ESTRO School

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Advanced Skills in Modern Radiotherapy

06-10 May 2018 - Rome, Italy

ESTRO School

Speakers

Course Director

- Rianne de Jong

Faculty

- Elizabeth Forde
- Mirjana Josipovic (not present)
- Martijn Kamphuis
- Jose Lopez
- Peter Remeijer
- Sofia Rivera

Guest Lecturers

- Maaike Milder
- Marco Schwarz
- Local lecturers: Veronica Pollutri & Francesco Cellini

Programme: DAY 1

Time	Description	Speaker
09.00 – 09.15	Welcome & Introduction of teachers	R.de Jong
09.15 – 09.45	RTT's Perspective on modern radiation therapy	R. de Jong
09.45 – 10.15	Patient preparation and positioning	M. Kamphuis
10.15 – 10.45	Coffee break	
10.45 – 11.30	Pre-treatment Imaging Modalities	P. Remeijer
11.30 – 12.15	Delineation Target Volumes	S. Rivera
12.15 – 13.00	Delineation Organs at Risk	E. Forde
13.00 – 14.00	Lunch break	
14.00 – 14.15	Workshop on delineation of OAR: Introduction to the software	S.Rivera / E. Forde / P. Remeijer
14.15 – 15.30	Workshop on delineation of OAR	S.Rivera / E. Forde / P. Remeijer
15.30 – 16.00	Coffee break	
16.00 – 17.00	Workshop on delineation of OAR	S.Rivera / E. Forde / P. Remeijer

Programme: DAY 2

Time	Description	Speaker
08.30 – 09.00	Errors and Margins	P. Remeijer
09.00 – 09.30	In room imaging modalities	M. Kamphuis
09.30 – 10.00	Correction Strategies	P. Remeijer
10.00 – 10.30	*Coffee break*	
10.30 – 12.15	Workshop on margin calculation: part I	P. Remeijer
12.15 – 13.15	*Lunch break*	
13.15 – 13.45	Motion Management	P. Remeijer
13.45 – 14.15	Image registration	P. Remeijer
14.15 – 14.45	Treatment Planning I	E. Forde
14.45 – 15.15	*Coffee break*	
15.15 – 15.45	Treatment Planning II	E. Forde
15.45 – 16.15	Clinical rationale for IGRT	J. Lopez
16.15 – 16.45	Workshop on margin calculation: part II	P. Remeijer

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Programme: DAY 3

Time	Description	Speaker
08.30 – 10.15	Lower Abdomen: Prostate & cervix (6x 15 min)	Faculty
10.15 – 10.45	*Coffee break*	
10.45 – 12.30	Thorax: Lung and breast (6x 15min)	Faculty
12.30 – 13.30	*Lunch break*	
13.30 – 14.15	Image registration and Evaluation: Part I (CBCT XVI)	R. de Jong
14.15 – 15.00	Image registration and Evaluation: Part II (CBCT Varian)	E. Forde
15.00 – 15.30	*Coffee break*	
15.30 – 17.15	Break up sessions Image registration and evaluation Varian & Elekta	

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Programme: DAY 4

Time	Description	Speaker
09.00 – 09.30	Recap Registration Workshop	R. de Jong
09.30 – 11.15	Head&Neck (3x 15min) / Brain (3x 15min)	Faculty
11.15 – 11.45	*Coffee break*	
11.45 – 12.15	Implementing and managing IGRT	M. Kamphuis
12.15 – 13.00	Who is doing what in radiation therapy - *interactive* -	R. de Jong
13.00 – 14.00	*Lunch break*	
14.00 – 15.30	Workshop: Safety issues and prospective risk analysis	M. Kamphuis
15.30 – 16.00	*Coffee break*	
16.00 – 16.30	Cyberknife – *Skype lecture*	M. Milder
16.30 – 17.00	Error management	P. Remeijer

Programme: DAY 5

Time	Description	Speaker
08.30 – 10.00	Theory & Workshop: Plan of the day	R. de Jong
10.00 – 10.30	Incident management	M. Kamphuis
10.30 – 11.00	*Coffee break*	
11.00 – 11.30	Adverse Event Reporting and the Role of the RTT	E. Forde
11.30 – 12.00	Protons	M. Schwarz
12.00 – 12.30	MR guided treatment	Local lecturer
12.30 – 13.30	Wrap-up & Closure	Faculty

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Patient Preparation and Positioning

Martijn Kamphuis MSc MBA

(Slides: Rianne de Jong)
Academic Medical Center, Amsterdam
Prague 2017

m.kamphuis@amc.nl

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Aim of Patient preparation and positioning

→ Minimize the difference in patient position

1. between simulation and treatment sessions
2. during the treatment session

→ Maximize the distance between target volume and organs at risk

Tools:

- Immobilization and fixation
- Patient compliance

Tools of Patient preparation and positioning

→ Immobilization

Daily set-up **reproducibility** and **stability** through the use of fixation or aiding devices





Expectation management

- This aim of this talk is not to show the best devices
- Understanding the rationale behind it
- Choice for device will be based on:
  - Economics
  - Local availability
  - Literature
  - Experience
- Link to important review at the end of the .ppt

Tools of Patient preparation and positioning

"My diabetic research shows that test subjects are 98% more likely to take their diabetic pills if the pills are covered in chocolate."

Minimize the difference in patient position

→ **Minimize the difference in patient position**

1. **between simulation and treatment sessions**
2. during the treatment session

→ Maximize the distance between target volume and organs at risk

Tools:

- Patient compliance
- Immobilization and fixation

Aim of Patient preparation and positioning

→ **<u>Minimize</u> the difference in patient position between simulation and treatment sessions: *inter*-fraction motion**

Tools:

Patient compliance:

- Pelvic patients using diet / drinking protocol

Immobilization and fixation:

- Head&Neck using head support
- Lung using 4D CBCT.

Prostate patients

Reconstructed

CBCT

Prostate patients

To improve image quality:

Dietician

- Mild regimen of laxatives
- Diet

Fixed treatment times

Prostate patients

	gas	faeces	moving gas
no diet	68%	61%	45%
with diet	42%	23%	22%

- reduced percentage of faeces and gas
- reduced percentage of moving gas, hence improved image quality

Prostate patients

Lips et al. Ijrobp 2011

- 739 patients without diet, 205 patients with diet
- Diet instructions on leaflet
- No reduction of **intrafraction** movement

McNair et al. 2011

- 22 patients using questionaires
- Rectal filling consistency not improved
- Diet + fixed treatment times, **no laxatives**

Conclusion:

- Drinking and dietery protocol are needed for clear patient communication **BUT**
- **Won't solve the whole problem of intra/interfraction motion (additional tools are needed)**

Aim of Patient preparation and positioning

→ **<u>Minimize</u> the difference in patient position between simulation and treatment sessions: *inter*-fraction motion**

Tools:

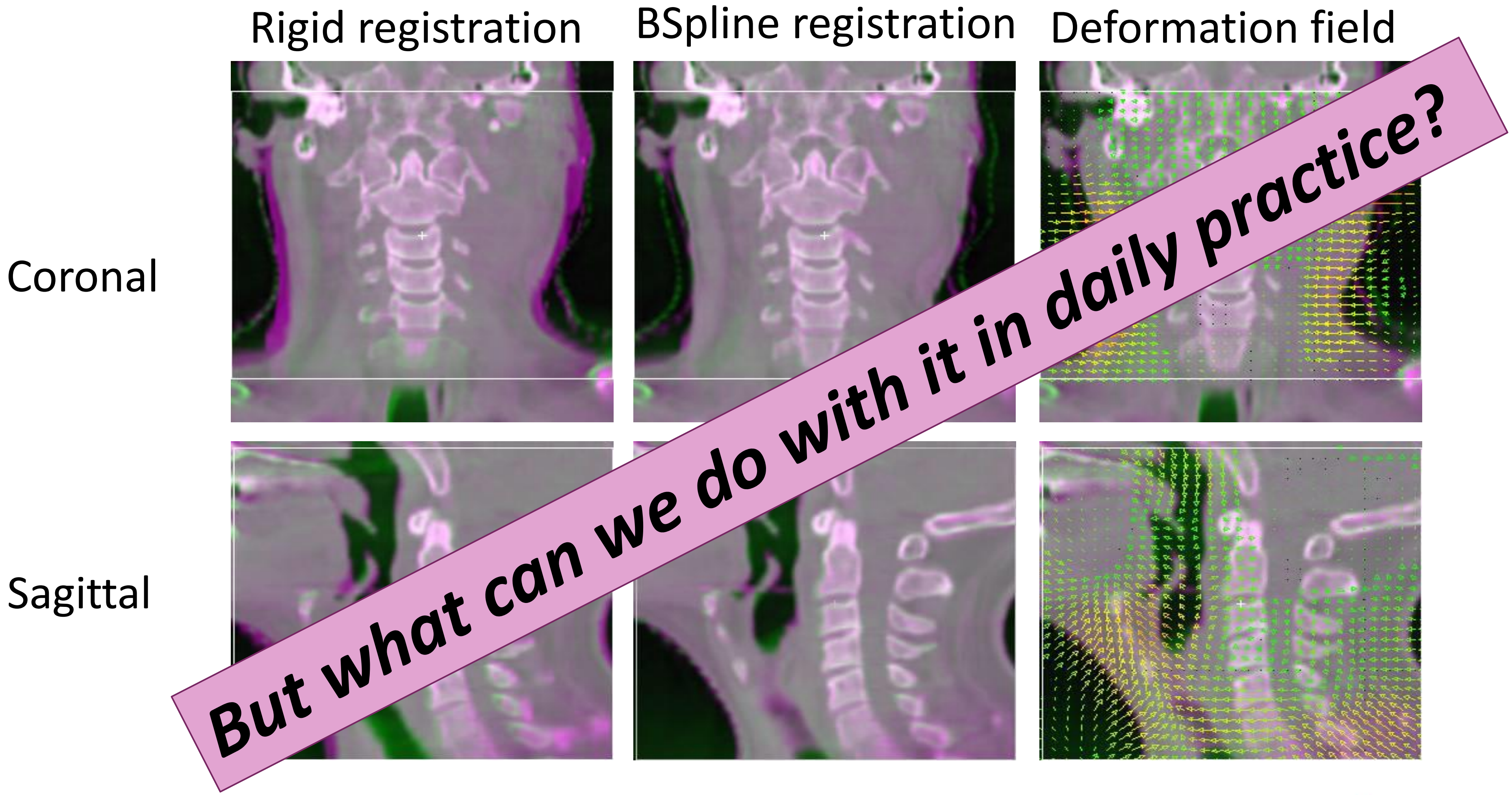
Patient compliance:

- Pelvic patients using diet / drinking protocol

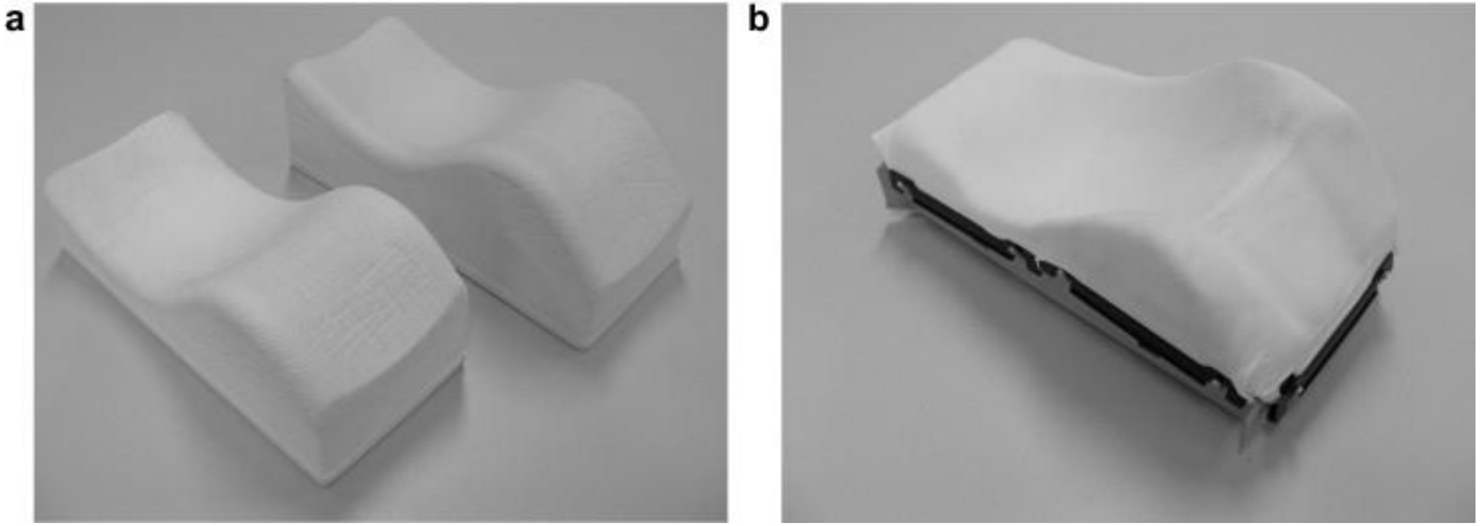
Immobilization and fixation:

- **Head&Neck using head support**
- **Unfortunate differences**

Head&Neck patients: head support



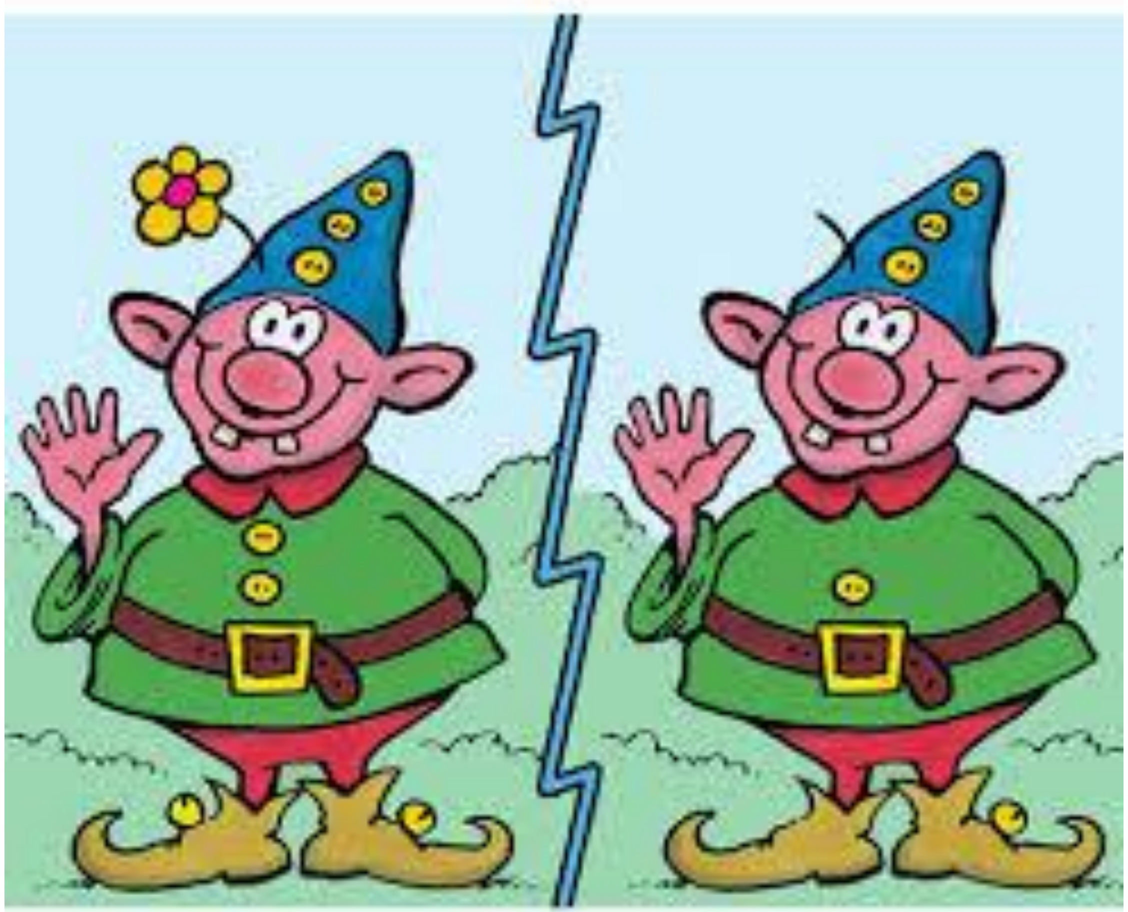
Head&Neck patients: head support



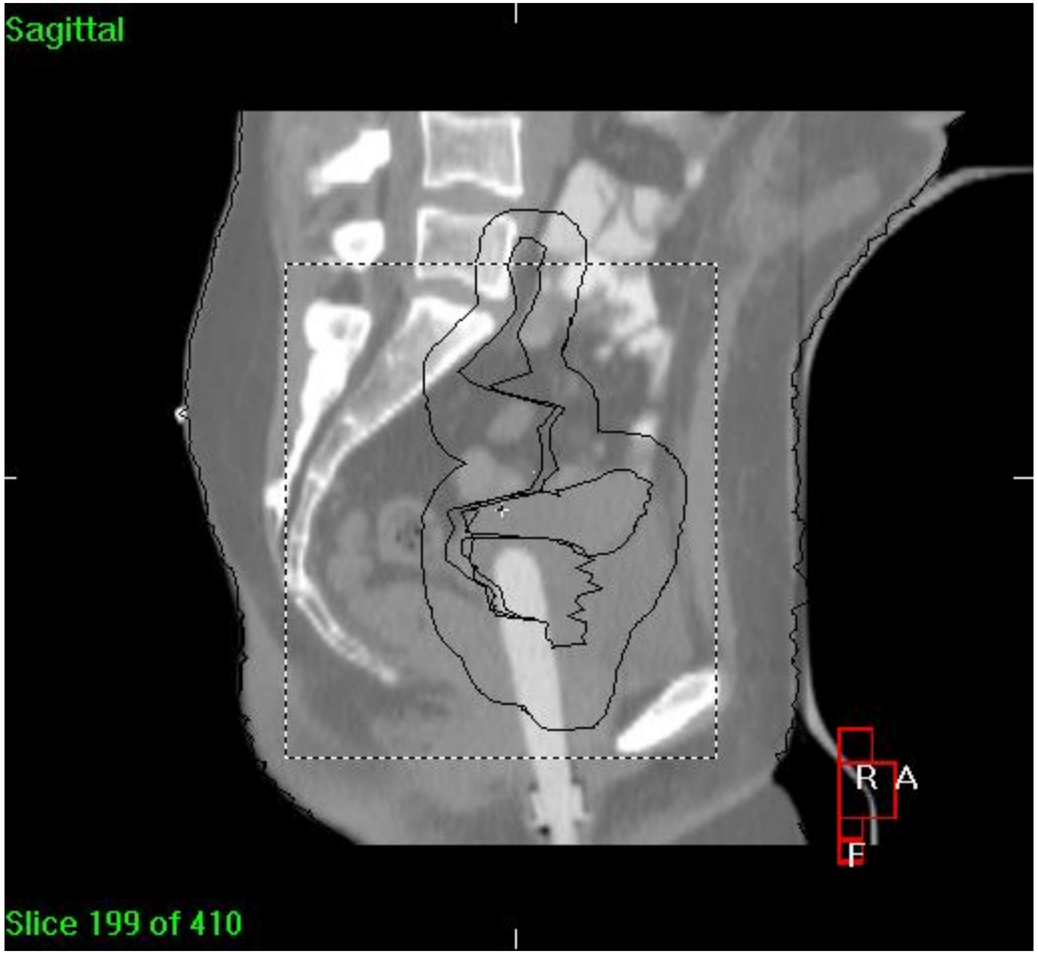
- Reduction of the average difference between fractions in set up of the bony anatomy.
- Reduction in the difference of the shape of the bony anatomy between fraction.

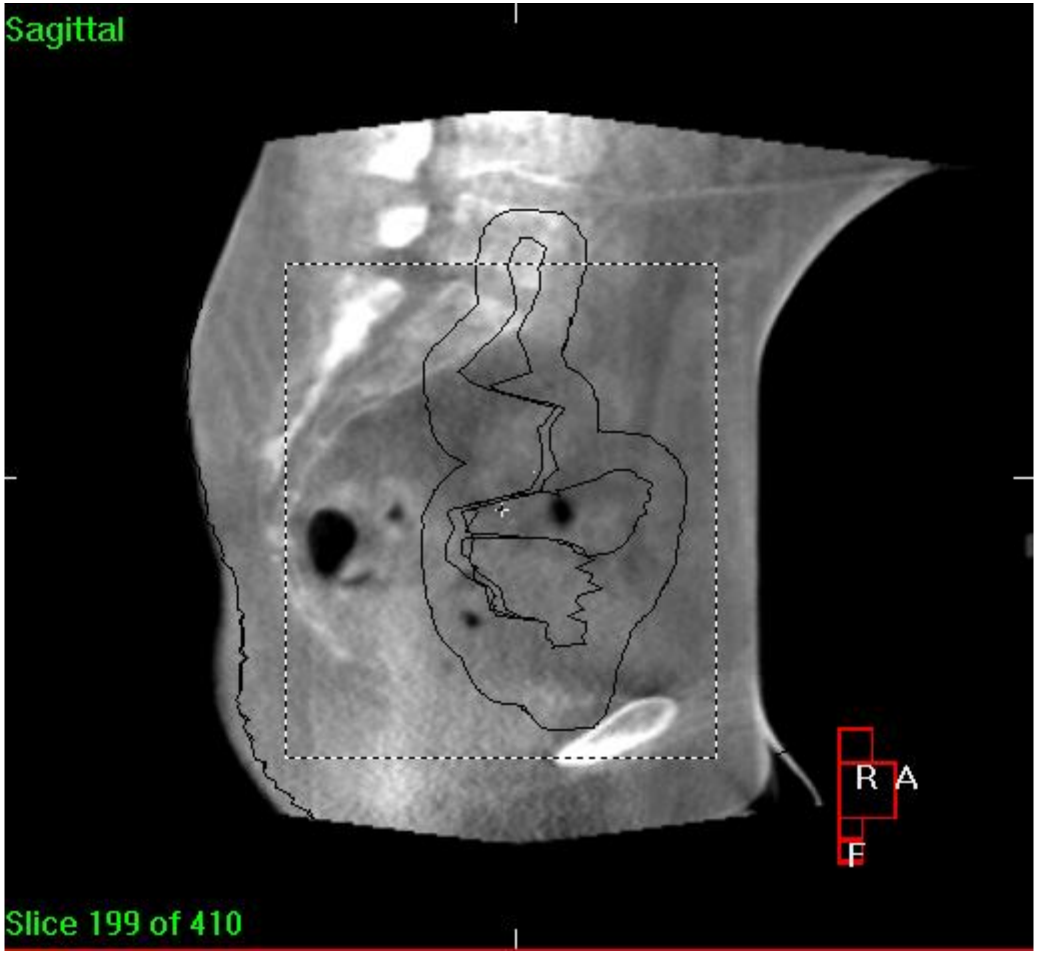
Creating unfortunate differences

- Between CT and treatment

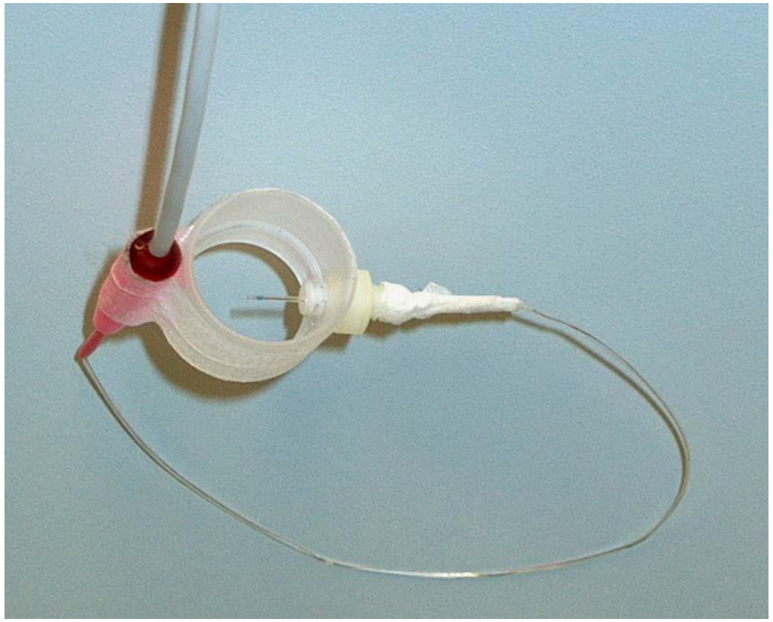


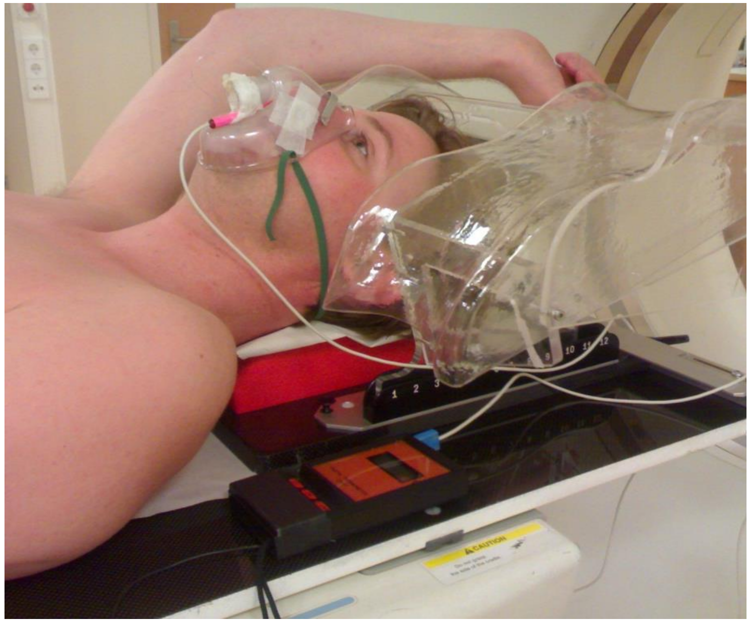
Example 1: Look for differences..





Example 2: Respiratory monitoring system





- 4D CBCT scans with and without oxygen mask
- 3D tumor motion was assessed for tumor mean position and amplitude

Respiratory monitoring system

With oxygen mask

	LR (cm)	CC (cm)	AP (cm)
Σ	0.18	0.23	0.23
σ	0.16	0.19	0.19
Mean	0.06	0.03	0.00

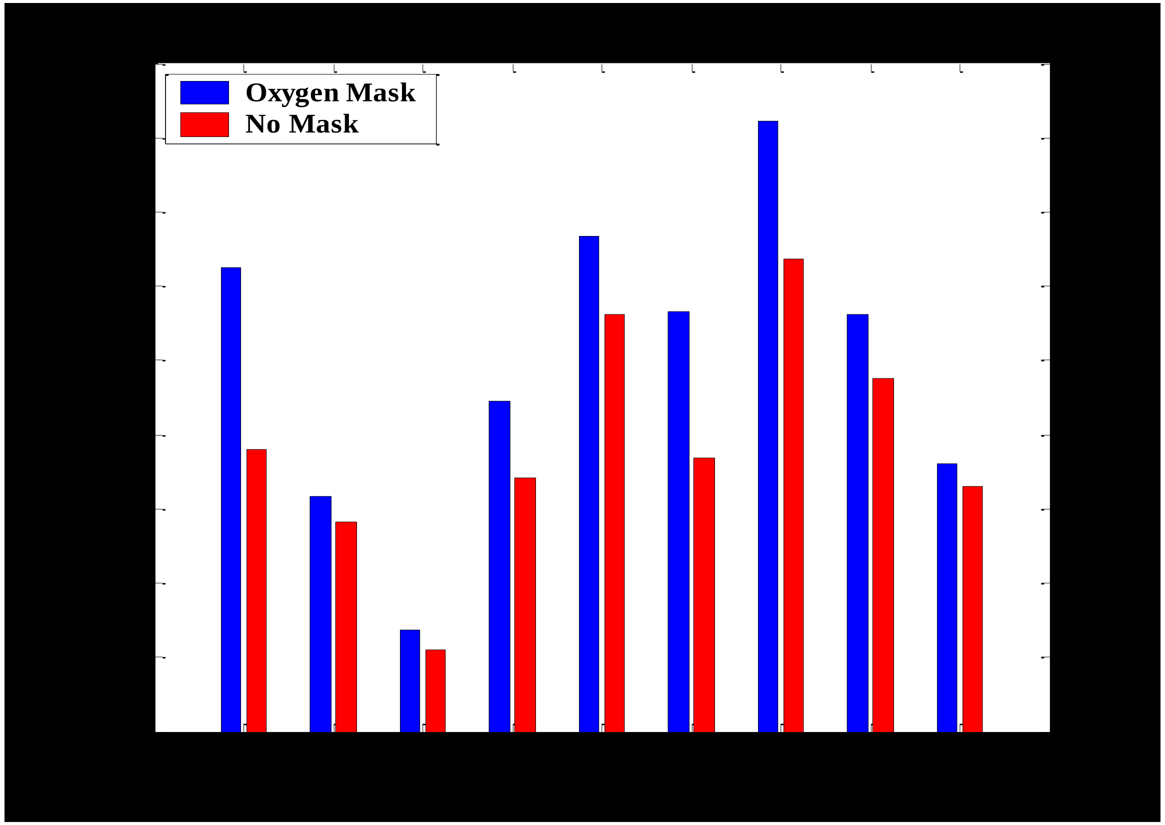
Without oxygen mask

	LR (cm)	CC (cm)	AP (cm)
Σ	0.15	0.21	0.22
σ	0.18	0.17	0.20
Mean	0.04	0.08	-0.09

No significant difference in tumour mean position

J. Wolthaus, M. Rossi

Respiratory monitoring system



M = 29%, SD = 19%, p = 0.0017

Difference in breathing amplitude!

J. Wolthaus, M. Rossi

Deformable registration decreases the need for good immobilization

A. True
B. False

Aim of Patient preparation and positioning

→ **Minimize the difference in patient positioning during the treatment session: *intra*-fraction motion**

Tools:

Increasing patient compliance:

- Practical session SBRT

Immobilization and fixation:

- Lung using 4D CBCT.

Practical session

In case of hypofractioned RT:

- Patient visit the linac
- Session is completely performed but no Gray's are given

Advantages:

- Patient gets acquinted with workflow
- Set-up accuracy can be assesed:
  - ➢ is the intra# motion acceptable?
- Is it do able for the patient?
- Is the image quality sufficient?
- Precautions can be made:
  - ➢ Pain/stress relief
  - ➢ Additional margins/replanning

Stability with prolonged treatment time

Hypo fractionated lung

On-line lung tumor match with CBCT: 3 x 18 Gy

(first protocol design without arc therapy and inline scanning)

Aligning the patient:	5 min
First CBCT scan:	4 min
Registration:	5 min
Manual table shift:	3 min
Second CBCT scan:	4 min
Evaluation CBCT scan:	1 min
Beam delivery:	25 min
Post treatment CBCT scan:	4 min

Stability with prolonged treatment time

Antoni van Leeuwenhoek Hospital

100x real speed

Stability with prolonged treatment time

Antoni van Leeuwenhoek Hospital

Stability with prolonged treatment time

59 Patients, 3 fractions per patient

		LR (mm)	CC (mm)	AP (mm)
Residual Inter-fraction	GM	0.2	0.6	-0.6
	Σ	0.8	0.8	1.0
	σ	1.1	1.1	1.4
Intra-fraction	**GM**	**0.0**	**1.0**	**-0.9**
	Σ	**1.2**	**1.3**	**1.9**
	σ	**1.2**	**1.4**	**1.7**

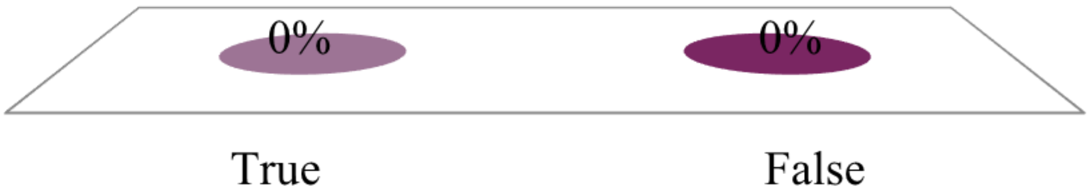
Intrafraction motion is the motion of a patient within a session

A. True

B. False

Patient compliance won't impact intrafraction motion

A. True
B. False



Minimize the difference in patient position

→ Minimize the difference in patient position

1. between simulation and treatment sessions
2. during the treatment session

→ **Maximize the distance between target volume and organs at risk**

Tools:

- **Immobilization and fixation**
- **Patient compliance**

Minimize the difference in patient position

→ **<u>Maximize</u> the distance between target volume and organs at risk**

Tools:

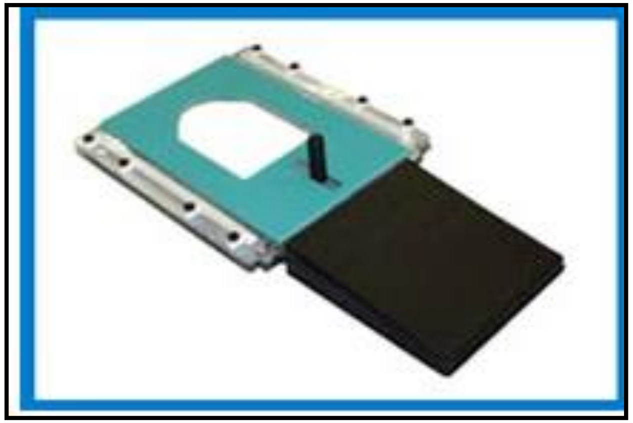
Immobilization and fixation:

- Bellyboard for pelvic patients

Patient compliance:

- Breath hold for breast patients

Belly board pelvic patients



Belly board

Belly board pelvic patients

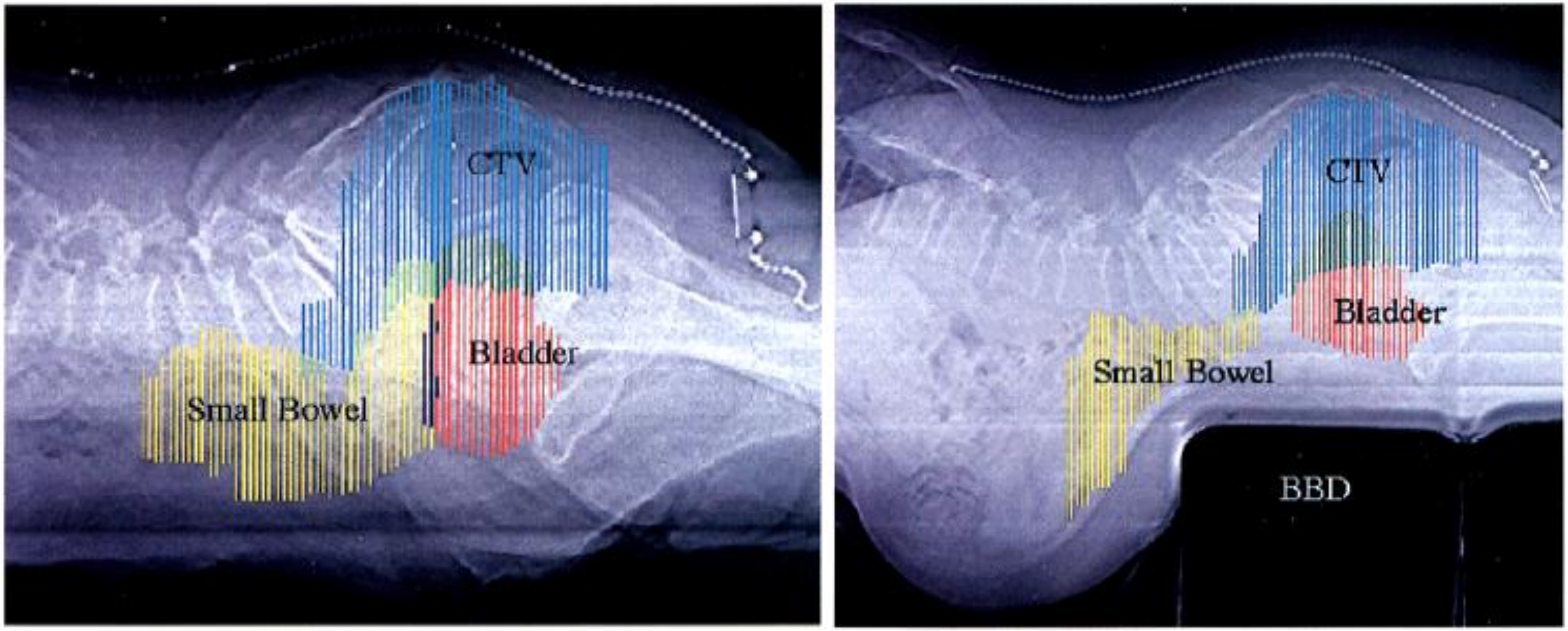
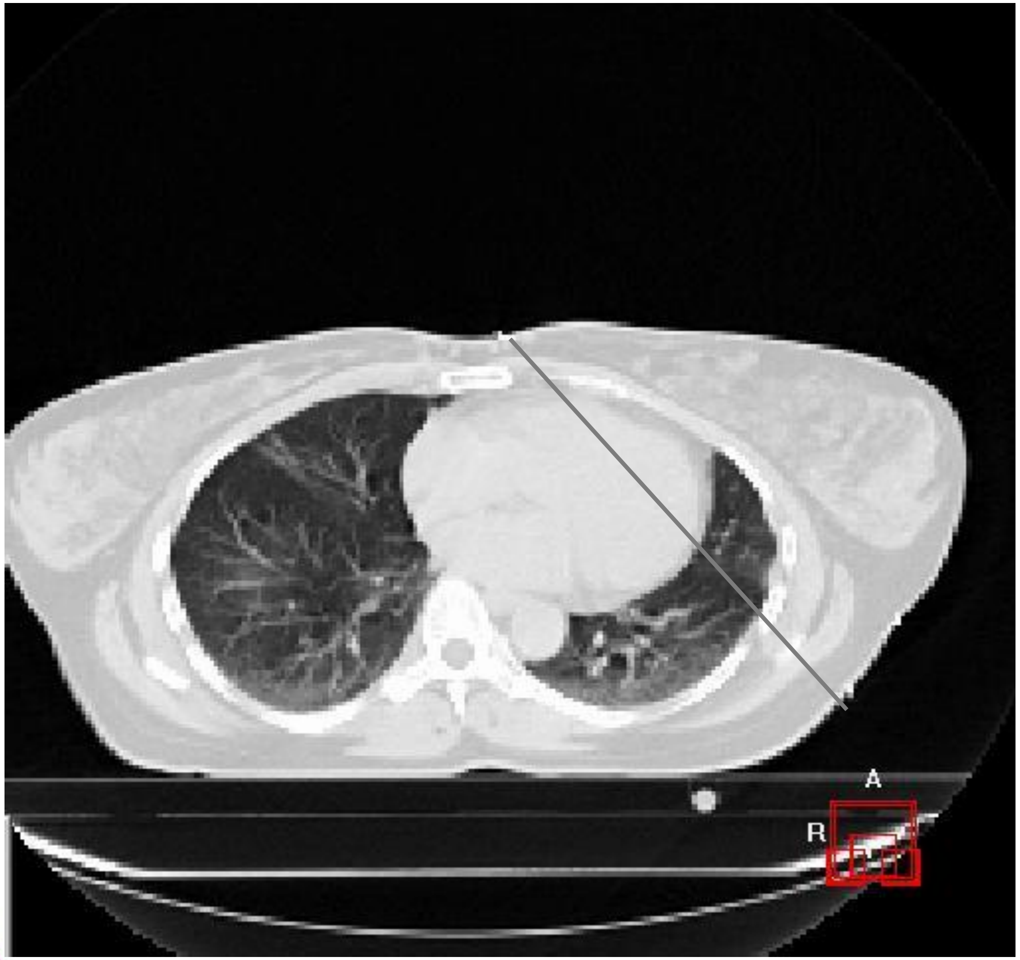


Fig. 2. Pilot localization, lateral view is shown (a) for simulation without BBD and (b) with BBD. The clinical target volume (CTV), small bowel, and bladder are shown. Note a dramatic shift in small bowel in the cephalic direction with the BBD.

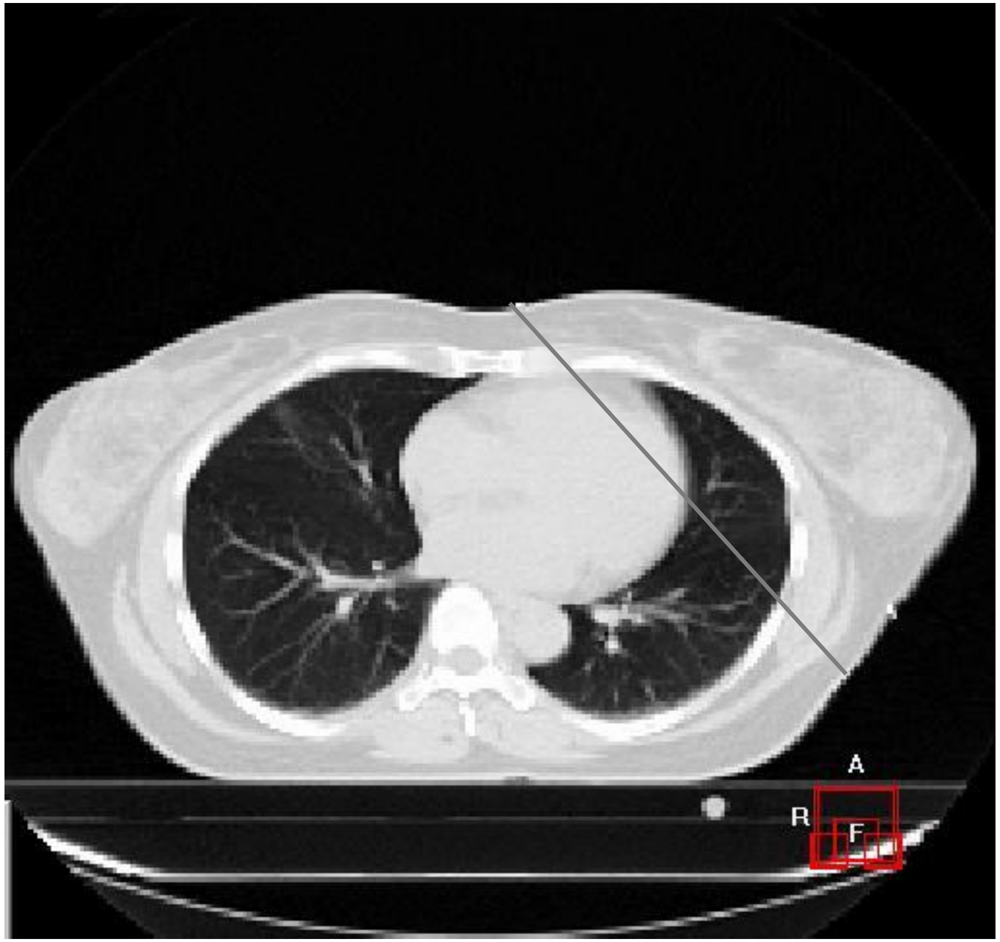
Das *et al,* 1997

Breath hold for breast patients

Normal inspiration

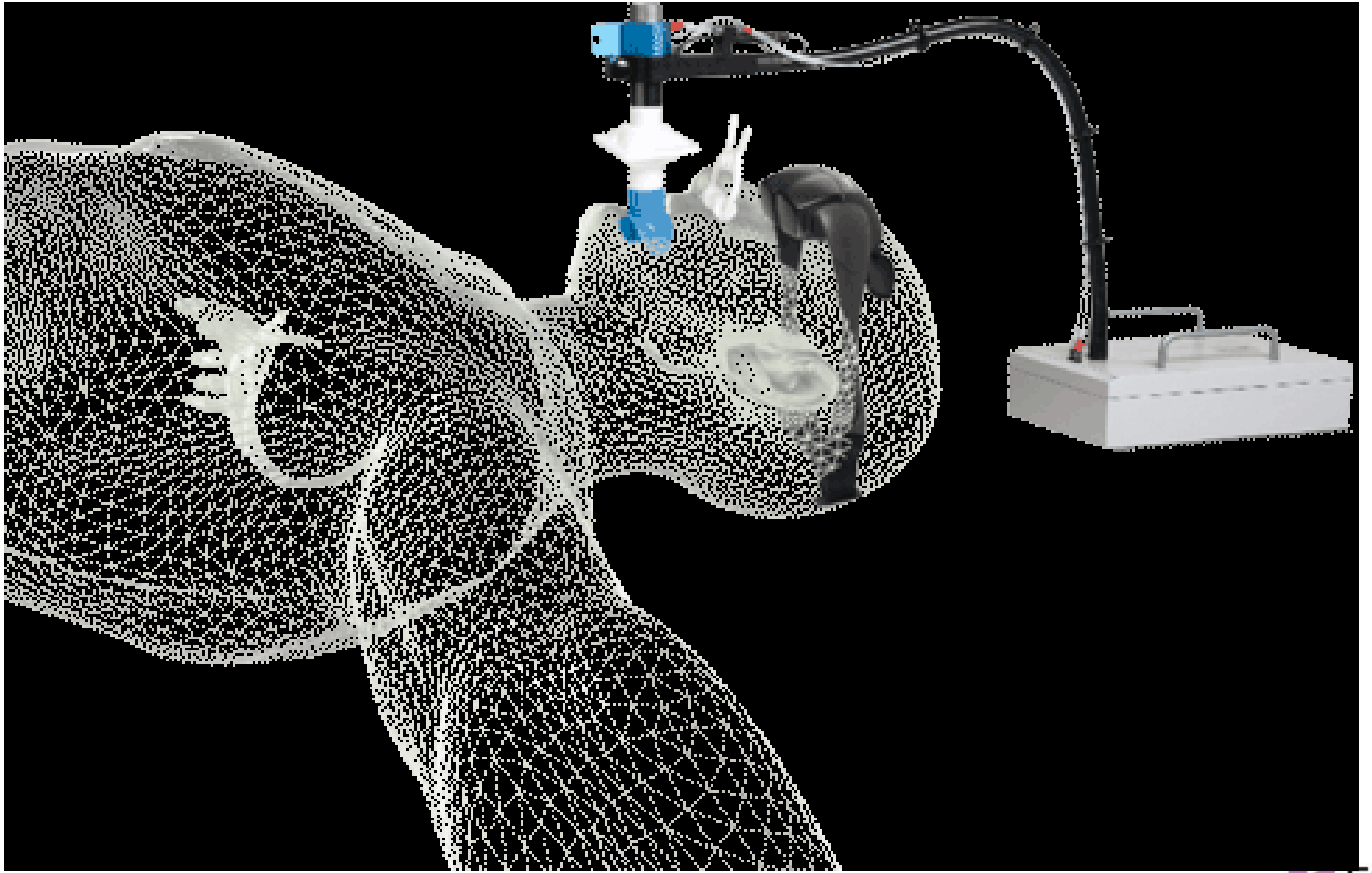


Deep inspiration



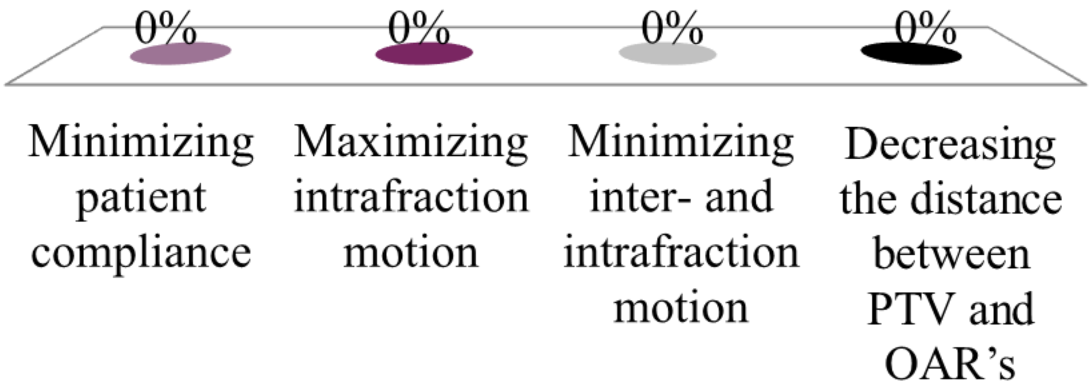
J. Sonke

Essential: education & compliance



Patient preparation and immobilization aims at:

A. Minimizing patient compliance
B. Maximizing intrafraction motion
C. Minimizing inter- and intrafraction motion
D. Decreasing the distance between PTV and OAR's



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Conclusion

The first step in radiation therapy is to <u>minimize</u>

- the difference in patients anatomy and set-up between CT en treatment
- the difference in patients anatomy and set-up between treatment days

and to <u>maximize</u>

- patient stability
- the distance between target volume and organs at risk

Conclusion

The first step in radiation therapy is to minimize

- the difference in patients anatomy and set-up between CT en treatment
- the difference in patients anatomy and set-up between treatment days

and to maximize

- patient stability
- the distance between target volume and organs at risk

IGRT & ART?

Rotations

Deformations

Offline protocol

OAR

Conclusion

https://espace.cern.ch/ULICE-results/Shared%20Documents/D.JRA_5.1_public.pdf

‘Recommendations for organ depending optimized fixation systems’

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Pre-treatment imaging

Mirjana Josipovic

Dept. of Oncology, Rigshospitalet

& Niels Bohr Institute, University of Copenhagen

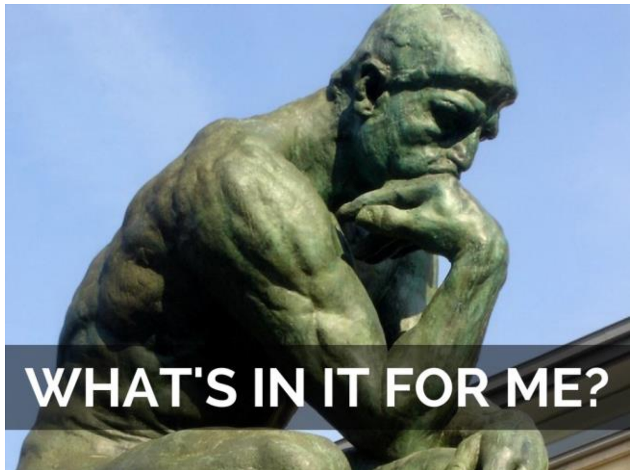
Denmark

Advanced skills in modern radiotherapy

May 2018

Intended learning outcomes

- Illustrate the importance of a particular pre-treatment imaging modality for radiotherapy
- Comprehend the additional value of applying combined information from several imaging modalities for radiotherapy planning
- Identify uncertainties of pre-treatment imaging modalities



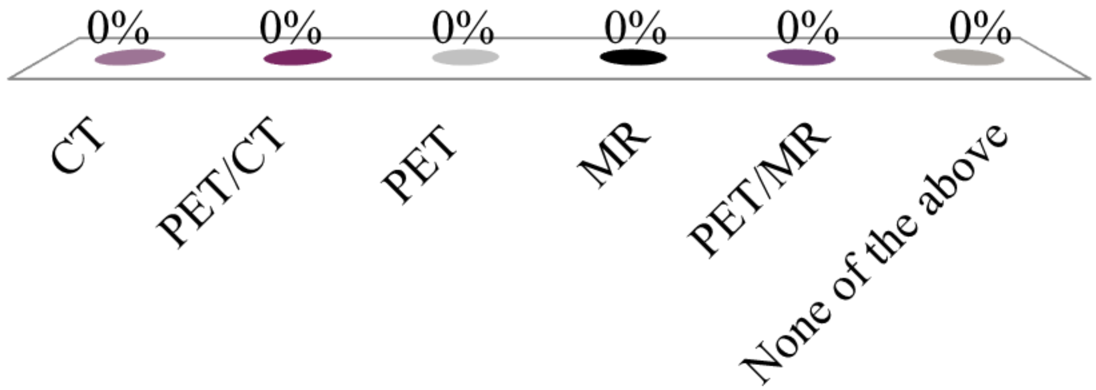
Pre-treatment imaging for radiotherapy

- CT: computed tomography
- PET: positron emission tomography
- MR: magnetic resonance

Do you have experience with…?

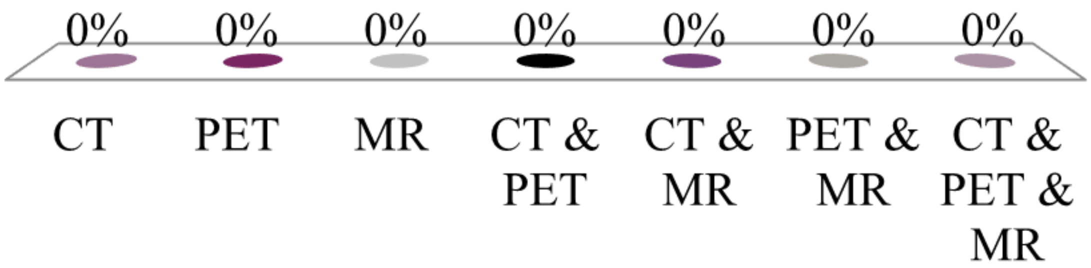
A. CT
B. PET/CT
C. PET
D. MR
E. PET/MR
F. None of the above

Multiple answers possible!



Which imaging modalities do we need for modern state of the art radiotherapy?

A. CT
B. PET
C. MR
D. CT & PET
E. CT & MR
F. PET & MR
G. CT & PET & MR



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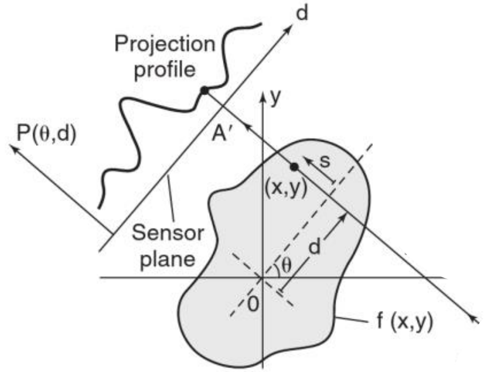
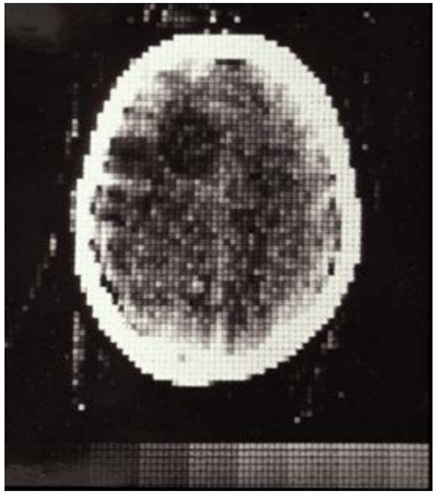
CT chronology



- 1917 mathematical grounds for CT reconstruction
- 1971 first clinical CT
- 1990 spiral CT
- 1993 dual slice
- 2003 32-slice
- Today : ultrafast volume-scanning
  dual source, dual energy



80x80 matrix
5 min rotation time

1024x1024 matrix
< 0.3 s rotation time

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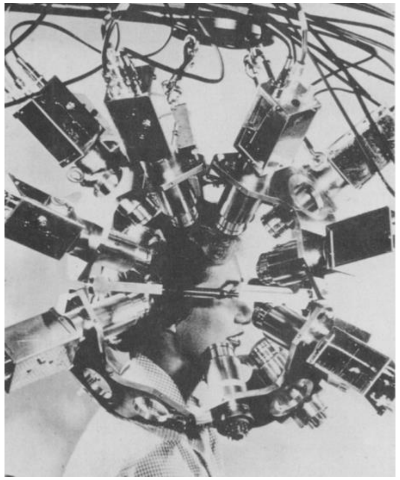
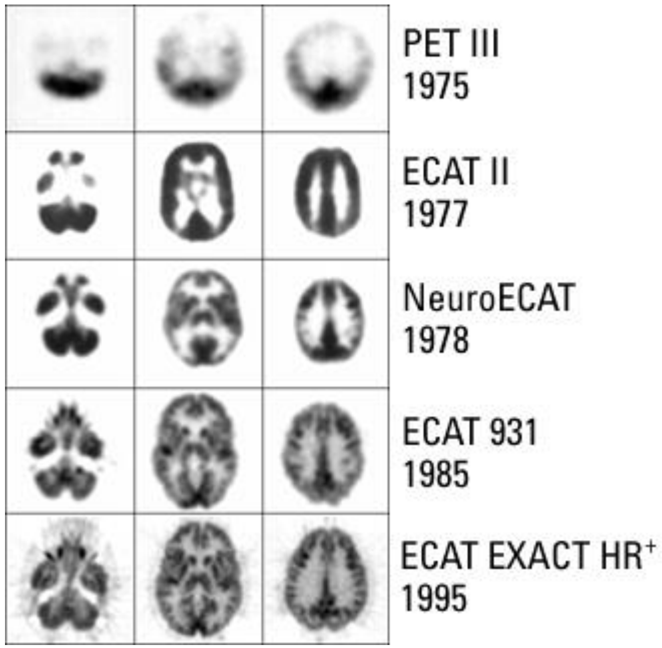
PET chronology

- 1930's radioactive tracers
- 1953/66 multidetector device
- 1975 back projection method for PET
- 1979 fluorine 18 deoxy glucose (FDG)
- 2000 PET/CT "medical invention of the year"



Wagner et al. 1998



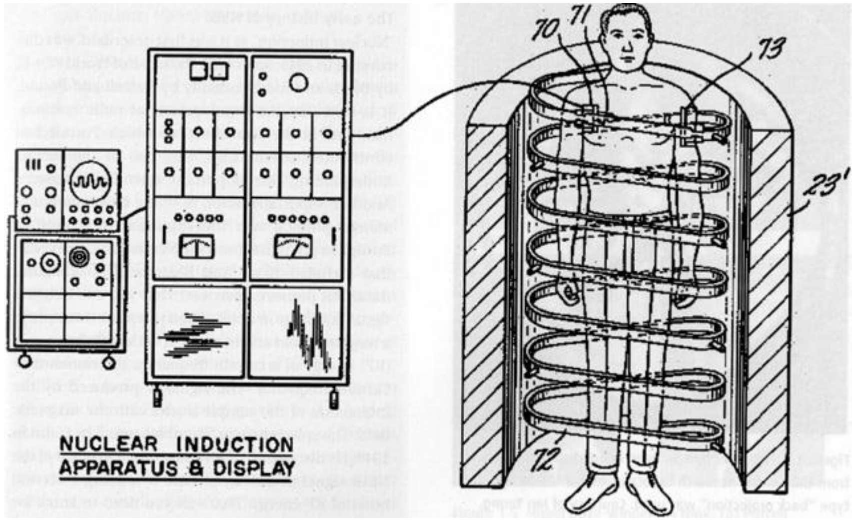
MR chronology

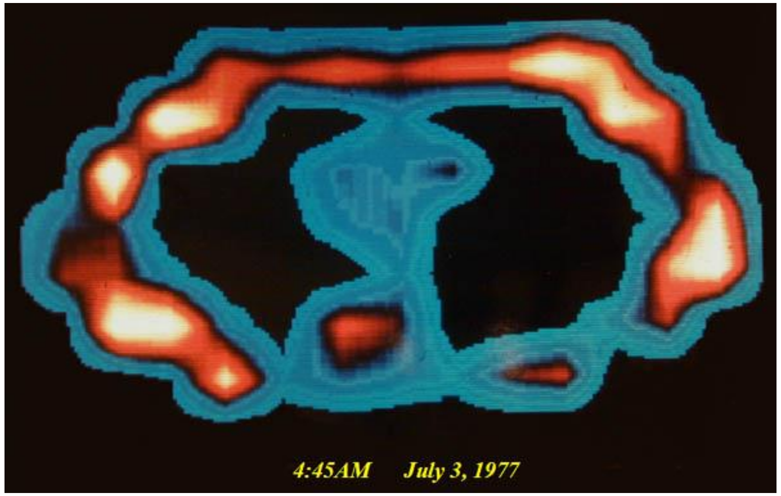
- 1937 nuclear magnetic resonance

- 1956 Tesla unit
- 1972 Damadian invention

- 1977 first MR scan

- 1993 functional MR

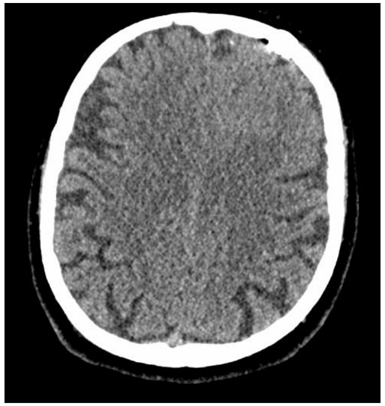


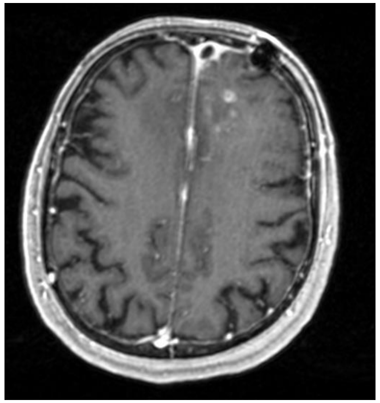


CT

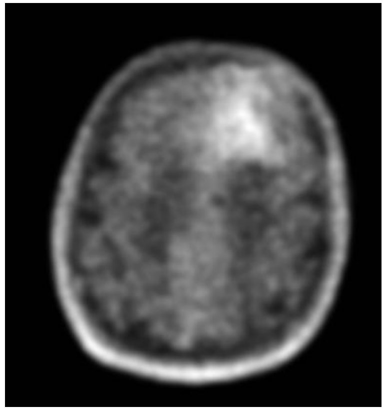
MR

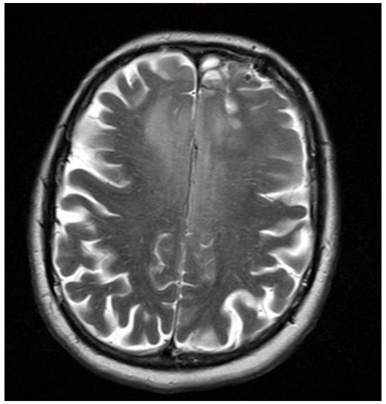
PET

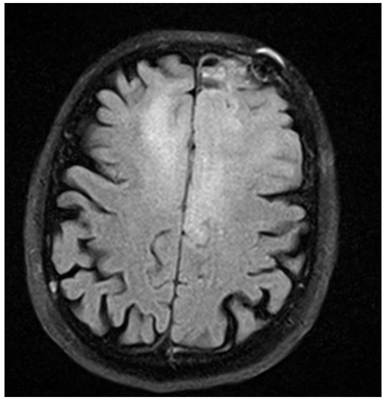


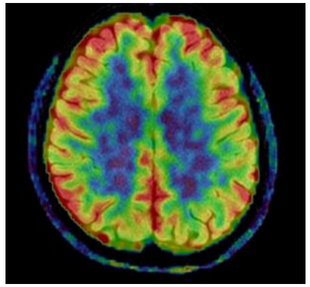


T1



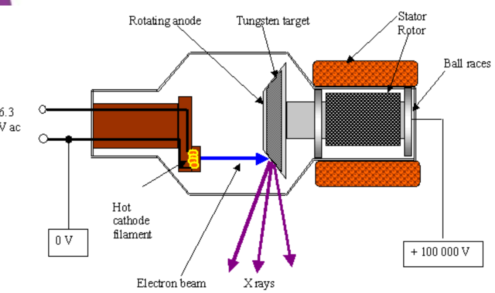


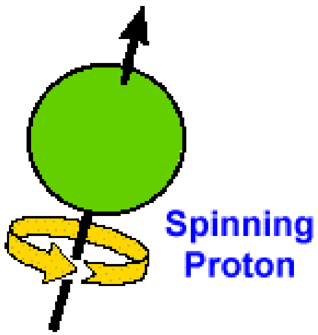


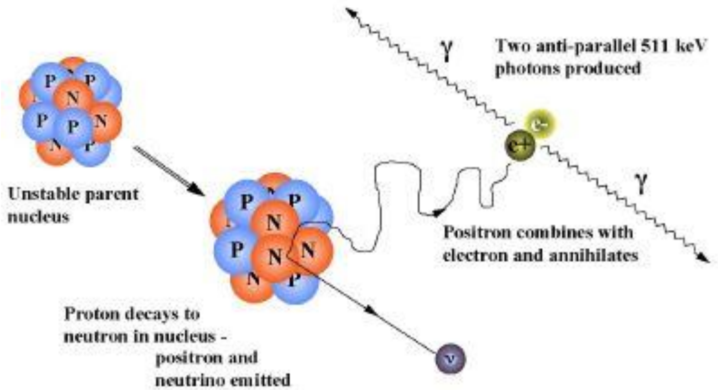


T2

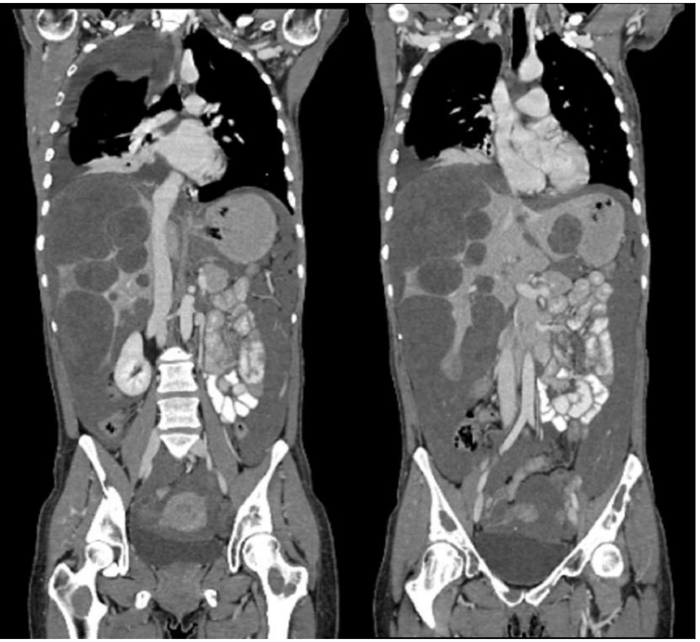
flair



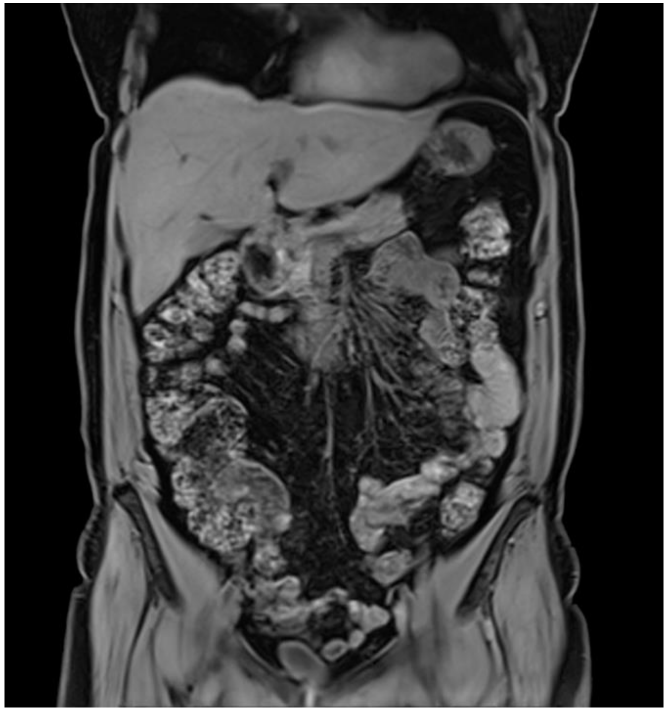




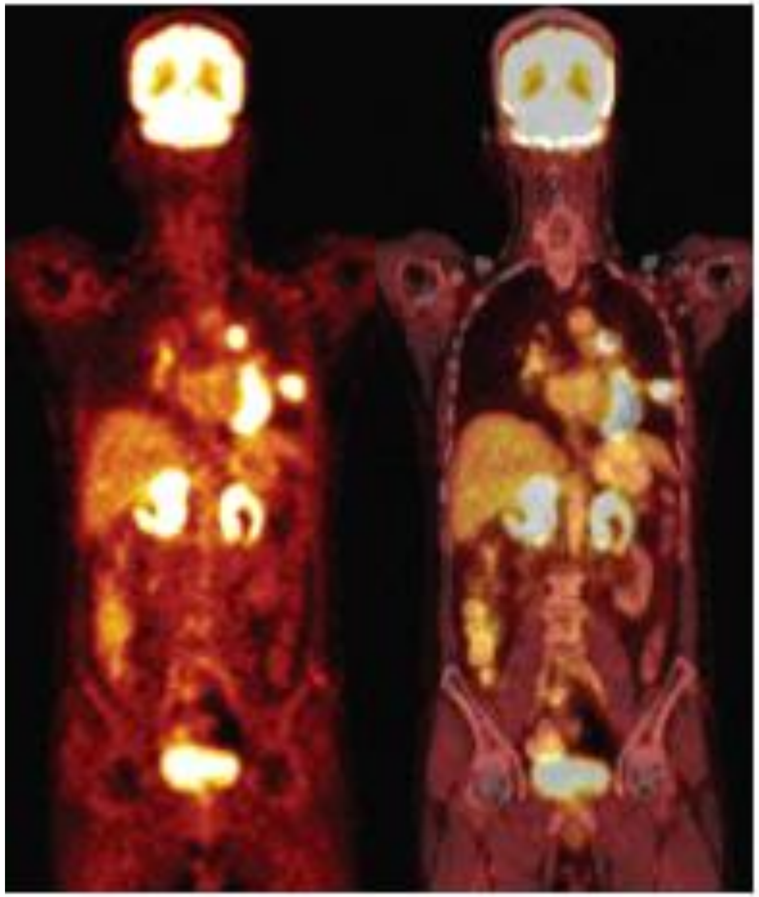
CT



MR



PET



What do we see?

- Morphology
  - ➢ CT, MR

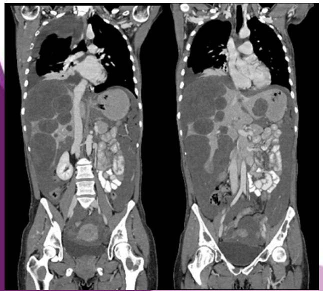
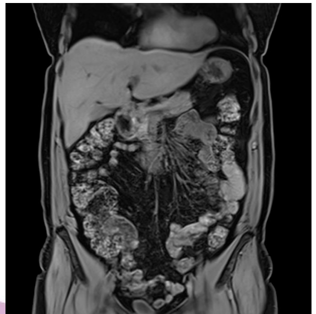
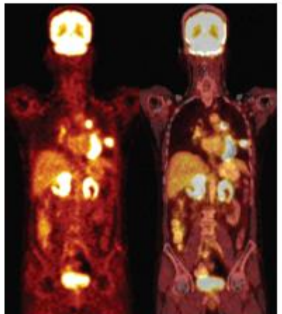
→ (patologic) anatomy

- Biological processes
  - ➢ PET, MR

→ Tumour metabolism

Perfusion

Organ function

Diagnostic imaging vs RT imaging

- Diagnostic
  - ➢ What is this?

- RT planning
  - ➢ Where is this?

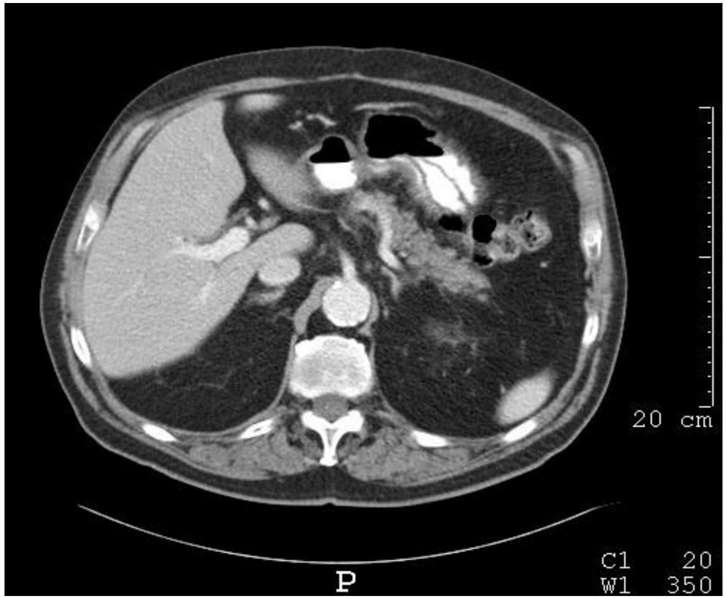
Why we need CT

CT numbers = Hounsfield units

The grey tones on the CT image represent the attenuation in every pixel/voxel

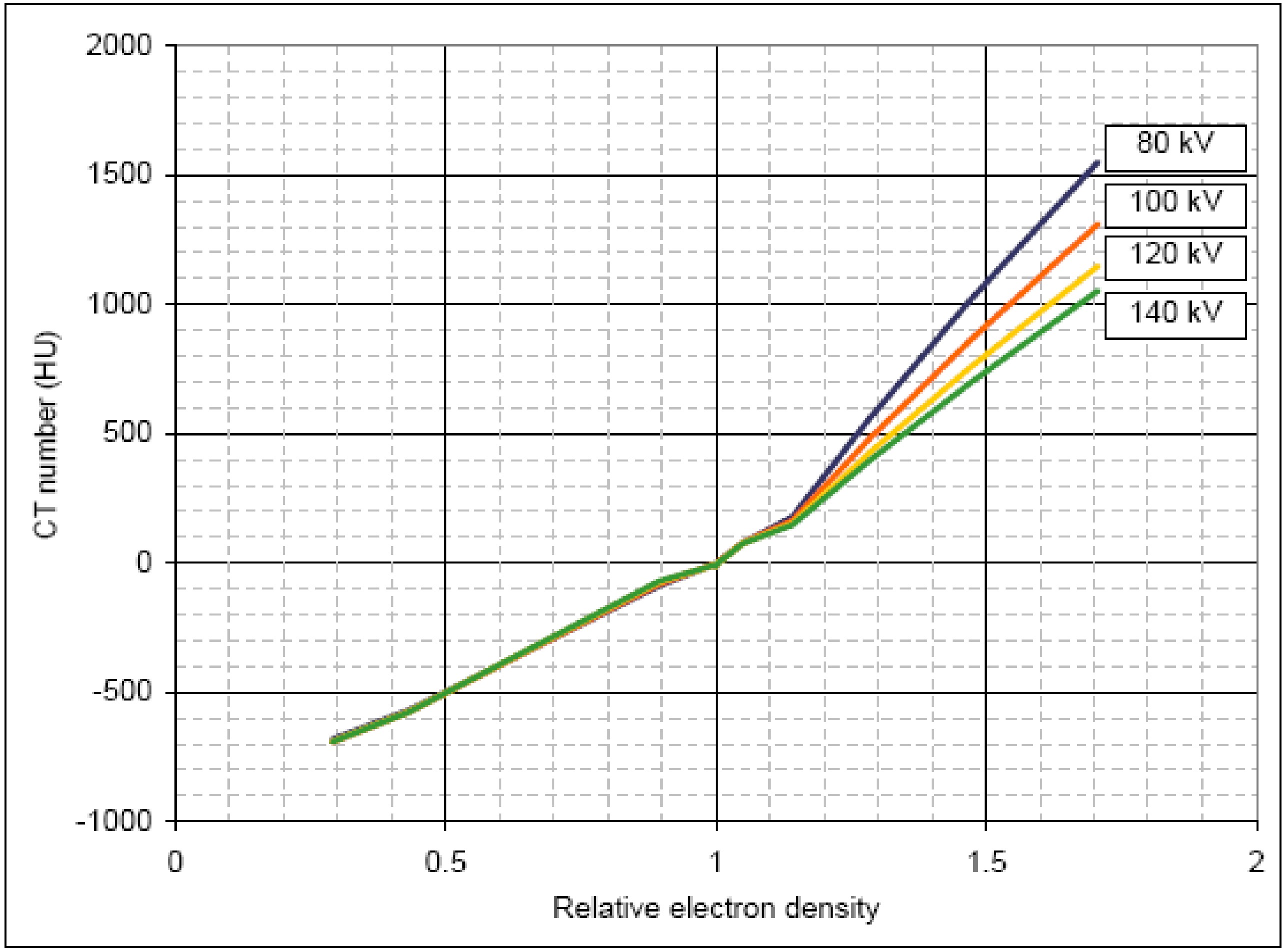
The grey tones are expressed in Hounsfield units (HU)
– CT numbers:

$$HU = \frac{\mu_{obj} - \mu_{water}}{\mu_{water}} \times 1000$$



Hounsfield units → electron density

Figure 4. CT number against electron density at a range of kVs



Necessary for dose calculation

Calibration curve needed for each applied kV

How well can we trust the imaging information?

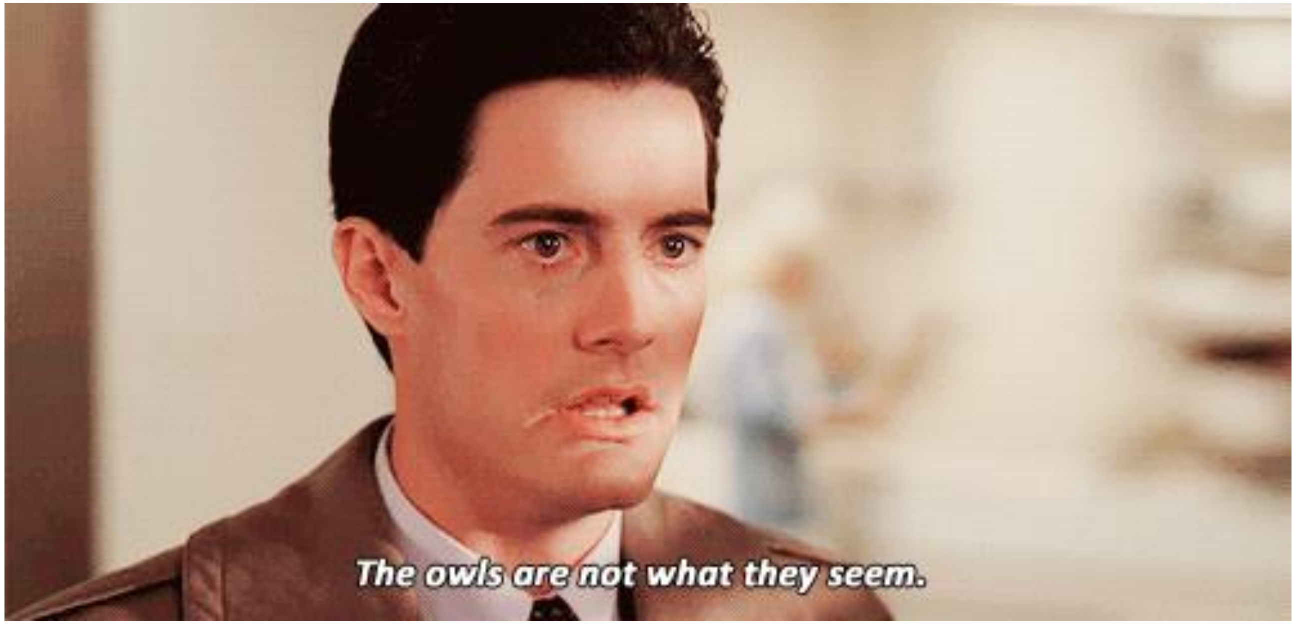


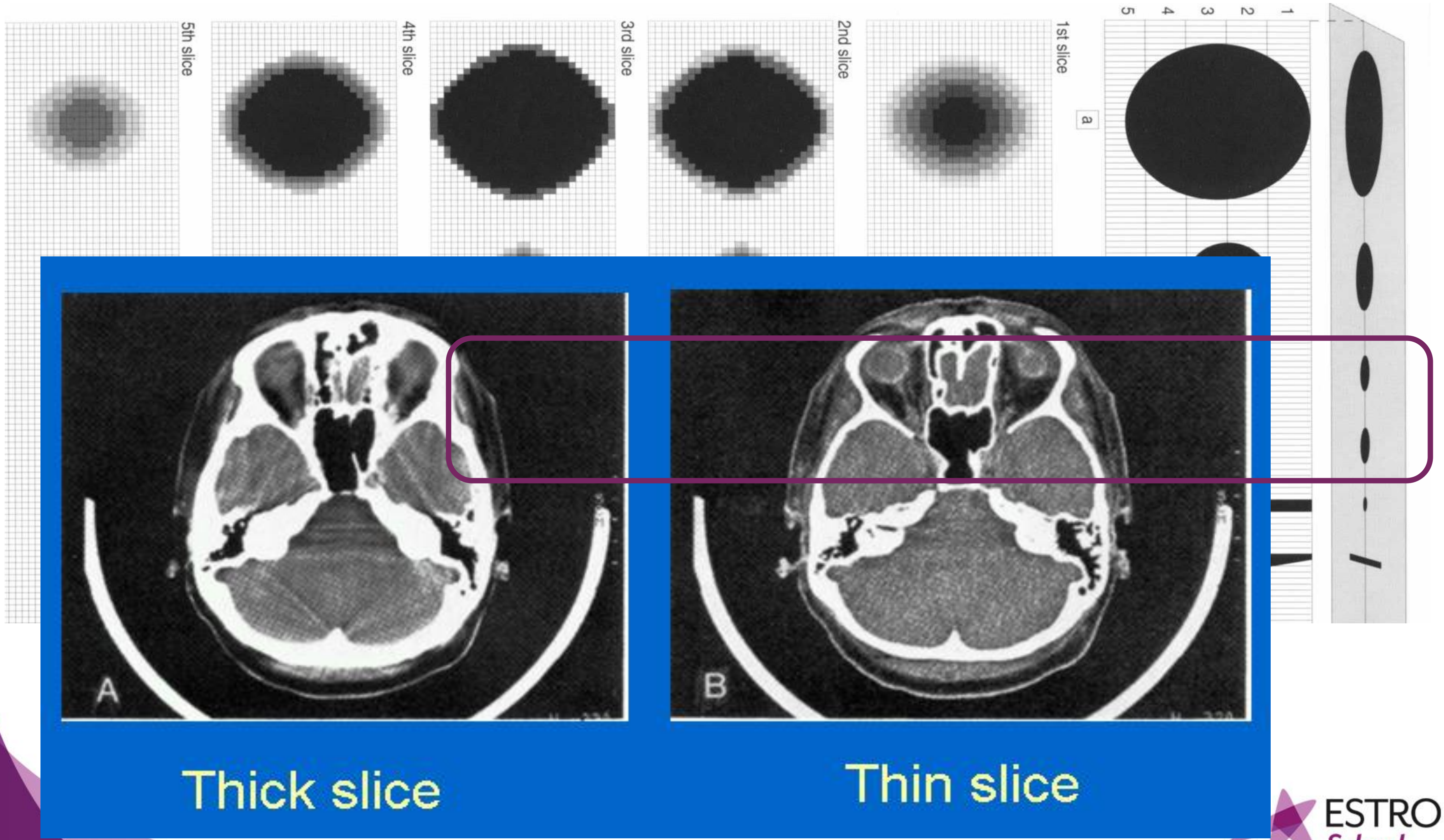
Image artifacts

Definition :

Systematic deviation between the HU in the reconstructed image and the objects correct attenuation’s coefficient

- **Partial volume artefacts**
- **Streak artefacts**
- Ring artefacts
- Motion artefacts
- Noise

Partial Volume artefacts



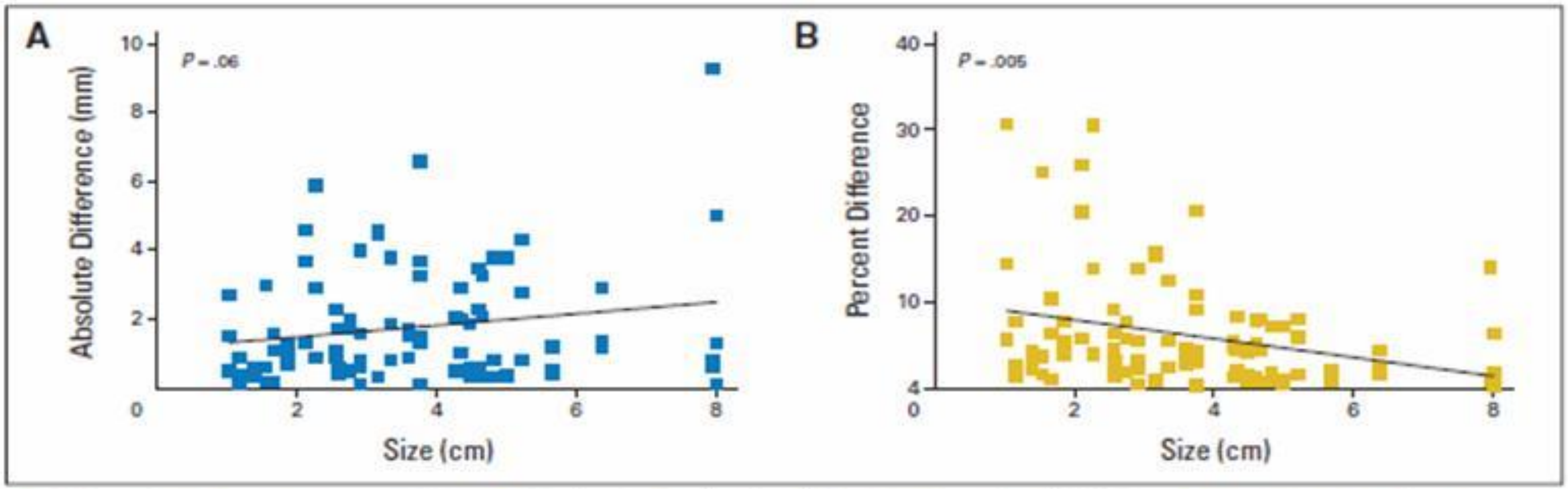
Oxnard et al. JCO 2011

Variability of Lung Tumor Measurements on Repeat Computed Tomography Scans Taken Within 15 Minutes

Table 3. Differences in Measurement Variability Depending on Lesion Size, As Calculated From Repeat CT Scans Performed Within 15 Minutes of Each Other

		Example Tumor		
Size of Tumor (cm)	Standard Deviation (mm)	Size (cm)	Range As a Result of Variability (cm)*	% Change As a Result of Variability
1-3	2.0	2	1.6-2.4	± 20
3-5	2.3	4	3.5-4.5	± 12
5-8	3.3	7	6.3-7.7	± 9

For a lesion measuring 4 cm,
CT variability can lead to measurements from 3.5 to 4.5 cm



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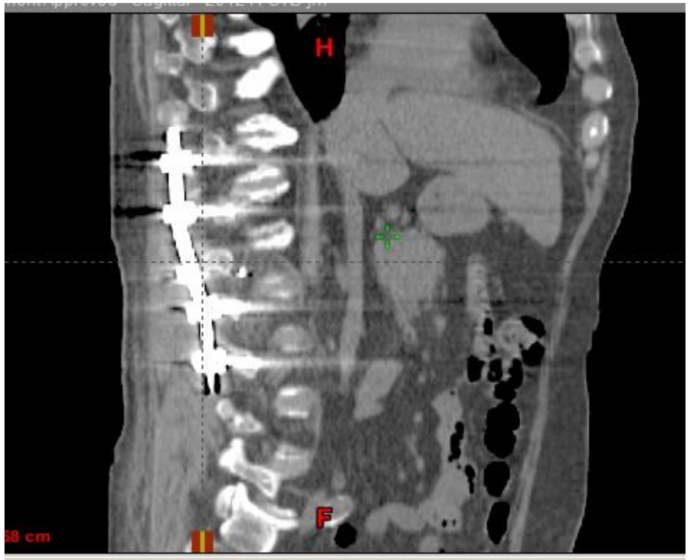
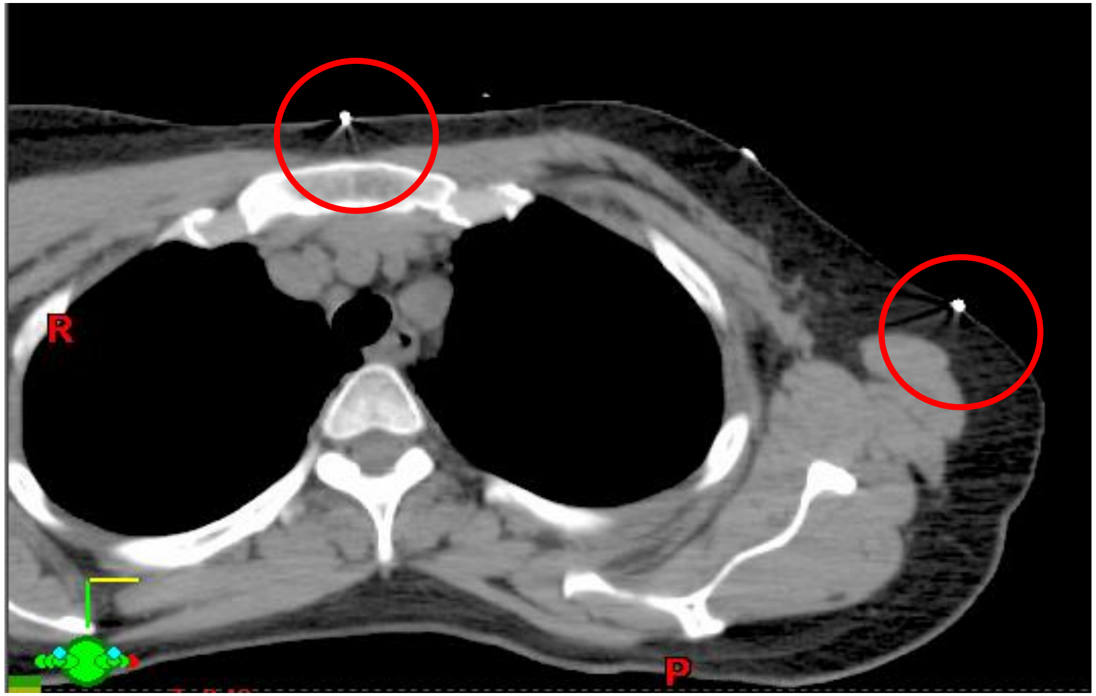
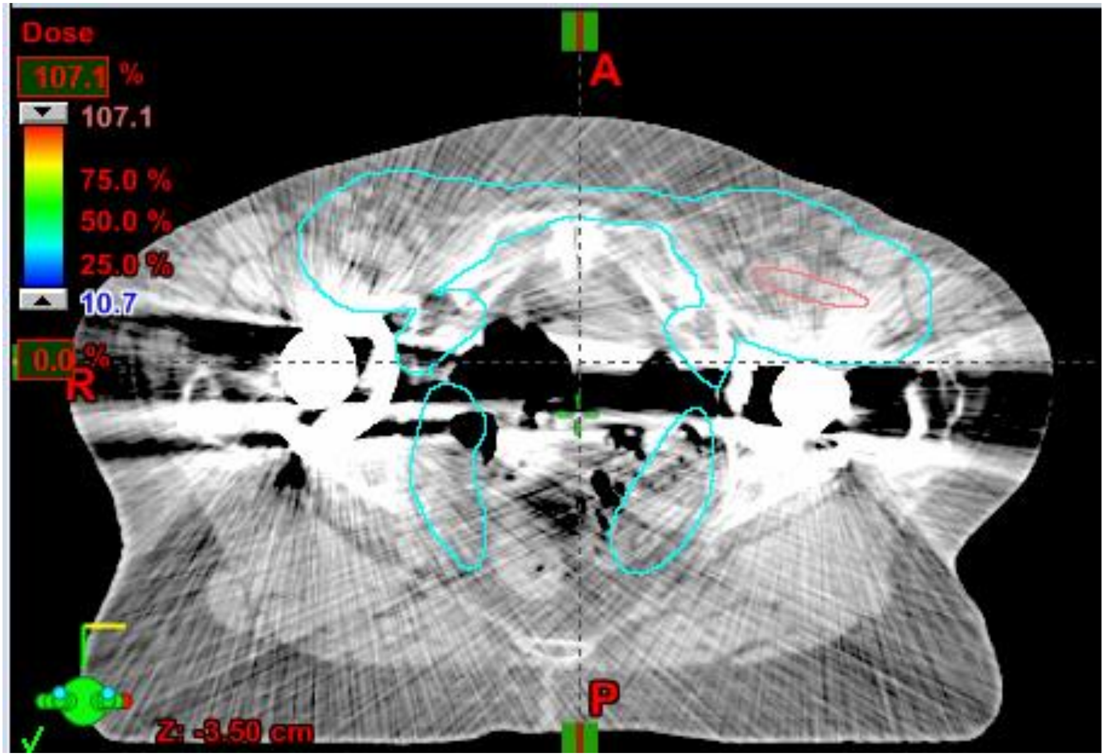
Streak artefacts







Metal artifact reducton sw

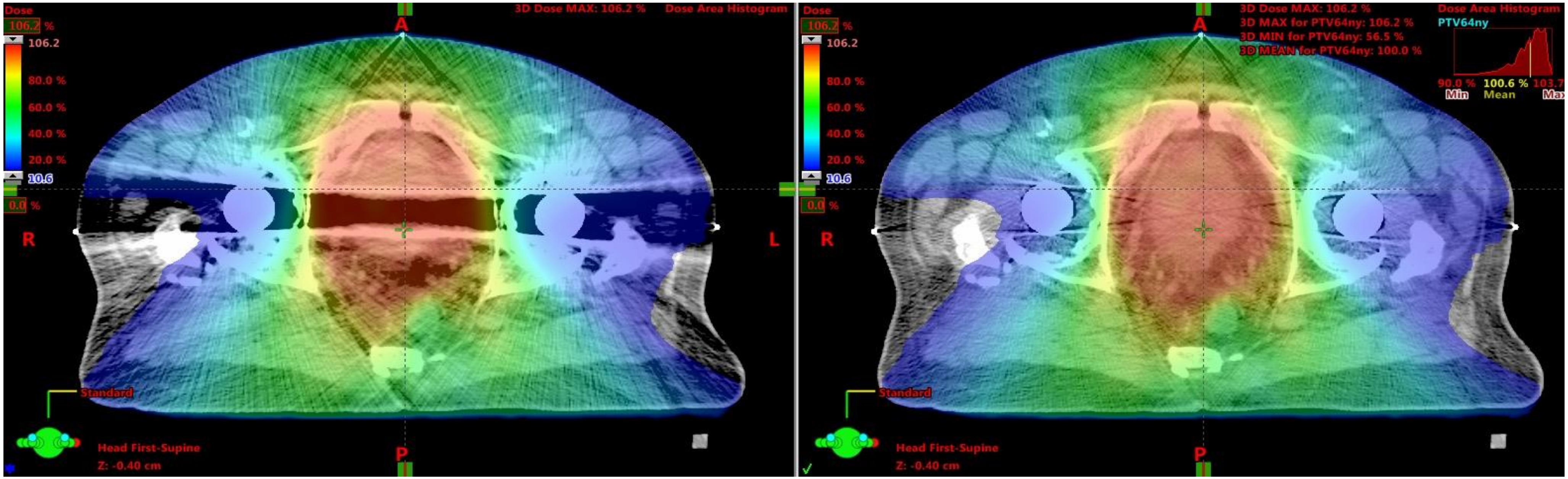
- Dual Energy CT (DECT)
  - Used two different X-ray energies
  - “Virtual monochromatic” scans

- Iterative metal artifact reduction software
  - MAR, iMAR, O-MAR…

MAR - impact on dose planning

Dose calculation for 10 patients with iMAR

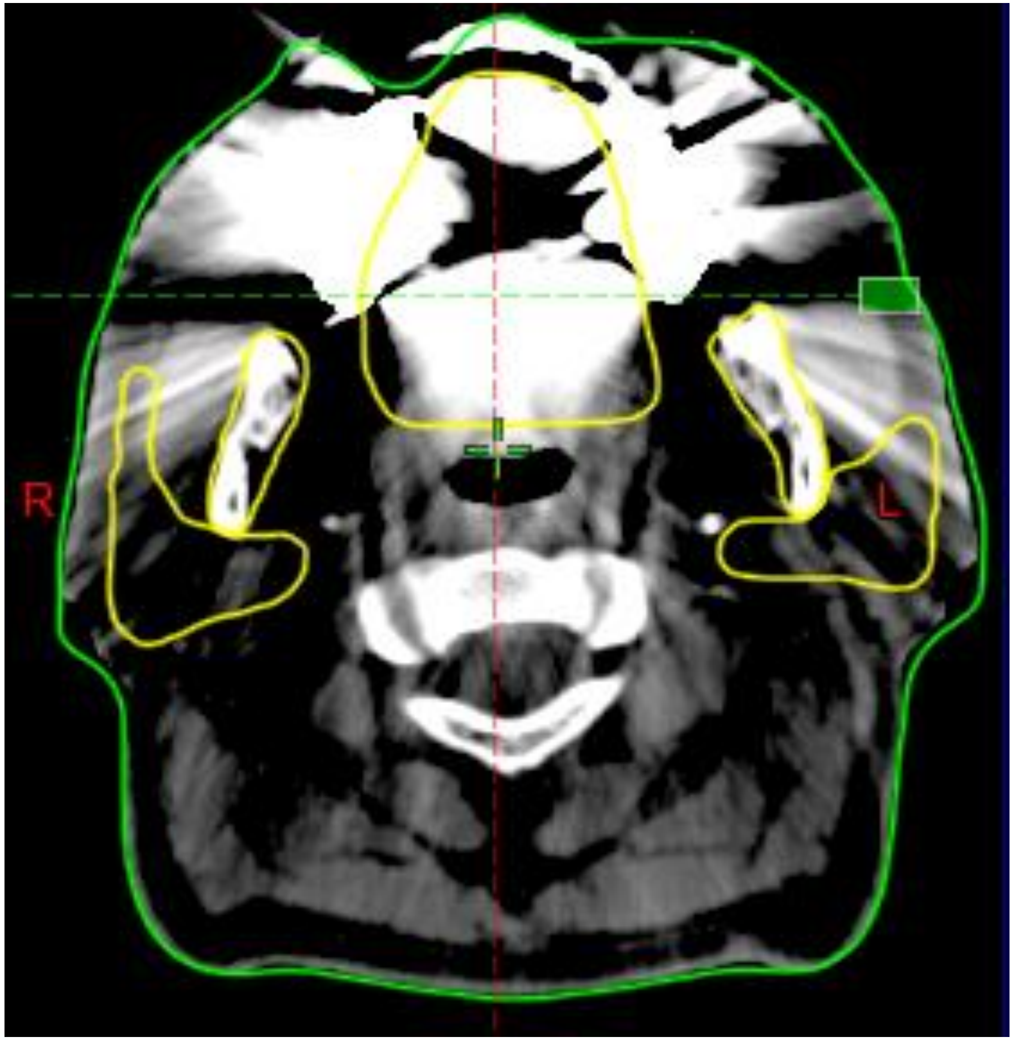
- No difference in dose compared to manual override

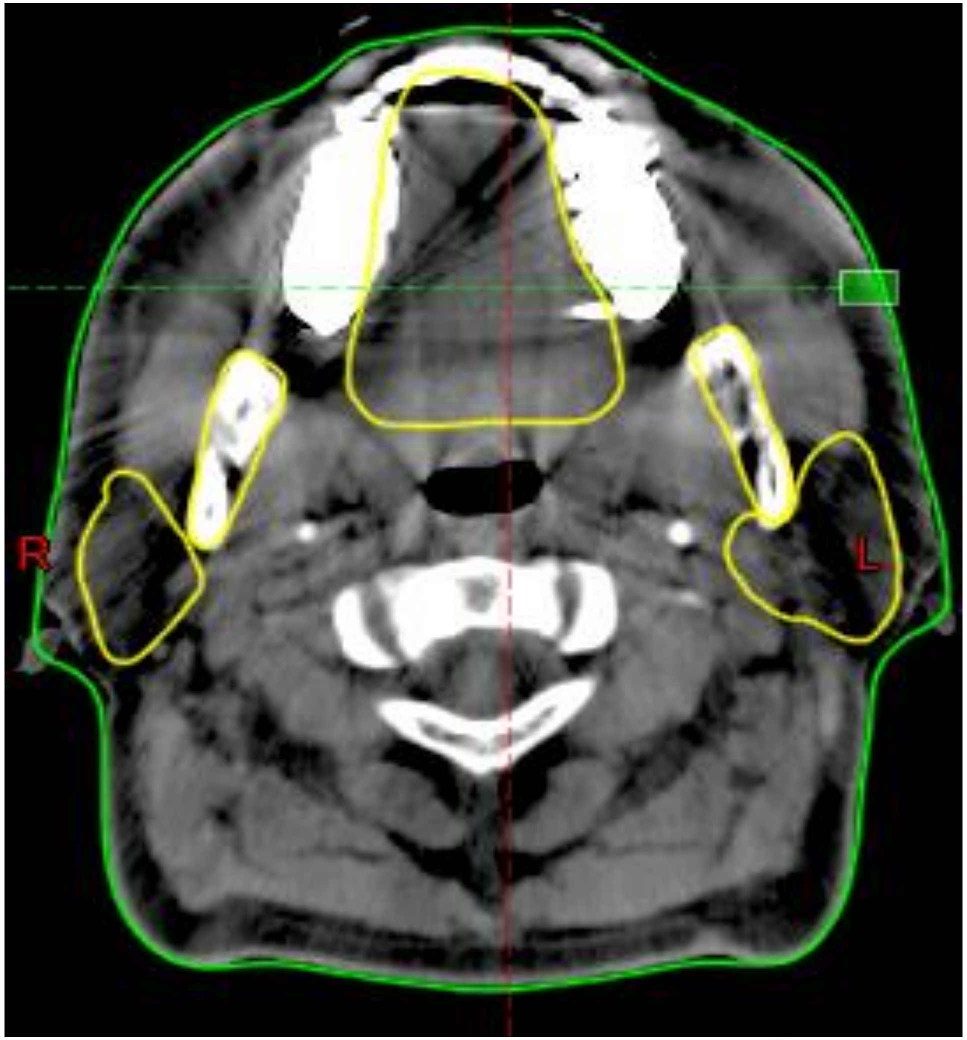


Images courtesy of Laura Rechner, Rigshospitalet

MAR- impact on contouring

- Head and neck contouring by a radiation oncologist

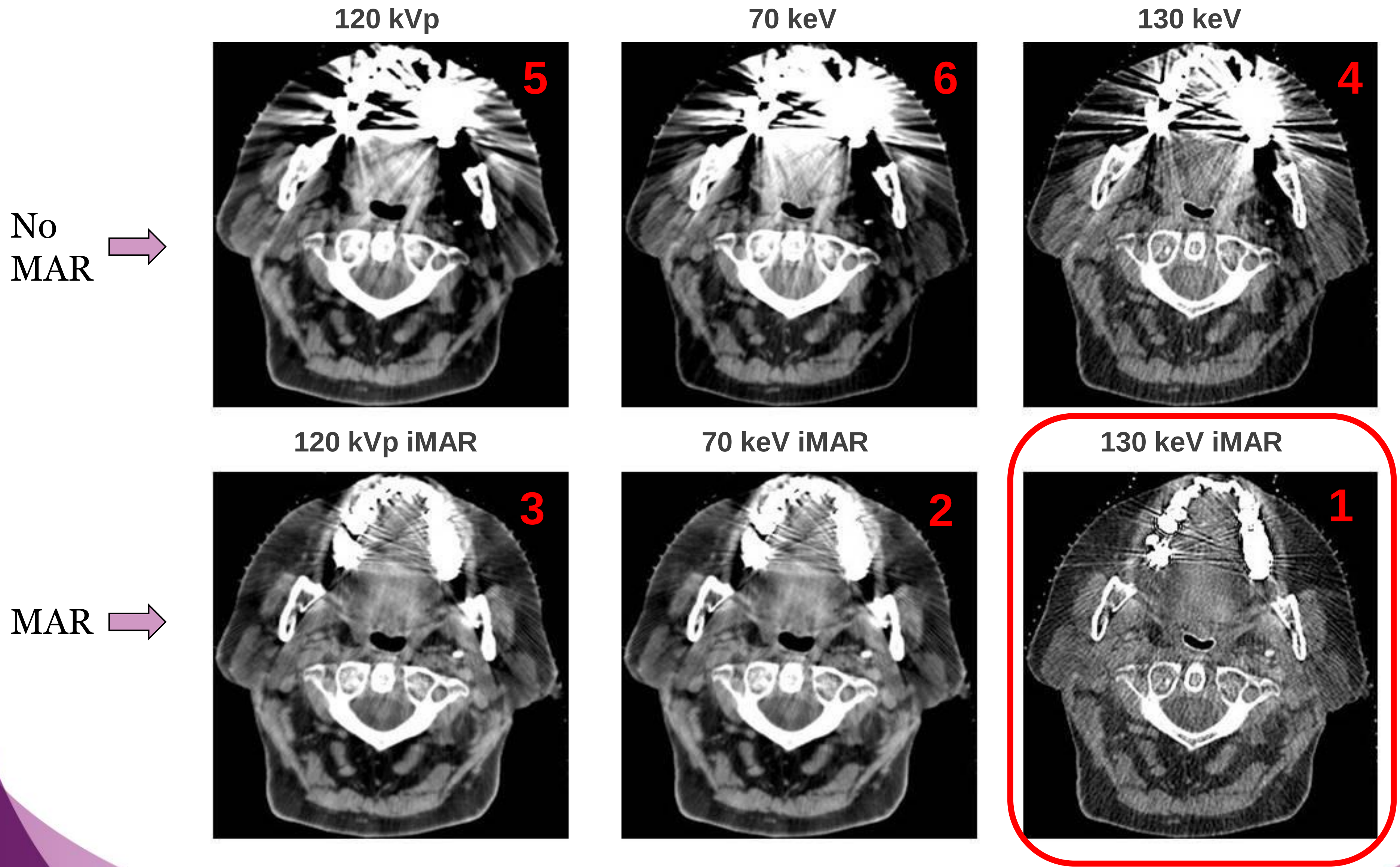




Images courtesy of Jeppe Friborg, Rigshospitalet

MAR combined with dual energy scan

- **Which images do radiologists & oncologists prefer?**



Kovacs et al. RO 2018

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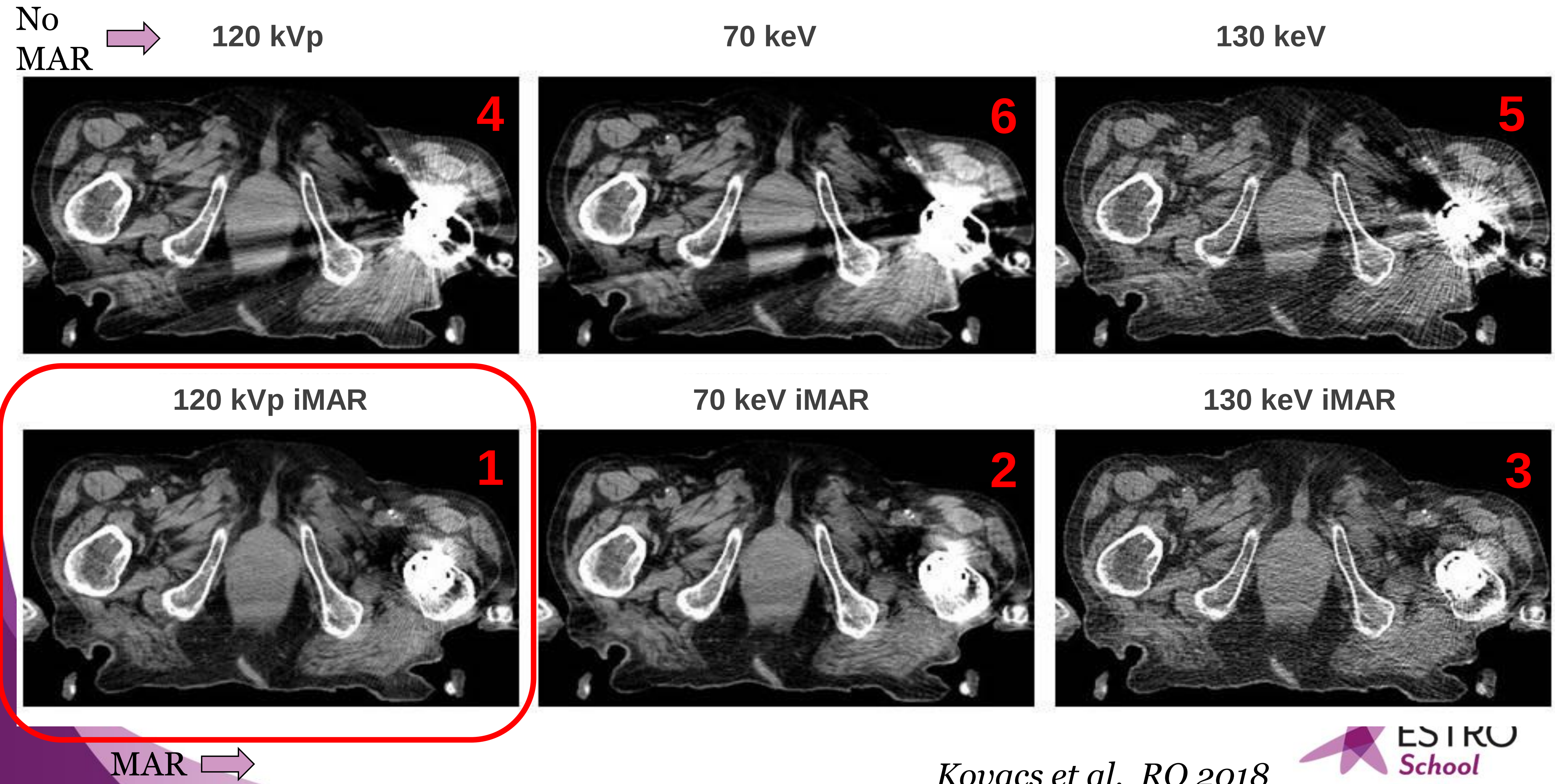
MAR combined with dual energy scan

- **Which images do radiologists & oncologists prefer?**



Kovacs et al. RO 2018

Imaging for RT planning

- Has to be precise
- Has to provide safe judgment of the extent of the disease

- CT images are base for treatment planning

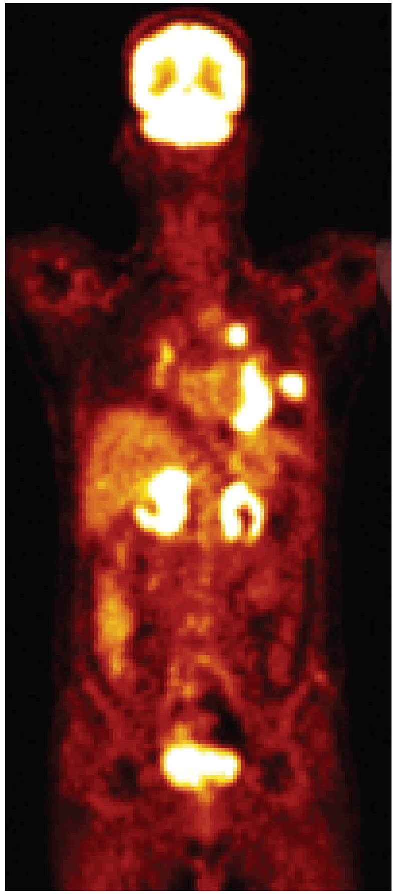
BUT

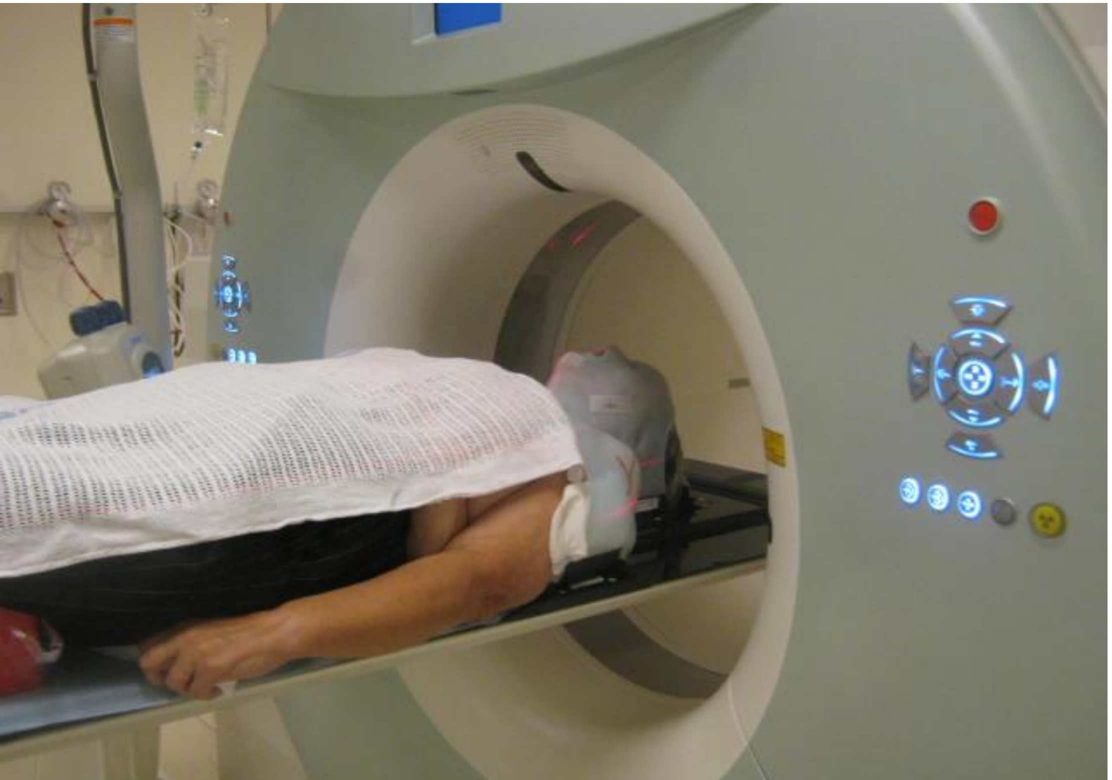
- On CT, it can be difficult to discriminate vital tumour tissue from scar tissue, oedema, atelectasis, surrounding soft tissu…

- CT can not stage correctly
    - ➢ detect small metastases
    - ➢ detect distant metastases

Added value of PET CT for radiotherapy

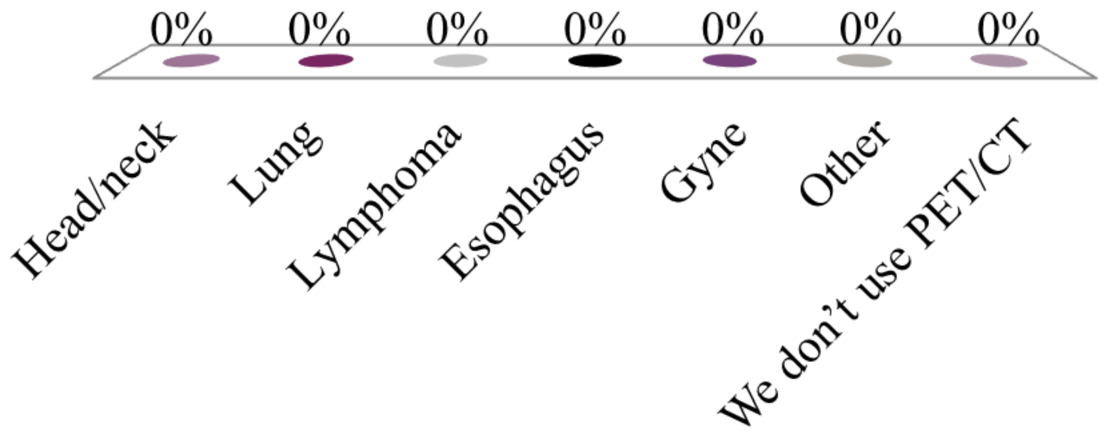
- Improved delineation consistency
- Improved staging





Which sites do you plan with PET/CT?

A. Head/neck
B. Lung
C. Lymphoma
D. Esophagus
E. Gyne
F. Other
G. We don't use PET/CT



Multiple answers possible!

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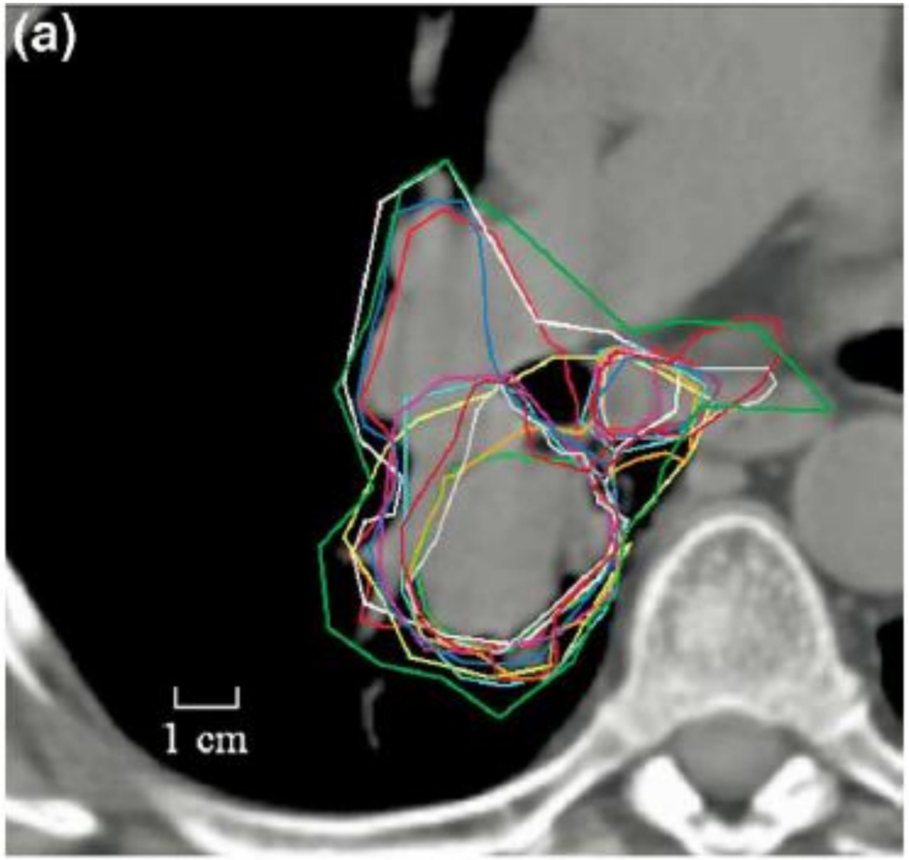
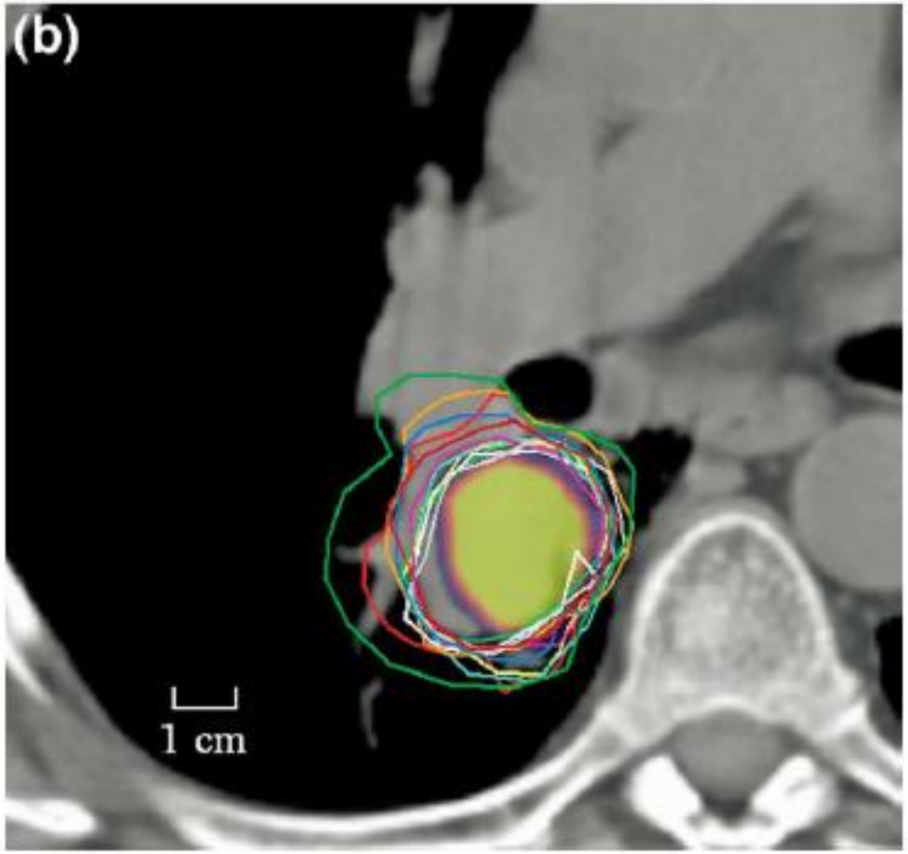
Improved delineation consistency

CT based



PET/ CT based



Steenbakkers IJROBP 2006

Impact of PET in lung cancer RT

- Change in target definition: in 2 out of 5 patients
- Change in treatment intent: in 1 out of 5 patients

Radiotherapy and Oncology 123 (2017) 71–77

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

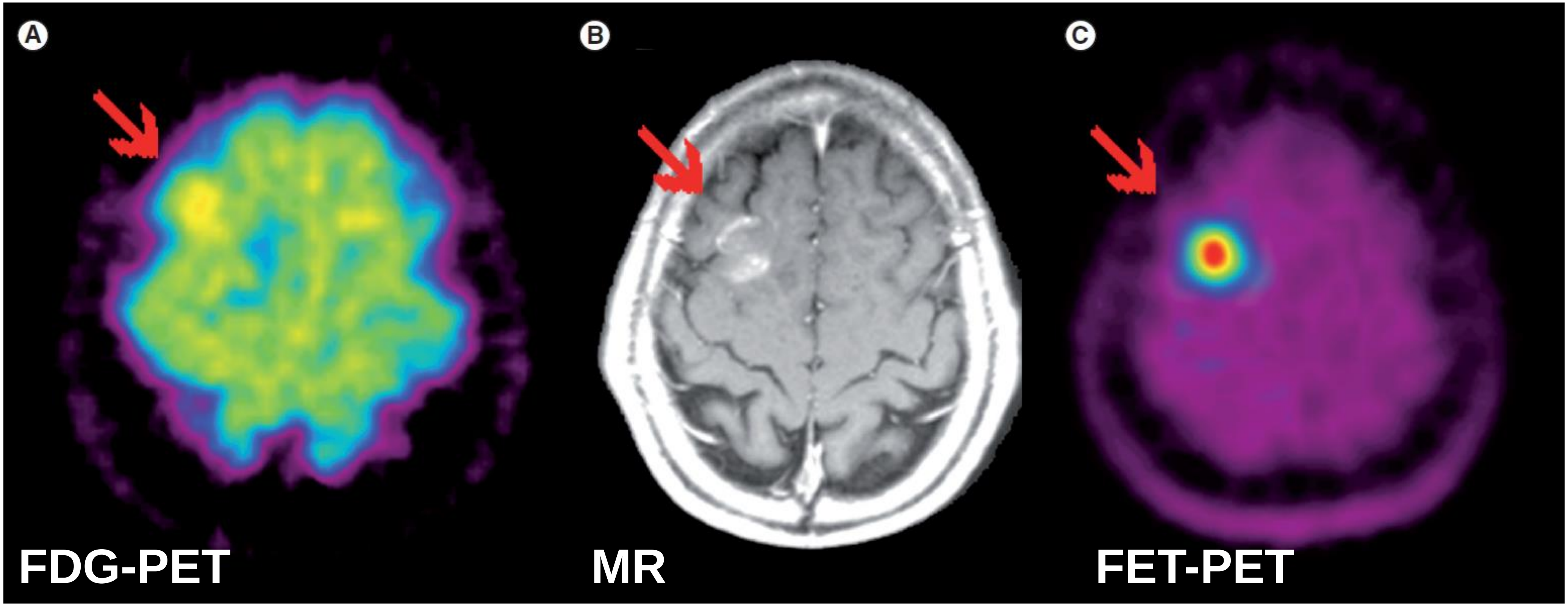
ELSEVIER

Systematic review

Positron emission tomography and computed tomographic imaging (PET/CT) for dose planning purposes of thoracic radiation with curative intent in lung cancer patients: A systematic review and meta-analysis

Andreas Hallqvist [a,*], Charlotte Alverbratt [a], Annika Strandell [b], Ola Samuelsson [b], Emil Björkander [c], Ann Liljegren [c], Per Albertsson [a]

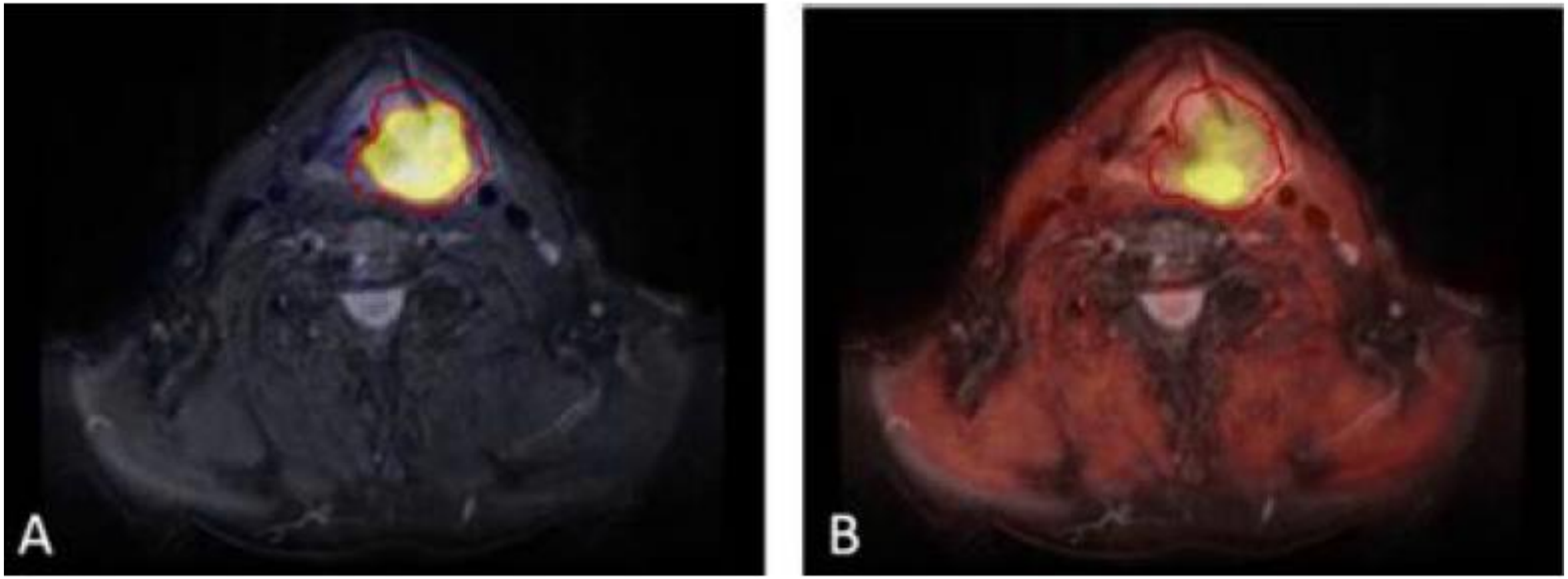
PET imaging of brain tumours



- 18F-Fluoro-Ethyl-Tyrosin (FET), aminoacid uptake

BD Kläsner et al. *Expert Rev. Anticancer Ther 2010*

PET imaging of hypoxia with FMISO

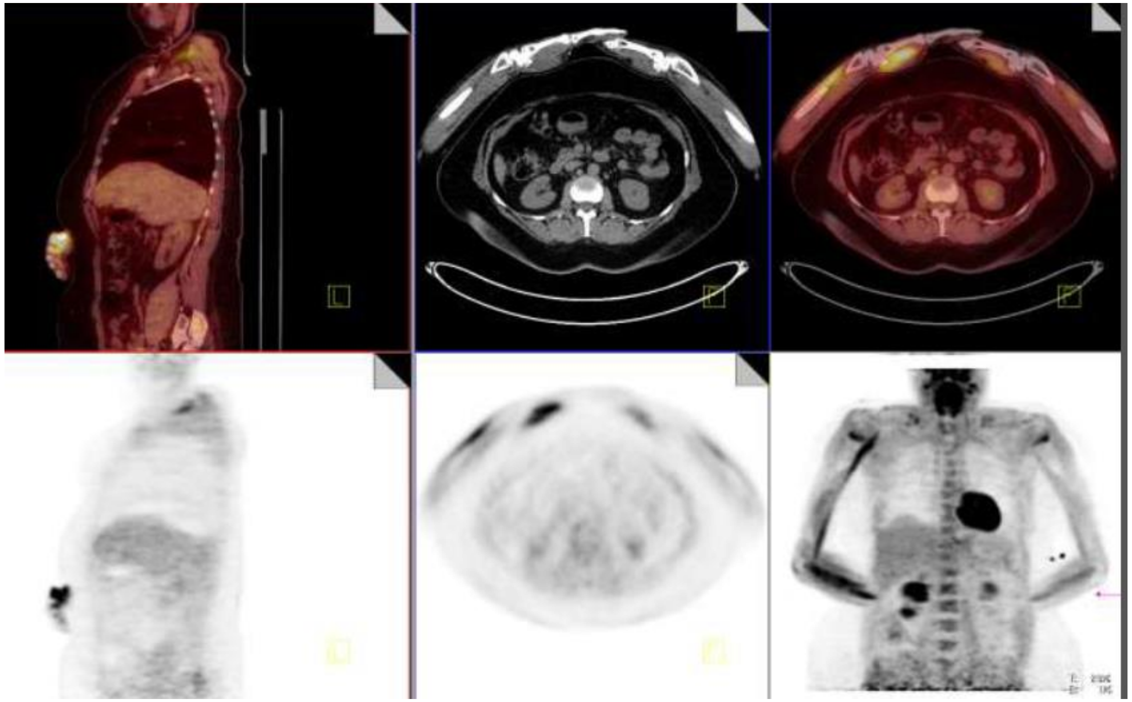


- Hypoxia area is associated with high risk of locoregional failure

Thorwarth BJR 2015

Pitfalls

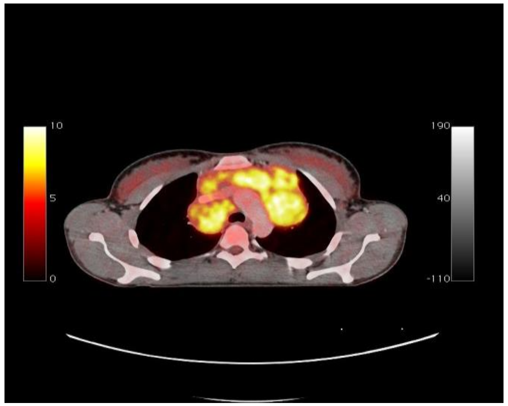
- FDG is not specific
  - ➢ Not all ”hot-spots” are malignant



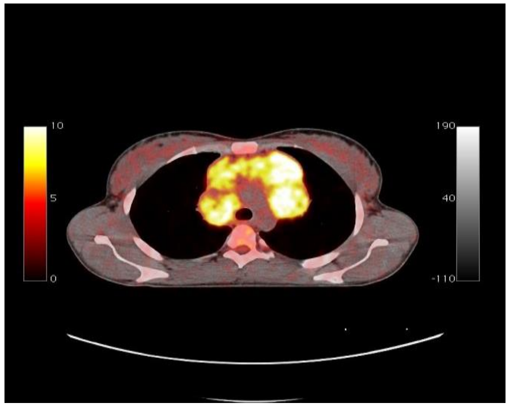
Courtesy of TL Klausen

- Motion blurs the FDG uptake
  - ➢ Is it a small lesion, with high degree of motion and high SUV uptake?
  - ➢ Is it a large lesion, without motion and low SUV uptake?

Free breathing



Breath hold



Courtesy of M Aznar

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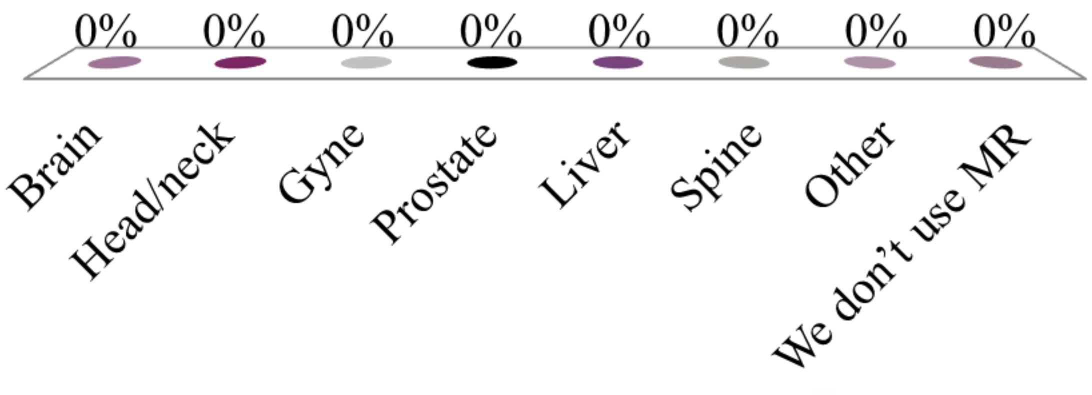
Added value of MR imaging for RT

- Superior soft tissue contrast

Which sites do you plan with MR?

A. Brain
B. Head/neck
C. Gyne
D. Prostate
E. Liver
F. Spine
G. Other
H. We don’t use MR



Multiple answers possible!

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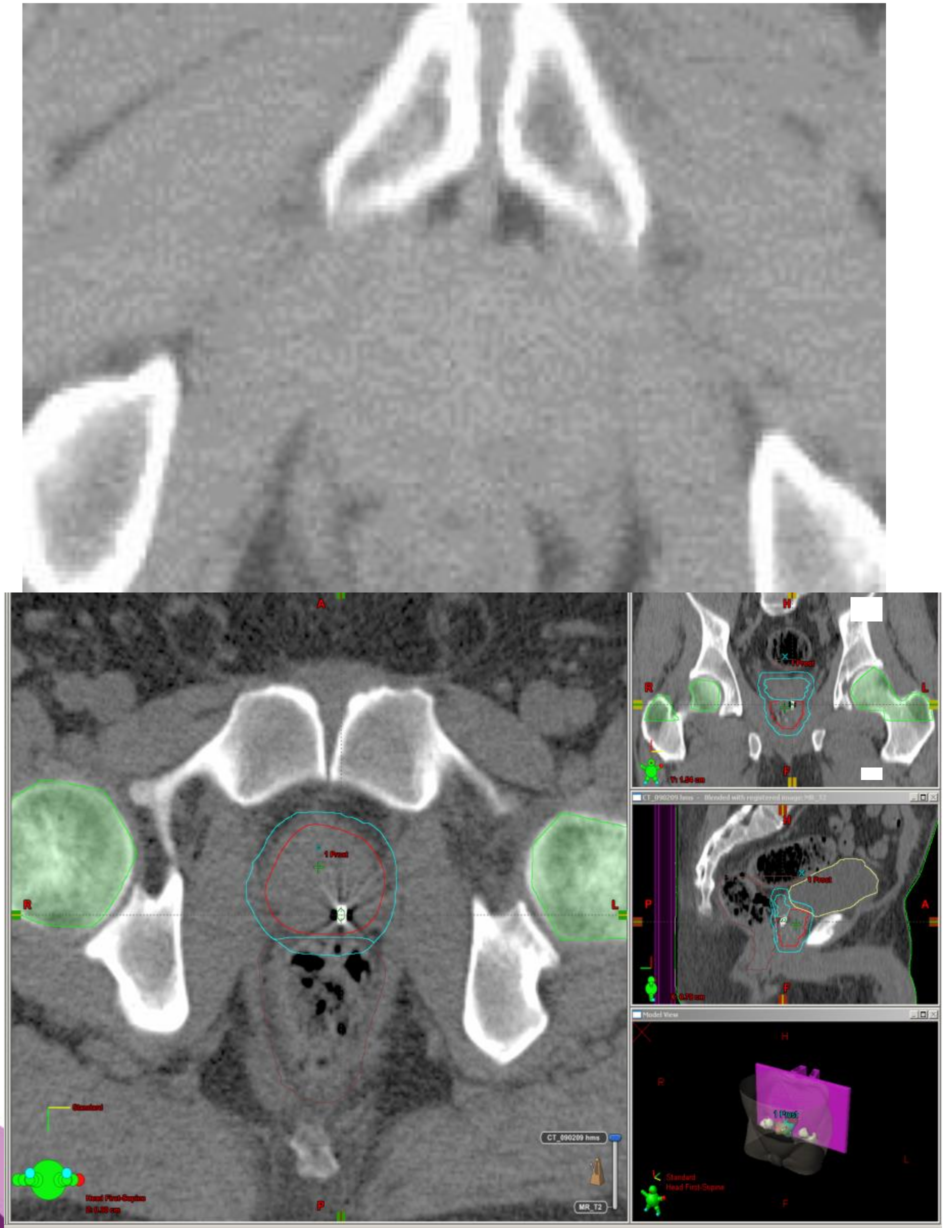
Prostate cancer

CT



MR

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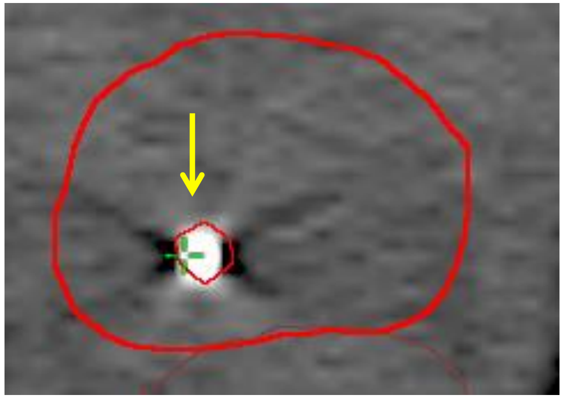
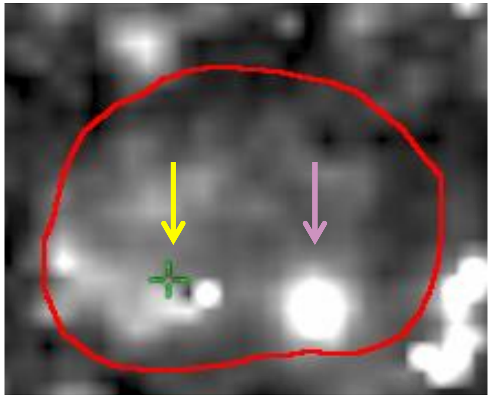
Functional imaging with MR

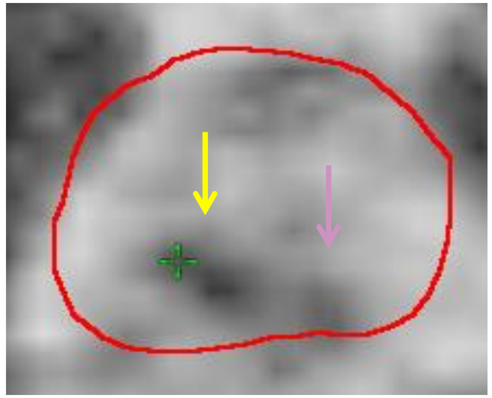


CT

T2



DCE (ktrans)



ADC

DCE = dynamic contrast enhanced
- high signal due to increase in capilar permeability

ADC = apparent diffusion coefficient
- lack of signal due to high cell density

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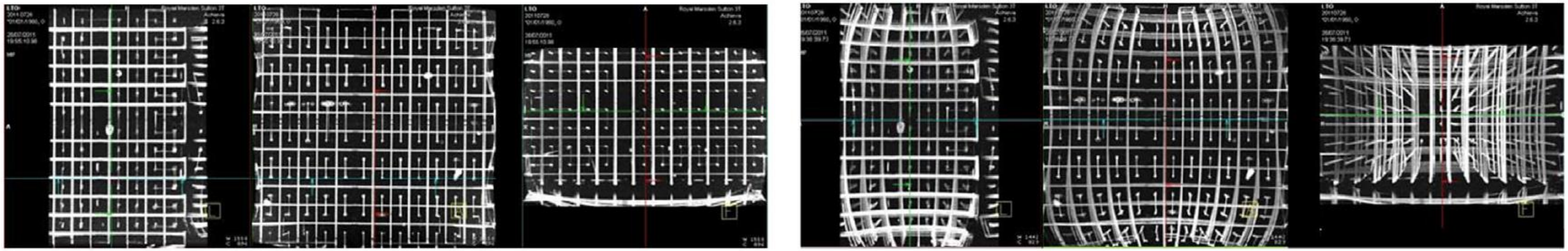
Pitfalls

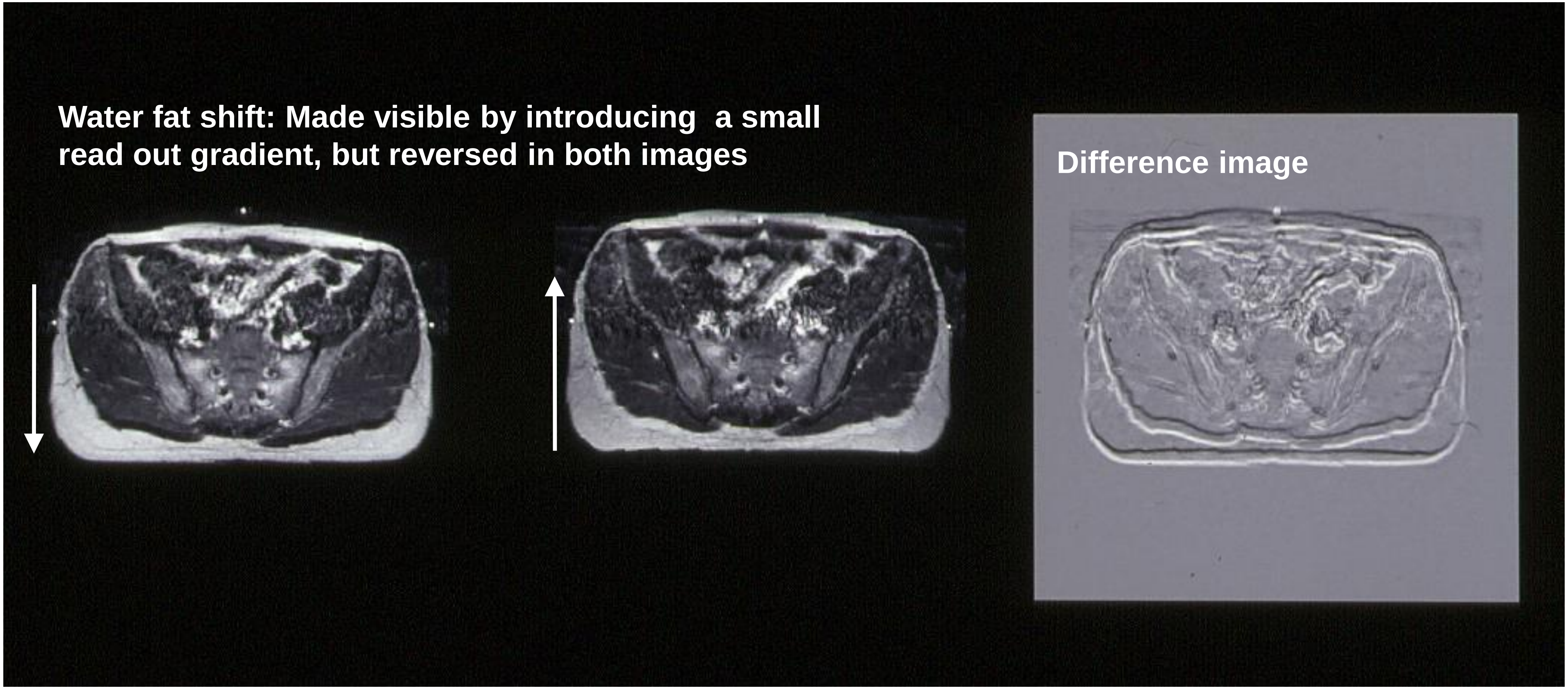
- Geometric distortion



Schmidt & Payne PMB 2015

- No direct relation with electron density
  - ➢ CT atlas corregistration
  - ➢ MR segmentation

MRI artifacts can cause invisible geometrical errors!



→ Relative position of bone and tumor geometrically incorrect

Courtesy U. van der Heide

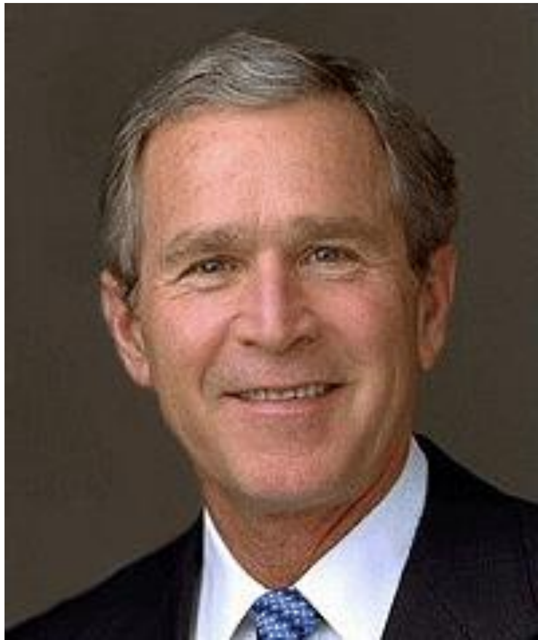
Registration

- Planning and image guidance is CT and CBCT based
- Delineation often based on MRI or PET

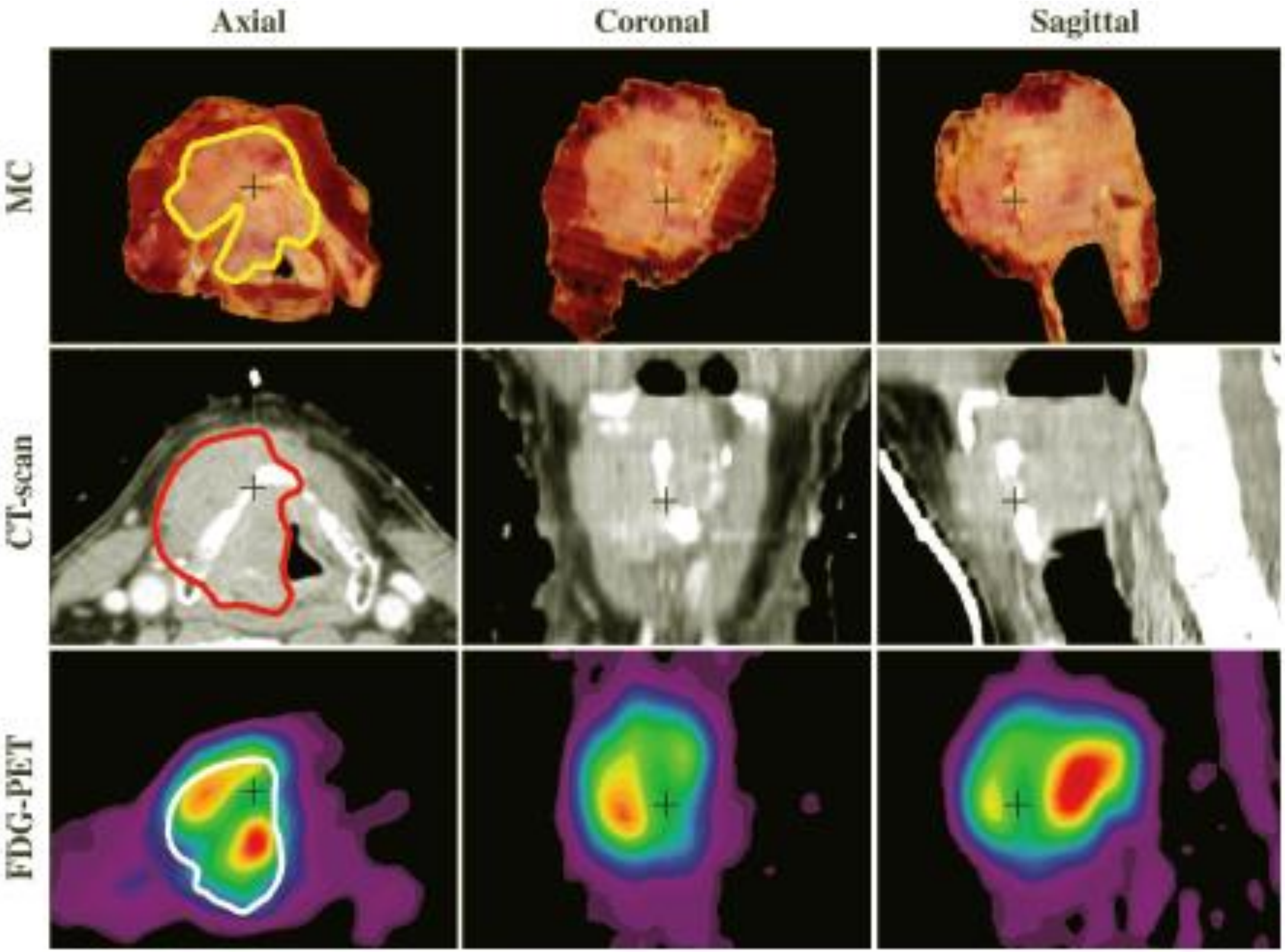
→ Registration error = Delineation error!

- Be careful with registrations – especially deformable

Anything can be deformed in anything else…
But is it true?



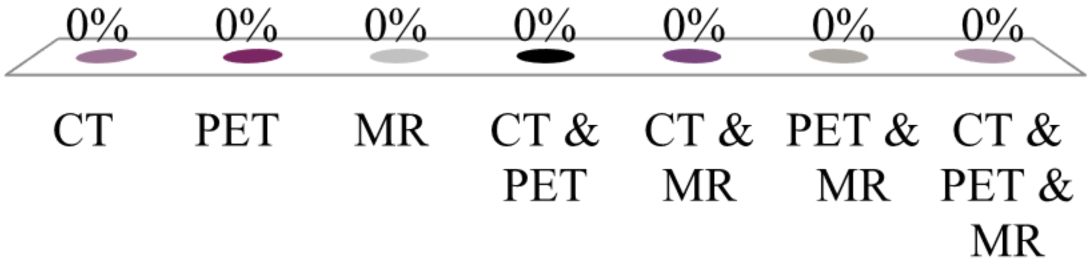
Challenge of multi modality imaging



Daisne et al. *Radiology 2004*

Which imaging modalities do we need for modern state of the art radiotherapy?

A. CT
B. PET
C. MR
D. CT & PET
E. CT & MR
F. PET & MR
G. CT & PET & MR



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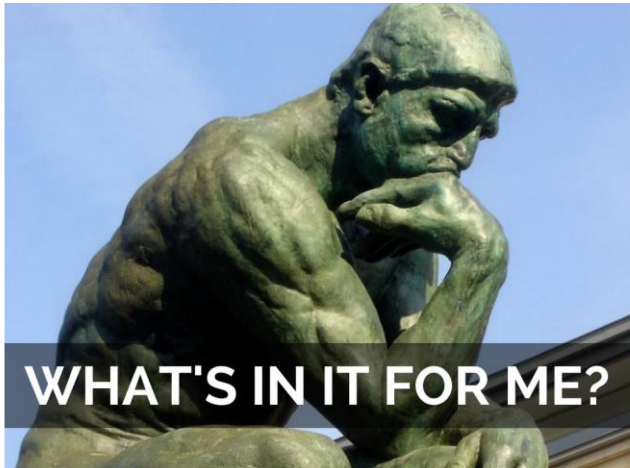
Conclusion (1)

- Illustrate the importance of a particular pre-treatment imaging modality for radiotherapy

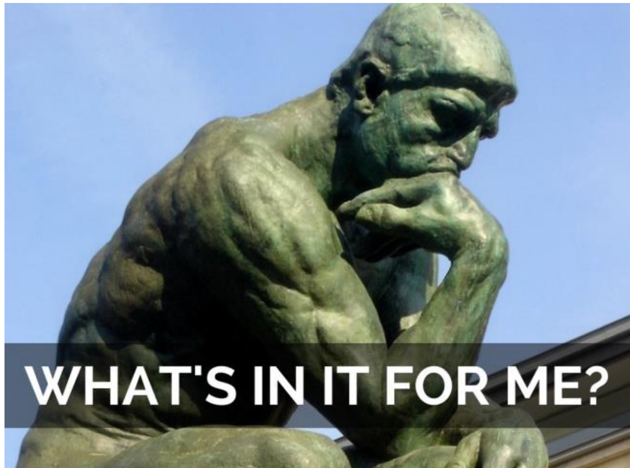
    - ➢ CT is needed for calculation of dose distribution
    - ➢ PET adds value for staging, distinguishing tracer avid areas/volumes
    - ➢ MR increased soft tissue contrast



Conclusion (2)

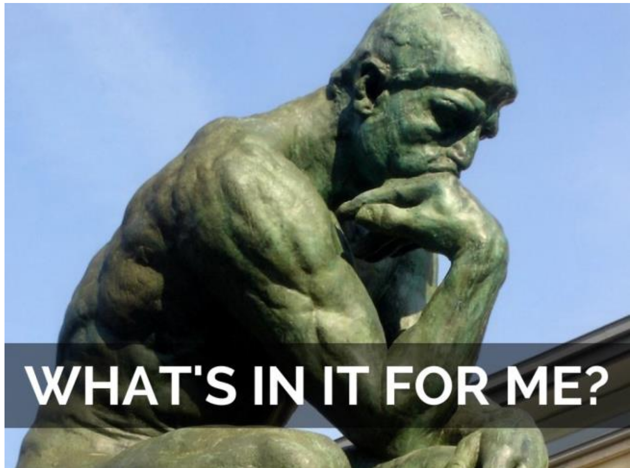
- Comprehend the additional value of applying combined information from several imaging modalities for radiotherapy planning

    - ➢ More reproducible target definition
    - ➢ More precise target definition
    - ➢ Optimal treatment strategy



Conclusion (3)

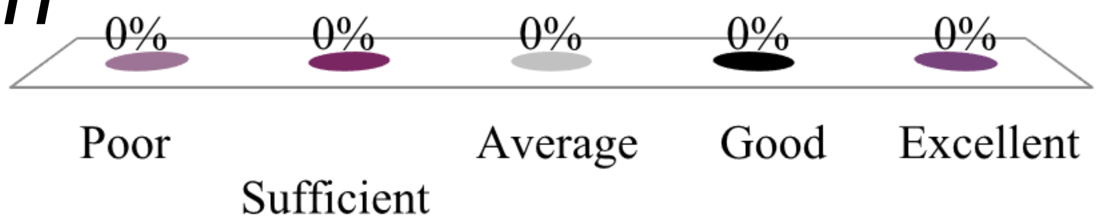
- Identify uncertainties of pre-treatment imaging modalities
  - ➢ Artefacts in images
  - ➢ Differences in (spatial) info on each modality



Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



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WWW.ESTRO.ORG/SCHOOL

TARGET VOLUME DELINEATION

ESTRO School

Sofia Rivera, MD, PhD
Radiation Oncology Department
Gustave Roussy
Villejuif, France

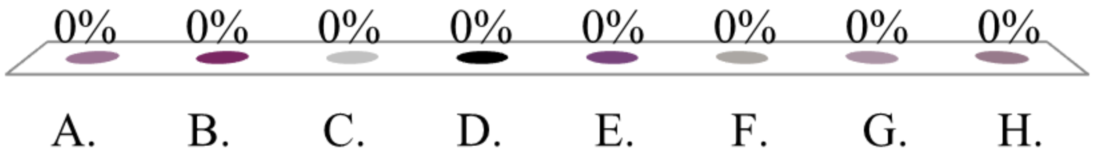
GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Advanced skills in modern radiotherapy
May 06, 2018

WWW.ESTRO.ORG/SCHOOL

What is the weakest point in our modern radiotherapy treatment chain?

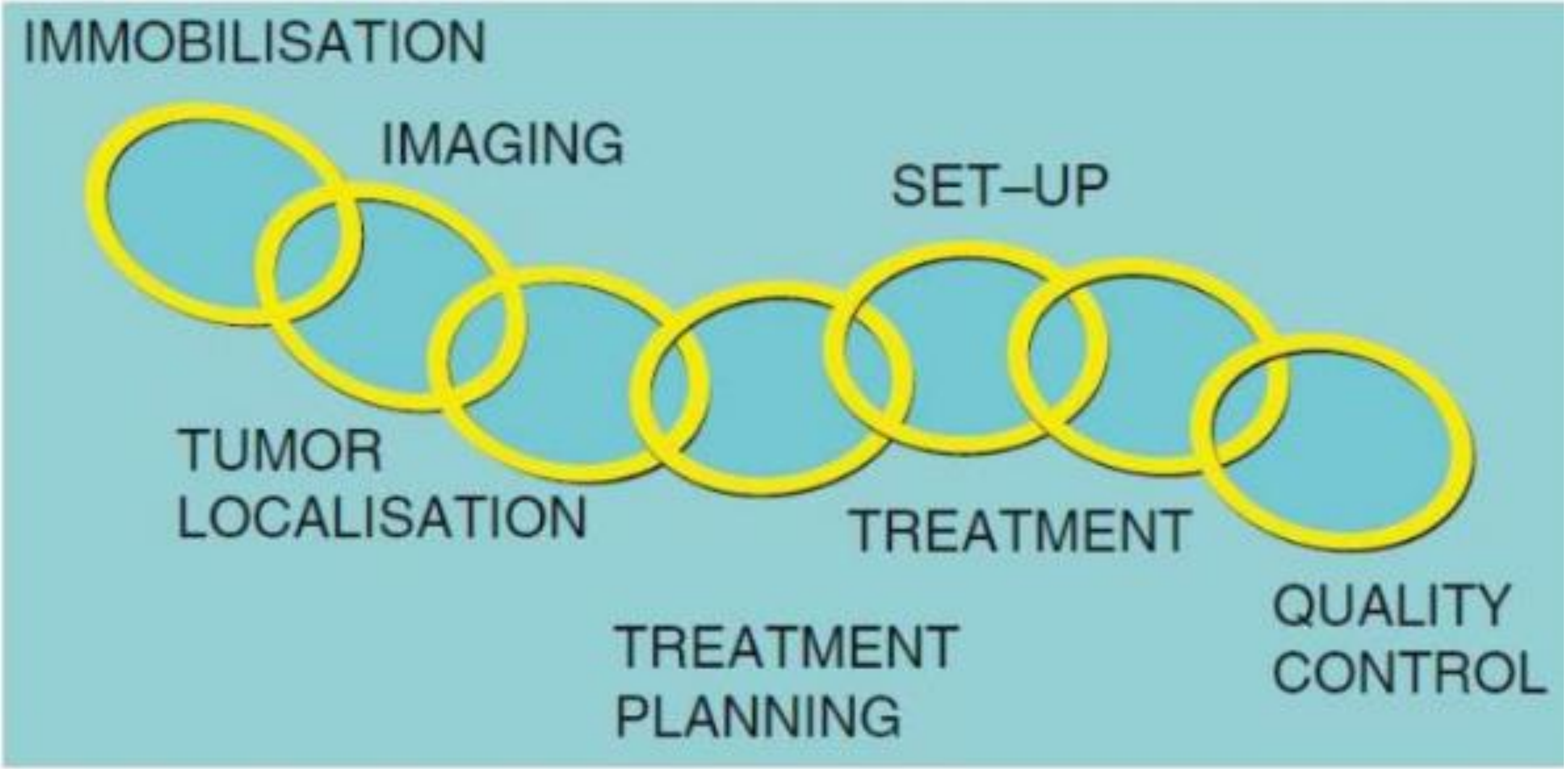
A. Dose calculation?
B. Positioning uncertainties?
C. Contouring uncertainties?
D. Quality control of the treatment machine?
E. Patient changes (weight loss, movements…)?
F. RTTs?
G. Physicists?
H. Physicians?



Learning outcomes

- Understand why heterogeneity in contouring is a major weak point in modern radiotherapy
- Discuss the challenges in contouring target volumes
- Identify skills required to delineate target volumes
- Identify tools for improving learning in delineation
- Identify adequate imaging modalities according to the target to delineate
- Discuss the impact and consequences of inaccurate delineation of target volumes

Delineation: one of the links in the treatment chain



Why is delineation important?

- Radiotherapy planning is nowadays mostly based on delineation
- Constraints for dose distribution are used
- DVH are calculated based on the contours
- Field arrangements are becoming more complex
- An error in contouring will therefore translate in a **systematic error** all along the treatment and may have consequences:
  - Jeopardizing treatment efficacy
  - Impacting treatment toxicity

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Do we need to improve?

NIH Public Access
Author Manuscript
Radiother Oncol. Author manuscript; available in PMC 2013 June 27.

Published in final edited form as:
Radiother Oncol. 2012 April ; 103(1): 92–98. doi:10.1016/j.radonc.2012.02.010.

Heterogeneity in head and neck IMRT target design and clinical practice

Theodore S. Hong[a], Wolfgang A. Tomé[b,c,d], and Paul M. Harari[b,*]

Abstract

Purpose—To assess patterns of H&N IMRT practice with particular emphasis on elective target delineation.

Materials and methods—Twenty institutions with established H&N IMRT expertise were solicited to design clinical target volumes for the identical H&N cancer case. To limit contouring variability, a primary tonsil GTV and ipsilateral level II node were pre-contoured. Participants were asked to accept this GTV, and contour their recommended CTV and PTV. Dose prescriptions, contouring time, and recommendations regarding chemotherapy were solicited.

Results—All 20 institutions responded. Remarkable heterogeneity in H&N IMRT design and practice was identified. Seventeen of 20 centers recommended treatment of bilateral necks whereas 3/20 recommended treatment of the ipsilateral neck only. The average CTV volume was 250 cm^3 (range 37–676 cm^3). Although there was high concordance in coverage of ipsilateral neck levels II and III, substantial variation was identified for levels I, V, and the contralateral neck. Average CTV expansion was 4.1 mm (range 0–15 mm). Eight of 20 centers recommended chemotherapy (cisplatin), whereas 12/20 recommended radiation alone. Responders prescribed on average 69 and 68 Gy to the tumor and metastatic node GTV, respectively. Average H&N target volume contouring time was 102.5 min (range 60–210 min).

Conclusion—This study identifies substantial heterogeneity in H&N IMRT target definition, prescription, neck treatment, and use of chemotherapy among practitioners with established H&N IMRT expertise. These data suggest that continued efforts to standardize and simplify the H&N IMRT process are desirable for the safe and effective global advancement of H&N IMRT practice.

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How can we answer that need ?

- Adequate imaging, training and use of contouring guidelines are the main strategies to minimize delineation uncertainties (Petrič et al 2013)

- Establishing and using consensus and guidelines have shown to reduce heterogeneity in contouring

Table III. Mean and ranges of DSC before and after consensus.

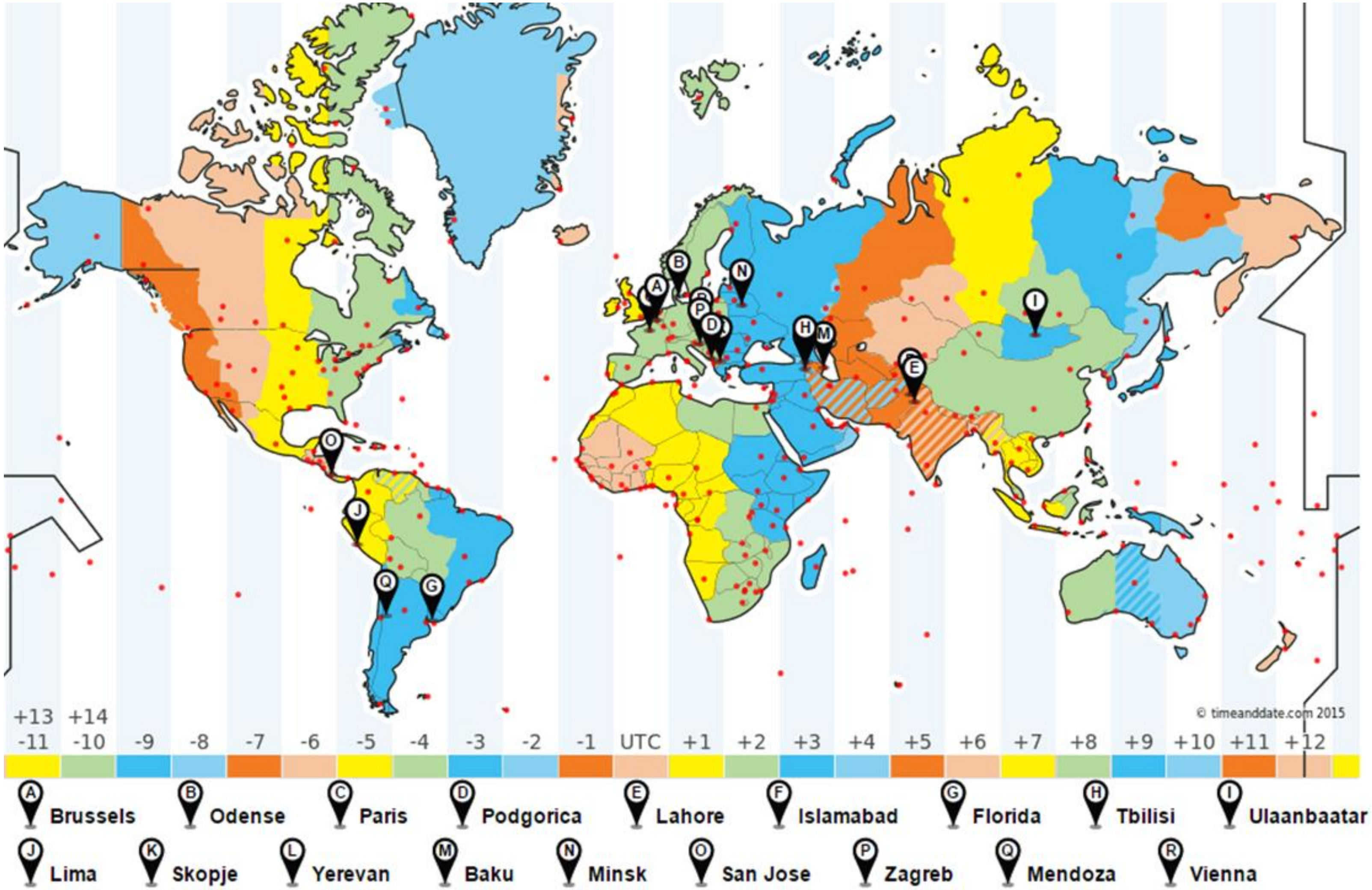
Volume	Consensus volume (ml)	Mean DSC (range) Before consensus	Mean DSC (range) After consensus
Breast	1247	0.93 (0.89–0.96)	0.95 (0.93–0.96)
Boost	40	NA	0.75 (0.60–0.89)
Internal mammary LN	15	0.59 (0.32–0.72)	0.71 (0.63–0.81)
Axillary LN level I	108	0.65 (0.59–0.75)	0.70 (0.60–0.77)
Axillary LN level II	32	0.56 (0.35–0.69)	0.76 (0.67–0.84)
Axillary LN level III	17	0.56 (0.39–0.73)	0.74 (0.66–0.82)
Periclavicular LN	47	0.41 (0.34–0.56)	0.56 (0.43–0.73)
Interpectoral LN	33	0.54 (NA)	0.66 (0.55–0.78)
Heart	731	0.91 (0.88–0.94)	0.94 (0.90–0.96)

DSC, Dice similarity coefficient; NA, not available.

NIELSEN et al 2013

Participants in the FALCON-IAEA study

14 centers from 13 countries that recently shifted from 2D to 3D

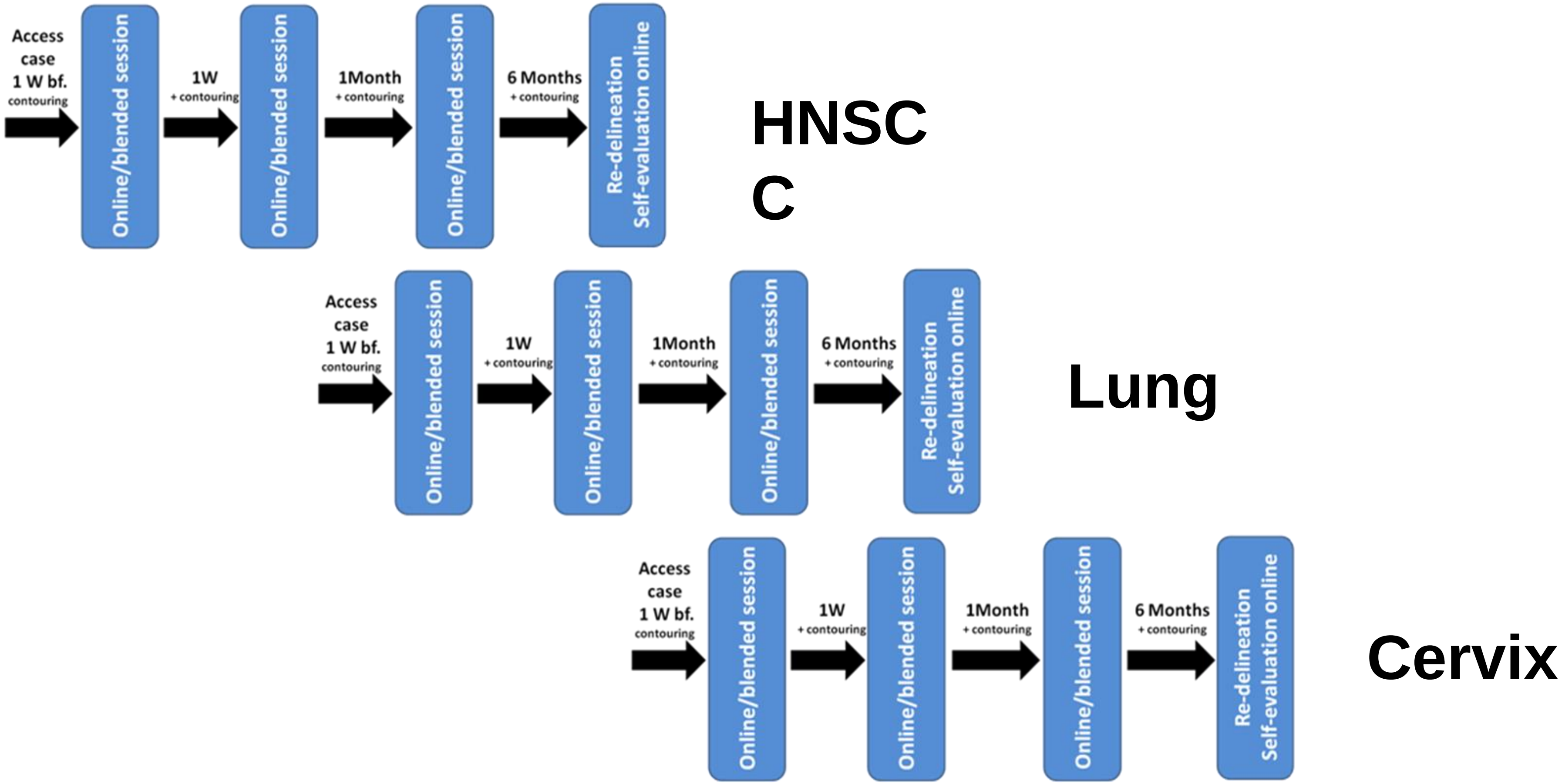


FALCON

IAEA International Atomic Energy Agency *Atoms for Peace*

ESTRO *School*

Structure of the FALCON-IAEA study



Participants characteristics

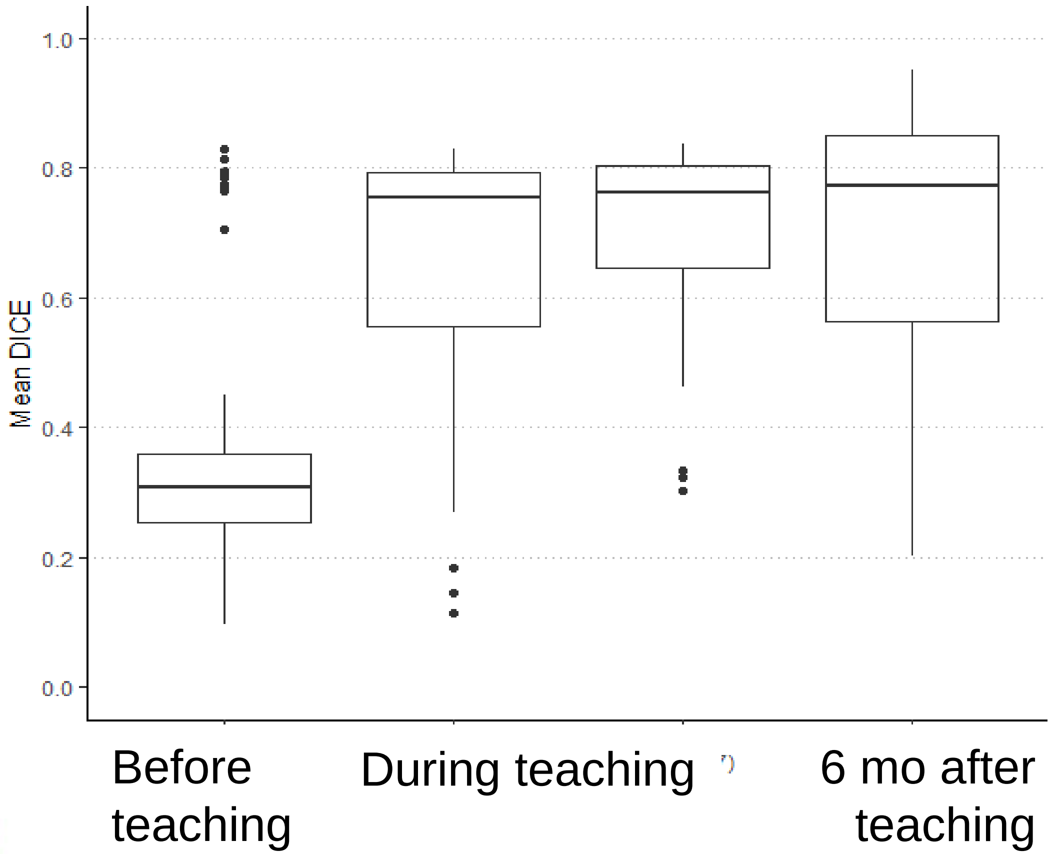
- 60 physicians were invited
- 57 joined and delineated

Characteristic	Frequency
Female	**39/57 (68%)**
Public hospitals	**45/57 (80%)**
Qualified specialist	**44/57 (77%)**
Rutinely use 3D confomal RT	**50/57 (88%)**
Use IV contrast	**34/57 (60%)**
Image fusion	**35/57 (61%)**
Use intl. guidelines/atlas	**52/57 (91%)**
Regular peer-review	**26/57 (46%)**
Confident radiology	**39/57 (68%)**
Confident contouring	**51/57 (89%)**

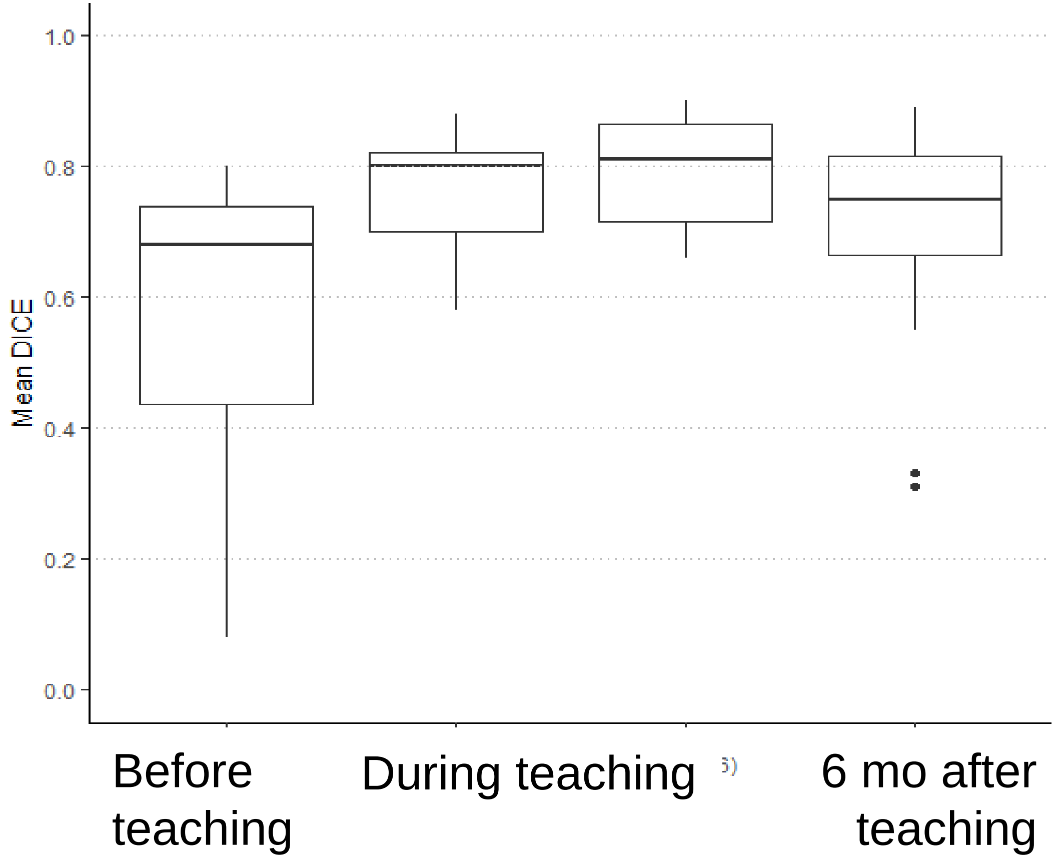
FALCON IAEA International Atomic Energy Agency *Atoms for Peace* ESTRO School

Increased homogeneitey to reference contour – also 6 months after teaching

Level II-IV, Neck



CTV-T, Cervical cancer



FALCON IAEA International Atomic Energy Agency *Atoms for Peace* ESTRO School

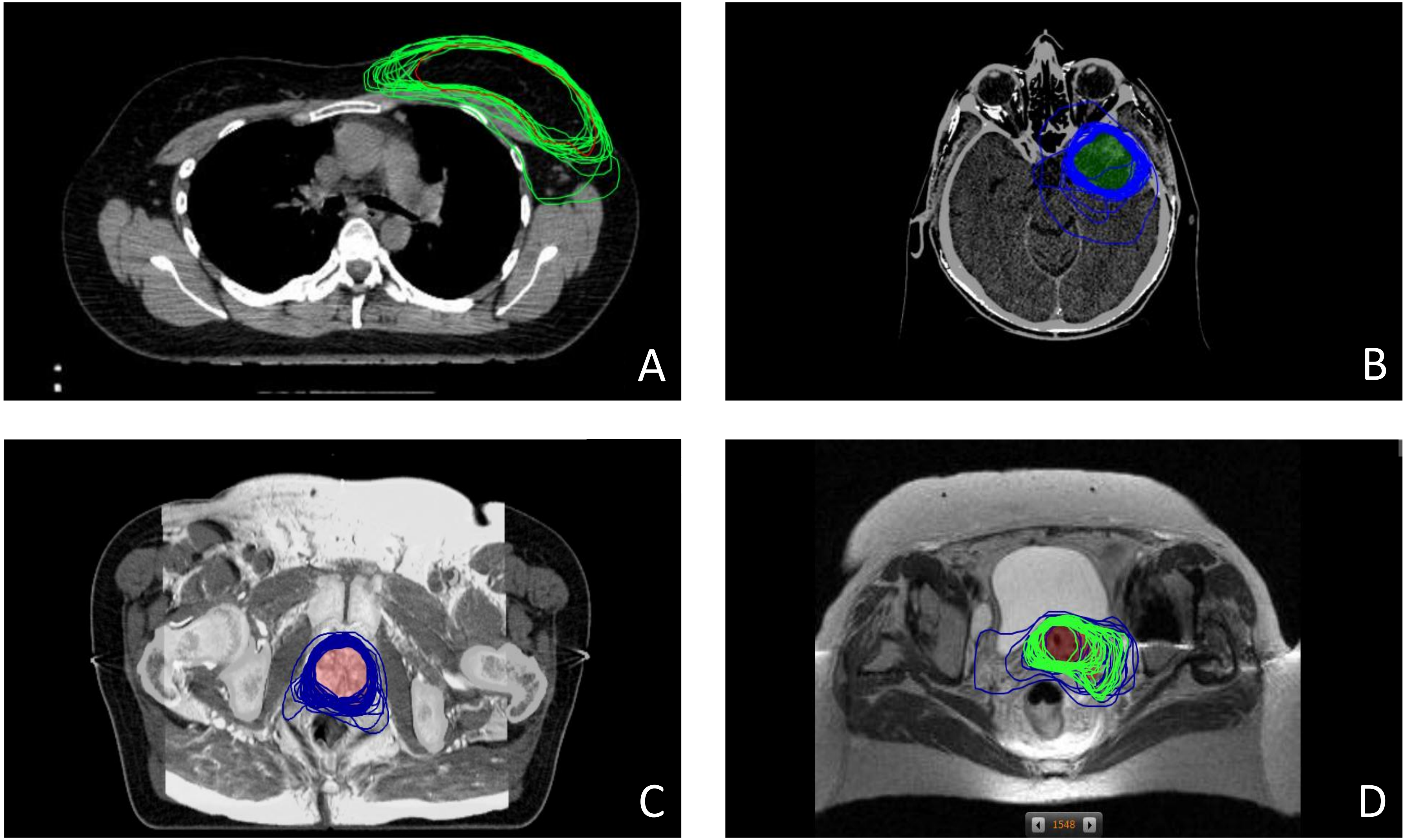
Did you know before this course that ESTRO provides a platform for hands on exercises on contouring?

A. YES

B. NO

Inter-observer variability in contouring

Examples of participant contours from ESTRO FALCON workshops.
A: CTV breast, B: GTV Brain tumour, C: CTV prostate and D: GTV cervix cancer



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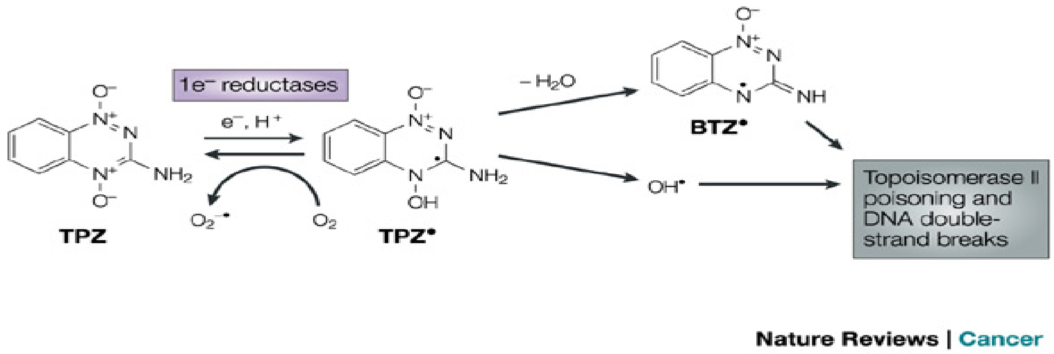
Does heterogeneity in RT matters?

- Bioreductive agent
- Radiosensitizer in hypoxia



Multicentric international
Randomized phase III
853 locally advanced
H&N patients

RT + CDDP

RT + CDDP
+ Tyrapazamine

Hypoxia radioresistance

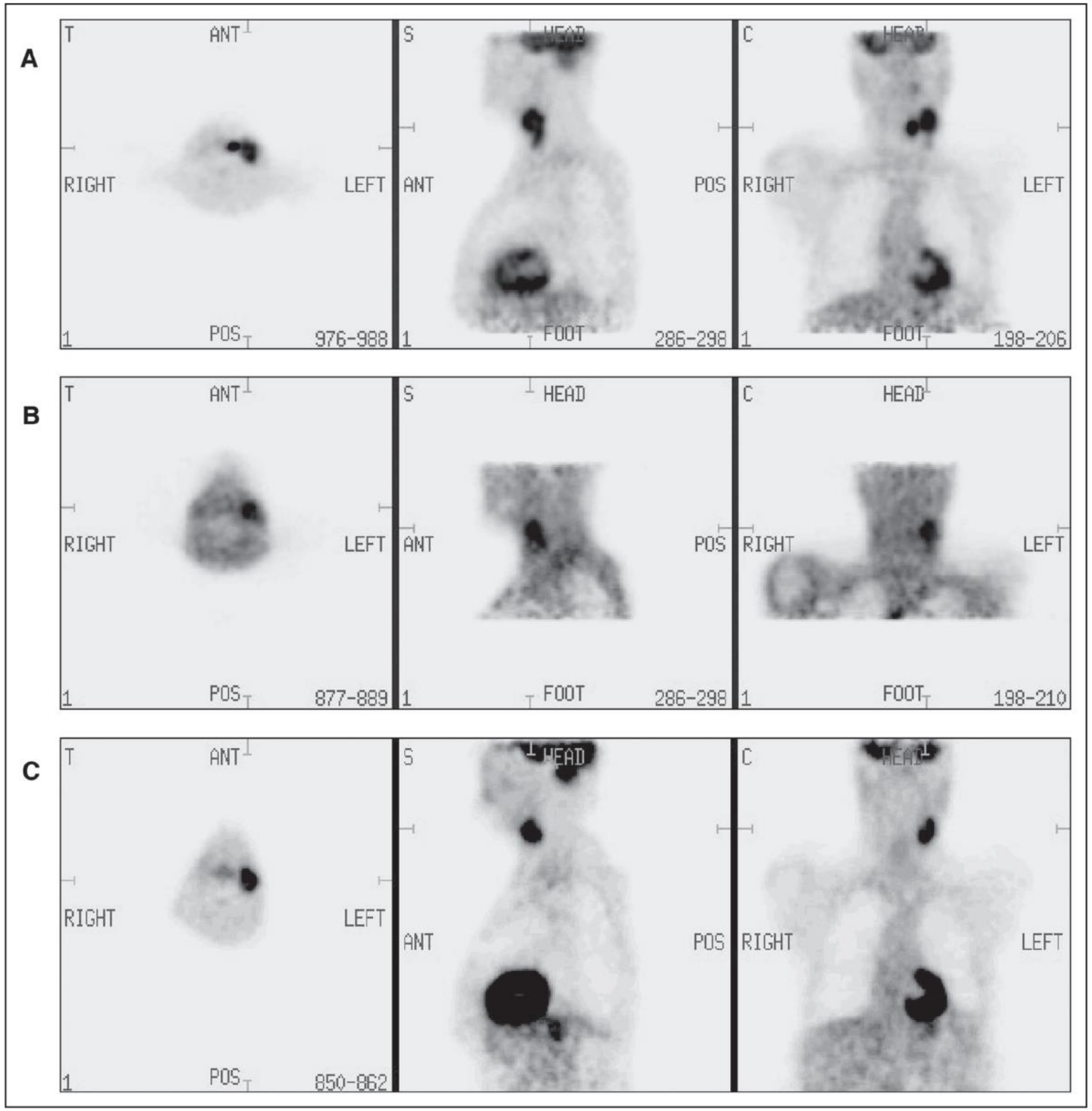
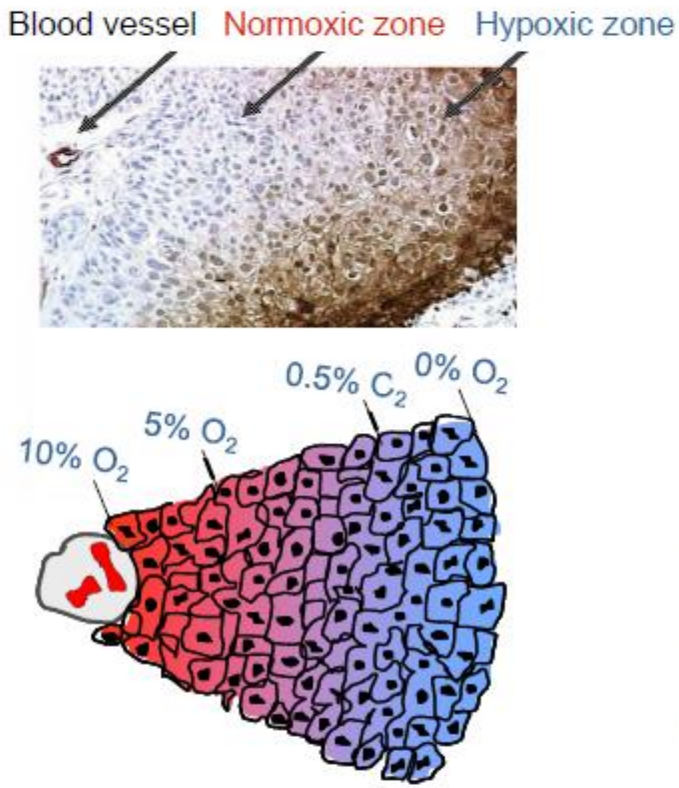


Fig 1. (A) Baseline [^{18}F]-fluorodeoxyglucose (FDG) positron emission tomography (PET) of patient with T2N2b squamous cell carcinoma of the pyriform fossa with left nodal mass. (B) [^{18}F]-fluoromisonidazole (FMISO) -PET at baseline, nonhypoxic primary tumor, and hypoxic node. (C) FDG-PET 12 weeks after chemoboost, complete response in nonhypoxic primary tumor, and poor response in hypoxic node. Residual tumor in nodal mass was confirmed pathologically after neck dissection.



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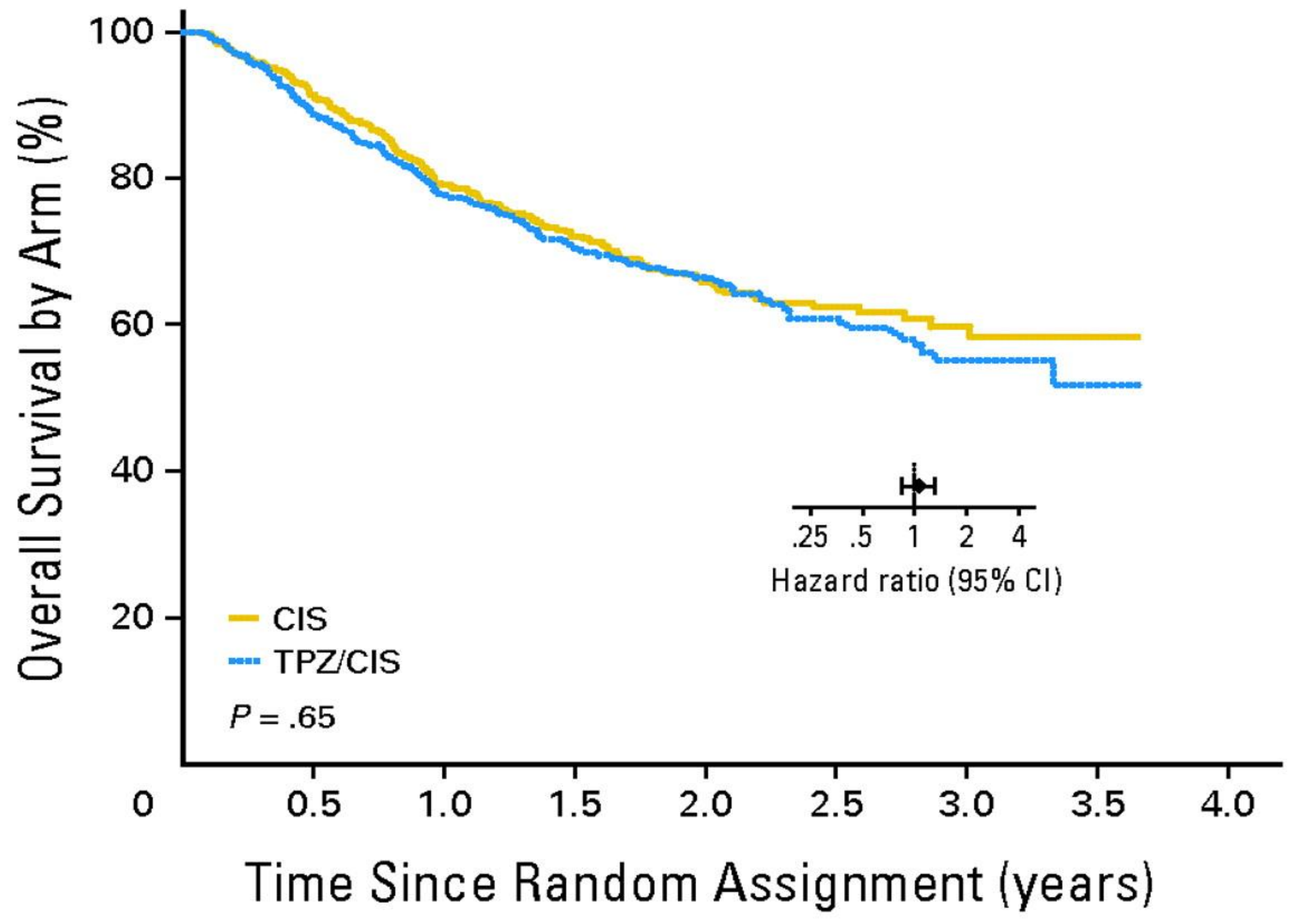
No benefit in overall survival



No. at risk									
CIS	428	389	332	294	248	91	45	6	0
TPZ/CIS	425	374	326	291	252	98	42	7	0

Rischin D et al. JCO 2010;28:2989-2995

JOURNAL OF CLINICAL ONCOLOGY

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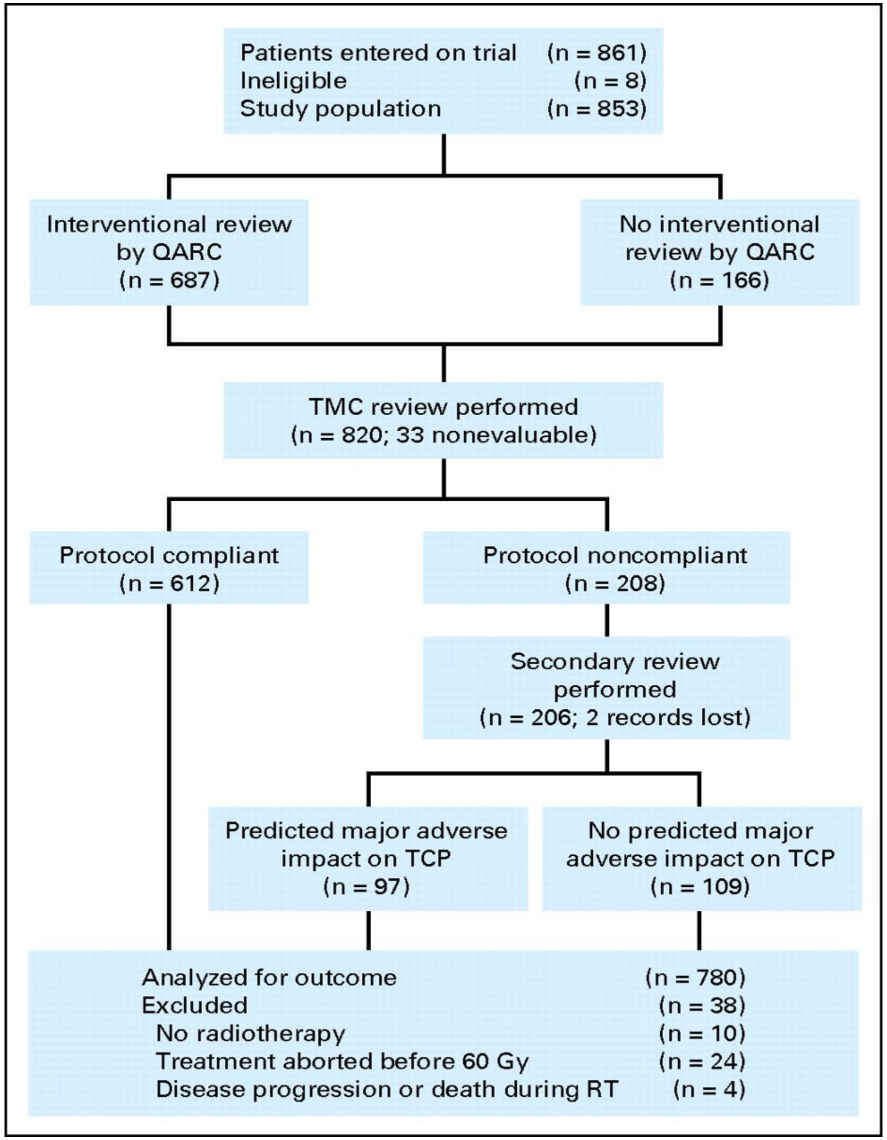
But… Trial quality control



Peters L J et al. JCO 2010;28:2996-3001

JOURNAL OF CLINICAL ONCOLOGY

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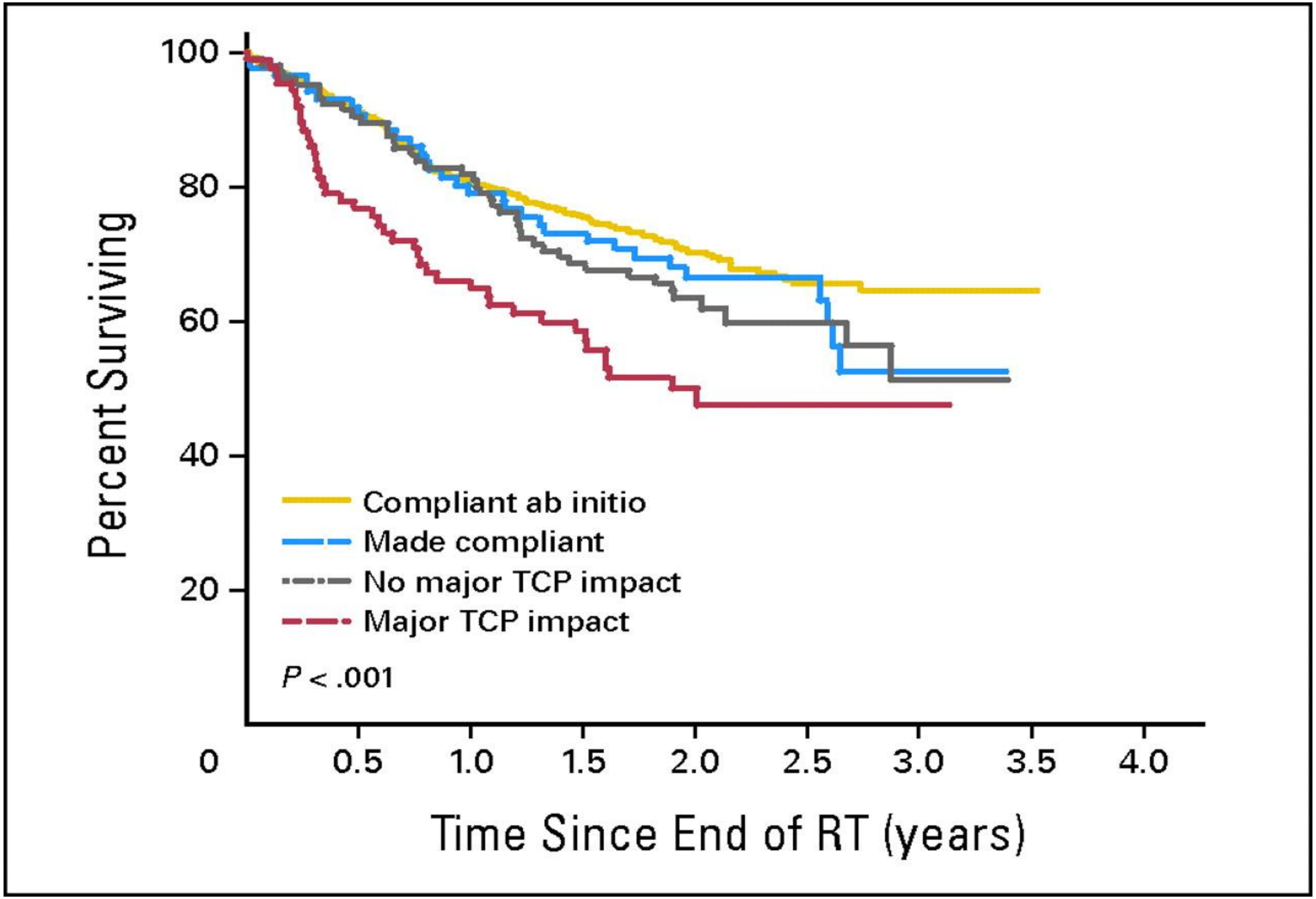
Impact of radiotherapy quality



Peters L J et al. JCO 2010;28:2996-3001

JOURNAL OF CLINICAL ONCOLOGY

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How to improve?

- Need for a common language: ICRU
- Need for delineation guidelines and anatomical knowledge
- No absolute truth so need to specify according to which guidelines we contour
- Heterogeneity in understanding/interpreting the guidelines
- Need for teaching in contouring
- Need for evaluation in contouring

ICRU Guidelines (ICRU50): volume definition

- Volumes defined prior/ during treatment planning:
  - ➢ Gross Tumor Volume (GTV)
  - ➢ Clinical Target Volume (CTV)
  - ➢ Planning Target Volume (PTV)

  - ➢ Organs At Risk (OAR)

  - ➢ Treated Volume
  - ➢ Irradiated Volume

- Volumes might be redefined during treatment for adaptive RT

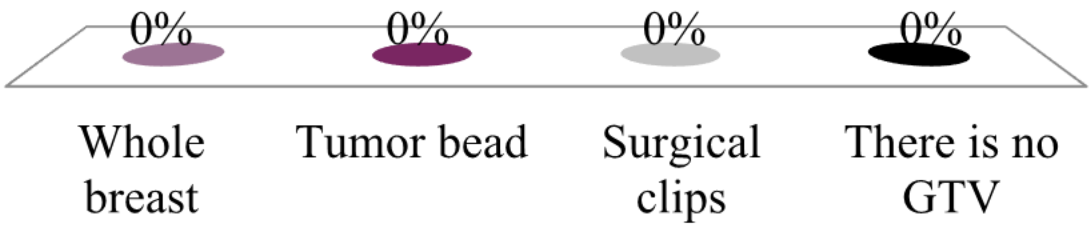
Tumor Gross Volume: GTV

- Macroscopic tumor volume visible or palpable

- Includes:
  - Primary tumor
  - Macroscopically involved lymph nodes
  - Metastases

What is your GTV when the tumor has been removed surgically like in a lumpectomy for breast cancer?

A. Whole breast
B. Tumor bead
C. Surgical clips
D. There is no GTV



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Tumor Gross Volume: GTV

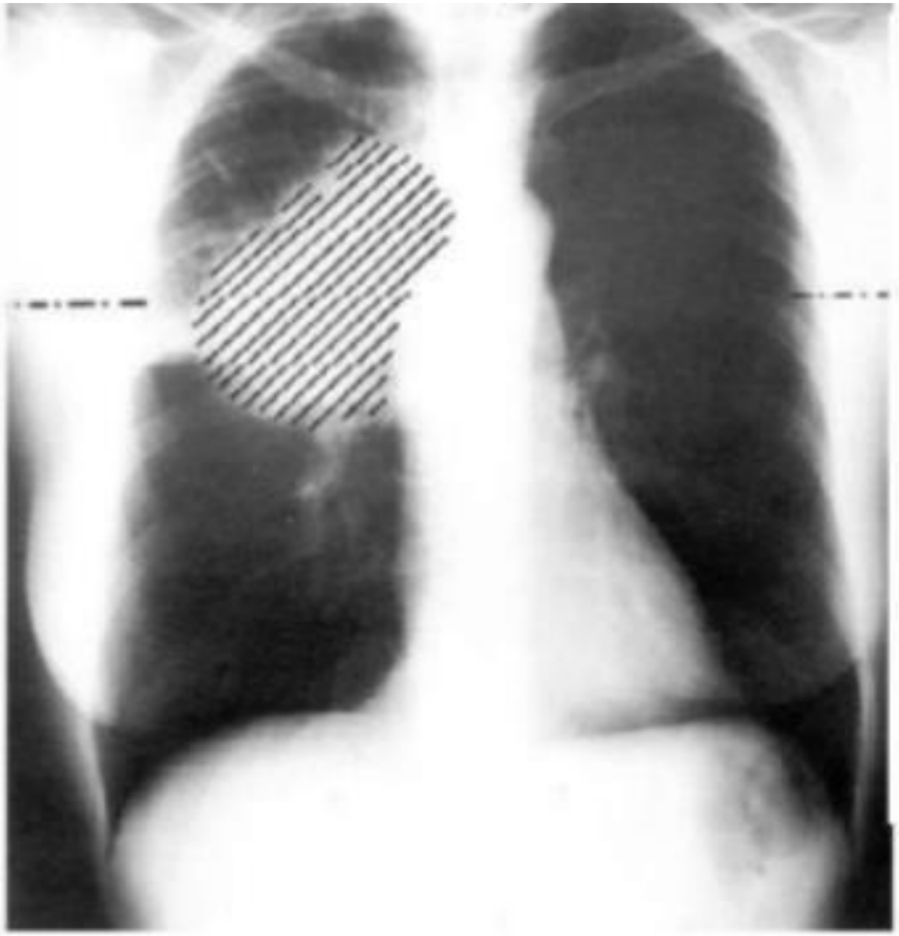
- GTV is defined based on clinical data (inspection, palpation) and imaging (CT, MR, US, PET depending on it's relevance for the tumor site)

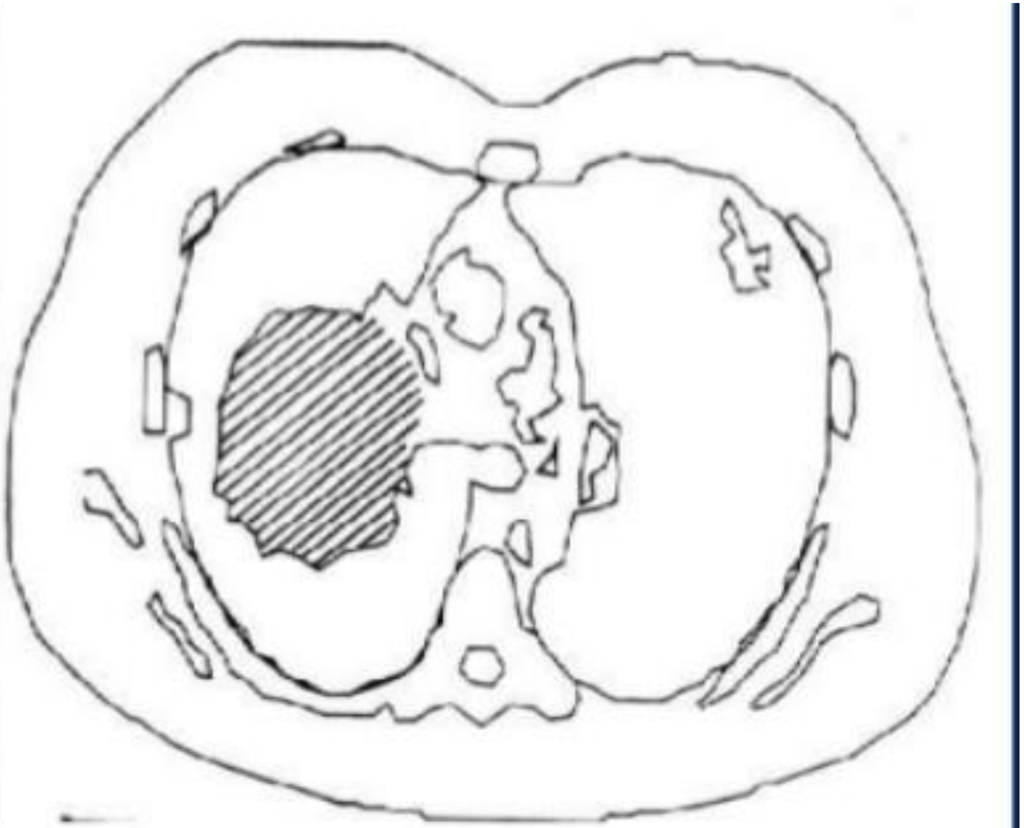
- Definition of the GTV allows for TNM classification of the disease

- Definition of the GTV allows for tumor response assessment

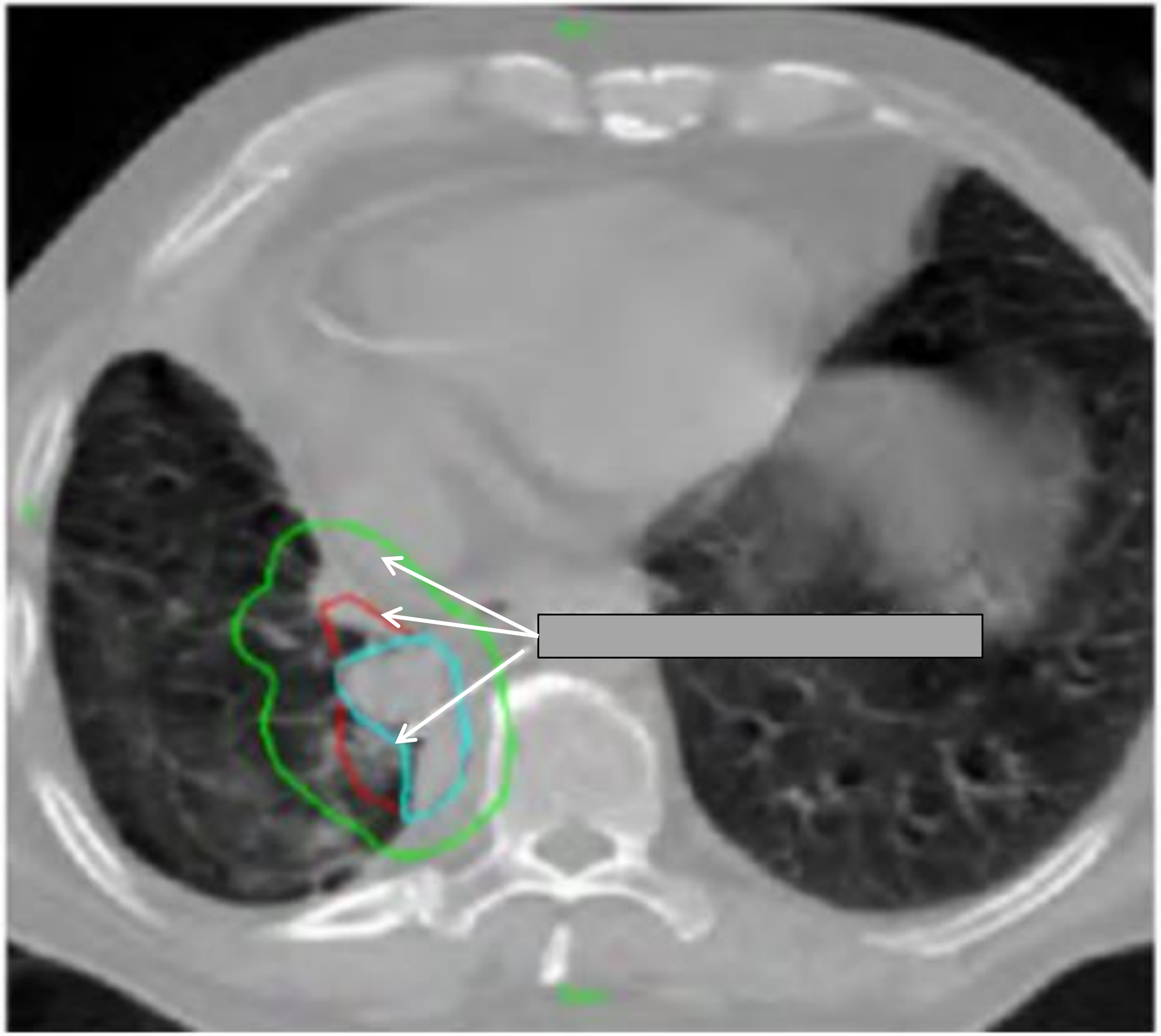
- Adequate dose to GTV is therefore crucial for tumor control

Tumor Gross Volume: GTV





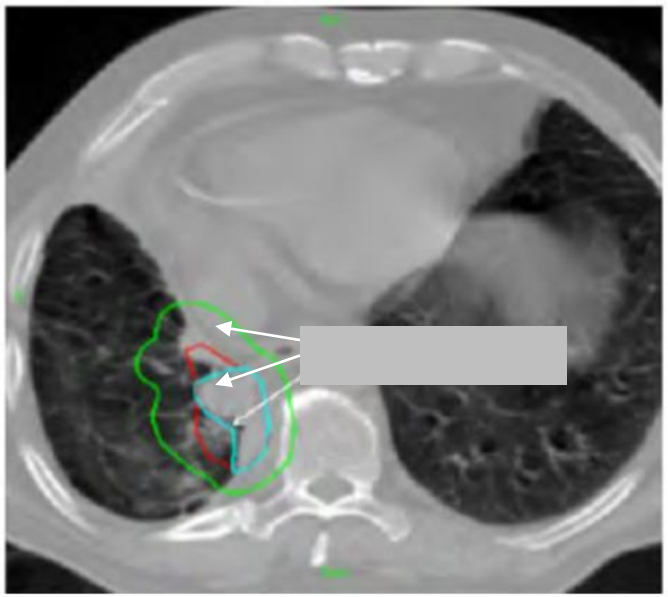
Which contour is the GTV?



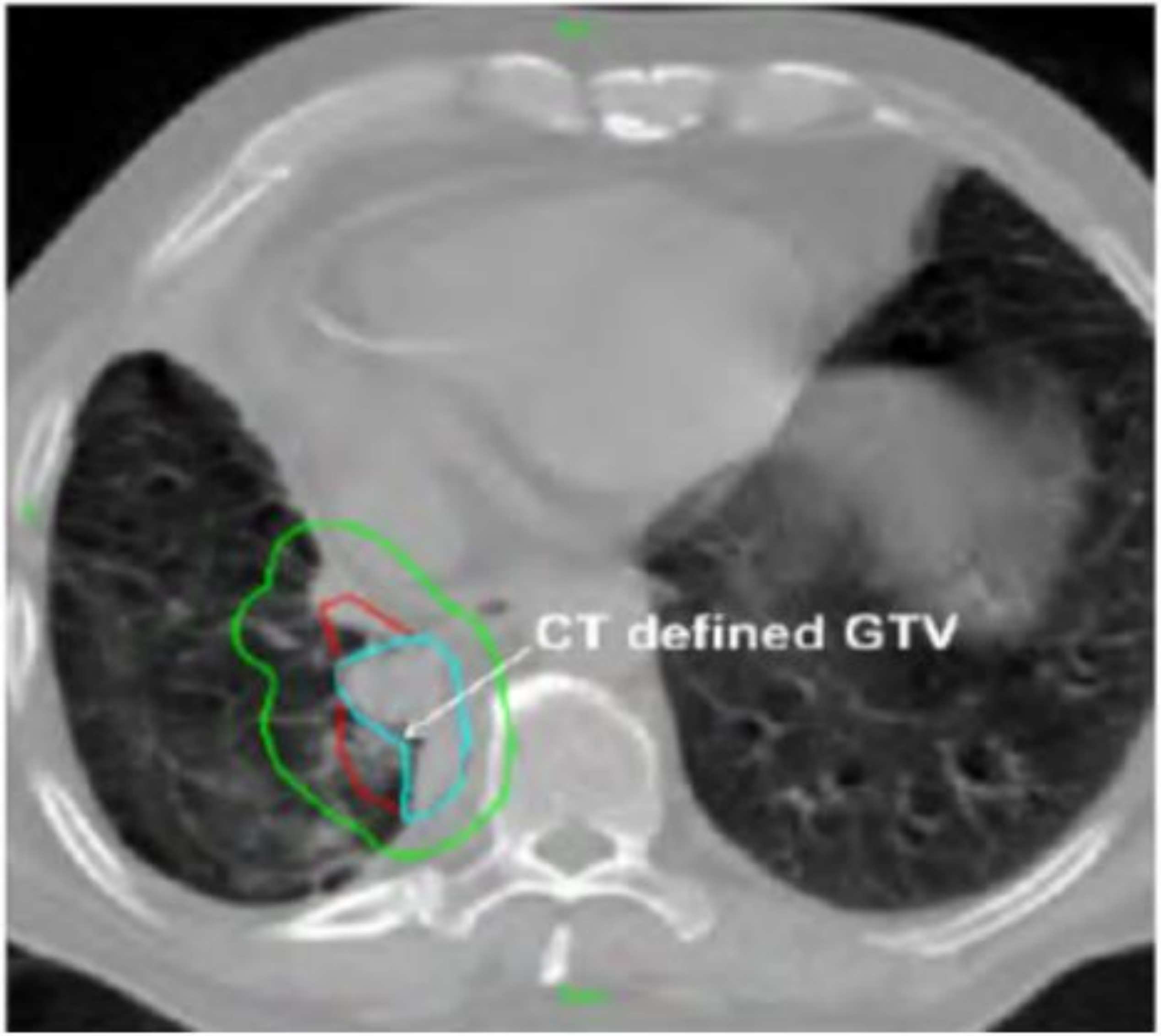
A/ Blue
B/ Red
C/ Green

Which contour is the GTV?

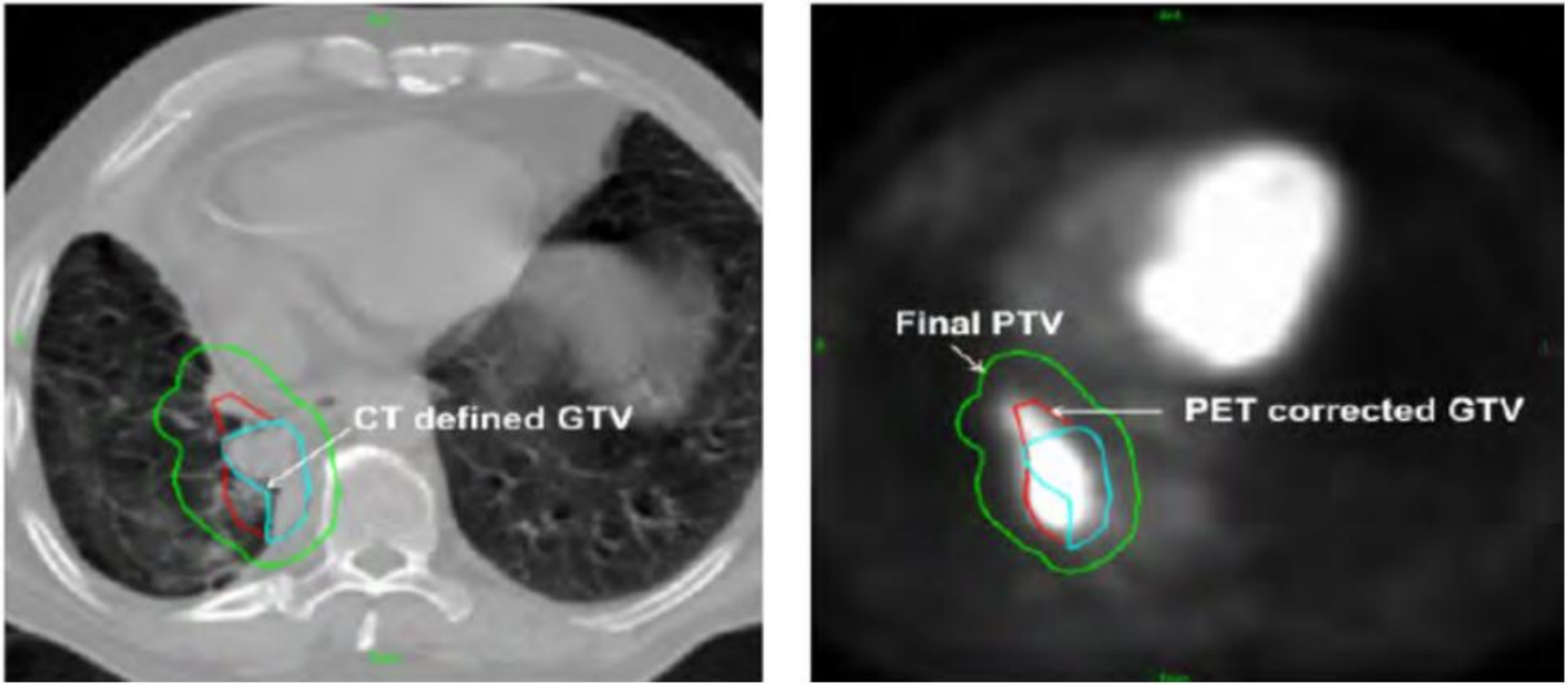
A. Blue
B. Red
C. Green



Which one is the GTV?



Are you sure about your GTV????



PET scans in delineation of lung cancer

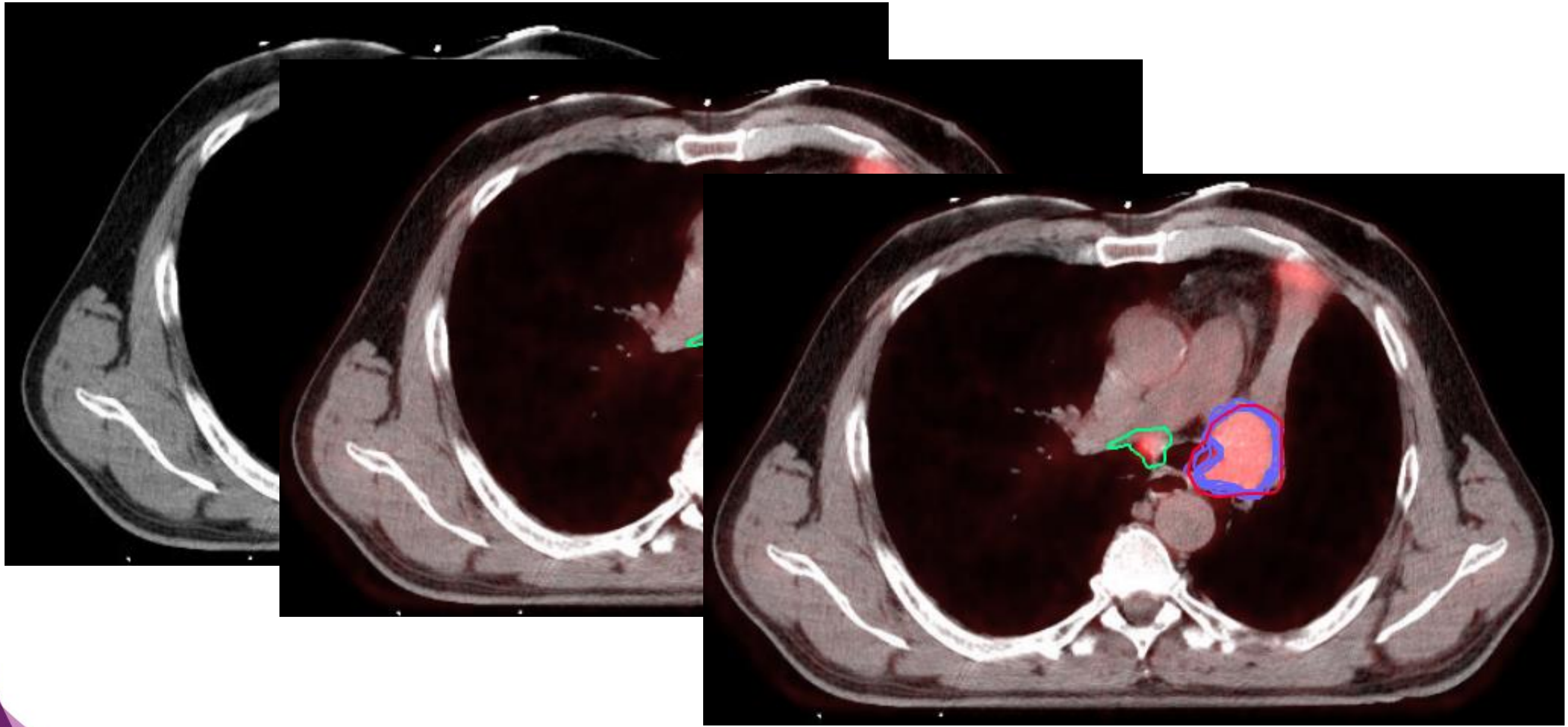
Contents lists available at ScienceDirect
Radiotherapy and Oncology 101 (2011) 284–290
Radiotherapy & Oncology

Contents lists available at ScienceDirect
Radiotherapy

- FDG-PET has an established role in contouring NSCLC
- Changes the tumor GTV in about 30–60% of patients
- Changes the nodal GTV in 9–39% of patients mainly through detection of occult metastases not seen on CT, lowering the risk of nodal recurrences

Tumor Gross Volume: GTV

- Adequate high quality imaging is a key point



Images from the FALCON platform; case Lung PET: Vienna 2013

Clinical Target Volume: CTV

- Includes GTV + microscopic extension of the tumor
- Volume to adequately cover to ensure treatment efficacy weather treatment is delivered with a curative or a palliative intent
- CTV delineation is based on local and loco regional capacity/probability of extension of the tumor
- Includes potential micromets surrounding the GTV
- Includes potential micromets in tumor’s drainage territory

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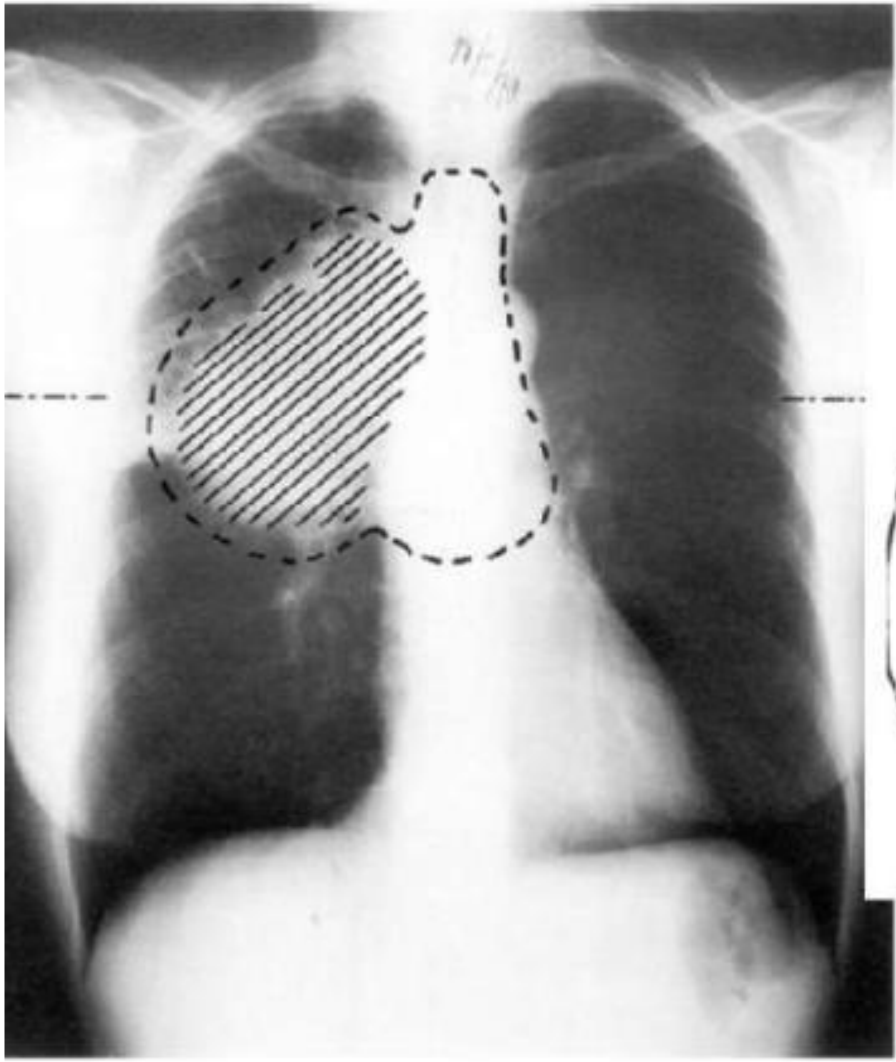
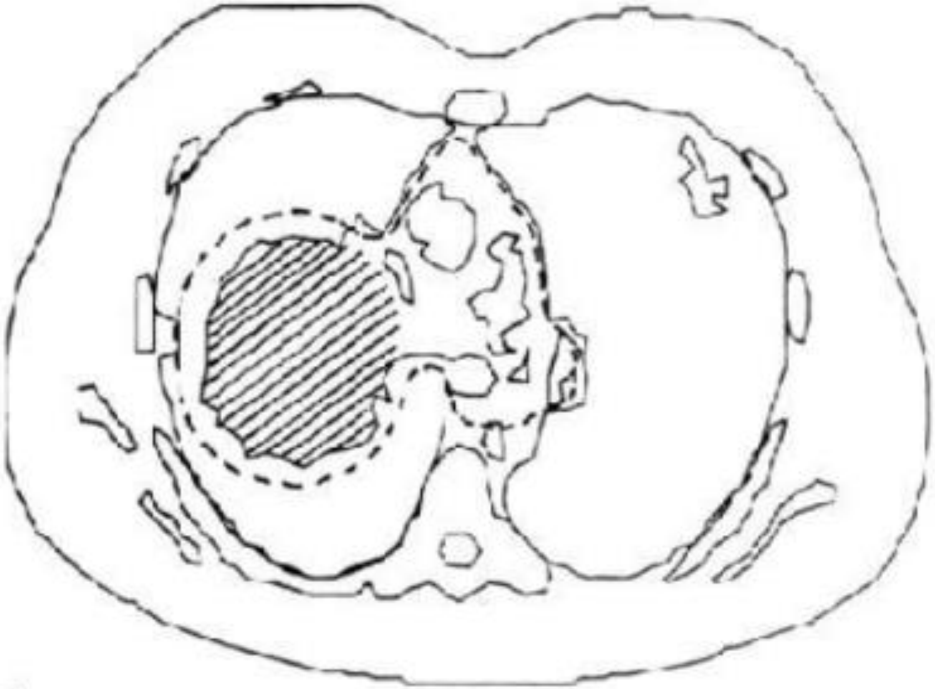
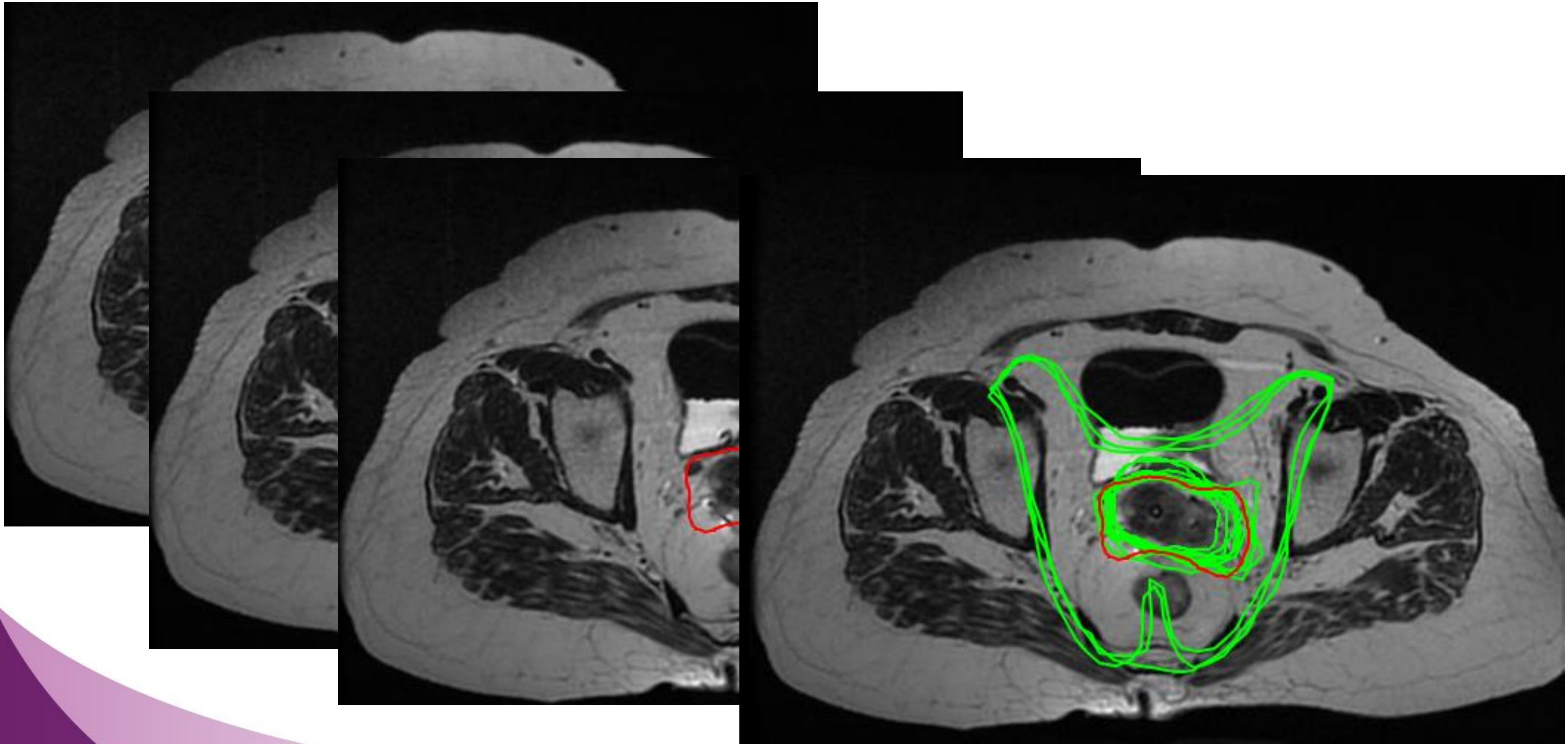
CTV





Clinical Target Volume: CTV

- High quality images are a key point for CTV delineation as well
- Margins adapted to anatomical boundaries



GTV and CTV

- Definition based on:
  - Anatomy
  - Morphology
  - Imaging
  - Biology
  - Natural history of each tumor site

- **But GTV and CTV delineation are independent of the radiotherapy technique used**

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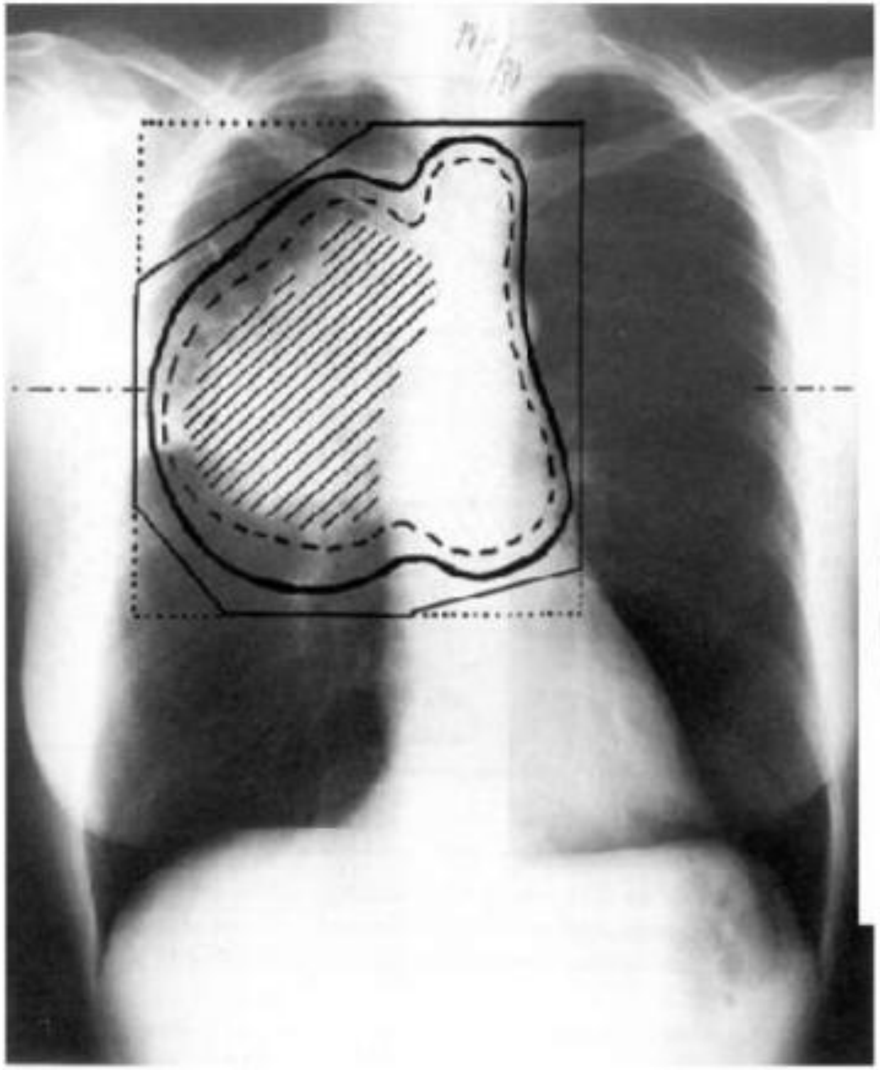
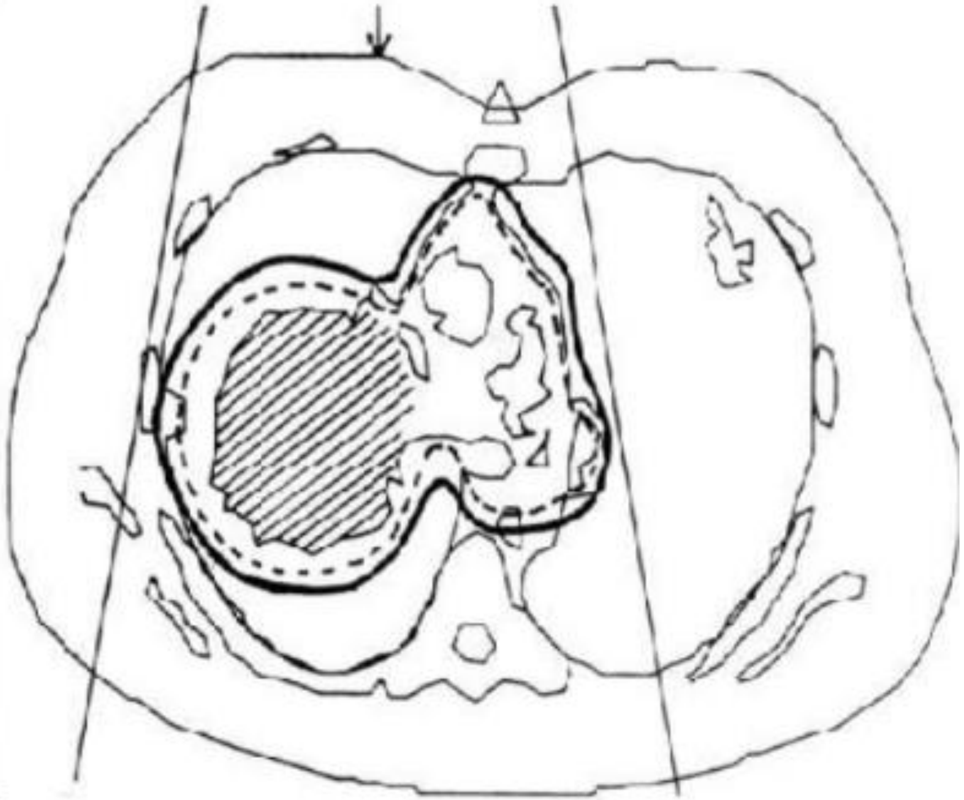
Planning Target Volume: PTV

- Geometric concept
- Meant to allow for an adequate coverage of the CTV what ever the technique, the movements, the set up uncertainties are
- Volume used for treatment planning
- Volume used for reporting

PTV

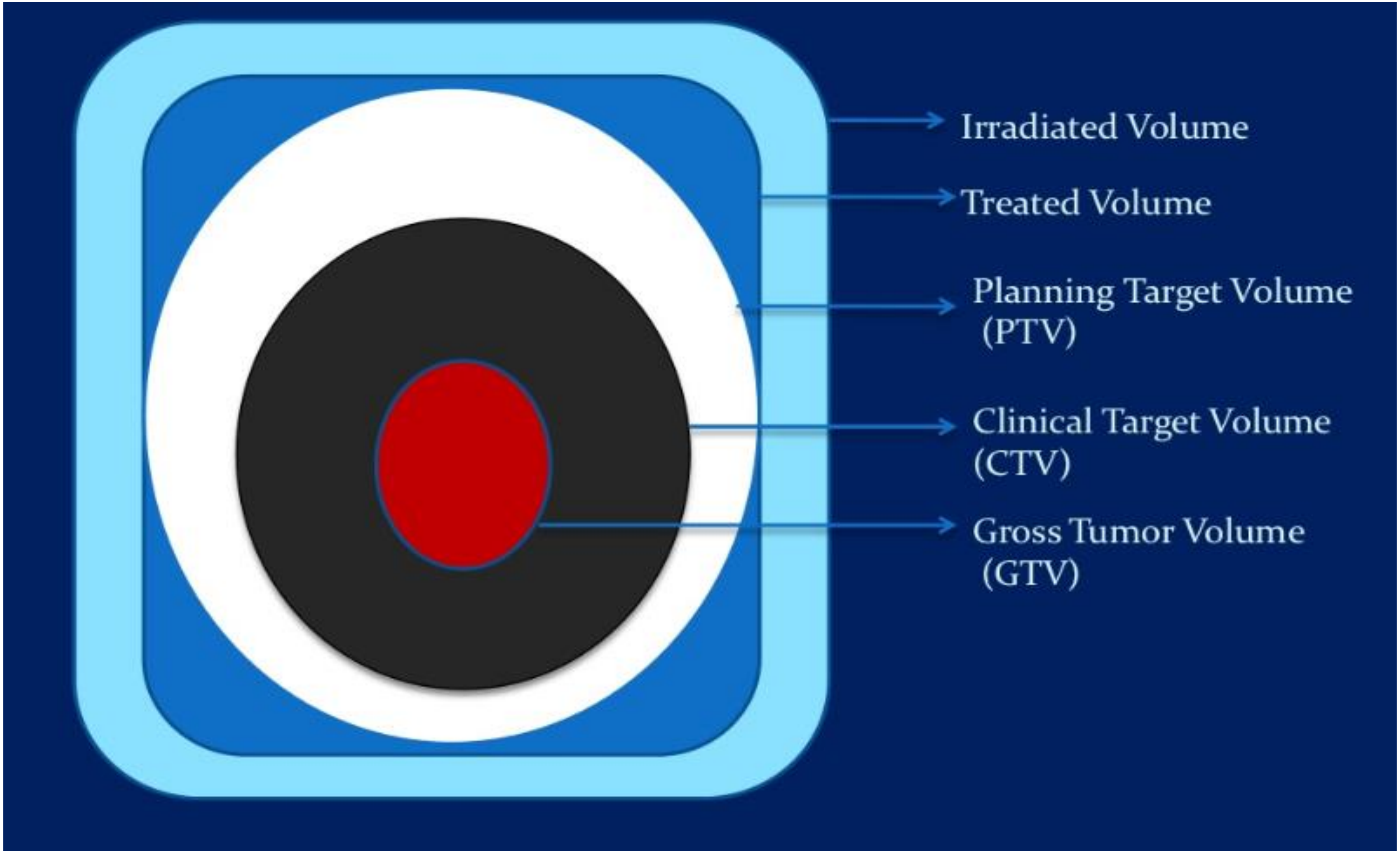




Irradiated Volume and Treated Volume: IRV and TV

- **IRV**: Defined as the volume receiving a significant dose on surrounding normal tissues / **Organs At Risk**
- Different from the **treated volume which is meant to be treated**
- Both depend on the technique used
- Both can be evaluated on the dosimetry but IRV evaluation is rather limited by most TPS
  - Ex: dose estimation outside of the treated field when using non coplanar beams

ICRU 50



Irradiated Volume
Treated Volume
Planning Target Volume (PTV)
Clinical Target Volume (CTV)
Gross Tumor Volume (GTV)

ICRU 62 (in addition to ICRU 50)

- Introduces the **Conformity Index**: **CI= treated volume/ PTV**
- Recommendations on anatomical and geometrical margins
- **Internal Margins**: **IM** are margins integrating physiological movements (breathing, bowel/ rectum/ bladder repletion, swallowing…)
- **Internal Target Volume**: **ITV** is defined as the CTV taking into account Internal Margins

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Set up Margin: SM

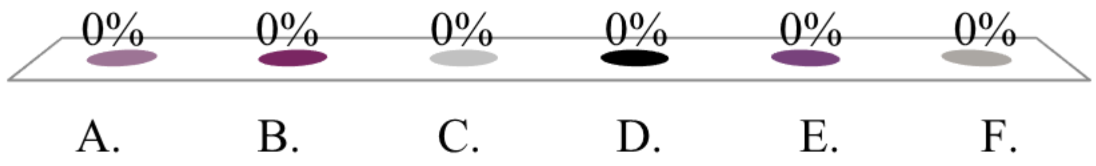
- Margins related to patient positioning:

  - Positioning uncertainties due to patient external movements
  - Positioning uncertainties due to body markers
  - Mechanical uncertainties due to immobilization device precision

- Depend on the technique (ex: tracking) and immobilization material and protocols (ex: thickness of painting markers or tattoos)

What is the definition of the ITV?

A. ITV= GTV + IM
B. ITV= CTV + IM
C. ITV= PTV + IM
D. ITV= GTV + SM
E. ITV= CTV + SM
F. ITV= PTV + SM



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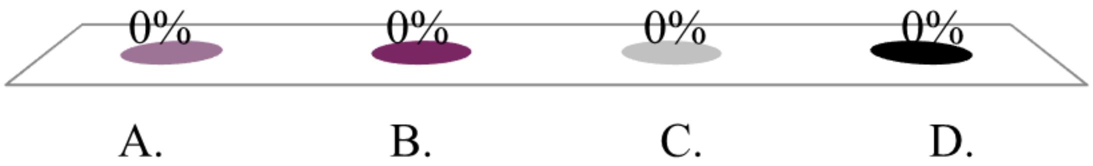
What is the definition of the PTV?

A. PTV= GTV + CTV

B. PTV= CTV + IM

C. PTV= CTV + SM

D. PTV= CTV+ IM + SM



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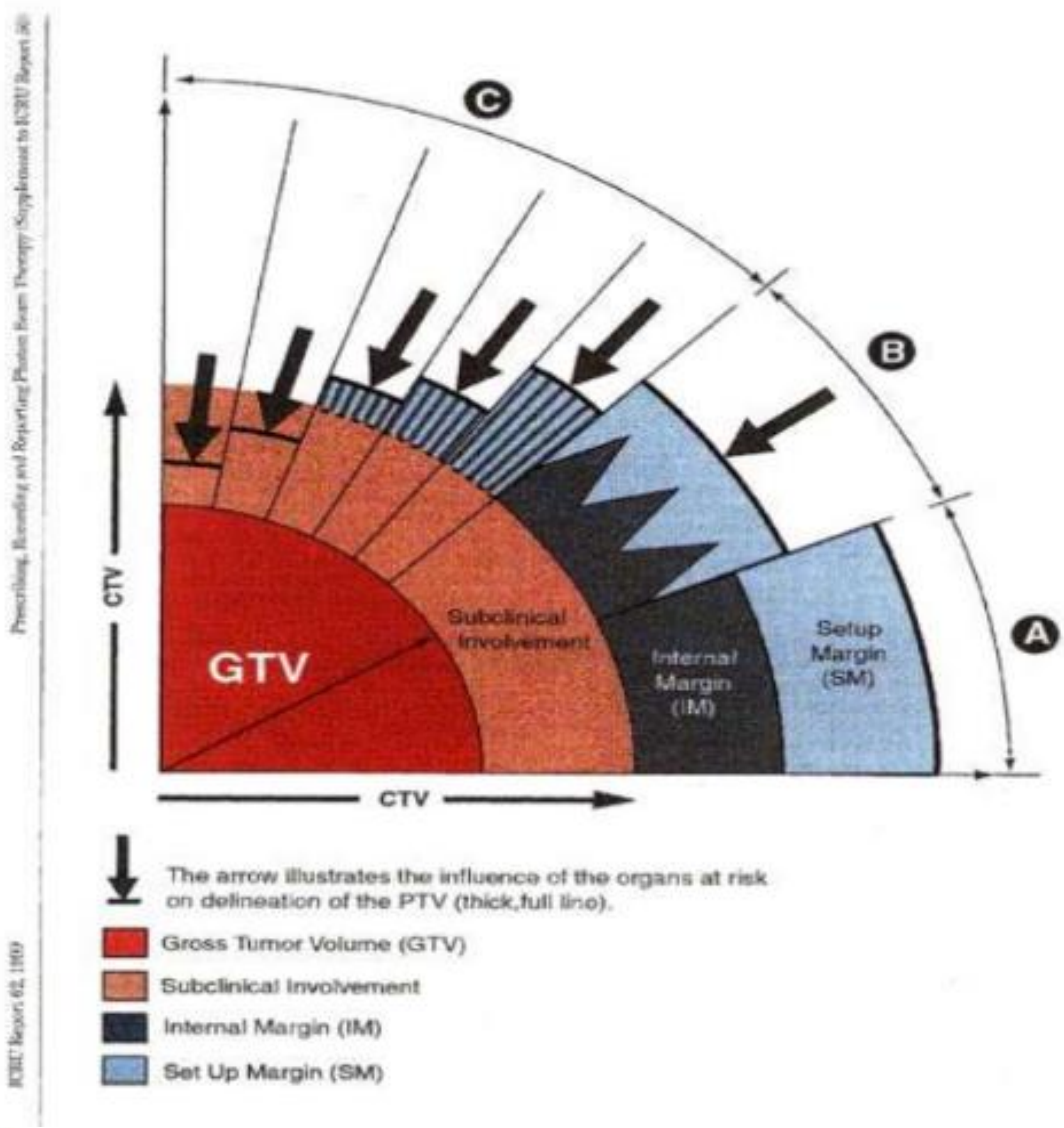


C
B
A
GTV
Subclinical Involvement
Internal Margin (IM)
Setup Margin (SM)
CTV
CTV
The arrow illustrates the influence of the organs at risk on delineation of the PTV (thick,full line).
Gross Tumor Volume (GTV)
Subclinical Involvement
Internal Margin (IM)
Set Up Margin (SM)
Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50)
ICRU Report 62, 1999

Contouring Guidelines

- Ex: ESTRO breast guidelines

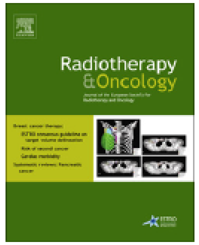
Radiotherapy and Oncology 114 (2015) 3–10

ELSEVIER

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



ESTRO consensus guidelines

ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer

CrossMark

Birgitte V. Offersen [a,*], Liesbeth J. Boersma [b], Carine Kirkove [c], Sandra Hol [d], Marianne C. Aznar [e], Albert Biete Sola [f], Youlia M. Kirova [g], Jean-Philippe Pignol [h], Vincent Remouchamps [i], Karolien Verhoeven [j], Caroline Weltens [j], Meritxell Arenas [k], Dorota Gabrys [l], Neil Kopek [m], Mechthild Krause [n], Dan Lundstedt [o], Tanja Marinko [p], Angel Montero [q], John Yarnold [r], Philip Poortmans [s]

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Contouring Guidelines

Table 1
ESTRO delineation guidelines for the CTV of lymph node regions, breast and postmastectomy thoracic wall for elective irradiation in breast cancer (see figures).

Borders per region	Axilla level 1 CTVn_L1	Axilla level 2 CTVn_L2	Axilla level 3 CTVn_L3	Lymph node level 4 CTVn_L4	Internal mammary chain CTVn_IMN	Interpectoral nodes CTVn_interpectoralis	Residual breast CTVp_breast	Thoracic wall CTVp_thoracic wall
Cranial	Medial: 5 mm cranial to the axillary vein Lateral: max up to 1 cm below the edge of the humeral head, 5 mm around the axillary vein	Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein)	Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein)	Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein)	Caudal limit of CTVn_L4	Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein)	Upper border of palpable/ visible breast tissue; maximally up to the inferior edge of the sterno-clavicular joint	Guided by palpable/visible signs; if appropriate guided by the contralateral breast; maximally up to the inferior edge of the sterno-clavicular joint
Caudal	To the level of rib 4 – 5, taking also into account the visible effects of the sentinel lymph node biopsy	The caudal border of the minor pectoral muscle. If appropriate: top of surgical ALND	5 mm caudal to the subclavian vein. If appropriate: top of surgical ALND	Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of CTVn_IMN	Cranial side of the 4th rib (in selected cases 5th rib, see text)	Level 2's caudal limit	Most caudal CT slice with visible breast	Guided by palpable/visible signs; if appropriate guided by the contralateral breast

B.Offersen et al radiother oncol 2015

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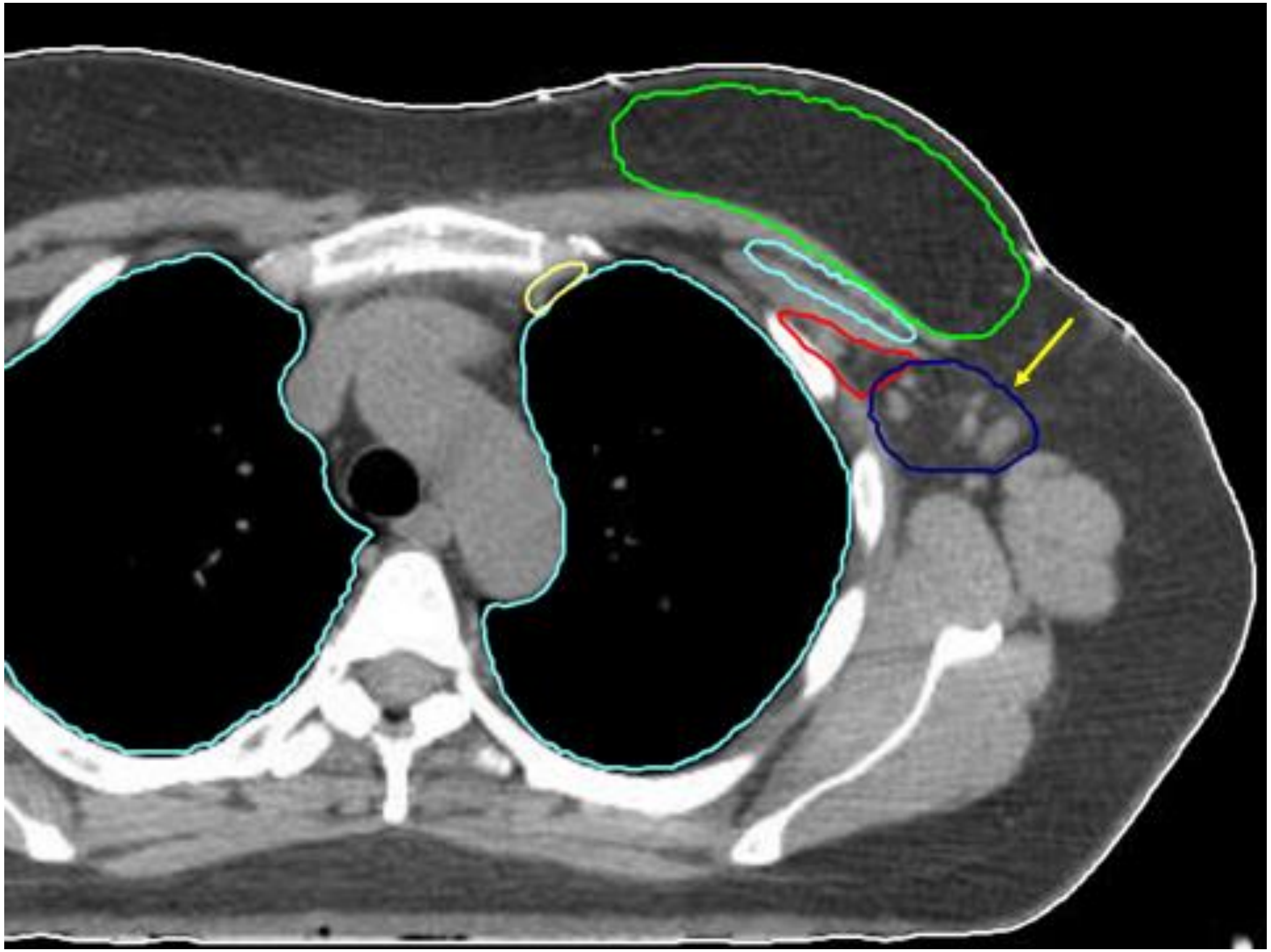
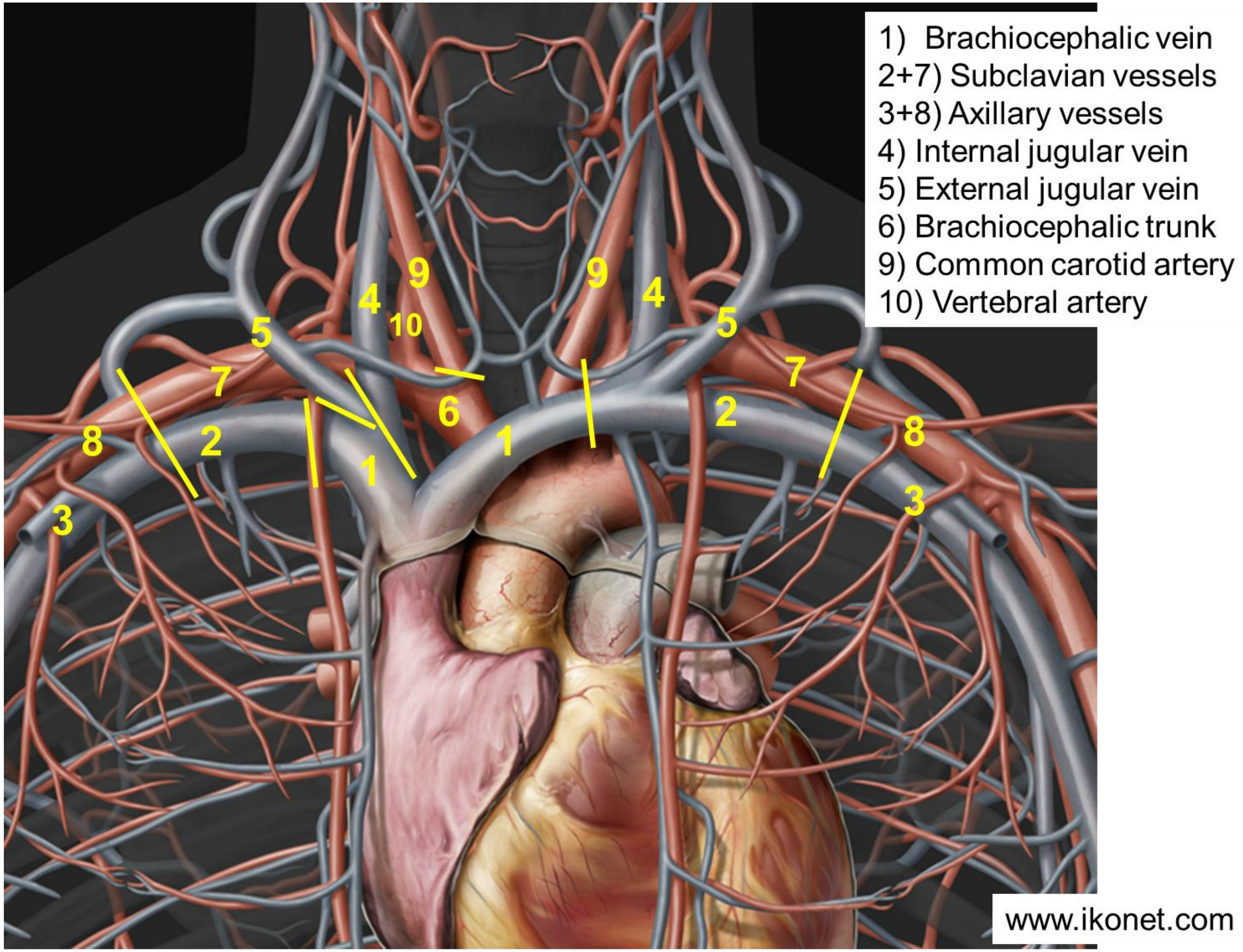
Contouring Guidelines

- Ex: ESTRO breast guidelines



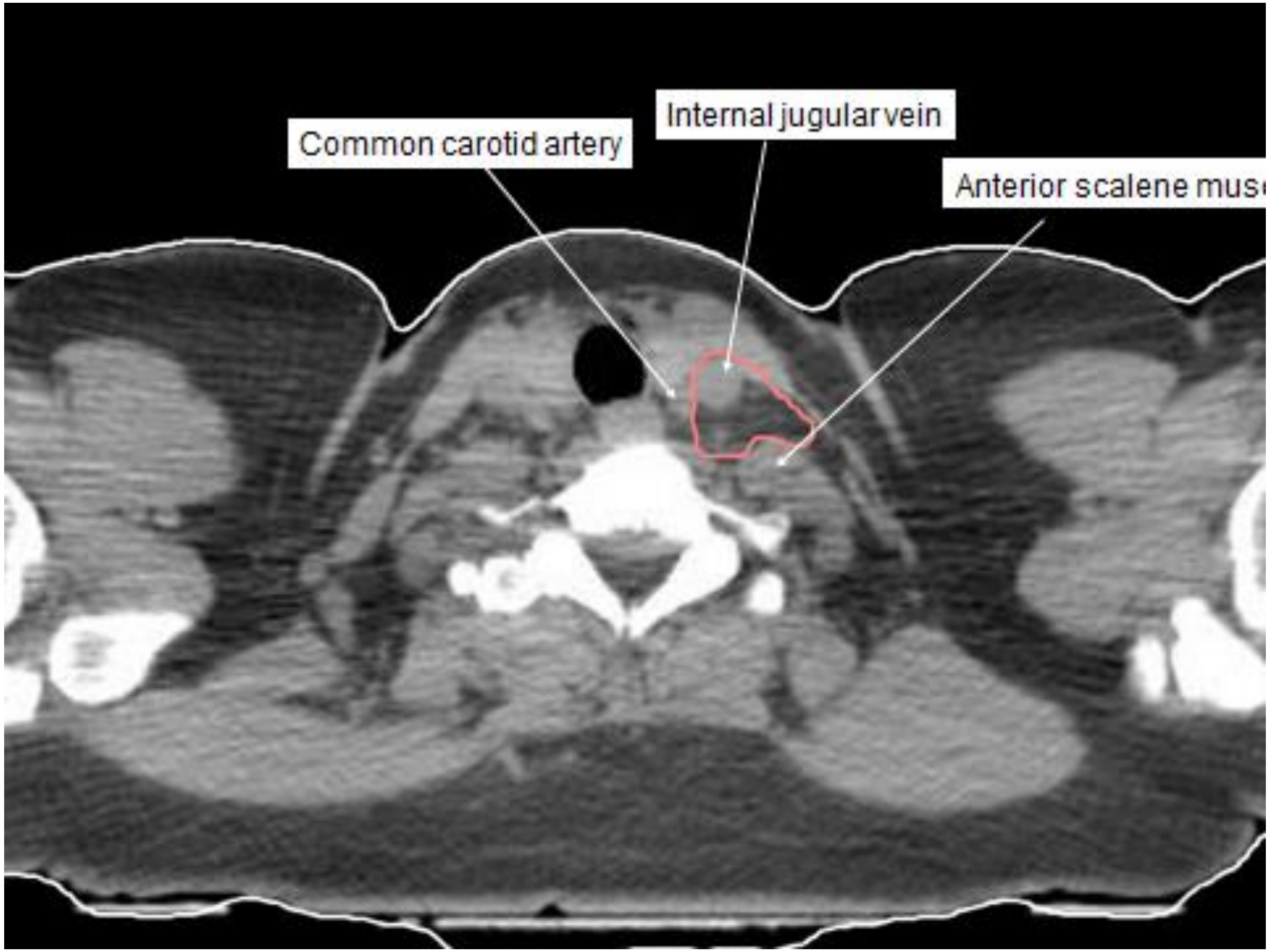
Contouring guidelines

- Anatomical basis are the key!



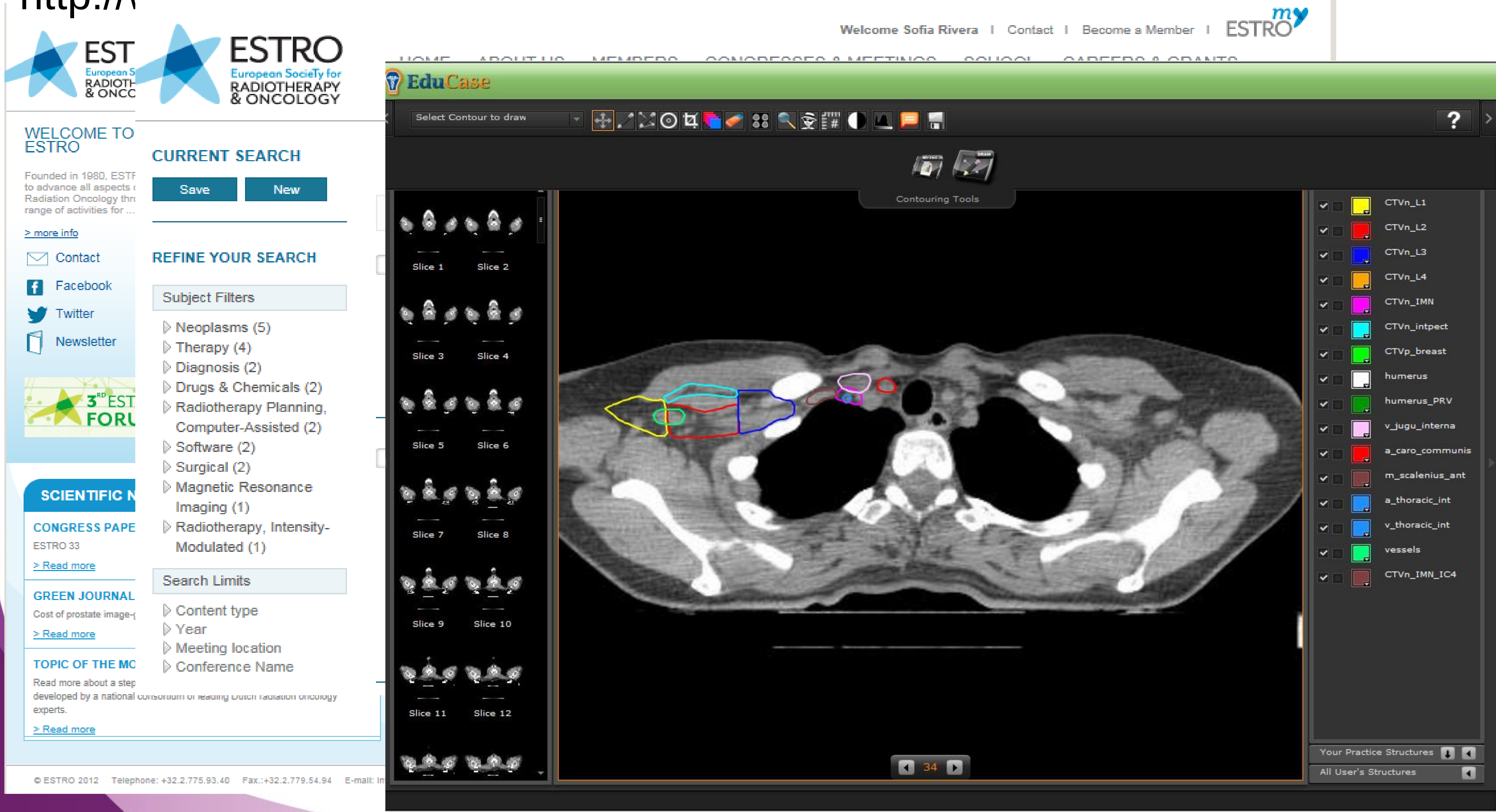
Contouring guidelines

- Anatomical basis are the key!



ESTRO guidelines

http://



Take home messages:

- Inter observer variability in contouring can translate in a systematic error

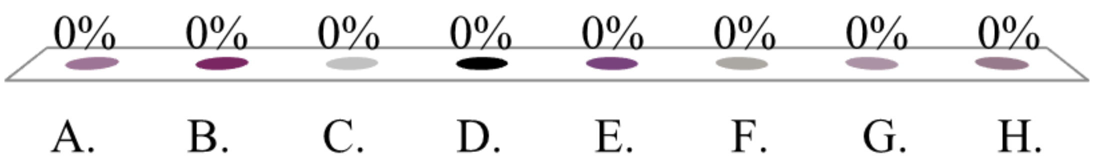
- Need for a common language: ICRU

- Need for delineation guidelines

- Need for teaching in contouring

What is the weakest point in our modern radiotherapy treatment chain?

A. Dose calculation?
B. Positioning uncertainties?
C. Contouring uncertainties?
D. Quality control of the treatment machine?
E. Patient changes (weight loss, movements…)?
F. RTTs?
G. Physicists?
H. Physicians?



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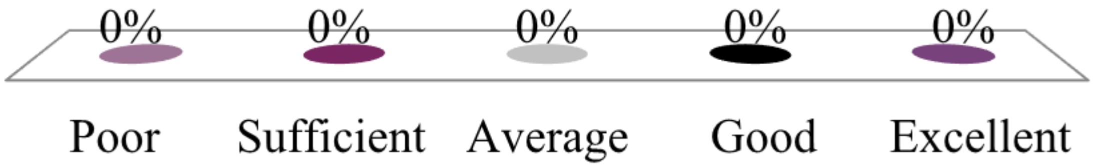
Thank you for you attention

Any question?

How would you score this lecture?

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on Survey Monkey



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TARGET VOLUME DELINEATION

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Delineation

ISc), RTT

rofessor

iation Therapy

ge Dublin

Sofia Rivera, MD, PhD
Radiation Oncology Department
Gustave Roussy
Villejuif, France

Advanced skills in modern radiotherapy
May 06, 2018

GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS

WWW.ESTRO.ORG/SCHOOL

ARTT Applied Radiation Therapy Trinity Research Group

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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Learning Outcomes

- Discuss the changing roles and responsibilities of RTTs with respect to Organ at Risk (OAR) delineation
- Discuss the impact inaccurate OAR delineation can have on treatment planning
- Discuss the application of dose volume constraints based on delineation protocols
- Identify resources available to support consistency and accuracy in OAR delineation

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Why Are OARs So Important?

- Do no harm culture of medicine
  - ➢ Decrease impact of radiation to our patients
- Requirement for inverse planning optimisation process
  - ➢ IMRT
  - ➢ VMAT
- Generates DVH information and assists in prediction of toxicity
  - ➢ Serial and Parallel structures
  - ➢ Assessment of clinical impact and disturbance on daily activities

Why Is ***Accuracy*** So Important?

- Consistency and uniformity
  - Within the department
    - Prospective data collection
    - Analysis of local practice and impact on patients
  - Within the context of clinical trials
    - Compliance with trial specifications
    - Allows for collections of data and comparison of outcomes and toxicity at a larger international scale

Why Is *Accuracy* So Important?

- OAR delineation has significant impact on dose calculation and plan quality in dosimetry

- IMRT and VMAT are inverse planning techniques and as such are driven by volumes
  - Target and OAR relationship

- Accurate imaging ensures:
  - Decrease in interobserver variability
  - DVH calculation
  - Greater confidence in predicting toxicity
  - "reduction in inter- and intra-observer variability and therefore unambiguous reporting of possible dose-volume effect relationships" *(van der Water, 2009)*

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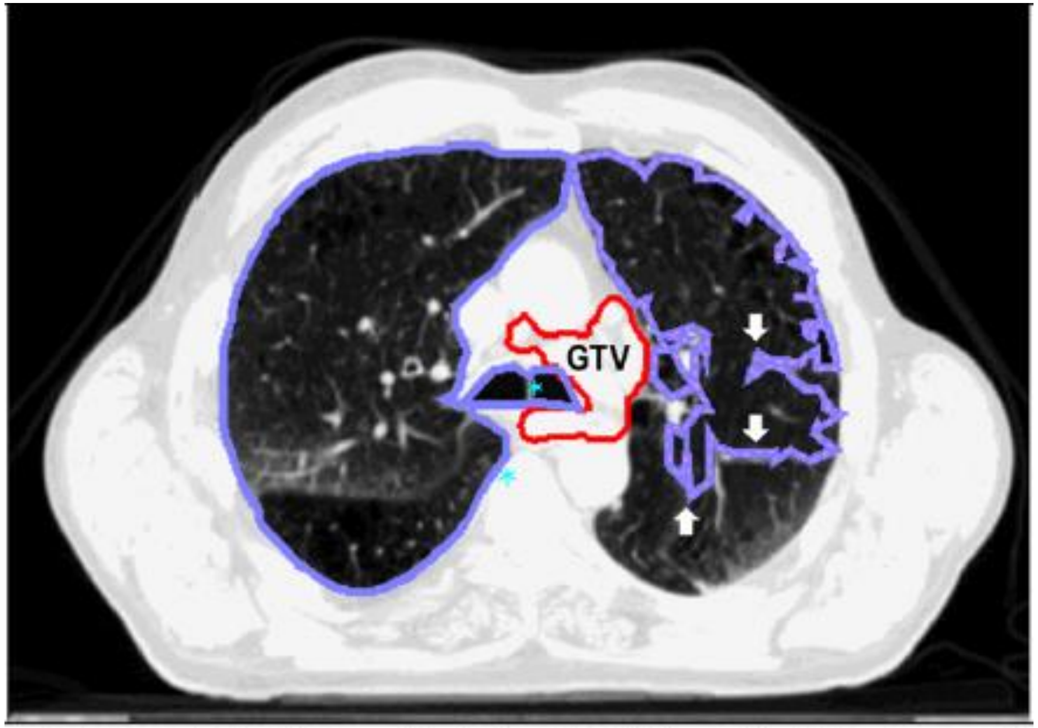
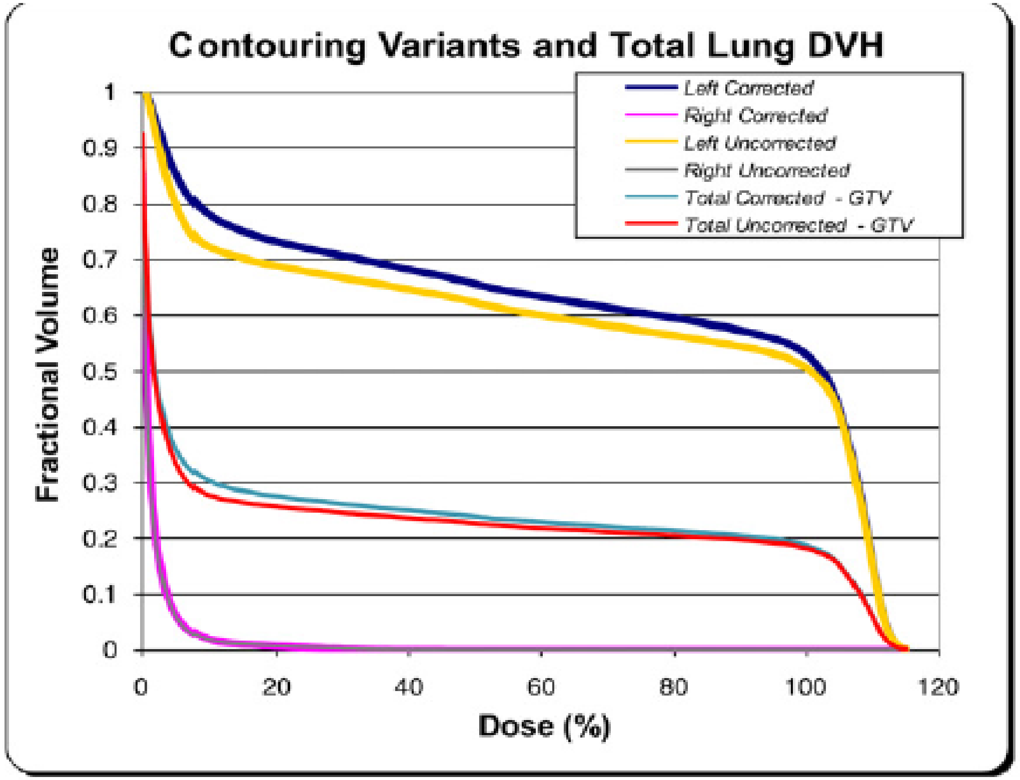
Impact on Planning



A: Lung Contour - Autotrack Failure (white arrows)

What is wrong in this picture?
What has caused this?
What impact would this have?



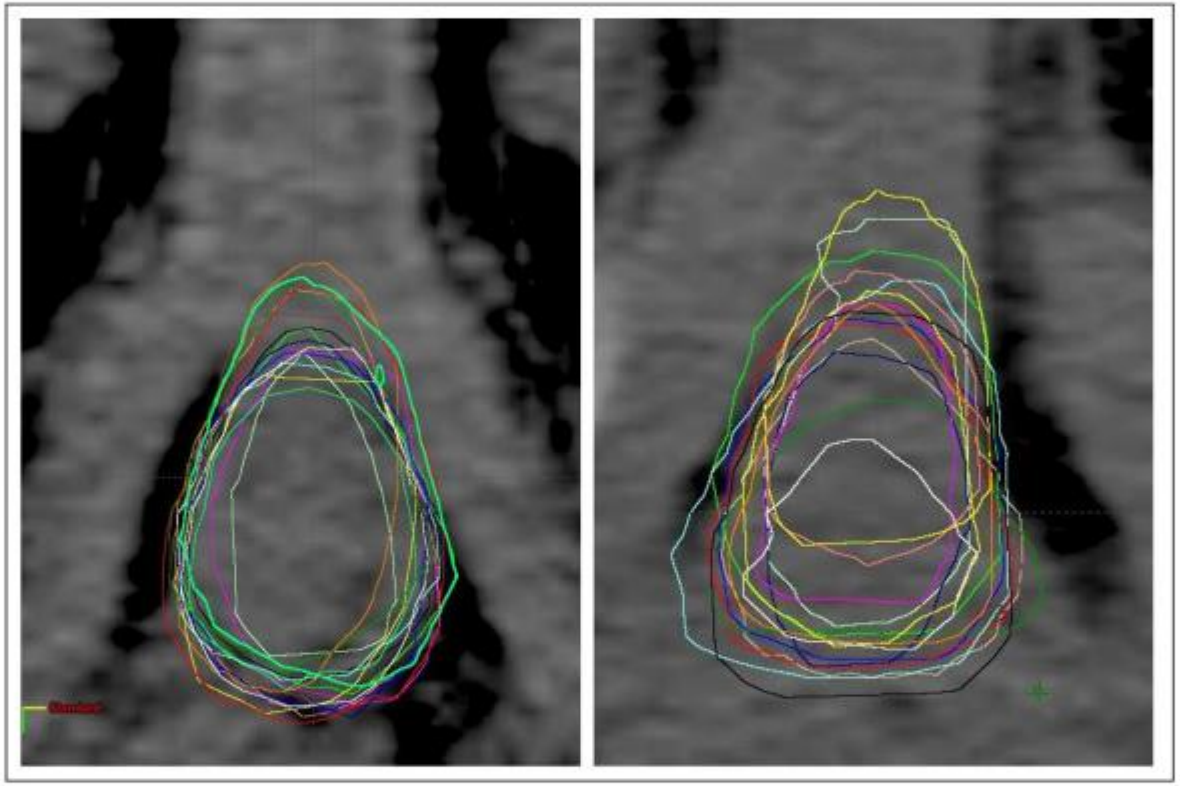
C: Lung DVH differences of contouring variants

Research

Open Access

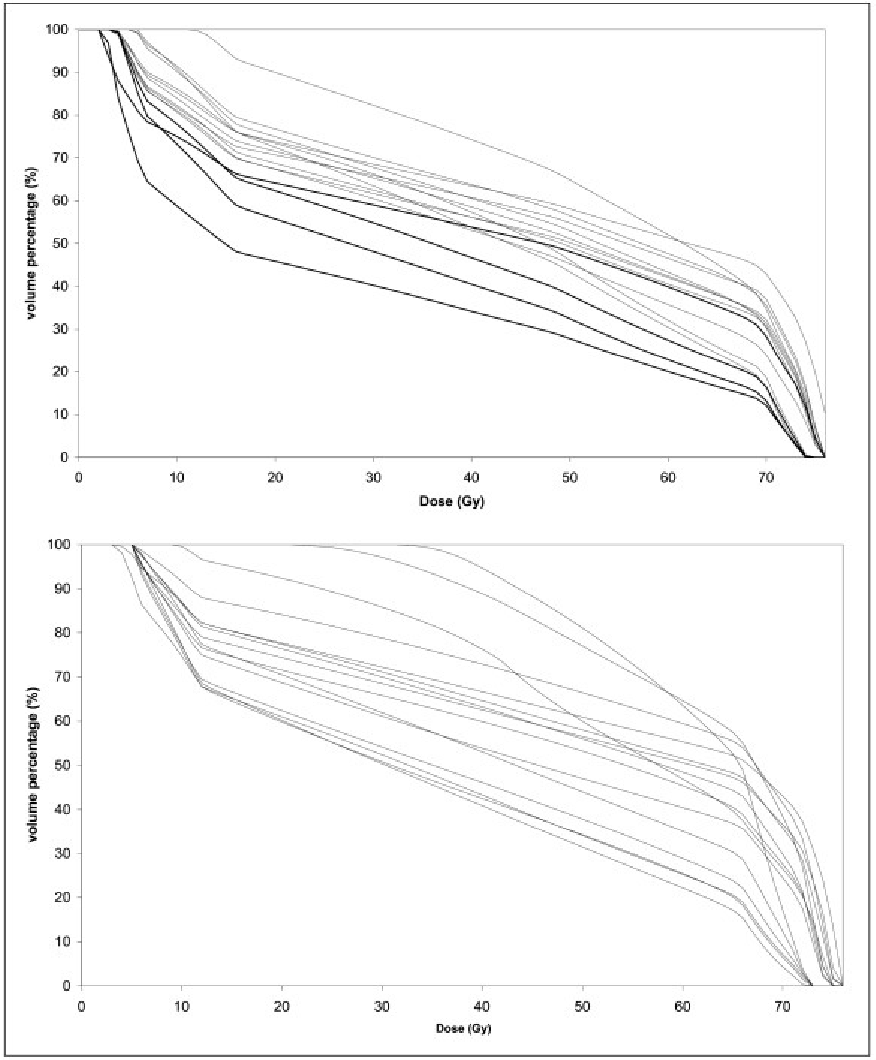
Inter-observer variability in contouring the penile bulb on CT images for prostate cancer treatment planning

Lucia Perna[1]*, Cesare Cozzarini[2], Eleonora Maggiulli[1], Gianni Fellin[3], Tiziana Rancati[4], Riccardo Valdagni[4], Vittorio Vavassori[5], Sergio Villa[6] and Claudio Fiorino[1]



A plot of the central slice of PB contours drawn by all observers of two patients: one with the lowest inter-observer volume variation (left side) and one with the largest inter-observer volume variation (right side).

Perna et al. Radiation Oncology 2011 6:123 doi:10.1186/1748-717X-6-123



Graphs showing PB dose-volume histograms relative to the two patients in figure 5: the first (top of figure) with the lowest impact of inter-observer variation on DVH parameters, and the second (bottom of the figure) with the largest impact of inter-observer variation on DVH parameters.

Possible recommendations put forward by the authors:

- Contouring by a single user
- Introduction of MRI into practice
- Improving the agreement between observers (consensus)

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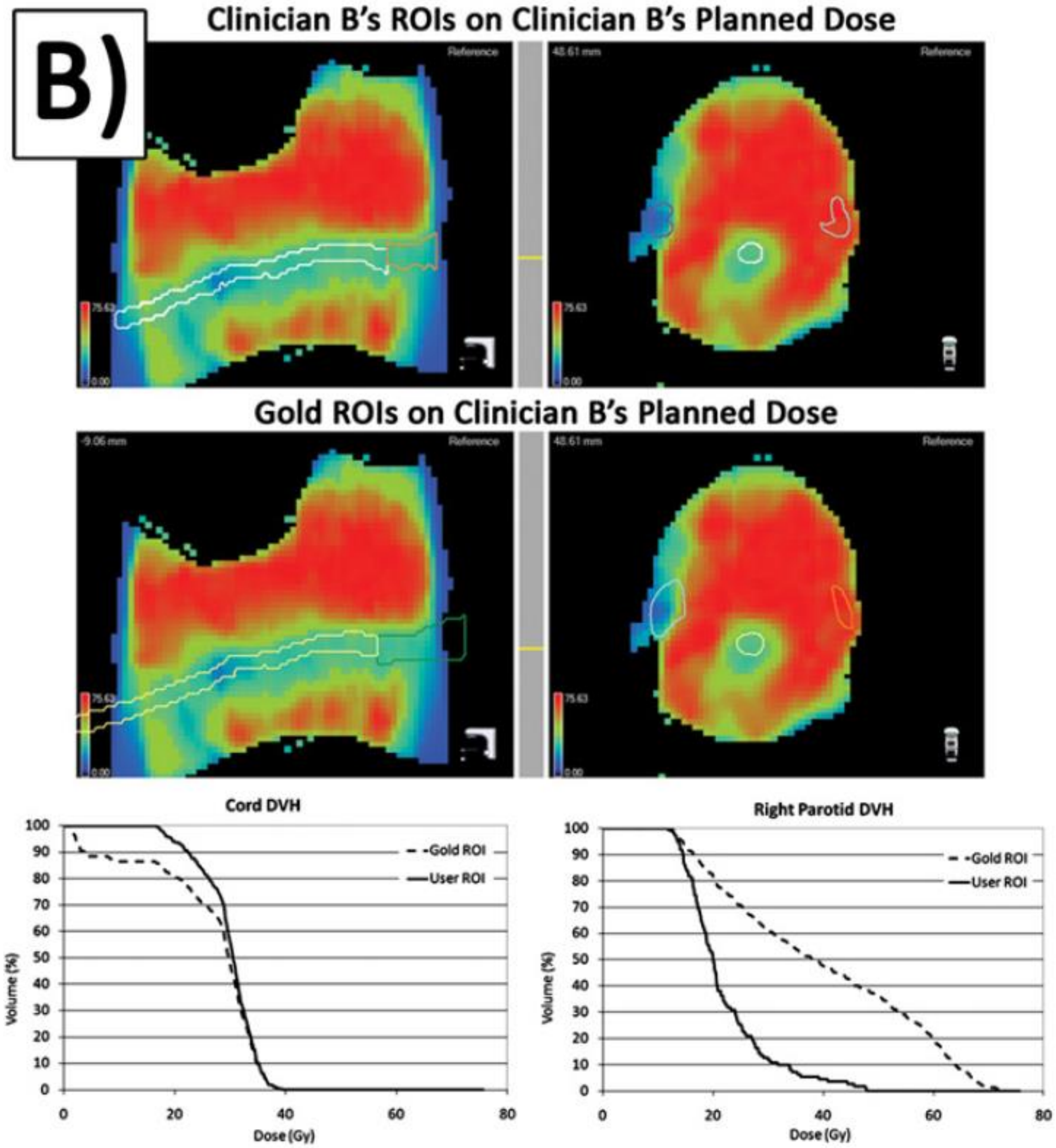
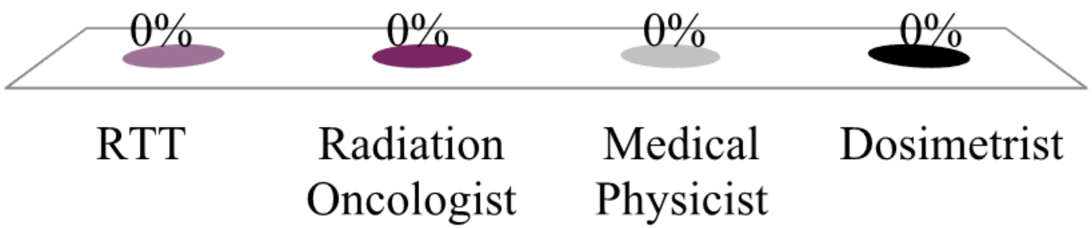


Nelms B et al., Variations in the contouring of organs at risk: test case from a patient with oropharyngeal cancer. IJROBP. 2012; 82(1): 368-378

Question Time!

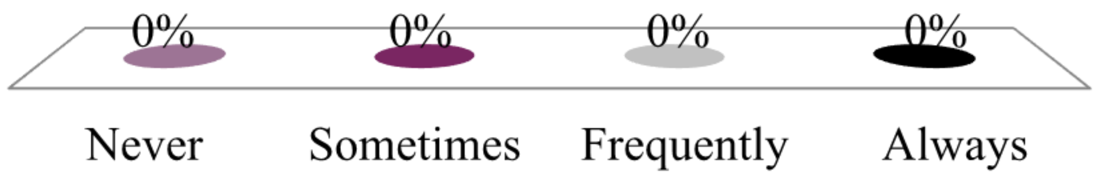
In my current practice organs at risk are contoured by the:

A. RTT
B. Radiation Oncologist
C. Medical Physicist
D. Dosimetrist



I personally am involved in OAR delineation:

A. Never
B. Sometimes
C. Frequently
D. Always



The New RTT!

"flexible inter professional boundaries" Schick et al., 2011

"The goal of a radiation therapist undertaking OAR delineation is logical role expansion." (Schick et al 2011)

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The New RTT

ELSEVIER

Journal of Medical Imaging and Radiation Sciences xx (2014) 1-8

Journal of Medical Imaging and Radiation Sciences

Journal de l'imagerie médicale et des sciences de la radiation

www.elsevier.com/locate/jmir

Role Development for Radiation Therapists: An Examination of the Computed Tomographic Simulation Procedure for Patients Receiving Radiation Therapy for Breast Cancer

Bonnie Bristow, MRT(T), BSc*, Saffiyya Saloojee, MRT(T), Michele Silveira, MRT(T), Shila Vakani, MRT(T) and Angela Turner, MRT(T), BA(Hons)

Department of Radiation Therapy, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

- Comparison of practice and confidence
- Identified tasks performed at CT Simulation
- Results: 84% no change made by RO

Table 4

Responses for Confidence Levels (n = 9 ROs, n = 21 RTs)

I have confidence in RTs performing the following tasks:
Placement of baseline
Contouring of cardiac volume
Lung volume
Scar/seroma delineation
Cardiac contour
Spinal contour
Placement of field junction
Humeral shielding
Selection of immobilization

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Tools for Implementation and Facilitating Change

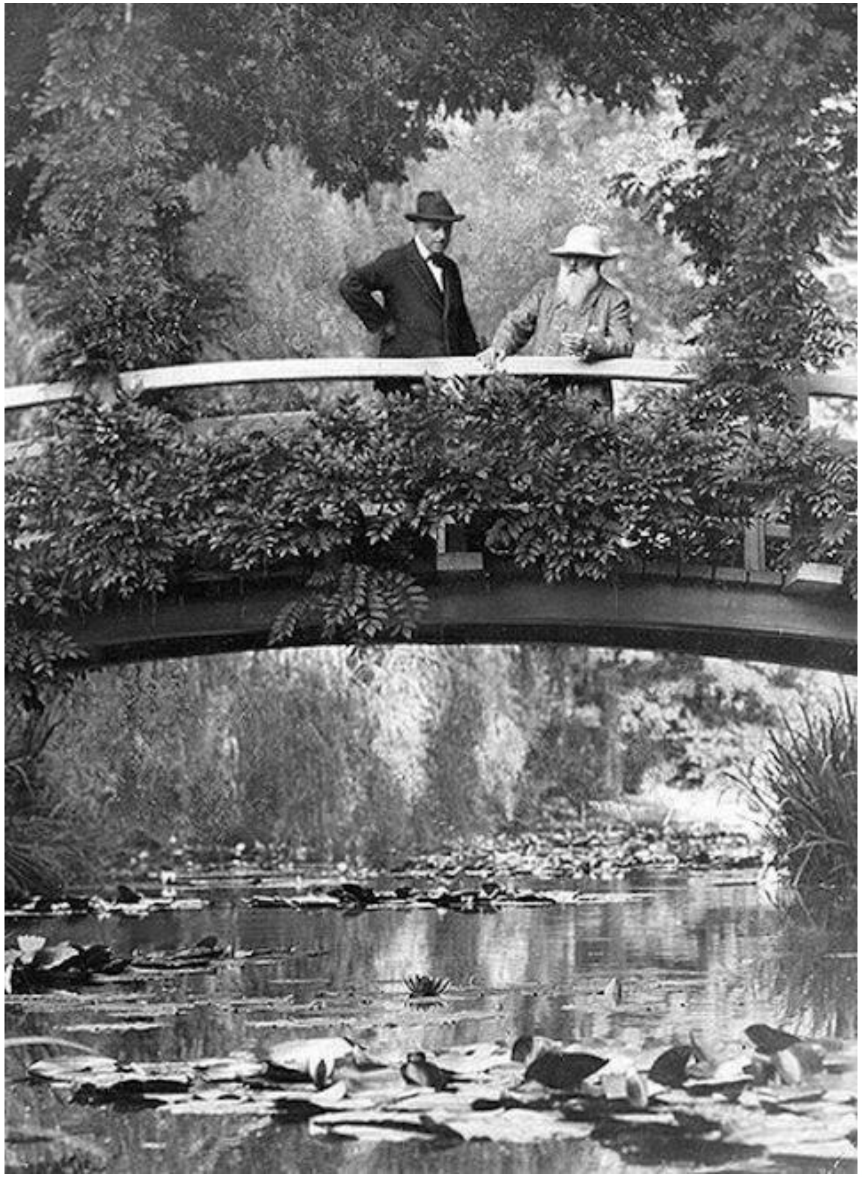
- Culture of the department
  - ➢ Clinical mentorship
  - ➢ Commitment to evidence based practice
  - ➢ Commitment to role development
  - ➢ Shared goals within the MDT
  - ➢ Open communication

- Prior and ongoing education!

- Even in an ideal environment uncertainties in delineation exist…

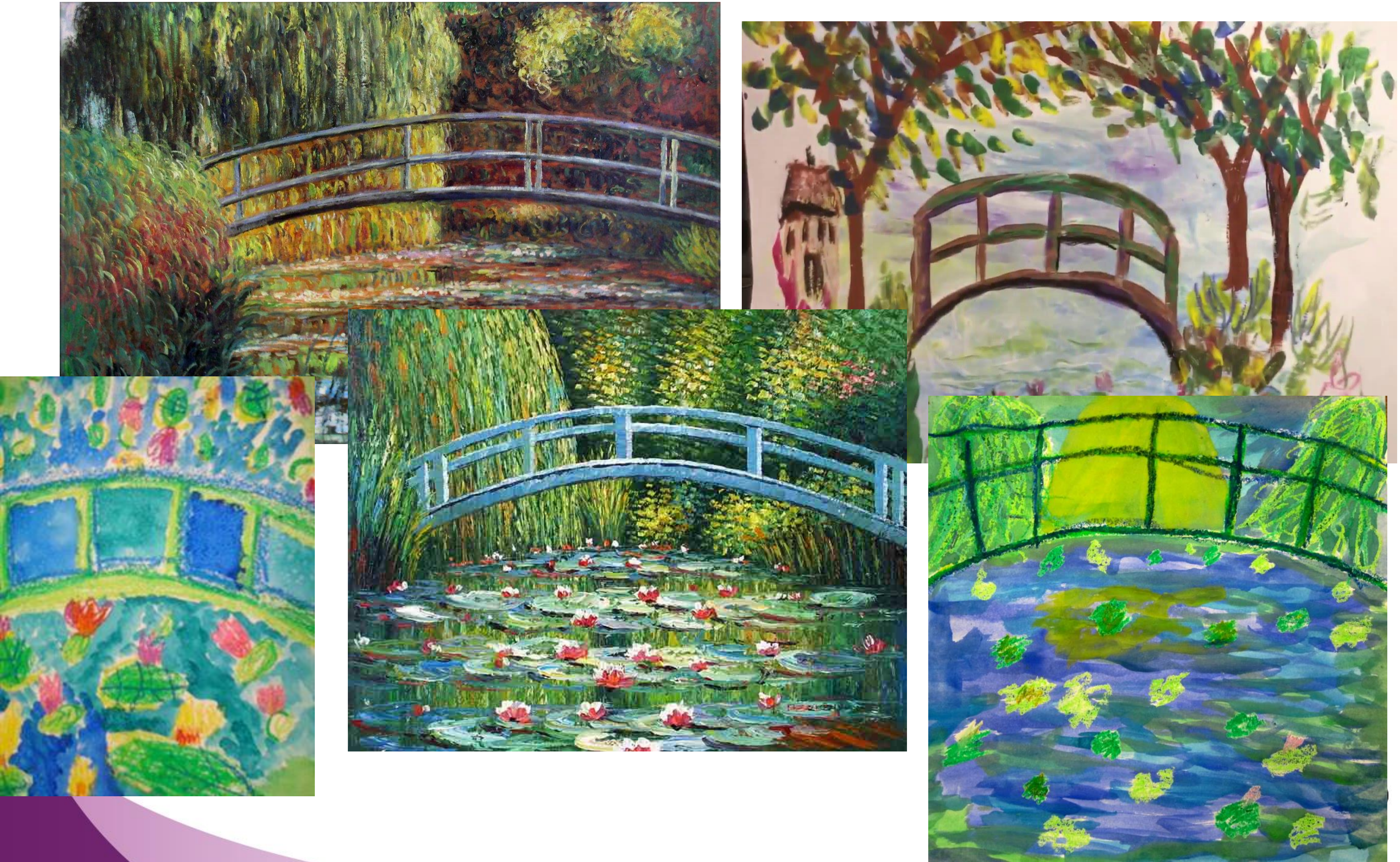
Observer Variability in Delineation

- Claude Monet
- Photo
- 1922



Intra Observer Variability

Inter Observer Variability



Recommendations to Decrease Observer Variability

- Use of contouring guidelines and atlases
- Use of secondary imaging data sets
- Use of auto-contouring tools
  - Not to be used in an isolated fashion but to be adjusted for each individual patient
- Attendance at contouring workshops
- Multidisciplinary input – open communication
- Peer review of contours, regardless of who completed the delineation
- Education within the clinic and competency based approach to new roles/responsibilities *(Bristow et al., 2014)*

Vinod S et al., A review of interventions to reduce inter-observer variability in volume delineation in radiation oncology. JMIRO. 2016, 60(3): 393-406

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Auto – Segmentation

- **Image content or greyscale method**
  - Appropriate for very high or low contrast structures

- Segmentation without prior knowledge

- Widely available (e.g. flood fill, spindle snake)

- "Common errors include…using the auto-threshold contouring tools in the TPS and not editing the resulting errors" *(Gay et al., 2012)*

Whitfield G et al., Automated delineation of radiotherapy volumes: are we going in the right direction? BJR. 2013 86(1021): 20110718

Auto – Segmentation

- **Atlas based segmentation**

- Propagation of segmented structures from an atlas onto the patient image using deformable registration *(Lim and Leech, 2017)*

- Atlas can be based on:
  - ➢ Single patient dataset
  - ➢ Multiple patient data (based on an average of a range of patients from multiple libraries)
  - ➢ Model based (using library of previously manually contoured patients)

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Auto – Segmentation

- **Shape model based segmentation**

- Concept is extending an active snake approach into an active mesh approach
  - ➢ Driven by greyscale and constrained by shape

Whitfield G et al., Automated delineation of radiotherapy volumes: are we going in the right direction? BJR. 2013 86(1021): 20110718

Auto – Segmentation: Vendor Solutions

Vendor	Product Name	Segmentation Approach	Reference
Varian	Eclipse (smart segmentation)	Atlas-based	11
MIM software	MIM Maestro 6+	Atlas-based	12
Velocity	VelocityAI 3.0.1	Atlas-based	13
BrainLab	iPlan	Atlas-based	14
Dosisoft	IMAgo	Atlas-based	15
Mirada	RTx 1.4, workflow box	Atlas-based	16
OSL	OnQ RTS	Atlas-based	17
Elekta	ABAS 2.01	Atlas- and model-based	18
Philips	SPICE 9.8	Atlas- and model-based	19
RaySearch	RayStation 4.0	Atlas- and model-based	20

Raudaschl P et al., Evaluation of segmentation methods in head and neck CT: Auto-segmentation challenge 2015. Medical Physics. 2017; 44(5): 2020-2036

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Auto-segmentation – Beware!

- Attractive due to time saving aspects and support of adaptive RT, but…

- Beware of automaticity!

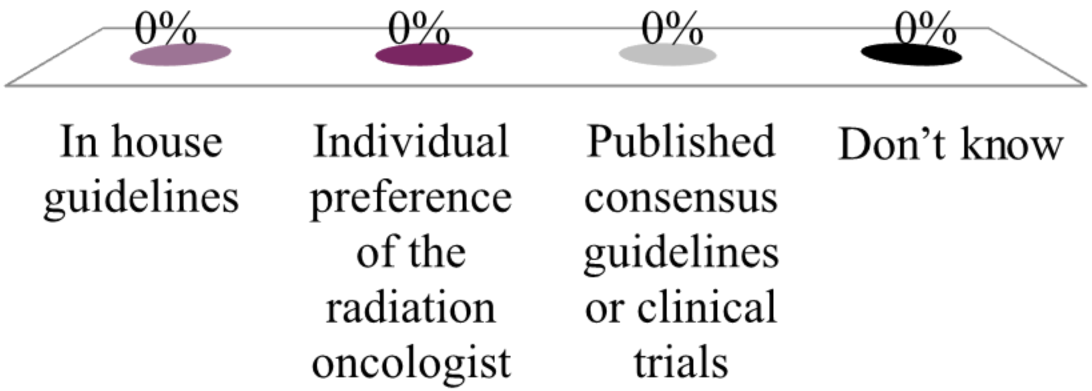
    - "Even with the implementation of AS software in the future, it should be reinforced that manual editing is still a necessity for patient safety." *(Lim and Leech, 2017)*

    - "atlas-based automatic segmentation tool … is timesaving but still necessitates review and corrections by an expert" *(Daisne and Blumhofer, 2013)*

Question Time!

In your current practice what defines how organs at risk are contoured?

A. In house guidelines
B. Individual preference of the radiation oncologist
C. Published consensus guidelines or clinical trials
D. Don’t know



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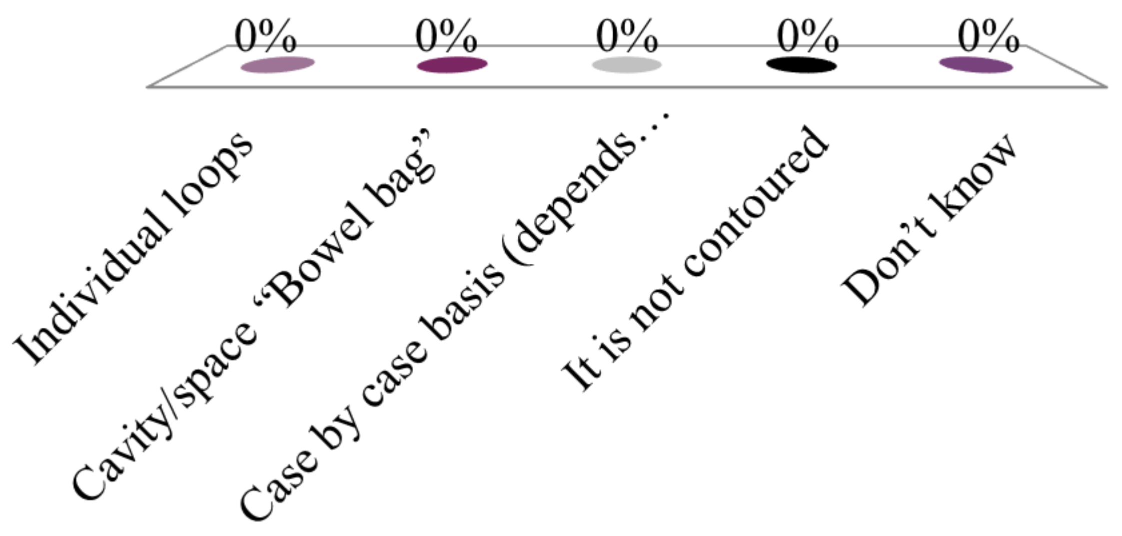
In your current practice how is the small bowel contoured?

A. Individual loops
B. Cavity/space "Bowel bag"
C. Case by case basis
D. It is not contoured
E. Don't know



Is there Consensus?

QUANTEC

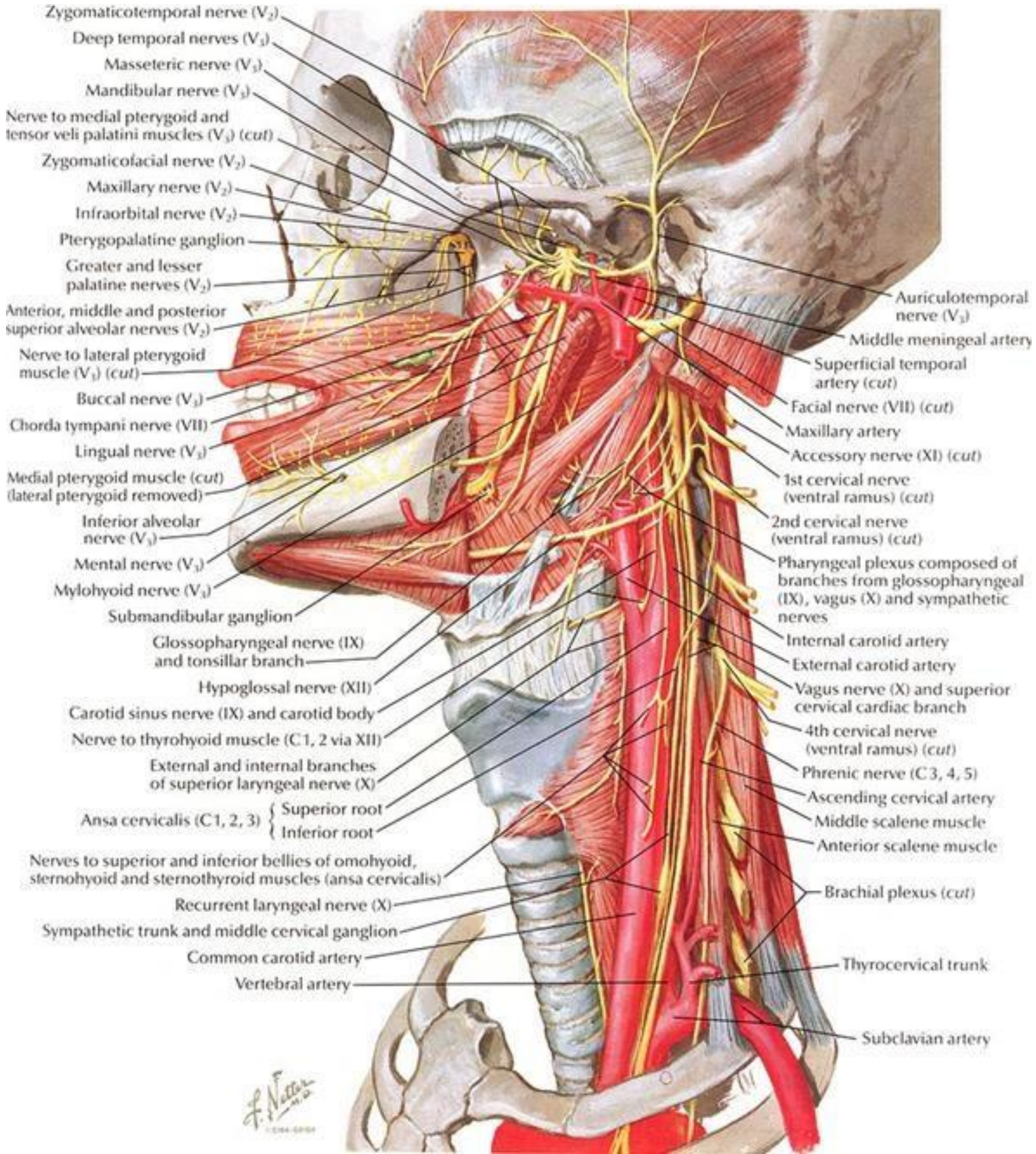
eLearning Modules by Experts

Published Literature

Clinical Trials

Contouring Atlases

So Let's take a look at the Head and Neck...



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Head and Neck

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0615

A PHASE II STUDY OF CONCURRENT CHEMORADIOTHERAPY USING THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY (3D-CRT) or INTENSITY-MODULATED RADIATION THERAPY (IMRT) + BEVACIZUMAB (BV) FOR LOCALLY OR REGIONALLY ADVANCED NASOPHARYNGEAL CANCER

NCI-supplied agent: Bevacizumab (NSC 704865; IND 79211)

A lot of contouring!

Critical Normal Structures

Surrounding critical normal structures, including the brainstem, spinal cord, optic nerves, chiasm, parotid glands, pituitary, temporo-mandibular (T-M) joints and middle and inner ears, skin (in the region of the target volumes), oral cavity, mandible, eyes, lens, temporal lobes, brachial plexus, esophagus (including postcricoid pharynx) and glottic larynx should be outlined.

Critical structures are ***critical***!

Planning Priorities

Critical normal structure constraints followed by the prescription goals are the most important planning priorities. The priorities in addressing the protocol aims and constraints will be in the following order:

1) Critical Normal Structure Constraints (Section 6.5);
2) Dose Specifications (Section 6.1);
3) Planning Goals: Salivary glands (Section 6.5.3);
4) Planning Goals: Other normal structures (Section 6.5.3).

Head and Neck

- RTOG Atlases for H&N do not cover OARs!!!

Head and Neck

Radiation Oncology, Head and Neck, Organs at Risk (OAR)

ID: 001523 | Approved:08 Aug 2013 | Last Modified: 02 Oct 2013 | Review Due:08 Se

Head and Neck Organs At Risk (OAR)

- Doses listed in the table below are based on radiation doses of 2Gy per fraction

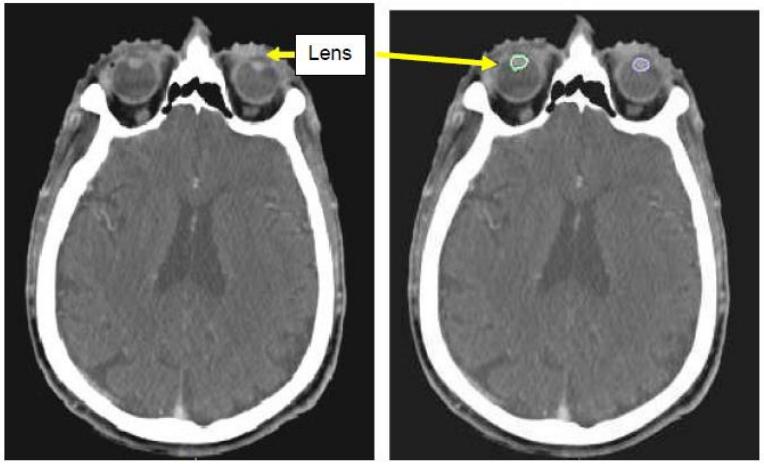
OAR Structure	Description based on RTOG 0920	True structure constraint (ideal)	Notes (Aim to keep doses as low as possible)
Brainstem	The inferior most portion of the brainstem is at the cranial-cervical junction where it meets the spinal cord. The superior most portion of the brainstem is approximately at the level of the top of the posterior clinoid. The brainstem shall be defined based on the treatment planning CT scan.	▪ Max dose ≤ 54Gy	Additional goals may include: ▪ ≤ 1% of PRV to exceed 60Gy ▪ small volumes (1-10cc) max dose ≤ 59Gy for fraction doses ≤ 2Gy [1]
Optic nerves		▪ Max dose ≤ 50Gy	Additional goals may include: ▪ ≤ 1% of PRV to exceed 60Gy ▪ To keep the risk of radiation induced optic neuropathy (RION) ≤ 3-7%, max dose 55-60Gy ▪ The risk of RION increases to 7-20% for doses > 60Gy in 1.8-2Gy fractions [2]
Optic Chiasm		▪ Max dose ≤ 54Gy	Additional goals may include: ▪ ≤ 1% of PRV to exceed 60Gy ▪ To keep risk of radiation induced optic neuropathy (RION) < 3-7%, max dose 55-60Gy ▪ The risk of RION increase to 7-20% for doses > 60Gy in 1.8-2Gy fractions [2]

Available from www.eviq.org.au

eviQ Head and Neck Critical Structures Atlas

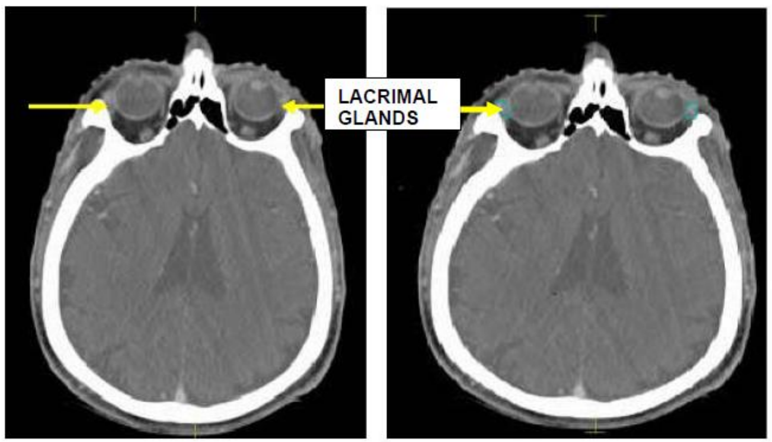
LENSES

Description: The lens is an anterior structure 5-8mm in length
Window level: W600/L40
Typical tolerance dose: 5Gy maximum



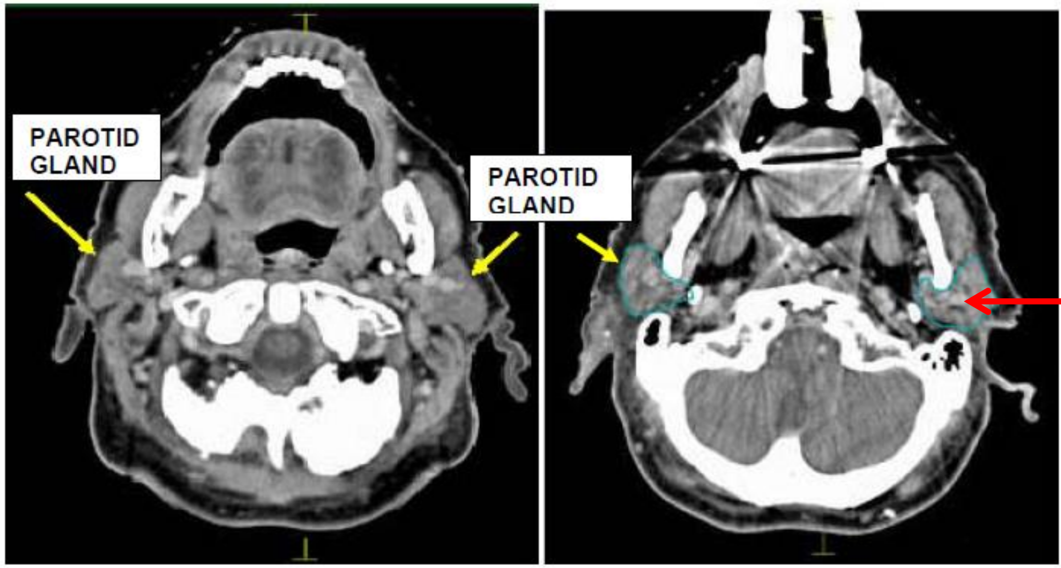
LACRIMAL GLAND

Location: Bilateral structure located supero-laterally to the orbits.
Length: Contoured extends approximately 10-15mm
Scroll through the images first to distinguish between muscle and the gland itself.
Window level: use approximately W270/L40 or W500/L60.
Typical Tolerance dose: <40Gy



- Shows adjacent images with and without contour
- Provides anatomical location, description, suggested window level and tolerance dose

eviQ Head and Neck Critical Structures Atlas



Note: degradation of image quality due to dental artefact

PAROTID GLAND

Location: The parotid gland is a bilateral glandular tissue lying anterior to the ear between the masseter muscle and the skin. It lies inferior to the zygomatic arch beneath the skin that covers the lateral and posterior surface of the mandible.
Length: approximately 50-60mm.
Borders: Medial Border is at the styloid process. Anteriorly hooks around the posterior aspect of anterior ramus of mandible.
Window level: use approximate window levels W290/L40 or W400/L80.
Typical tolerance doses: Mean parotid dose <26Gy (in at least one gland) or at least 50 % of one gland should receive <30Gy mean. (Doses to the parotid should be kept as low as reasonably achievable)

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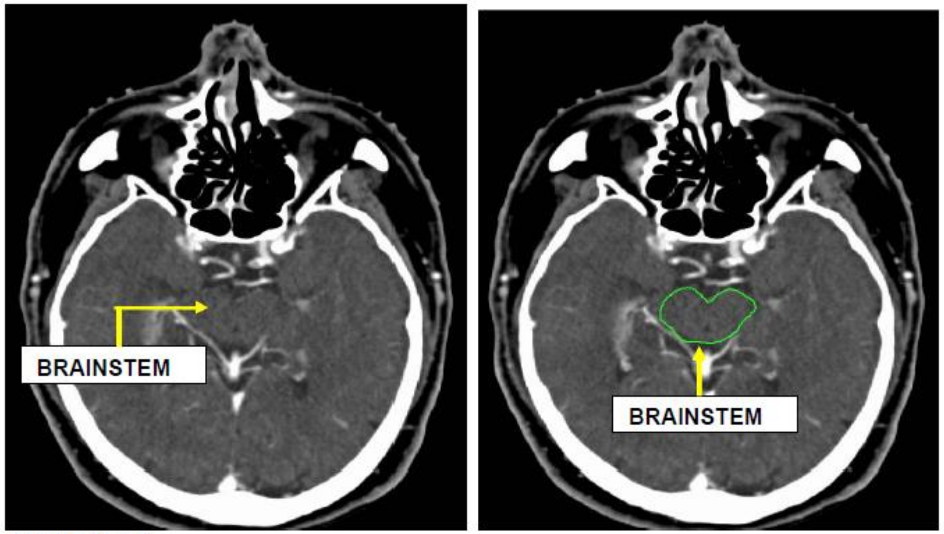
eviQ Head and Neck Critical Structures Atlas

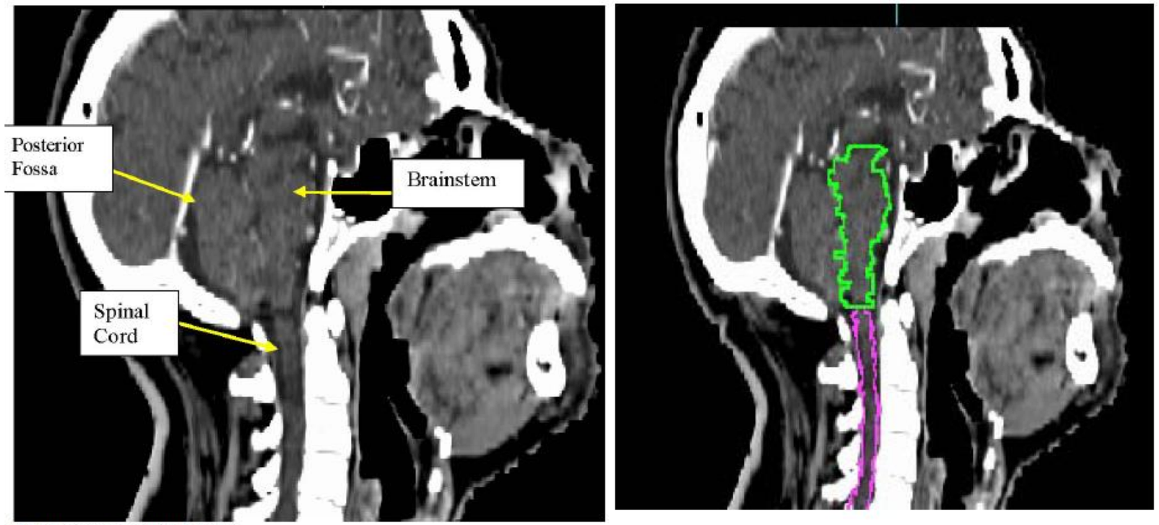
BRAINSTEM

Location: Superior to as well as a continuous structure from the proximal spinal cord, the brain stem is characterised by a sudden increase in width compared to the spinal cord above the level of the foramen magnum. The brain stem sits inferior to the optic chiasm. The brainstem is composed of the medulla, the pons and midbrain. It lies posterior to the bony clivus. Use sagittal view for ant/post definition; inferiorly it may be over contoured as spinal cord, due to tighter dose constraints.
Window level: Approximate window level of W200/L80.
Typical tolerance doses: <54Gy maximum.

Remember to view structures in all planes



Superior level



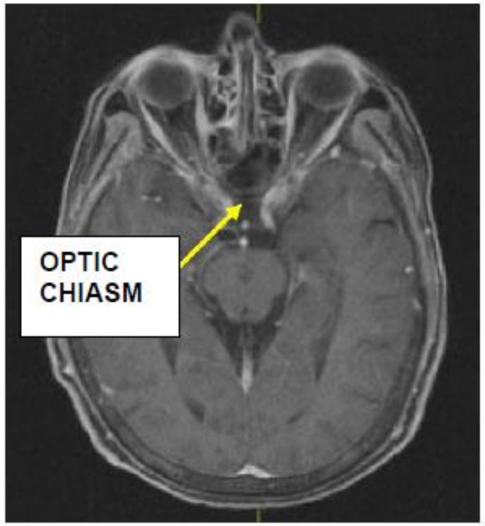
Brainstem sagittal view

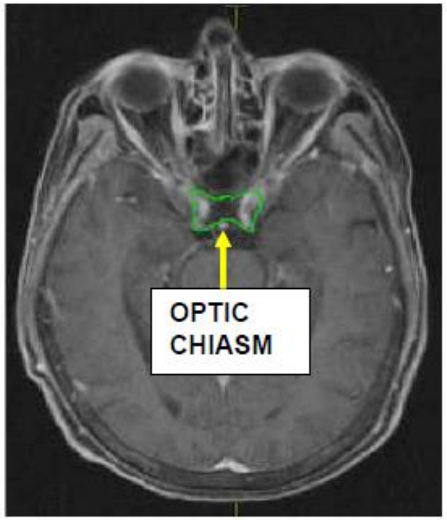
Note: It is important to avoid a gap between the brainstem and spinal cord contours as the emetic centre which controls nausea is located in this space. To avoid dose dumping in this region it is advised to overlap the contours by 1 CT slice to avoid a gap between these structures. (Monroe et al 2008 Radiother Oncol 87(2):188-194).

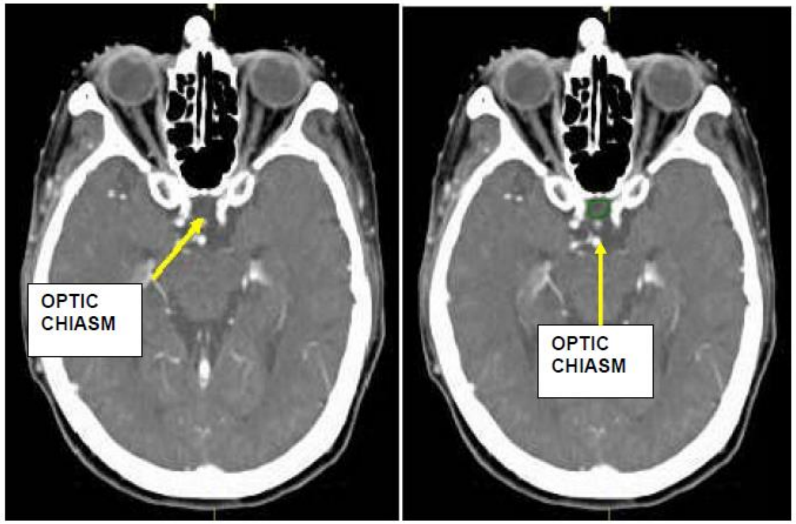
OPTIC CHIASM

Location: A butterfly-shaped structure which sits directly above the pituitary fossa. To aid in contouring trace the optic nerves to the point of posterior intersection to help with identifying the optic chiasm.
Course: Anterior it begins directly posterior to the optic canal. Begin contouring at this position. At this area it lies medial to the carotid arteries (which enhance with contrast) but anterior to the pituitary stalk. The optic chiasm joins in front of the pituitary stalk and then divides again posteriorly to travel to the most superior/anterior part of the brainstem (ie gives position of the most superior limit of the brainstem). It should look butterfly shaped.
Length: Approximately 5-8mm, consider using an MRI study set if it is available for easier visualisation of the optic chiasm.
Window level: use approximate window level of W220/L70.
Typical Tolerance dose: Ideally <50Gy with a maximum of <54Gy

Remember to use all imaging available for that patient







Published Literature

Radiotherapy and Oncology 117 (2015) 83–90

ELSEVIER

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Head and neck guidelines

CT-based delineation of organs at risk in the head and neck region: DAHANCA, EORTC, GORTEC, HKNPCSG, NCIC CTG, NCRI, NRG Oncology and TROG consensus guidelines

CrossMark

Charlotte L. Brouwer [a,*,1], Roel J.H.M. Steenbakkers [a,1], Jean Bourhis [b], Wilfried Budach [c], Cai Grau [d], Vincent Grégoire [e], Marcel van Herk [f], Anne Lee [g], Philippe Maingon [h], Chris Nutting [i], Brian O'Sullivan [j], Sandro V. Porceddu [k], David I. Rosenthal [l], Nanna M. Sijtsema [a], Johannes A. Langendijk [a]

Consensus panel of Radiation Oncologists from Europe, North America, Asia and Australia

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Head and Neck

- Don’t worry – even the “experts” have significant inter-observer variability

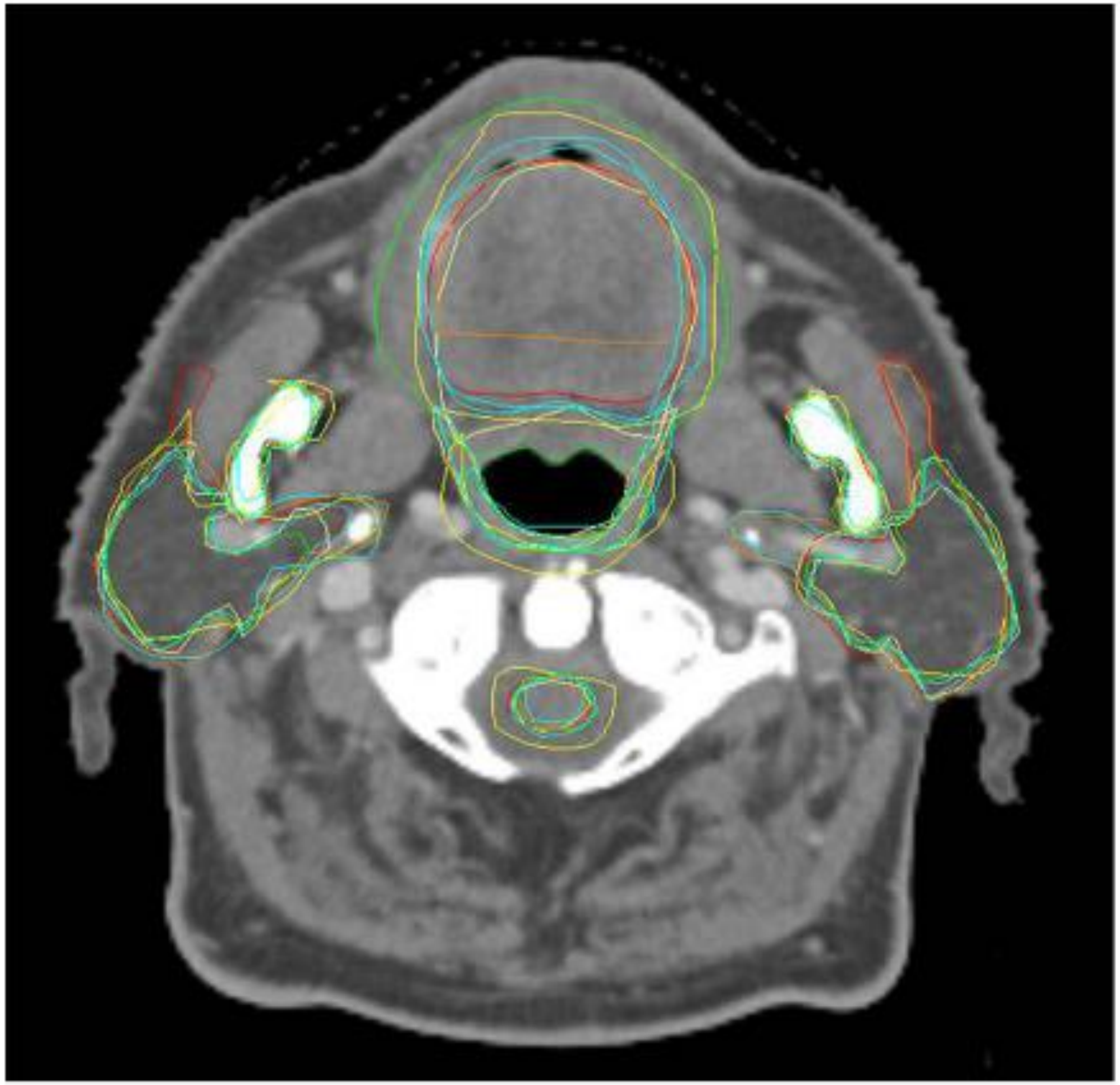


Fig. 1. Delineation results of 7 members of the panel for the parotid glands, spinal cord, pharyngeal constrictor muscles and the oral cavity, projected on an axial CT slice.

Head and Neck

- But still worth a read!
- Test and table description of anatomy with multimodality images to show

Supraglottic larynx

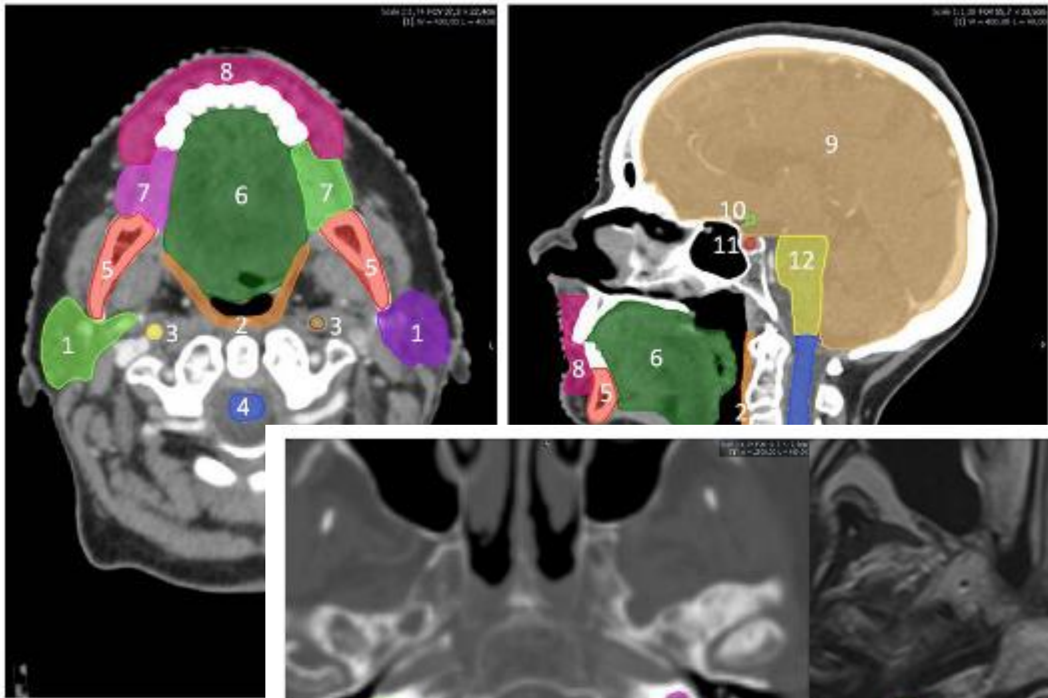
The supraglottic larynx is delineated according to Christianen et al. [7]. Anatomic borders are listed in Table 1. An axial slice of the supraglottic larynx is depicted in Fig. 4a.

Glottic area

We decided to define the glottic area structure, including the vocal cords and paraglottic fat. Air should be excluded from the contour. Cranial, caudal and posterior borders can be found in Table 1. An axial slice of the glottic area is depicted in Fig. 4b.

Arytenoids

The arytenoids (or arytenoids cartilage) are defined as a separate structure. The base (caudal edge) of each arytenoid is broad for articulation with the cricoid cartilage. The apex (cranial edge) is pointed.



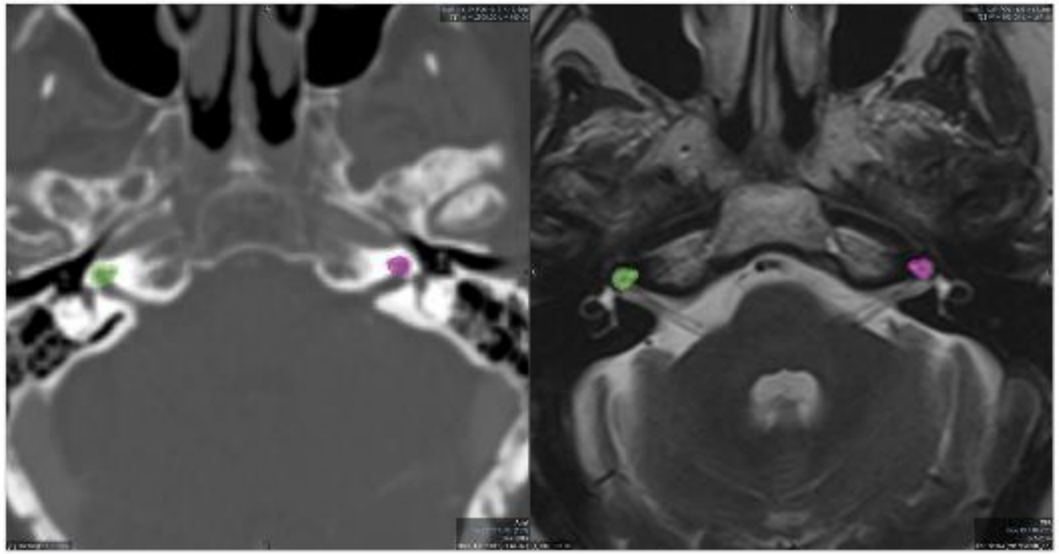
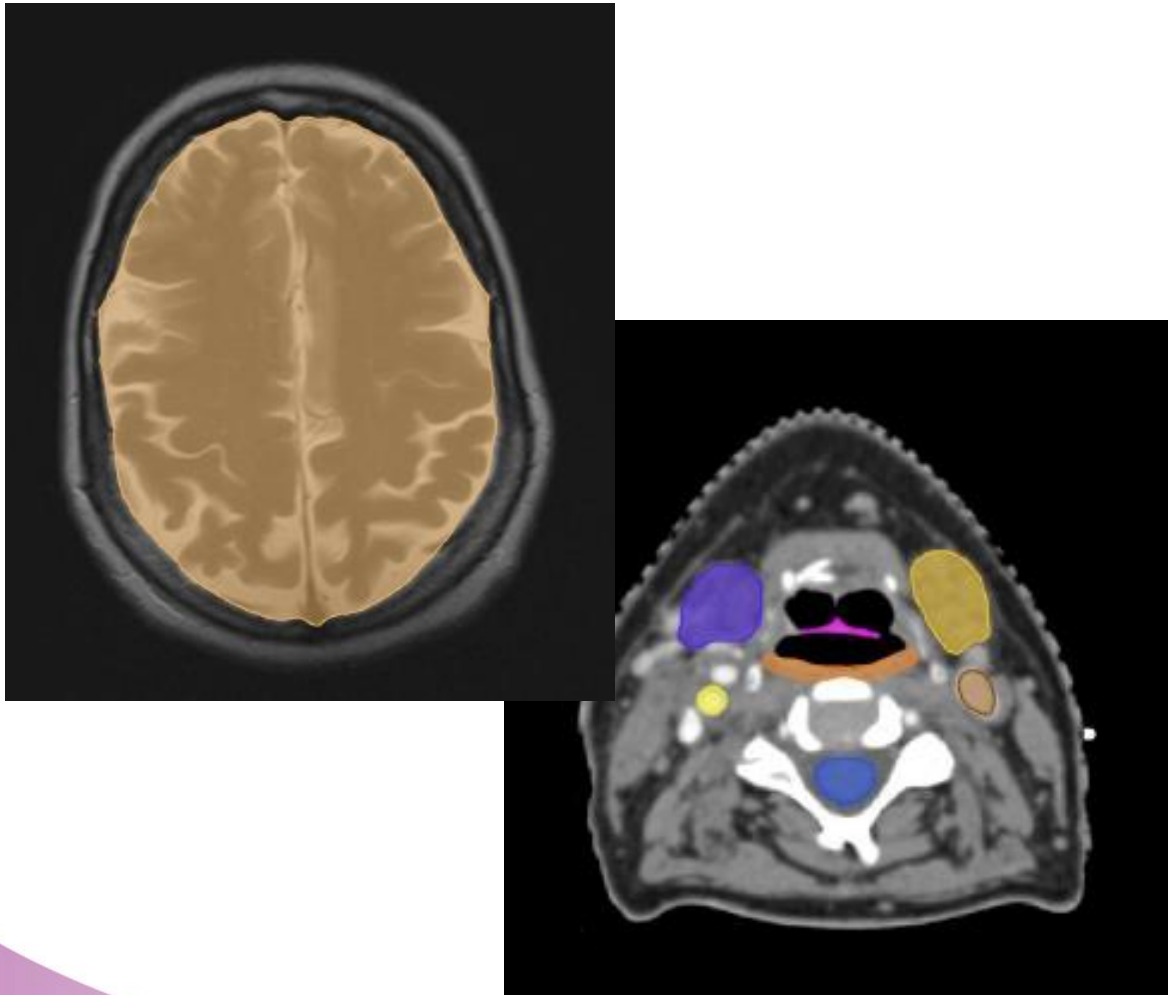


Fig. 2. Delineation of the cochlea in CT bone settings (left), matched to MRI-T2 (right).

Head and Neck

- Thank you – they have an atlas published as supplementary material



- Anterior segment of the eyeball L
- Anterior segment of the eyeball R
- Posterior segment of the eyeball L
- Posterior segment of the eyeball R
- Lacrimal gland L
- Lacrimal gland R
- Parotid gland L
- Parotid gland R
- Submandibular gland L
- Submandibular gland R
- Extended oral cavity
- Lips
- Mandible
- Cochlea L
- Cochlea R
- Pharyngeal constrictor muscles
- Glottic area
- Brachial plexus L
- Brachial plexus R
- Thyroid gland
- Brain
- Brainstem
- Pituitary gland
- Optic chiasm
- Optic nerve L
- Optic nerve R
- Spinal cord
- Carotid artery L
- Carotid artery R
- Buccal mucosa R
- Buccal mucosa L
- Arytenoid L
- Arytenoid R
- Crico-pharyngeal inle
- Cervical esophagus
- Supraglottic larynx

Head and Neck – ESTRO Support

Contouring of normal tissues in head and neck radiotherapy

Sandra Hol[Dr. Bernard Verbeeten Instituut]

ESTRO 35, Turin - Italy

Abstract text
In the head and neck region, there are a lot of organs at risk (OAR) to take into account when making a treatment plan. The radiation fields are often very large and can go up to the brain and down to the lungs. The OAR in this region are responsible for a lot of body functions, like walking, talking, swallowing and taste. Some of the OAR are parallel organs, so they will be able to compensate the loss of part of the organ and others are serial organs, which implies that the dose to the entire organ has to be below a threshold value in order to maintain the functionality.

In recent years most hospitals have started delineating more OAR in the head and neck region, but for some, there is no concensus on the constraints that have to be applied. Recently, consensus guidelines for head and neck OAR delineation were defined by Brouwer et al (1) To make sure that in the future we will be able to define constraints for these OAR we need a lot of data. This can only be obtained if there is consensus among institutes on delineation and reporting in the same manner.

In this presentation the different OAR will be discussed and a short summary of recently published guidelines will be provided.

(1) CT-based delineation of organs at risk in the head and neck region: DAHANCA, EORTC, GORTEC, HKNPCSG, NCIC CTG, NCRI, NRG Oncology and TROG consensus guidelines. Brouwer, C. et al. Radiother. Oncol. 2015; 117: 83–90.

[...less]

Head and Neck – ESTRO Support

Online Contouring Workshop Schedule for 2018

WORKSHOP DATES	WORKSHOP TOPIC
23 January 30 January	CNS Cancer
13 February 20 February	Head and Neck Cancer
20 March 27 March	OAR - Head and Neck

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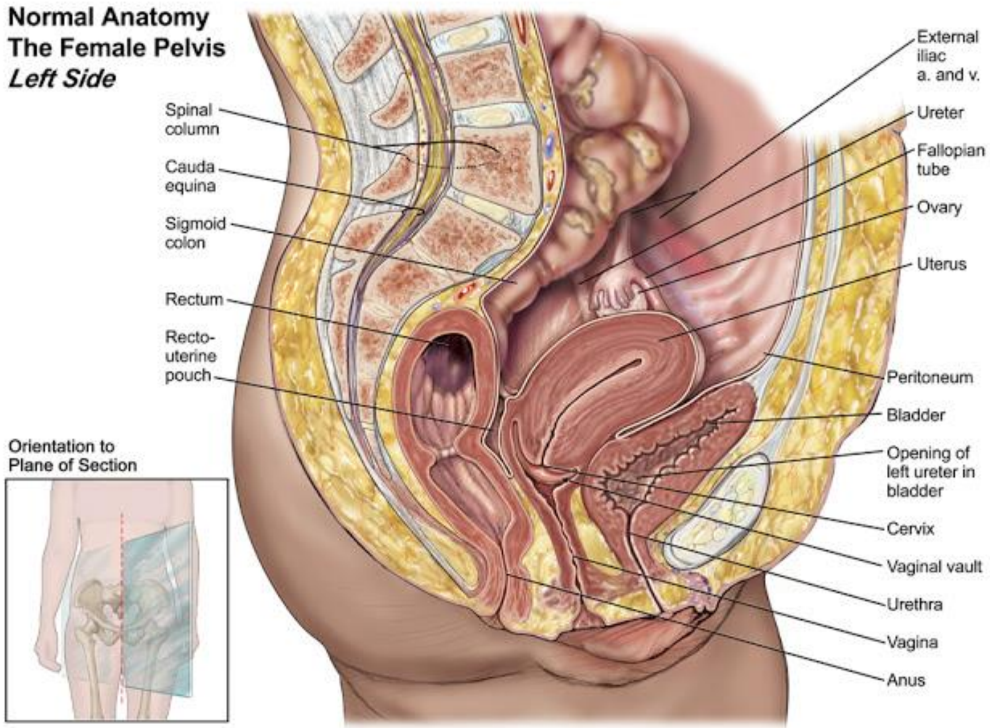
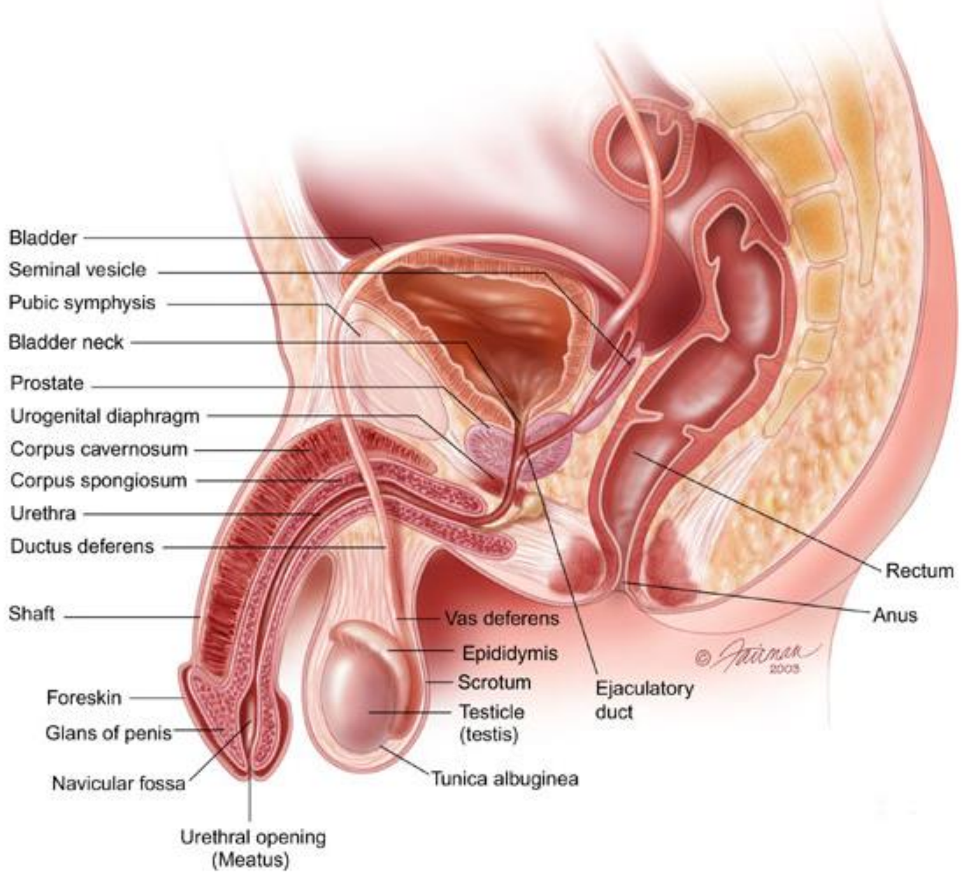
What about clinical trials?

So Let's take a look at the Pelvis...





RADIATION THERAPY ONCOLOGY GROUP

RTOG 0529

A Phase II Evaluation of Dose-Painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for Reduction of Acute Morbidity in Carcinoma of the Anal Canal

Critical Normal Structures: In addition, surrounding critical normal structures, including the femoral heads (right and left), bladder, external genitalia, iliac crest, small bowel, large bowel outside the CTVs, and perianal skin should be outlined. The normal tissues will be contoured and considered as solid organs. The tissue within the skin surface and outside all other critical normal structures and PTVs is designated as unspecified tissue.

Critical normal structures: DVHs must be generated for all critical normal structures.
NOTE: Effort should be made to achieve the listed dose constraints to normal tissues below. Failure to meet the 6.5.1.1 and 6.5.1.2 dose constraints will result in minor deviation. The dose constraints are listed in order from most to least important.

AGITG – For Anus

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation: Gastrointestinal Cancer

Australasian Gastrointestinal Trials Group (AGITG) Contouring Atlas and Planning Guidelines for Intensity-Modulated Radiotherapy in Anal Cancer

Michael Ng, M.B.B.S.(Hons), F.R.A.N.Z.C.R.,[*]
Trevor Leong, M.B.B.S., M.D., F.R.A.N.Z.C.R.,[†,‖]
Sarat Chander, M.B.B.S., F.R.A.N.Z.C.R.,[†] Julie Chu, M.B.B.S., F.R.A.N.Z.C.R.,[†]
Andrew Kneebone, M.B.B.S., F.R.A.N.Z.C.R.,[‡,**]
Susan Carroll, M.B.B.S., F.R.A.N.Z.C.R.,[§,**] Kirsty Wiltshire, M.B.B.S., F.R.A.N.Z.C.R.,[†]
Samuel Ngan, M.B.B.S., F.R.C.S.Ed., F.R.A.N.Z.C.R.,[†,‖] and Lisa Kachnic, M.D.[¶]

*Radiation Oncology Victoria, Victoria, Australia; [†]Department of Radiation Oncology, Peter MacCallum Cancer Centre, Victoria, Australia; [‡]Department of Radiation Oncology, Northern Sydney Cancer Centre, Royal North Shore Hospital, NSW, Australia; [§]Department of Radiation Oncology, Sydney Cancer Centre, Royal Prince Alfred Hospital, NSW, Australia; [¶]Department of Radiation Oncology, Boston Medical Center, Boston University School of Medicine, Boston, MA; [‖]University of Melbourne, Australia; and **University of Sydney, Australia

Received Jun 19, 2011, and in revised form Dec 13, 2011. Accepted for publication Dec 18, 2011

- Bladder
  - Entire outer wall
- Femoral Heads
  - Inferior – Cranial edge of the *lesser trochanter*
- Bowel
  - Small and large bowel
  - *15mm superior of PTV* down to the rectosigmoid junction
- External Genitalia
  - Male – penis, scrotum, skin and fat anterior to the pubic symphysis
  - Female - clitoris, labia majora and minora, skin and fat anterior to pubic symphysis
- Bone Marrow
  - Iliac crests, both contoured and combined
  - Superior - top of the iliac crests
  - Inferior - superior part of the acetabulum

Take note of positioning at Sim!

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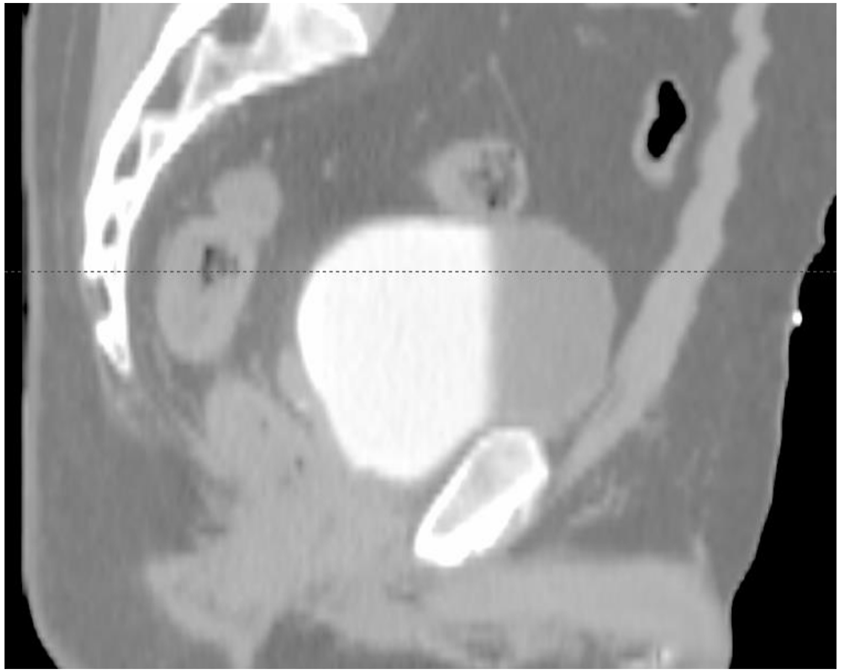
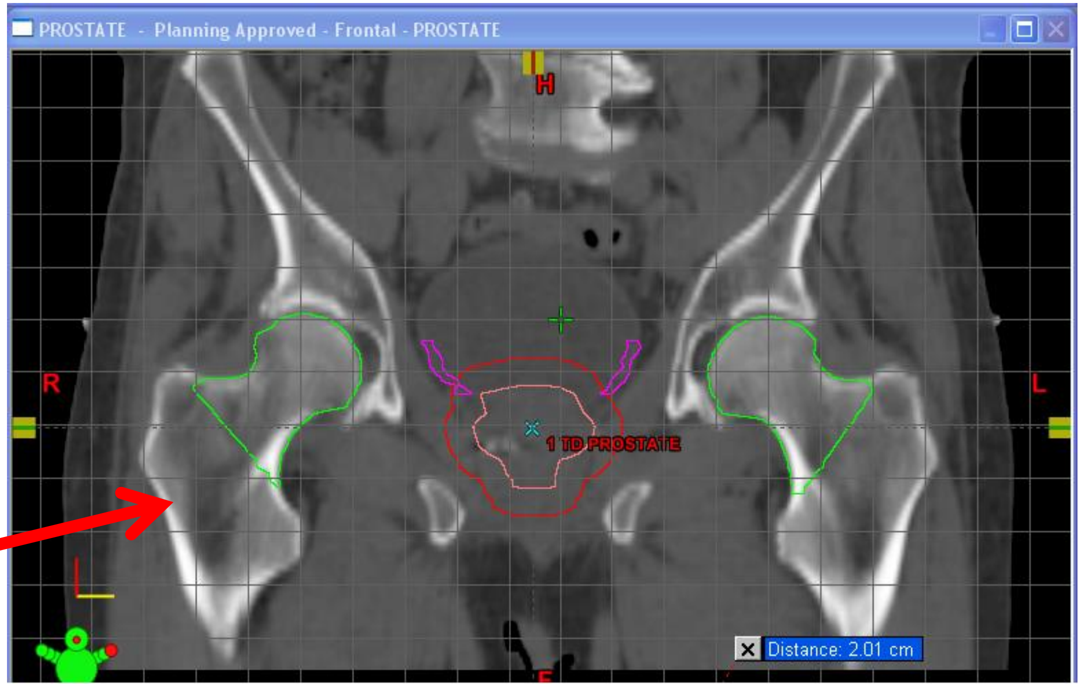
RAVES

- Femoral head:
  - ➢ Superior – acetabulum
  - ➢ Inferior – *inferior edge of the treatment field*
- Bladder:
  - ➢ Whole structure with bulk homogeneity correction for contrast
- Rectum:
  - ➢ Superior – rectosigmoid junction
  - ➢ Interior – *15mm inferior to the CTV*



PROFIT Trial

- Rectal *Wall*
- Bladder *Wall*
- Femoral Head and Neck



Let’s Look at Some Common OARs in the *Thorax*

Heart

Ribs

Lungs

Spinal Cord

Oesophagus

Main Bronchus

Brachial Plexus

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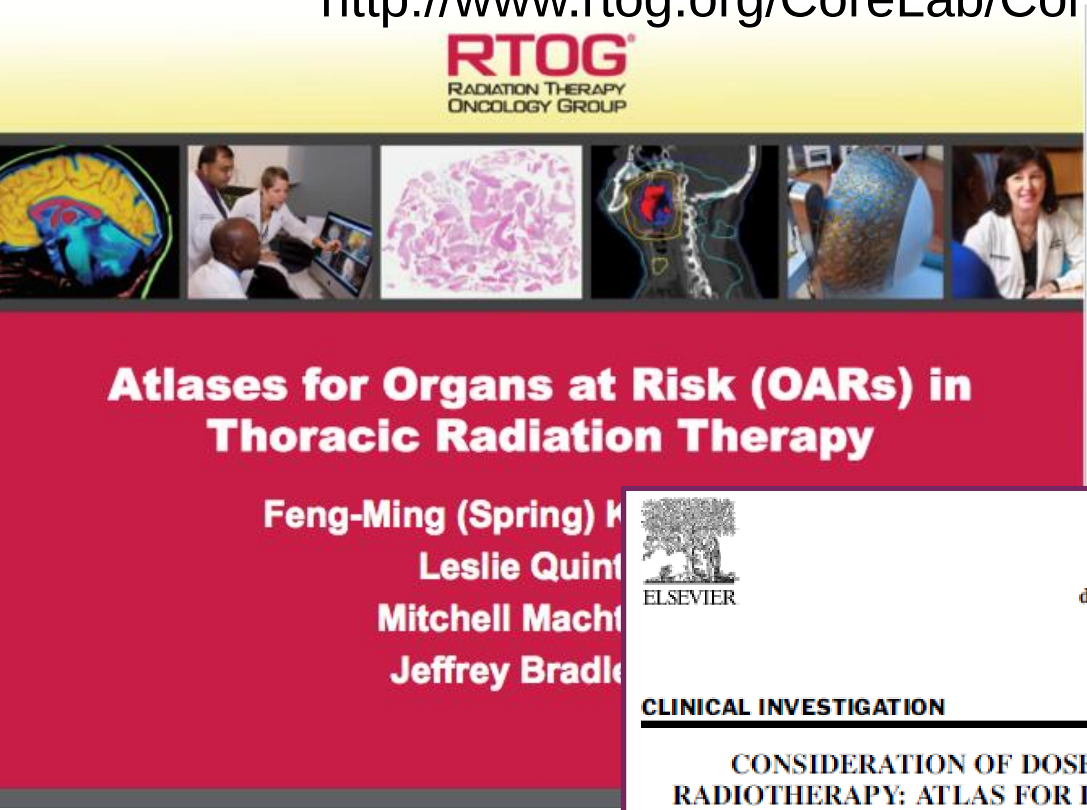
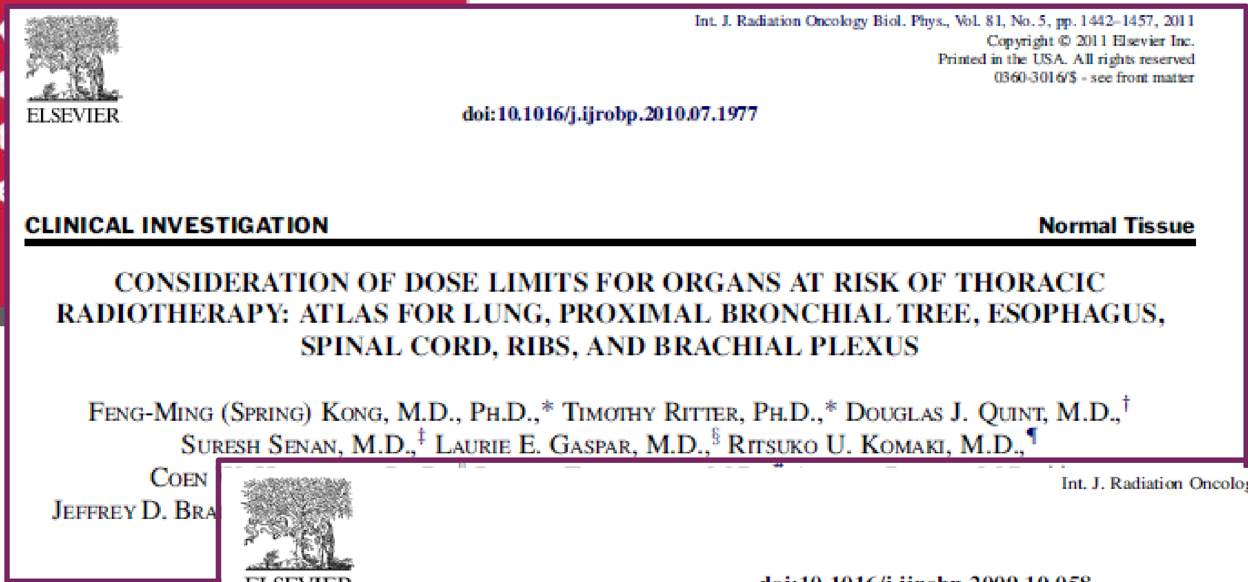
What Are Some of the Challenges You Faced?

- Windowing
- Length to contour
- Contrast
- Motion
- Exclusion of disease

RTOG Thoracic Atlas available from:

http://www.rtog.org/CoreLab/ContouringAtlases/LungAtlas.aspx





Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 5, pp. 1442–1457, 2011

0360-3016/$ - see front matter

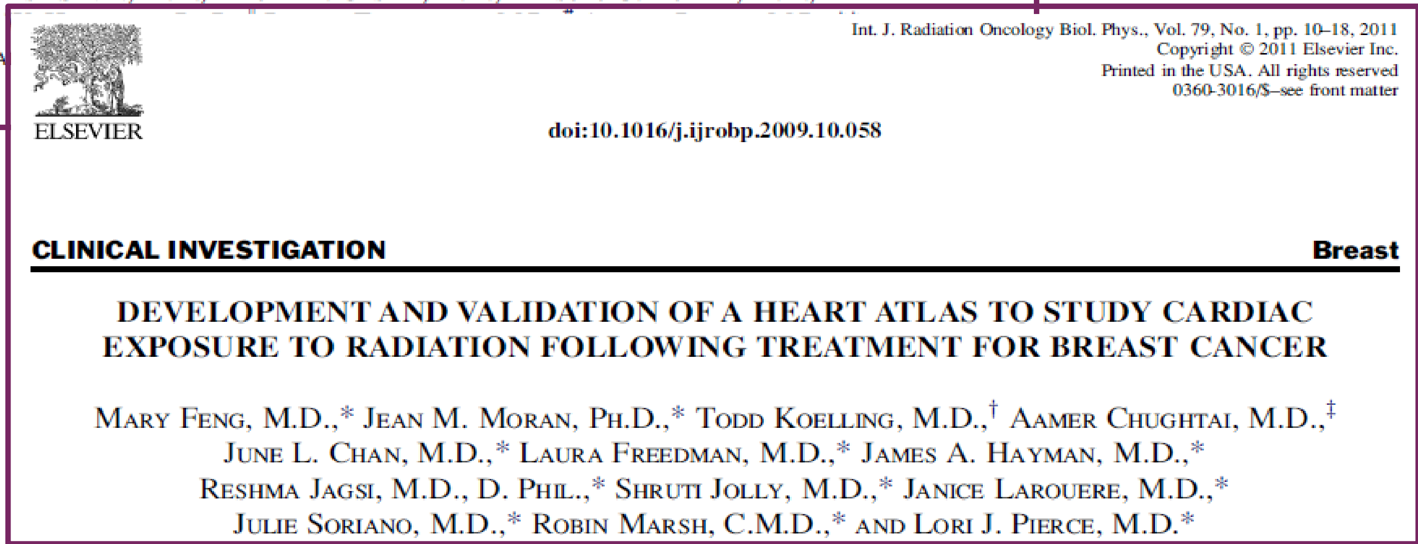
ELSEVIER

doi:10.1016/j.ijrobp.2010.07.1977

CLINICAL INVESTIGATION **Normal Tissue**

CONSIDERATION OF DOSE LIMITS FOR ORGANS AT RISK OF THORACIC RADIOTHERAPY: ATLAS FOR LUNG, PROXIMAL BRONCHIAL TREE, ESOPHAGUS, SPINAL CORD, RIBS, AND BRACHIAL PLEXUS

Feng-Ming (Spring) Kong, M.D., Ph.D.,* Timothy Ritter, Ph.D.,* Douglas J. Quint, M.D.,†
Suresh Senan, M.D.,‡ Laurie E. Gaspar, M.D.,§ Ritsuko U. Komaki, M.D.,¶
Coen
Jeffrey D. Bra



Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 1, pp. 10–18, 2011

0360-3016/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2009.10.058

CLINICAL INVESTIGATION **Breast**

DEVELOPMENT AND VALIDATION OF A HEART ATLAS TO STUDY CARDIAC EXPOSURE TO RADIATION FOLLOWING TREATMENT FOR BREAST CANCER

Mary Feng, M.D.,* Jean M. Moran, Ph.D.,* Todd Koelling, M.D.,† Aamer Chughtai, M.D.,‡
June L. Chan, M.D.,* Laura Freedman, M.D.,* James A. Hayman, M.D.,*
Reshma Jagsi, M.D., D. Phil.,* Shruti Jolly, M.D.,* Janice Larouere, M.D.,*
Julie Soriano, M.D.,* Robin Marsh, C.M.D.,* and Lori J. Pierce, M.D.*

What Do the Experts Say? - ***Lung***

Challenges

- Inappropriate window settings!
- Exclusion of disease from healthy lung?
- Inclusion of vessels?

Recommendations

- Air inflated lung only
  - Do not include fluid
- Contoured as single or combined structures
- Exclude lung GTV
- Exclude trachea/bronchus
- Exclude vessels >1cm
- Auto-segmentation is allowed combined with manual inspection
- Ensure appropriate windowing

What Do the Experts Say? – ***Spinal Cord***

Challenges

- Difficult to see true cord on CT
- Often not specifically covered in atlases
- Circumferential extend?
  - Contour cord or canal?
- Superior/Inferior extent
  - Entire length visible on planning scan or set distance from PTV?

Recommendations

- Use MRI fusion, if available
- Contour to the bony limits of the canal
- For lung cases, superior limit is the same as oesophagus (cricoid cartilage)
- Inferior limit is L2/L3 junction

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What Do the Experts Say? – ***Heart***

Challenges

- Contour specific structures within the heart?
- Superior limit

Recommendations

- Superiorly: Just inferior to the left pulmonary artery, include the great vessels in a rounded contour
- Inferiorly: to diaphragm, include pericardium
- If contrast is used, contour SVC separately

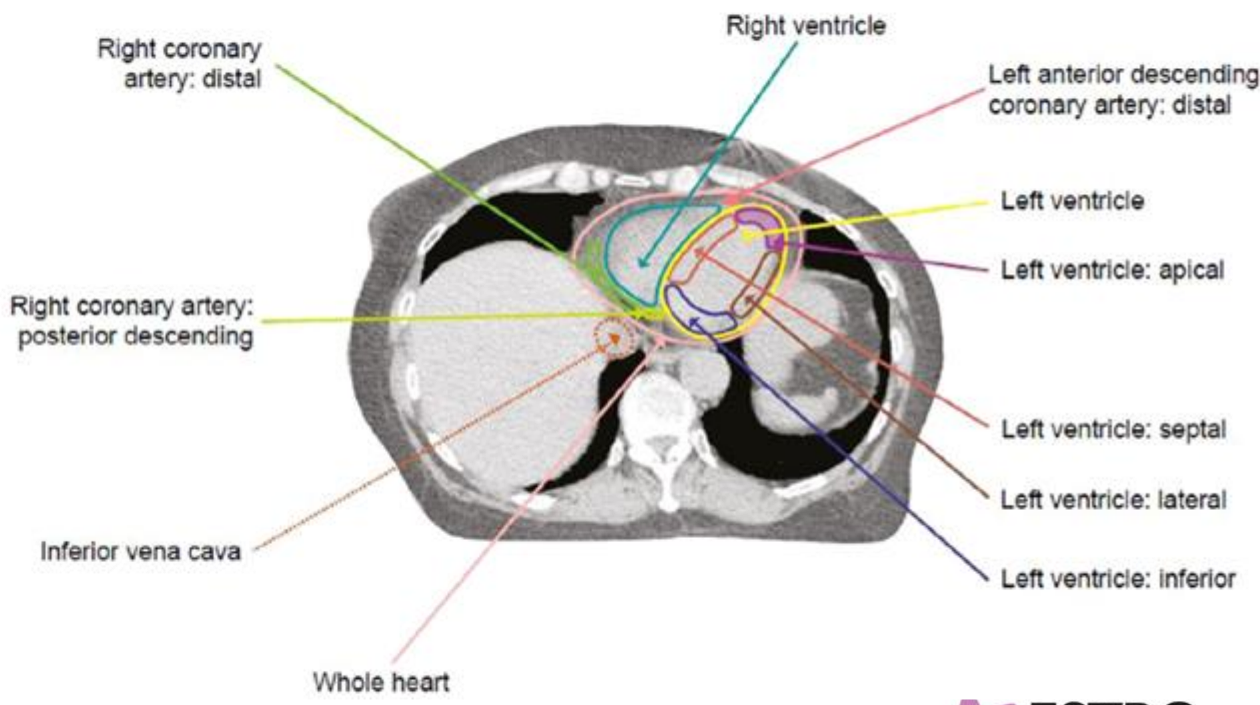
What Do the Experts Say? – ***Heart (Substructures)***

2017 Atlas in Green Journal

- Whole heart dose may not be the best predictor for the different types of radiation induced cardiac toxicity

- Focus on left ventricle and coronary arteries

F. Duane et al. / Radiotherapy and Oncology 122 (2017) 416–422



Dunane et al., 2017

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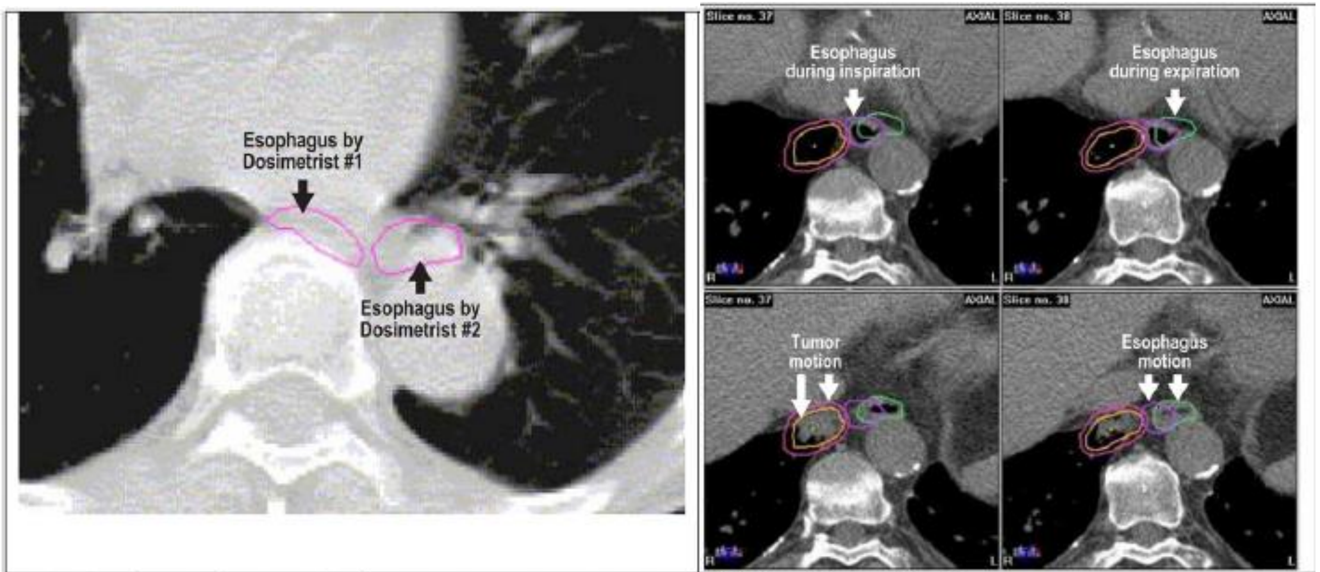
What Do the Experts Say? – ***Oesophagus***

Challenges

- Impact of windowing
- Impact of oral contrast
- Motion
- Inclusion of the muscular wall
- Length of contour

Recommendations

- Use mediastinal windowing level
- Contour from cricoid cartilage to gastro oesophageal junction
- Avoid oral contrast
    - Distorts shape and density



A: Esophagus Contour Variants B: Esophagus Motion

Other Points to Consider

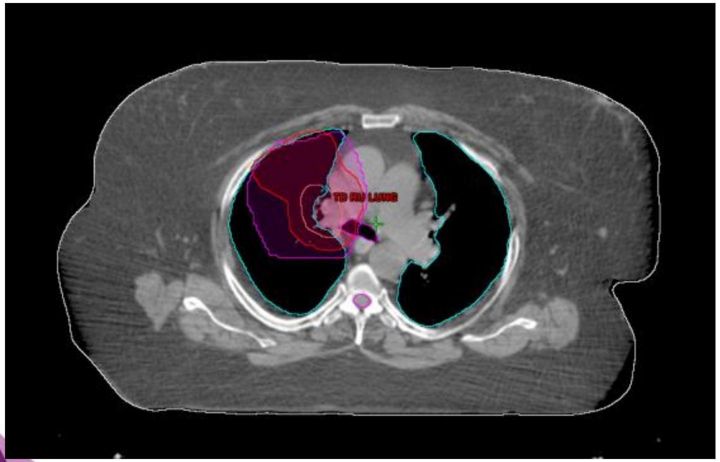
- Planning Risk Volume
  - Margin added to true structure
  - ICRU 83
  - RTOG H&N Trials

- Understand your potential errors
  - Recalculate plan with a error or shift induced to determine potential impact
    - Eg. Shift isocentre 3mm posterior for Head and Neck patient and review DVH

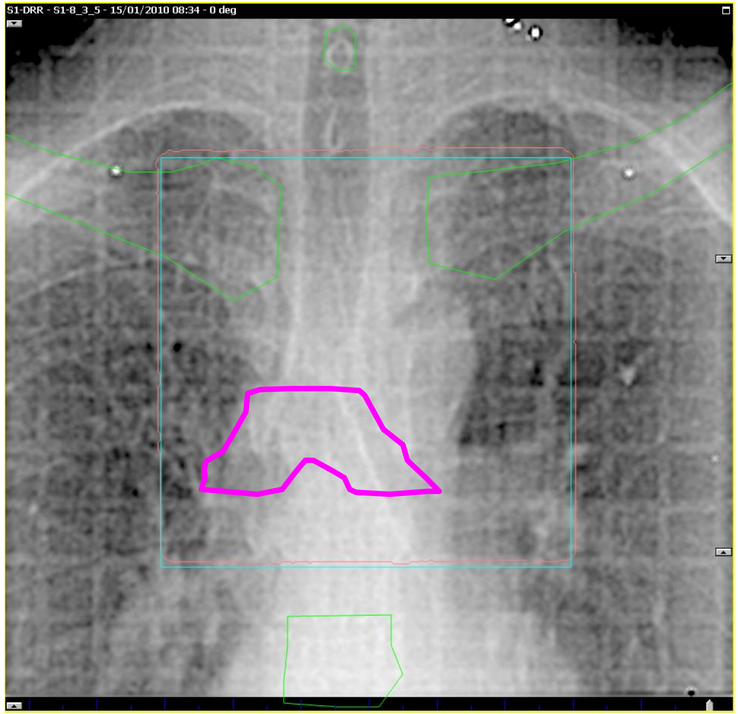
Other Structures for IGRT at the Linac

- What is the best surrogate for the target?
- What else can you see that might help you match?

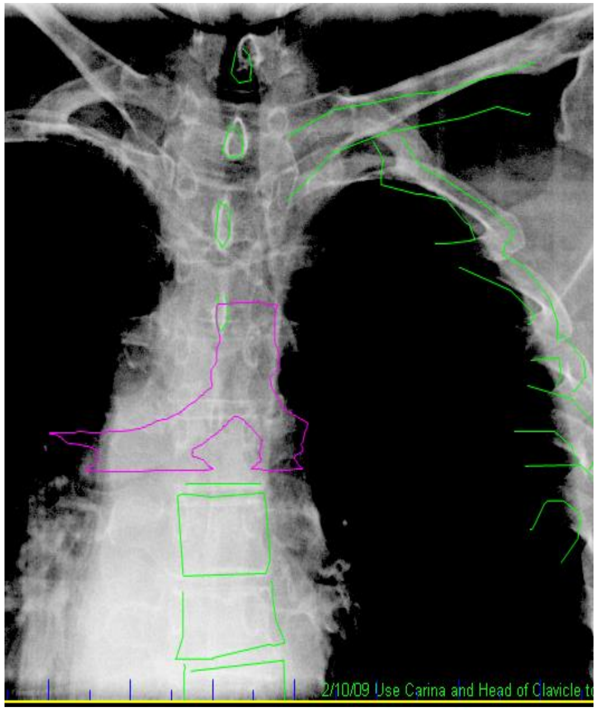
Planning CT



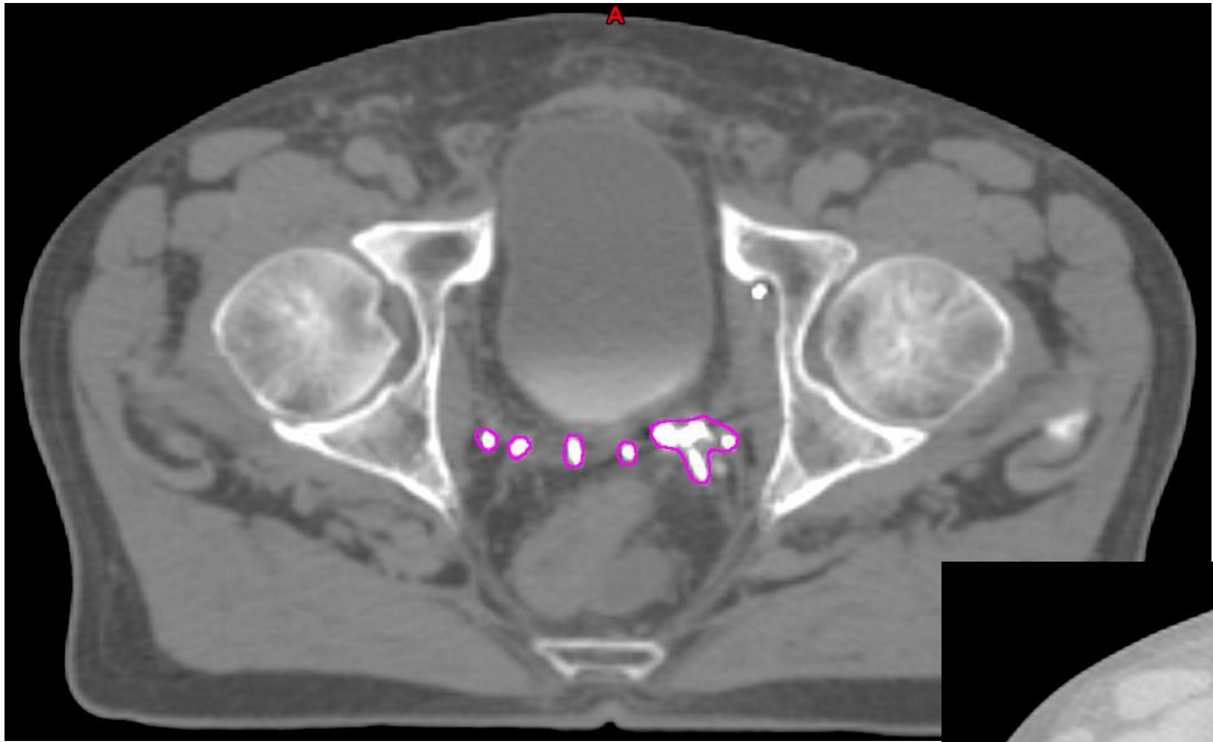
2D MV EPI

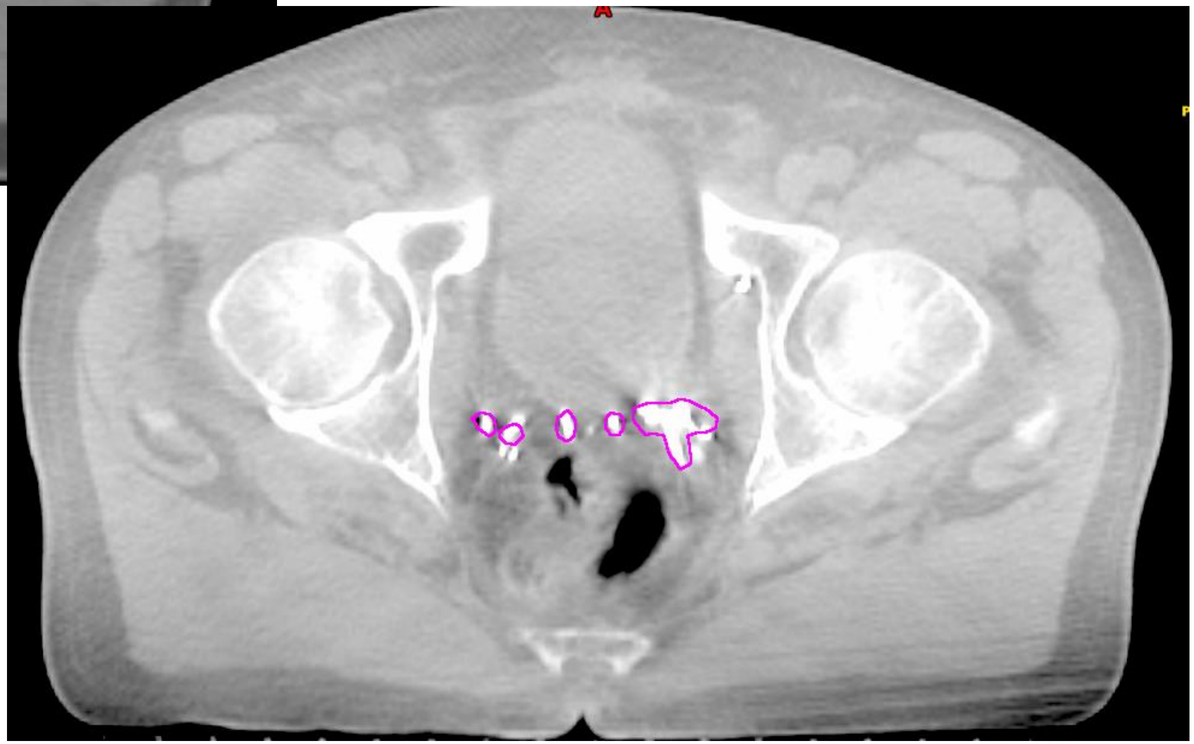


2D kV OBI



Other Structures for IGRT at the Linac





Take Home Message

- Quality assurance of organ delineation is vital regardless of who is responsible for OAR delineation
- "The accuracy of any autosegmenting tools should be carefully assessed" *(Marks et al., 2010)*
- Use all imaging modalities and viewing planes that you have available for that patient
- Think about the whole patient pathway
  - ➢ What will these contours impact on?
- Be consistent!
  - ➢ Preferably with international recommendations/consensus
  - ➢ At least at a local level

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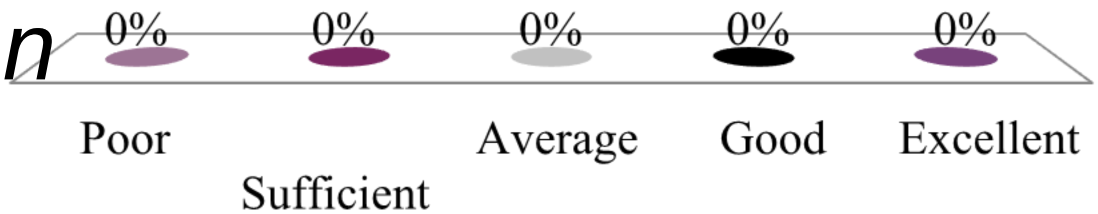
"Inaccuracy and variation in defining critical volumes will affect everything downstream: treatment planning, dose–volume histogram analysis, and contour based visual guidance used in image-guided radiation therapy"

(Nelms et al., 2012)

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on Survey Monkey



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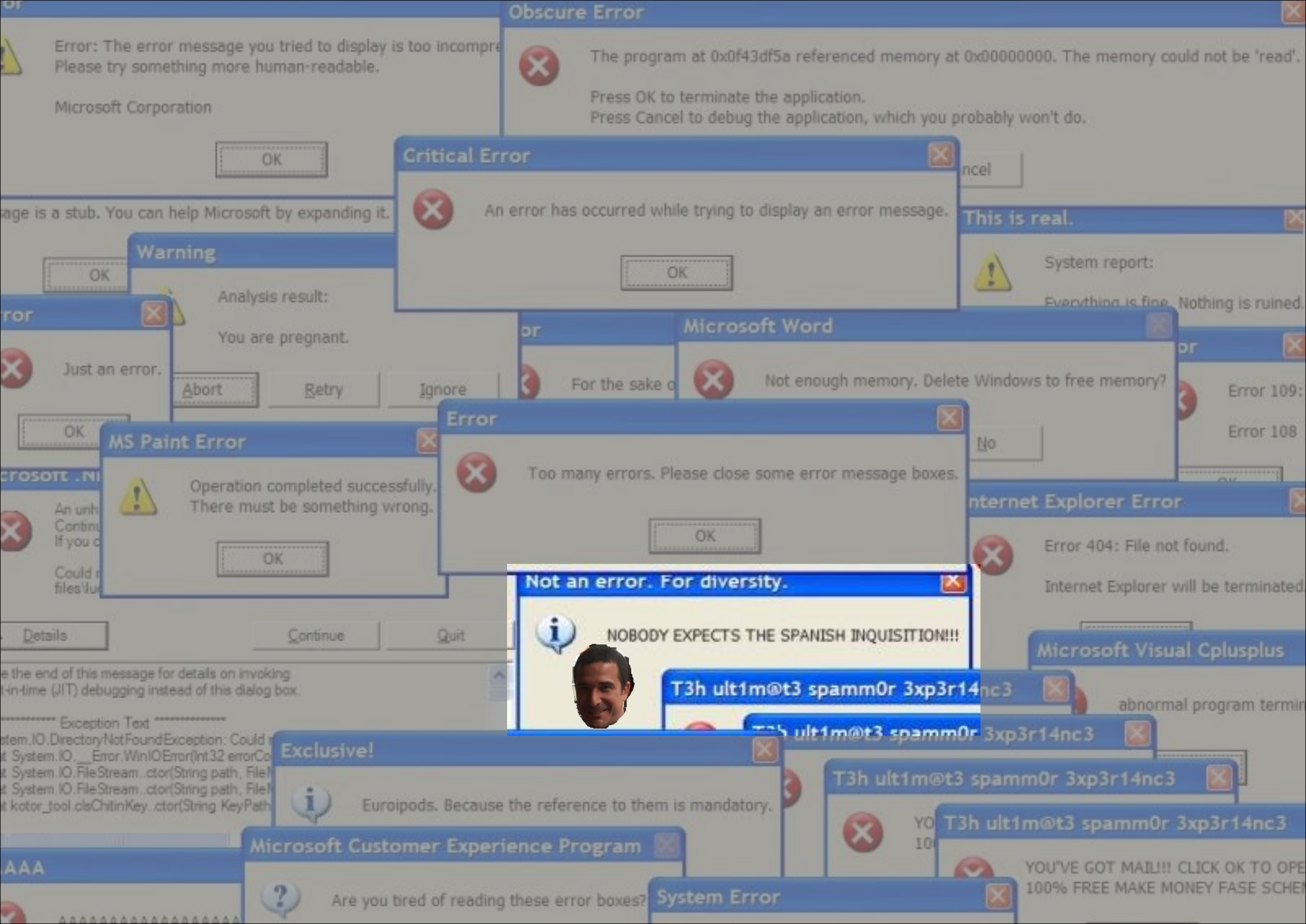
WWW.ESTRO.ORG/SCHOOL

Error management

Peter Remeijer
Department of Radiation Oncology
The Netherlands Cancer Institute

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

ESTRO School


Error: The error message you tried to display is too incompre
Please try something more human-readable.
Microsoft Corporation
OK
Obscure Error
The program at 0x0f43df5a referenced memory at 0x00000000. The memory could not be 'read'.
Press OK to terminate the application.
Press Cancel to debug the application, which you probably won't do.
ncel
Critical Error
An error has occurred while trying to display an error message.
OK
age is a stub. You can help Microsoft by expanding it.
OK
Warning
Analysis result:
You are pregnant.
Abort
Retry
Ignore
This is real.
System report:
Everything is fine. Nothing is ruined.
ror
Just an error.
OK
or
For the sake o
Microsoft Word
Not enough memory. Delete Windows to free memory?
No
Error 109:
Error 108
MS Paint Error
Operation completed successfully.
There must be something wrong.
OK
Error
Too many errors. Please close some error message boxes.
OK
nternet Explorer Error
Error 404: File not found.
Internet Explorer will be terminated
Not an error. For diversity.
NOBODY EXPECTS THE SPANISH INQUISITION!!!
Microsoft Visual Cplusplus
abnormal program termin
T3h ult1m@t3 spamm0r 3xp3r14nc3
Details
Continue
Quit
e the end of this message for details on invoking
t-in-time (JIT) debugging instead of this dialog box.
Exception Text
Exclusive!
Euroipods. Because the reference to them is mandatory.
T3h ult1m@t3 spamm0r 3xp3r14nc3
T3h ult1m@t3 spamm0r 3xp3r14nc3
YOU'VE GOT MAIL!!! CLICK OK TO OPE
100% FREE MAKE MONEY FASE SCHE
AAA
Microsoft Customer Experience Program
Are you tired of reading these error boxes?
System Error

More errors?

- Transfer errors (planning → linac)
- Linac errors (both dosimetric and geometric)
- Dosimetric errors in plan
- Input errors
- Patient setup (e.g. CT reference to isoc shifts)
- Select the right patient / treatment in all systems

More errors?

- Transfer errors (planning → linac)
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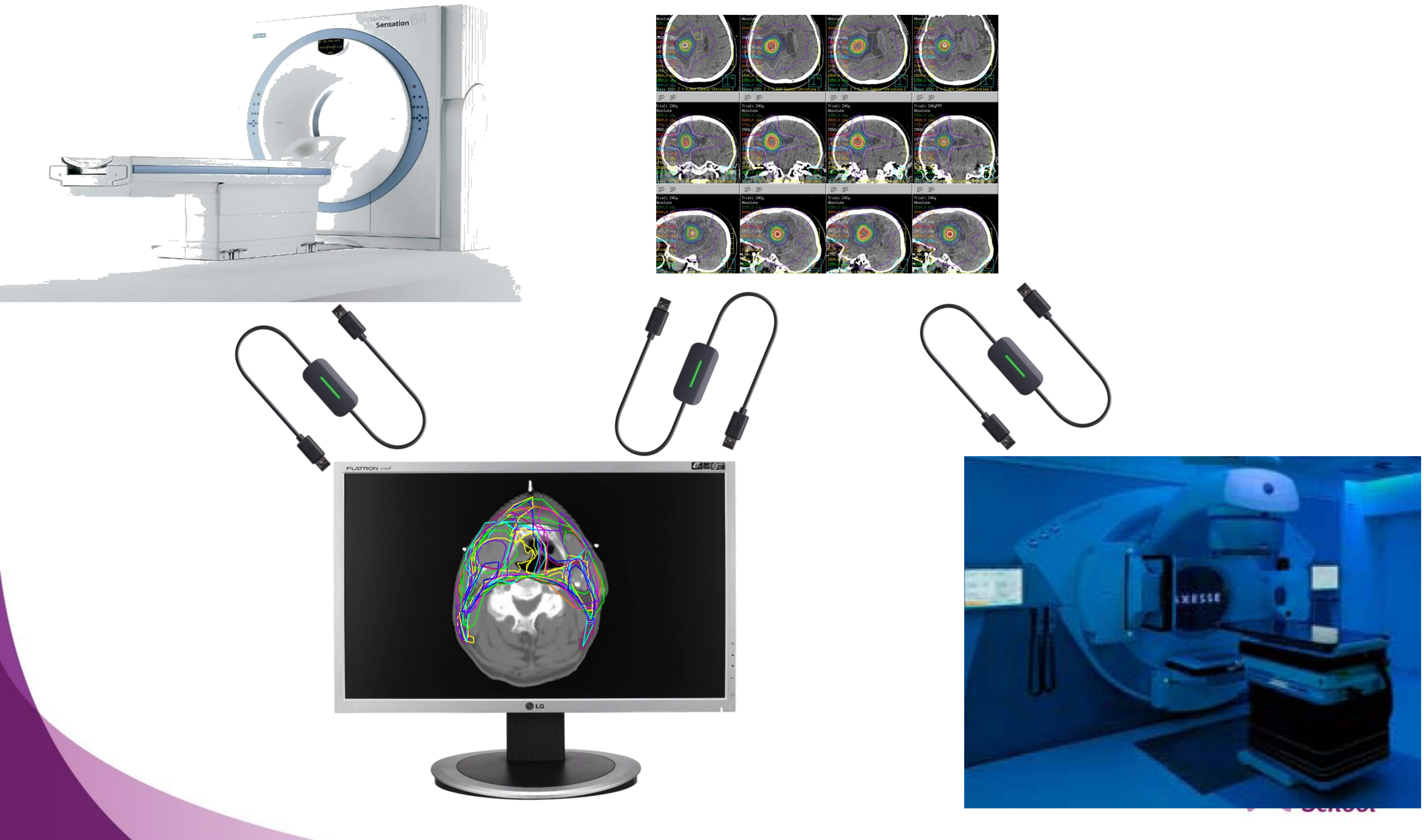
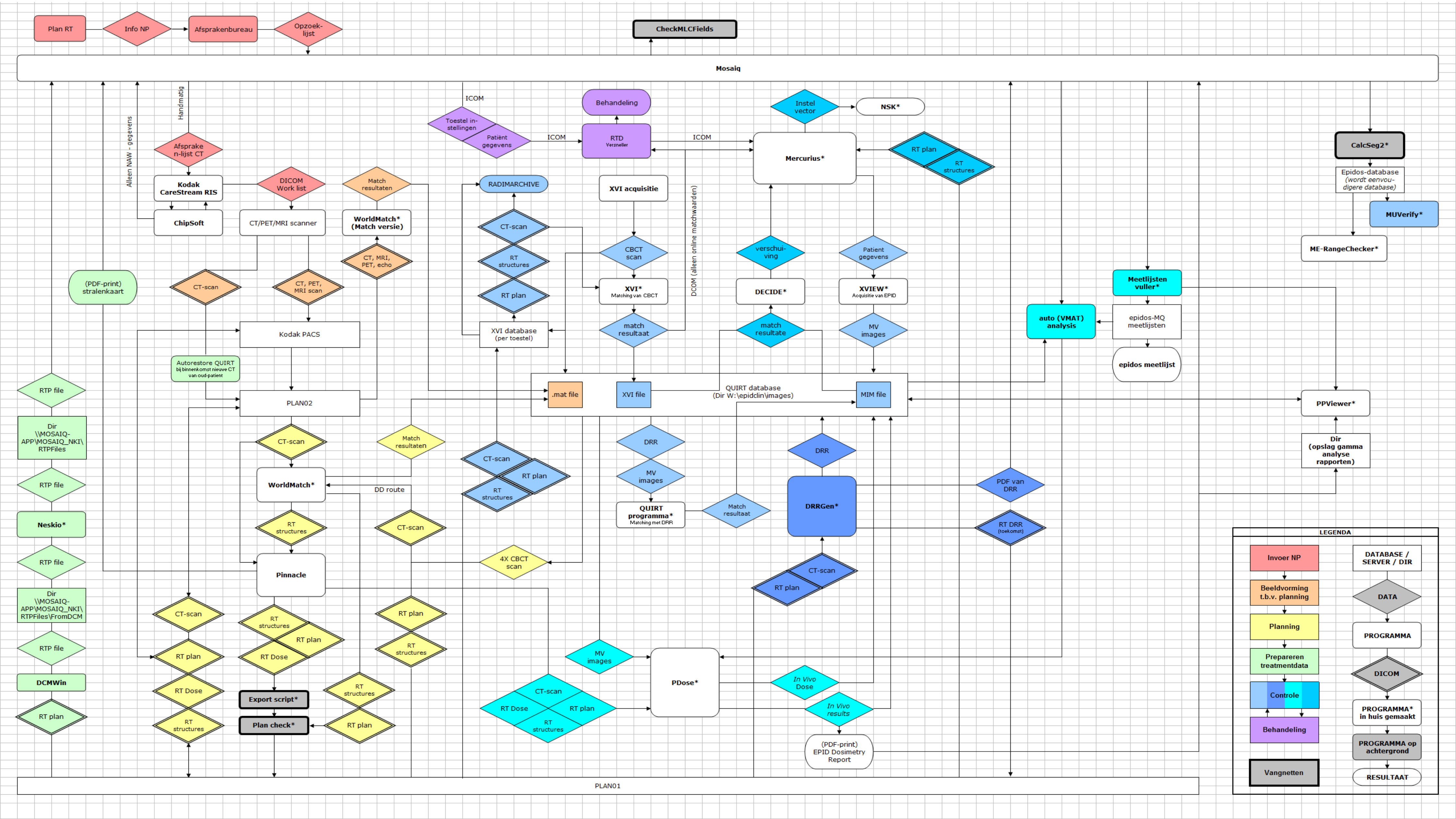
- Patient setup (e.g. CT reference to isoc shifts)
- Input errors
- Select the right patient / treatment in all systems

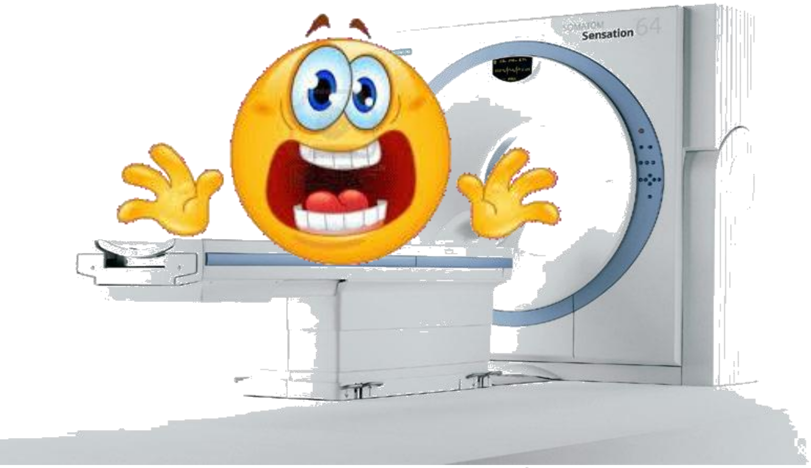
Errors and the radiotherapy "chain"

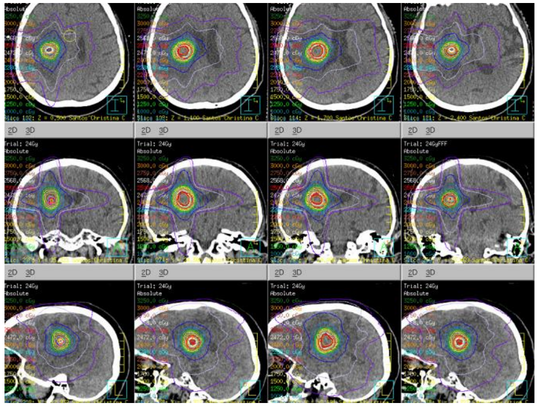


The radiotherapy “chain”



“Chain test” a.k.a regression test with phantom





Regression testing

- Run a phantom through the whole treatment chain and check for problems / errors
  - May be necessary to do this for different situations, i.e. HFS, HFP, etc
  - New methods, e.g. ART, library of plans, new planning techniques (VMAT)
- This will check
  - Connectivity
  - Systematic equipment and software errors
  - Overall dosimetry
  - Overall geometry

More errors?

- Transfer errors (planning → linac)
- Linac errors (both dosimetric and geometric)
- Dosimetric errors in plan
- Patient setup (e.g. CT reference to isoc shifts)
- Input errors
- Select the right patient / treatment in all systems

Independent MU checks

- Recalculates the dose, based on the plan parameters from the planning system (or v.v.)

- This will check (in theory)
  - Amount of monitor units
  - Problems with plan normalization
  - Computation errors of planning system

- Third party software
  - Lots of software around (small companies)
  - Check what it really checks
  - Test with intentional errors

MU range checking

- In house NKI development, but easy to build
- Plans following a certain protocol, e.g. prostate
  - Amount of MU for a VMAT plan will be similar for each patient
  - Depends a little on patient size, etc

→ MU range check

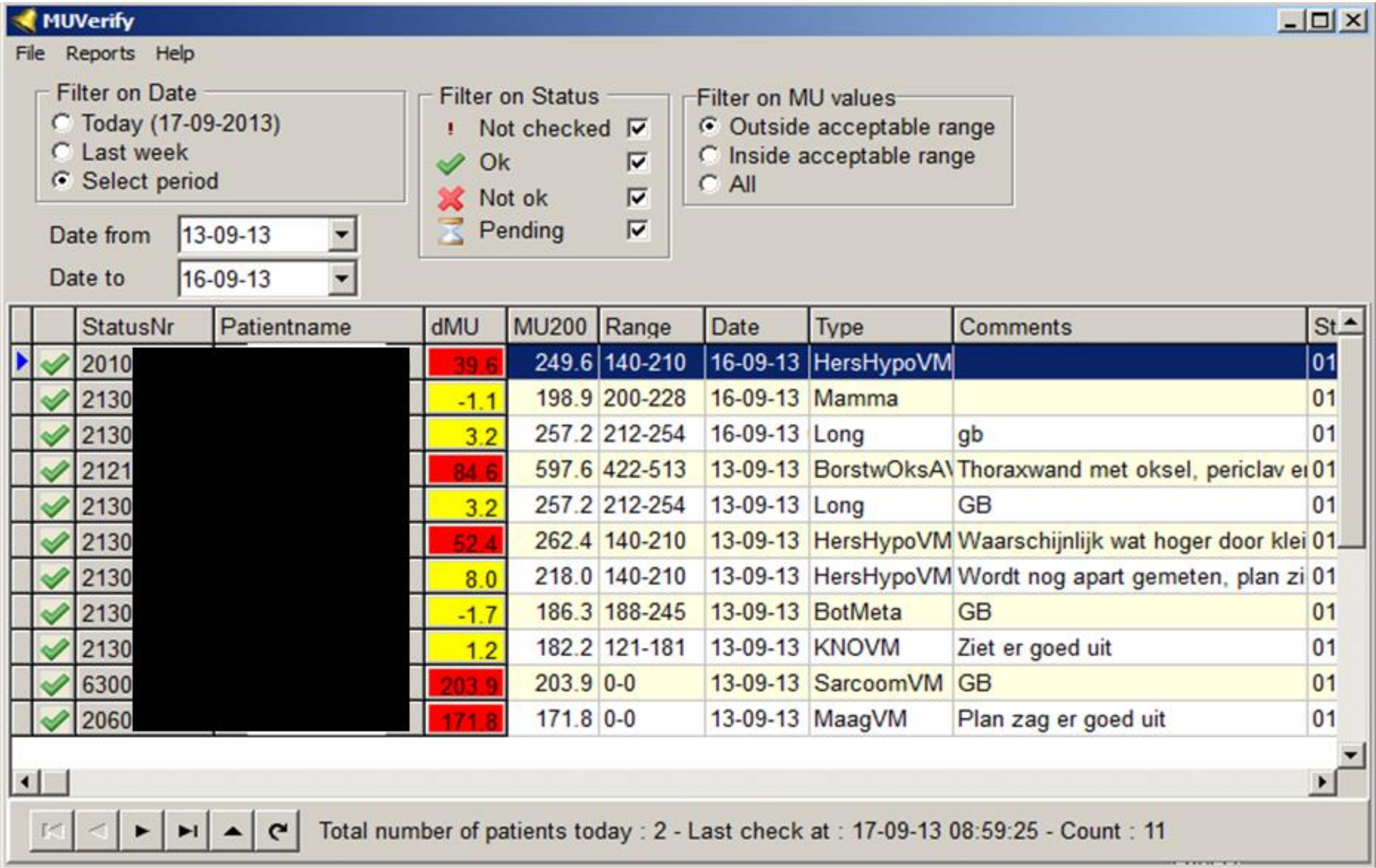
- If patient does not fall within the range, something may have gone wrong
- Check by physics
- About 5-10%
- Usually anatomical reasons
- Some errors found (wrong dose specification point, #fractions)

MU range checking

- Plan type depends on
  - Careplan name (brain, breast, prostate, etc)
  - RX-site name (plan name), e.g. Sacrum <231290>
  - Number of beams
  - Number of segments
  - Energy
  - Fraction dose
- Range for each type

CP	Nbeam		Nsegm		Energy		Fr.Dosis		Type	Min	Max
Anus	2	8	2	70	6	10	180	300	Anus	188	261
Blaas	1	2	70	180	6	10	180	400	BlaasVM	158	218
Cervix	2	10	2	60	6	10	180	800	Gyn	221	284

Automated message on desktop of physicist



StatusNr	Patientname	dMU	MU200	Range	Date	Type	Comments	St
2010	[redacted]	39.6	249.6	140-210	16-09-13	HersHypoVM		01
2130	[redacted]	-1.1	198.9	200-228	16-09-13	Mamma		01
2130	[redacted]	3.2	257.2	212-254	16-09-13	Long	gb	01
2121	[redacted]	84.6	597.6	422-513	13-09-13	BorstwOksA\	Thoraxwand met oksel, periclav e	01
2130	[redacted]	3.2	257.2	212-254	13-09-13	Long	GB	01
2130	[redacted]	52.4	262.4	140-210	13-09-13	HersHypoVM	Waarschijnlijk wat hoger door klei	01
2130	[redacted]	8.0	218.0	140-210	13-09-13	HersHypoVM	Wordt nog apart gemeten, plan zi	01
2130	[redacted]	-1.7	186.3	188-245	13-09-13	BotMeta	GB	01
2130	[redacted]	1.2	182.2	121-181	13-09-13	KNOVM	Ziet er goed uit	01
6300	[redacted]	203.9	203.9	0-0	13-09-13	SarcoomVM	GB	01
2060	[redacted]	171.8	171.8	0-0	13-09-13	MaagVM	Plan zag er goed uit	01

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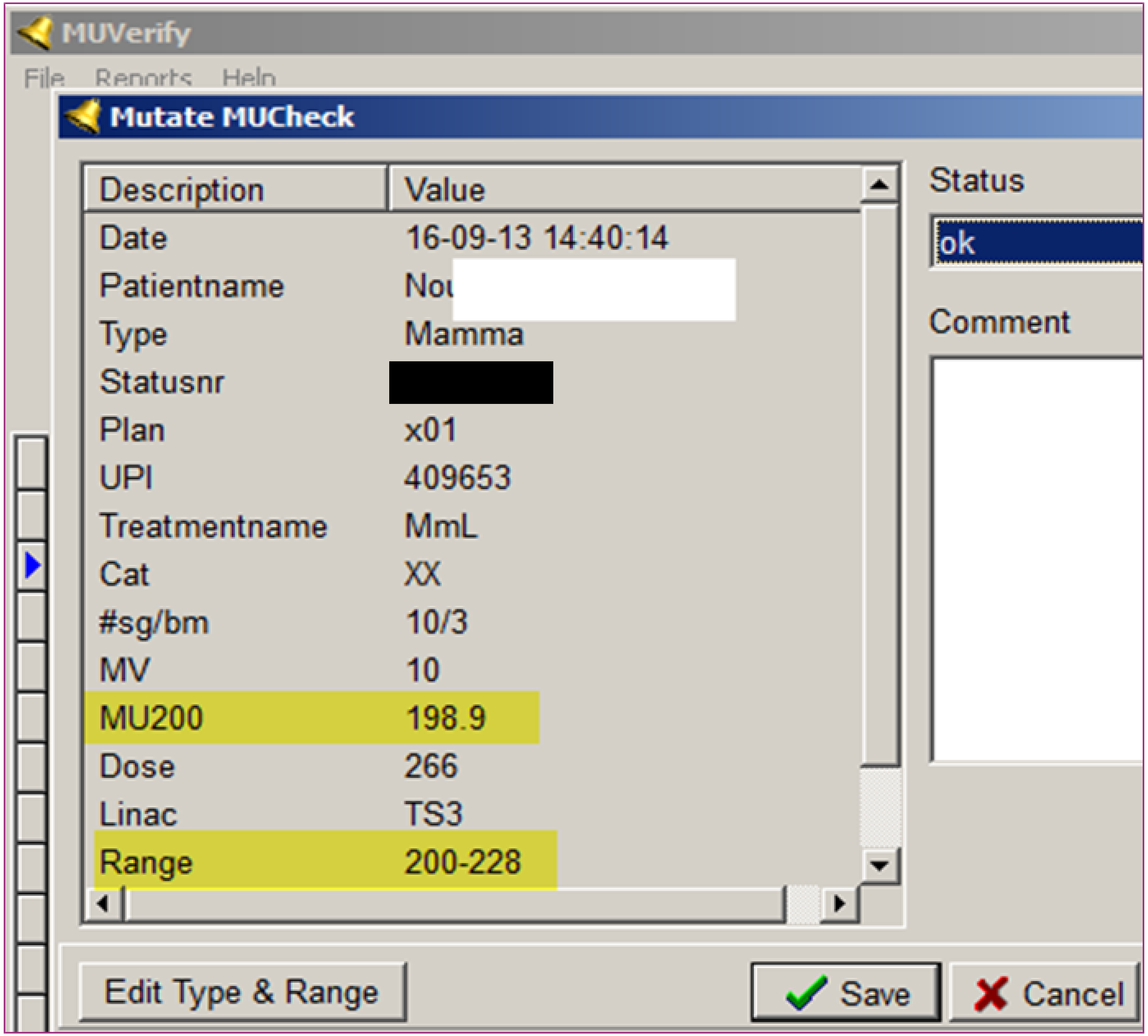
Automated message on desktop of physicist

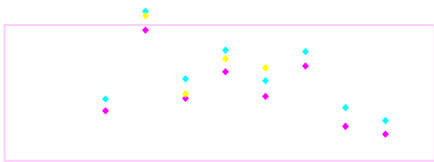


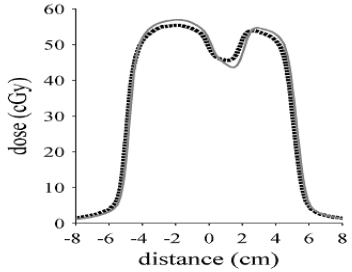
In-vivo portal dosimetry

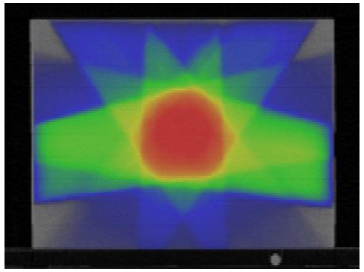
in most centres today:

	0D	1D	2D

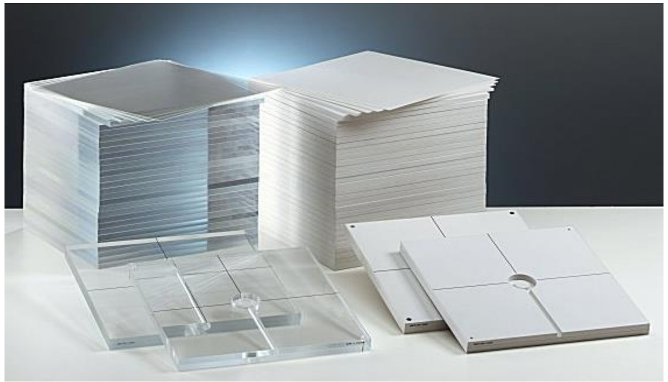
not 3D



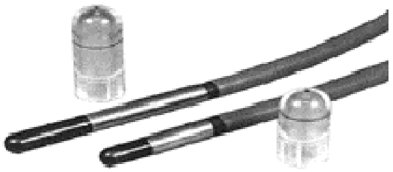


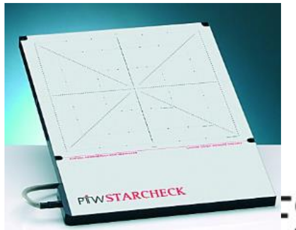


not *in vivo*



not with an EPID





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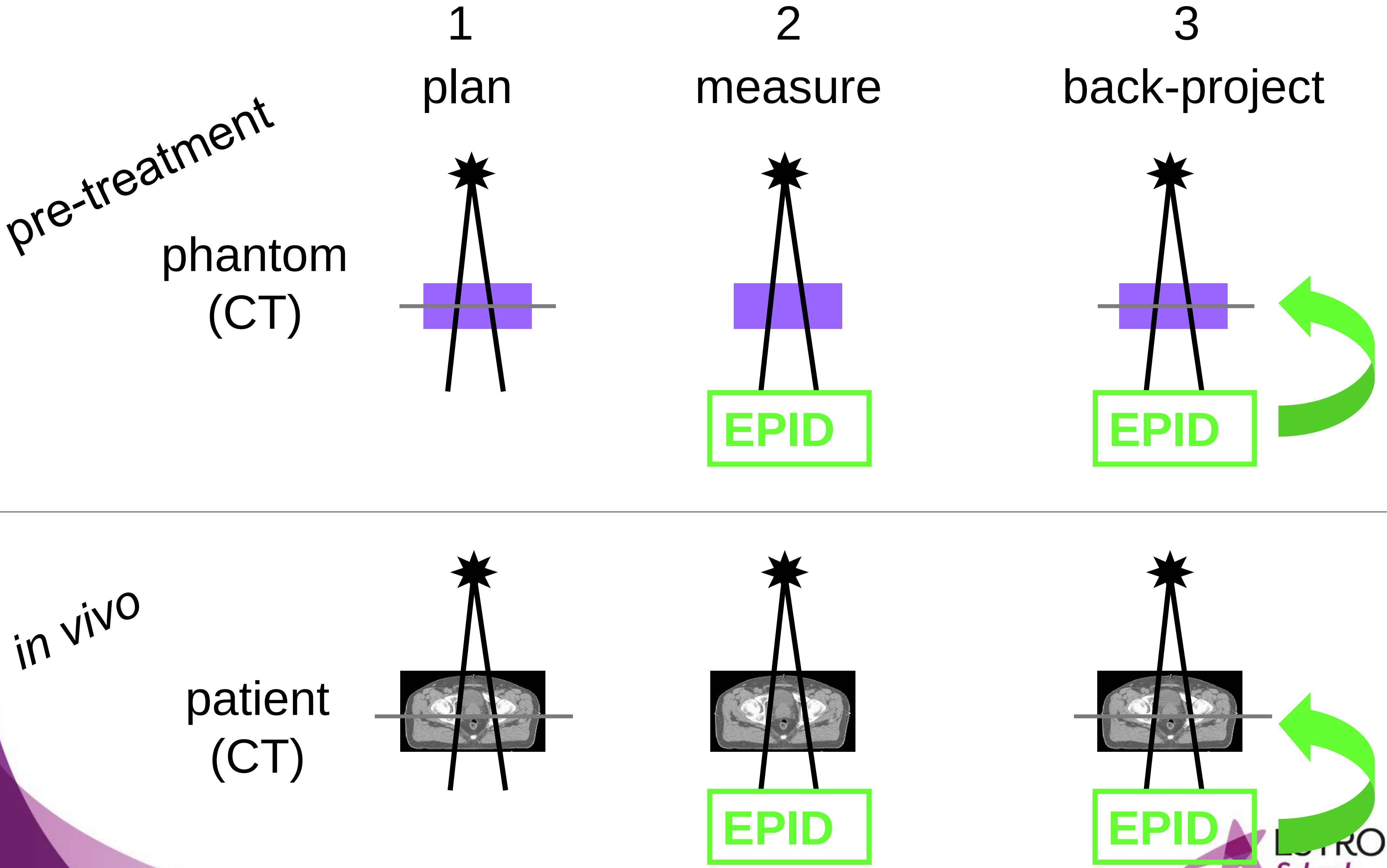
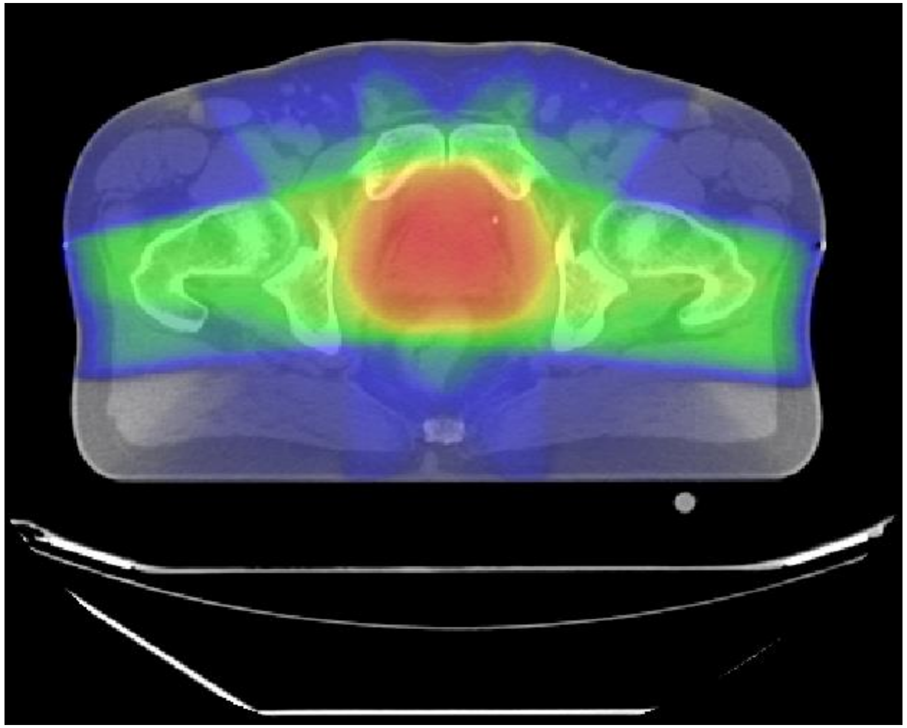
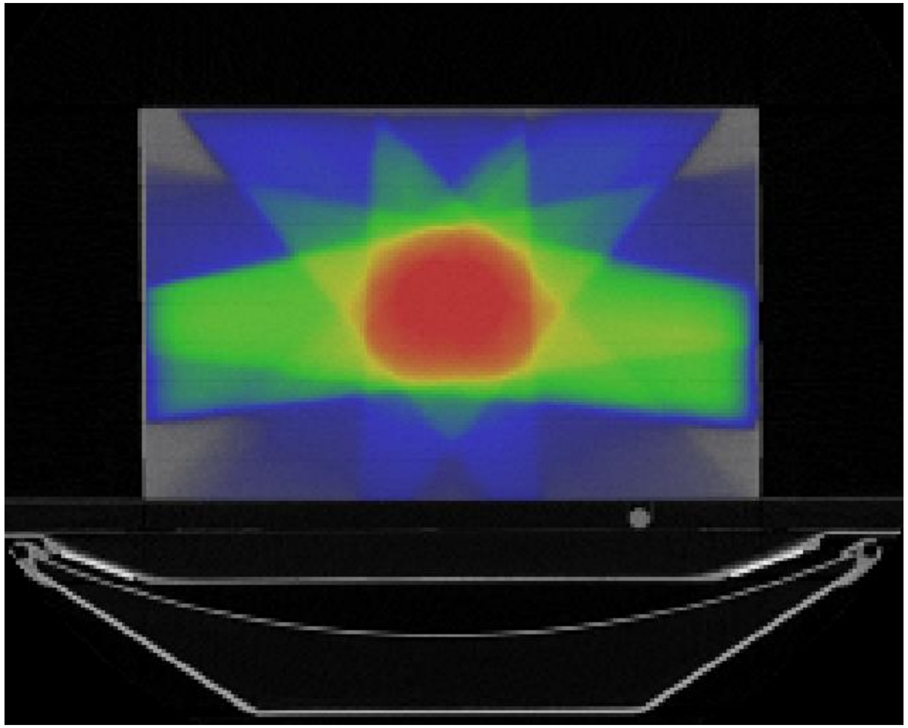
The NKI back-projection approach



Pre-treatment : in a phantom



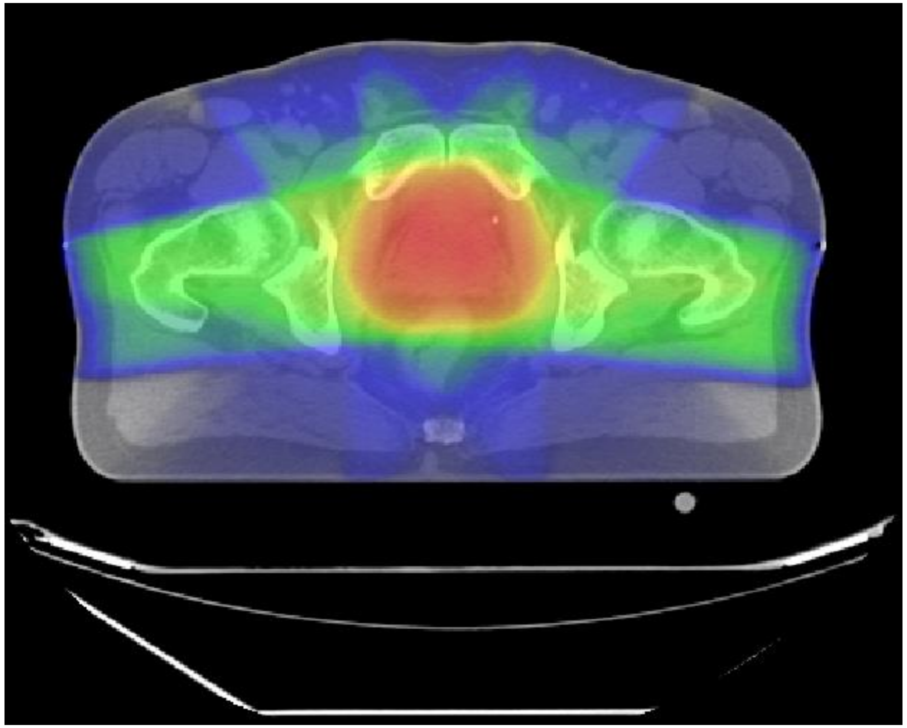


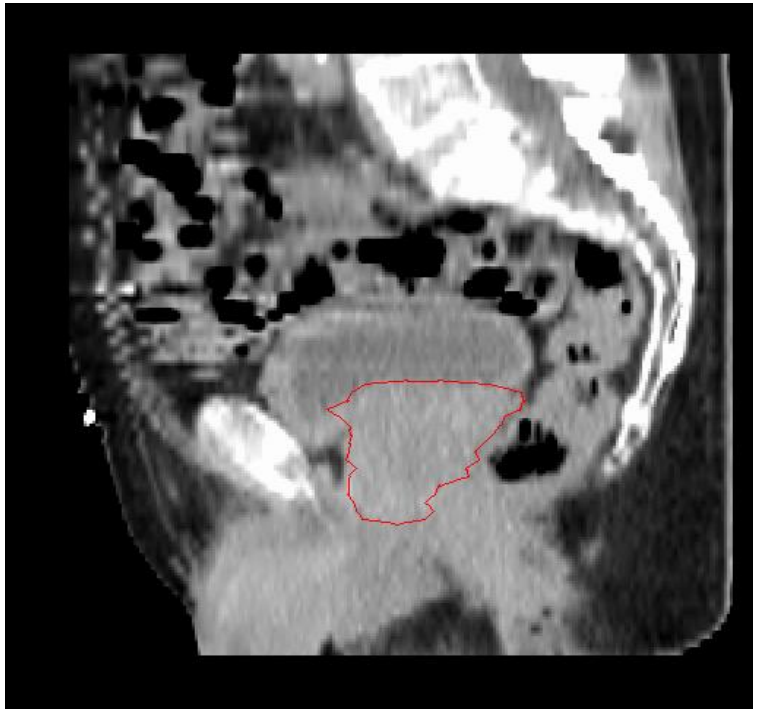
checks: plan deliverability

dose calculation

extra time : about 1 hour

In vivo : in the patient





checks: plan deliverability

dose calculation

anatomy changes

random delivery errors

extra time : ~ 25 min in case of an error
+ 30s/day

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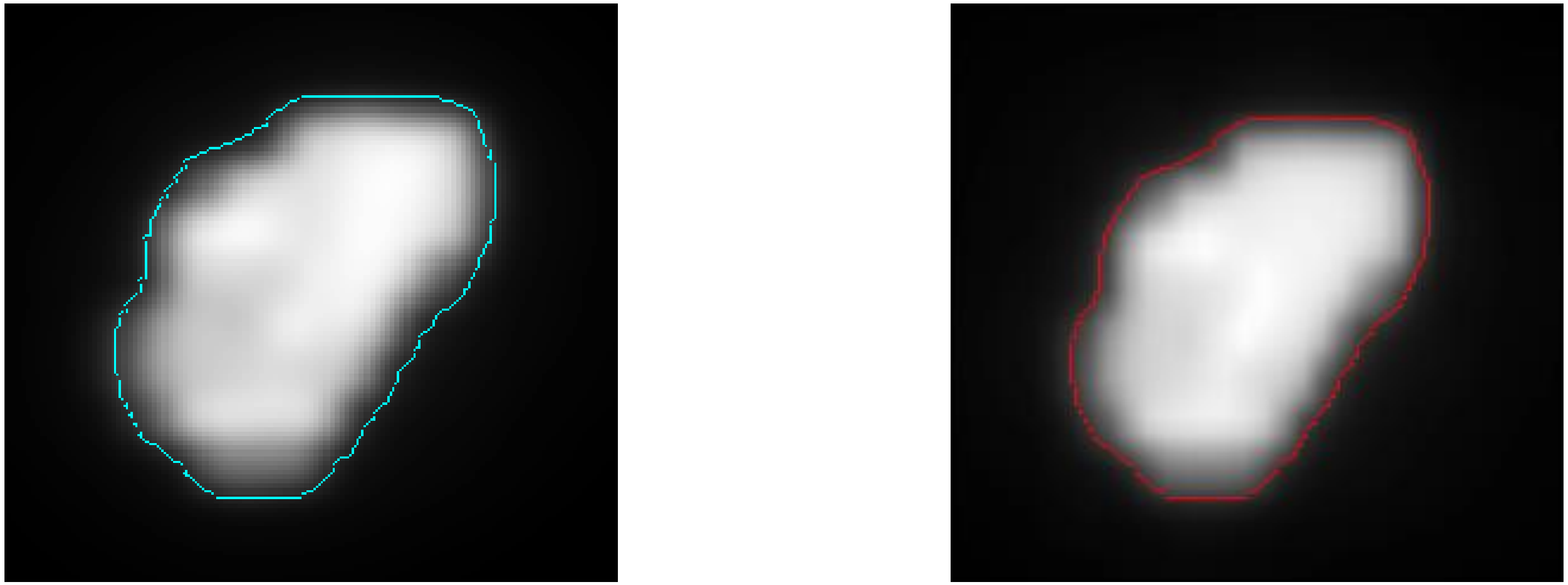
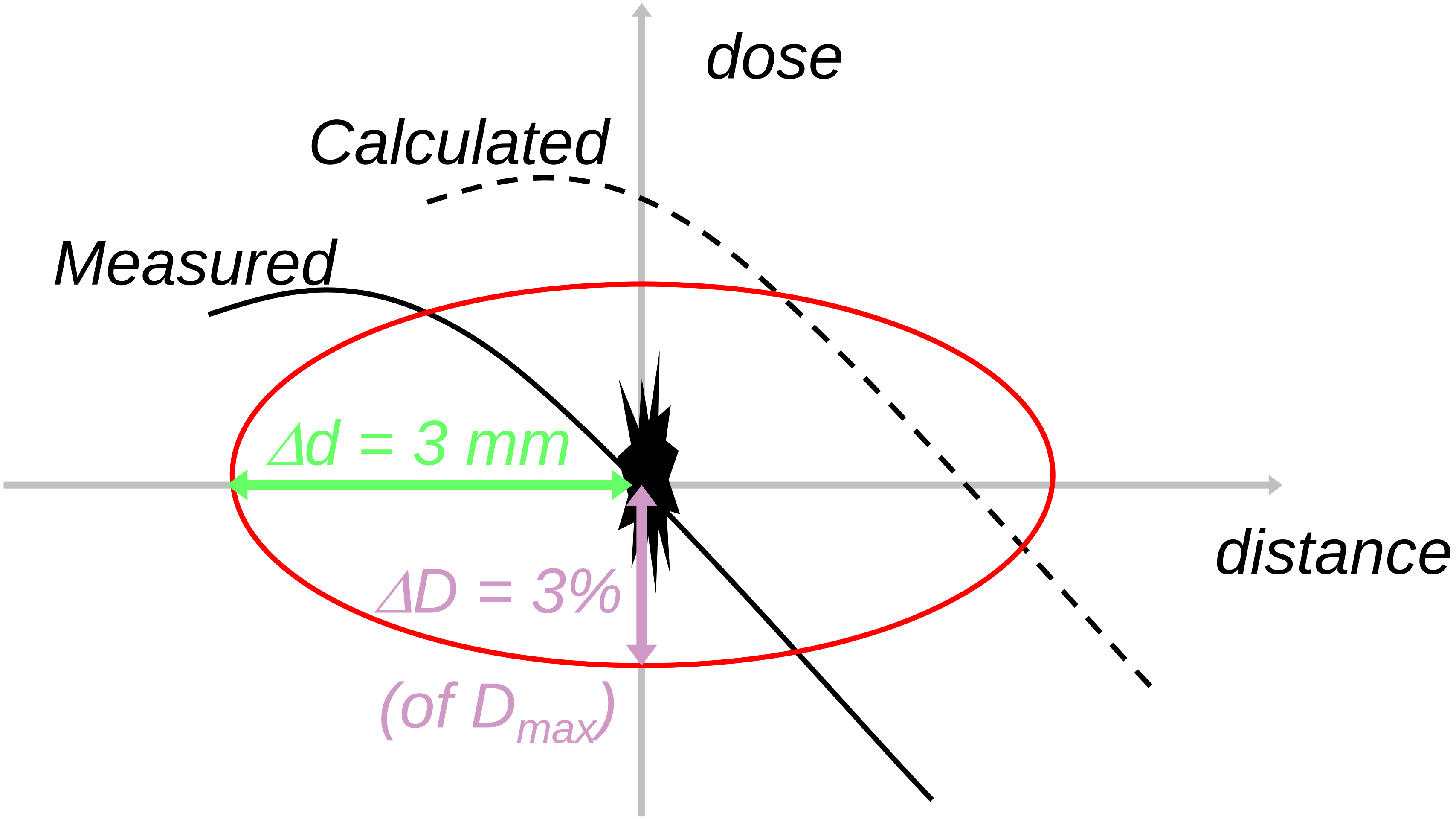
Field-by field
reference vs calculated or measured dose

how do we compare them in 2D?



PLAN EPID

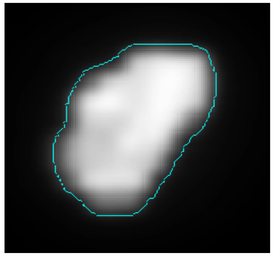
γ-evaluation: calculation vs measurement



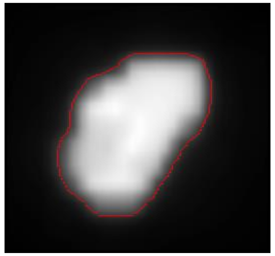
combines dose and distance criterion

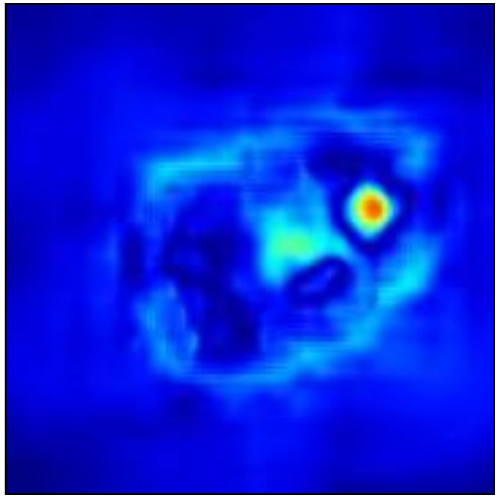
To compare the dose in 2D

plan

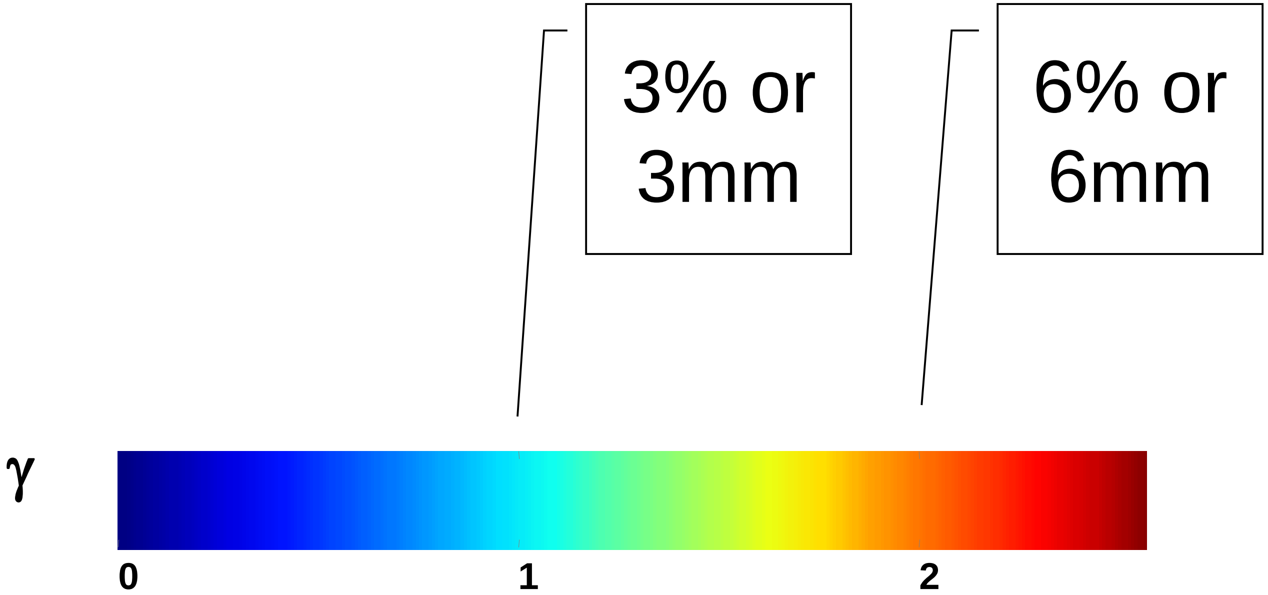


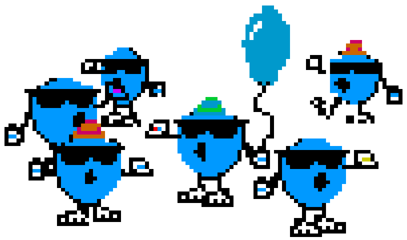
EPID

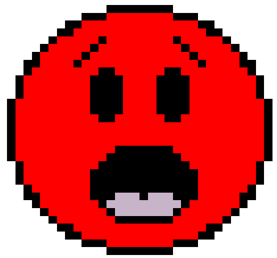




γ image

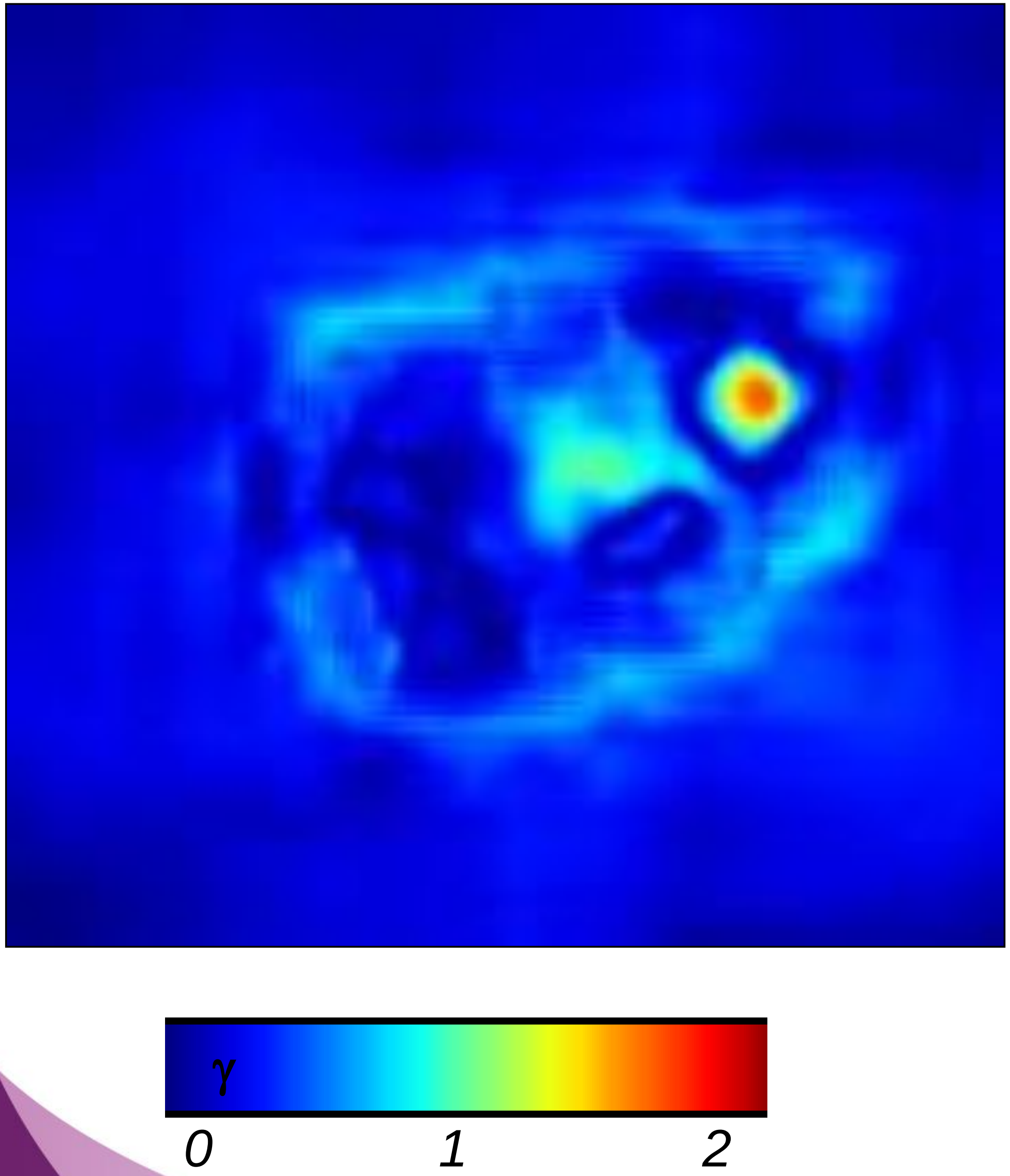


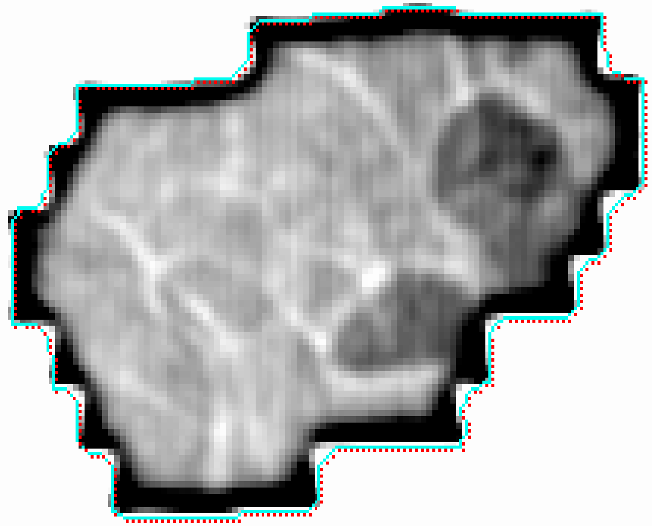




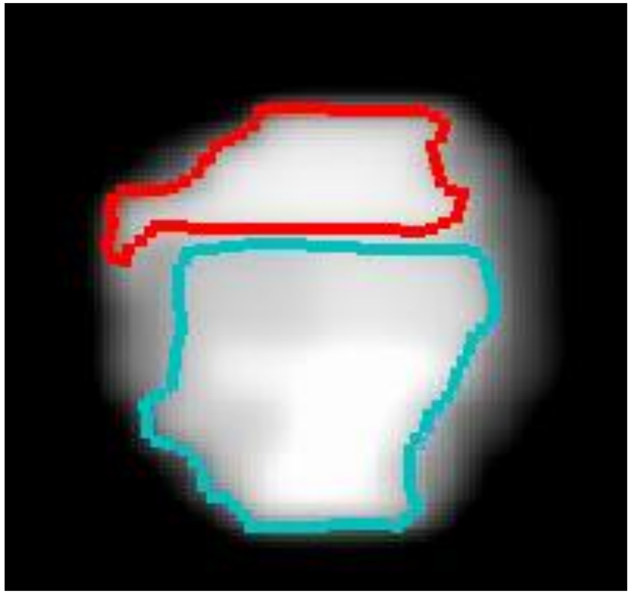
What can you detect?

Gas pockets

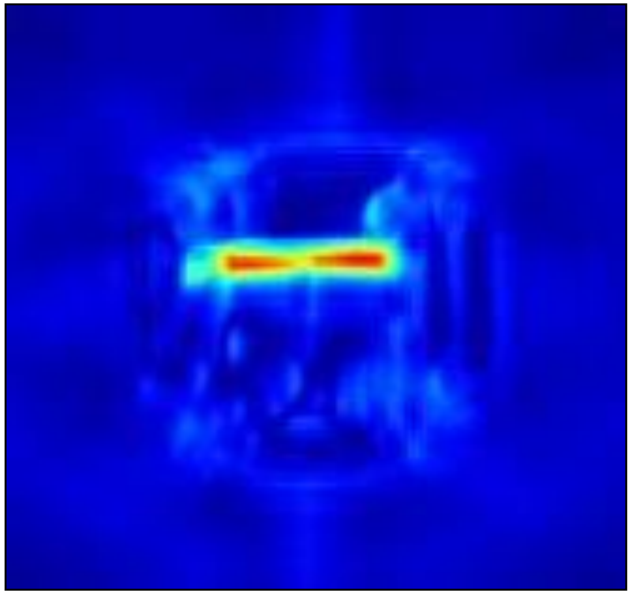




abutting leaves



isodose lines
segments 3 & 6



γ-evaluation
3% / 3mm
EPID vs plan

More errors?

- Transfer errors (planning → linac)
- Linac errors (both dosimetric and geometric)
- Dosimetric errors in plan
- Patient setup (e.g. CT reference to isoc shifts)
- Input errors
- Select the right patient / treatment in all systems

Patient setup

- CT reference to isocenter shift
  - Potentially really large errors (e.g. 10cm!)
  - They DO occur

- Possible countermeasures
  - Online imaging for ALL patients
  - Table shift surveillance software

ZERO

LCS: B2 PATID:

Please align patient

to CT Ref

Automatically retrieved from planning system

Includes shifts from offline protocols as well

Height: Lateral: Longitudinal

-10.0 **2.4** **-3.1**

TABLE:

Height: Lateral: Longitudinal:

0.0 **0.0** **0.0**

ZERO

Interlock released when numbers are the same

Height: -10.0

Lateral: 2.4

Longitudinal -3.1

TABLE:

Height: -10.0

Lateral: 2.4

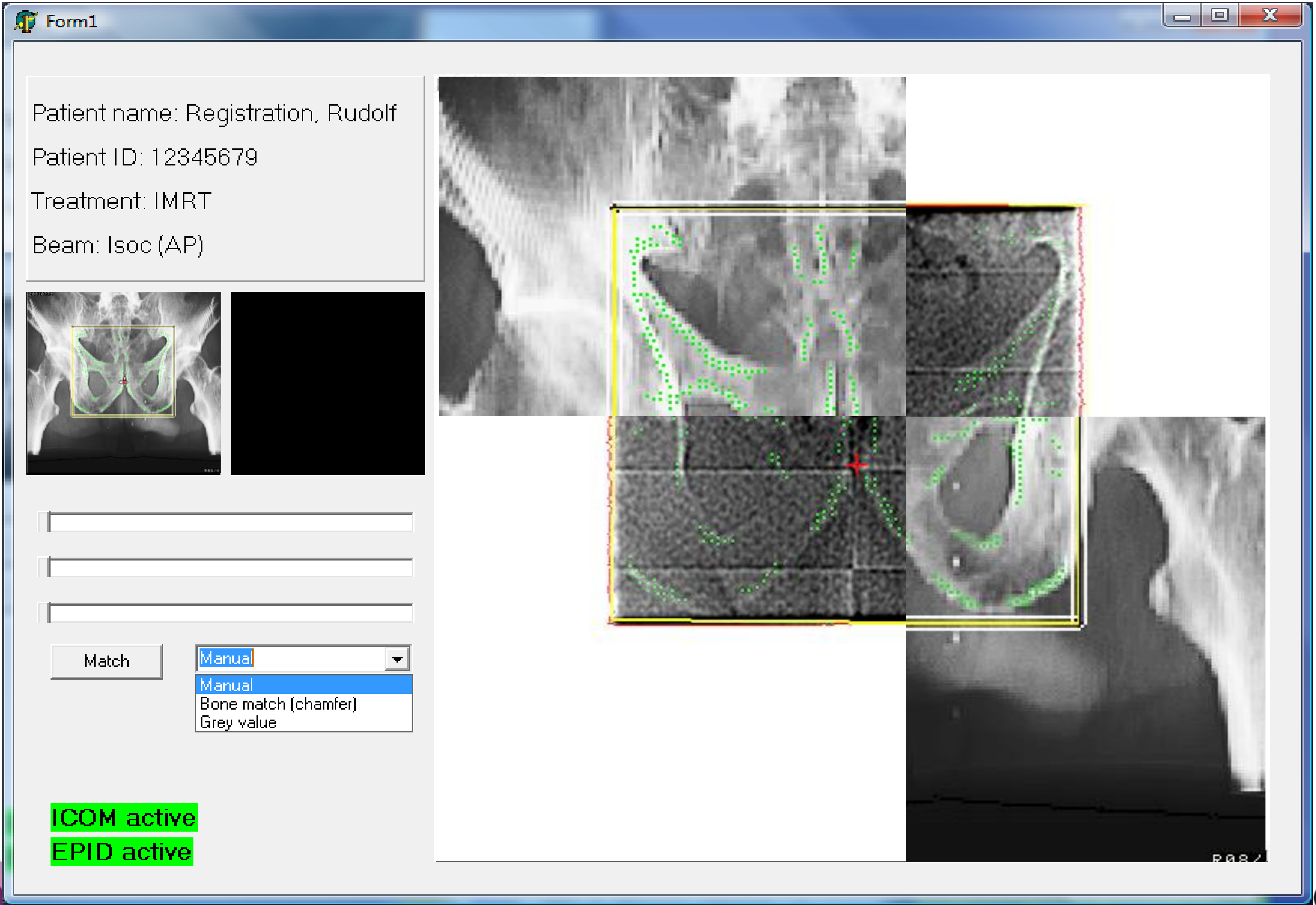
Longitudinal -3.1

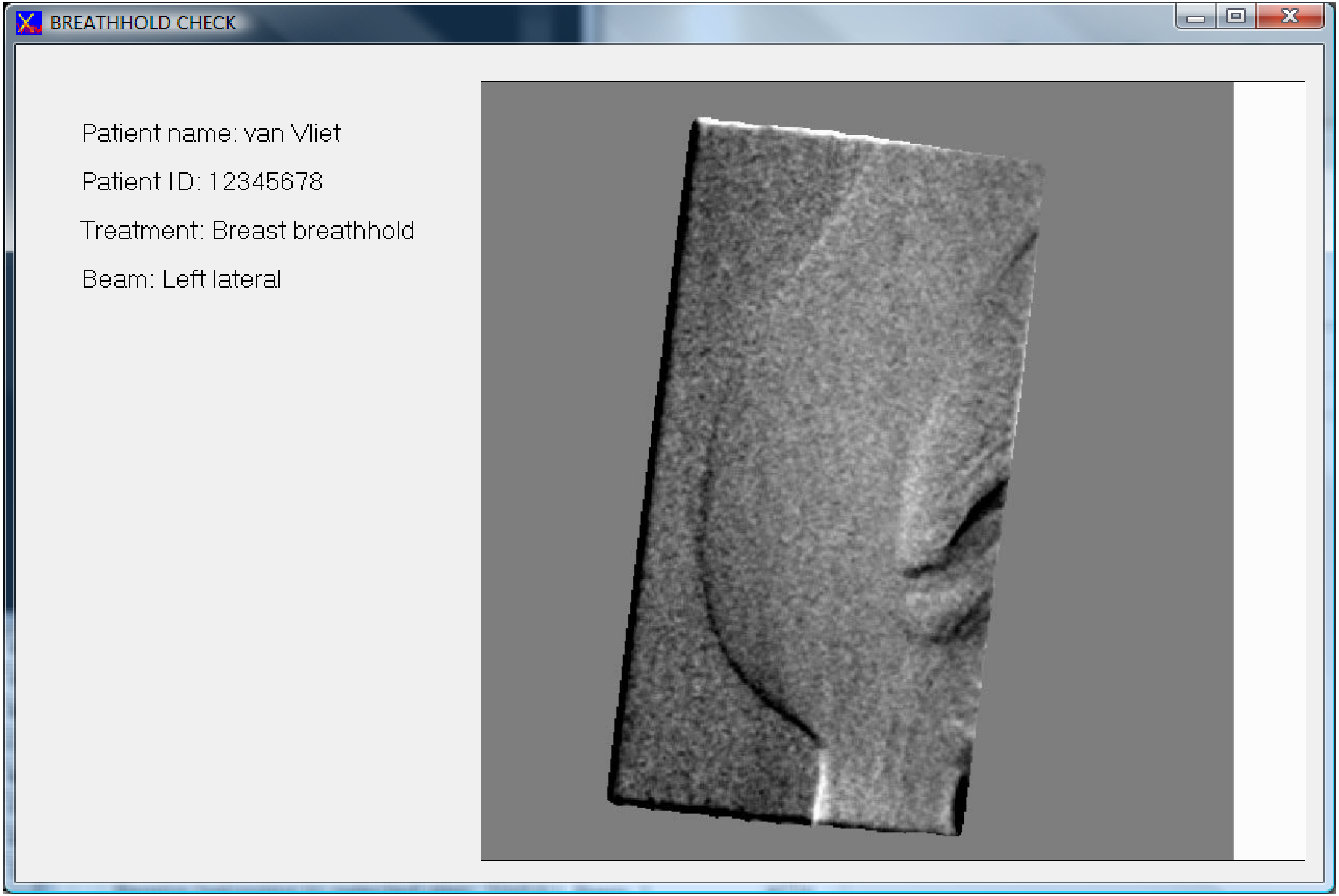
Input errors / patient / treatment selection

- Automation. Make the number of user interaction as small as possible
- Intuitive user interfaces
- Double checks
- New technology, like RFIDs?

Automation: EPID acquisition

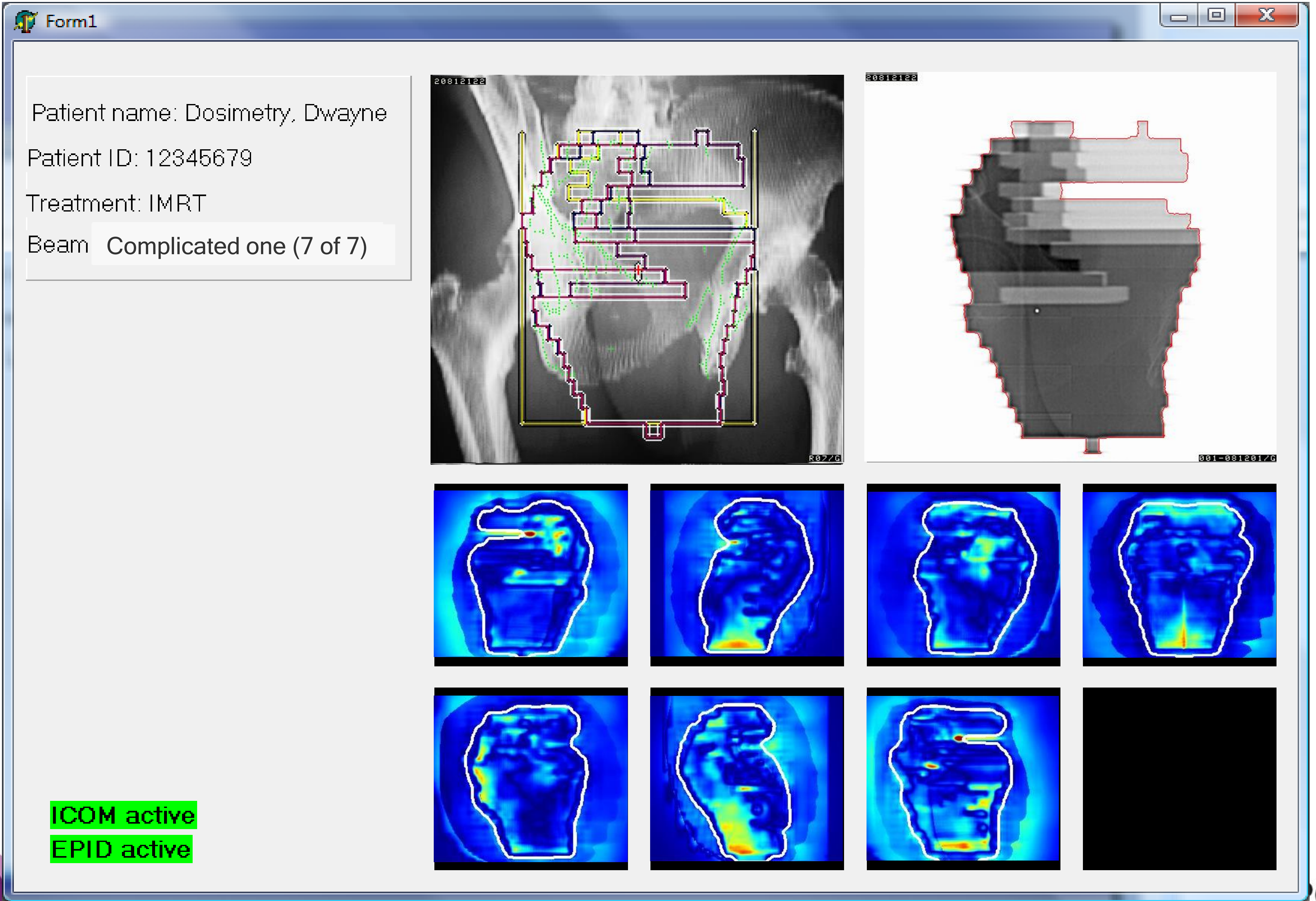
- Radiographer…
  - Deploys the imager
- Application…
  - Selects patient and beam
  - Saves data in database without any user intervention
- Different screens, depending on beam property, e.g.
  - Dosimetry screen
  - Online registration screen
  - Breathhold screen


Form1
Patient name: Registration, Rudolf
Patient ID: 12345679
Treatment: IMRT
Beam: Isoc (AP)
Match
Manual
Manual
Bone match (chamfer)
Grey value
ICOM active
EPID active


BREATHHOLD CHECK
Patient name: van Vliet
Patient ID: 12345678
Treatment: Breast breathhold
Beam: Left lateral

Automation: Zero button EPID dosimetry

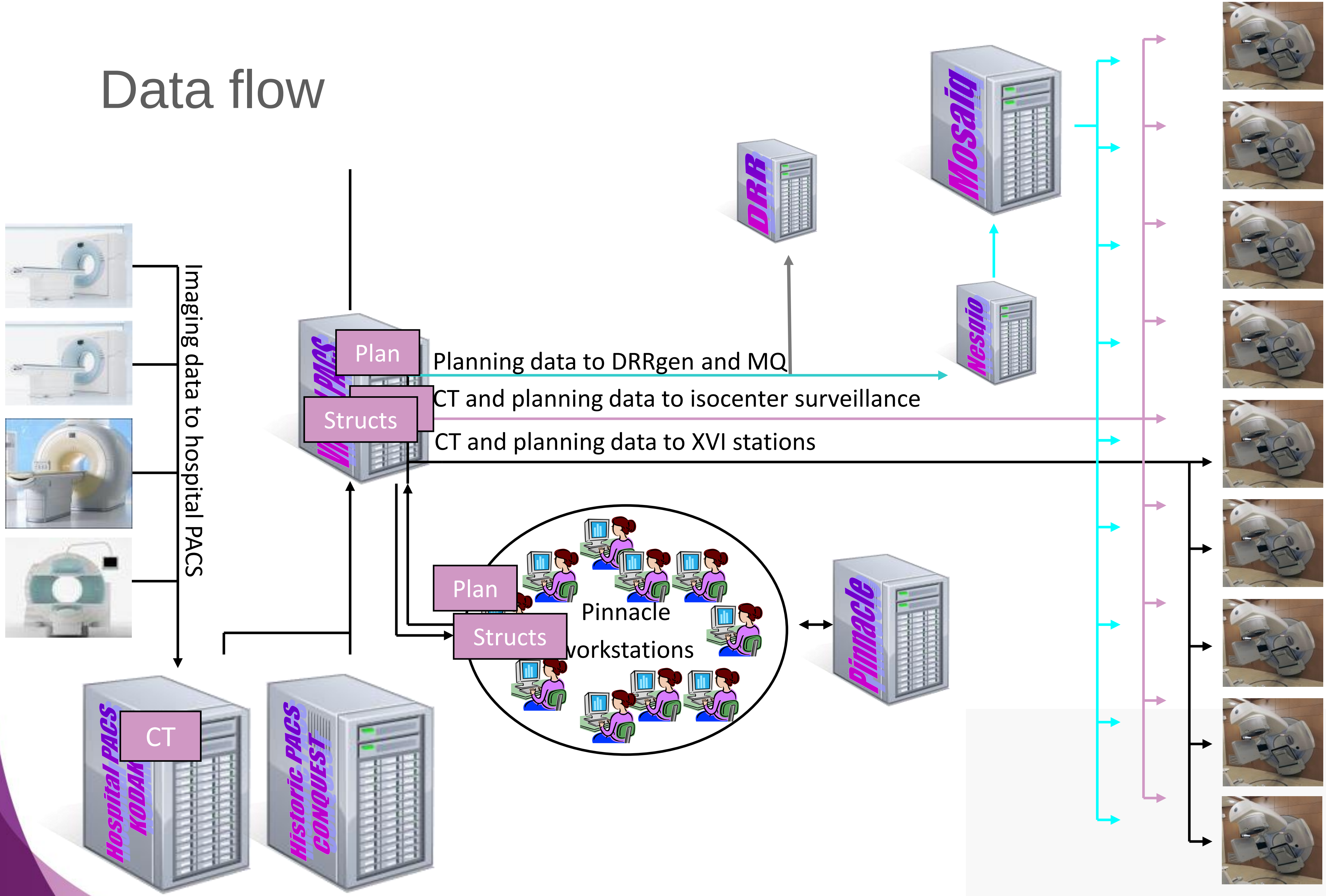
- Radiographer…
  - Deploys the imager and treats the patient
- Application…
  - ‘Triggers’ on new images from EPID acquisition application
  - Computes dose
  - Sends a report to physics
  - Notifies physics when something is wrong


Form1
Patient name: Dosimetry, Dwayne
Patient ID: 12345679
Treatment: IMRT
Beam
Complicated one (7 of 7)
ICOM active
EPID active

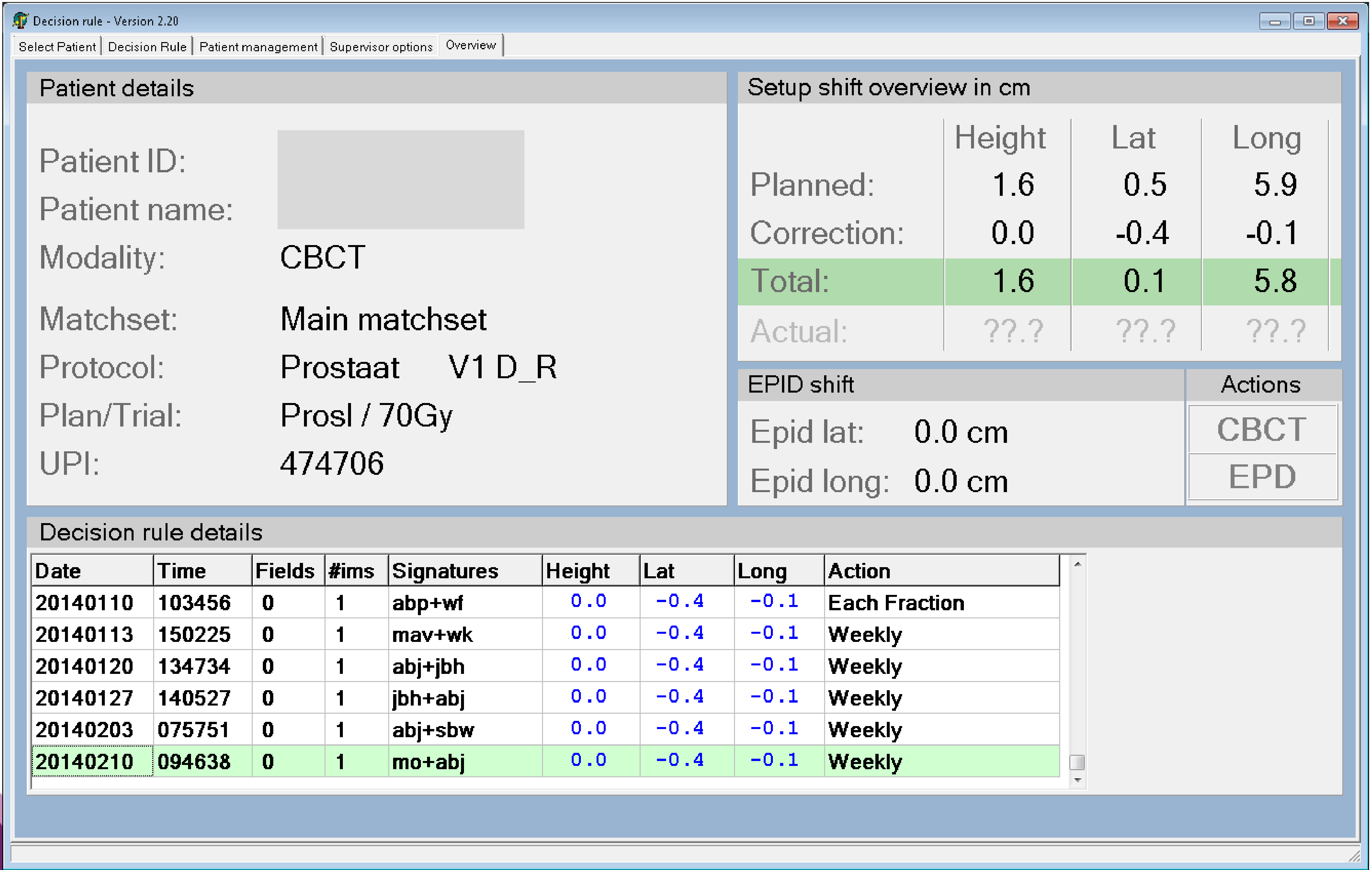
Automated dataflow example

- Dosimetrist sends plan for linac B5 to central server
- Server finds corresponding CT scan and structure set
- All data is then automatically sent to XVI station on B5
- Plan is sent to Mosaiq
- Plan and structures are sent to hospital PACS
- DRRs are automatically generated
- Patient is automatically entered in imaging database

Data flow


Imaging data to hospital PACS
Hospital PACS
KODAK
CT
Historic PACS
CONQUEST
Plan
Structs
Planning data to DRRgen and MQ
CT and planning data to isocenter surveillance
CT and planning data to XVI stations
DRR
Mosaiq
Plan
Structs
Pinnacle
workstations
Pinnacle

User interface



Decision rule - Version 2.20

Select Patient | Decision Rule | Patient management | Supervisor options | Overview

Patient details

Patient ID:

Patient name:

Modality: CBCT

Matchset: Main matchset

Protocol: Prostaat V1 D_R

Plan/Trial: Prosl / 70Gy

UPI: 474706

Setup shift overview in cm

	Height	Lat	Long
Planned:	1.6	0.5	5.9
Correction:	0.0	-0.4	-0.1
Total:	1.6	0.1	5.8
Actual:	??.?	??.?	??.?

EPID shift

Epid lat: 0.0 cm

Epid long: 0.0 cm

Actions

CBCT

EPD

Decision rule details

Date	Time	Fields	#ims	Signatures	Height	Lat	Long	Action
20140110	103456	0	1	abp+wf	0.0	-0.4	-0.1	Each Fraction
20140113	150225	0	1	mav+wk	0.0	-0.4	-0.1	Weekly
20140120	134734	0	1	abj+jbh	0.0	-0.4	-0.1	Weekly
20140127	140527	0	1	jbh+abj	0.0	-0.4	-0.1	Weekly
20140203	075751	0	1	abj+sbw	0.0	-0.4	-0.1	Weekly
20140210	094638	0	1	mo+abj	0.0	-0.4	-0.1	Weekly

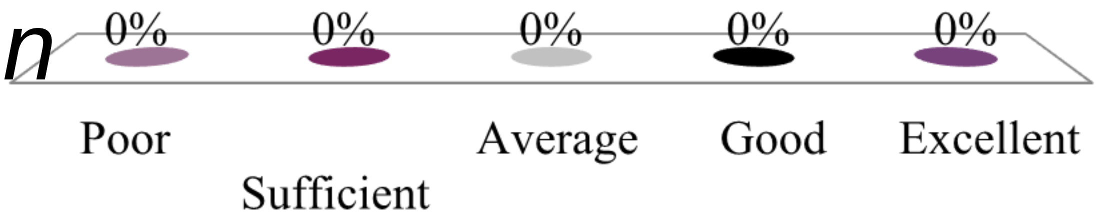
Take home messages

- IGRT is good but not enough
- Take countermeasures to catch gross errors
- Try to find the simplest workflow (user interface, protocols, forms)
- **Be especially aware when introducing new systems, protocols, or technologies**

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



In-room imaging modalities

Martijn Kamphuis MSc MBA
Research Radiation Therapist IGRT

Department of Radiotherapy
Amsterdam, the Netherlands

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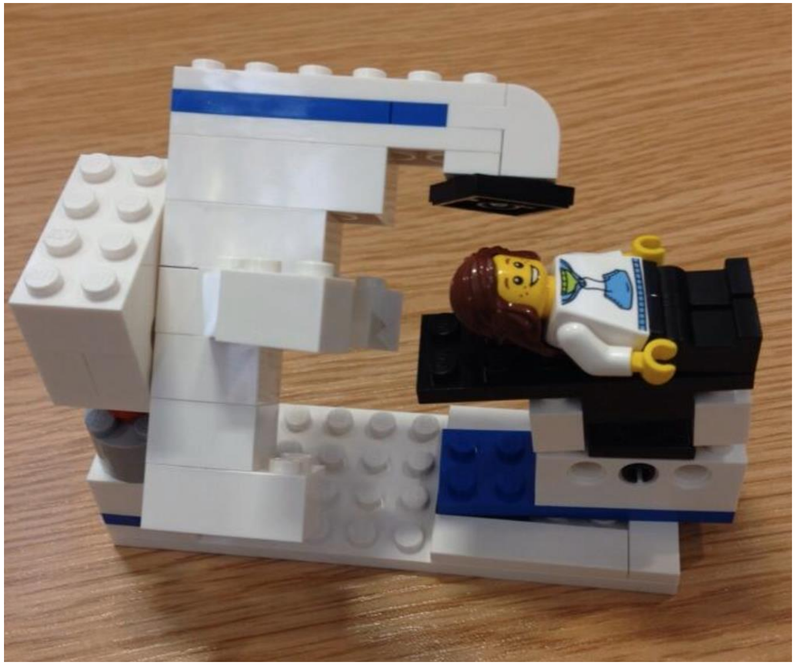
Content of the presentation

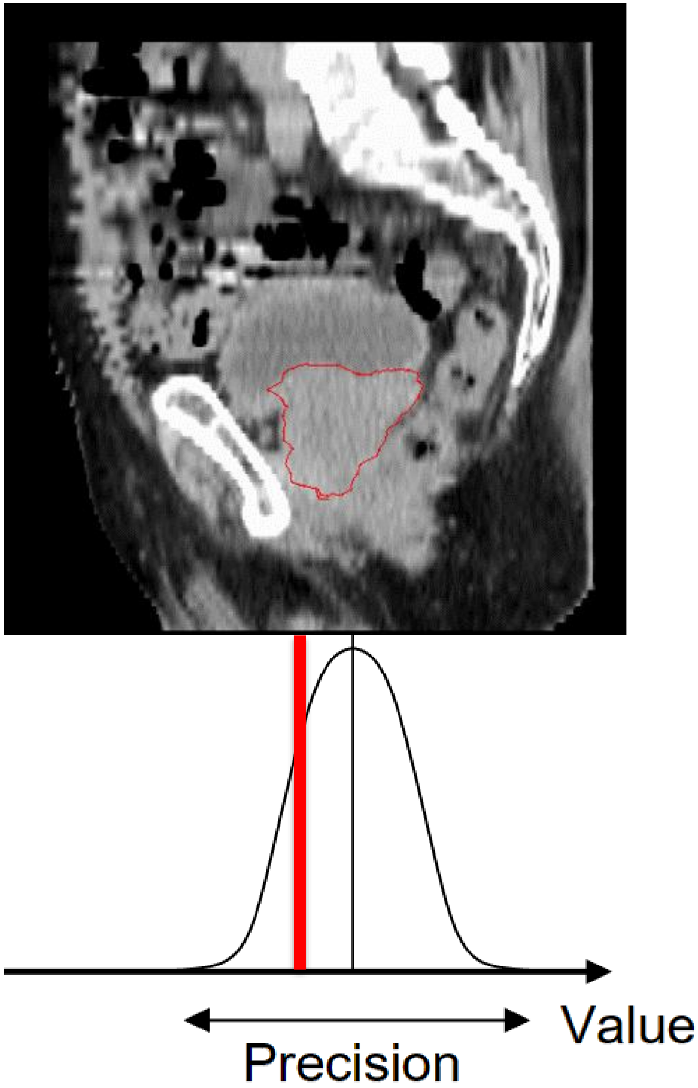
- Why do we need imaging on the linac?

- Imaging modalities
  - How do the work?
  - What can we do with them?
  - Pros and cons



At the start of treatment

- Single CT introduces systematic errors*:
  - Delineation errors
  - Organ position and shape at time of localization
  - Phantom transfer errors
    - Geometric imaging error
    - Treatment planning system error
    - Linear accelerator geometry error
    - Set-up error at time of localization
  - TPS beam algorithm error
  - Breathing positional error



*McKenzie et al., BIR 2003
Image courtesy: Marcel van Herk

In fact…it's just a snapshot

www.facetimewithsharon.com

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Why do we need imaging on the linac?

- To reduce systematic and random geometrical errors

- Monitor/adapt to patient anatomy/pathology
  - ➢ Plan of the day
  - ➢ (Ad hoc) replanning

- To document the treatment accuracy
  - ➢ Margin calculation
  - ➢ Incident analyses

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Imaging modalities

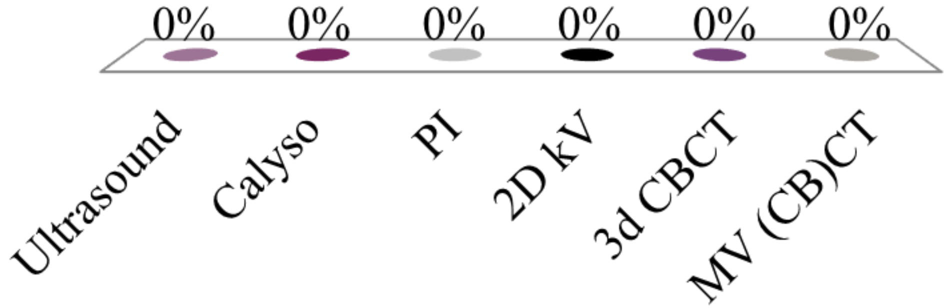
- Ultrasound systems
- Electromagnetic tracking

- Portal Imaging (EPID)
- kV cone beam CT
- 3D CBCT
- MV (CB)CT

- Surface scanning
- MR linac

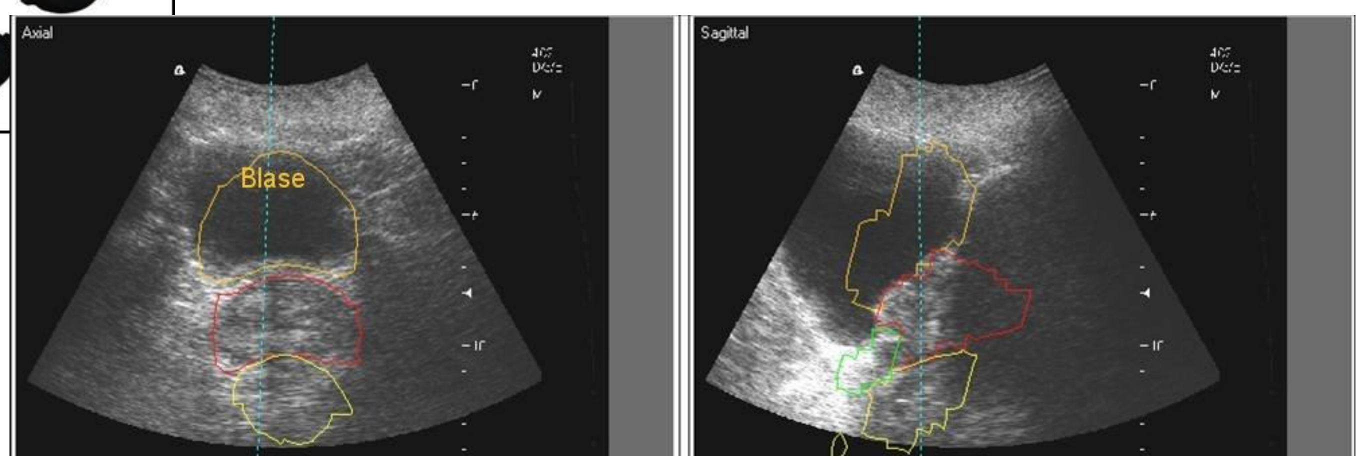
Polling: Who is using what?

A. Ultrasound
B. Calyso
C. PI
D. 2D kV
E. 3d CBCT
F. MV (CB)CT

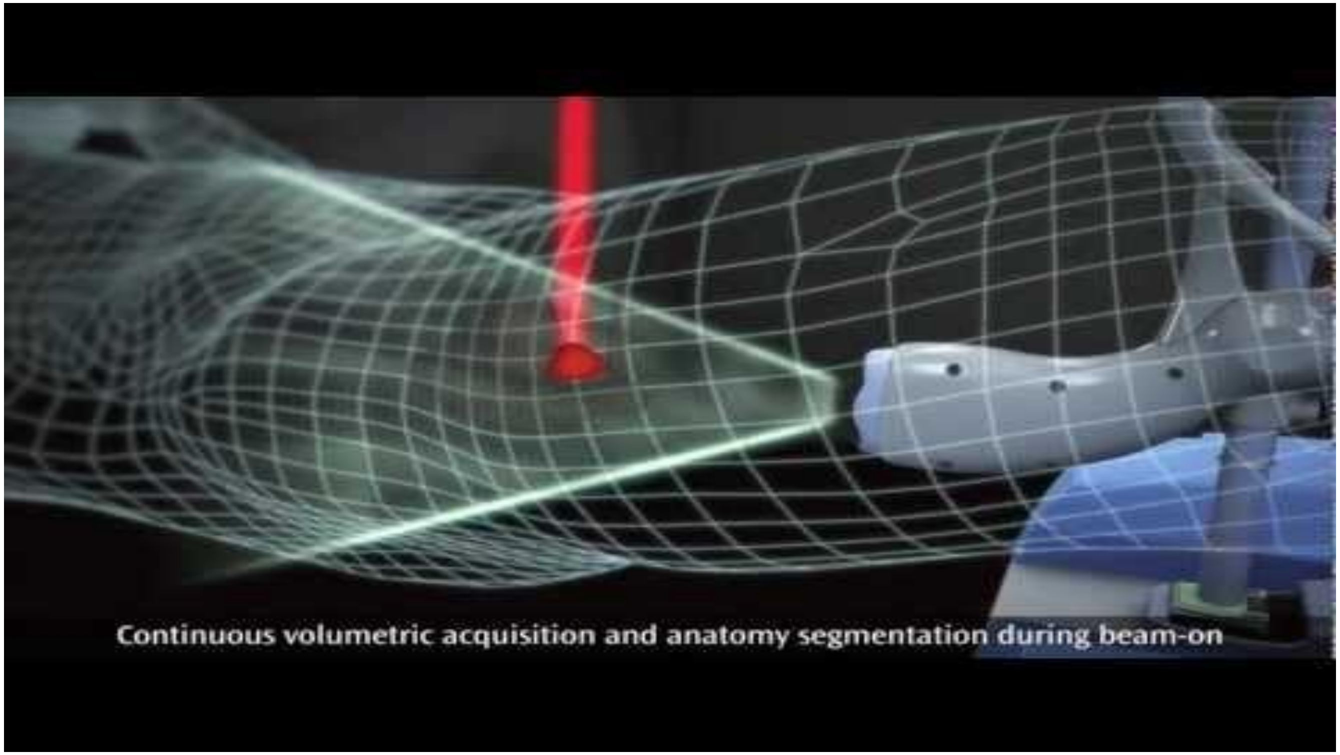


Ultrasound systems

- With probe define position target
- Infrared enables correlation with linac



More recent developments



https://www.elekta.com/software-solutions/treatment-management/imaging/clarity/?utm_source=clarity&utm_medium=redirect&utm_campaign=redirects

Ultrasound system

Pros:

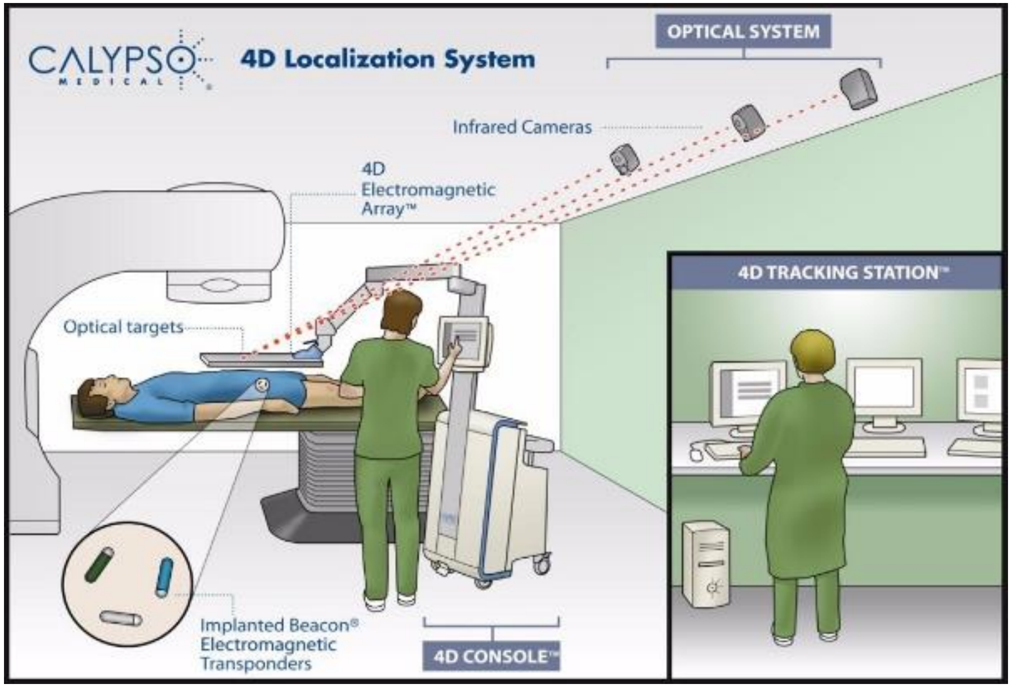
- Non invasive
- No imaging dose
- (Intra fraction imaging)

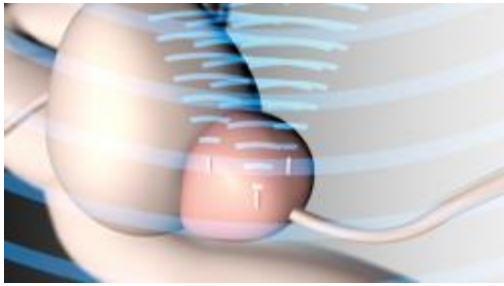
Cons:

- (User dependent accuracy)
- (No intra fraction information)
- Limited number of indications
  - ➢ Prostate
  - ➢ Upper abdominals
- (Probes influences position target)
  - ➢ Systematic error

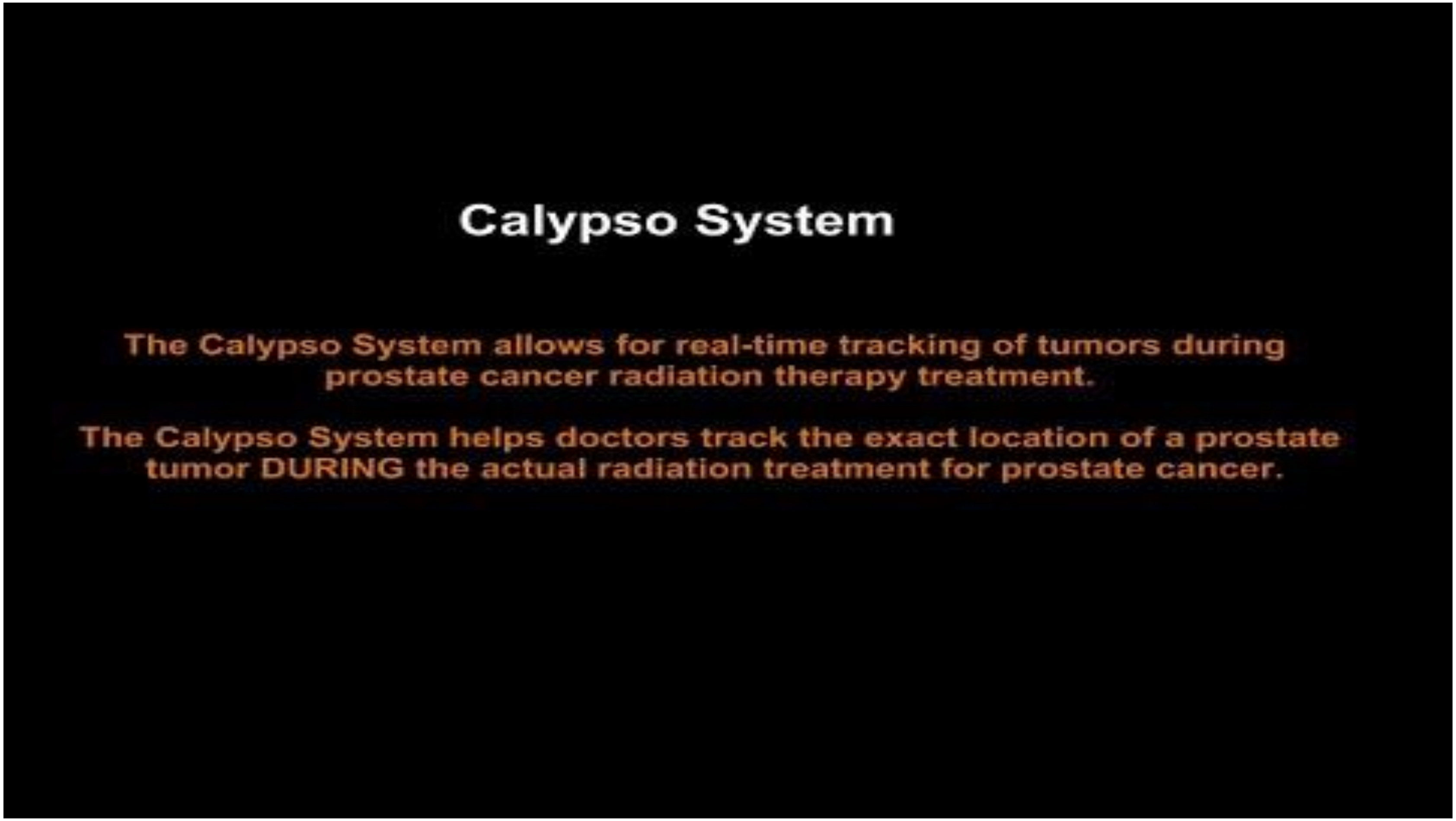
Electromagnetic tracking

- Uses implanted fiducials
- Lower magnetic field
- Transponder emits RF





Electromagnetic tracking



Electromagnetic tracking (GPS)

Pros:

- Continuous real time measurements (10Hz)
  - Intra fraction monitoring is used for others sites as well
- Non ionizing

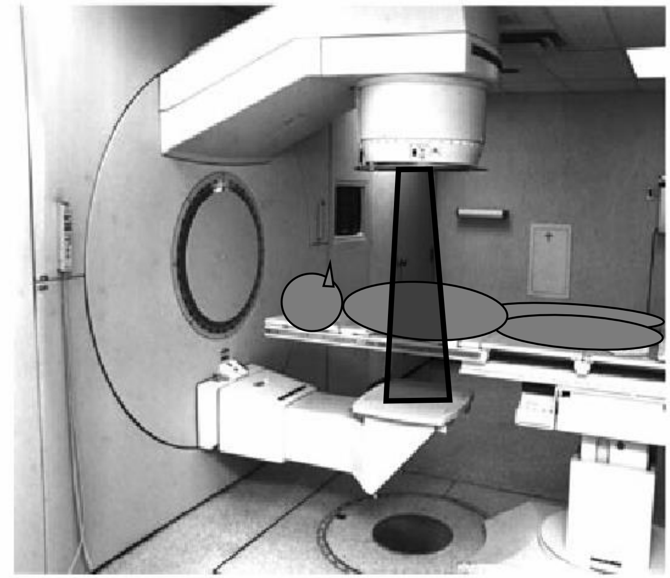
Cons:

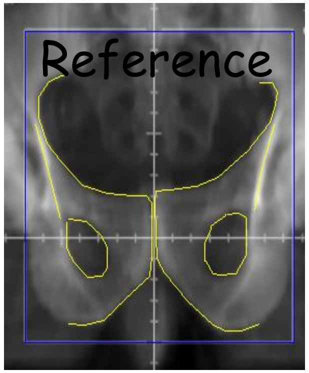
- Limited number of indications
  - Mostly prostate
  - Lung
  - Breast (PBI)
  - Pancreas
- No anatomical information
- Invasive pre imaging procedure

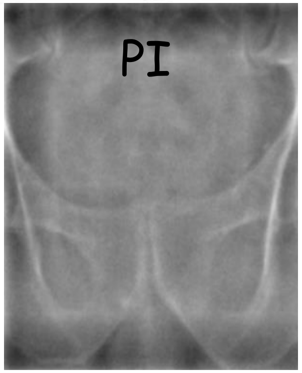
Portal Imaging - physics

- An imager used to detects the photons that cross the patient

- The portal image is compared to a reference image







Goals of Portal Imaging

- Position verification

- Documentation of treatment
- Portal dosimetry (in-vivo)
- QA (MLC adjustment)

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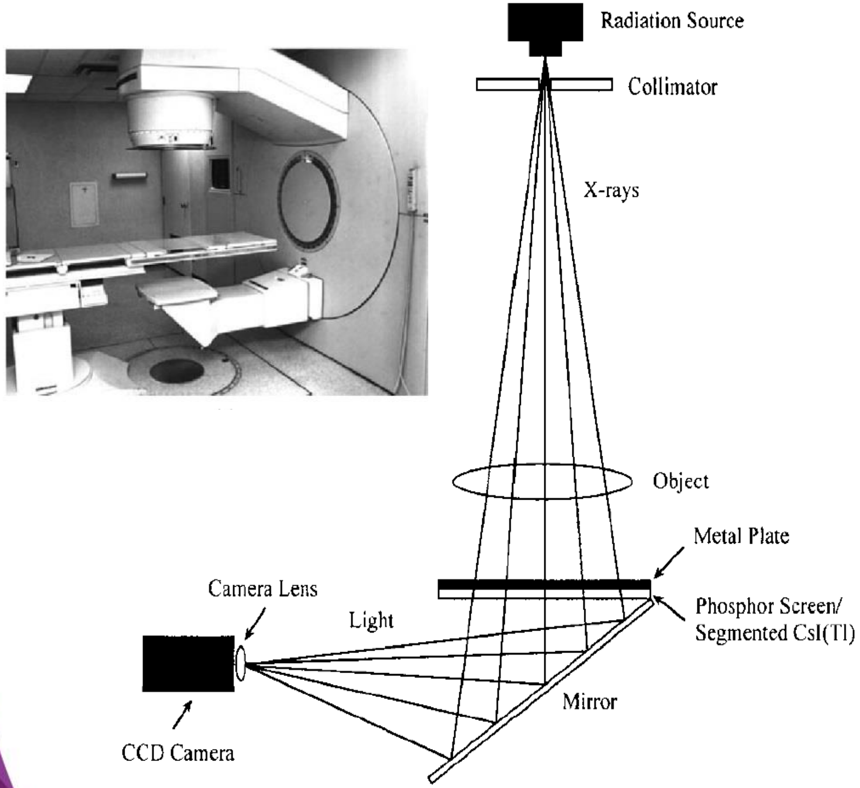
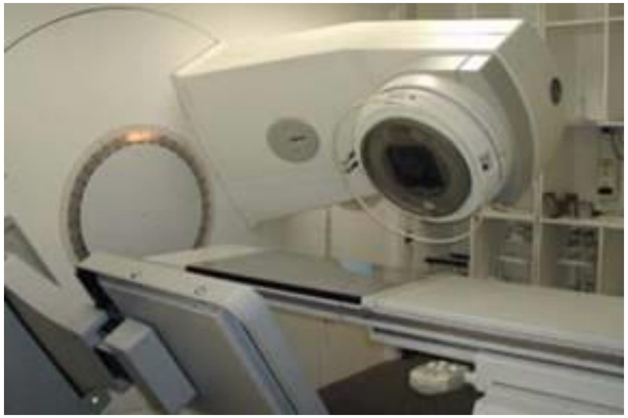
Technical aspects of EPIDs

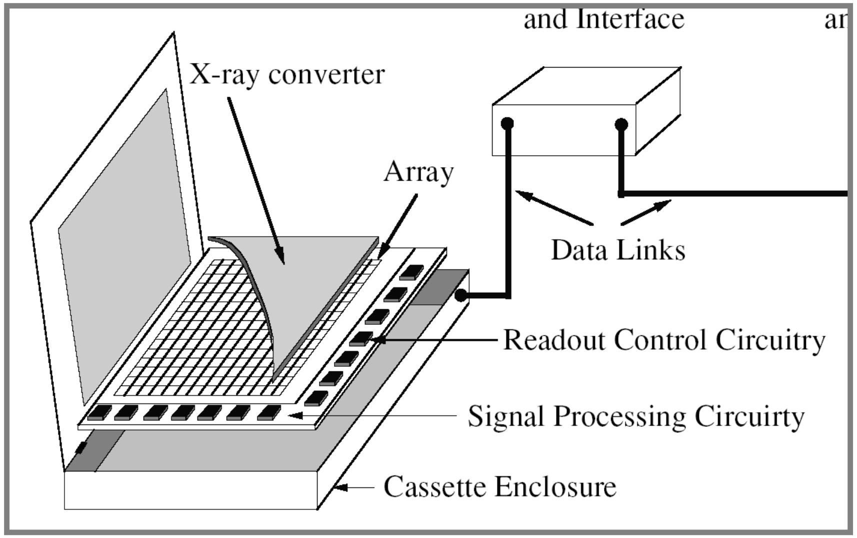
Camera-mirror based systems



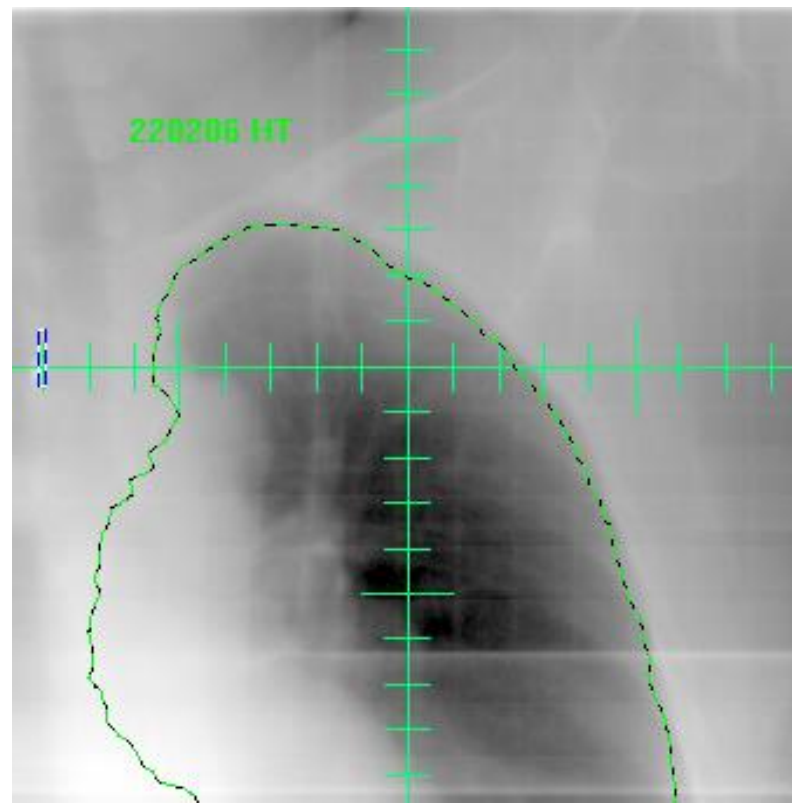
Active matrix flat panel imagers (AMFPI)

- also called amorphous silicon imagers



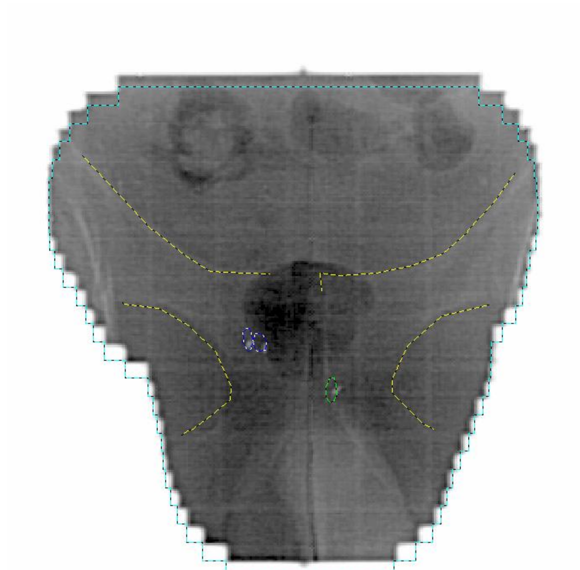


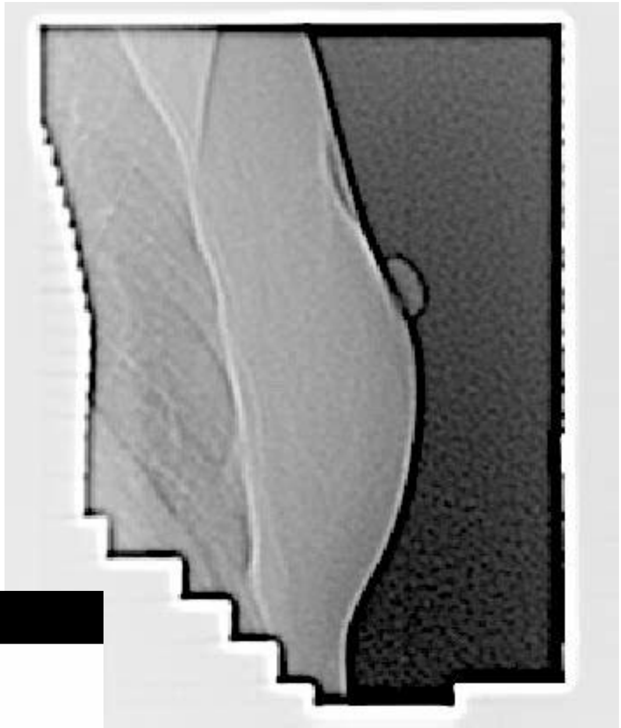
Examples of portal images (open field)

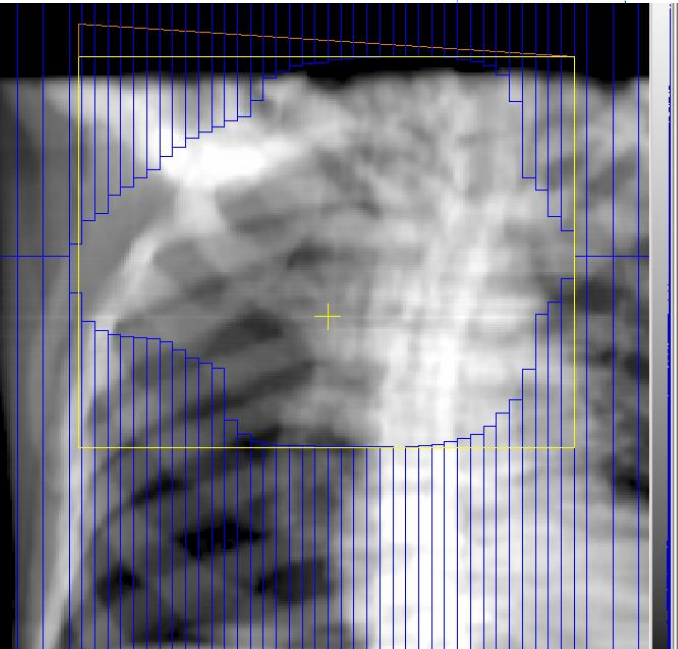


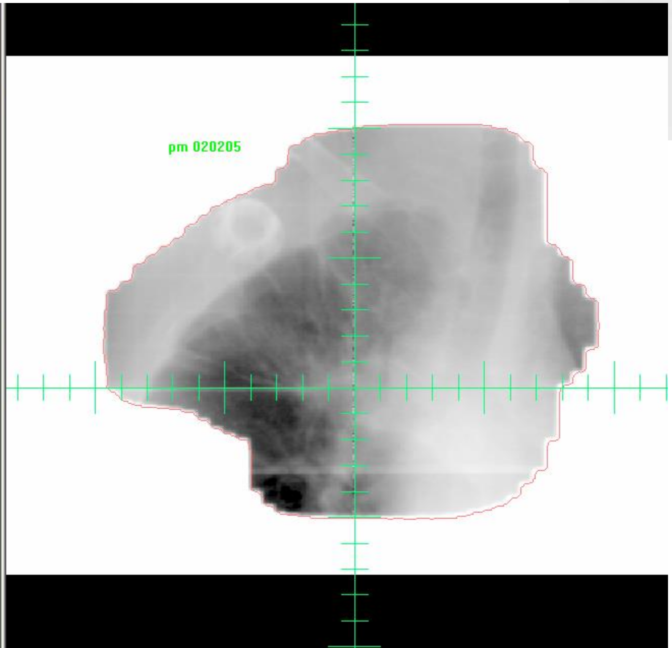
Images: M. Josipovic

EPID – field images









Images: M. Josipovic

Electronic Portal Imaging

Pros

- Image made with treatment beam
- Imaging during treatment
- Possible to perform dosimetry

Cons

- Surrogate imaging
  - ➢ Additional margins
- Imaging dose
  - ➢ Although it is possible to compensate for
- Imaging quality

2D kV imaging

kV source & detector panel

Different approaches:

- kV source moutend on linac
- kV sources on fixed position in room

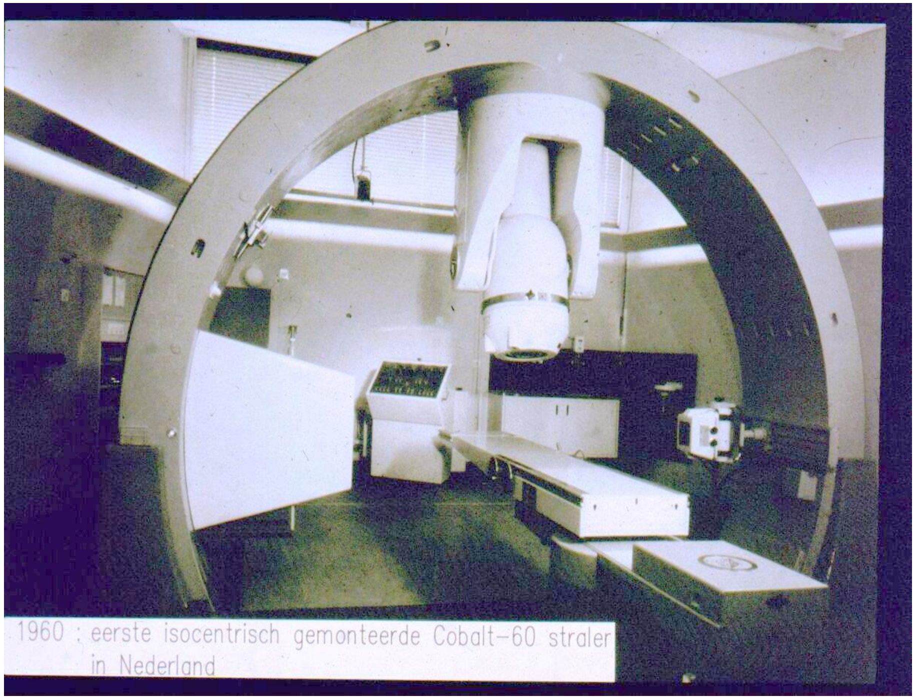
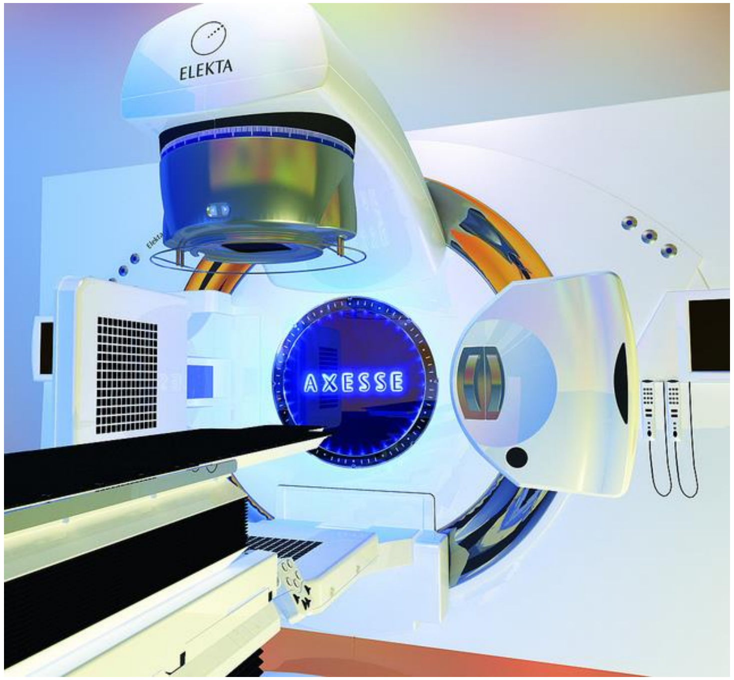


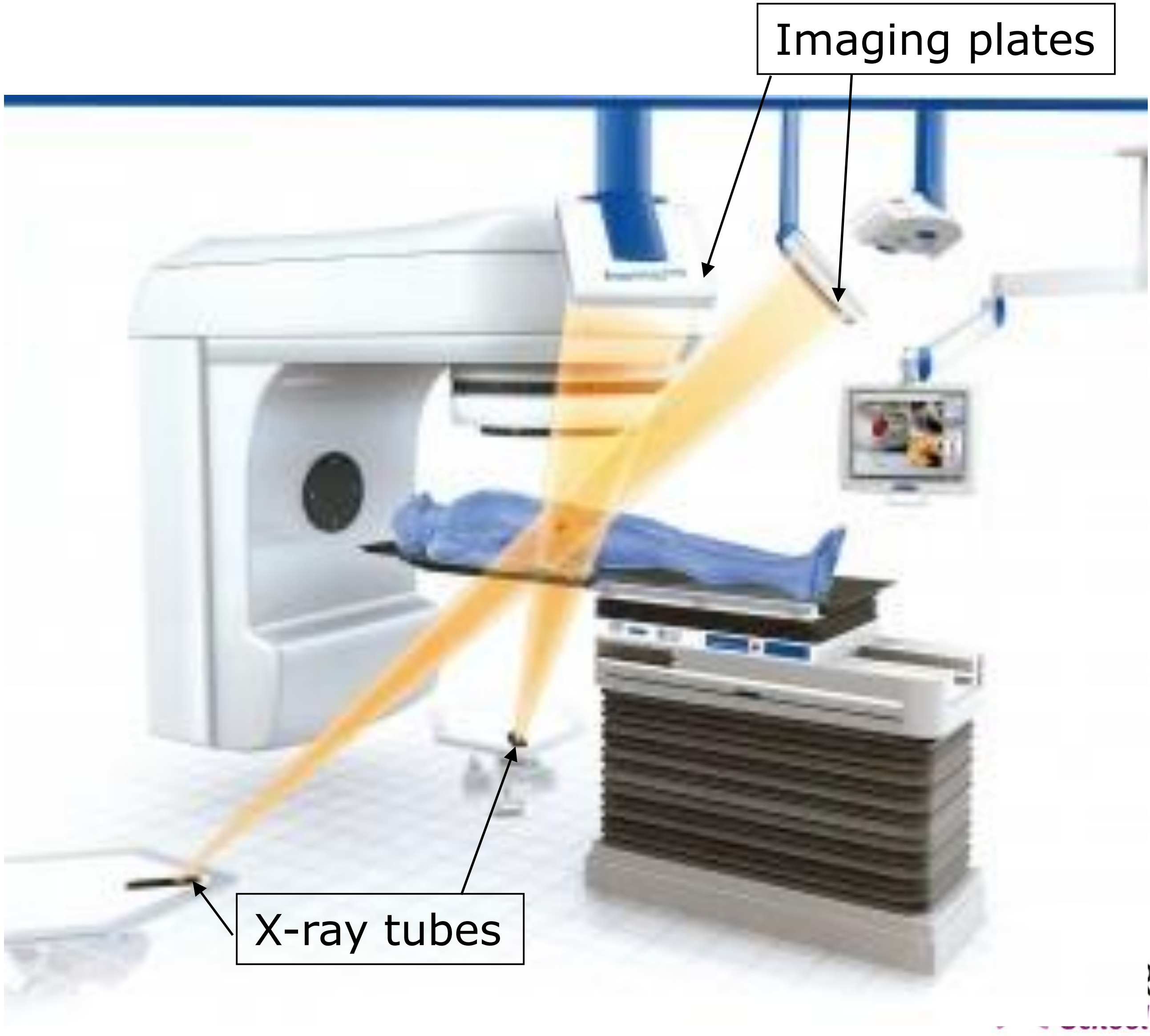
Image: Ben Mijnheer (NKI)

kV source moutend on linac

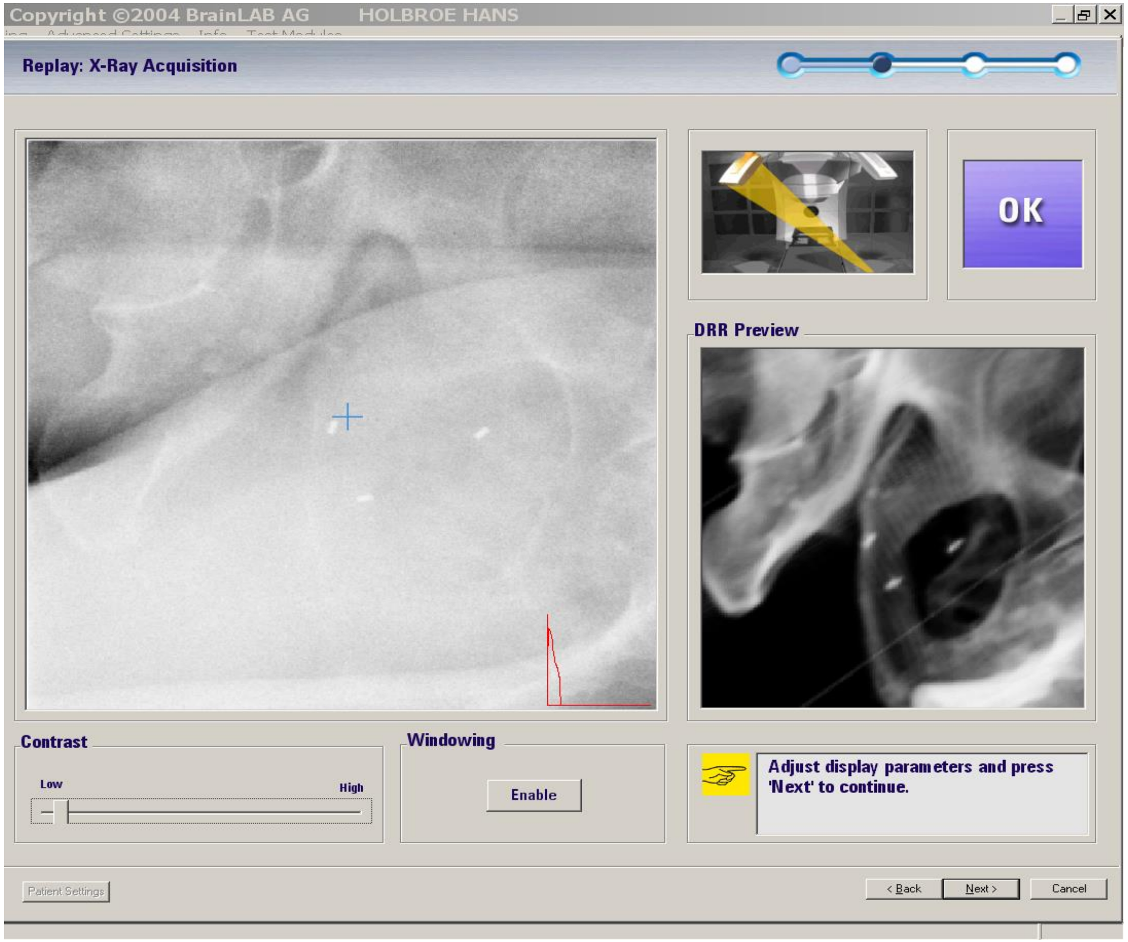


kV imaging: Cyberknife

Exac Trac® IGRT system



Exac Trac® IGRT system



Images: M.Josipovic

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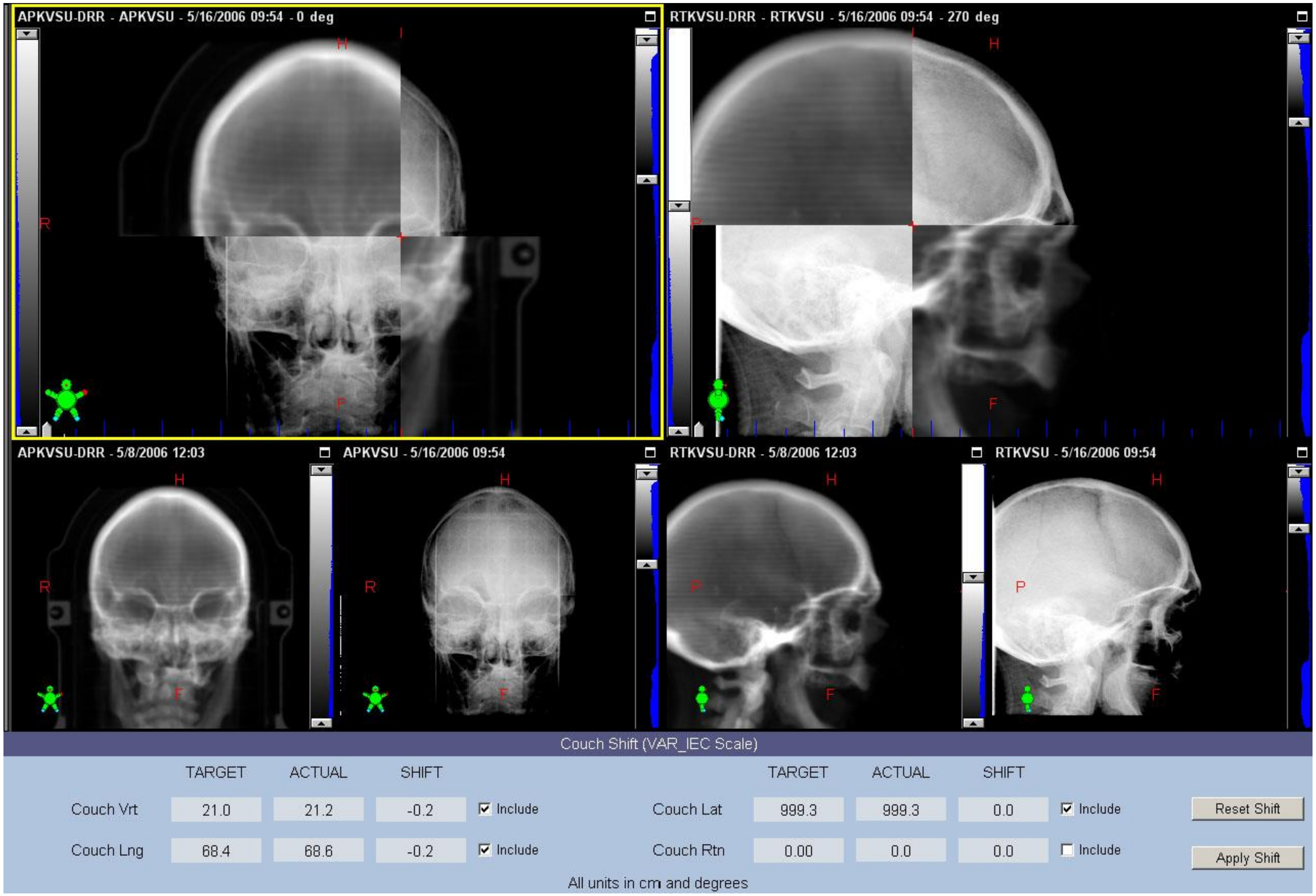
OBI kV imaging



Images: M.Josipovic

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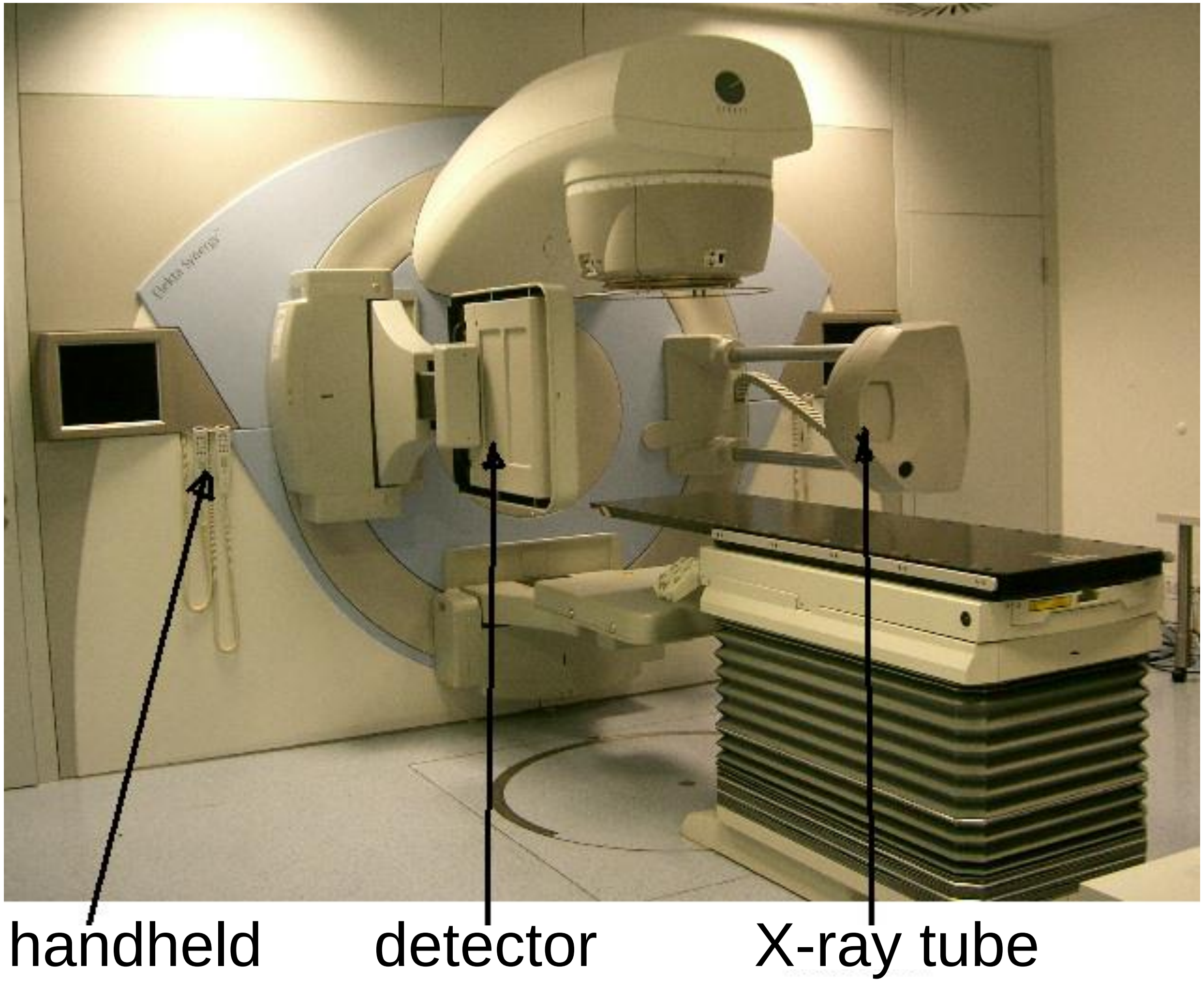
kV imaging

Pros:
- Imaging dose is low
- High 2D imaging quality
- Real time imaging in some systems (all angles)

Cons
- Limited anatomical information
- In most times it is a surrogate
- Oblique images are difficult to interpret.

Cone beam CT



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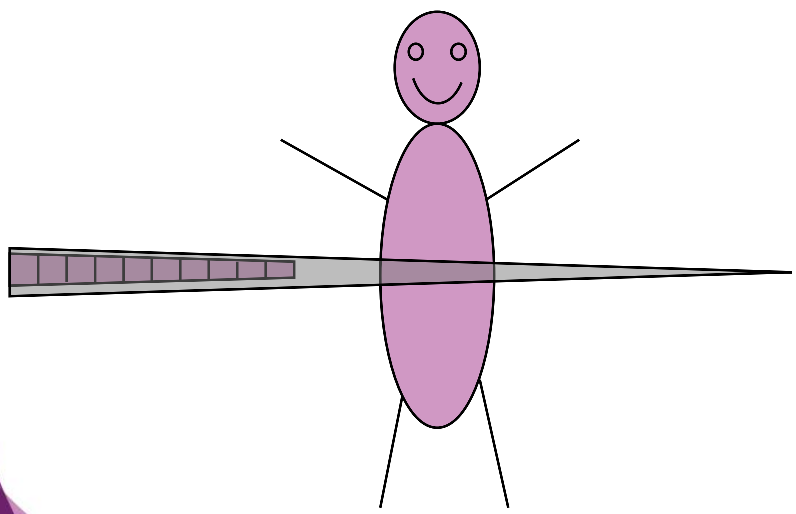
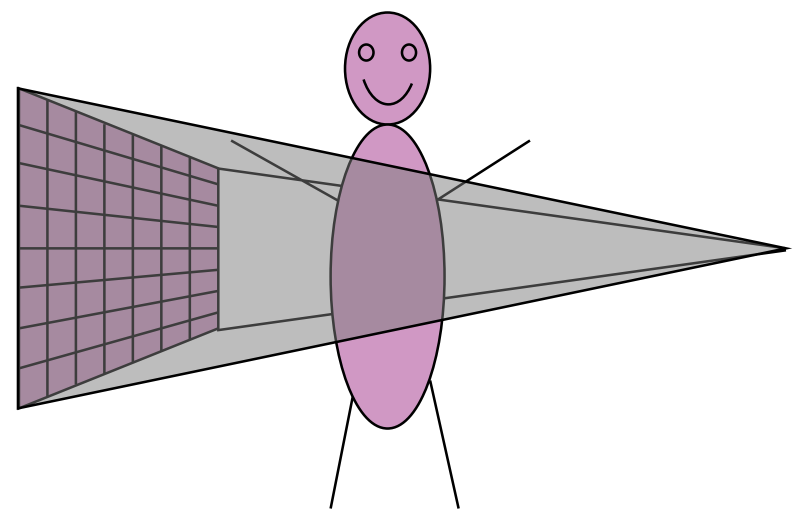
CBCT Acquisition

Conventional CT
- ‘Fan’ beam
- 1D detector
- 1 rotation = 1 slice



Cone-beam CT
- ‘Cone’ beam
- 2D detector
- 1 rotation = volume (many slices)



Courtesy: Peter Remeijer

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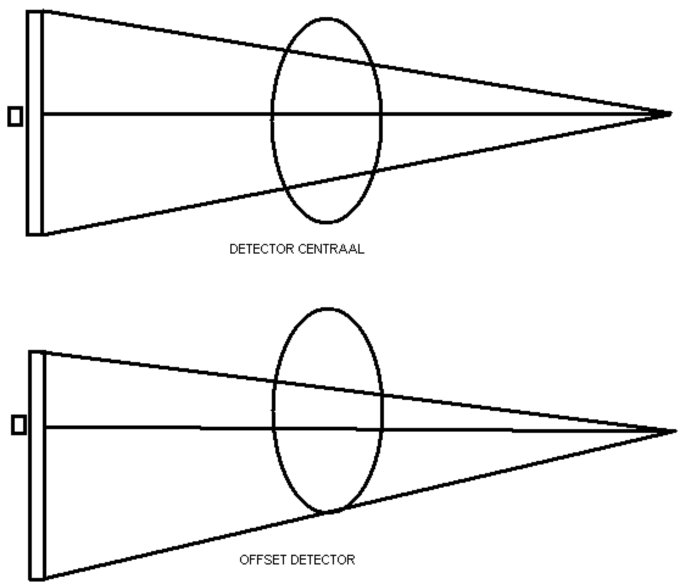
How does it work?

Variable detector position



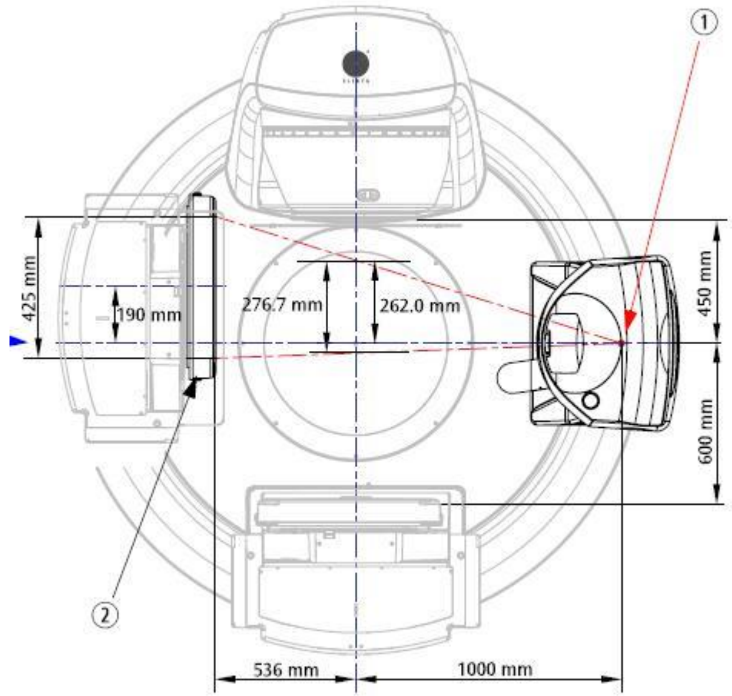


Image registration: Defining the ROI

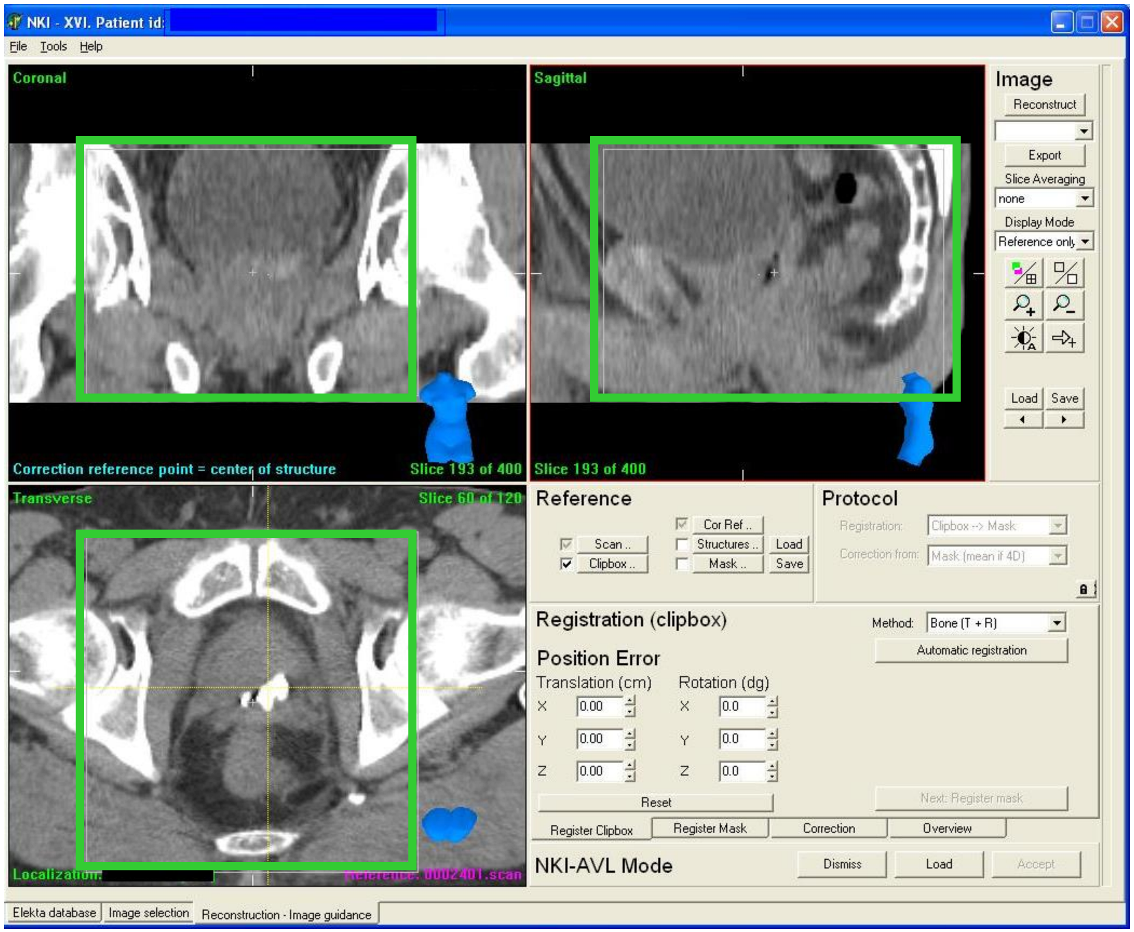


Image registration: Defining the ROI

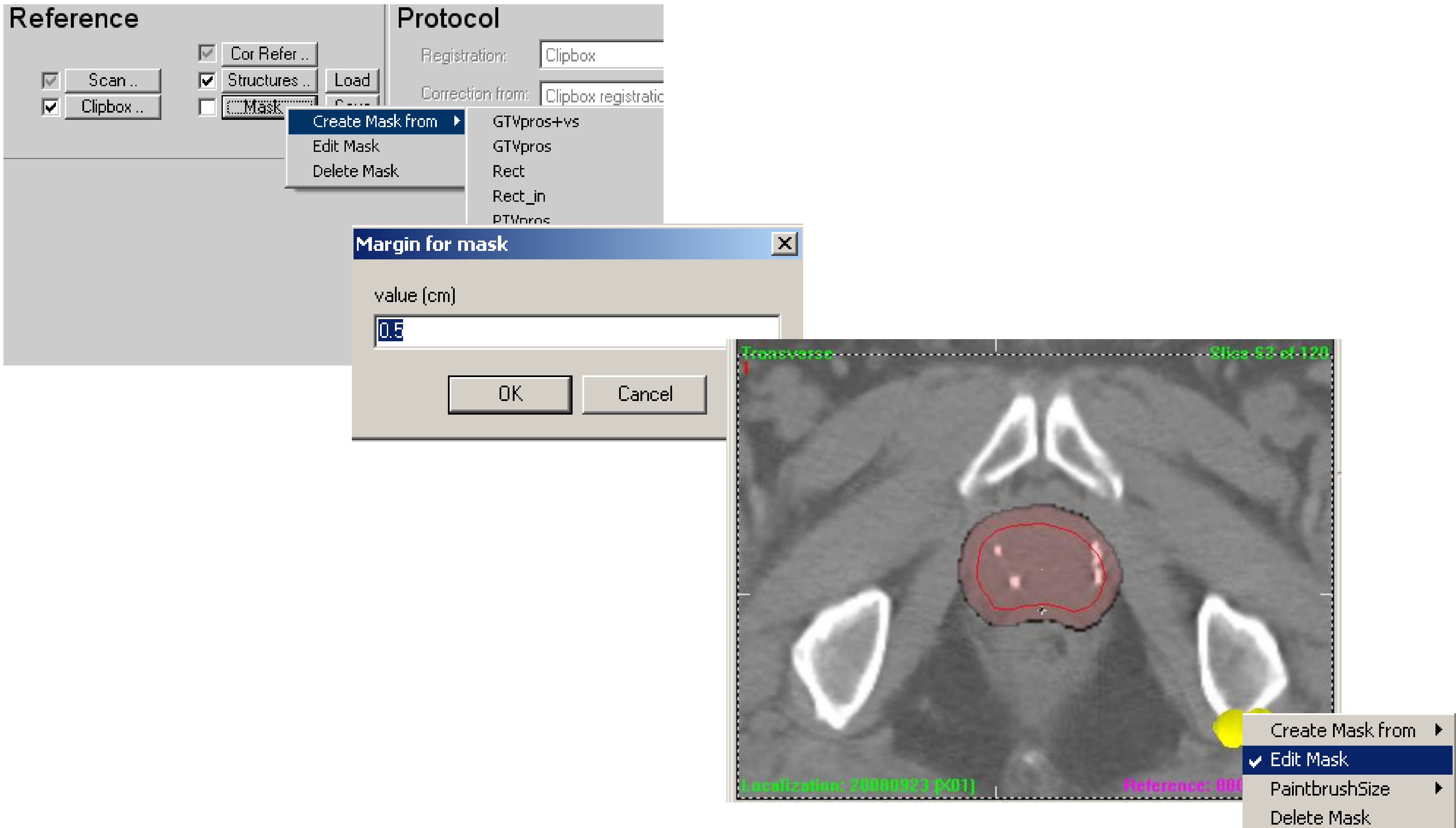


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Image registration

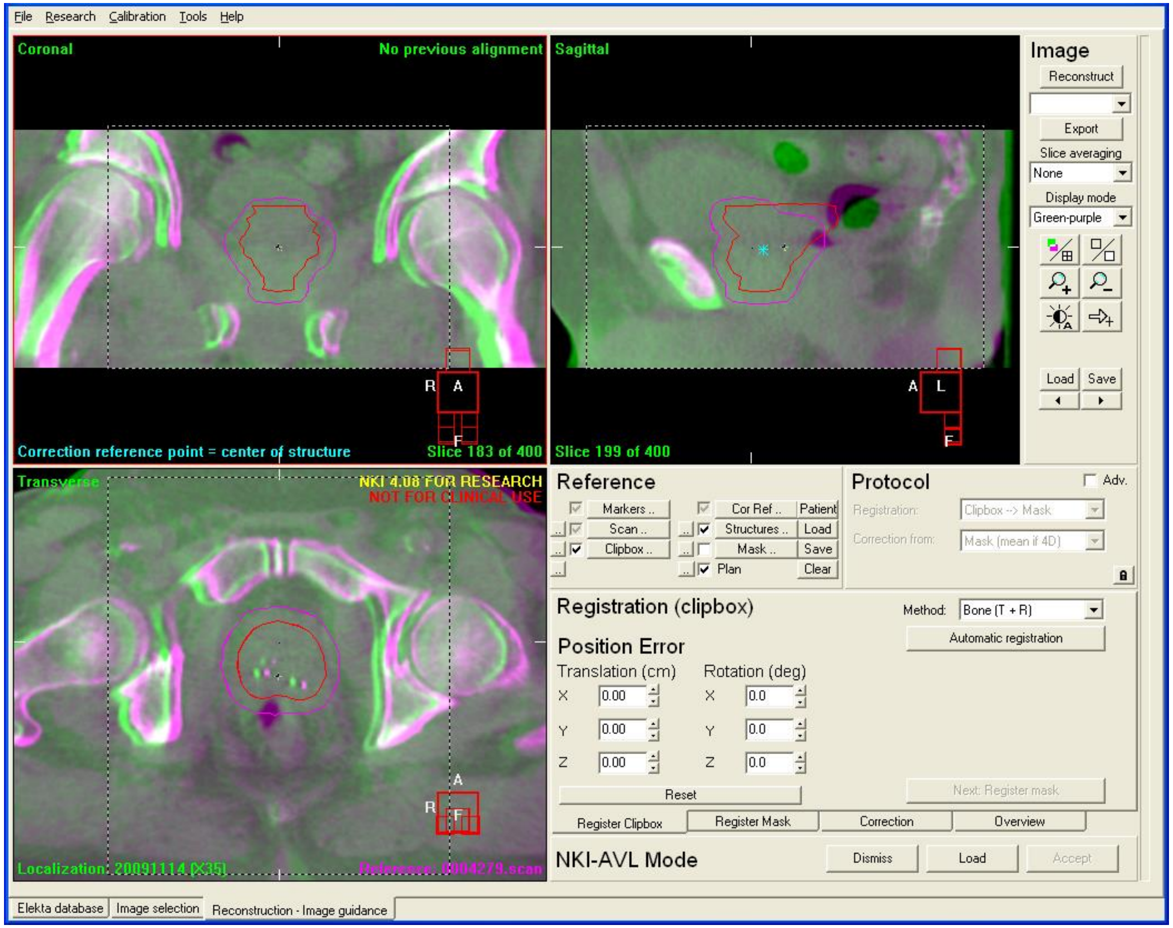


Image registration: bony anatomy

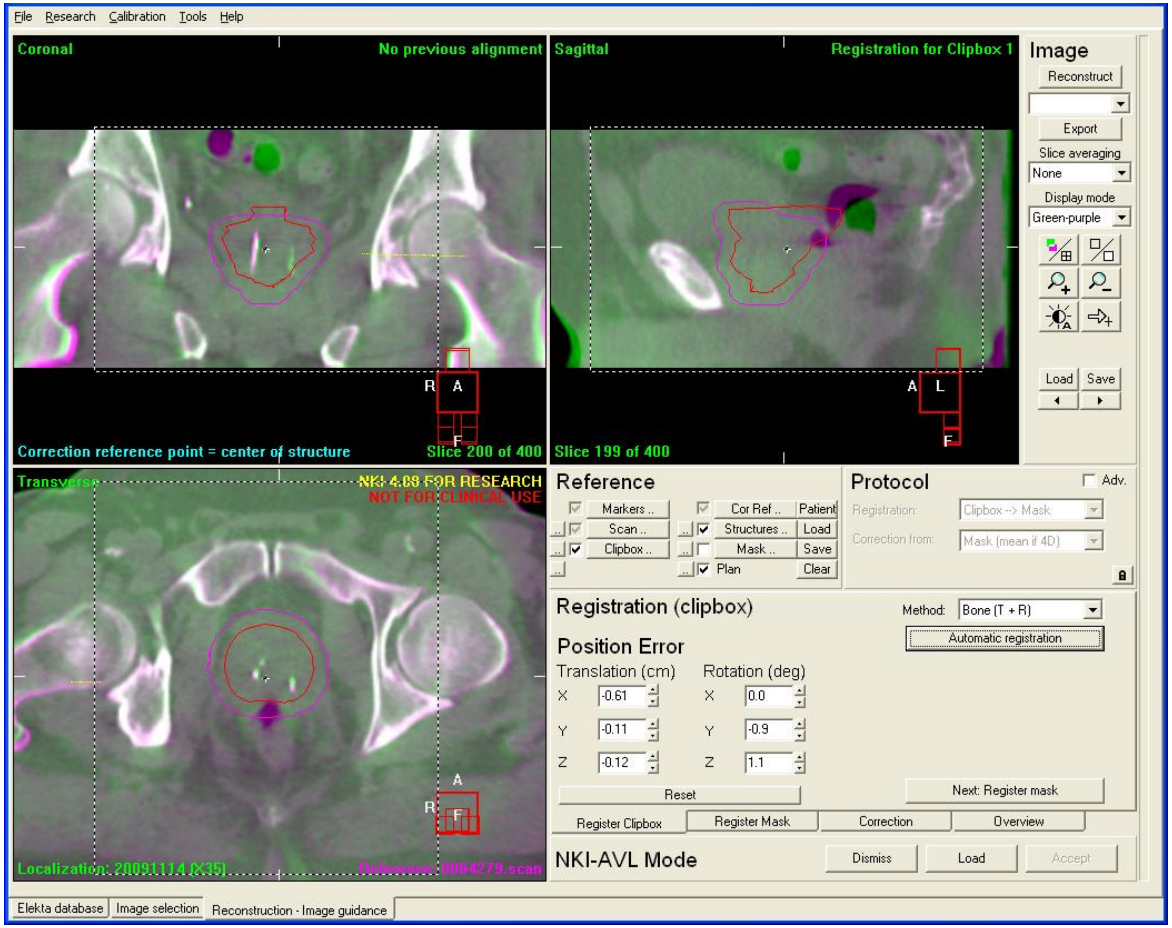
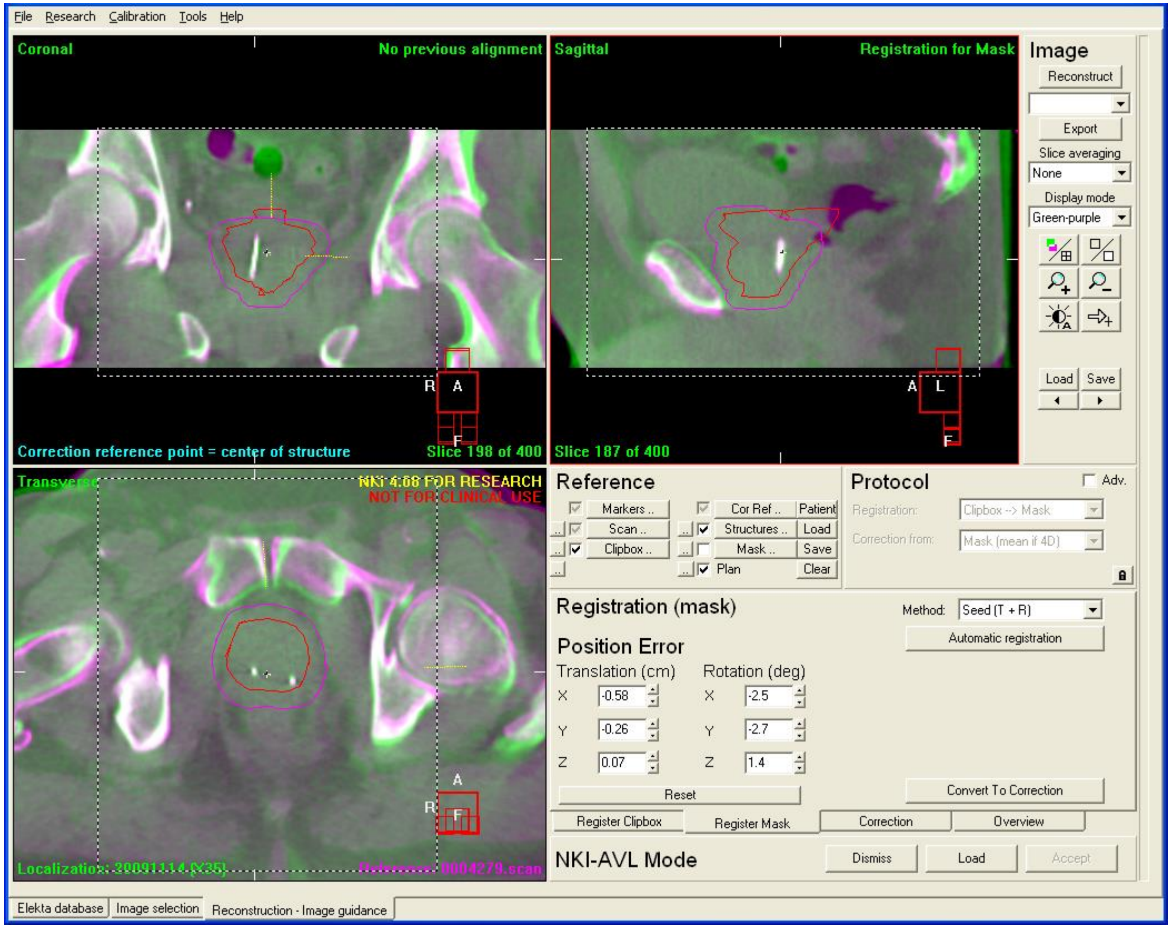


Image registration: fiducial markers



CBCT imaging

Pros:

- Anatomical information
- Imaging dose can be low
- Relatively high imaging quality
- Good to excellent registration algoritms

Cons

- Imaging dose can be substantial
- No real time imaging in some systems
  - ➢ Inline scanning still leads to retrospective analyses

MV-(CB)CT

Using:

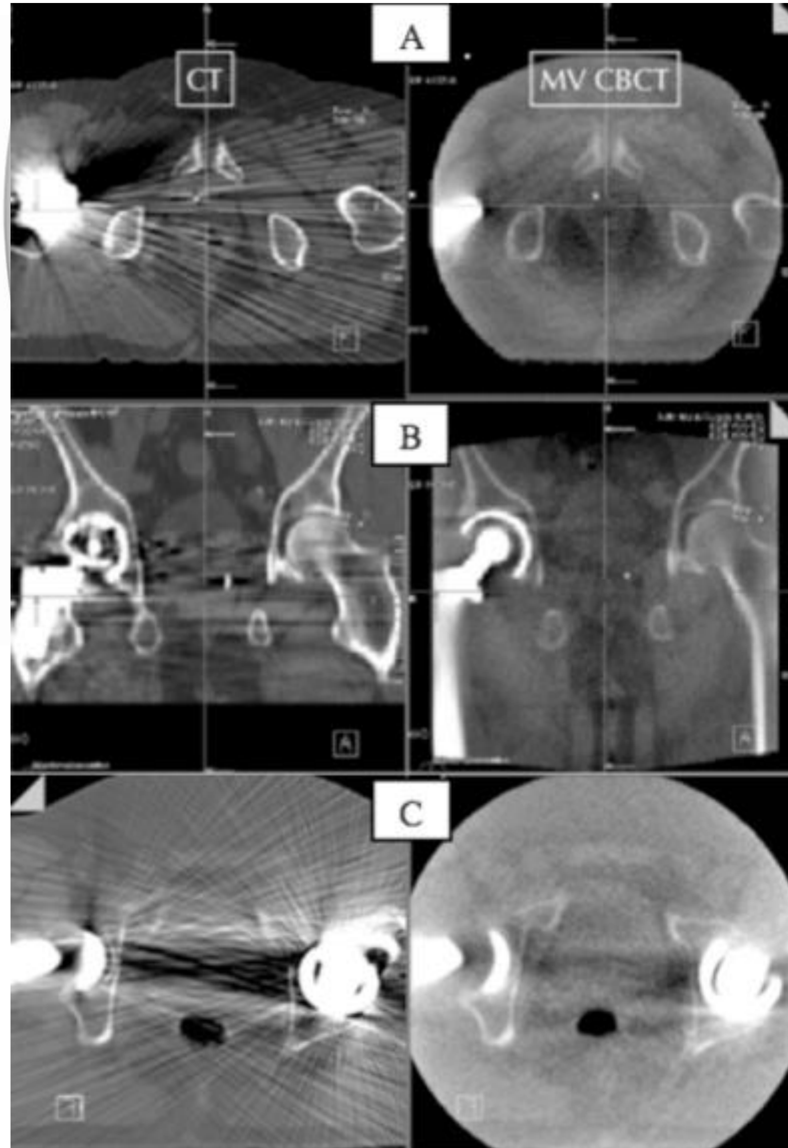
- Treatment beam
- Flat panel
- 3D acquisition

MV-CT:

- Helical acquisition
- TomoTherapy

MV-CBCT:

- 360 degrees acq.
- Siemens Oncor



MV-CT

Pros:

- Anatomical information
- Limited influence of high densities (prostheses)
- Image of the actual absorbed dose

Cons

- Image quality not as good as kV CBCT
- Imaging dose
- Only available as Siemens

Videosystems

Different approaches:

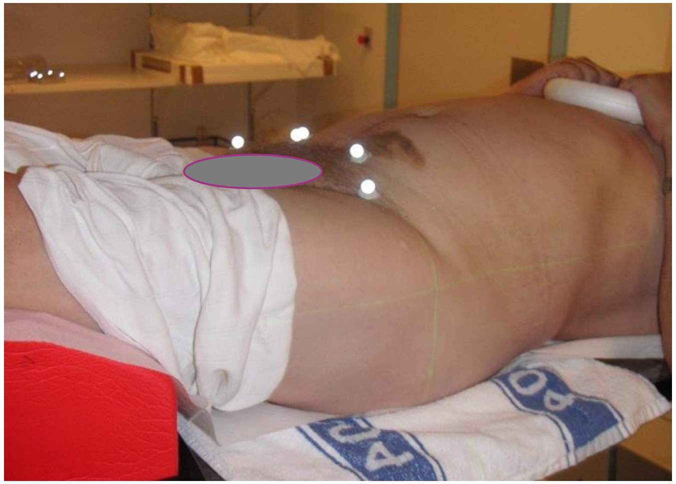
- Infrared tracking of external markers
- Surface scanning

What can you do with these systems?

- Set-up aid
- More important: monitor the patient during treatment:
  1. Passive: monitoring set-up accuracy
  2. Active: correlate motion with treatment (e.g. gating or DIBH)

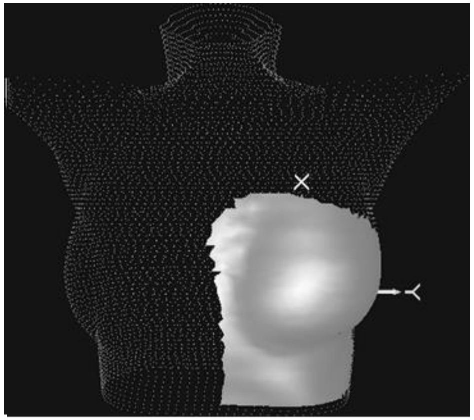
Exac trac infrared

- Infrared marker,
  - ➢ placed on fixed spots
- Tracking of the markers during RT
  - ➢ Correlate with respiration (tracking/gating)

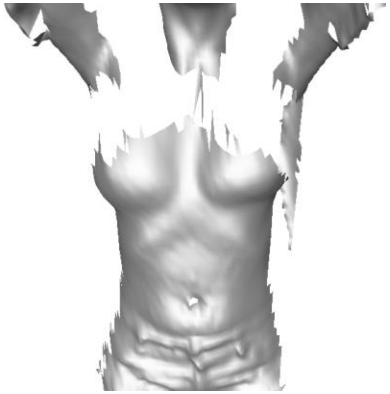


Images: M.Josipovic

Surface scanning



Left side



Images: T.Alderliesten

Infra red systems

Pros

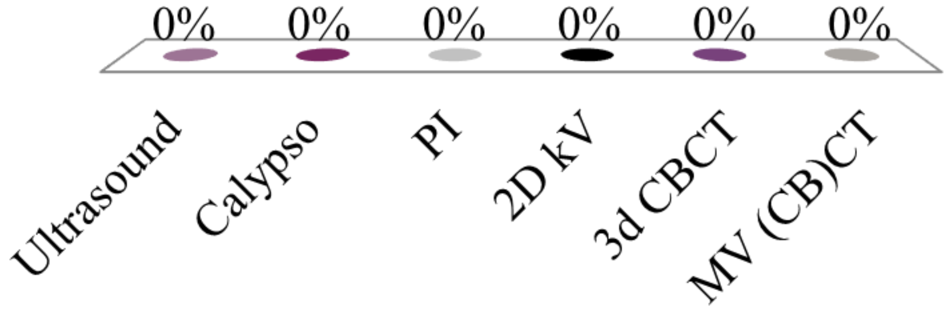
- No imaging dose
- Enables tracking and gating
- Real time measurements
- Surface scanning:
  - ➢ Pre treatment set-up check

Cons

- It’s an aid
  - ➢ Can never be a stand alone system
- Surrogate

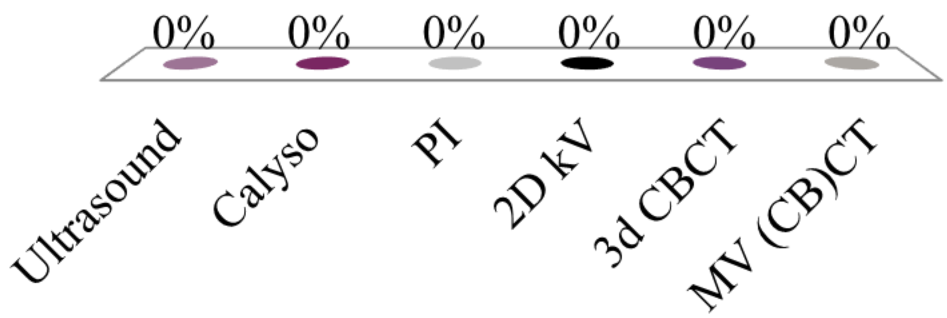
Which one do you prefer most in prostate?

A. Ultrasound
B. Calypso
C. PI
D. 2D kV
E. 3d CBCT
F. MV (CB)CT

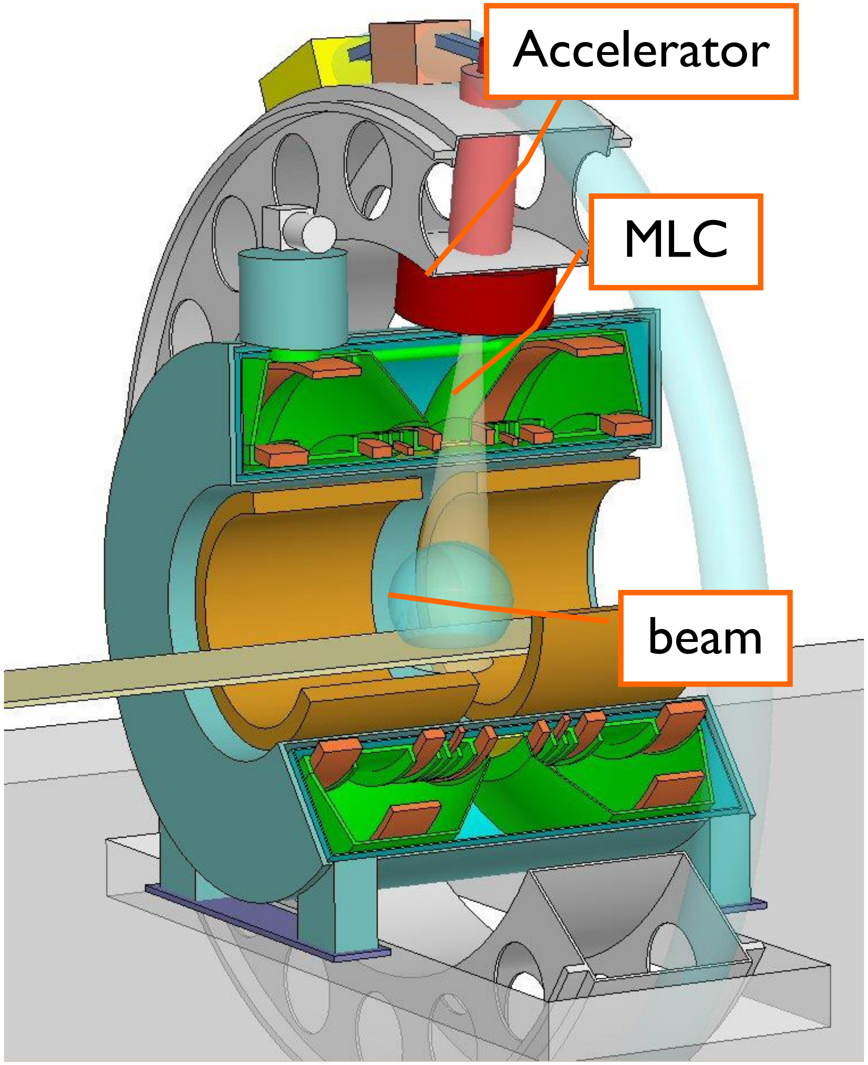


Which one do you prefer most in lung?

A. Ultrasound
B. Calyso
C. PI
D. 2D kV
E. 3d CBCT
F. MV (CB)CT



Integrating MRI functionality with external beam radiotherapy



Integrating MRI functionality with external beam radiotherapy

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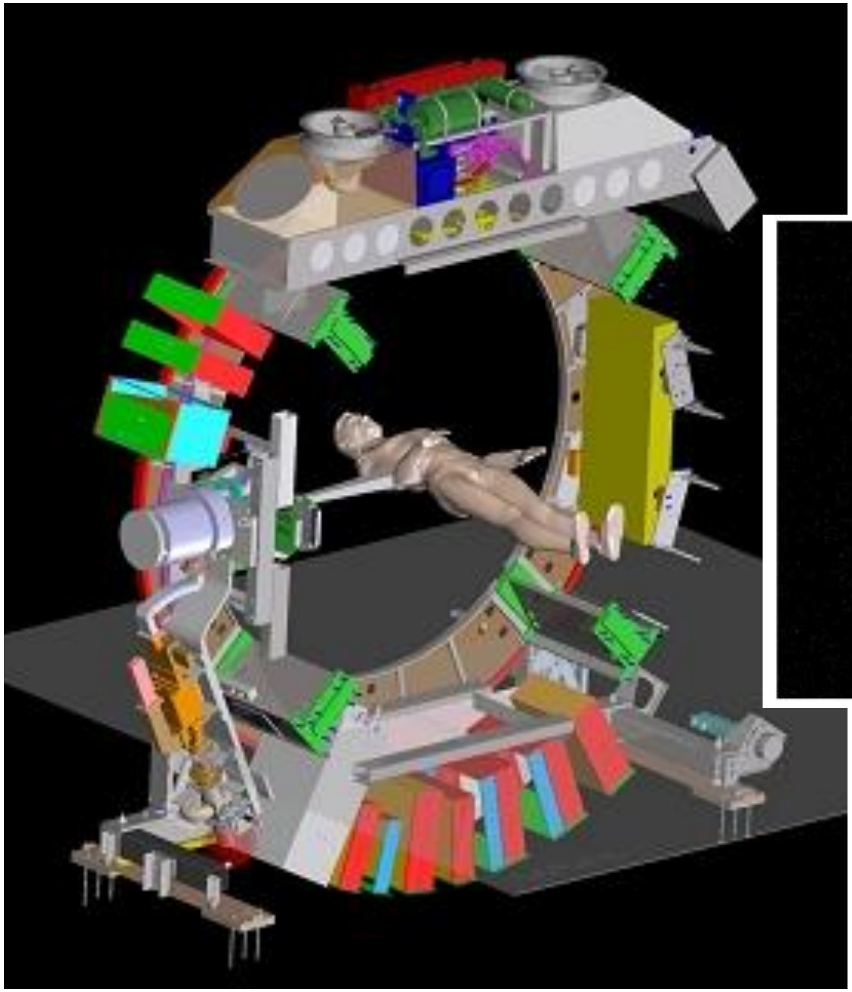
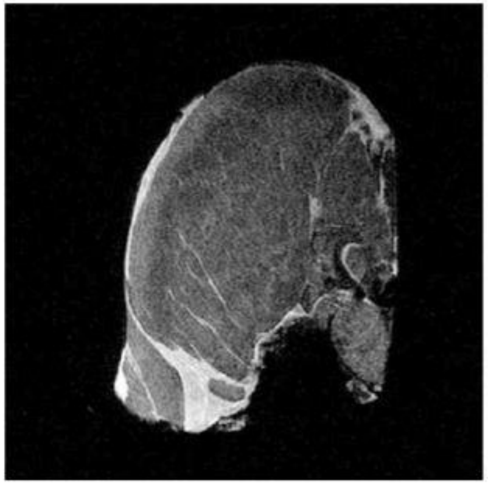
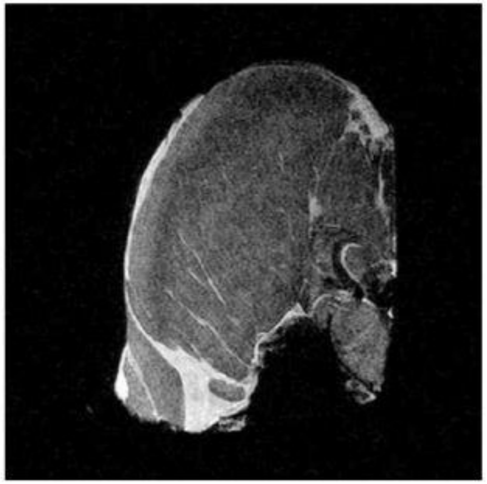
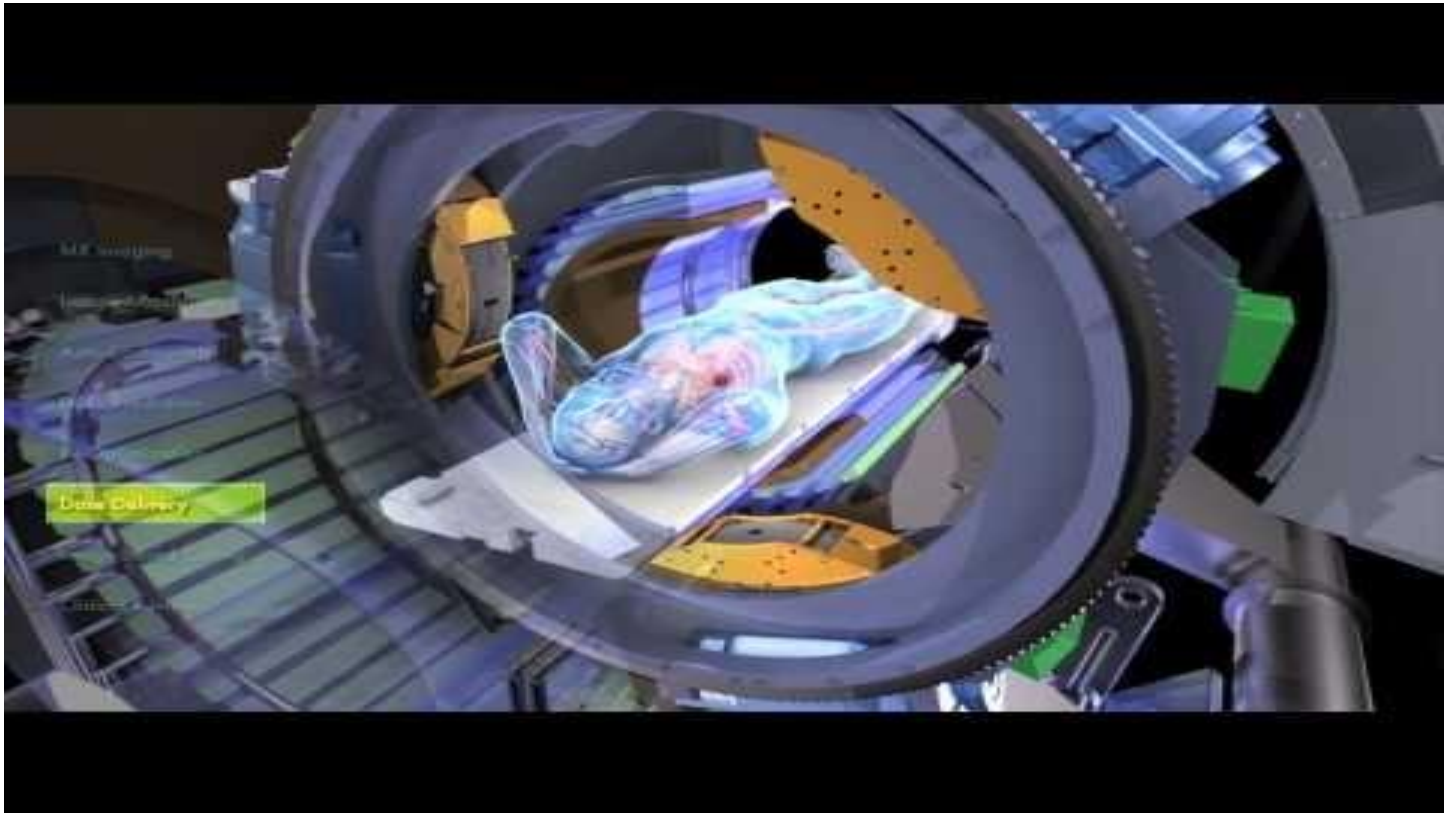
Gantry design MRL: (MRI-Linac)







MRIdian: MR Cobalt



MR linac

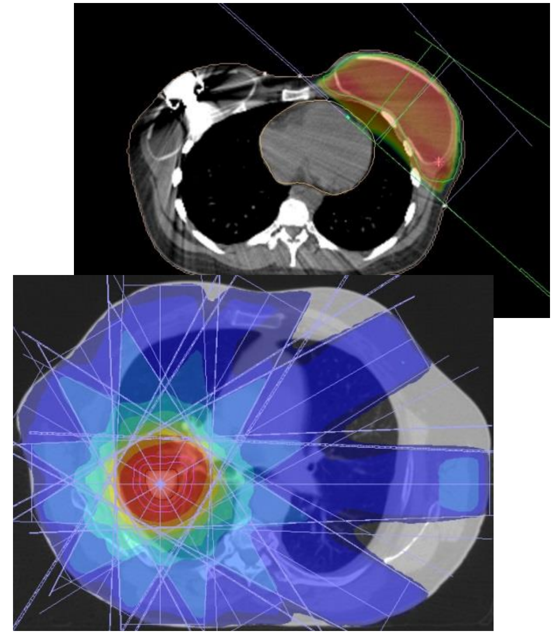
Pros

- Optimal image quality
- Intra fraction imaging

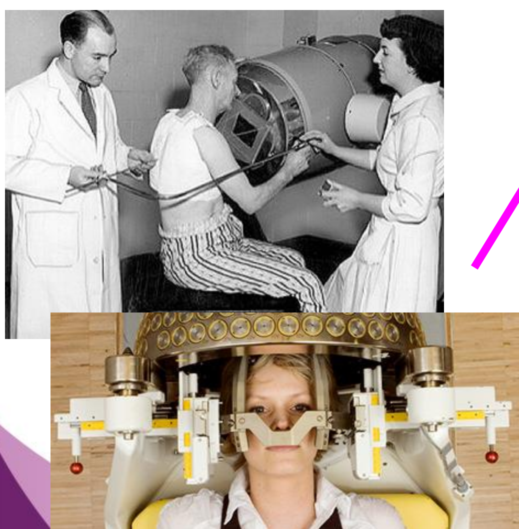
Cons

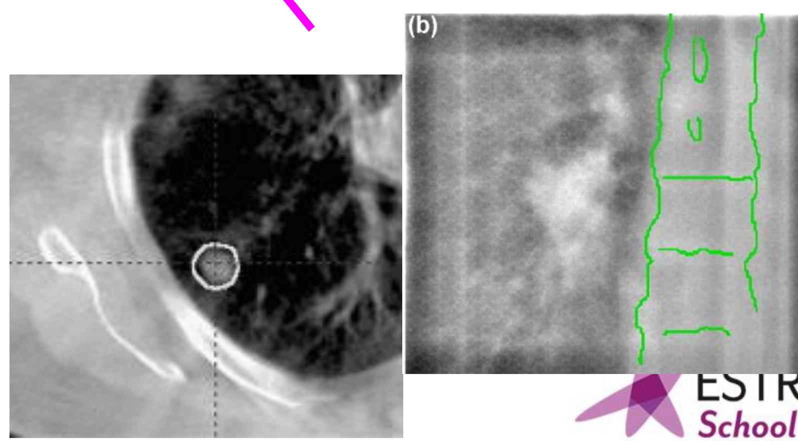
- MR-Linac:
  - ➢ quite expensive
  - ➢ Under development, mainly research
- Cobalt treatment: linac upcoming
- Challenging Treatment planning (1,5 Tesla)
  - ➢ Secondary electrons are influenced by the magnetic field

How accurate should the delivery be?



Balance!





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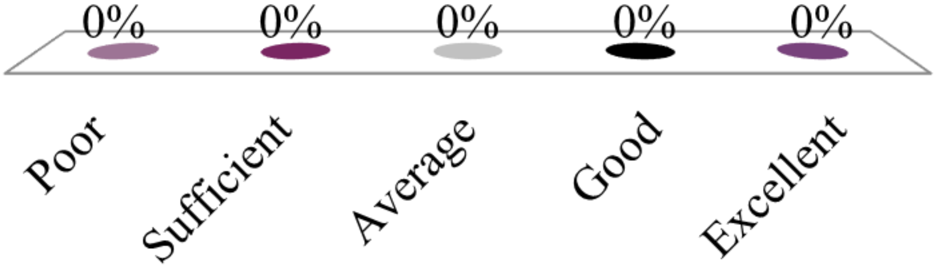
Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



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Management of respiratory motion in radiation therapy

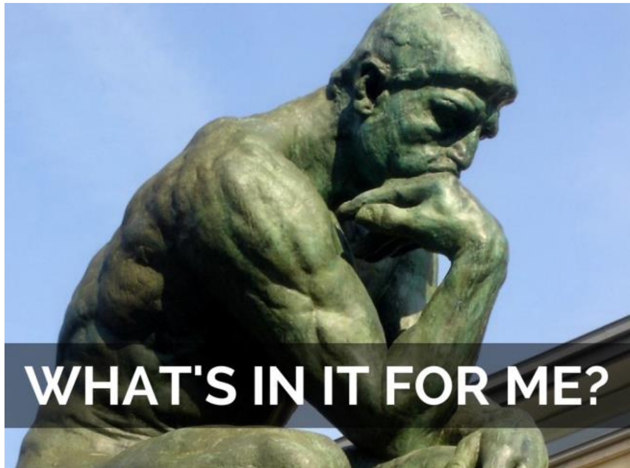
Mirjana Josipovic

Dept. of Oncology, Rigshospitalet
& Niels Bohr Institute, University of Copenhagen
Denmark

Advanced skills in modern radiotherapy
May 2018

Intended learning outcomes

- Differentiate between different motion management strategies in RT
- Interpret the purpose of motion management for different patient groups
- Identify the limitations in motion management



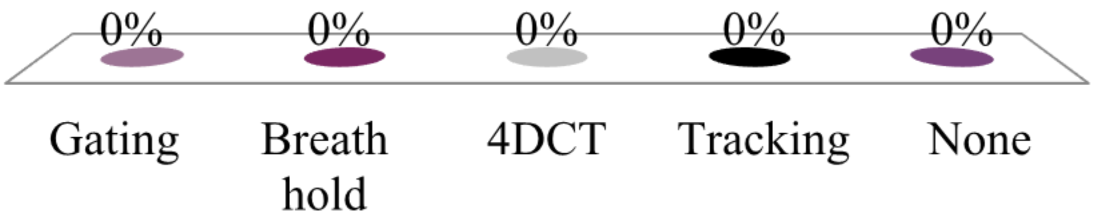
Management of respiratory motion in RT

- Respiratory gating technique
- Breath hold methods
- Motion encompassing methods
- Respiration synchronized techniques

AAPM TG 76 definition

Which motion management do you use?

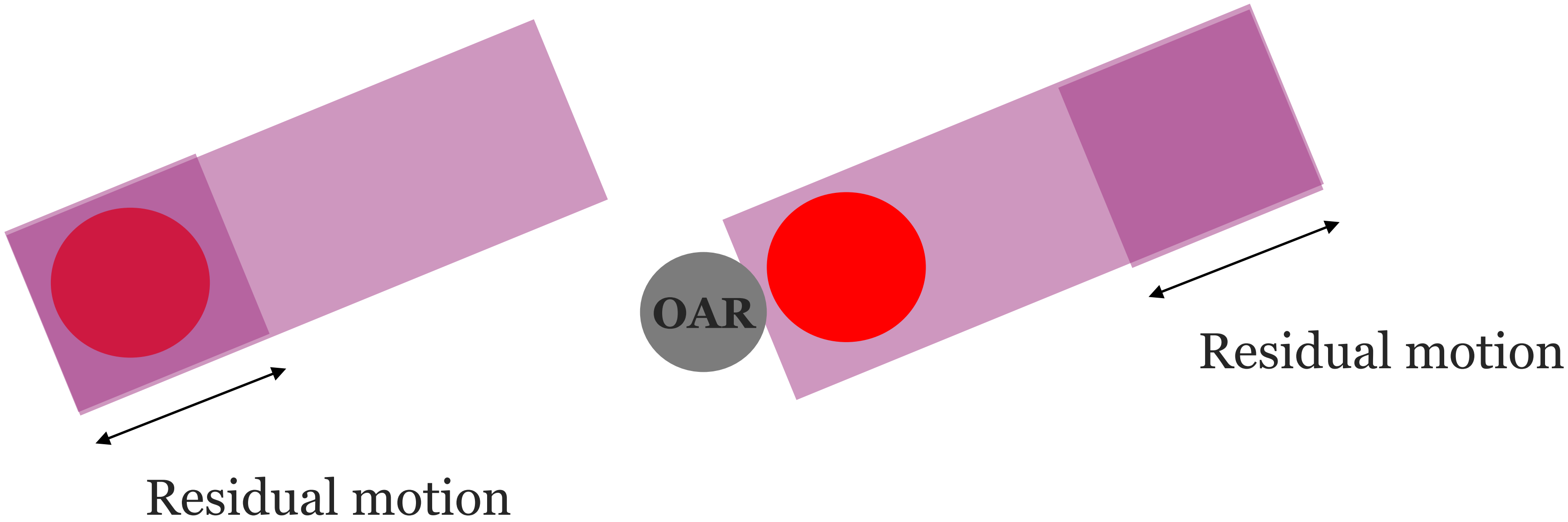
A. Gating
B. Breath hold
C. 4DCT
D. Tracking
E. None



Multiple answers allowed

What is respiratory gating?

- Applying radiation within a particular part of the patient's breathing cycle



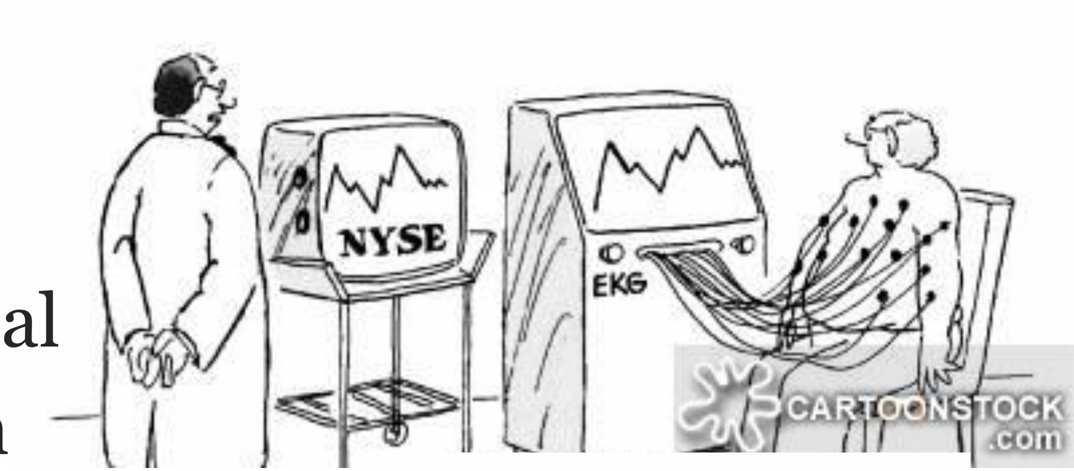
→ Reduce motion during treatment
→ Move target away from OAR

Condition for success with gating

Strong correlation

Internal organ motion - External chest motion

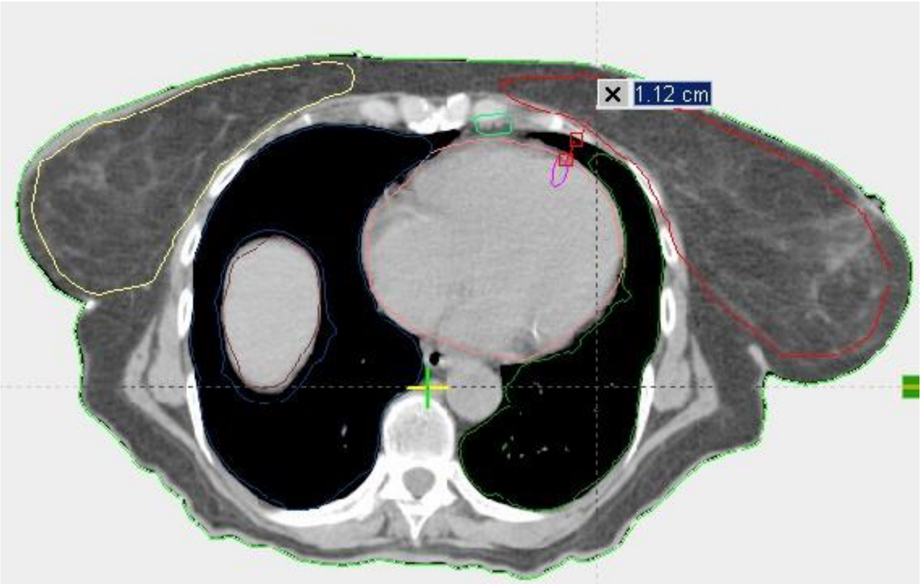
- Tumour type and location
- Source of the respiratory signal
- Reproducibility of respiration



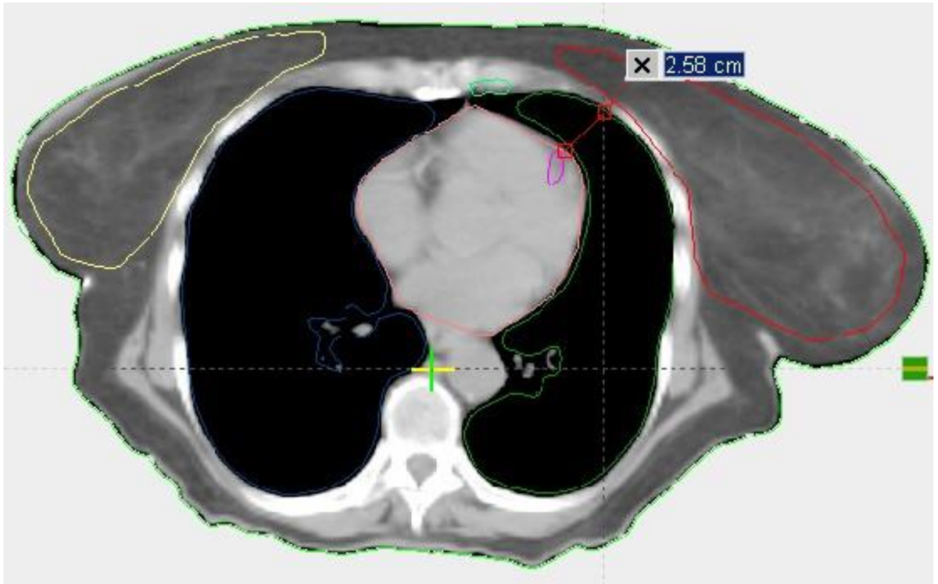
" Amazing . . the patterns are the same ! "

External vs. "internal" motion - breast

- Good correlation



Spontaneous breathing



Enhanced inspiration gating

External vs. internal motion - lung

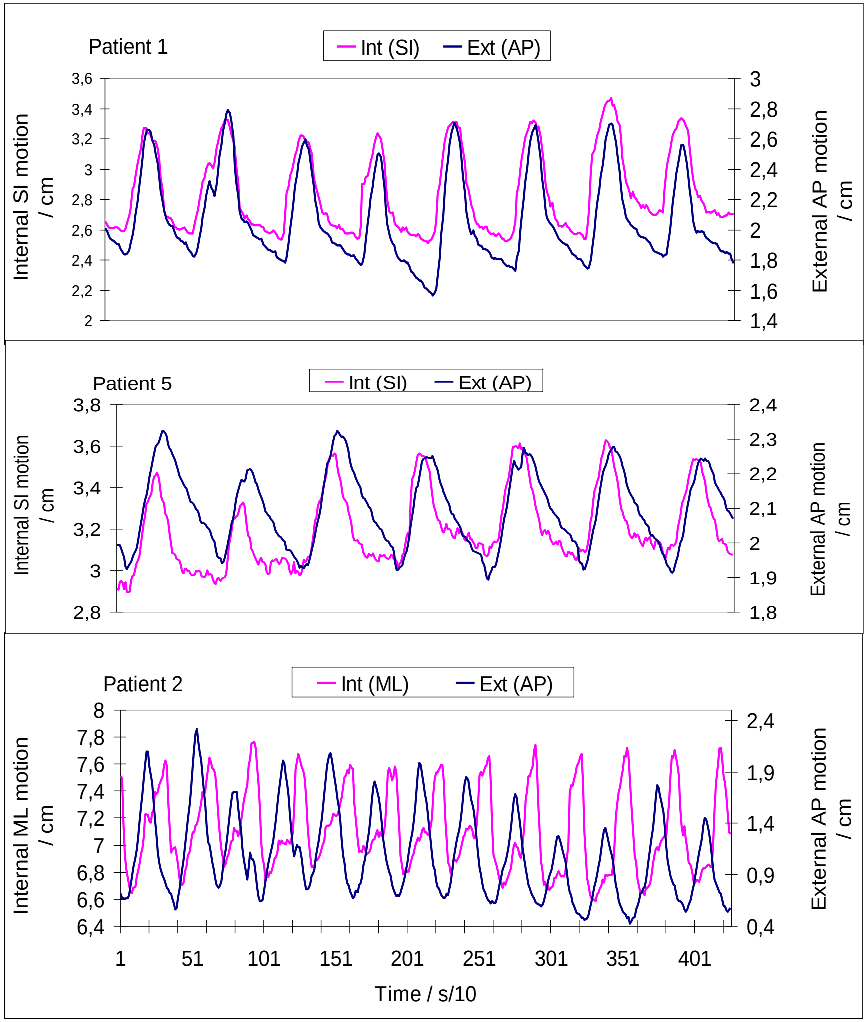


Image courtesy of S Korreman

Correlation can be established

Phase difference

Phase drift

– No correlation

No external vs. internal motion correlation

Simple approach:

- Don't do gating

Complicated approach:

- Monitor the target position during (gated) treatment

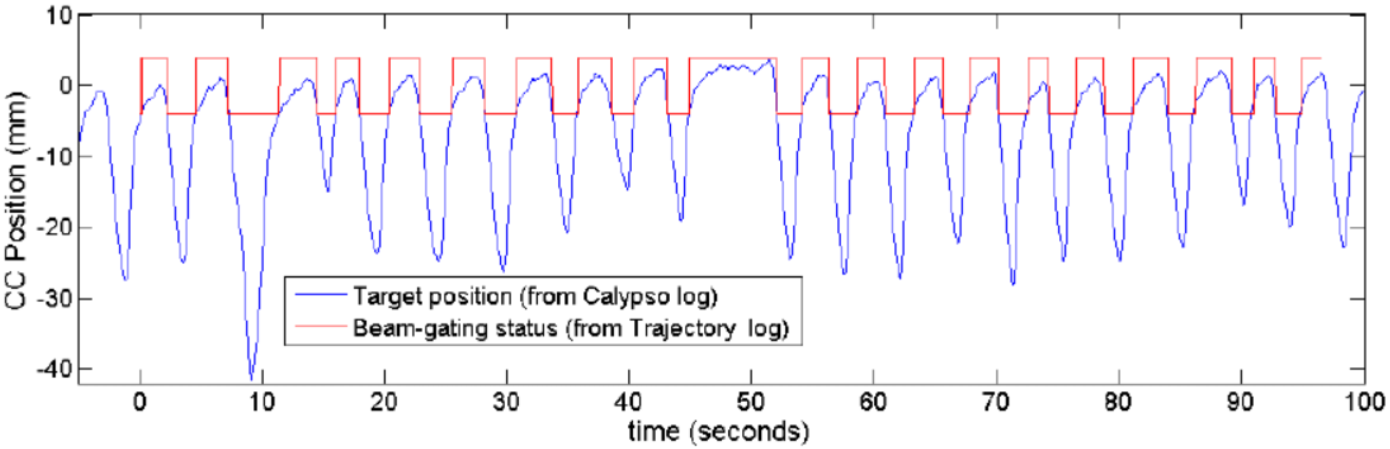
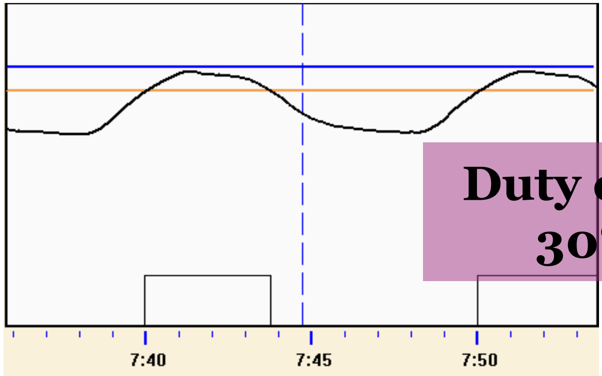


Image courtesy of PR Poulsen

- Free breathing respiratory gating can be applied if there is a good correlation between the respiratory signal and the tumour motion

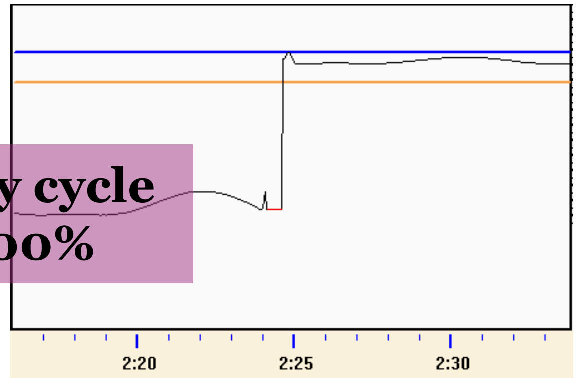
The choice of breathing technique

Inspiration gating



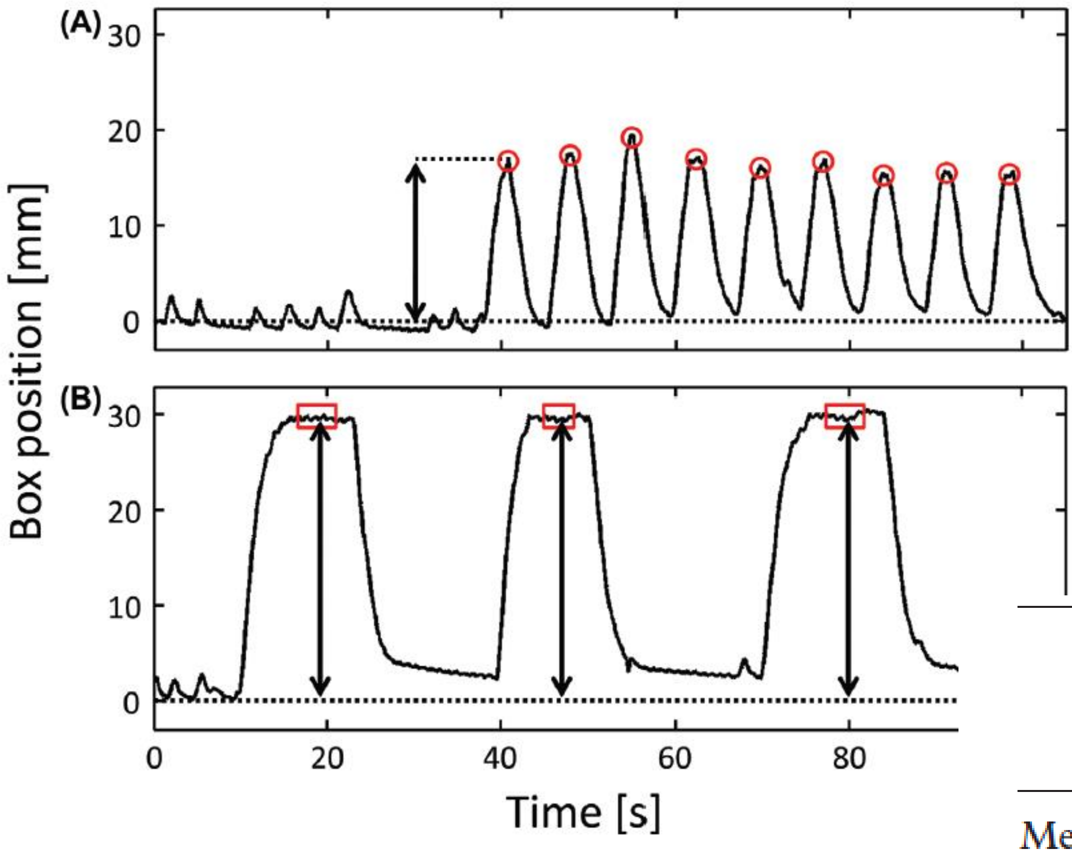
Duty cycle 30%

Deep inspiration breath hold (DIBH)



Duty cycle 100%

Respiration reprodicibility



← audio coaching + insp.gating

← visual guidance + DIBH

	Audio-coached EIG mean (range)	Visually guided DIBH mean (range)
Mean inspiration level [mm]	16.6 (5–35)	20.5 (5–34)
Mean standard deviation [mm]	1.66 (0.5–3.5)	0.38 (0.2–0.6)

Damkjær et al. Acta Oncologica, 2013

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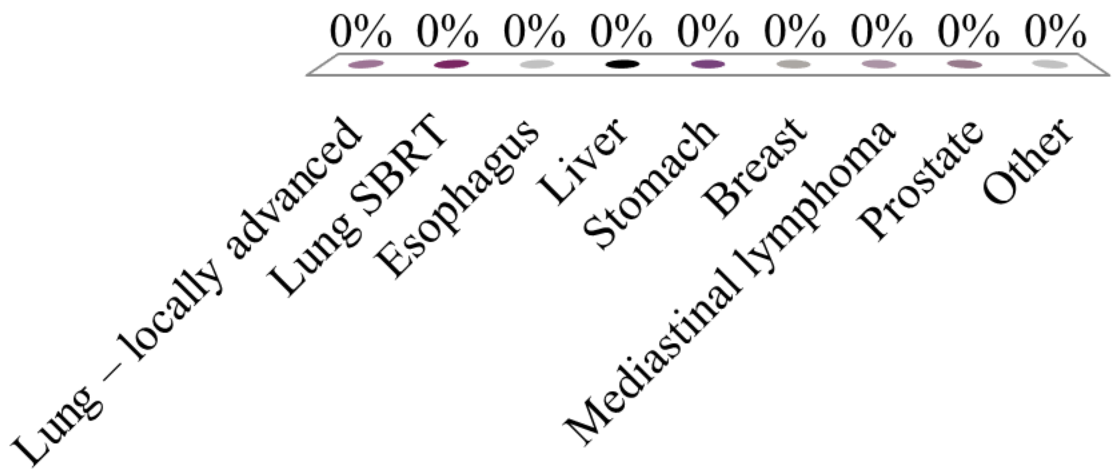
In which sites do you use gating / DIBH?

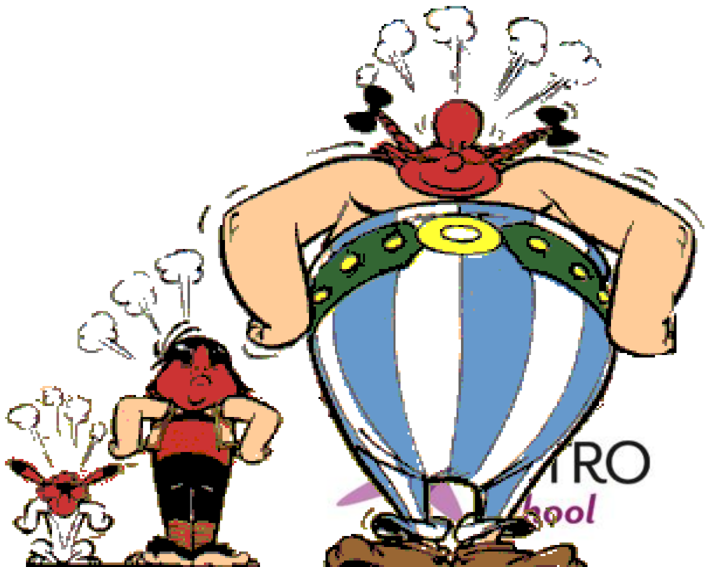
A. Lung – locally advanced
B. Lung SBRT
C. Esophagus
D. Liver
E. Stomach
F. Breast
G. Mediastinal lymphoma
H. Prostate
I. Other



How to DIBH?

- Free DIBH 

- Computer-controlled
  - ➢ Breathing volume based
  - ➢ Optical surface tracking



Boda-Heggemann IJROBP 2016

Breathing volume based DIBH

- Spirometry

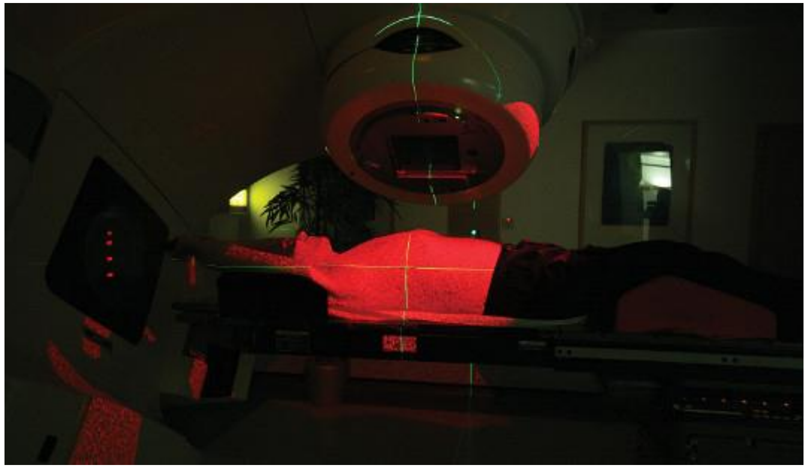
SDX™

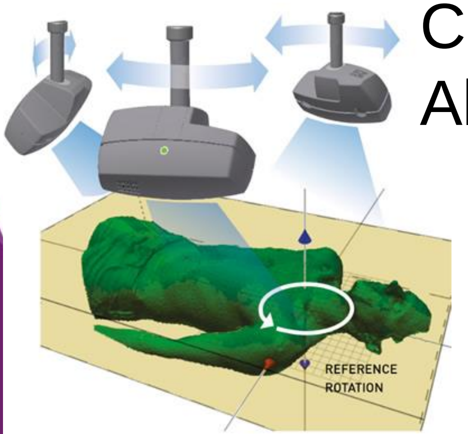
ABC™

Optical surface tracking based voluntary DIBH

Surface tracking

(Surface Guided RT)

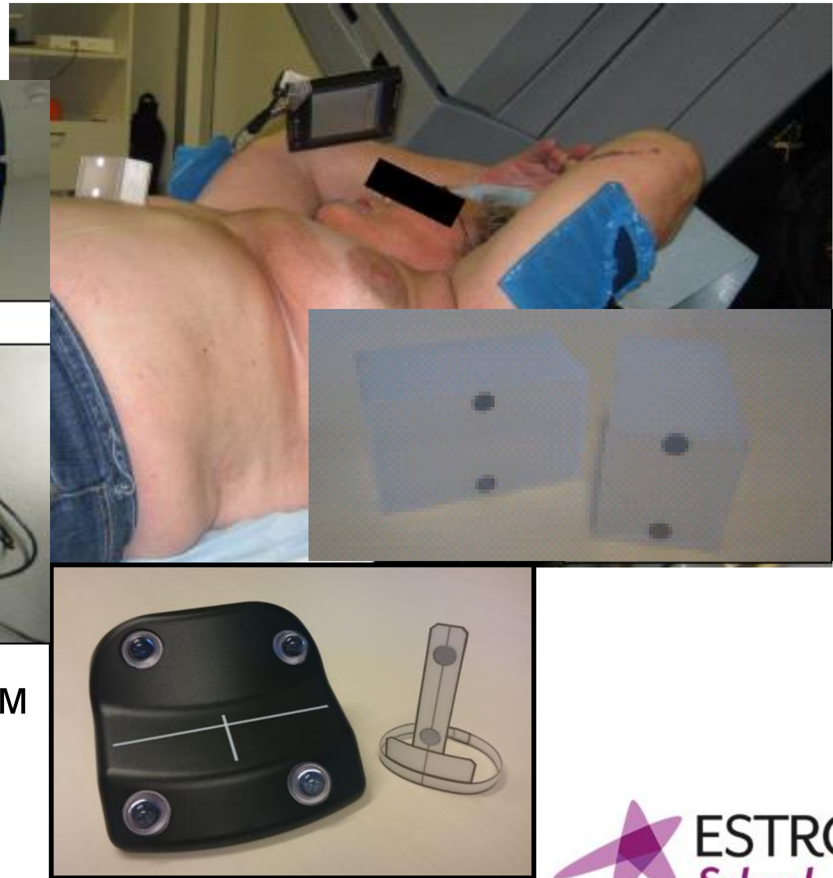




C-RAD Sentinel™

Align RT®

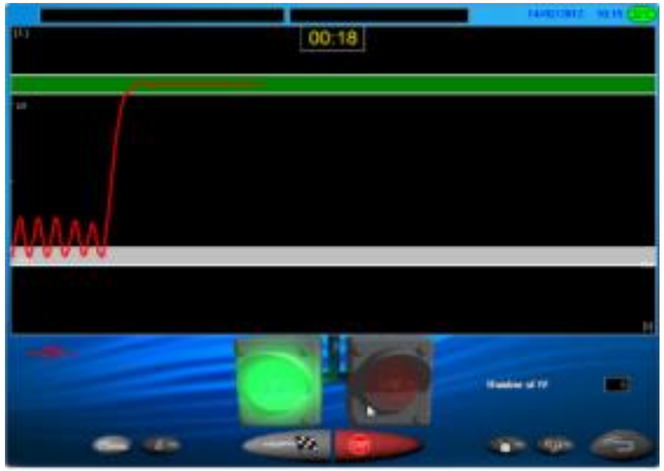
Marker tracking



Varian RPM™

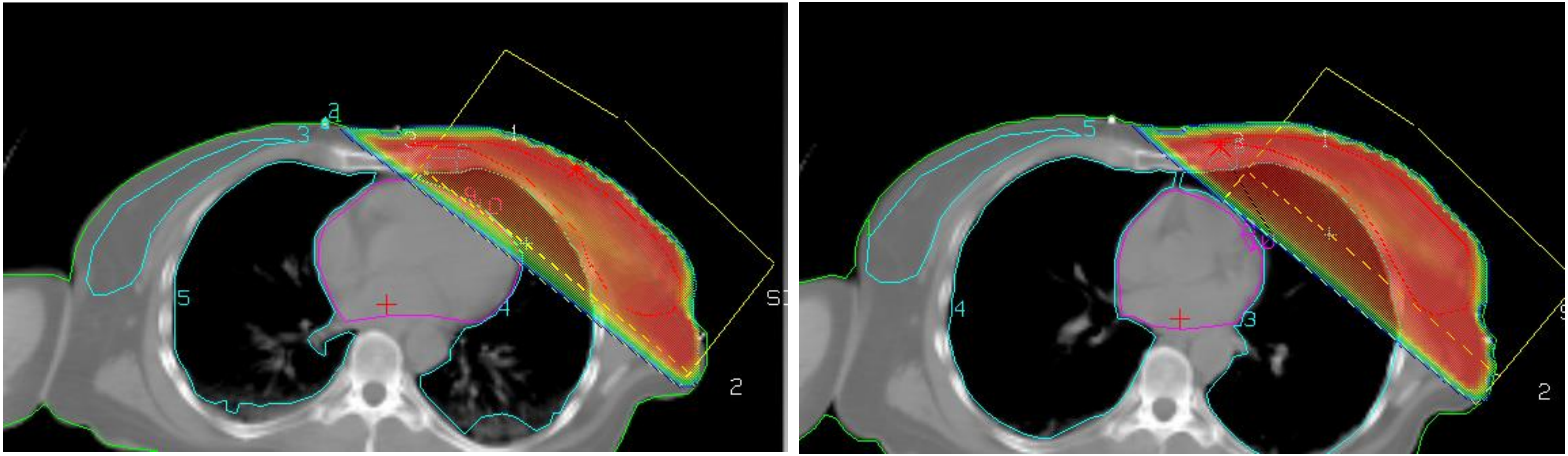
Patient training & QA

- Patient information
- Patient coaching



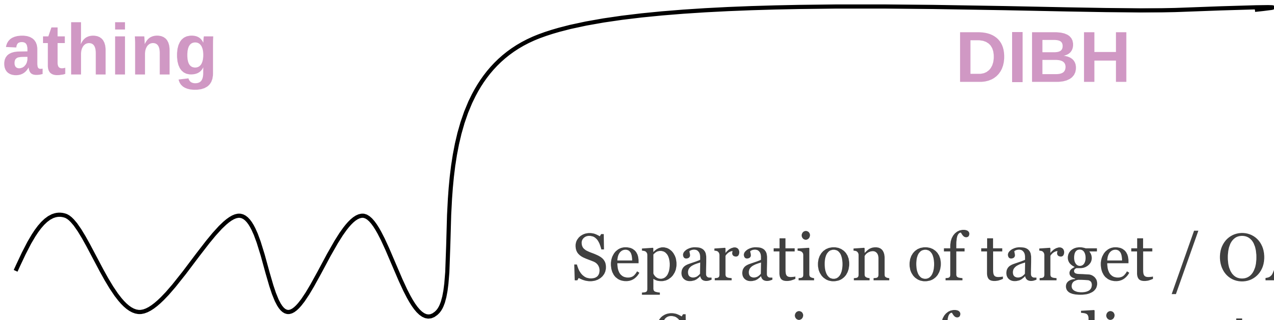
- DIBH level / volume individually adjusted!
- DIBH duration 15-30 s
  - If the patient doesn’t comply – exclude!

Dosimetric potential of DIBH – breast



Free breathing

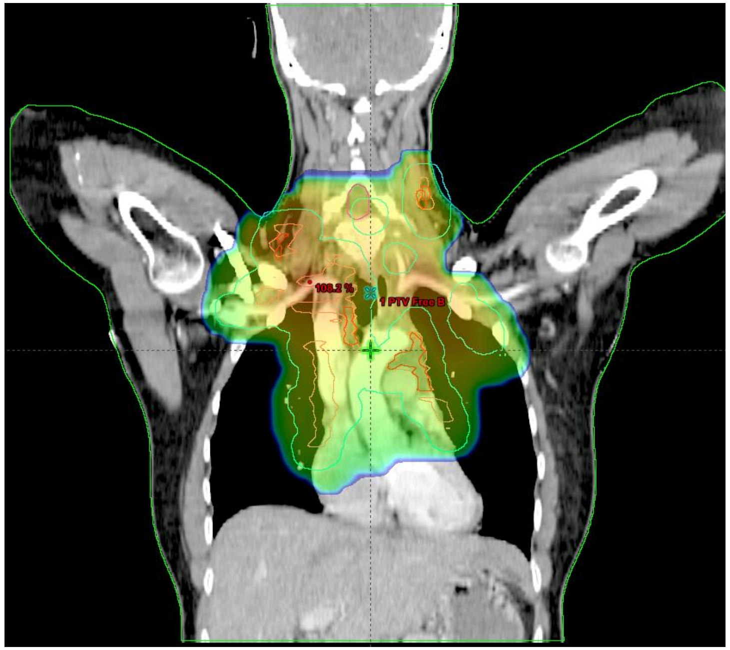
DIBH



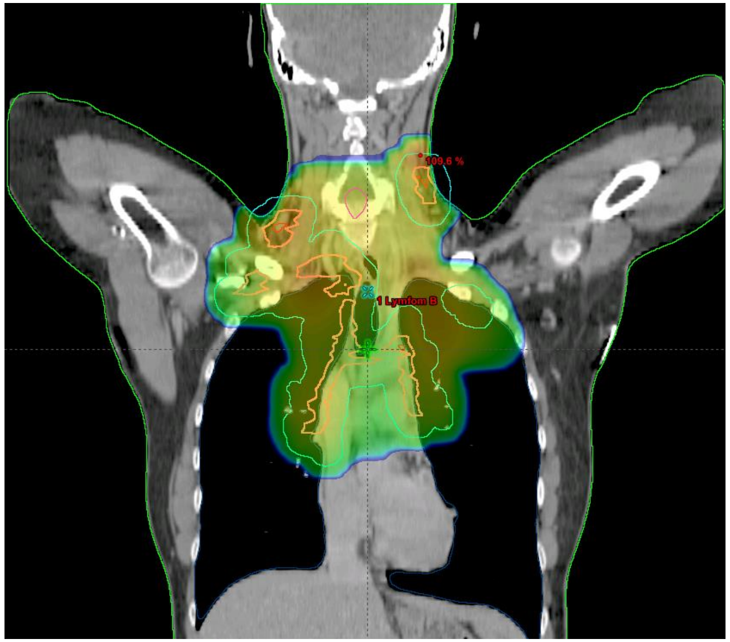
Separation of target / OAR

- Sparing of cardiac structures
- IMN coverage not compromised

Dosimetric potential of DIBH – lymphoma



Free breathing

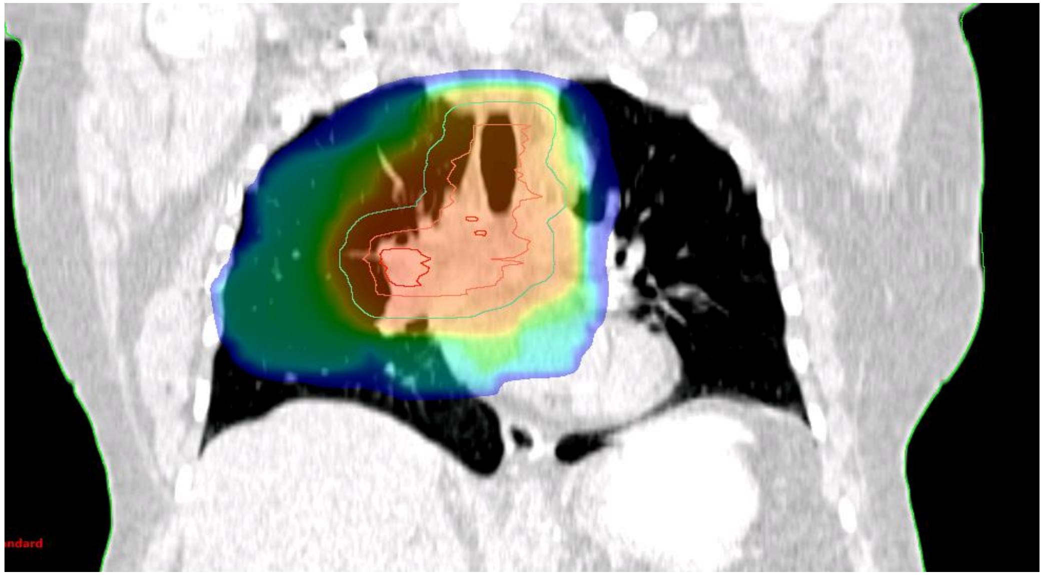


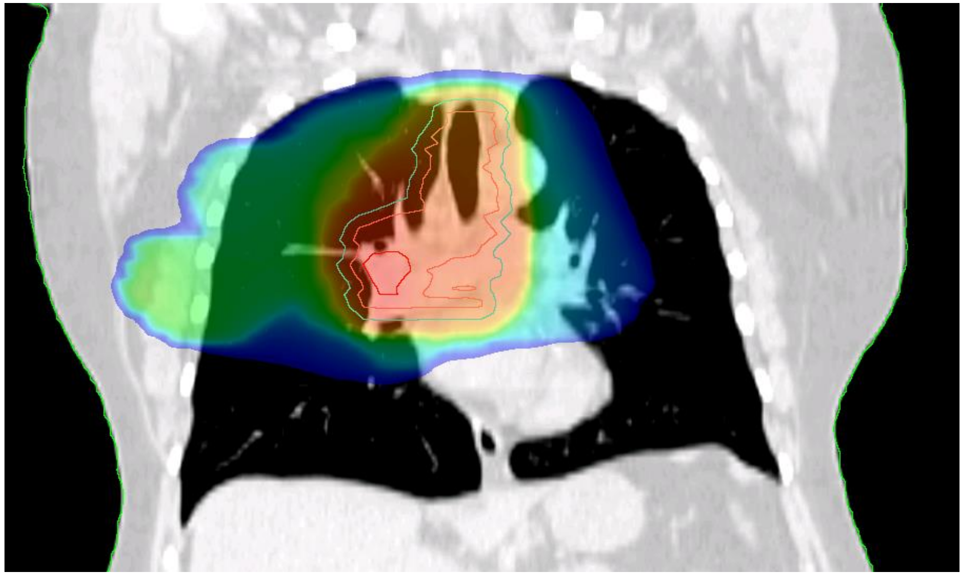
DIBH

- Sparing of heart & lung
- Separation of target & OAR

Images courtesy of Marianne Aznar

Dosimetric potential of DIBH – lung





Free breathing

DIBH

- Sparing of heart & lung
- Maintain curative treatment intent
- Tumour motion reduction

Josipovic et al, Acta Oncologica 2013 & 2014

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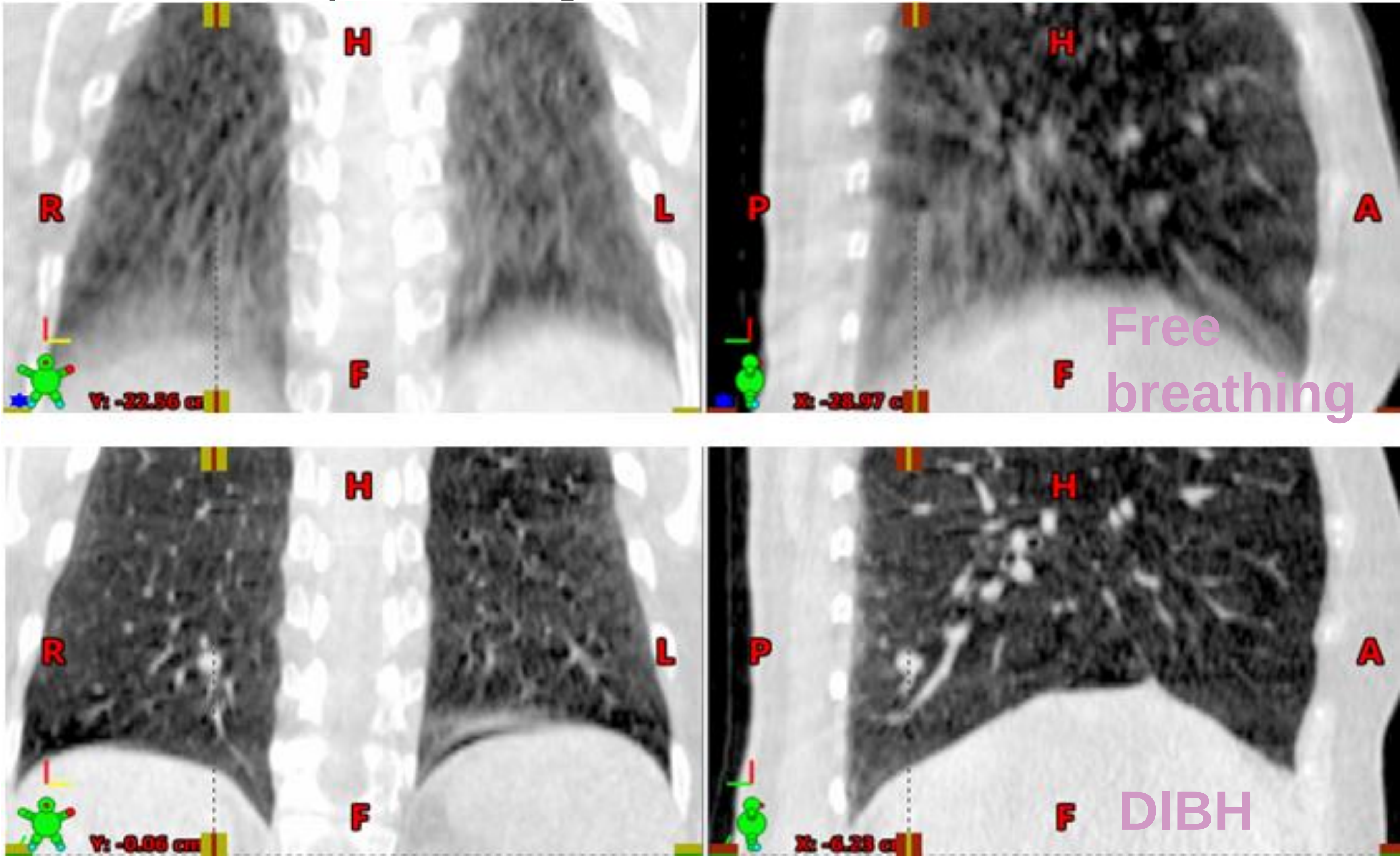
Special case: lung SBRT

SBRT – very small targets

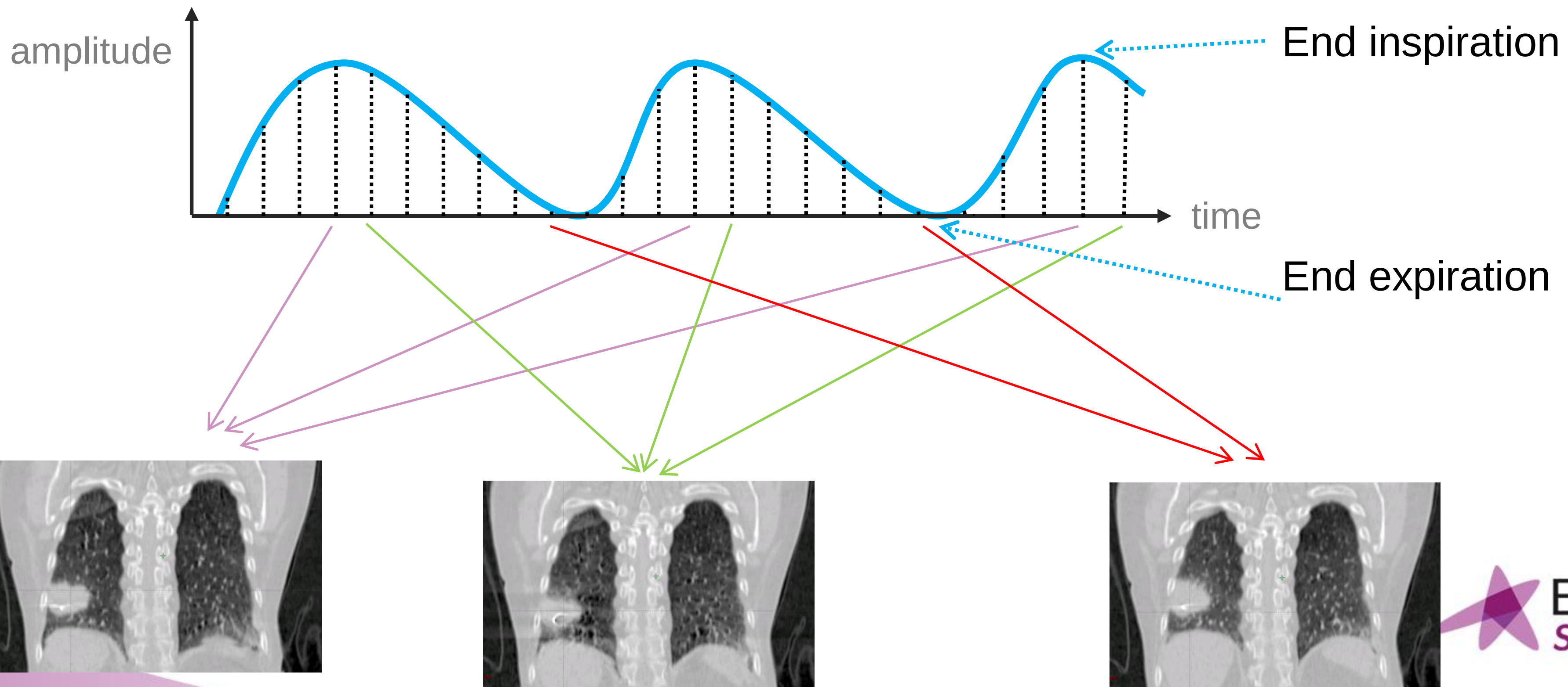


Aznar et al. Physica Medica 2018

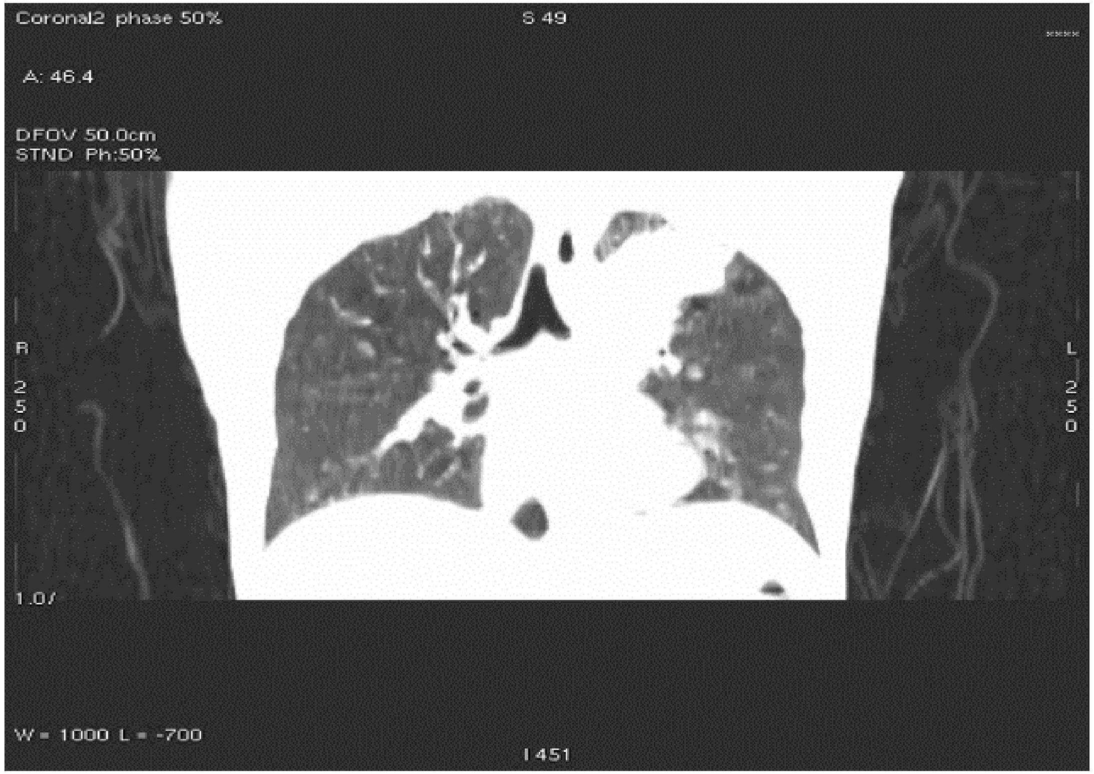
- DIBH gating is more reproducible than inspiration gating
- DIBH facilitates anatomical separation of target & OAR
- DIBH mitigates target motion

4DCT – a motion encompassing method

- A very slow CT
- Sorting of images acc. to respiration
  - Resp. phase
  - Resp. amplitude



4DCT – a motion encompassing method



4DCT facilitates

- Tumour motion evaluation

- Delineation of ITV

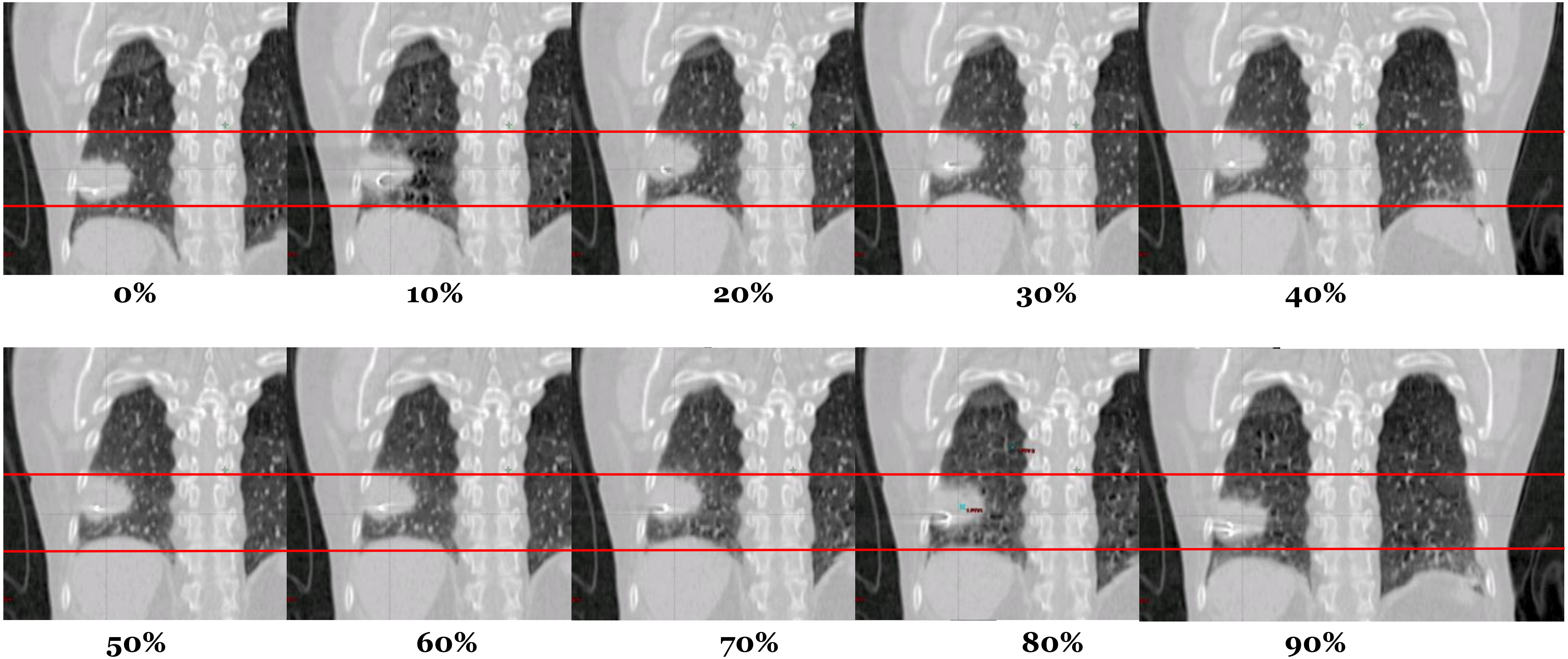
  or

- Selection of midventilation phase

- Correlation of tumour position
  respiratory phase

- 4DCT is only a snapshot!

4DCT = 10 3D CTs from 10 respiratory phases



Gitte Persson, Rigshospitalet

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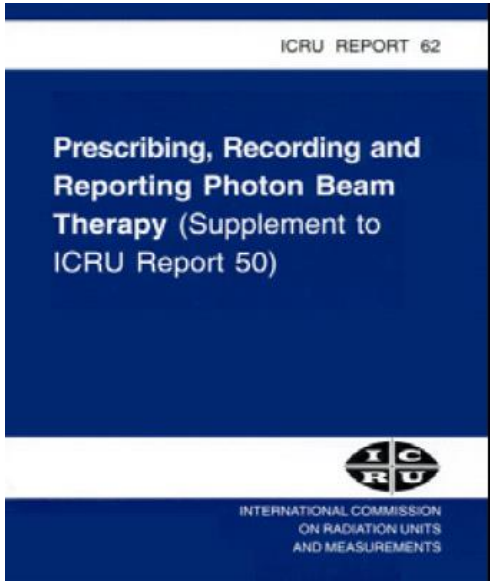
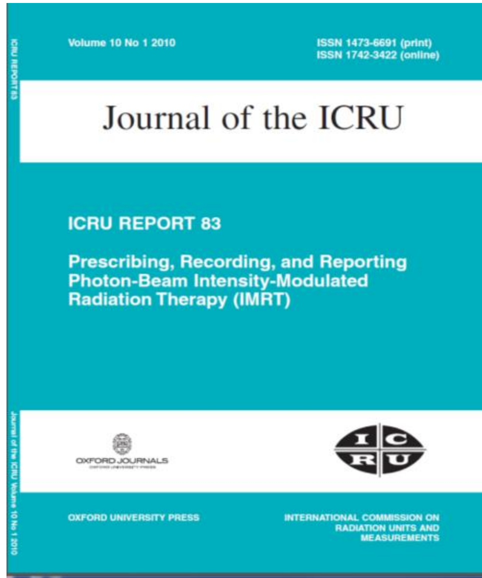
ITV = internal target volume

- ITV = margin for tumor motion added to CTV
- *ICRU 62: "ITV = CTV + margin for uncertainties in size, shape & position of CTV <u>within</u> the patient"*

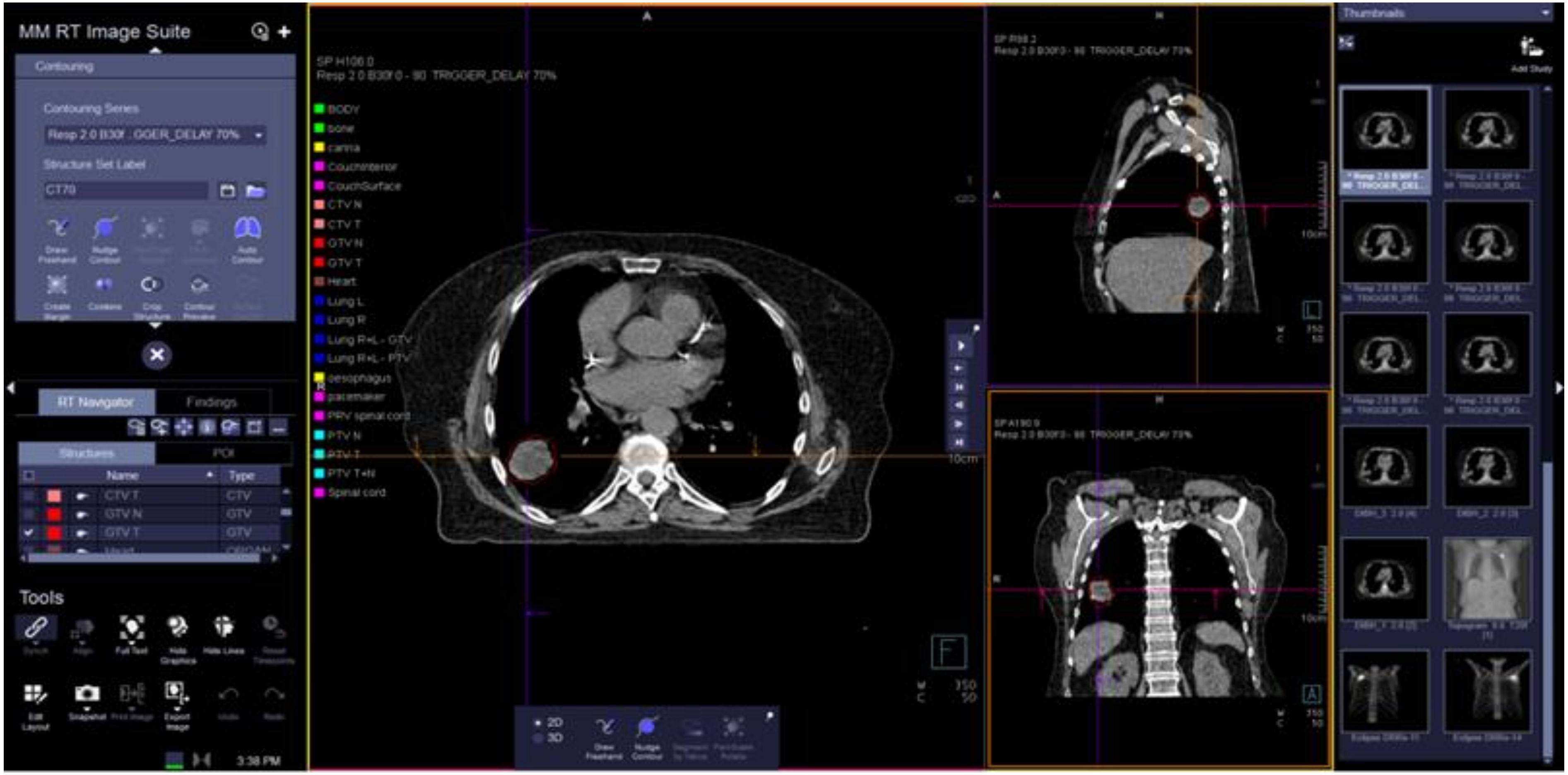
- iGTV = sum of GTVs in al phases of 4DCT

- ICRU 83: *"resulting PTVs were too big"*



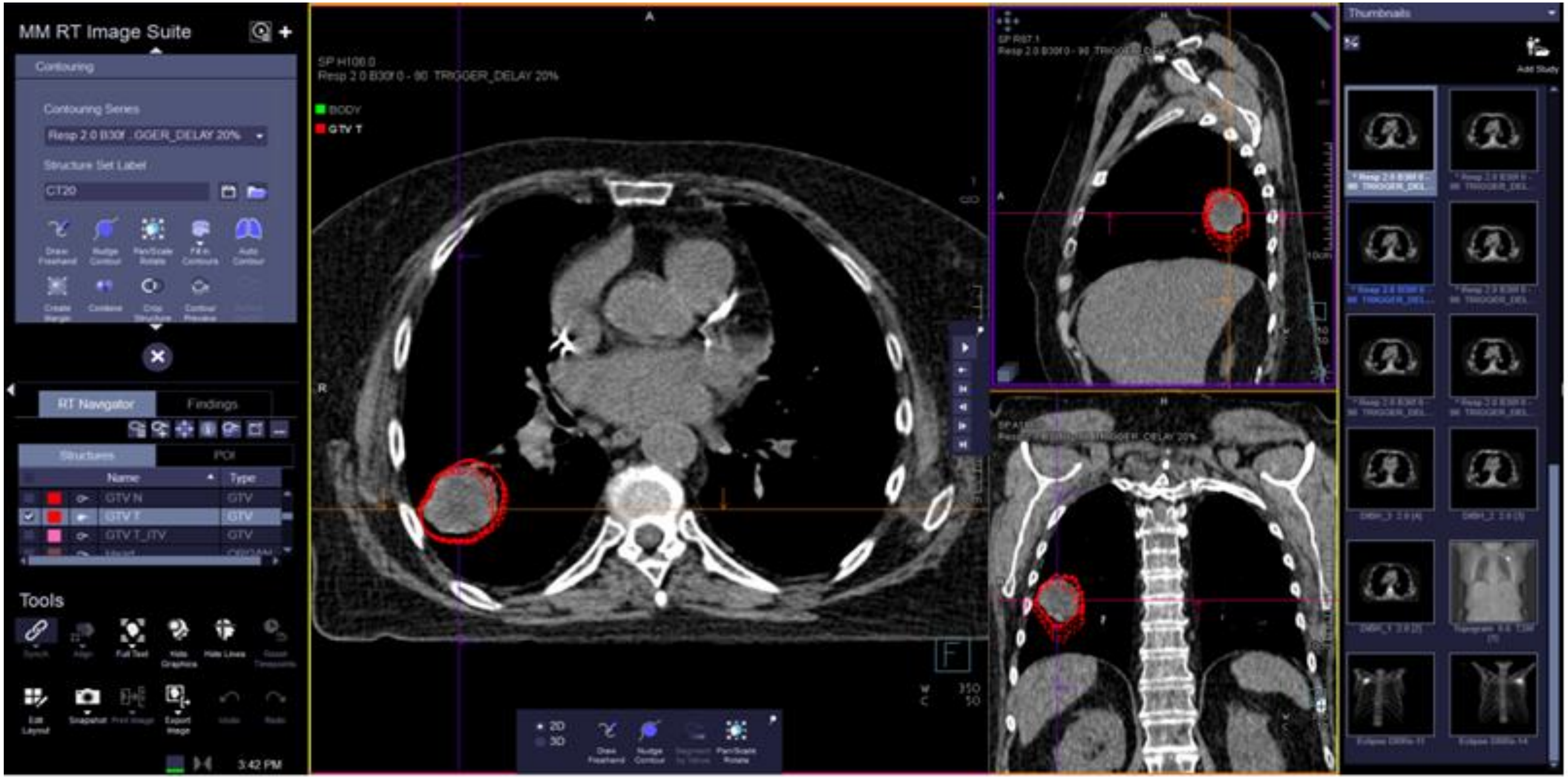


4DCT: ITV-like approach

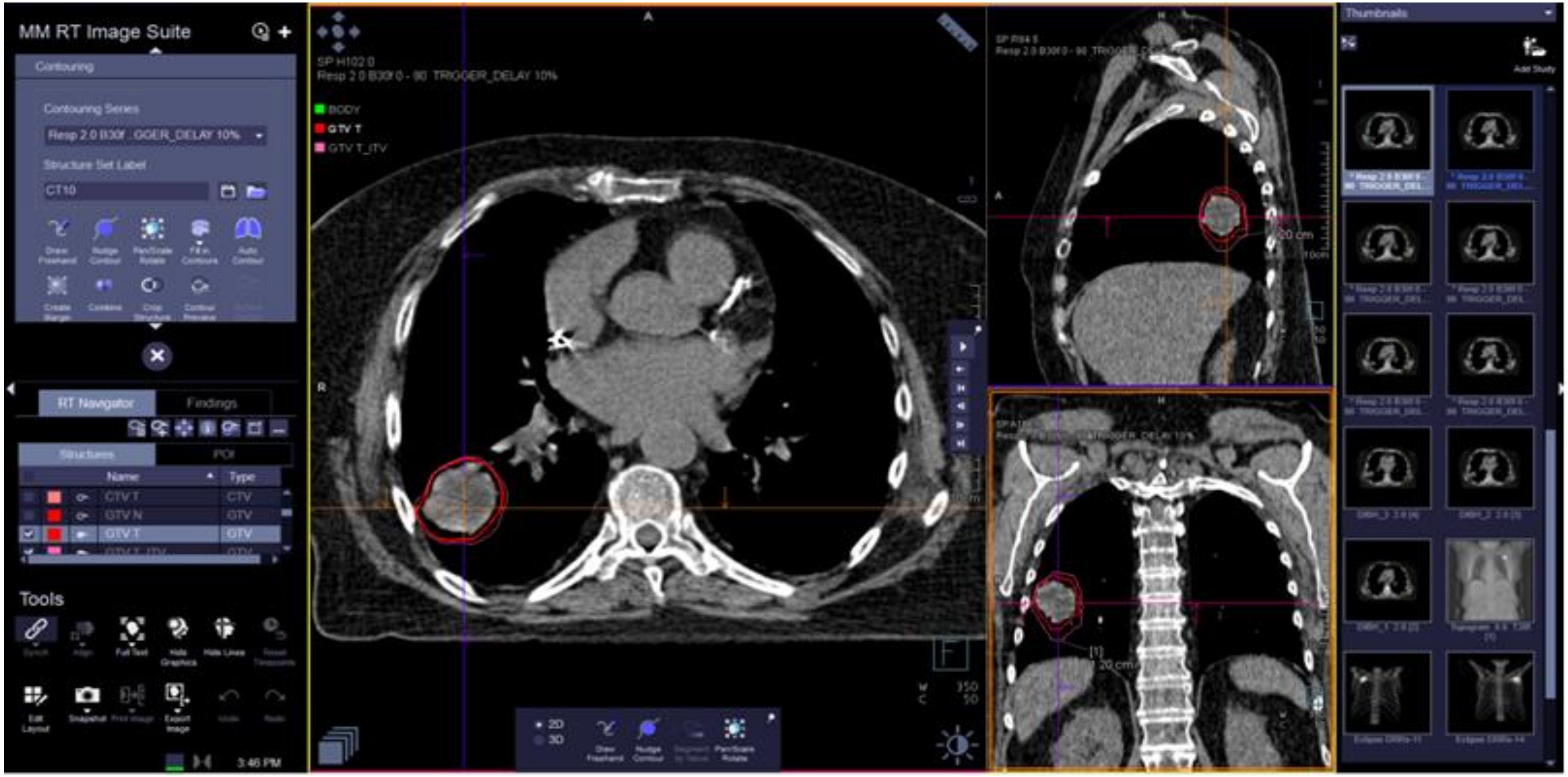


4DCT: ITV-like approach

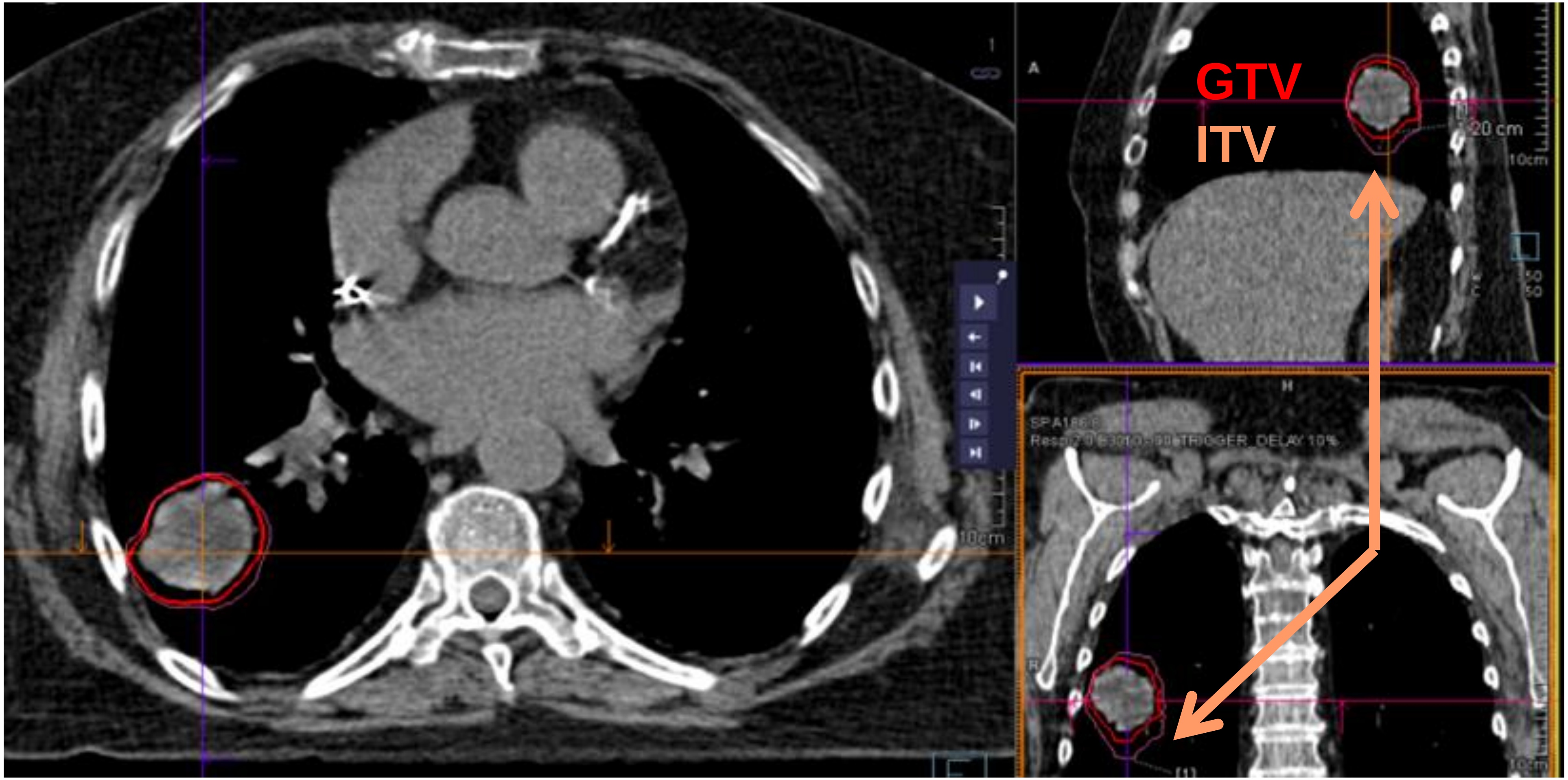
4DCT: ITV-like approach



4DCT: ITV-like approach



4DCT: ITV-like approach



4DCT: Midventilation

Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 5, pp. 1560–1571, 2006

0360-3016/06/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2006.04.031

PHYSICS CONTRIBUTION

MID-VENTILATION CT SCAN CONSTRUCTION FROM FOUR-DIMENSIONAL RESPIRATION-CORRELATED CT SCANS FOR RADIOTHERAPY PLANNING OF LUNG CANCER PATIENTS

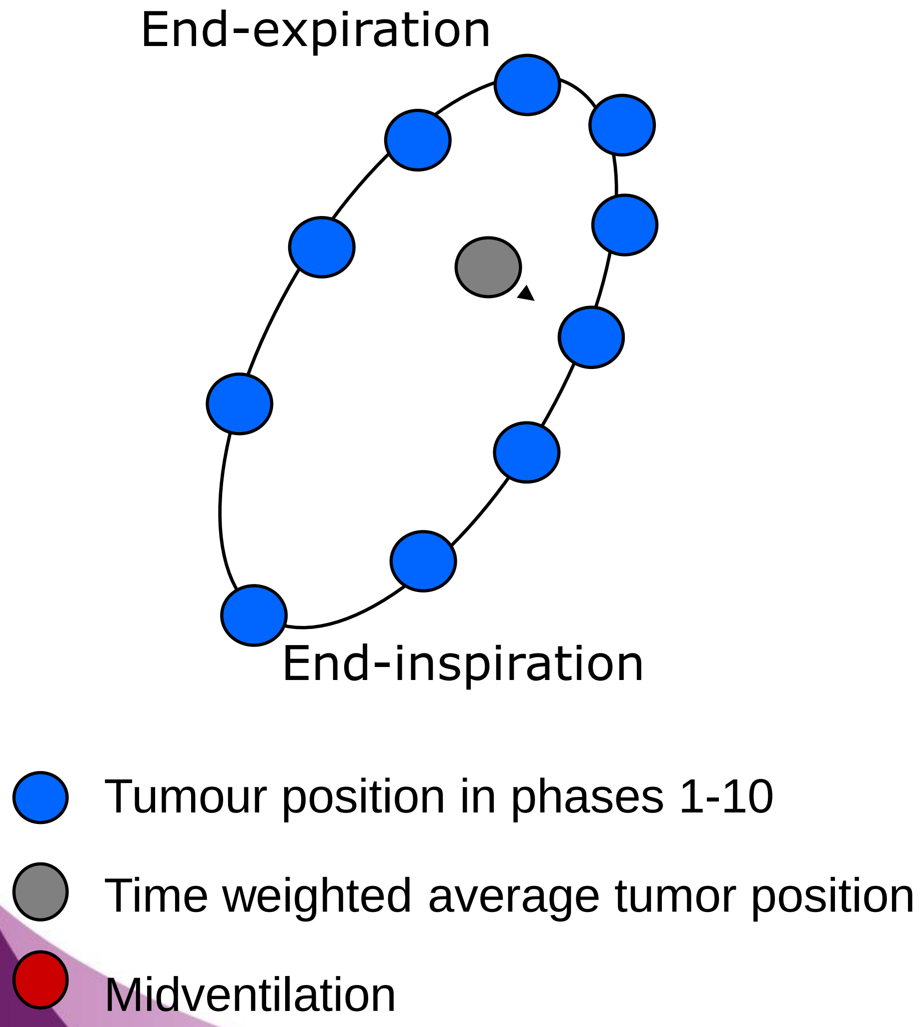
Jochem W. H. Wolthaus, M.Sc., Christoph Schneider, Ph.D., Jan-Jakob Sonke, Ph.D., Marcel van Herk, Ph.D., José S. A. Belderbos, M.D., Maddalena M. G. Rossi, D.C.R.(R), R.T.T., Joos V. Lebesque, M.D., Ph.D., and Eugène M. F. Damen, Ph.D.

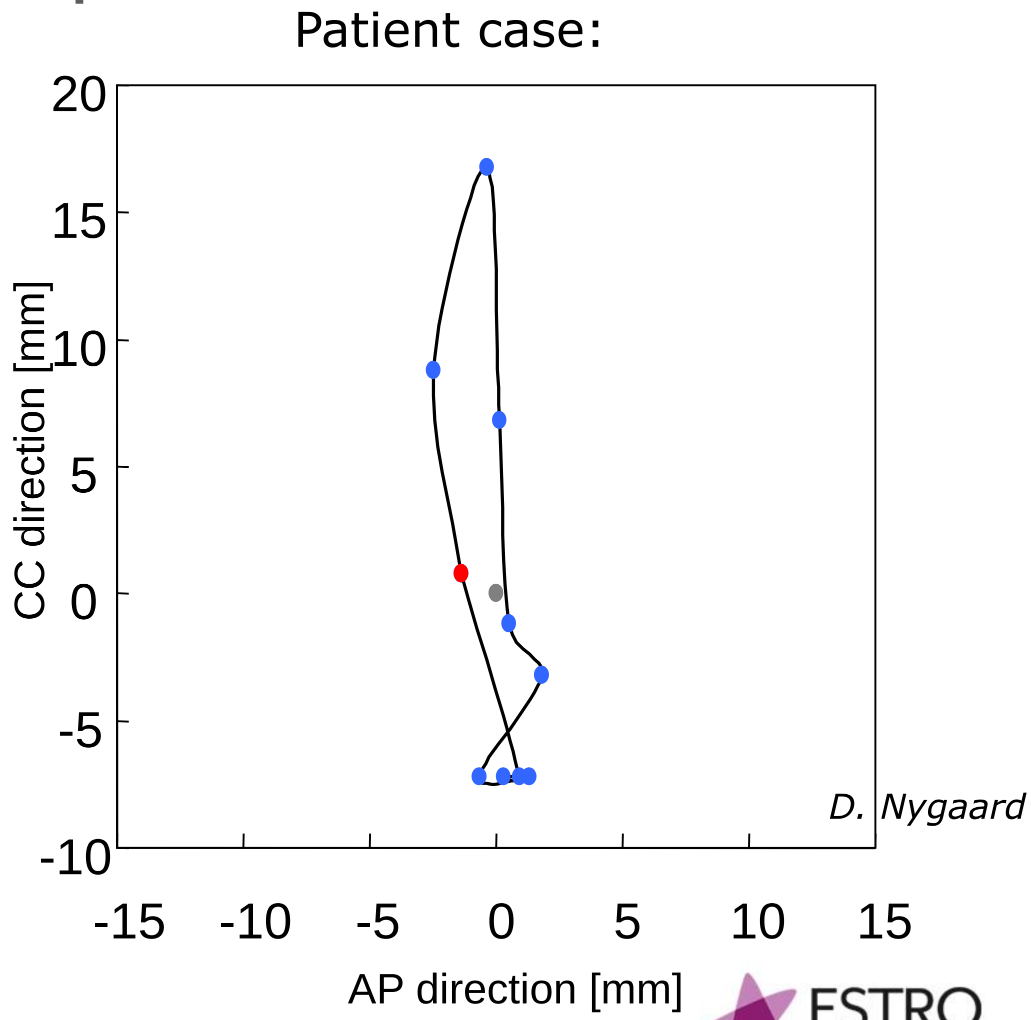
Department of Radiation Oncology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

Purpose: Four-dimensional (4D) respiration-correlated imaging techniques can be used to obtain (respiration) artifact-free computed tomography (CT) images of the thorax. Current radiotherapy planning systems, however, do not accommodate 4D-CT data. The purpose of this study was to develop a simple, new concept to incorporate patient-specific motion information, using 4D-CT scans, in the radiotherapy planning process of lung cancer patients to enable smaller error margins.

4DCT: Midventilation

= time weighted average position of tumour





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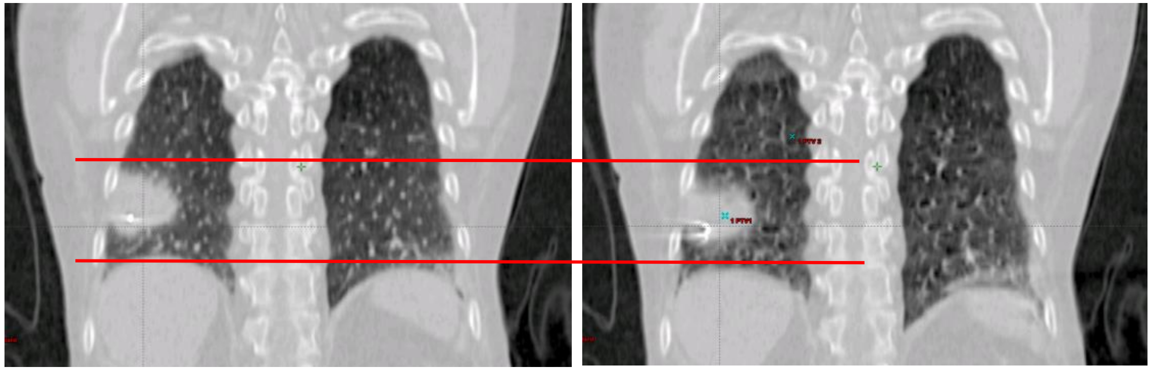
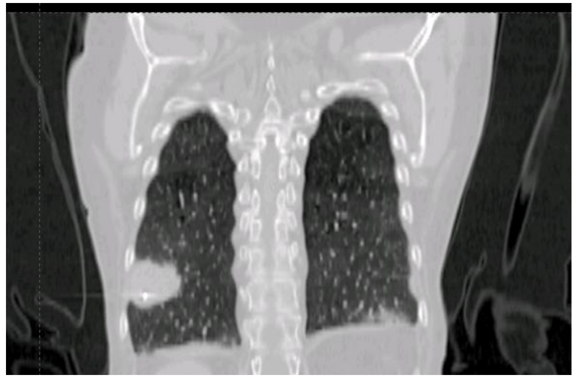
Midventilation

- choice of the correct phase



50% 80%

- Comparisson of tumour size & shape with the breath hold scan

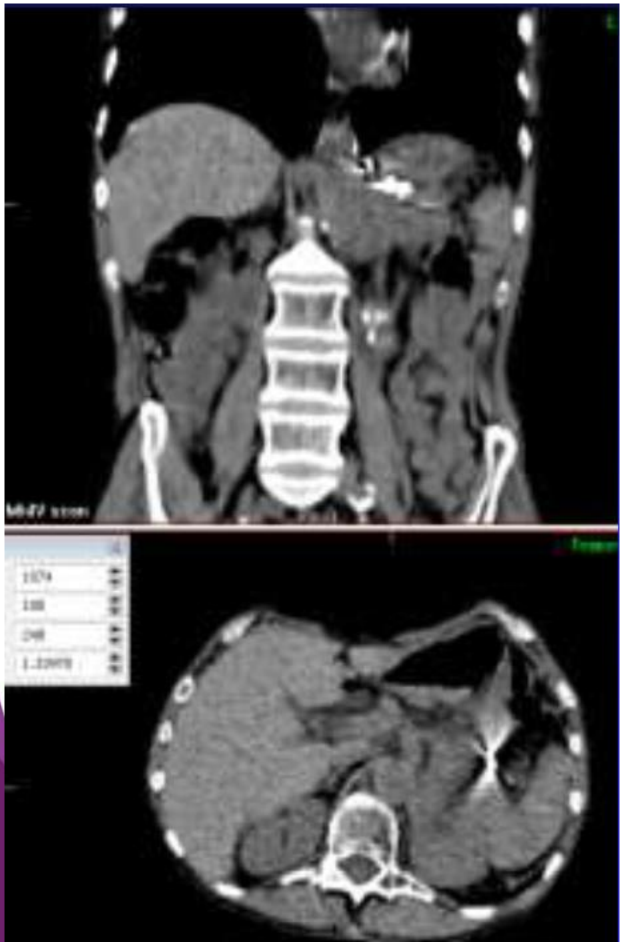


Breath Hold scan

Midventilation vs. midposition

MIDVENTILATION =

1 phase of the 4DCT



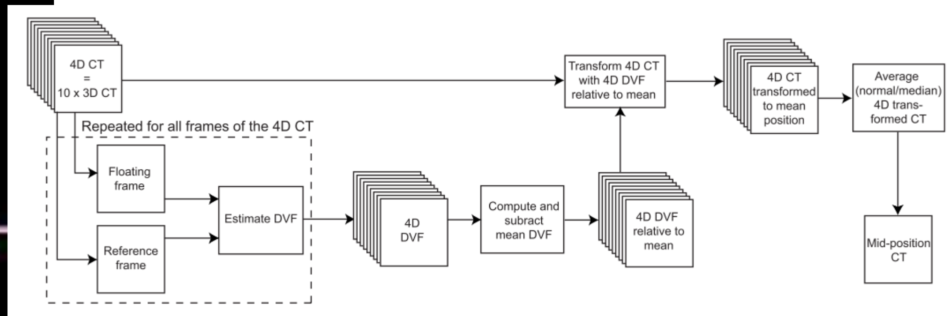
Images courtesy of Marcel van Herk

MIDPOSITION =

Deformable registration

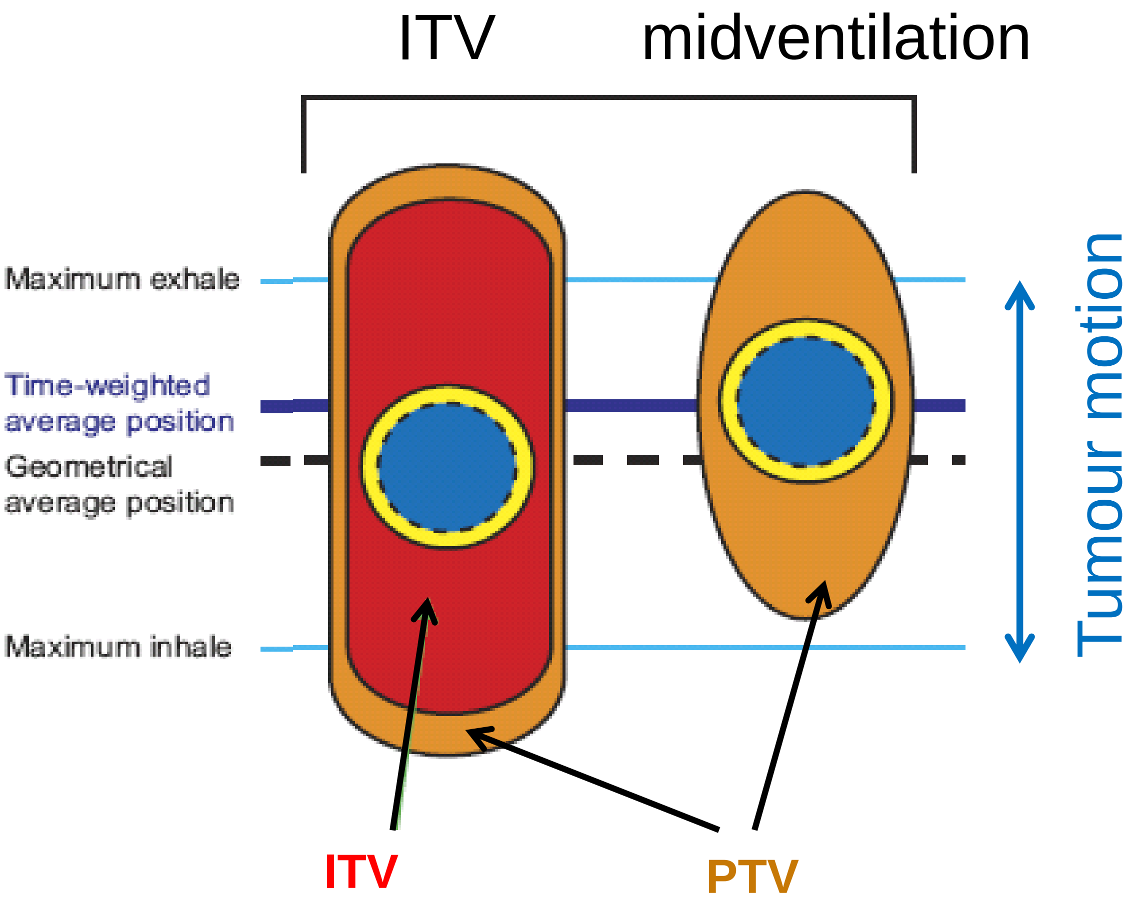
Deforming phases to time-weighted midposition

Averaging (median)

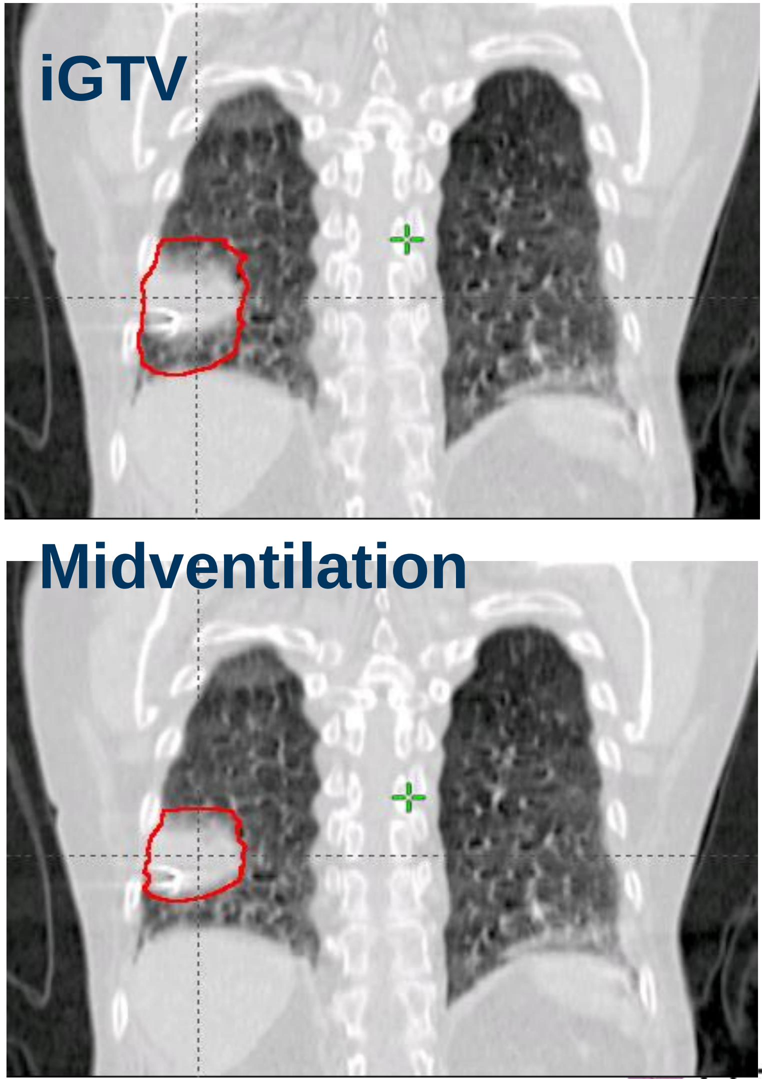


Wolthaus 2008

ITV or midventilation – impact on PTV



adapted from J Wolthaus IJROBP 2008



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ITV-like approach

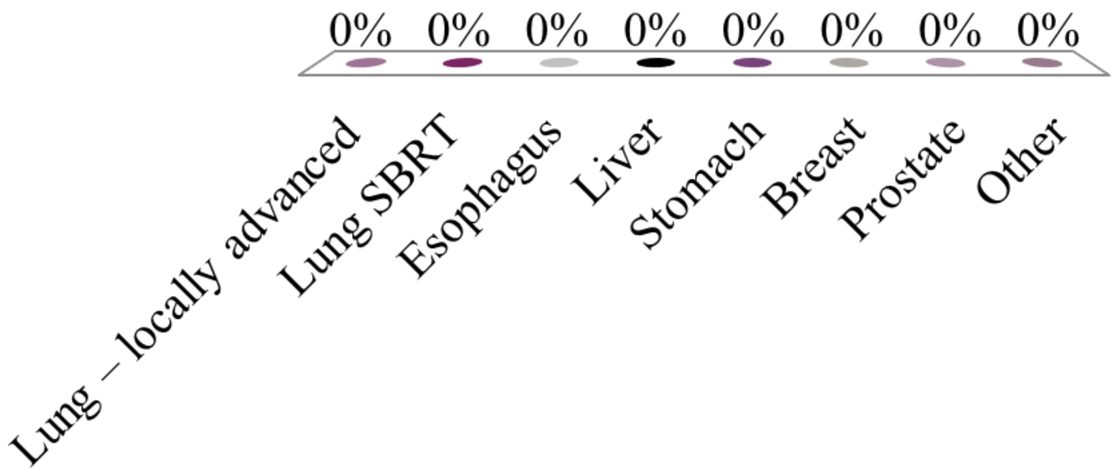
- Larger GTV
- Smaller GTV-PTV margin
- Larger PTV
- Beneficial if hysteresis in tumour motion

Midventilation

- Smaller GTV
- Larger GTV-PTV margin
- Smaller PTV
- Problem if hysteresis in tumour motion

In which sites do you use 4DCT ?

A. Lung – locally advanced
B. Lung SBRT
C. Esophagus
D. Liver
E. Stomach
F. Breast
G. Prostate
H. Other



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Respiration synchronised techniques

Rationale of motion tracking…

Letting the beam move with the target

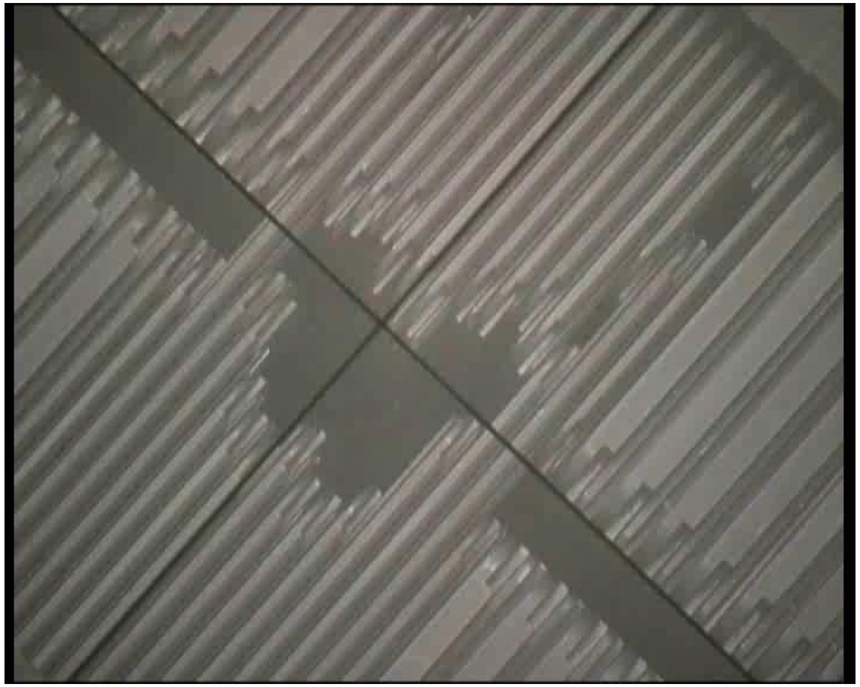
How

- By using surrogate for tumor motion:
  - external or internal
- Prediction algorithms

Respiration synchronised techniques

Tracking on linac

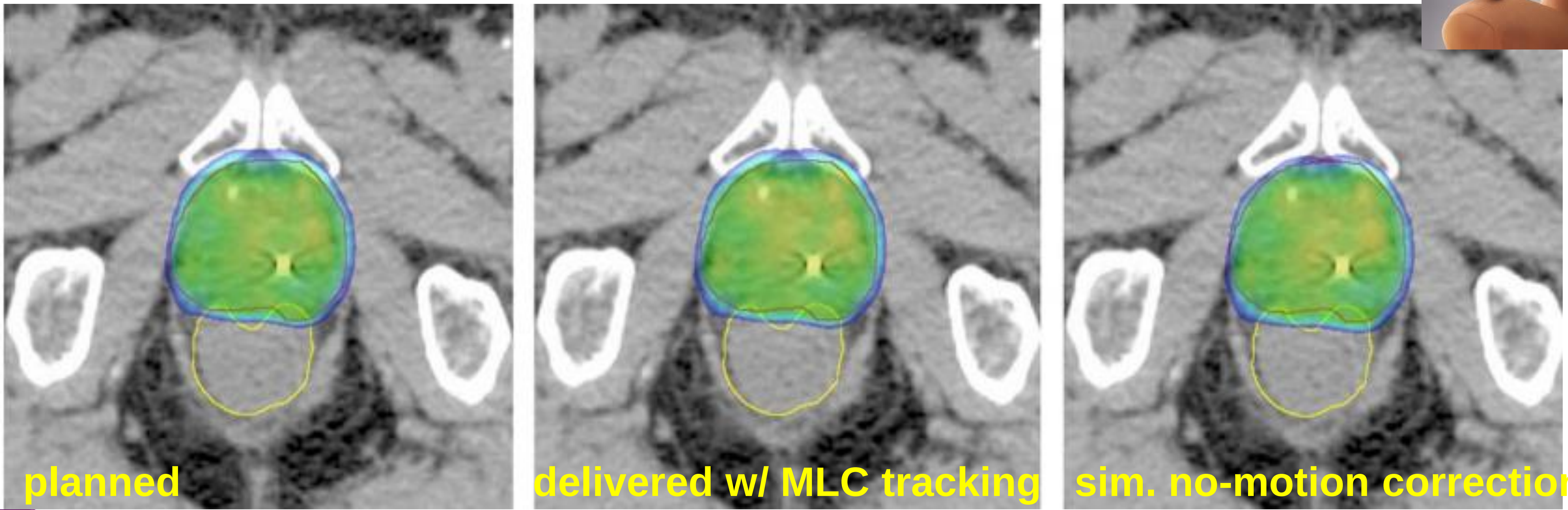
- MLC shape adjusted to compensate for target motion in real-time



You need to KNOW the target motion!

Motion synchronised techniques

First patient treated with electromagnetic transponder MLC tracking



Keall Med Phys 2014

Take home messages

- Different motion management strategies
  - Gating
  - Breath hold
  - Tracking

  } Dosimetric benefit!
  - 4D imaging
- Good correlation between respiration surrogate & target motion
- Patient training improves reproducibility

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form

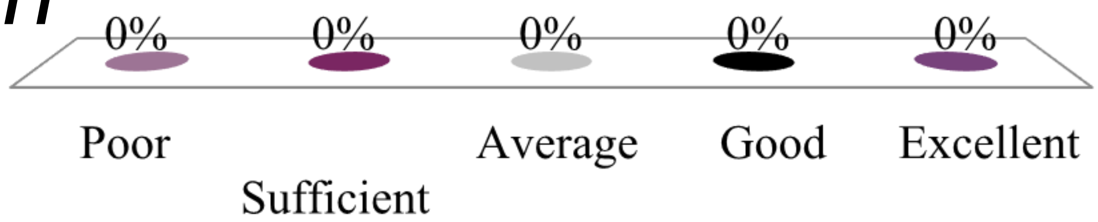


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Image registration

Mirjana Josipovic

Dept. of Oncology, Rigshospitalet
Niels Bohr Institute, Uni. of Copenhagen
Denmark

Peter Remeijer

NKI-AVL
Amsterdam
The Netherlands

Advanced skills in modern radiotherapy
May 2018

Intended learning outcomes

- Describe basic principles of image registration process

- Identify limitations in image registration process

Image registration

You may also call it

- Image fusion
- Image matching
- Image warping

= process of aligning two (or more) images

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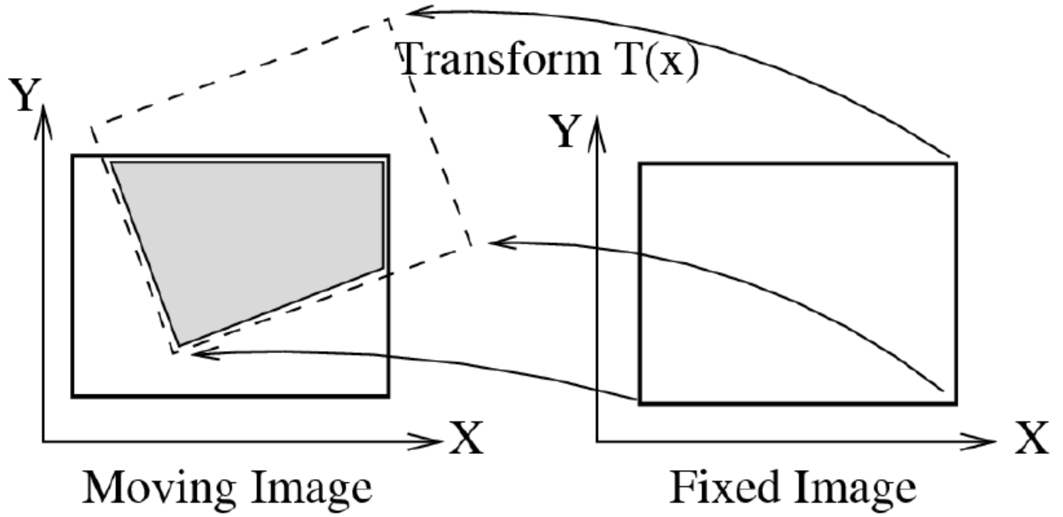
Definition: Image registration

- Determine **rigid transformation** between two scans

e.g. shift 3.2 cm to the
right and 4.1 cm up
and rotate



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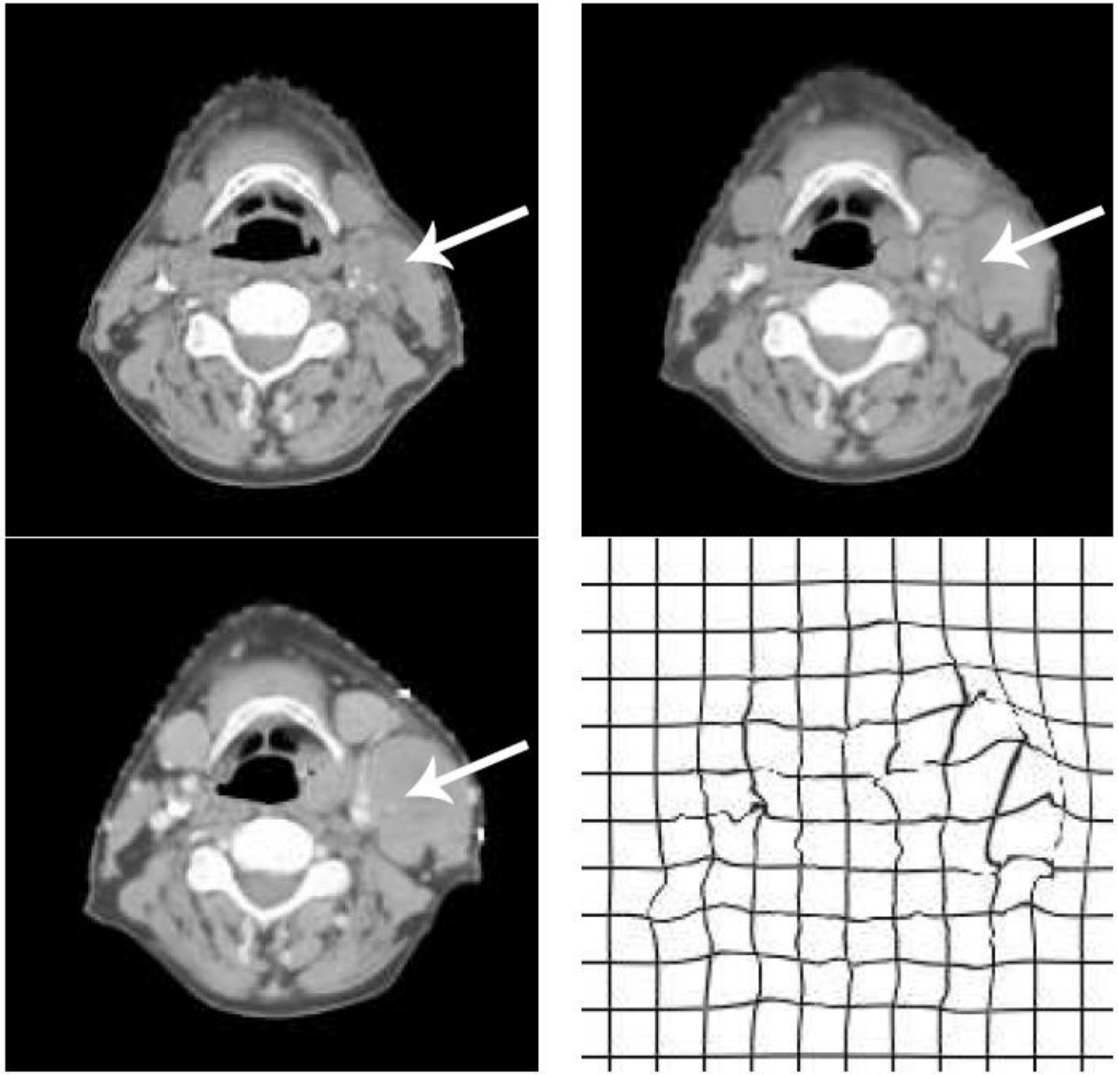
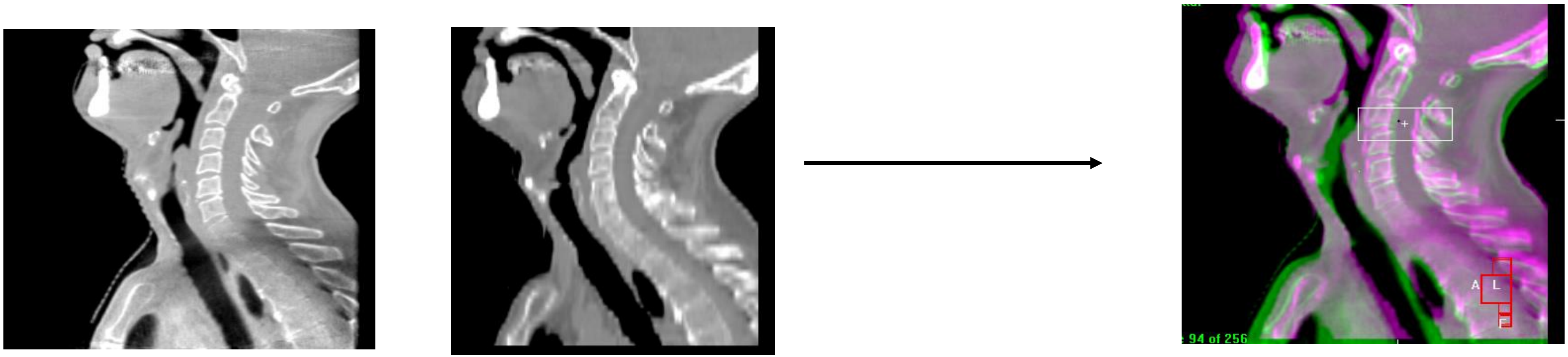
Definition: Image registration

- Determine **deformable transformation** between two scans



Definition: Image fusion

- Combine the information of two images



- **Viewing and validation** of registration result

Image registration in radiotherapy

- In the RT planning process
  - ➢ Inclusion of PET/MRI
  - ➢ Pre-chemo CT scans
- During RT delivery - IGRT
  - ➢ Reduction of setup uncertainty
  - ➢ Detect patient anatomy changes during treatment
    - ▪ Daily dose assesment / plan adaptation
- After RT
  - ➢ Follow up (tumour response, normal tissue damage)
  - ➢ Re-irraditaion

Image registration in radiotherapy

- Algorithms
- Validation
- Challenges

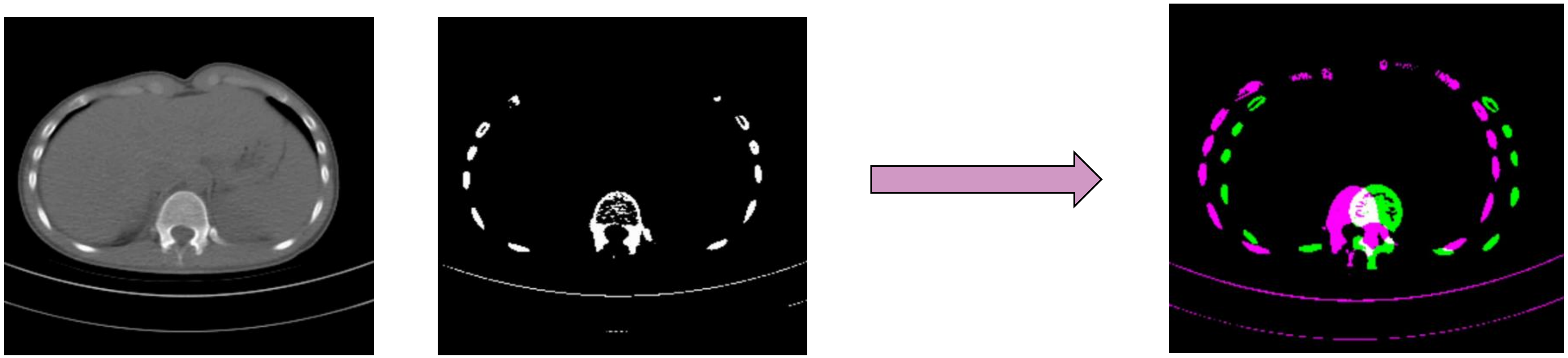
Manual image registration

- Simple ‘algorithm’
- Good for gross alignment

- Difficult in 3-D
- Not very precise

Automatic image registration

- Geometry based
  - ➢ Point matching (anatomic landmarks, implanted fiducial markers)
  - ➢ Surface matching (skull surface, pelvic bones)
    - ▪ Fx Chamfer matching



Automatic image registration

- Feature based
  - ➢ Numerical gray scale

- Uses gray values in all pixel values
  - ➢ Inside the regions of interest

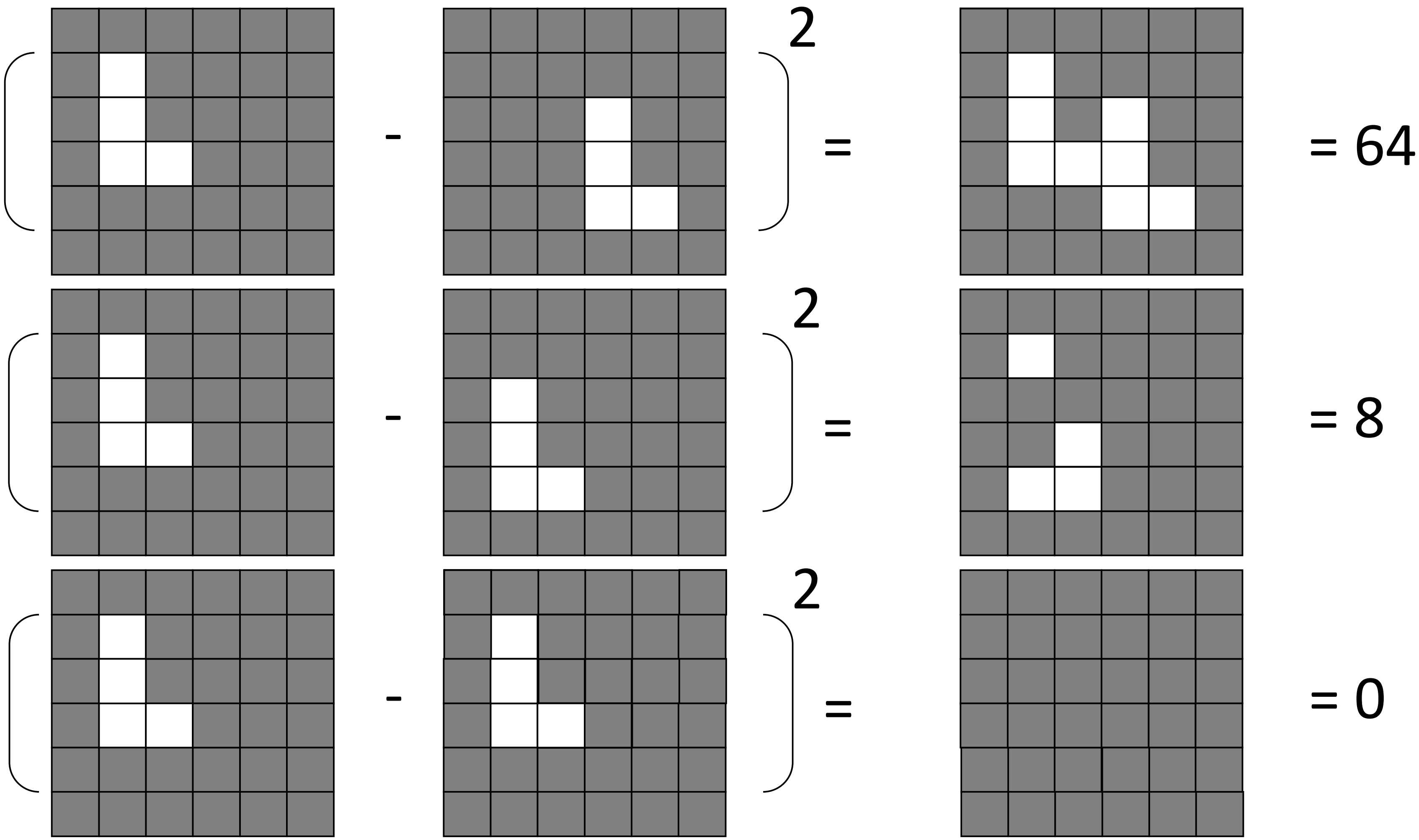
- Slower than chamfer matching
  - ➢ not really an issue today due to more computing power ☺

Similarity assessment

- How good is the resulting image registration?

- Similarity metrics / cost functions
  - ➢ Root mean square
  - ➢ Correlation ratio
  - ➢ Mutual information
  - ➢ …

Grey value registration example



Mutual information cost function

Understand your registration algorithm

- You see:

The computer sees:

$$
\begin{aligned}
R &= \begin{bmatrix} \cos\theta_z & -\sin\theta_z & 0 \\ \sin\theta_z & \cos\theta_z & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} \cos\theta_y & 0 & \sin\theta_y \\ 0 & 1 & 0 \\ -\sin\theta_y & 0 & \cos\theta_y \end{bmatrix} \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\theta_x & -\sin\theta_x \\ 0 & \sin\theta_x & \cos\theta_x \end{bmatrix} \\
&= \begin{bmatrix} \cos\theta_y \cos\theta_z & -\cos\theta_x \sin\theta_z + \sin\theta_x \sin\theta_y \cos\theta_z & \sin\theta_x \sin\theta_z + \cos\theta_x \sin\theta_y \cos\theta_z \\ \cos\theta_y \sin\theta_z & \cos\theta_x \cos\theta_z + \sin\theta_x \sin\theta_y \sin\theta_z & -\sin\theta_x \cos\theta_z + \cos\theta_x \sin\theta_y \sin\theta_z \\ -\sin\theta_y & \sin\theta_x \cos\theta_y & \cos\theta_x \cos\theta_y \end{bmatrix}
\end{aligned}
$$

Specify how the algorithm should handle image registration:

- Define region of interest
- Choose the appropriate algorithm

Check the result!

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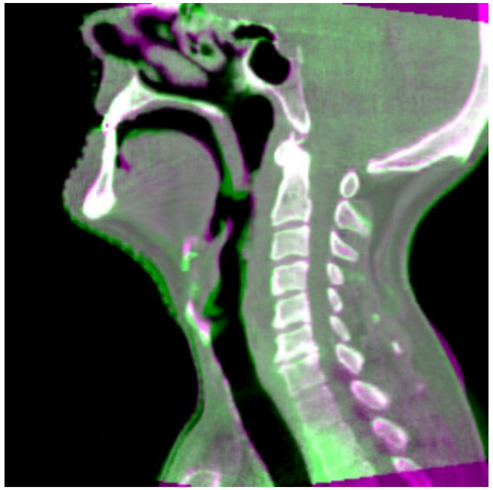
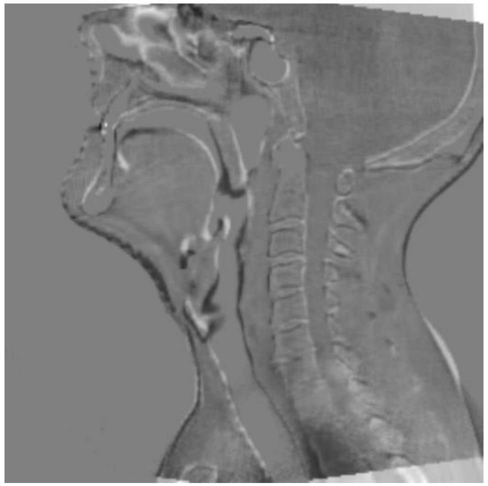
Image fusion

- Viewing & validation of the image registration



Overlay

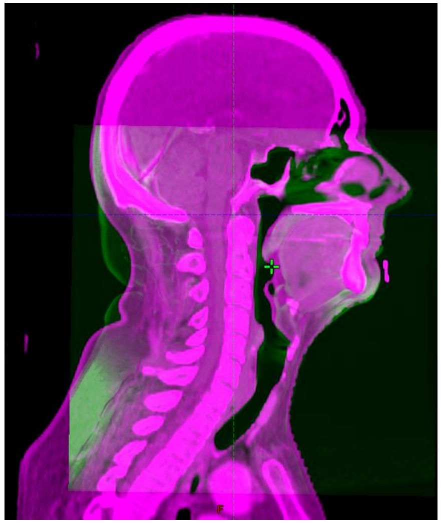


Substract

Checker

Why does this overlay look so purple?

A. Shown images are not weighted equally
B. Two different patients
C. Error in registration process
D. Two different imaging modalities
E. I have no idea



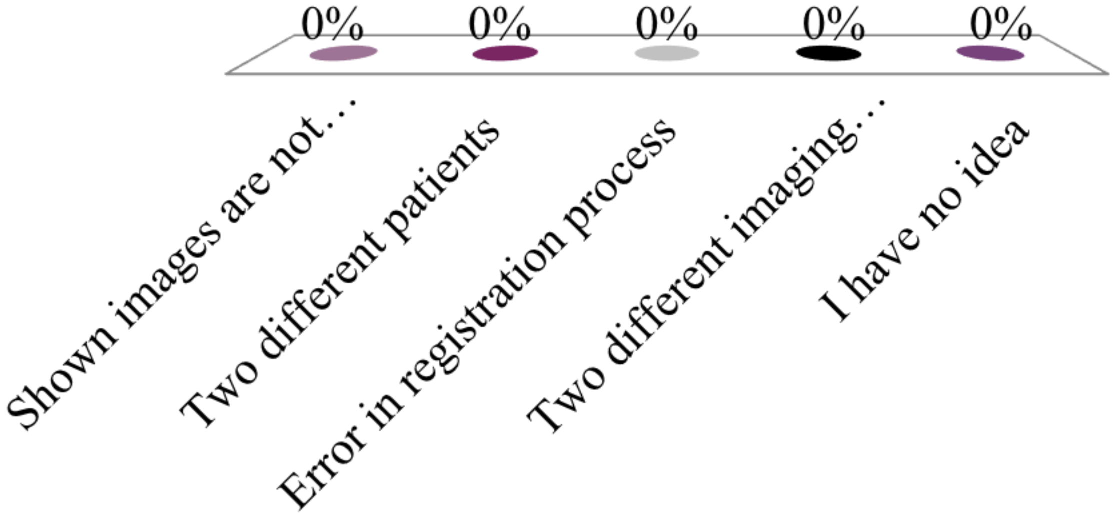


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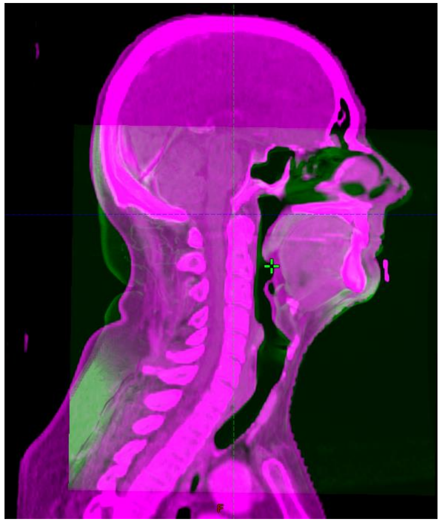
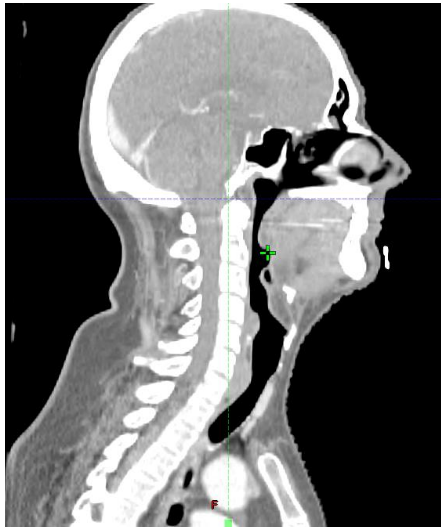
Image fusion

- Viewing & validation of the image registration





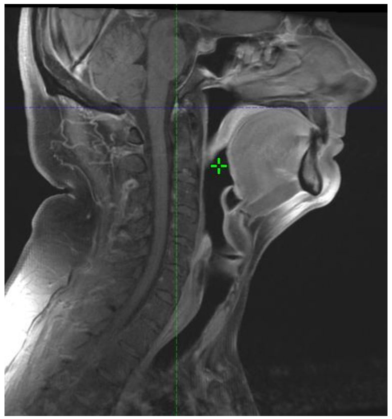
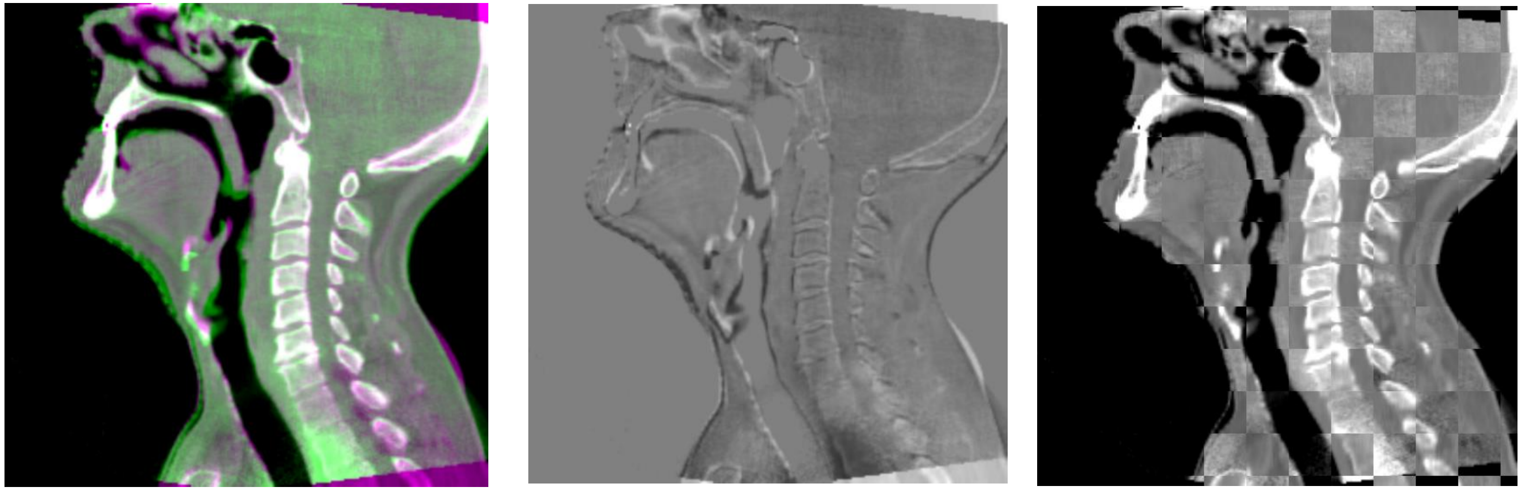


Image fusion

- Viewing & validation of the image registration



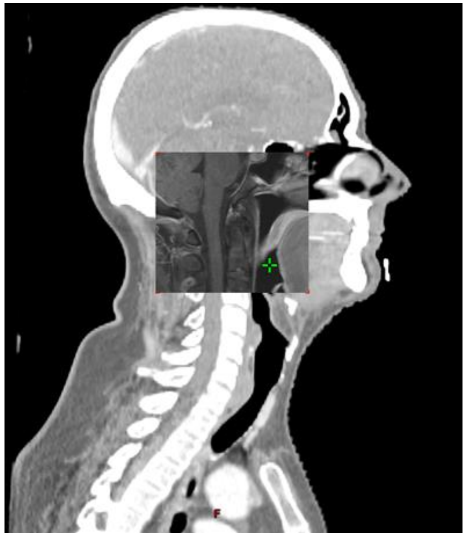
Overlay Substract Checker

Same modality

Image fusion

- Viewing & validation of the image registration

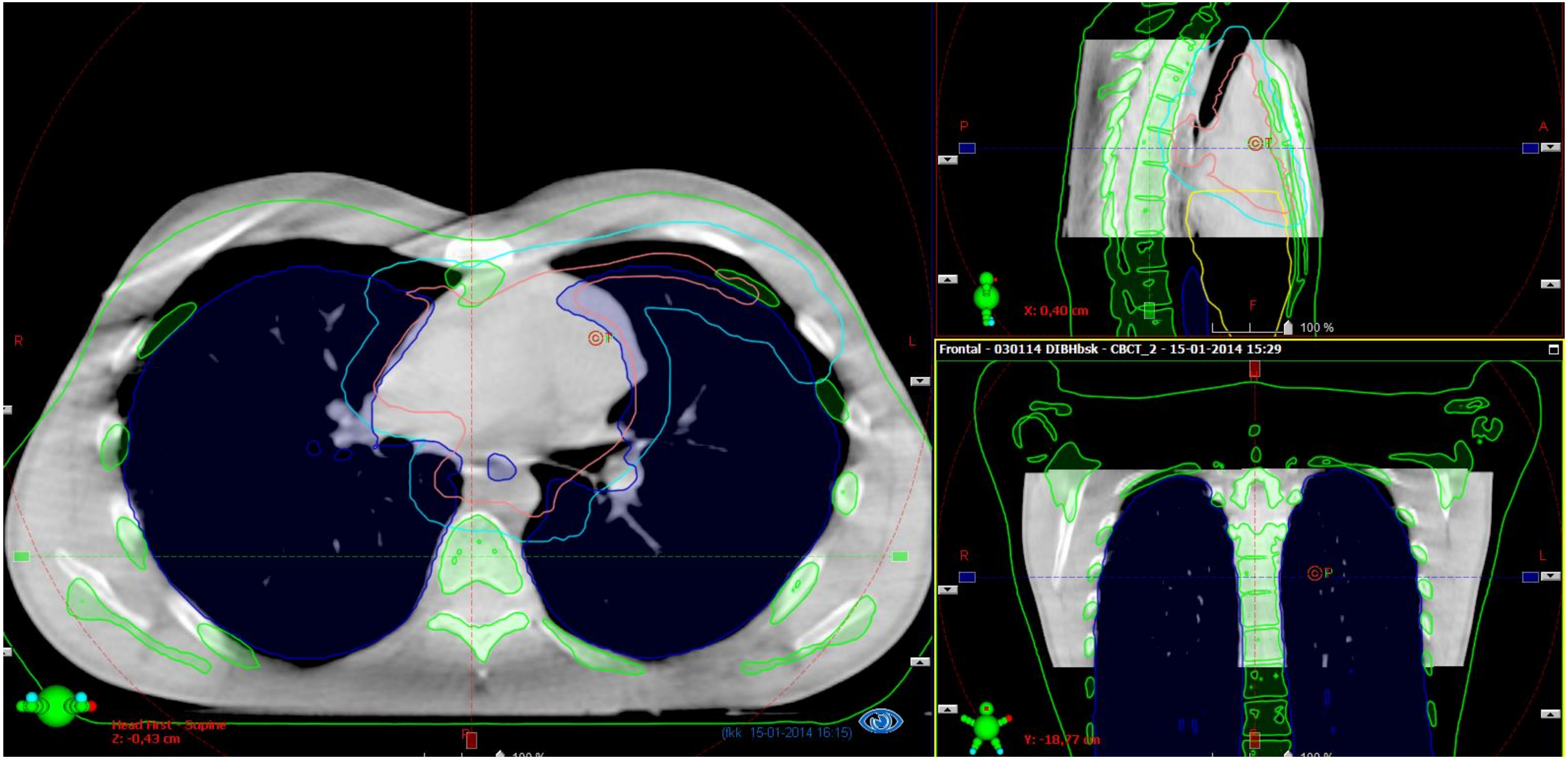
Split window



Spy glass

Different modalities

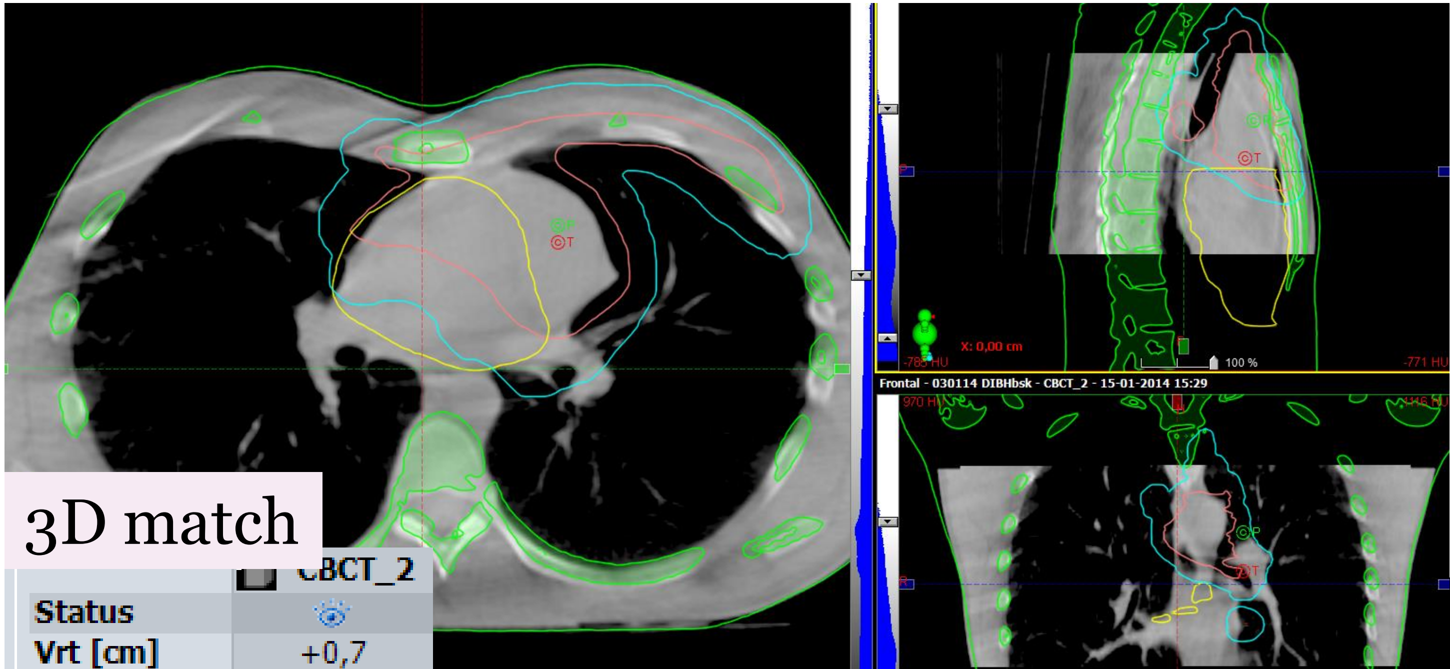
Case: error in automatic image registration



Automatic image registration has to be evaluated!

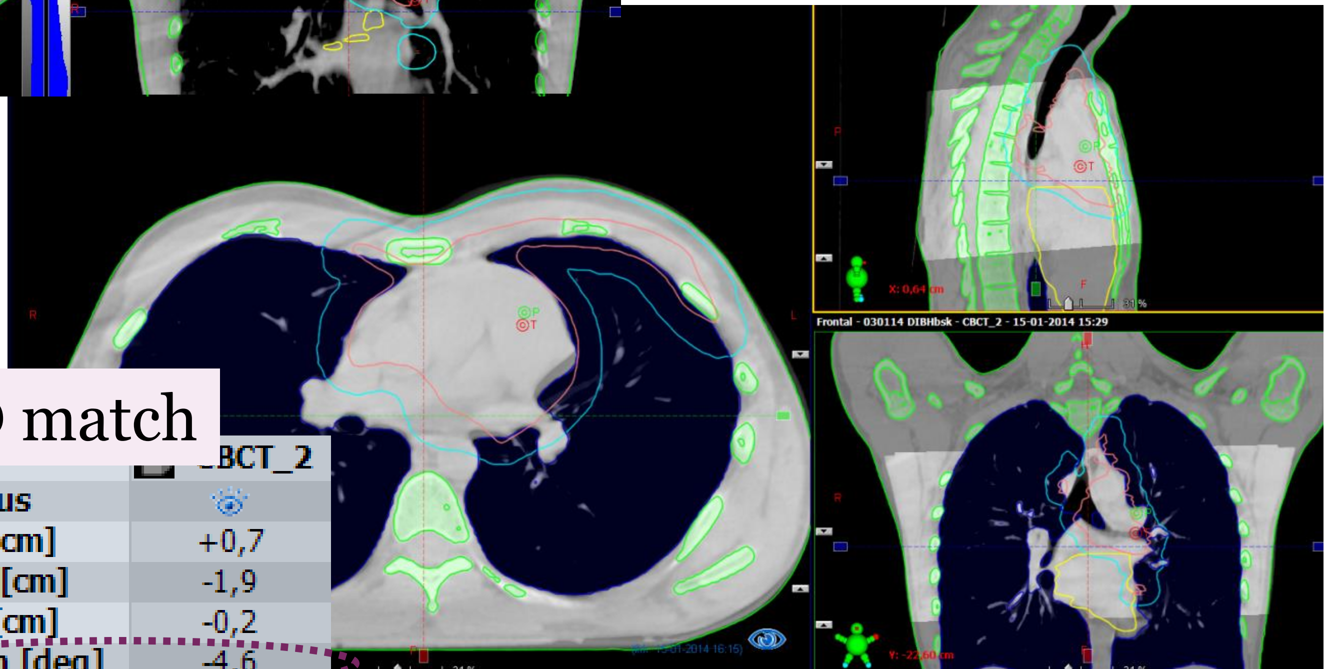
Focus not only on the primary structures of interest, but on the whole image!

Case: error in automatic image registration



3D match

	CBCT_2
Status	
Vrt [cm]	+0,7
Lng [cm]	-3,0
Lat [cm]	0,0
Pitch [deg]	0,0
Roll [deg]	0,0
Rtn [deg]	0,0

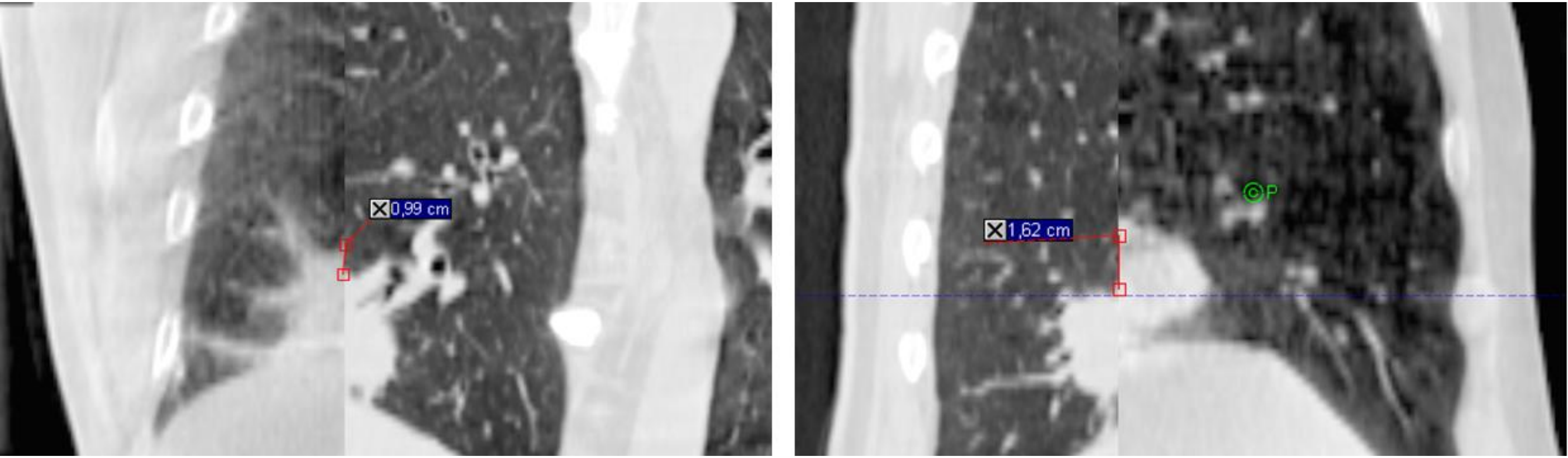


6D match

	CBCT_2
Status	
Vrt [cm]	+0,7
Lng [cm]	-1,9
Lat [cm]	-0,2
Pitch [deg]	-4,6
Roll [deg]	-1,4
Rtn [deg]	-1,1

Focus on the patient set-up!

Lung tumour baseline shift



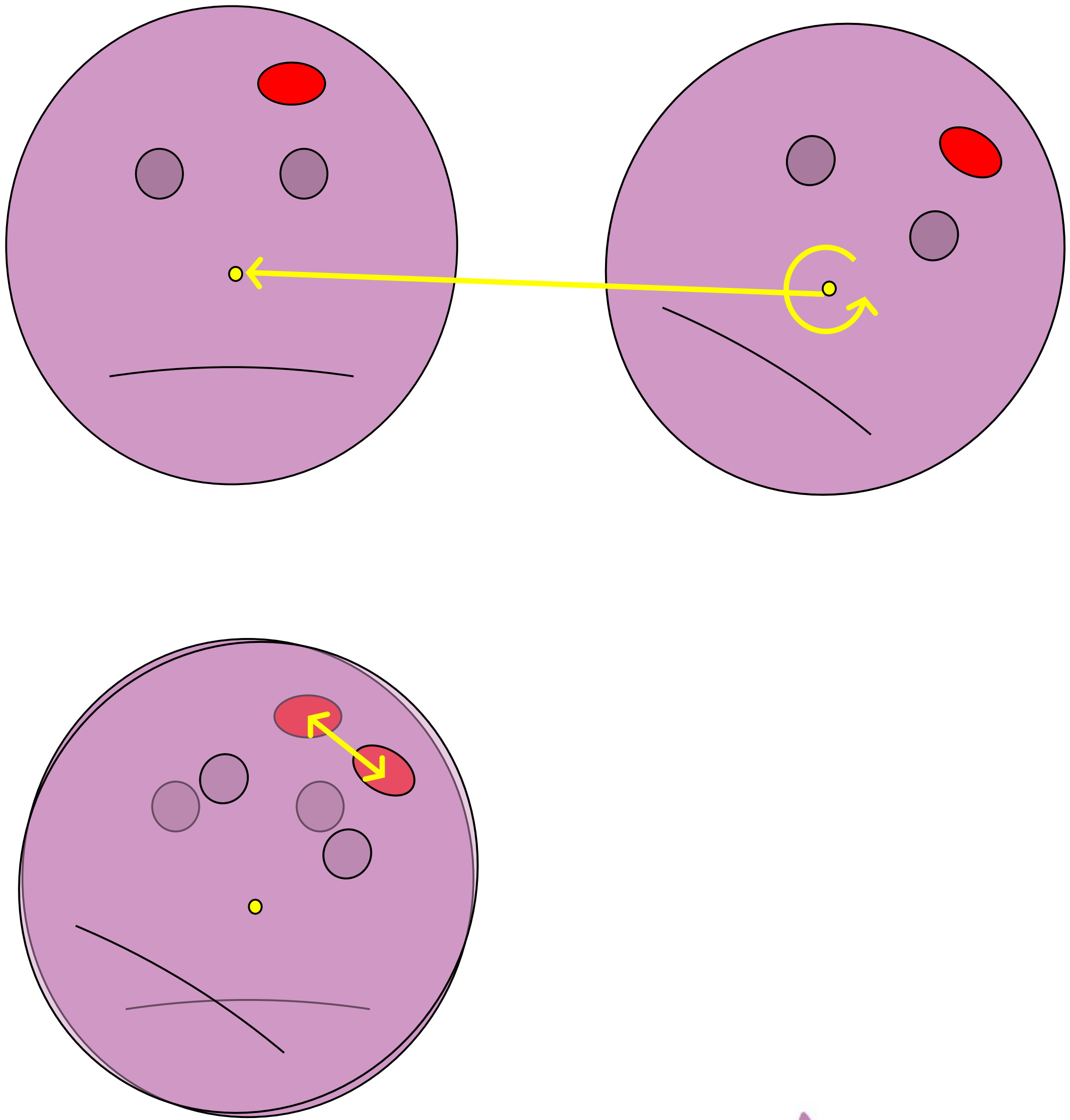
… misalignment of the peripheral tumour
after registration on vertebrae

Challenges in image registration

Impact of rotations on image registration

- Registration
  - Bony anatomy
  - Translations and rotations
  - Very accurate

- Correction
  - Only translations
  - Potentially large errors



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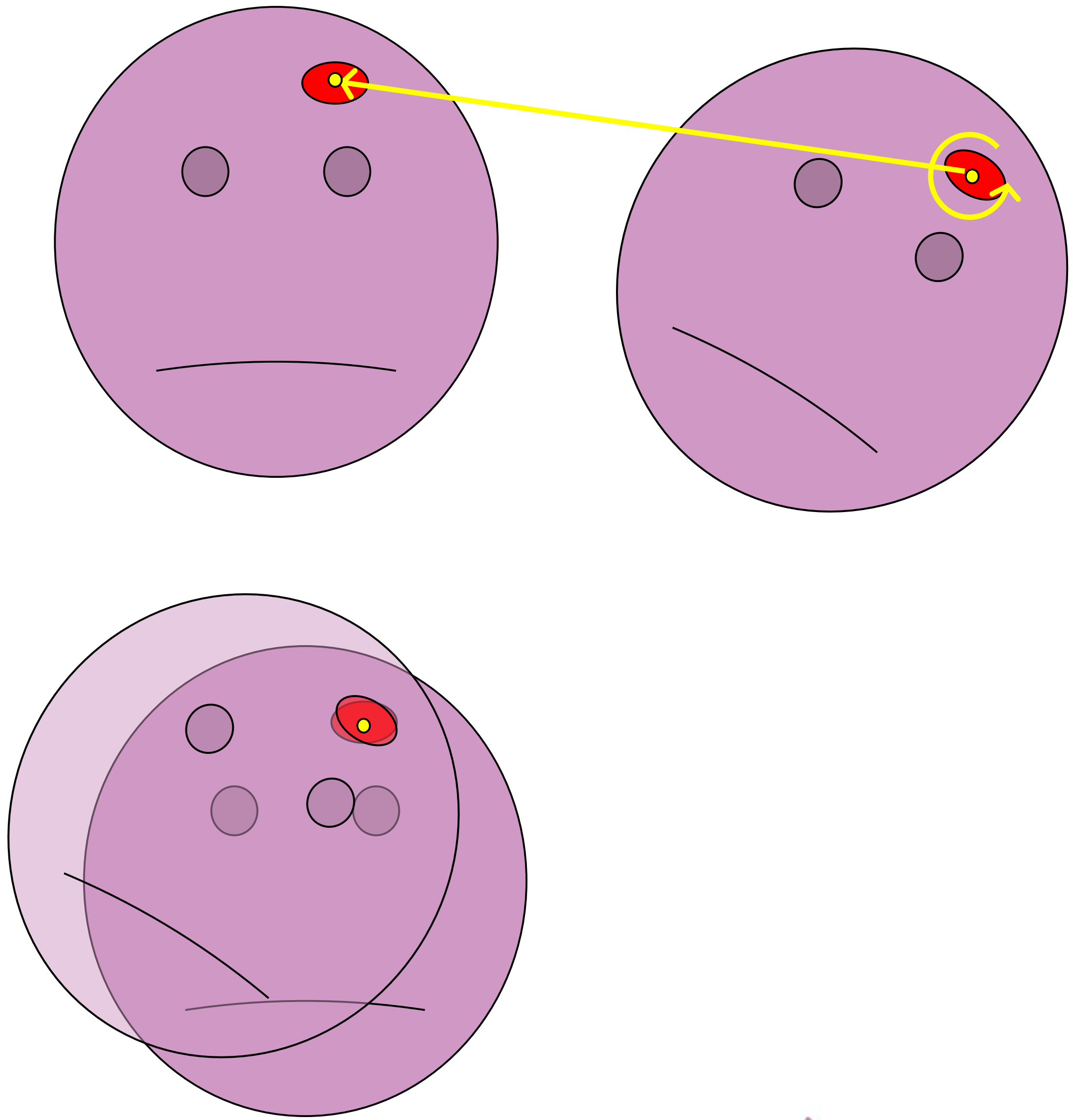
Impact of rotations on image registration

- Registration
  - Redefine match volume
  - Isocenter position
- Correction
  - Only translations
  - Rotational errors are small close to rotation center



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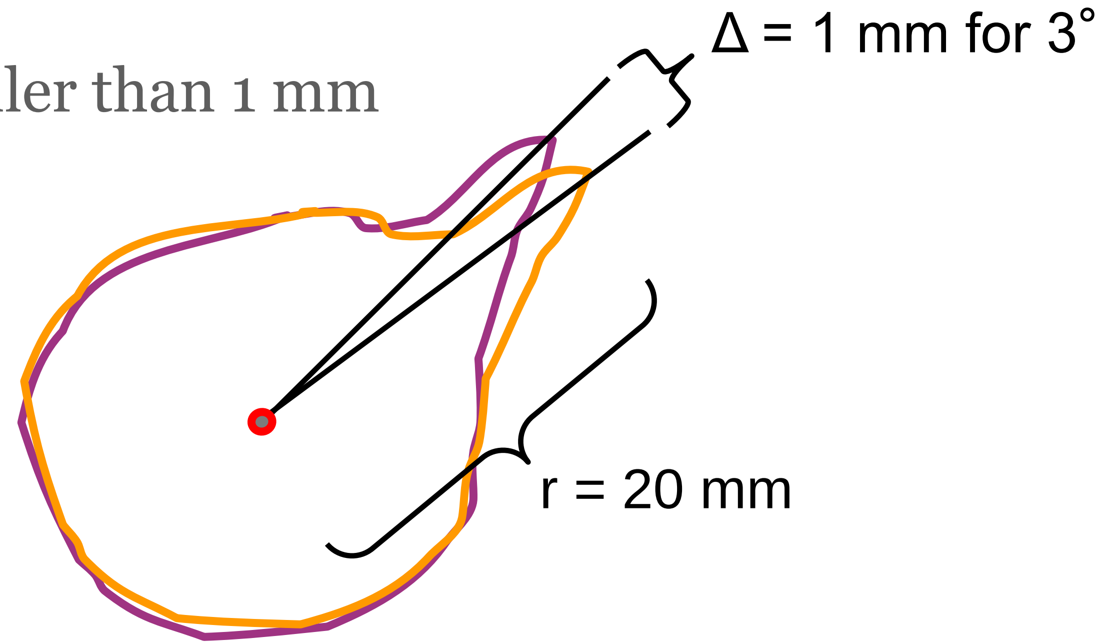
Corrections without rotations

Rule of thumb: $\Delta = 0.02 \times \varphi \times r$ (mm)

- 3° rotation
- CTV diameter is 40 mm (r = 20 mm)
- Rotation centre is in CTV

  →Errors to CTV will be smaller than 1 mm



Corrections without rotations

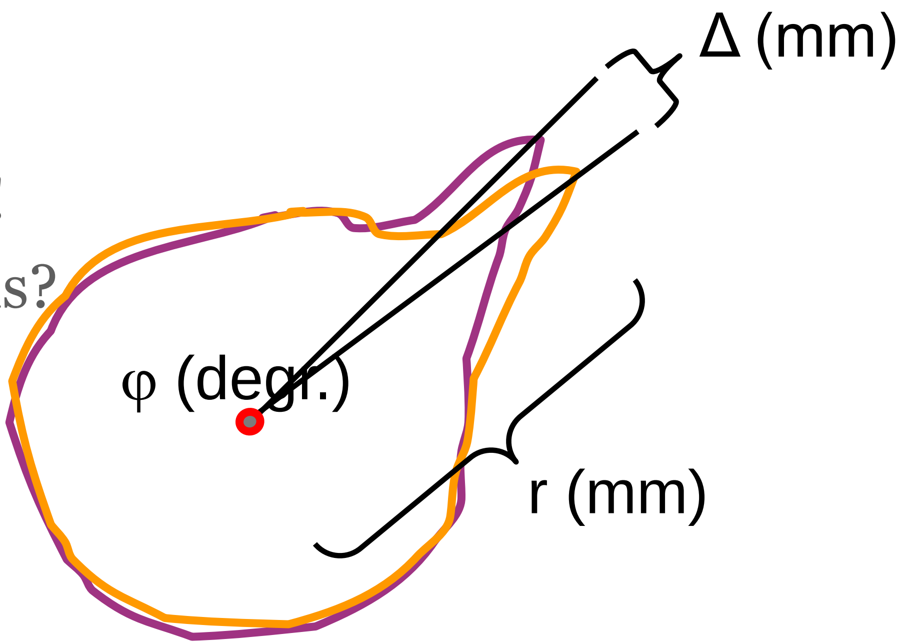
Rule of thumb: $\Delta = 0.02 \times \varphi \times r$ (mm)

Problem for structures far from rotation center

- 3° rotation
- Rotation centre is in CTV

→ 6 mm shift at 10 cm distance!

→ does treatment plan allow this?



Lung stereotactic body radiotherapy

- Residual positional error when only translations were used for image registration

	AP [mm]	CC [mm]	LR [mm]	pitch [°]	roll [°]	rot [°]
M	−0.1	0.1	−0.1	0.31	−0.06	−0.56
Σ	1.3	1.0	0.8	1.20	1.23	1.42
σ	1.5	1.0	1.1	0.79	1.33	0.85

AP, anterior-posterior; CC, cranio-caudal; LR, left-right.

Josipovic et al, Acta Oncol 2012

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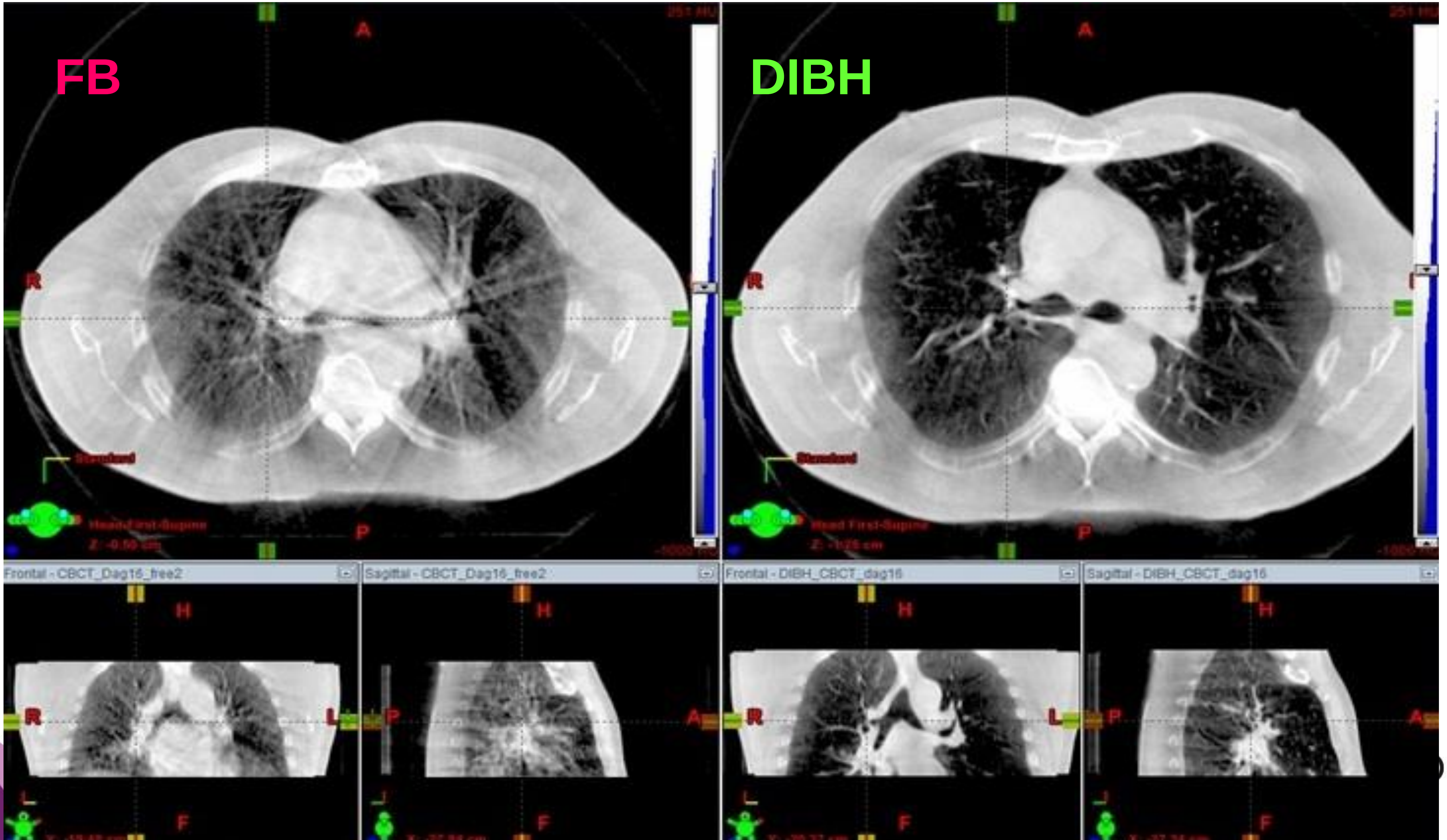
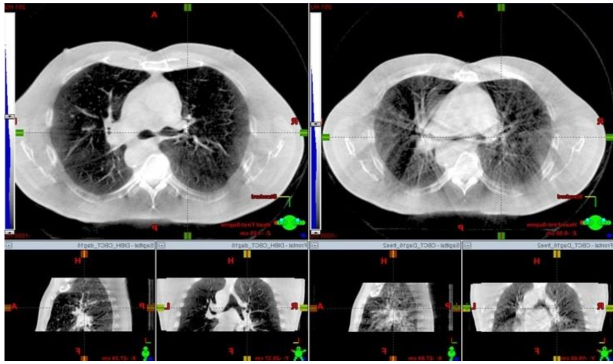
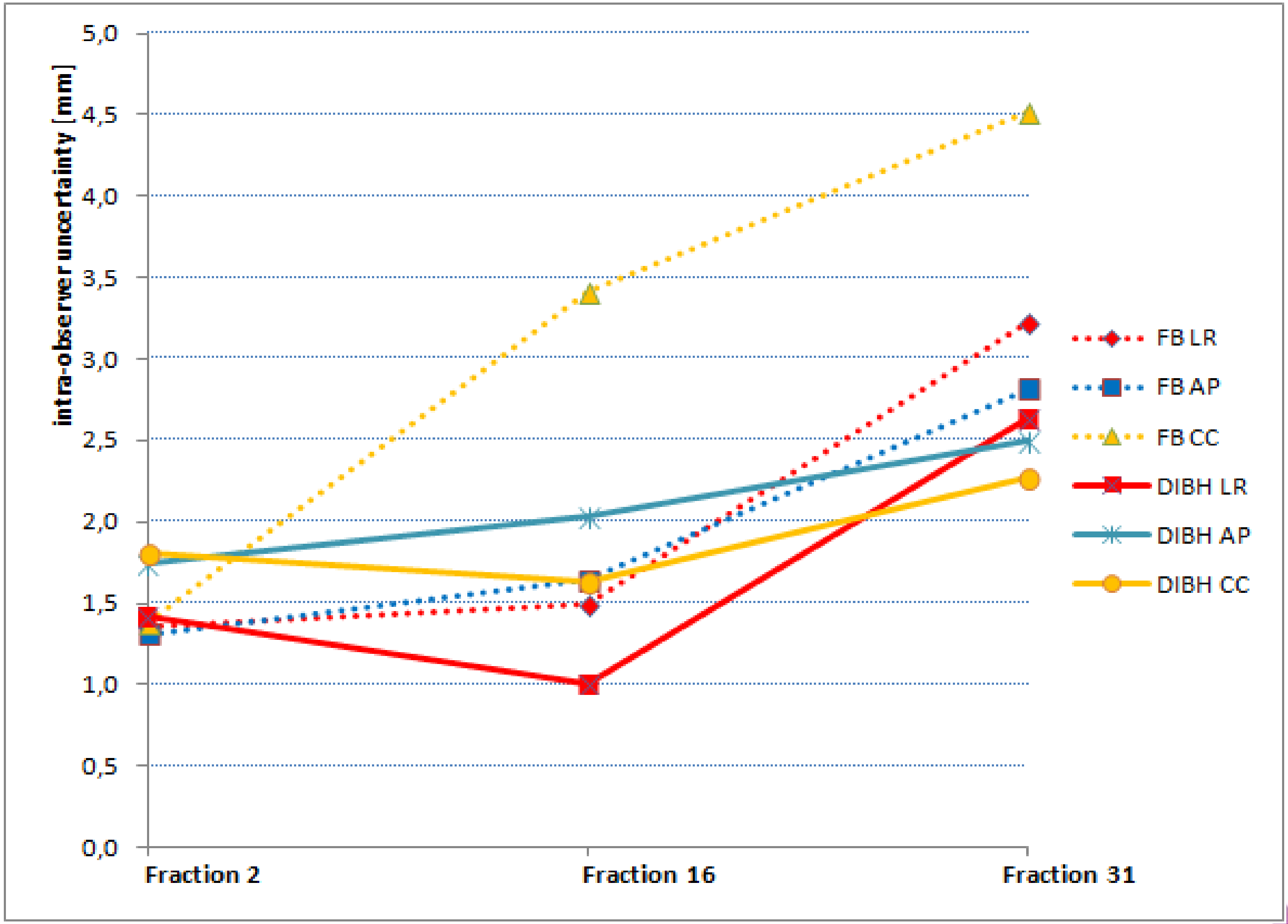
Impact of image quality



Impact of image quality



Observer uncertainties in CBCT registration



Josipovic et al. *BJR 2016*

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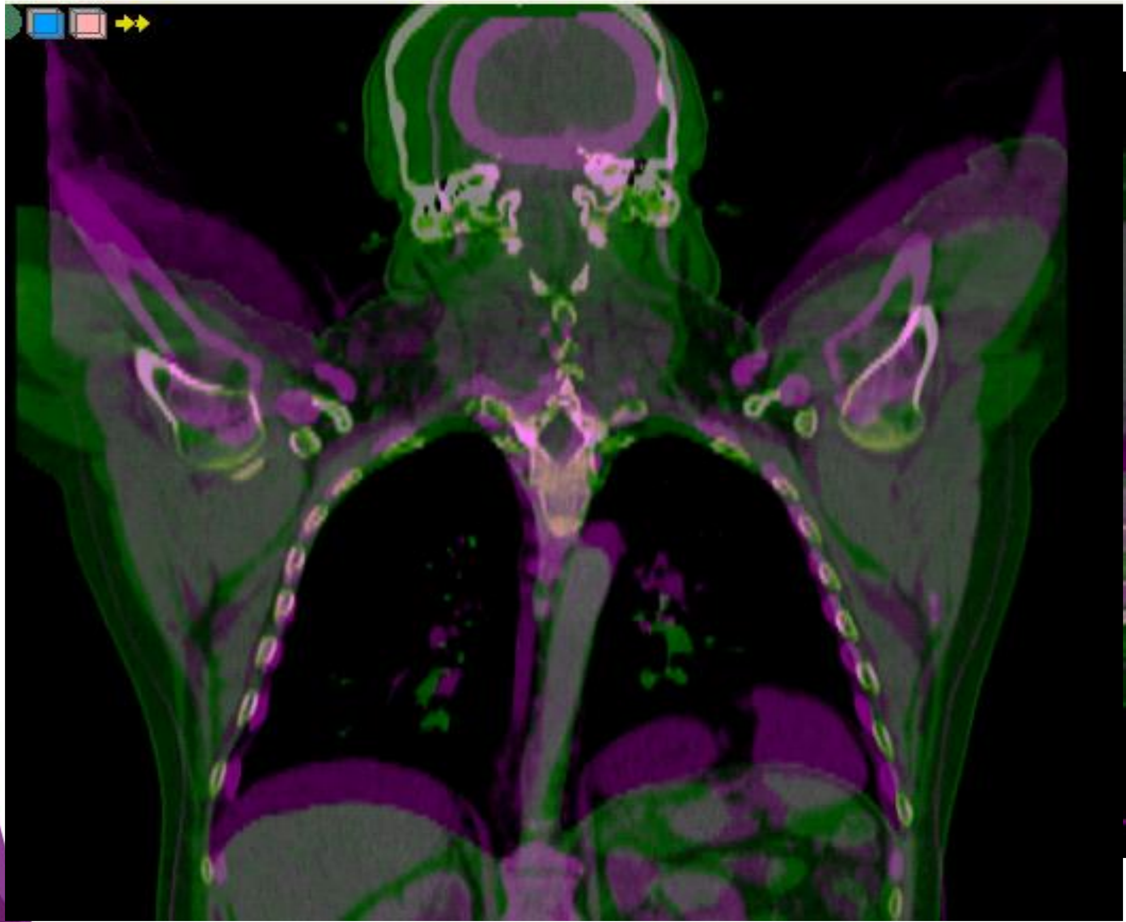
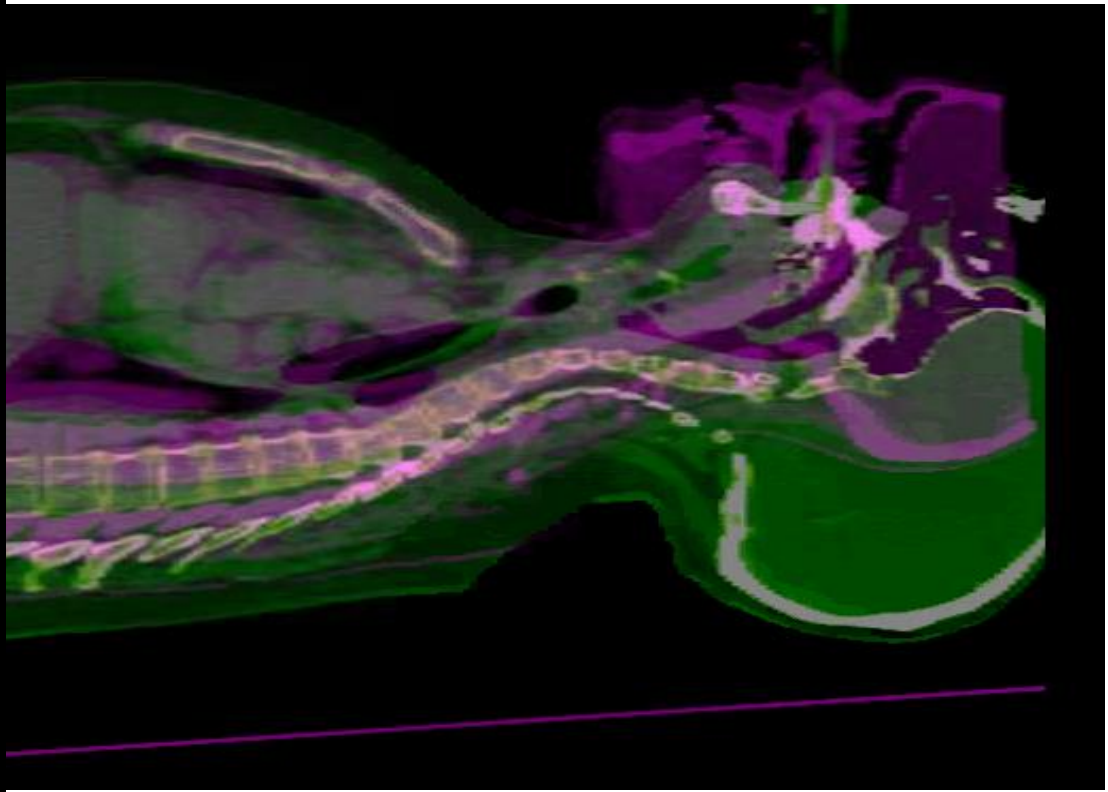
Case: fusion of pre- and post-chemo scan

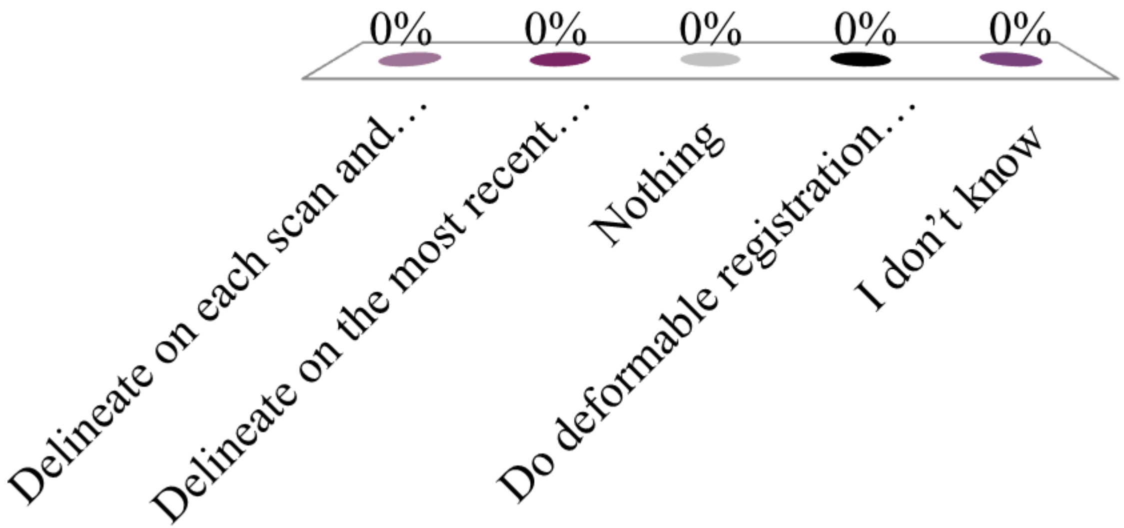




Courtesy M. Aznar

What would you do (or your radiation oncologist)?

A. Delineate on each scan and combine contours
B. Delineate on the most recent scan
C. Nothing
D. Do deformable registration before delineation
E. I don’t know



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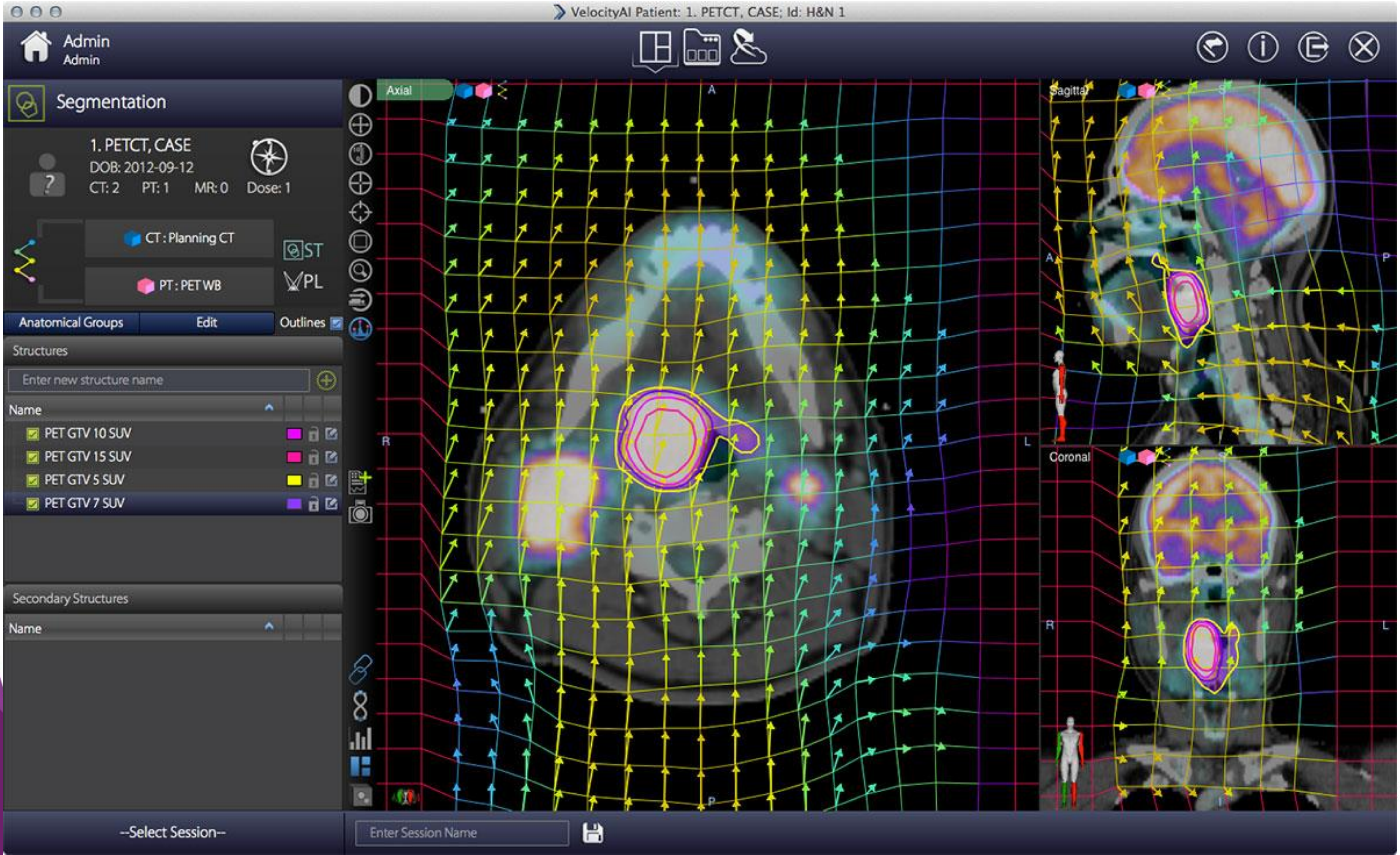
How to handle registration uncertainties ?

- Ensure a treatment-like position already at staging
  - ➢ Flat table top
  - ➢ Arms up
  - ➢ Chest board
  - ➢ Motion management

- Good collaboration with the PET / MR department!

Deformable image registration - DIR



Deformable image registration

- How do you know the result is good?
  - It looks ok ☺
- Getting the contours / outlines of organs right
  - Ok for IGRT
- Getting the heterogeniety/tissue cells inside the organs right
  - Necessary for dose accumulation
- Different challenges with different organs
- DIR needs to be evaluated for each clinical problem

Take home messages

- Image registration plays an important role for:
  - routine treatment planning
  - routing treatment delivery
  - Follow up, clinical studies, re-irradiation

- Consider the effect of rotations and anatomical changes

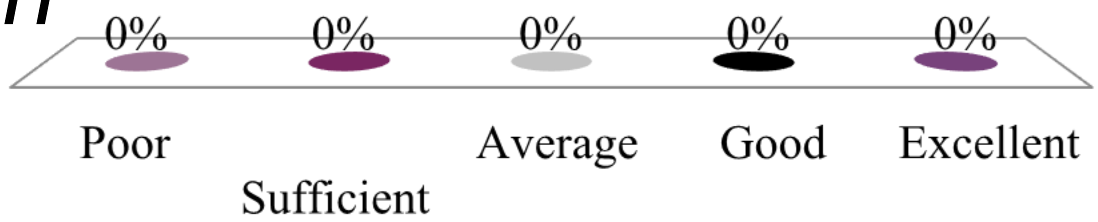
- There is no perfect solution:
  - use best registration algorithm for each problem
  - **<u>always</u>** include a visual inspection step in the process

Additional reading: **AAPM TG 132 report**

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



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Treatment Planning I

Liz Forde, MSc (RTT)
Assistant Professor
Discipline of Radiation Therapy
Trinity College Dublin

ARTT
Applied Radiation Therapy
Trinity Research Group

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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Learning Outcomes

- Discuss the role of the RTT in the treatment planning process
- Discuss key concepts of ICRU 50, 62 and 83
- Identify key features of inverse planning techniques
  - IMRT
  - VMAT
- Identify evidence for the use of inverse planning
- Describe the inverse planning process for IMRT and VMAT
- Describe the importance of target and organ definition and it's impact on the inverse planning process
- Review the benefits of inverse planning to "non standard" sites

RTT Lead Planning

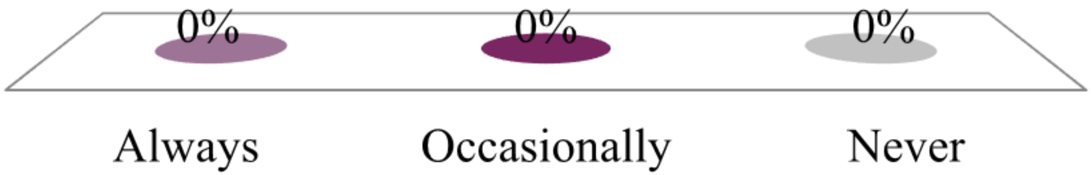
- Scope of practice may vary significantly

- Often seen as a "Specialist role"
  - ➢ Rotations may be limited

- Regardless of level of involvement in planning, a basic understanding of key principles increase your ***"clinical intelligence"***

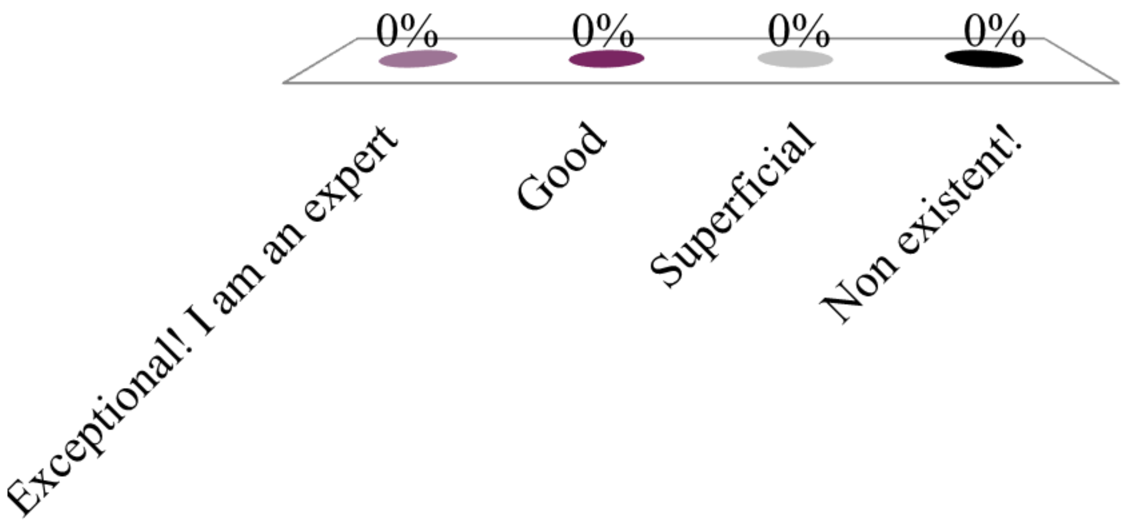
In my work, I am involved in treatment planning:

A. Always
B. Occasionally
C. Never



My knowledge and understanding of treatment planning and theoretical concepts is:

A. Exceptional! I am an expert
B. Good
C. Superficial
D. Non existent!



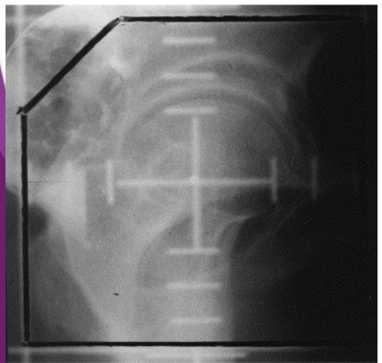
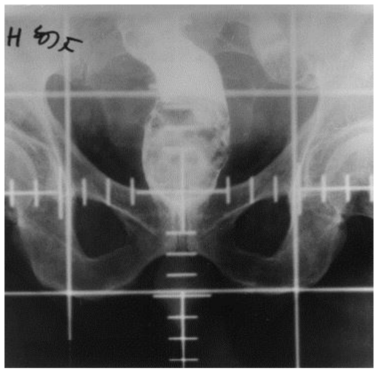
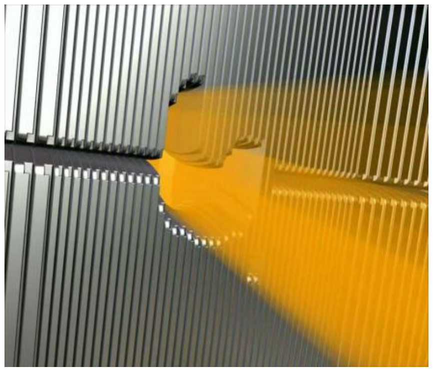
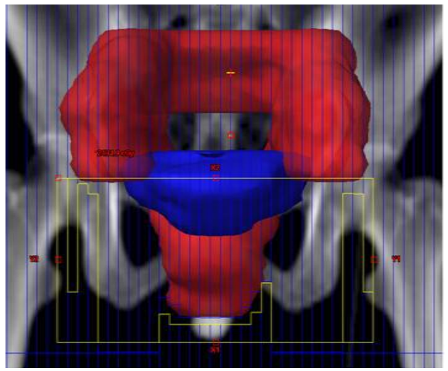
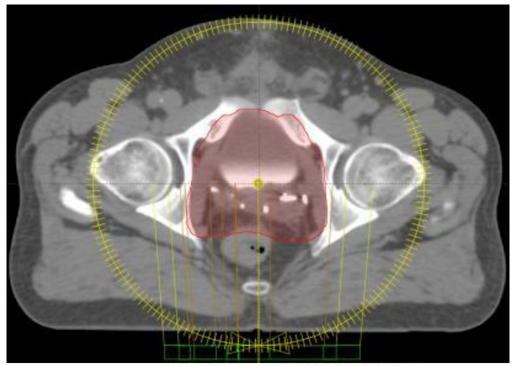
Planning: Where are we now?

- Technology boom

- From 2D to 3D
- From 3D to 4D, ART and tumour tracking

- From block shielding to conformal shielding
- From conformal shielding to dynamic shielding

- Inverse planning allows for greater control

"it is important that clear well defined unambiguous, and universally accepted concepts and terminology are used to ensure a common understanding" *(ICRU 62)*

ICRU 50

- GTV
- CTV
- PTV
- Irradiated Volume
- Treated Volume
- OAR
- ICRU reference point
- Dose heterogeneity
- (>95%, <107%)

ICRU 62

- Reference points
- Coordinate Systems
- PRV
- ITV
- CI

Target Conformity

- Conformity is achieved when the “treated volume is reduced towards the target volume and still covers the target volume in all dimensions”

- Conformity Index: the quotient of the Treated Volume and the volume of the PTV

- CI = TV/PTV

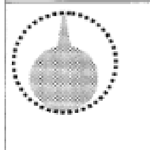
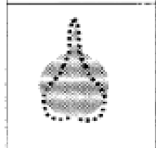
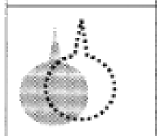
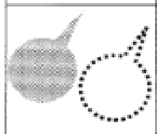
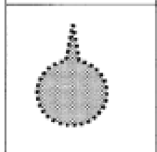
$$CI95 = \frac{\text{volume encompassed by the 95\% isodose line}}{\text{volume of the PTV}}$$

e.g. CI95 = volume encompassed by the 95% isodose line / volume of the PTV

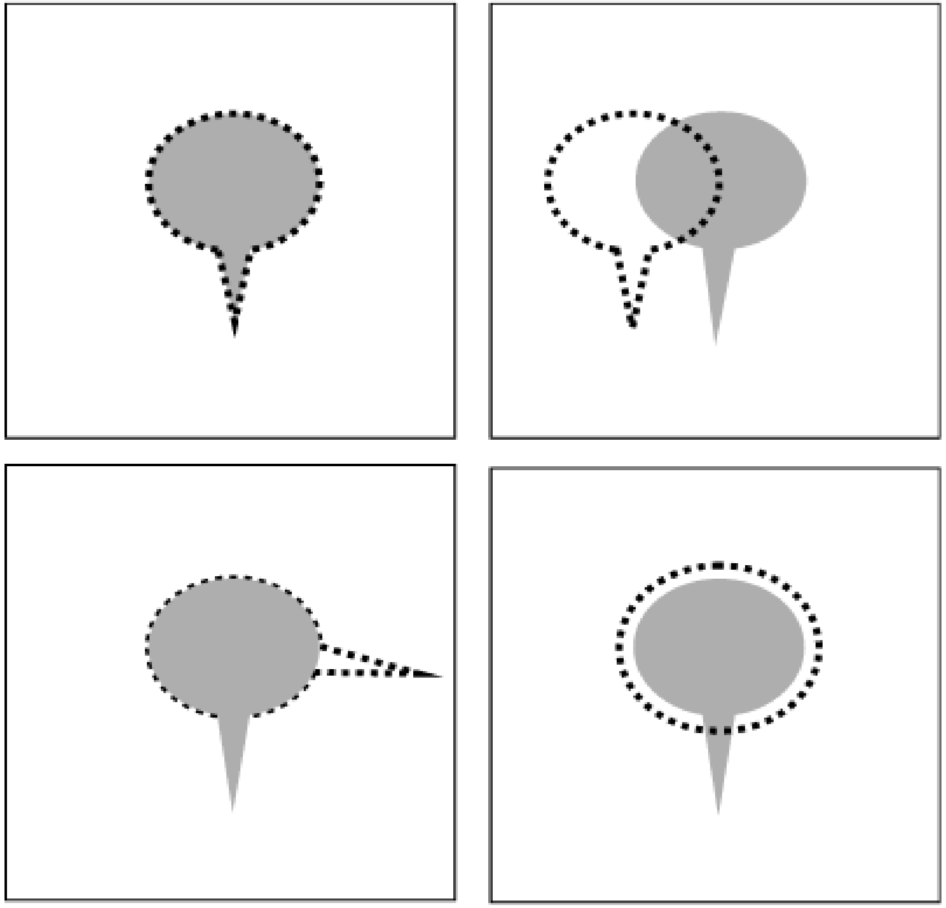
- This is Level 3 reporting

CI: A Word of Warning

Table 2. Comparison of the various volume-based conformity indices in various clinical settings

Treatment plan	Parameters	$\frac{V_{RI}}{TV}$ RTOG (1)	$\frac{TV_{RI}}{TV}$ SALT-Lomax (28,32)	$\frac{TV_{RI}}{V_{RI}}$ Lomax (32)	$\frac{TV_{RI} \times TV_{RI}}{TV \times V_{RI}}$ Van't Riet (33)
	$TV = 5\ cm^3$* $V_{RI} = 10\ cm^3$ § $TV_{RI} = 5\ cm^3$ ¶	**2**	**1**	**0.50**	**0.50**
	$TV = 5\ cm^3$ $V_{RI} = 3\ cm^3$ $TV_{RI} = 3\ cm^3$	**0.60**	**0.60**	**1**	**0.60**
	$TV = 5\ cm^3$ $V_{RI} = 5\ cm^3$ $TV_{RI} = 4\ cm^3$	**1**	**0.80**	**0.80**	**0.64**
	$TV = 5\ cm^3$ $V_{RI} = 5\ cm^3$ $TV_{RI} = 2.5\ cm^3$	**1**	**0.50**	**0.50**	**0.25**
	$TV = 5\ cm^3$ $V_{RI} = 5\ cm^3$ $TV_{RI} = 0\ cm^3$	**1**	**0**	**0**	**0**
	$TV = 5\ cm^3$ $V_{RI} = 5\ cm^3$ $TV_{RI} = 5\ cm^3$	**1**	**1**	**1**	**1**

Abbreviations: TV = Target Volume (gray); V_{RI} = Volume of the Reference Isodose (dotted line); TV_{RI} = Target volume covered by the Reference Isodose = intersection of TV and V_{RI}.



Feuvret L, Noel G, Mazeron JJ, Bey P. Conformity Index: A Review. IJROBP. 2005; 64(2): 333-342

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ICRU 50

- GTV
- CTV
- PTV
- Irradiated Volume
- Treated Volume
- OAR
- ICRU reference point
- Dose heterogeneity
- (>95%, <107%)

ICRU 62

- Reference points
- Coordinate Systems
- PRV
- ITV
- CI

ICRU 83

- Detailed labelling of structures
- Volumetric prescription
- Near min (D98%)
  Near max (D2%)
  Median dose (D50%)
- CI (again)
- HI

ARTICLE

J Natl Cancer Inst 2008;100:300–307

Intensity-Modulated Radiation Therapy Dose Prescription, Recording, and Delivery: Patterns of Variability Among Institutions and Treatment Planning Systems

Indra J. Das, Chee-Wai Cheng, Kashmiri L. Chopra, Raj K. Mitra, Shiv P. Srivastava, Eli Glatstein

Aim: Examined the variation in dose prescription, planning, recording and delivery at different institutes

Data was retrospectively analysed for patients treated between 2004 – 2006 in 5 US institutes using 5 different TPS

2008 Publication

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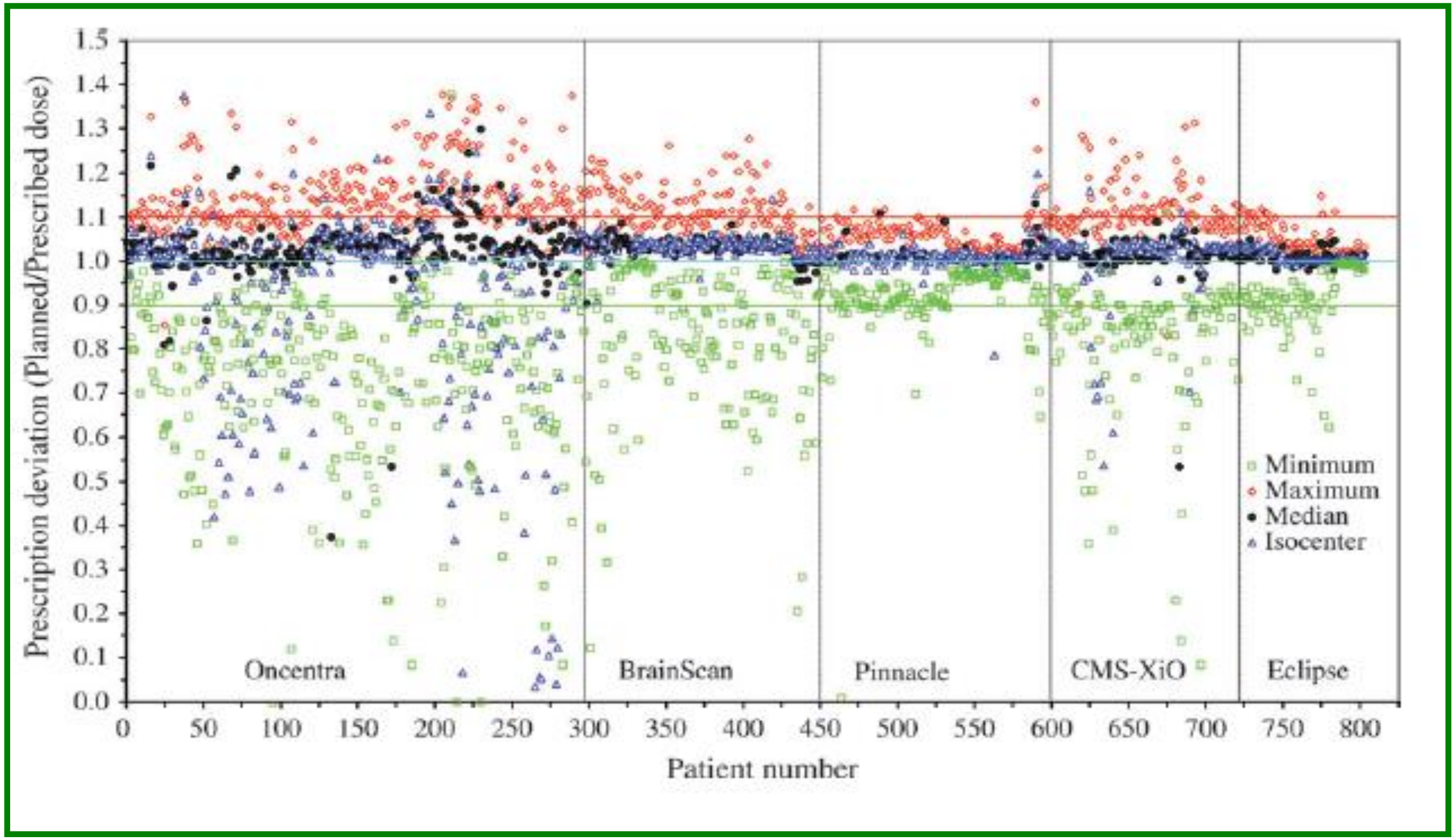

Across all institutions and all TPS, the Median dose to the target was least variable and closest to 100% of the total dose

The Need for Standardised Reporting

- Green Journal Editorial, 2013 *(Yartsev, Muren and Thwaites)*
- Planning papers are interesting to everyone (RO, MP and RTTs)
- Pick up practical tips and share outcome data ***BUT…***

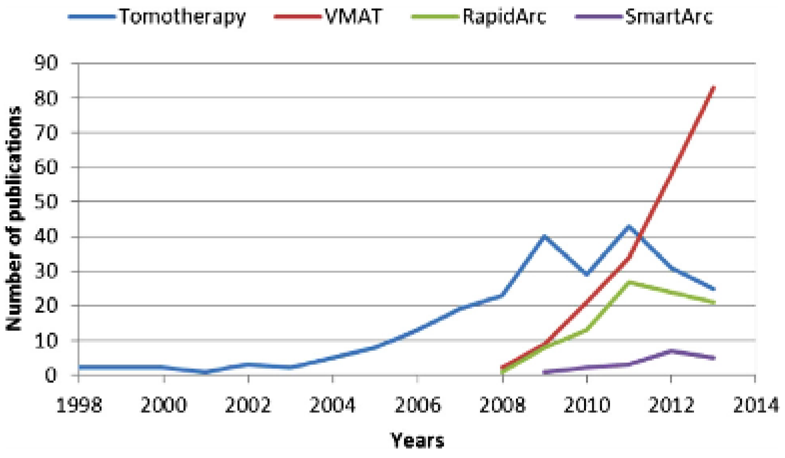

Fig. 1. Number of publications per year for rotational IMRT planning studies. (The data for 2013 is limited to 11 months.)

A third group of readers includes treatment planners who need solid information about the details of the planning procedure applicable to the current case. Unfortunately, there is a variety of definitions and a confusion in terminology that makes it difficult to compare publications of plans performed by different groups. For example, we have found nine different definitions used to describe conformity of the prescribed dose to the target, and seventeen (!) for the homogeneity of dose distribution within the target. The included DVHs should be reproduced in high-quality, allowing for exact numerical values to be derived. It is also essen-

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The Price of Target Homogeneity

- Previous ICRU reports recommended that the dose values in the PTV be confined within 95% and 107% of the prescribed dose.
- With IMRT, these constraints may be confining if the avoidance of OARs is more important than target dose homogeneity

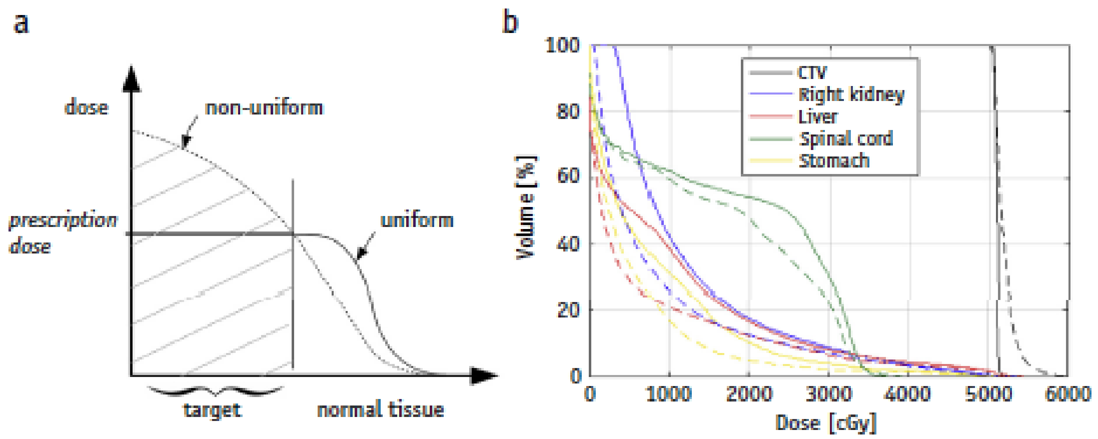

Fig. 1. "More dose in the tumor can mean less dose in the healthy tissue." Demonstrations showing that forcing target dose uniformity can result in increased organ at risk doses. Panel a) is a schematic illustration of the concept and panel b) demonstrates it for a clinical plan. The hot plan is plotted with dashed lines and the clinical plan (striving for a uniform target dose) with solid lines. *Abbreviation:* CTV = clinical target volume.

"No data have demonstrated that uniform doses are radiobiologically preferable in general"

Craft et al., 2016 IJROBP

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Fine, But What is Happening in Clinical Practice?

Practical Radiation Oncology (2017) 7, e145-e155

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Original Report

State of dose prescription and compliance to international standard (ICRU-83) in intensity modulated radiation therapy among academic institutions

Indra J. Das PhD, FACR, FASTRO [a,*], Aaron Andersen MS [b], Zhe (Jay) Chen PhD [c], Andrea Dimofte MS [d], Eli Glatstein MD, FASTRO [d], Jeremy Hoisak PhD [e], Long Huang PhD [f], Mark P. Langer MD [b], Choonik Lee PhD [g], Matthew Pacella MS [h], Richard A. Popple PhD [i], Roger Rice PhD [e], Jennifer Smilowitz PhD [j], Patricia Sponseller MS [k], Timothy Zhu PhD [d]

Aim: Assess current state of compliance to ICRU-83 for dose prescribing among academic institutions

2017 Publication

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10 US academic institutes with >10 years IMRT experience

Data was retrospectively collected between 2013 - 2015

Data collected:

Disease site

PTV name

Target Volume

DVH (including D100, D98, D95, D50 and D2)

TPS

Technique

MUs

Anonymised planner and consultant ID

"Nearly 95% of patient treatments deviated from the ICRU-83 recommended D50 prescription dose delivery."

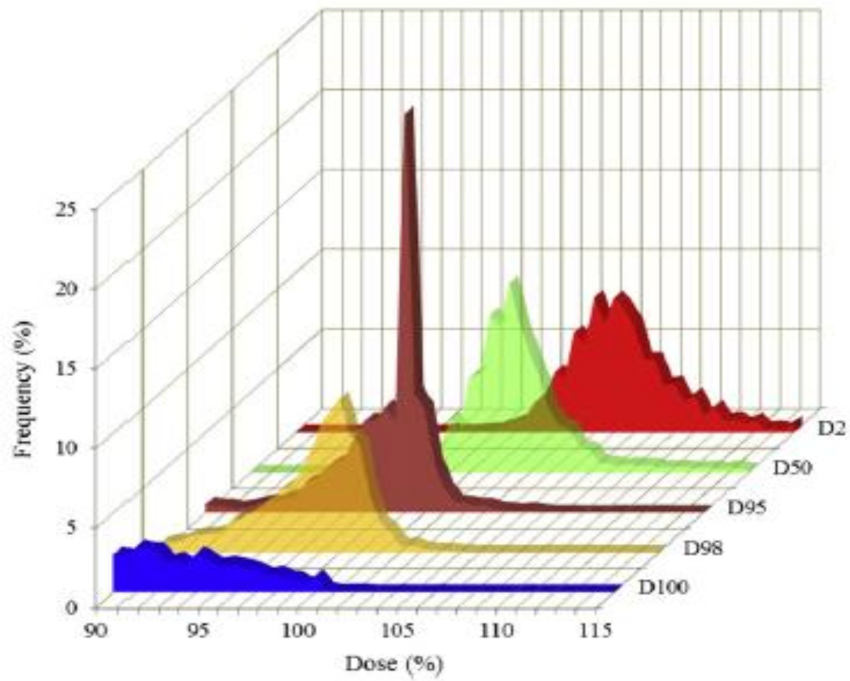

Figure 2 Frequency distribution of International Commission on Radiation Units & Measurements (ICRU)-83 parameters, of doses delivered to 100% (D_{100}), 98% (D_{98}), 95% (D_{95}), 50% (D_{50}), and 2% (D_2) of sites for the 5094-patient population indicating a larger variation in the shape of these prescription point distributions. D_{100} is widely distributed. D_{95} seems to have a peak distribution centered at 100% with (mean ± 1 SD) (97.1 ± 8.3%), which might be common practice. D_{50}, which is the recommended prescription point in ICRU-83, peaks at around 103% (102.9 ± 9.4%).

The majority of institutes appear to be prescribing to the D95 ***– not even mentioned in ICRU-83***

Fine, but that is clinical practice, not current literature!

Practical Radiation Oncology (2017) xx, xxx xxx

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Basic Original Report

Adherence to ICRU-83 reporting recommendations is inadequate in prostate dosimetry studies

Aishling Mohan BSc (Hons), Elizabeth Forde MSc*

Applied Radiation Therapy Trinity, Discipline of Radiation Therapy, School of Medicine, Trinity College Dublin, Ireland

Received 28 April 2017; revised 29 June 2017; accepted 21 August 2017

Aim: Collate the endpoints reported in prostate planning studies and evaluate whether they adhere to ICRU-83 recommendations

48 papers published in peer reviewed journals since 2010 were analysed

2017 Publication

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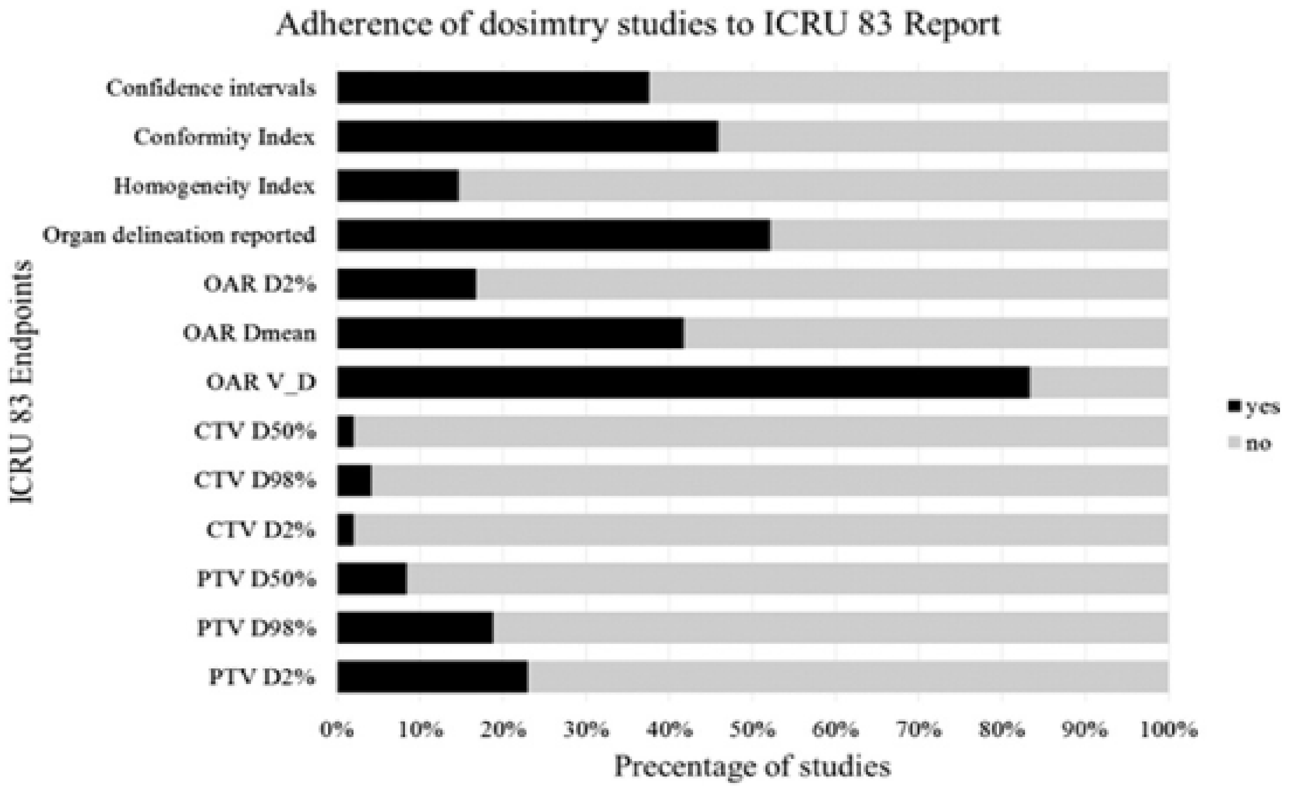


Figure 1 Adherence of dosimetry studies to ICRU 83 report. CTV, clinical target volume; D2%, dose received by 2% of the volume; D50%, dose received by 50% of the volume; D98%, dose received by 98% of the volume; Dmean, mean dose; ICRU, International Commission on Radiation Units and Measurements; OAR, organ at risk; PTV, planning target volume; V_D, the volume of tissue receiving a specified dose.

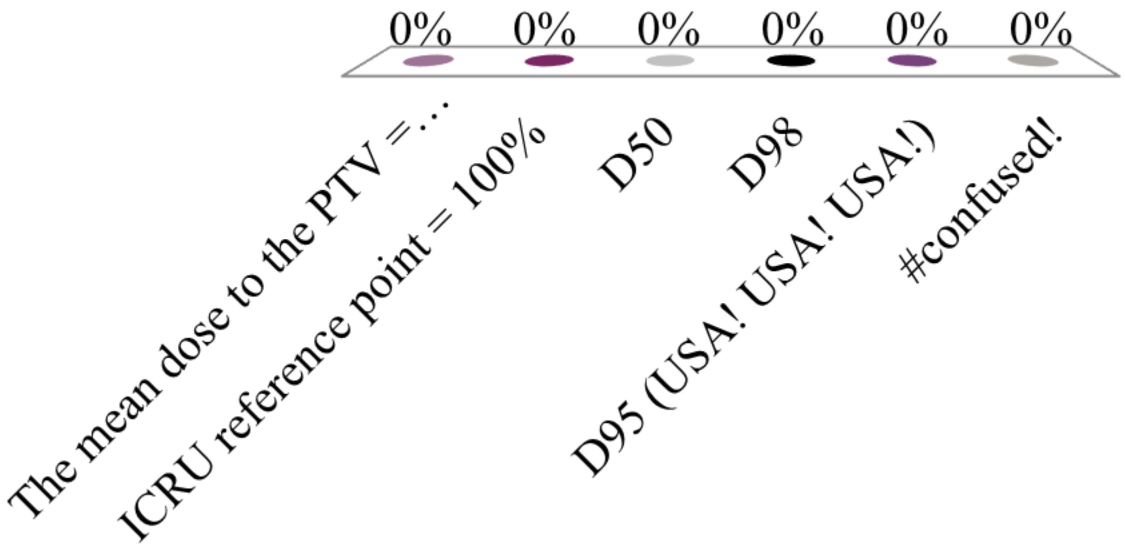
22.9% reported PTV D2%
18.8% reported PTV D98%
8.3% reported PTV D50%

Significance of this Variation

- We are not able to pool multi-instititional data
- We are not able to benchmark the quality of our plans to others in the RO community
- We are not able to clearly link dosimetric endpoints with clinical outcomes for our patients

In my department we prescribe our IMRT/VMAT prostate plans to:

A. The mean dose to the PTV = 100%
B. ICRU reference point = 100%
C. D50
D. D98
E. D95 (USA! USA! USA!)
F. #confused!



The Planning Process

What do you think is missing from this flowchart?

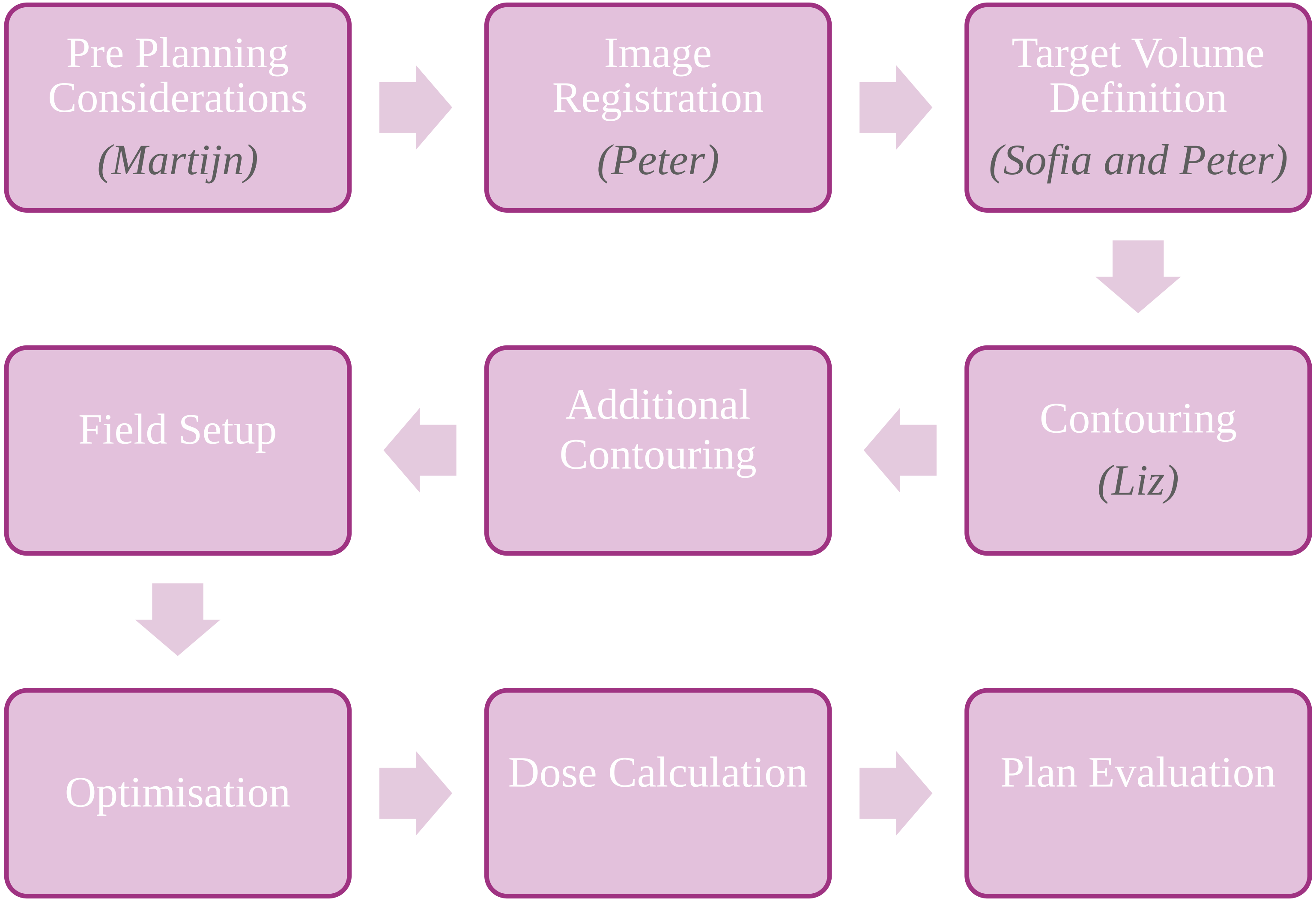
Field Setup

Optimisation

Dose Calculation

Plan Evaluation

This is a dynamic process



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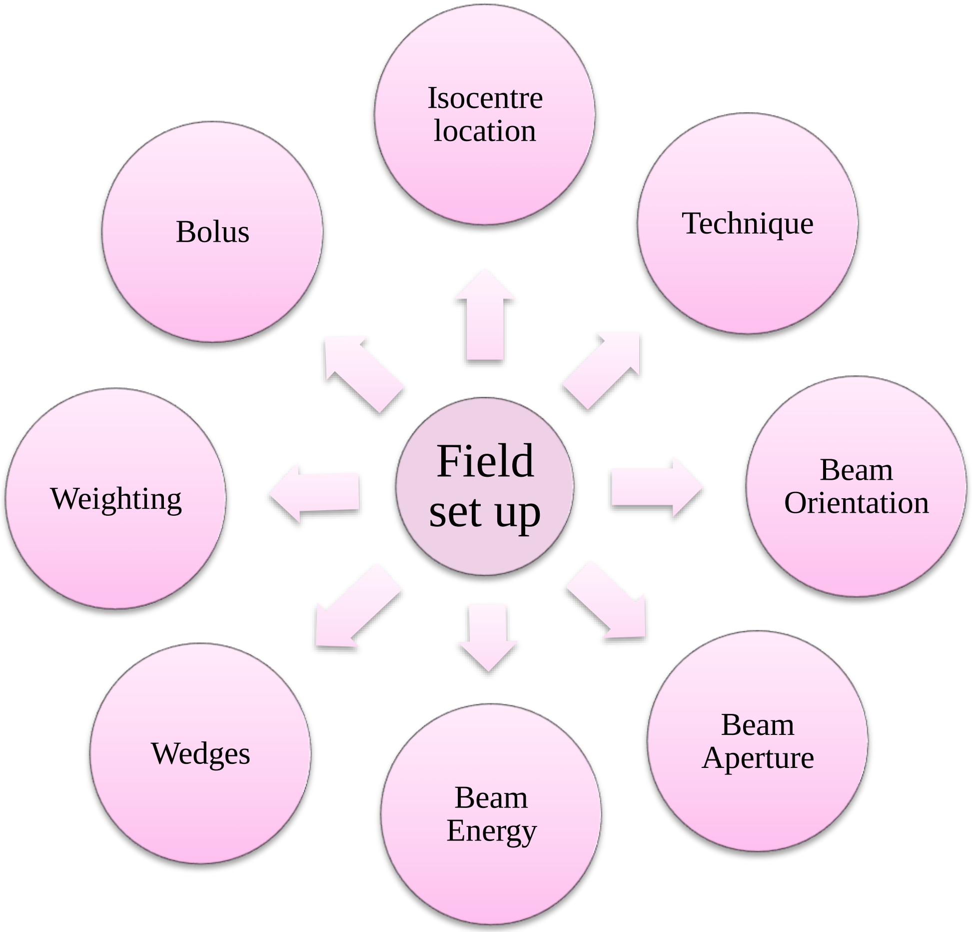
Key Concepts of 3DCRT

- Field set up… “*Finally we get to put some beams on!*”

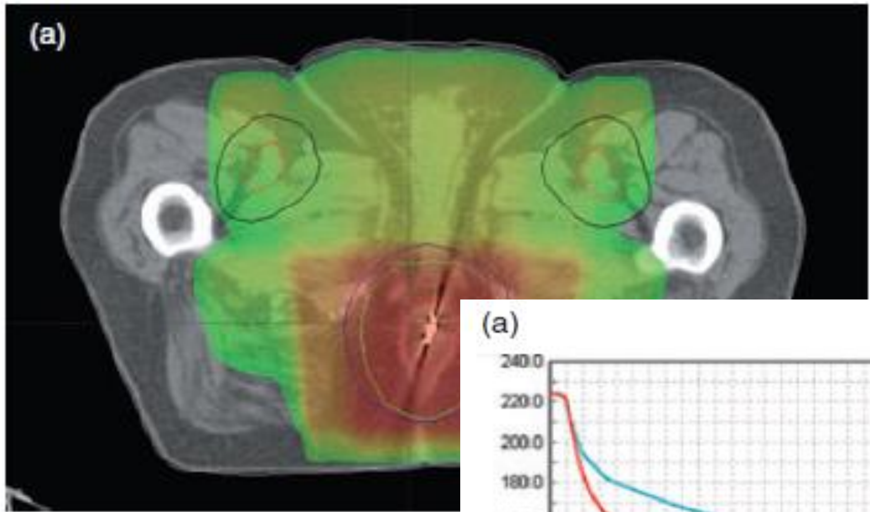
- User defines:

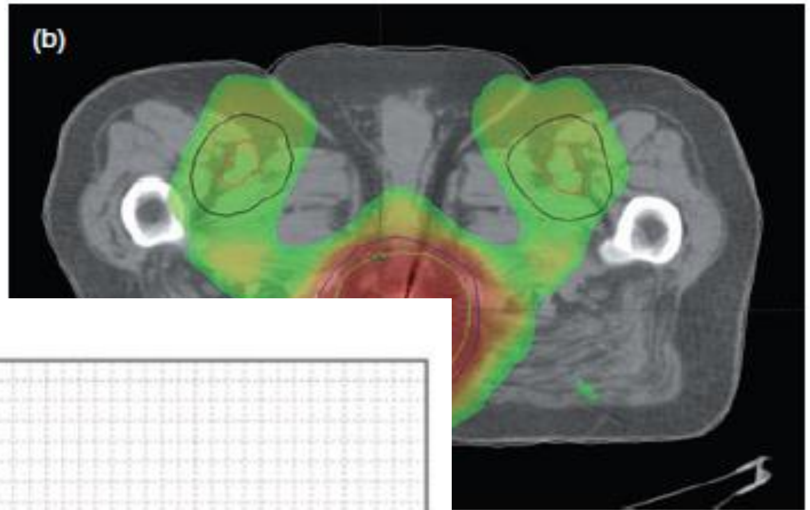


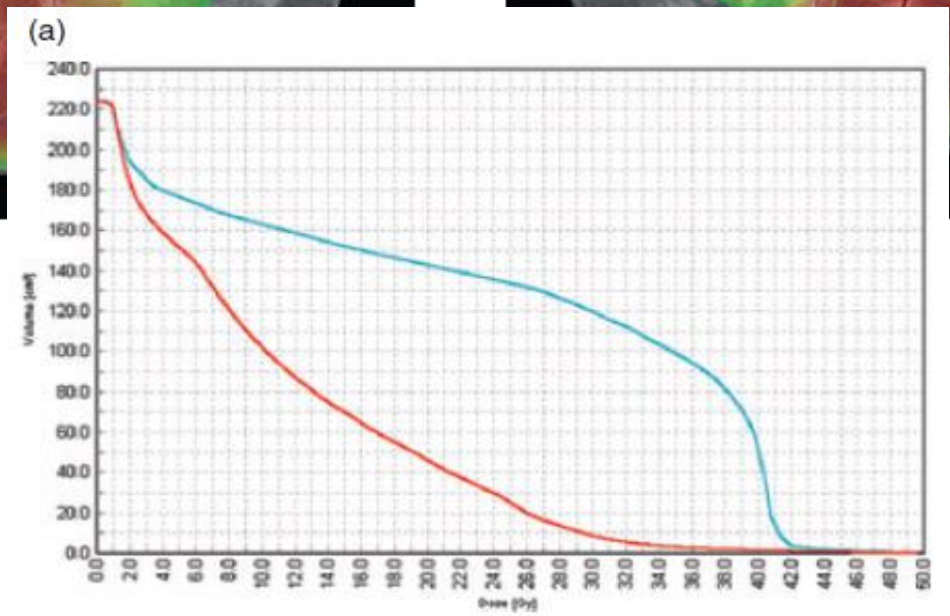
Planning Techniques Explored...

- With 3D targets now being delineated, 3DCRT techniques have become more complex

- “Genital sparing” technique







Bui et al., 2009

Key Concepts of 3DCRT

- But…
- How many fields are we up to now?
- ***Enter IMRT…***

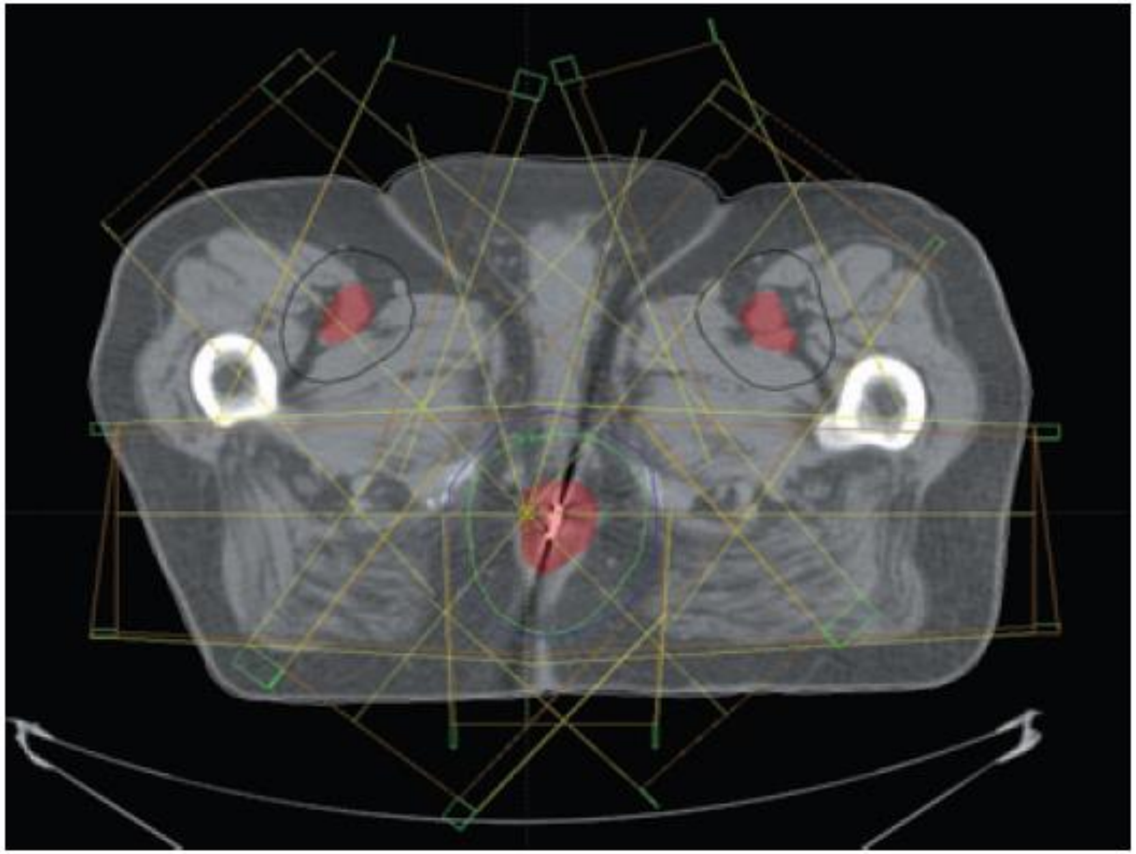


Fig. 2. Example of three-dimensional conformal radiotherapy technique field arrangement. Gross tumour anus and inguinal, red; planning target volume (PTV) anus, green; PTV inguinal, black; PTV pelvis, dark blue.

Bui et al., 2009

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Key Concepts of IMRT

- The multiple-static-field MLC technique
  - Step and Shoot
- The dynamic MLC technique
  - Sliding Window
- Intensity modulated arc therapy
  - IMAT
- Intensity modulated proton therapy
  - IMPT

- "*IMRT requires expertise and careful target design to avoid reduction in local control by marginal miss*" *(NCCN 2013)*

Key Concepts of IMRT

- IMRT is the delivery of radiation to the patient via fields that have a non-uniform radiation distribution across a field.
- Progression from geometric to **fluence** shaping of a field

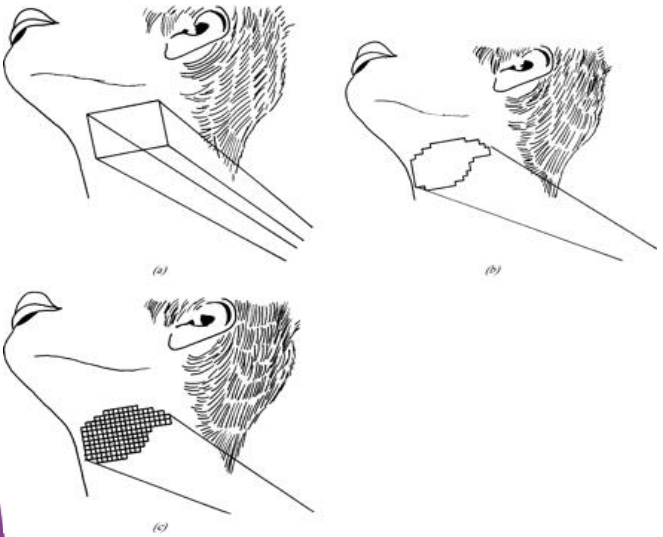
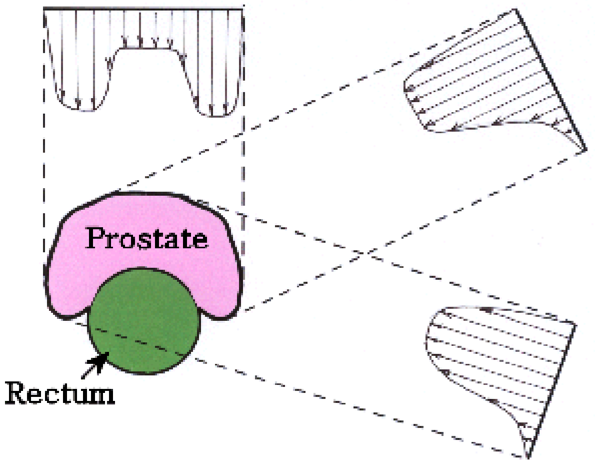
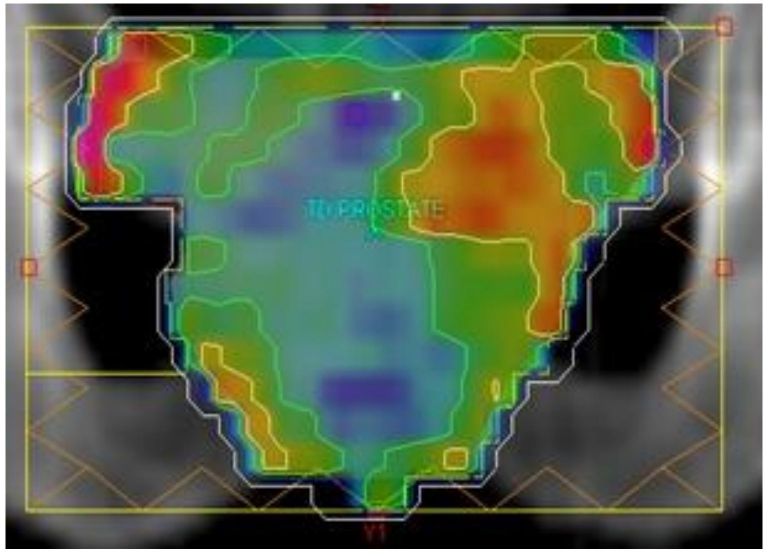


Image taken from: S Webb (2003) The physical basis of IMRT and inverse planning British Journal of Radiology 76: 678-689



Sketch illustrating intensity modulated beams of radiation.



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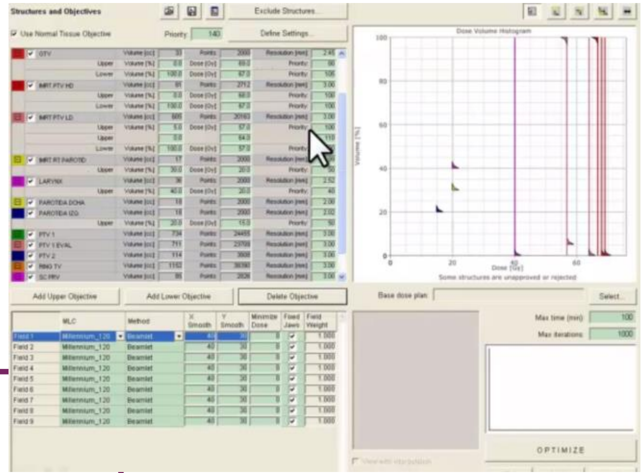
Key Concepts of IMRT

- This fluence is **modulated**
- The intensity of the fluence changes across the beam
- This changing intensity is based on the required dose to be delivered across a field
- This modulated fluence will determine the dMLC leaf motion

Key Concepts of IMRT

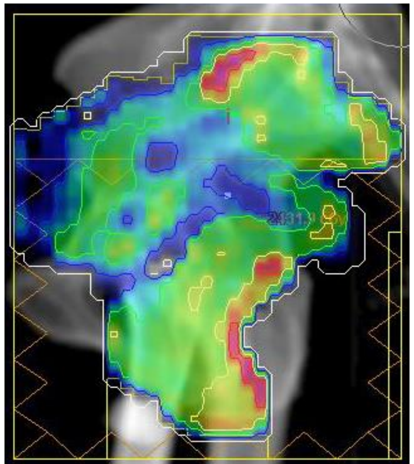
- Limitations of IMRT…

1. Multiple PTVs
2. Complex PTVs (close to skin edge)
3. Multiple OARs with multiple DVCs



Sophisticated optimisation parameters

Complex fluence patterns



High MUs

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Key Concepts of IMRT

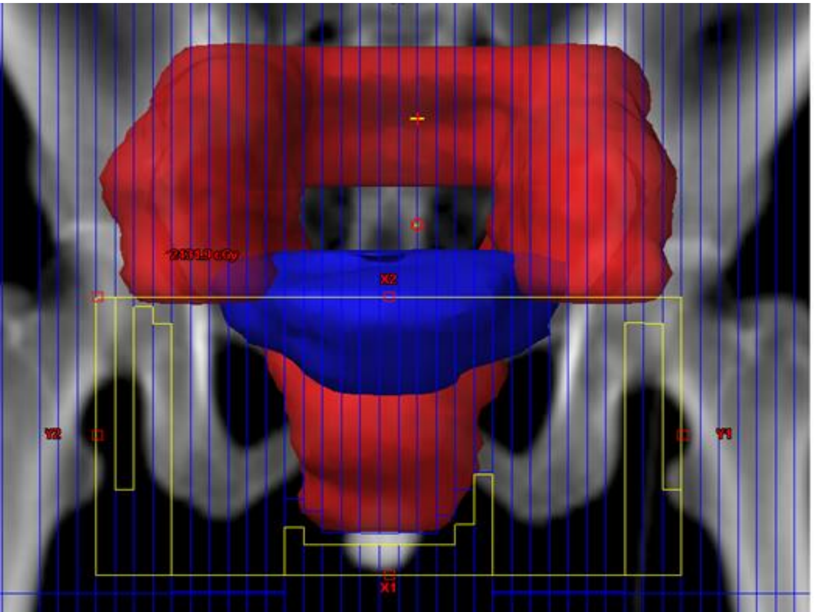
- Limitatio f IMRT…

Large PTVs

Increased number of planning fields

Enter VMAT…

Due to restrictions r motion for SW IMRT, even more eatment fields (for some Varian machines)



NB: this image demonstrates the concept of split carriages

Key Concepts of VMAT

- Simultaneously changing 3 main features
  - ➢ MLC leaf motion
  - ➢ Gantry speed
  - ➢ Variably dose rate

- Inverse planning based on Progressive Resolution Optimisation Algorithm (PRO)

- PRO 3
  - ➢ 4 multi resolution levels
  - ➢ All 178 control points are included in each level
  - ➢ Internal logic
  - ➢ Intermediate dose calculation

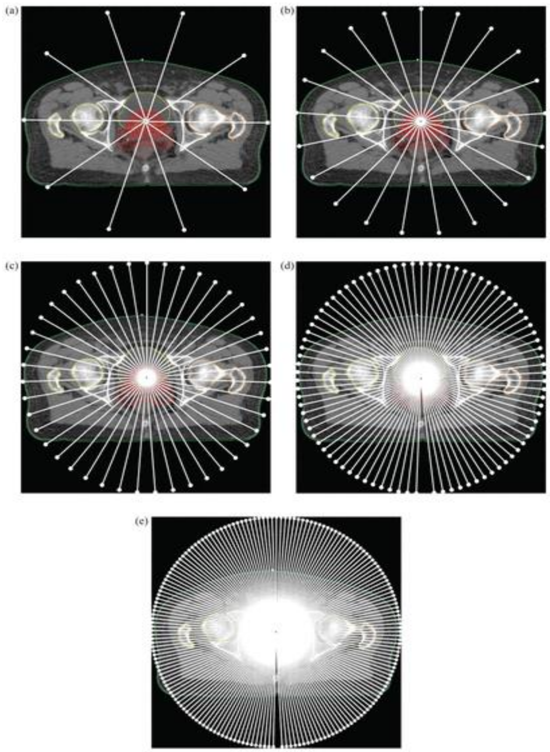


Image taken from: Jolly D, Alahakone D and Meyer J A RapidArc planning strategy for prostate with integrated boost. J Appl Clin Med Phys 2010

Clinical Applications of VMAT

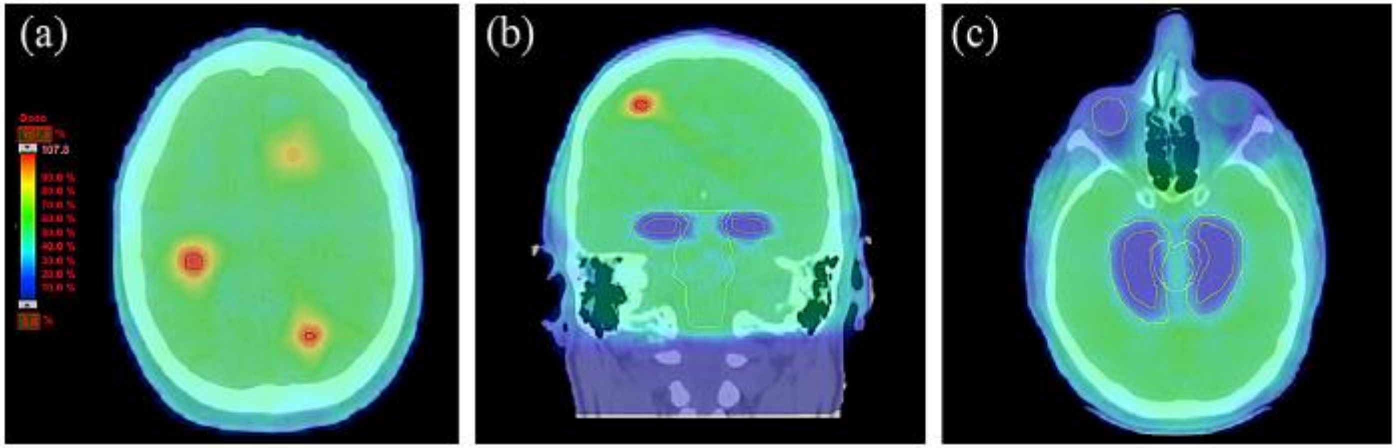
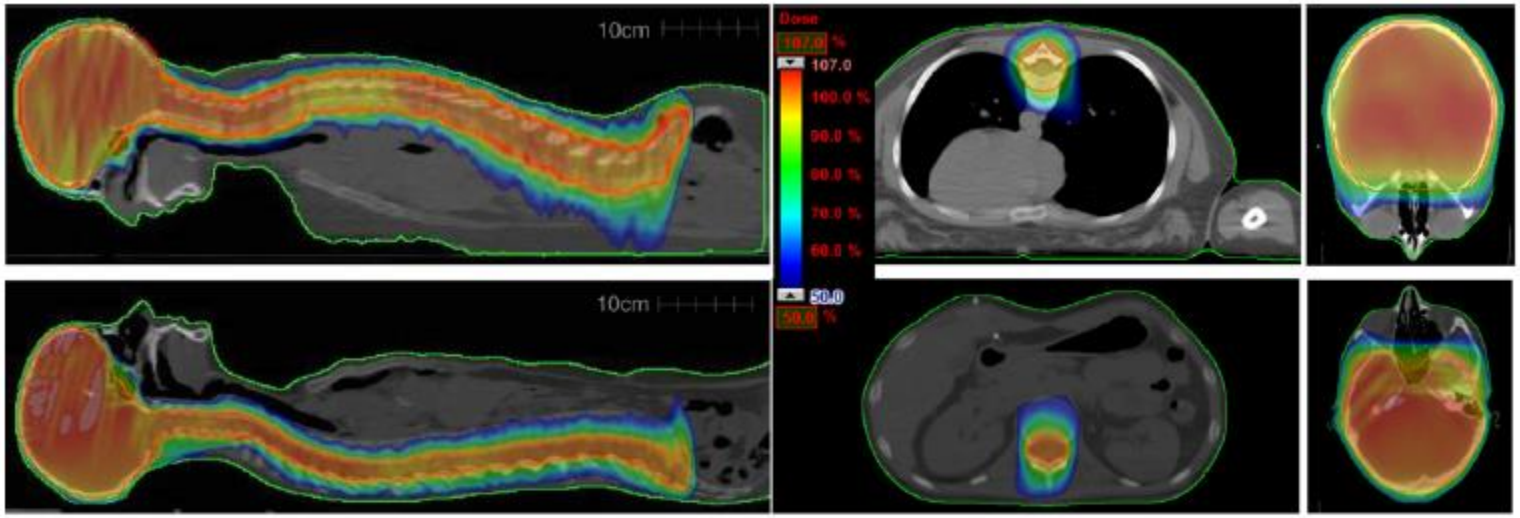


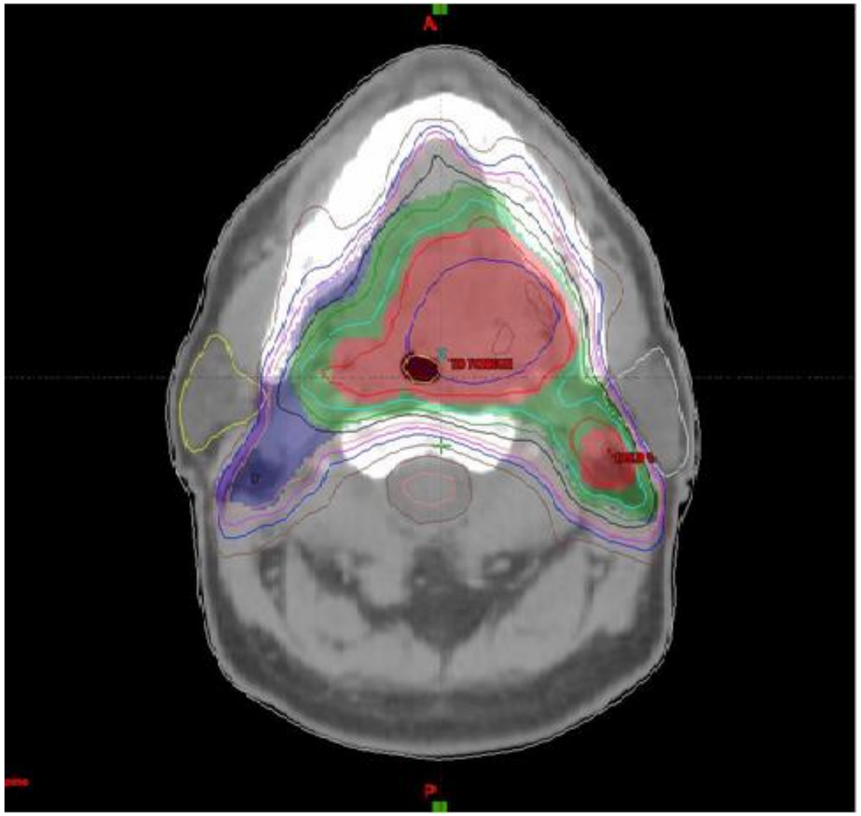
Fig. 1. Examples of isodose distributions for whole brain radiotherapy with hippocampal avoidance and simultaneous integrated boost for three brain metastases using volumetric modulated arc therapy. The whole brain clinical target volume was prescribed to 32.25 Gy in 15 fractions. Three metastases were prescribed 70.8 Gy in 15 fractions. (a) Axial image with three metastases. (b) Coronal image with one metastasis and the hippocampi. (c) Axial image with the hippocampi and eyes.

Hsu et al., 2010

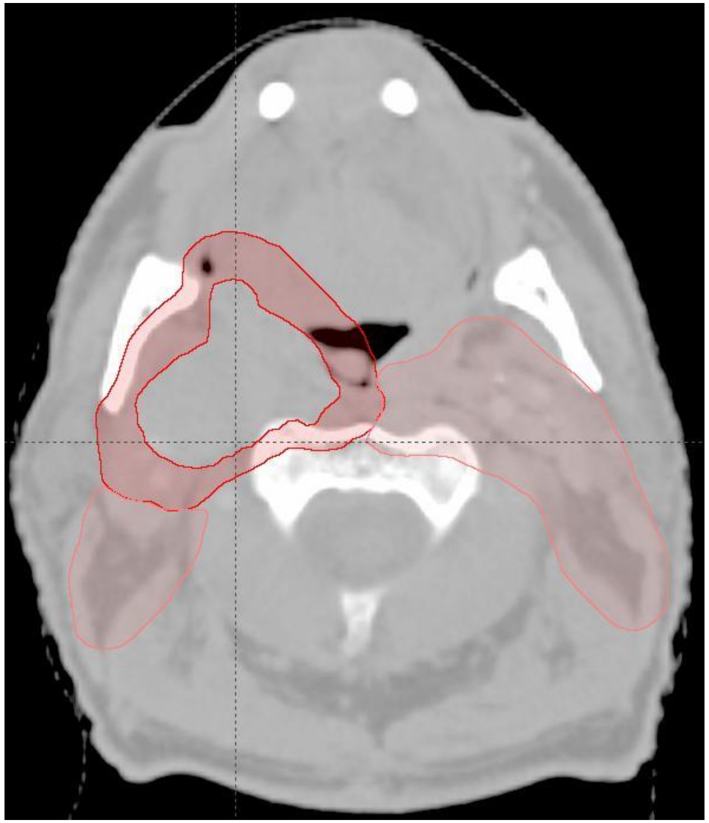


Fogliata et al., 2011

The Benefits of Inverse Planning



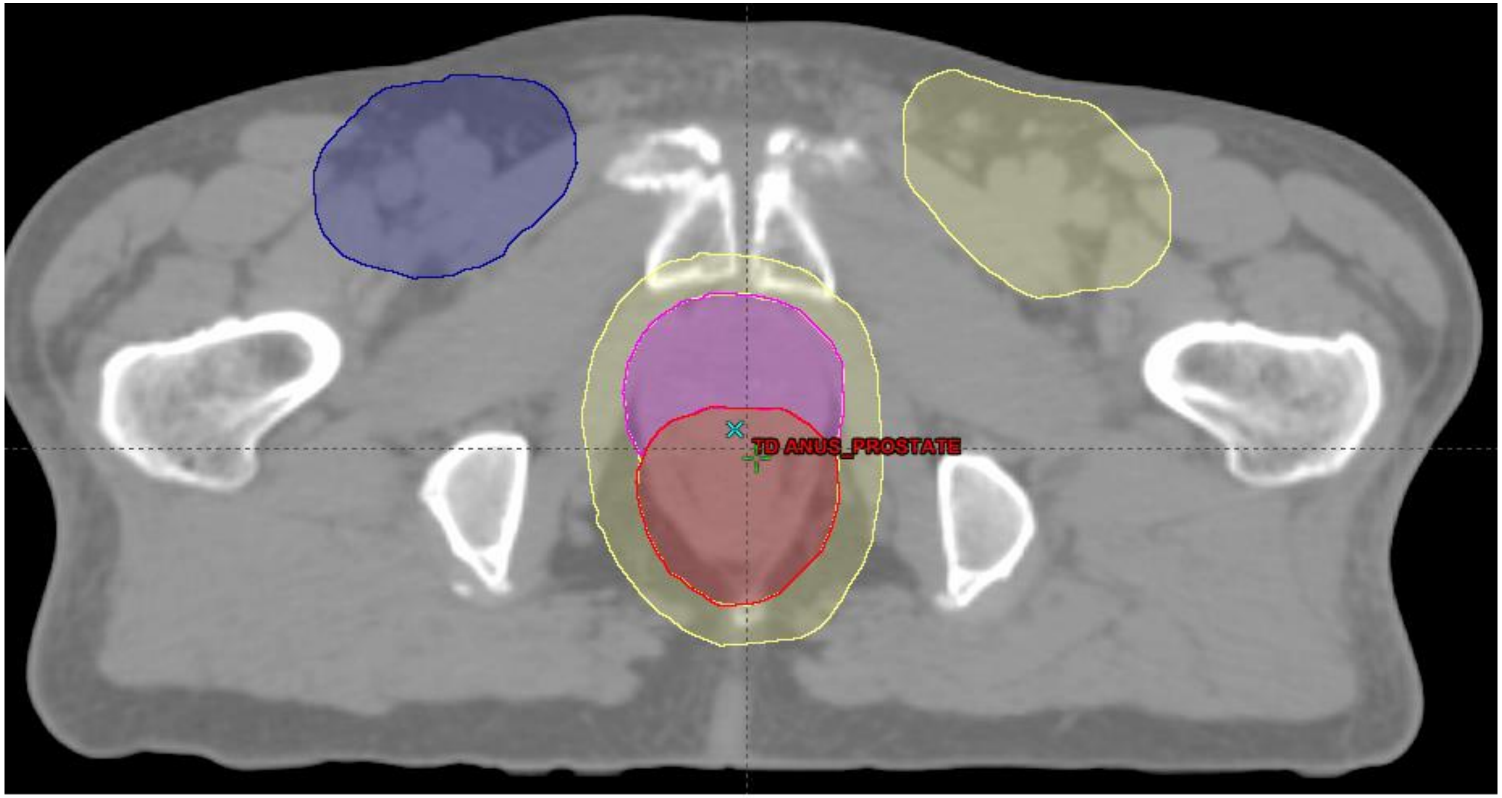
Complex concave volumes



Increased control over distribution

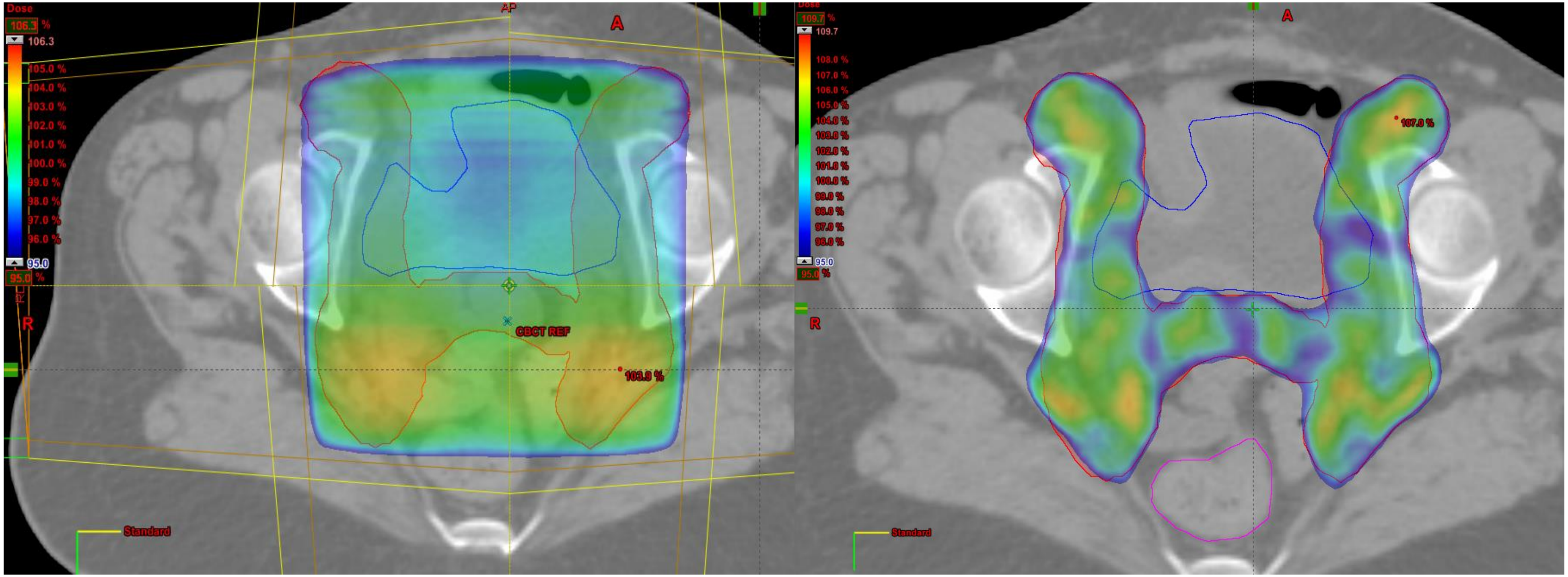
Boosting targets within targets

The Benefits of Inverse Planning



Multiple targets
Simultaneous integrated boost

The Benefits of Inverse Planning



Sharp dose fall off
Improved OAR sparing

Need robust IGRT!

Let's Look at the Inverse Planning Process in Closer Detail...

Contouring → Additional Contouring → Field Setup → Optimisation → Dose Calculation → Plan Evaluation

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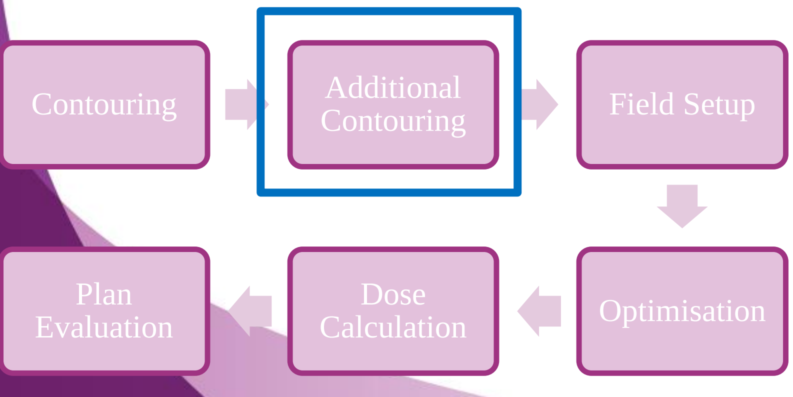
Additional Contouring

- Virtual contours used only in optimisation but ***not*** plan evaluation

- Ease the optimisation process/algorithm

- How and when you use them will depend on the case and also on your experience as a planner
    - ➢ Also what point of the optimisation process you are at for VMAT



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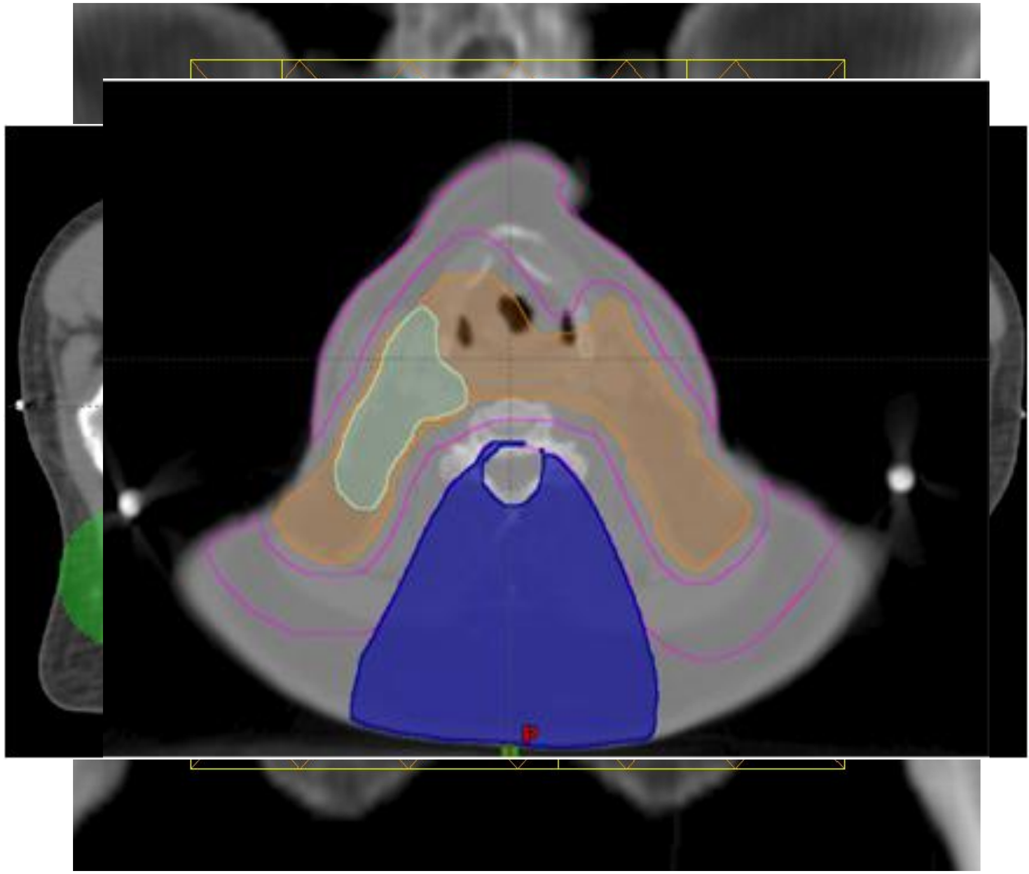
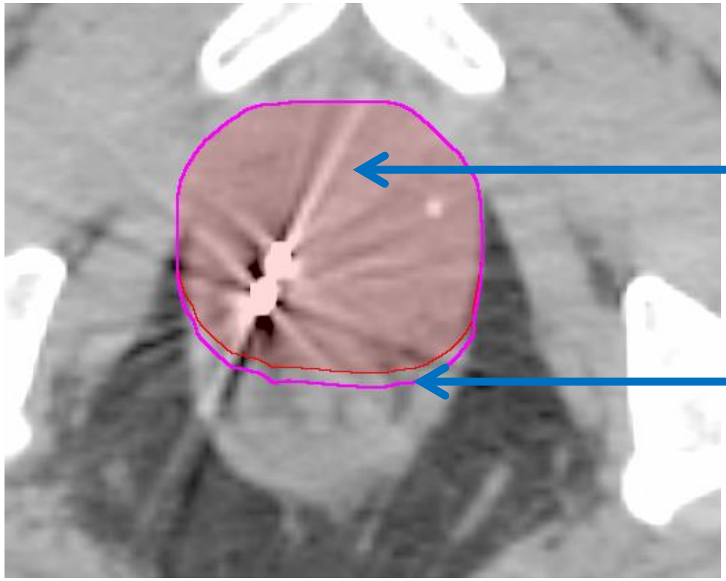
Additional Contouring

- Increase control over dose distribution
  - Dose escalate within a PTV
  - Dose fall off across a structure
  - Dose directly surrounding PTV
  - Dose dumping in healthy tissue



Additional Contouring

- Improve coverage of whole or partial target
  - ➢ We can’t manually adjust the MLC
  - ➢ Inverse planning is volume based planning
  - ➢ Can be “cold” on superior or inferior slices
  - ➢ Can be “cold” where there is a competition between structures
  - ➢ “IMRT PTV”



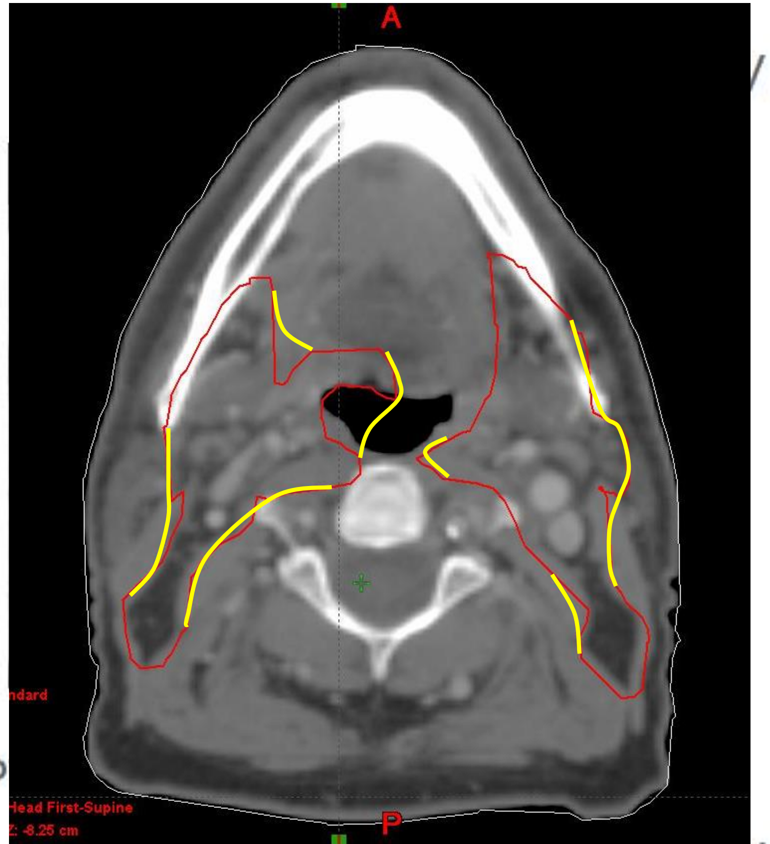
“True” PTV
Used for plan evaluation

“IMRT” PTV
Used for optimisation

Additional Contouring

- Lessen the competition between structures
  - OAR and target

- Smoother contours and gradients between slices of target structure

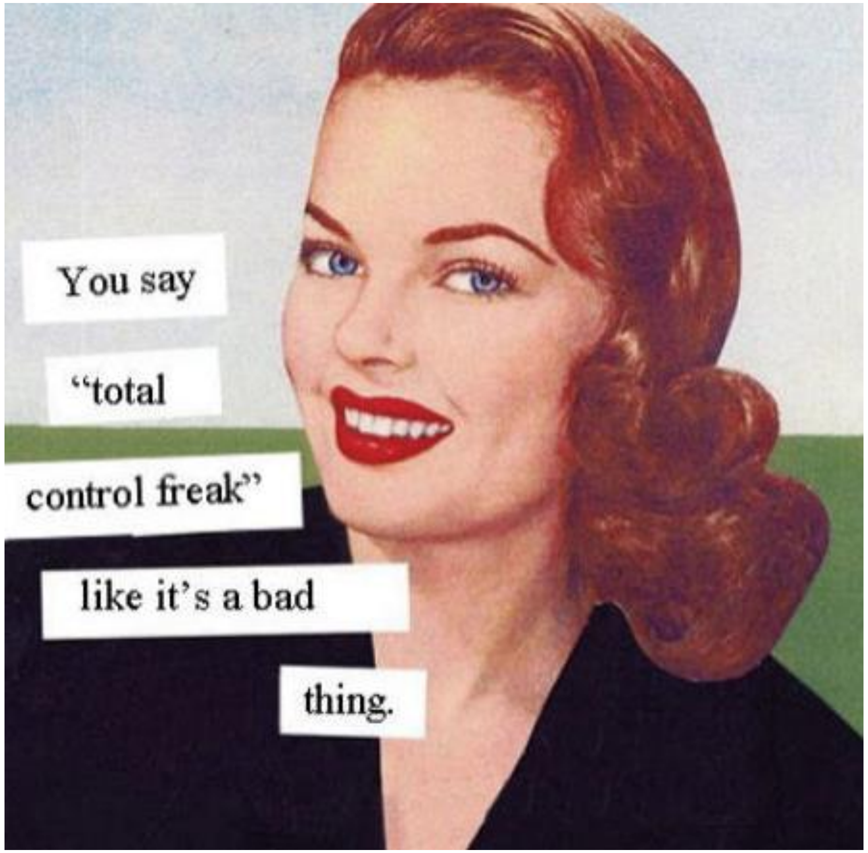


P

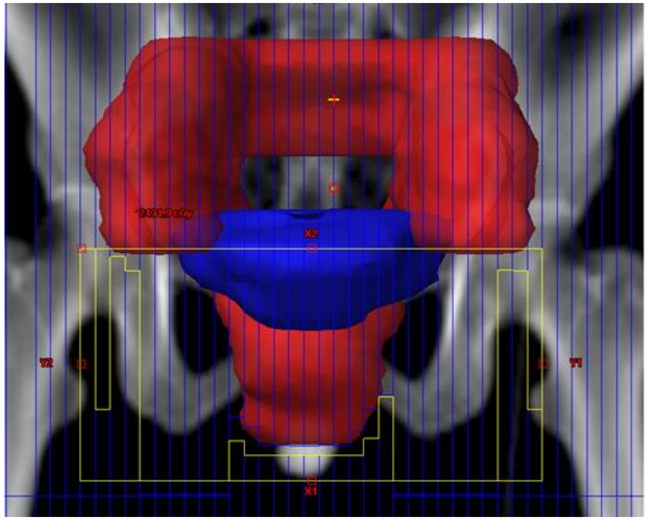
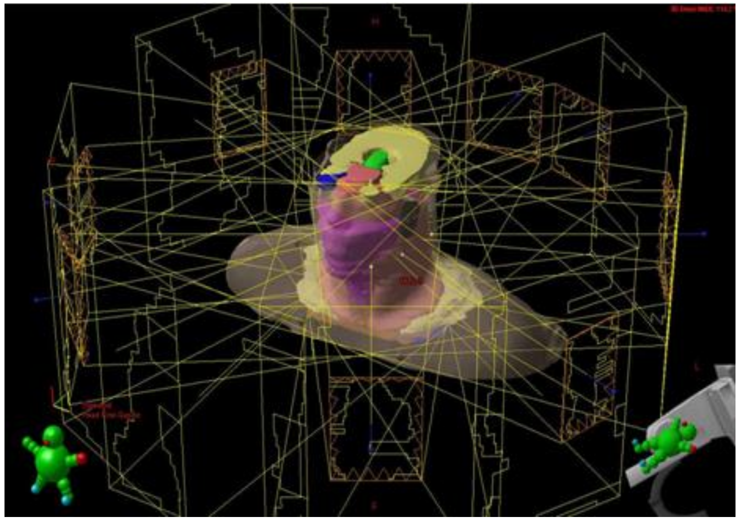
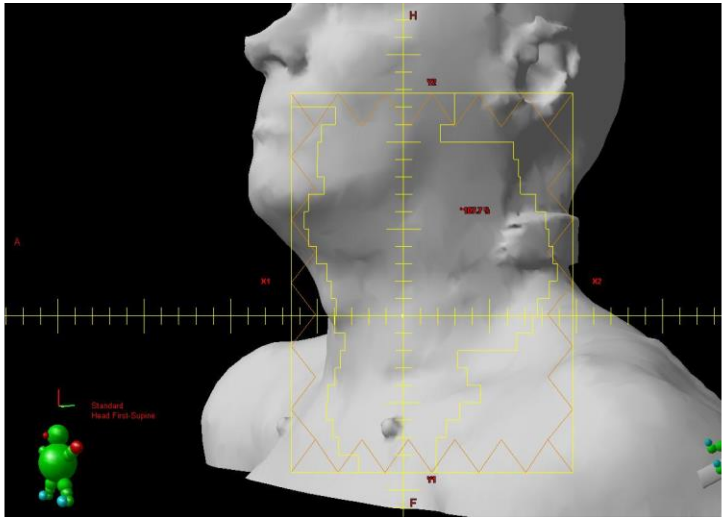
Bladder inside PTV

Field Setup

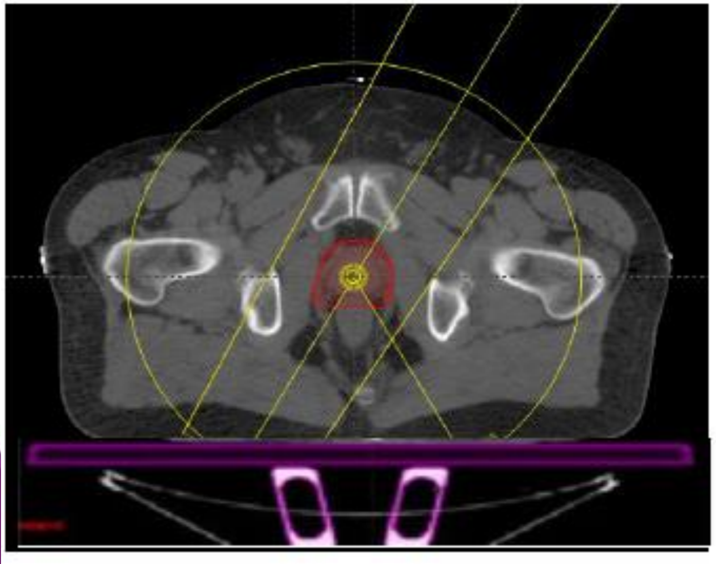
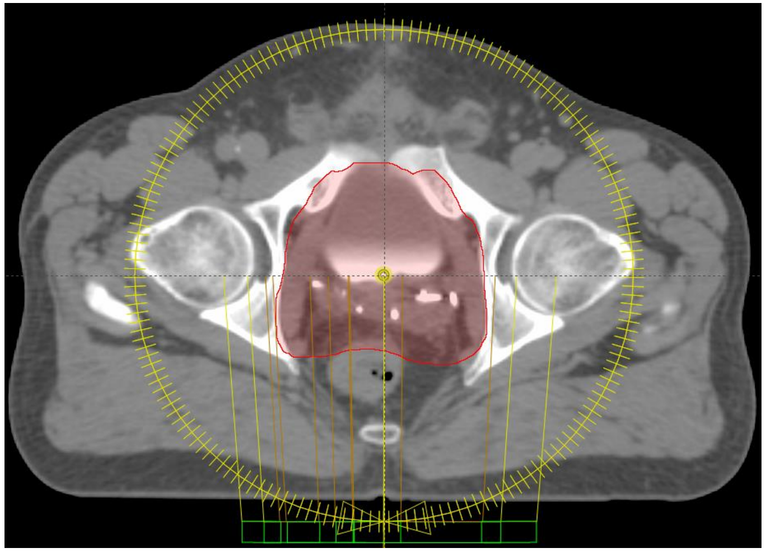
- Isocentre placement
- Beam arrangement
- Field size
- Collimator angle
- Dose rate



IMRT

VMAT

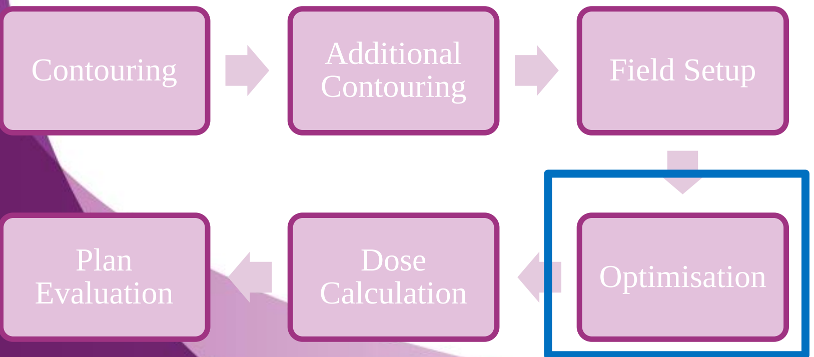
Shoulders:
Angle gantry to avoid
Angle couch to avoid
Fix jaw to avoid
(sup or ant/post)

Inverse Planning Optimisation

- Planner decides on required dose coverage with dose constraints for surrounding structures
    - ➢ Cost function algorithm

- Upper and lower dose limits are to be nominated
    - ➢ Target structures have both

- Planning systems allow for dose constraints to be specified
    - ➢ Either as a dose max, mean dose or as a %volume to receive a specified dose
    - ➢ Can have either a single point, a series of points or a line



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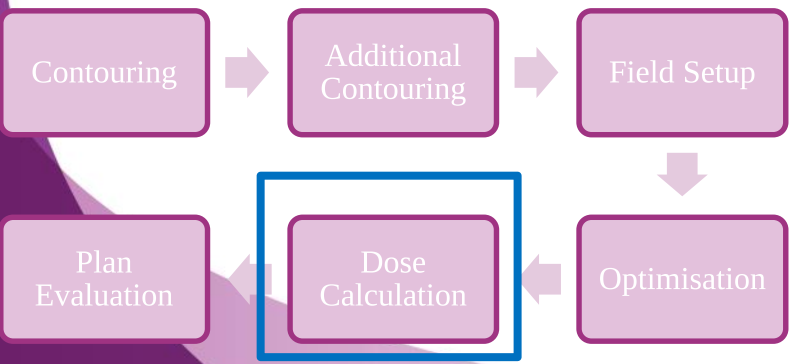
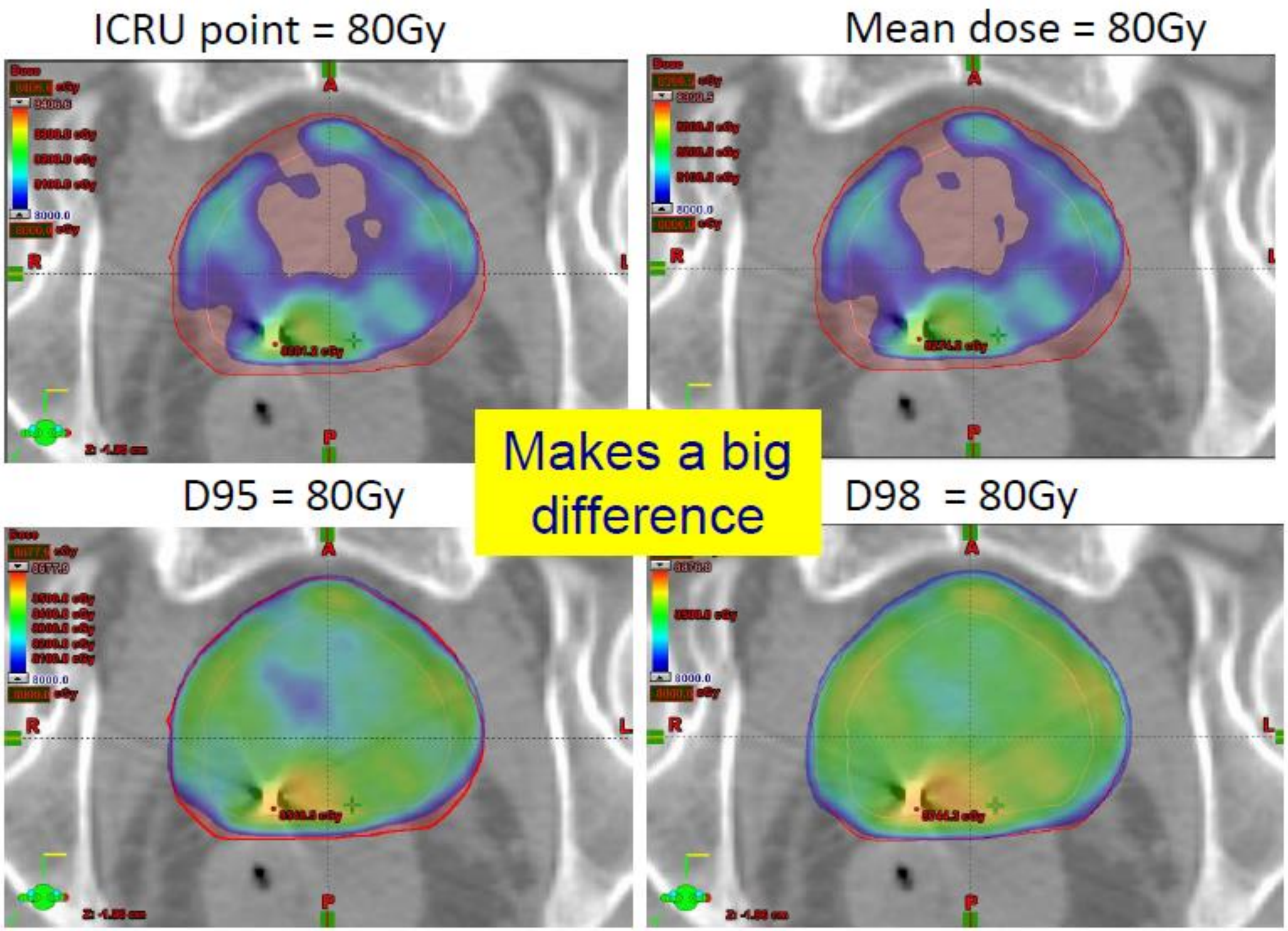
IMRT Dose Calculation

- The fluence maps are generated at the time of optimisation
- The leaf motion is then calculated to enable the delivery of this
- The 3D dose calculation is then carried out generating a dose distribution
- Note the subtle changes:
  - ➢ Fluence now reflected the deliverable values
  - ➢ The DVH is now based on AAA as opposed to PBC



Plan Normalisation

What happened to ICRU 83?



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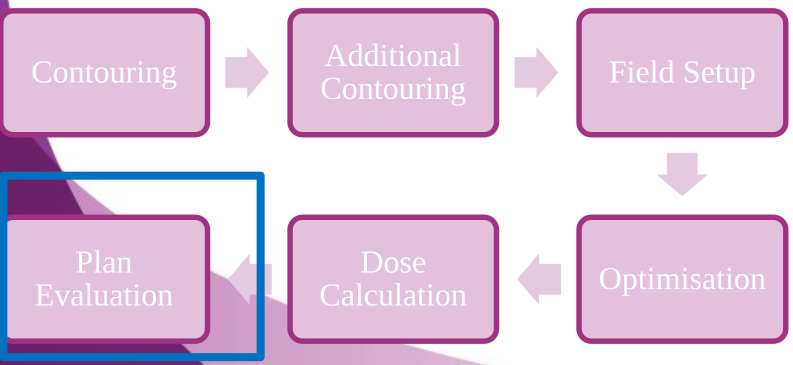
Plan Evaluation

- This is a crucial component of the planning process and should not be rushed or undervalued

- Target Coverage
- Target Conformity
- Target Homogeneity
- OAR doses
- Integral Dose
- Field arrangement used
- Fluence maps or segments for IMRT
- Monitor Units
- Treatment time



Plan Evaluation

- Select appropriate tools
  - ➢ Modern TPS are developed to make our life easier but are only as good as the user who is interpreting the information

- Qualitative
  - ➢ Visual inspection is vital
  - ➢ Clinical judgement

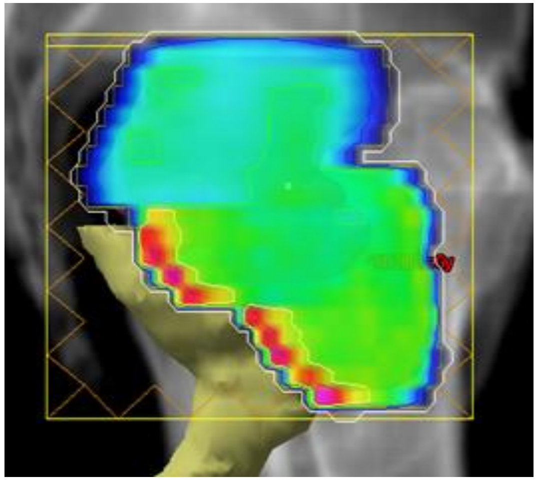
- Quantitative
  - ➢ ICRU 56, 62, 83
  - ➢ DVH
  - ➢ Conformity and homogeneity indices

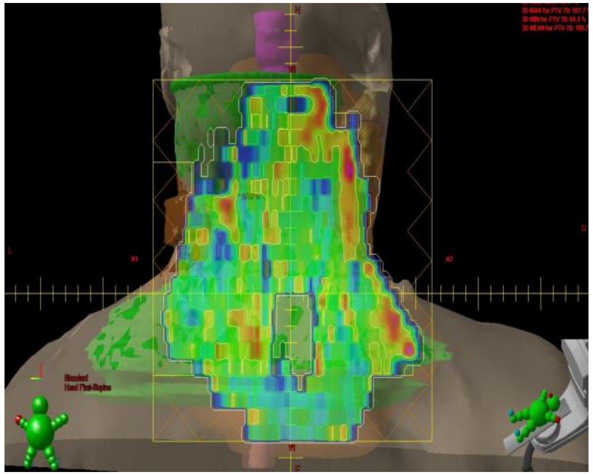
Revise ICRU!
You must know and use the correct terminology
You must know the main recommendations

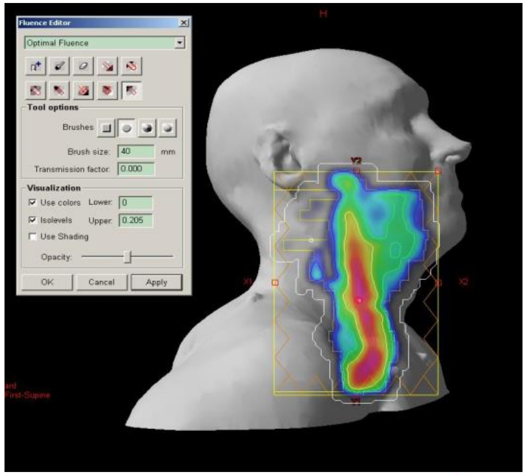
Plan Evaluation

- RTTs care about fluence maps too!

- What is level of modulation
- Is this necessary
- What impact does this have on the dose distribution
- What impact does this have on treatment delivery







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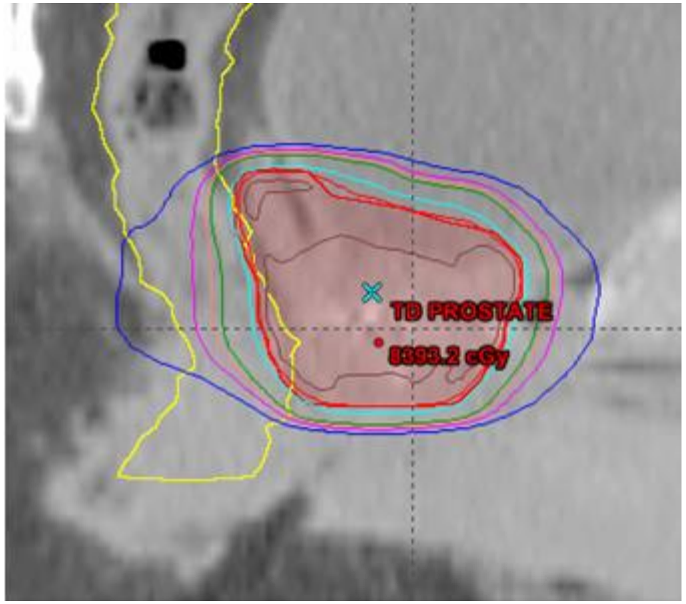
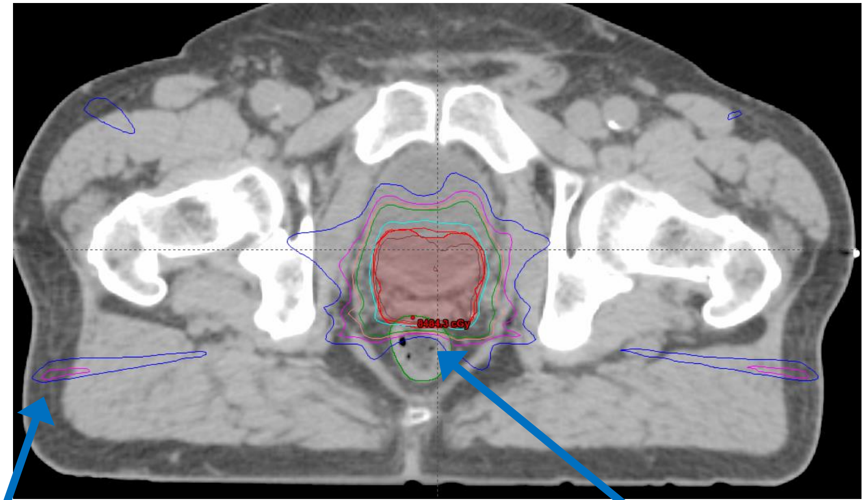
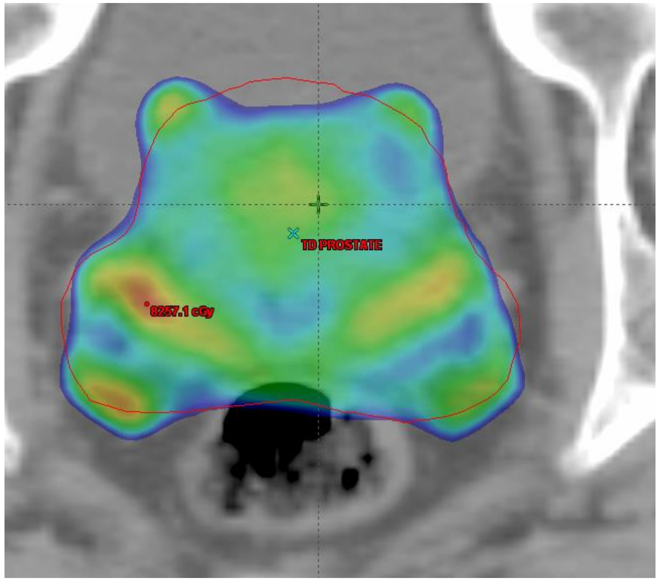
Plan Evaluation

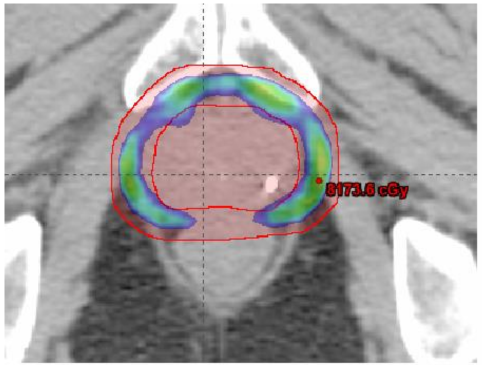


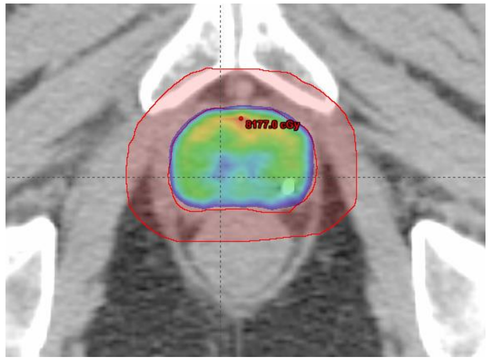


Lateral Hot Spot 50Gy

Max in Rectum







How To Improve a Bad Plan

- Beam Angles
  - ➢ Number and position
  - ➢ Bare in mind length of treatment

- Plan normalisation
  - ➢ Heat up or cool down the whole plan
  - ➢ Quick, does not require re calc

- Reoptimise
  - ➢ Think about what you are trying to achieve
  - ➢ Relax constraints if possible
  - ➢ Try to keep it simple

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Just Remember...

Planning is a collaborative and dynamic process

I want a better plan!

This is the best plan!

Advances in Treatment Planning: Is the "Evidence" There?

- Understanding the Literature and the Evidence

- Caution!
  - Small patient numbers
  - Retrospective in nature
  - Important to recognise fundamental differences in planning techniques between centres
    - Target dose and coverage stipulated
      - ICRU Pt or Volumetric
    - OAR constraints (protocol or department specific)
    - Beam energy
    - Number of fields/arcs
    - Planning system used
      - Sliding window vs. step and shoot IMRT

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Read the Literature Carefully!

An example from 3DCRT

Research | **Open Acce**

Optimal organ-sparing intensity-modulated radiation therapy (IMRT) regimen for the treatment of locally advanced anal canal carcinoma: a comparison of conventional and IMRT plans

Cathy Menkarios[1,2], David Azria*[2], Benoit Laliberté[1,2], Carmen Llacer Moscardo[2], Sophie Gourgou[3], Claire Lemanski[2], Jean-Bernard Dubois[2], Norbert Aillères[2] and Pascal Fenoglietto[2]

Address: [1]Département de Radio-Oncologie, Hôpital Maisonneuve-Rosemont, Montréal, Canada., [2]Département d'Oncologie Radiothérapie et de Radiophysique, CRLC Val d'Aurelle-Paul Lamarque, Montpellier, France. and [3]Unité de Biostatistiques, CRLC Val d'Aurelle-Paul Lamarque, Montpellier, France.

AP and PA fields, respectively. The radiation dose was prescribed to the PTV, such that 100% of the PTV received > 95% of the prescribed dose and that no region in the field received greater than 107% of the prescribed dose. Varia-

Good, that sounds like ICRU 50

All treatment plans showed adequate coverage of the target volume, with more than 95% of volume of PTV1 and PTV2 receiving greater than 95% of the prescribed dose.

Hang on a minute?!

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Read the Literature Carefully!

An example from IMRT

CLINICAL INVESTIGATION **Prostate**

ULTRA-HIGH DOSE (86.4 GY) IMRT FOR LOCALIZED PROSTATE CANCER: TOXICITY AND BIOCHEMICAL OUTCOMES

OREN CAHLON, M.D.,* MICHAEL J. ZELEFSKY, M.D.,* ALISON SHIPPY, B.A.,* HEATHER CHAN, B.A.,* ZVI FUKS, M.D.,* YOSHIYA YAMADA, M.D.,* MARGIE HUNT, M.S.,† STEVEN GREENSTEIN, B.A.,* AND HOWARD AMOLS, PH.D.†

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

METHODS AND MATERIALS

Between August 1997 and March 2004, 478 consecutive patients with localized prostate cancer were treated with definitive IMRT to a dose of 86.4Gy at the Memorial Sloan-Kettering Cancer Center.

dose. On average, this resulted in 87% of the PTV volume receiving the prescribed dose of 86.4 Gy or more (V100) (standard deviation 6.5%) and an average dose to 95% of the PTV (D95) of 83.1 Gy (standard deviation 2.1 Gy). PTV regions receiving less than the prescribed

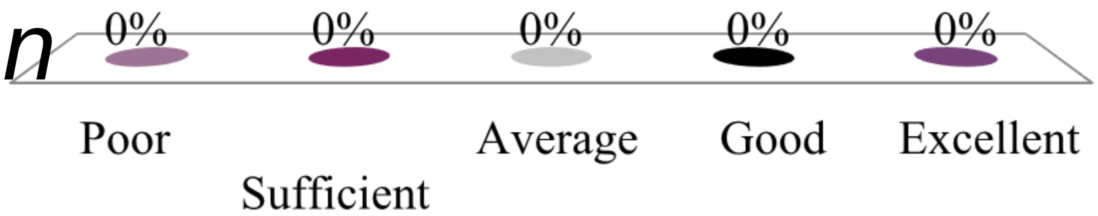
Take Home Messages

- Have an awareness of what to expect from your plan
- Despite the efforts of ICRU, inconsistencies in clinical practice and published literature still exist
- Encourage standardisation at a local level allowing for comparison with international practice
- Be guided by the literature
  - ➢ Almost all dosimetry papers will outline their planning process
  - ➢ Critical analysis is needed!

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



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Treatment Planning II

Liz Forde, MSc (RTT)
Assistant Professor
Discipline of Radiation Therapy
Trinity College Dublin

ARTT
Applied Radiation Therapy
Trinity Research Group

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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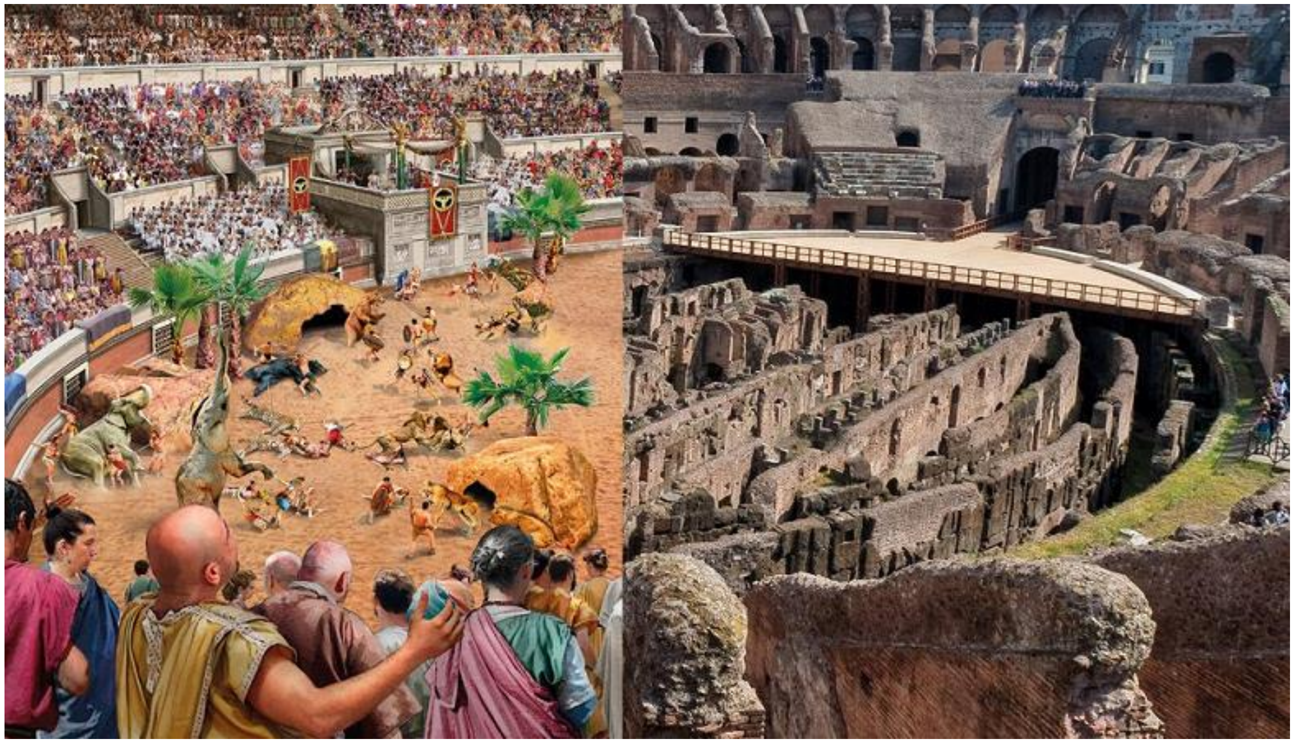
The Changing Landscape of Treatment Planning

1. Stereotactic planning
2. Isotoxic planning
3. Biological based planning
4. Adaptive planning
5. Automated planning



Stereotactic Planning

- The goal stereotactic RT is to deliver *very* high doses/fx to the target to induce maximum damage
  - “ablative” doses

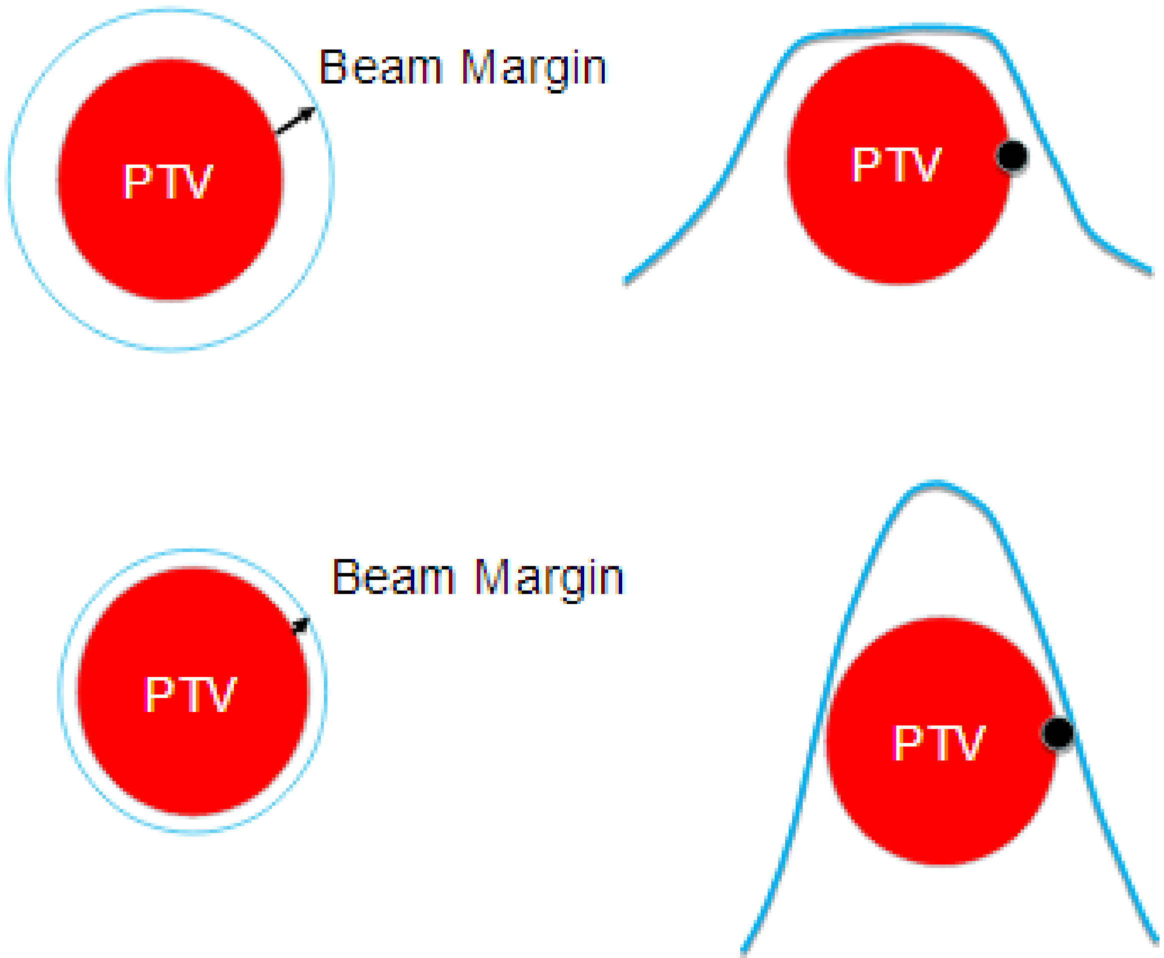
- Aim to minimise the volume of healthy tissue receiving a high dose per fraction
  - Dose to OARs is very important due to high dose/fx and increased risk of toxicity

- Traditional dose homogeneity is less of a concern
  - Up to 160% dose maximum is not uncommon

Stereotactic Planning

Standard approach

SBRT approach



Stereotactic Planning

- ICRU Report 91
- Level 2 Reporting as a minimum
- Level 3 Reporting for R&D
  - ➢ Software versions (P&T)
  - ➢ Integral dose
  - ➢ Confidence intervals
  - ➢ Biology based evaluation metrics

should be reported relative to the GTV (and this should be explicitly stated for clarity). However, in the planning process it may be useful to calculate them relative to the PTV. Only through more rigorous and uniform reporting of these parameters will it be possible to better associate these parameters with treatment complication.

For radiosurgery in the brain, extra parameters may be considered such as the dose gradient index, GI, defined as:

Journal of the International Commission on Radiation Units and Measurements, Volume 14, Issue 2, 1 December 2014, Pages 101–109, https://doi.org/10.1093/jicru/ndx010

Published: 25 July 2017

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7.3.1 Recommendation for Reporting at Level 2

Stereotactic Planning

Level 2 reporting should include the following items:

- Brief clinical history including description of the clinical examination, location, diagnostic technique used, histopathological evaluation if any, staging, prior treatment, performance status.
- Treatment intent (*i.e.*, palliative, curative)
- Patient simulation (*i.e.*, immobilization devices, accessories, planning image acquisition, and protocols)
- Target volumes and OAR selection and delineation
  - (1) Target volumes
    - (i) GTV (cm^3)
    - (ii) CTV (cm^3)
    - (iii) ITV, PTV (cm^3)
  - (2) Normal tissues
    - (i) OAR (cm^3)
    - (ii) PRV (cm^3)
    - (iii) RVR (cm^3)
- Planning aims and dose–volume constraints
- Description of treatment planning system (*i.e.*, algorithm, voxel size, calculation dose grid, type-A uncertainty for MC-based systems)
- Prescription
- Patient-specific QA
- Delivery (*i.e.*, treatment unit and energy, image verification device, and data set)
- Dose reporting
  - (1) Dose in PTV and, if applicable in CTV and/or GTV
  - (2) Dose in OAR and PRV.

For dose reporting (Item 10), the present report recommends the following metrics:

- PTV median absorbed dose, $D_{50\,\%}$: As this report recommends a CTV be defined for each case, the $D_{50\,\%}$ can be also reported for CTV. In the specific case of peripheral lung lesions, where the dose distribution is strongly affected by tissue density variations, a dose to a target, which does not include uninvolved lung parenchyma ($D_{50\,\%}$ (GTV/CTV)), should be systematically reported.
- The SRT near-maximum dose, $D_{\text{near-max}}$: For PTV V larger than or equal to 2 cm^3, the volume near-max represents 2 % of the PTV, as recommended in ICRU Report 83 ($D_{2\,\%}$). For PTV V of less than 2 cm^3, near-max is an absolute volume of 35 mm^3, in which case D_{35mm^3} is reported.
- The SRT near-minimum dose, $D_{\text{near-min}}$: For PTV V larger or equal than 2 cm^3, the volume near-min represents 98 % of the PTV, as recommended in ICRU Report 83 ($D_{98\,\%}$). For PTV V of less than 2 cm^3, near-min is an absolute volume of 35 mm^3, in which case D_{V-35mm^3} is reported.

Homogeneity and Conformity is also discussed

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“**Isotoxic**” Treatment Planning

- Pioneered by MAASTRO

- Moves away from the “one size fits all” approach for dose prescription
  - ➢ Dose escalation is based on patient specific OAR DVH results

- Dose escalate the PTV until the OARs reach their tolerance

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Isotoxic Planning

- The risk of toxicity is standardised, not the prescription dose

Mean lung dose = 18Gy

Prescribed dose = 79Gy

Mean lung dose = 18Gy

Prescribed dose = 66Gy

Isotoxic Planning

- Most data for this approach comes from lung cancer with Spinal Cord and MLD as the toxic endpoints

- Why lung?
  - ➢ Radiation dose improves both local control and survival (Kong et al., 2005)

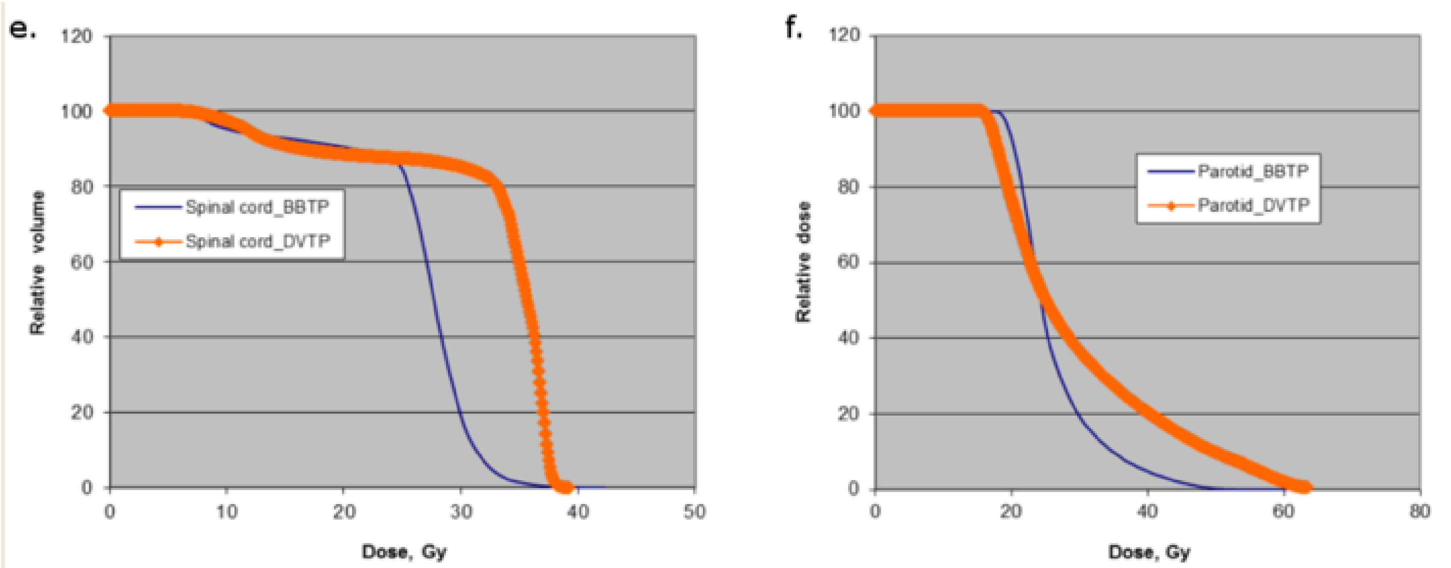
- Future work identified by Warren et al.,
  - ➢ Could we escalate just a specific portion of the PTV
  - ➢ Modulated techniques allow for multiple dose levels within a target

Biologically Based Planning

- Vendor Solutions to support advanced planning based on radiobiological models
  - ➢ Optimisation also uses the TCP and NTCP

- Combines physical and biological criteria

- Plan evaluation includes standard DVH as well as add on



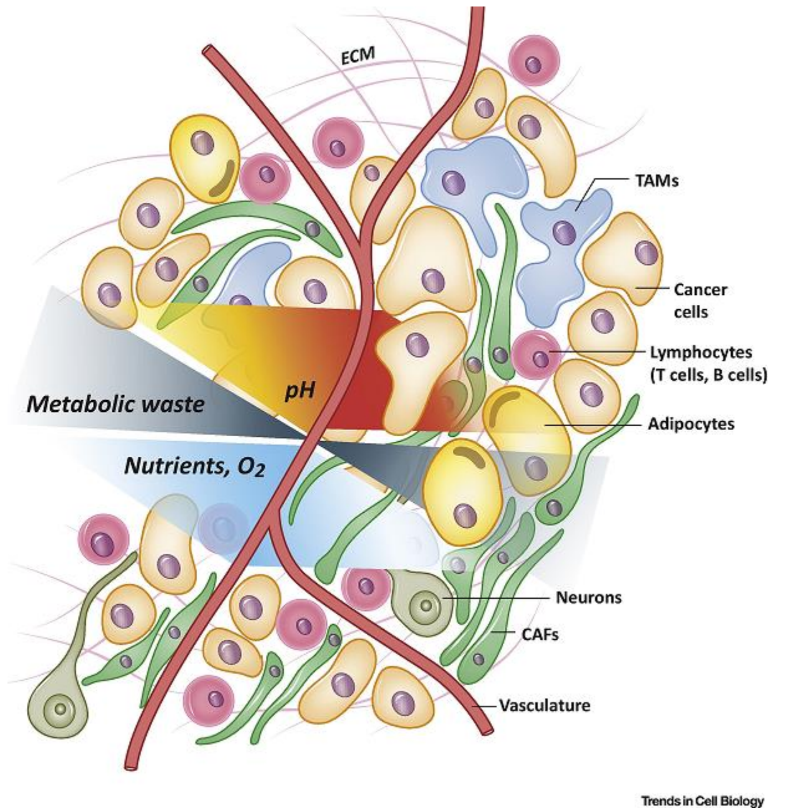
Kan M et al., The use of biologically related model (Eclipse) for the intensity modulated radiation therapy planning of nasopharyngeal carcinomas. 2014 https://doi.org/10.1371/journal.pone.0112229

Dose Painting Approach

- Tumours are heterogeneous in nature
  - ➢ Cell type
  - ➢ Metabolic activity

- Some regions are more hypoxic than others indicating greater radioresistance

- So how do we identify these hypoxic regions?



Dose Painting Approach

- **Functional Imaging**

- Range of options all providing different information specific to tumour type
  - ➢ Diffusion weighted MRI
  - ➢ FMISO PET
  - ➢ FDG PET

- FDG uptake is related to metabolic activity (hypoxia)

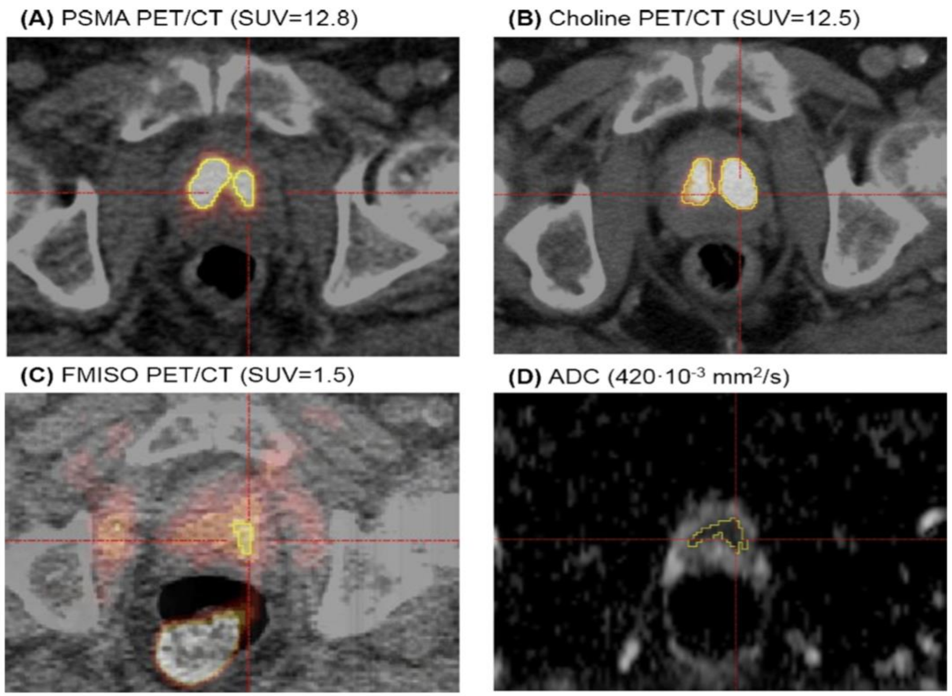


Figure 1. Screenshots of the same anatomical position of PET/CTs with tracer accumulation in the prostate for PSMA (A), Choline (B) and FMISO (C) and the ADC map derived from DW-MRI (D). Additionally, in each image the PET- or ADC-positive contour is shown. Those contours were defined automatically using a threshold of 50% SUV_{max} for PSMA and Choline PET/CT, TMR = 1.4 for FMISO PET/CT and 30% ADC_{min} for DW-MRI.

Biological Target Volume

- A **biological target volume** is defined based on functional rather than anatomical imaging.
- The BTV is often a sub volume within a traditional GTV or CTV that has been anatomically delineated.
- It can represent an area of increased activity within the tumour volume or an area of presumed resistance where by we want to increase the dose to this region.

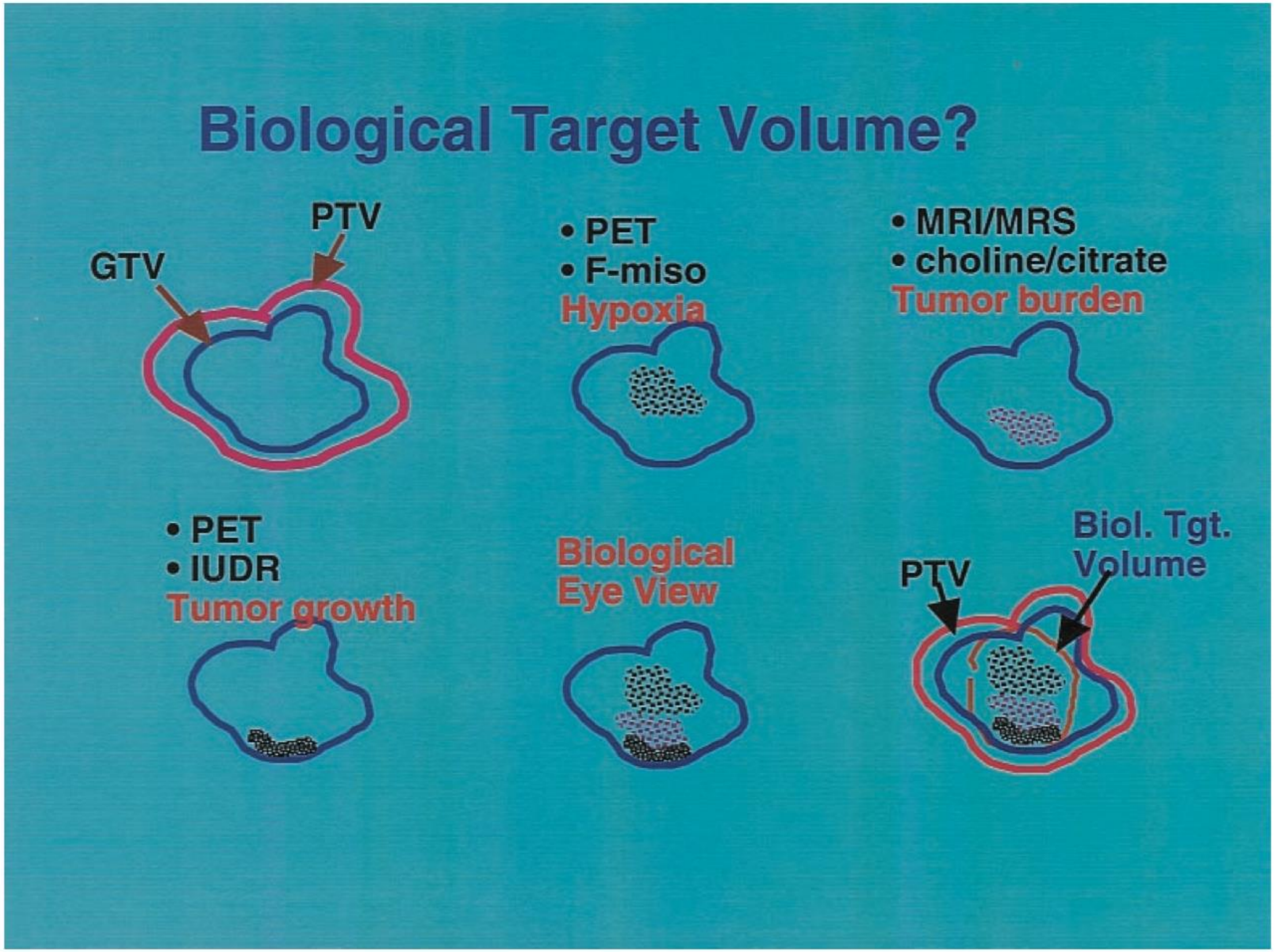


Fig. 2. An idealized schematic illustrating the concept of biological target volume (BTV). Whereas at present the target volume is characterized by the concepts of GTV, CTV, and PTV, biological images as depicted in Fig. 2 may provide information for defining the BTV to improve dose targeting to certain regions of the target volume. For example, regions of low pO_2 level may be derived from PET-^{18}F-misonidazole study, high tumor burden from MRI/MRS data of choline/citrate ratio, and high proliferation from PET-^{124}IUdR measurement.

TRO
ool

Slide Credit: Bruno Speleers

Dose Painting Approach

- First step towards intentional dose heterogeneity

- Dose Painting – a concept of intentionally non uniform radiation dose prescription and delivery based on (multimodality) biologic imaging

Acta Oncologica 26 (1987) Fasc. 5

FROM THE DEPARTMENT OF RADIATION PHYSICS, KAROLINSKA INSTITUTET AND THE UNIVERSITY OF STOCKHOLM, S-10401 STOCKHOLM, AND THE DEPARTMENT OF HOSPITAL PHYSICS, SÖDERSJUKHUSET, S-10064 STOCKHOLM, SWEDEN.

OPTIMAL DOSE DISTRIBUTION FOR ERADICATION OF HETEROGENEOUS TUMORS

A. BRAHME and A.-K. ÅGREN

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Dose Painting Approach

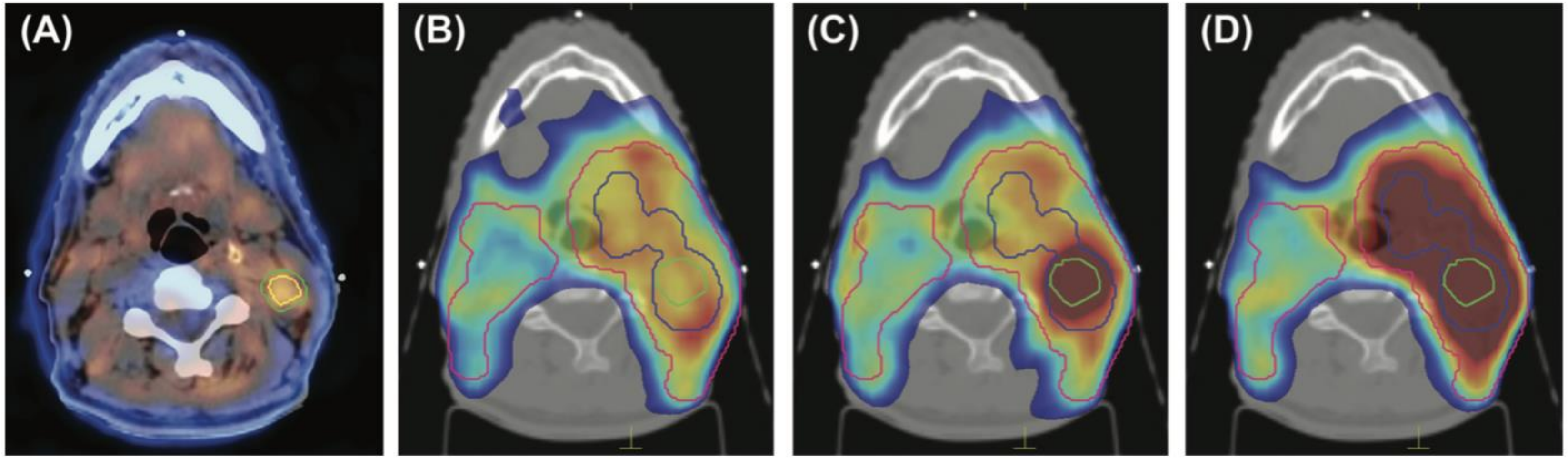

Figure 1. The FMISO PET/CT scan of a patient with a T3N2b oropharyngeal squamous cell carcinoma is shown (A). The GTVH, PTVH, PTV3 and PTV1 are outlined in yellow, green, blue and red, respectively. The dose distributions for the STD plan (B), the HDP plan (C) and the UDE plan (D) are demonstrated using 'colorwash' with red indicating higher doses and blue indicating lower doses.

The Price of Target Homogeneity

- Previous ICRU reports recommended that the dose values in the PTV be confined within 95% and 107% of the prescribed dose.
- With IMRT, these constraints may be confining if the avoidance of OARs is more important than target dose homogeneity

914 Craft et al. International Journal of Radiation Oncology • Biology • Physics

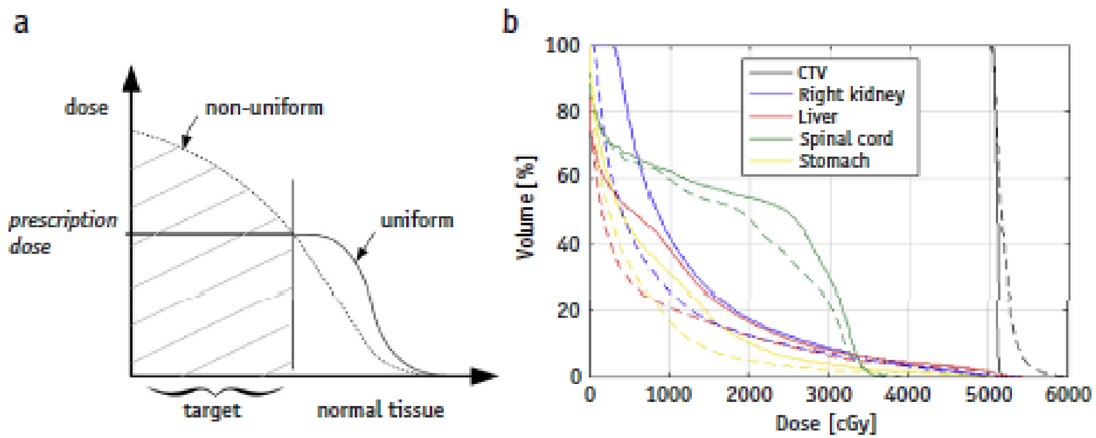

Fig. 1. "More dose in the tumor can mean less dose in the healthy tissue." Demonstrations showing that forcing target dose uniformity can result in increased organ at risk doses. Panel a) is a schematic illustration of the concept and panel b) demonstrates it for a clinical plan. The hot plan is plotted with dashed lines and the clinical plan (striving for a uniform target dose) with solid lines. *Abbreviation:* CTV = clinical target volume.

"No data have demonstrated that uniform doses are radiobiologically preferable in general"

Craft et al., 2016 IJROBP

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Image courtesy of Bruno Speleers

Dose Painting Approach

- New challenges to ICRU 83

New concept: biologic conformity

$$Q_p = \frac{D_{obtained}}{D_{prescribed}}$$

$$QF = \frac{1}{n}\sum_p \left|Q_p - 1\right|$$

$D_{obtained}$: dose obtained by plan optimization

$D_{prescribed}$: dose calculated in every point p randomly seeded in the dose-painted target volume in total n points

In an ideal plan, $Q_p = 1$

QF-factor ≤ 0.05 or 5%

Vanderstraeten B, et al. *Radiother Oncol* 2006;79:249-58.

Stability of BTV throughout RT

- Consideration must be given to the impact that the treatment delivery will have on the biology of the tumour and its micro-environment.

- With our GTV we can monitor clear changes to volume on our daily imaging however BTVs can also change and we may need to introduce *longitudinal functional imaging* to evaluate this.

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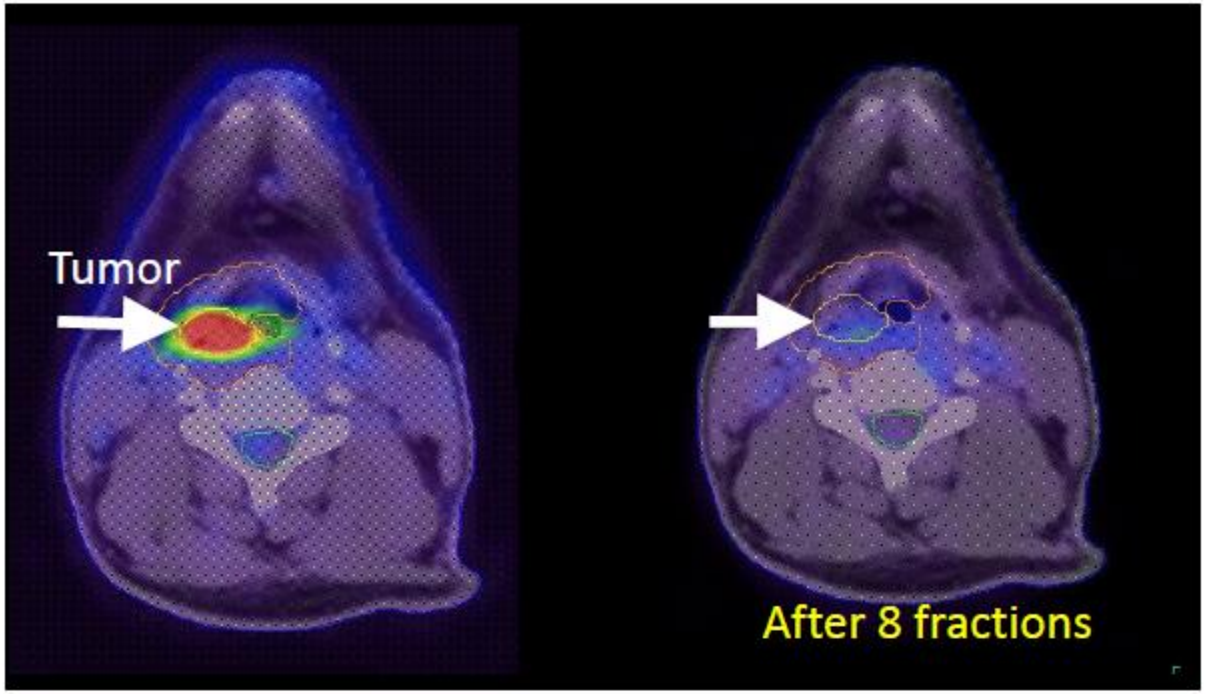
Image courtesy of Bruno Speleers

Stability of BTV throughout RT

- Procedure for biological based ART is cumbersome and resource demanding



Decrease in FDG-uptake by the tumor during the 2nd week of fractionated radiotherapy.

Adapting the FDG-PET based dose-painted target volume in the 1st half of treatment?

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Adaptive Radiotherapy

- Definition: “Adaptive radiotherapy involves changes to the radiotherapy plan during treatment on the basis of patient specific observations that were not taken into account during initial planning” *(Gregoire et al., 2012)*

- Incorporates systematic measurements of treatment variations into a closed-loop RT treatment process

- Provides feedback to re-optimise the treatment plan early on during the fractionated course of RT

- Delivers treatment that is customised to the **daily** patient target volumes

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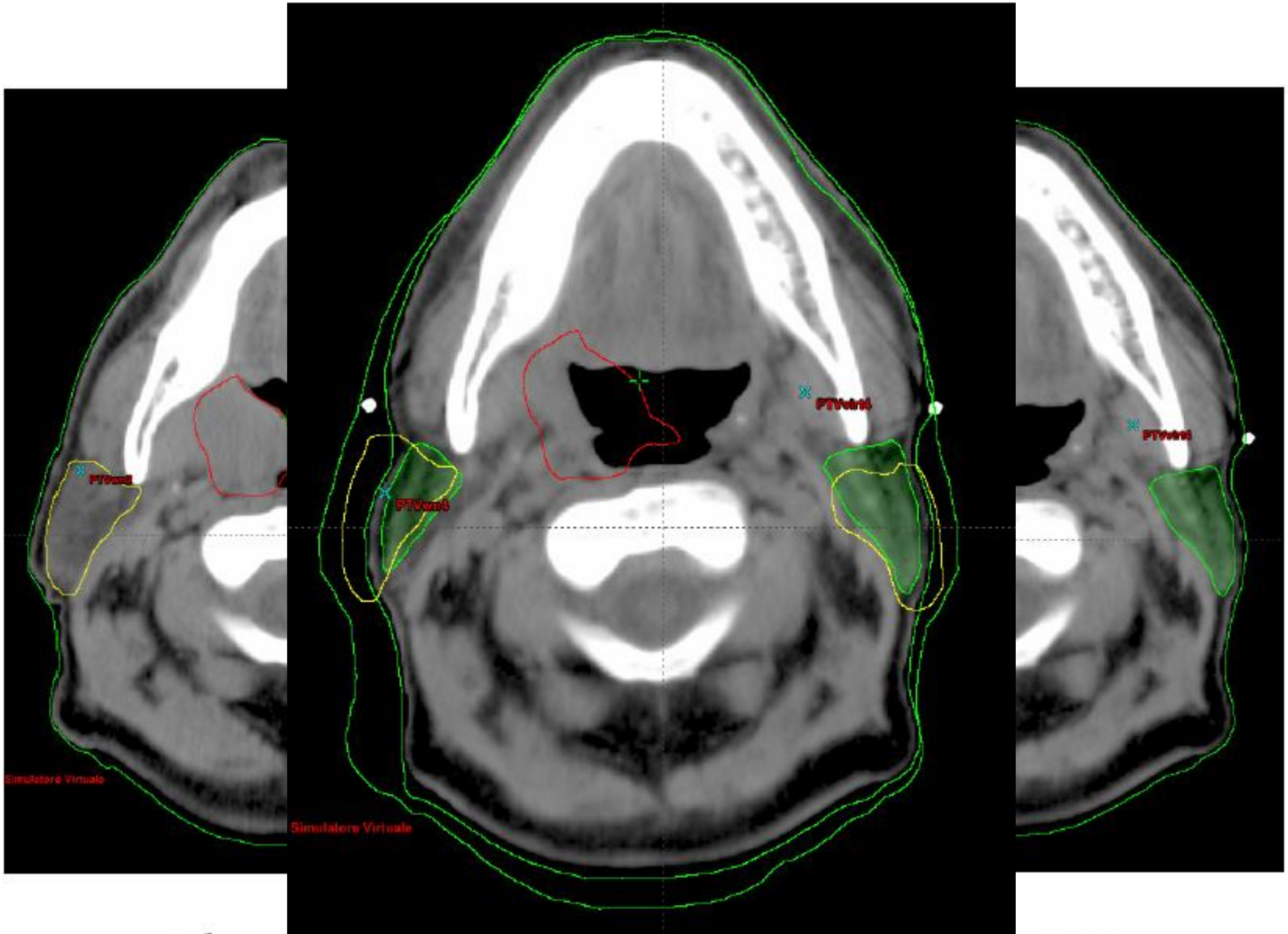
Principles of ART

- Can be adapting to changing geometry or changing geometry and delivered dose

- Approaches:
  - Completely Online
  - Library of Plans
  - Offline
    - Composite CTV at treatment initiation
    - Scheduled replan
    - Unsceduled replan

Slide courtesy of Michelle Leech

Adapting Planning on CT

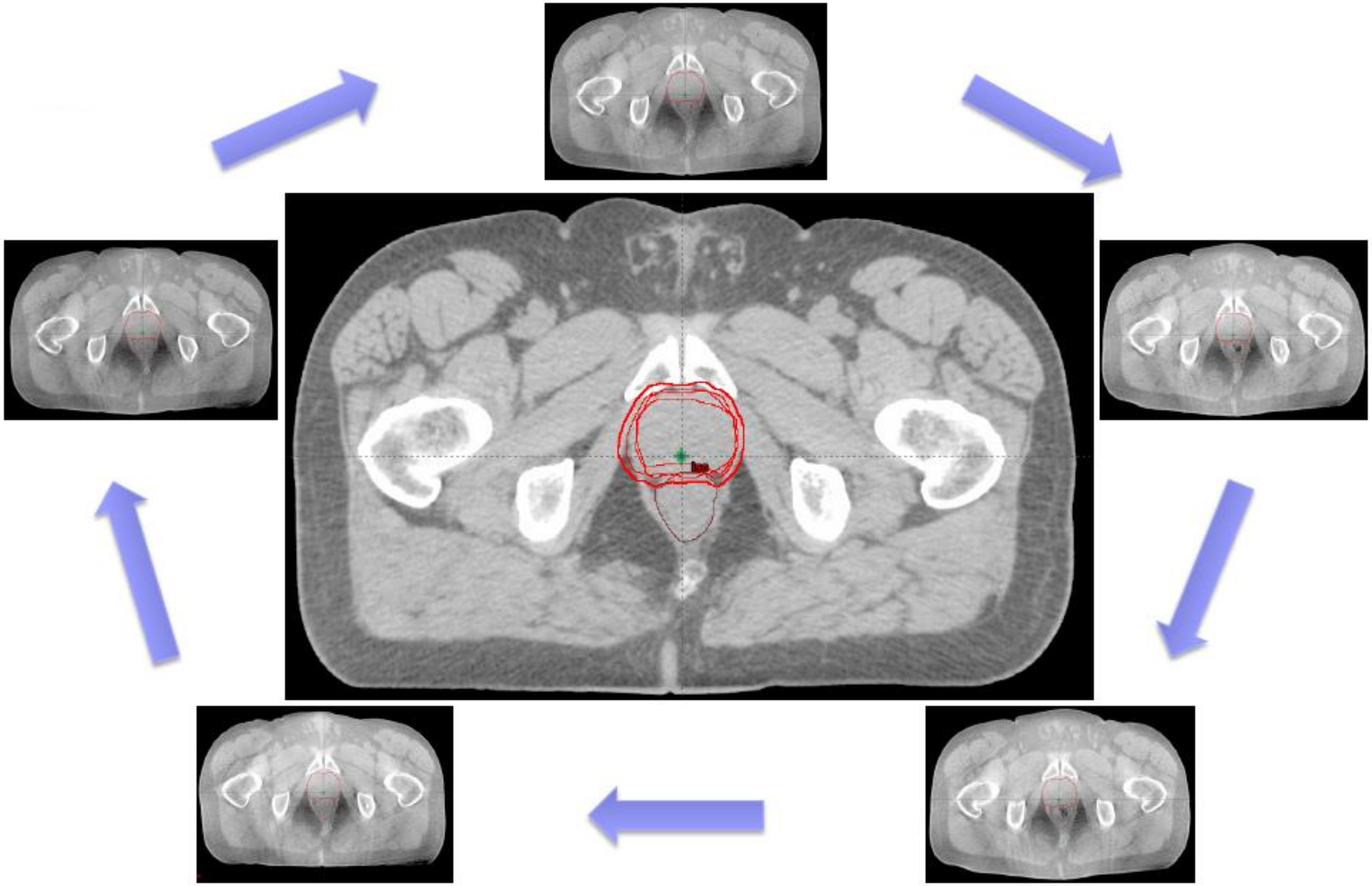


Planning CT

New CT

Slide courtesy of Michelle Leech

Adaptive Planning Based on CBCT 1



Adaptive Planning Based on CBCT 2

- Recalculation of planned dose using CBCT

- Are HU on CBCTs accurate?
  - Some conflicting evidence in the literature
  - Depends on the quality of your CBCT

- Options to overcome these uncertainties:
  - Pixel correction technique
    - CT numbers from conventional CT are applied to CBCT
  - Deformable registration
    - Deform planning CT to the CBCT to calculate “dose of the day”
    - This is a move towards “online” ART

Be Careful of Potential Limitations!

Slide courtesy of Michelle Leech

Geometric accuracy of bladder plan libraries

- A plan library strategy does not necessarily **guarantee** geometric accuracy
  - Risk of geographical miss due to intra-fractional bladder filling in 6 directions (Murthy, 2011)
  - No suitable plan in plan libraries (Foroudi, 2011, Lalondrelle 2011, Tuomikoski 2011, Gronborg 2015, Vestergaard 2014)
  - Confusion in plan selection (Tuomikoski 2011, Meijer 2012)
  - Inappropriate plan selection (Foroudi 2014, Meijer 2012)

Slide courtesy of Michelle Leech

Logistics of implementation of plan libraries

- ART is not currently feasible for **all** clinical departments
  - Interobserver variability in plan choice post-education (Kuyumcian et al 2012, Hutton et al 2013)
  - Availability of technology may hinder ART implementation (Hutton et al 2013, Murthy et al 2011, Meijer et al 2012)
  - Additional education: Cost and Time (MacDonald et al 2013, Lalondrelle 2013, Meijer et al 2012, Wright et al 2008)
  - Resource implications on daily workflow (Burridge et al 2006, Hutton et al 2013, Wright et al 2008)

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Automated Planning

- Planners! Let's not panic! You are still loved!

- Advantages:
  - ➢ Improved uniformity
  - ➢ Plan quality is less dependant on planners experience
  - ➢ Faster generation of plans
  - ➢ Free up planners time for other tasks and research

TUESDAY 24 APRIL 2018

	ROOM 116	ROOM 111	ROOM 120-121	ROOM 117	ROOM 113-114	ROOM 112	ROOM 115	ROOM 129-130
	SYMPOSIUM	SYMPOSIUM	SYMPOSIUM	SYMPOSIUM	DEBATE	JOINT SYMPOSIUM	SYMPOSIUM	DEBATE
11:00 - 12:15	Implications of the ageing population for radiation oncology	Salvage prostate radiotherapy	Radiation induced senescence	Immunotherapy	This house believes that stereotactic radiosurgery will replace whole brain radiotherapy in patients with ten brain metastases	*ESTRO-EFOMP* CBTC in radiotherapy: Improving and sharing best practice	Dose painting – from bench to bed(?)	Autoplanning, is there still a bright future for RTTs after automation?

12:20 - 13:20: CLOSING DEBATE This house believes that innovative radiotherapy is superior to innovative drugs to maximise value in cancer care - ROOM 112

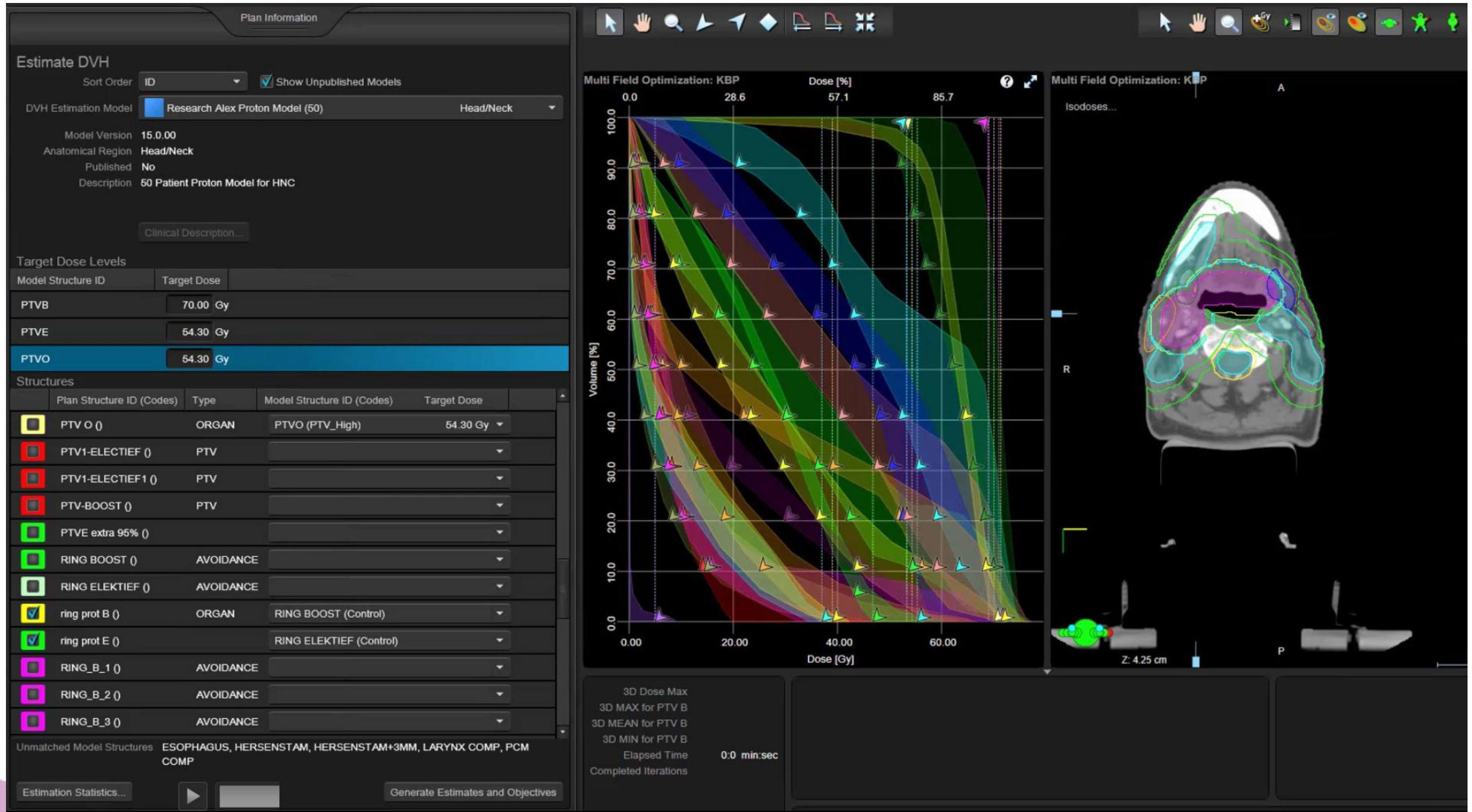
Automated Planning: Basic Class Solutions

- Range of treatment sites
  - Whole brain w/ hippocampal sparing
  - Post prostatectomy
  - Spine SBRT

- Tested solution across difference vendor TPS (Huang et al., 2013)
- Tested across different VMAT algorithms (Forde et al., 2014)
- Tested across different planners experience (Weksberg et al., 2012)

- All demonstrate viable class solutions

Automated Planning: Vendor Solutions



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Automated Planning: “In House” Solutions

Erasmus MC

Patient care | Research | Education | About us

↳ Radiotherapy

... / ... / ... / ... / Projects / Automated treatment plan generation

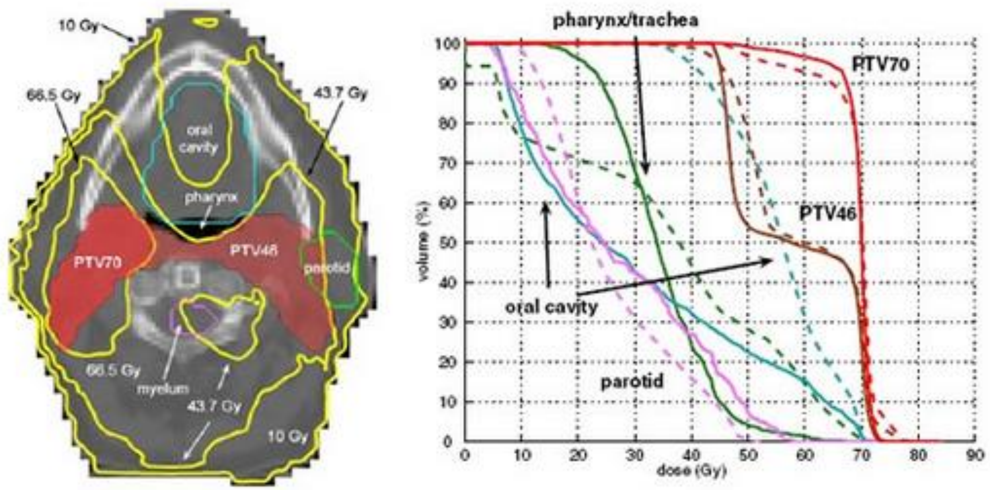
Automated treatment plan generation

- Organization
- Research
- Education
- Vacancies
- Erasmus MC Cancer Institute

Research aimed at development, clinical implementation, and clinical evaluation of new algorithms for treatment plan generation.

Scope and outline

The research aims at development, clinical implementation, and clinical evaluation of new algorithms for treatment plan generation. Main research lines are beam angle optimization (developed algorithm: ‘Cycle’), inclusion of geometrical uncertainties in inverse planning, and multi-criteria optimization. Part of the research is done in collaboration with Delft University of Technology (Prof. dr. A.W. Heemink, Dr. M. Keijzer).



Multi-criteria optimized IMRT treatment plan for an exceptionally difficult head and neck case. Left figure shows isodose lines, right figure compares the plan generated with multi-criteria optimization (solid lines) with the clinically applied IMRT plan (dashed lines). (Breedveld et al. Phys Med Biol. 2007; 52(20): 6339-53).

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:hool

What Will Planning Look Like in the Future?

- Will continue to increase in complexity
  - Biological optimisation
    - Continued integration of radiobiology
  - ART and personalised approach based on Radiomics based analysis of pre treatment and during treatment imaging

- ***Radiomics*** is the extraction of quantitative imaging features that can be combined with clinical data

- Will move from a separate planning room to the linac
  - MRI linac and MRI based dose calculation
  - Online reoptimisation
  - *Online* ART

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Take Home Messages

- The integration of radiobiology continues to strengthen
  - Collaboration is key
- Don’t be afraid of automation – this will simply change our practice
- Roles and responsibilities of ***all*** RTTs is changing
- Standardisation in reporting will aid in mass data collection and comparisson

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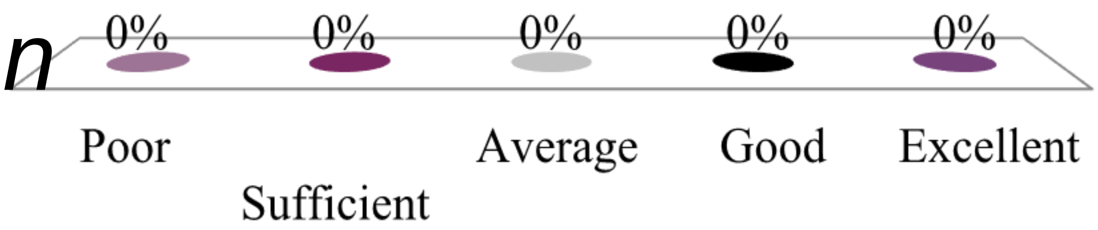
Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written in Survey Monkey



Clinical rationale for image-guided radiation therapy (IGRT)

ESTRO School

Jose Lopez, M.D., Ph.D
Radiation Oncology
University Hospital Virgen del Rocio
Seville, Spain

Advanced skills in modern radiotherapy

Time challenge

15:45pm 16:45pm 9:45am 21:45pm 1:45am

Italy Turk/Jor US Hong Kong NZ

Learning Objectives (IGRT)

- Learn the **clinical rationale** for IGRT
  Why we should do it
- Learn the **challenges** in achieving **precision and accuracy**
- Understand the **benefits and limitations** of IGRT
- Learn the **evidence** that supports the use of IGRT

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Wikipedia

- IGRT is the process of frequent **two and three-dimensional imaging**, during a course of RT, **utilizing the imaging coordinates**.

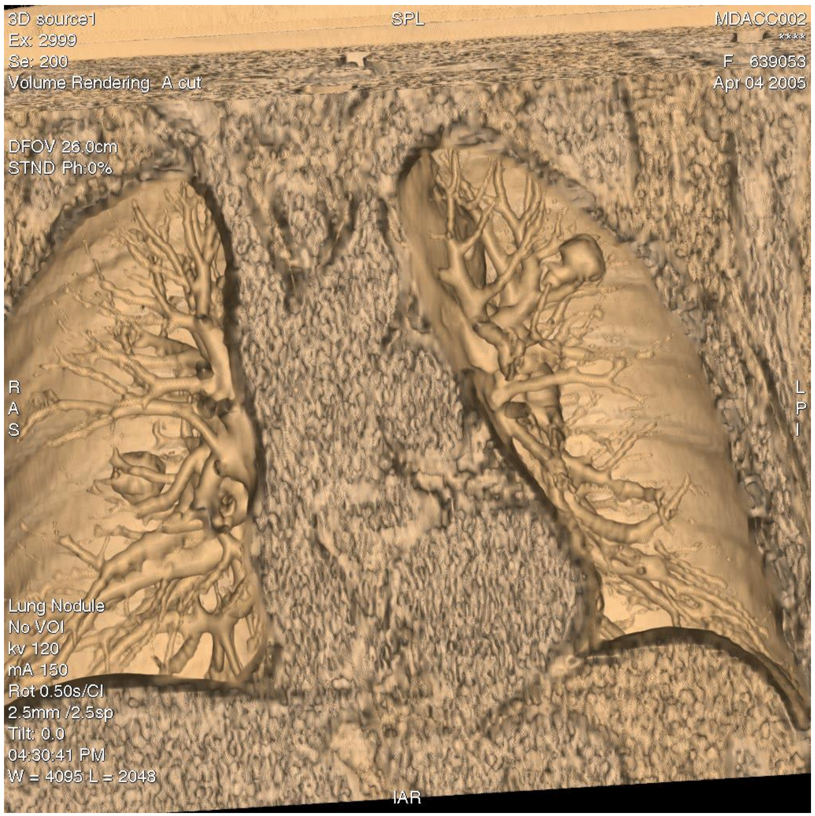
- The patient is localized in the treatment room in the **same position as planned** from the reference imaging dataset.

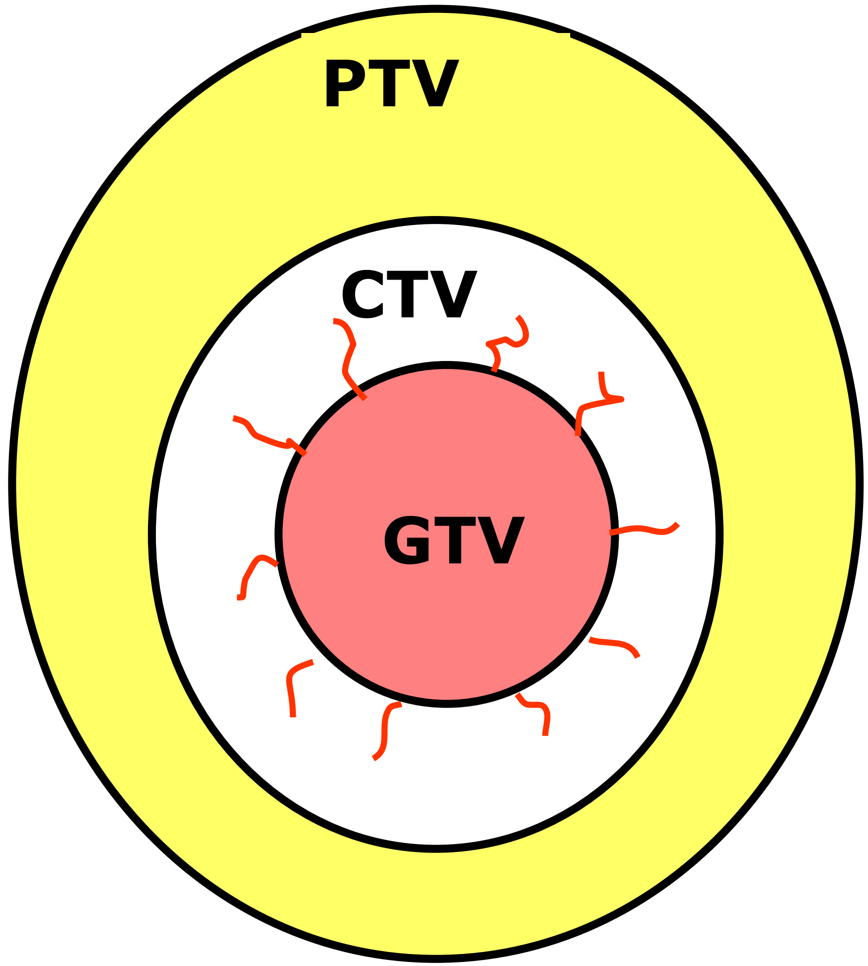
- An example of IGRT would include:

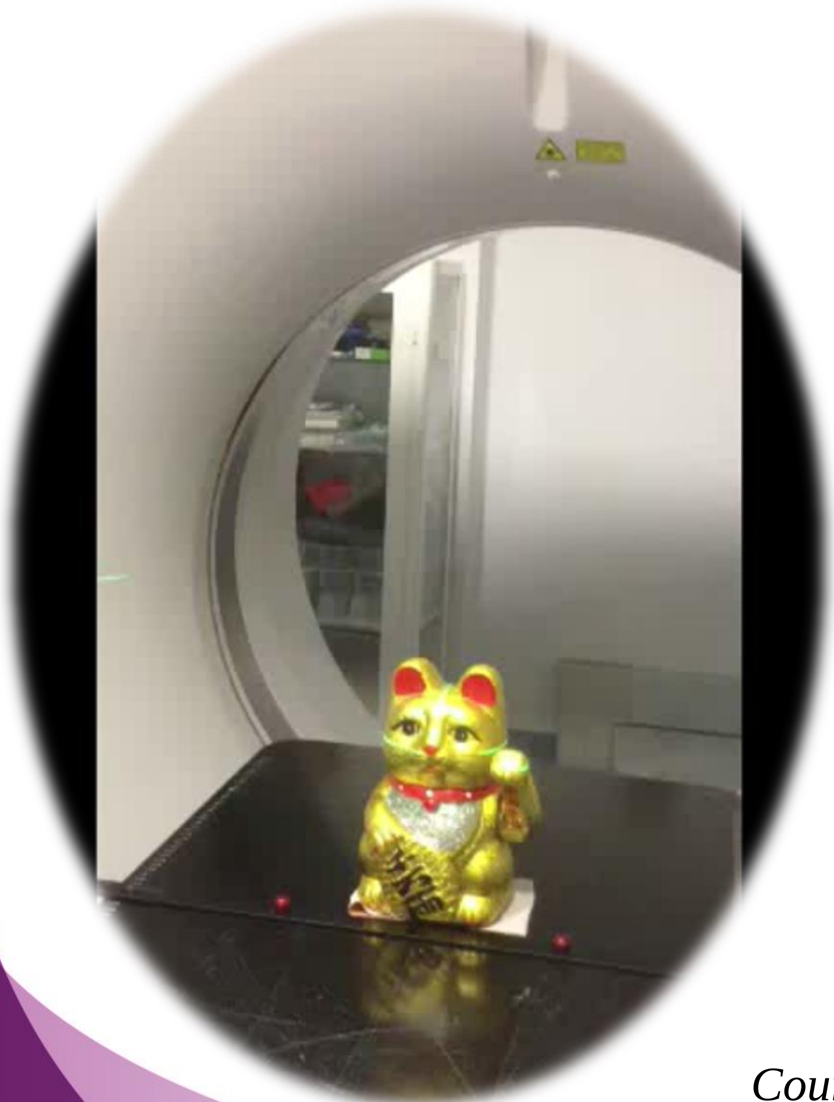
- localization of a **CBCT** dataset with the planning **CT** dataset
- matching planar **kV** or **MV** images with **DRRs**

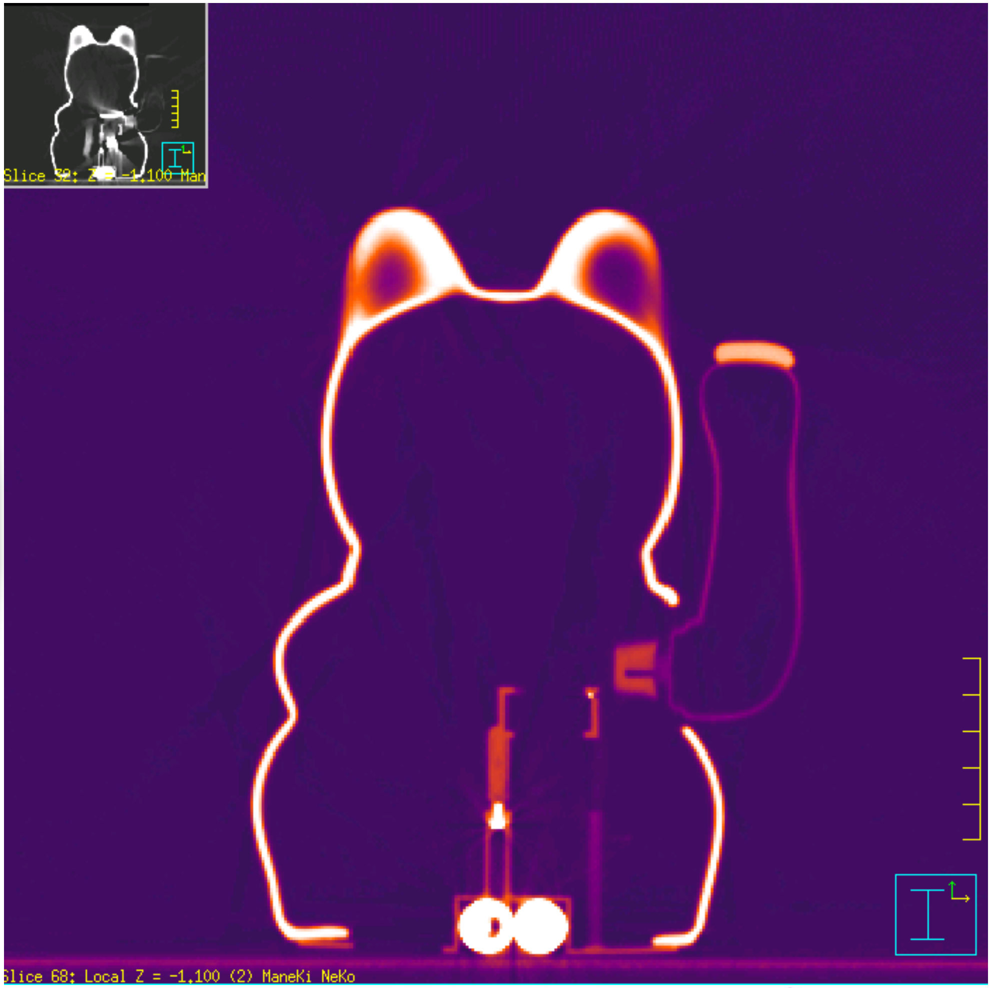
Why do we need IGRT?

Tumor motion

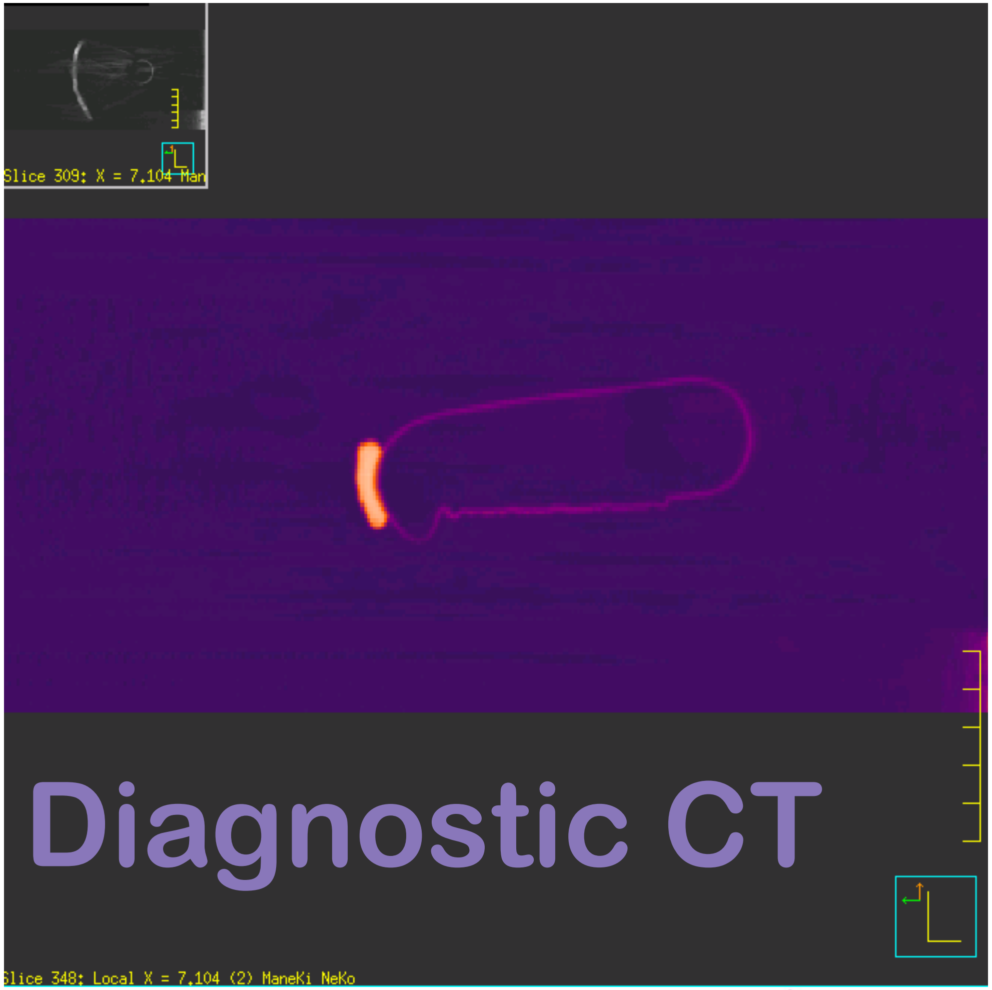




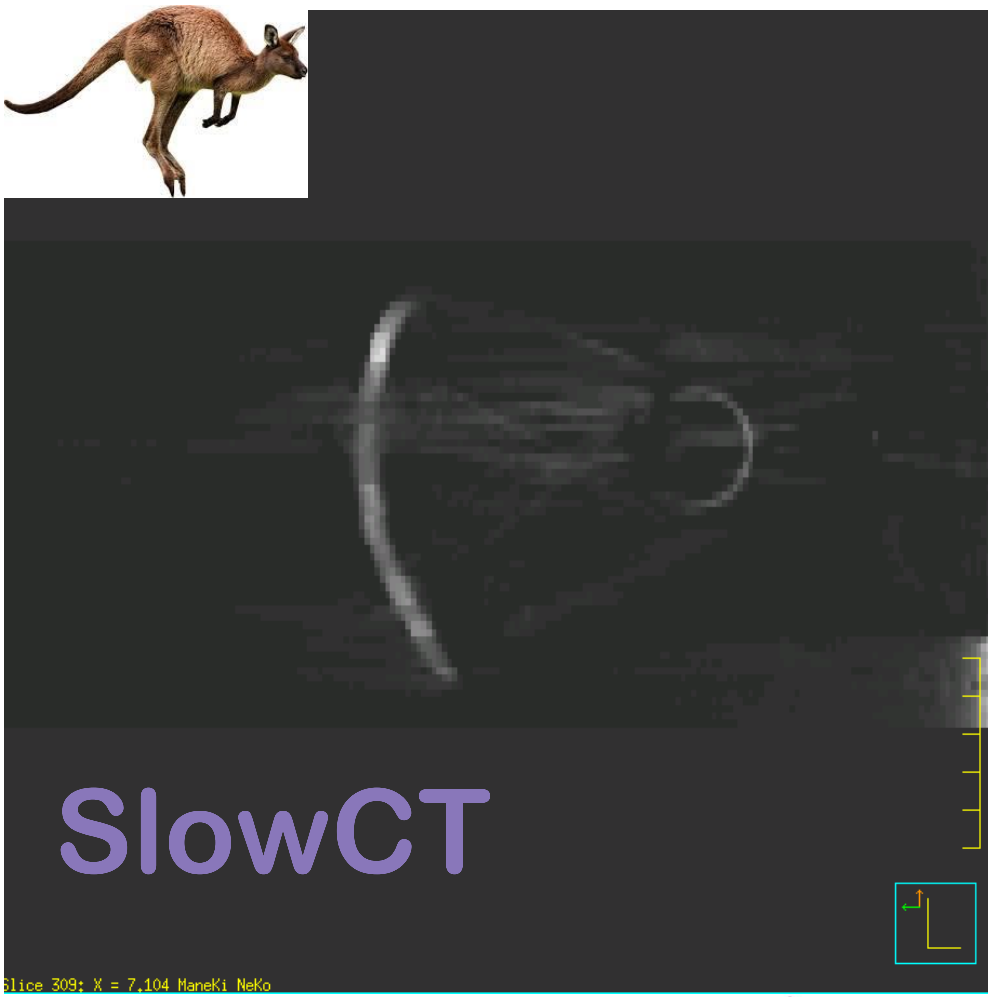




Courtesy Santiago Velazquez

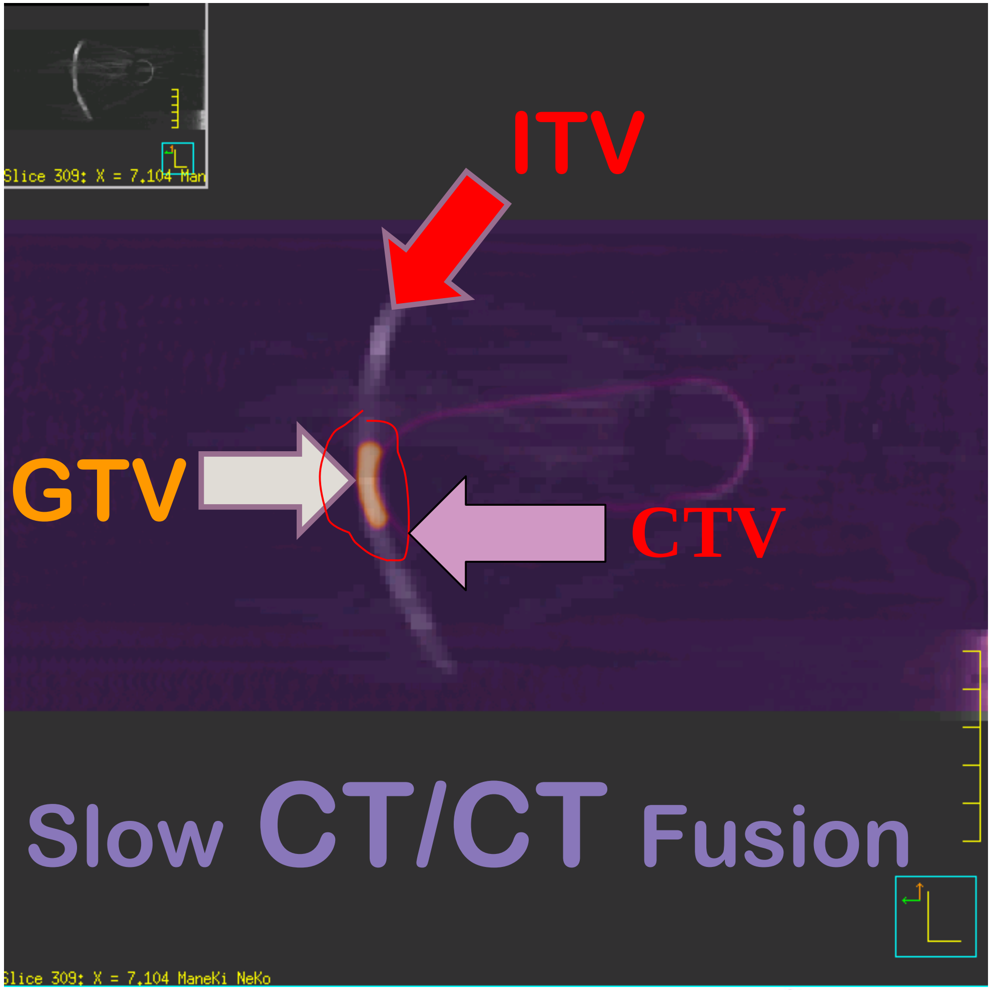


Courtesy Santiago Velazquez

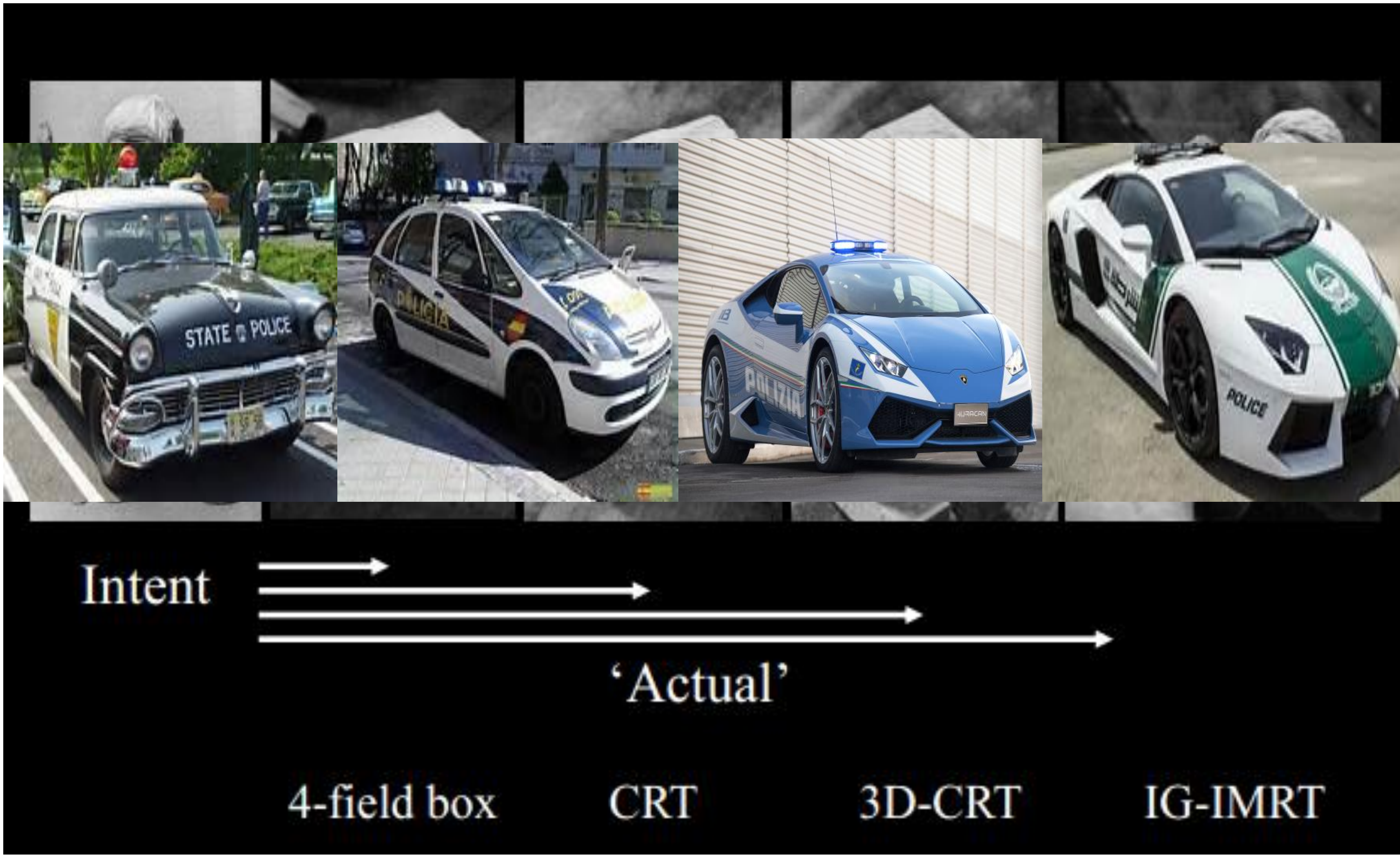


Courtesy Santiago Velazquez

SlowCT/CT Fusion



Courtesy Santiago Velazquez


STATE POLICE
POLICIA
POLIZIA
POLICE
Intent
'Actual'
4-field box
CRT
3D-CRT
IG-IMRT

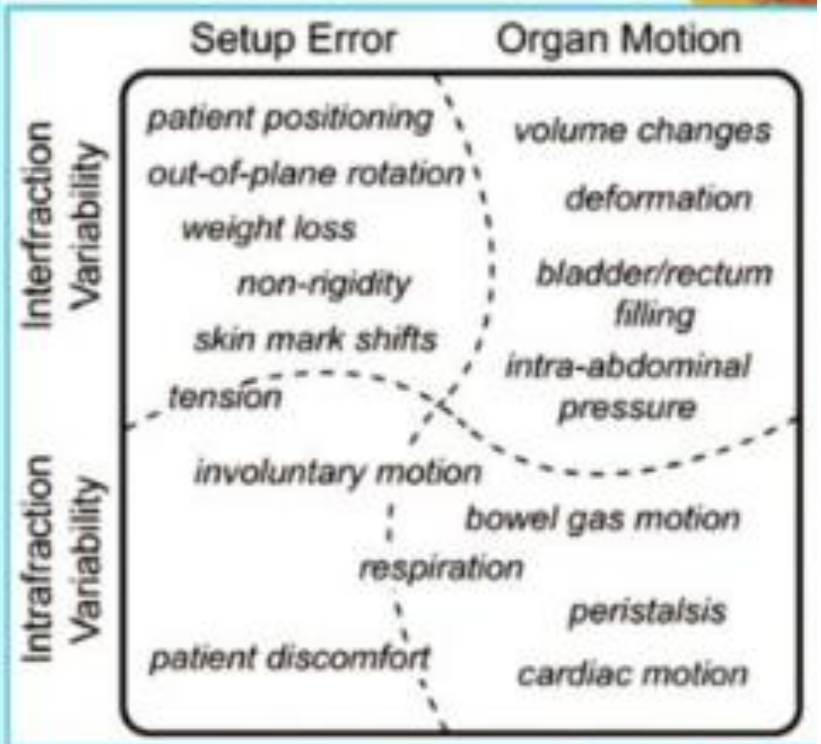
Rationale for IGRT

Quality of Radiotherapy Delivery

- Quality of radiotherapy (RT) delivery is one of the important determinants of patient outcomes
- Efforts to improve the quality of RT delivery include:
  - Accurate target delineation
  - Robust plan optimization
  - Minimizing day-to-day setup variation
  - Tracking intra-fractional organ motion
  - Monitoring & adapting to inter-fractional tumor and normal tissue changes
  - Enhance deliverability (spatial access)

IGRT

Geometric Uncertainty in RT



Jaffray – ASTRO 2012

VOLUME 28 · NUMBER 18 · JUNE 20 2010

JOURNAL OF CLINICAL ONCOLOGY

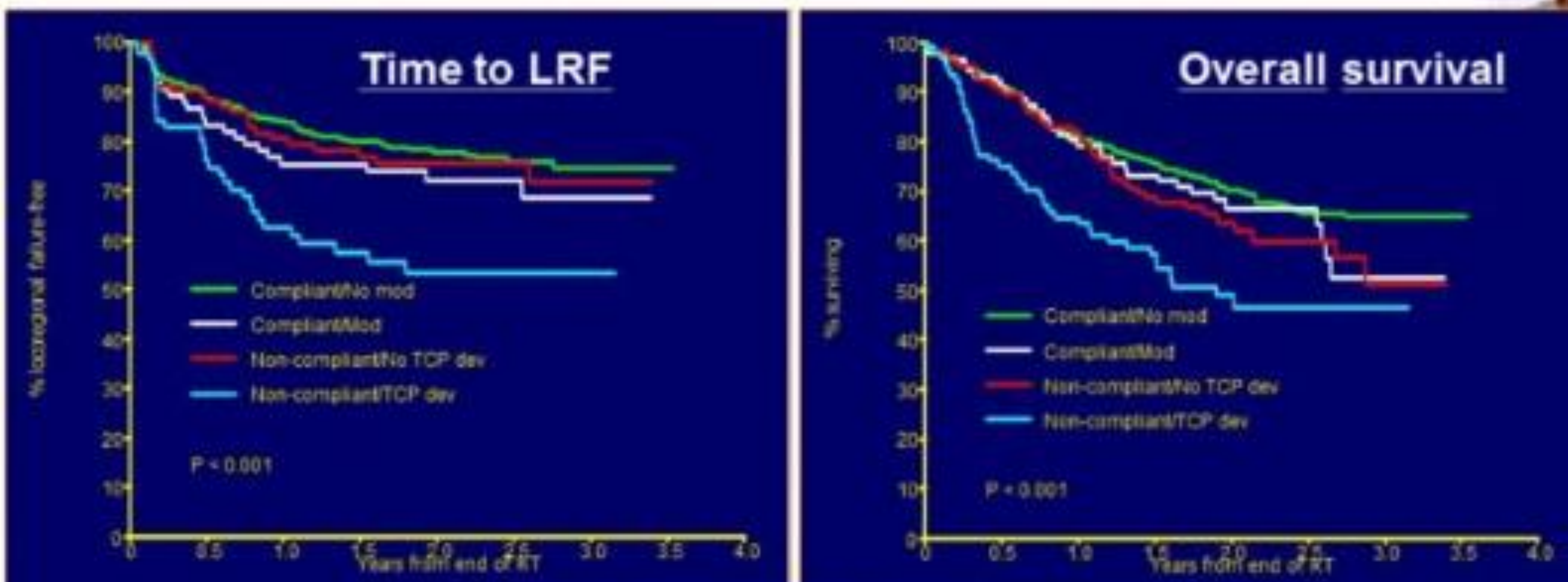
ORIGINAL REPORT

- >800 patients across four Continents
- Influence by accrual numbers

Critical Impact of Radiotherapy Protocol Compliance and Quality in the Treatment of Advanced Head and Neck Cancer: Results From TROG 02.02

Lester J. Peters, Brian O'Sullivan, Jordi Giralt, Thomas J. Fitzgerald, Andy Trotti, Jacques Bernier, Jean Bourhis, Kally Yuen, Richard Fisher, and Danny Rischin

Radiation Quality Matters: Results by deviation status



Patients who had received at least 60 Gy to PTV2

Imaging for treatment verification

1980's – port films	
1990's -	emergence of MV portal imagers
	in-room ultrasound localization
	marker-based localization
	Fluoroscopic tracking
2000's –	flat panel imaging
	KV digital imaging
	CBCT
	MV CBCT
	CT "on rails"
Emerging -	Electromagnetic localization and tracking
	surface tracking
	in-room MRI

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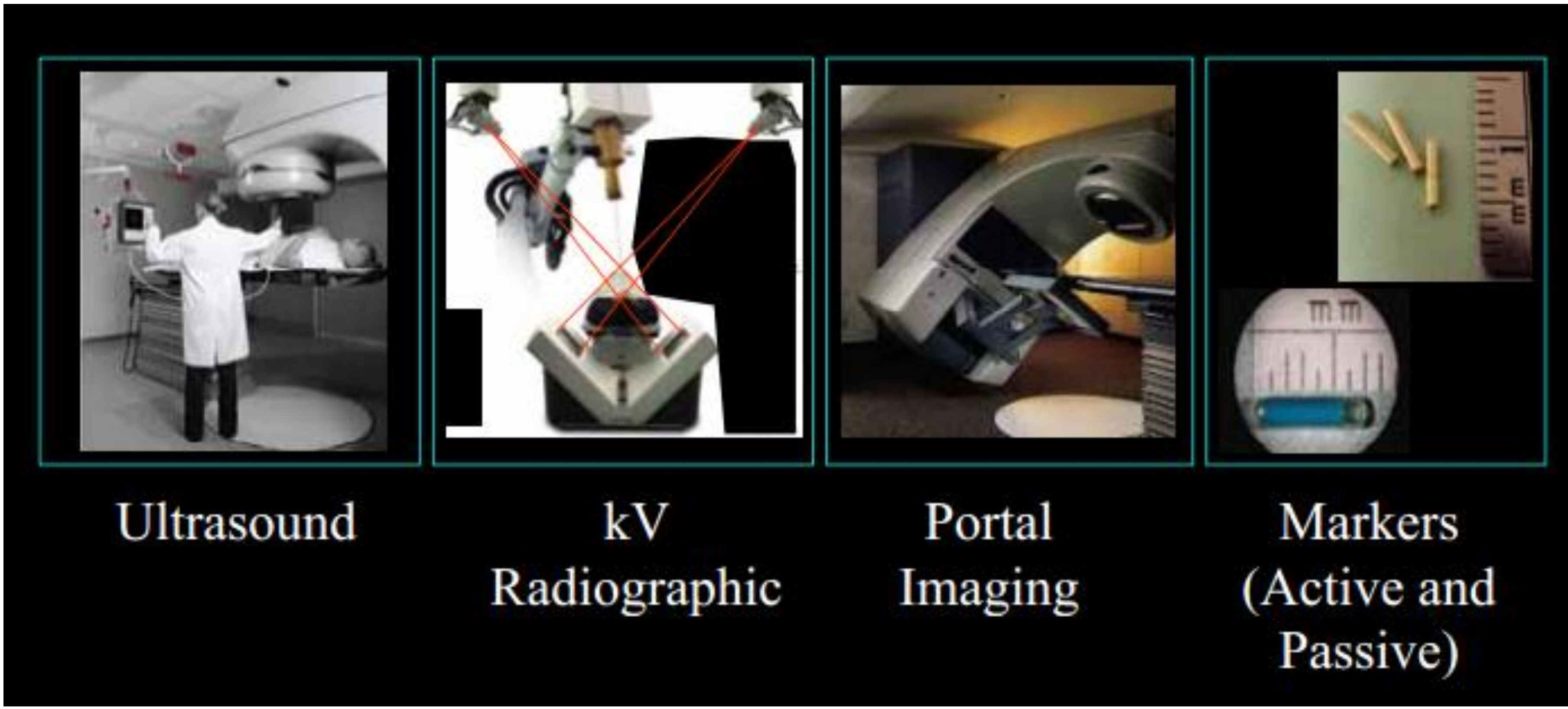
Technologies available for IGRT



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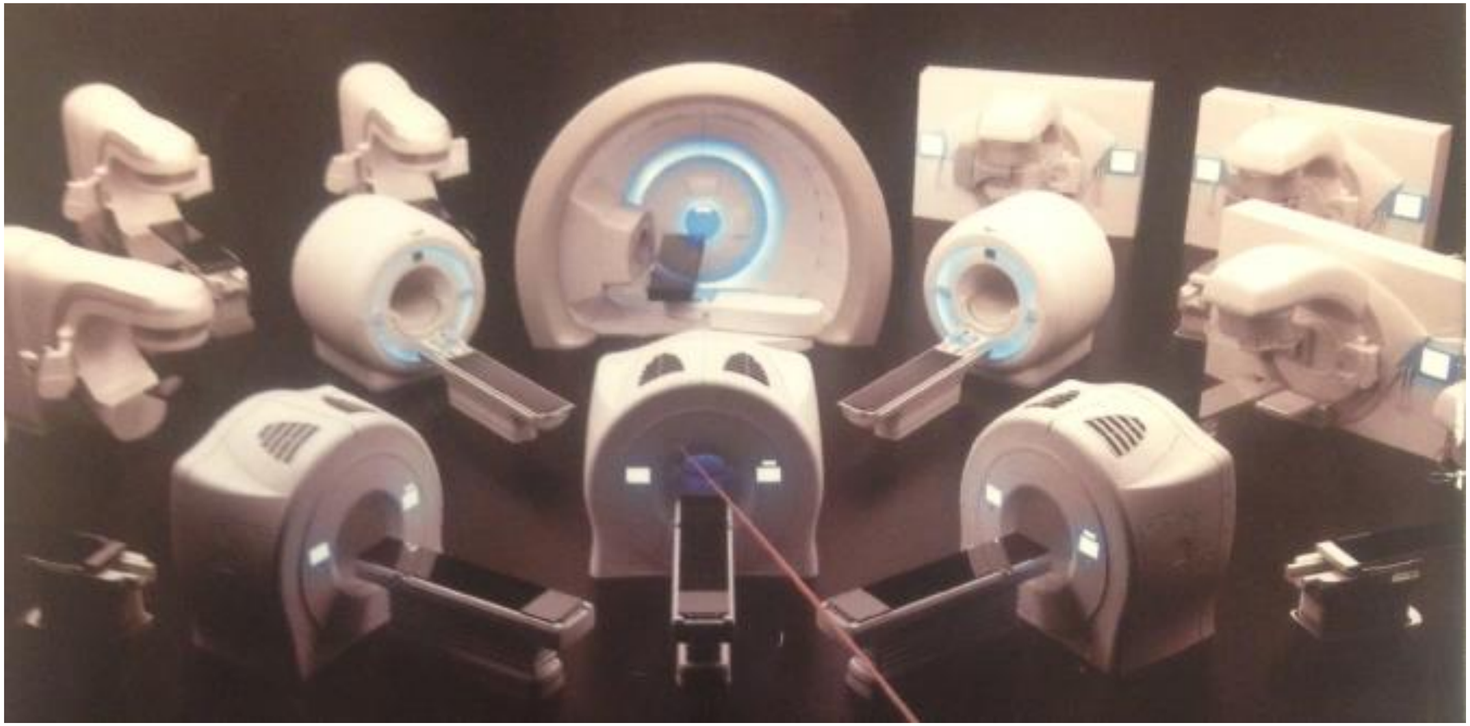
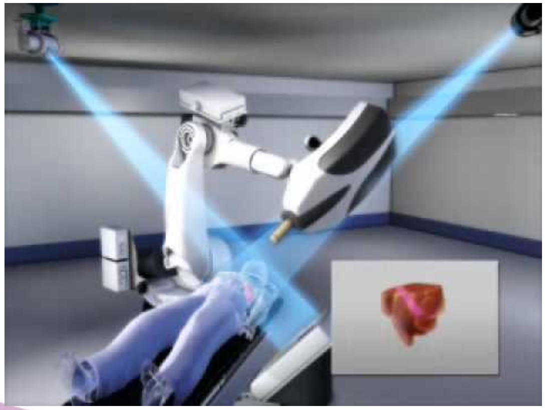
Technologies available for IGRT





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Adoption of new RT Technology

- Vendor and developer motivation
- Healthcare provider´s incentive
- Patient and their family´s perception
- Public health provider and Policy maker´s concern
- Adoption of these techniques is often hasty

Mainly focus on **technological capacity** rather than **evidence-based** sptepwise approach

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IGRT, What else ?

Rising Cost of Radiotherapy

Radiotherapy and Oncology

The cost of radiotherapy in a decade of technology evolution

Evelyn Van de Werf, Jan Verstraete, Yolande Lievens

Table 2
Comparison of the costs at the activity-group level for respectively 2000 and 2009.

	2000 (€)	%	2009 (€)	%
Treatment preparation	839,247	31	1,480,112	27
First patient contact	137,066	5	197,612	4
Simulation	423,162	16	667,324	12
Delineation	25,540	1	114,611	2
Dose calculation	253,479	9	500,565	9
Treatment delivery	1,872,695	69	4,059,947	73
Quality assurance (QA)	283,192	10	1,252,789	23
General at start	40,561	1	102,459	2
Patient specific		0	48,678	1
Supervision plan	69,606	3	68,519	1
Portal imaging	60,324	2	791,248	14
In vivo dosimetry	32,423	1	76,064	1
Chart round	80,278	3	165,821	3
Daily radiotherapy delivery	1,508,306	56	2,501,649	45
Clinical follow up	44,820	2	116,816	2
Discharge	36,377	1	188,693	3
Total	2,711,942	100	5,540,059	100

Rationale for IGRT

Adoption of new IGRT techniques should be based on clinical rationale/evidence and clinical needs:

- **What is the clinical evidence for the claims**
  - ➢ It is better/lower cost than current standard
  - ➢ It can tackle a currently unsolvable clinical problem
  - ➢ It is any purported benefit
- **What is the clinical indication**
- **What are the limitations/risks**
- **Do we have resources and demand**

- **CLAIM IS NOT EVIDENCE!!**

Challenges in RT delivery:

- Day-to-day setup variation
- Intra-fractional organ motion
- Inter-fractional tumor and normal tissue deformation

IGRT Claims: (compared to conventional 3D Conformal)

- IGRT improves the precision and accuracy of RT delivery
  - ➢ Minimizes day-to-day setup variation with daily image-guidance using appropriate matching surrogate
  - ➢ Tracks intra-fractional organ motion
  - ➢ Tracks inter-fractional tissue deformation (adaptive)

- ***Does it translate into better clinical outcomes?***

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IGRT

Radiotherapy and Oncology 78 (2006) 119-122
www.thegreenjournal.com

Special commentary

From IMRT to IGRT: Frontierland or Neverland?

C. Clifton Ling[a,*], Ellen Yorke[a], Zvi Fuks[b]

[a]*Department of Medical Physics, and* [b]*Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Abstract

The recent enthusiasm for real-time image guidance in radiotherapy (IGRT) is in part due to the commercial availability of advanced on-line imaging technologies. Perhaps more important than its potential to improve conventional radiotherapy, IGRT may lead to a paradigm shift in facilitating hypo-fractionated or single-dose treatment. However, there are uncertainty regarding features and approaches of competing IGRT systems and as to whether a sub-set of the features of an ideal IGRT system would suffice for specific disease sites and clinical applications. Clinical studies are necessary for the quantification of benefit needed for evidence-based medicine (Bentzen, SM. Radiation therapy: intensity modulated, image guided, biologically optimized and evidence based. Radiat Oncol 2005;77:227-230).

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IGRT

Acta Oncologica, 2008; 47: 1186–1187

informa
healthcare

EDITORIAL

Will IGRT live up to its promise?

MARCEL VAN HERK

The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands

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Evidence levels

Levels		Type of Evidence
I	1A	Systemic review (with homogeneity) of RCTs
	1B	Individual RCT (with narrow confidence intervals)
	1C	All or none study
II	2A	Systematic review (with homogeneity) of cohort studies
	2B	Individual cohort study (including low quality RCT, e.g. <80% follow-up)
	2C	"Outcomes" research: Ecological studies
III	3A	Systematic review (with homogeneity) of case-control study
	3B	Individual Case-control study
IV	4	Case series (and poor quality cohort and case-control study)
V	5	Expert opinion without explicit critical appraisal or based on physiology bench research or "first principles"

Guyatt et al. JAMA 2000

Improved Clinical Outcomes With High-Dose Image Guided Radiotherapy Compared With Non-IGRT for the Treatment of Clinically Localized Prostate Cancer

Michael J. Zelefsky, M.D.,* Marisa Kollmeier, M.D.,* Brett Cox, M.D.,* Anthony Fidaleo, B.A.,* Dahlia Sperling, B.A.,* Xin Pei, Ph.D.,* Brett Carver, M.D., Ph.D.,† Jonathan Coleman, M.D.,† Michael Lovelock, Ph.D.,† and Margie Hunt, B.S.†

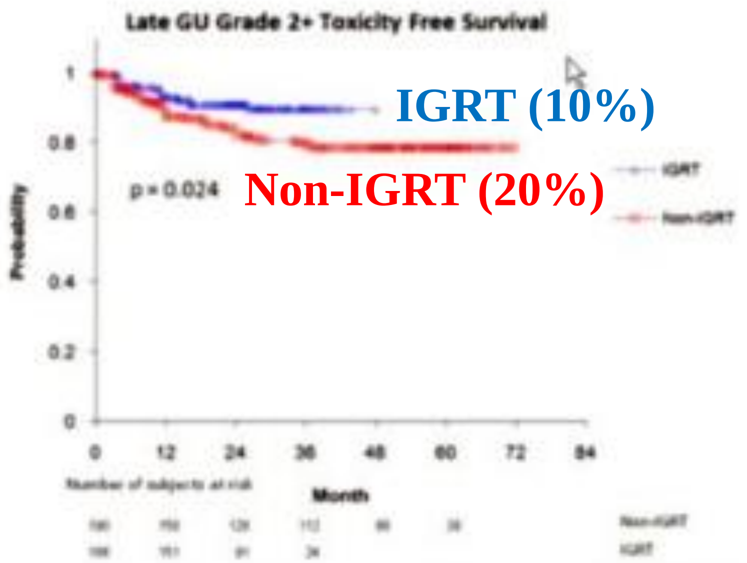

Fig. 1. Comparison of actuarial likelihood of grade 2 or higher late urinary toxicity for patients treated with image-guided radiotherapy (IGRT) to 86.4 Gy vs. intensity-modulated radiotherapy.

IGRT (daily imaging with fiducial marker) vs. non-IGRT (weekly imaging without marker):

- ✓ Same Rx dose: 86.4 Gy
- ✓ Same PTV margin
- ✓ Similar delivery technique: IMRT

IGRT vs non-IGRT

- Lower G2+ GU toxicity (3-y: 10 vs 20%)
- Higher biochemical tumor control in high-risk cohort
- Limitation:
  - ✓ Retrospective review
  - ✓ Slightly different study period
    - Non-IGRT: 2006-2008
    - IGRT: 2007-2009
  - ✓ Short follow-up: median 2.8 years, esp. IGRT cohort

IGRT reduced daily setup variation ⇒ better clinical outcomes
(level 3B evidence)

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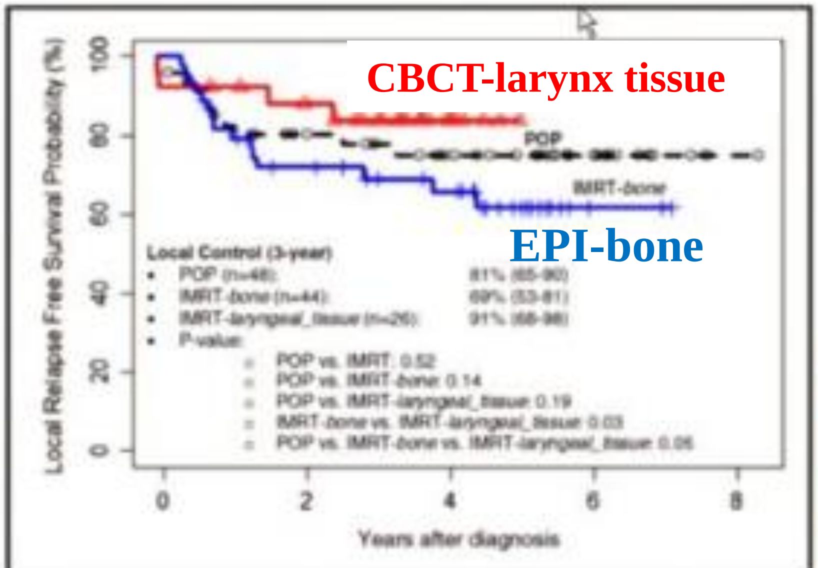
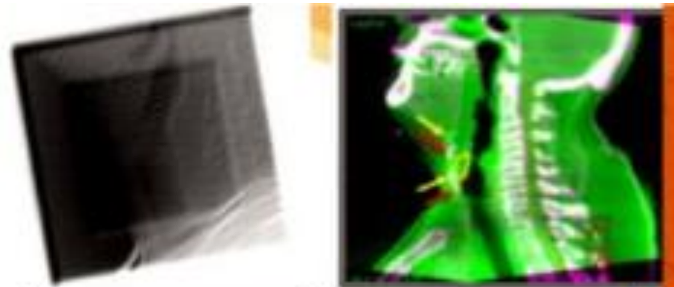
CBCT (vs. MV-EPID): better soft tissue visualization

Outcome following IMRT for T2 glottic cancer: the potential impact of image-guidance protocols on local control

Albert Tiong · Shao Hui Huang · Brian O'Sullivan · Indrasil Mallick · John Kim · Laura A. Dawson · John Cho · Jolie Ringash · Andrew Bayley · Andrew Hope · Eugene Yu · Stephen Breen · Andrea McNiven · Ralph Gilbert · Wei Xu · John Waldron





IMRT (CBCT to laryngeal tissue) vs IMRT (MV-EPID to bone)

- Higher LC (97 vs 69% at 3-yr)
- Limitations:
  - ✓Retrospective review
  - ✓Different study period
    - Non-IGRT: 2006-2008
    - IGRT: 2008-2010
  - Smaller sample size (44 vs 26 patients)

- IMRT with MV-EPID matching to bone could result in geographic miss
- IGRT with CBCT allows selecting appropriate matching surrogate (laryngeal soft tissue) ⇒ improved setup accuracy ⇒ improved clinical outcomes

Level 4 evidence

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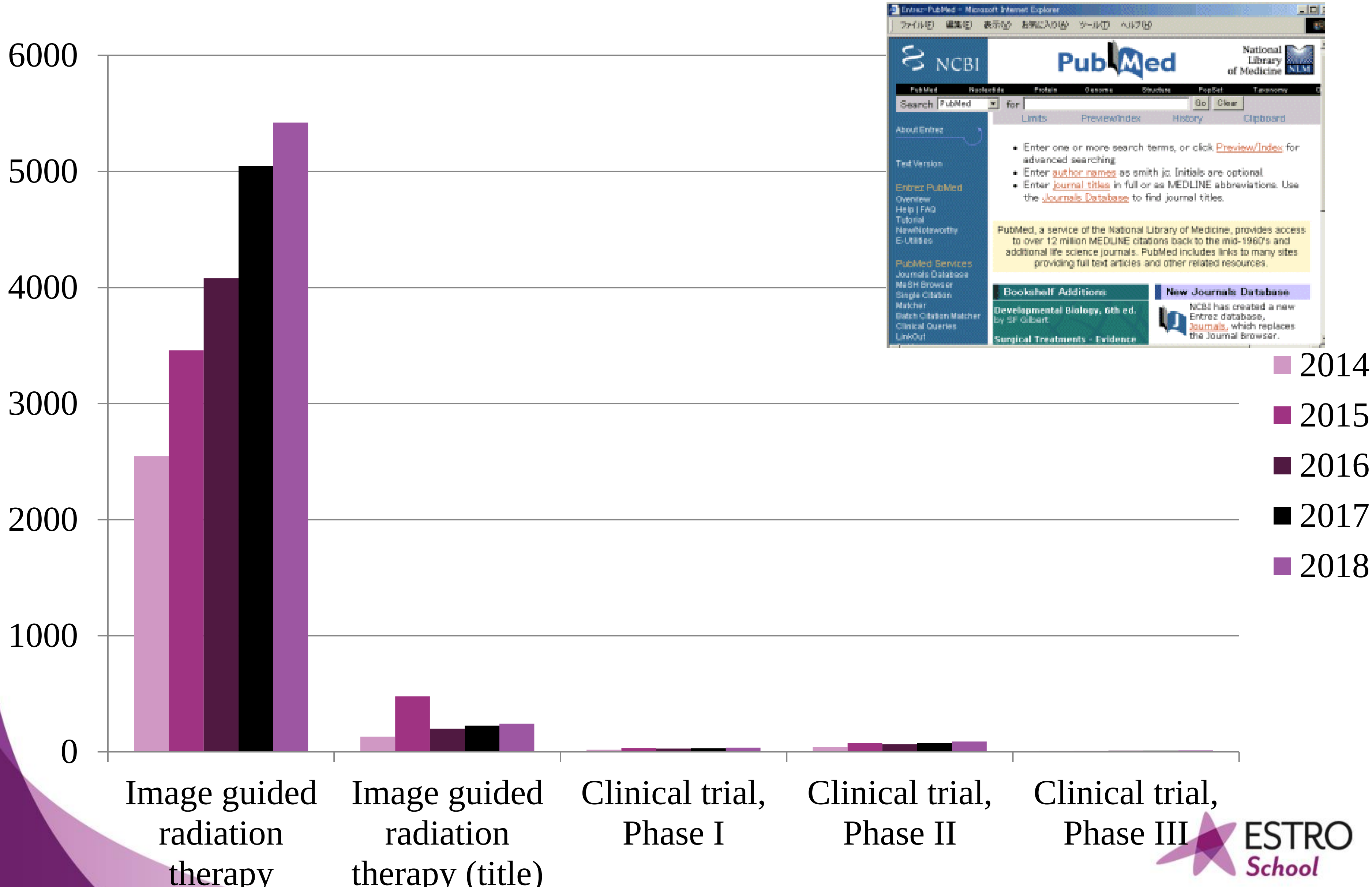
Sources for Clinical Rationale

- Premarketing research work:
  - Randomized trial is ideal but often lacking
    - Difficult to conduct (small "*window of opportunity*")
- Published literature
  - Various quality: high level of evidence is scant
  - Be aware of publication bias, reporting bias, reviewers' bias, omission bias
- Official and unofficial communication
  - Conference, courses, symposium, expert narration
    - Subject to bias, especially vendor sponsored symposium
- Own institutional experience following implementation
  - Cumulative, prospective, and reflective
    - Requires close monitoring and timely feedback

Cites in Pubmed (2014-2017)



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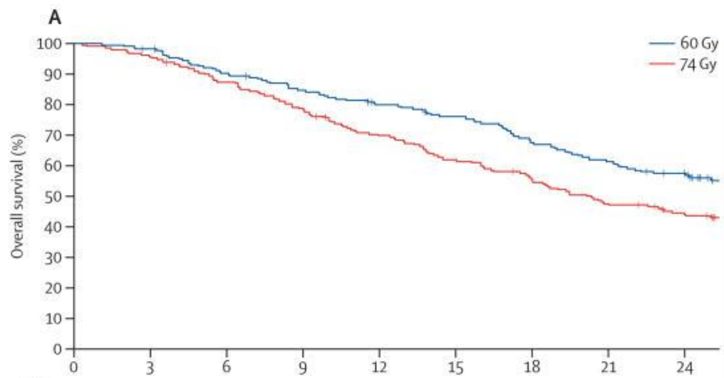
Clinical trial, Phase III
(compare new treatments with the standard)

Standard-dose (60Gy) vs high-dose RT (74Gy) for NSCLC patients (RTOG 0617): negative results



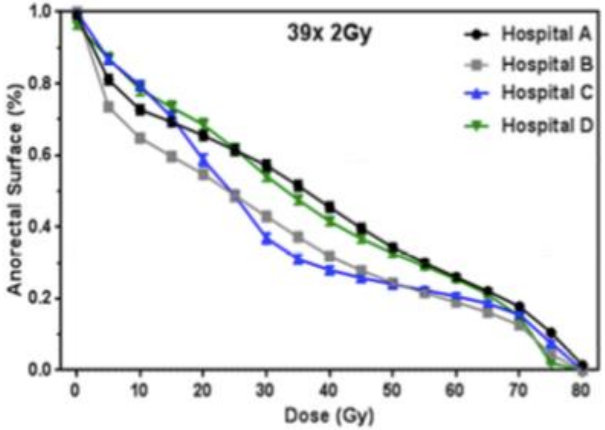
- RT planning was more likely to be noncompliant in the high-dose group (26% vs 17%, *P* = .02)
- They used both 3D and IMRT
- No details about IGRT

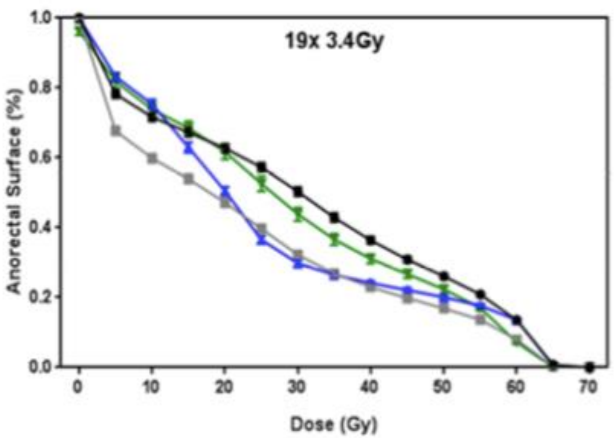
Local protocol variations for Image-Guided Radiotherapy in the multicenter Dutch hypofractionation (HYPRO) trial: impact of rectal balloon and MRI delineation on anorectal dose and gastrointestinal toxicity levels

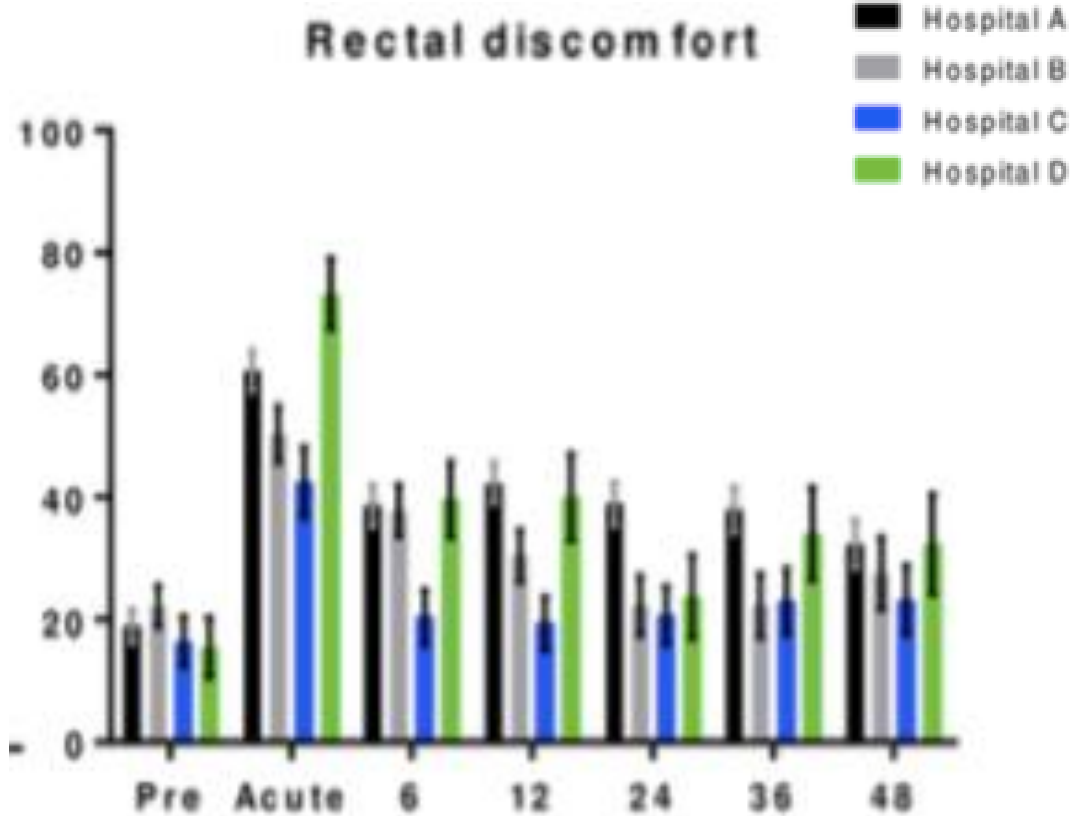
Table 2. Treatment characteristics per treatment center

	A	B	C	D
Patients (%)	242	170	85	75
Conventional treatment	121 (50%)	81 (48%)	42 (49%)	37 (49%)
Hypofractionated treatment	121 (50%)	89 (52%)	43 (51%)	38 (51%)
Seminal vesicle dose group (%)				
1	46 (19%)	35 (21%)	25 (29%)	12 (16%)
2	126 (52%)	85 (50%)	39 (46%)	32 (43%)
3	70 (29%)	50 (29%)	21 (25%)	31 (41%)
ADT (%)				
No ADT	119 (49%)	21 (12%)	42 (51%)	19 (25%)
6 months	7 (3%)	79 (46%)	37 (43%)	7 (9%)
12-24 months	4 (2%)	0	4 (5%)	0
36 months	104 (43%)	66 (39%)	2 (2%)	47 (63%)
Unknown	8 (3%)	4 (2%)	0	2 (3%)
Days between start of ADT and first fraction (median, IQR)	90 (72-100)	54 (34-86)	183 (173-196)	25 (7-55)
Treatment planning imaging modality	CT	CT+ MRI	CT	CT
Fiducial Markers	Yes	Yes*	Yes	Yes
Delineated prostate volume (cm3) (median, IQR)	56.8 (43.8-75.4)	39.3 (29.9-52.5)	42.3 (33.7-60.0)	59.6 (46.9-71.5)
Delineated prostate volume in ADT-naïve patients (cm3) (median, IQR)	66.3 (51.7-93.7)	45.2 (34.8-54.6)	52.7 (40.7-66.7)	63.7 (52.7-74.9)
PTV margins (mm)	5-6	7	7	8
PTV margins seminal vesicles (mm)	8-10	7	7	8-10
Rectal balloon	No	No	Yes	No

Wortel et al IJROBP 2017

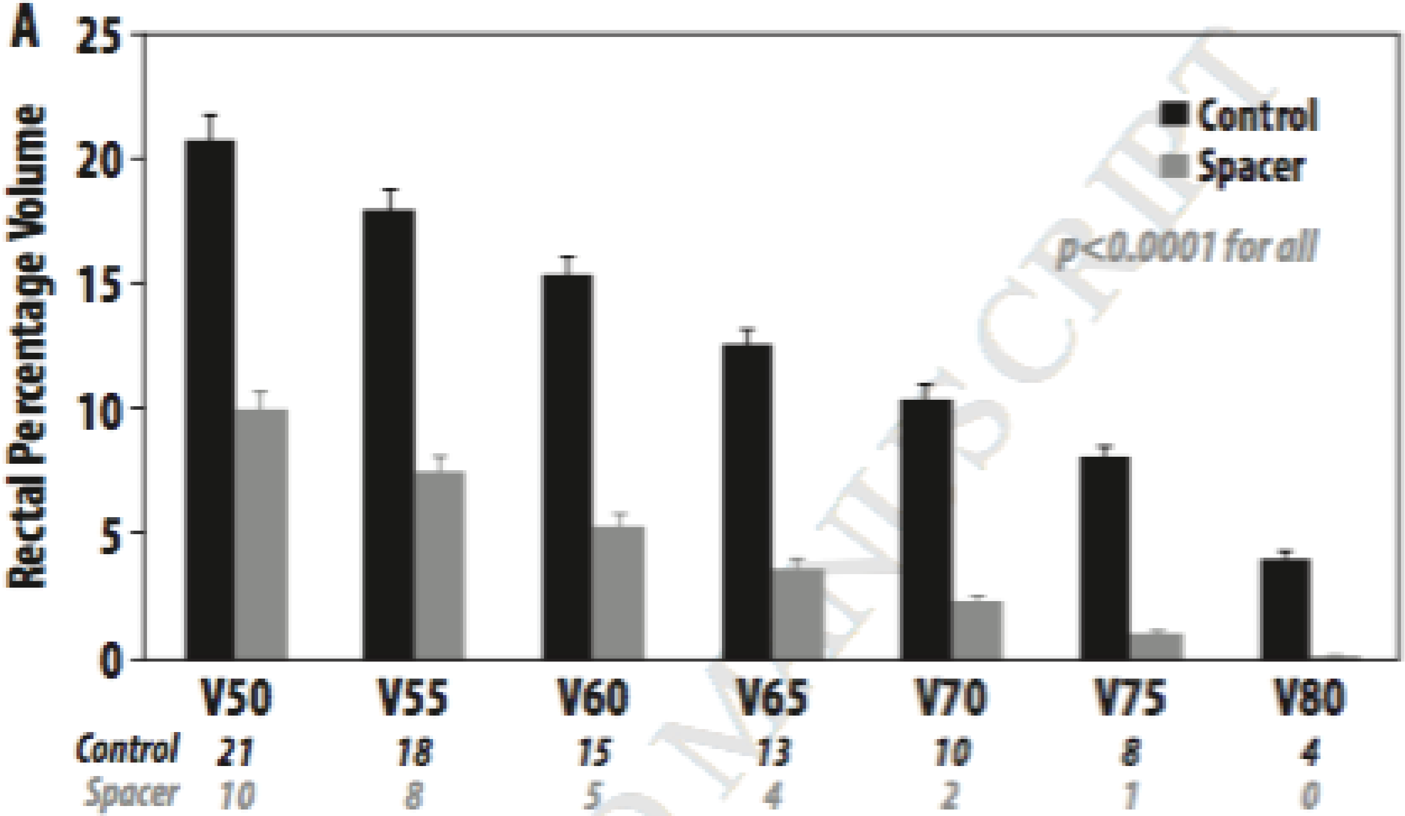




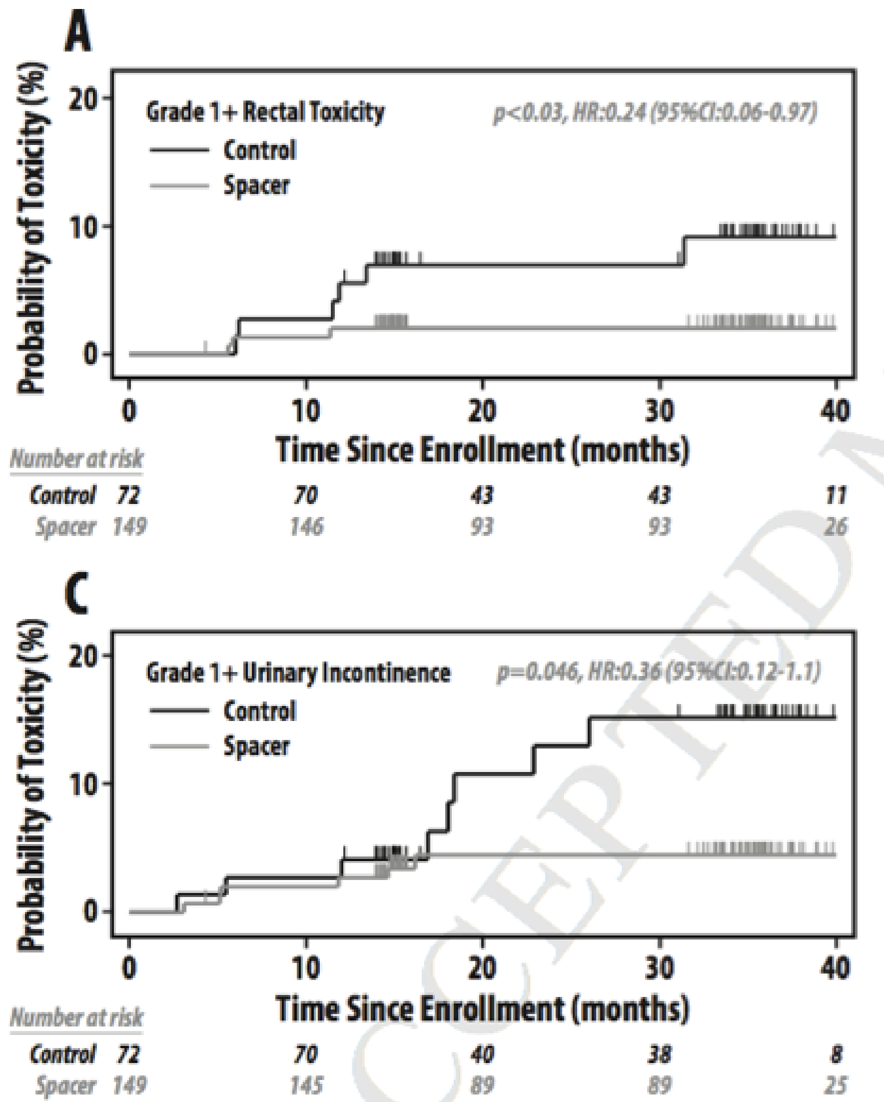


Wortel et al IJROBP 2017

Continued Benefit to Rectal Separation for Prostate RT: Final Results of a Phase III Trial



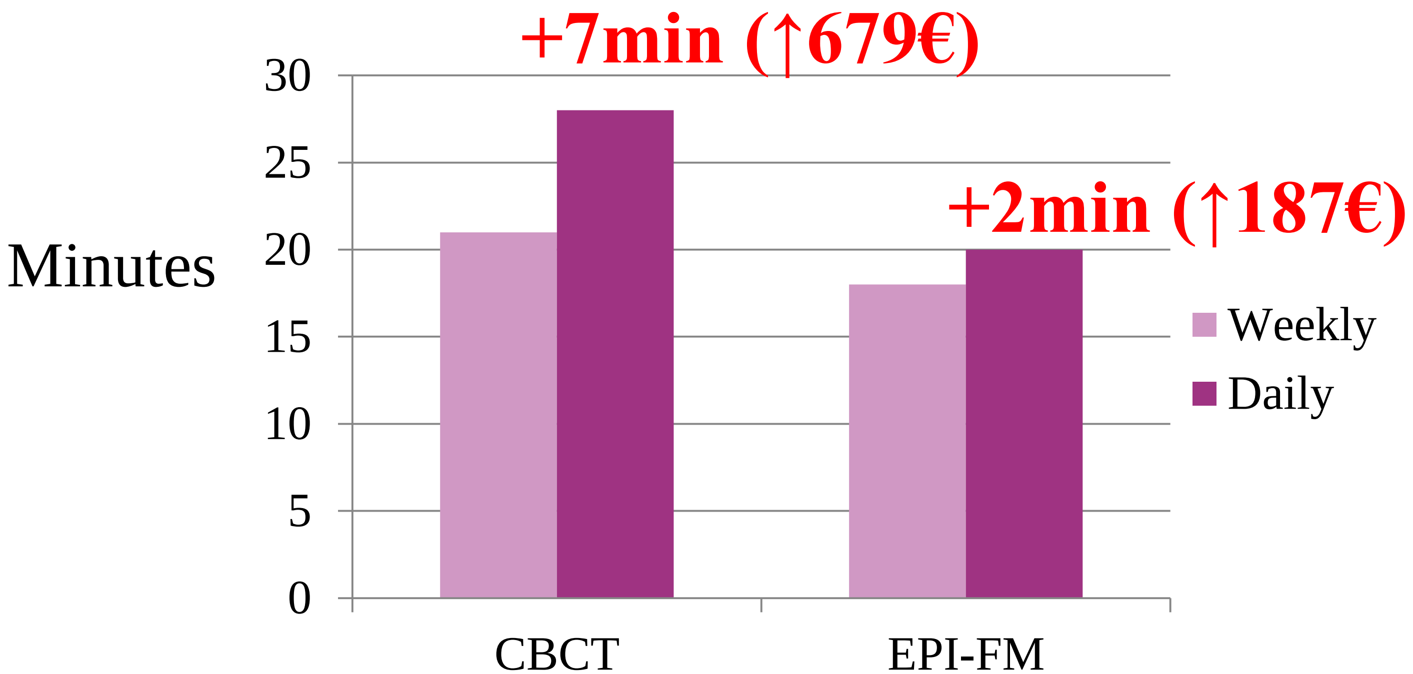
Hamstra et al IJROBP 2017



Hamstra et al IJROBP 2017

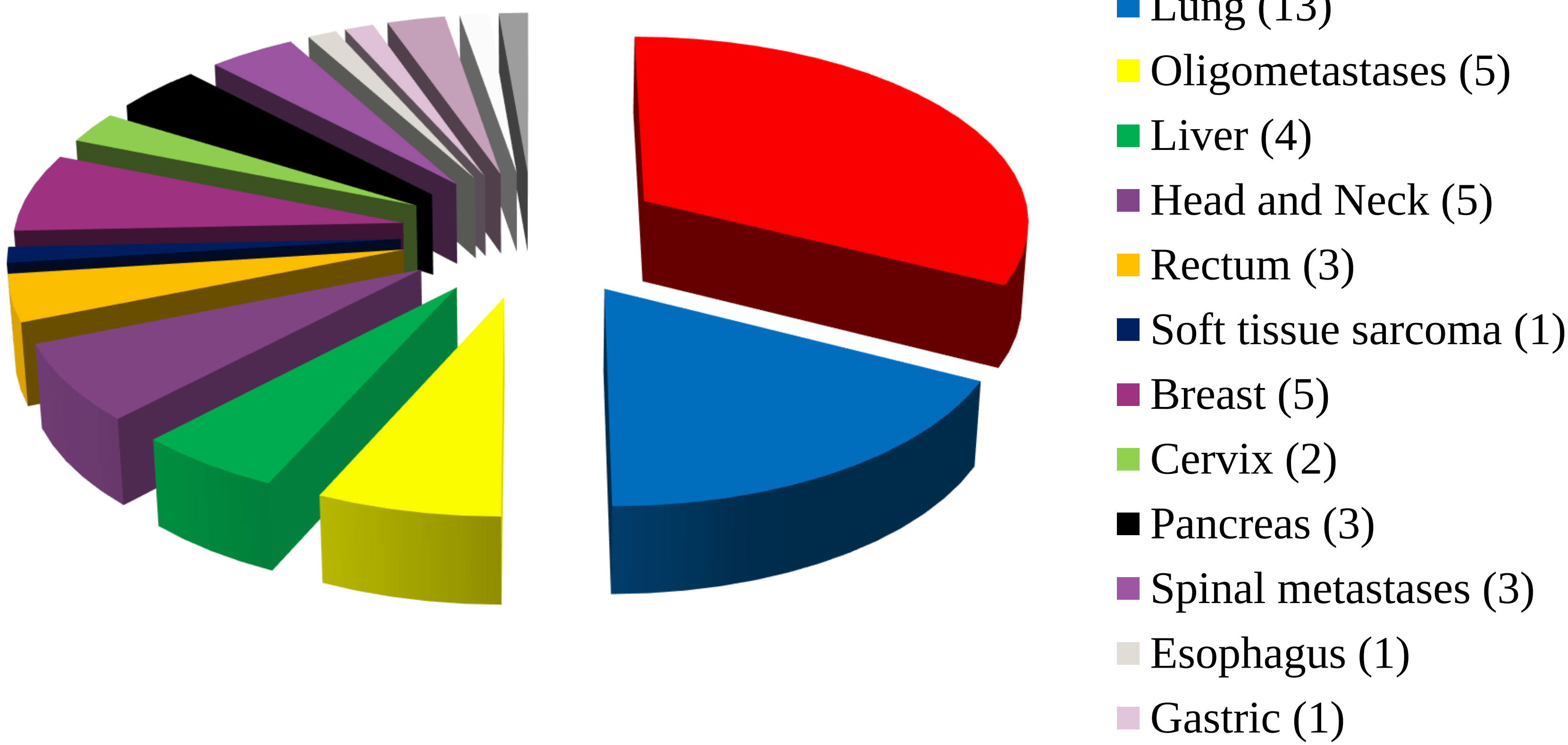
Cost of prostate IGRT: results of a randomized trial

- N=208 patients (France)



- The incremental costs due to different IGRT strategies are relatively **moderate**.

Clinical trial, Phase II (N = 87)
(if a new treatment works well)



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Toxicity

Grade 0	None
Grade 1	Mild
Grade 2	Moderete
Grade 3	Severe
Grade 4	Intensive care
Grade 5	Fatal

Phase II (Prostate)

Table 1 Patient and treatment characteristics

Variable	3D-CRT (n=215)	IG-IMRT (n=260)
Mean (±SD), y	68.9 (±6.3%)	70.5 (±6.0%)
T category		
1	36 (16.7%)	40 (15.4%)
2	97 (45.1%)	89 (34.2%)
3a	53 (24.7%)	102 (39.2%)
3b	29 (13.5%)	28 (10.8%)
4	0	1 (0.4%)
Gleason score		
2-6	106 (49.3%)	75 (28.8%)
7	81 (37.7%)	119 (45.8%)
8-10	28 (13.0%)	66 (25.4%)
Median prehormone PSA concentration, Indeed "Median initial PSA concentration" µg/L (range)	11.3 (0.4-57.0)	15.0 (1.8-59.6)

SIMILAR GROUPS

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Int J Radiation Oncol Biol Phys, Vol. 91, No. 4, pp. 737–744, 2015

Treatment

	3D	IG-IMRT
Risk category		
Low	34 (15.8%)	0
Intermediate	72 (33.5%)	75 (28.8%)
High	109 (50.7%)	185 (71.2%)
Seminal vesicle dose (Gy)		
0	43 (20.0%)	50 (19.2%)
50	35 (16.3%)	0
68	101 (47.0%)	0
70	0	125 (48.1%)
78	36 (16.7%)	85 (32.7%)
Planning margins (mm)		
5	0	107 (41.3%)
6-8	0	151 (58.3%)
10	215 (100%)	1 (0.4%)
Hormone therapy	42 (19.5%)	174 (66.9%)
TURP	24 (11.2%)	28 (10.8%)
Diabetes mellitus	12 (5.6%)	29 (11.2%)
Abdominal surgery	57 (26.5%)	65 (25.0%)
Smoking	34 (15.8%)	28 (15.0%)

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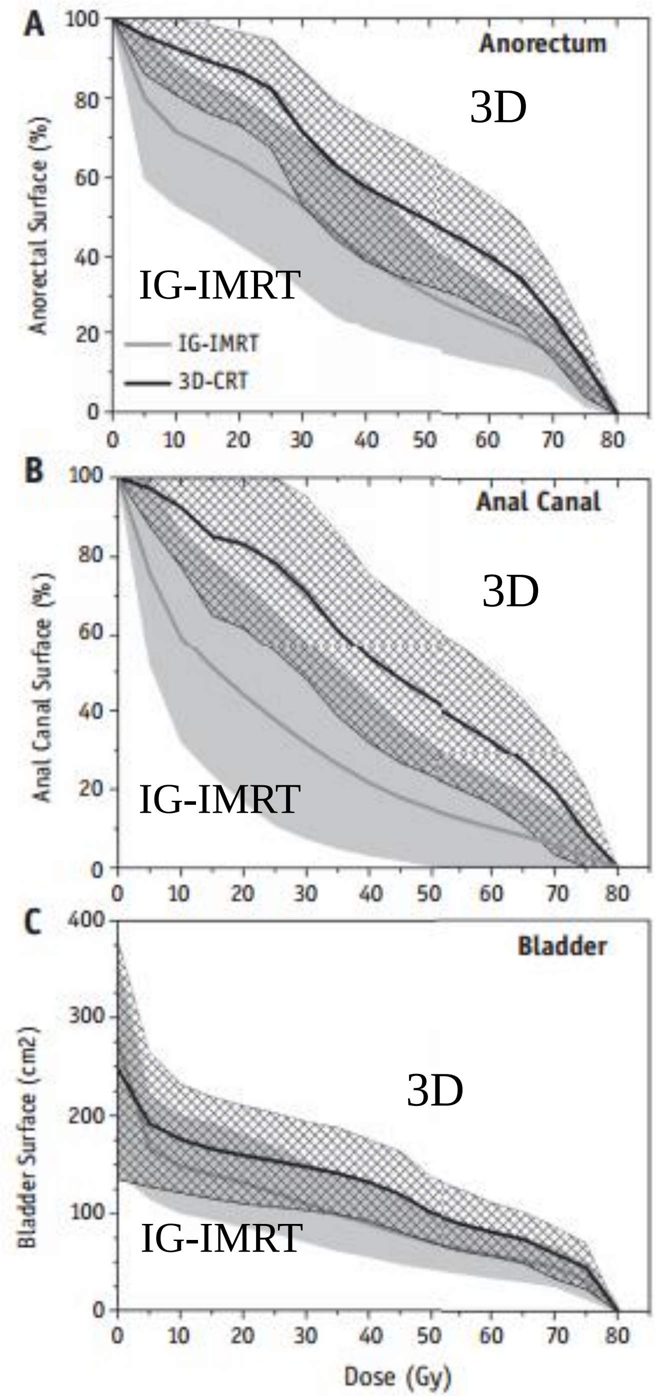
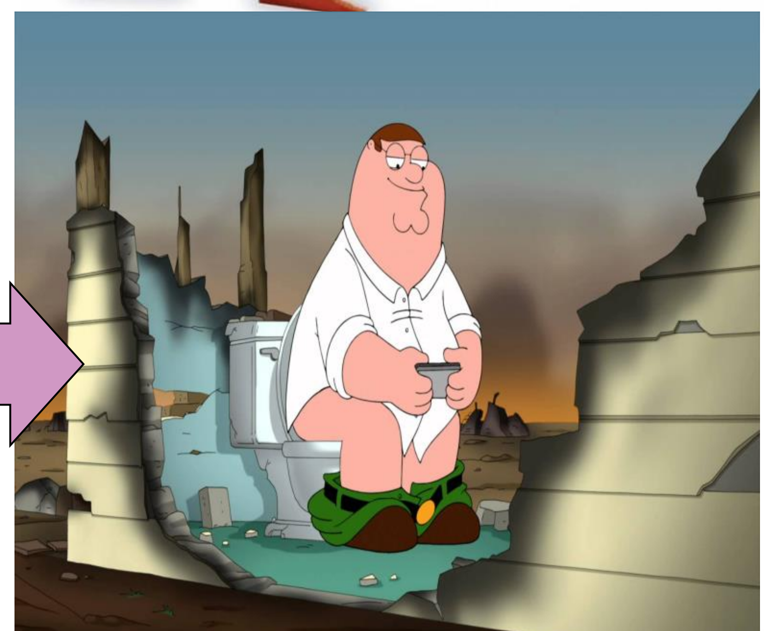
Int J Radiation Oncol Biol Phys, Vol. 91, No. 4, pp. 737–744, 2015



Mean dose and 10th to 90th percentiles are shown

Int J Radiation Oncol Biol Phys, Vol. 91, No. 4, pp. 737−744, 2015



Int J Radiation Oncol Biol Phys, Vol. 91, No. 4, pp. 737–744, 2015

Prostate IGRT

ARTICLE IN PRESS

Radiotherapy and Oncology xxx (2014) xxx–xxx

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Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Is "pelvic radiation disease" always the cause of bowel symptoms following prostate cancer intensity-modulated radiotherapy?

Myo Min [a,*], Benjamin Chua [a], Yvonne Guttner [d], Ned Abraham [d], Noel J. Aherne [a], Matthew Hoffmann [b], Michael J. McKay [c,*,1], Thomas P. Shakespeare [a,1]

[a] North Coast Cancer Institute, Coffs Harbour; [b] North Coast Cancer Institute, Port Macquarie; [c] North Coast Cancer Institute, Lismore; [d] Coffs Harbour Hospital, Australia

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Prostate IGRT

- Multicenter study
- N=102
- Prostate cancer
- Bowel symptoms persisting >90 days post-RT
- IMRT-IGRT
- Dose: 74-78 Gy at 1,8-2 Gy/fx
- Bowel symptoms + **ENDOSCOPIC EXAMINATION**
- Endoscopy findings:
  56% Polyps
  49% Diverticular disease
  38% Haemorrhoids
  29% radiation proctopathy with associated pathology
  4% radiation proctopathy alone

M Min et al. Radiother Oncol 110 (2), 278-283. 2014

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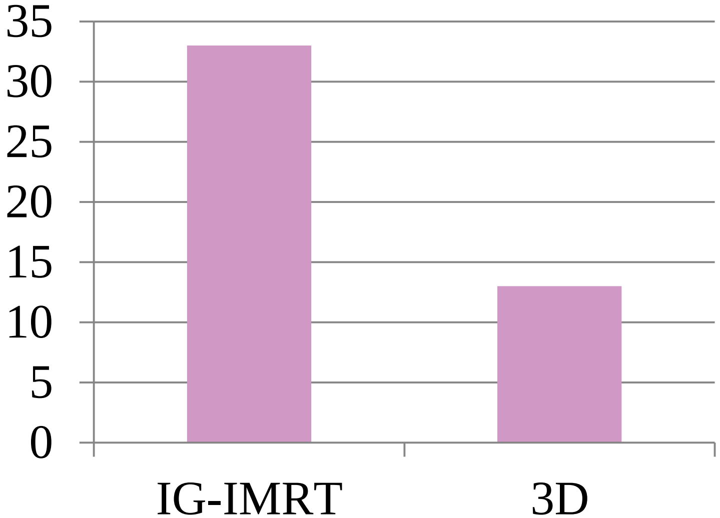
Clinical trial, Phase II (hepatocellular carcinoma)

- IG-IMRT (N=65) vs 3D (N=122)
- Stage III-IV
- Period: 2006-2011
- Retrospective
- Dose: 62 Gy for IG-IMRT and 53 Gy for 3D

- **No differences in toxicity**
- **Survival at 3 years:**



J Cancer Res Clin Oncol. 2014 Sep;140(9):1595-605

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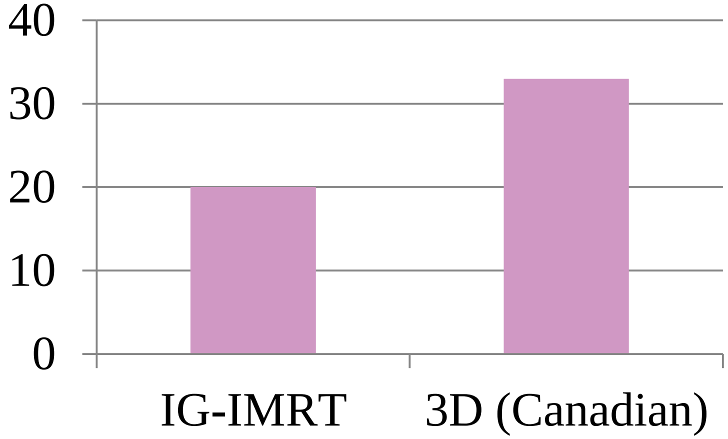
Clinical trial, Phase II (Sarcoma)

- Single Institution study
- Lower extremity soft tissue sarcoma
- N=56
- Period: 2005-2009
- IG-IMRT
- Dose: 50 Gy at 2 Gy/fx

- **Acute wound complication:**
- Local control 88%
- OS: 74%



O'Sullivan B, et al. Cancer. 2013 May 15;119(10):1878-84.

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Clinical trial, Phase II (Lung)

- Multicenter study
- Prospective
- Inoperable T1/T2 NSCLC
- N=60
- Period: 2003-2005
- SBRT
- Dose: 45 Gy at 15 Gy/fx

- **Grade 3 toxicity: 21%**
- Local control 96%
- OS: 65%

Table 3
Lung-related toxicity maximum grade per patient number of affected patients

Toxicity	CVD (17 patients)		COPD (40 patients)	
	Gr 1–2	Gr 3	Gr 1–2	Gr 3
Cough	4	–	11	1
Dyspnoea	2	2	8	2
Pneumonia	–	–	1	1
Pneumonitis	3	–	7	–
Fibrosis	8	1	12	1
Atelectasis	3	1	3	–
Pleural effusion	6	2	5	–
Heart disorder	1	–	–	1
Esophagitis	1	–	1	–

Toxicity grading was done according to CTC v2. Radiation-related pulmonary fibrosis >90 days post-treatment was graded according to RTOG/EORTC Late Radiation Morbidity Scoring Scheme.
Maximum grade refers to the highest degree of toxicity recorded during follow-up. CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease.

Baumann et al. Radiotherapy and Oncology 88 (2008) 359–367

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Clinical trial, Phase II (oligometastases)

- Single Institution study
- Oligometastases
- N=25
- Period: 2004-2006
- SBRT
- Dose: 50 Gy at 5 Gy/fx + sunitinib

- **Grade 3 toxicity: 28%**
- Local control 75%
- OS: 71%; PFS: 56%

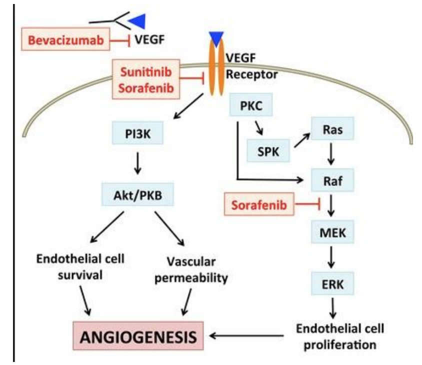

Table 2. Adverse Events.

Adverse Event	All grades	Grade 3	Grade 4	Grade 5
Anemia	18	2	0	0
Neutropenia	14	2	0	0
Fatigue	18	0	0	0
LFT abnormalities	15	1	0	0
Thrombocytopenia	15	4	0	0
Mucositis/stomatitis	8	0	0	0
Nausea/vomiting	7	0	0	0
Skin changes	4	0	0	0
Diarrhea	5	0	0	0
Hypertension	3	0	0	0
Bleeding	4	1	0	1*
Metabolic abnormalities	2	1 (PO_4)	0	0
Increased creatinine	5	0	0	0

*One case occurred after sunitinib treatment and was likely related to reirradiation performed prior to protocol therapy.

doi:10.1371/journal.pone.0036979.t002

Tong CC, et al. PLoS One. 2012;7(6):e36979.

Clinical trial, Phase II (head and neck)

- Multicenter study
- Reirradiation
- N=60
- Period: 2007-2010
- SBRT

- Dose: 36 Gy at 6 Gy/fx + cetuximab
- **Grade 3 toxicity: 18%**
- OS: 47,5%

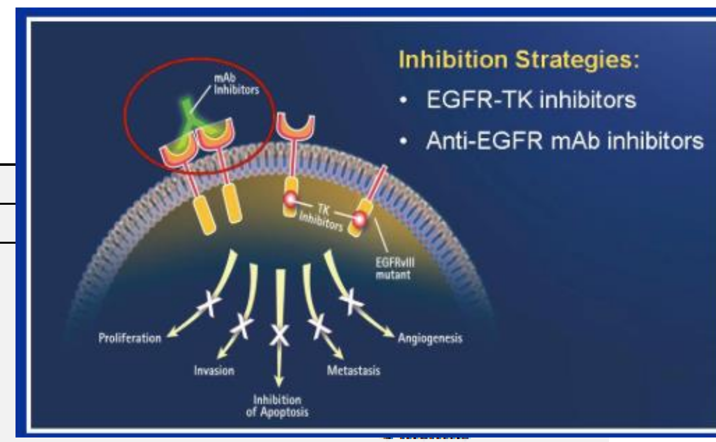

Table 1
Grade 3 toxicities and cutaneous toxicity.

Grade ⩾ 3 AE related to study treatment		
(*N* = 56)	*n*	
Cutaneous		
Rash	4	
Cutaneous toxicity	1	
Fibrosis	1	
Gastrolntestinal		
Mucositis	4	
Dysphagia	3	
Xerostomia	2	3–6 months
Fistula (oral cavity)	1	>6 months
Dysgeusia	1	<3 months
Cutaneous toxicity (*N* = 56)	Related to cetuximab and/or radiotherapy	Related to cetuximab
Cutaneous toxicity, *n* (%)	47 (84)	41 (73)
NK	1 (2)	1 (2)
Grade 1	14 (25)	14 (25)
Grade 2	27 (48)	22 (39)
Grade 3	[illegible] (9)	[illegible] (7)

Lartigau et al. Radiotherapy and Oncology 109 (2013) 281–285

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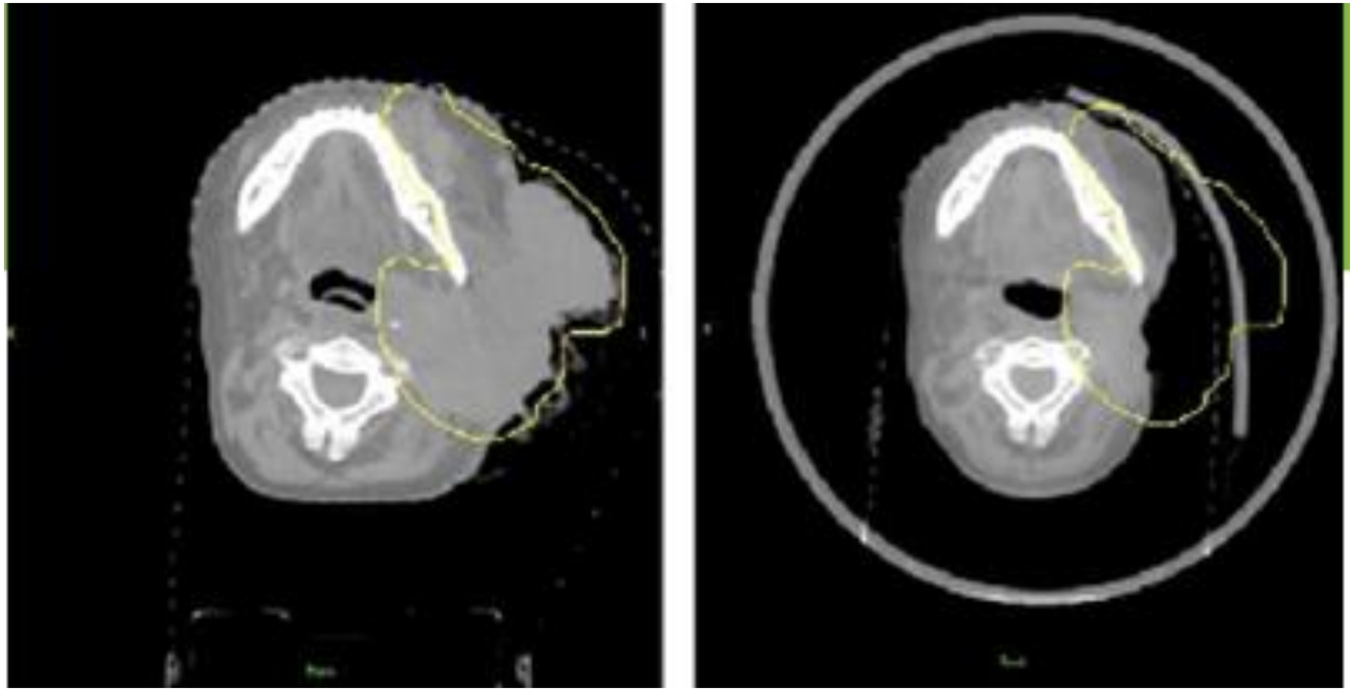


Corresponding axial CT slices from the beginning and the end of treatment.

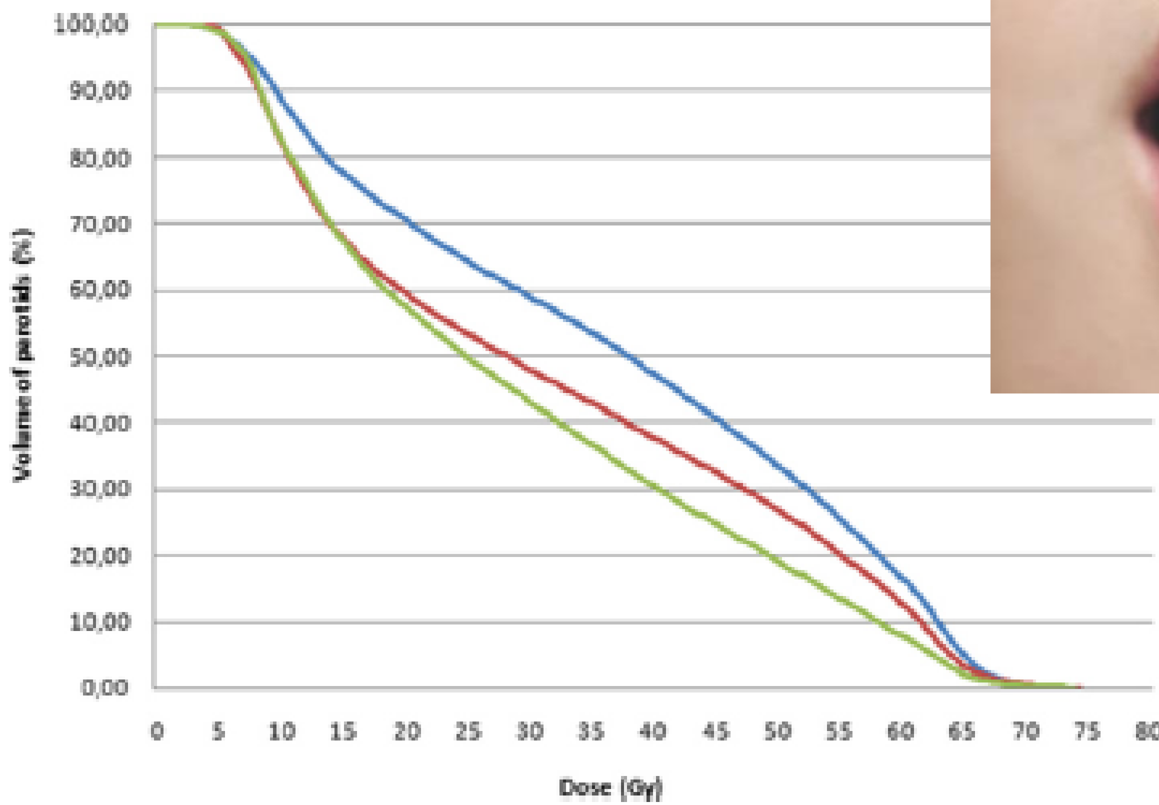
The volume of the PTV changed from 606 to 336 cm3 over treatment, a decrease of 45%.

Spinal cord D05 differed from the planned value by:

3.5% (average) +/- 9.8% (standard desviation)

Mechalakos J et al. Med Dosim. 2009 Fall;34(3):250-5.

Adaptive radiotherapy



Head and Neck
N=15
IG-IMRT

•

Replanning decreased the PG mean dose by 5 Gy, and 11% the xerostomia

LEVEL 2B: INDIVIDUAL COHORT STUDY

Castelli et al. Radiation Oncology (2015) 10:6

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FUTURE DIRECTIONS (phase III studies on-going)

- A Randomised, Two Centre Trial on Daily Cone-beam vs Standard Weekly Orthogonal IGRT for **Prostate**
- Hypofractionated IGRT in Patients With Stage II-III Non-Small Cell **Lung Cancer**
- Biological Image Guided Antialgic SBRT of **Bone Metastases**: a Randomized Phase II/III Trial
- Evaluation of 3DCRT Versus IGRT and Analysis of Early Response in **Head and Neck Cancer**.
- Tomotherapy vs Conventional Radiation for Adjuvant Pelvic RT in **Ca Cervix.**
- Can 3D Ultrasound Be Used Reproducibly by RTTs in Partial **Breast** IGRT?

Daily real time planning (RTP)—Treatment of prostate cancer, clinical implementation, and technique

- 60 RTP's were delivered (10 daily RTP/patient) in 6 consecutive patients.

- In 20% of the cases, the CTV-DVH by RTP improved by >10%.

Plans	V40 (%)	V50 (%)	V60 (%)	V70 (%)
RTP	47.1	29.9	18.6	7.8
IGRT	63.8	49.3	38.0	26.5

↓ 20%

Journal of Clinical Oncology 2013;31:191.

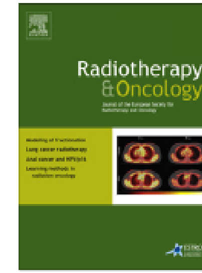
FUTURE DIRECTIONS

Radiotherapy and Oncology 109 (2013) 165–169

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Learning methods in radiation oncology

The utility of e-Learning to support training for a multicentre bladder online adaptive radiotherapy trial (TROG 10.01-BOLART)

CrossMark

Farshad Foroudi [a,*], Daniel Pham [a], Mathias Bressel [b], David Tongs [a], Aldo Rolfo [a,1], Colin Styles [a], Suki Gill [a], Tomas Kron [a]

[a] Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, Australia; [b] Centre for Biostatistics and Clinical Trials, Peter MacCallum Cancer Centre, Melbourne, Australia

ESTRO School

IGRT confidence and knowledge

- To demonstrate the utility of an e-Learning programme for providing training regarding a multi-centre **IGRT** trial.
- Participants : **185 RTTs** from 12 centres.
- There was **an increase confidence after** modules ($p < 0.001$).
- The pre **scores increased** from 67 ± 11 ⇨ 79 ± 8 ($p < 0.001$)

IGRT confidence and knowledge

Confidence questions	Pre e-Learning		Post e-Learning		p-Value
	n	Percentage	n	Percentage	
Identifying bladder on CT					<0.001
Not confident	0	0.0	0	0.0	
A little confident	20	10.8	4	2.2	
Somewhat confident	60	32.4	31	16.8	
Quite confident	69	37.3	102	55.1	
Very confident	36	19.5	48	25.9	
Identifying soft tissue anatomies on pelvic CBCT					<0.001
Not confident	13	7.0	0	0	
A little confident	49	26.5	7	3.8	
Somewhat confident	80	43.2	71	38.4	
Quite confident	39	21.1	91	49.2	
Very confident	4	2.2	16	8.6	
Implementing the BOLART at your centre					<0.001
Not confident	28	15.1	1	0.5	
A little confident	40	21.6	9	4.9	
Somewhat confident	58	31.4	48	25.9	
Quite confident	45	24.3	86	46.5	
Very confident	14	7.6	41	22.2	

57% → 81%

23% → 56%

32% → 69%

E-LEARNING WAS FEASIBLE AND IMPROVED CONFIDENCE AND KNOWLEDGE

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CONCLUSIONS: Why IGRT?

- Security
- Precision
- Accuracy (dose escalation)
- Homogeneity
- Potentially, less toxicity:

Clinical trials needed? Evidence is enough.

- Reliability
- Adapt to changes in antomy
- Shortening RT
- Quality matters!!

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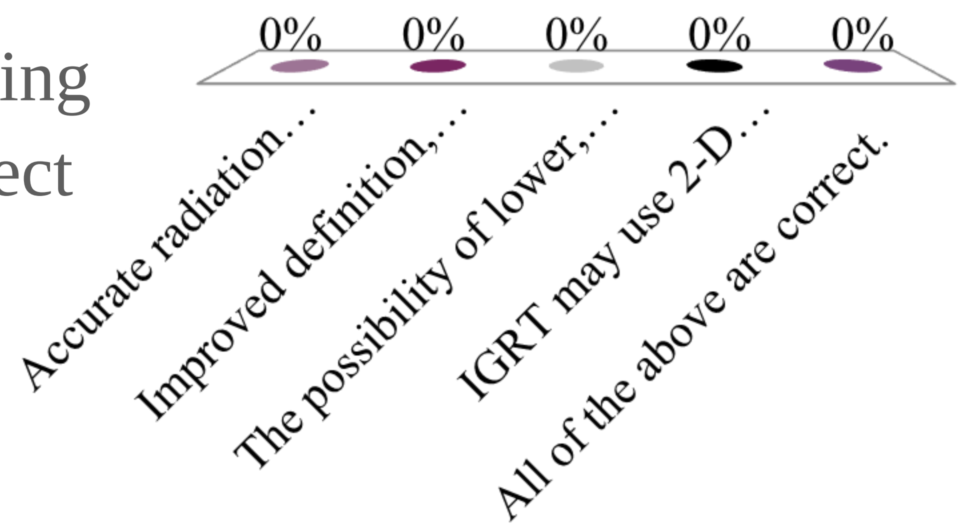
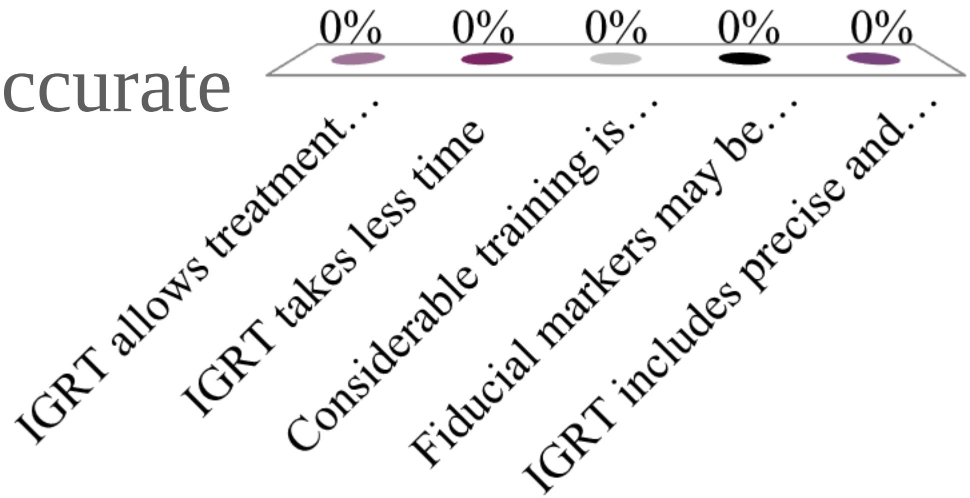
Which of the following statement is TRUE for IGRT?:

A. Less cost and complexity
B. Better definition and delineation
C. The possibility of lower, targeted radiation dosage to improve tumor control
D. IGRT may use 2-D imaging
E. All of the above are correct



Select the FALSE statement about IGRT from the following:

A. Allows treatment monitoring
B. CBCT takes less time
C. Training is needed
D. Fiducial markers may be used
E. Includes precise and accurate imaging



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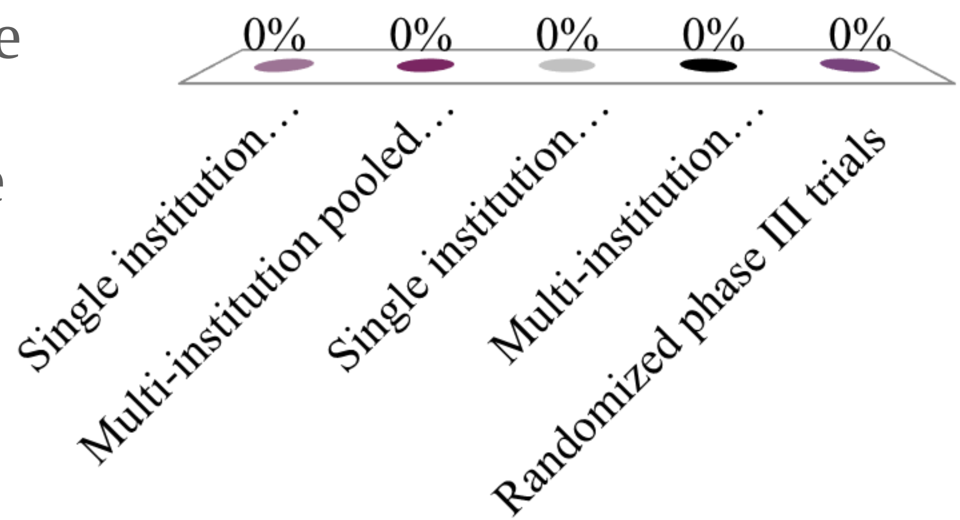
What is the highest level of evidence that supports the clinical benefit of IGRT?

A. Single institution retrospective trials
B. Multi-institution pooled retrospective
C. Single institution prospective phase I/II
D. Multi-institution prospective phase I/II
E. Randomized phase III trials




Thank you!
Triana (Sevilla, Spain)

Prostate

Jose Lopez, M.D., Ph.D
Radiation Oncology
University Hospital Virgen del Rocio
Seville, Spain

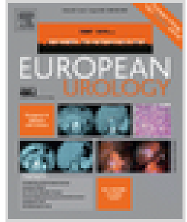
Advanced skills in modern radiotherapy

Outline of Talk

- Clinical data supporting benefit to local treatment in lymph node metastasized prostate cancer
- Delineation/Preparation
- Case report
- Discussion of current multidisciplinary (physician, phisyc and RTTs) management

European Urology

Volume 58, Issue 2, August 2010, Pages 261–269



Review – Prostate Cancer

Does Local Treatment of the Prostate in Advanced and/or Lymph Node Metastatic Disease Improve Efficacy of Androgen-Deprivation Therapy? A Systematic Review

Paul C.M.S. Verhagen[a], Fritz H. Schröder[a], Laurence Collette[b], Chris H. Bangma[a]

[a] Department of Urology, Erasmus MC, Rotterdam, The Netherlands

[b] European Organisation of Research and Treatment of Cancer Headquarters, Statistics Department, Brussels, Belgium

Conclusions

The local therapy in T3 and/or lymph node–positive disease is an essential part of the optimal treatment.

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Lymph node metastasized prostate cancer

- N=80
- T1-4, N1M0
- Intensity modulated arc radiotherapy (IMAT) + androgen deprivation
- Dose: 69,3 Gy in 25 fractions; SIB (intraprostatic lesion): 72 Gy
- F/u: 3 years
- **3-year late grade 3 GI: 8%**
- **3-year late grade 3/4 GU: 6%**
- **3-year bRFS and cRFS was 81% and 89%, respectively.**

Radiotherapy and Oncology 109 (2013) 229–234

T1

T1 Clinically inapparent; tumor not palpable or visible by imaging

T1a Incidental finding during transurethral resection of prostate; < 5% of tissue resected

T1b Incidental finding during transurethral resection of prostate; > 5% of tissue resected

T1c Tumor identified by needle biopsy (e.g. because of elevated PSA)

T2

T2 Tumor confined within prostate (palpable or visible on TRUS)

T2a Involves half of a lobe or less

T2b Involves more than half of a lobe one lobe but not both lobes

T2c Tumor involves both lobes

T3

T3 Tumor extends through prostatic capsule, bladder neck or seminal capsule

T3a Unilateral extracapsular extension

T3b Bilateral extracapsular extension

T3c Tumor invades seminal vesicle(s)

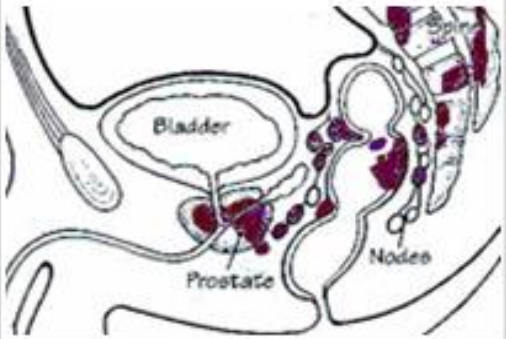
T4

T4 The tumor has spread or attached to tissues next to the prostate (other than the seminal vesicles).

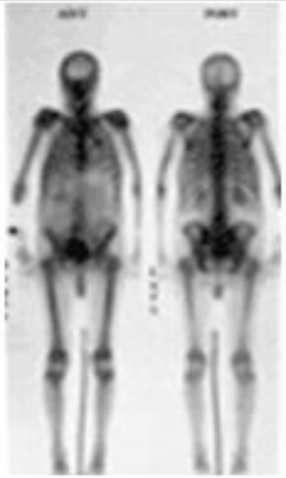
T4a The tumor has spread to the neck of the bladder, the external sphincter (muscles that help control urination), or the rectum.

T4b The tumor has spread to the floor and/or the wall of the pelvis.

N0-3



M0-1



N0 Cancer has not spread to any lymph nodes.
N1 Cancer has spread to a single regional lymph node (inside the pelvis) and is not larger than 2 centimeters
N2 Cancer has spread to one or more regional lymph nodes and is larger than 2 centimeters (¾ inch), but not larger than 5 centimeters
N3: Cancer has spread to a lymph node and is larger than 5 centimeters

M0: The cancer has not metastasized (spread) beyond the regional lymph nodes
M1: The cancer has metastasized to distant lymph nodes (outside of the pelvis), bones, or other distant organs such as lungs, liver, or brain

Lymph node metastasized prostate cancer

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Radiotherapy and Oncology 109 (2013) 229–234

Lymph node metastasized prostate cancer

- N=80
- T1-4, N1M0
- Intensity modulated a[…] deprivation
- Dose: 69,3 Gy in 25 fra[…]
- F/u: 3 years
- **3-year late grade 3 […]**
- **3-year late grade 3/[…]**
- **3-year bRFS and cRFS was 81% and 89%, respectively.**

Grade 1 Mild

Grade 2 Moderate

Grade 3 Severe

Grade 4 Life-threatening consequences

Grade 5 Death

Radiotherapy and Oncology 109 (2013) 229–234

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Lymph node metastasized prostate cancer

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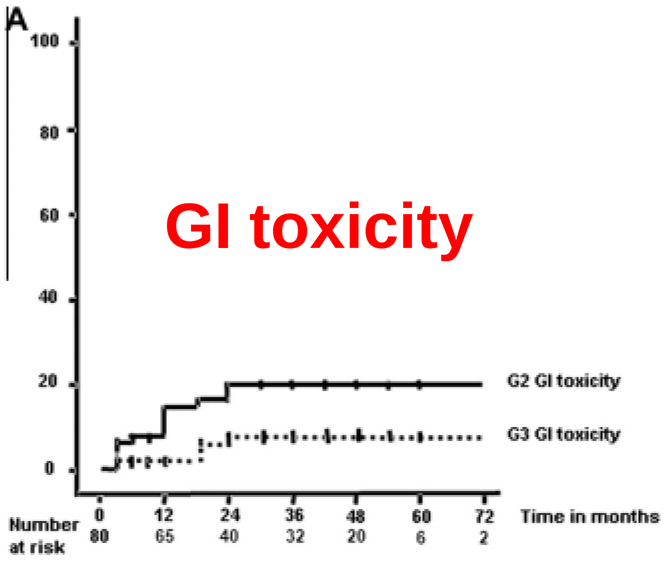
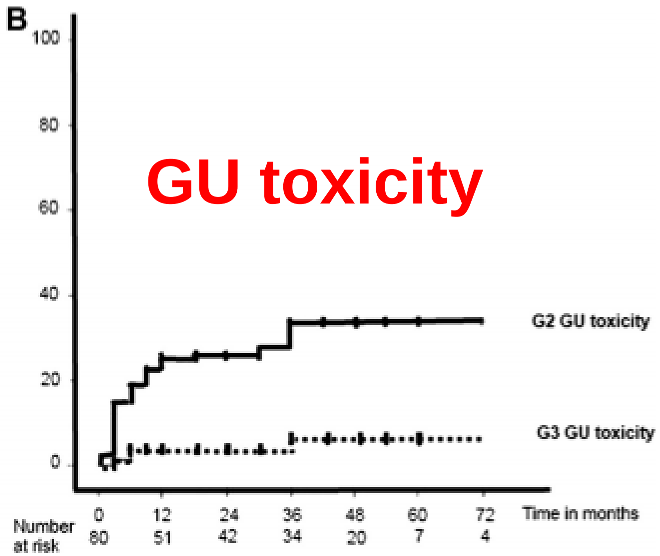
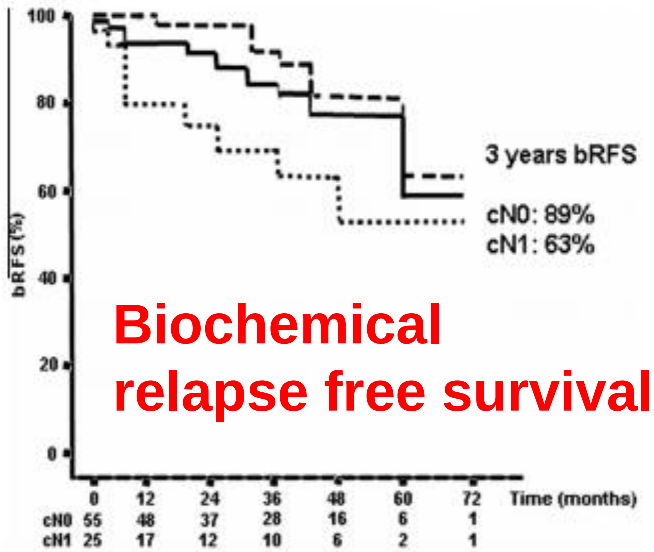
Radiotherapy and Oncology 109 (2013) 229–234

Lymph node metastasized prostate cancer







Radiotherapy and Oncology 109 (2013) 229–234

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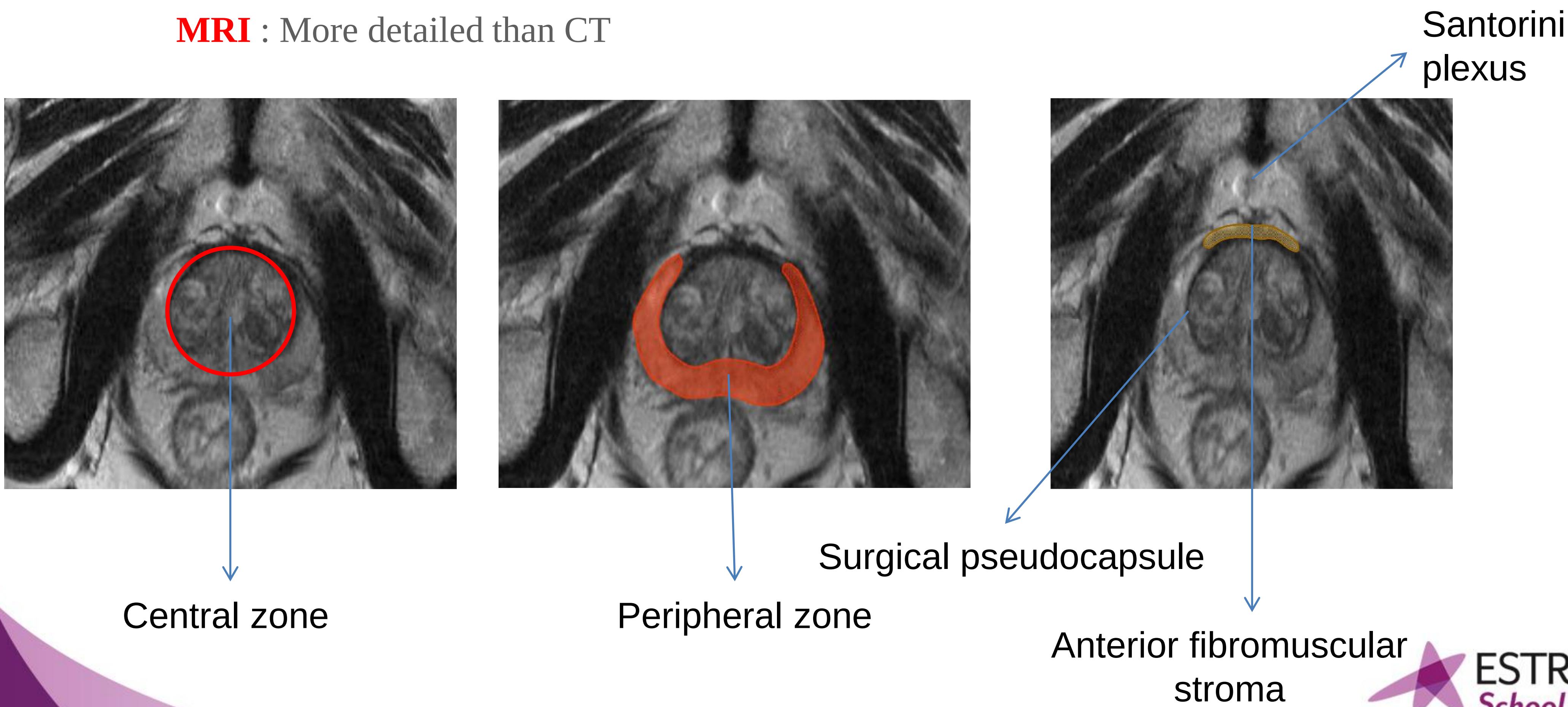
Prostate Contourning

- **GTV:** Usually subclinical malignant disease
- **CTV:** Whole prostate (it contains the GTV at a certain probability level)
- **PTV**: Geometrical concept to compensate, among others, physiological movements, variations in size, shape, and position of the CTV during RT.

MRI : More detailed than CT



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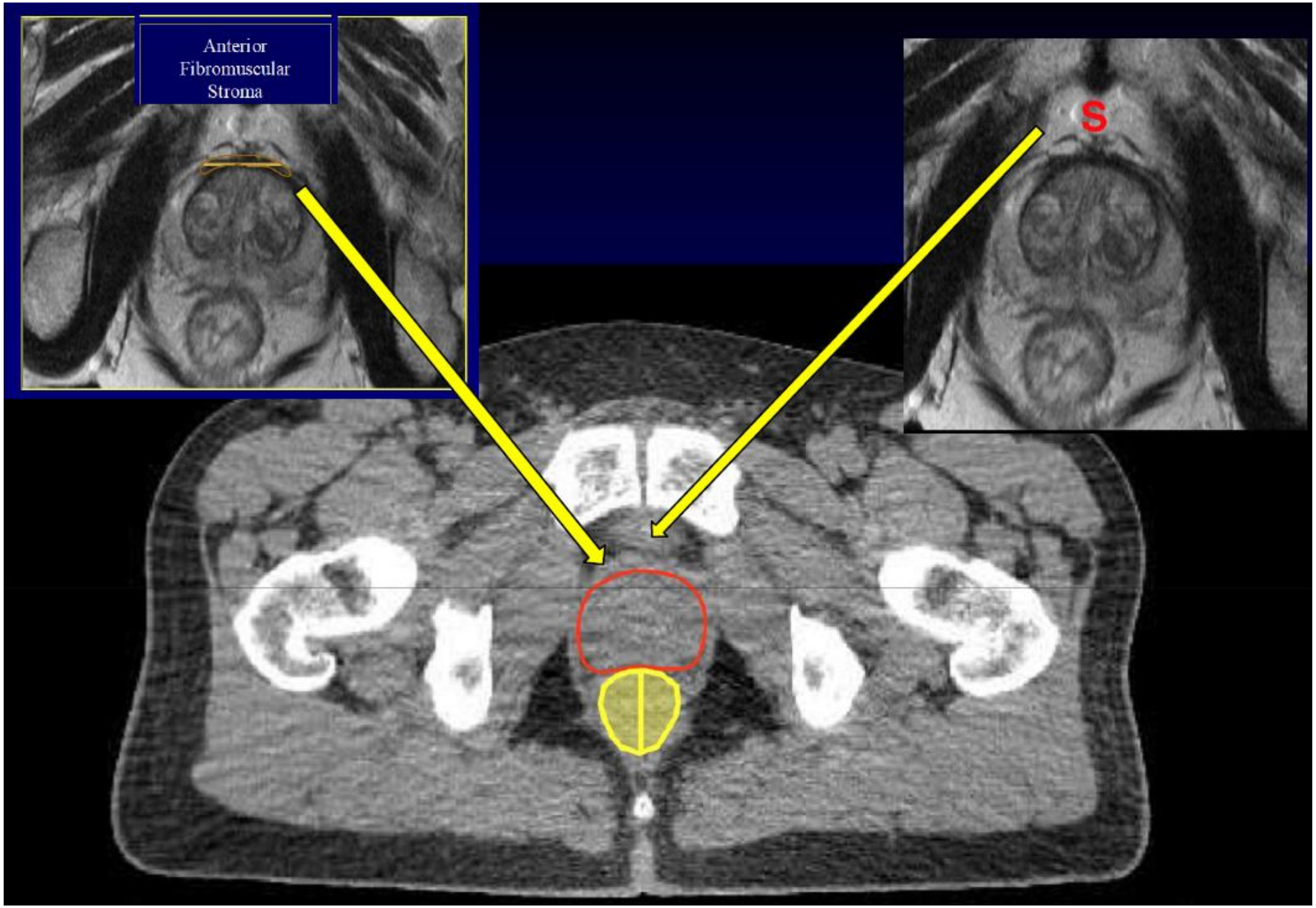
Delineation on CT-scan



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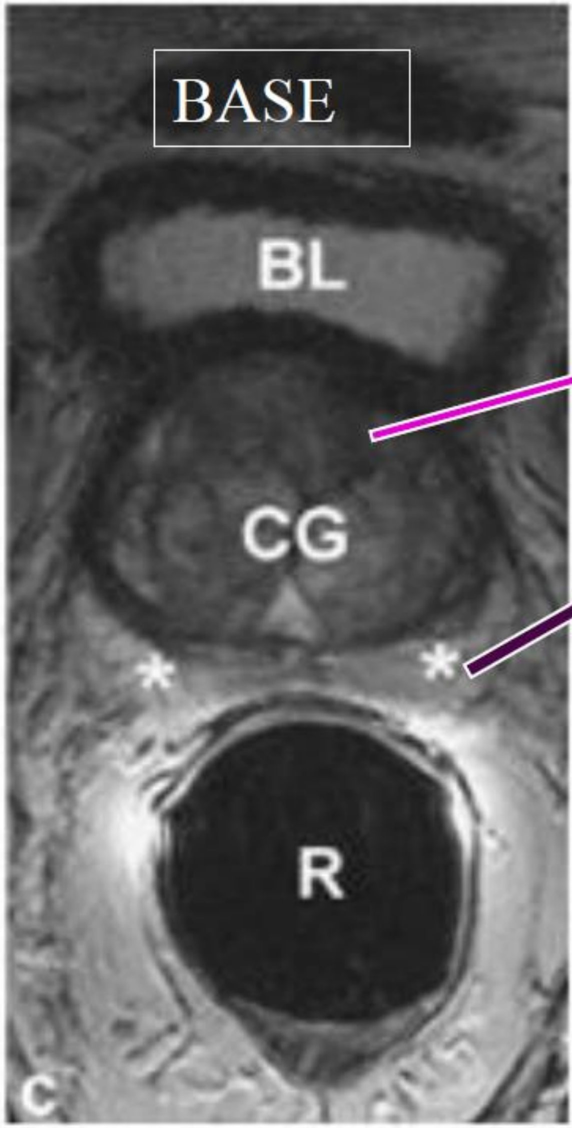
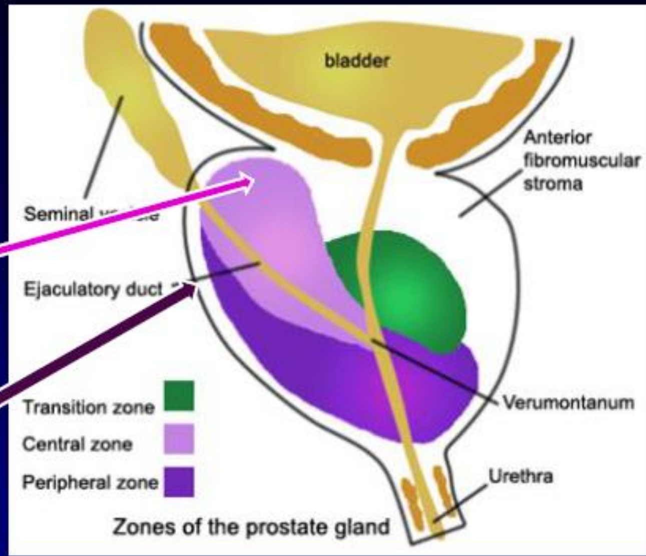
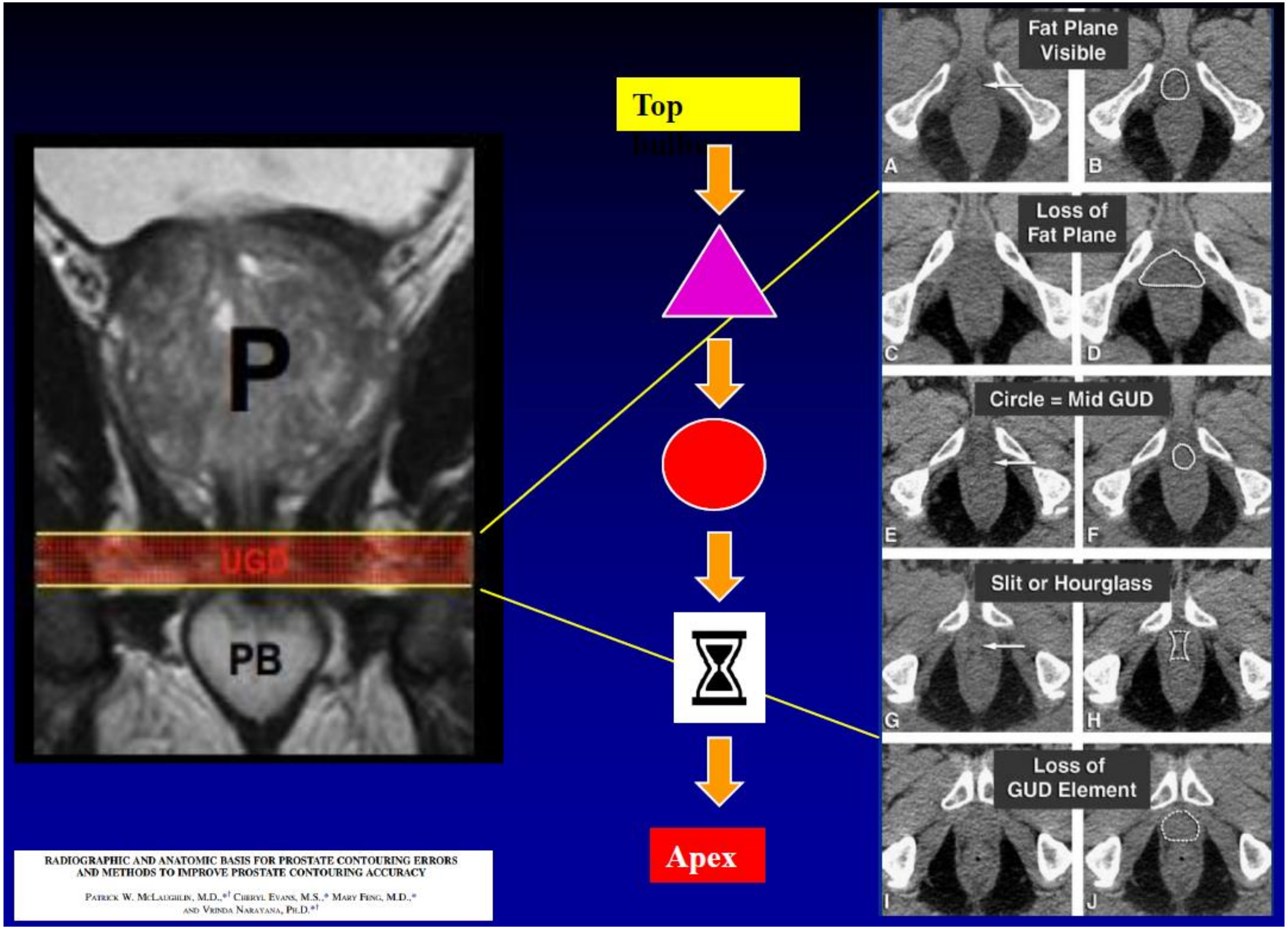




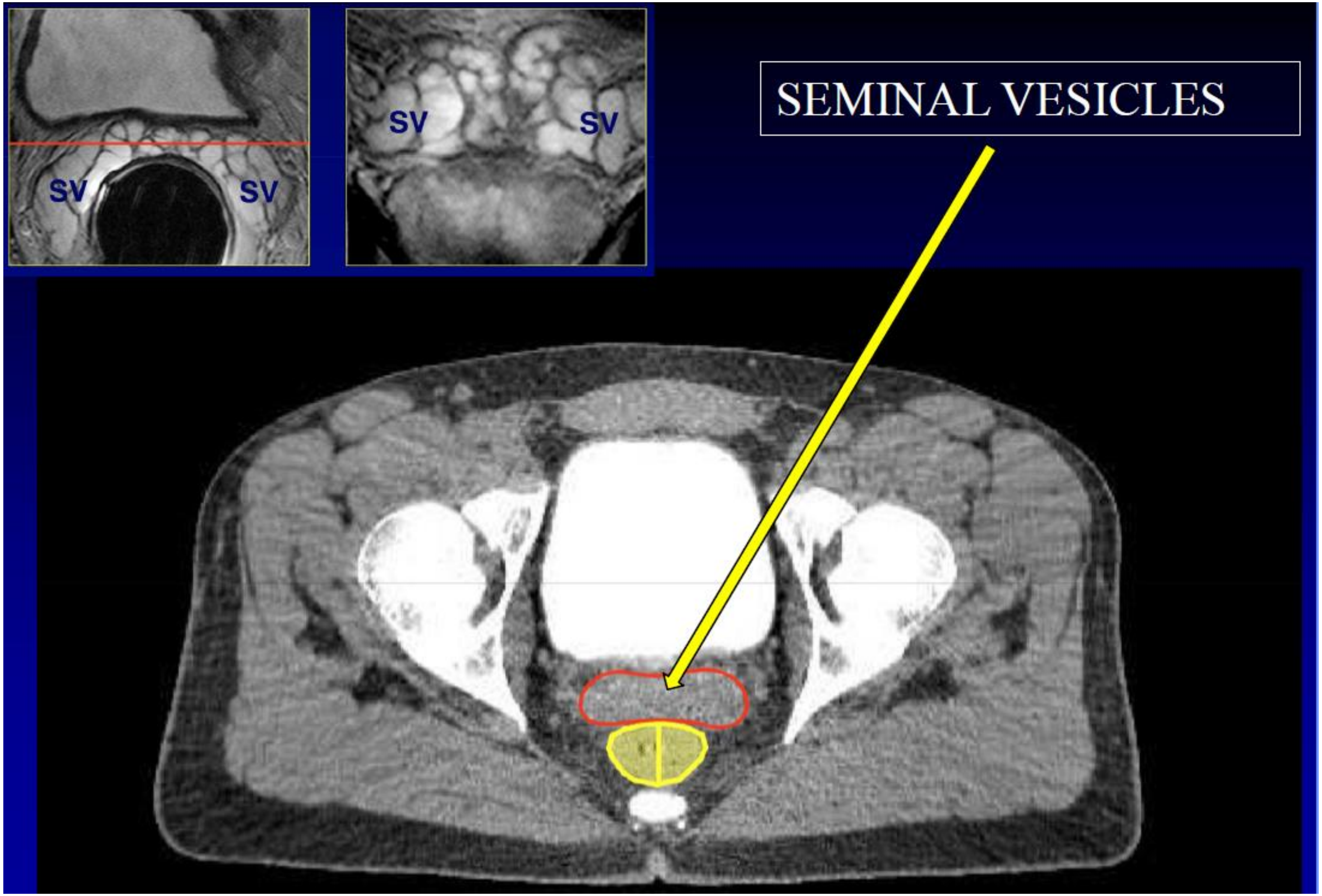
- Almost entirely composed of mixed signal-intensity central gland
- Narrow posterior band of high signal-intensity peripheral zone tissue

Where is the apex??



Looking for the apex…

- Distal part of the prostatic urethra
- High signal-intensity peripheral zone tissue


SV
SV
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SV
SEMINAL VESICLES

Analysis of fiducial marker-based position verification in the external beam radiotherapy of patients with prostate cancer

Uulke A. van der Heide*, Alexis N.T.J. Kotte, Homan Dehnad, Pieter Hofman, Jan J.W. Lagenijk, Marco van Vulpen

Department of Radiation Oncology, University Medical Center, CX Utrecht, The Netherlands

Abstract

Purpose: Evaluate the fiducial marker-based position verification in the external-beam radiotherapy of patients with prostate cancer.

Methods: Four hundred and fifty-three patients with prostate cancer received an IMRT treatment combined with fiducial marker-based position verification. Portal images were taken in all 35 treatment fractions. This database was used to study the accuracy of detecting the prostate position as well as the presence of time trends and the effectiveness of commonly used off-line correction protocols.

Results: The variation in inter-marker distance shows that the prostate position can be detected with an accuracy better than 0.6 mm. Significant time trends in prostate position occurred in 35%, 18% and 48% of the patients in the vertical, lateral and longitudinal directions, respectively, with 34%, 9% and 35% deviating more than 3 mm over the course of the treatment. Off-line correction protocols that estimate a deviation only in the first fractions of the treatment (shrinking action level (SAL), no action level (NAL)) are not effective in following these trends. With daily off-line position correction using an adapted SAL protocol we reduced systematic positioning errors in clinical practice to less than 0.8 mm in all directions.

Conclusion: Fiducial markers are a reliable tool for prostate position verification. Time trends occur frequently. Correction procedures must take such trends into account.

 Radiotherapy and Oncology 82 (2007) 38–45.

Radiotherapy and Oncology 82 (2007) 38–45

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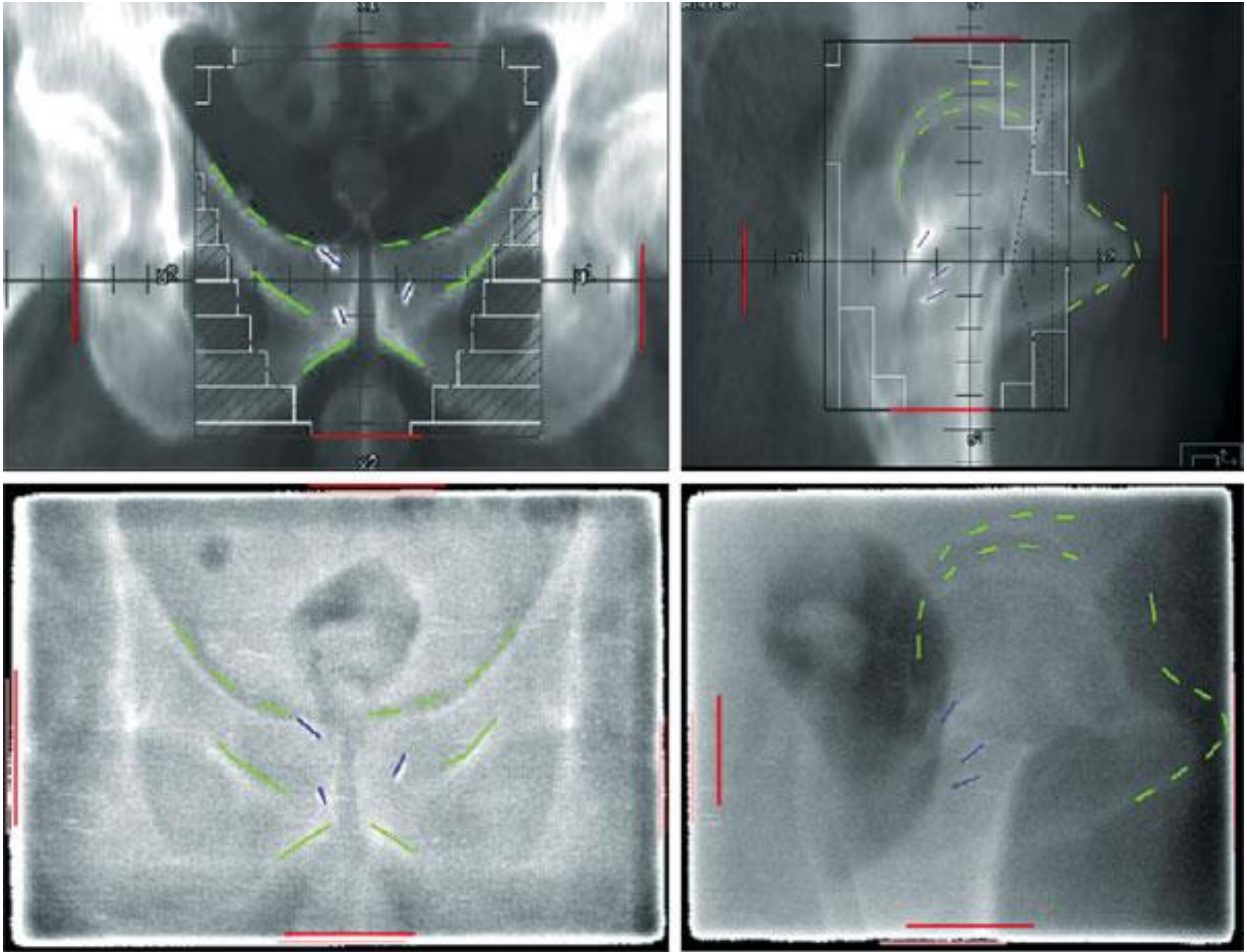
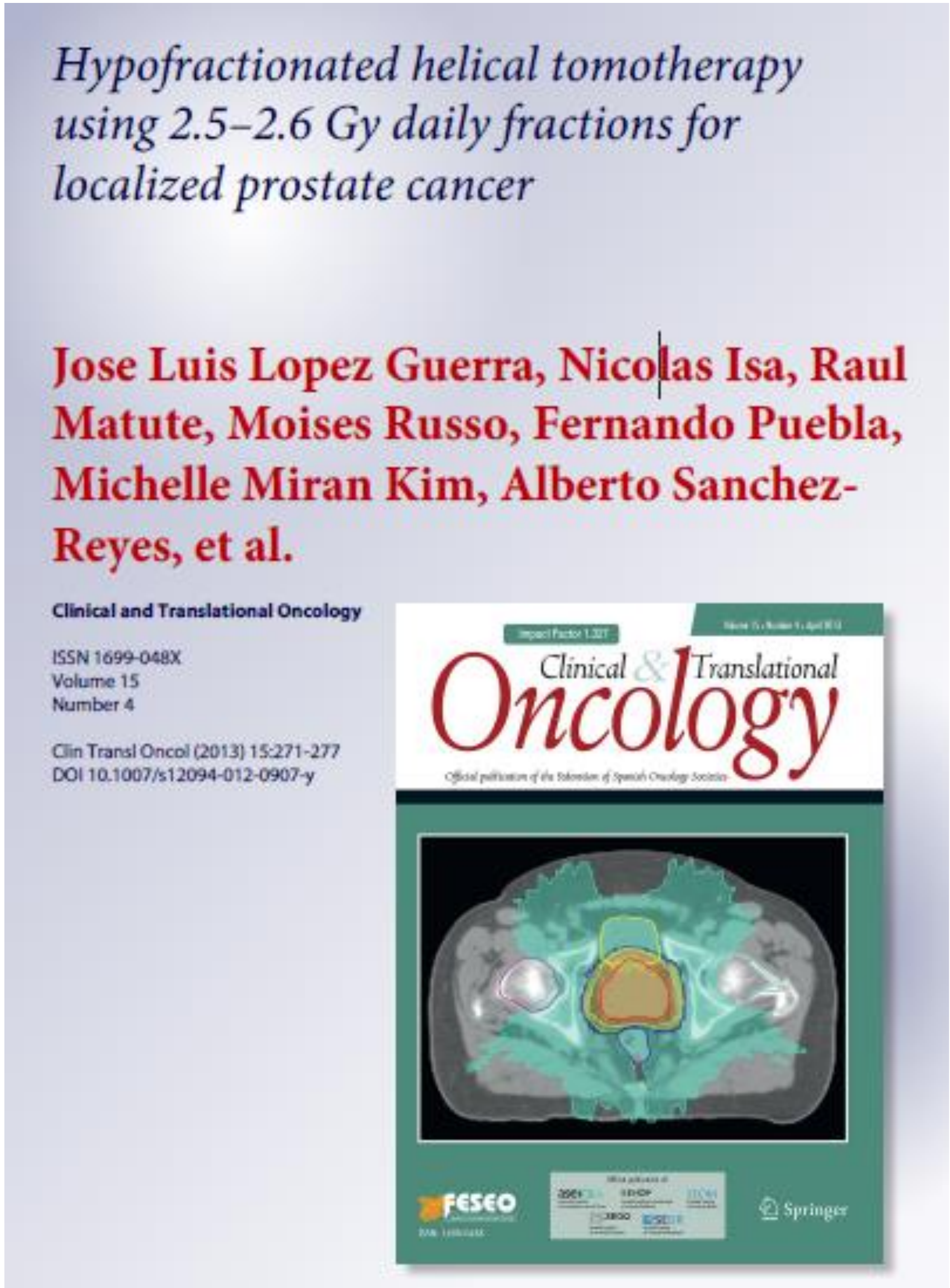


http://www.nature.com/nrclinonc/journal/v7/n10/images/nrclinonc.2010.135-f4.jpg

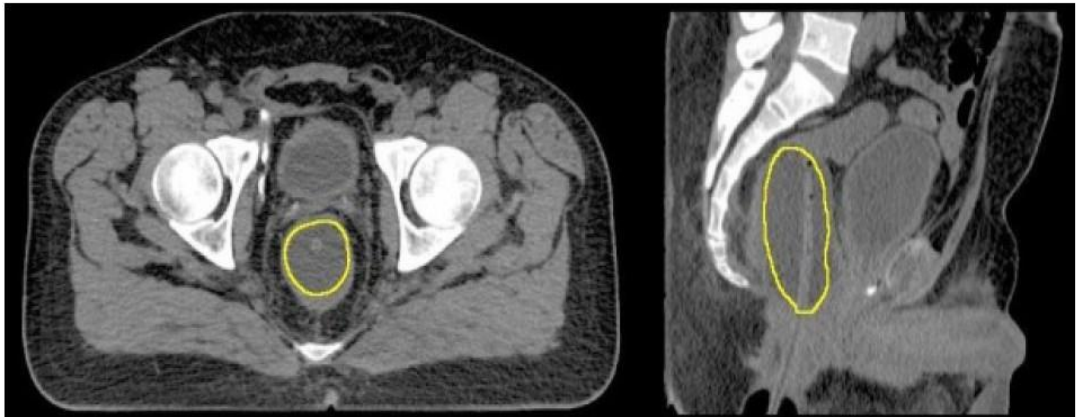

Hypofractionated helical tomotherapy using 2.5–2.6 Gy daily fractions for localized prostate cancer

Jose Luis Lopez Guerra, Nicolas Isa, Raul Matute, Moises Russo, Fernando Puebla, Michelle Miran Kim, Alberto Sanchez-Reyes, et al.

Clinical and Translational Oncology

ISSN 1699-048X
Volume 15
Number 4

Clin Transl Oncol (2013) 15:271-277
DOI 10.1007/s12094-012-0907-y

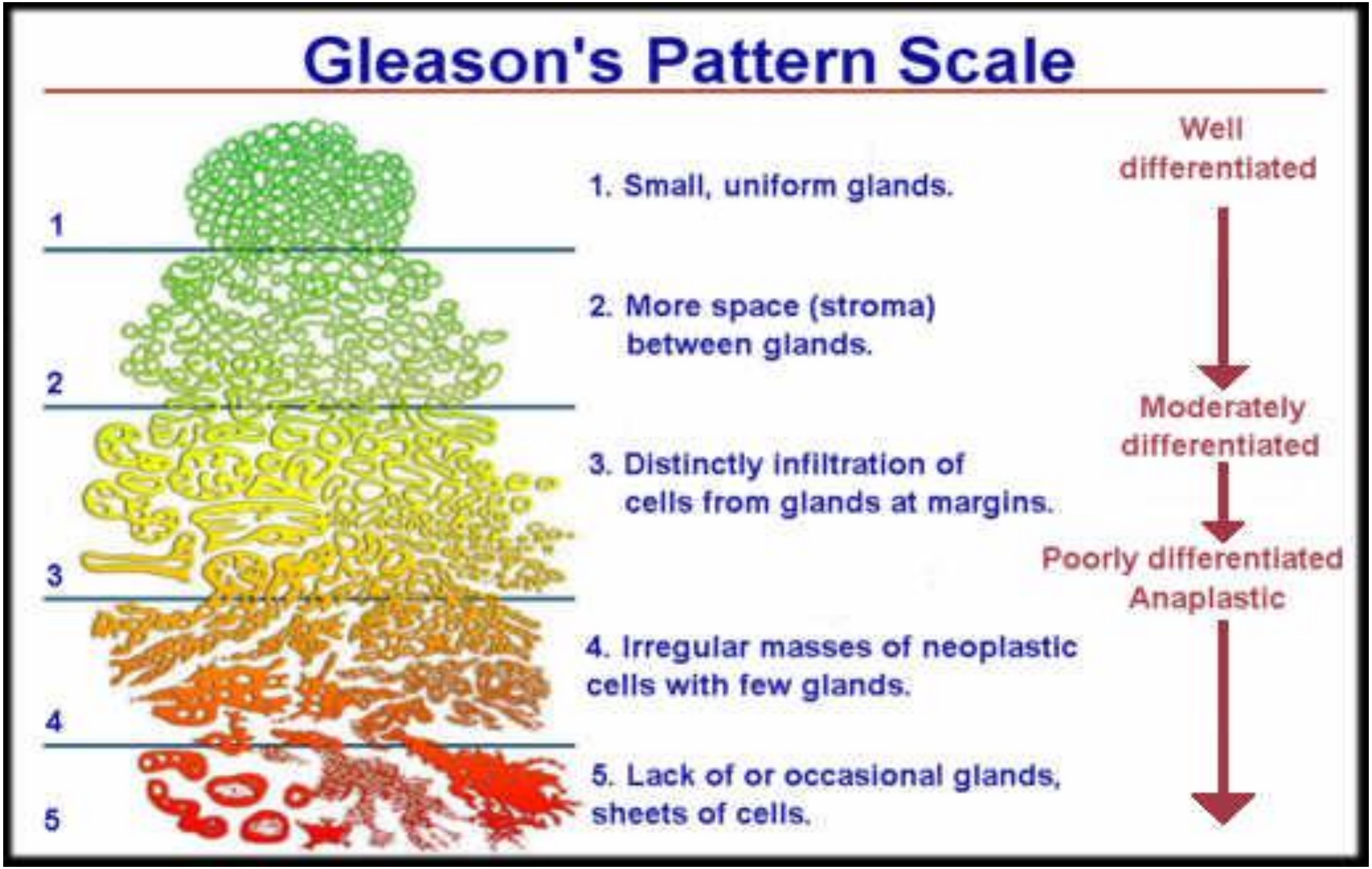


"Various trials did not find any relation between the percentage of bladder/rectum volume receiving a certain radiation dose and ***acute*** *urinary/rectal toxicity"*

2017 updated data showed a significant association between Rectum V50-V70 and ***late*** *GI toxicity*

Case 1: patient with stage N+ (D1) disease

- A 78-year-old man was shown to have a prostate-specific antigen (PSA) level of 18 ng/mL in a routine evaluation.
- His physical exam was normal and the digital rectal examination revealed a slightly enlarged prostate (87 cc by transrectal ultrasound).
- Prostatic biopsy revealed a Gleason score 8 (4 + 4) adenocarcinoma in 7 of 12 specimens.
- His past medical history was significant for systemic hypertension and dyslipidemia.

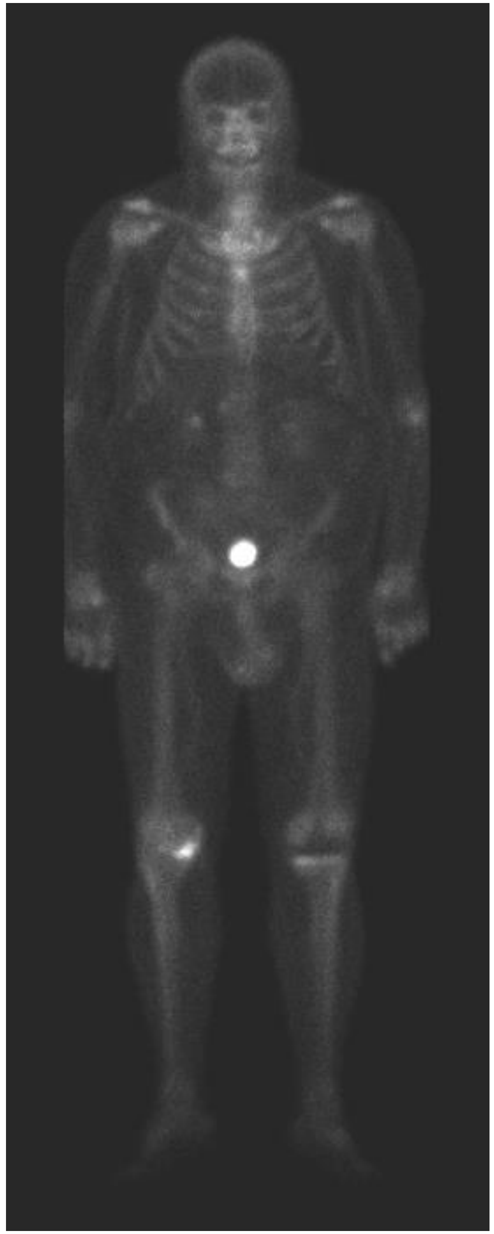

Gleason's Pattern Scale
1
2
3
4
5
1. Small, uniform glands.
2. More space (stroma) between glands.
3. Distinctly infiltration of cells from glands at margins.
4. Irregular masses of neoplastic cells with few glands.
5. Lack of or occasional glands, sheets of cells.
Well differentiated
Moderately differentiated
Poorly differentiated
Anaplastic

Case 1: patient with stage N+ (D1) disease

- A 78-year-old man was shown to have a prostate-specific antigen (PSA) level of 18 ng/mL in a routine evaluation.
- His physical exam was normal and the digital rectal examination revealed a slightly enlarged prostate (87 cc by transrectal ultrasound).
- Prostatic biopsy revealed a Gleason score 8 (4 + 4) adenocarcinoma in 7 of 12 specimens.
- His past medical history was significant for systemic hypertension and dyslipidemia.

- Laboratory data: normal values
- Chest X-ray negative

- ...ing... e ch... over the body and no definite evidence of metastatic bone disease was noted.



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- Abdominal CT scan showed enlarged pelvic lymph nodes (left obturator area, right internal iliac)

Prostate

- **Regional lymph nodes:**
  Pelvic
  Hypogastric
  Obturador
  Iliac (internal, external)
  Sacral (lateral, presacral, promontory)

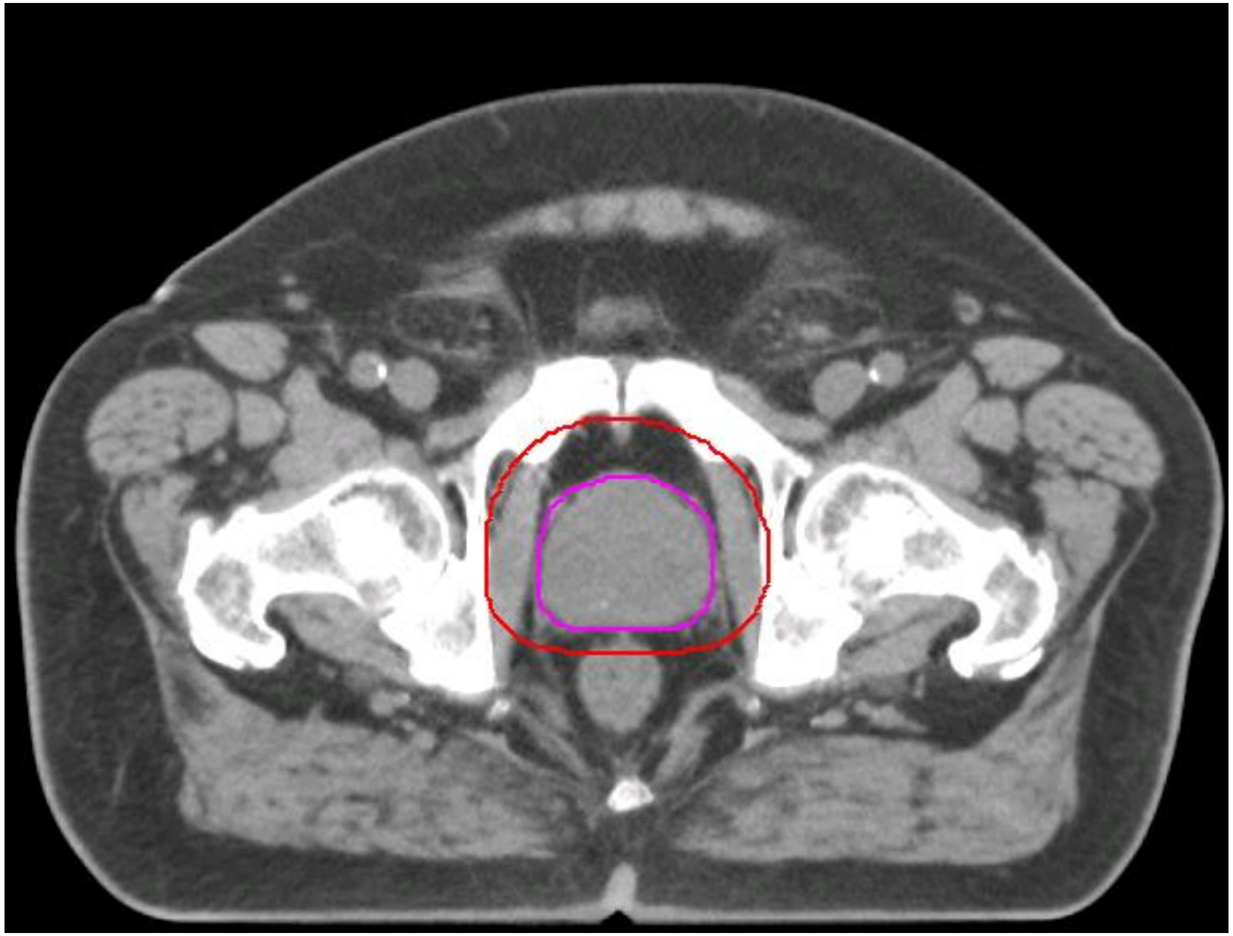
- **Distant lymph nodes:**
  Aortic (para-aortic lumbar)
  Common iliac
  Inguinal, deep
  Superficial inguinal (femoral)
  Supraclavicular
  Cervical
  Escalene
  Retroperitoneal

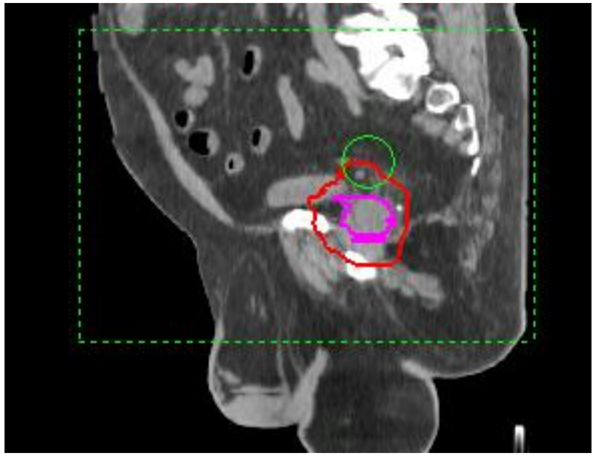
- Diagnosis: Stage IV Prostate Cancer (cT1cN1M0)
- Treatment: Hormonal Therapy + Radiation Therapy

Hormonal therapy:
- Neoadjuvant and Adjuvant Androgen deprivation therapy.

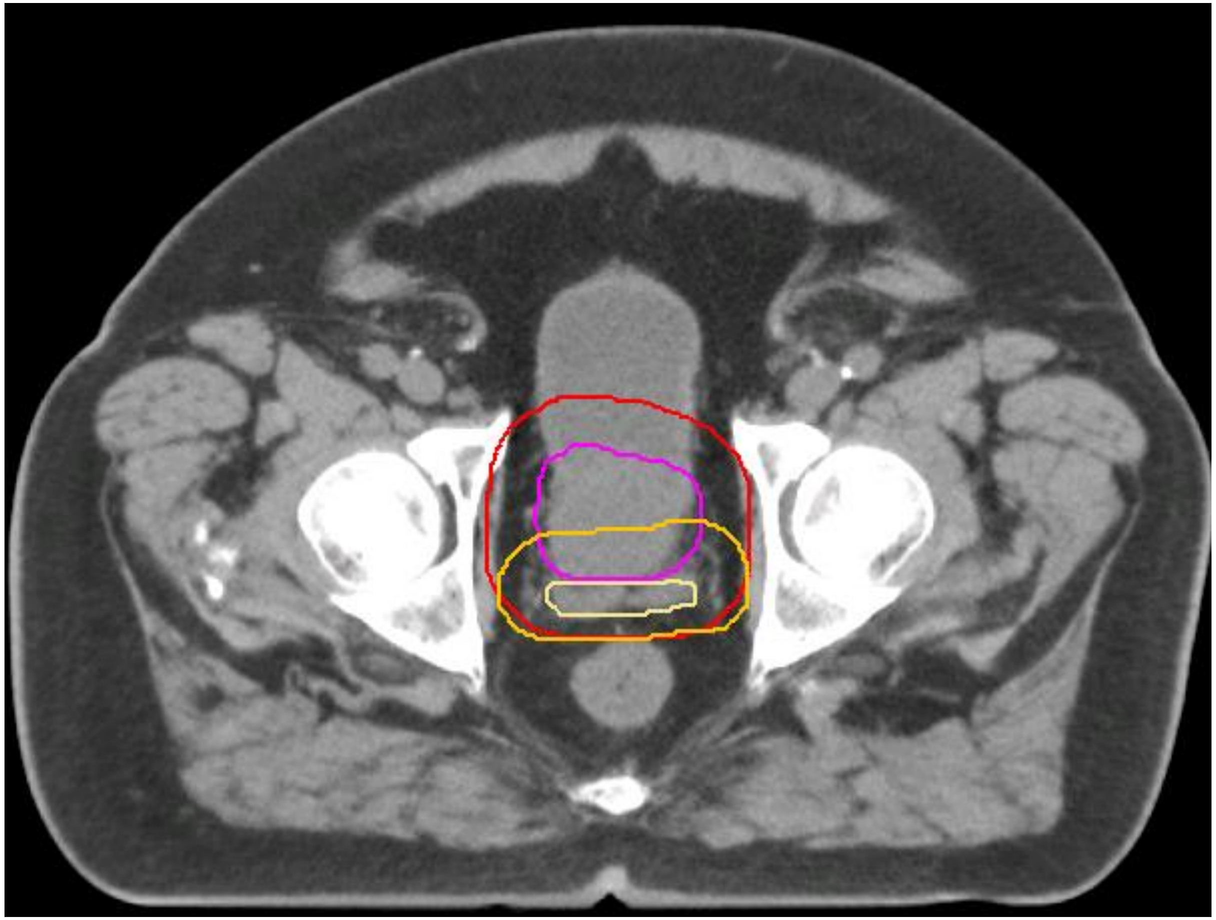
Radiation Therapy Dose Prescription:
- PTV (prostate gland+5mm margin): 65 Gy at 2.32 Gy/fraction
- Seminal vesicles: 60 Gy at 2.14 Gy/fraction
- Enlarged left obturator and right internal iliac lymph nodes, 60 Gy at 2.14 Gy/fraction
- Pelvic lymph nodes , 50 Gy at 1.78 Gy/fraction

PTV (prostate gland+5mm margin)

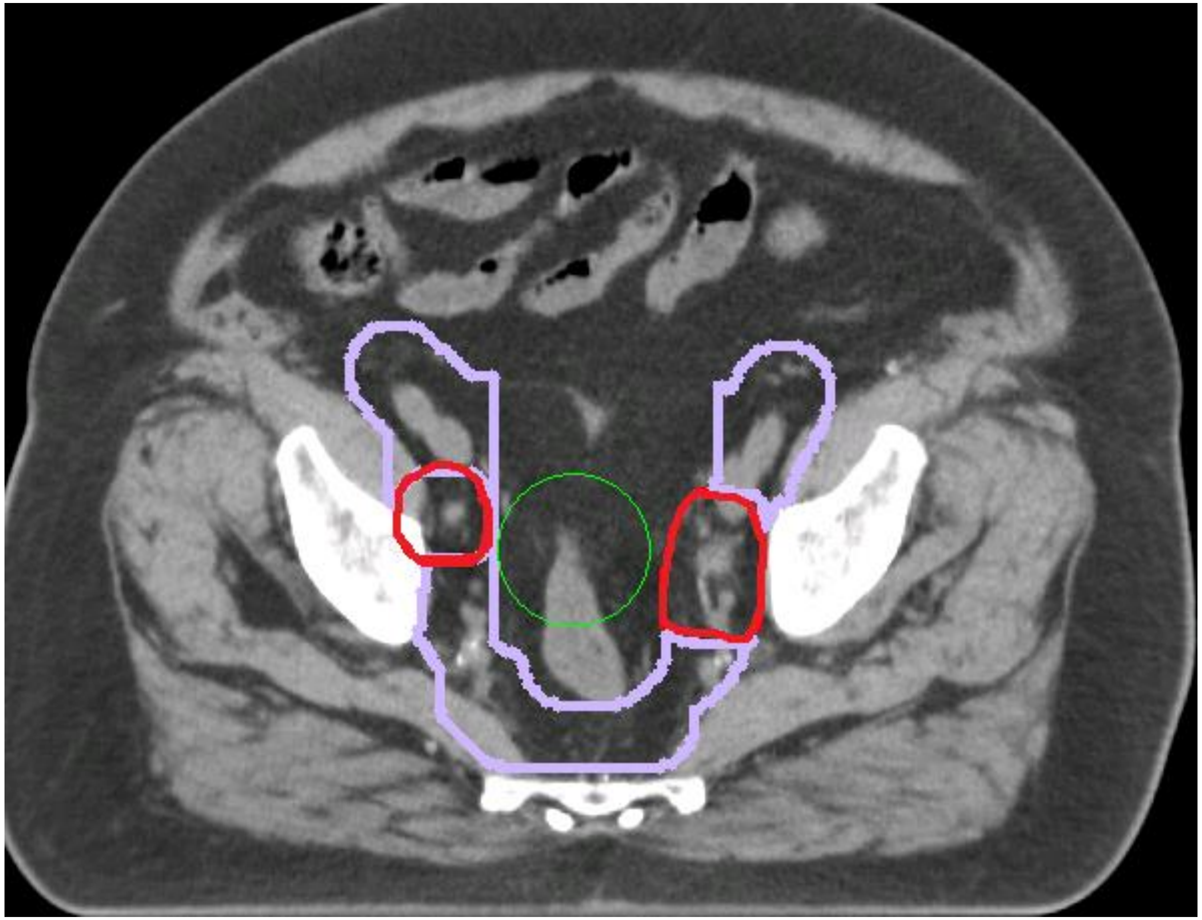




Seminal vesicles planning volume (orange)

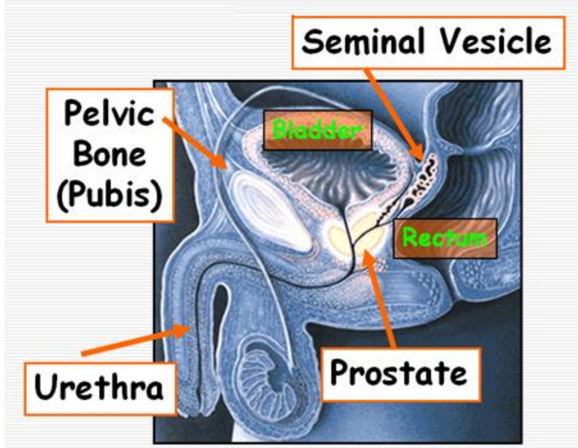


Pelvic lymph nodes planning volume (prophylactic [purple], positive [red])



Take home message

- The local therapy in lymph node metastasized prostate cancer seems to have benefit.
- Different strategies such as fiducial markers are needed for tumor location control with 2D technology
- OAR preparation is needed in order to decrease the risk of toxicity



Questions:

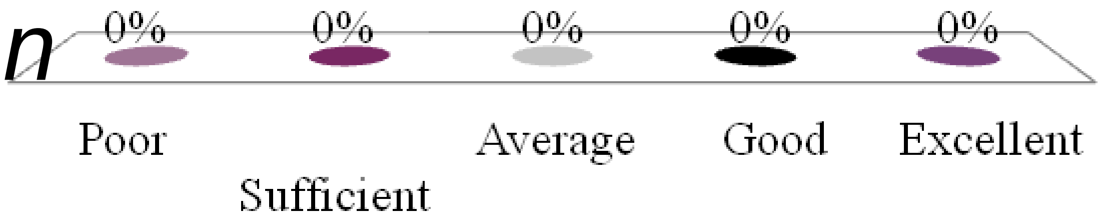
- Preparation (bladder, rectum)
- Positioning
- Tattoos
- Organ at risk contouring
- Set-Up
- Verification
- Radiation technique
-

???

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



Case report: **Cervix**

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Sofia Rivera, Gustave Roussy, Villejuif, France

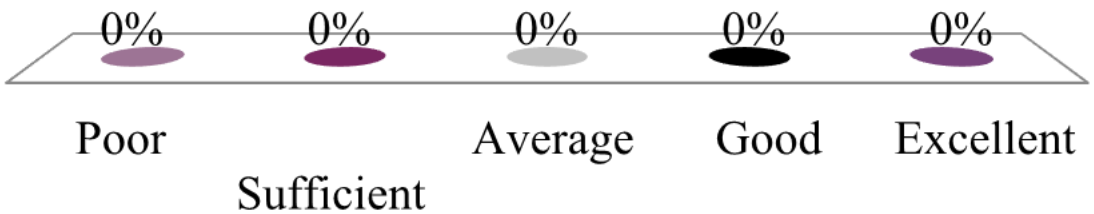
Case from the Gyn GEC ESTRO Network / FALCON WS
Courtesy of Pr Pötter

Advanced skills in modern radiotherapy
May 2018

FALCON
Fellowship in Anatomic deLineation & CONtouring

What are the true statements?

A. Cervical cancer is due to bad luck
B. cervical cancer is due to all HPV viruses
C. Cervical cancer is due to HPV 16 and 18 mostly
D. Cervical cancer is avoidable by screening smear
E. Cervical cancer is avoidable by vaccination



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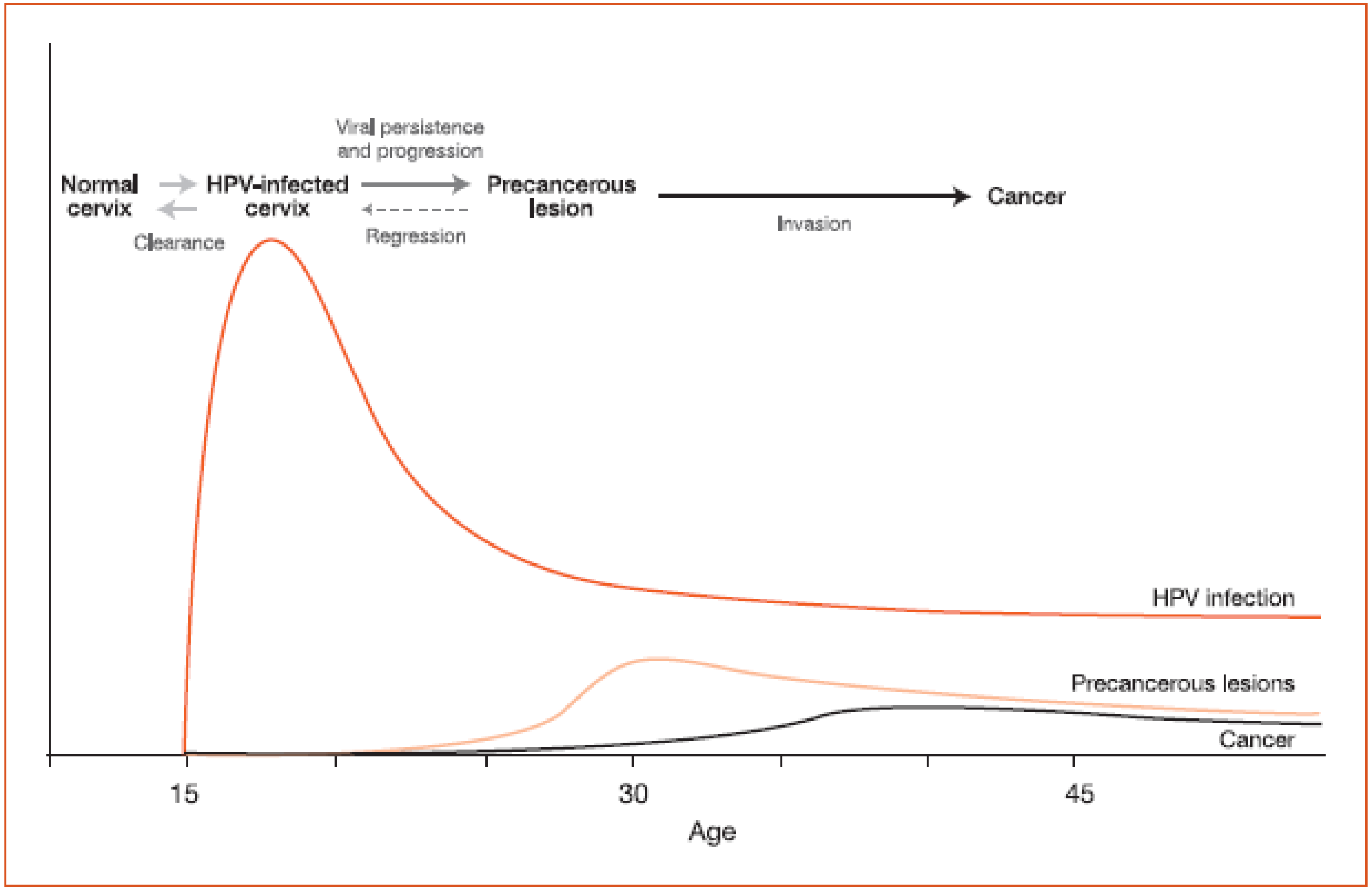
HPV infection natural history

Figure 1. Prevalence of HPV infection, precancerous lesions and cervical cancer by age of women



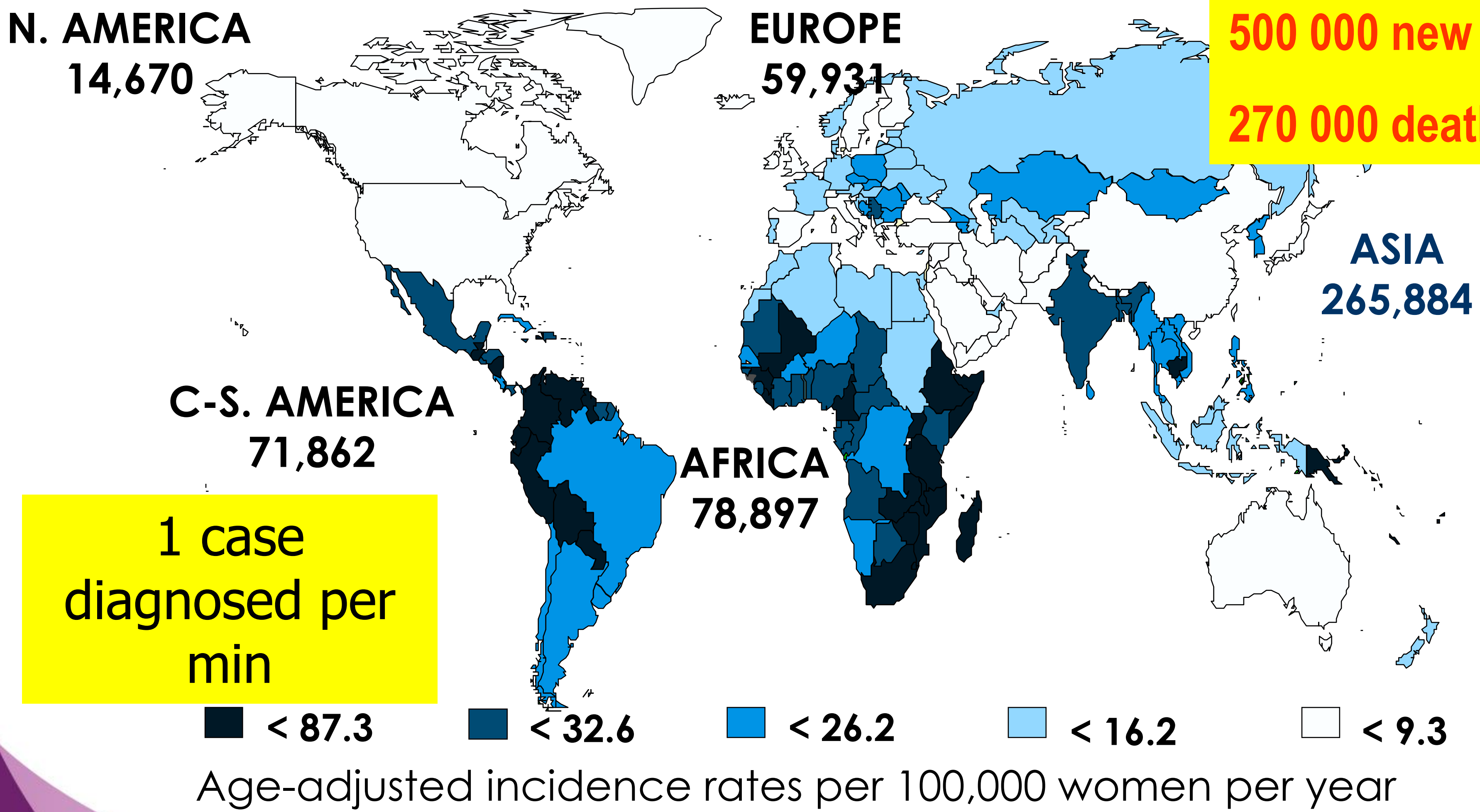
Source: Schiffman M, Castle PE. The promise of global cervical-cancer prevention. *New England Journal of Medicine*, 2005, 353(20): 2101–2103. (© 2005 Massachusetts Medical Society. Adapted with permission.)

Cervix cancer diagnosis OMS (2002)

1,4 Million cases

500 000 new cases/ year

270 000 death / year



1 case diagnosed per min

Whosis Statistical Database, 2012.

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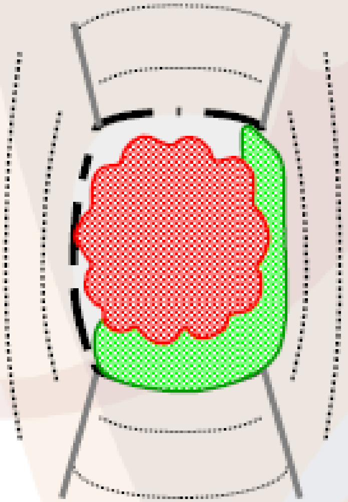
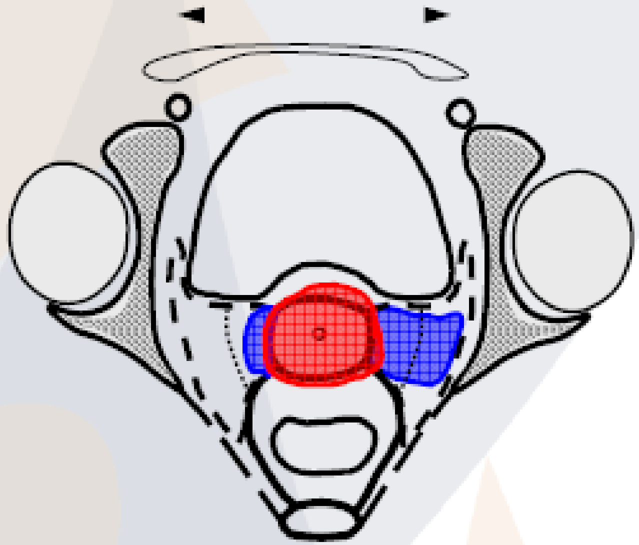
Patient History

- 42-year old woman.
- WHO performance status=0
- No clinical symptom
- No palpable node
- Squamous cell carcinoma, grade 3
- TNM: T3b N1 M0

Clinical findings of gyn. examination: at DIAGNOSIS

	Infiltrative	Exophytic
Cervix		
Vagina		
Parametria		





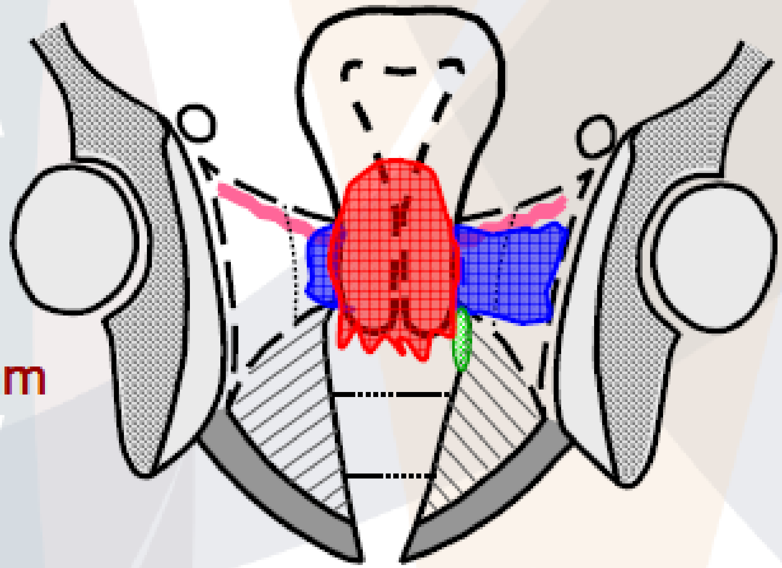
Dimensions:

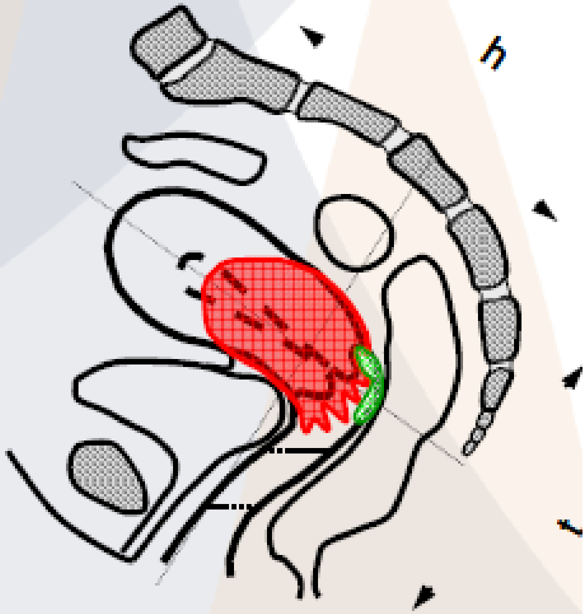
Width: 90 mm

Thickness: 50 mm

Height: 60 mm

Vaginal inv.: 20 mm





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Gyn contouring workshop
Barcelona, May 2012

*Radiological findings integrated on the drawing

Clinical findings of gyn. examination: SUMMARY

FIGO stage: IIIB

	At diagnosis	At brachytherapy
Width	90 mm	
Thickness	50 mm	
Height*	60 mm	
Left parametrium	Infiltration to pelvic wall	
Right parametrium	Proximal infiltration	
Vagina	20 mm: left & posterior wall	
Bladder**	Not infiltrated	
Rectum**	Not infiltrated	

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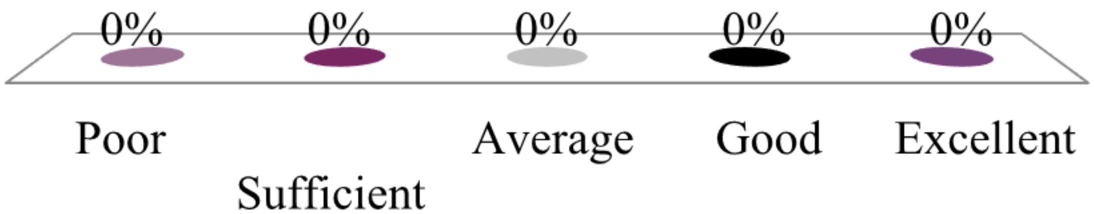
*Some uncertainty in assessment of height

**Endoscopy at diagnosis

What is the best imaging modality for volume definition in the pelvic region?

A. CT
B. PET CT
C. MRI
D. PET MRI
E. Ultrasound



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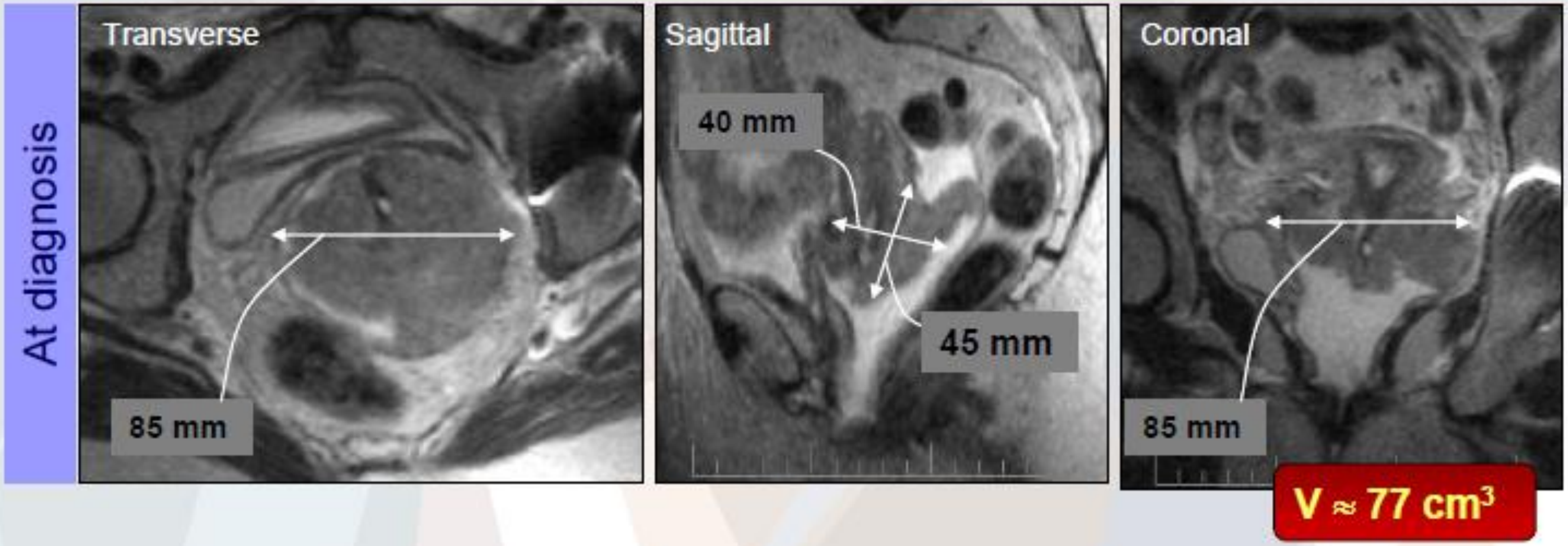
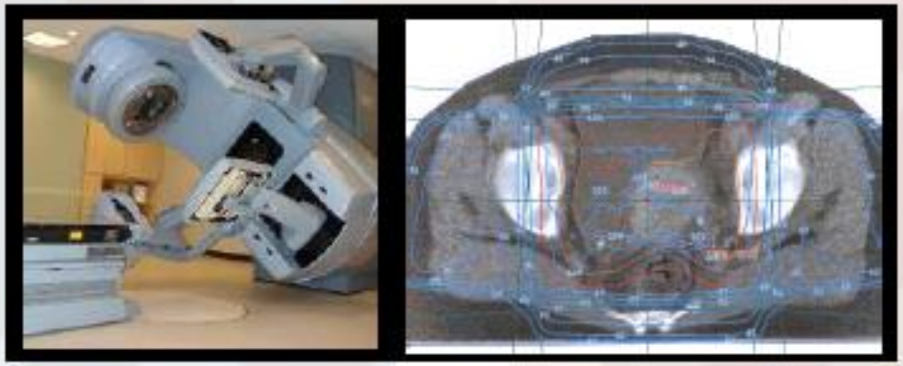
MRI findings



Comment:

Only the representative slices are shown here. Use the information from complete initial MRI data set to fully understand the extent and topography of the tumour.

EBRT, Chemotherapy & timing of BT



Technique: 3D, CT based CRT; box
TD: 45 Gy
Dose per fraction: 1,8 Gy

Concomitant chemotherapy:
Cisplatin 40 mg/m2 weekly, 5 cycles

2 x 7 Gy 2 x 7 Gy

Prescribed to HR CTV

High Dose Rate

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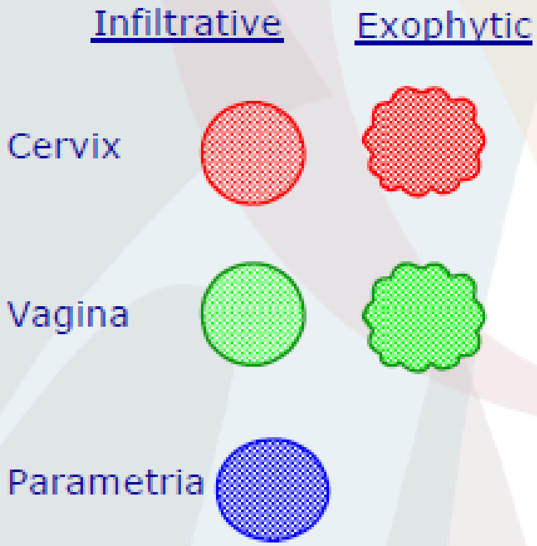
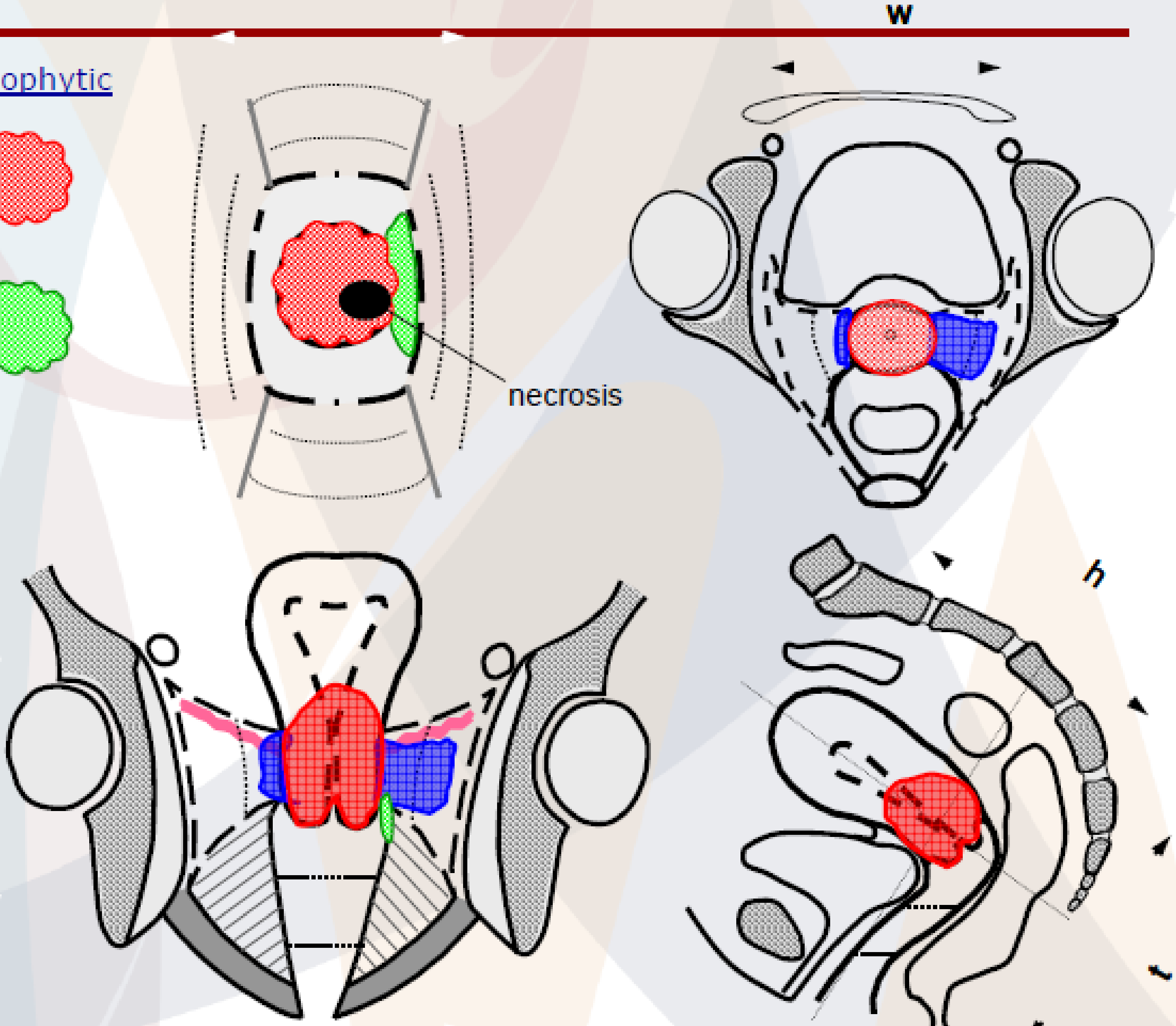
Barcelona, May 2012

Clinical findings of gyn. examination: at Brachytherapy





Dimensions:

Width: 70 m

Thickness: 40

Height: 40

Vaginal inv.: 10

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Clinical findings of gyn. examination: SUMMARY

FIGO stage: IIIB

	At diagnosis	At brachytherapy
Width	90 mm	70 mm
Thickness	50 mm	40 mm
Height*	60 mm	40 mm
Left parametrium	Infiltration to pelvic wall	Distal infiltration (≈ 30 mm)
Right parametrium	Proximal infiltration	Proximal infiltration (≈ 10 mm)
Vagina	20 mm: left & posterior wall	10 mm: left fornix
Bladder**	Not infiltrated	NA
Rectum**	Not infiltrated	NA

*Some uncertainty in assessment of height

**Endoscopy at diagnosis

Brachytherapy application

Tandem & Ring

Interstitial parametrial needles according to tumour spread

↳ Following applicator insertion:

pelvic MRI with the applicator in place

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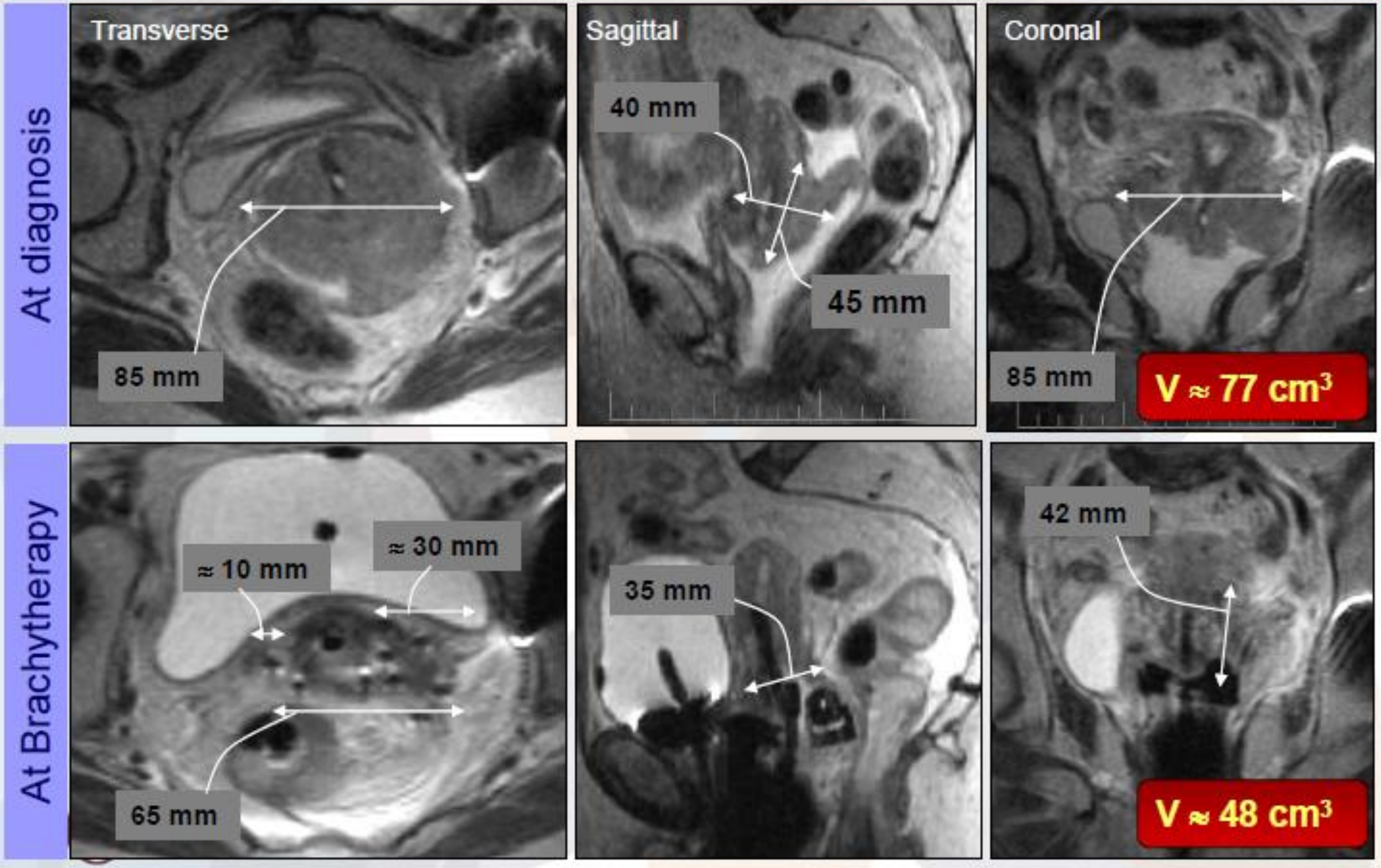
Barcelona, May 2012

MRI findings



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]

[a]*Department of Radiotherapy and Radiobiology, Medical University of Vienna, Austria,* [b]*Department of Radiotherapy, Brachytherapy Unit, Institut Gustave Roussy, Villejuif, France,* [c]*Department of Radiotherapy, University Hospital Gasthuisberg, Leuven, Belgium,* [d]*Department of Radiation Oncology, Centre George-Francois Leclerc, Dijon, France,* [e]*Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI, USA,* [f]*Service de Radiodiagnostic, Institut Curie, Paris, France*

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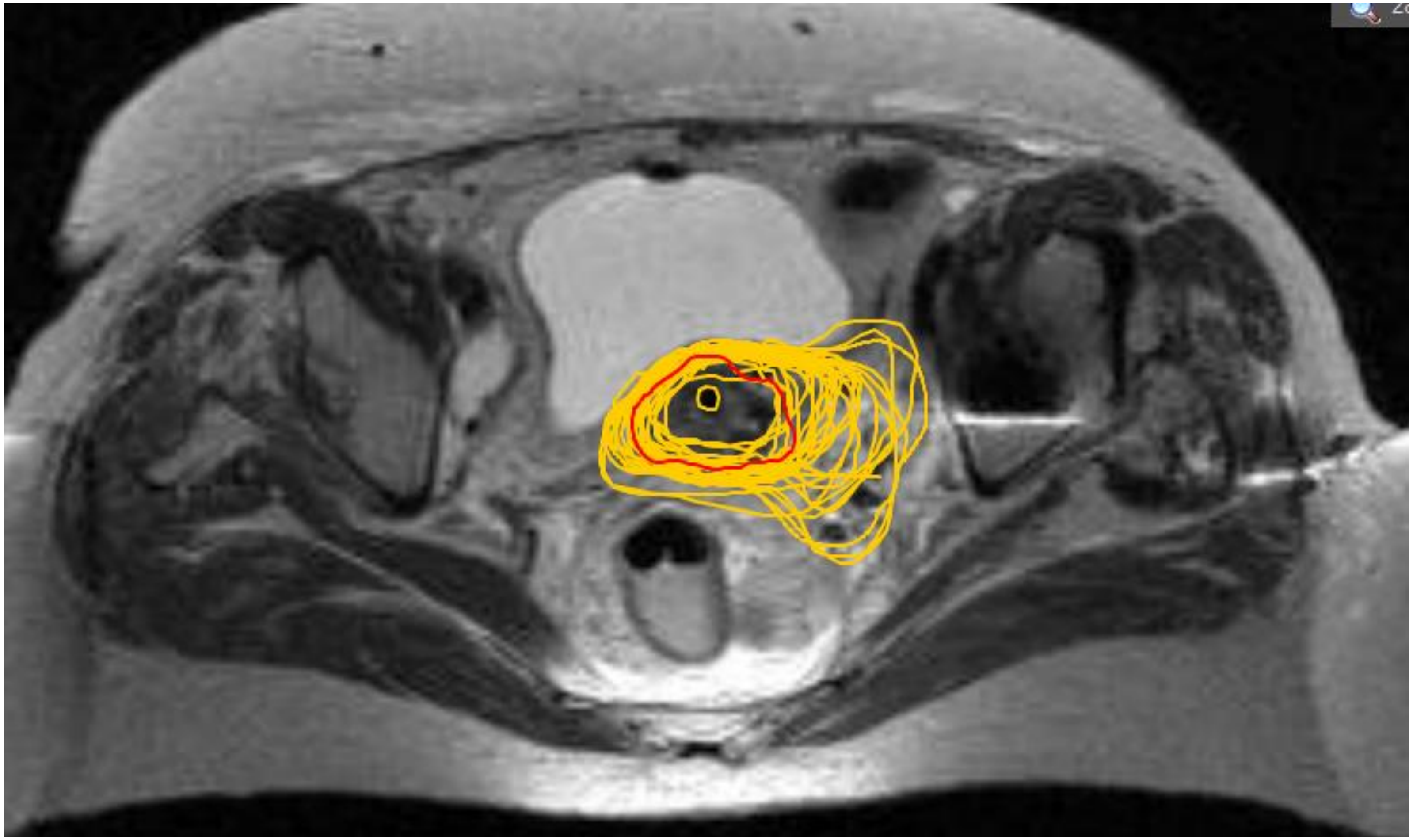
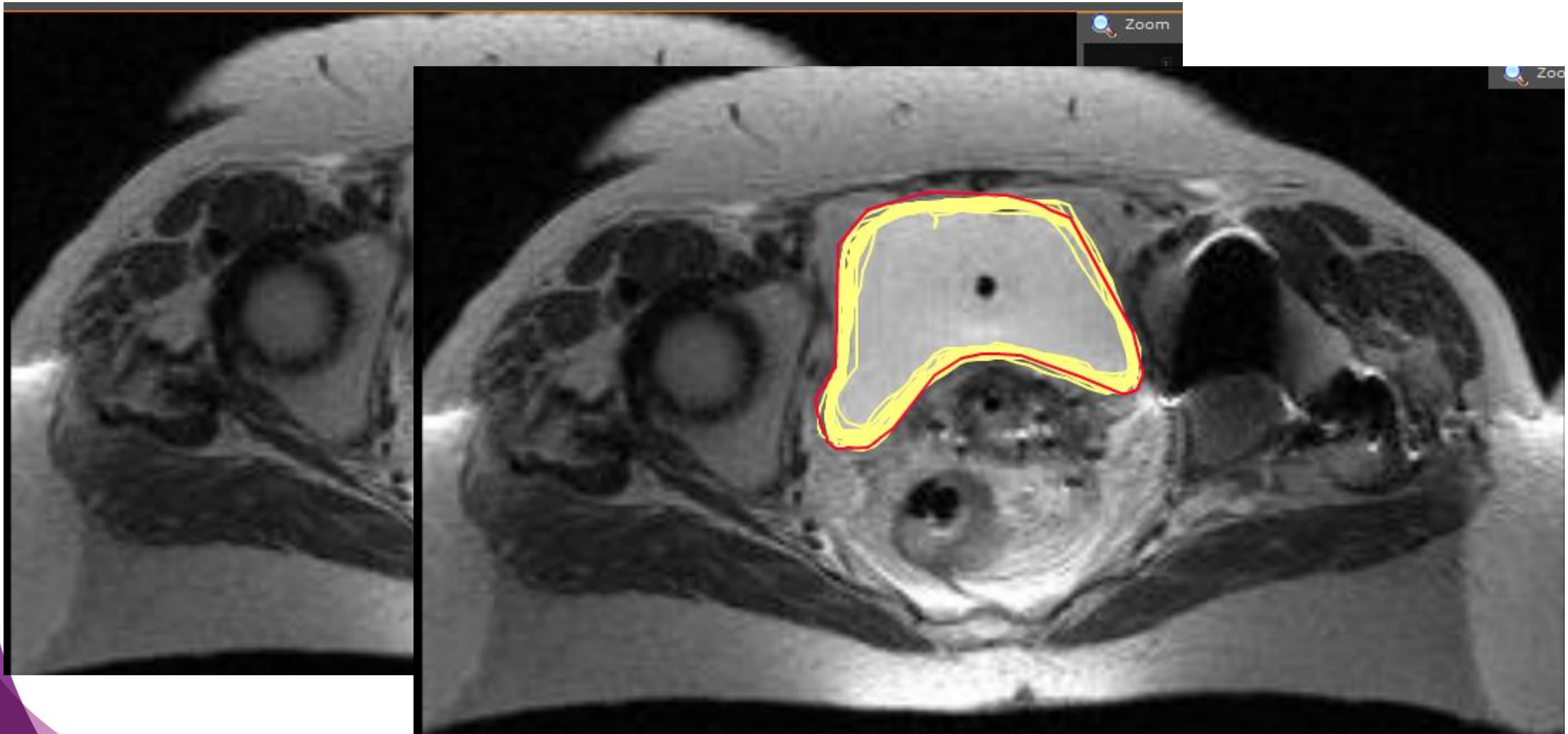
Heterogeneity in contouring target volumes besides the use of guidelines

- High Risk CTV



Quite good homogeneity in some OAR contouring

- Where anatomical bundaries are well visible



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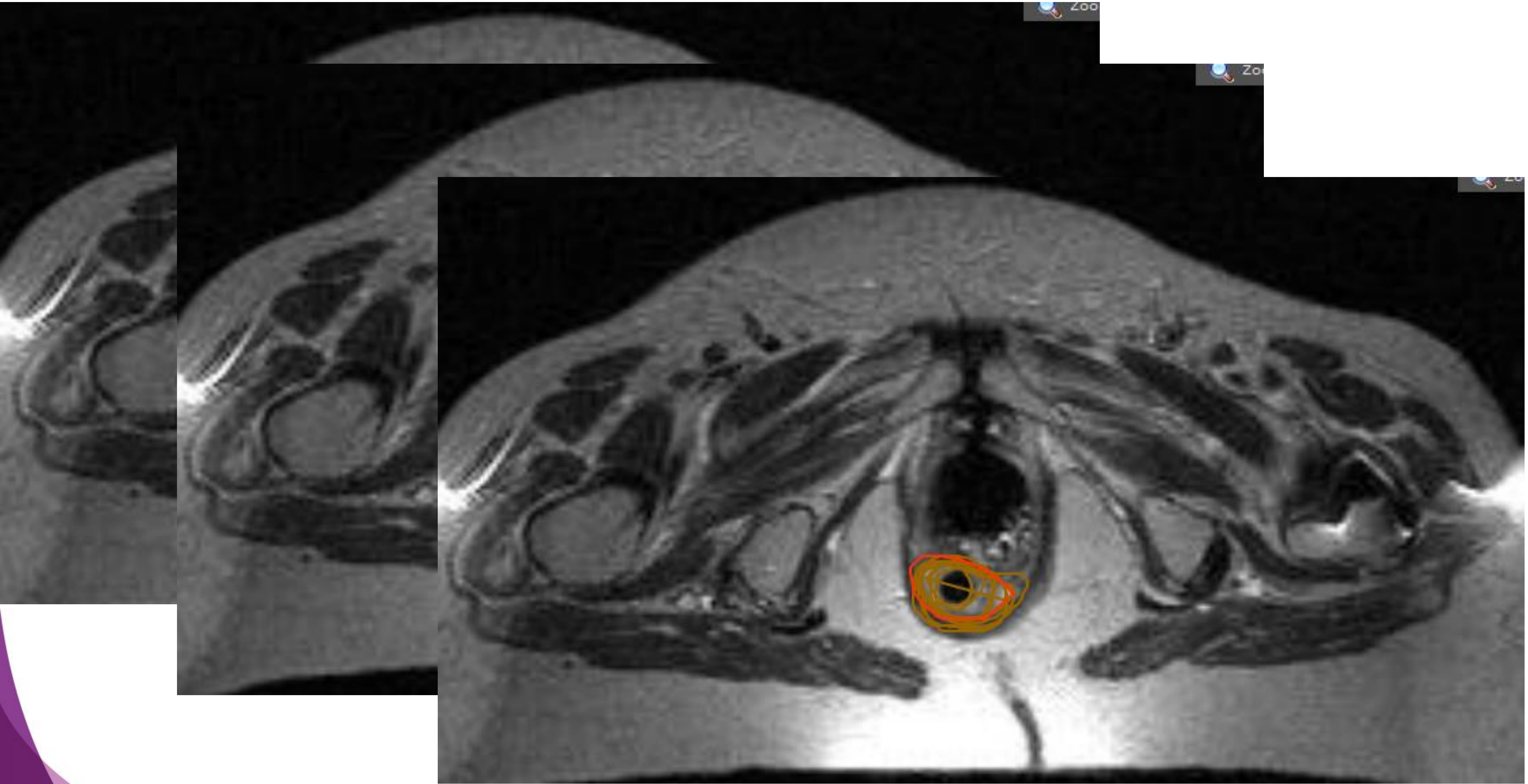
But it's not always the case!



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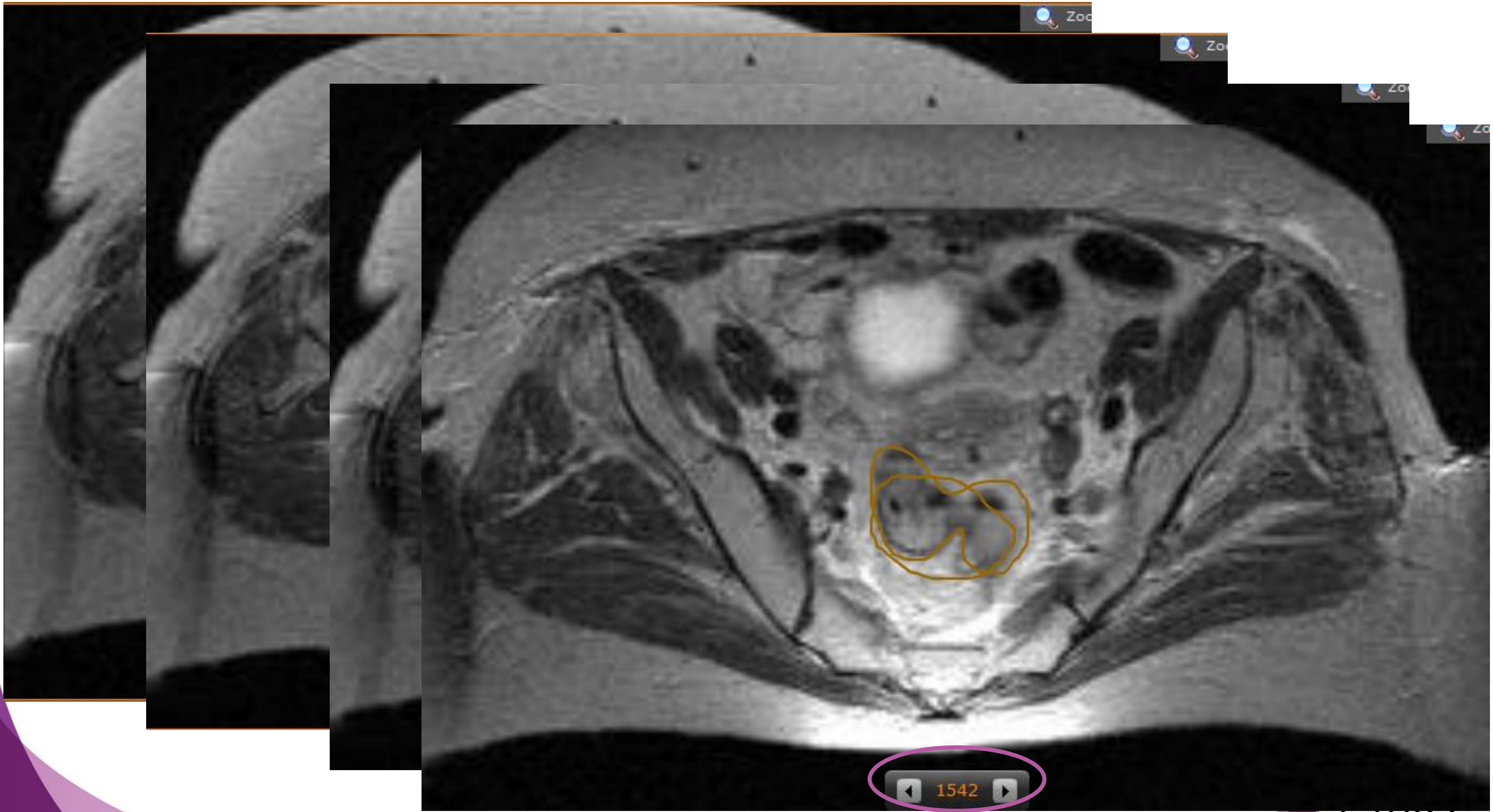
Upper and lower limits are a source of heterogeneity in contouring as well



5 slices = 1,5cm difference in the upper limit of the rectum

Take home messages:

- High quality CT, MR imaging and clinical examination are crucial for contouring targets and OAR in the pelvic region

- High quality re-imaging and clinical examination are key points in cervical cancer to adapt contours for brachytherapy dosimetry

- MR is a key imaging modality in gynecology

Breast IGRT:
An RTT Perspective

Liz Forde, RTT
Assistant Professor
The Discipline of Radiation Therapy
School of Medicine
Trinity College Dublin

Fundamental IGRT Questions

- ***When*** *should I image?*
  - *Frequency*
- ***How*** *should I image?*
  - *Technology*
  - *Projection*
- ***What*** *can I see?*
  - *What is my target*
- ***What*** *should I match to?*
  - *Surrogate for target position*

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Site Specific Points to Consider

- Laterality
  - ➢ Right/Left
    - ▪ Cardiac dose
- Patient positioning
  - ➢ Supine, Prone or lateral decubitus
- Target volume
  - ➢ Whole or Partial Breast
  - ➢ Boost
- Simulation
  - ➢ 3D or 4D
- Breathing motion
  - ➢ DIBH
  - ➢ Free breathing

All of these factors will influence how we image this patient group

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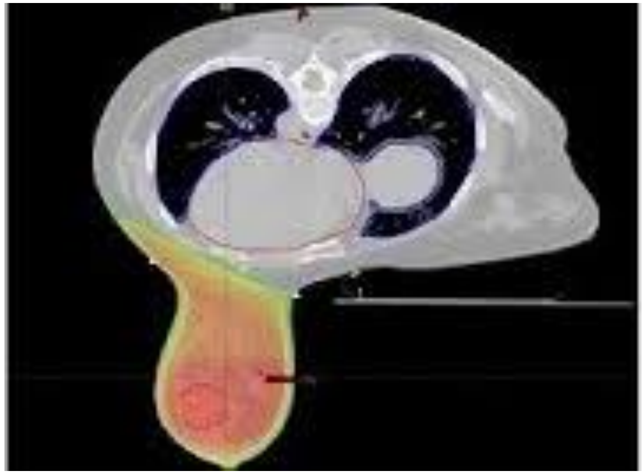
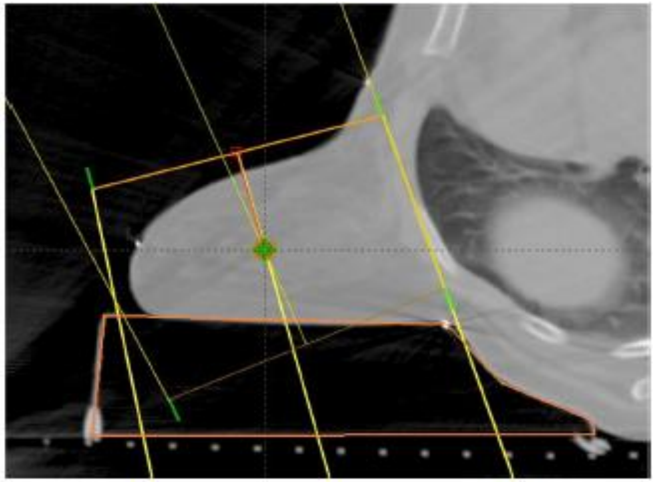
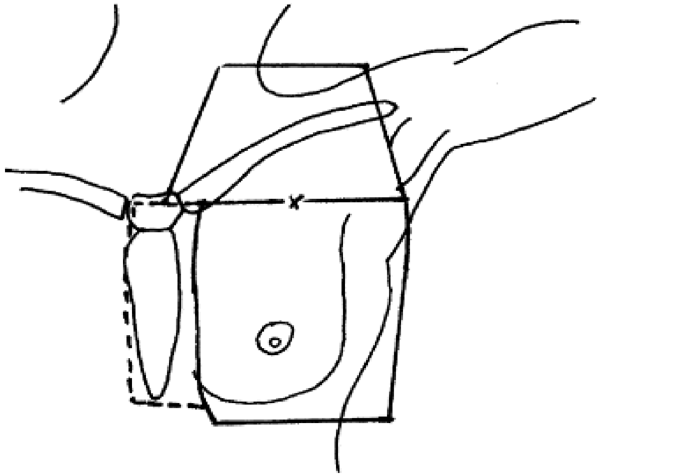


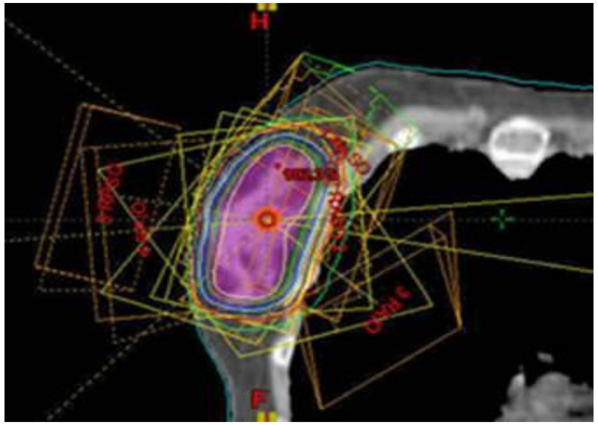
Prone



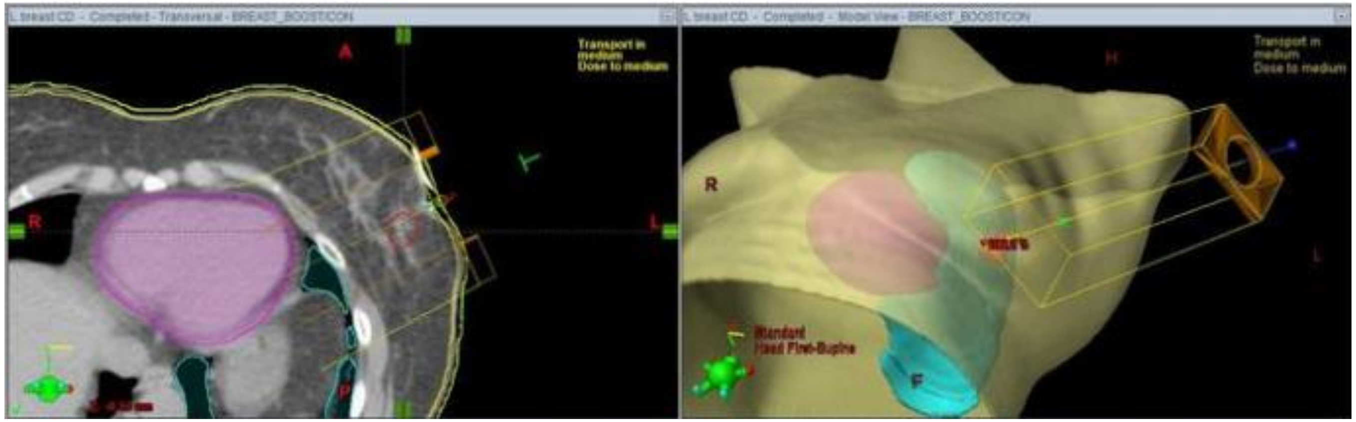
Lateral decubitus



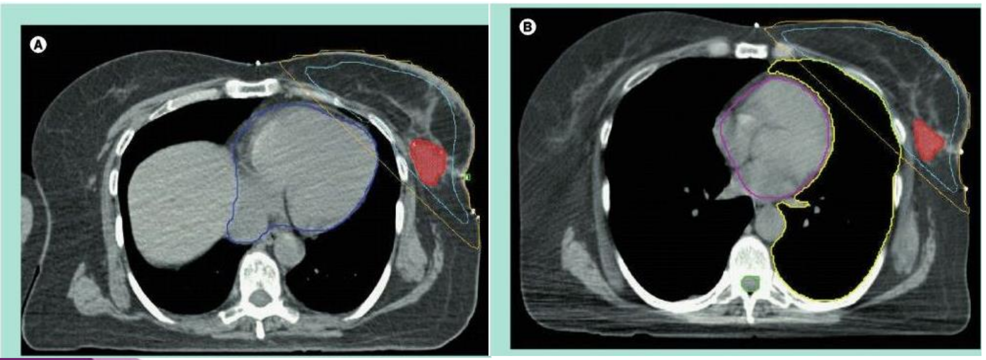
Supine: IMC (ph/e junx)



APBI



Electron boost to surgical bed



DIBH

IMRT and VMAT

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On Treatment Verification

- ***Look! There is it! I can see the target!***
  - ➢ Whole breast RT

- Confirm gross external positioning information
  - ➢ Light field
  - ➢ FSDs

- What else do we want to see?
  - ➢ Contour changes
  - ➢ Tumour bed
  - ➢ Seroma
  - ➢ Surgical clips

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Match Anatomy

- Breast contour
- Lung volume
- Ribs
- Seroma
- Surgical Clips

Surgical Clips

- Act as a surrogate for the tumour bed
- Improve accuracy in delineation and used for positional verification
- Clip insertion after breast conservation surgery
- Caution artefact on planning CT
  - ➢ Impact on electron beam dosimetry?

- Either use directly in match or export isodose lines from planning to ensure they fall within required dose
  - ➢ Donovan *et al.*, 2012
  - ➢ Similar to Post Prostatectomy clips

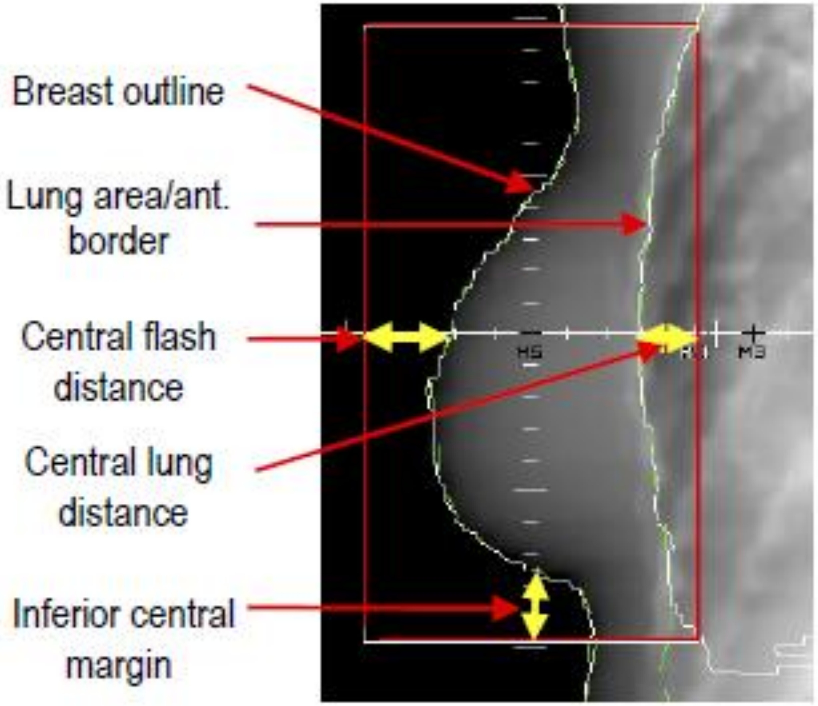
On Treatment IGRT

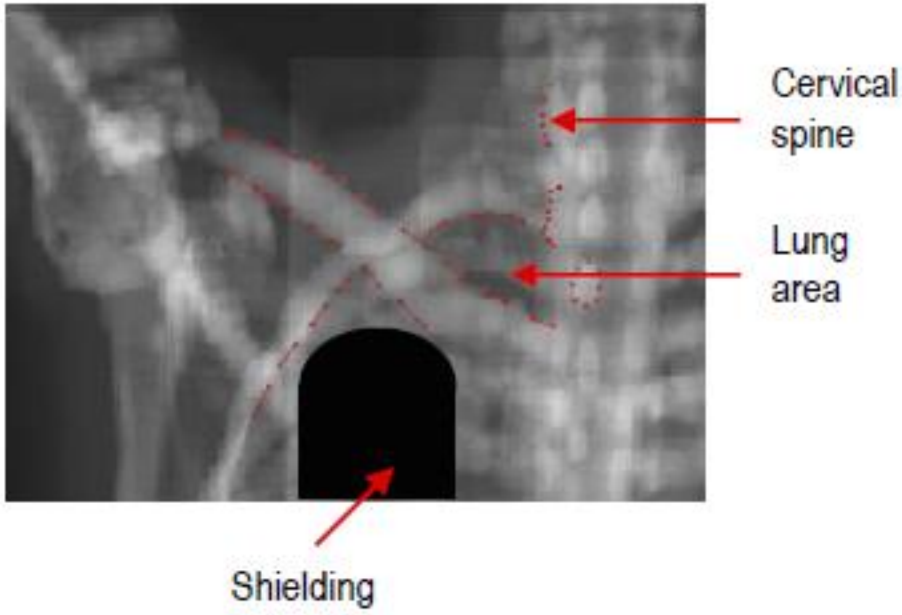
- Largely driven by what is available to you
- Make the most of it
- Consider the clinical impact
  - ➢ Tighter margins?
  - ➢ Reduced Toxicity?

MV 2D

- Widely available
- Ability to acquire continuous "snapshot" during the fraction
- Will provide field border information
- Will provide assessment of lung volume, breast contour
- Adequate for whole breast RT with standard fractionation
- Typically 5mm tolerance is acceptable
- Difficult to visualise surgical clips
- Depending on lung in field, generally sufficient information from a "single" acquisition

MV 2D





On Target: Ensuring geometric accuracy in radiotherapy. 2008

2D/2D (Paired orthogonal 2D)

Used for isocentre position check

Field border information is not displayed

A minimum requirement for all advanced techniques

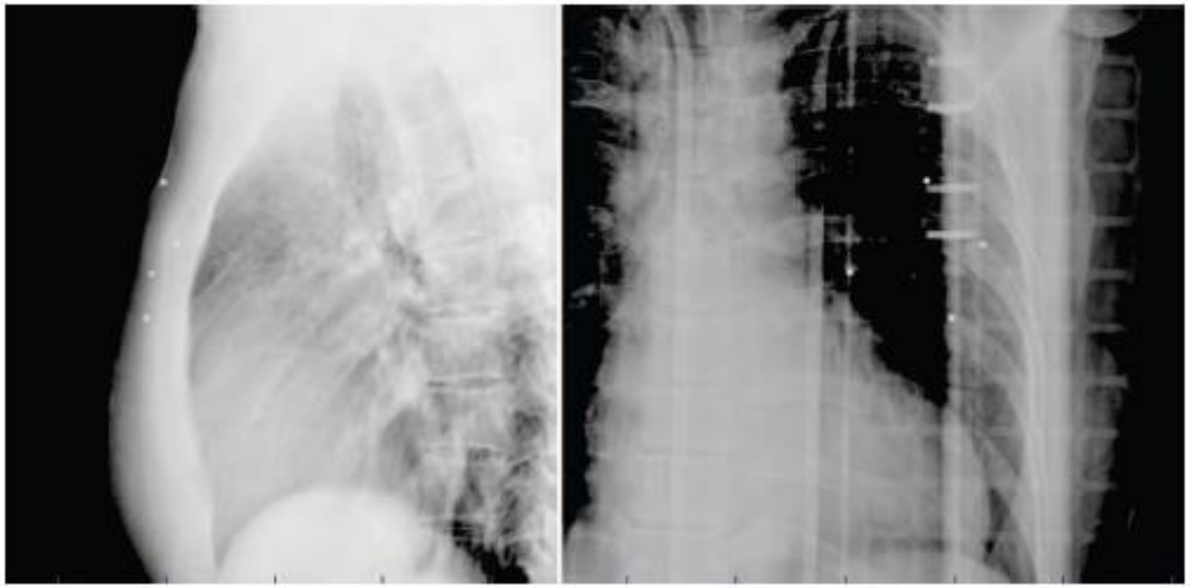


FIG. 2. Anterior–posterior and lateral paired kV images of a patient on treatment day 1. *Yue at al., 2013*

kV decreases dose burden and increases image quality

3D (CBCT)

- Provides:
  - Isocentre position verification
  - Internal soft tissue anatomy
  - Clearer image of clips
  - Information on changes in target during treatment
    - Seroma changes

- Consider:
  - Dose
  - Collision risk
  - Ease of accurate registration and match

3D (CBCT)

- Limitations
  - ➢ Collision
  - ➢ Field of view
  - ➢ Increased dose to contra lateral breast

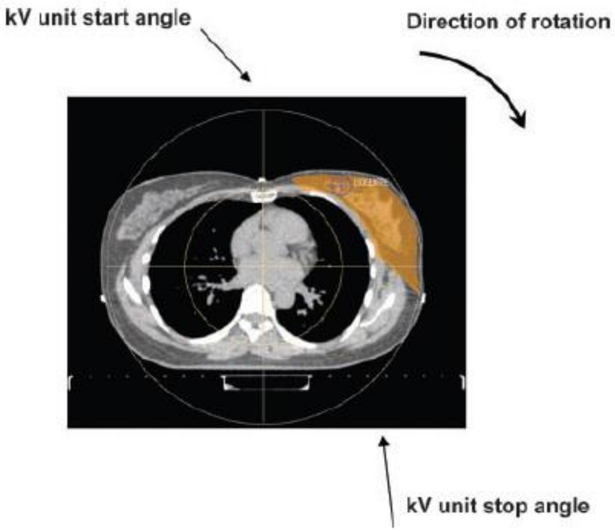
- CBCT not acquired at the isocentre to avoid collision

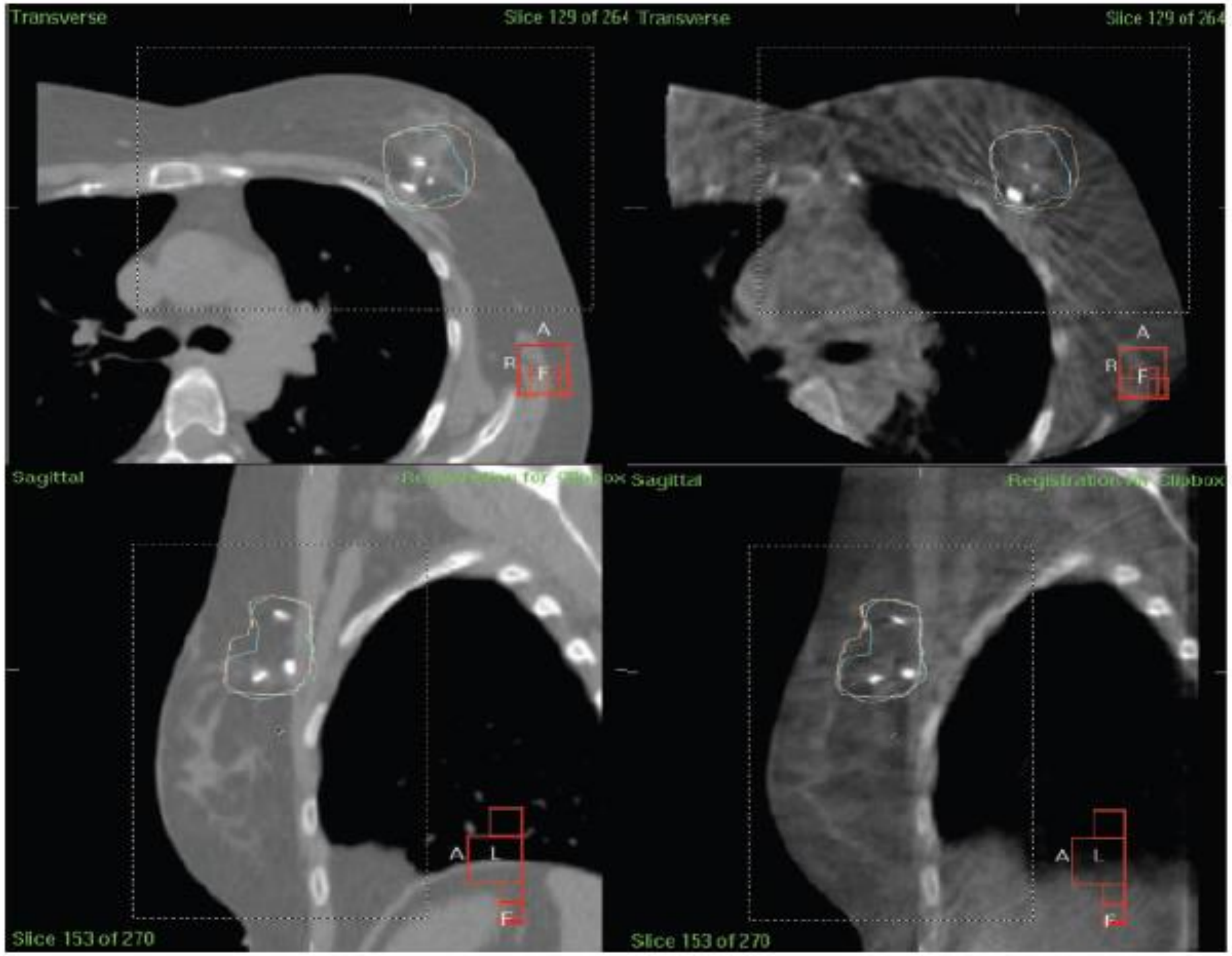
- Then once matched the shift includes the offset from isocentre position

- Adds time and potential errors

- Donovan et al. (2012) stipulate limitations on iso position to account for this

3D (CBCT): Clarity of Surgical Clips





Note: size of clip box

Isodose lines have been exported to confirm coverage

Donovan et al., 2012

3D (CBCT): Clarity of Surgical Bed

Setup error for EPID and cone-beam CT ● R. Topolnjak *et al.*

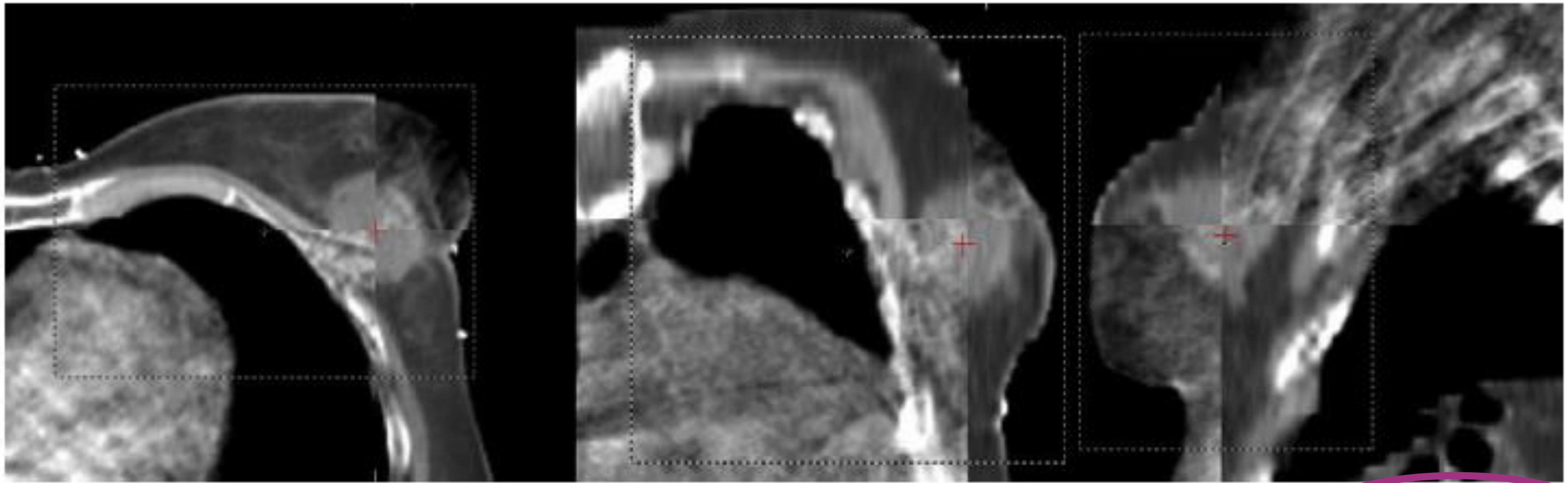


Fig. 2. Match of planning computed tomography (CT) and cone-beam CT (CBCT) images after bony (sternum and rib) anatomy registration. A bony anatomy rigid registration was performed based on image data in a user-defined, three-dimensional, box-shaped region of interest (white dashed line) using a chamfer matching algorithm.

Topolnjak et al., 2009

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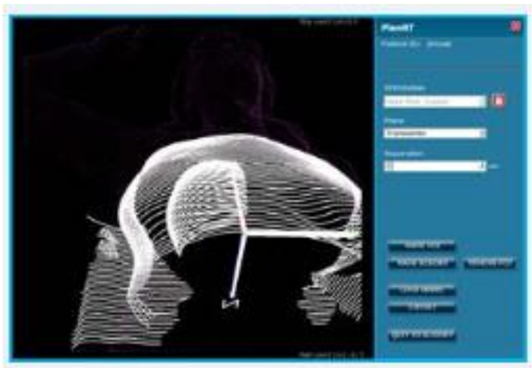
Video-Based Surface Mapping

- Whole surface shape matching
  - ➢ Some use this to setup and replace the need for tattoos

- Provides surface anatomy information and can demonstrate the impact of breathing and confirmation for DIBH

- Can this be correlated to provide shift/positional information?
  - ➢ Often used in conjunction with other imaging devices

- No additional radiation



A Look at the Literature

Table 4.5 Articles that discuss doses, anatomy matching methods and seroma visualisation

KV imaging Method	Author	Matched Method	Sample Size>20	Seroma Visible	Surgical clips	Auto co-registration	Reported imaging dose to patient.	Safe to acquire at iso centre
CBCT	Jain et al.(2009)	Bones	No	No	No	Yes	Yes	No
	White et al. (2007)	Lung/external contour	Yes	Yes	No	Potential	Yes	Yes
	Kim et al. (2007)	Clips	No	Yes	Yes	Yes	Yes	No
	Topolnjak et al. (2010)	Sternum/ribs	Yes	Unknown	No	Yes	No	Unknown
	Yang et al.(2010)	Unknown	No	Yes	No	Yes	Yes	Unknown
	Donovan et al.(2012)	Clips	Yes	Yes	Yes	Yes	Yes	Yes
kV*	Yue et al. (2011)	Bony to gold fiducials	Yes	Yes	Yes	Unknown	No	Unknown
	Lawson et al. (2008)	Bony	Yes	Unknown	Yes	No	Yes	Unknown
kV* vs. CBCT	Fatunase et al. (2008)	Bones, then soft tissue	No	Yes	Yes	No	Yes	No for both.

*orthogonal kV imaging

L. Lewis Improving Radiotherapy for Breast Cancer: Identification of the tumour bed and characterisation of target volume changes. 2013 MSc Thesis, available online

Do You Represent Europe?

- **2010** Survey of EORTC affiliated institutions
- "Electronic portal imaging for patient set-up is used by **92%** of the institutions." *(van der Laan et al., 2010)*
- So what does Europe look like in 2018?

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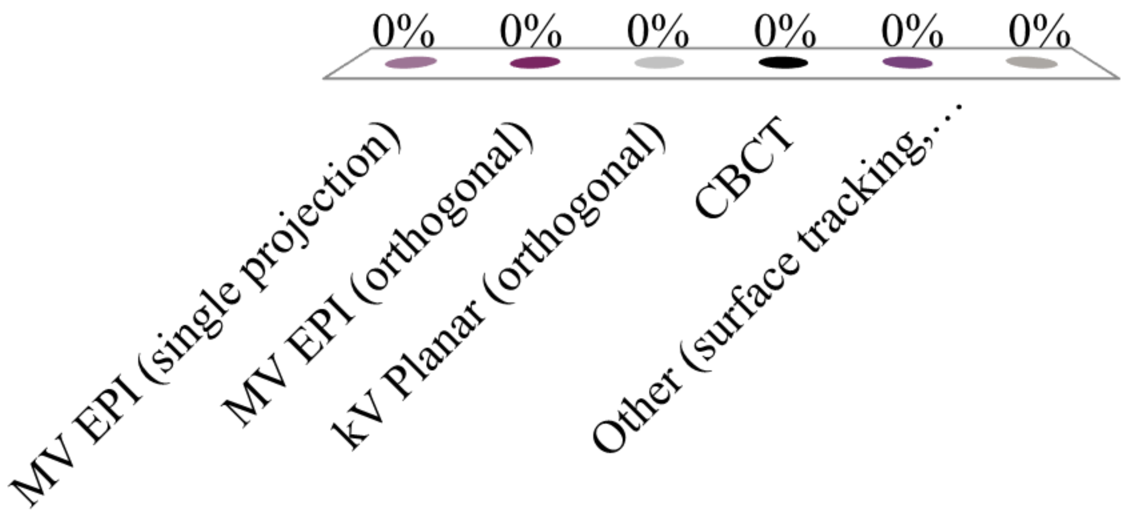
In my clinical department, for standard WBRT, we image using:

A. MV EPI (single projection)
B. MV EPI (orthogonal)
C. kV Planar (orthogonal)
D. CBCT
E. MV CT (tomotherapy)
F. Surface Guidance



How did you compare with The US?
2016 Survey of ASTRO Members *(Nabavizadeh et al., 2016)*

Technology Used

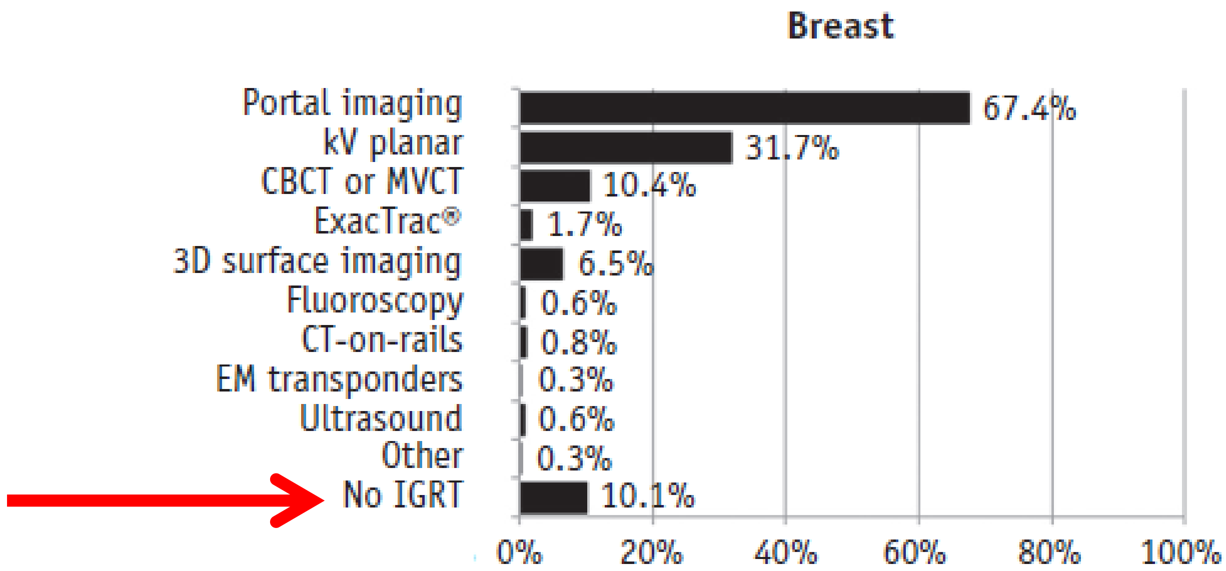


Fig. 2. Physician-reported image guided radiation therapy frequency (black) and on-line image verification frequency (gray) for standard fractionation treatments, by disease site. *Abbreviations:* 3D-CRT = 3-dimensional conformal radiation therapy; fx = fractions; IMRT = intensity modulated RT.

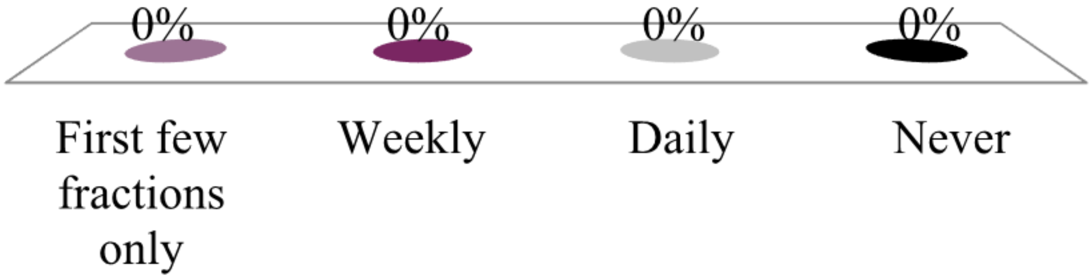
In my clinical department, for standard WBRT, we image :

A. First few fractions only

B. Weekly

C. Daily

D. Never



How did you compare with The US?
2016 Survey of ASTRO Members *(Nabavizadeh et al., 2016)*

Frequency of Imaging

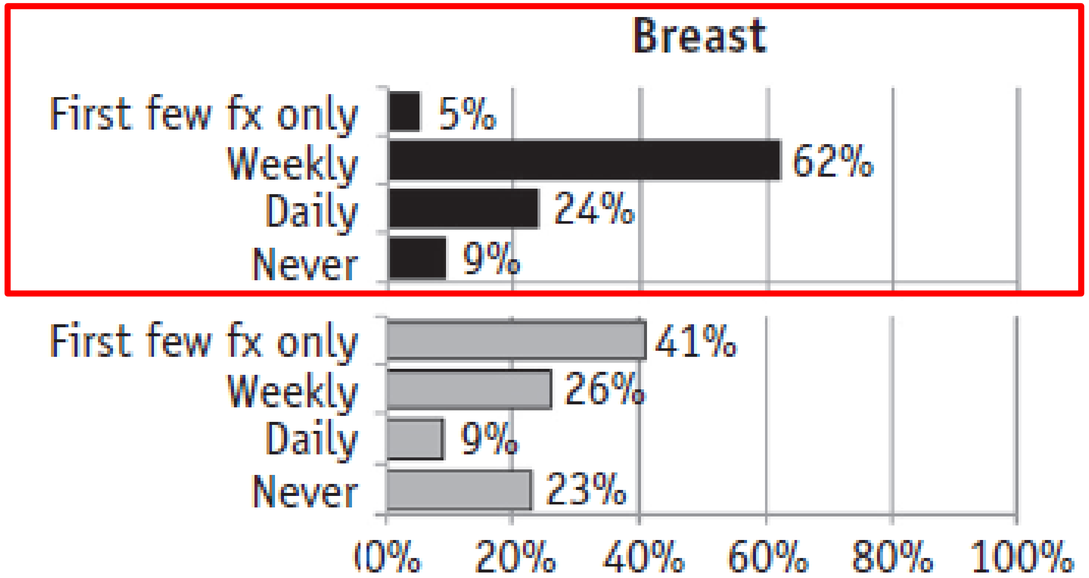
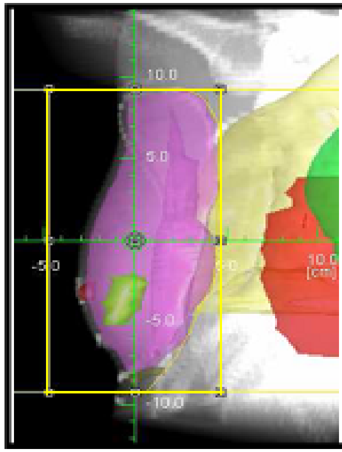


Fig. 2. Physician-reported image guided radiation therapy frequency (black) and on-line image verification frequency (gray) for standard fractionation treatments, by disease site. *Abbreviations:* 3D-CRT = 3-dimensional conformal radiation therapy; fx = fractions; IMRT = intensity modulated RT.

Therapeutic strategy: Which radiotherapy?

Two changing practice concepts have modified the standard whole breast irradiation 50Gy +/- boost has been replaced



Hypo fractionated whole breast irradiation

Whelan NEJM 2010; START A and B Lancet Oncol 2008

Accelerated partial breast irradiation

Vaidya Lancet 2010; Bourgier IJROBP 2010 ; Lemanski IJROBP 2010; Taghian IJROBP 2005; Polgar IJROBP 2004 ; Vicini IJROBP 2003; Formenti IJROBP 2003;

IGRT for *(Supine)* APBI: What are people doing?

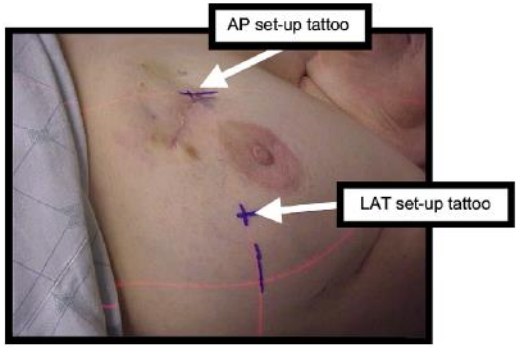


Fig. 1. Patient with skin marker crosshairs representing isocentric setup at surgical cavity.

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 2, pp. 528–534, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.02.001

CLINICAL INVESTIGATION **Breast**

CLINICAL EXPERIENCE WITH IMAGE-GUIDED RADIOTHERAPY IN AN ACCELERATED PARTIAL BREAST INTENSITY-MODULATED RADIOTHERAPY PROTOCOL

Charles E. Leonard, M.D.,* Michael Tallhamer, M.S.,* Tim Johnson, Ph.D.,* Kari Hunter, C.M.D.,* Kathryn Howell, M.D.,* Jane Kercher, M.D.,[†] Jodi Widener, M.D.,[†] Terese Kaske, M.D.,[‡] Devchand Paul, M.D.,[§] Scot Sedlacek, M.D.,[§] and Dennis L. Carter, M.D.*

*Rocky Mountain Cancer Centers, Littleton, CO; [†]Arapahoe Surgical Associates, Littleton, CO; [‡]Sally Jobe Diagnostic Breast Center, Greenwood Village, CO; and [§]Rocky Mountain Cancer Centers, Rose Hospital, Denver, CO

2010
One of the first reports on IGRT APBI

Orthogonal **MV** images taken **daily**

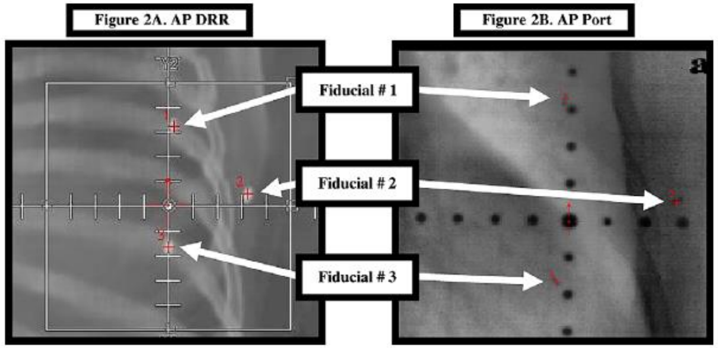


Fig. 2. Anterior/posterior digital reconstruction radiograph and corresponding port film (arrows indicate respective fiducial location).

Imaging dose included in plan

Table 5. Individual and total dose contribution of AP and lateral port films for 5 patients over the course of accelerated partial breast radiotherapy to the isocenter and 100% of PTV using image-guided radiotherapy

	ISO dose (cGy)			
Patient	AP	Lateral	Total	100% PTV
1	30.7	25.3	56	45
2	28.1	30.7	58.8	48
3	26.4	30.1	56.5	50
4	29.7	28	57.6	49
5	30.3	29.9	60.2	54
As a percentage of prescription dose of 3,850 cGy				
1	0.8	0.7	1.5	1.2
2	0.7	0.8	1.5	1.3
3	0.7	0.8	1.6	1.3
4	0.8	0.7	1.5	1.3
5	0.8	0.8	1.6	1.4

IGRT for *(Supine)* APBI: What are people doing?

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 2, pp. 528–534, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.02.001

CLINICAL INVESTIGATION **Breast**

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Because of the reliability of these fiducial markers, we have reduced the size of port films for IGRT. Before the use of fiducials, reviewing physicians required visualization of the surrounding anatomy, specifically the ribs, clavicle, and sternum. This required the more traditional double-exposure port with the second larger field exposure. When it is not necessary to view surrounding anatomical landmarks because of fiducial placement in proximity to the target cavity, it is possible to reduce port field sizes.

cerning their use in partial breast treatment. This could suggest that margins might be reduced for a smaller PTV volume than is used currently. Up to this time, an additional margin of 1 cm from the CTV had been used. However, owing to the use of these fiducial markers, this additional margin may be reduced by 5 mm. This would be well within two standard deviations of the average mean error of our IGRT experience.

IGRT for *(Supine)* APBI: What are people doing?

Distinction b/w surgical clips and fiducials

Textured gold fiducials for stability and visualisation

Daily orthogonal MV EPI

Published 2012

Clinical Investigation: Breast Cancer

Validating Fiducial Markers for Image-Guided Radiation Therapy for Accelerated Partial Breast Irradiation in Early-Stage Breast Cancer

Catherine K. Park, M.D., M.P.H.,* Jakub Pritz, M.S.,† Geoffrey G. Zhang, Ph.D.,* Kenneth M. Forster, Ph.D.,* and Eleanor E.R. Harris, M.D.*

*From the *Department of Radiation Oncology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; and †Department of Physics, University of South Florida, Tampa, FL*

Received Jan 12, 2011, and in revised form Jun 22, 2011. Accepted for publication Jul 18, 2011

Visualisation of fiducials on 100% MV images
Centre of fiducials correlated to centre of seroma

When matching to fiducials margins can be reduced to 6mm compared to bone (10mm)

IGRT for *(Supine)* APBI: What are people doing?

Aim: to assess the residual and intrafraction errors

PTV = CTV+10mm
5 fld non coplanar
95%/95%

Cai *et al. Radiation Oncology* 2010, 5:96
http://www.ro-journal.com/content/5/1/96

RADIATION ONCOLOGY

RESEARCH Open Access

Impact of residual and intrafractional errors on strategy of correction for image-guided accelerated partial breast irradiation

Gang Cai[1†], Wei-Gang Hu[1*†], Jia-Yi Chen[1*], Xiao-Li Yu[1], Zi-Qiang Pan[1], Zhao-Zhi Yang[1], Xiao-Mao Guo[1], Zhi-Min Shao[2], Guo-Liang Jiang[1]

Pre and post fx XVI
Grey value match
Manual adjustment
2-3 mins
Matched by RO

CBCT does not guarantee absolute accuracy
13mm margin required to account for initial setup and intrafraction errors

MRI Based IGRT – The Future?

Clinical Investigation

Magnetic Resonance Image Guided Radiation Therapy for External Beam Accelerated Partial-Breast Irradiation: Evaluation of Delivered Dose and Intrafractional Cavity Motion

Sahaja Acharya, MD, Benjamin W. Fischer-Valuck, MD, Thomas R. Mazur, PhD, Austen Curcuru, BS, Karl Sona, MS, Rojano Kashani, PhD, Olga Green, PhD, Laura Ochoa, ANP, PhD, Sasa Mutic, PhD, Imran Zoberi, MD, H. Harold Li, PhD, and Maria A. Thomas, MD, PhD

Department of Radiation Oncology, Washington University School of Medicine, St. Louis, Missour

Received Jan 9, 2016, and in revised form Jul 8, 2016. Accepted for publication Aug 10, 2016.

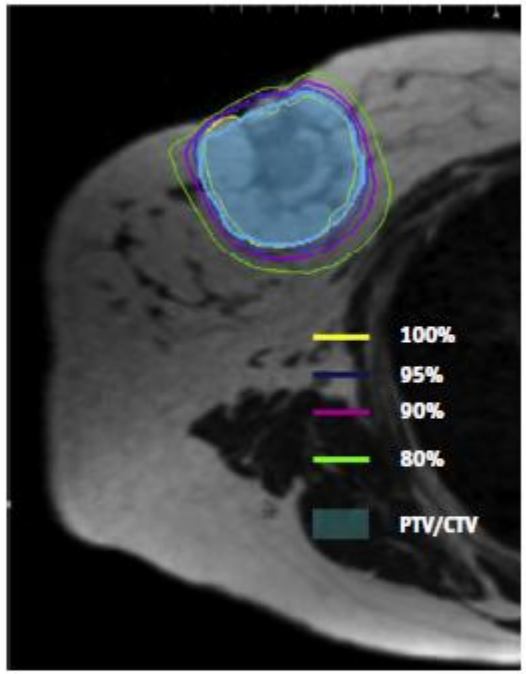


Fig. 1. Plan visualized on magnetic resonance simulation. Planning target volume (PTV) (= clinical target volume [CTV]) is shown in light blue color wash. Isodose lines: 100% (yellow), 95% (dark blue), 90% (magenta), 80% (green). (A color version of this figure is available at www.redjournal.org.)

Take Home Message

- There is an abundance of imaging technologies and strategies available for this site

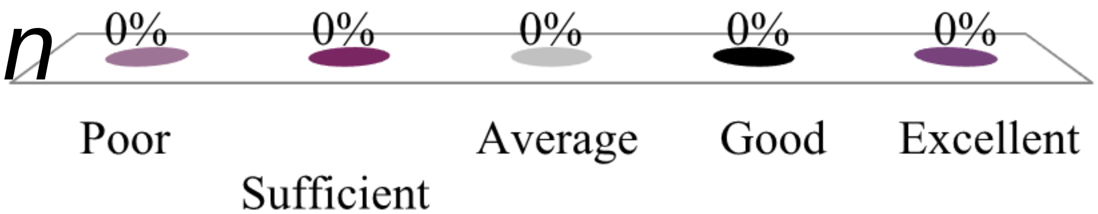
- IGRT for breast is largely dependant not only what is available to you, but the planning technique that is used

- Advanced treatment techniques require more sophisticated imaging techniques
  - APBI, IMRT, VMAT

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



Lung

Jose Lopez, M.D., Ph.D
Radiation Oncology
University Hospital Virgen del Rocio
Seville, Spain

Advanced skills in modern radiotherapy

The Lancet Oncology 2015; vol 16: Issue 10

Outline of Talk

- Preclinical rationale behind **oligometastatic** state
- **Clinical data supporting** benefit to local treatment in oligometastatic NSCLC
- Case report
- Discussion of current multidisciplinary (physician, phisyc and RTTs) management

Introduction

- Definitive radiotherapy has historically been reserved for patients with stage I-III disease.
- The most common indication for RT in patients with metastatic lung cancer has been palliation for pain or other symptoms
- However, stage IV lung cancer is a very broad category , and prior studies have suggested that some patients with stage IV lung cancer and only a few distant metastases (‘**oligometastasis**’) may benefit from local therapy to both the primary tumor and the distant sites of disease .

Introduction

- Spectrum of metastatic patients exists
  - ➢ Indolent vs. aggressive course
- In-between locoregionally confined and true metastatic state, there appears to exist intermediate state of low disease burden systemically=oligometastasis
  - ➢ Can these patients be “cured”?

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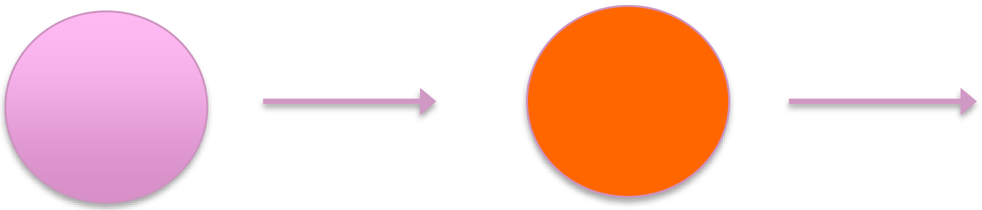
"Oligo" means "having few, having little."

Studies with lung cancer have defined oligometastatic disease as up to 5 metastatic lesions.



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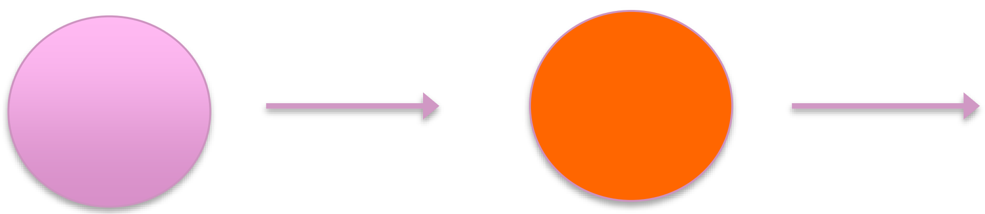
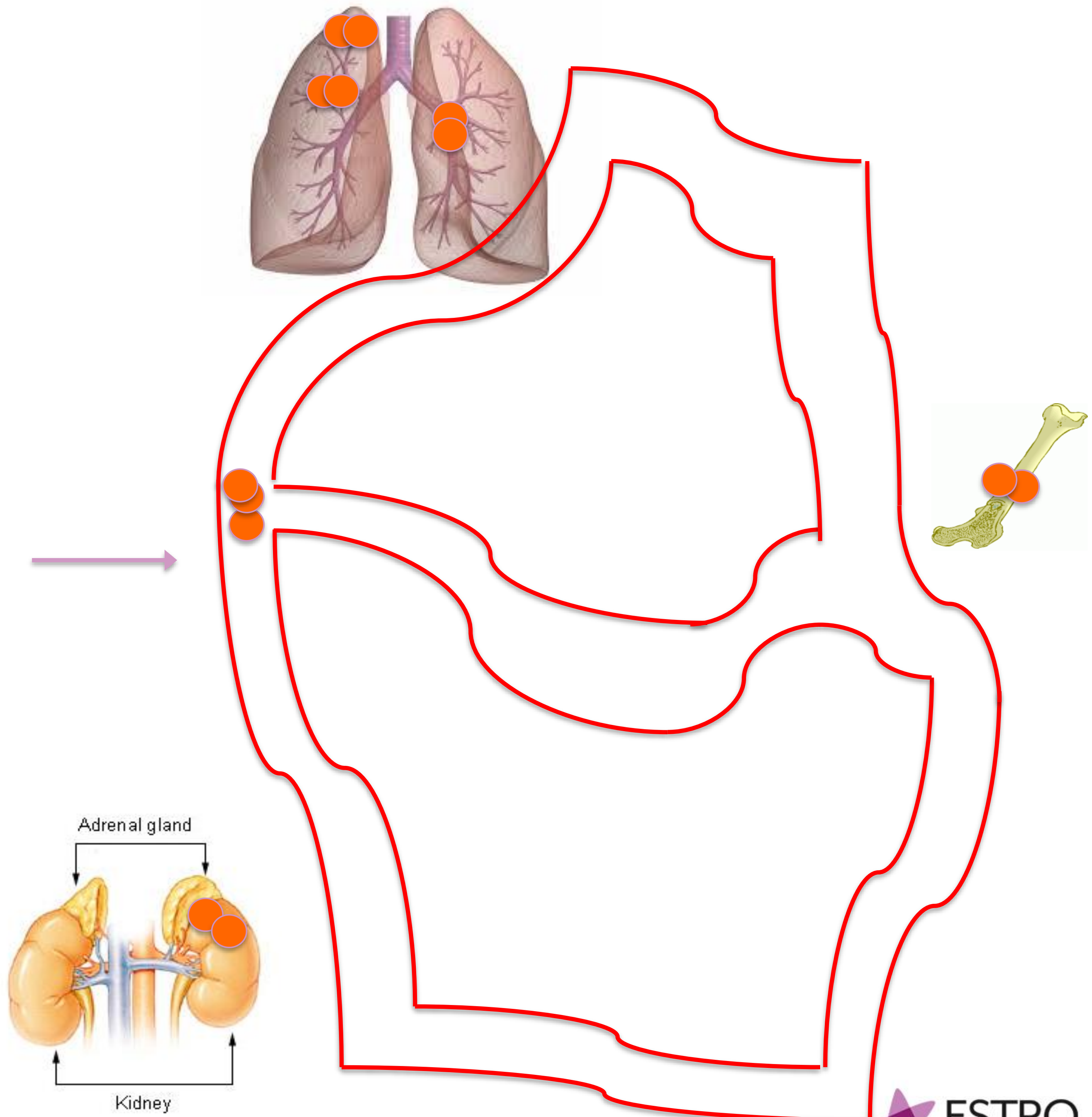
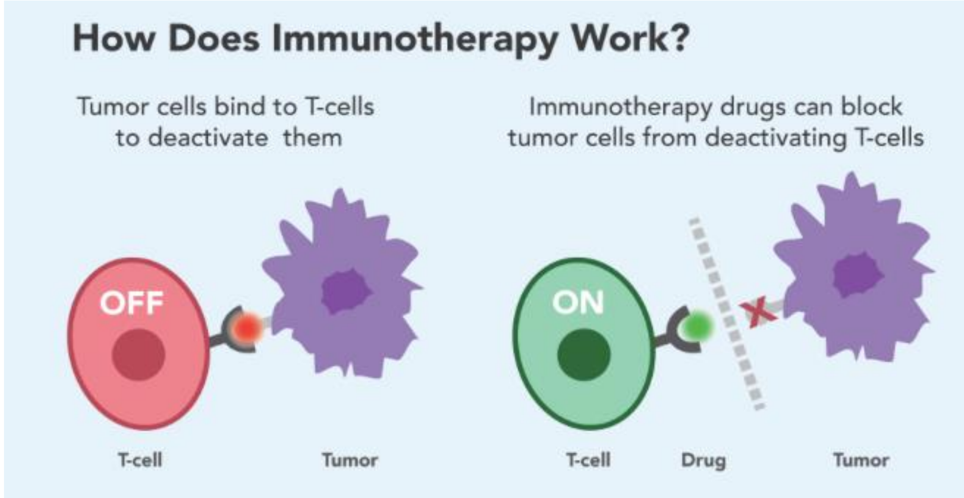




Dr Daniel Gomez. MD Anderson Cancer Center

Recent Trials Addressing Management of Oligometastatic NSCLC



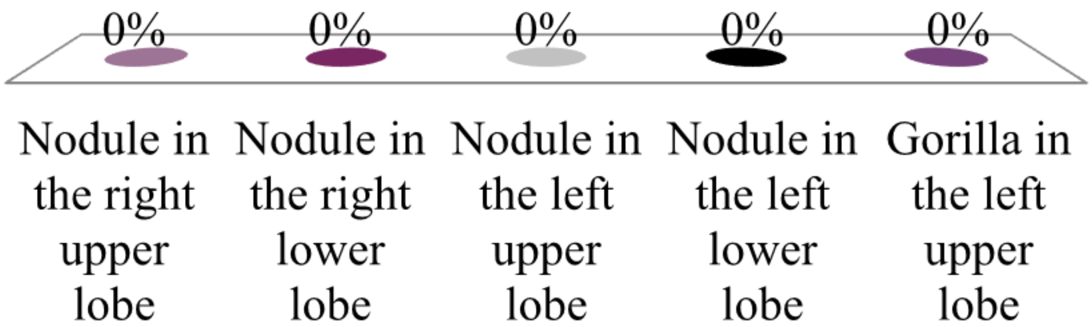
- Recent developments
  - ➢ Targeted agents
  - ➢ Maintenance chemotherapy
  - ➢ Technologic advances permitting ablative doses of radiation therapy

Do you notice anything unusual?

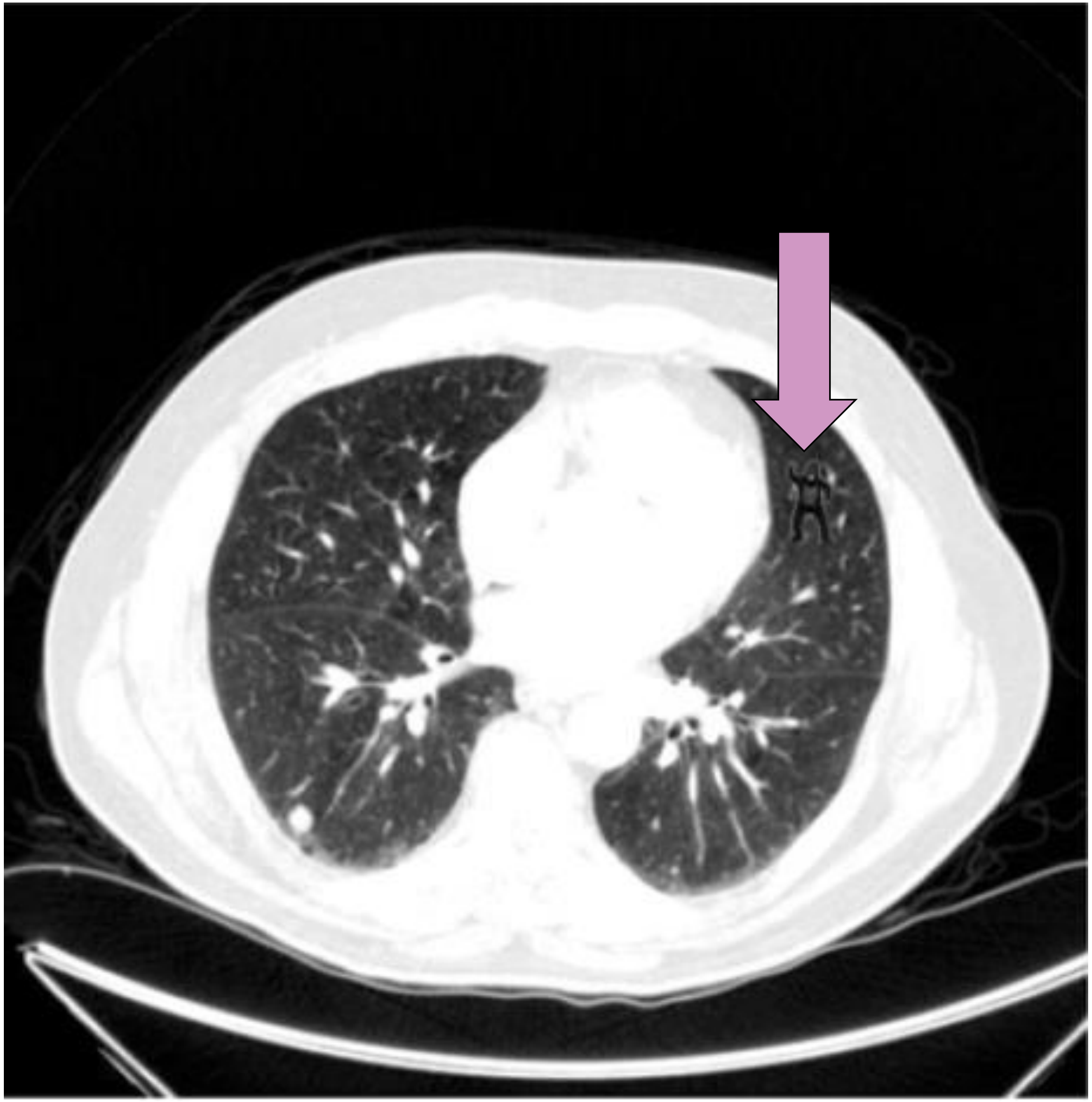
Psychological Science 2013 24: 1848

Do you notice anything unusual?

A. Nodule in the right upper lobe
B. Nodule in the right lower lobe
C. Nodule in the left upper lobe
D. Nodule in the left lower lobe
E. Gorilla in the left upper lobe



Inattentional blindness



Psychological Science 2013 24: 1848

Clinical Data Supporting Local Treatment in Oligometastatic Setting

Author	Year	n	Timespan (years)	Single institution
Twomey	1982	2	14	Yes
Reyes	1990	5	4	Yes
Raviv	1990	3	nr	Yes
Kirsch	1993	1	6	Yes
Higashiyama	1994	5	12	Yes
Ayabe	1995	3	9	Yes
Urschel	1997	1	9	Yes
Bendinelli	1998	4	4	Yes
Tsuji	1998	1	2	Yes
Linos	1998	1	1	Yes
Porte	1998	11	8	Yes
Wade	1998	14	7	No (159 centers)
de Perrot	1999	1	5	Yes
Bretcha-Boix	2000	5	nr	Yes
Ambrogi	2000	5	7	Yes
Porte	2001	43	12	No (8 centers)
Mercier	2004	23	14	Yes
Lucchi	2005	11	10	Yes
Pfannschmidt	2005	11	7	Yes
Sebag	2006	9	9	Yes
Munoz	2006	1	5	Yes
Strong	2007	29	11	Yes

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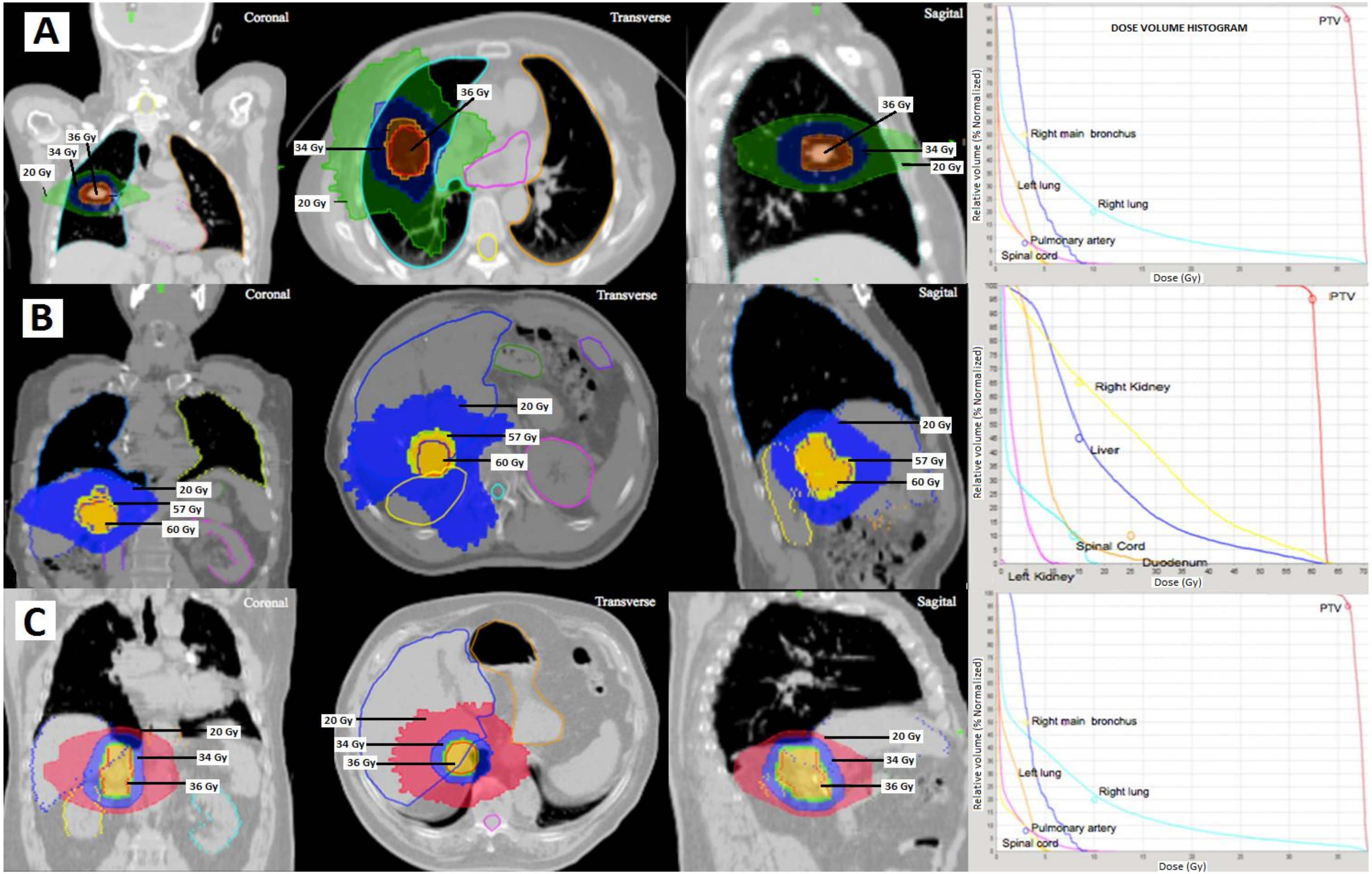
STEREOTACTIC ABLATIVE RADIOTHERAPY DELIVERED BY HELICAL TOMOTHERAPY FOR EXTRACRANEAL OLIGOMETASTASIS



Sole CV, Lopez Guerra JL, et al. Clin Transl Oncol. 2013

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STEREOTACTIC ABLATIVE RADIOTHERAPY DELIVERED BY HELICAL TOMOTHERAPY FOR EXTRACRANEAL OLIGOMETASTASIS

CONTOURS

- GTV: defined only as the solid abnormality on CT + PET
- ITV: using a multiple CT scan (free breathing, maximal inspiration, and maximal expiration)
- PTV: 0.5 cm in the axial plane and 1.0 cm in the craneocaudal plane

DOSE PRESCRIPTION

- Lung (not chest wall): 3 fractions of 20 Gy
- Lung (chest wall): 3-5 fractions of 12 Gy for lesions
- Lung (central): 8 fractions of 7.5 Gy

CHEMOTHERAPY (90%)

- FOLFOX/FOLFIRI

Sole CV, Lopez Guerra JL, et al. Clin Transl Oncol. 2013

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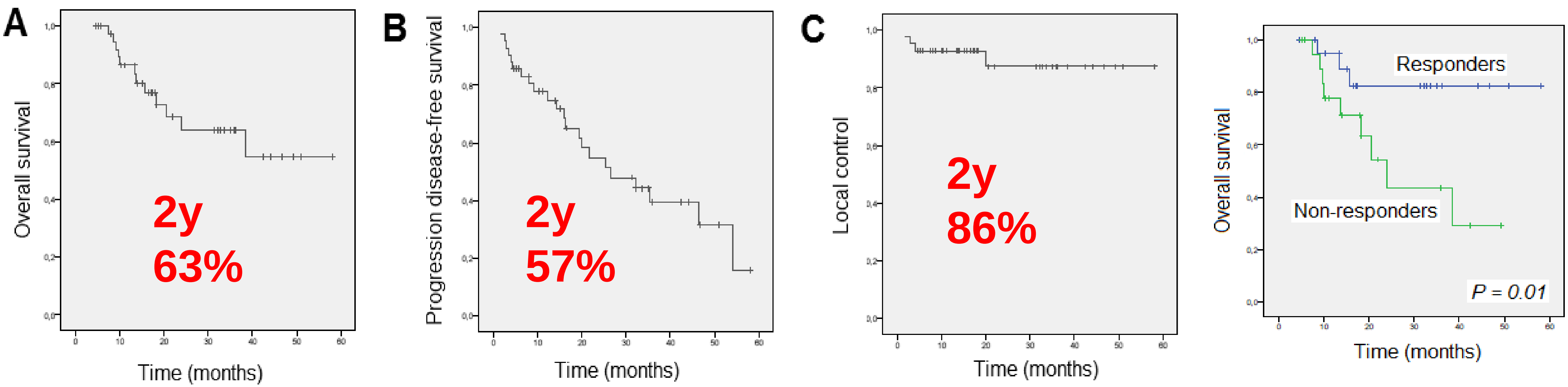
DOSE CONSTRAINTS

THORAX

- Chronic lung disease: 70% of the lungs <17 Gy.
- Healthy lungs: 60 % of the lungs <20 Gy.
- Esophagus: Dmax < was 4.0 Gy per fraction.
- Chest wall: <30 Gy to 30 cc and <60 Gy to 3 cc.
- Spinal cord: <2 Gy per fraction and <45 Gy total.



Toxicity (N=28)	Grade I	Grade II	Grade III
Pneumonitis	11 (39%)	3 (11%)	1 (4%)
Chest wall pain	6 (21%)		
Skin	6 (21%)		
Esophagitis	3 (11)		

Select group of patients that benefit from aggressive local treatment for oligometastatic disease

Sole CV, Lopez Guerra JL, et al. Clin Transl Oncol. 2013

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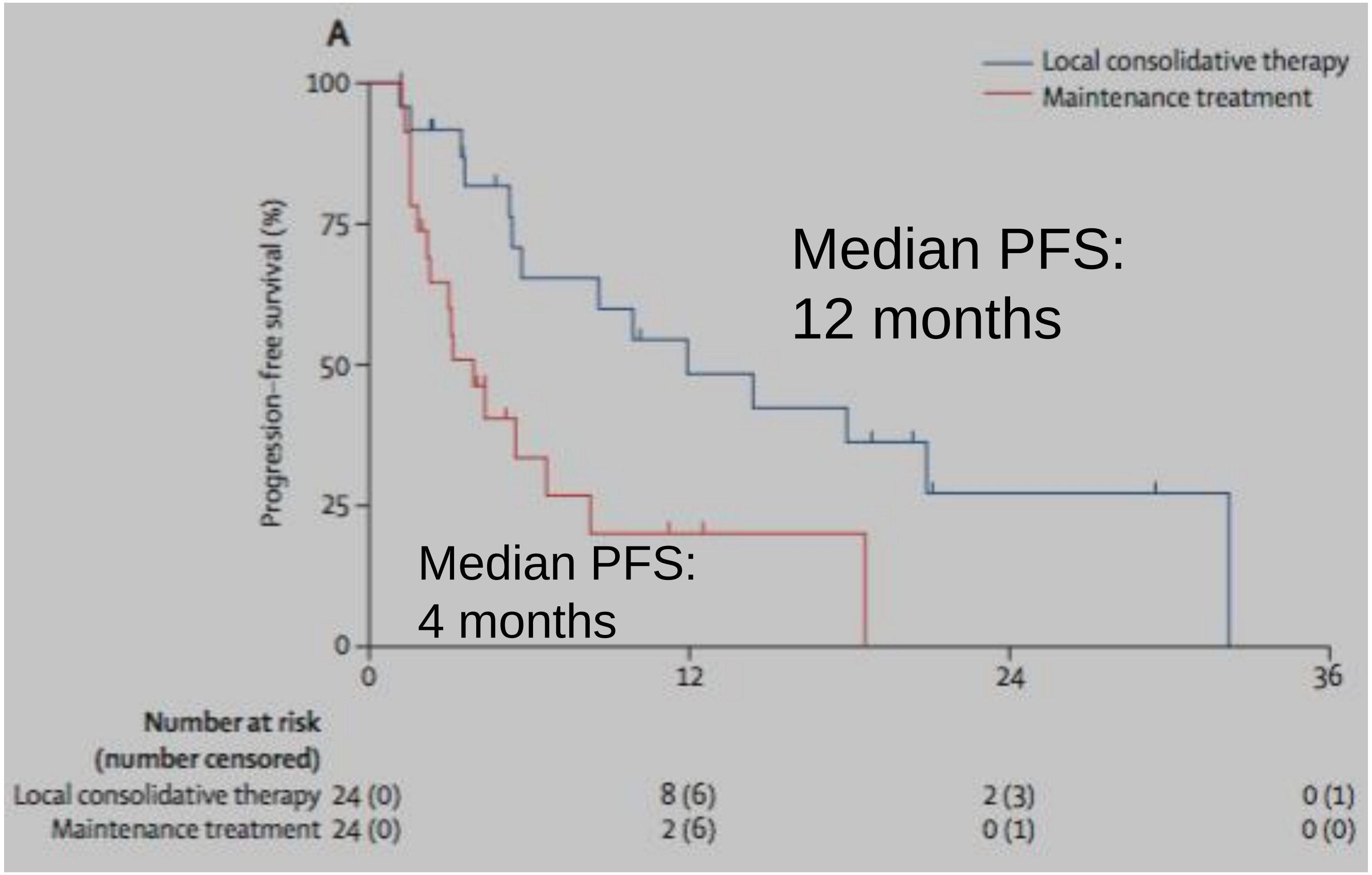
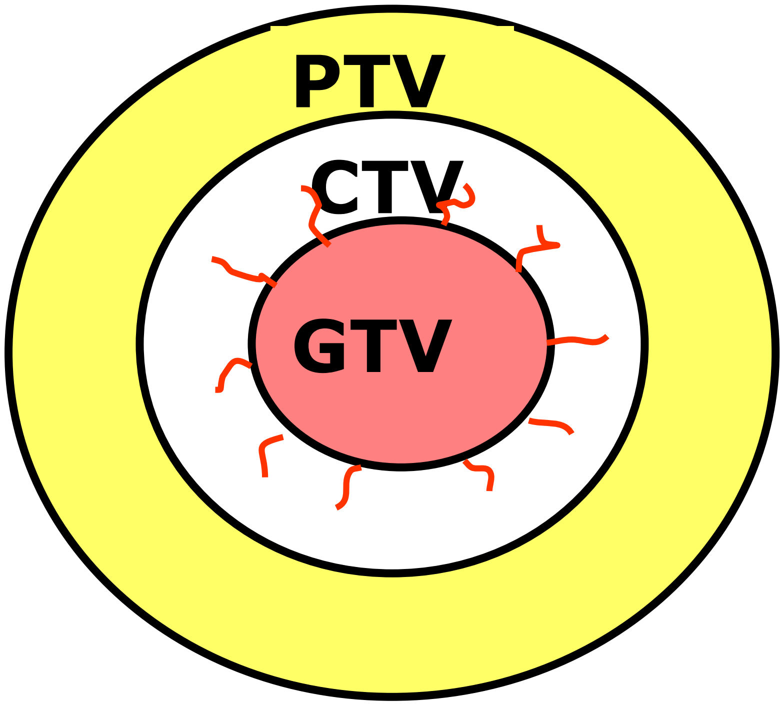
Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic NSCLC

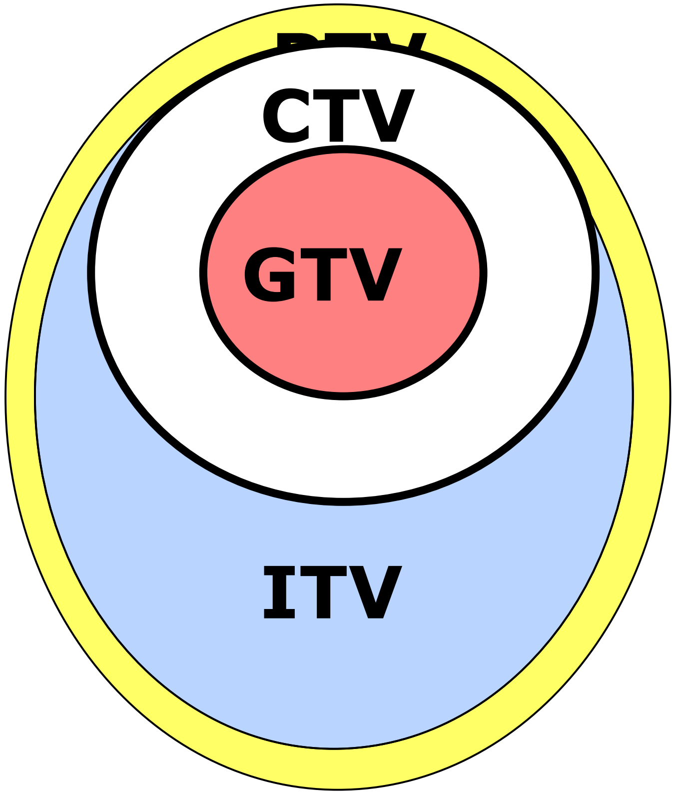


Gomez D et al. Lancet 2016

ICRU 50

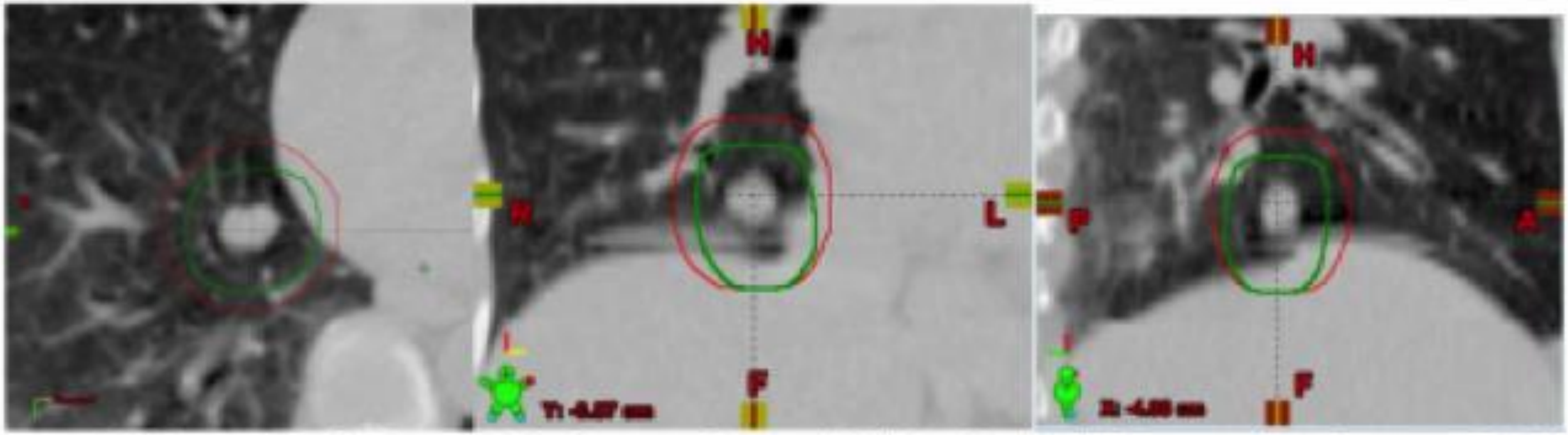


ICRU 62

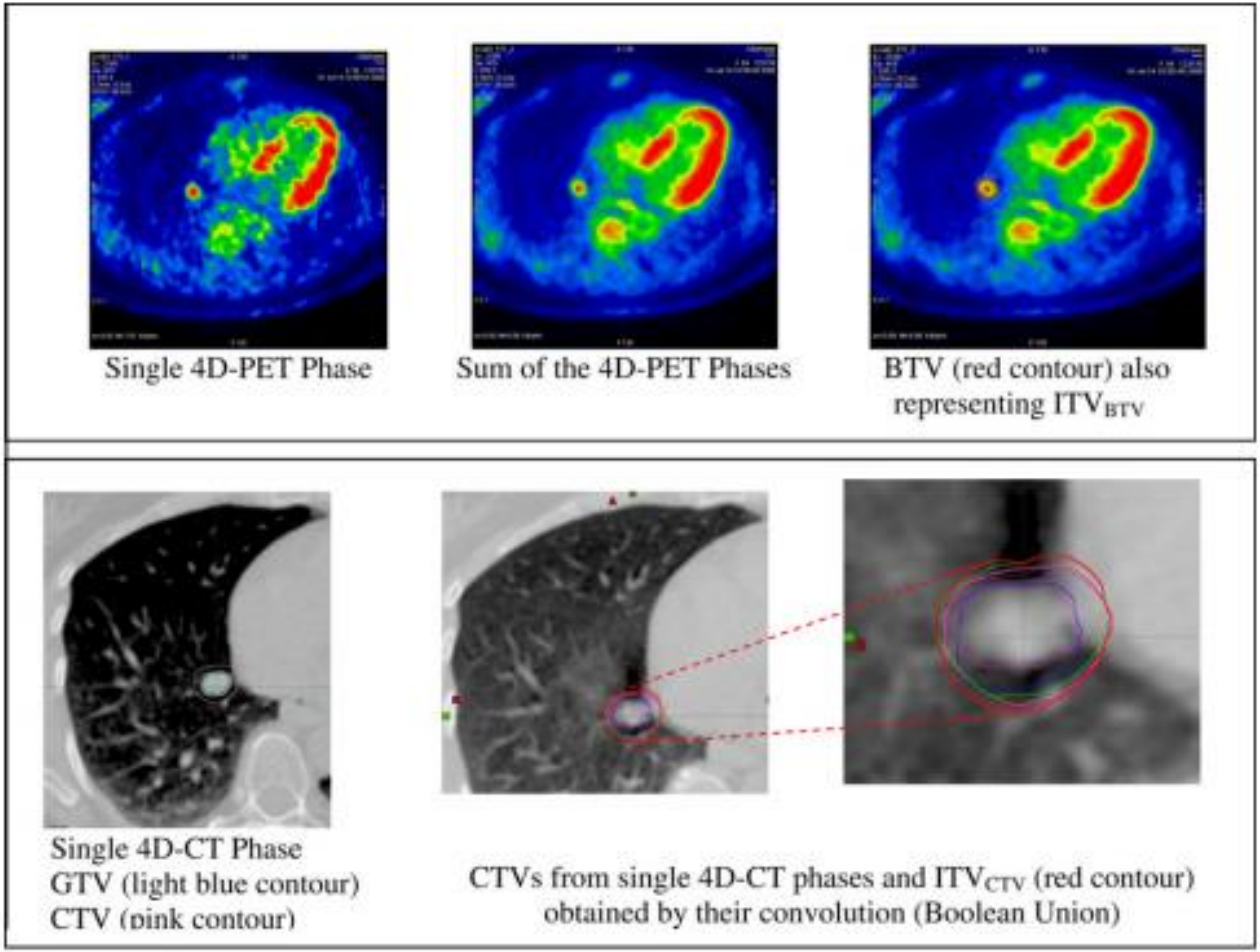


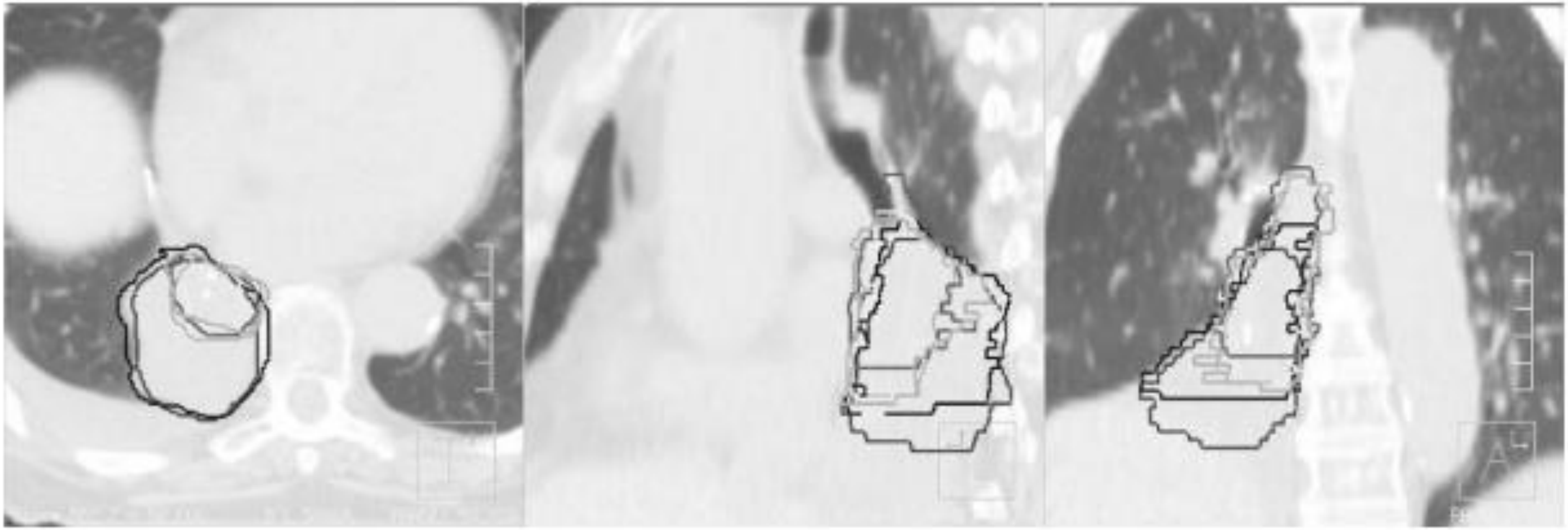
GTV= Gross Tumor Volume, CTV=Clinical Target Volume, PTV=Planning Target Volume, ITV=Internal Target Volume

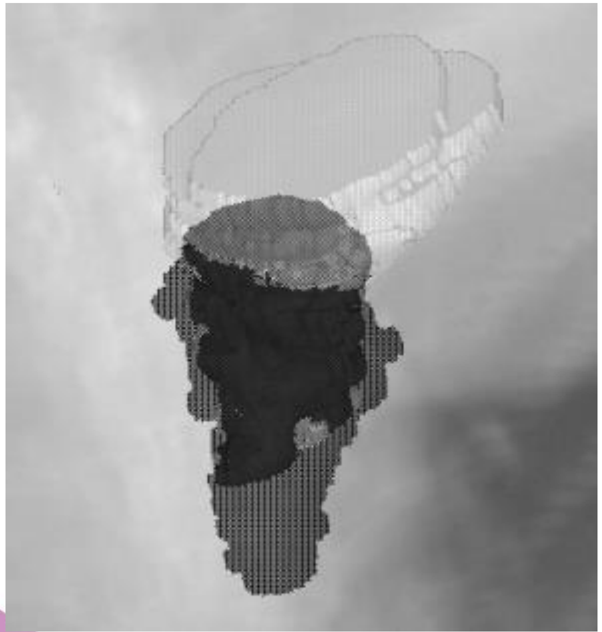
V. Bettinardi et al./Radiotherapy and Oncology 96 (2010) 311–316



CT Image (Left Transaxial, Center: Coronal, Right: Sagittal).Comparison between PTV_{4D} (green contour) and PTV obtained by standard expansions (red contour)


Single 4D-PET Phase
Sum of the 4D-PET Phases
BTV (red contour) also representing ITV_{BTV}
Single 4D-CT Phase
GTV (light blue contour)
CTV (pink contour)
CTVs from single 4D-CT phases and ITV_{CTV} (red contour) obtained by their convolution (Boolean Union)





Inter-observer and intra-observer reliability for lung cancer target volume delineation in the 4D-CT era

Radiotherapy and Oncology 95 (2010) 166–171

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Radiotherapy and Oncology 101 (2011) 322–328

ELSEVIER

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Lung cancer radiotherapy

An evaluation of an automated 4D-CT contour propagation tool to define an internal gross tumour volume for lung cancer radiotherapy

Stewart Gaede[a,b,c,d,*], Jason Olsthoorn[e], Alexander V. Louie[b], David Palma[b,c], Edward Yu[b,c], Brian Yaremko[b,c], Belal Ahmad[b,c], Jeff Chen[a,b,c,d], Karl Bzdusek[g], George Rodrigues[b,c,f]

[a] *Physics and Engineering Department; and* [b] *Department of Radiation Oncology, London Regional Cancer Program, Canada;* [c] *Department of Oncology; and* [d] *Department of Medical Biophysics, University of Western Ontario, Canada;* [e] *Department of Mathematics, University of Waterloo, Canada;* [f] *Department of Epidemiology and Biostatistics, University of Western Ontario, Canada;* [g] *Philips Radiation Oncology Systems, Fitchburg, WI, USA*

Conclusions: Automated 4D-CT propagation tools can significantly decrease the IGTV delineation time without significantly decreasing the inter- and intra-physician variability.

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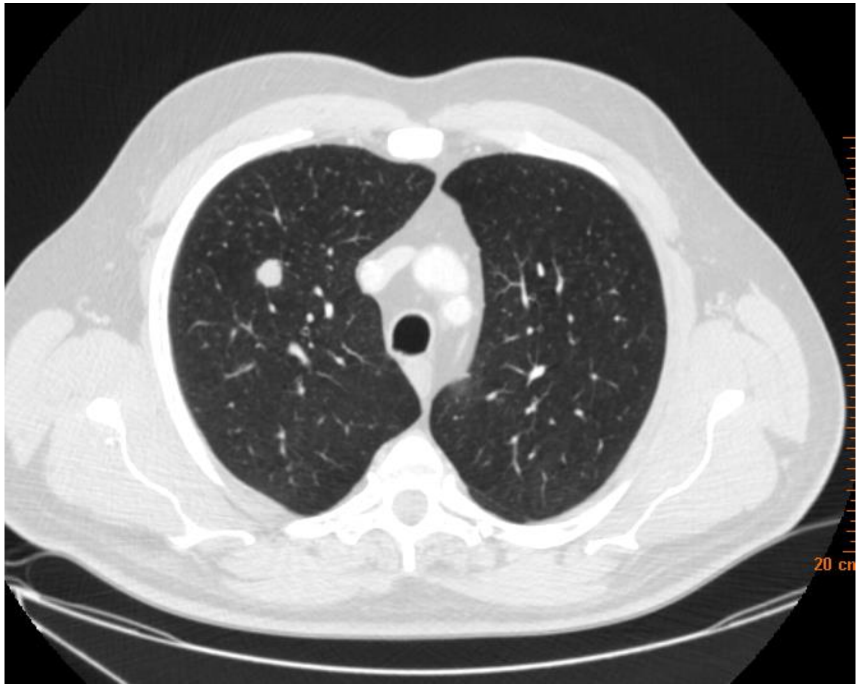
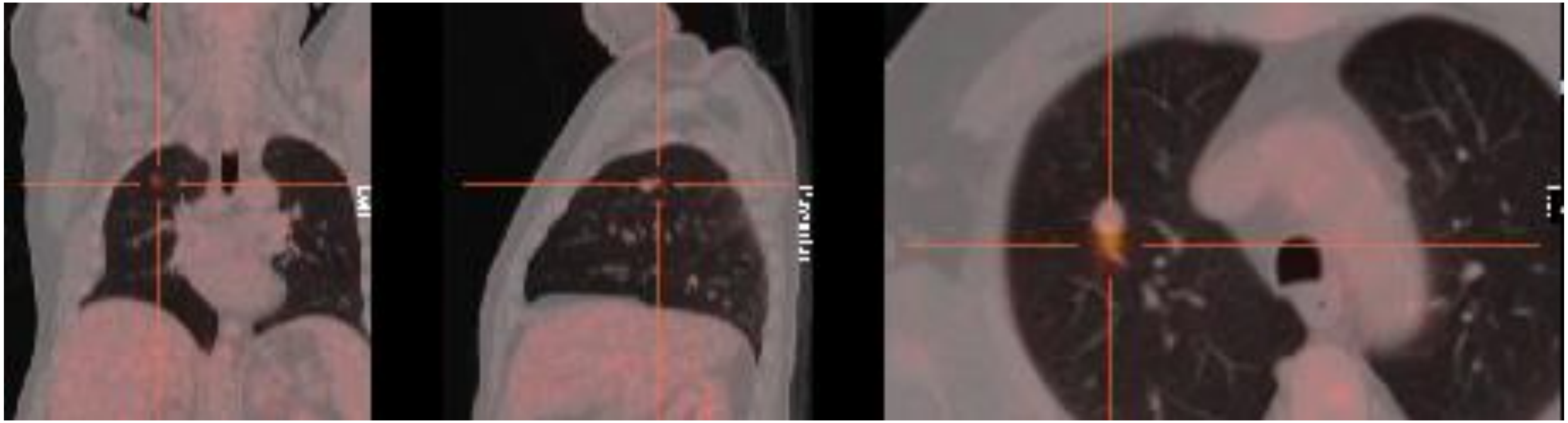
Case 1: Oligorecurrence of lung cancer

- A 65-year-old male presented to the emergency department with a two-week history of upper back pain
- Pertinent social history includes a 34-pack year history of tobacco smoking, as well as history of heavy alcohol consumption in the past.
- Chest X-ray and CT scan showed a RUL nodule (14 mm)

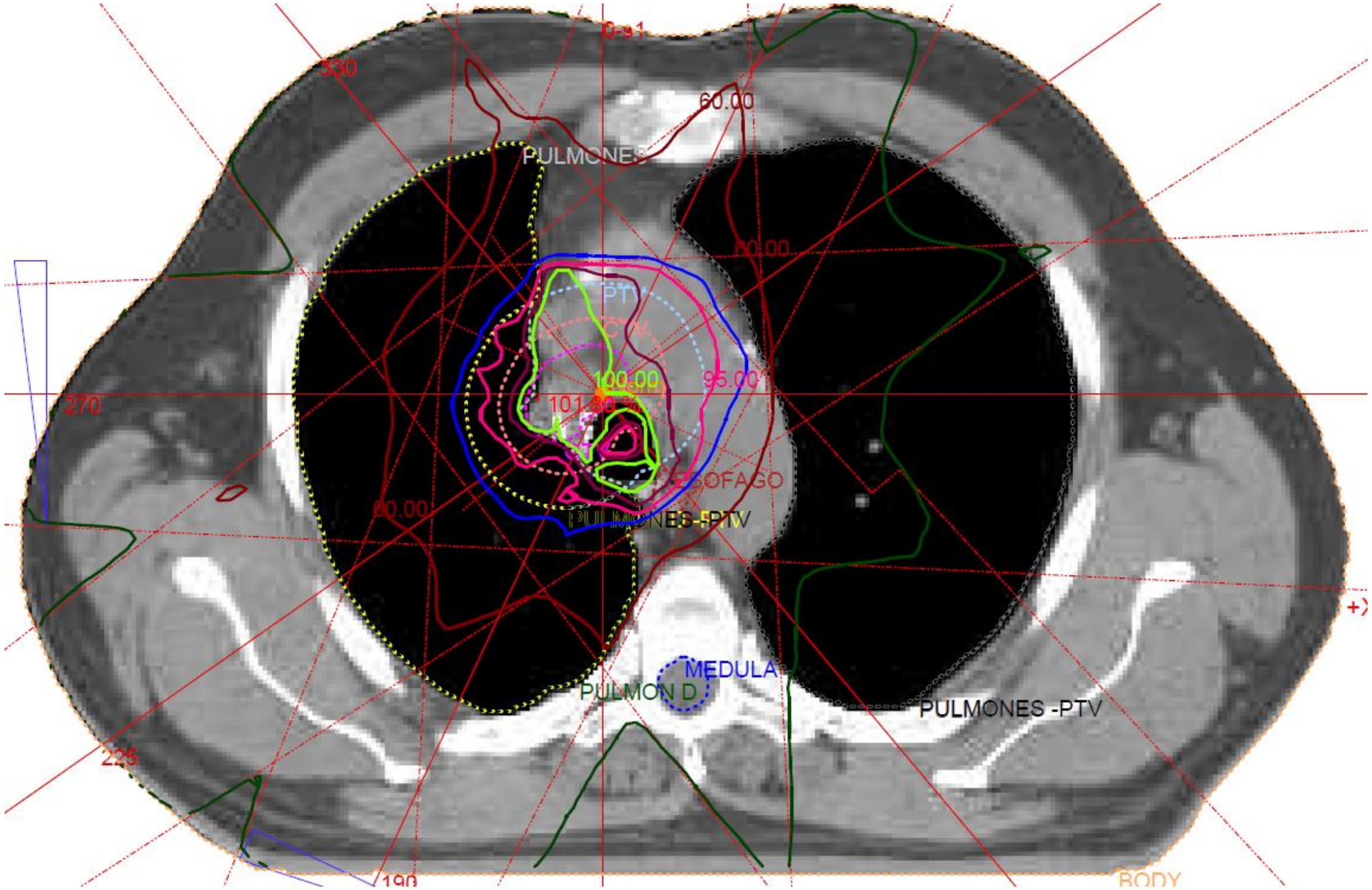


- PET/CT: SUVmax 5,1



- The patient underwent RUL lobectomy and mediastinal lymph node dissection.
- Final pathology report was consistent with high-grade large cell neuroendocrine carcinoma.

- At 2 years follow up , the CT scan showed mediastinal recurrence that was treated with concomitant radiochemotherapy (total radiation dose 66 Gy at 2 Gy/fraction).

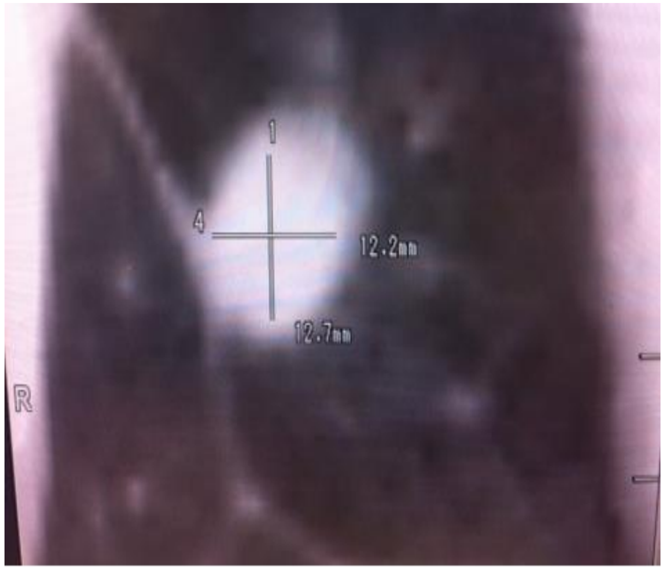


- At 3 years follow up , the CT scan showed a RML recurrence (15 mm nodule).

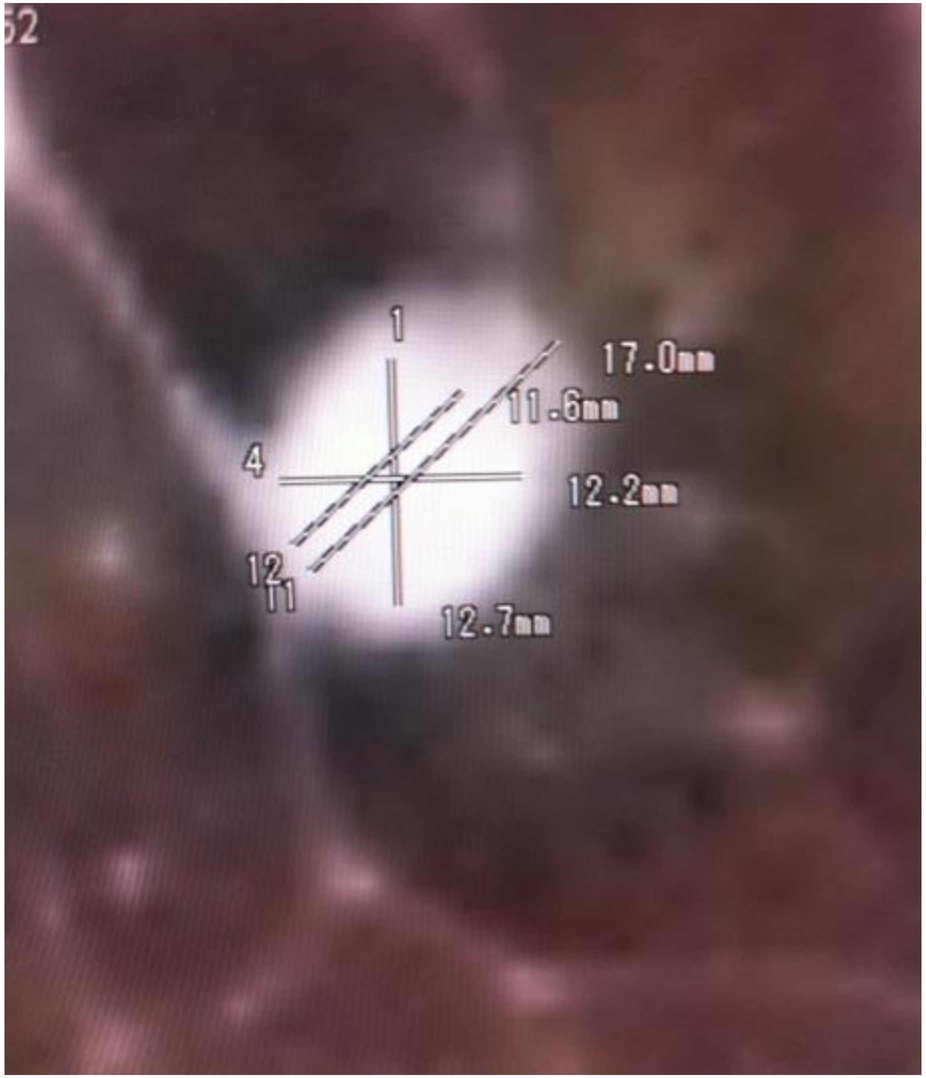
IMG_4190 (1).MOV

Motion artifacts are commonly seen with thoracic CT images

Motion artifacts



Tumor movement



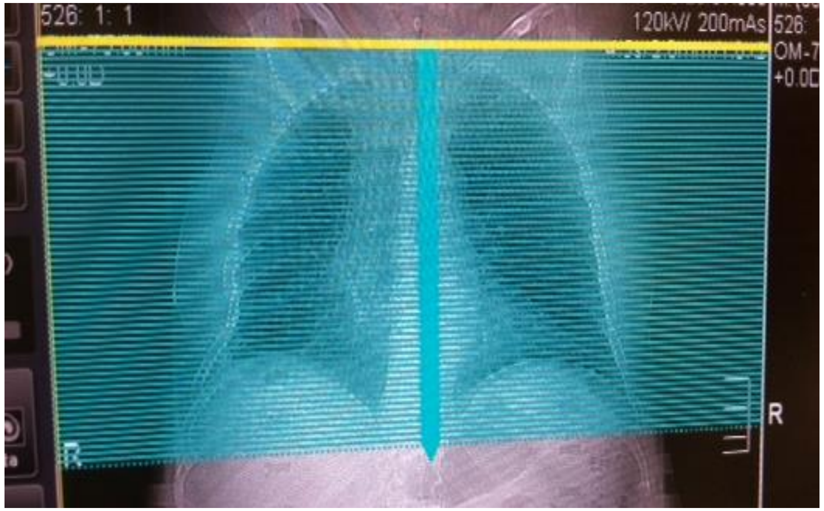
- Diagnosis
- Oligorecurrence of lung cancer

- Treatment
- Radiation Therapy (SBRT)

- Radiation Therapy Dose Prescription:
- PTV (RML nodule): 50 Gy at 12,5 Gy/fraction

Take home message

- Further research is necessary to assess the survival outcome and late toxicity with a longer follow-up for oligometastatic lung cancer
- Different strategies such as 4D repiratory gated acquisition techniques are needed for tumor motion control
- The consecuences of lower doses ("bath dose") in the OAR is still unknown



Questions:

- Immobilization
- Positioning
- Organ at risk contouring
- Set-Up
- Verification
- Radiation technique

???

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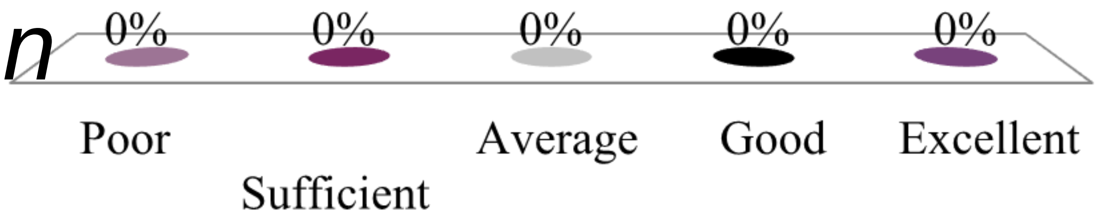
Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written in Survey Monkey



Case report: **Breast**

ESTRO School

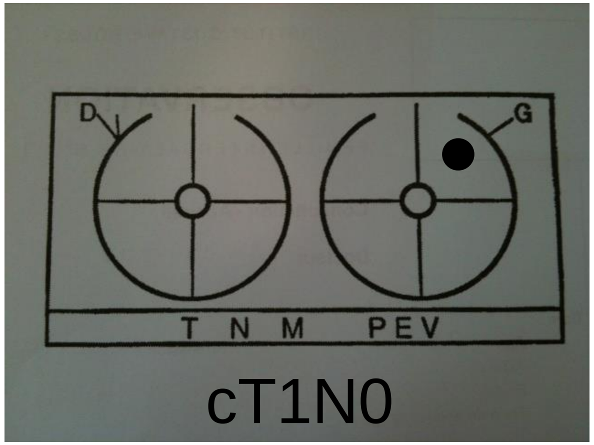
Sofia Rivera, MD,PhD
Radiation Oncology Department
Gustave Roussy
Villejuif, France

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Advanced skills in modern radiotherapy
May 2018

WWW.ESTRO.ORG/SCHOOL

Clinical case

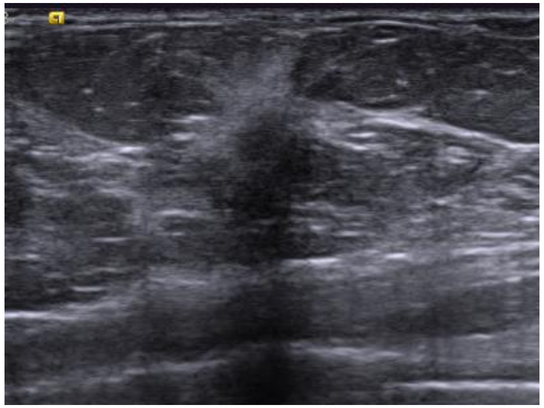


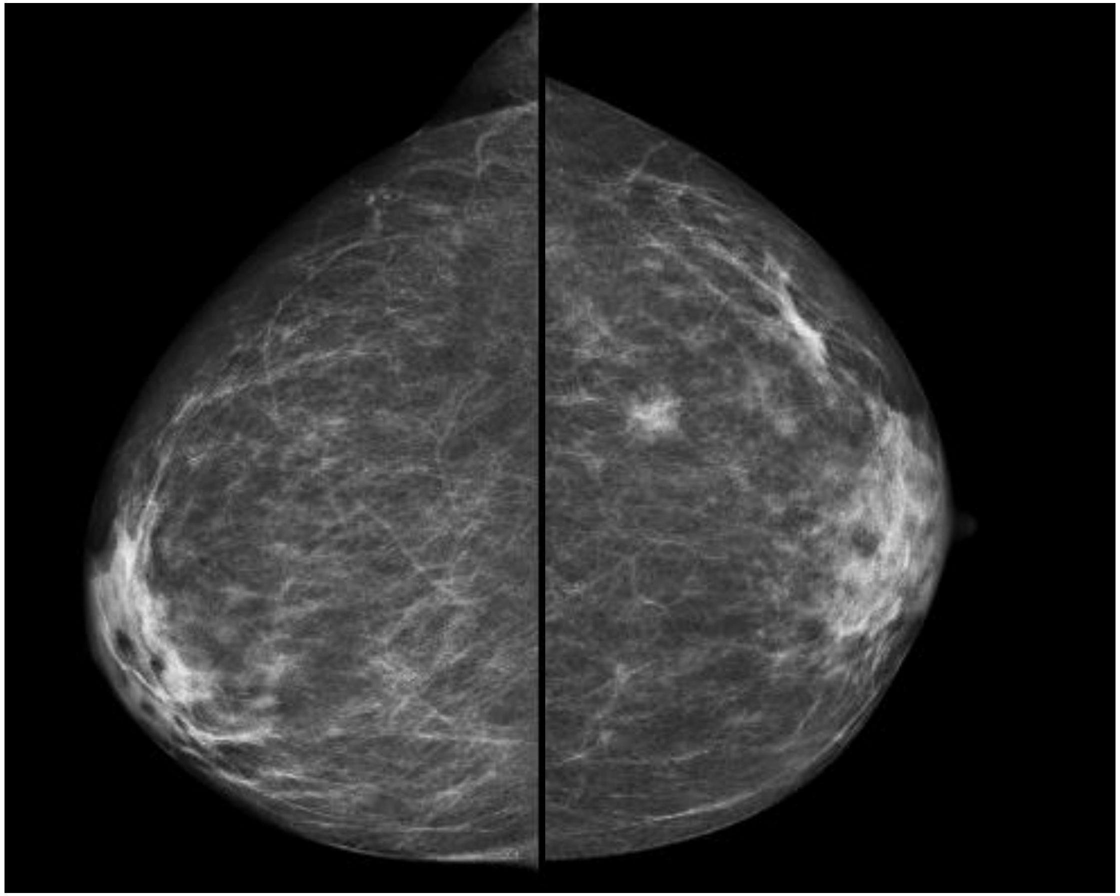
•72 years old female patient referred by her GP after palpation of a supra areolar hard mass of the left breast external upper quadrant measuring 1cm with no axillary or supraclavicular palpable node (breast cup: 95 D)

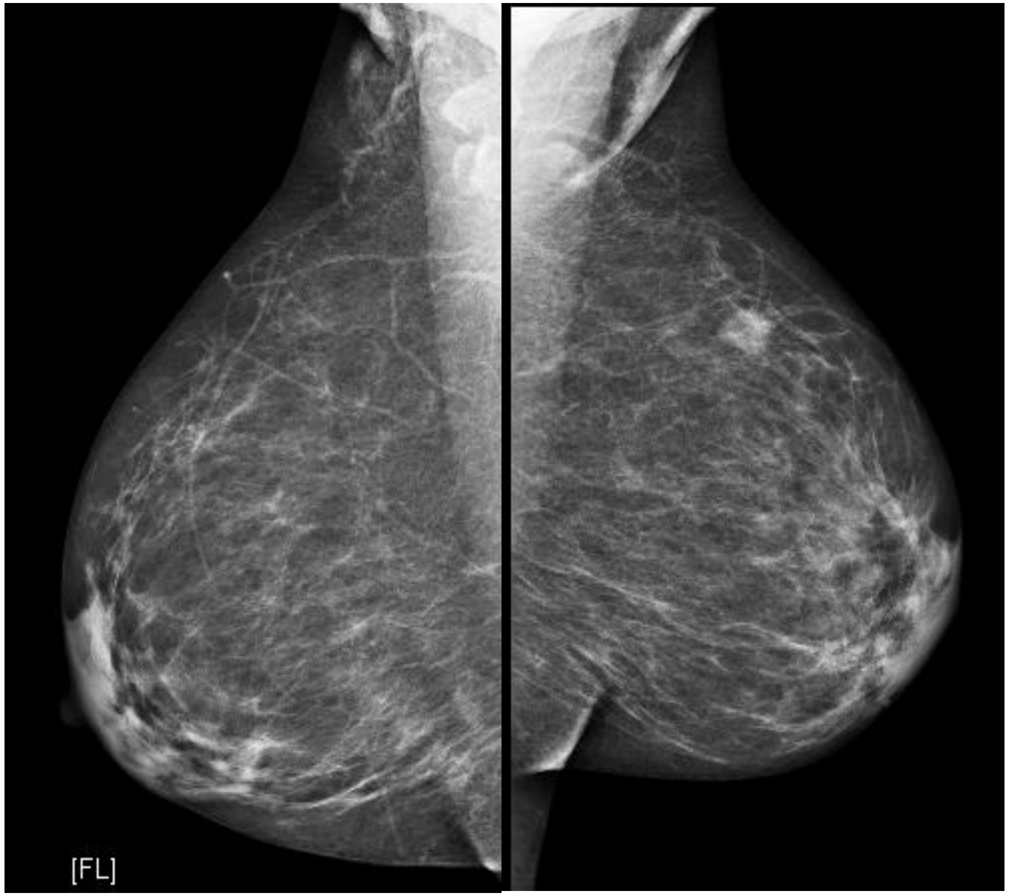
•Retired, yoga teacher, autonomous, living in an individual house with 5 cats

•Medical history of hypertension, diabetes and ischemic cardiopathy

Mammograms + US





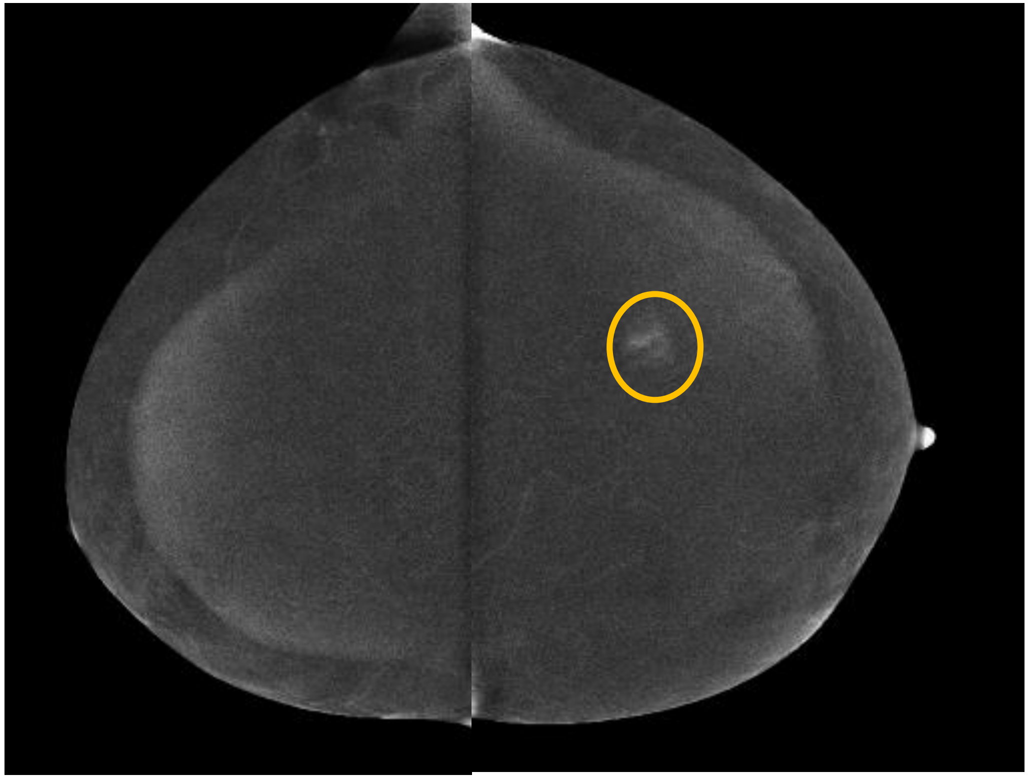


Do you see where the lesion is?

A. YES

B. NO

Angio mammography



Clinical case

•Imaging: confirmation of a single lesion without any suspicious lymph node

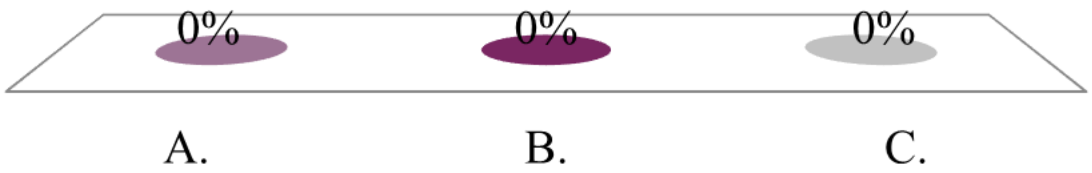
•Biopsy: Infiltrating ductal carcinoma, ER: 90%, PR: 80%, HER2- Ki67: 2%, grade I

•Lumpectomy + sentinel lymph node procedure: pT1cN0 in complete resection

•Adjuvant radiotherapy followed by hormonotherapy for 5 years

Which radiotherapy schema would you recommend?

A. Whole breast irradiation 50Gy in 25 fractions
B. Whole breast irradiation 50Gy in 25 fractions + boost Whole breast irradiation 40Gy in 15 fractions
C. Partial breast irradiation



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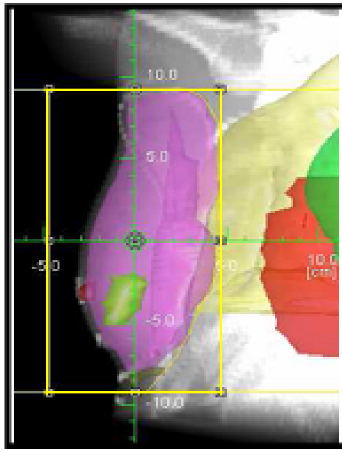
Therapeutic strategy: Which radiotherapy?

Two changing practice concepts have modified the standard whole breast irradiation 50Gy +/- boost



Hypo fractionated whole breast irradiation

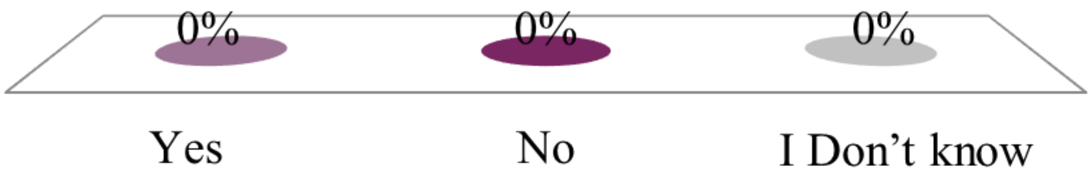
Whelan NEJM 2010; START A and B Lancet Oncol 2008

Accelerated partial breast irradiation

Vaidya Lancet 2010; Bourgier IJROBP 2010 ; Lemanski IJROBP 2010; Taghian IJROBP 2005; Polgar IJROBP 2004 ; Vicini IJROBP 2003; Formenti IJROBP 2003;

Do you perform hypofractionated treatments for breast cancer?

A. Yes
B. No
C. I Don’t know



Whole breast irradiation

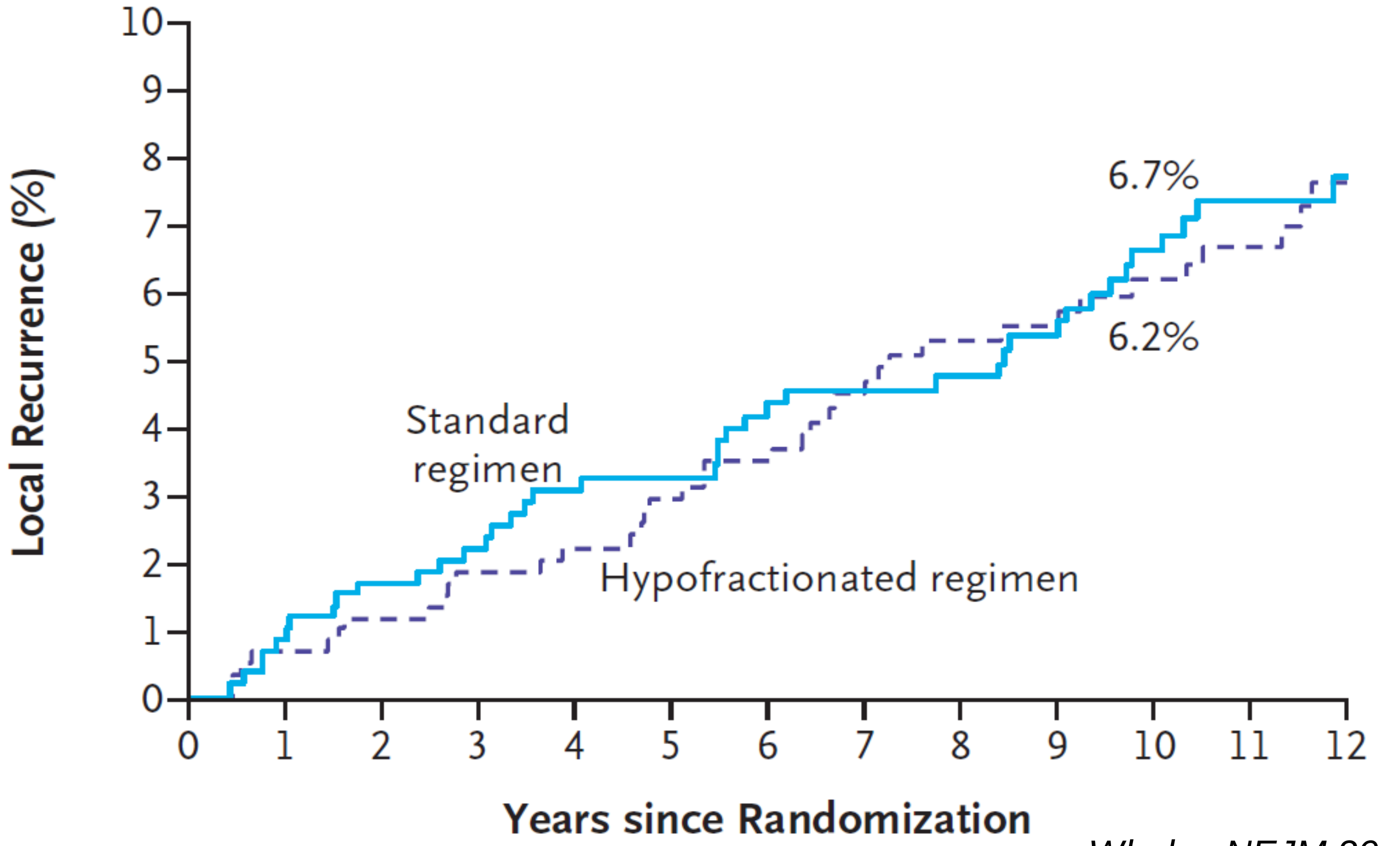
ORIGINAL ARTICLE

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D.,

N=1234

Short fractionated schedule	Long fractionated schedule
N=622	N=612
42.5Gy /16f	50Gy /25f



Whelan NEJM 2010

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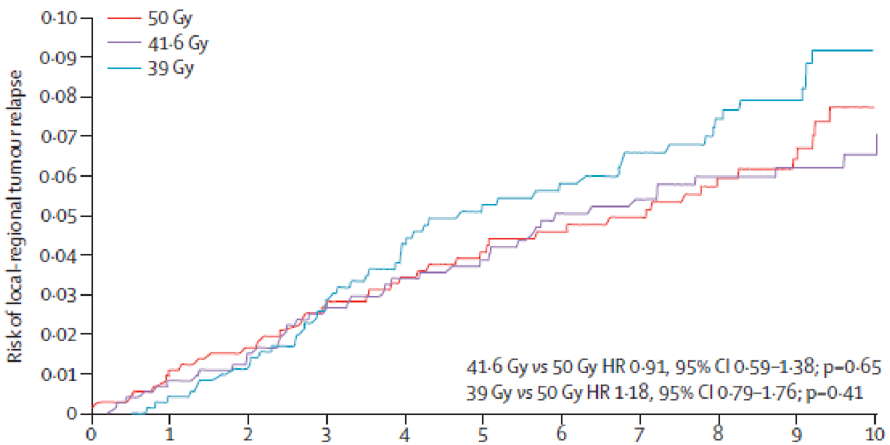
Whole breast irradiation

START A
2236 patients

50 Gy/25 fractions/ 5 weeks

41.6 Gy/13 fractions/ 5 weeks

39 Gy/13 fractions/ 5 weeks



Number at risk

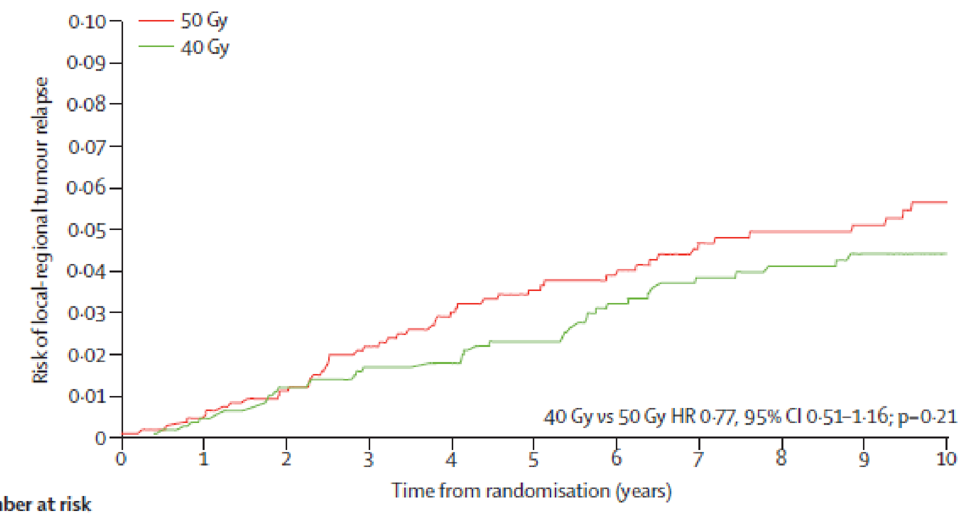
50 Gy	749	725	702	674	645	607	563	534	470	368	196
41·6 Gy	750	732	710	689	662	623	574	547	501	408	206
39 Gy	737	724	702	668	631	583	540	500	452	362	184

Median follow up = 9,3 yrs
LRR-10y (50Gy) : 7,4% [5,5-10]

START B
2215 patients

50 Gy/25 fractions/ 5 weeks

40 Gy/15 fractions/ 3 weeks



Number at risk

50 Gy	1105	1077	1047	1002	952	893	816	749	688	620	388
40 Gy	1110	1085	1055	1016	982	927	843	772	710	639	412

Median follow up = 9,9 yrs
LRR-10y (50Gy) : 5,5% [4.2-7,2]

JS Haviland; Lancet Oncol 2013

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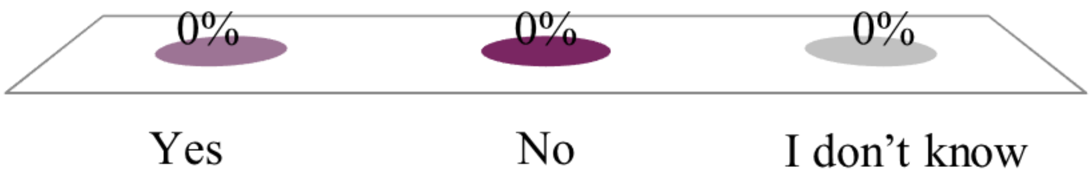
Do you perform partial breast irradiation?

A. Yes
B. No
C. I don’t know



Partial breast irradiation indication guidelines

ESTRO	ASTRO
• >50 years	• ≥60 years
• IDC, mucinous, tubular, medullary, and colloid cc.	• Invasive ductal or other favorable subtypes
• Associated LCIS allowed but not DCIS	• Pure DCIS not allowed
• Any grade, ER, PR	• ER status positive
• pT1–2 (⩽30 mm)	• pT1 : ≤2 cm
• Negative surgical margins (⩾2 mm)	• Negative surgical margins by at least 2 mm
• Unicentric, Unifocal	• Unicentric only, Clinically unifocal with total size ≤2.0 cm
• pN0 (by SLNB or ALND)	• pN0 (i^-, i^+) (by SLNB or ALND)

Polgar, Radiother Oncol 2010

Smith IJROBP 2009

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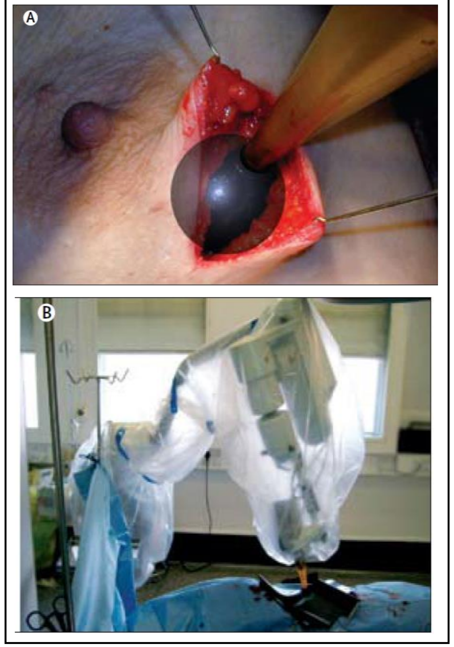
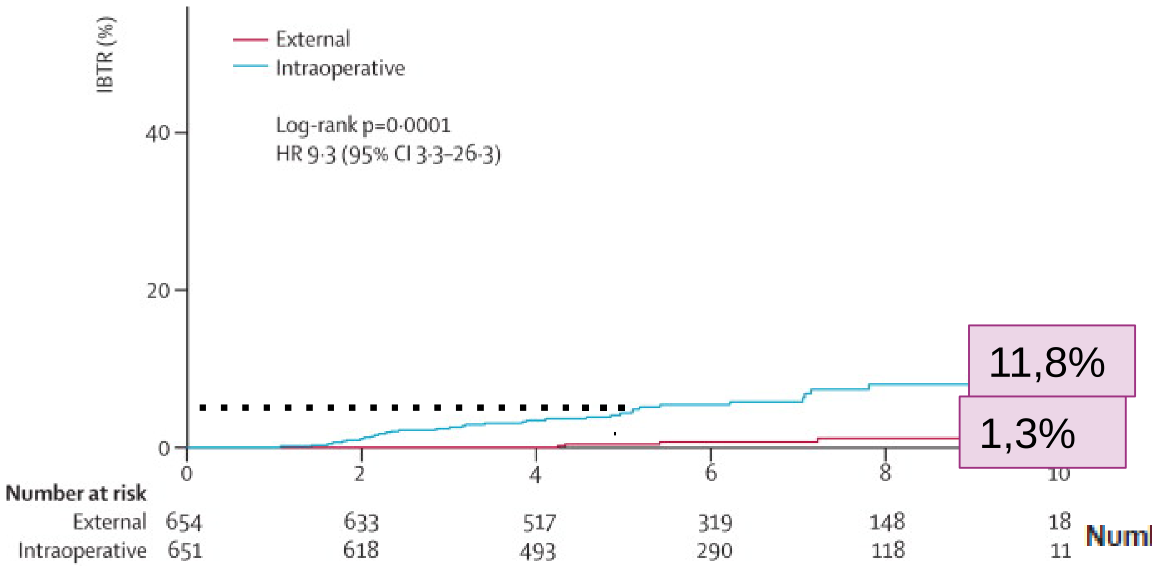
Intraoperative Partial breast versus whole breast irradiation



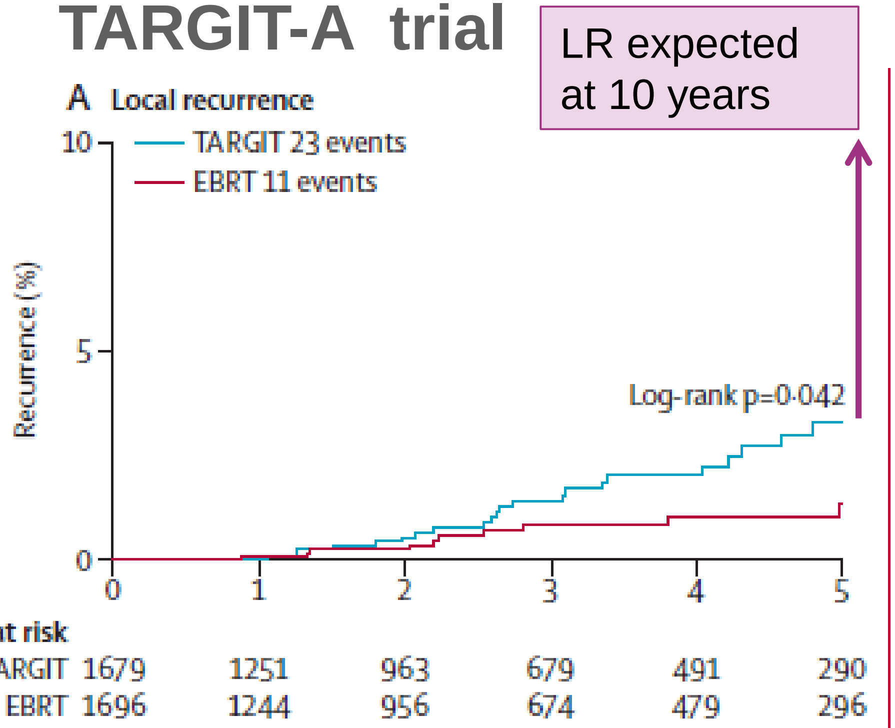
•Ipsilateral breast recurrence

ELIOT trial



Veronesi et al; lancet oncol 2013

TARGIT-A trial



Vaidya et al; lancet oncol 2013

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Radiotherapy and Oncology xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Special commentary

Has partial breast irradiation by IORT or brachytherapy been prematurely introduced into the clinic?

Harry Bartelink [a,*], Celine Bourgier [b], Paula Elkhuizen [a]

[a] Netherlands Cancer Institute, The Netherlands; [b] Institut Gustave Roussy, France

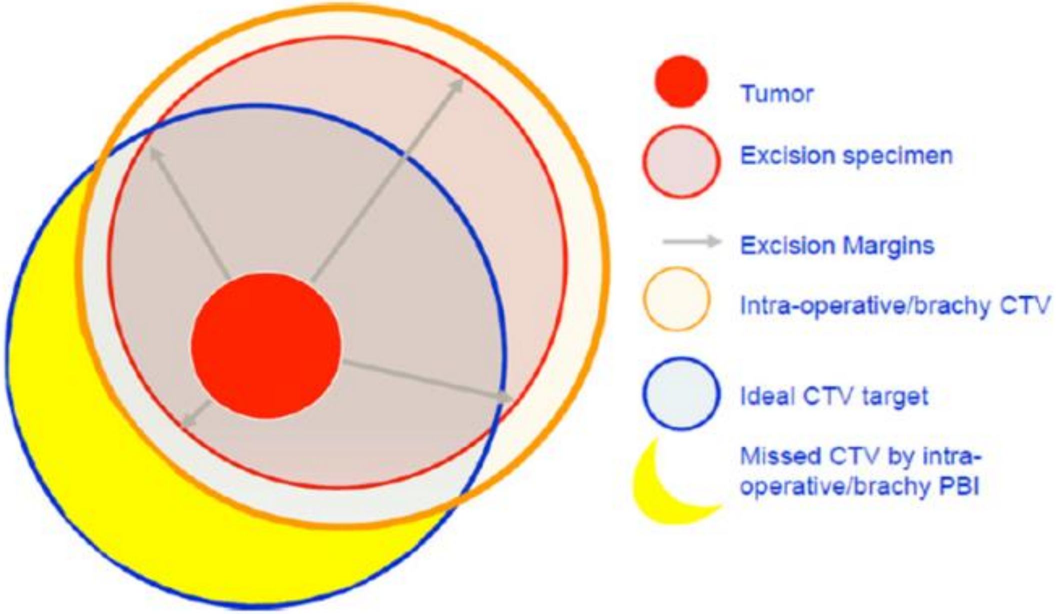

Fig. 1. Breast tumors are often eccentric located with highest risk of residual tumor in the region of the narrowest resection margin, therefore CTV by brachy or IORT is not covered.

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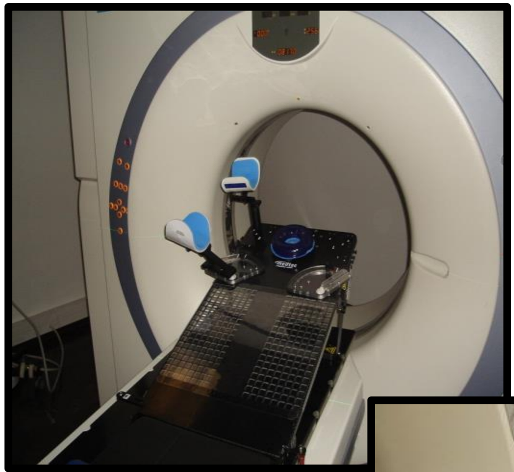
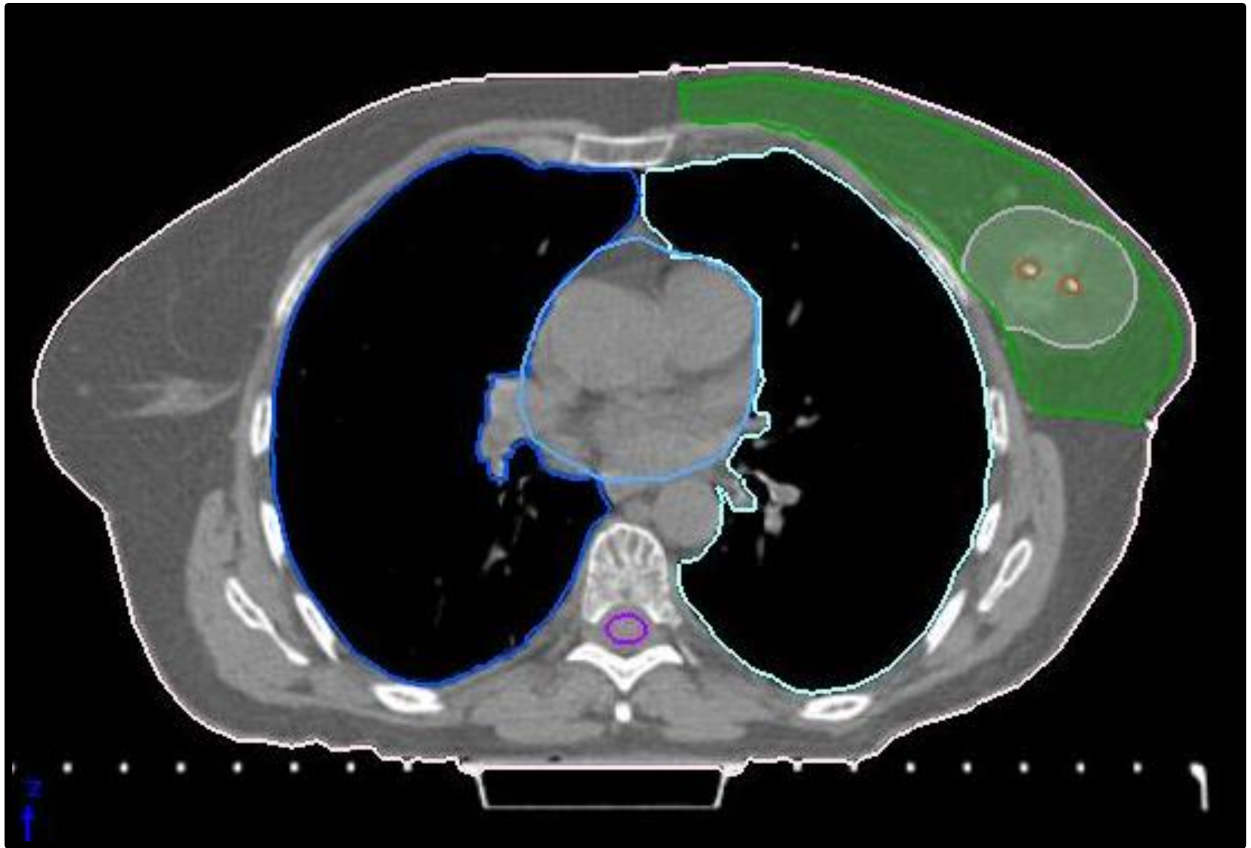
EBRT allows for conformal treatment

- In pre operative or post operative (several ongoing trials)
- Positioning and contouring are essential : more risks to miss the target as we don't treat the whole breast!





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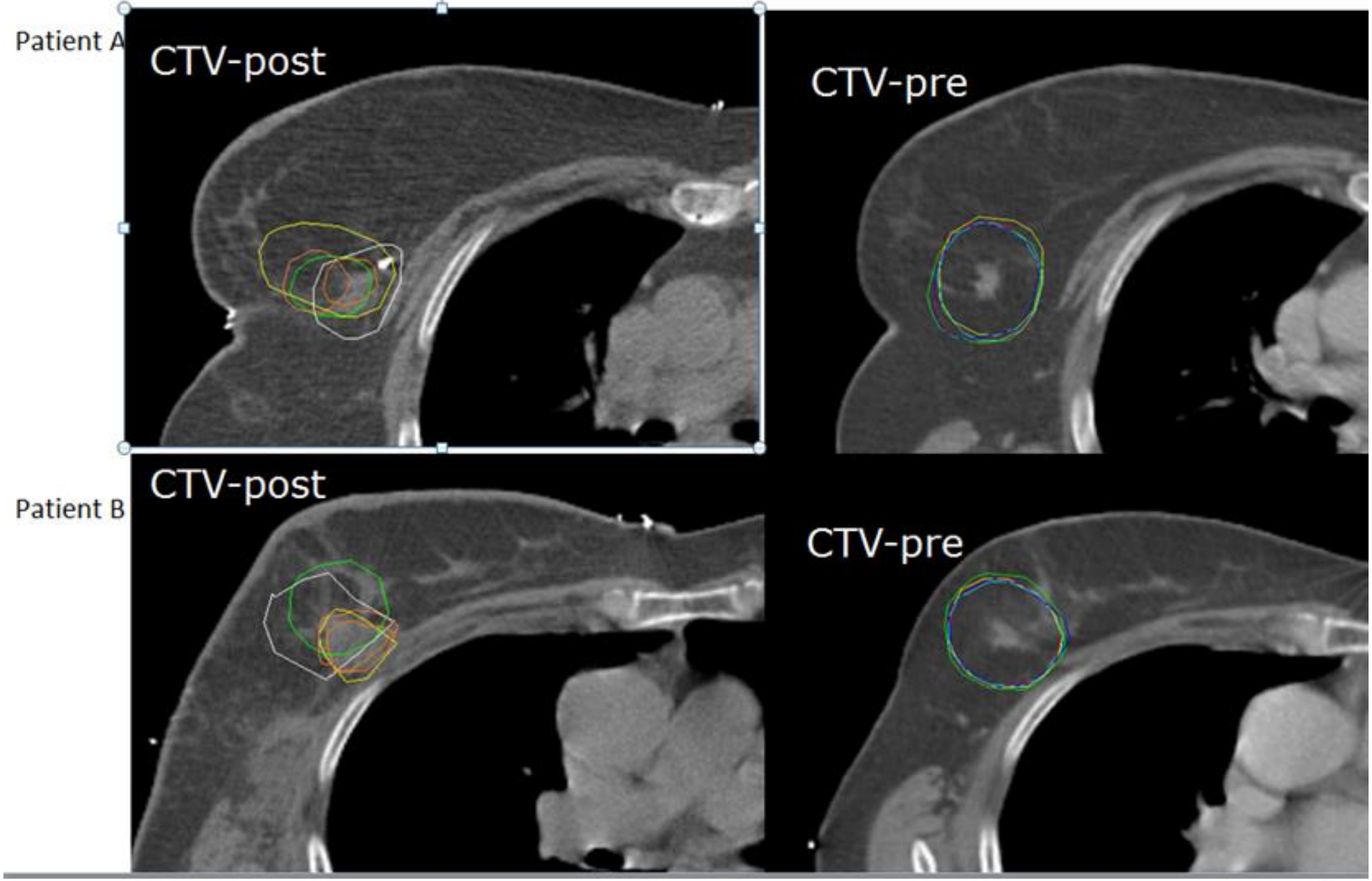
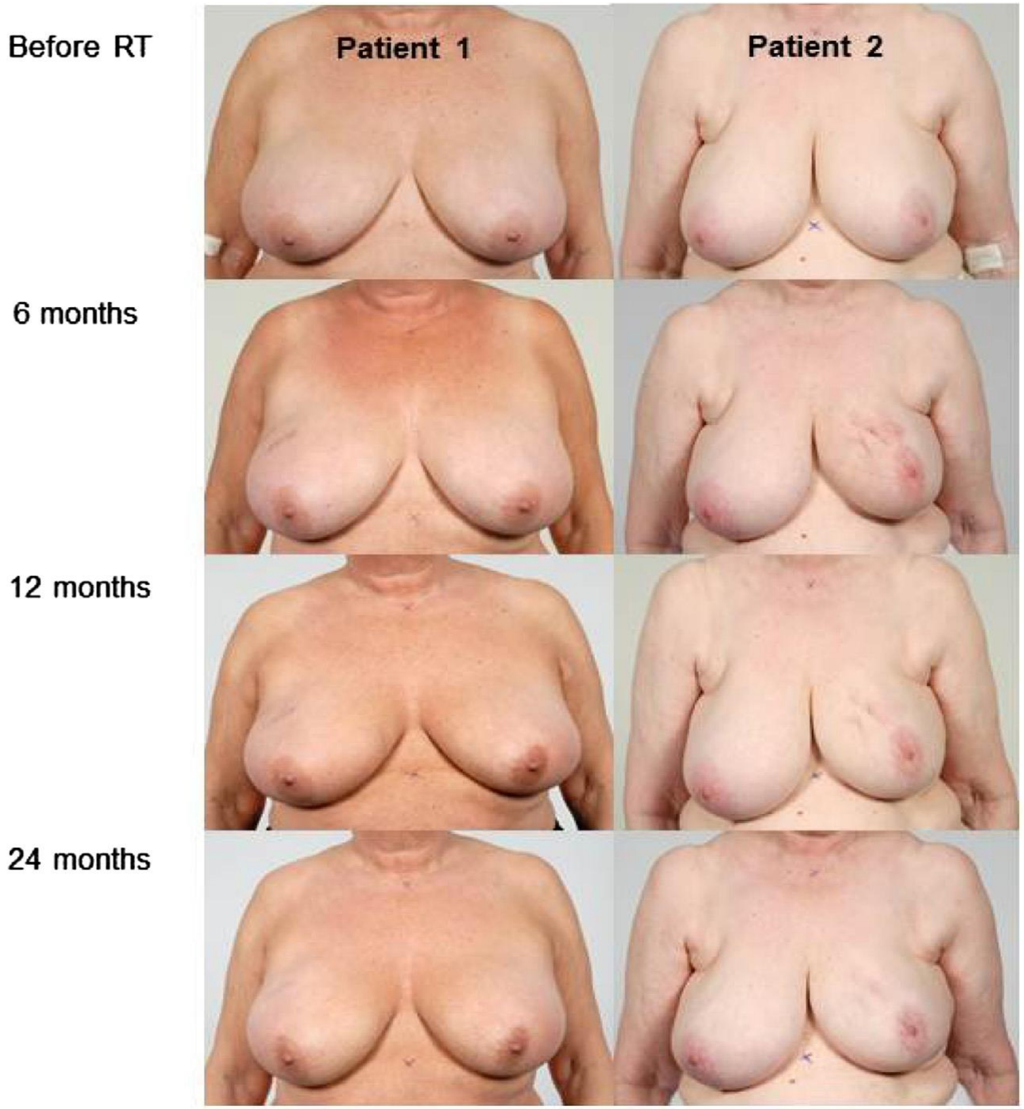
Preop. vs postop. delineation

van der Leij et al *Radiother Oncol 2014*



Pre-op APBI ⟹ improved homogeneity in contouring

PAPBI: first résults

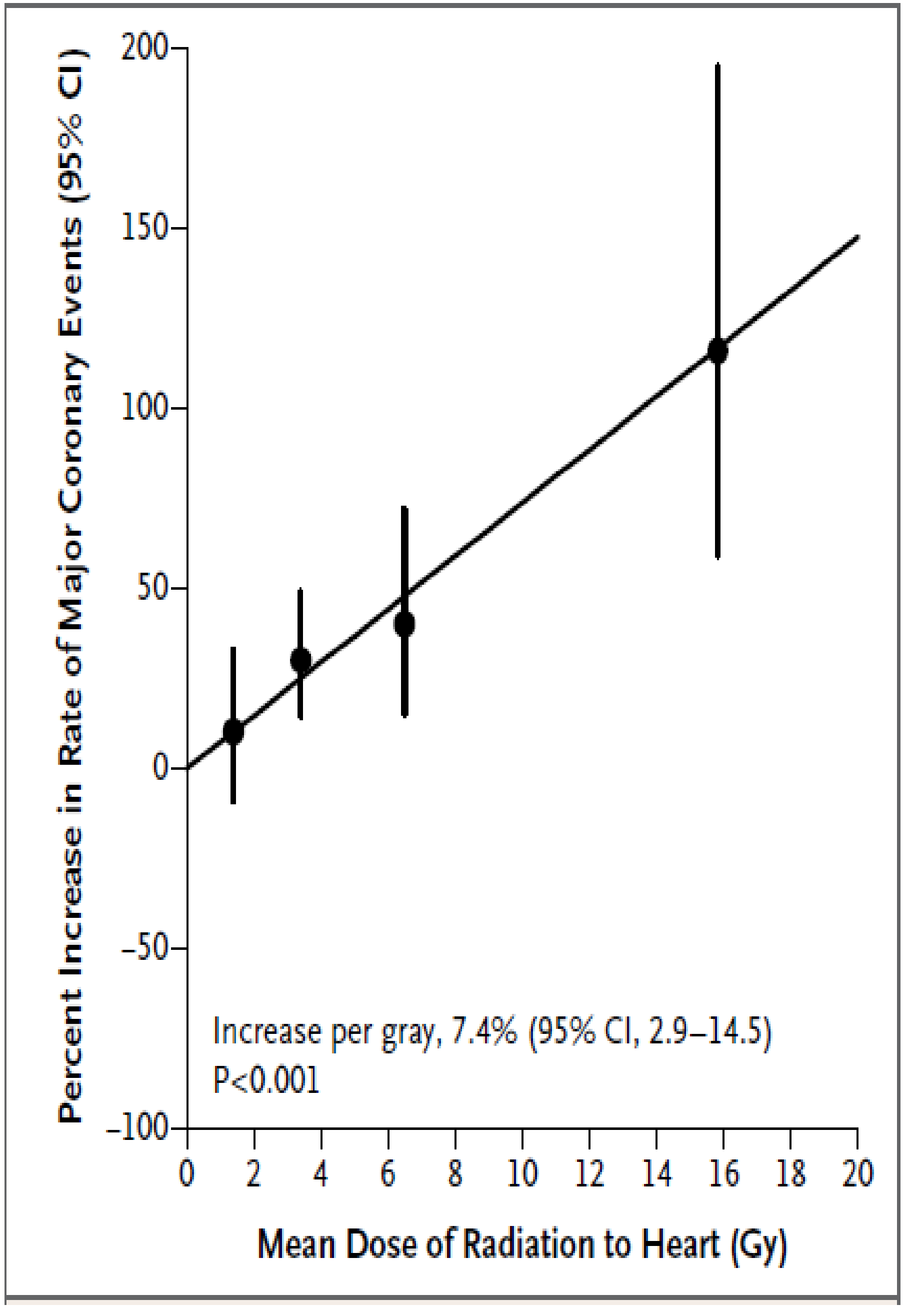


Pre-op APBI → improved cosmesis over time

F. Van Der Leij, Radiot Oncol 2015

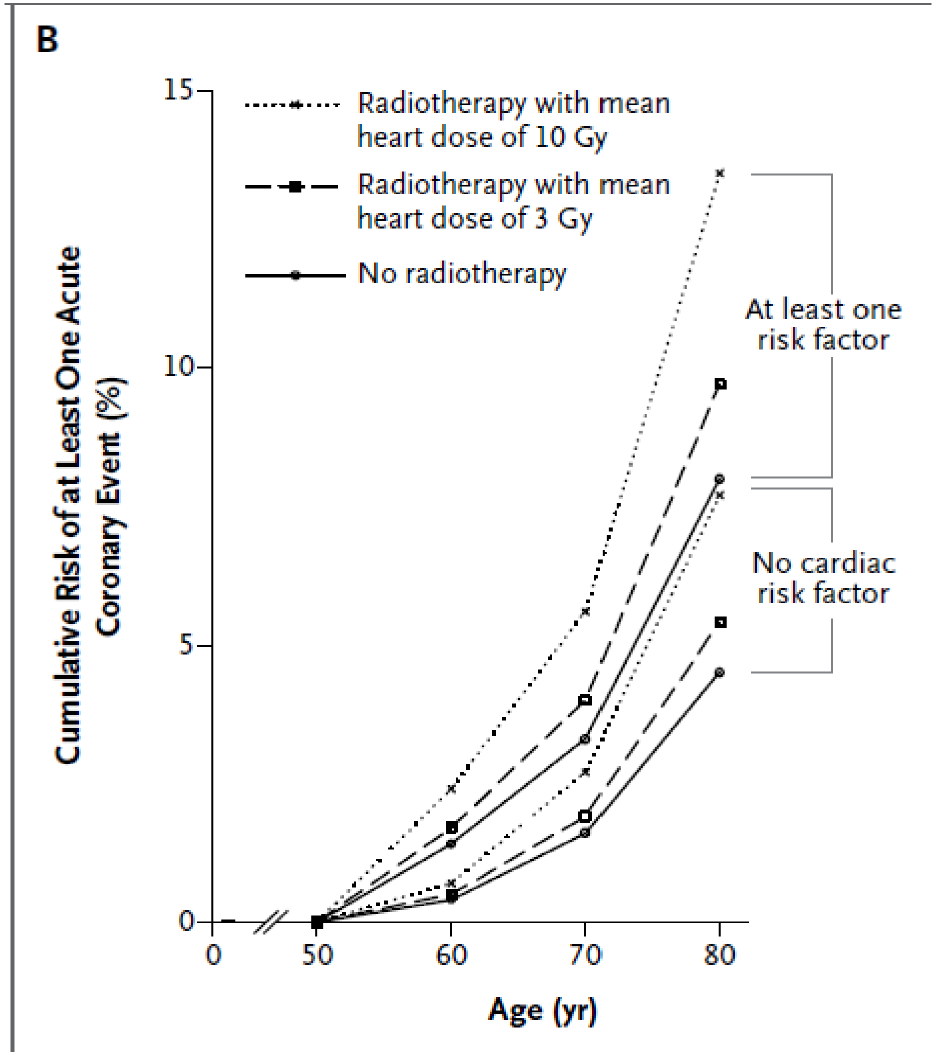
Heart Toxicity

- “The overall average of the mean doses to the whole heart was 4.9 Gy (range, 0.03 to 27.72). Rates of major coronary events increased linearly with the mean dose to the heart by 7.4% per gray (95% confidence interval, 2.9 to 14.5; P<0.001), with no apparent threshold. The increase started within the first 5 years after radiotherapy and continued into the third decade after radiotherapy. The proportional increase in the rate of major coronary events per gray was similar in women with and women without cardiac risk factors at the time of radiotherapy”



Darby NEJM 2013

Cardiac risk is increased by cardiovascular risk factors

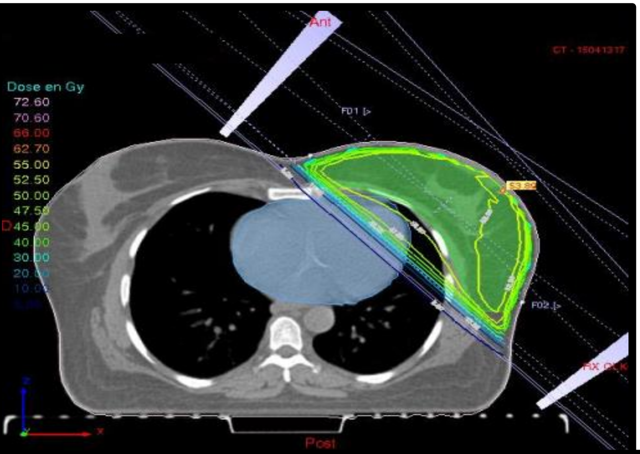


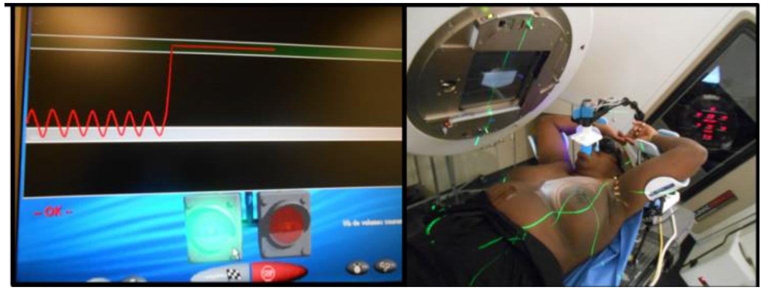
Darby NEJM 2013

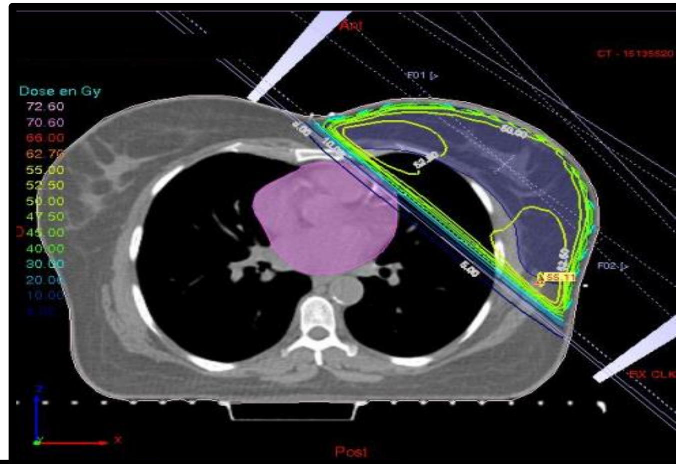
Improved heart sparing by breath hold

Free breathing

Breath hold inspiration



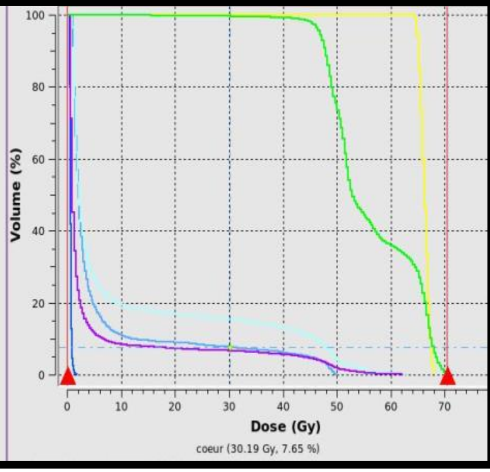




Statistiques

	1	2	3	4	5	6
Structure	coeur	poumon D	poumon G	Poumons	PTV boost	PTV sein
Vol. Géom. (cm3)	488.6	1065.4	843.0	1881.9	52.8	1190.1
Points Aléatoires	6756	7779	7433	8823	4937	7957
Dose Min. (Gy)	0.75	0.34	0.86	0.35	63.90	9.10
Dose Max. (Gy)	50.31	2.13	63.34	63.47	67.88	70.44
Dose Med. (Gy)	1.98	0.63	2.06	0.83	66.09	52.69
Dose Moy. (Gy)	6.18	0.66	9.86	4.66	66.09	56.22
Ecart Type	11.73	0.17	16.47	11.77	0.81	8.29
Borne Dose Min. (Gy)	0.00	0.00	0.00	0.00	0.00	0.00
Borne Dose Max. (Gy)	70.44	70.44	70.44	70.44	70.44	70.44
Vol. sélection (cm3)	488.6	1065.3	842.9	1881.8	52.8	1190.0
Vol. sélection (%)	100.0	100.0	100.0	100.0	100.0	100.0
Dose à 95% (Gy)				0.37	64.78	46.66
Dose à 2% (Gy)	48.50	1.14	53.99	49.70		

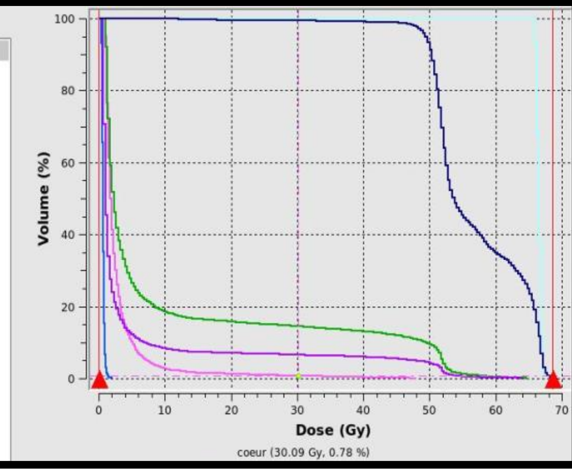
Heart mean dose: 6.8Gy



Statistiques

	1	2	3	4	5	6
Structure	coeur	poumon D	poumon G	Poumons	PTV boost	PTV sein
Vol. Géom. (cm3)	550.4	2007.8	1714.2	3686.4	46.5	1301.6
Points Aléatoires	6891	8965	8628	10648	4858	8109
Dose Min. (Gy)	0.83	0.34	0.71	0.33	65.29	7.86
Dose Max. (Gy)	48.92	2.29	65.88	65.67	67.21	68.53
Dose Med. (Gy)	1.71	0.64	2.06	0.90	66.40	53.50
Dose Moy. (Gy)	2.82	0.67	9.81	4.83	66.40	56.68
Ecart Type	4.20	0.19	16.89	12.29	0.36	7.38
Borne Dose Min. (Gy)	0.00	0.00	0.00	0.00	0.00	0.00
Borne Dose Max. (Gy)	68.53	68.53	68.53	68.53	68.53	68.53
Vol. sélection (cm3)	550.3	2007.6	1714.2	3686.3	46.5	1301.5
Vol. sélection (%)	100.0	100.0	100.0	100.0	100.0	100.0
Dose à 95% (Gy)				0.38	65.78	49.30
Dose à 2% (Gy)	12.72	1.17	53.27	51.97		

Heart mean dose: 2.82Gy



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Take home messages:

- Accelerated hypofractionated whole breast and partial breast irradiation are changing our practices for early breast cancers with good prognosis factors

- Contouring and positioning remain key points for these treatment strategies

- Moving toward better sparing OAR means we need to assess low dose consequences as well

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Image Registration and Evaluation: Part 2 CBCT (Varian)

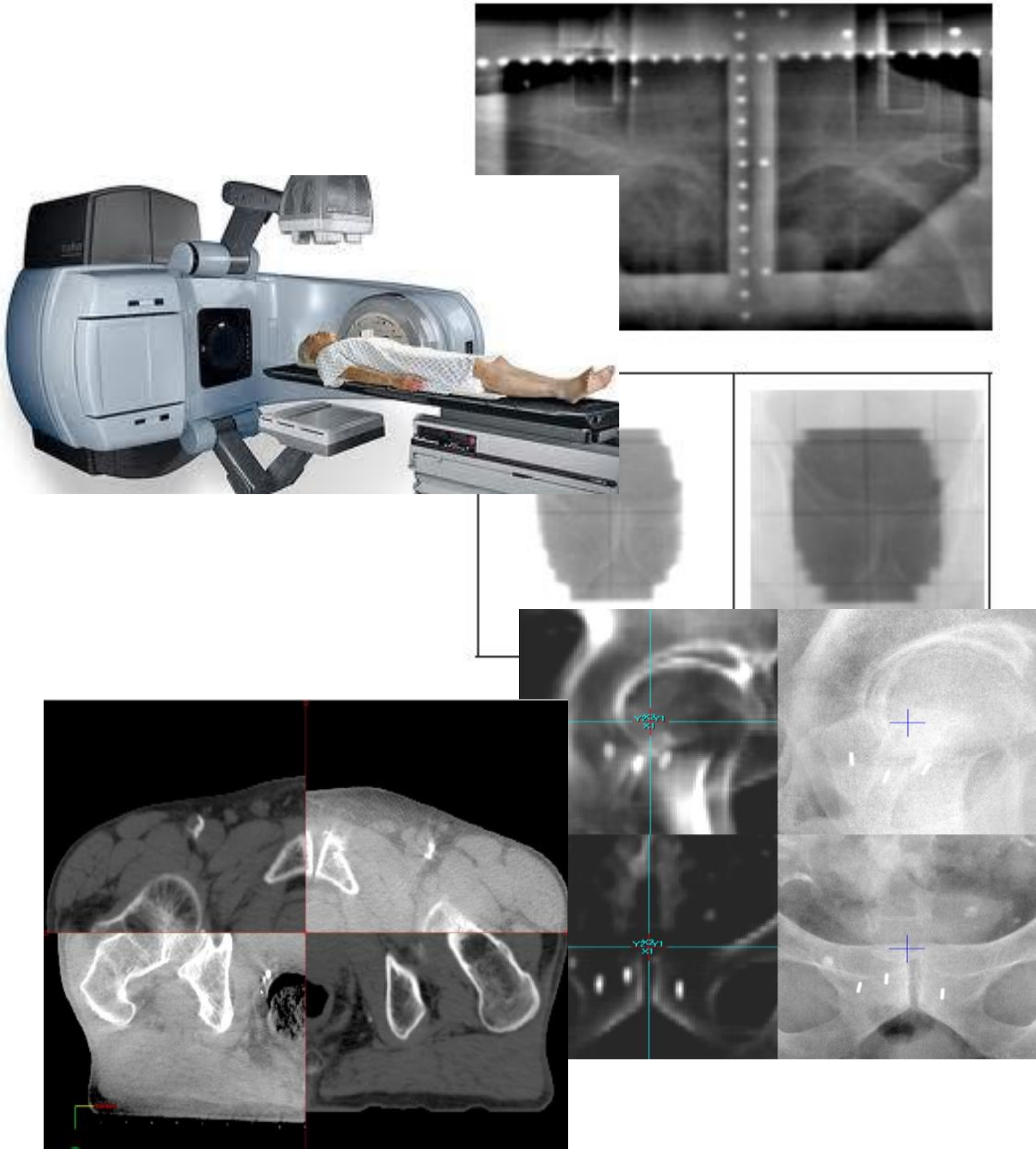
Liz Forde, RTT
Assistant Professor
The Discipline of Radiation Therapy
School of Medicine
Trinity College Dublin

Learning Outcomes

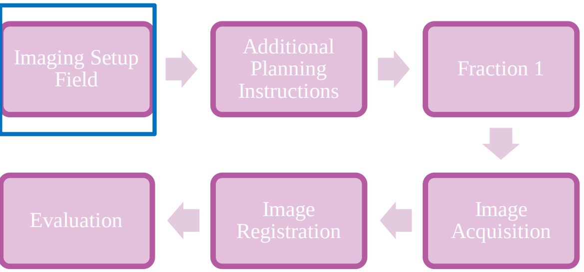
- Identify the key features of the Varian OBI system
  - ➢ 2D and 3D image acquisition, registration and verification
- Outline the CBCT acquisition, registration and evaluation process
- Discuss what influences CBCT image quality
- Identify appropriate match structures for the main tumour sites
  - ➢ kV 2D/2D and CBCT
- Discuss possible clinical scenarios that require troubleshooting

Key Features of Varian OBI

- 2D
  - ➢ MV and kV
- 2D/2D
  - ➢ MV and kV
- 3D
  - ➢ kV
- Fluoroscopy (2D + time)



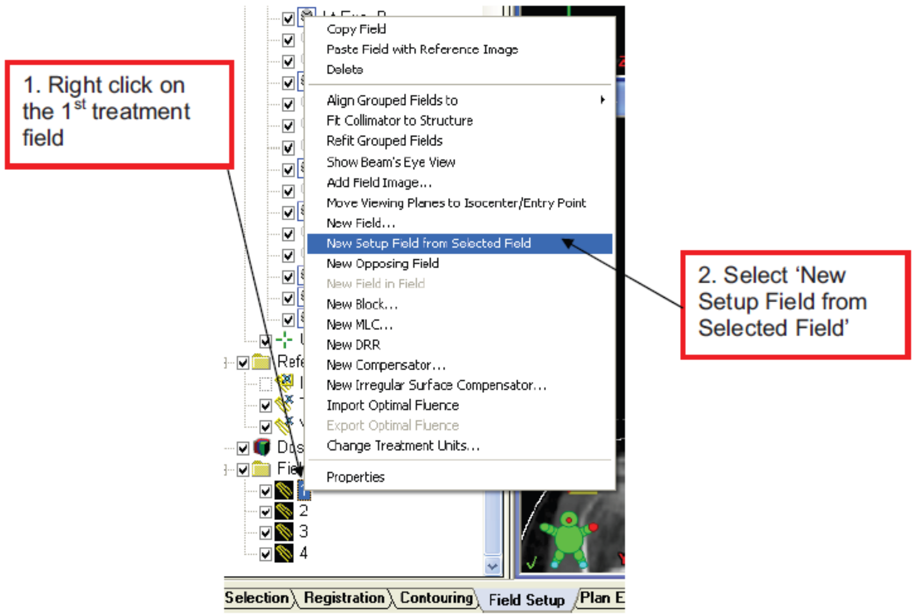
The IGRT Process

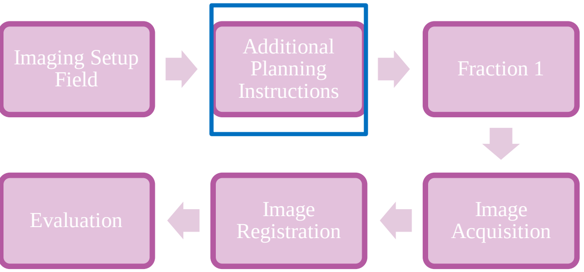


IGRT Setup in Planning

- Create setup fields in planning

- Consider the position of the **isocentre**
    - Varian does not have a “Correction reference point”
    - IMRT and VMAT are forgiving with isocentre placement
    - CBCT may need to shift laterally for clearance
    - You will be prompted on the linac

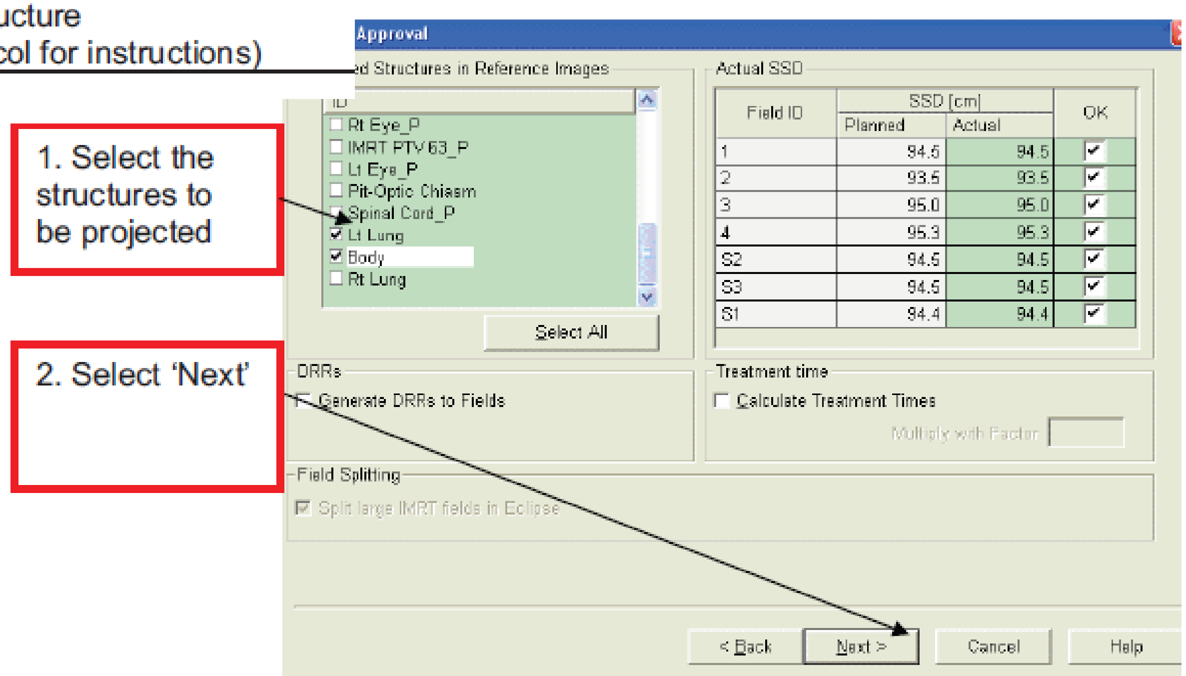




IGRT Setup in Planning

- Additional contours to be outlined and/or "sent across" for image verification

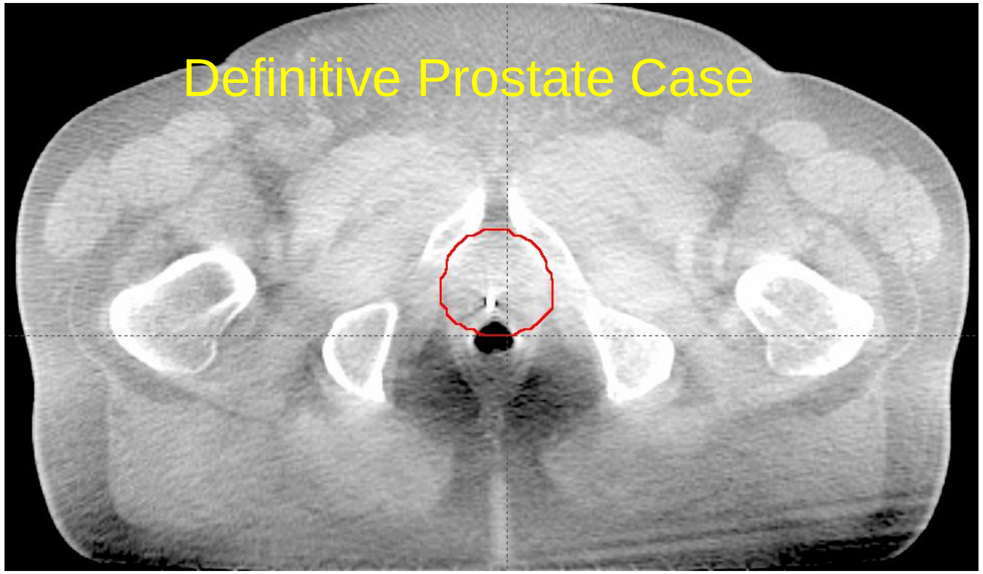
Treatment Area	Imaging Type	Extra Contouring
All treatment areas	CBCT, kV or MV	PTV
All treatment areas	CBCT	FSD tolerance rings (see site specific planning protocols for instructions and size of the rings)
Chest	kV or MV or CBCT	Carina
Abdomen	kV or MV or CBCT	Carina
Breast/Chest Wall	MV	Lung (treatment side) and Body
Prostate	CBCT	Convert dose to structure (see prostate protocol for instructions)
Post-Prostatectomy	CBCT	Convert dose to structure (see prostate protocol for instructions)



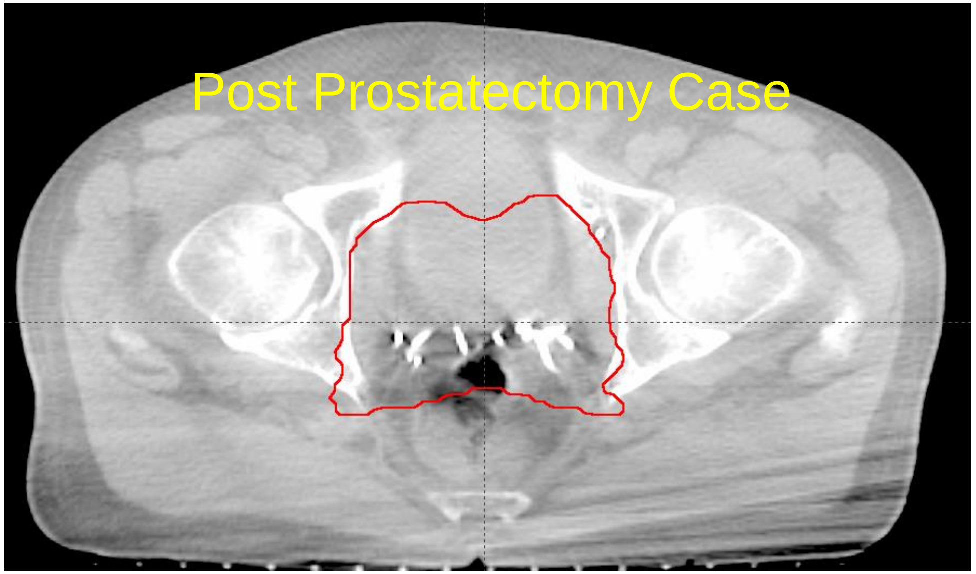
IGRT Setup in Planning

- Additional contours to be outlined and/or "sent across" for image verification
  - In Field Setup (Eclipse TPS) "Convert isodose line to structure"

80Gy isodose line



68Gy isodose line



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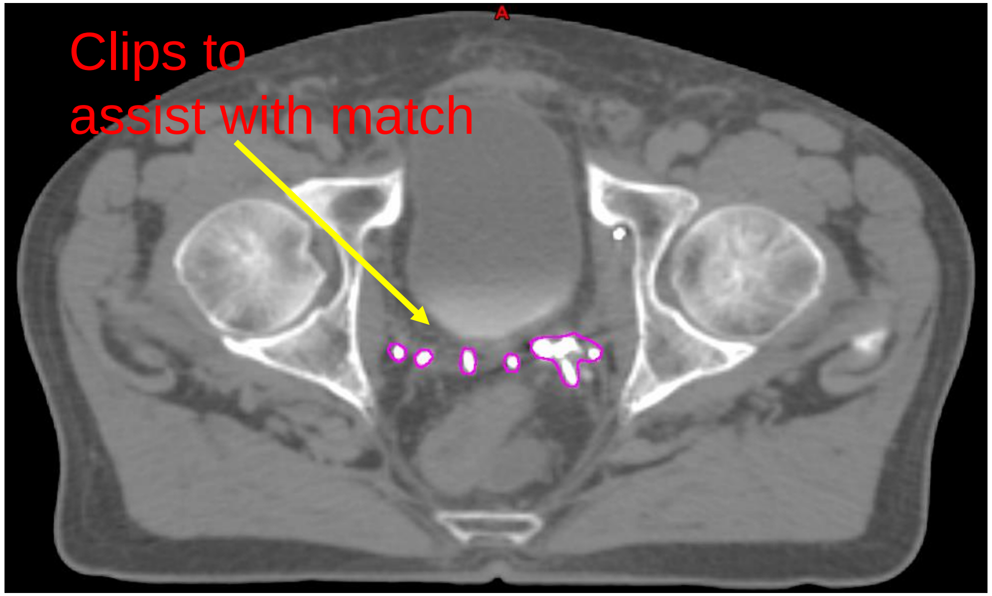
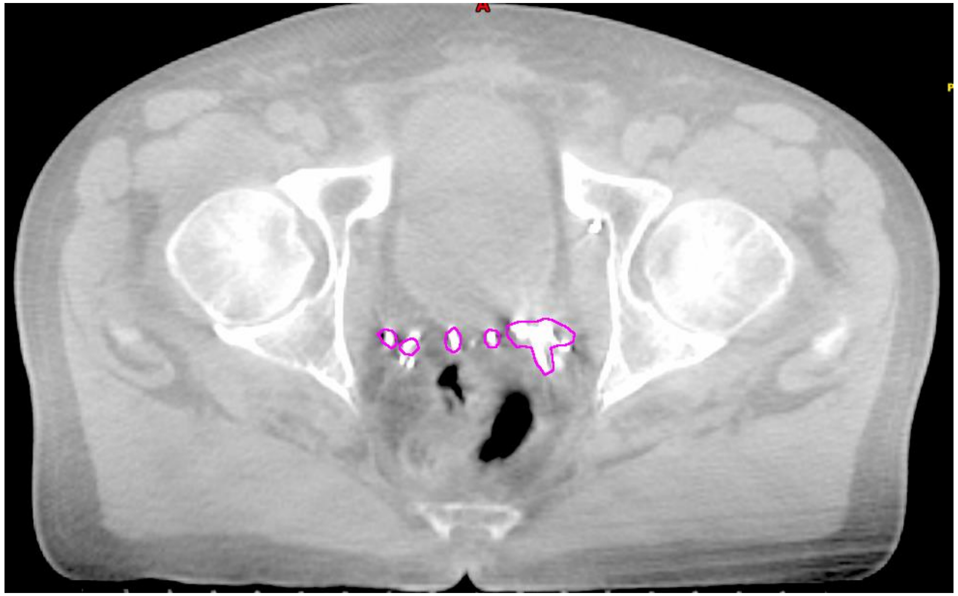
IGRT Setup in Planning

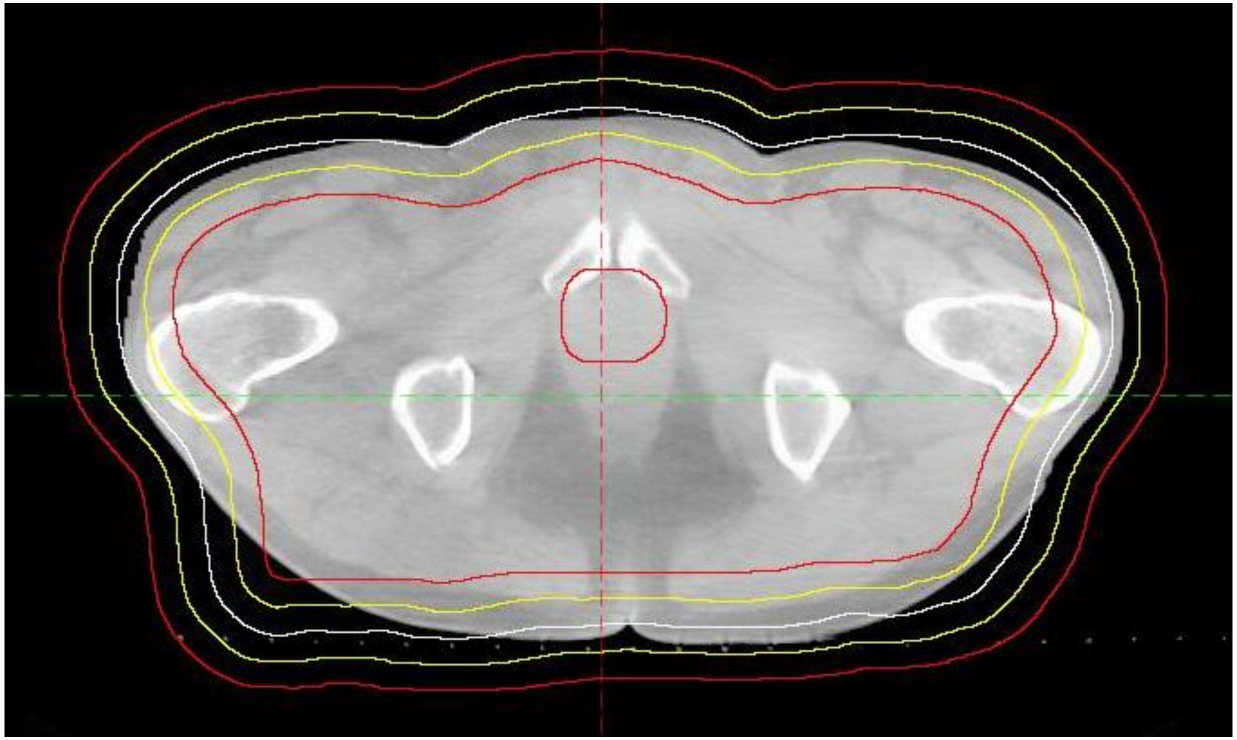
- Additional contours to be outlined and/or "sent across" for image verification
  - ➢ In Contouring Workspace in Eclipse TPS

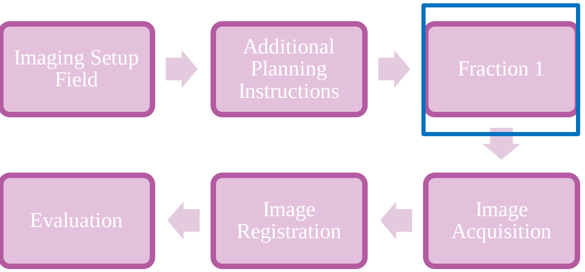




IGRT Setup in Planning

- Additional contours to be outlined and/or “sent across” for image verification
    - ➢ In Contouring Workspace in Eclipse TPS “Wall Extraction” tool from Body contour





Fraction 1 Considerations

- Clearance

- Education
  - ➢ Who should be present for first day scan?
  - ➢ RO, MP, RTT responsible for plan, Senior RTT

- Documentation!
  - ➢ Anything weird and wonderful
  - ➢ Structures to include/avoid

- Set VOI box and decide on additional registration variables
  - ➢ This will ensure consistency throughout the course of treatment

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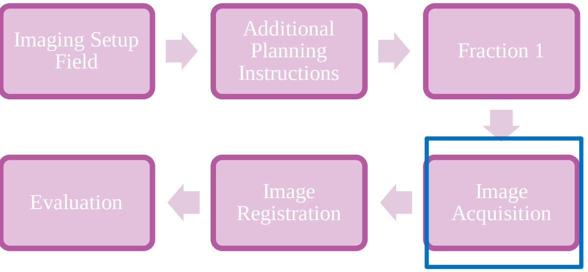


The Image Acquisition Process - CBCT

1. Select correct bow tie filter for treatment site
2. On fraction 1 consider checking rotation/clearance whilst in room
3. Mode up CBCT setup imaging field
    1. Note this is incorporated in the individual patient's plan

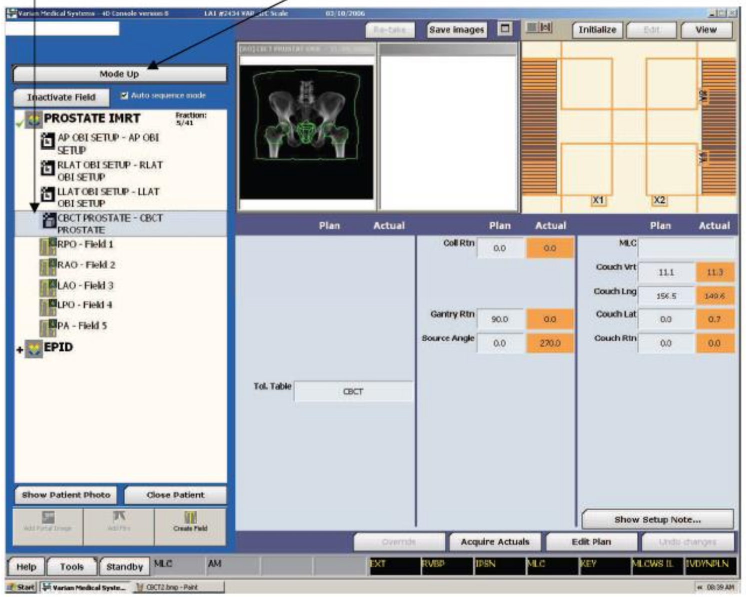
Scan Name	Gantry Rotation Required	Bow-tie Filter Required	Treatment sites to be used on	Field of View
Standard-dose head	200	Full	-	24cm
Low-dose head	200	Full	-	24cm
High-quality head	200	Full	Head & Neck Brain	24cm
Pelvis	360	Half	Pelvis (includes: Prostate Rectum Bladder Gynecological)	45cm
Pelvis spotlight	200	Full	-	24cm
Low-dose thorax	360	Half	Chest Abdomen	45cm

NB: See pictures below to distinguish between the bow-tie filters

1. Call up the patient on the 4DTC and mode up the CBCT field.

Click on the CBCT field

Select mode up



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The Image Acquisition Process - CBCT

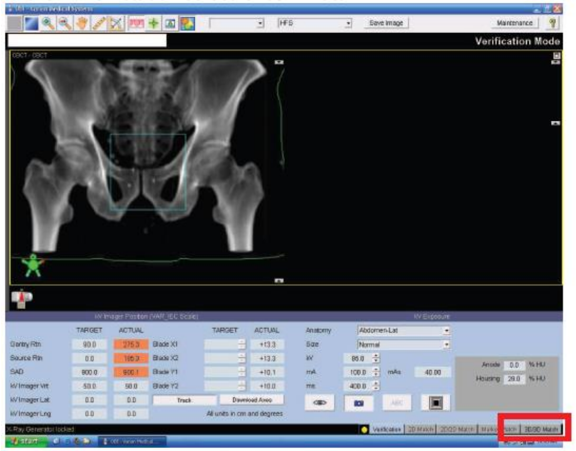
4. Select 3D/3D match

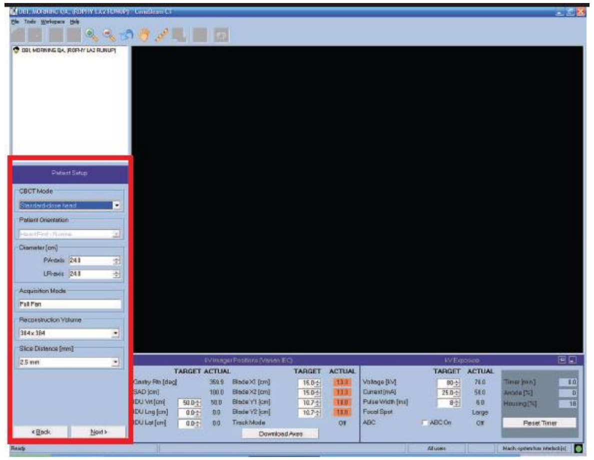
5. Acquire new scan

6. Complete details
    1. Slice thickness
    2. Orientation
    3. Full fan or half fan

7. Start scan

8. Accept and export





CBCT Image Quality

- What impacts on image quality?
  - CBCTs use a large flat panel detector – increases scatter
  - Permanent anti scatter filter built into detector panel

Scatter decreases image contrast, increases noise, possible registration errors and also patient dose

↓

CT Numbers (HU) affected

CBCT Image Quality

- Machine characteristics
  - ➢ MV or kV
  - ➢ Acquisition time
  - ➢ Scan length
  - ➢ Filters used
    - o Bow Tie filter added to source panel

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Bow Tie Filters

- Decrease patient dose
- Two types used in different modes: Full fan or half fan mode
- Full fan mode: image is acquired at the central axis on the detector panel and images acquired from 200º rotation
- Half fan mode: the detector is offset laterally acquiring only half of the projection of the patient
    - ➢ Detector panel is offset laterally, rotates a full 360º captures only half a projection and reconstructs the image from that
    - ➢ Recommended for larger FOV (pelvis)
    - ➢ Half fan filters result in the greatest HU discrepancy b/w CT and CBCT (Ding *et al.*, Yoo and Fang-Fang, Seet *et al.*)

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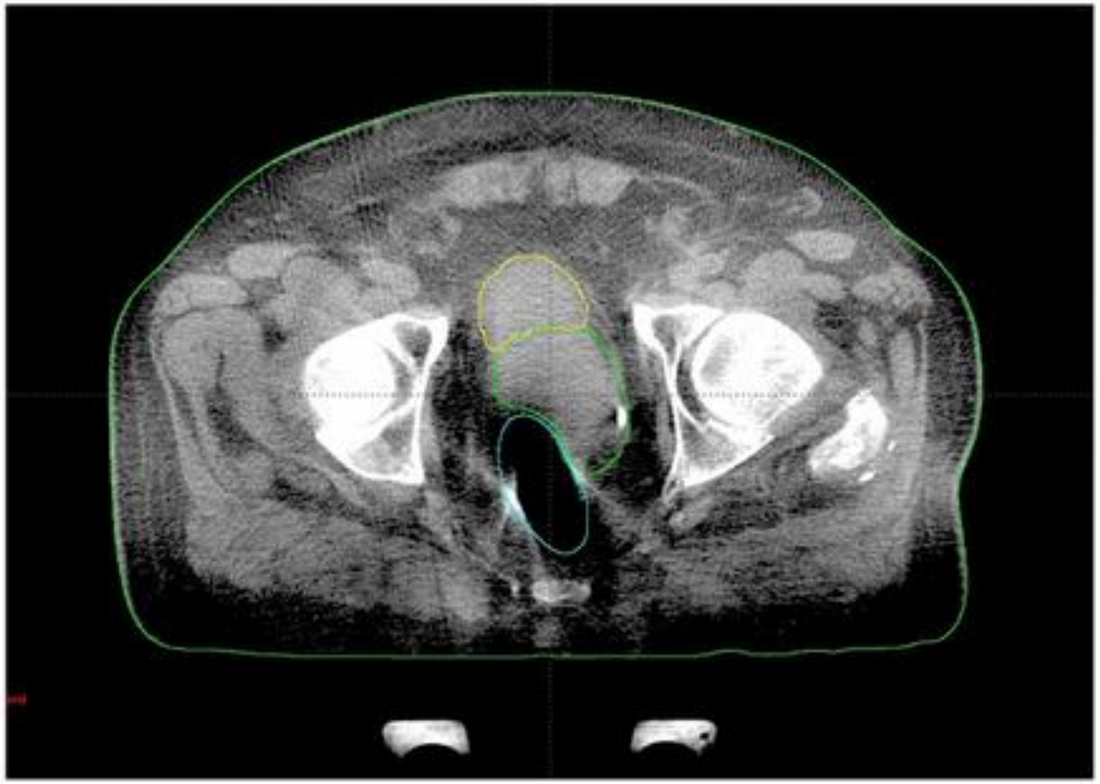
CBCT Image Quality

- Patient characteristics

  - Size
    - Poor image quality as the patient contour approached the limits of the FOV
  - Tissue heterogeneity
  - High dense structures
    - Hip prosthesis
  - Motion
    - Increased risk of motion with slow scan time
    - E.g. peristalsis, breathing and gas

CBCT Image Quality

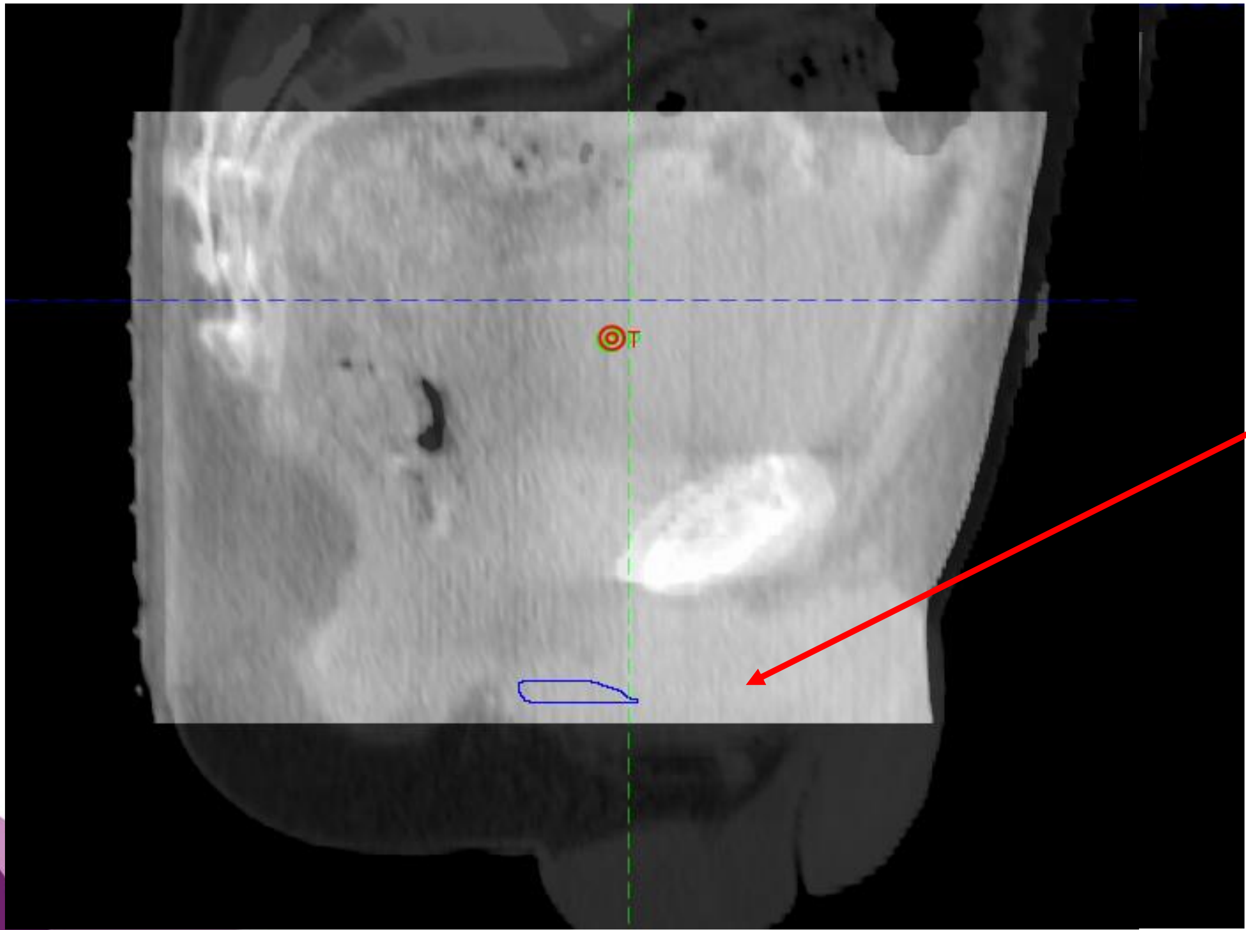


Reggiori et al., 2010

Degradation of image quality due to patient size and gas passing through rectum at time of scan

The Image Acquisition Process

- Make sure you image what you need to match and review to
- Option to offset the couch to ensure appropriate anatomy is visualized



Definitive Prostate Case

Couch now offset to include Penile Bulb in image

The Image Acquisition Process

- Option to offset the couch to ensure appropriate anatomy is visualized

Missing Superior PTV

Excessive inferior

Radiotherapy and Oncology 94 (2010) 129–144

Contents lists available at ScienceDirect

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journal homepage: www.thegreenjournal.com

Martijn will discuss IGRT implementation tomorrow

Review

The European Society of Therapeutic Radiology and Oncology–European Institute of Radiotherapy (ESTRO–EIR) report on 3D CT-based in-room image guidance systems: A practical and technical review and guide

Stine Korreman[a], Coen Rasch[b], Helen McNair[c], Dirk Verellen[d], Uwe Oelfke[e], Philippe Maingon[f], Ben Mijnheer[b], Vincent Khoo[c,g,*]

[a] Department of Radiation Oncology, The Finsen Centre, Rigshospitalet, Copenhagen, Denmark; [b] Department of Radiation Oncology, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; [c] Department of Clinical Oncology, Royal Marsden NHS Foundation Trust, Chelsea and Sutton, London, UK; [d] UZ Brussel, Oncologisch Centrum, Radiotherapie, Brussels, Belgium; [e] Department of Medical Physics in Radiation Oncology, Deutsches Krebsforschungzentrum, Heidelberg, Germany; [f] Département de Radiothérapie, Centre Georges-François-Leclerc, Dijon, France; [g] Institute of Cancer Research, Chelsea, London, UK

Table 1
Factors for consideration in image acquisition and their relevance.

What field of view (FOV) length is available in the cranio-caudal direction?
Determines the length of scan available and possible solutions if longer scan lengths are required
What size is the reconstruction circle?
Determines the lateral FOV
Are filters required? – Which filters are available?
Involves time to select and insert, and affects image quality
Are filters interlocked?
If not, then risk of poor quality or unusable scans from incorrect filters selection
Can panel be positioned remotely? If so, does this the system come with an anti-collision system?
Will involve time to position if not remotely accessed
What are the available rotation speeds?
Determines the acquisition time
What are the possible angles of rotation?
Affects the flexibility of scanning; e.g. the possibility of performing half-scans for small regions, rotations through 180 degrees (underneath the patient) and using preset or flexible start and stop angles
How ergonomic is the operation?
One- or two-button operation, foot- or hand-control, several screens affects the ease of operation and the risk of aborted scans
Can the scan be stopped and restarted?
Will result in extra dose if the scan is interrupted inadvertently, and has to be started from the beginning
Also allows the scan to be acquired with the patient in several breath holds.

The Image Registration Process

Automatic Match

- Uses matching algorithm based on “Mutual Information” within the defined field of view

Manual Match

- Allows adjustments to be made using either mouse or keyboard
- User dependant
  - Respect the learning curve

The Image Registration Process

- The Region of Interest Box
- Used for the automatic registration algorithm
- Defines the greyscale range (HU) that the algorithm will use for the solution

- The interface has additional options
  - Consider the "Structure VOI" option
  - Margin added to the Structure VOI will help drive the MI algorithm
  - Intensity Range
  - Be willing to adjust settings to ensure you are getting the most out of your system!

!

- Similar to Elekta, the anatomy included is very important

The Image Registration Process

- Correctional shifts are displayed to the nearest 1mm
- Any automatic match ***must*** be reviewed by both the RTTs prior to treatment
- No machine can replace clinical judgement
- Know your volumes
  - ➢ Be aware of possibility of additional “planning volumes”

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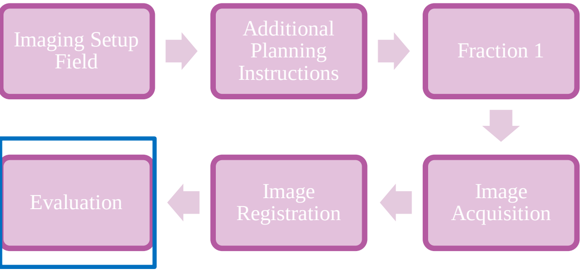
The Image Registration Process

- How can we decrease inter observer variability?

  - ➢ Education of staff (encourage CPD, training packages, competency based assessment)

  - ➢ Protocolised imaging methods

  - ➢ Protocolised matching methods
    - ▪ Sequence of matching process
      - o Automatic Match ***must be followed by manual review***
    - ▪ VOI and intensity levels set for each site and “locked” on Fx 1
      - o Anatomy to include in VOI box



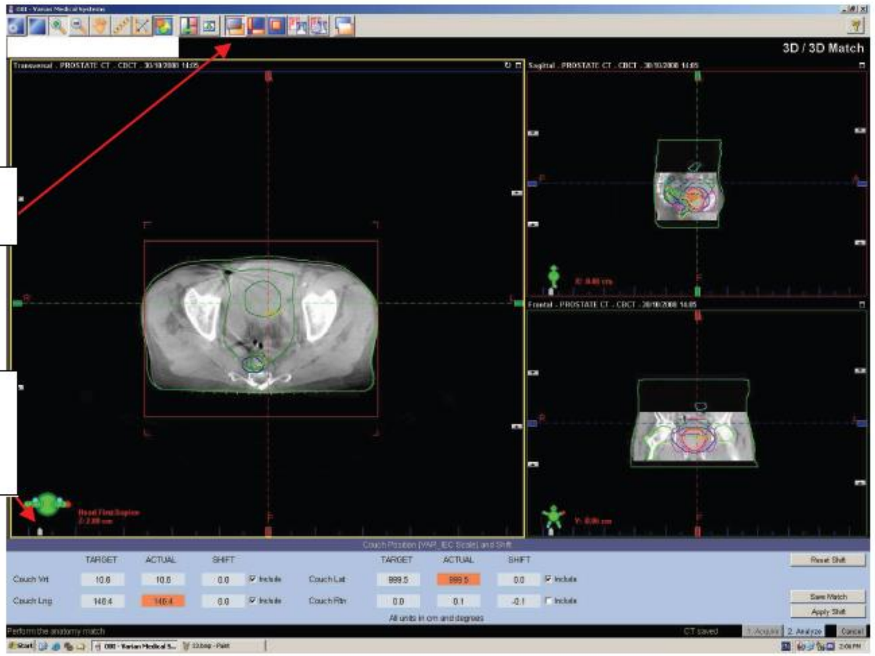
The Image Evaluation Process

- Processes available to assist in image evaluation

- Blending
  - ➢ Blending of the planned and acquired image
  - ➢ Colour or greyscale

Select the blend tool.

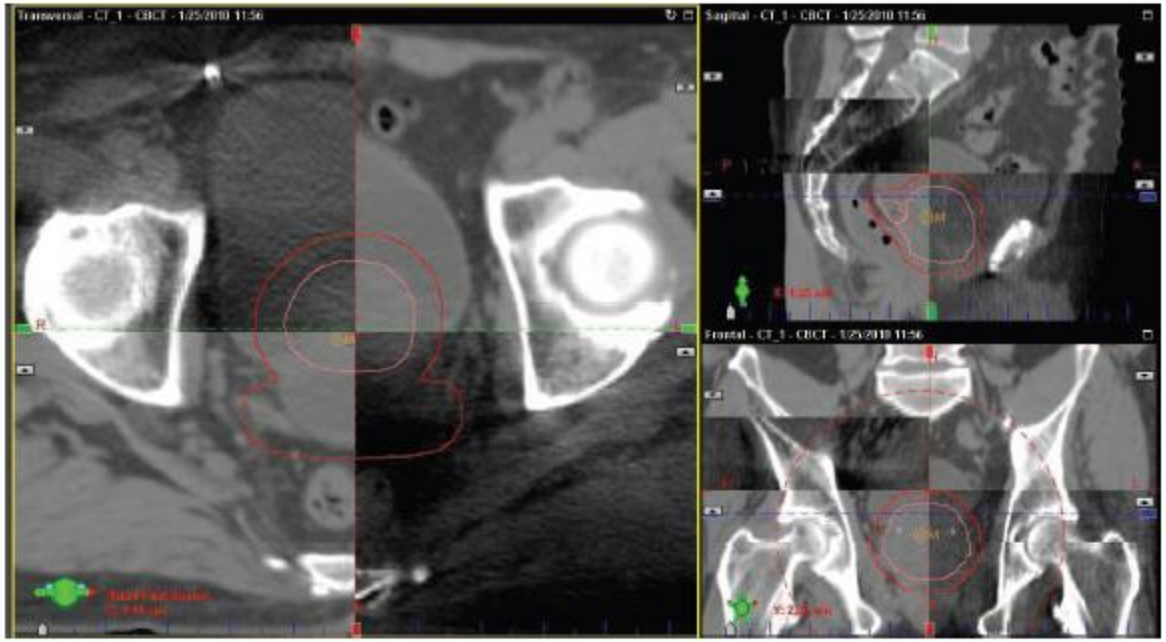
Drag the blend arrow to the LEFT to see the CBCT



The Image Evaluation Process

- Processes available to assist in image evaluation

- Split screen

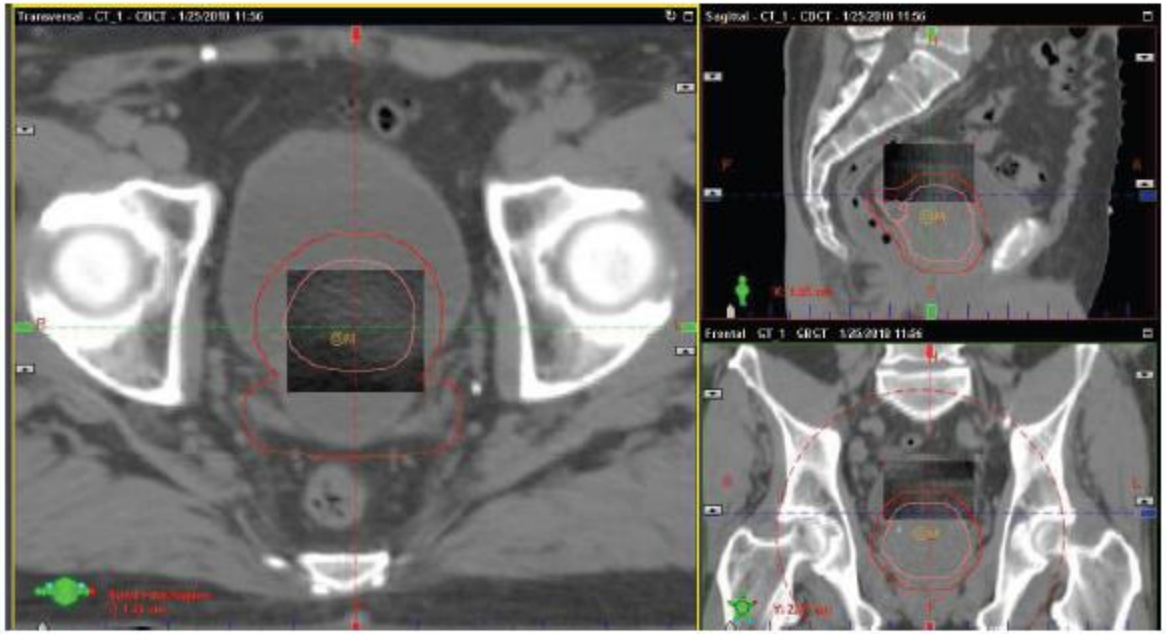


Don't forget to adjust the window level and move your views around

The Image Evaluation Process

- Processes available to assist in image evaluation

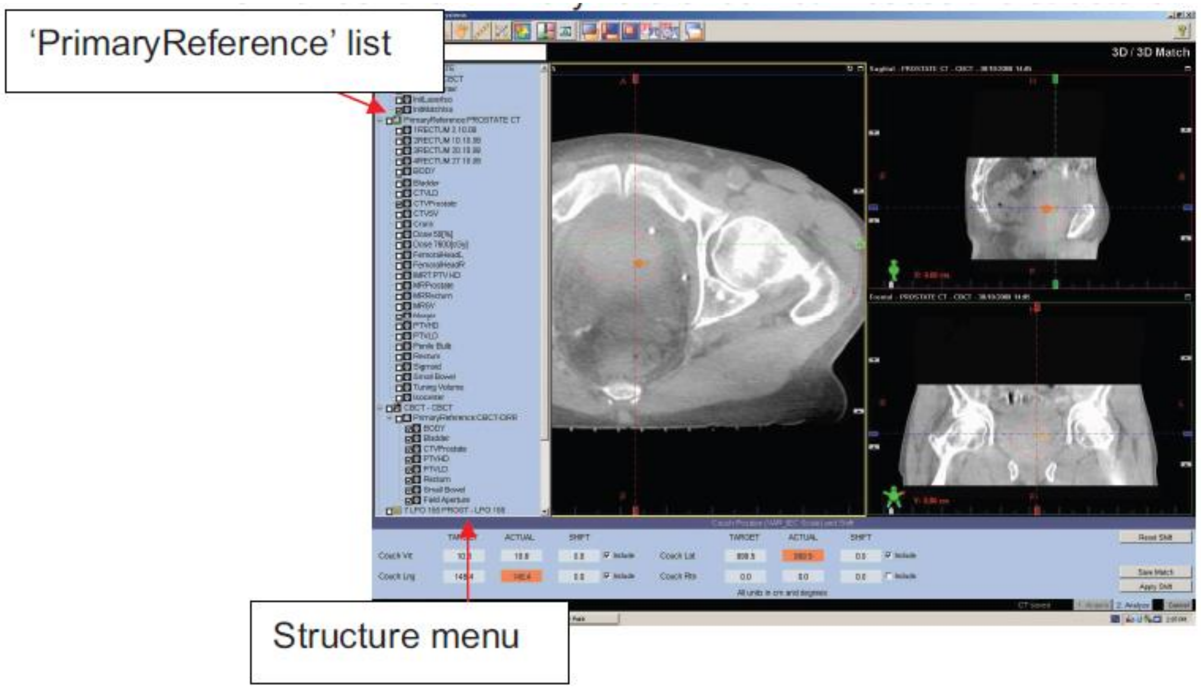
- Moving window tool



Don't forget to adjust the window level and move your views around

The Image Evaluation Process

- Overlay Structure
  - ➢ Volumes that were contoured at the planning stage



The Image Evaluation Process

- The evaluation process must not be rushed
  - ➢ Check that the shifts are *sensible*
- Both RTTs must confirm the match
- It is better be check than treat the patient incorrectly
- IGRT is a team approach and if unsure there are always people to help
- Communicate!
  - ➢ Aria, Alerts, annotation on the image

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"the importance of this visual inspection cannot be over-emphasized and the user is encouraged to assess the accuracy of these automated registration tools" (Korreman et al., 2010)

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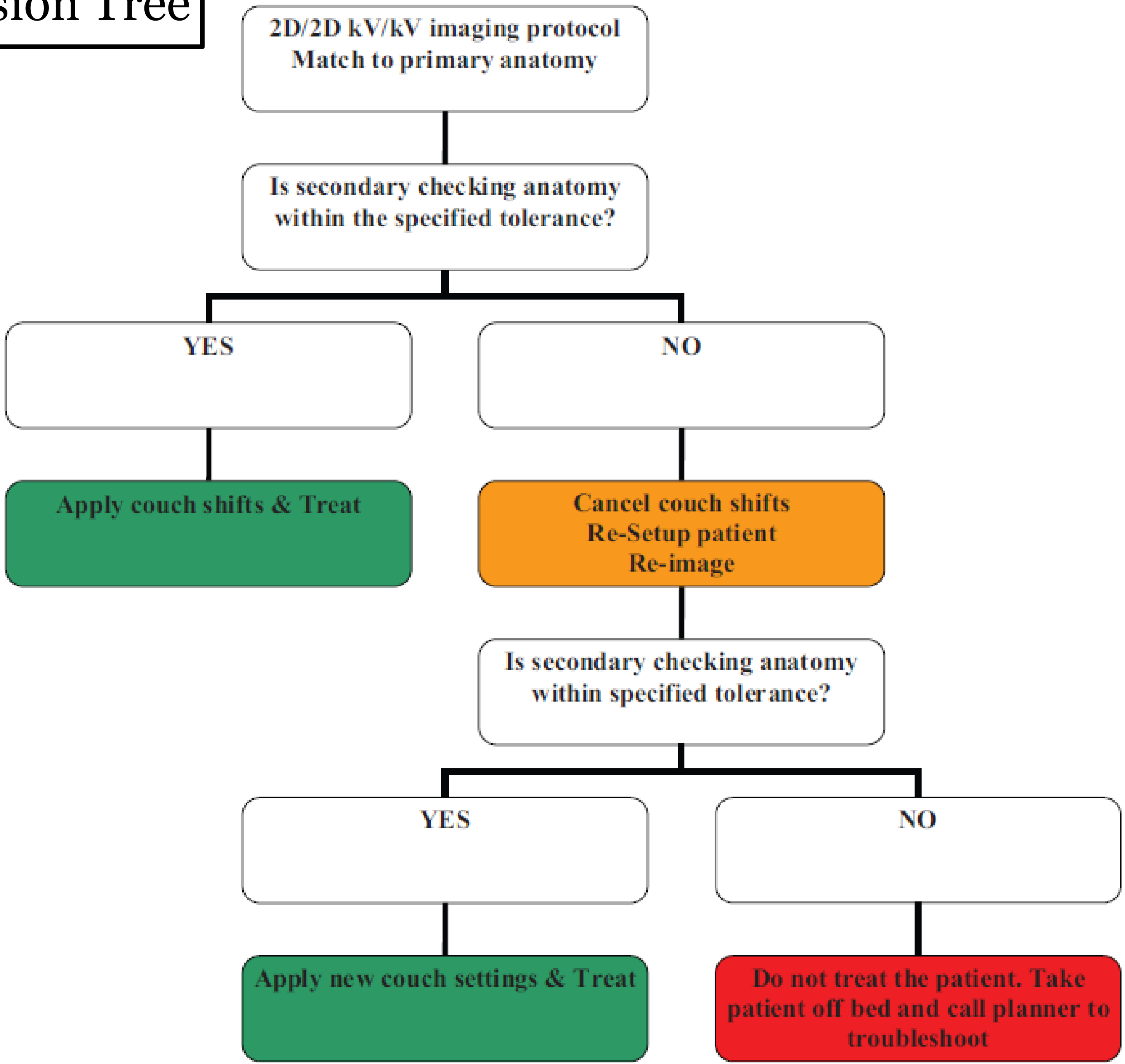
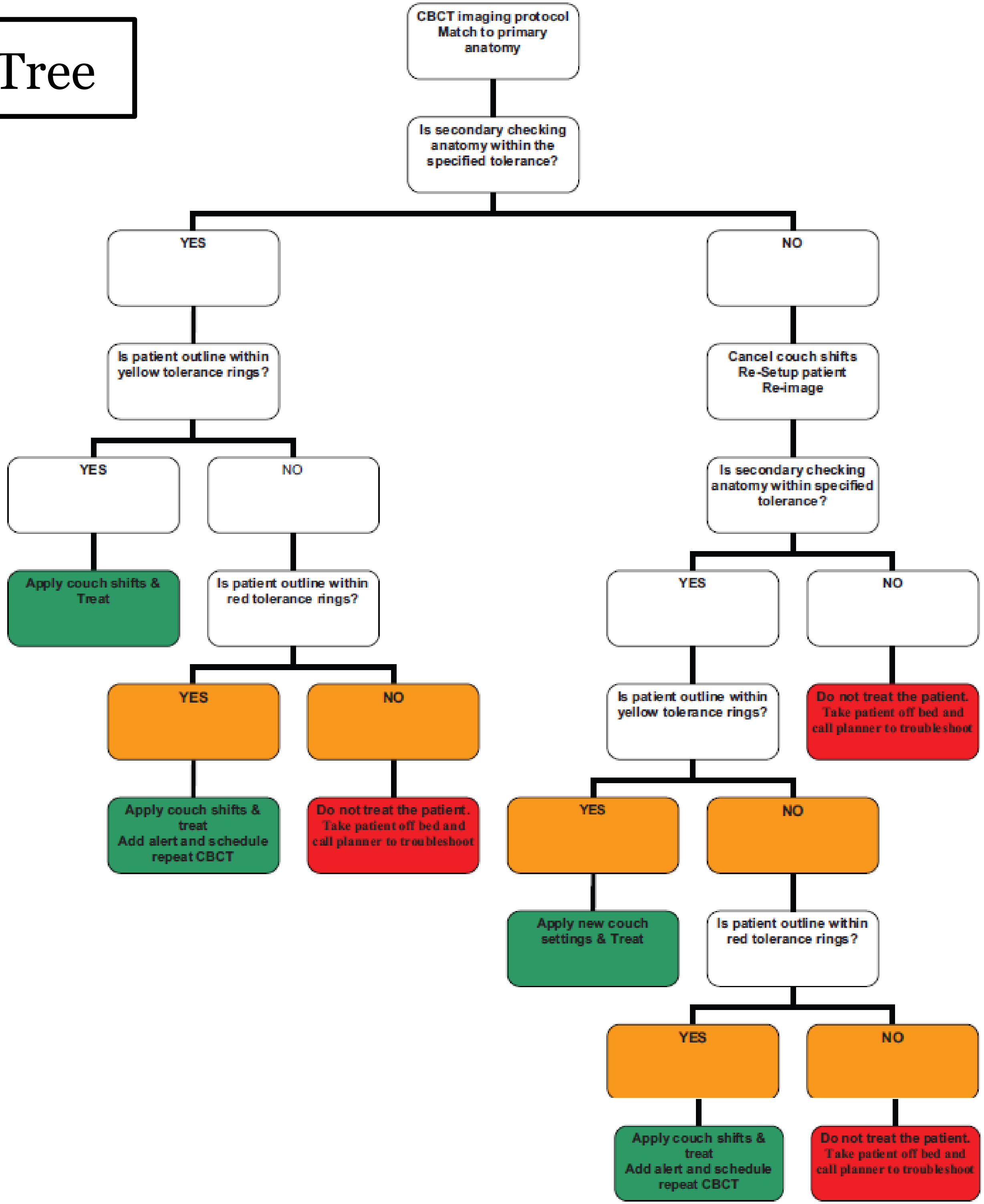
2D/2D Decision Tree



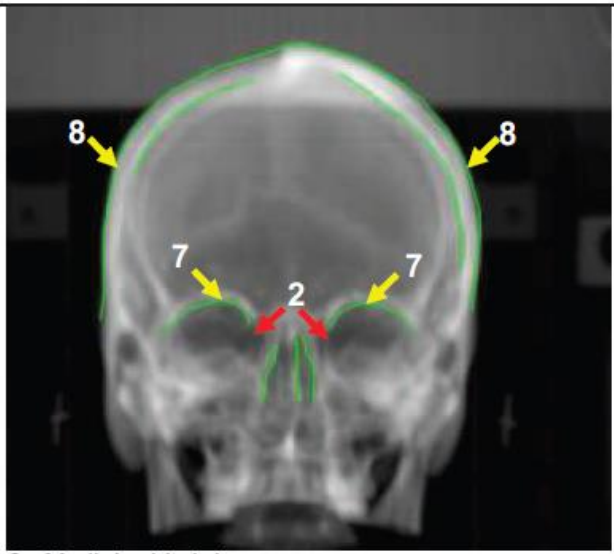
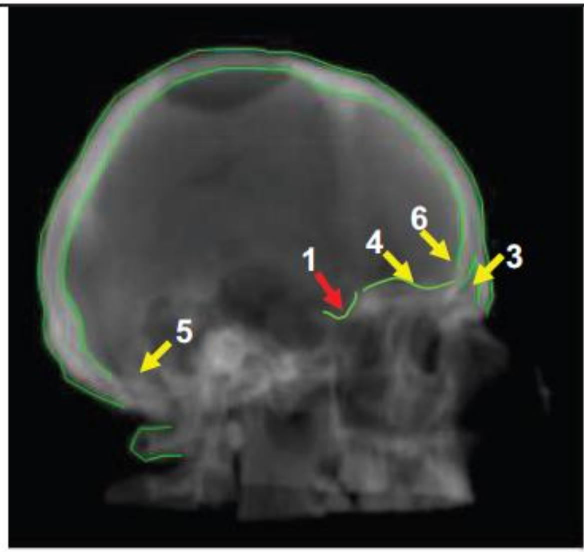
CBCT Decision Tree



Site Specific Application

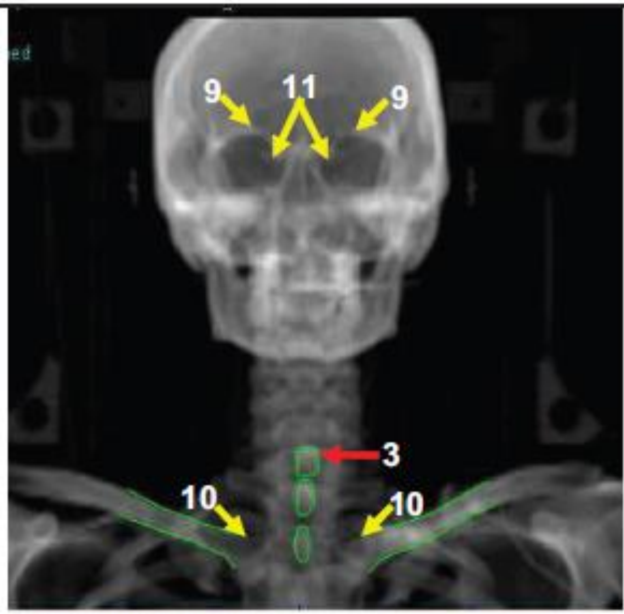
Radical CNS

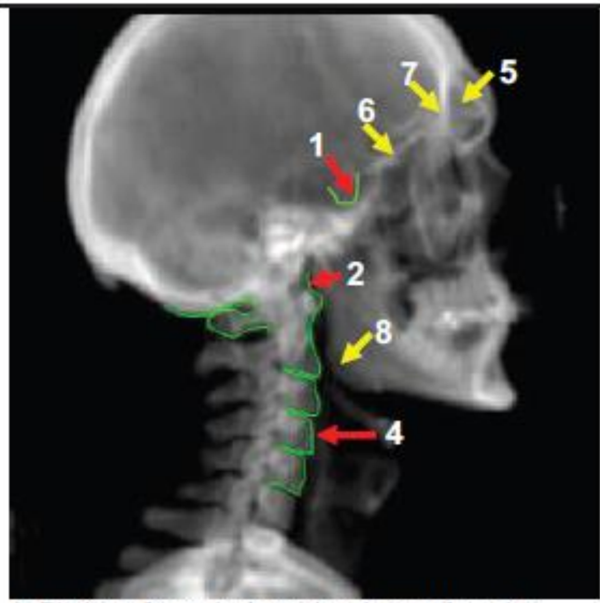
- Examples of structures to outline on DRR for 2D/2D match

Site	Image type	Primary (red) and Confirming (yellow) matching anatomy	
Brain	KV & CBCT	 2. Medial orbital rims 7. Superior orbital rims 8. Lateral skull wall (parietal region)	 1. Pituitary fossa (volumend and transferred to reference image) 3. Frontal sinus 4. Base of skull in pituitary fossa region 5. Base of skull in Occipital bone region 6. Anterior cranial fossa

Head and Neck

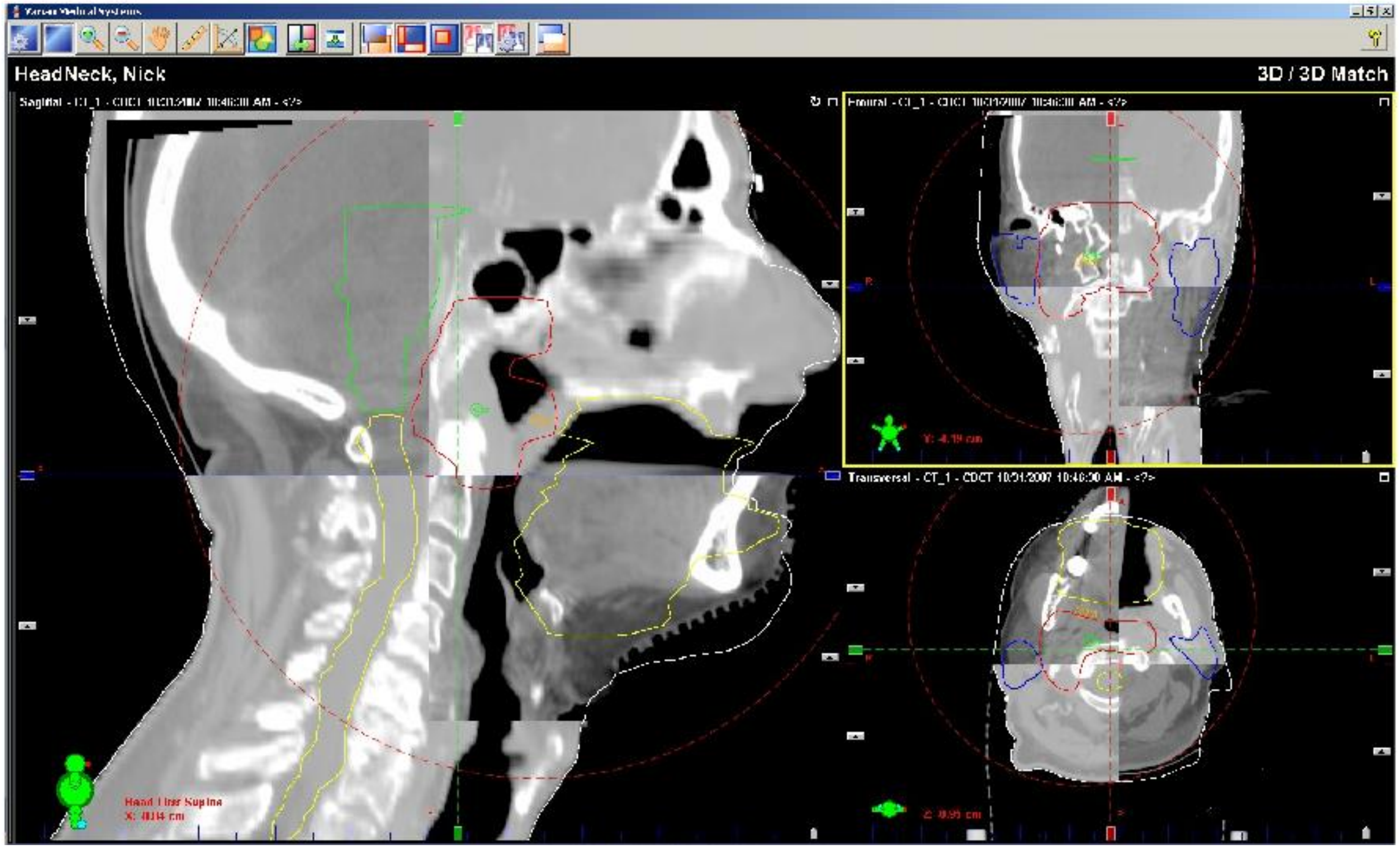
- Examples of structures to outline on DRR for 2D/2D match

<table>
<tr>
<td>Naso-
Pharynx</td>
<td>kV &
CBCT</td>
<td>


3. Spinuous processes
9. Superior orbital rim
10. Head of Clavicles
11. Medial orbital rims
</td>
<td>


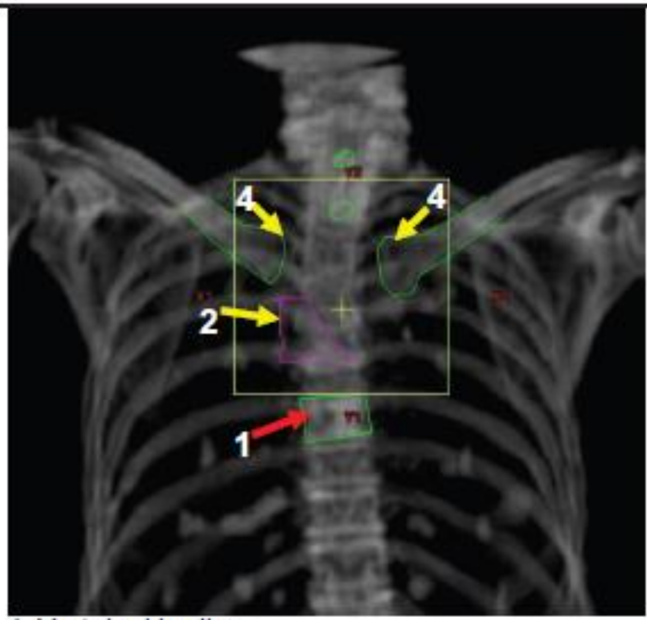
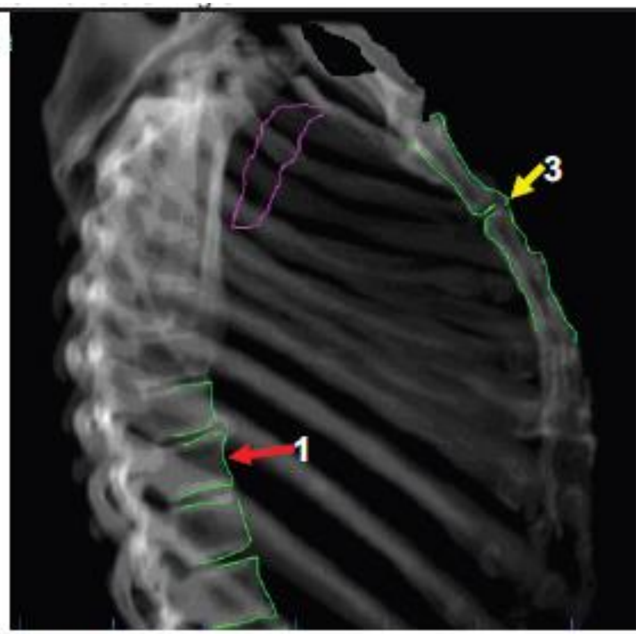
1. Pituitary fossa (volumed and transferred to reference image)
2. Intersection of anterior vertebral column and base of skull
4. Vertebral bodies
5. Frontal sinus
6. Base of skull in pituitary fossa region
7. Anterior cranial fossa
8. Mandible angle
</td>
</tr>
</table>

Head and Neck



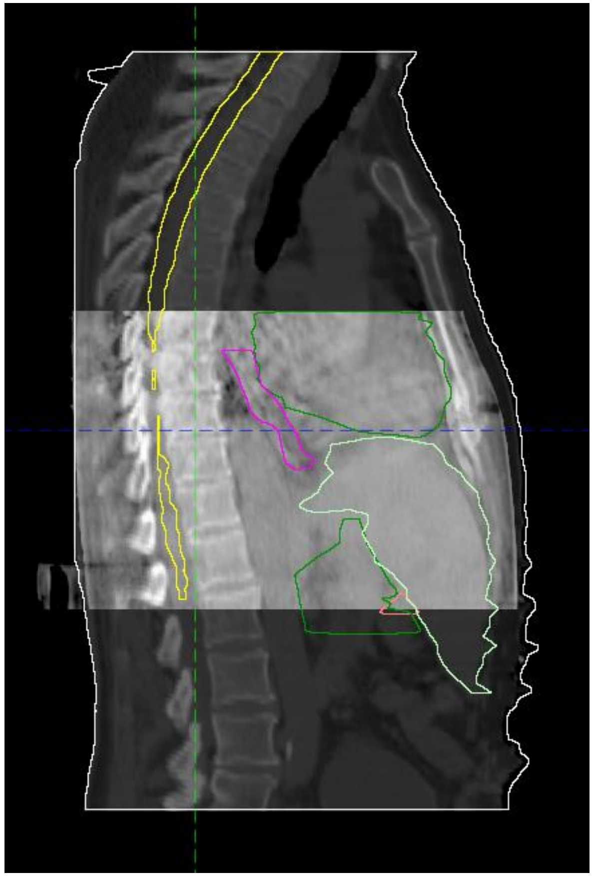
Thorax and Upper Abdomen

- Examples of structures to outline on DRR for 2D/2D match

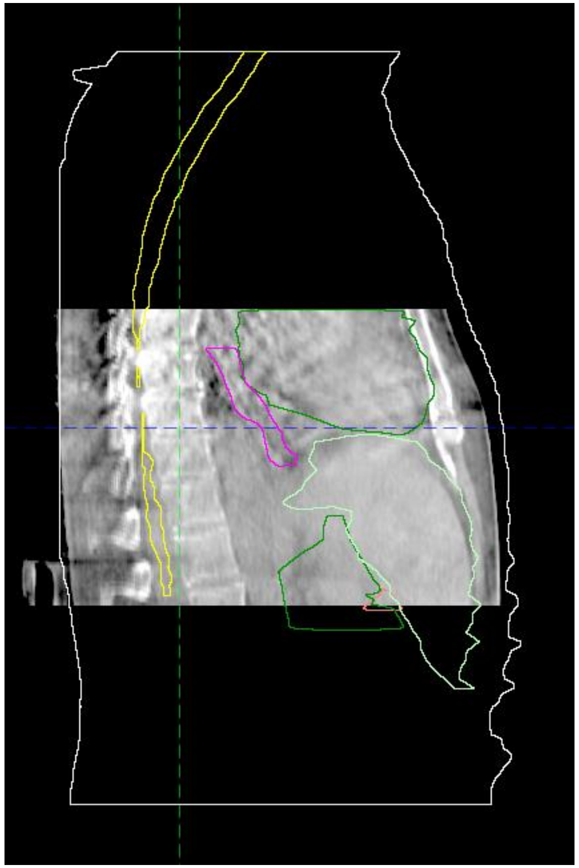
Chest	kV & CBCT	 1. Vertebral bodies 2. Contoured Carina 4. Head of Clavicles	 1. Vertebral bodies 3. Manubrial-sterno joint

Thorax and Upper Abdomen

Blended View

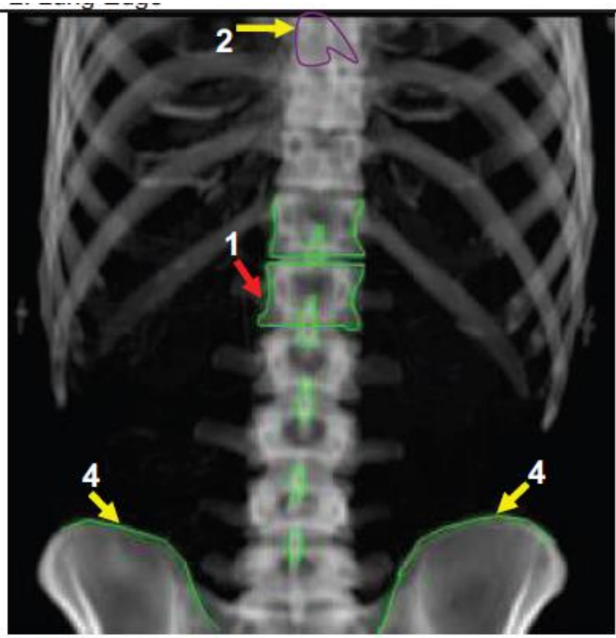
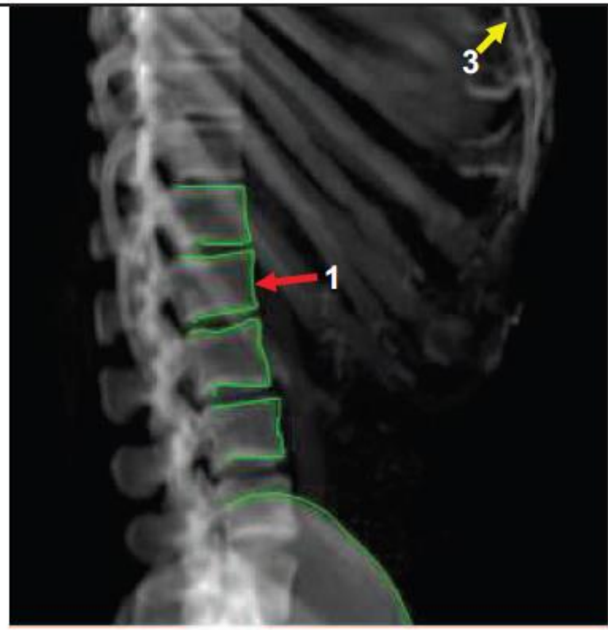


Contour Overlay



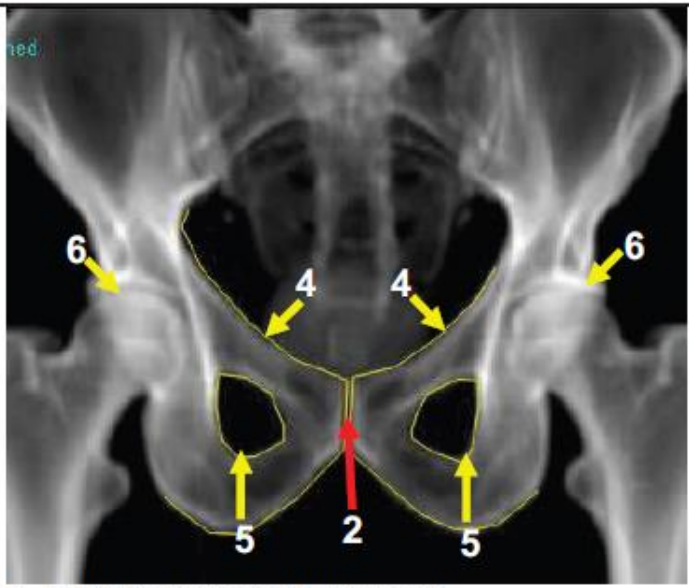
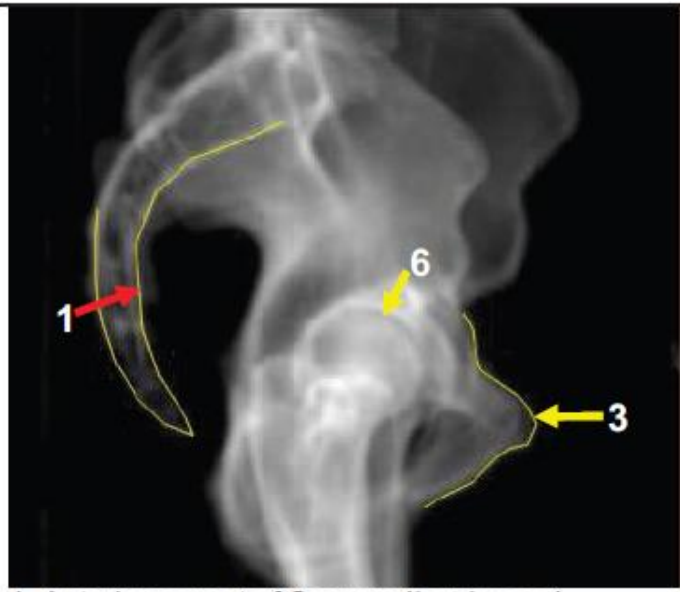
Abdomen

- Examples of structures to outline on DRR for 2D/2D match

Abdomen Pancreas Adrenal Gastric	kV & CBCT	 1. Vertebral bodies 2. Contoured Carina (if on image) 4. Iliac crest	 1. Vertebral bodies 2. Contoured Carina (if on image) 3. Manubrial-sterno joint

Rectum

- Examples of structures to outline on DRR for 2D/2D match

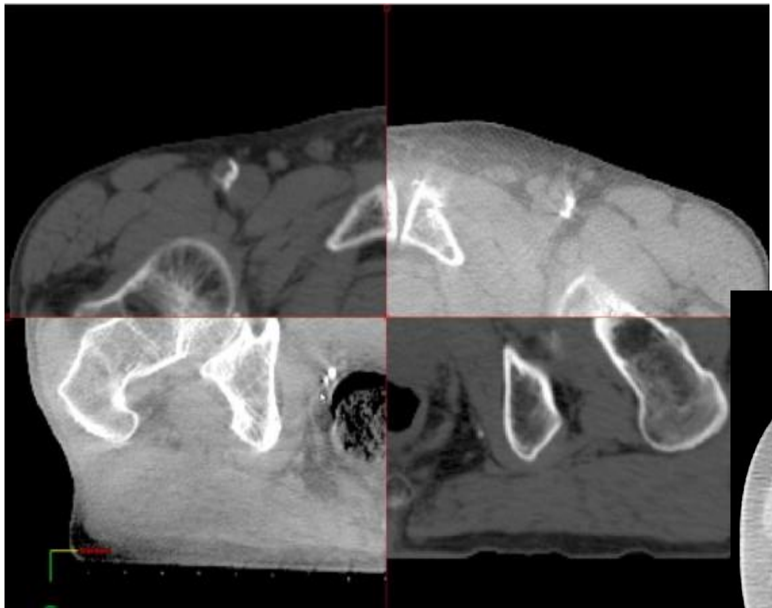
Rectum/ Anus	kV & CBCT	 2. Pubic Symphasis **(AP image)** 4. Pelvic Rim 5. Obturator Foramen 6. Head of Femur	 1. Anterior aspect of Sacrum **(Lat image)** 3. Pubic Symphasis 6. Head of Femur

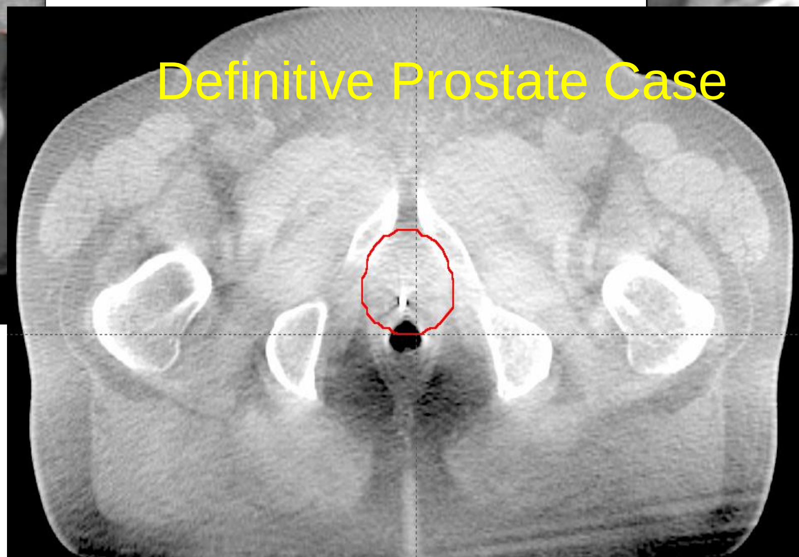
Prostate

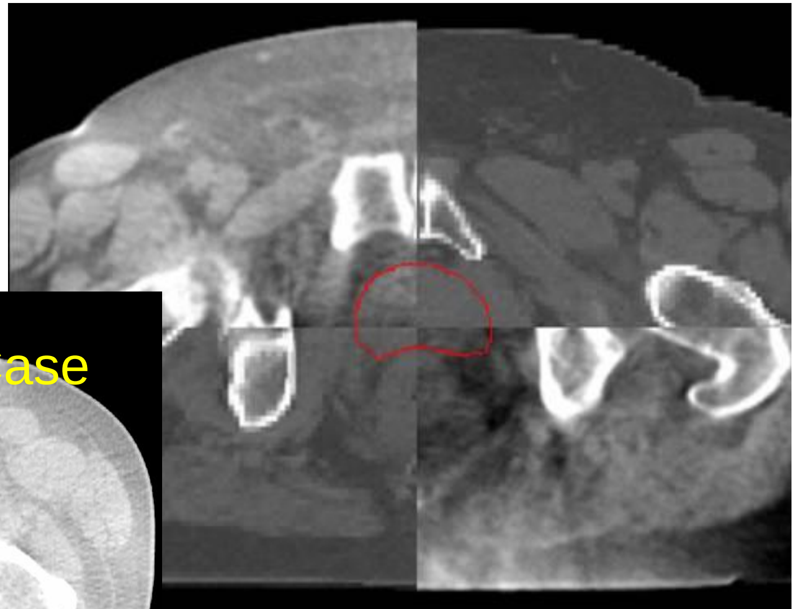
Remember the results from Peter's workshop!

- Do ***not*** match to bones for definitive cases

Definitive Prostate (seeds)	kV	All fractions except CBCT	Daily moves
	CBCT	1,2,3,5,10,15,20,25,30,35,40	
Definitive Prostate (soft tissue)	CBCT	All fractions	Daily moves

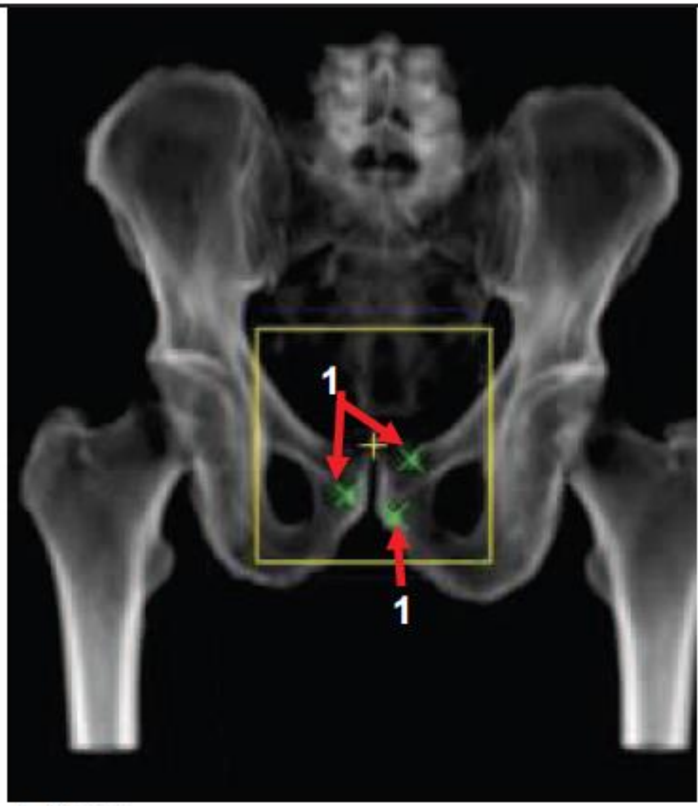
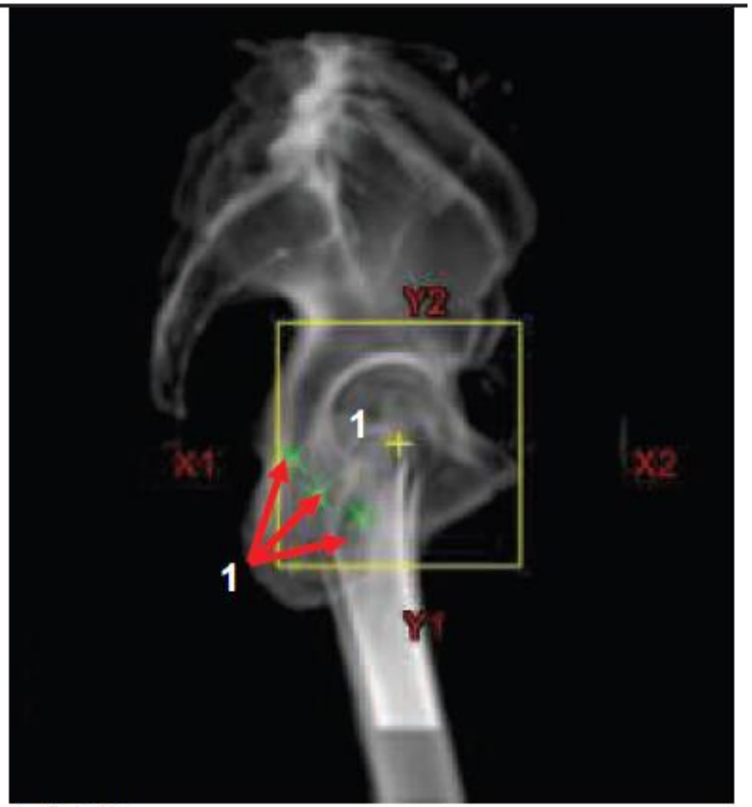




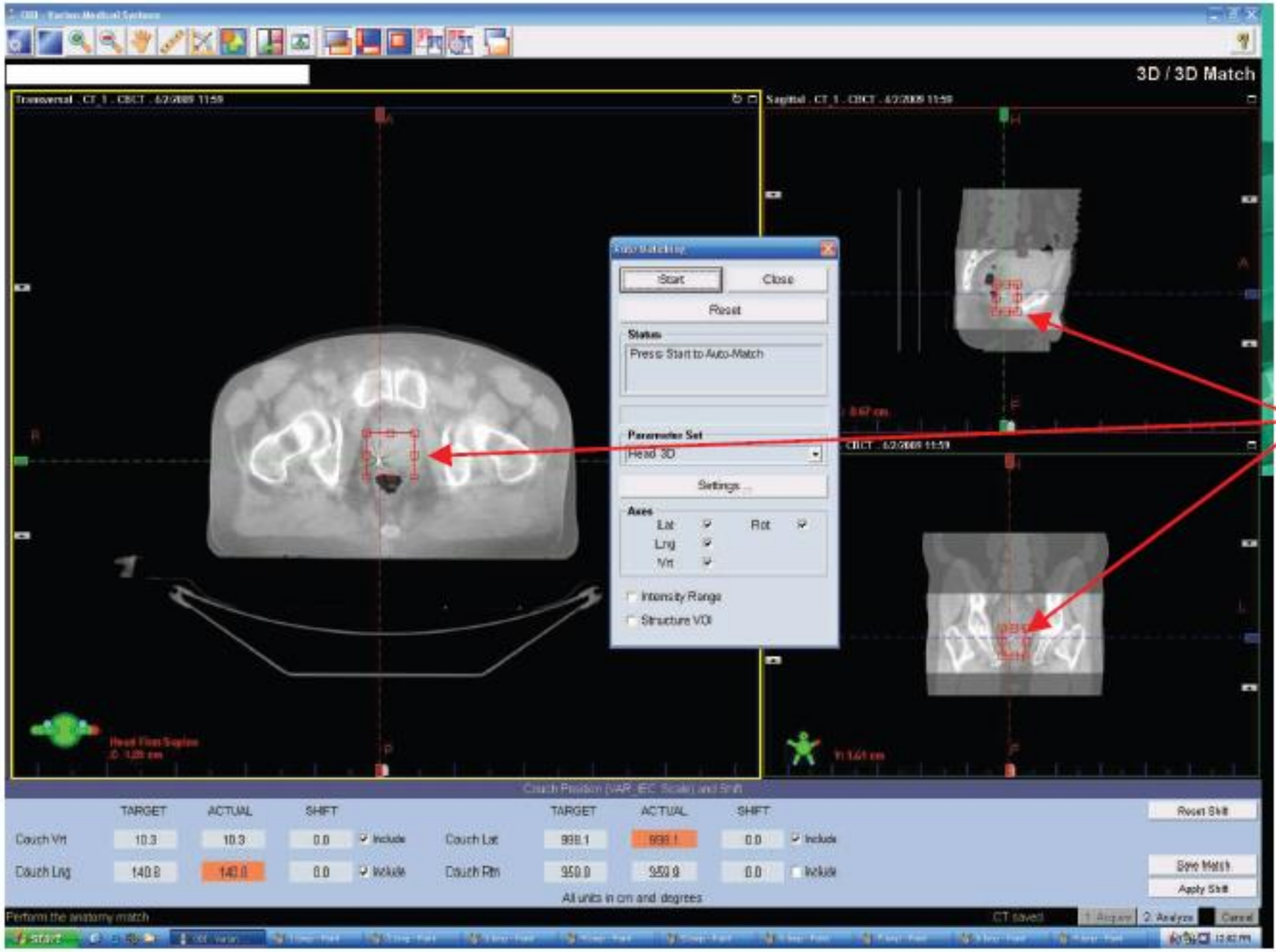


Prostate – 2D/2D fiducial match

- Match points used for 2D/2D fiducial match

Prostate (Seeds)	kV & CBCT	 1. Seeds	 1. Seeds

Prostate – CBCT fiducial match



Move the VOI box on all three views to cover the matching area.
Eg in this picture the fiducial markers

Always scroll through the entire length of the PTV and view in all 3 planes

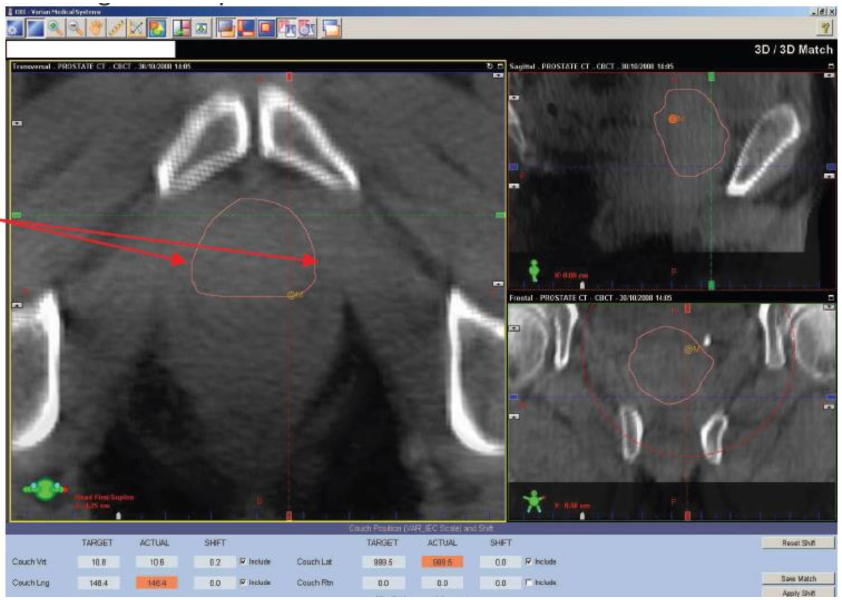
Prostate – Soft tissue

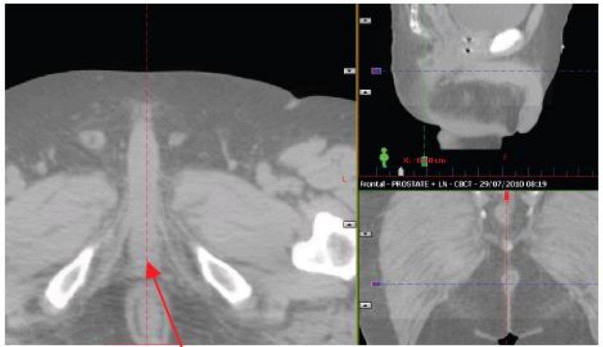
- Process for CBCT soft tissue match
  - *Manual confirmation* of match

1. Change window level to visualise rectum & superior prostate
2. Position superior CTV prostate contour to superior aspect of prostate at junction with bladder
3. Position posterior edge of CTV prostate structure (at mid prostate) to the anterior rectal wall
4. Check inferior CTV prostate structure to inferior edge of prostate, using penile bulb to assist
5. Position lateral edges of CTV prostate to pelvis muscles

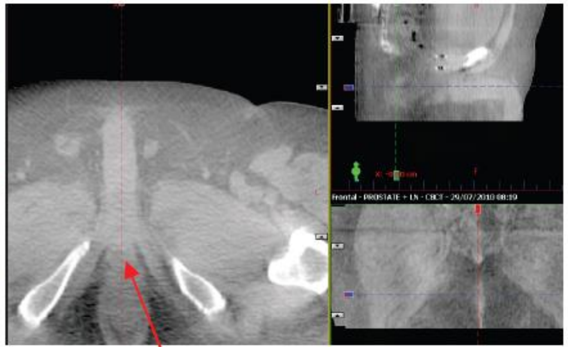
Prostate – Soft tissue

Check the Prostate CTV contour is positioned to the lateral edges of the prostate

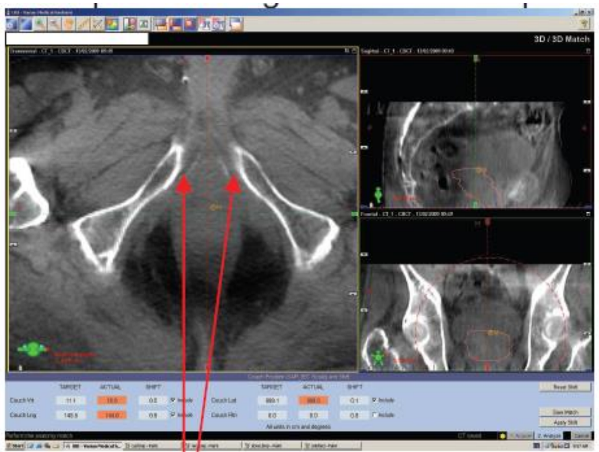


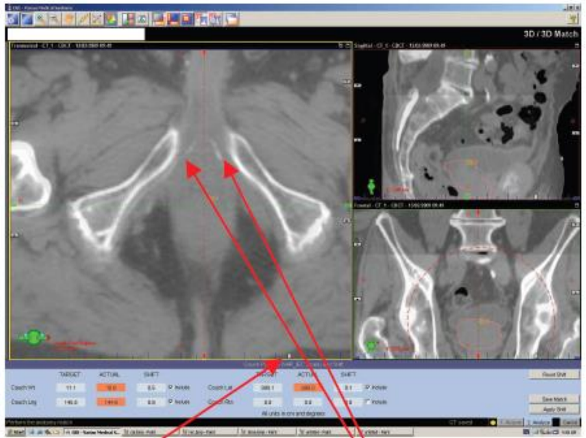


Penile Bulb seen on the GE scan



Penile Bulb seen on the CBCT scan

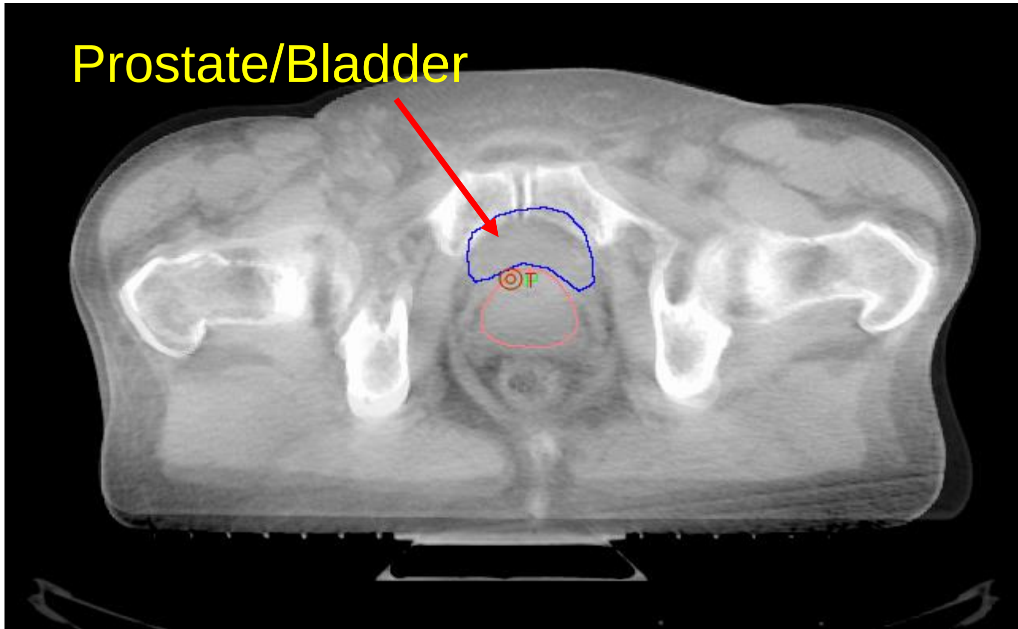




Calcifications seen on the CBCT scan

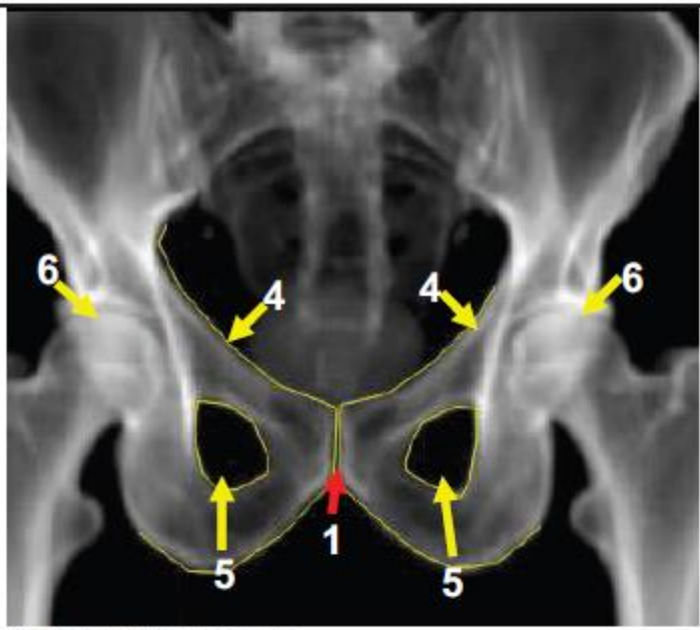
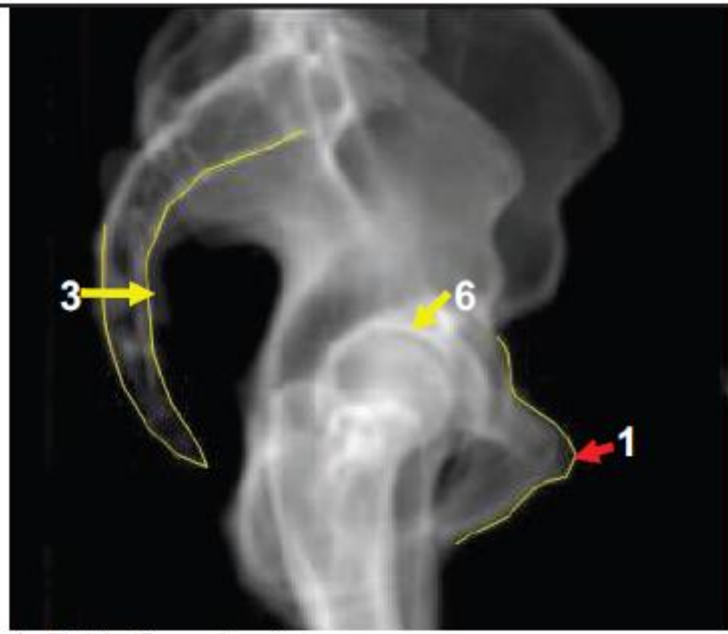
Slide the blend tool to see the GE scan

Calcifications seen on the GE scan



Prostate Bed

- Example of 2D anatomy to outline on the DRR

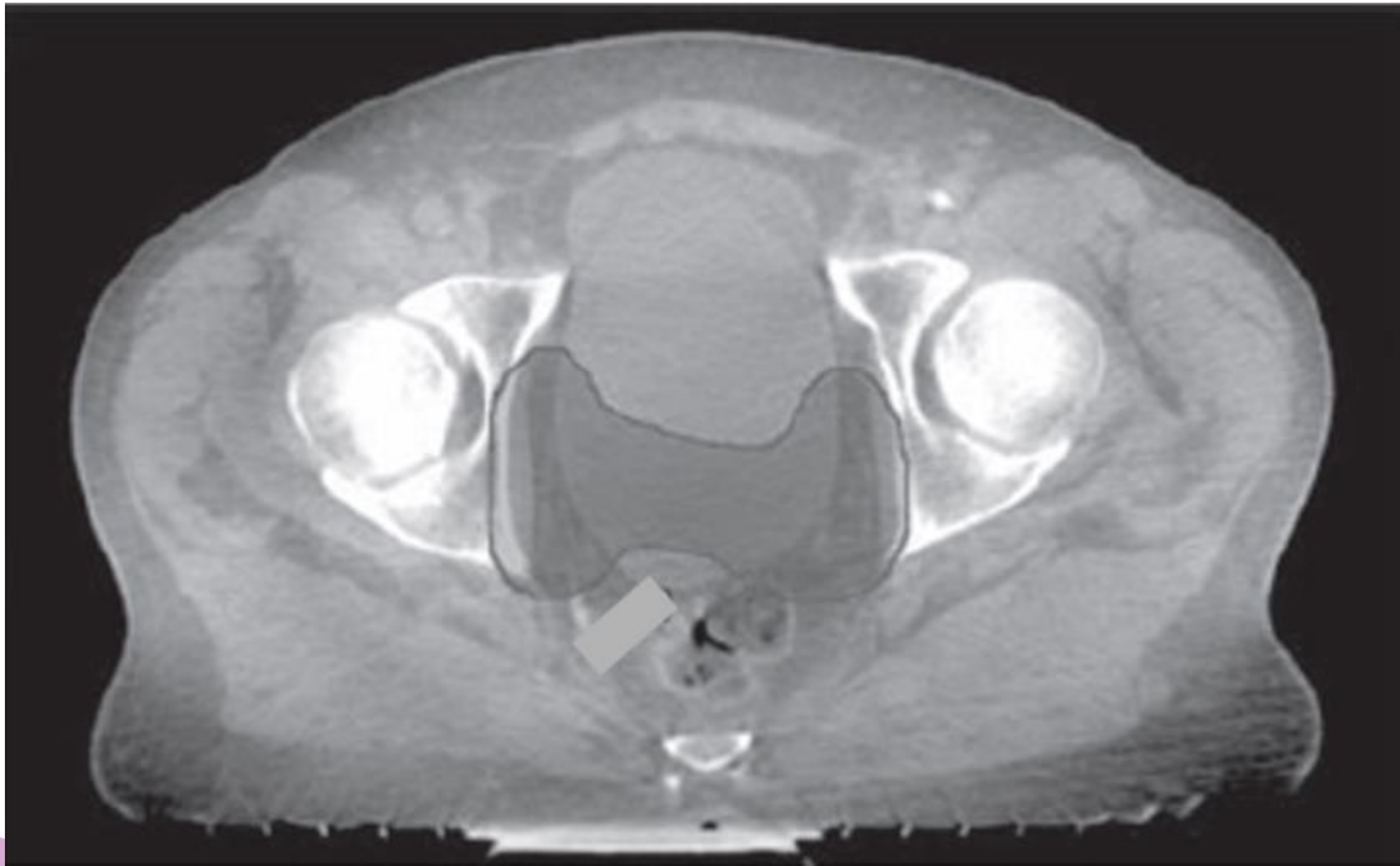
Prostate (Bone)	kV & CBCT	 1. Pubic Symphasis 2. Check any clips are covered with PTV for CBCT 4. Pelvic Rim 5. Obturator Foramen 6. Head of Femur	 1. Pubic Symphasis 2. Check any clips are covered with PTV for CBCT 3. Anterior Sacrum 6. Head of Femur

Troubleshooting

- These are all well suited and ideal cases
- What about when things aren't so clear?! *Troubleshoot*

Prostate Bed

- Instructions – match to bones
- All bony anatomy aligned perfectly
- Isodose lines hug the PTV very nicely



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Prostate Bed

- Have an anatomical understanding of exactly what the target is post surgery

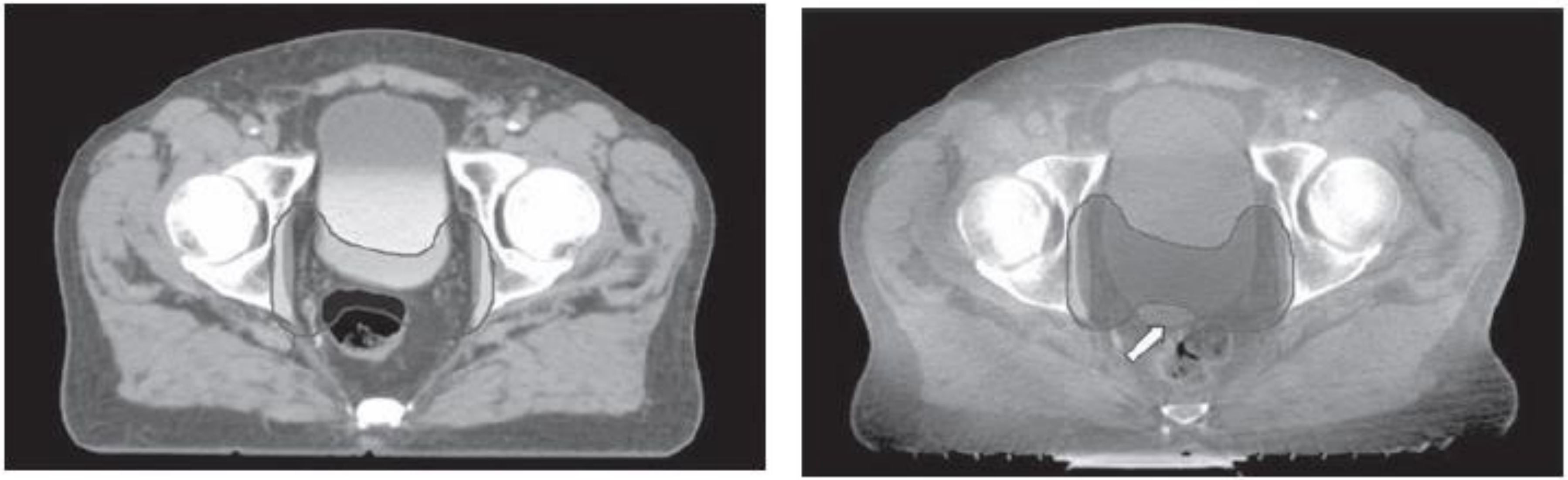

Fig. 4. CBCT of a patient undergoing radiotherapy following radical prostatectomy. Panel (a) shows the initial planning scan with the PTV displayed. Panel (b) shows a change in rectal volume resulting in the treated volume shifting outside the planning PTV (white arrow). CBCT, cone beam computed tomography; PVT, planning target volume.

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Prostate Bed

Radiation Oncology—Original Article

Prostate bed motion may cause geographic miss in post-prostatectomy image-guided intensity-modulated radiotherapy

Linda J Bell[1,2,*], Jennifer Cox[1,2], Thomas Eade[1], Marianne Rinks[1,†], Andrew Kneebone[1]

Article first published online: 9 JUL 2013

DOI: 10.1111/1754-9485.12089

Issue

Journal of Medical Imaging and Radiation Oncology

Volume 57, Issue 6, pages 725–732, December 2013

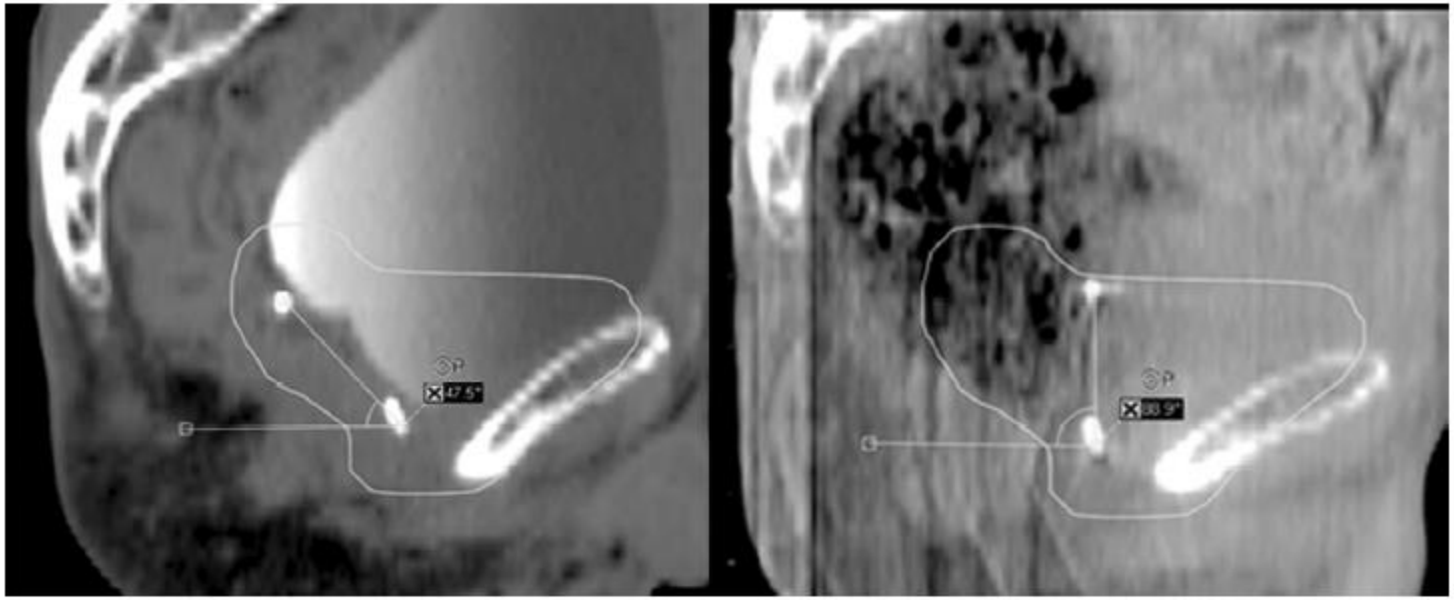

Fig. 1. Method used to measure prostate bed tilt. The angle between the superior and inferior clip relative to a horizontal line at the inferior clip was measured on the planning CT scan (left) and the cone beam CT scans (right). The angle-measuring tool in the Varian Offline Review® software was used to calculate this on the sagittal slice closest to midline of each scan where the clips could be visualised. The difference between the planning CT and cone beam CT angles was calculated. In this extreme case the angle on the planning CT (left) is 47.5° and that on the cone beam CT scan (right) is 88.9°. This is a difference of 41.4°. The FROGG-acceptable planning target volume expansion is delineated on these scans.

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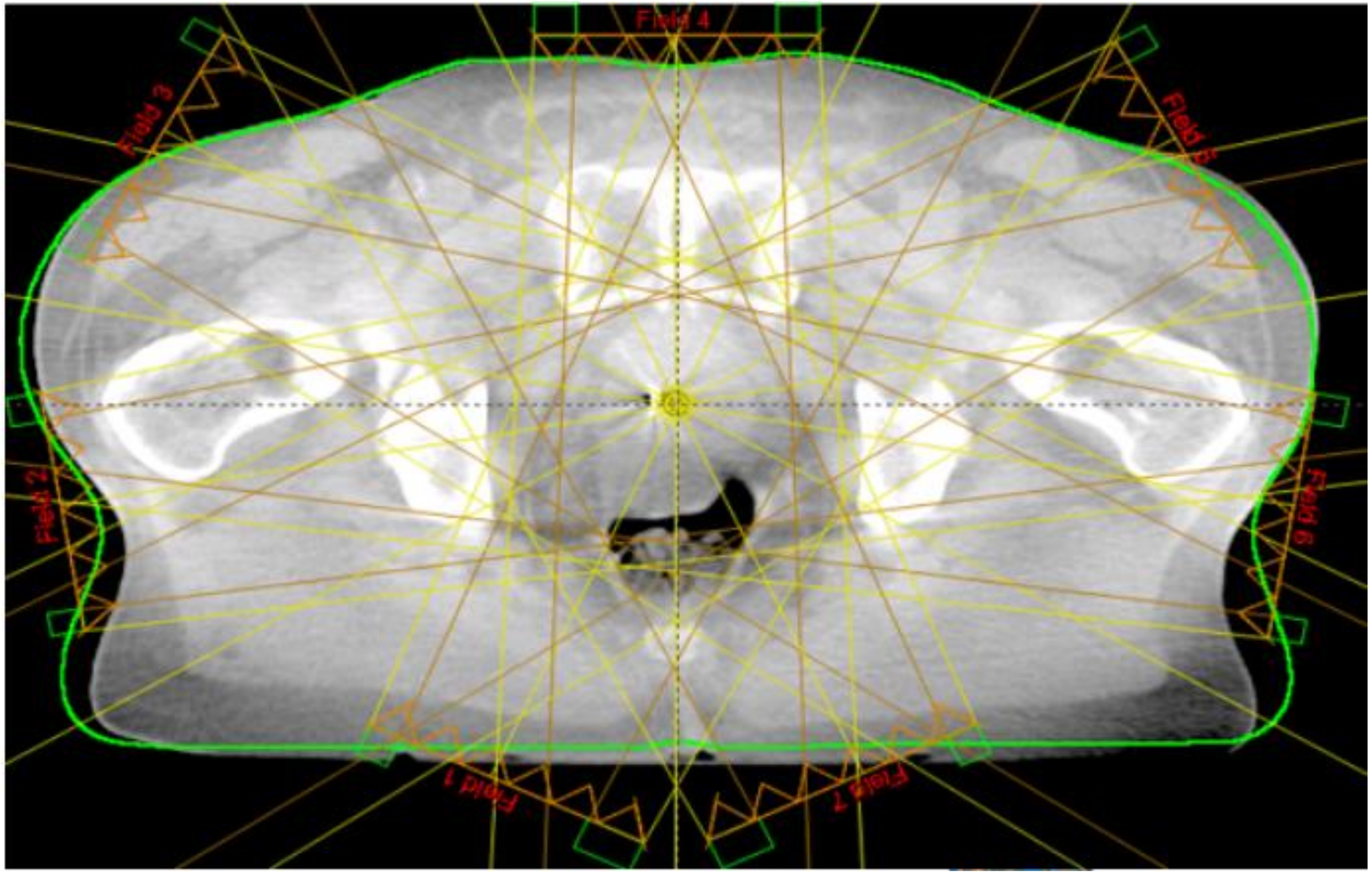
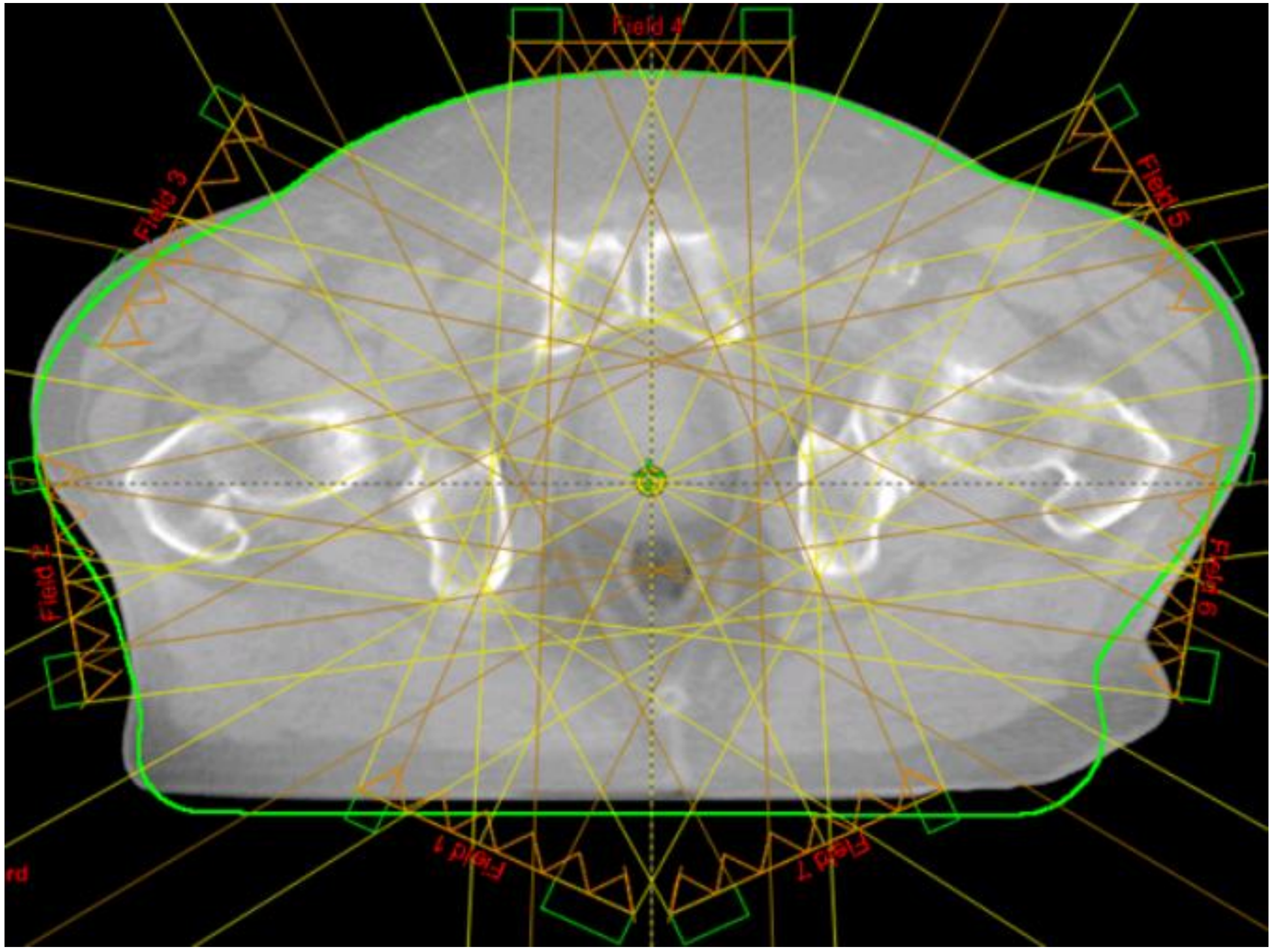
Definitive Prostate

- IMRT
- Daily online
- Match to implanted fiducials
- All fiducials aligned well; bladder and rectal volumes were consistent with planning scan



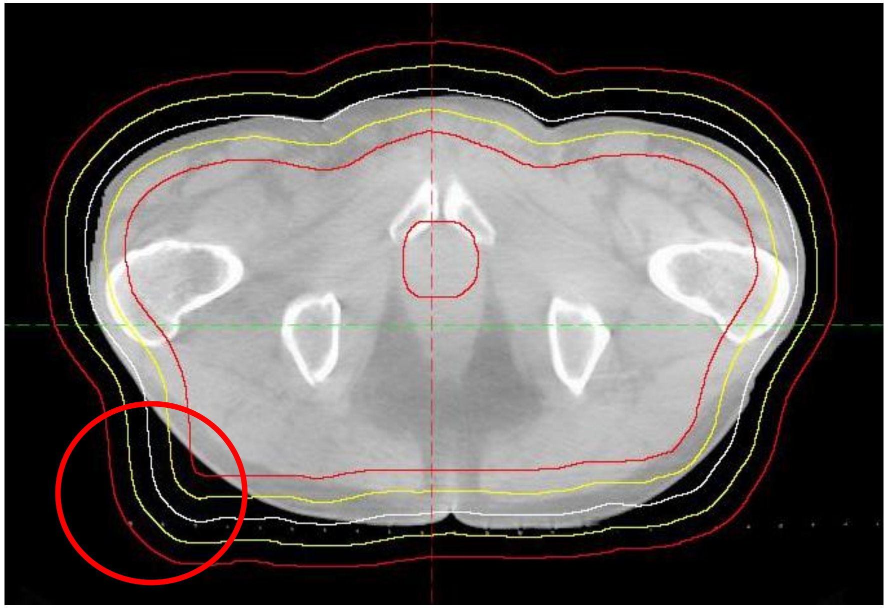
Troubleshooting

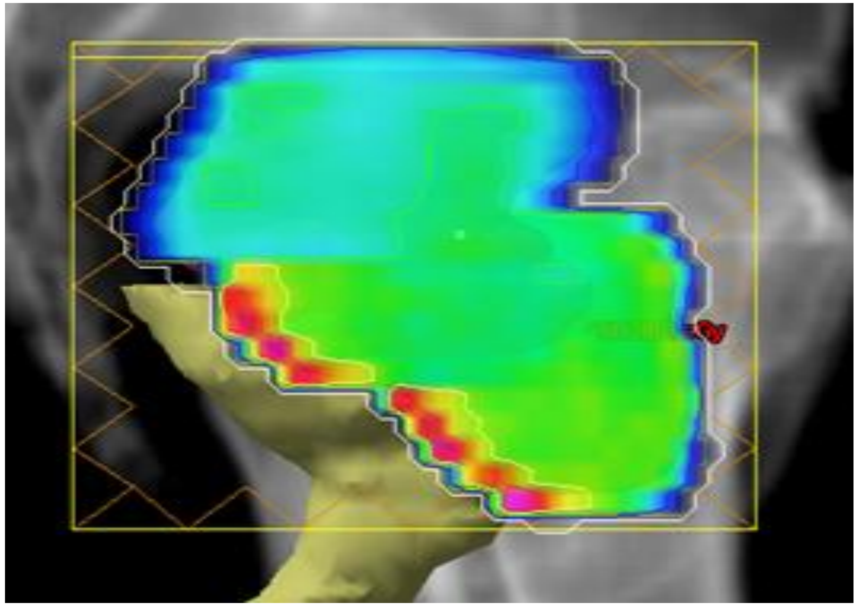
- Look beyond the target!
- Impact not on target ***position***, but on target ***dosimetry***

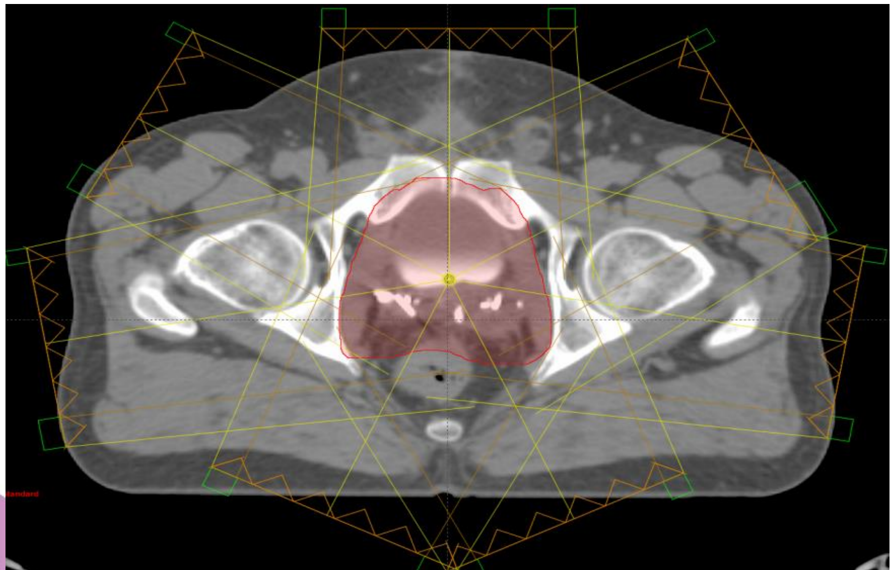


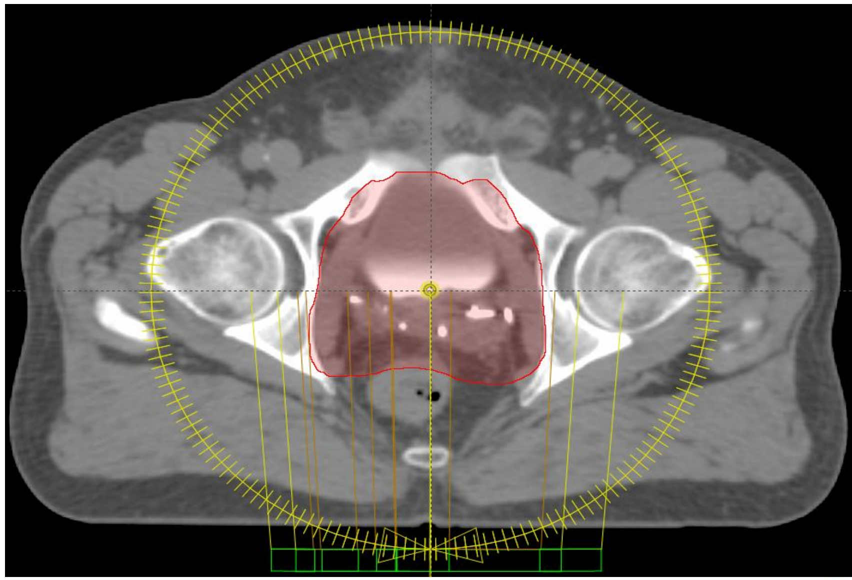
Troubleshooting

Integrate your planning knowledge –
Clinical Intelligence!



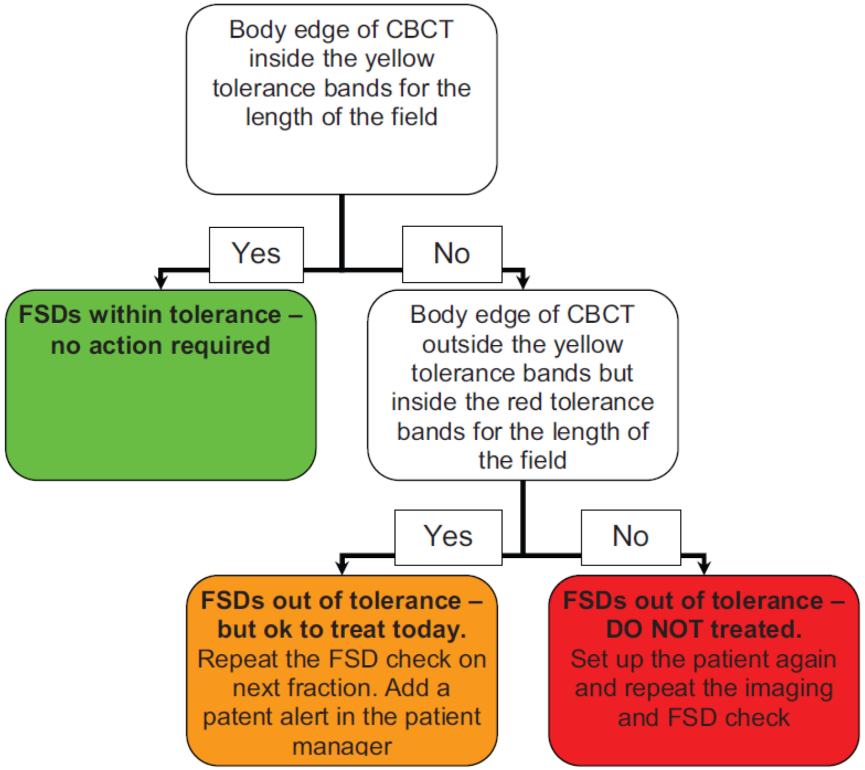






Troubleshooting

- What about when things aren't so clear?! *Troubleshoot*
  - ➢ Contour Variation
    - ▪ Weight Loss/Gain
    - ▪ Shoulder position
      - ○ Neubauer et al 2012



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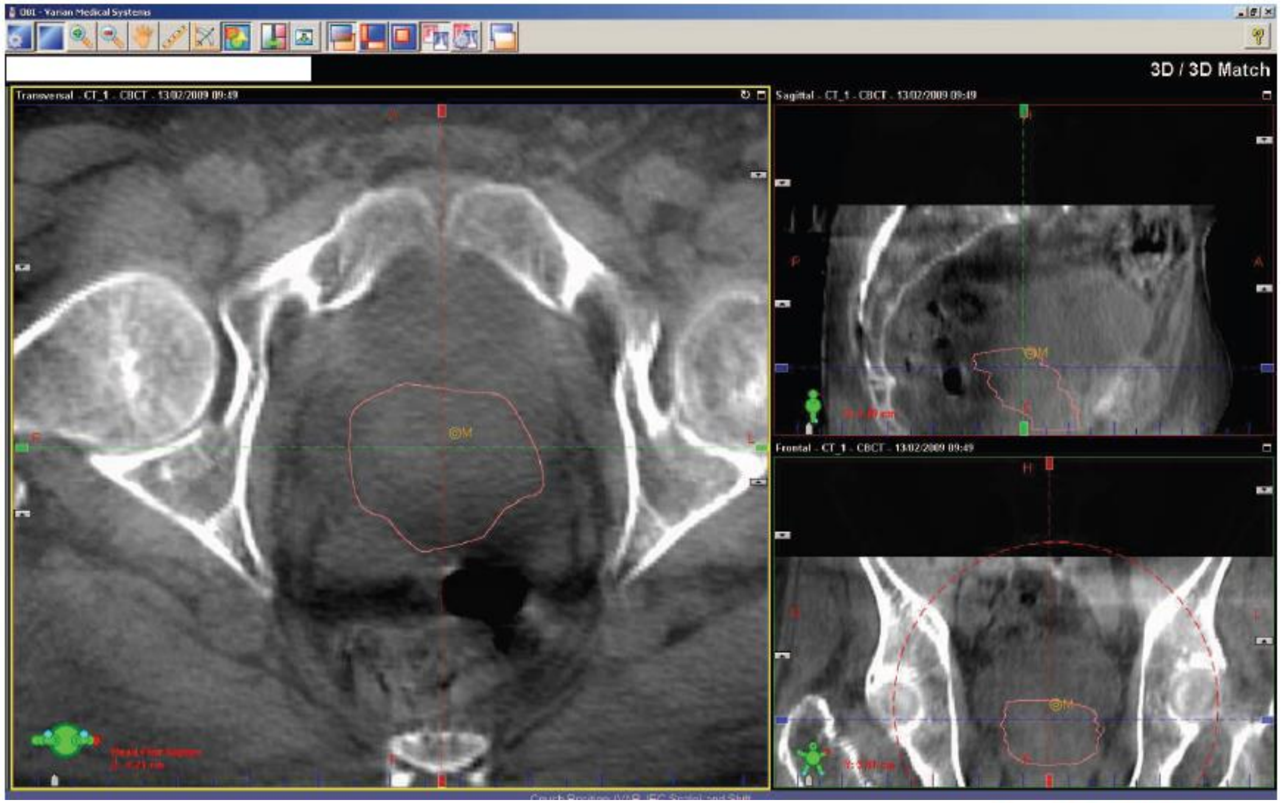
Troubleshooting

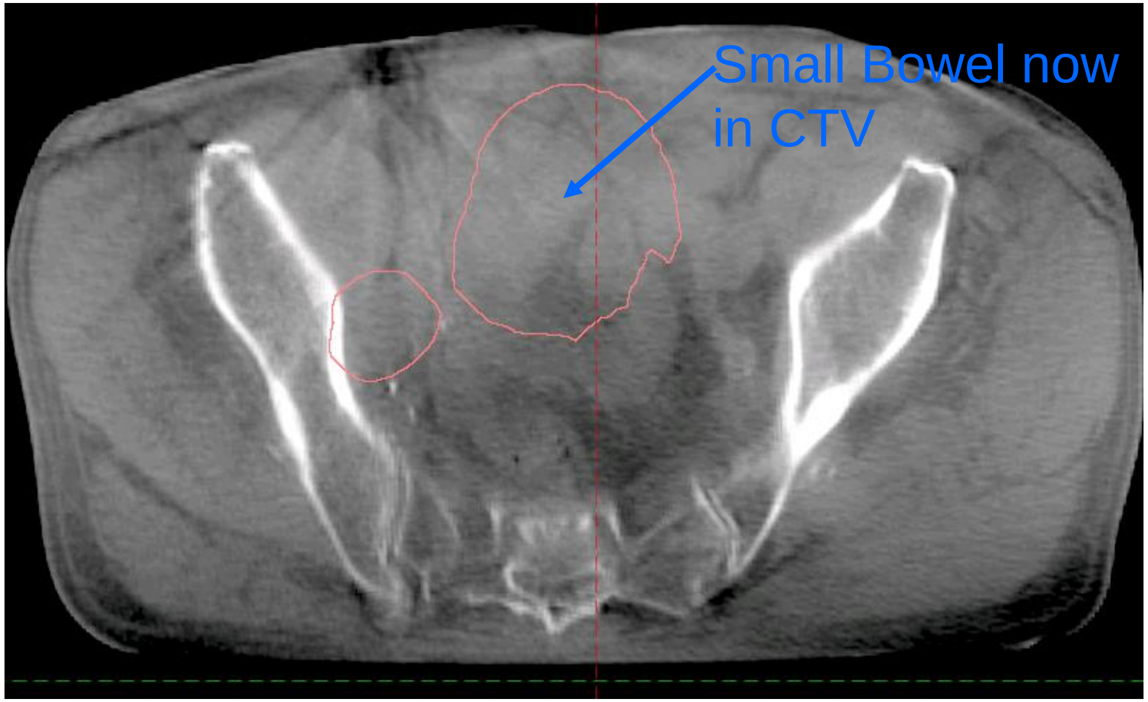
- What about when things aren't so clear?! *Troubleshoot*
  - ➢ Internal organ motion
    - ▪ Inter and intrafraction
      - ○ Gas



Troubleshooting

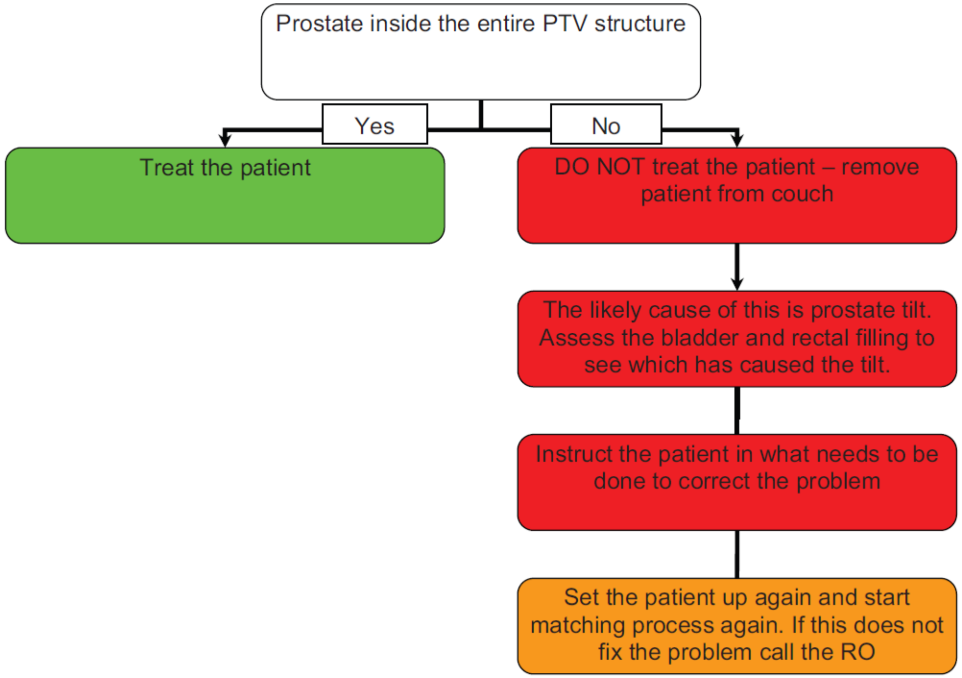
- What about when things aren't so clear?! *Troubleshoot*
  - ➢ Changes in bowel and bladder filling
    - ▪ Impact on target position and possibly dose
    - ▪ Impact on OAR dose

This is a bladder case, but also applicable to other sites (prostate bed)



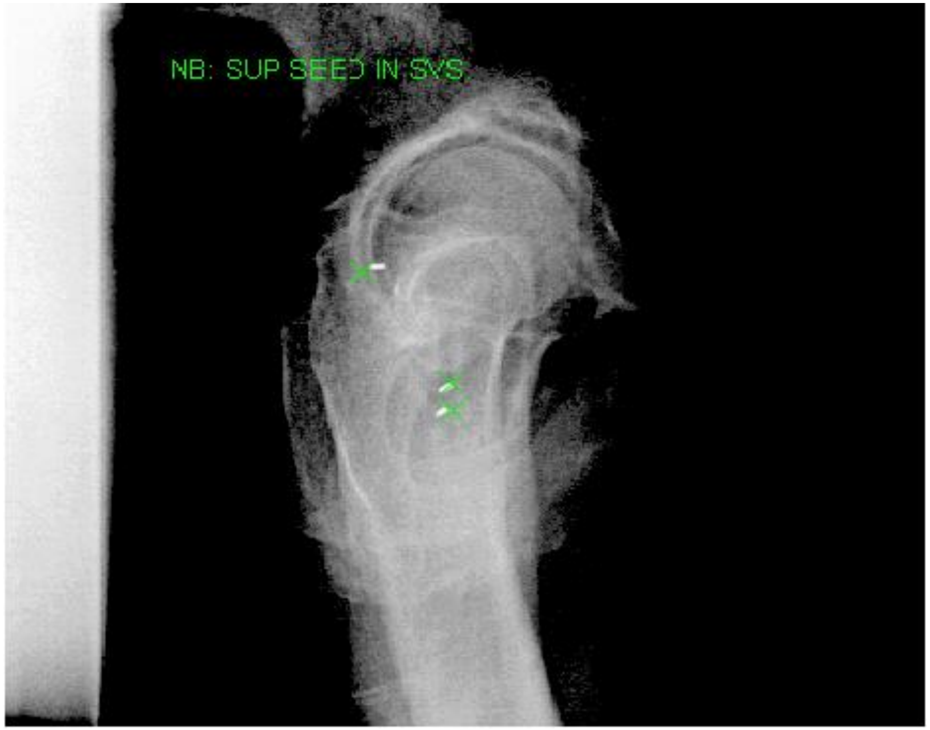
Troubleshooting

- What about when things aren't so clear?! *Troubleshoot*
  - ➢ Displacement of CTV/PTV
    - Likely cause rotation or tilt
    - Motion of adjacent structures
    - Anatomical changes of target



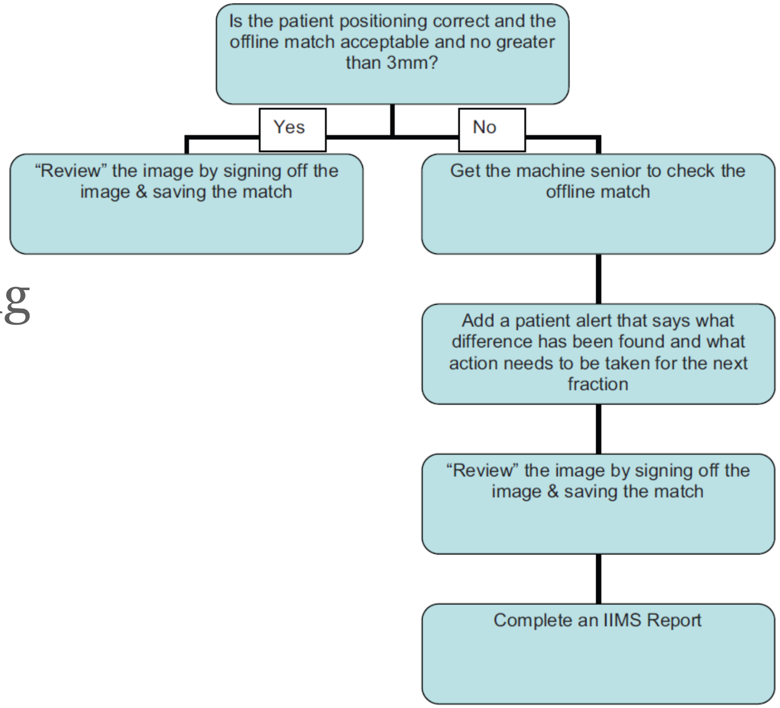
Troubleshooting

- What about when things aren't so clear?! *Troubleshoot*
  - ➢ Seed Migration
  - ➢ Poorly placed fiducials (SVs, Rectal wall etc)



Troubleshooting

- Online IGRT protocols should still include an offline review by an independent party
  - ➢ RTT on machine
  - ➢ RTT in planning
  - ➢ RO
    - ▪ Can also then feedback to patient
    - ▪ Patient education
  - ➢ Discuss at weekly MDT Audit Meeting



“The therapists are the front-runners for execution of the developed IGRT programs, and the quality of their performance will have a substantial impact on the success of IGRT” *(AAPM Report 104)*

Take Home Message!

- Use your “clinical intelligence”
  - ➢ Don’t just automatch and hit apply to whatever the result is.
  - ➢ ***Think!*** Does the match result make sense?

- Dosimetric Impact – Thinking beyond the treatment unit

- Good idea to overlay the relevant isodose lines (95% or 100%) on the CTV position

- Consider what is your target and what is the best surrogate for that

- Include the whole MDT

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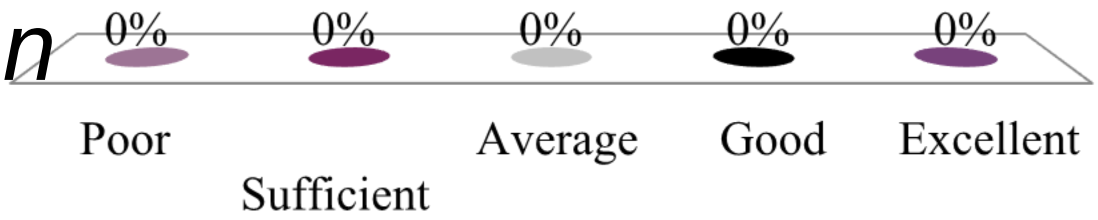
Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



Head and Neck IGRT: An RTT Perspective

Liz Forde, RTT
Assistant Professor
The Discipline of Radiation Therapy
School of Medicine
Trinity College Dublin

ARTT Applied Radiation Therapy Trinity Research Group

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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Fundamental IGRT Questions

- ***When*** *should I image?*
  - *Frequency*
- ***How*** *should I image?*
  - *Technology*
  - *Projection*
- ***What*** *can I see?*
  - *What is my target*
- ***What*** *should I match to?*
  - *Surrogate for target position*

Site Specific Points to Consider

- The head and neck is a regions rich in radiosensitive structures (serial organs)

- Margins are typically tight
  - 0.3cm -0.5cm

- IMRT or VMAT are now standard and carry with them highly conformal dose distributions and multiple targets

Site Specific Points to Consider

- In addition to standard match structures also review:

- Position of mouth bung (if used) is correctly in place

- Bolus is positioned correctly (no gaps)

- Change in tumour size

Site Specific Points to Consider

- Gaps between skin and mask
- Shoulder position
  - Neubauer *et al.*, 2012
- Direct clinical impact of translations and rotations have on adjacent structures
  - True OAR
  - OAR PRV

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Pre Treatment

CT Simulation

Slice thickness

- Accurate delineation
- Accurate dose calculation
- Improved DRR resolution
- 2.5-3.0mm

Registration of diagnostic imaging

Contrast

IV

No pre contrast scan

Bolus

Scan with bolus on

Planning

3DCRT

IMRT
VMAT
} Standard for this patient group

Beware the steep dose gradients

Shoulders

Avoid?

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Match Anatomy

- Bony landmarks

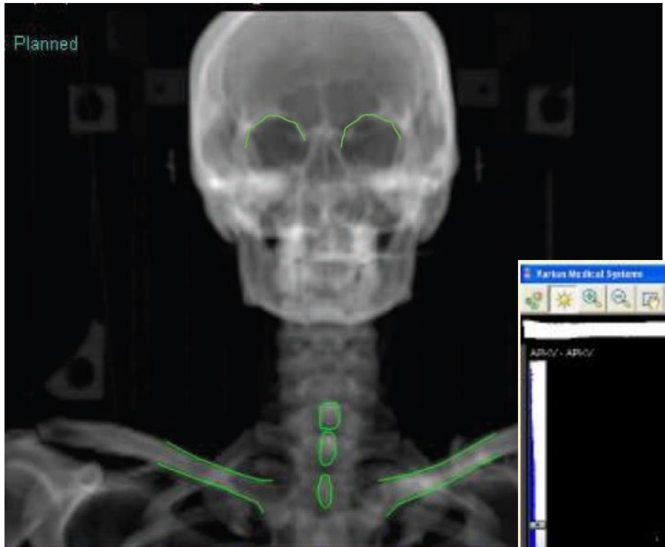
- Vertebrae
- Angle of mandible
- Orbital rim
- Frontal sinus
- Pituitary fossa

2D

- MV (EPI) is adequate for visualisation of bony anatomy
- Single projection ***not*** recommended for H&N
- Need to confirm isocentre in two planes
- Of less value when treating with IMRT
  - ➢ Field borders
  - ➢ Ciao images
- Impact of dose when imaging daily with MV

2D/2D

- Improved visualisation and image quality
- Large FOV assess anatomy across whole target volumes and patient straightening

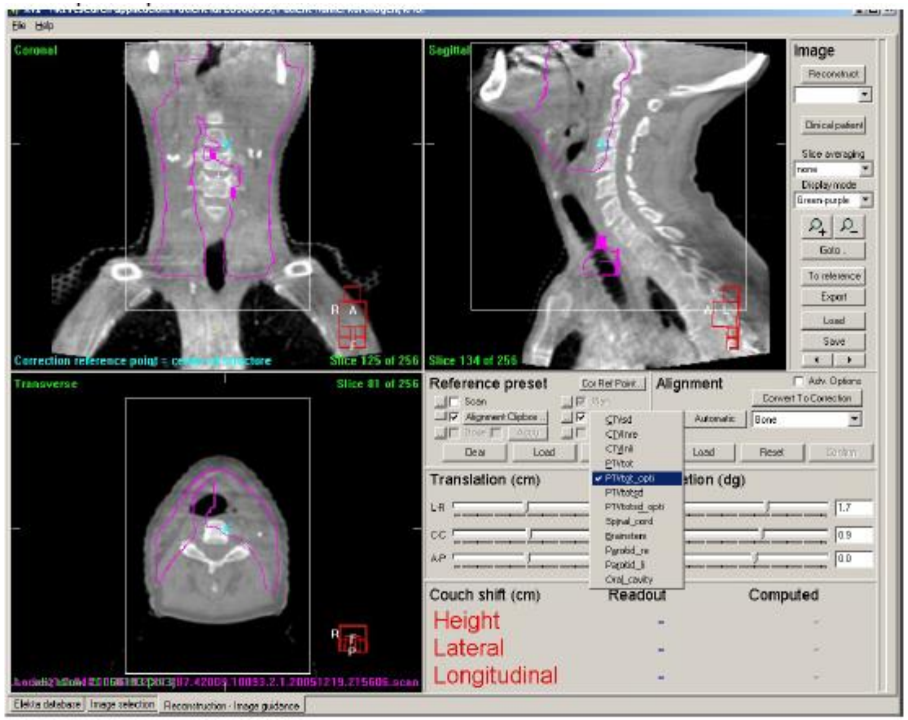


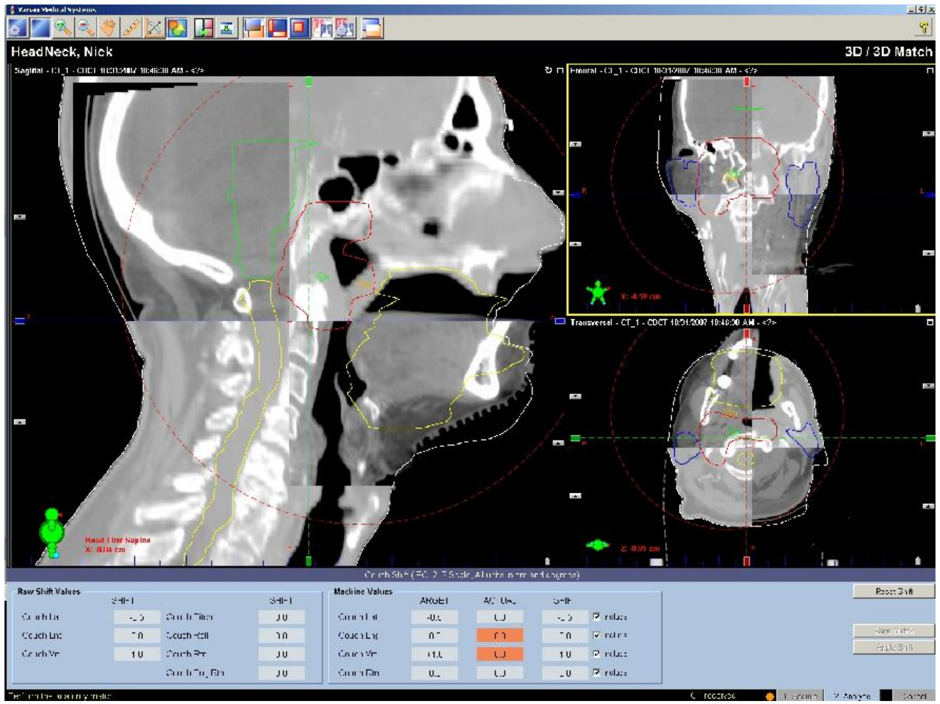
Mechalakos et al., 2007

3D

- Peter has covered this in excellent detail!

- Consider other structures to review
  - ➢ 45Gy isodose line





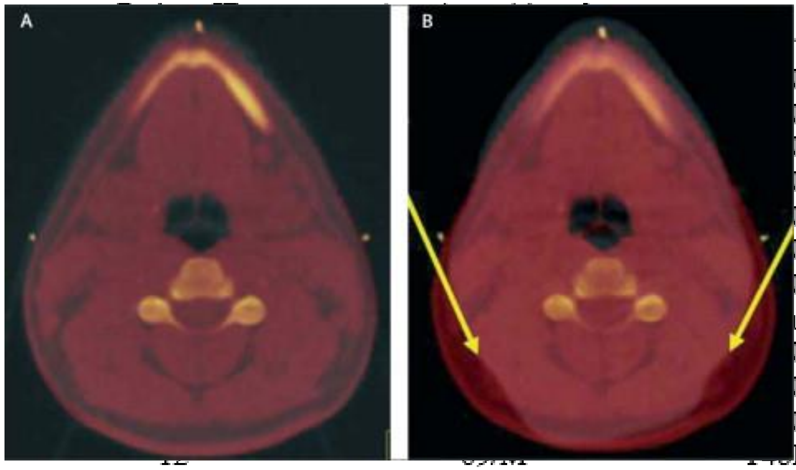
All Very Straightforward!

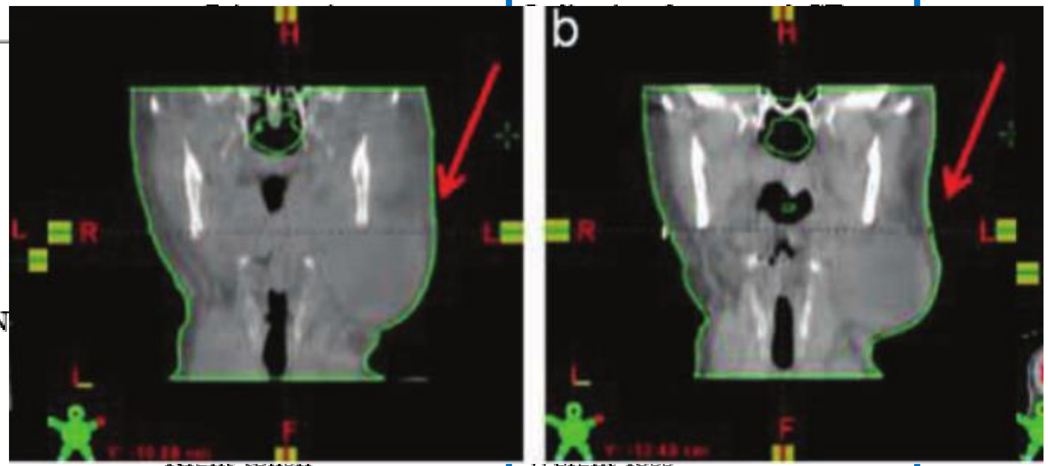
- But wait…there's more…

Tumour Shrinkage and Weight Loss

- Despite nutritional support these patients typically suffer significant weight loss during treatment
  - ➢ Impact on setup accuracy
  - ➢ Role of prophylactic PEG

Table 1. Patient characteristics





		Stage		
13	54/M	TXN2b	Unknown primary	Weight loss, tumor shrinkage

Abbreviations: ID = identification number; M = male; F = female; NPX = nasopharynx; BOT = base of tongue.
* Patient died of pneumonia after completing 23 fractions.

Tumour Shrinkage and Weight Loss

- Dosimetric Impact!

Replanning during IMRT for H&N cancer ● E. K. HANSEN *et al.*

Table 3. Dosimetric comparisons of the 2nd portion of treatment with and without replanning

Dosimetric end point (mean values)	1st portion of treatment (1st CT/1st plan)	2nd portion of treatment: Replanned (2nd CT/2nd plan)	2nd portion of treatment: Not replanned (2nd CT/1st plan)	*p* value
PTV_{GTV}				
D_{99}	38.1 Gy	28.3 Gy	26.0 Gy	0.05
D_{95}	40.3 Gy	30.3 Gy	28.1 Gy	0.02
V_{93}	99.5%	99.4%	92.5%	<0.001
PTV_{CTV}				
D_{99}	30.9 Gy	22.9 Gy	18.3 Gy	<0.001
D_{95}	34.0 Gy	25.7 Gy	22.7 Gy	0.003
V_{93}	98.7%	98.7%	90.5%	<0.001
Spinal cord				
D_{max}	25.7 Gy	19.3 Gy	23.3 Gy	0.003
$D_{1\ cc}$	23.0 Gy	17.1 Gy	20.2 Gy	0.04
Brainstem				
D_{max}	28.2 Gy	22.3 Gy	24.9 Gy	0.007
$D_{1\ cc}$	25.0 Gy	19.4 Gy	21.7 Gy	0.20
$D_{1\%}$	26.1 Gy	20.2 Gy	22.9 Gy	0.12
Right parotid	(n = 12)			
D_{mean}	15.5 Gy	12.0 Gy	14.9 Gy	0.05
D_{50}	13.0 Gy	10.6 Gy	13.6 Gy	0.06
V_{26}	44.6%	45.5%	55.5%	0.04
Left parotid				
D_{mean}	15.2 Gy	11.9 Gy	12.1 Gy	0.81
D_{50}	13.2 Gy	10.2 Gy	11.2 Gy	0.47
V_{26}	45.2%	42.9%	42.2%	0.89
Mandible (n = 9)				
D_{max}	39.2 Gy	29.6 Gy	31.3 Gy	0.01
V_{60}	11.0%	11.3%	18.2%	0.08
V_{70}	0.04%	0.05%	4.5%	0.32

Abbreviations: PTV_{GTV} PTV_{CTV} = planning target volumes of gross tumor volume and clinical tumor volume, respectively; D_{max} = maximum dose; D_{99} = dose to 99% of the volume; D_{95} = dose to 95% of the volume; V_{93} = percent of volume receiving ≥93% of the prescribed dose; $D_{1\ cc}$ = dose to 1 cc of the volume; $D_{1\%}$ = dose to 1% of the volume; D_{mean} = mean dose; D_{50} = dose to 50% of the volume; V_{26}, V_{60}, and V_{70} = percent of volume receiving ≥26 Gy, ≥60 Gy, and ≥70 Gy, respectively.

Assessed impact on OAR doses not target dose

Contoured OARs on CBCTs and recalc'd with correction for HU differences

Clinical Investigation: Head-and-Neck Cancer

Monitoring Dosimetric Impact of Weight Loss With Kilovoltage (KV) Cone Beam CT (CBCT) During Parotid-Sparing IMRT and Concurrent Chemotherapy

Kean Fatt Ho, F.R.C.R.,* Tom Marchant, Ph.D.,[†] Chris Moore, Ph.D.,[†] Gareth Webster, Ph.D.,[†] Carl Rowbottom, Ph.D.,[†] Hazel Penington, B.Sc.,[‡] Lip Lee, F.R.C.R.,[§] Beng Yap, F.R.C.R.,[§] Andrew Sykes, F.R.C.R.,[§] and Nick Slevin, F.R.C.R.[§]

*From *Academic Radiation Oncology, [†]North Western Medical Physics, [‡]Wade Radiotherapy Research Centre, and [§]Department of Clinical Oncology, The Christie NHS Foundation Trust, Manchester, UK*

Received Oct 10, 2010. Accepted for publication Jul 6, 2011

Where did this weight loss occur?

Weight loss and parotid shrinking did occur, but insignificant impact on OAR doses

Results inconsistent with previous studies
Impact of neoadjuvant therapy?

Demonstrates the benefit of 3D imaging
Discusses options of dose calculation from CBCT

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Tumour Shrinkage and Weight Loss

- A lot of literature!!!
- Every patient is individual
  - RTTs treat them and can see these subtle changes
- Dosimetric (and clinical) impact will depend on original DVH results
- Without 3D imaging, you cannot accurately visualise or account for this
- *"The dosimetric impact of anatomic changes during radiotherapy was of lesser importance than the effects of IGRT repositioning"* (Graff et al., 2012)

What Else?
Variation in Shoulder Position

- The shoulders move independently from the isocentre
- This shoulder motion changes the path length of the beam
- Superior shoulder shift results in target coverage loss

Table 3 Target coverage in the C6-C7 region

	IMRT			VMAT		
	100%	98%	95%	100%	98%	95%
C6-C7						
No shift	97	98	100	94	97	99
5 mm superior	90	98	100	84	96	99
15 mm superior	23	53	94	16	35	72
C7-T2						
No shift	98	100	100	–	–	–
15 mm posterior	89	99	100	–	–	–

Percentage of the clinical target volume (CTV) in the C6-C7 region covered by the 100%, 98%, and 95% isodose lines with no shift and with superior shifts for IMRT and VMAT plans, as well as the percent coverage of the CTV in the C7-T2 region with no shift and a 15 mm posterior shift. All percentages were evaluated for Patient 1.

What Else?
Variation in Shoulder Position

- This positional variation cannot be corrected with translational or rotational corrections

- This variation also caused an increase in OAR dose
    - Brachial Plexus increased by up to 7.2Gy

- In the absence of CBCT the angle of clavicle on AP EPI

Take Home Message

- *"Complex and multifactorial dosimetric variations occur during head and neck IMRT."* (Graff et al., 2012)
- Take caution due to tight margins, conformal techniques and proximity of radiosensitive structures
- Have an understanding of dosimetric impact of weight loss and shoulder motion
- Appropriate immobilisation is key. IGRT may help in assessment of this, but can not always correct for this.
- Recommend clear protocols to mandate imaging frequency and match structures

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RTTs! If you are going to read one head and neck paper this year...
Let it be this one!

Technical Innovations & Patient Support in Radiation Oncology 1 (2017) 1–7

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Technical Innovations & Patient Support in Radiation Oncology

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tipsRO Technical Innovations and Patient Support in Radiation Oncology

Practice guidelines

ESTRO ACROP guidelines for positioning, immobilisation and position verification of head and neck patients for radiation therapists

CrossMark

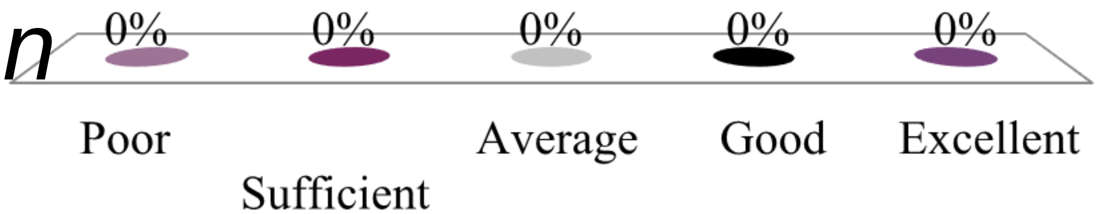
Michelle Leech [a,*], Mary Coffey [a], Mirjam Mast [b], Filipe Moura [c], Andreas Osztavics [d], Danilo Pasini [e], Aude Vaandering [f]

[a] *Applied Radiation Therapy Trinity (ARTT), Discipline of Radiation Therapy, School of Medicine, Trinity College, Dublin 2, Ireland*
[b] *Radiotherapy Centre West/Medical Center Haaglanden, The Hague, The Netherlands*
[c] *Hospital CUF Descobertas, Lisboa, Portugal*
[d] *Universitätsklinik für Strahlentherapie, Vienna, Austria*
[e] *USCU Policlinico A. Gemelli, Rome, Italy*
[f] *Radiation Oncology Department, Cliniques Universitaires St Luc, Brussels, Belgium*

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



Brain

Jose Lopez, M.D., Ph.D
Radiation Oncology
University Hospital Virgen del Rocio
Seville, Spain

Advanced skills in modern radiotherapy

Outline of Talk

- General pearls for Pediatric (CNS) tumors
- Protons
- Case report
- Discussion of current multidisciplinary (physician, phisyc and RTTs) management

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Pearls

- The number one cause of death in children is accidents (44%), followed by cancer (10%).
- Of childhood cancers, leukemias are the most common followed by CNS neoplasms (~20%)
- Of pediatric CNS neoplasms, gliomas are most common (lowgrade astrocytomas ~35–50%, brainstem gliomas ~15%, malignant astrocytomas ~10%, optic pathway gliomas ~5%)

Inmovilization

Planning images

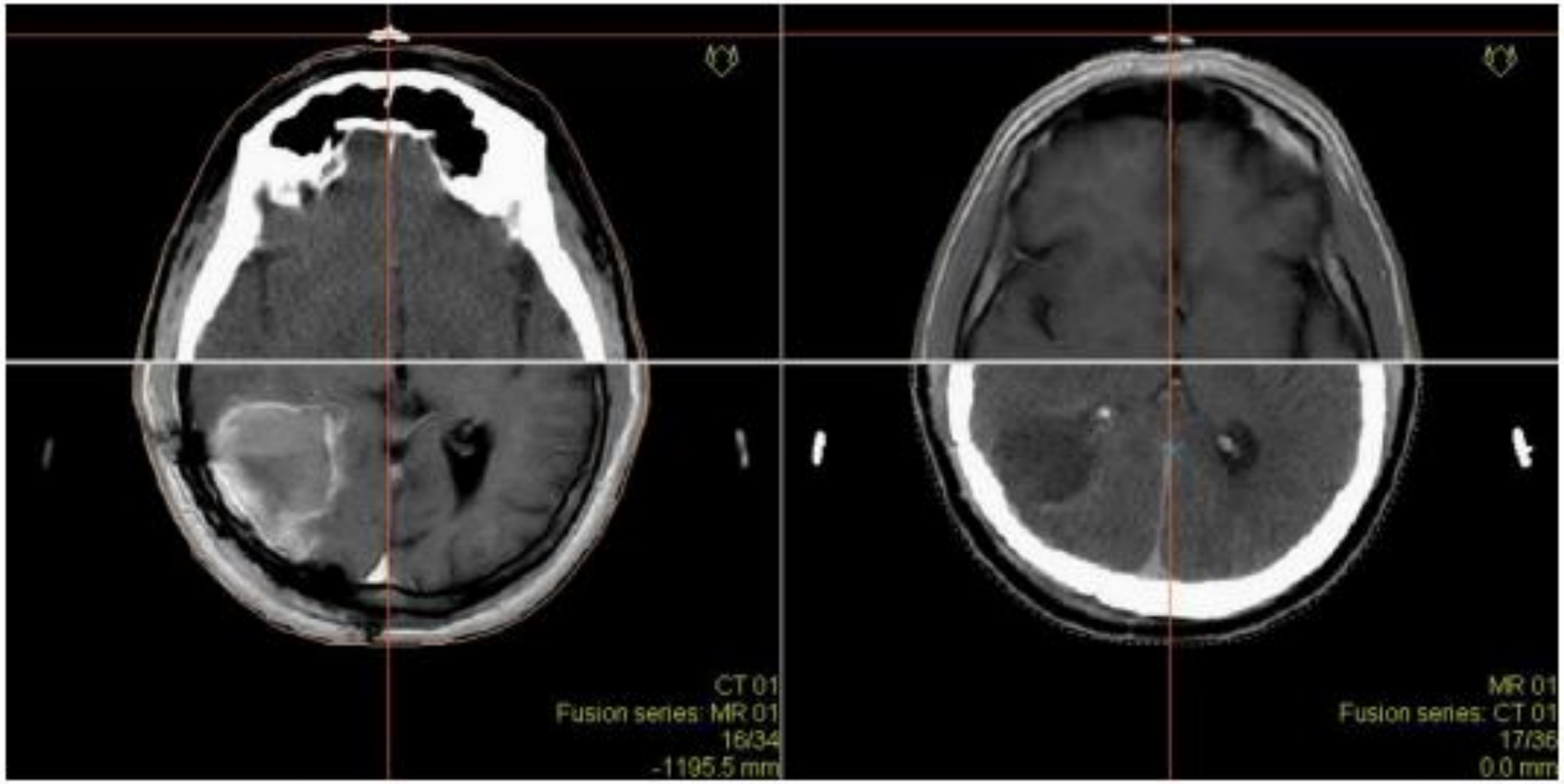
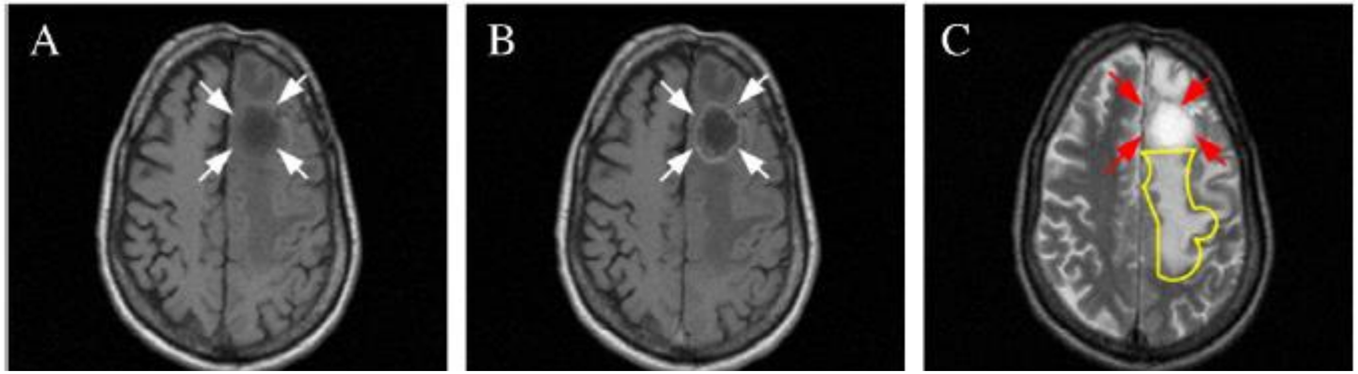


Fig. 2. Image registration of CT and MR image sets. Left image: top (CT), bottom (MR). Right image: top (MR), bottom (CT). The center of the middle fiducial marker pointed out on the left image is shown via registration on the right.

Radiotherapy and Oncology 87 (2008) 100–109



T1 without contrast T1 with contrast T2

Fig. 4. Appearance of astrocytoma tumor on three sequences. (A) Isointense tumor (diffused) on T1-weighted image. (B) Isointense, peripherally enhanced homogeneous tumor on postcontrast T1-weighted image. (C) The tumor is seen as a homogeneous, hyperintense mass on T2-weighted image (in red) as is the edema, which, however, is less bright (in yellow).

T1 hyperintense

T1 isointense

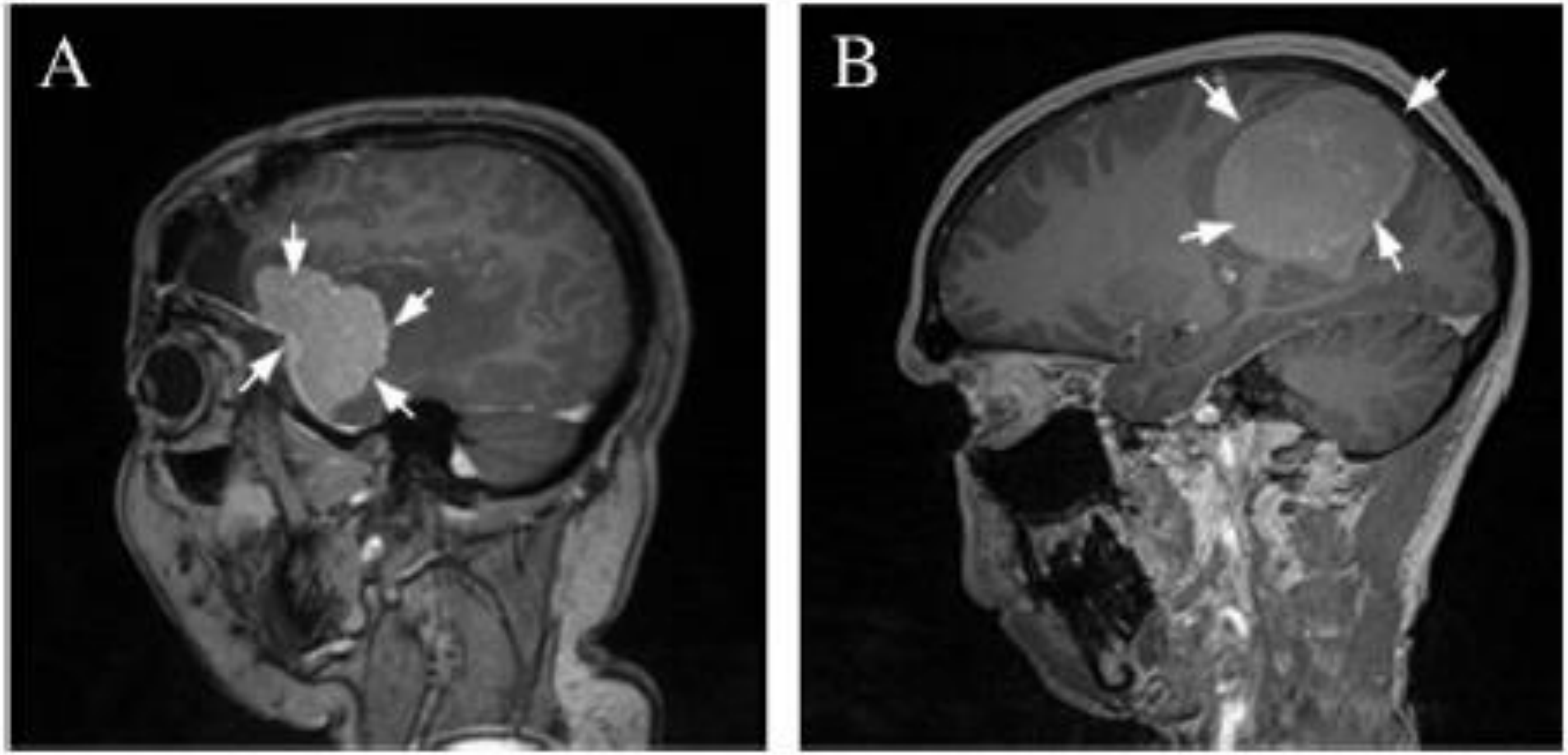


Fig. 2. Degree of enhancement of same tumor (meningioma) of different patients on postcontrast T1-weighted images. (A) Full enhancement of meningioma tumor (hyperintense signal). (B) No enhancement of meningioma tumor (isointense signal).

Homogeneous Heterogeneous

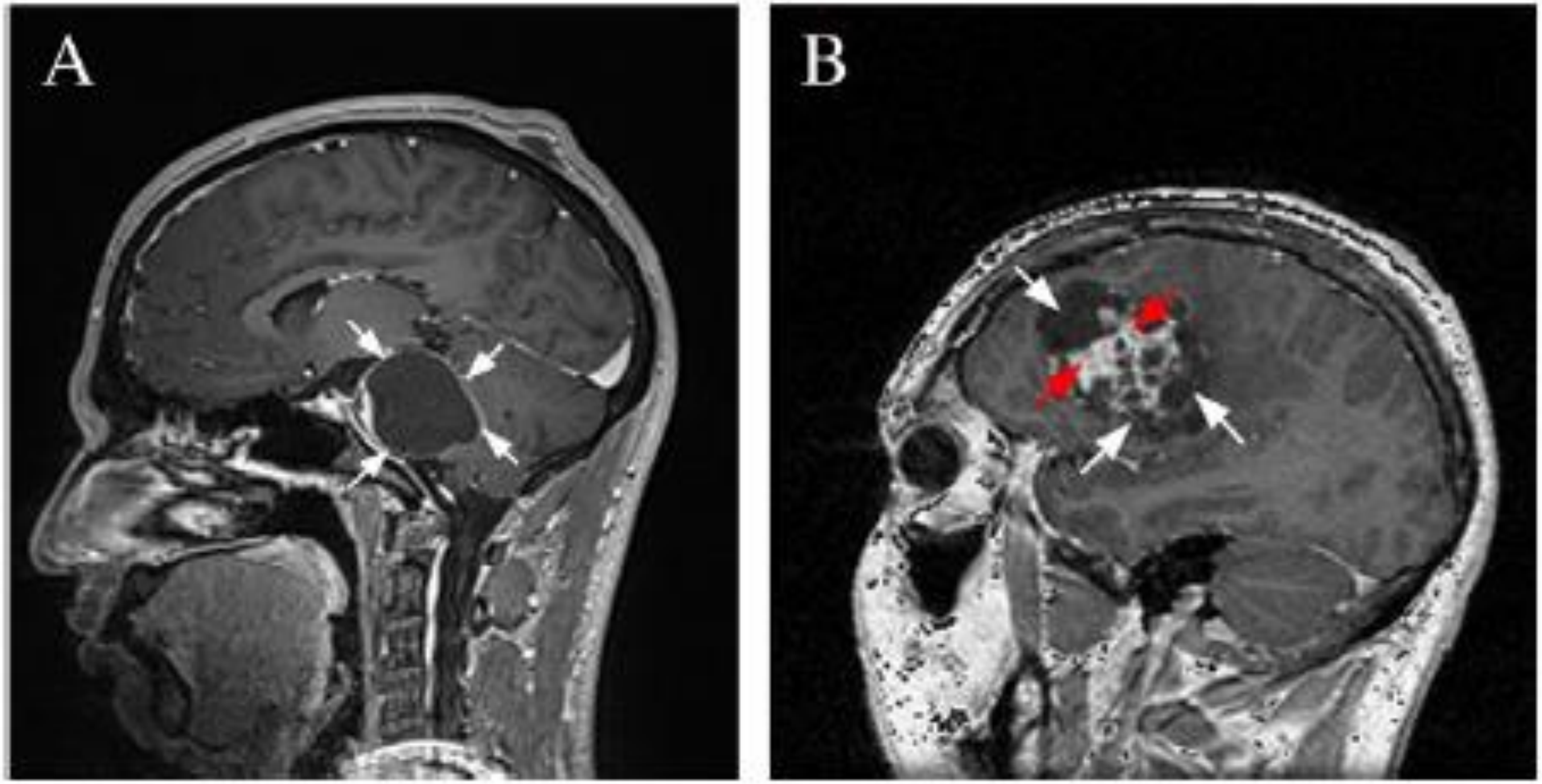


Fig. 3. Homogeneous and heterogeneous tumors. (A) Homogeneous astrocytoma tumor — hypointense signal, peripheral enhancement. (B) Heterogeneous glioma tumor with hypointense necrotic part (in red) and hyperintense-cystic components (in white).

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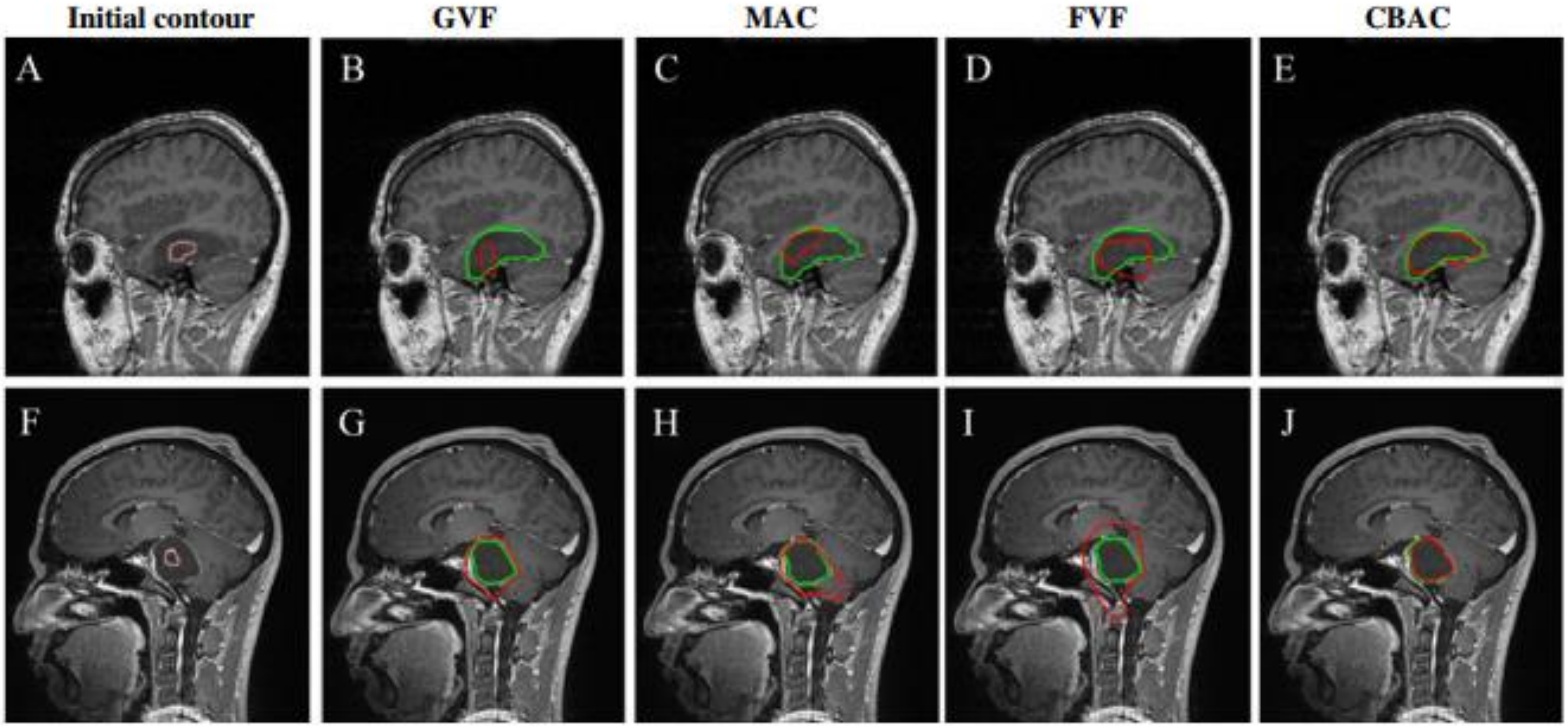
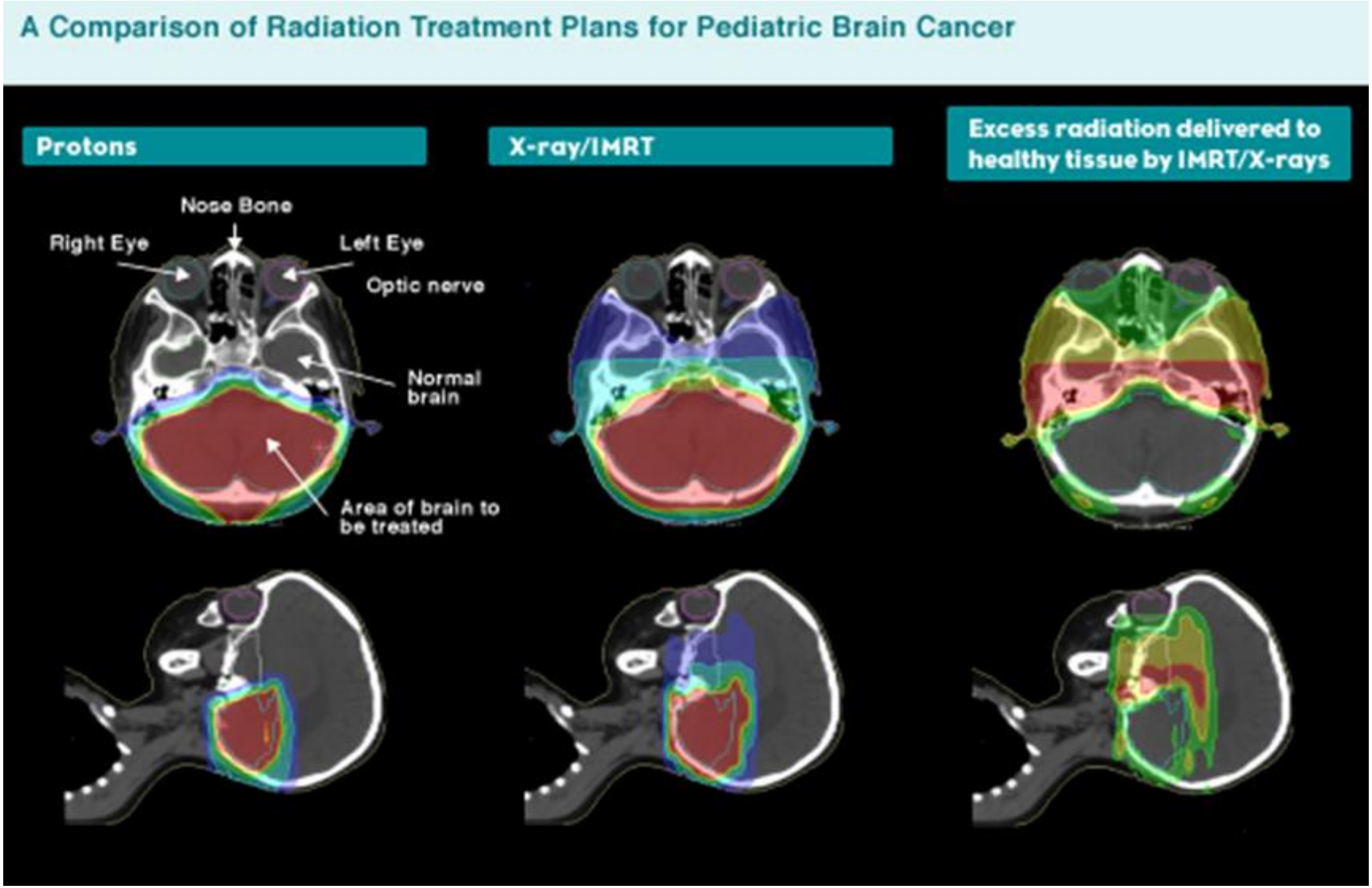


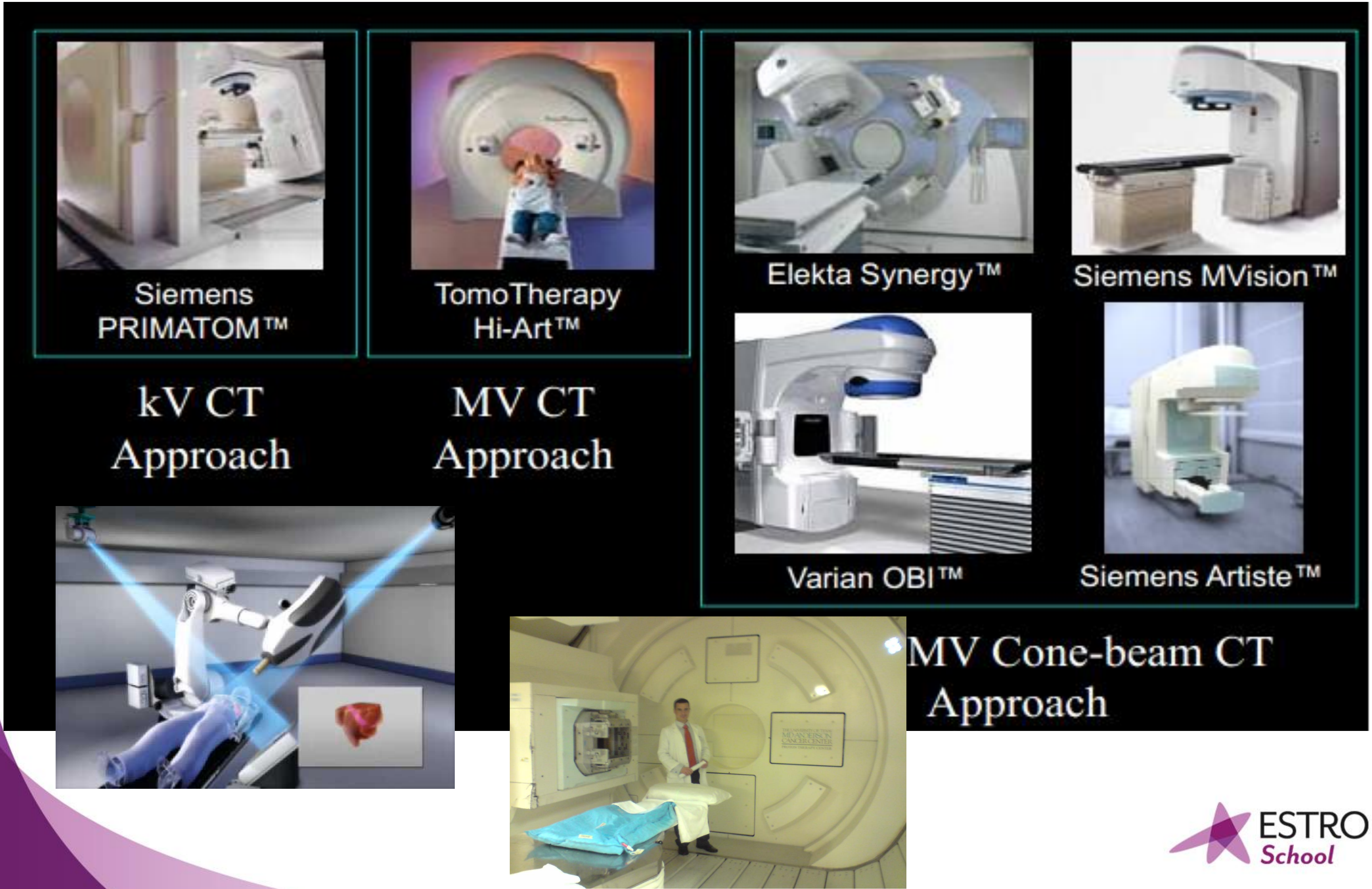
Fig. 10. Comparative segmentation results on postcontrast T1-weighted image. Green — ground truth marked by the radiologist; red — tumor boundary extracted by different methods. Row 1: tumor type, low-grade glioma; appearance, homogeneous tumor with isointense signal; the tumor shows no enhancement. Row 2: tumor type, astrocytoma; appearance, homogeneous tumor with hypointense signal; the tumor shows peripheral enhancement.

Magnetic Resonance Imaging 30 (2012) 694–715



http://www.procure.com/ForMedicalProfessionals/ClinicalIndications.aspx

Technologies



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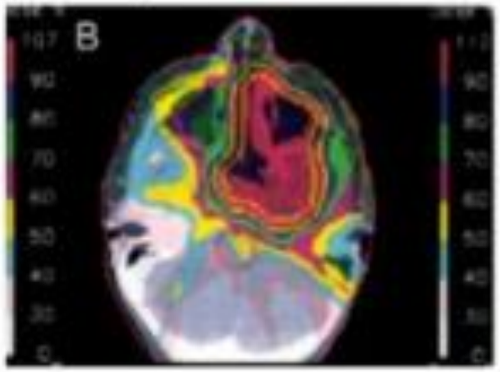
Proton Therapy

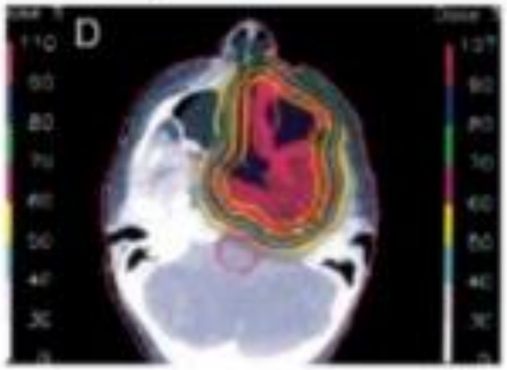
Claims:

- Opportunity to treat previously untreatable disease because of challenging geometry
  - ➢ Concave CTV/PTV partially surrounding a convex OAR

IMRT



Proton



- Second cancer reduction

CLINICAL INVESTIGATION — Pediatric Tumors

POTENTIAL REDUCTION OF THE INCIDENCE OF RADIATION-INDUCED SECOND CANCERS BY USING PROTON BEAMS IN THE TREATMENT OF PEDIATRIC TUMORS

Raymond Miralbell, M.D.,* Antony Lomax, Ph.D.,† Laura Cella, M.Sc.,* and Uwe Schneider, Ph.D.†

Controversies of cost-effectiveness with new technologies, e.g. protons

Is proton beam therapy for prostate cancer worth the cost?

February 20, 2013

By Durado Brooks, MD, MPH

Proton therapy popular and profitable

The lack of evidence has not slowed the rapid increase in the use of proton treatment for prostate cancer. One recent study documented a 67% increase in the number of cases of proton treatment for prostate cancer billed to Medicare between 2006 and 2009. This rate of growth is particularly noteworthy given the limited access to proton therapy: there are at present only 10 proton beam centers operating in the United States, and each center treats only a few hundred cancer patients each year.

- Cost of proton therapy nearly double compared to IMRT
- Benefit of proton therapy in prostate cancer is unproven
  - ➢ Neither better tumor control nor lower toxicity
    - A few studies suggest that toxicity rates might even be higher

pace? Financial incentives may be playing a role. Proton beam therapy for prostate cancer is reimbursed at a much higher rate than traditional radiation treatment for the same condition. Medicare pays about $19,000 for a full dose of standard radiation therapy for prostate cancer, but it pays nearly double for proton therapy - more than $32,000.

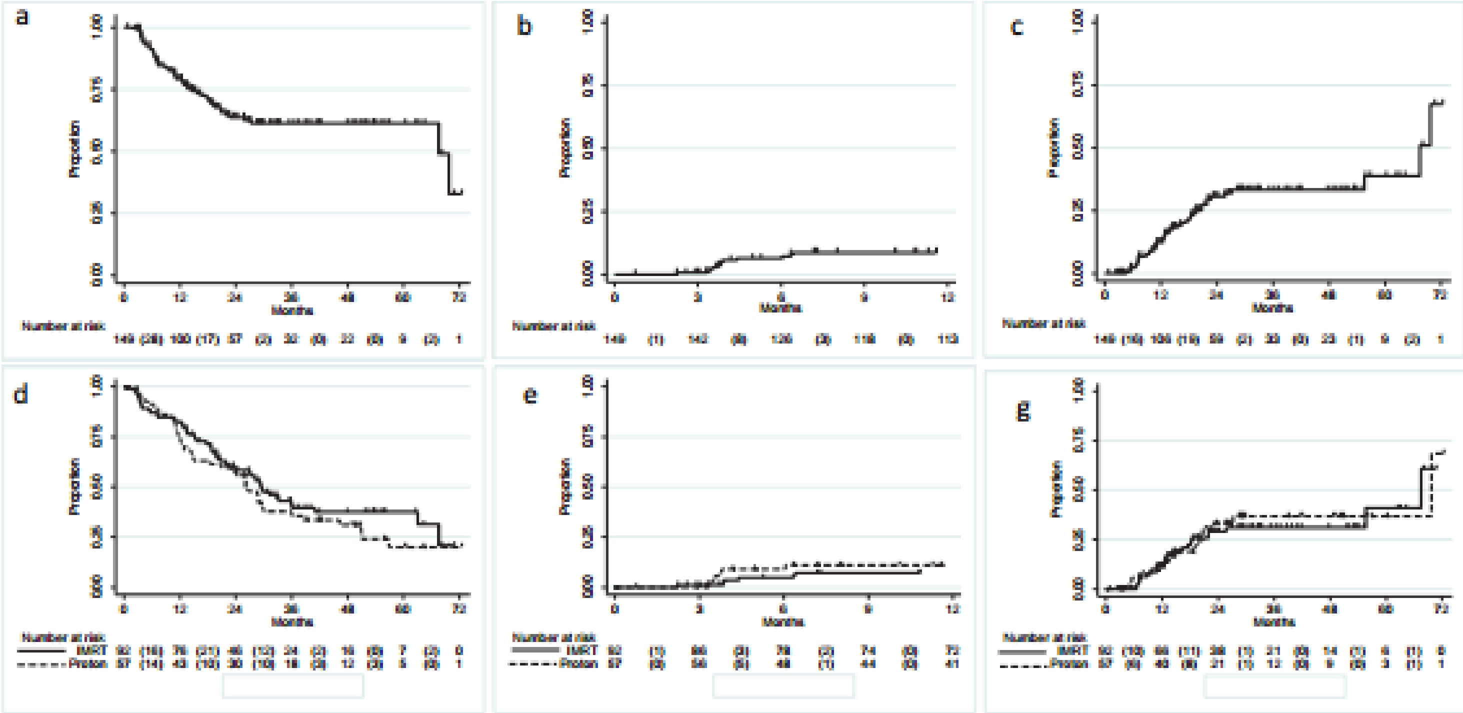


Figure 2. Time to treatment failure defined as 1) grade ≥ 3 RP, 2) Local recurrence as first occurence in randomised patients. Upper panels show the time to the development of (a) combined treatment failure, (b) grade ≥ 3 RP, and (c) local recurrence as a whole group. Lower panels shox the comparison between IMRT (solid) vs. 3D-PBT (dashed) in time to the development of (d) combined treatment failure, (e) grade ≥ 3 RP, and (g) local recurrence.

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Lung cancer
Photons vs protons
Phase III
MDA

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International Journal of Radiation Oncology biology • physics
www.redjournal.org
Vol. 87, No. 1, pp. 46-52, 2013

Clinical Investigation: Late Effect

Incidence of Second Malignancies Among Patients Treated With Proton Versus Photon Radiation

Christine S. Chung, MD, MPH,[*] Torunn I. Yock, MD, MCh,[†] Kerrie Nelson, PhD,[‡] Yang Xu, MS,[§] Nancy L. Keating, MD, MPH,[‖,¶] and Nancy J. Tarbell, MD[†,#]

- Conflicting hypotheses:
  - ➢ whether proton radiation has less risk than photon therapy
    - scattering with photons vs neutron contamination with protons
- 558 proton pts treated from 1973 to 2001 Harvard cyclotron vs 558 matched photon pts from SEER
- Second Ca: 29 protons (5.2%) and 42 Photons (7.5%)
- No evidence for or against (adjusted for age at treatment, sex, site, year diagnosed)

A systematic literature review of the clinical and cost-effectiveness of hadron therapy in cancer

Mark Lodge[a,*], Madelon Pijls-Johannesma[b], Lisa Stirk[c], Alastair J. Munro[d], Dirk De Ruysscher[b,e], Tom Jefferson[a]

[a]Cochrane Cancer Network, Oxford, UK, [b]MAASTRO Clinic, Maastricht, The Netherlands, [c]Centre for Reviews & Dissemination, University of York, UK, [d]University of Dundee, Scotland, UK, [e]University Hospital Maastricht, GROW, MAASTRO Clinic, Maastricht, The Netherlands

Table 1
Results literature review in comparison with conventional therapy classified by tumour site

Tumour site	Protons		Ions	
	n studies/*N*	Result	*n* studies/*N*	Result
Head and neck	2/62	No firm conclusions	2/65	Similar to protons
ACC (locally advanced)	—	—	1/29	Superior
Prostate cancer	3/1751	Similar	4/201	No firm conclusions
Ocular tumours	10/7708	Superior	2/1343	Similar to protons
Gastro-intestinal cancer	5/369	No firm conclusions	2/73	No firm conclusions
Lung cancer (non-small cell)	3/156	No firm conclusions	3/205	Similar to SRT
CNS[a]	10/839	Similar	3/405	Similar to protons
Chordomas of skull base	3/302	Superior	2/107	Similar to protons
Sarcoma's	1/47	No firm conclusions	1/57	No firm conclusions
Pelvic tumours	3/80	No firm conclusions	2/49	No firm conclusions

Abbreviations: *N*, number of patients; ACC, adenoid cystic carcinomas; SRT, stereotactic radiotherapy.
[a] CNS, central nerve system tumours; inclusive skull base, spinal cord chondroma and chondrosarcomas.

- Brada et al. (JCO 2008) concluded that there is insufficient evidence at the present to recommend the use of proton therapy in any disease sites
- Reviewers / Authors have different views as to what constitutes evidence

Radiotherapy and Oncology 103 (2012) 8–11

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journal homepage: www.thegreenjournal.com

Systematic review

An evidence based review of proton beam therapy: The report of ASTRO's emerging technology committee

Aaron M. Allen[a,*], Todd Pawlicki[b], Lei Dong[c], Eugene Fourkal[d], Mark Buyyounouski[d], Keith Cengel[e], John Plastaras[e], Mary K. Bucci[c], Torunn I. Yock[f], Luisa Bonilla[a], Robert Price[d], Eleanor E. Harris[g], Andre A. Konski[h]

- In pediatric CNS malignancies PBT appears superior to photon approaches but more data is needed.
- In large ocular melanomas and chordomas, we believe that there is evidence for a benefit of PBT over photon approaches.
- PBT is an important new technology in radiotherapy
  - Current evidence provides a limited indication for PBT
  - More robust prospective clinical trials are needed to determine the appropriate clinical setting for PBT


Essen, Germany
Berlin, Germany
Uppsala, Sweden
Munich, Germany
St. Petersburg, Russia
Vancouver, Canada
Dubna, Russia
Clatterbridge, England
Moscow, Russia
Wakasa, Japan
San Francisco, CA
Heidelberg, Germany
Austron, Austria
Seoul, South Korea
Tsukuba, Japan
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Trento, Italy
Koeln, Germany
Zibo, China
Bloomington, IN
Kashiwa, Japan
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Loma Linda, CA
Villigen, Switzerland
Milan, Italy
Shuzuoka, Japan
Orsay, France
Houston, TX
Jacksonville, FL
Nice, France
Hyogo, Japan
Gauteng, South Africa
Western Cape, South Africa
Physics research-based facility
Medical facility
Planned or under construction

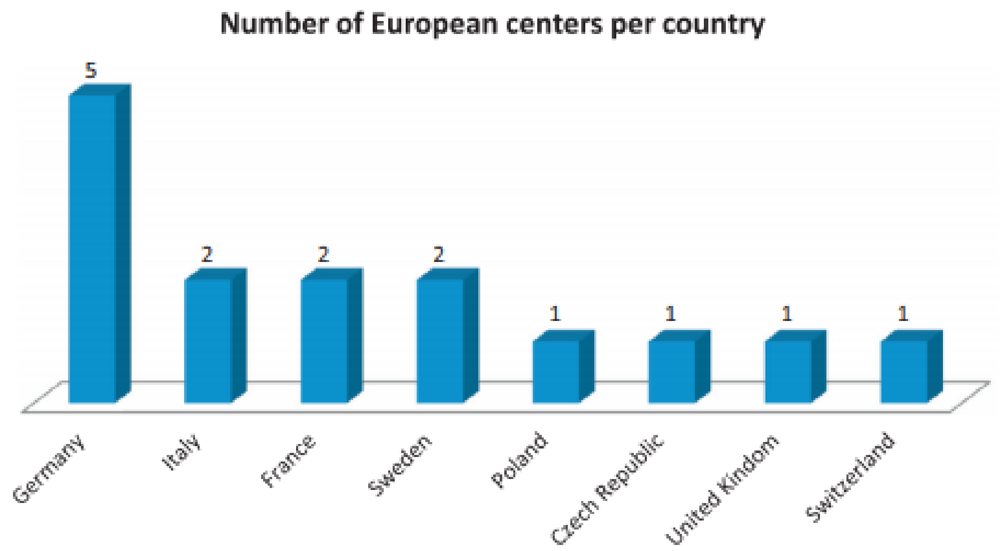
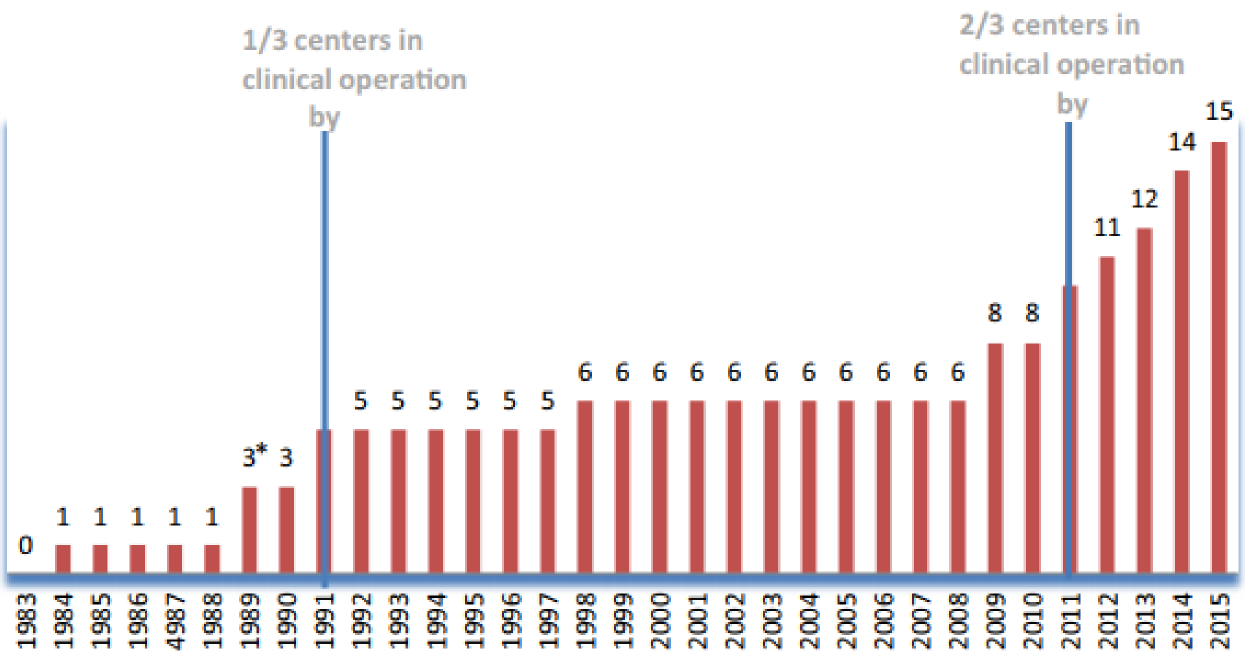
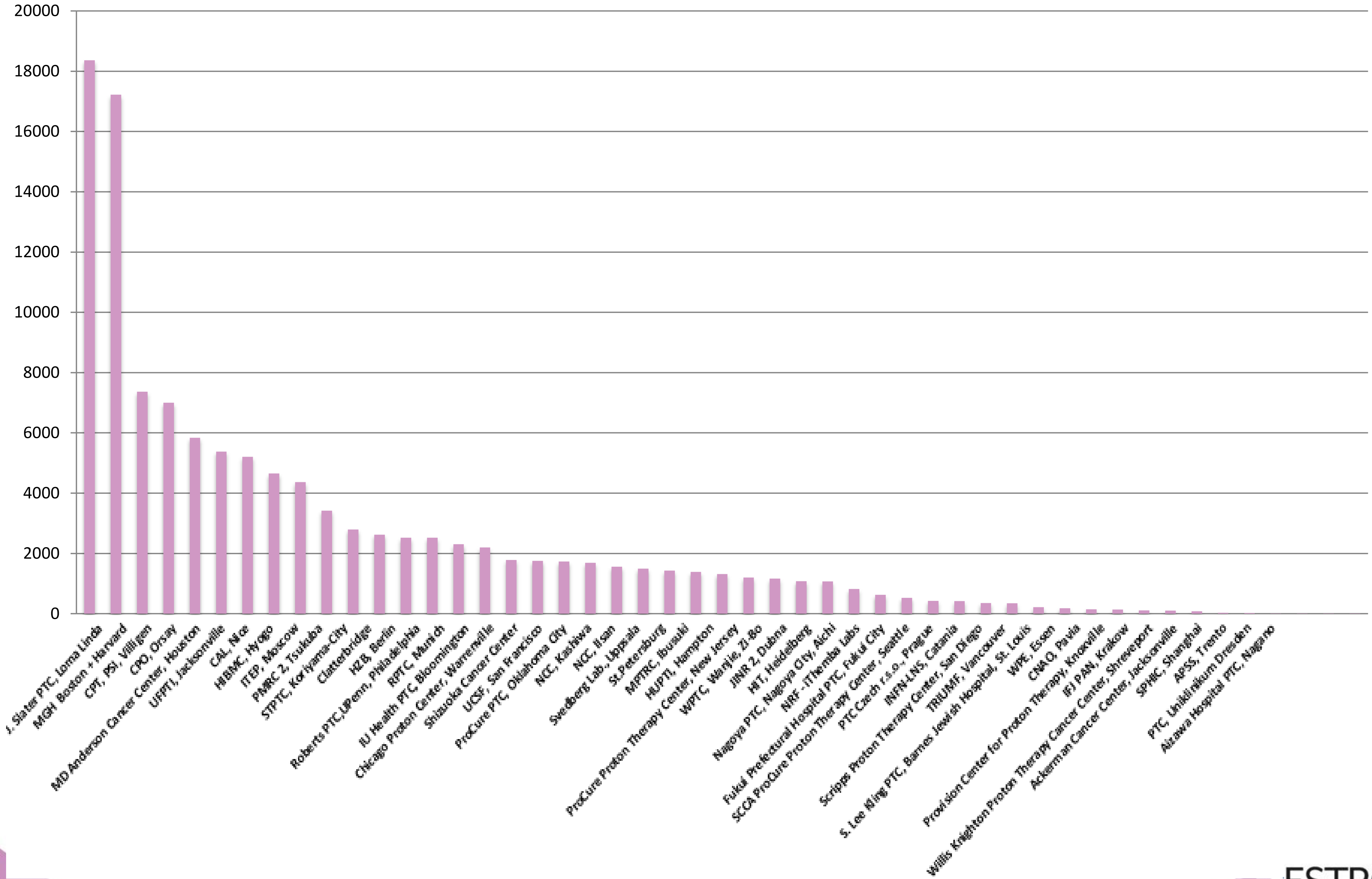


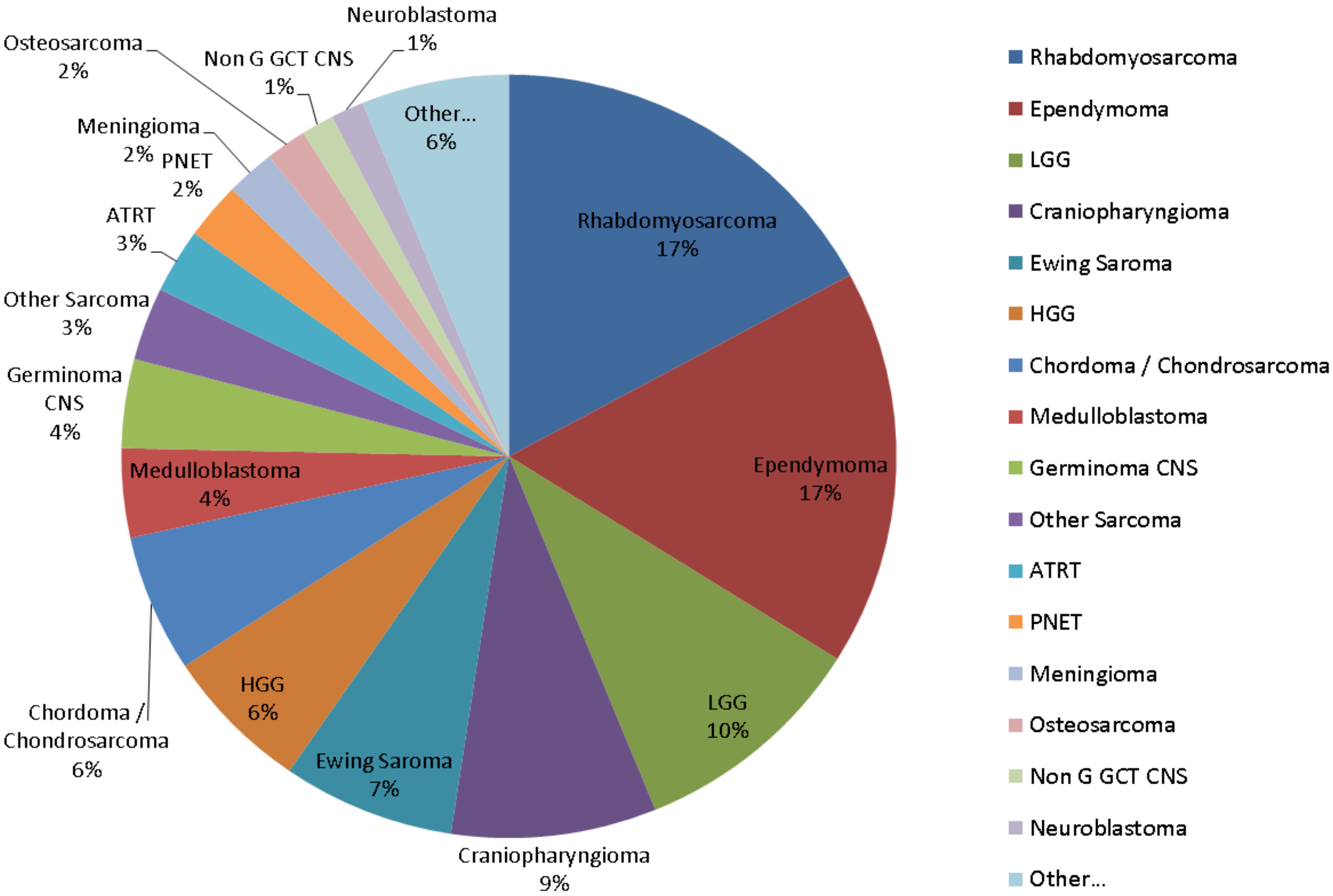
Fig. 1. Number of queried European centers per country.



Number of patients treated per center in the world



Proton Therapy for Children in Europe in 2014 : 297 cases



CNS: 57%

C.Alapetite et al, 2016

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Children treated with Proton beams in Europe - Until

Centre	Number Pats end 2014	1st child	Total nb children [end 2014]	Chidren treated in 2014	% children In 2014	% with General Anesthesia	% from abroad
CPO Orsay	7004	1994	450	65	32%	37%	12%
PSI Villigen	7364	1996	370	45	41%	55%	55%
HIT Heidelberg *protons* *C-ion*	824 1723	2010	275 *44*	73 *13*	(from start) 33% *2.5%*	*24%*	- -
WPE Essen	139	2013	85	63	59%	52%	41%
PTC Prague	357	2013	65	31	13%	29%	45%
TSL Uppsala	1431	1997	95	10	19%	30%	10%
RPTC Munich	2307	2009?	-	10	-	20%	70%
CNAO Pavia *protons* *C-ion*	111 318	- -	- -	- -	-		- -
Total	21578		1384	297	13-59%	38%	10-70%

Claire Alapetite et al, PTCOG 2016

Inter-comparison of dose reporting, delivery techniques, patient throughput and staffing levels (2015).

Particle beam Center#	Dose reporting	Treatment of eye tumors	PBS delivery[b]	Total number of patients per center	Annual number of patients	# of FTE ROs per center	Ratio # patients per FTE (RO)	# of FTE MedPh. per center	Ratio # patients per FTE (MedPh.)	# of FTE RTTs per center	Ratio # patients per FTE (RTT)	# of FTE Nurses per center
1	GyRBE	Yes	Yes	6048	330	3.2	*103.1*	5.5	*60*	11	*30.0*	1
2	cGy	Yes[a]	No	2800	185	0.3	*616.7*	2.5	*74*	1.4	*132.1*	0
3	CGE	Yes	No	7416	557	2.1	*265.2*	5	*111.4*	11.5	*48.4*	0.5
4	CGE	Yes	Yes	300	108	6	*18.0*	4.5	*24*	16	*6.8*	3
5	CGE	No	Yes	2548	494	4	*123.5*	5	*98.8*	6	*82.3*	6.5
6	Gy	No	Yes	55	40	2.5	*16.0*	6	*6.7*	3	*13.3*	0
7	CGE	Yes[a]	No	2600	210	2	*105.0*	3	*70*	2	*105.0*	0
8	GyE	No	Yes	1075	350	62	*5.6*	12	*29.2*	22	*15.9*	4
9	GyE	No	Yes	85	72	5	*14.4*	6	*12*	6	*12.0*	3
10	GyRBE	No	Yes	65	100	1	*100.0*	4.75	*21.1*	7.25	*13.8*	0.45
11	GyE	No	Yes	145	52	6	*10.5*	6	*8.7*	16	*3.3*	4
12	Gy	Yes[a]	Yes	700	400	6	*66.7*	6	*66.7*	10	*40.0*	4
13	Gy	No	No	5301	270	2	*132.0*	3	*90*	3	*90.0*	1
14	Gy	Yes[a]	Yes	135	45	1	*45.0*	6	*7.5*	4	*11.3*	0
15	Gy	Yes	No	1483	95	1	*95.0*	1.5	*63.3*	3	*31.7*	0
Mean			66.7%	2050.4 (total, 30,756)	220.5	6.9	*114.4*	5.1	*49.6*	8.1	*42.4*	1.8

RBE = radio-biological equivalent, FTE = full time equivalent, RO = ra ion oncologist, MedPhy = medical physicist, RTT = radiation t py tech gist, PBS = Pencil beam delivery.

[a] Center treating eye tumor only.

[b] PBS delivery and raster scanning.

The number of patients treated per radiation therapy technologist's (RTT) FTE was significantly (P = 0.009) higher for eye tumor centers only (mean, 72.1) when compared to noneye tumor only centers (mean, 31.6)

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Indications for non-pediatric patients treated with particle therapy at European centers.

Indications	Number of center ($n = 11$[a])	% of centers treating this indication
Chordoma/chondrosarcoma	11	100
Sarcoma	11	100
Meningioma	11	100
Brain tumors (non meningioma)	11	100
Head and Neck cancers	8	73
Prostate cancer	7	64
Uveal melanoma	6[b]	40[b]
Breast cancer	2	18
Other[c]	4	36

[a] Non-eye tumor only center.

[b] Eye tumor only center and non-eye tumor only center ($n = 15$).

[c] Liver/pancreas/rectum/lymphoma/lung.

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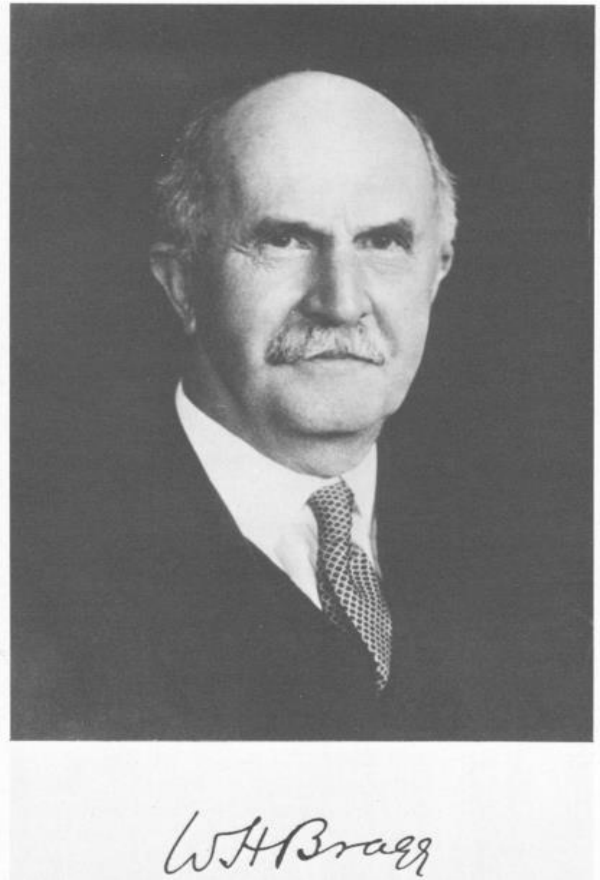
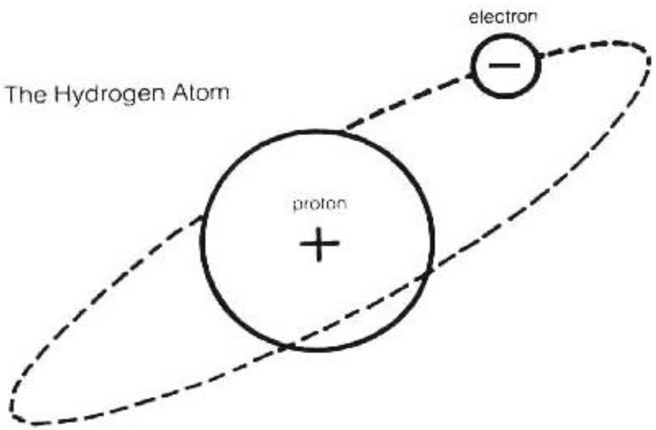
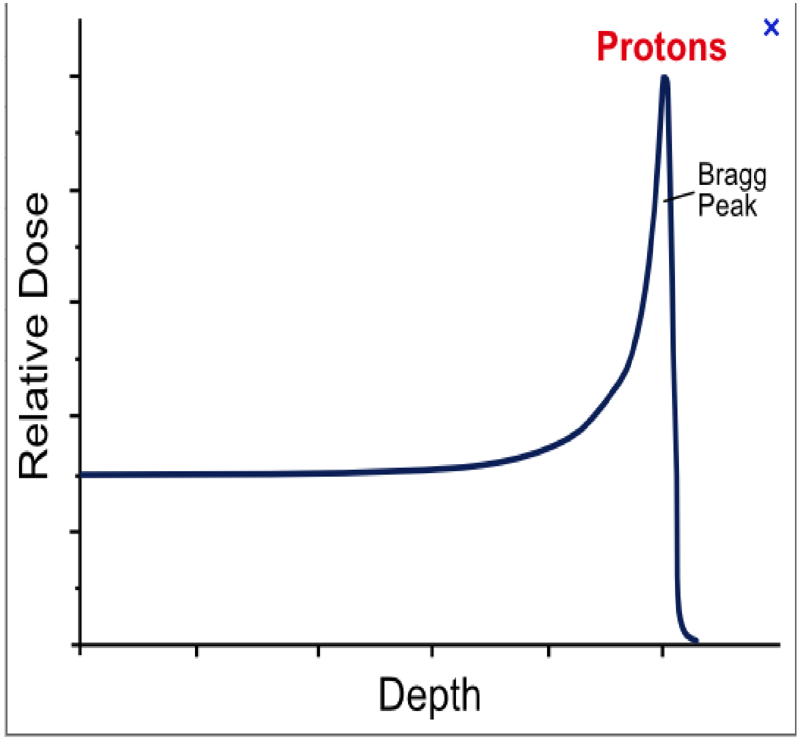
BRAGG PEAK


W.H. Bragg

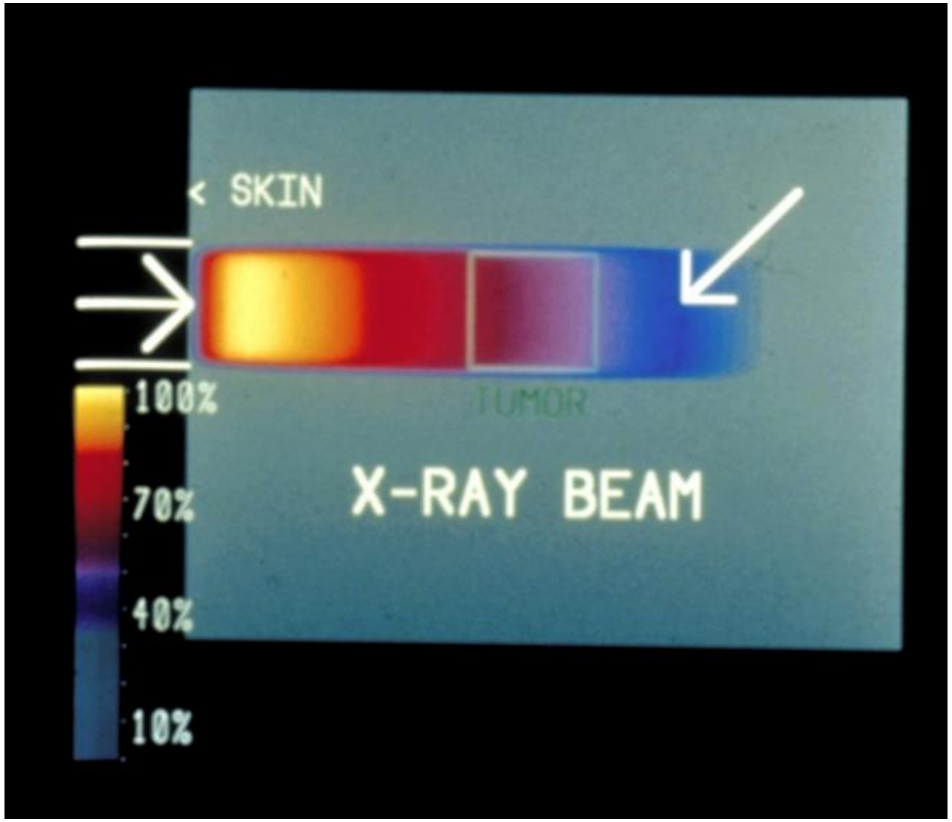

The Hydrogen Atom
electron
proton
+
−


Protons
Bragg
Peak
Relative Dose
Depth

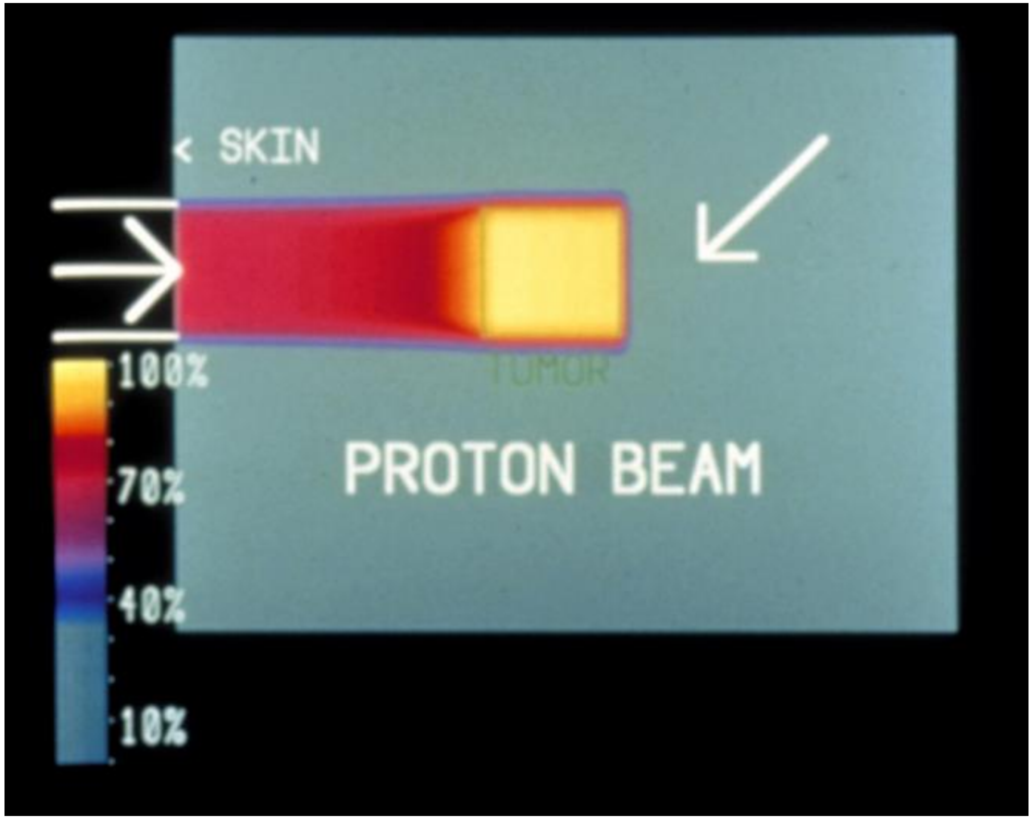
How precise is proton therapy?

- Photons:

- Protons:



< SKIN
100%
70%
40%
10%
TUMOR
X-RAY BEAM



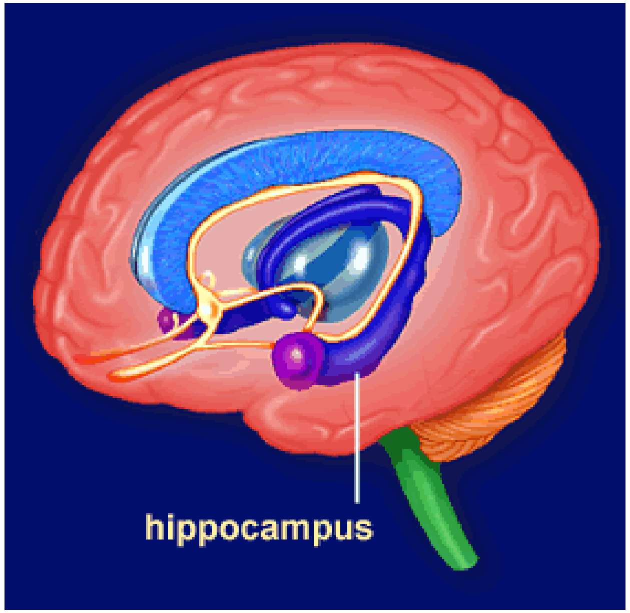
< SKIN
100%
70%
40%
10%
TUMOR
PROTON BEAM


2460
2460
2575
2460
2460
2460
2575
2460
2575
2460
2460
2460
2460
2460
2460
2225
2460
2000
2460
2460

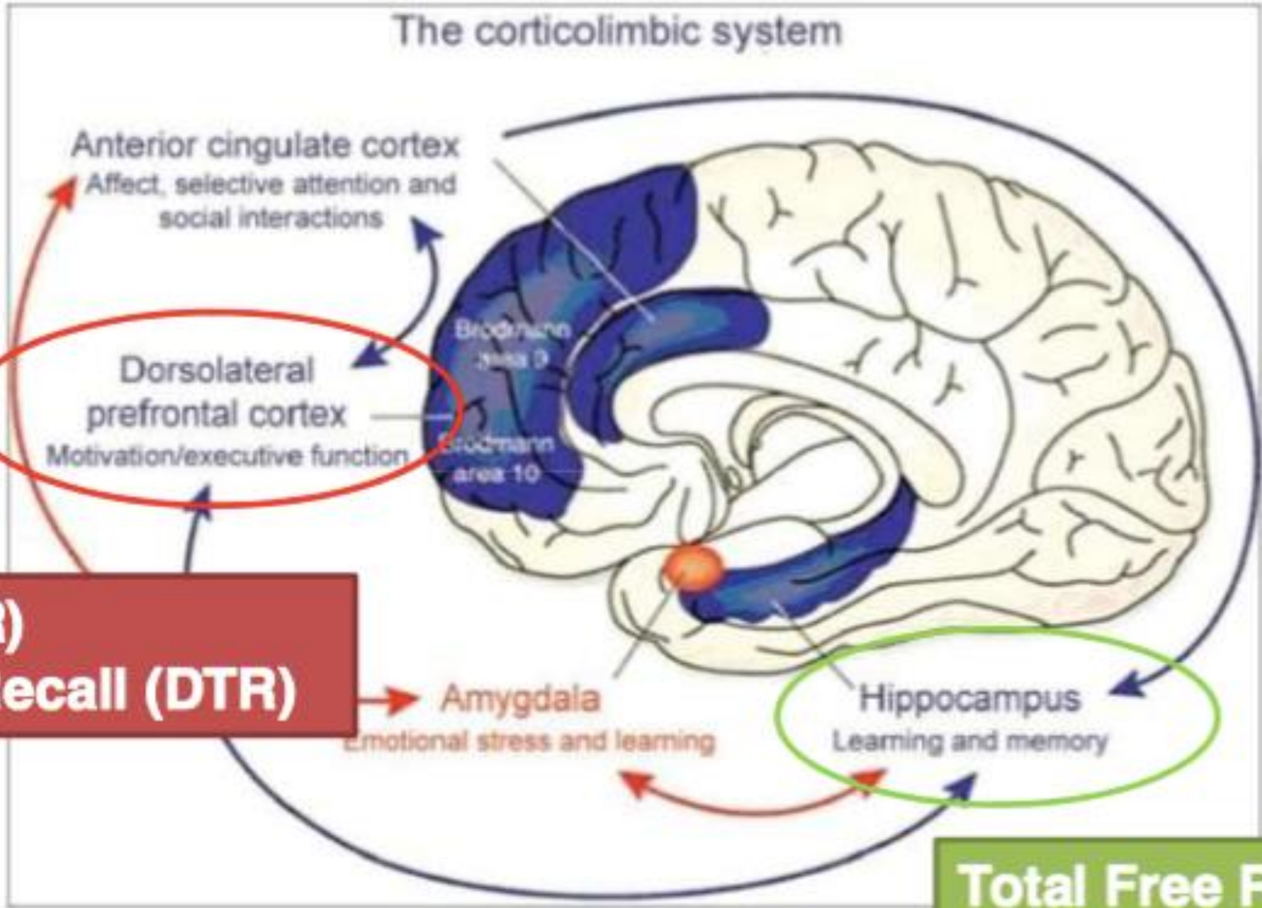
PTC

Association between hippocampal dosimetry and impairment in Wechsler Memory Scale-III Word Lists Delayed Recall at 18 months

Dosimetry	Dosimetric cut point	No impairment	Impairment*	*p* value
Bilateral hippocampi				
Maximum	≤24.7 Gy	66.7%	33.3%	0.500
	>24.7 Gy	55.6%	44.4%	
D30%	≤8.2 Gy	77.8%	22.2%	0.167
	>8.2 Gy	44.4%	55.6%	
D40%	≤7.3 Gy	88.9%	11.1%	0.025
	>7.3 Gy	33.3%	66.7%	
D50%	≤3.8 Gy	66.7%	33.3%	0.500
	>3.8 Gy	55.6%	44.4%	
D80%	≤0.5 Gy	55.6%	44.4%	0.500
	>0.5 Gy	66.7%	33.3%	
D100%	≤0.0 Gy	76.9%	23.1%	0.047
	>0.0 Gy	20.0%	80.0%	
Left hippocampus				
Maximum	≤15.0 Gy	55.6%	44.4%	0.500
	>15.0 Gy	66.7%	33.3%	



Int J Radiat Oncol Biol Phys. 2012 Jul 15;83(4):e487-93.



Total Recall (TR)
Delayed Total Recall (DTR)

Total Free Recall (TFR)
Delayed Free Recall (DFR)

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SPANISH LUNG GROUP 2017

	FIRST TIME	TOTAL FREE RECALL (TFR)	FREE RECALL (TR)	DELAYED FREE RECALL (DFR)	DELAYED T. RECALL (DTR)
BASAL-3					
PCI	2 (6,7%)	4 (13,3%)	7 (23,3%)	8 (26,7%)	8 (26,7%)
Hippocampal sparing	4 (13,3%)	2 (6,7%)	3 (10%)	1 (3,3%)	5 (16,7%)
	NS	NS	NS	**0,01** **RR 8 [1,06- 60,08]**	NS
BASAL-6					
PCI	11 (40,7%)	9 (33,3%)	14 (51,9%)	13 (48,1%)	14 (51,9%)
Hippocampal sparing	3 (14,3%)	1(4,8%)	3 (14,3%)	1 (4,8%)	5 (23,8%)
	0,06 RR 2,8 [0,9- 8,9]	**0,01** **RR 7 [0,9- 50,9]**	**0,01** **RR 3,6 [1,19- 11,0]**	**0,001** **RR 10 [1,4- 71,23]**	0,07 RR 2,1 [0,9- 5,08]

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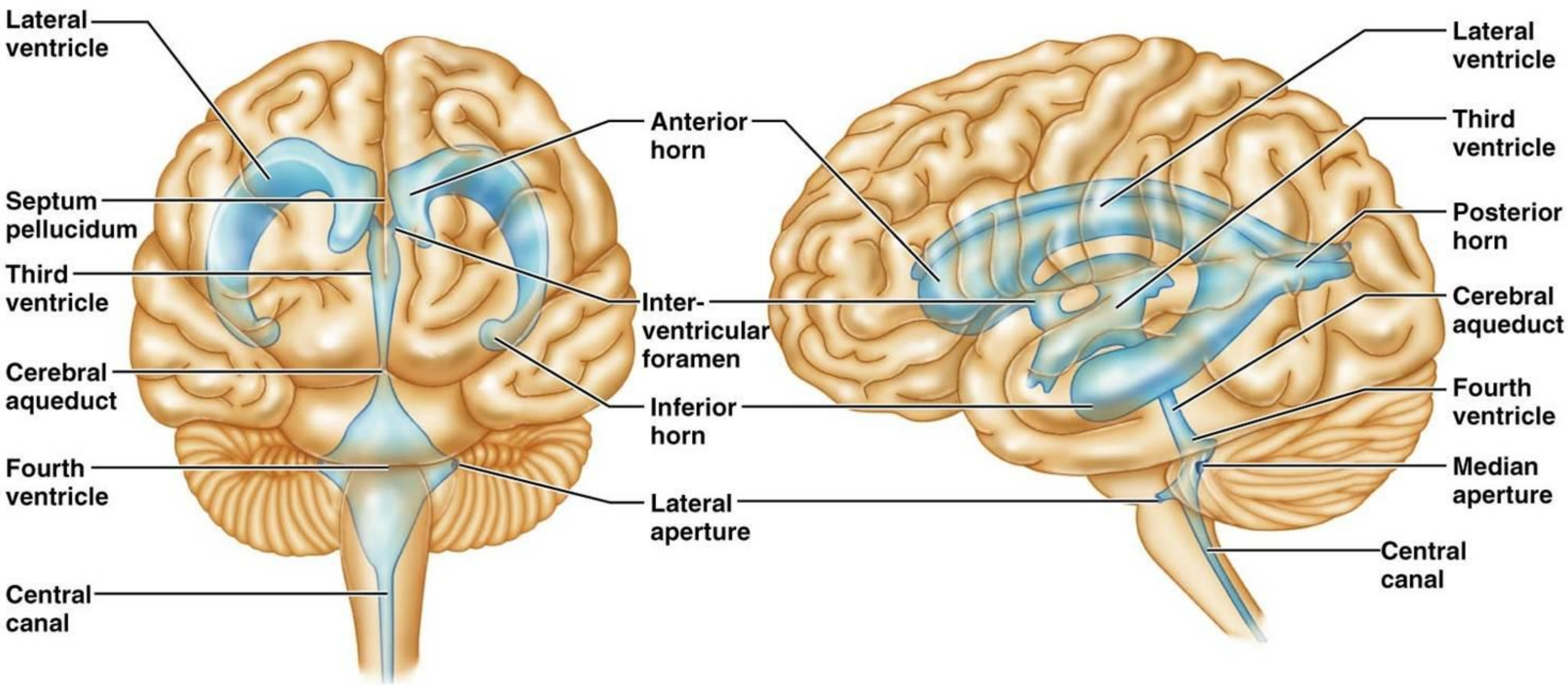
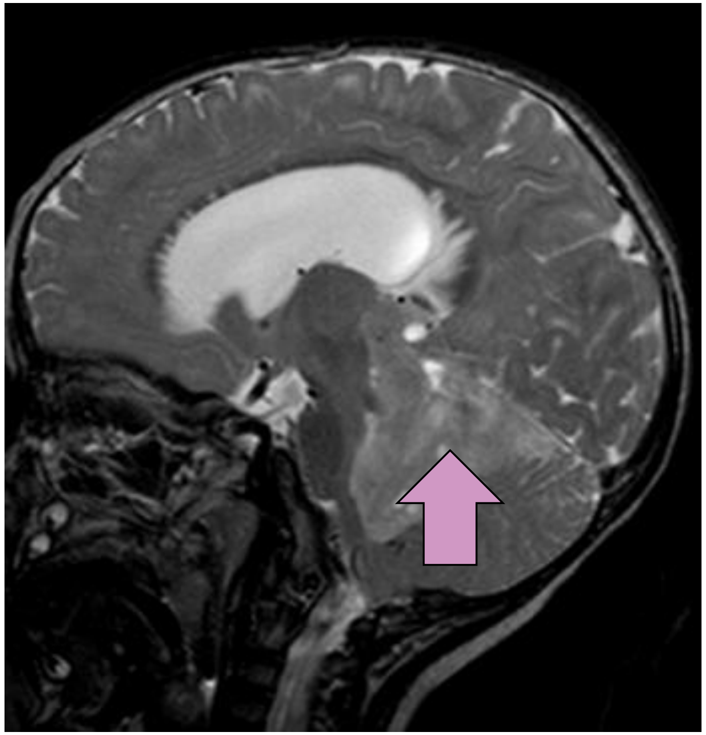
Case 1: patient with teratoid rhabdoid tumor

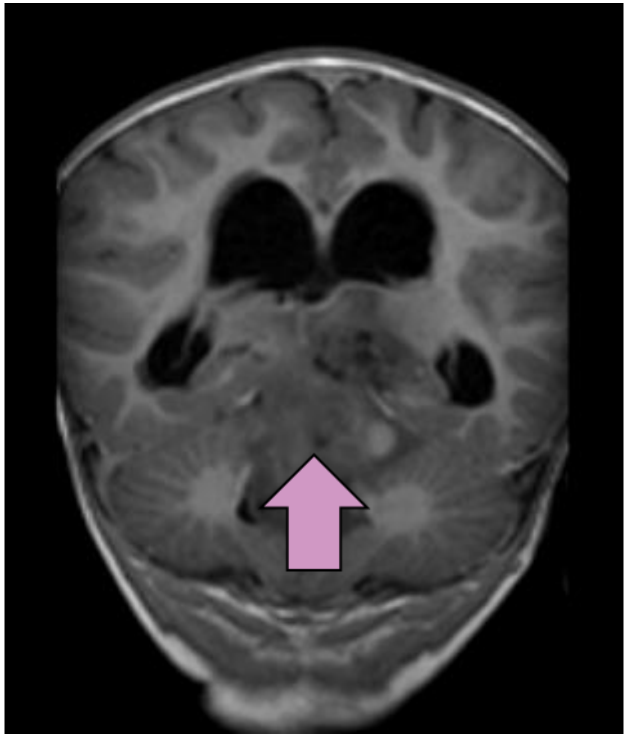
- A 19-month-old female infant was referred because of headache and weakness
- Magnetic resonance imaging revealed a mass that occupied the fourth ventricle

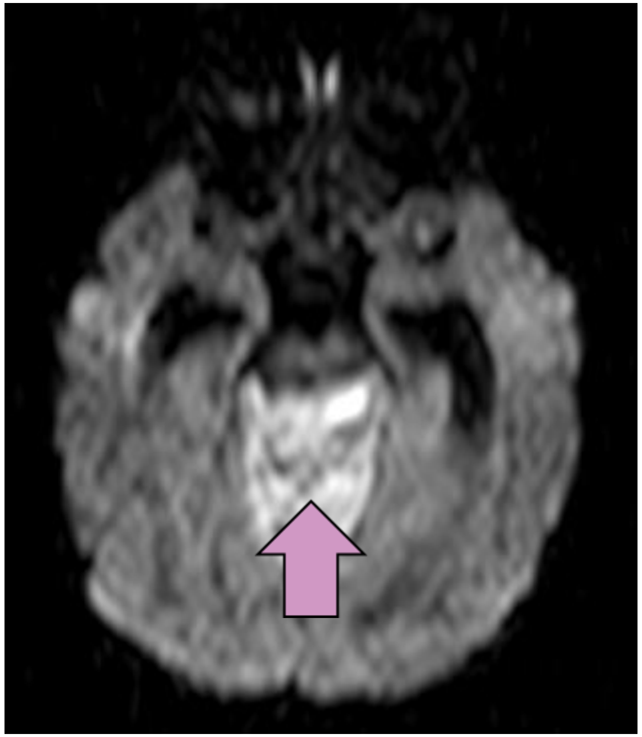


(a) Anterior view **(b) Left lateral view**

Mass at the fourth ventricle







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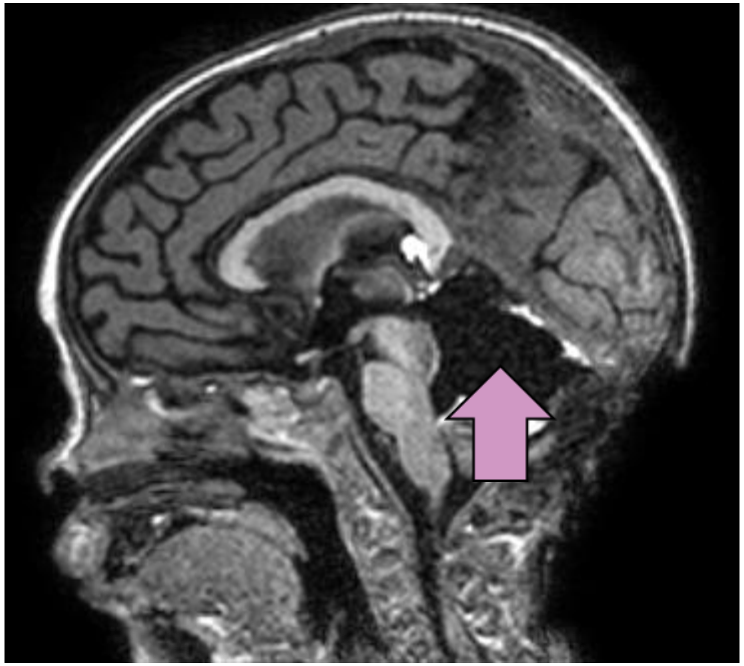
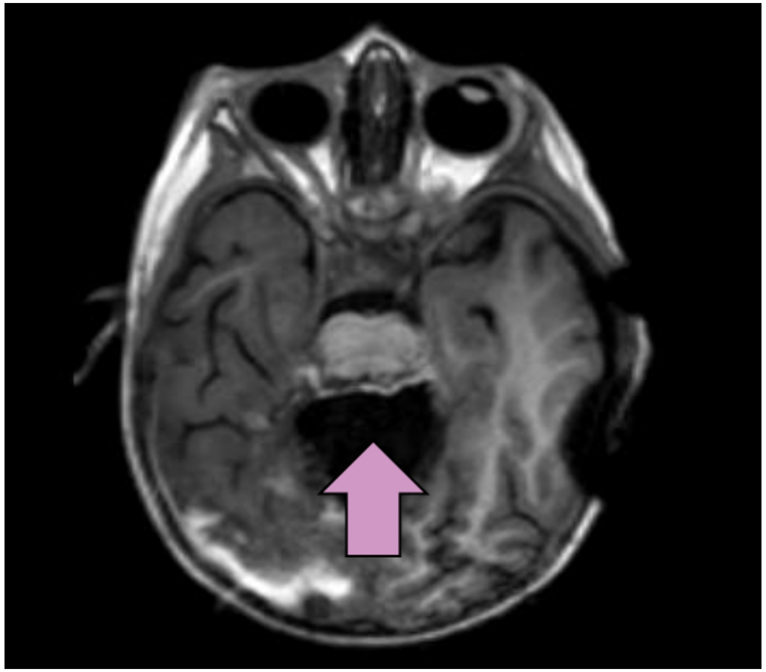
- The child underwent total removal of the tumor mass





- Pathological findings showed an **atypical teratoid/rhabdoid tumor**

- Diagnosis

- Atypical teratoid/rhabdoid tumor

- Treatment

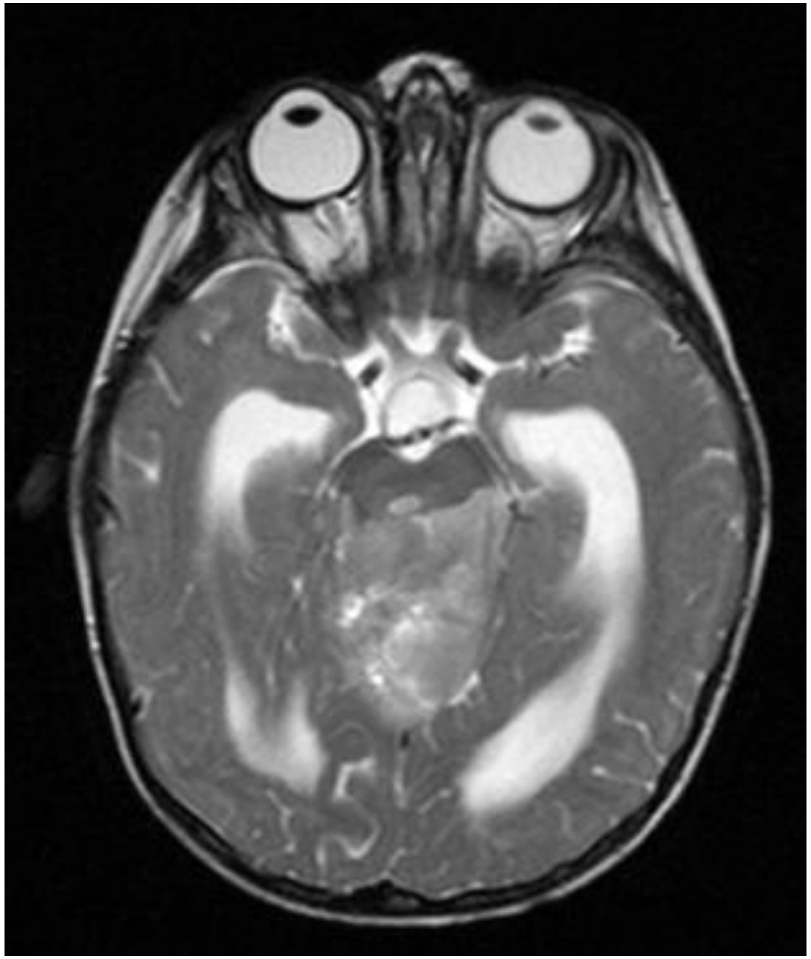
- Chemotherapy + Surgery + Radiation Therapy

- Radiation Therapy Dose Prescription:

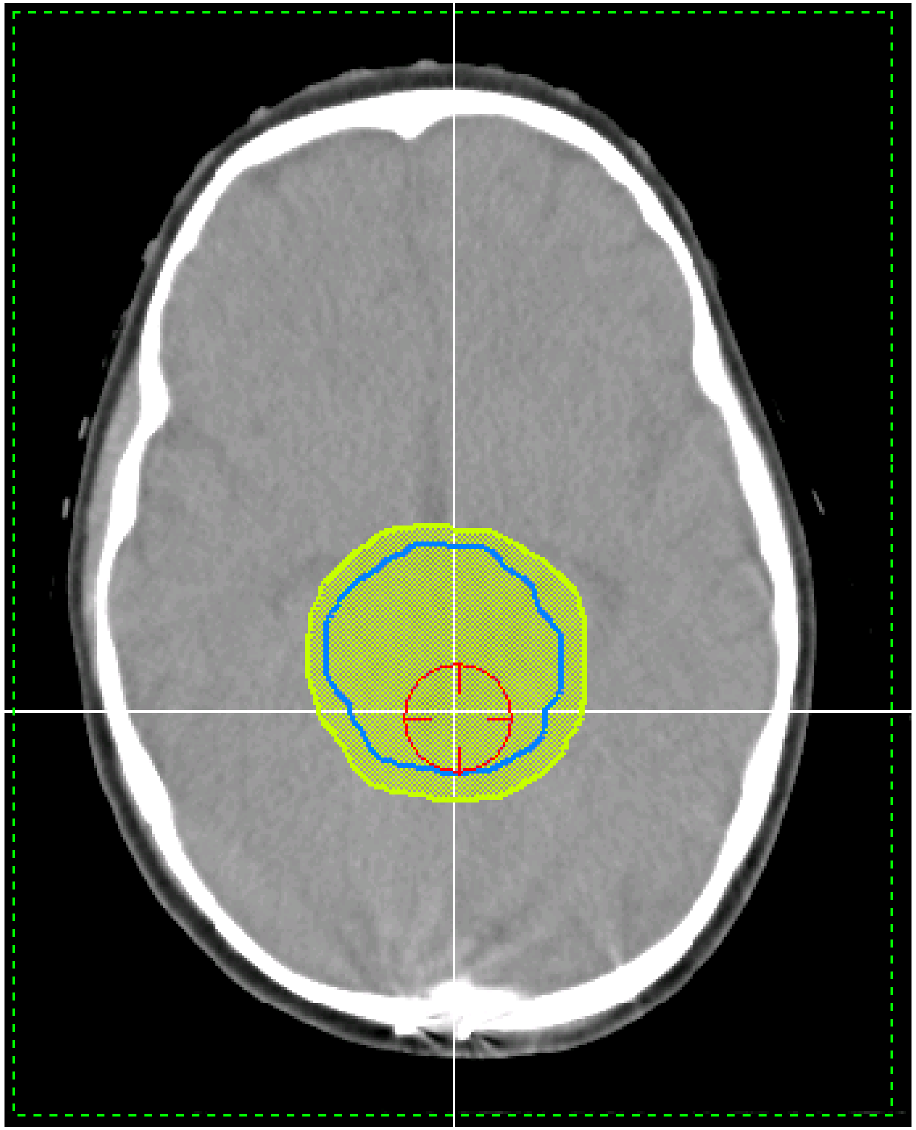
- PTV (surgical bed + 5mm margin): 54 Gy at 2 Gy/fraction

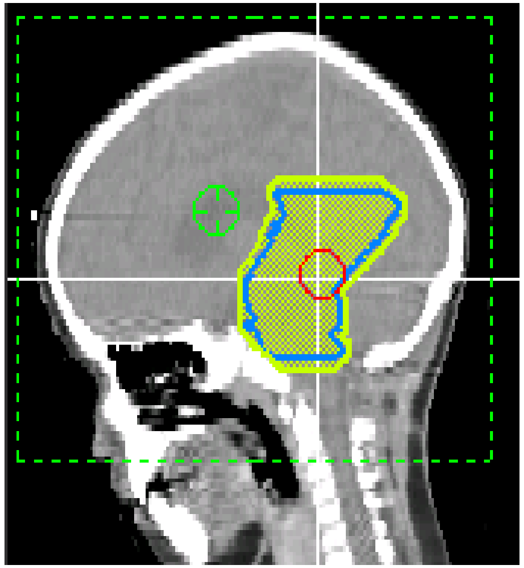
- **Organ at risk**

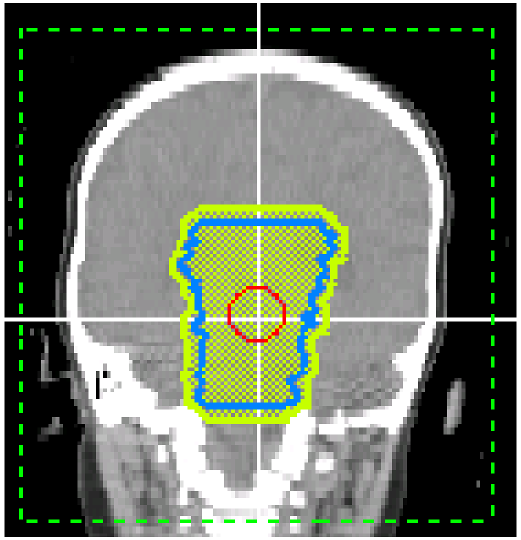
  Whole brain
  Braim stem
  Chiasm
  Pituitary
  Eyes
  Crystalline lens
  Nerve optic



PTV (surgical bed + 5 mm margin)







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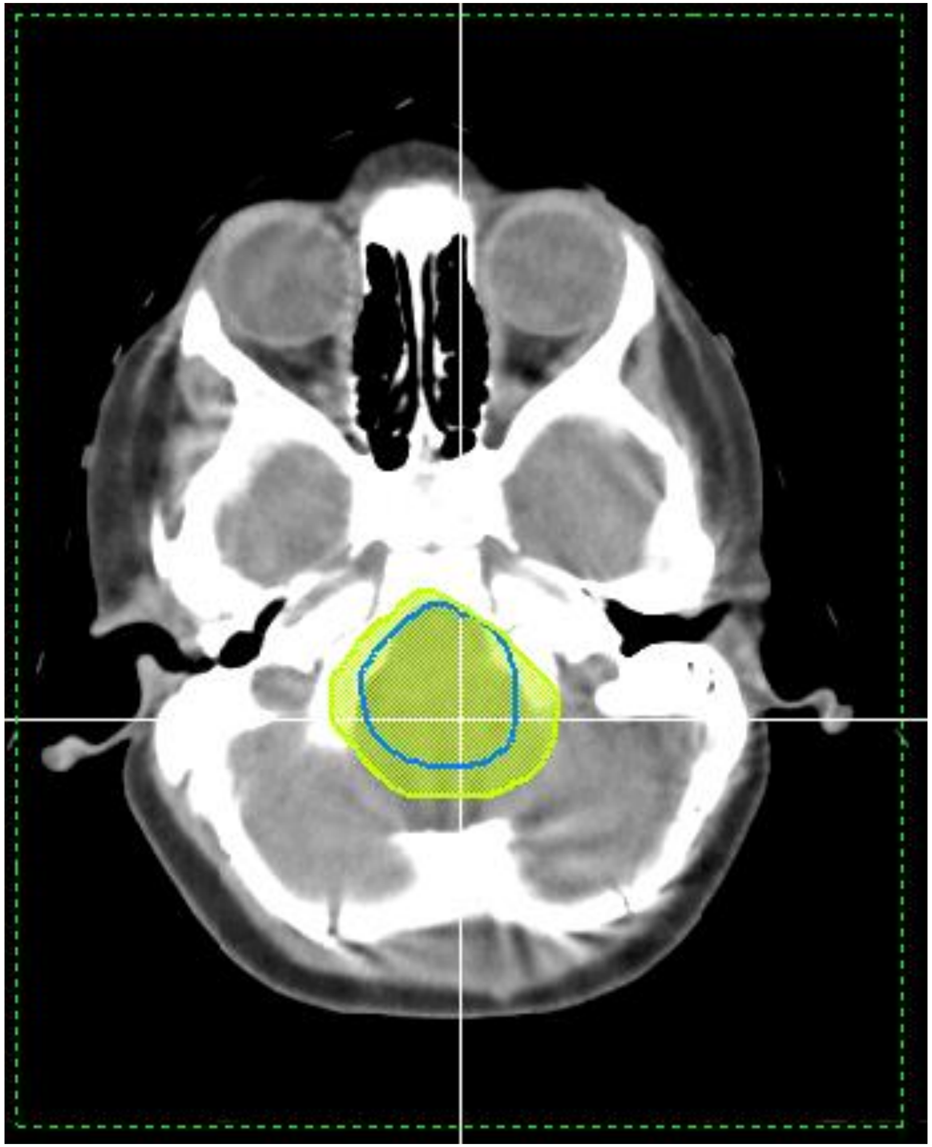
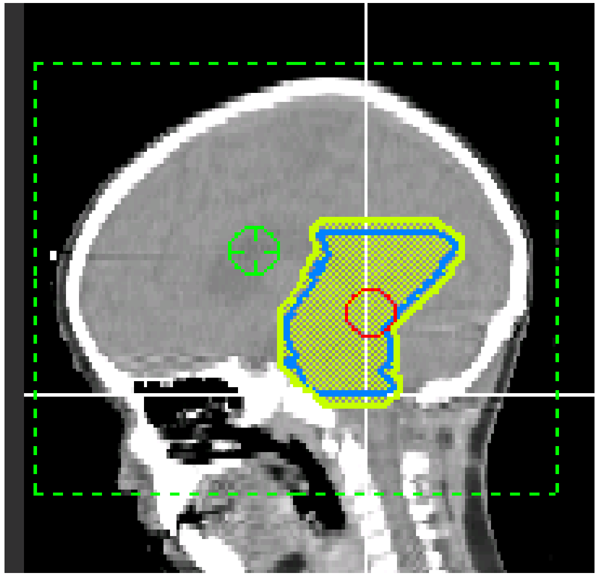
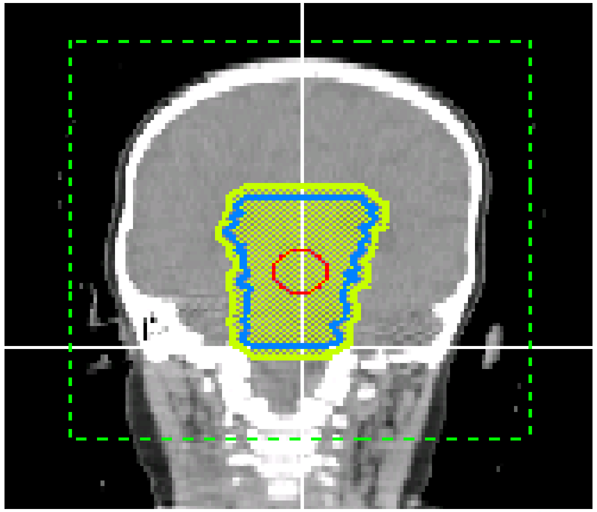
PTV(yellow)







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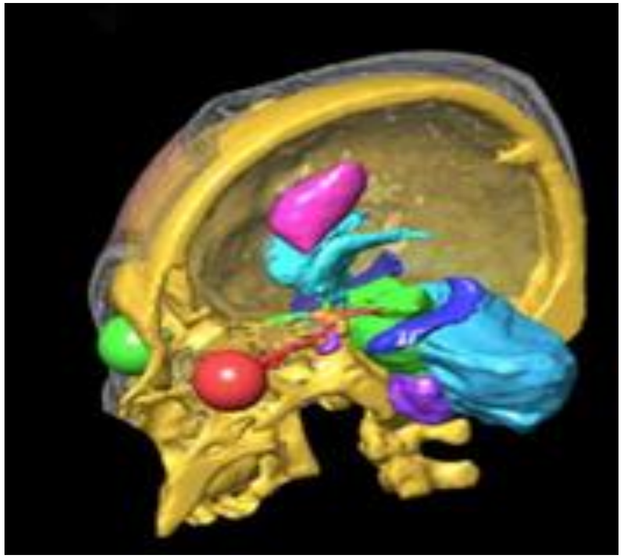
Take home message

- Inmovilization is crucial to reduce toxicity
- The addition of MRI gives vastly superior soft-tissue visualization
- The radiation technique (IMRT, Tomotherapy, Protons, Cyberknyfe) should be individualised for each patient



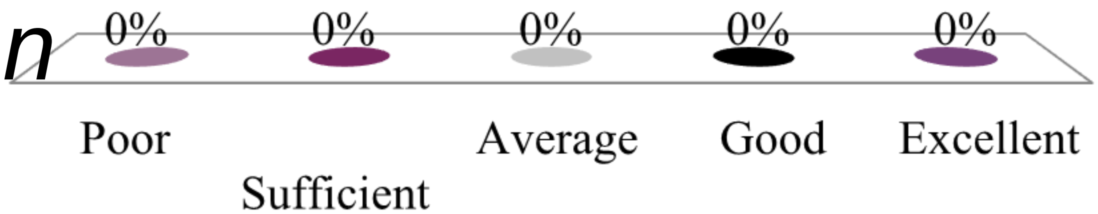
Questions:

- Preparation (thermoplastic mask)
- Positioning
- Organ at risk contouring
- Set-Up
- Verification
- Radiation technique

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



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Case reports: **Brain**

a physicist's perspective

Mirjana Josipovic

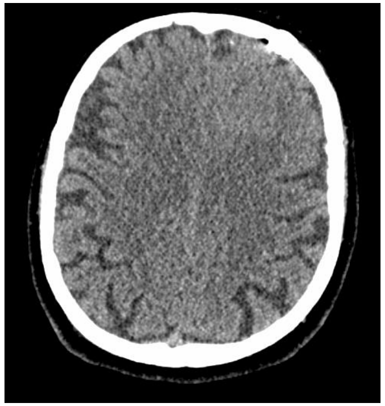
Dept. of Oncology, Rigshospitalet
& Niels Bohr Institute, University of Copenhagen
Denmark

Advanced skills in modern radiotherapy
May 2018

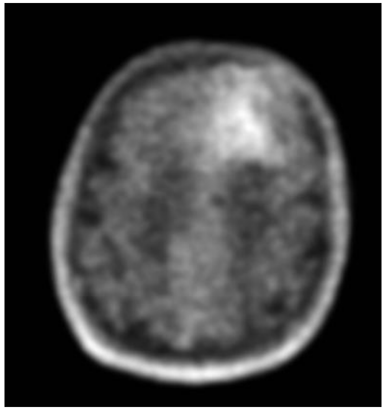
Imaging for brain RT planning

Imaging immobilised patient in the treatment position

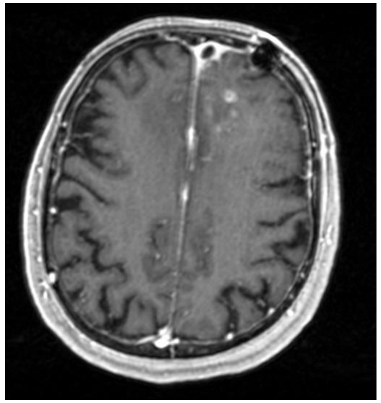
CT scan

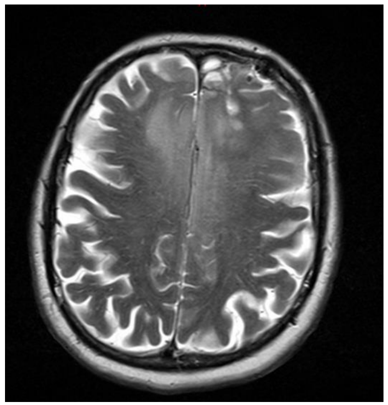


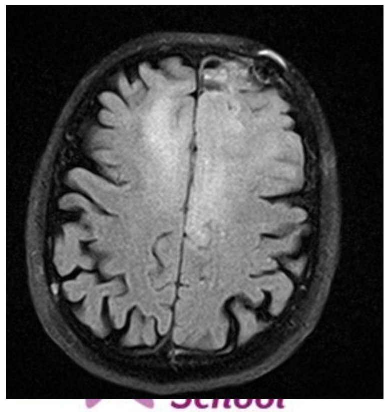
FET PET scan



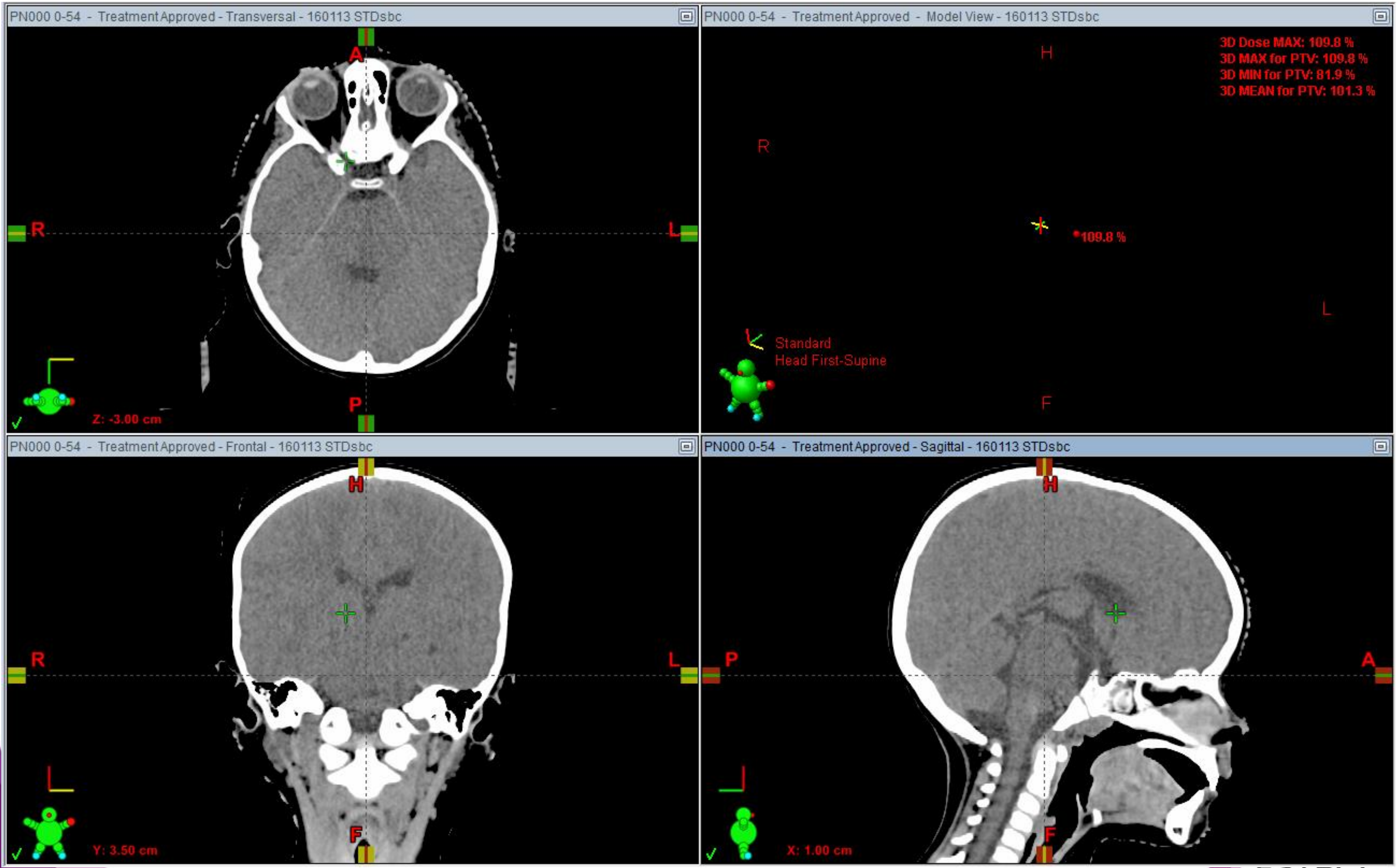
MR scan (T1,T2,FLAIR)

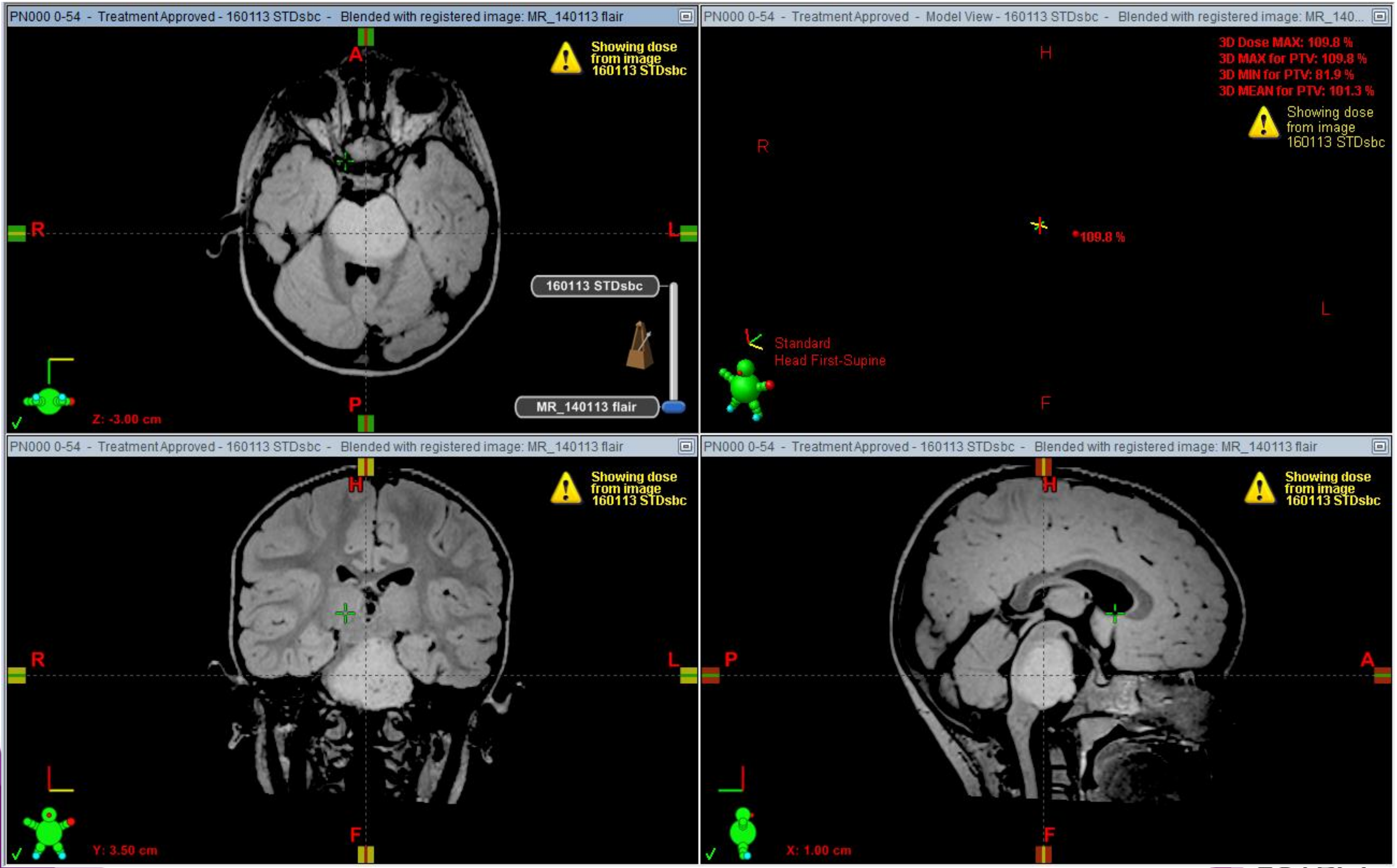


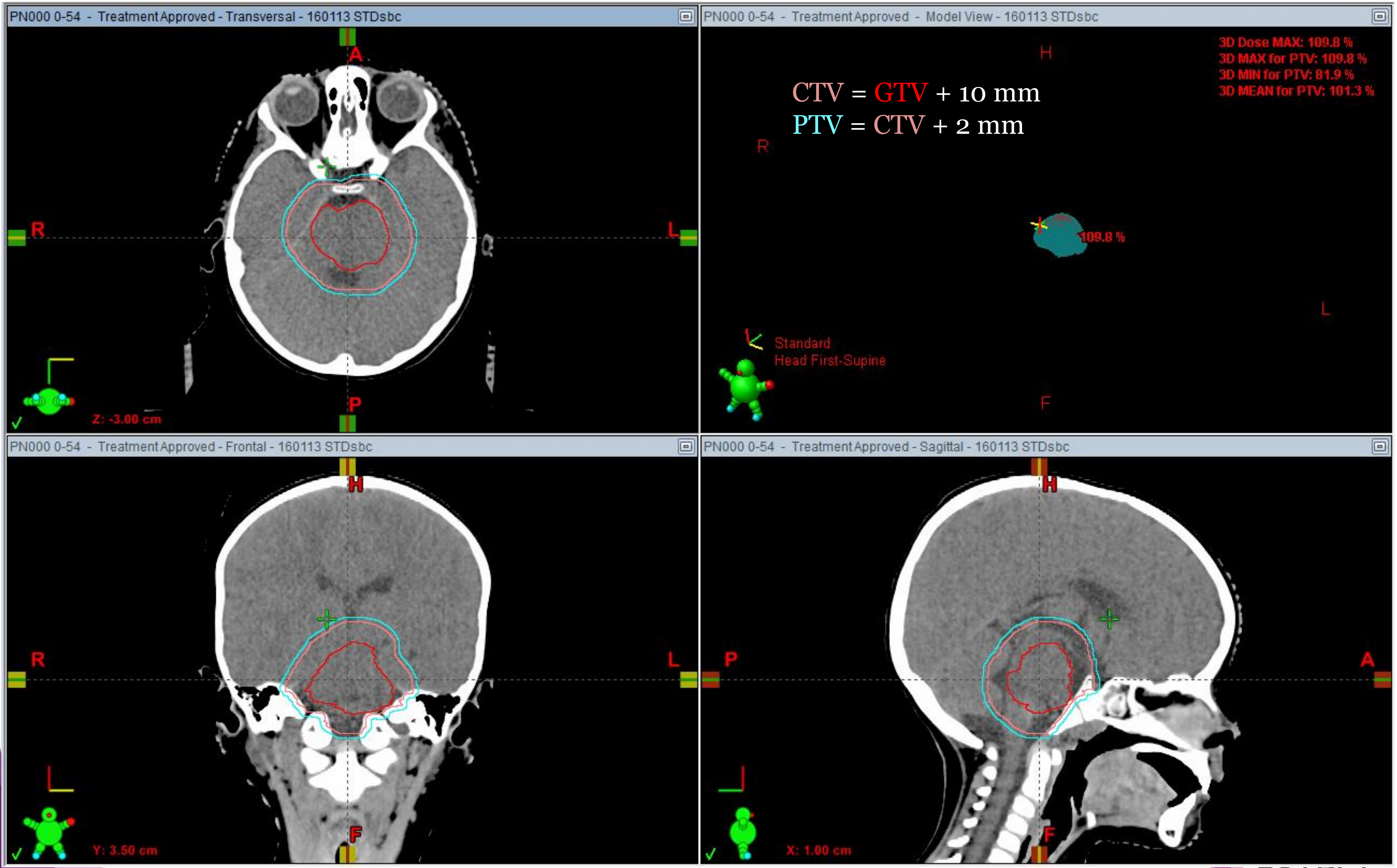




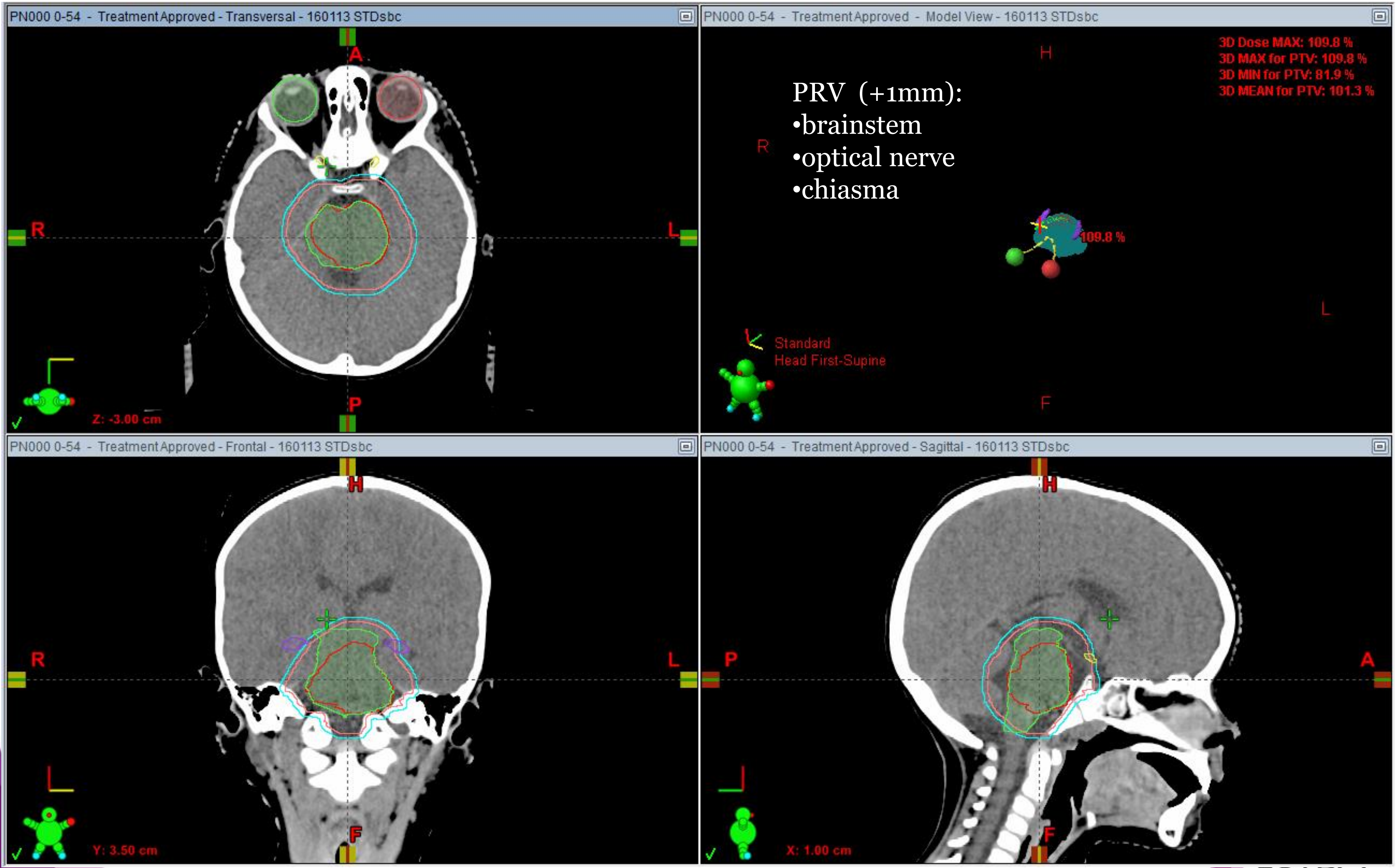
Thin scan slices ~1 mm


PN000 0-54 - Treatment Approved - Transversal - 160113 STDsbc
A
R
L
P
Z: -3.00 cm
PN000 0-54 - Treatment Approved - Model View - 160113 STDsbc
H
3D Dose MAX: 109.8 %
3D MAX for PTV: 109.8 %
3D MIN for PTV: 81.9 %
3D MEAN for PTV: 101.3 %
R
109.8 %
L
Standard
Head First-Supine
F
PN000 0-54 - Treatment Approved - Frontal - 160113 STDsbc
H
R
L
F
Y: 3.50 cm
PN000 0-54 - Treatment Approved - Sagittal - 160113 STDsbc
H
P
A
F
X: 1.00 cm


PN000 0-54 - Treatment Approved - 160113 STDsbc - Blended with registered image: MR_140113 flair
Showing dose from image 160113 STDsbc
A
R
L
P
160113 STDsbc
MR_140113 flair
Z: -3.00 cm
PN000 0-54 - Treatment Approved - Model View - 160113 STDsbc - Blended with registered image: MR_140...
3D Dose MAX: 109.8 %
3D MAX for PTV: 109.8 %
3D MIN for PTV: 81.9 %
3D MEAN for PTV: 101.3 %
Showing dose from image 160113 STDsbc
H
R
109.8 %
L
Standard
Head First-Supine
F
PN000 0-54 - Treatment Approved - 160113 STDsbc - Blended with registered image: MR_140113 flair
Showing dose from image 160113 STDsbc
H
R
L
F
Y: 3.50 cm
PN000 0-54 - Treatment Approved - 160113 STDsbc - Blended with registered image: MR_140113 flair
Showing dose from image 160113 STDsbc
H
P
A
F
X: 1.00 cm

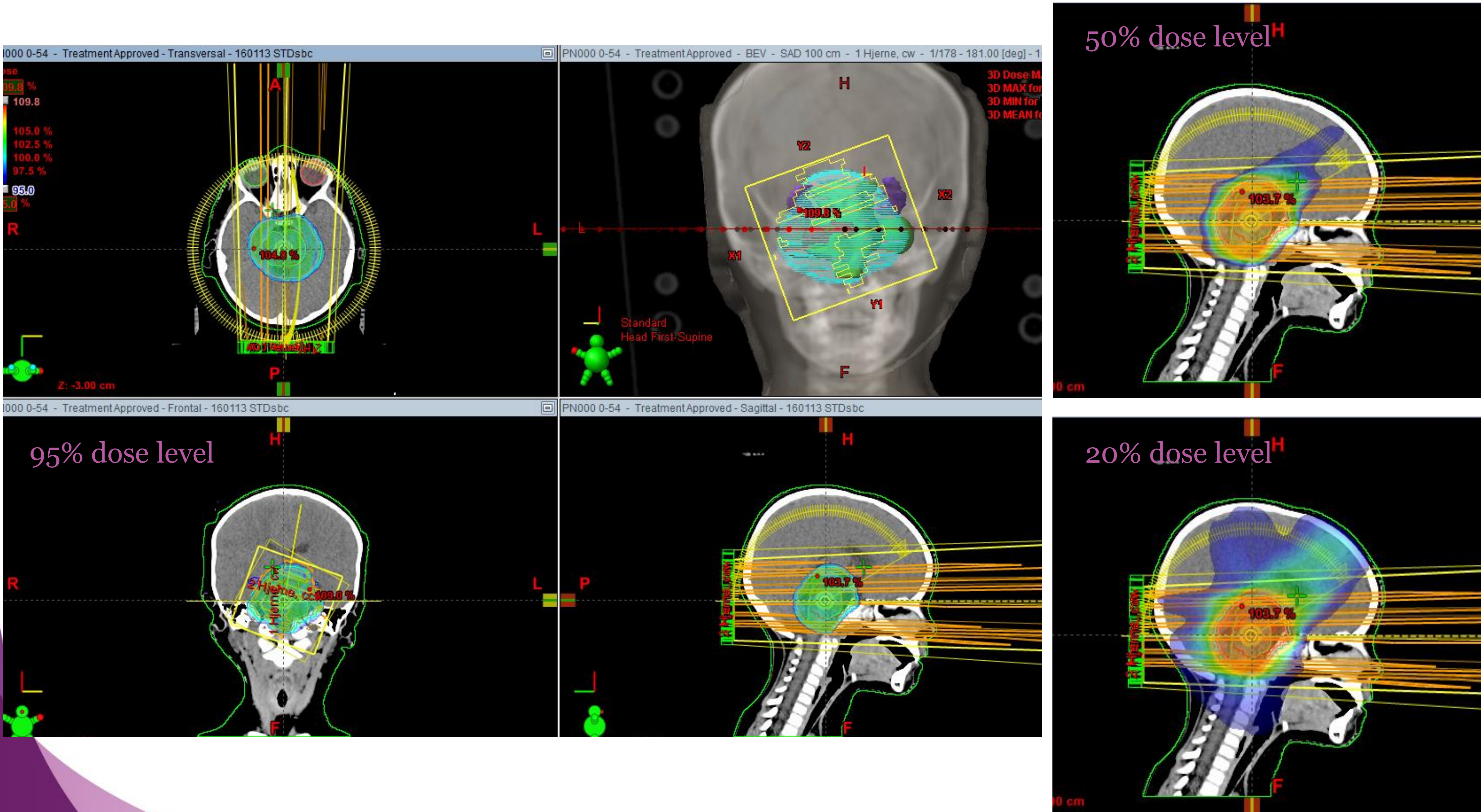


PN000 0-54 - Treatment Approved - Transversal - 160113 STDsbc
A
R
L
P
Z: -3.00 cm
PN000 0-54 - Treatment Approved - Model View - 160113 STDsbc
CTV = GTV + 10 mm
PTV = CTV + 2 mm
3D Dose MAX: 109.8 %
3D MAX for PTV: 109.8 %
3D MIN for PTV: 81.9 %
3D MEAN for PTV: 101.3 %
H
R
109.8 %
L
Standard
Head First-Supine
F
PN000 0-54 - Treatment Approved - Frontal - 160113 STDsbc
H
R
L
F
Y: 3.50 cm
PN000 0-54 - Treatment Approved - Sagittal - 160113 STDsbc
H
P
A
F
X: 1.00 cm



PRV (+1mm):
- brainstem
- optical nerve
- chiasma

VMAT plan – 2 arcs



Radiotherapy

Radiotherapy techniques

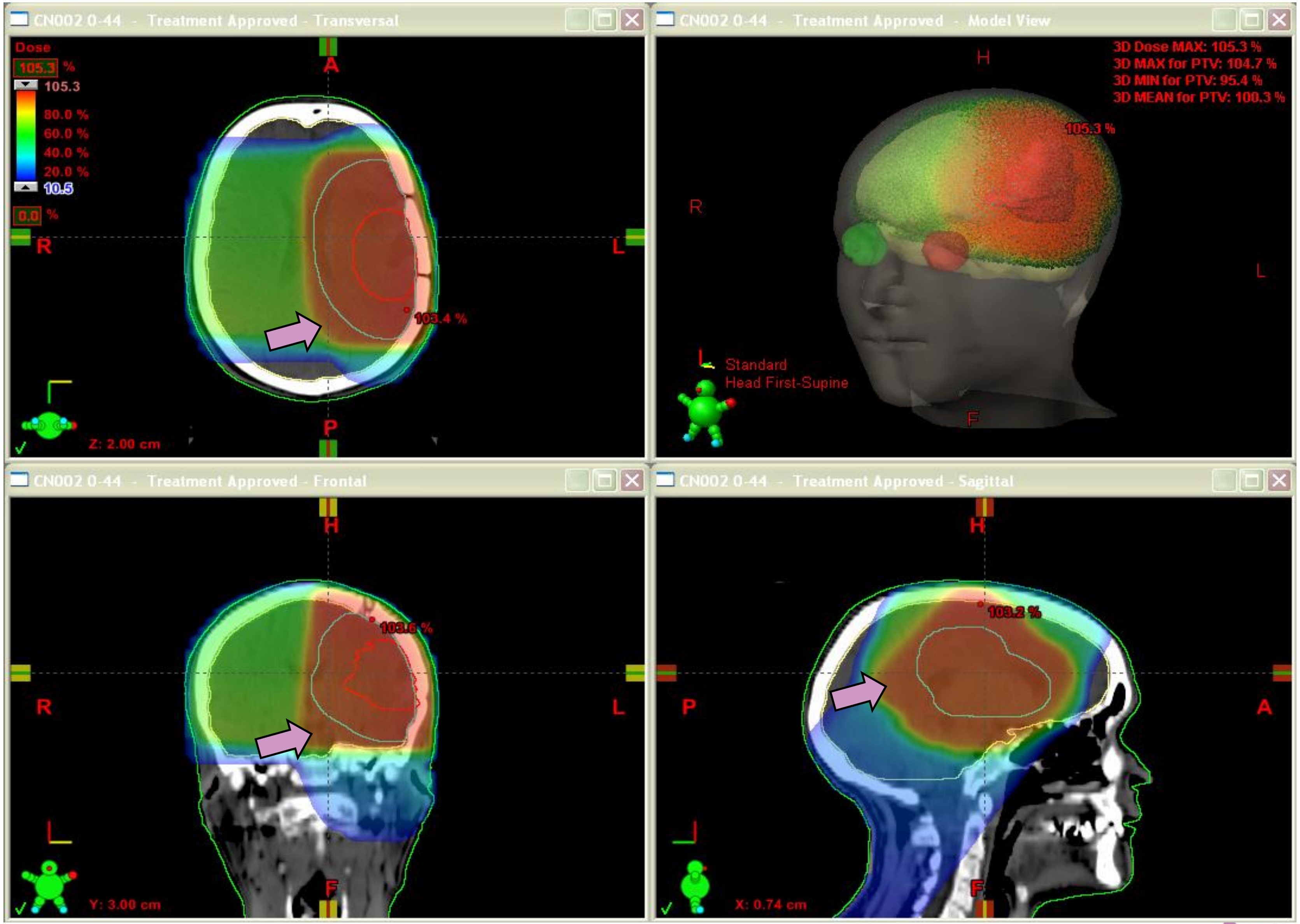
- 3DC
- IMRT
- VMAT
- Proton therapy

Fractionation schemes (Rigshospitalet, CPH)

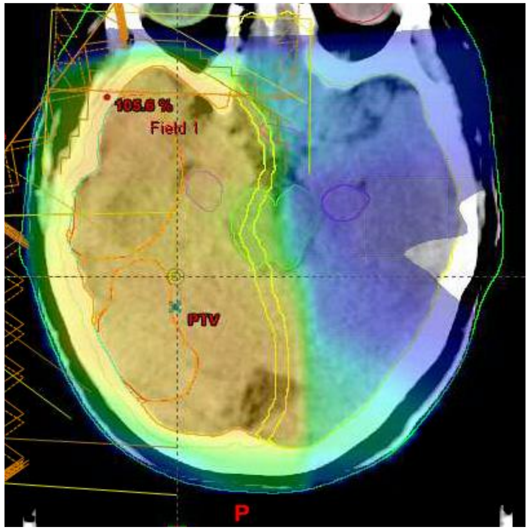
- 2 Gy x 30
- 1.8 Gy x 30 (if brainstem is involved)

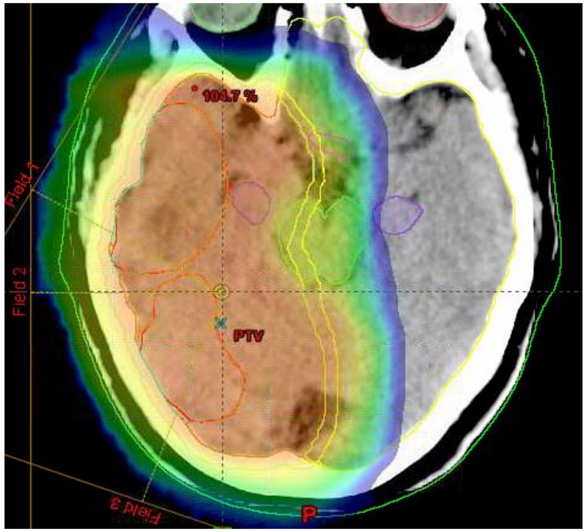
- 18 Gy x 1 (very small targets, stereotactic RT)
  - Prescribed as minimum dose to target

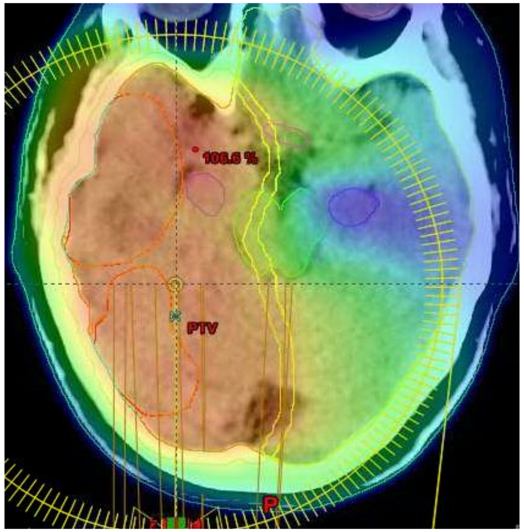
3DC plan

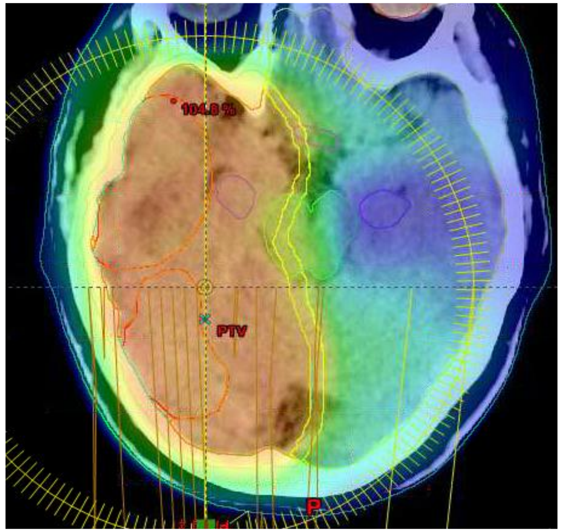

CN002 0-44 - Treatment Approved - Transversal
Dose
105.3 %
105.3
80.0 %
60.0 %
40.0 %
20.0 %
10.5
0.0 %
A
R
L
P
103.4 %
Z: 2.00 cm
CN002 0-44 - Treatment Approved - Model View
3D Dose MAX: 105.3 %
3D MAX for PTV: 104.7 %
3D MIN for PTV: 95.4 %
3D MEAN for PTV: 100.3 %
H
R
L
F
105.3 %
Standard
Head First-Supine
CN002 0-44 - Treatment Approved - Frontal
H
R
L
F
103.6 %
Y: 3.00 cm
CN002 0-44 - Treatment Approved - Sagittal
H
P
A
F
103.2 %
X: 0.74 cm

IMRT vs. protons vs. VMAT









IMRT

IMPT
protons

VMAT (co-planar)

VMAT (non co-planar)

worst plan conformity

best plan conformity

Courtesy of P Munck af Rosenschöld

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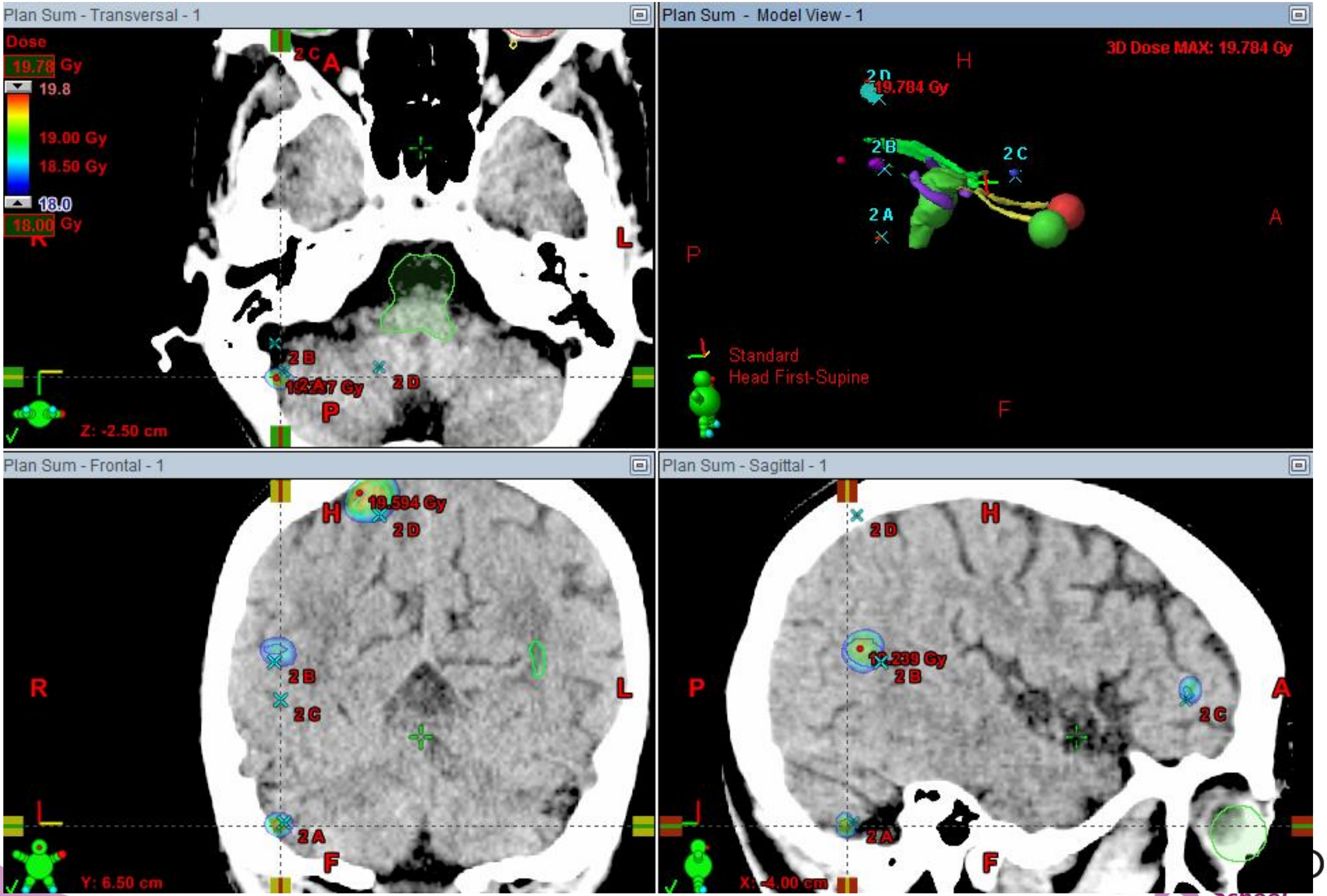
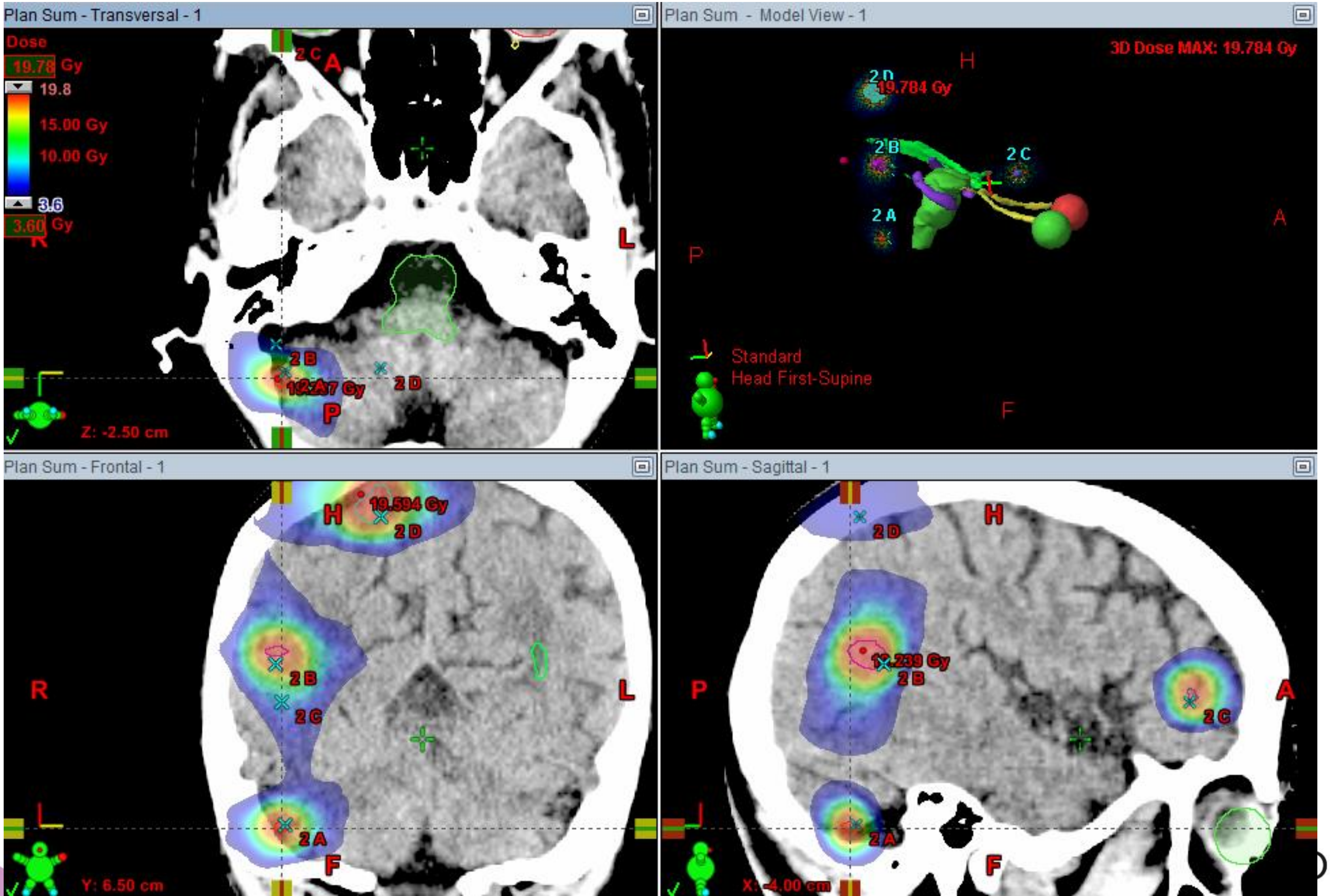
Stereotactic treatment – brain metastases

Stereotactic treatment – 4 targets!



Stereotactic treatment – 4 targets!



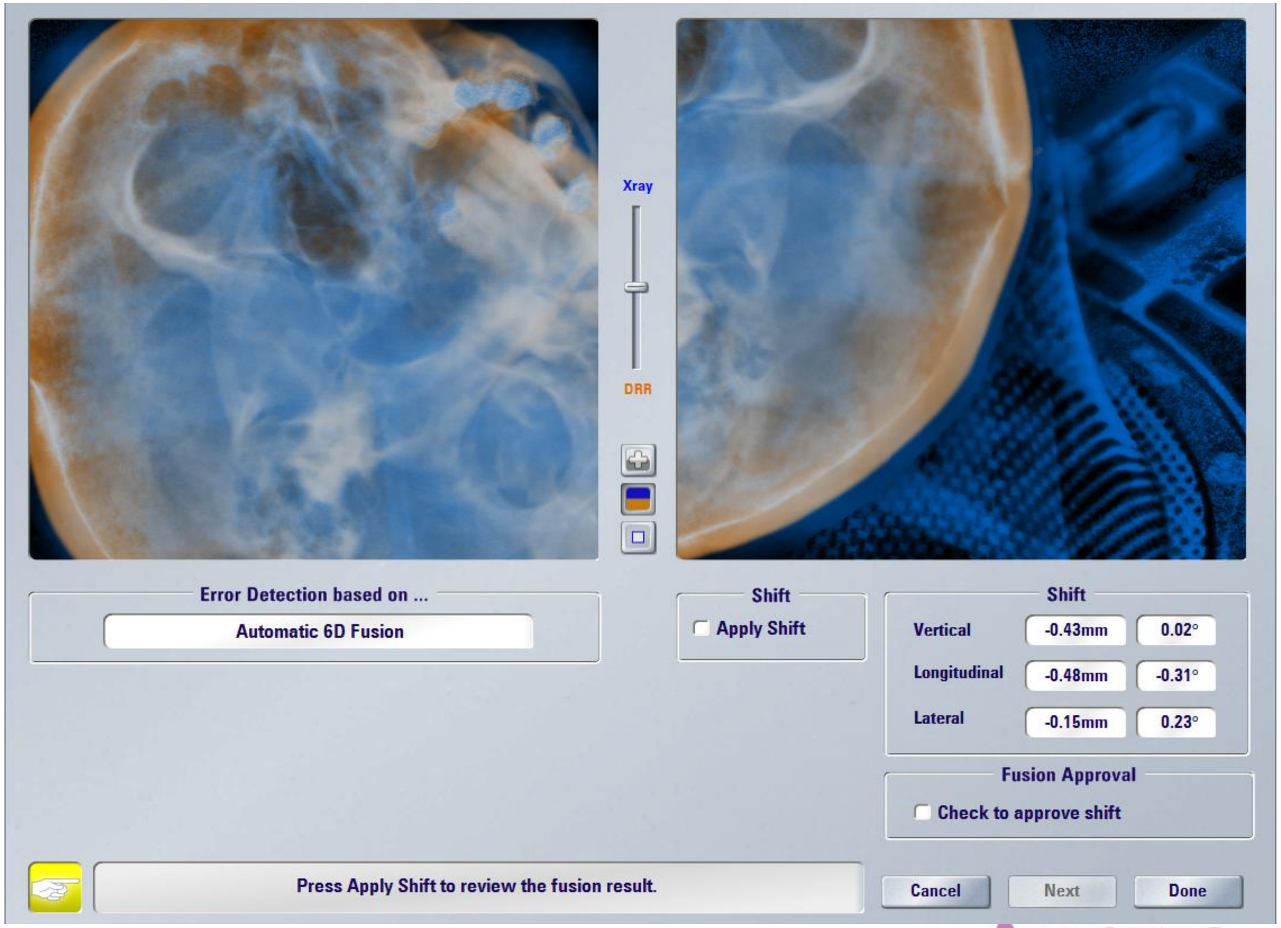
Delivery of stereotactic brain RT

IGRT

- Small PTV margins
- 6D corrections

- Rigs tolerance:
  - <1mm
  - <1°

- Non-coplanar RT delivery
  - Repeat imaging after couch rotation



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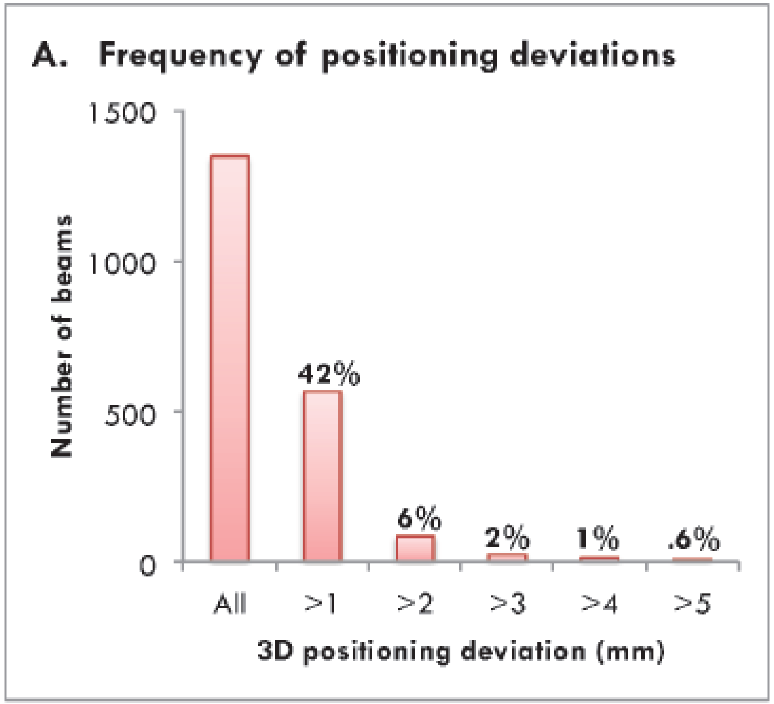
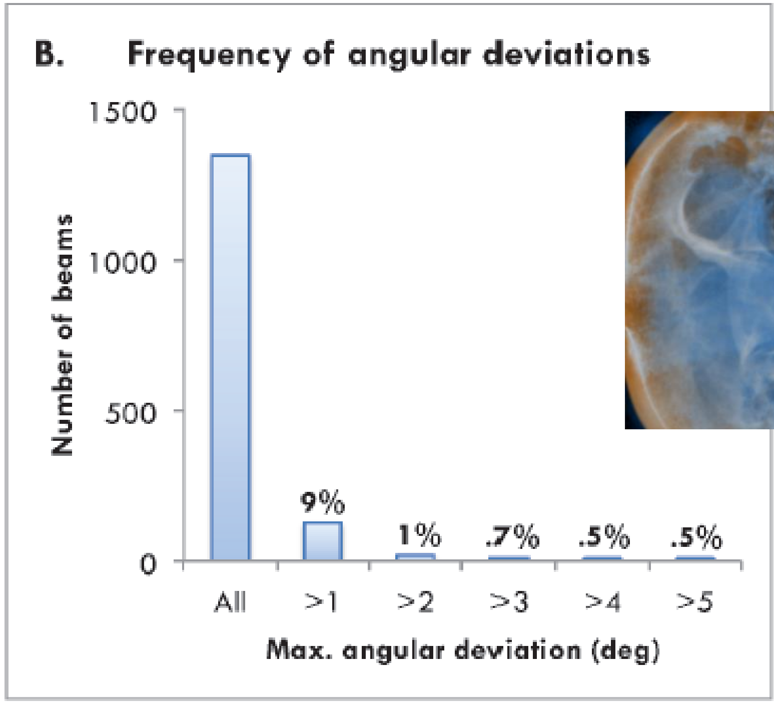
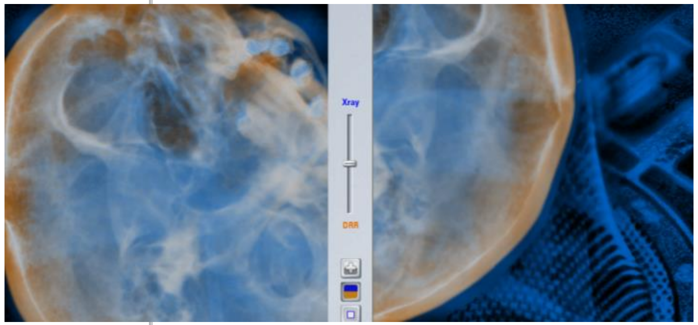
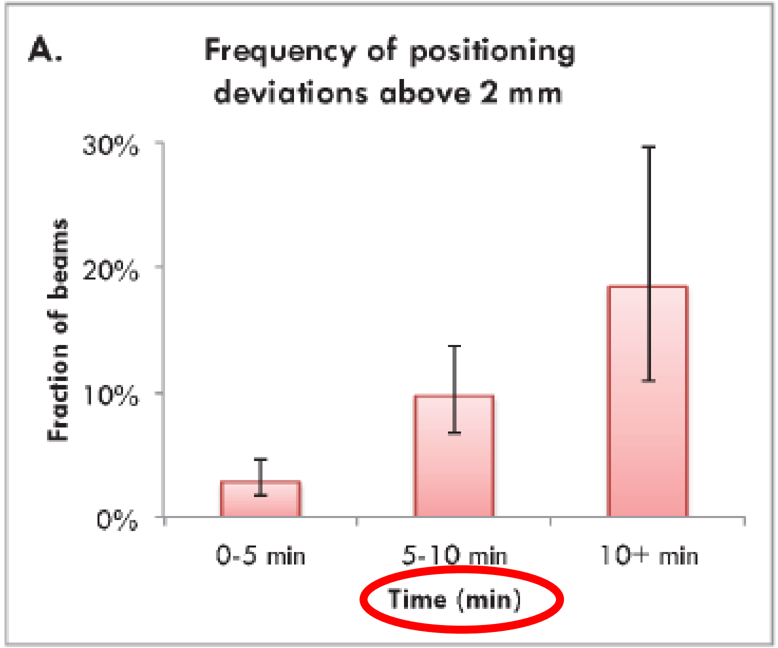
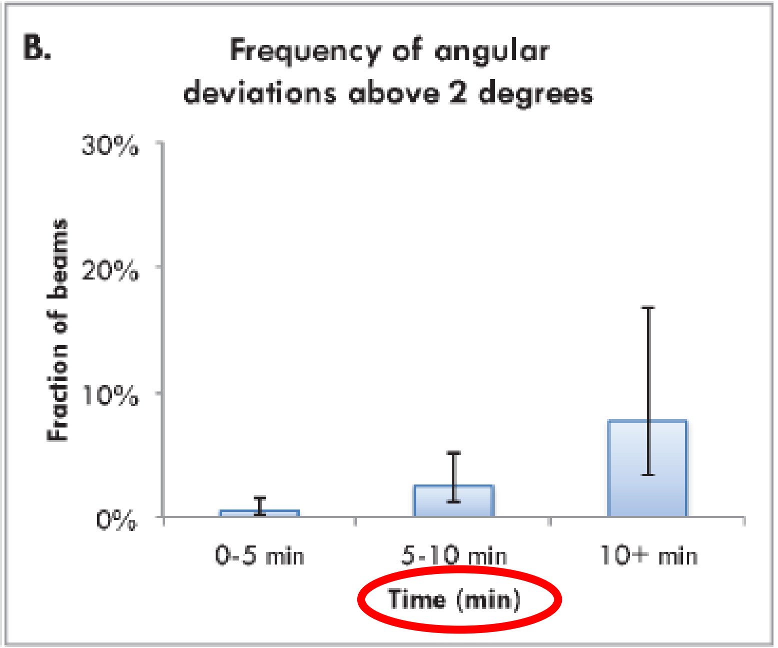






Intra-fractional uncertainties





Tarnavski et al. Jour. of Radiosurgery and SBRT 2016

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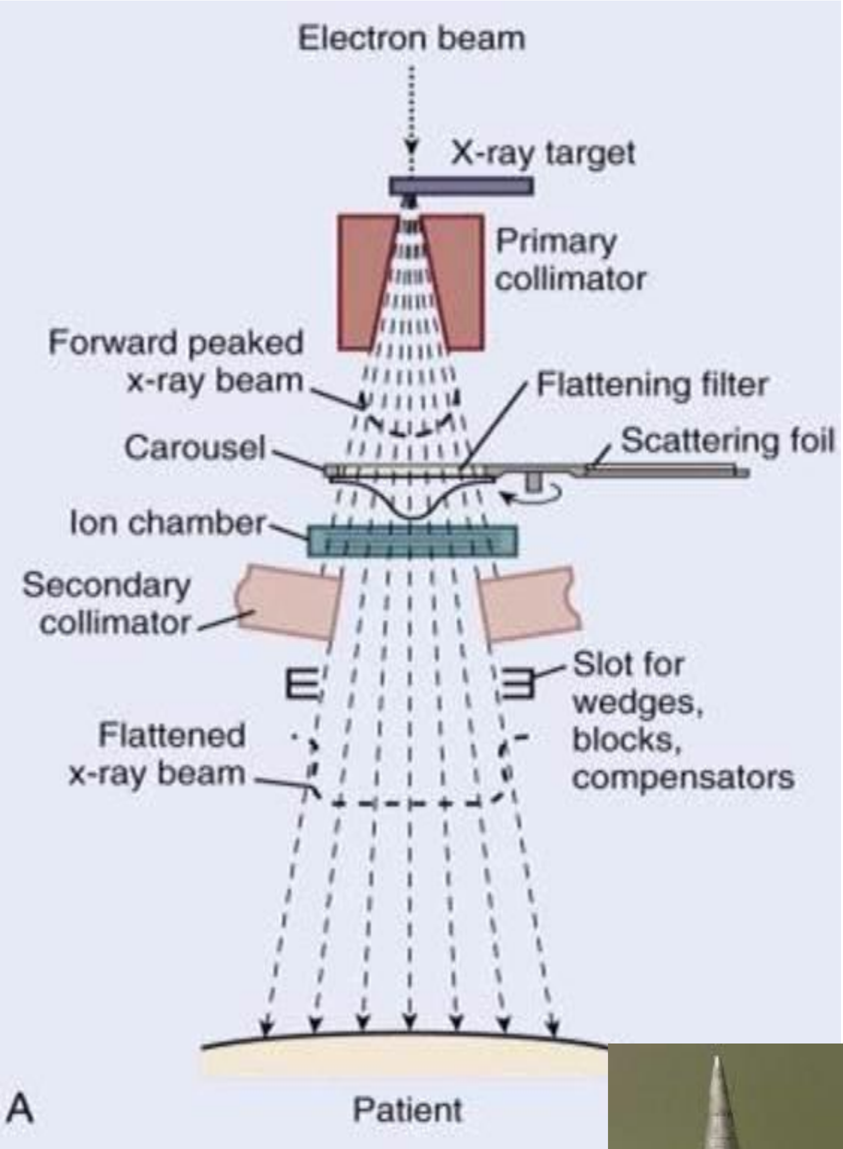
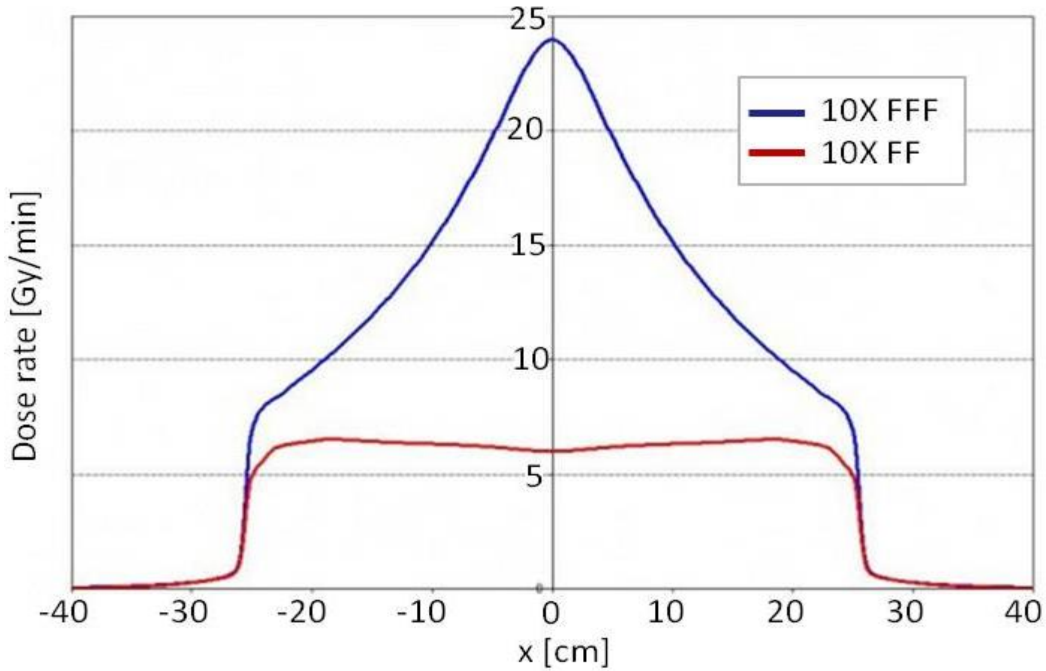
FFF – flattening filter free



Intensity modulated RT does not necessitate flat beams



FFF facilitates increase in dose rate & decrease in beam time by a factor of up to 6

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A bit about the margins…

Margins depend on:

- RT technique
- IGRT strategy

Example:

- 3DC RT & field verification at first treatment
  - ➢ 5 mm CTV-PTV margin

- VMAT & daily IGRT with 6D:
  - ➢ 1-3 mm CTV-PTV margin

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Considering the margins vs. daily IGRT workload

margins of 5 mm increase the treated volume by 50%

D. Verellen et al. nature reviews | **cancer** volume 7 | december 2007 | 949

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Case report: **Head and Neck**

ESTRO School

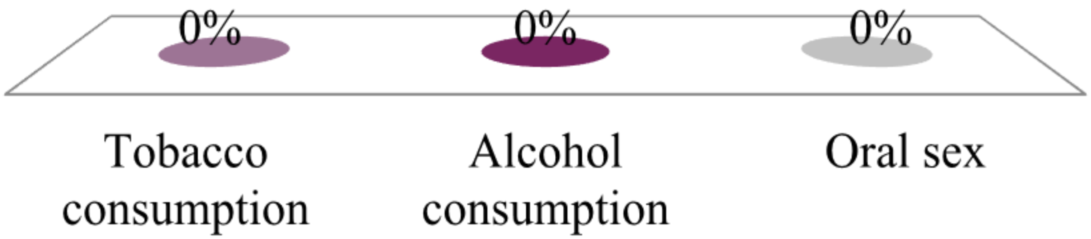
Jesper Eriksen, Odense University hospital, Denmark
Sofia Rivera, Gustave Roussy, Villejuif, France

Advanced skills in modern radiotherapy
May 2018

FALCON
Fellowship in Anatomic deLineation & CONtouring

What are head and neck cancer main risk factors?

A. Tobacco consumption
B. Alcohol consumption
C. Oral sex



Changing traditional scenario in H&N cancer

- Increasing incidence of HPV positive tumors (+++ Oral Cavity)
- Improved outcome compared with HPV-negative tumors
- younger patients with limited comorbidity and good performance status, less likely to abuse tobacco and alcohol

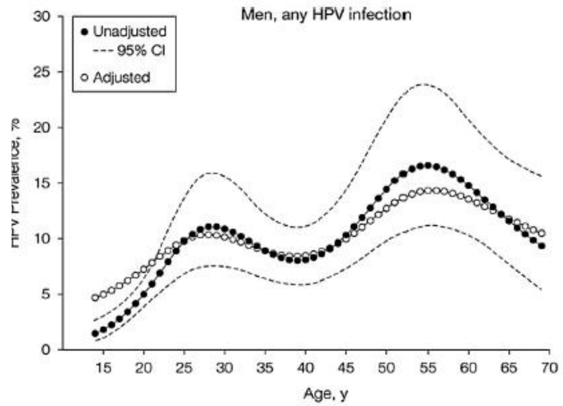
Epidemiology of oral human papillomavirus infection

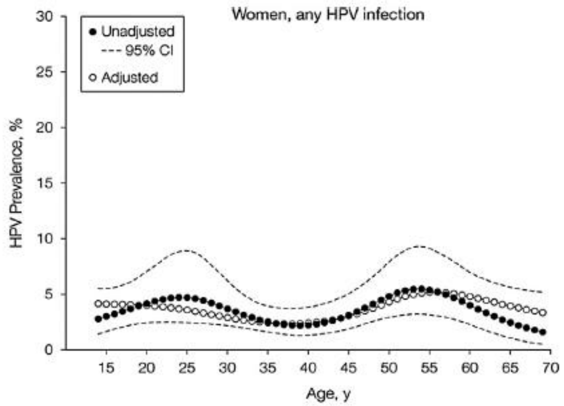
Christine H. Chung [a,b], Ashley Bagheri [a], Gypsyamber D'Souza [c,*]

[a] Department of Oncology, Johns Hopkins Medical Institute, Baltimore, MD, United States
[b] Department of Otolaryngology, Head and Neck Surgery, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medical Institute, Baltimore, MD, United States
[c] Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

S U M M A R Y

Objective: To describe what is known about the epidemiology of oral human papillomavirus (HPV) infection.
Methods: In this article we review current data on HPV prevalence, natural history, mode of acquisition, and risk factors for oral HPV infection.
Results & Conclusion: Over the past several years new studies have informed our understanding of oral HPV infection. These data suggest oral HPV prevalence is higher in men than women and support the sexual transmission of HPV to the mouth by oral sex. Data is emerging suggesting that most oral HPV infections usually clear within a year on and describing risk factors for prevalent and persistent infection. Recent data support likely efficacy of the HPV vaccine for oral HPV, suggesting vaccination may reduce risk of HPV-related oropharyngeal cancer.





Lassen et al ;Radiother oncol 2013
Chung et al; oral oncol 2013

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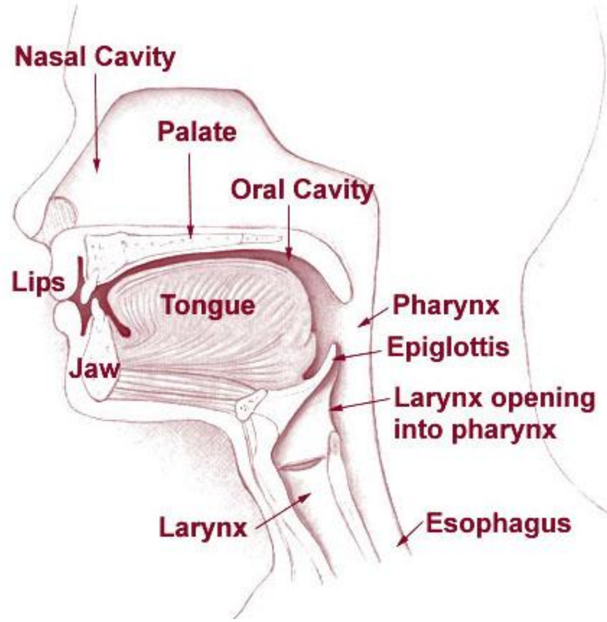
Patient history



- 60-year old man.
- 3 week history of nodal swelling , left side of the neck.
- No pain or dysphagia. No weight loss.
- No co-morbidity except from back pain.
- Ceased smoking in 1990, 10 pack-years.
- No daily use of alcohol.

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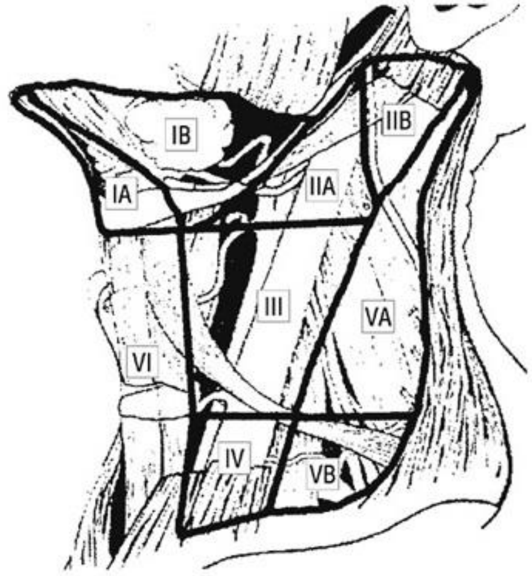
Clinical examination



•Good performance (WHO PS 0)

• Base of tongue/vallecula area a 3x2x2cm large tumour is seen.

•Proximal border of the tumour seems to be close to the lower pole of the left tonsil

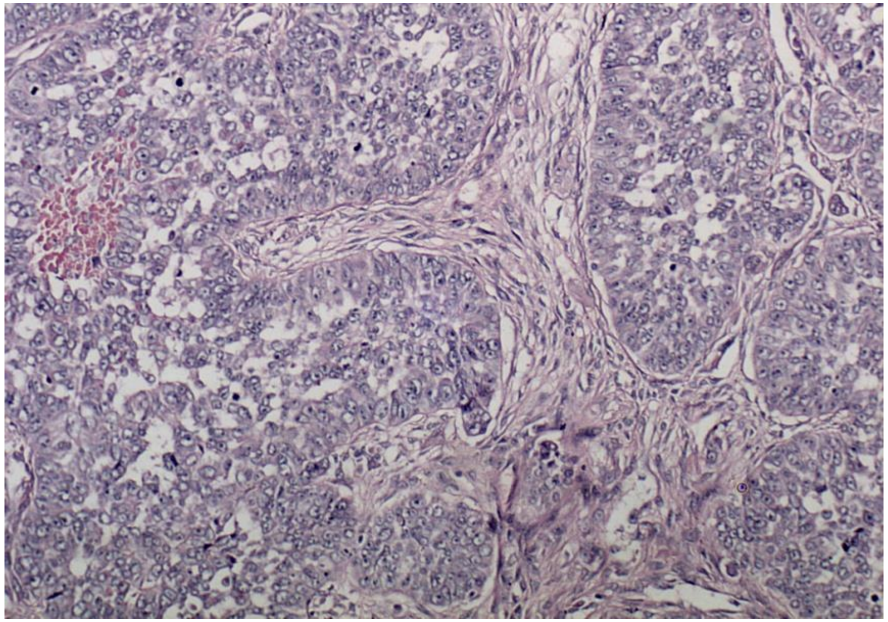
• Otherwise normal fiber optic examination.

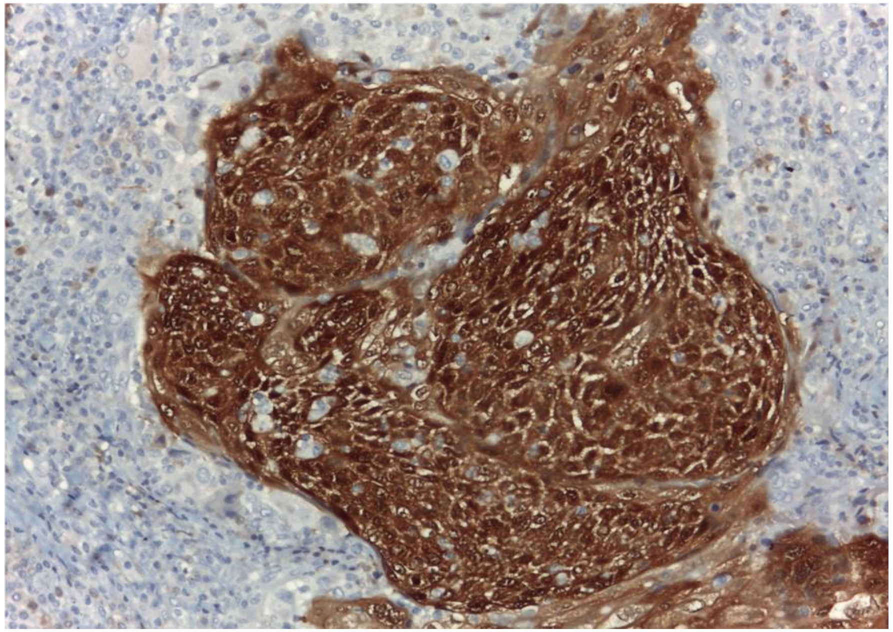
• Palpable node in region II, left side.

• Contralateral side normal.

Pathology

- Moderate differentiated squamous cell carcinoma (G2).
- p16 positive (HPV marker)





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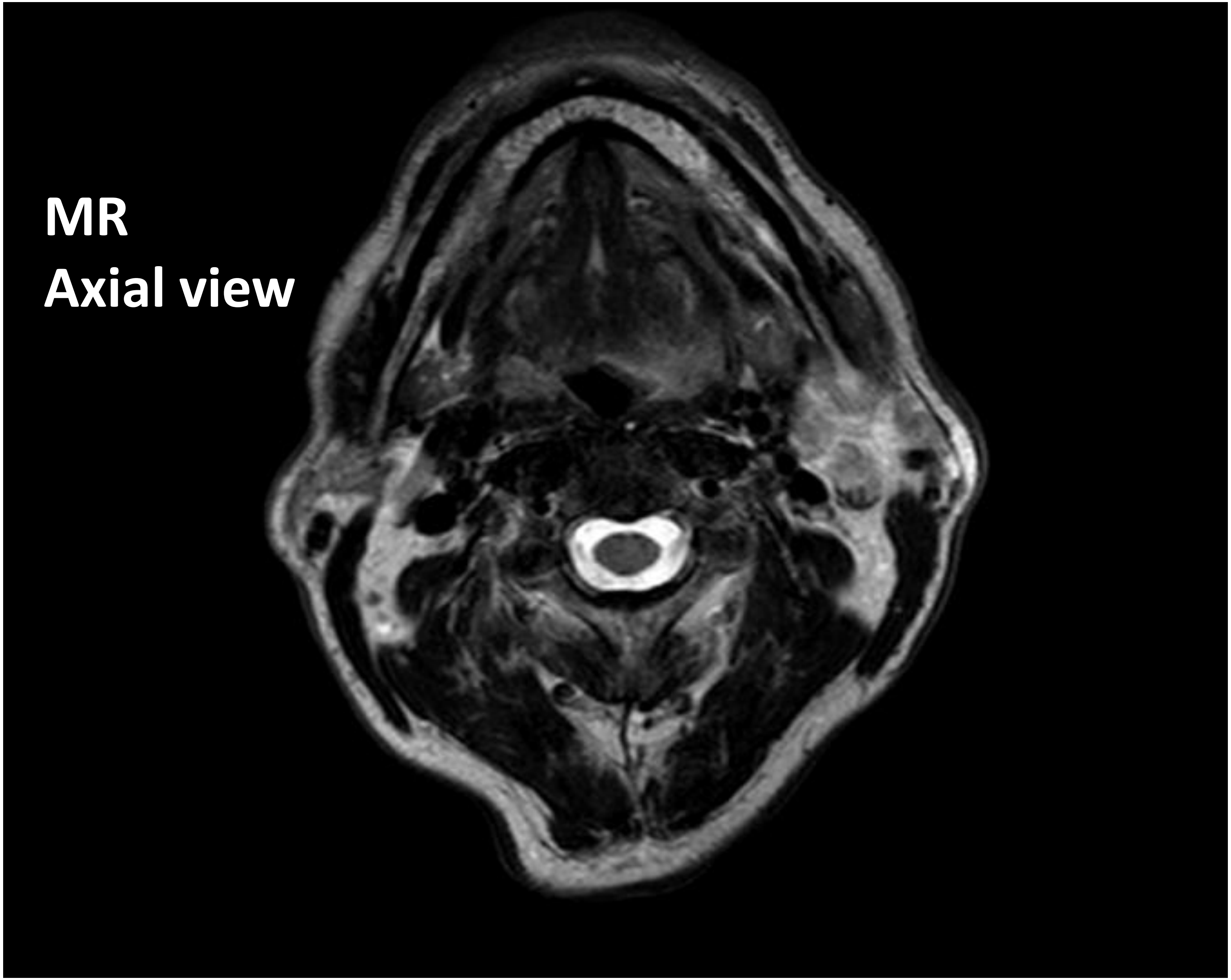
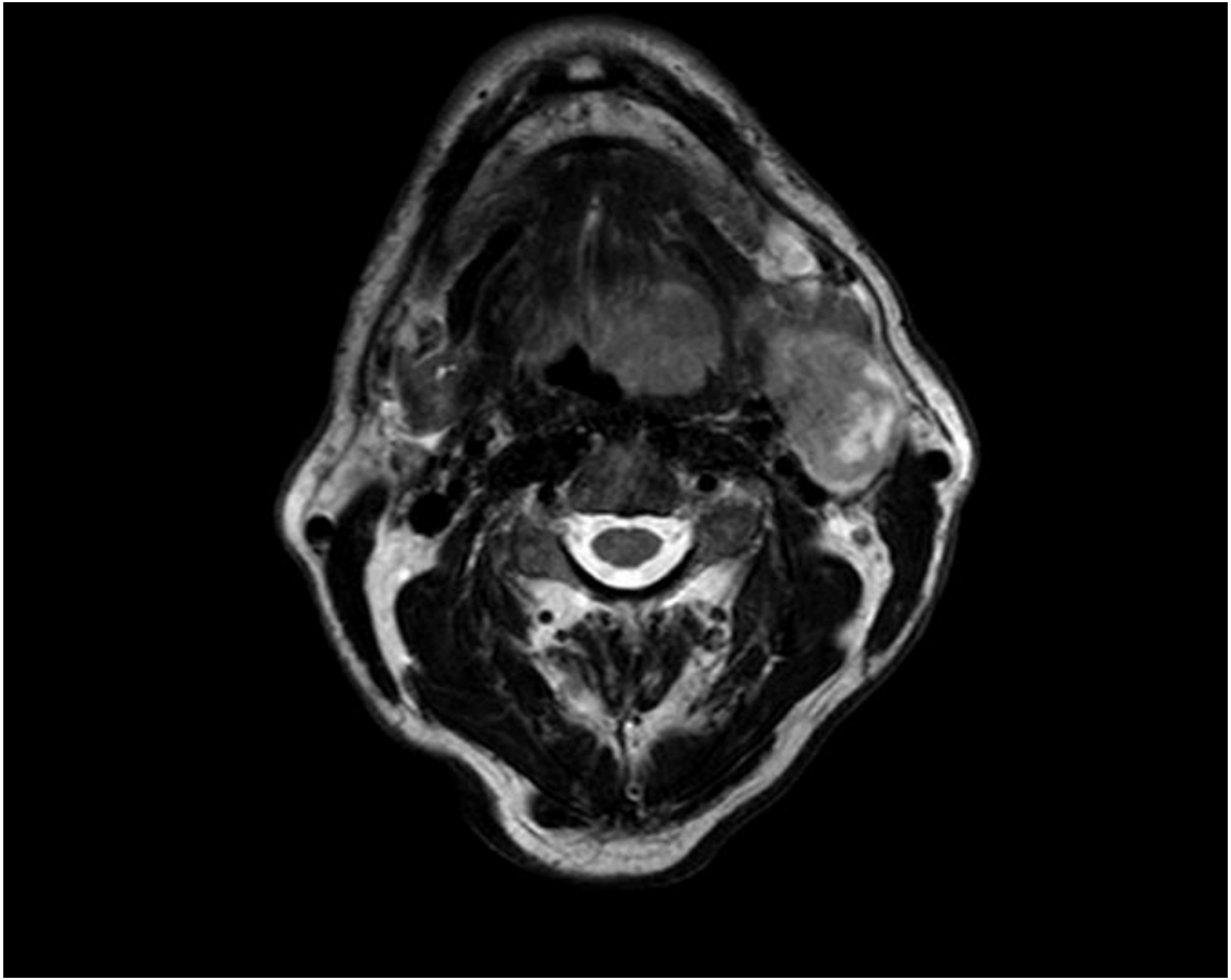
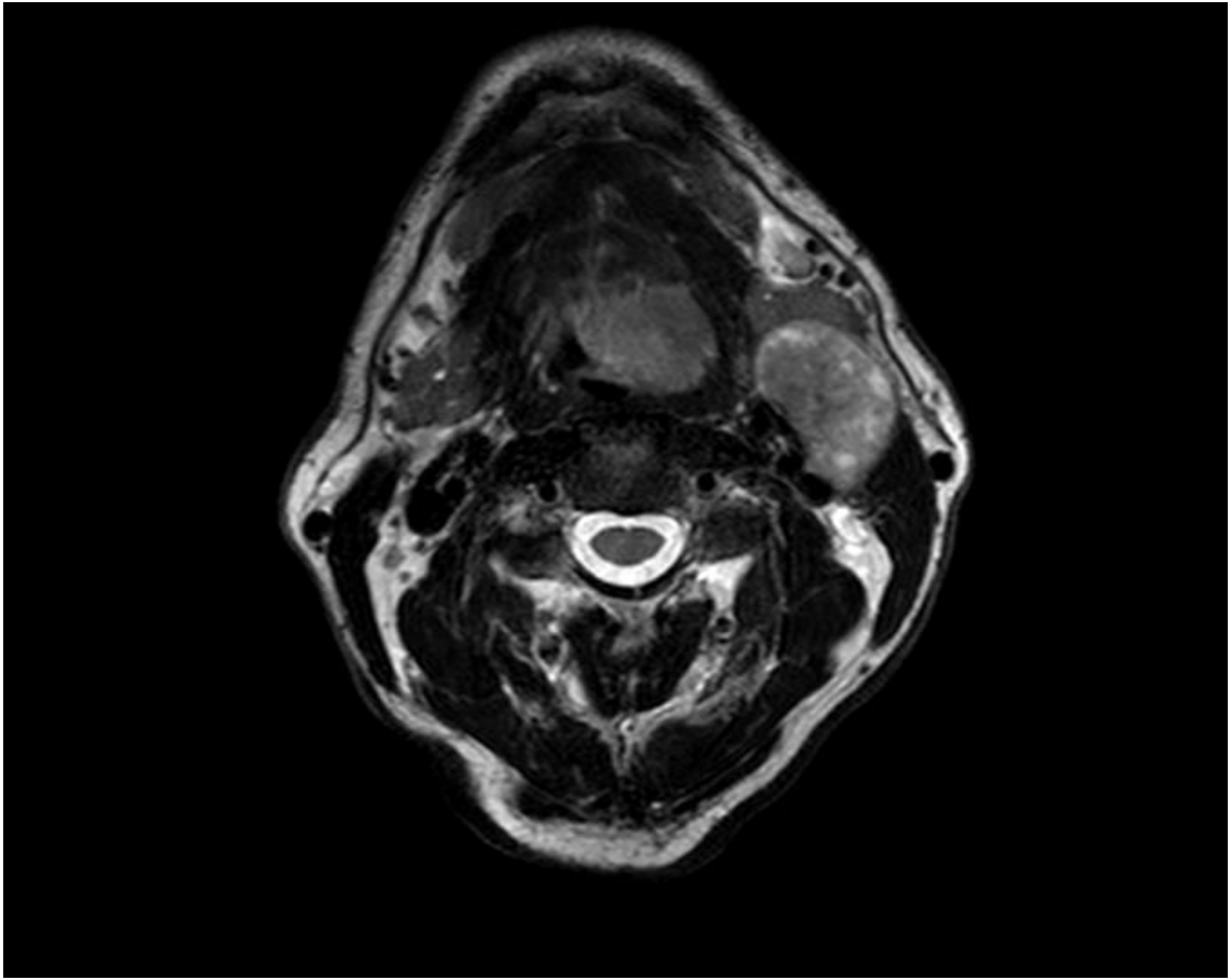
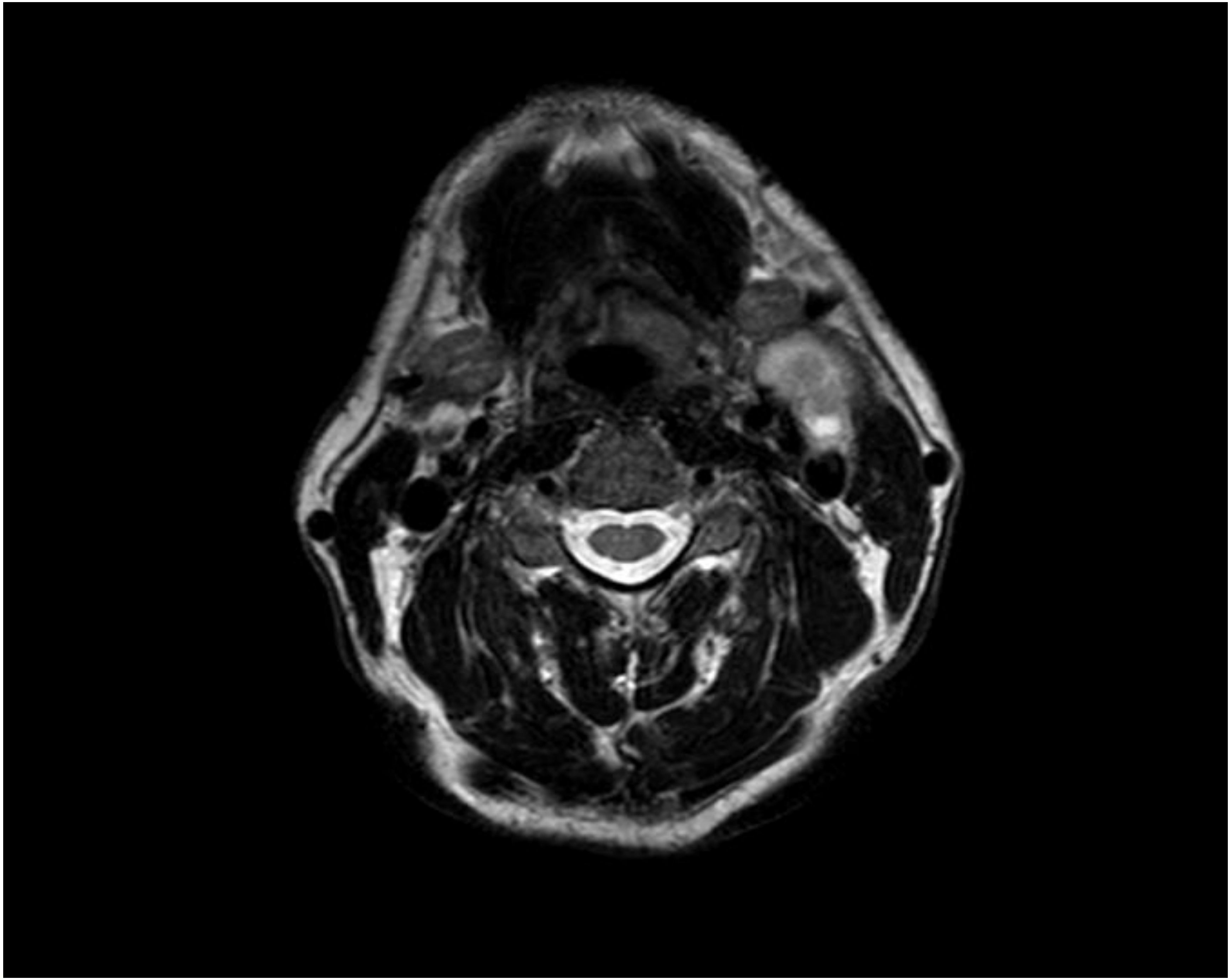
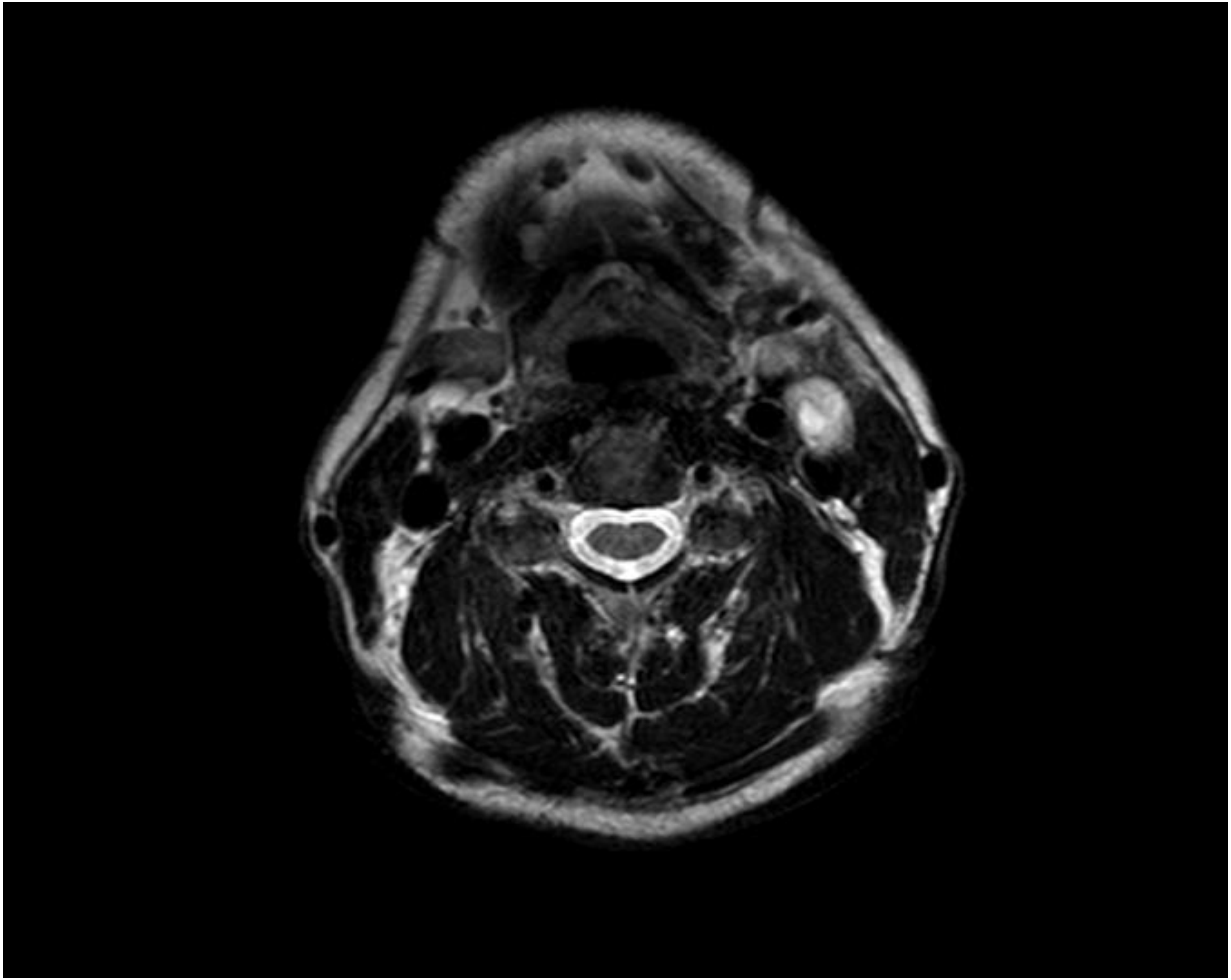
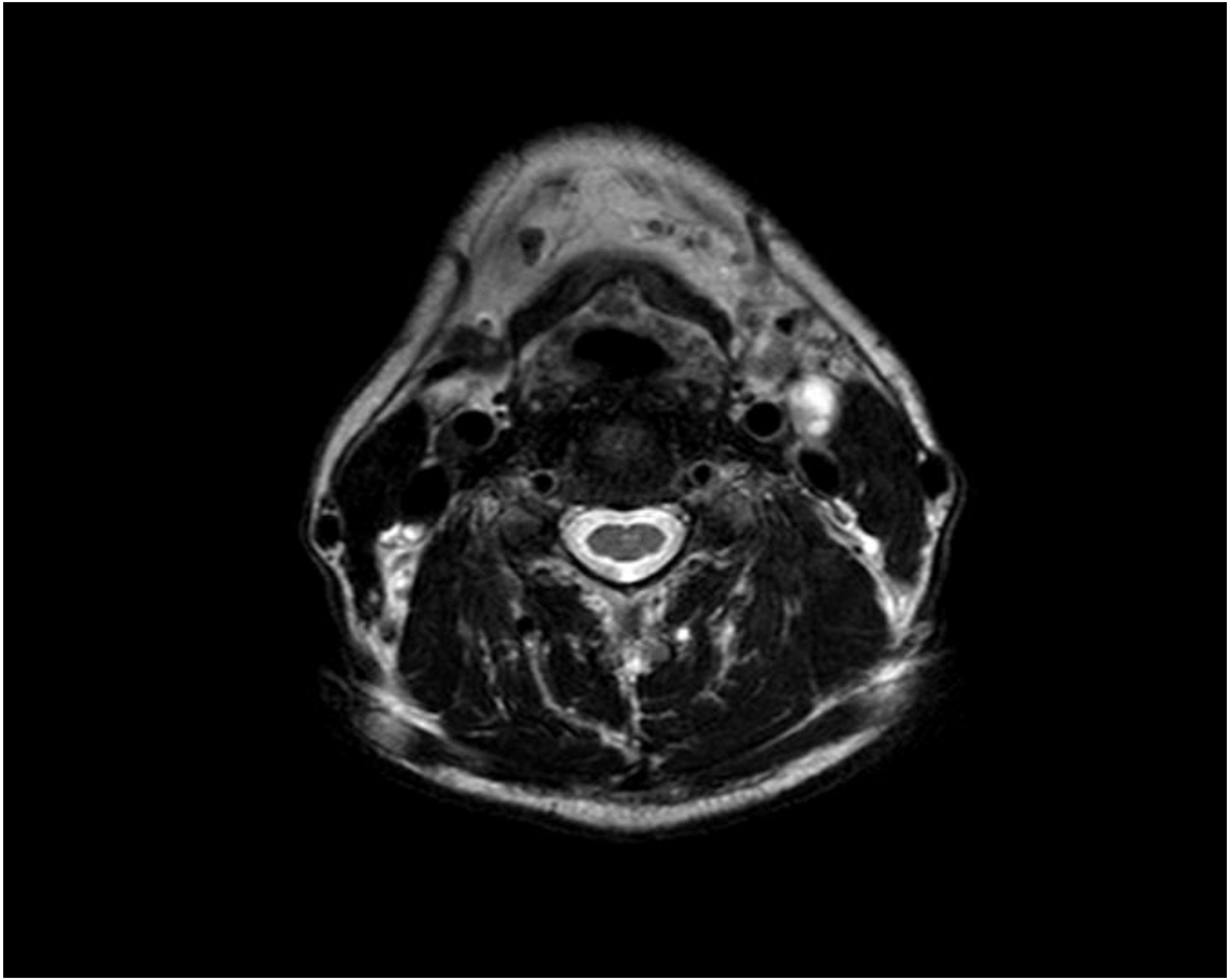

MR
Axial view

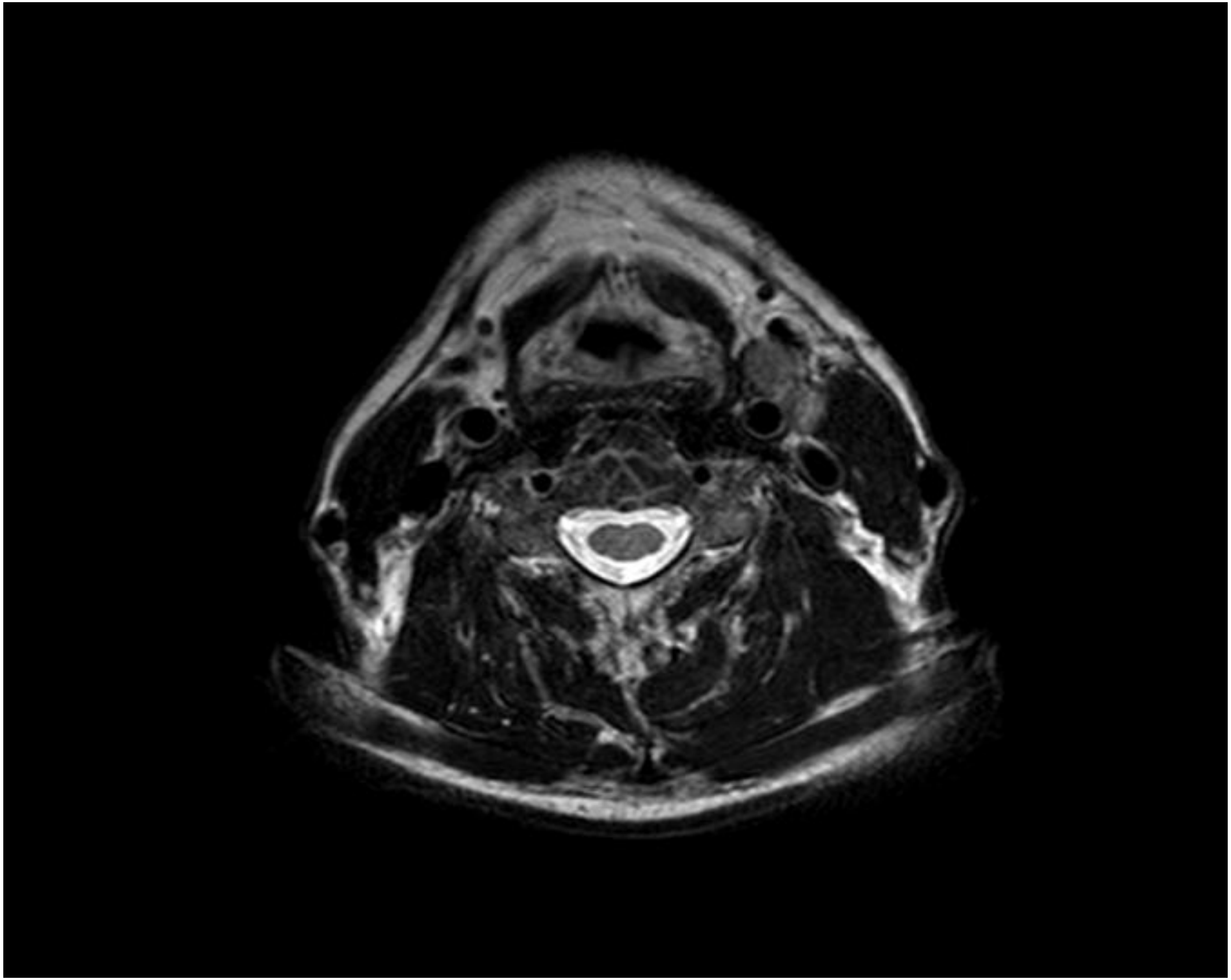




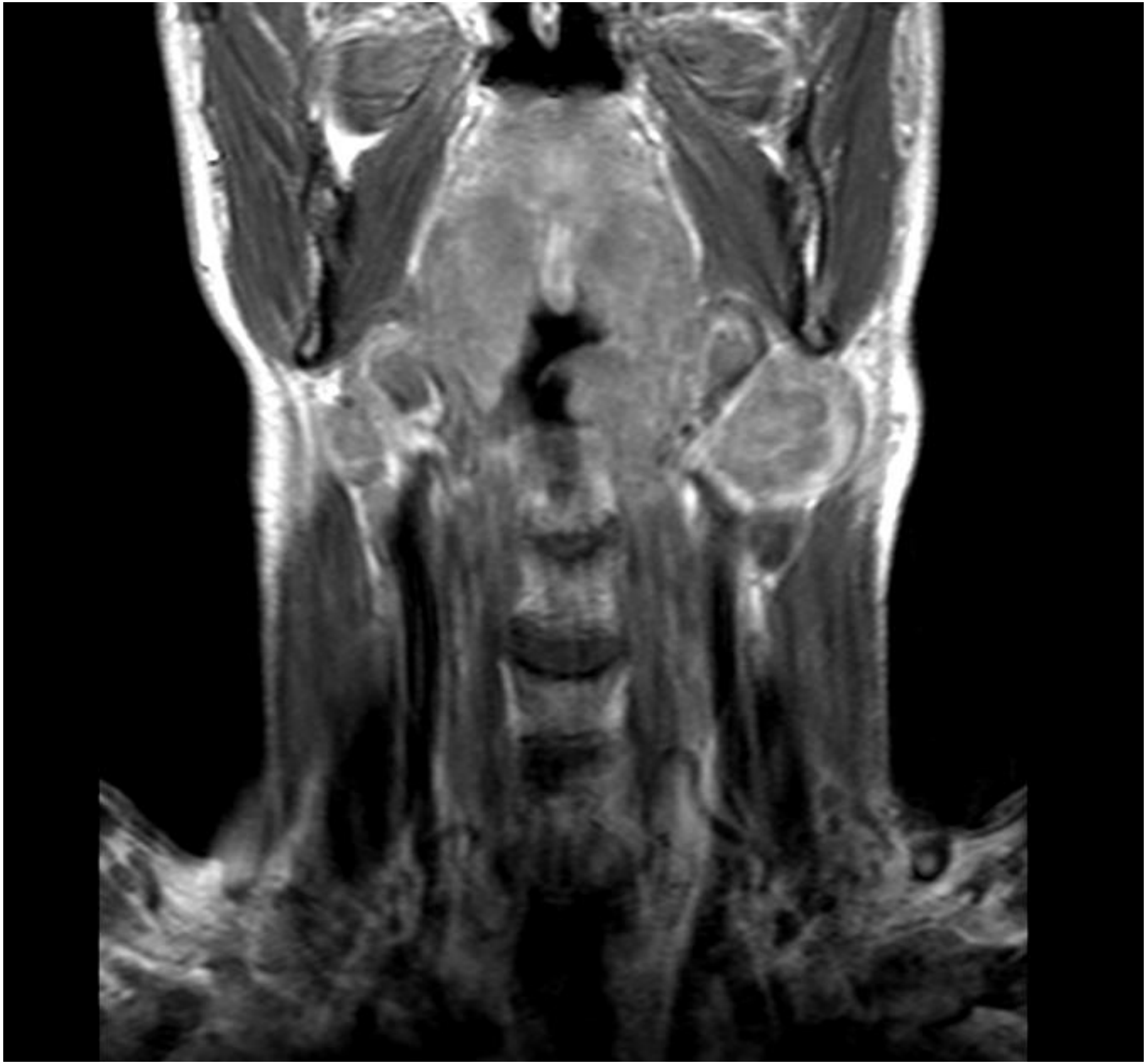


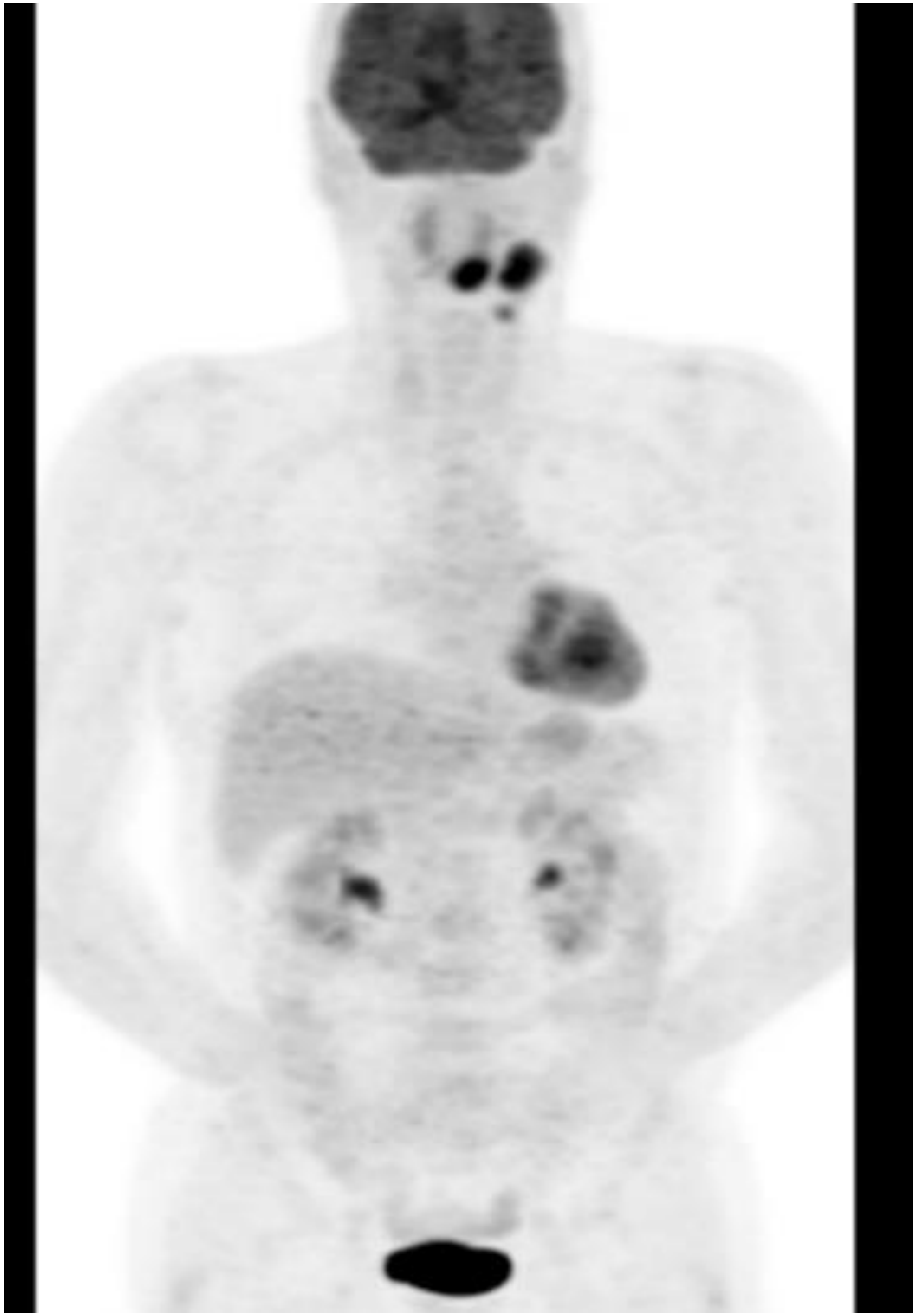


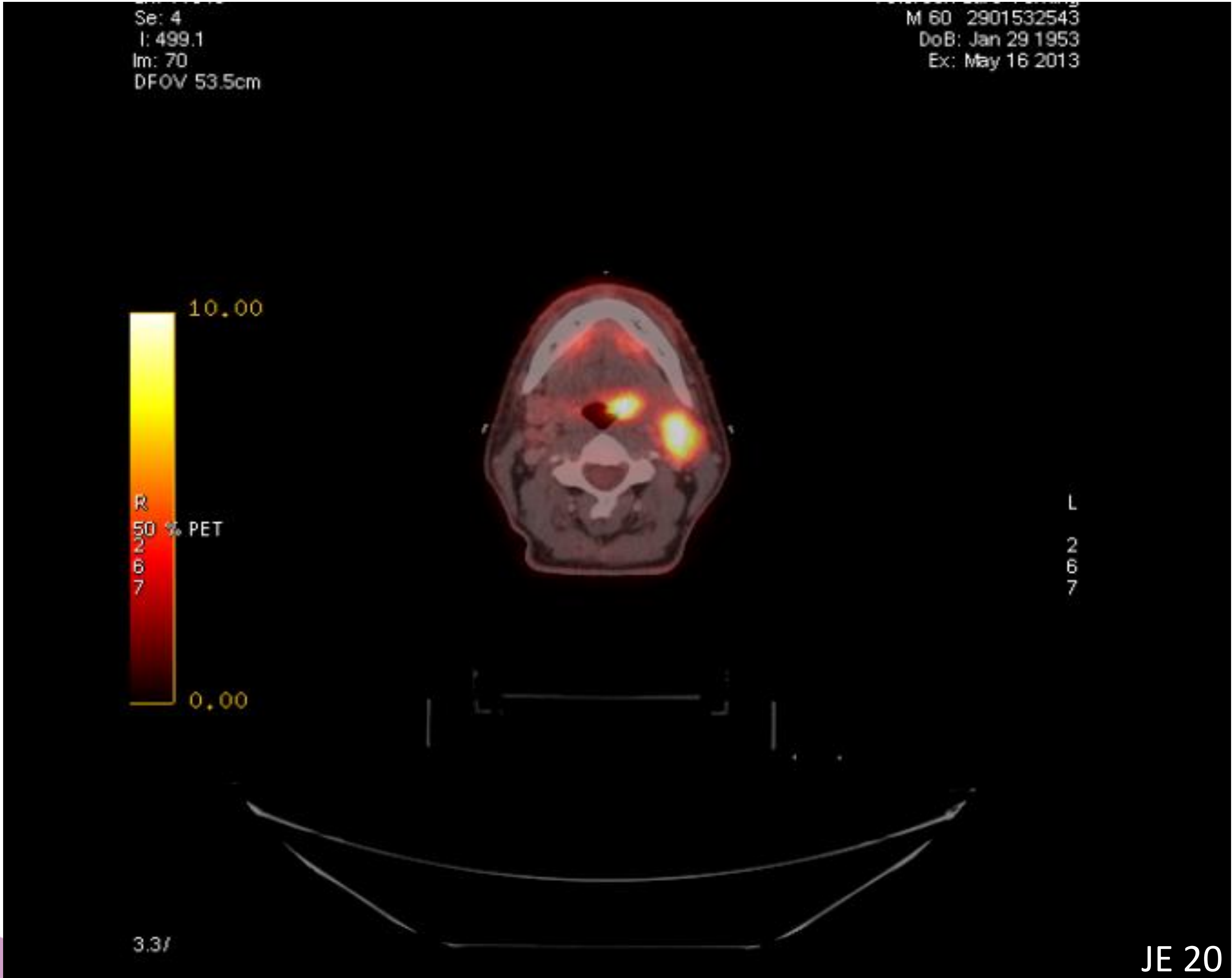


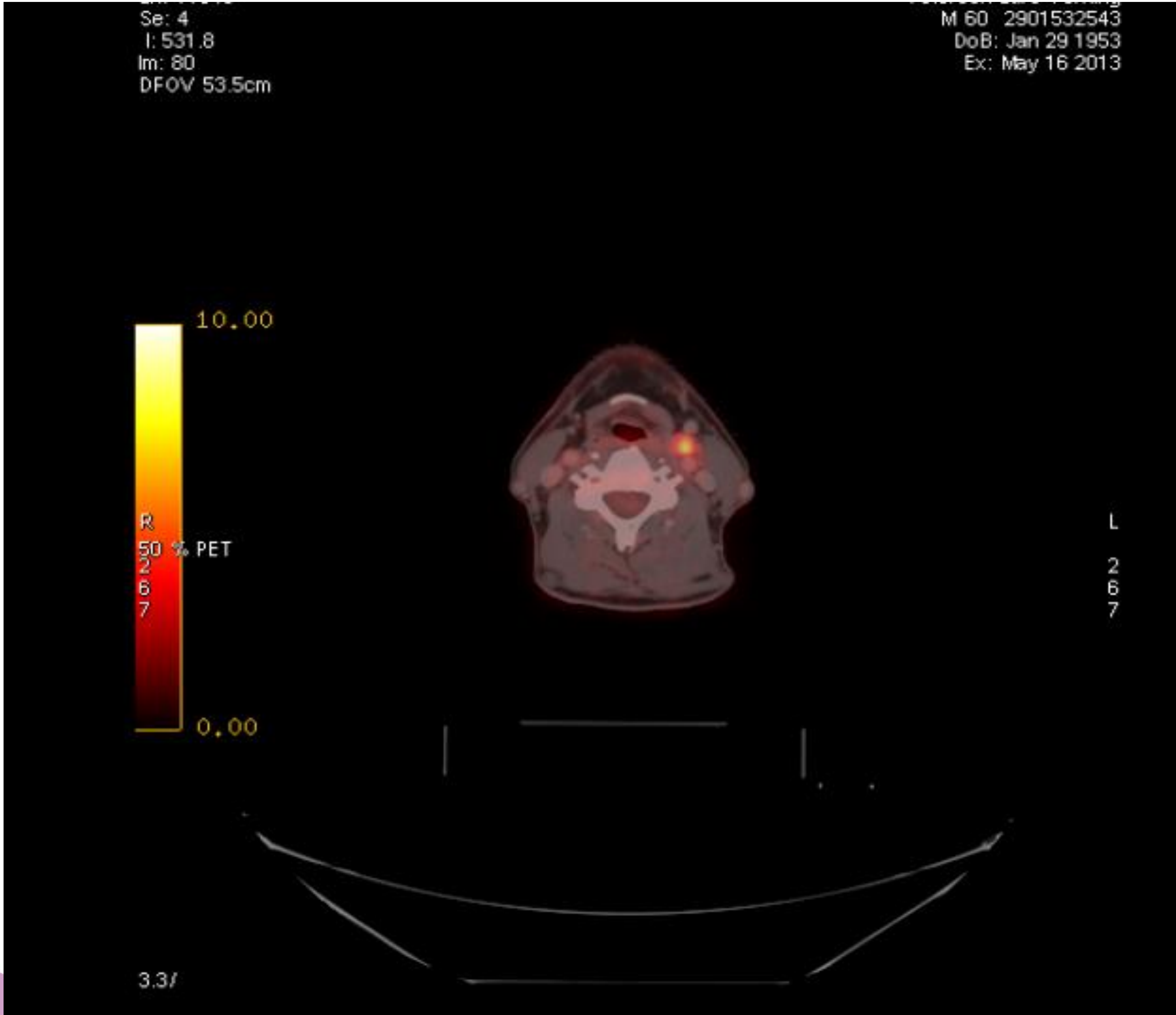


MR
Coronal view






Se: 4
I: 499.1
Im: 70
DFOV 53.5cm
M 60 2901532543
DoB: Jan 29 1953
Ex: May 16 2013
10.00
R
50 % PET
2
6
7
0.00
L
2
6
7
3.3/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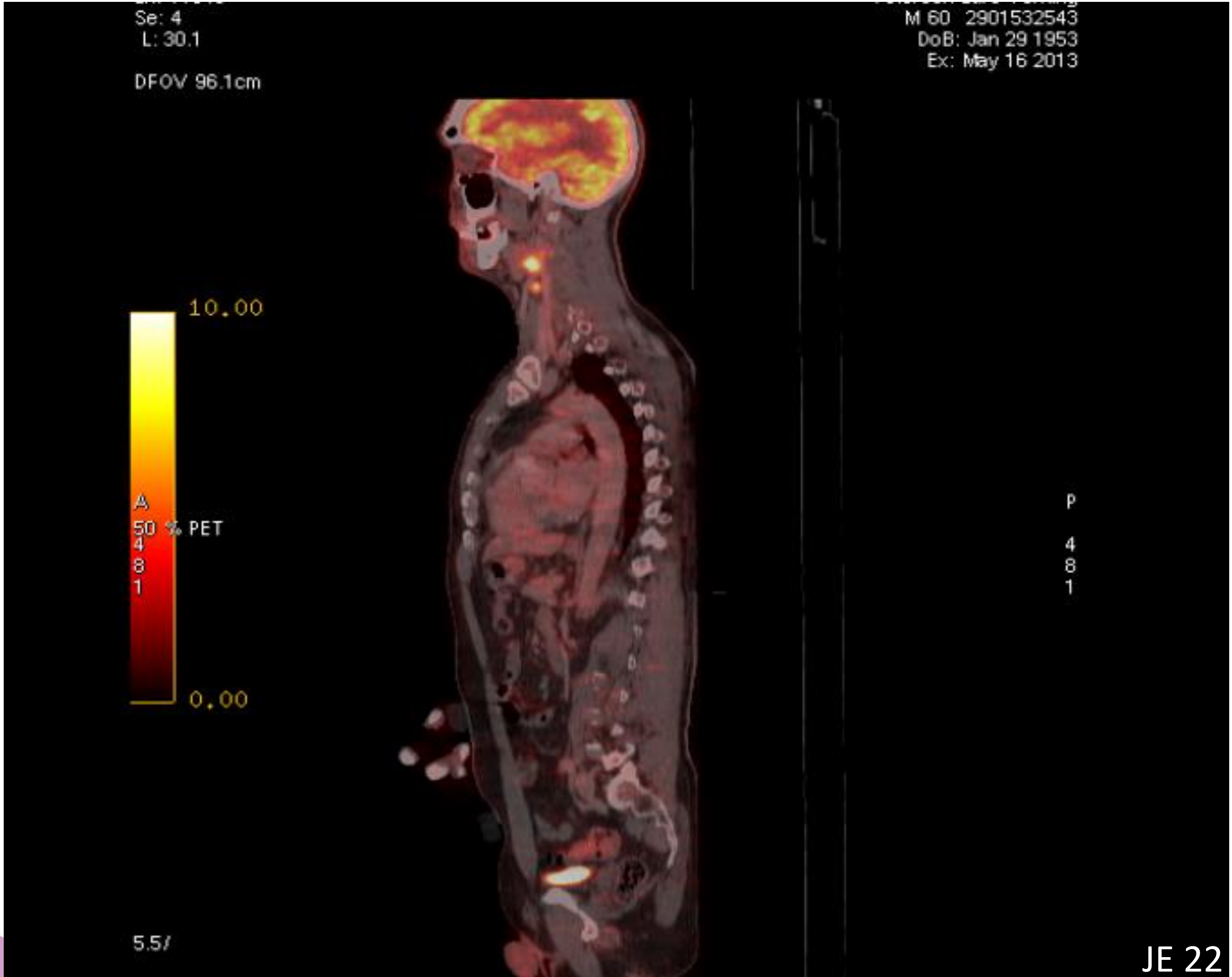
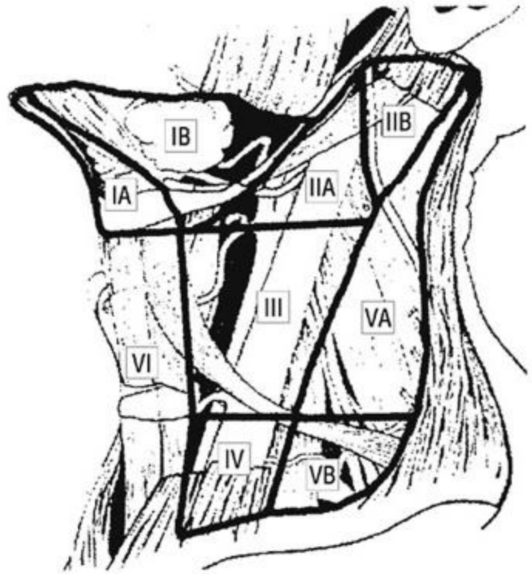
I: 531.8
Im: 80
DFOV 53.5cm
M 60 2901532543
DoB: Jan 29 1953
Ex: May 16 2013
10.00
R
50 % PET
2
6
7
0.00
L
2
6
7
3.37


Se: 4
L: 30.1
DFOV 96.1cm
M 60 2901532543
DoB: Jan 29 1953
Ex: May 16 2013
10.00
A
50 % PET
4
8
1
0.00
P
4
8
1
5.5/
JE 22

Ultrasound of neck

- One necrotic node in the upper part of left region II close to the submandibular gland; 3.5x2x2 cm.
- One node in left region III, 1.5x1x1 cm without preserved hilar region.
- Right side of the neck is normal.



Conclusions after diagnostic workup

- T2N2bM0 (stage IVa) SCC oropharyngeal tumour.
- Patient in a good performance with no relevant co-morbidity.

Treatment done

- 66 Gy/33 Fx; 2 Gy/Fx; 6 Fx/week.
- Concomitant weekly low-dose cisplatinum
  40 mg/m² (maximum 70 mg/m²).
- Concomitant hypoxic radiosensitization with
  nimorazole according to DAHANCA guidelines

Contouring guidelines

ARTICLE IN PRESS

Radiotherapy and Oncology xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

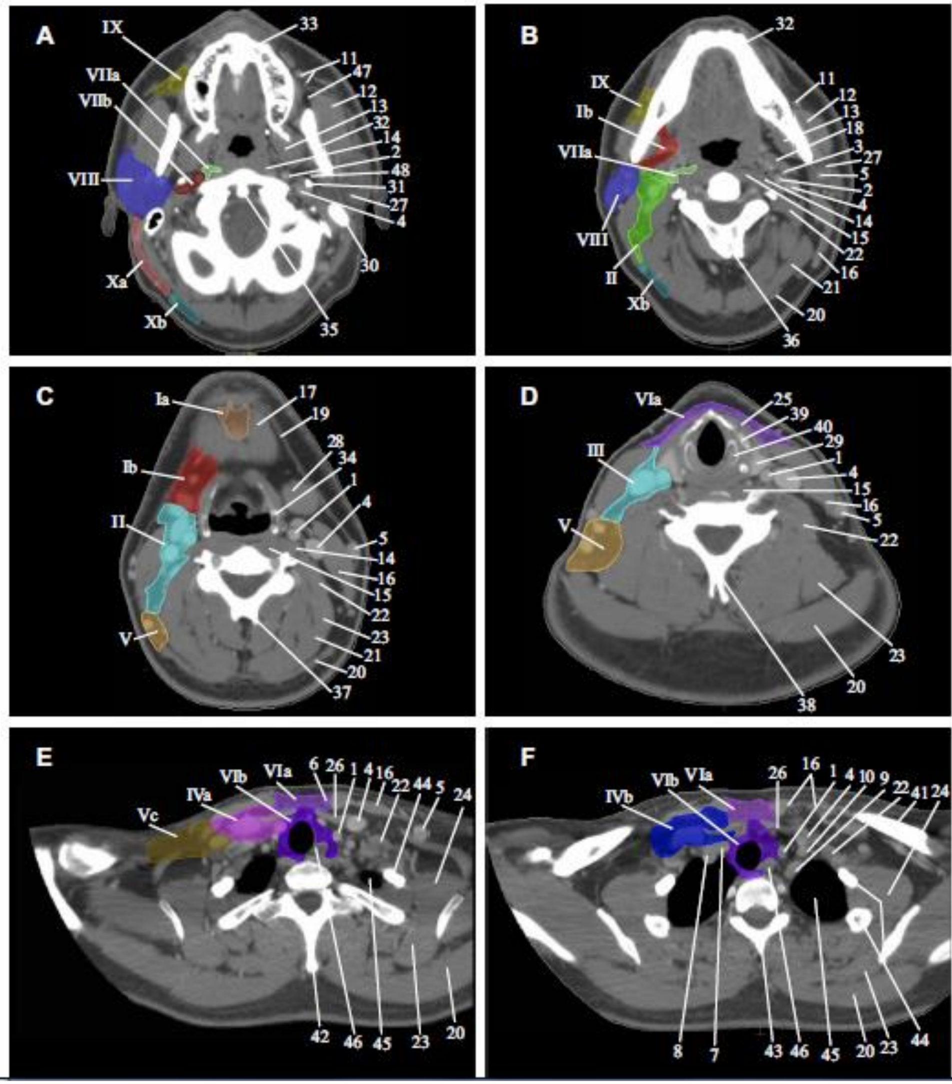
Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Delineation of the neck node levels for head and neck tumors: A 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines ☆

Vincent Grégoire [a,*], Kian Ang [b], Wilfried Budach [c], Cai Grau [d], Marc Hamoir [e], Johannes A. Langendijk [f], Anne Lee [g], Quynh-Thu Le [h,i], Philippe Maingon [j], Chris Nutting [k], Brian O'Sullivan [l], Sandro V. Porceddu [m], Benoit Lengele [n]



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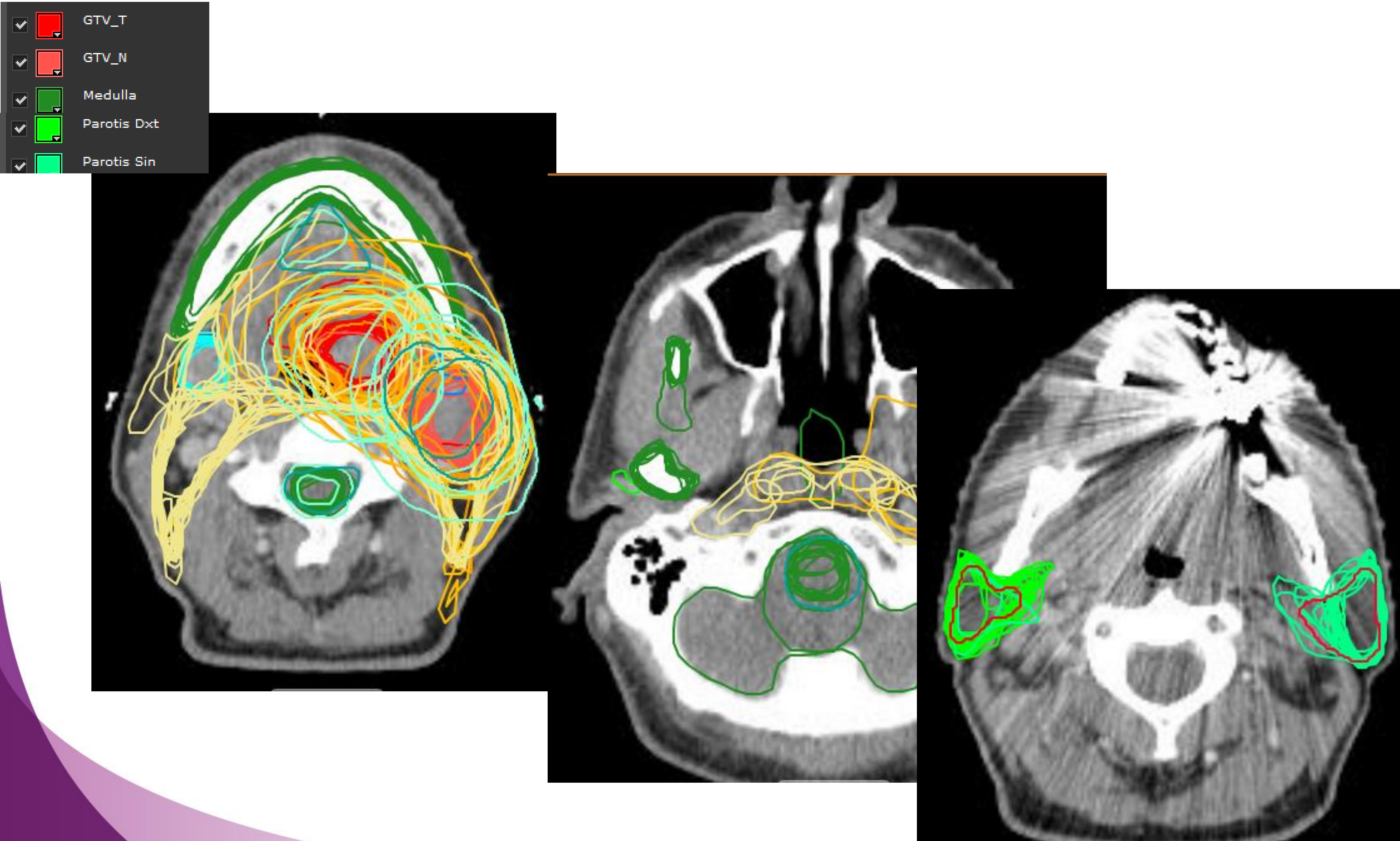
Case used for H&N Falcon online WS



Take home messages:

- HPV positive tumors are changing H&N cancer traditional scenario

- Positioning remain key points for these highly conformal treatments (IMRT+++)

- Target and OAR contouring remains an issue: Highly heterogeneous contours

- Crucial need for contouring guidelines and training

Who is doing what in Radiation Therapy

Rianne de Jong *RTT*,
Amsterdam Medical Centre

m.a.j.dejong@amc.uva.nl

NKI-AVL
The Netherlands Cancer Institute
Antoni van Leeuwenhoek Hospital

Survey

Questionnaires to participants of ESTRO course on "IGRT in clinical practice" in 2006-2010:

48 hospitals

19 countries

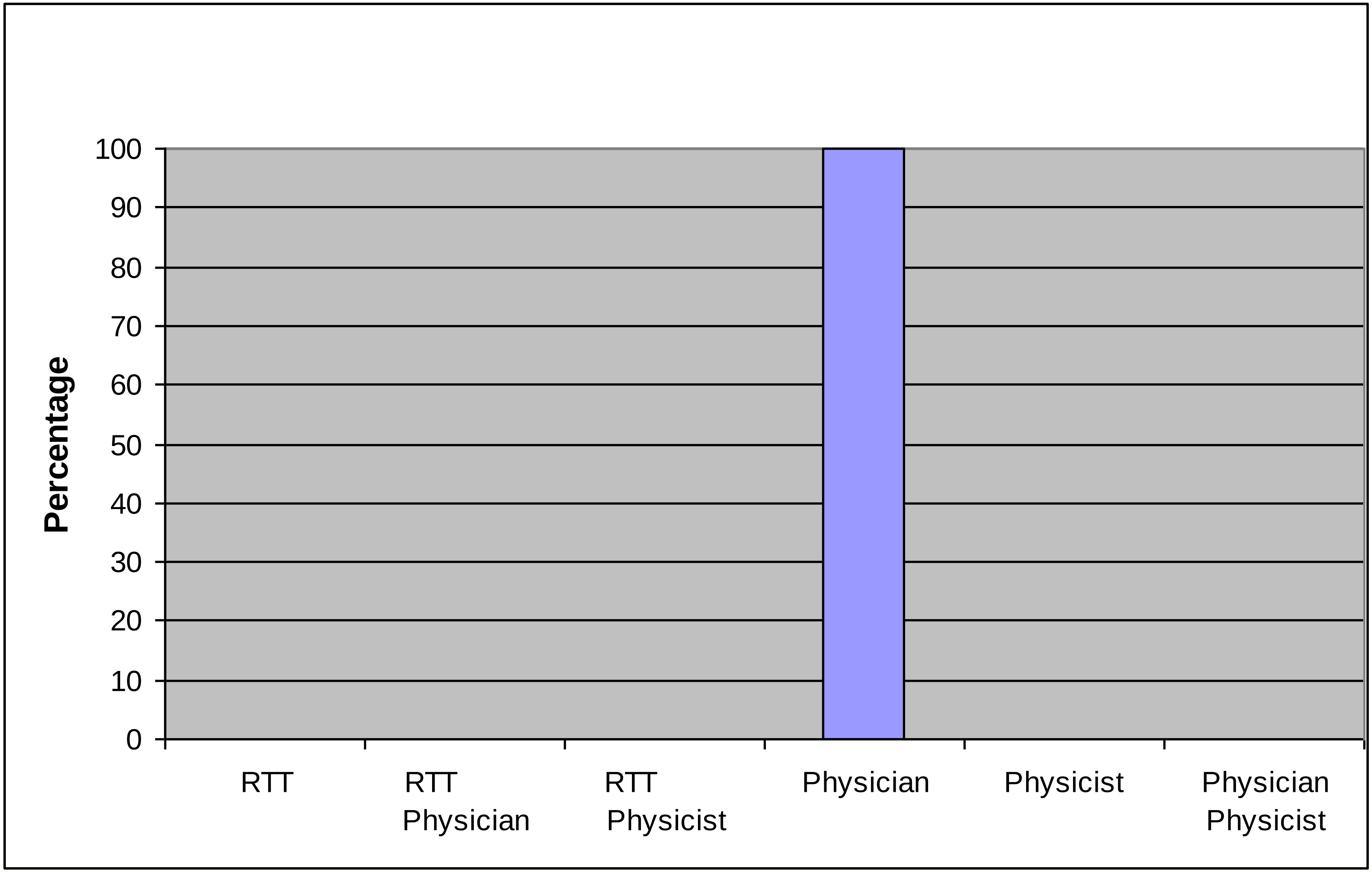
Survey

1. Indication/Design of Radiation Treatment
2. Pre treatment imaging: CT/simulation
3. Delineation
4. Treatment Planning
5. Treatment
6. Image Guidance/Adaptation treatment

→

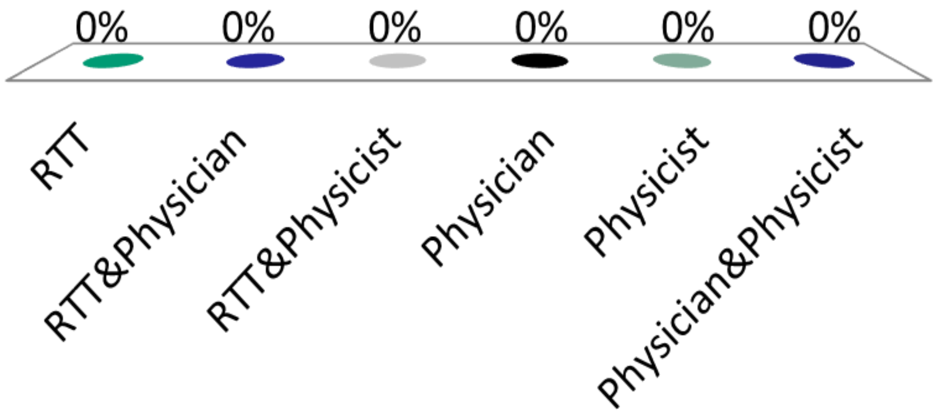
- Radiation Therapy Technicians (RTT)
- Physicians
- Physicists

1. Indication of treatment

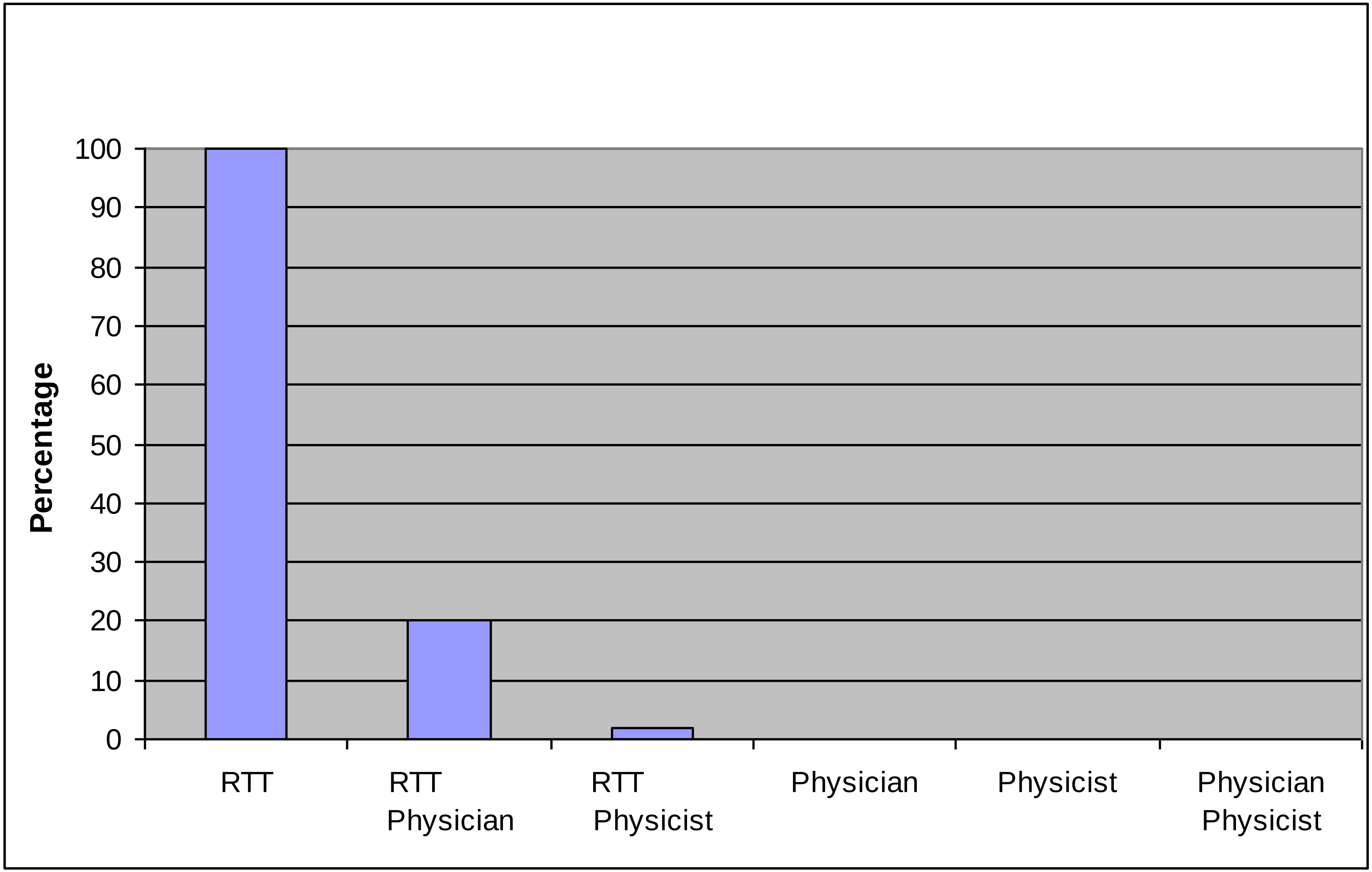


1. Indication of treatment

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

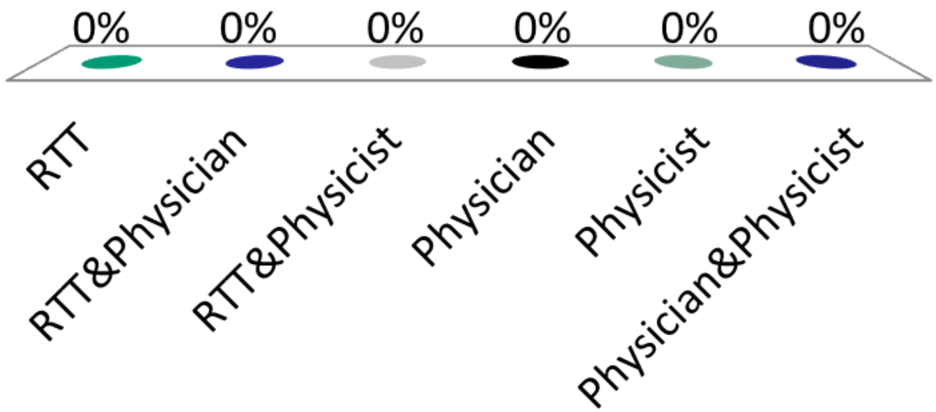


2. Pre-treatment Imaging

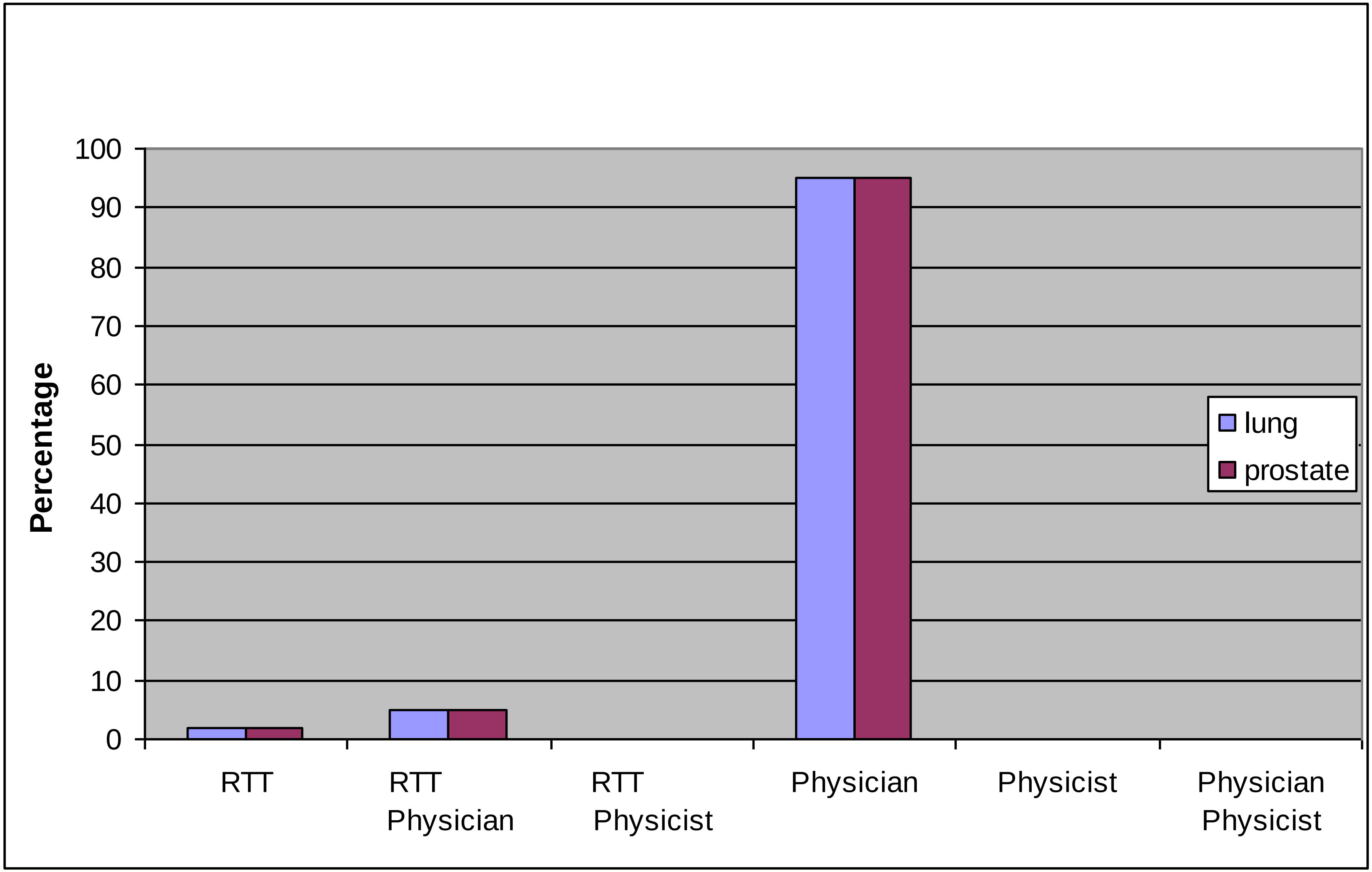


2. Pre treatment Imaging

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

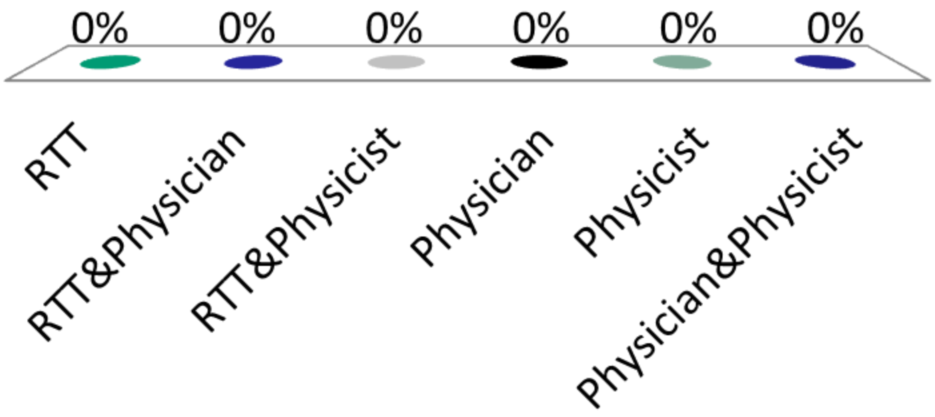


3. Delineation: Target Volume

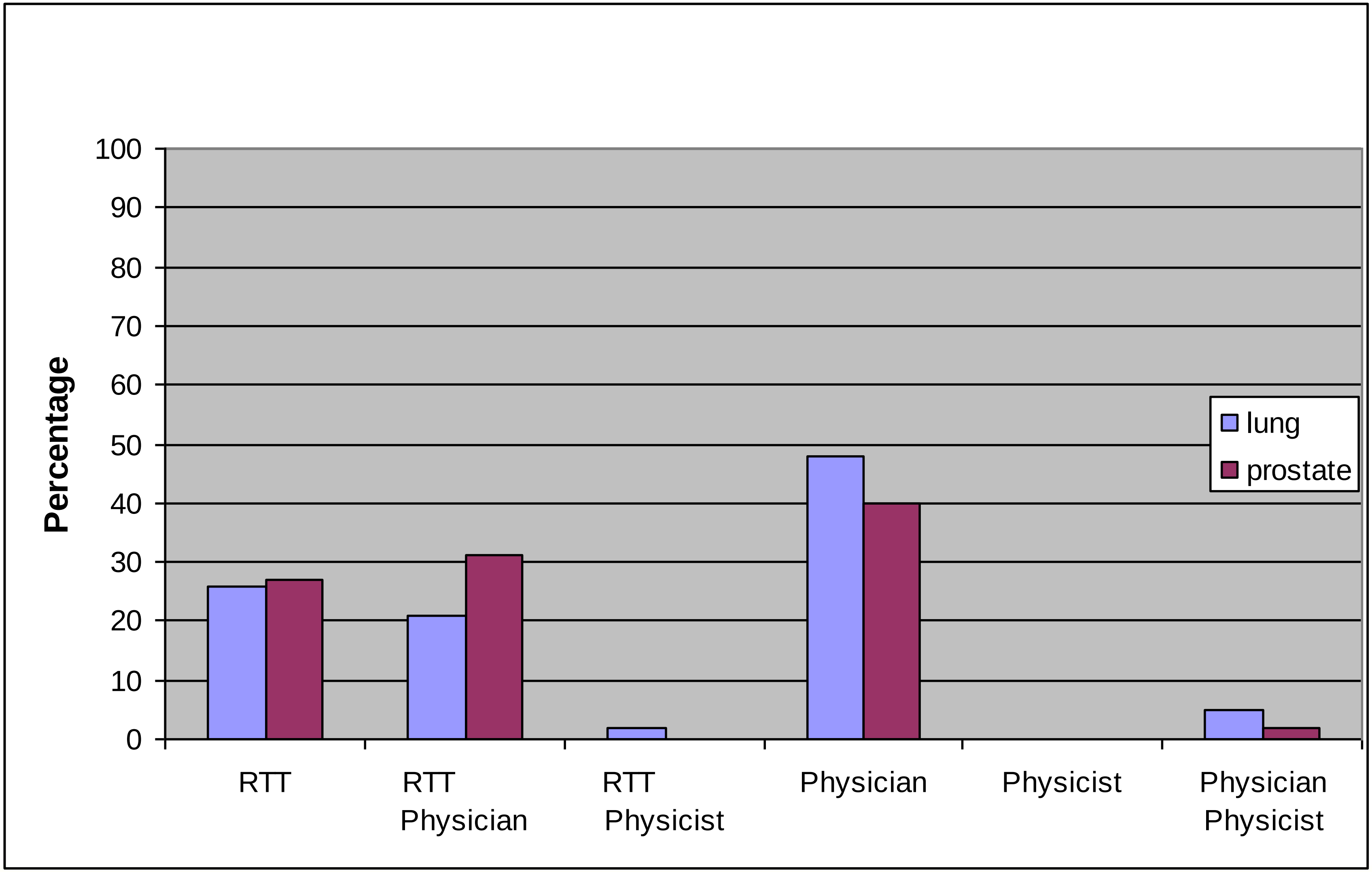


3. Delineation Target Volume

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

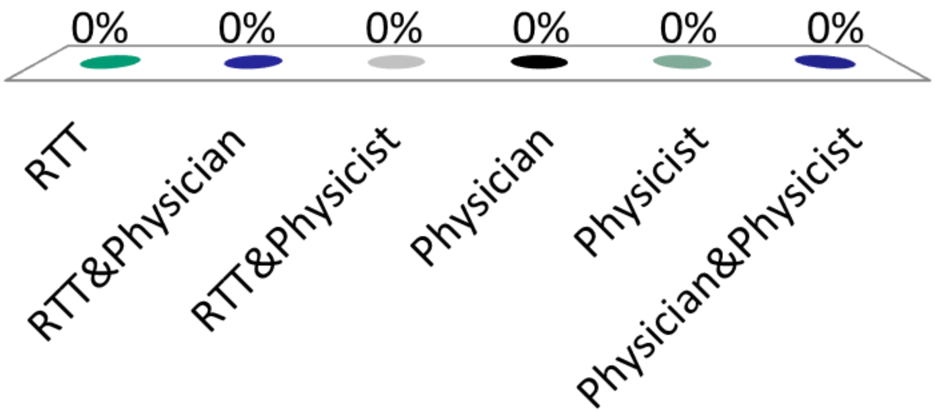


3. Delineation: Organs at Risk

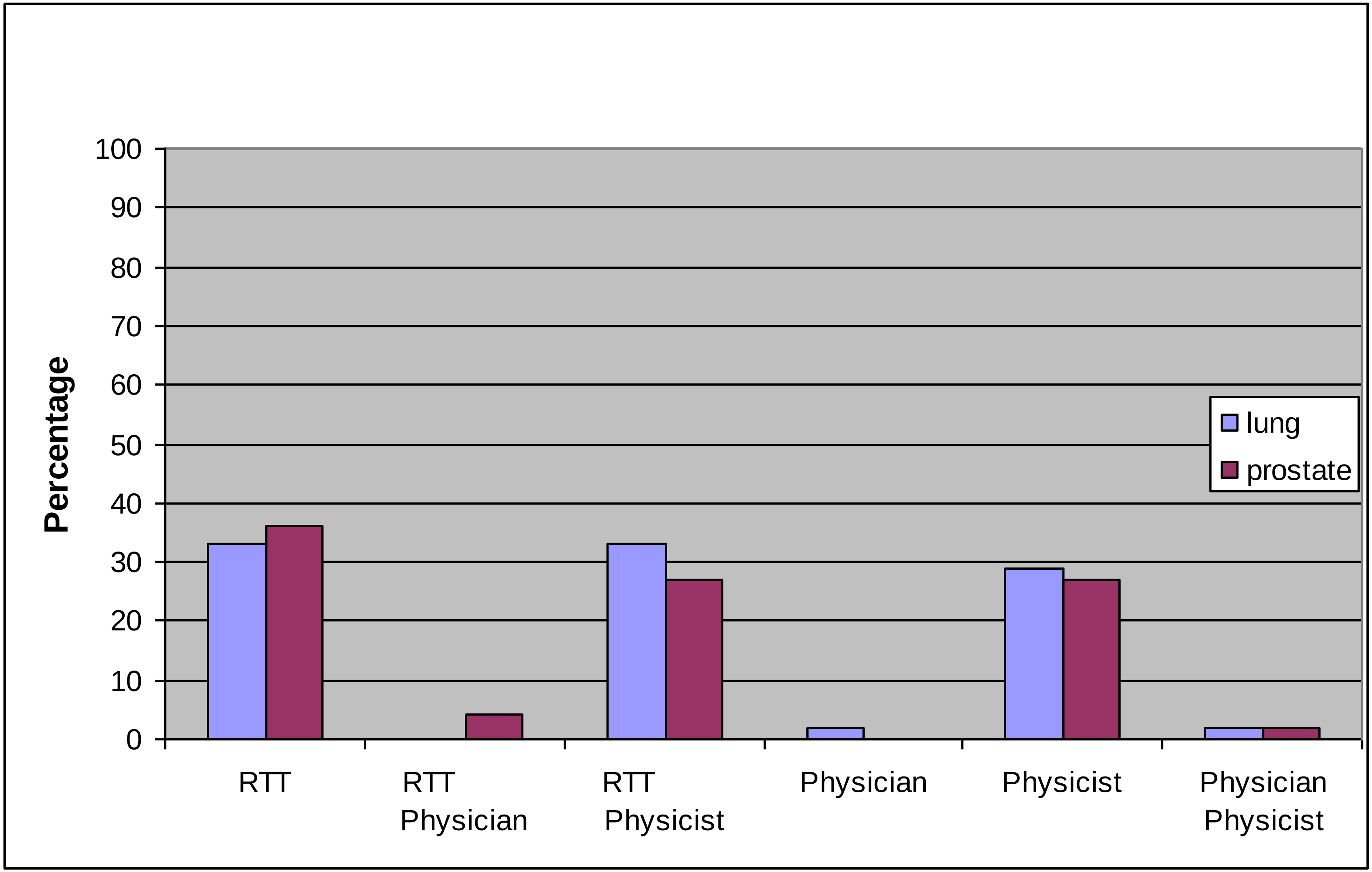


3. Delineation Organs at Risk

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist



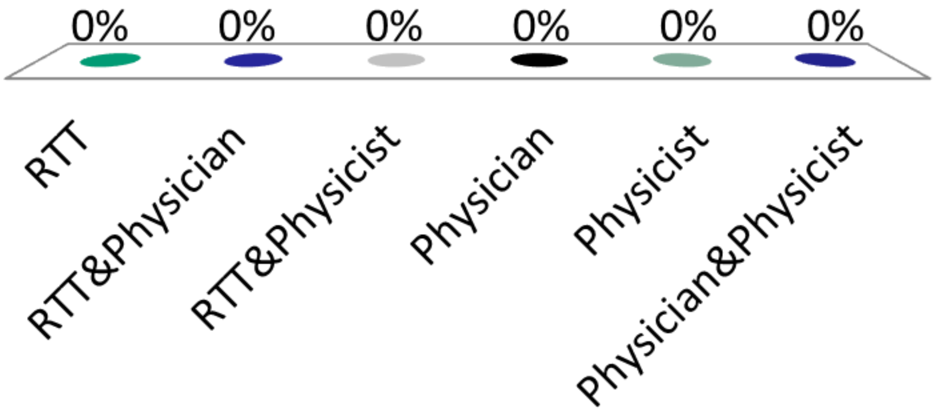
4. Treatment Planning



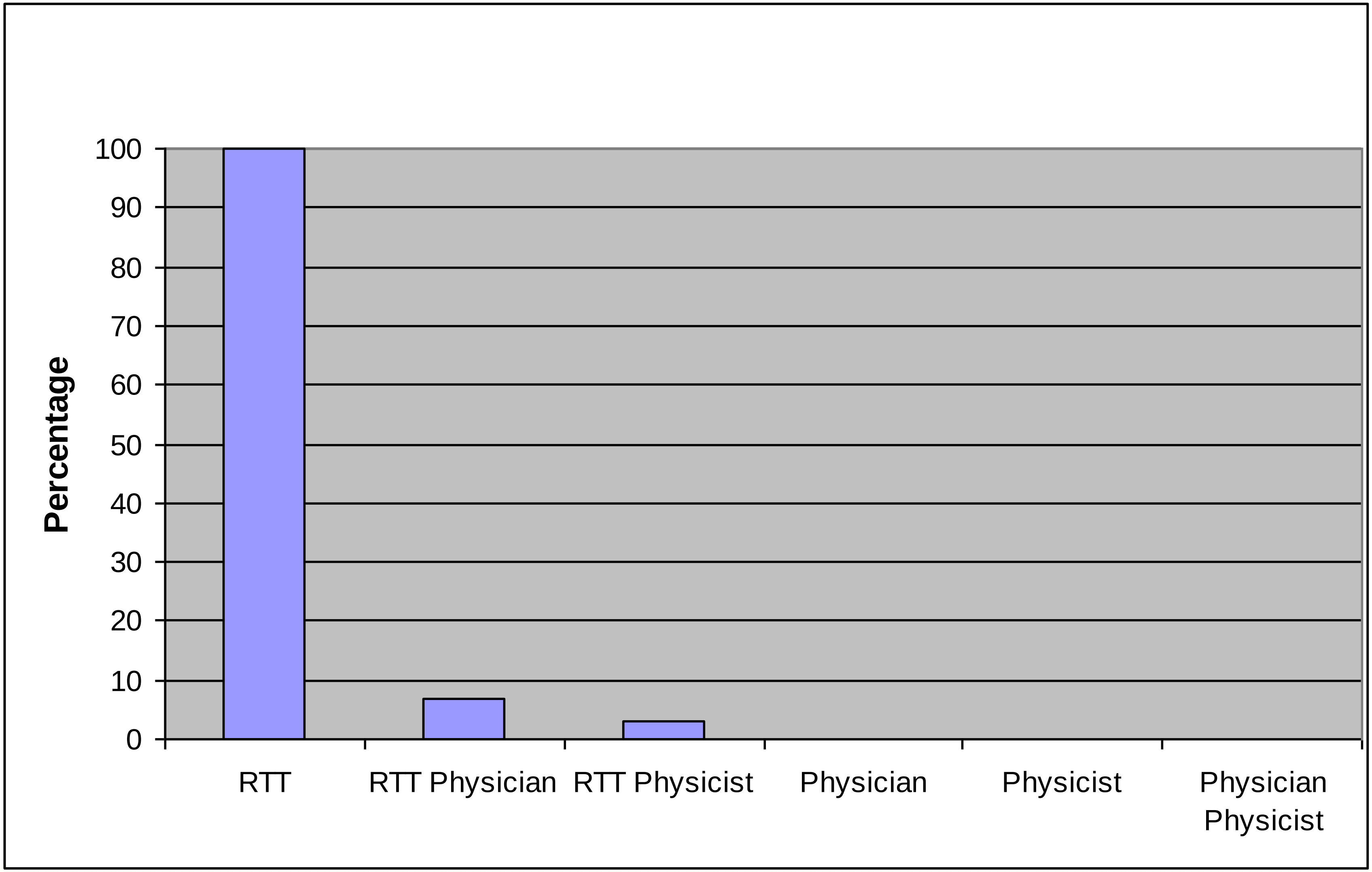
RTT: supervised and/or accepted by physician or physicist

4. Treatment Planning

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

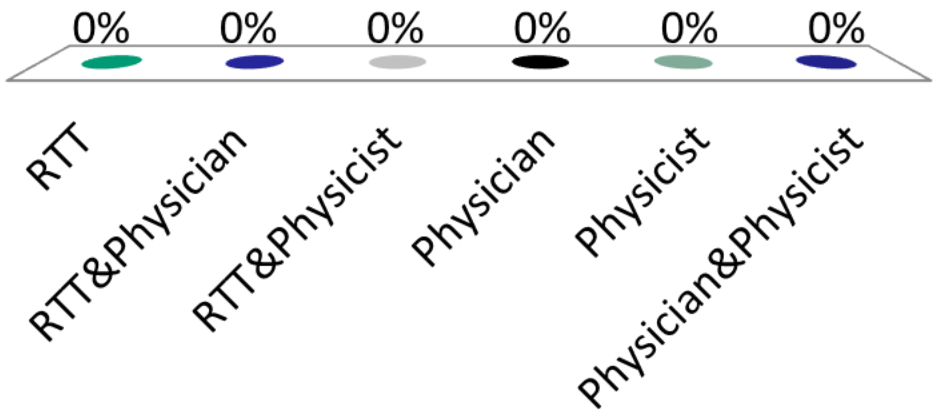


5. Treatment Delivery

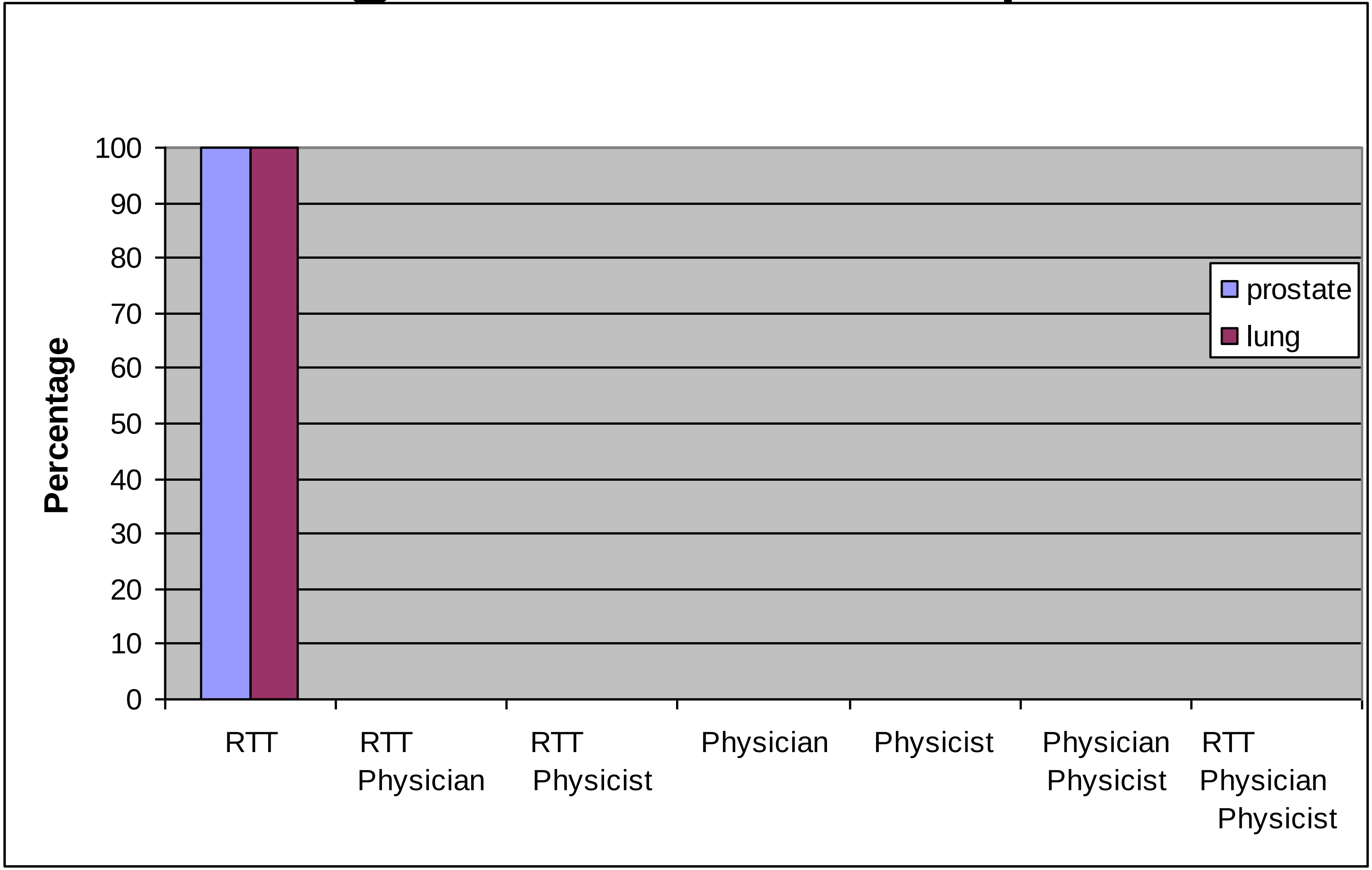


5. Treatment Delivery

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

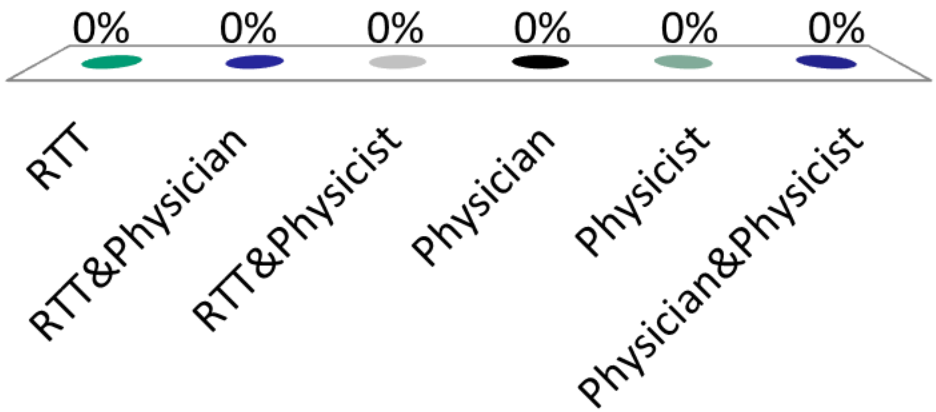


6a. Image Guidance: Acquisition

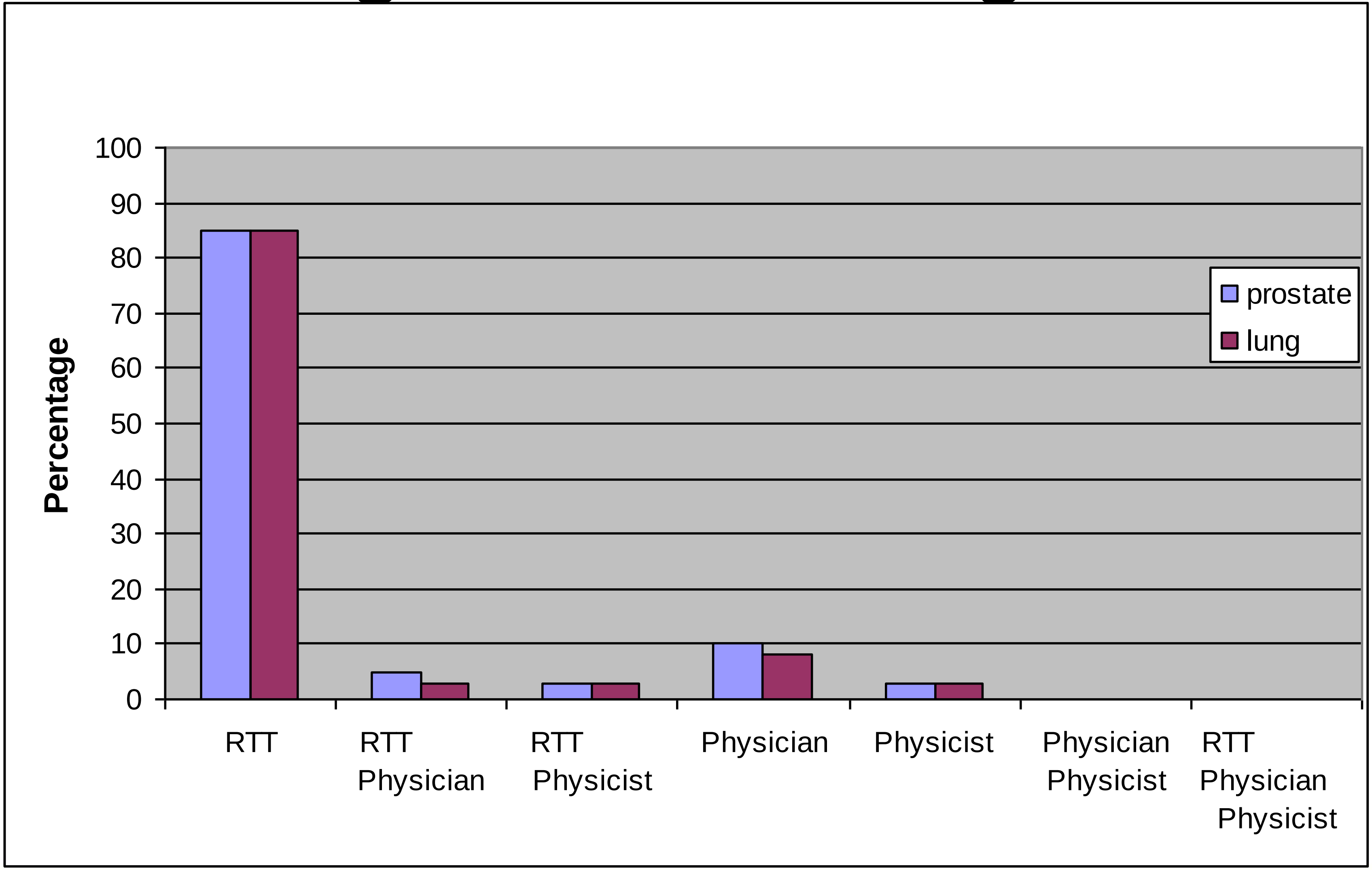


6a. Image guidance: Acquisition

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

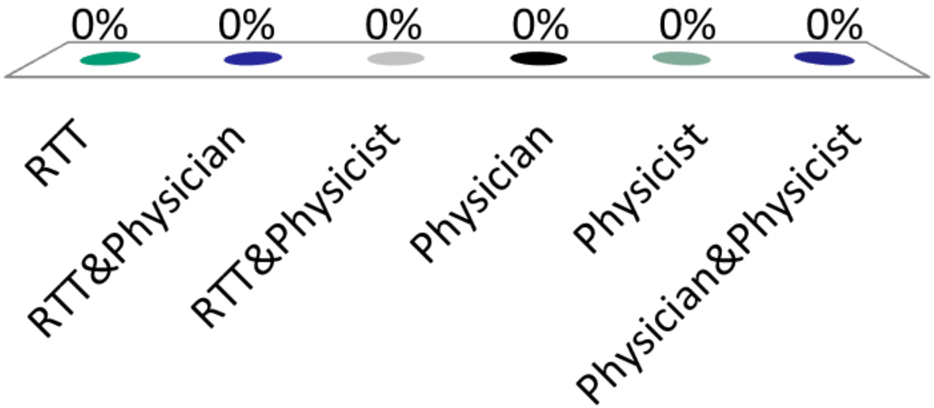


6b. Image Guidance: Registration

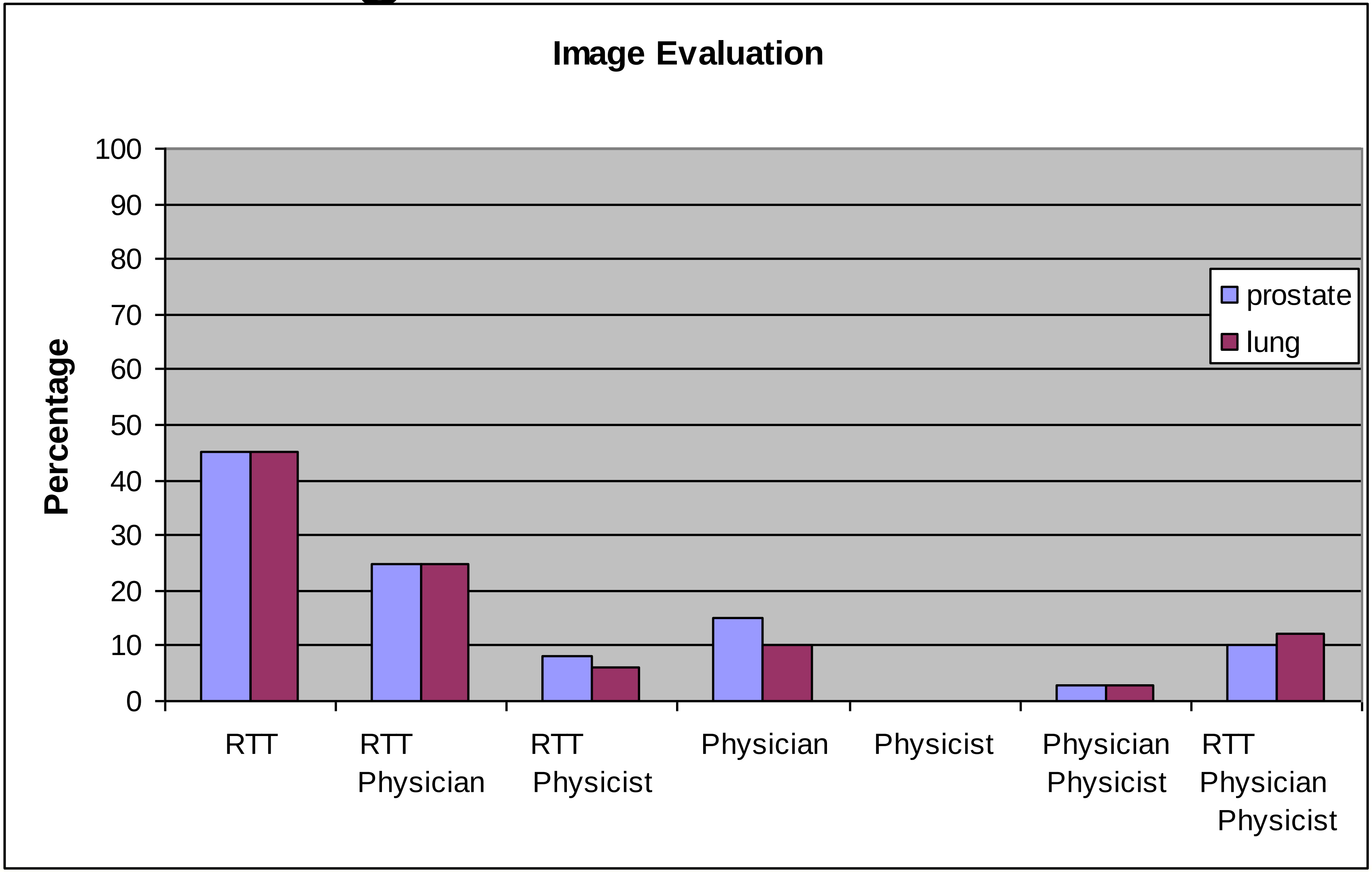


6b. Image Guidance: Registration

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist

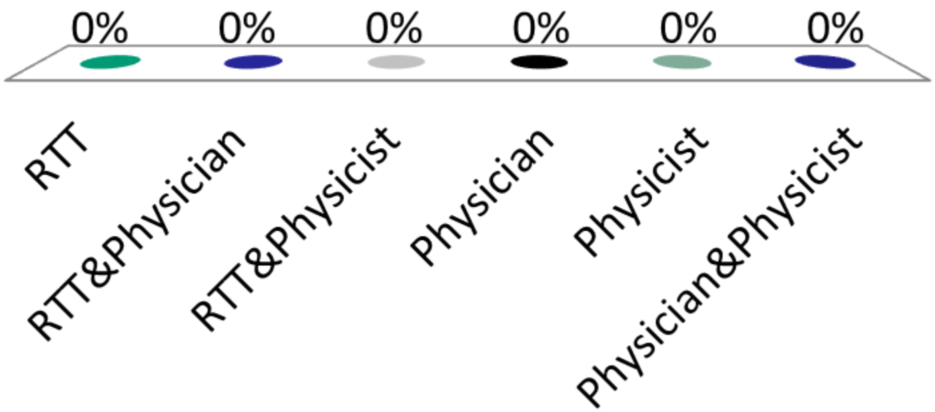


6c. Image Guidance: Evaluation



6c. Image Guidance: Evaluation

A. RTT
B. RTT&Physician
C. RTT&Physicist
D. Physician
E. Physicist
F. Physician&Physicist



Who is doing what?

Conclusion: Largest differences in ***Treatment Planning*** and ***Image Guidance***.

Why? What are the **variables** in the different departments that could have an influence on these differences?

- RTT – education / training
- Department size
- Resources per treatment machine
- IGRT modalities
- *Culture / History*
- *Money*

RTT training / Education

Majority:

- 3 years of classroom combined with clinical intern hours

→ bachelor degree

Also:

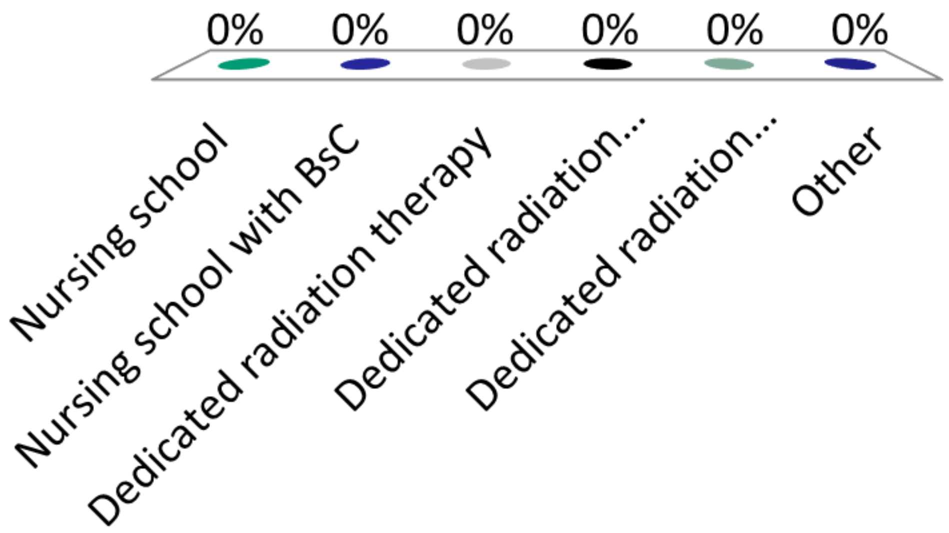
- 2 or 4 years of classroom combined with clinical intern hours

→ bachelor degree

- 3 years of nursing school with bachelor degree with additional theoretical or clinical RTT training ~1 year.

Training & Education

A. Nursing school
B. Nursing school with BsC
C. Dedicated radiation therapy
D. Dedicated radiation therapy with Bsc
E. Dedicated radiation therapy with MsC
F. Other



RTT training / Education

Majority:

- 3 years of classroom combined with clinical intern hours

  → bachelor degree

Does not correlate

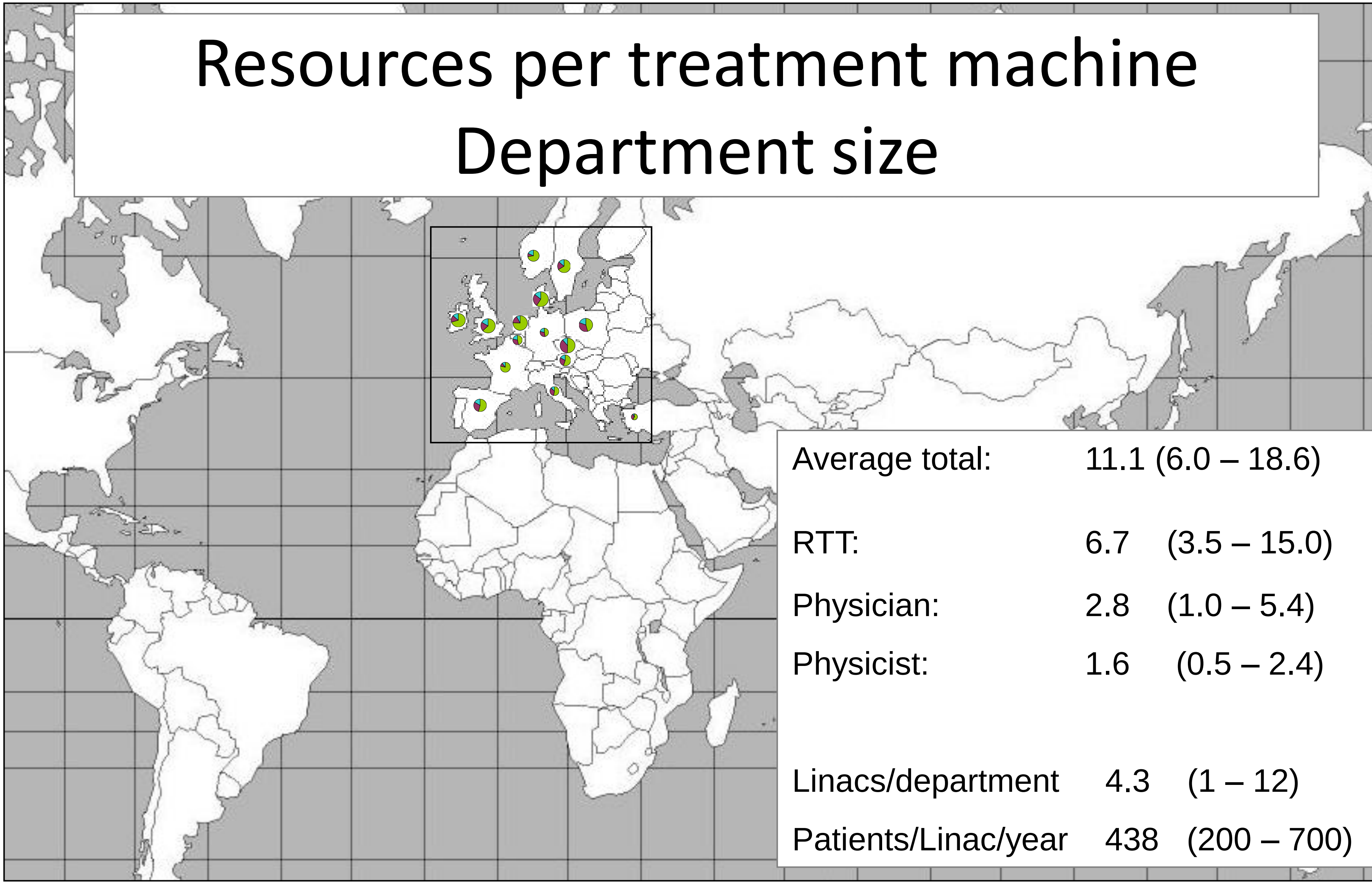
Also:

- 2 or 4 years of classroom combined with clinical intern hours

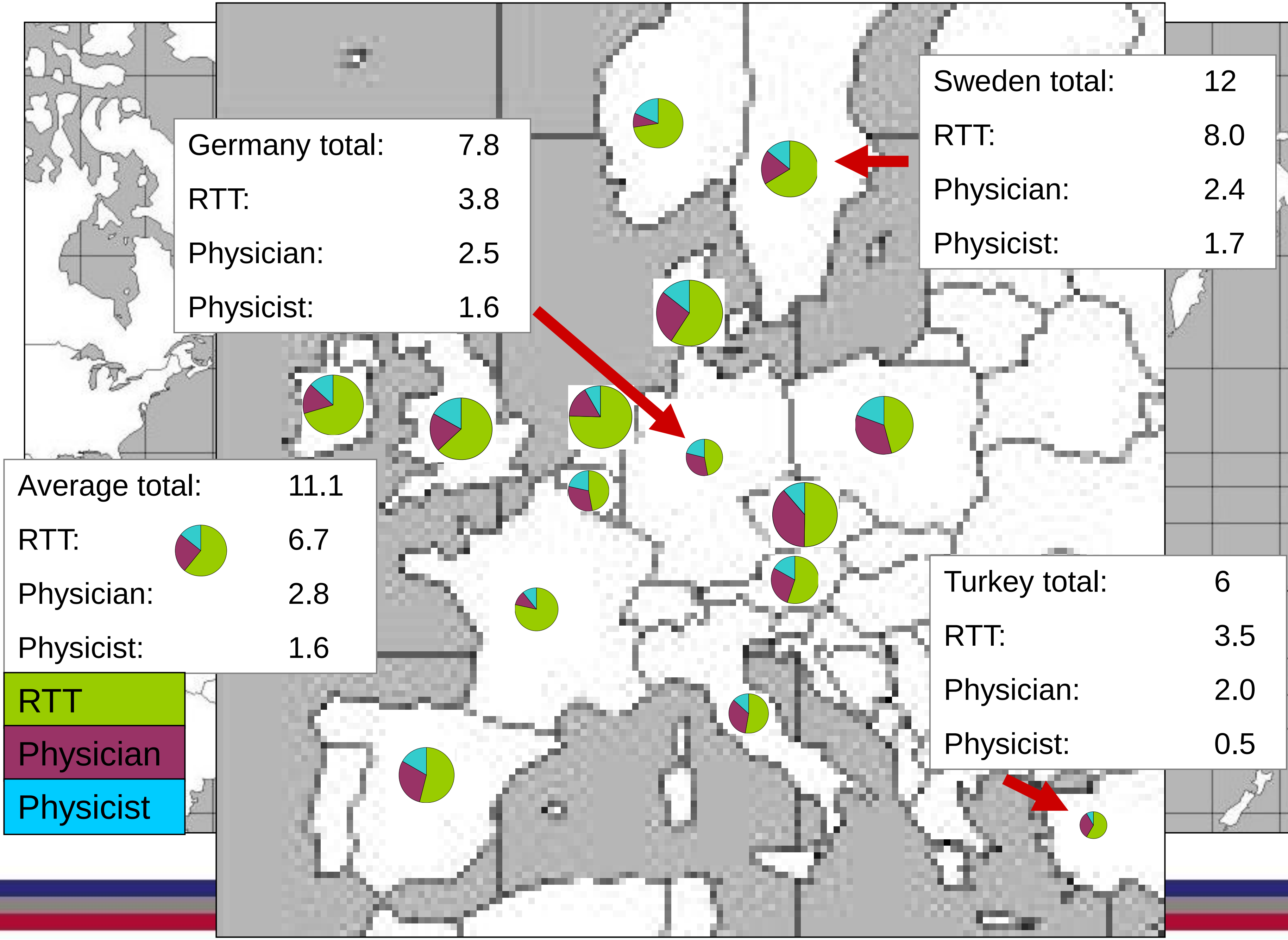
  → bachelor degree

- 3 years of nursing school with bachelor degree with additional theoretical or clinical RTT training ~1 year.

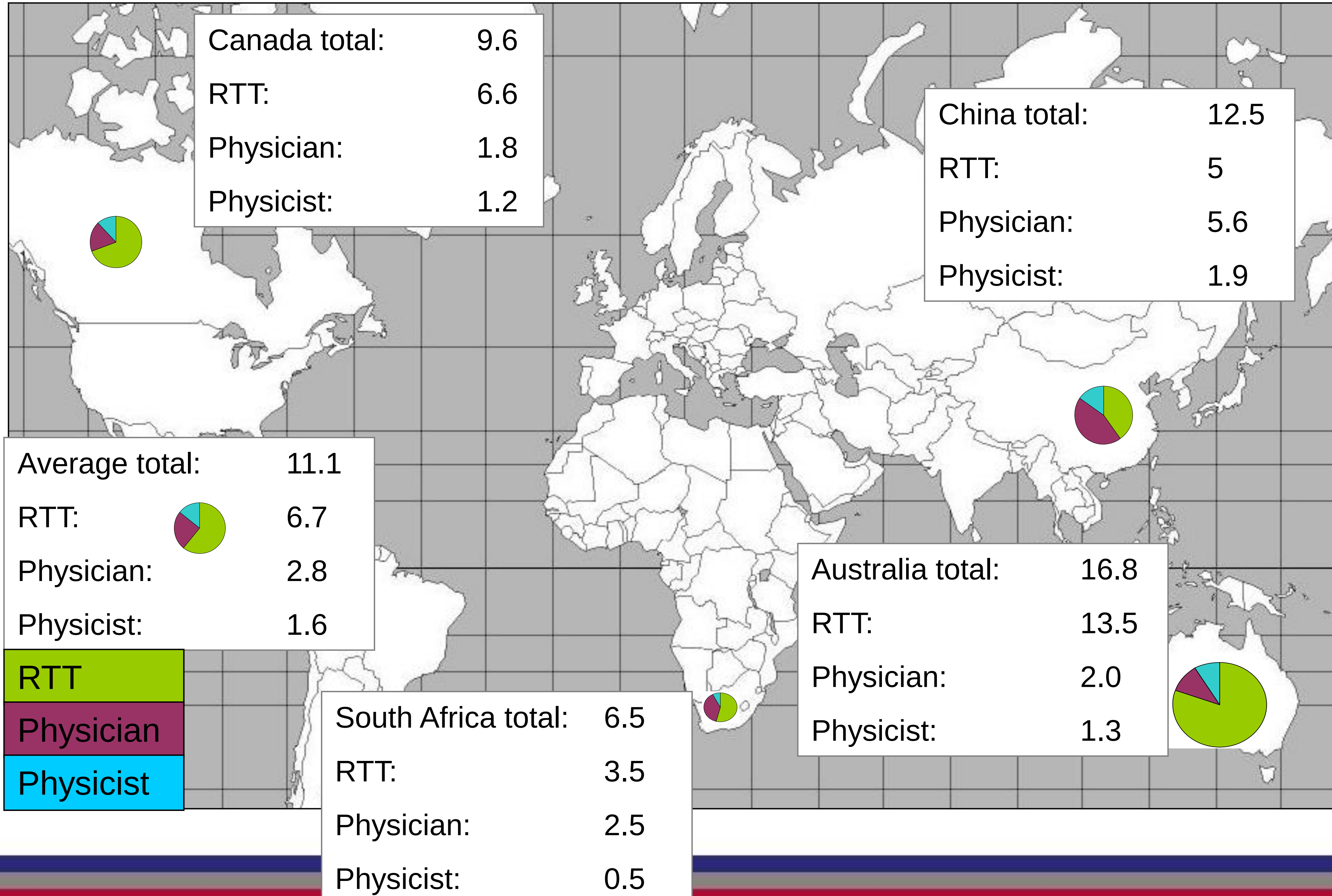
Resources per treatment machine
Department size



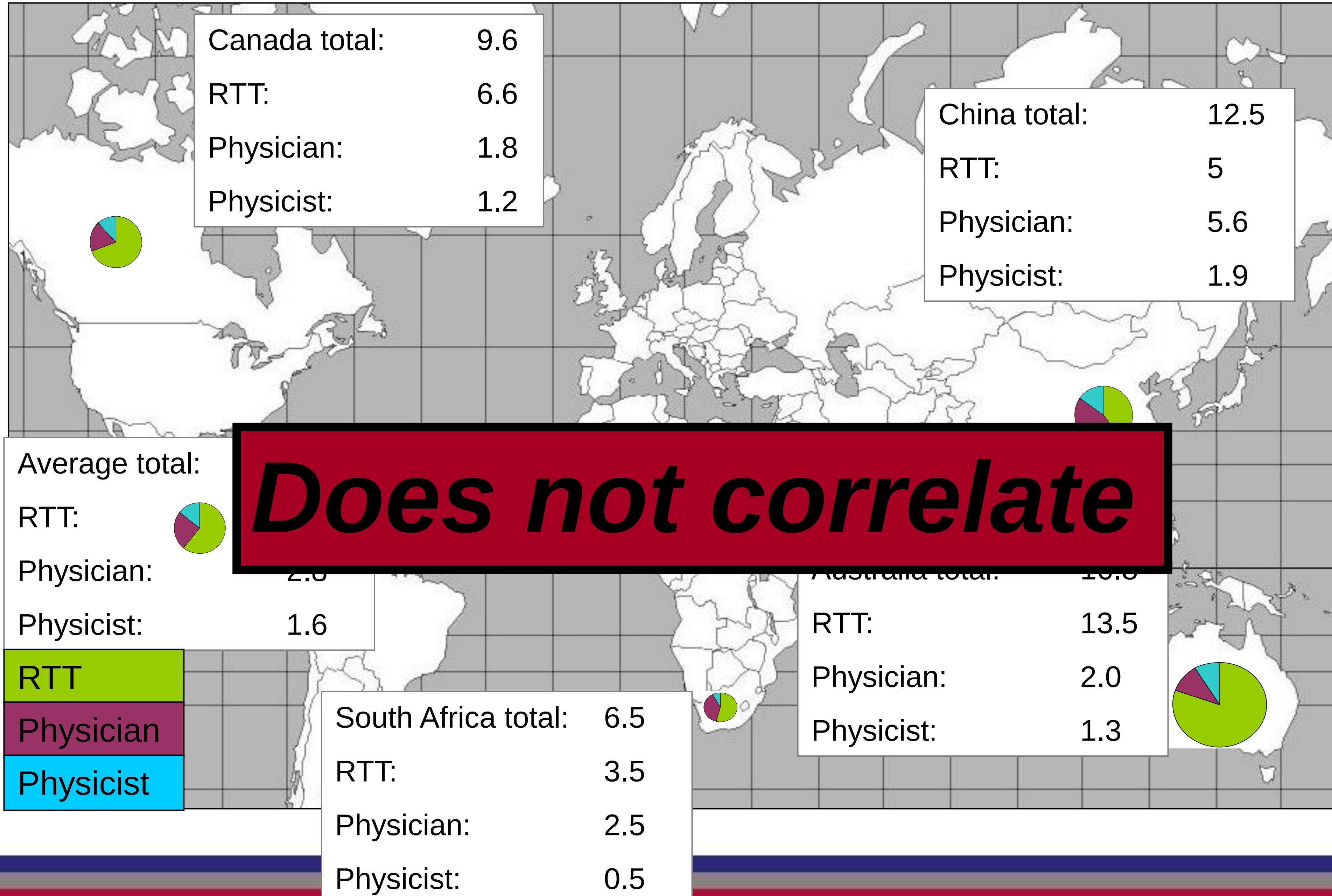
Average total:	11.1	(6.0 – 18.6)
RTT:	6.7	(3.5 – 15.0)
Physician:	2.8	(1.0 – 5.4)
Physicist:	1.6	(0.5 – 2.4)
Linacs/department	4.3	(1 – 12)
Patients/Linac/year	438	(200 – 700)



Germany total: 7.8
RTT: 3.8
Physician: 2.5
Physicist: 1.6
Sweden total: 12
RTT: 8.0
Physician: 2.4
Physicist: 1.7
Average total: 11.1
RTT: 6.7
Physician: 2.8
Physicist: 1.6
Turkey total: 6
RTT: 3.5
Physician: 2.0
Physicist: 0.5
RTT
Physician
Physicist



Canada total: 9.6
RTT: 6.6
Physician: 1.8
Physicist: 1.2
China total: 12.5
RTT: 5
Physician: 5.6
Physicist: 1.9
Average total: 11.1
RTT: 6.7
Physician: 2.8
Physicist: 1.6
RTT
Physician
Physicist
Australia total: 16.8
RTT: 13.5
Physician: 2.0
Physicist: 1.3
South Africa total: 6.5
RTT: 3.5
Physician: 2.5
Physicist: 0.5


Canada total: 9.6
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Physicist: 1.2
China total: 12.5
RTT: 5
Physician: 5.6
Physicist: 1.9
Average total:
RTT:
Physician:
Physicist: 1.6
Does not correlate
RTT: 13.5
Physician: 2.0
Physicist: 1.3
South Africa total: 6.5
RTT: 3.5
Physician: 2.5
Physicist: 0.5
RTT
Physician
Physicist

IGRT

<u>IGRT Modalities:</u>

2D Portal Images		79%
2D kV Images		6%
kV Conebeam CT	66%	
MV Conebeam CT	17%	

<u>IGRT protocols are:</u>

– **Tumor site specific**		**100%**
– Patient specific	18%	
– Physician specific		2%

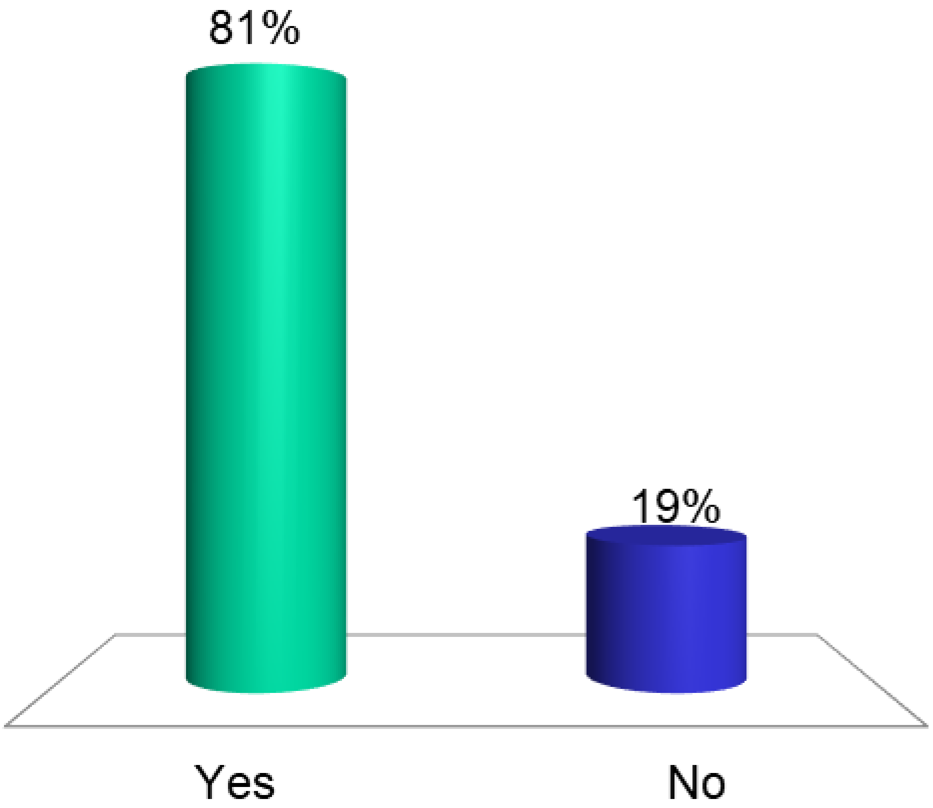
IGRT modalities: 2D MV

A. Yes

B. No

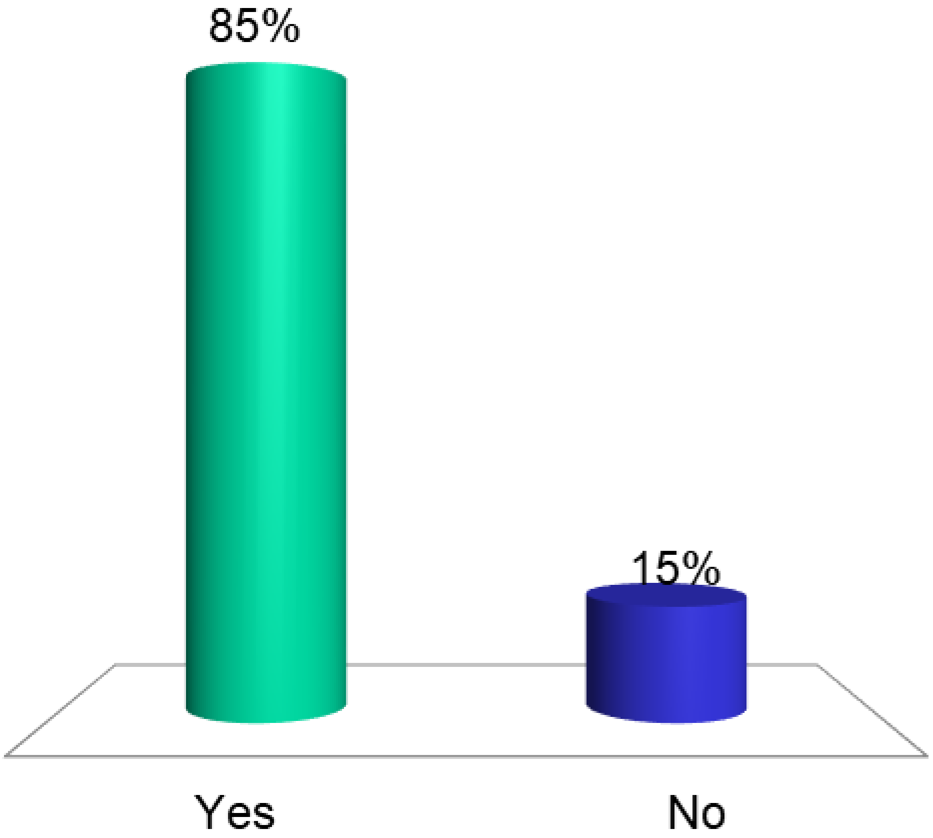
IGRT modalities: 2D kV

A. Yes
B. No



IGRT modalities: 3D kV

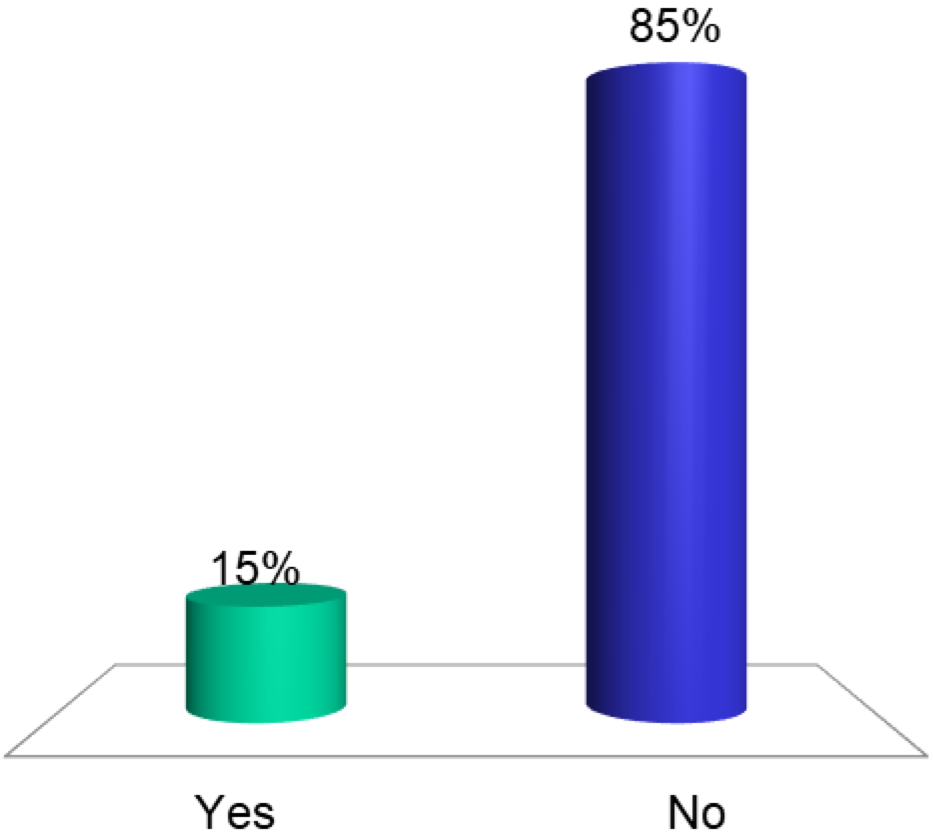
A. Yes
B. No



IGRT modalities: 3D MV

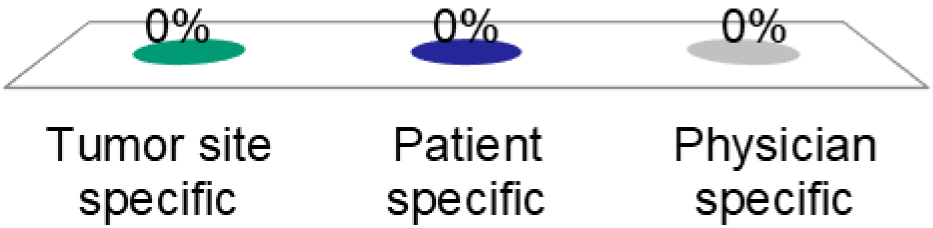
A. Yes

B. No



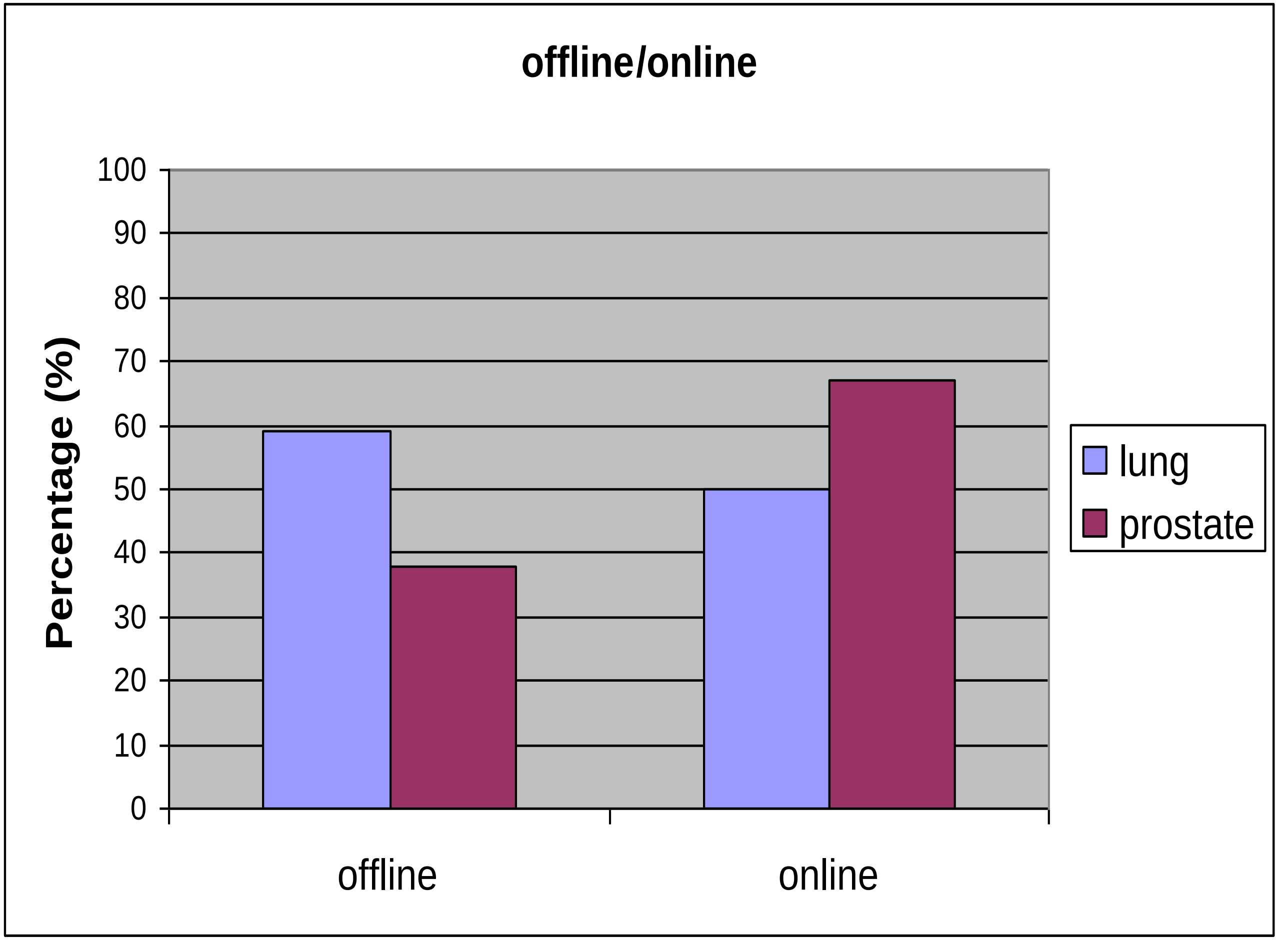
IGRT protocols are

A. Tumor site specific
B. Patient specific
C. Physician specific



IGRT

2D Portal Images	69%
kV Conebeam CT	67%
MV Conebeam CT	18%



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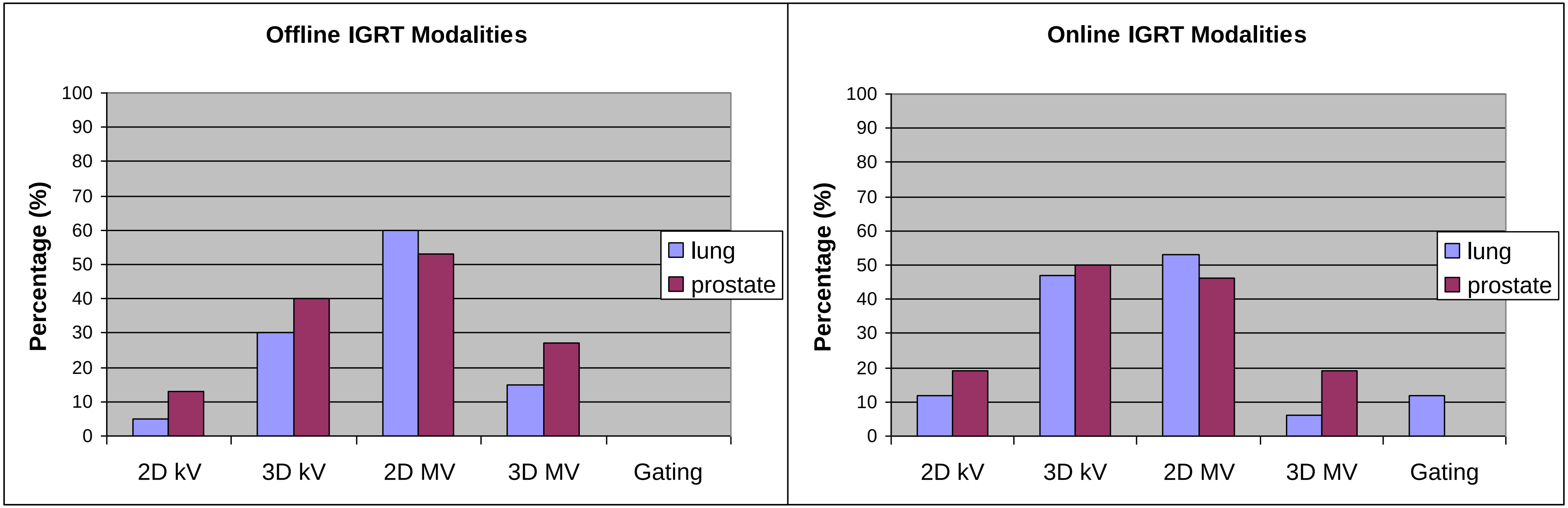

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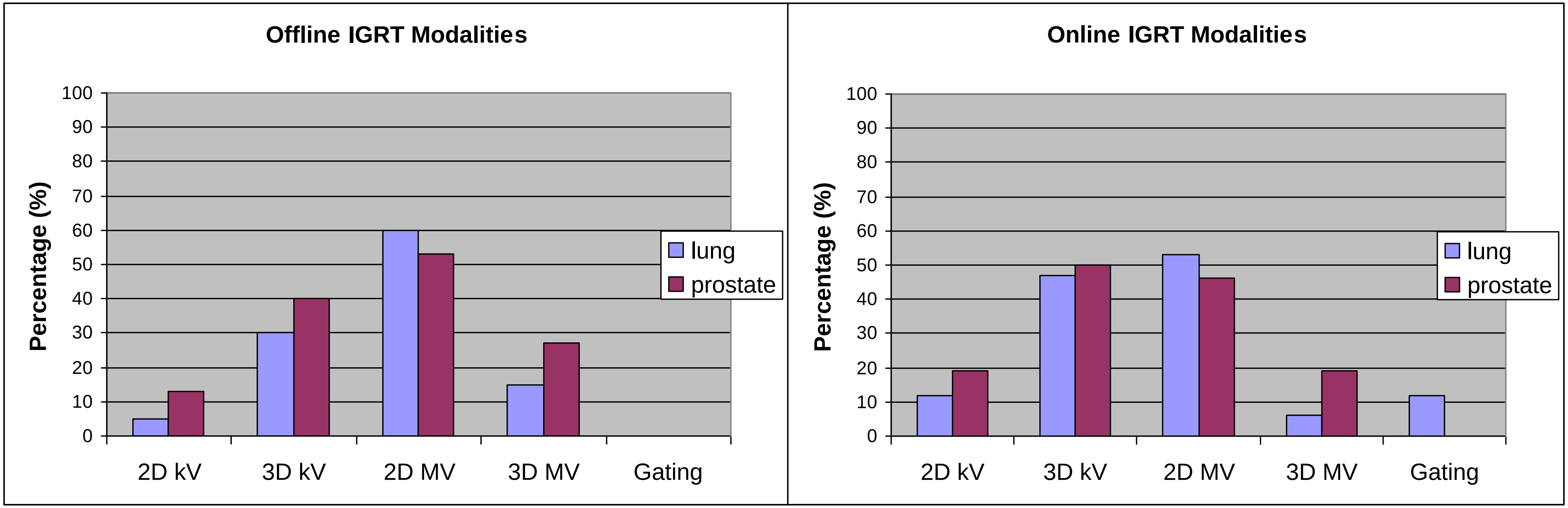
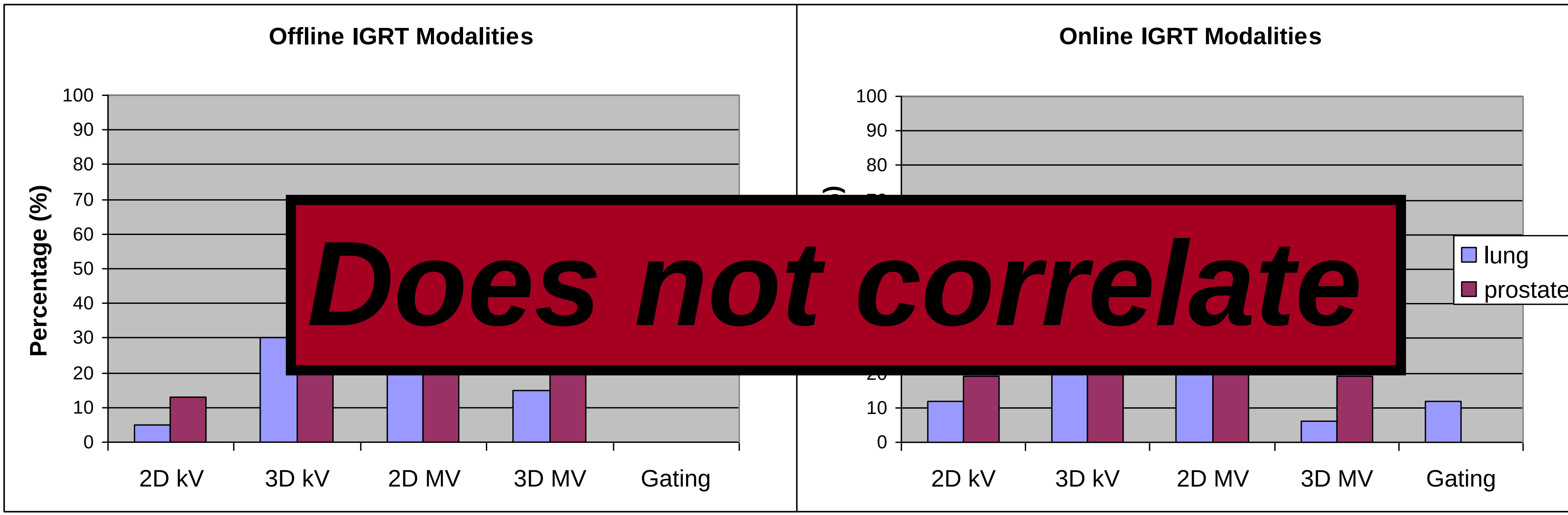


→ Adaptive Radiation Therapy… 0%

IGRT

2D Portal Images	69%
kV Conebeam CT	67%
MV Conebeam CT	18%

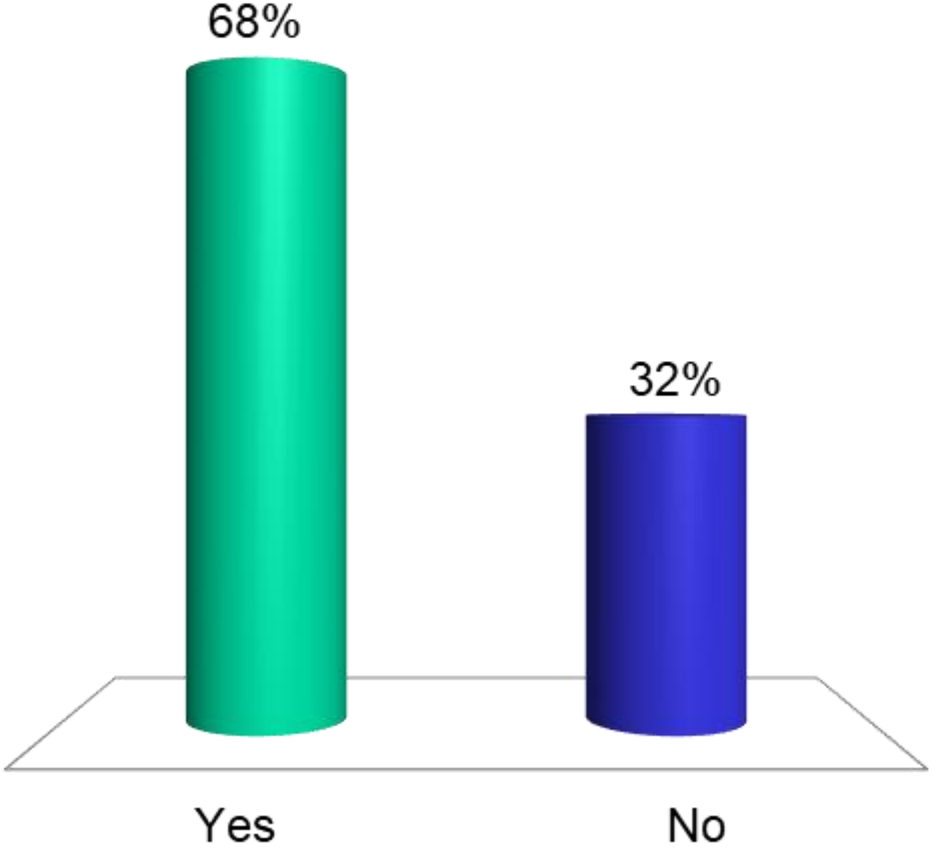


Adaptive Radiation Therapy… 0%

Who is doing ART?

A. Yes

B. No



Summary

Large variation between departments in:

- Amount of resources per linac
- Their distribution in different disciplines:
  - Treatment planning
  - IGRT evaluation

Some Variables

- RTT training and education
- Department size
- Resources per treatment machine
- IGRT Modalities
  - » Culture – History
  - » Money

Not decisive

Might consider different solutions?

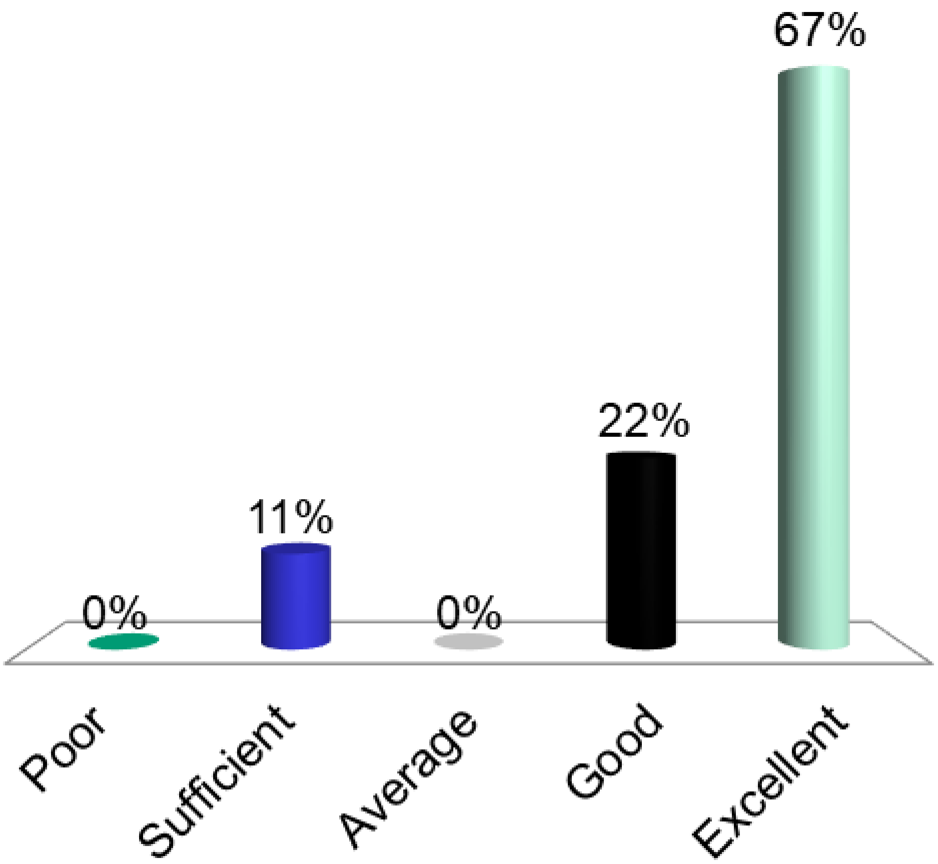
Questions & Discussion

m.a.j.dejong@amc.uva.nl

NKI-AVL
The Netherlands Cancer Institute
Antoni van Leeuwenhoek Hospital

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent



comments can be written in Survey Monkey

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Incident management

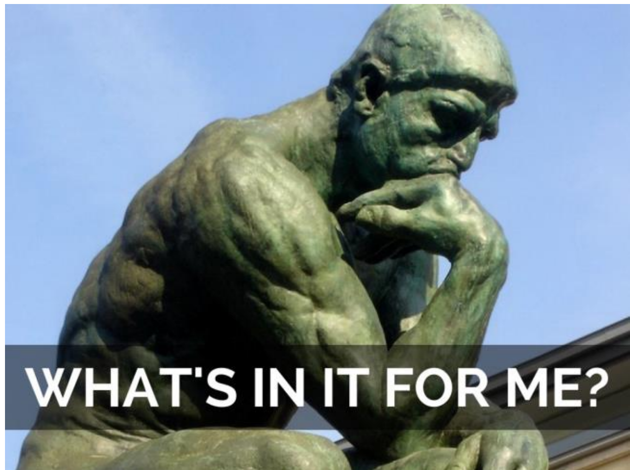
Mirjana Josipovic

Dept. of Oncology, Rigshospitalet
& Niels Bohr Institute, University of Copenhagen
Denmark

Advanced skills in modern radiotherapy

Intended learning outcomes

- Define an incident in radiotherapy context
- Discuss the importance of an incident reporting system
- Analyse the potential causes for an incident to have happened



Definitions

Incident

- Any unintended event, including operating errors, equipment failures, initiating events, accident precursors, near misses or other mishaps, or unauthorized act, malicious or non-malicious, the consequences or potential consequences of which are not negligible from the point of view of protection or safety.

(IAEA Safety Glossary, 2007)

Radiation incident

- The delivery of radiation during a course of RT is other than intended by prescription, and could have or did result in unnecessary harm to the patient.

(Towards safer radiotherapy, BJR 2008)

Incident

- An *unplanned, undesired* event that hinders completion of a task and may cause injury, illness, or property damage or some combination of all three in varying degrees from minor to catastrophic. Unplanned and undesired do not mean *unable to prevent*.

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Unintended does not mean *unable to prevent!*

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Incidents

Actual incident = accident:

- The unforeseen event, that has affected the treatment of the patient

Potential incident:

- "Near miss"
- The unforeseen event, that was discovered and halted before it affected the treatment of the patient

From IAEA database of radiation incidents

Independent calculation checks 1998-2003 on 27830 charts/plans

An unintended “potential incident” was found:
• in ~3 % of all plans, during primary check
• in ~½ % of all plans, during secondary check

Actual incidents = accidents:
• in ~¼ % of cases

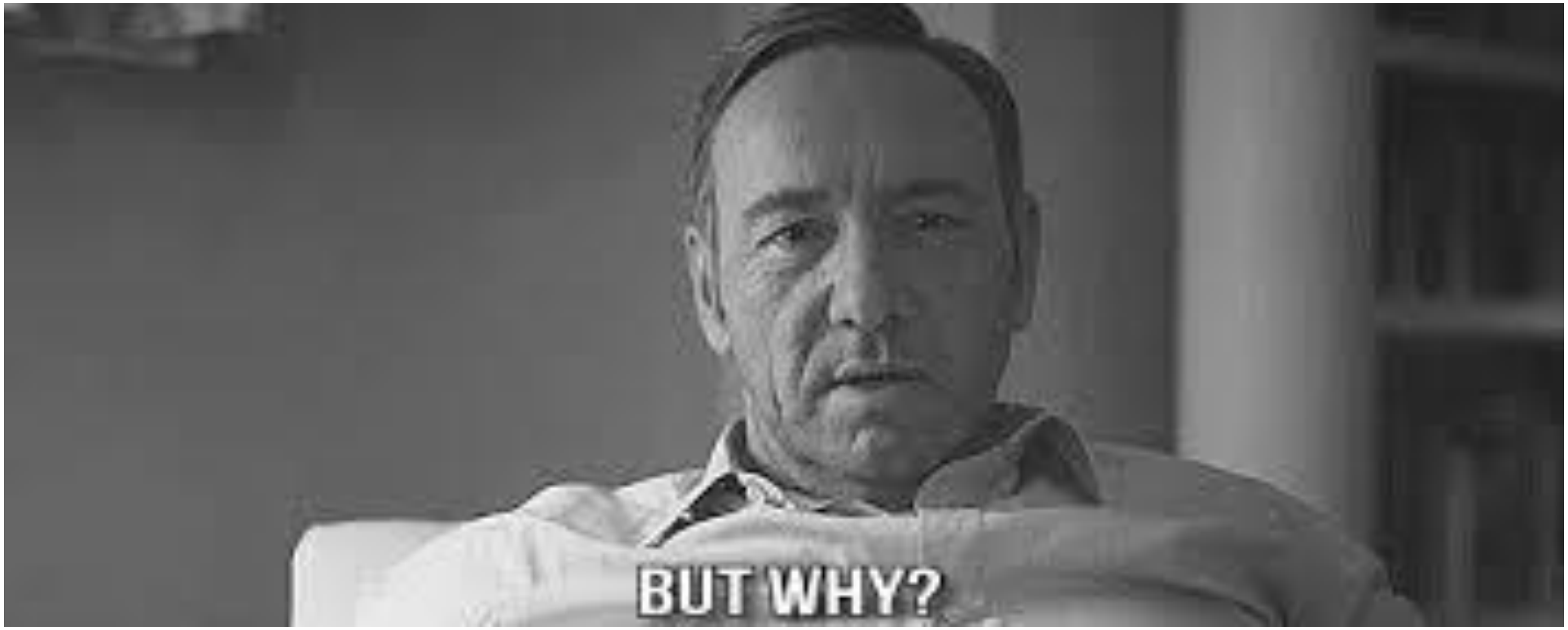
For each actual incident, ~14 potential incidents were found through checking.

An incident frequency of 3% could be seen in a “typical clinic”.

Incidents are more numerous than accidents:

- there are more opportunities to learn and improve the safety, than by only looking at major accidents.

But we do have a check procedure…



Incident frequency in modern radiotherapy

3011 reported incidents from 2012-2015 in single institution

- 552 potentially severe or critical

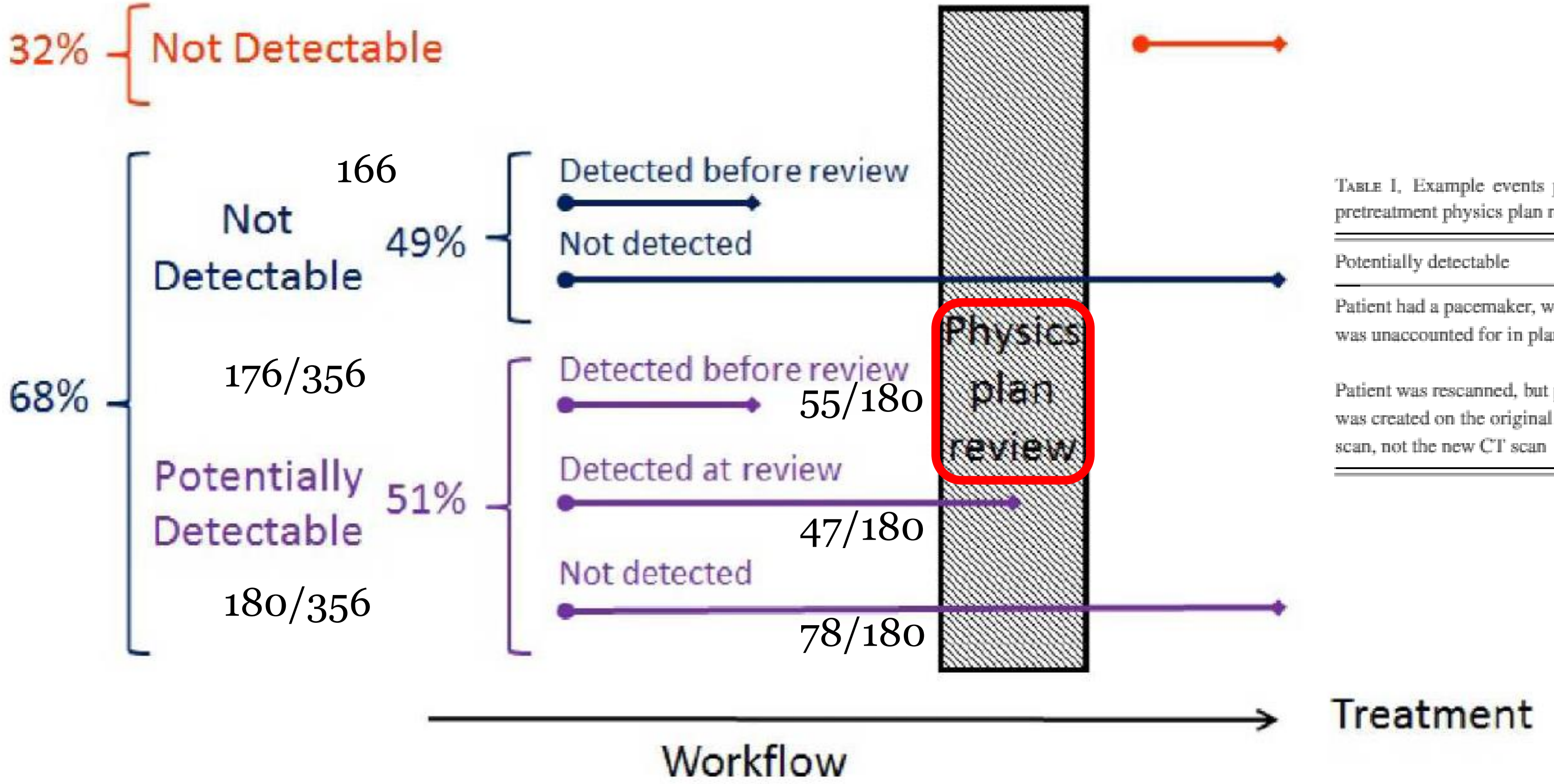


TABLE I. Example events potentially detectable and not detectable by the pretreatment physics plan review.

Potentially detectable	Not detectable
Patient had a pacemaker, which was unaccounted for in planning	Patient starts oral chemotherapy not on the day of radiation therapy as prescribed, but earlier
Patient was rescanned, but plan was created on the original CT scan, not the new CT scan	Physician changes the prescription midway through the treatment, but the change is not communicated

Gopan et al Med Phys 2016

Incident frequency in modern radiotherapy

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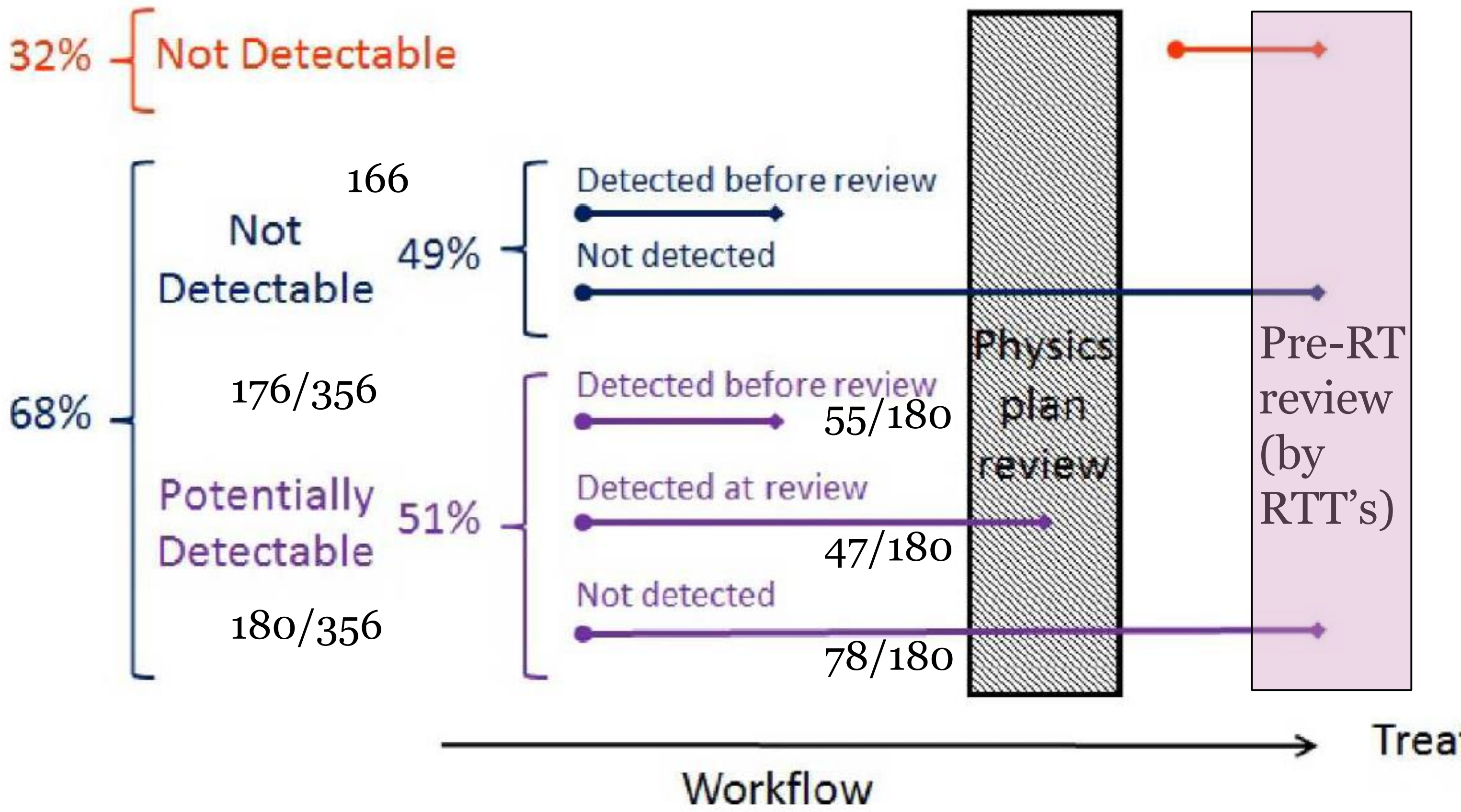

	Departmental ($n = 180$)
Isocenter verified (i.e., localization in TPS)	39
DRR's associated with correct beams and are appropriate (e.g., structures on)	17
Plan matched Rx (dose, normalization, etc.)	12
Fields scheduled appropriately (including imaging)	8
Field parameters verified vs plan (angles, MU, wedges, etc.)	7

- Majority of potentially severe incidents occure before physics review (68%) – ~1/3 of them is detected by review

Gopan et al Med Phys 2016

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Incident frequency in modern radiotherapy

3011 reported incidents from 2012-2015 in single institution

TABLE III. The percentage of potentially detectable and all events from the institutional ILS, which originated and were found at each step in the radiation therapy process.

Workflow step	% of potentially detectable events originating at this step	% of potentially detectable events found at this step	% of ALL events originating at this step	% of ALL events found at this step
Patient assessment	7.7	0.6	22.4	3.5
Simulation	28.2	3.3	13.0	8.2
Treatment planning	49.2	26.5	29.6	18.9
Plan review	1.7	38.1	4.7	22.3
Treatment delivery	2.8	14.9	8.9	29.1
On-treatment QM	1.6	8.8	2.8	9.4
Post-tx completion	0	0.6	11.4	6.6
Equipment and software QM	2.2	6.1	0.3	1.4
Not-defined	6.6	1.1	6.8	0.5

- Manual checks
- Majority detected by plan review – need for improvement
- Recommendation for automatisation of check procedures

Gopan et al Med Phys 2016

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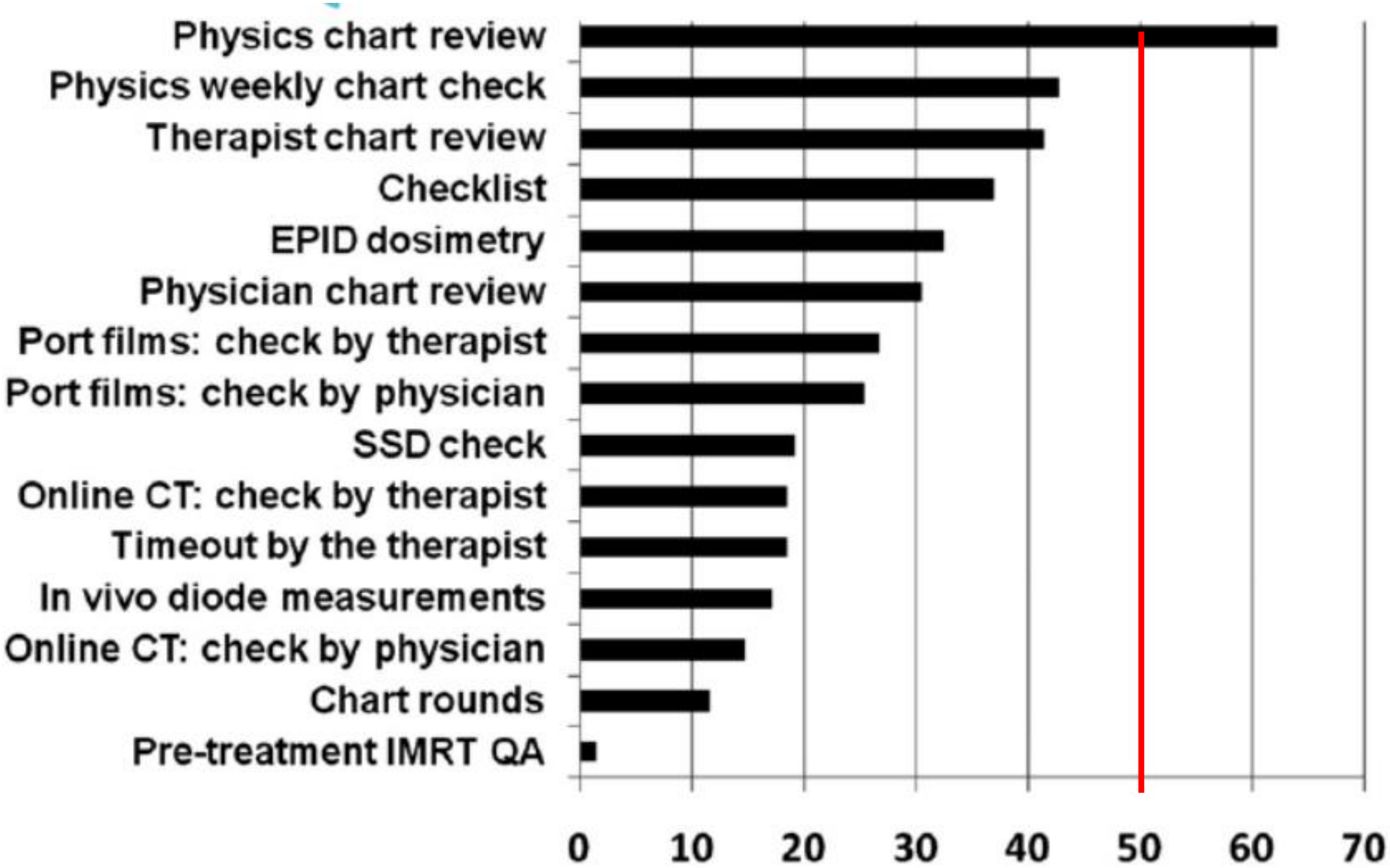
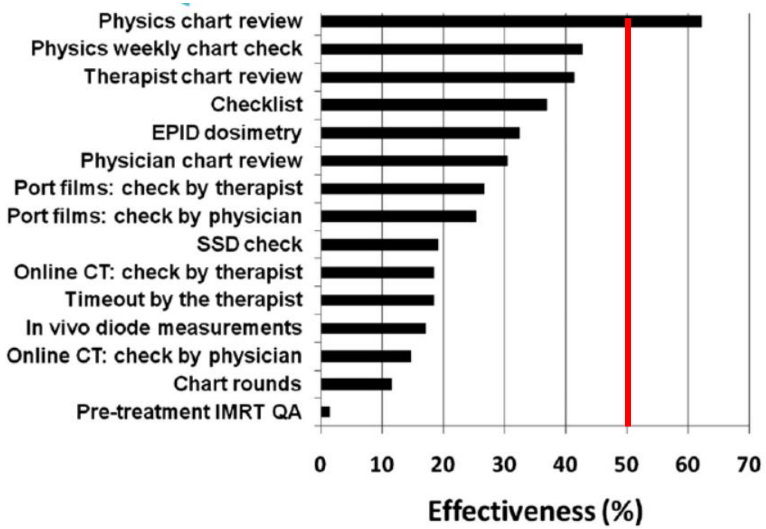
Are the check tools / procedures effective?



Effectiveness of a SINGLE check procedure [%]

Ford et al IJROBP 2012

Are the check tools / procedures effective?

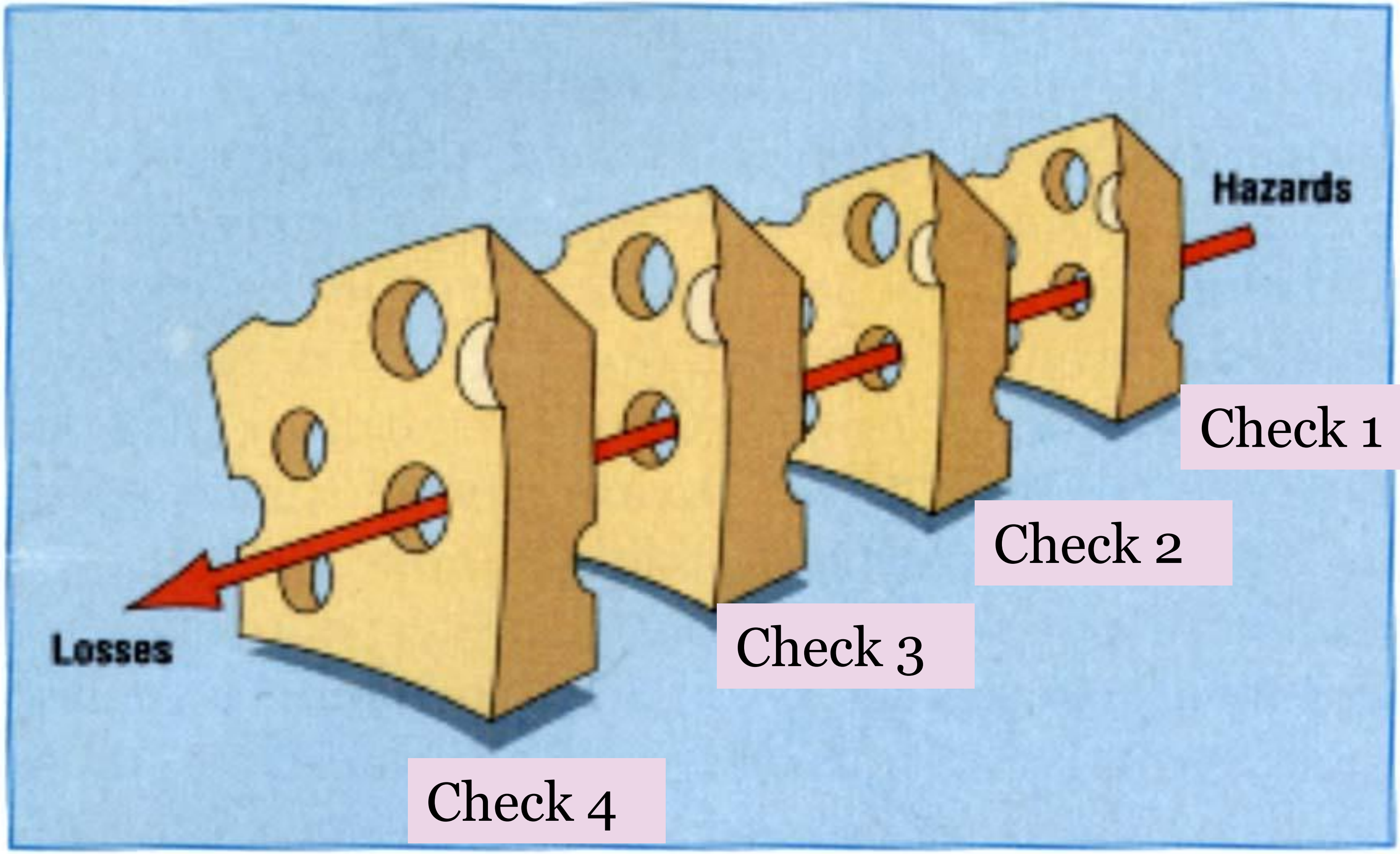


Combined effect of check procedures:

- 7 checks → 97% effectiveness

Ford et al IJROBP 2012

Swiss cheese model of accident causation



J Reason BMJ 2000

Many incidents have a variable magnitude:

- same type of incident can have different impact on different patients / treatment sites

- next time the same incident happens, it may become an accident

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Incident prevention to improve patient safety

Proactive

- Patient safety rounds
- Leadership tool

Reactive

- Reporting and analysing incidents

Incident reporting

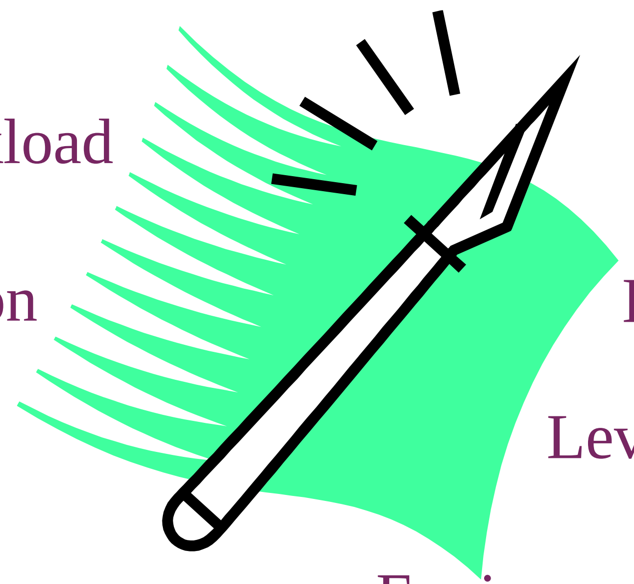
- Blaming individuals is emotionally more satisfying than targeting institutions

- We cannot change the human condition, but we can change the conditions under which the humans work

Human Error: models and management - J Reason, BMJ 2000

Incident reporting

- Incident reporting must not result in disciplinary investigation as a consequence of reporting



Incident reporting

internal ⟷ external

- locally
- inside your dept / institution

external

- outside your organisation
- sharing with peers

mandatory ⟷ voluntary

- to regulatory authorities

voluntary

- to professional (inter)national organisation

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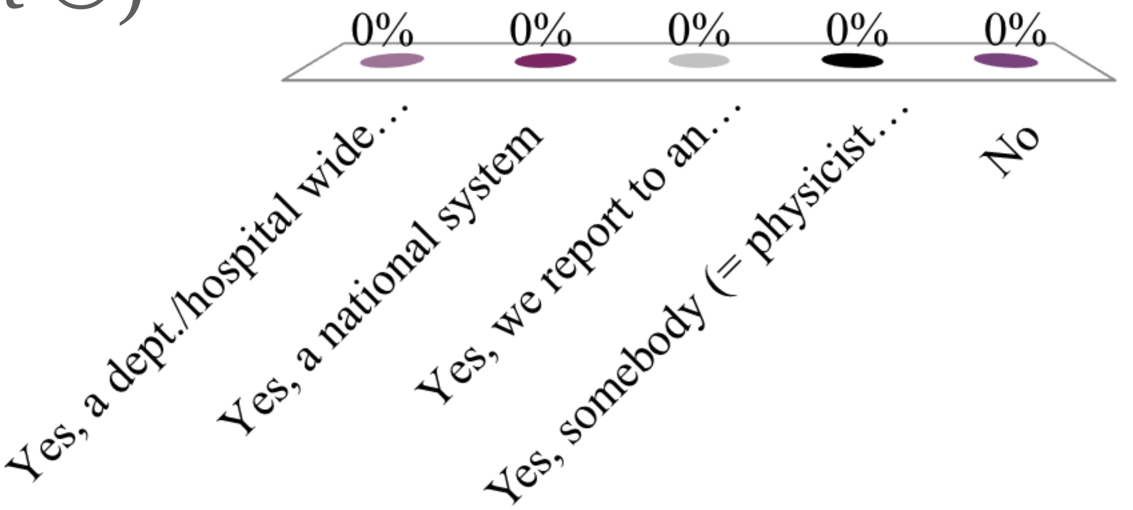
Incident reporting

internal ⟷ external

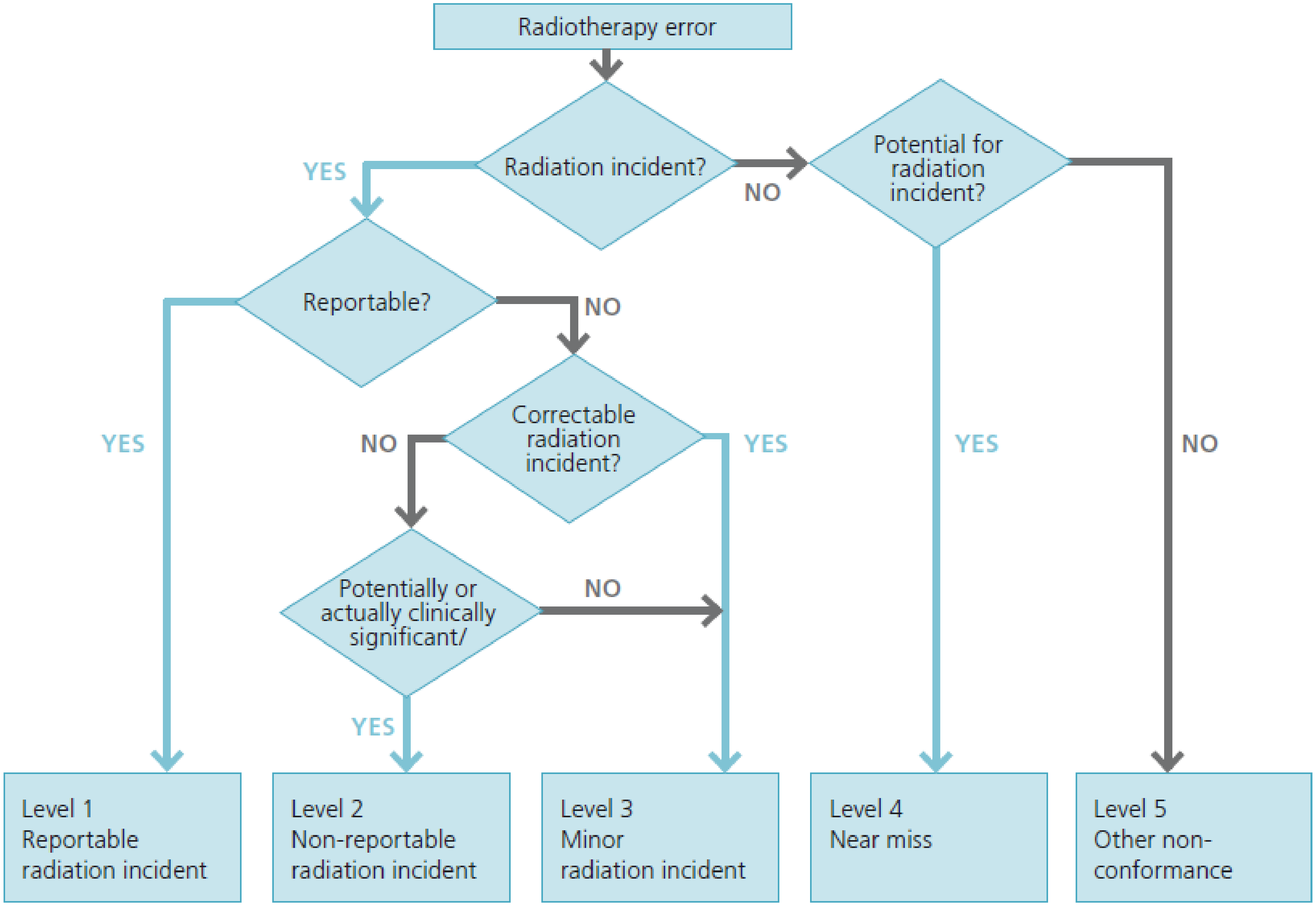
- Bigger “pool of events” facilitate better identification of safety critical steps in the process of radiotherapy
- Incidents from another hospital can lead to early identification of hazard in your own hospital, before an actual incident occurrence
- Providing general culture of safety awareness

Do you have an incident reporting system?

A. Yes, a dept./hospital wide system
B. Yes, a national system
C. Yes, we report to an international database
D. Yes, somebody (= physicist ☺) has an excel spreadsheet
E. No



What to report?



from *Towards safer radiotherapy*

You should report an incident that…

A. involved a clear error, even if it did not result in treatment correction / change of treatment

B. as above, but with a potential of resulting in an accident

C. required treatment correction

D. resulted in irradiation of radiotherapy professionals,

E. where treatment corrections can not be facilitated, but where negative consequences for the patient are unlikely

F. where treatment corrections can not be facilitated, but where negative consequences for the patient are likely to occur

What to report?

You should report all unintended incidents:

- Observed by you, during involvement in the incident
- Observed by observing others
- Made to attention at a later point in time

All incidents
affecting patient safety
or
potentially affecting patient safety

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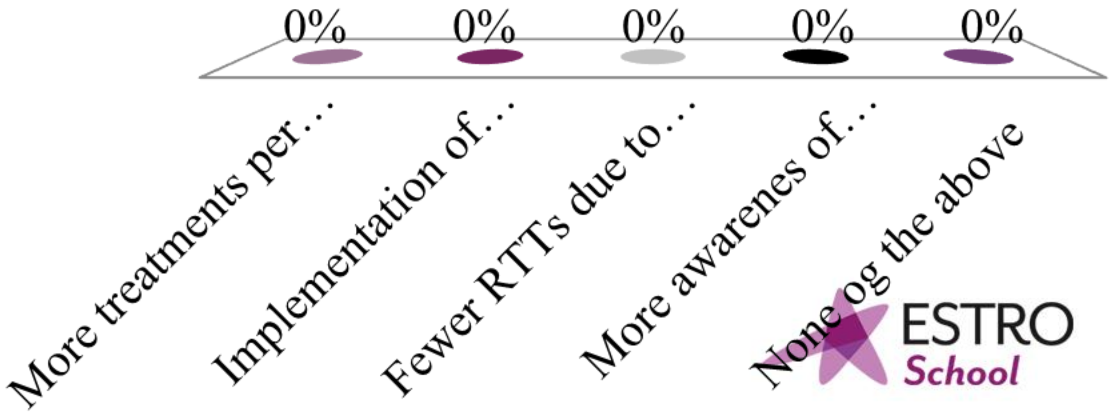
How to explain the increase of incidents?

Year	2008	2009	2010	2011
# of incidents reported	14	30	115	122

A. More treatments per linac
B. Implementation of advanced technology
C. Fewer RTTs due to budget cut downs
D. More awarenes of incident reporting
E. None og the above



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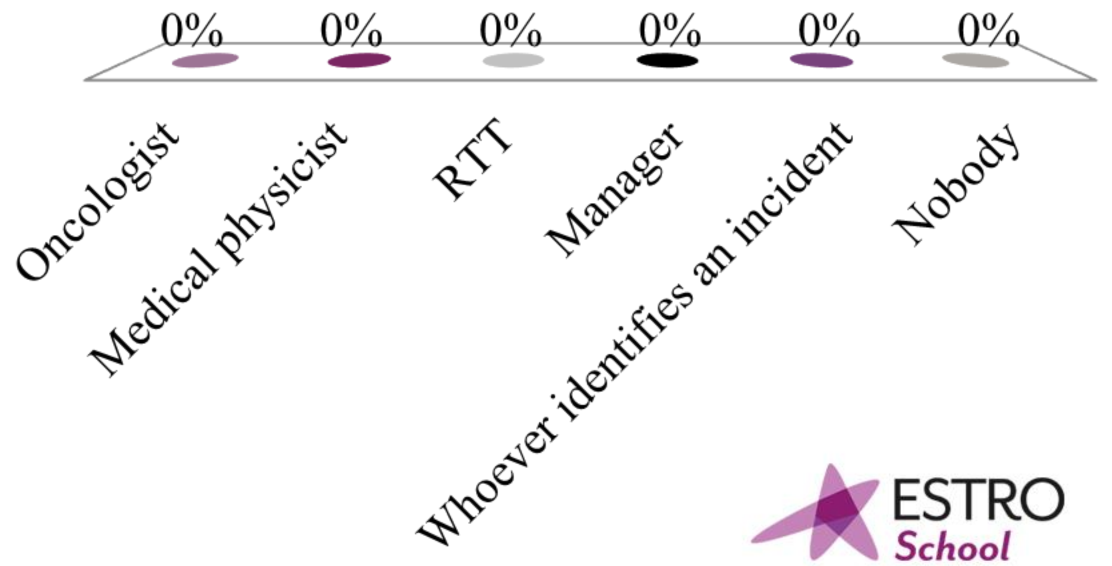
Who reports an incident at your clinic?

A. Oncologist
B. Medical physicist
C. RTT
D. Manager
E. Whoever identifies an incident
F. Nobody



Role of incident reporting system

- To **identify** system design flaws and critical steps in the radiotherapy pathway
- To highlight **critical problems and patterns** of causes of these problems
- To **spread knowledge** on new risks or involving new technology
- To **promote safety culture** and awareness through involvement of and feedback to staff and managers
- To **prevent** repeated incidents

Role of incident reporting system

Incident reporting system has to be a part of a longer chain:

- Incident Identification
- Reporting
- Investigation
- Analysis
- Management
- Learning

Analysis methods

- Root cause analysis
- Journalaudit
- Mortality analysis
- Global Trigger Tool

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Root cause analysis

A systematic method to identify

- WHAT happened
  …the actual chain of events leading to the incident

- WHY could it happen
  …identification of what caused the incident

- HOW to prevent the incident to happen again
  …action plan & follow up

•…NEVER, who caused the incident

Take home message

- Incidents are more numerous and varying than actual accidents
- By learning from the incidents happening in your clinic you can avoid a potential future accident
- Incident report is an essential tool for safer radiotherapy

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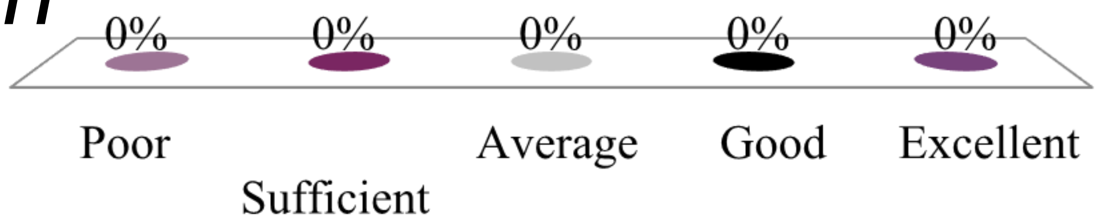
Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



Adverse Event Reporting and the Role of the RTT

Liz Forde, MSc (RTT)
Assistant Professor
The Discipline of Radiation Therapy
School of Medicine
Trinity College Dublin

ARTT
Applied Radiation Therapy
Trinity Research Group

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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Toxicity in Oncology

- Toxicity and tolerance differs for each organ
- Toxicity has an undeniable impact on patients psychosocial well being and quality of life
- Factors impacting on toxicity and patient tolerance:
  - ➢ Biological
  - ➢ Subjective
  - ➢ Duration of reaction
  - ➢ Response to medical intervention

Toxicity in Oncology

- Acute reactions
  - ➢ During or shortly after treatment
  - ➢ Common for epithelial tissue damage
  - ➢ Typically temporary
  - ➢ Support through the most severe phase
    - Medical intervention
  - ➢ Psychosocial
  - ➢ ***Do not ignore unexpected acute toxicities***

- Late reactions
  - ➢ Months or even years following treatment
  - ➢ Too late for a change in treatment
  - ➢ Often in deeply seated organs
  - ➢ Clinical observation difficult

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Need for Recording and Reporting

- Survival and success stories frequently reported
- Adverse events and poor outcome data rarely reported

- Large variation in grading, analysing and reporting
  - ➢ Standardisation is required
  - ➢ Comparison between trials, patients groups, institutions

- More combined therapies
- More aggressive therapies
- More complex treatment regimes

} Associated with higher acute toxicity

Need for Recording and Reporting

- Routine reporting involves commitment to prospective documentation, analysis and long term follow up

- Culture of the department and education of staff
  - ➢ Radiation oncology vs. Medical oncology vs. Surgical oncology
  - ➢ Single modality vs. multi modality trials

The Four Domains of Adverse Event Reporting

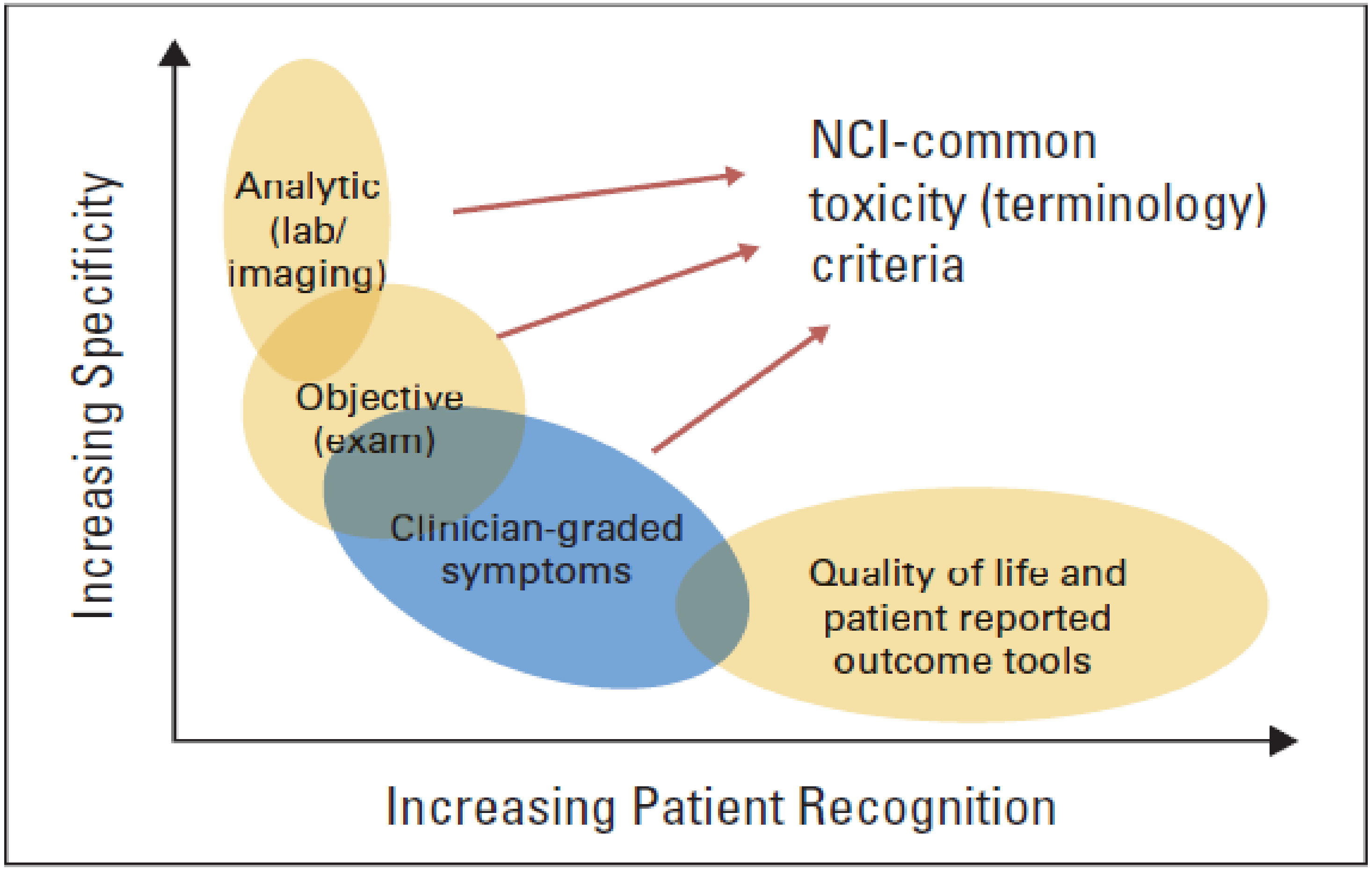

Fig 1. Adverse effects domains. NCI, National Cancer Institute. Adapted with permission.[8]

Trotti et al., Patient reported outcomes and the evolution of adverse reporting in oncology. J Clin Oncol. 2007; 25(32): 5121-5127

Assessment and Reporting of Adverse Events

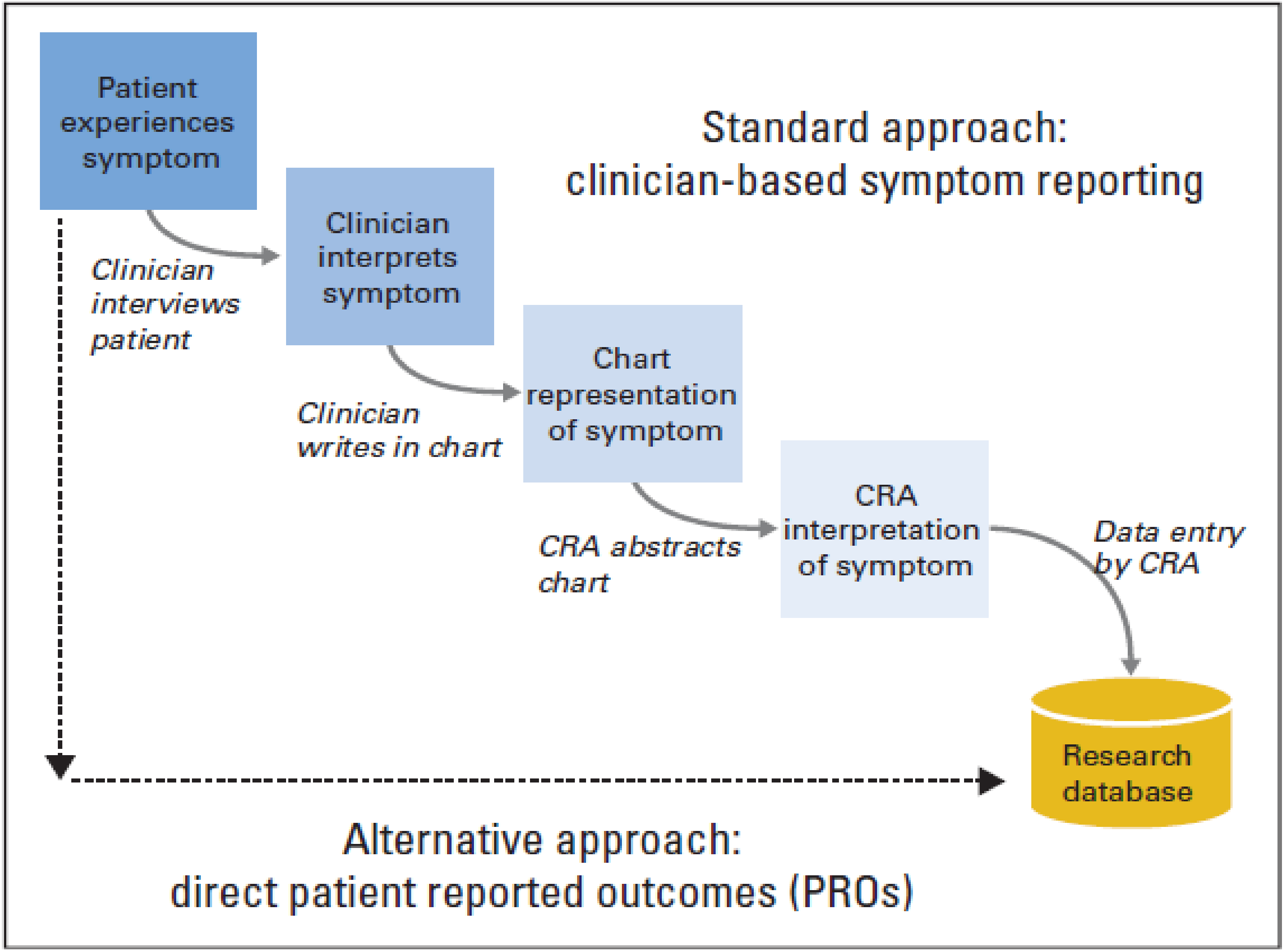

Fig 2. Flow of symptom information in cancer treatment trials. CRA, clinical research assistant. Reprinted with permission.[36]

Trotti et al., Patient reported outcomes and the evolution of adverse reporting in oncology. J Clin Oncol. 2007; 25(32): 5121-5127

Features of a Scoring System

- Specific descriptions
- Unambiguous language
- Consistency and reliability
  - Decreased inter-user variation and misinterpretation
- Grading of severity
  - Intervention required
  - Impact on QoL or daily activities

Systems Developed

- WHO – 1979
- NCI - CTC – 1983
- RTOG – 1984
- RTOG/EORTC – 1984
- Franco-Italian Dictionary
- The Dische grading dictionary
- ***LENT-SOMA – 1995***
- CTCAE Version 3 - 2003
- CTCAE Version 4 – 2010
- CTCAE Version 5 - 2017

Chemotherapy only

Radiation Oncology, Acute Only

- All with varying degrees of content and severity of scaling
- Need for standardisation and amalgamation of acute and late effects…

LENT SOMA

- Perception of toxicity between patient and physician can be very different
  - ➢ Irreversible
  - ➢ Protracted
  - ➢ Uncontrollable
  - ➢ Social debilitating

- Combination of data from functional tests and also a ***subjective*** score

The Work of the NCI

- CTC v1.0 developed in 1983
    - ➢ Chemotherapy only
    - ➢ Acute reactions only

- CTC v2. updated in 1997
    - ➢ Intended for ***all oncology modalities***
    - ➢ >250 descriptive criteria
    - ➢ Still only addressed grading of ***acute*** toxicity

NCI - CTCAE v3.0

- 2003
- All organ systems covered with a total of 370 criteria listed
- Amalgamation of ***acute and late*** effects
- Can be applied to ***all modalities*** (Surgical, medical and radiation oncology)
- Duration and sequence of an adverse event should be recorded
- This is a "grading dictionary" not intended to assess treatment regimes or determine what is acceptable or not
  - This is still a clinical judgement of risks vs. benefits

CTCAE v4

- 2010
- Harmonise terminology with MedDRA
- Organisation of document changes
  - Version 3 was divided into categories based on either pathophysiology or anatomy
  - Version 4 is based on system organ class (SOC)
- Result: Decreased number of terms (1059 down to 790)

CTCAE v5.0

- 2017
- A lot of quite small changes mainly relating to clarification of phrasing and terminology
- Spreadsheet of changes are available online

	A	B	C	D	E	F	G	H	I	J	K	L
1	MedDRA Coc	MedDRA SOC	CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Definition	Navigational Not	CTCAE v5.0 Change	
2	10002272	Blood and lyr	Anemia	Hemoglobin	Hgb <10.0 - 8.	Hgb <8.0 g/dL	Life-threaten	Death	A disorder characterized by an		Clarification: Definition	
3	10005329	Blood and lyr	Blood and lyr	Asymptomat	Moderate; m	Severe or me	Life-threaten	Death	-		Clarification: Grade 3	
4	10048580	Blood and lyr	Bone marrow	Mildly hypoc	Moderately h	Severely hyp	Aplastic pers	Death	A disorder characterized by the inability of the bone marrow to p			
5	10013442	Blood and lyr	Disseminated	-	Laboratory fi	Laboratory fi	Life-threaten	Death	A disorder characterized by systemic pathological activation of b			
6	10014950	Blood and lyr	Eosinophilia	>ULN and >Ba	-	Steroids initi	-	-	A disorder characterized by lal		Addition: Term	
7	10016288	Blood and lyr	Febrile neutr	-	-	ANC <1000/m	Life-threaten	Death	A disorder characterized by an ANC <1000/mm3 and a single tem			
8	10019491	Blood and lyr	Hemolysis	Laboratory ev	Evidence of h	Transfusion c	Life-threaten	Death	A disorder characterized by lal		Clarification: Grade 2	
9	10019515	Blood and lyr	Hemolytic ur	[Grade delete	-	Laboratory fi	Life-threaten	Death	A disorder characterized by a f		Deletion: Grade 1	
10	10024378	Blood and lyr	Leukocytosis	-	-	>100,000/mm	Clinical mani	Death	A disorder characterized by laboratory test results that indicate a			
11	10025182	Blood and lyr	Lymph node	Mild pain	Moderate pa	Severe pain;	-	-	A disorder characterized by a sensation of marked discomfort in			
12	10027506	Blood and lyr	Methemoglo	-	>ULN	Requiring urg	Life-threaten	Death	A disorder characterized by lal		Addition: Term	
13	~~10041633~~	~~Blood and lyr~~	~~Spleen disord~~	[Term delete	[Term delete	–	[Term delete	[Term delete	[Term deleted. Map to Blood a		Deletion: Term	
14	10043648	Blood and lyr	Thrombotic t	[Grade delete	-	Laboratory fi	Life-threaten	Death	A disorder characterized by th		Deletion: Grade 1	
15	~~10051592~~	~~Cardiac disor~~	~~Acute corona~~	–	[Term delete	[Term delete	[Term delete	[Term delete	[Term deleted. Map to Chest p		Deletion: Term	
16	10061589	Cardiac disor	Aortic valve d	Asymptomat	Asymptomat	Symptomatic	Life-threaten	Death	A disorder characterized by a defect in aortic valve function or st			

Common Terminology Criteria for Adverse Events (CTCAE) v5.0

Publish Date: November 27, 2017

Introduction

The NCI Common Terminology Criteria for Adverse Events is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

SOC

System Organ Class (SOC), the highest level of the MedDRA[1] hierarchy, is identified by anatomical or physiological system, etiology, or purpose (e.g., SOC Investigations for laboratory test results). CTCAE terms are grouped by MedDRA Primary SOCs. Within each SOC, AEs are listed and accompanied by descriptions of severity (Grade).

CTCAE Terms

An Adverse Event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Each CTCAE v4.0 term is a MedDRA LLT (Lowest Level Term).

Grades

Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.

Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**.

Grade 4 Life-threatening consequences; urgent intervention indicated.

Grade 5 Death related to AE.

A Semi-colon indicates 'or' within the description of the grade.

A single dash (-) indicates a Grade is not available.

Not all Grades are appropriate for all AEs. Therefore, some AEs are listed with fewer than five options for Grade selection.

Grade 5

Grade 5 (Death) is not appropriate for some AEs and therefore is not an option.

Definitions

A brief Definition is provided to clarify the meaning of each AE term. A single dash (-) indicates a Definition is not available.

Navigational Notes

A Navigational Note is used to assist the reporter in choosing a correct AE. It may list other AEs that should be considered in addition to or in place of the AE in question. A single dash (-) indicates a Navigational Note has not been defined for the AE term.

Activities of Daily Living (ADL)

*Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

**Self care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

[1] CTCAE v5.0 incorporates certain elements of the MedDRA terminology. For further details on MedDRA refer to the MedDRA MSSO Web site (https://www.meddra.org/).

CTCAE v5.0

- Example of AEs potentially experienced by prostate radiotherapy patients

Gastrointestinal disorders					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of >=7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an increase in frequency and/or loose or watery bowel movements.					
Navigational Note: -					

Proctitis	Rectal discomfort, intervention not indicated	Symptoms (e.g., rectal discomfort, passing blood or mucus); medical intervention indicated; limiting instrumental ADL	Severe symptoms; fecal urgency or stool incontinence; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by inflammation of the rectum.					

General disorders and administration site conditions					
CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities.					

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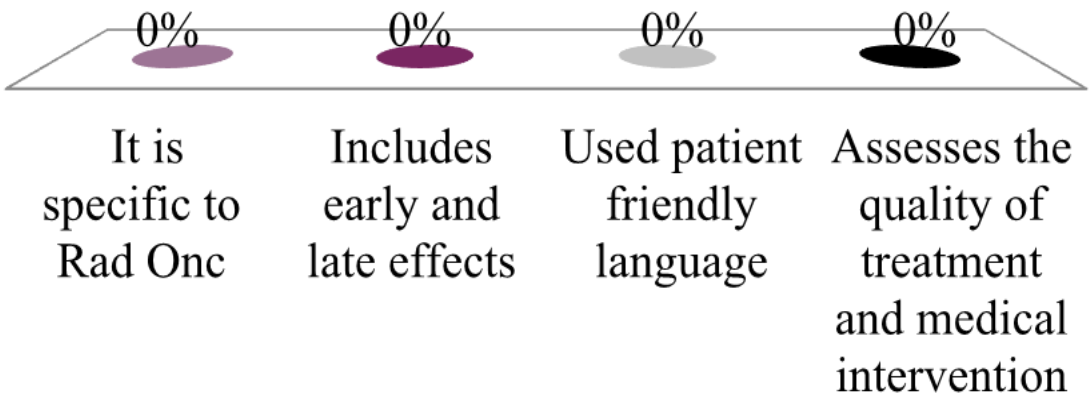
Which is a key feature of the CTCAE systems?

A. They are specific to Rad Onc
B. Includes early and late effects
C. Used patient friendly language
D. Assesses the quality of treatment and medical intervention



Even with advances in toxicity reporting using CTCAE variability still remains

Patient Reported Outcomes (PRO)

- HCP generally ***underestimate*** side effect presentation, severity and duration compared with patients

- Agreement is generally closer for observable side effects than for subjective ones
  - ➢ E.g. diarrhoea is observable and fatigue is subjective

- PROs cover the ***subjective*** domain
  - ➢ E.g. Pain

- Issues re literacy
  - ➢ Questionnaires to guide a consult is not considered a true PRO as there is still some level of interpretation and collection by someone other than the patient

PROs

- The NCI have since developed a web based PRO for the CTCAE
- 81 symptoms have been identified for inclusion in a PRO
- 126 questions assess the different attributes of these symptoms
- Language has been adjusted for patients
  - Myalgia is “translated” as aching muscles

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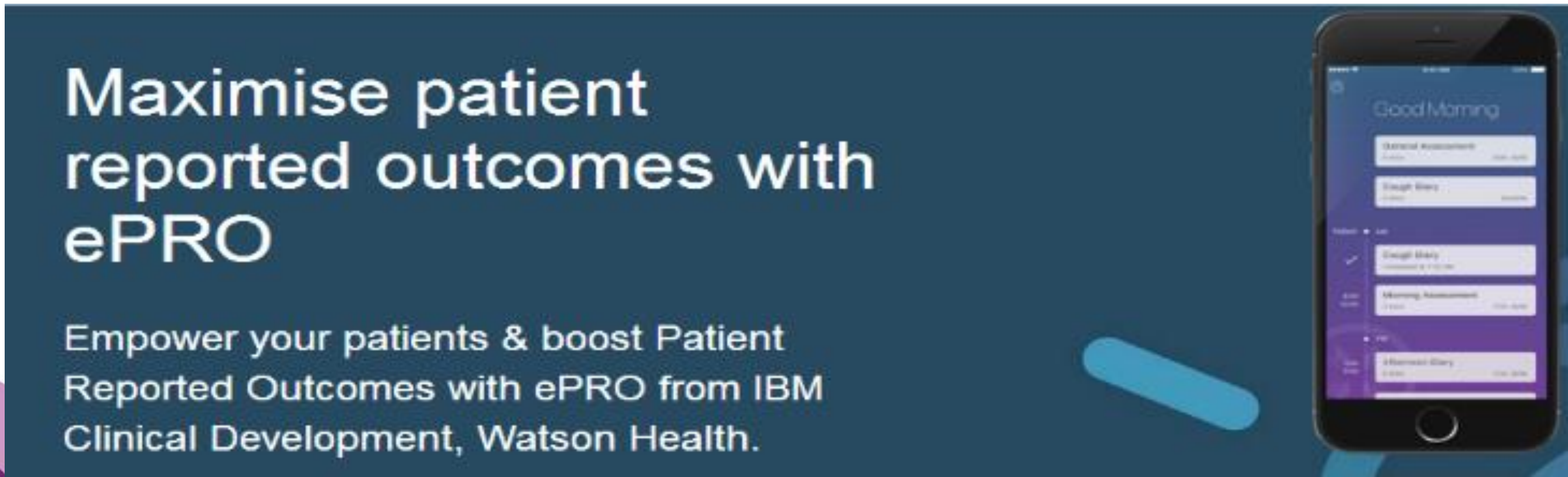
ePRO

- Basche presented at ASCO in June 2017
  - ➢ >700 patients treated at MSKCC
  - ➢ Breast and lung
- "Real time" reporting of side effects
- Web based PRO for chemo patients
- Works on smart phones
- Nurses get sent an email when side effects worsen



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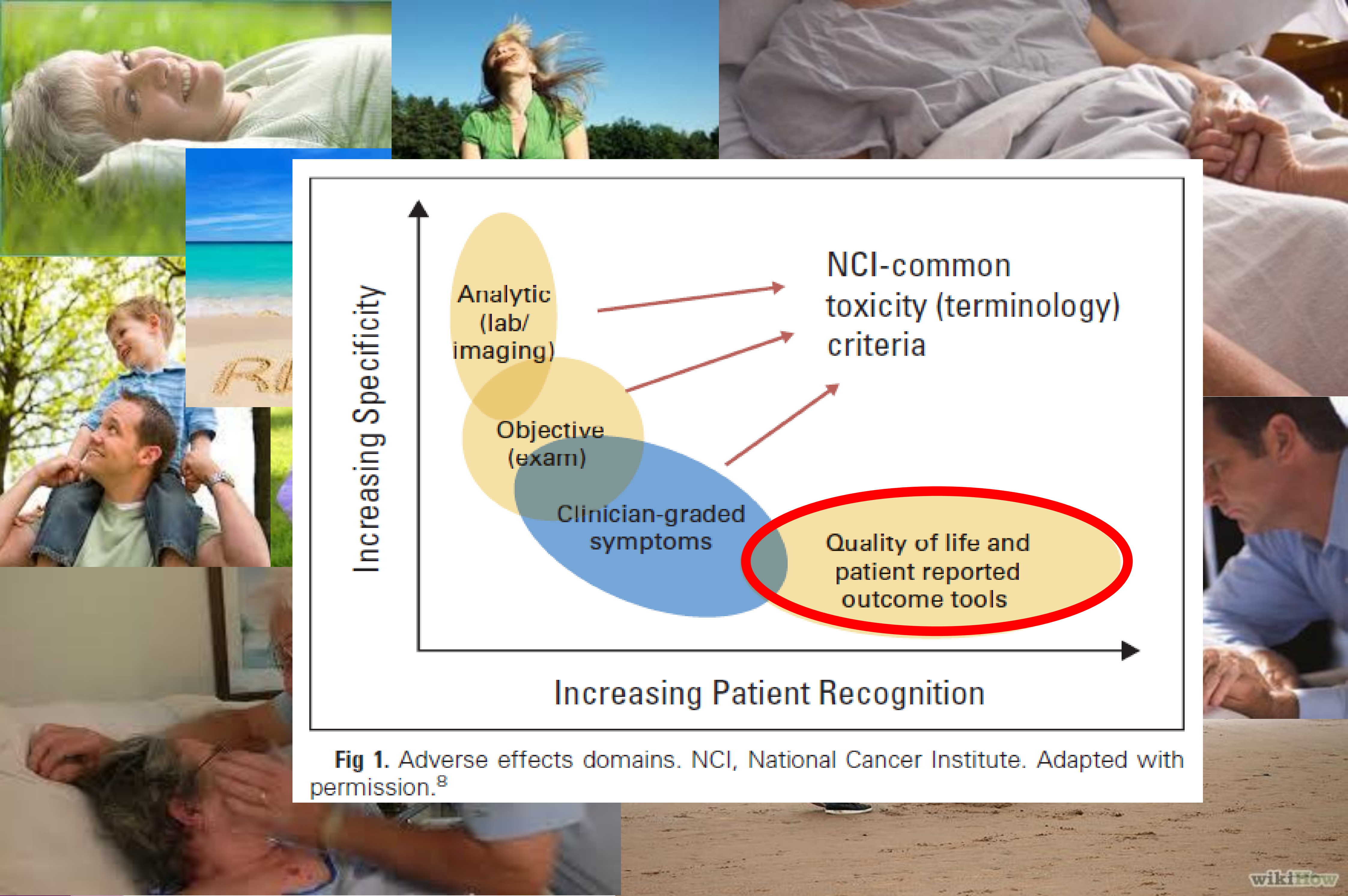

Fig 1. Adverse effects domains. NCI, National Cancer Institute. Adapted with permission.[8]

Quote read directly from: *Pavy et al., Late effects toxicity scoring: the SOMA scale. Radiother Oncol. 1995;*

"To the clinician and the biologist the preservation of functions that are essential to life would seem of paramount importance. But to the patient, the obligation to live a long and painful existence may be worse than death itself. The economic consequence of being unable to work, and even more, being utterly dependent on others for day to day activities like feeding, dressing and washing are not easy for a third person to appreciate. Similarly facial disfigurement and anal or bladder incontinence may impose such social consequences on the patient that may become effectively housebound even though their other vital organs function, motor activities and pain threshold are virtually unimpaired."

Pavy et al., Late effects toxicity scoring: the SOMA scale. Radiother Oncol. 1995; 35:11-15

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Quality of Life Assessment

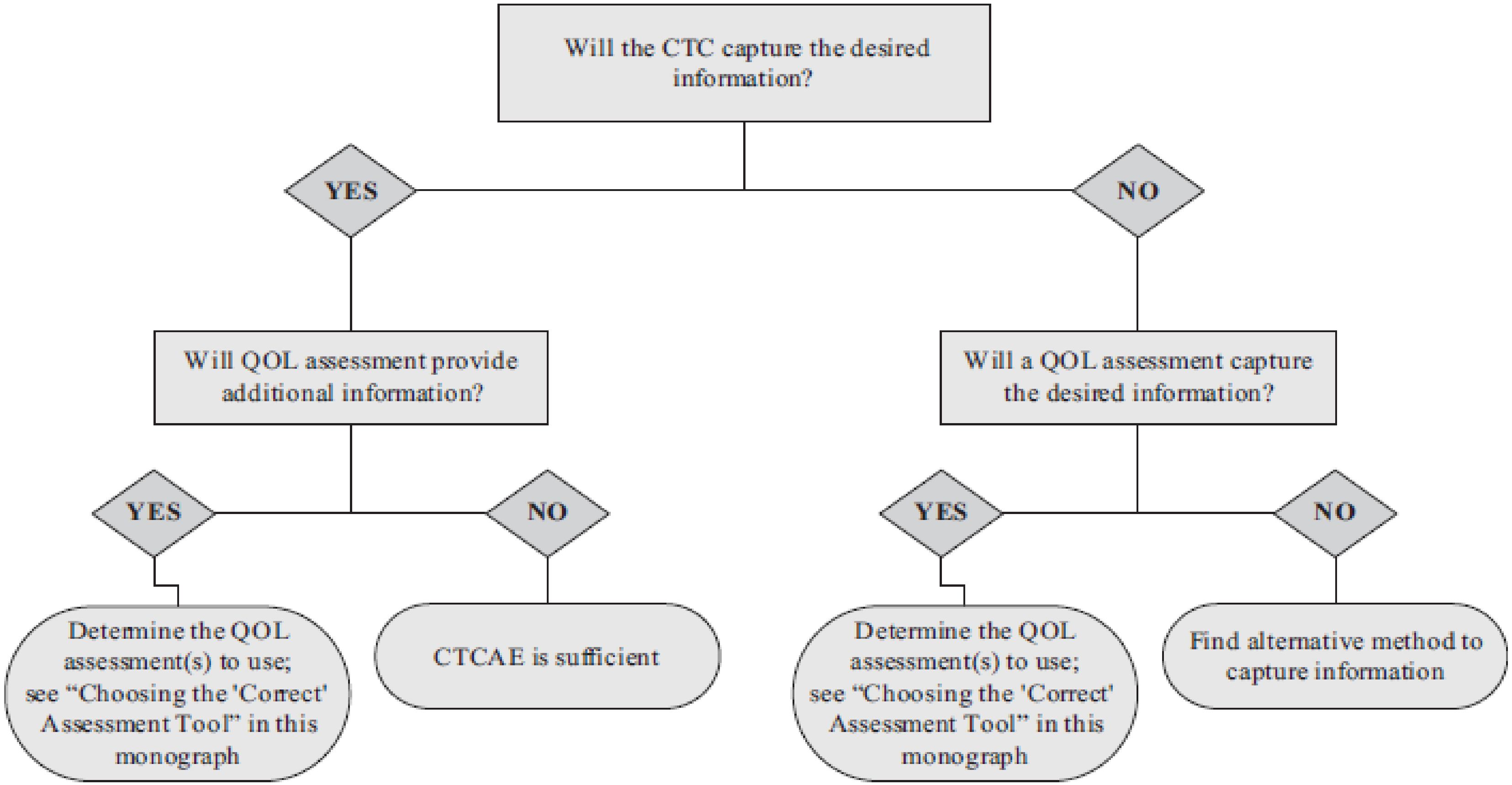

FIG 2. Flow diagram to determine the method for adverse event and QOL data collection.

Huschka M and Burger K. Does QOL provide the same information as toxicity data? Curr Probl Cancer. 2006; 30(6): 244-254

QoL Assessment

- QoL is ***subjective*** and depends on patients ability to adapt to a certain extent
  - ➢ QoL measures not the AE itself but the how it impacts on daily activities

- QoL includes psychosocial support networks and patient’s spirituality

- QoL and AE reporting are complimentary to each other

- This combination strengthens the patient physician relationship
  - ➢ Recognition of different goals
  - ➢ Overall survival, but at what cost

QoL Assessment

- QoL assessment also lacks consistency between trials, countries, departments and patient groups

- Assessment Scales available
  - ➢ The Symptom Distress Scale
  - ➢ The Lung Cancer Symptom Scale
  - ➢ Functional Assessment of Chronic Illness Therapy – Diarrhoea
  - ➢ The International Prostate Symptom Score
    - 8 questions includes 1 QoL question
  - ➢ The Expanded Prostate Cancer Index Composite (EPIC)
    - Urinary
    - Bowel
    - Sexual function
    - Hormonal changes

EORTC Quality of Life

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QUESTIONNAIRES

The EORTC Quality of Life questionnaires are developed to assess the quality of life of cancer patients.

The EORTC QLQ-C30 assesses the quality of life of cancer patients. It has been translated and validated into 81 languages and is used in more than 3,000 studies worldwide. Various modules have been developed for disease specific treatement measurements.

- EORTC QLQ-C30
- EORTC CAT
- EORTC QLQ-C15-PAL
- EORTC IN-PATSAT32
- MODULES Specific Diseases

LATEST NEWS

03/10/2013

Quality of Life Department 20 Year Anniversary

13/09/2013

EORTC QLQ-CML24 has just been published in "Quality of Life Research"

EVENTS

12/09/2013

Autumn 2013 Quality of Life Group Meeting

Canterbury, UK

24/04/2014

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QoL Assessment

- QLQ - C30
- Current version = version 3
- Translated into 81 languages
- 3000 studies internationally

- Disease specific modules also available for use:
  - Breast, Lung, Head & Neck, Oesophageal, Ovarian, Gastric, Cervical cancer, Multiple Myeloma, Oesophago-Gastric, Prostate, Colorectal Liver Metastases, Colorectal and Brain

During the past week:	Not at All	A Little	Quite a Bit	Ve Mu
17. Have you had diarrhea?	1	2	3	
18. Were you tired?	1	2	3	
19. Did pain interfere with your daily activities?	1	2	3	
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	
21. Did you feel tense?	1	2	3	
22. Did you worry?	1	2	3	
23. Did you feel irritable?	1	2	3	
24. Did you feel depressed?	1	2	3	
25. Have you had difficulty remembering things?	1	2	3	
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	
28. Has your physical condition or medical treatment				

Some Limitations of Scoring Systems in General

- Inconsistencies in the timing of data recording

- Time consuming and resource intensive data collection

- Transfer of information and data collection
  - Interpretation of information from patient to clinician
  - Manually entered into database

- Underreporting of lower grades (Grade 1 and Grade 2)

Is There a Role for the RTT?

Treatment Review Clinics

- Clinical examination
- Side effects are explained and assessed
- Medication or intervention may be required
- Nutritional advice
- CAM advice
- Psycho social issues are addressed
- Documentation of intervention and progress
- Unrelated medical advice
- Quality assurance for the progression on treatment is addressed
- Logistical information

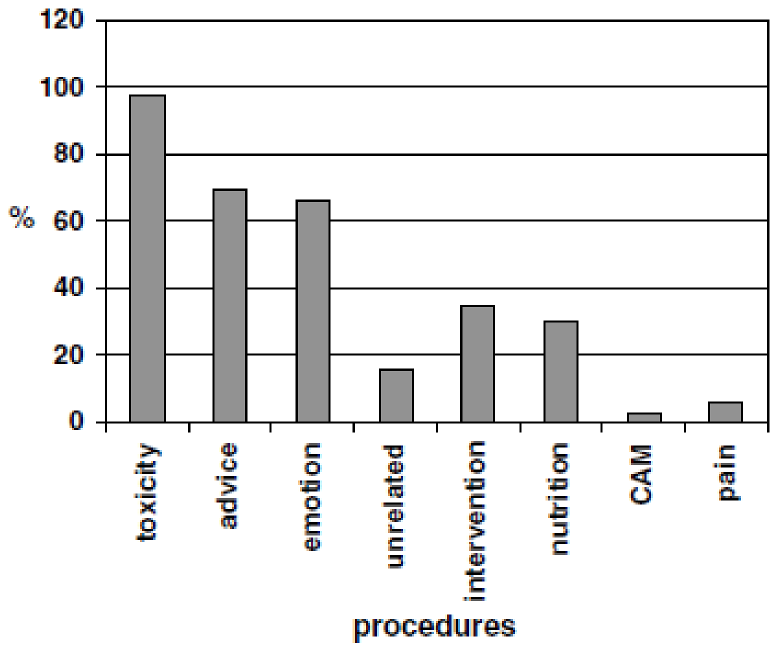

Fig. I. Frequency of procedures observed during treatment reviews. Toxicity, toxicity scoring indicated; Advice, advice on side effects; Emotion, emotional support given in terms of assurance and information given; Unrelated, unrelated medical problems addressed; Intervention, medical intervention given in the form of drug prescription, liaison with other physicians, ordering of wound dressing, or any other investigations; Nutrition, nutritional advice given; CAM, complementary and alternative medicine addressed; Pain, pain score taken.

Shi et al., 2009

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Table I
Medical intervention rates versus treatment site observed in Phase 2

Treatment site	Breast	Brain	H & N	Thorax	Pelvis	Other	Total	Pearson's Chi-square
Number (% within site)	11 (19%)	6 (54.5%)	13 (40.6%)	8 (38.1%)	15 (65.2%)	3 (20%)	56 (35%)	$P = 0.001$

Shi et al., 2009

Table 1. Breakdown of treatment review clinics requiring medical intervention (MI) and no MI according to the site of the cancer being treated.

Treatment site	MI required *n* (%)	No MI required *n* (%)	Total clinics *n* (%)
Head and neck	41 (93)	3 (7)	44 (22)
Prostate	11 (28)	29 (73)	40 (20)
Chest	18 (78)	5 (22)	23 (12)
Rectum	13 (59)	9 (41)	22 (11)
Breast	7 (33)	14 (67)	21 (11)
Brain	8 (73)	3 (27)	11 (6)
Gynaecological	10 (91)	1 (9)	11 (6)
Bladder	3 (33)	6 (67)	9 (5)
Superficial	2 (33)	4 (67)	6 (3)
Bone metastases	2 (40)	3 (60)	5 (3)
Pelvis	2 (50)	2 (50)	4 (2)
Abdomen	1 (50)	1 (50)	2 (1)
Extremity	0 (0)	2 (100)	2 (1)
Total clinics	118 (59)	82 (41)	200 (100)

Monk et al., 2013

As an initial step limit RT lead review to sites of low MI

Table III
ROs' and RTTs' concerns with regards to RTT-led treatment reviews

ROs' concerns	RTTs' concerns
(1) Training [9]	(1) Medico-legal responsibility [21]
(2) Scope of practice – RTTs must know when to refer to ROs [7]	(2) Training [18]
(3) Medico-legal responsibility [5]	(3) Resource, time and manpower constraints [16]
(4) Resource, time and manpower constraints [4]	(4) Remuneration [14]
(5) Patients' perspective [2]	(5) Support from ROs and management [14]
(6) Compromise in RTT work performance due to diversification of role [1]	(6) Patients' perspective [13]
(7) Overconfidence of RTTs [1]	(7) Increase workload for RTTs [12]
	(8) Lack of licensing – prescription, decision making, recognition for leading reviews [6]
	(9) Sensitivities of job overlap with nurses and ROs [5]

Shi et al., 2009

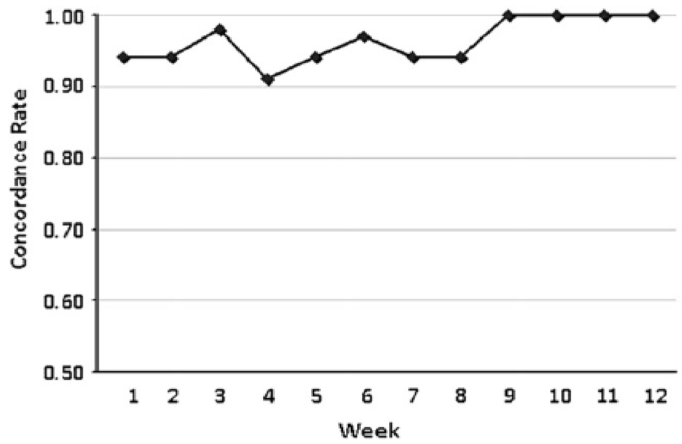

Figure 2. Average weekly concordance rates between the clinical specialist radiation therapist and radiation oncologist.

Lee et al., 2012

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Impact of This Approach?

For the *Individual*?

- Increased job satisfaction
- Mutual respect as a professional
- Specialisation
- Autonomy in the workplace
- Personal growth
- Career advancement in a field that has a historical "ceiling"

For the *Institution?*

- Improved MDT dynamics
- Increased efficiency
- Better use of staff skills
- Education of peers
  - Mentorship

Take Home Messages

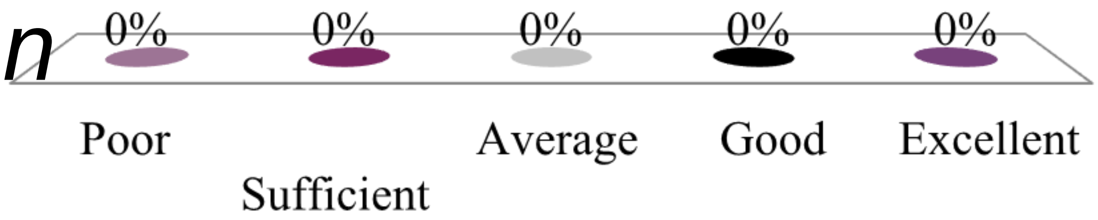
- ***Diligent*** adverse event reporting should not be reserved for clinical trials
- ***Prospective*** data collection that is electronic and easily accessible
- Language needs to be clear for ***all*** members of the team accessing patient notes
- Better equipped to assess impact of treatment in an evidence based approach


OUTBACK
AUSTRALIA

Please score this lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

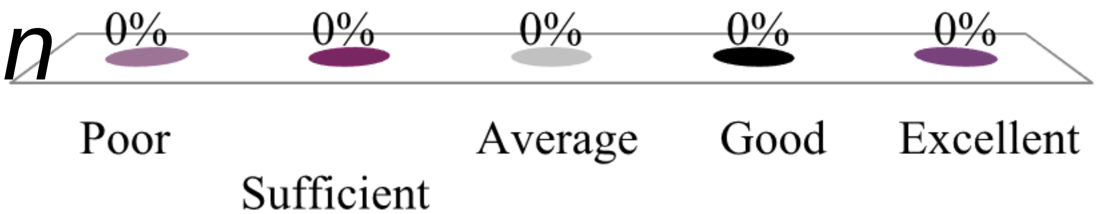
comments can be written on the paper form



Please score ***Advances in Treatment Planning*** lecture

A. Poor
B. Sufficient
C. Average
D. Good
E. Excellent

comments can be written on the paper form



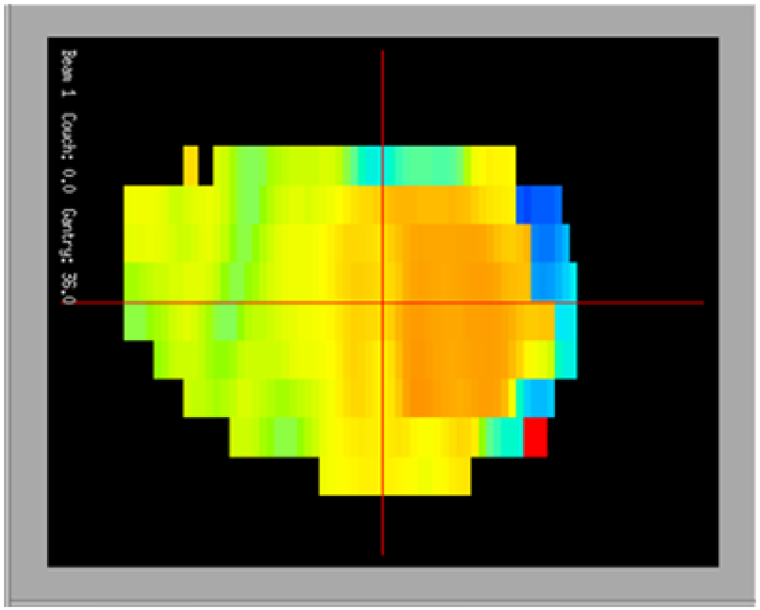
Protontherapy Dpt.
S. Chiara Hospital
Trento, Italy

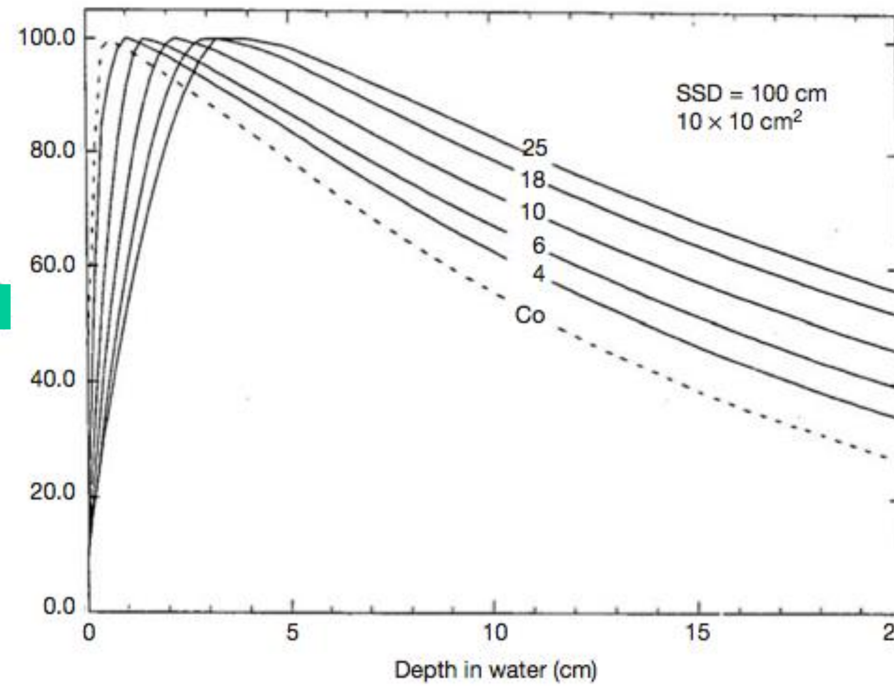
Protontherapy -
A crash course

Marco Schwarz
marco.schwarz@apss.tn.it

Roma– 10 Maggio 2018

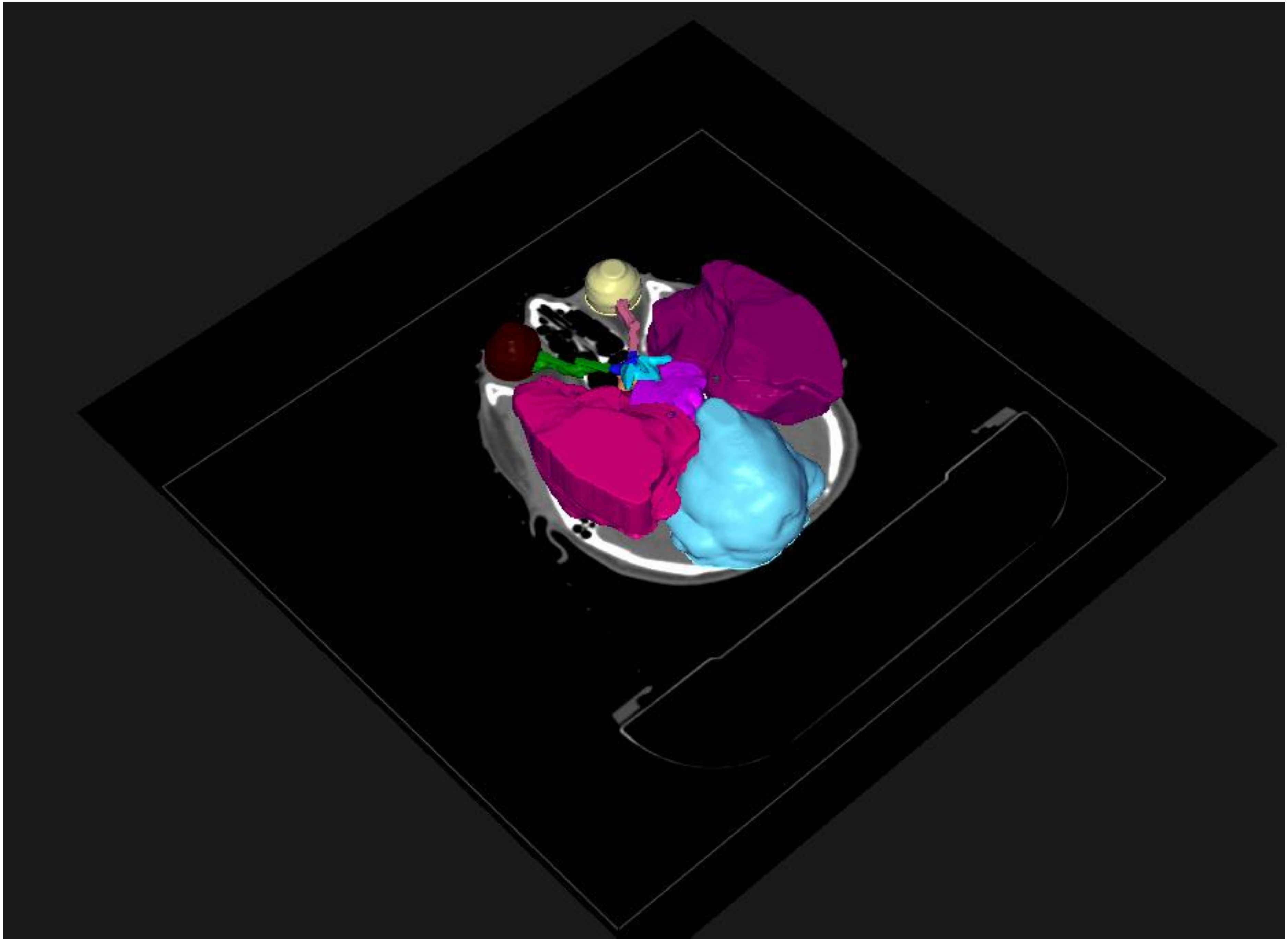
What can we do in photon RT?

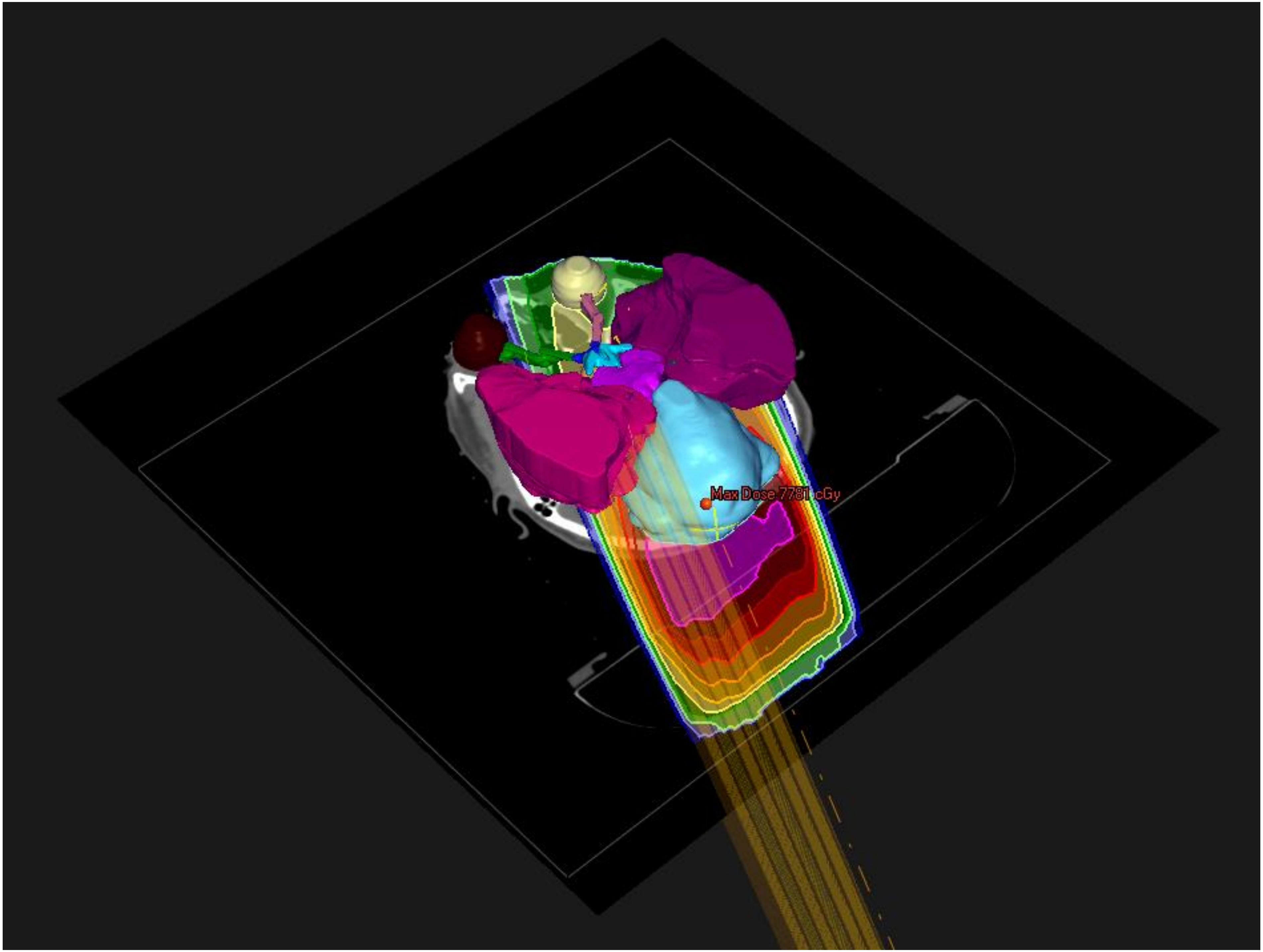


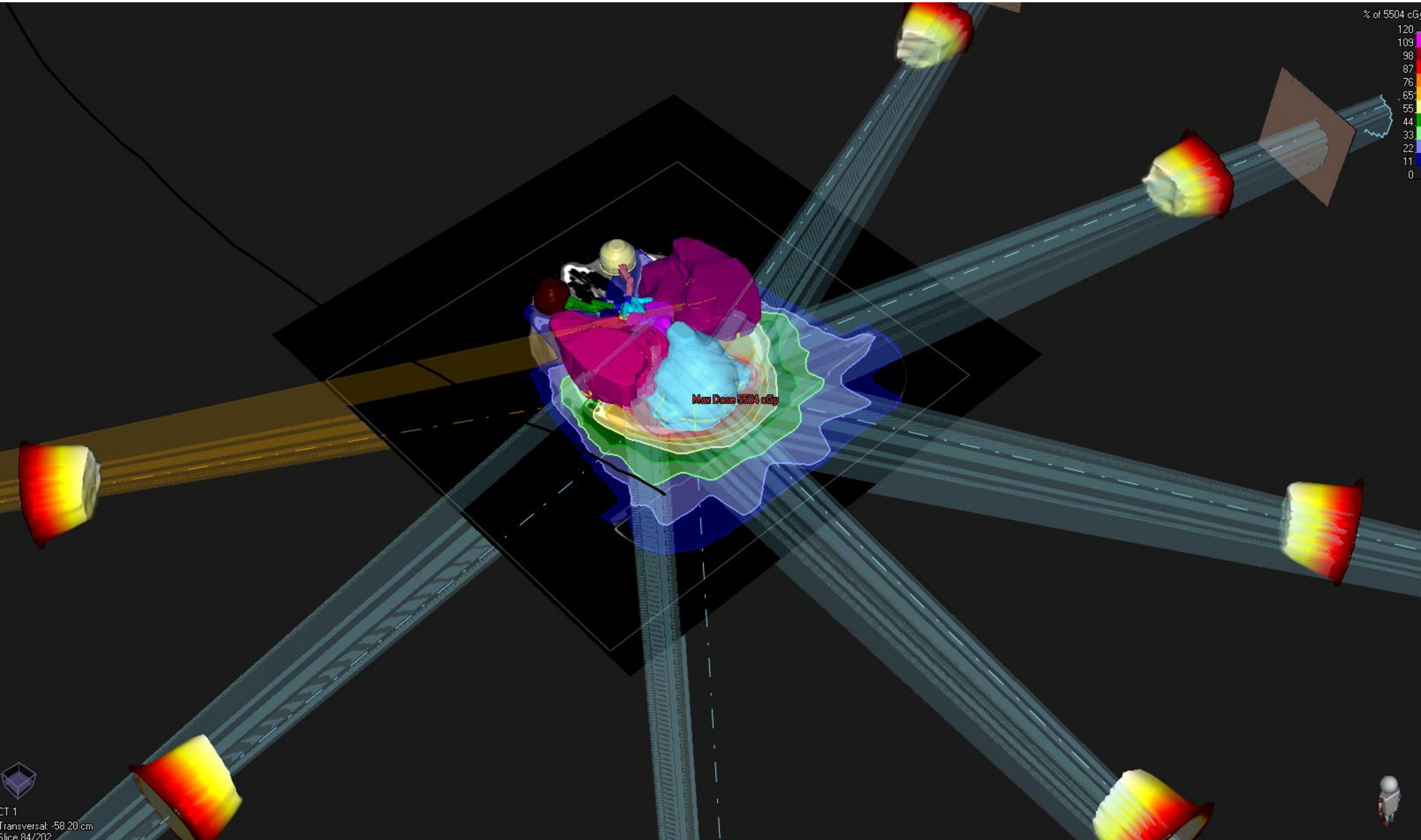


We can modulate beam intensity in the transversal plane

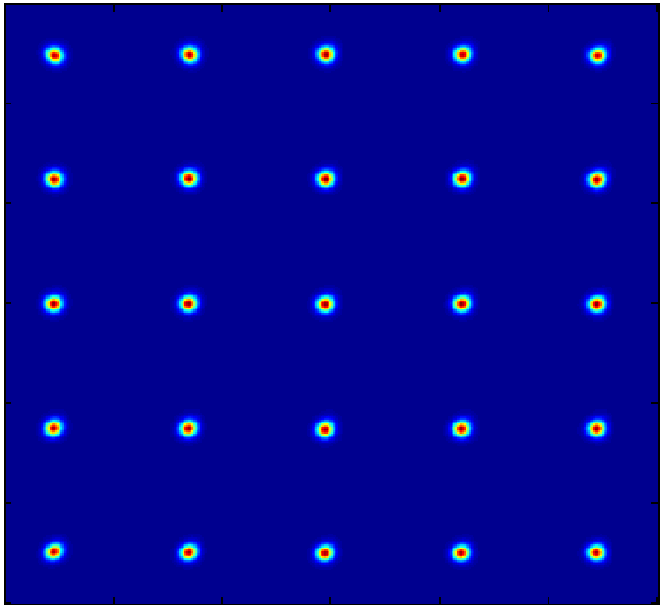
We can not modulate the dose distribution in depth

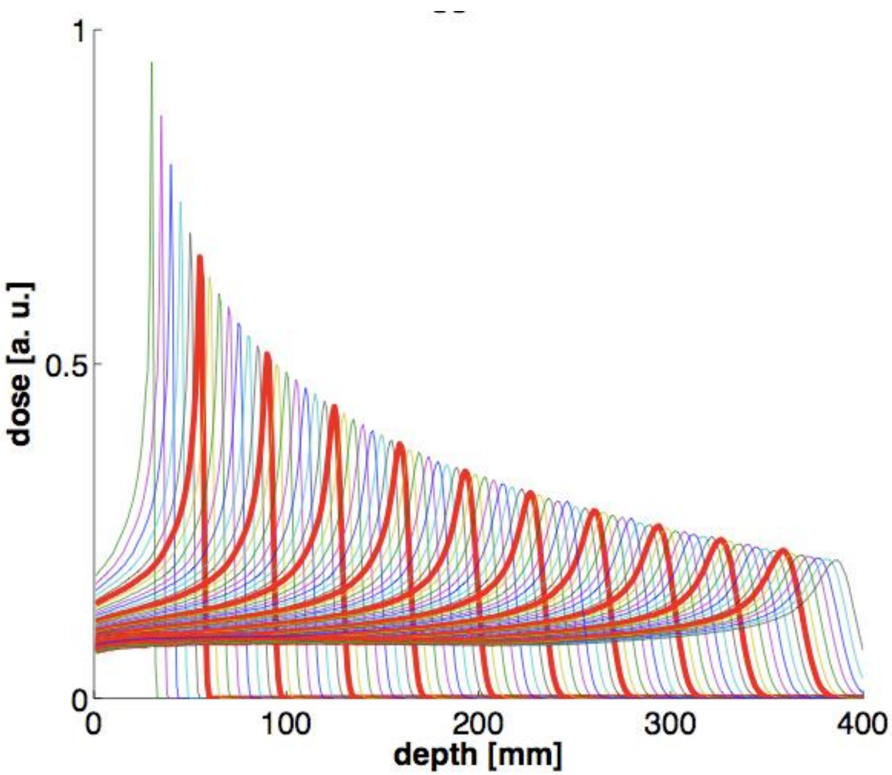



Max Dose 7781 cGy


% of 5504 cGy
120
109
98
87
76
65
55
44
33
22
11
0
Max Dose 5504 cGy
CT 1
Transversal: -58.20 cm
Slice 84/202

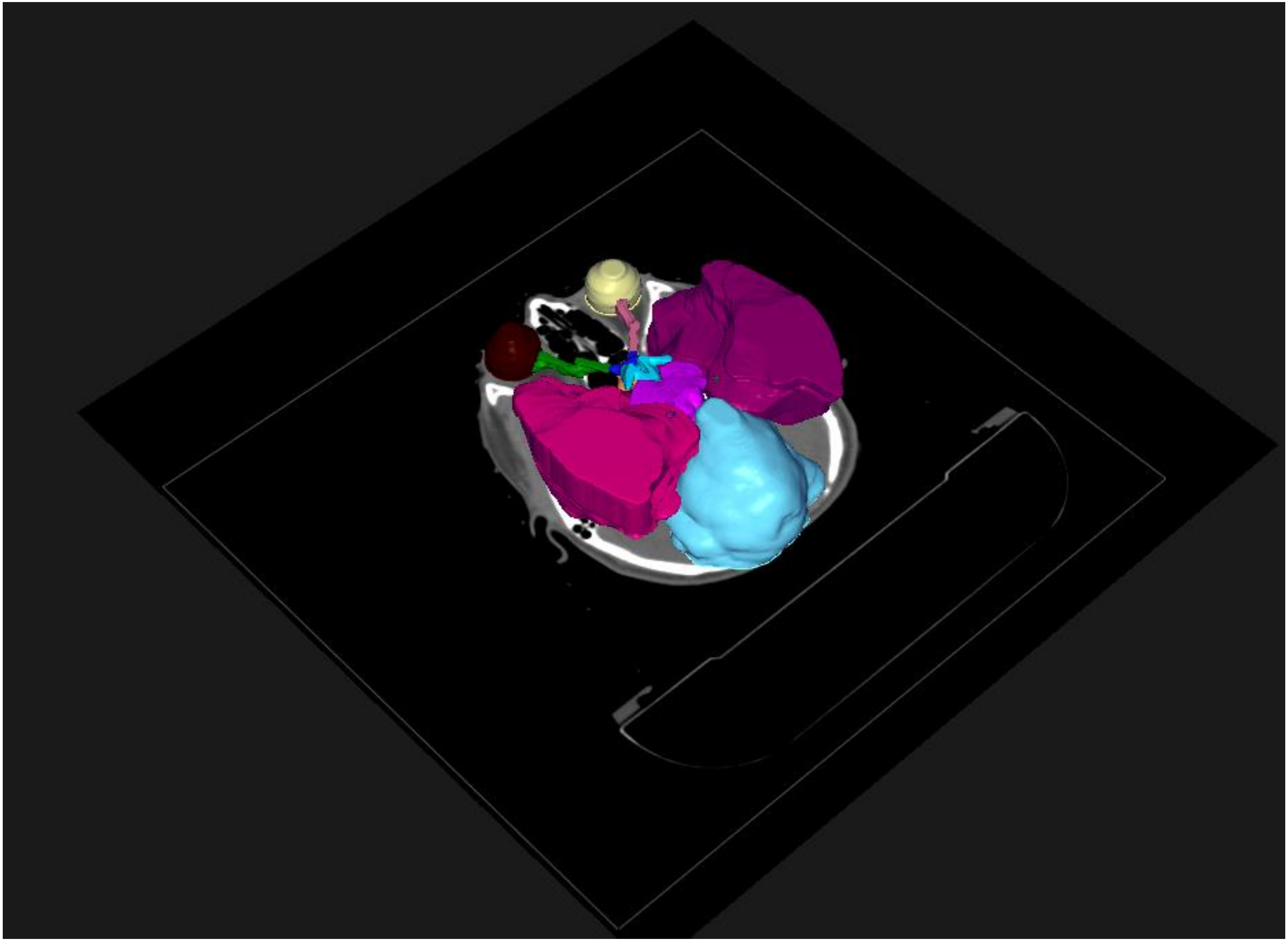
What can we do in photon RT?

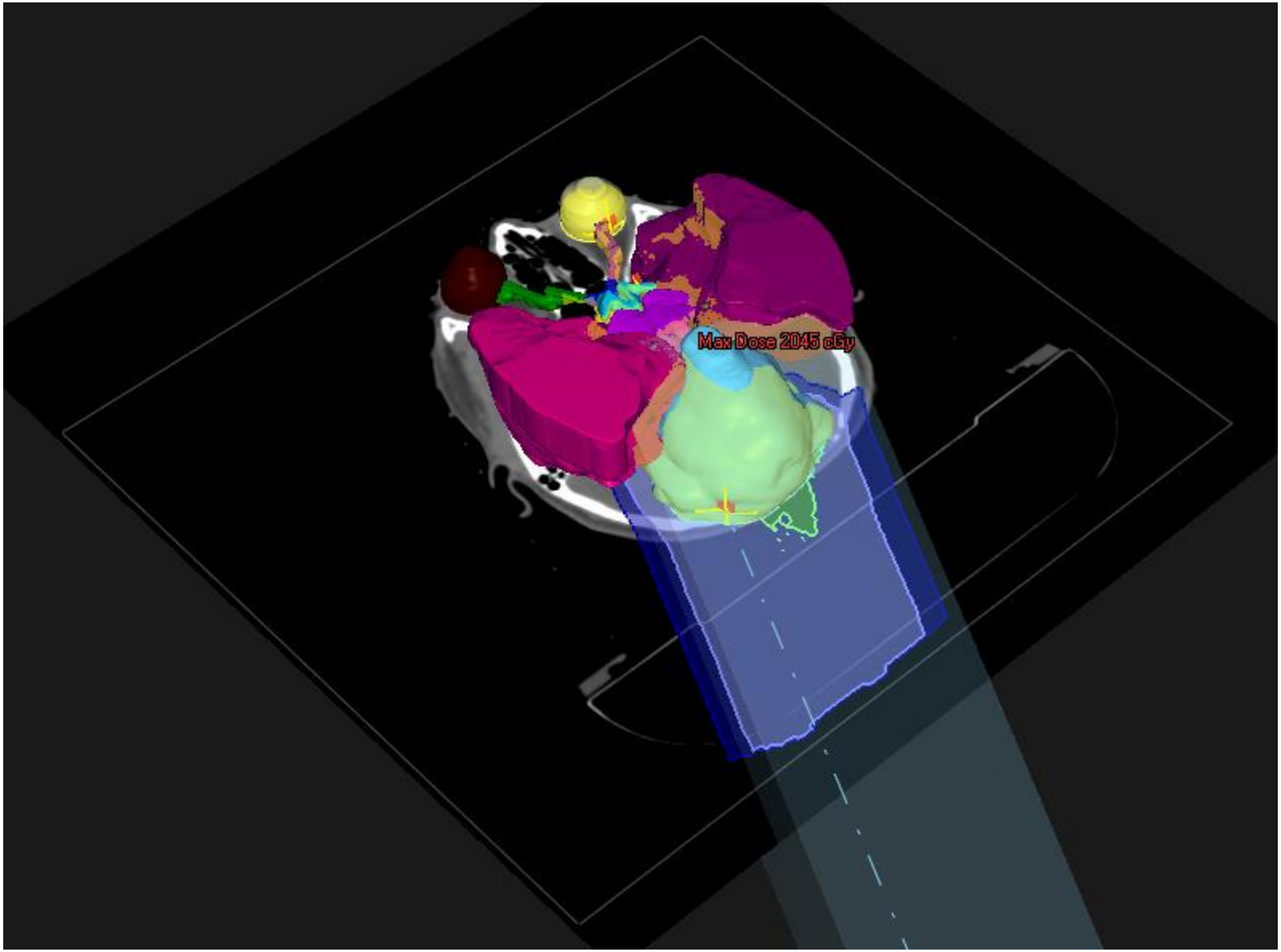


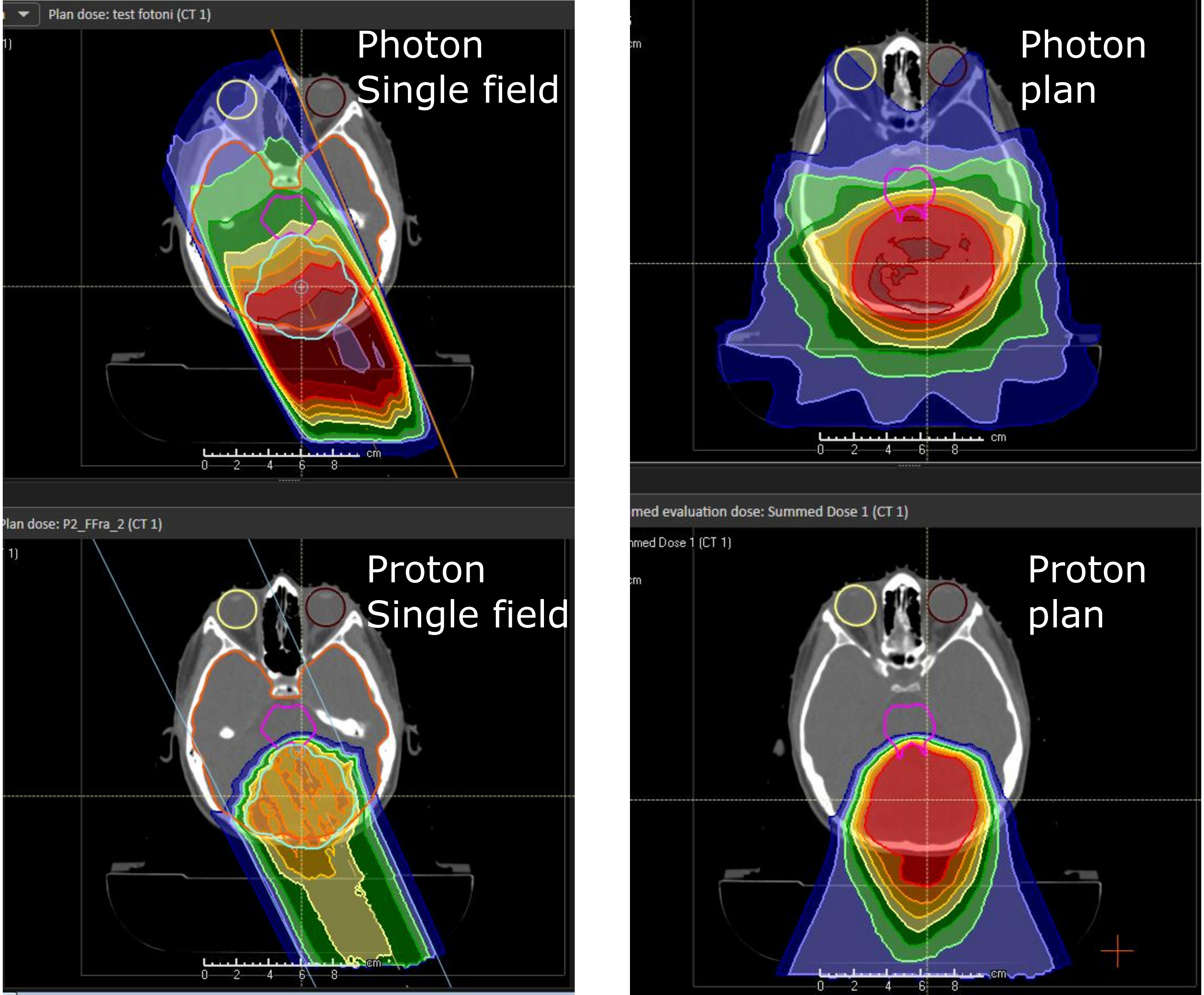


We can modulate beam intensity in the transversal plane

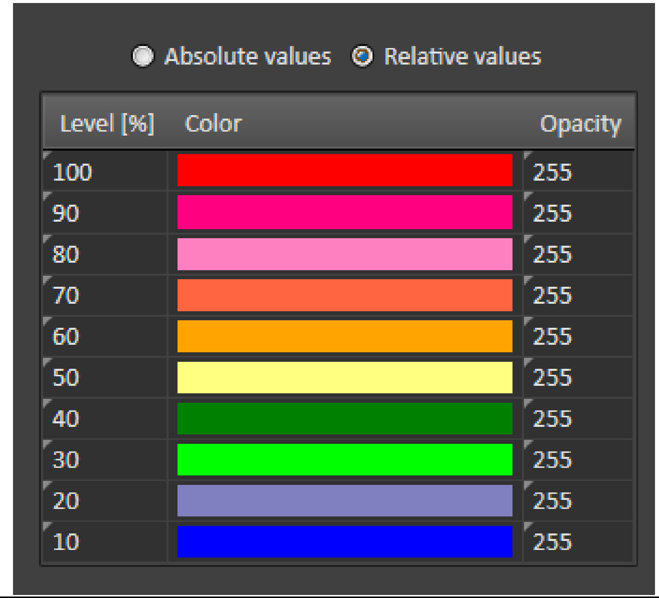
We can also modulate the dose distribution in depth

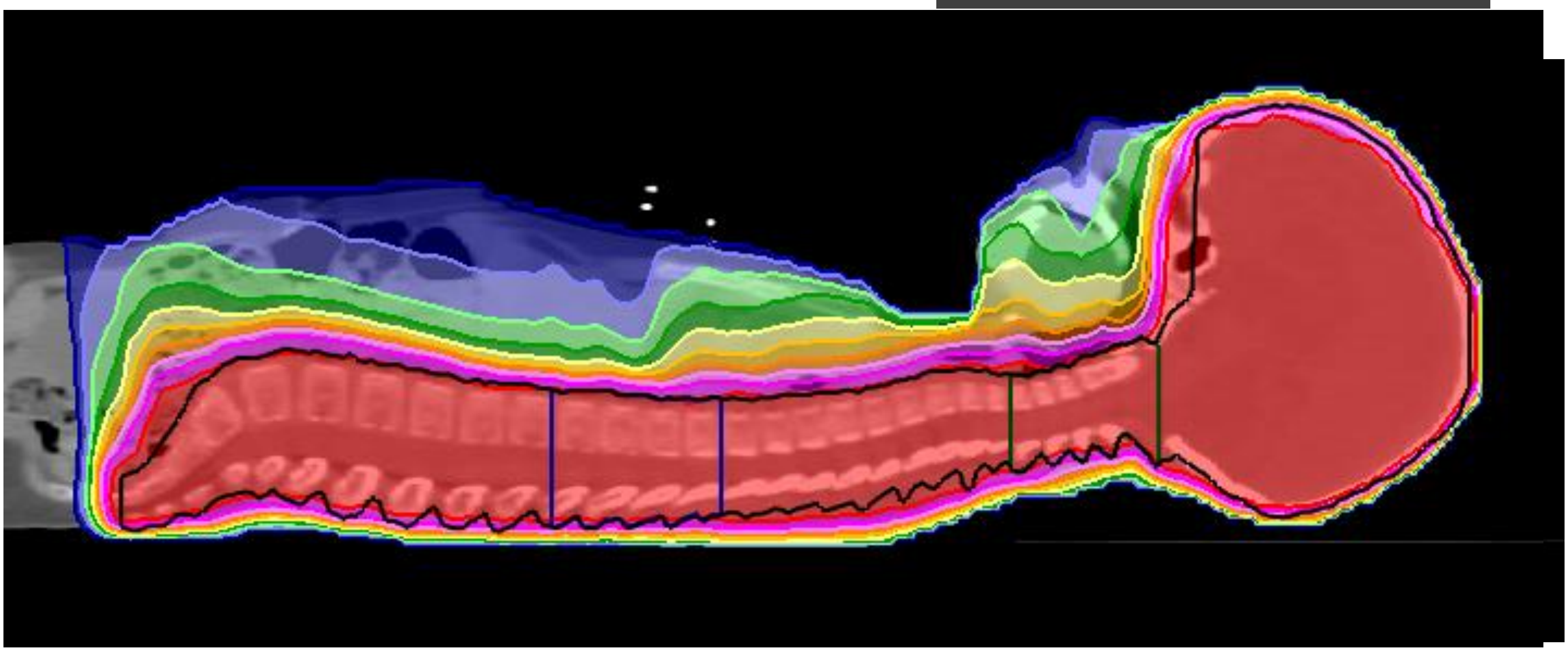



Max Dose 2045 cGy


Plan dose: test fotoni (CT 1)
Photon
Single field
Photon
plan
Plan dose: P2_FFra_2 (CT 1)
Proton
Single field
med evaluation dose: Summed Dose 1 (CT 1)
Proton
plan
0 2 4 6 8 cm

Protons vs. fotons in craniospinal axis irradiation



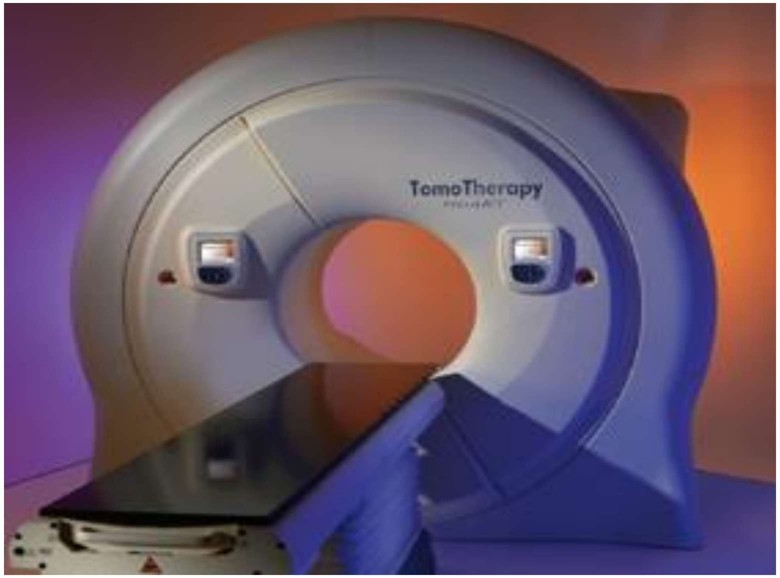


Why don’t we treat all patients with protons then?

1. Because generating a proton beam is much more difficult

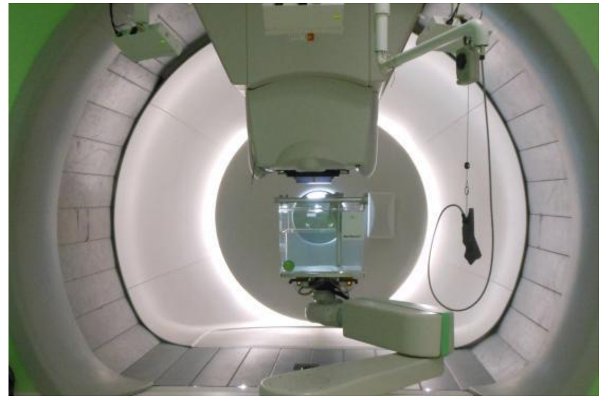
In X-rays therapy we accelerate electrons (about 0.5MeV/c^2) at 10-15MeV

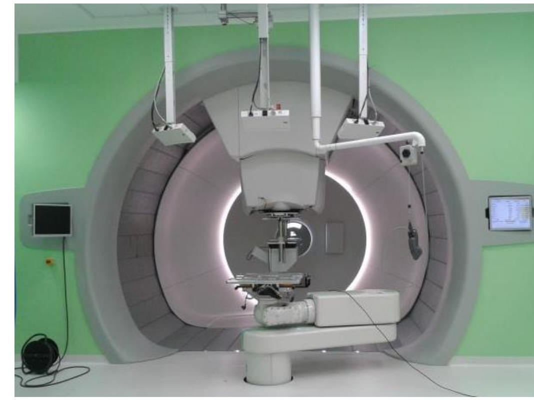
In protontherapy we accelerate protons (about 1000MeV/c^2) at 200-250MeV

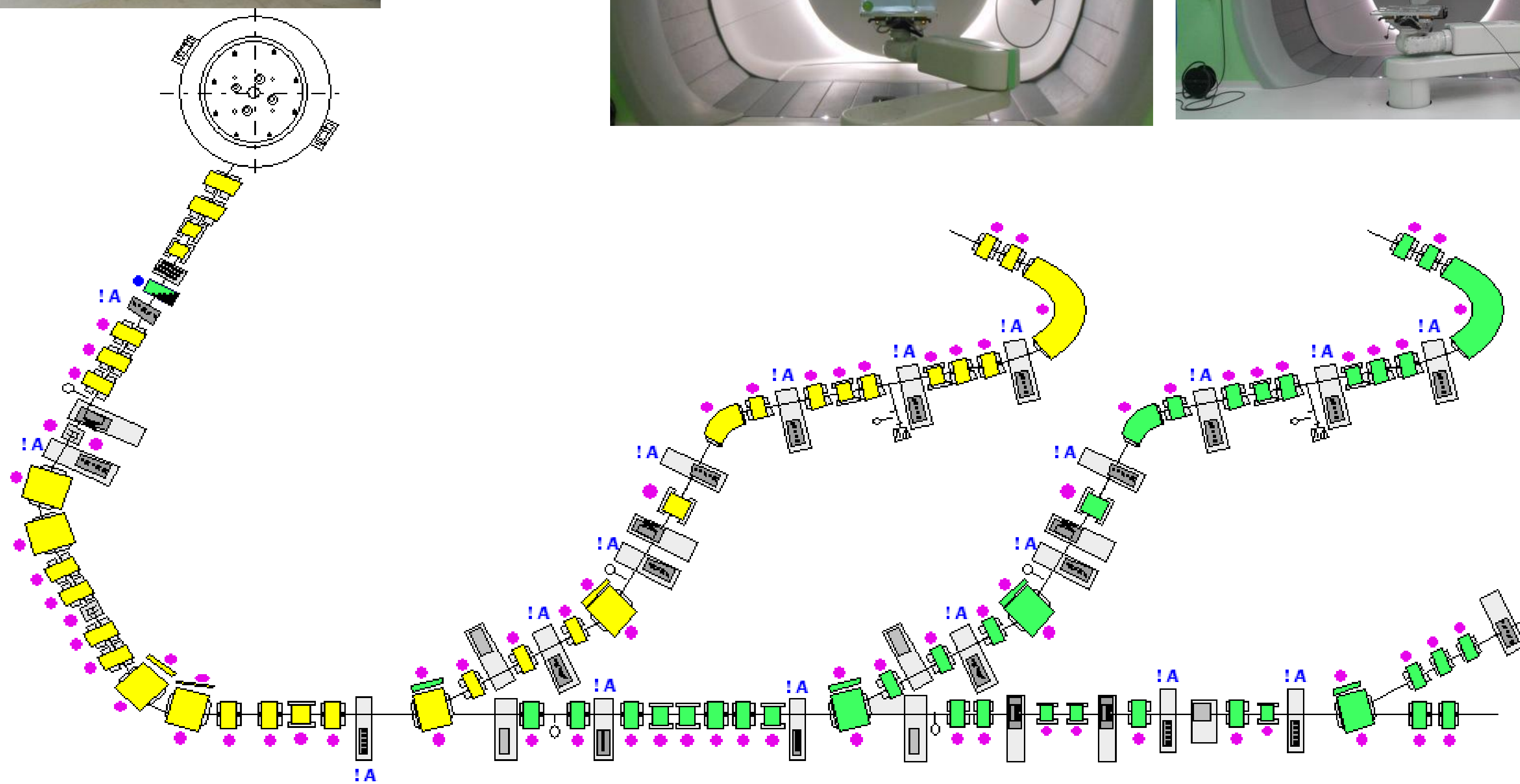


Devices for X RT are cheaper and simpler


CAUTION
NO
STEP
ATTENZIONE
1

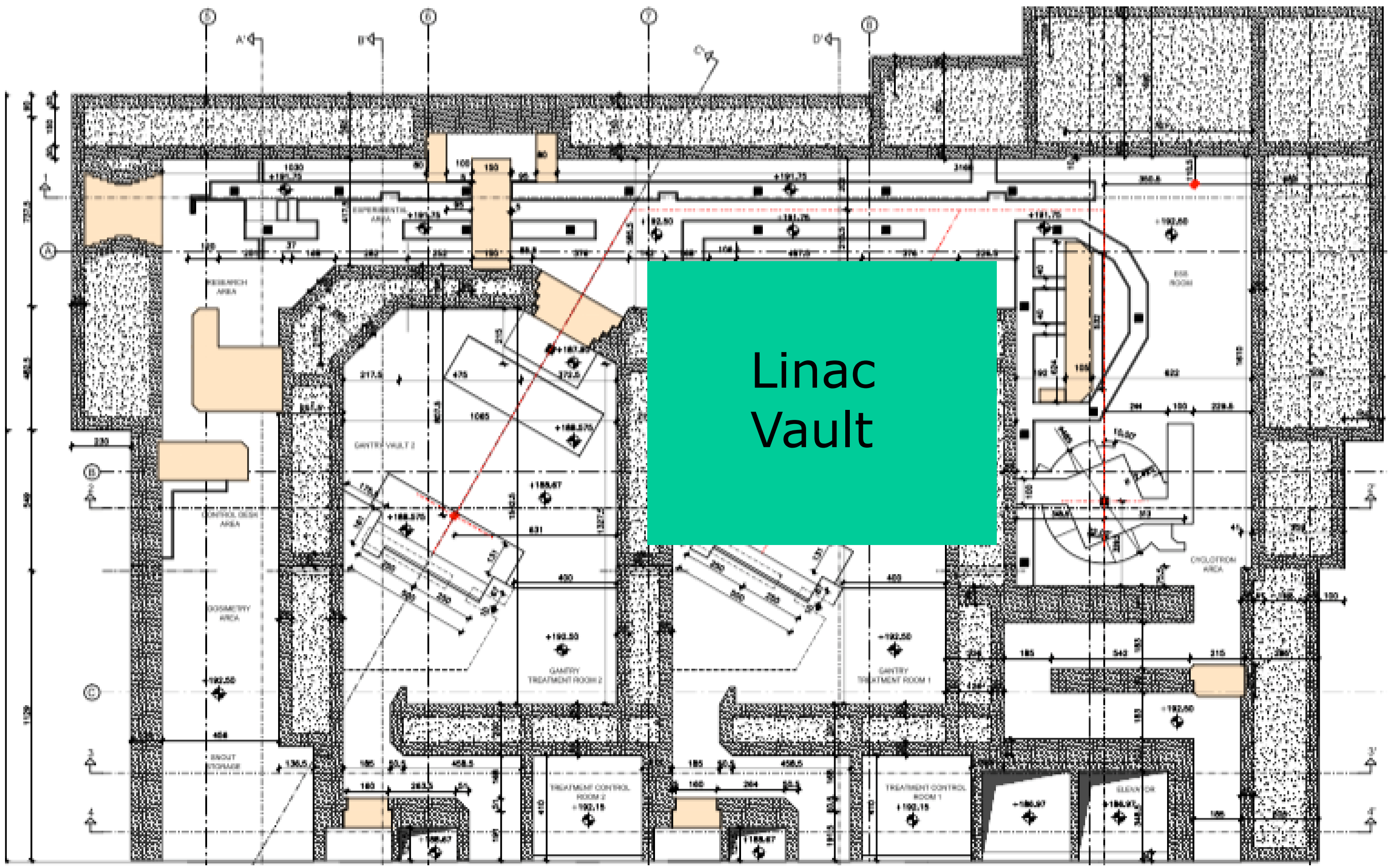






Protons vs. photons in Trento

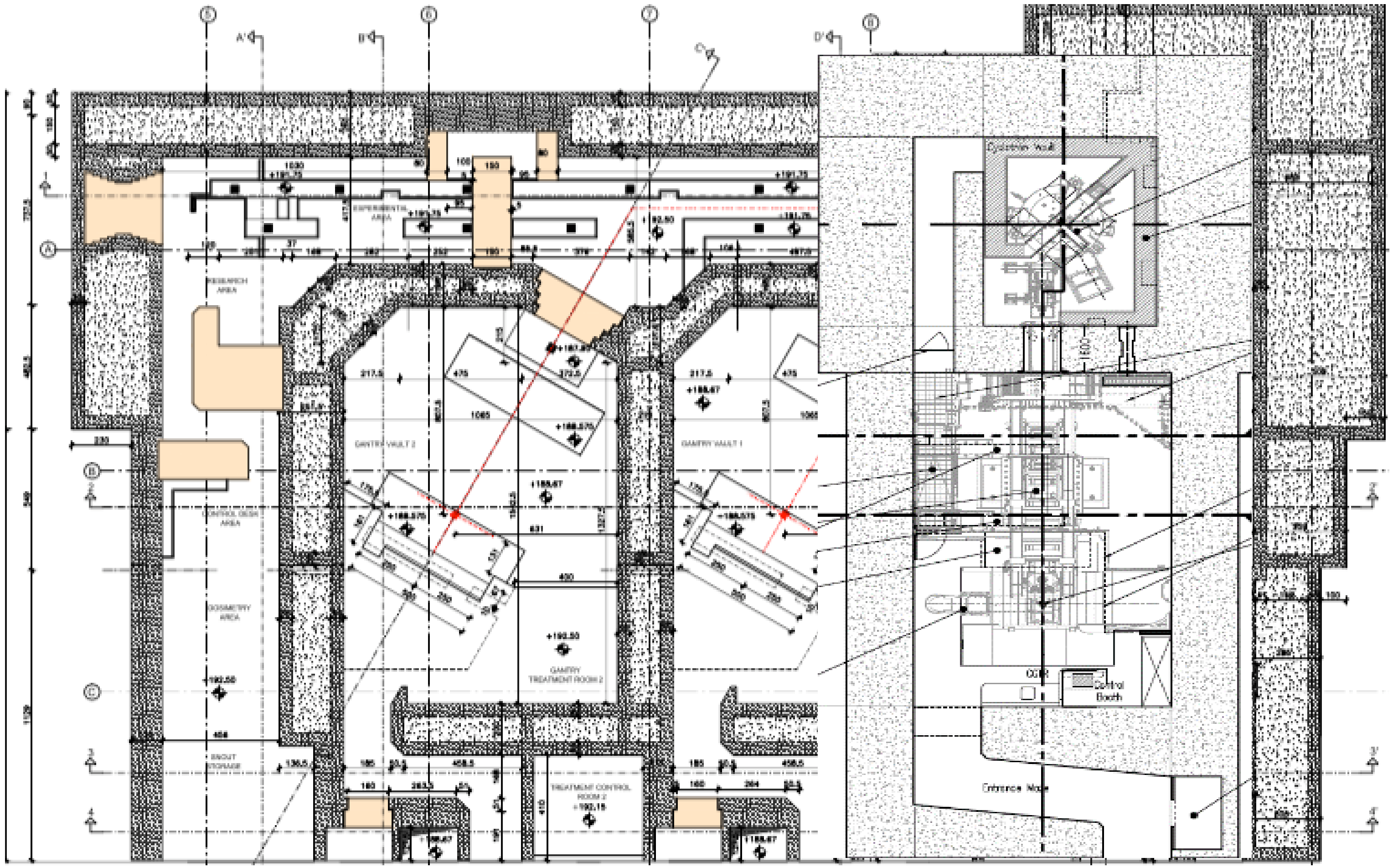
About 30m



About 45m

Single vs multiple room facilities

About 30m



About 45m

What are the changes/compromises?

Courtesy of J Habrand

The beam has a time structure (possible impact on dosimetry)

Compact gantry →

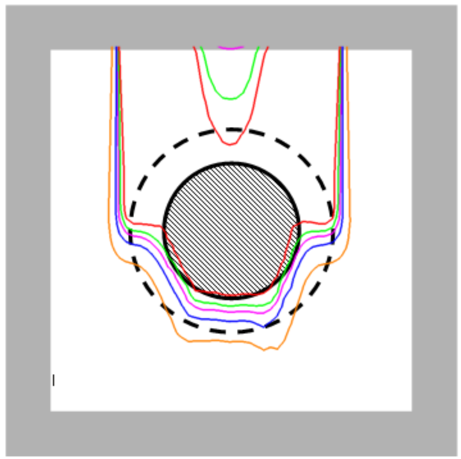
- more couch rotations (possible impact on accuracy and treatment time)
- does not allow for a 360° CBCT acquisition

Smaller field size →

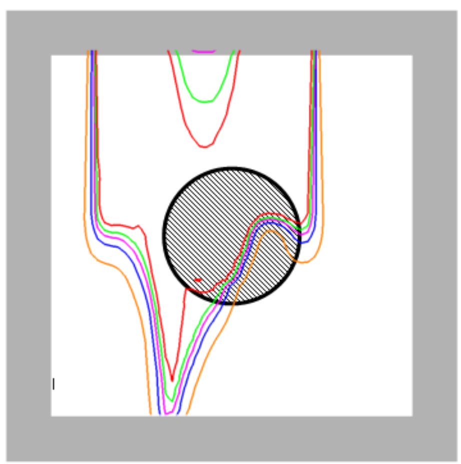
- More «patched» fields are needed
- Increased treatment time in some cases (e.g. CSI)

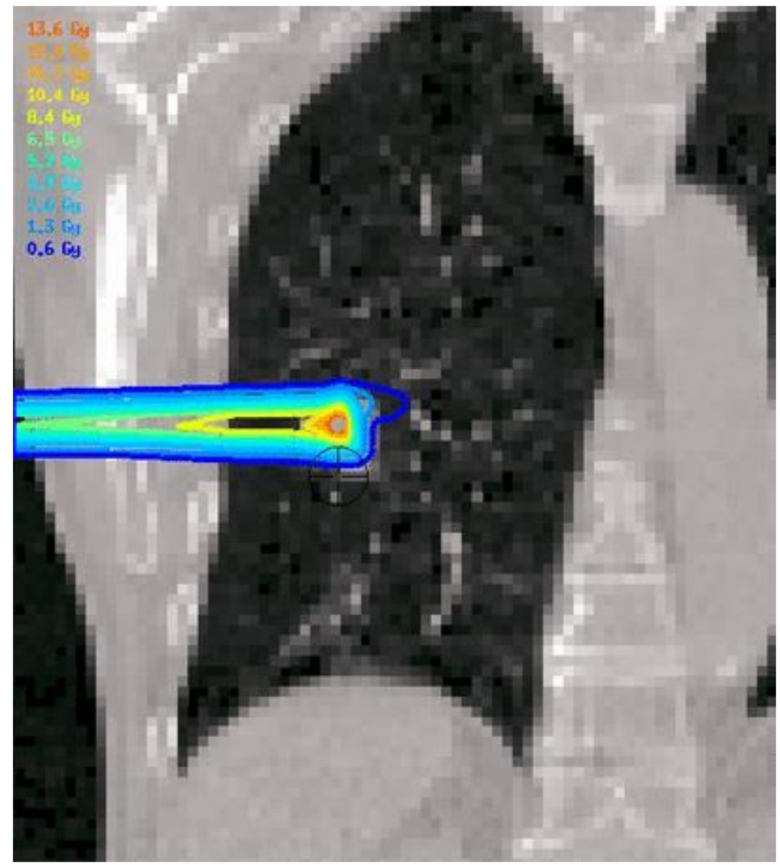
Protons are more sensitive to geometrical uncertainties

No setup error



10mm error



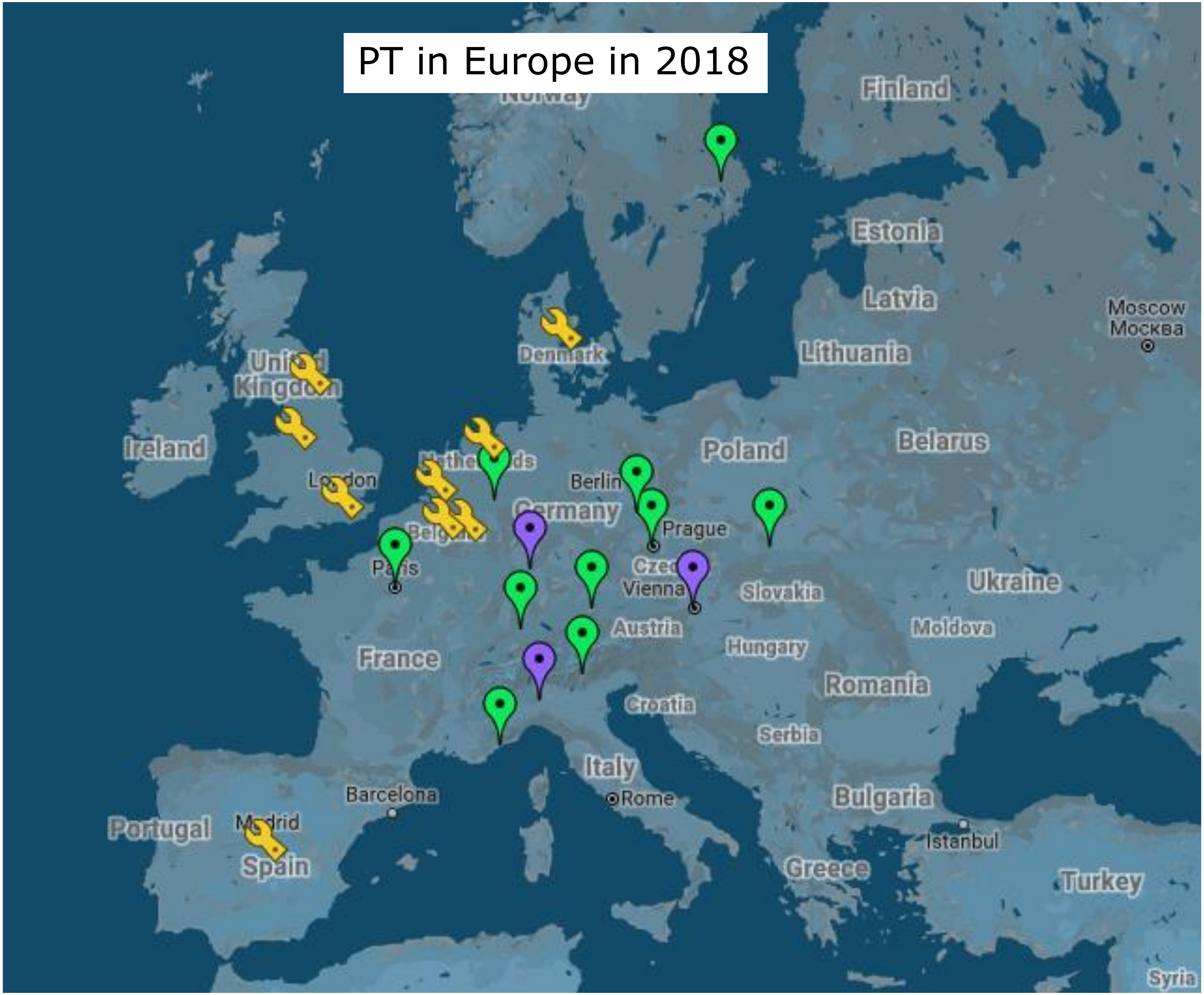


Courtesy M. Sohn

High image quality for positioning is needed (even though it is not standard yet)

PT in Europe in 2008

PT in Europe in 2018



Protontherapy is and will remain a scarce resource: how to select patients?

In Italy(LEA): histology/disease location-based approach

1. Chordomas/condrosarcomas (selected localizations)
2. Spinal cord and (most) brainstem tumors
3. Sarcomas (selected localizations
4. Meningiomas (critical localizations)
5. Orbital and periorbital
6. Ocular melanoma
7. Salivary gland ACC
8. Solid pediatric tumors
9. Highly radiosensitive patients (e.g. genetic syndroms)
10. Recurrencies in the same area previously treated

(not a single patient treated in this setting yet)

Pros and cons of this patient selection approach

Pros:
- Same approach used in the past to send patients abroad
- Usually justified with the need of being based on “evidence”
- Safe and predictable from the budget perspective.

Cons:
- It is more or less the opposite of “personalized medicine”
- Lacks a clear path for testing new indications
- It does not take advantage of a unique feature of RT, i.e. treatment planning.

Can we do things differently, better?

Can we use validated multivariable NTCP-models for evidence-based *selection of patients* and *clinical validation* of proton therapy aiming at reduction of side effects?

H. Langendijk

The "model-based" approach

Langendijk R&O 2013

Multivariable Normal Tissue Complication Probability (NTCP) models

In silico planning comparative studies

Comparison of dose distributions

Estimation of the potential benefit

integrating step 1 and 2

Selection

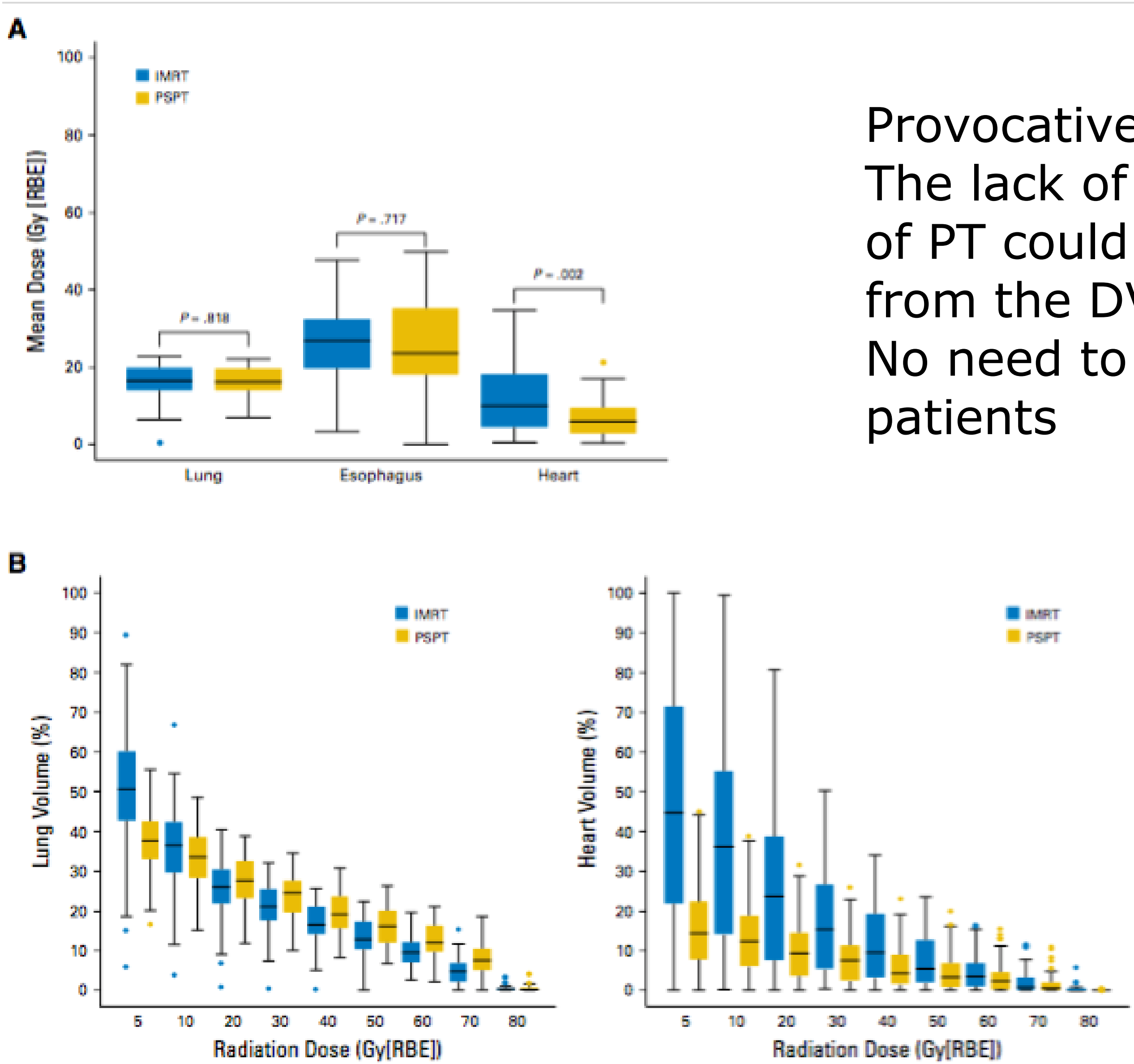
Clinical validation:

(RCT's)

Model-based validation studies

Validation

Model-based approach may help running more useful trials



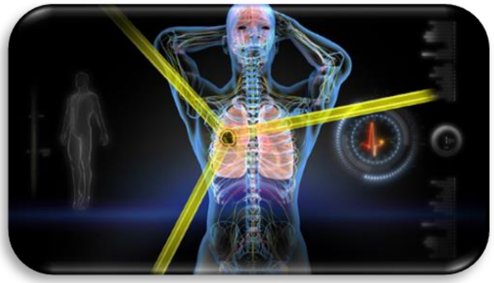
Provocative thought:
The lack of superiority of PT could be inferred from the DVHs.
No need to treat 149 patients

Liao
JCO 2018

Conclusions

Protontherapy

- Has solved most technological problems (in beam delivery)
- Will be part of the future of radiation oncology
- The current challenge is to select the patient who will benefit the most and prove such benefit.



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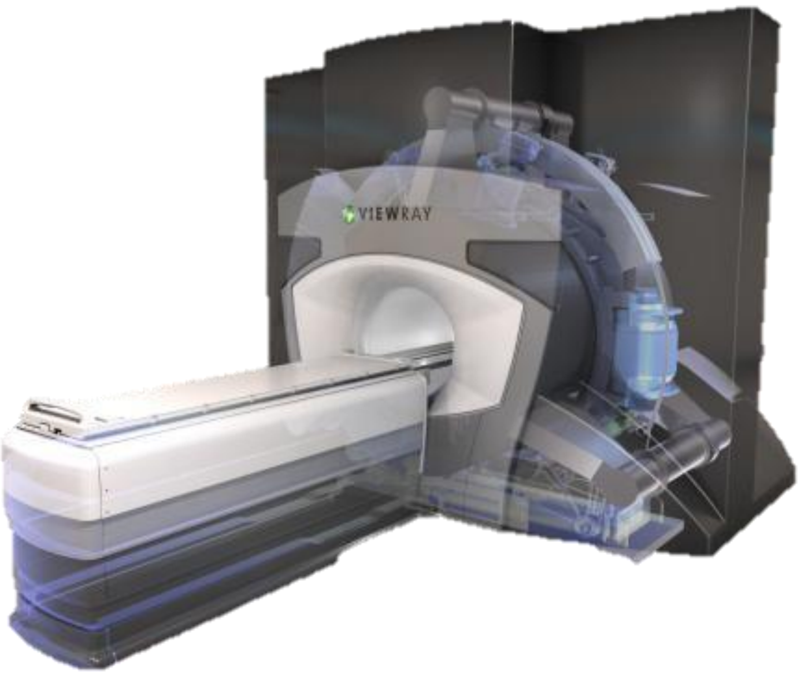
The MRIdian System

Dr. Veronica Pollutri

Radiation Therapist
Medipass Srl
Fondazione Policlinico Universitario Gemelli
veronicapollutri@gmail.com

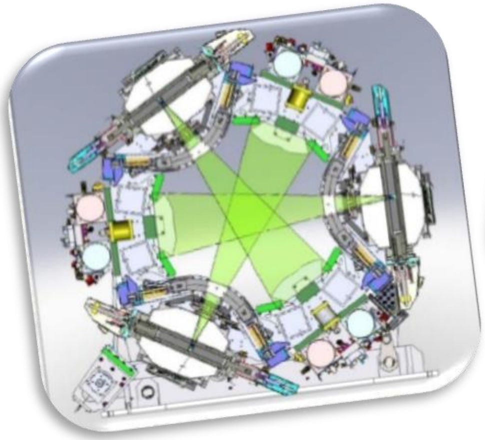
The MRIdian system

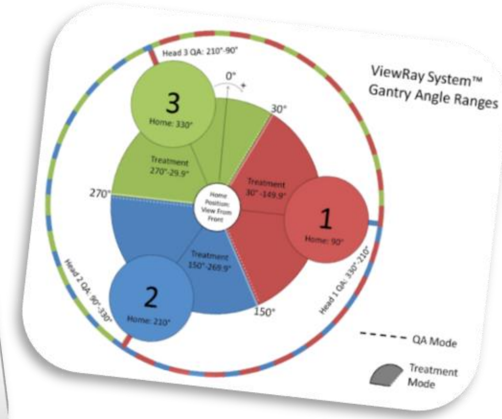


TOPICS

- **System Overview**
- ***Setup in MRI***
- ***Simulation***
- ***Delivery***

MRIdian RT Components





- ❖ *3 headed Cobalt 60 system*
- ❖ *Dose rate 550cGy/min*
- ❖ *Step and Shoot Modality*
- ❖ *Leaf width: 1.05 cm*
- ❖ *Maximum field: 27.3 x 27.3 cm^2*
- ❖ *Minimum field: 1.05 x 1.05 cm^2*

MRIdian MR Components

❖ *0.35 T Magnetic Field*

❖ *Faraday Cage*

❖ *Metal Detector*

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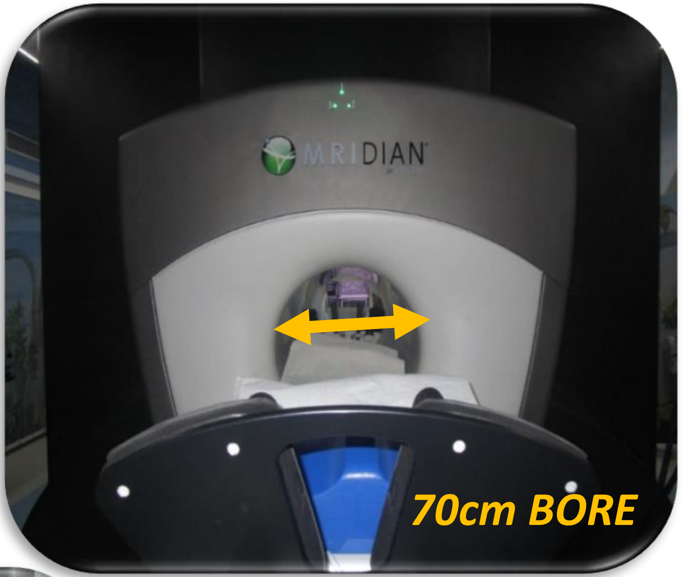
MRIdian Treatment Components

- ❖ 3 DOF Couch
- ❖ MR isocenter = RT isocenter
- ❖ 2 Control Panels inside the bunker
- ❖ 70 cm Bore



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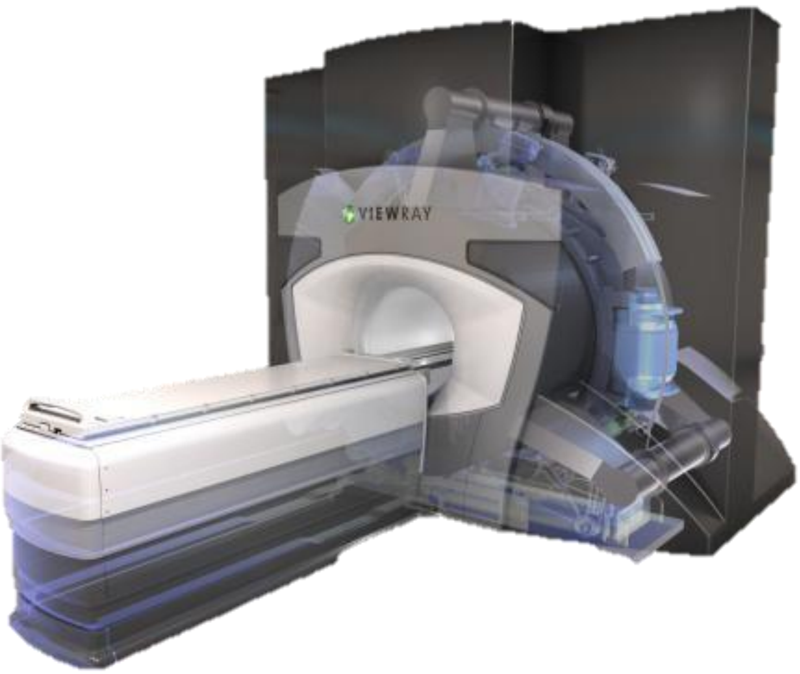
The MRIdian system



TOPICS

- System Overview
- **Setup in MRI**
- Simulation
- Delivery

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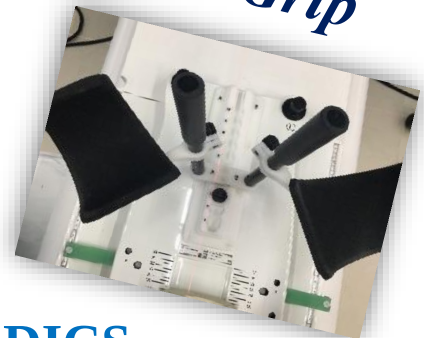
T-Grip

MRIdian SETUP

U-Grip

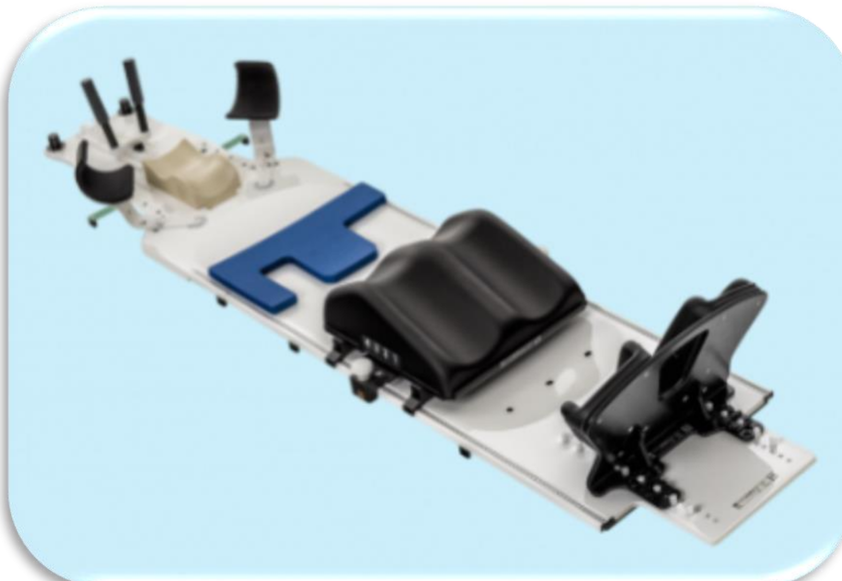


FLUXBOARD *by* MACROMEDICS

dedicated treatment Couch-Top for the ViewRay MRIdian

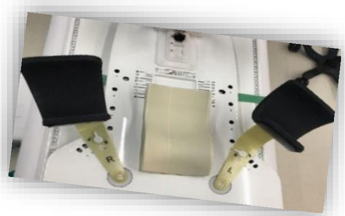
***CONVENTIONAL FEATURES*:**

FEET FIX, KNEE FIX, SUPPORTS FOR HEAD AND CONFORTABLE ARMS POSITIONING



***SPECIFIC FEATURES*:**

MR SAFE AND CUSTOM MIRROR



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MRIdian SETUP

Bore of 70 cm

+

Borderline Claustrophobia

+

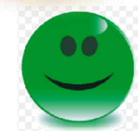
Long treatment time

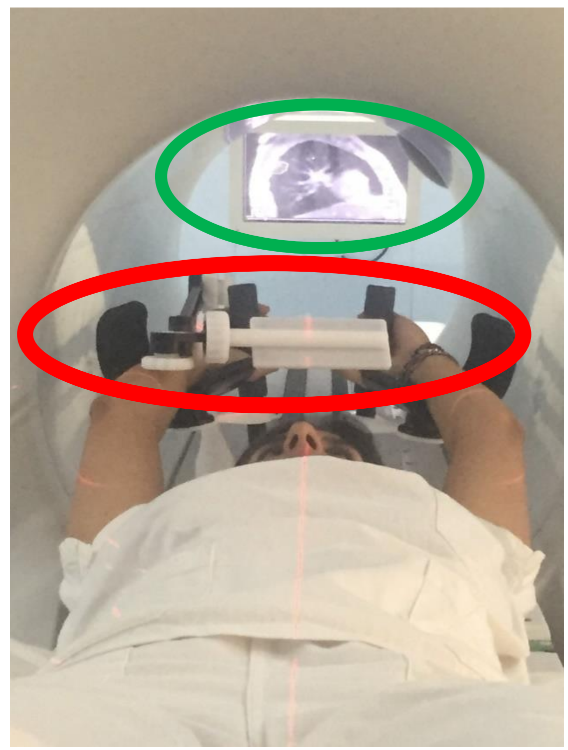
⇩

Decrease COMPLIANCE

Squeeze bulb

Headphones





HEADPHONES
To decrease background noise

+

Alarm

+

CUSTOM MIRROR

+

MONITOR

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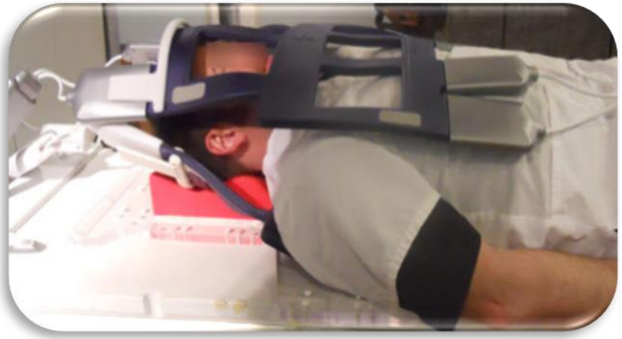
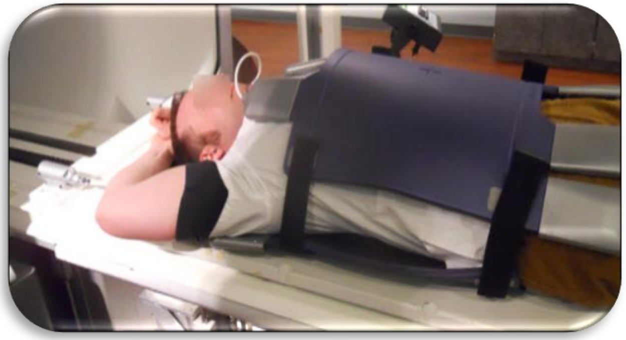
MRIdian SETUP

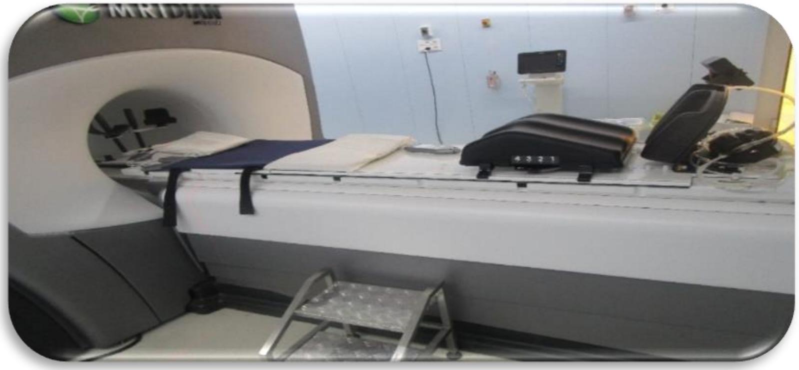
Head and Neck Coils



SURFACE COILS
to receive the signal

Torso Coils





Part of the immobilization system.

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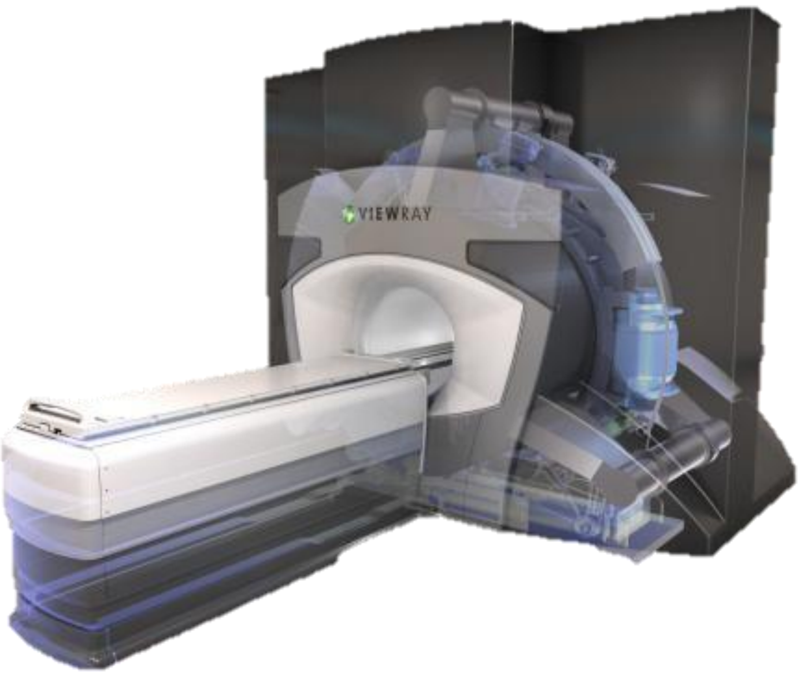

TOPICS

- System Overview
- Setup in MRI
- **Simulation**
- Delivery

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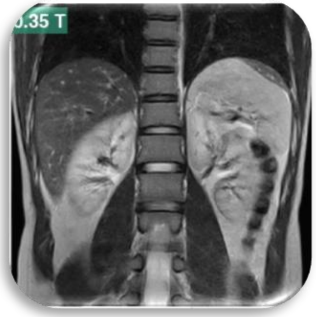
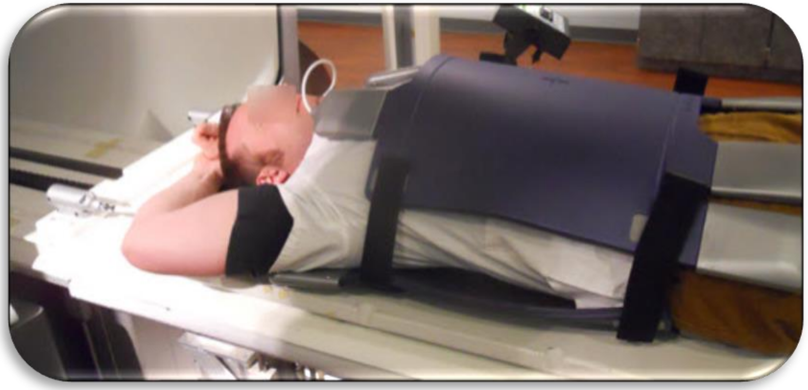
MRIdian Simulation





MR simulation

CT simulation

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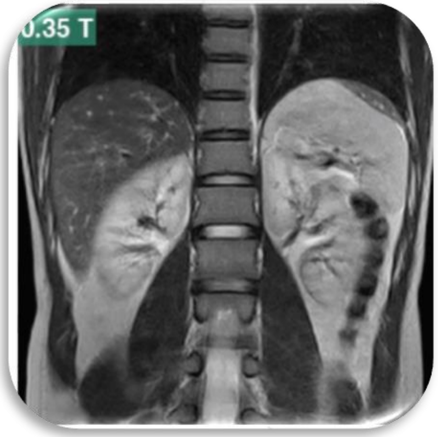
MR Simulation

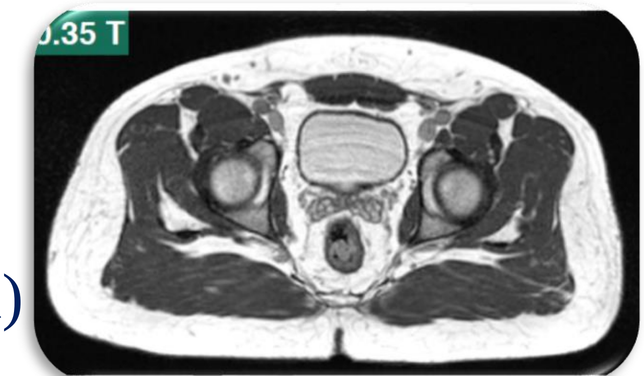
3D image scan



True FISP Sequence

(T2/T1)*

Imaging Type	Available FOV (mm)	Available Resolution (mm)	Scan Time
Pilot Scan (3D)	540 x 540 x 480	3.0 x 3.0 x 3.0	15 sec
Planning Scan (3D)	19 defined FOVs convering the 1, 50 and 99 percentile of the US population	0.75 x 0.75 x 0.75 1.5 x 1.5 x 1.5 1.5 x 1.5 x 3.0	Less than 3 min (except for sub millimeter resolution)
Treatment Scan (2D) 1 or 3 parallel slices	270 x 270 350 x 350 450 x 450	3.5 x 3.5 x 3.5 3.5 x 3.5 x 5.0 3.5 x 3.5 x 7.0	4 fr/sec for 1 slice 2 fr/sec for 3 slices



- BREATHING MODALITY
  (Free Breathing or Breath Hold Inspiration)

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Hu, Yanle, et al., *Characterization of the onboard imaging unit for the first clinical magnetic resonance image guided radiation therapy system*.
Med Phys 42(10), 2015 5828-5837.

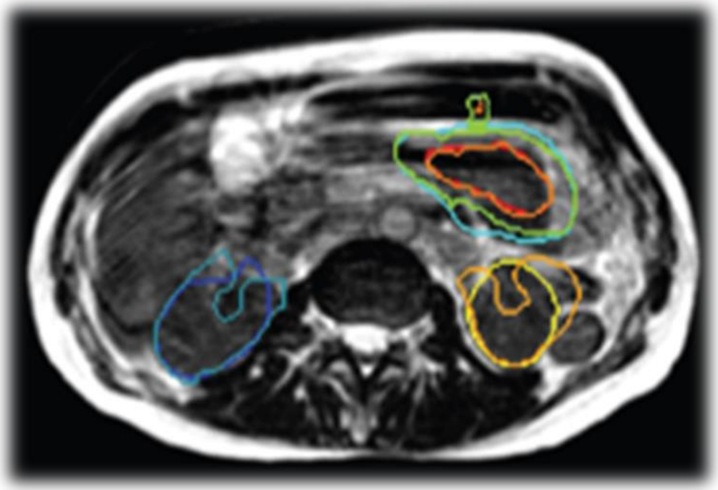
MR Simulation

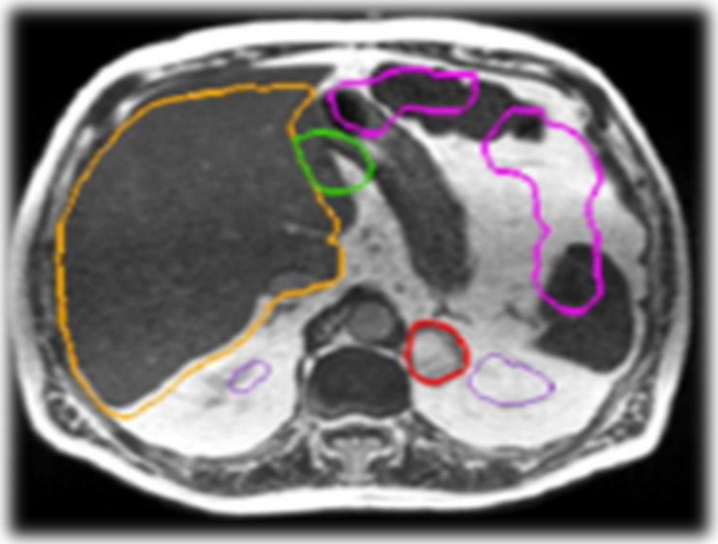
3D image scan

To hold or not to hold?

Breath Hold:

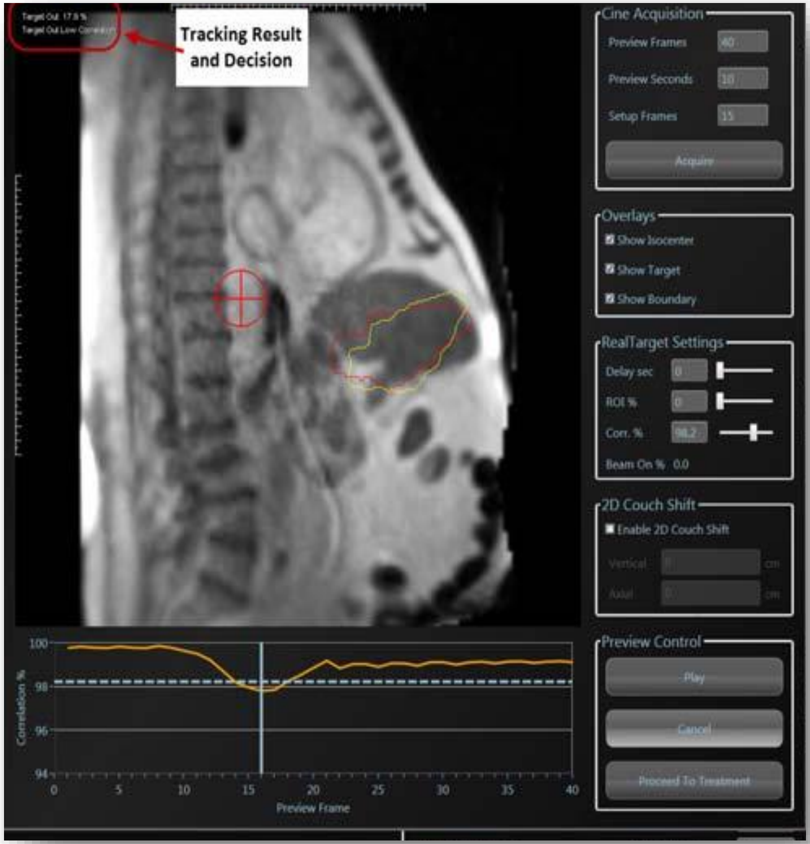
- *Can impact on image quality, Timing and Volume Consistency*
- *Site dependent*





MR Simulation

2D Cine



IMAGING MRI CINE

- REAL TARGET MOVEMENT
- OAR motion
- PATIENT COMPLIANCE

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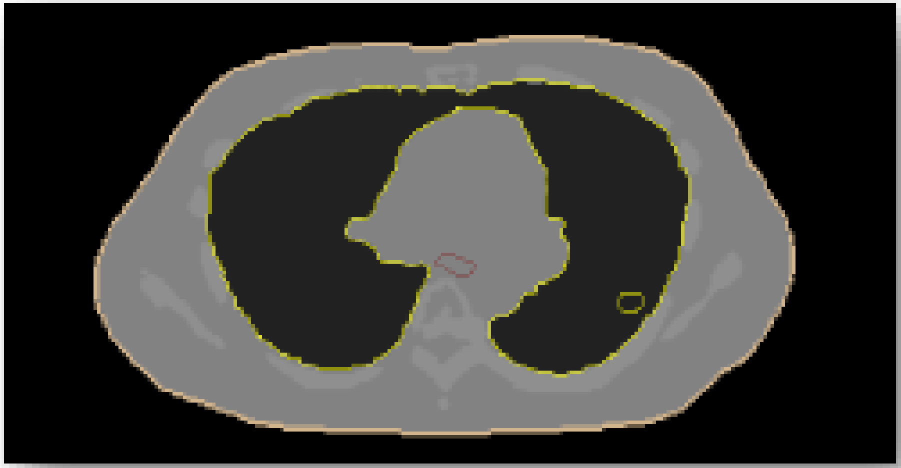
CT Simulation



- **Same immobilisation device**
- **Electron Density Map to perform Dose Calculation**

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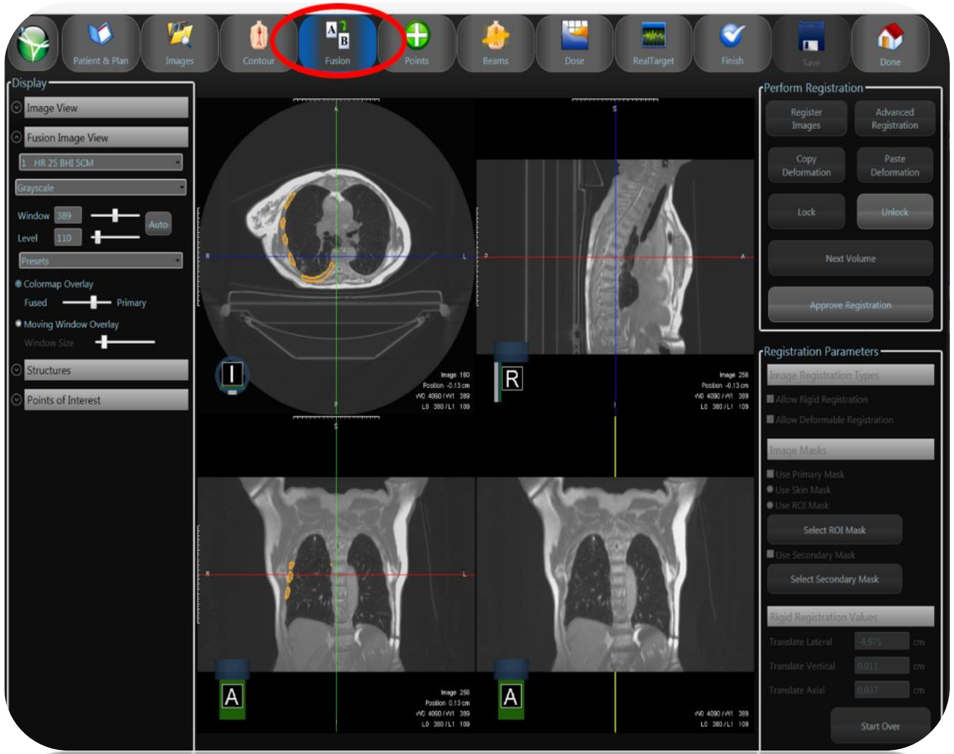
CT Simulation

FUSION BETWEEN MR-IMAGES AND CT-IMAGES to provide electron density



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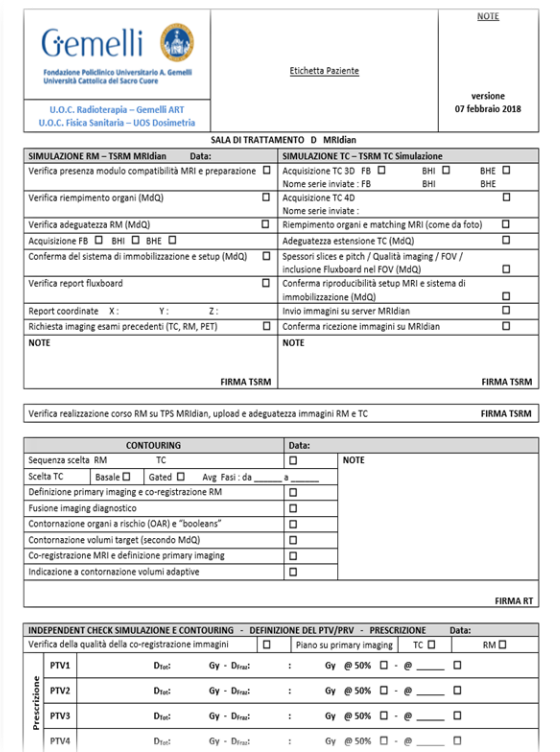
Gemelli ART Procedures
MRIdian Workflow



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U.O.C. Radioterapia – Gemelli ART
U.O.C. Fisica Sanitaria – UOS Dosimetria

Etichetta Paziente

NOTE

versione
07 febbraio 2018

SALA DI TRATTAMENTO D MRIdian

SIMULAZIONE RM – TSRM MRIdian Data:	SIMULAZIONE TC – TSRM TC Simulazione
Verifica presenza modulo compatibilità MRI e preparazione ☐	Acquisizione TC 3D FB ☐ BHI ☐ BHE ☐ Nome serie inviate : FB BHI BHE
Verifica riempimento organi (MdQ) ☐	Acquisizione TC 4D ☐ Nome serie inviate :
Verifica adeguatezza RM (MdQ) ☐	Riempimento organi e matching MRI (come da foto) ☐
Acquisizione FB ☐ BHI ☐ BHE ☐	Adeguatezza estensione TC (MdQ) ☐
Conferma del sistema di immobilizzazione e setup (MdQ) ☐	Spessori slices e pitch / Qualità imaging / FOV / inclusione Fluxboard nel FOV (MdQ) ☐
Verifica report fluxboard ☐	Conferma riproducibilità setup MRI e sistema di immobilizzazione (MdQ) ☐
Report coordinate X : Y : Z :	Invio immagini su server MRIdian ☐
Richiesta imaging esami precedenti (TC, RM, PET) ☐	Conferma ricezione immagini su MRIdian ☐
NOTE FIRMA TSRM	NOTE FIRMA TSRM

Verifica realizzazione corso RM su TPS MRIdian, upload e adeguatezza immagini RM e TC FIRMA TSRM

CONTOURING	Data:	
Sequenza scelta RM TC	☐	NOTE
Scelta TC Basale ☐ Gated ☐ Avg Fasi : da _____ a _____		
Definizione primary imaging e co-registrazione RM	☐	
Fusione imaging diagnostico	☐	
Contornazione organi a rischio (OAR) e "booleans"	☐	
Contornazione volumi target (secondo MdQ)	☐	
Co-registrazione MRI e definizione primary imaging	☐	
Indicazione a contornazione volumi adaptive	☐	
		FIRMA RT

INDEPENDENT CHECK SIMULAZIONE E CONTOURING - DEFINIZIONE DEL PTV/PRV - PRESCRIZIONE Data:

Verifica della qualità della co-registrazione immagini ☐ | Piano su primary imaging | TC ☐ RM ☐

Prescrizione
PTV1 Dtot: Gy - Dfraz: : Gy @ 50% ☐ - @ _____ ☐
PTV2 Dtot: Gy - Dfraz: : Gy @ 50% ☐ - @ _____ ☐
PTV3 Dtot: Gy - Dfraz: : Gy @ 50% ☐ - @ _____ ☐
PTV4 Dtot: Gy - Dfraz: : Gy @ 50% ☐ - @ _____ ☐

Each step is governed by a Check-List

Follow a scheme helps to decrease issues and speeds up the workflow

<u>RTT tasks:</u>

✓ Reporting the coordinates

✓ Reporting data and immobilization system

✓ Type of preparation to ensure always reproducing same conditions

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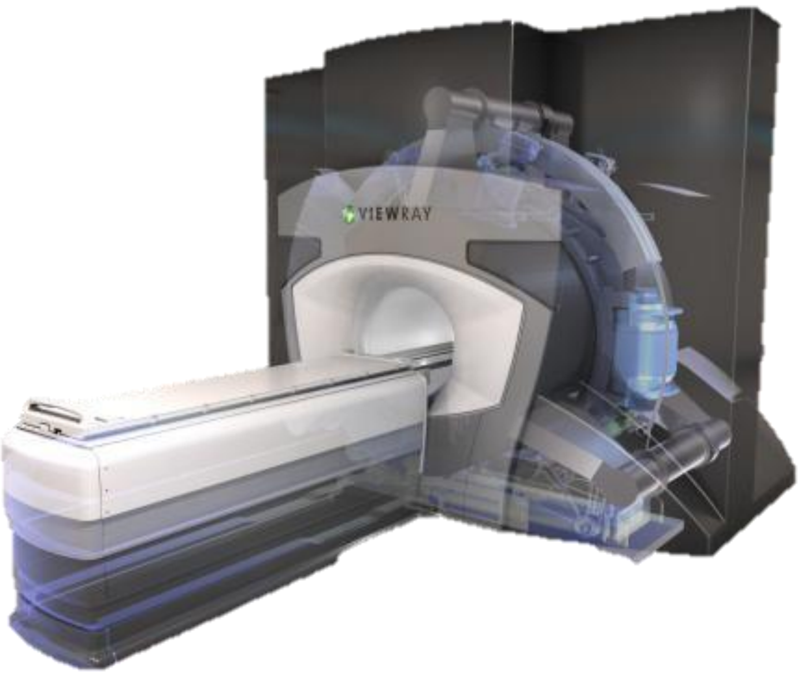

TOPICS

- System Overview
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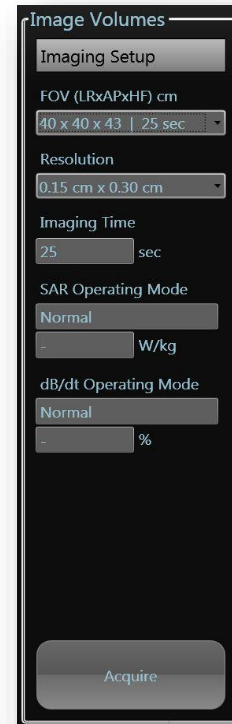
- **Delivery**

MRIdian Delivery



HIGH RESOLUTION

25 SEC scan

3D MATCH

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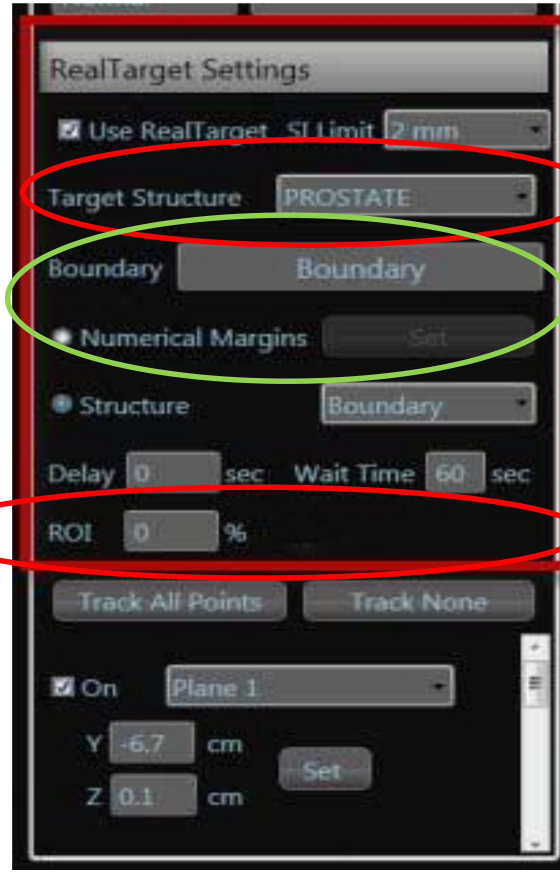

REAL TARGET

IN A SAGITTAL SLICE WE SET THE TARGET TO TRACK, ITS MARGIN , NAMED BOUNDARY, AND THE % ROI THAT ENABLE THE GATING SISTEM TO STOP THE DELIVERY

Delay: 0

Wait Time: 60

ROI: 5%

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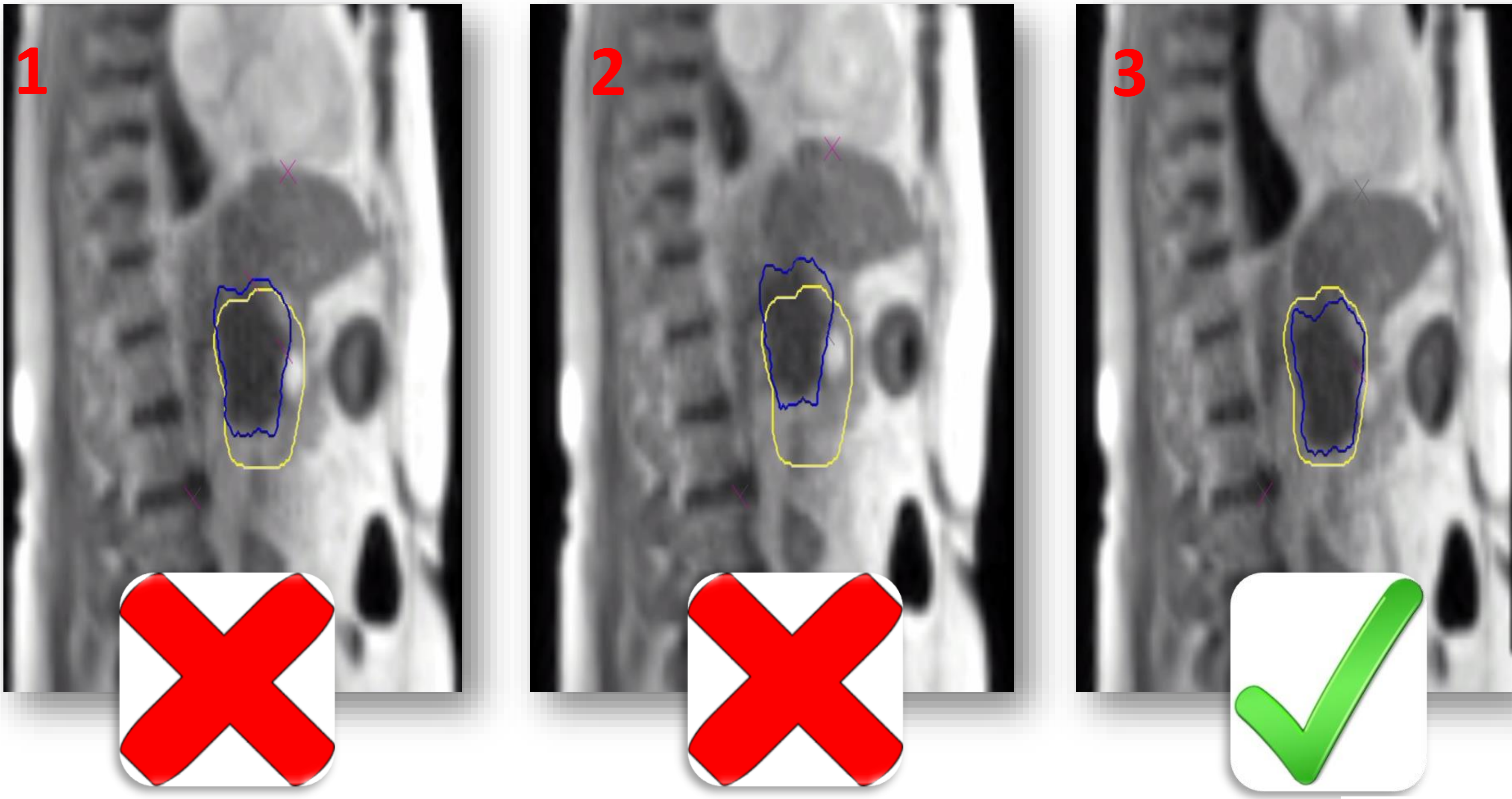
MRIdian Delivery

Target OUT = Beam Hold

Target OUT = Beam Hold

Target IN = Beam ON



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The Future…
MRIdian Linac

The Mridian Linac system, courtesy of Viewray Inc.

6 MV Linac

(FFF; D_{rate}=1000 cGy/min)

+

RM Siemens @ 0,35 T

8 FPS

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Many Thanks and Enjoy ESTRO!!!