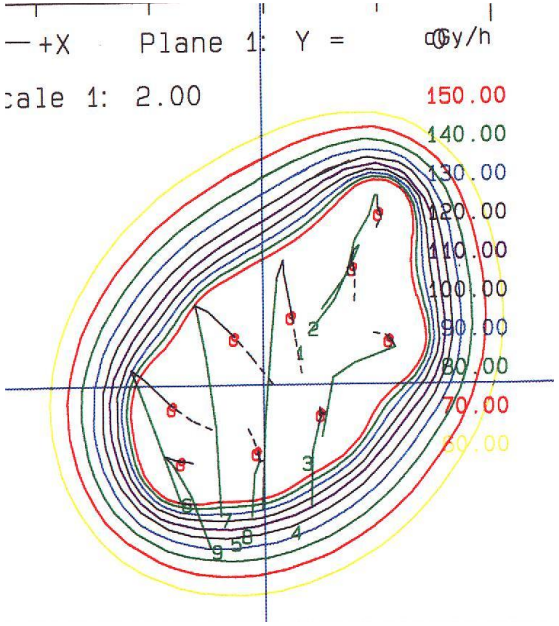
CTV

R.K. Das Int J Radiat Oncol Biol Phys, 2004;59:1224-1228



Present





Past

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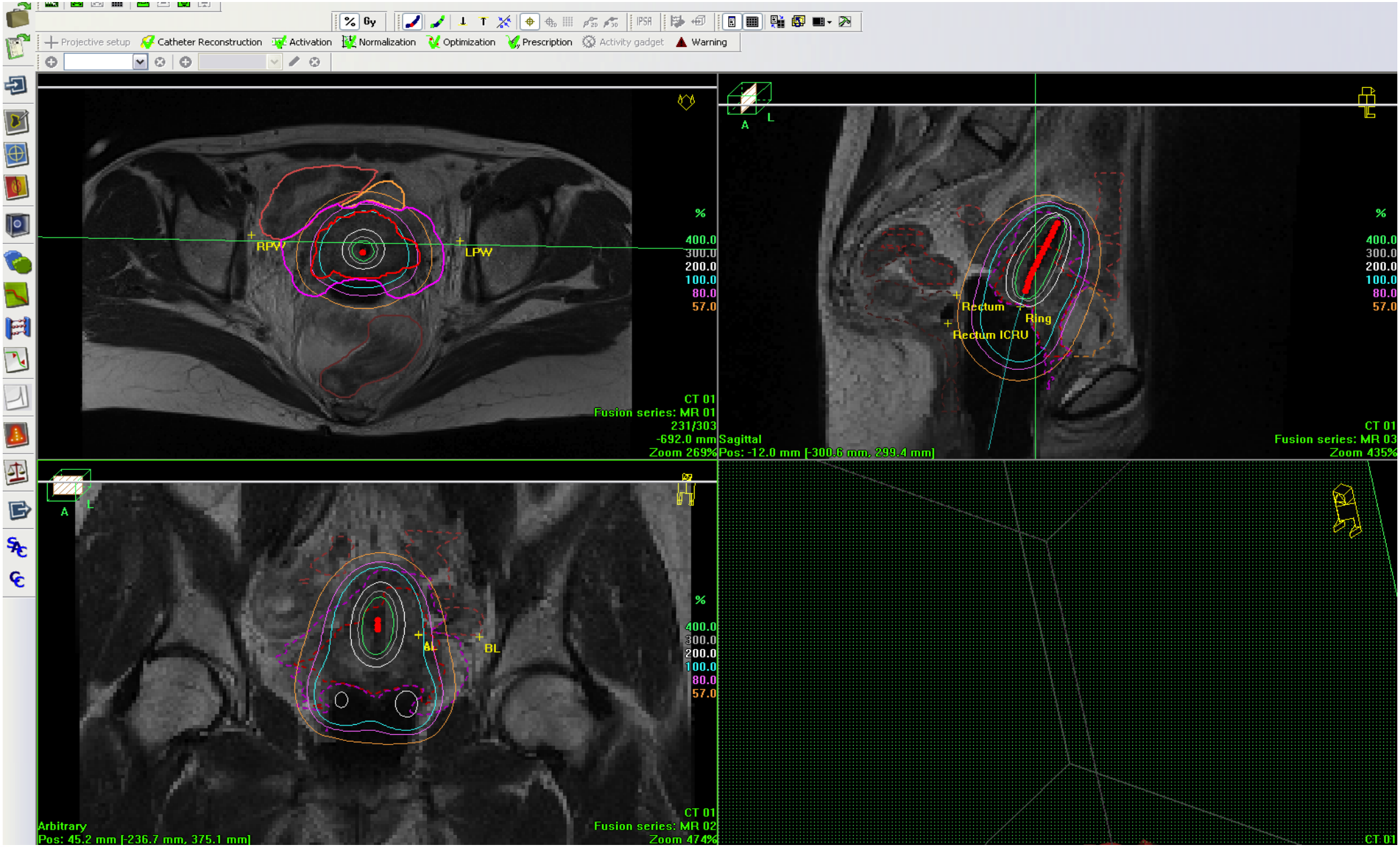

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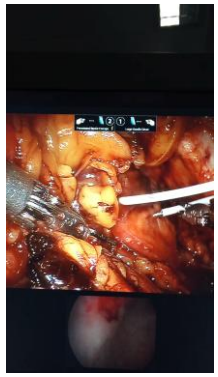
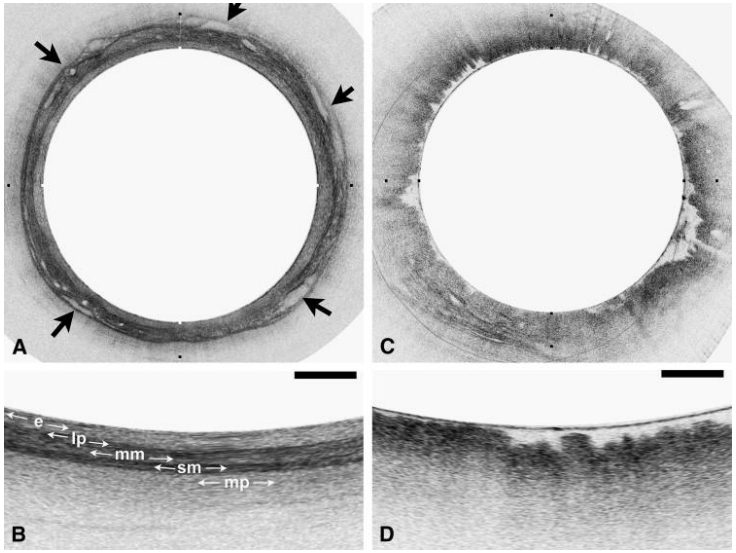
Optical Imaging

- White light endoscopy



- Fluoroscene (emerging)

- Optical Coherence Tomography (emerging)



Suter et al. Gastrointestinal Endoscopy 2008

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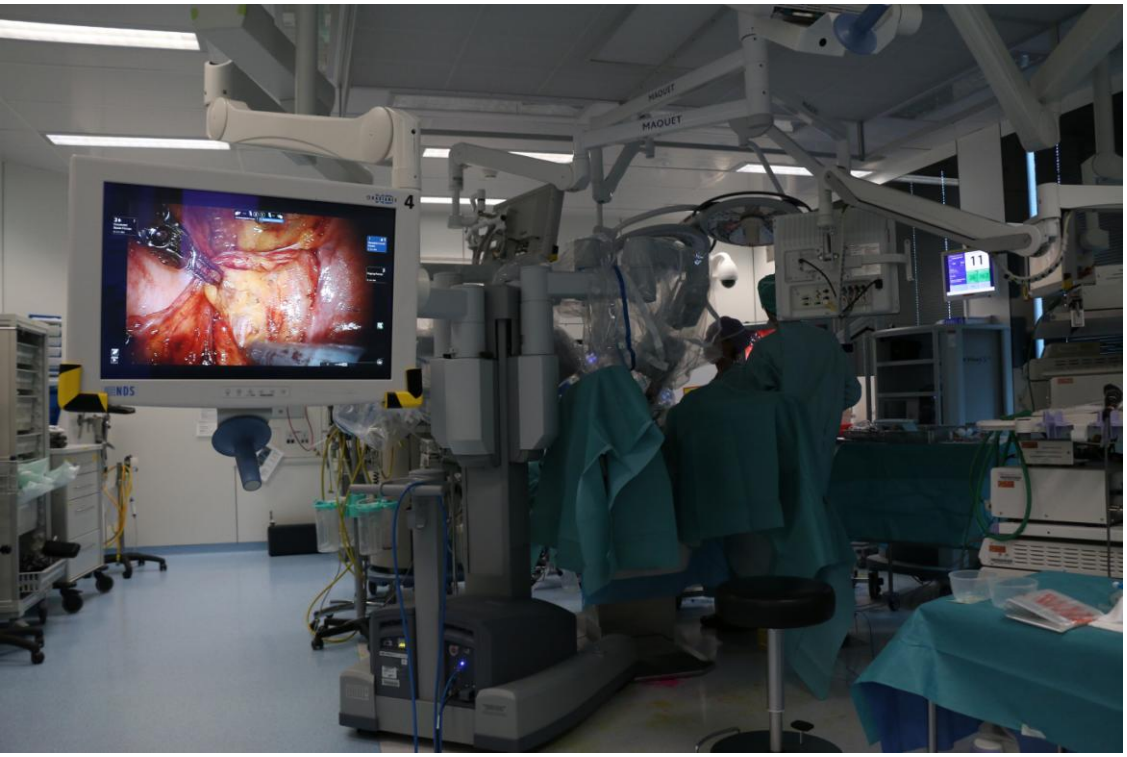
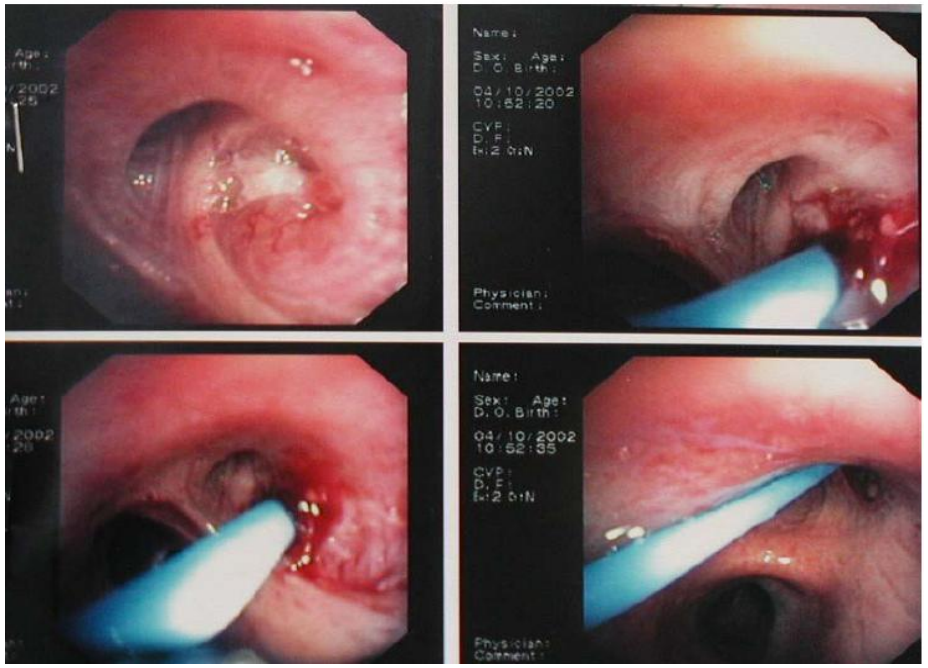


Laparoscopy



Bronchial endoscopy

Esophageal endoscopy

Ultrasound

- Easy to use while perfoming the implantation
- Visualization of needles
- Adaptation of needle position
- Usable in every operation room

- Except for prostate, not connected to a planning system

Ultrasound

Applicable for:

- Prostate
- Anal canal
- Paravaginal
- Cervix
- Breast

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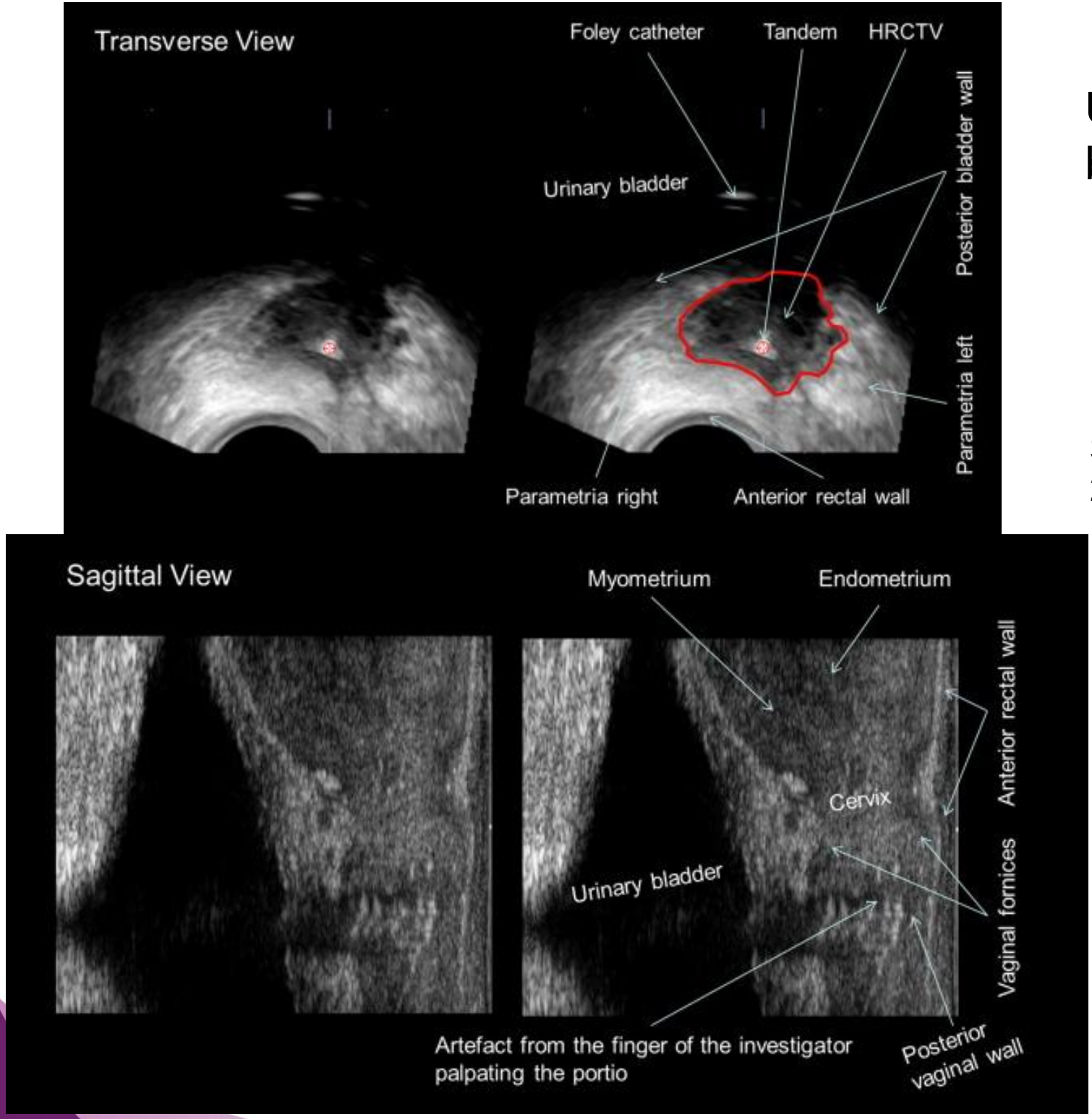
US for cervical brachytherapy



Schmid et al. Radiother Oncol 2016;120:467-472

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Functional Ultrasound (multiparametric)

- Contrast-enhanced Ultrasound
- Doppler
- Elastography

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Sonovue (Bracco) contrast agent

Philips IU22 ultrasound device

Contrast Enhanced Ultrasound Microvessel Imaging

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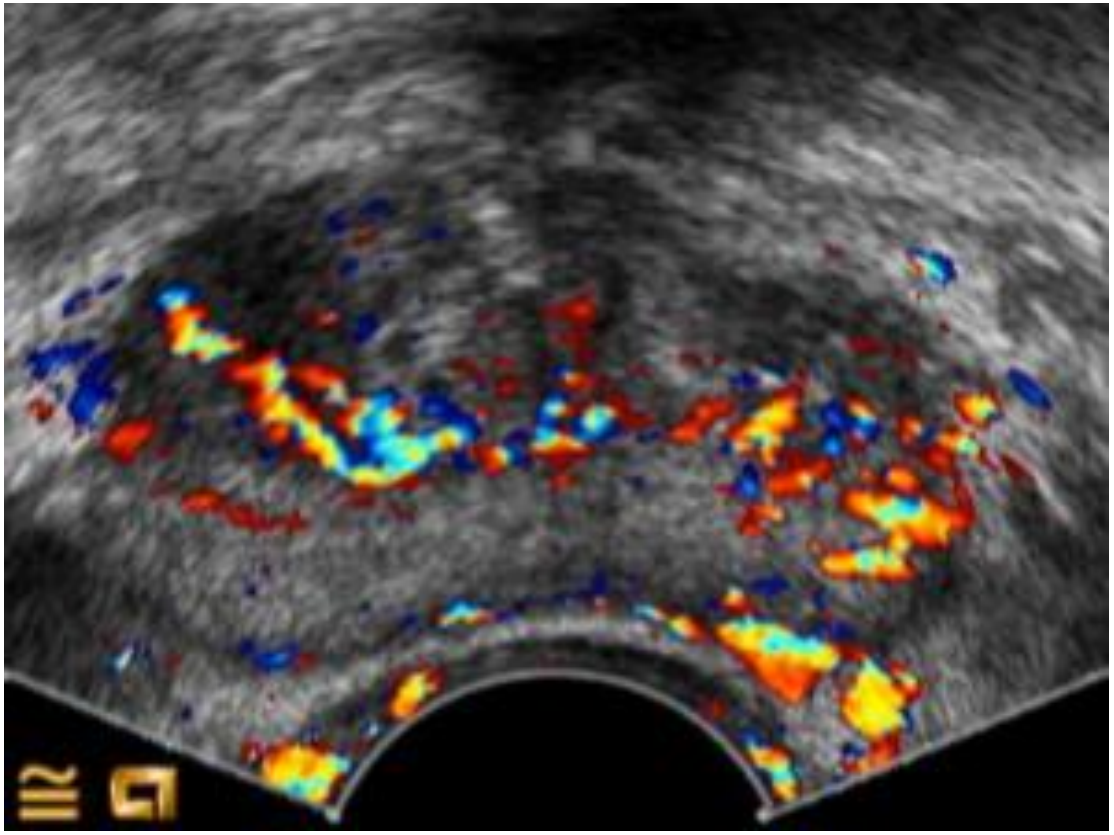
Doppler Ultrasound



X-ray and CT-scan

- Orthogonal X-ray imaging largely abandoned
- Fluoroscopic images at different angels
- CBCT
- CT-scan

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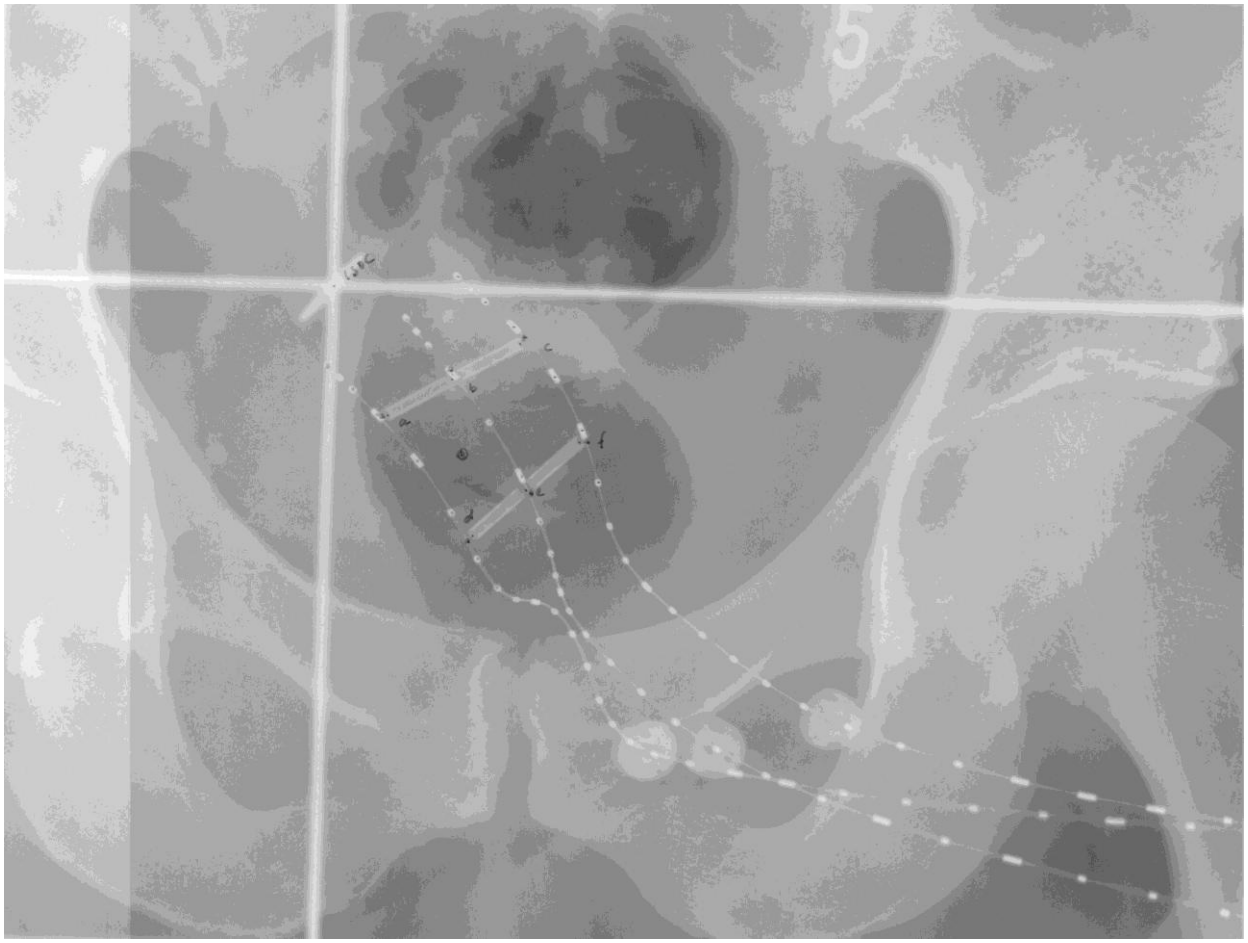
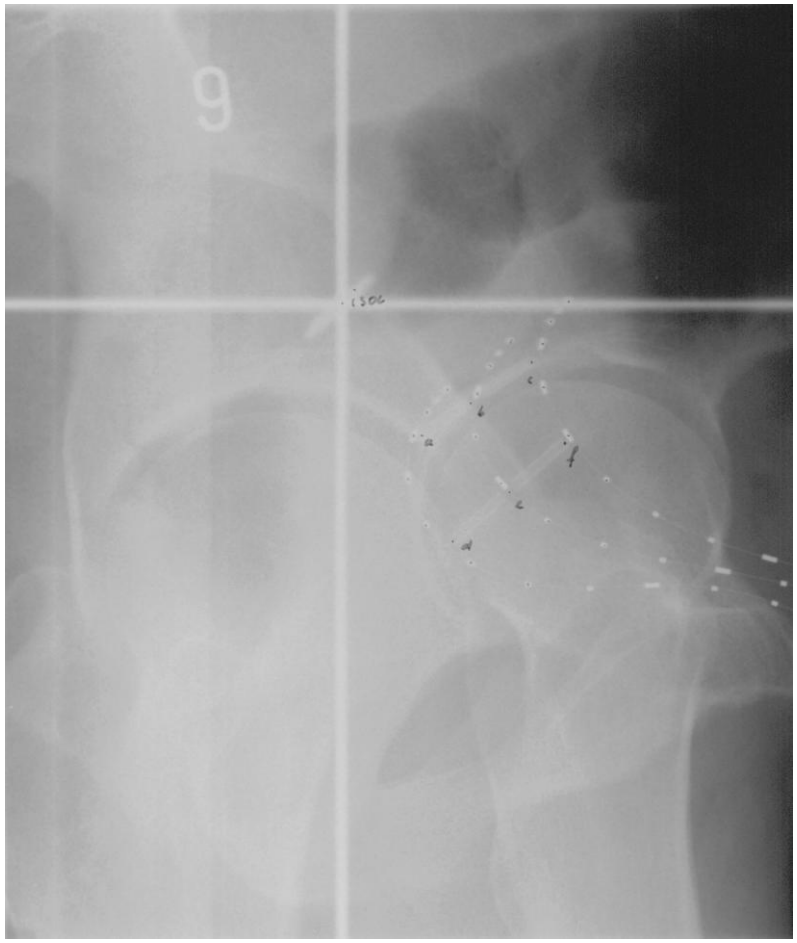
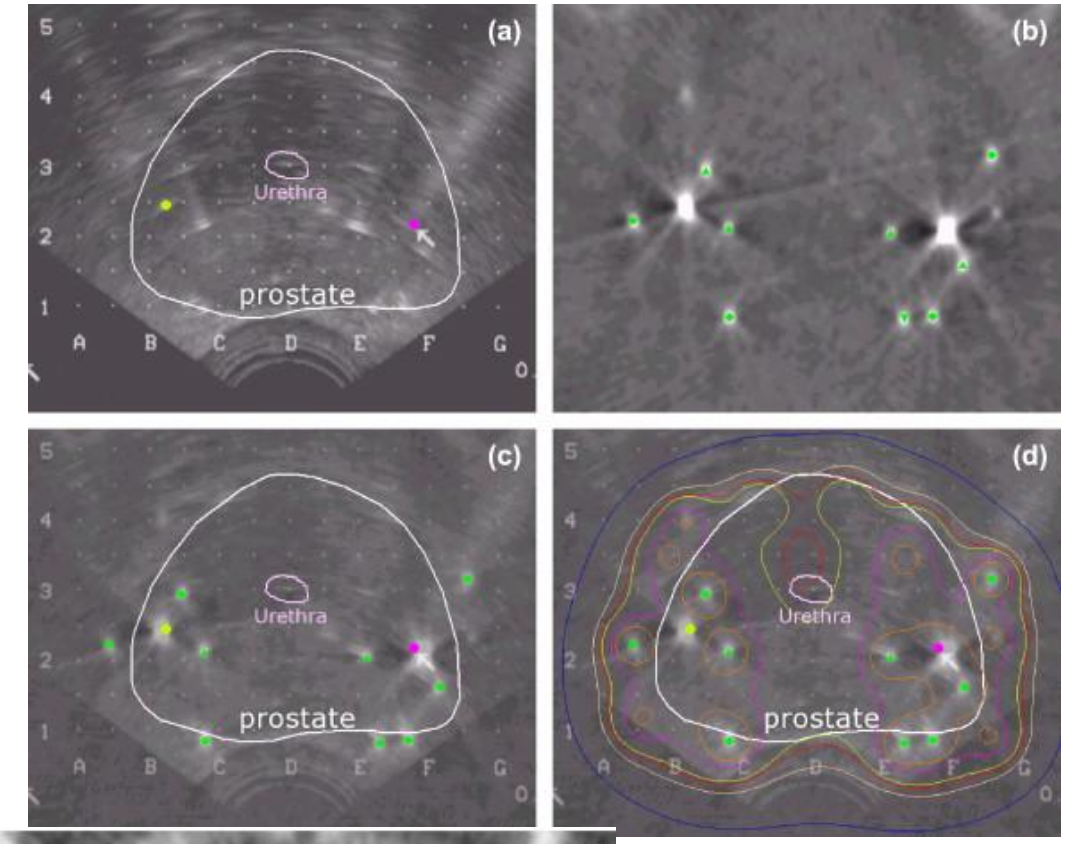
Orthogonal X-ray

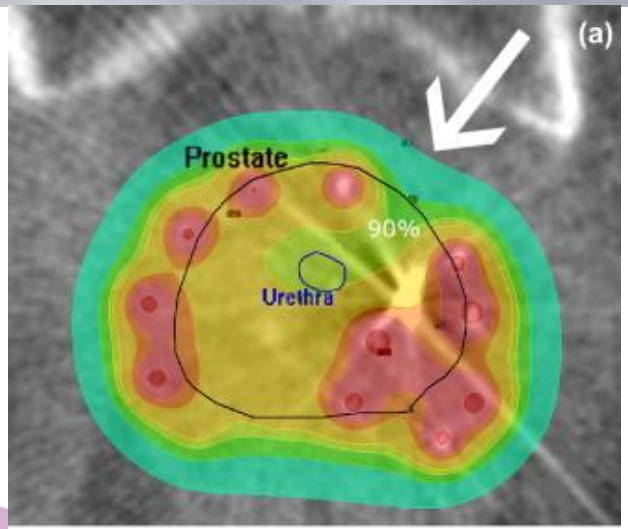


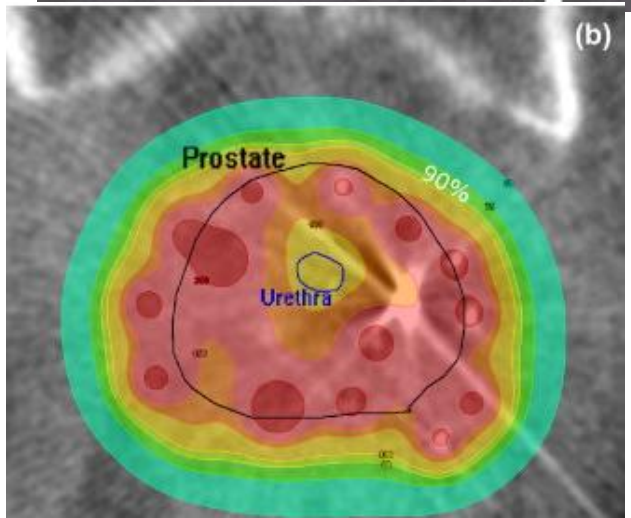


CBCT

Westendorp et al. Brachytherapy 2007;6:231-237







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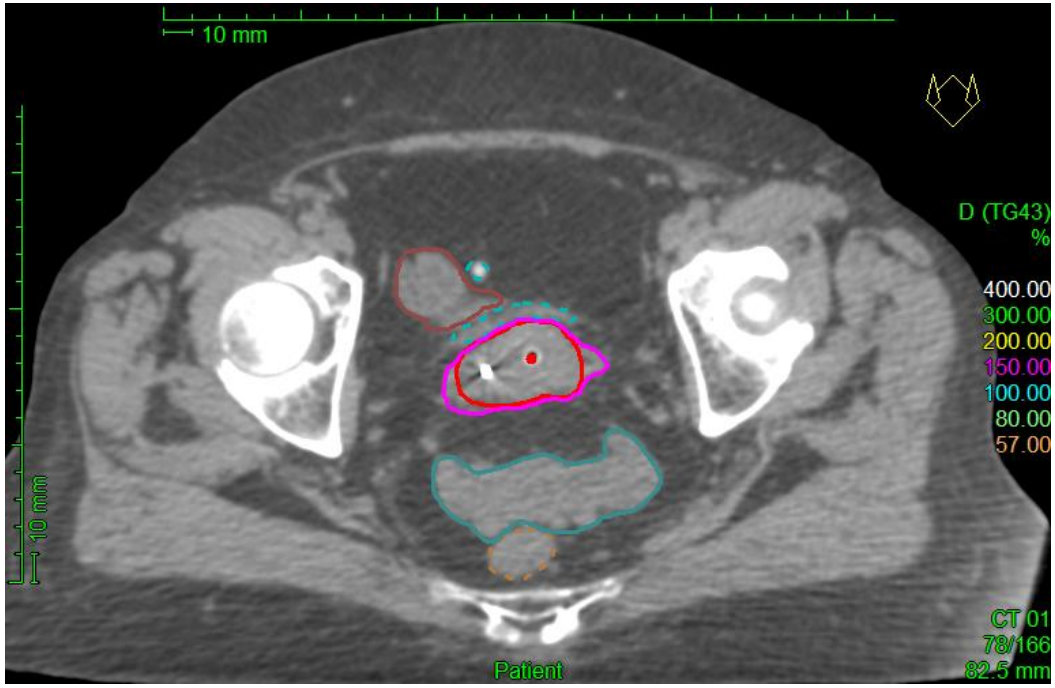
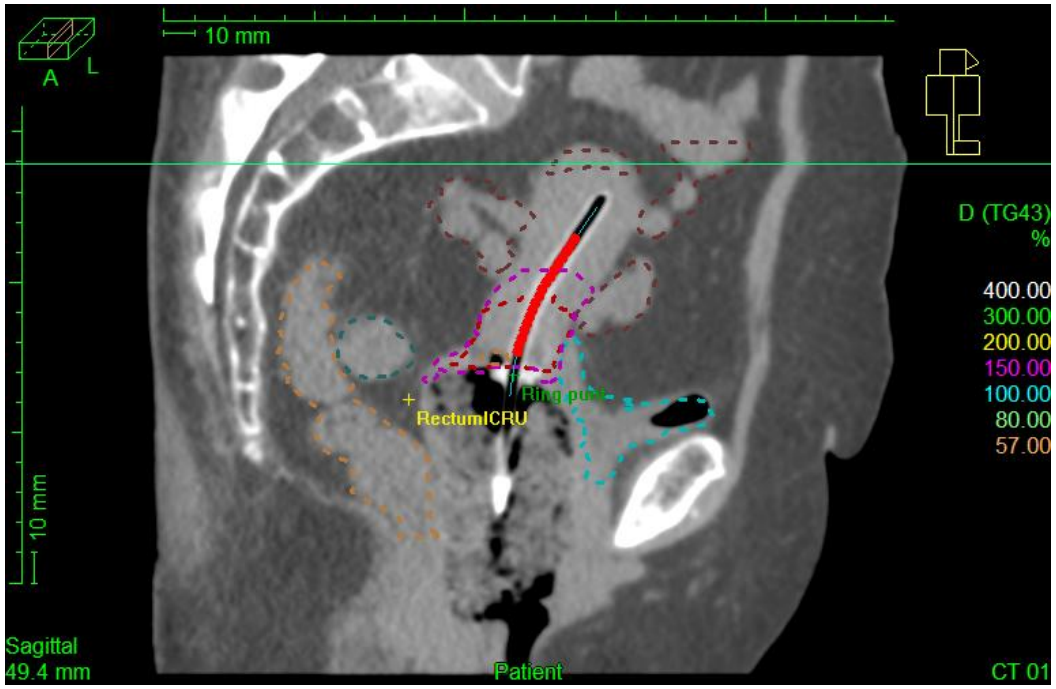
CT





Low soft tissue contrast (for target volume delineation)
Adequate for OAR contouring
Adequate for applicator localization

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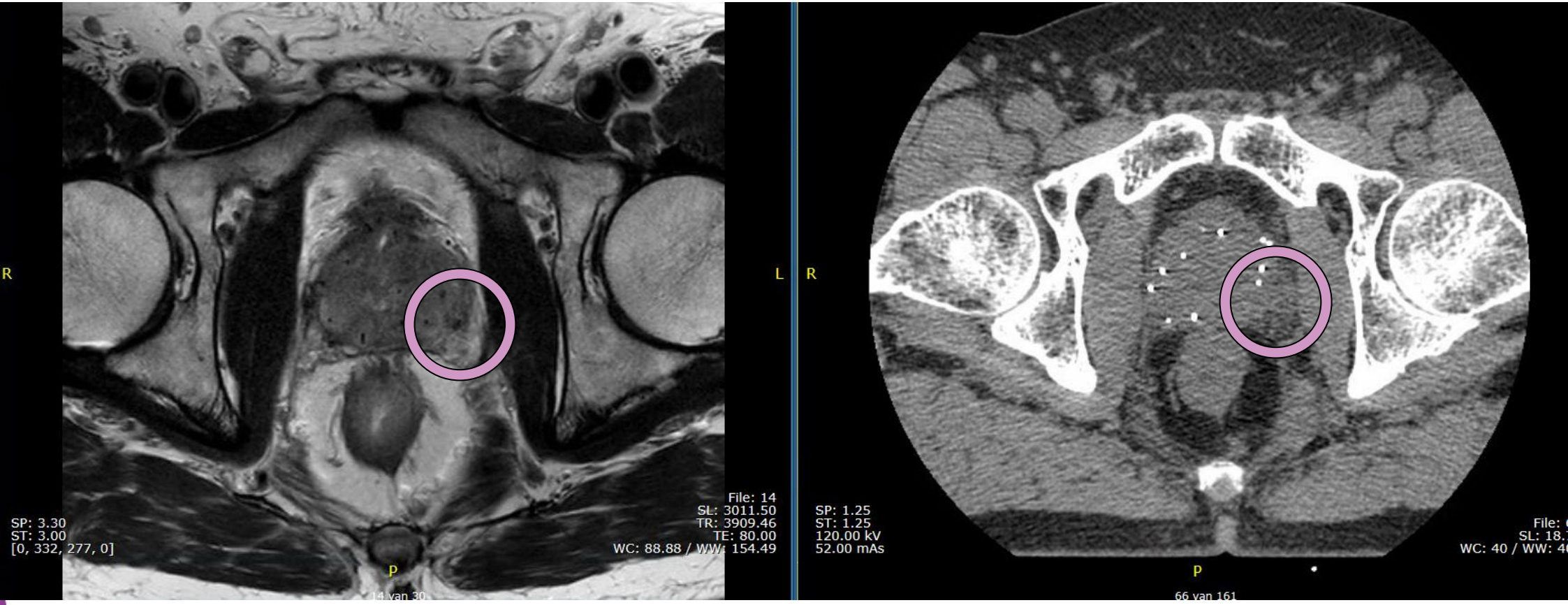
CT vs MR



Contouring on CT is influenced by position of sources
D90 on CT usually higher than on MRI
Sources better visible on CT

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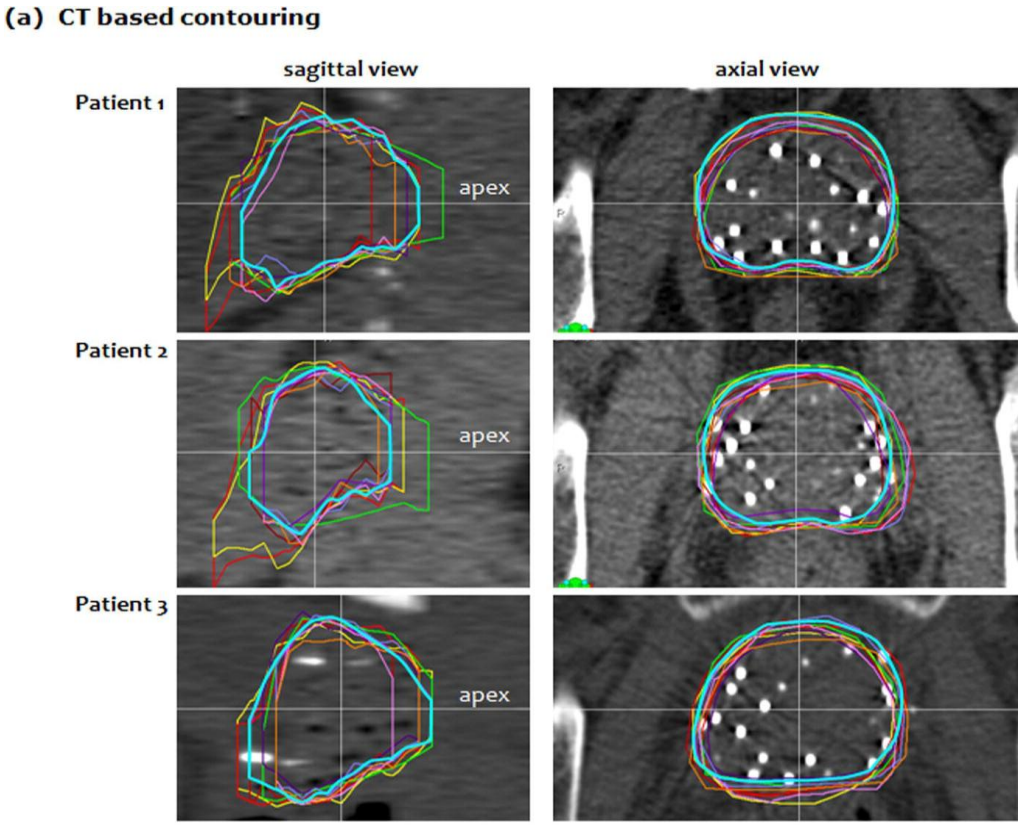
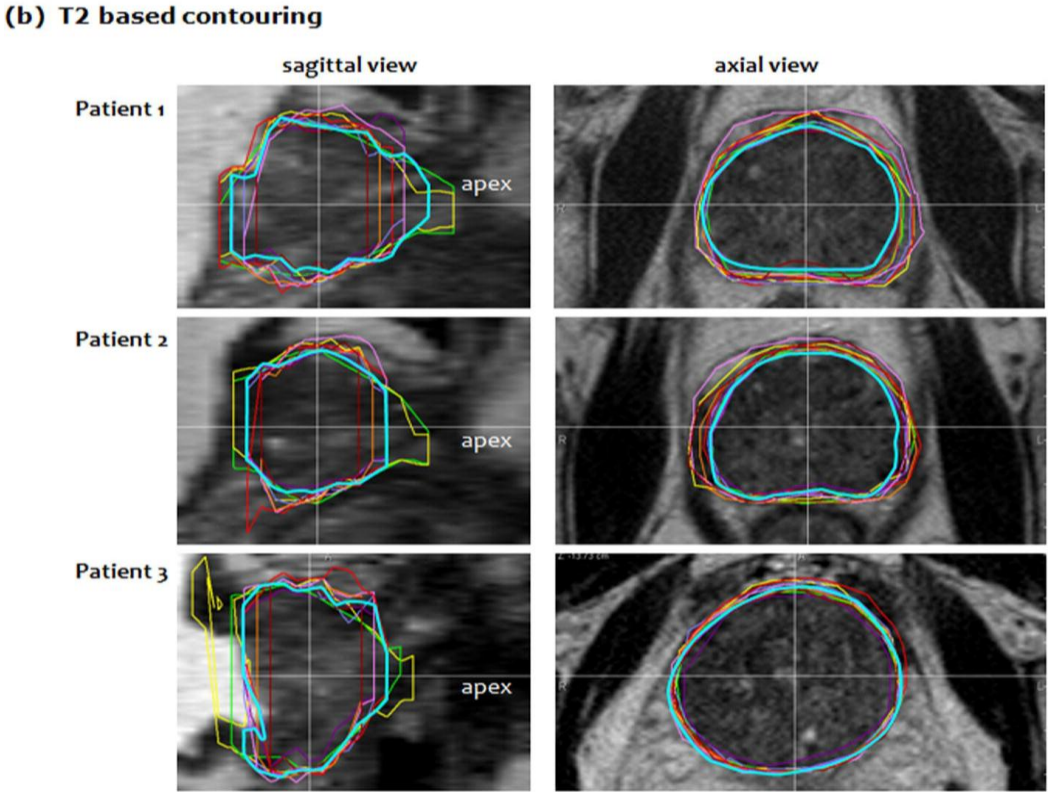
Source Localization CT vs. MR





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

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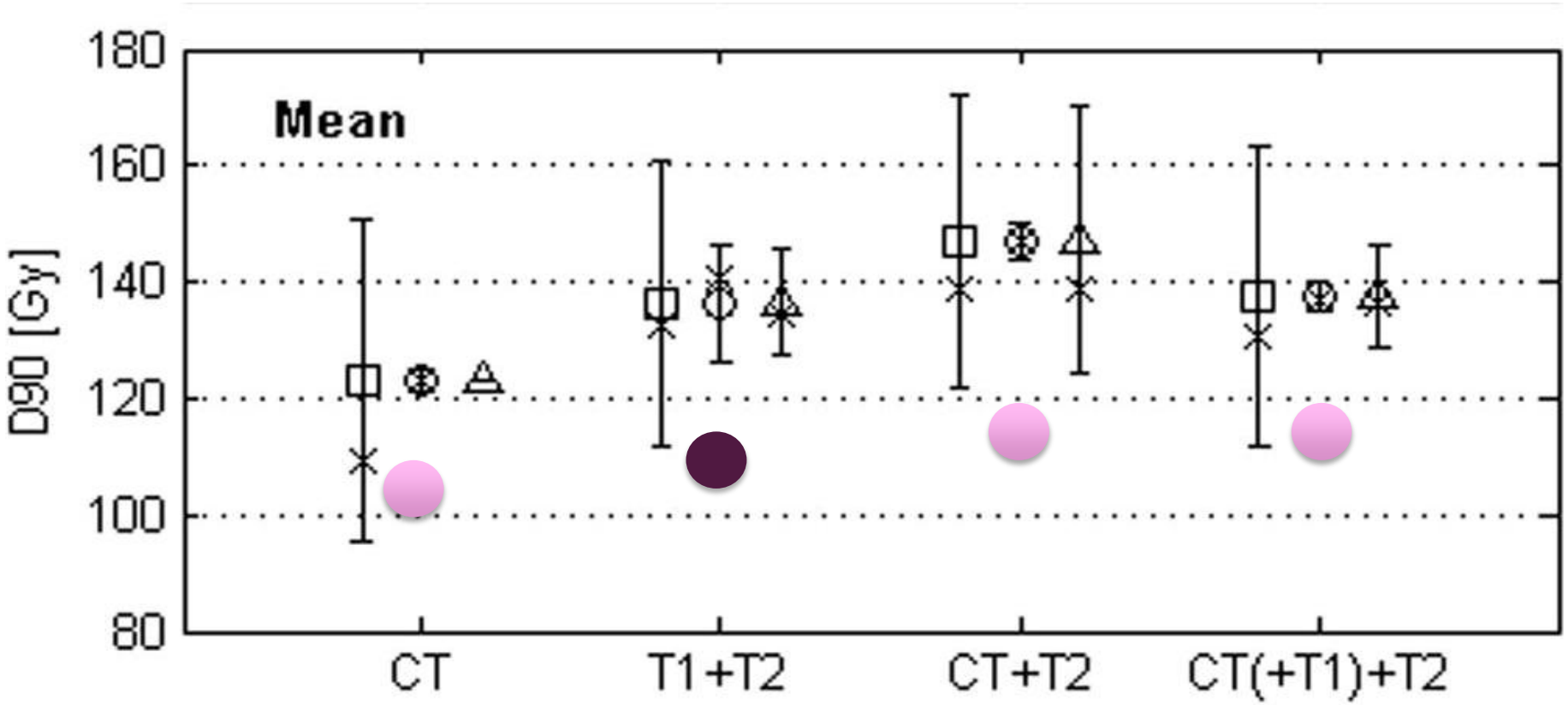
Seed Reconstruction Prostate Brachytherapy



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

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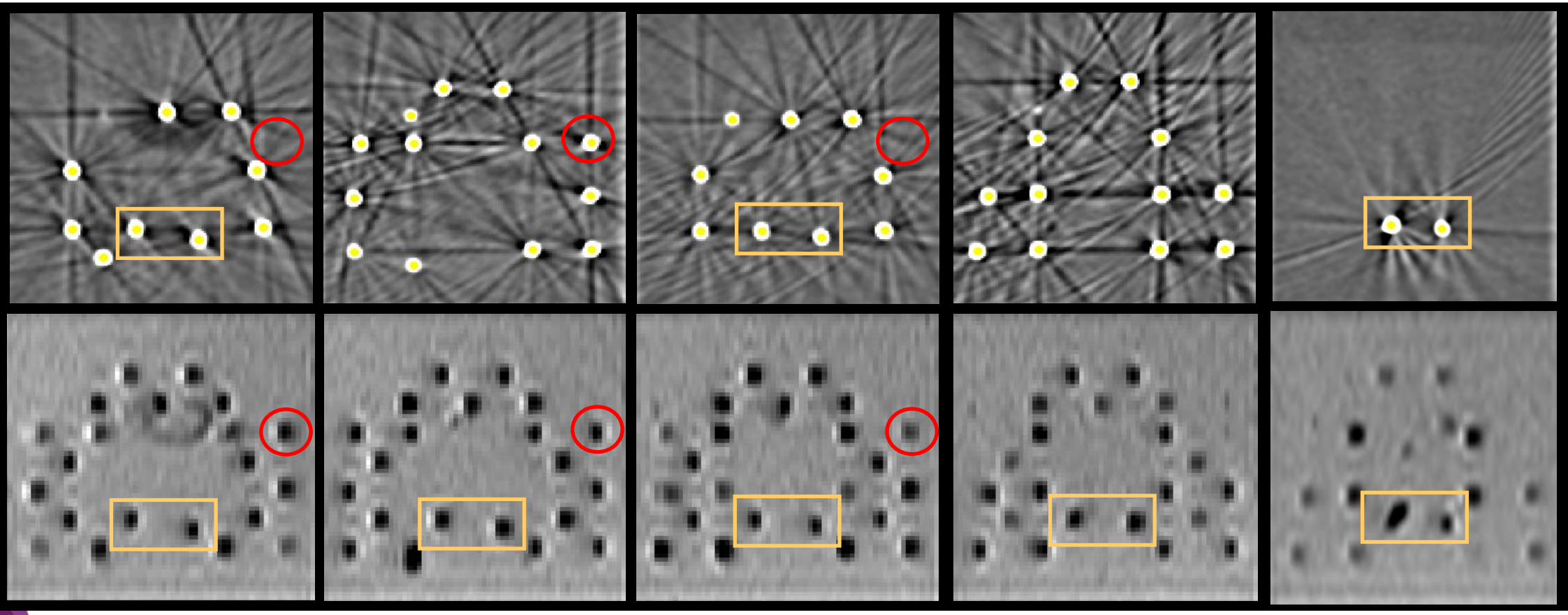
Positioning Deviation

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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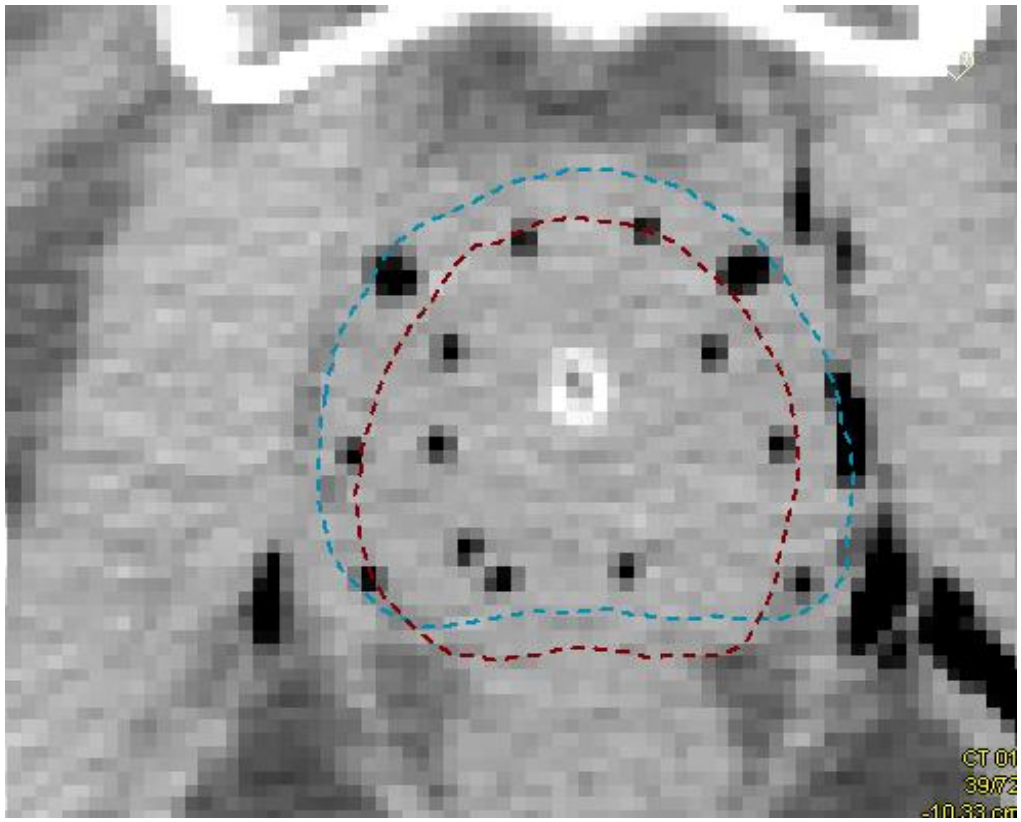
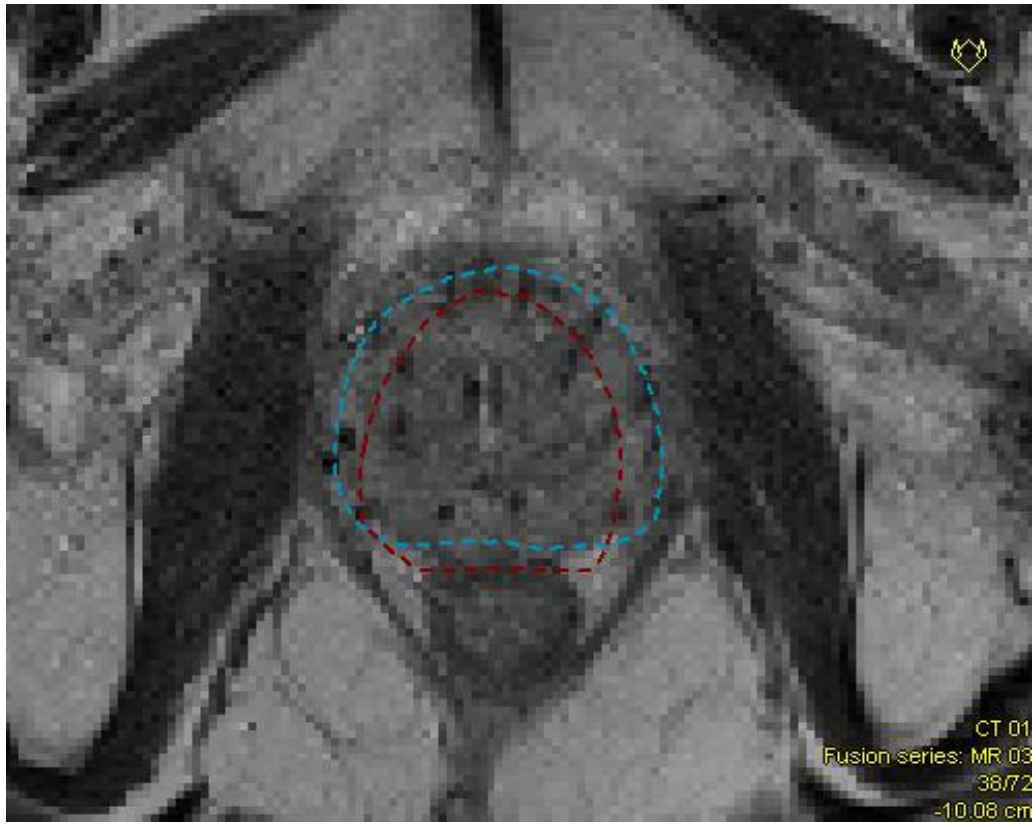
Comparison Treatment Planning on CT vs MR





PTV-MRI vs PTV-CT

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

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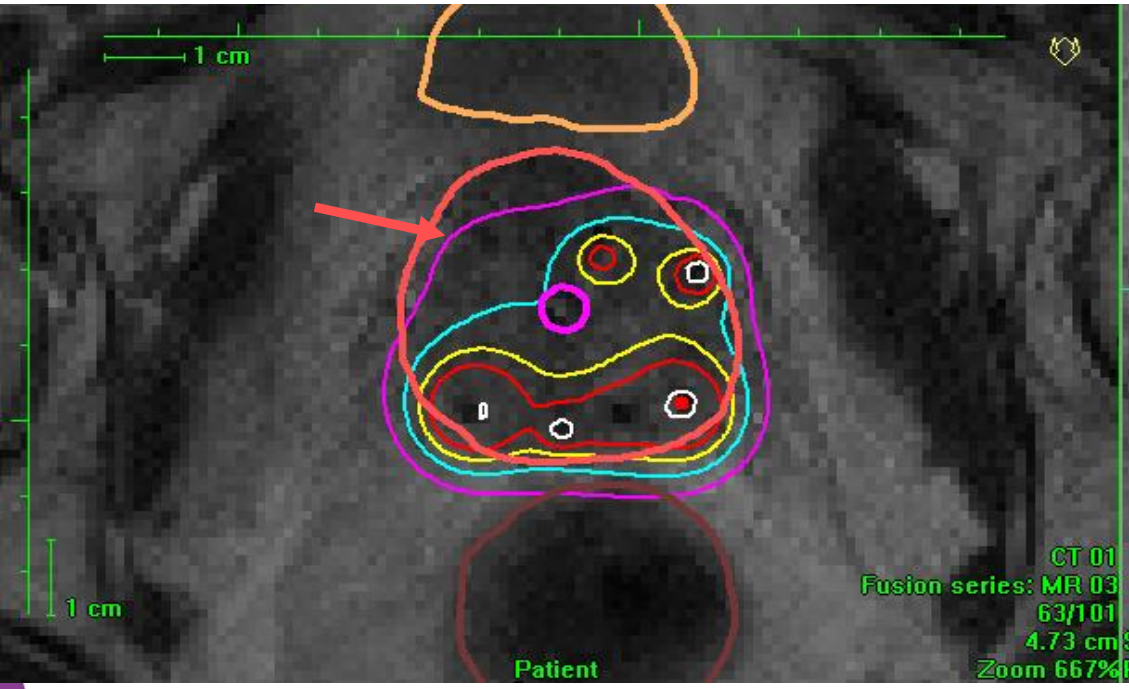
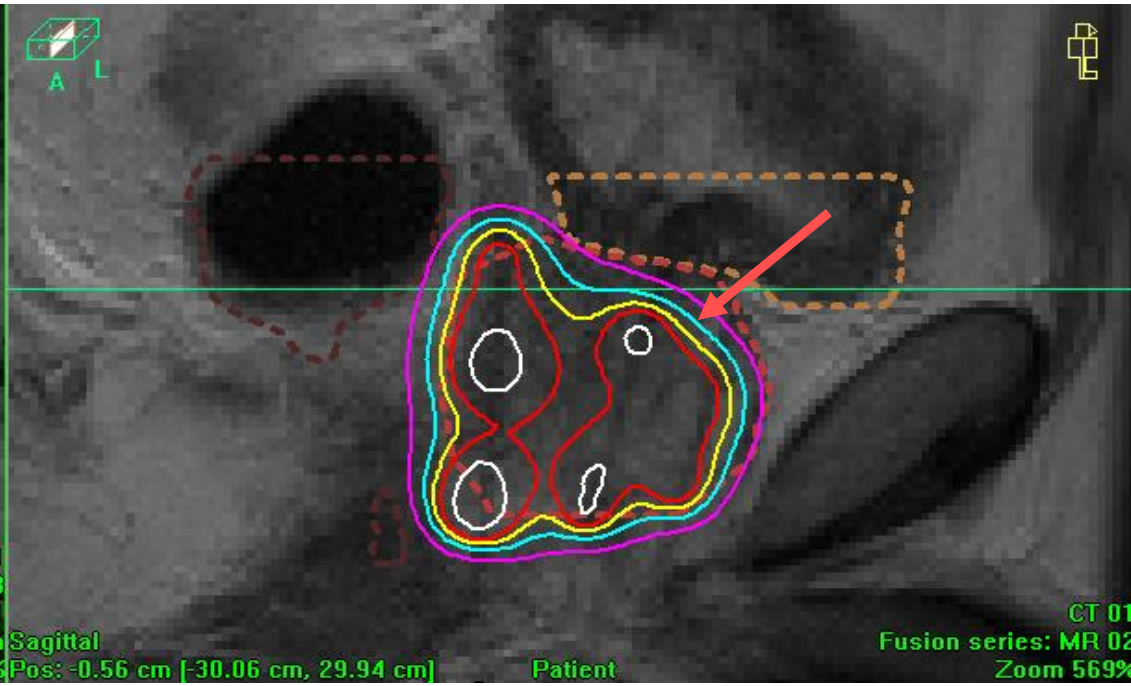
Example

CT-plan, projected on MRI contours:

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



(1)



(2)

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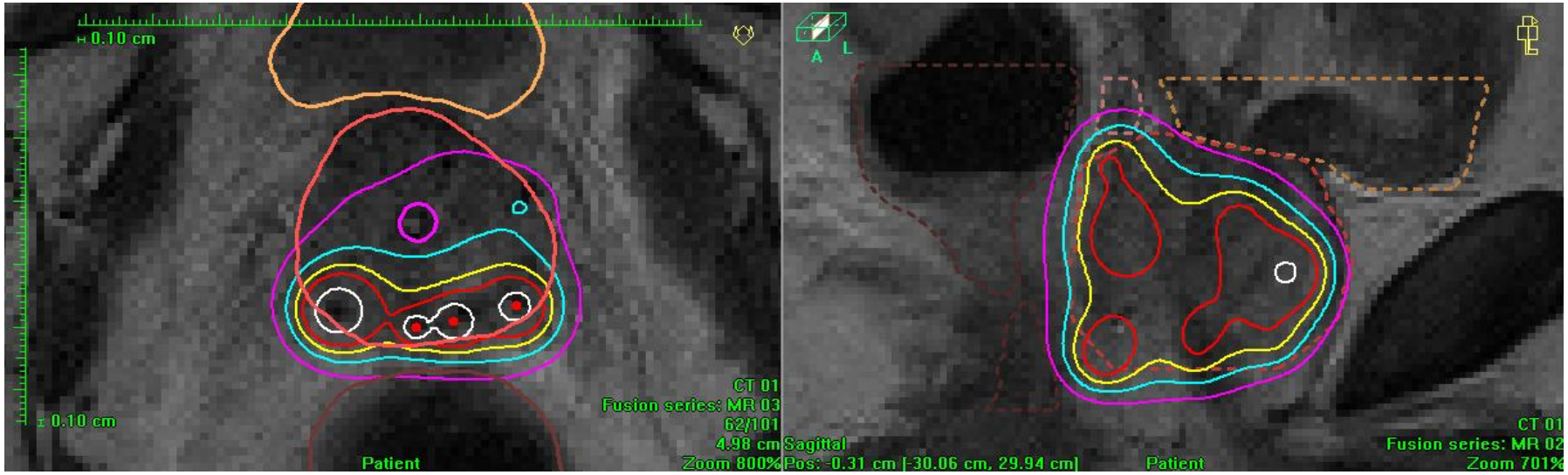
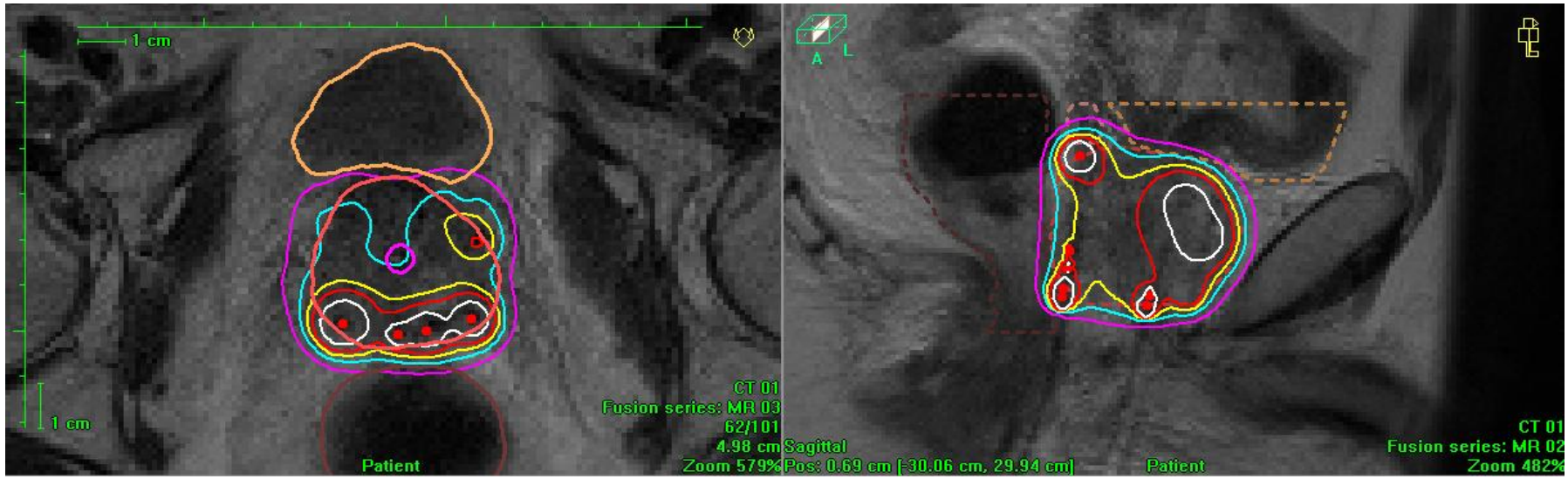
Example: Improved coverage with MRI-based planning

CT-based plan



MRI-Based plan



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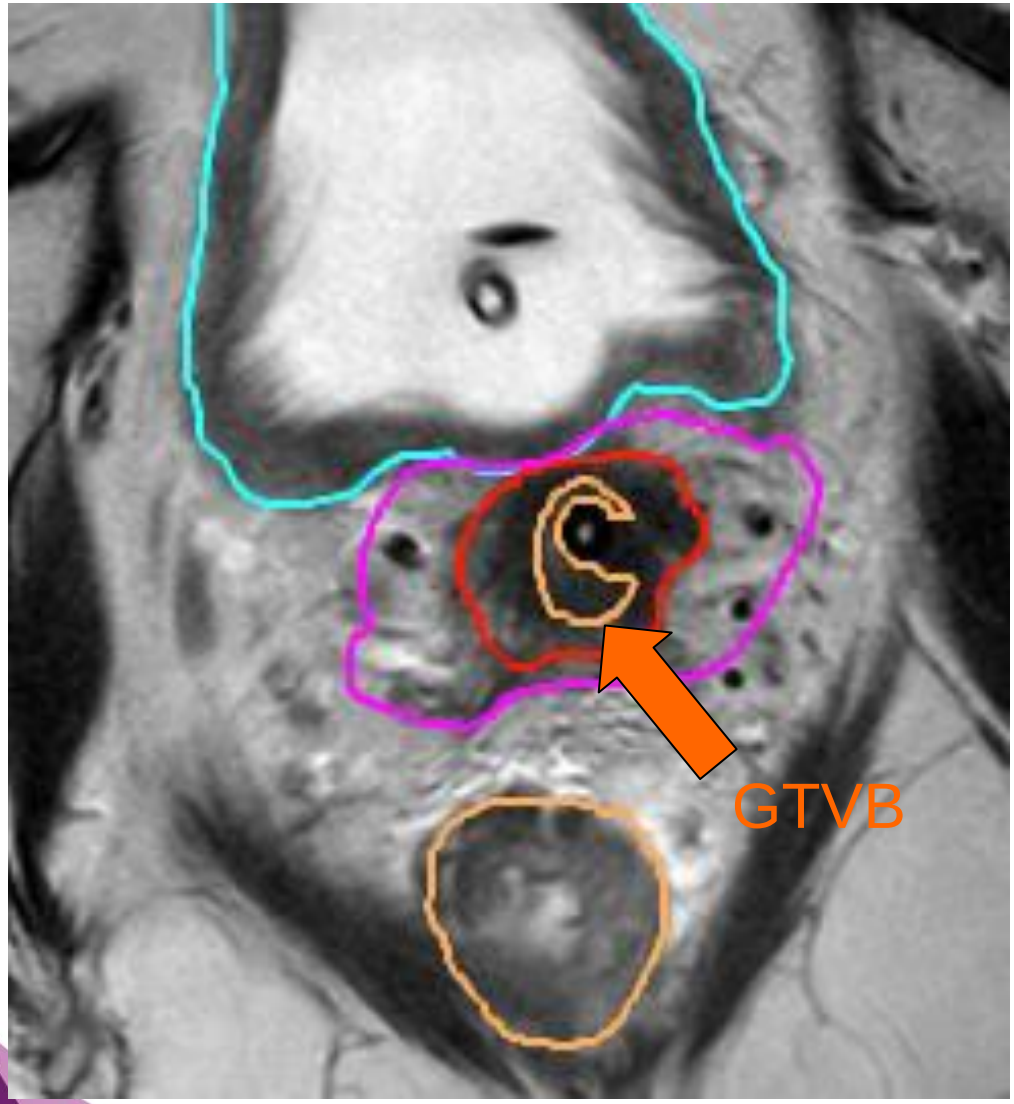
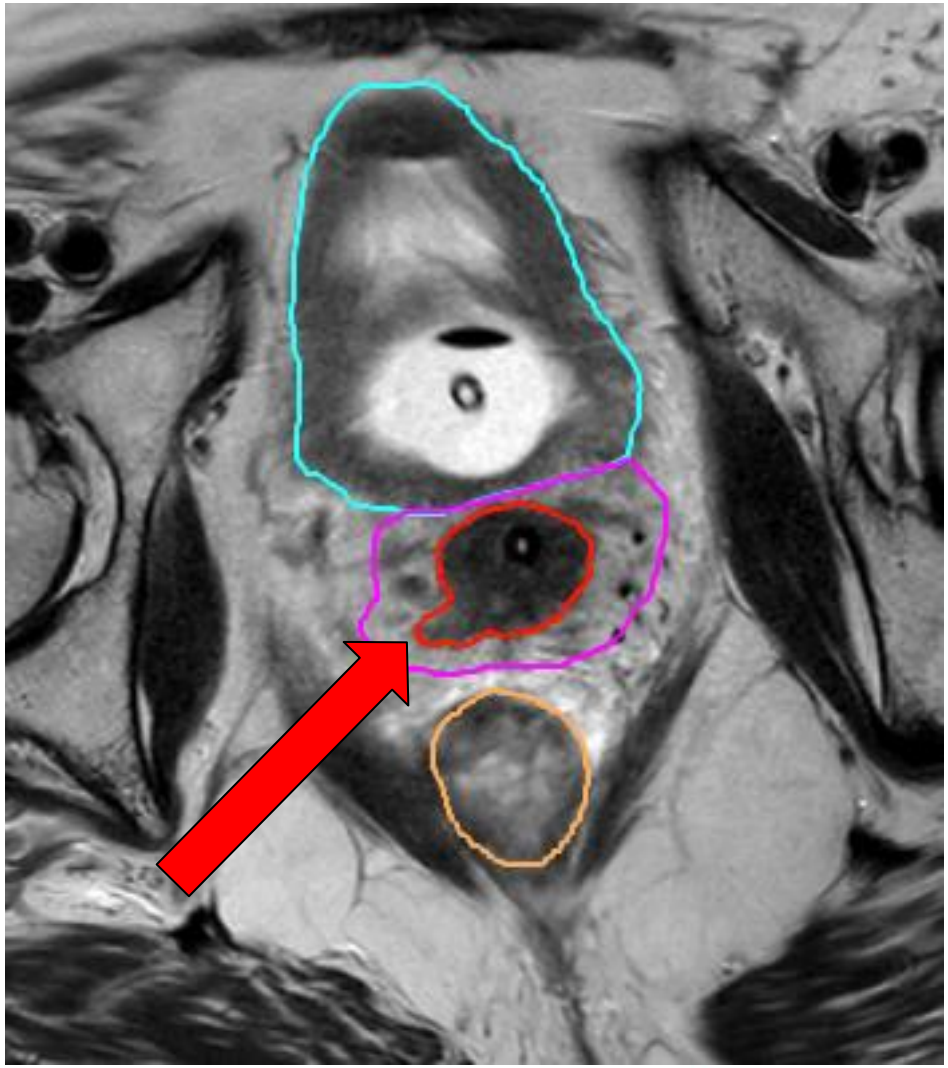
MRI

- High tissue contrast, ideal for target volume contouring
- Demands MR-compatible applicators
- Not widely available
- Localization of applicator (source track) is not easy
- Spatial fidelity can be compromised because of strong magnetic fields and magnetic susceptibility

MRI
High tissue contrast





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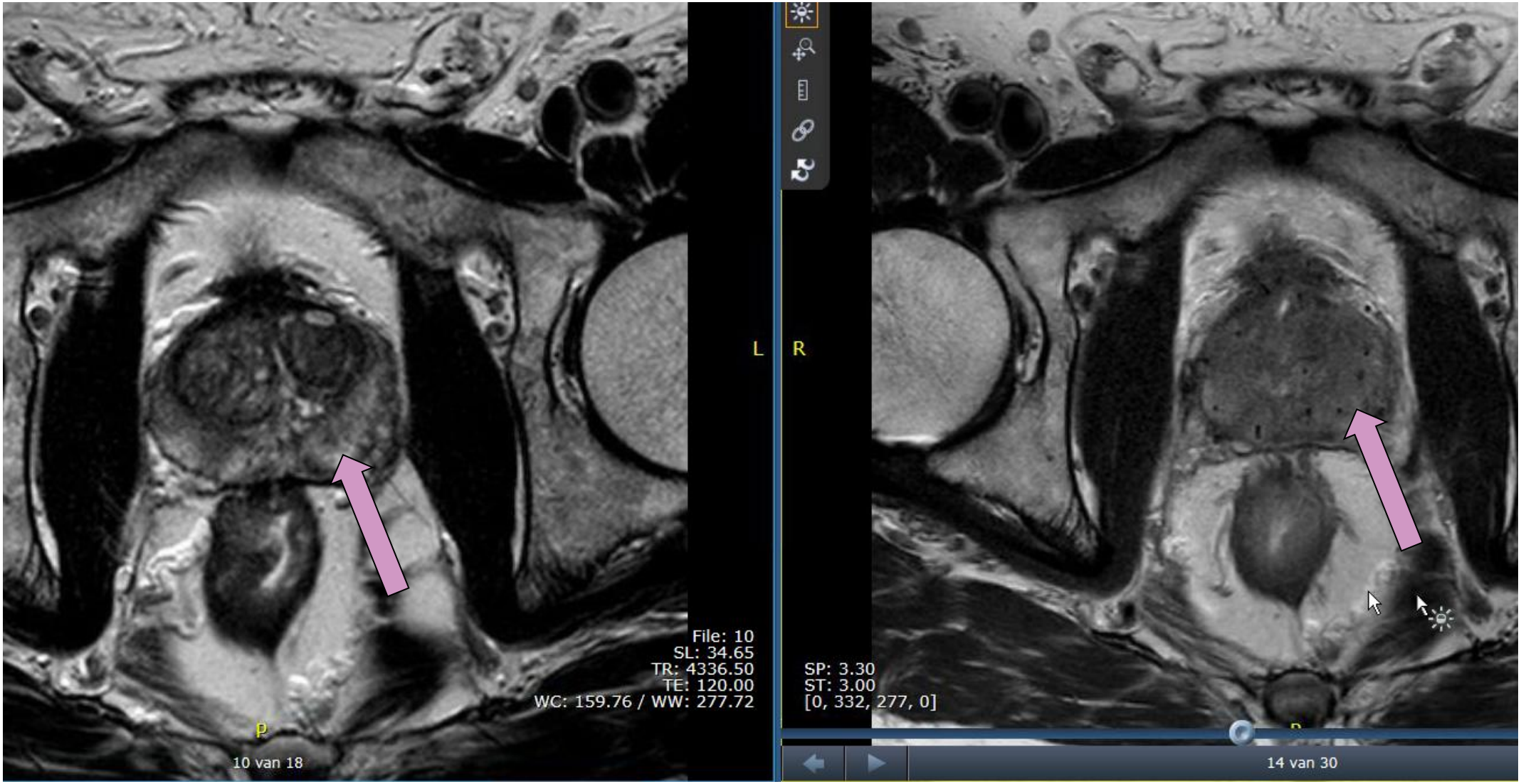

Pre-implantation

Post-implantation

Disappearance of peripheral zone

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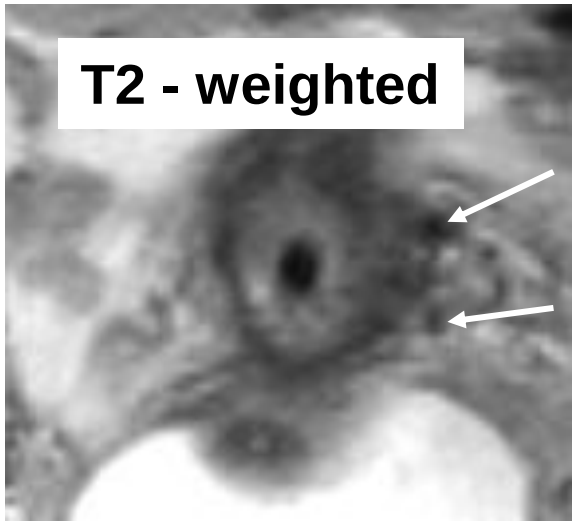
MRI

Balance between accurate target delineation and visibility of applicator

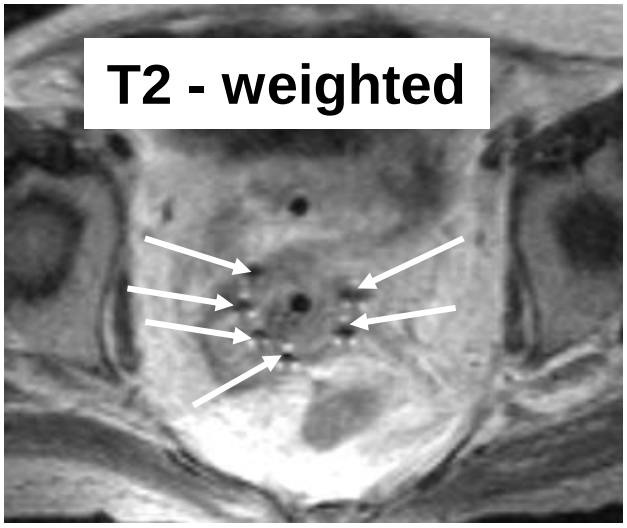
Solutions

- Reducing echo-time (TE) and increasing Proton density (PD)
- Make T2-images and separate PD image
- Registering fixed applicator geometries using identified landmarks

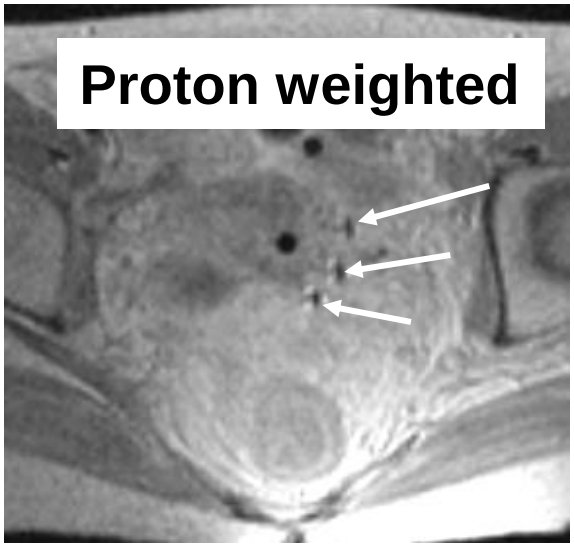
Needle Depiction

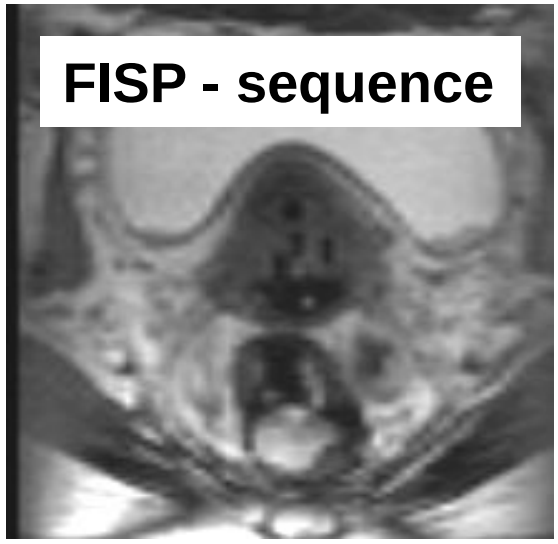


poor quality



excellent depiction





improvement for needles / loss of soft tissue depiction quality

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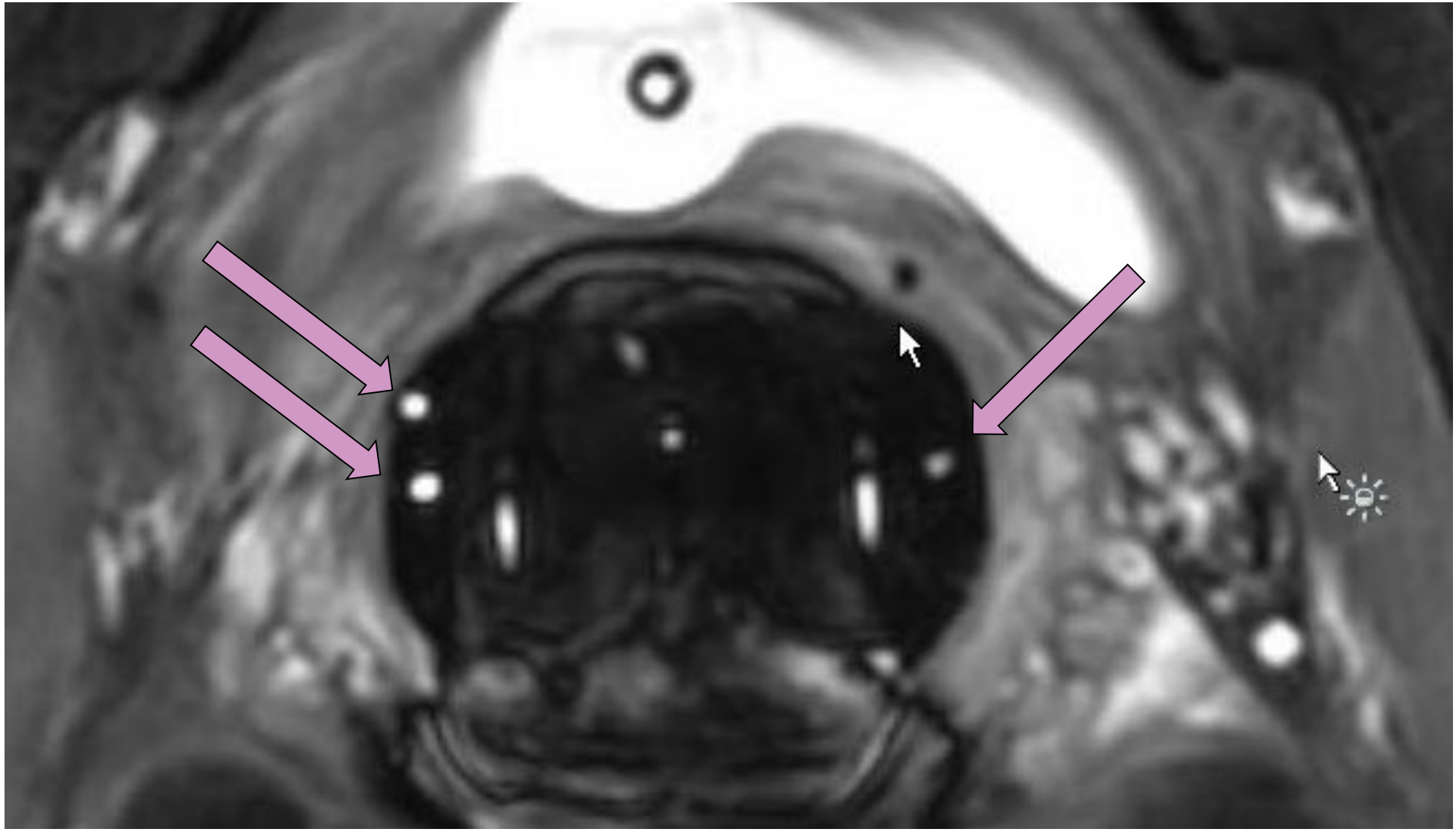
Applicator registration



MR Protocol

Specifically designed for pelvic brachytherapy

	1	2	3
Sequence name	Sag T2W	Tra T2W	Cor T2W
Sequence type	TSE	TSE	TSE
Scan time	5.09 min	5.36 min	3.39 min
Number slices	31	45	30
Slice thickness	3 mm	3 mm	3 mm
Slice gap	default	default	default
Scan direction	Sagital	Tranversal	Coronal
Fase direction	FH	RL	RL
TR	Shortest (4170 ms)	Shortest (5995 ms)	Shortest (3909 ms)
TE	80 ms	80 ms	80 ms
Flip degree	90°	90°	90°
NSA	1	1	1
FOV	180 x 180 mm	200 x 200 mm	200 x 200 mm
Acq matrix	300 x 255 mm	332 x 276 mm	332 x 276 mm
Pixel-/voxel size	0.6 x 0.7 mm	0.6 x 0.7 mm	0.6 x 0.7 mm
Bandwidth (WFS(pix)/BW(Hz))	0.990/438.6	0.992/437.8	0.992/437.8
Sense	-	Yes	Yes
Sense factor	-	RL: 1.3	RL: 1.3
Turbofactor	19	19	19
Fat Supression	-	-	-

Neither ESTRO nor anybody else can accept any legal responsibility or liability for using this example MR protocol.

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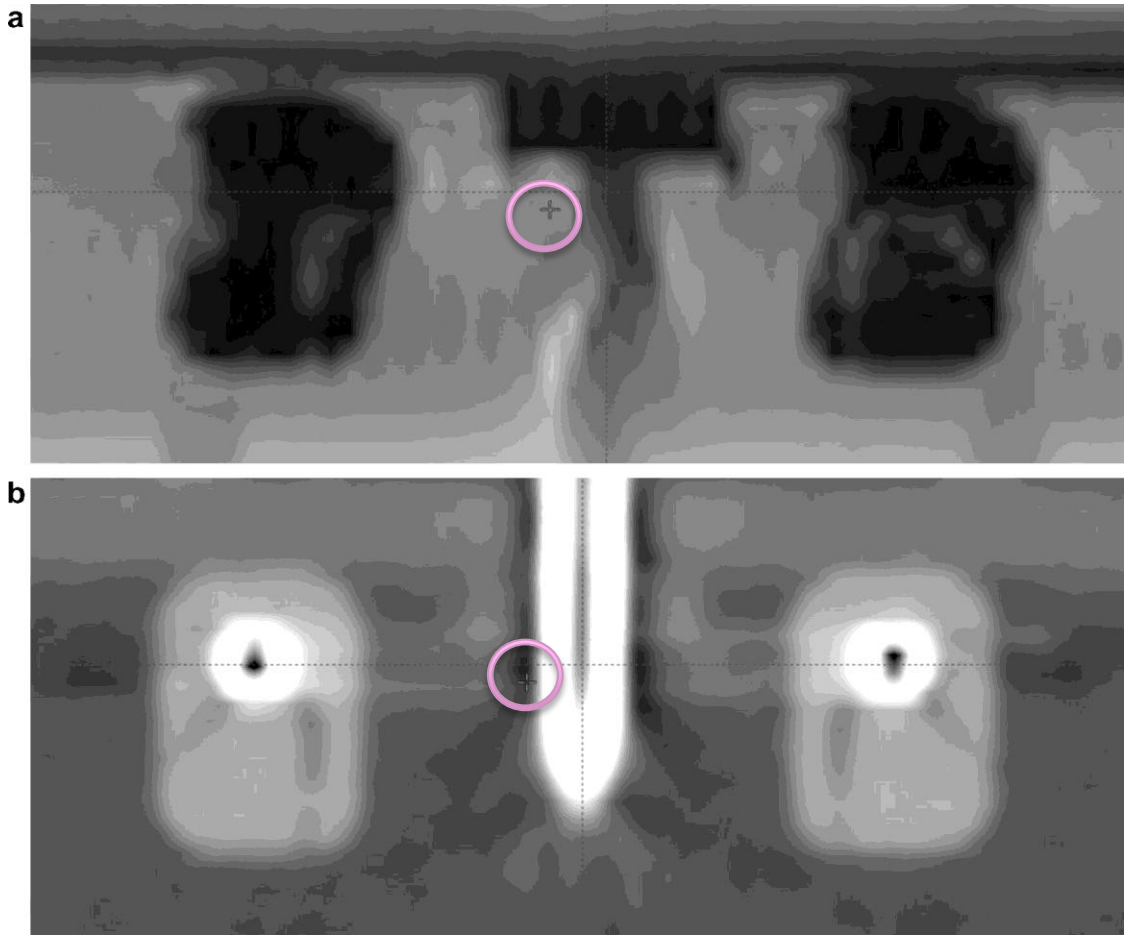
MR Distorsions

T1W MRI

CT



Titanium applicator

Haack et al. Radiother Oncol 2009;91:187

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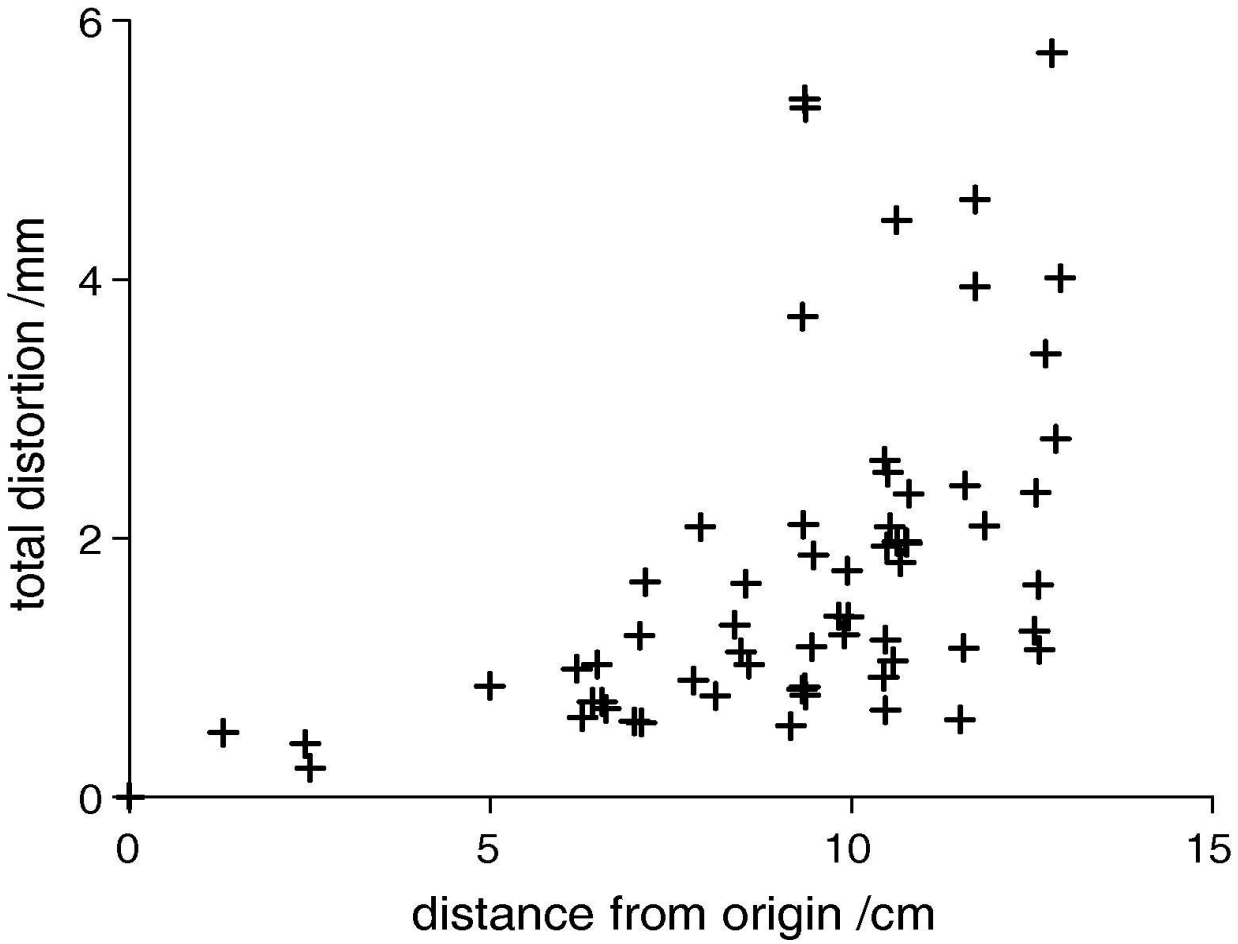
MR Distorsions



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

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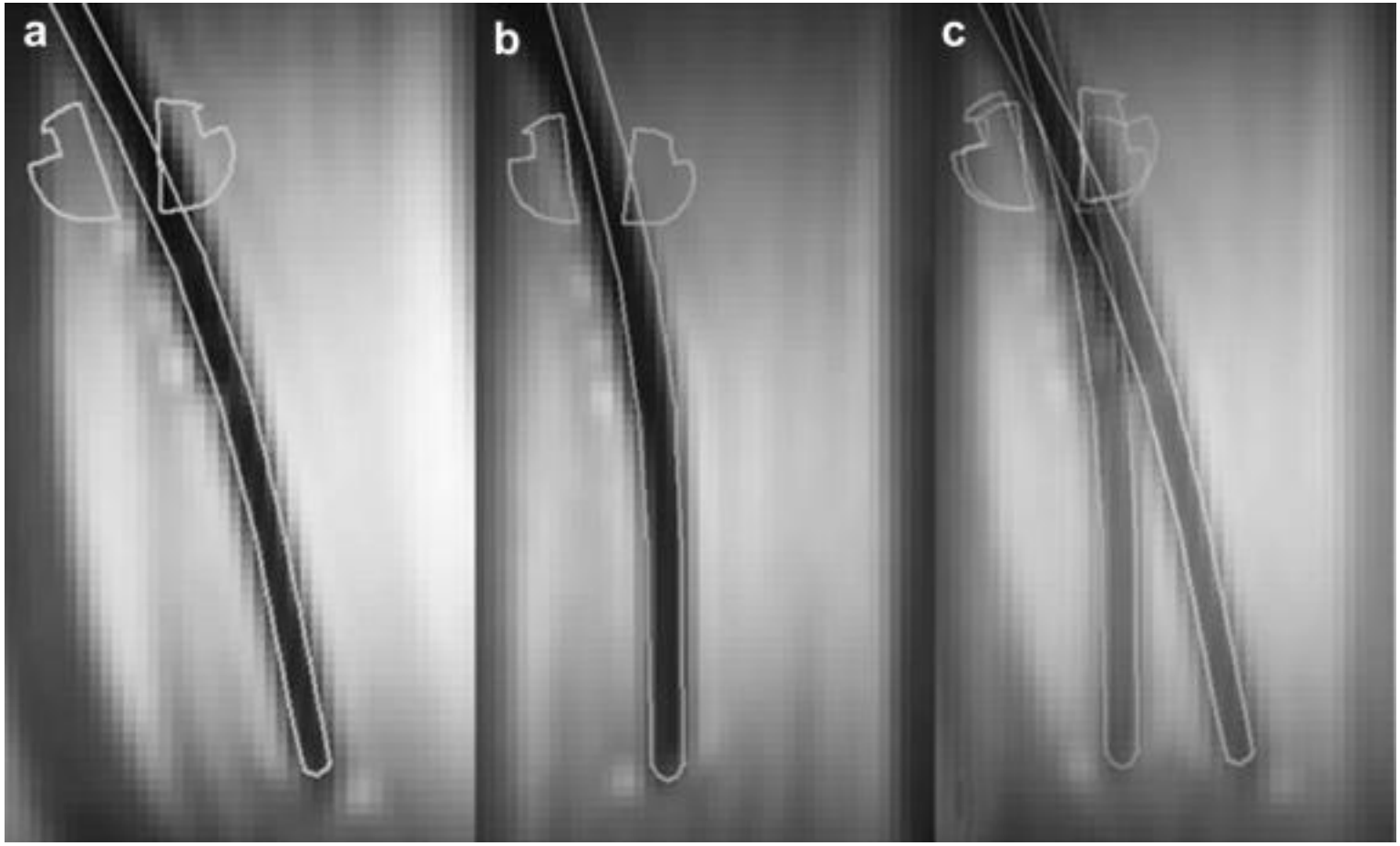
B0 inhomogeneity

Example of deformation at low scanning bandwidth (63.1 Hz) after applicator reconstruction with opposing readout directions.



Van Heerden, Brachytherapy 2016;15:118-126

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MR Distorsions aspects to brachytherapy

- Magnetic field homogeneous in center of the scanner
  - Relevant for brachytherapy

- Distorsions by the patient itself at the interface of air and metal/tissue
  - Susceptibility distorsions reduced by increasing the read-out bandwith

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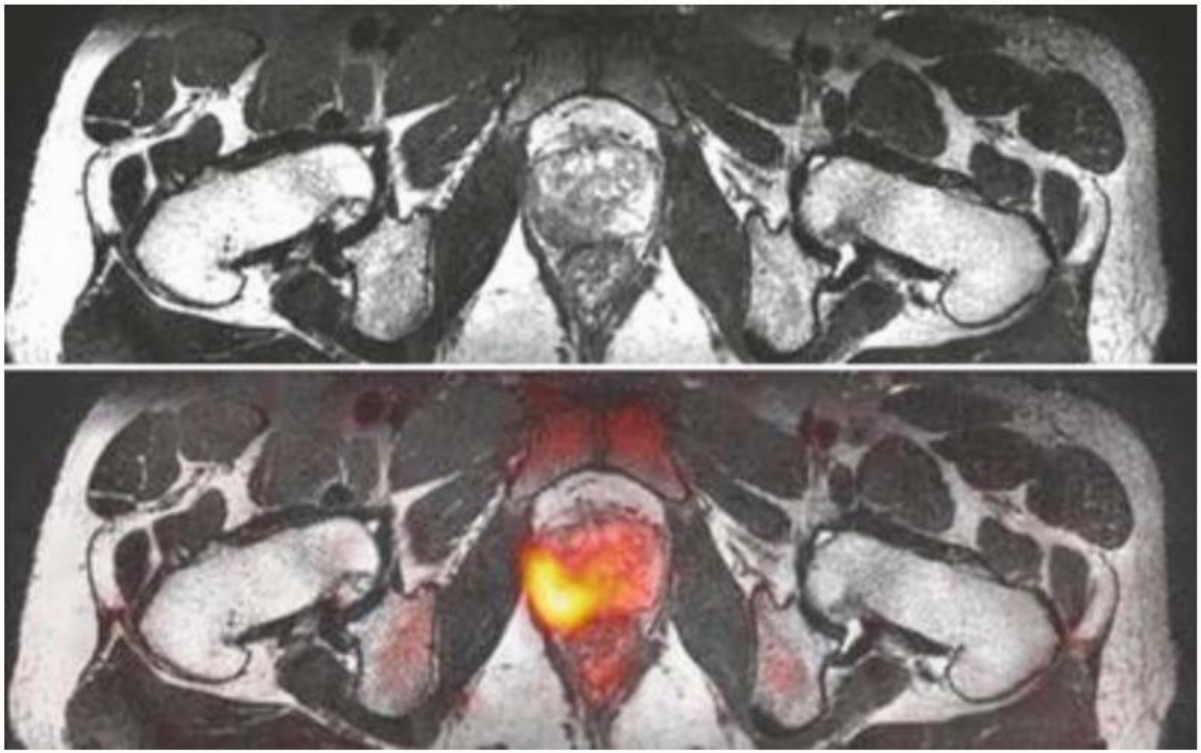
PET-imaging

- Lack of tissue contrast and therefore inadequate for brachytherpay planning
- Probably new perspectives with PET/MRI techniques



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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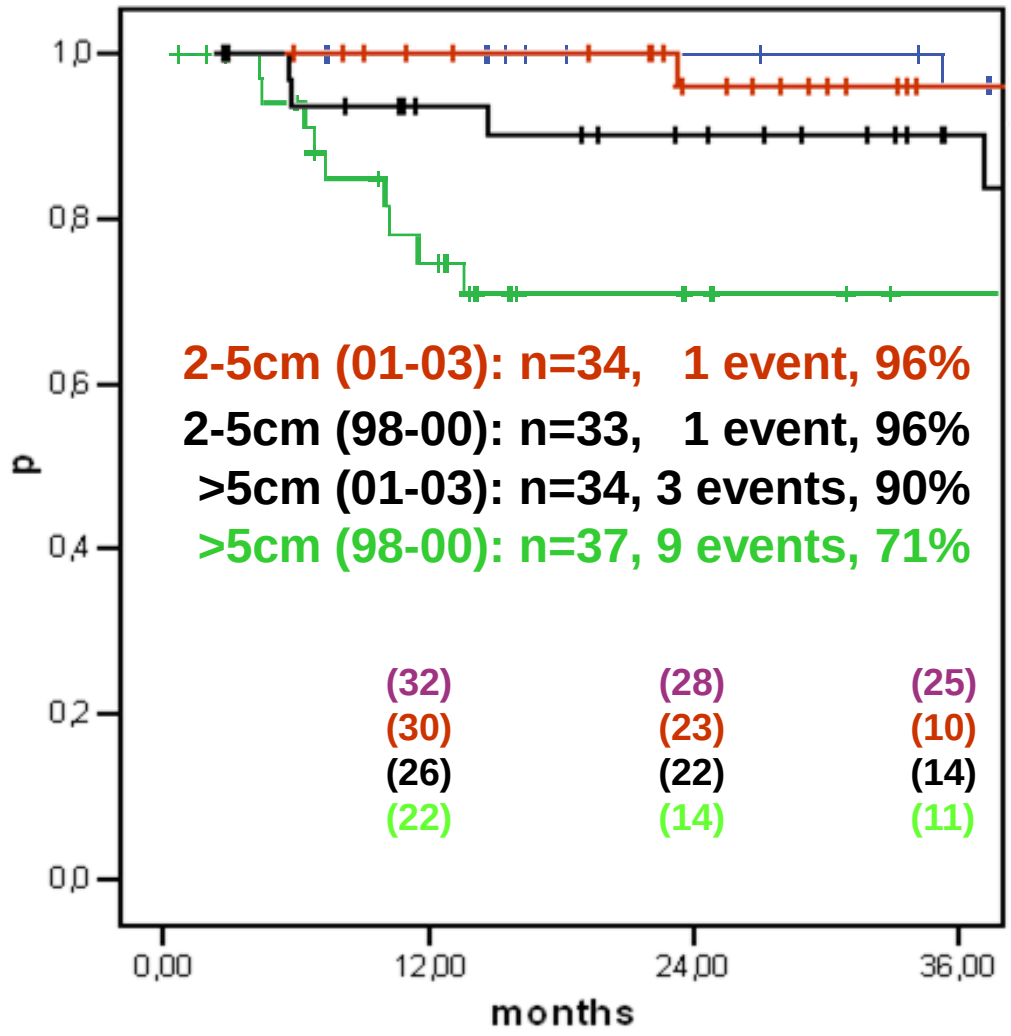
Dose Optimization with MRI Based Planning

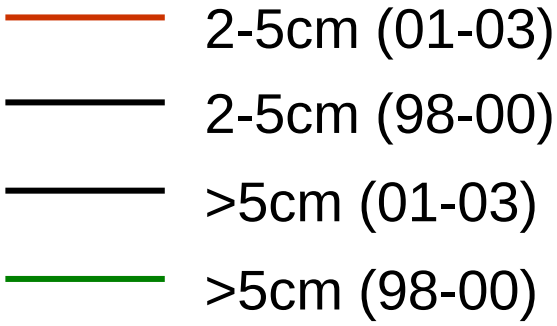
	X-ray	MRI/optimized
HR-CTV D90	76 Gy	79 Gy
IR-CTV D90	65 Gy	69 Gy
Bladder D2cc	86 Gy	82 Gy
Rectum D2cc	59 Gy	62 Gy
Sigmoid D2cc	70 Gy	68 Gy

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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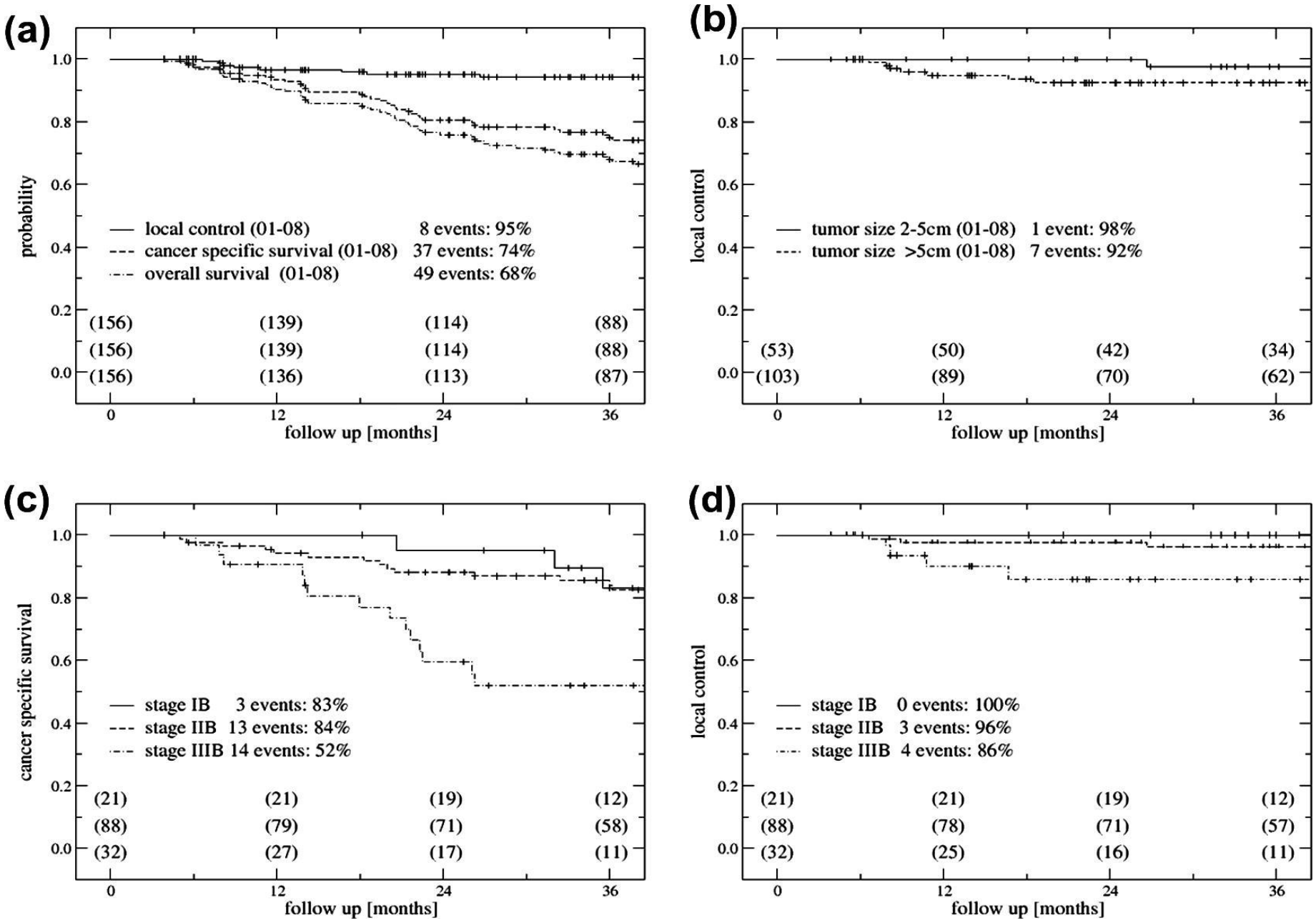

Pötter et al. Radiother Oncol, 2011;100:116-123

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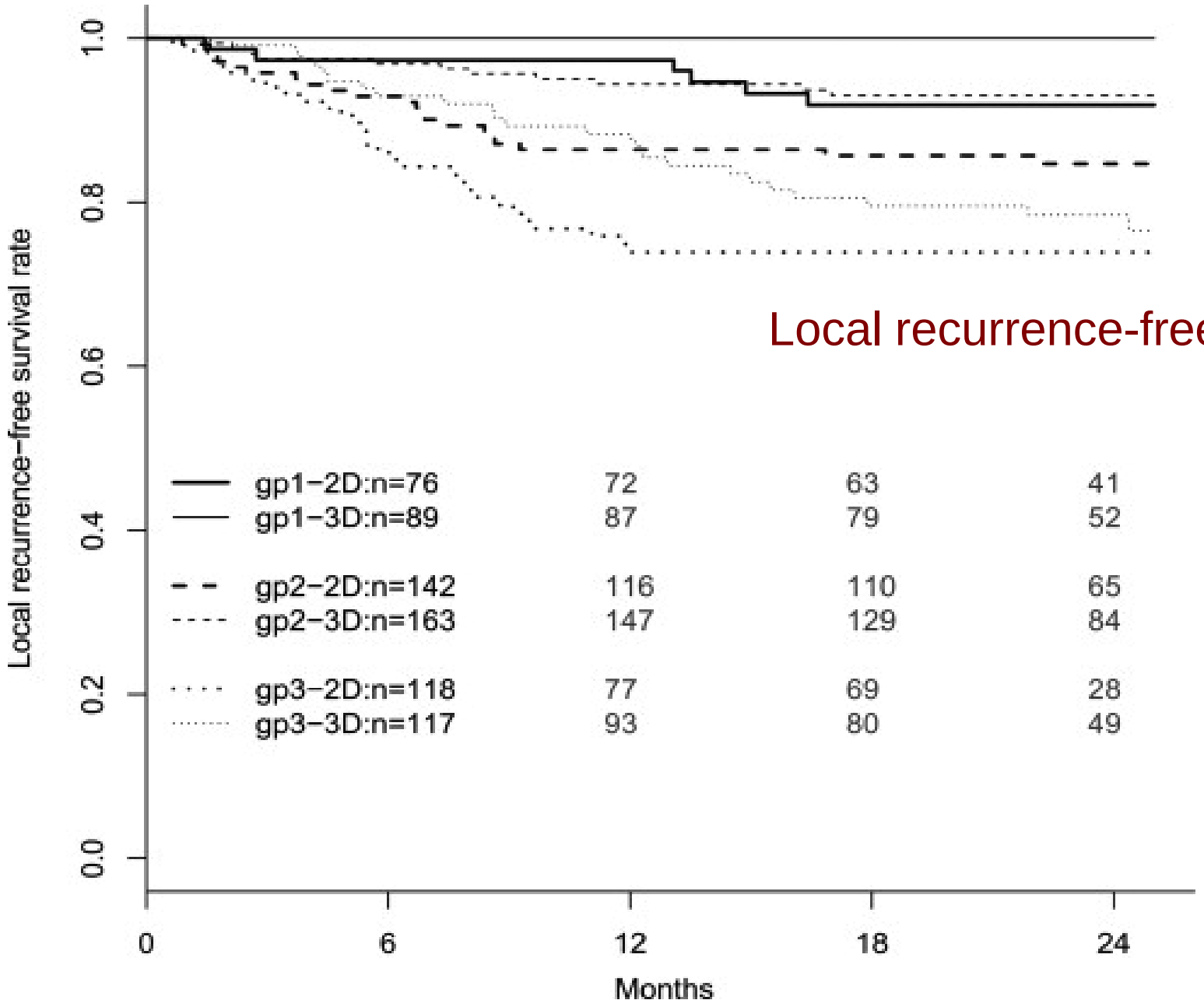

Local recurrence-free survival

Multicenter French study

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

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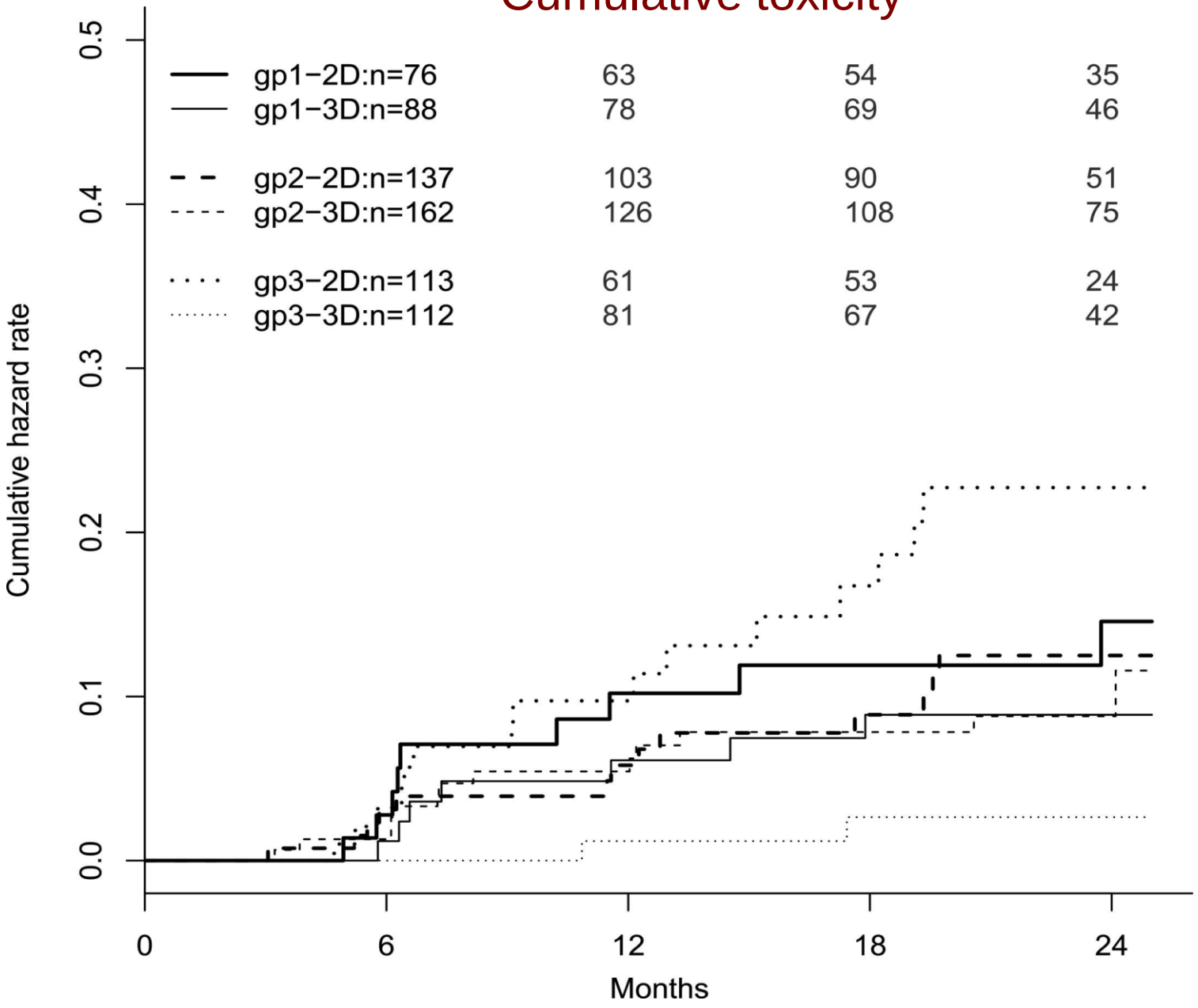
Cumulative toxicity



Multicenter French study

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

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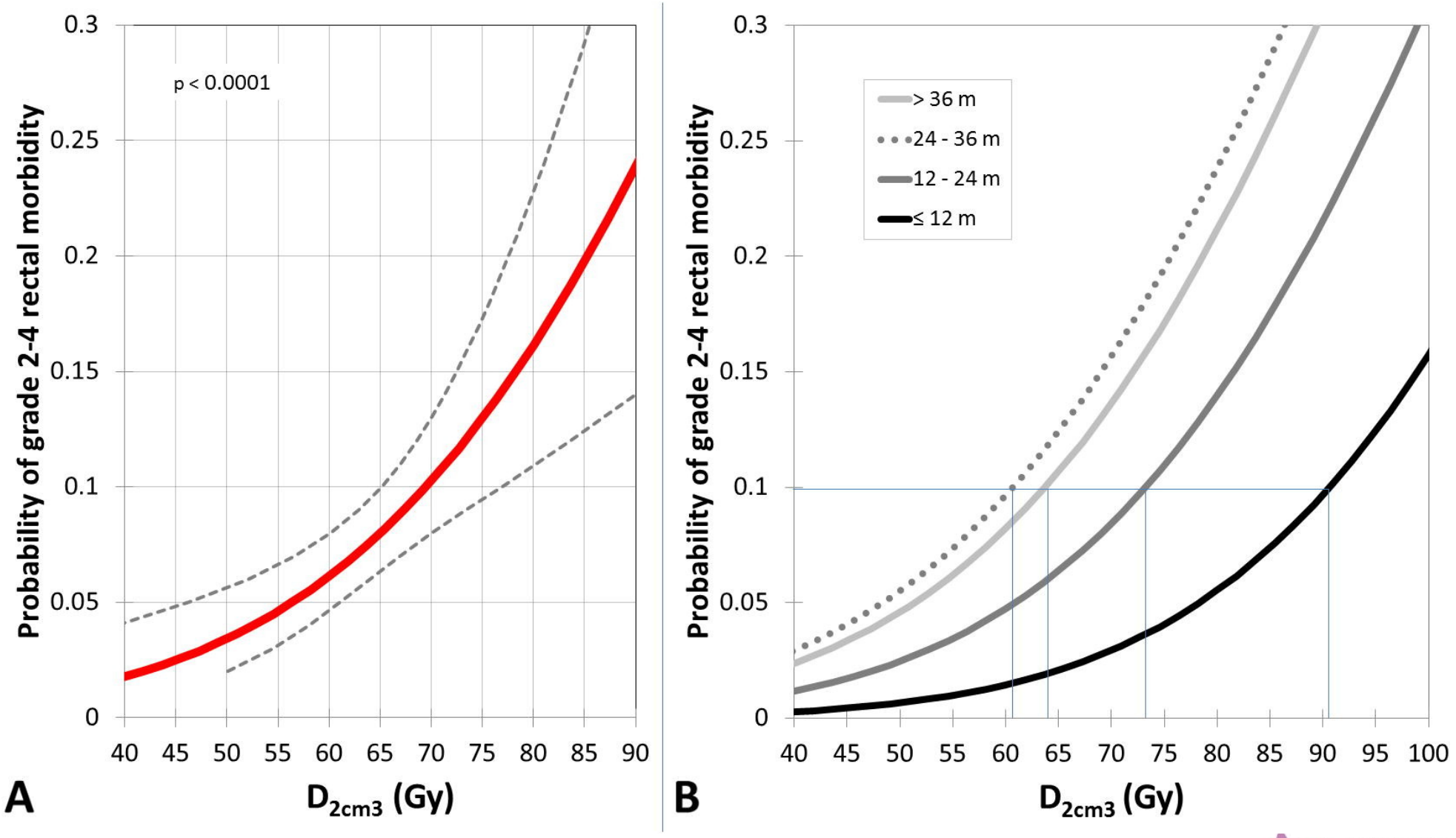
Prediction of late effects using DVH-parameters obtained from imaging



Mazeron et al. Radiother Oncol;2016;120:412-419

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Take home messages

- Different usage
  - Preplan
  - Image guided application
  - Definitive planning
  - Quality control of dose delivery
- Several imaging modalities available for specific usage
- Be aware of drawbacks and uncertainties related to specific imaging
- Main advantage of imaging is illustration of applicator in relation to target volume and OAR.
- Treatment planning using DVH-parameters is possible

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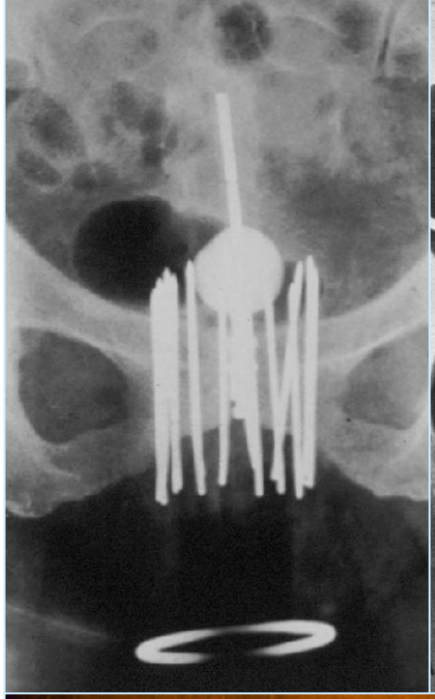
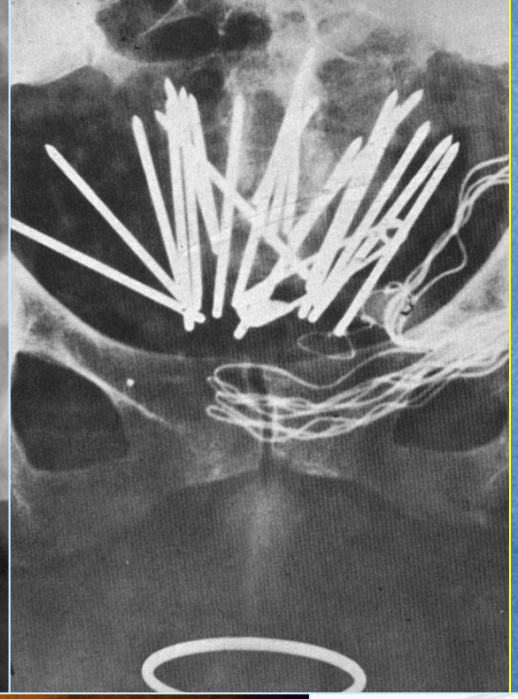
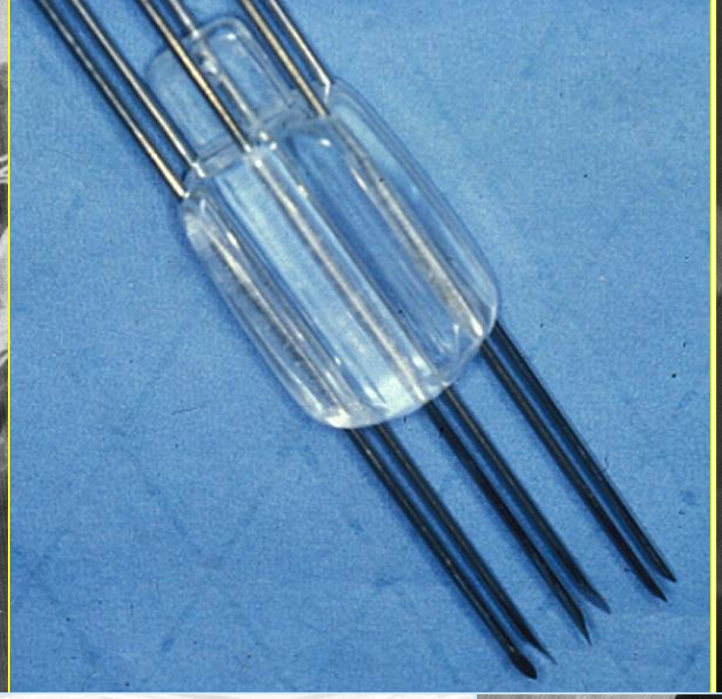
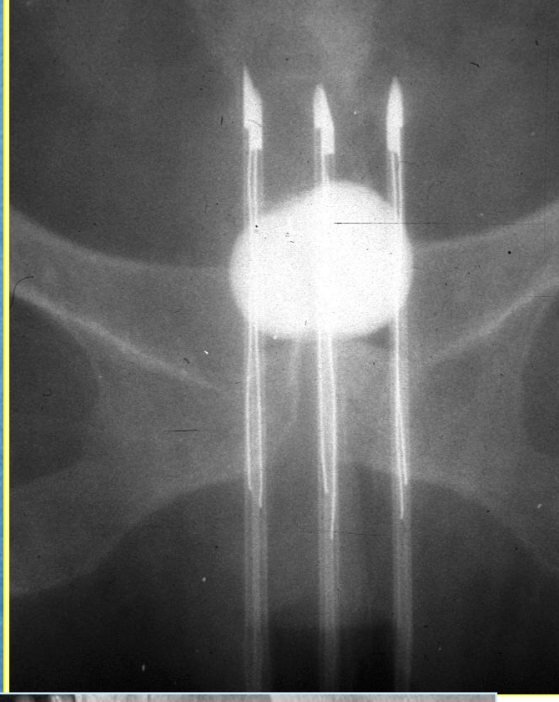
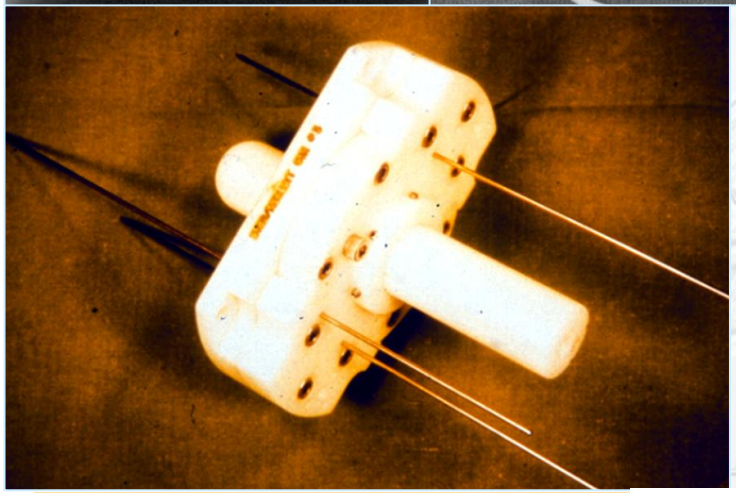
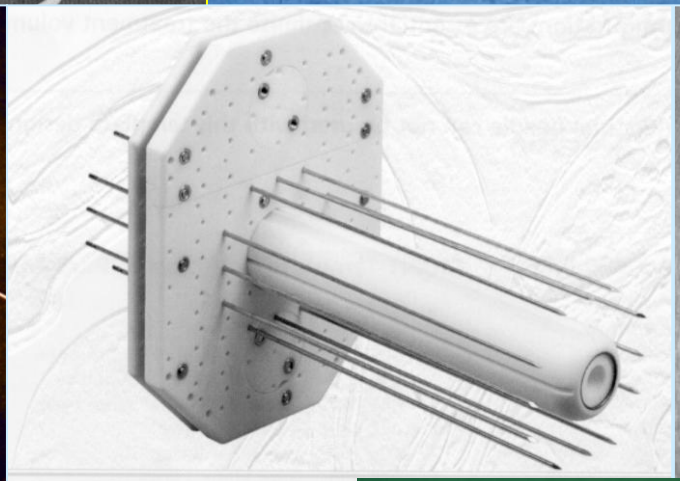
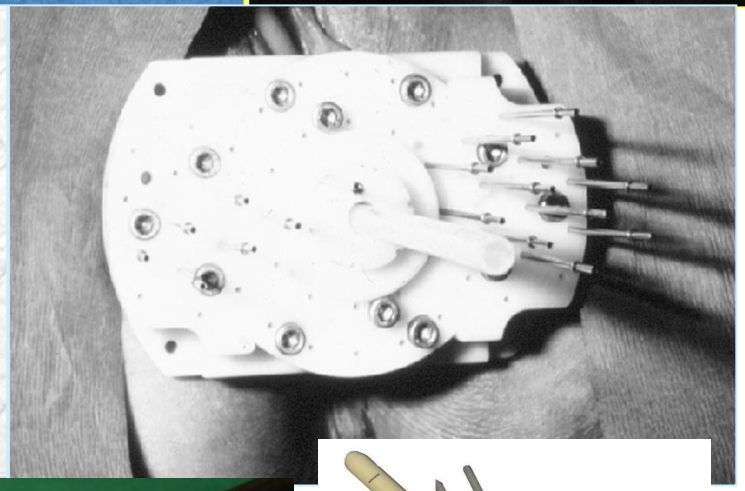
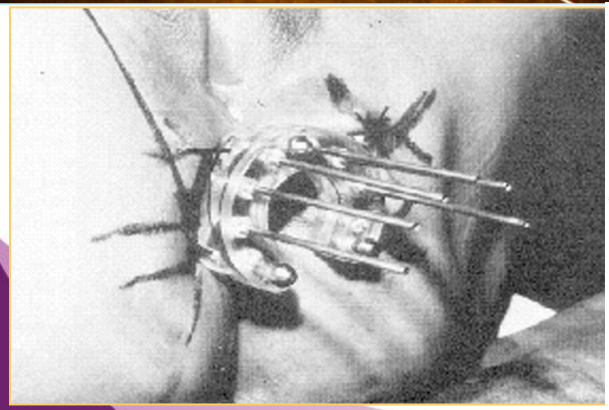
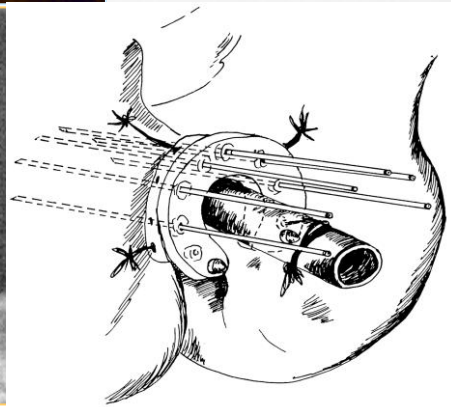
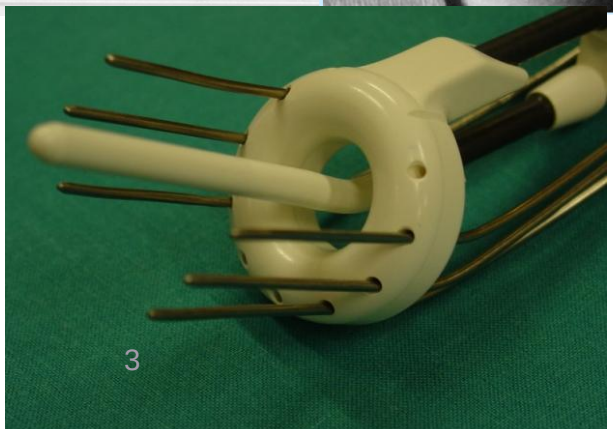
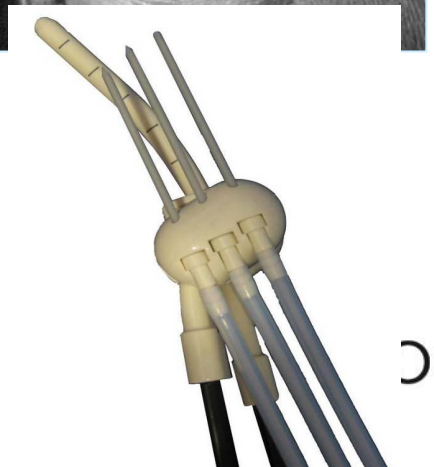
Interstitial Brachytherapy Techniques

Gynecological tumors

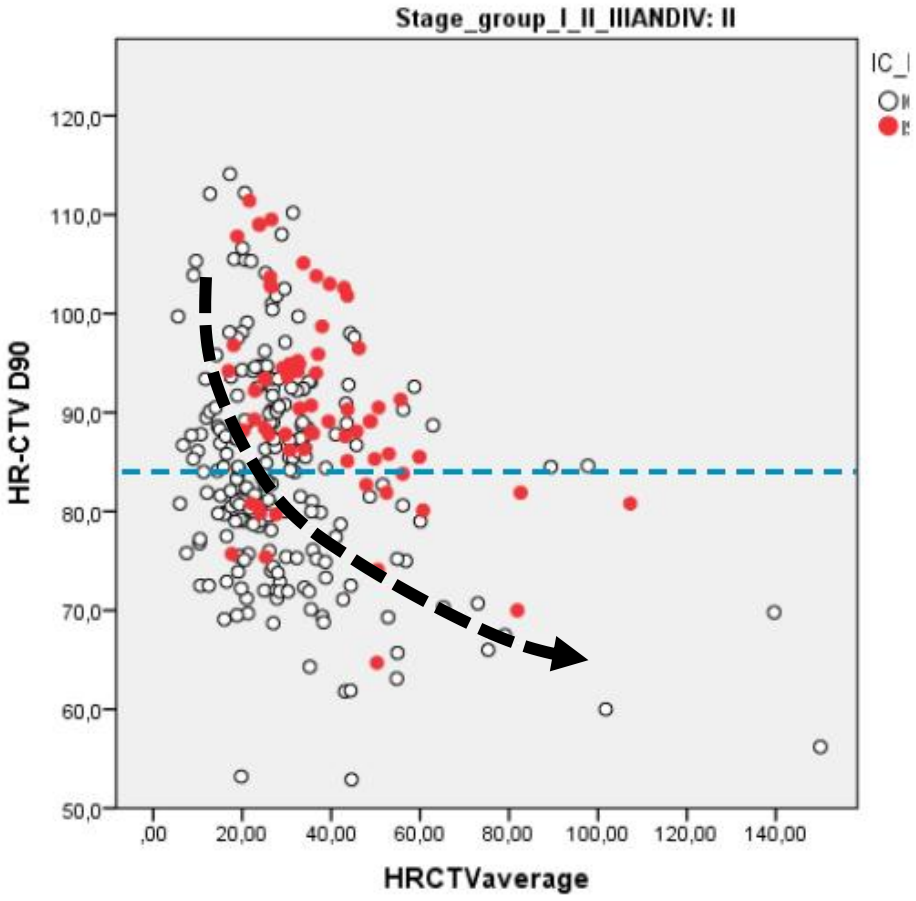
Renaud Mazeron

Gustave Roussy

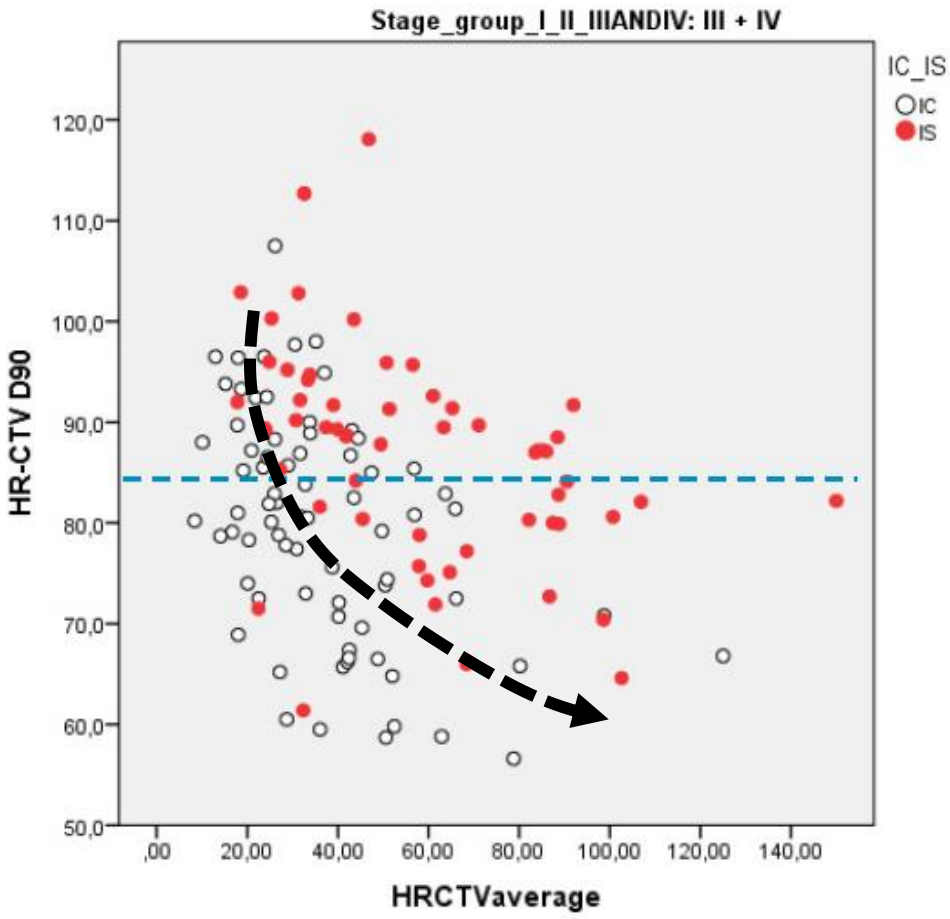












Importance of needles

Stage II

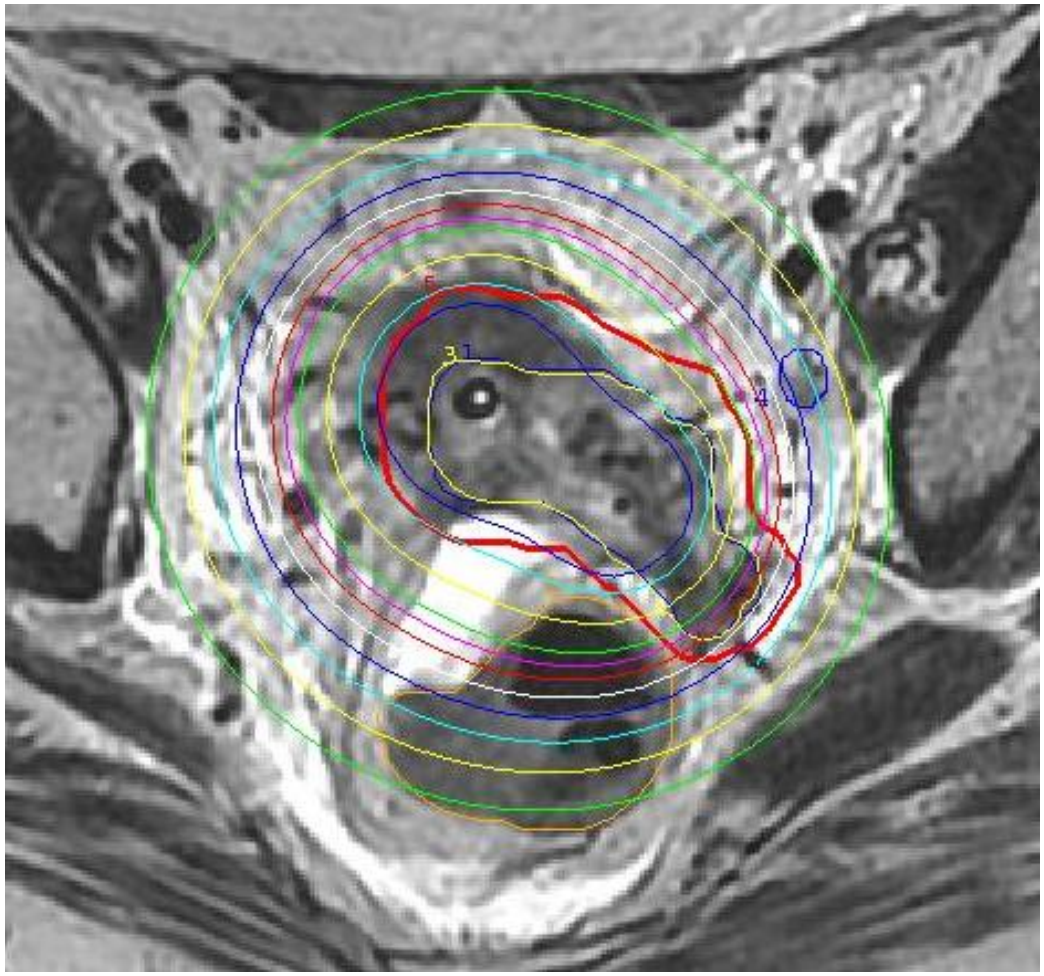


Stage III+IV



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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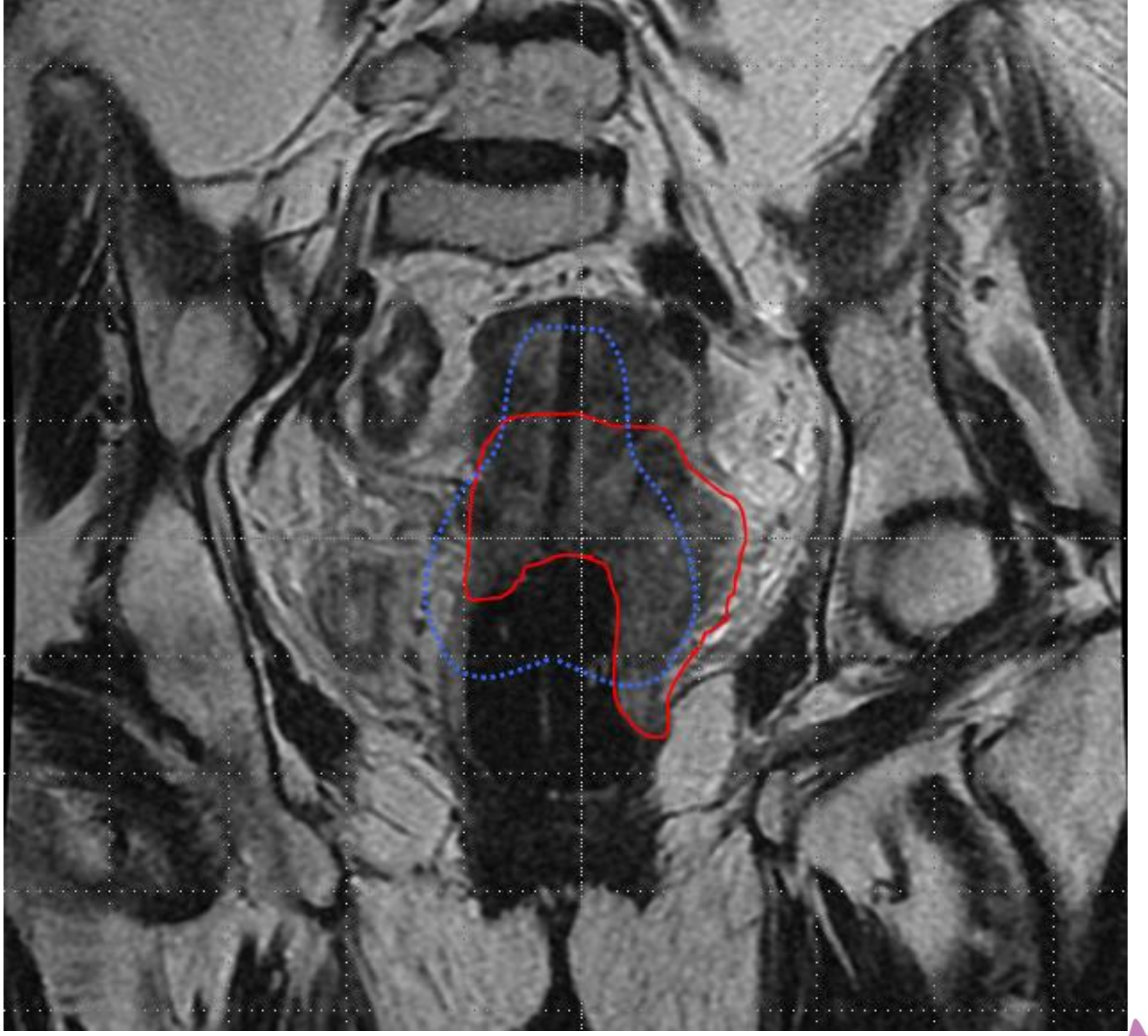

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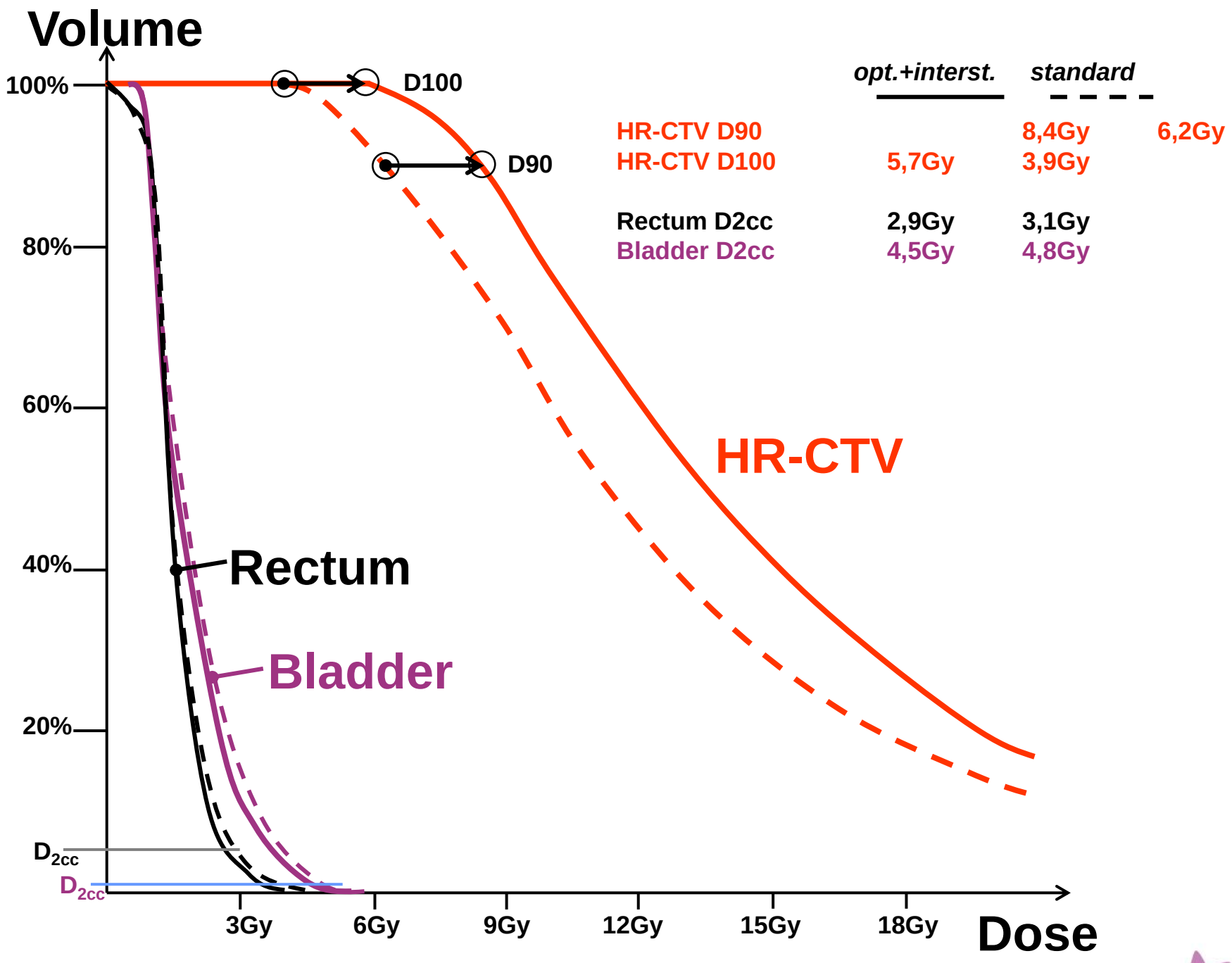

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Intracavitary techniques limitations with conventional applicators

- 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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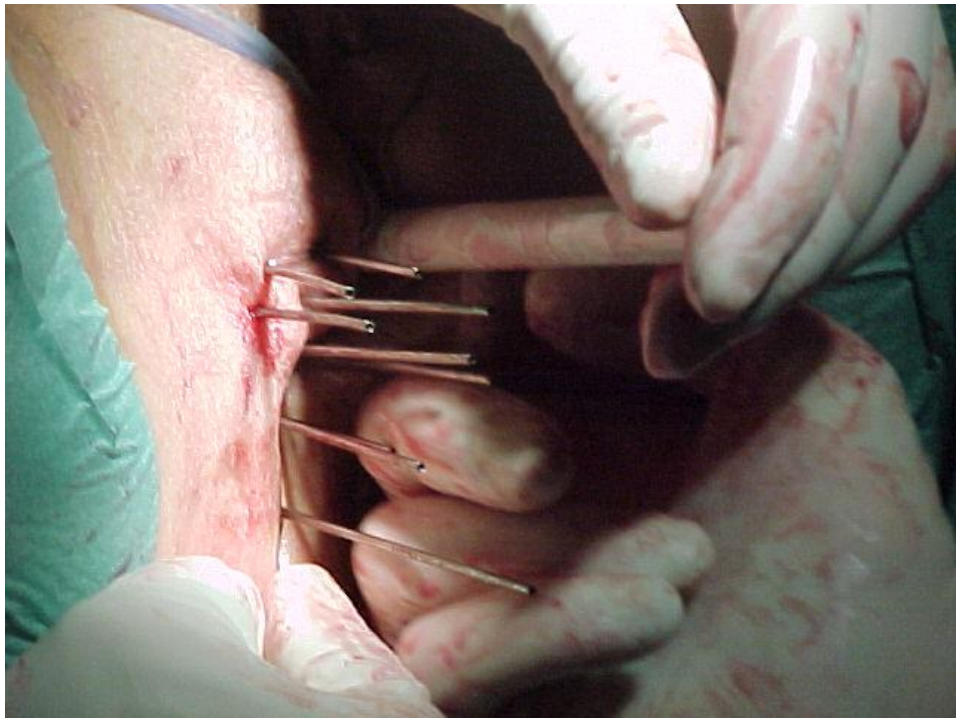
CLASSICAL INTERSTITIAL TECHNIQUES
FREEHAND PLACEMENT



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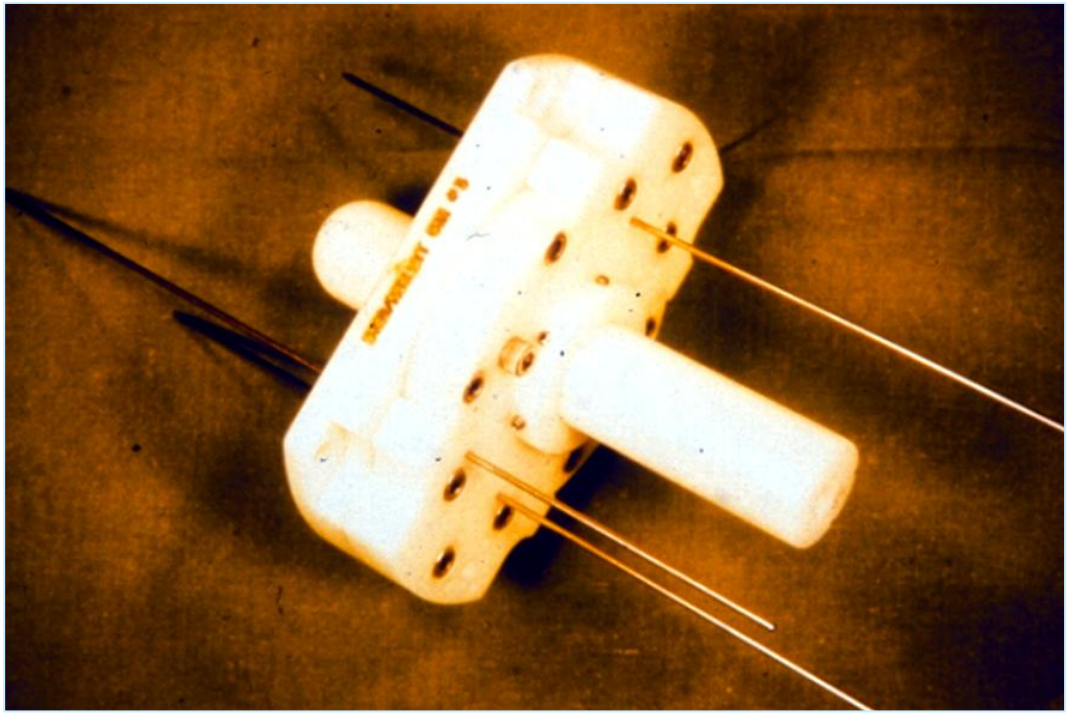
CLASSICAL INTERSTITIAL TECHNIQUES
PERINEAL TEMPLATES

SYED



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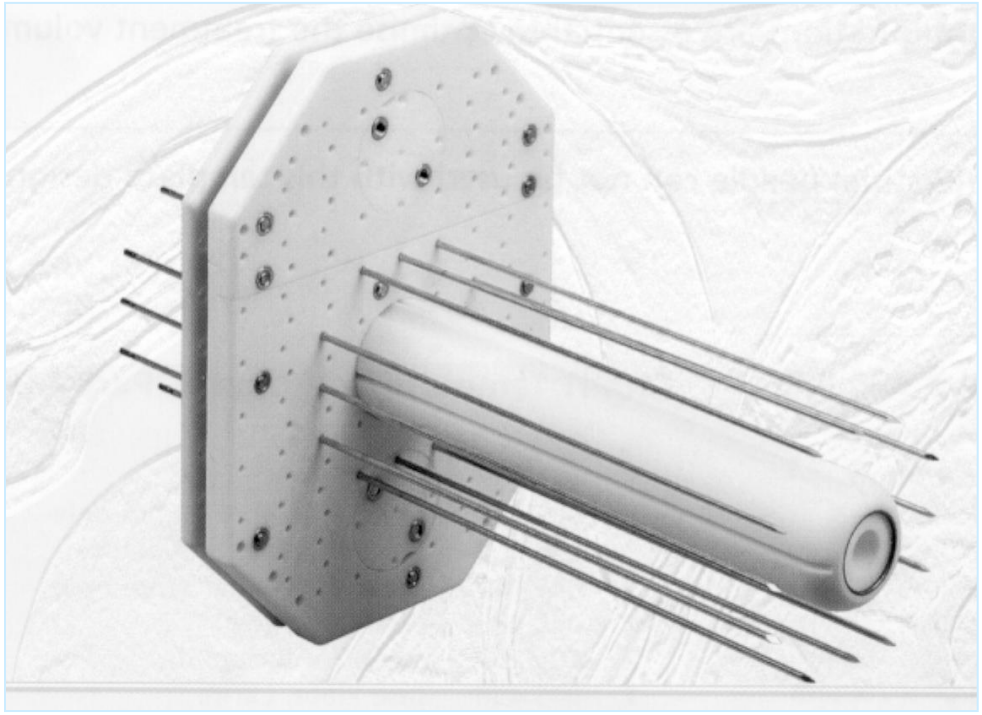

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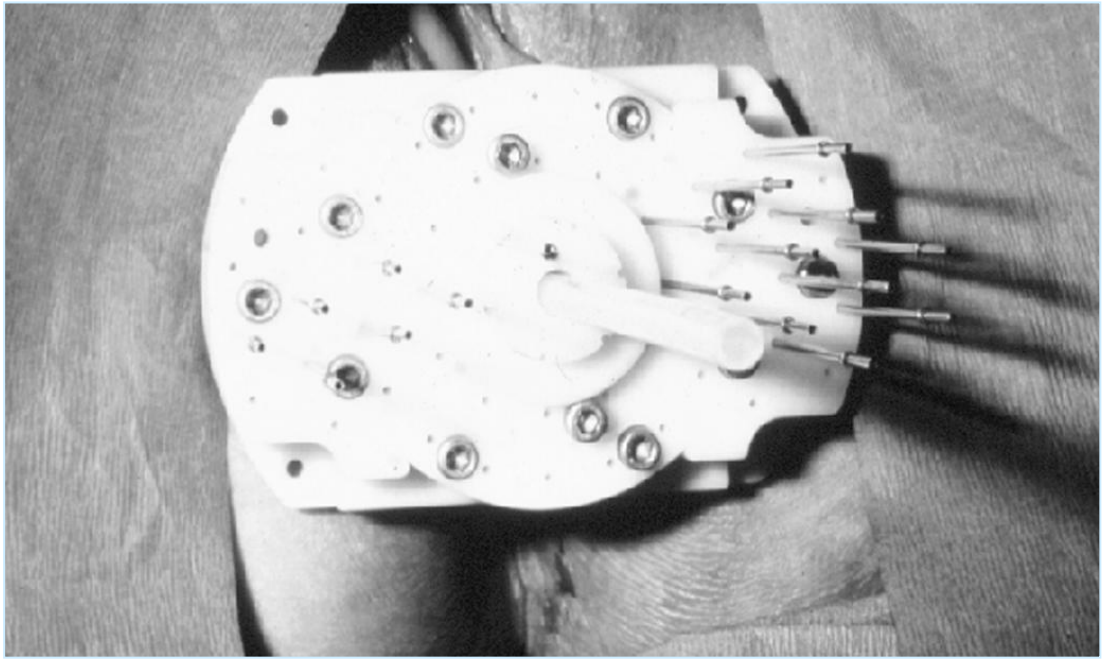
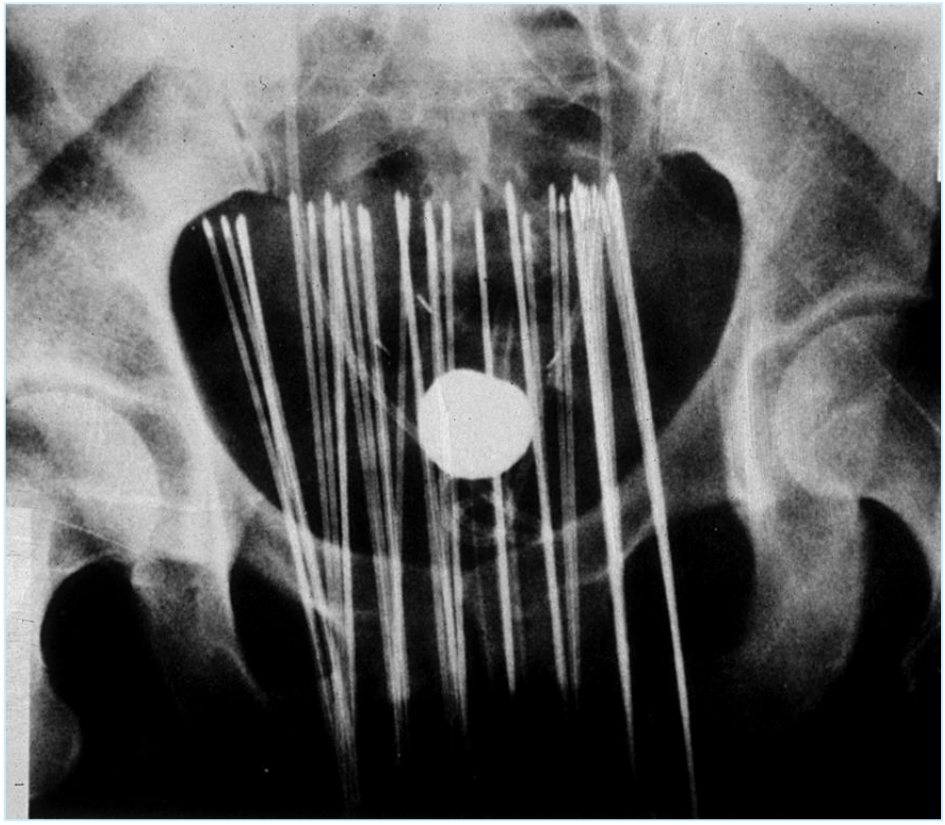
CLASSICAL INTERSTITIAL TECHNIQUES
PERINEAL TEMPLATES

SYED





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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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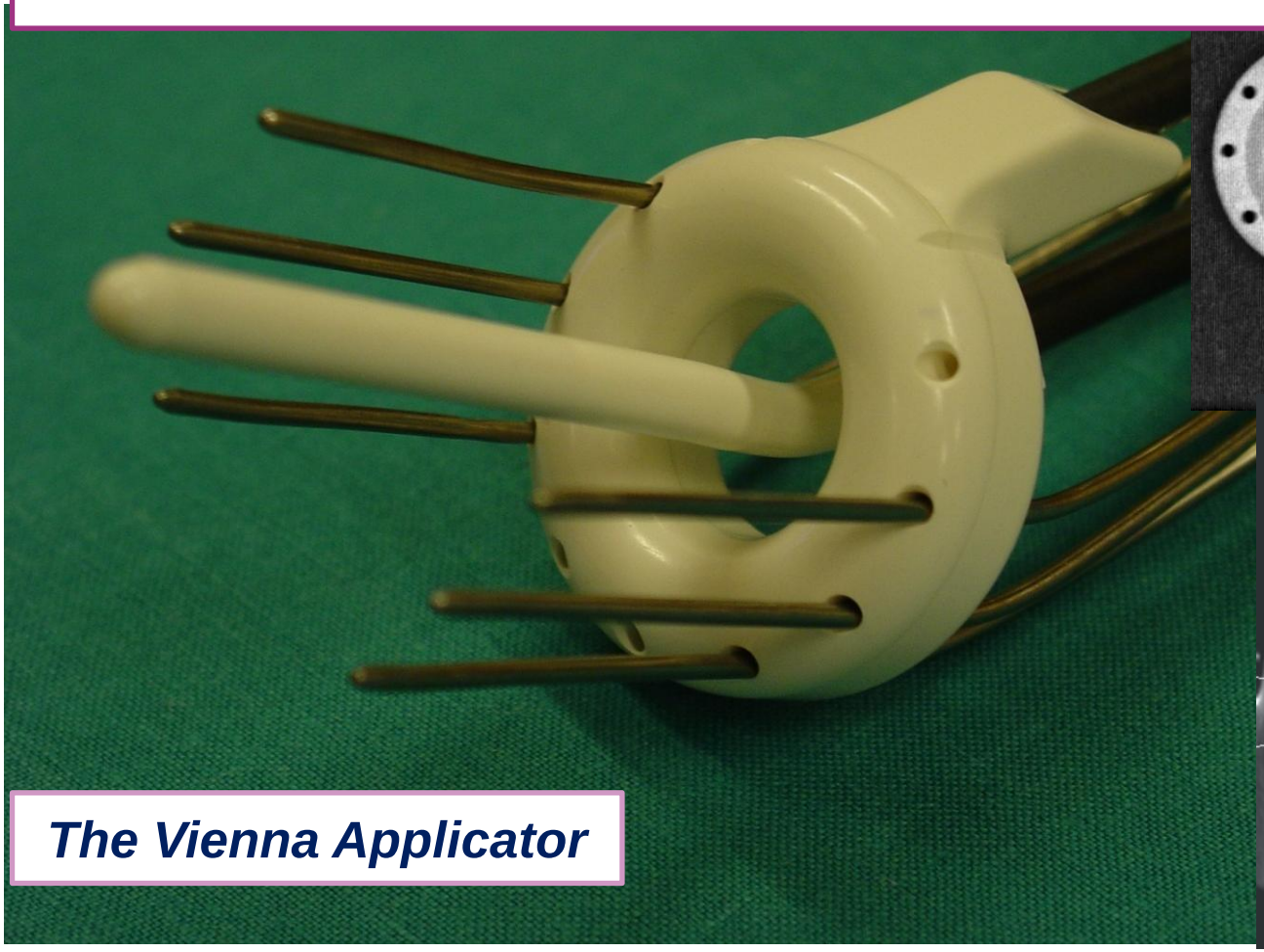
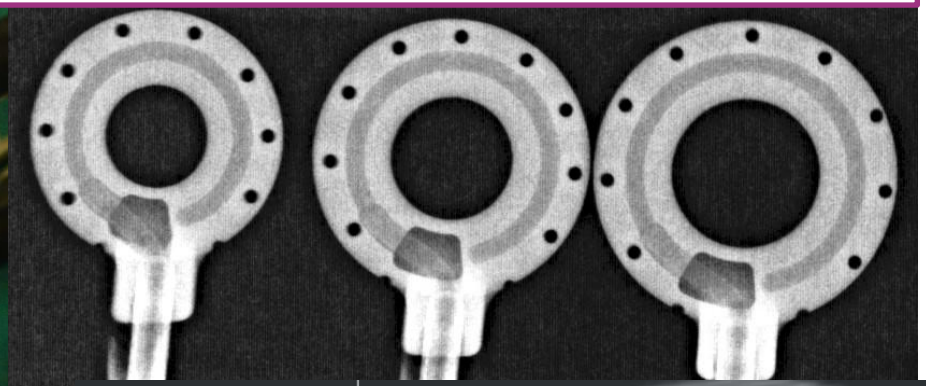
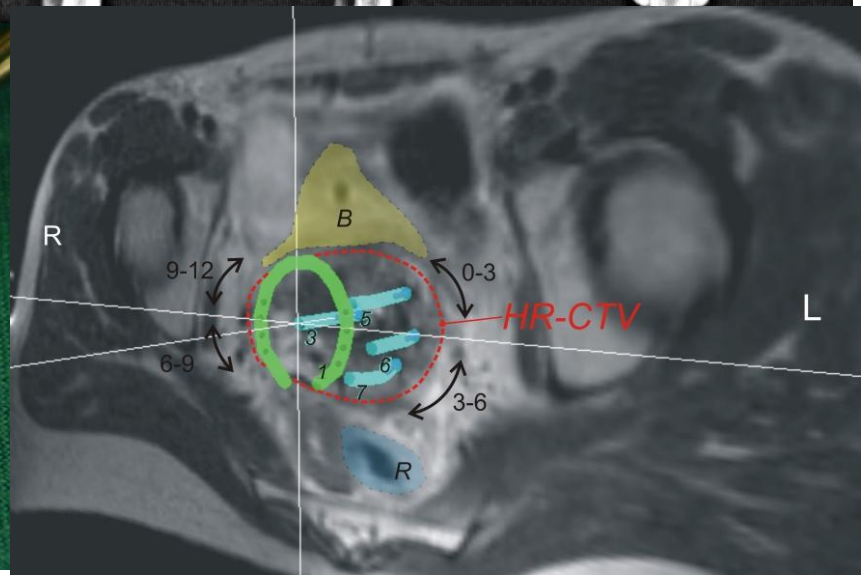
NOVEL INTERSTITIAL TECHNIQUES



The Vienna Applicator





Kirisits et al. IJROBP 2006

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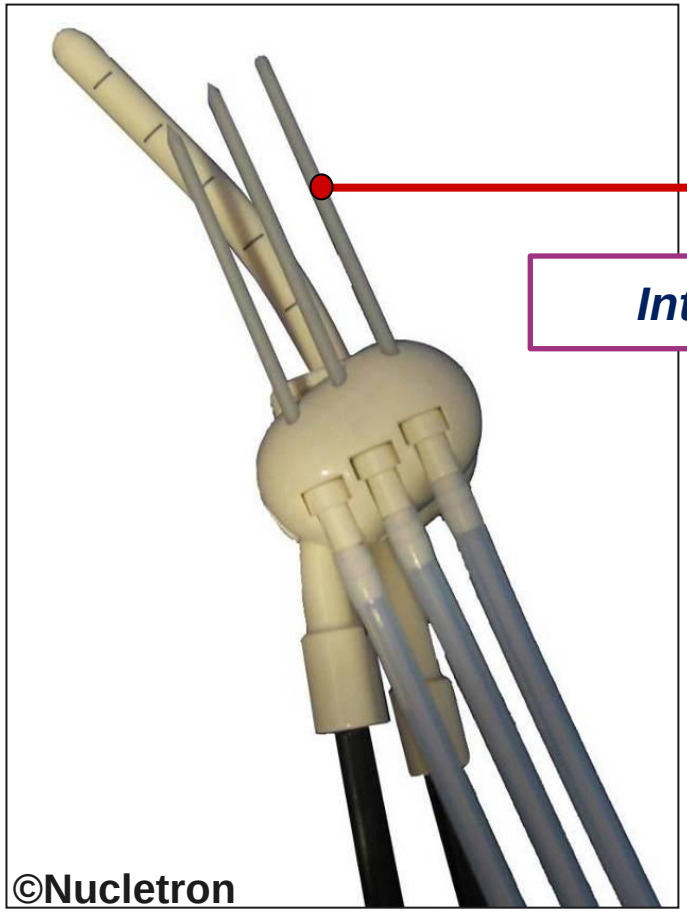
NOVEL INTERSTITIAL TECHNIQUES

The Utrecht Applicator



Interstitial needles

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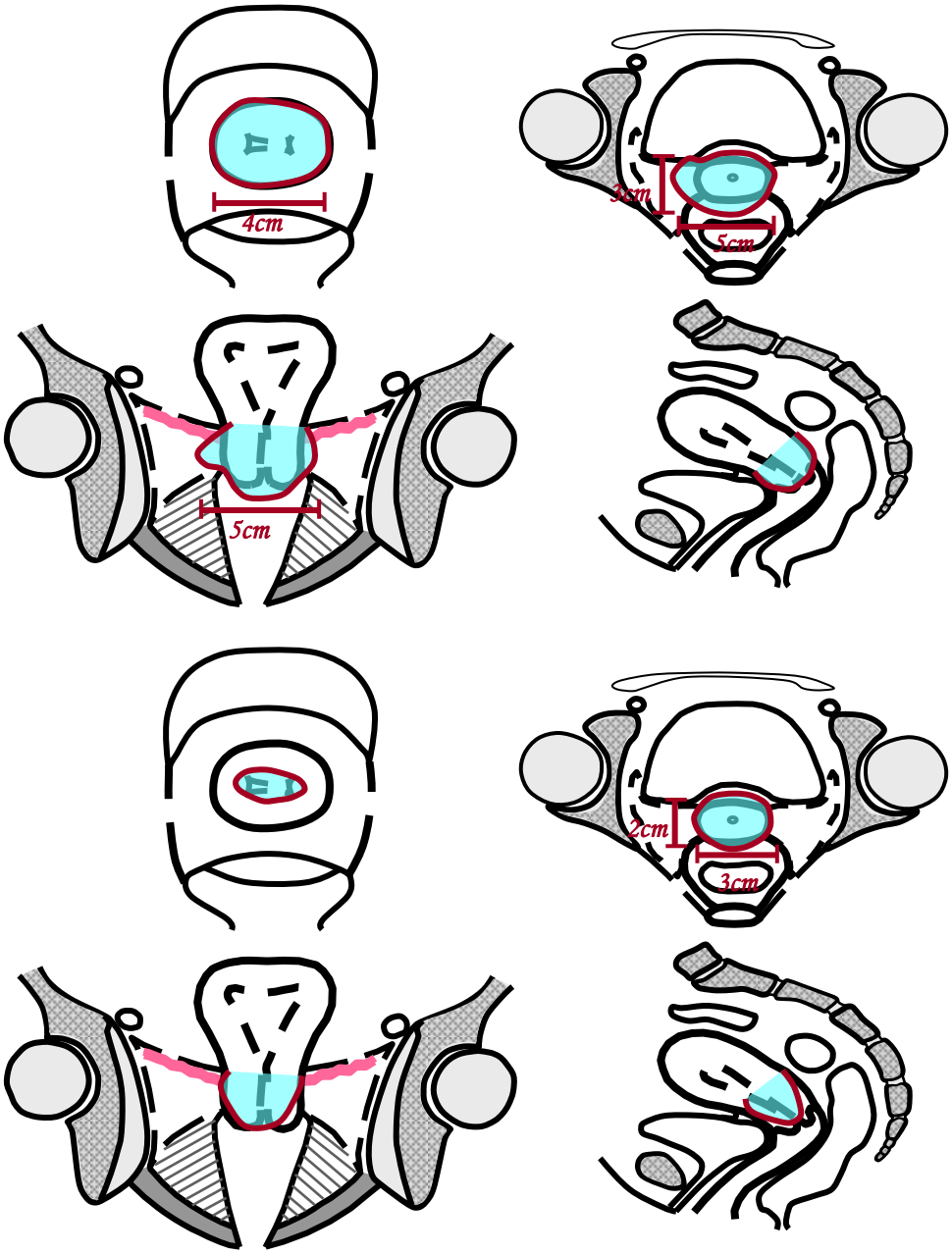
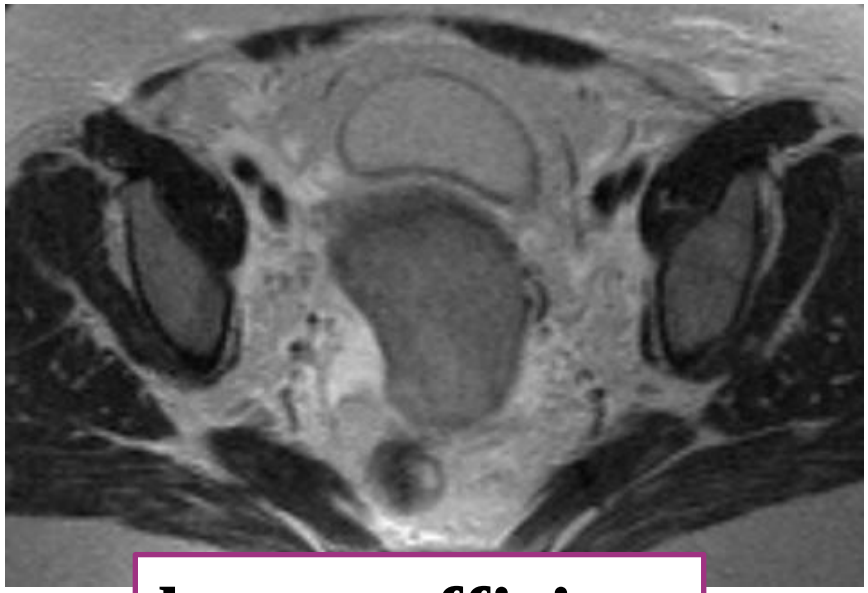
modern application techniques

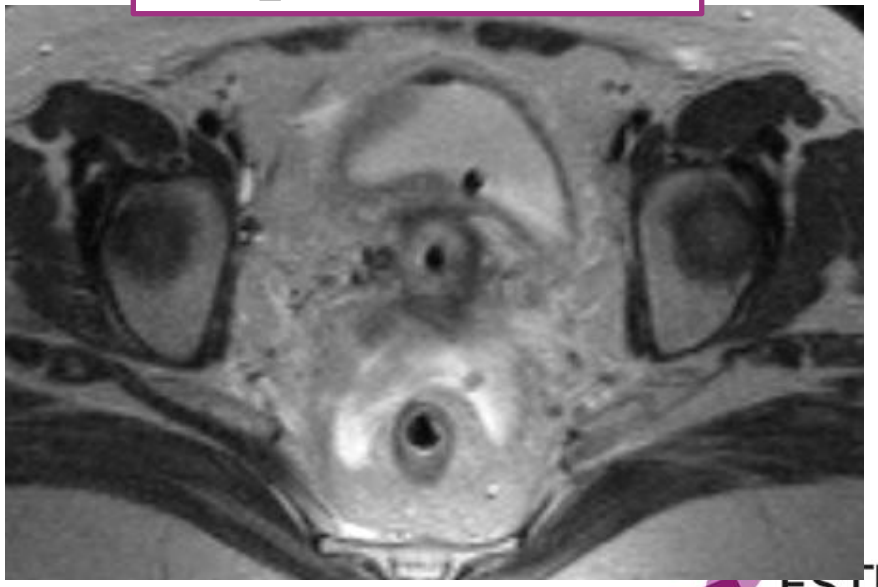
- improve control over the placement of needles: short distance between template and the target (accurate and reproducible insertion)
- lower number of needles to achieve an adequate target coverage
- to be combined with individualised CT/MRI based treatment planning to tailor the dose distribution (improve local control without increasing side effects)

Pattern of tumor regression I





large sufficient proximal



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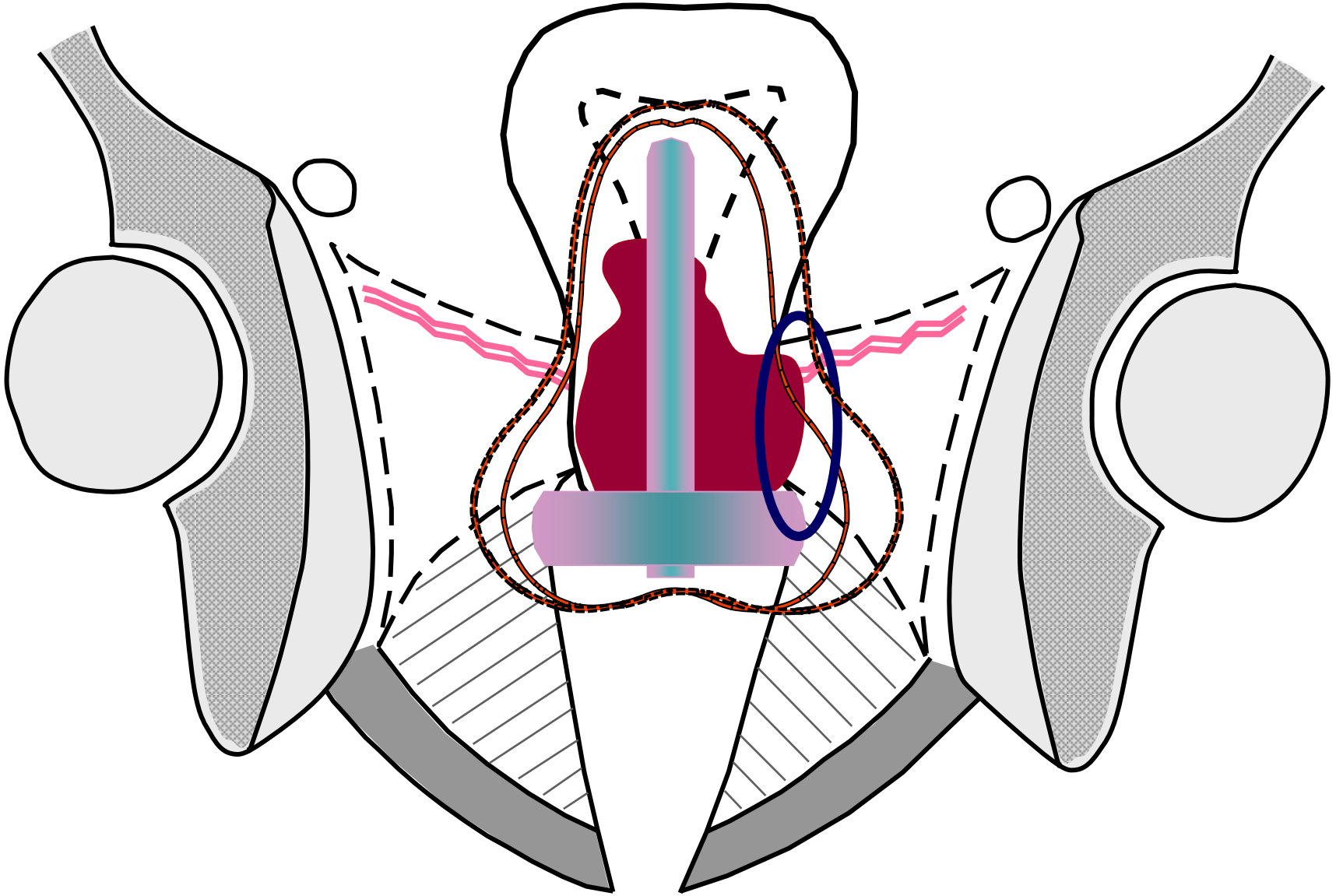
Lateral tumoral extension coverage



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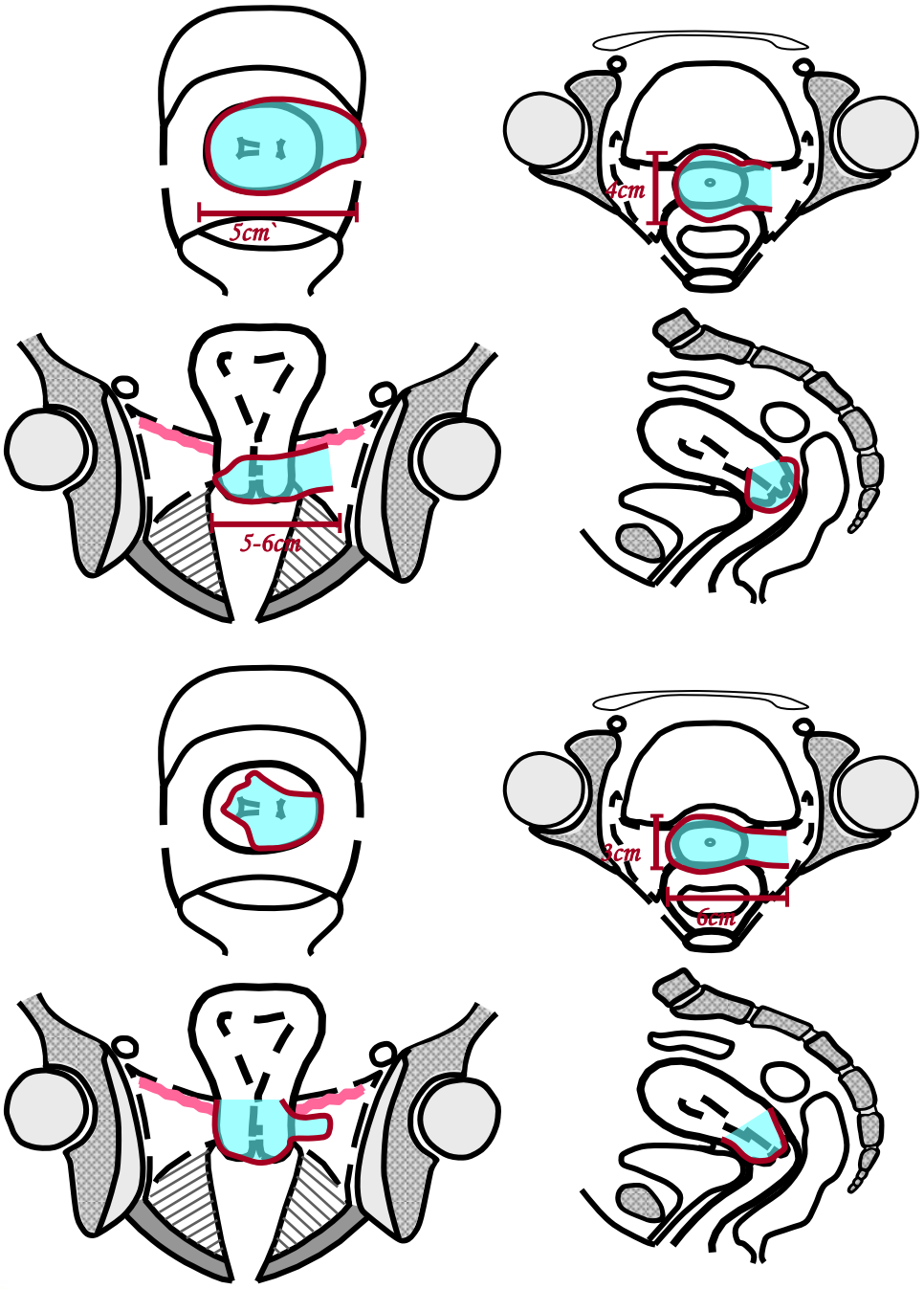
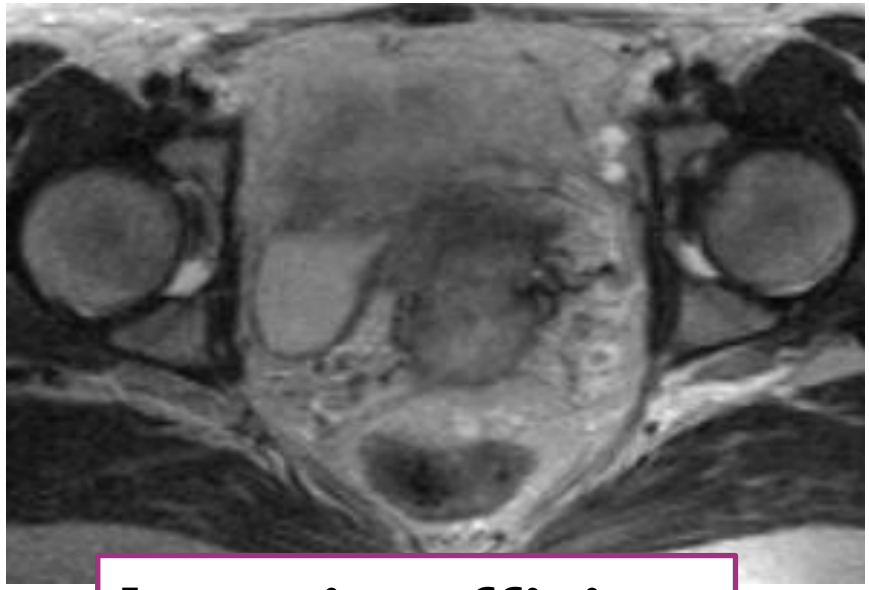
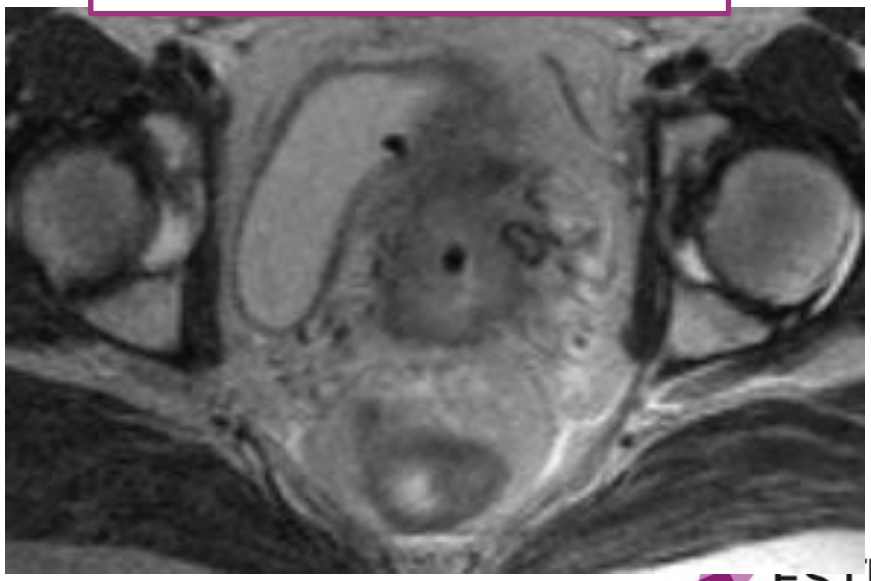
Pattern of tumor regression II





large insufficient middle



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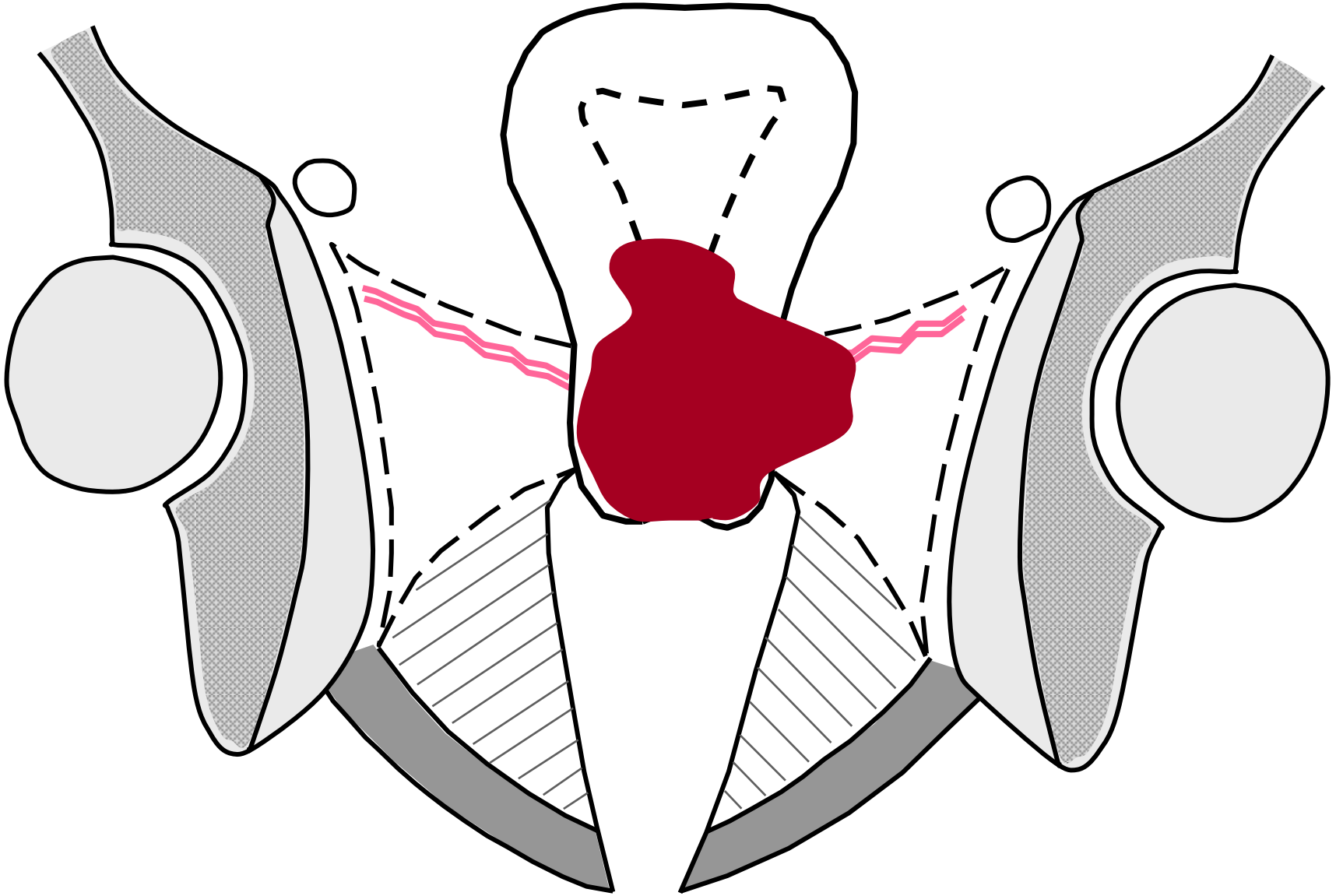
Pattern of tumor regression II



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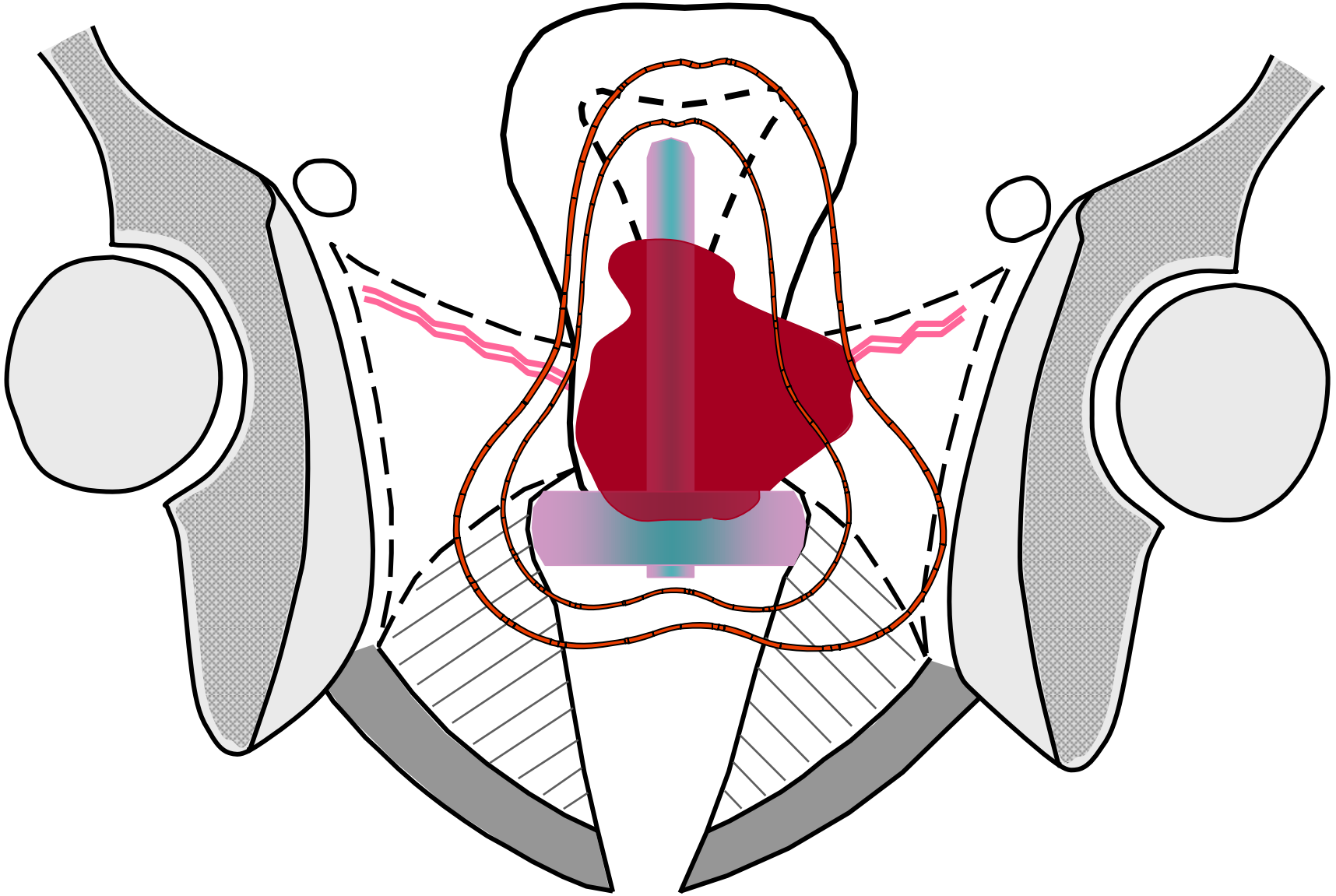
Pattern of tumor regression II



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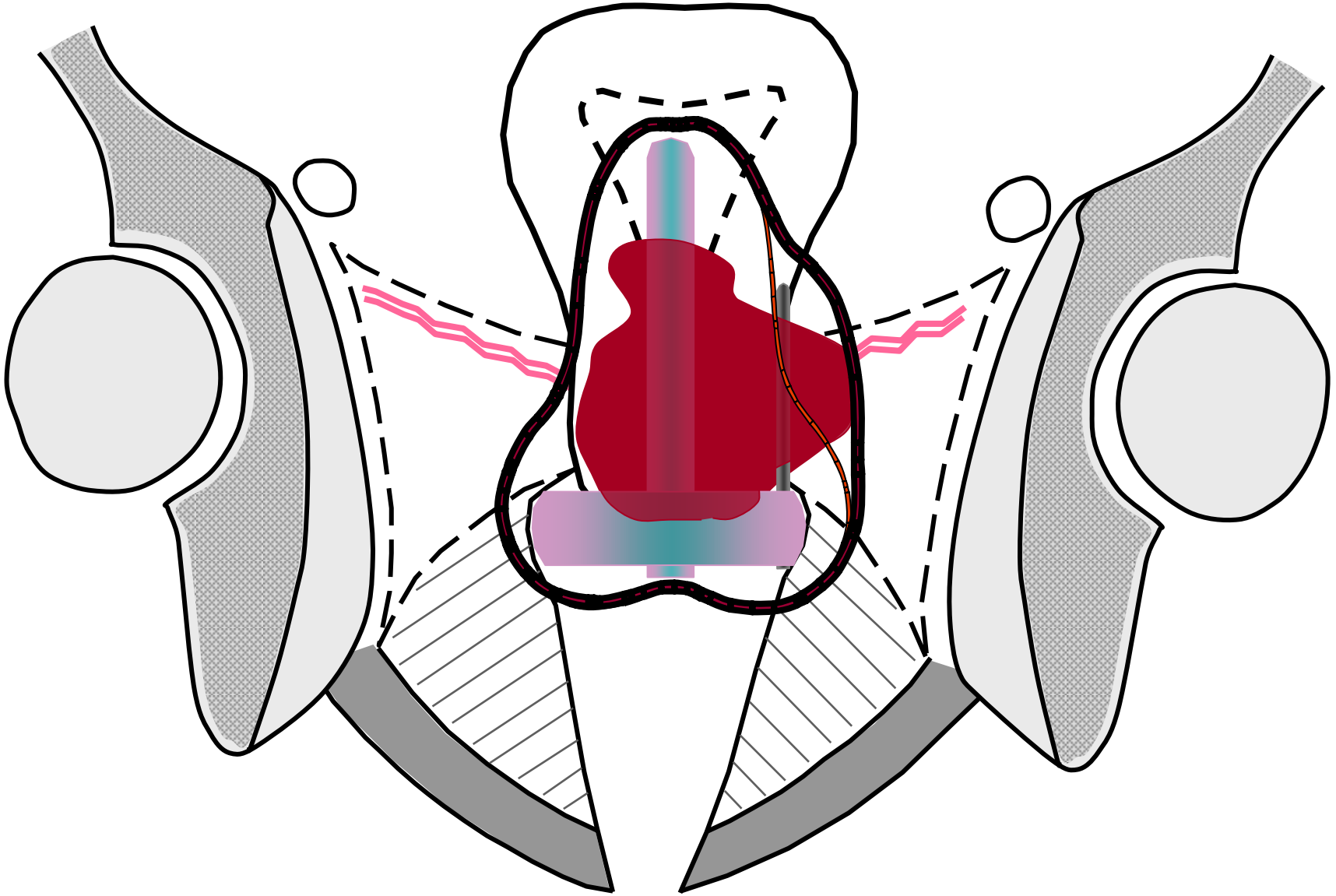
Pattern of tumor regression II



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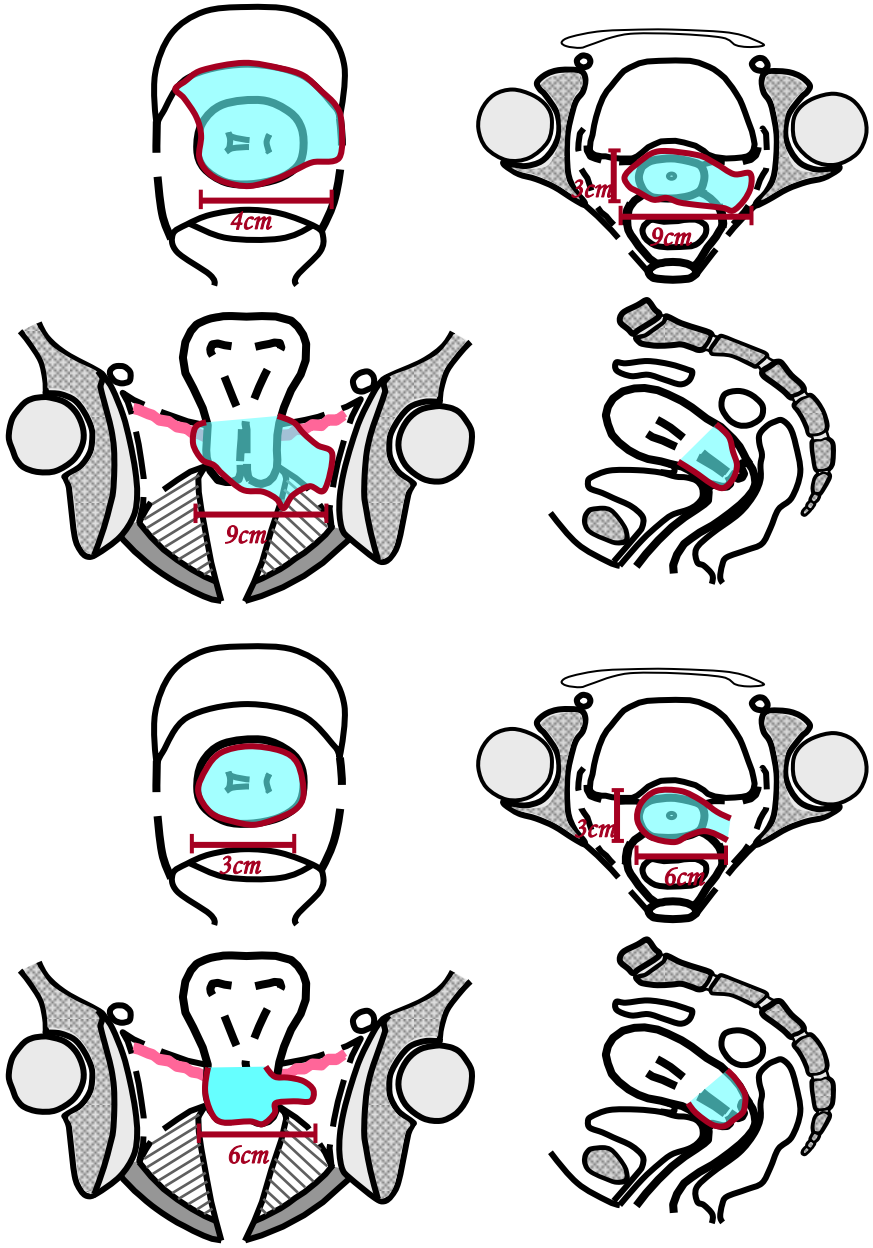
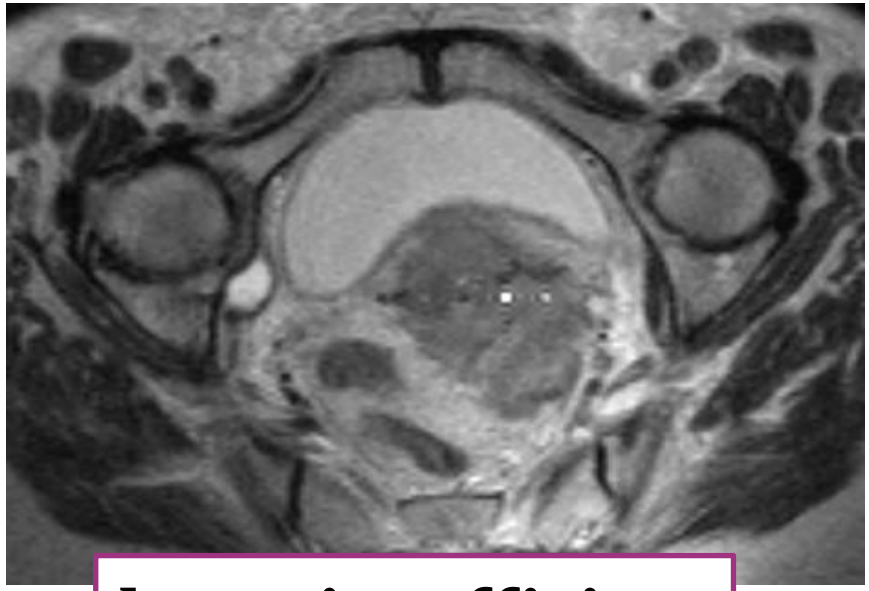
Pattern of tumor regression III





large insufficient distal

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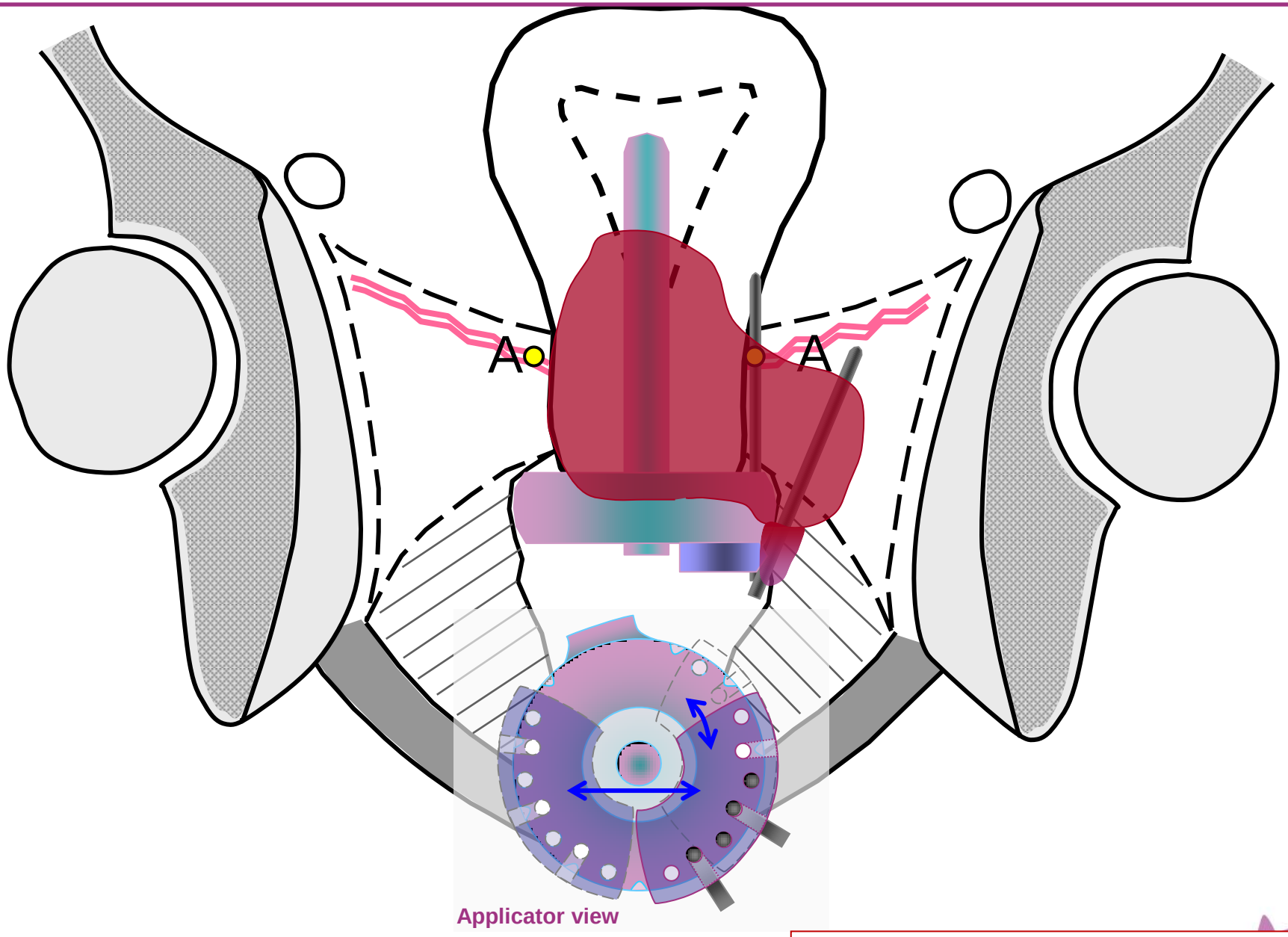
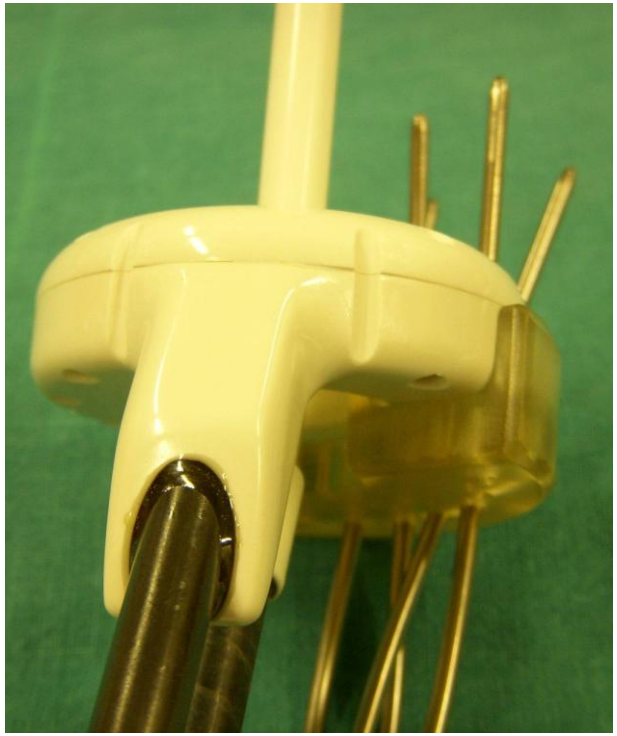
Applicator for distal parametrial disease

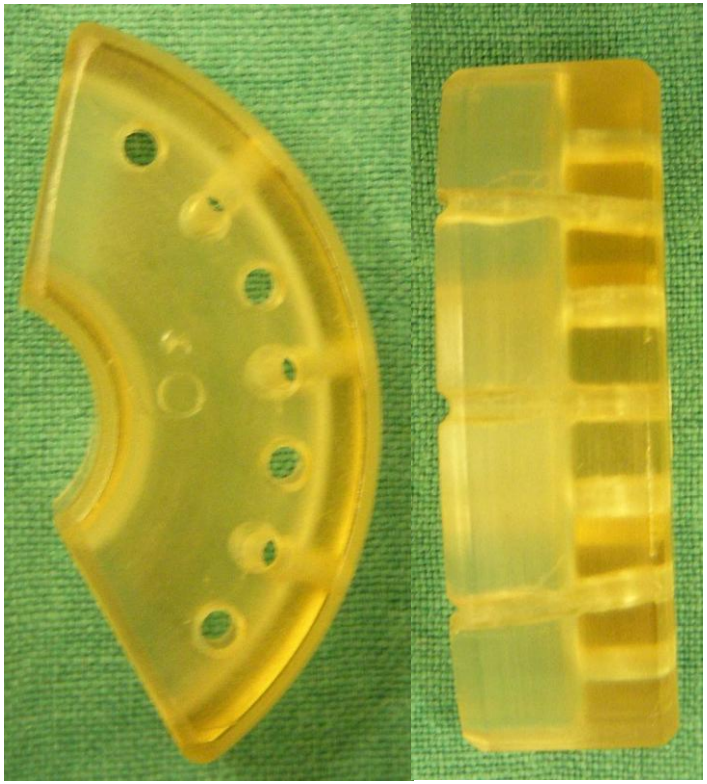
additional parallel and divergent template guided needles

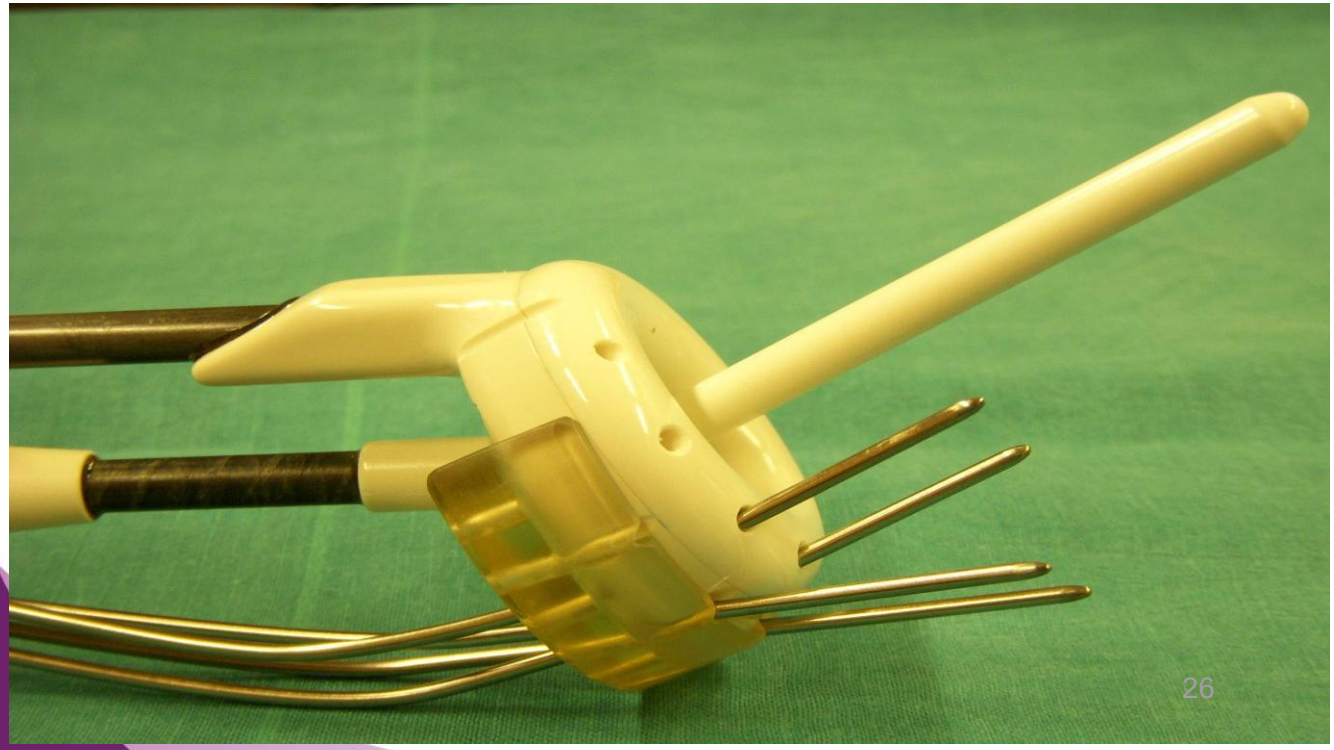


The Vienna II Applicator



Modified Vienna Ring
Vienna II





Provided by Dimopoulos et al

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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

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 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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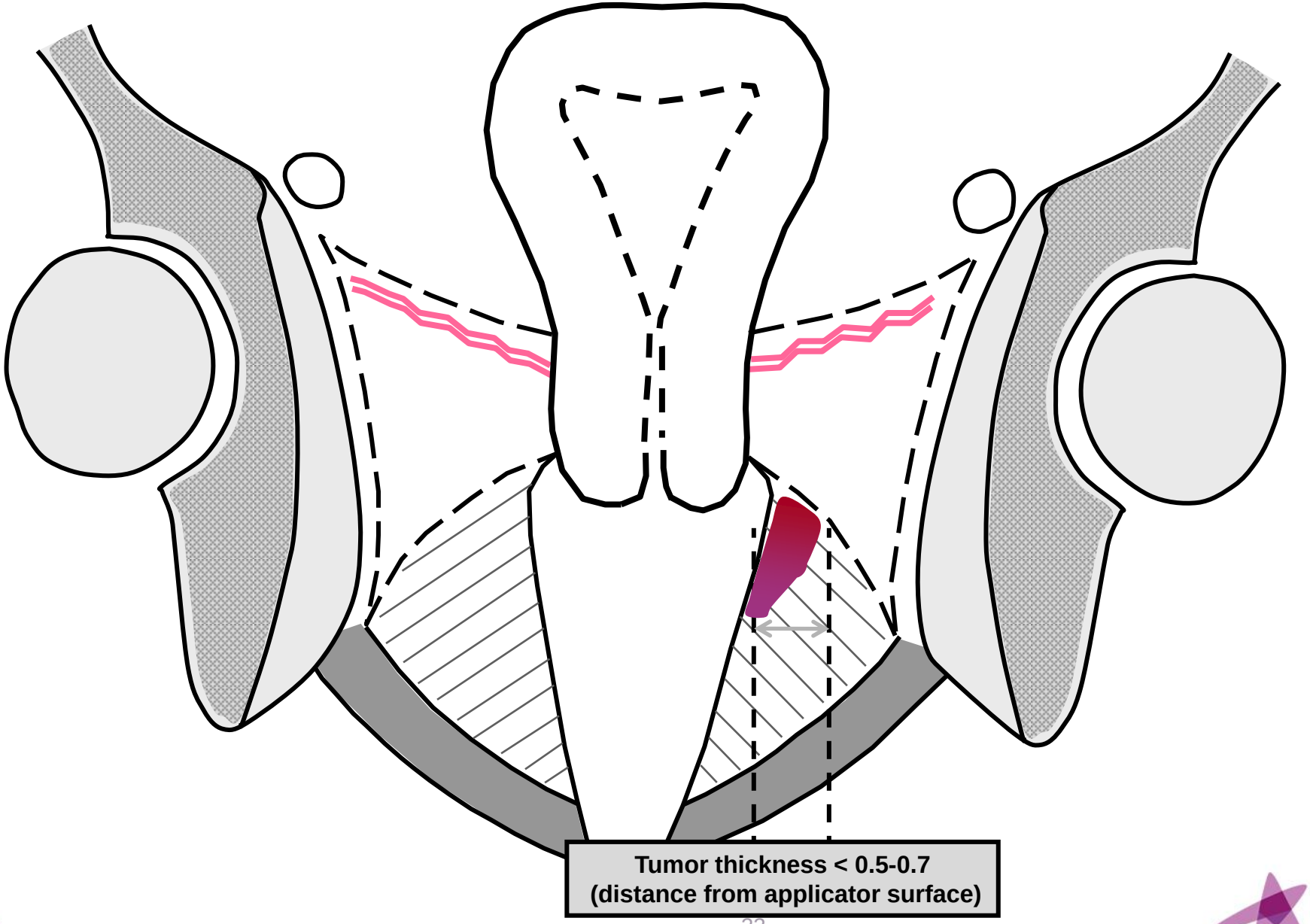
Interstitial Techniques Vagina

Pattern of tumor regression



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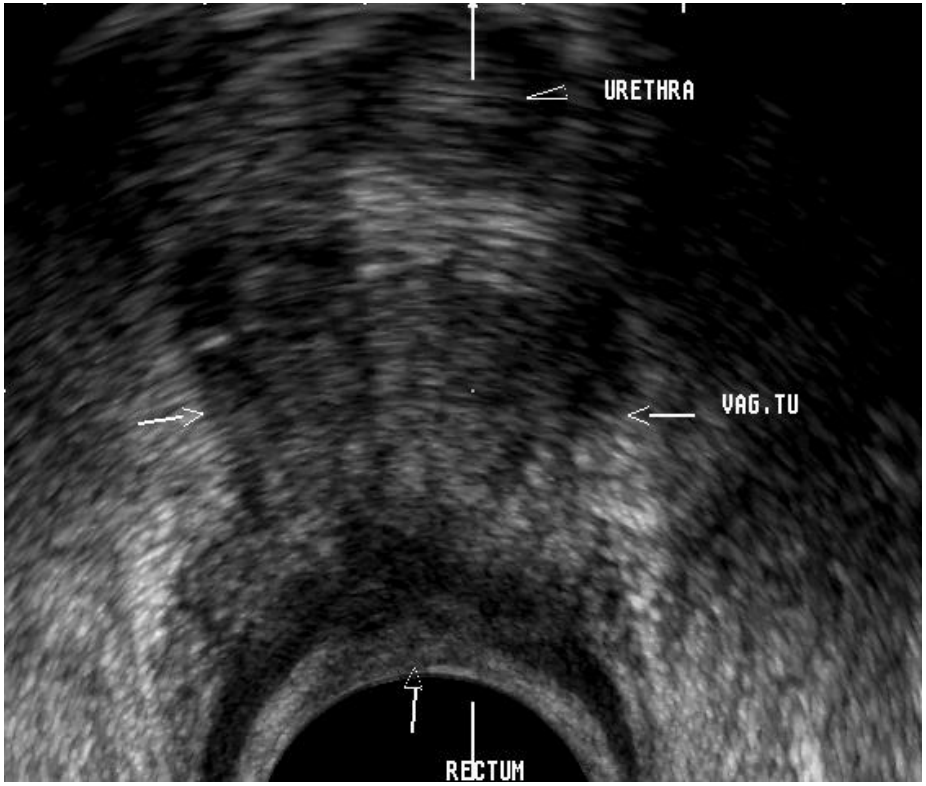
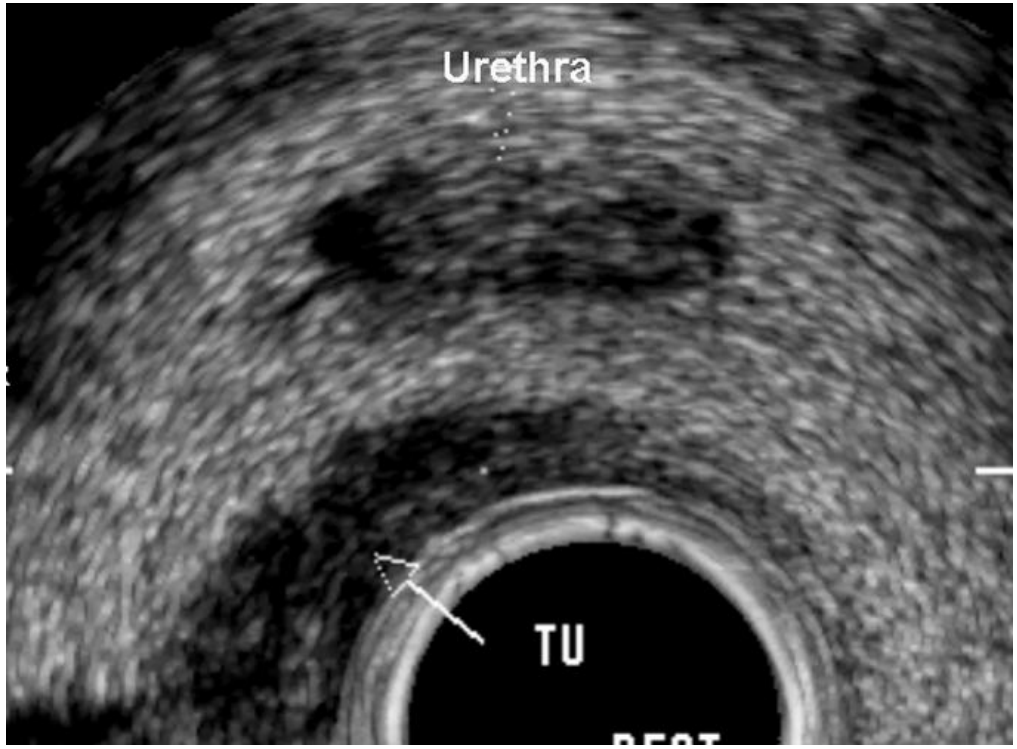
Interstitial Techniques Vagina

Importance of initial work-up

Assessment of tumor thickness with endosonography

decisive for selection of appropriate application technique





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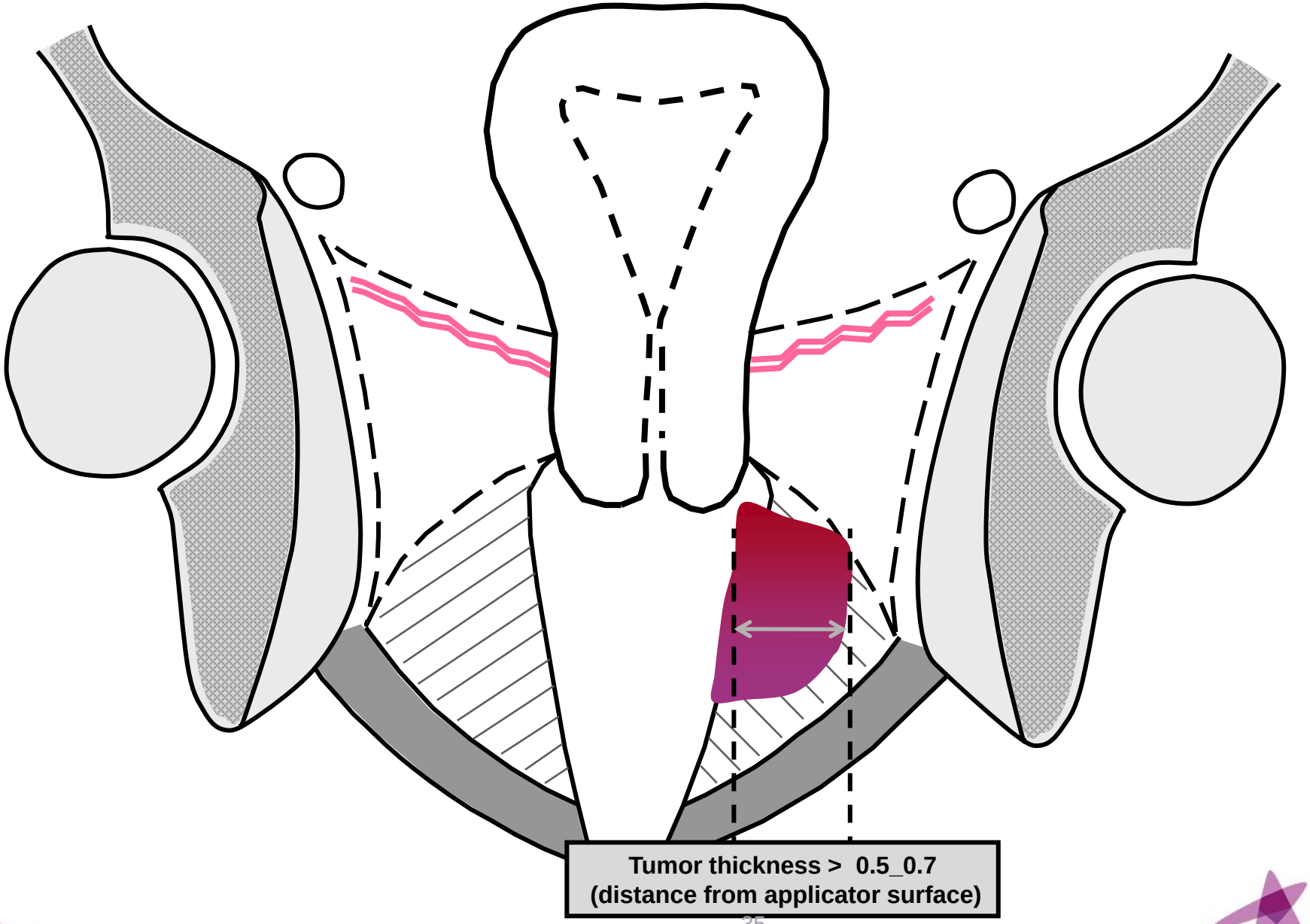
Interstitial Techniques Vagina

Pattern of tumor regression



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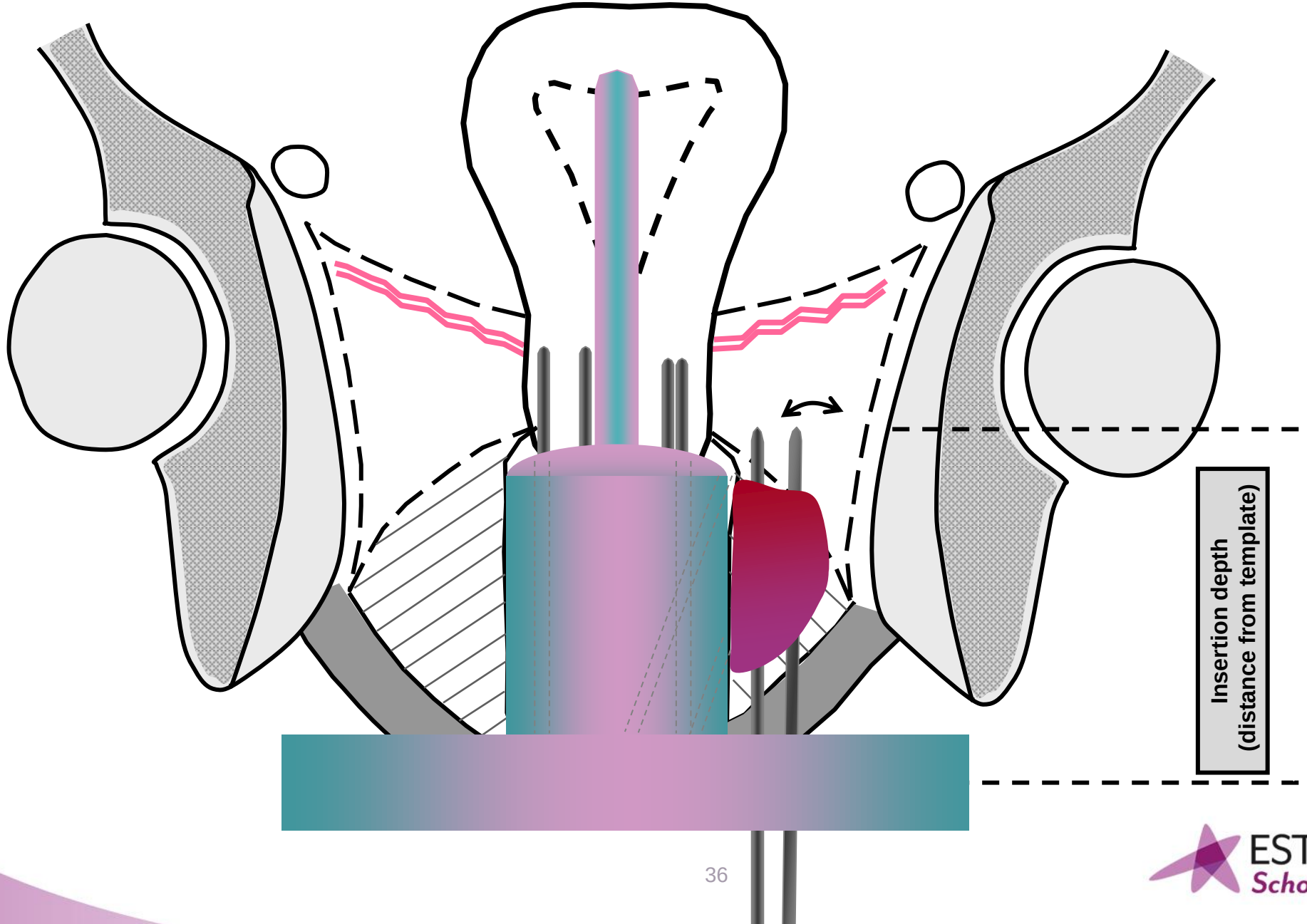
Interstitial Techniques Vagina

Pattern of tumor regression



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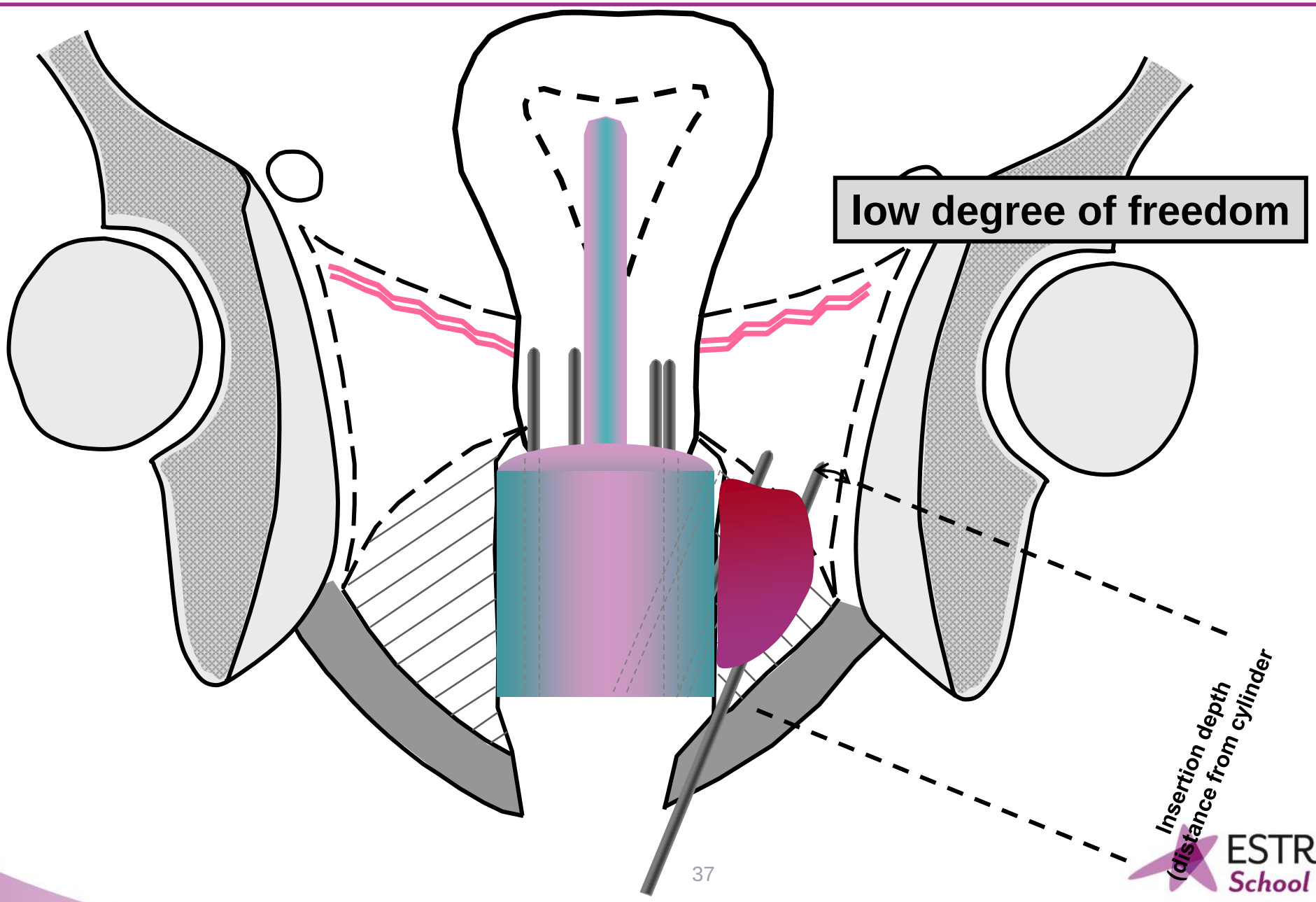
Interstitial Techniques Vagina

Pattern of tumor regression



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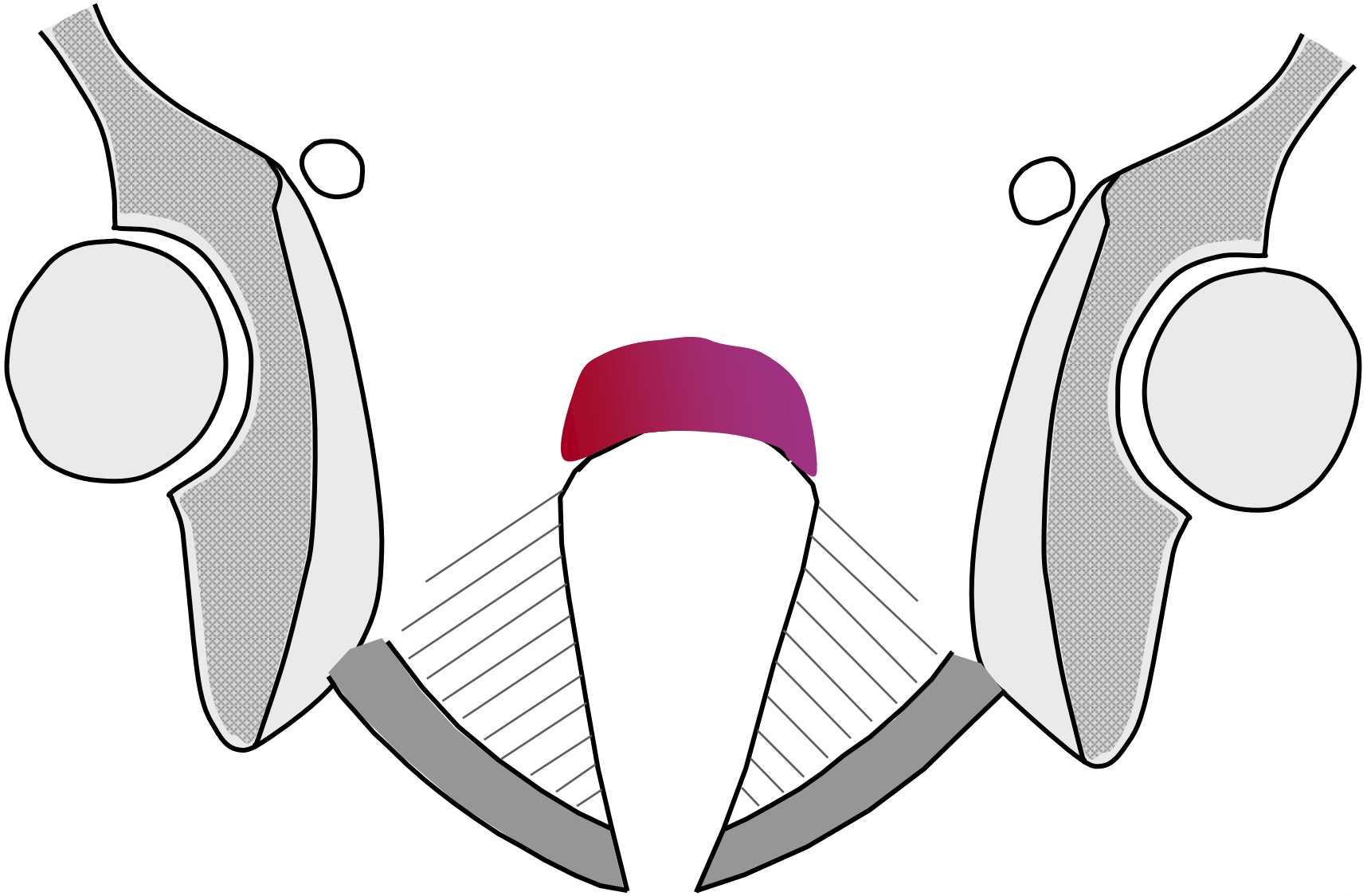
Interstitial Techniques Vagina

Vaginal Cuff



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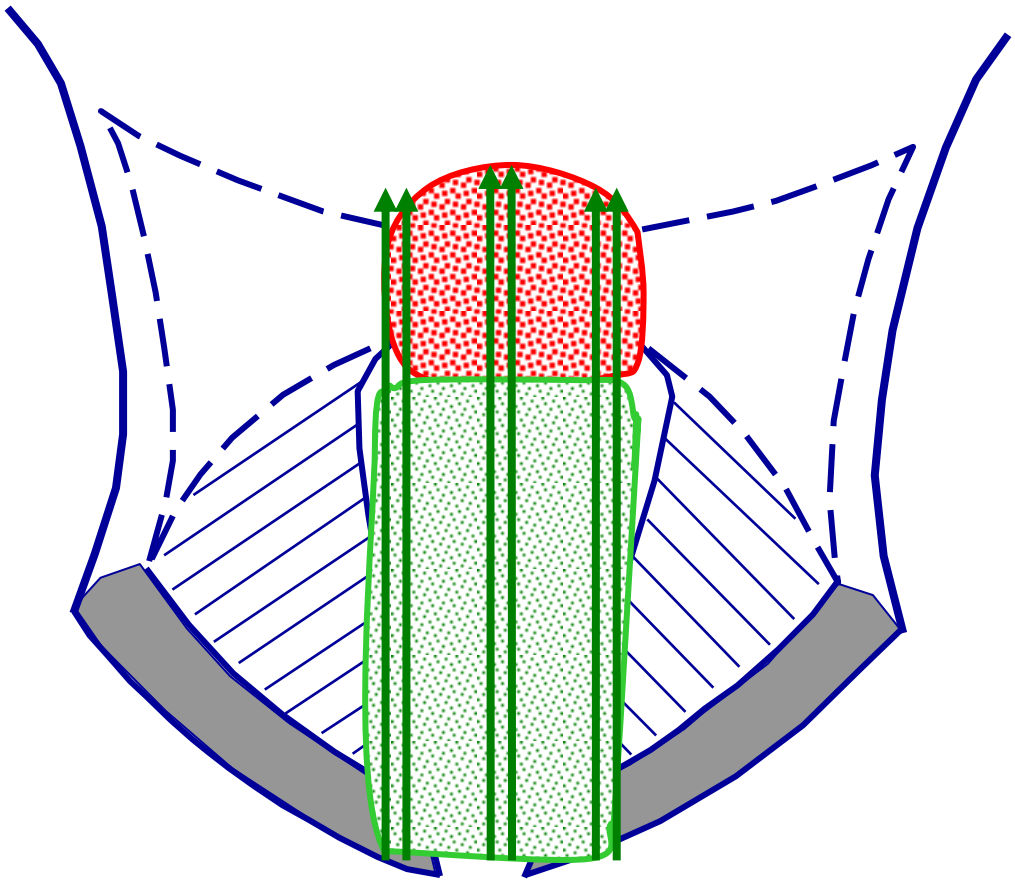
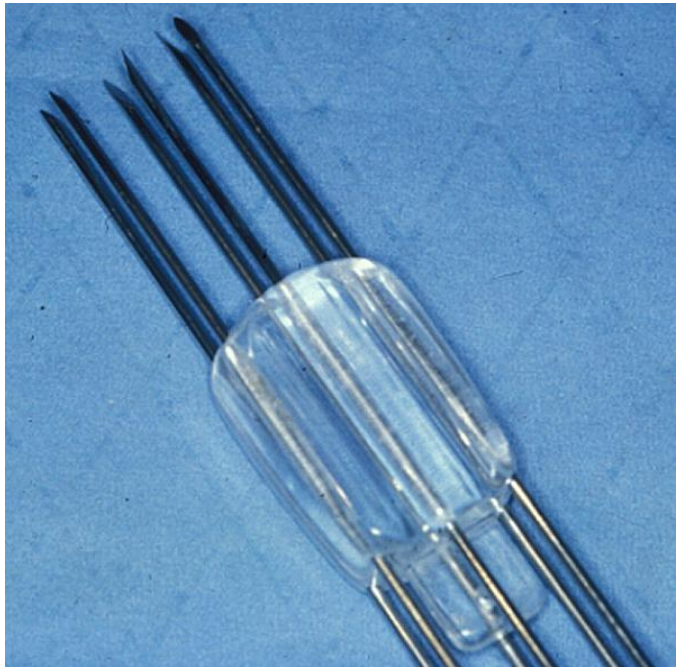
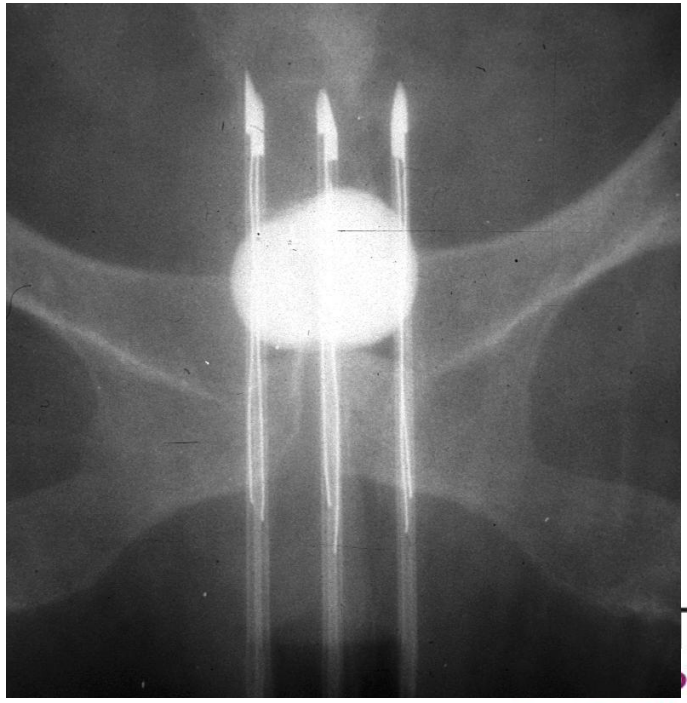
Apical tumors
> 10 mm thickness

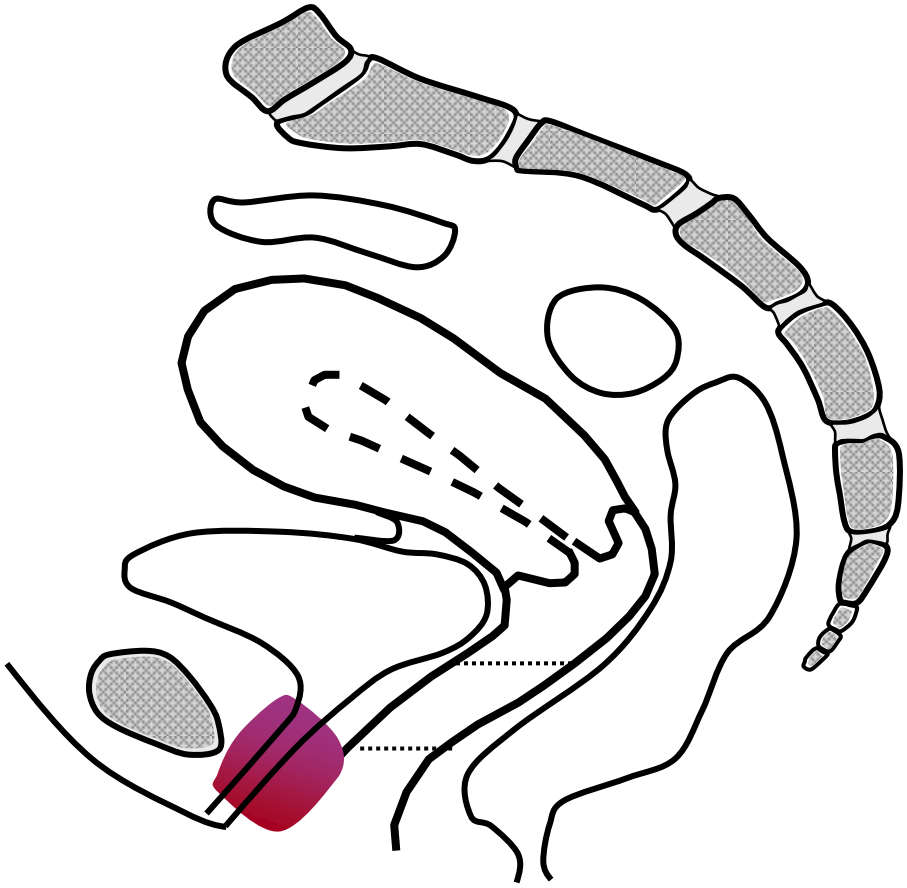


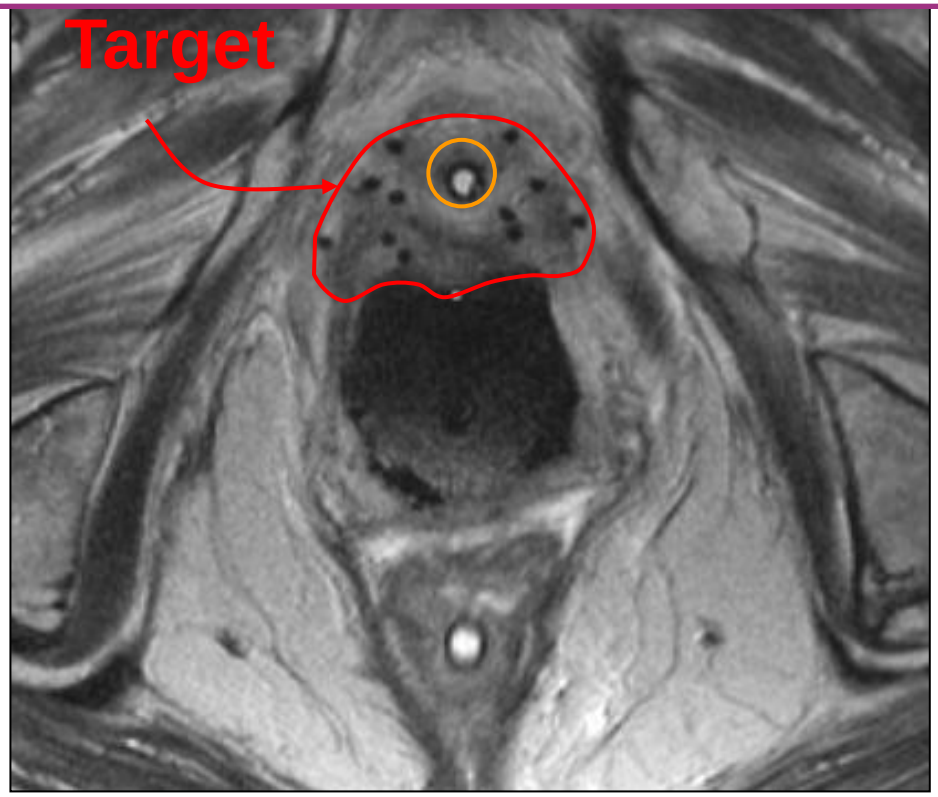


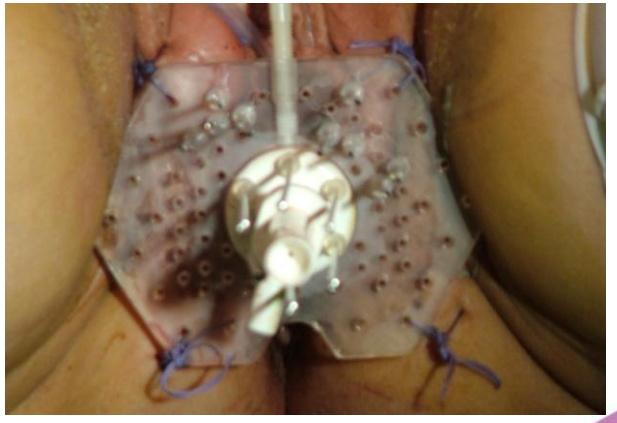


Interstitial Techniques Vagina

Pattern of tumor regression







Suburethral tumour

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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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Interstitial techniques

Better coverage of target volume
Reducing dose in OAR

Template based
Imaging based

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GYNAECOLOGICAL IMPLANTATION

COMPREHENSIVE AND PRACTICAL BRACHYTHERAPY

ESTRO Teaching Course, Budapest 2017

Emmie Kaljouw
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ESTRO School

Gynaecological implantation

- Performing a CT scan
- Digitising ring applicator based on CT
- Ring applicator, standard plan
- Performing an MRI scan
- Digitising fletcher applicator in TPS
- Digitising catheters in TPS
- Library planning
- ICRU 89 points A
- Fletcher applicator, optimisation
- EQD2 calculation
- Registration of CT and MRI

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Performing a CT scan

- Imaging after applicator placement

- Catheter visualisation
  - Metal applicator
  - Synthetic applicator
  - Line markers
  - Slice thickness
  - Slice spacing

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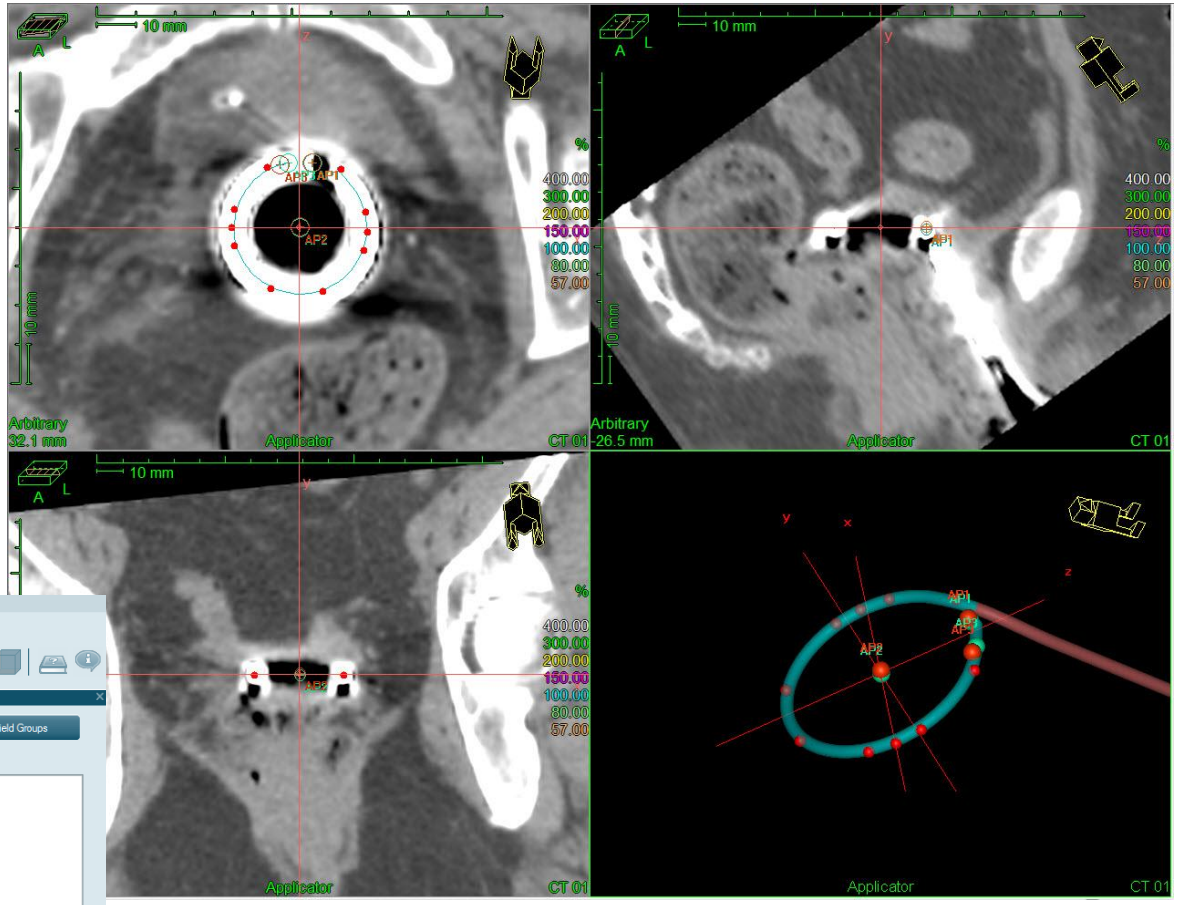
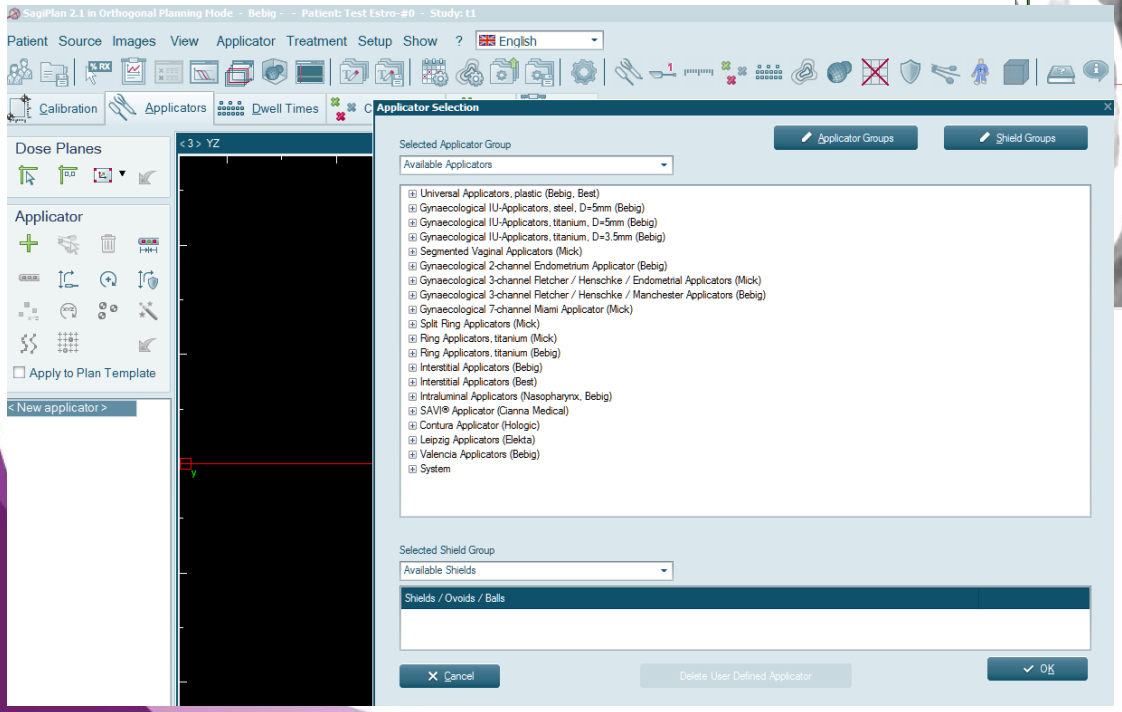
Digitising ring applicator based on CT

- Import images in treatment planning system
- Select the right applicator from the applicator library
- Digitise the entire applicator





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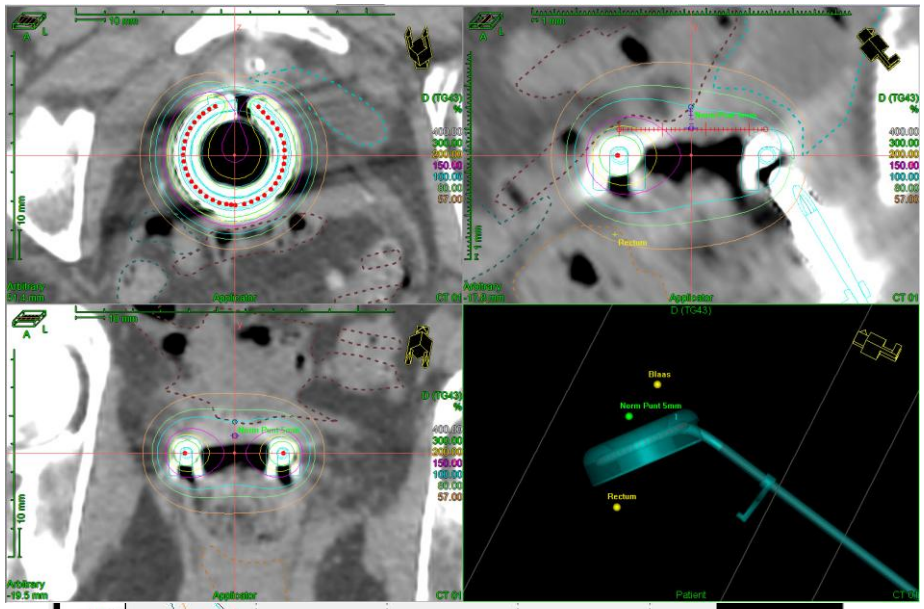
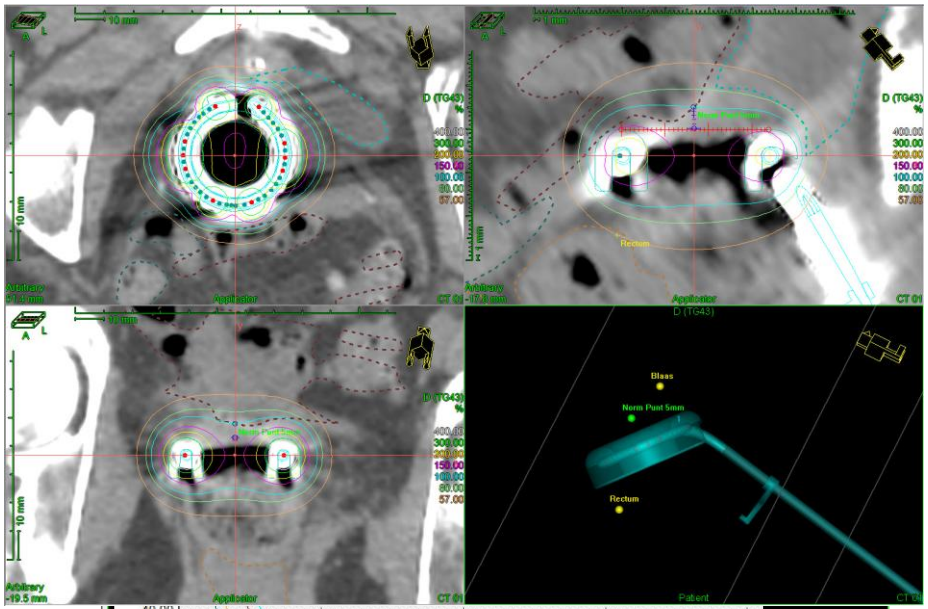
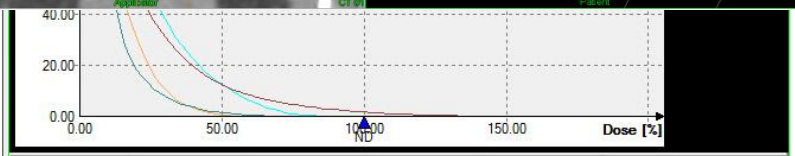
Ring applicator, standard plan



ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
bladder	62.46	437.21	3.01	**2.00**
bowel	111.54	780.78	1.65	**2.00**
rectum	43.36	303.54	2.81	**2.00**
sigmoid	47.02	329.14	3.00	**2.00**

Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	1	-33.1	37.3	27.5	1.00	0.00	5.54	
1	2	-35.2	37.7	26.5	1.00	0.00	5.54	
1	3	-37.2	38.3	25.2	1.00	0.00	5.54	
1	4	-38.6	38.9	24.1	1.00	0.00	5.54	
1	5	-40.3	39.8	22.5	1.00	0.00	5.54	
1	6	-41.6	40.9	20.8	1.00	0.00	5.54	
1	7	-42.6	42.1	19.0	1.00	0.00	5.54	
1	8	-43.4	43.5	17.1	1.00	0.00	5.54	
1	9	-43.9	45.0	15.2	1.00	0.00	5.54	
1	10	-44.0	46.5	13.4	1.00	0.00	5.54	
1	11	-43.8	48.0	11.6	1.00	0.00	5.54	
1	12	-43.3	49.5	9.8	1.00	0.00	5.54	
1	13	-42.4	51.1	8.2	1.00	0.00	5.54	
1	14	-41.3	52.6	6.6	1.00	0.00	5.54	
1	15	-39.9	54.1	5.3	1.00	0.00	5.54	
1	16	-38.3	55.3	4.2	1.00	0.00	5.54	
1	17	-36.3	56.6	3.2	1.00	0.00	5.54	
1	18	-34.0	57.8	2.5	1.00	0.00	5.54	
1	19	-31.7	58.6	2.0	1.00	0.00	5.54	
1	20	-29.4	59.3	1.9	1.00	0.00	5.54	
1	21	-27.8	59.6	1.9	1.00	0.00	5.54	
1	22	-26.3	59.9	2.0	1.00	0.00	5.54	
1	23	-23.3	60.0	2.7	1.00	0.00	5.54	
1	24	-21.0	59.9	3.5	1.00	0.00	5.54	





ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
bladder	67.24	470.66	3.01	**2.00**
bowel	100.58	704.05	1.65	**2.00**
rectum	40.71	284.97	2.81	**2.00**
sigmoid	41.82	292.76	3.00	**2.00**

Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	1	-33.1	37.3	27.5	1.00	0.00	22.44	
1	8	-43.4	43.5	17.1	1.00	0.00	22.44	
1	10	-44.0	46.5	13.4	1.00	0.00	22.44	
1	12	-43.3	49.5	9.8	1.00	0.00	22.44	
1	18	-34.0	57.8	2.5	1.00	0.00	22.44	
1	24	-21.0	59.9	3.5	1.00	0.00	22.44	
1	30	-10.5	54.4	13.0	1.00	0.00	22.44	
1	32	-9.6	51.7	16.6	1.00	0.00	22.44	
1	34	-10.0	48.5	20.3	1.00	0.00	22.44	
1	40	-18.5	39.0	28.7	1.00	0.00	22.44	

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Performing an MRI scan

- Imaging after catheter/ applicator placement

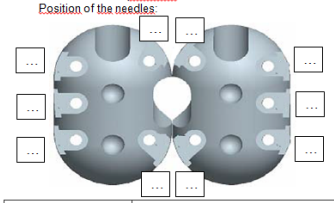
- Catheter/ applicator visualisation
  - Synthetic needle/ applicator
  - Line markers
  - Slice thickness
  - Slice spacing

MRI fletcher

Date:
Fysician:
Technician:

Patient Name:
Patient number:
Date of birth:

☐ Needles used (ProGuide Needles Round 6F x 294 110.230)
Position of the needles:



EBRT dose:

Intra-uterine:	▫ 15° ▫ 30°		
Ovoids	**left:**	mm	**right:** mm
Needle angle:	▫ 15° ▫ 25°		

Total dose	cGy	
Dose per fraction	cGy	
Number of fractions		
Stepsize	▫ 2,5mm ▫ 5mm	
Period time	……hour ……min.	
PDR	▫ Blue F5-230	▫ Green F5-237
HDR	▫ Red F5-234	
Transfertubes fletcher		
Transfertubes naalden		

Catheter Number (= chanal number)	Catheter Length (mm)	Transfer tubes	Indexer (mm)	Offset (mm)	External lenght catheter (extending from the tubes)	Catheter depth (depth of needle into the patient)
1	Applicator library	Rechtstreeks	1500	0		
2	Applicator library	Rechtstreeks	1500	0		
3	Applicator library	Rechtstreeks	1500	0		
4	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
5	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
6	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
7	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
8	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
9	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
10	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
11	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
12	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		
13	293	Rechtstreeks	1293 (1005 + 293 - 5)	-5		

Remarks:

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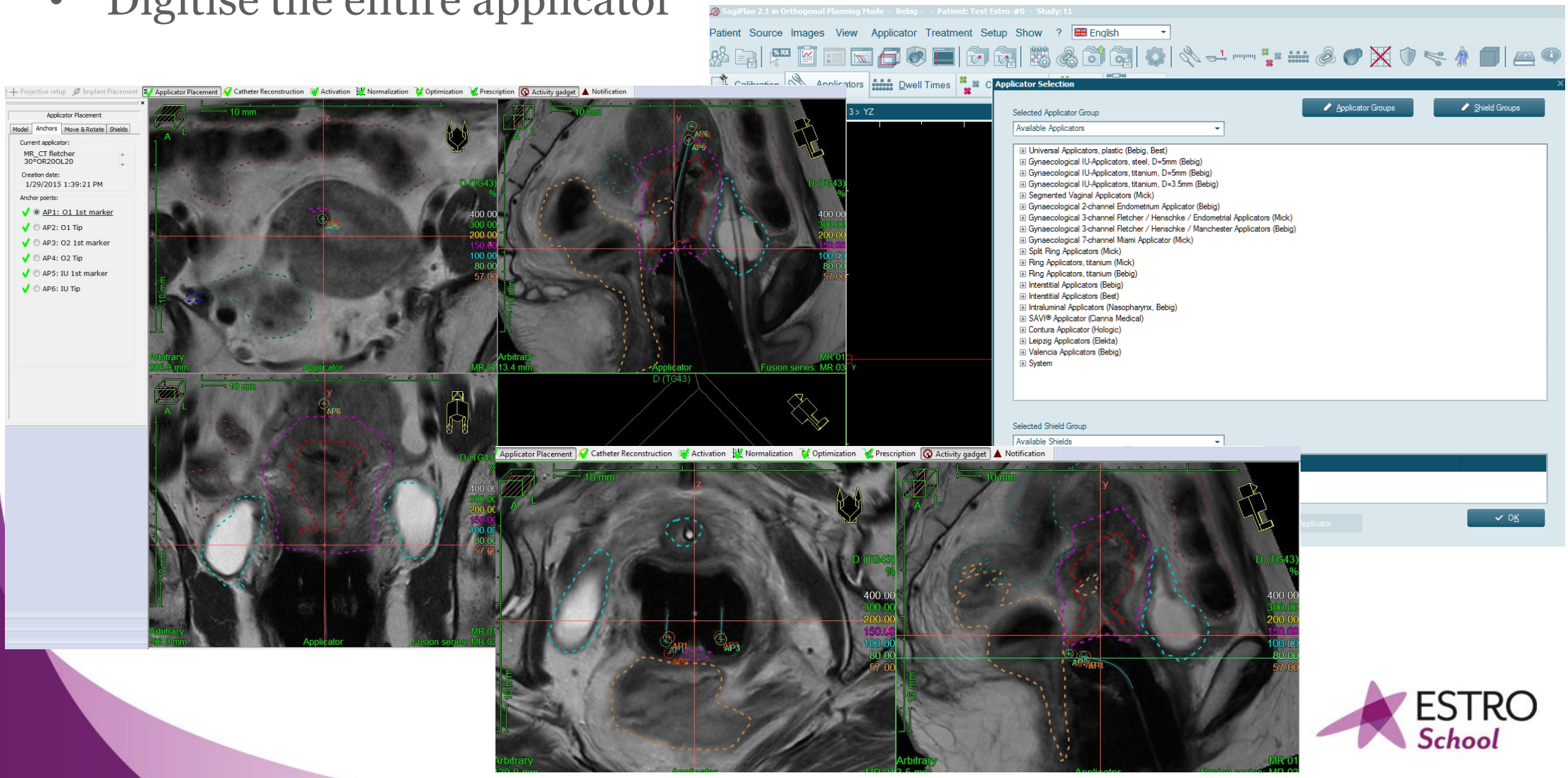
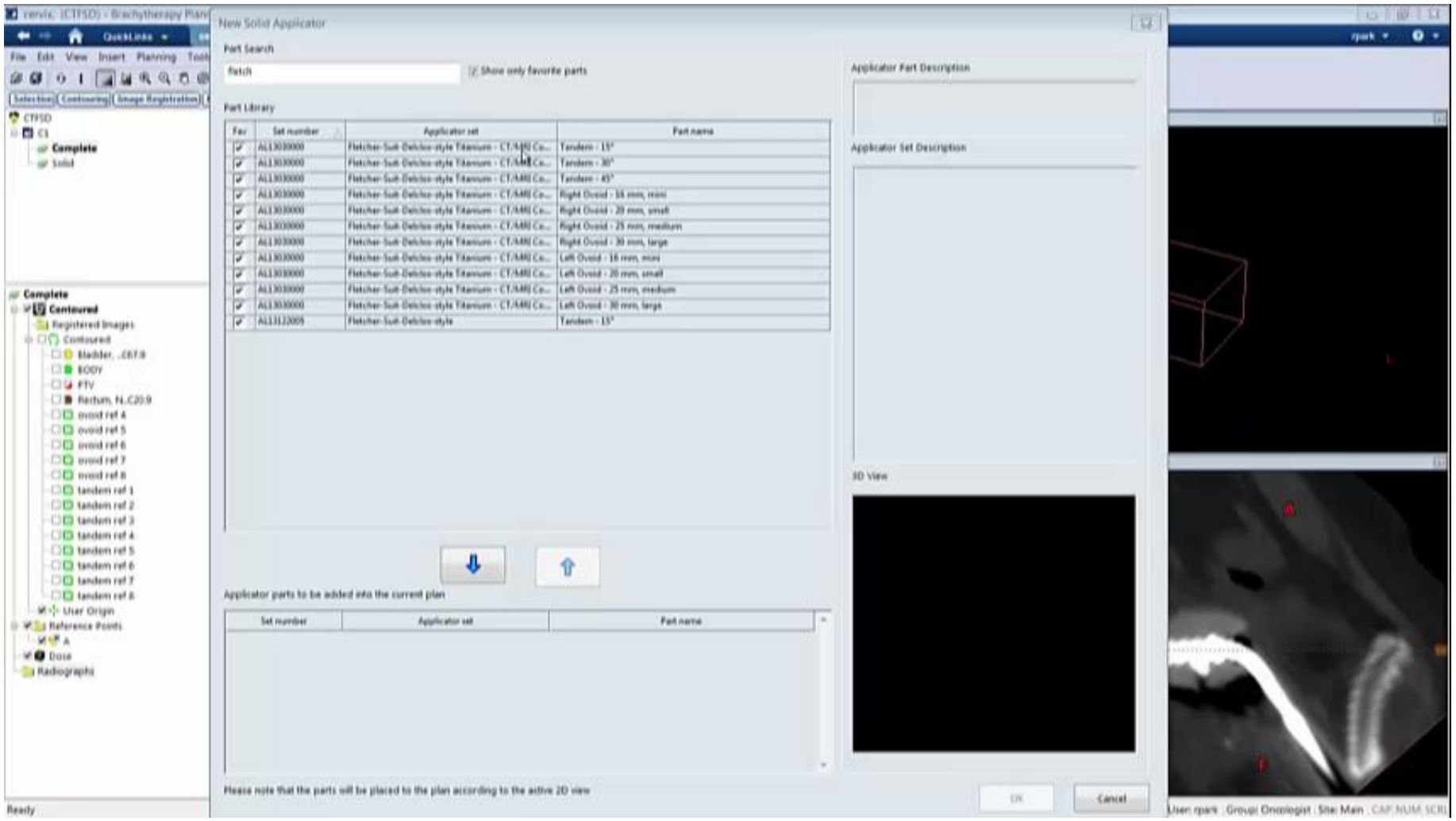
Digitising fletcher applicator in TPS

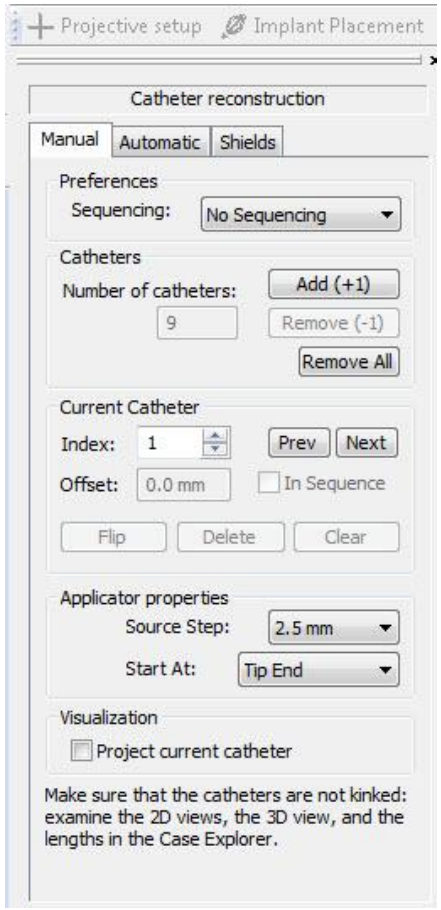
- Import images in treatment planning system
- Select the right applicator from the applicator library
- Digitise the entire applicator

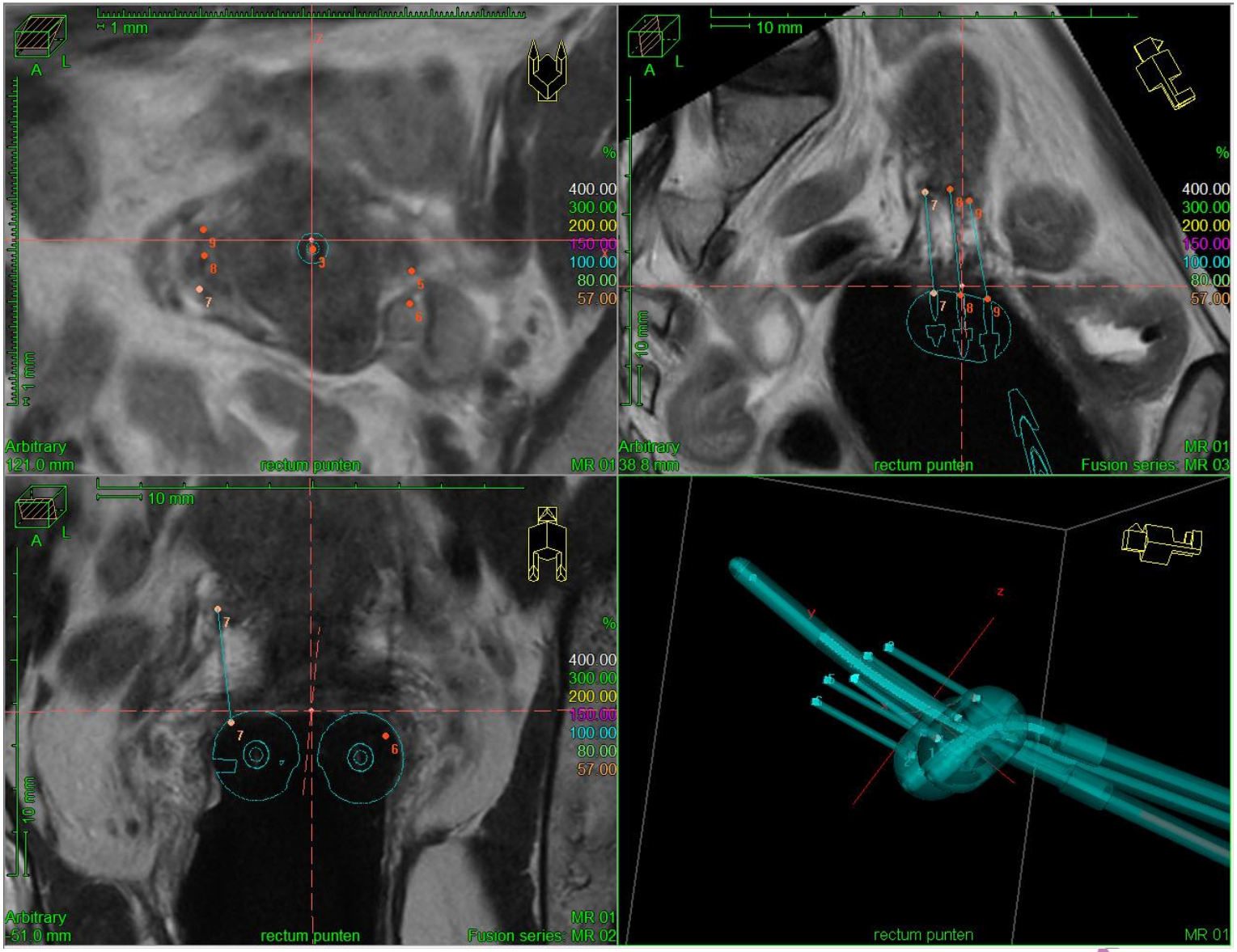


Digitising fletcher applicator in TPS



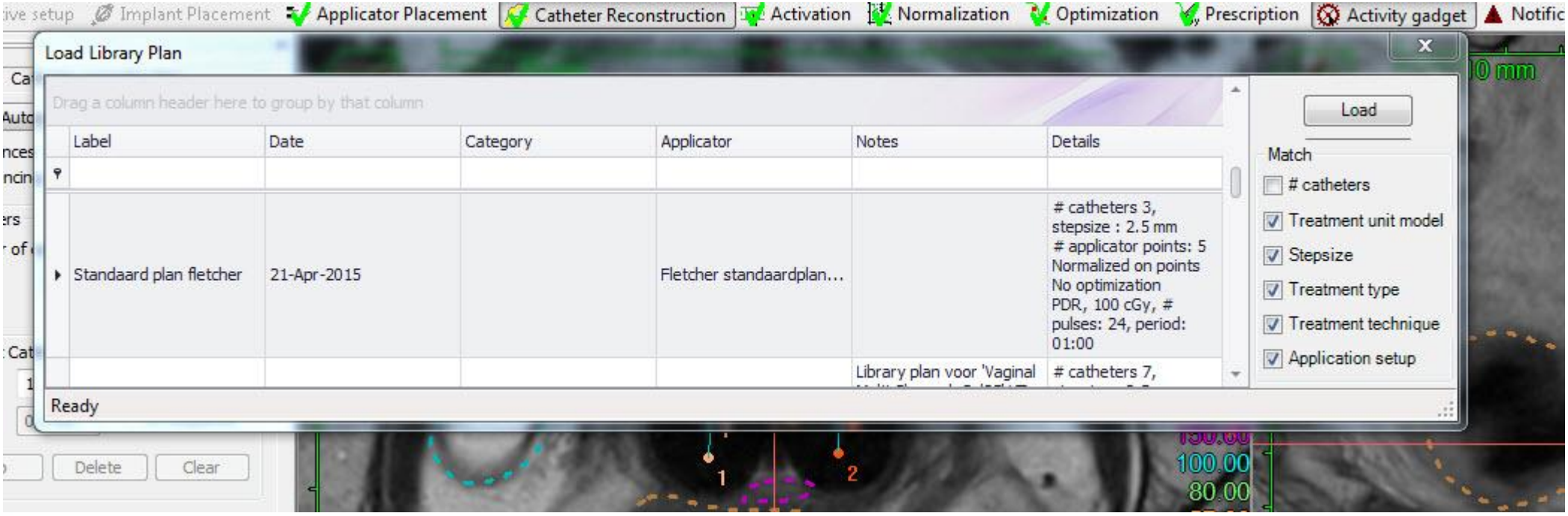
Digitising catheters in TPS



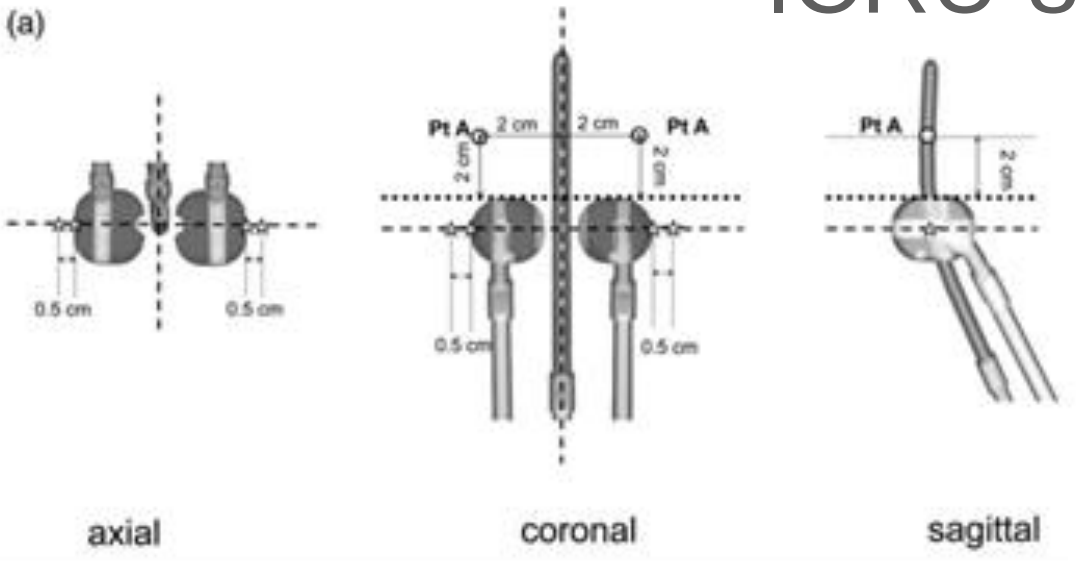


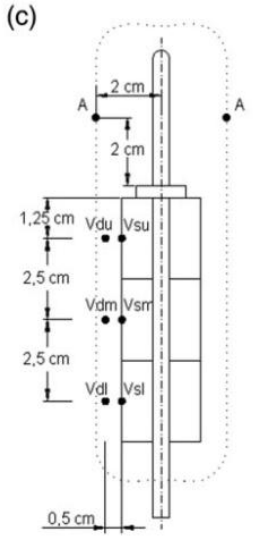
Library plan

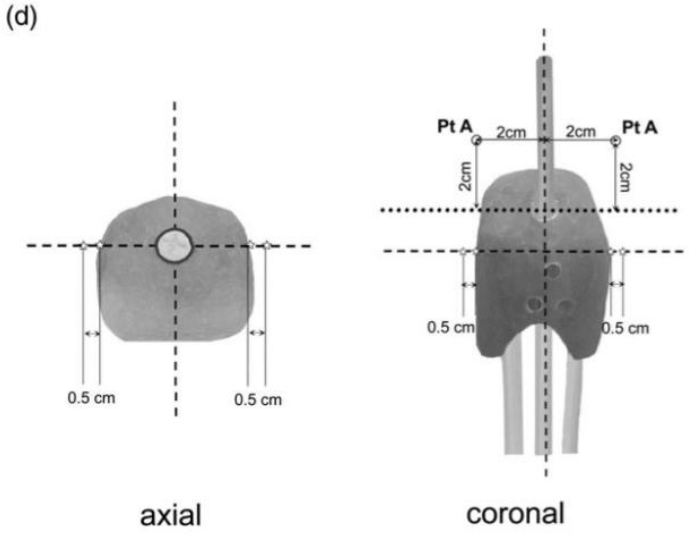
- Basic treatment planning saved in the computer
  - Involving for example stapsize, applicator points, dose, pulses and period time
- Loaded after reconstruction of the applicator

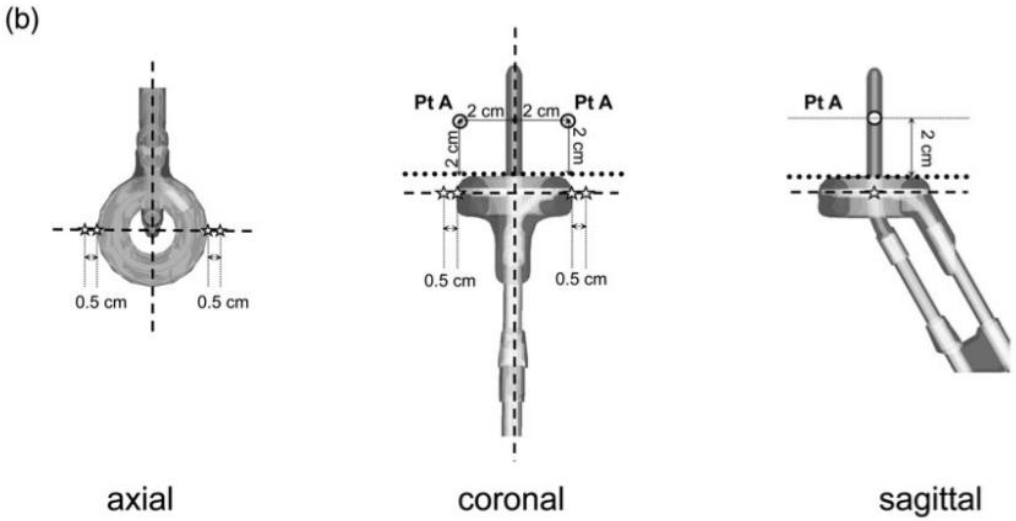


ICRU 89 points A

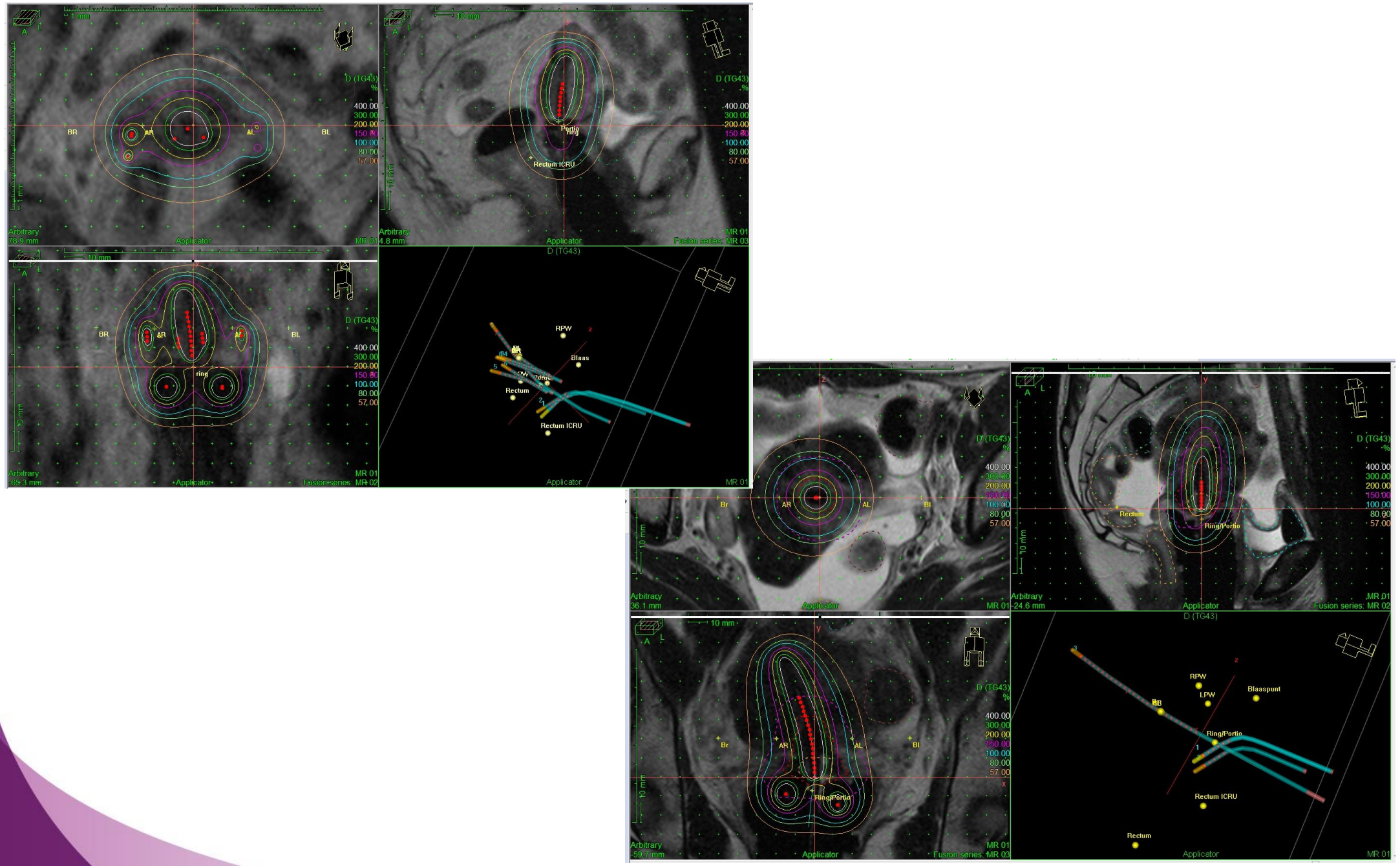




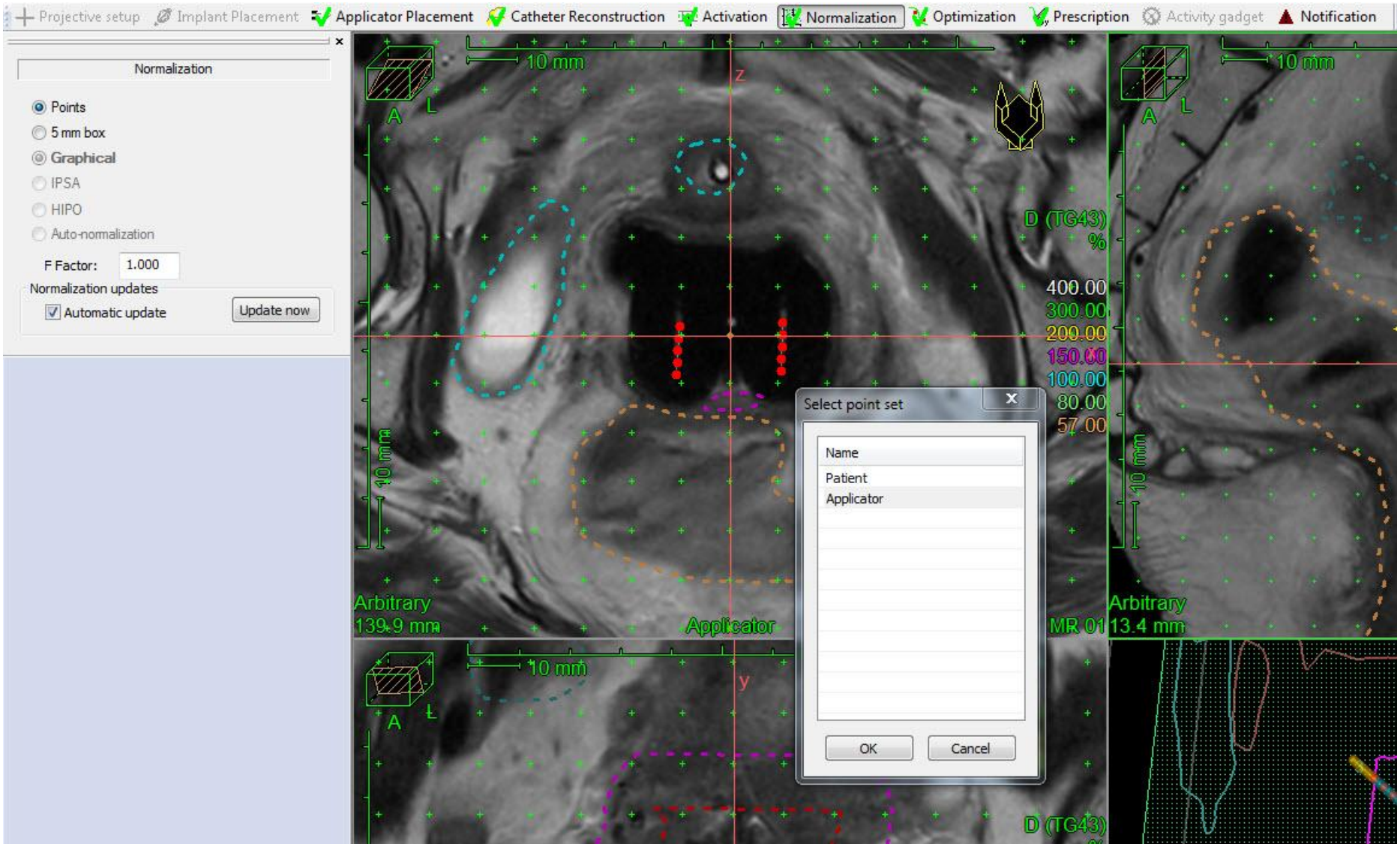




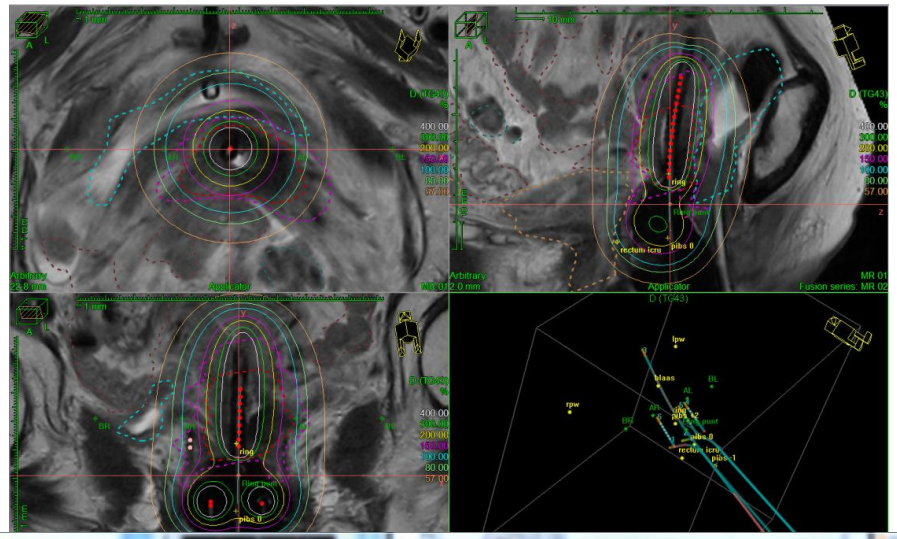
ICRU 89 points A

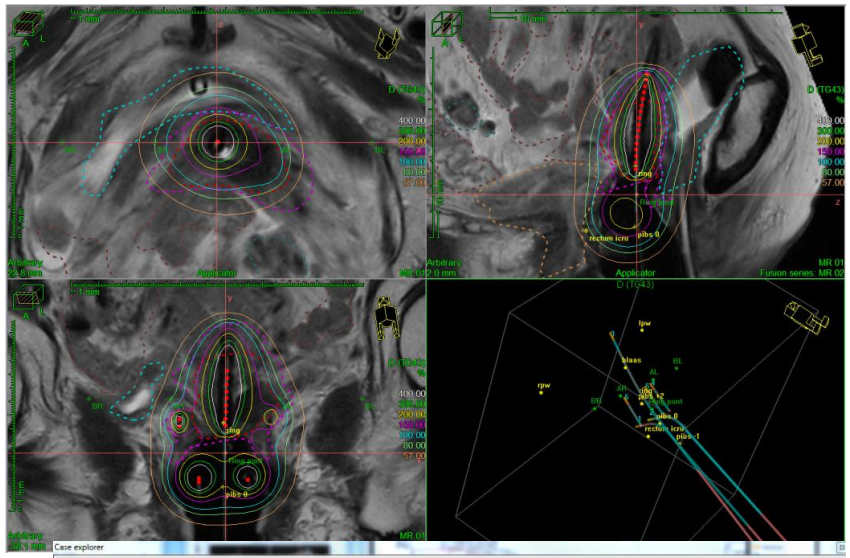


ICRU 89 points A



Flechter applicator, optimisation





Case explorer

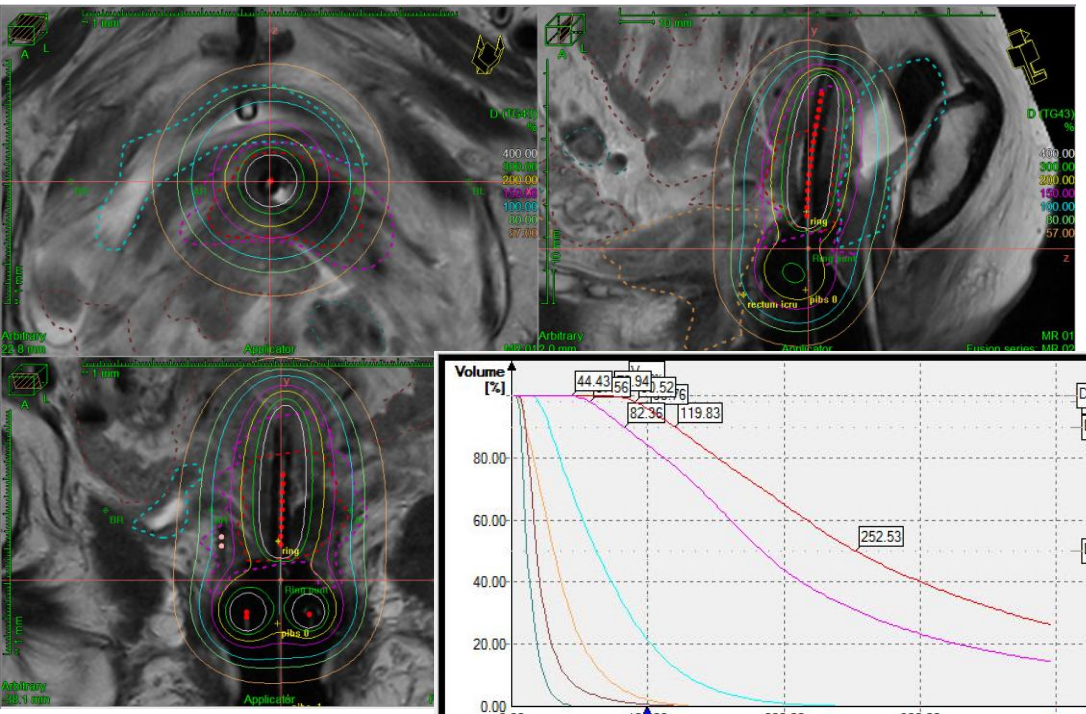
ROI Set
Plans
Brachy plan
Applicator
Anchor Points
Active Dwell Positions
#1/O1
#2/O2
#3/IU
#4
#5
#6
Points
Patient
Applicator

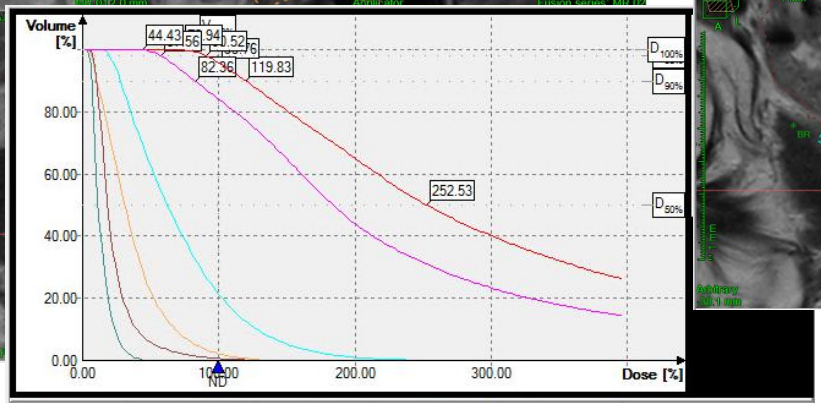
Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	2	-7.6	15.0	-43.3	1.00	0.00	33.97	
1	3	-7.8	13.3	-41.5	1.00	0.00	33.97	
1	4	-8.0	11.6	-39.7	1.00	0.00	33.97	
1	5	-8.2	9.8	-37.9	1.00	0.00	33.97	
1	6	-8.4	7.8	-36.4	1.00	0.00	33.97	
2	2	9.7	13.8	-45.6	1.00	0.00	33.97	
2	3	9.6	12.1	-43.7	1.00	0.00	33.97	
2	4	9.6	10.4	-41.9	1.00	0.00	33.97	
2	5	9.5	8.7	-40.1	1.00	0.00	33.97	
2	6	9.4	6.7	-38.6	1.00	0.00	33.97	
3	5	11.4	60.4	-11.6	1.00	0.00	33.97	
3	6	10.9	58.3	-12.9	1.00	0.00	33.97	
3	7	10.5	56.2	-14.3	1.00	0.00	33.97	
3	8	10.0	54.1	-15.6	1.00	0.00	33.97	
3	9	9.5	52.1	-16.9	1.00	0.00	33.97	
3	10	9.1	50.0	-18.2	1.00	0.00	33.97	
3	11	8.6	47.9	-19.5	1.00	0.00	33.97	
3	12	8.2	45.8	-20.8	1.00	0.00	33.97	
3	13	7.7	43.7	-22.0	1.00	0.00	33.97	
3	14	7.3	41.6	-23.3	1.00	0.00	33.97	
3	15	6.8	39.4	-24.4	1.00	0.00	33.97	
3	16	6.4	37.2	-25.6	1.00	0.00	33.97	
3	17	5.9	35.0	-26.7	1.00	0.00	33.97	
3	18	5.5	32.8	-27.8	1.00	0.00	33.97	
3	19	5.1	30.6	-28.9	1.00	0.00	33.97	
3	20	4.6	28.4	-29.9	1.00	0.00	33.97	
3	21	4.2	26.1	-30.9	1.00	0.00	33.97	
4	1	21.4	27.4	-32.0	0.00	0.00	0.00	
4	2	20.9	25.1	-32.8	0.00	0.00	0.00	
4	3	20.5	22.8	-33.6	0.00	0.00	0.00	
4	4	20.1	20.5	-34.4	0.00	0.00	0.00	
4	5	19.6	18.2	-35.2	0.00	0.00	0.00	
5	1	21.1	30.7	-37.5	0.00	0.00	0.00	

Name	X [mm]	Y [m...	Z [m...	Coord....	Abs. Dos...	Rel. Dose [%]	Normalization	Norm. Dose [%]	Optimization
Ring punt	0.0	0.0	0.0	Applic...	162.00	216.00	No	100.00	No
AR	-20.0	20.0	0.0	Applic...	73.12	97.49	Yes	100.00	No
AL	20.0	20.0	0.0	Applic...	76.88	102.51	Yes	100.00	No
BR	-50.0	20.0	0.0	Applic...	17.90	23.86	No	100.00	No
BL	50.0	20.0	0.0	Applic...	18.20	24.26	No	100.00	No

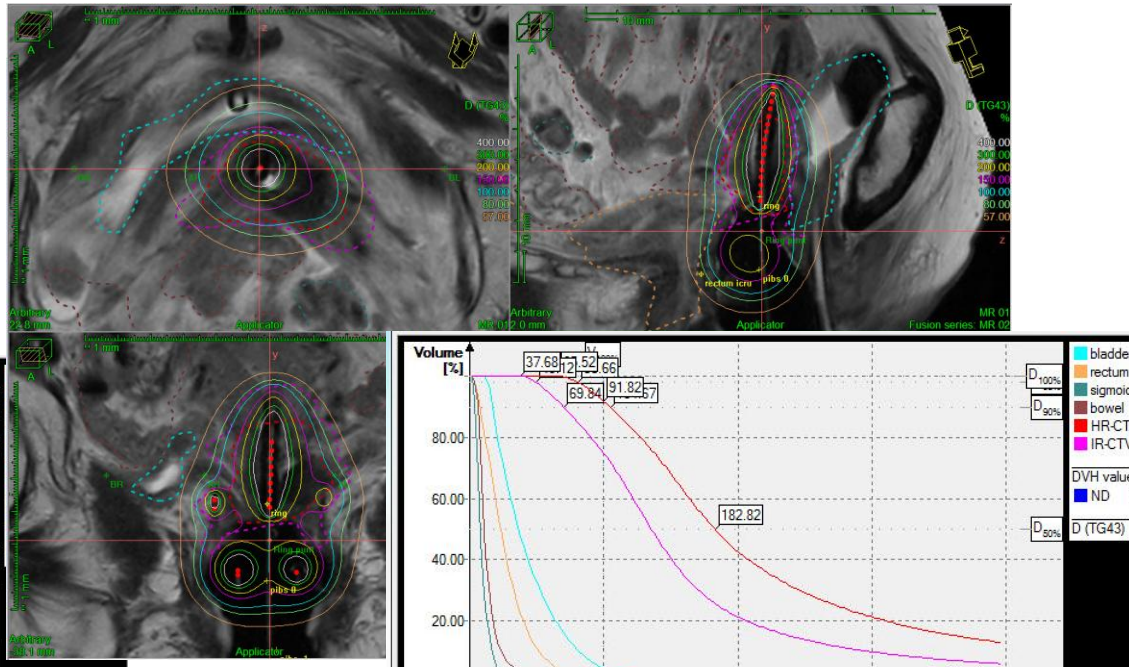
Name	X [mm]	Y [m...	Z [m...	Coord....	Abs. Dos...	Rel. Dose [%]	Normalization	Norm. Dose [%]	Optimization	Opt. Rel. Dose
Ring punt	0.0	0.0	0.0	Applic...	116.43	155.23	No	100.00	No	10
AR	-20.0	20.0	0.0	Applic...	58.96	78.61	No	100.00	No	10
AL	20.0	20.0	0.0	Applic...	71.54	95.39	No	100.00	No	10
BR	-50.0	20.0	0.0	Applic...	12.46	16.62	No	100.00	No	10
BL	50.0	20.0	0.0	Applic...	13.19	17.59	No	100.00	No	10

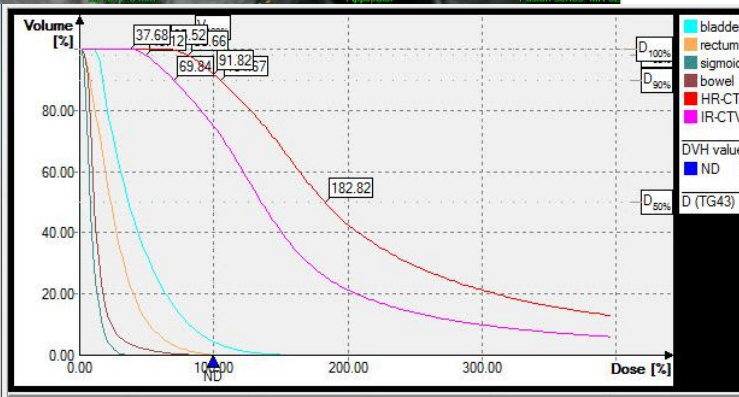
Fletcher applicator, optimisation





ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
HR-CTV	**100.00**	75.00	95.76	12.96
HR-CTV	72.94	54.71	**100.00**	13.53
HR-CTV	252.53	189.40	**50.00**	6.77
HR-CTV	119.83	89.87	**90.00**	12.18
HR-CTV	90.52	67.89	**98.00**	13.26
IR-CTV	44.43	33.32	**100.00**	34.35
IR-CTV	82.36	61.77	**90.00**	30.92
IR-CTV	57.56	43.17	**98.00**	33.66
bladder	235.69	176.76	0.21	**0.10**
bladder	157.07	117.80	4.19	**2.00**
bowel	144.34	108.25	0.04	**0.10**
bowel	95.46	71.59	0.77	**2.00**
rectum	129.27	96.95	0.21	**0.10**
rectum	86.41	64.81	4.27	**2.00**
sigmoid	43.23	32.42	0.24	**0.10**
sigmoid	28.48	21.36	4.90	**2.00**





ROI	Dose [%]	Dose [cGy]	Volume [%]	Volume [ccm]
HR-CTV	**100.00**	75.00	91.82	12.43
HR-CTV	65.52	49.14	**100.00**	13.53
HR-CTV	182.82	137.11	**50.00**	6.77
HR-CTV	104.67	78.50	**90.00**	12.18
HR-CTV	80.66	60.49	**98.00**	13.26
IR-CTV	37.68	28.26	**100.00**	34.35
IR-CTV	69.84	52.38	**90.00**	30.92
IR-CTV	49.12	36.84	**98.00**	33.66
bladder	148.73	111.55	0.21	**0.10**
bladder	100.85	75.64	4.19	**2.00**
bowel	100.48	75.36	0.04	**0.10**
bowel	64.11	48.08	0.77	**2.00**
rectum	97.35	73.01	0.21	**0.10**
rectum	65.89	49.42	4.27	**2.00**
sigmoid	32.41	24.31	0.24	**0.10**
sigmoid	20.59	15.45	4.90	**2.00**

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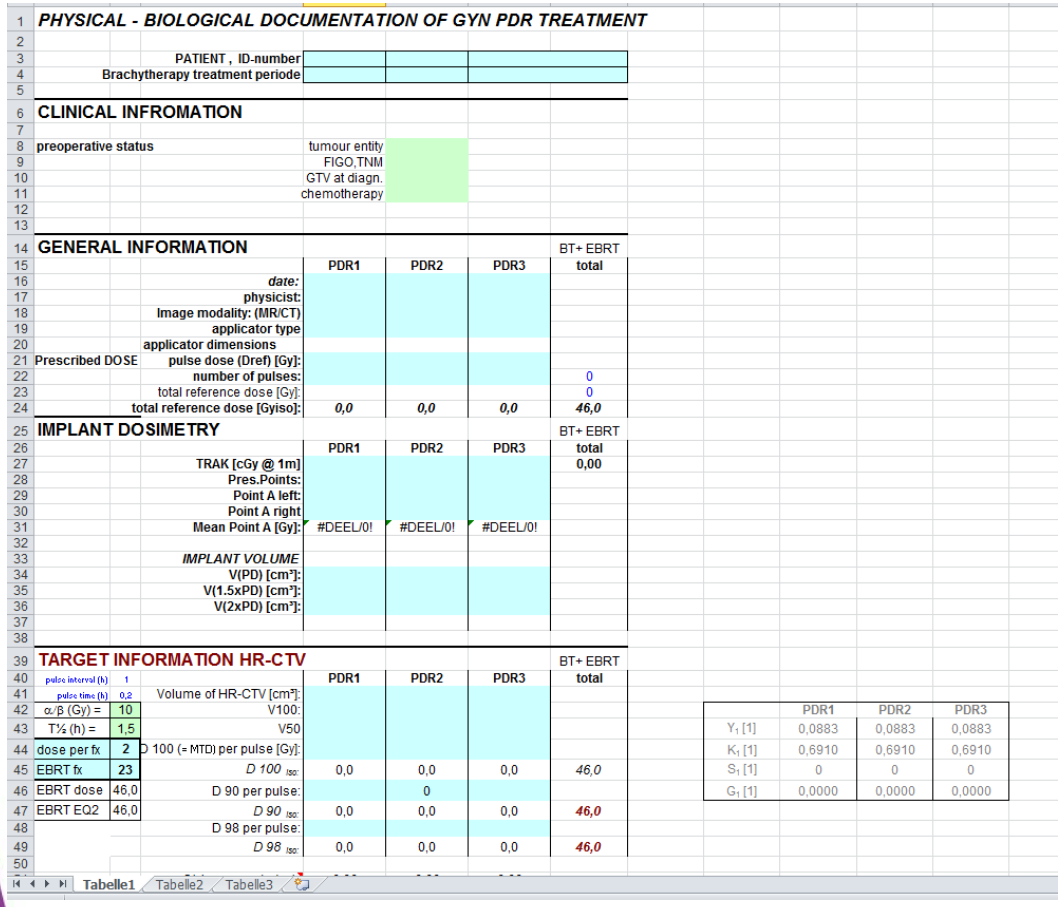
EQD2 calculation



PHYSICAL - BIOLOGICAL DOCUMENTATION OF GYN PDR TREATMENT

PATIENT , ID-number
Brachytherapy treatment periode

CLINICAL INFROMATION

preoperative status
tumour entity
FIGO,TNM
GTV at diagn.
chemotherapy

GENERAL INFORMATION

	PDR1	PDR2	PDR3	BT+ EBRT total
date:				
physicist:				
Image modality: (MR/CT)				
applicator type				
applicator dimensions				
Prescribed DOSE pulse dose (Dref) [Gy]:				
number of pulses:				0
total reference dose [Gy]:				0
total reference dose [Gyiso]:	0,0	0,0	0,0	46,0

IMPLANT DOSIMETRY

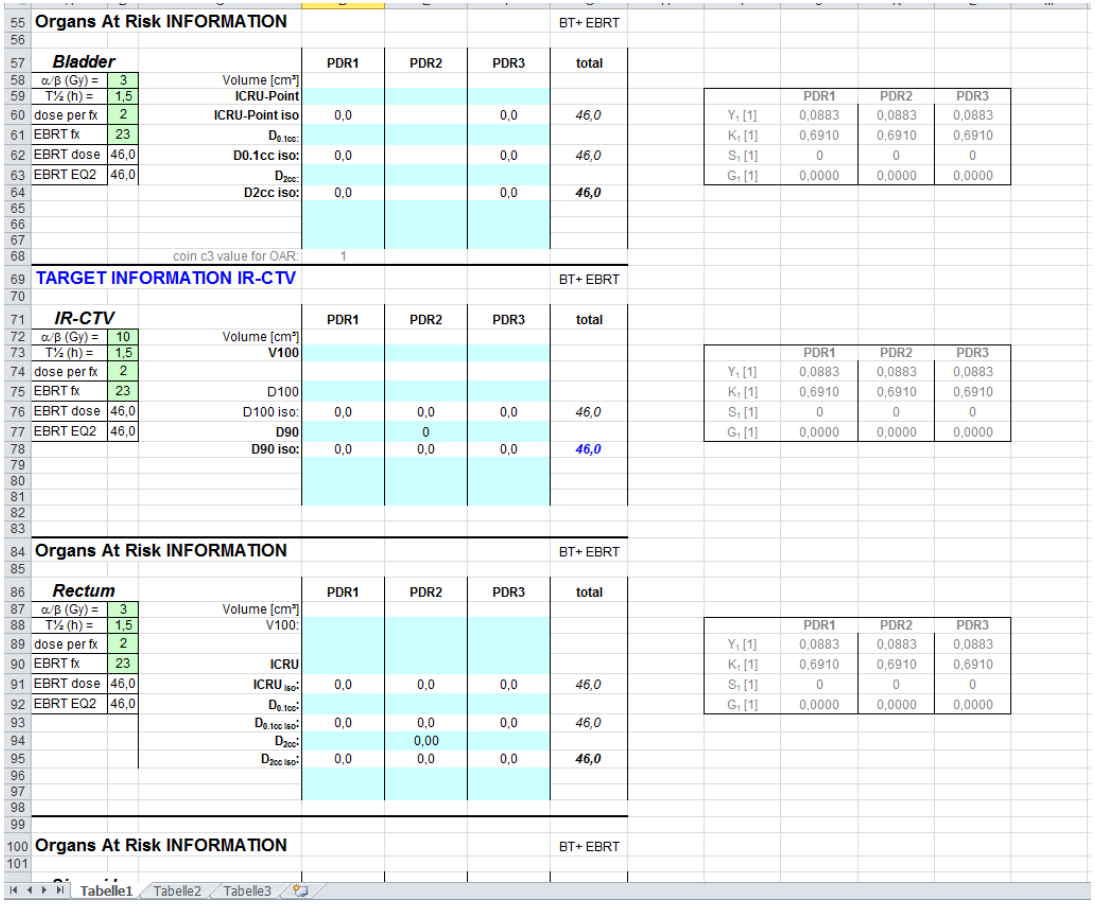
	PDR1	PDR2	PDR3	BT+ EBRT total
TRAK [cGy @ 1m]				0,00
Pres.Points:				
Point A left:				
Point A right				
Mean Point A [Gy]:	#DEEL/0!	#DEEL/0!	#DEEL/0!	
IMPLANT VOLUME				
V(PD) [cm³]:				
V(1.5xPD) [cm³]:				
V(2xPD) [cm³]:				

TARGET INFORMATION HR-CTV

			PDR1	PDR2	PDR3	BT+ EBRT total
pulse interval (h)	1					
pulse time (h)	0,2	Volume of HR-CTV [cm³]:				
α/β (Gy) =	10	V100:				
T½ (h) =	1,5	V50				
dose per fx	2	D 100 (= MTD) per pulse [Gy]:				
EBRT fx	23	D 100 iso:	0,0	0,0	0,0	46,0
EBRT dose	46,0	D 90 per pulse:		0		
EBRT EQ2	46,0	D 90 iso:	0,0	0,0	0,0	46,0
		D 98 per pulse:				
		D 98 iso:	0,0	0,0	0,0	46,0

	PDR1	PDR2	PDR3
Y_1 [1]	0,0883	0,0883	0,0883
K_1 [1]	0,6910	0,6910	0,6910
S_1 [1]	0	0	0
G_1 [1]	0,0000	0,0000	0,0000

Tabelle1 Tabelle2 Tabelle3



Organs At Risk INFORMATION — BT+ EBRT

Bladder

		PDR1	PDR2	PDR3	total
α/β (Gy) =	3	Volume [cm³]			
T½ (h) =	1,5	ICRU-Point			
dose per fx	2	ICRU-Point iso	0,0	0,0	46,0
EBRT fx	23	$D_{0.1cc}$:			
EBRT dose	46,0	D0.1cc iso:	0,0	0,0	46,0
EBRT EQ2	46,0	D_{2cc}:			
		D2cc iso:	0,0	0,0	46,0
		coin c3 value for OAR:	1		

	PDR1	PDR2	PDR3
Y_1 [1]	0,0883	0,0883	0,0883
K_1 [1]	0,6910	0,6910	0,6910
S_1 [1]	0	0	0
G_1 [1]	0,0000	0,0000	0,0000

TARGET INFORMATION IR-CTV — BT+ EBRT

IR-CTV

		PDR1	PDR2	PDR3	total
α/β (Gy) =	10	Volume [cm³]			
T½ (h) =	1,5	V100			
dose per fx	2				
EBRT fx	23	D100			
EBRT dose	46,0	D100 iso:	0,0	0,0	46,0
EBRT EQ2	46,0	D90		0	
		D90 iso:	0,0	0,0	46,0

	PDR1	PDR2	PDR3
Y_1 [1]	0,0883	0,0883	0,0883
K_1 [1]	0,6910	0,6910	0,6910
S_1 [1]	0	0	0
G_1 [1]	0,0000	0,0000	0,0000

Organs At Risk INFORMATION — BT+ EBRT

Rectum

		PDR1	PDR2	PDR3	total
α/β (Gy) =	3	Volume [cm³]			
T½ (h) =	1,5	V100:			
dose per fx	2				
EBRT fx	23	ICRU			
EBRT dose	46,0	ICRU iso:	0,0	0,0	46,0
EBRT EQ2	46,0	$D_{0.1cc}$:			
		$D_{0.1cc\ iso}$:	0,0	0,0	46,0
		D_{2cc}:		0,00	
		$D_{2cc\ iso}$:	0,0	0,0	46,0

	PDR1	PDR2	PDR3
Y_1 [1]	0,0883	0,0883	0,0883
K_1 [1]	0,6910	0,6910	0,6910
S_1 [1]	0	0	0
G_1 [1]	0,0000	0,0000	0,0000

Organs At Risk INFORMATION — BT+ EBRT

Tabelle1 Tabelle2 Tabelle3

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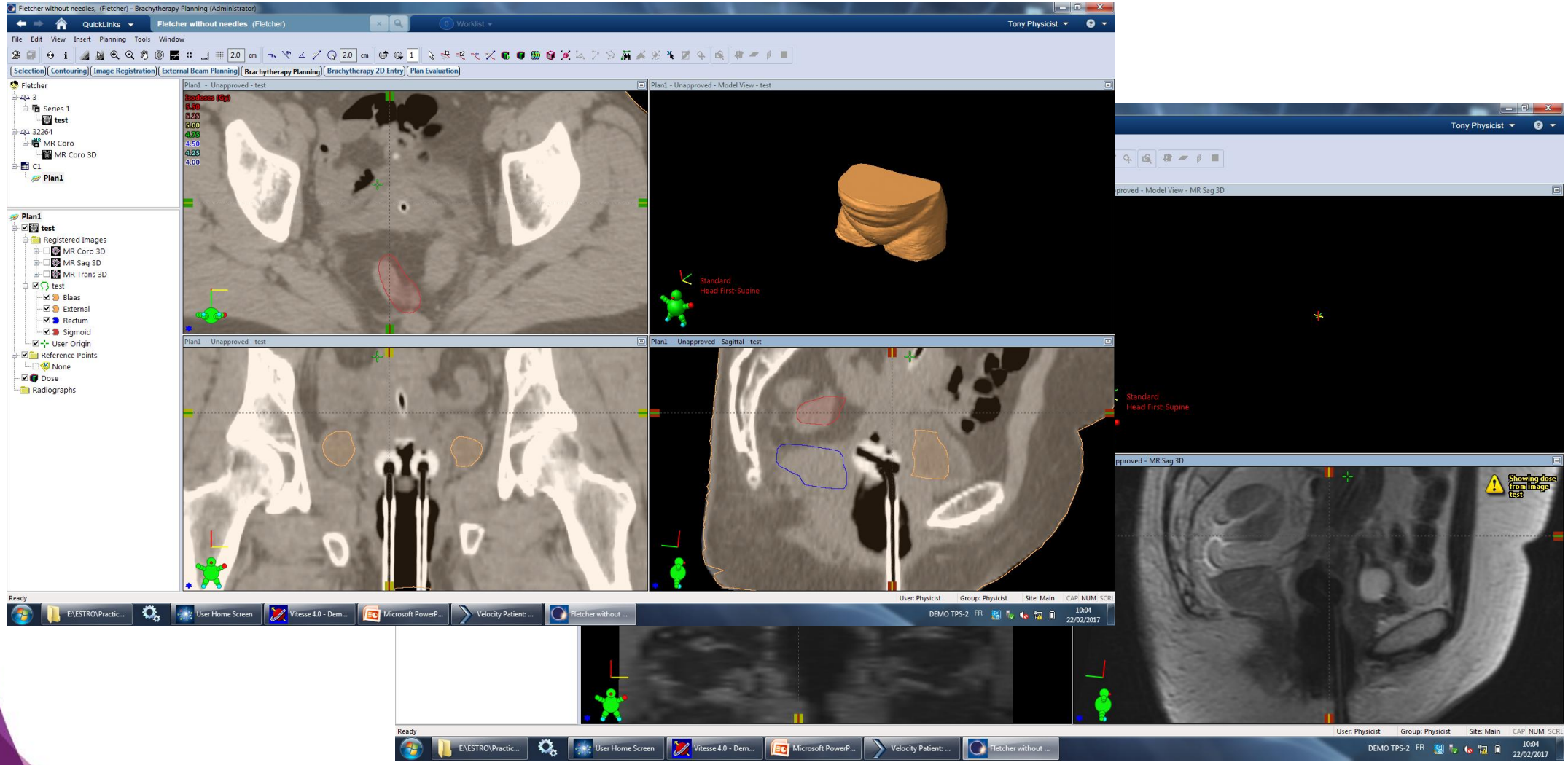
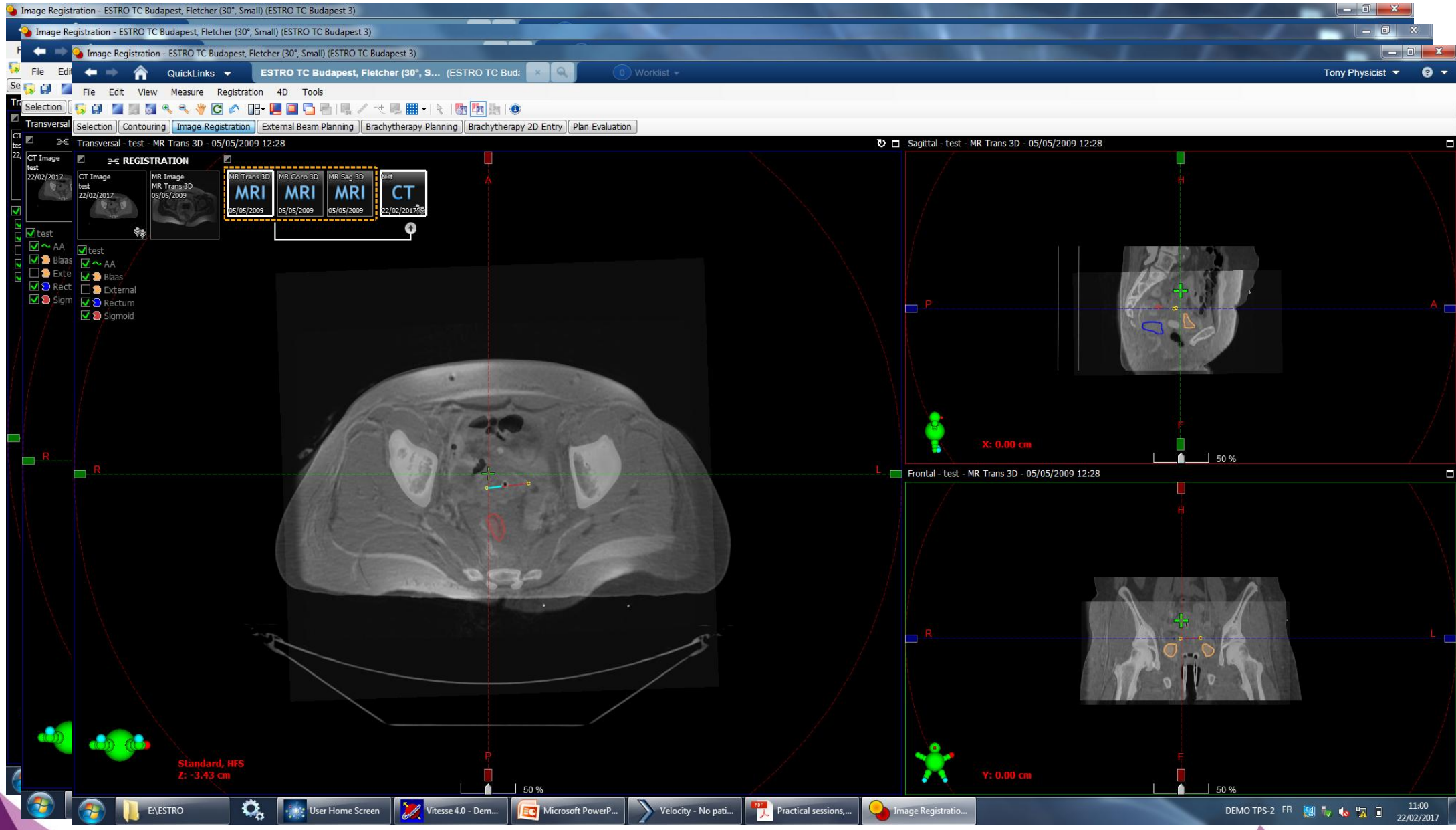
Registration of CT and MRI



Registration of CT and MRI



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Thank you for your attention

- Now you've seen some possibilities
- This afternoon you have the opportunity to work with the treatment planning systems yourself

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WWW.ESTRO.ORG/SCHOOL

Radiation Safety – Radiation Prootection
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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Topics

- **Overview on Events in BRT**
- Overview of Physicist´s Tasks
- Radiation Protection
- Introduction on Shielding Calculations

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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**

Prevention of High-dose-rate Brachytherapy Accidents, Volume 35 No. 2, 2005

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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.

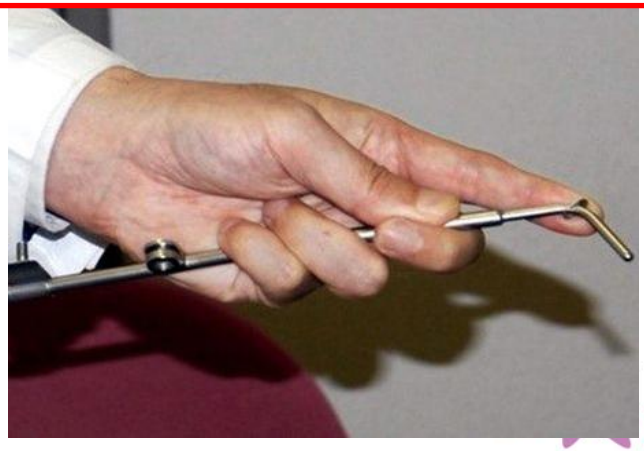
The hospital has set up an investigation board, which also includes third parties, to determine what precisely went wrong.

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.

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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Topics

- Overview on Events in BRT
- **Overview of Physicist´s Tasks**
- Radiation Protection
- Introduction on Shielding Calculations

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Important physicist' tasks in the development of QA programs for Brachytherapy

- Applicator insertion
- Treatment prescription
- Dose computation
- Source preparation
- Source insertion
- **Radiation protection**
- Source removal

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Topics

- Overview on Events in BRT
- Overview of Physicist´s Tasks
- **Radiation Protection**
- Introduction on Shielding Calculations

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General rules for radioprotection when applying radiation

- **Justification of the application**
  (proper medical use is an accepted application)
- **Dose limits**
  (ICRP, IAEA, Euratom, national legislation)
- **ALARA principle**
  (*as low as reasonably achievable)*

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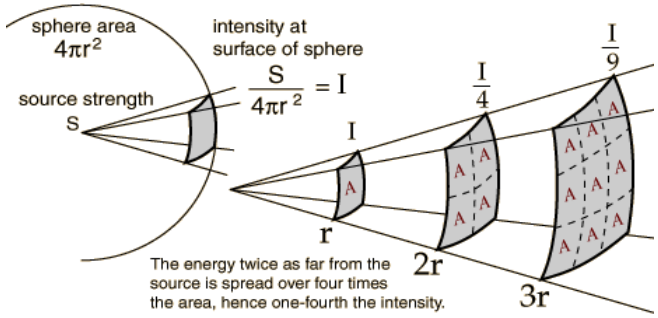
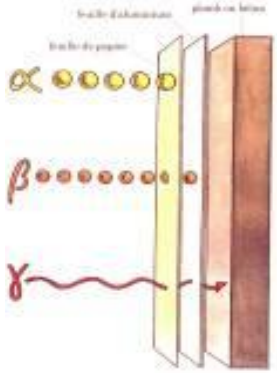
Reduce the exposure as much as possible

1. **Increase distance from the source of exposure (inverse square law)**



2. **Reduce time of exposure**

3. **Use of shielding:**



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Topics to be discussed:

- Source handling
- Facility
- Use of afterloaders
- Radiation protection devices
- Shielding (calculation principles)

and the QC checks of these items

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Risks:

Do not allow too much improvisation;
Try to educate your people ….
Use written protocols !!!

It's all about:

"training of the personnel"

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Facility, Equipment

Source handling

- special preparation room
- shielding
- long forceps
- small amounts of activity
- radiation detector(s)

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Facility, Equipment

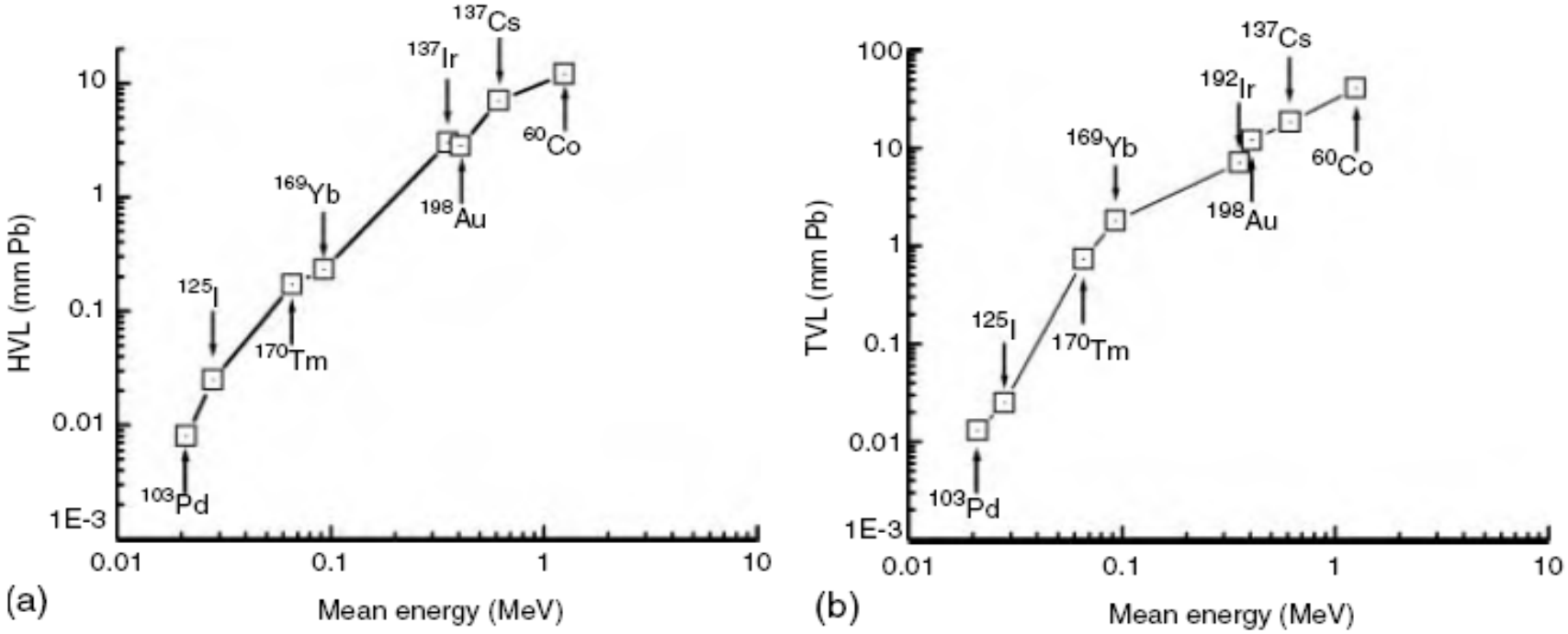

FIGURE 5.2
Thickness of lead required (a) for 50% transmission, HVL, and (b) for 10% transmission, TVL for the different radionuclides handled in this chapter. HVL values are according to the data presented in Table 5.2, where the tenth value layer data are according to Williamson.[19] The TVL values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

Source preparation: contamination due to leakage

- **Basically: wipe testing of sealed sources**

- **Testing of contamination of “catheters” in case of HDR/PDR afterloading sources**

According to national regulations

(frequency, documentation)

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Requirements for QC Checks

Minimum Requirements [NCS Rep. 13, 2000]

Test	Test frequency	
	HDR / PDR	LDR
Leakage radiation	Source Exchange	Annually
Contamination	Source Exchange	Annually

Tables taken from: NCS Report 13, the Netherlands Commission on Radiation Dosimetry, November 2000. NCS: Delft, The Netherlands (see www.ncs-dos.org)
See also www.estro.org for ESTRO Booklet No 8

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Personal Dose Detectors

Detectors,

used in a prep-room,

personal detectors

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Surface contamination detectors

Detectors, used in a prep-room, surface contamination

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Types of Transport Containers

For Emergencies:

- cutting device
- long forceps
- instructions available
- practicing

For seed delivery

Emergency HDR

For shipment of (HDR) sources

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Lead aprons, for X-ray and low energy photons

Use of protective devices, but only if this is useful (with energies e.g. smaller than 100keV)

Consider the extra time needed vs. extra shielding

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Simple behaviour rules

In summary, protective measures during source preparation:

- **sources in a vault**
- **using long forceps**
- **wire-cutter (with manual loadings)**
- **use only what is needed (the rest should be safely put away)**
- **stay behind a screen, lead glass**
- **no eating, drinking, smoking (absolutely prohibited!)**

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Facility Requirements

Facility

- Radiation safety measures
- Availability and functioning of radiation detectors
- Warning systems
- Door interlocks
- CCTV system

Facility Requirements

Use of radiation detectors in vault, in patient / treatment room

Facility Requirements

- warning signals for radiation area

Facility Requirements

Afterloader - interrupt:

contact on door of treatment room

Facility Requirements

Video camera observation, audio contact with patient

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Requirements for QC Checks

Minimum Requirements for QC Checks

Test	Test frequency	
	HDR / PDR	LDR
Warning lights	4M*	4M
Room radiation monitor	4M	4M
Audio/visual communication system	4M	4M

[NCS Rep. 13, 2000, also in ESTRO Booklet 8]

*** For quarterly source exchange, it can be part of the exchange procedure**

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Afterloaders: Overview (HDR & PDR)

Varian, GammaMed Plus

Varian, Varisource

Varian, Varisource

ELEKTA-Nucletron, MicroSelectron Vs. 3

ELEKTA-Nucletron, Flexitron

BEBIG, SagiNova®

BEBIG, MultiSource

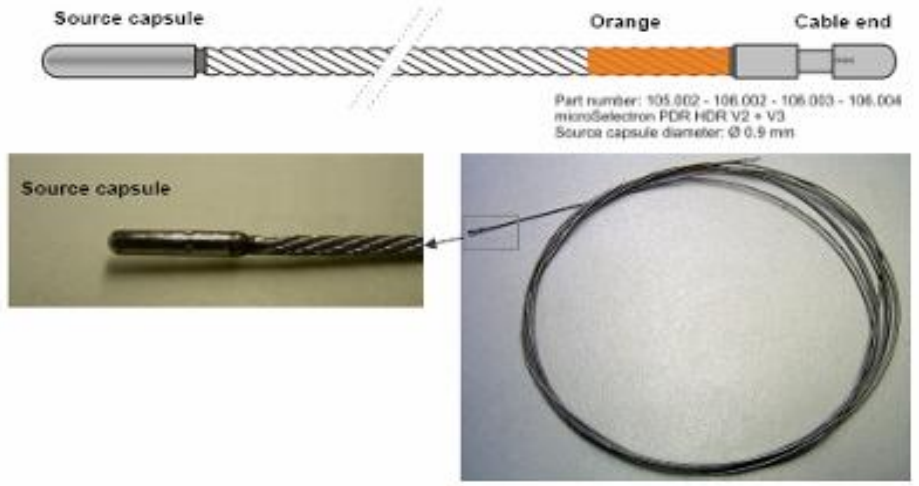
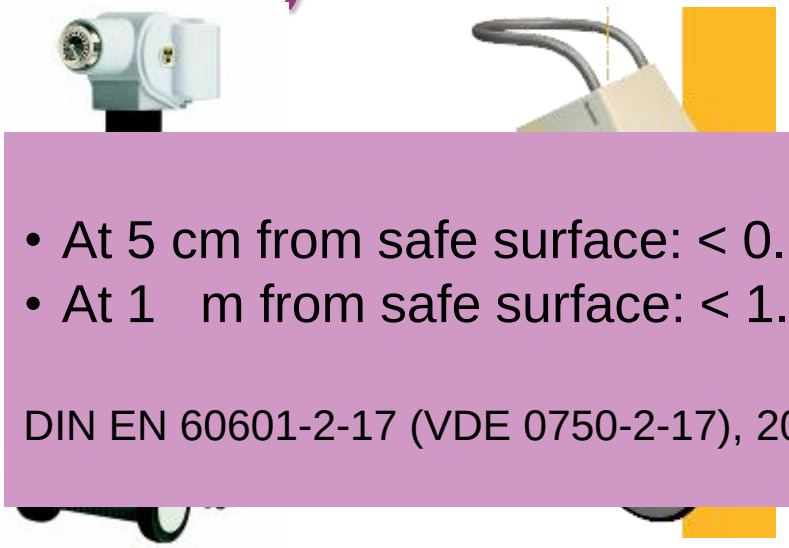


Figure 2: Source cable: microSelectron HDR V2 + V3

Afterloaders: Overview (HDR & PDR)

Varian, GammaMed Plus

Varian, Varisource



ELEKTA-Nucletron, MicroSelectron Vs. 3

ELEKTA-Nucletron, Flexitron

- At 5 cm from safe surface: < 0.01 mSv h^{-1}
- At 1 m from safe surface: < 1.0 µSv h^{-1}

DIN EN 60601-2-17 (VDE 0750-2-17), 2016

BEBIG, SagiNova®

BEBIG, MultiSource

Afterloader (radiation protection)

- **Designed to reduce dose the radiation workers**
- **Radiation levels near source safe and @ 1 m**
- **Emergency procedures, interrupts**

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Emergency Procedures (Afterloaders)

- Backup storage batteries
- Interrupts
- Reaction to power loss
- Reaction to air pressure loss
- Availability of operating instructions
- Availability of emergency instructions

Note: QC of functionality goes with radiation protection considerations

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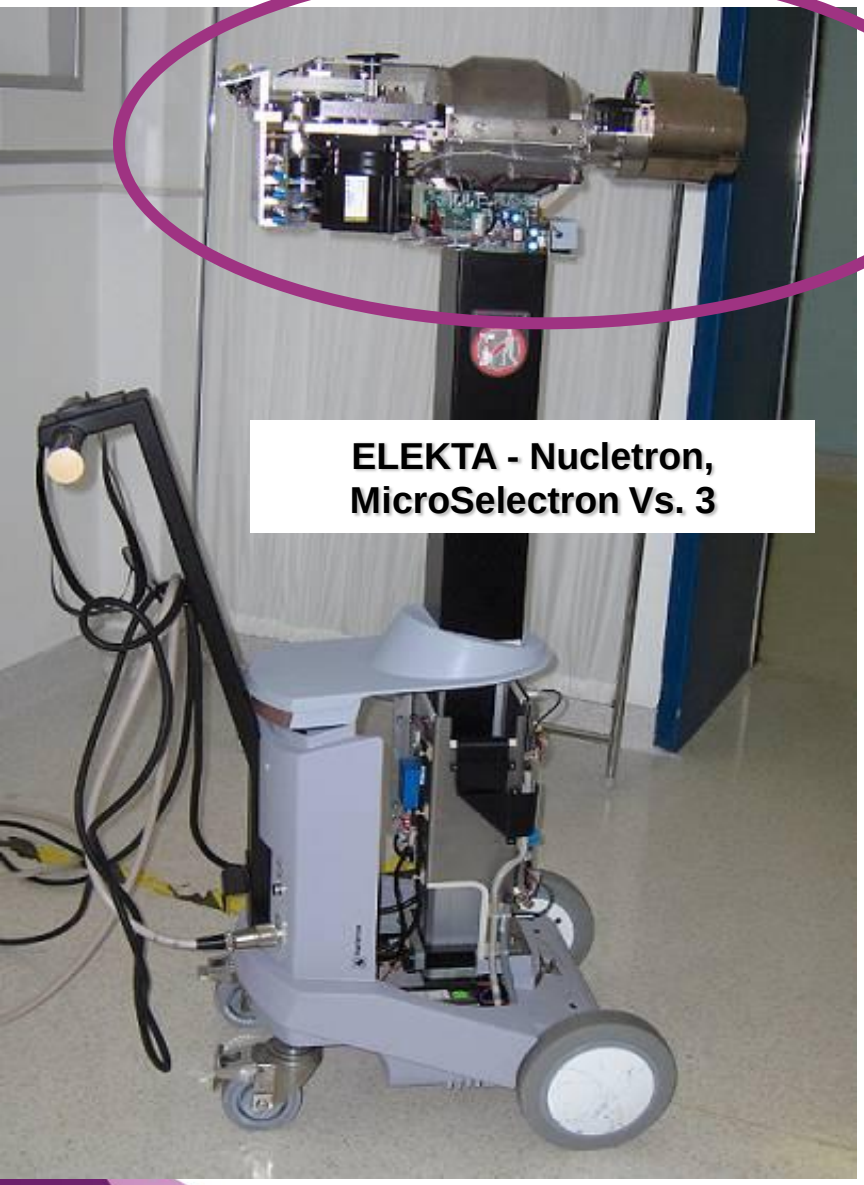
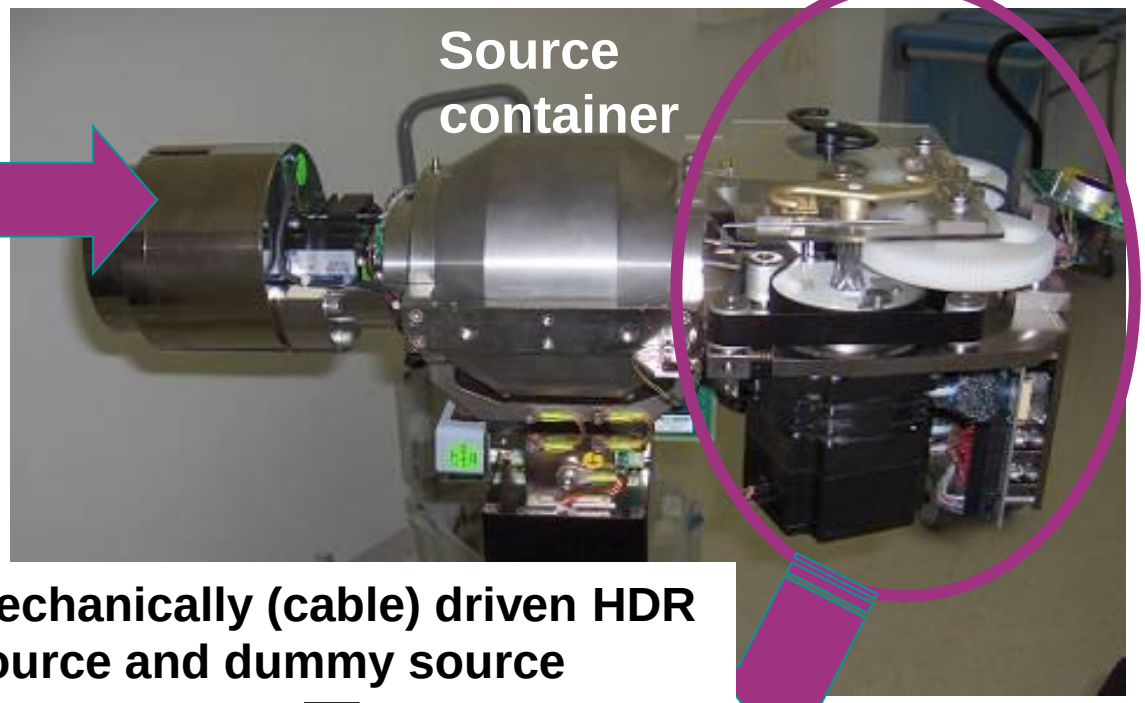
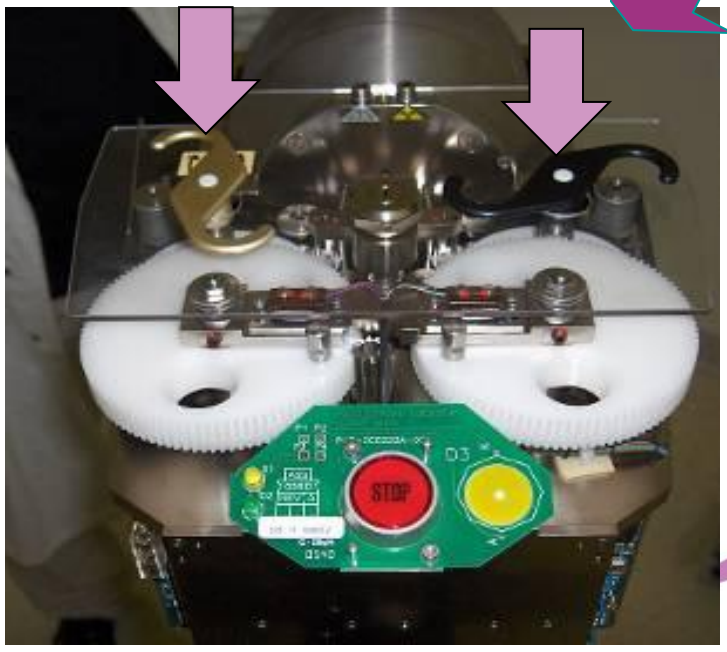
Modern Afterloaders: Some Details on Mechanisms



ELEKTA - Nucletron, MicroSelectron Vs. 3



Mechanically (cable) driven HDR source and dummy source



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Requirements for QC Checks

Minimum Requirements for QC (afterloaders)

Test	Test frequency	
	HDR / PDR	LDR
Emergency stop push buttons	4M	6M
Interrupt button	4M	6M
Door interlock	4M	6M
Power loss	4M	6M
Air pressure loss	-	6M
Unlocked indexer ring	4M	-
Obstructed applicator	4M	6M
Missing applicator	4M	6M

[NCS Rep. 13, 2000, also in ESTRO Booklet 8]

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Requirements for QC Checks

IAEA TECDOC-1040

Design and implementation of a radiotherapy programme: Clinical, medical physics, radiation protection and safety aspects

INTERNATIONAL ATOMIC ENERGY AGENCY IAEA

September, 1998

I.10.4. Measurement Equipment for Brachytherapy

I.10.4.1. Well-Type Ionization Chambers

QC procedures for well-type ionization chambers are given in Table I.X.

TABLE I.X. QC TESTS FOR BRACHYTHERAPY SOURCE CALIBRATOR

I, initial use or following malfunction and repairs[a], S, isotope/source specific, D, documented and correction applied or noted in report of measurement, when appropriate, and E, each use (measurement sequence) or ongoing evaluation. Reproduced with permission of AAPM TG-40.

Instrument type	Test	Frequency	Tolerance
Well ionization chamber	Standards Laboratory calibration	I,S[a]	D
	Precision	I	2%
	Linearity	I, 2 year	1%
	Collection Efficiency	I	1%
	Geometrical/length dependence	I	D
	Energy dependence	I	D
	Source wall dependence	I	D
	Venting	I	D
	Redundant check	E	2%
	Leakage	E	D
In-air calibration chamber and external source holder	SSDL calibration	I,S[a]	D
	Accuracy of source chamber distance	1 yr, S	1%, D
	Redundancy See Table I.III. for other tests	E	D

[a] Instruments or sources must have a calibration directly traceable to a Standards Laboratory.

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Requirements for QC Checks

I.10.3. QC of Remote Afterloading Devices

Recommended QC tests for remote afterloading devices are given in Table I.IX.

TABLE I.IX. QC OF REMOTE AFTERLOADING BRACHYTHERAPY UNITS

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Frequency	Test	Tolerance
Each treatment day	Room safety door interlocks, lights, and alarms	Functional
	Console functions, switches, batteries, printer	Functional
	Visual inspection of source guides	Free of kinks and firmly attached
	Verify accuracy of ribbon preparation	Autoradiograph
Weekly	Accuracy of source and dummy loading (dummies used for spacing and/or simulation/verification)	1 mm
	Source positioning	1 mm
At each source change or quarterly	Calibration[a]	3%
	Timer function	1%
	Check accuracy of source guides and connectors	1 mm
	Mechanical integrity of applicators (by X-ray if appropriate)	Functional
Annual	Dose calculation algorithm (at least one standard source configuration for each isotope)	3%, 1 mm
	Simulate emergency conditions	
	Verify source inventory	

[a] It is worthwhile at source change to calibrate both new and old sources to establish and document reproducibility of calibration method.

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Requirements for QC Checks: Sources & Afterloaders

Table 11.22

Test frequencies and action levels for various brachytherapy procedures. HDR = high dose rate, PDR = pulsed dose rate, LDR = low dose rate, MDR = medium dose rate. (Adapted from [207].)

DESCRIPTION	MINIMUM REQUIREMENTS	
	TEST FREQUENCY	ACTION LEVEL
HDR/PDR		
Source calibration	Source exchange	5%
Source position	Daily/quarterly	2 mm
Length of treatment tubes	Annually	1 mm
Irradiation timer	Annually	1%
Date, time, source strength	Daily	-
Transit time effect	Annually	-
LDR/MDR		
Source calibration, mean of batch	Source exchange	3%
Source calibration, individual source, decay	Source exchange	5%
Linear uniformity	Source exchange	5%
Source position, source length	Half yearly	2 mm
Irradiation timer	Annually	2%
Date, time, source strength in treatment unit	Daily	-
Manual Afterloading		
Source calibration, decay calculation	Source exchange	5%
Linear uniformity, source length	Source exchange	5%
Source identification	Daily/annually	—

Venselaar, J., and J. Pérez-Calatayud, eds. *A Practical Guide to Quality Control of Brachytherapy Equipment.* ESTRO Booklet Number 8.

Accuracy and Uncertainty Considerations in Modern Radiation Oncology, The Modern Technology of Radiation Oncology, J. Van Dyk, 2013

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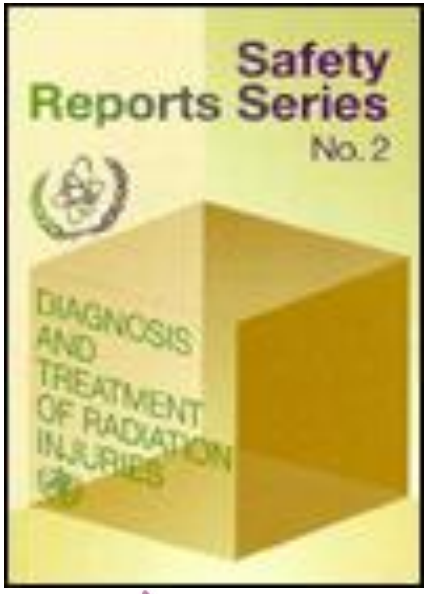
Training aiming at avoiding accidents

Training:

- **Radiographers, nursing staff**
- **Physicians and residents**
- **Patient instructions**

Note: many of the accidents with unintended medical exposures in BT were due to lack of training and procedures (source: IAEA Safety Report Series 2)



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Topics

- Overview on Events in BRT
- Overview of Physicist´s Tasks
- Radiation Protection
- **Introduction on Shielding Calculations**

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The GEC ESTRO Handbook of Brachytherapy

SECOND EDITION

PART I: THE BASICS OF BRACHYTHERAPY

3

Radiation Protection in Brachytherapy

Panagiotis Papagiannis, Jack Venselaar

Editors

Erik Van Limbergen
Richard Pötter
Peter Hoskin
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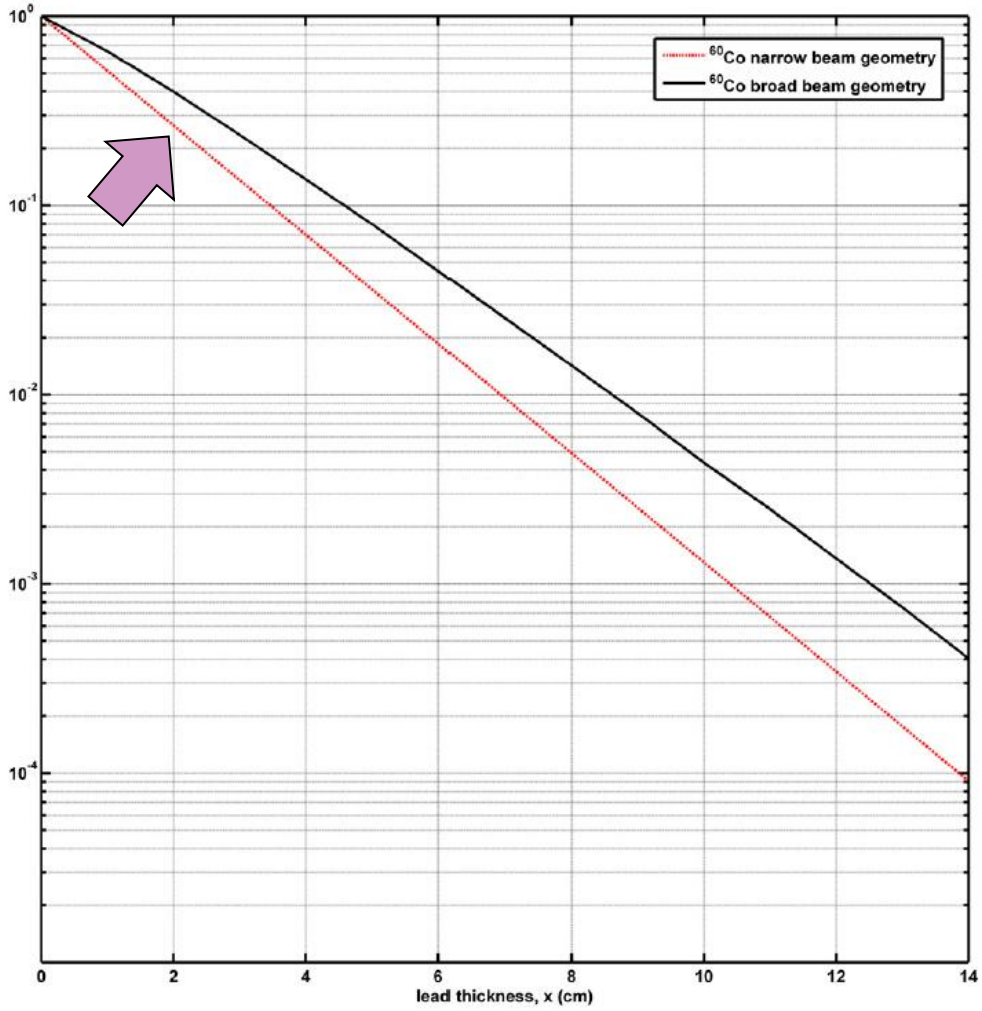

Fig. 3.2 ^{60}Co radiation transmission factor *T* for a lead shielding barrier in narrow and broad beam geometry conditions. (Courtesy: P. Papagiannis)

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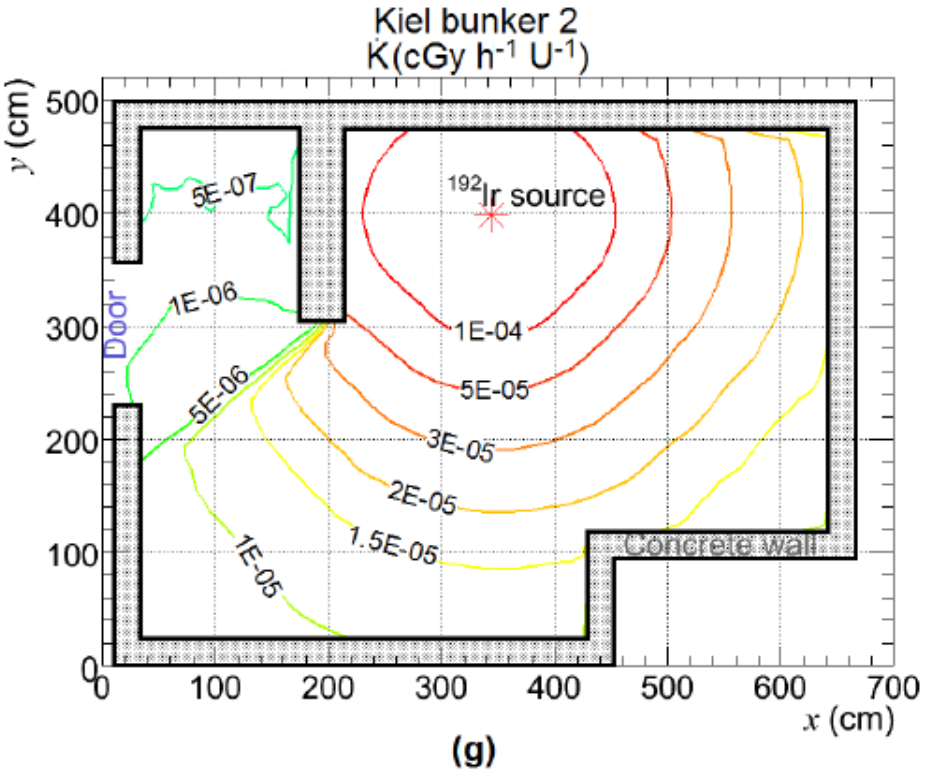
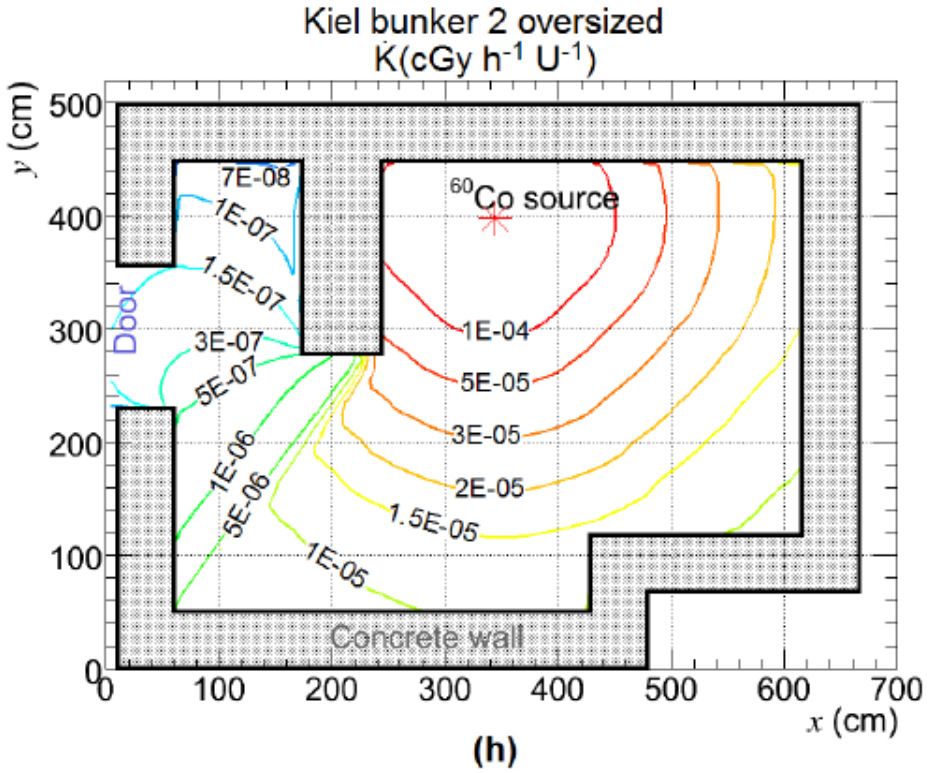
Shielding Calculations, Principles: Examples





Air-kerma rate distribution on the plane parallel to the floor and containing the source for five different facility designs for ^{192}Ir (left) and ^{60}Co (right) of a given strength. See the original article for more details. (Courtesy: M.C. Pujades)

Remember for ^{192}Ir 370 GBq ≈ 40.4 kU
For ^{60}Co ≈ 1/3 of contained activity of ^{192}Ir …

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Shielding Calculations, Principles

Shielding Calculations, determine the "workload" W in your department:

$$W = N \times S_K \times t$$

- **W = workload, in air @ 1 m distance from the source(s) per period (week, month, year)**
- **N = number of applications per time period (week, month, year)**
- **S_K = Reference air kerma rate in air**
- **t = time of exposure (average/application)**

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Shielding Calculations, Principles

Shielding Calculations: does your facility fulfil the radiation protection requirements (limits)?

$$W \times f_{dist} \times f_{occup} \times T_{patient} \times T_{trans} < limit$$

- f_{dist} = inverse square law (distance factor)
- f_{occup} = occupancy factor
- $T_{patient}$ = transmission through the patient
- T_{trans} = transmission factor through the wall or shielding material
- limit = requirement for the specific point per time period (w, m, y; e.g. 1 mSv/year)

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Shielding Calculations, Principles: Dose Limits

Table 3.1: Dose limits recommended by the ICRP (24)

	PUBLIC EXPOSURE	OCCUPATIONAL EXPOSURE
Effective dose limit:	1 mSv per year	20 mSv per year averaged over 5 years and less than 50 mSv in any single year
Eye lens equivalent dose limit:	15 mSv	150 mSv*
Skin equivalent dose limit:	50 mSv	500 mSv
Hands and feet equivalent dose limit:	-	500 mSv

**After review of epidemiological evidence suggesting threshold doses might be lower than previously considered, irrespective of rate of dose delivery, ICRP issued a statement on tissue reactions (25) and an equivalent dose limit for the lens of the eye of 20 mSv in a year, averaged over defined periods of 5 years, was recommended for occupational exposure in planned exposure situations. This recommendation, which is significantly lower than corresponding ICRP 103 (24) recommendations, was adopted in the IAEA Basic Safety Standards (15) and will very likely be implemented in national dose limits in the coming years.*

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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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Published Radiation Protection Data

You may wish to take data from NCRP publications, in concrete….

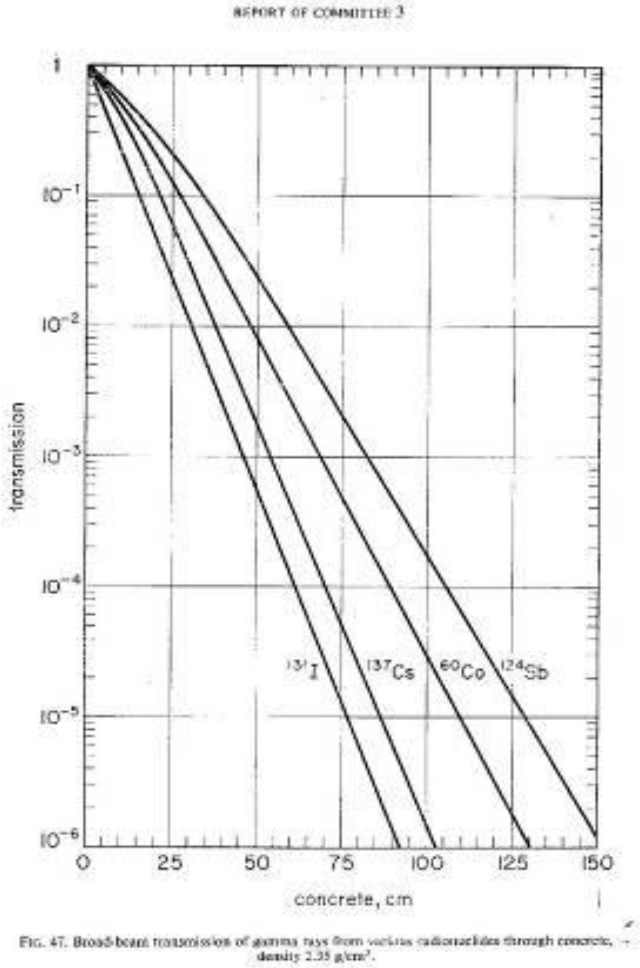

FIG. 47. Broad-beam transmission of gamma rays from various radionuclides through concrete, density 2.35 g/cm³.

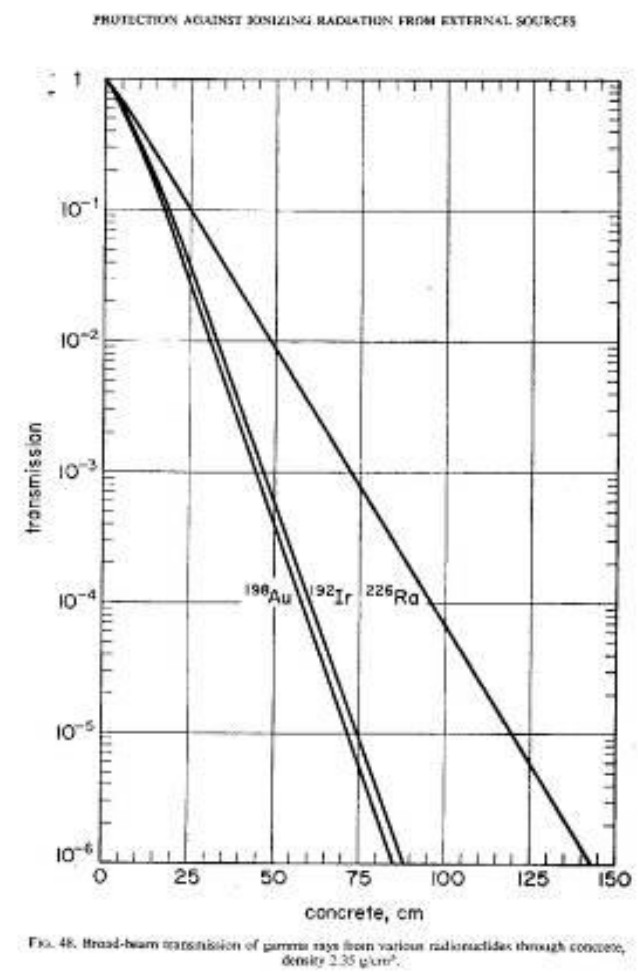

FIG. 48. Broad-beam transmission of gamma rays from various radionuclides through concrete, density 2.35 g/cm³.

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Published Radiation Protection Data

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)

To address the limited availability of radiation shielding data for brachytherapy as well as some disparity in existing data, Monte Carlo simulation was used to generate radiation transmission data for ^{60}Co, ^{137}Cs, ^{198}Au, ^{192}Ir, ^{169}Yb, ^{170}Tm, ^{131}Cs, ^{125}I, and ^{103}Pd photons through concrete, stainless steel, lead, as well as lead glass and baryte concrete. Results accounting for the oblique incidence of radiation to the barrier, spectral variation with barrier thickness, and broad beam conditions in a realistic geometry are compared to corresponding data in the literature in terms of the half value layer (HVL) and tenth value layer (TVL) indices. It is also shown that radiation shielding calculations using HVL or TVL values could overestimate or underestimate the barrier thickness required to achieve a certain reduction in radiation transmission. This questions the use of HVL or TVL indices instead of the actual transmission data. Therefore, a three-parameter model is fitted to results of this work to facilitate accurate and simple radiation shielding calculations. © *2008 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2986153]

Key words: brachytherapy, radiation protection, shielding, HVL, TVL, Monte Carlo

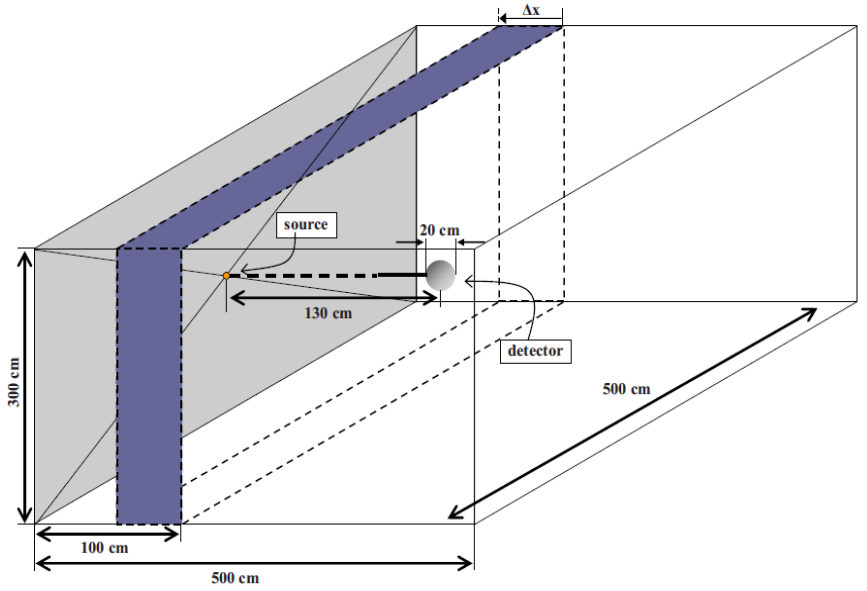

FIG. 1. A schematic diagram illustrating the simulation geometry used in this work.

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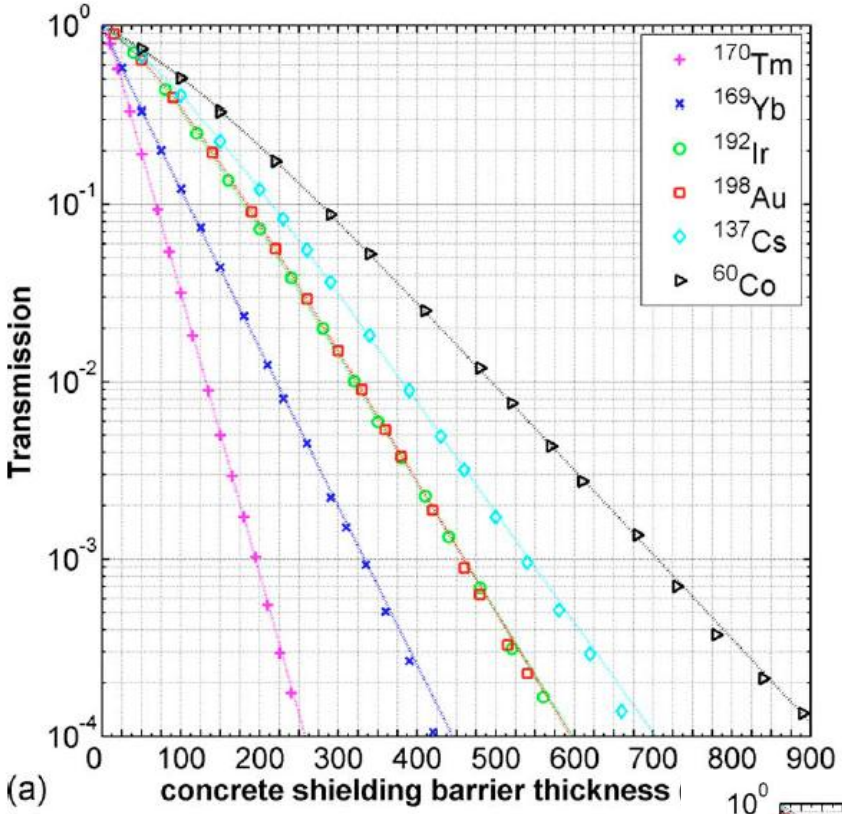
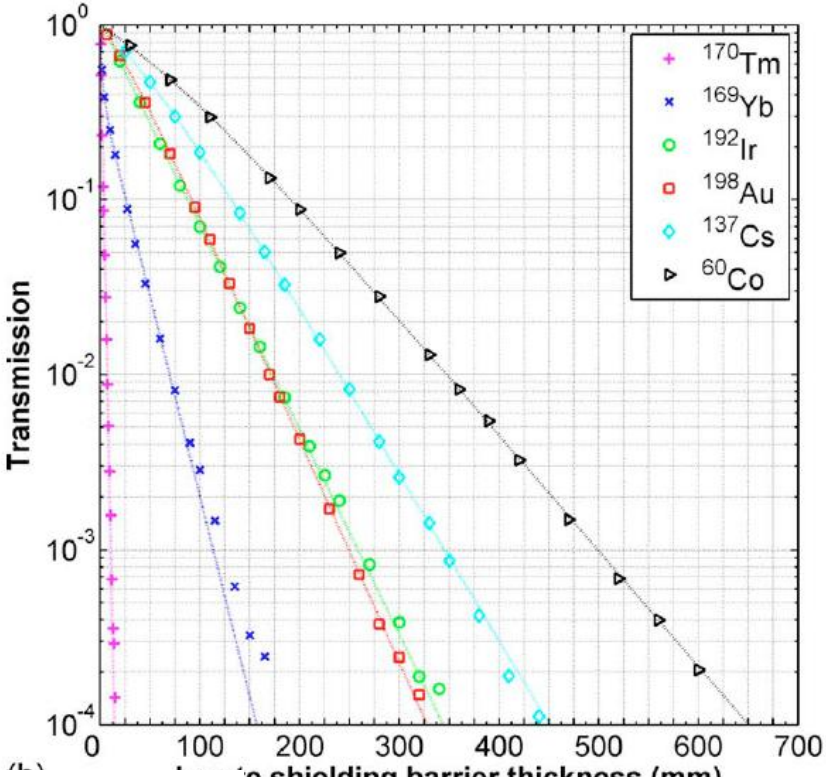
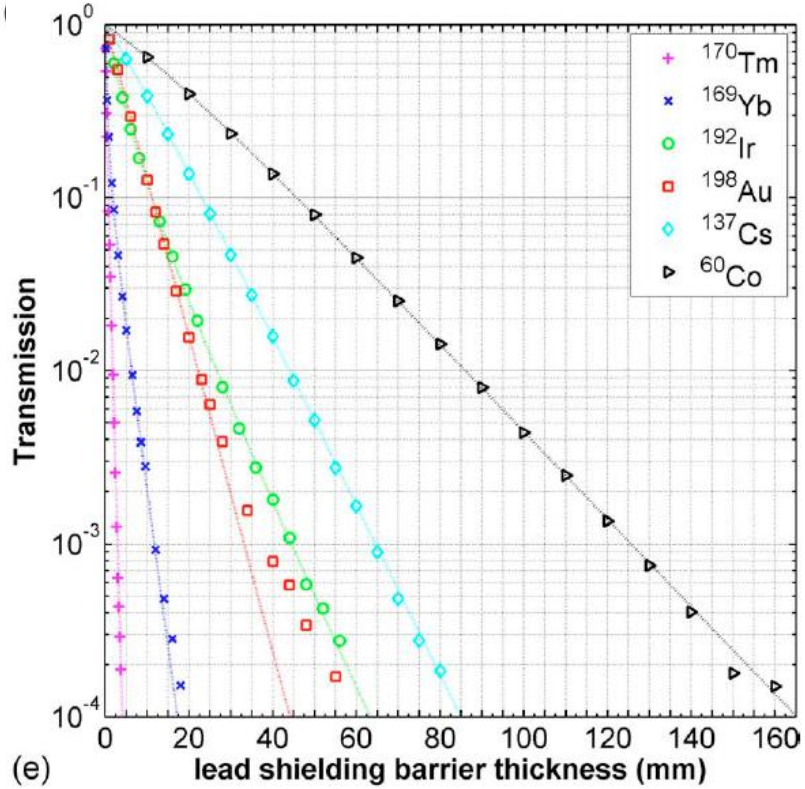


(a)





(e)

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TABLE III. First and equilibrium HVL and TVL results of this work compared to corresponding results in the literature. All values are in mm.

		This work[a]		Corresponding values in the literature	
Radionuclide	Material	HVL_e (HVL_1)	TVL_e (TVL_1)	HVL_e (HVL_1)	TVL_e (TVL_1)
^{170}Tm	Concrete	19 (24)	63 (68)	—	—
	Baryte concrete	1.0 (1.1)	3.5 (3.5)	—	—
	Stainless steel	1.9 (0.98)	6.5 (4.4)	(1)[b]	(5)[b]
	Lead glass	0.80 (0.39)	2.7 (1.7)	—	—
	Lead	0.34 (0.17)	1.1 (0.73)	(<1)[b]	(<1)[b]
^{169}Yb	Concrete	34 (31)	112 (109)	34[c] (32)[c]	114[c] (106)[c]
	Baryte concrete	13 (2.1)	44 (26)	—	—
	Stainless steel	8.8 (2.2)	29 (22)	(3)[b]	(26)[b]
	Lead glass	3.6 (0.59)	12 (4.1)	—	—
	Lead	1.7 (0.25)	5.5 (1.7)	1.6,[d] (<1),[b] (0.25)[d]	5.3,[d] (2),[b] (1.8)[d]
^{192}Ir	Concrete	42 (70)	139 (180)	43,[e,f] 42,[d] (65)[d]	152,[e] 147,[f] 141,[d] (176)[d]
	Baryte concrete	26 (28)	86 (88)	—	—
	Stainless steel	12 (18)	41 (48)	13,[e,f] (23),[b] (19)[e]	43,[e,f] (49),[e] (56)[b]
	Lead glass	14 (6.4)	47 (24)	—	—
	Lead	5.8 (2.8)	19 (11)	6,[e,f] 5.7,[d] (3),[b] (2.3),[g] (2.8)[d]	16,[e,f] 18.7,[d] 9,[g] (12),[b] (9),[g] (11)[d]
^{198}Au	Concrete	41 (71)	136 (184)	—	—
	Baryte concrete	24 (32)	79 (92)	—	—
	Stainless steel	12 (19)	39 (50)	(24)[b]	(58)[b]
	Lead glass	7.1 (7.7)	23 (24)	—	—
	Lead	3.3 (3.5)	11 (11)	(4)[b]	(12)[b]
^{137}Cs	Concrete	48 (80)	161 (214)	48[e,f]	175[e,f]
	Baryte concrete	32 (46)	105 (131)	—	—
	Stainless steel	14 (23)	48 (63)	16,[e,f] (30),[e] (29)[b]	53,[e] 50,[f] (69),[e] (72)[b]
	Lead glass	12 (15)	41 (47)	—	—
	Lead	6.2 (7.5)	20 (23)	6.5,[e,f] (8),[b] (5.6)[g]	22,[e,f] 18.5,[g] (24),[b] (18.5)[g]
^{60}Co	Concrete	63 (102)	210 (276)	62[e,f]	218,[e] 220,[f] (245)[e]
	Baryte concrete	46 (68)	151 (191)	—	—
	Stainless steel	20 (30)	65 (84)	21,[e,f] (35),[e] (36)[b]	71,[e] 67,[f] (87),[e] (93)[b]
	Lead glass	22 (30)	74 (86)	—	—
	Lead	12 (16)	40 (46)	12,[e,f] (15),[e] (16)[b]	41,[e] 42,[f] (46)[b]

[a]HVL_e and TVL_e calculated as $HVL_e=\ln(2)/\alpha$ and $TVL_e=\ln(10)/\alpha$ using data in Table II. HVL_1 and TVL_1 calculated using Eq. (2) with data in Table II.

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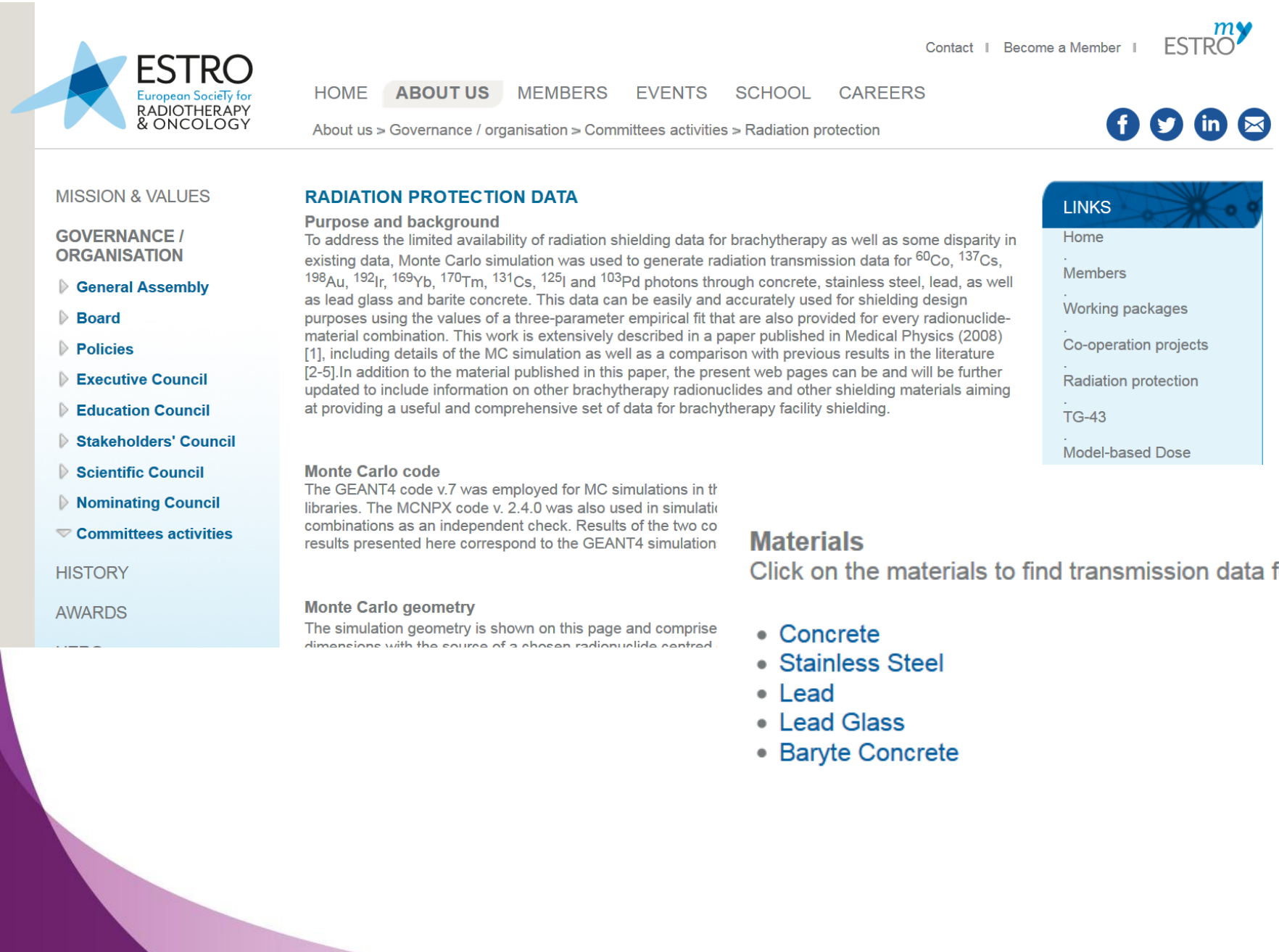
http://www.estro.org/about/governance-organisation/committees-activities/radiation-protection



BRAPHYQS

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For Shielding Calculations and Limits:

Follow your National Regulations!

Summary

- Quality management program
- written procedures
- Training program !!!

8. KEY MESSAGES

- Radiation protection policies are revised dynamically by the work of several international bodies (ICRP, UNSCEAR, IAEA) leading to international consensus on sets of rules that can be integrated to national legislation. These rules are equally applicable to brachytherapy.

- Structural shielding must be used when workload and distance are such that acceptable levels of protection cannot be ensured. The methodology for calculating the required thickness is presented, including references for the data for radionuclide / shielding material combinations. Examples of different treatment room designs are shown in this chapter.

- A quality management program should be developed for each brachytherapy department. Written procedures, clearly defined tasks for each member of the brachytherapy team, and an appropriate training program with frequent reevaluation and repeated practice by the team members, contribute to a safe treatment for the patient while ensuring minimized risks of radiation exposure and accidents.

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WWW.ESTRO.ORG/SCHOOL

Radiation Safety – Radiation Prootection
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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Topics

- **Overview on Events in BRT**
- Overview of Physicist´s Tasks
- Radiation Protection
- Introduction on Shielding Calculations

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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**

Prevention of High-dose-rate Brachytherapy Accidents, Volume 35 No. 2, 2005

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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.

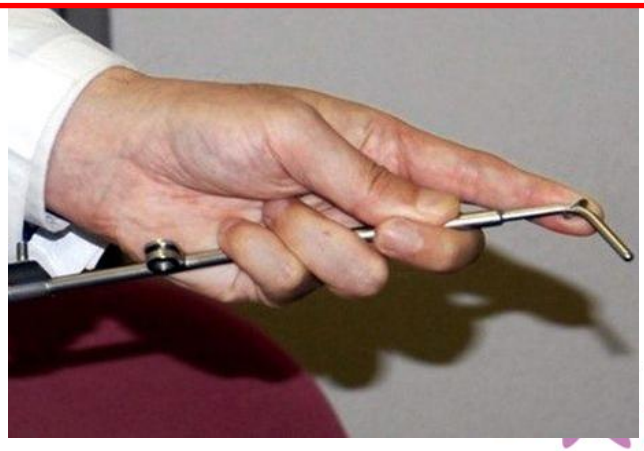
The hospital has set up an investigation board, which also includes third parties, to determine what precisely went wrong.

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.

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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Topics

- Overview on Events in BRT
- **Overview of Physicist´s Tasks**
- Radiation Protection
- Introduction on Shielding Calculations

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Important physicist' tasks in the development of QA programs for Brachytherapy

- Applicator insertion
- Treatment prescription
- Dose computation
- Source preparation
- Source insertion
- **Radiation protection**
- Source removal

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Topics

- Overview on Events in BRT
- Overview of Physicist´s Tasks
- **Radiation Protection**
- Introduction on Shielding Calculations

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General rules for radioprotection when applying radiation

- **Justification of the application**
  (proper medical use is an accepted application)
- **Dose limits**
  (ICRP, IAEA, Euratom, national legislation)
- **ALARA principle**
  (*as low as reasonably achievable)*

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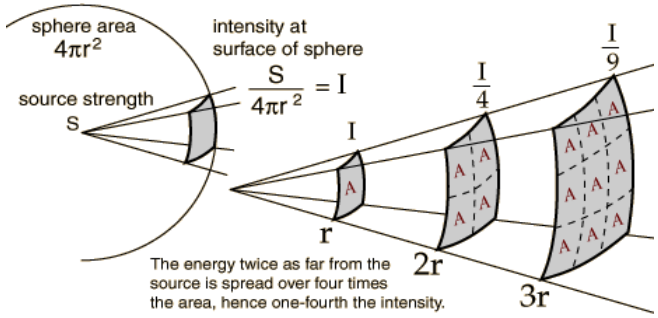
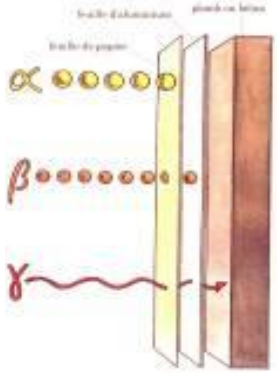
Reduce the exposure as much as possible

1. **Increase distance from the source of exposure (inverse square law)**



2. **Reduce time of exposure**

3. **Use of shielding:**



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Topics to be discussed:

- Source handling
- Facility
- Use of afterloaders
- Radiation protection devices
- Shielding (calculation principles)

and the QC checks of these items

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Source preparation: contamination due to leakage

- **Basically: wipe testing of sealed sources**

- **Testing of contamination of “catheters” in case of HDR/PDR afterloading sources**

According to national regulations

(frequency, documentation)

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Requirements for QC Checks

Minimum Requirements [NCS Rep. 13, 2000]

Test	Test frequency	
	HDR / PDR	LDR
Leakage radiation	Source Exchange	Annually
Contamination	Source Exchange	Annually

Tables taken from: NCS Report 13, the Netherlands Commission on Radiation Dosimetry, November 2000. NCS: Delft, The Netherlands (see www.ncs-dos.org)
See also www.estro.org for ESTRO Booklet No 8

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Types of Transport Containers

Emergency HDR

For Emergencies:

- cutting device
- long forceps
- instructions available
- practicing

For seed delivery

For shipment of (HDR) sources

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Lead aprons, for X-ray and low energy photons

Use of protective devices, but only if this is useful (with energies e.g. smaller than 100keV)

Consider the extra time needed vs. extra shielding

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Facility Requirements

Facility

- Radiation safety measures
- Availability and functioning of radiation detectors
- Warning systems
- Door interlocks
- CCTV system

Facility Requirements

Use of radiation detectors in vault, in patient / treatment room

Facility Requirements

- warning signals for radiation area

Facility Requirements

Afterloader - interrupt:

contact on door of treatment room

Facility Requirements

Video camera observation, audio contact with patient

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Requirements for QC Checks

Minimum Requirements for QC Checks

Test	Test frequency	
	HDR / PDR	LDR
Warning lights	4M*	4M
Room radiation monitor	4M	4M
Audio/visual communication system	4M	4M

[NCS Rep. 13, 2000, also in ESTRO Booklet 8]

*** For quarterly source exchange, it can be part of the exchange procedure**

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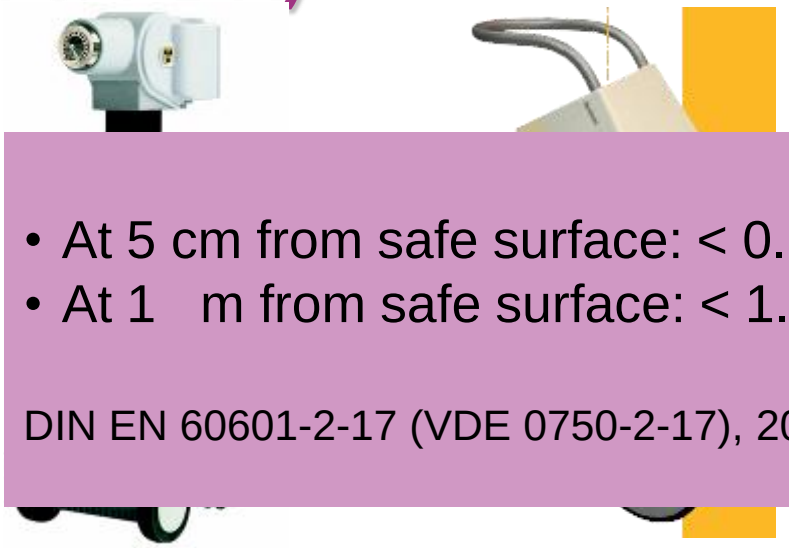
Afterloaders: Overview (HDR & PDR)

Varian, GammaMed Plus

Varian, Varisource



ELEKTA-Nucletron, MicroSelectron Vs. 3

ELEKTA-Nucletron, Flexitron

- At 5 cm from safe surface: < 0.01 mSv h^{-1}
- At 1 m from safe surface: < 1.0 µSv h^{-1}

DIN EN 60601-2-17 (VDE 0750-2-17), 2016

BEBIG, MultiSource

BEBIG, SagiNova®

Afterloader (radiation protection)

- **Designed to reduce dose to personnel**
- **Radiation levels near source safe and @ 1 m**
- **Emergency procedures, interrupts**

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Emergency Procedures (Afterloaders)

- Backup storage batteries
- Interrupts
- Reaction to power loss
- Reaction to air pressure loss
- Availability of operating instructions
- Availability of emergency instructions

Note: QC of functionality goes with radiation protection considerations

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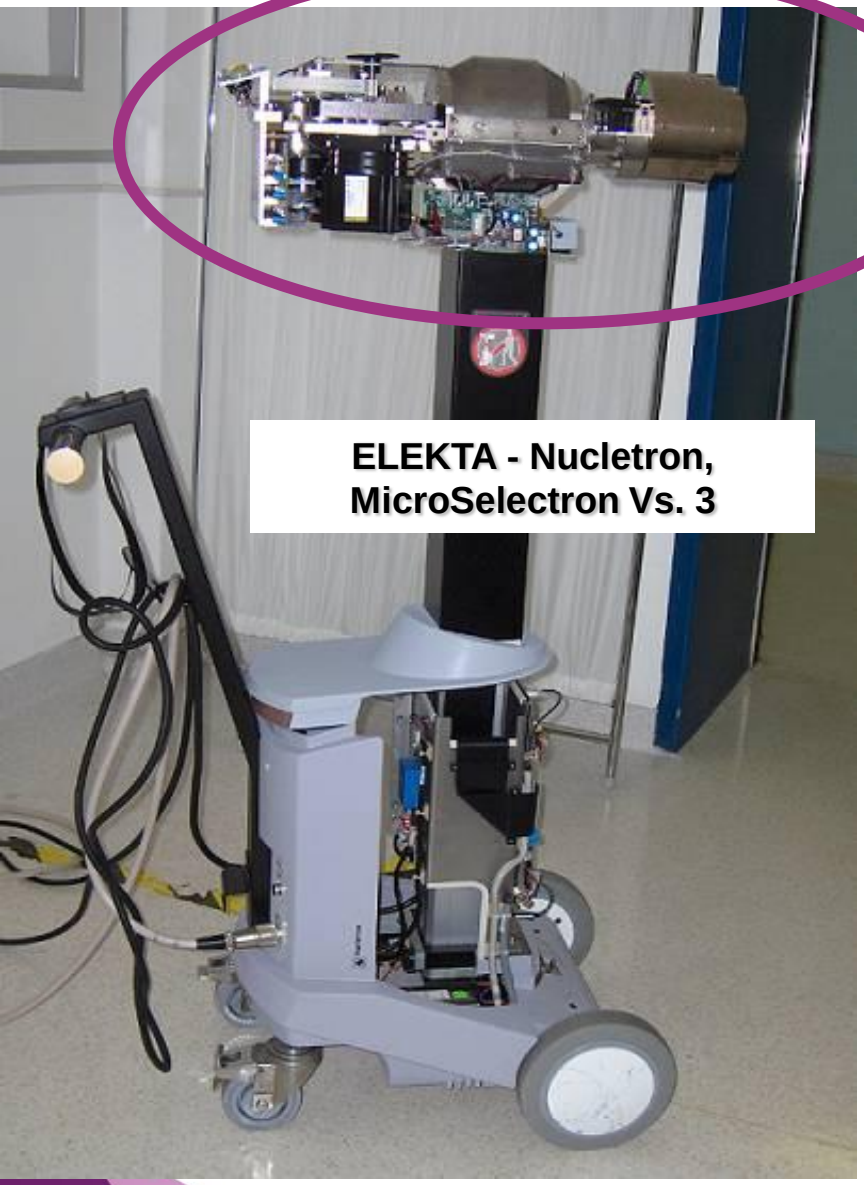
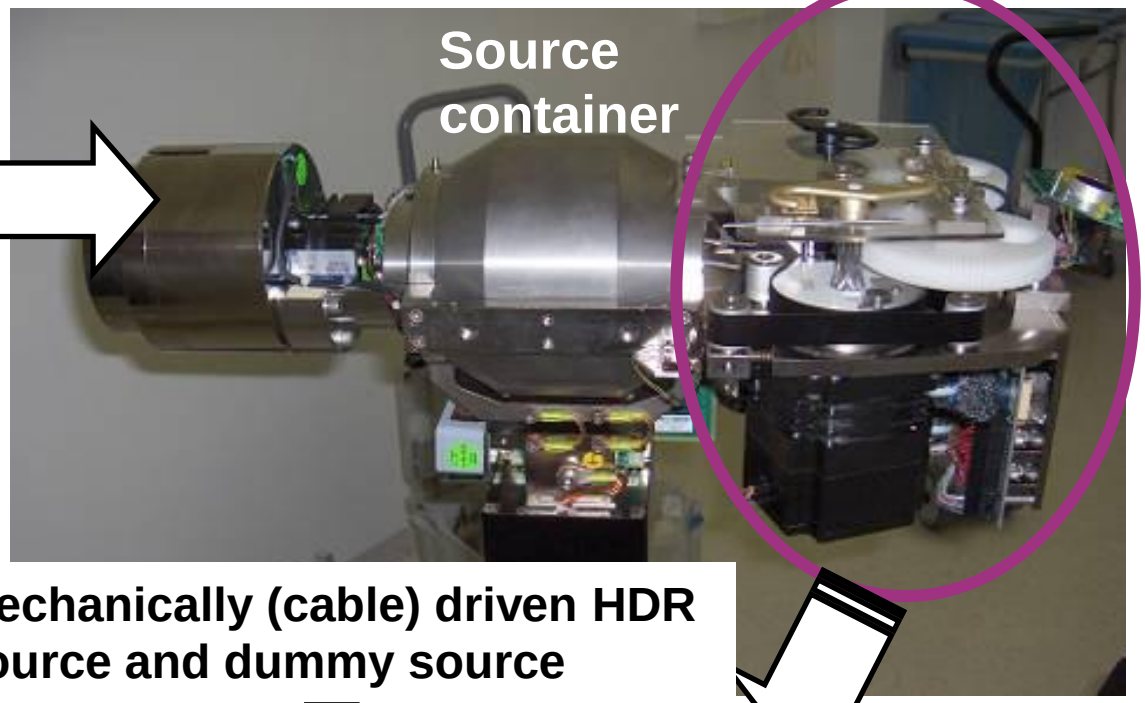
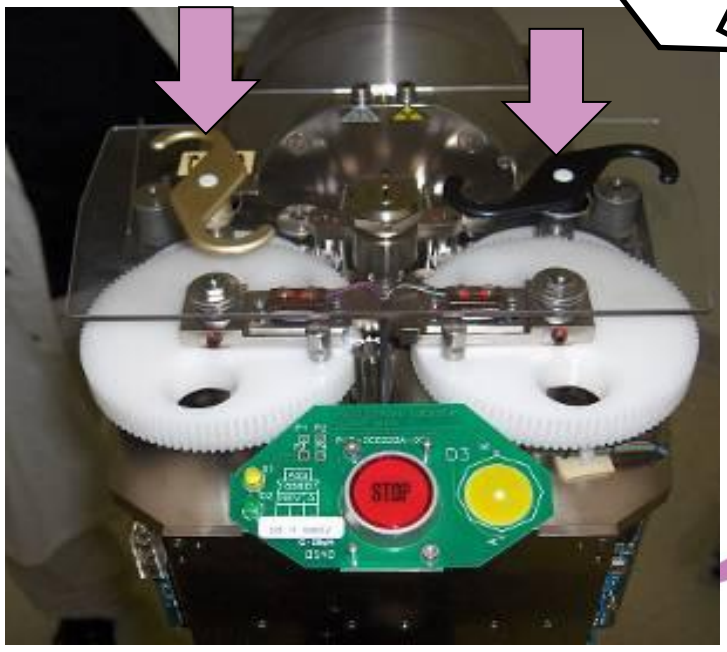
Modern Afterloaders: Some Details on Mechanisms



ELEKTA - Nucletron, MicroSelectron Vs. 3



Mechanically (cable) driven HDR source and dummy source



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Requirements for QC Checks

Minimum Requirements for QC (afterloaders)

Test	Test frequency	
	HDR / PDR	LDR
Emergency stop push buttons	4M	6M
Interrupt button	4M	6M
Door interlock	4M	6M
Power loss	4M	6M
Air pressure loss	-	6M
Unlocked indexer ring	4M	-
Obstructed applicator	4M	6M
Missing applicator	4M	6M

[NCS Rep. 13, 2000, also in ESTRO Booklet 8]

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Requirements for QC Checks

IAEA TECDOC-1040

Design and implementation of a radiotherapy programme: Clinical, medical physics, radiation protection and safety aspects

INTERNATIONAL ATOMIC ENERGY AGENCY IAEA

September, 1998

I.10.4. Measurement Equipment for Brachytherapy

I.10.4.1. Well-Type Ionization Chambers

QC procedures for well-type ionization chambers are given in Table I.X.

TABLE I.X. QC TESTS FOR BRACHYTHERAPY SOURCE CALIBRATOR

I, initial use or following malfunction and repairs[a], S, isotope/source specific, D, documented and correction applied or noted in report of measurement, when appropriate, and E, each use (measurement sequence) or ongoing evaluation. Reproduced with permission of AAPM TG-40.

Instrument type	Test	Frequency	Tolerance
Well ionization chamber	Standards Laboratory calibration	I,S[a]	D
	Precision	I	2%
	Linearity	I, 2 year	1%
	Collection Efficiency	I	1%
	Geometrical/length dependence	I	D
	Energy dependence	I	D
	Source wall dependence	I	D
	Venting	I	D
	Redundant check	E	2%
	Leakage	E	D
In-air calibration chamber and external source holder	SSDL calibration	I,S[a]	D
	Accuracy of source chamber distance	1 yr, S	1%, D
	Redundancy See Table I.III. for other tests	E	D

[a] Instruments or sources must have a calibration directly traceable to a Standards Laboratory.

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Requirements for QC Checks

I.10.3. QC of Remote Afterloading Devices

Recommended QC tests for remote afterloading devices are given in Table I.IX.

TABLE I.IX. QC OF REMOTE AFTERLOADING BRACHYTHERAPY UNITS
Reproduced with permission of AAPM TG-40.

Frequency	Test	Tolerance
Each treatment day	Room safety door interlocks, lights, and alarms	Functional
	Console functions, switches, batteries, printer	Functional
	Visual inspection of source guides	Free of kinks and firmly attached
	Verify accuracy of ribbon preparation	Autoradiograph
Weekly	Accuracy of source and dummy loading (dummies used for spacing and/or simulation/verification)	1 mm
	Source positioning	1 mm
At each source change or quarterly	Calibration[a]	3%
	Timer function	1%
	Check accuracy of source guides and connectors	1 mm
	Mechanical integrity of applicators (by X-ray if appropriate)	Functional
Annual	Dose calculation algorithm (at least one standard source configuration for each isotope)	3%, 1 mm
	Simulate emergency conditions	
	Verify source inventory	

[a] It is worthwhile at source change to calibrate both new and old sources to establish and document reproducibility of calibration method.

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Requirements for QC Checks: Sources & Afterloaders

Table 11.22

Test frequencies and action levels for various brachytherapy procedures. HDR = high dose rate, PDR = pulsed dose rate, LDR = low dose rate, MDR = medium dose rate. (Adapted from [207].)

DESCRIPTION	MINIMUM REQUIREMENTS	
	TEST FREQUENCY	ACTION LEVEL
HDR/PDR		
Source calibration	Source exchange	5%
Source position	Daily/quarterly	2 mm
Length of treatment tubes	Annually	1 mm
Irradiation timer	Annually	1%
Date, time, source strength	Daily	-
Transit time effect	Annually	-
LDR/MDR		
Source calibration, mean of batch	Source exchange	3%
Source calibration, individual source, decay	Source exchange	5%
Linear uniformity	Source exchange	5%
Source position, source length	Half yearly	2 mm
Irradiation timer	Annually	2%
Date, time, source strength in treatment unit	Daily	-
Manual Afterloading		
Source calibration, decay calculation	Source exchange	5%
Linear uniformity, source length	Source exchange	5%
Source identification	Daily/annually	—

Venselaar, J., and J. Pérez-Calatayud, eds. *A Practical Guide to Quality Control of Brachytherapy Equipment.* ESTRO Booklet Number 8.

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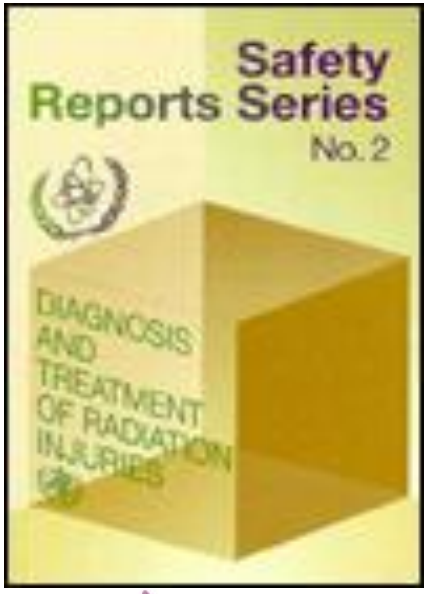
Training aiming at avoiding accidents

Training:

- **Radiographers, nursing staff**
- **Physicians and residents**
- **Patient instructions**

Note: many of the accidents with unintended medical exposures in BT were due to lack of training and procedures (source: IAEA Safety Report Series 2)



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Topics

- Overview on Events in BRT
- Overview of Physicist´s Tasks
- Radiation Protection
- **Introduction on Shielding Calculations**

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The GEC ESTRO Handbook of Brachytherapy

SECOND EDITION

PART I: THE BASICS OF BRACHYTHERAPY

3

Radiation Protection in Brachytherapy

Panagiotis Papagiannis, Jack Venselaar

Editors

Erik Van Limbergen
Richard Pötter
Peter Hoskin
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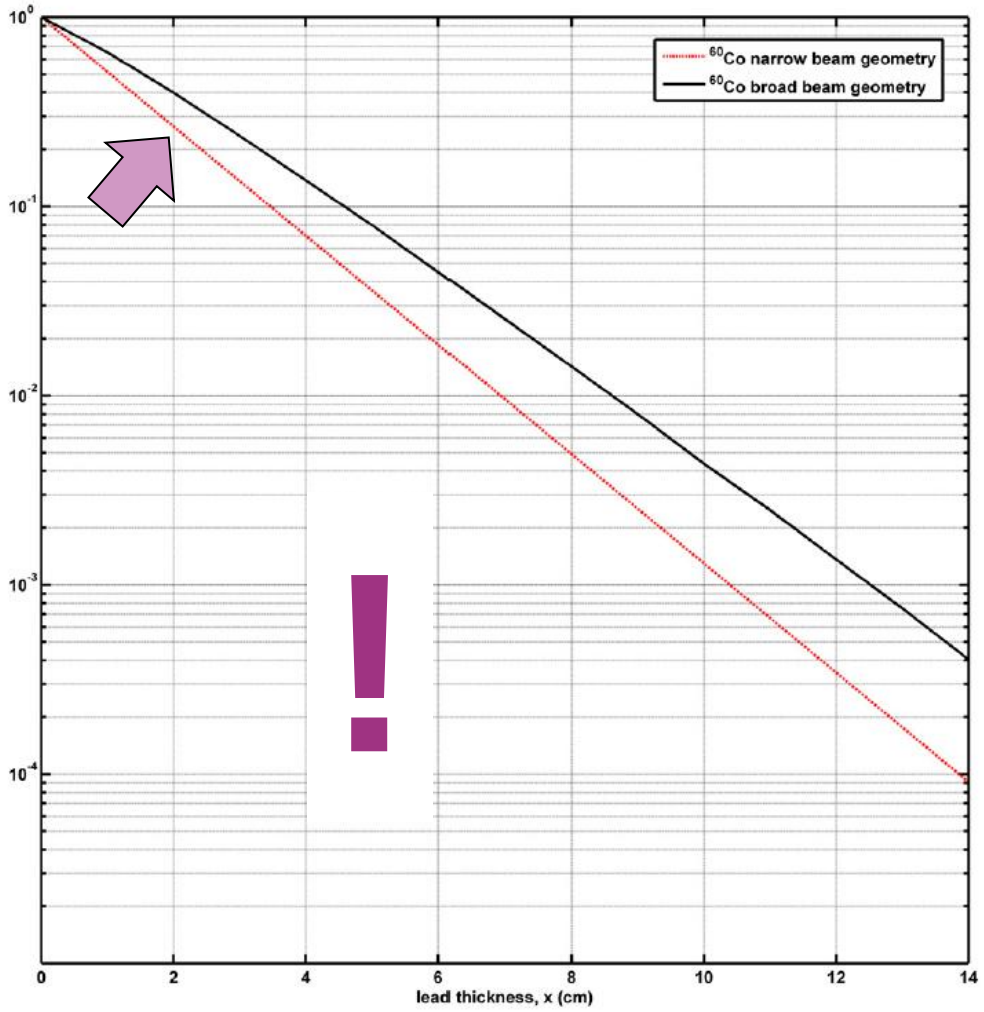

Fig. 3.2 ^{60}Co radiation transmission factor *T* for a lead shielding barrier in narrow and broad beam geometry conditions. (Courtesy: P. Papagiannis)

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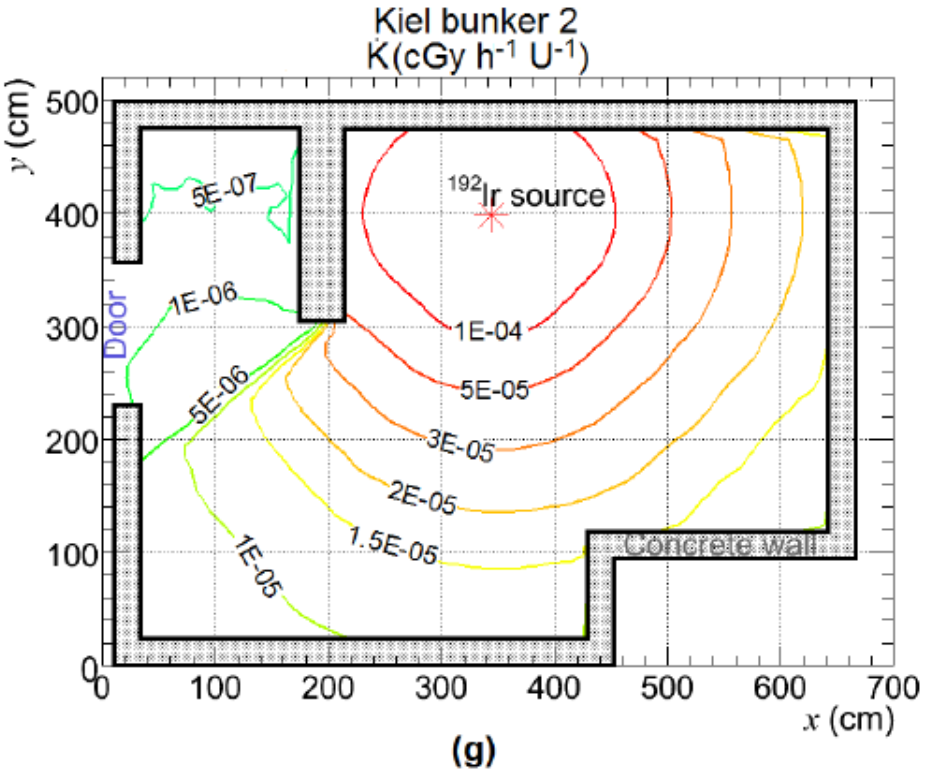
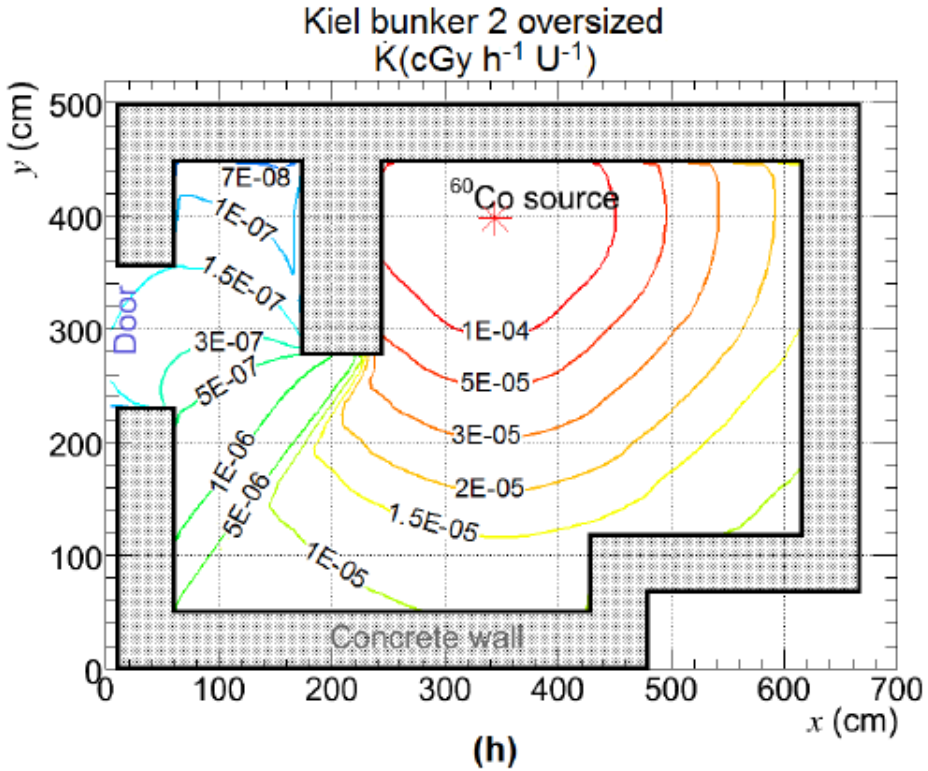
Shielding Calculations, Principles: Examples





Air-kerma rate distribution on the plane parallel to the floor and containing the source for five different facility designs for ^{192}Ir (left) and ^{60}Co (right) of a given strength. See the original article for more details. (Courtesy: M.C. Pujades)

Remember: for ^{192}Ir 370 GBq ≈ 40.4 kU
for ^{60}Co ≈ 1/3 of contained activity of ^{192}Ir …

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Shielding Calculations, Principles

Shielding Calculations, determine the "workload" W in your department:

$$W = N \times S_K \times t$$

TRAK

- **W = workload, in air @ 1 m distance from the source(s) per time period (week, month, year)**
- **N = number of applications per time period (week, month, year)**
- **S_K = Reference air kerma rate**
- **t = time of exposure (average/application)**

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Shielding Calculations, Principles

Shielding Calculations: does your facility fulfil the radiation protection requirements (limits)?

$$W \times f_{dist} \times f_{occup} \times T_{patient} \times T_{trans} < \text{limit}$$

- f_{dist} = inverse square law (distance factor)
- f_{occup} = occupancy factor
- $T_{patient}$ = transmission through the patient
- T_{trans} = transmission factor through the wall or shielding material
- limit = requirement for the specific point per time period (w, m, y; e.g. 1 mSv/year)

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Shielding Calculations, Principles: Dose Limits

Table 3.1: Dose limits recommended by the ICRP (24)

	PUBLIC EXPOSURE	OCCUPATIONAL EXPOSURE
Effective dose limit:	1 mSv per year	20 mSv per year averaged over 5 years and less than 50 mSv in any single year
Eye lens equivalent dose limit:	15 mSv	150 mSv*
Skin equivalent dose limit:	50 mSv	500 mSv
Hands and feet equivalent dose limit:	-	500 mSv

**After review of epidemiological evidence suggesting threshold doses might be lower than previously considered, irrespective of rate of dose delivery, ICRP issued a statement on tissue reactions (25) and an equivalent dose limit for the lens of the eye of 20 mSv in a year, averaged over defined periods of 5 years, was recommended for occupational exposure in planned exposure situations. This recommendation, which is significantly lower than corresponding ICRP 103 (24) recommendations, was adopted in the IAEA Basic Safety Standards (15) and will very likely be implemented in national dose limits in the coming years.*

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Published Radiation Protection Data

You may wish to take data from NCRP publications, in concrete….

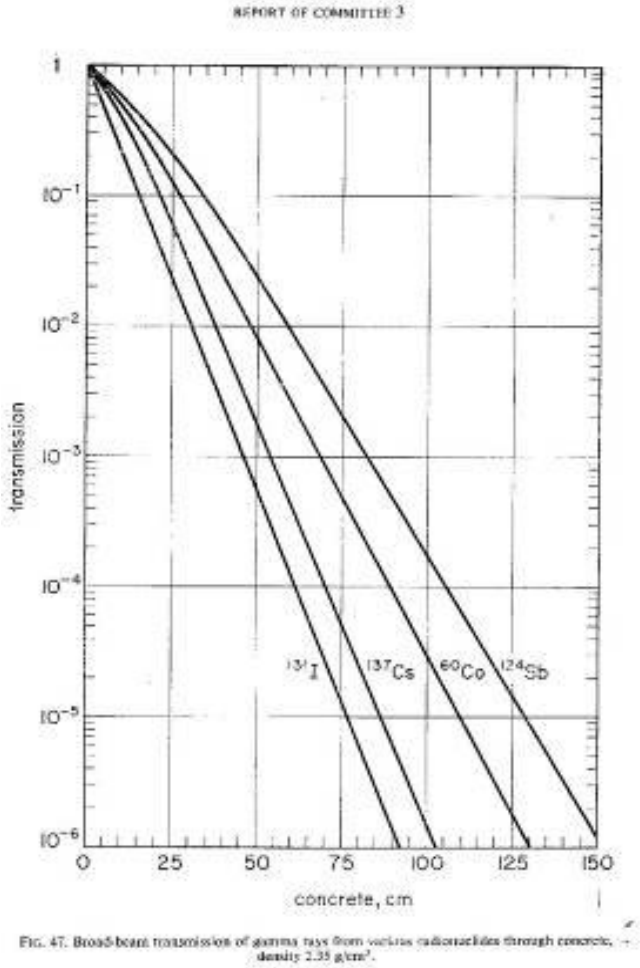

FIG. 47. Broad-beam transmission of gamma rays from various radionuclides through concrete, density 2.35 g/cm³.

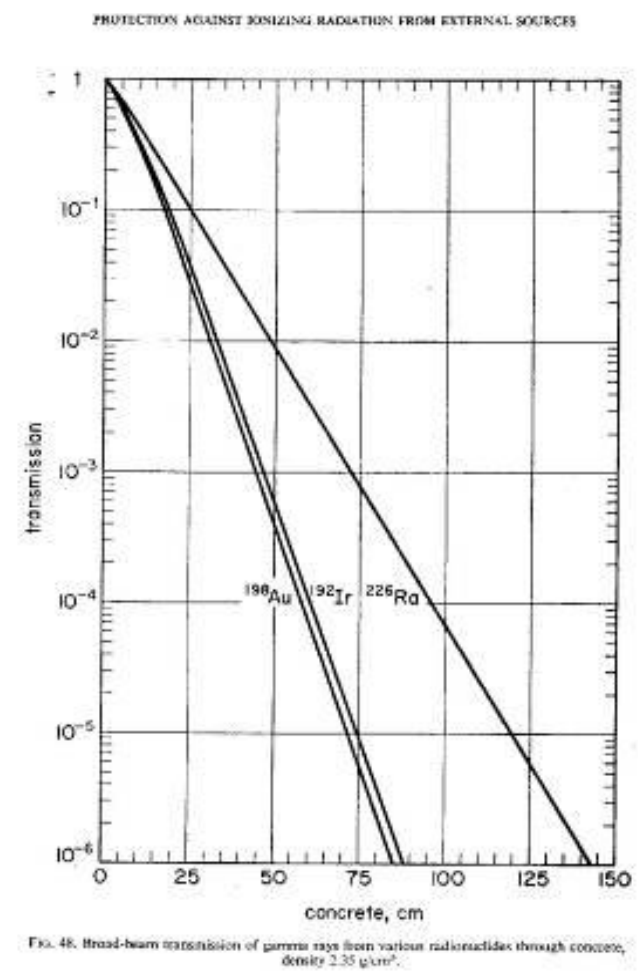

FIG. 48. Broad-beam transmission of gamma rays from various radionuclides through concrete, density 2.35 g/cm³.

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Published Radiation Protection Data

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

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Department of Medical Physics, Dr. B. Verbeeten Instituut, P.O. Box 90120, 5000 LA, Tilburg, The Netherlands

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

To address the limited availability of radiation shielding data for brachytherapy as well as some disparity in existing data, Monte Carlo simulation was used to generate radiation transmission data for ^{60}Co, ^{137}Cs, ^{198}Au, ^{192}Ir, ^{169}Yb, ^{170}Tm, ^{131}Cs, ^{125}I, and ^{103}Pd photons through concrete, stainless steel, lead, as well as lead glass and baryte concrete. Results accounting for the oblique incidence of radiation to the barrier, spectral variation with barrier thickness, and broad beam conditions in a realistic geometry are compared to corresponding data in the literature in terms of the half value layer (HVL) and tenth value layer (TVL) indices. It is also shown that radiation shielding calculations using HVL or TVL values could overestimate or underestimate the barrier thickness required to achieve a certain reduction in radiation transmission. This questions the use of HVL or TVL indices instead of the actual transmission data. Therefore, a three-parameter model is fitted to results of this work to facilitate accurate and simple radiation shielding calculations. © *2008 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2986153]

Key words: brachytherapy, radiation protection, shielding, HVL, TVL, Monte Carlo

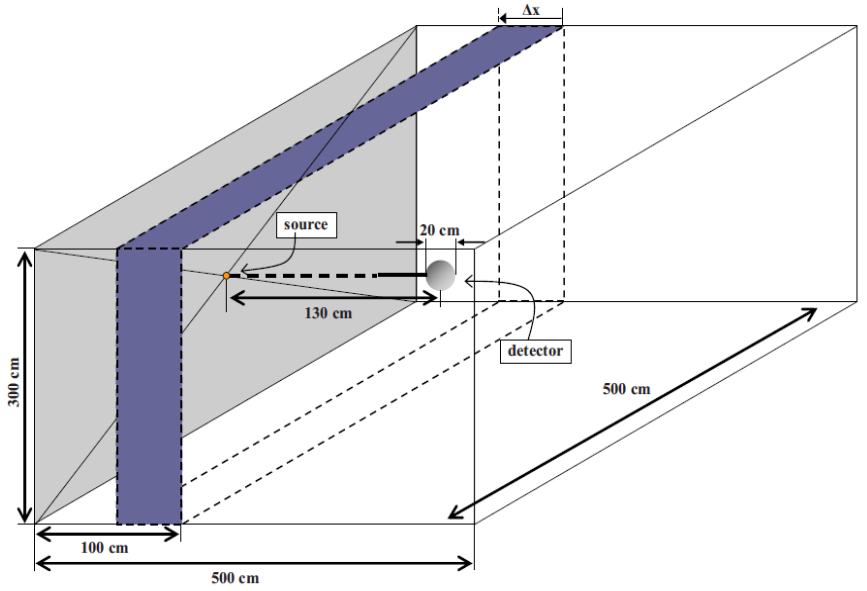

FIG. 1. A schematic diagram illustrating the simulation geometry used in this work.

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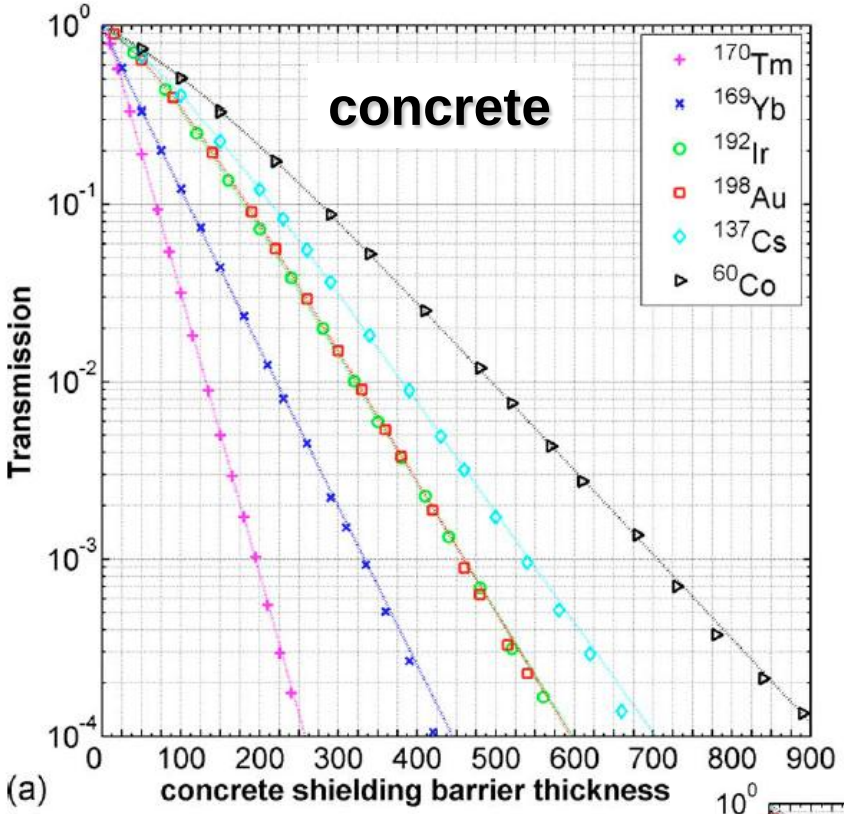

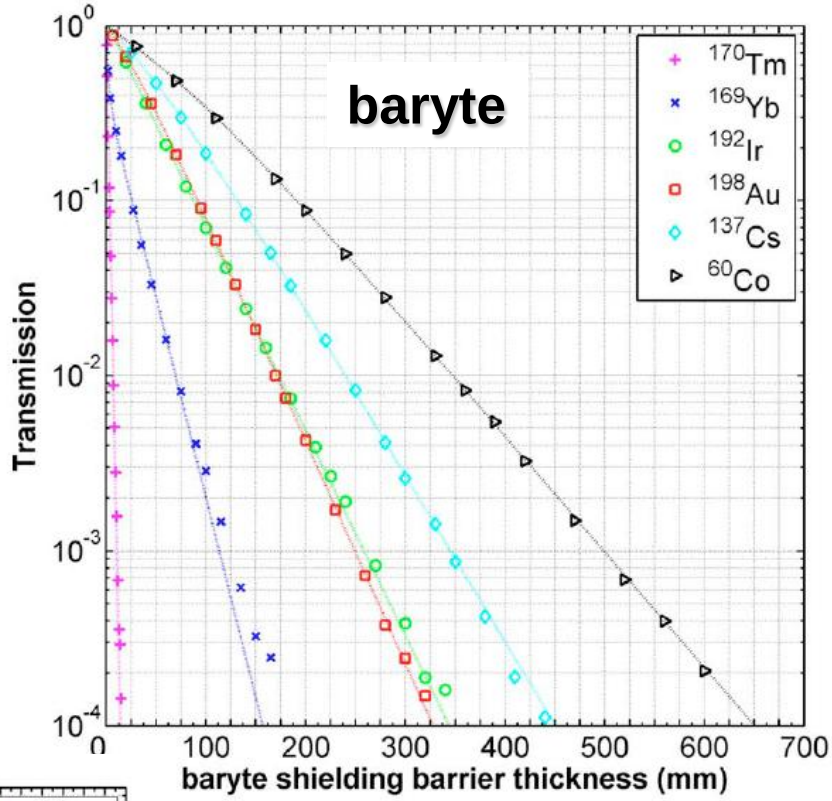

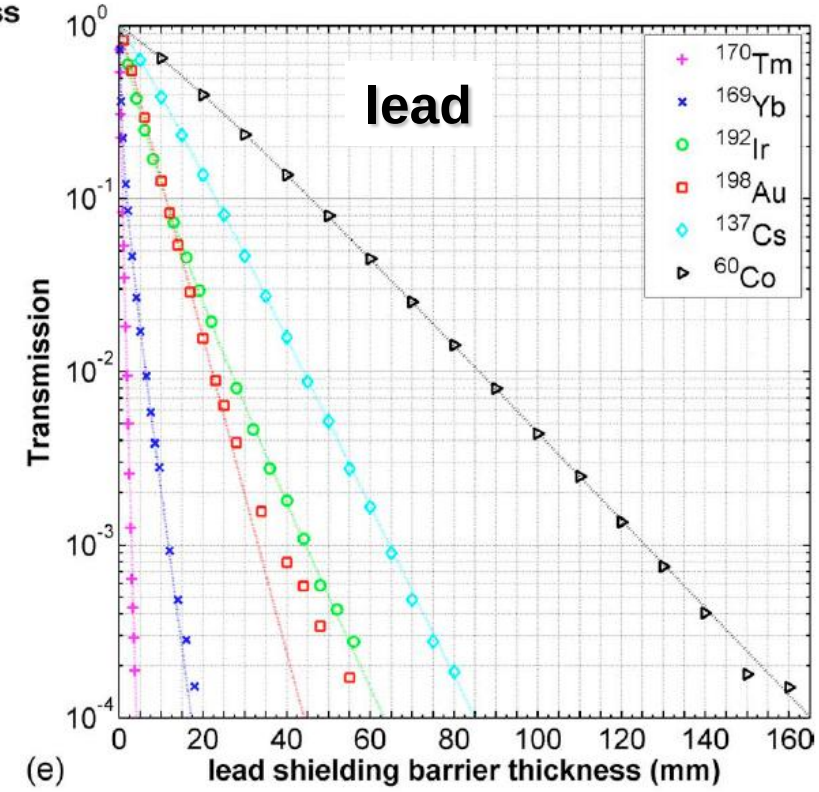

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TABLE III. First and equilibrium HVL and TVL results of this work compared to corresponding results in the literature. All values are in mm.

		This work[a]		Corresponding values in the literature	
Radionuclide	Material	HVL_e (HVL_1)	TVL_e (TVL_1)	HVL_e (HVL_1)	TVL_e (TVL_1)
^{170}Tm	Concrete	19 (24)	63 (68)	—	—
	Baryte concrete	1.0 (1.1)	3.5 (3.5)	—	—
	Stainless steel	1.9 (0.98)	6.5 (4.4)	(1)[b]	(5)[b]
	Lead glass	0.80 (0.39)	2.7 (1.7)	—	—
	Lead	0.34 (0.17)	1.1 (0.73)	(<1)[b]	(<1)[b]
^{169}Yb	Concrete	34 (31)	112 (109)	34[c] (32)[c]	114[c] (106)[c]
	Baryte concrete	13 (2.1)	44 (26)	—	—
	Stainless steel	8.8 (2.2)	29 (22)	(3)[b]	(26)[b]
	Lead glass	3.6 (0.59)	12 (4.1)	—	—
	Lead	1.7 (0.25)	5.5 (1.7)	1.6,[d] (<1),[b] (0.25)[d]	5.3,[d] (2),[b] (1.8)[d]
^{192}Ir	Concrete	42 (70)	139 (180)	43,[e,f] 42,[d] (65)[d]	152,[e] 147,[f] 141,[d] (176)[d]
	Baryte concrete	26 (28)	86 (88)	—	—
	Stainless steel	12 (18)	41 (48)	13,[e,f] (23),[b] (19)[e]	43,[e,f] (49),[e] (56)[b]
	Lead glass	14 (6.4)	47 (24)	—	—
	Lead	5.8 (2.8)	19 (11)	6,[e,f] 5.7,[d] (3),[b] (2.3),[g] (2.8)[d]	16,[e,f] 18.7,[d] 9,[g] (12),[b] (9),[g] (11)[d]
^{198}Au	Concrete	41 (71)	136 (184)	—	—
	Baryte concrete	24 (32)	79 (92)	—	—
	Stainless steel	12 (19)	39 (50)	(24)[b]	(58)[b]
	Lead glass	7.1 (7.7)	23 (24)	—	—
	Lead	3.3 (3.5)	11 (11)	(4)[b]	(12)[b]
^{137}Cs	Concrete	48 (80)	161 (214)	48[e,f]	175[e,f]
	Baryte concrete	32 (46)	105 (131)	—	—
	Stainless steel	14 (23)	48 (63)	16,[e,f] (30),[e] (29)[b]	53,[e] 50,[f] (69),[e] (72)[b]
	Lead glass	12 (15)	41 (47)	—	—
	Lead	6.2 (7.5)	20 (23)	6.5,[e,f] (8),[b] (5.6)[g]	22,[e,f] 18.5,[g] (24),[b] (18.5)[g]
^{60}Co	Concrete	63 (102)	210 (276)	62[e,f]	218,[e] 220,[f] (245)[e]
	Baryte concrete	46 (68)	151 (191)	—	—
	Stainless steel	20 (30)	65 (84)	21,[e,f] (35),[e] (36)[b]	71,[e] 67,[f] (87),[e] (93)[b]
	Lead glass	22 (30)	74 (86)	—	—
	Lead	12 (16)	40 (46)	12,[e,f] (15),[e] (16)[b]	41,[e] 42,[f] (46)[b]

[a]HVL_e and TVL_e calculated as $HVL_e=\ln(2)/\alpha$ and $TVL_e=\ln(10)/\alpha$ using data in Table II. HVL_1 and TVL_1 calculated using Eq. (2) with data in Table II.

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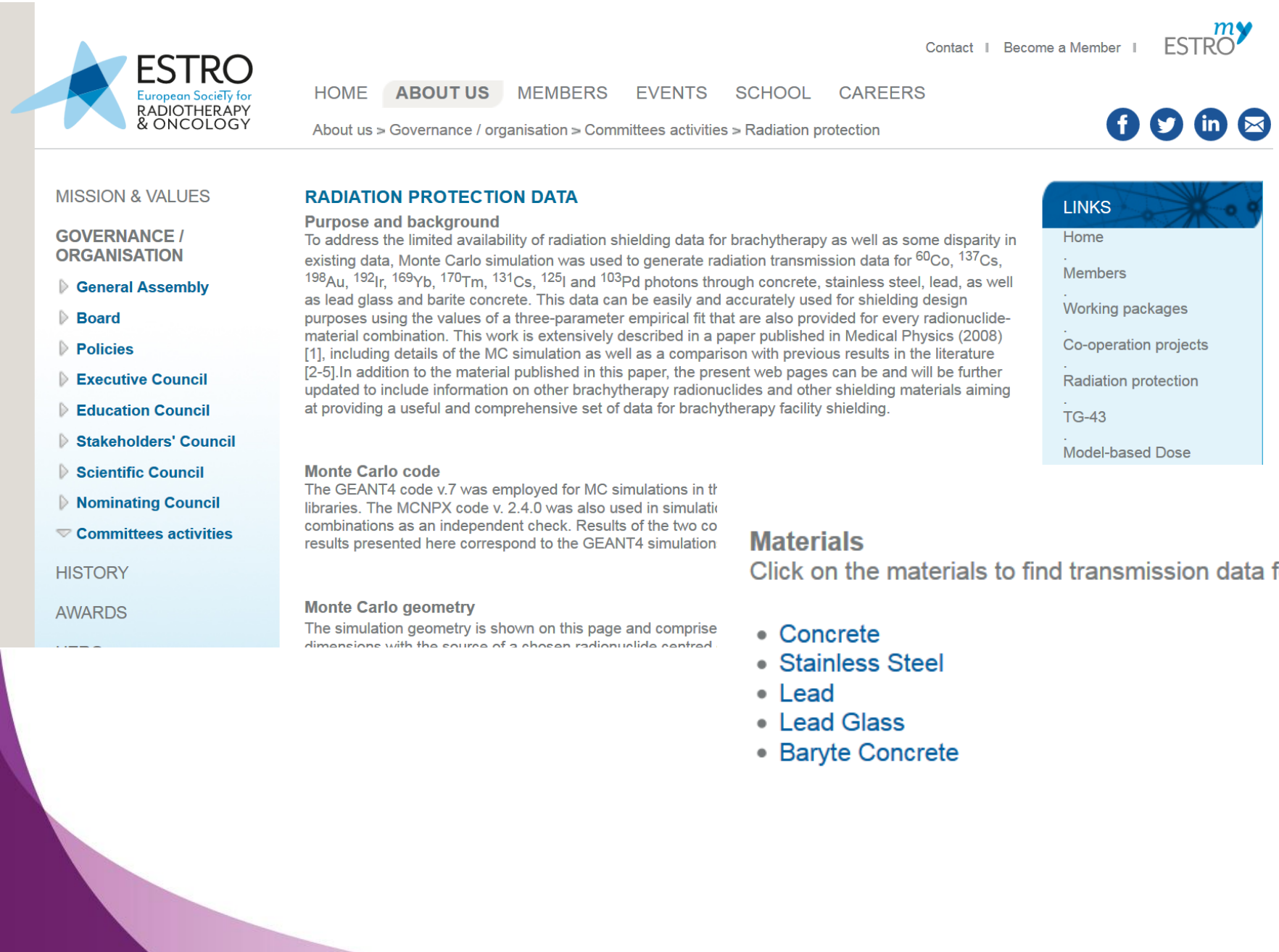
http://www.estro.org/about/governance-organisation/committees-activities/radiation-protection



BRAPHYQS

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For Shielding Calculations and Limits:

Follow your National Regulations!

Summary

- Quality management program
- written procedures
- Training program !!!

8. KEY MESSAGES

- Radiation protection policies are revised dynamically by the work of several international bodies (ICRP, UNSCEAR, IAEA) leading to international consensus on sets of rules that can be integrated to national legislation. These rules are equally applicable to brachytherapy.

- Structural shielding must be used when workload and distance are such that acceptable levels of protection cannot be ensured. The methodology for calculating the required thickness is presented, including references for the data for radionuclide / shielding material combinations. Examples of different treatment room designs are shown in this chapter.

- A quality management program should be developed for each brachytherapy department. Written procedures, clearly defined tasks for each member of the brachytherapy team, and an appropriate training program with frequent reevaluation and repeated practice by the team members, contribute to a safe treatment for the patient while ensuring minimized risks of radiation exposure and accidents.

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WWW.ESTRO.ORG/SCHOOL

Uncertainties
ESTRO Teaching Course

Budapest, 2017

Dimos Baltas

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

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Topics

- Definition of Uncertainty
- Accuray and Precision
- Types of Uncertainty
- Categories of Uncertainty
- Technology Related Uncertainties
- Human Related Uncertainties
- Summary

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Definition of Uncertainty

There are some things that you know to be true, and others that you know to be false; yet, despite this extensive knowledge that you have, there remain many things whose truth or falsity is not known to you. We say that you are uncertain about them. You are uncertain, to varying degrees, about everything in the future; much of the past is hidden from you; and there is a lot of the present about which you do not have full information. **Uncertainty is everywhere and you cannot escape from it.**

Dennis Lindley, Understanding Uncertainty (2006)

Definition of Uncertainty

Uncertainty (of measurement):

parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand.

- The parameter may be, for example, a standard deviation (or a given multiple of it), or the half-width of an interval having a stated level of confidence.
- Uncertainty of measurement comprises, in general, many components. Some of these components may be evaluated from the statistical distribution of the results of a series of measurements and can be characterized by experimental standard deviations. The other components, which also can be characterized by standard deviations, are evaluated from assumed probability distributions based on experience or other information.
- It is understood that the result of the measurement is the best estimate of the value of the measurand, and that all components of uncertainty, including those arising from systematic effects, such as components associated with corrections and reference standards, contribute to the dispersion.

NIST: http://physics.nist.gov/cuu/Uncertainty/glossary.html

Topics

- Definition of Uncertainty
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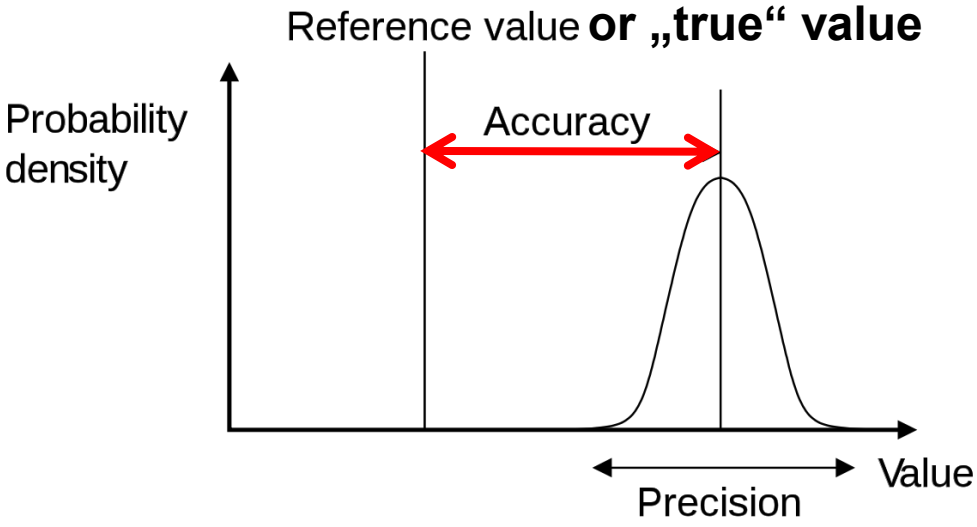
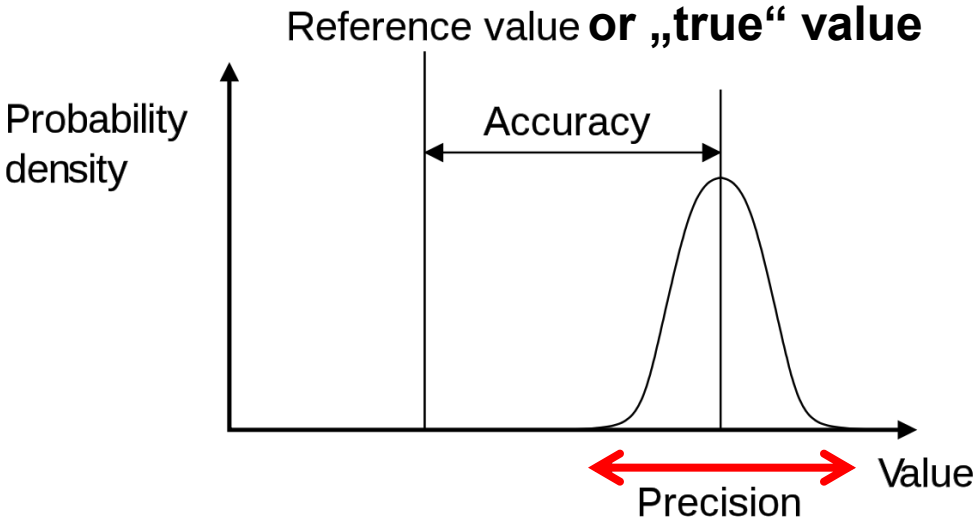
Accuracy and Precision



Accuracy is the closeness of agreement between a measured quantity and its “true value.”
Trueness is the closeness of agreement between the average value obtained from a large series of test results and the accepted true value.

Accuracy and Uncertainty Considerations in Modern Radiation Oncology, The Modern Technology of Radiation Oncology, J. Van Dyk, 2013

Accuracy and Precision

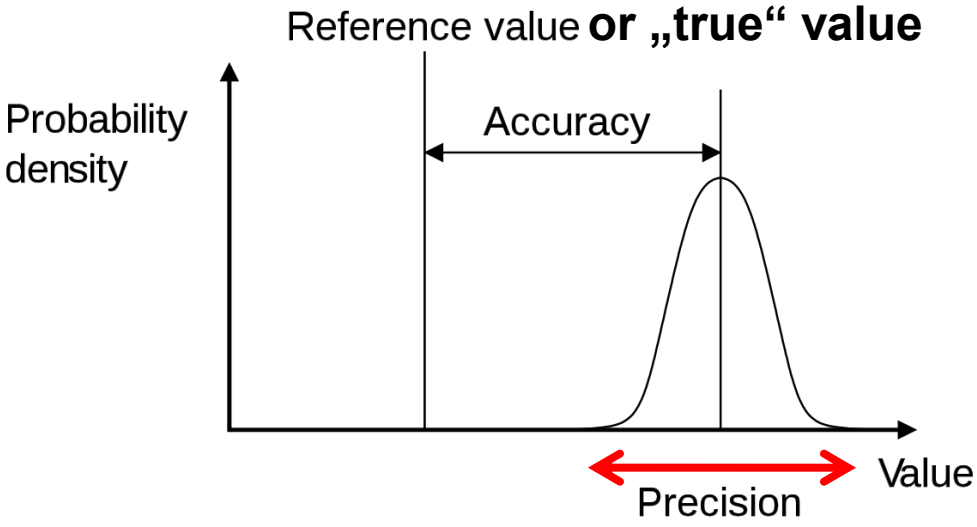


Precision is the closeness of agreement of the results when the same measurement is made repeatedly.

Error is the difference between the measured quantity and its reference value.
Note that error in this context is not to be confused with a production error or mistake. In the radiation oncology context, however, the word “error” tends to be used for both measurement errors and mistakes.

Accuracy and Uncertainty Considerations in Modern Radiation Oncology, The Modern Technology of Radiation Oncology, J. Van Dyk, 2013

Accuracy and Precision



Systematic error is a set of results of measurements that deviate by a consistent amount from the true value of the measurement. Once a systematic error is known, a correction can be applied to compensate for it.

Random error occurs when the same measurement is performed repeatedly and the resulting variations lead to the measurable values being inconsistent.

Topics

- Definition of Uncertainty
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Definition of Uncertainty: Types of Uncertainty

Type A of Uncertainty

If an uncertainty is based on a statistical analysis, it is to be treated as a Type A uncertainty. Most random uncertainties are Type A uncertainties. They vary each time a measurement is made. The uncertainty can be reduced by averaging lots of measurements, but it can never be totally eliminated.

Type B of Uncertainty

Any uncertainty not based on a statistical analysis is to be treated as a Type B uncertainty.
Most systematic uncertainties are Type B uncertainties.
Type B evaluations require critical thinking, intellectual honesty, and professional skill.

Wrongly classifying Type A and Type B uncertainties will lead to different intermediate numbers. **But the final uncertainty will be the same!**

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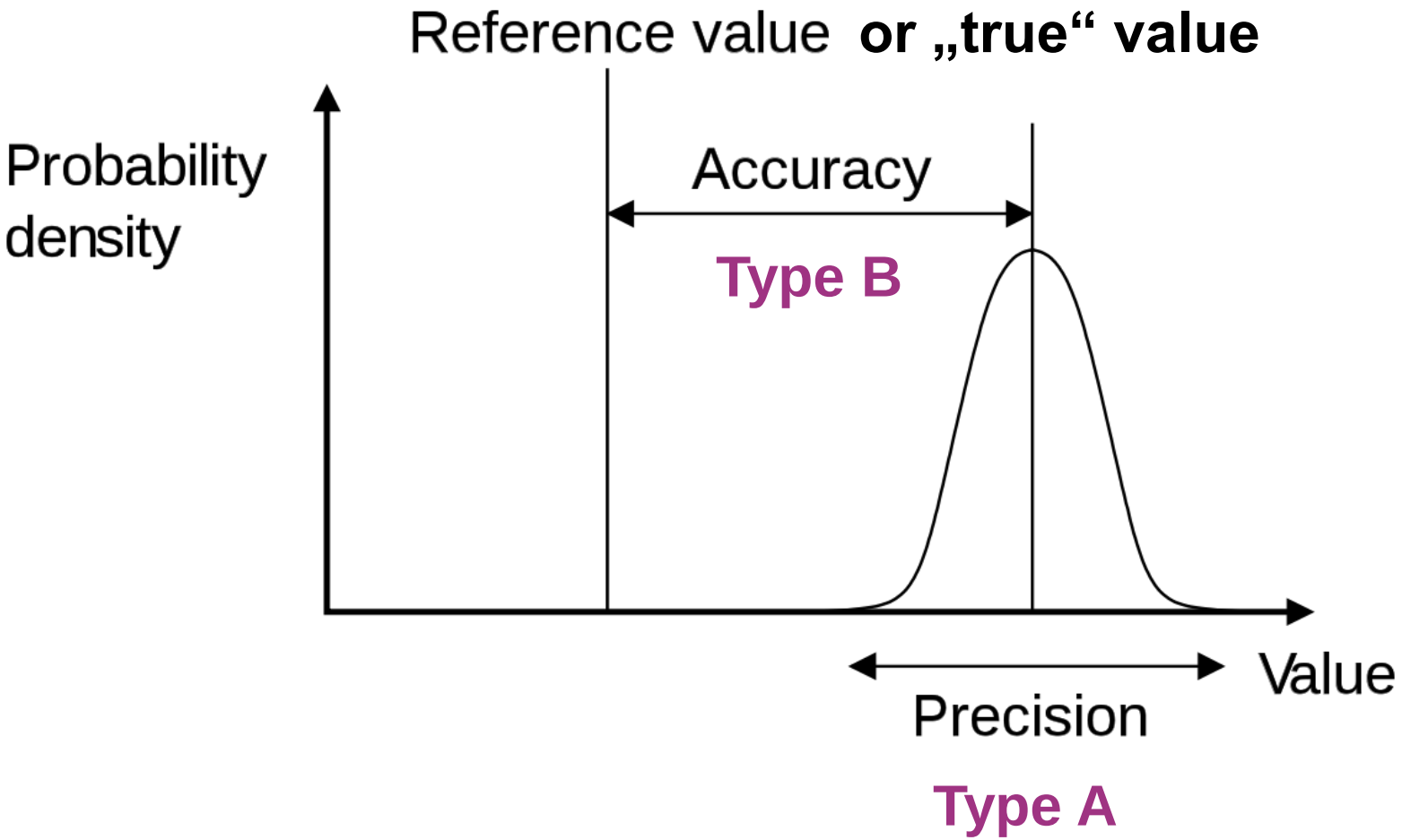
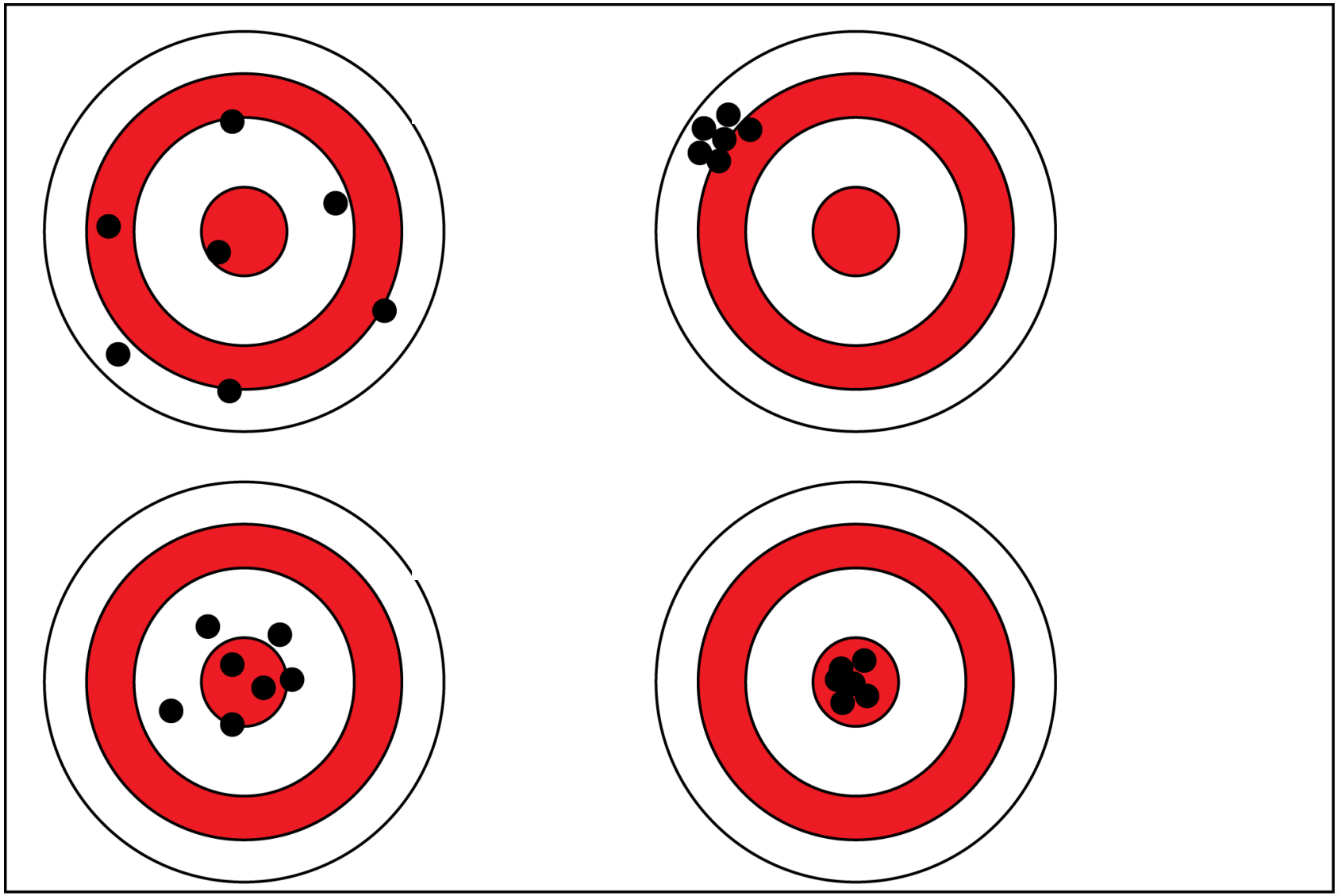
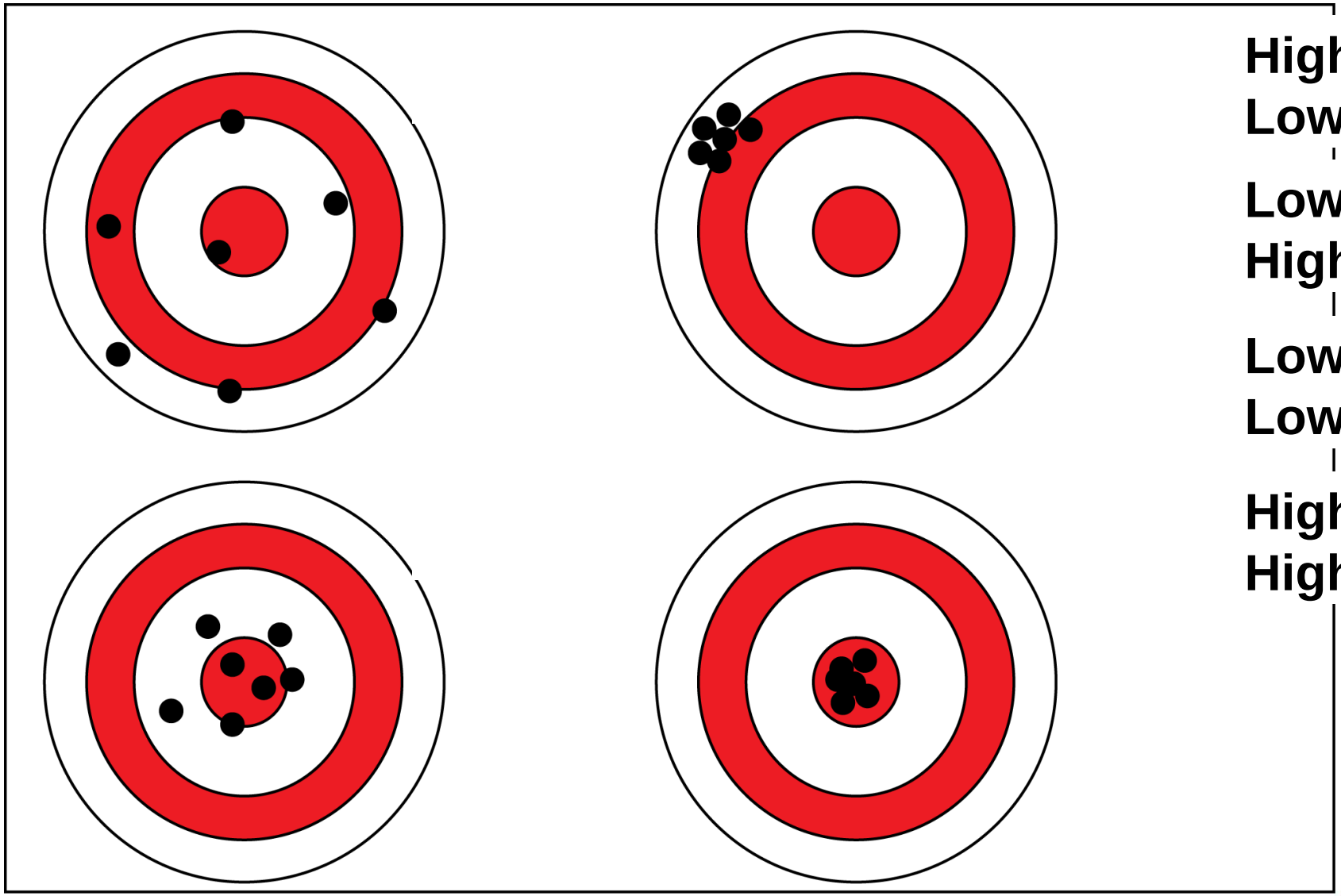
Definition of Uncertainty: Types of Uncertainty



Definition of Uncertainty: Types of Uncertainty



Definition of Uncertainty: Types of Uncertainty



High Type A
Low Type B

Low Type A
High Type B

Low Type A
Low Type B

High Type A
High Type B

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Definition of Uncertainty: Types of Uncertainty

Uncertainty is a parameter that characterizes the dispersion of values that can be obtained for a particular measurement when it is performed repeatedly. For such repeated measurements, the results can be represented by a statistical distribution, which can be summarized by specific statistical quantities such as mean, mode, standard deviation, and variance.

Standard uncertainty is the standard deviation. The symbol often attributed to the standard uncertainty is u.

Combined standard uncertainty is the standard uncertainty of a quantity that is composed of various components, each of which has its own uncertainty. The combined standard uncertainty is obtained by combining the square of the sums of the individual standard deviations and taking the square root. This assumes a gaussian distribution for each of the contributing uncertainties. This mathematical procedure for combining uncertainties is generally known as “addition in quadrature.”

Accuracy and Uncertainty Considerations in Modern Radiation Oncology,
The Modern Technology of Radiation Oncology, J. Van Dyk, 2013

Definition of Uncertainty: Types of Uncertainty

Expanded uncertainty is the standard uncertainty multiplied by a coverage factor, k, such that the statement of the expanded uncertainty gives a higher probability that the correct value lies within the range of the stated uncertainty.

Often the expanded uncertainty is given the symbol U such that

$$U = k\,u$$

Generally $k > 1$.

For *k* equal to 1, 2, or 3, there is approximately a 67%, 95%, or 99% probability, respectively, that *the true value* lies between $\pm U$ *of the measured mean value*. Often we will see uncertainties quoted, for example, “at the *k* 2 level” or “with $k = 2$”.

Topics

- Definition of Uncertainty
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The Radiation Therapy Process: Categories of Uncertainty

From the point of view of uncertainty analysis and uncertainty modeling, it is useful to sort uncertainties into two major categories:

1. ***Human-related*** *(patient or personnel)* uncertainties and
2. ***Technology*** **or** ***Dose-related*** uncertainties

Human-related uncertainties can be analyzed by considering the radiation therapy process from a patient's perspective (i.e., patient's-eye view), whereas technology-related uncertainties can be addressed by considering a machine perspective (i.e., machine's-eye view), including dosimetry, commissioning, and quality control processes.

The Radiation Therapy Process: Categories of Uncertainty

Table 11.3

Examples of human- and technology-related uncertainty components in the radiation treatment process. Note that these are not comprehensive lists but only some examples for illustration.

HUMAN-RELATED UNCERTAINTIES	TECHNOLOGY-RELATED UNCERTAINTIES
Target and organ-at-risk segmentation	Absolute dose determination
Patient repositioning	Machine calibration
Organ/tumour motion	Beam profiles
Interpretation of on-line image matching	Imaging quality/resolution
Deformation	Dose calculation
~~Couch position~~	Electron density
Organ full/empty	~~Beam energy~~
~~Weight change~~	Machine isocentricity
Contour change	Tissue inhomogeneity corrections
Source-to-surface distance	Beam modifiers
Immobilization devices	Leaf transit times
~~Accuracy of laser setup~~	Uncertainty in leaf position
Skin tattoo movement	~~Partial leaf transmission~~
Breathing motion	Optimization algorithm

Not relevant for BRT

Accuracy and Uncertainty Considerations in Modern Radiation Oncology, The Modern Technology of Radiation Oncology, J. Van Dyk, 2013

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Topics

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The Radiation Therapy Process: Technology Uncertainty

Imaging

Table 11.8

Summary of geometric uncertainties associated with imaging systems used for treatment planning. N/A = not applicable.

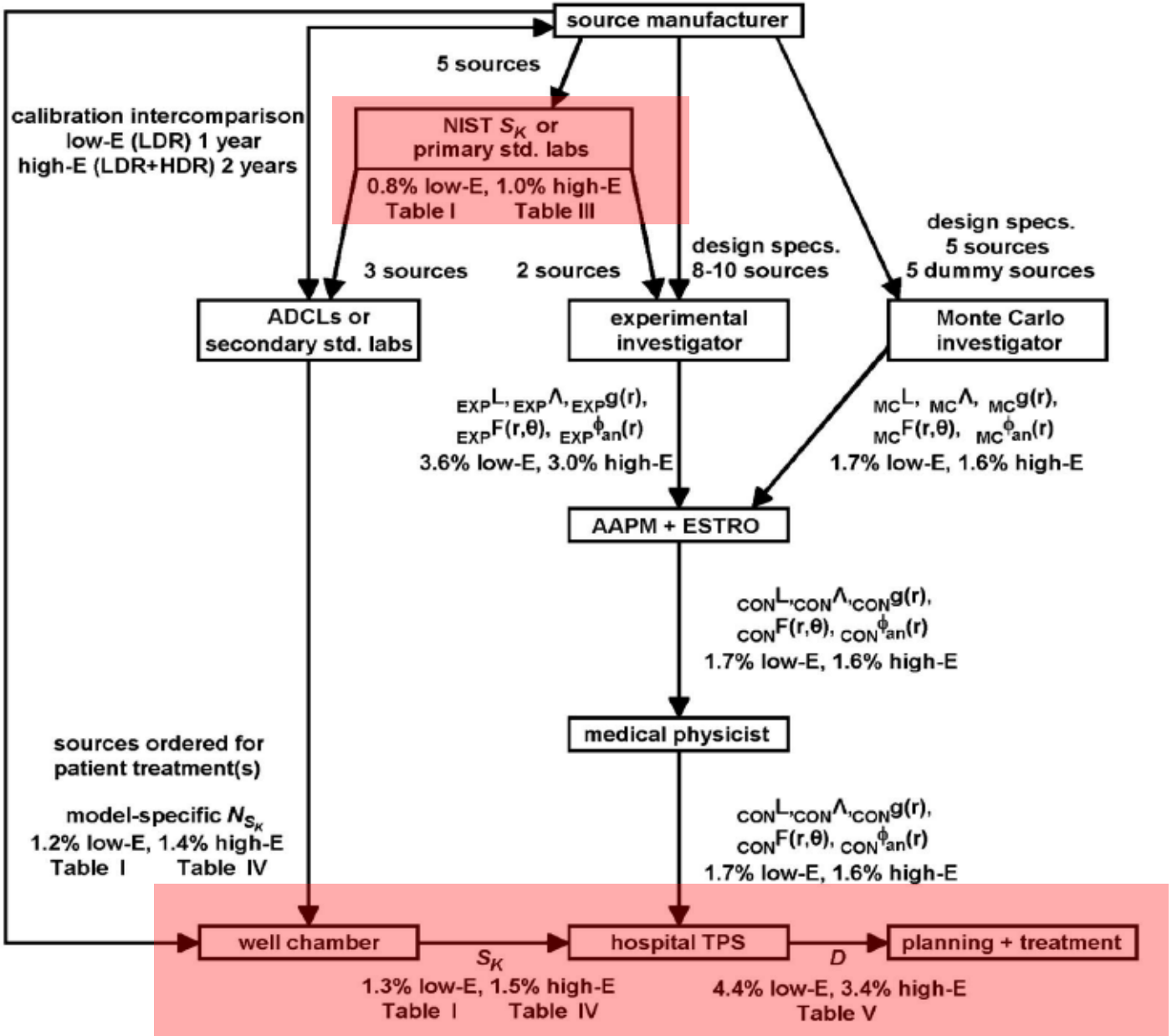
Imaging modality	Spatial Resolution	Overall geometric considerations	Derivation of Electron Density Relative to Water
Simulator film radiography	≤ 0.1mm	0.5 – 2 mm	N/A
Simulator fluoroscopy	≤ 0.5 mm	0.5 – 2 mm	N/A
CT	≤ 1 mm	1 – 2 mm	0.02 after conversion of CT number to electron density relative to water (1.00)
MRI	≤ 1 mm	2 – 7 mm (can be reduced to ≤ 1 mm with corrections) [211,212]	N/A
PET	4 – 8 mm	4 – 8 mm	N/A
SPECT	8 – 20 mm	8 – 20 mm	N/A
Ultrasound	1 – 3 mm	1 – 3 mm	N/A

Accuracy and Uncertainty Considerations in Modern Radiation Oncology, The Modern Technology of Radiation Oncology, J. Van Dyk, 2013

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.

Dosimetry / Calibration



TROOL

The Radiation Therapy Process: Technology Uncertainty

Dosimetry / Calibration

Table 11.19

Propagation of best practice uncertainties (k = 1 unless stated otherwise) associated with the transfer of air-kerma strength from NIST through the ADCL to the clinic for LDR high-energy brachytherapy sources. Well-chamber measurement uncertainty is estimated to be 0.5%. WAFAC = wide-angle free-air chamber. (Reproduced with permission from [45].)

Row	Measurement description	Quantity (units)	Relative propagated uncertainty (%)
1	NIST calibration	$S_{K,\mathrm{NIST}}$ (U)	1.0
2	ADCL well ion chamber calibration	$S_{K,\mathrm{NIST}}/I_{\mathrm{ADCL}}$ (U/A)	1.1
3	ADCL calibration of source from manufacturer	$S_{K,\mathrm{ADCL}}$ (U)	1.2
4	ADCL calibration of clinic well ion chamber	$S_{K,\mathrm{ADCL}}/I_{\mathrm{CLINIC}}$ (U)	1.3
5	Clinic measures source air-kerma strength	$S_{K,\mathrm{CLINIC}}$ (U)	1.4
	Expanded uncertainty (k = 2)	$S_{K,\mathrm{CLINIC}}$ (U)	2.8

DeWerd, L.A., G.S. Ibbott, A.S. Meigooni, M.G. Mitch, M.J. Rivard, K.E. Stump, B.R. Thomadsen, J.L. Venselaar. "A dosimetric uncertainty analysis for photon-emitting brachytherapy sources: report ofAAPMTask Group No. 138 and GECESTRO." *Med. Phys.* 38:782–801, 2011.

The Radiation Therapy Process: Technology Uncertainty

Dosimetry / Calibration

Table 11.20

Propagation of best practice uncertainties ($k = 1$ unless stated otherwise) associated with the transfer of air-kerma strength from a traceable NIST coefficient from the ADCL to the clinic for HDR high-energy brachytherapy sources. (Reproduced with permission from [45].)

Row	Measurement description	Quantity (units)	Relative propagated uncertainty (%)
1	ADCL calibration	$S_{K,\mathrm{NIST}}$ (U)	1.1
2	ADCL well ion chamber calibration	$S_{K,\mathrm{NIST}}/I_{\mathrm{ADCL}}$ (U/A)	1.2
3	ADCL calibration of source from manufacturer	$S_{K,\mathrm{ADCL}}$ (U)	1.3
4	ADCL calibration of clinic well ion chamber	$S_{K,\mathrm{ADCL}}/I_{\mathrm{CLINIC}}$ (U/A)	1.4
5	Clinic measures source air-kerma strength	$S_{K,\mathrm{CLINIC}}$ (U)	1.5
	Expanded uncertainty ($k = 2$)	$S_{K,\mathrm{CLINIC}}$ (U)	2.9

DeWerd, L.A., G.S. Ibbott, A.S. Meigooni, M.G. Mitch, M.J. Rivard, K.E. Stump, B.R. Thomadsen, J.L. Venselaar. "A dosimetric uncertainty analysis for photon-emitting brachytherapy sources: report ofAAPMTask Group No. 138 and GECESTRO." *Med. Phys.* 38:782–801, 2011.

The Radiation Therapy Process: Technology Uncertainty

Dosimetry / Calibration

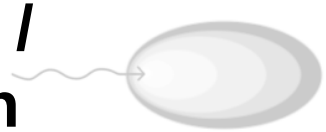


Table 11.21

Propagation of best practice uncertainties ($k = 1$ unless stated otherwise) in dose at 1 cm on the transverse plane associated with source-strength measurements at the clinic, brachytherapy dose measurements or simulation estimates, and treatment planning system dataset interpolation for low-energy (low-E) and high-energy (high-E) brachytherapy sources. (Reproduced with permission from [45].)

		Relative propagated uncertainty (%)	
Row	Uncertainty component	low-E	high-E
1	S_K measurements from row 5 of Tables 11.17 and 11.20	1.3	1.5
2	Measured dose	3.6	3.0
3	Monte Carlo dose estimate	1.7	1.6
4	TPS interpolation uncertainties	3.8	2.6
5	Total dose calculation uncertainty	4.4	3.4
	Expanded uncertainty ($k = 2$)	8.7	6.8

DeWerd, L.A., G.S. Ibbott, A.S. Meigooni, M.G. Mitch, M.J. Rivard, K.E. Stump, B.R. Thomadsen, J.L. Venselaar. "A dosimetric uncertainty analysis for photon-emitting brachytherapy sources: report ofAAPMTask Group No. 138 and GECESTRO." *Med. Phys.* 38:782–801, 2011.

The Radiation Therapy Process: Technology Uncertainty

Treatment Machine

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 k=1)

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The Radiation Therapy Process: Technology Uncertainty

Treatment Planning System

Radiotherapy and Oncology 84 (2007) 290–297
www.thegreenjournal.com

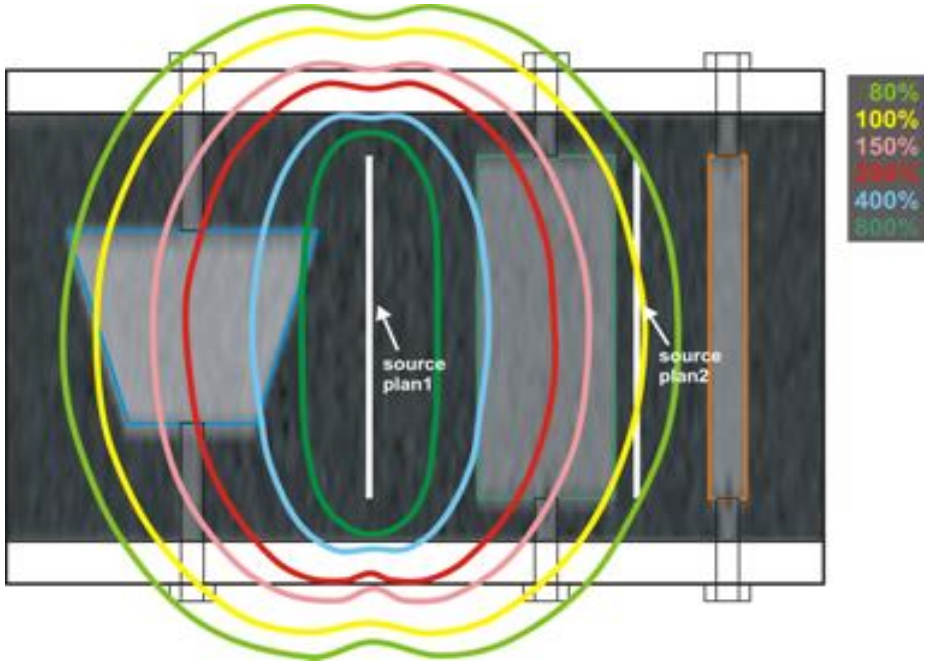
Brachytherapy

Accuracy of volume and DVH parameters determined with different brachytherapy treatment planning systems

Christian Kirisits[a,*], Frank-André Siebert[b], Dimos Baltas[c], Marisol De Brabandere[d], Taran Paulsen Hellebust[e], Daniel Berger[a], Jack Venselaar[f]

Table 2
Deviations of DVH parameters for the two different treatment plans and for the 4 mm slice thickness CT image set

	Inter-system variation	
	Large cylinder	Cone
Treatment plan 1		
$D_{0.1cc}$		
1 SD (%)	3	3
Maximum (%)	8	6
D_{1cc}		
1 SD (%)	1	5
Maximum (%)	2	11
D_{2cc}		
1 SD (%)	1	5
Maximum (%)	3	12



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Topics

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The Radiation Therapy Process: Human Uncertainty

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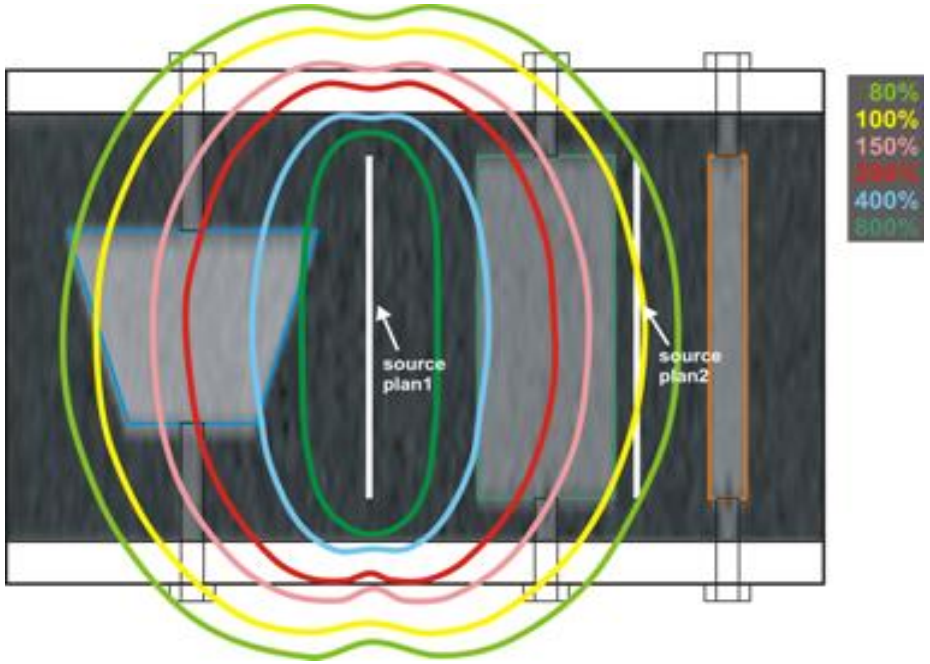
Table 2
Deviations of DVH parameters for the two different treatment plans and for the 4 mm slice thickness CT image set

	Inter-system variation		Inter-observer variation	
	Large cylinder	Cone	Large cylinder	Cone
Treatment plan 1				
$D_{0.1cc}$				
1 SD (%)	3	3	5	4
Maximum (%)	8	6	11	11
D_{1cc}				
1 SD (%)	1	5	1	2
Maximum (%)	2	11	1	5
D_{2cc}				
1 SD (%)	1	5	1	3
Maximum (%)	3	12	3	7



BRAPHYQS

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The Radiation Therapy Process: Human Uncertainty

Radiotherapy and Oncology 104 (2012) 192–198

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

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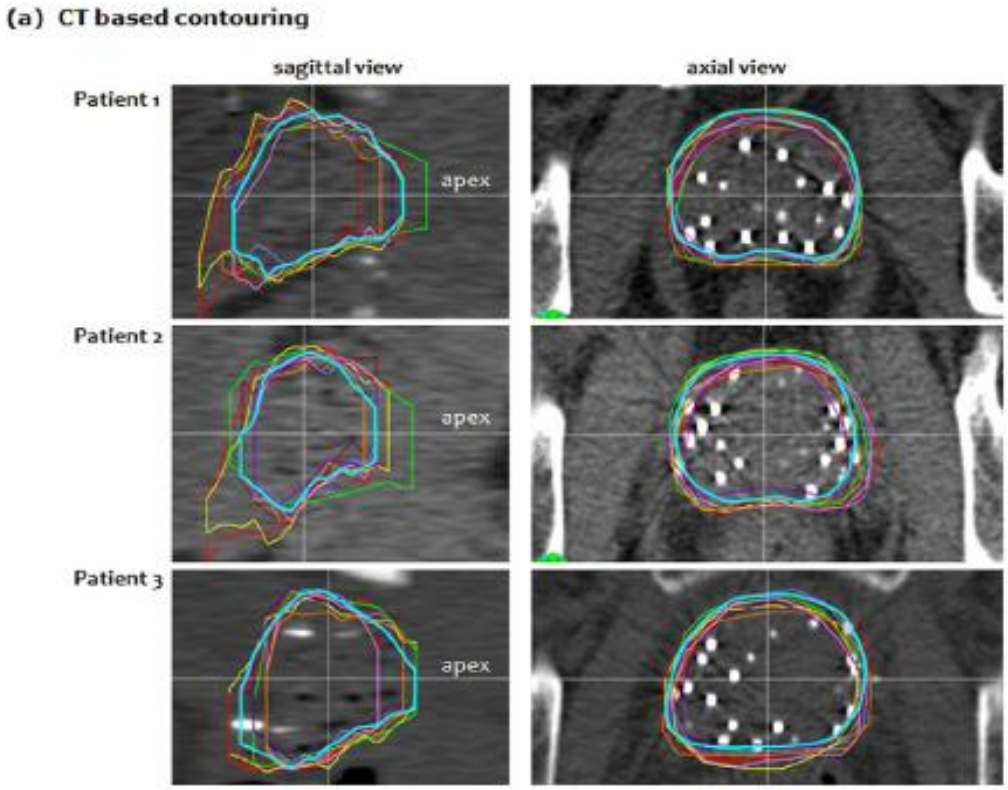
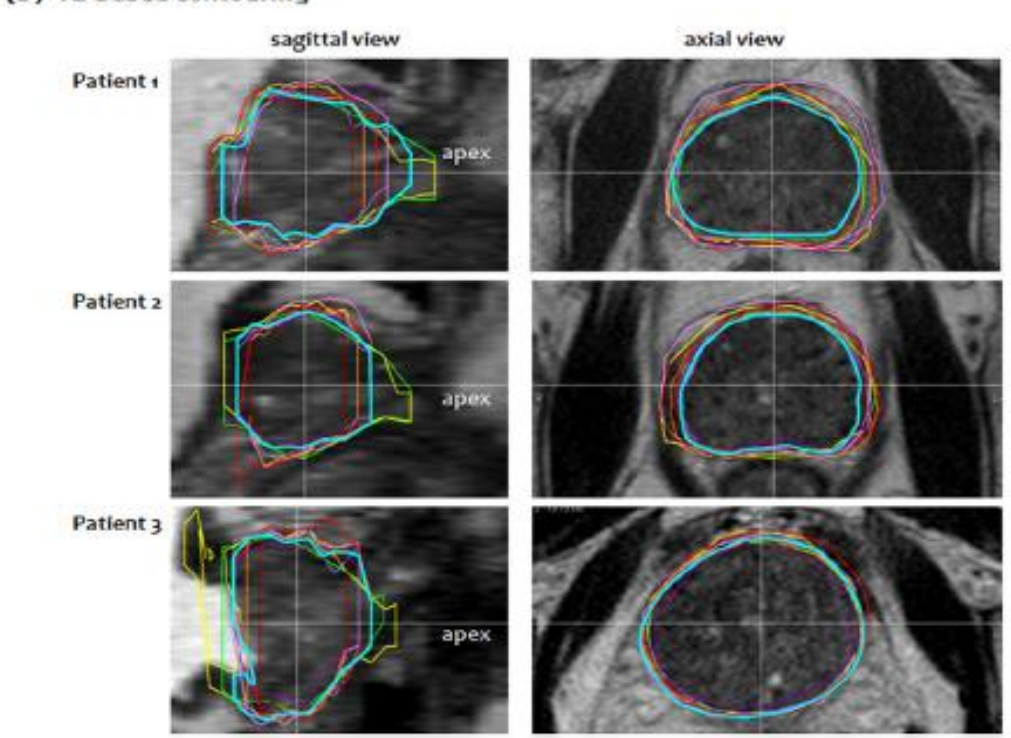
Prostate brachytherapy

Prostate post-implant dosimetry: Interobserver variability in seed localisation, contouring and fusion

Marisol De Brabandere [a,*], Peter Hoskin [b], Karin Haustermans [a], Frank Van den Heuvel [a], Frank-André Siebert [c]





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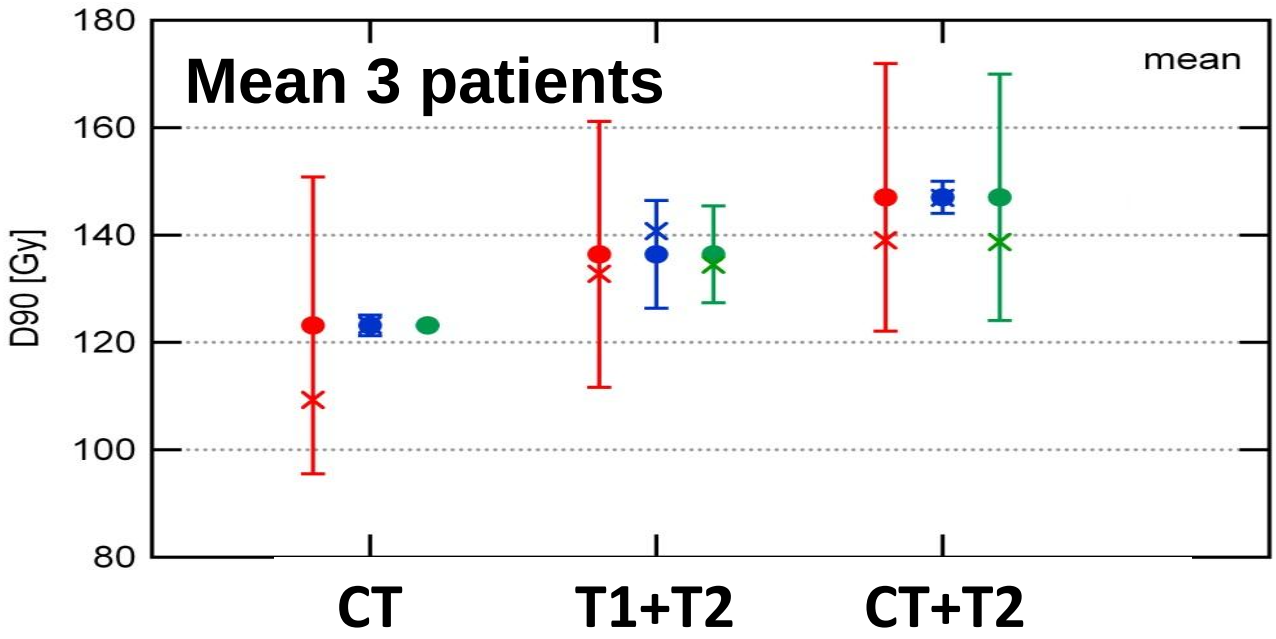
[a] University Hospital Gasthuisberg, Leuven, Belgium; [b] Mount Vernon Cancer Centre, Middlesex, UK; [c] University Hospital of Schleswig-Holstein, Kiel, Germany



Contouring
seeds
fusion

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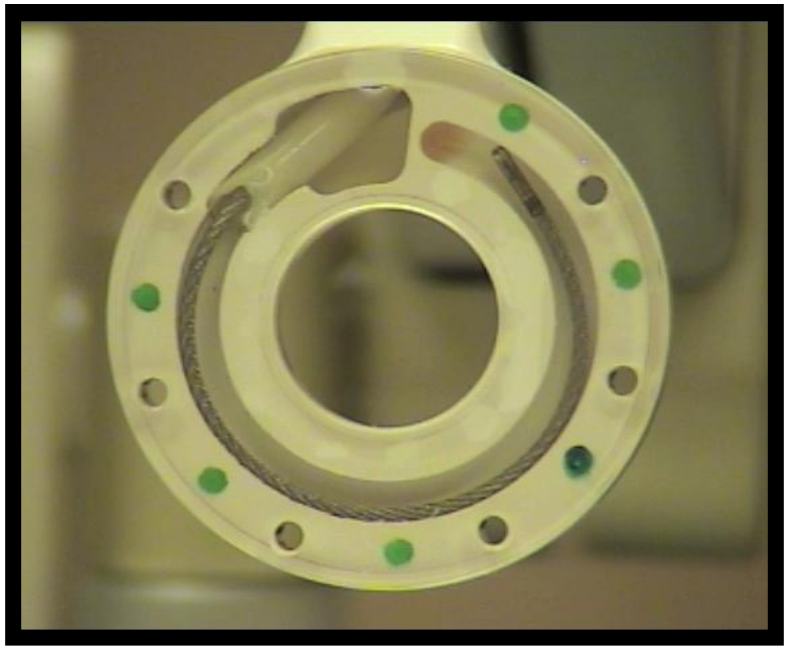
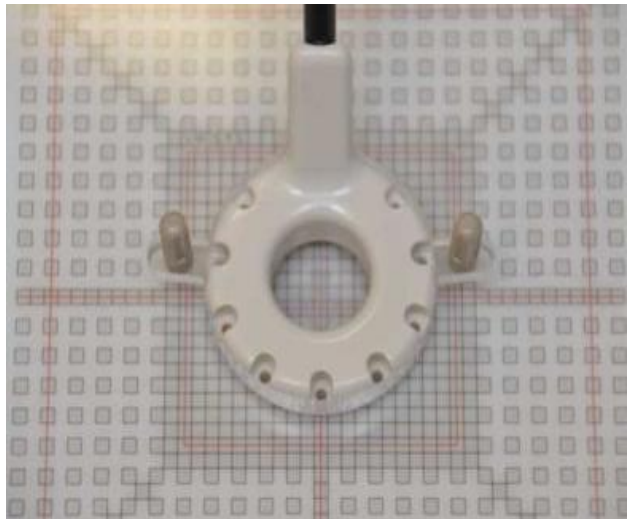
The Radiation Therapy Process: Human Uncertainty

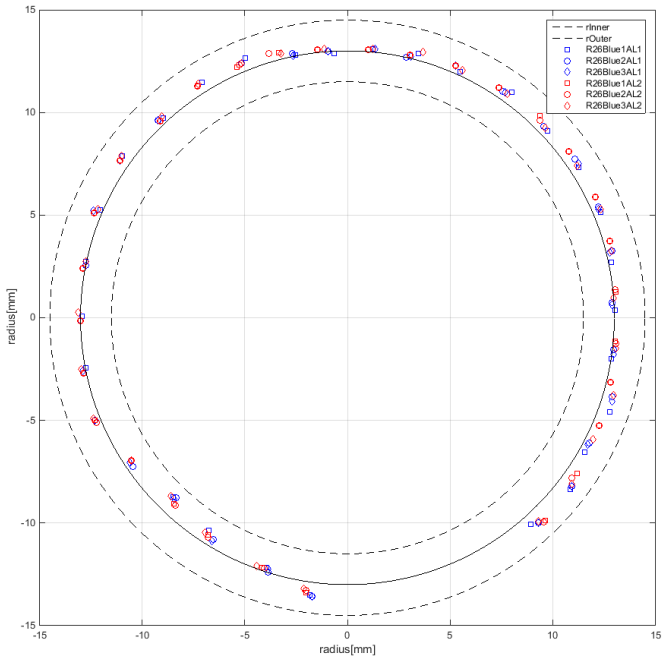
Measurement of the “real” source positions for the Vienna ring applicator

The Vienna “invasive” Method



The Freiburg “non-invasive” Method





2D time-resolved measurement with a high resolution ionisation chamber array (PTW-Freiburg SRS1000), M. Gainey, M. Kollefrath, D. Baltas et al., University of Freiburg, Germany

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The Radiation Therapy Process: Human Uncertainty

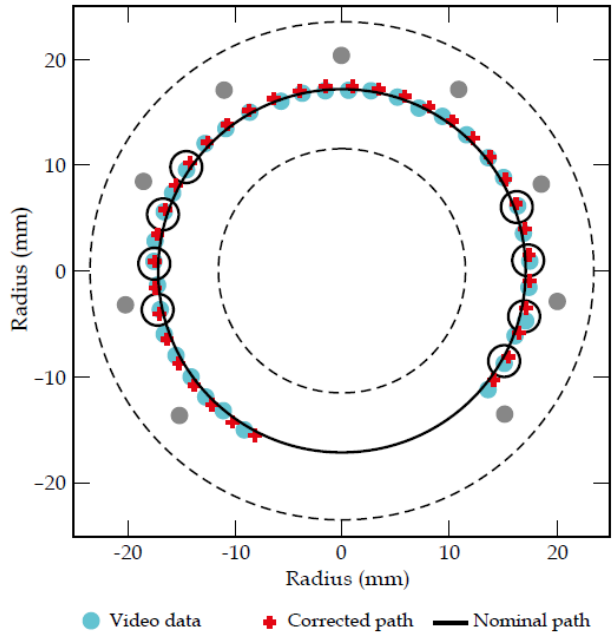

Table 3. Ranges for average deviations (mean ± 1σ) for D_{2cm^3} of organs at risk and D_{90} of targets caused by rotation of the loading pattern by one or two dwell positions in clockwise (+) or counter clockwise (–) direction

Rotation	–5.0 mm	–2.5 mm	+2.5 mm	+5.0 mm
D_{2cm^3} bladder	(+0.65 ± 5.25) %	(+0.15 ± 2.65) %	(+1.30 ± 1.90) %	(+3.15 ± 3.55) %
D_{2cm^3} rectum	(–1.80 ± 6.00) %	(–1.65 ± 2.95) %	(+2.55 ± 2.65) %	(+6.65 ± 5.05) %
D_{2cm^3} sigmoid	(–0.05 ± 3.55) %	(–0.35 ± 1.95) %	(–0.20 ± 2.30) %	(+0.05 ± 4.15) %
D_{90} CTV_{HR}	(+0.35 ± 2.65) %	(+0.35 ± 1.55) %	(–0.45 ± 1.25) %	(–1.20 ± 2.90) %
D_{90} GTV	(+0.30 ± 3.20) %	(+0.25 ± 1.65) %	(–0.40 ± 1.70) %	(–1.10 ± 3.50) %

Improved source path localisation in ring applicators and the clinical impact for gynaecological brachytherapy. I. Humer, C. Kirisits et al., al., Journal of Contemporary Brachytherapy (2015/volume 7/number 2).

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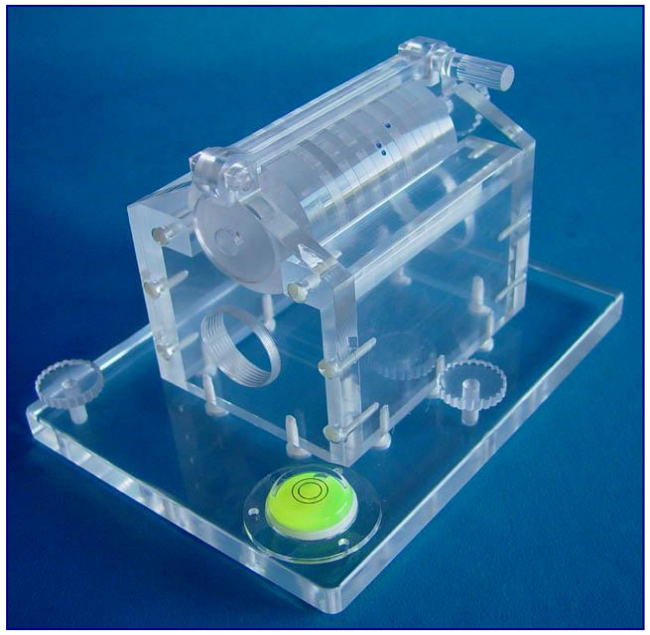

Accuracy of source/seeds localisation

CT phantom (solid)

Siebert et al. R&O 2007

- reconstruction uncertainty (1 SD)
  - < **1.4 mm** for 4-5 mm scans
  - < **1.0 mm** for 2-3 mm scans

MRI / CT phantom (agarose gel)

De Brabandere et al. R&O 2006

- uncertainties for MRI slightly larger than for CT
- reconstruction uncertainty
  - < **2 mm** for 3-5 mm scans

See also DeBrabandere et al. Brachyther 2013

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BRACHYTHERAPY

Brachytherapy 11 (2012) 111–118

Dosimetric effect of interfractional needle displacement in prostate high-dose-rate brachytherapy

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ABSTRACT

PURPOSE: To quantify the dosimetric deviations that would arise from delivering subsequent prostate high-dose-rate fractions with only needle readjustment and no replanning after the first fraction.

METHODS AND MATERIALS: Patients were treated with either two implant sessions (two 9.5-Gy fractions per session) separated by 2–4 weeks or with one implant session and external beam radiotherapy. After needle placement, needle positions were adjusted under CT guidance, after which dosimetric planning was performed before each fraction. To evaluate the consequence of not replanning before the second fraction, we analyzed the dosimetric parameters of 45 consecutive implants (26 patients). Needles with optimized dwell positions from the first fraction were transferred to the needle positions in the second fraction. Needle displacement between fractions was assessed as well as changes in plan metrics.

RESULTS: After adjustment, the mean interfractional needle displacement was 3.5 mm. If replanned, the probability of planning target volume $D_{90\%}$ ≥95% is 100%, prostate $V_{100\%}$ ≥95% is 87%, and urethra V_{115}% ≤10% is 78%. If treated without replanning, the probability of planning target volume $D_{90\%}$ ≥95% is 82%, prostate $V_{100\%}$ ≥95% is 53%, and urethra $V_{115\%}$ ≤10% is 69%. Even for implants with minimal needle displacement (<3 mm) and minimal prostate volume change (<3 cc), the dosimetric consequence of not replanning the second fraction would result in 46% of cases with a prostate $V_{100\%}$ <95%.

CONCLUSION: The dosimetric consequences of not replanning the second fraction for prostate high-dose-rate implants results in significantly inferior plan metrics. © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Prostate; HDR brachytherapy; Needle displacement; Dosimetry

Table 3

Mean needle and prostate base displacement evaluated based on the planning CT images (slice thickness of 1.25 mm) for Fraction 2 relative to Fraction 1 after adjustment of catheters

Landmark	Mean needle displacement	Prostate base displacement
Pubic symphysis	−1.4 to 1.3 cm (0.35 cm)	−1.7 to 1.0 cm (0.36 cm)
Center of markers	−1.8 to 0.9 cm (0.23 cm)	−1.8 to 0.8 cm (0.23 cm)

Negative values indicate displacement in caudal direction, whereas positive values indicate displacement in cranial direction. Number in parenthesis is the mean of absolute displacement values.

Table 5

Probability of obtaining optimal dosimetric parameters for prostate HDR treatment

	PTV $D_{90\%}$ ≥95%	Prostate $V_{100\%}$ ≥95%	Urethra $V_{115\%}$ ≤10%
With replanning	100%	87%[a]	78%
Without replanning	82%	53%[b]	69%

HDR = high dose rate; PTV = planning target volume.

[a] Prostate $V_{100\%}$ ≥92% = 98%.

[b] Prostate $V_{100\%}$ ≥92% = 71%.

CT-based

Use of reference:

- **bony structures**
- **Implanted markers**

RESULTS: After adjustment, the mean interfractional needle displacement was 3.5 mm. If replanned, the probability of planning target volume $D_{90\%}$ ≥95% is 100%, prostate $V_{100\%}$ ≥95% is 87%, and urethra V_{115}% ≤10% is 78%. If treated without replanning, the probability of planning target volume $D_{90\%}$ ≥95% is 82%, prostate $V_{100\%}$ ≥95% is 53%, and urethra $V_{115\%}$ ≤10% is 69%. Even for implants with minimal needle displacement (<3 mm) and minimal prostate volume change (<3 cc), the dosimetric consequence of not replanning the second fraction would result in 46% of cases with a prostate $V_{100\%}$ <95%.

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The Radiation Therapy Process: Human Uncertainty

Radiotherapy and Oncology 93 (2009) 253–258

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Prostate cancer brachytherapy

Justification for inter-fraction correction of catheter movement in fractionated high dose-rate brachytherapy treatment of prostate cancer

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ARTICLE INFO

Article history:
Received 23 December 2008
Received in revised form 5 June 2009
Accepted 19 September 2009

Keywords:
Catheter movement
Prostate
HDR brachytherapy

ABSTRACT

Background and purpose: Fractionated high dose rate (HDR) brachytherapy in the treatment of prostate cancer relies on reproducible catheter positions for each fraction to ensure adequate tumour coverage while minimising dose to normal tissues. Peri prostatic oedema may cause caudal displacement of the catheters relative to the prostate gland between fractions. This can be corrected for by changing source dwell positions or by physical re advancement of catheters before treatment.

Materials and methods: Data for 20 consecutive monotherapy patients receiving three HDR fractions of 10.5 Gy per fraction over 2 days were analysed retrospectively. Pre treatment CT scans were used to assess the effect of catheter movement between fractions on implant quality, with and without move ment correction. Implant quality was evaluated using dosimetric parameters.

Results: Compared to the first fraction (f1) the mean inter fraction caudal movement relative to the pros tate base was 7.9 mm (f2) (range 0 21 mm) and 3.9 mm (f3) (range 0 25.5 mm). PTV D90% was reduced without movement correction by a mean of 27.8% (f2) and 32.3% (f3), compared with 5.3% and 5.1%, respectively, with catheter movement correction. Dose to 2 cc of the rectum increased by a mean of 0.69 (f2) and 0.76 Gy (f3) compared with an increase of 0.03 and 0.04 Gy, respectively, with correction. The urethra V12 also increased by a mean of 0.36 (f2) and 0.39 Gy (f3) compared with 0.06 and 0.16 Gy, respectively, with correction.

Conclusions: Inter fraction correction for catheter movement using pre treatment imaging is critical to maintain the quality of an implant. Without movement correction there is significant risk of tumour under dosage and normal tissue over dosage. The findings of this study justify additional imaging between fractions in order to carry out correcti

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Mean shift:

- **f2-f1 = 7.9 mm**
- **f3-f1 = 3.9 mm**

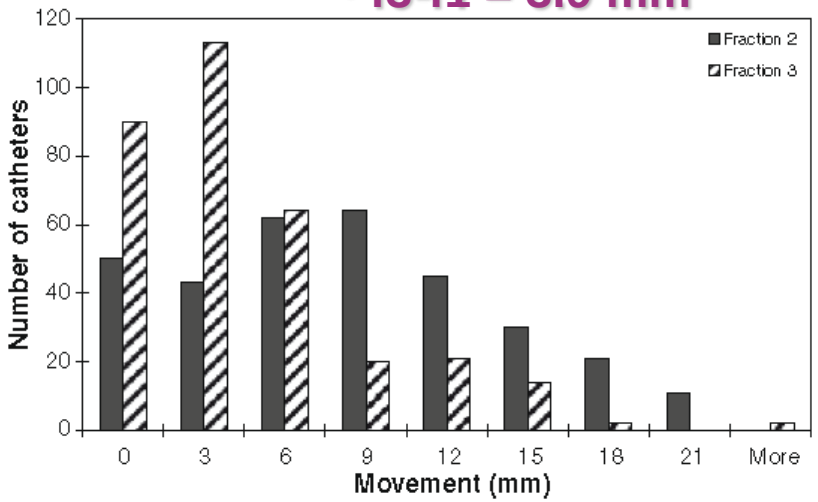

Fig. 1. Frequency histograms displaying the caudal movement in mm of each catheter at fractions 2 and 3 (326 in total).

Multi-fractions delivery with a single implant

Table 2
Mean change in DVH and COIN parameters for all patients relative to fraction 1, values ± standard deviation. Negative values indicate a lower value than that achieved for fraction 1.

Dosimetric parameter		Fraction 2			Fraction 3		
		With correction	Without correction	*P*-value	With correction	Without correction	*P*-value
CTV V100%	(%)	−3.48 ± 4.7	−12.61 ± 9.6	0.000	−4.76 ± 7.4	−15.17 ± 11.7	0.001
PTV	V100% (%)	−4.05 ± 5.1	−13.07 ± 9.2	0.000	−5.33 ± 7.8	−15.40 ± 11.7	0.001
	D90% (%)	−5.32 ± 6.6	−27.7 ± 22.8	0.000	−5.09 ± 8.3	−32.34 ± 24.6	0.000
Rectum	D2cc (Gy)	0.03 ± 0.7	0.69 ± 0.9	0.000	0.04 ± 0.9	0.76 ± 1.1	0.000
	V10Gy (cc)	0.14 ± 0.4	0.46 ± 0.8	0.001	0.22 ± 0.5	0.70 ± 1.0	0.001
Urethra	V12Gy (cc)	0.06 ± 0.2	0.36 ± 0.5	0.002	0.16 ± 0.4	0.39 ± 0.4	0.003
	D30% (Gy)	−0.35 ± 0.4	0.12 ± 0.7	0.000	−0.27 ± 0.6	0.27 ± 0.9	0.000
COIN index		−0.05 ± 0.1	−0.16 ± 0.1	0.000	−0.05 ± 0.1	−0.17 ± 0.1	0.000

Analysis performed using the Wilcoxon signed rank test in SPSS (v16.0 for Windows). *P*-values < 0.05 were considered significant at the 95% confidence level.

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Table 3
Summary of the current relevant literature documenting catheter migration in HDR brachytherapy treatment of prostate cancer.

Author	Kim (2007)	Damore (2000)	Mullokandov (2004)	Martinez (2001)	Hoskin (2002)
No. of patients	10	96	50 (groups of 12–17 analysed)	10 analysed	20
No. fractions over time	Two fractions over 24 h	Four fractions over 40 h	Four fractions over 24–28 h	Four fractions over 48 h	Two fractions over 24–28 h
Imaging method	CT scans	X-ray films	CT scans (2 mm)	X ray films	CT scans (3 mm)
Measurements relative to	Bony and gold seed markers	Bony and gold seed markers	Bony markers and tip at first fraction	Bony markers, gold seeds and bladder base	Tip at first fraction
Dosimetric analysis?	No	No	Yes	Yes	Yes

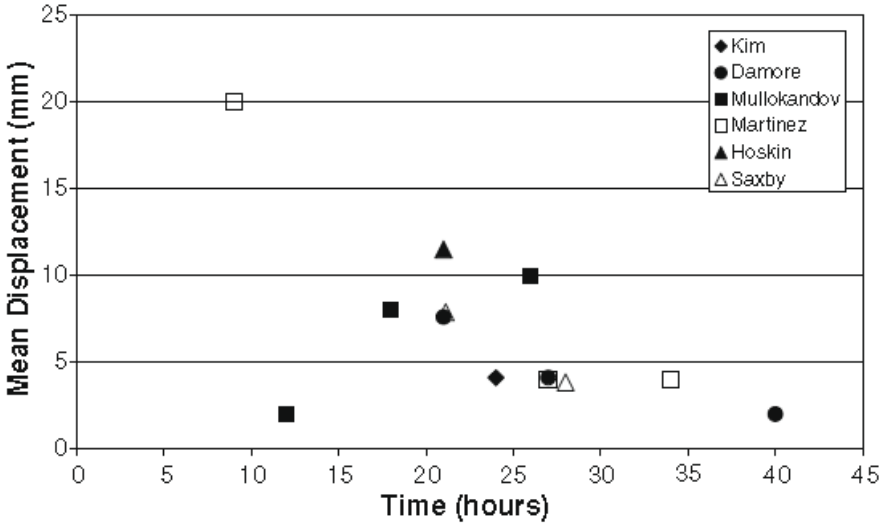

Fig. 4. Graphical interpretation of results in current literature documenting mean caudal catheter migration for prostate HDR brachytherapy. Time is in approximate hours since implant, with two exceptions: Martinez and this study (Saxby) show time in hours since obtaining fraction 1 images and are shown as non-solid symbols.

Multi-fractions delivery with a single implant

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The Radiation Therapy Process: Human Uncertainty

Radiotherapy and Oncology 101 (2011) 490–494

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Prostate cancer brachytherapy

Prostate HDR brachytherapy catheter displacement between planning and treatment delivery

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ARTICLE INFO

Article history:
Received 27 October 2010
Received in revised form 3 August 2011
Accepted 5 August 2011
Available online 31 August 2011

Keywords:
HDR prostate brachytherapy
Catheter displacement
Movement

ABSTRACT

Background and purpose: HDR brachytherapy is used as a conformal boost for treating prostate cancer. Given the large doses delivered, it is critical that the volume treated matches that planned. Our outpatient protocol comprises two 9 Gy fractions, two weeks apart. We prospectively assessed catheter displacement between CT planning and treatment delivery.

Materials and methods: Three fiducial markers and the catheters were implanted under transrectal ultrasound guidance. Metal marker wires were inserted into 4 reference catheters before CT; marker positions relative to each other and to the marker wires were measured from the CT scout. Measurements were repeated immediately prior to treatment delivery using pelvic X ray with marker wires in the same reference catheters. Measurements from CT scout and film were compared. For displacements of 5 mm or more, indexer positions were adjusted prior to treatment delivery.

Results: Results are based on 48 implants, in 25 patients. Median time from planning CT to treatment delivery was 254 min (range 81–367 min). Median catheter displacement was 7.5 mm (range 2.9–23.9 mm), 67% of implants had displacement of 5 mm or greater. Displacements were predominantly caudal.

Conclusions: Catheter displacement can occur in the 1–3 h between the planning CT scan and treatment. It is recommended that departments performing HDR prostate brachytherapy verify catheter positions immediately prior to treatment delivery.

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Table 2
Occurrence of displacement magnitude.

Magnitude (mm)	Number of implants
−3 to −0.1	3
0 to 4.9	13
5 to 9.9	18
10 to 14.9	9
>15	5

The frequency of occurrence for each group of displacement magnitude is shown here. The number of implants refers to the frequency of occurrence.

Median shift:
- **7.5 mm [2.9 , 23.9]**

Median Δt between CT & delivery
- **254 min [81 , 367]**

!

Conclusions: Catheter displacement can occur in the 1–3 h between the planning CT scan and treatment. It is recommended that departments performing HDR prostate brachytherapy verify catheter positions immediately prior to treatment delivery.

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Topics

- Definition of Uncertainty
- Accuray and Precision
- Types of Uncertainty
- Categories of Uncertainty
- Technology Related Uncertainties
- Human Related Uncertainties
- Summary

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Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and AAPM

Radiotherapy and Oncology xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and the AAPM ☆

Christian Kirisits [a,*], Mark J. Rivard [b], Dimos Baltas [c], Facundo Ballester [d], Marisol De Brabandere [e], Rob van der Laarse [f], Yury Niatsetski [g], Panagiotis Papagiannis [h], Taran Paulsen Hellebust [i,j], Jose Perez-Calatayud [k], Kari Tanderup [l], Jack L.M. Venselaar [m], Frank-André Siebert [n]

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ARTICLE INFO

Article history:
Received 20 August 2013
Received in revised form 30 October 2013
Accepted 4 November 2013
Available online xxxx

Keywords:
Brachytherapy
Dosimetry
Uncertainties
Treatment planning

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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BRAPHYQS

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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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Difference on uncertainty per fraction to uncertainty for total dose

For normal distributions the number of subsequent fractions (observations) results in compensation of variations

$1 / \sqrt{N}$

including constant EBRT results in

1 / 2

So 13% per fraction can be 3.5% for total dose

By courtesy of Prof. Christian Kirisits, Medical University of Vienna

Difference on uncertainty per fraction to uncertainty for total dose

Intracavitary Cervical BRT

For 4x Fractions multiply by 1 / √N

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 → **2%**	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 → **6%**	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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The Radiation Therapy Process: Summary

- **Errors**
  - Mainly resulting in systematic deviations
    - Wrong source strength in afterloader unit
    - Wrong offset for applicator tip to first dwell position
    - Wrong catheter connections, etc…

The Radiation Therapy Process: Summary

- **Uncertainties**
  - Type A (statistical)
  - Type B (everything else)

Analyze and present systematic effects
(target volume shrinkage, edema causing applicator shifts)

Analyze and present normal distributed effects
(random catheter shifts, reconstruction with finite slice thickness)

By courtesy of Prof. Christian Kirisits, Medical University of Vienna

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The Radiation Therapy Process: Summary

- **Variations**
  - Known effects which can be predicted.
    - E.g. bladder filling can have an impact on dose to bladder or bowel
    - Prostate swelling influences the D_{90} – if the variations over time are known the delivered dose can be predicted

Table 11.22

Test frequencies and action levels for various brachytherapy procedures. HDR = high dose rate, PDR = pulsed dose rate, LDR = low dose rate, MDR = medium dose rate. (Adapted from [207].)

DESCRIPTION	MINIMUM REQUIREMENTS	
	TEST FREQUENCY	ACTION LEVEL
HDR/PDR		
Source calibration	Source exchange	5%
Source position	Daily/quarterly	2 mm
Length of treatment tubes	Annually	1 mm
Irradiation timer	Annually	1%
Date, time, source strength	Daily	-
Transit time effect	Annually	-
LDR/MDR		
Source calibration, mean of batch	Source exchange	3%
Source calibration, individual source, decay	Source exchange	5%
Linear uniformity	Source exchange	5%
Source position, source length	Half yearly	2 mm
Irradiation timer	Annually	2%
Date, time, source strength in treatment unit	Daily	-
Manual Afterloading		
Source calibration, decay calculation	Source exchange	5%
Linear uniformity, source length	Source exchange	5%
Source identification	Daily/annually	—

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Head and Neck BT
Results ,Hazards, Complications

Erik Van Limbergen

Dep of Radiation Oncology

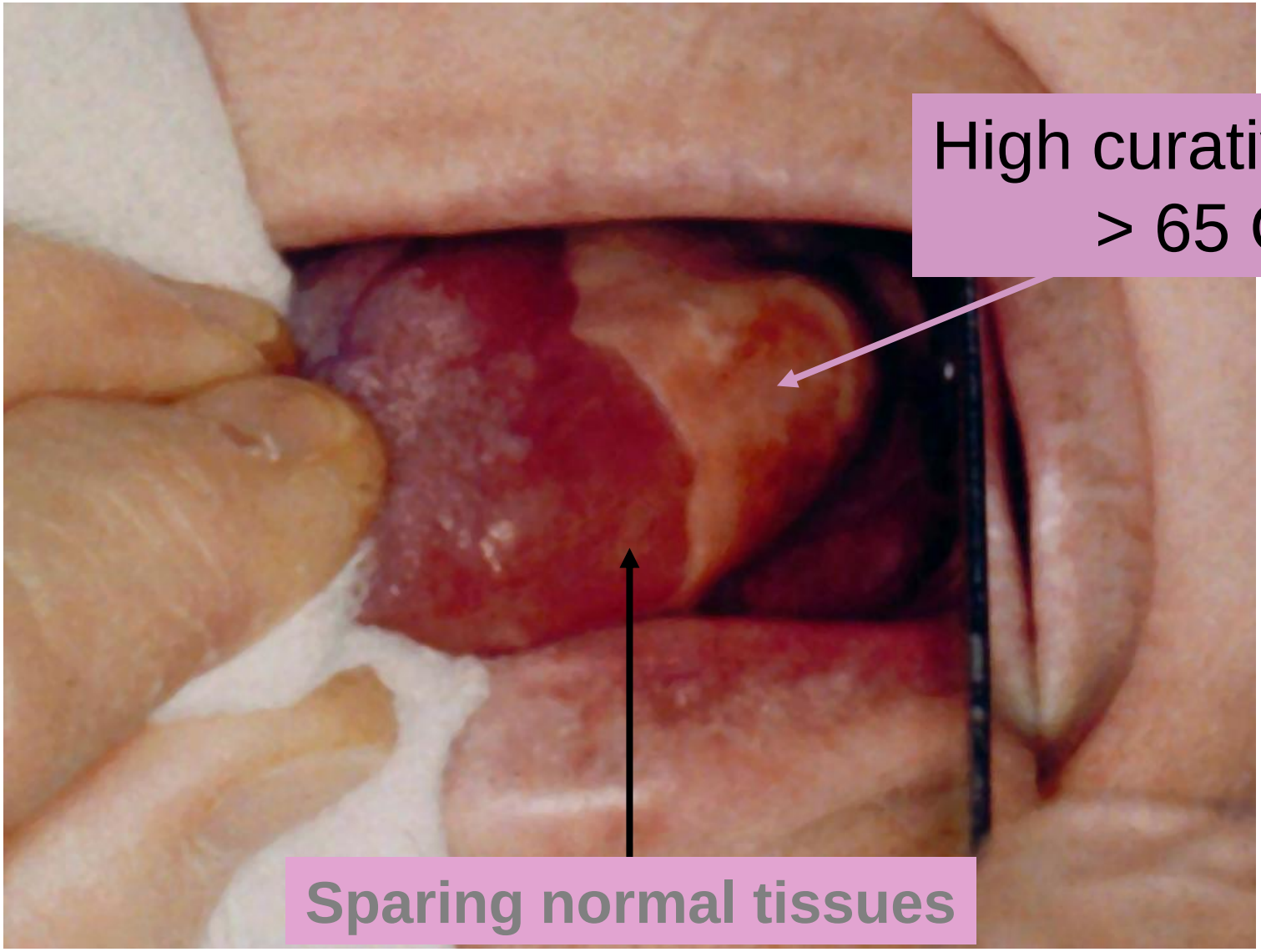
University Hospital Gasthuisberg

Leuven, Belgium

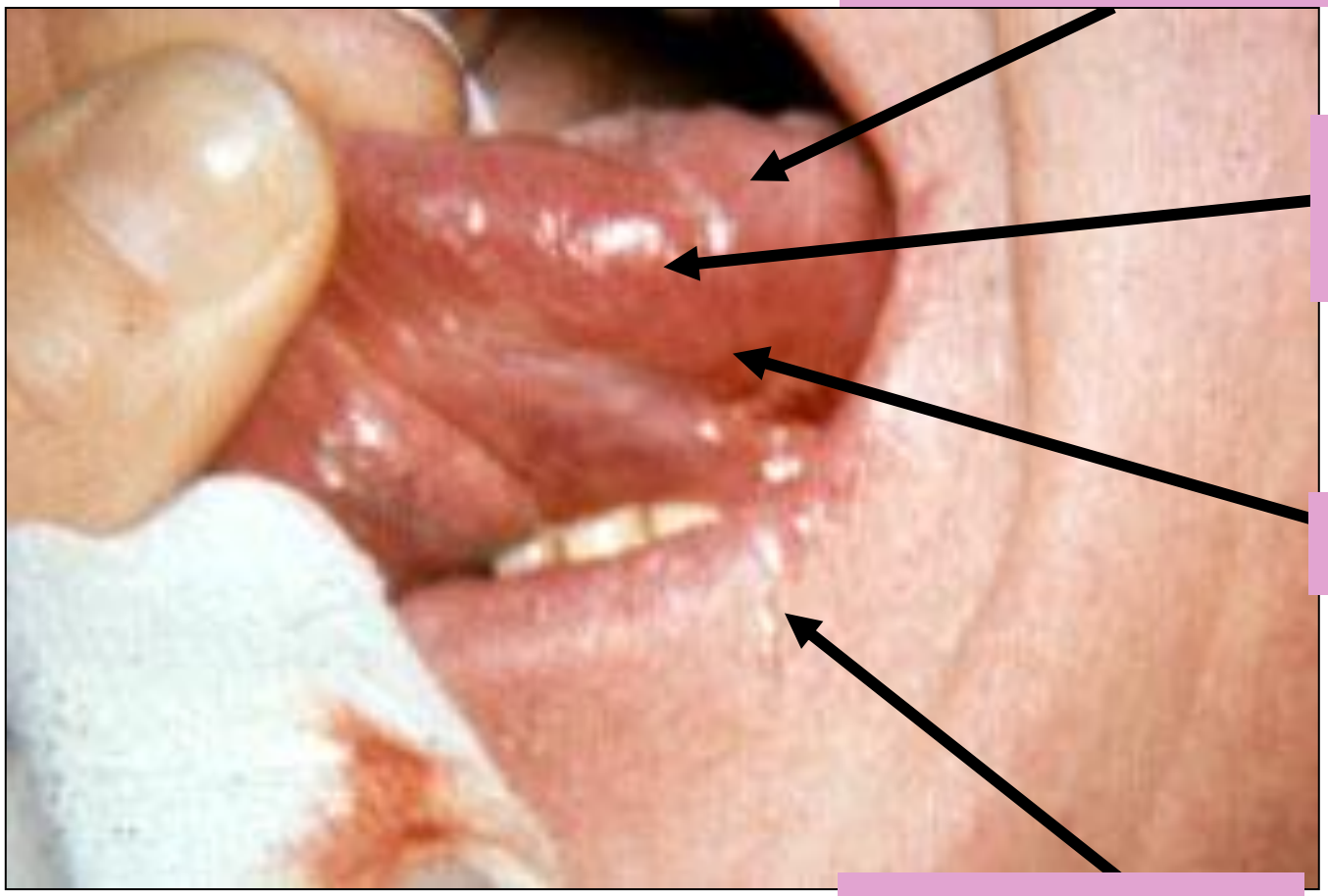
LDR (< 1 Gy/h)
« classical golden standard »

- Pro:
  - Radiobiology LDR is more forgiving in H&N
  - Clinical data
    - Long follow up+++
- Contra
  - Technical expertise needed
  - No SS dwell time optimizaion

MUCOSITIS (3-6 Weeks)



Healing after 2 Months



Factors influencing local control

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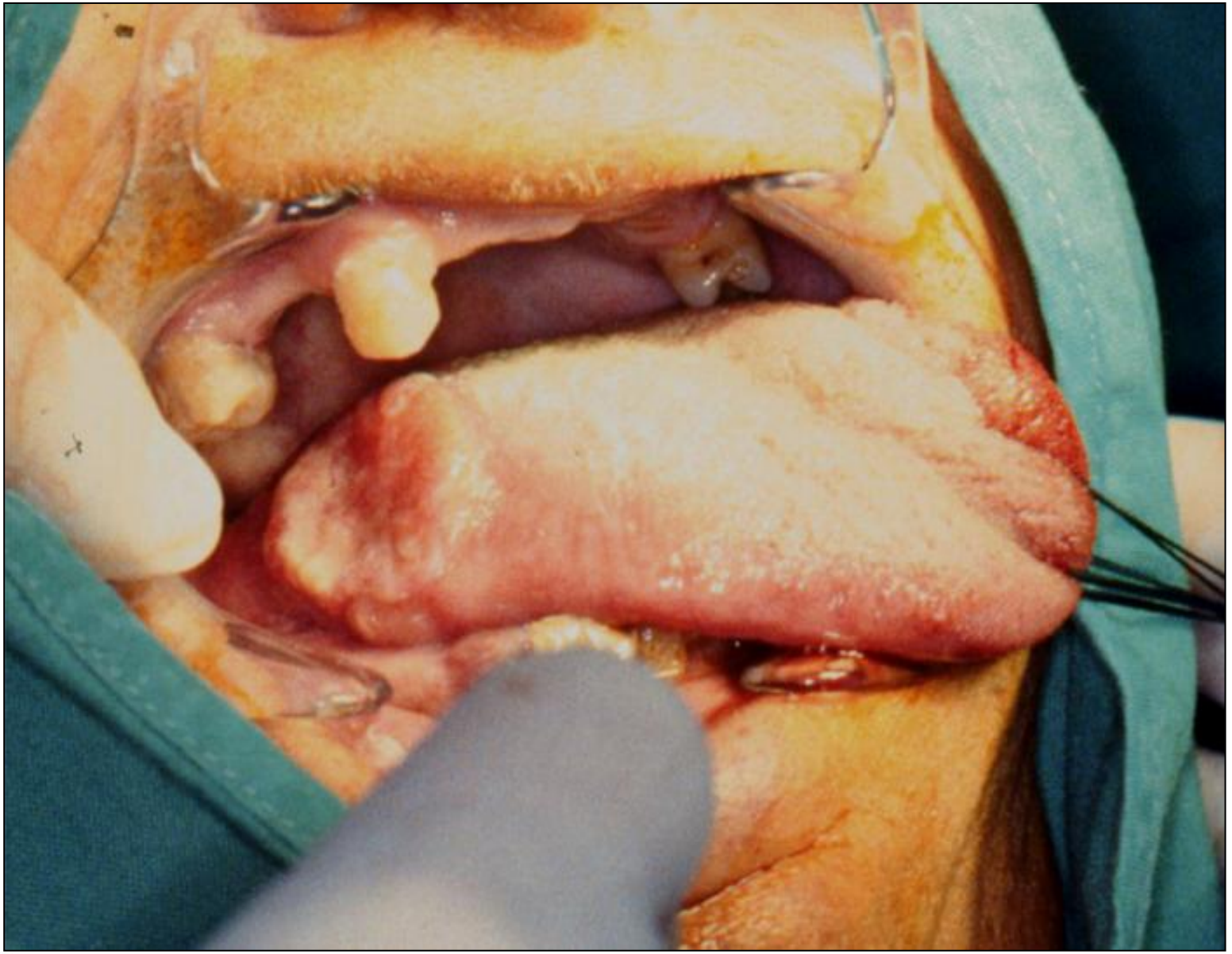
Mobile Tongue Tumors



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**	**87%**		62%
		EBI + BT	**49%**	8%	30%
Mazeron	121	**BT** 55-60 Gy	**73%**	T2 N0 7%	
		BT 65-75 Gy	**92%**		
Wendt	103	**BT**	**65%**	0	89%
		BT+ EBI <40 Gy	**92%**	4%	78%
		BT+ EBI >40 Gy	**69%**	17%	71%
		EBI	**28%**	0	57%
Nareyama	130	BT	**86%**		
		EBI + BT			
Shibuya	370	**BT**	**75%**	4%	
		BT + EBI	**48%**		
Lefebvre	283	**BT**	**83%**	6%	NP
Pernot	448	BT		9%	
		EBI + BT	**68%**	(3 % grade 3)	44%
Matsura	173	**BT**	**84 - 95%**		69 - 84%
		EBI + BT	**74 - 80%**		
		2500 Patients	65-95%		

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

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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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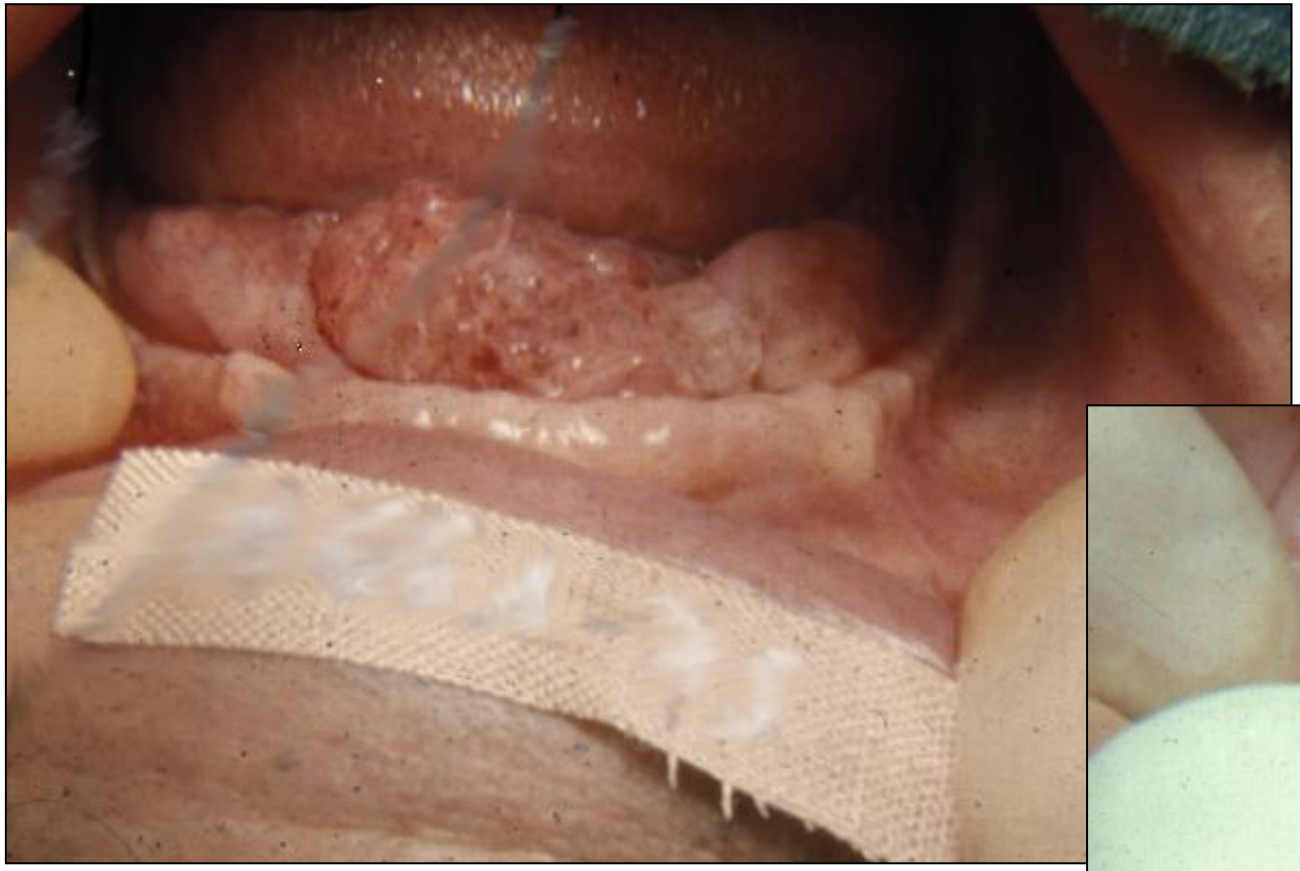
Floor of Mouth



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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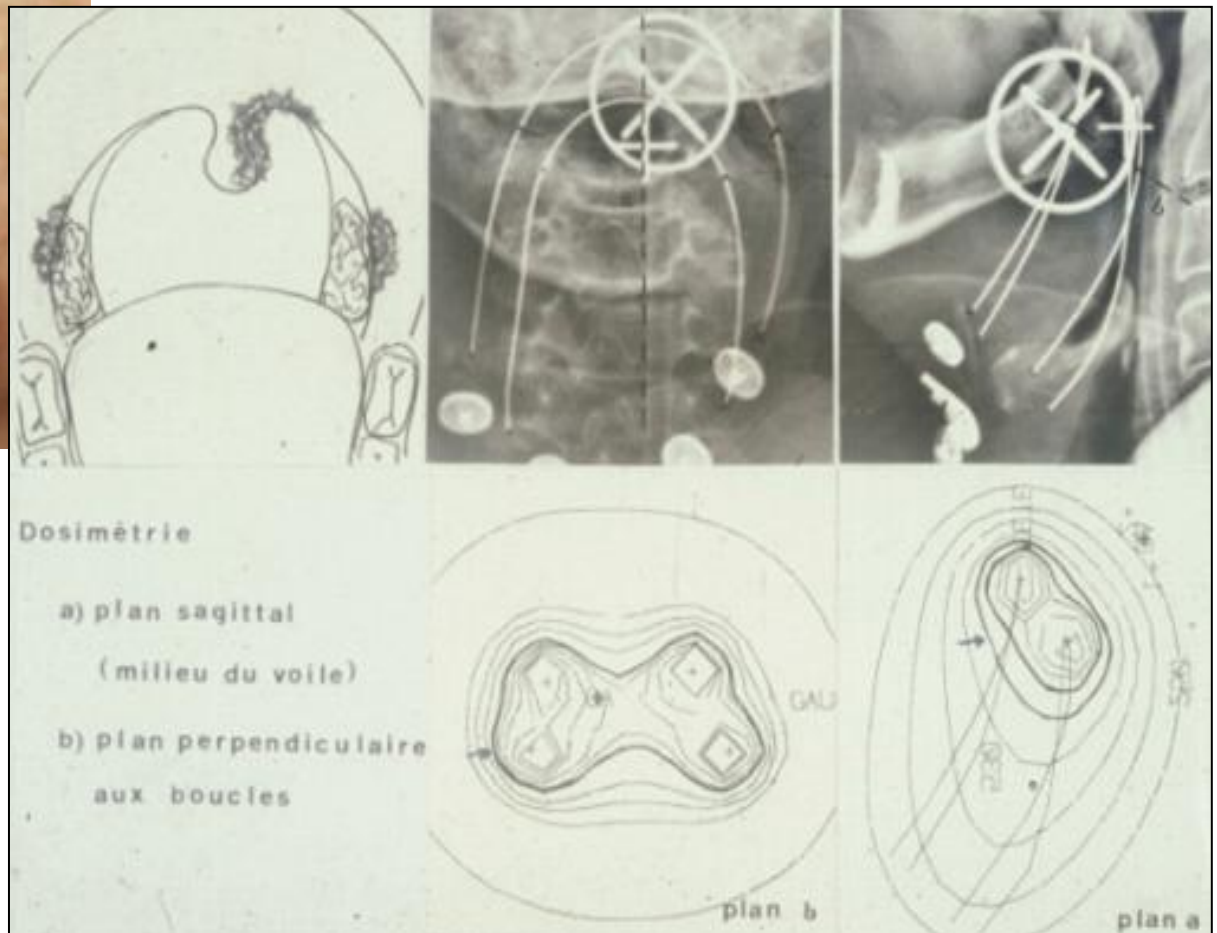
Velotonsillar Arch



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: 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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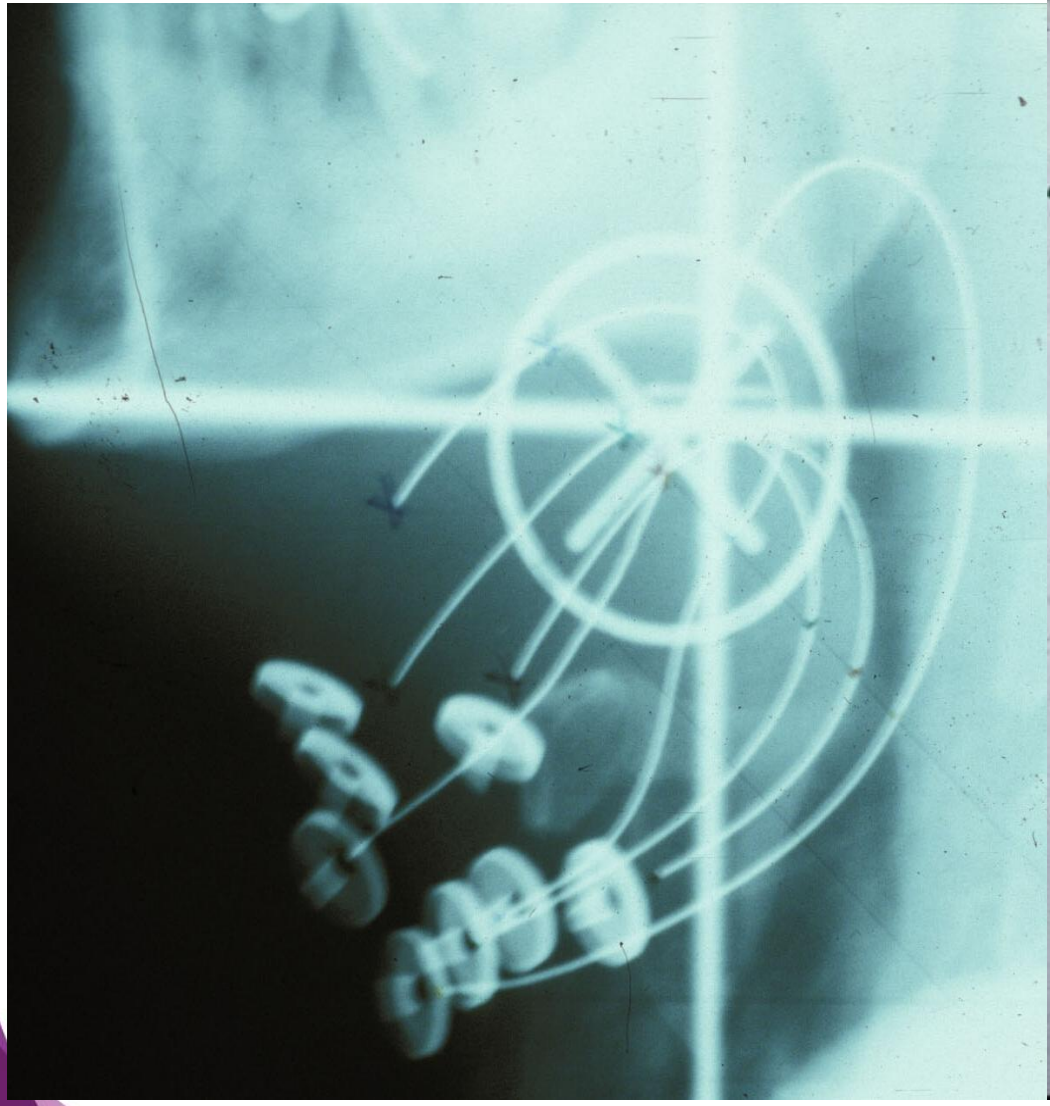
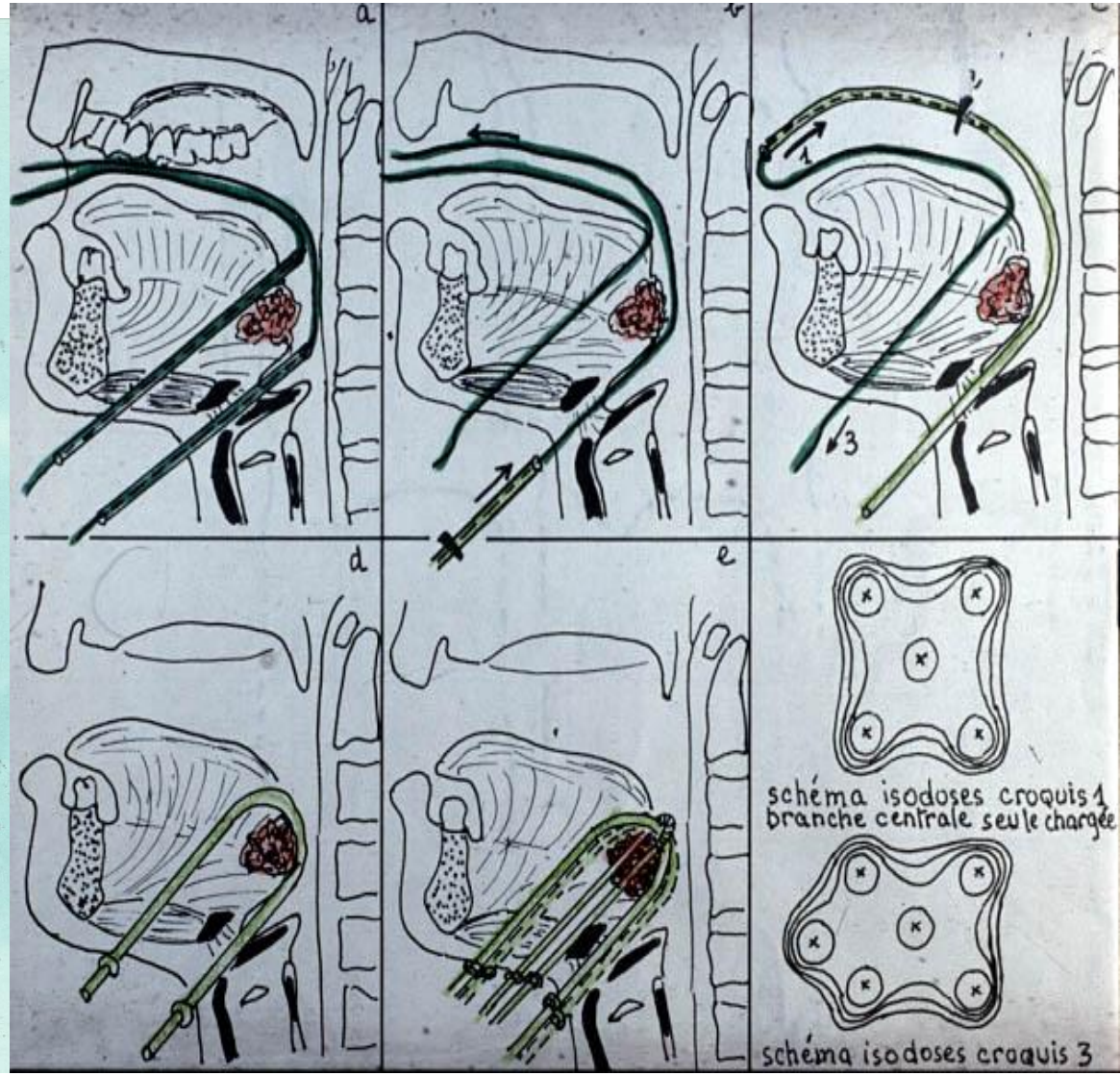
Base of tongue





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%

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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Factors influencing late complications

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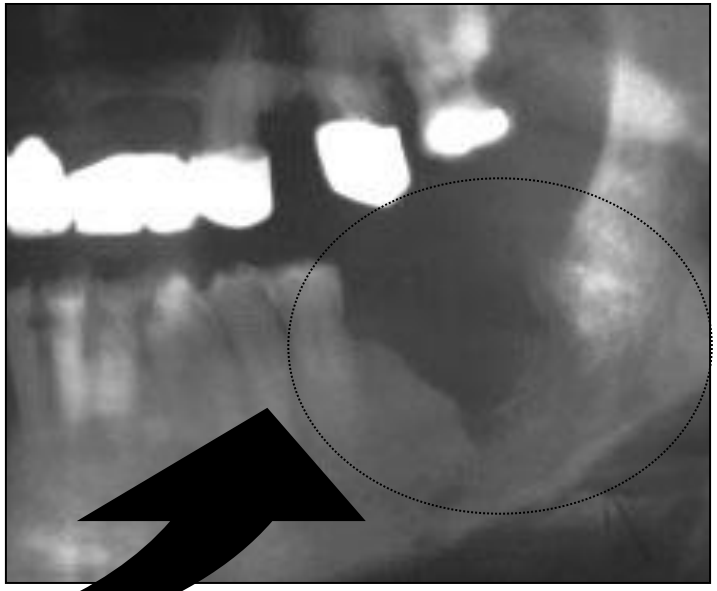
Late complications

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%

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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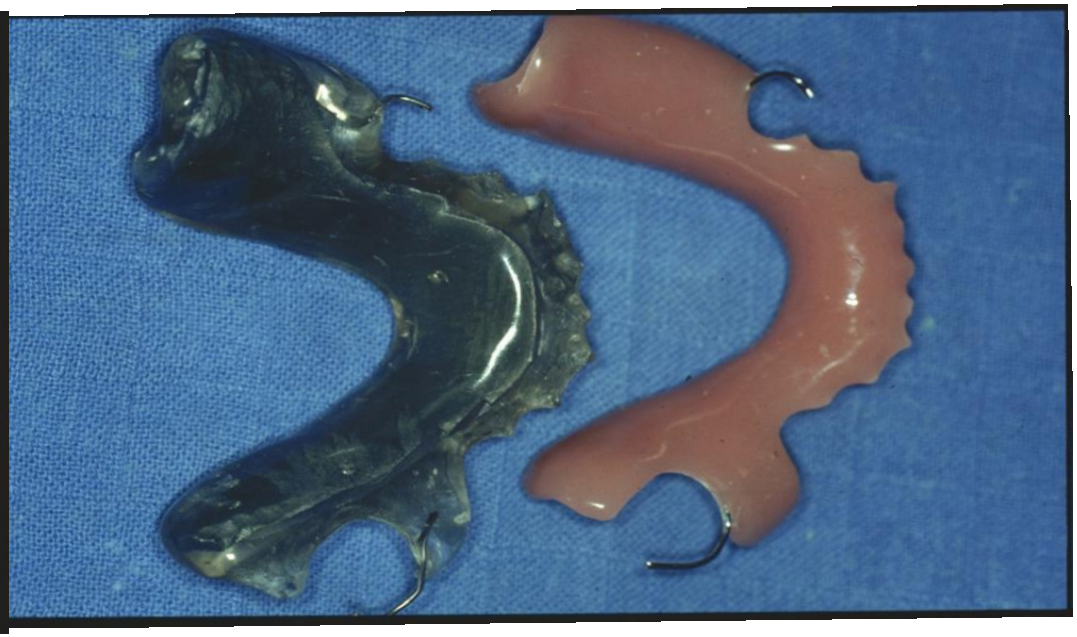
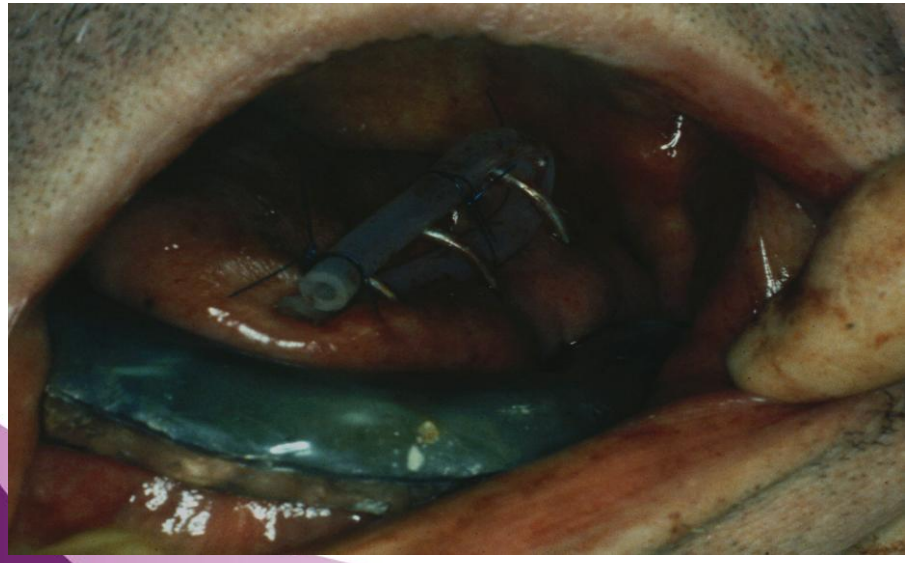
Lead shielding

- Tailored for each patient





Prophylaxis

- General measures
  - Alcohol / Tobacco abstinence
  - Balanced diet
  - Mouth wash
- Dental Care
  - Pre implantation tooth extraction:
    - Suture of the gum
    - 2-week delay for healing
- Mandibular Lead protectors
  - 50 % decrease of the dose to the bone

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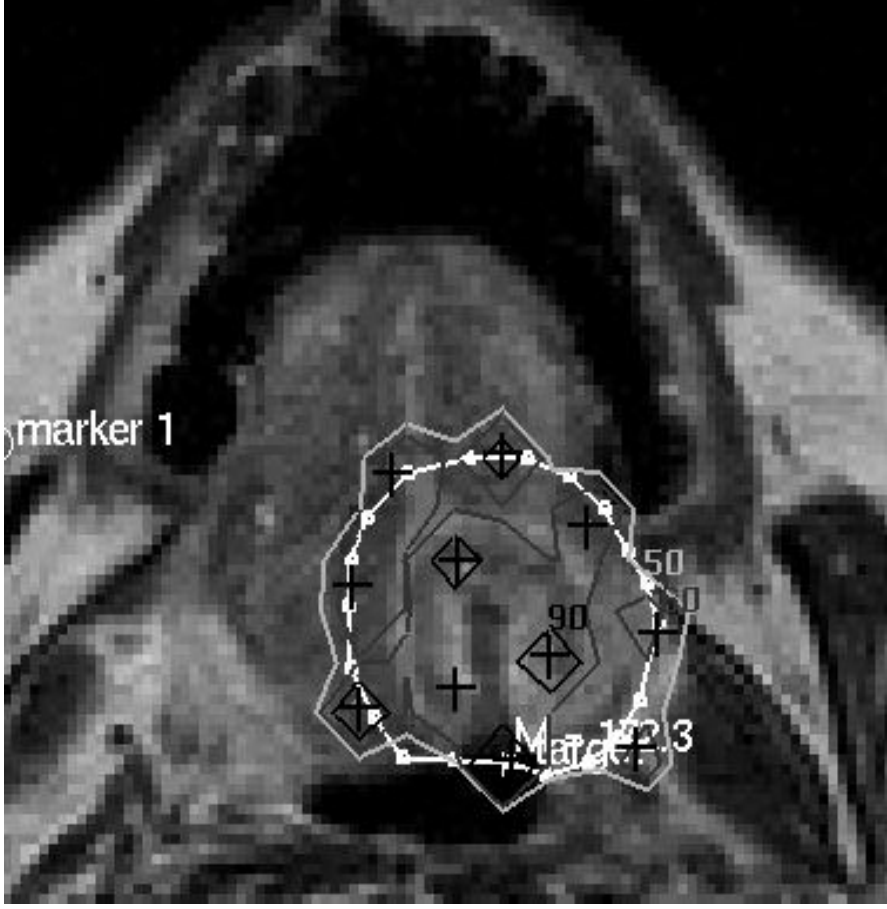
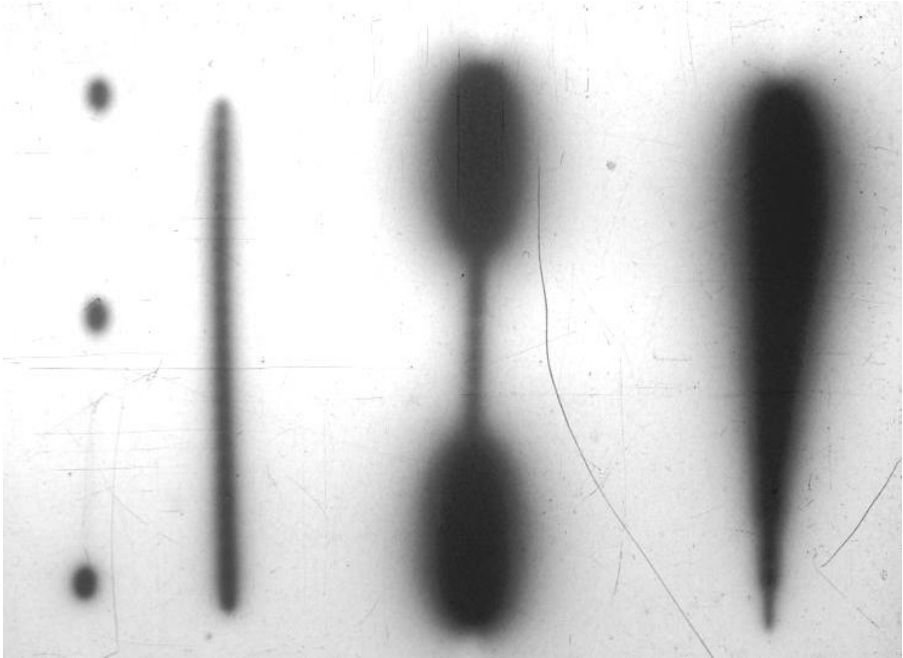
Nowadays

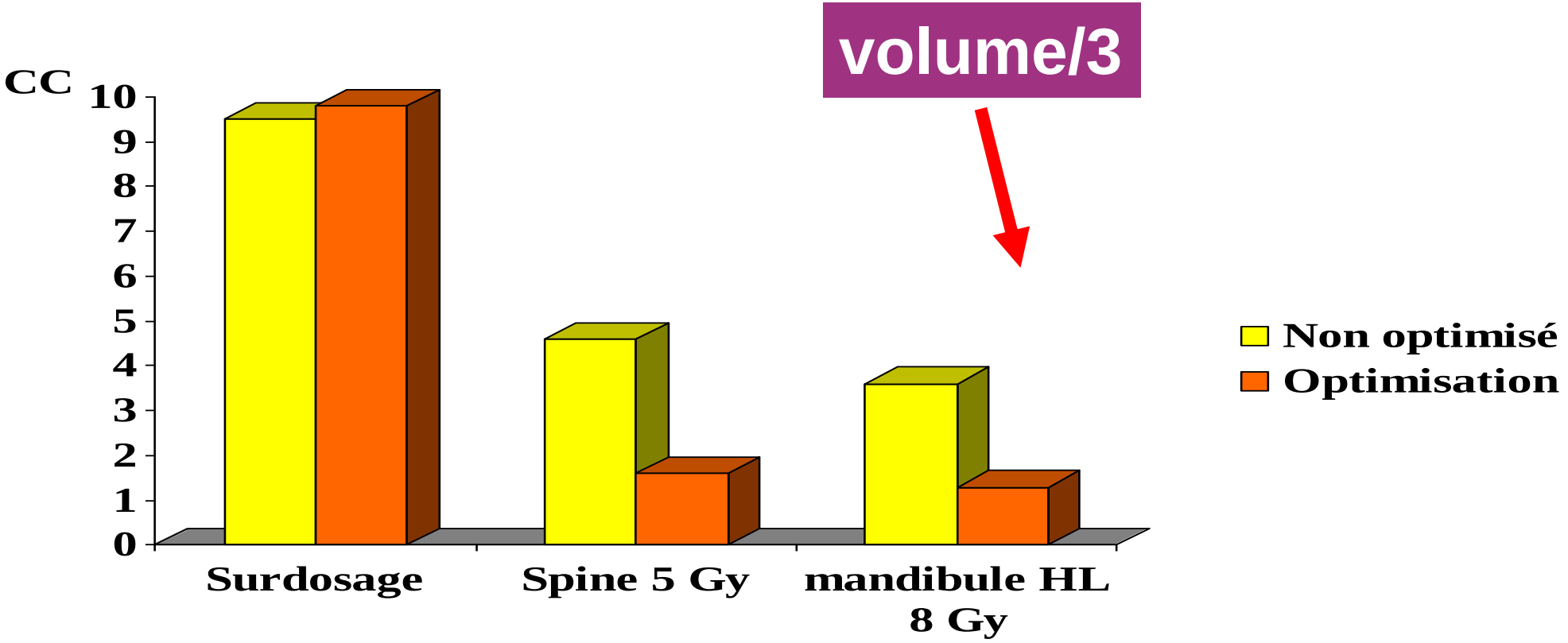
3D Imaging :
CT / MRI



Stepping Source
Technology



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

Auteurs	Pts	Gy/h	Nbre frac/J	Dose	Controle local	Complic
Levendag 1997	19	< 2Gy	4-8	56-70 20-28	100%	0% G3
De Pree 1999	17	0,4-0,75	/	41 Gy moy	59%	6%
Strnad 2000	40	0,5 0,7	24	50 Gy 24 Gy	92%	5%
Peiffert 2001	30	0,5	24	45 Gy 16-35 Gy	83%	16%
Ziemlewski 2007	45 50% lip	0,6-1 Gy/h	24	70 Gy 10 (boost)	88%	23%

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HDR H&N

	Pts	Gy/f	Fract	Control local	Complications
Donath 1995 CB	13	4,5 -5	10	90%	/
Lau 1996 CB	27	6,5	7	53%	35% G2-3
Levendag 1997 OP	15 (45 GY RT)	3-5	2	87%	30%
Leung 1998 CB	13	5,5-6	10	100%	1 G3
Inoue 2001 CB	25	6	10	87%	15%
Guinot 2003 lèvres	39	5-5,5	8-10	88%	G1-2
Nose 2004 OP	68 (46 Gy RT) 15	6 6	3-6 8-9	82% 84%	29% (?/100 +/-40cc, p=0,03)

peri-op HDR BT for ADP in irradiated areas

	Localisation	Dose	Controle survie	Complications
Pellizon 21 pts	ADP	12 à 48 Gy	52%	19%
Martinez- Monge 25 pts	10 ADP 15T	32 à 48 Gy 4 Gy/f	46 % (SG)	12%)

A. Pellizon Radiation Oncology 2006, 1:27. R. Martinez-Monge Brachytherapy 5 (2006) 32-40.

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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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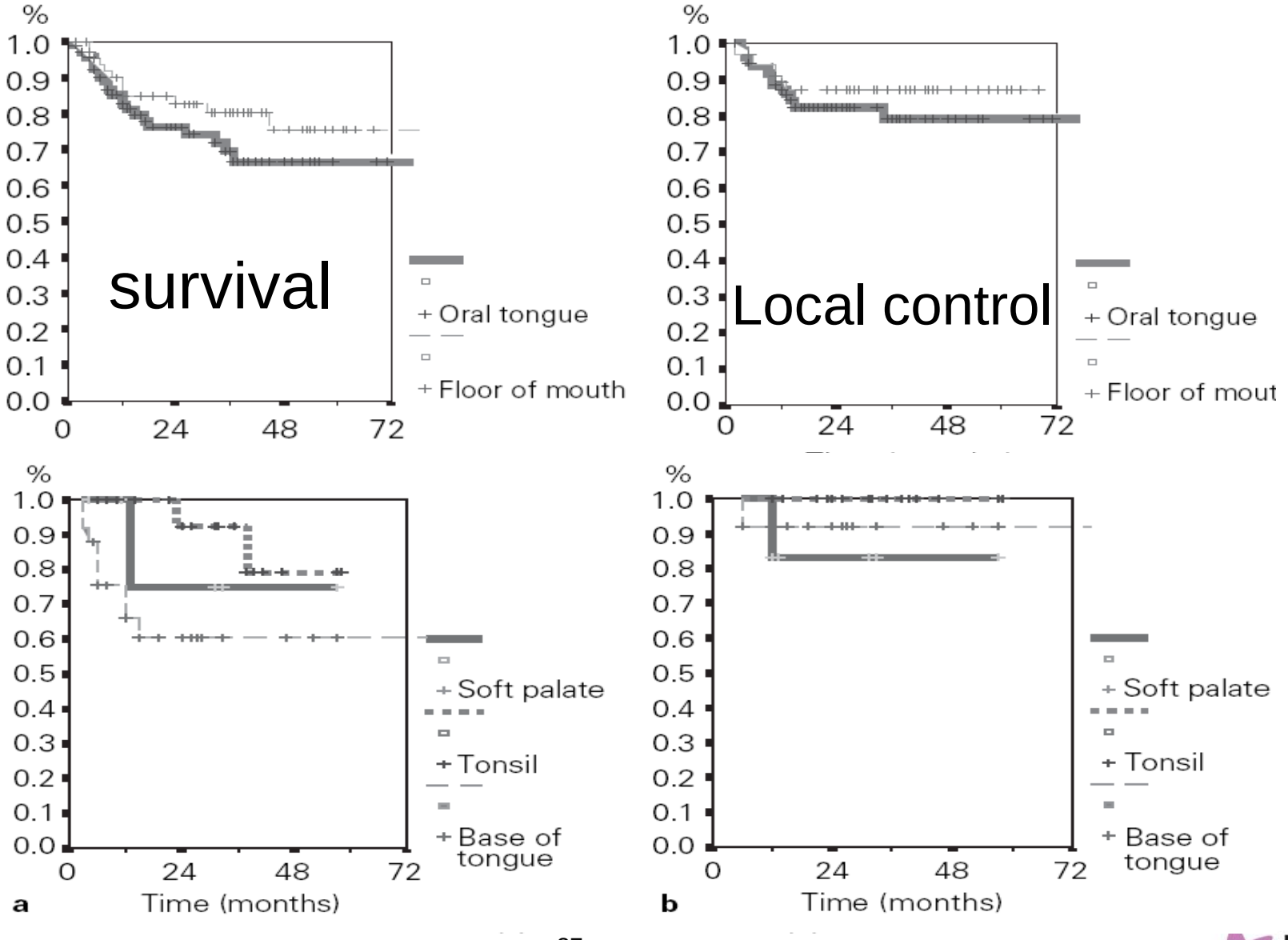
PDR in H&N



V. Strnad, W. Melzner, Strahlenther Onkol 2005;181:762–7

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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

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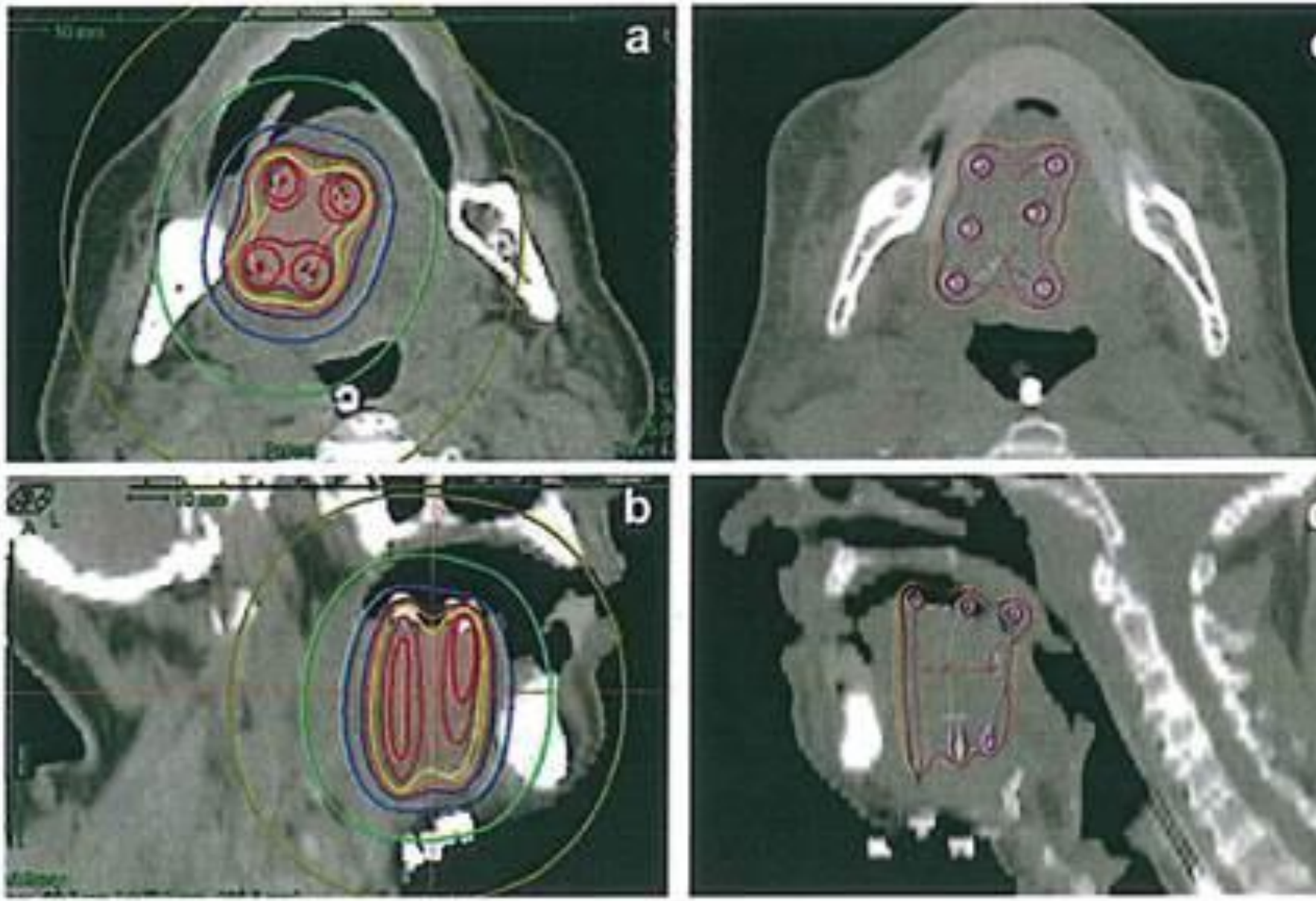

Fig. 1. Typical implant dose distributions. Left: (a) PDR 4-line implant in transverse and (b) sagittal views. Right: (c) LDR 6-l
(d) sagittal views. PDR = pulsed-dose-rate; LDR = low-dose-rate.

LDR vs PDR

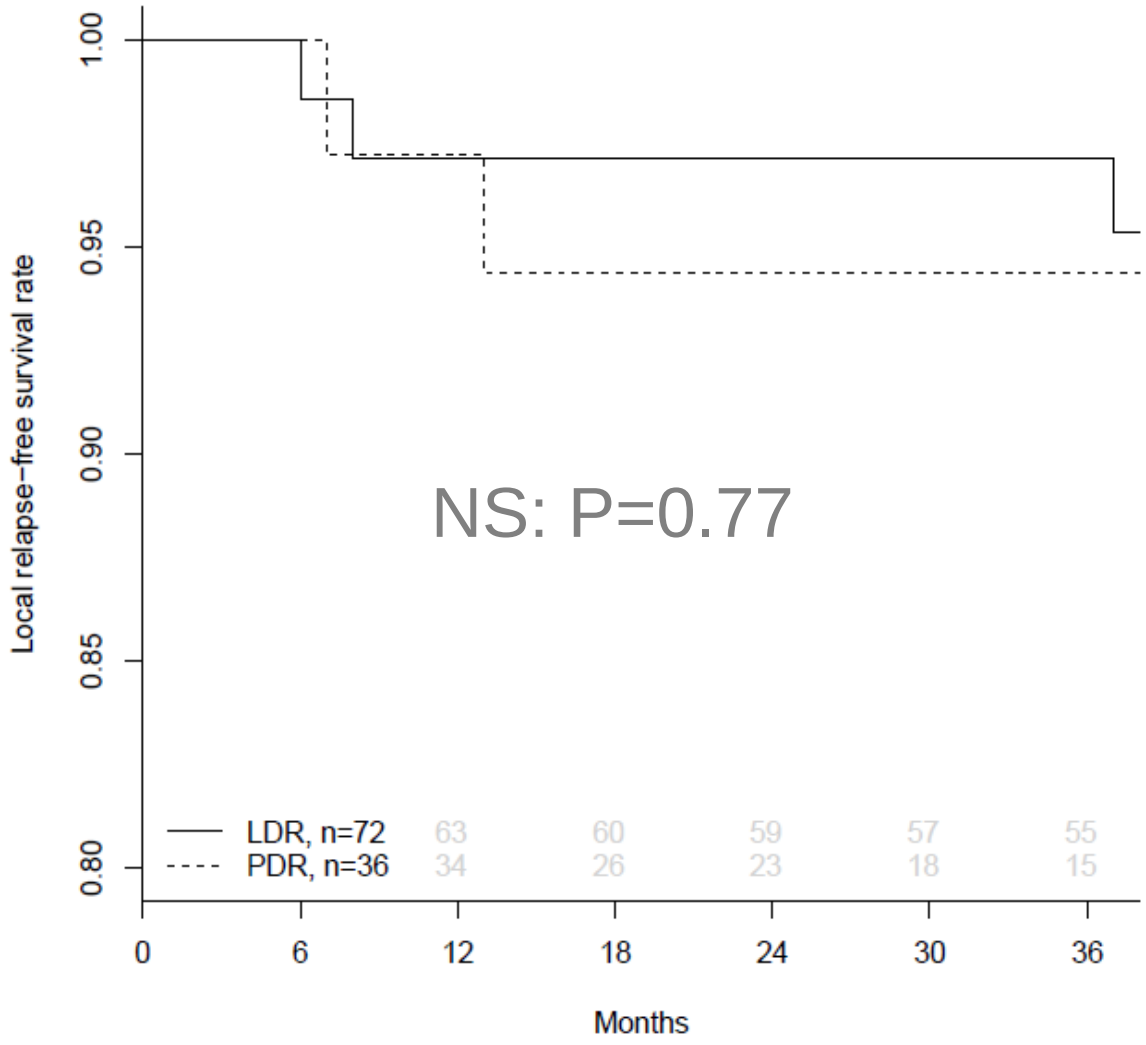

Figure 1 : Kaplan-Meier estimates of the Local Recurrence Free Survival (LRFS) for patients treated with Pulsed-Dose Rate (PDR) or continuous Low Dose Rate (cLDR) brachytherapy, showing no statiscally significant difference at 3 years (p=0.77).

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Complications LDR vs PDR

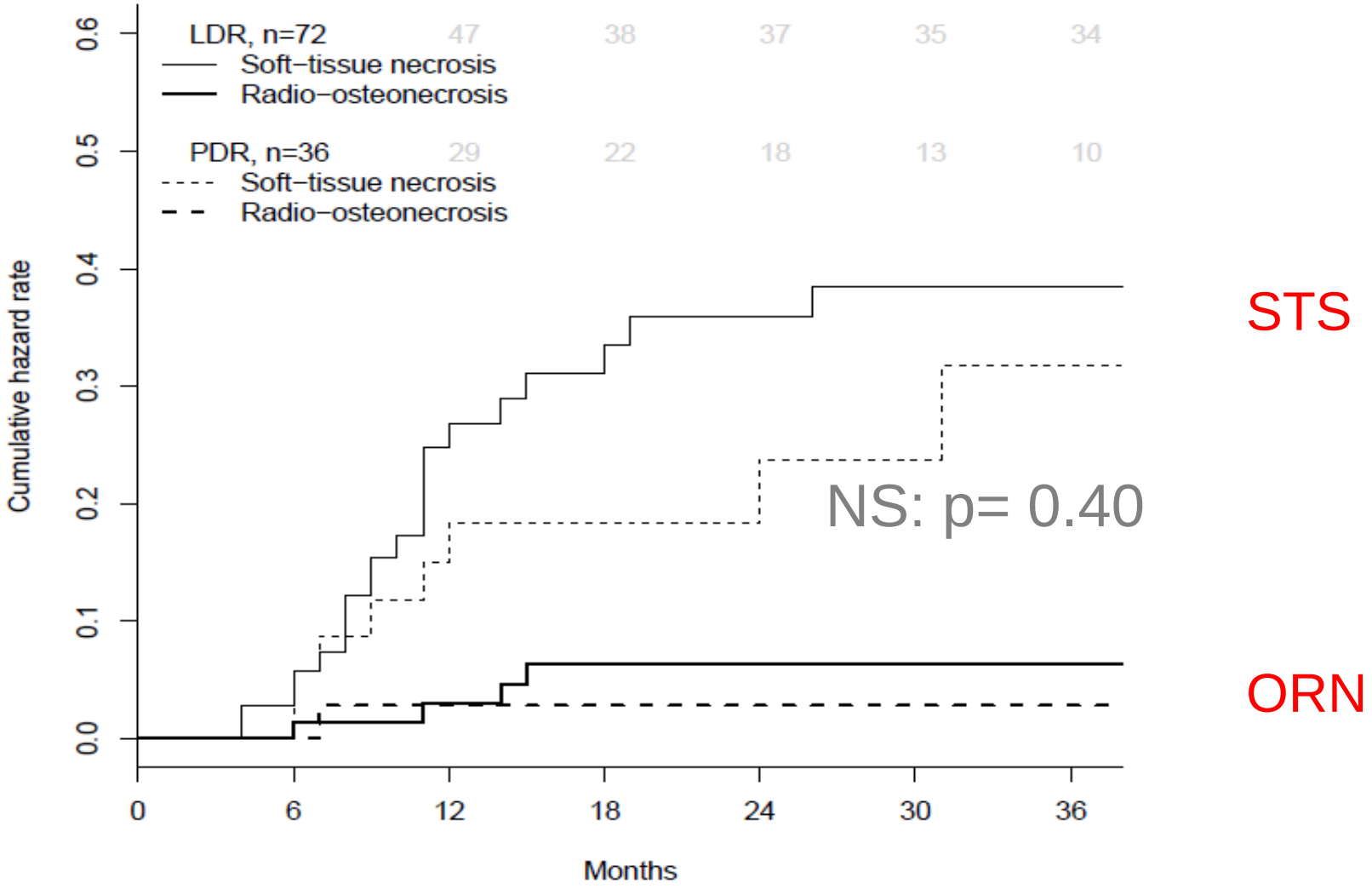

Figure 2 : Kaplan-Meier estimates of the cumulative risk of late grade 2-3 complications following Pulsed-Dose Rate (PDR) or continuous Low Dose Rate (cLDR) brachytherapy, showing no statistically significant difference at 3 years (p=0.4).

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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*

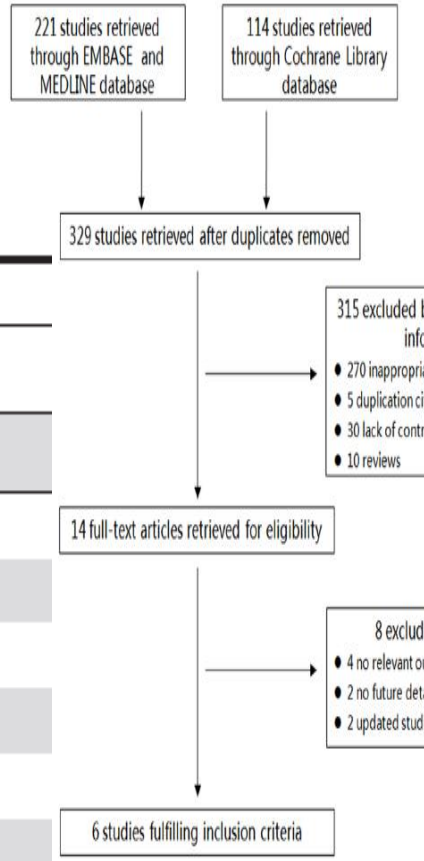
Department of Oral and Maxillofacial Surgery, Provincial Hospital Affiliated to Shandong University, Jinan, China

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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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

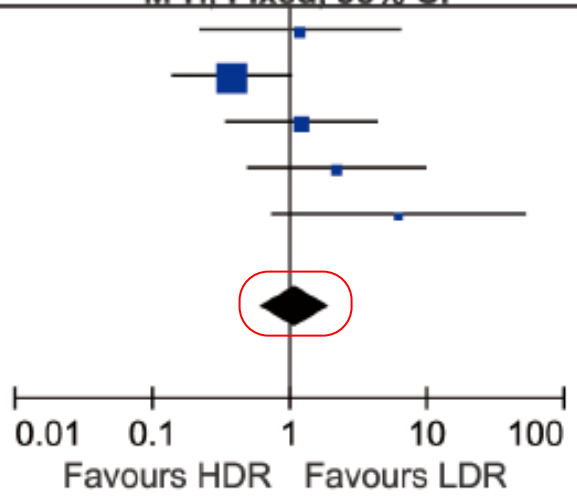
Local Recurrence LDR/HDR

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: $Z = 0.38$ ($P = 0.71$)



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: $Z = 0.60$ ($P = 0.55$)

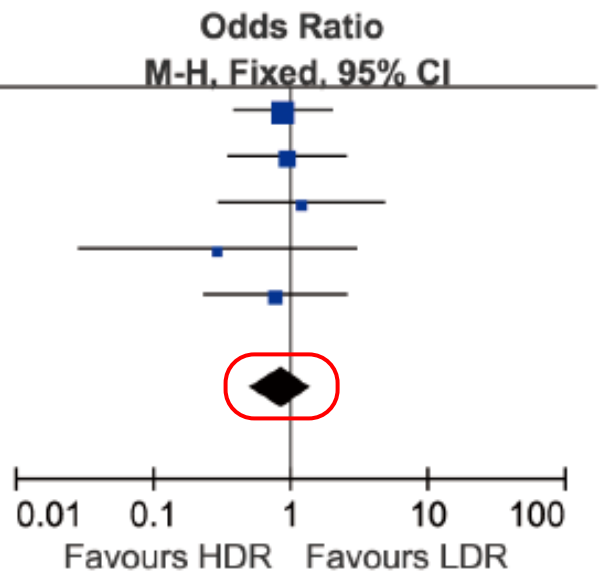


Figure 5. Grade 3 or Grade 4 complications of oral cancer treated with LDR vs. HDR brachytherapy.

doi:10.1371/journal.pone.0065423.g005

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Endometrium Postoperative: Indication, tools and requirements, performing application, hazards, results

Peter Hoskin

Mount Vernon Cancer Centre

ESTRO School

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

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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

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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

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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

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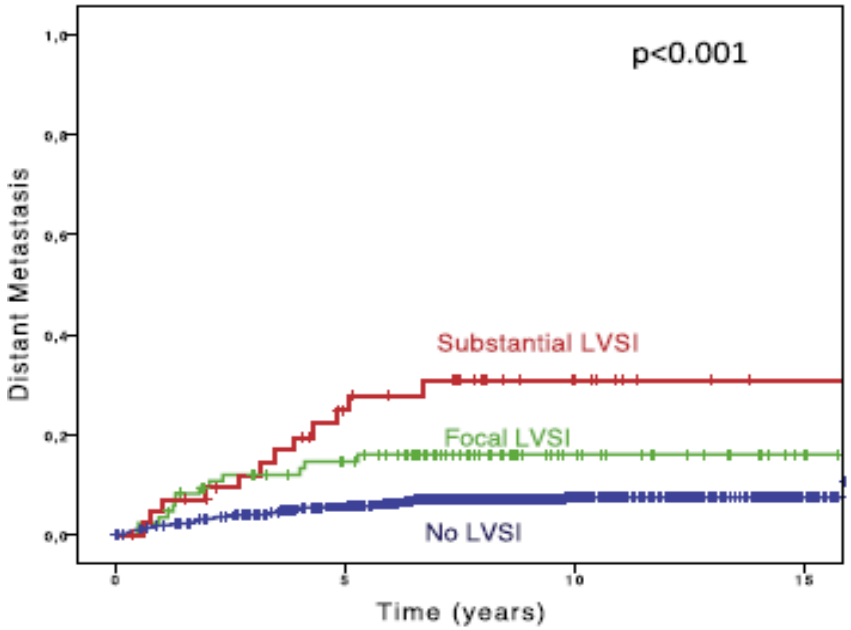
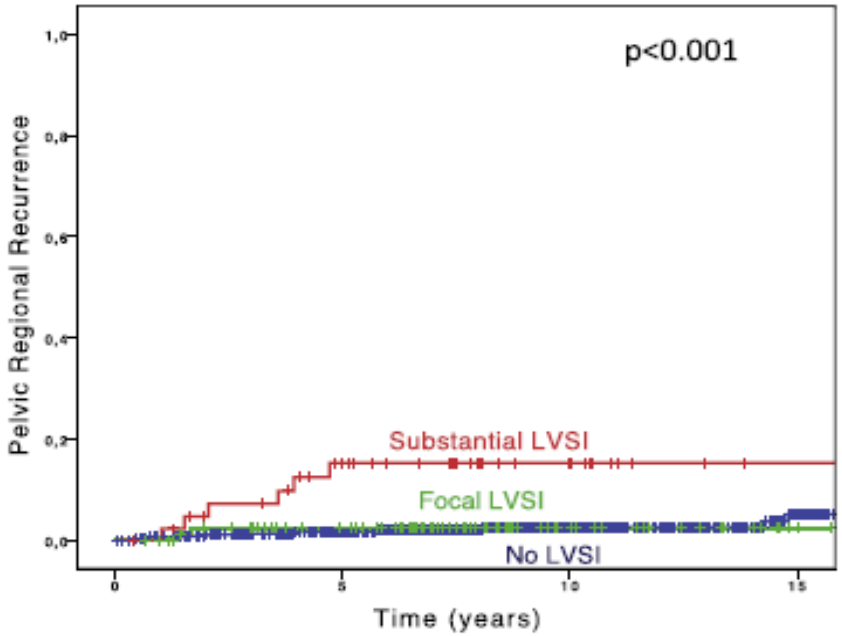
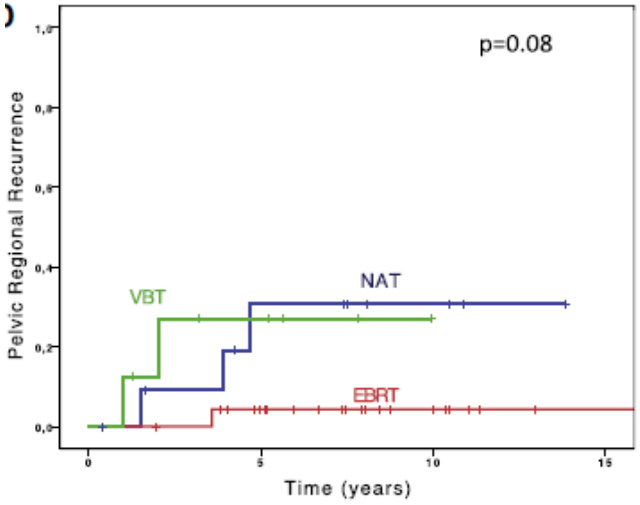
Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer – A pooled analysis of PORTEC 1 and 2 trials

Bosse et al European Journal of Cancer (2015) 51, 1742–1750





Subset all with Substantial LVSI



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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	3.1%	1.2%	[p=0.114]
G1/2 urinary toxicity	0.6%	2.8%	

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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

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Applicators

- Standard
  - Cylindrical single line source
  - Ovoids
  - Ring
  - Multichannel

- Customised
  - Individual moulds

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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

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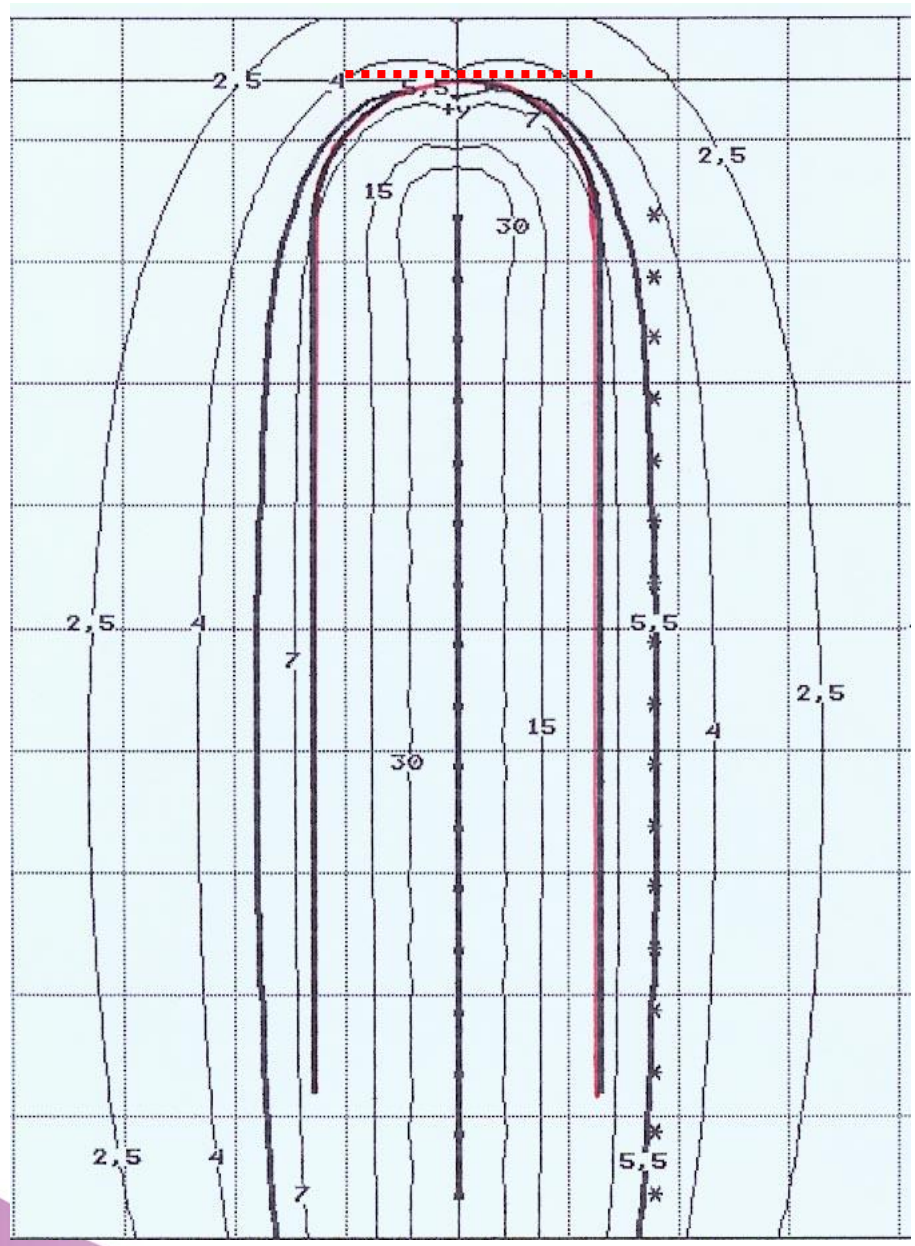
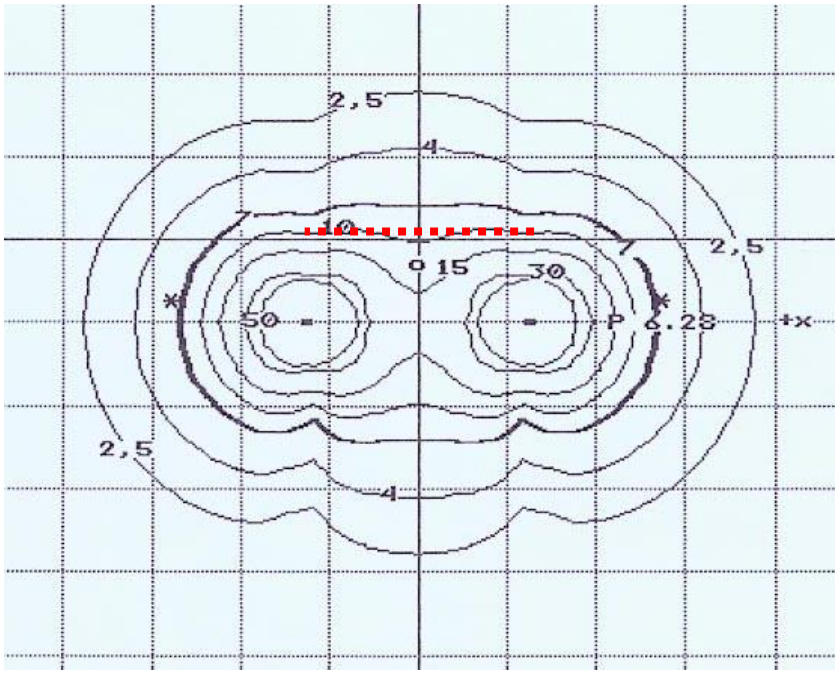
Weighted cylinder



Ovoids



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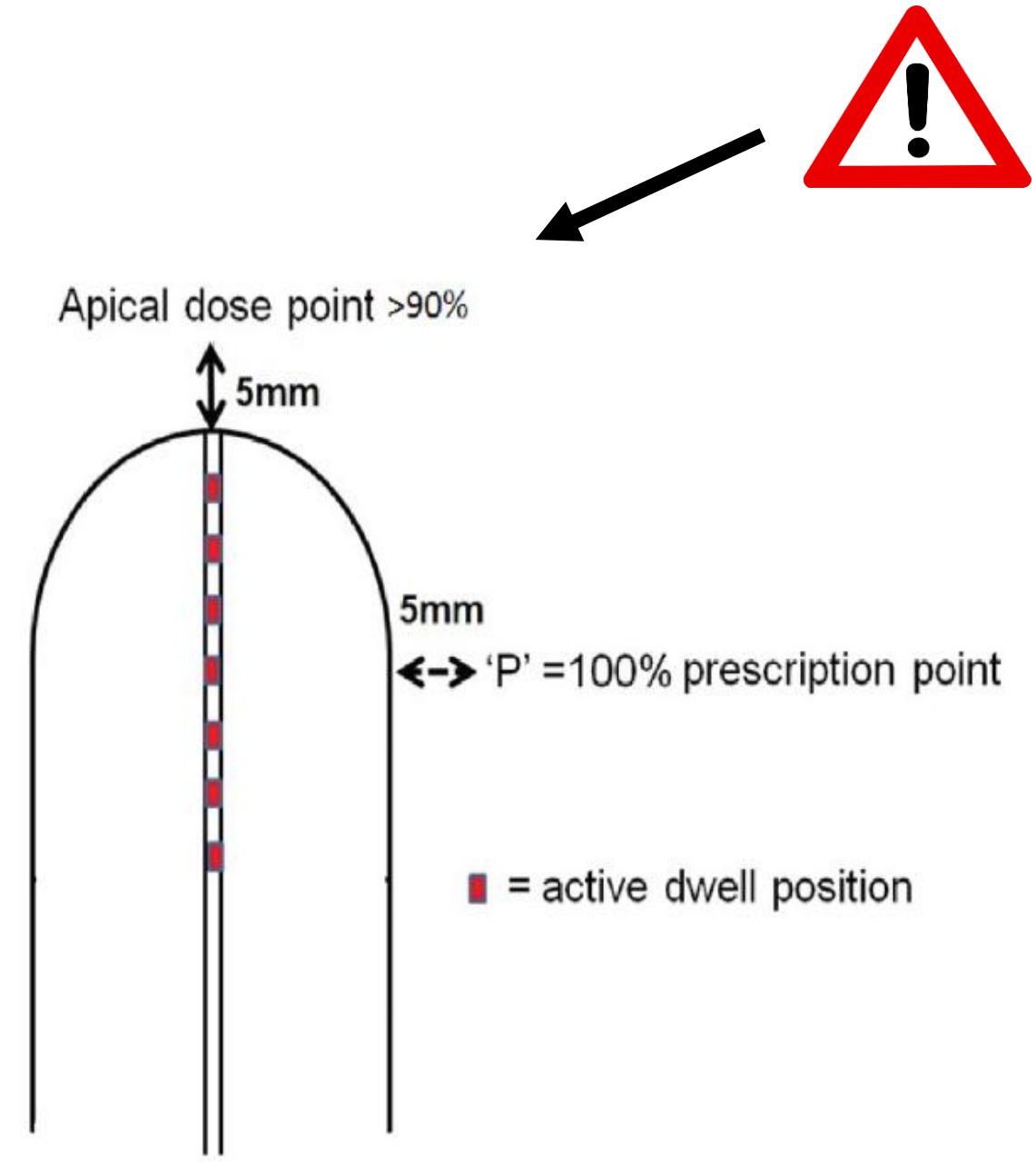
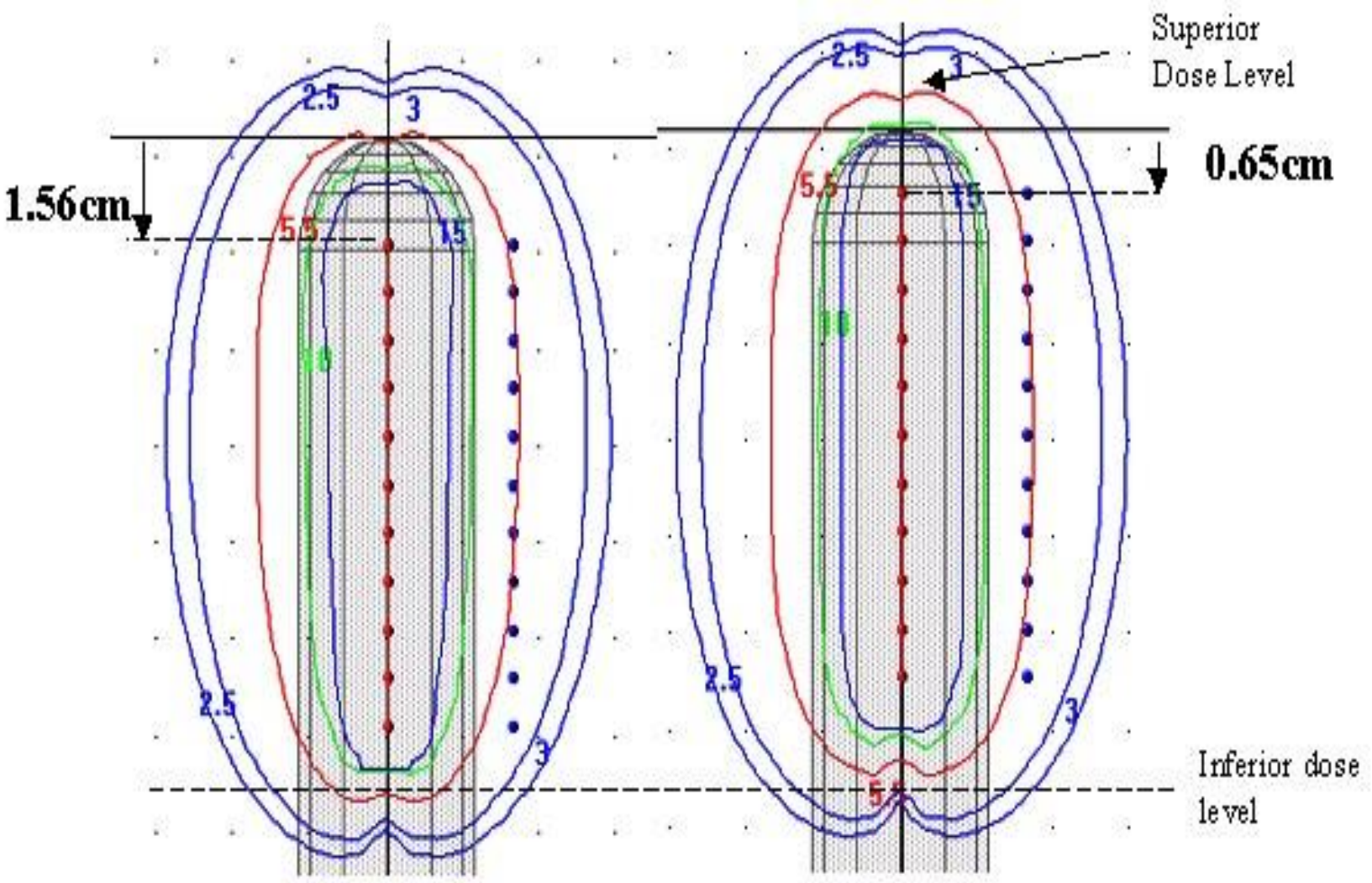

Apical dose point >90%
5mm
5mm
'P' =100% prescription point
= active dwell position


Superior
Dose Level
1.56cm
0.65cm
2.5
3
5.5
1.5
2.5
3
Inferior dose
level
2.3cm Diamaeter Vault Applicator
2.3cm Diameter Stump Applicator

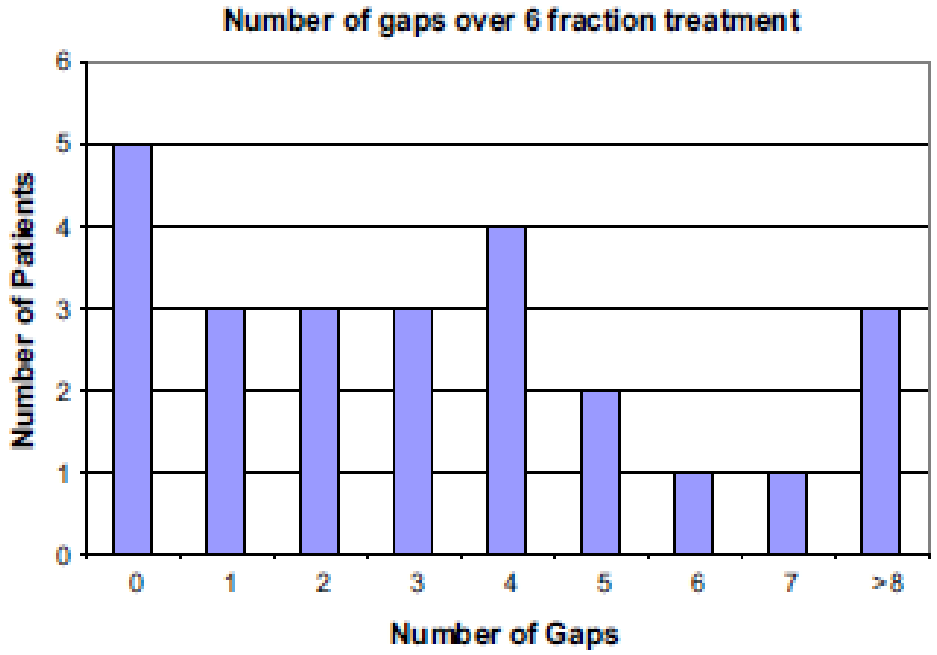
DOSIMETRIC EFFECTS OF AIR POCKETS AROUND HIGH–DOSE RATE BRACHYTHERAPY VAGINAL CYLINDERS

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: 6 FRACTION VAULT BRACHYTHERAPY



90 AIRPOCKETS IN 150 PROCEDURES (60%)

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DOSIMETRIC EFFECTS OF AIR POCKETS AROUND HIGH–DOSE RATE BRACHYTHERAPY VAGINAL CYLINDERS

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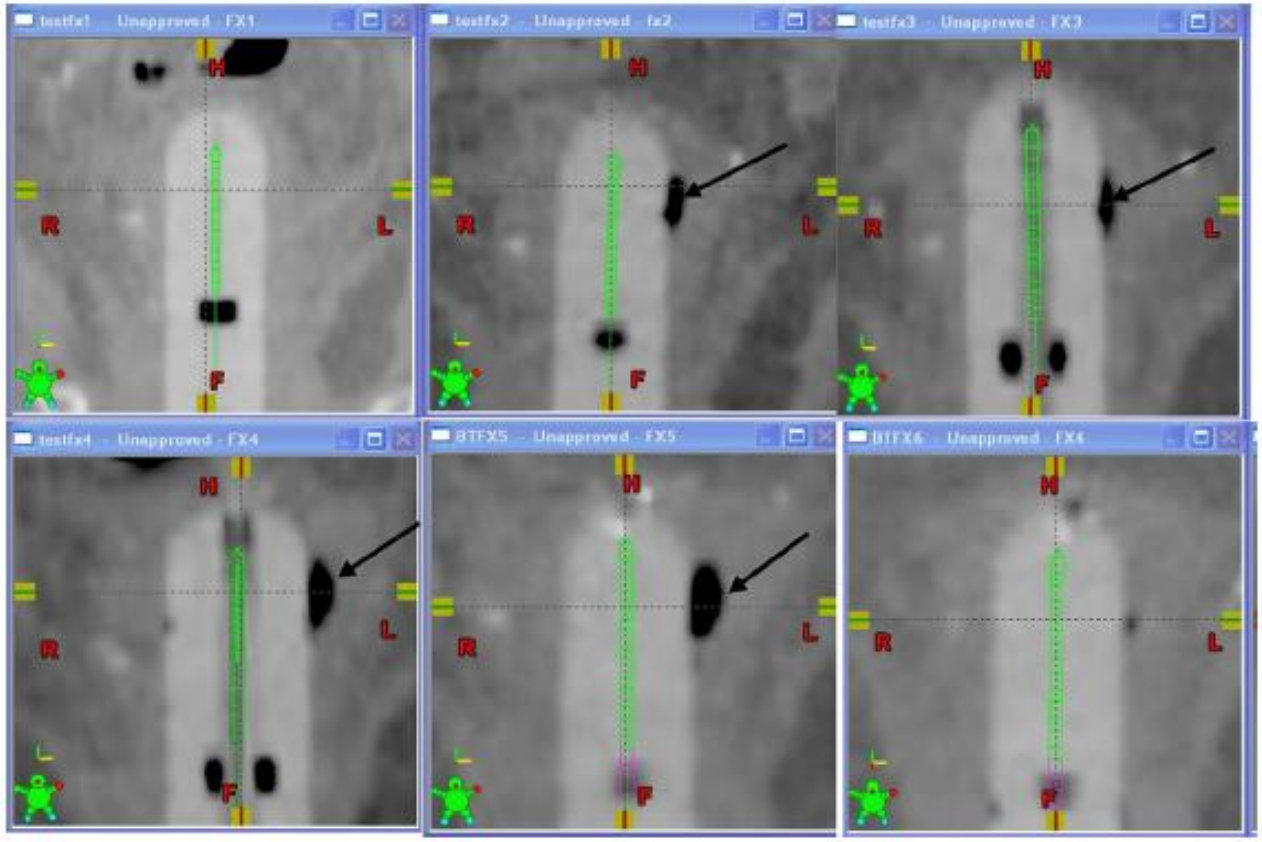
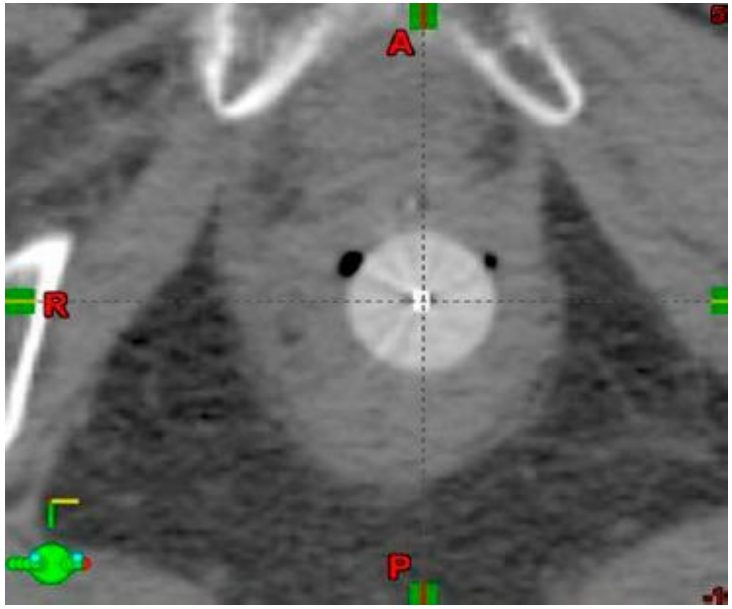


Persistent air pockets over 6 fractions

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 11 (2012) 58–67

BRACHYTHERAPY

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

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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

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Prescription dose

Brachytherapy alone

PDR: 30Gy at **5 mm**
(0.5Gy/hr)

HDR : 21Gy in 3 fr. at **5 mm**
(7 Gy per fraction)

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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

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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

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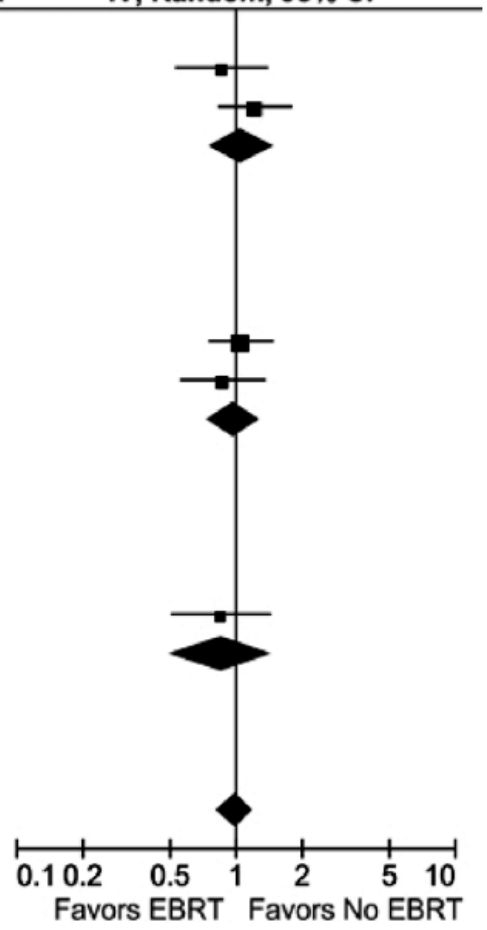
Adjuvant Radiotherapy for Stage I Endometrial Cancer: An Updated Cochrane Systematic Review and Meta-analysis

Anthony Kong,* Nick Johnson, Henry C. Kitchener, Theresa A. Lawrie*

J Natl Cancer Inst 2012;104:1625–1634

Overall survival

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	-0.15	0.25	190	202	15.0%	0.86 [0.53, 1.40]
PORTEC-1	0.2	0.2	354	360	23.5%	1.22 [0.83, 1.81]
Subtotal (95% CI)			**544**	**562**	**38.5%**	**1.06 [0.76, 1.48]**
Heterogeneity: Tau² = 0.01; Chi² = 1.20, df = 1 (*P* = .27); I² = 16%						
Test for overall effect: Z = 0.33 (*P* = .74)						
EBRT vs no additional treatment (VBT balanced across groups)						
ASTEC/EN.5 (1)	0.05	0.175	452	453	30.7%	1.05 [0.75, 1.48]
Sorbe 2011 (2)	-0.14	0.23	264	263	17.8%	0.87 [0.55, 1.36]
Subtotal (95% CI)			**716**	**716**	**48.4%**	**0.98 [0.75, 1.29]**
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 1 (*P* = .51); I² = 0%						
Test for overall effect: Z = 0.14 (*P* = .89)						
EBRT vs VBT						
PORTEC-2 (3)	-0.16	0.268	214	213	13.1%	0.85 [0.50, 1.44]
Subtotal (95% CI)			**214**	**213**	**13.1%**	**0.85 [0.50, 1.44]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.60 (*P* = .55)						
Total (95% CI)			**1474**	**1491**	**100.0%**	**0.99 [0.82, 1.20]**
Heterogeneity: Tau² = 0.00; Chi² = 2.16, df = 4 (*P* = .71); I² = 0%						
Test for overall effect: Z = 0.06 (*P* = .95)						
Test for subgroup differences: Chi² = 0.47, df = 2 (*P* = .79), I² = 0%						



(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 HRs in terms of VBT (VBT vs EBRT); we have expressed the HR in terms of EBRT.

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Adjuvant Radiotherapy for Stage I Endometrial Cancer: An Updated Cochrane Systematic Review and Meta-analysis

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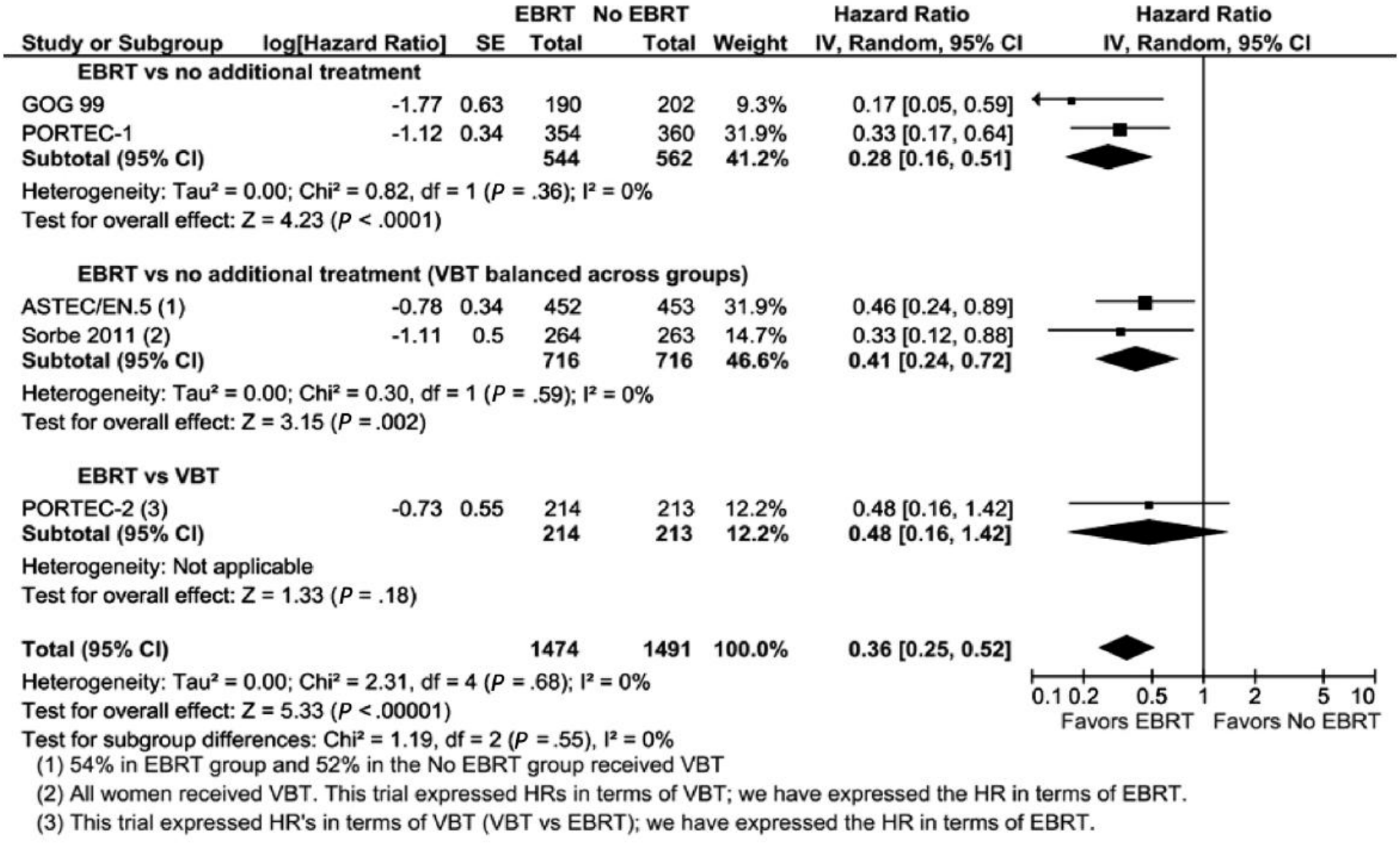

(1) 54% in EBRT group and 52% in the No EBRT group received VBT

(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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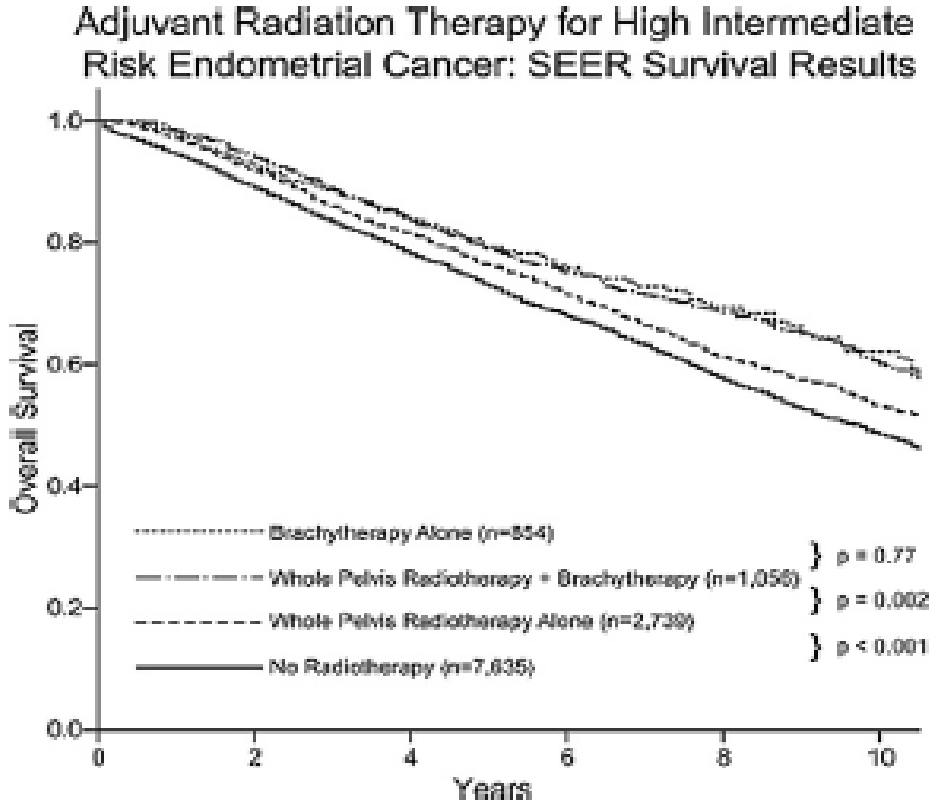
Brachytherapy for Stage I Endometrial Cancer: Survival Results from the SEER Registry

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

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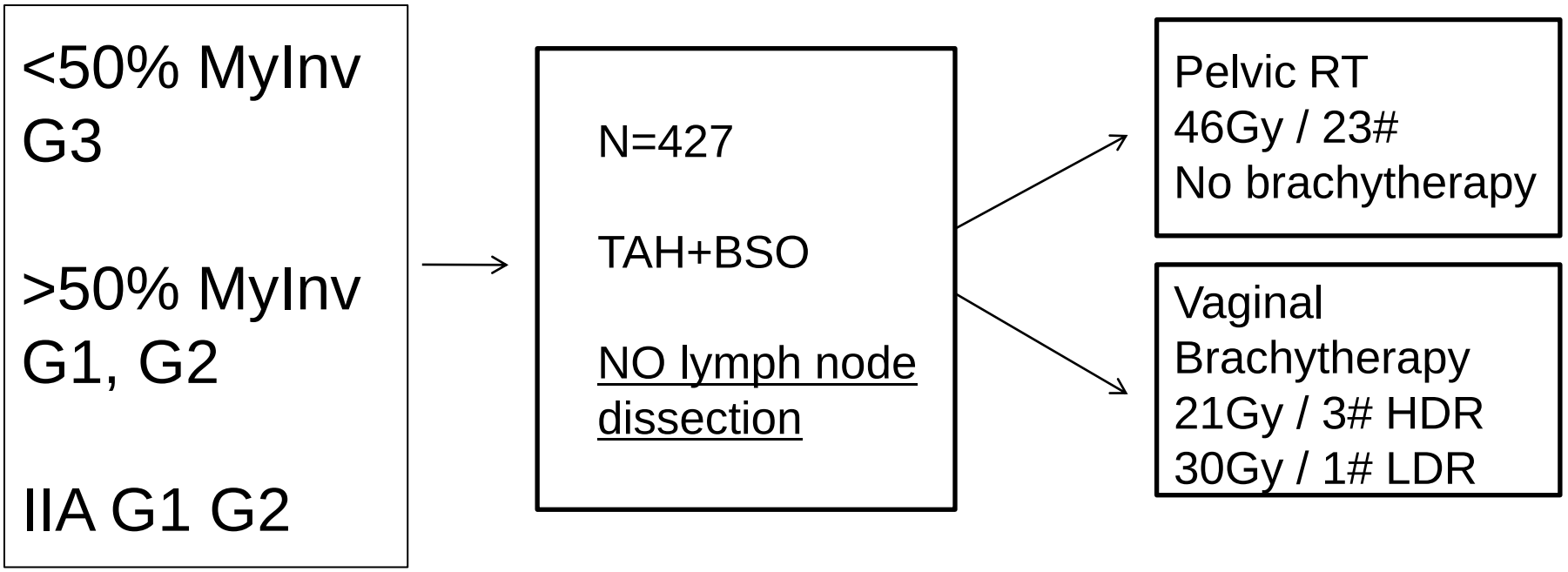
PORTEC 2 study



	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**

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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%

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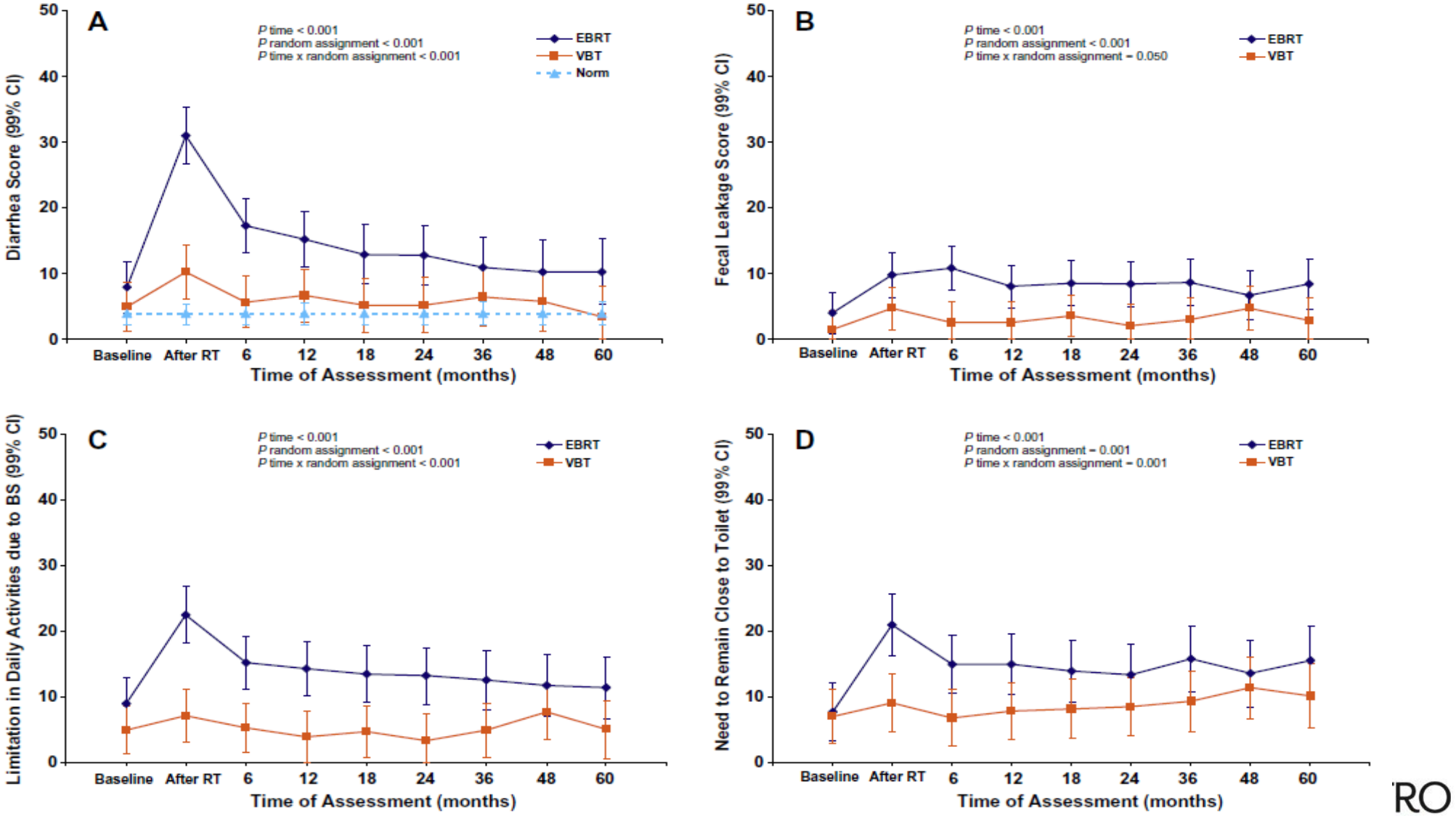
Five-year quality of life of endometrial cancer patients treated in the randomised Post Operative Radiation Therapy in Endometrial Cancer (PORTEC-2) trial and comparison with norm data ☆

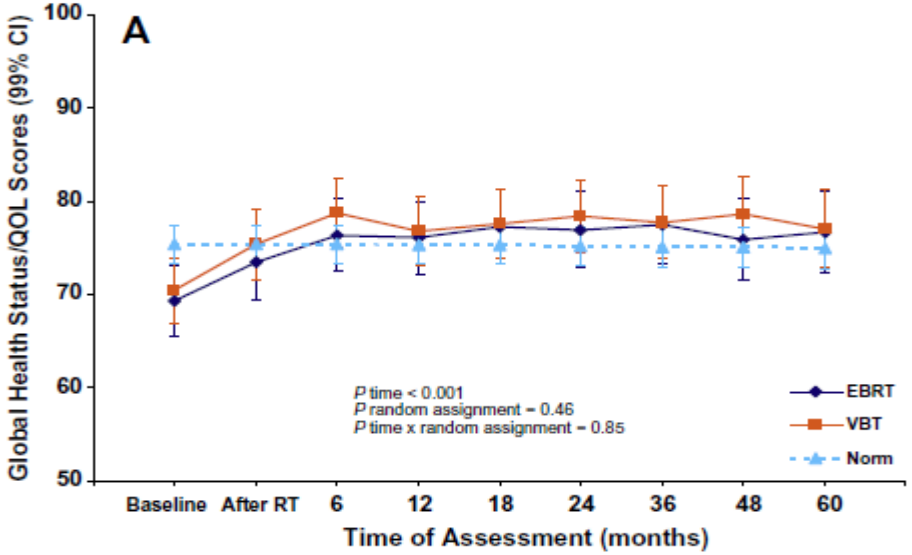
EUROPEAN JOURNAL OF CANCER 48 (2012) 1638–1648

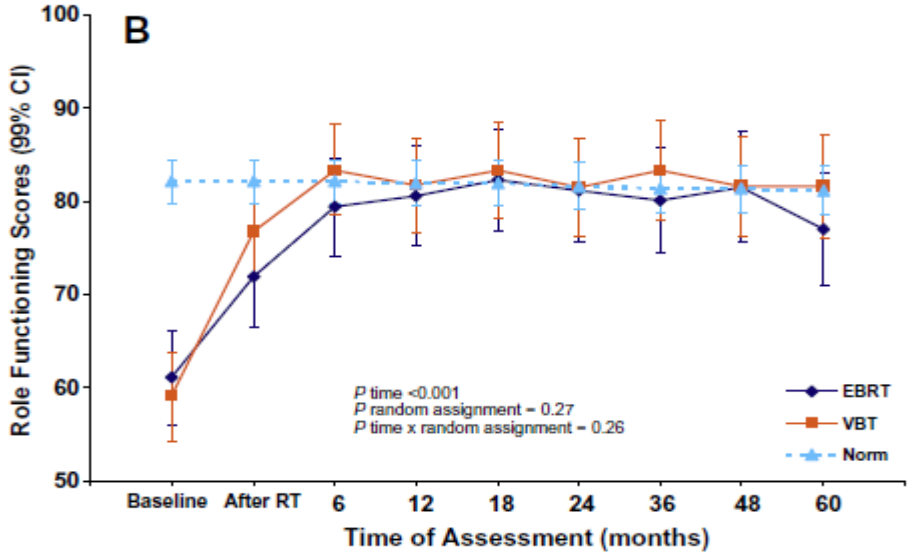


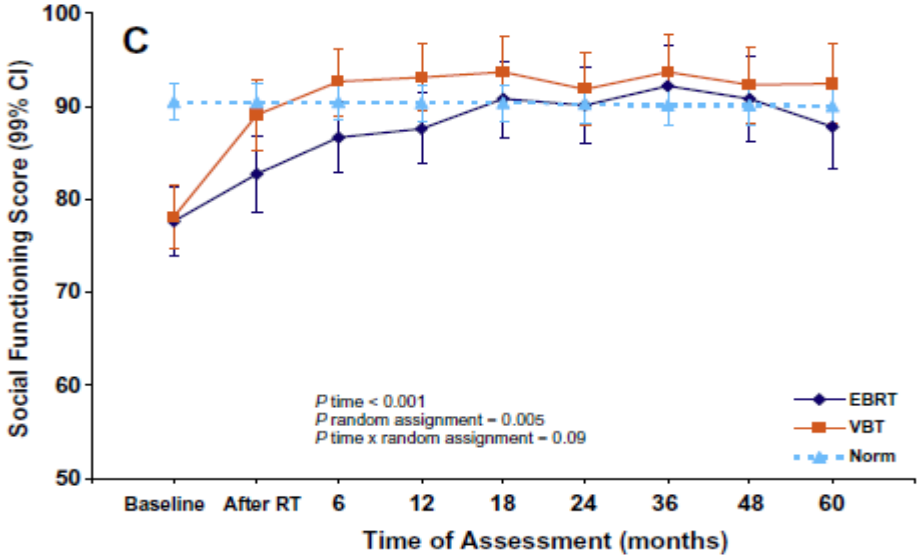
RO School

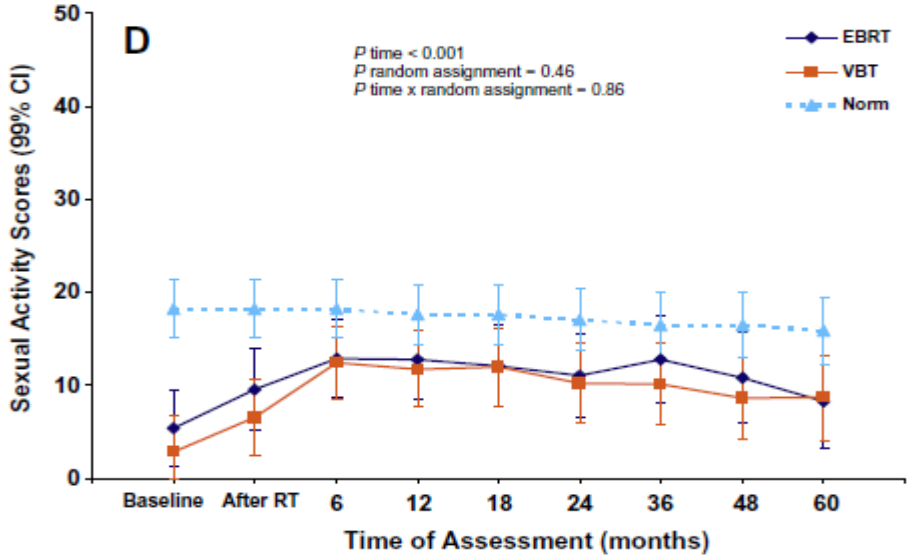
Five-year quality of life of endometrial cancer patients treated in the randomised Post Operative Radiation Therapy in Endometrial Cancer (PORTEC-2) trial and comparison with norm data ☆

EUROPEAN JOURNAL OF CANCER 48 (2012) 1638–1648









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

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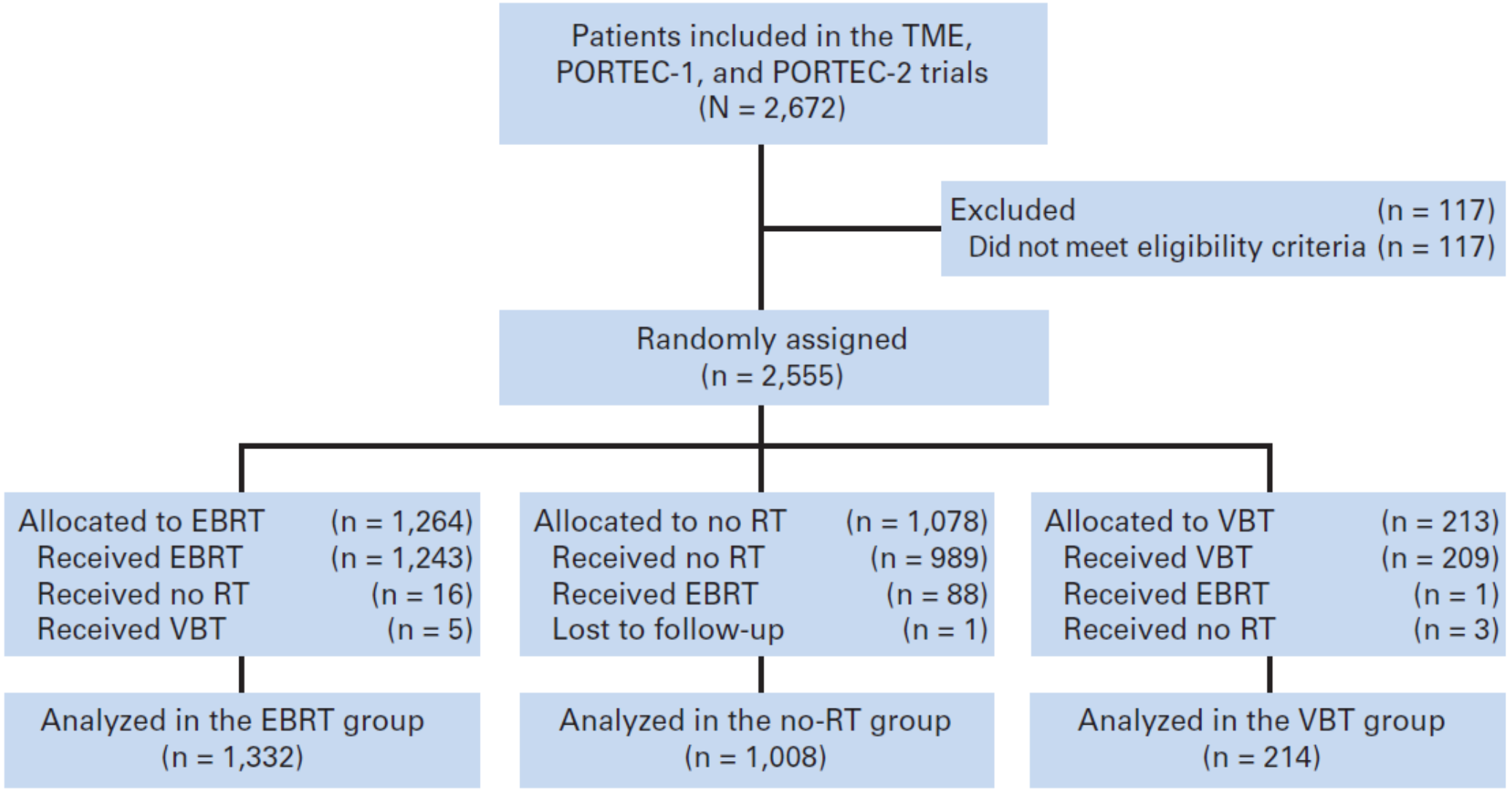
No Increased Risk of Second Cancer After Radiotherapy in Patients Treated for Rectal or Endometrial Cancer in the Randomized TME, PORTEC-1, and PORTEC-2 Trials

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 I



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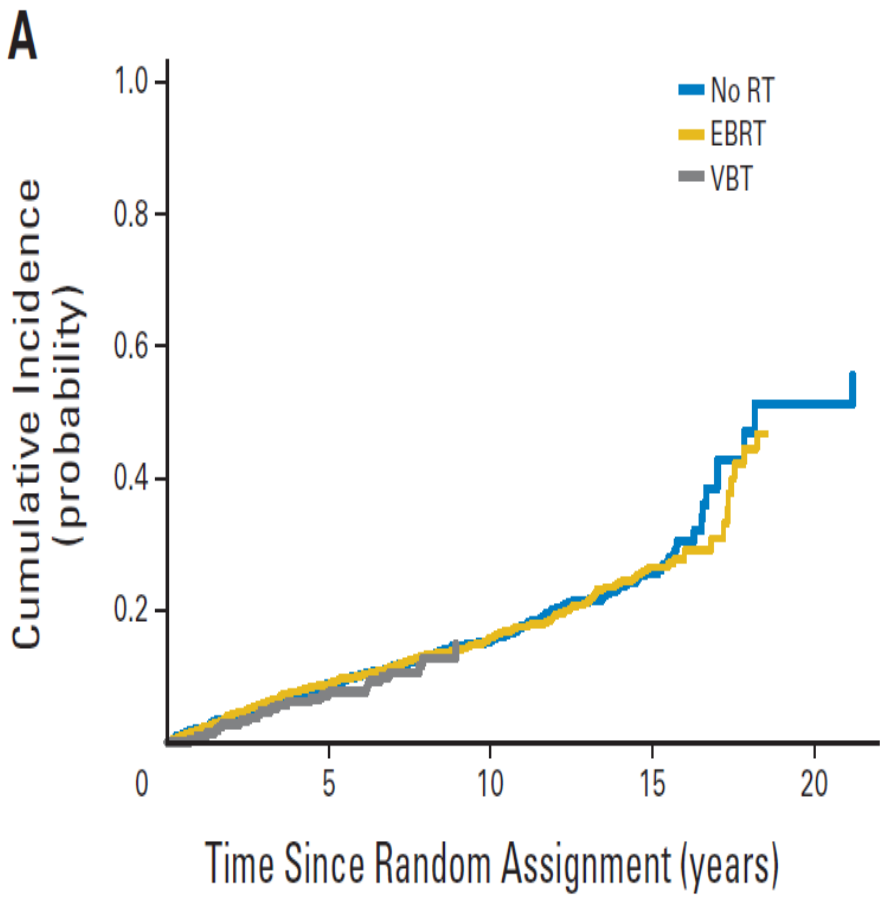
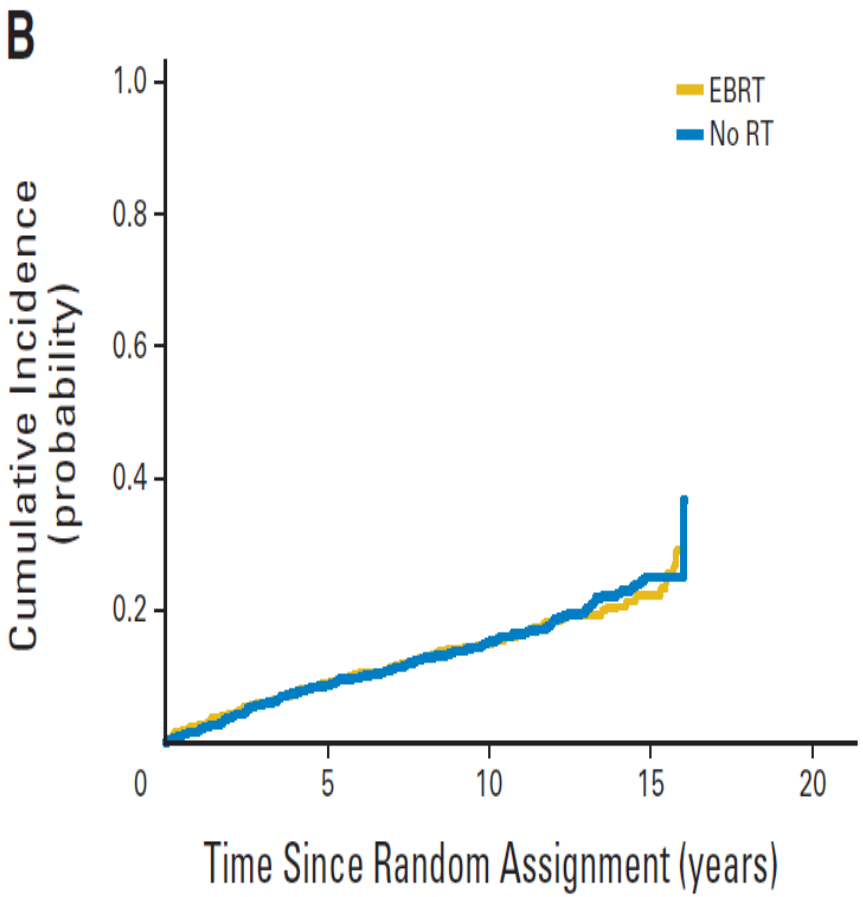


No. at risk					
No RT	1,008	708	496	84	2
EBRT	1,332	862	482	83	1
VBT	214	157	8	0	0



No. at risk					
EBRT	778	441	306	48	0
No RT	635	431	310	50	0

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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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Muscle-Invasive Bladder Cancer

ESTRO School

B. Pieters
Academic Medical Center / University of Amsterdam

MIBC

Standard

Radical cystectomy ± neo-adjuvant chemotherapy

Alternative in selected cases

Bladder preserving treatment

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Bladder Preserving Treatment

- Radio(chemo)therapy
- TUR-B + EBRT + Brachytherapy
- TUR-B alone

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Bladder Preservation with Brachytherapy

Techniques

- Open retropubic
- Laparoscopic

Radiotherapy and Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

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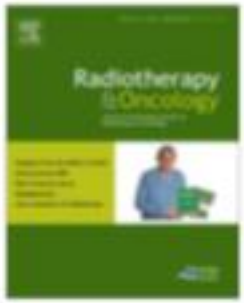


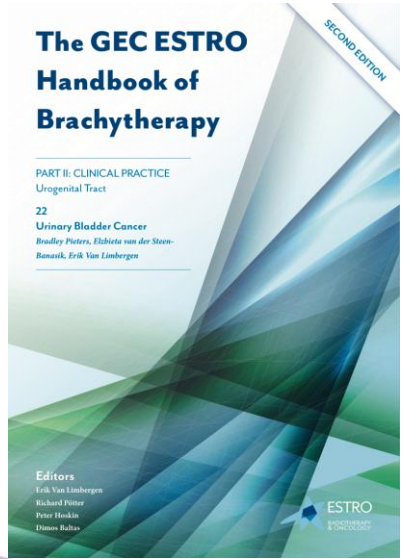
Original article

GEC-ESTRO/ACROP recommendations for performing bladder-sparing treatment with brachytherapy for muscle-invasive bladder carcinoma

Bradley R. Pieters [a,*], Elzbieta van der Steen-Banasik [b], Geert A. Smits [c], Marisol De Brabandere [d], Alberto Bossi [e], Erik Van Limbergen [d]

[a] Academic Medical Center/University of Amsterdam; [b] Radiotherapy Group; [c] Rijnstate Hospital, Arnhem, The Netherlands; [d] University Hospital Gasthuisberg, Leuven, Belgium; [e] Gustave Roussy Cancer Campus, Villejuif, France

http://dx.doi.org/10.1016/j.radonc.2016.12.022



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OPEN RETROPUBIC

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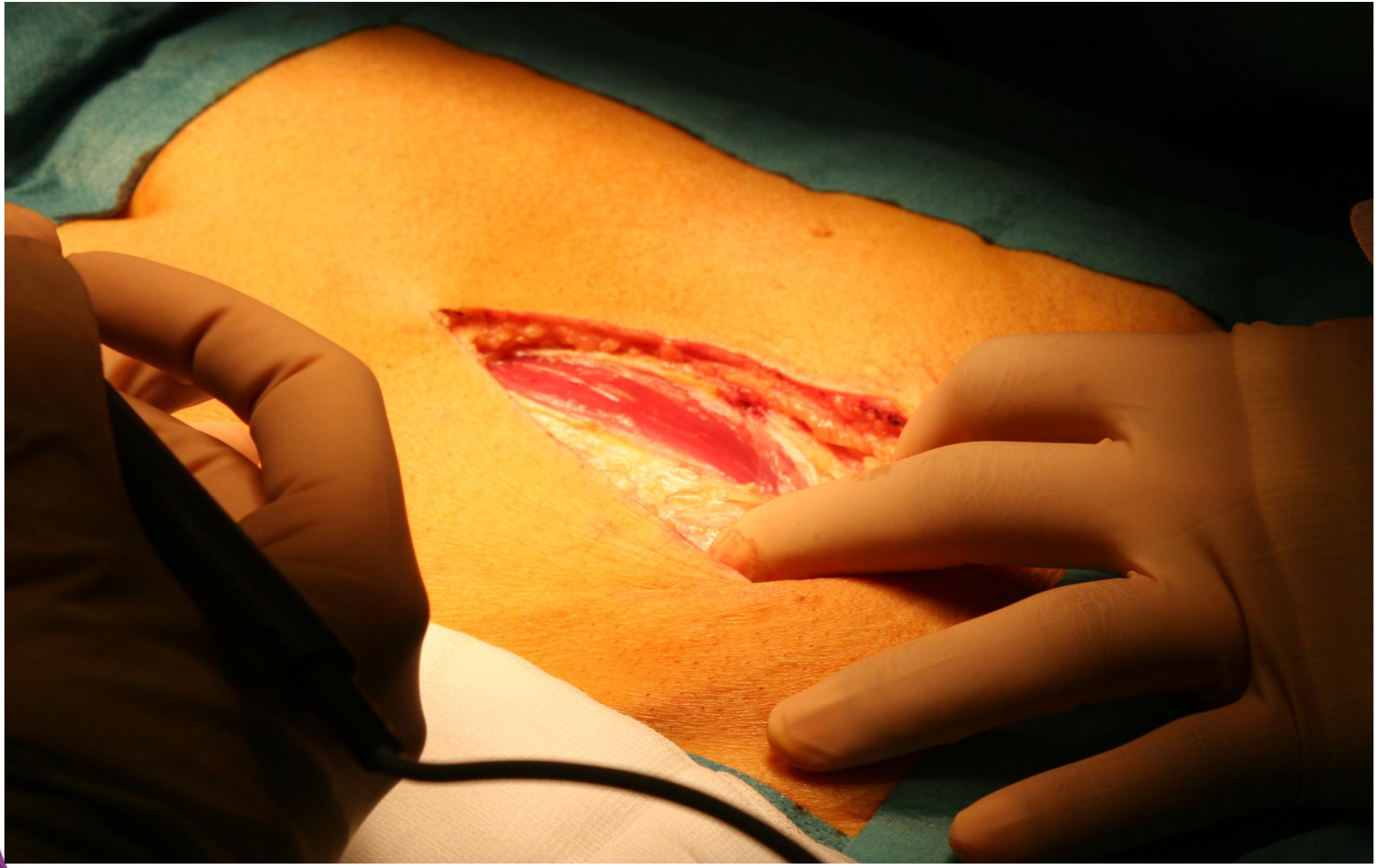
Median laparatomy incision



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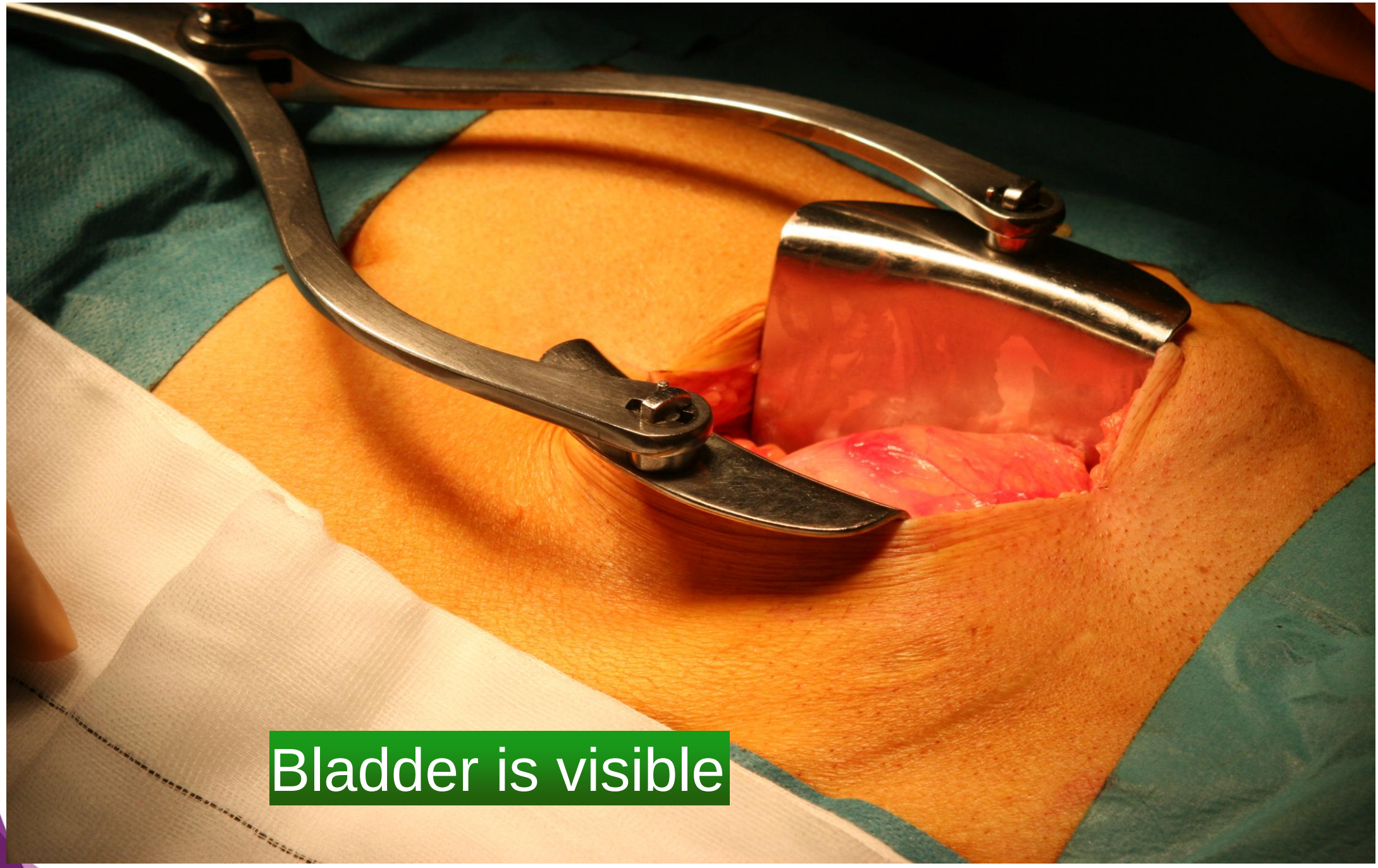
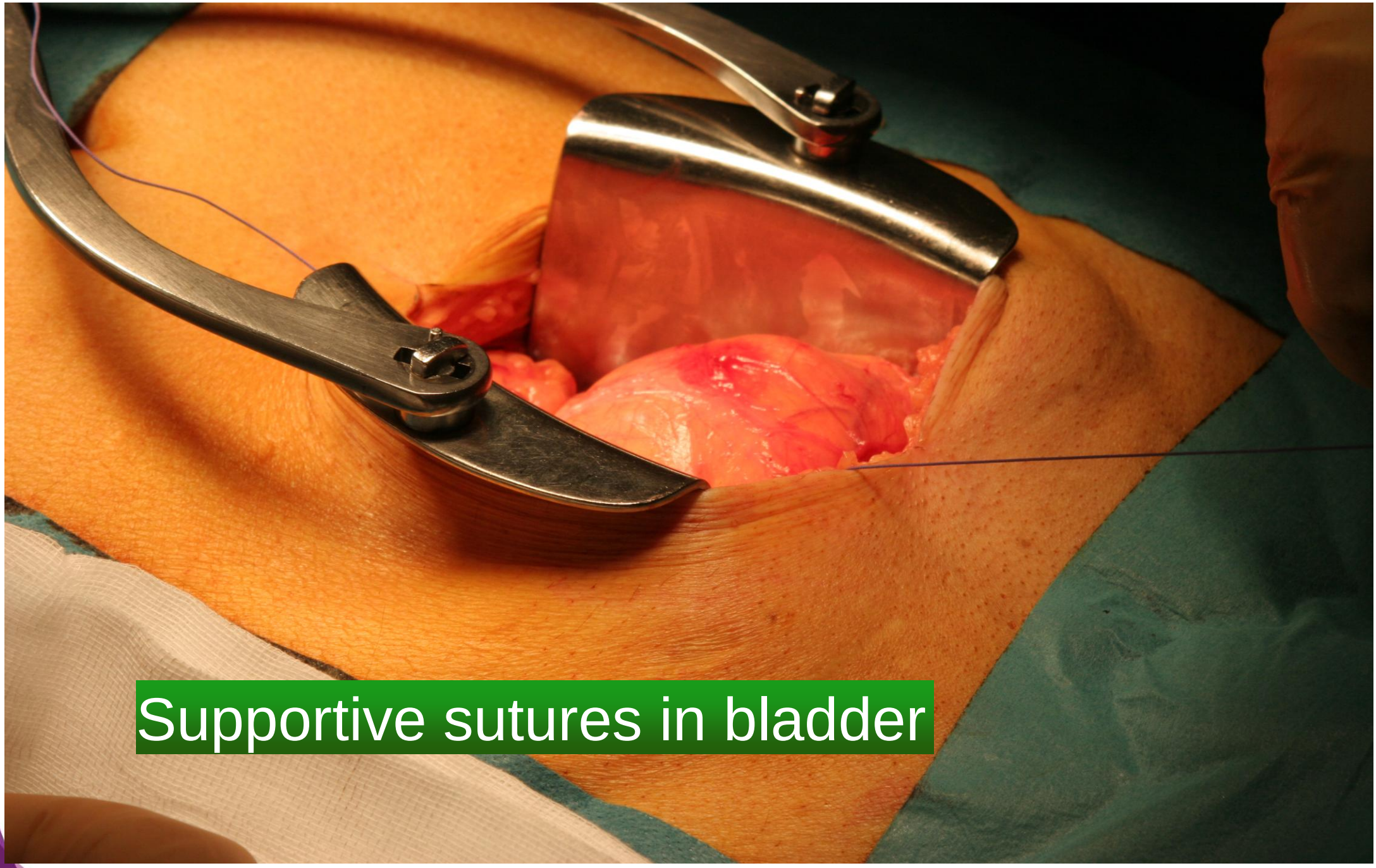

Bladder is visible



Supportive sutures in bladder

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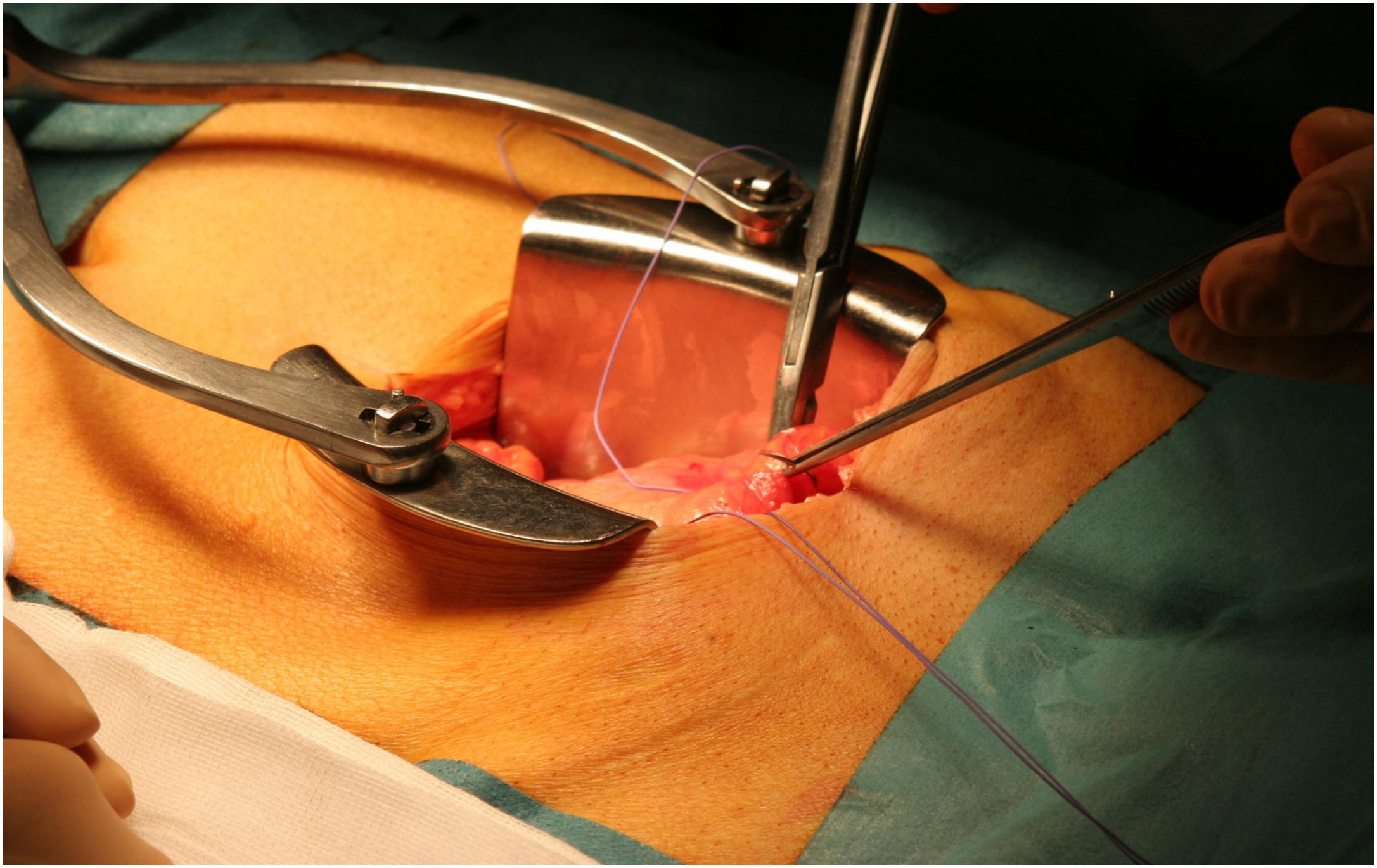

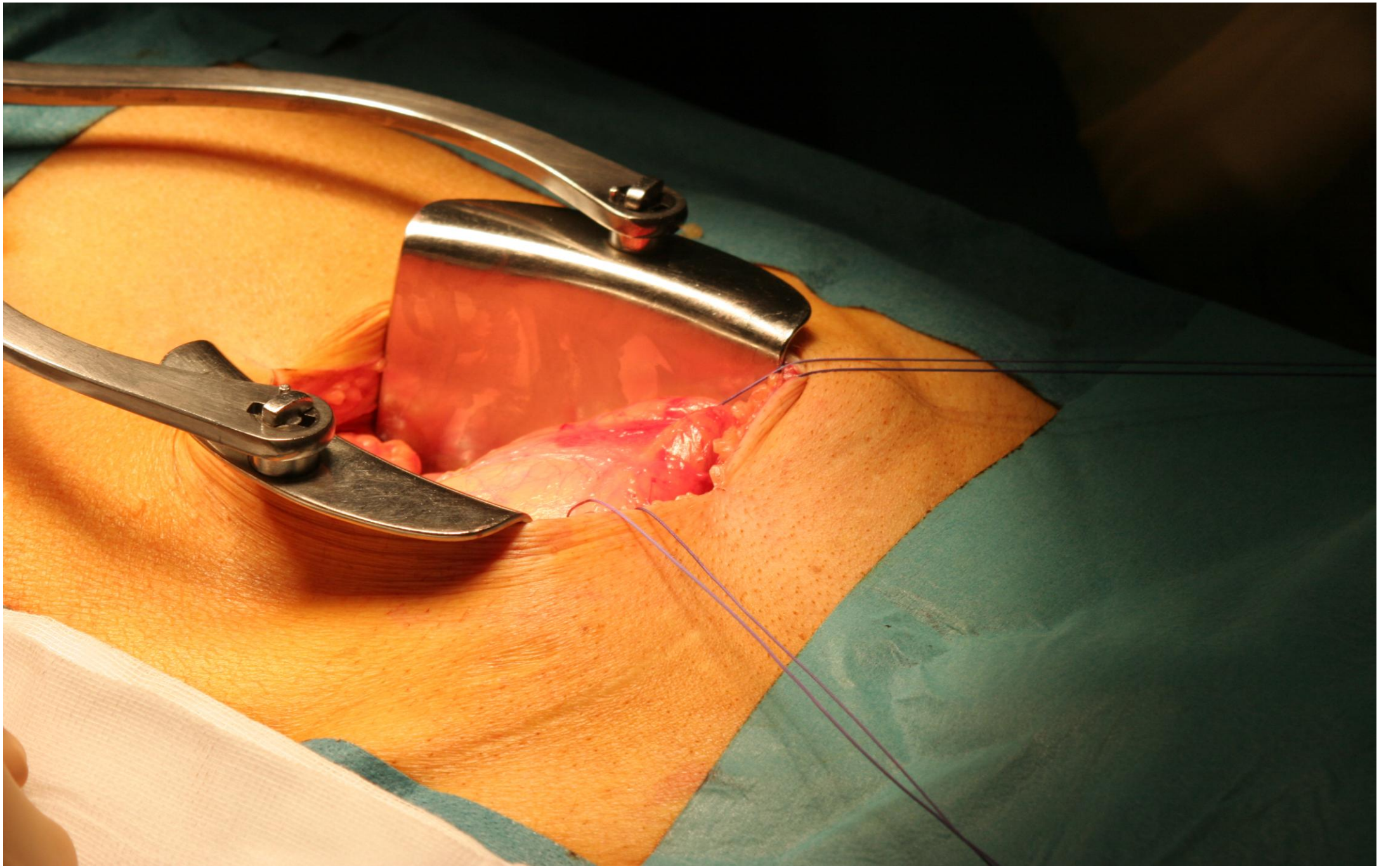

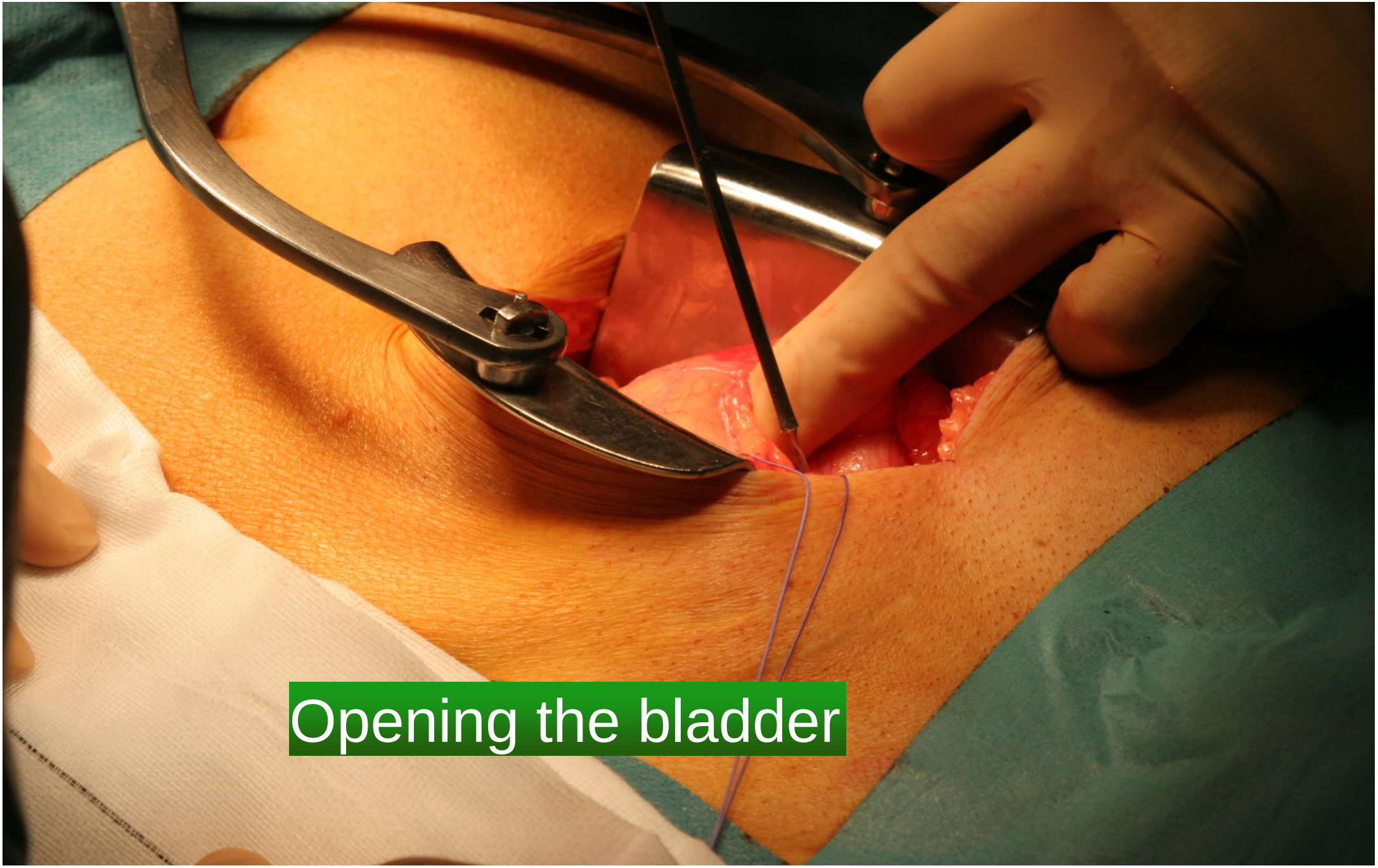

Opening the bladder

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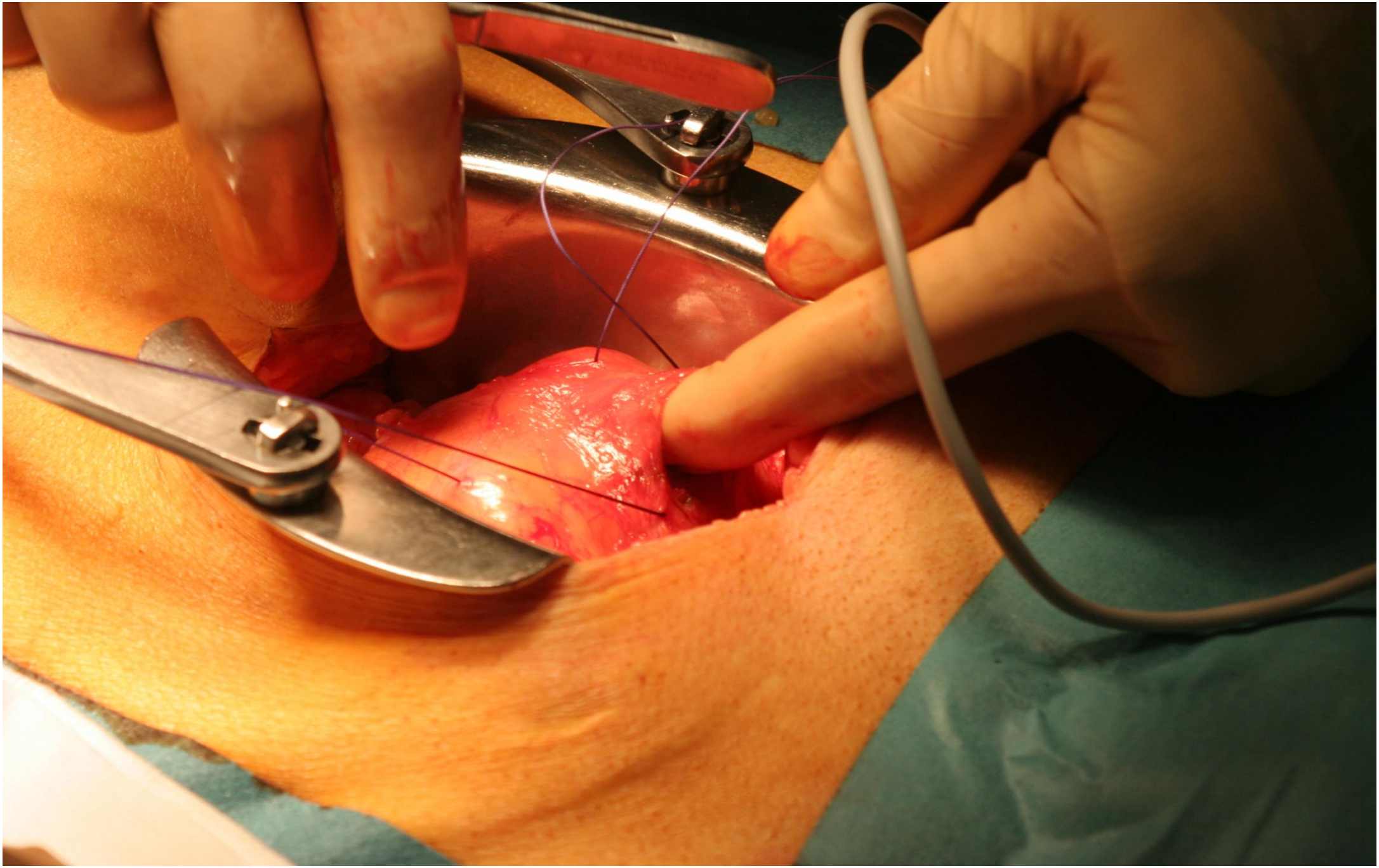

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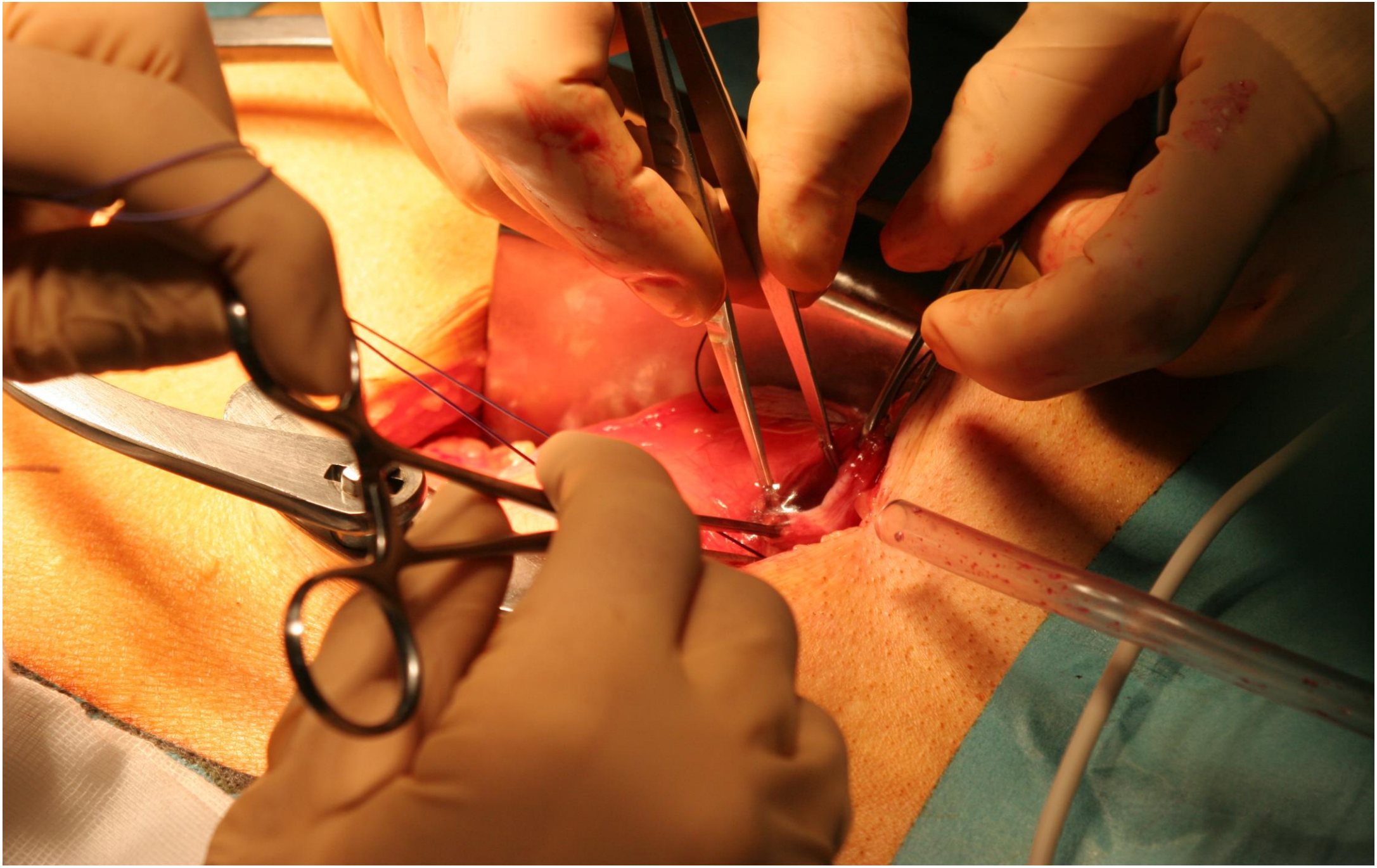

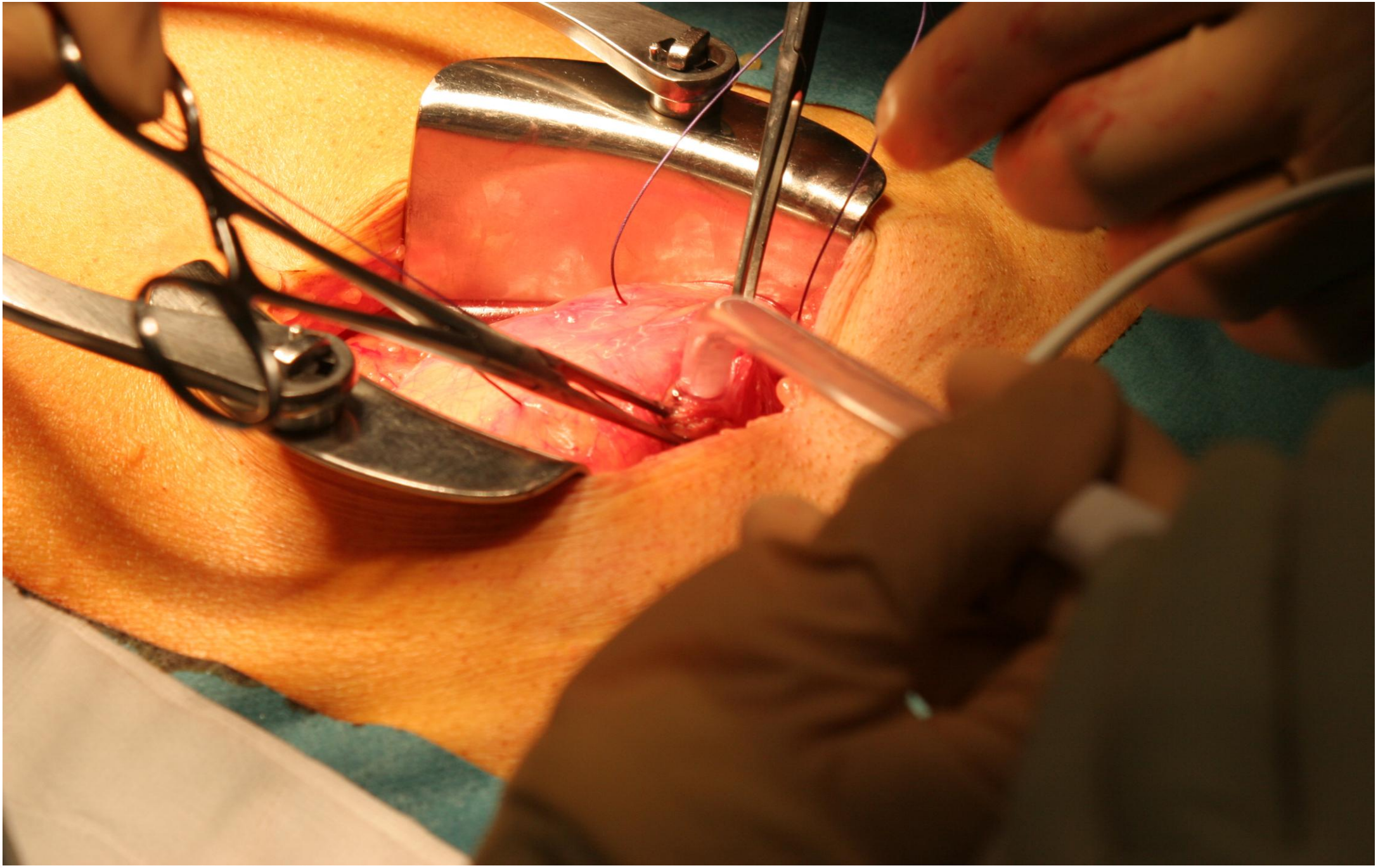

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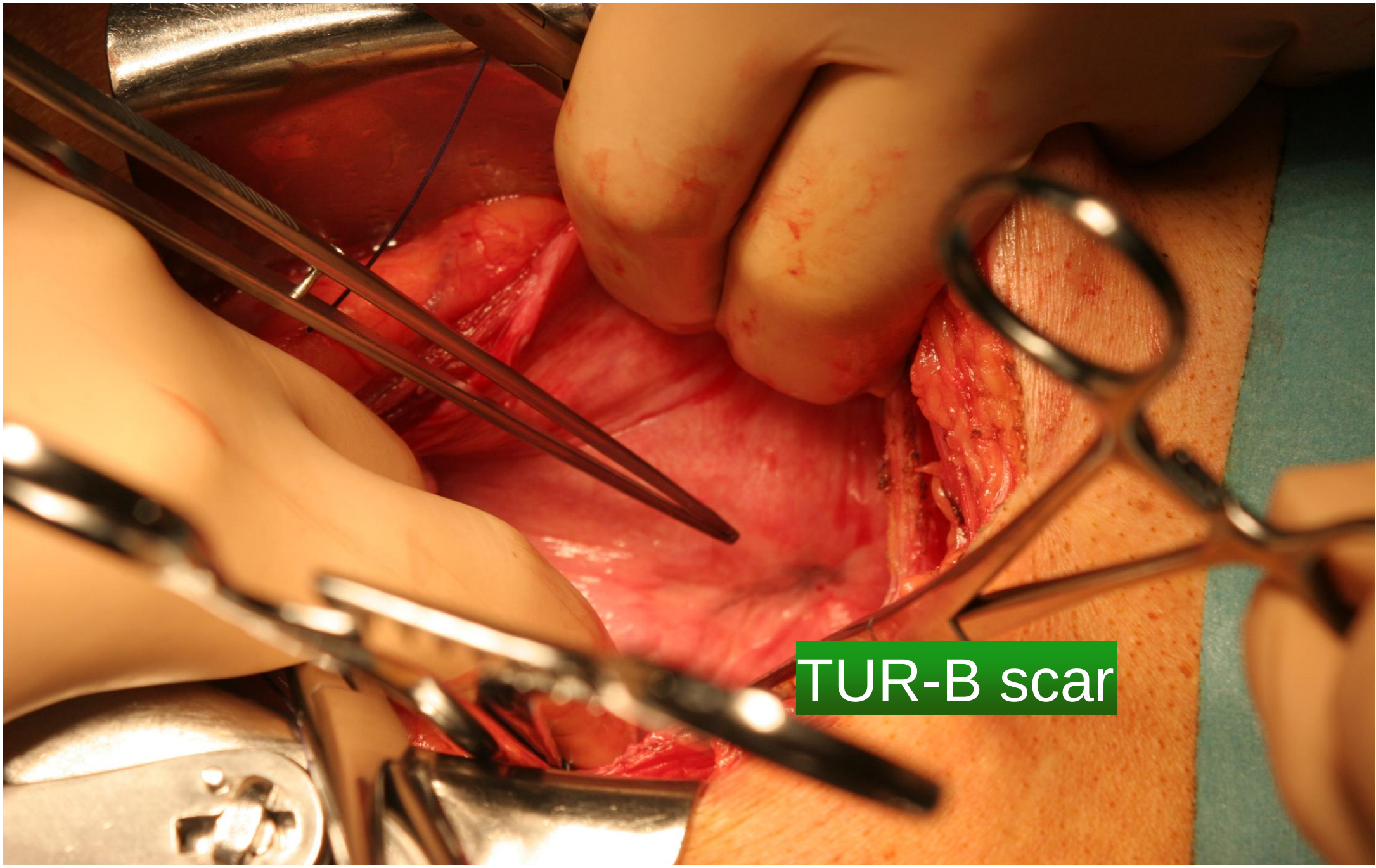
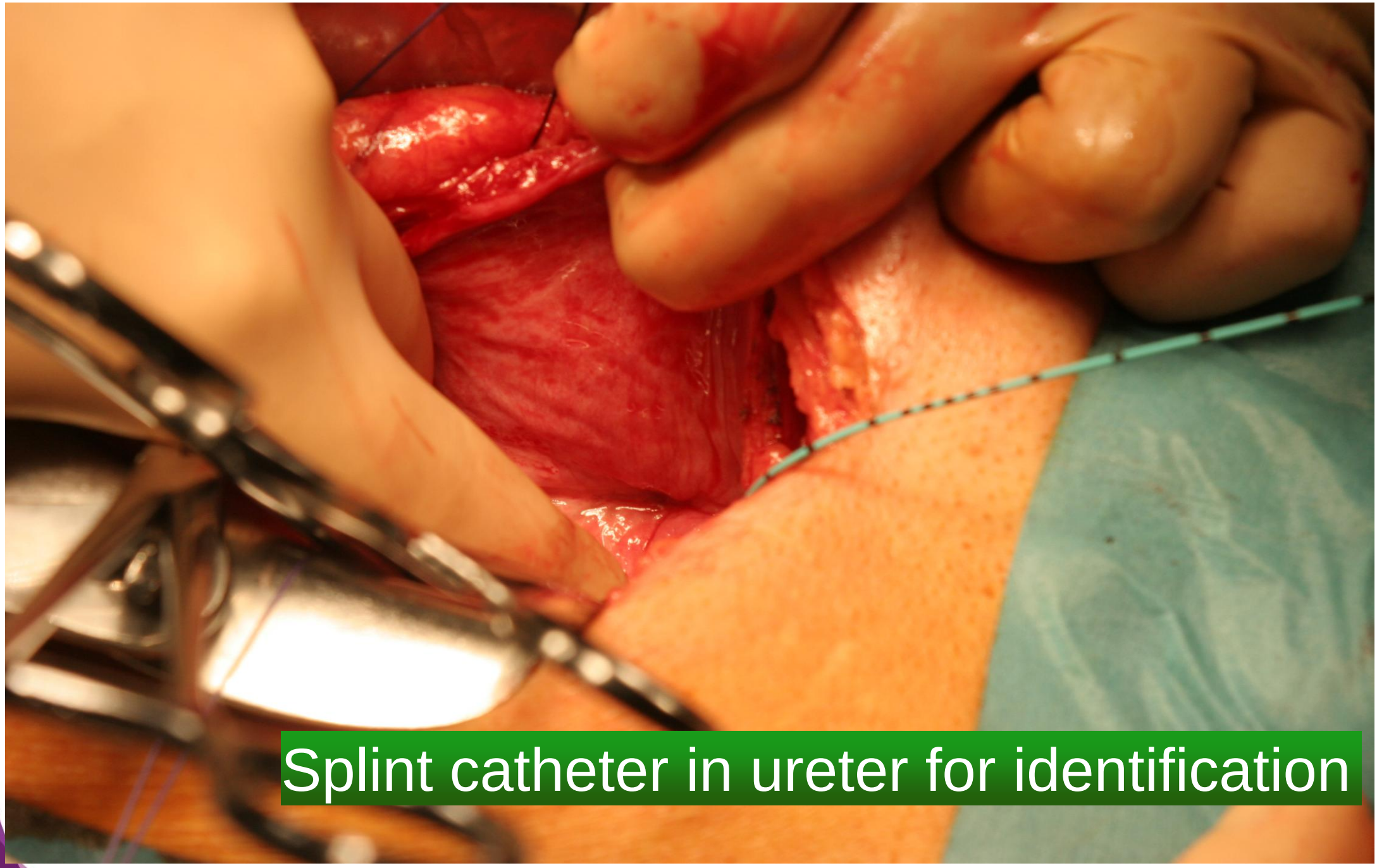
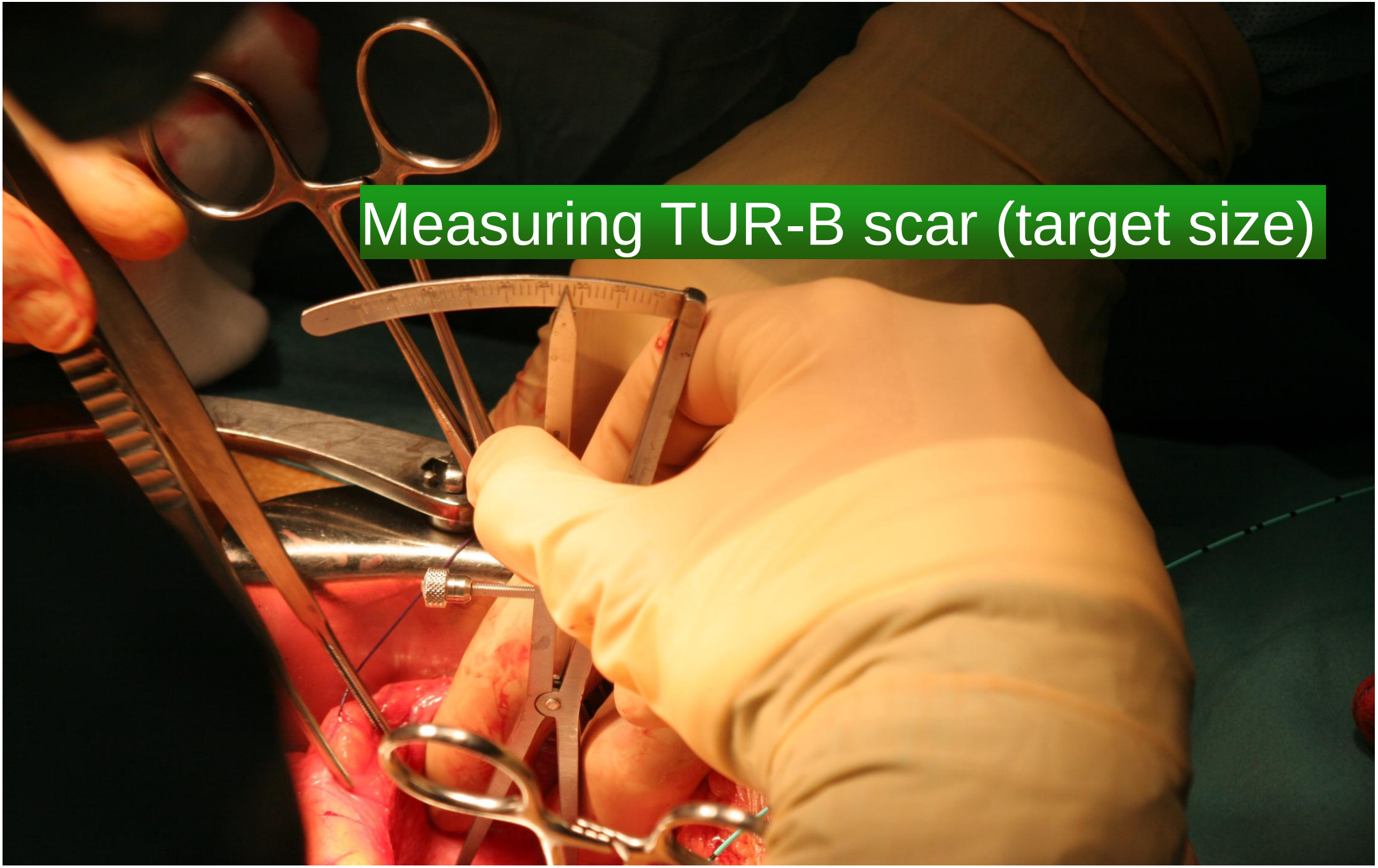
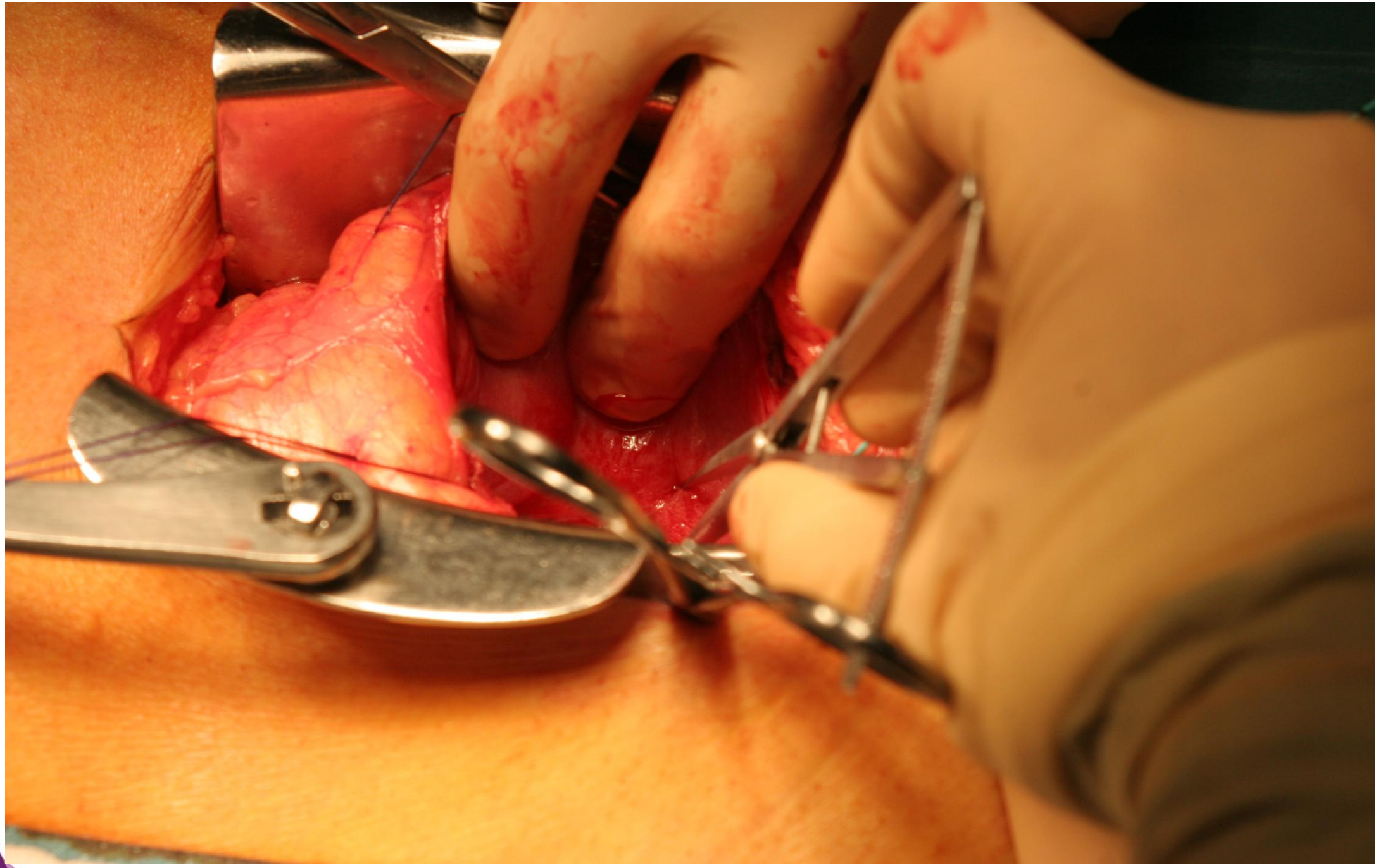
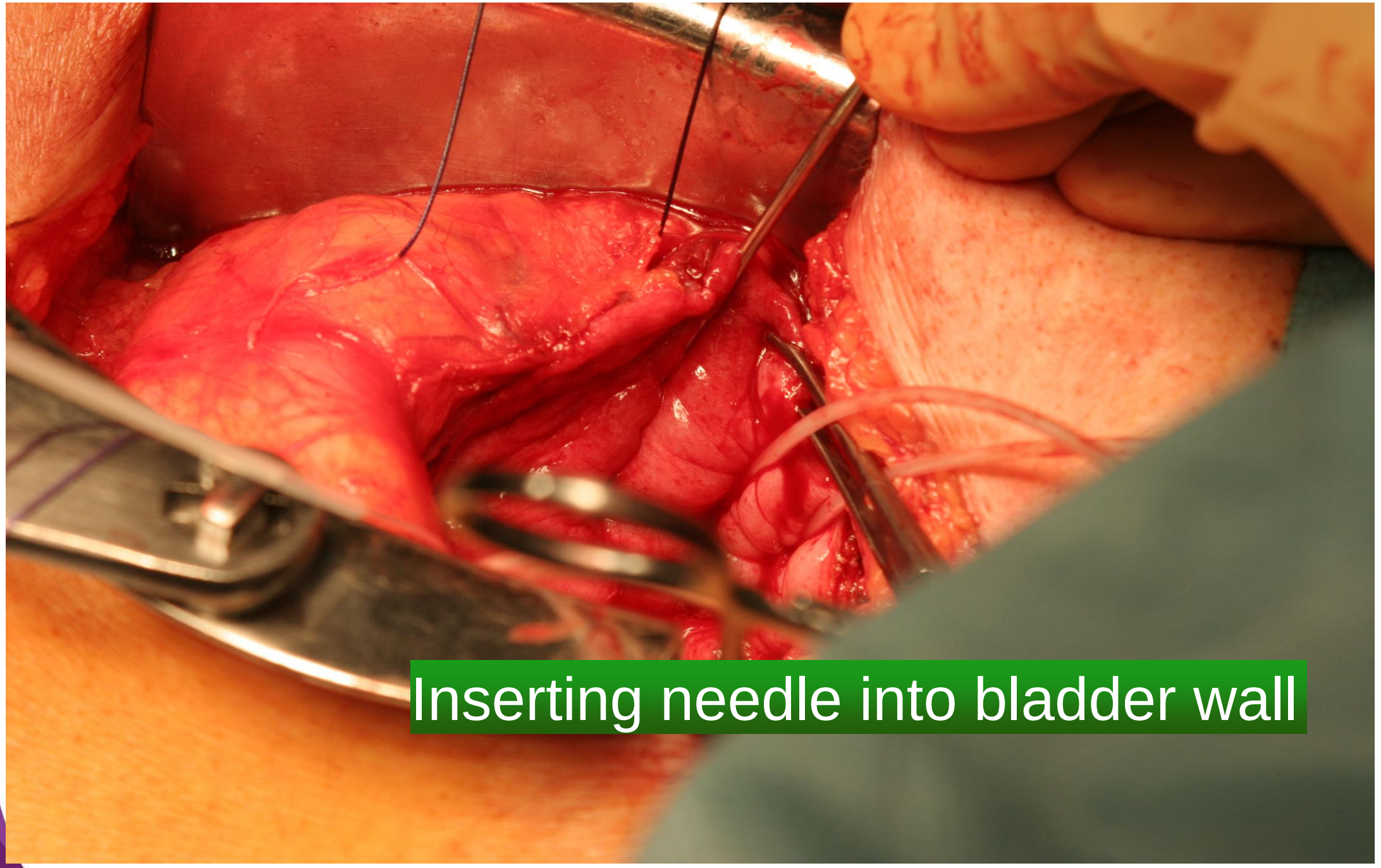

TUR-B scar


Splint catheter in ureter for identification


Measuring TUR-B scar (target size)





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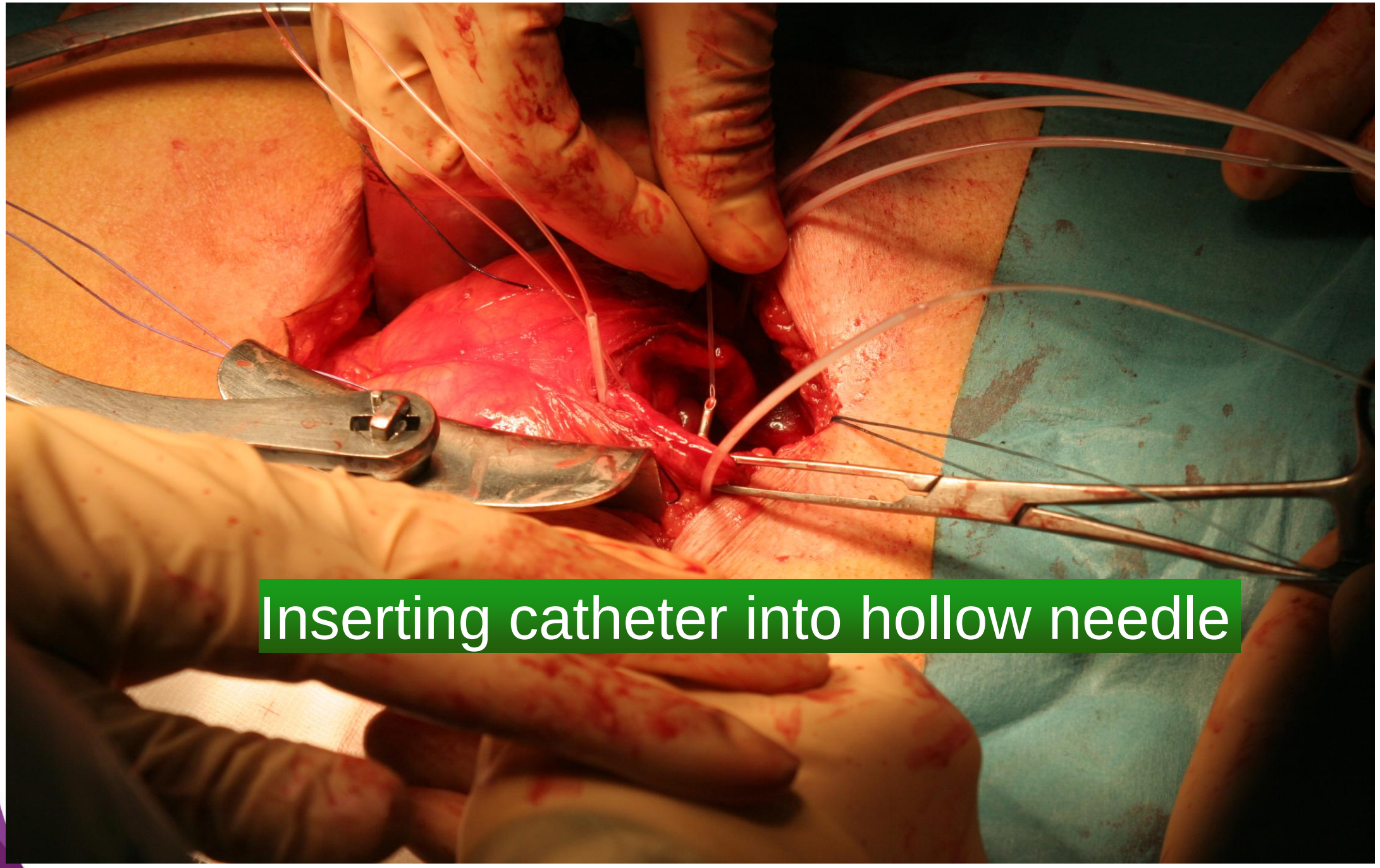

Inserting catheter into hollow needle

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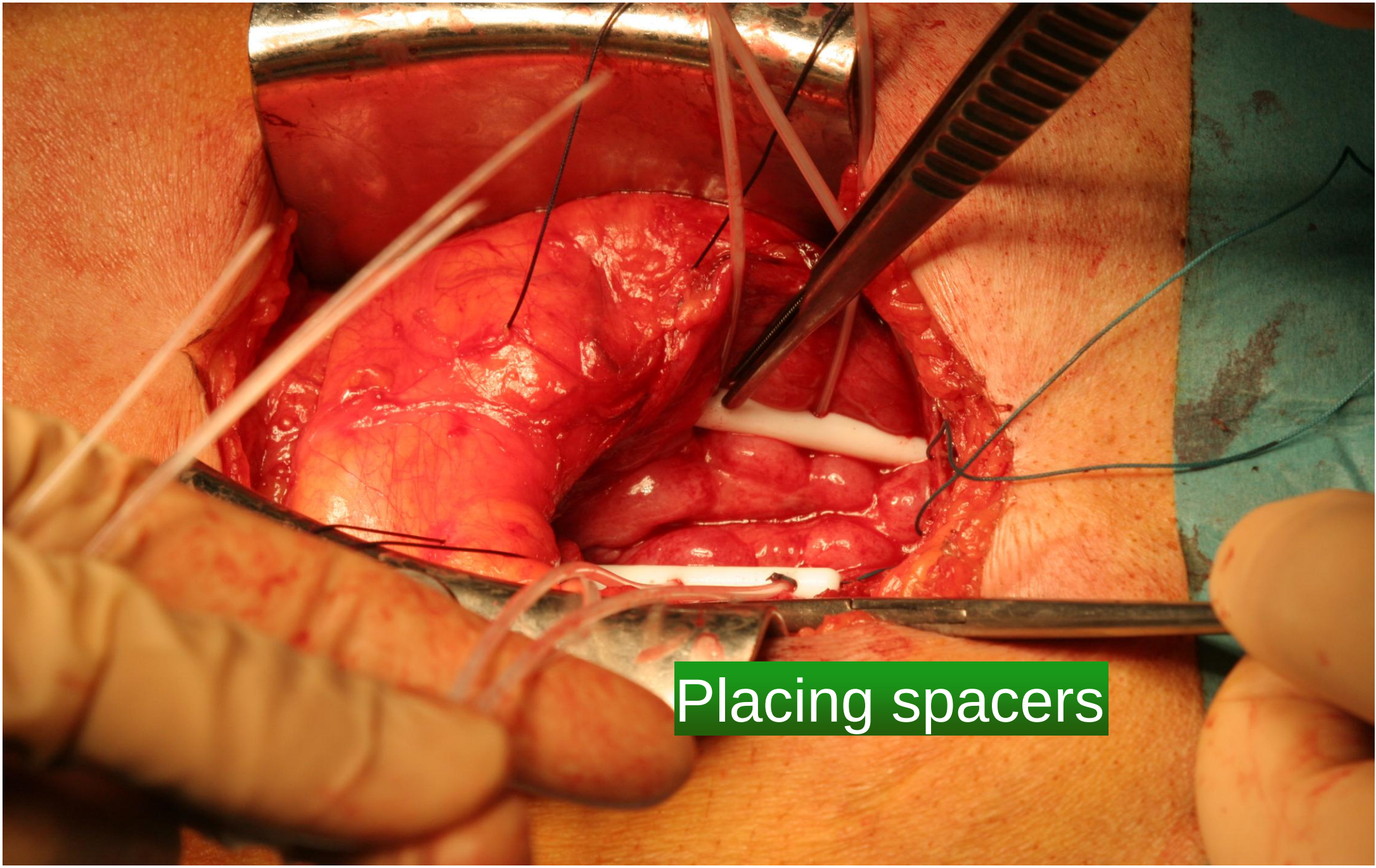

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Catheters through the bladder wall

Suturing spacers on the Foley-balloon catheter

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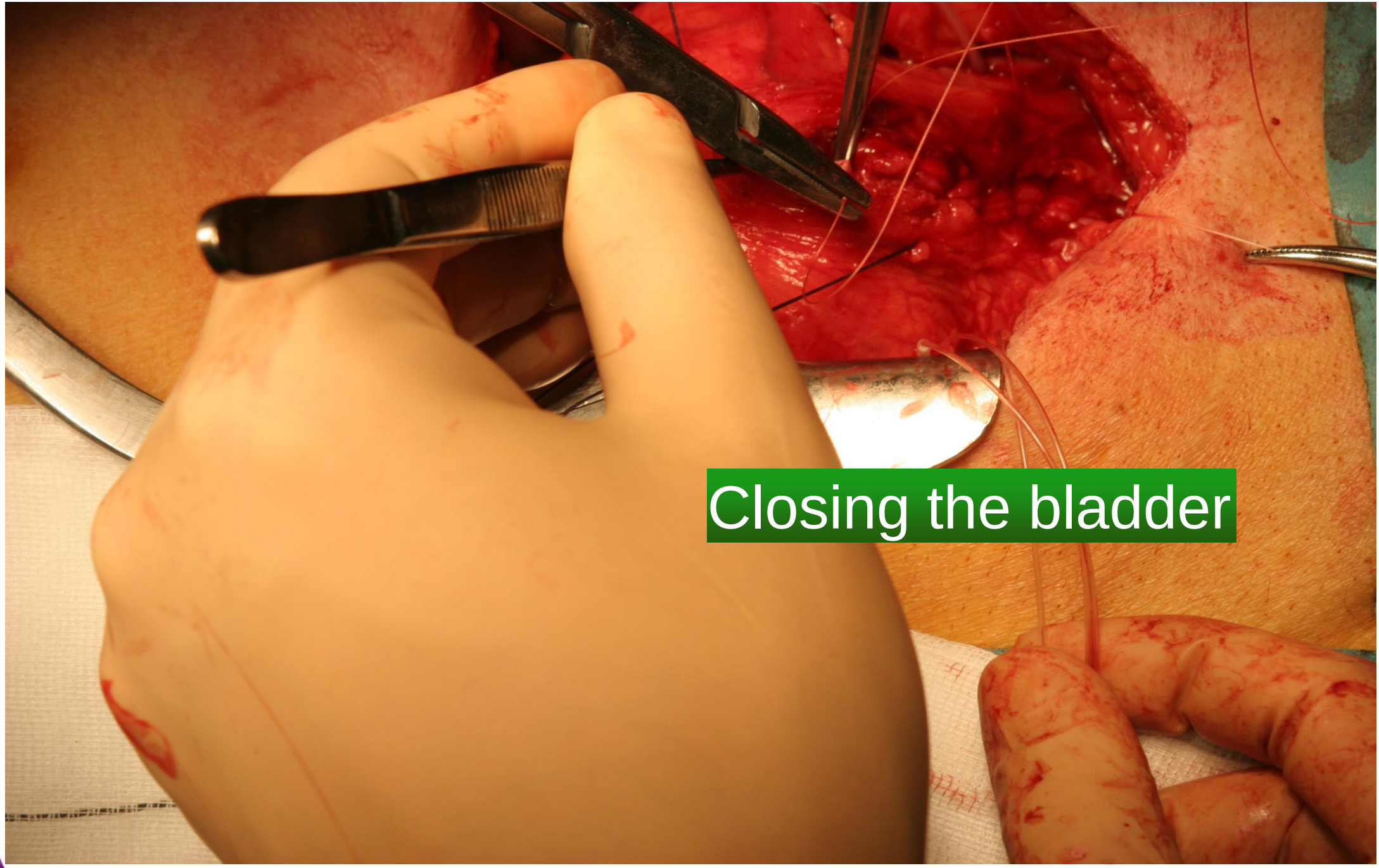
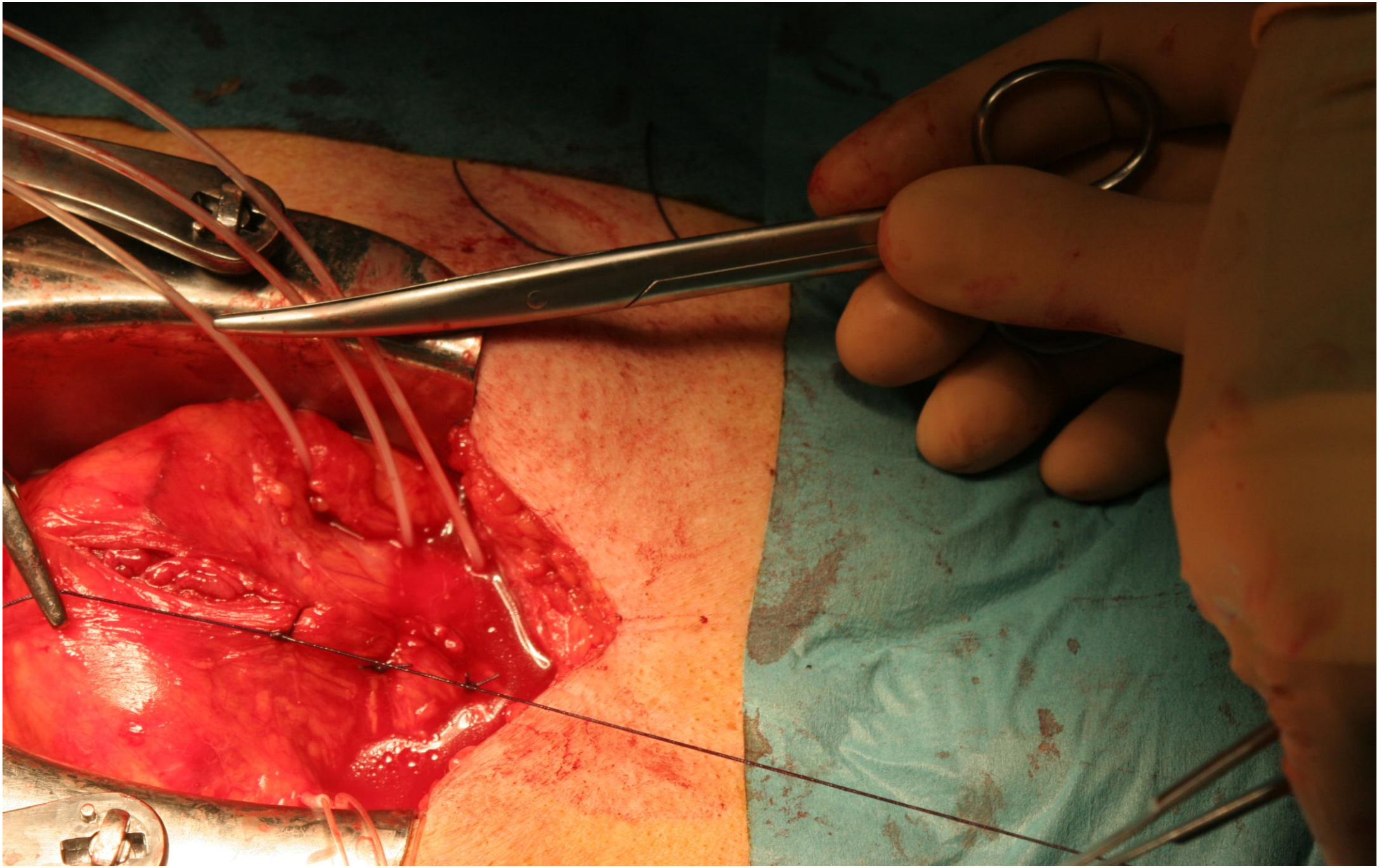

Closing the bladder



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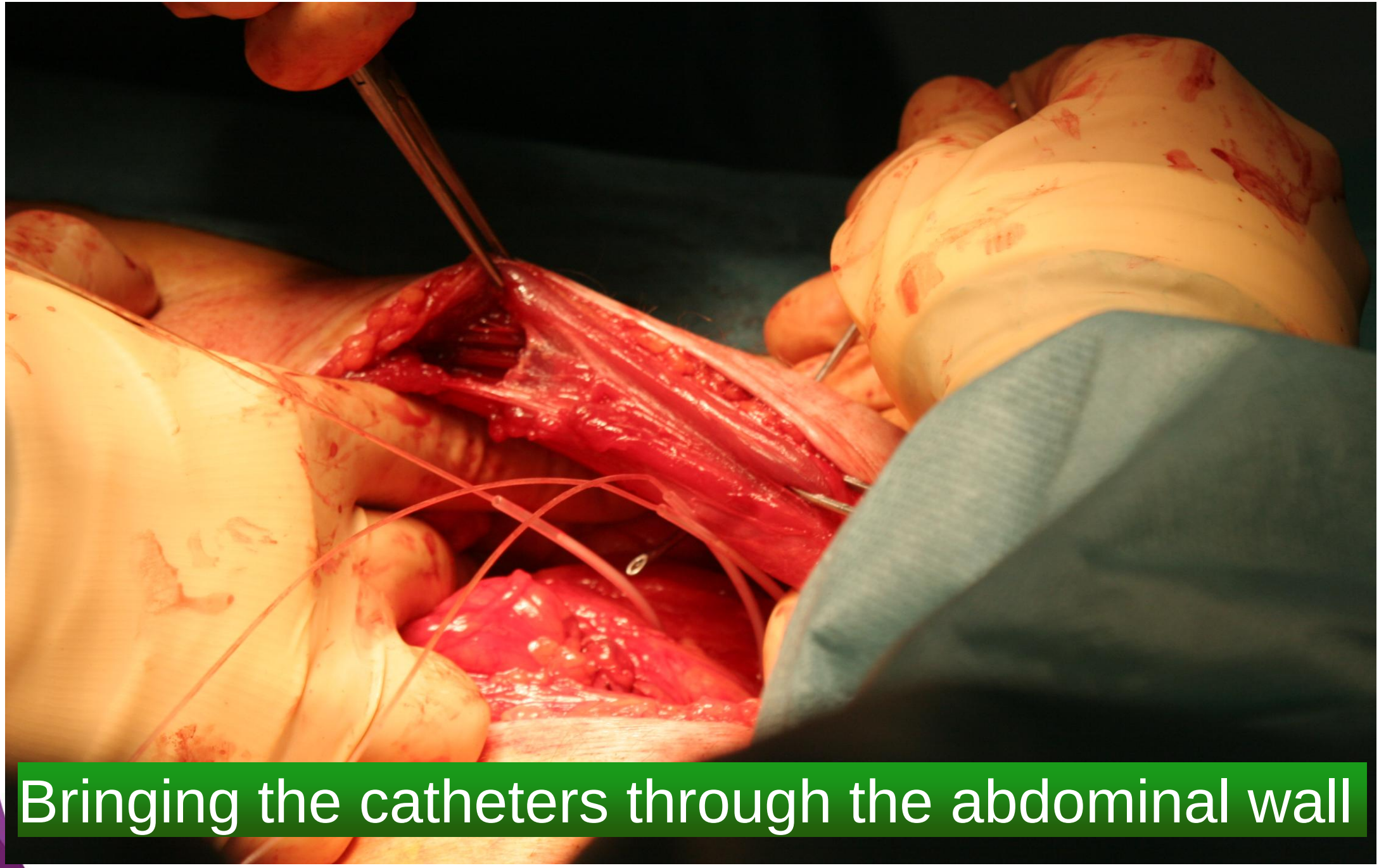

Bringing the catheters through the abdominal wall

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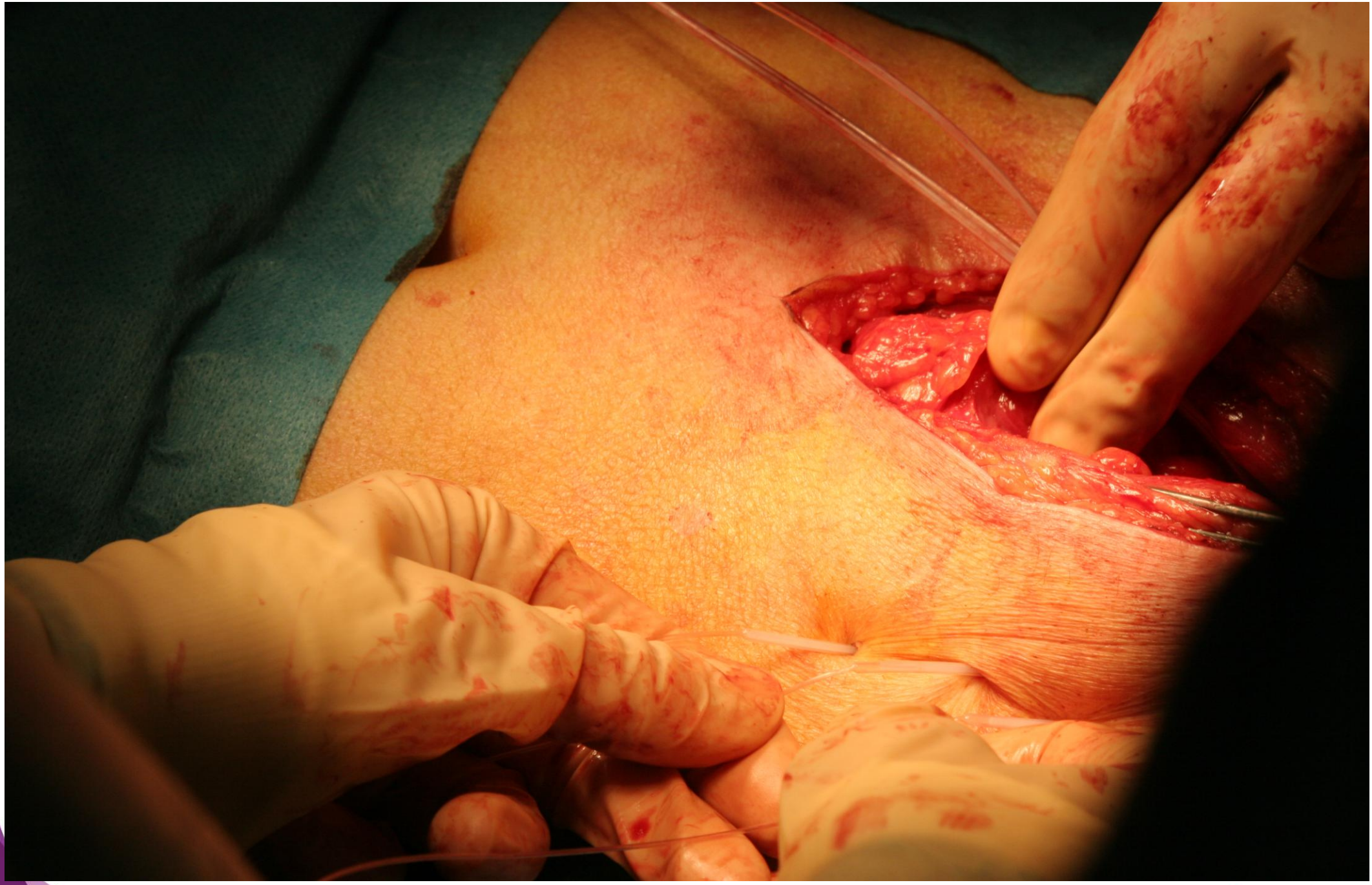

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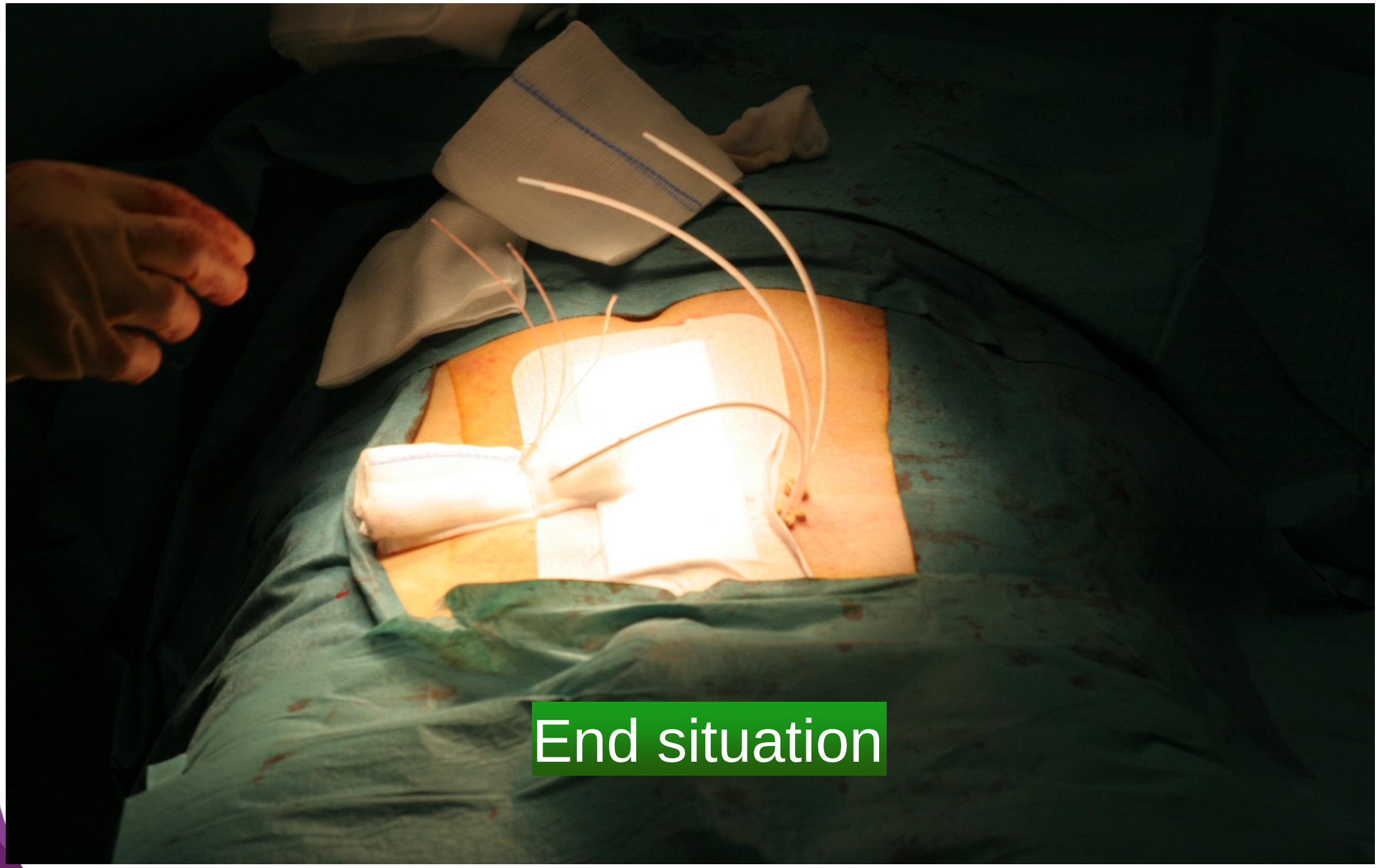

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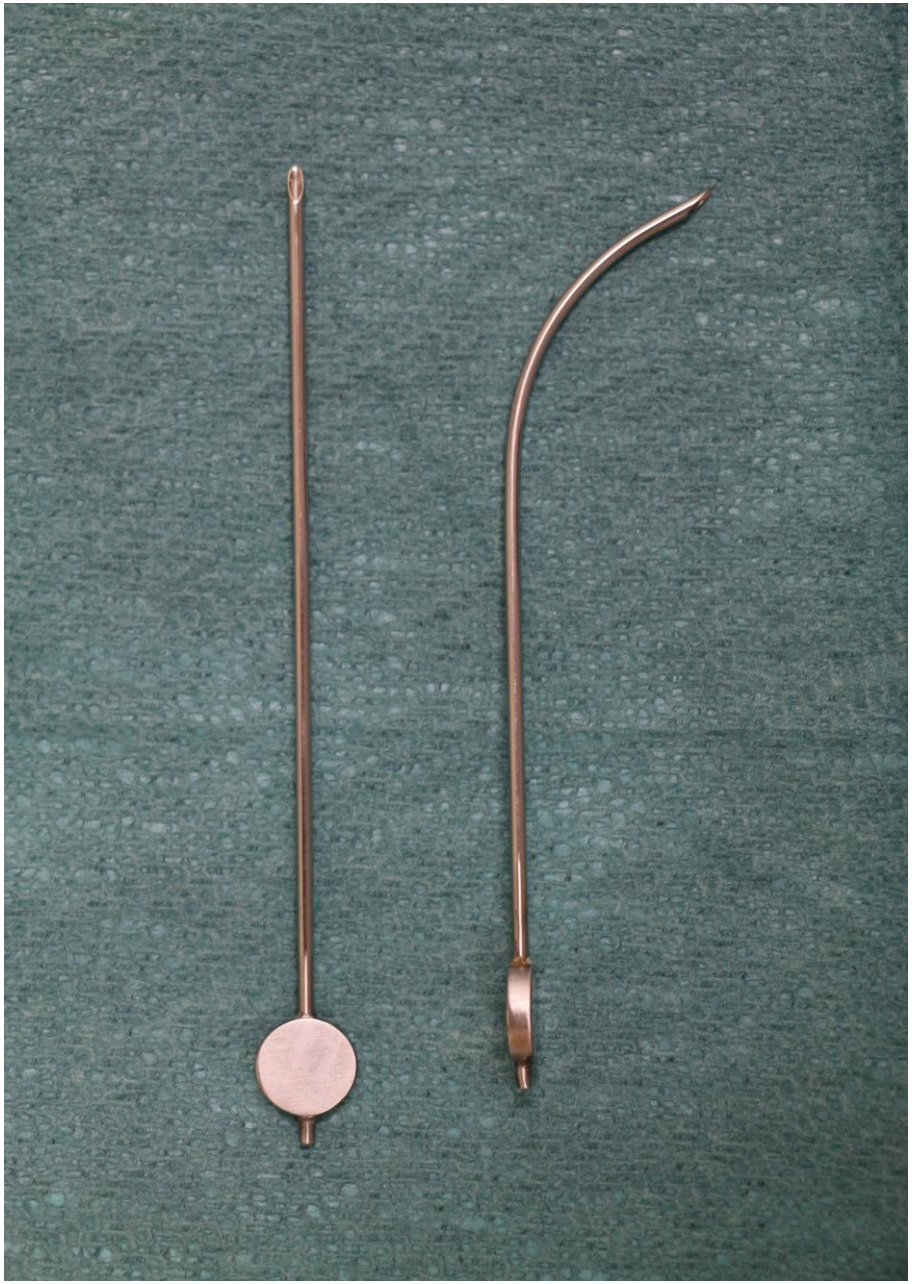

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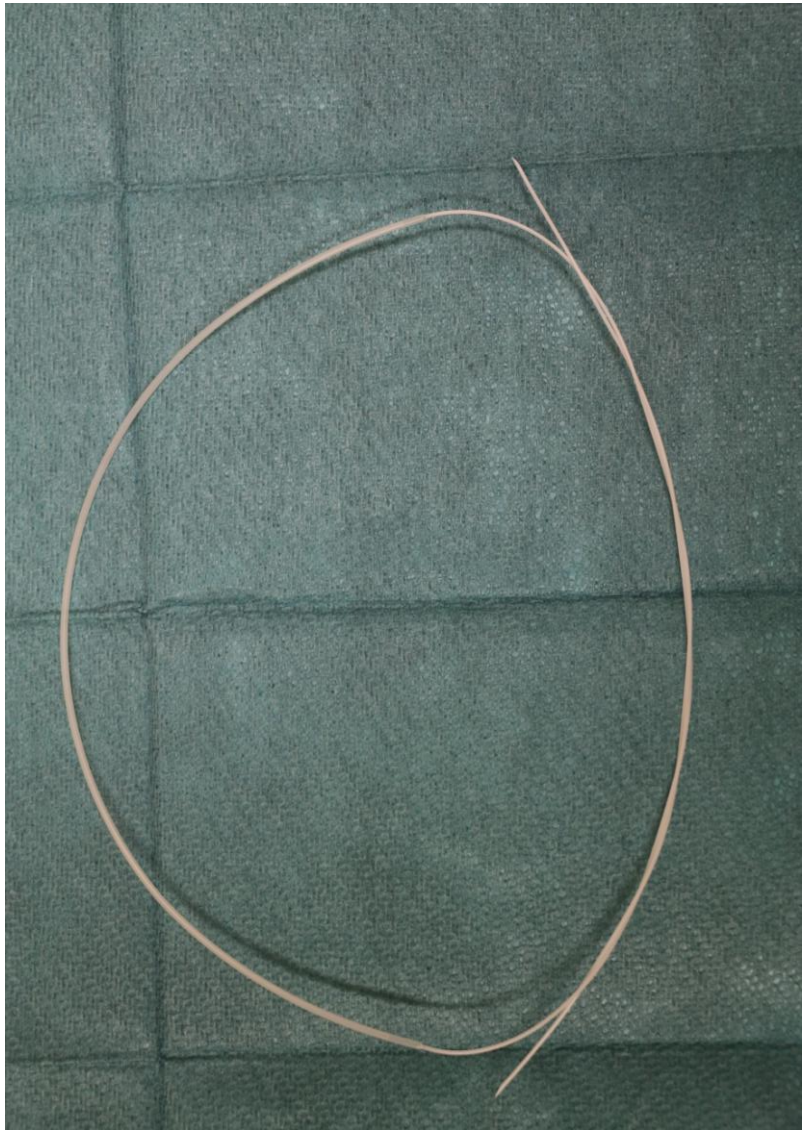

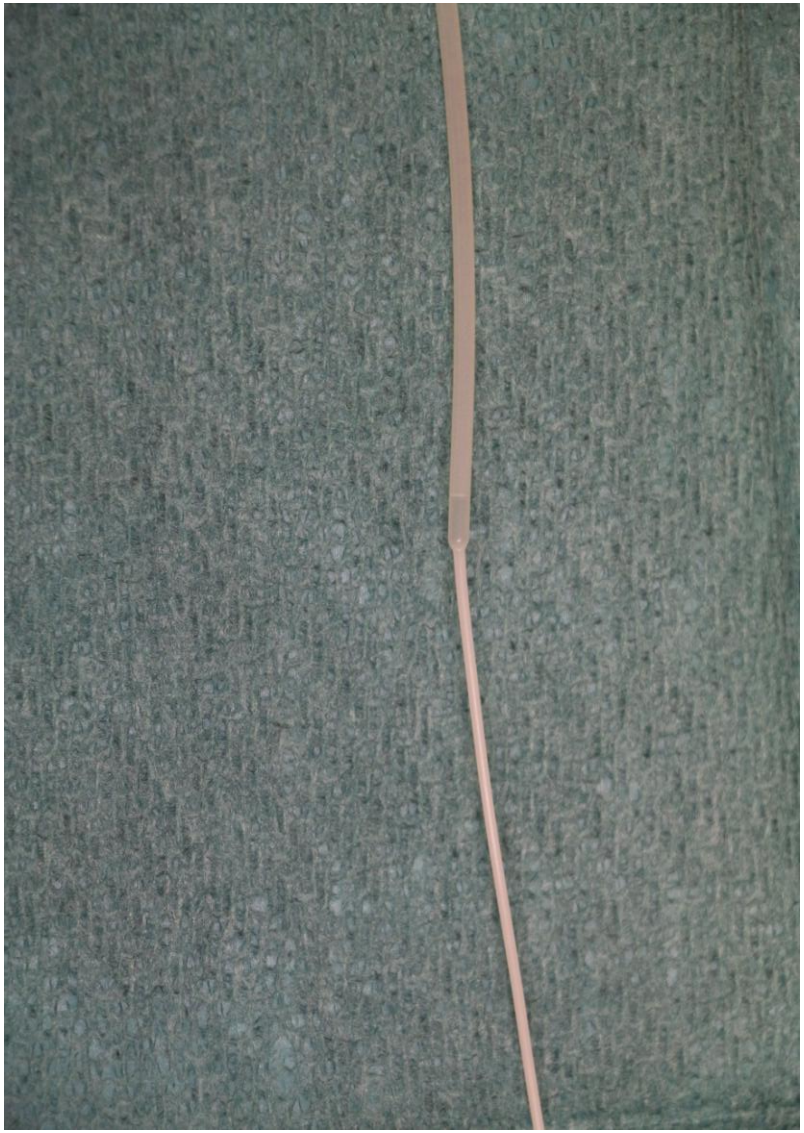

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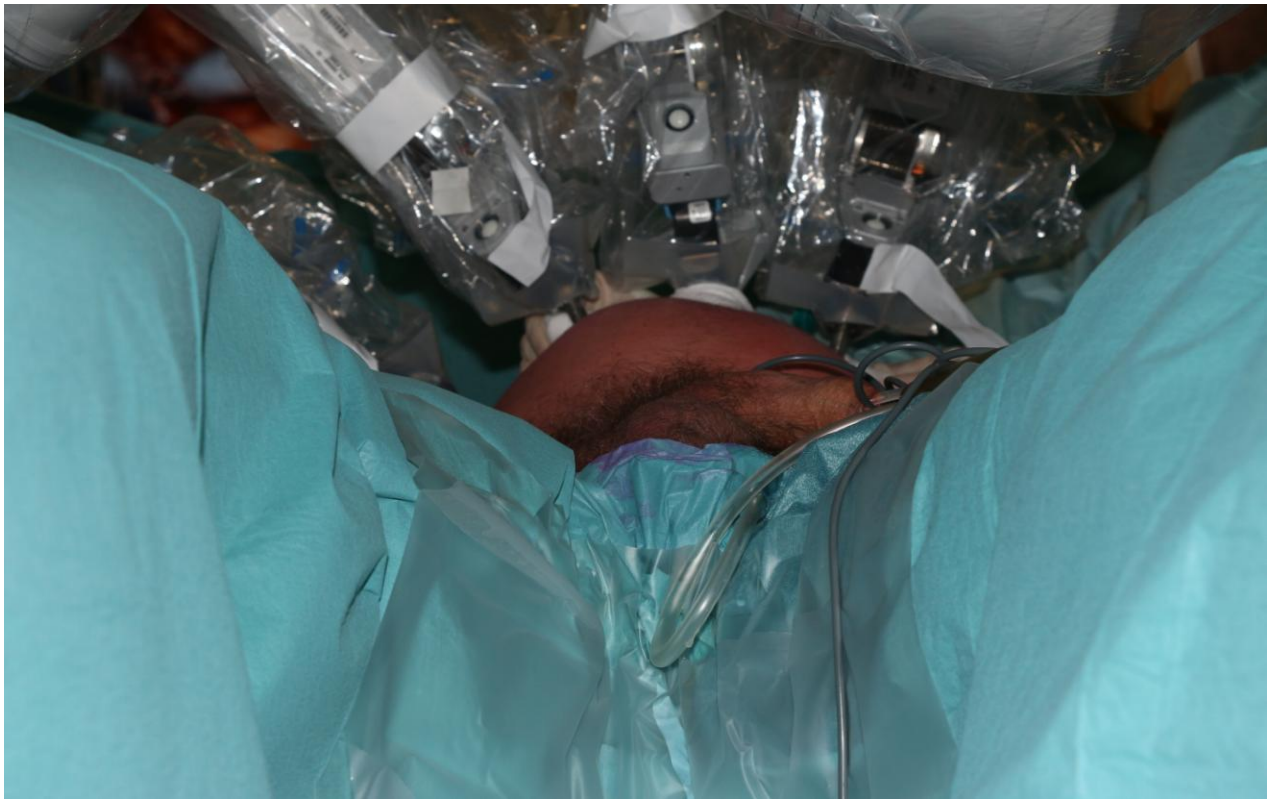
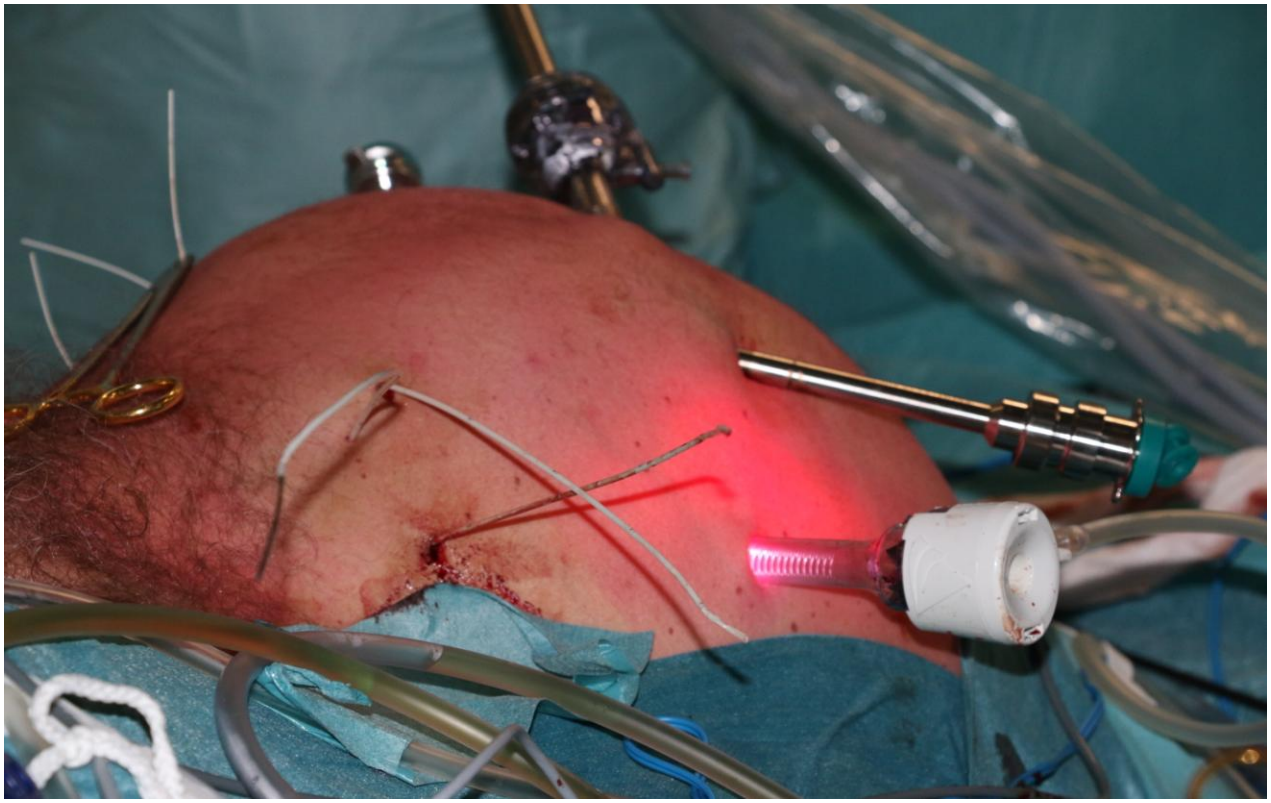
LAPAROSCOPIC ROBOT-ASSISTED





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Operating robotic arm

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Cytoscopy to identify TUR-B scar

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Laparoscopic view

Cystoscopic view

Courtesey of G. Smits

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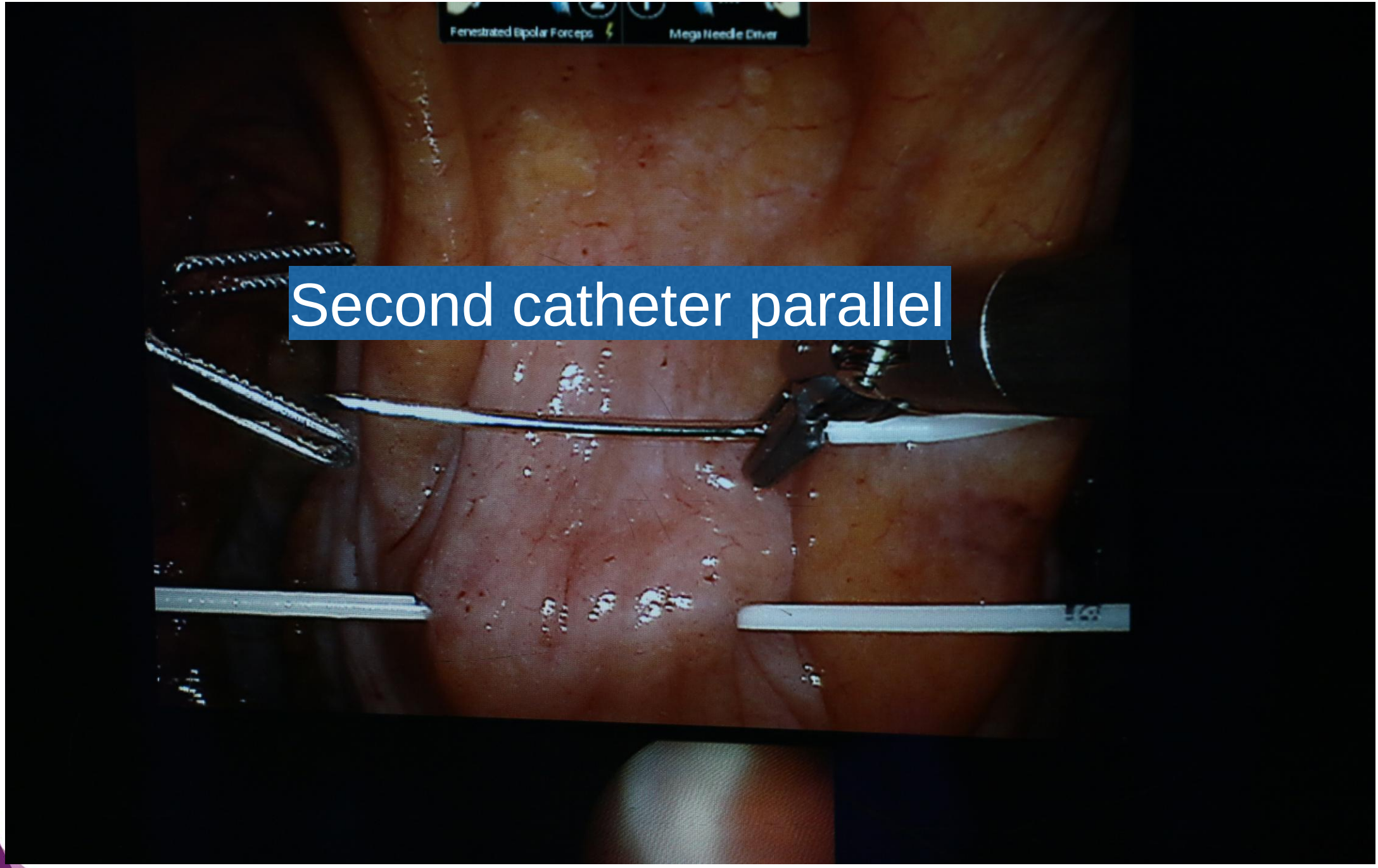
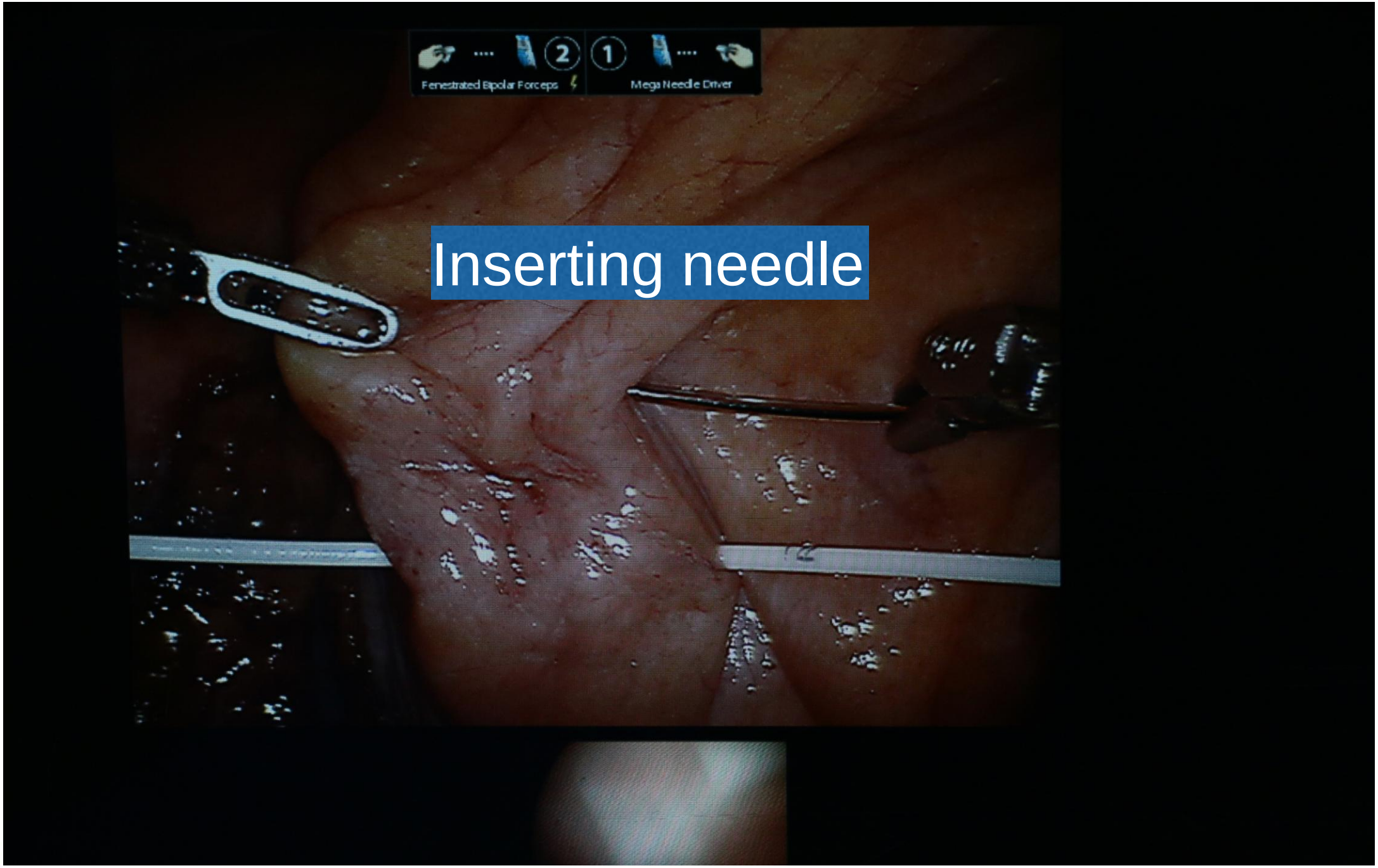
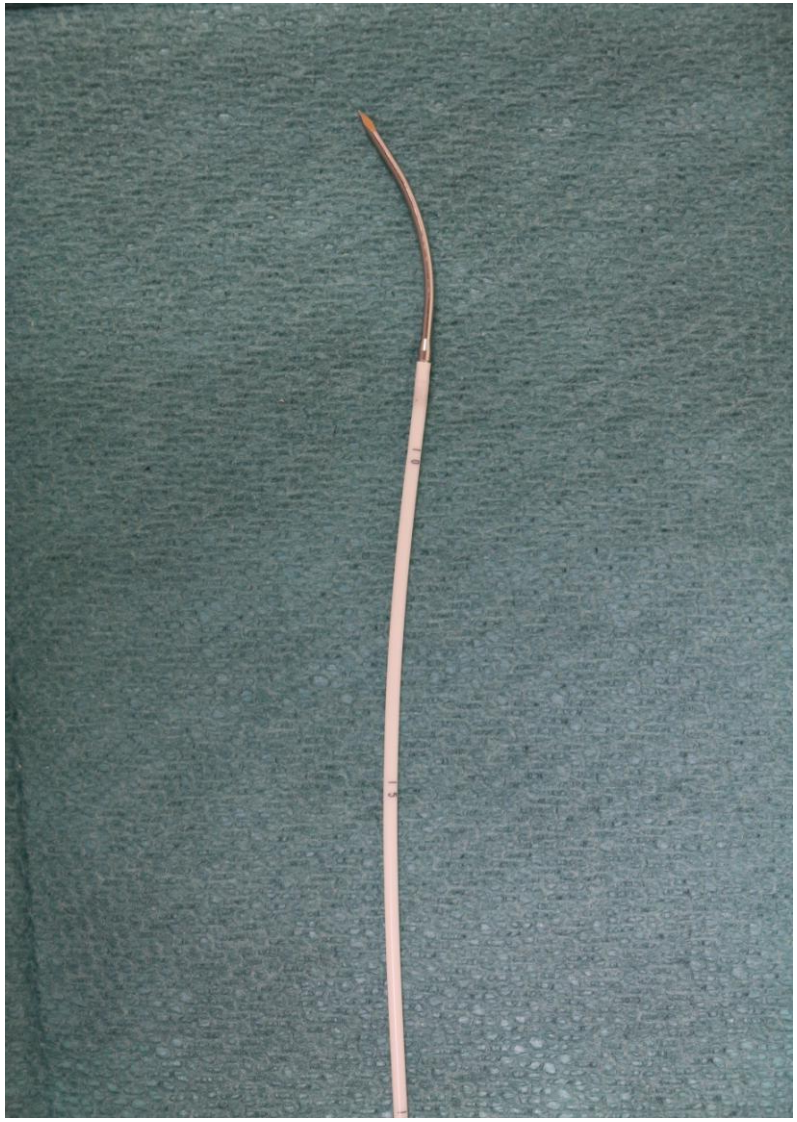
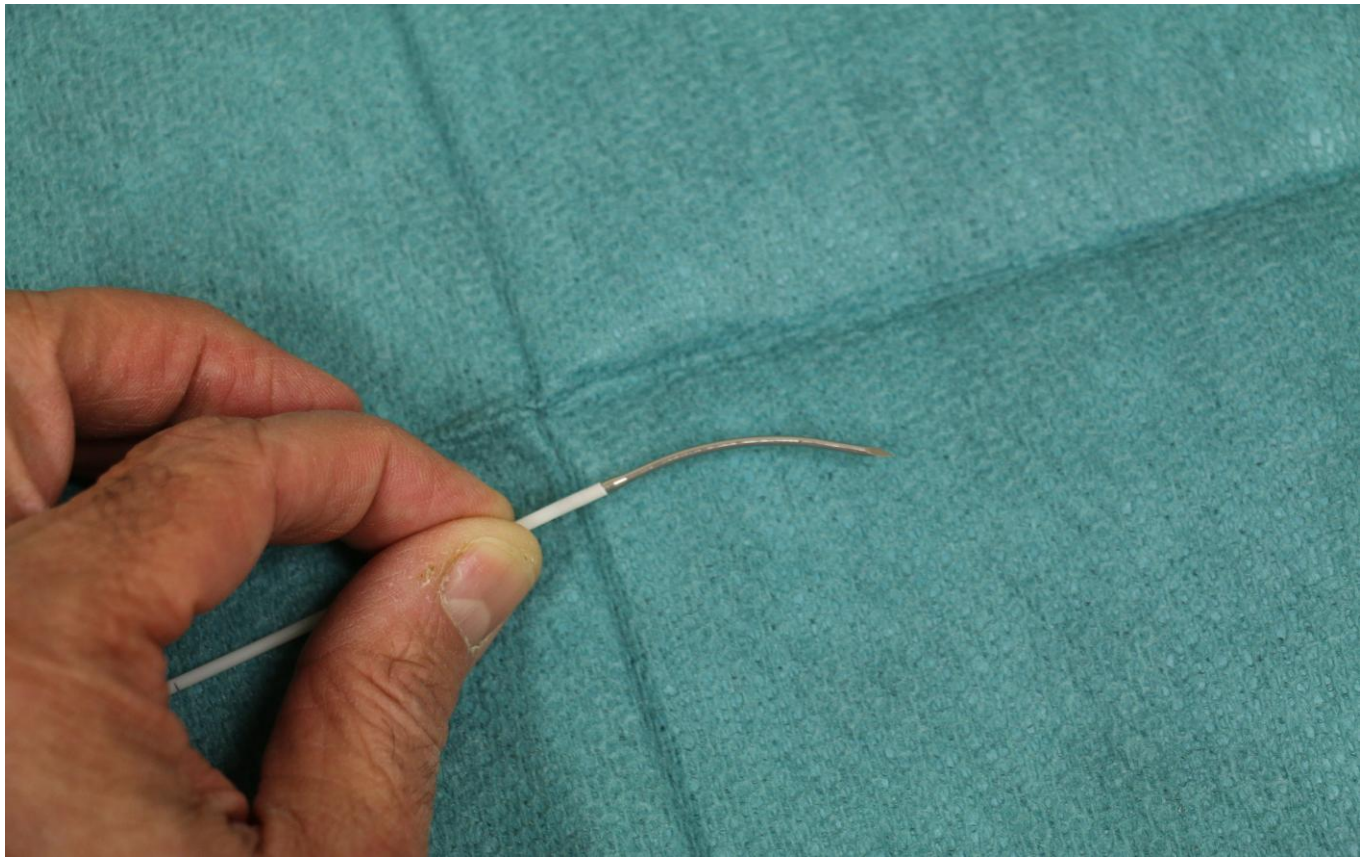
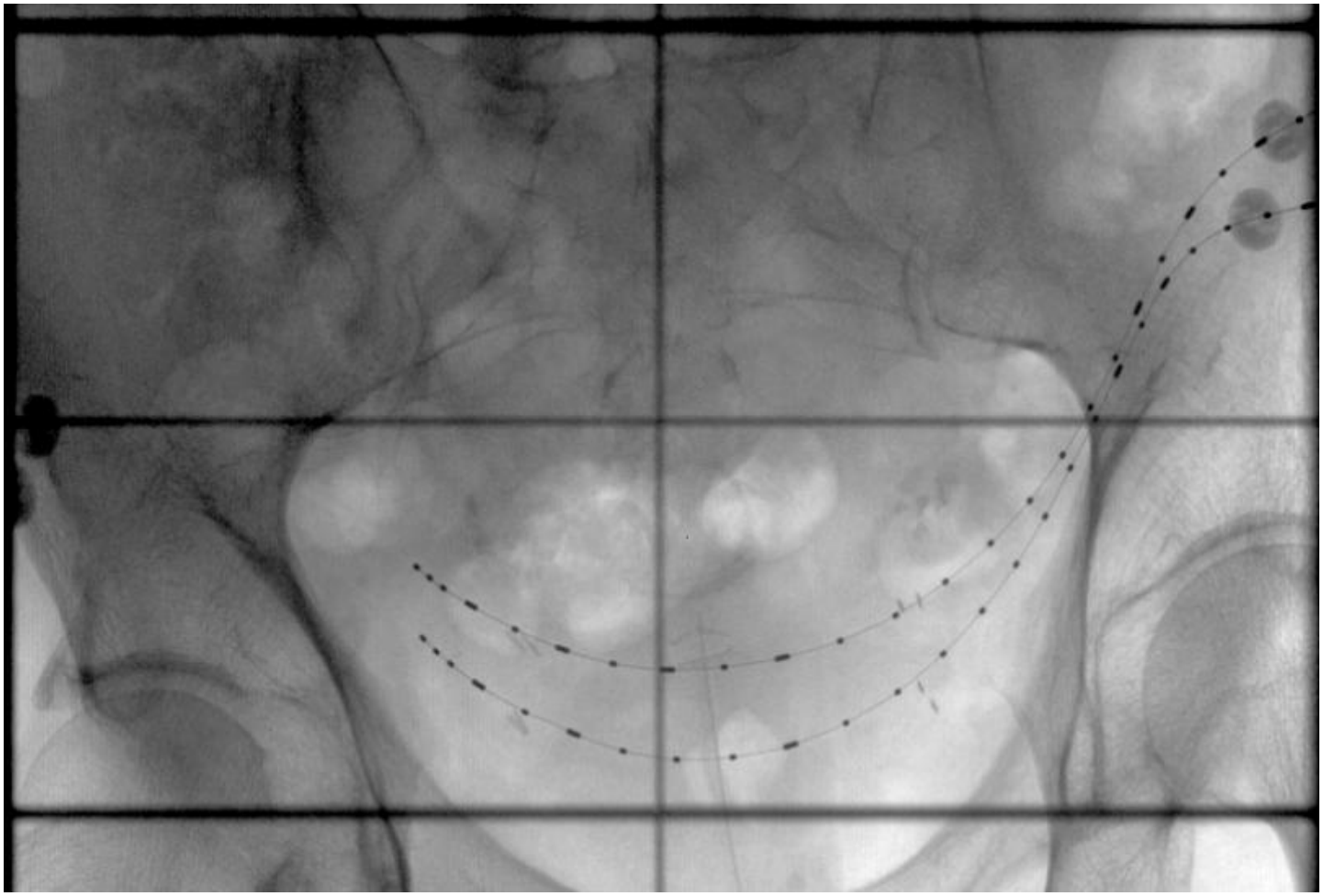

Fenestrated Bipolar Forceps
Mega Needle Driver
Second catheter parallel


Fenestrated Bipolar Forceps
Mega Needle Driver
Inserting needle



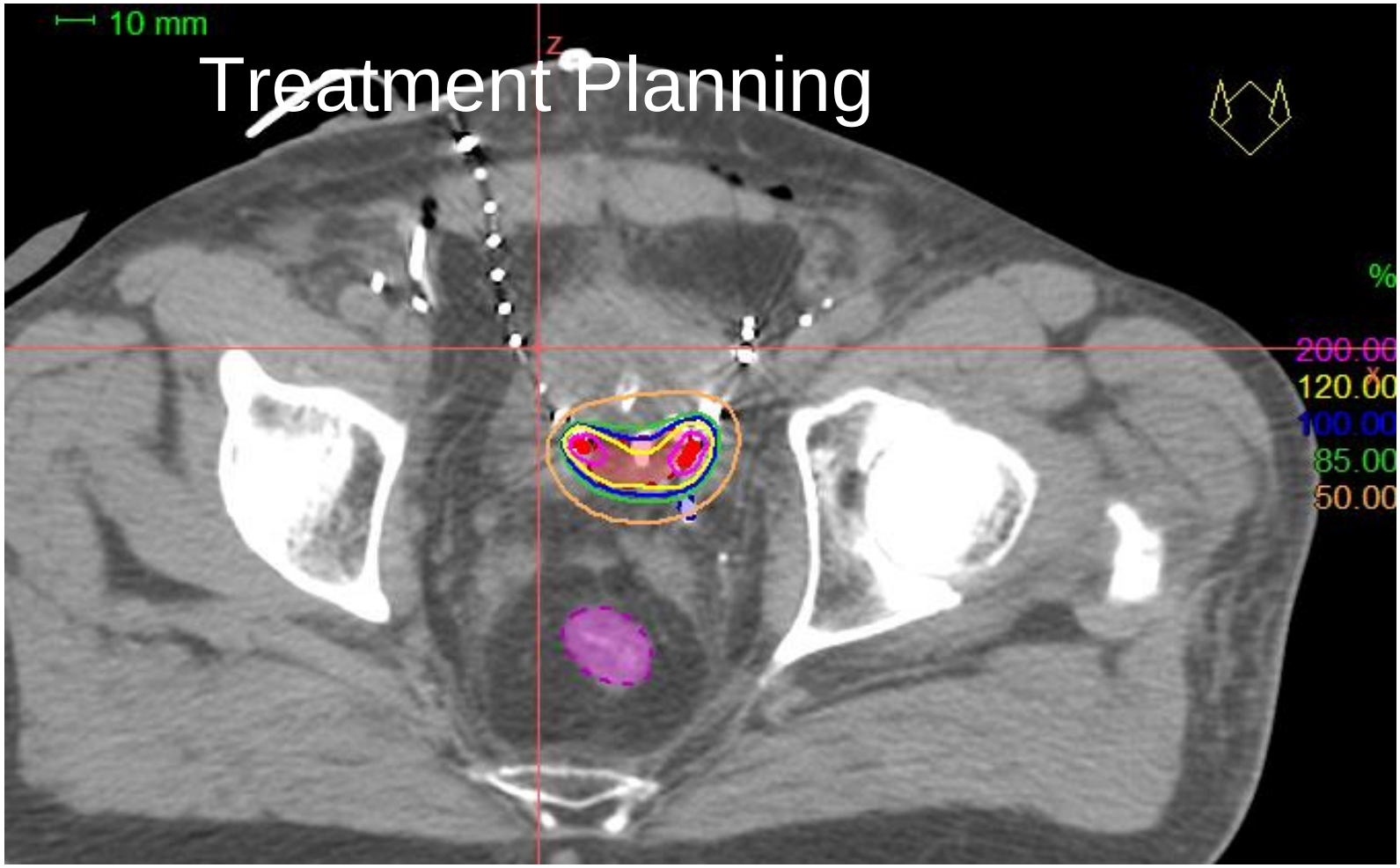


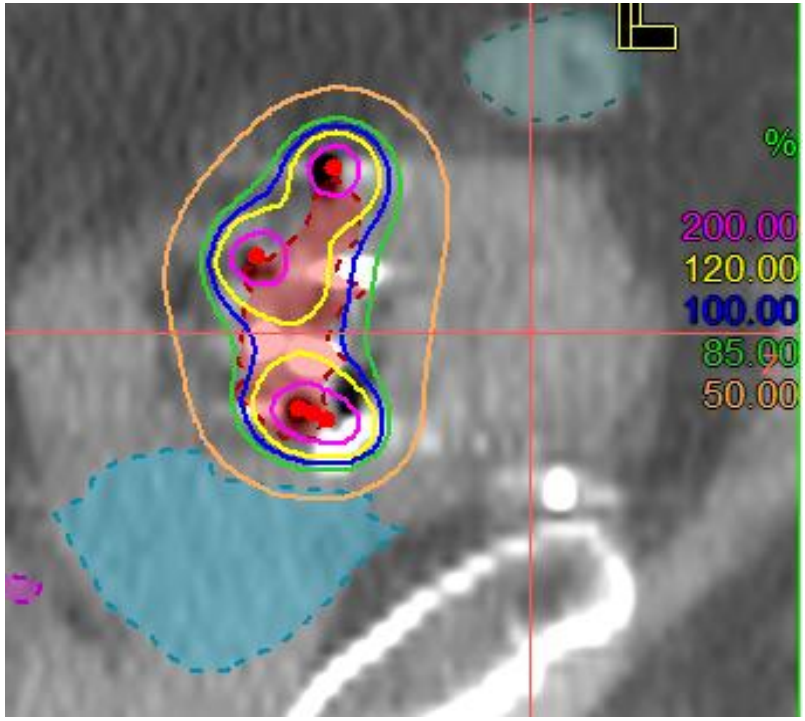


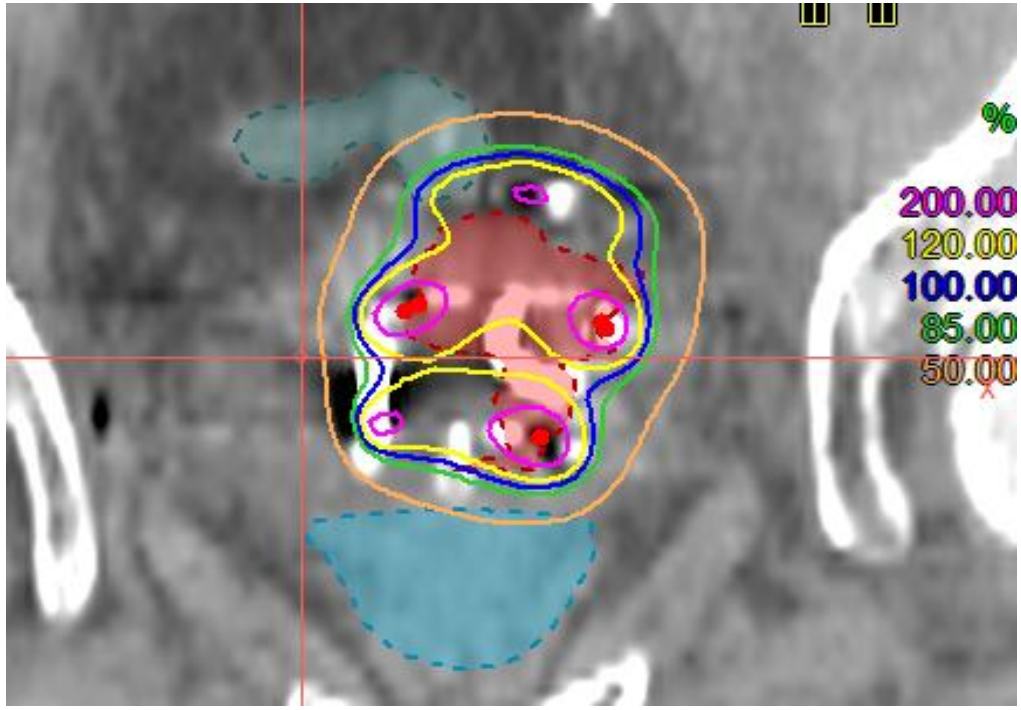
Laparoscopic implant

Courtesey of E. van der Steen-Banasik

Treatment Planning







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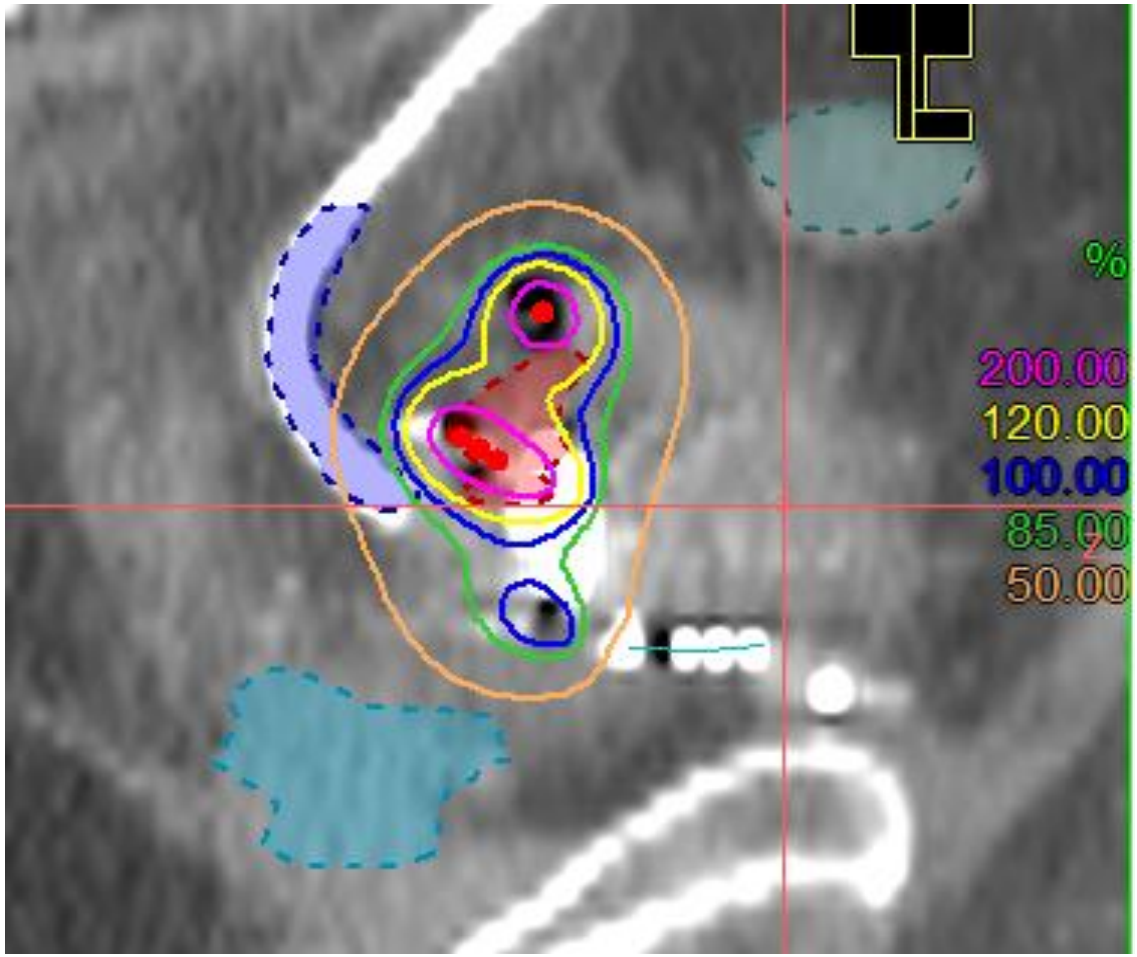
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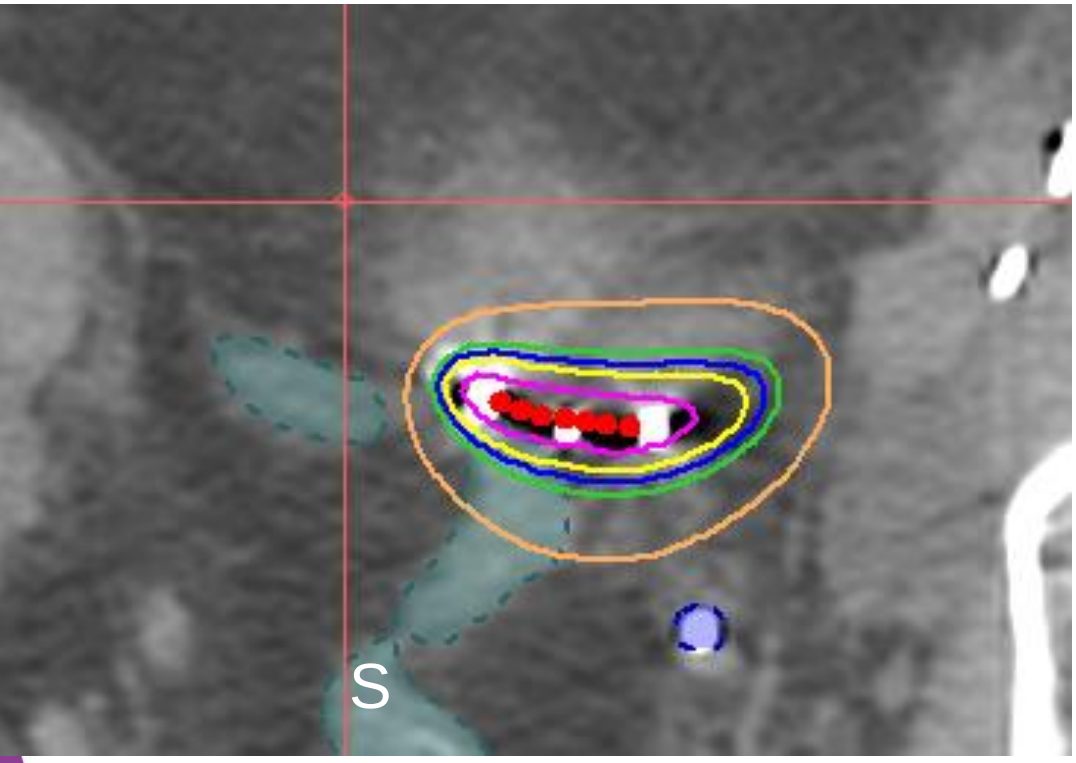
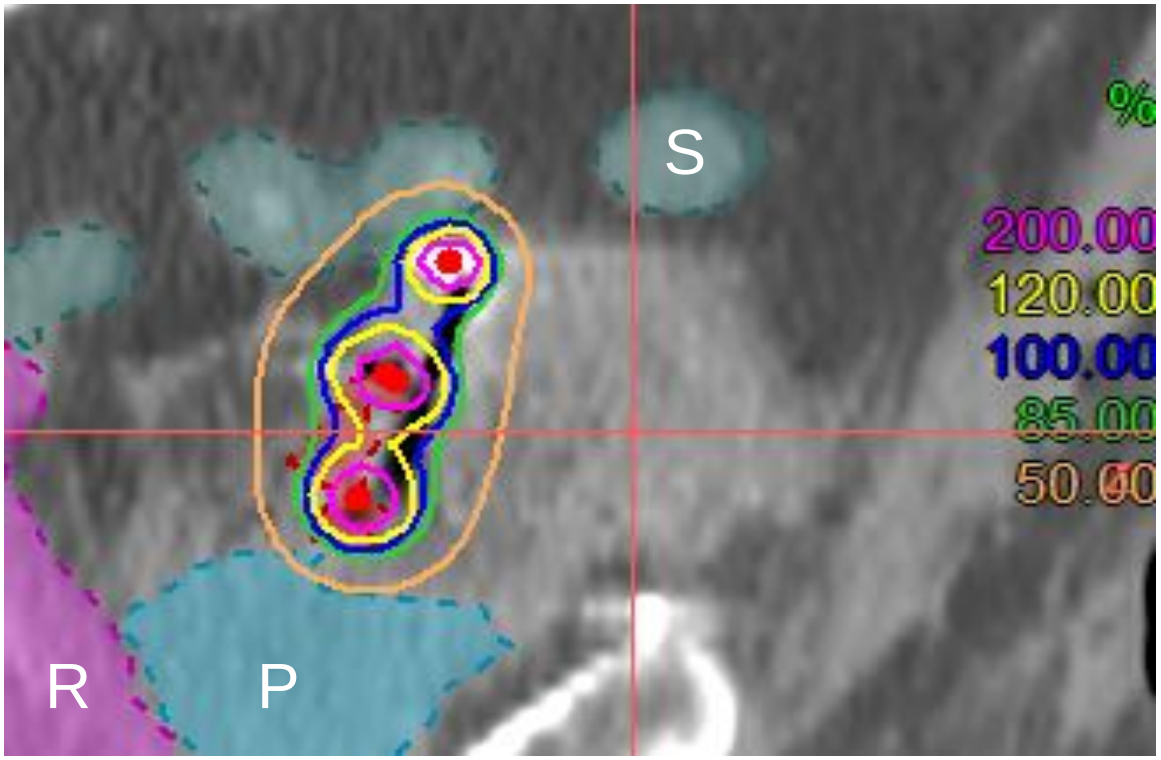
Sigmoid





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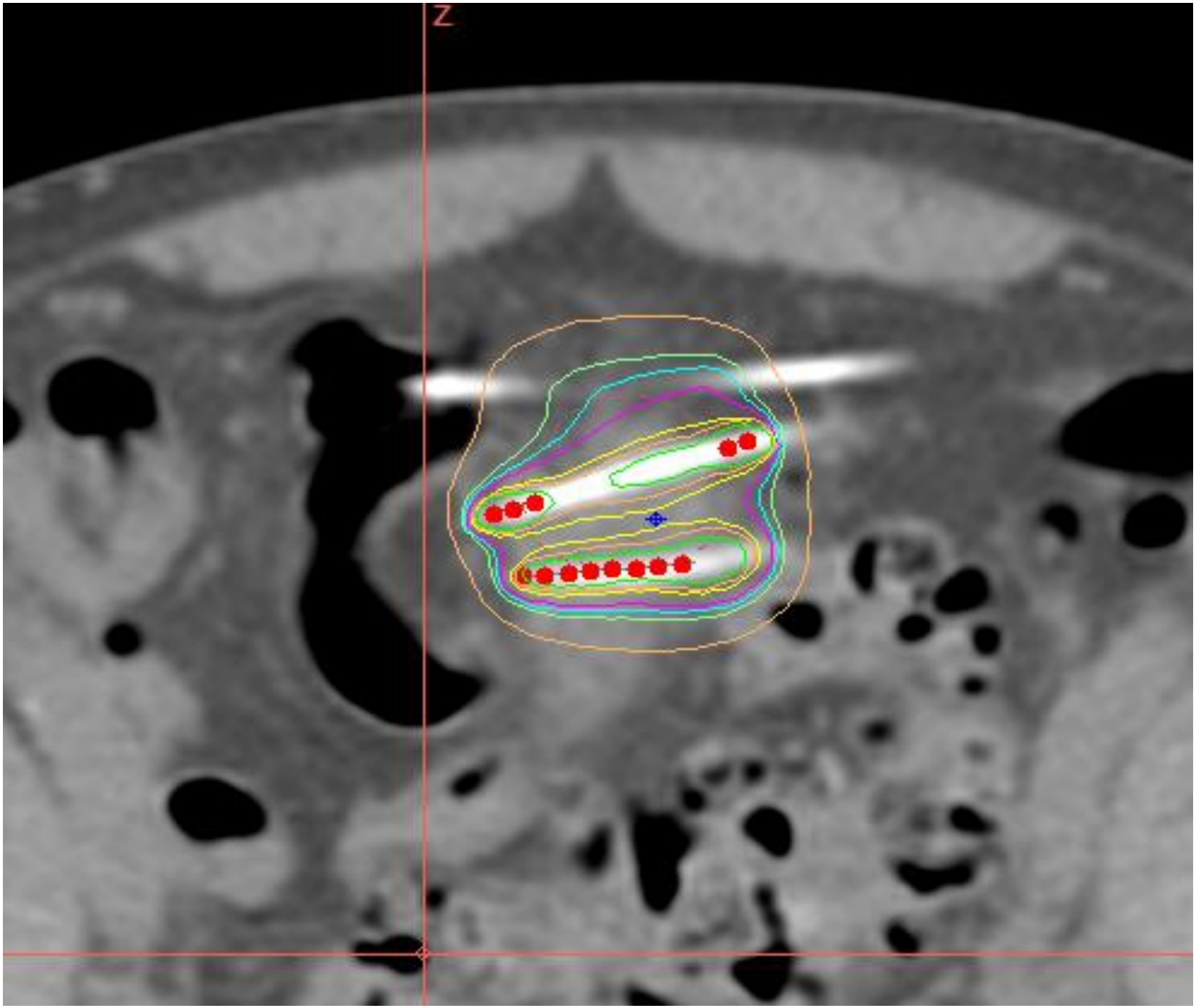

Non-parallel

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Patient selection

- Solitary tumors
- No carcinoma in situ
- ≤ 5 cm
- cT1-2, (small cT3)
- Not located in the bladder neck or prostatic urethra
- No distant metastasis

Dose

High Brachytherapy dose – (No pelvic lnn irradiation)
EBRT
3 x 3.5 Gy or 1 x 8.5 Gy
Brachytherapy
120 x 0.5 Gy PDR @ 1 h
59 x 1 Gy PDR @ 2 hr

Low Brachytherapy dose – (+ EBRT pelvic lnn irradiation)
EBRT
20 x 2 Gy
Brachytherapy
60 x 0.5 Gy PDR @ 1 h
30 x 1 Gy PDR @ 2 hr

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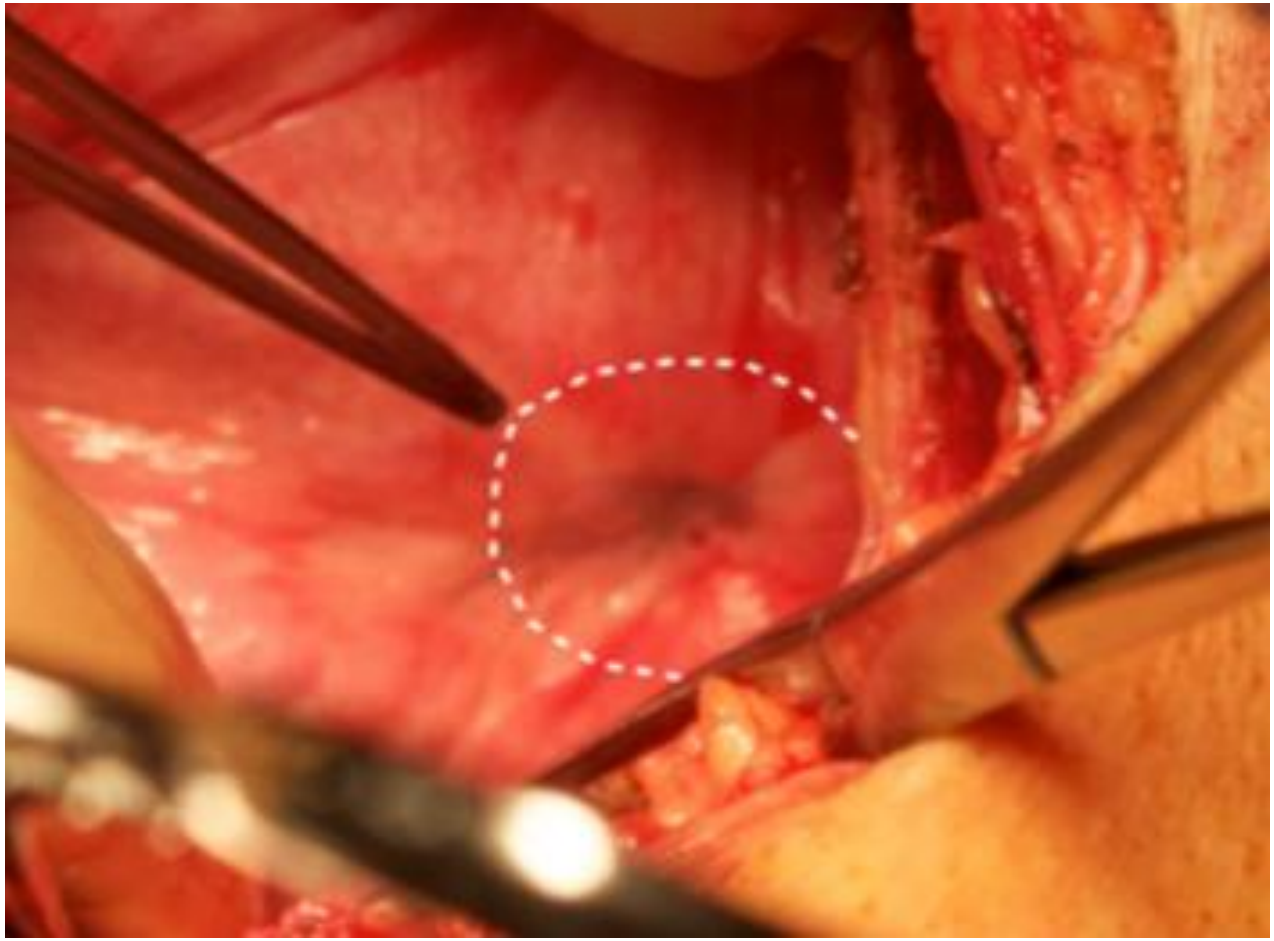
Clinical Target Volume



TUR-B scar with
5 mm margin

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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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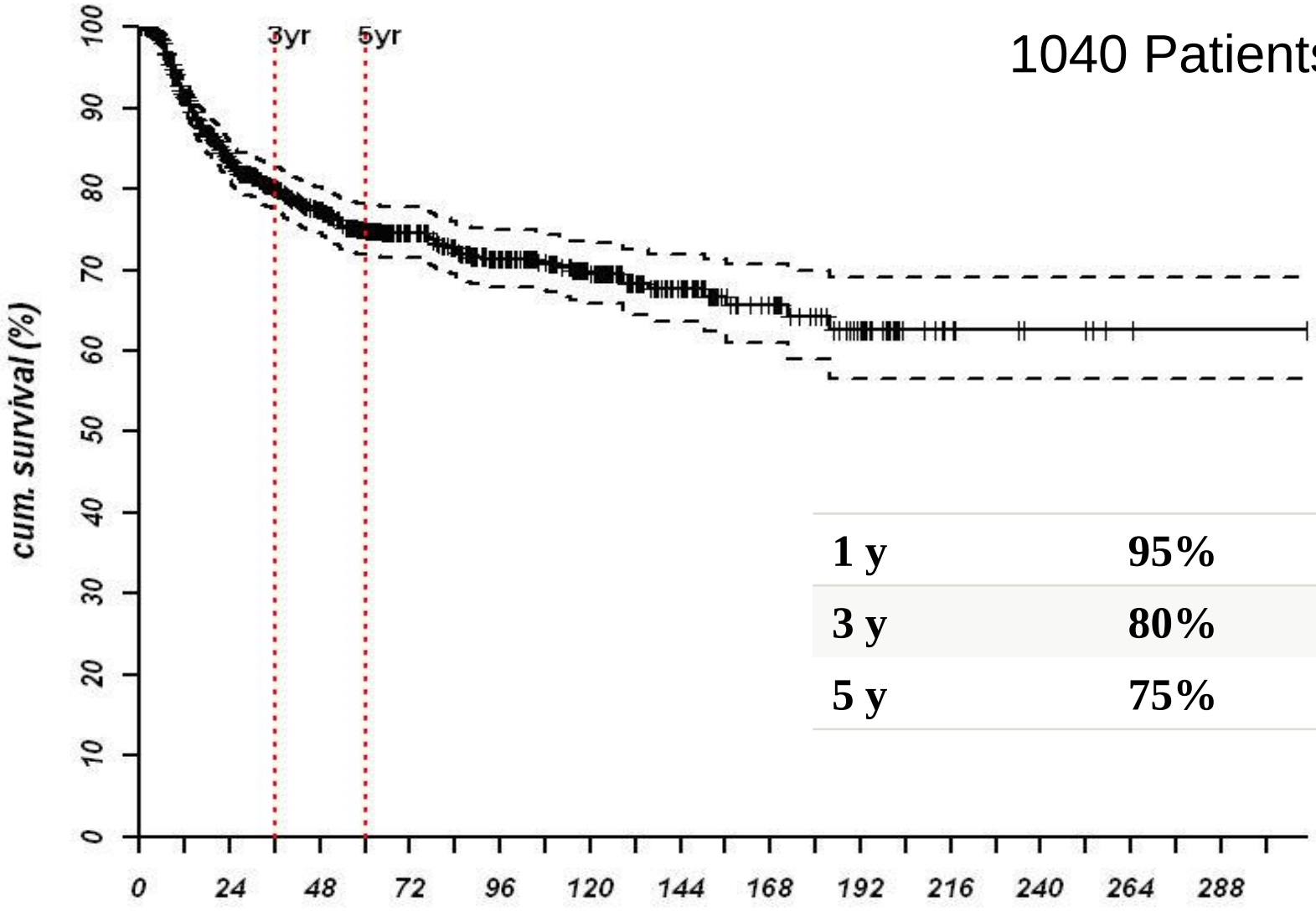
Local recurrence free survival

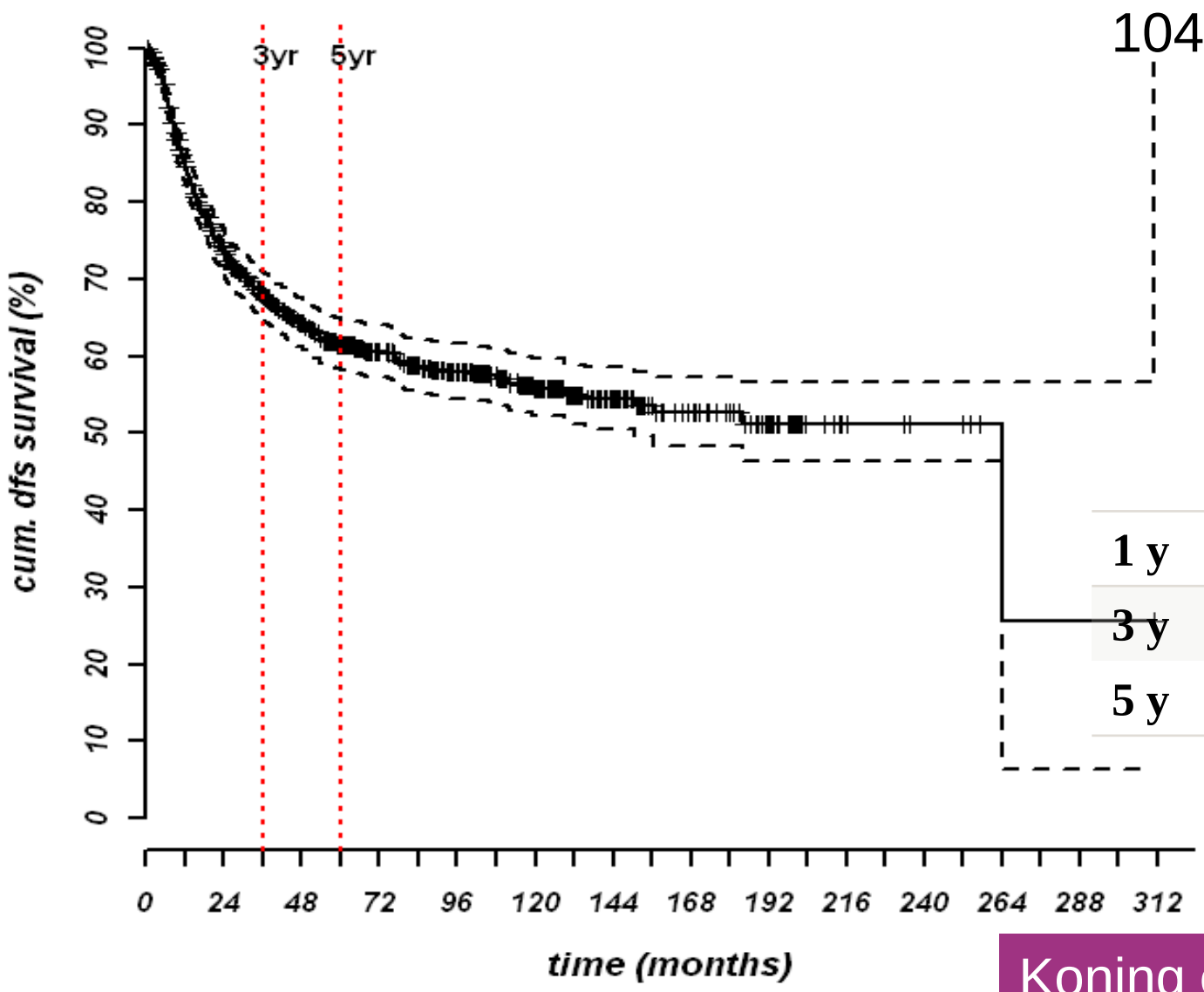


1040 Patients

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

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

Disease free survival

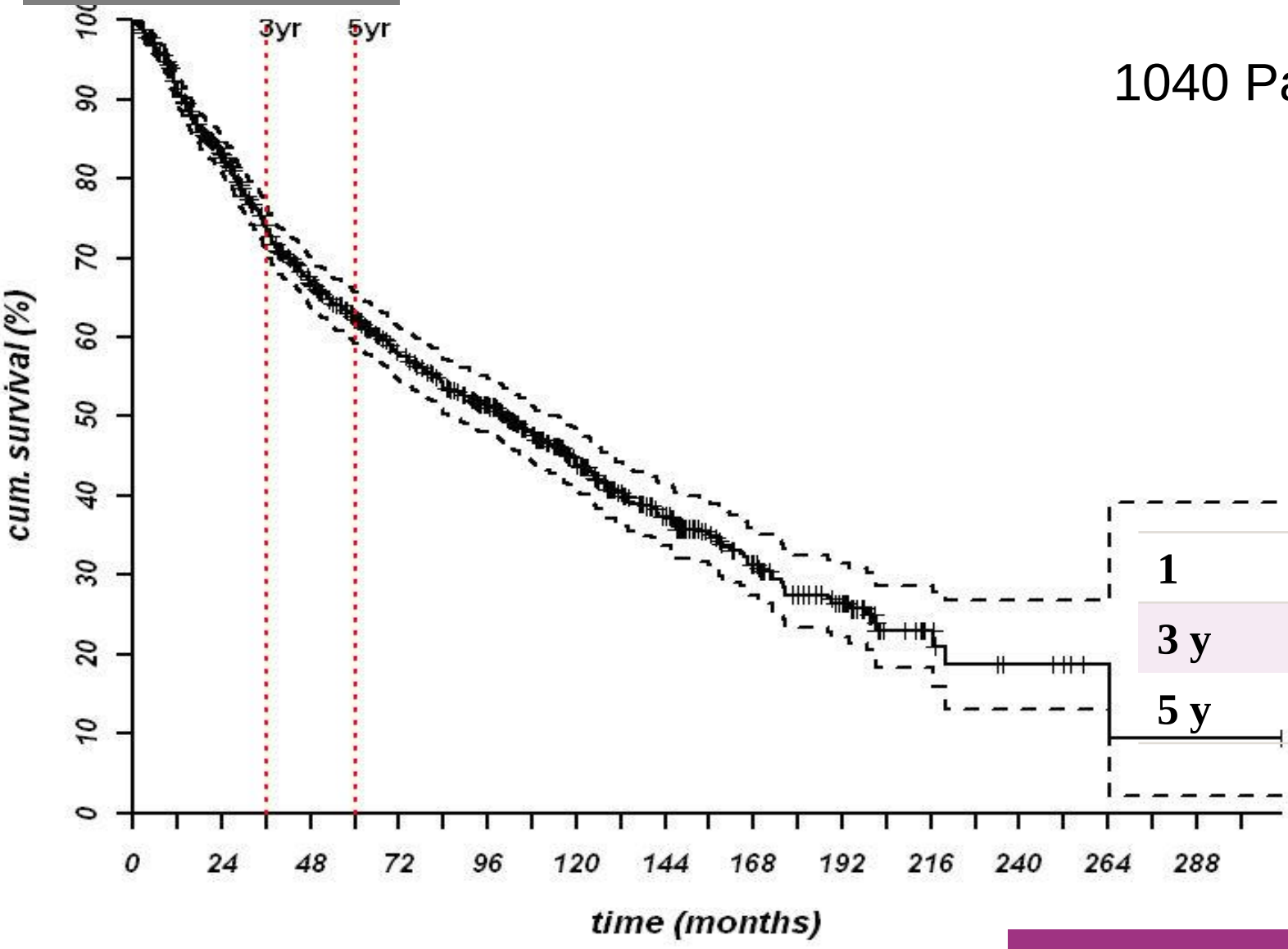


1040 Patients

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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Conclusion

- Bladder brachytherapy a solution for bladder preservation in MIBC
- Bladder brachytherapy indicated for selected group of patients
- Local control comparable to cystectomy series
- Functional outcome is good
- Laparoscopic / Robot-assisted technique is emerging

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Endometrium definitive treatment: Indication, tools and requirements, performing application, hazards, results

Peter Hoskin

Mount Vernon Cancer Centre

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Endometrial cancer: uterus in situ

- Surgery contraindicated:
  - gross obesity
  - general frailty
  - coexisting medical conditions:
    - diabetes
    - cardiovascular
    - thrombosis

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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

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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

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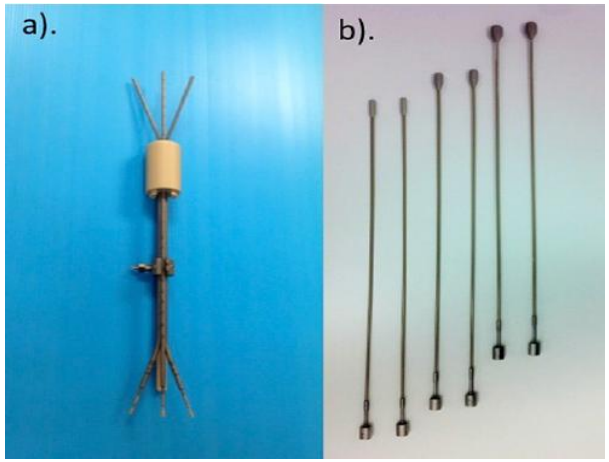
Image-guided high-dose-rate brachytherapy in inoperable endometrial cancer

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	

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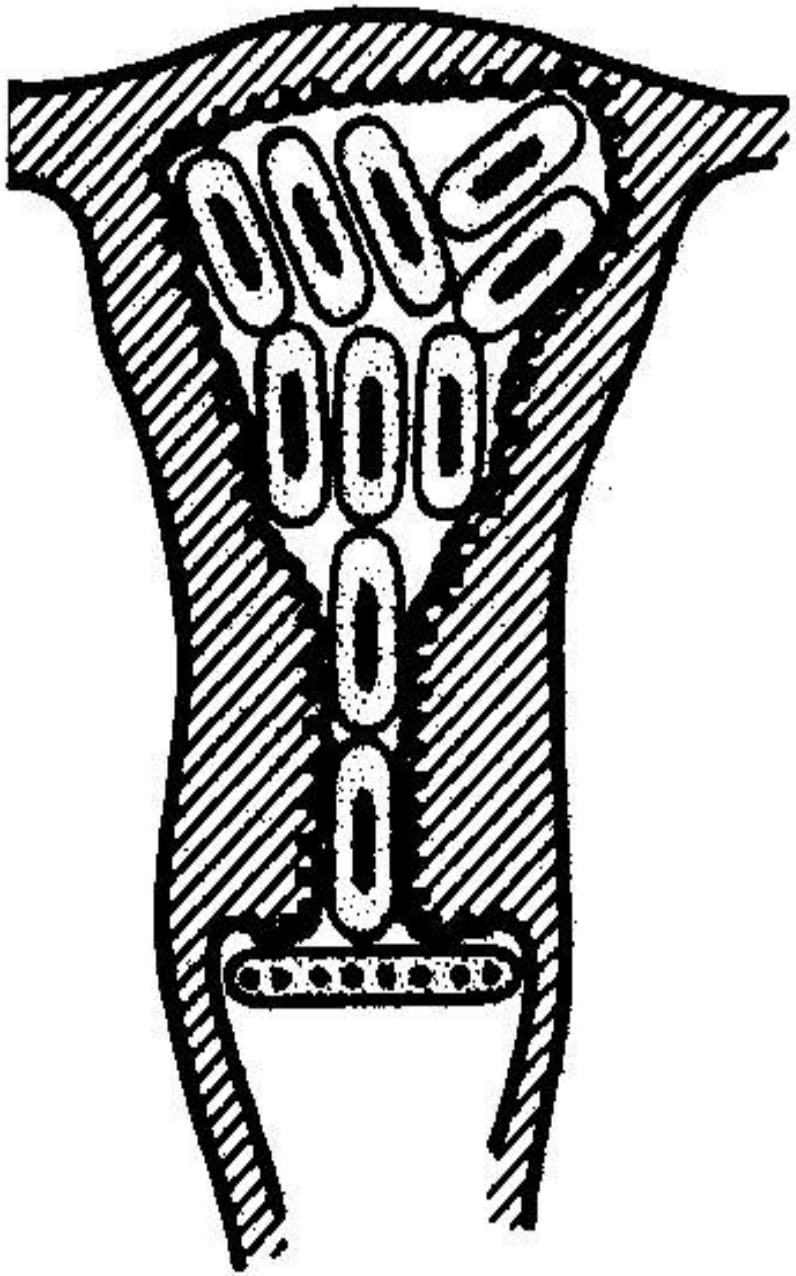
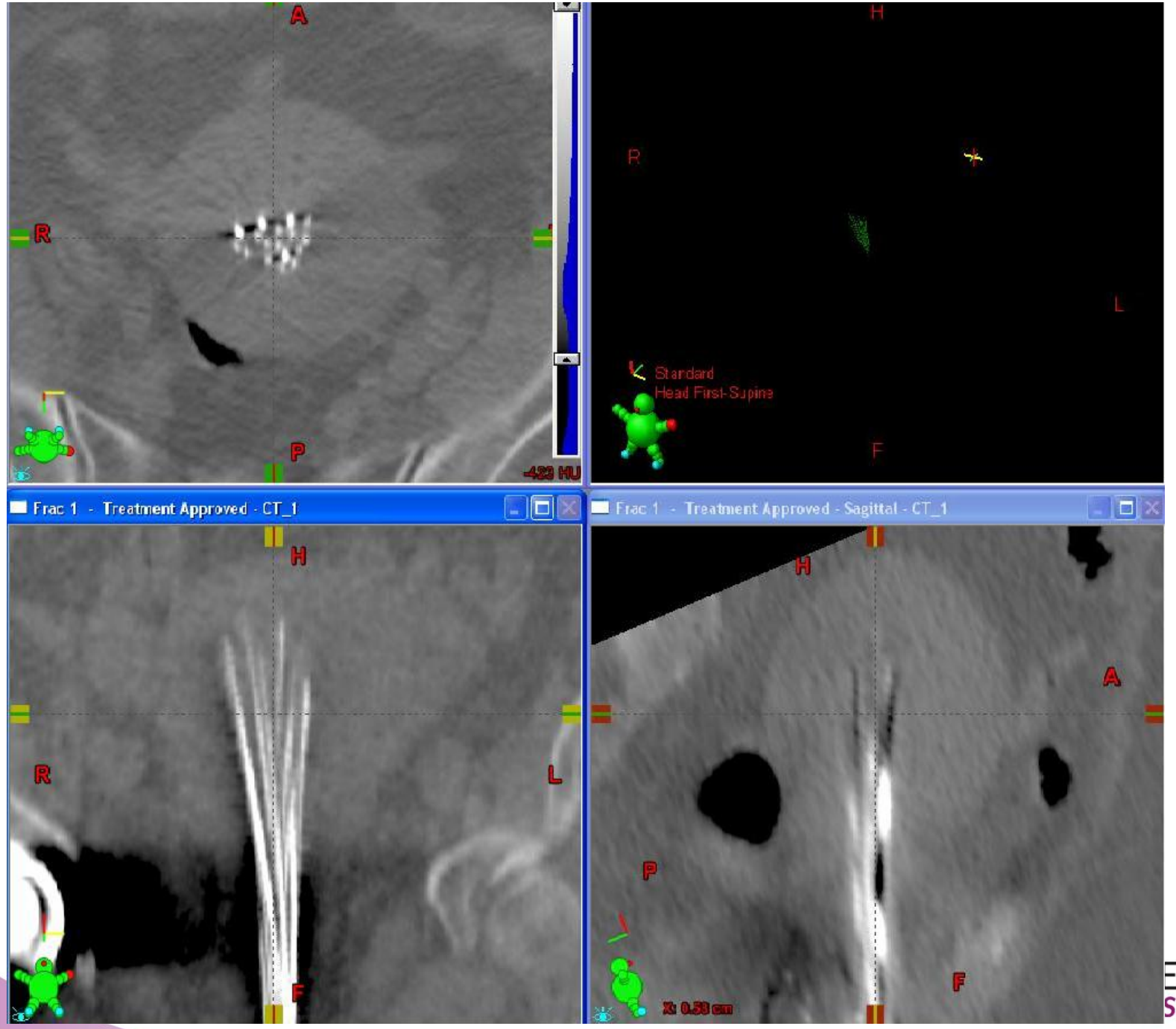
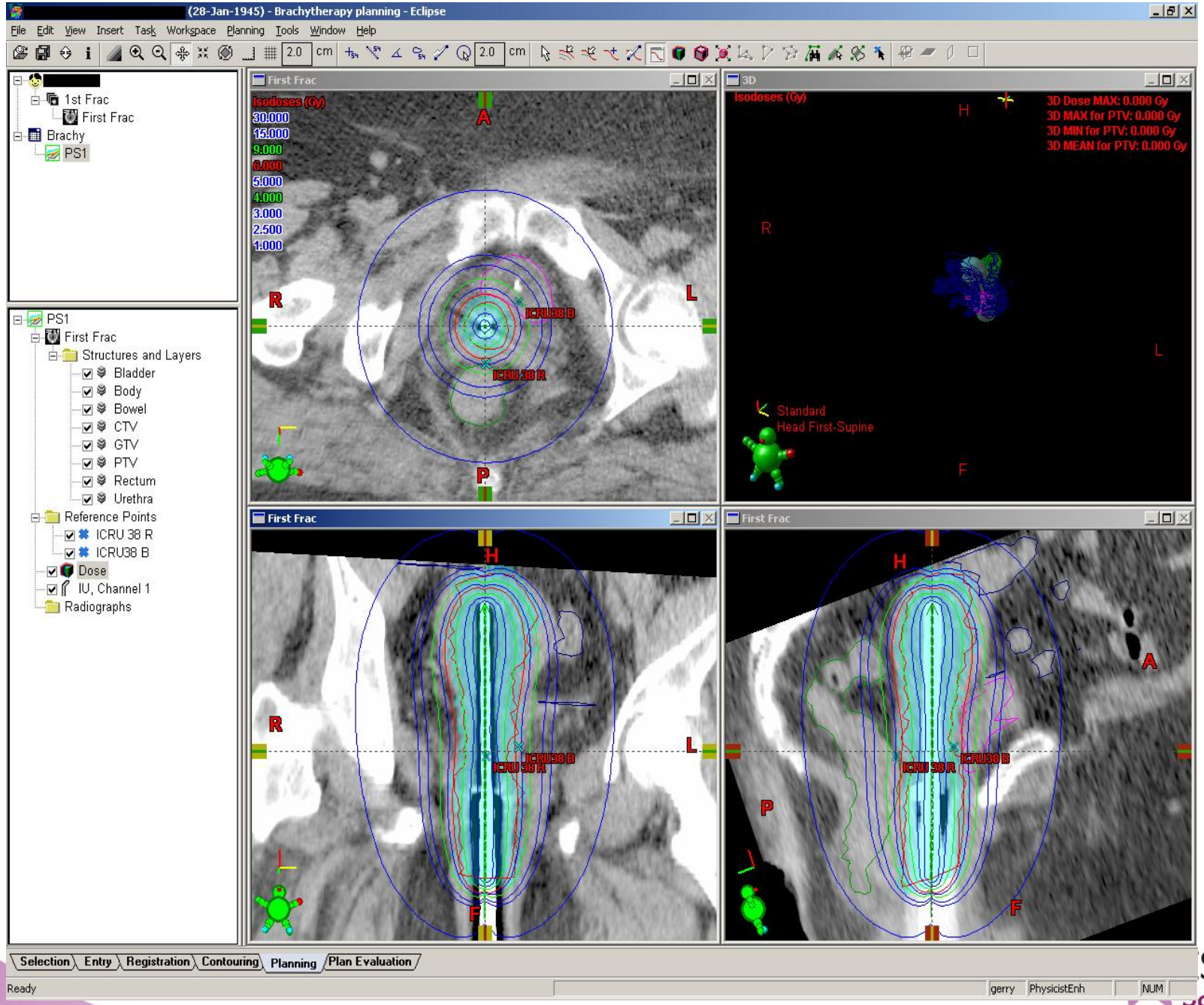
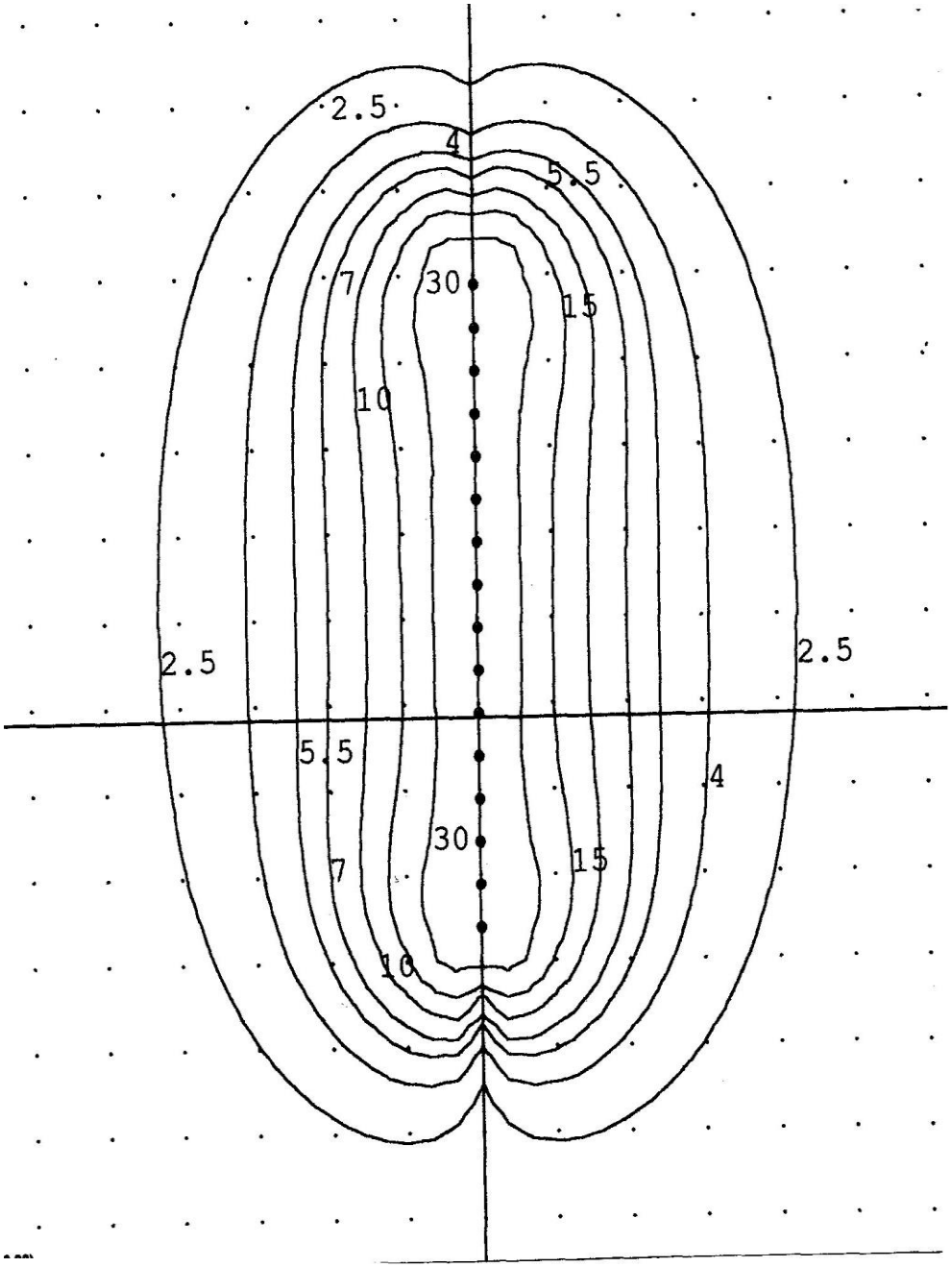
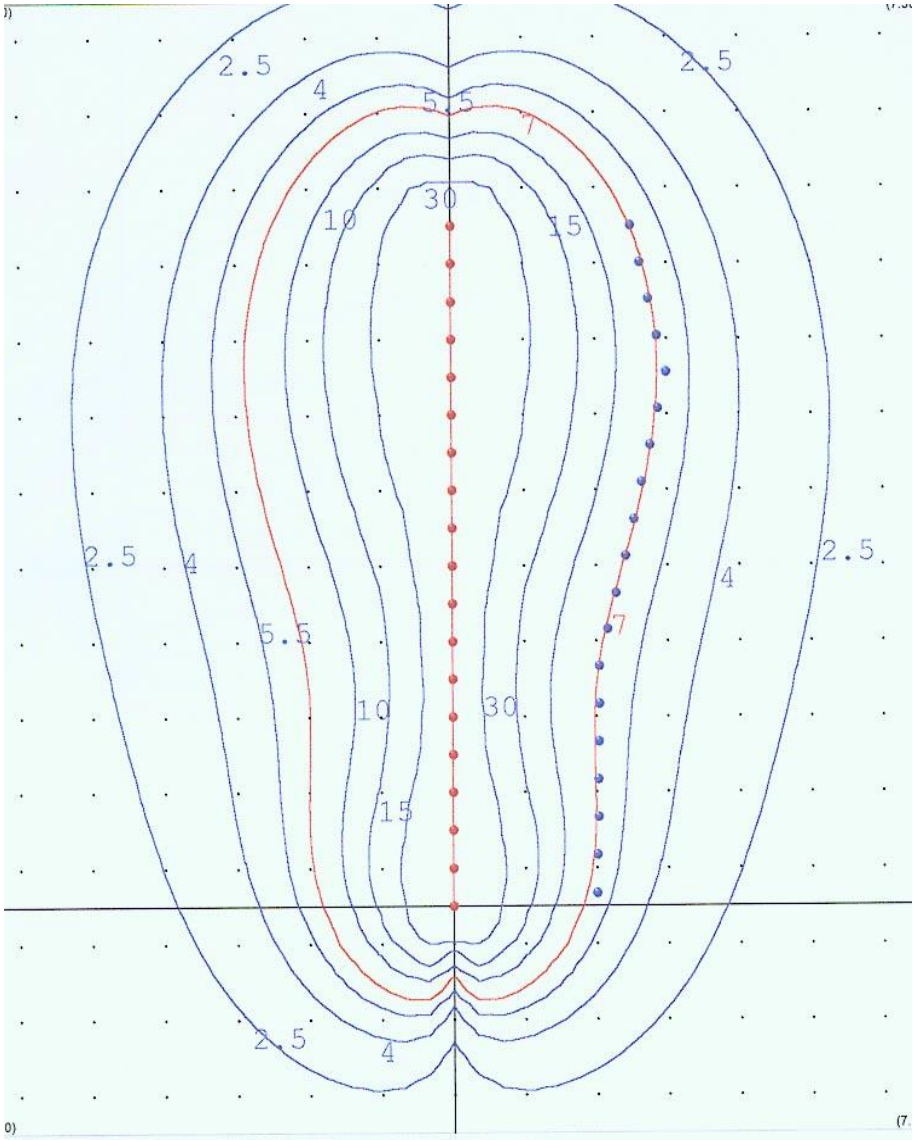
Heymans capsules
In situ




A
R
P
-433 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: 0.58 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

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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 should be reconstructed from diagnostic films

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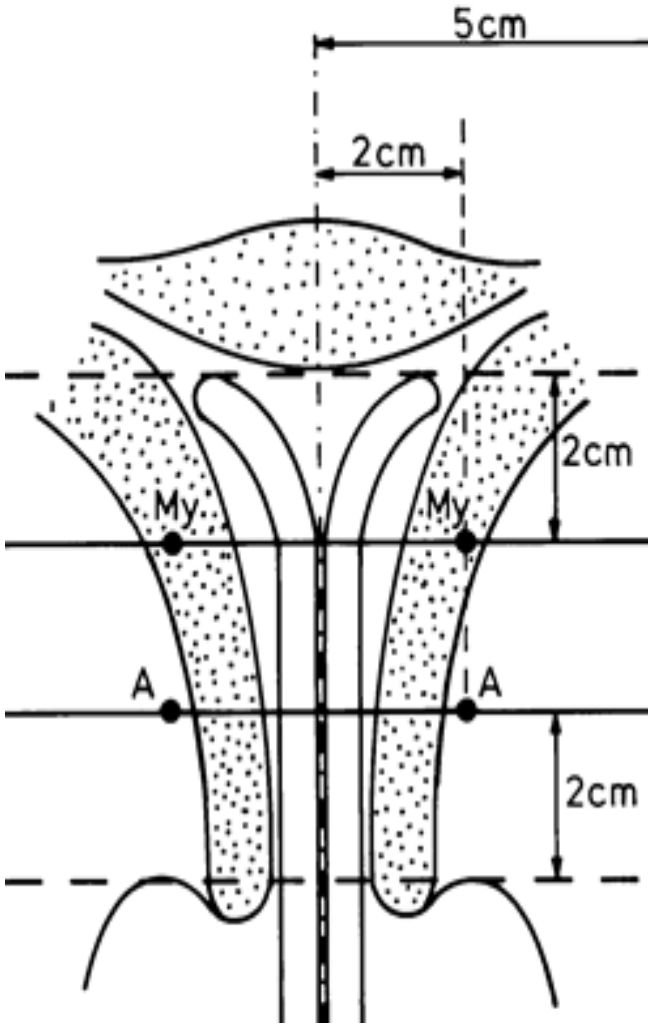
Dosimetry points for uterine BT



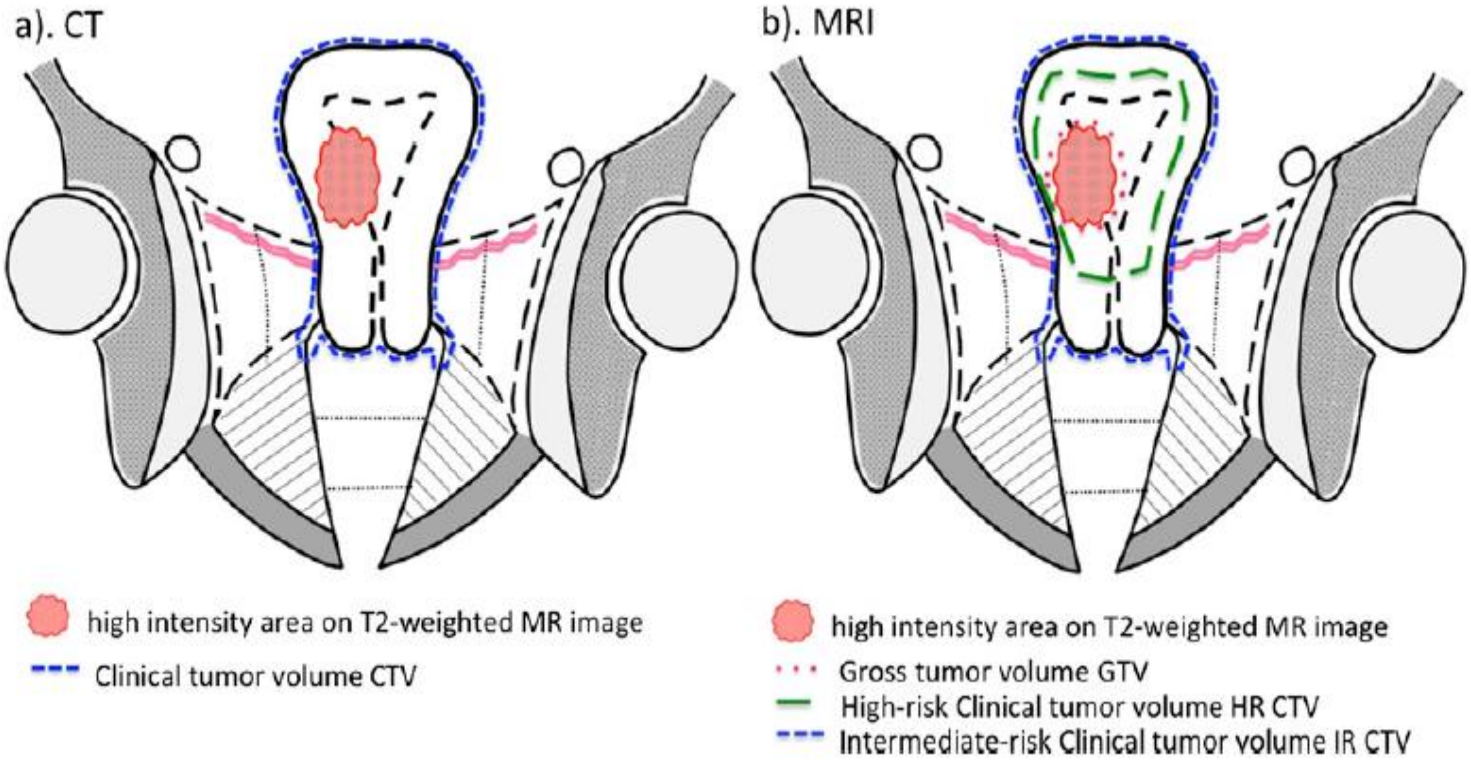
My = prescription point

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



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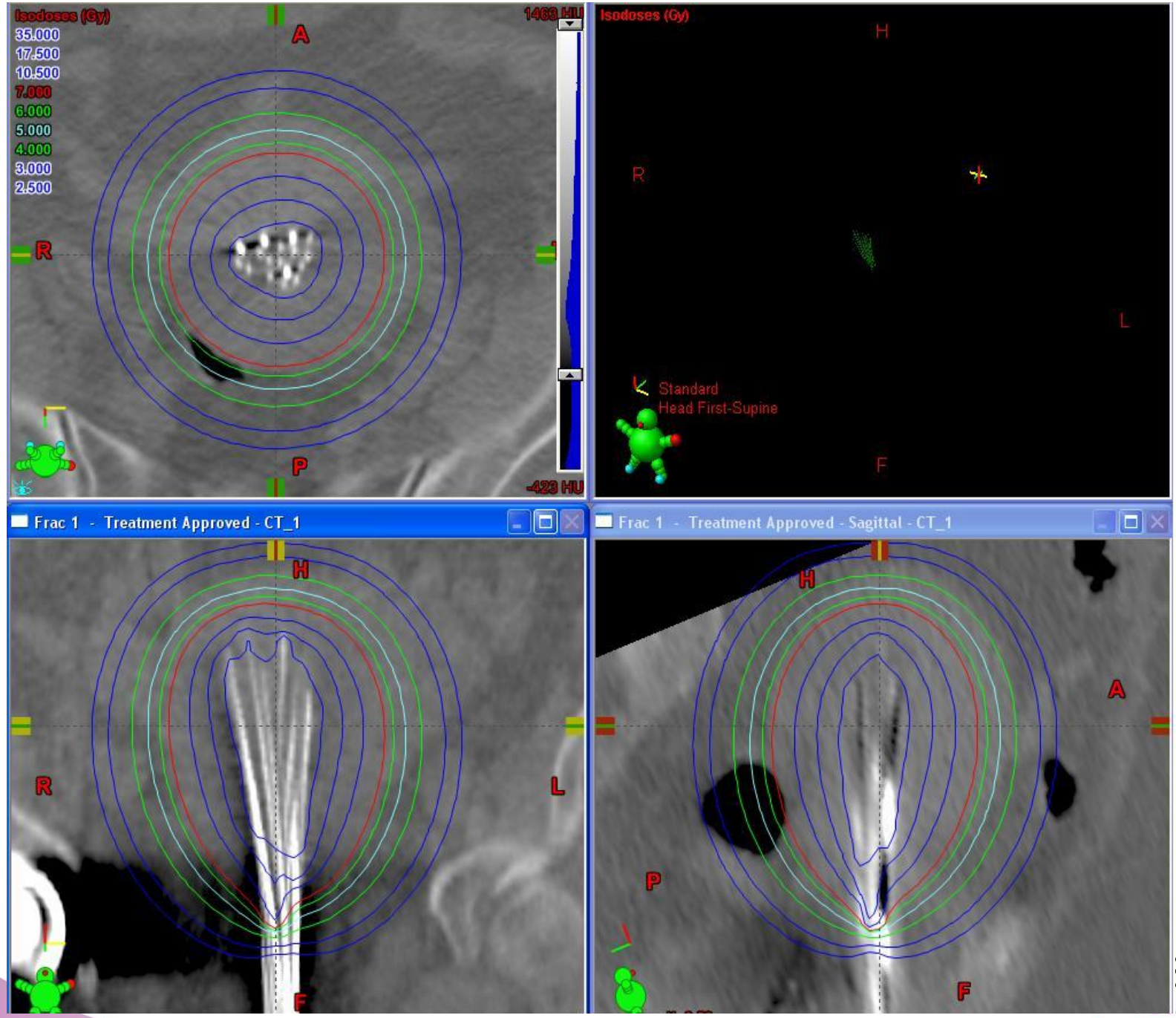
Isodoses (Gy)
35.000
17.500
10.500
7.000
6.000
5.000
4.000
3.000
2.500
1468 HU
-423 HU
A
P
R
Isodoses (Gy)
H
R
L
F
Standard
Head First-Supine
Frac 1 - Treatment Approved - CT_1
H
R
L
F
Frac 1 - Treatment Approved - Sagittal - CT_1
H
A
P
F

Actual dosimetry using modified Heyman's capsules

Weitmann et al 2005

	Min CTV Rectum dose	D90CTV dose	MinGTV dose	Bladder 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

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Uterus volume covered by reference volume

Mock et al. Strahlenther Onkol 1998

uterus volume outside reference isodose

reference isodose outside uterus volume

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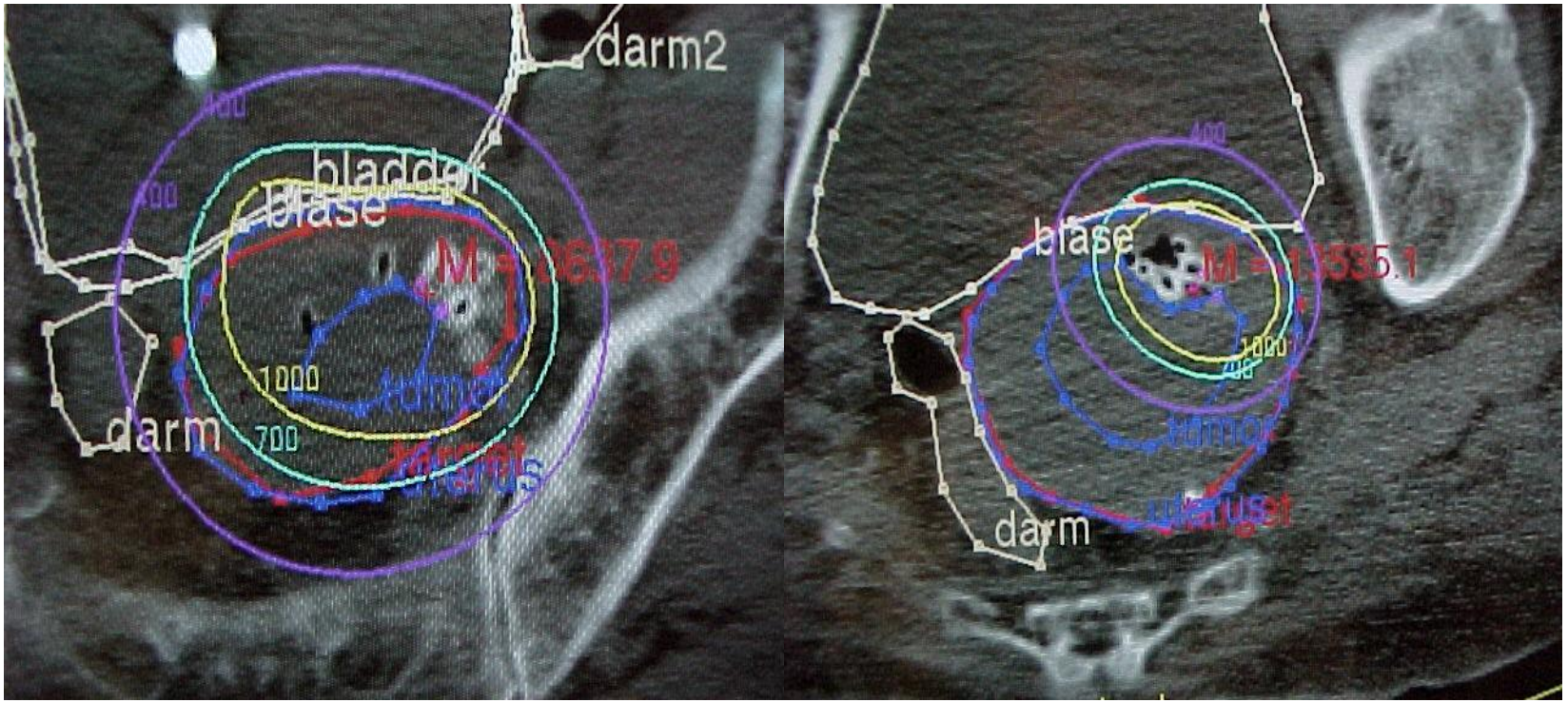
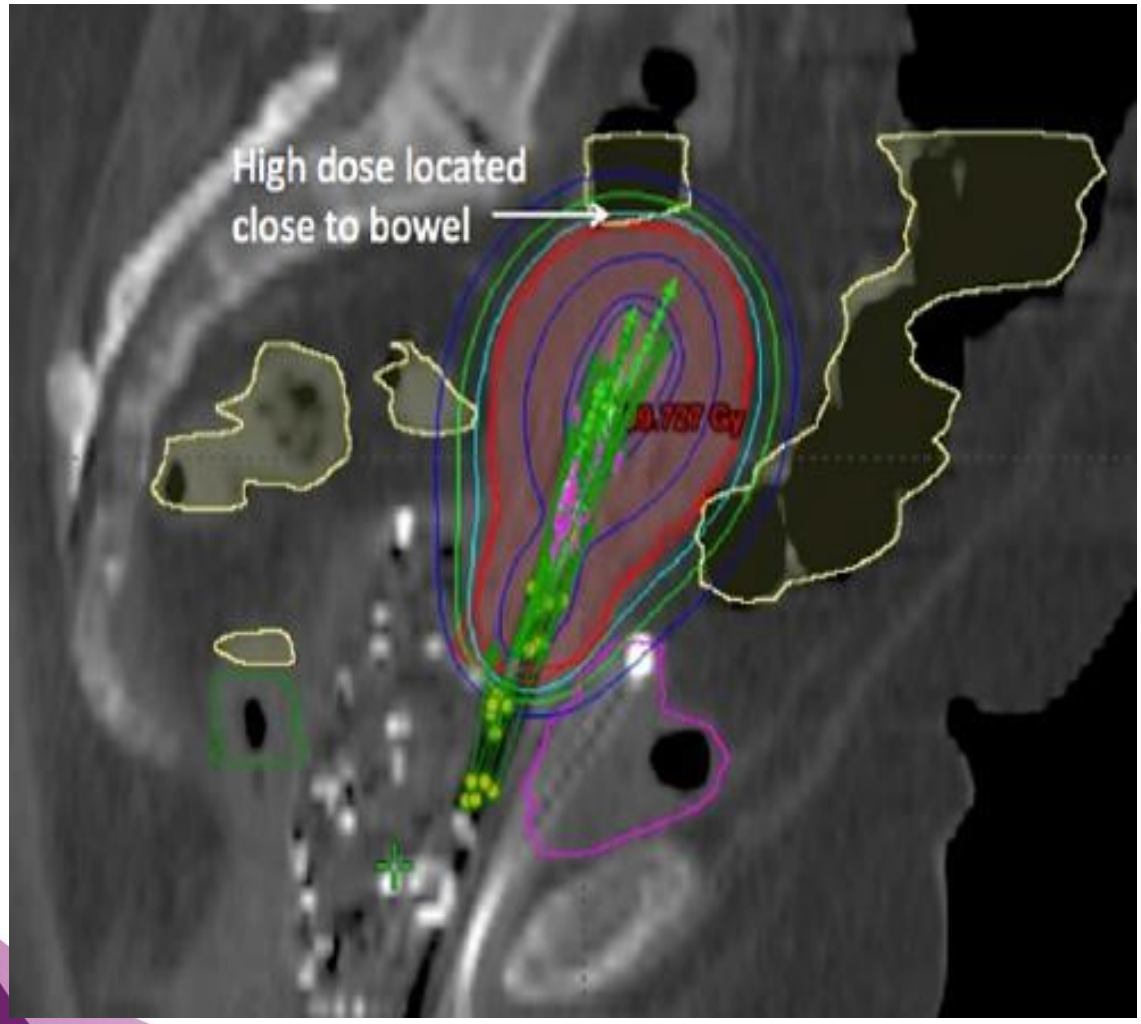
Poor dose distribution

Weitmann et al. IJROB 2005



OAR limitations



GEC ESTRO Gyn tolerances used:

Rectum<75Gy
Sigmoid < 70-75Gy
Bladder < 80Gy

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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.

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Intracavitary brachytherapy for endometrium: prescription

PDR	HDR	2Gyeq	
		αβ10	αβ3.5
BRACHYTHERAPY ALONE			
75Gy/2f	42Gy/6f	59.5Gy	80.2Gy
AFTER 45Gy EXT BEAM			
22Gy/1f	28Gy/4f	83.9Gy	96.9Gy

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Planning aim doses

2D orthogonal

- Point My: 50-60Gy
- Point A Line: 42Gy
- Upper vagina: 45-50Gy

3D IGBT

- CTV (outer uterine wall): 60Gy
- GTV: >80Gy
- HR-CTV: >70Gy
- IR-CTV: >60Gy

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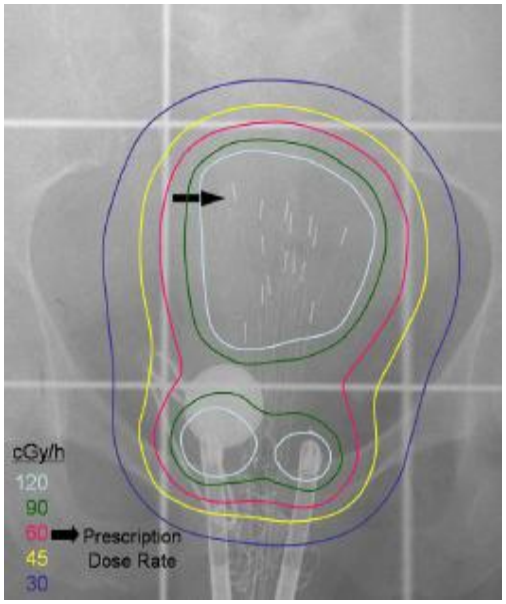
The management of inoperable Stage I endometrial cancer using intracavitary brachytherapy alone: A 20-year institutional review

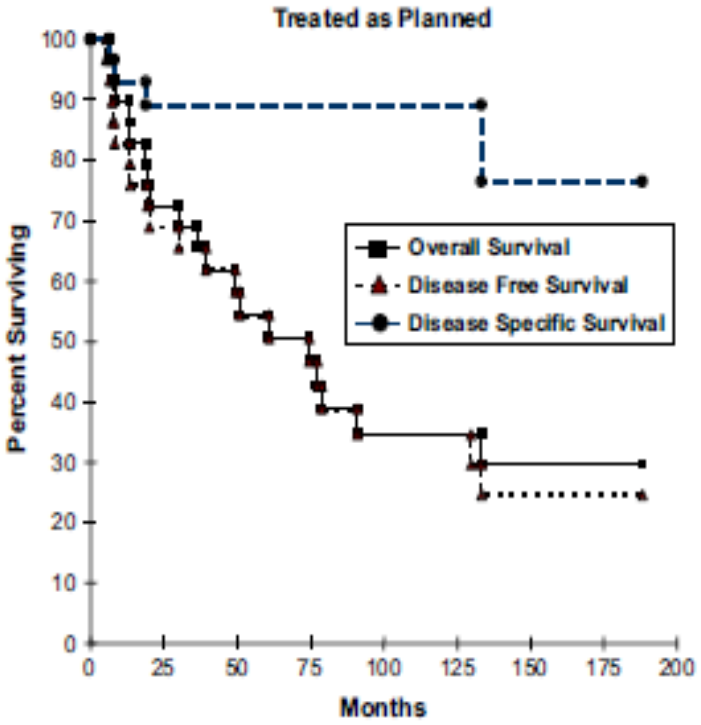
Carey B. Shenfield*, Robert G. Pearcey, Sunita Ghosh, George S. Dundas

Department of Radiation Oncology, Cross Cancer Institute, University of Alberta, Edmonton, Alberta, Canada

Brachytherapy 2009

1986-2006
44 PATIENTS





6000cGy LDR
(2 X 3000cGy)

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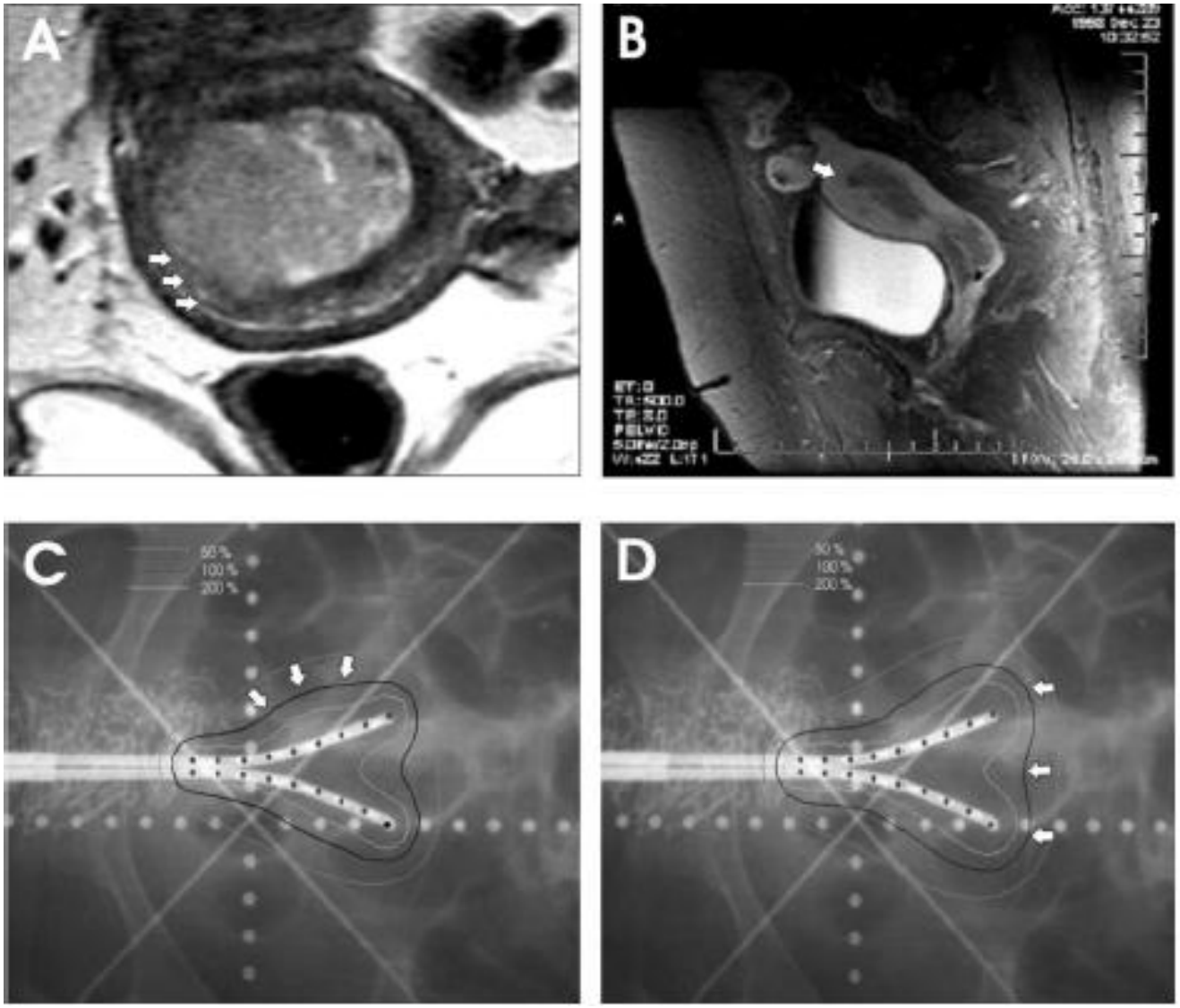
Inoperable endometrial cancer (Quebec)

Nyazi et al 2005



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Inoperable endometrial cancer (Quebec)

Nyazi et al 2005

n=38

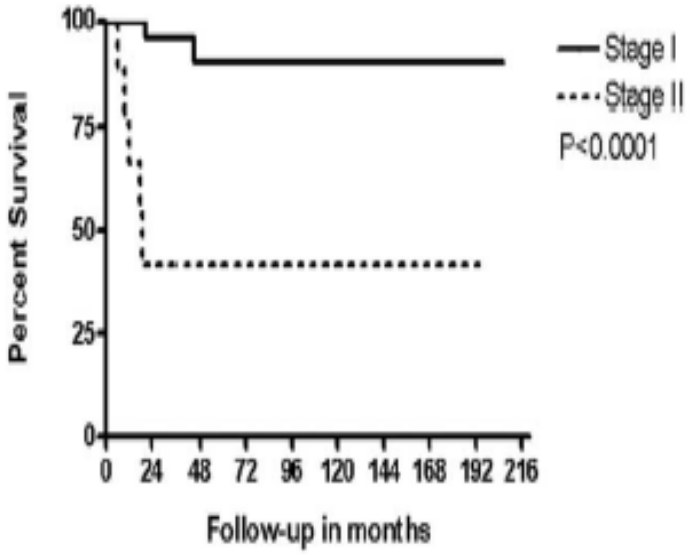

Fig. 2. Disease-specific survival for patients with Stage I and Stage II disease.

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

=15

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

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Image-based three-dimensional conformal brachytherapy for medically inoperable endometrial carcinoma

Brachytherapy 13 (2014) 542–547

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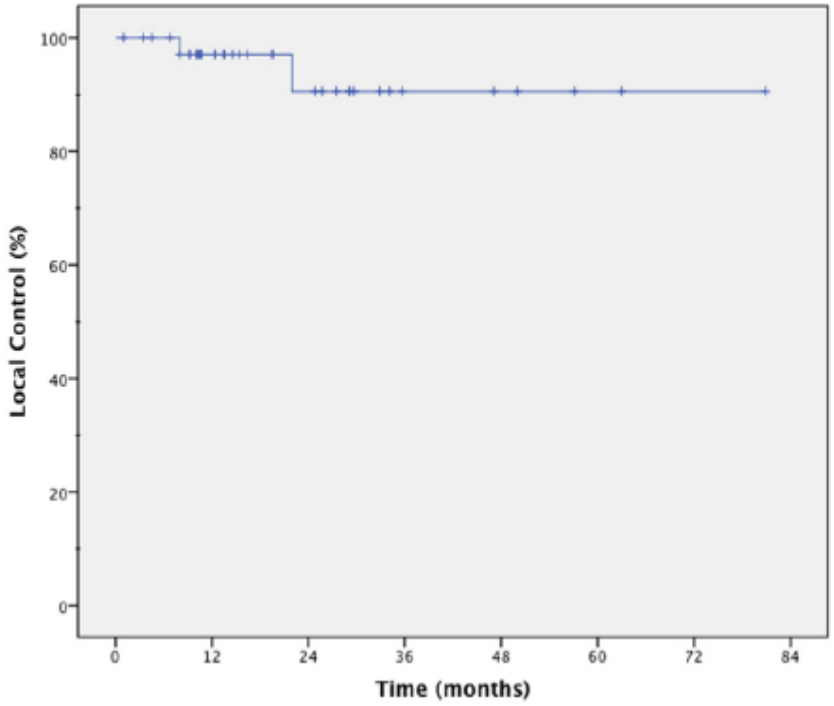

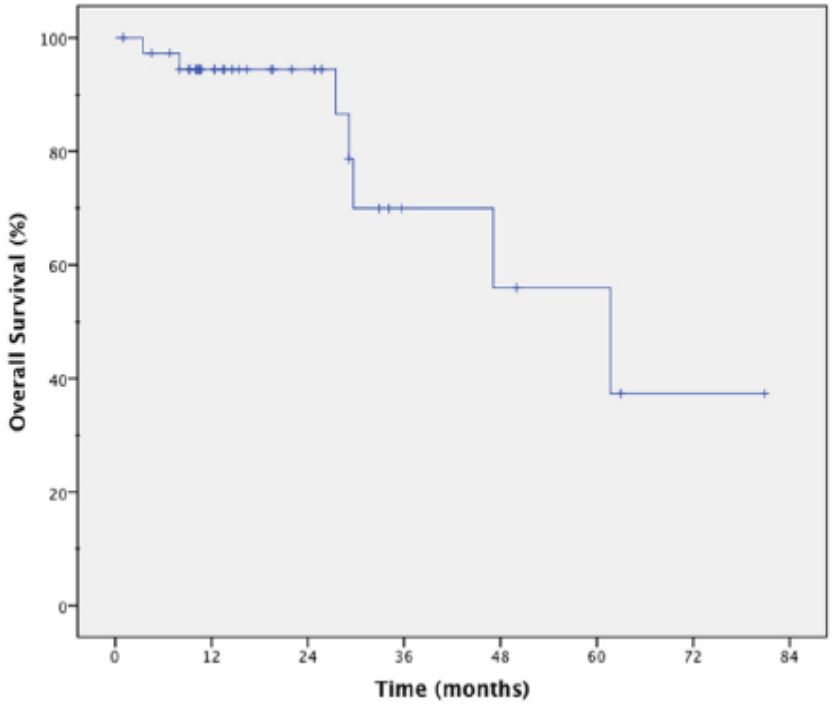

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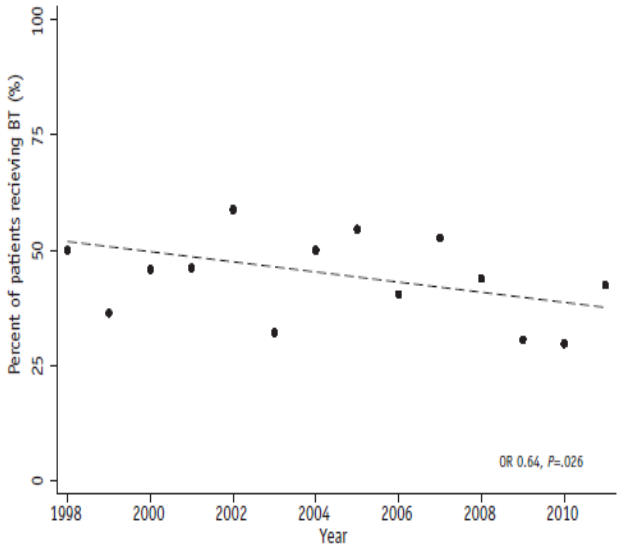
Brachytherapy Is Associated With Improved Survival in Inoperable Stage I Endometrial Adenocarcinoma: A Population-Based Analysis

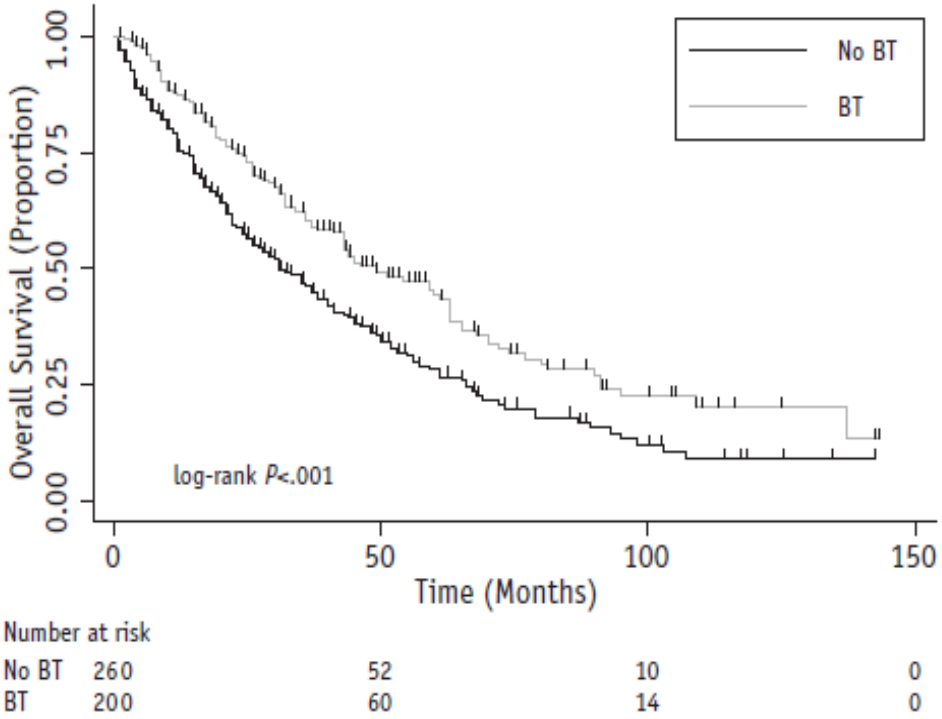
Int J Radiation Oncol Biol Phys, Vol. 93, No. 3, pp. 649–657, 2015

Sahaja Acharya, MD,* Stephanie M. Perkins, MD,* Todd DeWees, PhD,* et al

SEER analysis: 460 patients

Use of brachytherapy





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Pediatrics

Gustave Roussy experience

Renaud Mazeron

Gustave Roussy

Brachytherapy in pediatric malignancies

Tumor characteristics

- High chemosensitivity
- High cure rate
- Complication rate /sequelae = important issue
- Fertility preservation

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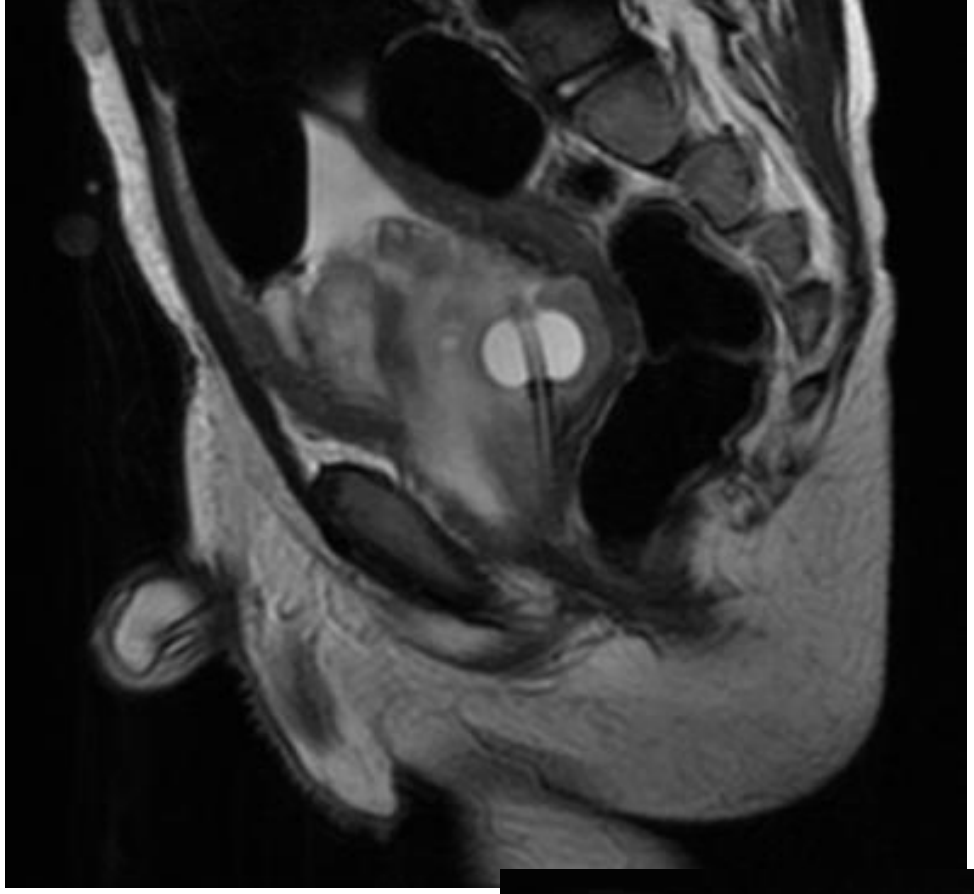
Prostate/bladder RMS

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 trigone

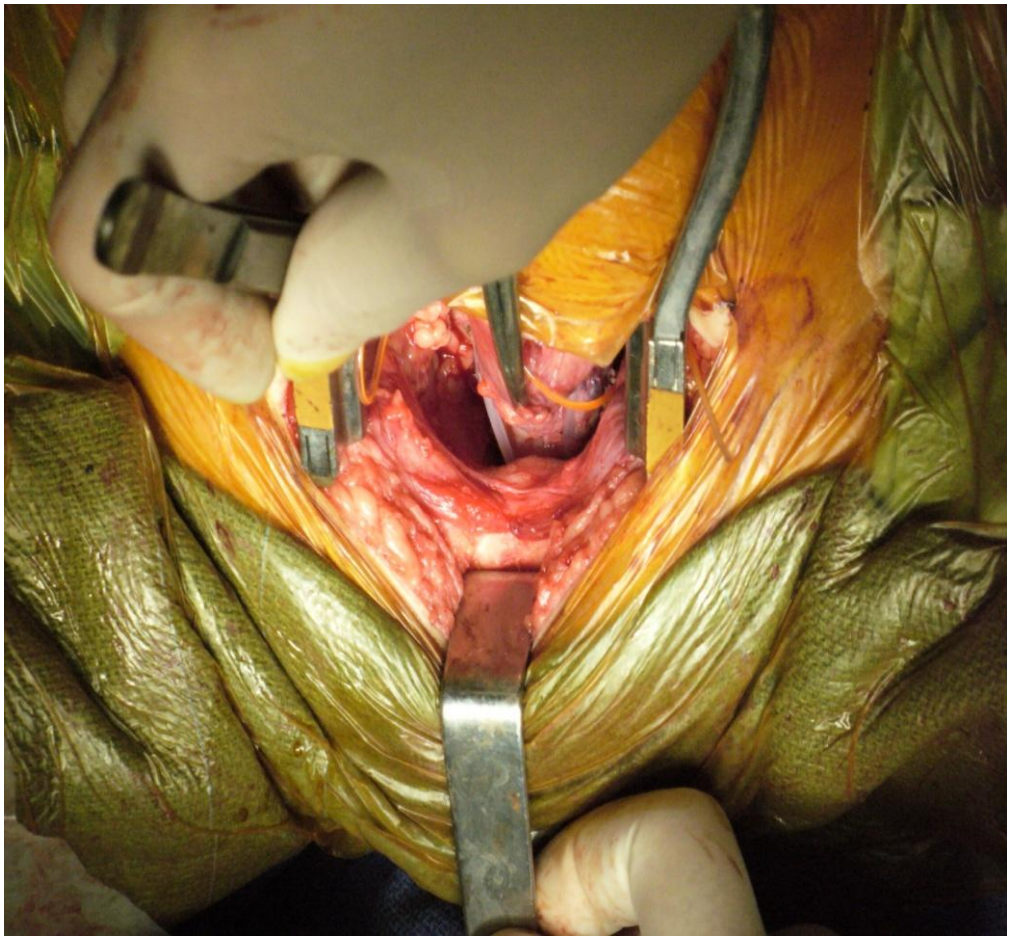
↓

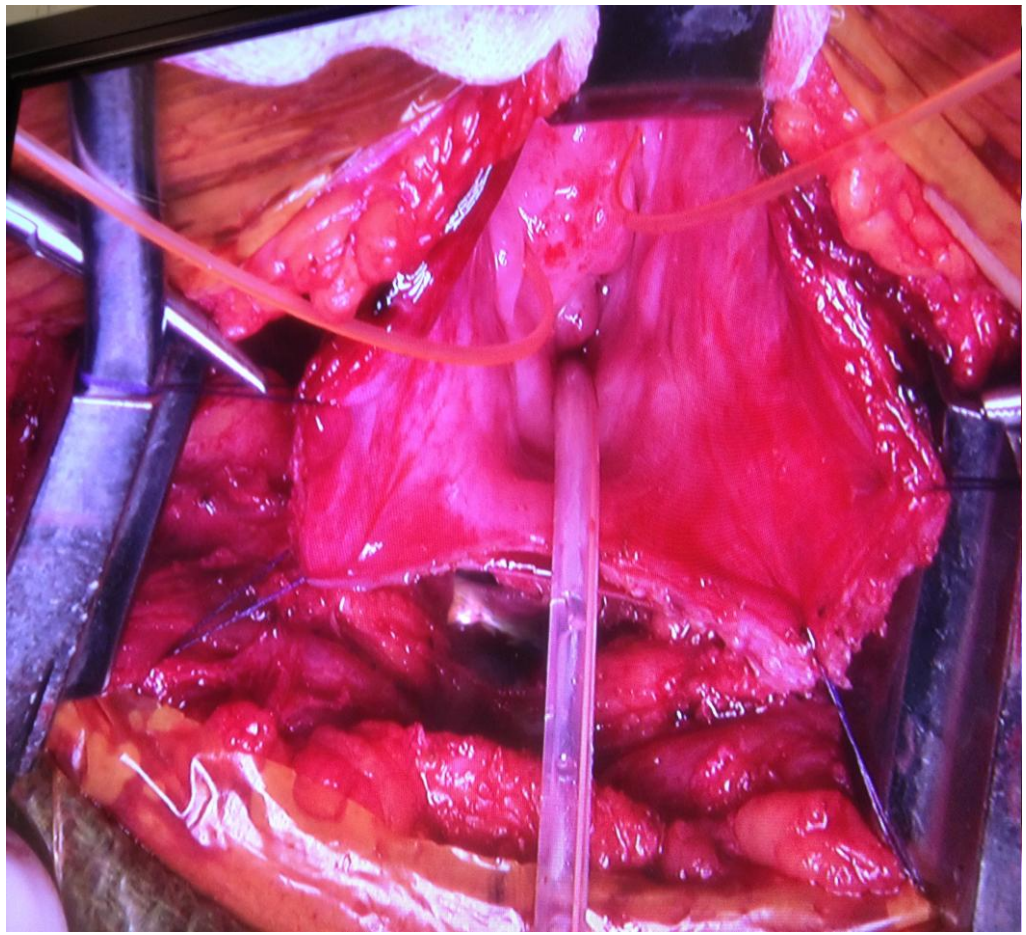
Partial prostatectomy

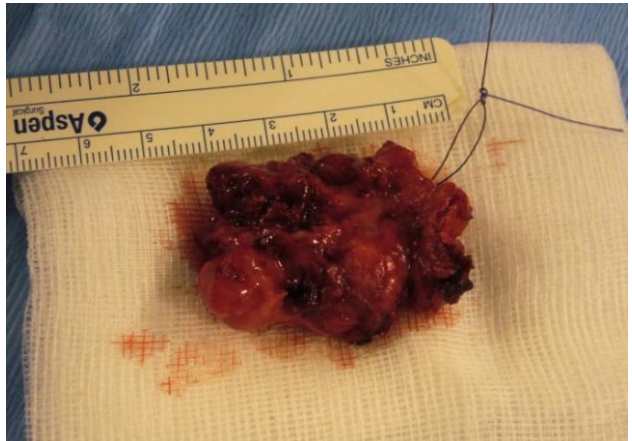
Partial cystectomy

+ BT

Prostate/bladder RMS







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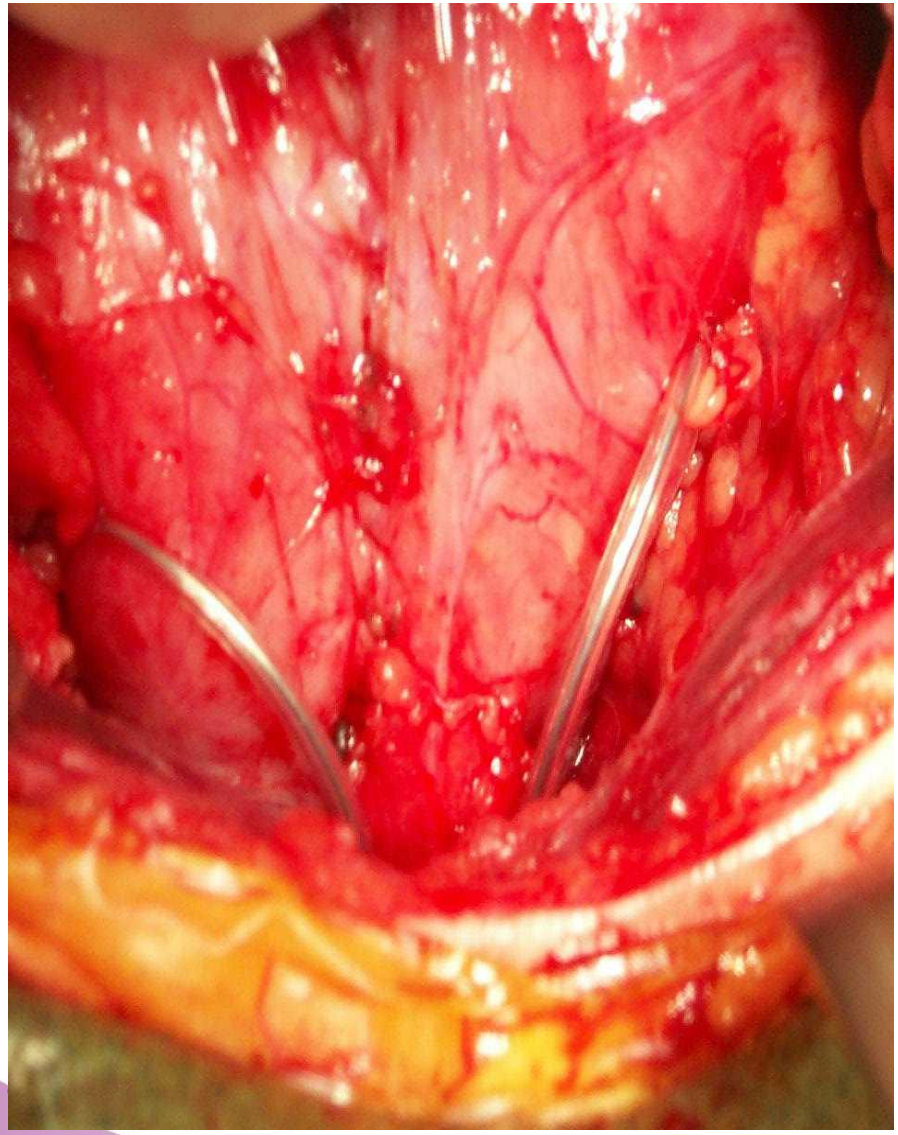
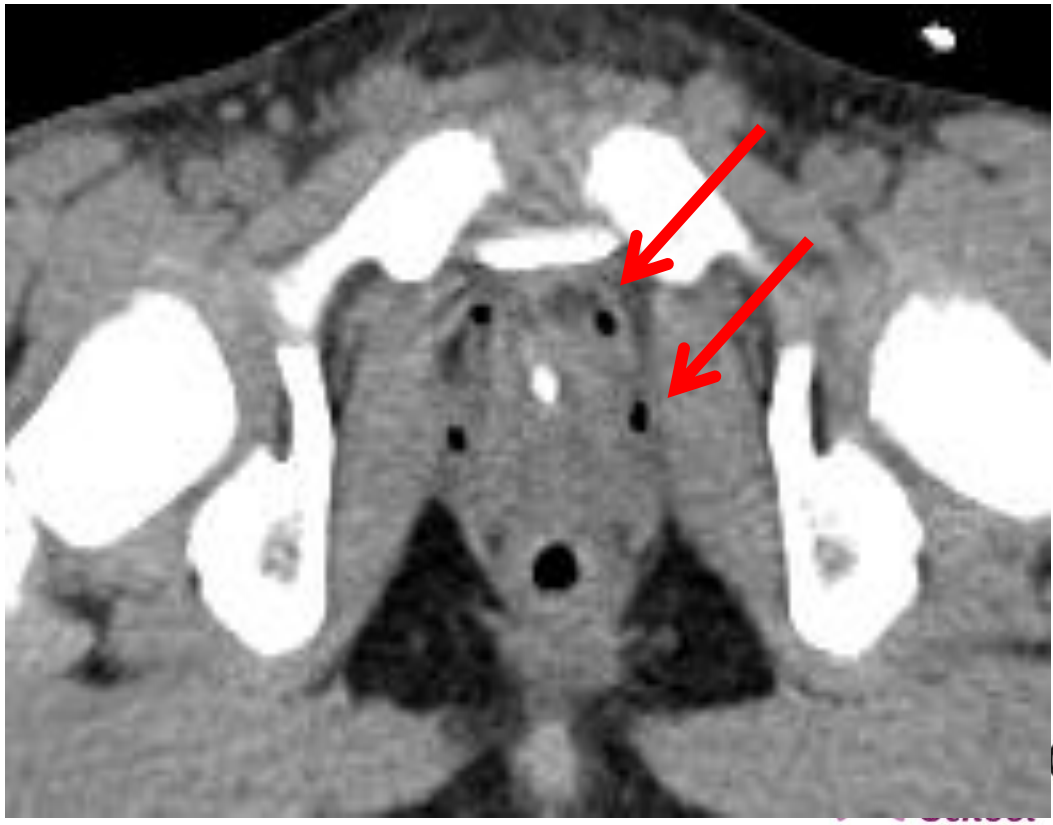
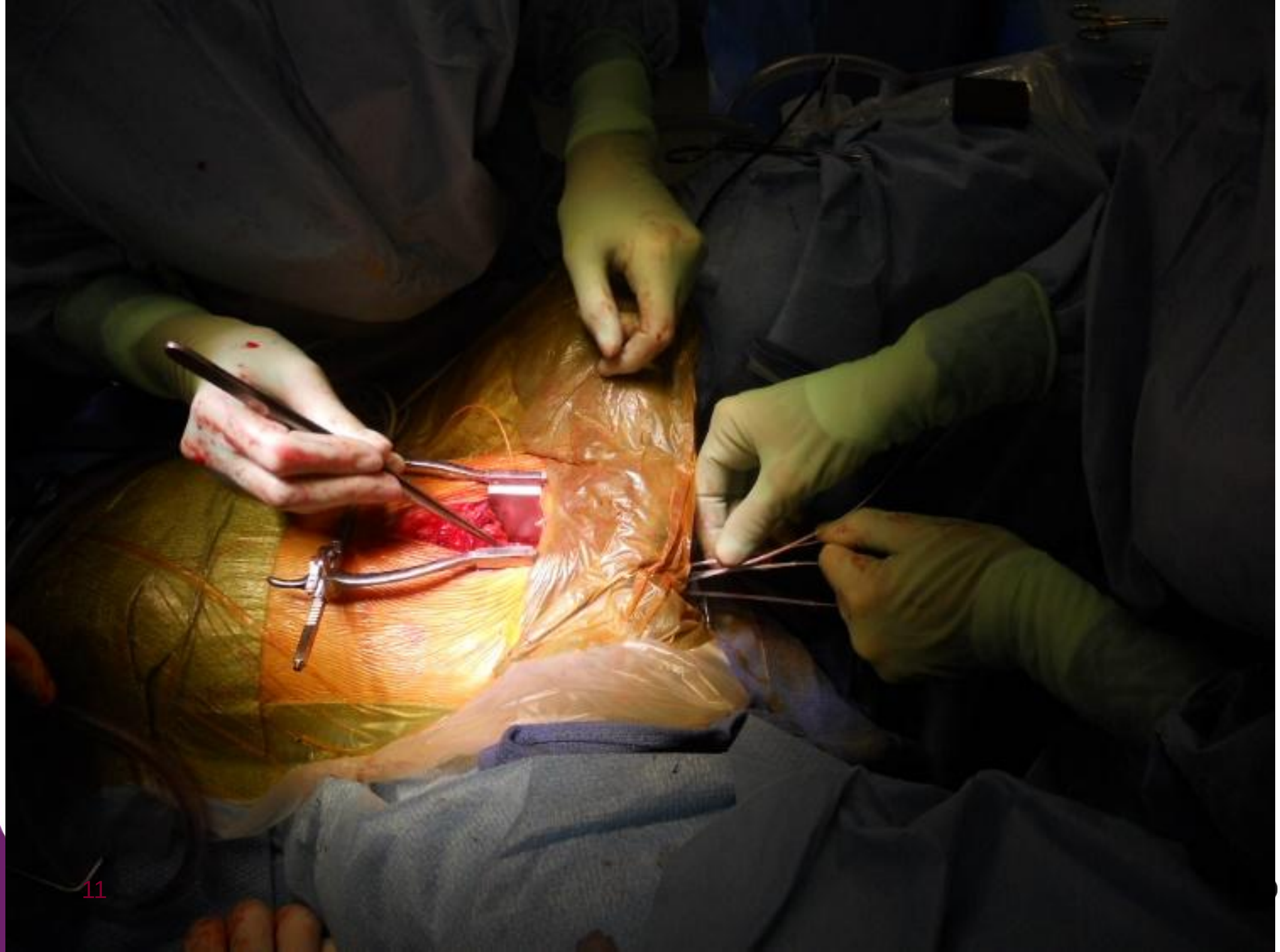
Prostate/bladder RMS



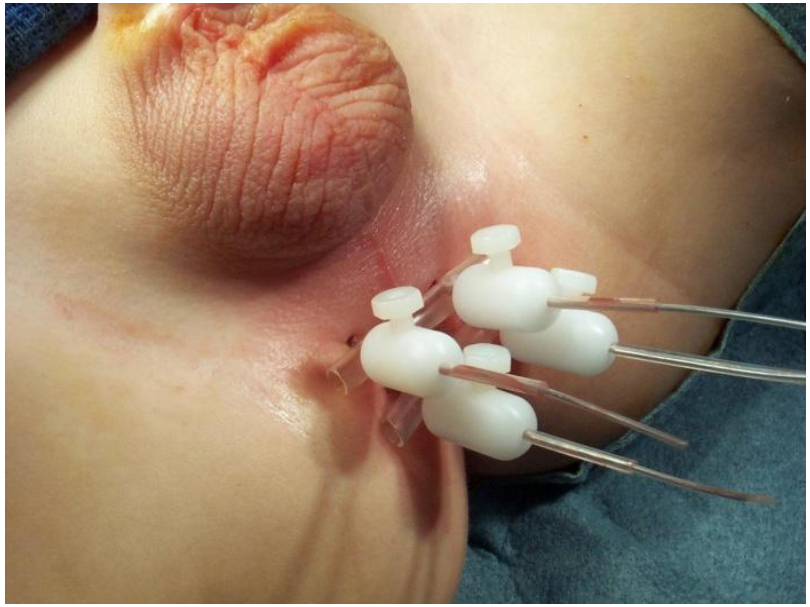
- 2 sagital loops
- Encompassing the prostate
- Perineal approach

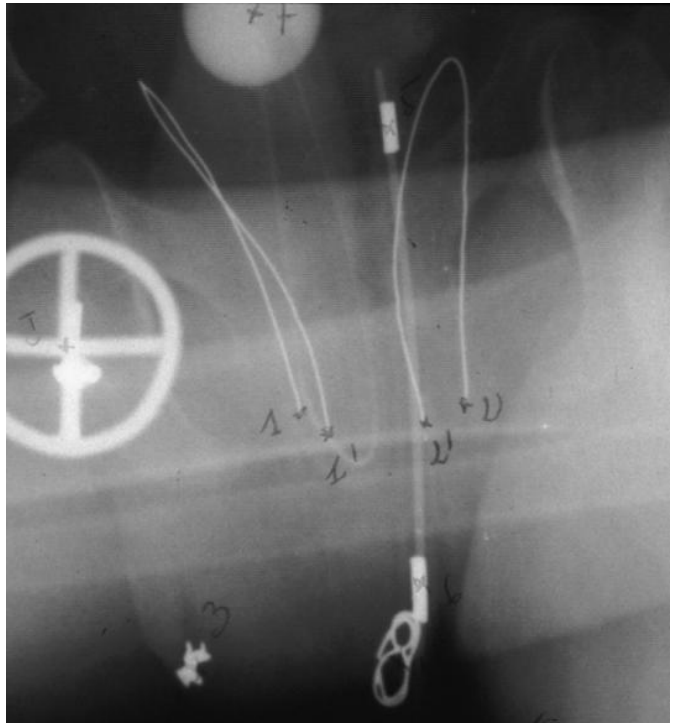


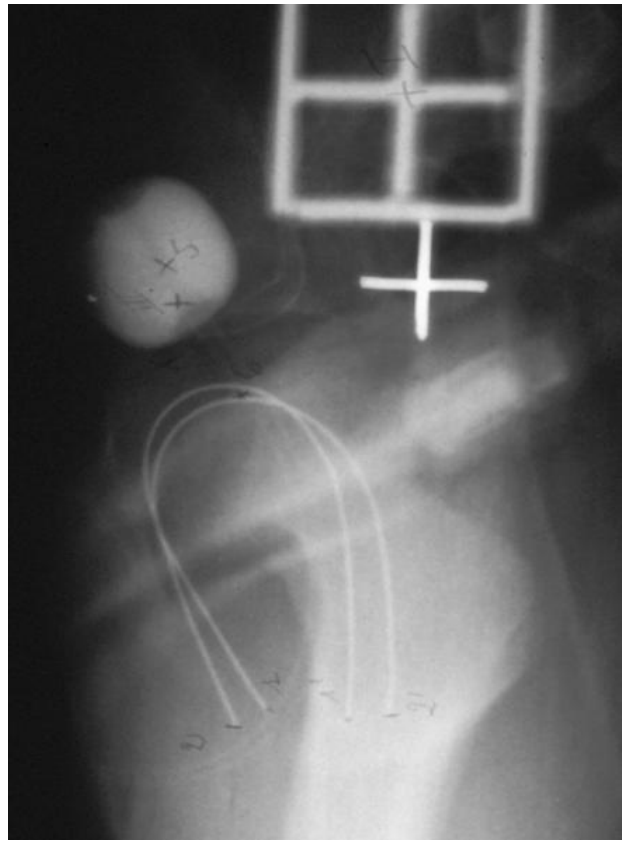
Per-operative implantation: perineal approach



Prostate/bladder RMS: loops techniques







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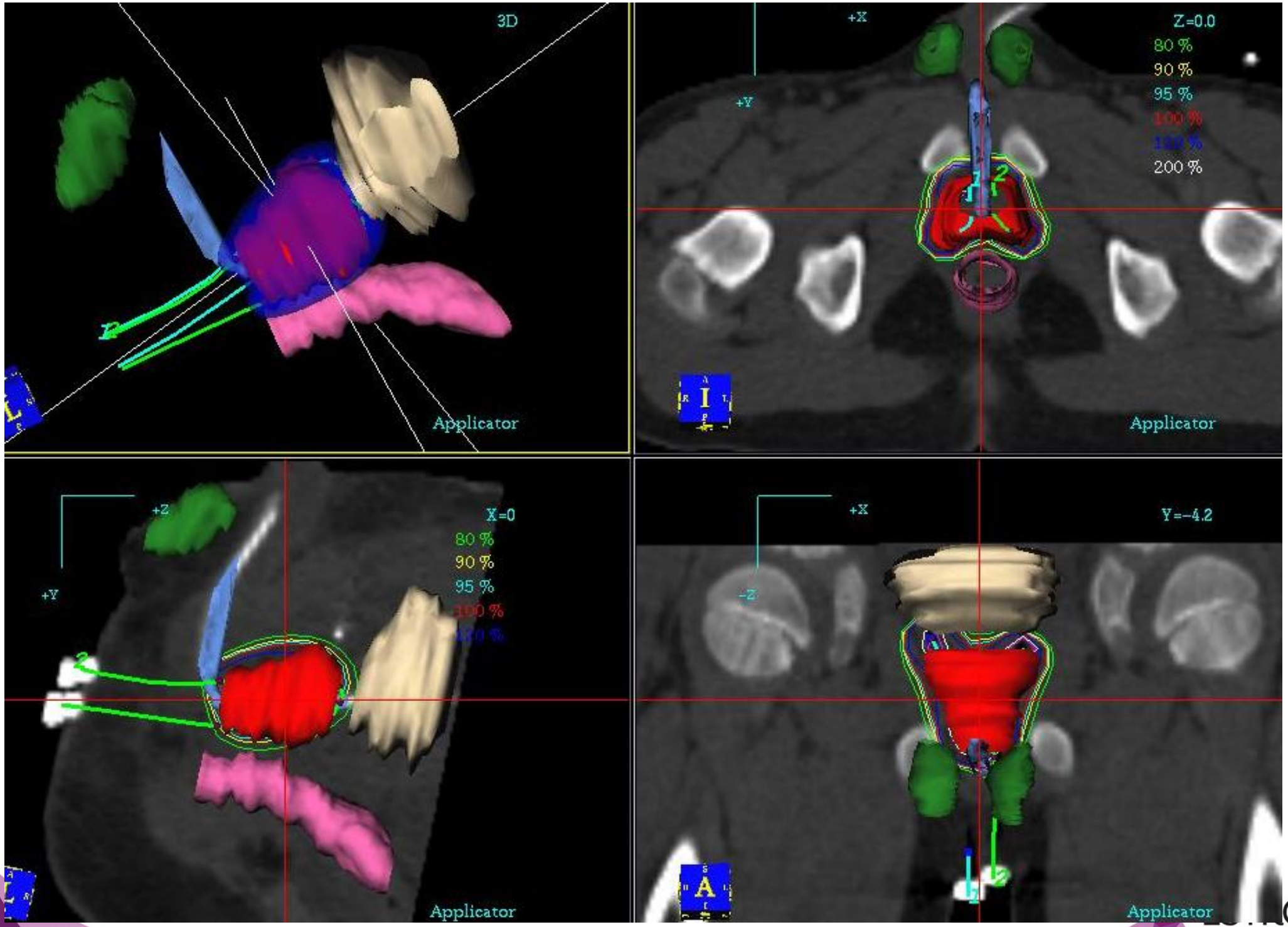
3D
Applicator
+X
+Y
Z=0.0
80 %
90 %
95 %
200 %
Applicator
+Z
+Y
X=0
80 %
90 %
95 %
Applicator
+X
-Z
Y=-4.2
Applicator

Loops technique

- Mimicking the LDR experience
  - 2 tubes and sagittal large loops
- Large curve
  - Enough for afterloaders
  - But one case of obstruction
- Technique adaptation
  - PDR
  - Paris system
  - 4 tubes

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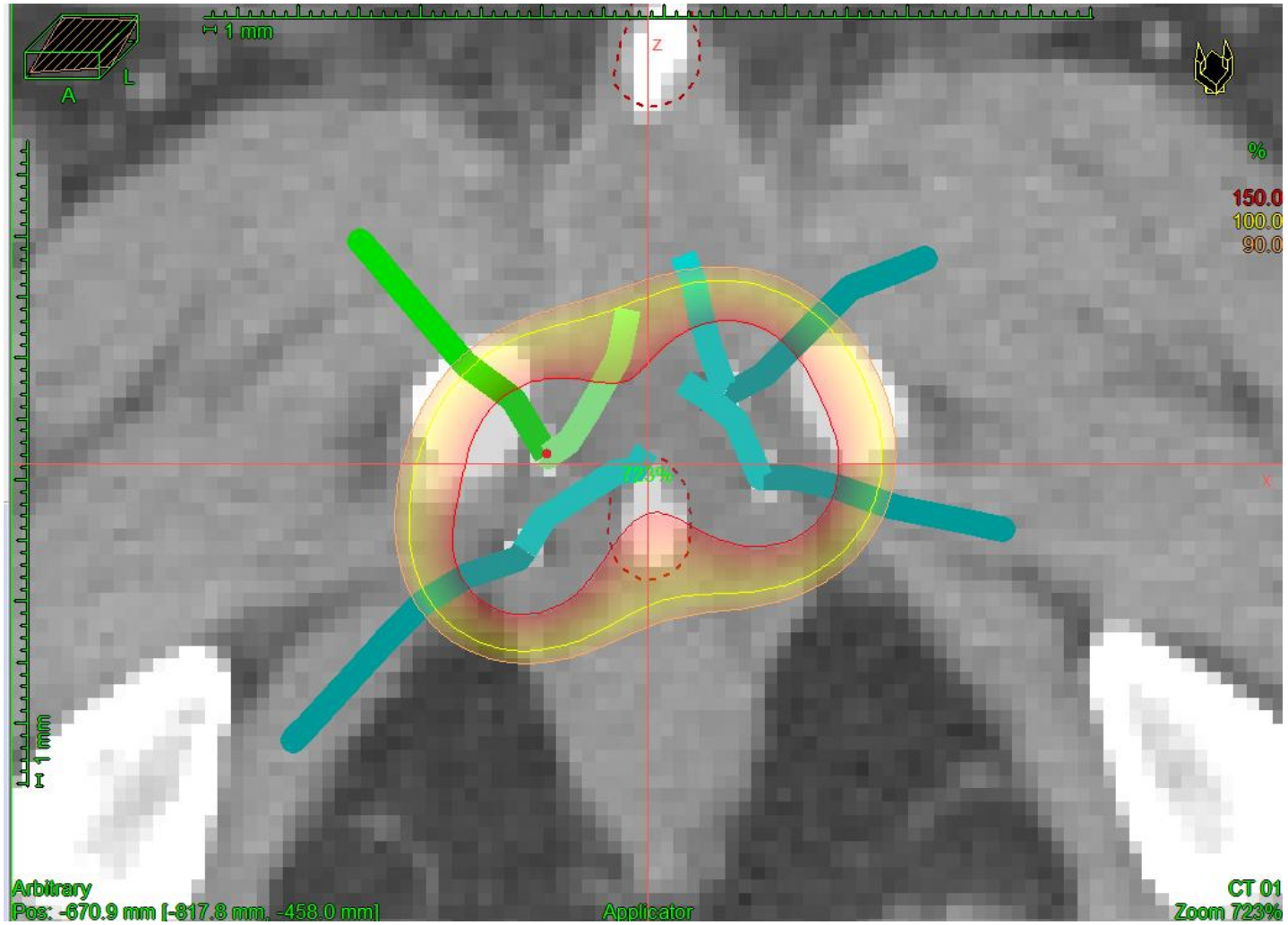

Catheter	Dwell pos.	X [m...	Y[mm]	Z[mm]	Weight	diff W	Time [s]	Dwell weight
1	8	-19.6	-750.6	149.1	1.00	0.00	23.82	
1	9	-19.1	-754.6	146.1	1.00	0.00	23.82	
1	10	-18.7	-758.6	143.1	1.00	0.00	23.82	
1	11	-18.6	-763.0	140.7	0.84	0.00	20.00	
1	12	-18.5	-767.4	138.3	0.84	0.00	20.00	
1	13	-18.0	-772.1	136.6	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

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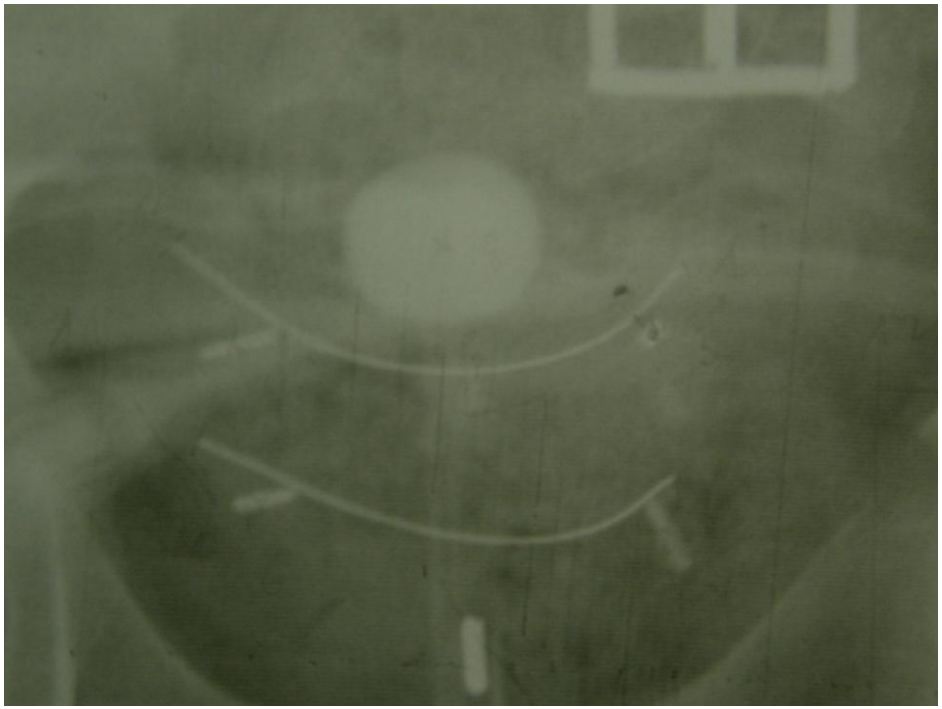
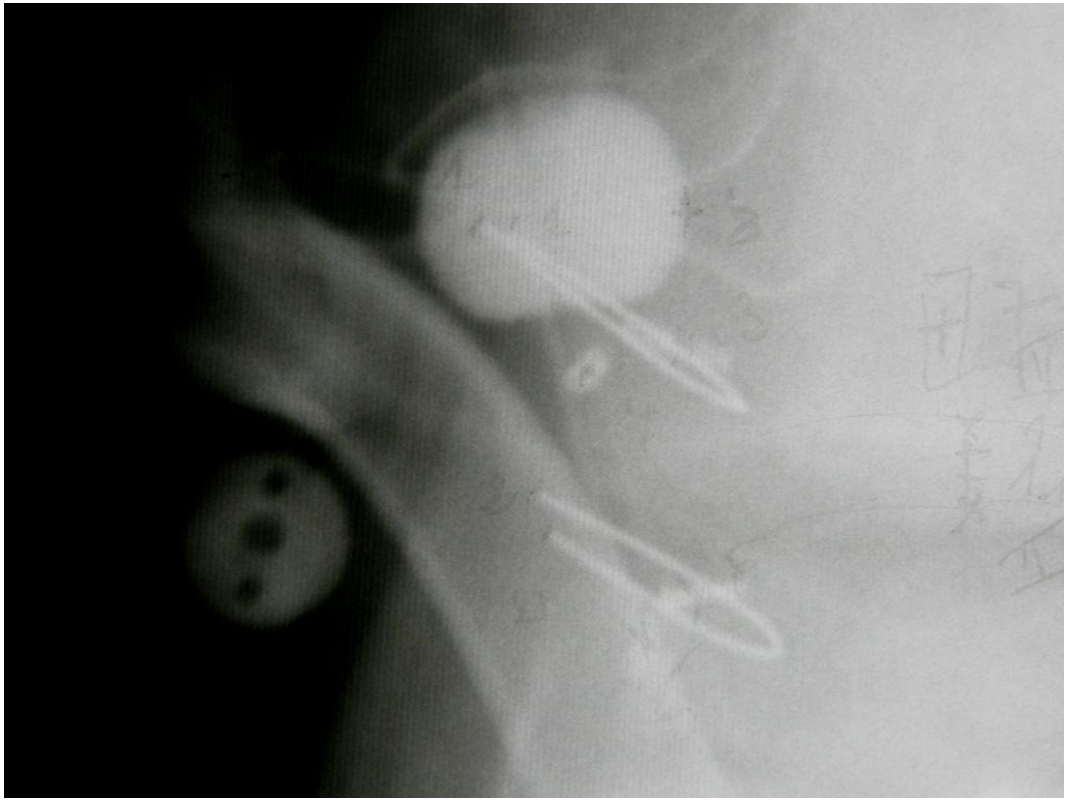
Prostate/bladder rhabdomyosarcoma





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

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

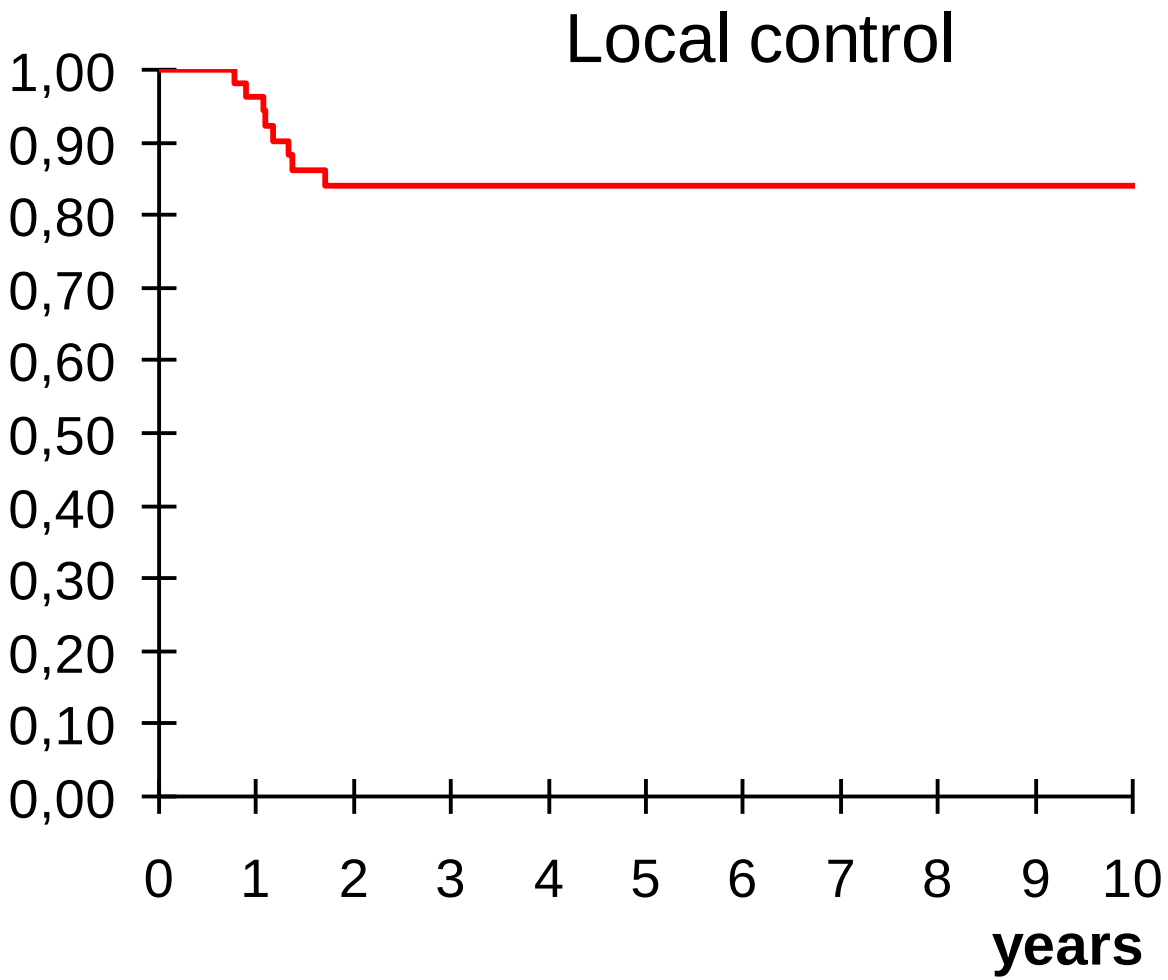
- Mean interval surgery-loading : 6 days
- Median prescribed dose: 60 Gy
- Paris system : 85% of basal dose
- Mean isodose volume : 29 cm^3
- 4 had a combination of external irradiation and brachytherapy (20-30 Gy + pelvic EBRT, 45 Gy)
- Mean bladder dose : 35 Gy
- Mean rectal dose : 35 Gy
- Mean testis dose : 3 Gy

Prostate/bladder RMS

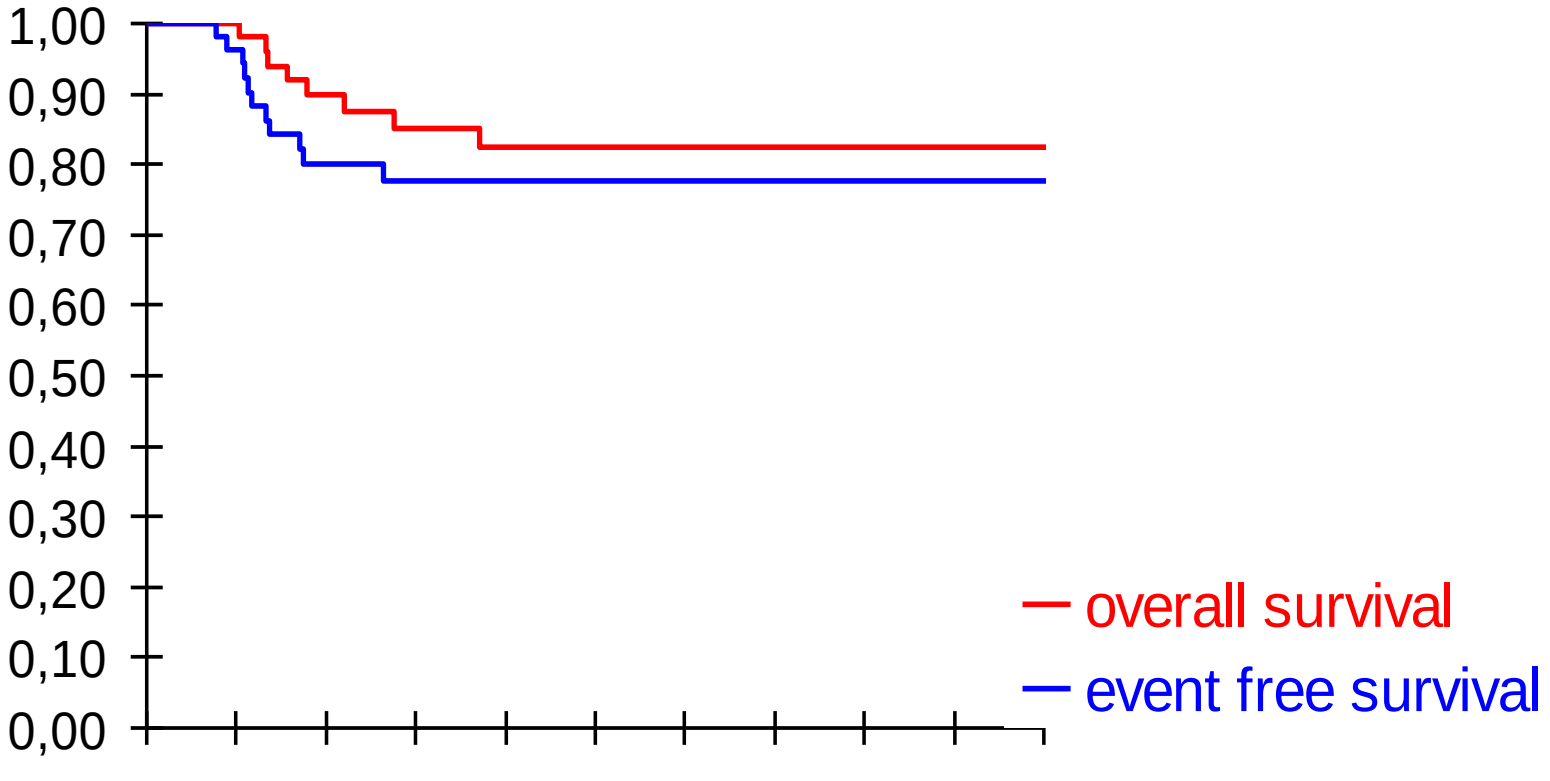
- Mean follow-up : 6.6 years (0.5-28.3)
- 7 recurrences within or above the treated BT volume (3 combined with regional/metastasis):
  - 5 before 2000 (out of 28)
  - 2 after 2000 (out of 39)
- Mean time to failure : 10.3 months

  (range : 5.2-14.1 months)
- 2 salvaged by surgery + chemotherapy

Prostate/bladder rhabdomyosarcoma



Prostate/bladder rhabdomyosarcoma



At risk

—	55	51	41	35	30	24	24	21	16	14	10
—	55	49	37	32	29	23	23	20	15	13	9

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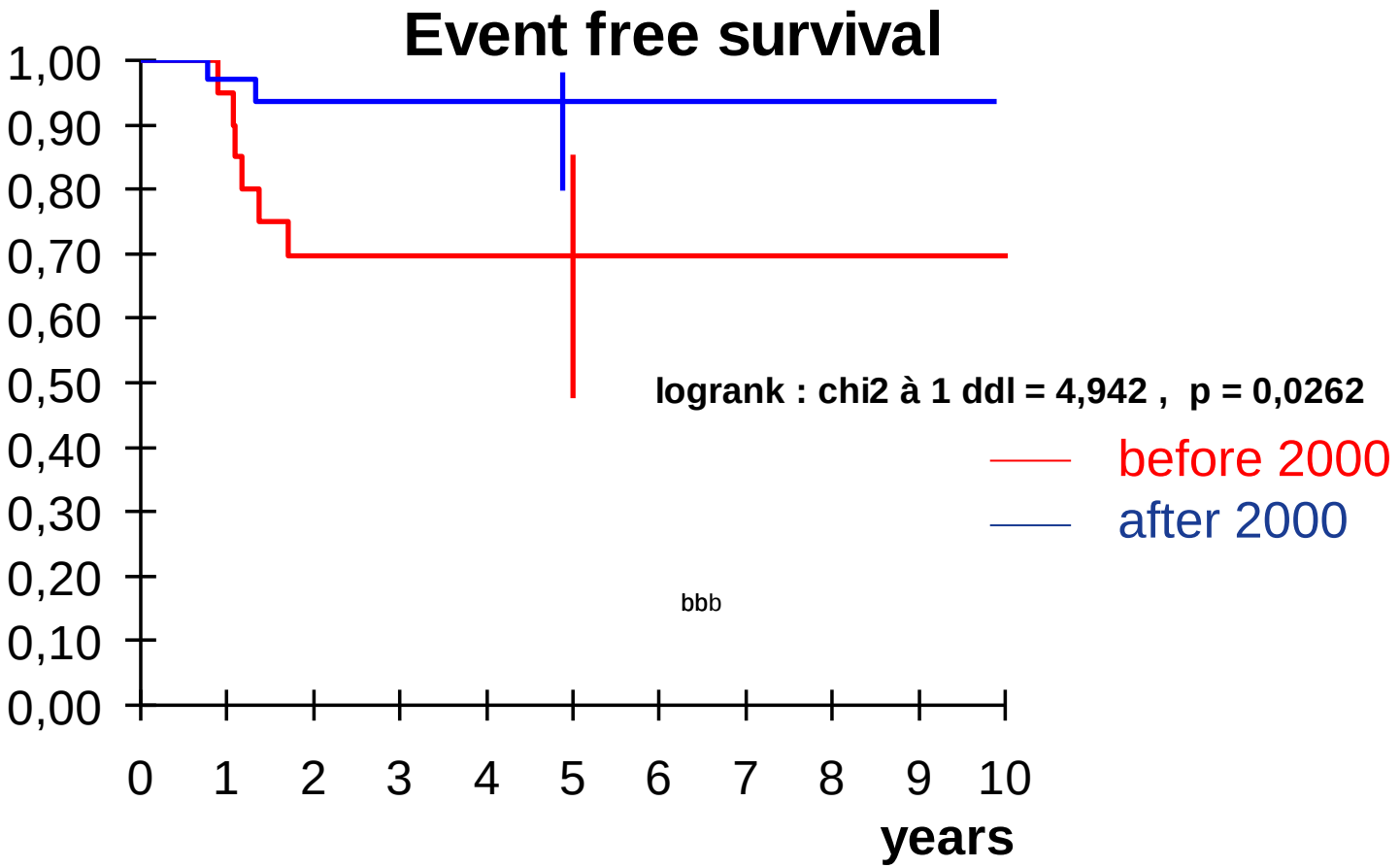
Prostate/bladder rhabdomyosarcoma



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)
- Median 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

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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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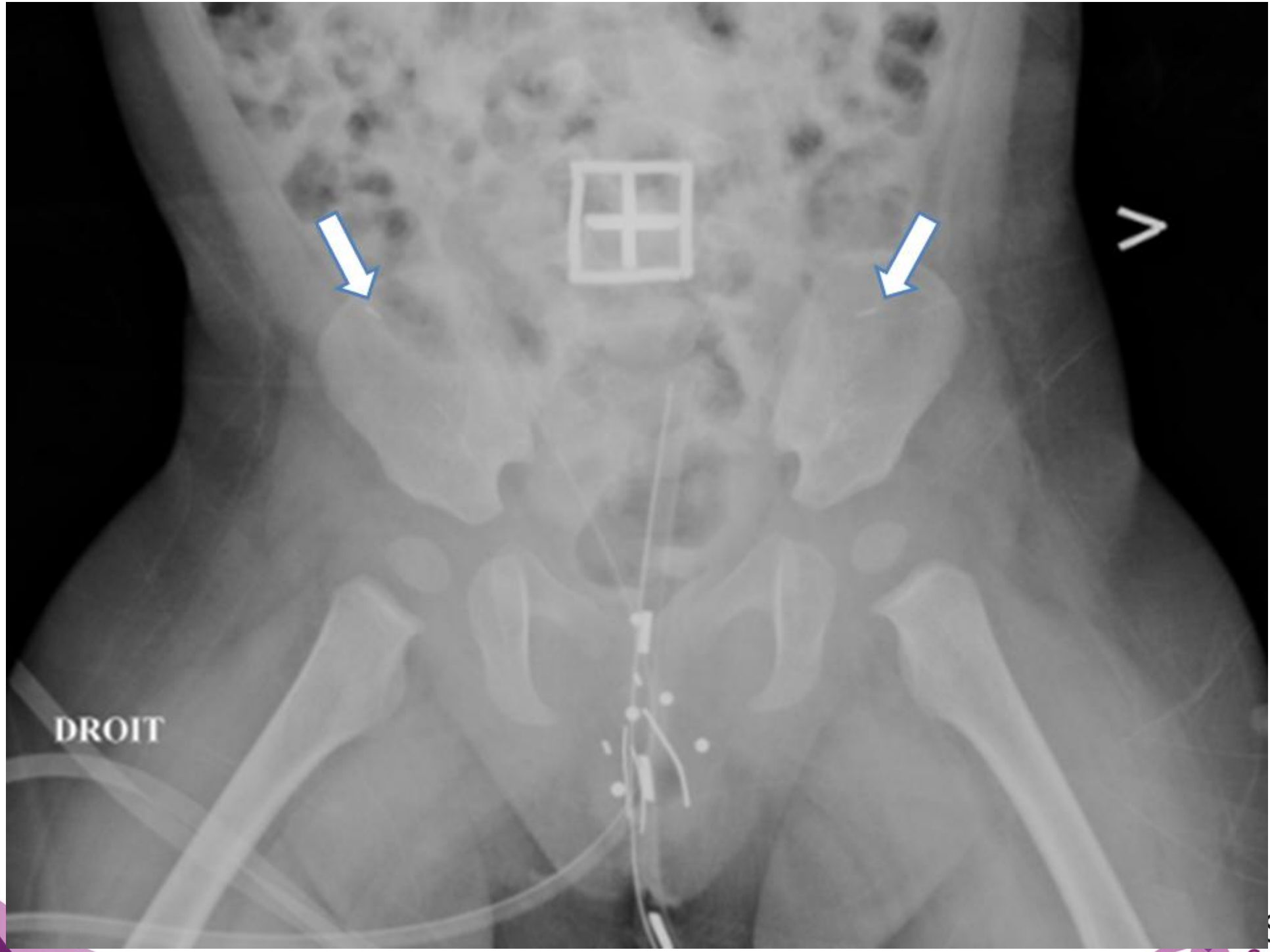
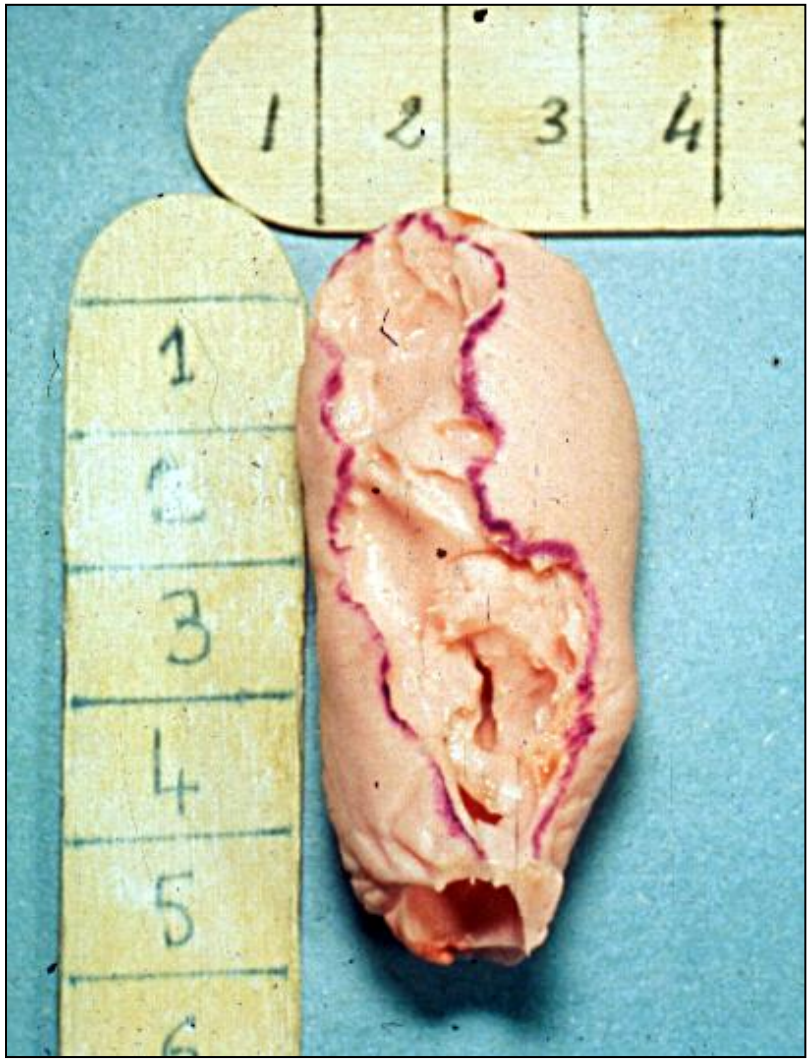
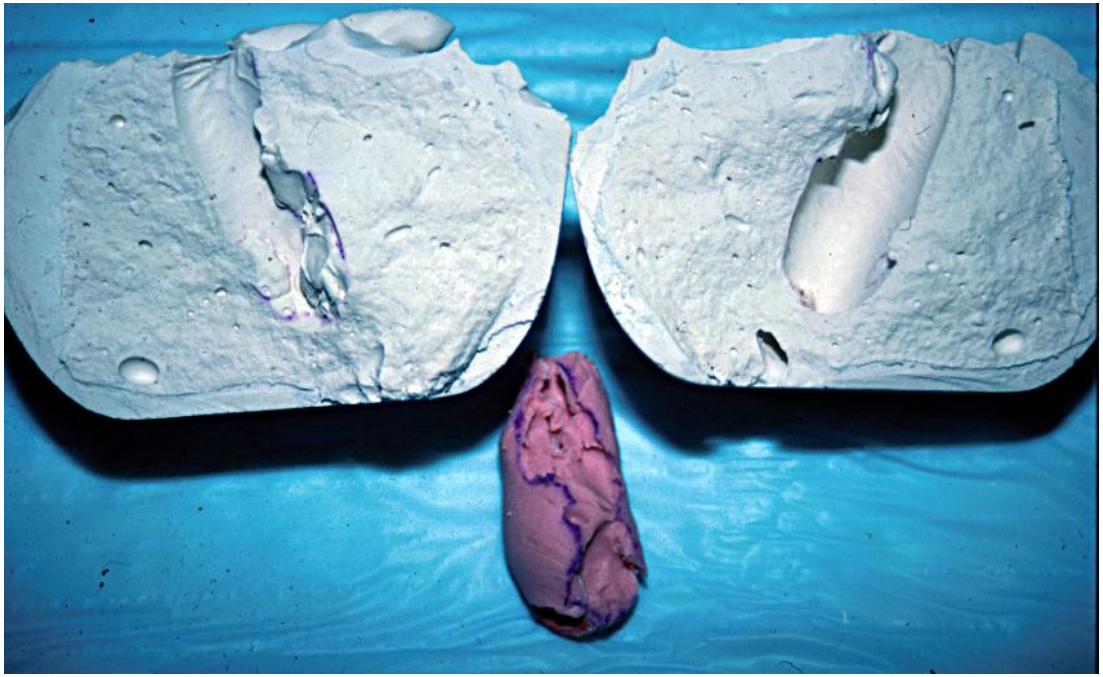
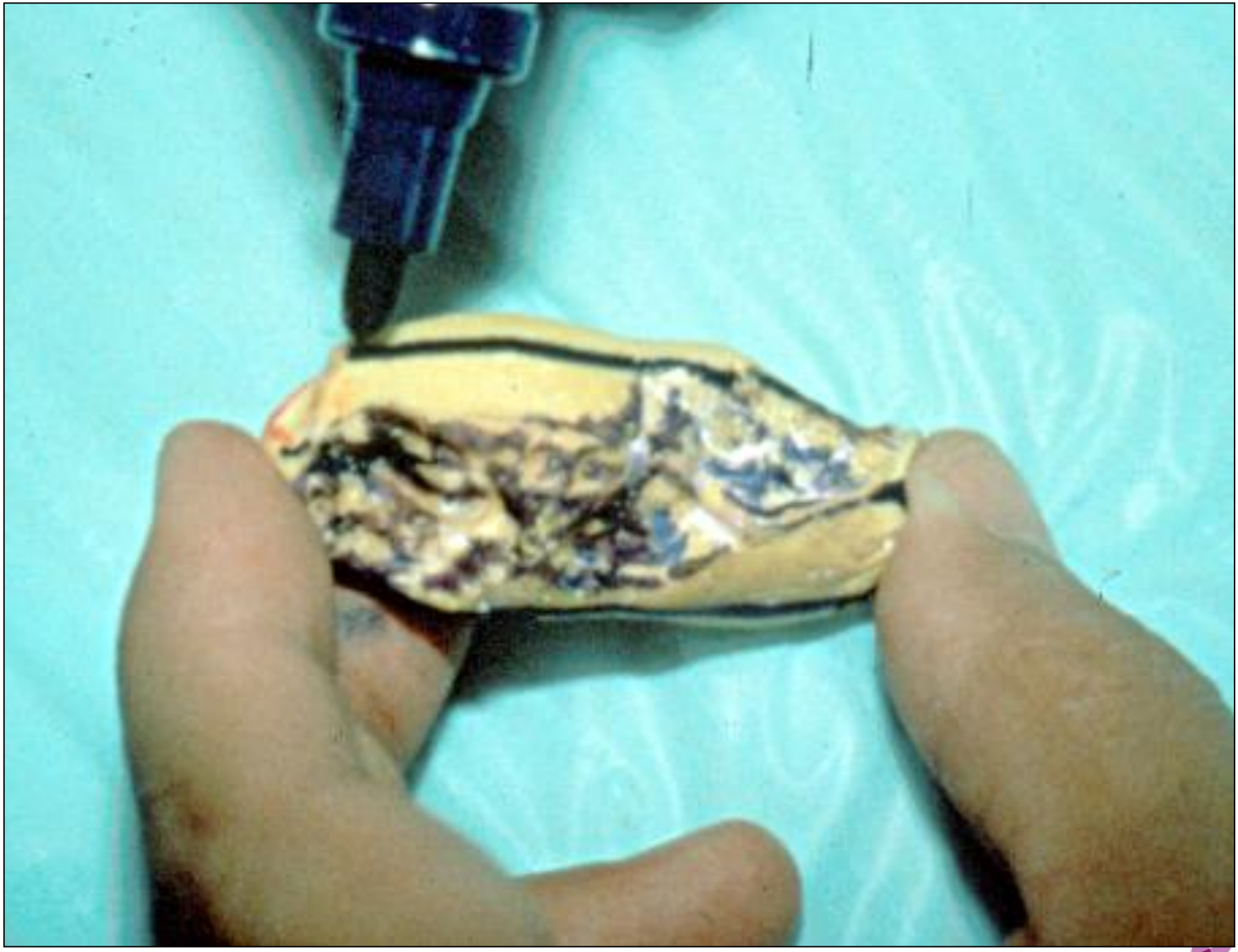
« Grape bunches »

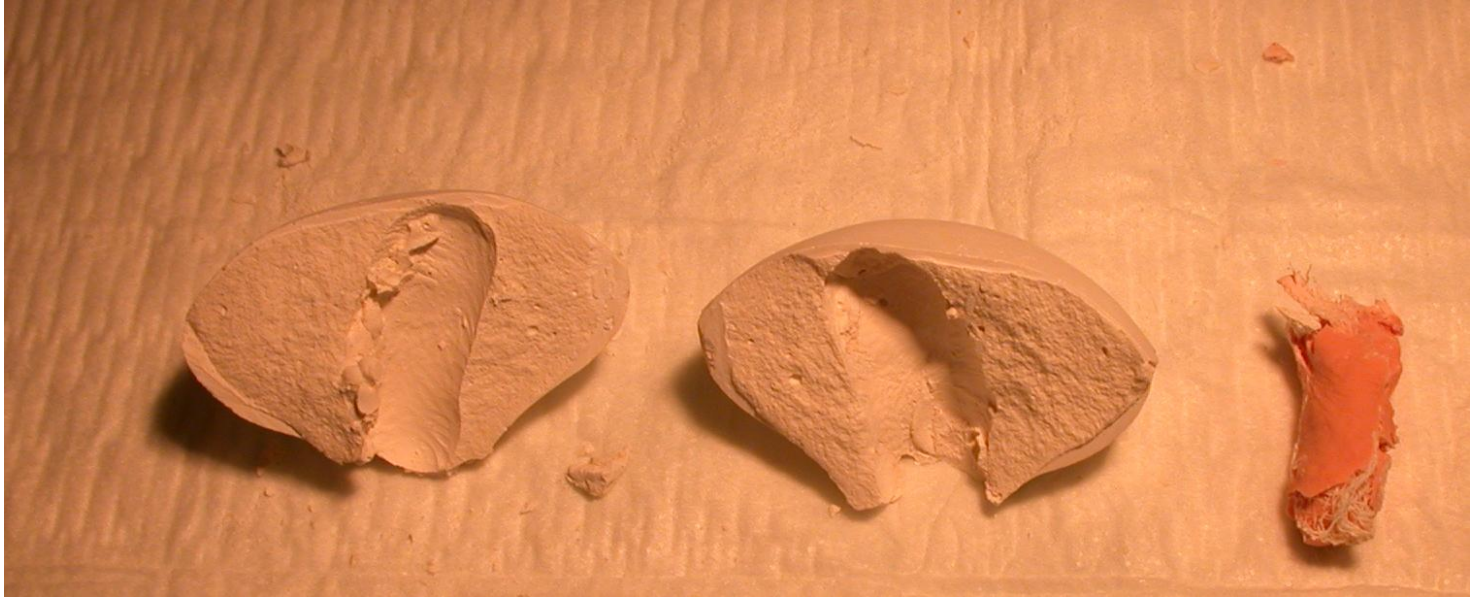

DROIT

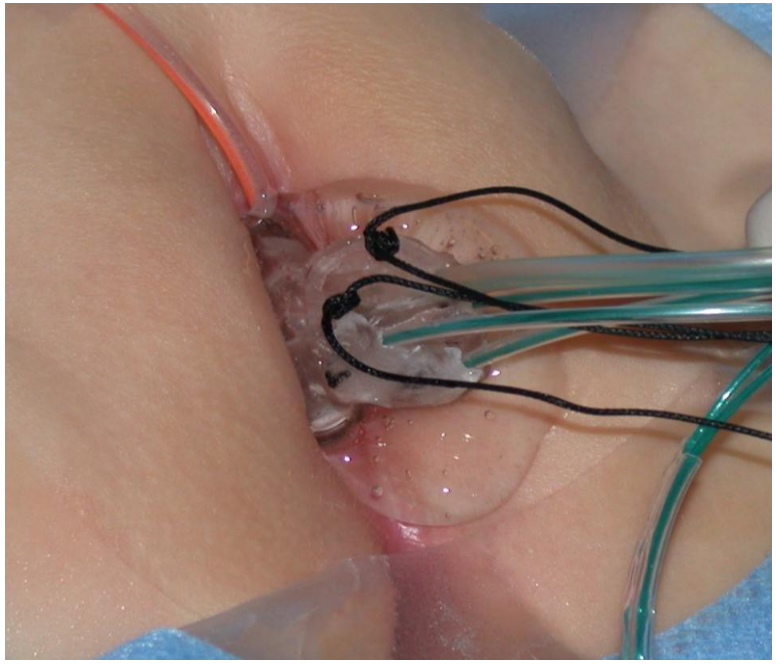
Vaginal impression

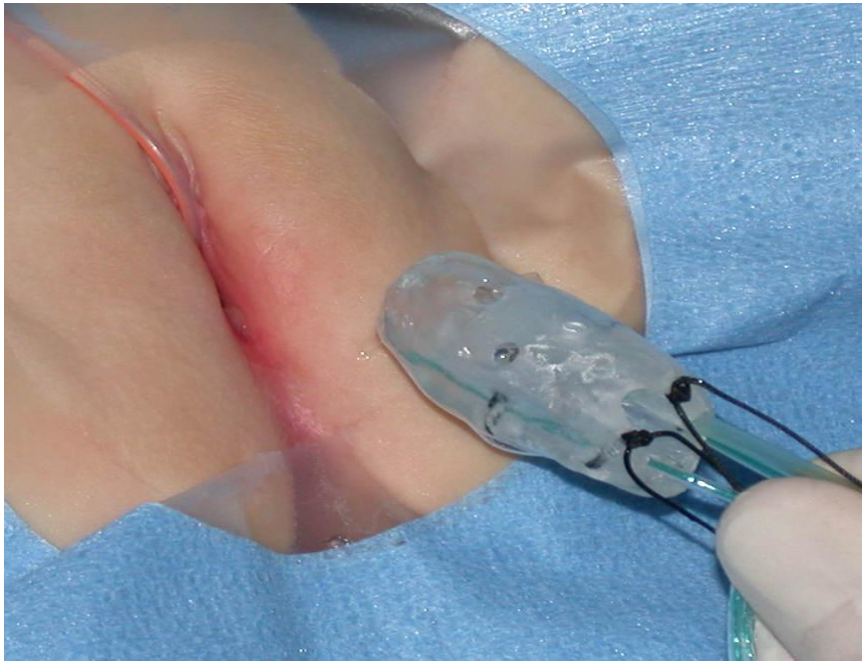


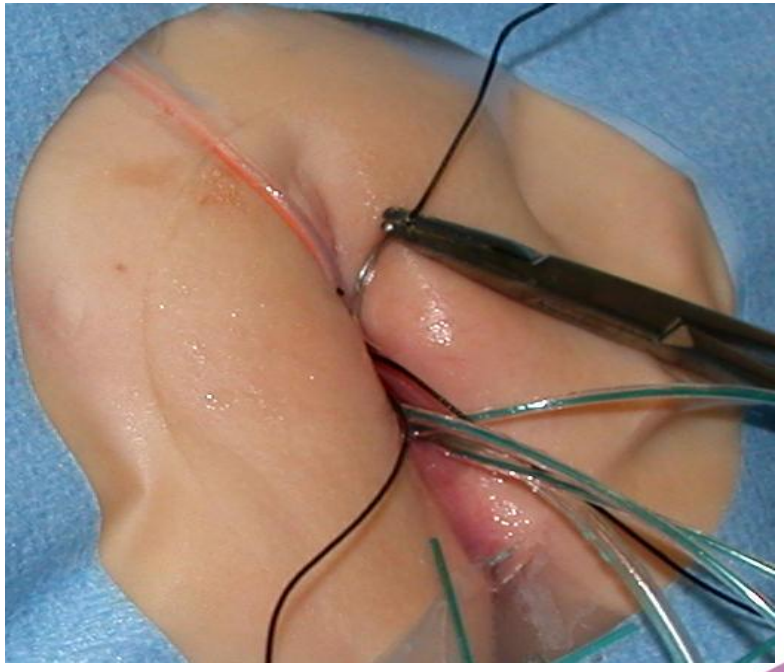


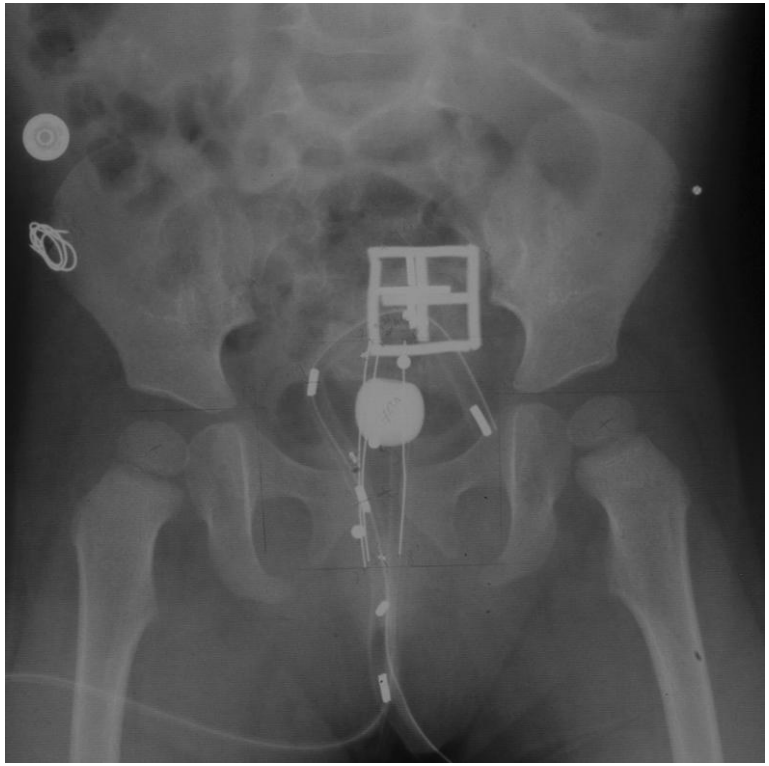


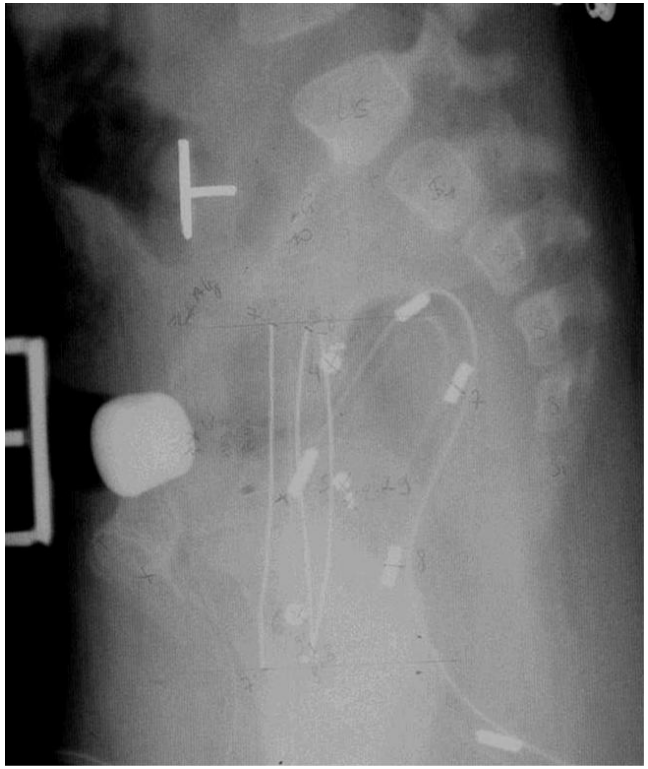


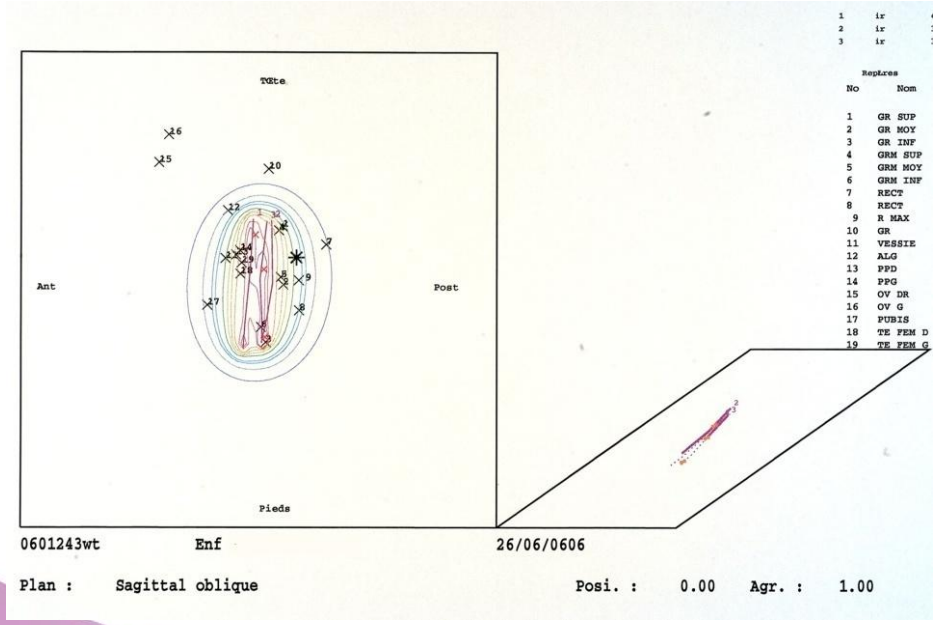








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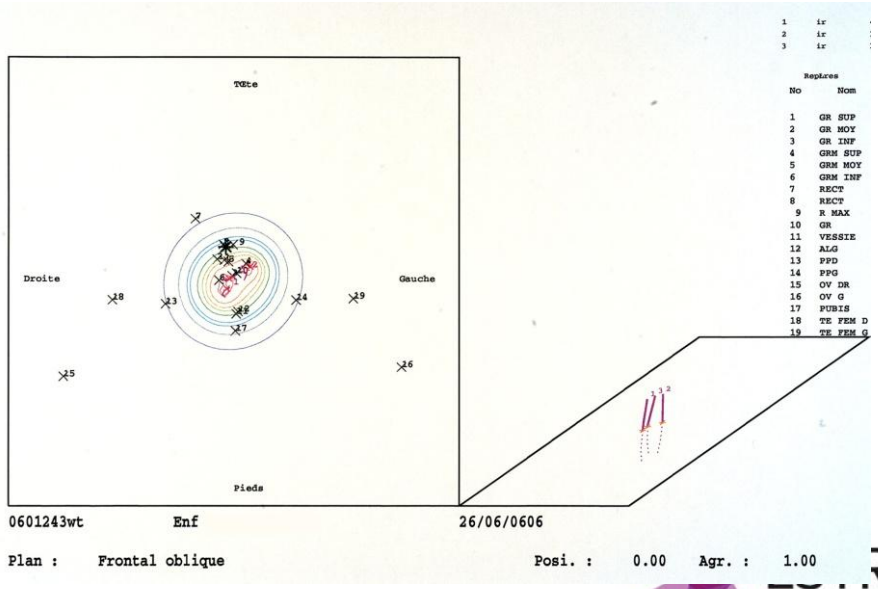
17 PUBIS
18 TE FEM D
19 TE FEM G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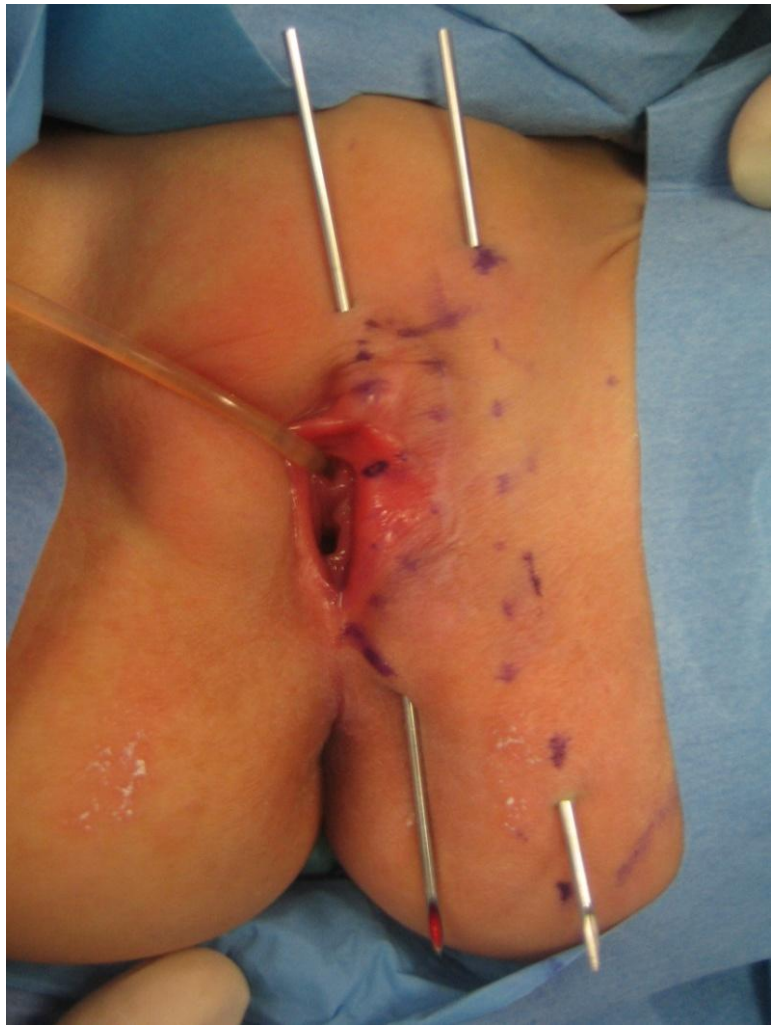
10 GR
11 VESSIE
12 ALG
13 PPD
14 PPG
15 OV DR
16 OV G
17 PUBIS
18 TE FEM D
19 TE FEM G

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

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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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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Head and Neck pediatric malignancies

The main aim for pediatric head and neck brachytherapy is …

A. To avoid the need for surgical excision
B. To increase survival
C. To reduce radiation associated side effects
D. To be used only as salvage radiation treatment after previous external beam radiotherapy

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Rhabdomyosarcoma

Classification according to localization

- Orbit
- Parameningeal
  - Nasopharynx, nasal cavity, parapharyngea area, paranasal sinuses, infratemporal and pterygopalatine fossa, middle ear, mastoid
- Non-parameningeal
  - Oral cavity, nose, ear, cheek, scalp, neck, salivary glands

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Rhabdomyosarcoma: 3-5% of all pediatric malignanies

Orbit: ± 10%
Non-parameningeal: ± 15%
Parameningeal: ± 20%

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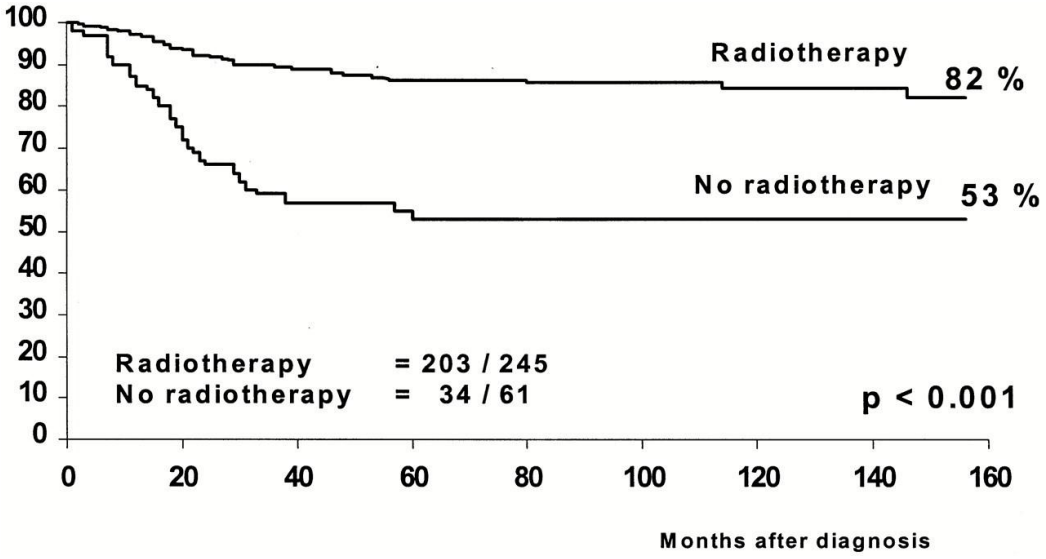
Results of treatment

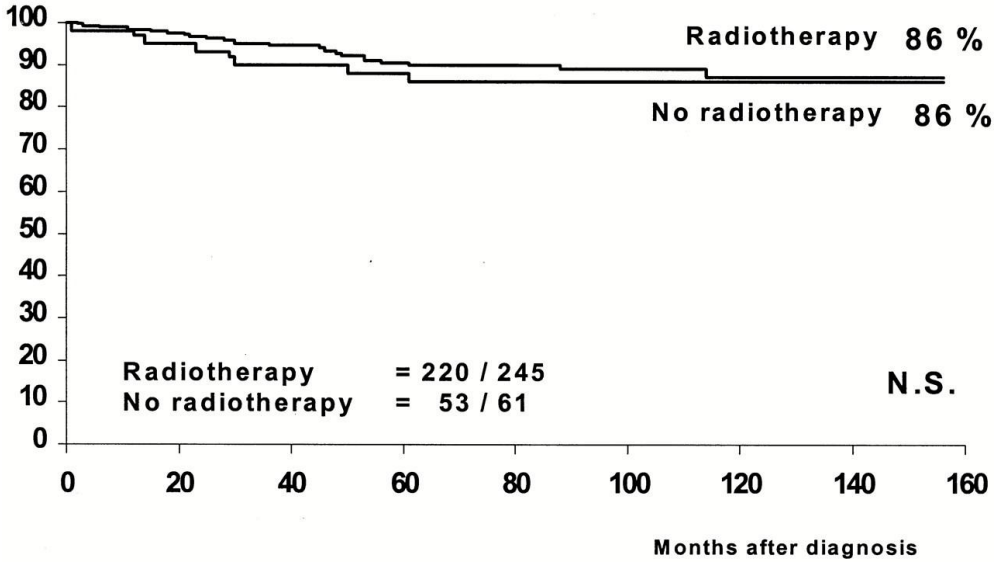
Orbital RMS

Prognostic risk factors

- Age < 3 years
- Alveolar subtype



Event Free Survival



Overall Survival

Oberlin et al. J Clin Oncol 2001;19:197-204

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Late sequelae radiotherapy orbital tumors

- Enucleation
- Cataract
- Reduced vision
- Dry eye
- Painful eye
- Keratitis
- Corneal ulcer
- Retinal damage
- Ptosis
- Orbital hypoplasia
- Maxillary hypoplasia

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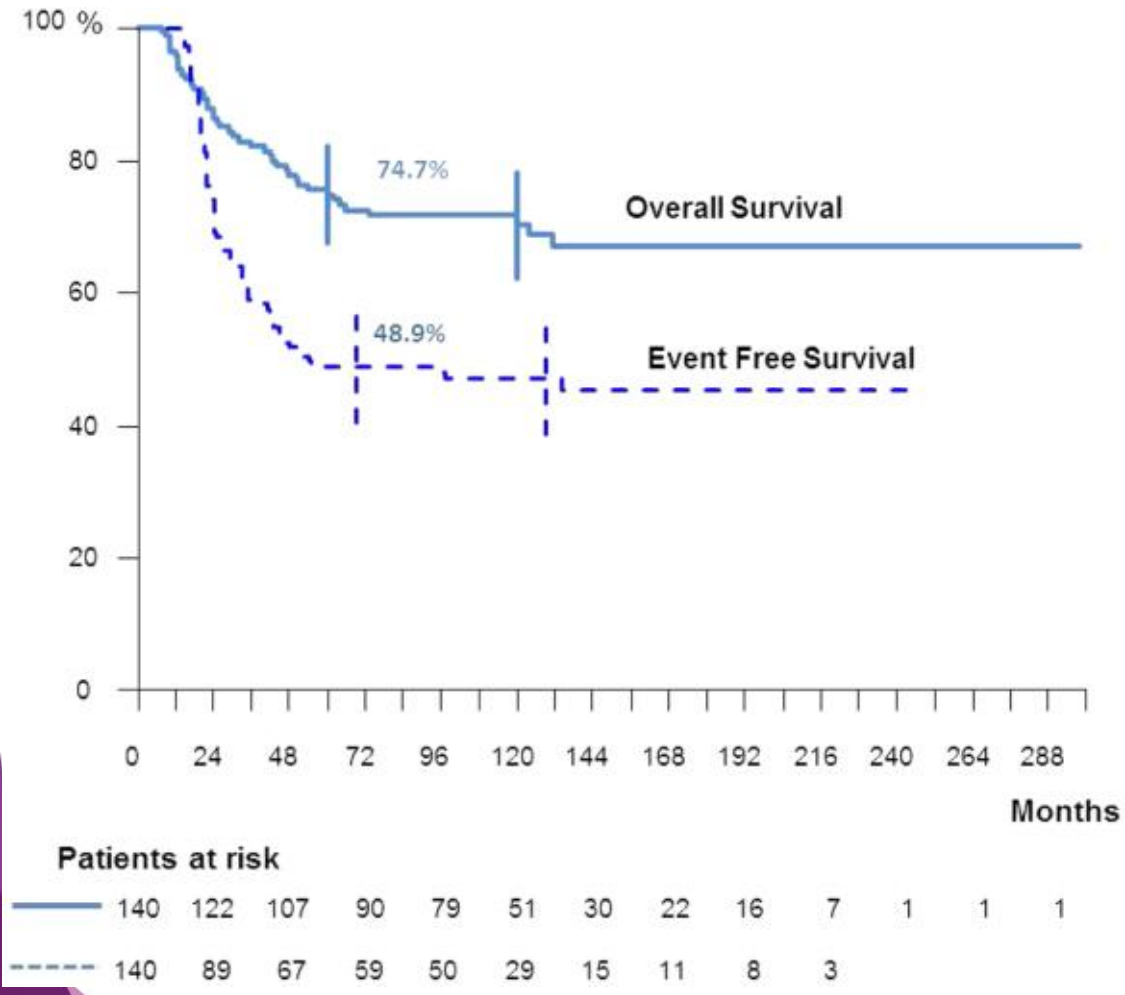
Results of treatment

Non-paramenigeal RMS



Prognostic risk factors

- N1
- Female
- Macroscopic residue (IRS group III)
- Salivary gland

Orbach et al. Head and Neck, 2016:DOI 10.1002/hed.24547

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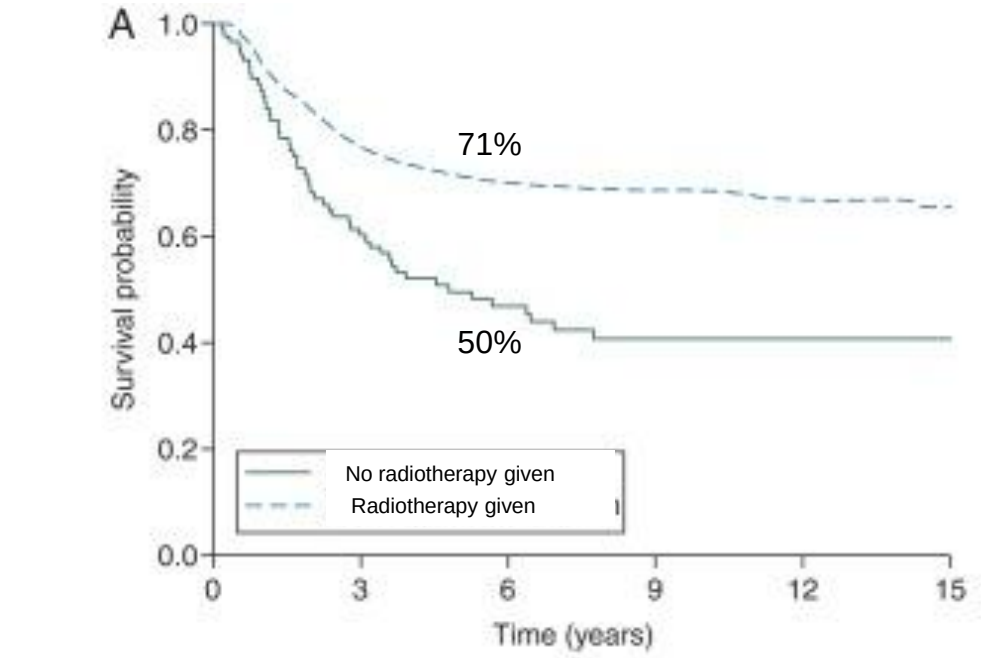
Results of treatment

Paramenigeal RMS



No. of patients at risk:

RT not given	89	53	33	24	11	1
RT given	1004	730	523	303	130	38

- Prognostic risk factors
- ≤ 1year, > 10 year
- Cranial nerve palsy, cranial base bone erosion, intra-cranial extension
- > 5 cm
- Alveolar subtype

Merks et al. Annals Oncol 2014;25:231-236

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Brachytherapy

Aim

To reduce frequency and severity of late sequelae of radiation therapy

Children; very sensitive to radiation

Large tumors

Lot of critical structures in head and neck area

Cosmetic appearance

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The AMORE Concept

- Ablative surgery
- MOld technique Brachytherapy
- REconstruction

in 1 week

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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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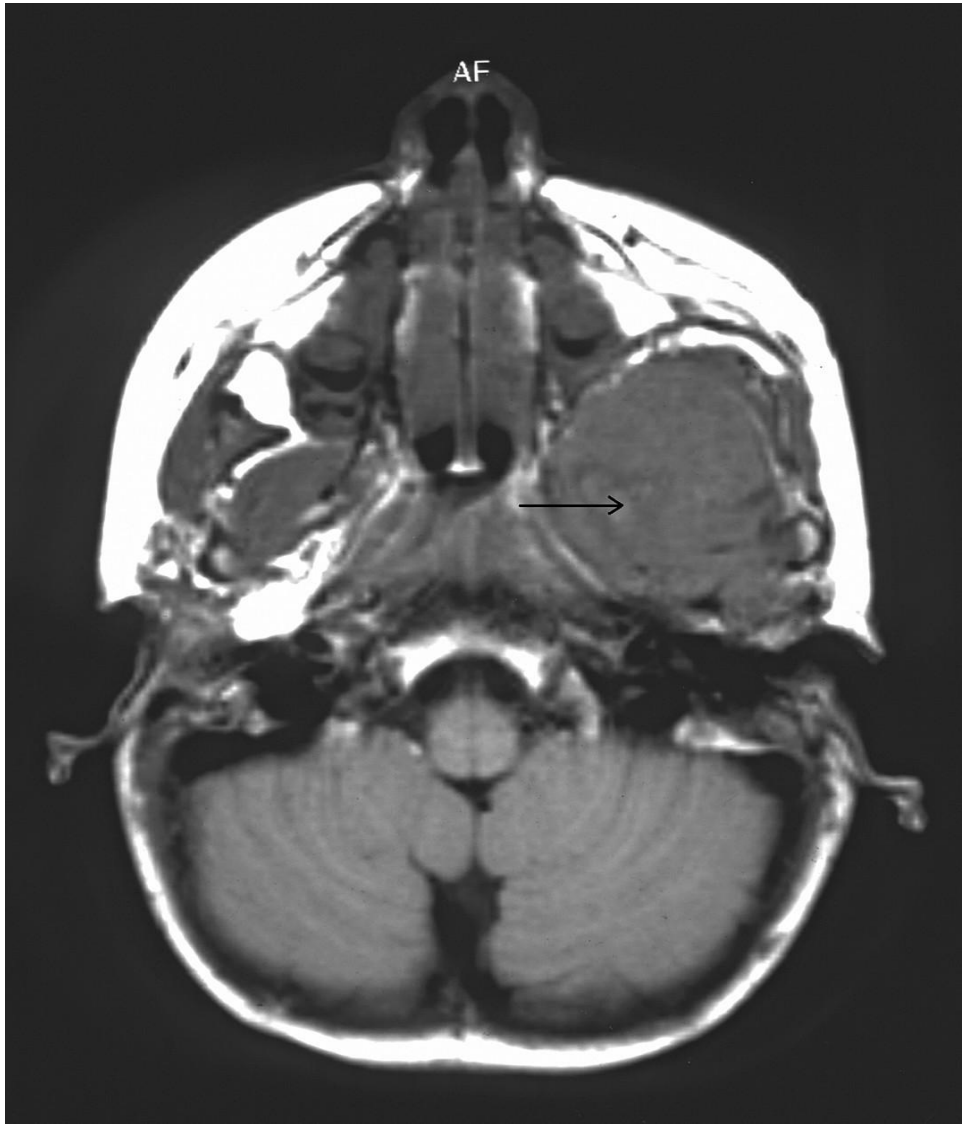
RMS in left pterygoid fossa



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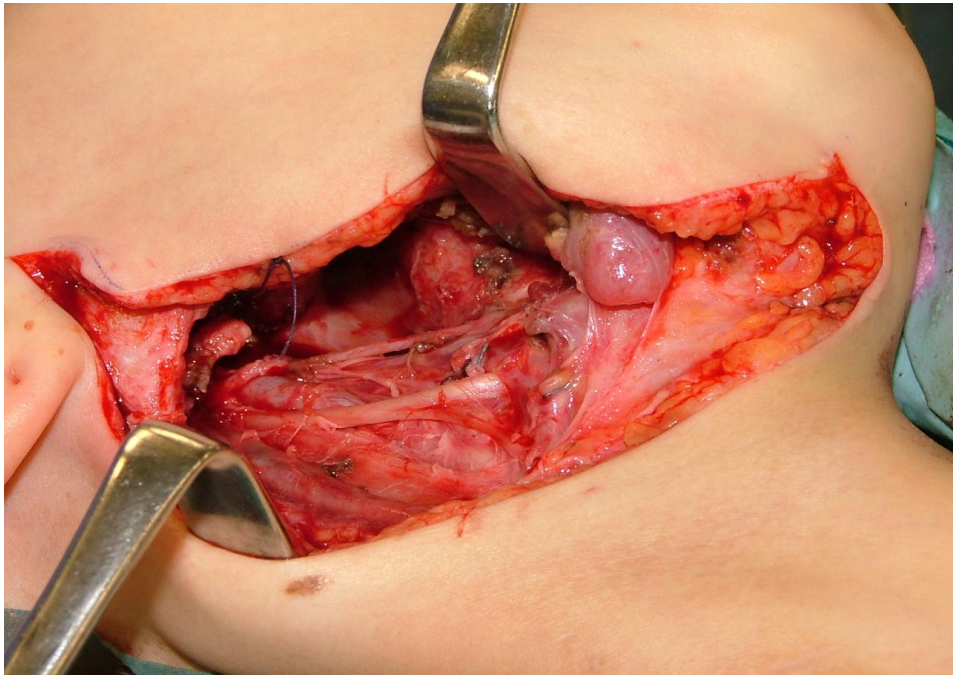
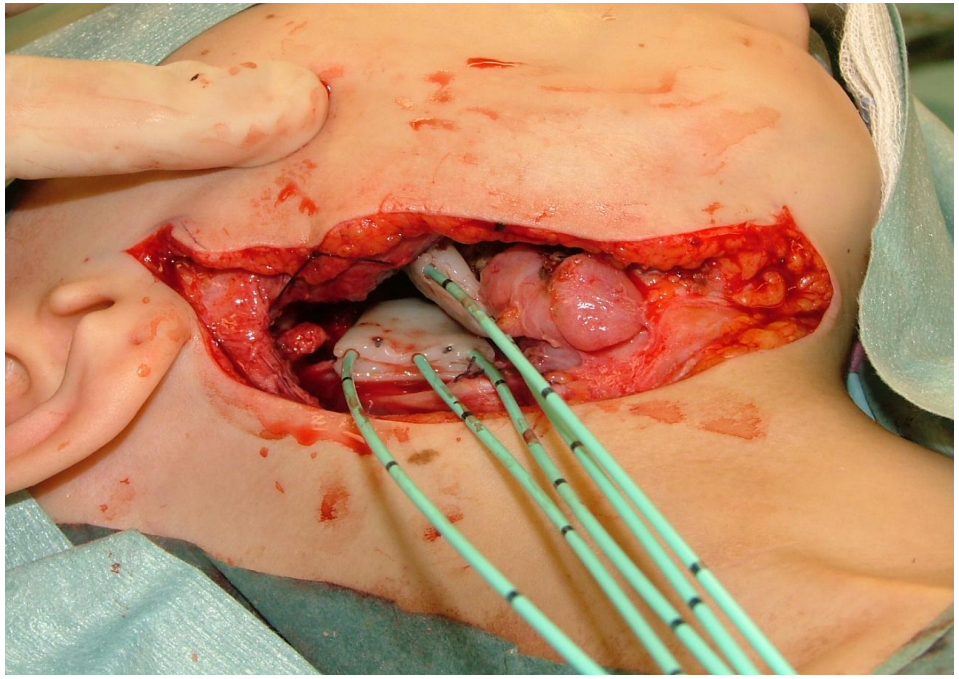
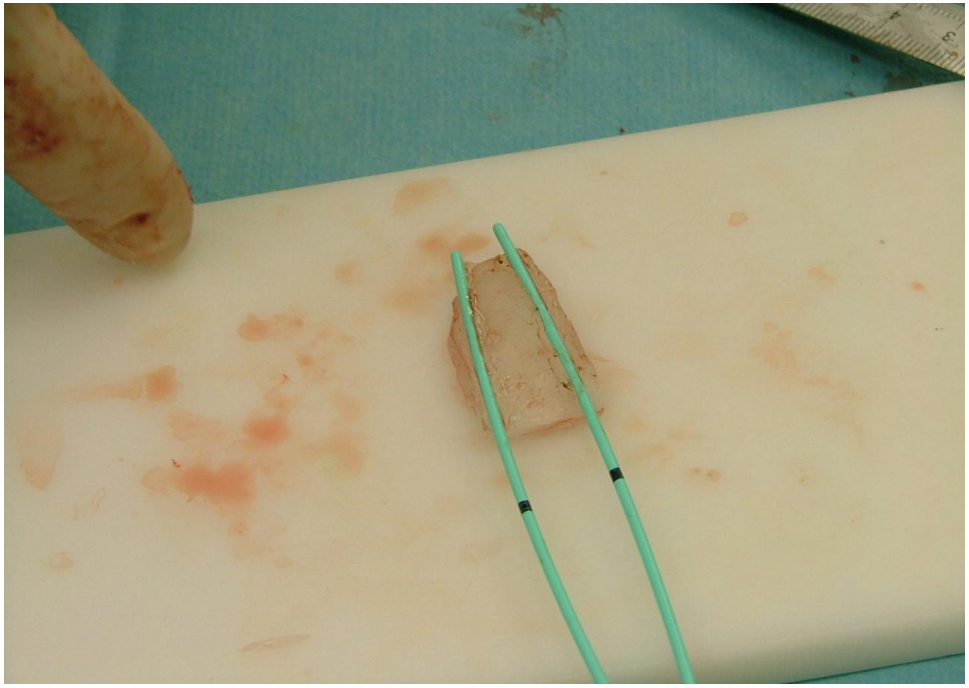




FastForm Percha

FastForm Research Ltd



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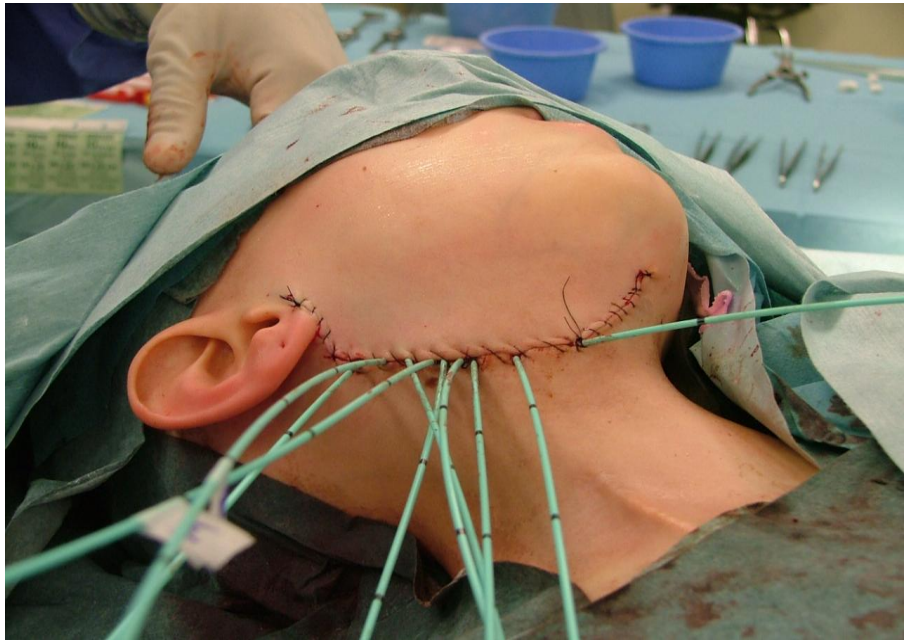

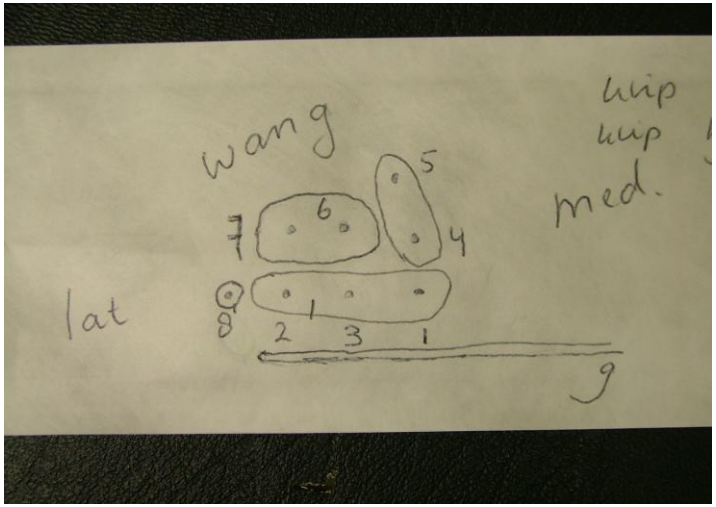
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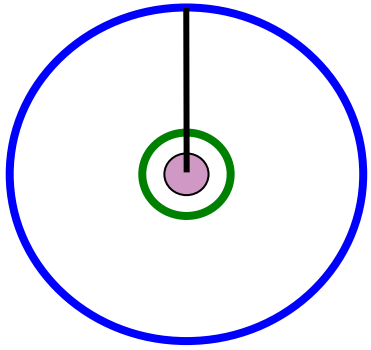
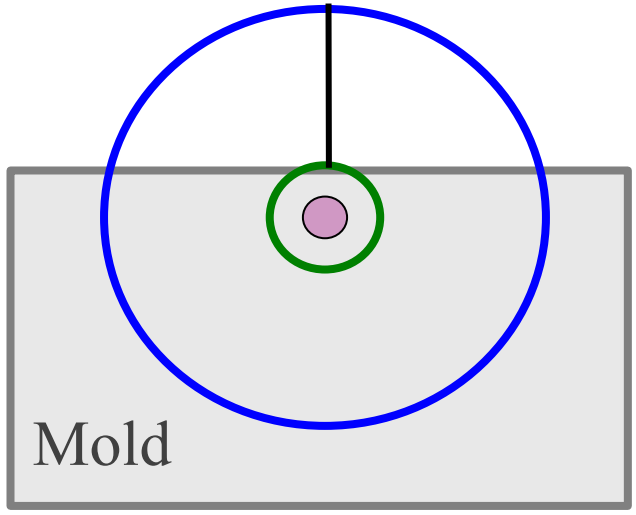
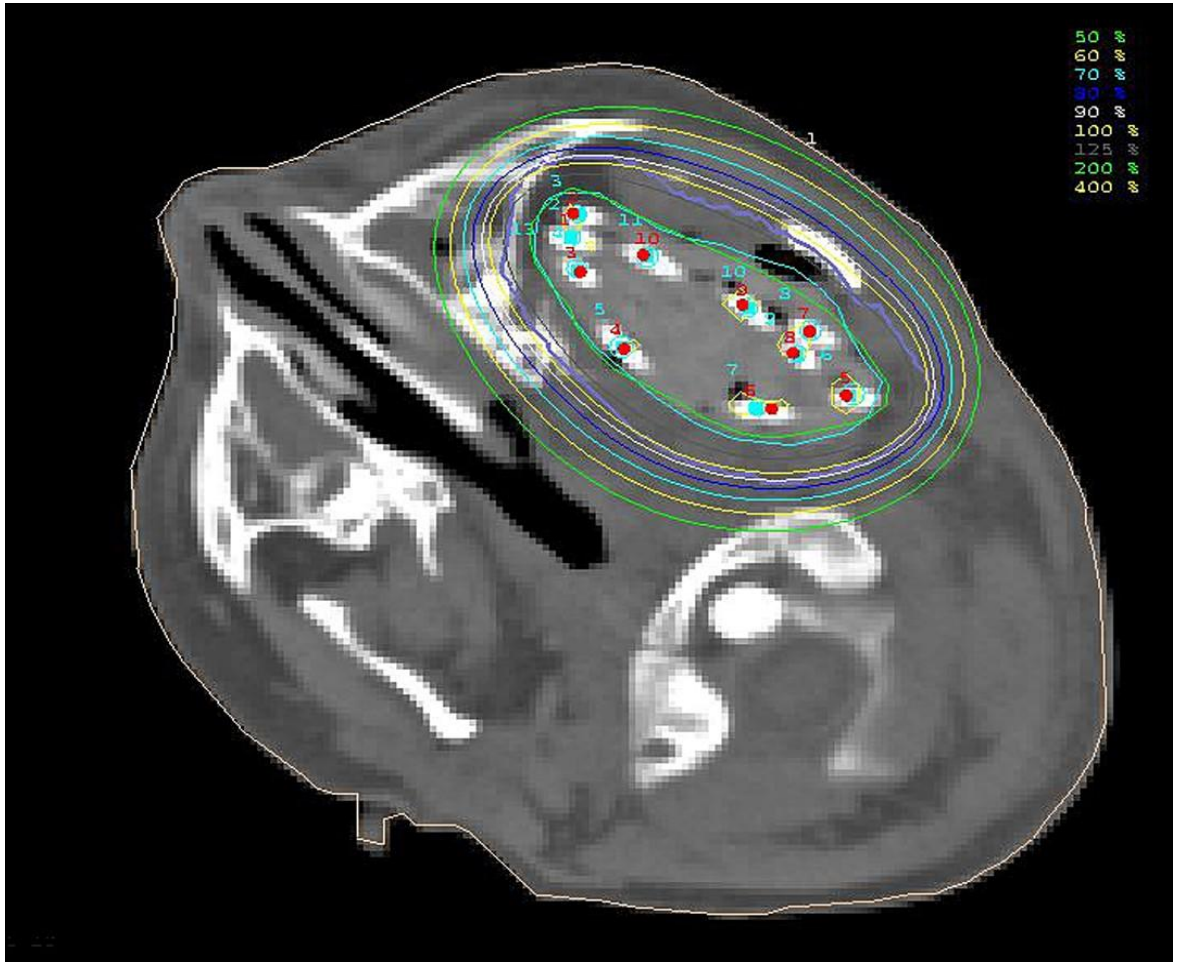


100% isodose

200% isodose



Planning of dose distribution



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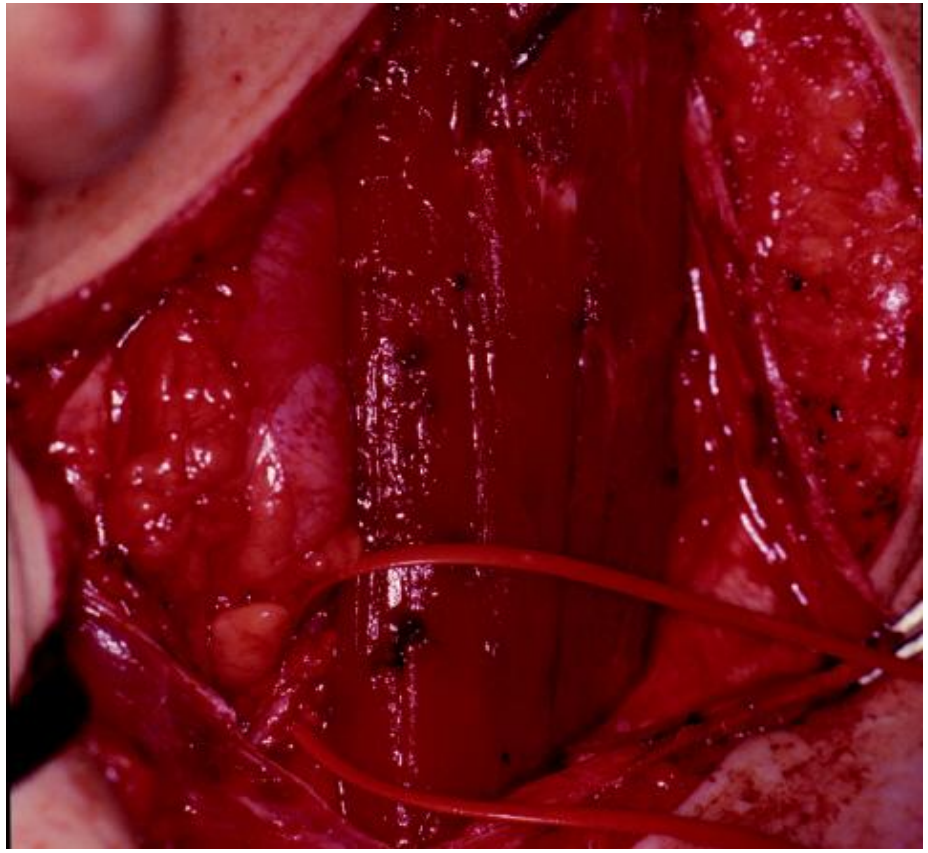
REconstruction: AMORE II

- Remove mold
- Surgical reconstruction

  -Free vascularised (microanastomosis)

  or -Transpositional muscle flap

REconstrucion



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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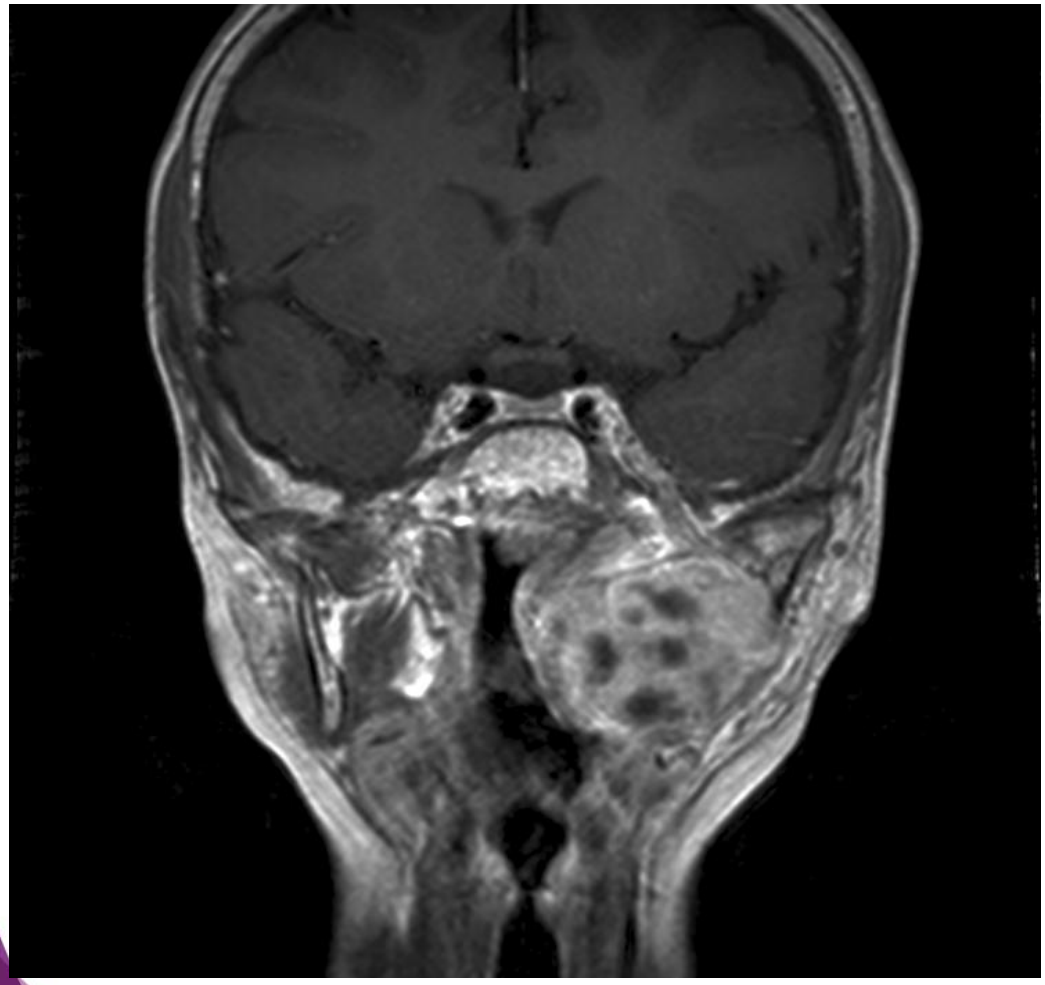
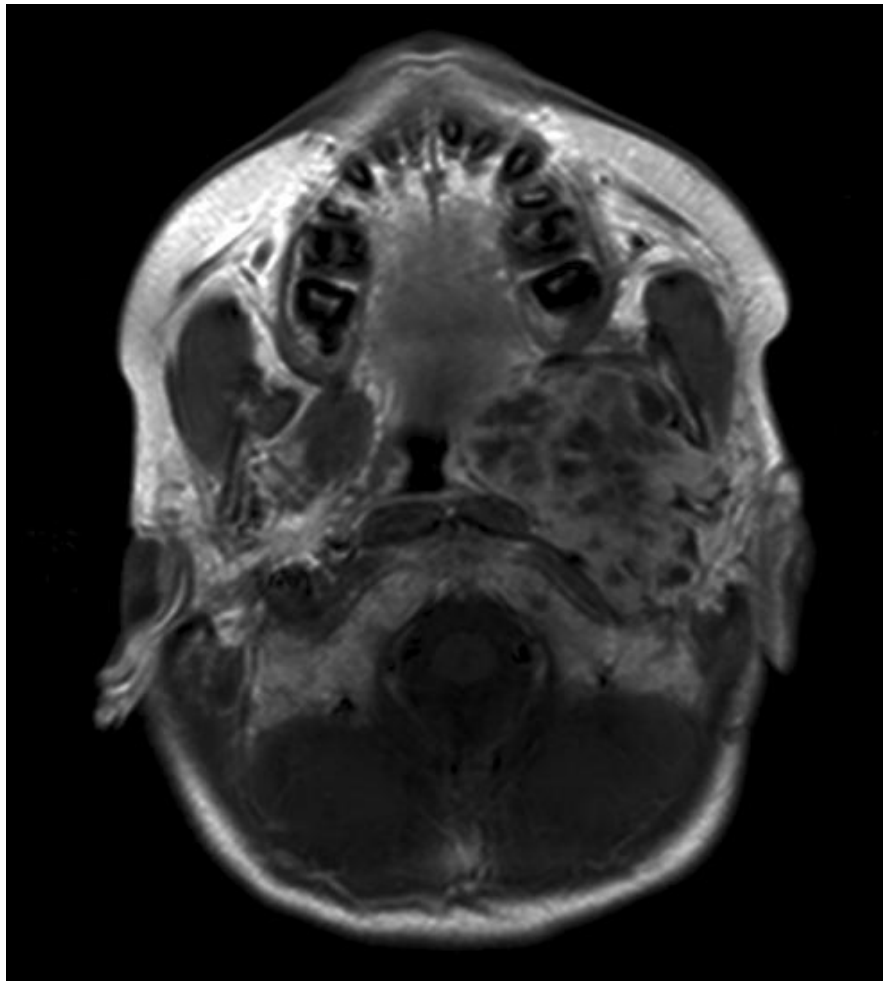
Examples

Recurrence after chemotherapy and EBRT





Before salvage chemotherapy

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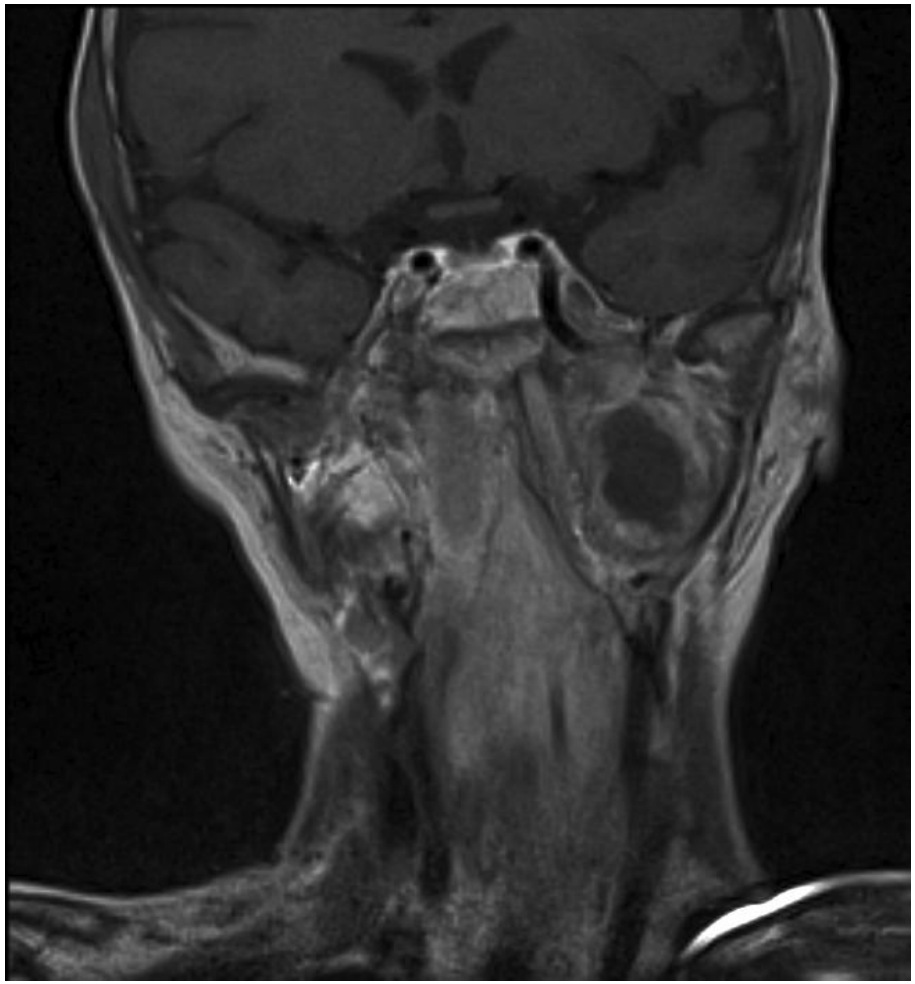
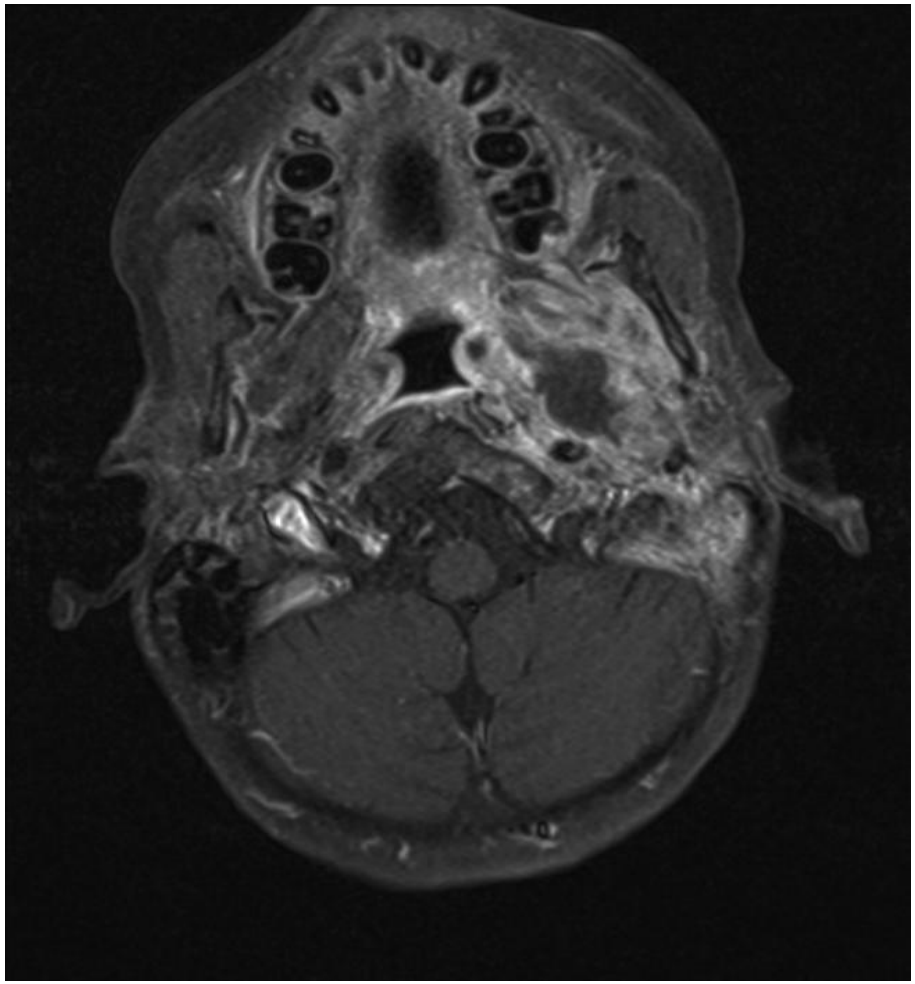
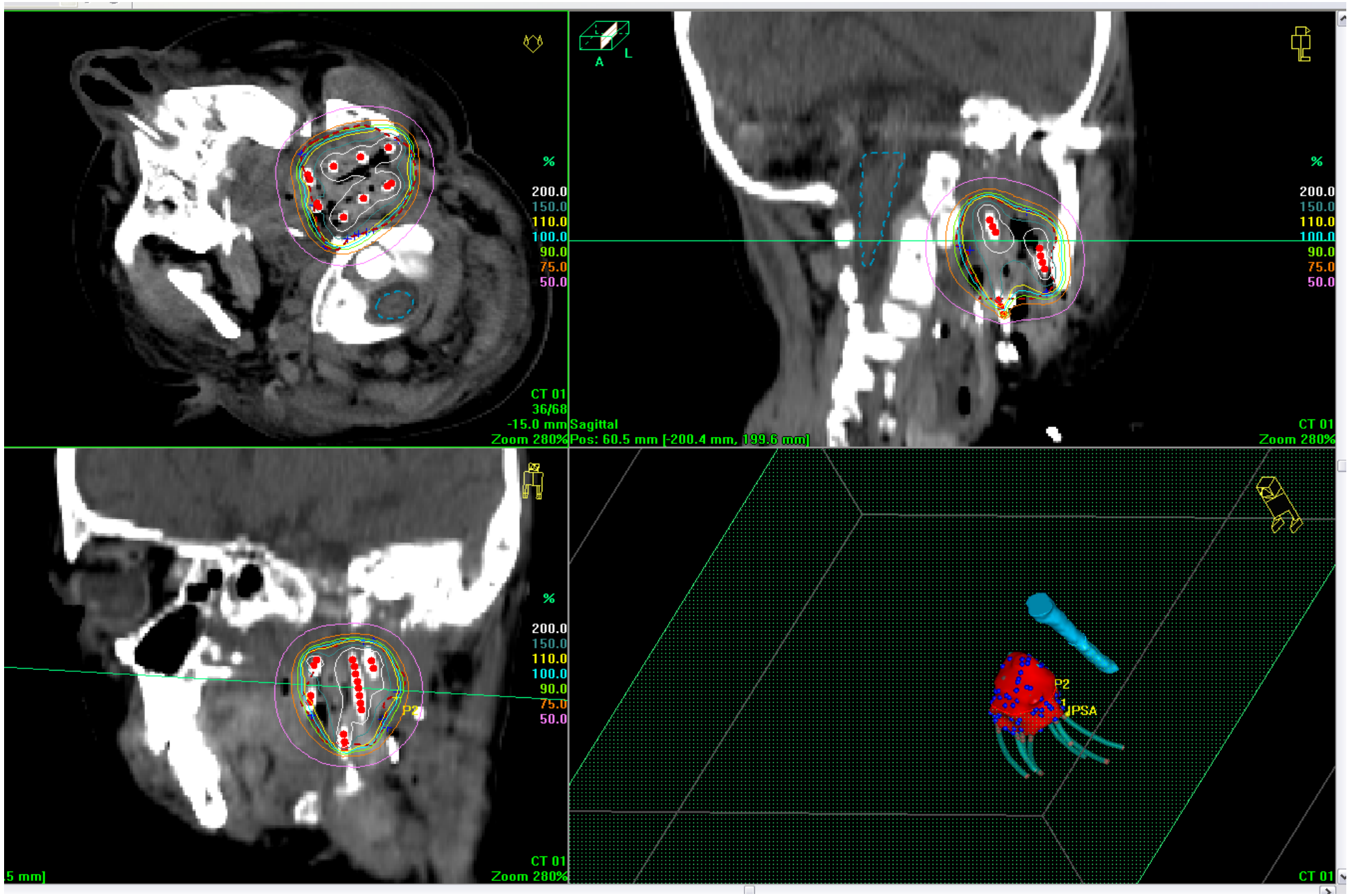


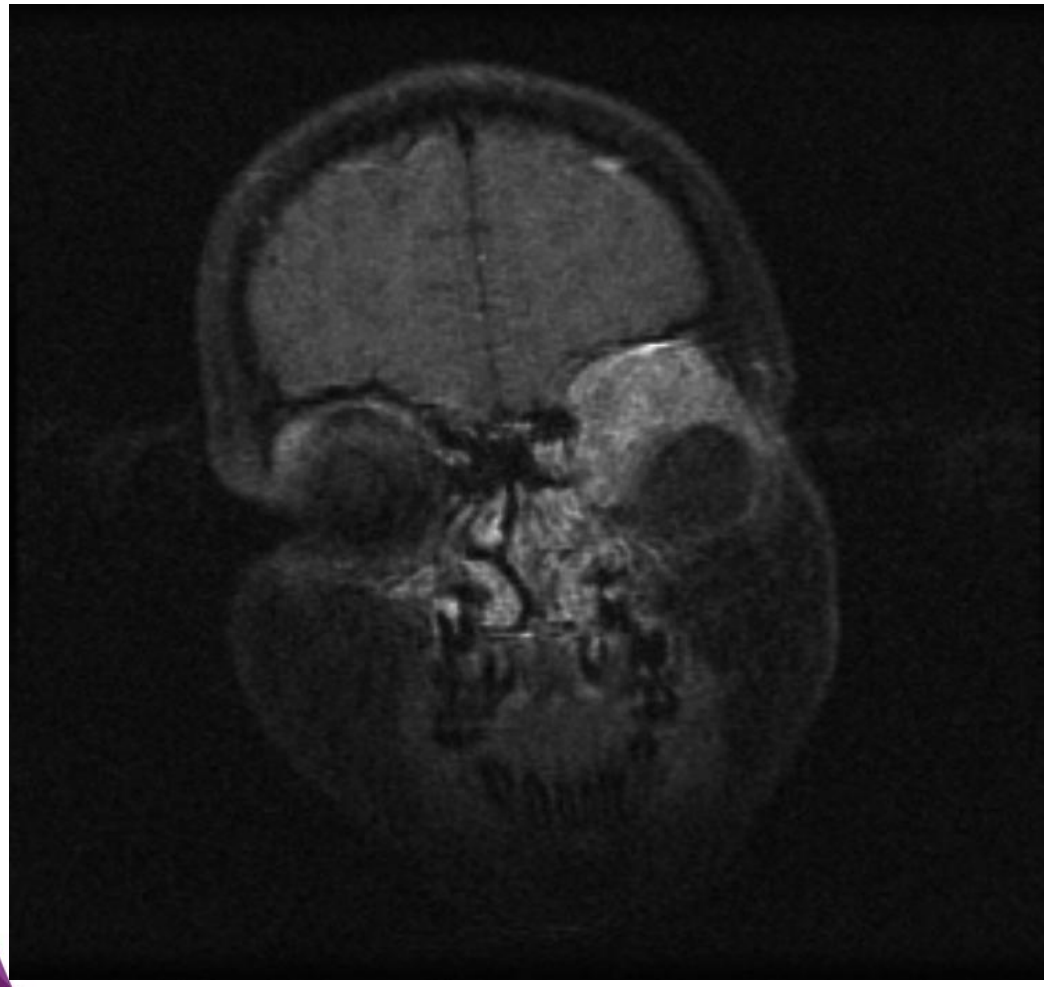


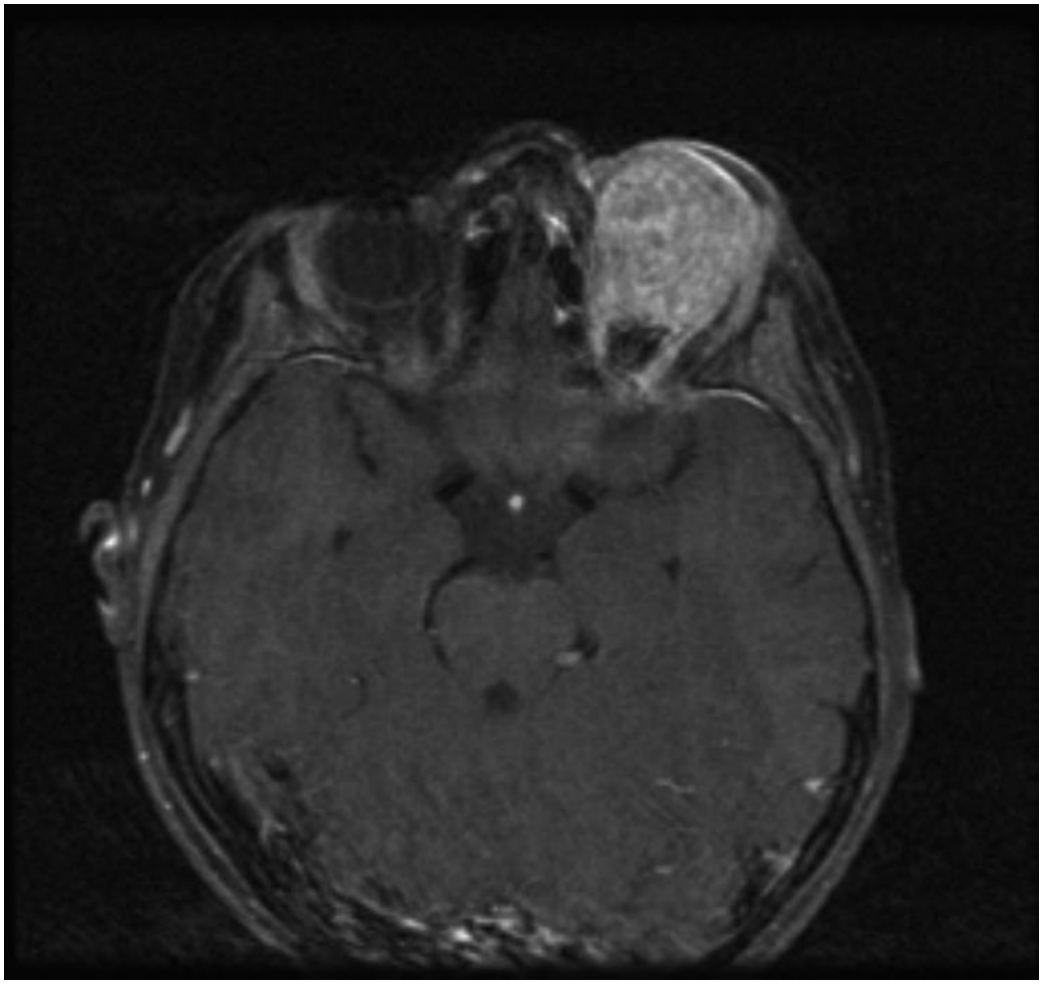
After salvage chemotherapy

ESTRO School


%
200.0
150.0
110.0
100.0
90.0
75.0
50.0
CT 01
36/68
-15.0 mm Sagittal
Zoom 280%
A
L
Pos: 60.5 mm [-200.4 mm, 199.6 mm]
CT 01
Zoom 280%
P2
UPSA

Orbital RMS





Before chemotherapy

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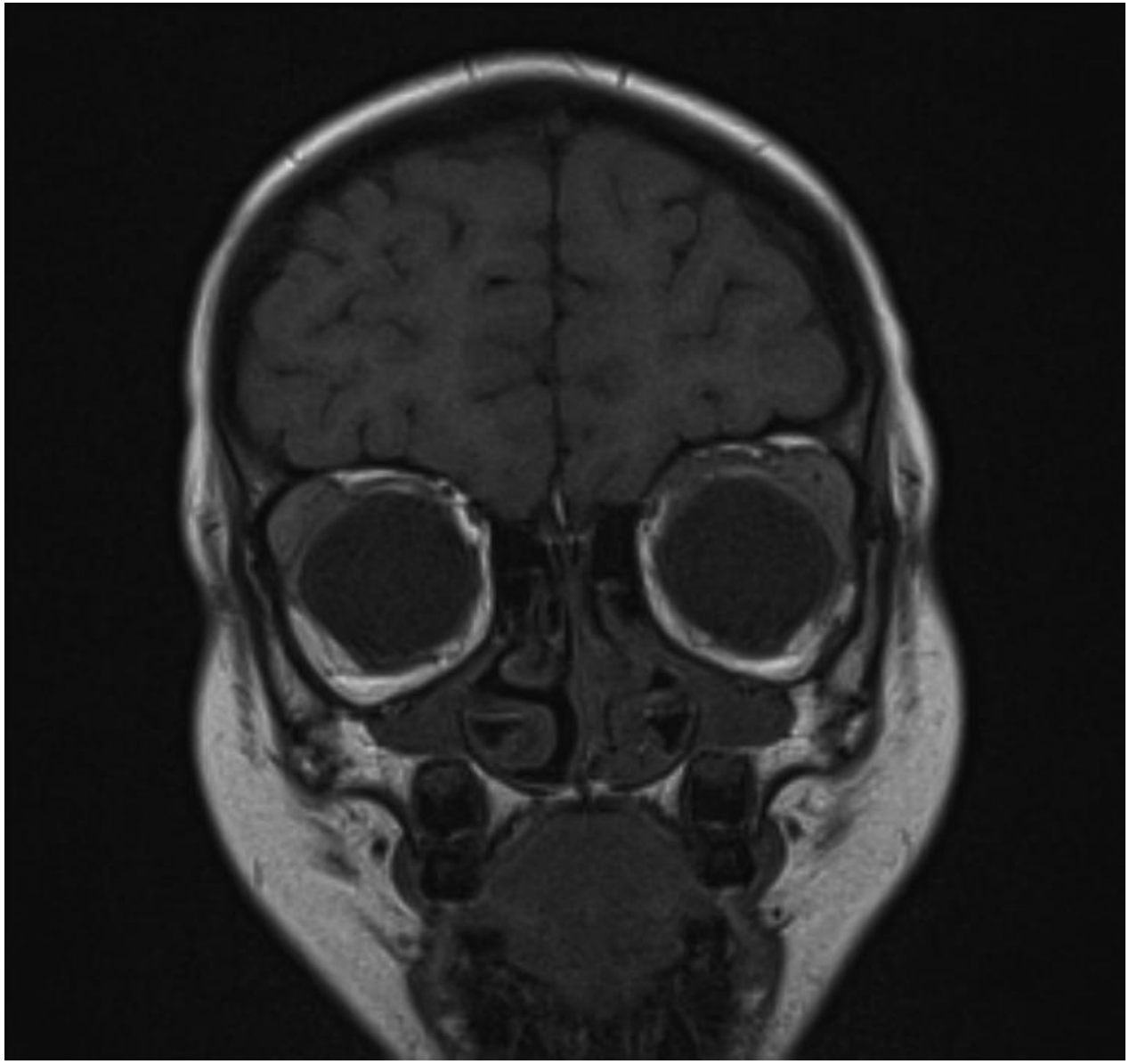
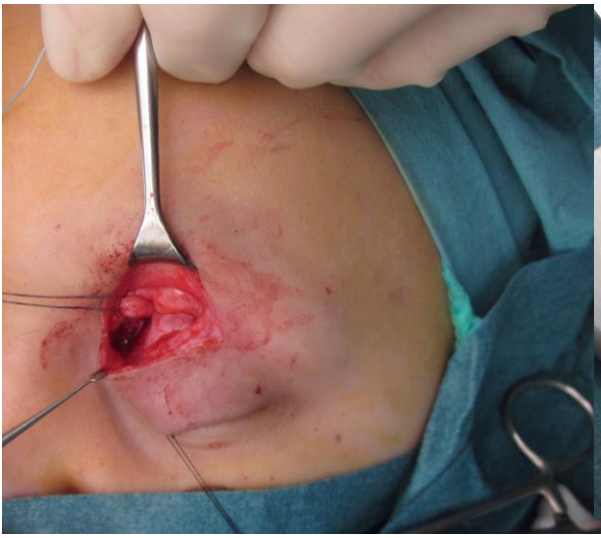
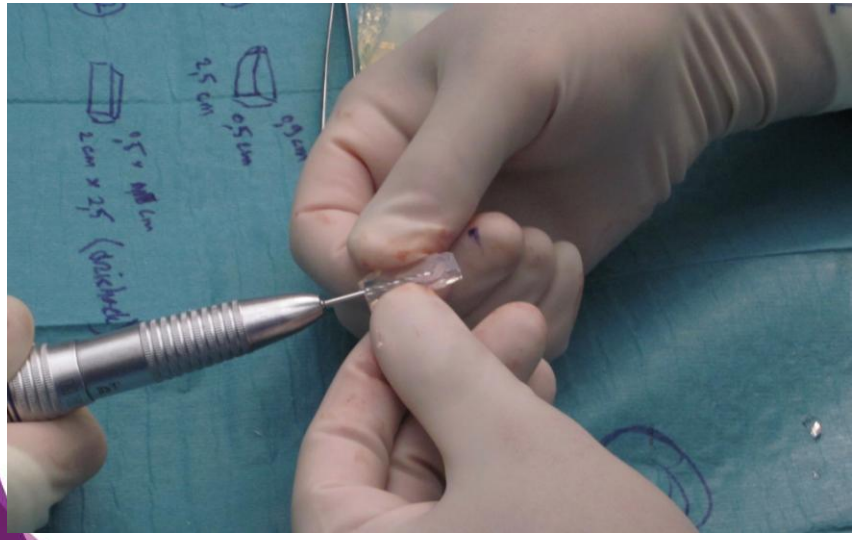
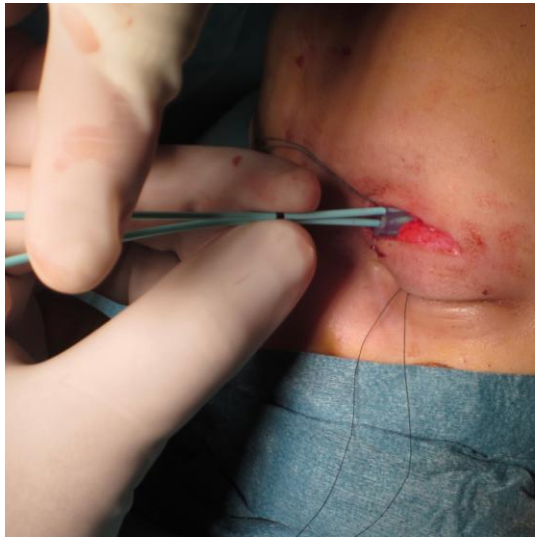


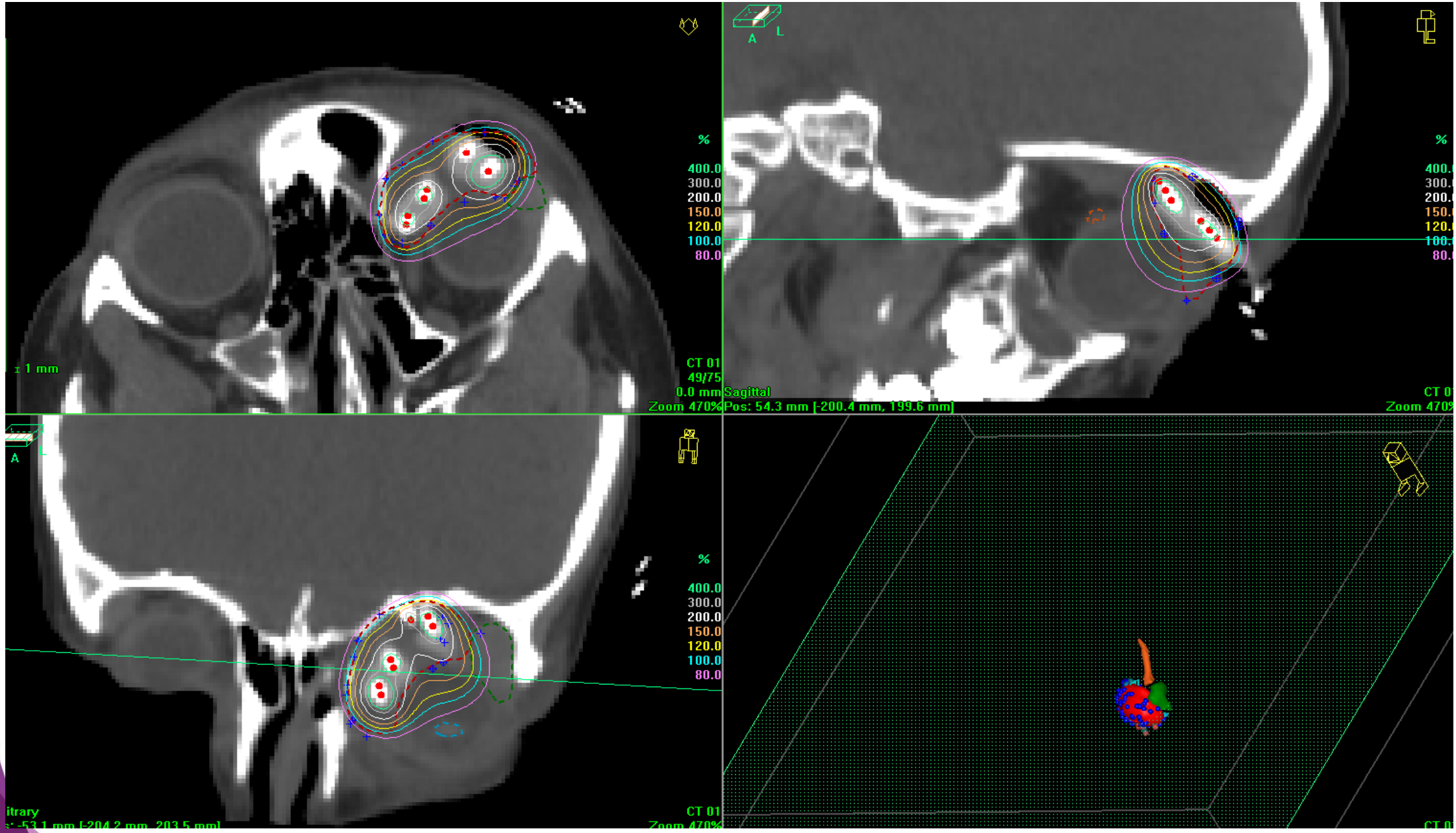
After chemotherapy

ESTRO School

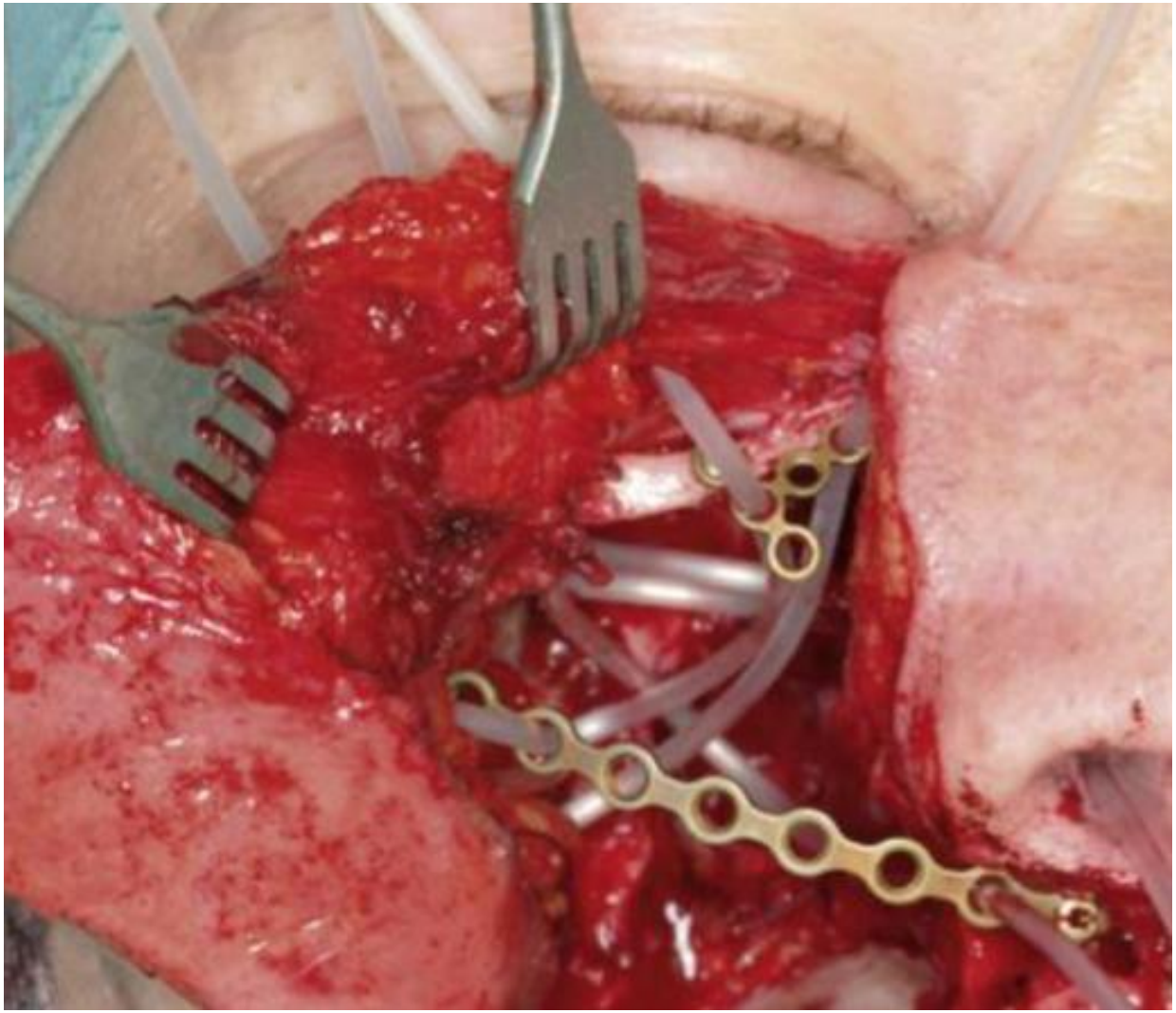






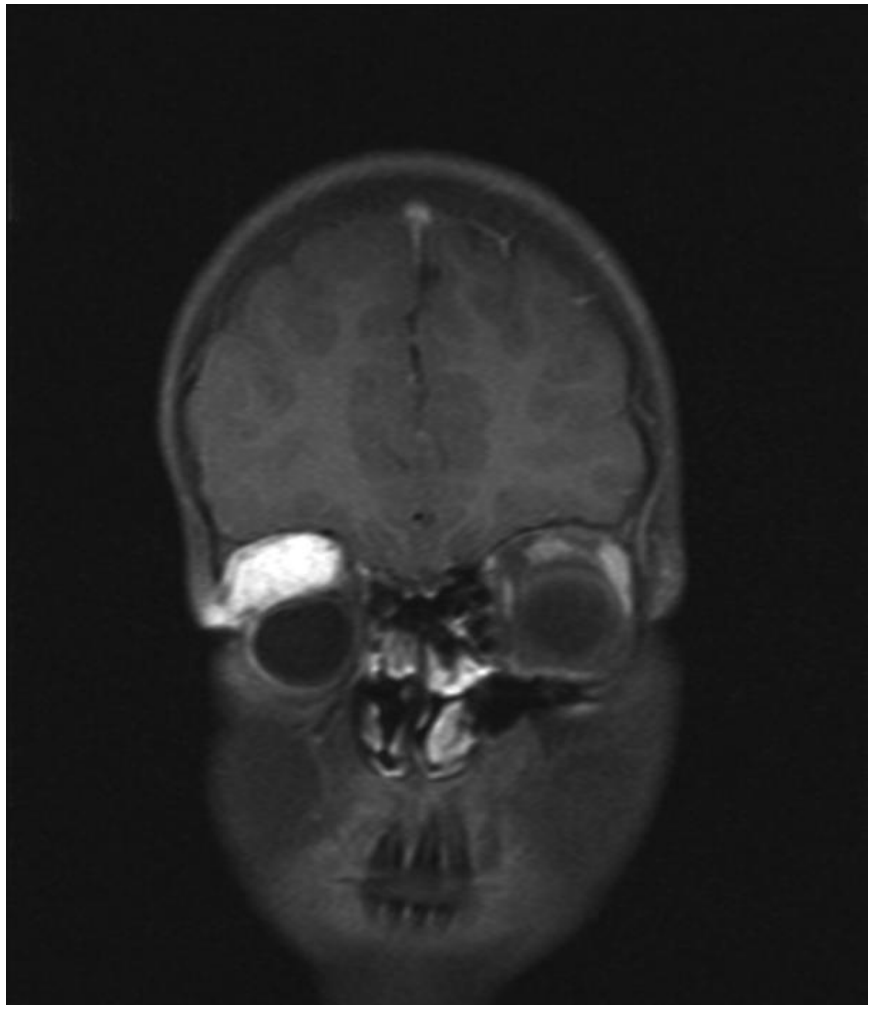

%
400.0
300.0
200.0
150.0
120.0
100.0
80.0
± 1 mm
CT 01
49/75
0.0 mm Sagittal
Zoom 470%
Pos: 54.3 mm [-200.4 mm, 199.6 mm]
A
L
CT 01
Zoom 470%

Other Techniques



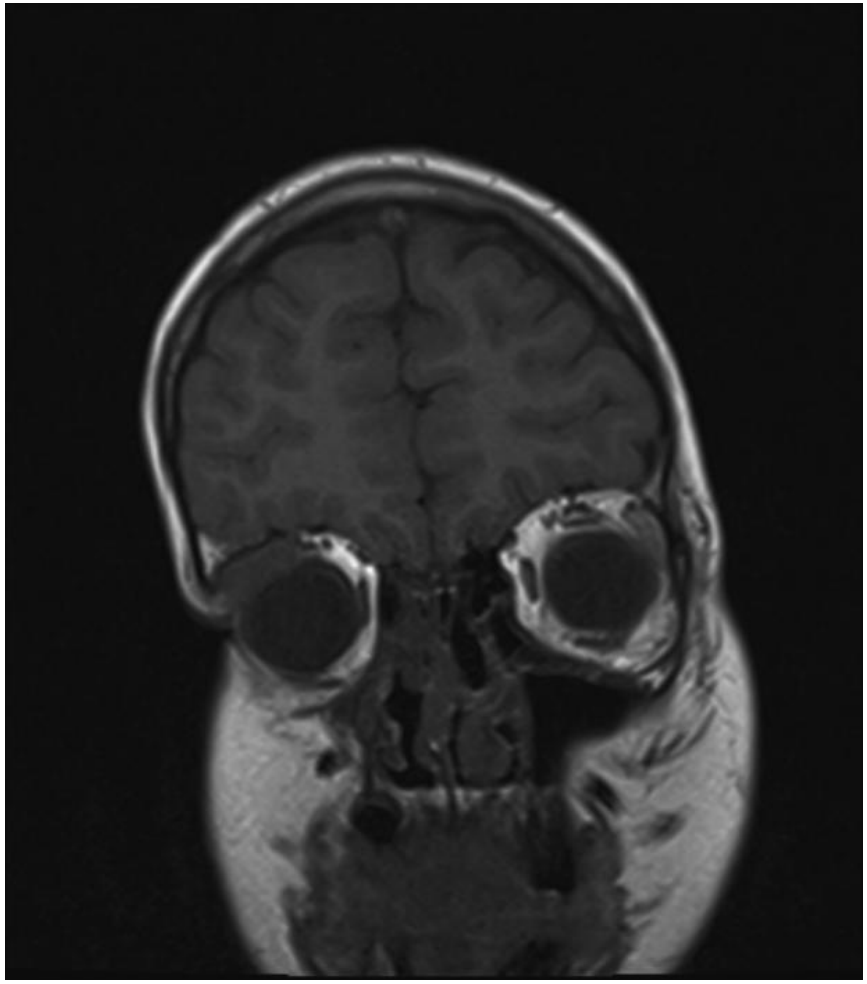
Courtesey of G. Kovács
University Lübeck

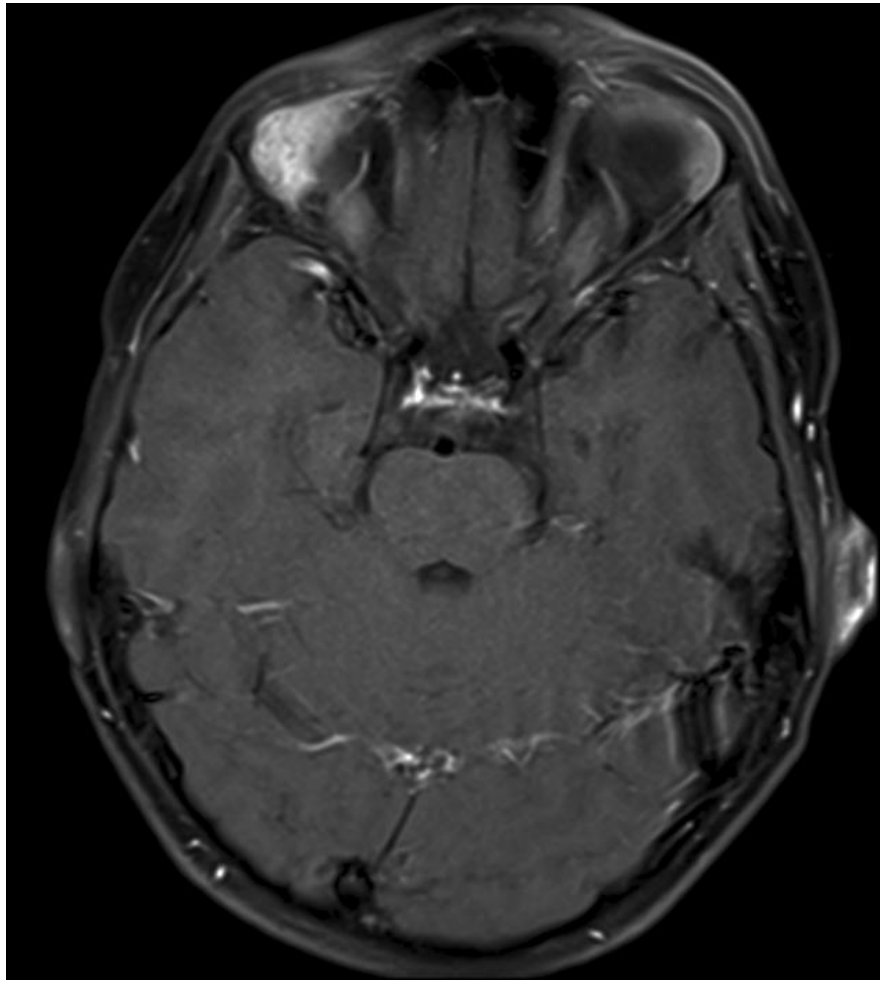
Recurrence after chemotherapy and EBRT



Before salvage chemotherapy

ESTRO School





After salvage chemotherapy

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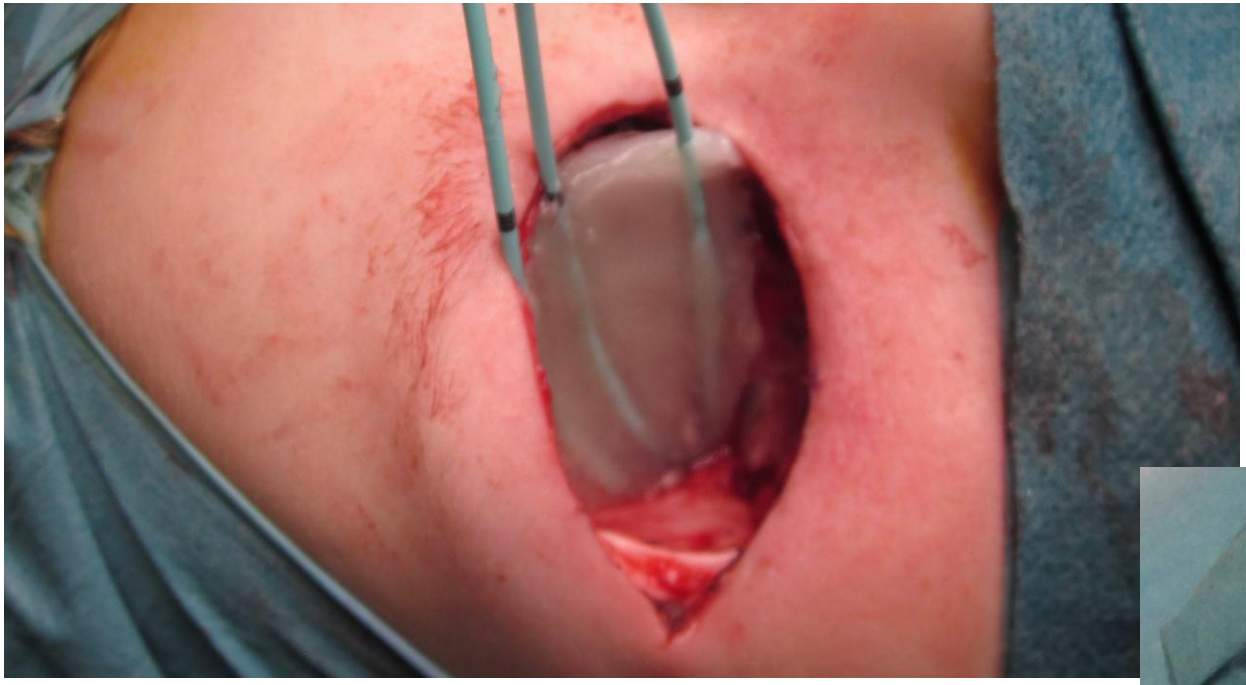
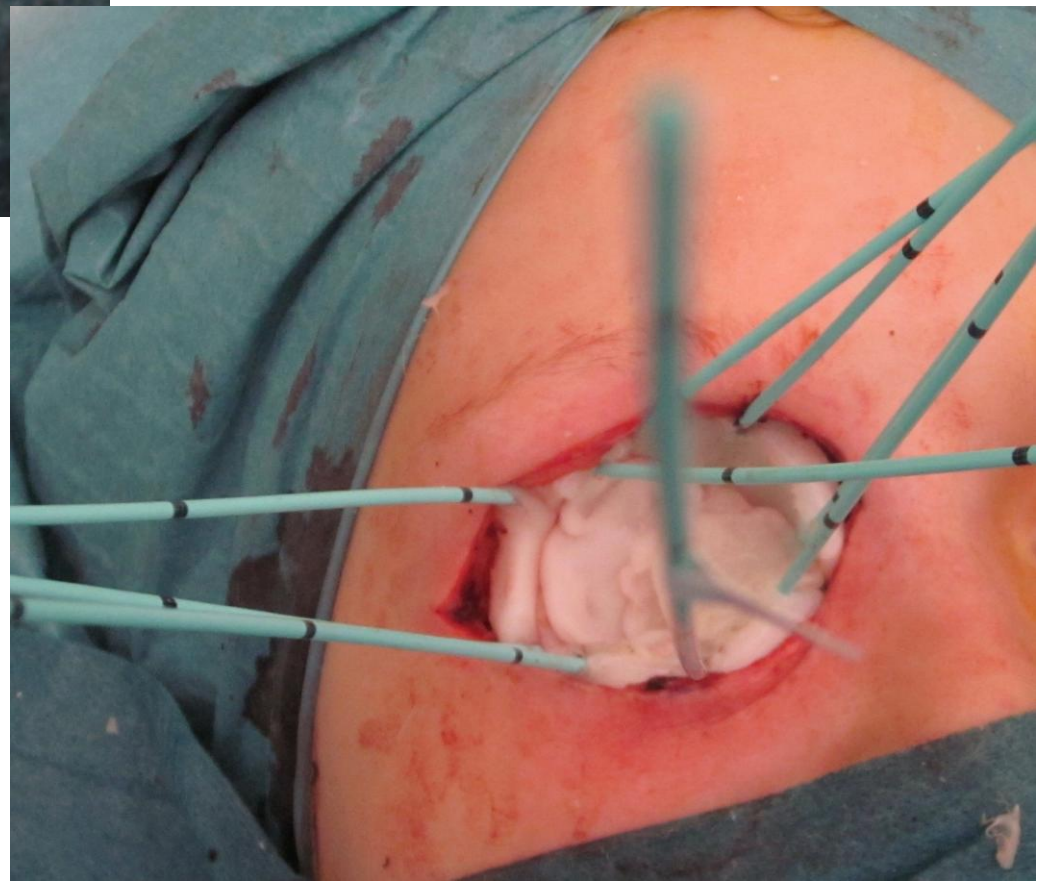
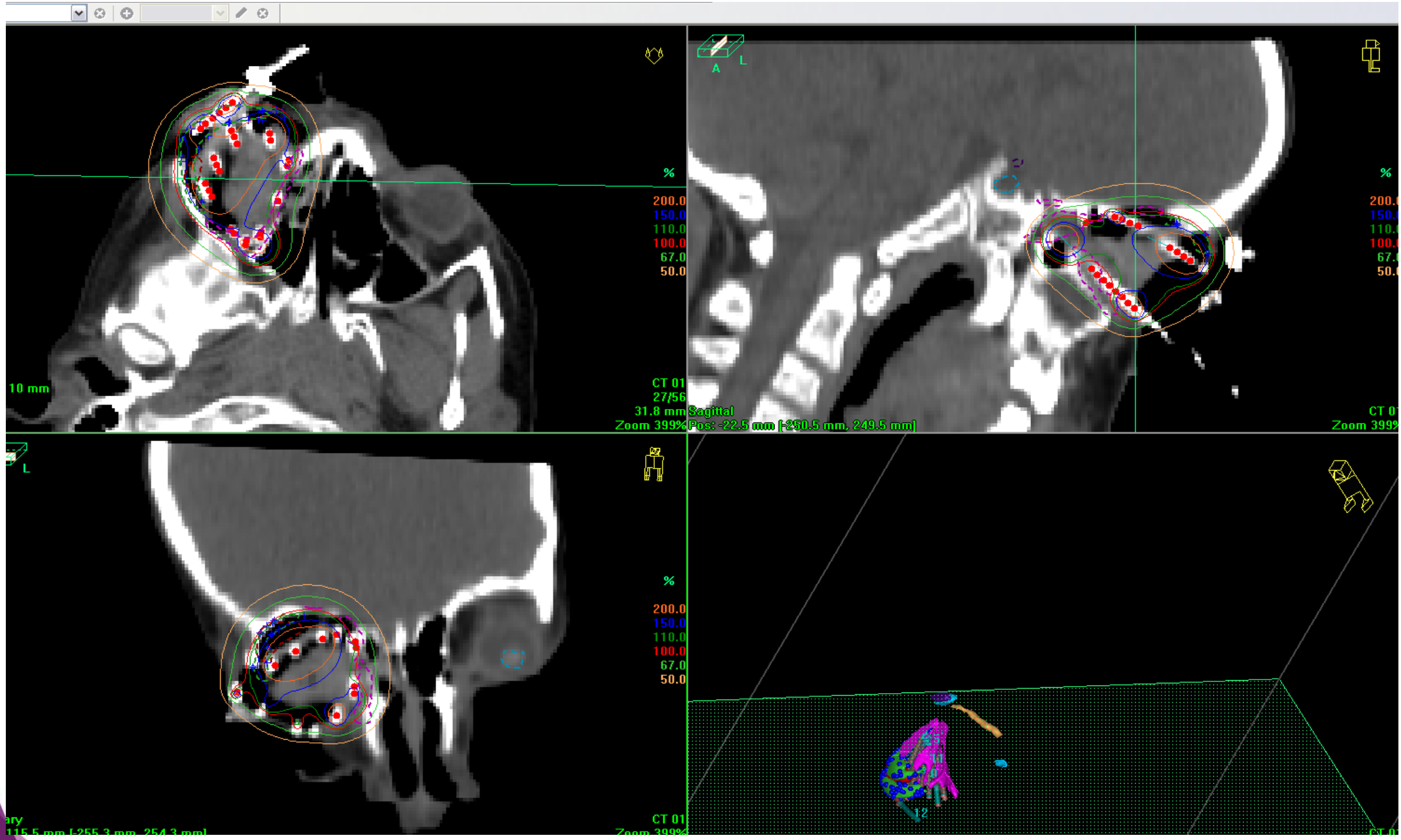


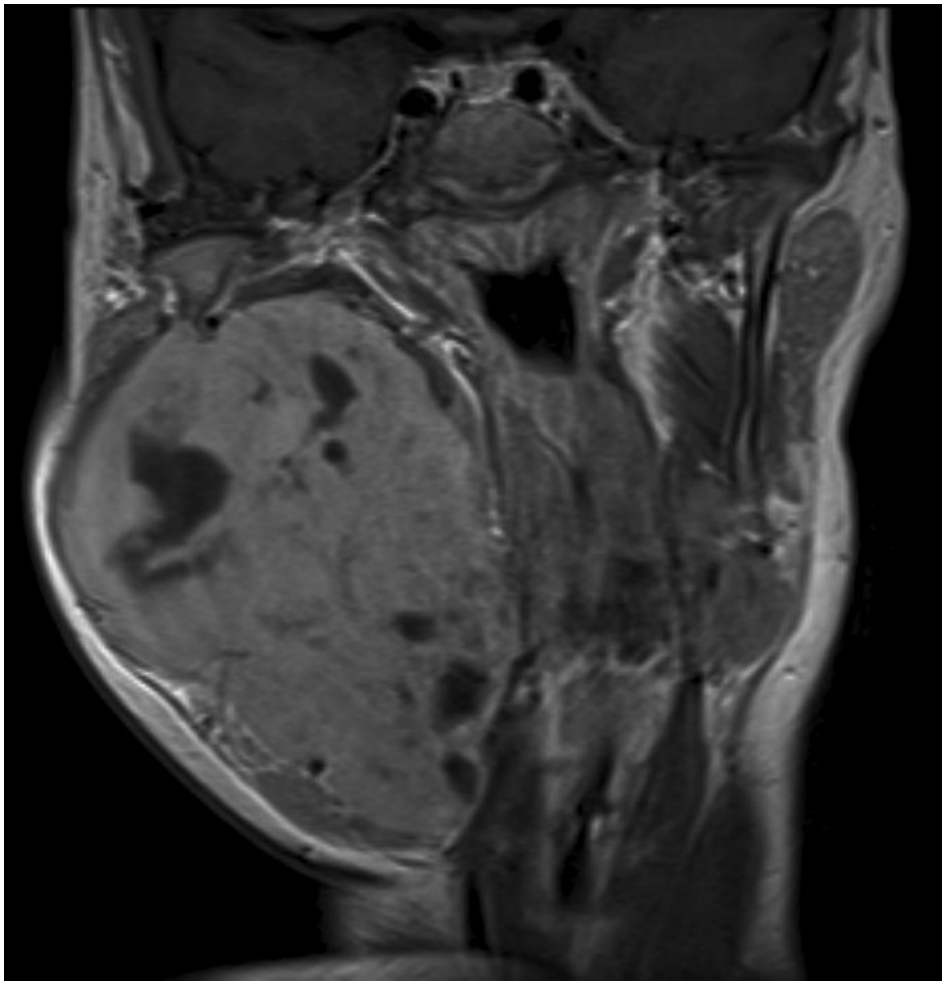


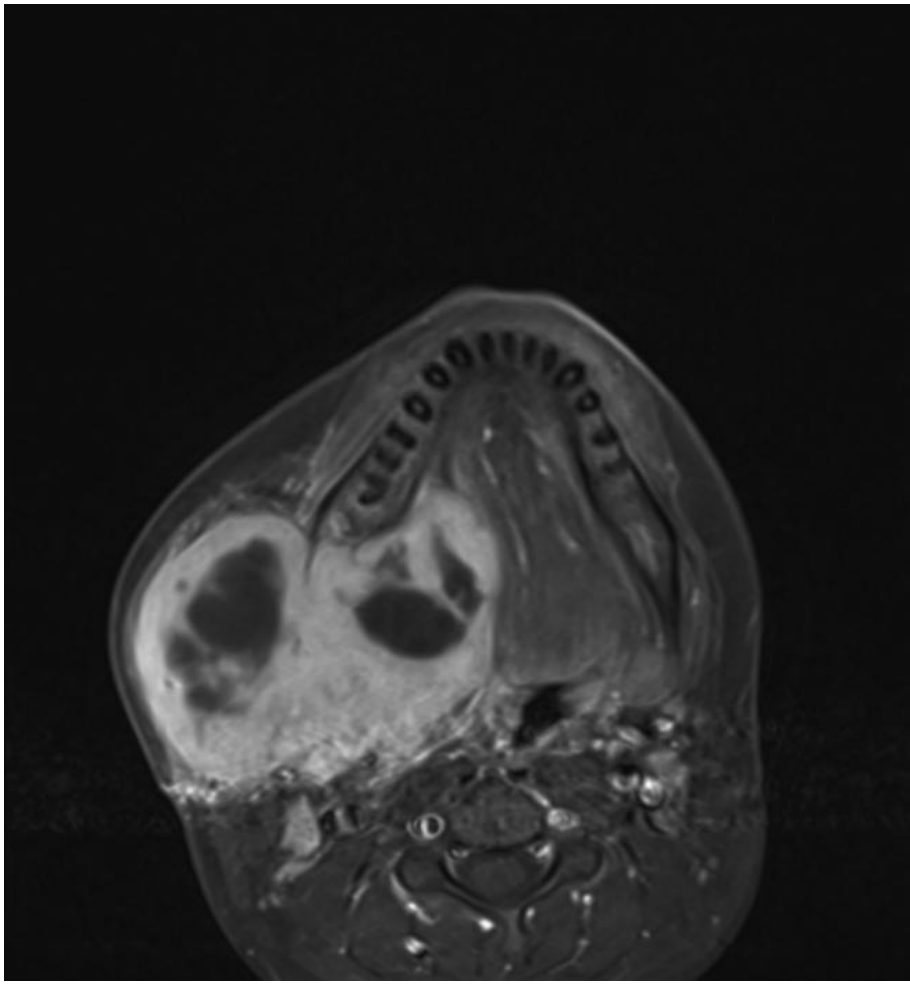
ESTRO School



ESTRO School

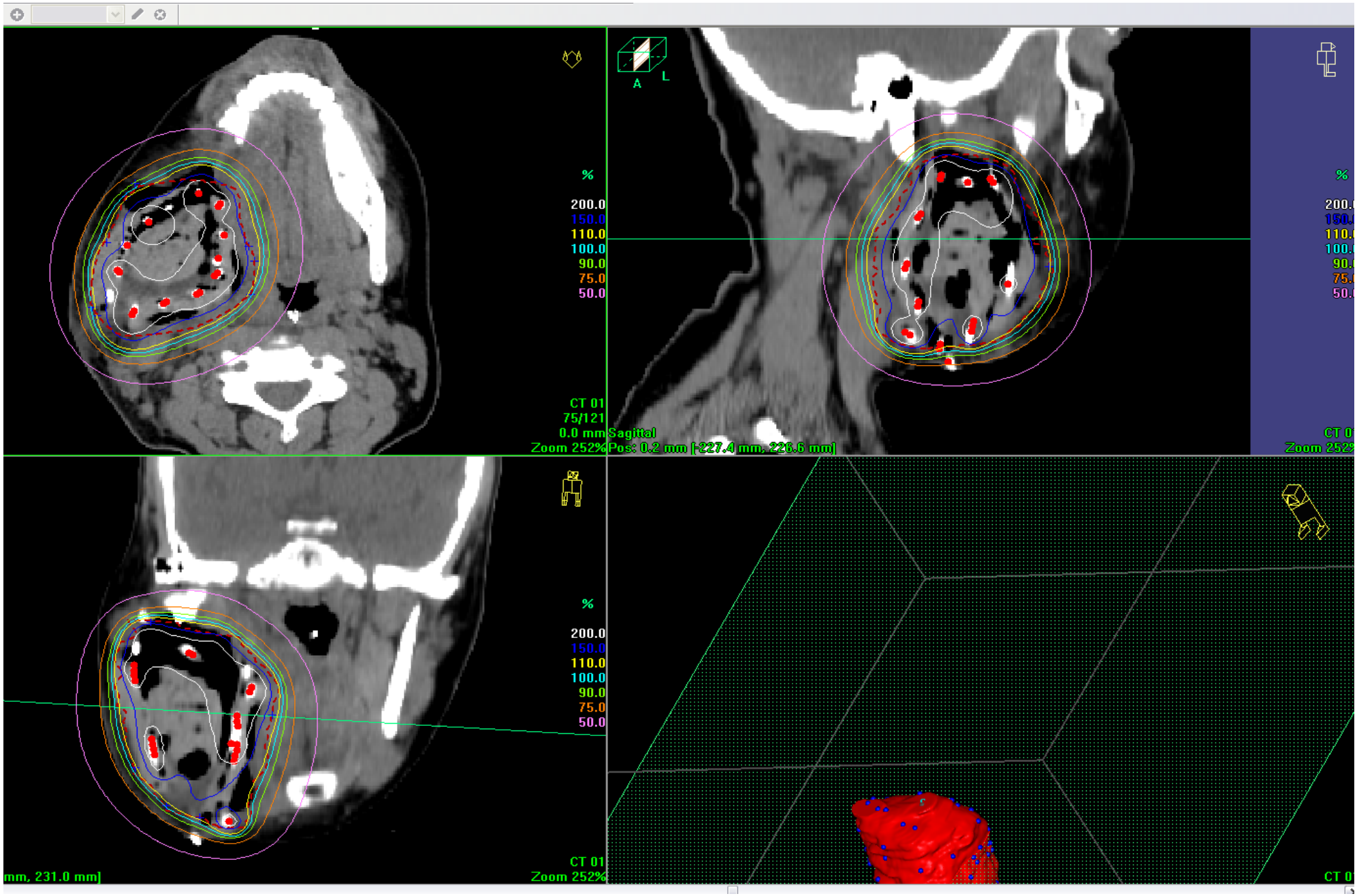
Undifferentiated sarcoma





After Chemotherapy

ESTRO School


%
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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%

Local adverse events clinic

Primary

- Assessment of adverse events (AEs)

Secondary

- Compare AEs between survivors treated with EBRT or AMORE

Eur J Cancer 2015;51:1424-34

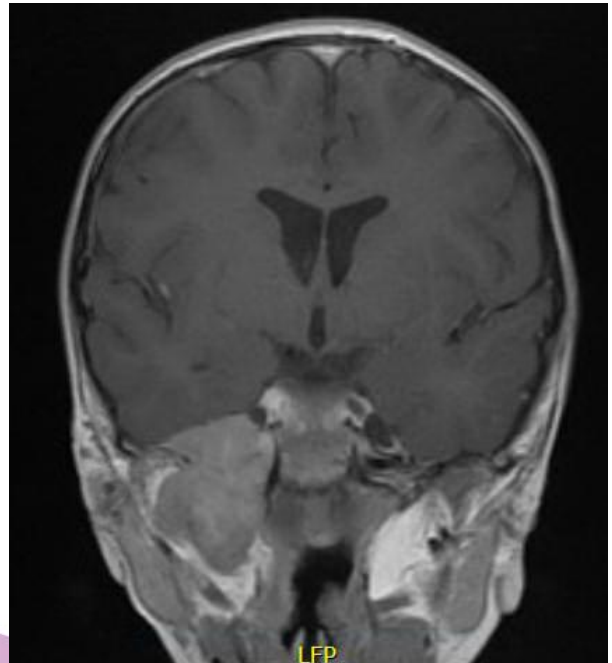
ESTRO School

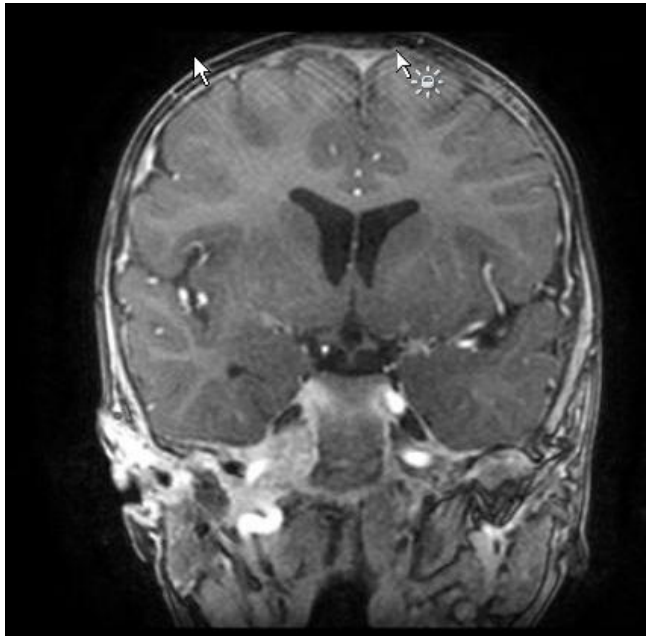
Contraindication

- Intracranial extension
- Invasion nasopharynx
- Involvement orbit leading to excenteration
- Encasement carotid artery
- Invasion in pterygopalatine fossa (relative contraindication)

Conclusion

- Macroscopic radical surgery possible
- Adequate mold position possible





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5-year survival

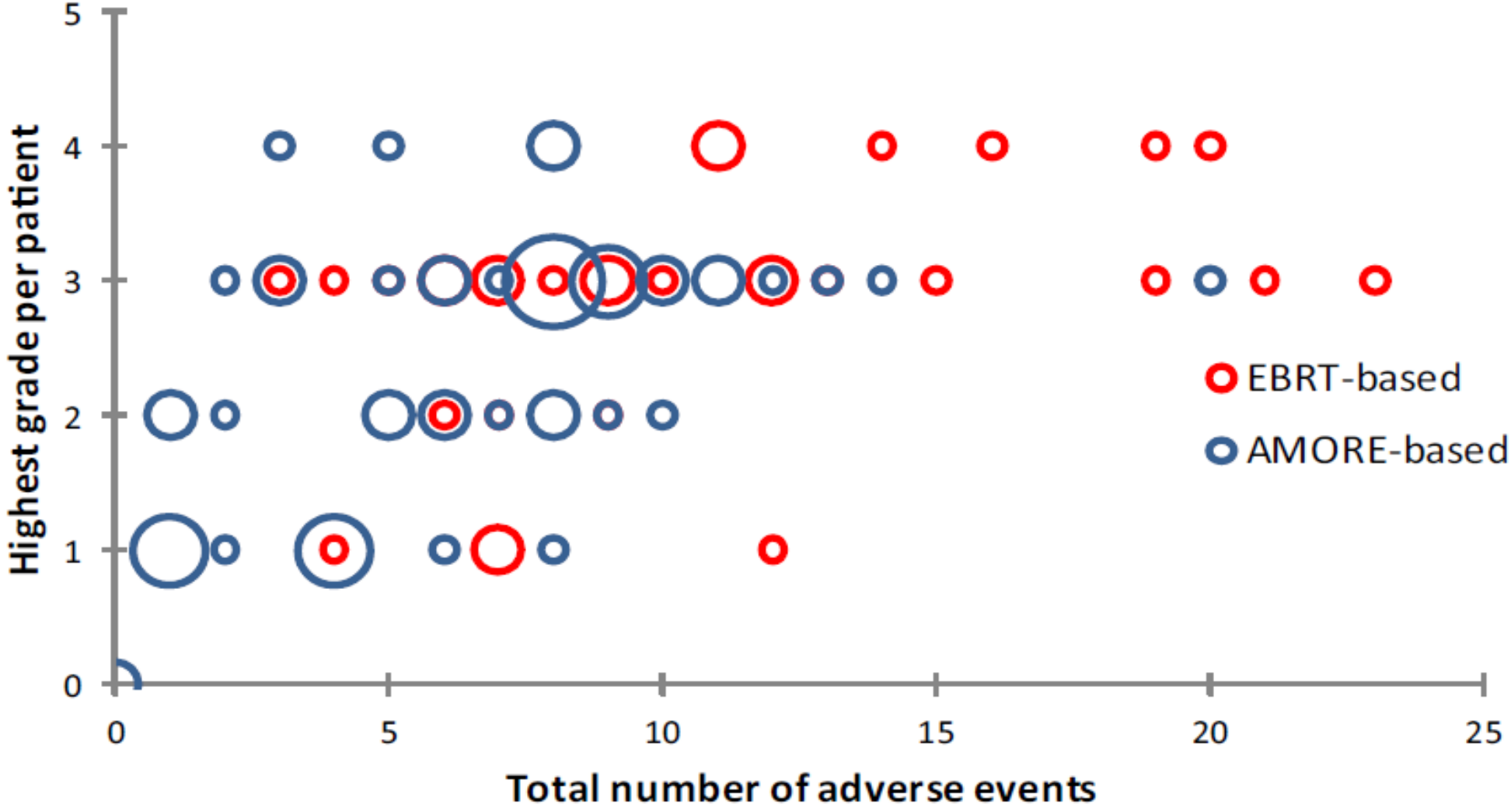
- All HNRMS both cohorts:
  FFS: 58.2% and OS: 76.0%

- EBRT-based:
  FFS: 63.8% and OS: 75.0%
- AMORE-based:
  FFS: 53.2% and OS: 76.9%
- (p = 0.37 and p = 0.56)

Failure-free survival
Overall survival

ESTRO School

Adverse Events



Eur J Cancer 2015;51:1424-34

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Number and grade of AEs

- Grade 3/4
  - 63% ≥1 grade 3/4 AE
  - 77% EBRT vs 53% AMORE (p = 0.028)
- ≥10 AEs
  - 48% EBRT vs 18% AMORE (p=0.04)
- Burden score
  - High: 22/80 (28%)
  - Severe: 5/80 (6%)
- EBRT higher burden than AMORE (p=0.04)

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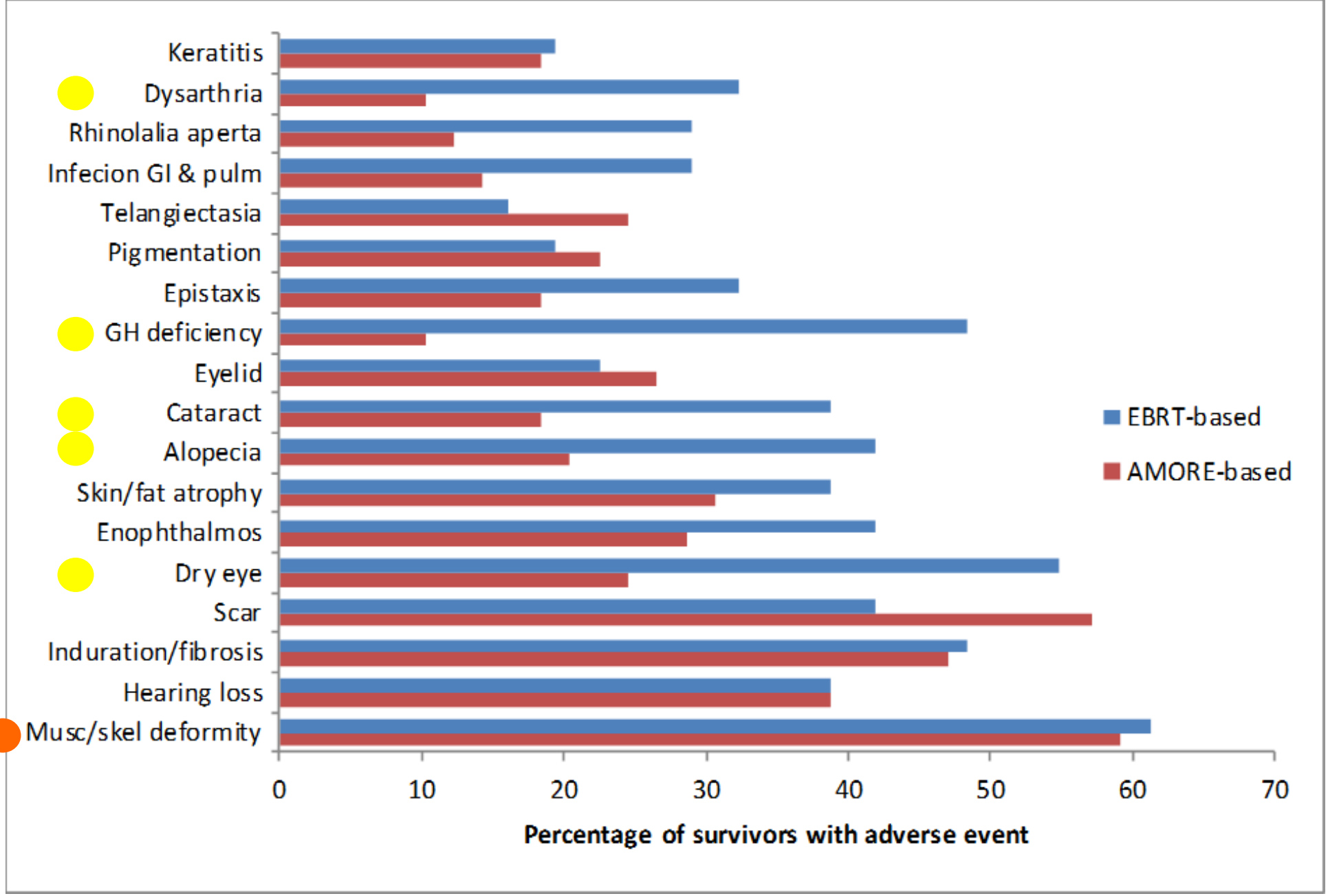

Eur J Cancer 2015;51:1424-34

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Take Home message

- Head and Neck RMS
  - Orbit
  - Non-parameningeal
  - Parameningeal
- Radiotherapy is essential for cure
- AMORE procedure only suitable if a macroscopic radical resection can be performed
- With Brachytherapy less and less severe adverse events