# Target volume determination- from imaging to margins.

ESTRO School

Barcelona, 10-13 April 2016

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France
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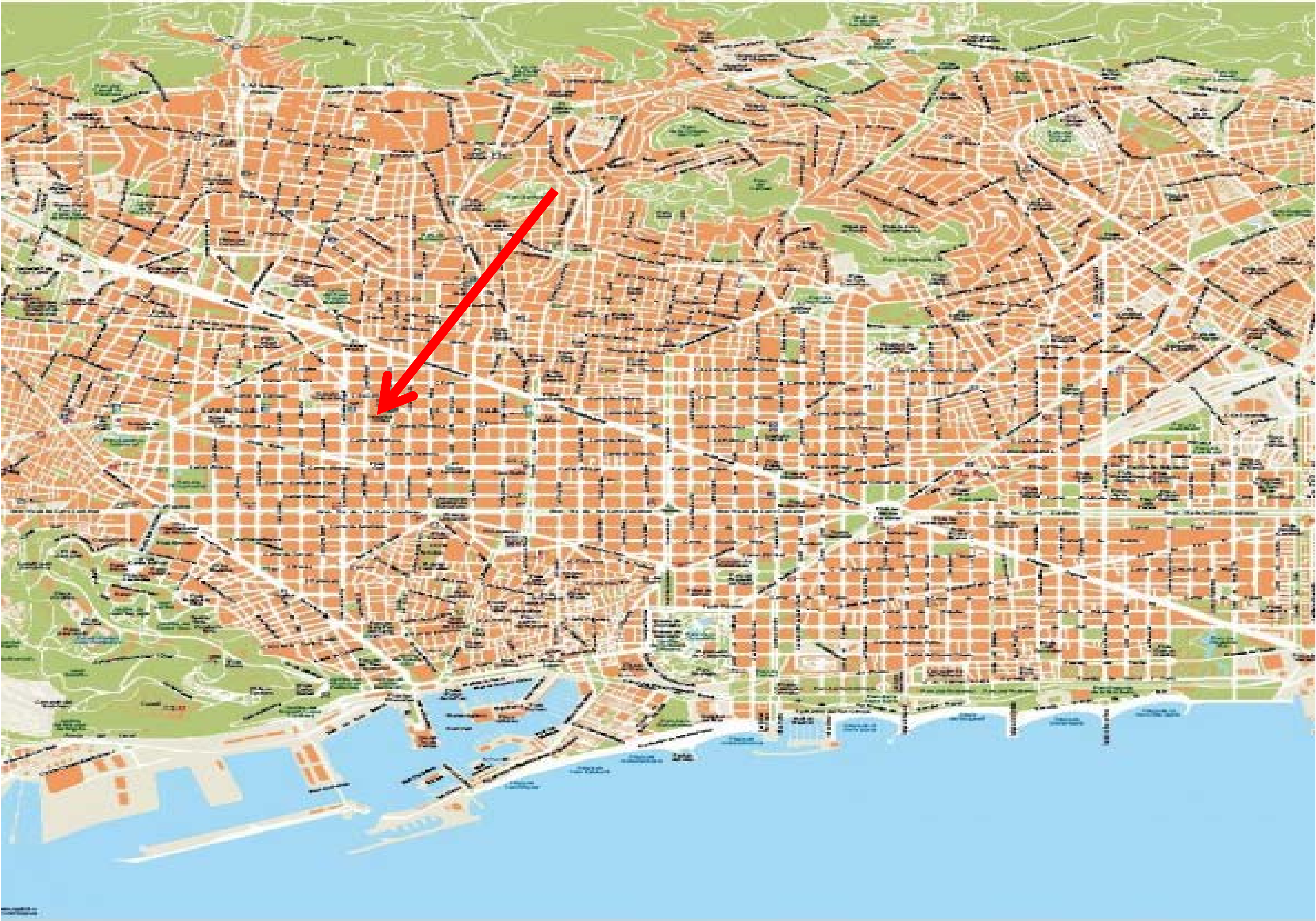
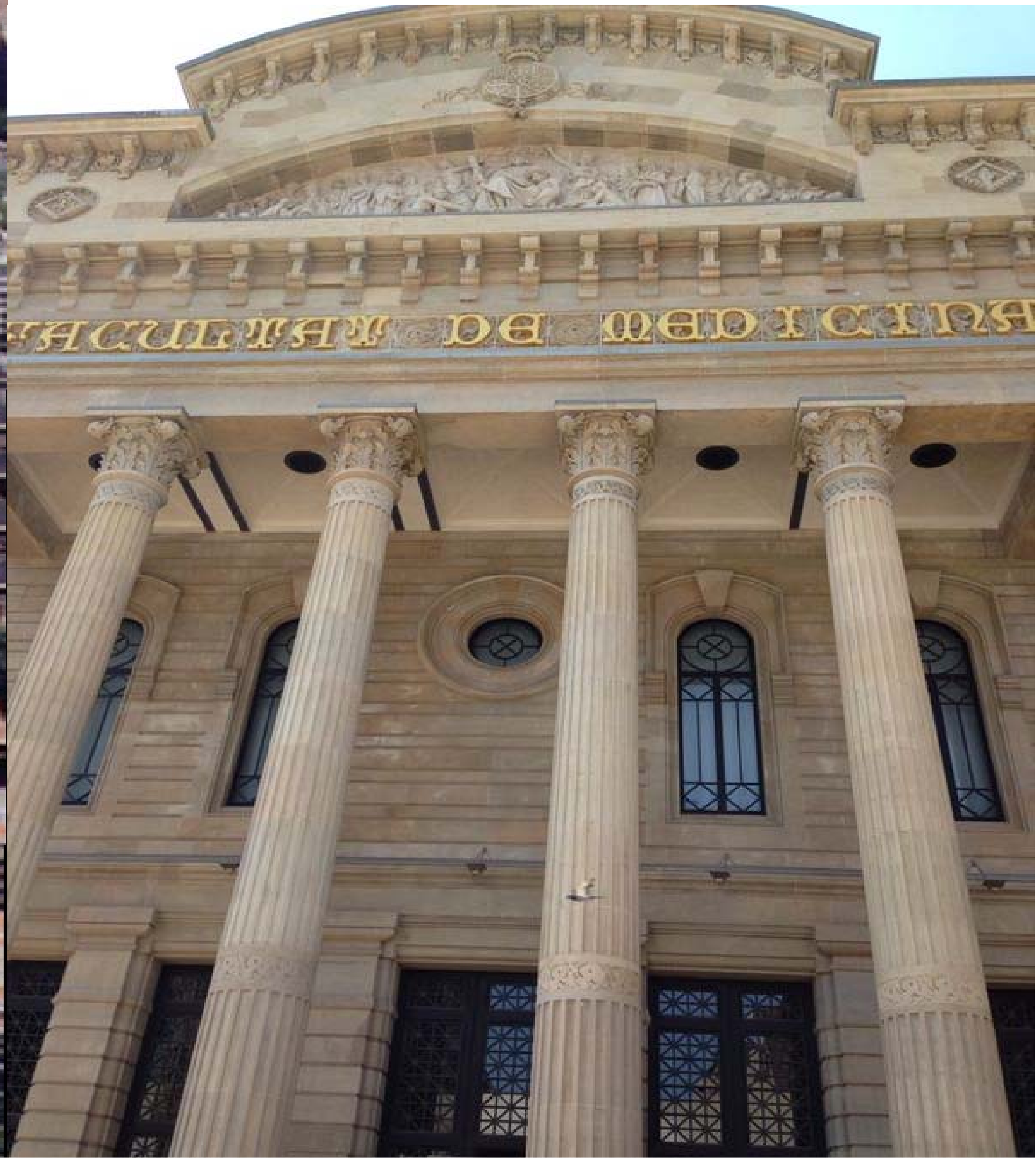
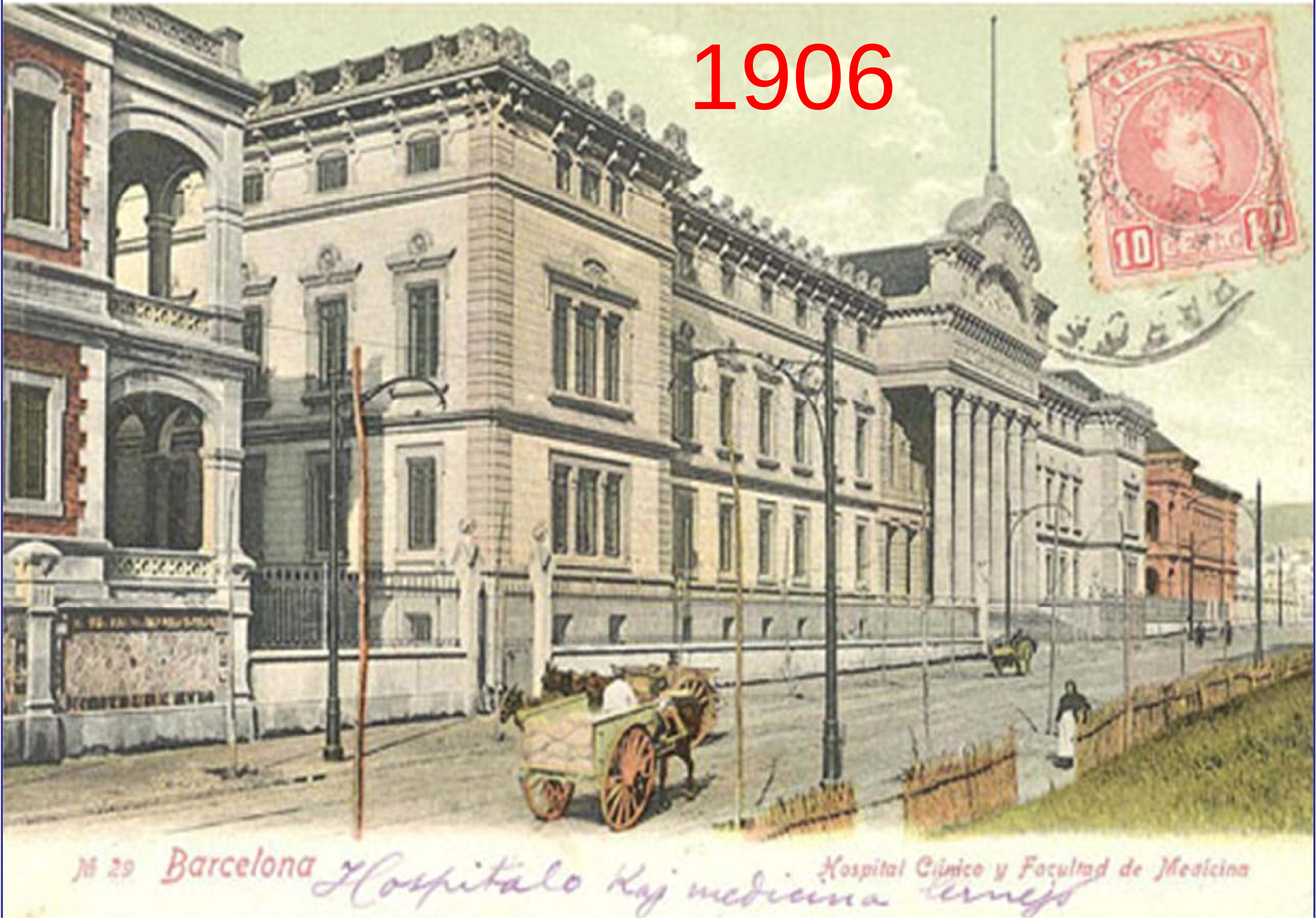
AP-7
C-33
C-32
C-16
Martorell
C-58
El Masnou
B-20
Parc Natural de la Serra de Collserola
Badalona
A-2
AP-2
N-340
B-23
Barcelone
Cornellà de Llobregat
C-31
C-32
Castelldefels
Rat-Penat
Map data ©2016 Google, Inst. Geogr. Nacional


Santiago de Compostela
Galicia
Asturias
Oviedo
Santander
Cantabria
Basque
Vitoria-Gasteiz
Castile and León
Valladolid
Logroño
La Rioja
Pamplona
Navarre
Aragon
Zaragoza
Catalonia
Barcelona
Madrid
Toledo
Extremadura
Mérida
Castile-La Mancha
Valencia
Valencian Community
Balearic Islands
Mallorca
Minorca
Palma
Ibiza
Formentera
Seville
Andalusia
Murcia
Murcia
Canary Islands
Provincia de Santa Cruz de Tenerife
La Palma
Tenerife
Santa Cruz de Tenerife
La Gomera
El Hierro
Gran Canaria
Las Palmas de Gran Canaria
Isla de Alegranza
Isla Graciosa
Lanzarote
Fuerteventura
Provincia de Las Palmas



HOSPITAL CLINIC I UNIVERSITARI
MEDICINE FACULTY
UNIVERSITAT DE BARCELONA




1906
Nº 29 Barcelona
Hospital Clínico y Facultad de Medicina
Hospitalo kaj medicina

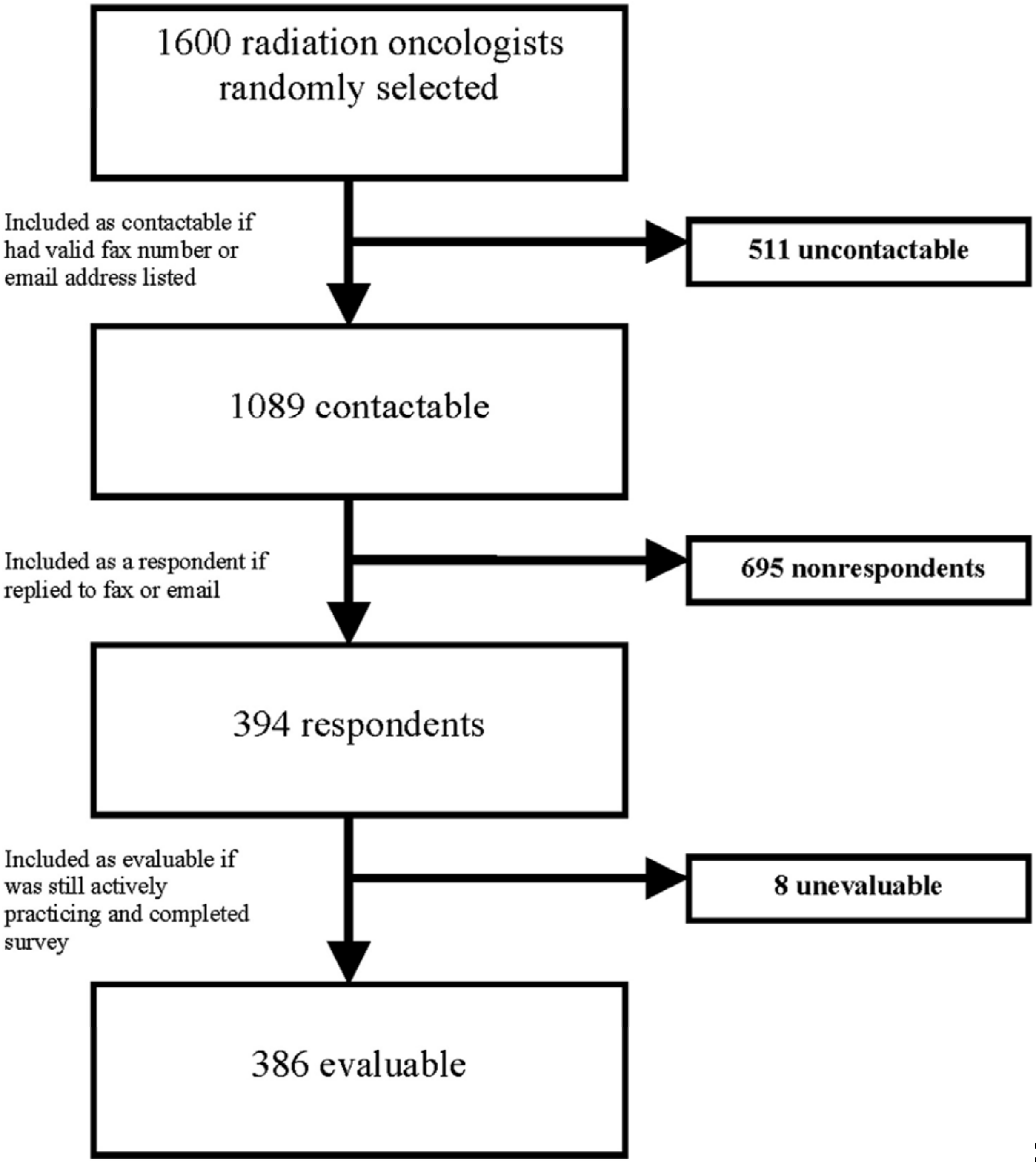
At its inception the institution catered almost exclusively to the poor, the doctors did not charge fees and the tasks of nursing fell to the nuns, and so the first directors often had to put their own money into it.

Despite the difficulties, the Clínic had some of the most prestigious physicians of the era, who in the 1920s converted the Clínic into a centre of research excellence.

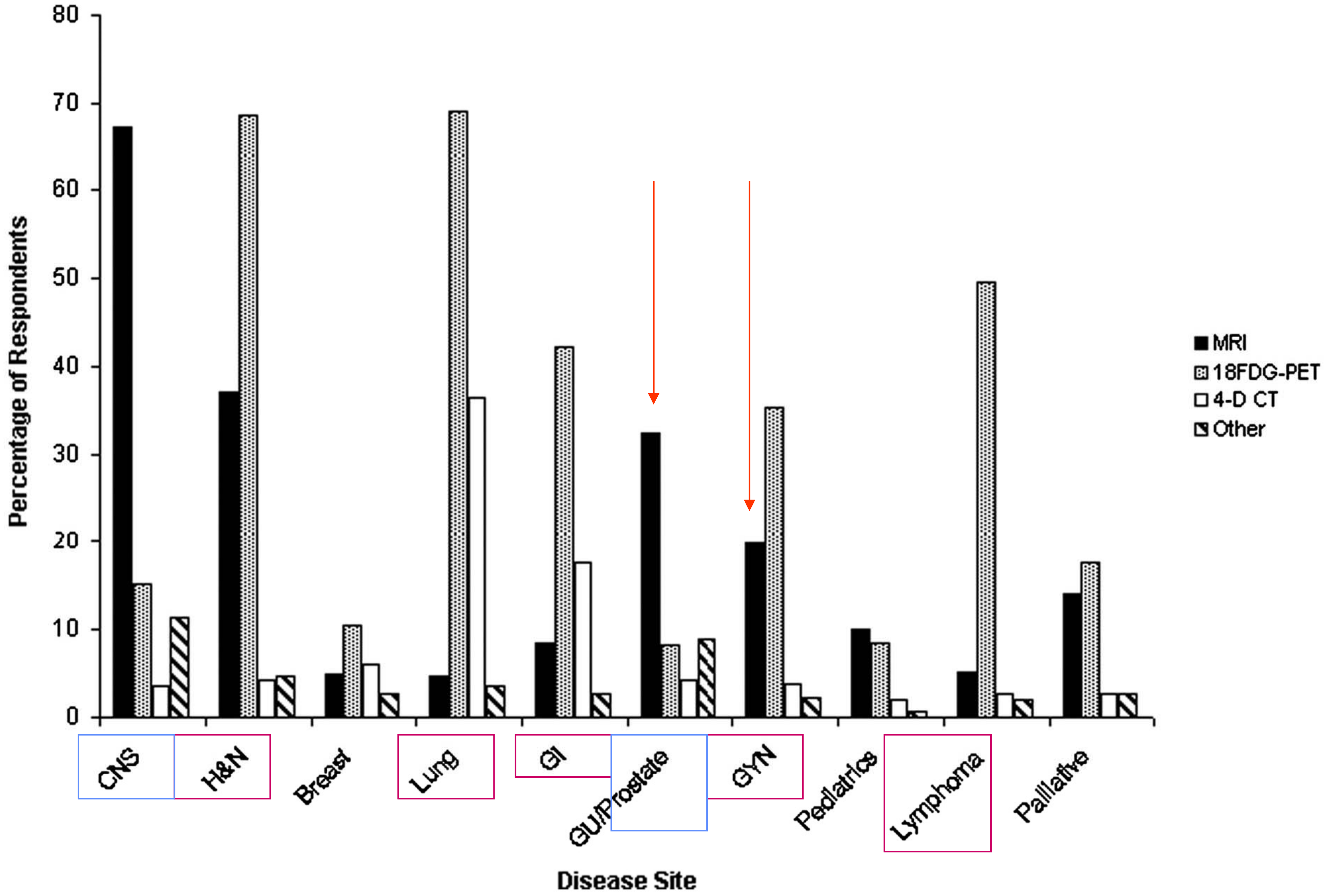

ecte
vecto
ect
vurf
et
getto

**Imaging for target volume delineation: the more, the better?**

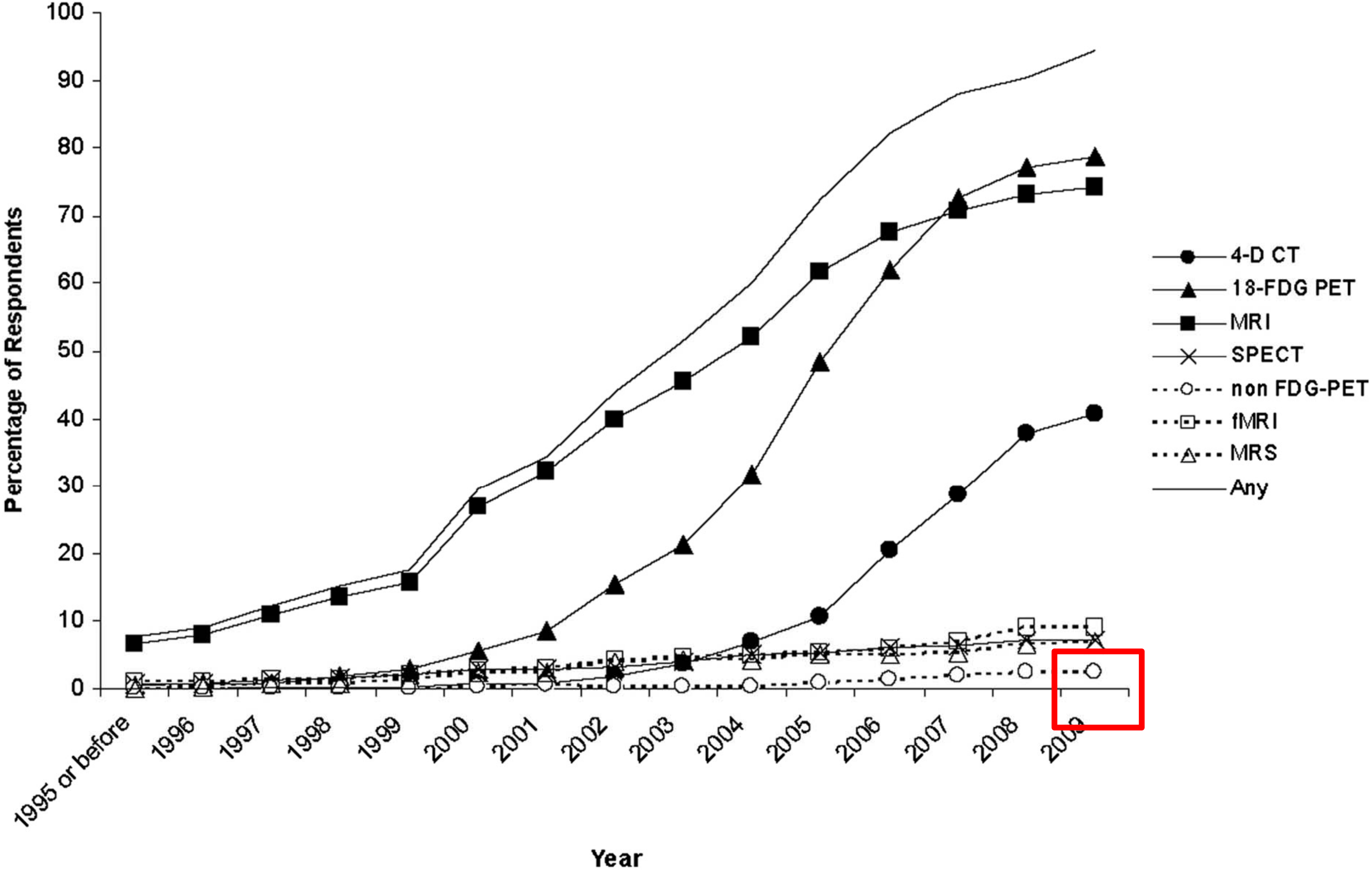
Gert De Meerleer
Esther Troost




Simpson et al, 2009



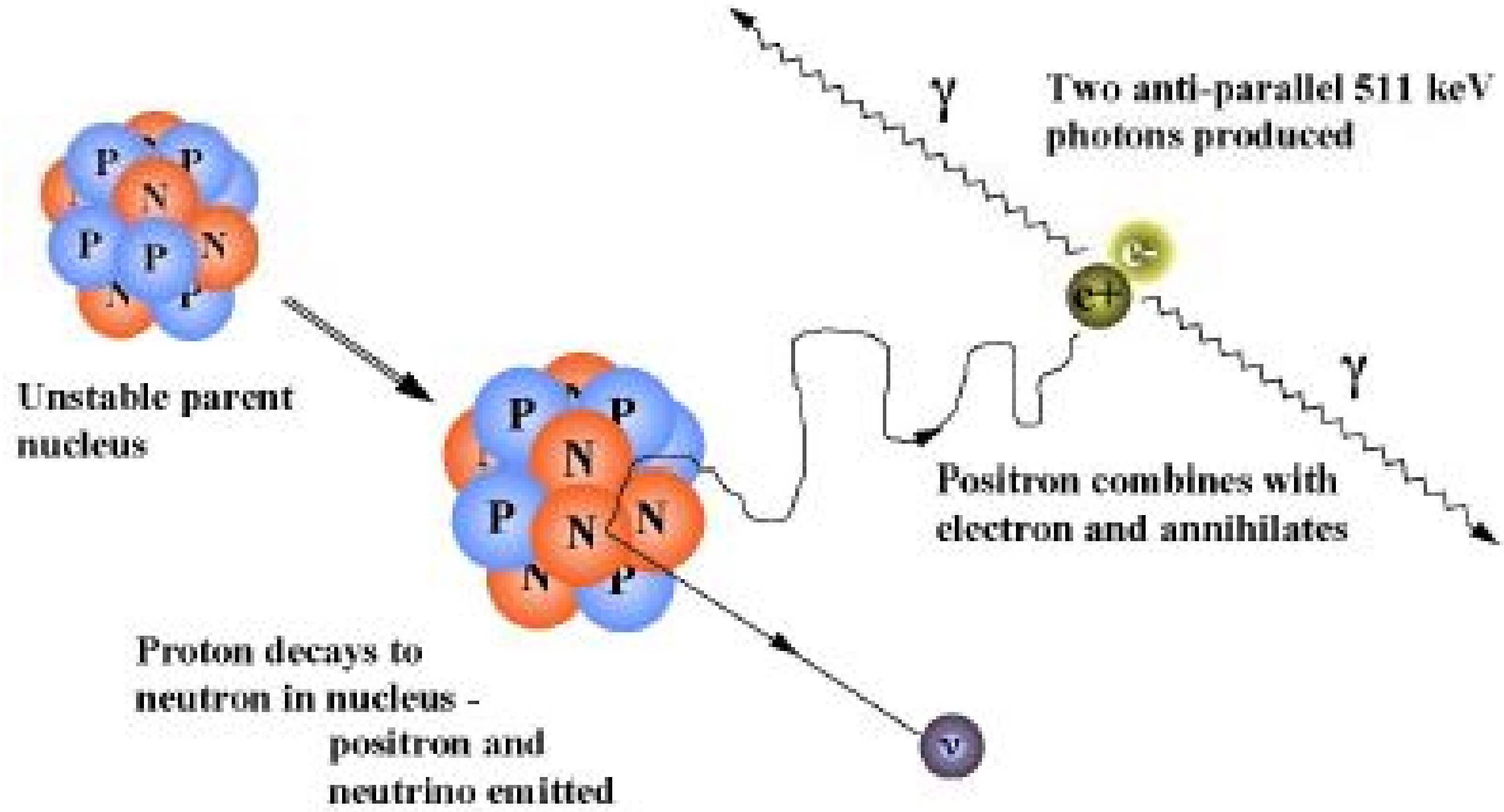
80
70
60
50
40
30
20
10
0
Percentage of Respondents
CNS
H&N
Breast
Lung
GI
GU/Prostate
GYN
Pediatrics
Lymphoma
Palliative
Disease Site
MRI
18FDG-PET
4-D CT
Other

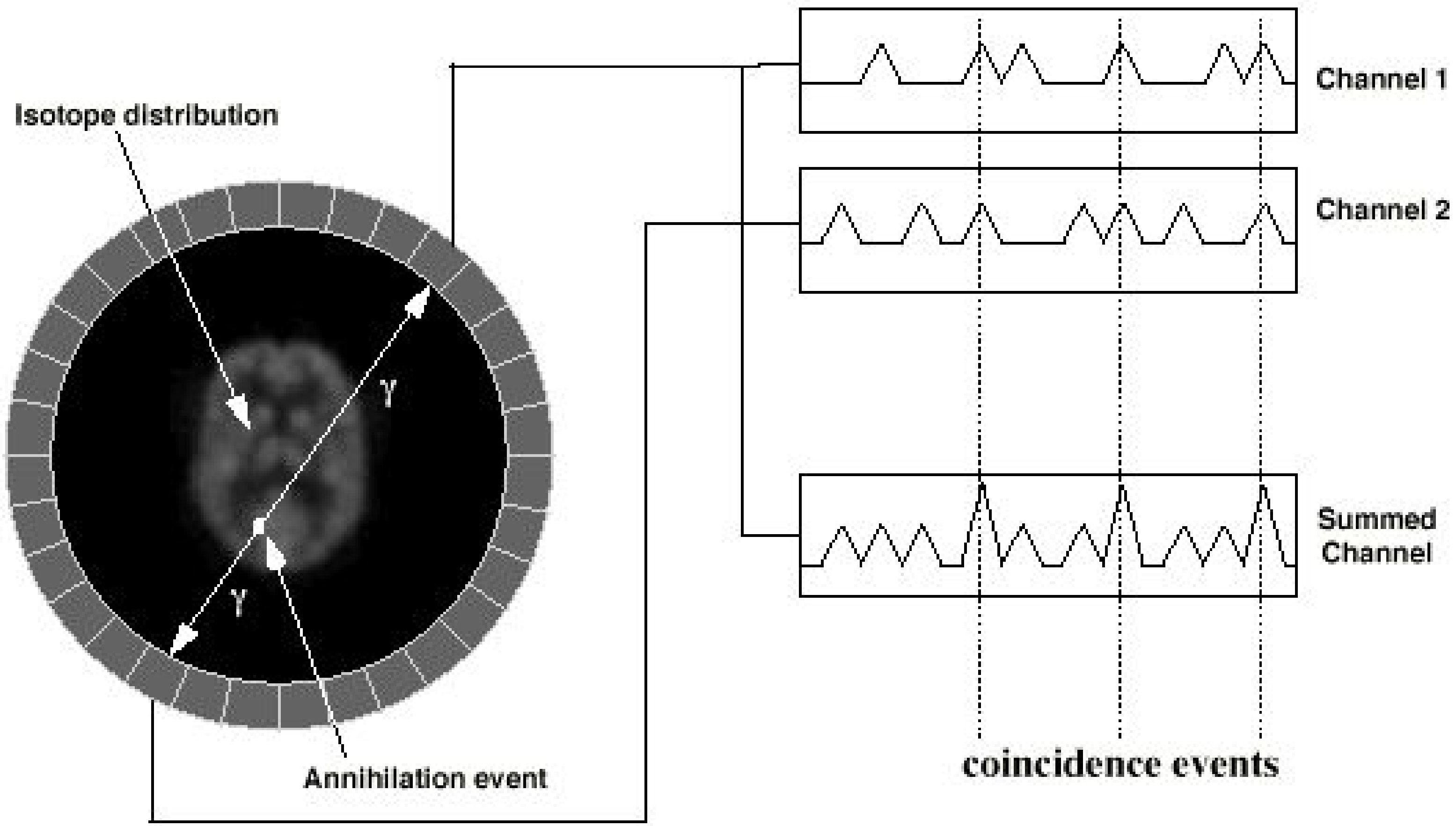


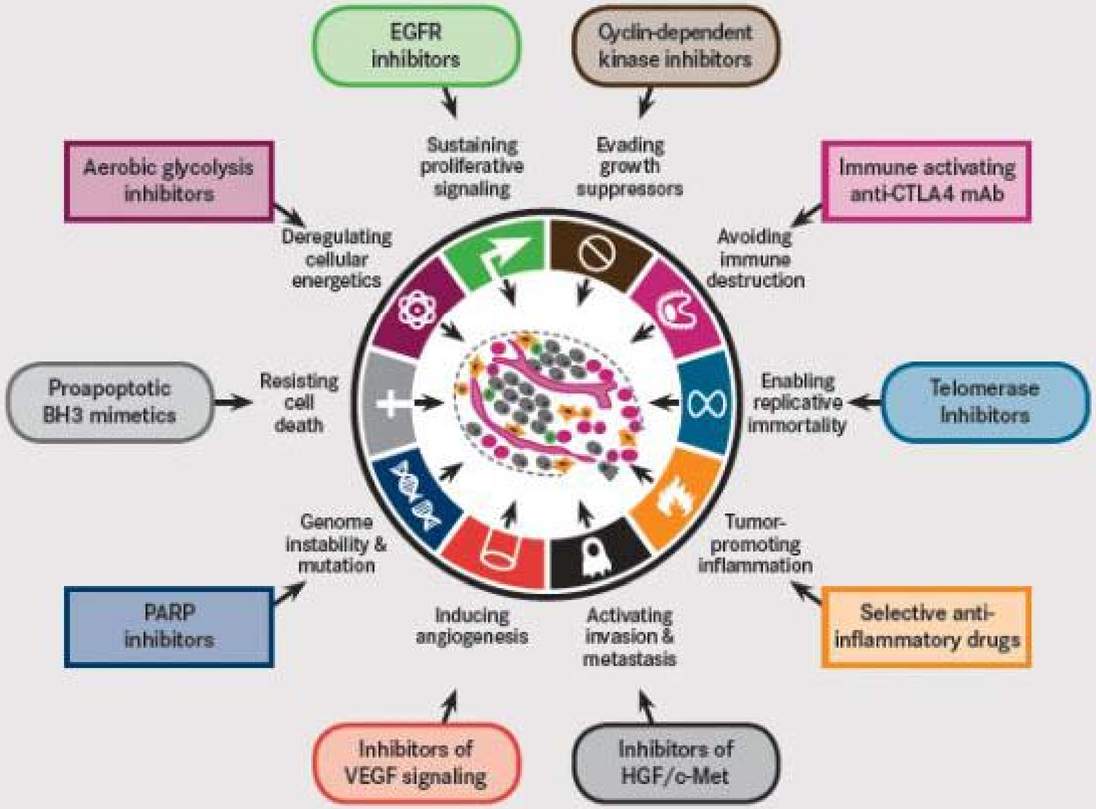
100
90
80
70
60
50
40
30
20
10
0
Percentage of Respondents
1995 or before
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
Year
4-D CT
18-FDG PET
MRI
SPECT
non FDG-PET
fMRI
MRS
Any


Ceci n'est pas une pipe.
Magritte

# PET


Two anti-parallel 511 keV
photons produced
γ
γ
e-
e+
P
N
Unstable parent
nucleus
Positron combines with
electron and annihilates
Proton decays to
neutron in nucleus -
positron and
neutrino emitted
ν


Isotope distribution
γ
γ
Annihilation event
Channel 1
Channel 2
Summed Channel
coincidence events

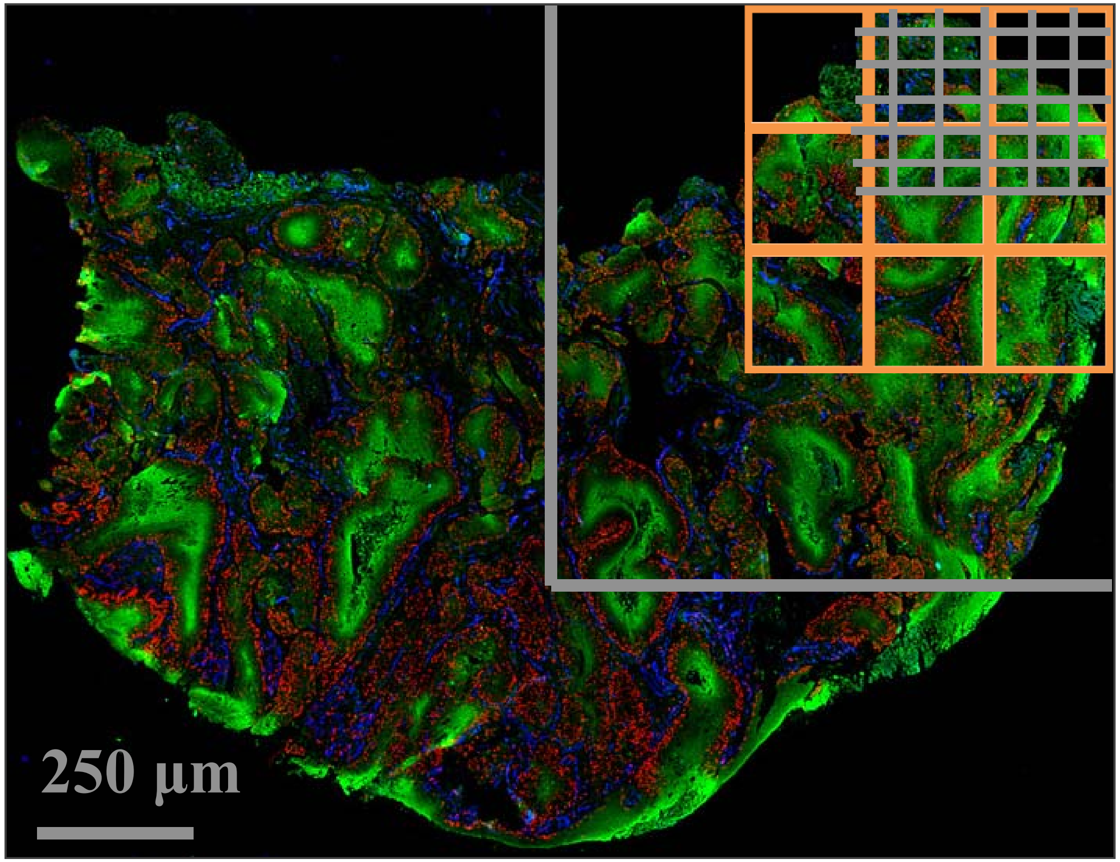



This figure illustrates some of the many approaches employed in developing therapeutics targeted to the known and emerging hallmarks of cancer.

EGFR indicates epidermal growth factor receptor; CTLA4, cytotoxic T lymphocyte-associated antigen 4; mAb, monoclonal antibody; HGF, hepatocyte growth factor; VEGF, vascular endothelial growth factor; PARP, poly-(ADP ribose) polymerase.

Source: Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*. 2011; 144: 646-674. Reprinted with permission.

GV




**Autoradiography (50 µm)**

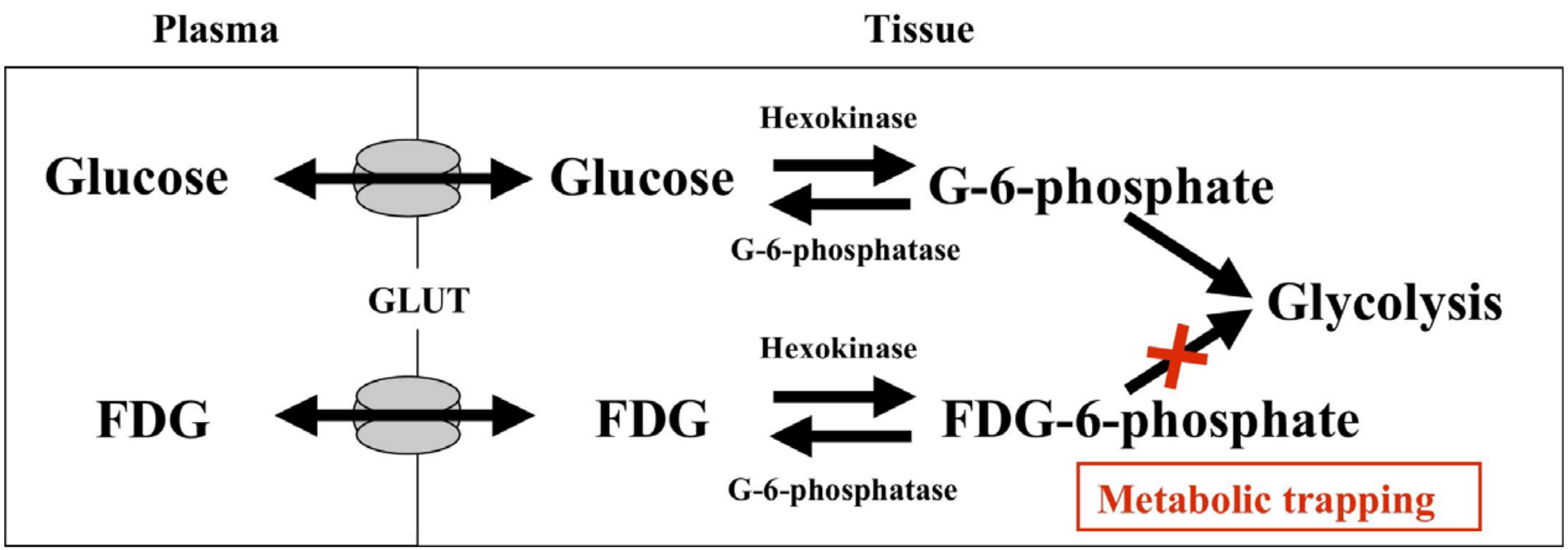
**microPET (1.5 mm)**

**PET (5-7 mm)**

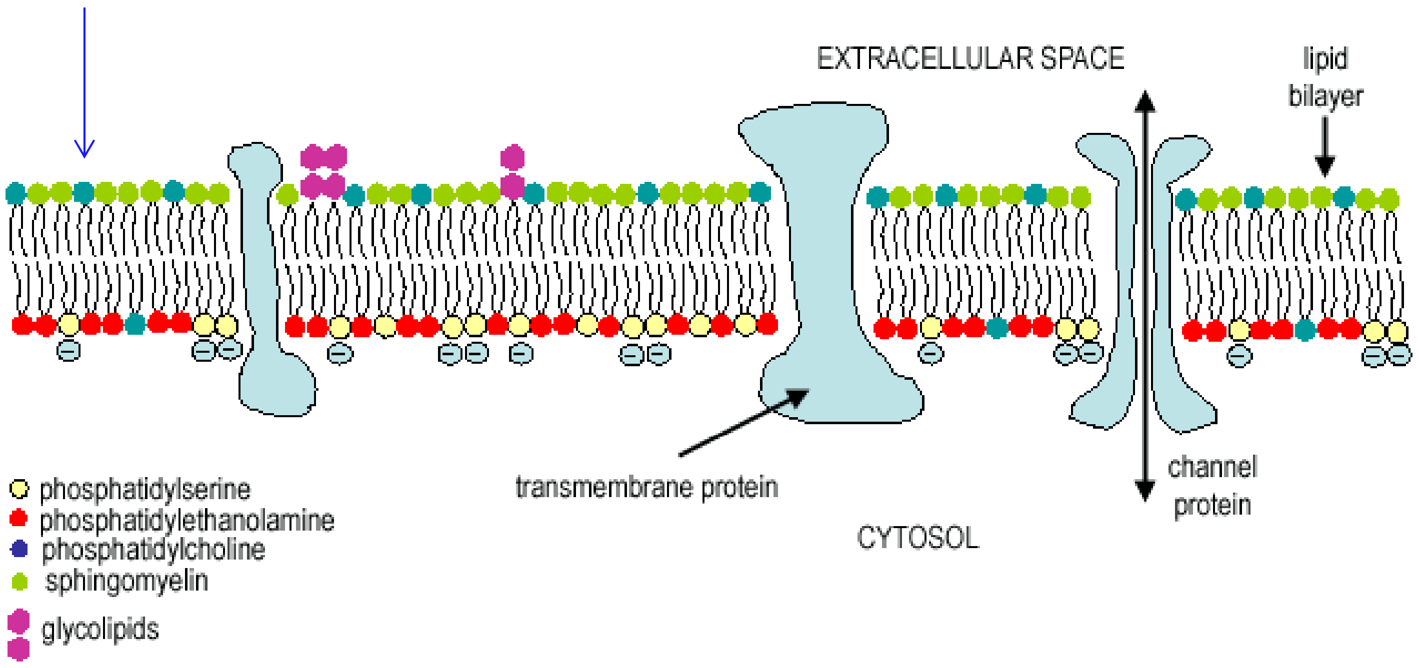
# Some famous PET tracers

| Radio-pharmaceutical | Depicted parameter | Possible RT-application | Clinically relevant neoplasms | Evidence for diagnostic value | Use in/state of evaluation for RT planning |
|---|---|---|---|---|---|
| FDG | Glucose metabolism | Tumour delineation | For example, lung cancer Head and neck cancer Esophageal Ca Lymphomas | Given for various tumours in staging and restaging | Probable, ongoing randomized clinical studies |
| AA | Protein metabolism | Tumour delineation | Primary and recurrent brain tumours | Given for brain tumours in staging and restaging | Probable, ongoing randomized clinical studies |
| MISO | Hypoxia | Hypoxic subvolume | HNC (SCC), NSCLC, Glioma, others | Under evaluation | Promising, practical implication not yet defined |

- $^{18}$F-FDG
  - most commonly used for various tumour types
  - based on increased uptake in tumour cells showing increased glucose metabolism
  - “Metabolic trapping”



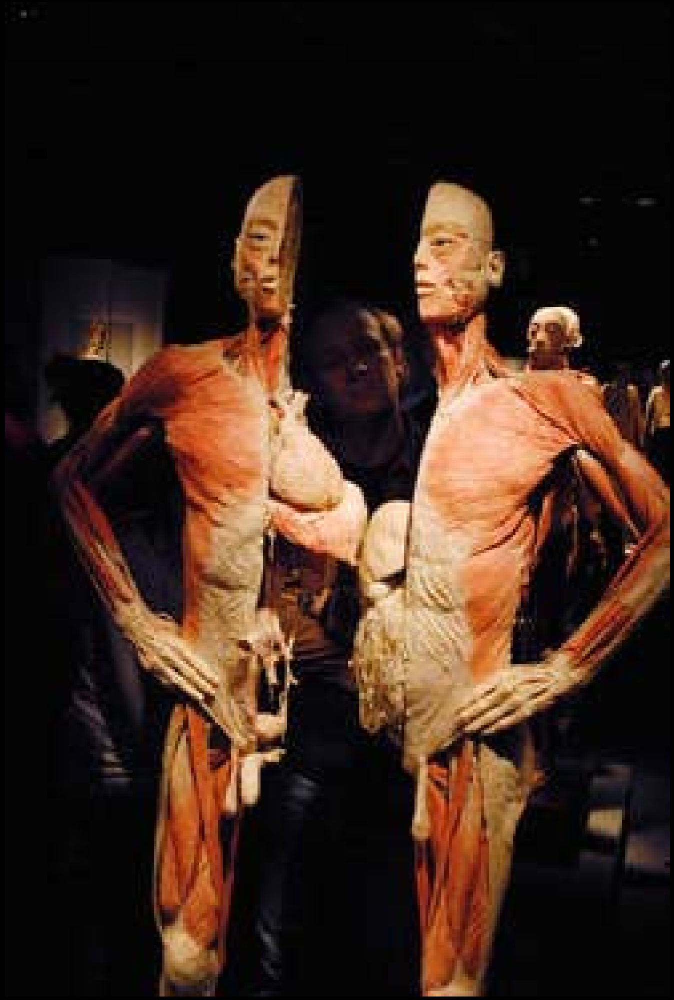
- $^{11}$C-choline – $^{18}$F-choline
  - marker of cell membrane turnover
  - based on increased phospholipid synthesis in tumour cells showing upregulation of choline kinase



- $^{11}C$-methionine
  - marker of proteine synthesis (essential AA)
  - based on increased cellular proliferation in tumour cells showing increased amino acid transport
  - > brain tumors

- $^{11}C$-methionine
  - marker of proteine synthesis
  - based on increased cellular proliferation in tumour cells showing increased amino acid transport
  - > brain tumors
- $^{11}C$-acetate
  - marker of lipid metabolism
  - based on increased fatty acid synthesis in tumour cells showing overexpression of fatty acid synthase
  - very similar to $^{11}C$-choline (also few urinary excretion)

- $^{11}C$-methionine
  - marker of proteine synthesis
  - based on increased cellular proliferation in tumour cells showing increased amino acid transport
  - > brain tumors
- $^{11}C$-acetate
  - marker of lipid metabolism
  - based on increased fatty acid synthesis in tumour cells showing overexpression of fatty acid synthase
  - very similar to $^{11}C$-choline (also few urinary excretion)
- $^{68}Ga$-PSMA
  - Glycoprotein with enzymatic function (NAAG to glutamate & NAA)
  - marker of lipid metabolism
  - based on increased fatty acid synthesis in tumour cells showing overexpression of fatty acid synthase



BRAIN

H & N

LUNG

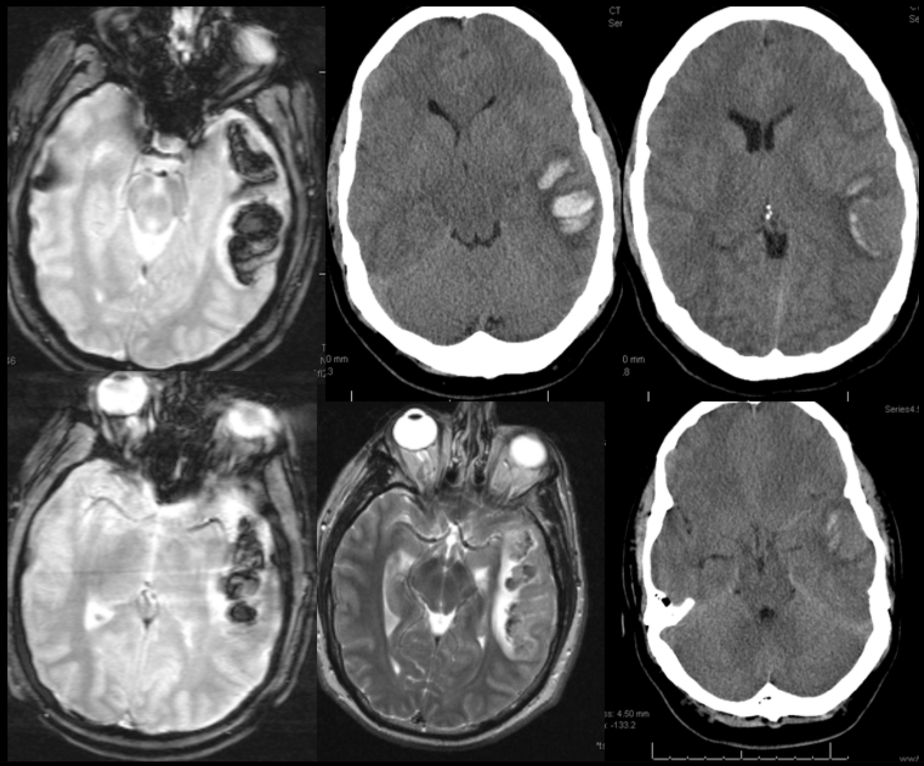
GYN

PROSTATE

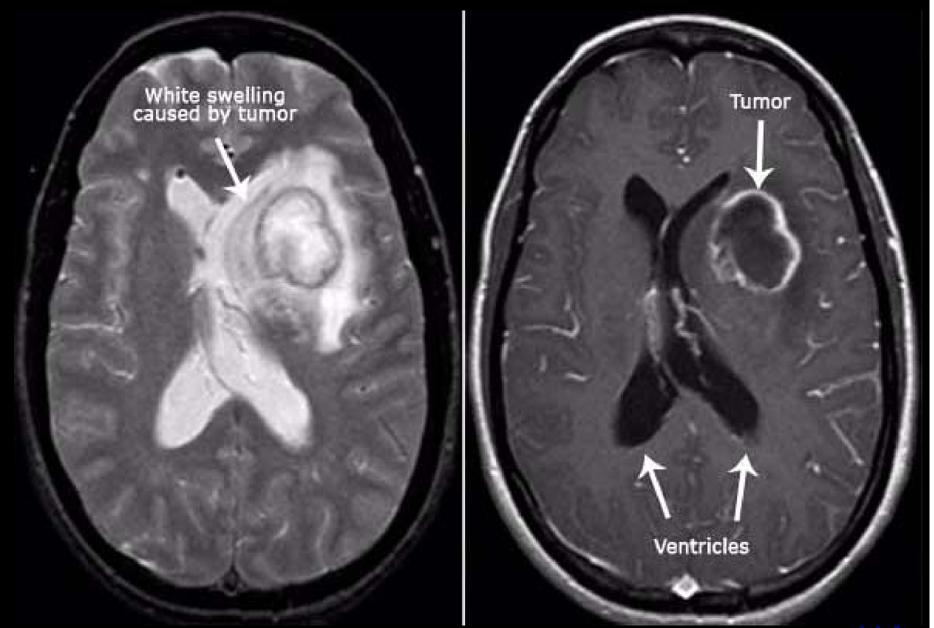
RECTUM

GV

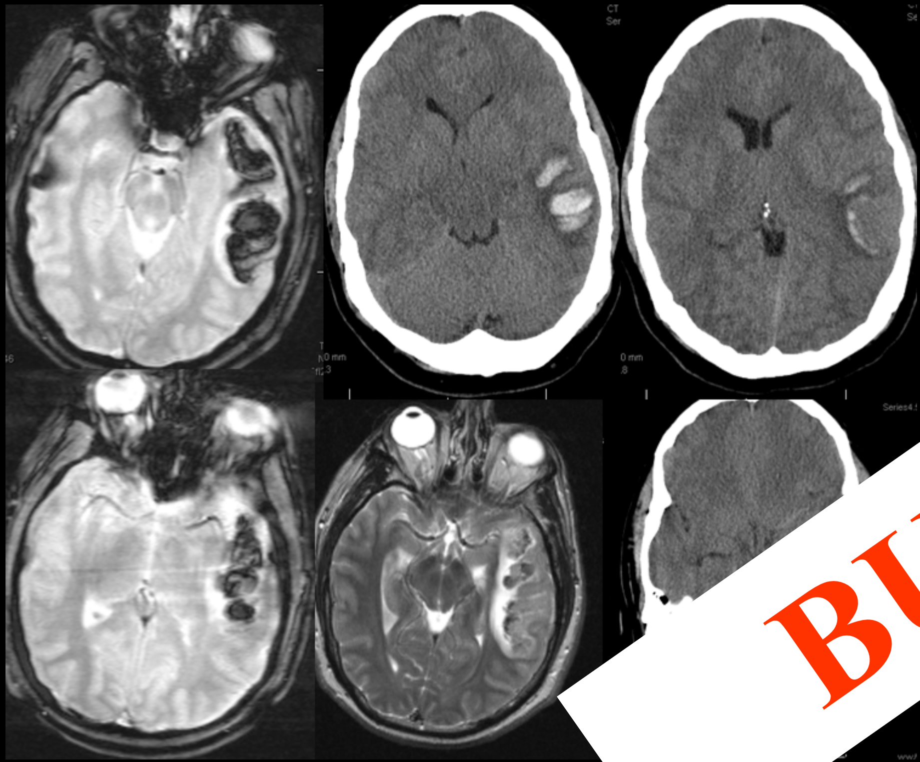
# BRAIN



Advantage MR unequivocal

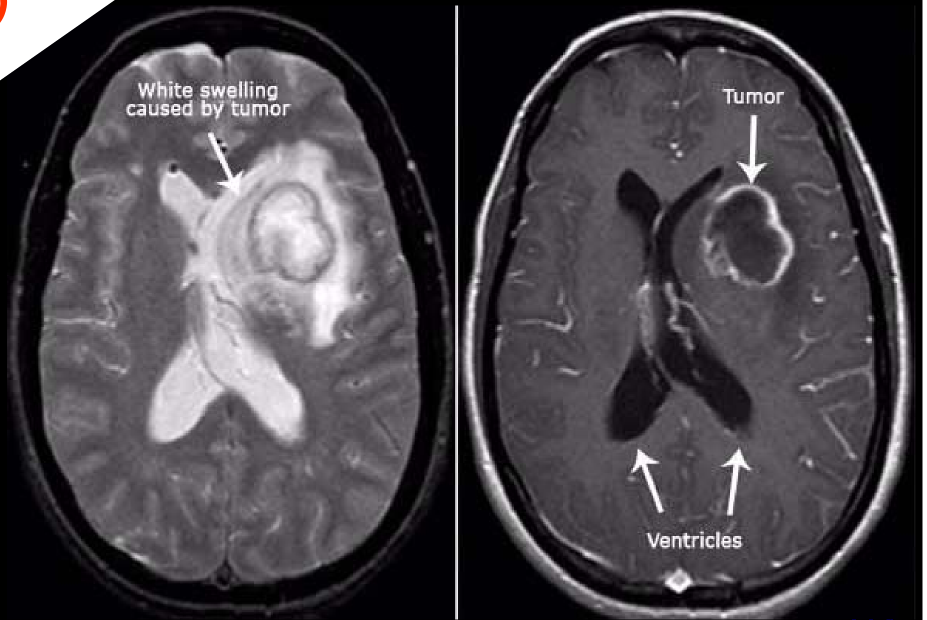


# BRAIN



Advantage MR unequivocal

**BUT**

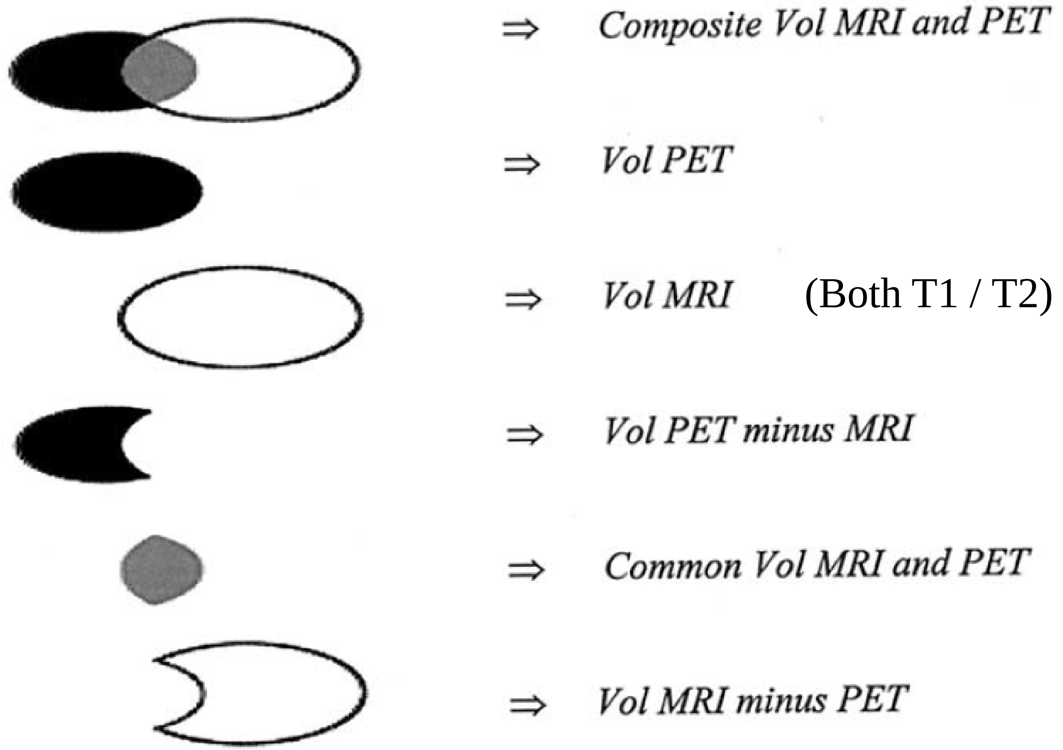


# BRAIN


Edema can be treatment related

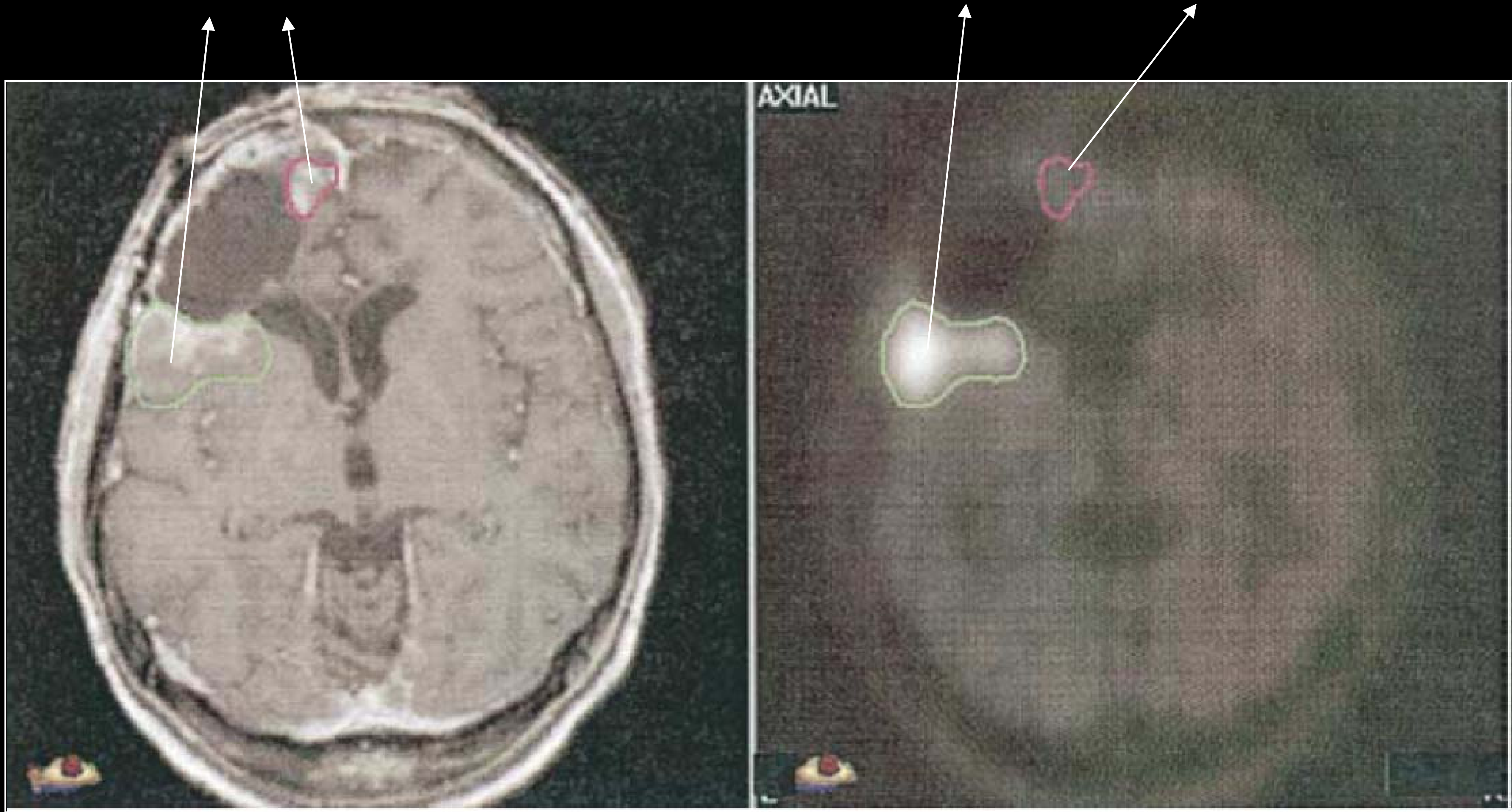
# L-(METHYL-11C) METHIONINE POSITRON EMISSION TOMOGRAPHY FOR TARGET DELINEATION IN RESECTED HIGH-GRADE GLIOMAS BEFORE RADIOTHERAPY

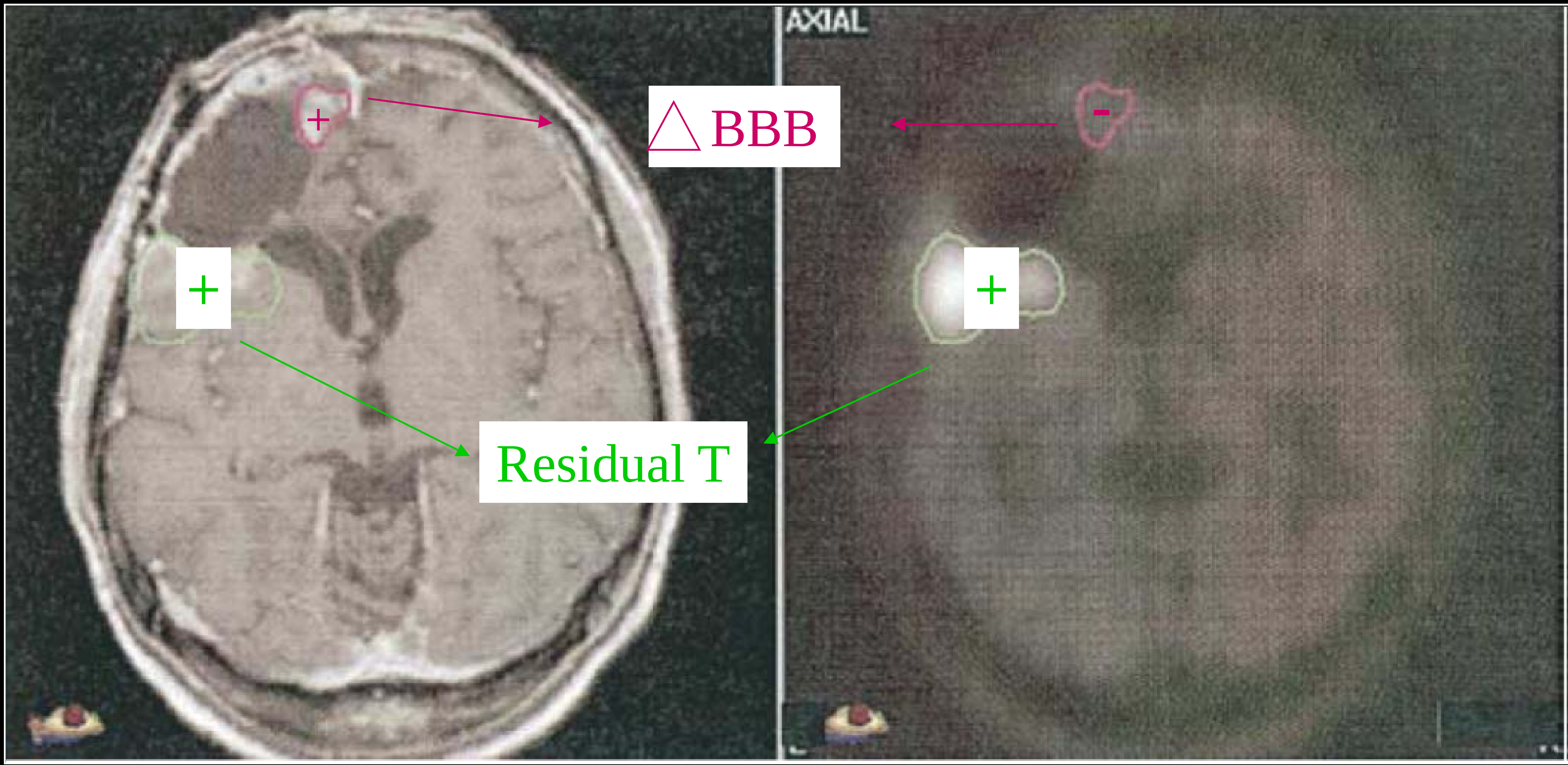
Anca-Ligia Grosu, M.D.,* Wolfgang A. Weber, M.D.,† Eva Riedel, M.D.,*
Branislav Jeremic, M.D.,* Carsten Nieder, M.D.,* Martina Franz,*
Hartmut Gumprecht, M.D., Ruprecht Jaeger, M.D.,§ Markus Schwaiger, M.D.,†
and Michael Molls, M.D.*

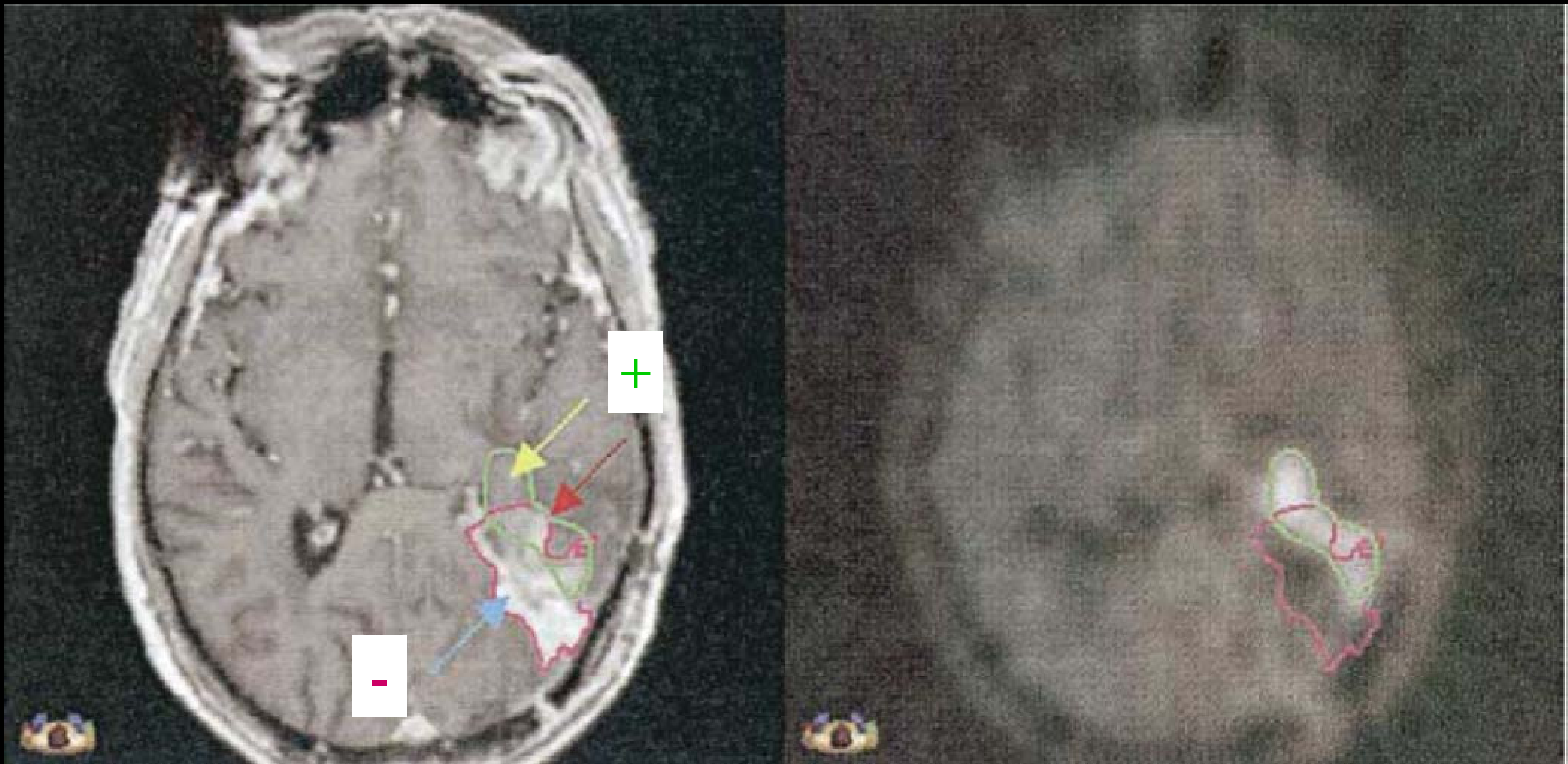


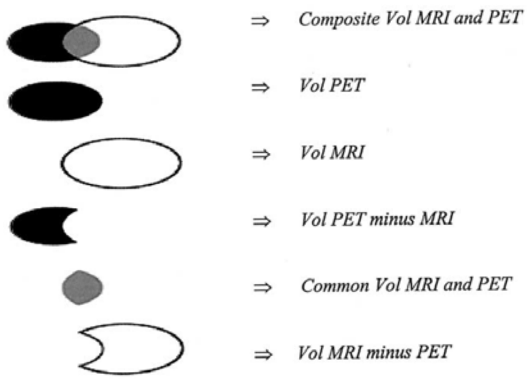
T1 MR1 MET-PET

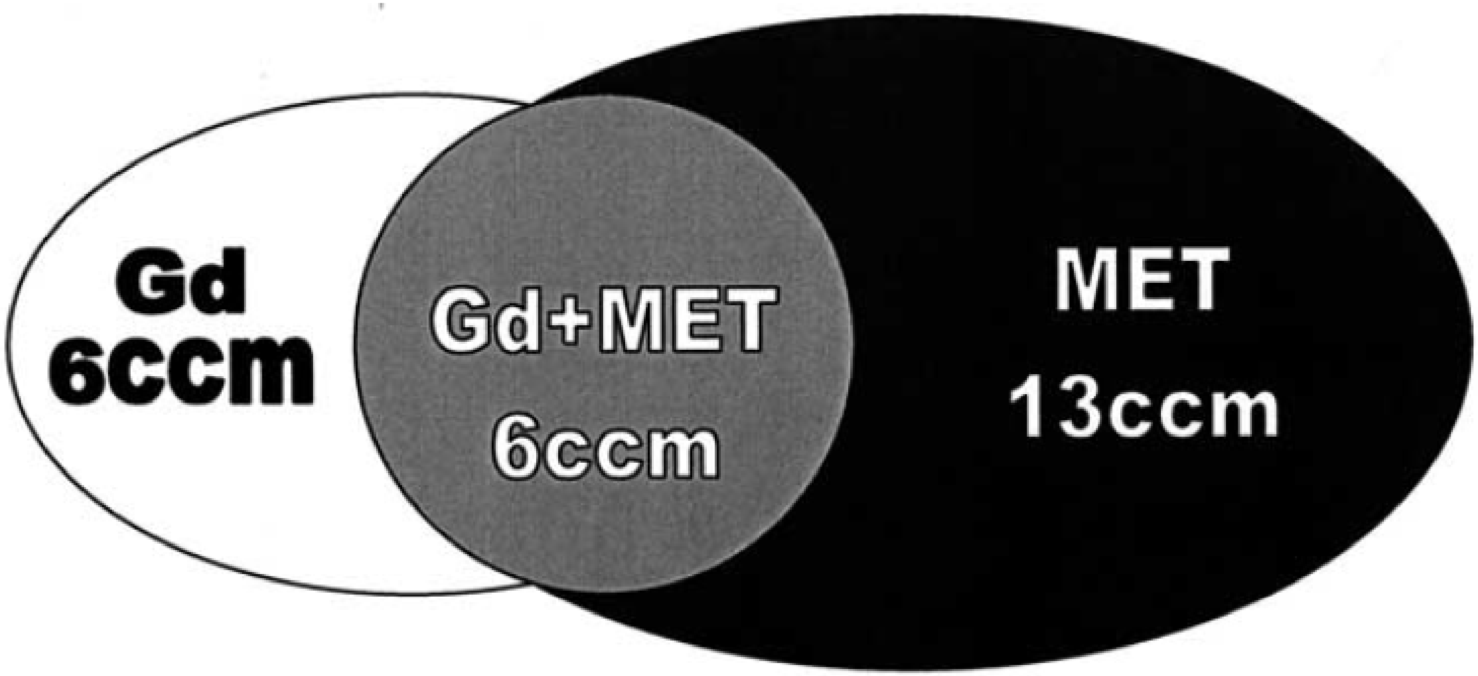
Gd enhancement MET uptake No MET uptake




AXIAL
+
△ BBB
-
+
+
Residual T



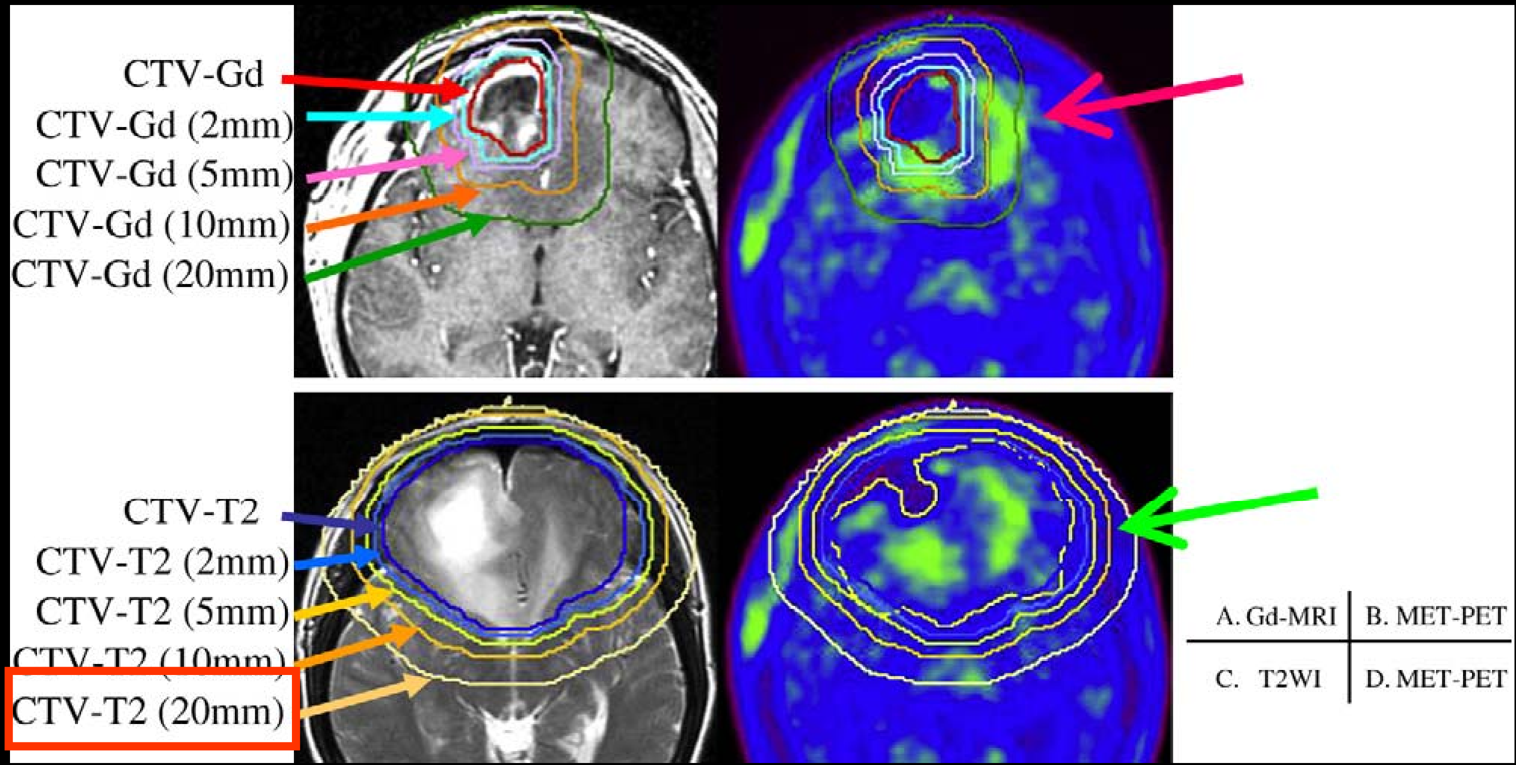

⇒ Composite Vol MRI and PET
⇒ Vol PET
⇒ Vol MRI
⇒ Vol PET minus MRI
⇒ Common Vol MRI and PET
⇒ Vol MRI minus PET


Gd
6ccm
Gd+MET
6ccm
MET
13ccm

MR vs. MET-PET

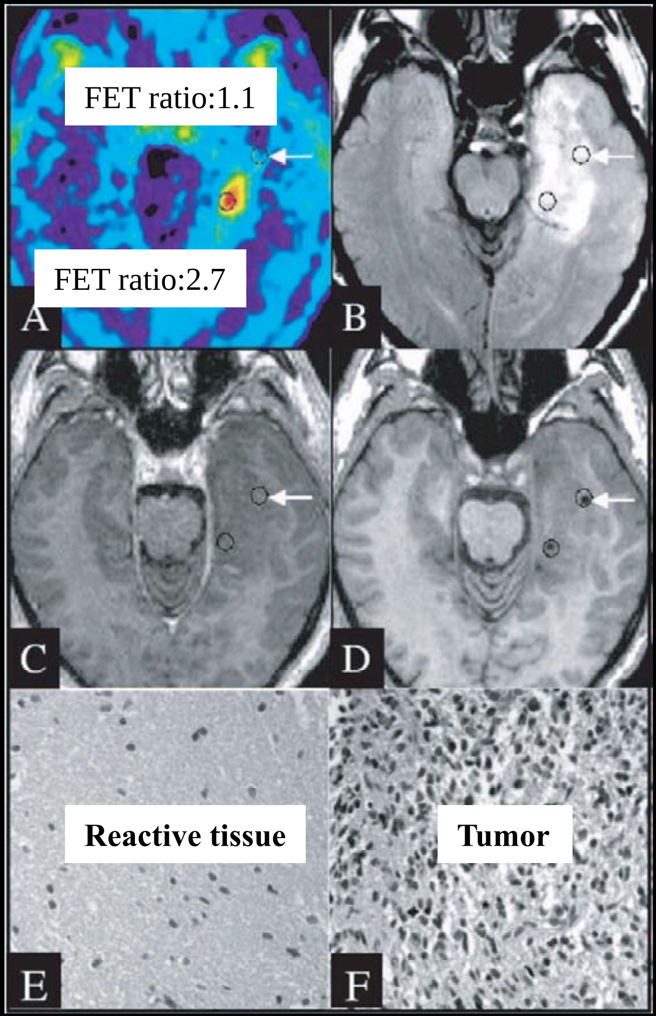
+: total extent of associated pathological changes
preferred: Gd contrast

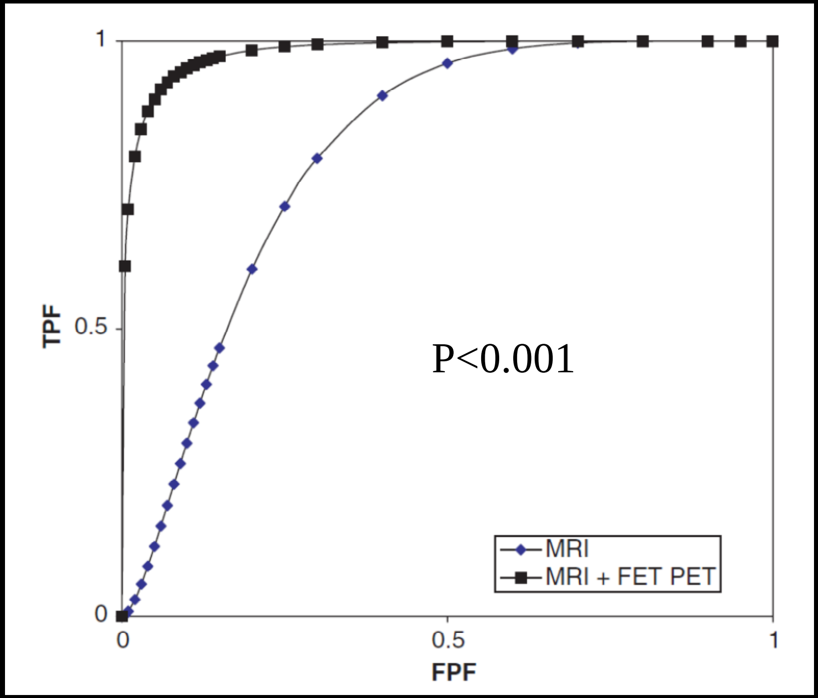
+: extent of viable tumor
methionine



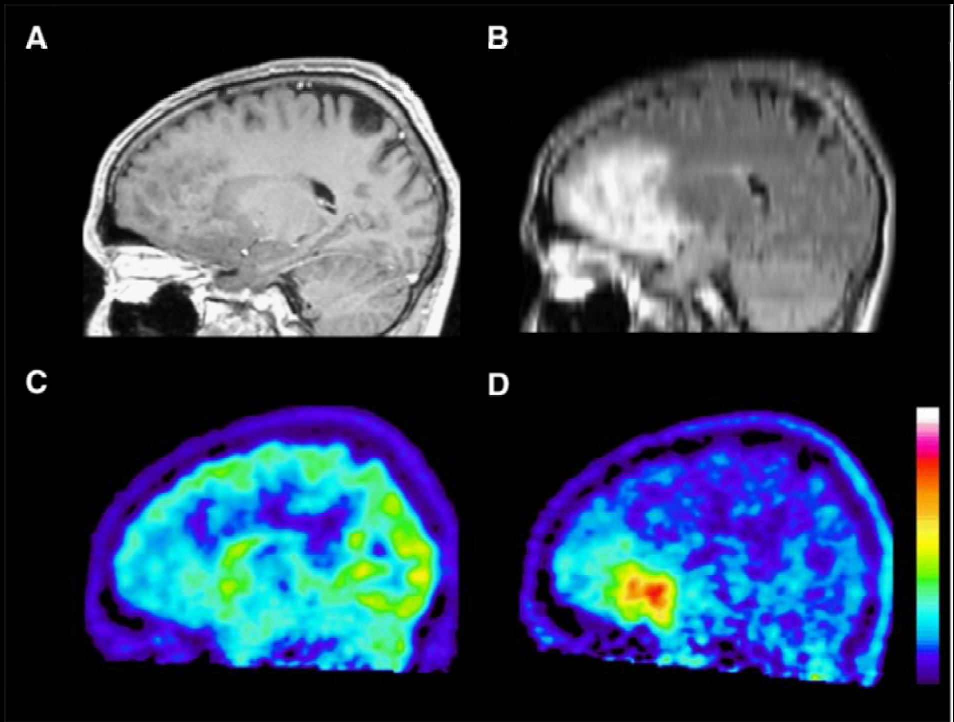
# Other PET tracers

## FET-PET



# FET-PET vs. FDG-PET




FDG-PET FET-PET

N=43 glioma patients (LGG / HGG)

- FET: uptake in 37 patients
- FDG: uptake in 15 patients

- FET: ok for delineation in all
- FDG: problem: gray matter!

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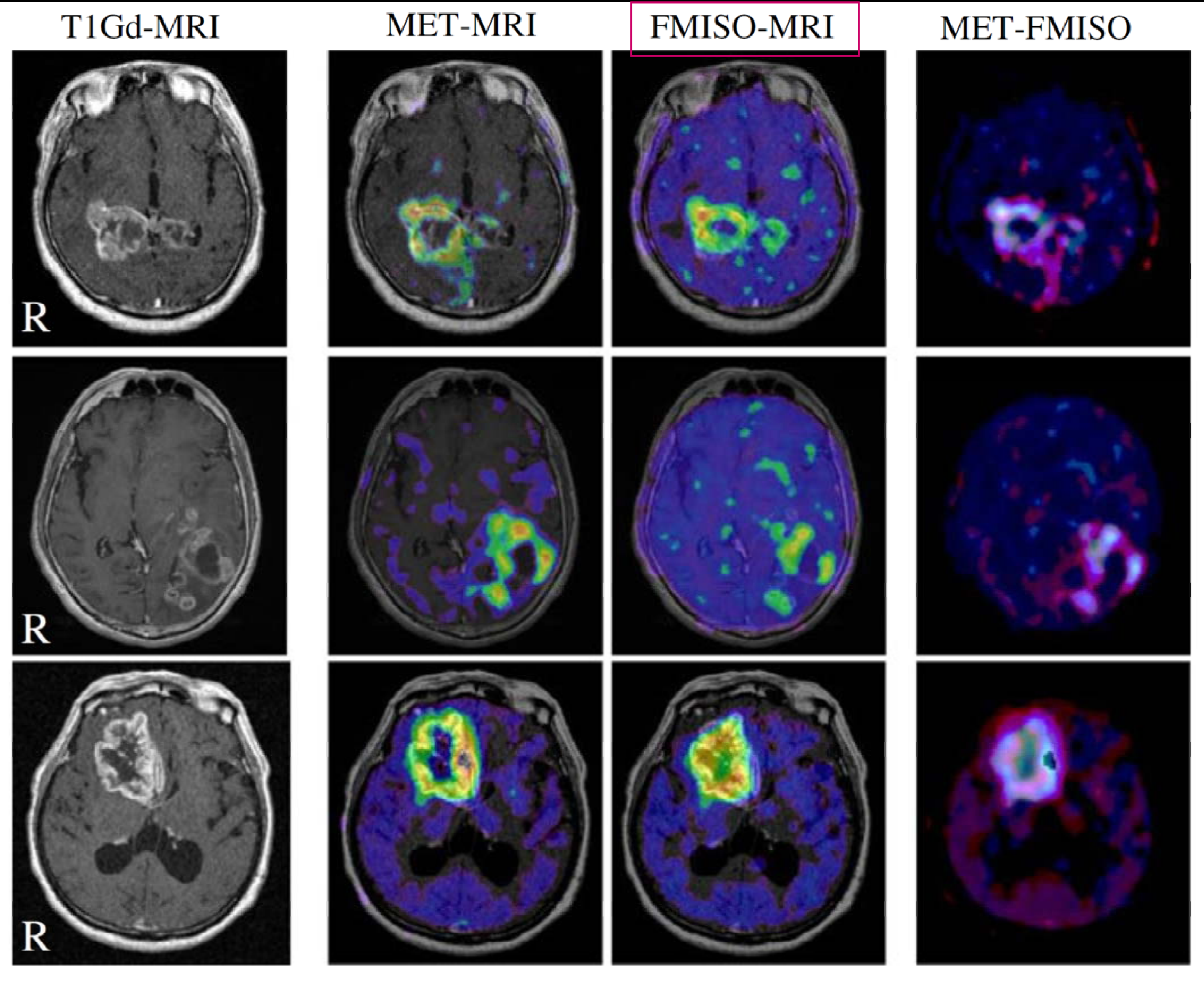
Available online at www.sciencedirect.com
ScienceDirect
Nuclear Medicine and Biology 36 (2009) 779–787
NUCLEAR MEDICINE AND BIOLOGY
www.elsevier.com/locate/nucmedbio

Comparison of $^{18}$F-FET and $^{18}$F-FDG PET in brain tumors

Dirk Pauleit[a], Gabriele Stoffels[a], Ansgar Bachofner[b], Frank W. Floeth[c], Michael Sabel[c], Hans Herzog[a], Lutz Tellmann[a], Paul Jansen[d], Guido Reifenberger[e], Kurt Hamacher[a], Heinz H. Coenen[a], Karl-Josef Langen[a,*]

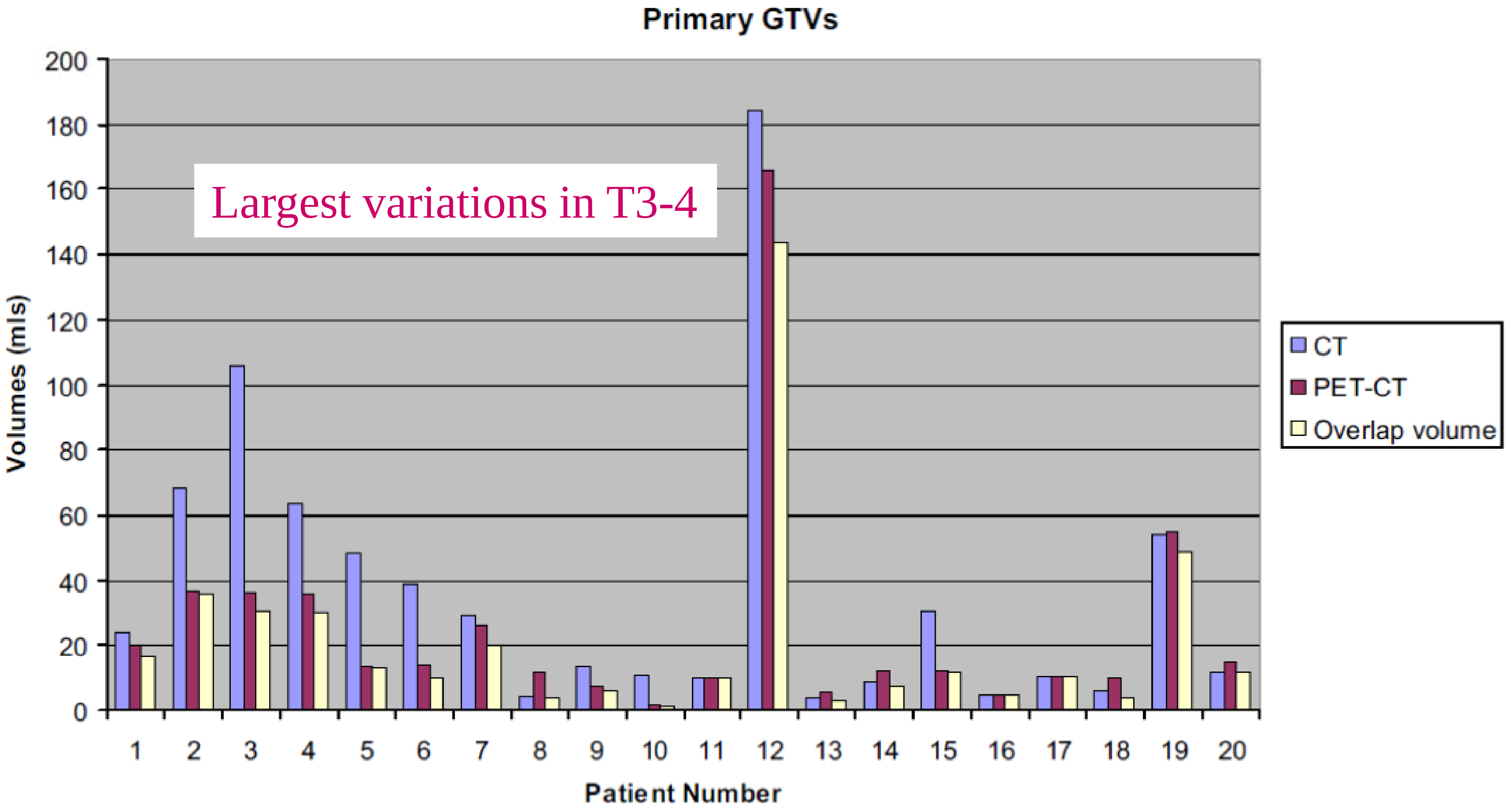
# Other PET tracers



# HEAD & NECK

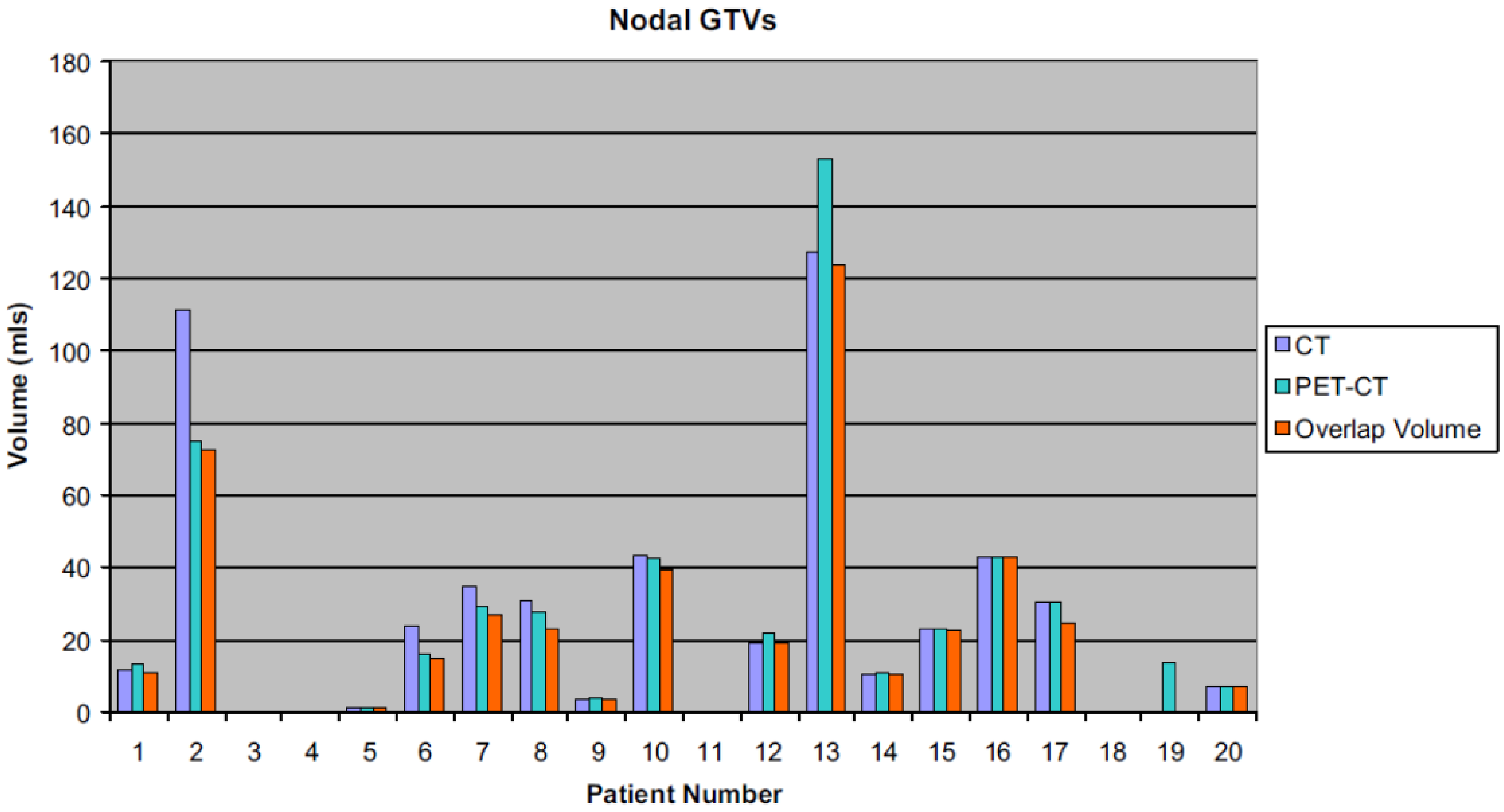
## FDG PET-CT: does it holds its promise?

# Oropharyngeal cancer: Delineations ~ imaging tool




Chatterjee 2012

# Oropharyngeal cancer: Delineations ~ imaging tool




Chatterjee 2012

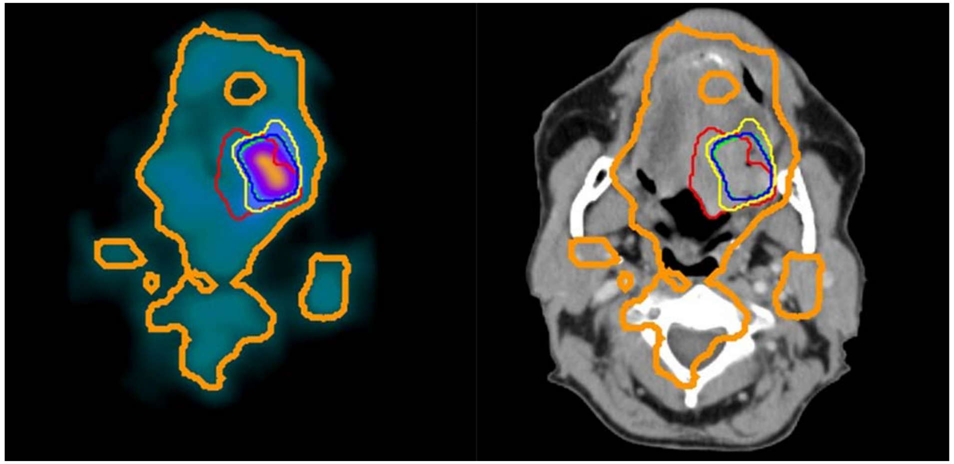
# PET segmentation tools

**Available methods**

- **Visual / manual**
- **SUV (different versions)**
- **% of tumor activity**
- **% of background activity**
- **Ratio tumor - background**
- **Advanced algorithms**

**This choice is not trivial !**

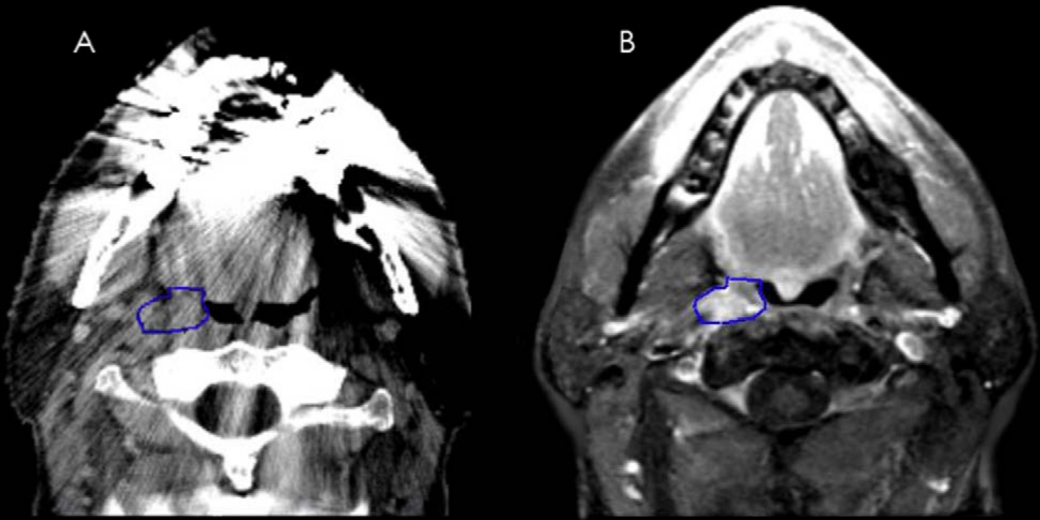
- **Fixed SUV is not suitable**
- **Volume depends on method**
- **Inter-observer variation**
- **Insufficient validation**

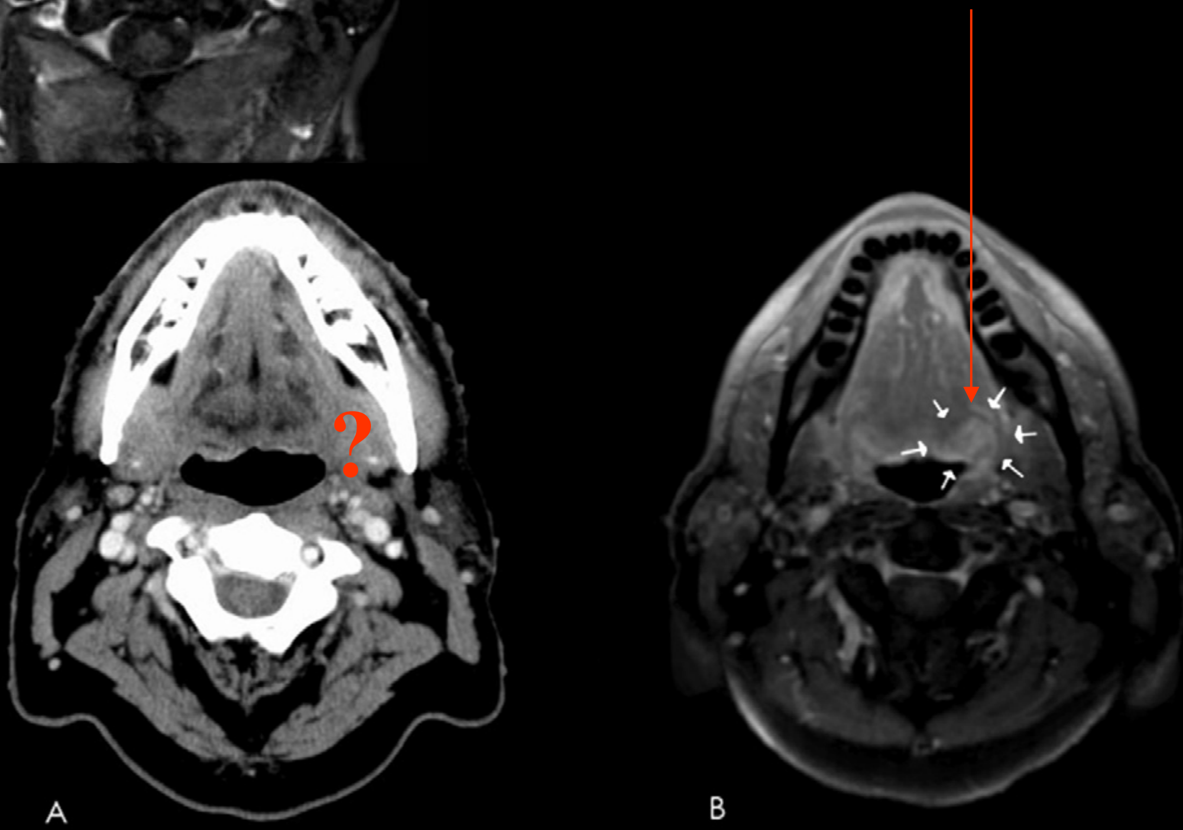


**Choose and standardize a method in your center!**

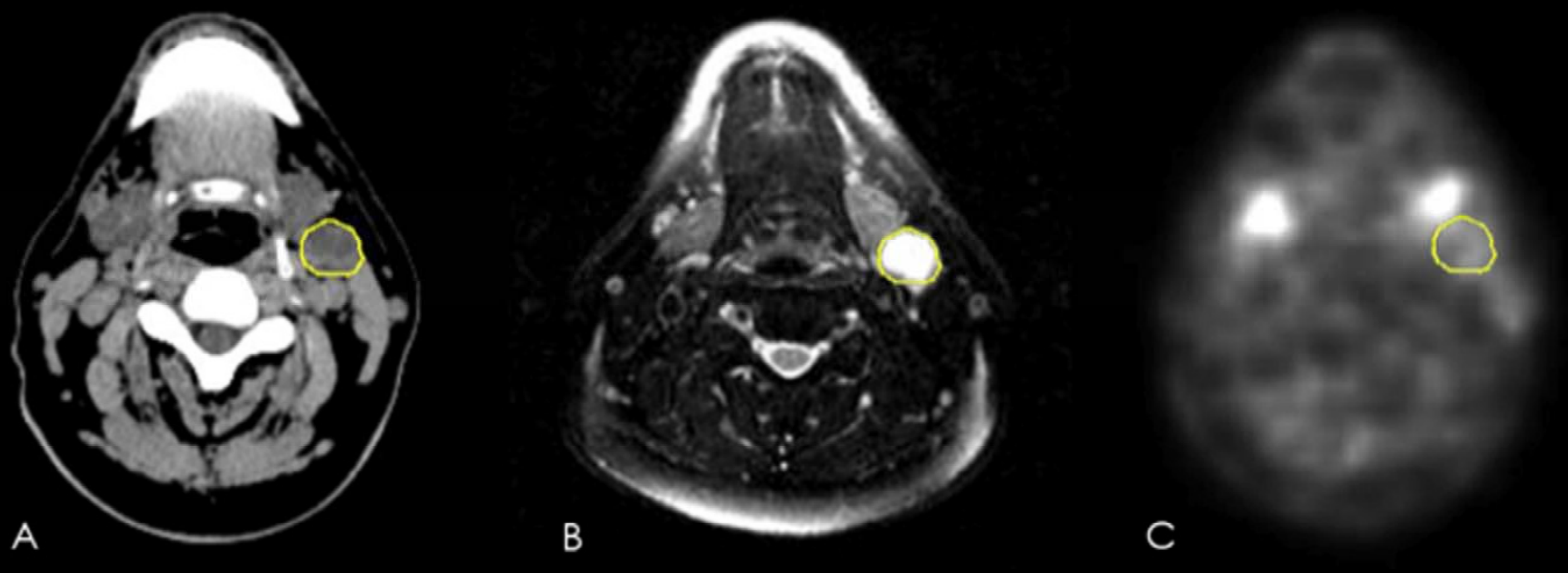
Schinagl 2007

# IS THERE a ROLE for MRI?



# IS PET-CT the HOLY GRALE?

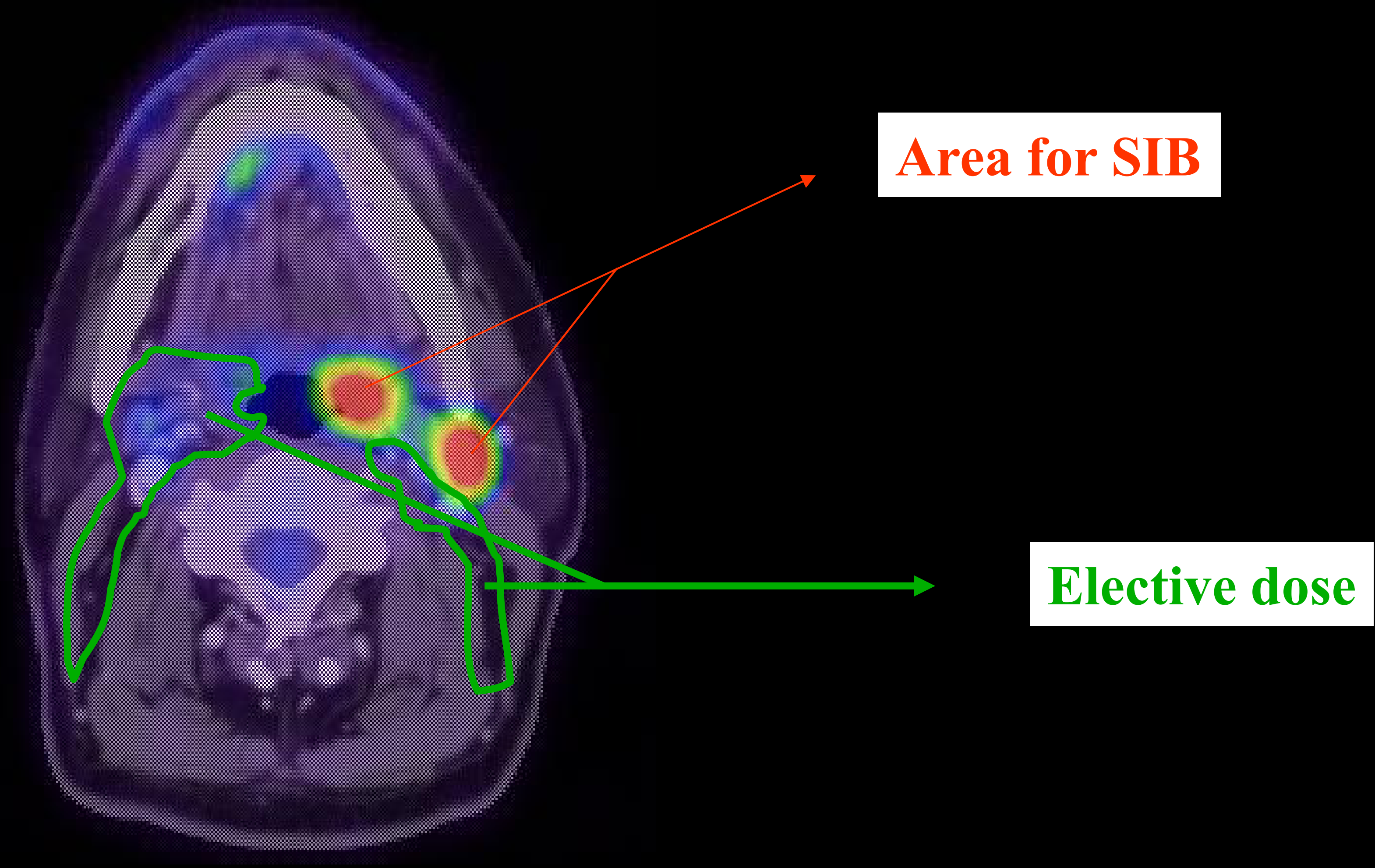



Problem: 30-50% of PET N0 contains tumor cells (AP)!

(Thiagarajan et al. 2011)

GV

# POSSIBLE IMPLICATIONS IN TP




GV

# A critical note …

## Is Image Registration of Fluorodeoxyglucose–Positron Emission Tomography/Computed Tomography for Head-and-Neck Cancer Treatment Planning Necessary?

David Fried, B.S.,* Michael Lawrence, Ph.D.,* Amir H. Khandani, M.D.,† Julian Rosenman, M.D., Ph.D.,*,‡ Tim Cullip, M.S.,* and Bhishamjit S. Chera, M.D.*,‡

**Conclusions:** PET and CT-defined tumor volumes received similar RT doses despite having less than complete overlap and the inaccuracies of image registration. LRF correlated with both CT and PET-defined volumes. The dosimetry for PET- and/or CT-based tumor volumes was not significantly inferior in patients with LRF. CT-based delineation alone may be sufficient for treatment planning in patients with HNSCC. Image registration of FDG-PET may not be necessary. 

IJROBP 2012

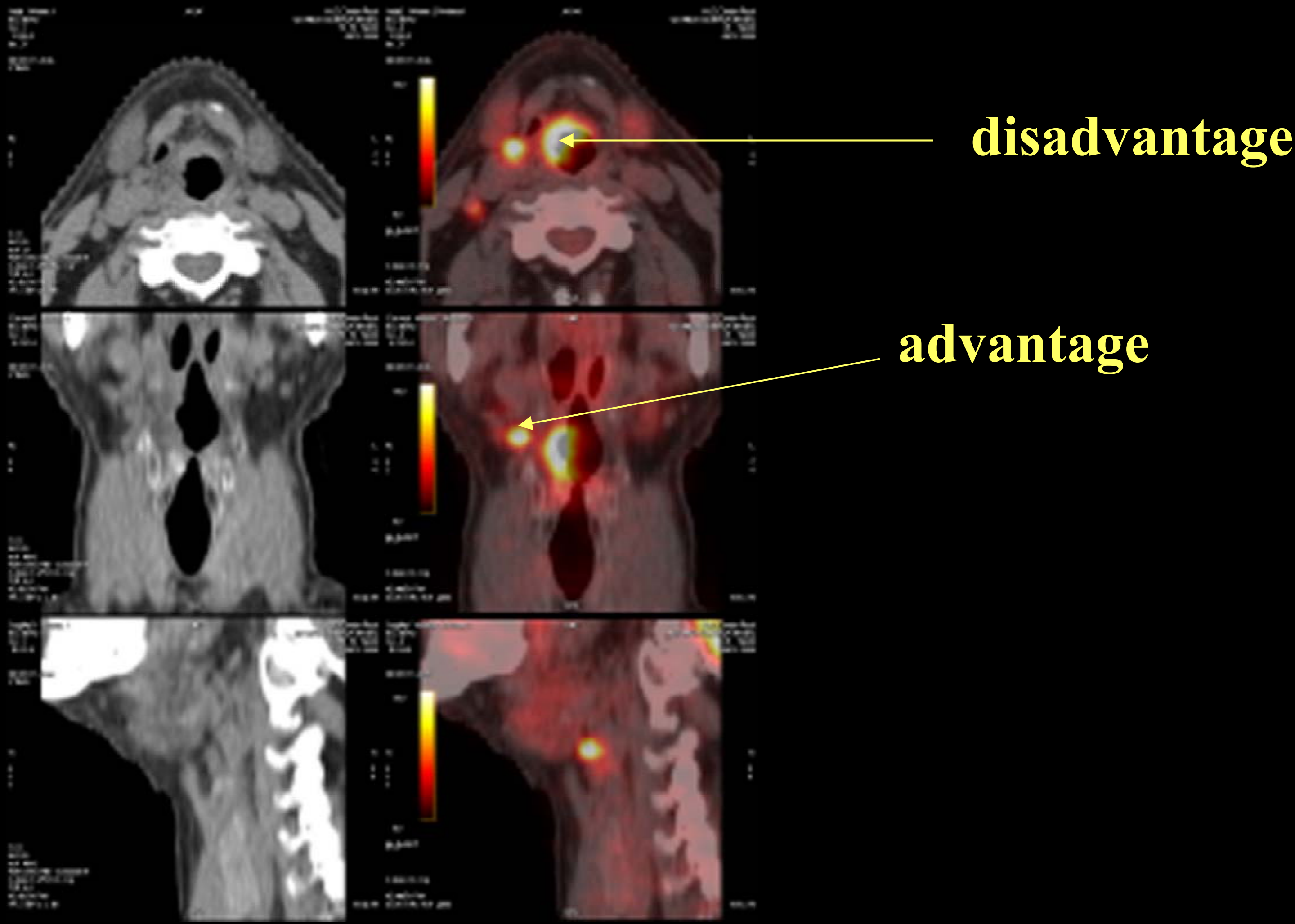
# LUNG CANCER

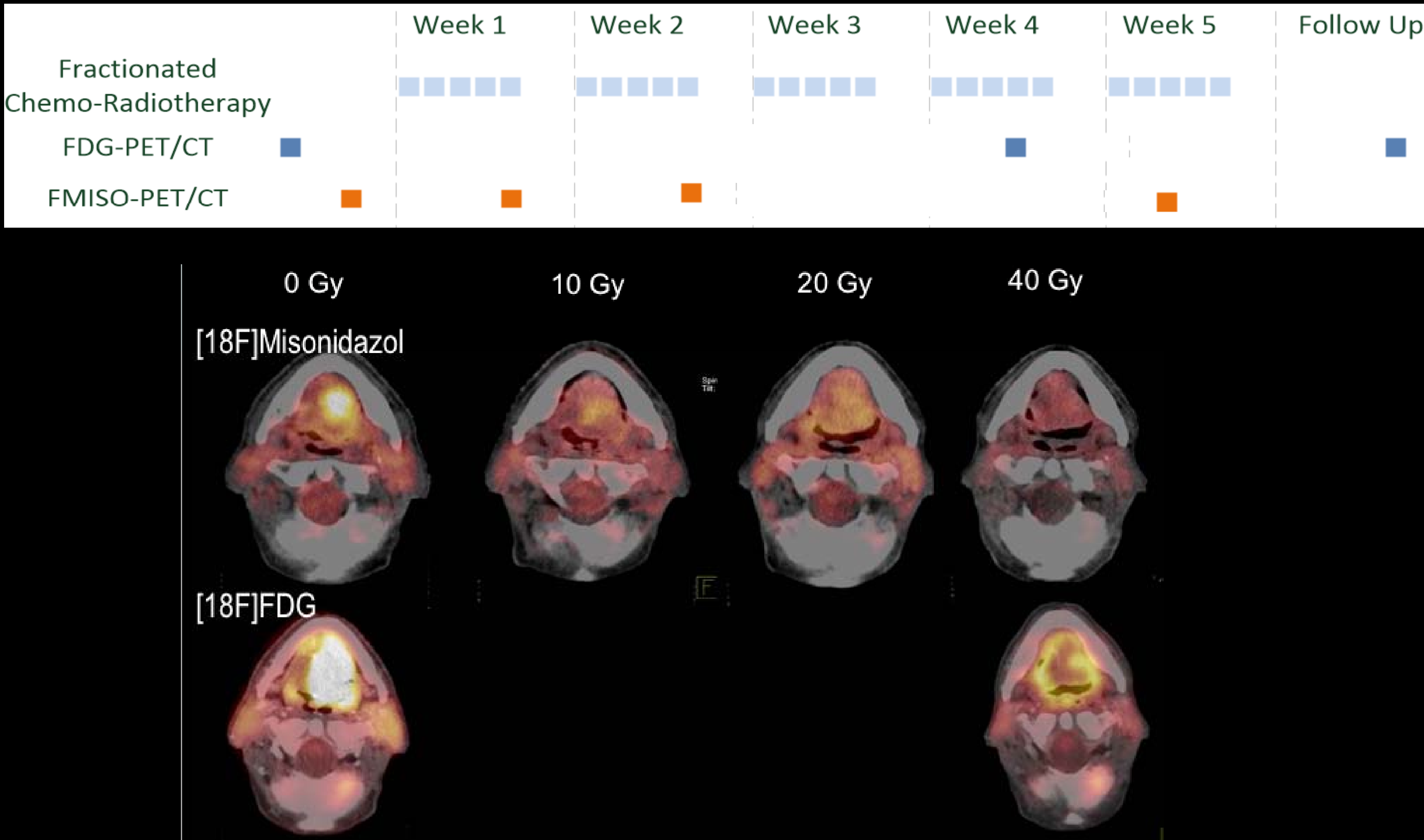
# PET can change staging & delineation

**N=167**

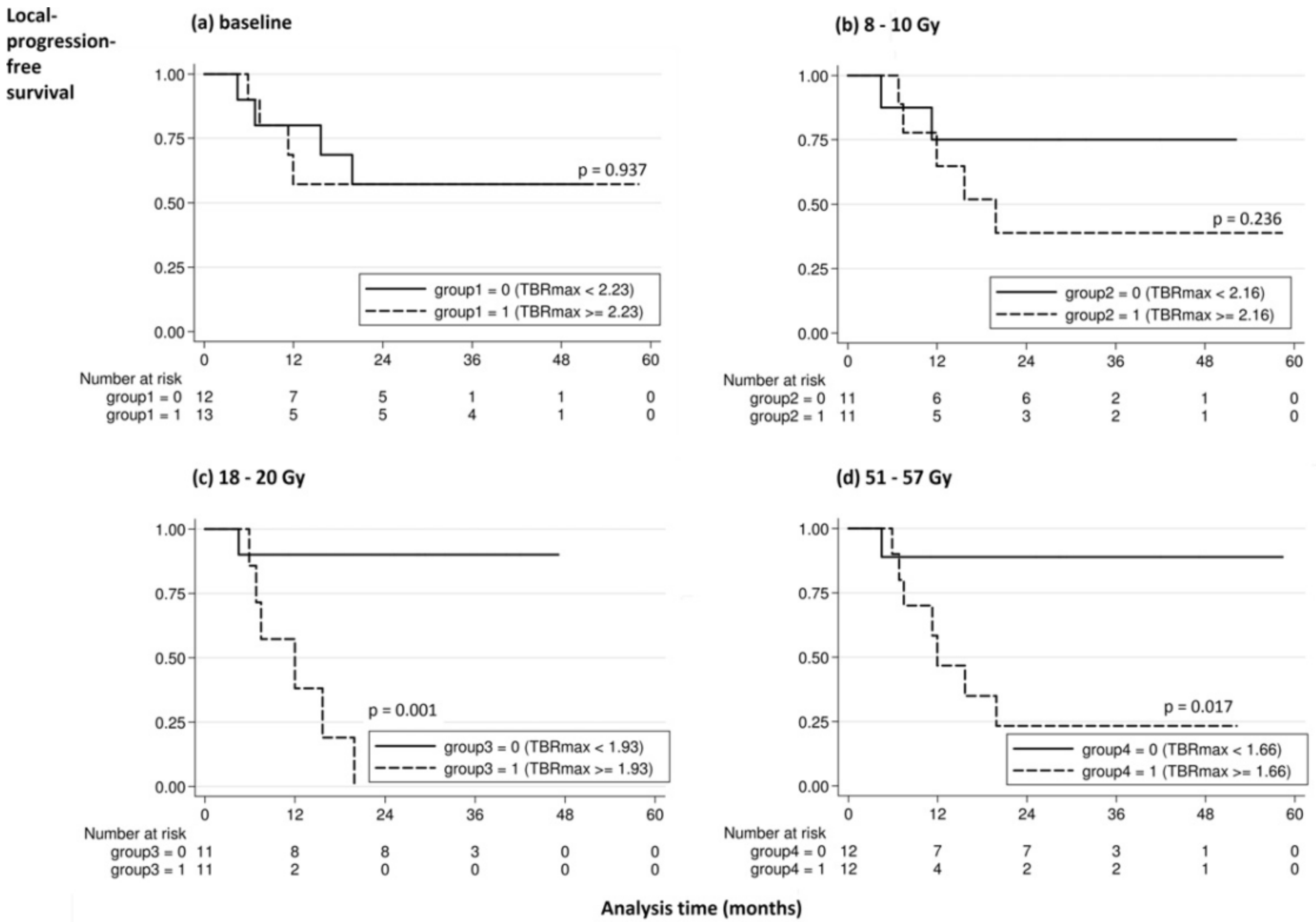
| Pre-PET stage | No. of patients | No. with metastasis | % |
|---|---|---|---|
| Stage IA | 21 | 0 | 0 |
| Stage IB | 18 | 3 | 17 |
| All Stage I | 39 | 3 | 8 |
| Stage IIA | 6 | 1 | 17 |
| Stage IIB | 22 | 4 | 18 |
| All Stage II | 28 | 5 | 18 |
| Stage IIIA | 62 | 16 | 26 |
| Stage IIIB | 38 | 8 | 21 |
| All Stage III | 100 | 24 | 24 |

**MacManus 2001**

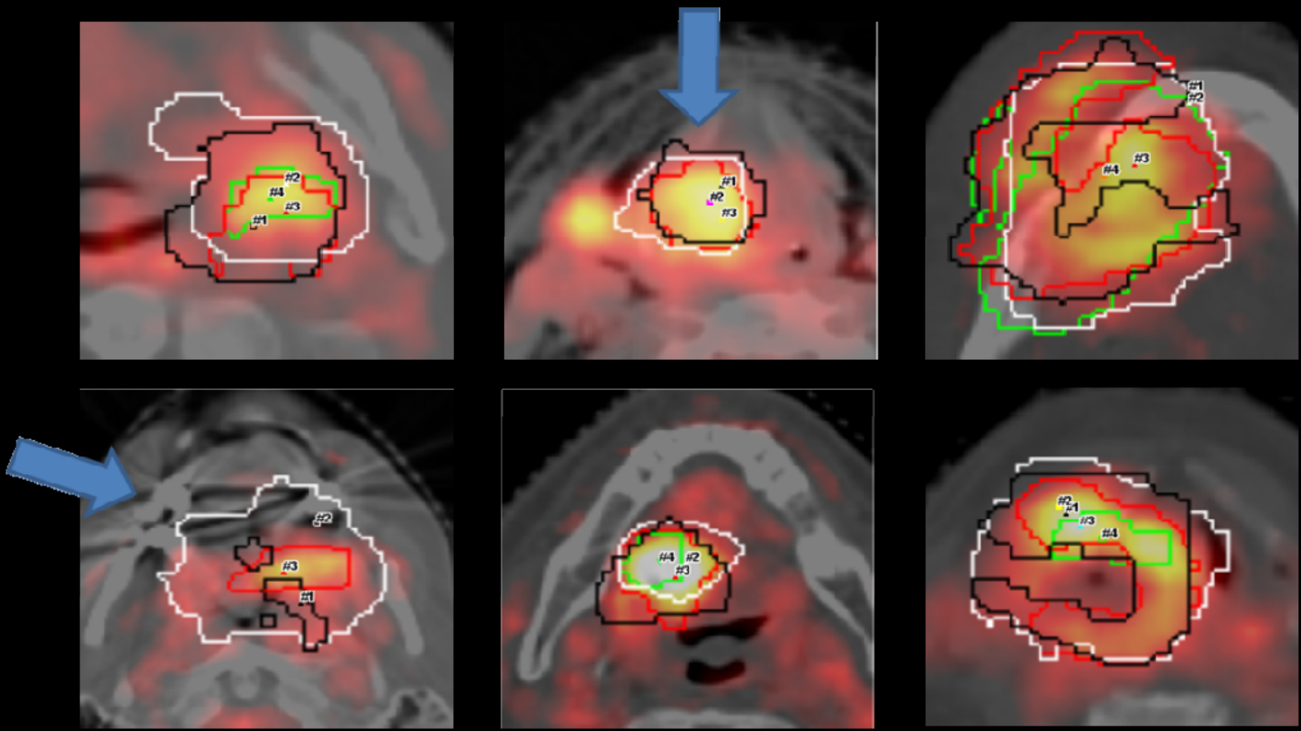

disadvantage
advantage


Week 1
Week 2
Week 3
Week 4
Week 5
Follow Up
Fractionated Chemo-Radiotherapy
FDG-PET/CT
FMISO-PET/CT
0 Gy
10 Gy
20 Gy
40 Gy
[18F]Misonidazol
[18F]FDG

Zips 2012


Local-progression-free survival
(a) baseline
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
p = 0.937
group1 = 0 (TBRmax < 2.23)
group1 = 1 (TBRmax >= 2.23)
Number at risk
group1 = 0 12 7 5 1 1 0
group1 = 1 13 5 5 4 1 0
(b) 8 - 10 Gy
p = 0.236
group2 = 0 (TBRmax < 2.16)
group2 = 1 (TBRmax >= 2.16)
Number at risk
group2 = 0 11 6 6 2 1 0
group2 = 1 11 5 3 2 1 0
(c) 18 - 20 Gy
p = 0.001
group3 = 0 (TBRmax < 1.93)
group3 = 1 (TBRmax >= 1.93)
Number at risk
group3 = 0 11 8 8 3 0 0
group3 = 1 11 2 0 0 0 0
(d) 51 - 57 Gy
p = 0.017
group4 = 0 (TBRmax < 1.66)
group4 = 1 (TBRmax >= 1.66)
Number at risk
group4 = 0 12 7 7 3 1 0
group4 = 1 12 4 2 2 1 0
Analysis time (months)

Zips 2012 GV

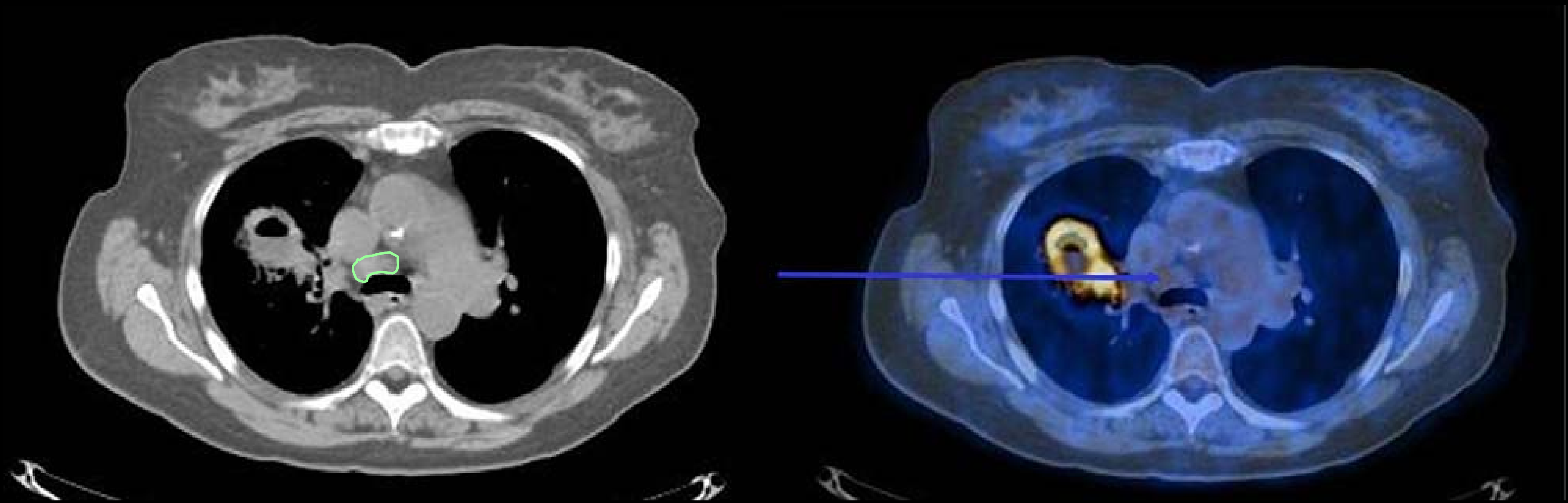


FMISO1black, FMISO2 white, FMISO3 red, FMISO4 green; 6 patients contoured by one observer

# FMISO-hypoxic volume changes during the course of RCHT

GV

# PET can change staging & delineation



PET -: APD confirmed

GV

| Pt. No. | CT scan | PET scan | Pathologic examination |
|---|---|---|---|
| 1 | 0 | 0 | 0 |
| 2 | 0 | 2 | 2 |
| 3 | 0 | 2 | 2 |
| 4 | 0 | 0 | 2 |
| 5 | 0 | 0 | 1 |
| 6 | 0 | 0 | 2 |
| 7 | 2 | 2 | 0 |
| 8 | 2 | 2 | 2 |
| 9 | 0 | 0 | 1 |
| 10 | 0 | 0 | 0 |
| 11 | 2 | 2 | 2 |
| 12 | 0 | 0 | 0 |
| 13 | 0 | 0 | 0 |
| 14 | 1 | 2 | 2 |
| 15 | 0 | 0 | 0 |
| 16 | 0 | 0 | 0 |
| 17 | 0 | 0 | 2 |
| 18 | 0 | 0 | 0 |
| 19 | 1 | 1 | 0 |
| 20 | 0 | 0 | 1 |
| 21 | 0 | 0 | 0 |
| 22 | 0 | 0 | 0 |
| 23 | 2 | 1 | 1 |
| 24 | 0 | 0 | 0 |
| 25 | 0 | 0 | 0 |
| 26 | 0 | 1 | 1 |
| 27 | 3 | 3 | 2 |
| 28 | 2 | 0 | 1 |
| 29 | 2 | 0 | 0 |
| 30 | 0 | 0 | 0 |
| 31 | 1 | 0 | 0 |
| 32 | 0 | 0 | 1 |

**32 patients**

**Changes in TN stage between CT and PET:**

**- For T: n=6**

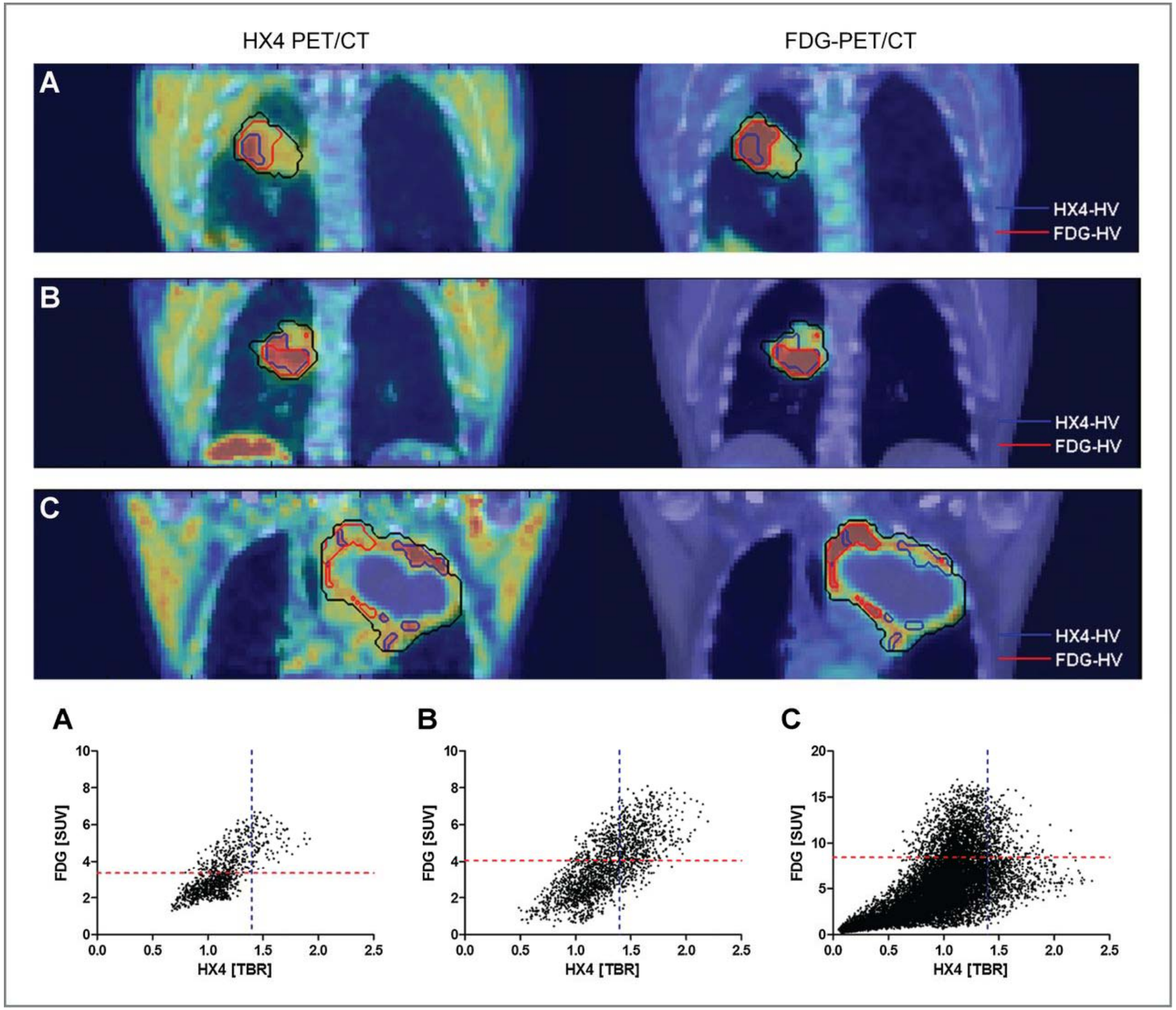
**- For N: n=9**

**APD confirmation in 7 N:**

**- 3 higher N (red)**

**- 4 lower N (green)**

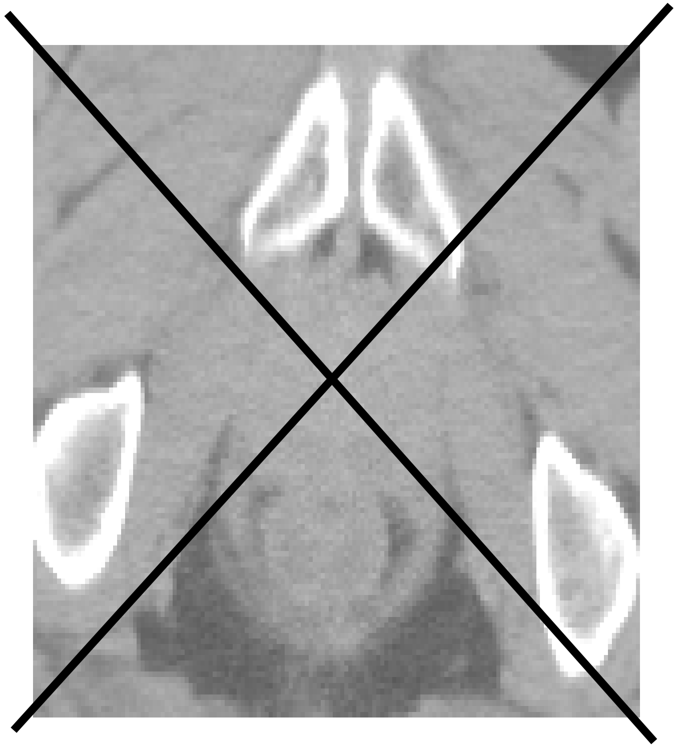
**Faria et al. 2008**




Zegers et al. 2014

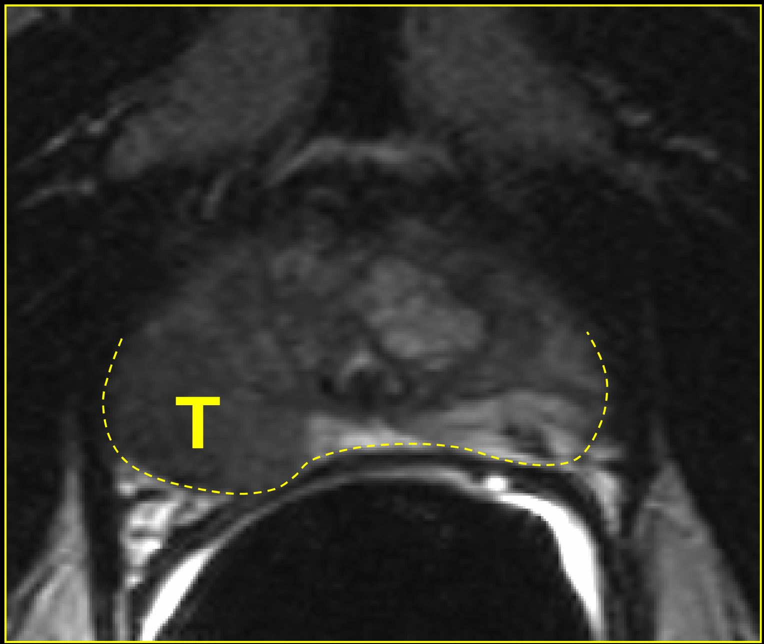
# PROSTATE CANCER

# Imaging of T



# Prostate Cancer Staging

## Extracapsular Tumor Spread

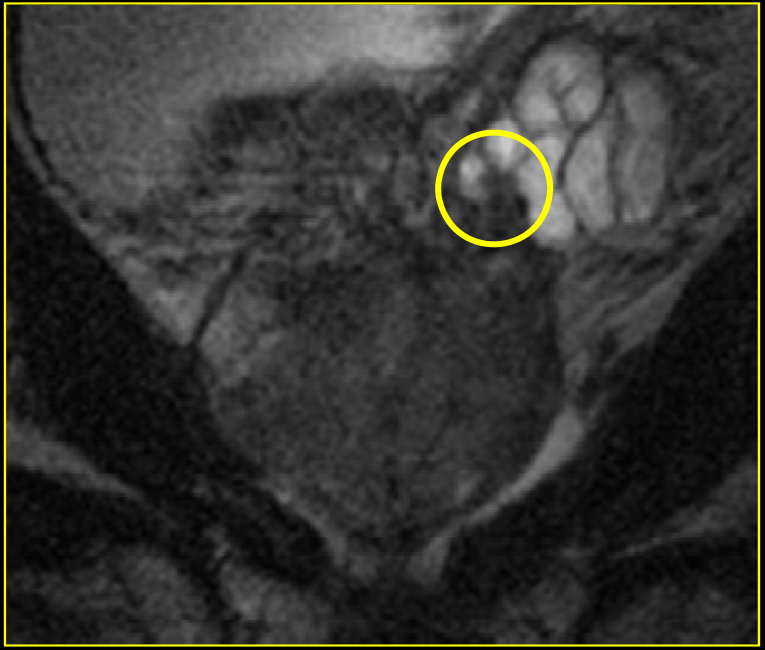


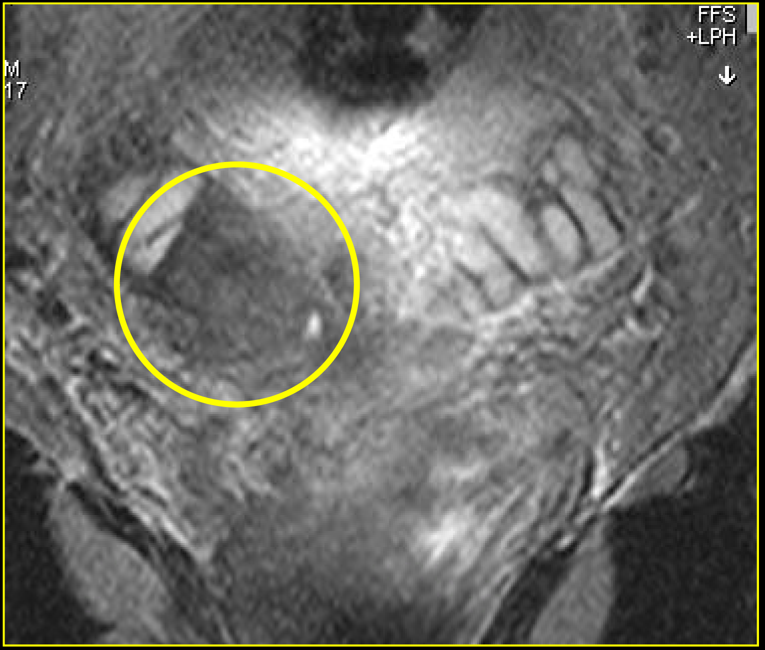

Capsular penetration = irregular capsular bulge OR infiltration of periprostatic fat OR neurovascular bundle asymmetry

GV

# Prostate Cancer Staging

## Seminal Vesicle Involvement






Seminal vesicle invasion =
abnormally low signal intensity within lumen/
focal thickening of seminal vesicle wall

GV

# MRI and its role in prognosis

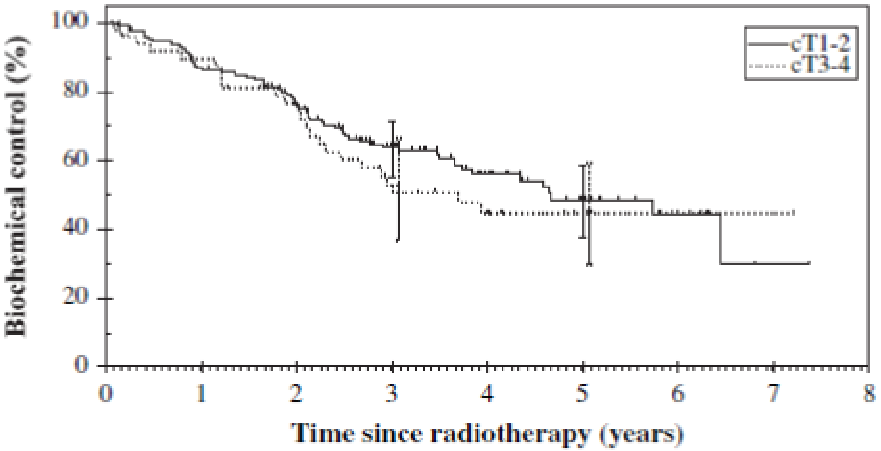



Fig. 1 – Biochemical control by clinical T stage.

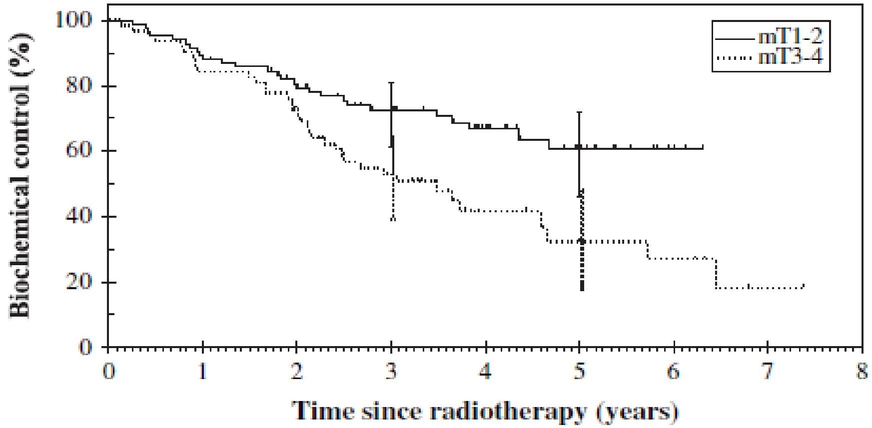



Fig. 3 – Biochemical control by magnetic resonance imaging T stage (cT1/2 cases only).

**Jackson et al. 2005; Clin Oncol: 167-71.**

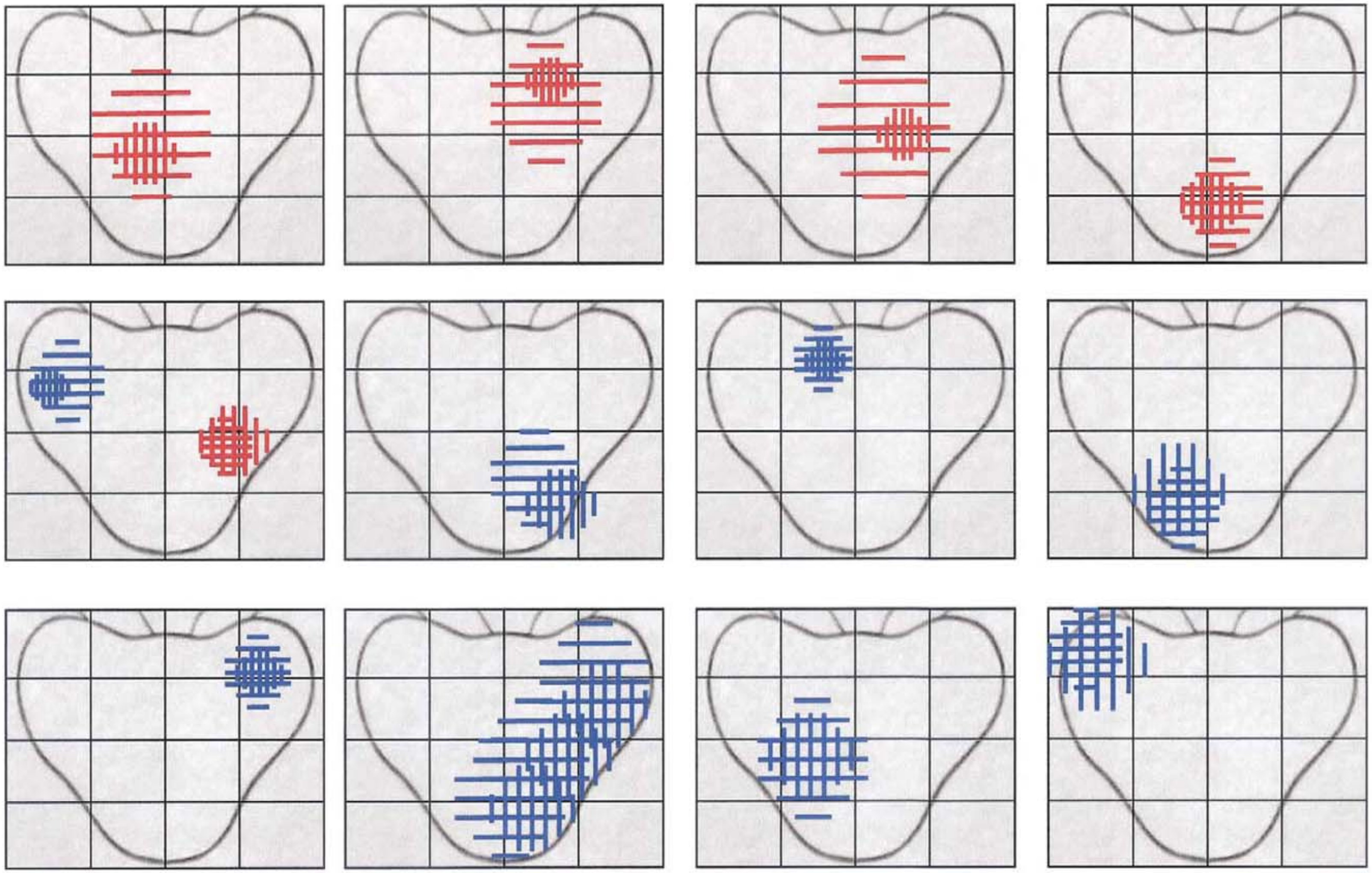
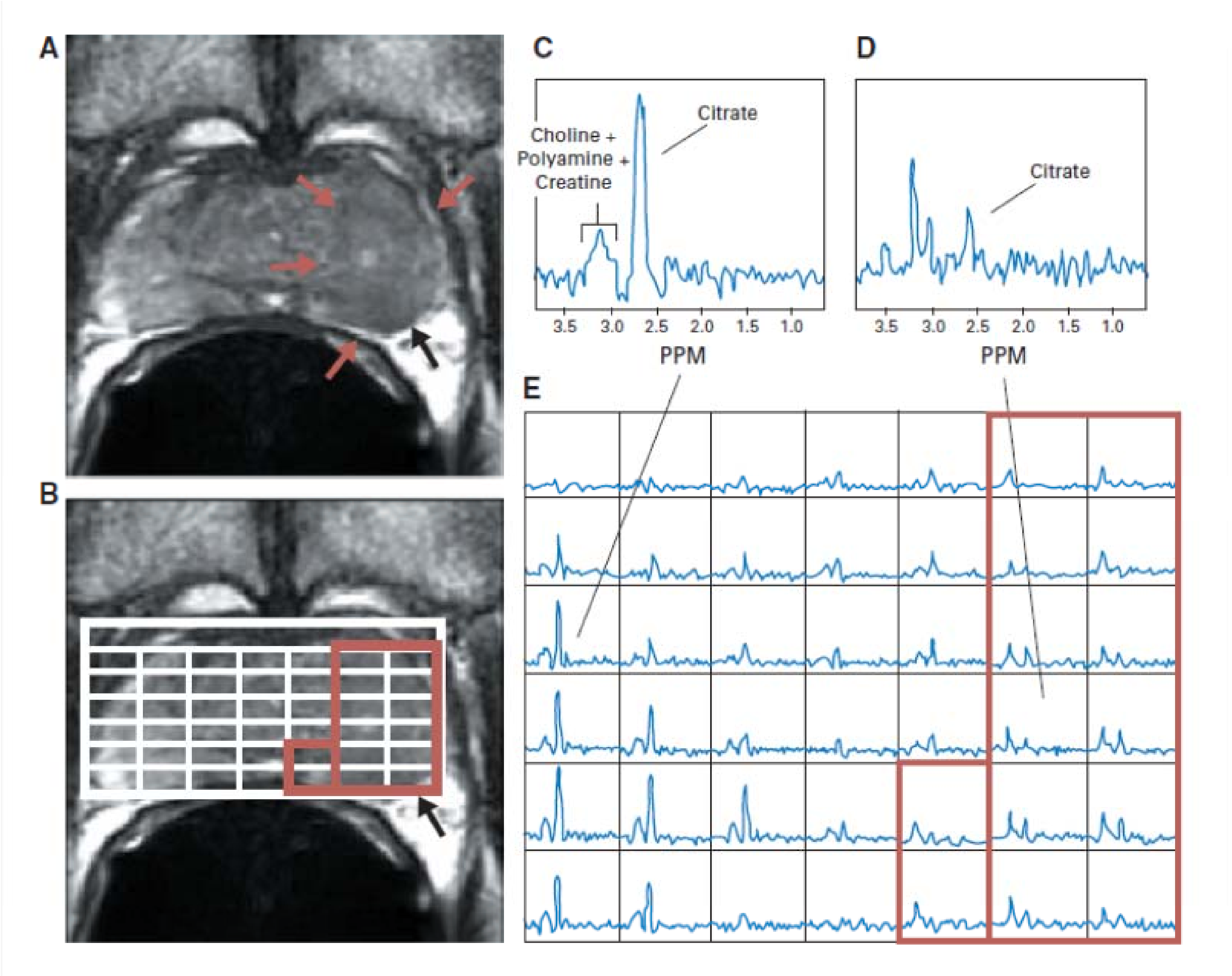


Fig. 3. Initial tumor extent (indicated with horizontal lines) and extent of disease progression at its identification (indicated with vertical lines) in 12 patients with local failure. Red lines indicate tumors with a complete response; blue lines indicate tumors with no or a partial response.

**Cellini et al, IJROBP 2002; 53:595-599: 12/12 local failures in the prostate.**

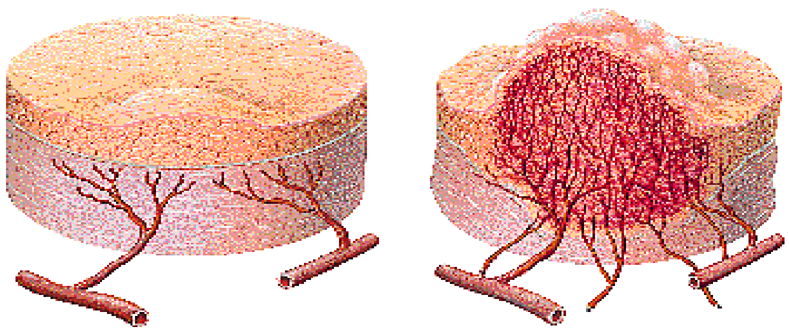


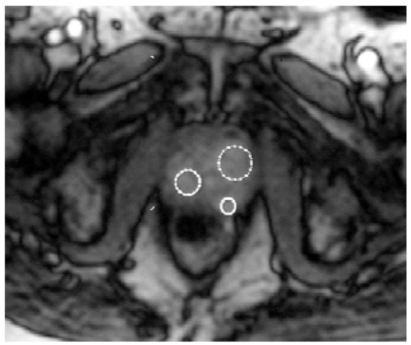

**Speight et al. 2007; JCO: 62-69.**

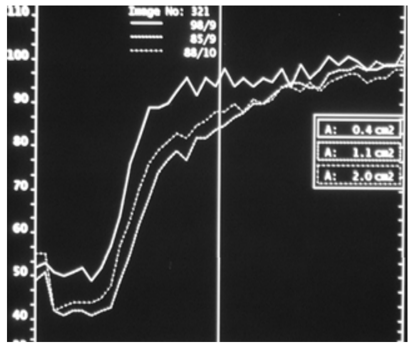
# Dynamic Contrast-Enhanced MRI

## Assessment of Angiogenesis

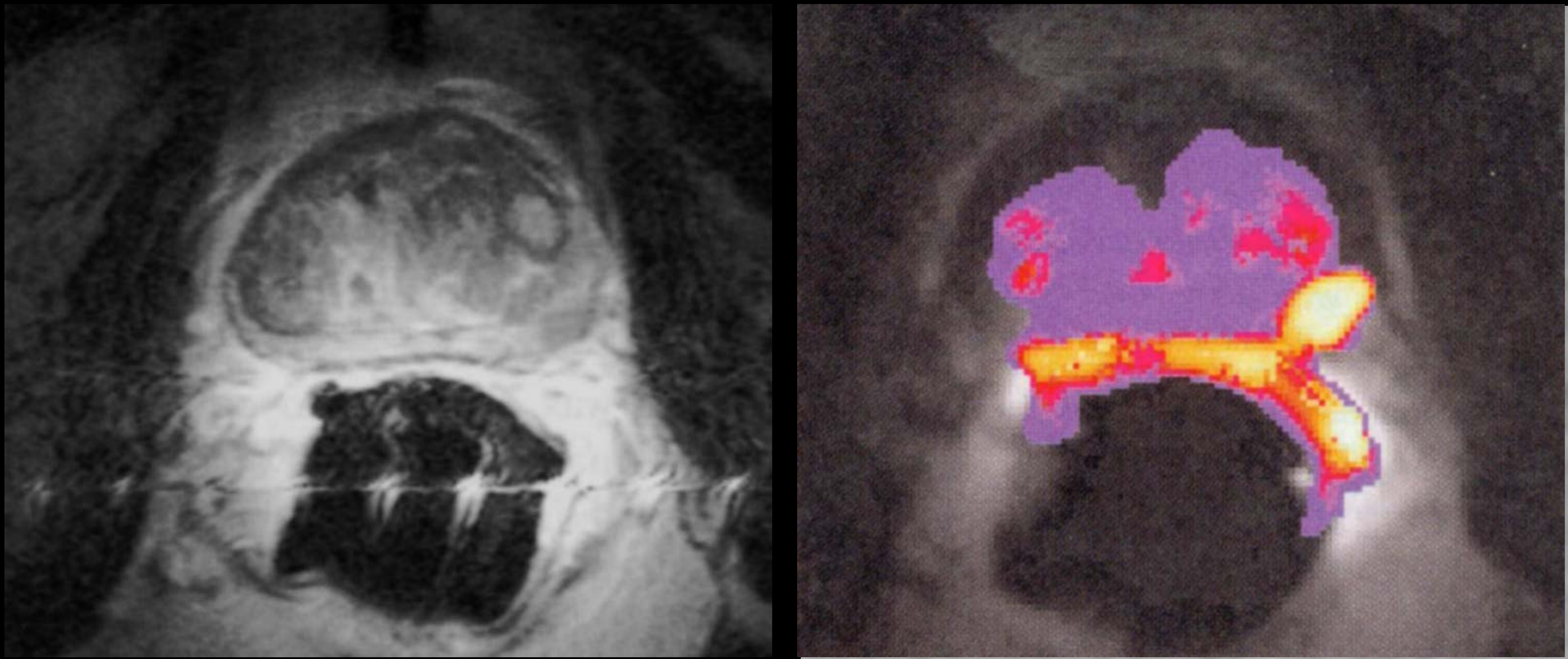
| Lesion Morphology | Enhancement |
| --- | --- |
| Angiogenic Factors | Increased in- en efflux<br>Expanded extracellular space<br>Increased extravasation |
| Growth of existing vessels<br>De novo angiogenesis | |
| Abnormal configuration: AV-shunts and defective endothelium | Earlier onset of enhancement<br>Increased slope |





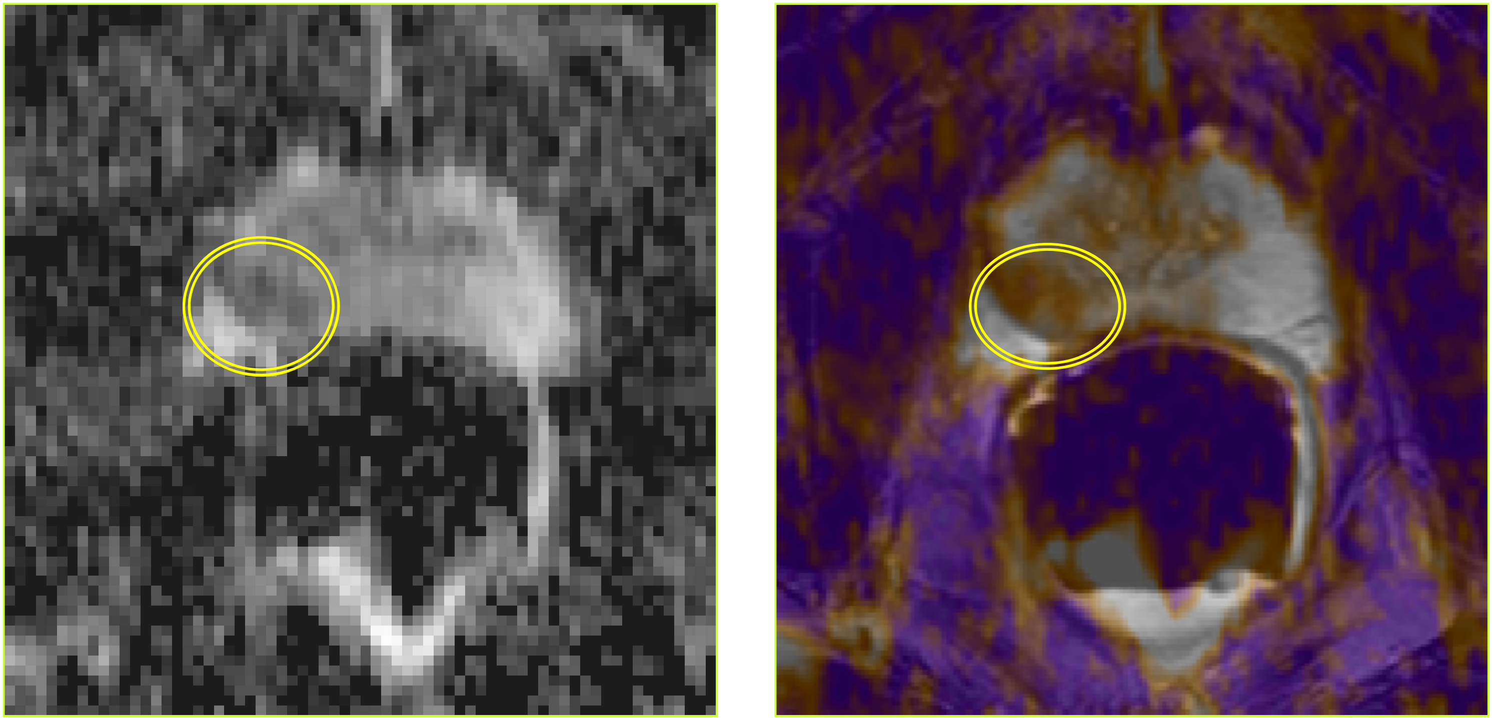


# Prostate cancer diagnosis with dCE



GV

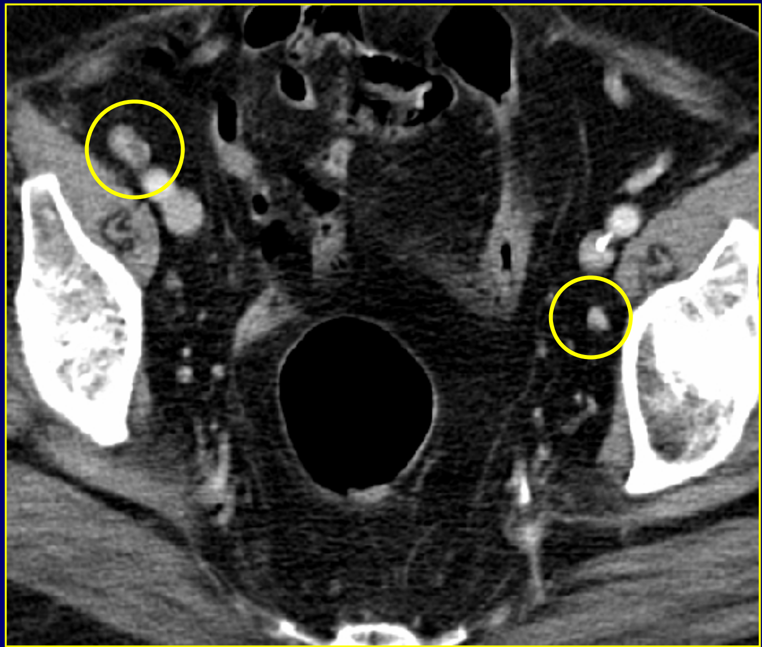
# Diffusion Weighted Imaging

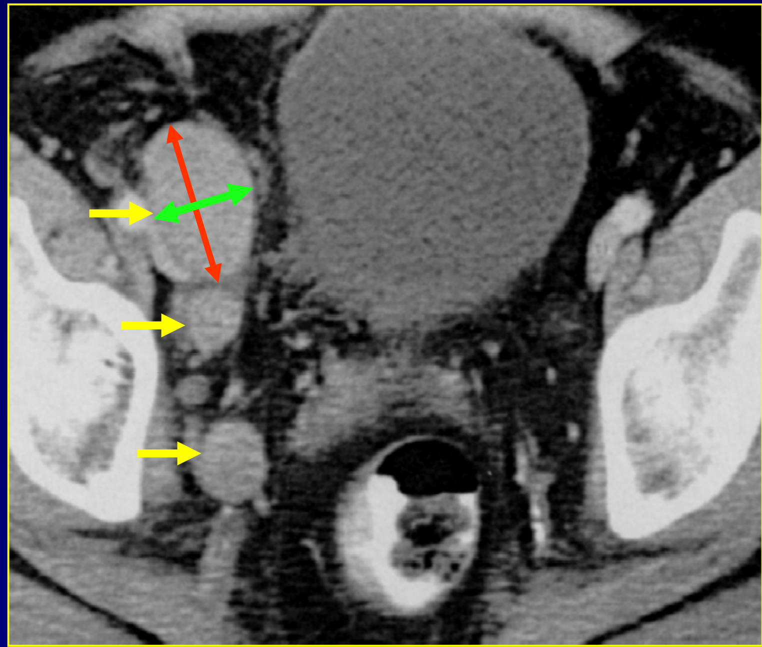


# Imaging of N

# Prostate Cancer Staging

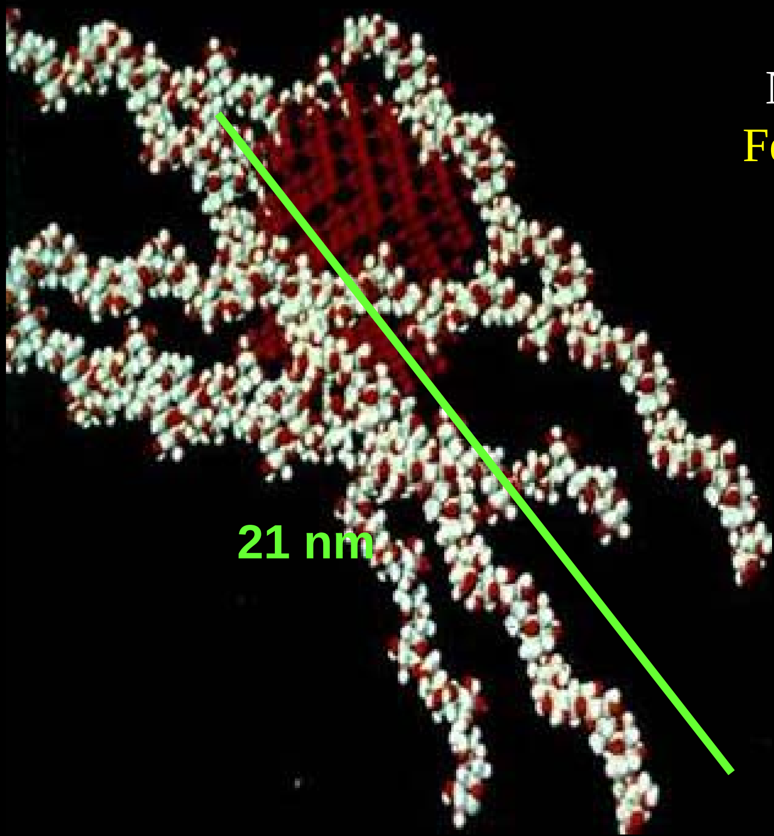
## Lymphatic Spread



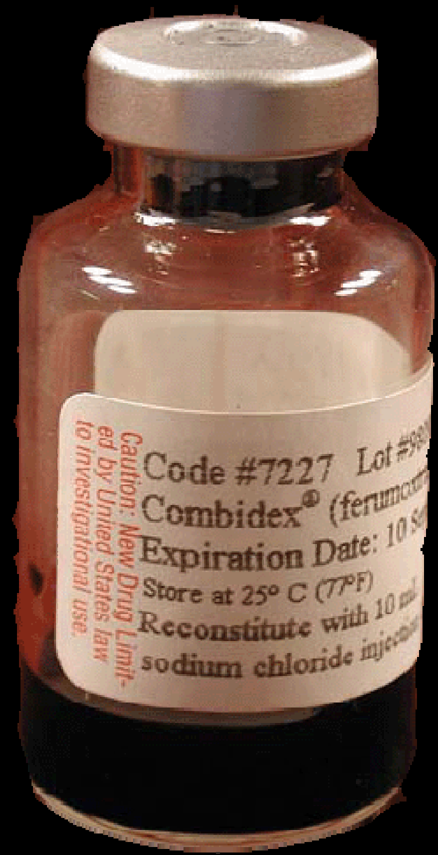


Lymph Node Staging
Oval node > 10 mm
Round node > 8 mm

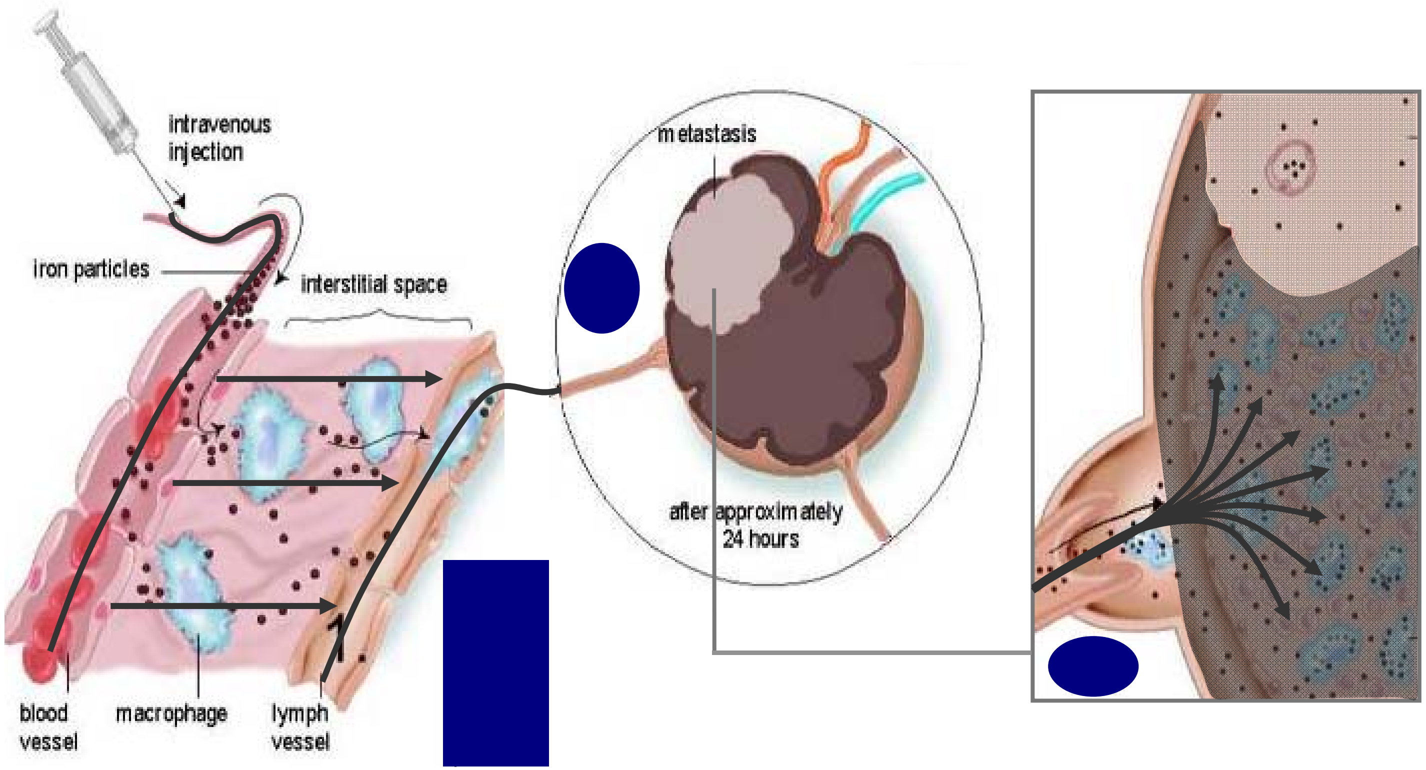
# IV injection of USPIO
# ("ultra small particles of iron oxide")




Nanoparticles
Ferumoxtran-10
Sinerem®
Combidex®

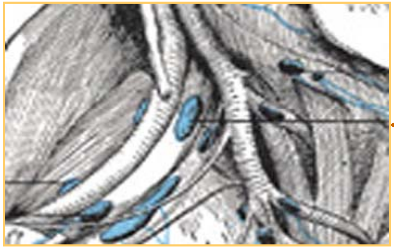


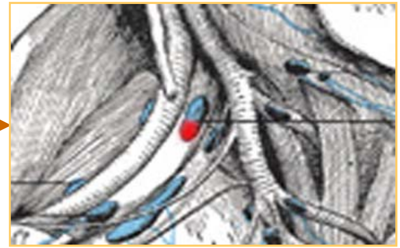
# IV injection of USPIO
# (“ultra small particles of iron oxide”)

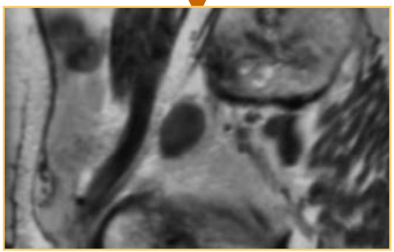


# IV injection of USPIO
# (“ultra small particles of iron oxide”)

*Captation in reticulo-endothelial system*







Detection limit up to 4 mm!

- The eternal “promise”: PET

GV

# Can imaging help?

**Prospective Evaluation of $^{11}$C-Choline Positron Emission Tomography/Computed Tomography and Diffusion-Weighted Magnetic Resonance Imaging for the Nodal Staging of Prostate Cancer with a High Risk of Lymph Node Metastases**

*Tom Budiharto [a,1,*], Steven Joniau [b,1], Evelyne Lerut [c], Laura Van den Bergh [a], Felix Mottaghy [d], Christophe M. Deroose [d], Raymond Oyen [e], Filip Ameye [b], Kris Bogaerts [f], Karin Haustermans [a], Hendrik Van Poppel [b]*

**n=36; 10-35% Partin**
**pN+: 47%**

| | No. of affected LNs | Dimension, mm |
|---|---|---|
| Isolated tumour cells | 2 | <0.2 |
| Micrometastases | 16 | 0.95 (range: 0.268–1.9) |
| Macrometastases | 20 | >2 |

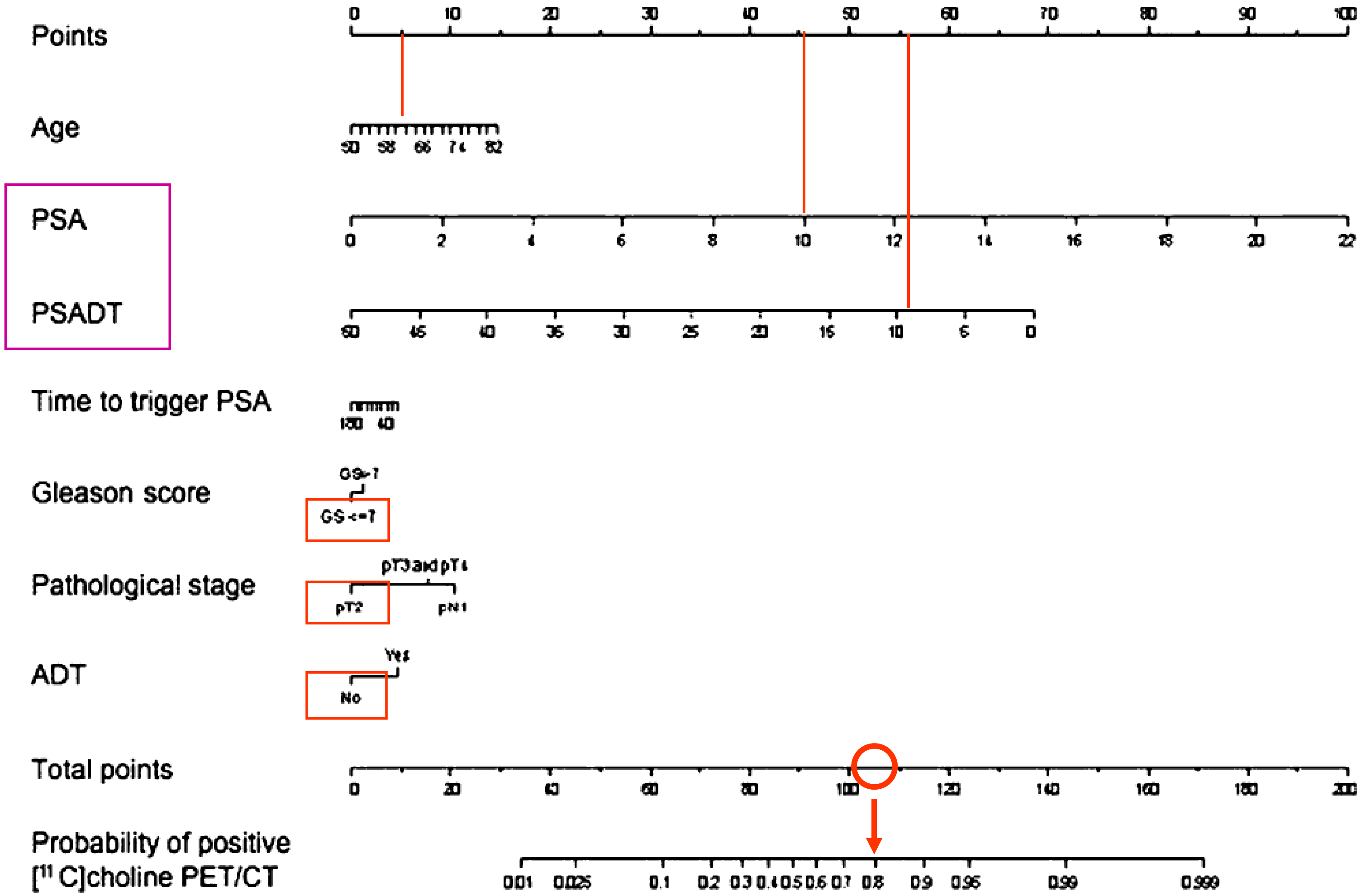
LN = lymph node.

| Choline Pet CT | Patient-based analysis | LN region-based analysis |
|---|---|---|
| No. of true-positive cases | 3 | 3 |
| No. of true-negative cases | 19 | 294 |
| No. of false-positive cases | 1 | 1 |
| No. of false-negative cases | 13 | 29 |
| Sensitivity | 18.8% | 9.4% |
| Specificity | 95% | 99.7% |
| PPV | 75% | 75% |
| NPV | 59.4% | 91.0% |

**Detection rate for macro LN: 18%**

| DWI | Patient-based analysis | LN region-based analysis |
|---|---|---|
| No. of true-positive cases | 6 | 6 |
| No. of true-negative cases | 18 | 288 |
| No. of false-positive cases | 4 | 7 |
| No. of false-negative cases | 8 | 26 |
| Sensitivity | 42.9% | 18.8% |
| Specificity | 81.8% | 97.6% |
| PPV | 60% | 46.2% |
| NPV | 69.2% | 91.7% |

**Detection rate for macro LN: 35%**

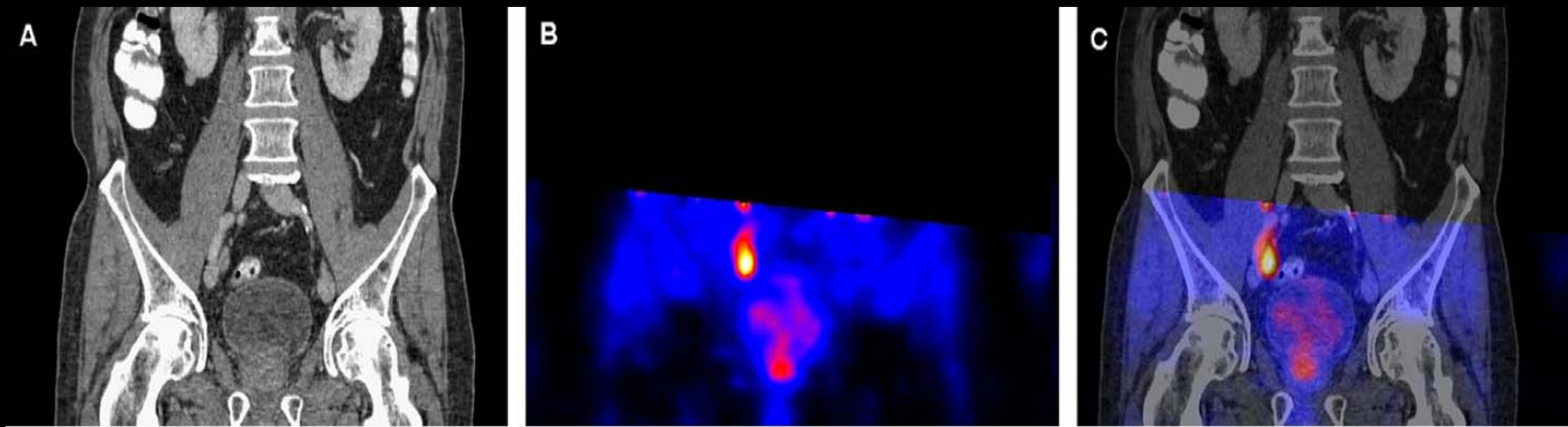





Giovacchini et al. Eur J Nucl Med Mol Imaging 2010; 37: 1106-1116.

## 11 C-choline PET and local relapse


## 11 C-choline PET and lymph node relapse



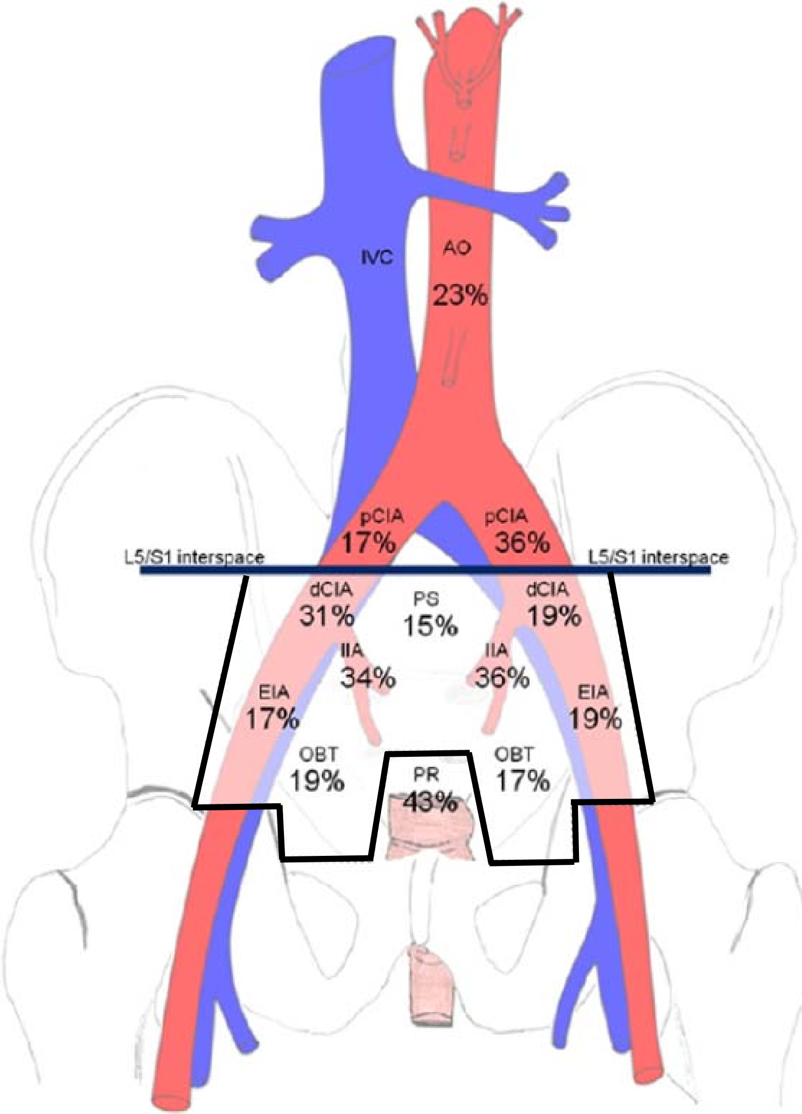
# Patients with PSA recurrence after radical prostatectomy

Table 1. Patient characteristics

| | |
|---|---|
| Age (y) | 65 (45–80) |
| Initial PSA (ng/mL) | 11.05 (2.30–92.50) |
| PSA at time of MRL (ng/mL) | 0.92 (0.23–34.00) |
| PSA doubling time (mo) | 4.23 (0.59–67.10) |
| Gleason score | |
| Unknown | 1 (2.1) |
| 6 | 2 (4.3) |
| 7 | 23 (48.9) |
| 8 | 8 (17.0) |
| 9 | 13 (27.7) |
| Pathologic T stage | |
| Unknown | 1 (2.1) |
| 1c | 1 (2.1) |
| 2a | 1 (1.5) |
| 2b | 2 (9.2) |
| 2c | 5 (15.4) |
| 3a | 15 (35.4) |
| 3b | 20 (32.3) |
| 4 | 2 (4.3) |
| Lymph node metastases at PLND | |
| Unknown | 1 (2.1) |
| No PLND performed | 7 (14.9) |
| Yes | 14 (29.8) |
| No | 25 (53.2) |
| Positive resection margin | |
| Unknown | 5 (10.6) |
| Yes | 14 (29.8) |
| No | 28 (59.6) |
| Extracapsular extension | |
| Unknown | 4 (8.5) |
| Yes | 29 (61.7) |
| No | 14 (29.8) |
| Seminal vesicle invasion | |
| Unknown | 1 (2.1) |
| Yes | 21 (44.7) |
| No | 25 (53.2) |
| PSA detectable postoperatively | |
| Yes | 23 (48.9) |
| No | 24 (51.1) |
| Hormonal treatment | |
| None | 30 (63.8) |
| Before RP | 1 (2.1) |
| After RP | 14 (29.8) |
| Before and after RP | 2 (4.3) |

**N=47**
**All underwent MRL**
**Aim: search for abberant nodes**

Meijer et al. IJROBP


IVC
AO
23%
pCIA
17%
pCIA
36%
L5/S1 interspace
L5/S1 interspace
dCIA
31%
PS
15%
dCIA
19%
IIA
34%
IIA
36%
EIA
17%
EIA
19%
OBT
19%
PR
43%
OBT
17%

# CERVIX CANCER

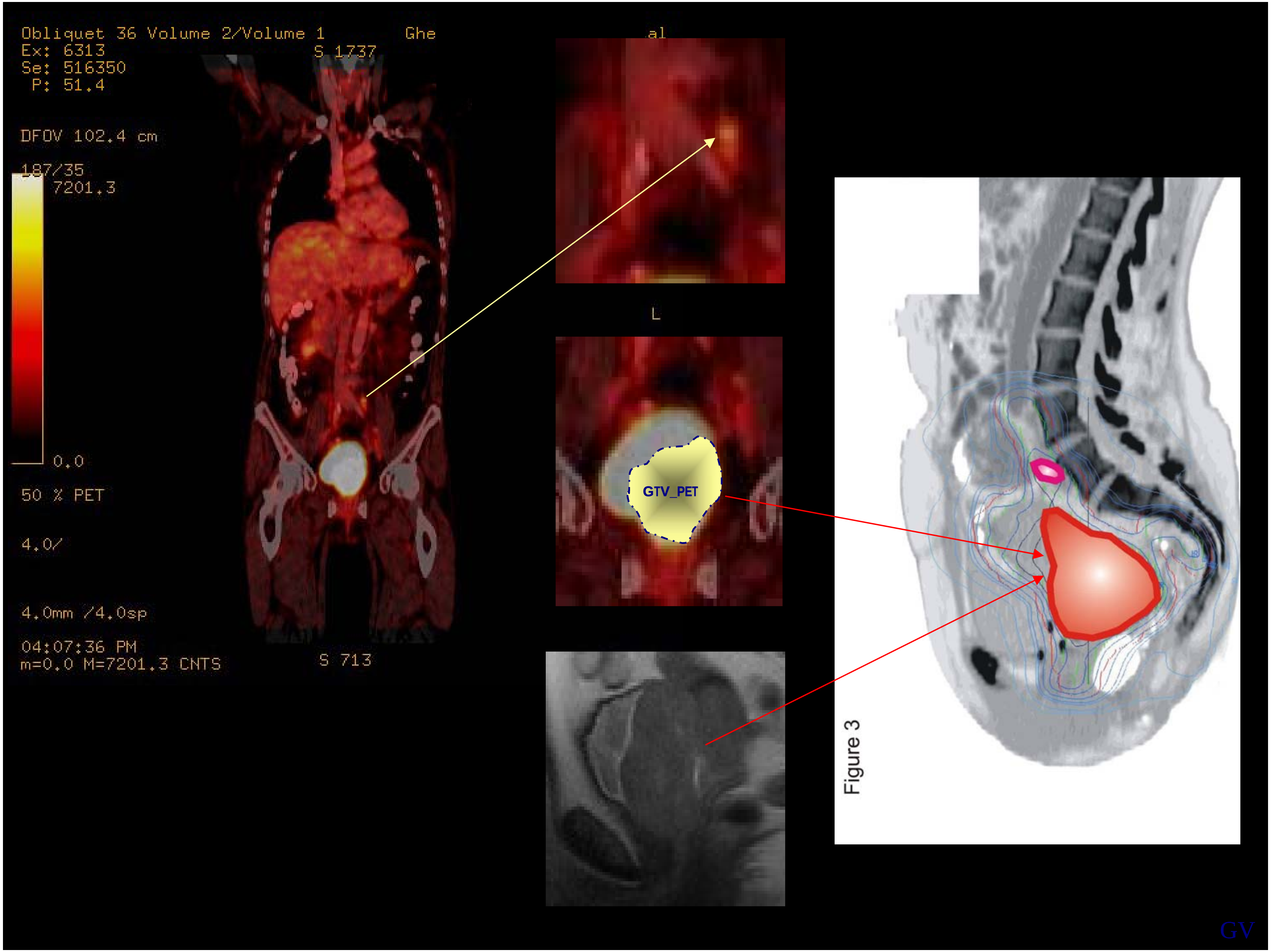
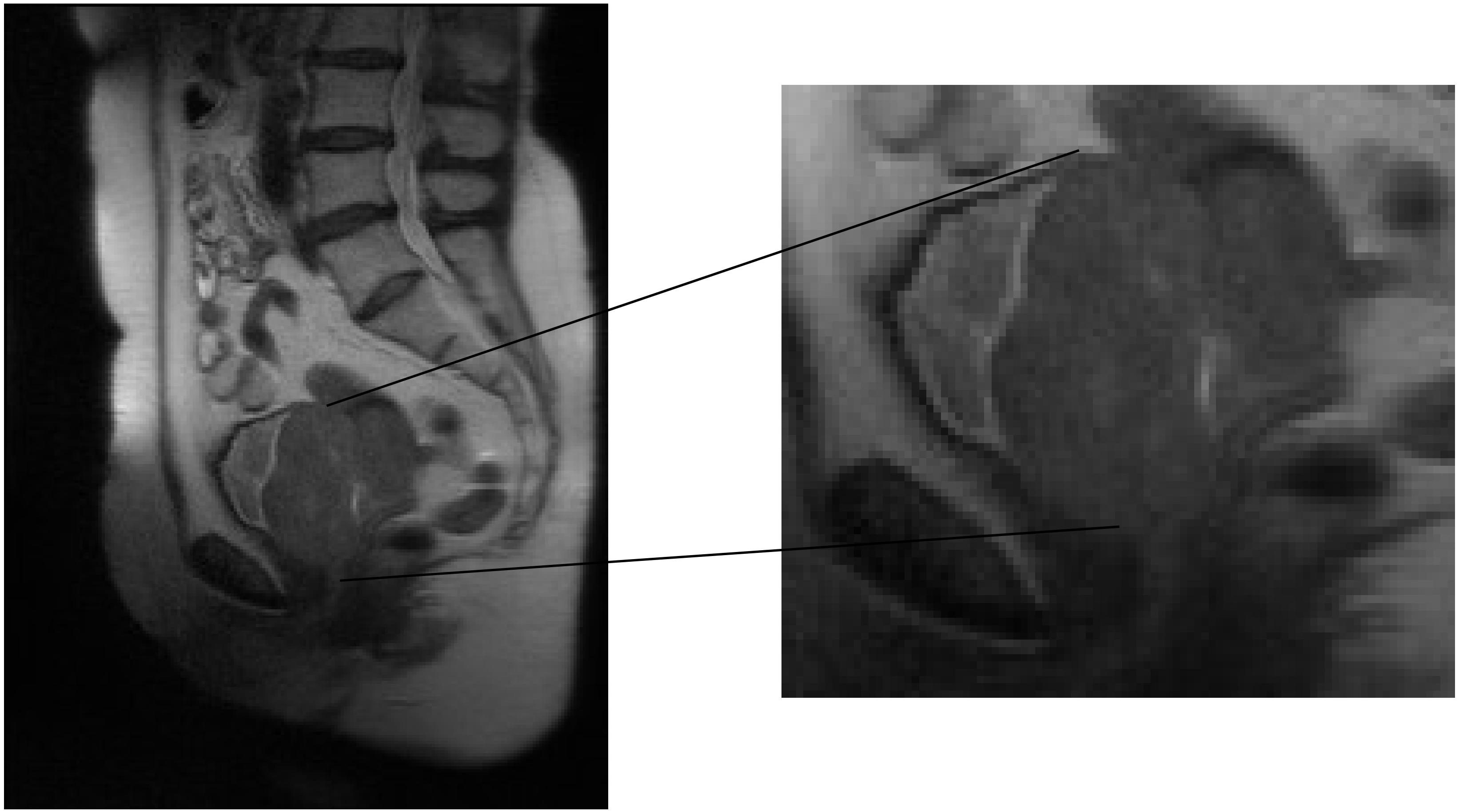

Obliquet 36 Volume 2/Volume 1
Ghe
al
Ex: 6313
S 1737
Se: 516350
P: 51.4
DFOV 102.4 cm
187/35
7201.3
0.0
50 % PET
4.0/
4.0mm /4.0sp
04:07:36 PM
m=0.0 M=7201.3 CNTS
S 713
L
GTV_PET
GV

Figure 3

## Pre – treatment investigations: magnetic resonance very useful

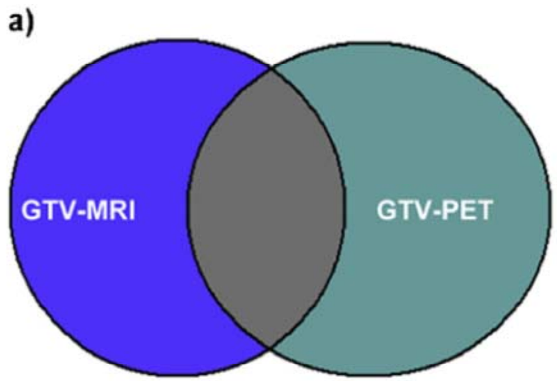


**sagital view of dose distribution**

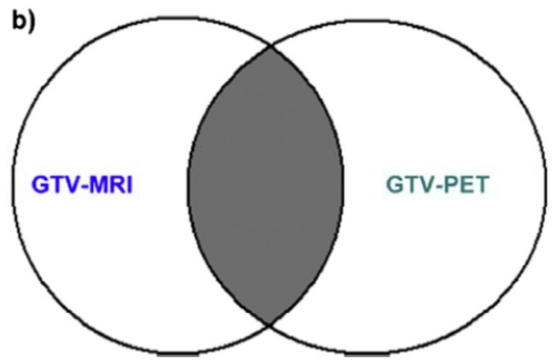
# RECTAL CANCER

# DELINEATION OF GROSS TUMOR VOLUME (GTV) FOR RADIATION TREATMENT PLANNING OF LOCALLY ADVANCED RECTAL CANCER USING INFORMATION FROM MRI OR FDG-PET/CT: A PROSPECTIVE STUDY

Morten Brændengen, M.D.,[*†] Karl Hansson, M.D.,[‡] Calin Radu, M.D.,[§] Albert Siegbahn, Ph.D.,[†]
Hans Jacobsson, M.D., Ph.D.,[‡] and Bengt Glimelius, M.D., Ph.D.[†§]



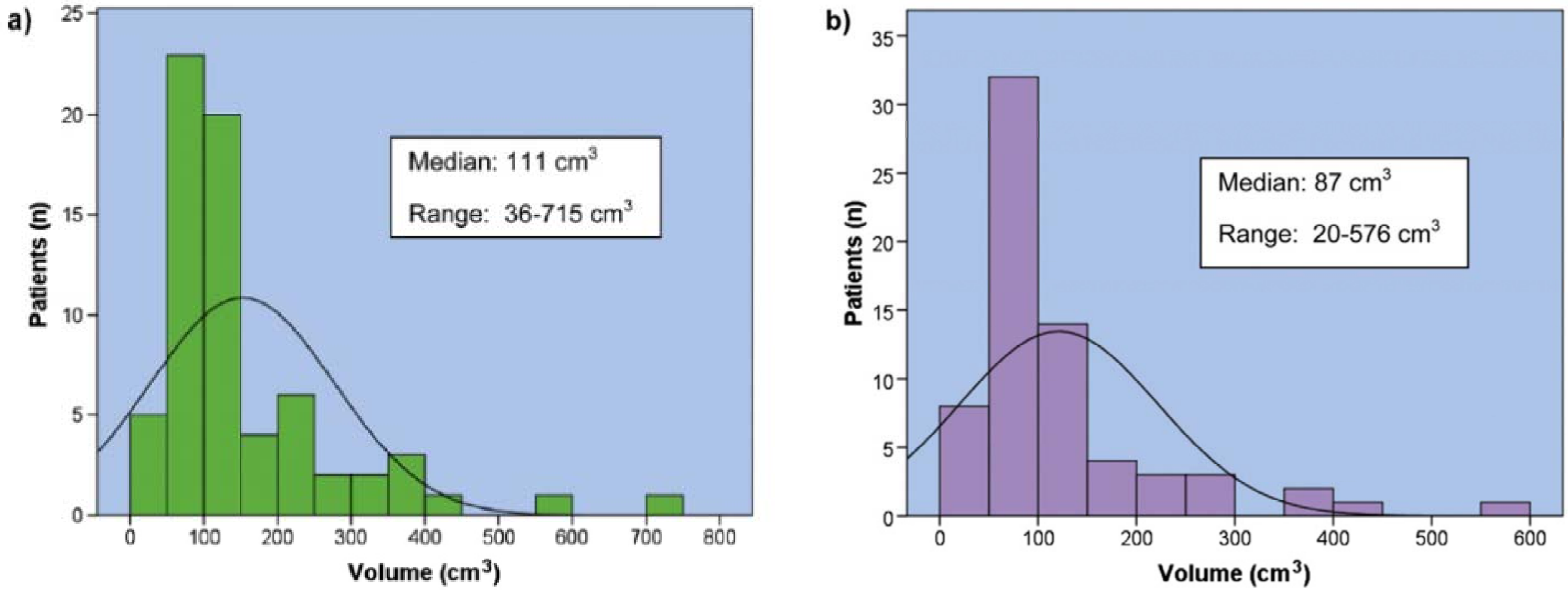

**Union**




**Intersection**

MRI

PET



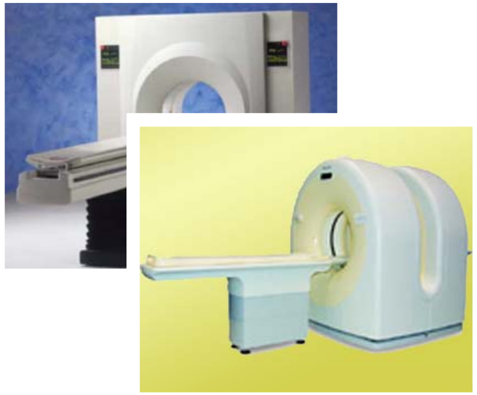
a)
Patients (n)
Volume (cm3)
Median: 111 cm3
Range: 36-715 cm3
b)
Patients (n)
Volume (cm3)
Median: 87 cm3
Range: 20-576 cm3

# THM

- Both MRI and PET improved target delineation
- MRI: use preferentially in:
    - cervix
    - rectum
    - prostate (prim)
    - brain / H&N if combined with PET

- PET: use preferentially in:
    - brain (no FDG), but combine with MRI
    - H&N (FDG / MISO)
    - prostate (no prim setting, choline in relapse, postop)
    - lung
    - rectum (sorry for limited data)
    - esophagus (?), pancreas (?)

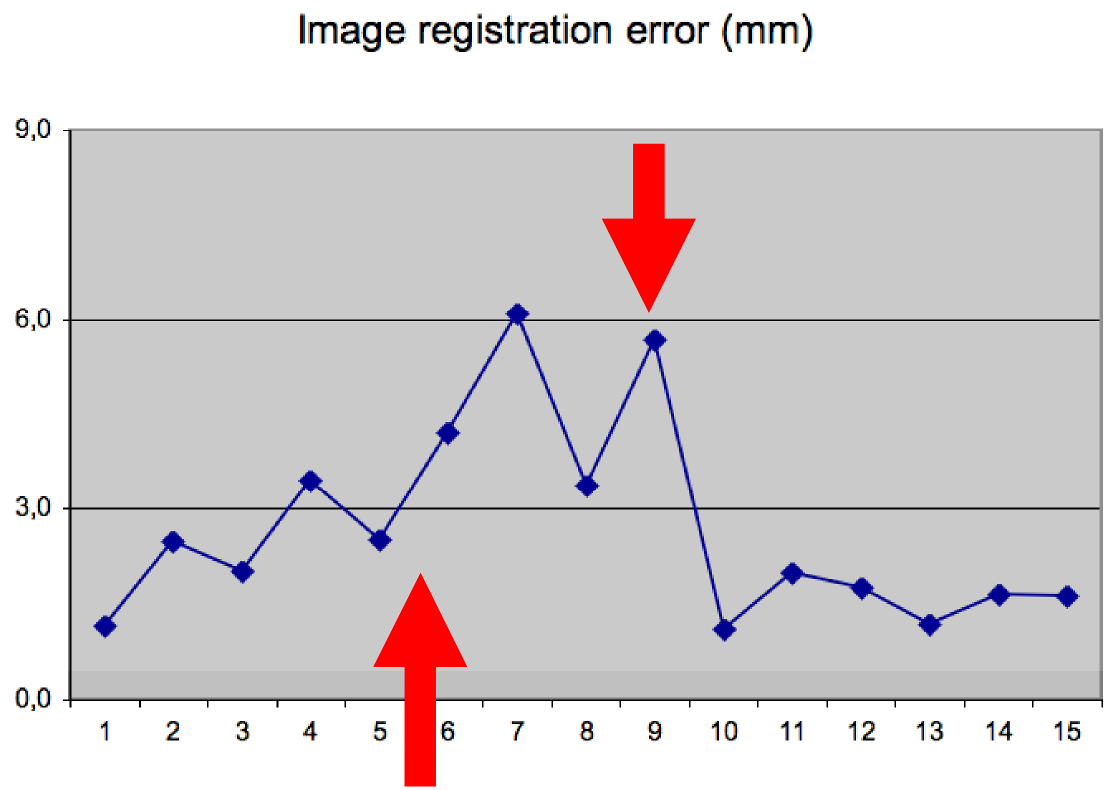
# Words of caution



| Modality | Repeats |
|---|---|
| ▪ Planning CT / MR | 1 – 2 |
| ▪ Additional PET | 1 |
| ▪ Radiation treatment | 25 – 50 |

# Words of caution

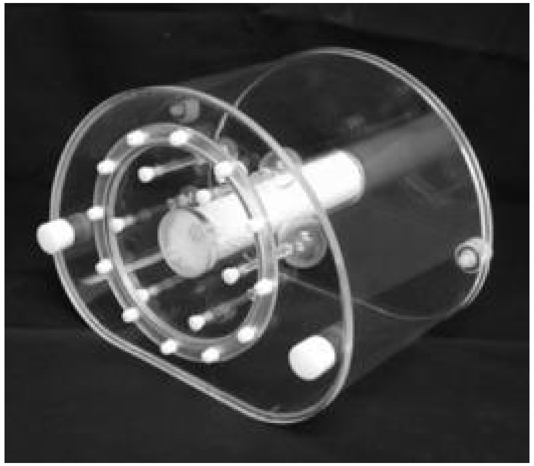
# Words of caution




**Recommendations**

- **Accept a learning curve for patient positioning**
- **Collaborate with radiotherapy department staff**
- **Train a dedicated PET planning staff**

# Words of caution



- PET resEARch 4 Life (EARL)
- Developed in 2010 by the EANM

- Until july 2014, 96 centers had their PET-CT scanners accredited.

Aims:

- Independent quality control by experts in the field of imaging;
- Comparable scanner output between centers, harmonisation of acquisition and interpretation of FDG-PET/CT scans;
- Accurate, reproducible und quantitative assessment;
- Quality certificate of accredited EARL-users.

# Words of caution

- **Quality assurance of anatomical and functional MR imaging**

# GTV, CTV and PTV
## (ICRU 62 + 83 and beyond)

,

**Sarah Jefferies PhD**

Department of Oncology,

Oncology Centre, Addenbrooke's Hospital, Cambridge, UK

# Learning Objectives

- To understand the concept of different planning volumes

- To understand definitions of
  - GTV, CTV, PTV

- To understand the relevance of Organs At Risk (OAR) and planning organs at risk volume (PRV)

- To understand how to manage overlapping volumes

- To understand prescribing


TomoTherapy
HI·ART

# The history of radiotherapy

- 1895 - Röntgen discovered X-rays
- 1896 - first treatment of cancer with X-rays
- ***120 years later the technology has changed!***

- ICRU reports are here to ***help*** us
- Series began with Report 50 and Supplement 62 (1993 + 1999)
- ICRU 71 (2004) added a few details
- ICRU 83 (2010) is designed for IMRT

# Target volumes

We need to consider, and define, how we describe target volumes

This is a prerequisite for integrating any diagnostic imaging

Think of an onion …

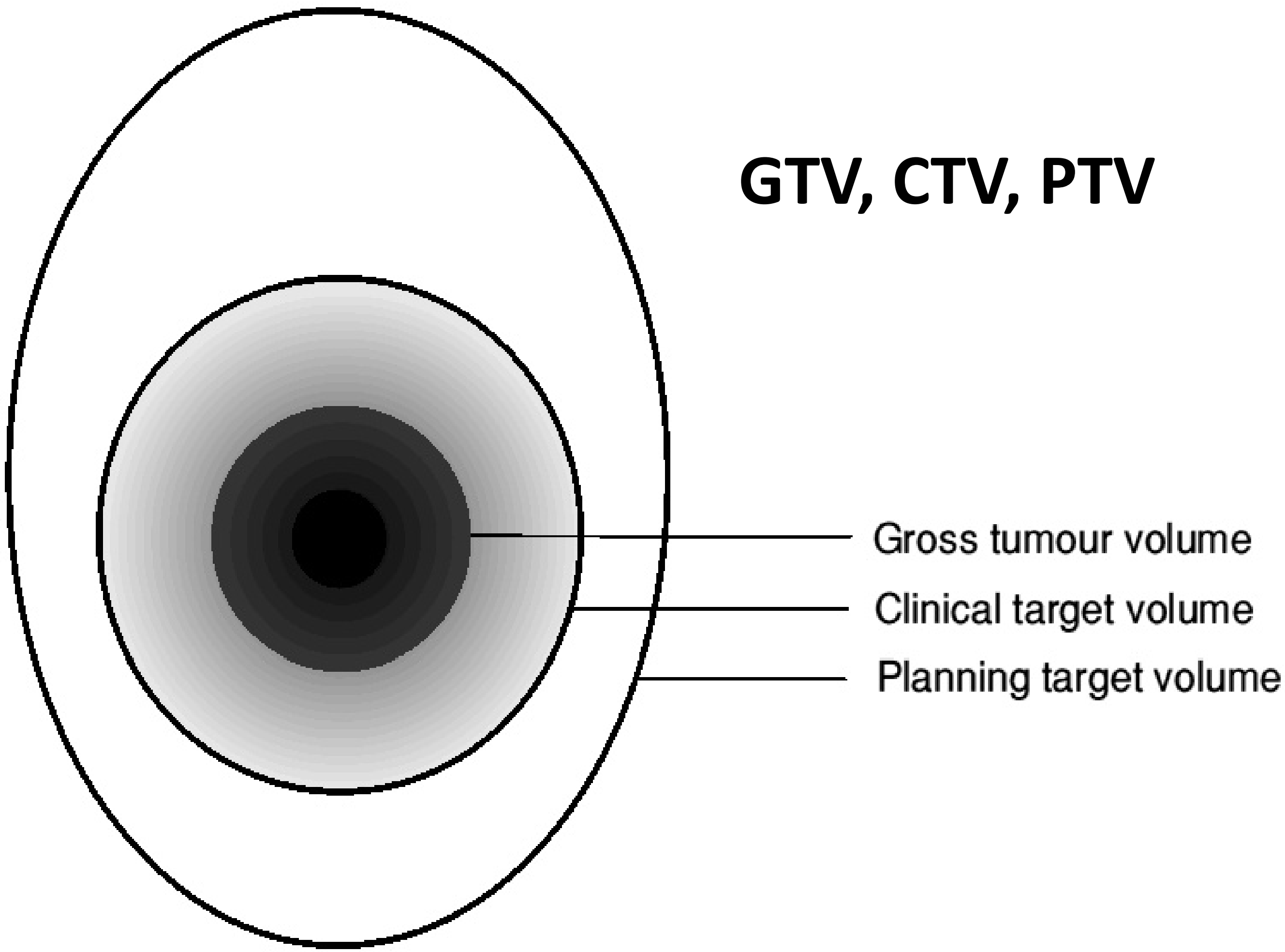
# Target volumes

Target volumes are like the concentric rings of an onion

# Target volumes

ICRU 50 target volumes

The PTV can be eccentric




**GTV, CTV, PTV**

# Target volumes

- ICRU report 50 and supplement 62 (1993 + 1999) specified definitions of different target volumes

- ICRU 62 was an update triggered by:
  i) increasing availability of conformal therapy where margins are more critical
  ii) need to describe normal tissues better

- ICRU 62 introduced the Planning organ at Risk Volume (PRV)

- ICRU 83 (2010) developed concepts for IMRT

# Target volumes - GTV

# Target volumes - GTV

- GTV - Gross Tumour Volume is the gross demonstrable extent and location of the tumour

- So, GTV is tumour you can:
  - **See, Feel, Image**

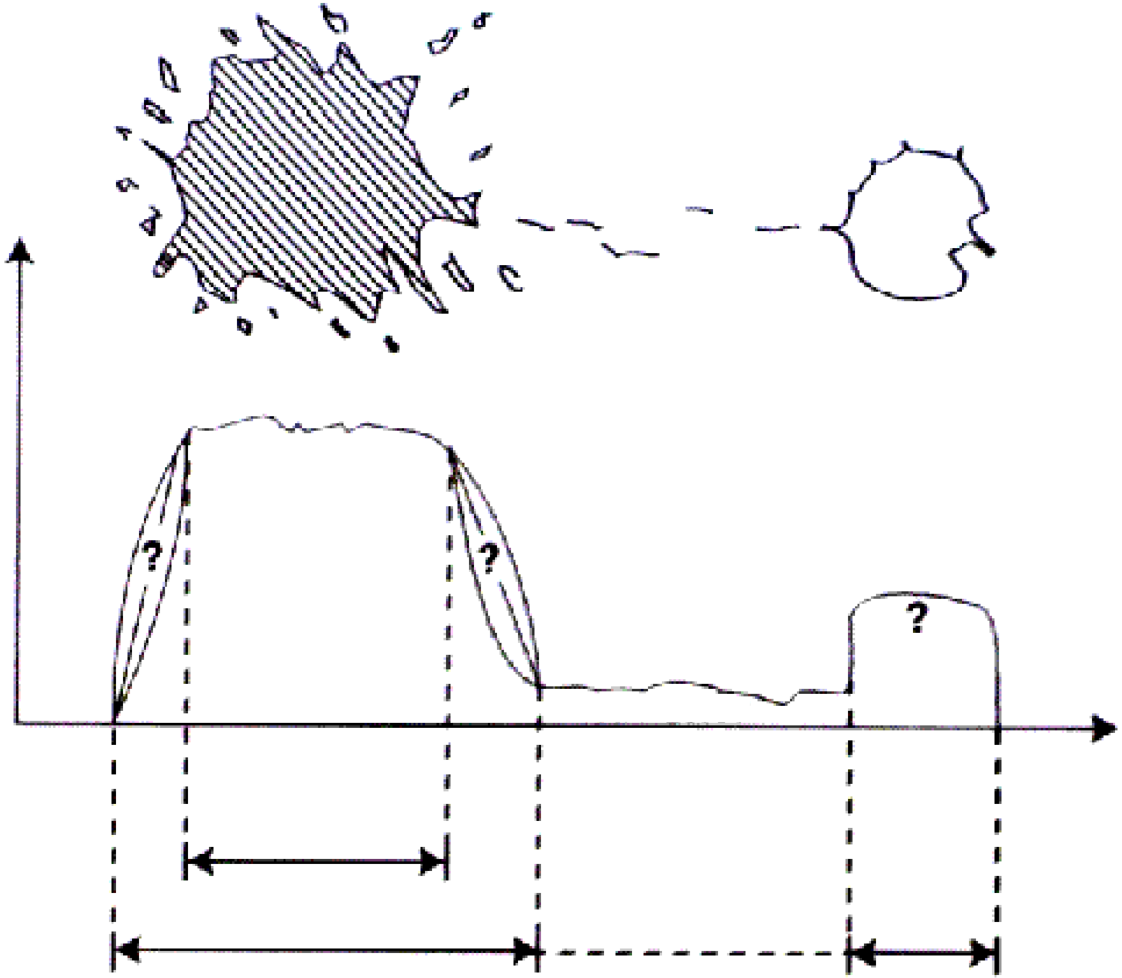
- Use different imaging modalities for different situations

- GTV can include lymph nodes or soft tissue spread as well as the primary tumour itself

# Target volumes - GTV

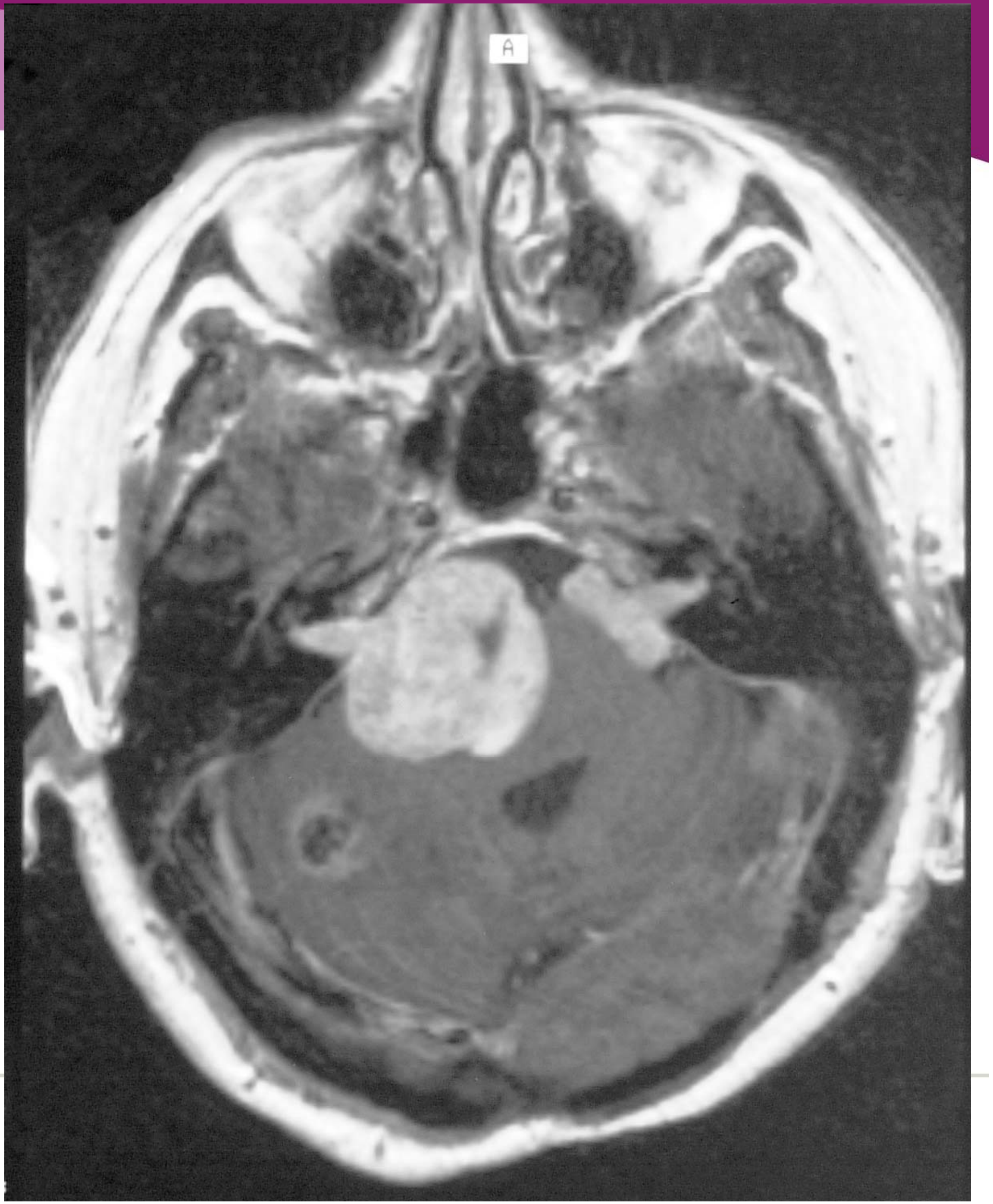
GTV – where tumour cell density is highest

(from ICRU 62)

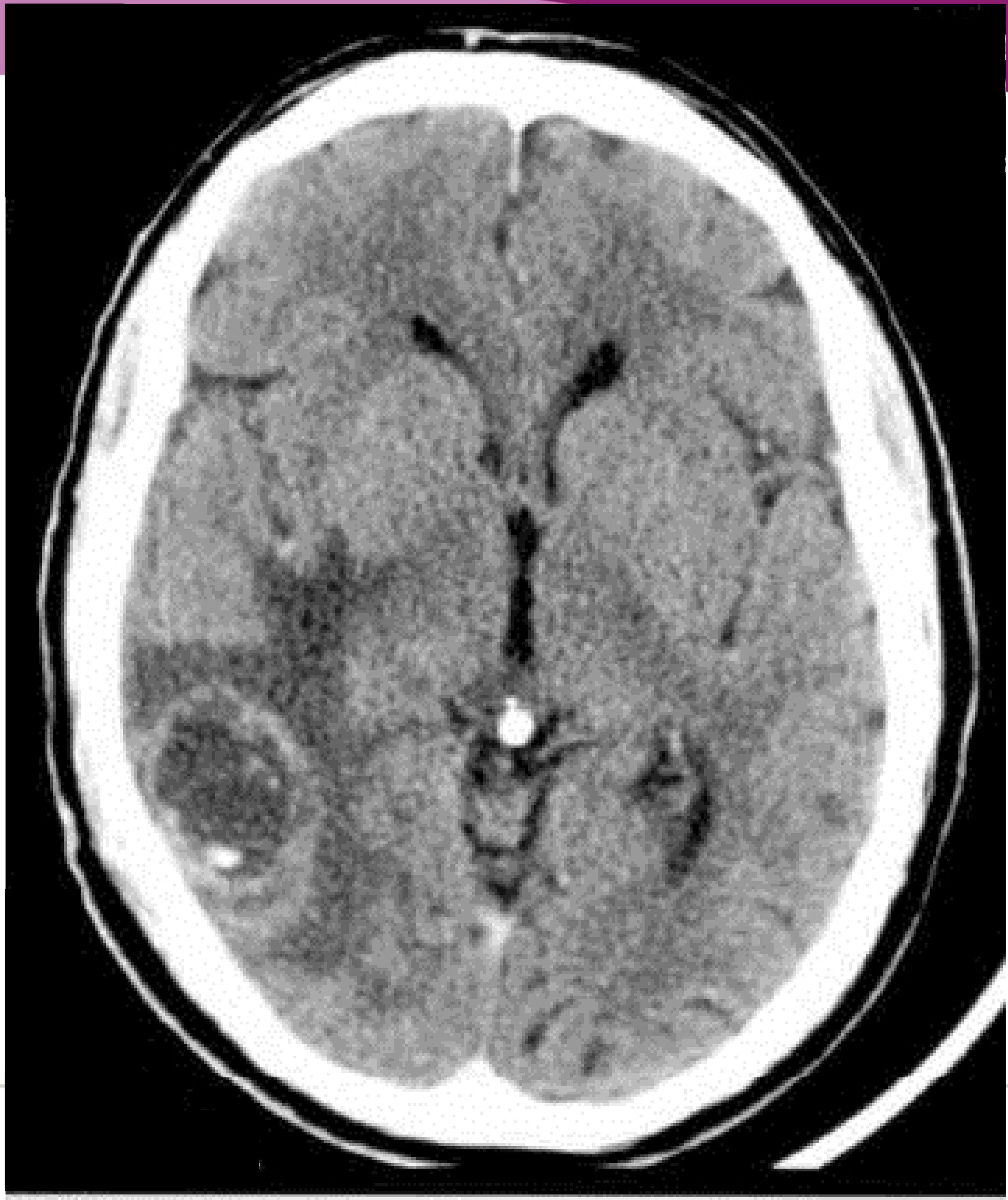


- GTV - completely obvious in this case

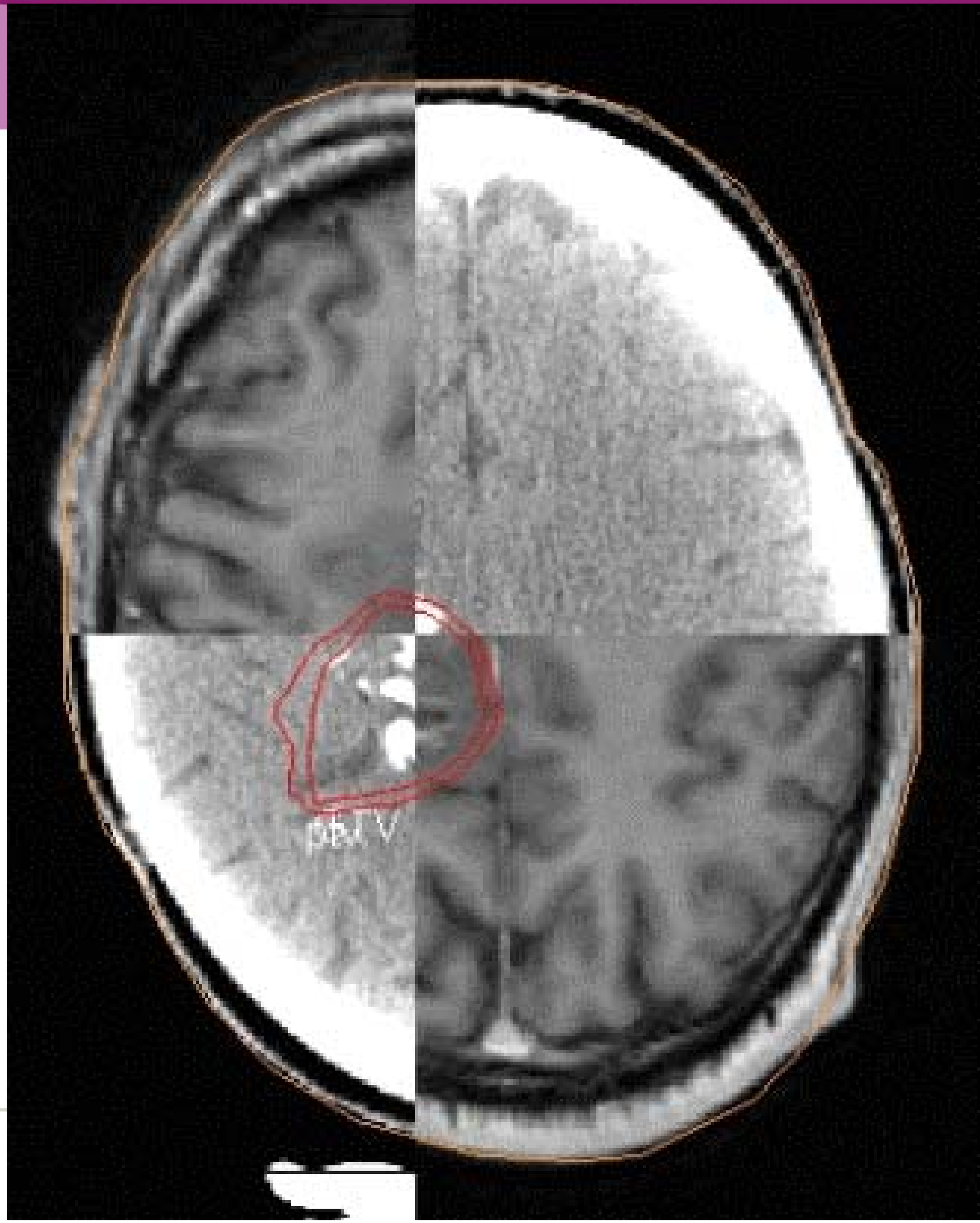
- (though not an easy clinical problem)



- GTV - reasonably obvious in this case
- (MRI would be better)



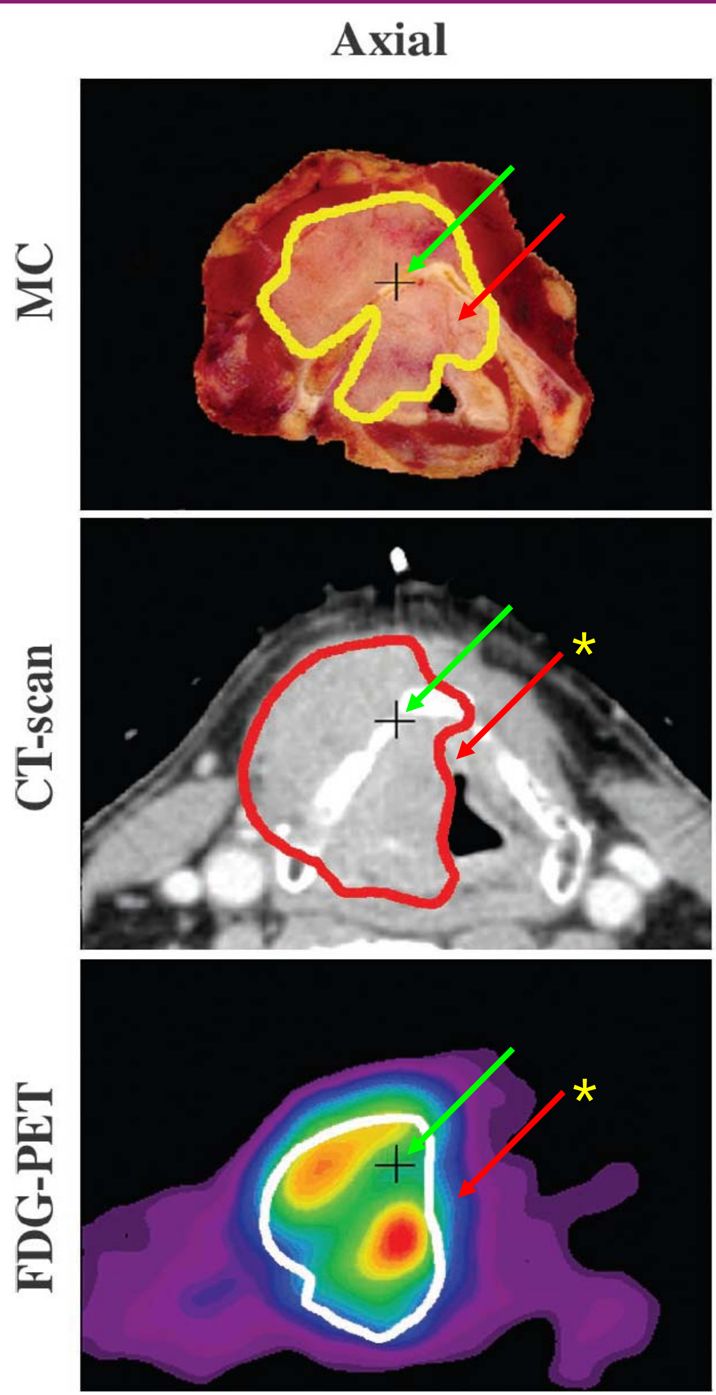
- GTV is hard to see on both CT and MRI
- The two modalities show different parts of the tumour



# Target volumes - GTV

- Imaging does ***not*** always correlate perfectly with
    - Other imaging
    - Pathology

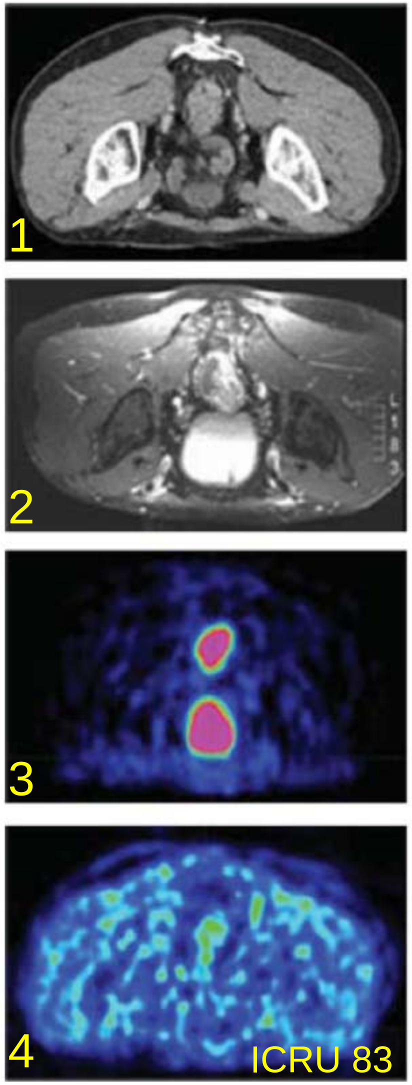
- Specimen to imaging: 10% mismatch




Daisne JF et al Radiology 2004; 233(1):93-100

# Target volumes - GTV

- ICRU 83 suggests specifying the modality used for GTV
- Primary rectal tumour (prone)
  - 1. GTV-T (CT)
  - 2. GTV-T (MRI T1 fat sat)
  - 3. GTV-T (FDG-PET)
  - 4. GTV-T (F-miso-PET)



# Target volumes - GTV

- Talk to your radiologists!

- They know ***lots*** about
  - Choosing the best imaging
  - The correct imaging sequences
  - Interpreting the imaging

# Improving concordance

Rasch *et al. Radiation Oncology* 2010, **5**:21
http://www.ro-journal.com/content/5/1/21

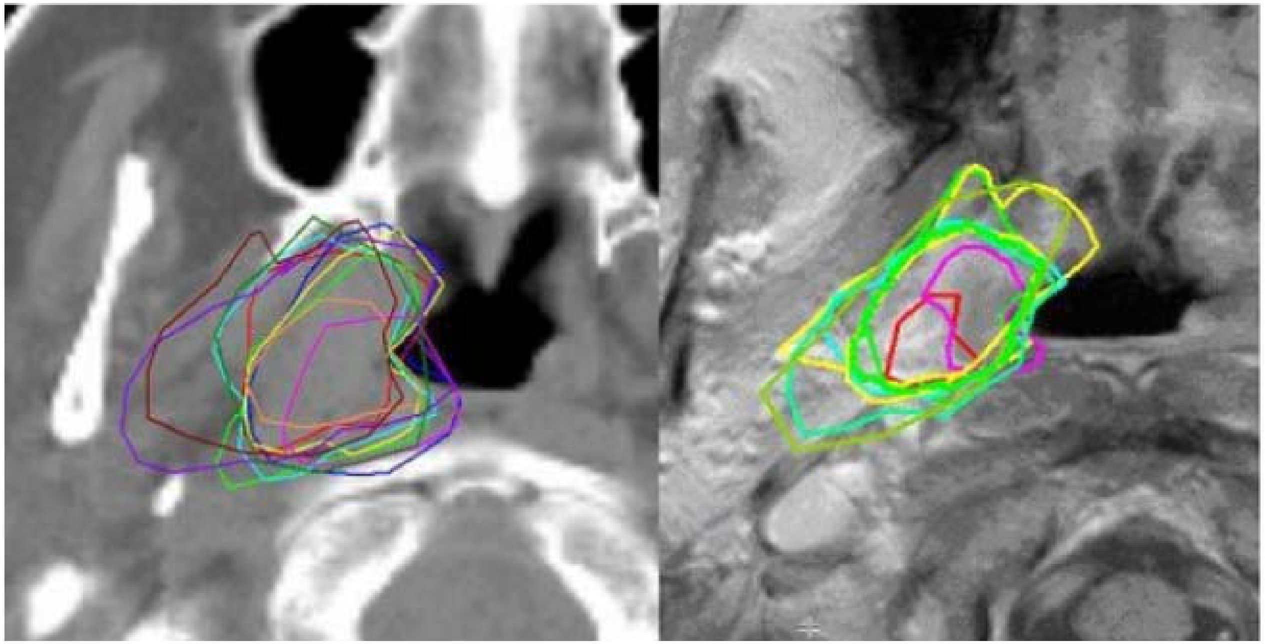
RADIATION ONCOLOGY

**RESEARCH** **Open Access**

## Decreased 3D observer variation with matched CT-MRI, for target delineation in Nasopharynx cancer

Coen RN Rasch[1*], Roel JHM Steenbakkers[2], Isabelle Fitton[3], Joop C Duppen[1], Peter JCM Nowak[4], Frank A Pameijer[5], Avraham Eisbruch[6], Johannes HAM Kaanders[7], Frank Paulsen[8], Marcel van Herk[1]

# Improving concordance



Better imaging improves consistency

# Improving concordance

- The largest impact was by improved target volume definitions = protocol

- Biggest differences seen at the top and bottom
  A problem of imaging

- Better concordance using sagittal image display

# Quality of RT affects outcome

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JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

(2010; 28(18): 2996-3001)

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*

Very scary results

Poor radiotherapy

↓ 20% in OS

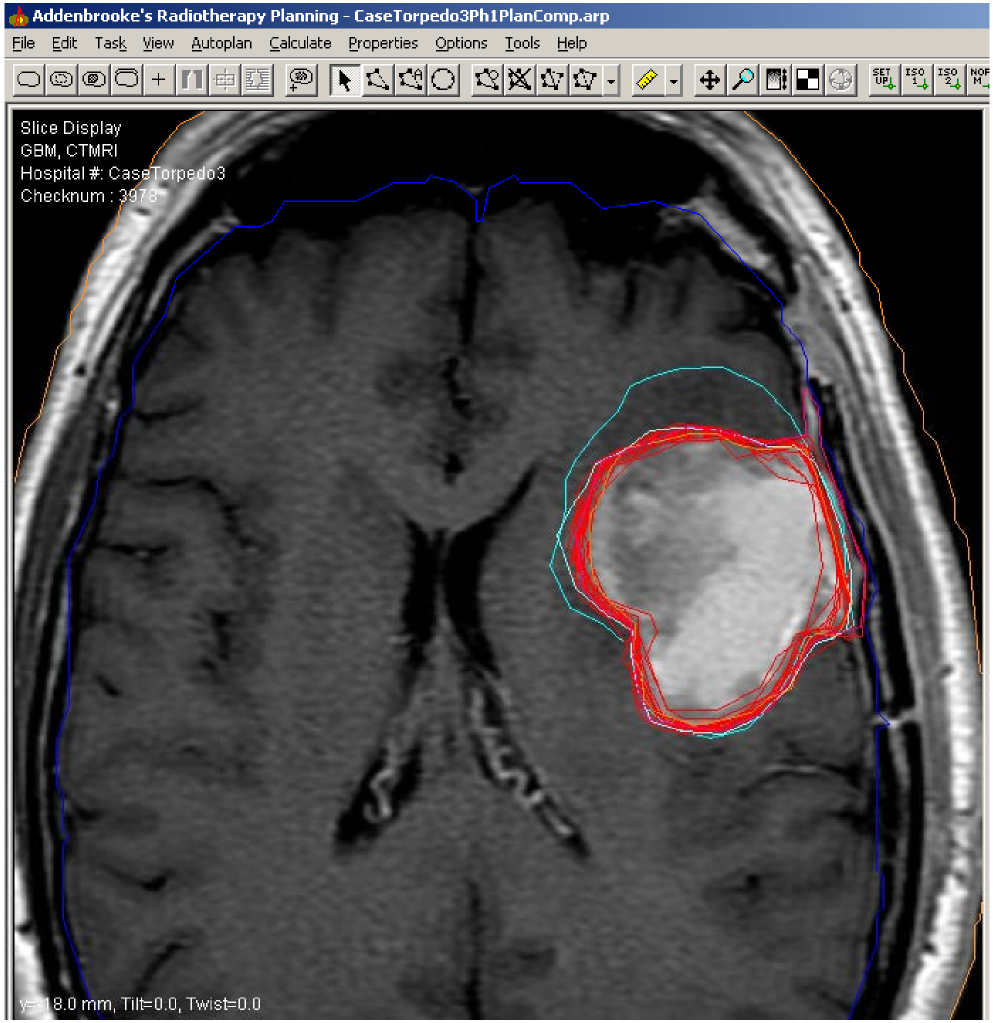
↓ 24% in DFS

In 3% contouring responsible for poor outcome

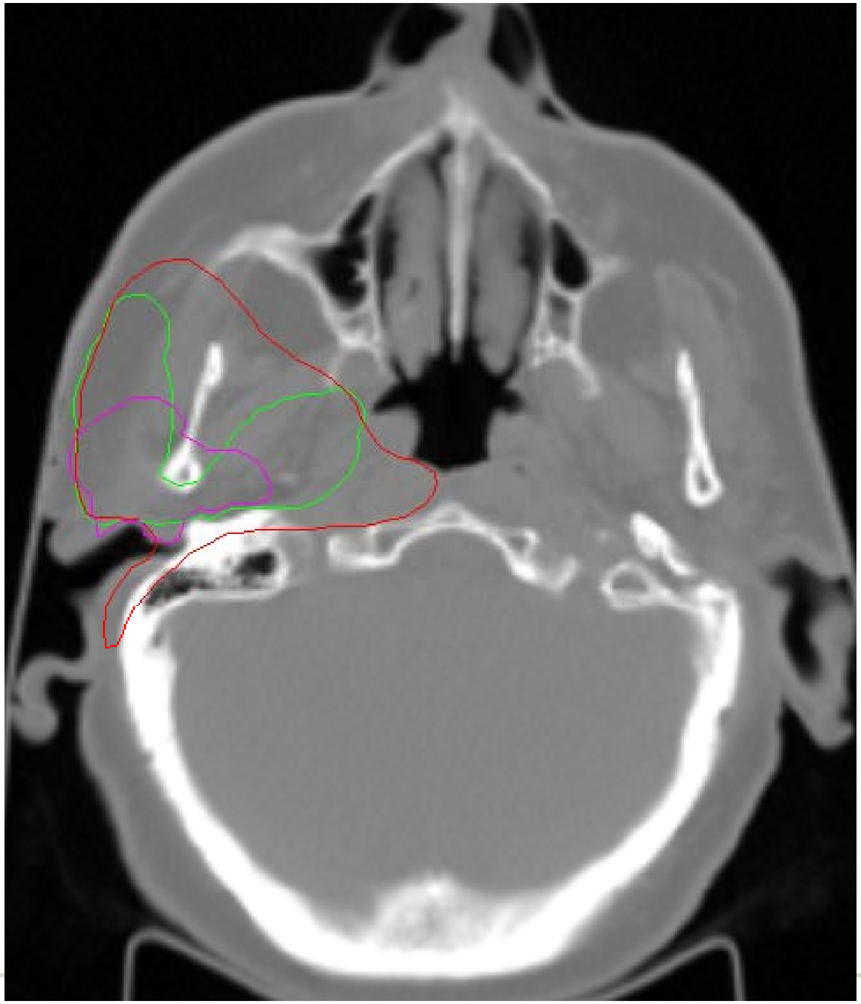
# Improving concordance

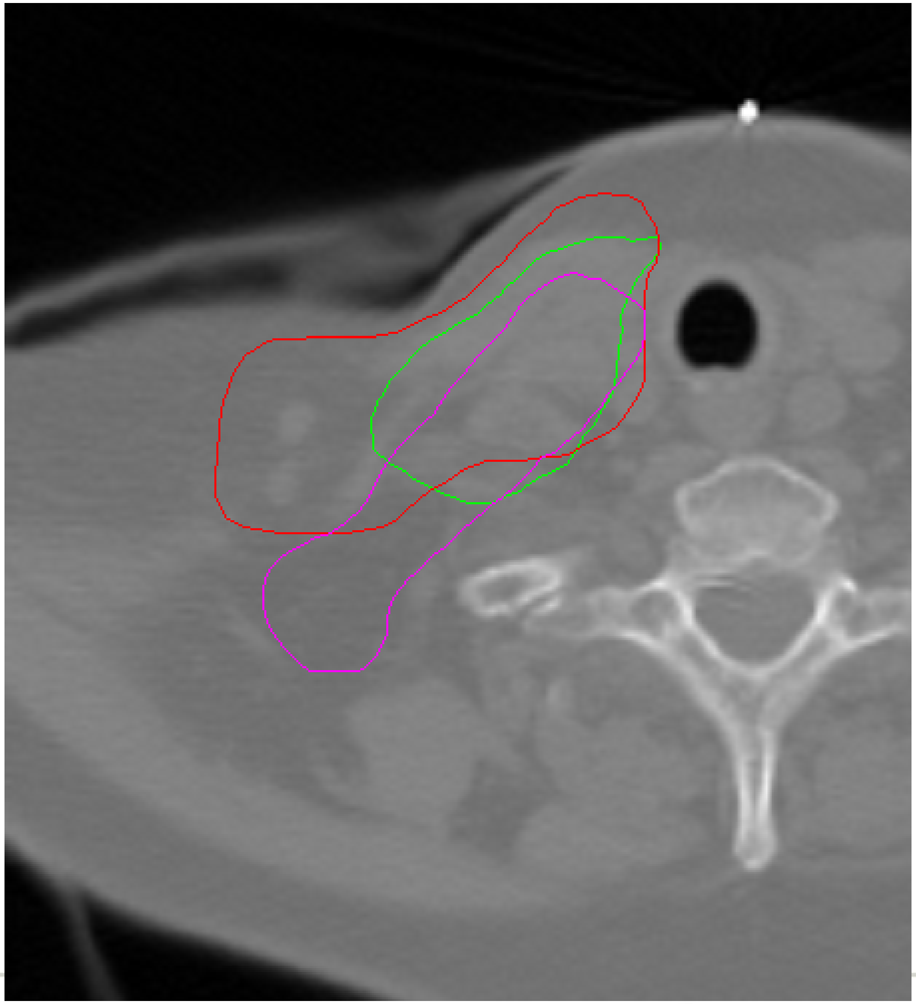
- Careful protocols required
  - Carefully written
  - Carefully followed

- The blue group ... ?



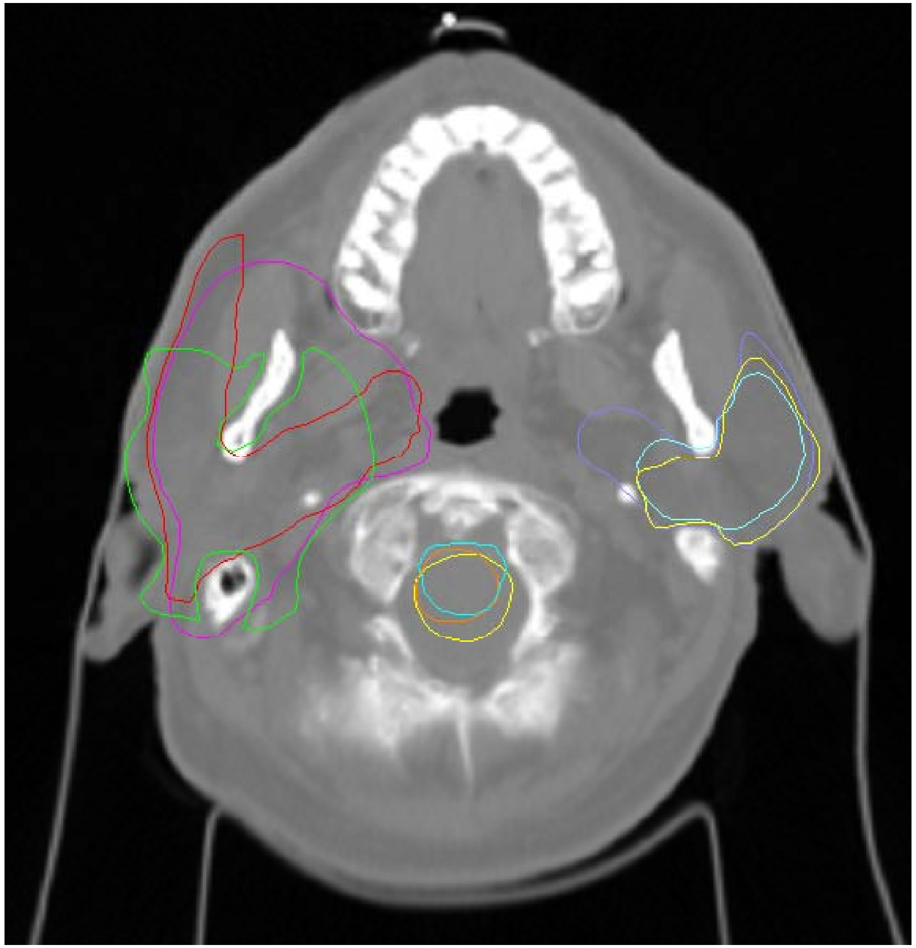
# Parotid and Neck Outlining

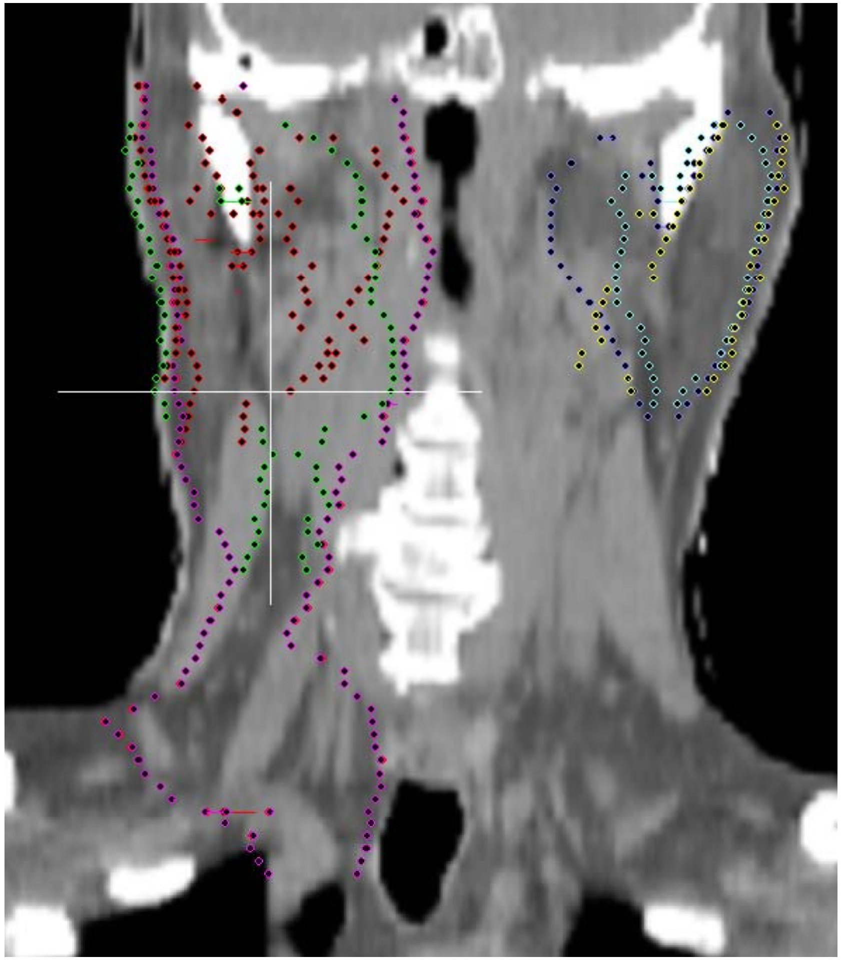




Mukesh, M et al, Br J Radiol 2012

# OAR Outlining





Mukesh, M et al, Br J Radiol 2012

# Target volumes - CTV

# Target volumes - CTV

- CTV - contains demonstrable GTV and/or sub-clinical disease,
- Typically tumour ***cannot*** be seen or imaged in the CTV
- This volume must be treated adequately for cure

# Target volumes - CTV

- Now includes the concept that the CTV contains sub-clinical disease ***with a certain probability***

- No consensus as to what probability actually requires treatment

- Probability of ~ 90-95% may be reasonable
  Should it be lower or higher?

- Concept of probability introduced in ICRU 83 (2010)

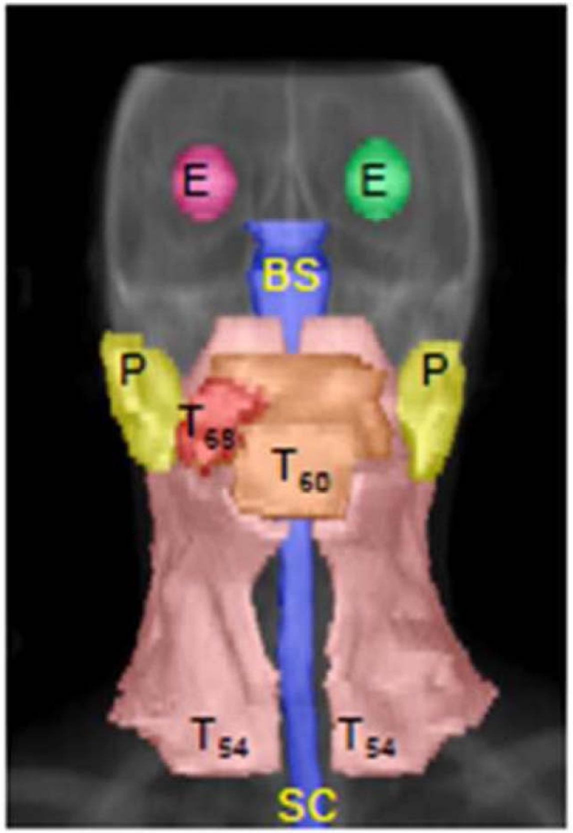
# Target volumes - CTV

- CTV is based on historical data
  - Derived from population data
  - Margin not individualised

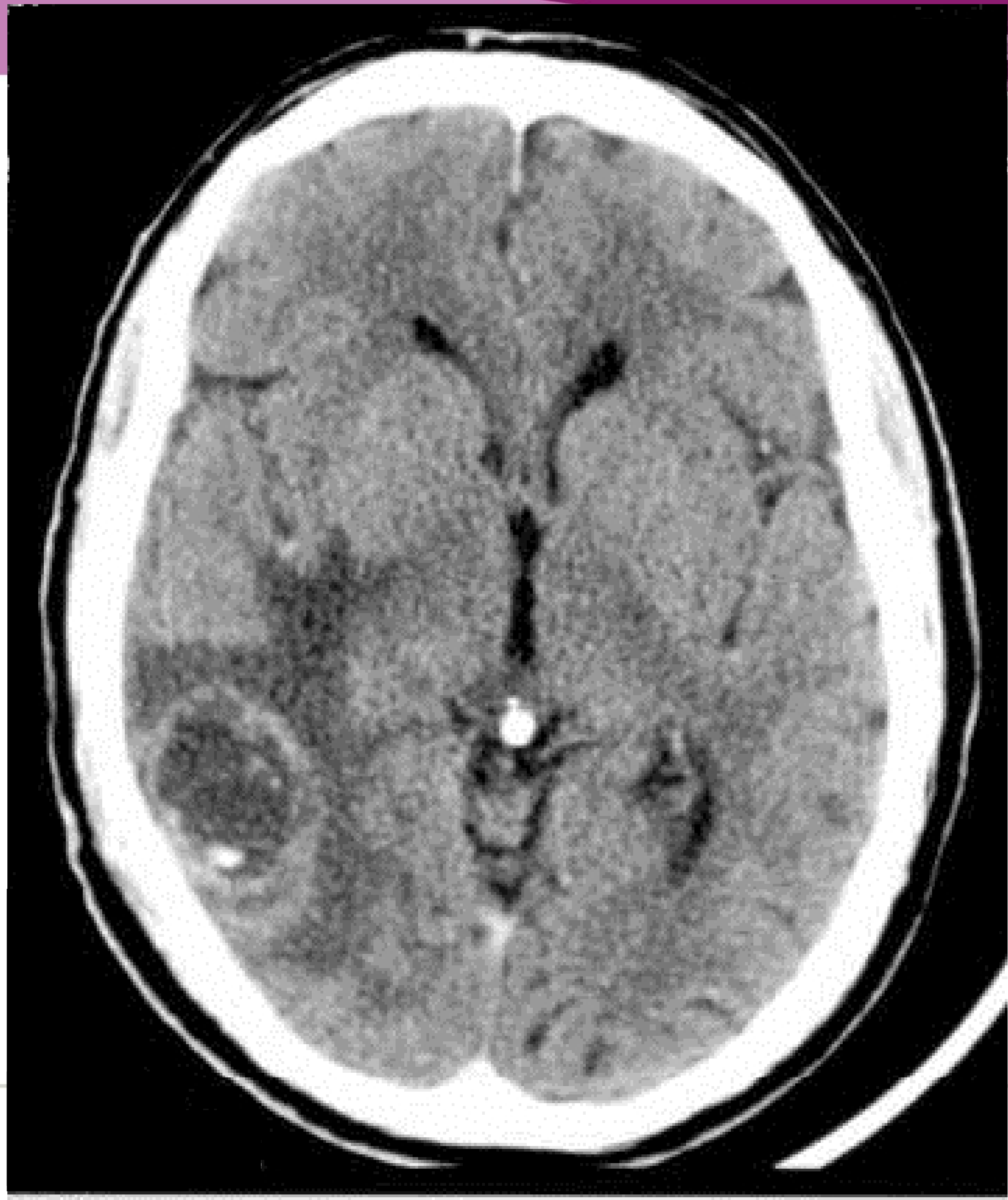
- Some individualisation according to anatomical boundaries is possible
  - This implies that isotropic growing is often ***not*** appropriate to derive the CTV

# Target volumes - CTV

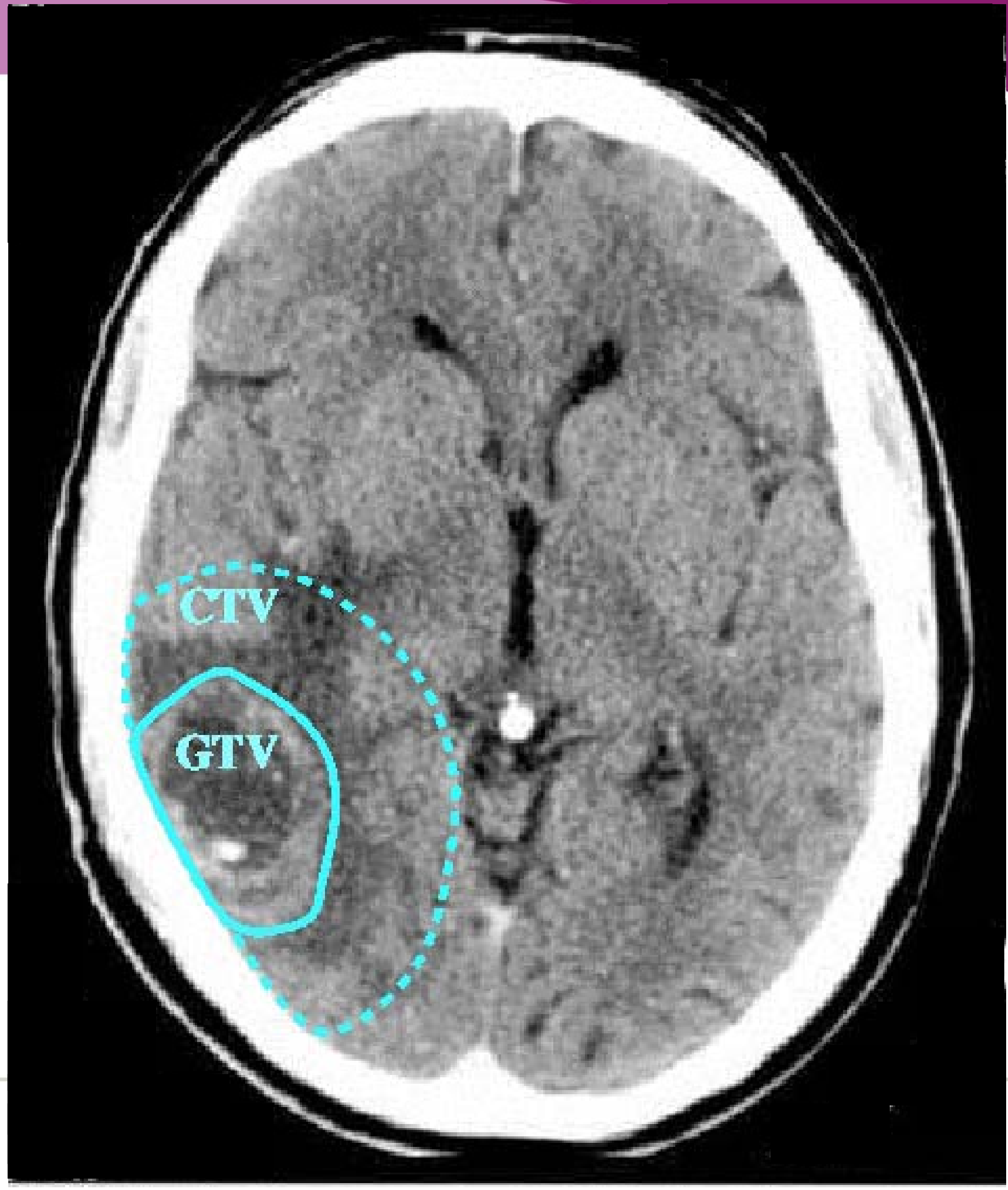
- It is allowable to have more than one CTV if necessary
- It is assumed that tumour cell density is lower in the CTV than in the GTV
- Therefore lower dose may be appropriate



- CTV - ***not*** obvious from the imaging
- CTV ***cannot*** be imaged
- Based on knowledge of population pathology



- CTV is an‘average’ volume
- CTV is enclosed by the skull
- Anatomical considerations useful



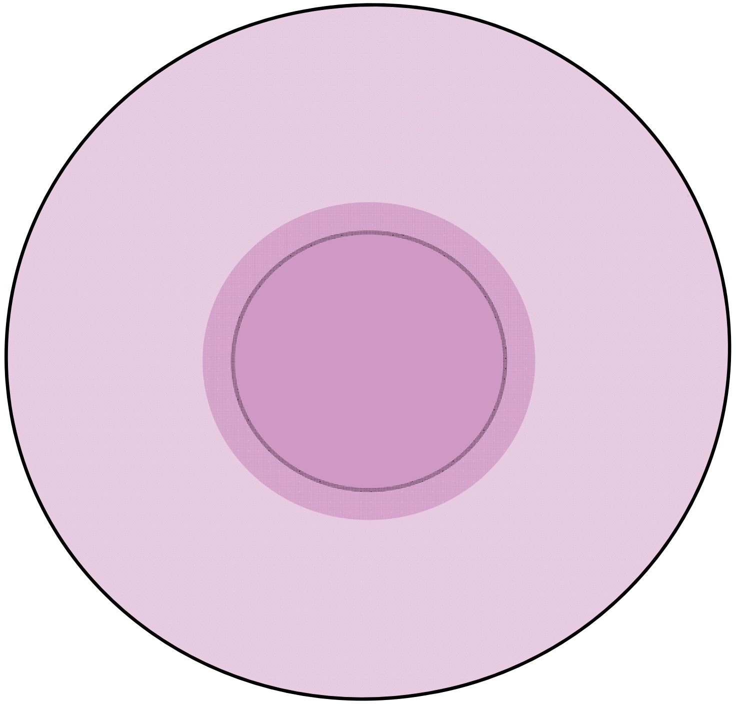
# Target volumes - CTV

Newer imaging may push the edge of the GTV outwards into the CTV

If CTV stays the same, the margin will change

May need new definitions

? "Imaging High-risk Volume" – IHV



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# Target volumes - PTV

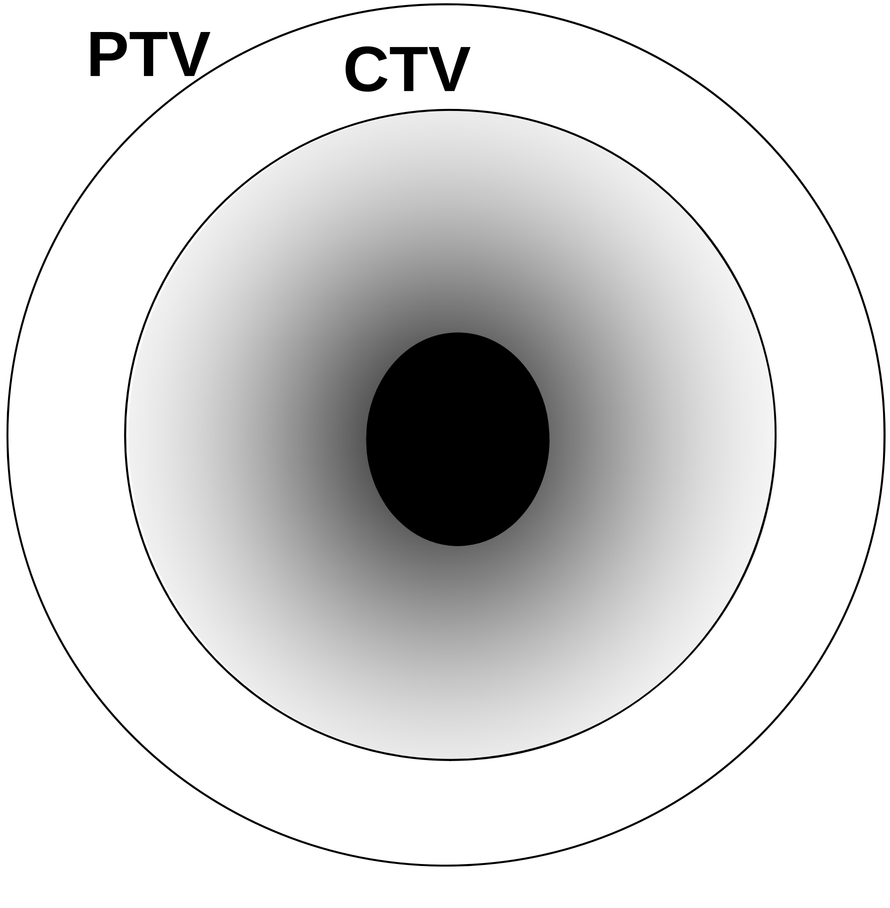
# Target volumes - PTV

PTV is a geometric concept designed to ensure that the prescription dose is actually delivered to the CTV

In a sense, it is a volume in space, rather than one directly related to the anatomy of the patient

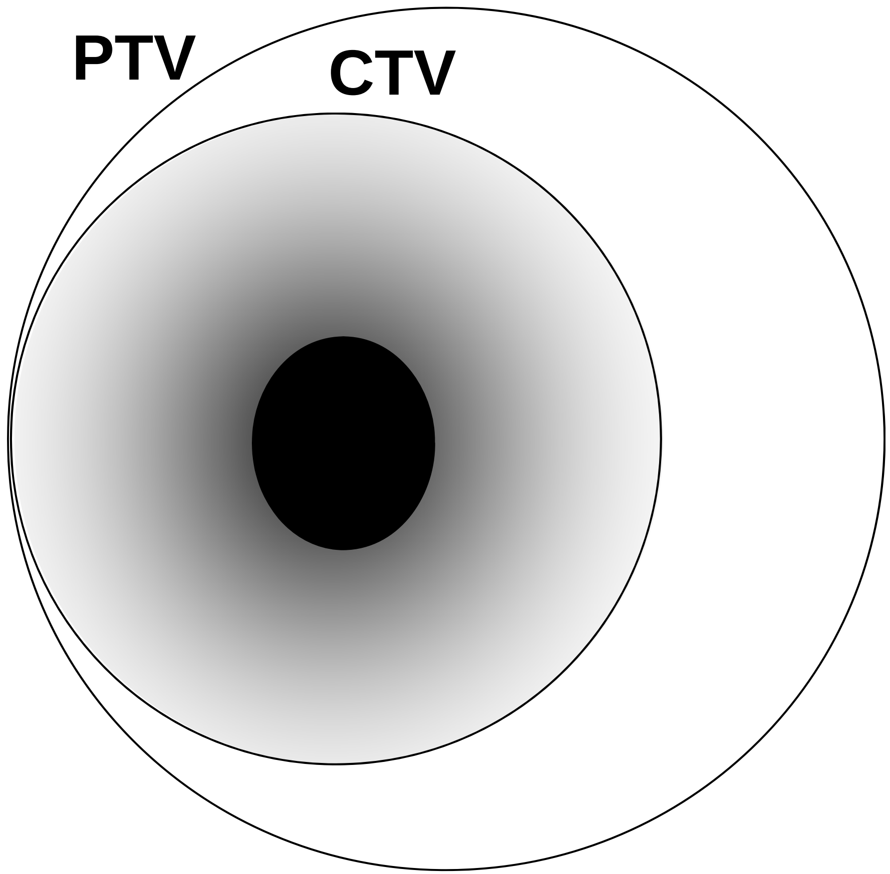
PTV may extend beyond bony margins, and even outside

# Target volumes - PTV




CTV safely enclosed within PTV

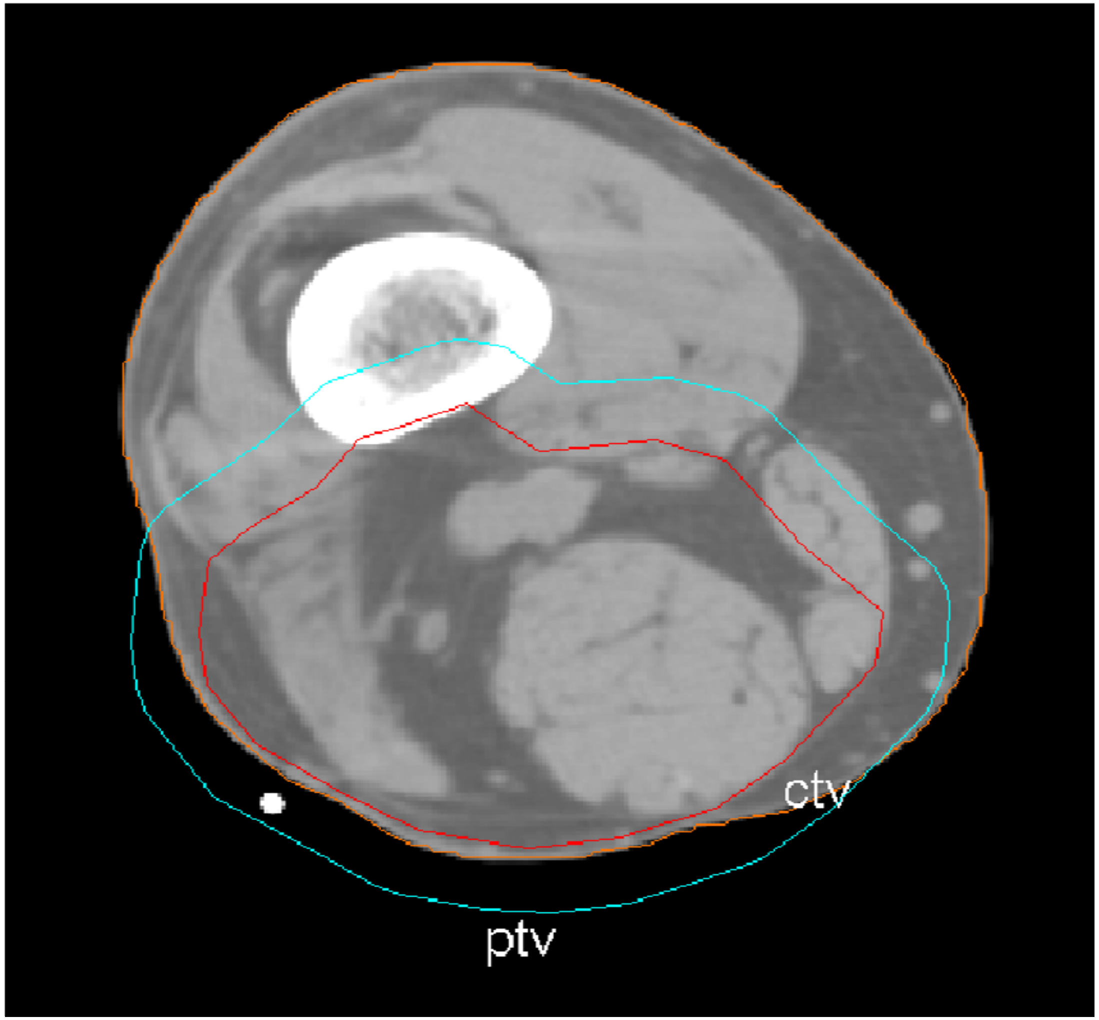
# Target volumes - PTV




CTV safely enclosed within PTV

# Target volumes - PTV

PTV outside the patient



# Target volumes - PTV

- The CTV must be treated adequately for cure
- The PTV is used to ensure that the CTV ***is*** properly treated
- PTV designed to allow for uncertainties in the process of planning and delivery
  - These uncertainties are many …

# Target volumes – PTV

- ICRU 62 suggested 2 components to the PTV:

  Internal Margin IM – for eg organ movement

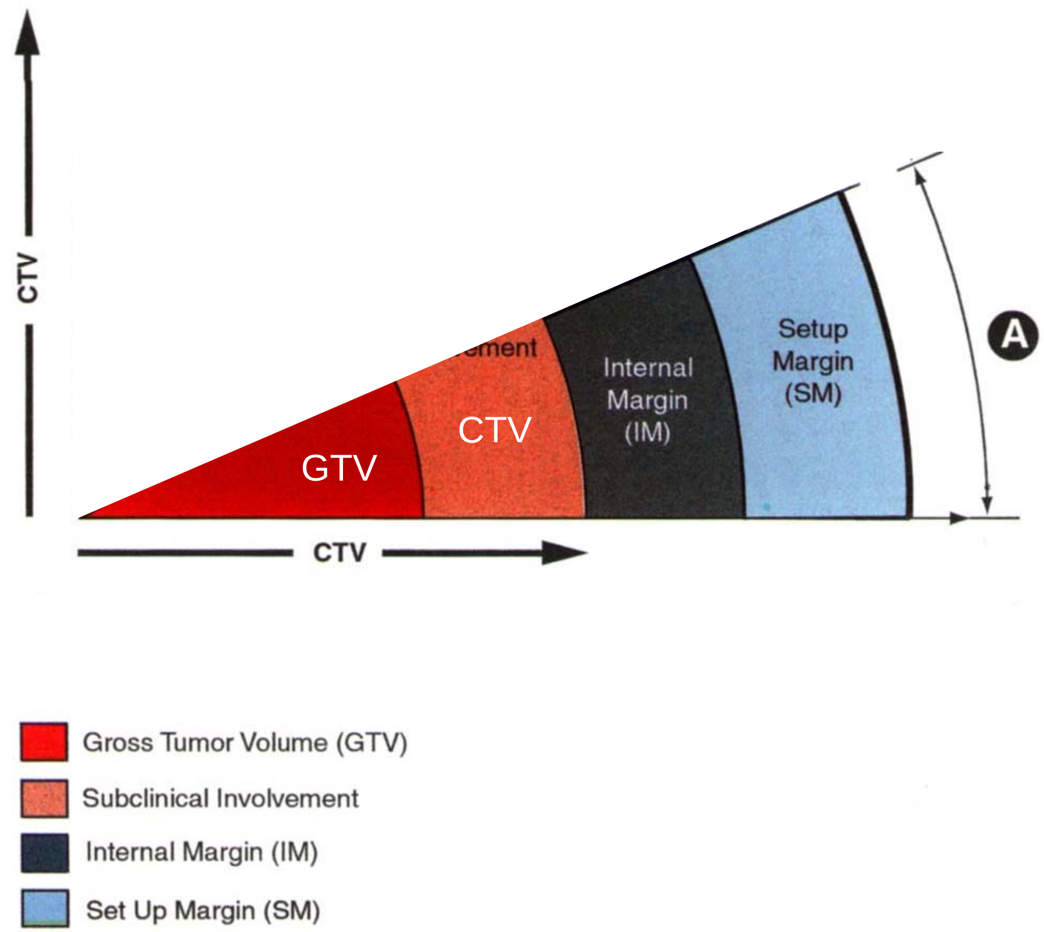
  Setup Margin SM – for set-up inaccuracies

  CTV + "Internal Margin" (IM) = ITV *

  ITV + "Set-up Margin" (SM) = PTV

- These are useful to remind about the basis of errors

* ITV= Internal Target Volume



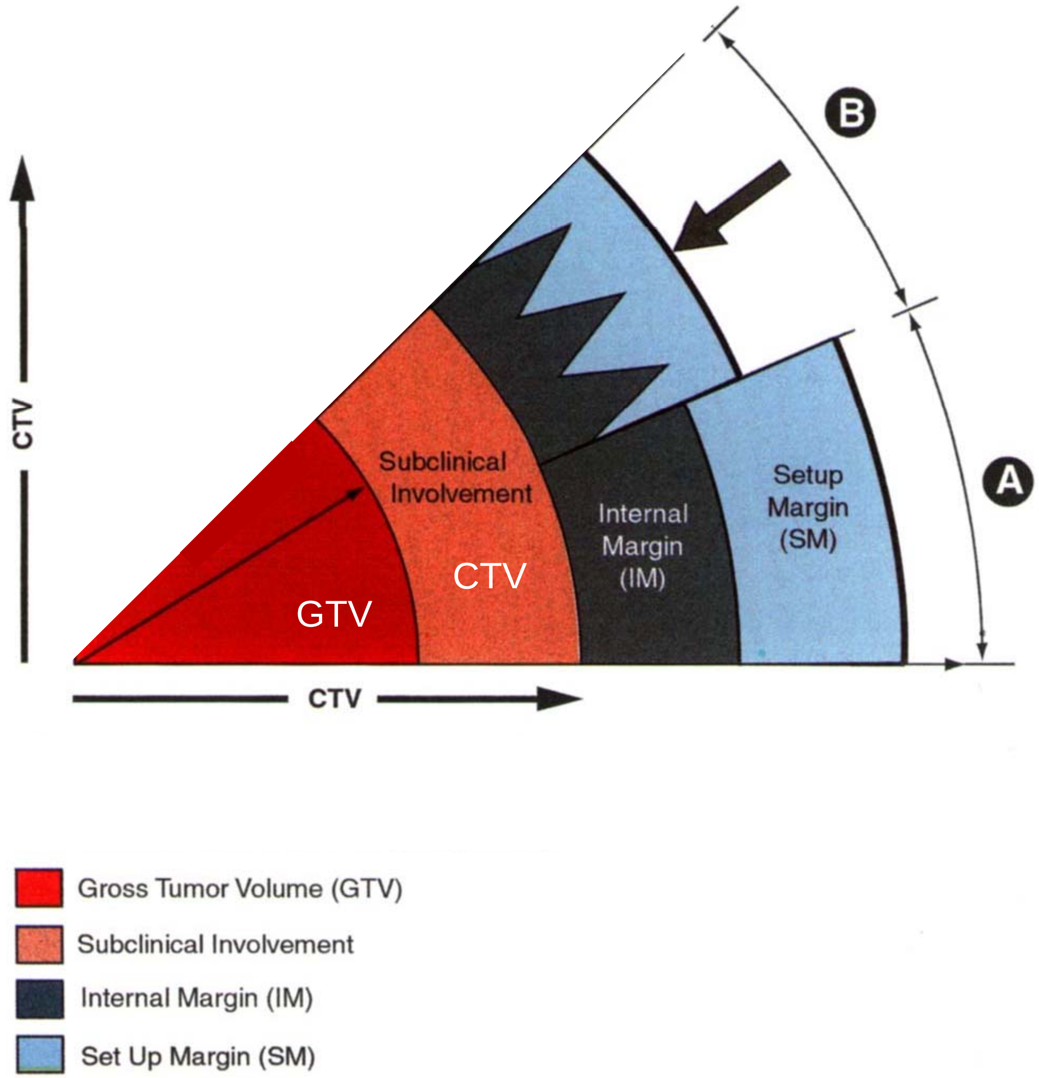

- Fig from ICRU 62 (also in ICRU 71)

- Adding IM + SM to reach the PTV

# Target volumes – PTV

- ICRU 62 also acknowledged that simple addition may not be :
  - realistic – because the margin becomes very large
  - correct – because not every error occurs in the same direction on the same occasion

- Components to be added in quadrature rather than arithmetically




- Scenario B
- Adding IM + SM in quadrature
- Specific margins must still be addressed

# Target volumes - PTV

- ***Systematic*** and ***random*** errors need to be quantified to produce the PTV margin

    - $\mathbf{PTV = 2.5\Sigma + 0.7\sigma}$

# Target volumes – PTV - Adaptation

To date PTV margins have been based on population data

Imaging during treatment – allows the concept of individualised PTV margins

Eg. Plan of the day for bladder cancer treatments

This could be a whole separate talk ………..

# Target volumes – OARs + PRVs

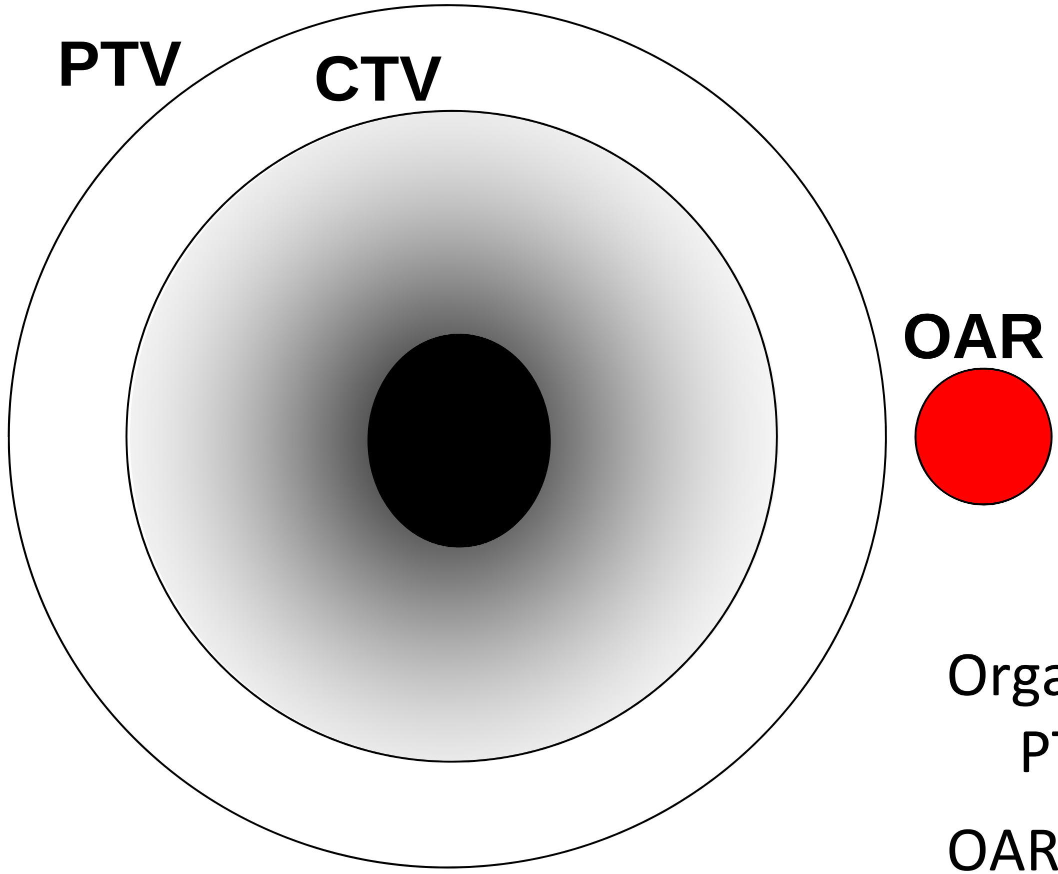
OAR - Organ at Risk

PRV - Planning organ at Risk Volume

# Target volumes – OARs

- Organs at Risk are normal tissues whose radiation tolerance influences treatment planning, and /or prescribed dose
- Now know as OARs
- Uncertainties apply to an OAR as well as to the CTV…

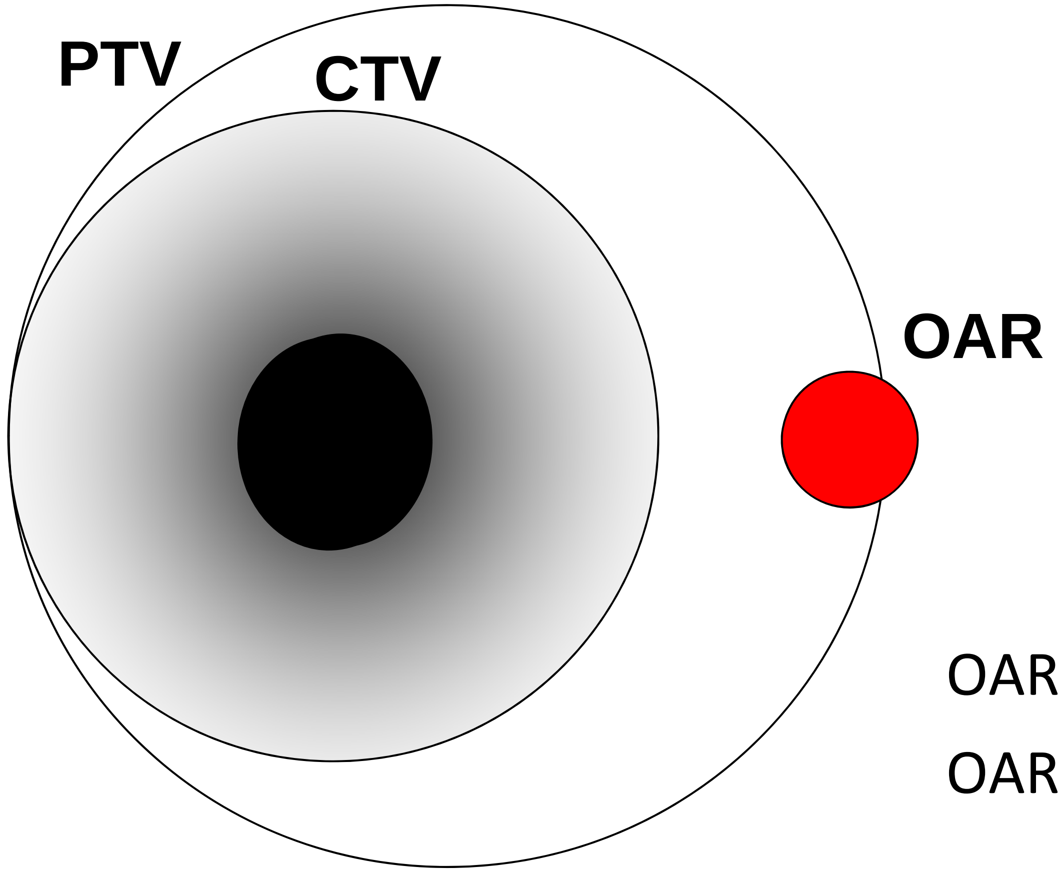
# OARs




Organ at Risk clear of PTV

OAR safe …

# OARs




OAR moves with CTV

OAR not so safe…

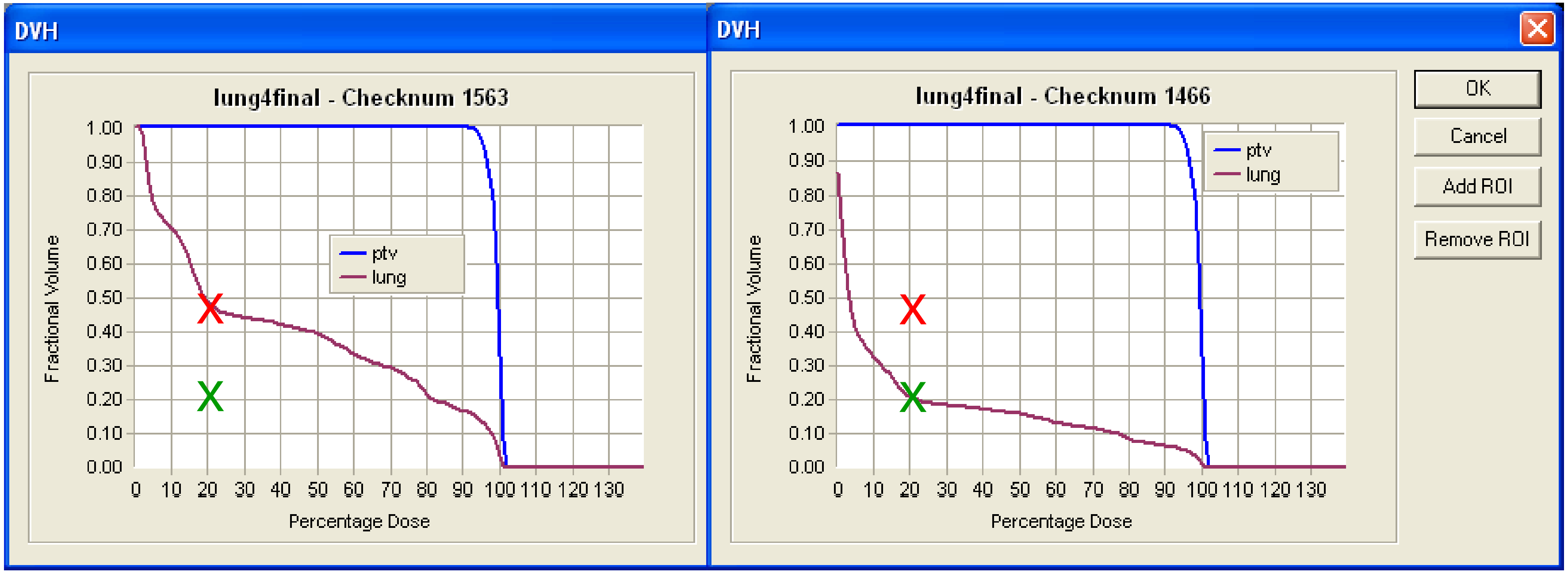
# Target volumes - OARs

- Imaging must also show critical normal structures (Organs At Risk - OARs)

- Essential to achieve a therapeutic gain

# Target volumes – OARs

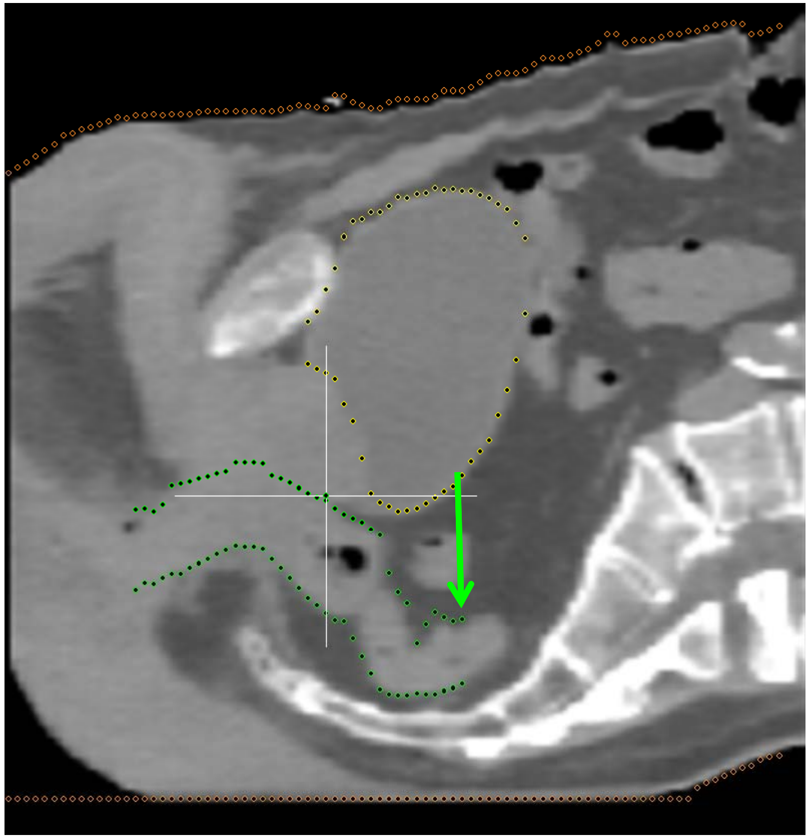
For parallel organs, comparison between plans, patients or centres requires the ***whole*** organ to be delineated, according to an agreed ***protocol***

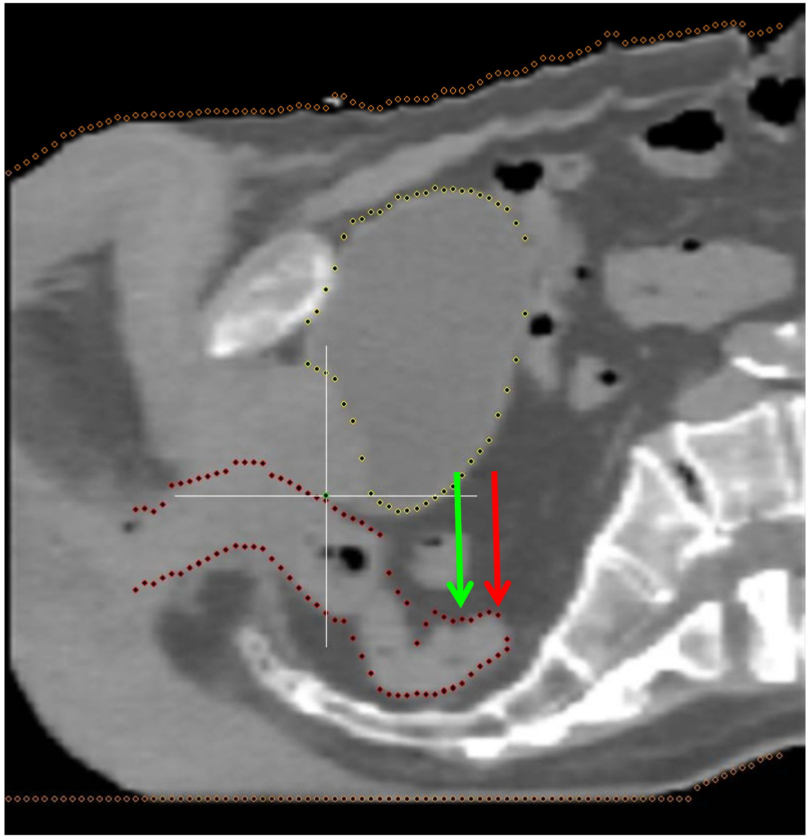



- Whole lung not outlined
- Better DVH!

# Target volumes – OARs

Rectum–clear delineation, according to an agreed ***protocol***





- Rectum correct
- Rectum on 4 slices more

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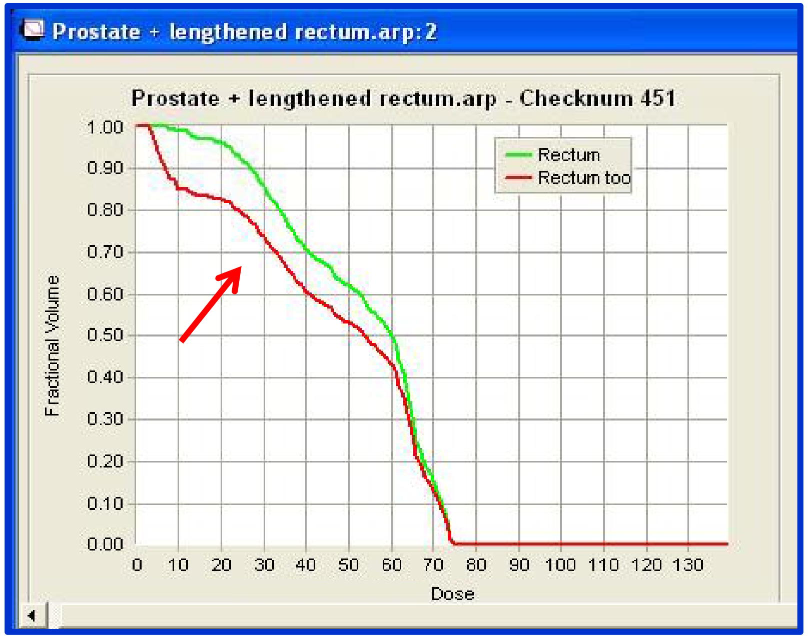
# Target volumes – OARs

For other parallel organs, over-contouring may lead to DVHs which appear better but are incorrect

Rectum– needs clear delineated, according to an agreed ***protocol***


- Rectum 'over-contoured'
- 'Better' DVH is incorrect

# Target volumes – OARs + PRVs

- Uncertainties apply to the OAR … so a 'PTV margin' can be added around it - to give the Planning organ at Risk Volume (PRV)

- But … the use of this technique will substantially increase the volume of normal structures

- May be smaller than PTV margin

  Component for systematic error can often be smaller

# Target volumes – PRV

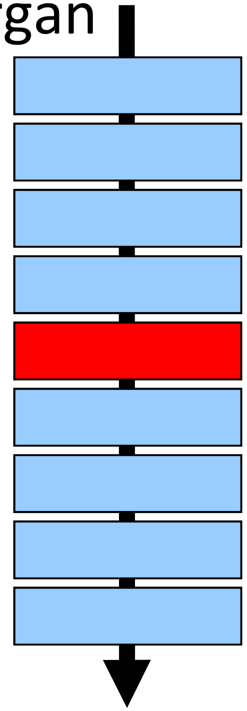
- The use of a PRV around an Organ at Risk is relevant for OARs whose damage is especially dangerous

- This applies to organs where loss of a ***small*** amount of tissue would produce a ***severe*** clinical manifestation

- A PRV is more critical around an OAR with serial organisation

# Tissue architecture

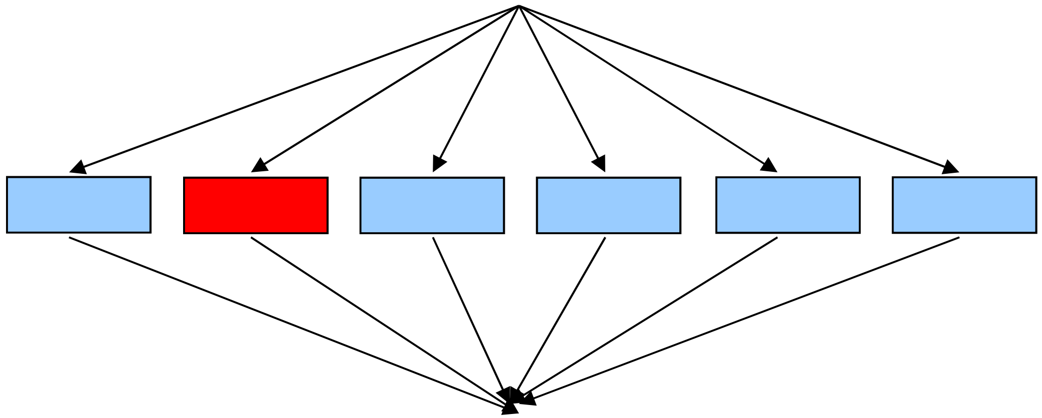
Serial organ



Damage to 1 part causes failure – eg spinal cord

Severe clinical consequence

- Parallel organ



- Damage to 1 part (only) does not compromise function
- Examples …

# Target volumes – PRV

- Spinal cord & optic nerves/chiasm perfect examples where a PRV may be helpful
  - serial tissue organisation
  - damage is clinically catastrophic

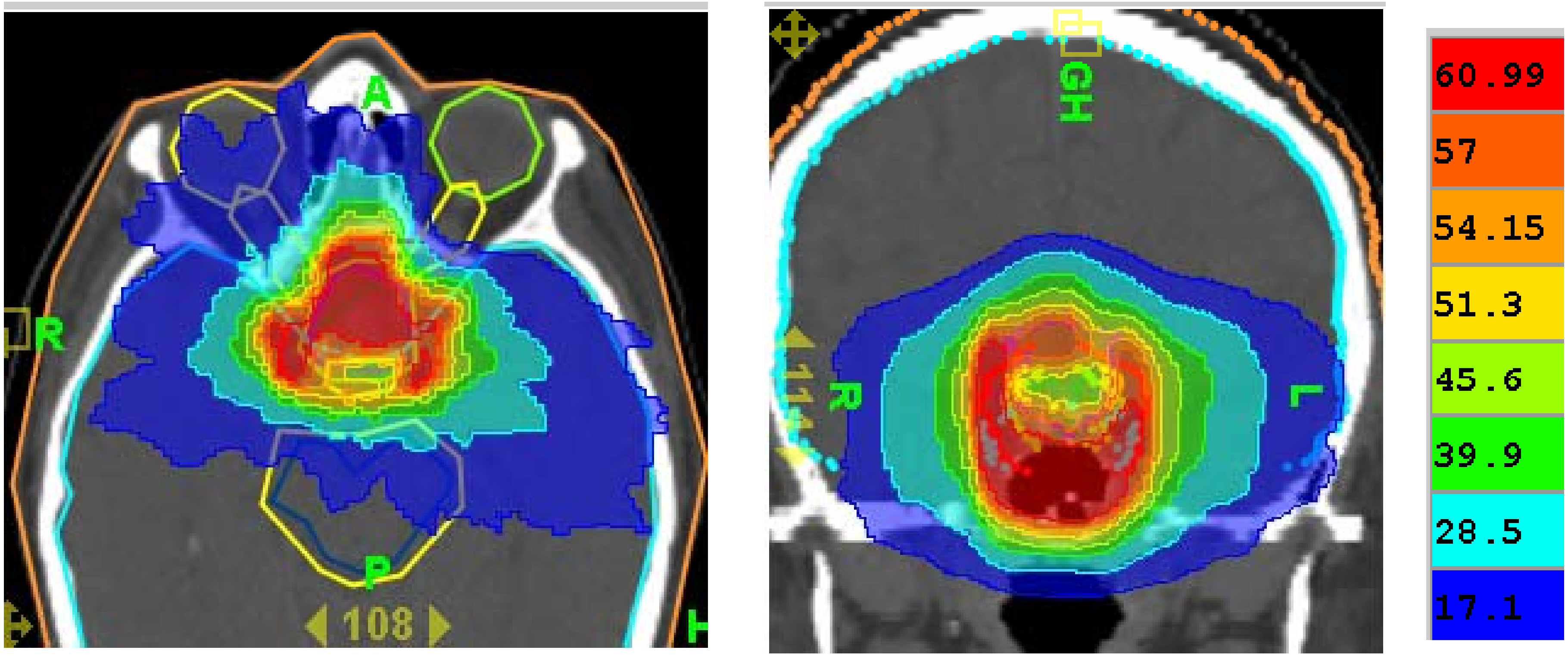
- Add a PRV, especially if high doses are planned
- Almost no other OARs where a PRV is needed
- PRV may be misleading for parallel organs

(This advice is more definitive than ICRU 83)

# Target volumes – PRV

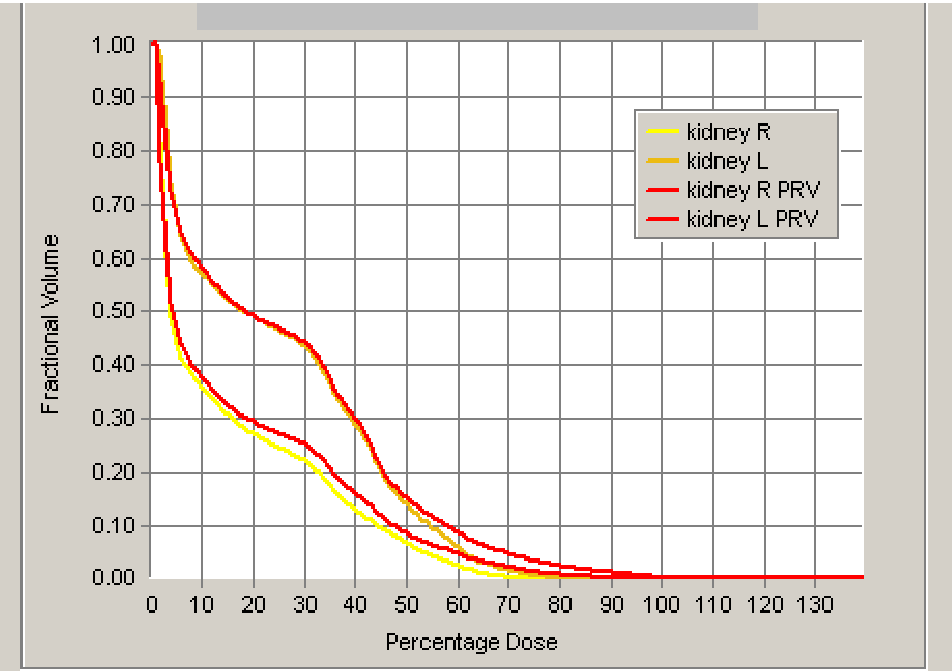
PRV around optic nerves and chiasm

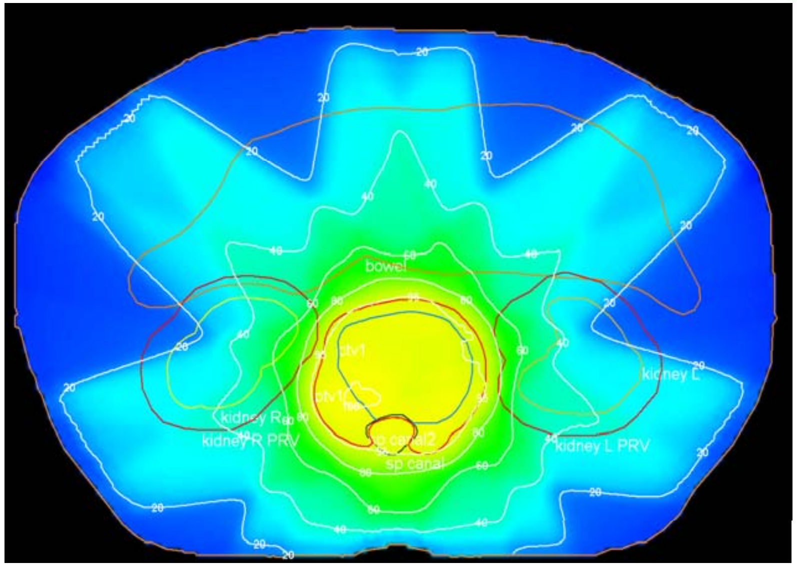
Allows dose escalation

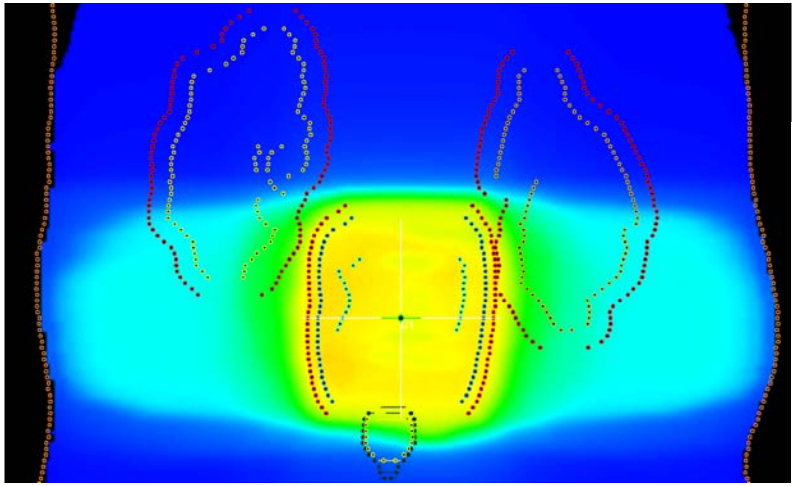


# Target volumes – PRV

- Kidney PRV 10mm
- DVH for PTVs ≈ PRVs
- PRV often not of particular value

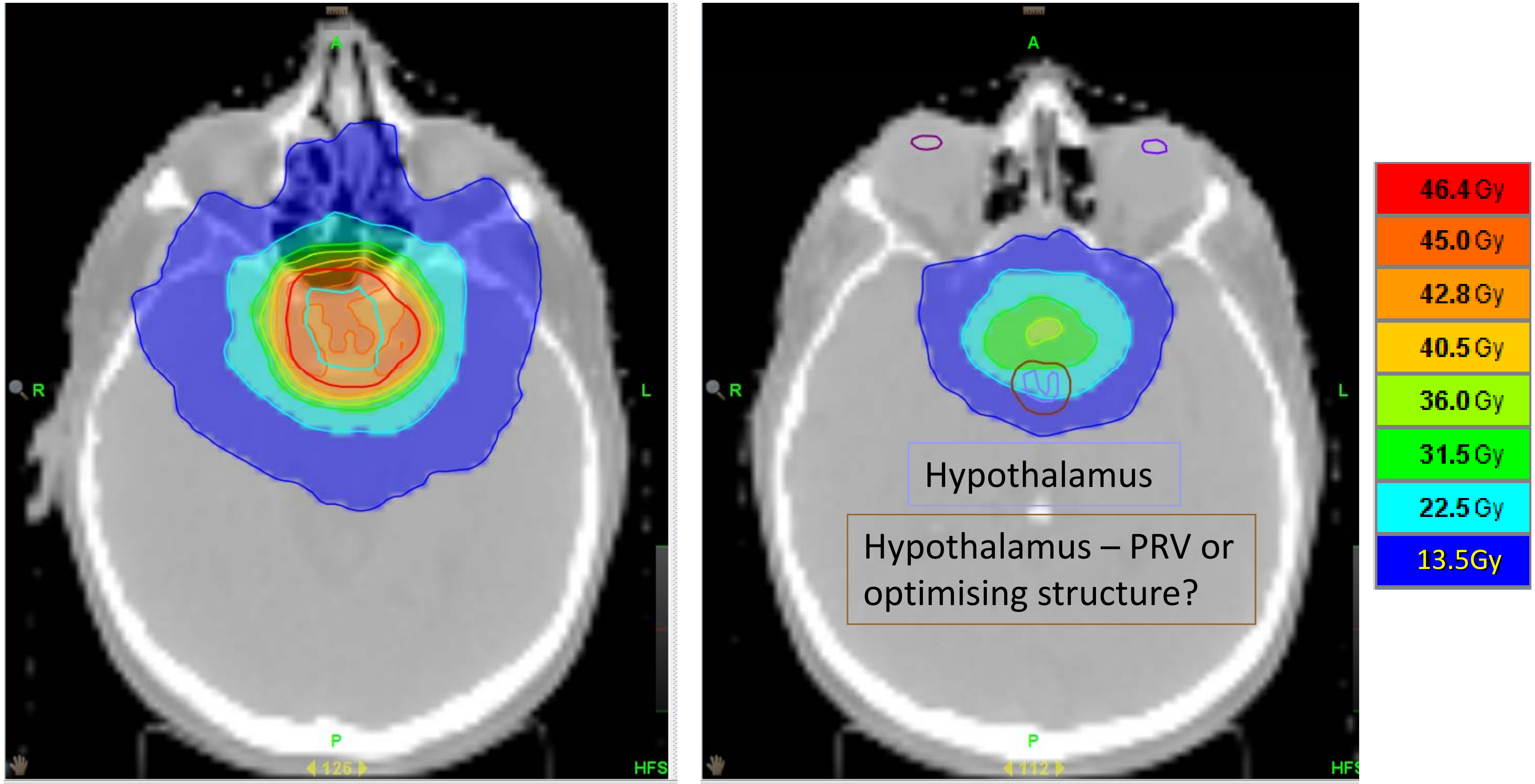


# Target volumes – PRV or optimising structure?

# Hypothalamus DVHs

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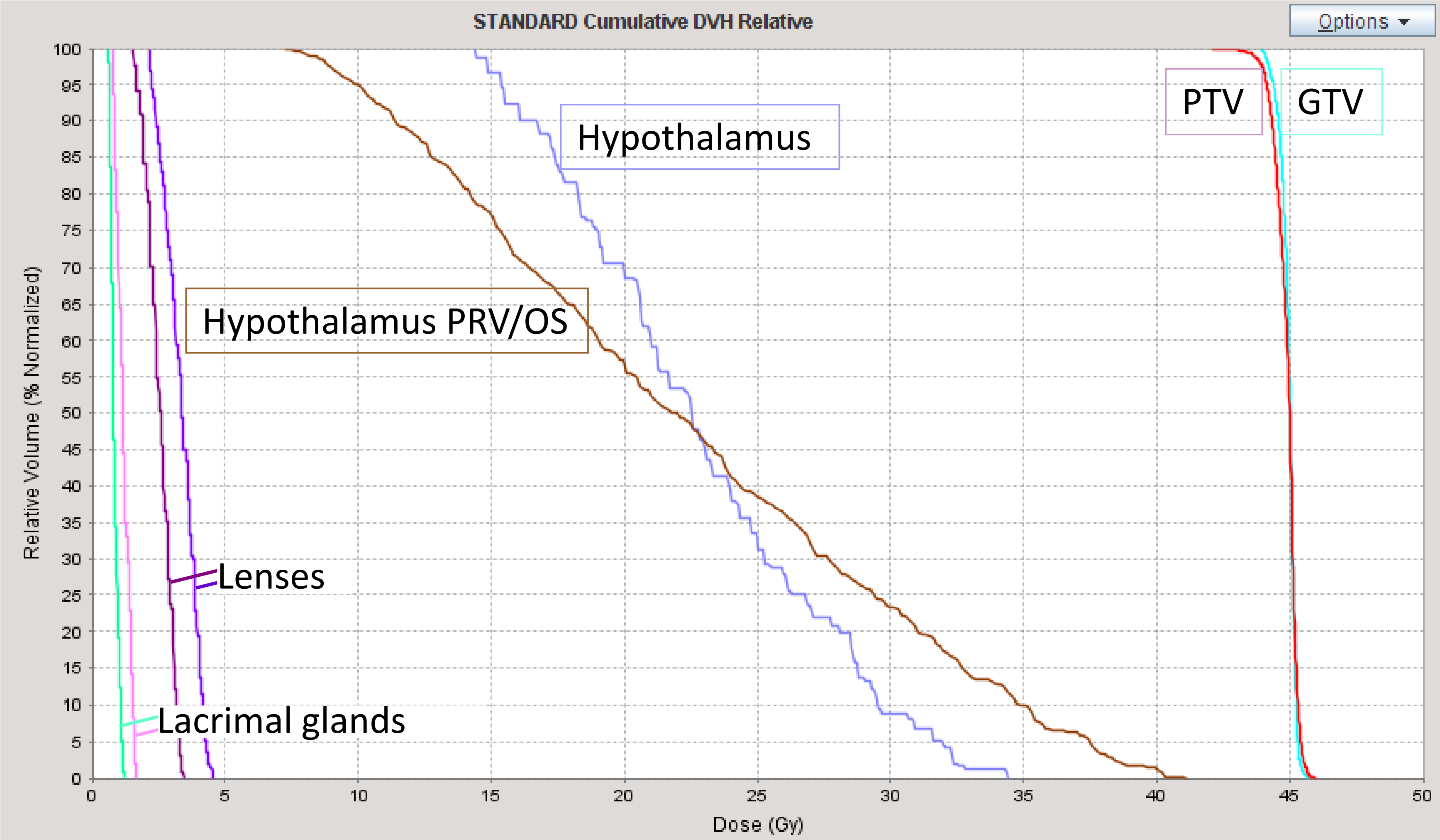
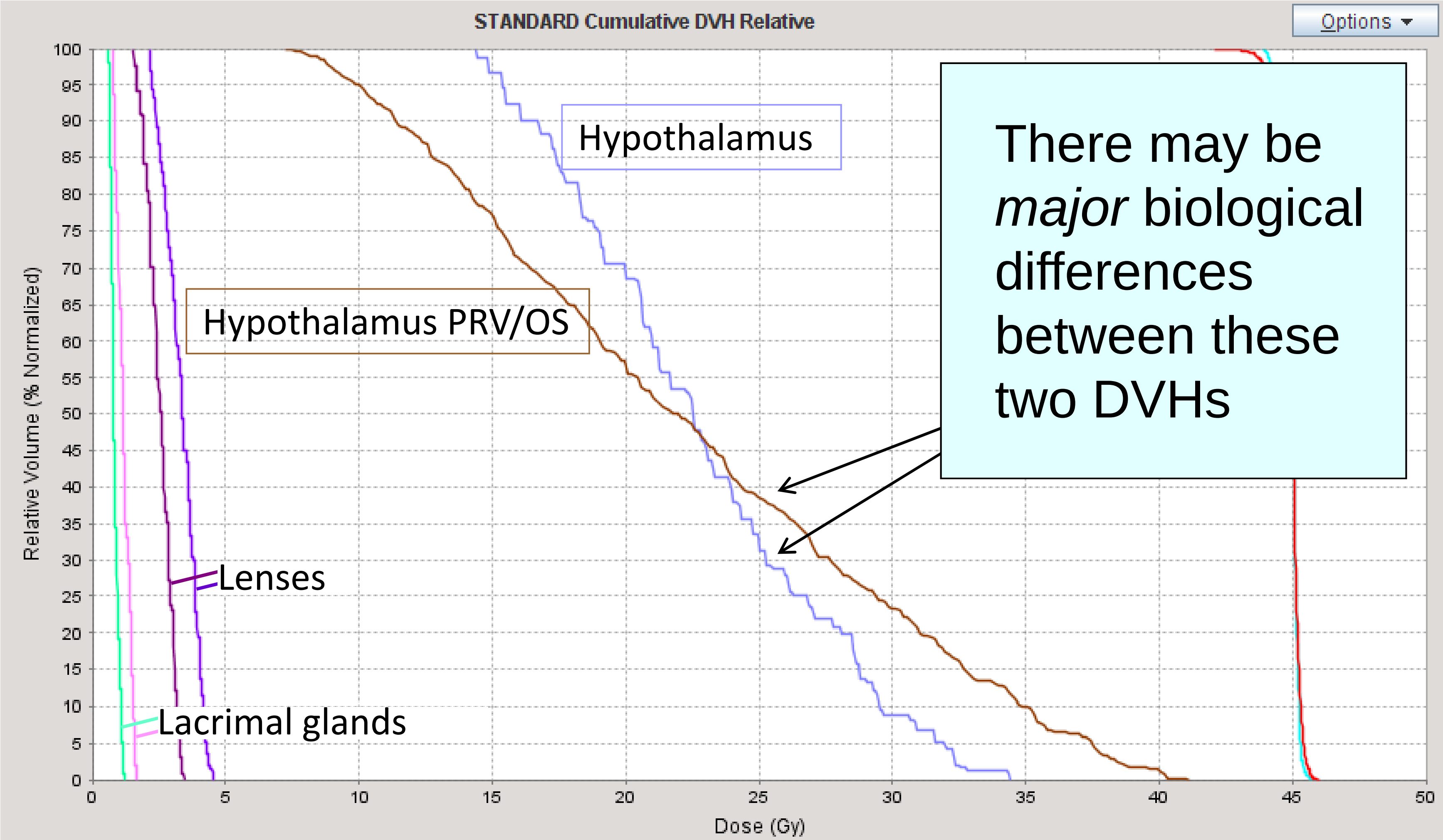
# Hypothalamus DVHs



# Hypothalamus DVHs




There may be *major* biological differences between these two DVHs

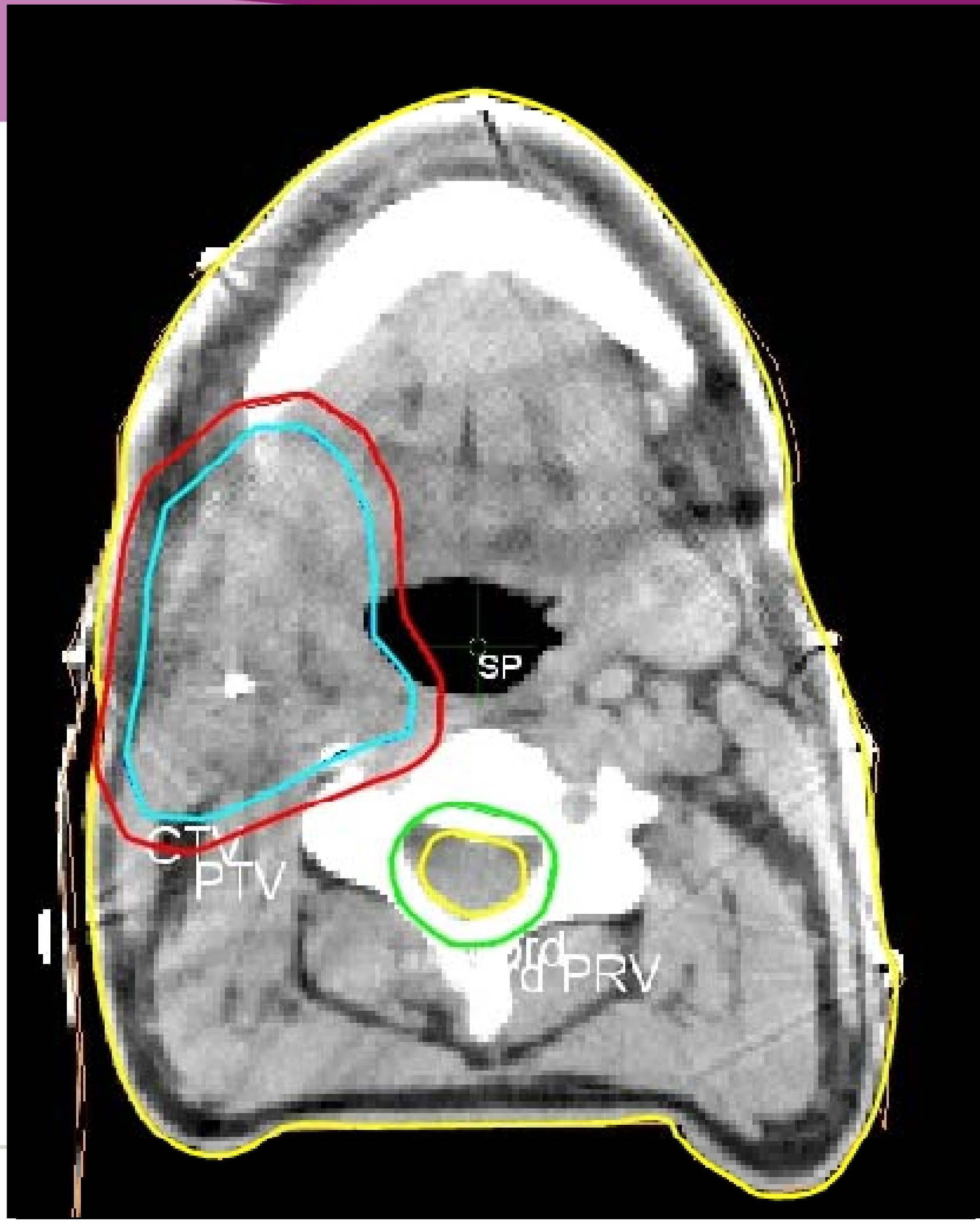
# PRV

Example

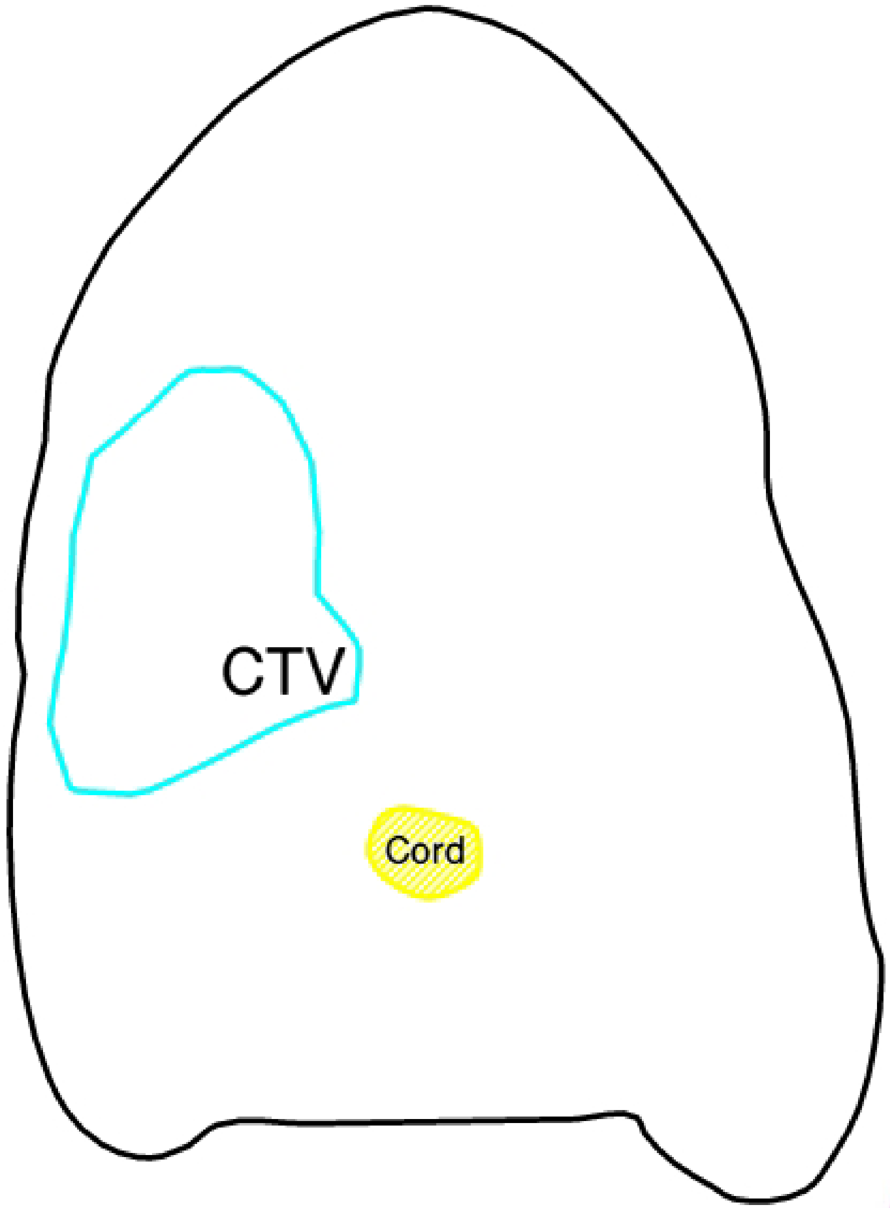
Ca tonsil

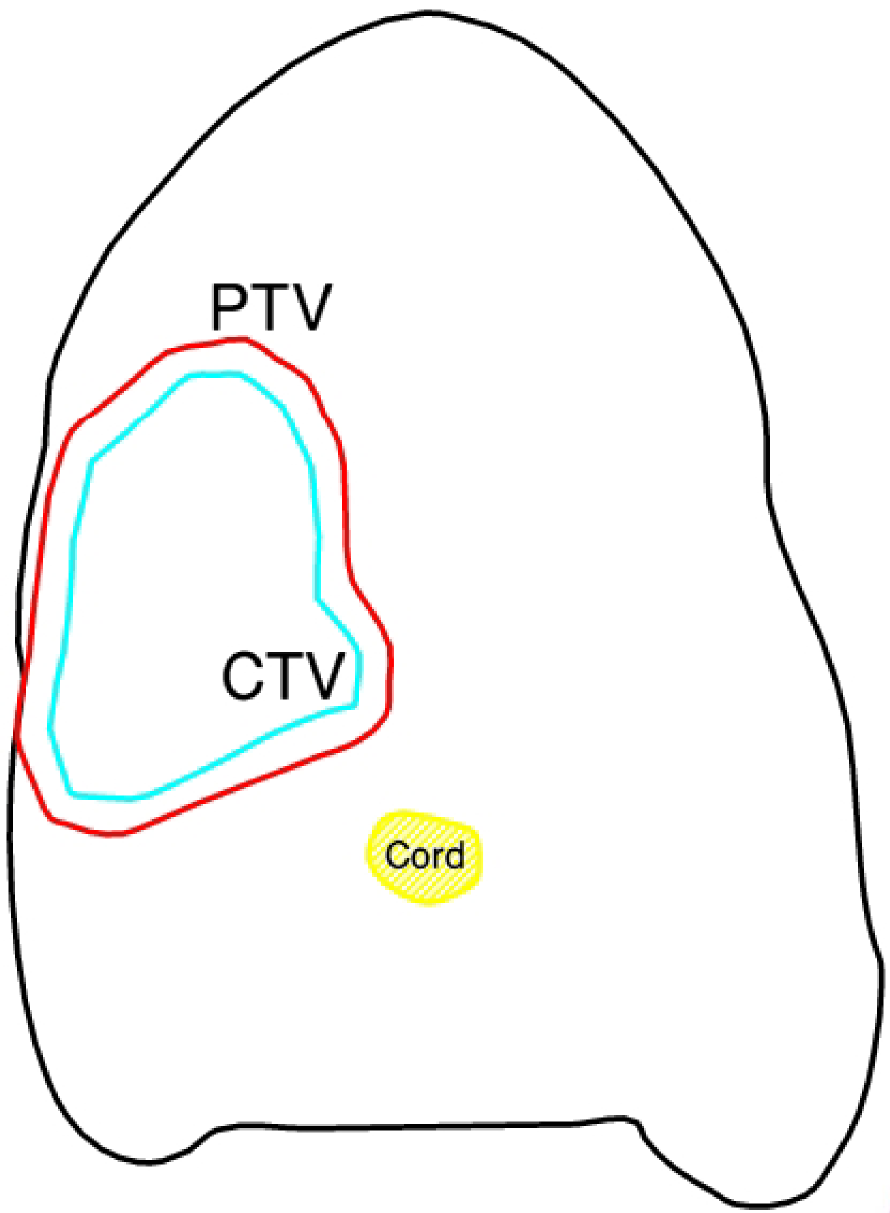
Spinal cord
close

Aim for 70 Gy



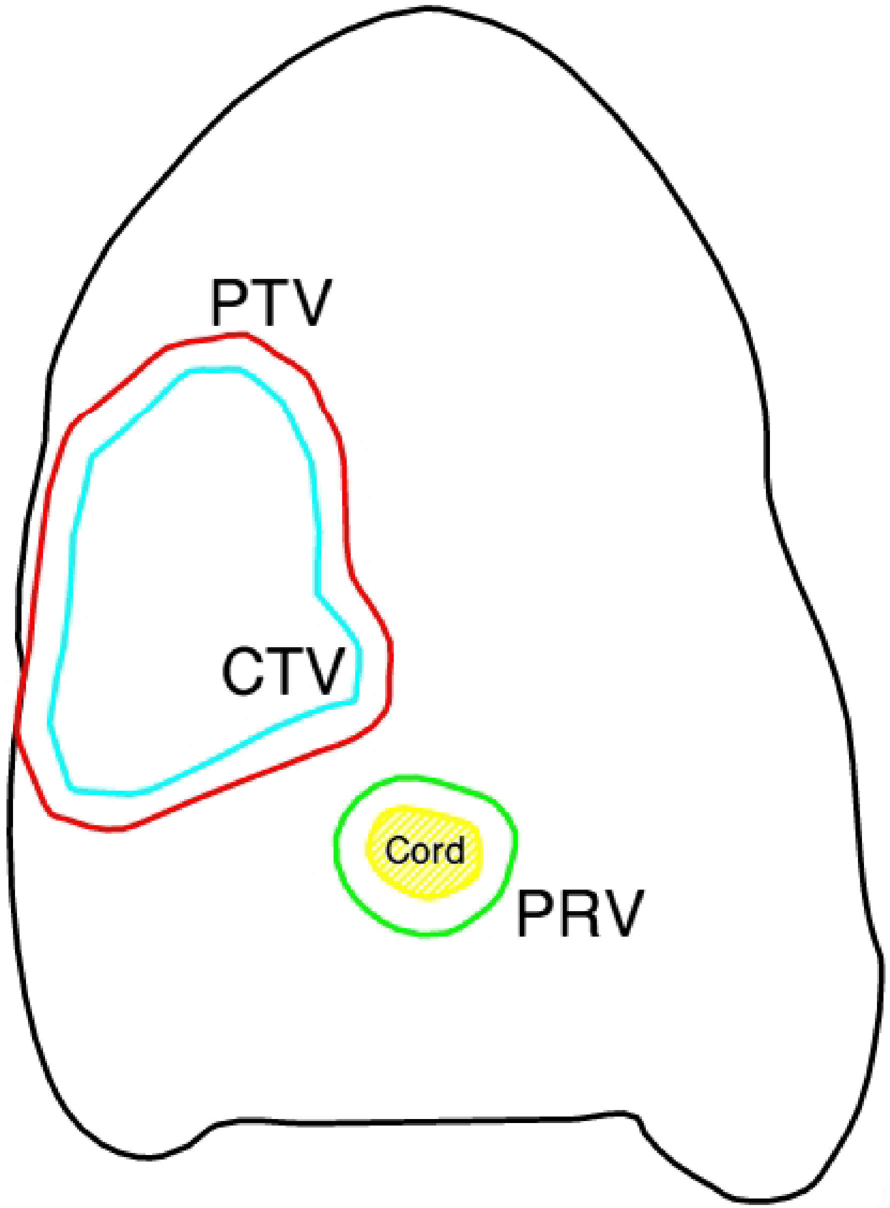
Simple outlines



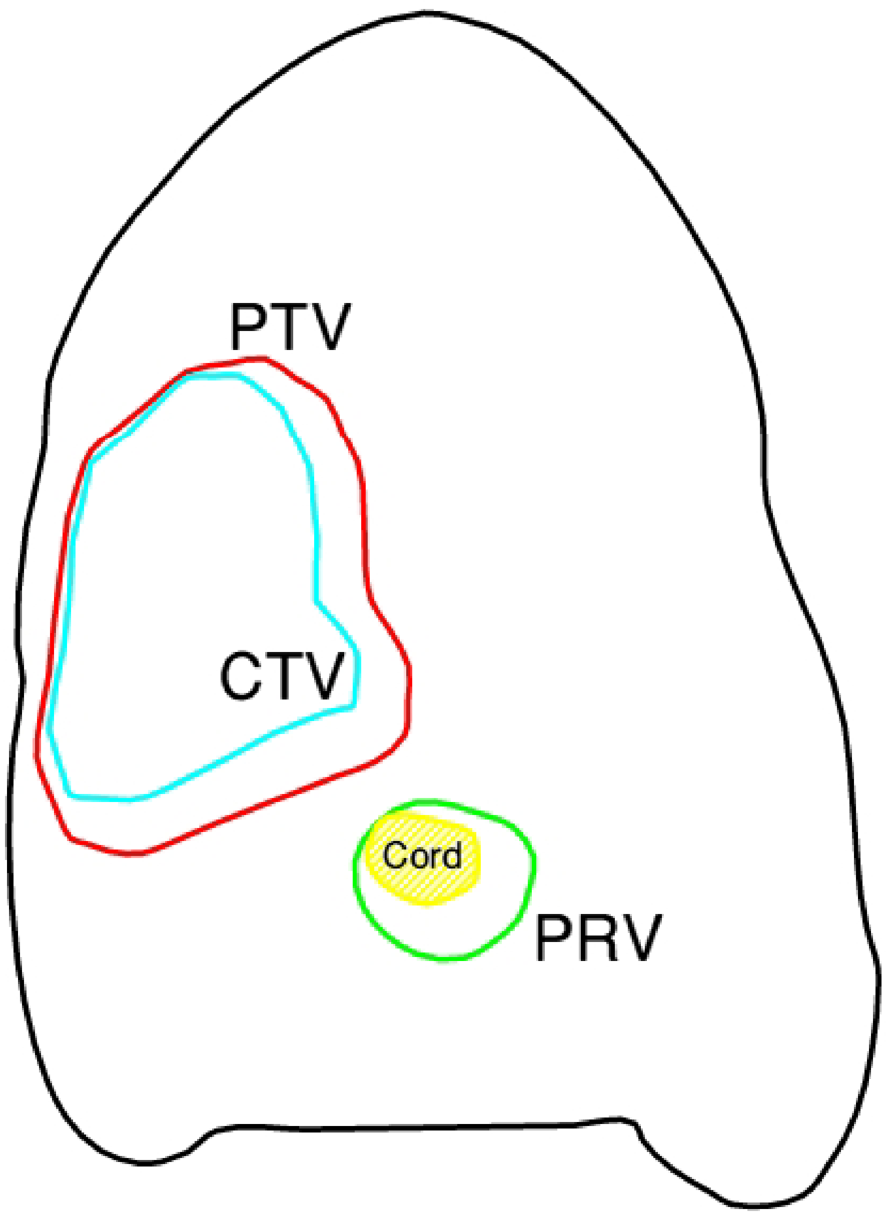

PTV
CTV
Cord

Cord should be
safe

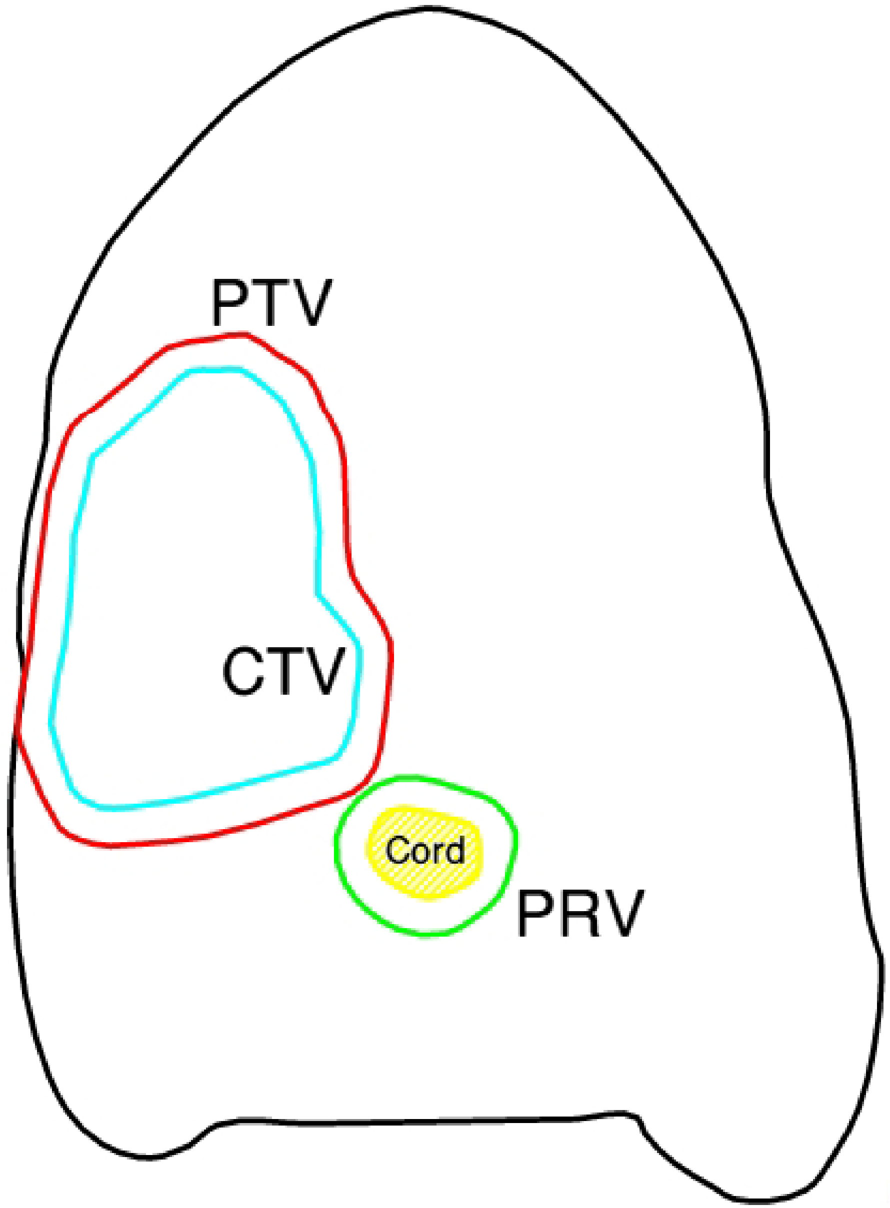
PRV is away from
PTV



- Cord still safe even if set up is imperfect
- Note: patient, CTV and cord have moved
- PTV and PRV have not moved



- PTV & PRV closer
- PRV shows area to avoid with high dose to ensure the cord is safe
- No conflict



# Target volumes – PTV + PRV

PRV margin can be ***smaller*** than the PTV margin

This is a helpful step for high dose treatments close to an OAR

This is because OAR movement is usually a 1D problem
(occasionally 2D, rarely 3D)

# Target volumes – overlaps

# Target volumes – overlaps

There are always occasions when the PTV and OARs/PRVs overlap

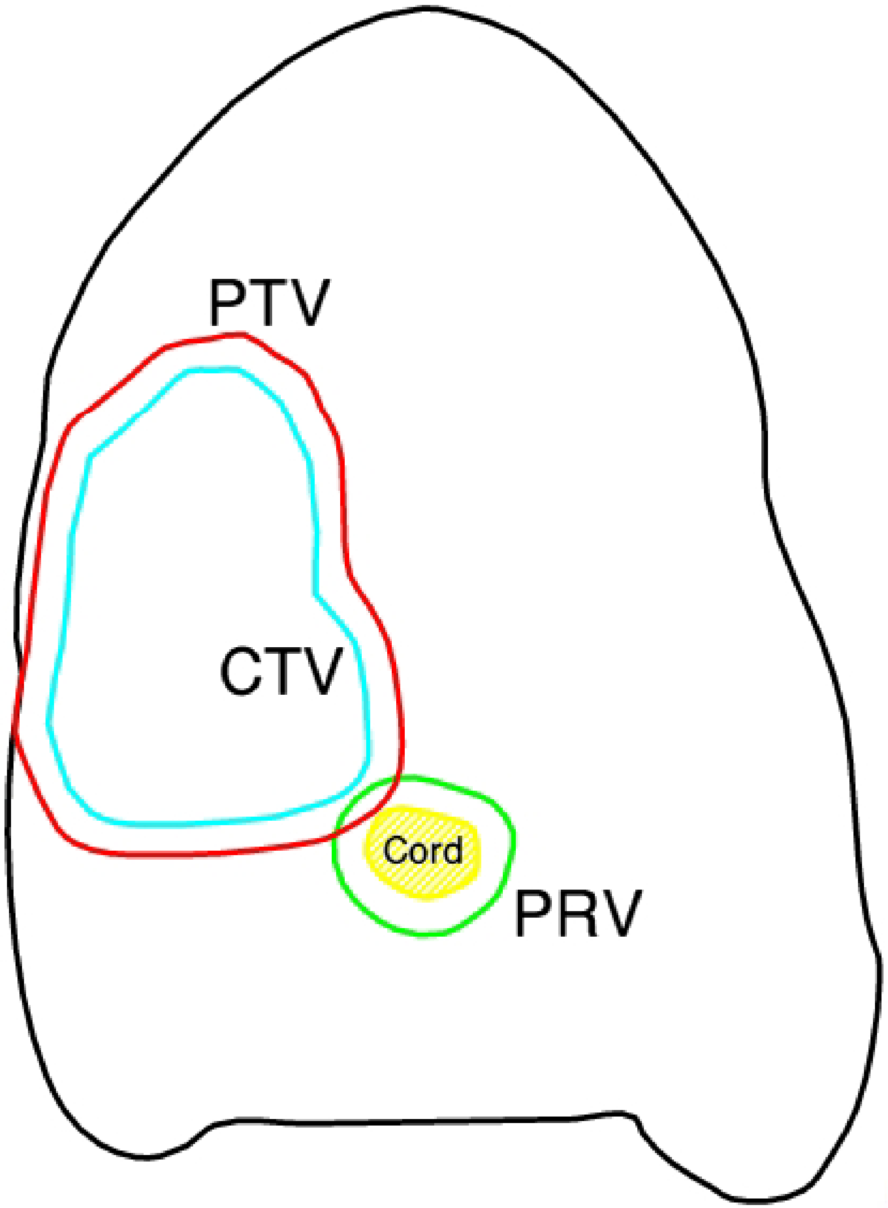
What is the best strategy?

The planning concept has changed between ICRU 62 and 83 …..
In fact changed ***completely*** in ICRU 83

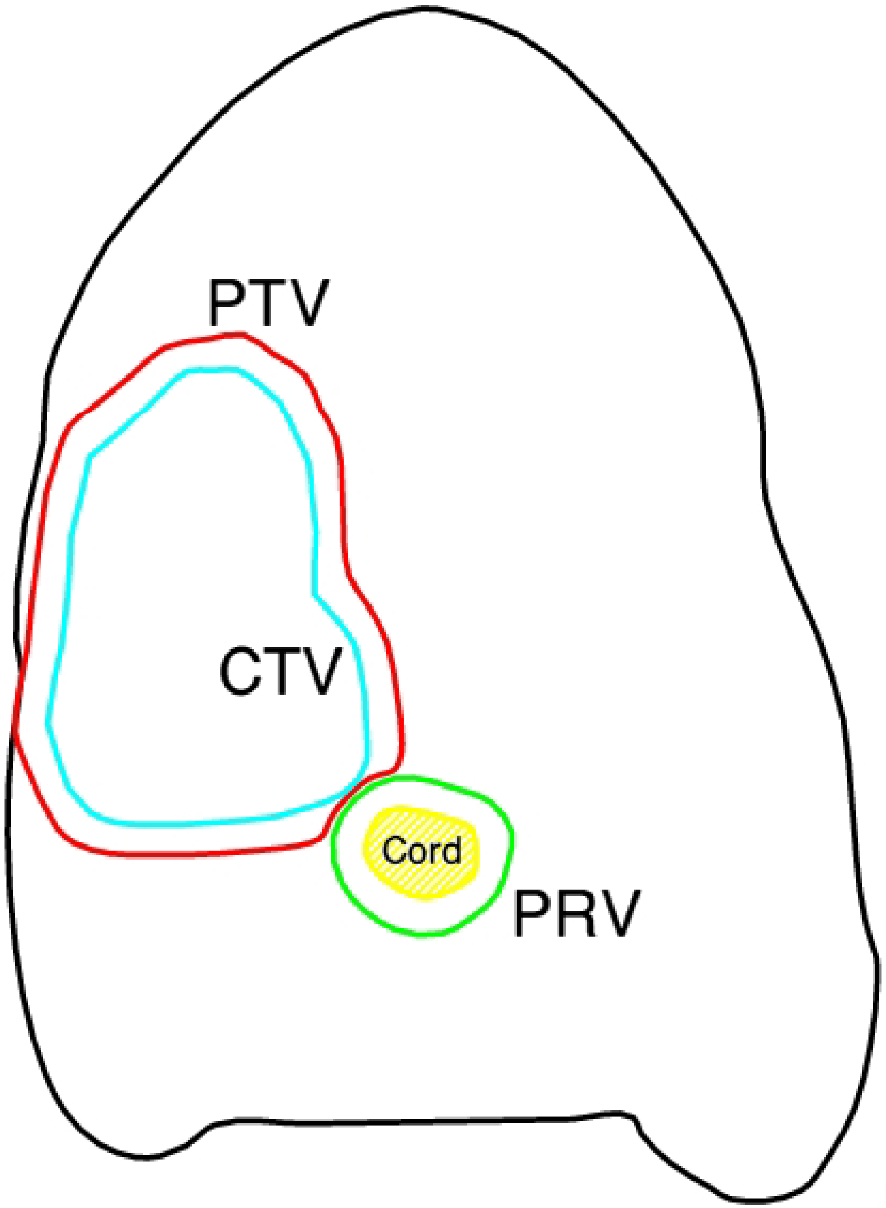
ICRU 62 – edit PTV (even CTV) – fine for CRT

ICRU 83 – ***do not*** edit – better for IMRT

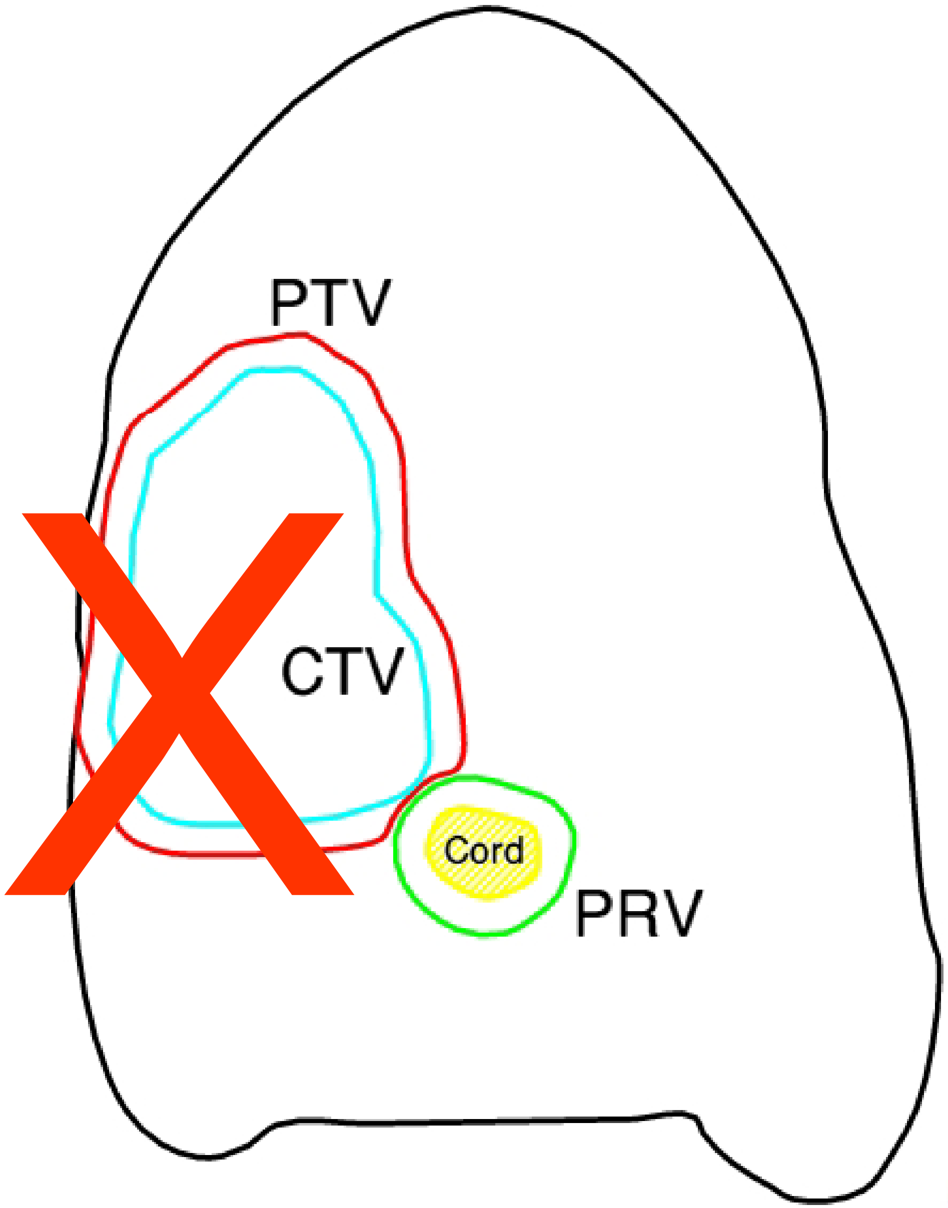
- PTV and PRV now overlap
- A problem for planning
- We need a solution to the dilemma

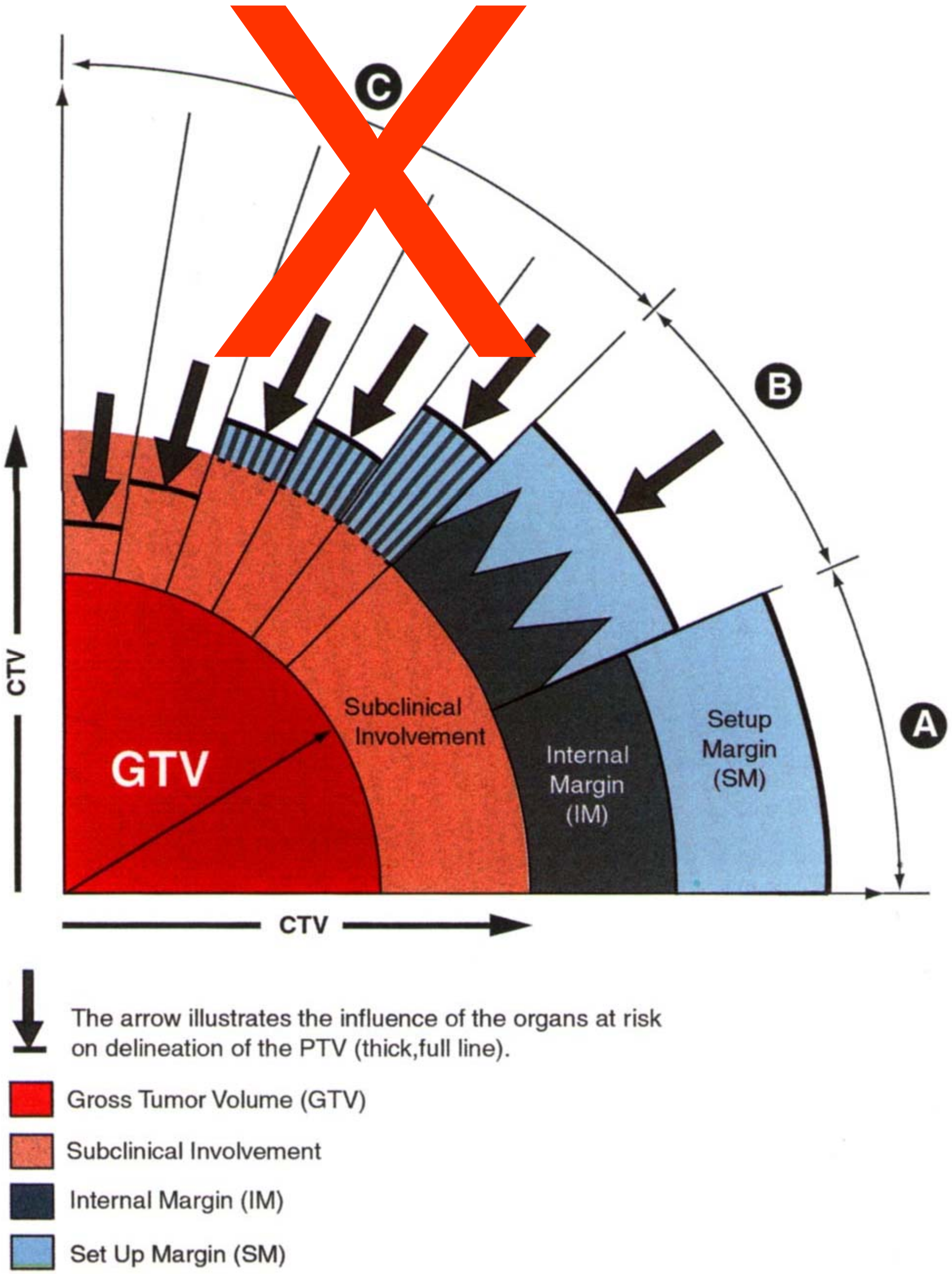


- ICRU 62 recommendation
- OAR would be safe
- Obscures target dose objective



- ICRU 62 recommendation
- OAR would be safe
- Obscures target dose objective
- Please don’t ...



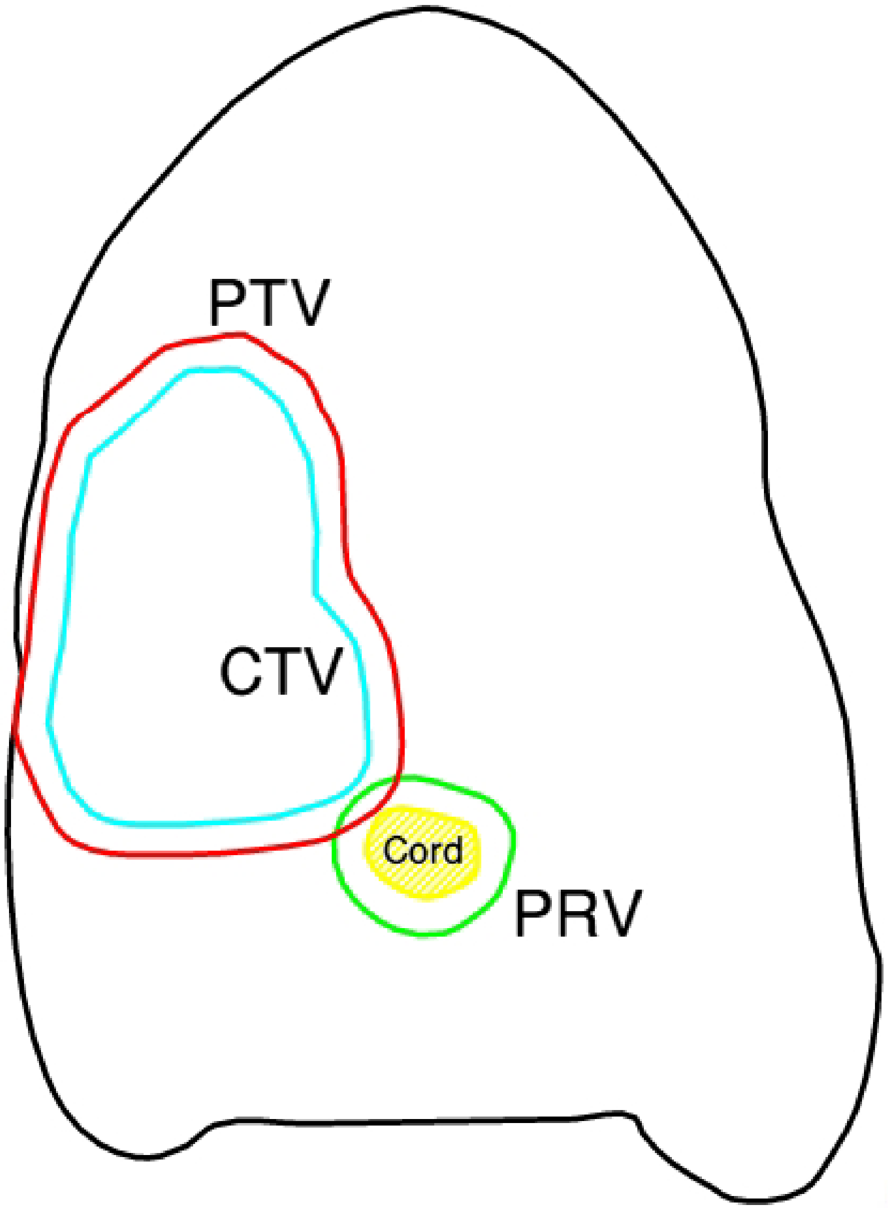



- Fig from ICRU 62 (also in ICRU 71)
- Scenario C not recommended now, in the era of IMRT

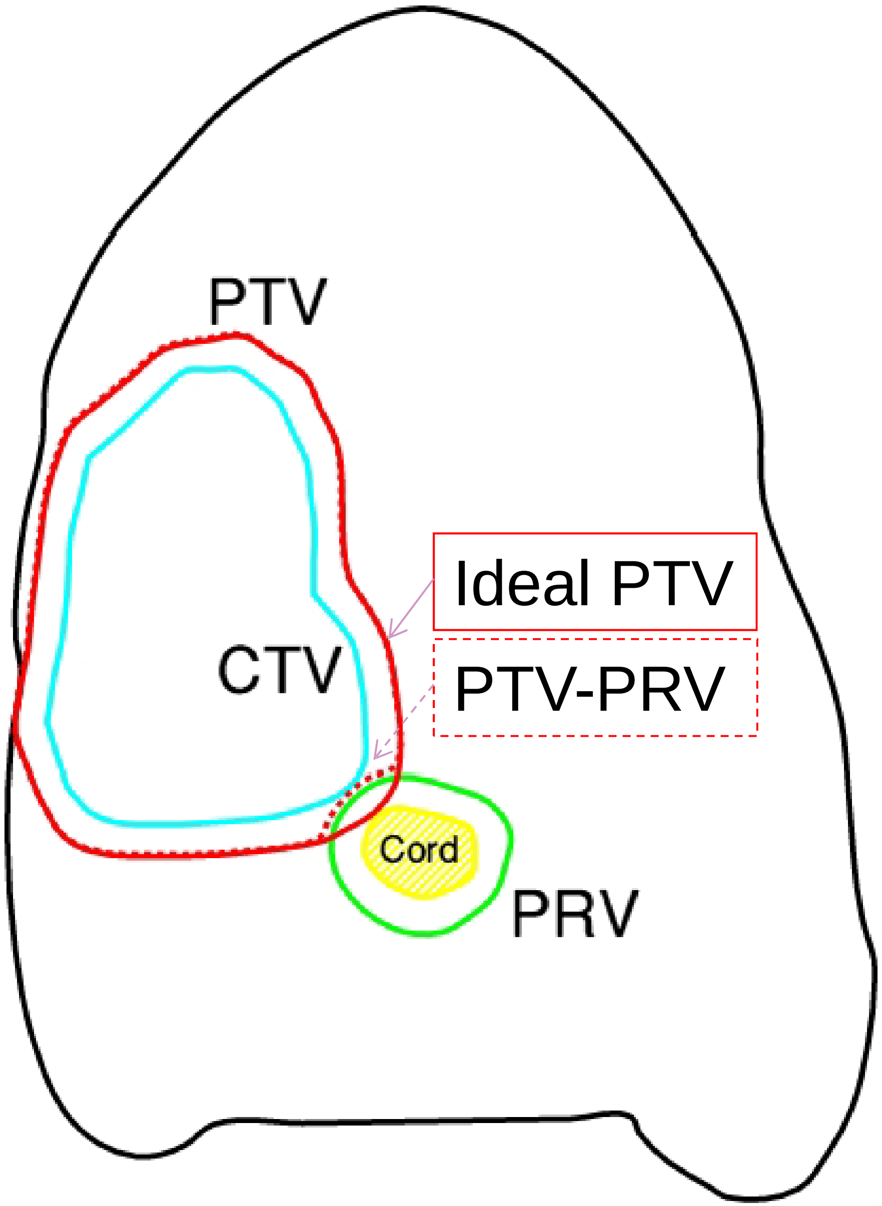
- PTV and PRV now overlap

- IMRT allows variable dose
- Therefore draw what you want

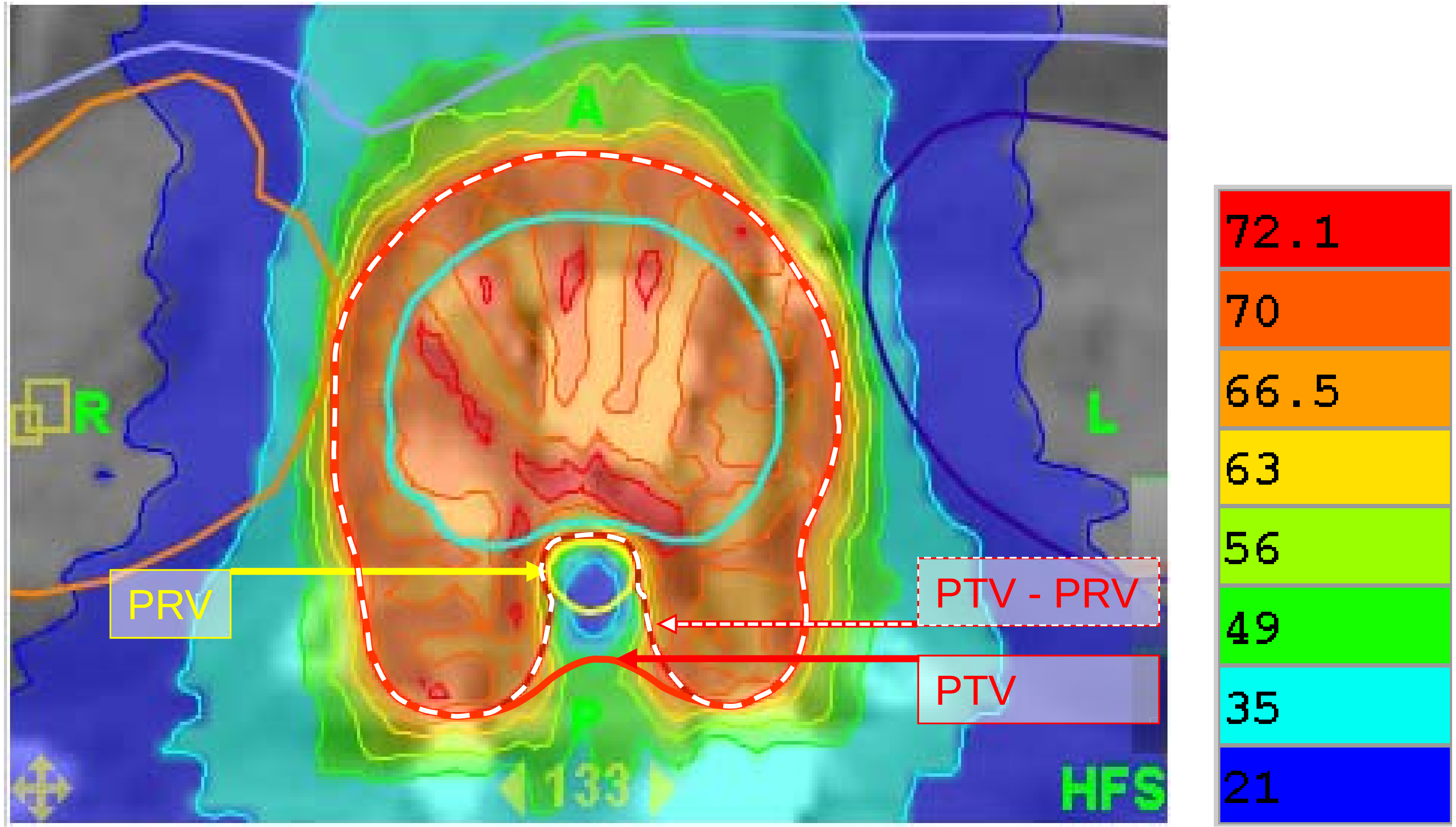
- ***Do not*** modify PTV



- ICRU 83 approach for IMRT
- Add 2nd volume avoiding overlap
- Specify priorities and doses



# Target volumes – PTV / PRV




PRV essential here to protect cord (so is IGRT)

Priority PRV > PTV

# Target volumes – overlaps

Overlapping volumes requires:

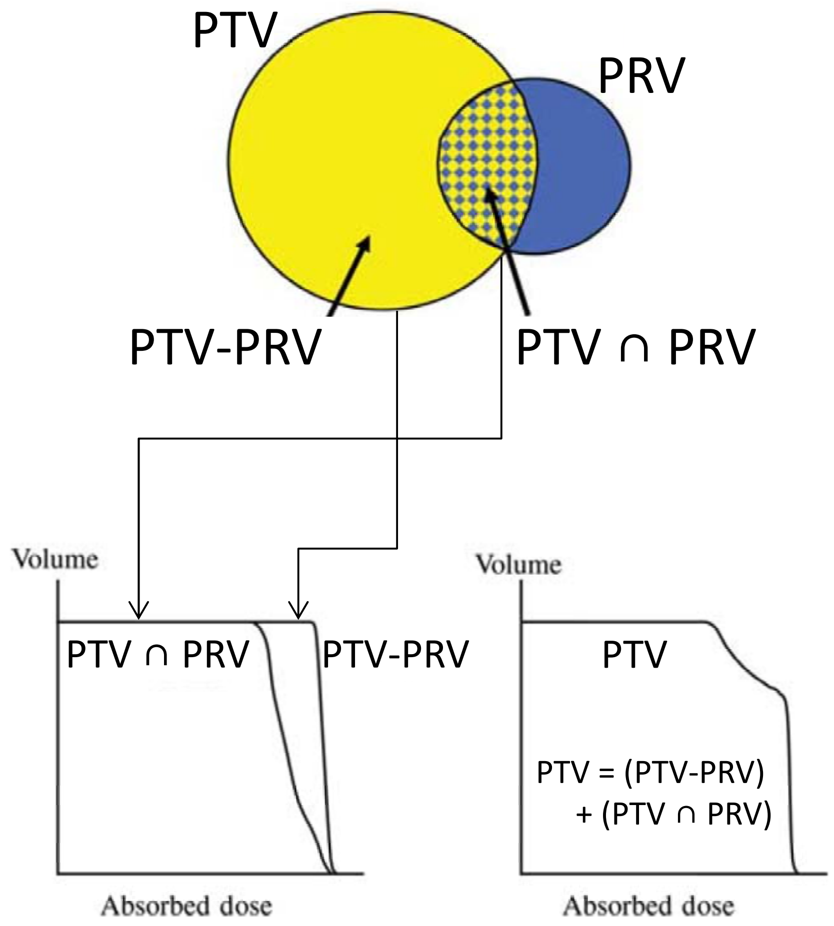
- Very clear objective setting
- Good communication between clinician & planner
    - Dialogue (i.e. 2 way communication) is recommended !
- Use optimiser to deliver different doses to different parts of the target
- Makes plan evaluation using DVH more difficult

# Target volumes – overlaps

From ICRU 83

Review DVHs carefully

Overall, more robust method



# ICRU guidance on planning and prescribing

# ICRU guidance

- ICRU 83 specifically dedicated to IMRT
- Recommendations for prescribing changed
- Introduces some specific aspects of reporting of dose to normal tissues

# ICRU guidance

- Advice on dose planning in the build up region or if PTV extends outside the body contour is given

- Concept of adaptive review introduced

  Possible to review dose and dose change during treatment

- Comments on QA given

  ***Not*** discussed here

# Prescribing

- Key changes in prescribing

Prescribe to ***median dose*** rather than ICRU reference point (≈ isocentre dose)

median dose = $D_{50\,\%}$

= dose to 50% of the volume

Report ***near-maximum*** and ***near-minimum***, rather than actual max & min

Still need to be aware of target coverage

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# Prescribing

- Specify median dose - $D_{median} = D_{50\ \%}$

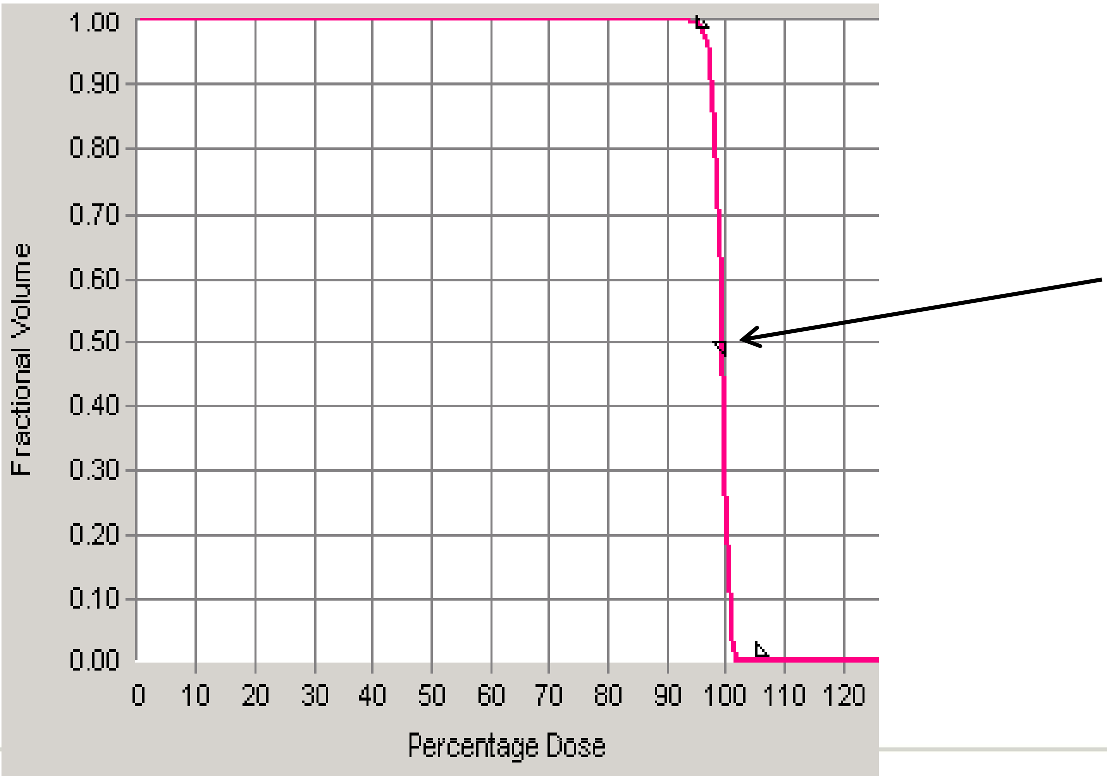
Corresponds best to previous ICRU reference point dose (≈ isocentre dose)

- Often close to mean dose
- Not influenced by 'tails' on the DVH
- Accurately calculated in TPSs

NB useful to add units e.g $D_{50\ \%}$ or $V_{20\ Gy}$

# Prescribing

Median dose = $D_{median}$ = $D_{50\ \%}$



# Prescribing

Prescribing to median dose without some restriction on the slope of the target DVH could allow a shallow slope and low target minimum dose

Need some agreement on minimum acceptable

At least 99% of the volume ($D_{99\ \%}$) to receive>95% of dose

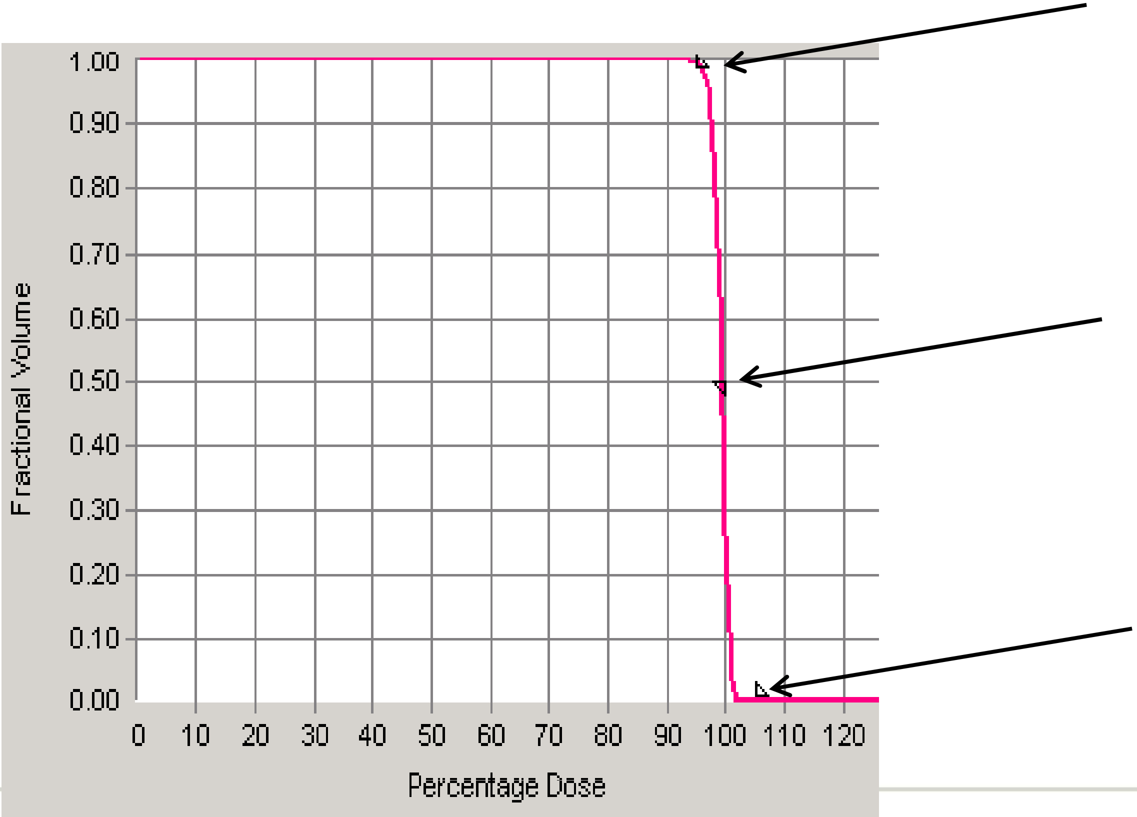
At least 98% of the volume ($D_{98\ \%)}$ to receive>95% of dose

Limit on maximum also needed, for example

Less than 1% of the volume >105% of dose

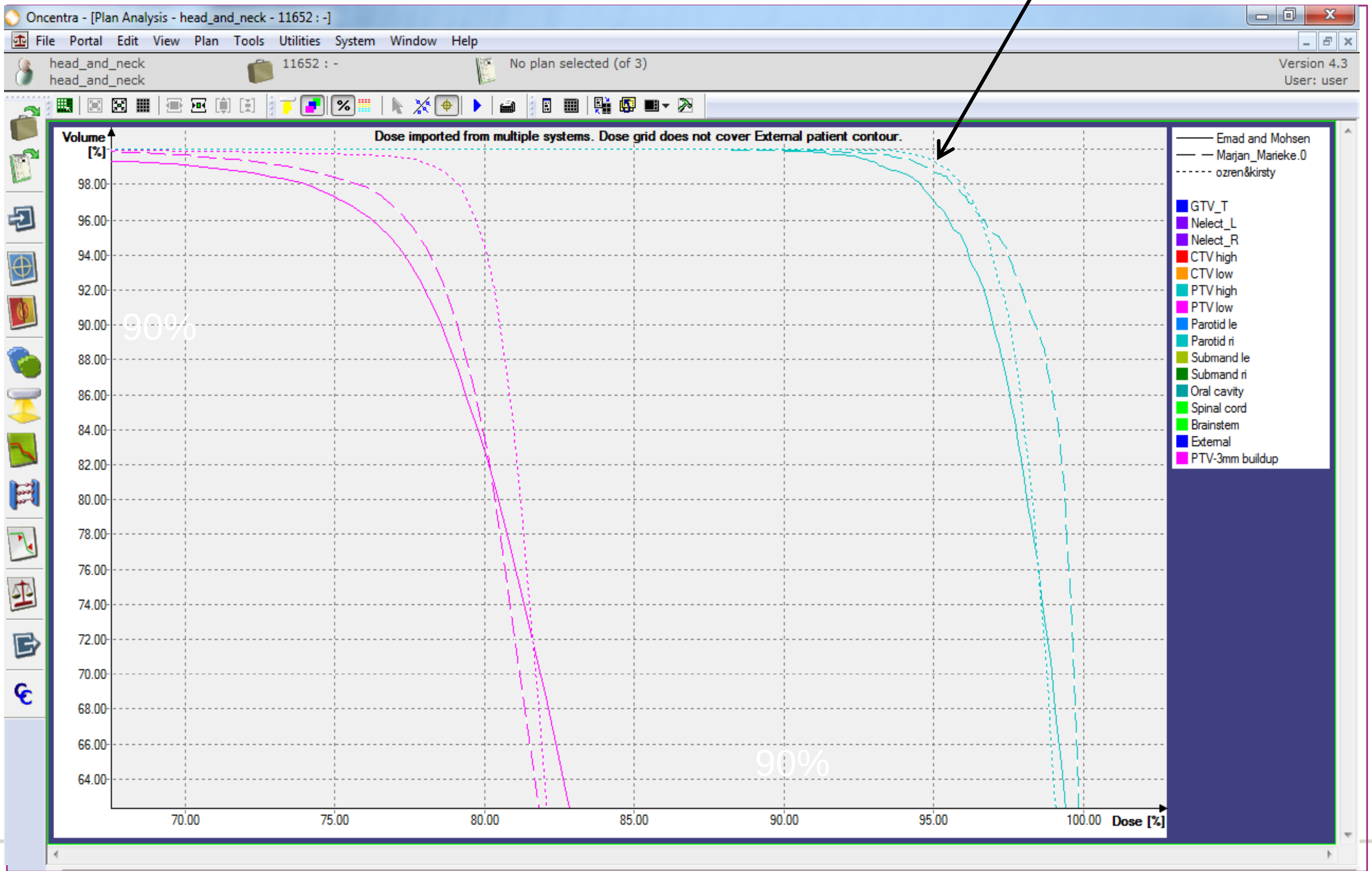
# Prescribing

Dose constraints (objectives) for min & max included (and median)



# Prescribing

$D_{99\ \%}$ >95%
(of prescription dose)

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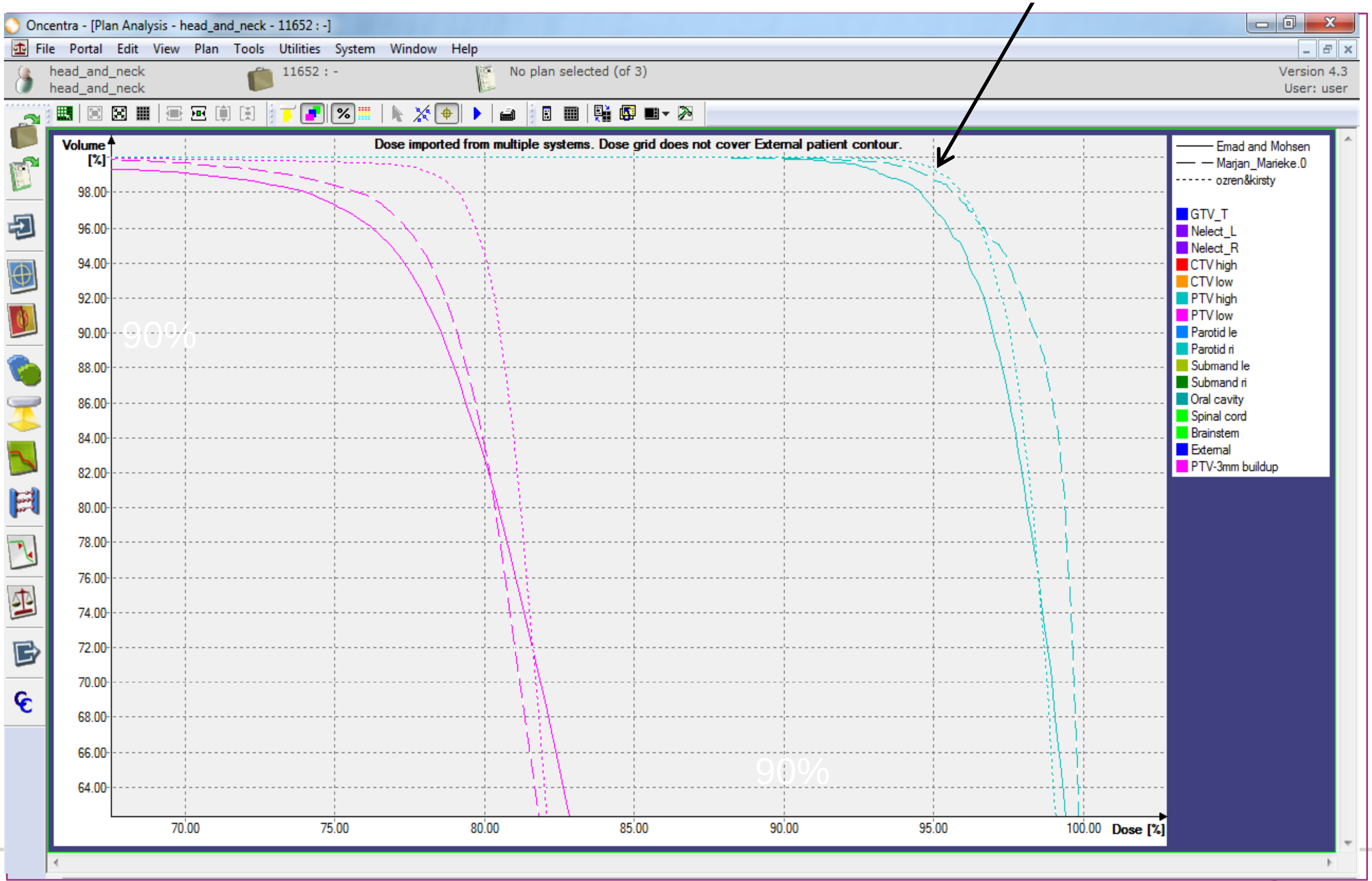
# Prescribing

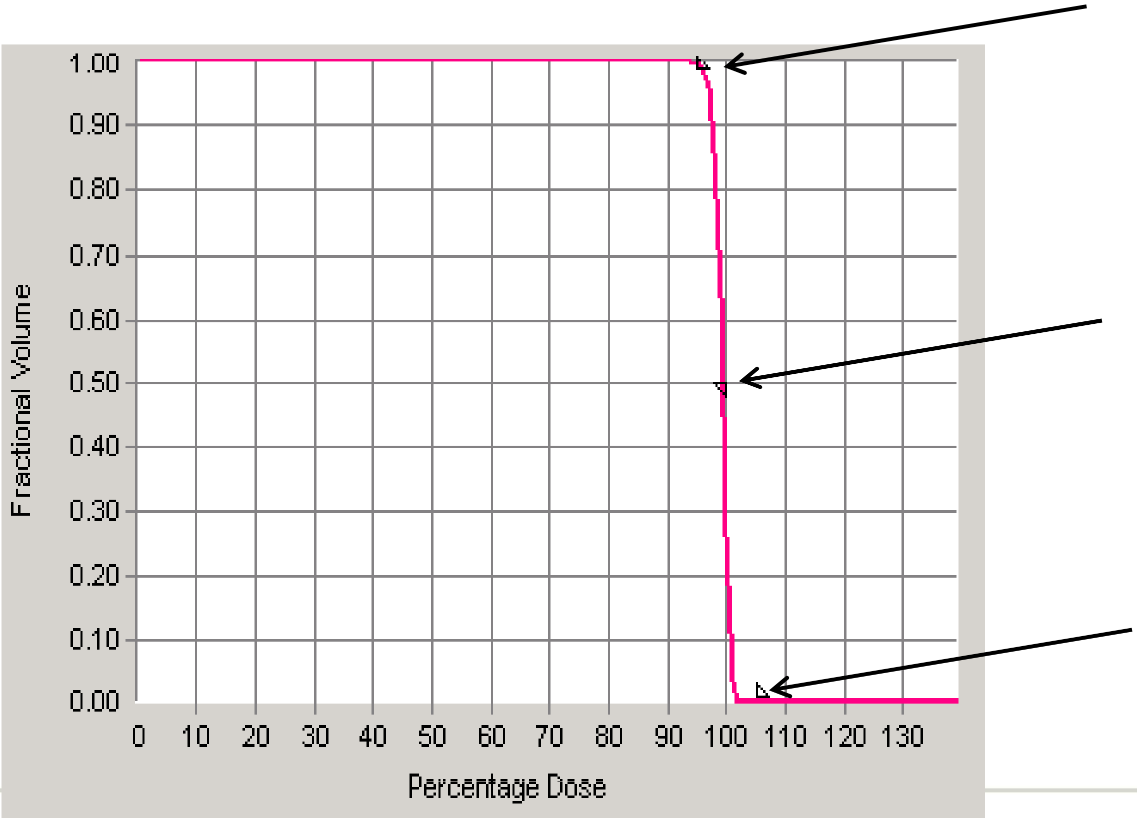
$D_{99\ \%}$ >95% (of prescription dose)

$V_{95\ \%}$ >99%



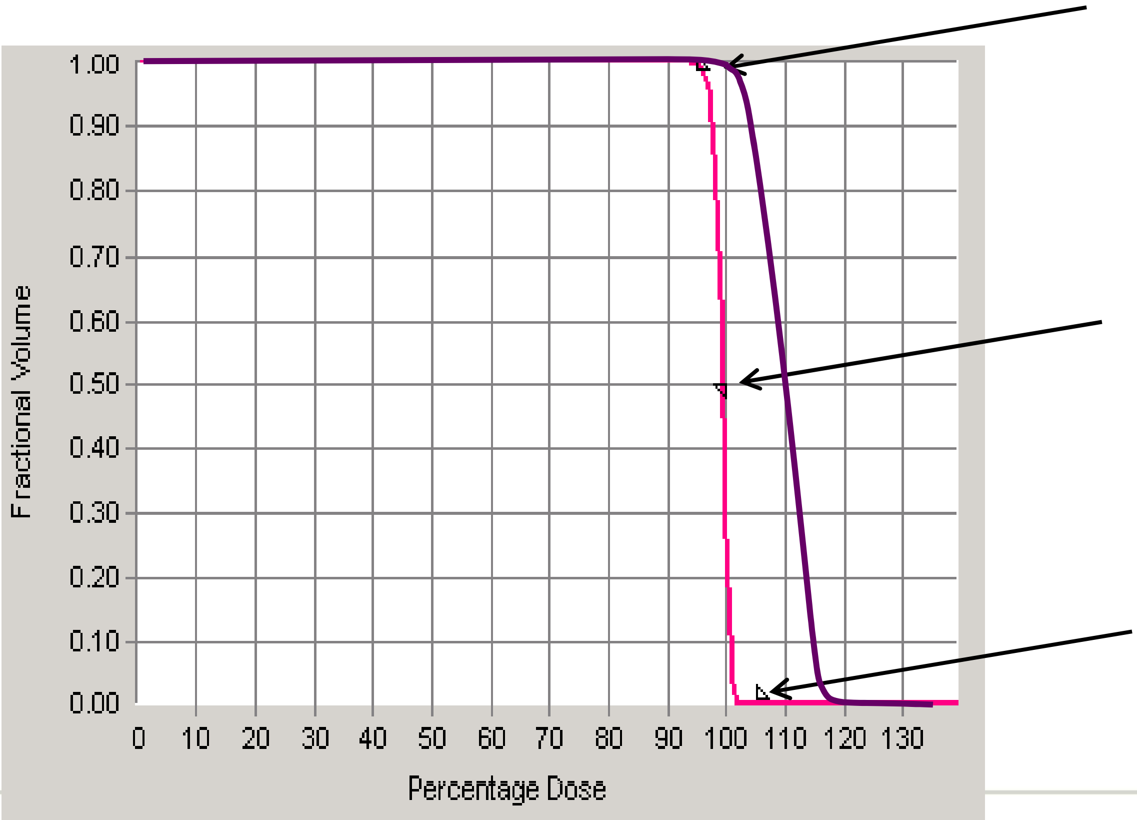
# Prescribing

Dose constraints (objectives) for min & max included (and median)



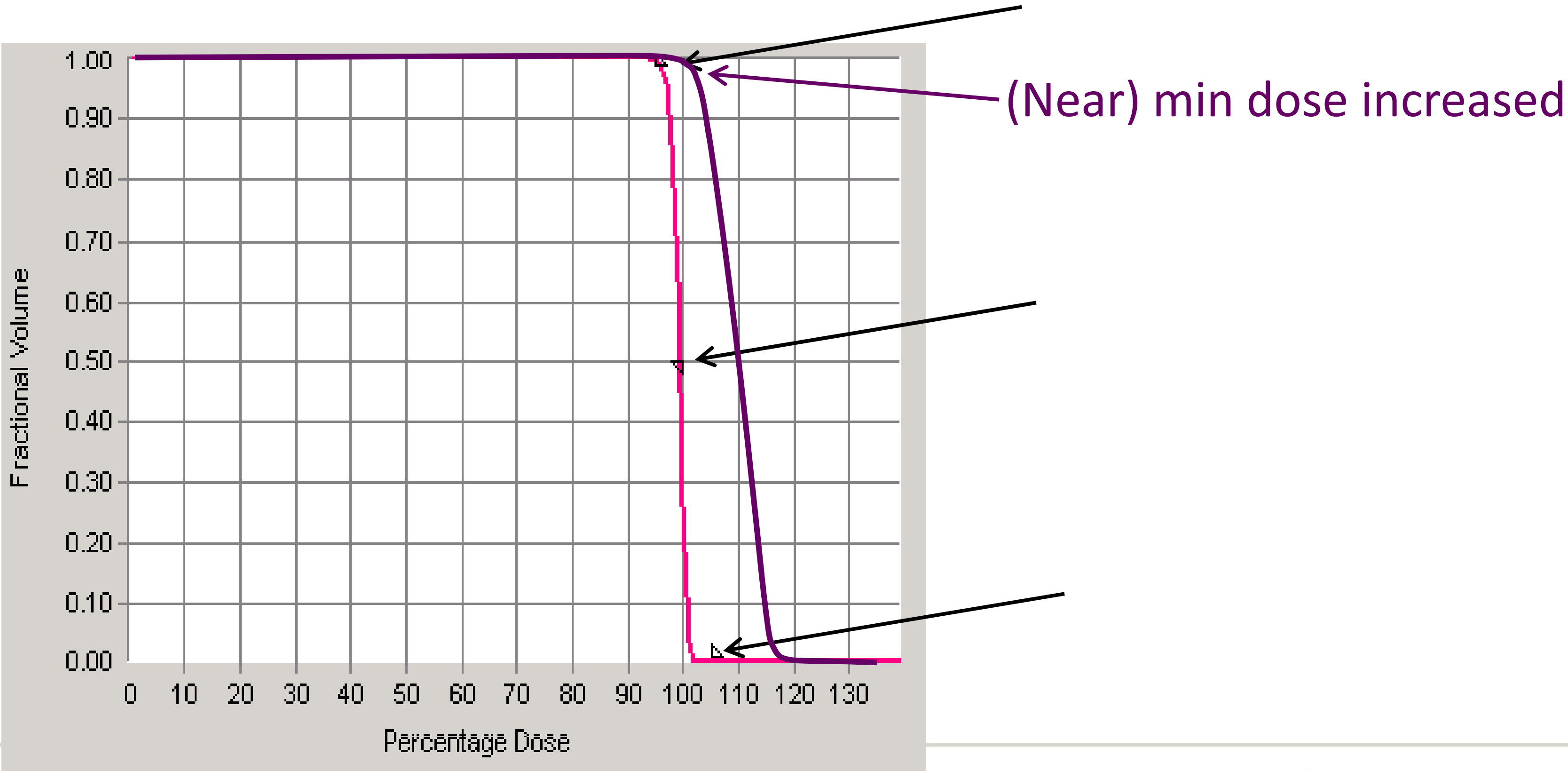
# Prescribing

Dose constraints (objectives) for min & max included (and median)



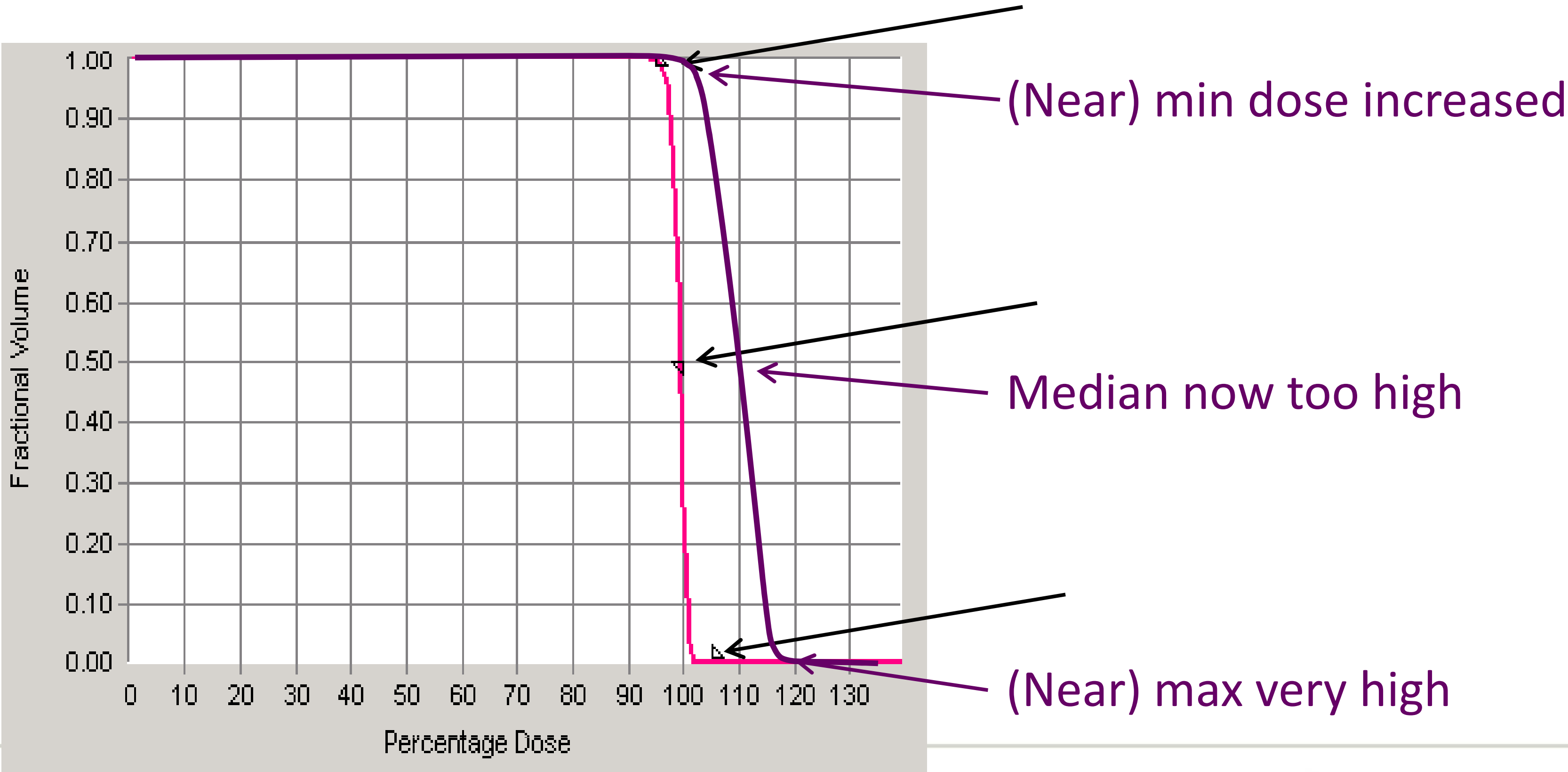
# Prescribing

Dose constraints (objectives) for min & max included (and median)



# Prescribing

Dose constraints (objectives) for min & max included (and median)



# Prescribing

- Report near-maximum and near-minimum in target volume, rather than actual max & min

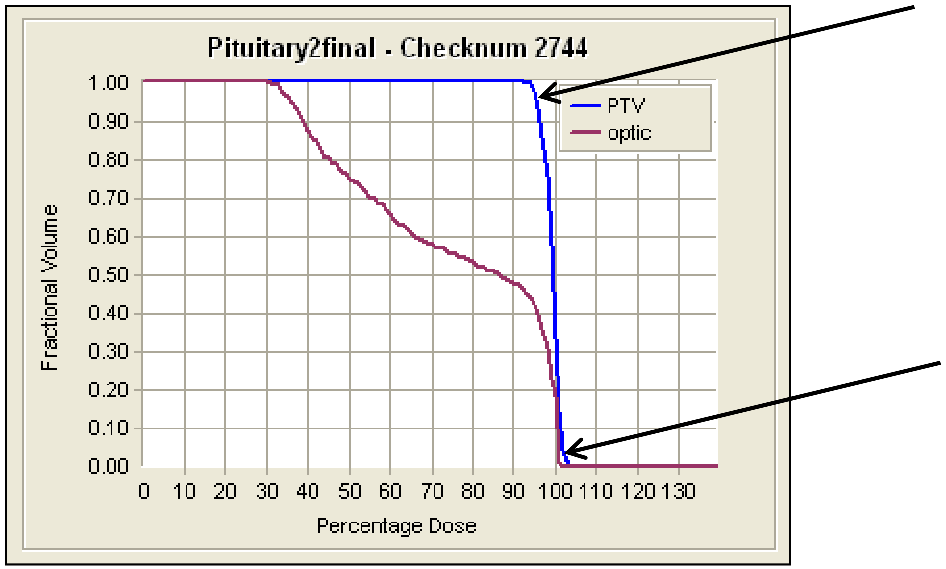
$D_{2\,\%}$ for near-max,

$D_{98\,\%}$ for near-min

# Prescribing

- Report near-maximum and near-minimum in target volume, rather than actual max & min

  $D_{2\,\%}$ for near-max, $D_{98\,\%}$ for near-min



# Prescribing

- Clinical relevance of minimum (near-min) dose point may depend on its position within the PTV

Minimum dose in edge of PTV may be of marginal significance

Minimum dose in centre (in GTV) may be rather important

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# Prescribing

- Concept of using dose volume histograms for dose specification is introduced in ICRU 83

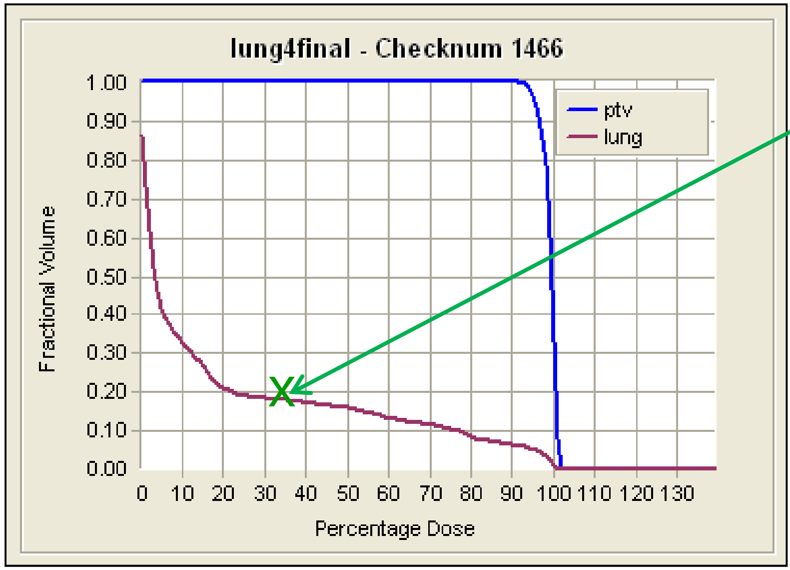
  Dose-volume prescribing in place of dose

  Dose-at-a-point specification is retained for purposes of comparison

- Contains worked examples, which may be helpful

# Prescribing

- Add volume parameters where relevant
  e.g. $V_{20\ Gy}$ for lung




$V_{20\ Gy}$

Relates to clinical outcome

NB $V_{20\ Gy} = V_{33\ \%}$ (for 60 Gy)

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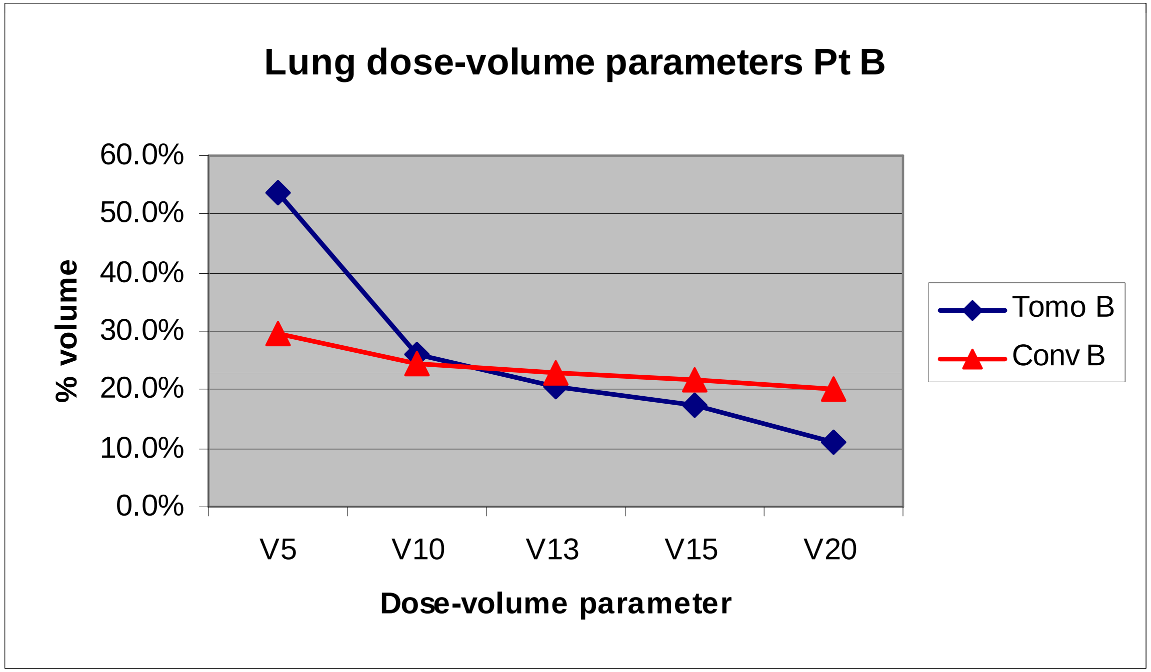
# Lung doses

- 2 plans compared
  - IMRT : 'CRT'
- Mean lung dose same = 9 Gy
- DVH different
- In reporting, the DVH (or some points on it) may be useful



# Prescribing

- For serial organs, maximum (near-max) dose is relevant parameter

ICRU recommends $D_{2\%}$ rather than $D_{Max}$ ($D_{0\%}$)

Overcomes problem of defining (knowing!) what volume of the structure is important

Note that $D_{2\%}$ not validated (yet); caution given !

But … it is logical

However, effect will depend on total volume of structure

In gynae brachtherapy often use $D_{2\,cm^3}$

# ICRU guidance

- ICRU 83 mentions the possibility of adding some additional parameters relating to dose
- Optional, but may become interesting

Homogeneity Index & Conformity Index

EUD – Equivalent Uniform Dose

TCP, NTCP

Probability of uncomplicated tumour control (PUC)

Remaining Volume at Risk (RVR)

# Remaining Volume at Risk (RVR)

- Remaining Volume at Risk risk assessment of the dose delivered to a patient
- To assess the risk of second cancers the whole patient volume must be considered
  - PTV
  - PRV
  - RVR
- Can potentially influence the choice of radiotherapy delivery – eg. IMRT vs dynamic arc therapy

# Take home messages

- GTV is tumour you can ***See - Feel – Image***
  - Outline what you see!
- CTV - contains GTV and/or sub-clinical disease
  - Tumour ***cannot*** be seen or imaged
  - Can be individualised to anatomy
- PTV is a geometric volume
  - Ensures prescription dose is delivered to the CTV
  - Includes systematic + random error components

# Take home messages

- Add PRV around CNS structures if giving high doses
- Overlaps can occur between PTV and OAR (or PRV)
  - Do ***not*** edit
- Use clear protocols & follow them
- Assess the treatment to see if adaptation required

# Radiation oncology

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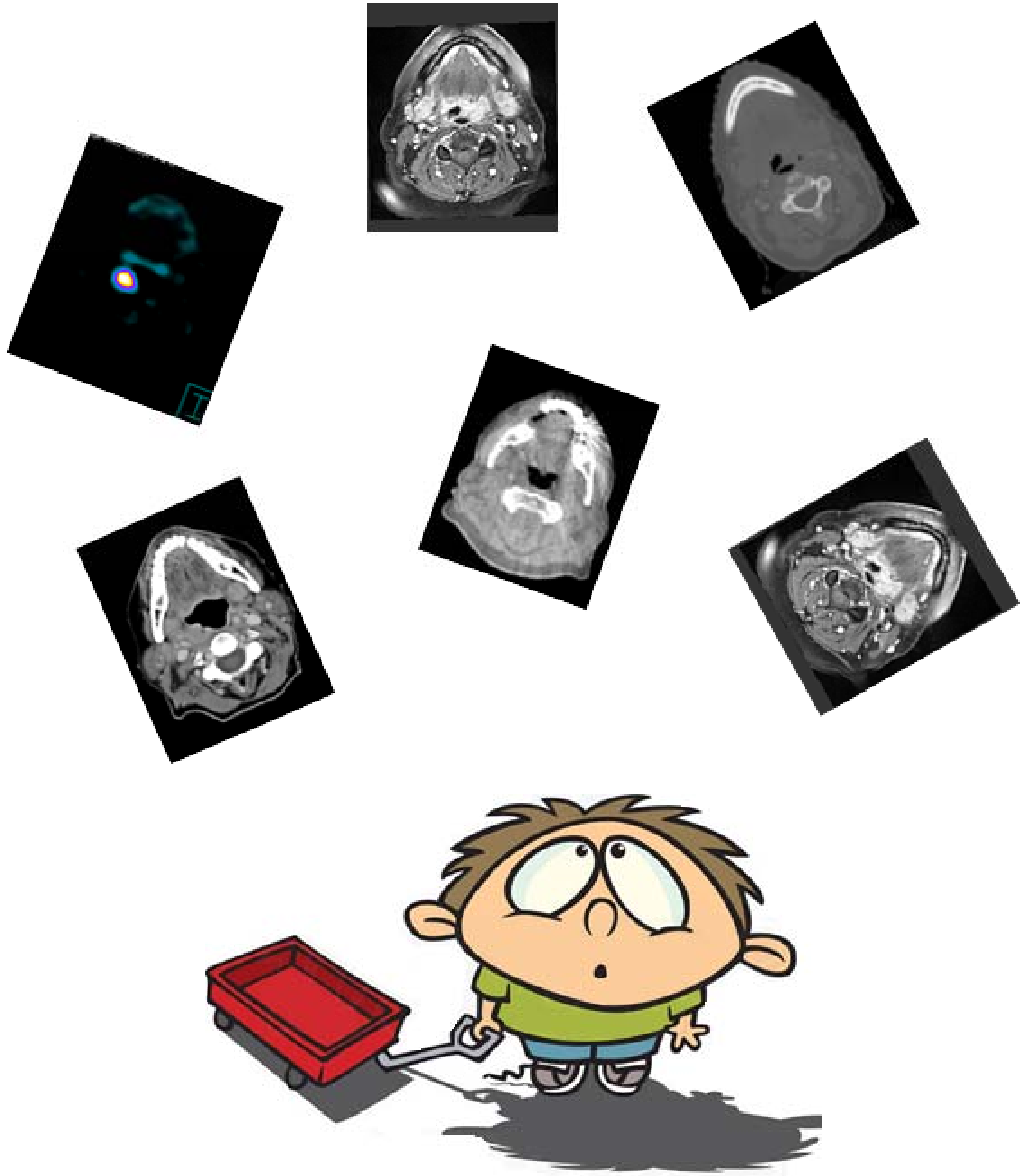
# Image Handling

## Role of images in Radiation Therapy

Martina Kunze-Busch
Radboud University Medical Center Nijmegen
The Netherlands



# Overview

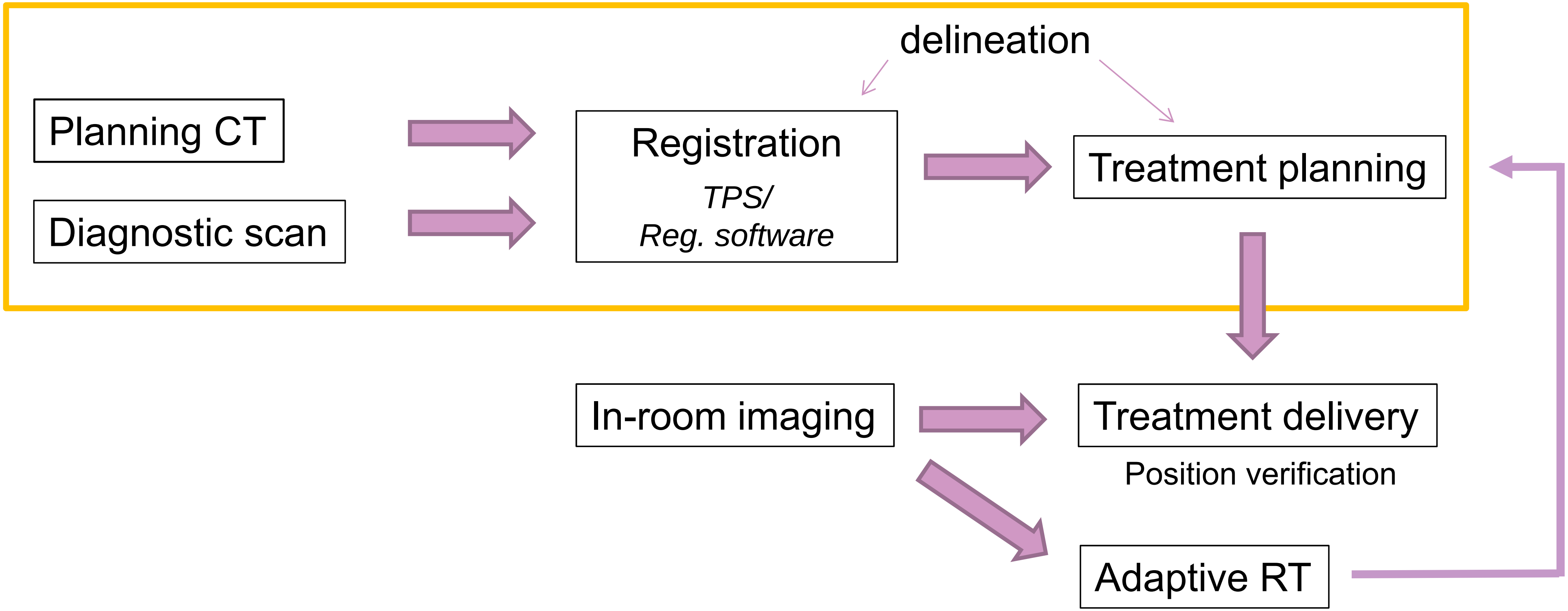
Image data in RT chain

- Treatment preparation (diagnostic scan, planning CT, registration, delineation, display)
  *purpose, potential errors, challenges*

- Treatment delivery (ImageGuidedRT)
  *examples*

- Adaptive RT

# Image data in RT chain

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# Treatment preparation – diagnostic scan

**Purpose**: tumor identification + staging

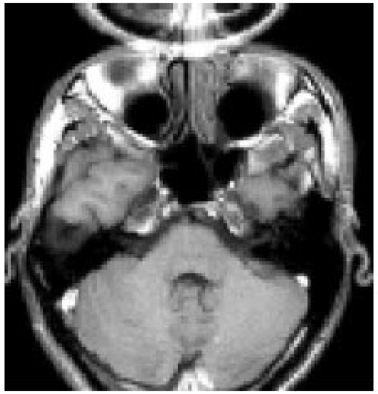
- different modalities CT – MRI – PET …

**Challenges**:

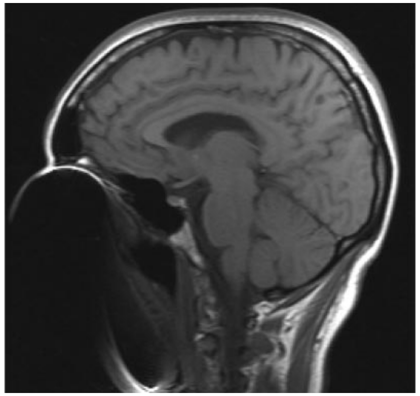
- imaging artefacts
- different modalities (registration)

# Treatment preparation – diagnostic scan

Example: MR imaging artefacts



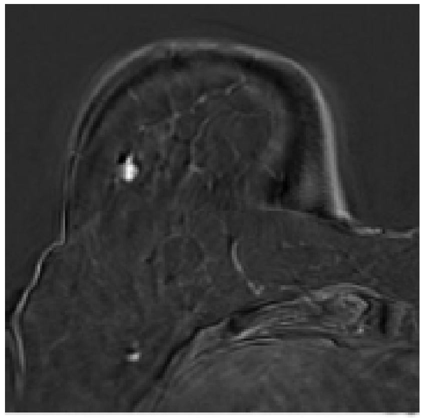
Wrap around



Susceptibility

RadioGraphics 2006

false positive in breast MRI
(pseudo-enhancement)



Millet et al., Br J Radiol 85 (2012)

# Treatment preparation – ~~diagnostic scan~~ dedicated MRI scan

Good collaboration with Radiology department

diagnostic scans → detection/staging

scans for treatment planning → tumor location/extent

↓

geometric accuracy of MR images

(can be compromised e.g. by
- inhomogeneity of main magnetic field
- magnetic field disturbance by imaged objects)

# Treatment preparation – planning CT

**Purpose**: delineation of tumor (→ PTV) and calculation of dose

! reproducible positioning of patient at simulation & treatment

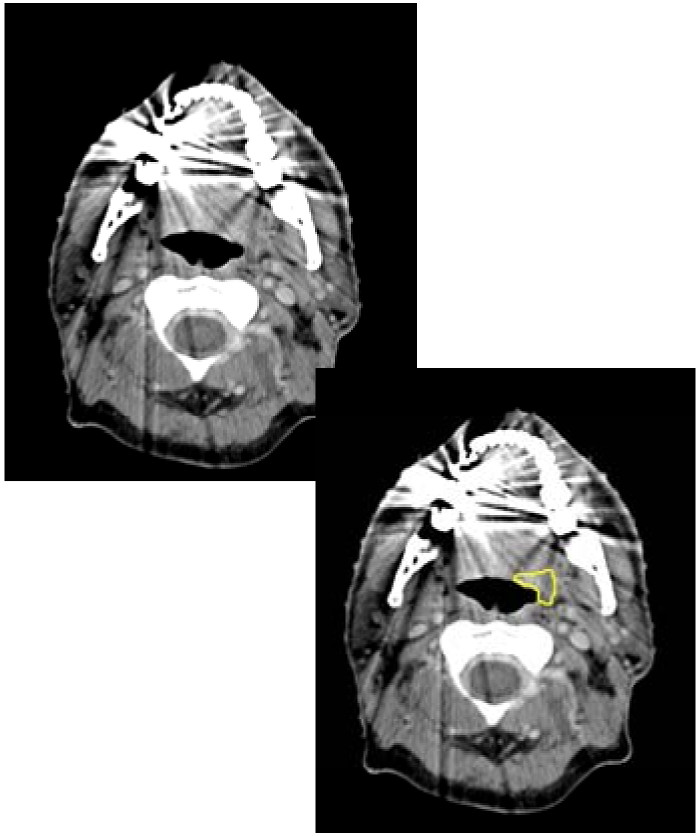
→ knee support
→ markers (skin)
→ fixation masks
→ …

**Potential errors/challenges**:

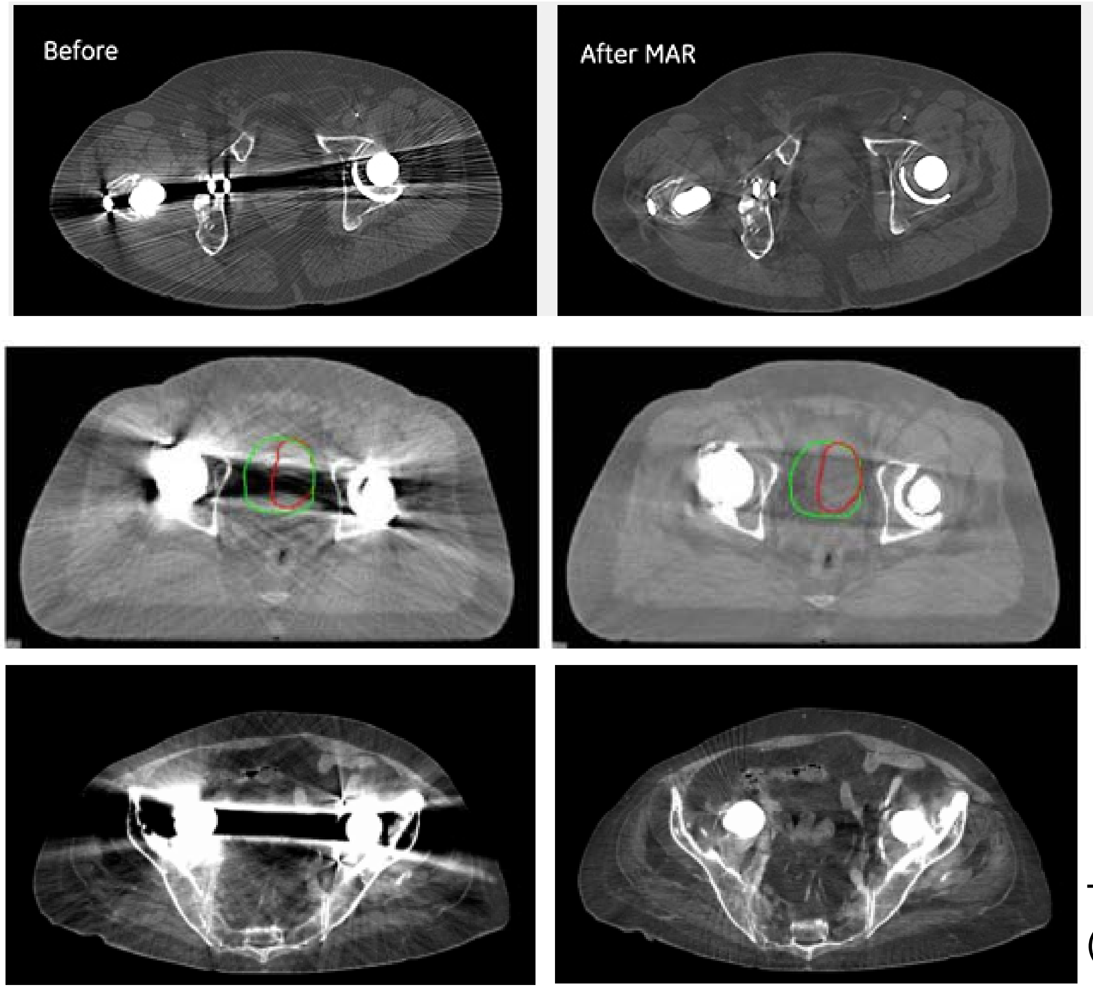
- set up error on scanner
- movement during scan (patient or tumor)
- metal
- ….

# Treatment preparation – planning CT

Example: metal



*Metal Artefact Reduction software*




GE (MAR)

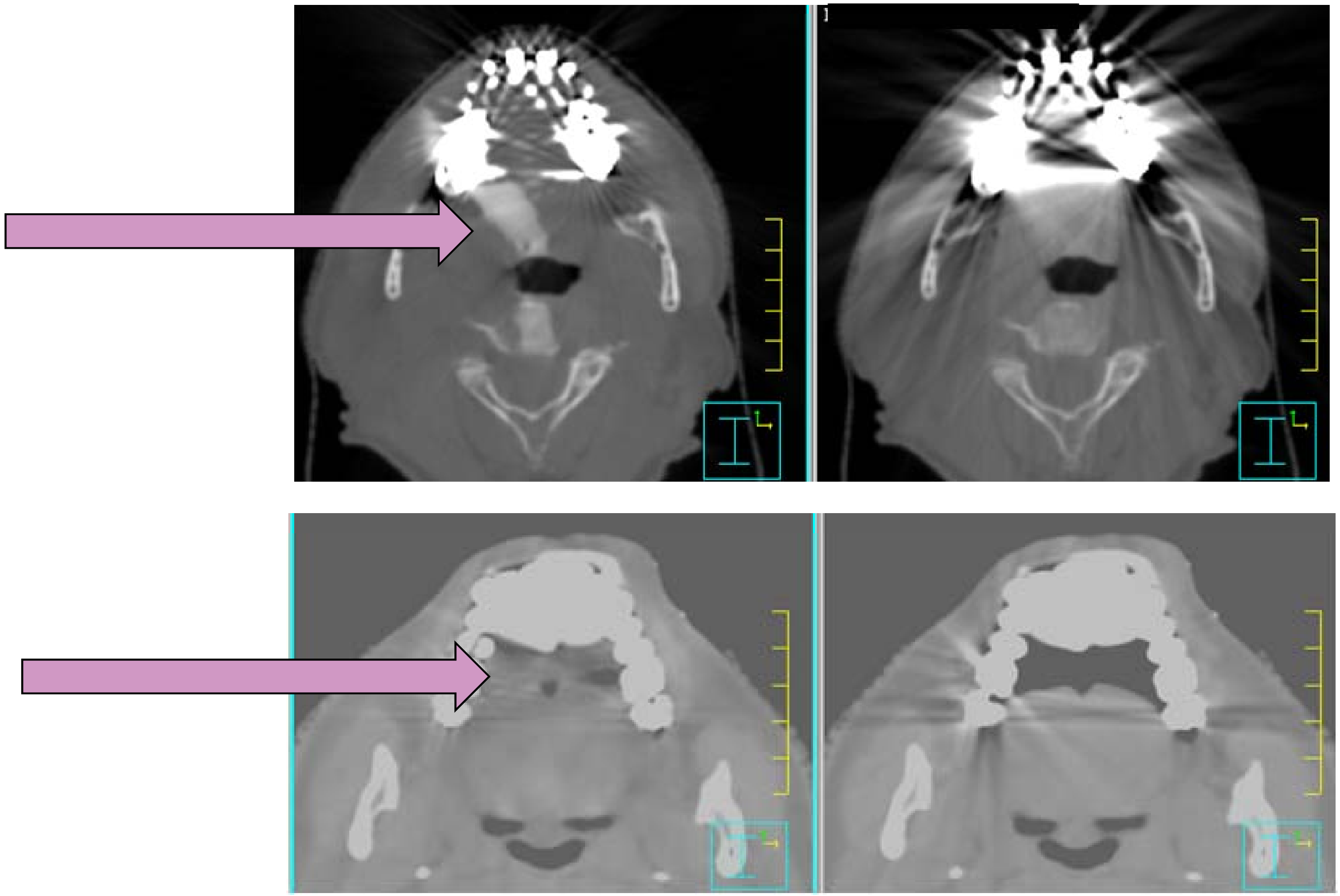
Philips (O-MAR)

Toshiba (SEMAR)

# Treatment preparation – planning CT

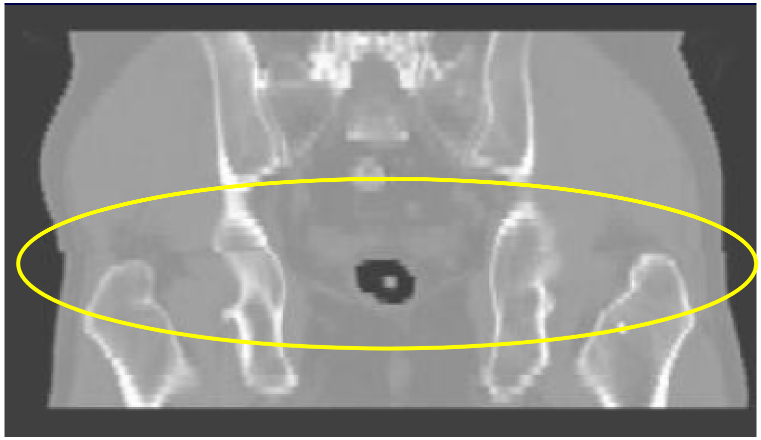
Metal Artefact Reduction software

Beware of artefacts being created by software!

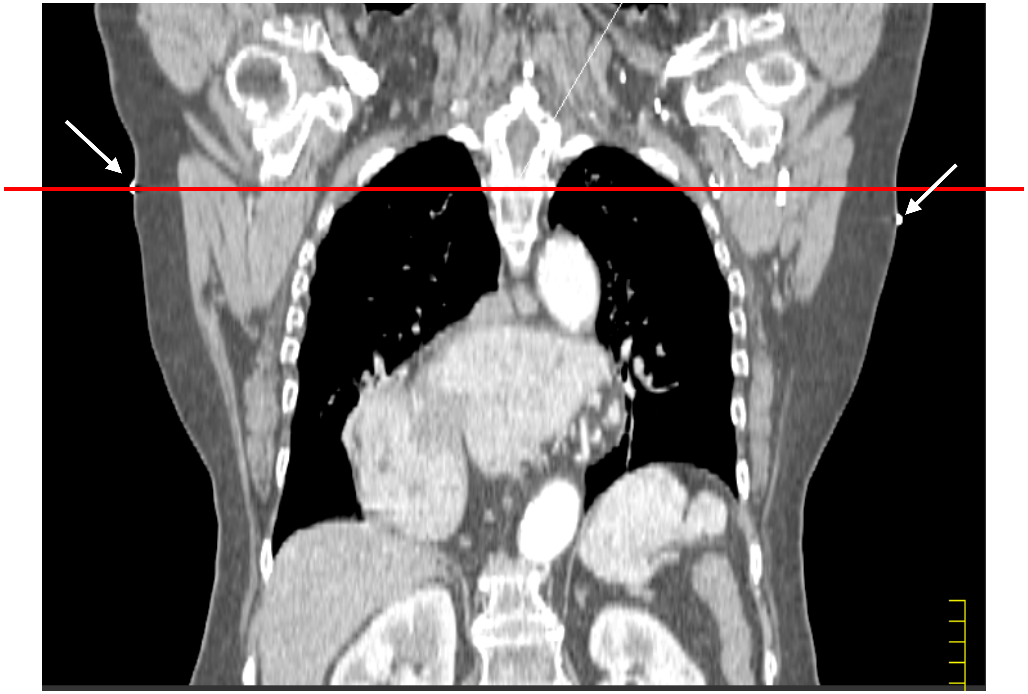


# Treatment preparation – planning (PET/)CT

Example: movement



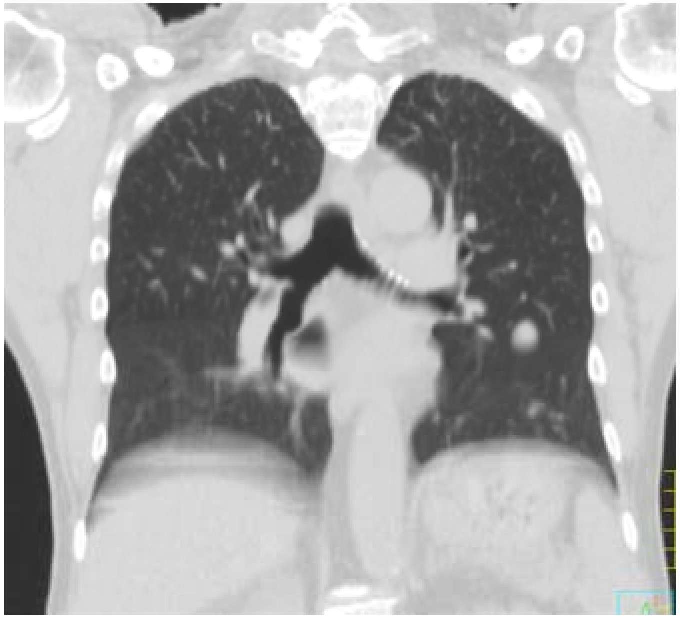
NKI-AVL



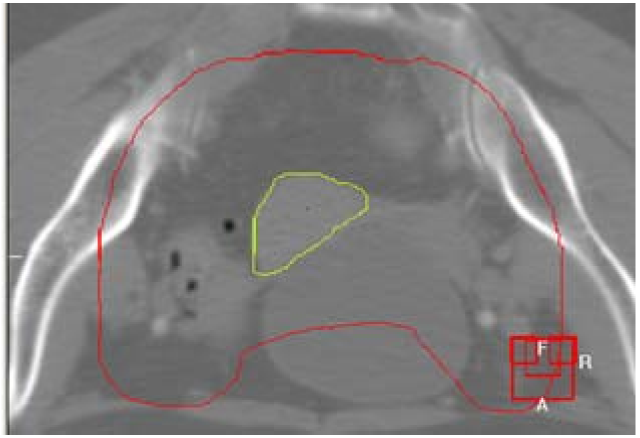
# Treatment preparation – delineation

Example: motion

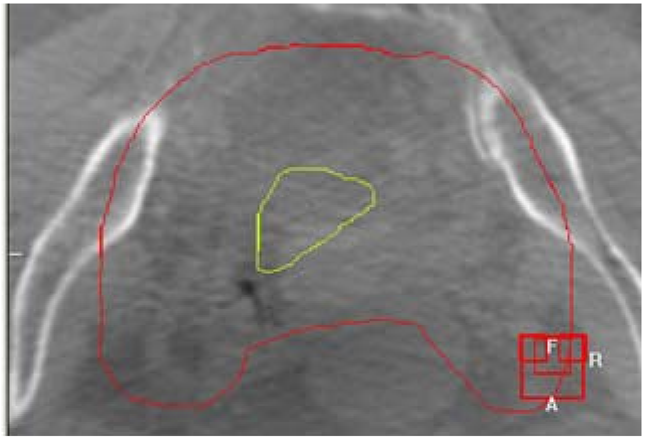
fast



slow




CT




CBCT

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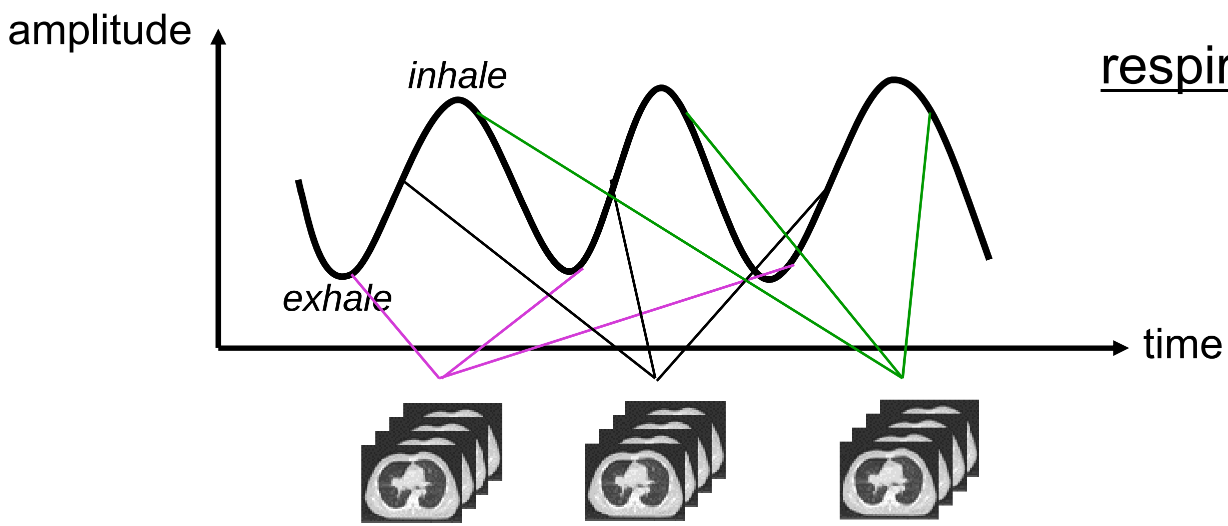
# Dealing with tumor motion

*Fast* motion

- breath-hold CT scan
- gated CT scan
- 4D CT scan
  = 3D scans at multiple phases

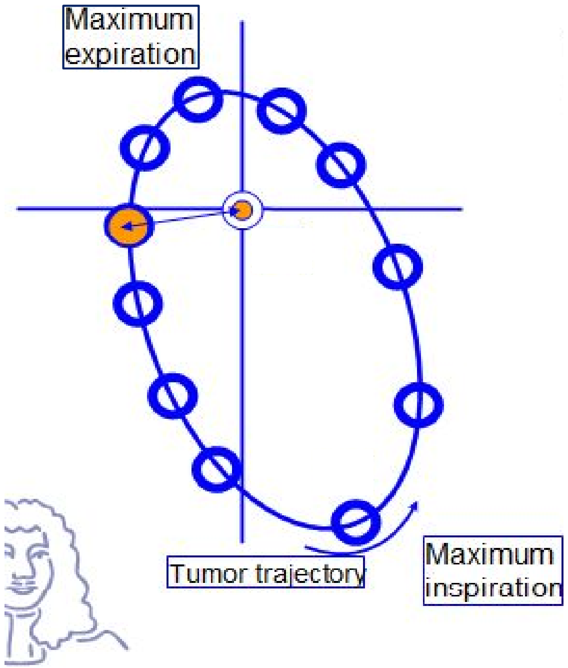


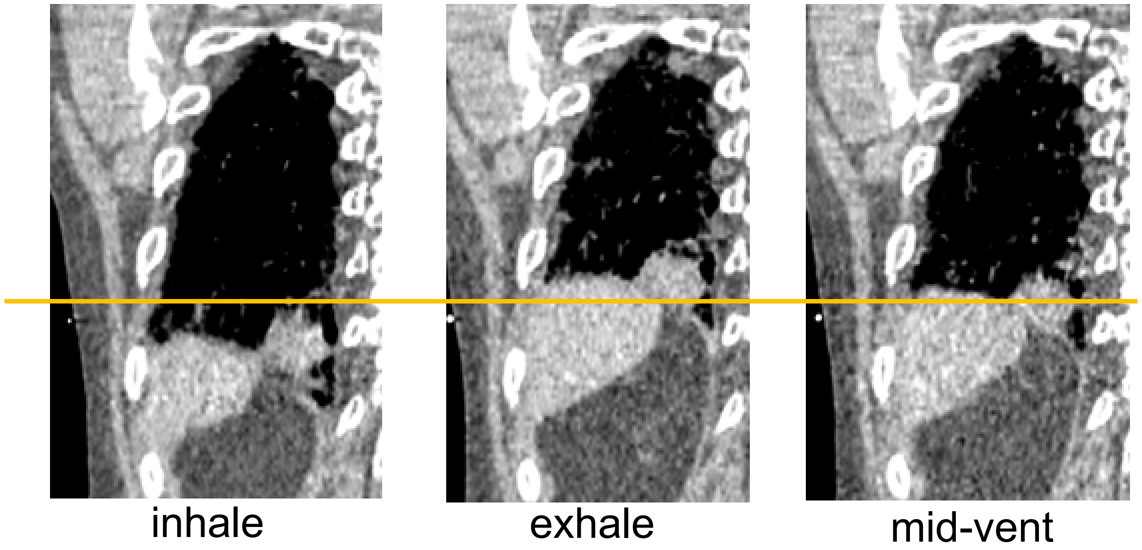

respiration correlated CT

# Dealing with tumor motion

4D CT – mid-ventilation

time-weighted average position



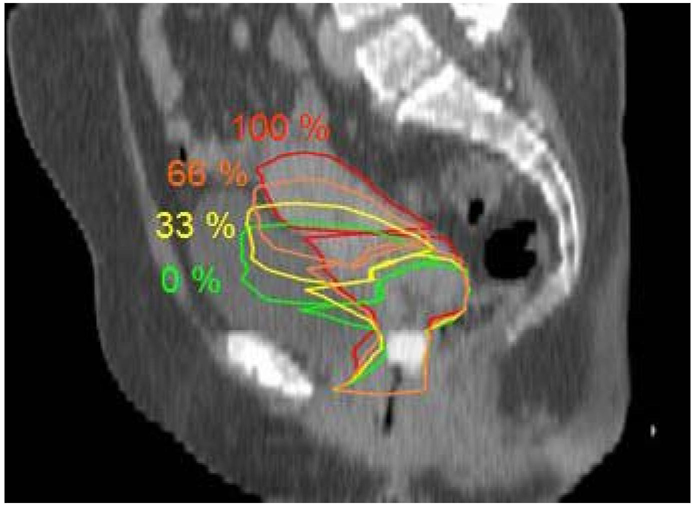



# Dealing with tumor motion

Interfraction changes

"plan of the day"

- >1 CT scan (e.g. with full and empty bladder)
- in-room imaging before treatment
- selection of daily plan from library

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Adaptive RT

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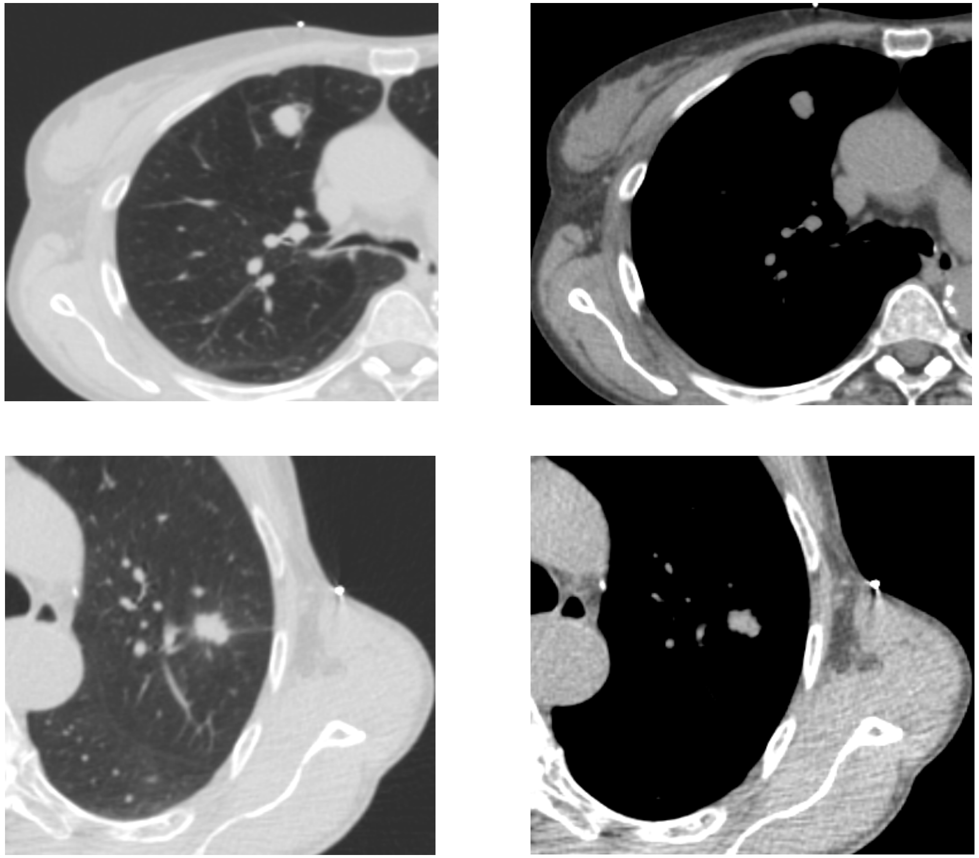
# Treatment preparation – display

Example CT: Window/Level (W/L)



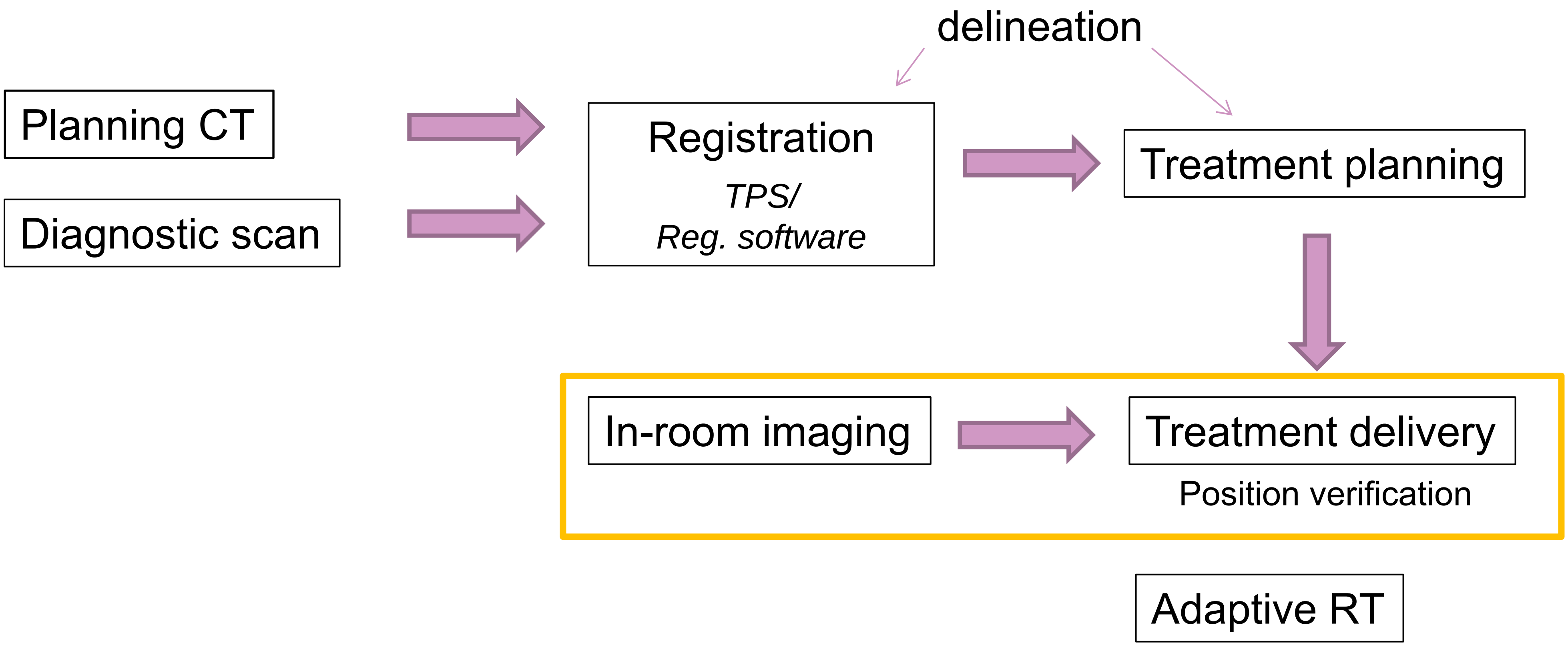
# Treatment preparation – registration

**Purpose**: accurate delineation of tumor and organs at risk

**Challenges/potential errors:**

→ Talk on image registration

# Image data in RT chain



# Treatment delivery – ImageGuidedRT

In-room imaging with

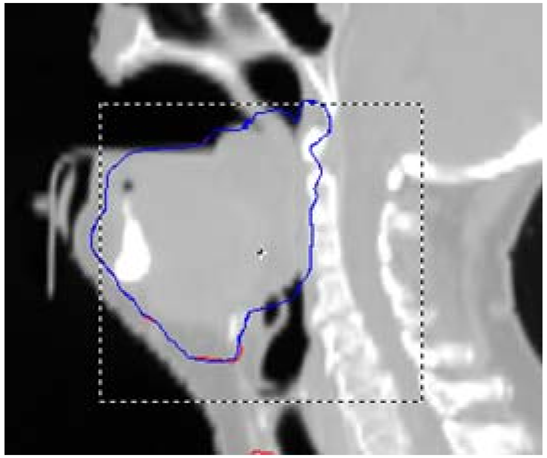
- Portal Imaging (2D)
- Cone Beam CT (e.g. Elekta, Varian)
- MV CT (e.g. Tomotherapy)

- MRI (Viewray, Elekta/Philips)

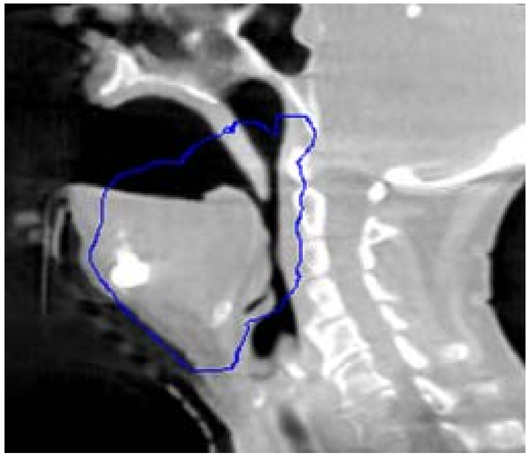
# Treatment delivery – IGRT

Example: CBCT

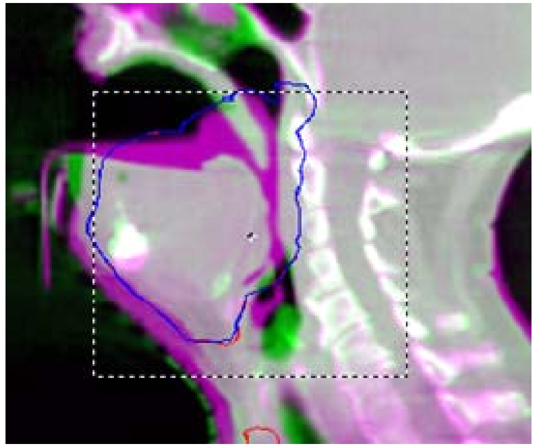
tumor regression



planning CT



CBCT



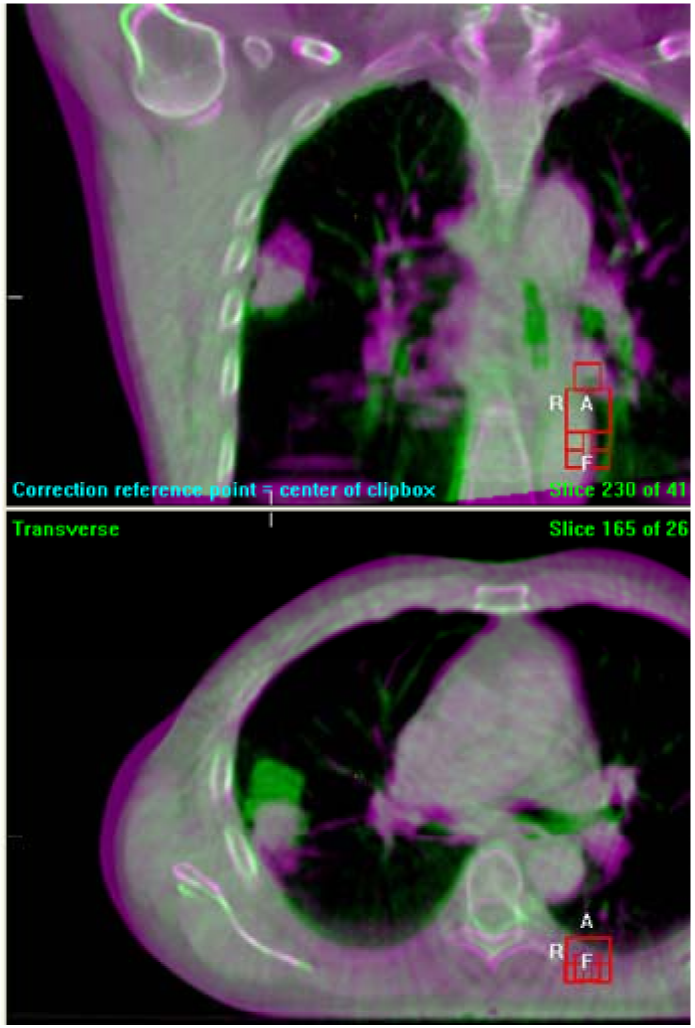
planning CT
CBCT

→ back to the CT scanner

# Treatment delivery – IGRT

Example: CBCT

tumor displacement




planning CT

CBCT

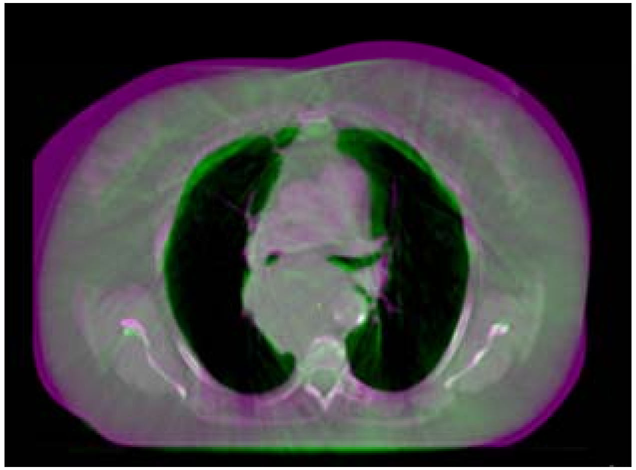
→ back to the CT scanner

# Treatment delivery – IGRT

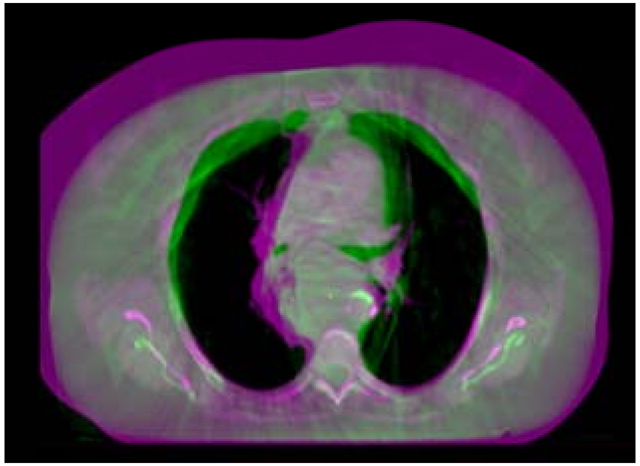
Example: CBCT

weight loss

1st week



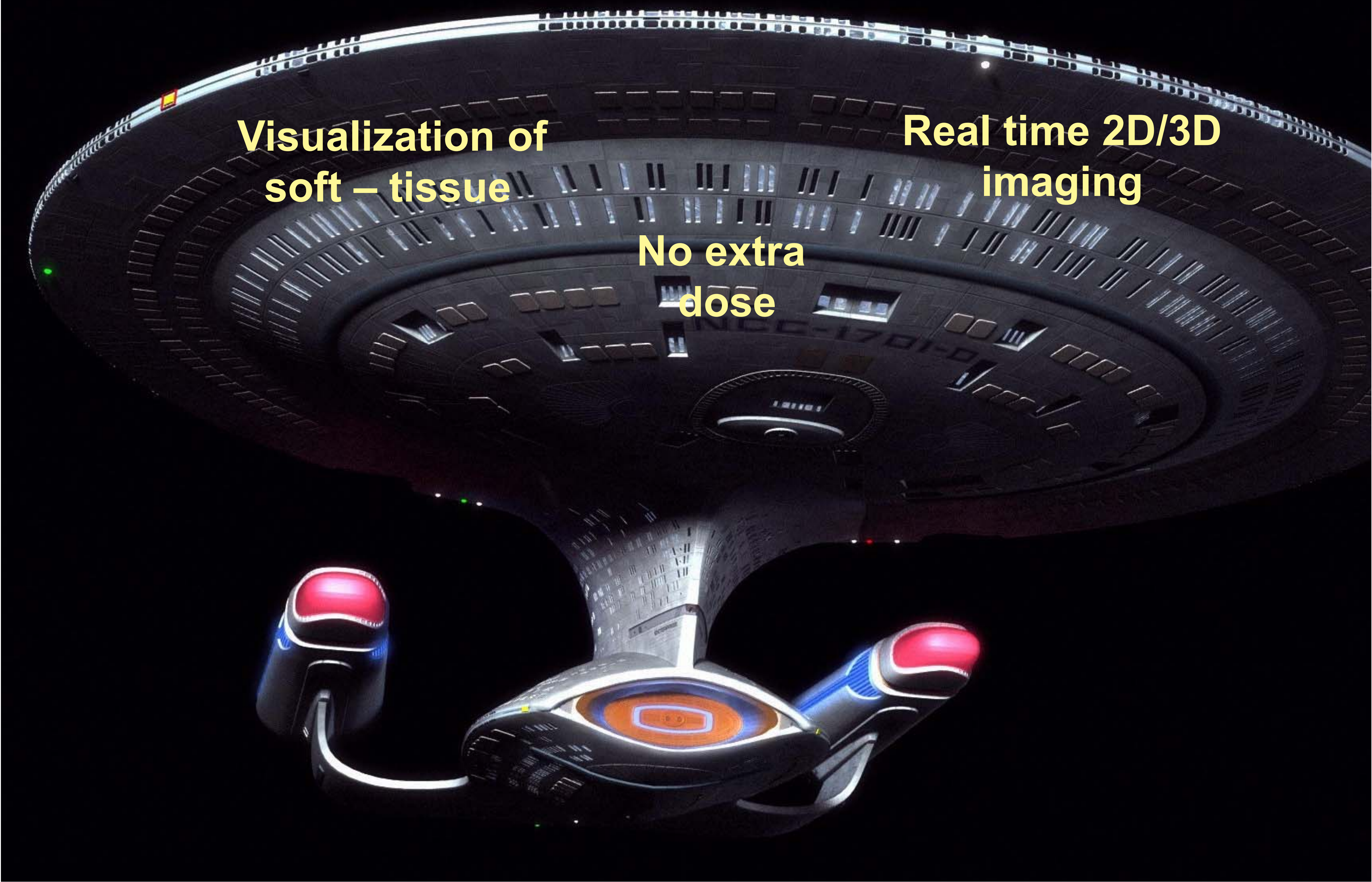
last week of treatment



planning CT

CBCT

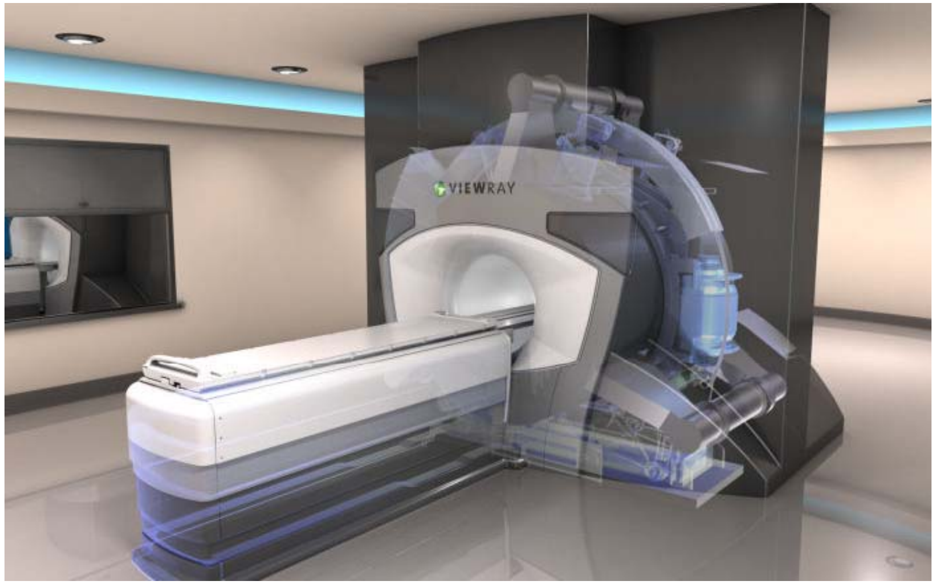
# Next IGRT generation: MR-guided RT



# Treatment delivery

*MR-guided RT*

<u>MRIdian</u> **Viewray**

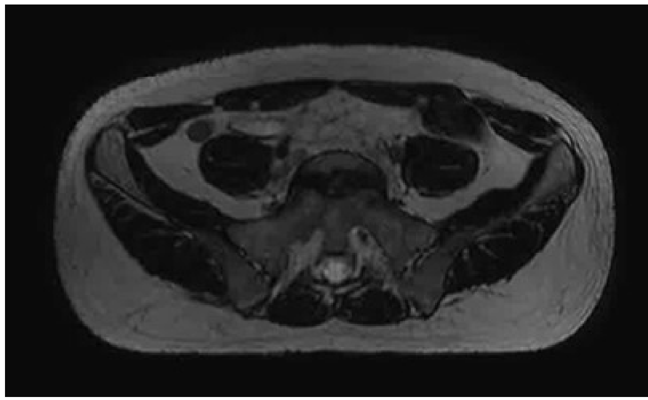



http://medicalphysicsweb.org/cws/article/research/5617916

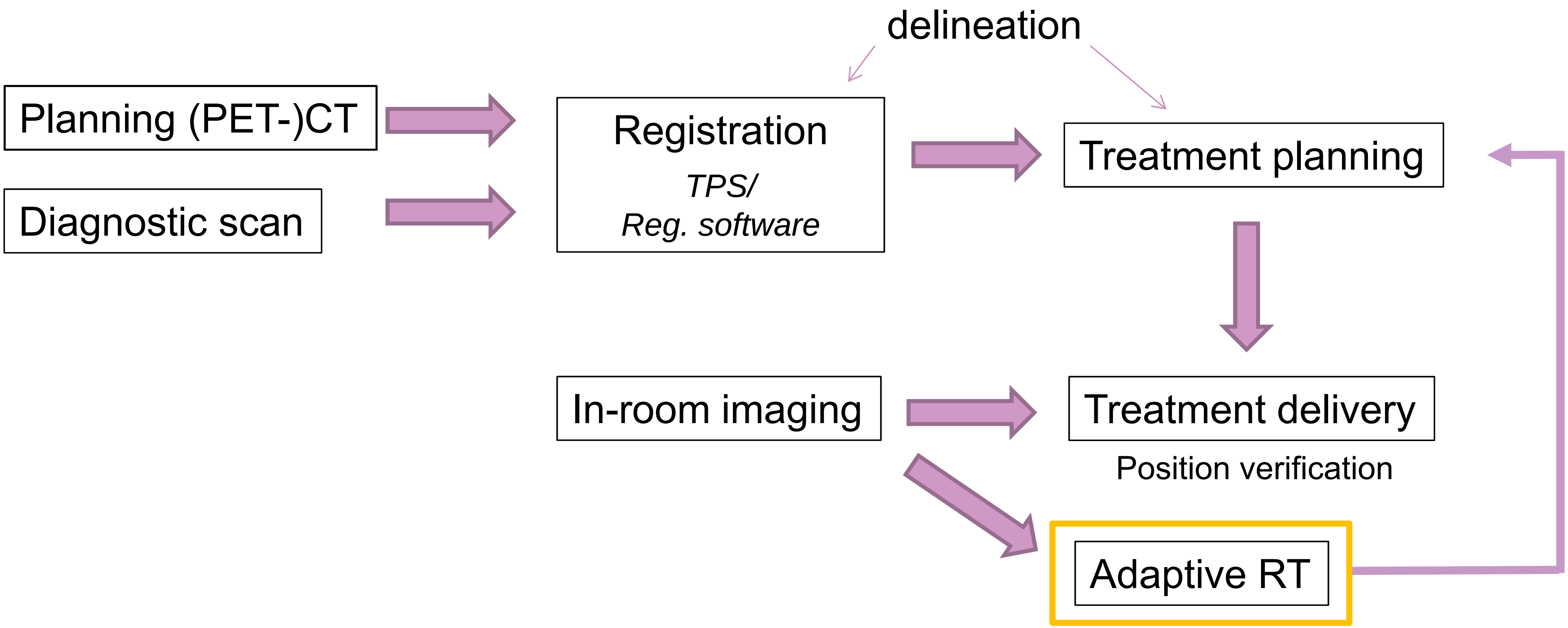
0.35 T split magnet MRI
3 Cobalt-60 teletherapy heads

<u>Atlantic</u> **Philips/Elekta**

CE marking expected 2017
cylindrical 1.5 T closed-bore MRI



# Image data in RT chain

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# Image guided Adaptive RT

= modify treatment plan due to anatomical (or physiological) changes

(**IGRT**: acquire image → (rigid) registration → move isocenter/table)

**Offline ART** ↔ **Online ART**

**Offline ART**

adapt treatment plan between fractions
→ re-contour & re-plan


**Online ART**

- choose plan from "library"
  → plan of the day
- adapt plan "online"
  (while patient on treatment table)

# Image guided Adaptive RT


…when ‘adapting’ tumor target volume as result of gross tumor shrinkage

→ potential of **geographical miss of residual microscopic tumor**

"With Great *Imaging* Comes Great Responsibility"

*Martina*

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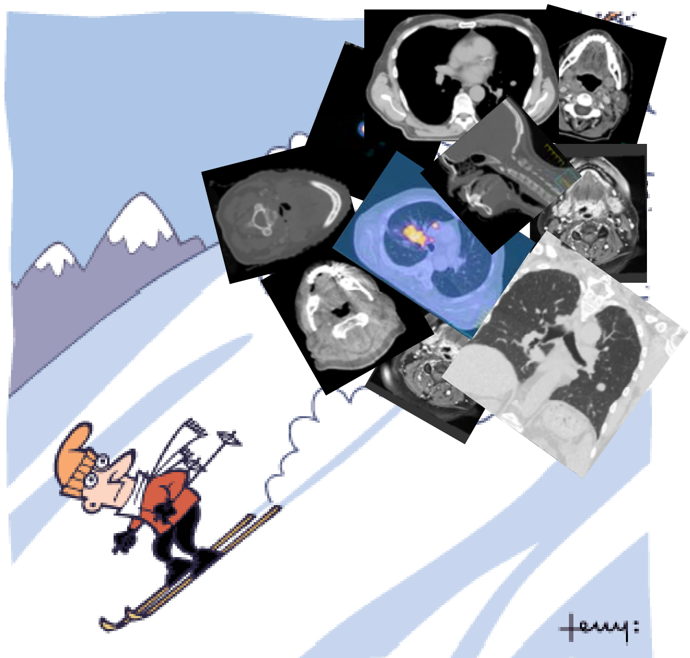
# Take home messages

- Understand imaging techniques and their limitations
- Additional imaging gives additional information & knowledge

→ increases responsibility

- Use extra information with care (e.g. be careful with reducing margins)



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USE

IMAGE WISELY®

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# From uncertainties to margins

Peter Remeijer

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

# Introduction

- Geometrical uncertainties are unavoidable
- Many are patient related
- What types of errors do we get?
- How large a margin do we need?

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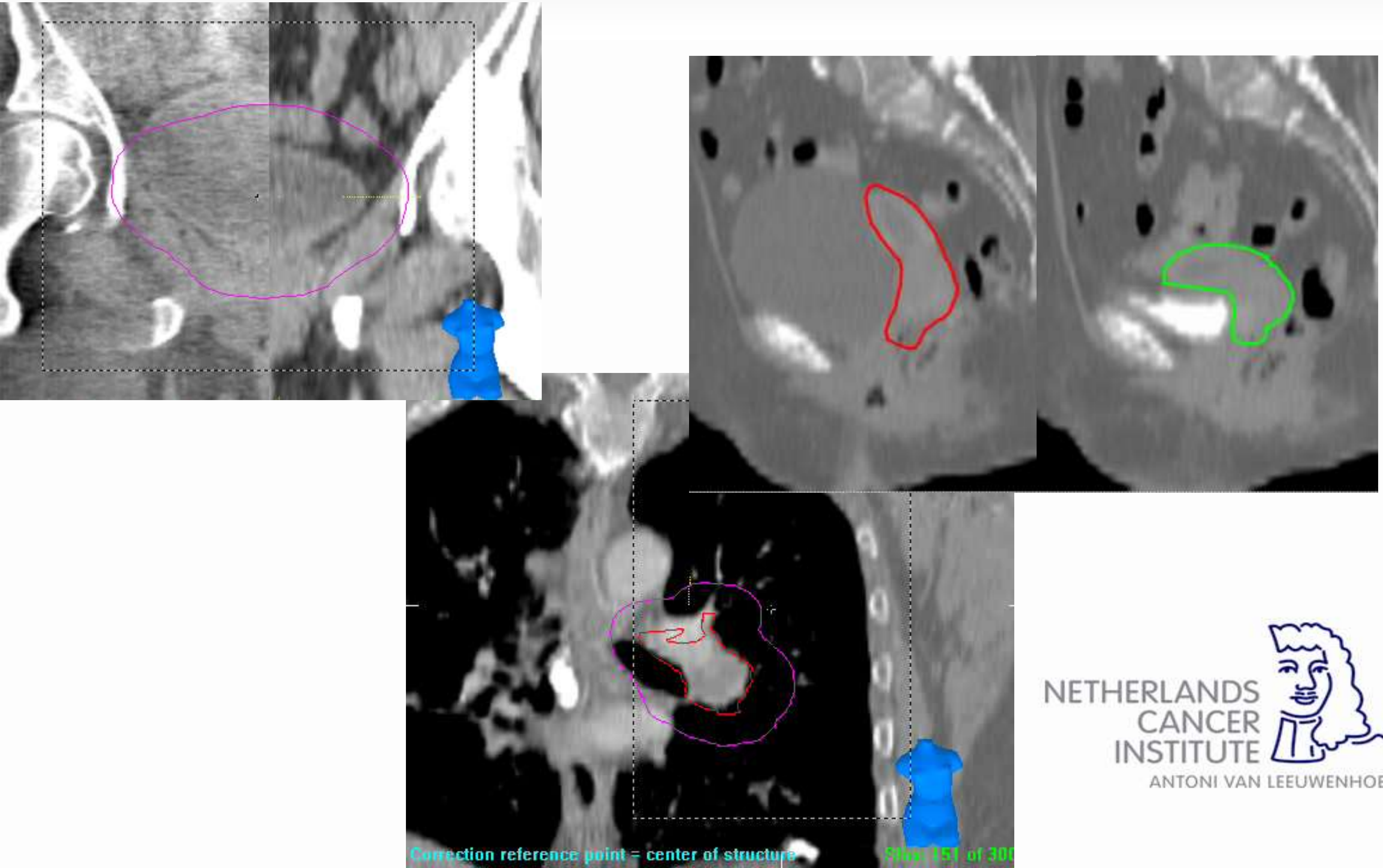
# Some examples

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# The basics

# The radiotherapy chain

1 x

35 x

Patient

Patient →

- CT room
- Lasers
- Skin markers

- Images
- Bone
- Tumor
- Delineation
- Margin
- Planned beam

- Treatment room
- Lasers
- Skin markers
- Bone
- Tumor

- Beam
- Accelerator
- Treatment room

Patient data

*17 steps with a lot of room for errors*

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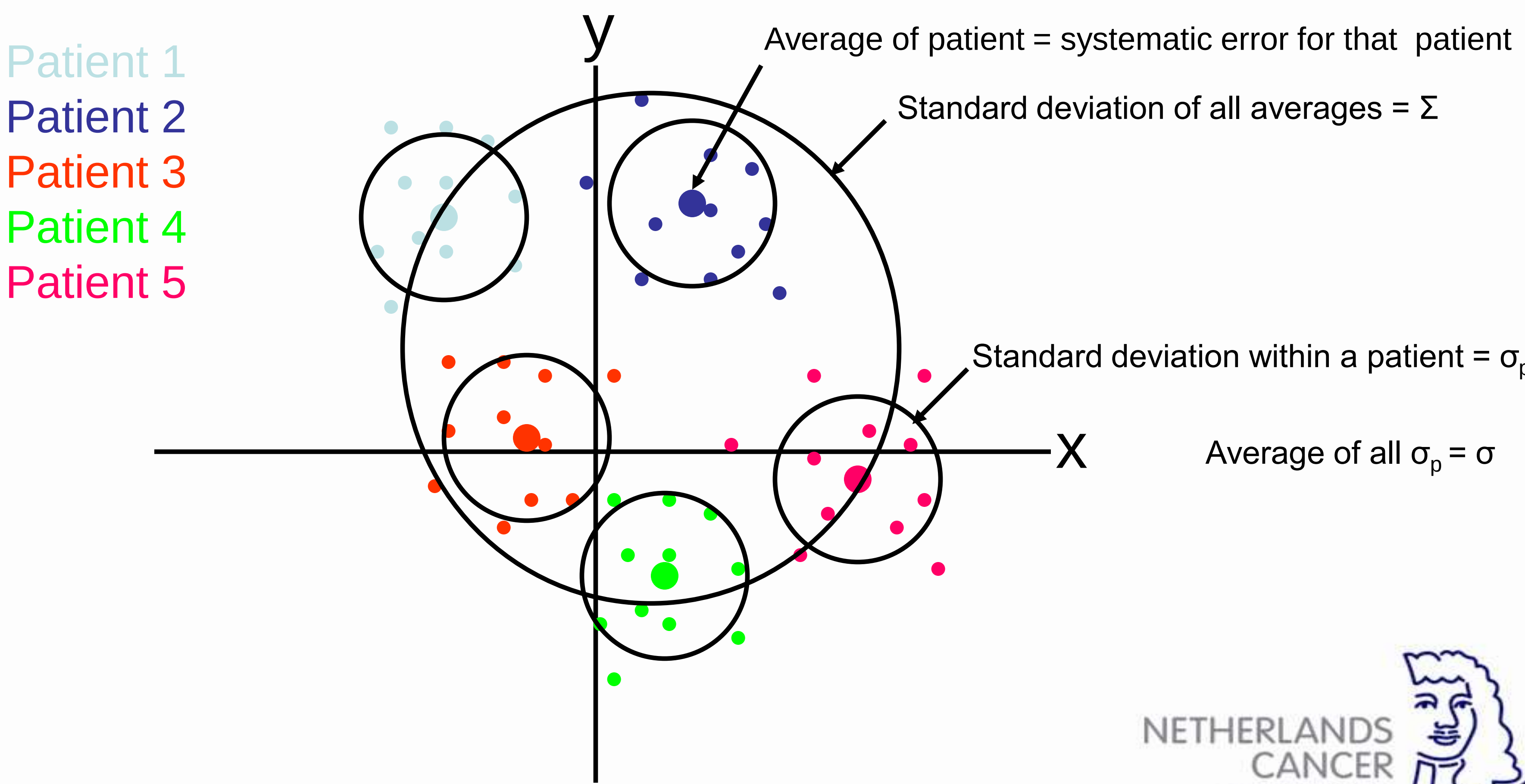
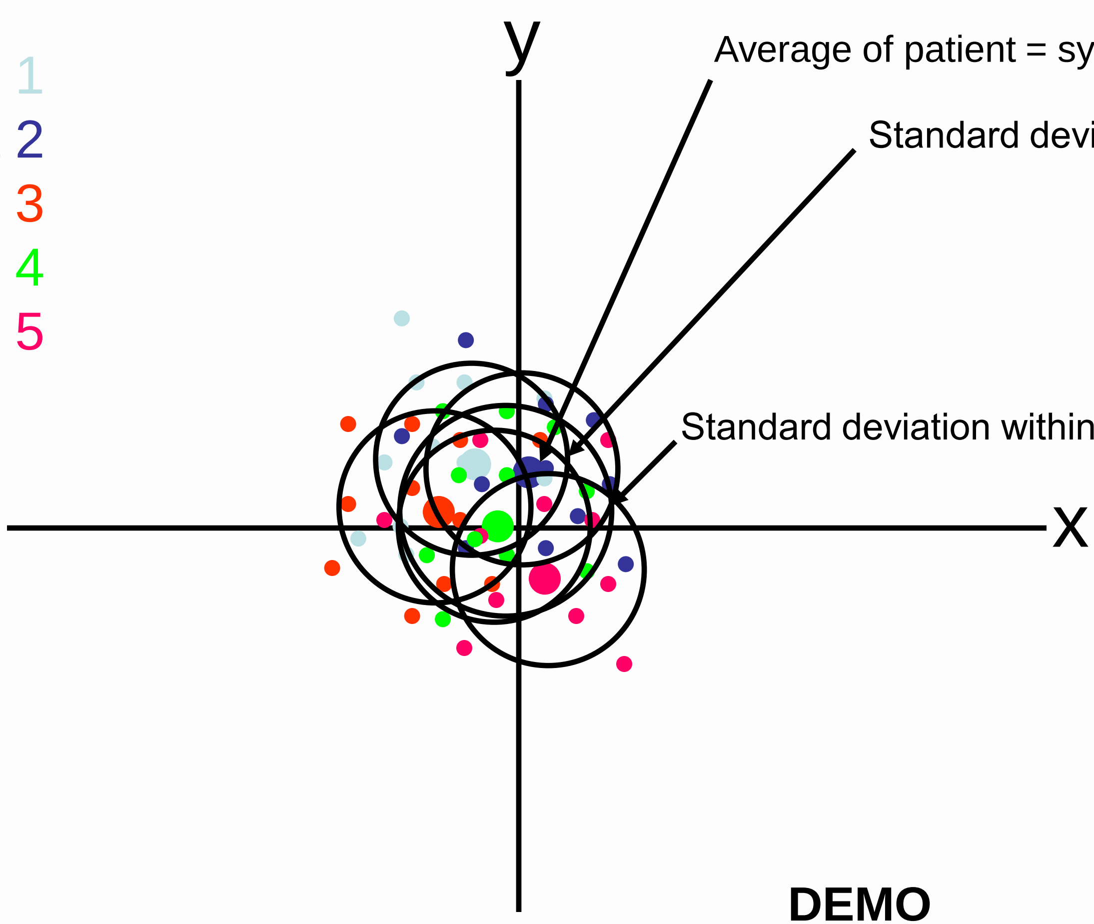
# Geometrical uncertainties



# Geometrical uncertainties

Patient 1
Patient 2
Patient 3
Patient 4
Patient 5




**DEMO**

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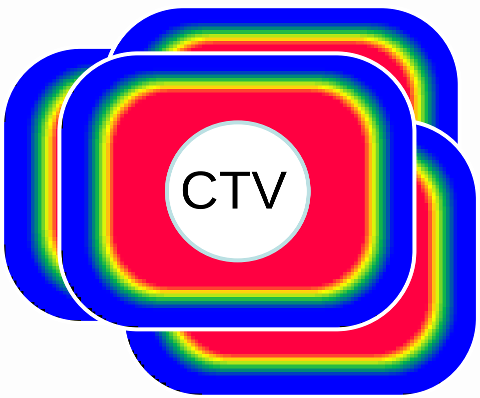
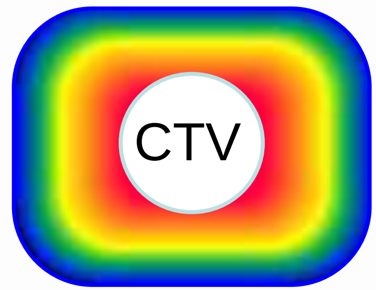
# Effect of geometrical errors

Random errors (σ) **blur** the cumulative dose distribution

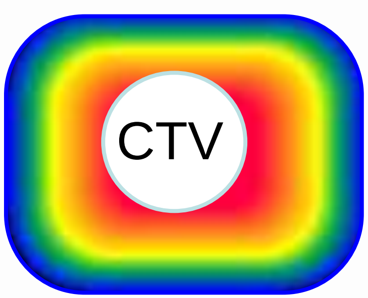


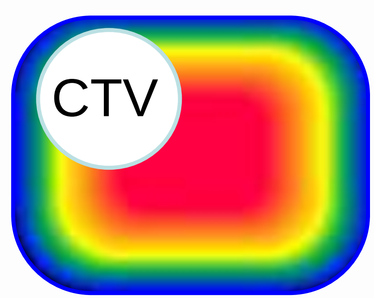

*Single fraction doses with random shifts*




*All fraction doses added*

Systematic errors (Σ) **shift** the cumulative dose distribution




*Average dose distribution shifts*

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# Geometrical uncertainties

- Systematic
  - Same for whole treatment
  - Shifts the dose distribution
  - May be different for each patient but the same for one patient
  - Quantified with standard deviation $\Sigma$

- Random
  - Different every day
  - Some patients may have larger variations from day to day than others
  - Blurs the dose distribution
  - Quantified with standard deviation $\sigma$

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# Many varieties

- Translational errors
- Rotational errors
- Shape changes

# But also different sources!

| Source | Systematic | Random | Solution |
|---|---|---|---|
| Delineation | 1-?? Mm | - | Multiple modalities |
| Setup | 1-5 mm | 1-5 mm | Portal imaging |
| Organ motion | <1-50 mm | <1-50mm | Markers<br>Repeat CT |

And all come as translations / rotations / deformations!

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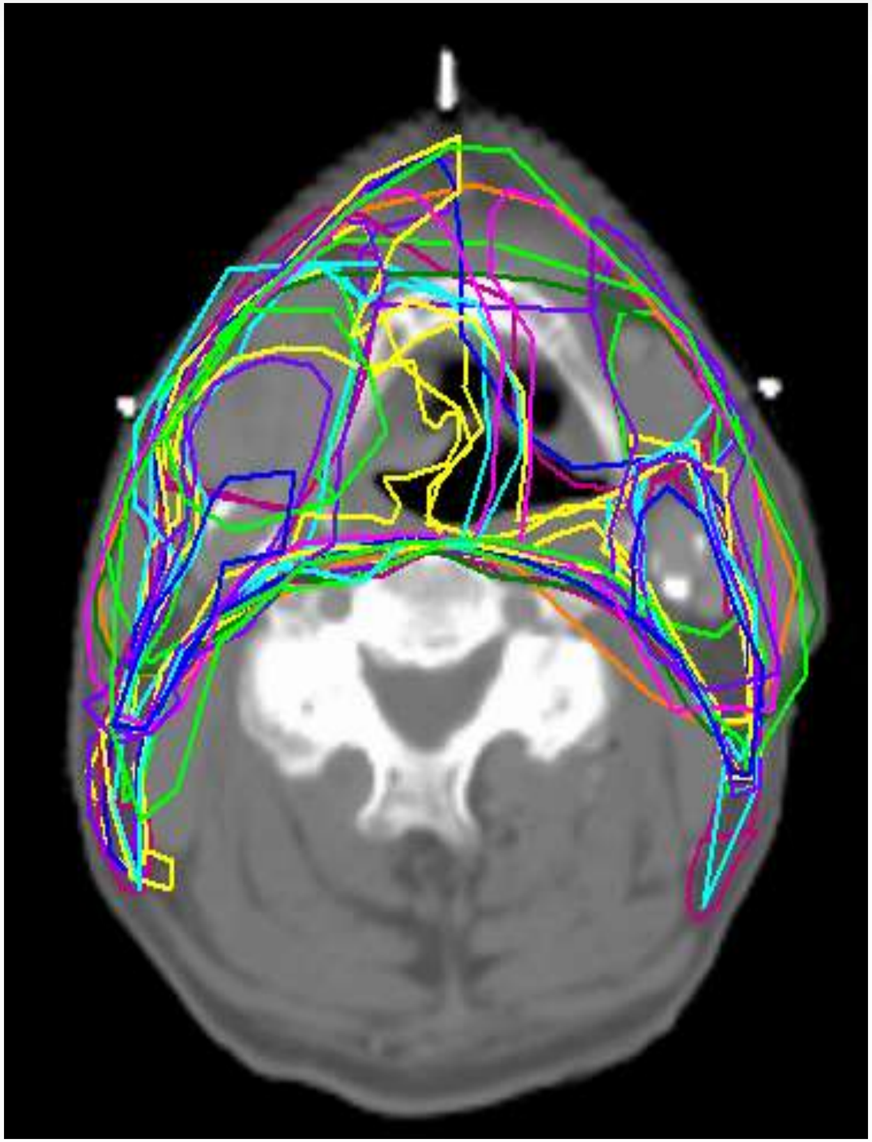
# Examples of geometrical uncertainties

# Delineation variation



- Previous TVD course
- Individual participants

back

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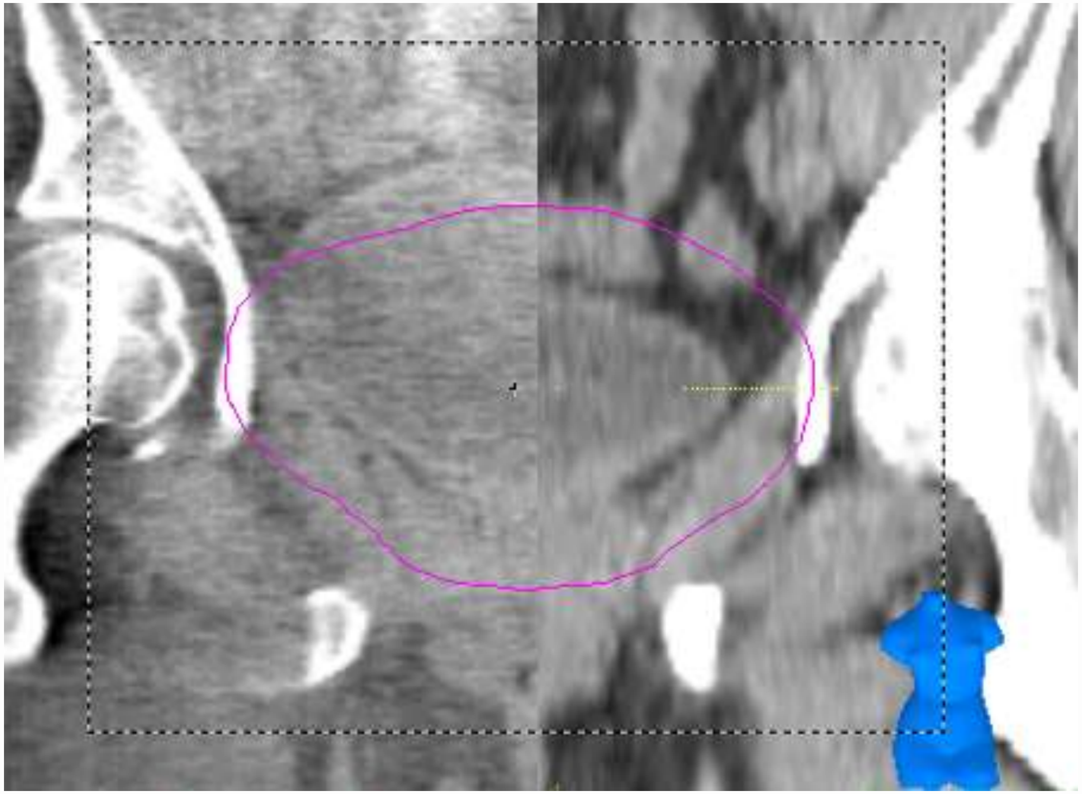
# Prostate motion

- Large amount of air in rectum during planning scan
- Not present during treatment

# Bladder filling changes

- Bladder volume is larger in the CBCT scan than in the planning scan



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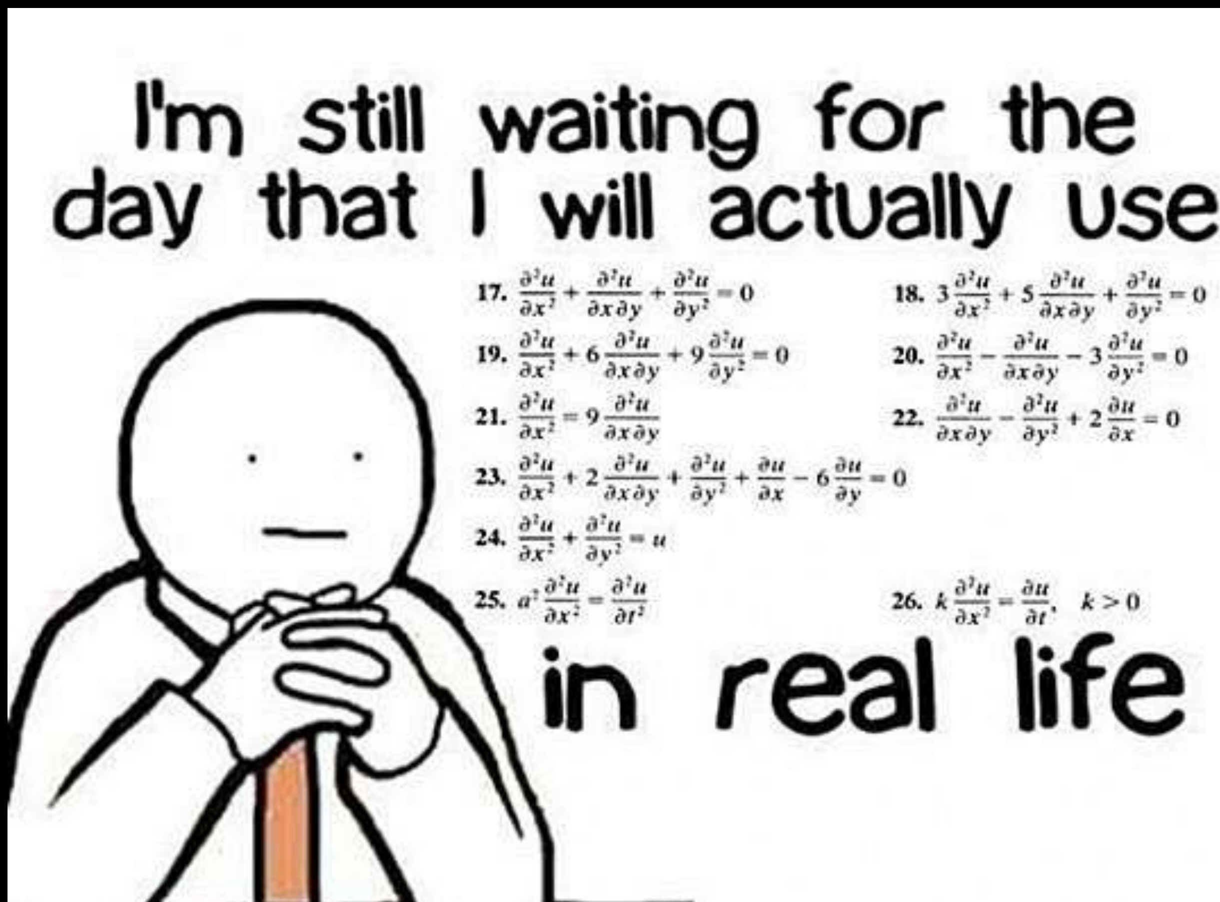
# So how do we determine these errors?



# Determining the uncertainties

- Imaging!

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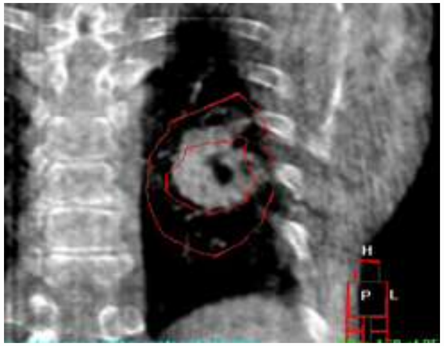
# Determining the uncertainties

- We can image the patient from fraction to fraction and analyze the geometrical changes
- Image tumor




- Use surrogates
  - Fiducials

  - Bony anatomy (margin for organ motion!)

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# Determining the uncertainties

- Register bony anatomy → Setup error

- Register tumor position → Organ motion

- Analyse re-delineation → Delineation variability

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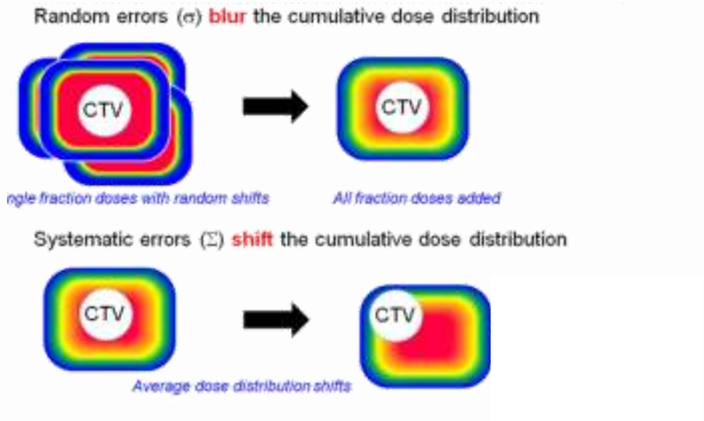
# Margins

# How do we determine the PTV margin?

- Effect of random and systematic errors on the dose distribution is different




→ We need a separate approach!

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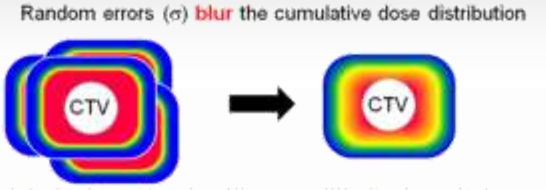
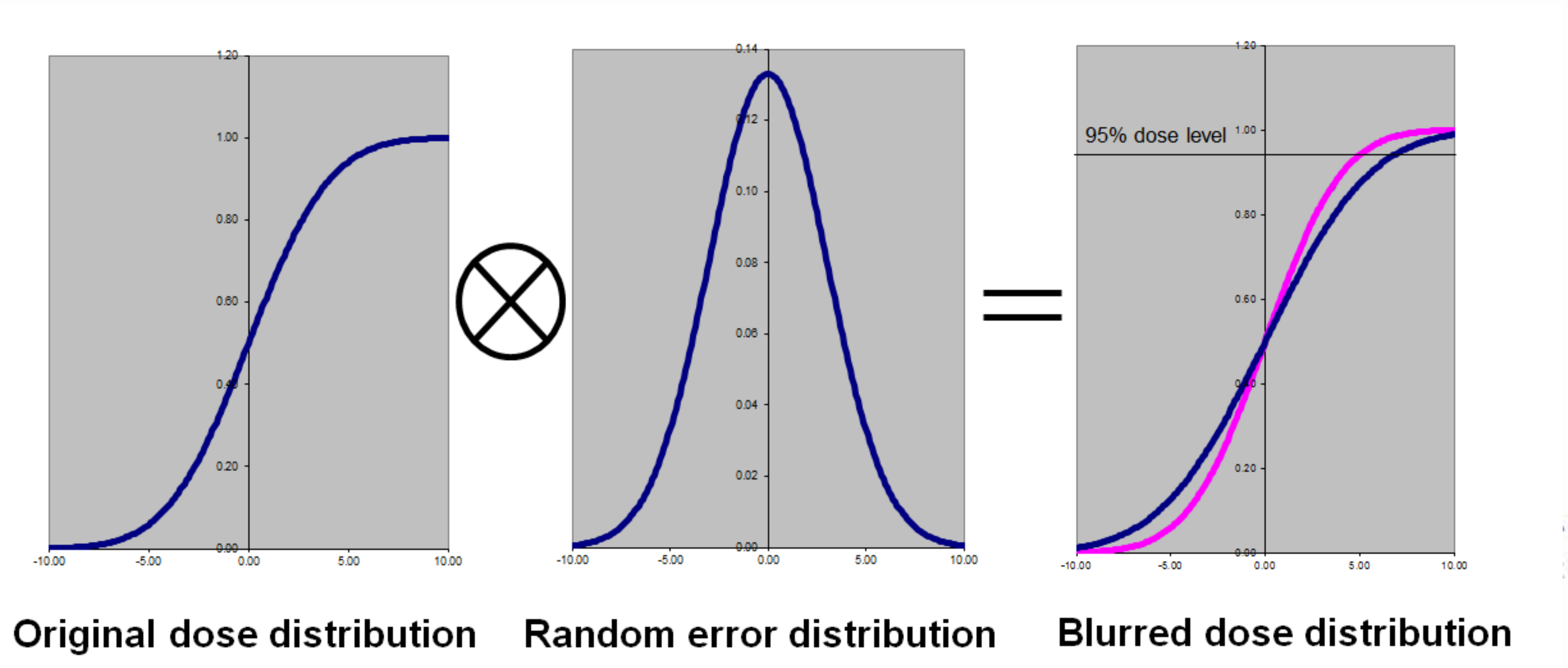
# Margins for random errors




- Random errors <u>blur</u> the dose distribution
  - Translations : Convolution dose with error distribution
  - Rotations : Convolution dose with error distribution (Bel)



# Margins for random errors

- Margin for random errors:

→Difference at 95 % dose level (i.e. the dose level of interest) before/after convolution

- Example

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# Margins for random errors

| Dose level | PTV margin | PTV margin* ($\psi$ = 3.2 mm) |
|---|---|---|
| 80% | $0.84 \sqrt{(\sigma^2 + \psi^2)} - 0.84\,\psi$ | $0.4\,\sigma$ |
| 85% | $1.03 \sqrt{(\sigma^2 + \psi^2)} - 1.03\,\psi$ | $0.5\,\sigma$ |
| 90% | $1.28 \sqrt{(\sigma^2 + \psi^2)} - 1.28\,\psi$ | $0.6\,\sigma$ |
| 95% | $1.64 \sqrt{(\sigma^2 + \psi^2)} - 1.64\,\psi$ | $0.7\,\sigma$ |

**$\sigma$ = SD of random errors,**

**$\psi$ = $\sigma$ of Gaussian penumbra**

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*linear approximation

# Margins for systematic errors


- Systematic errors <u>shift</u> the dose distribution
  - But we don't know in advance in which direction!

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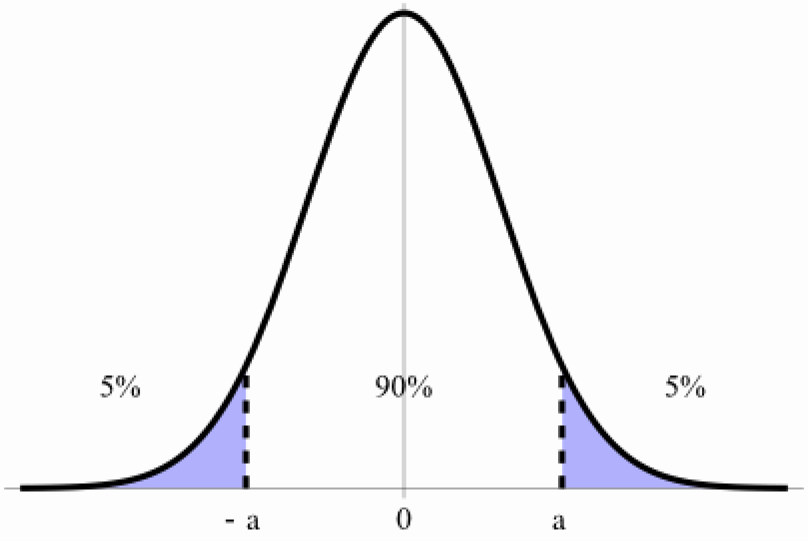
# Margins for systematic errors

- Systematic errors shift the dose distribution
  - But we can say something about the "target area' if we know the distribution of the errors, i.e. the standard deviation

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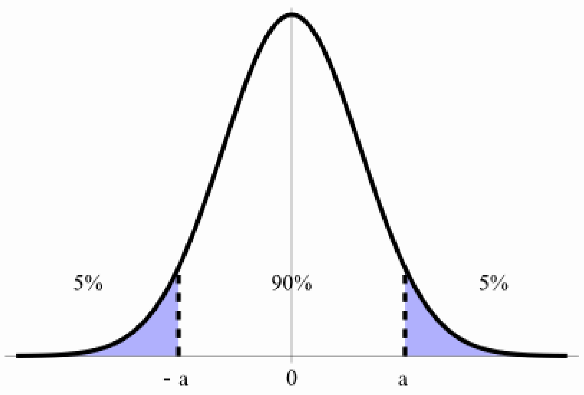
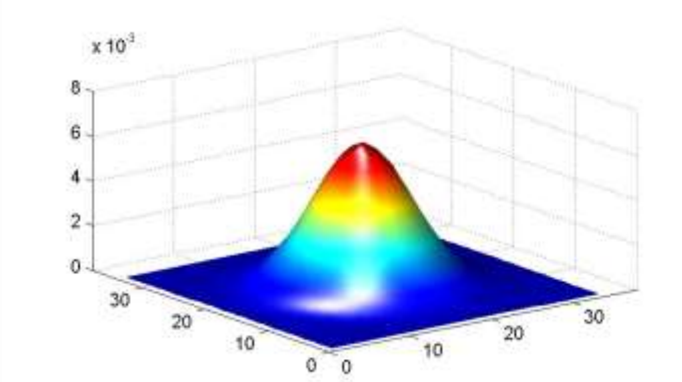
# PTV for systematic translations

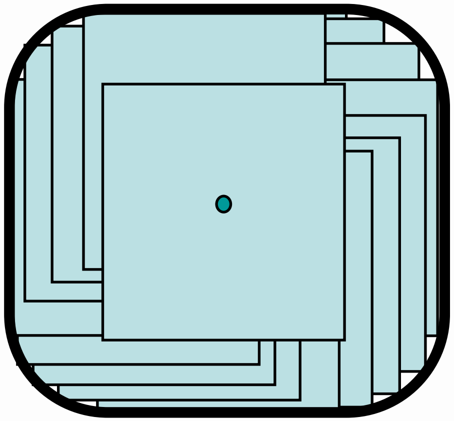
- 90 % Confidence interval
  - 1-D : $\pm 1.64\ \Sigma$
  - 2-D : Ellipse with radii 2.15 $\Sigma_{x,y}$
  - 3-D : Ellipsoid with radii 2.50 $\Sigma_{x,y,z}$

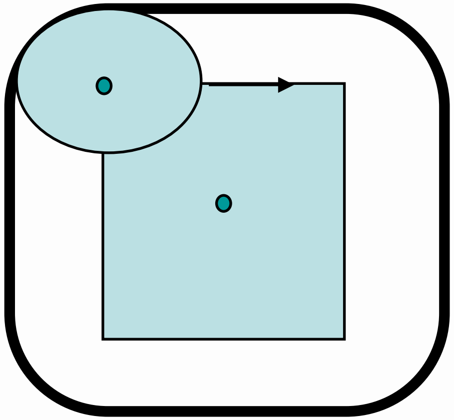


# Margins for systematic translations

- Select point in (square shaped) CTV
- Determine CI = Ellipse with radii $\alpha\Sigma_{x,y}$ mm *
- Determine envelope of all CTVs in CI





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*90% 2D CI: $\alpha$=2.15

# Margin for systematic errors

| Confidence level | 1-D errors | 2-D errors | 3-D errors |
|---|---|---|---|
| 80% | 1.28 Σ | 1.79 Σ | 2.16 Σ |
| 85% | 1.44 Σ | 1.95 Σ | 2.31 Σ |
| 90% | 1.64 Σ | 2.15 Σ | 2.50 Σ |
| 95% | 1.96 Σ | 2.45 Σ | 2.79 Σ |

Σ = SD of preparation/systematic errors

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# Margin recipe

- To cover 90% of the patients with the 95% isodose level:

**Margin = 2.5 * Σ + 0.7 * σ**

Where

$$\Sigma = \sqrt{\Sigma_{organmotion}^2 + \Sigma_{setup}^2 + \Sigma_{delineation}^2}$$

$$\sigma = \sqrt{\sigma_{organmotion}^2 + \sigma_{setup}^2}$$

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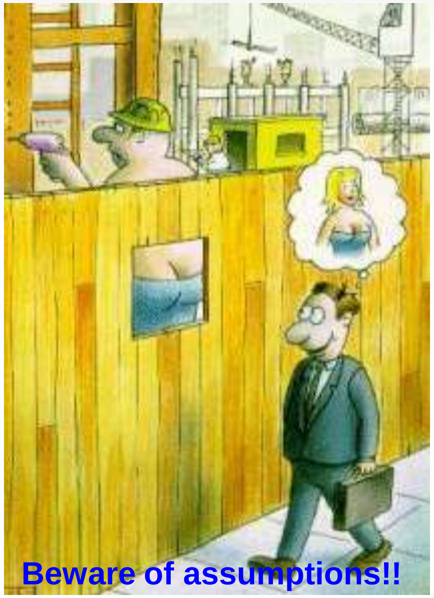
# Keeping things in perspective

- Margin recipe assumptions
  - Perfectly conformal dose distribution
  - Large and smooth (compared to penumbra size) CTV
  - Translational errors only
  - Homogeneous dose distribution
  - Large number of fractions (for the 0.7 part)




- Real life
  - Not conformal, i.e. margin will depend on shape of dose distribution
  - Not smooth
  - Lots of changes → translations, rotations, shape changes…
  - Inhomogeneous dose distributions
  - Any number of fractions (or very few!)

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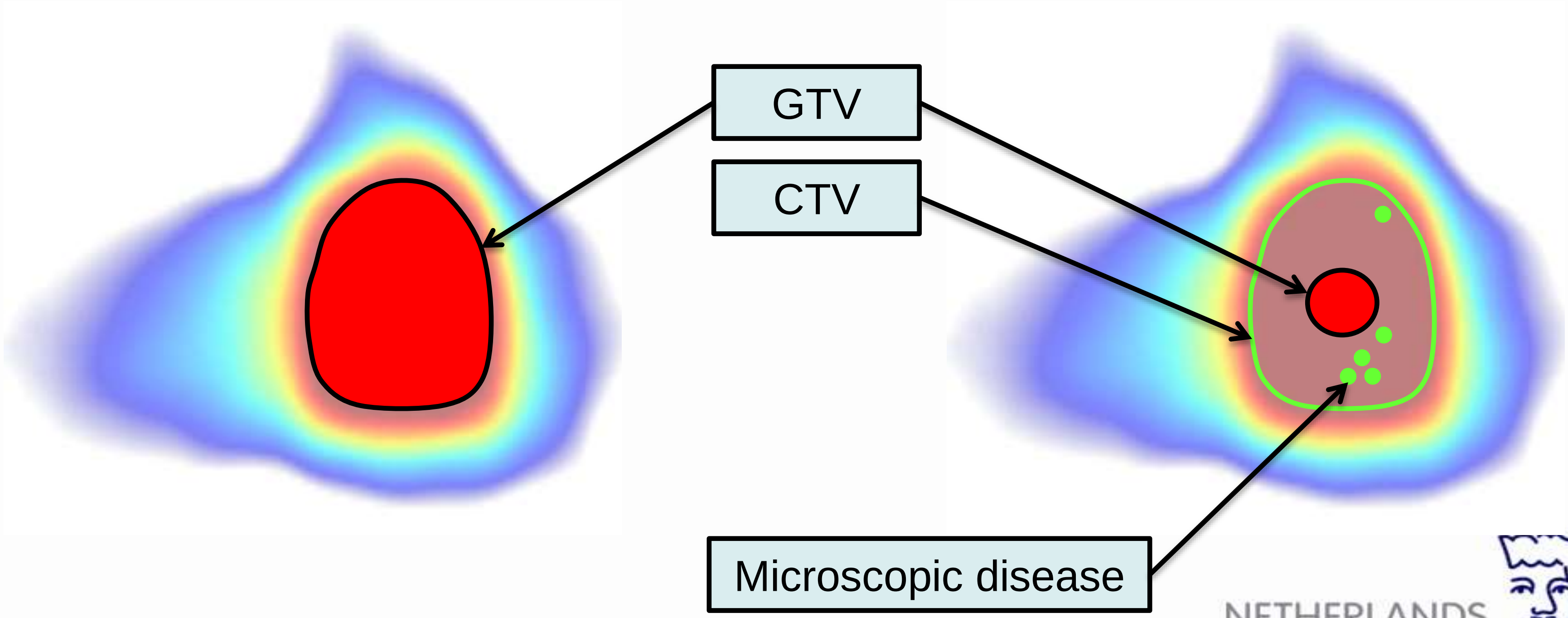
# GTV versus CTV underdosage

GTV: Whole volume tumor

CTV: Probability of tumor

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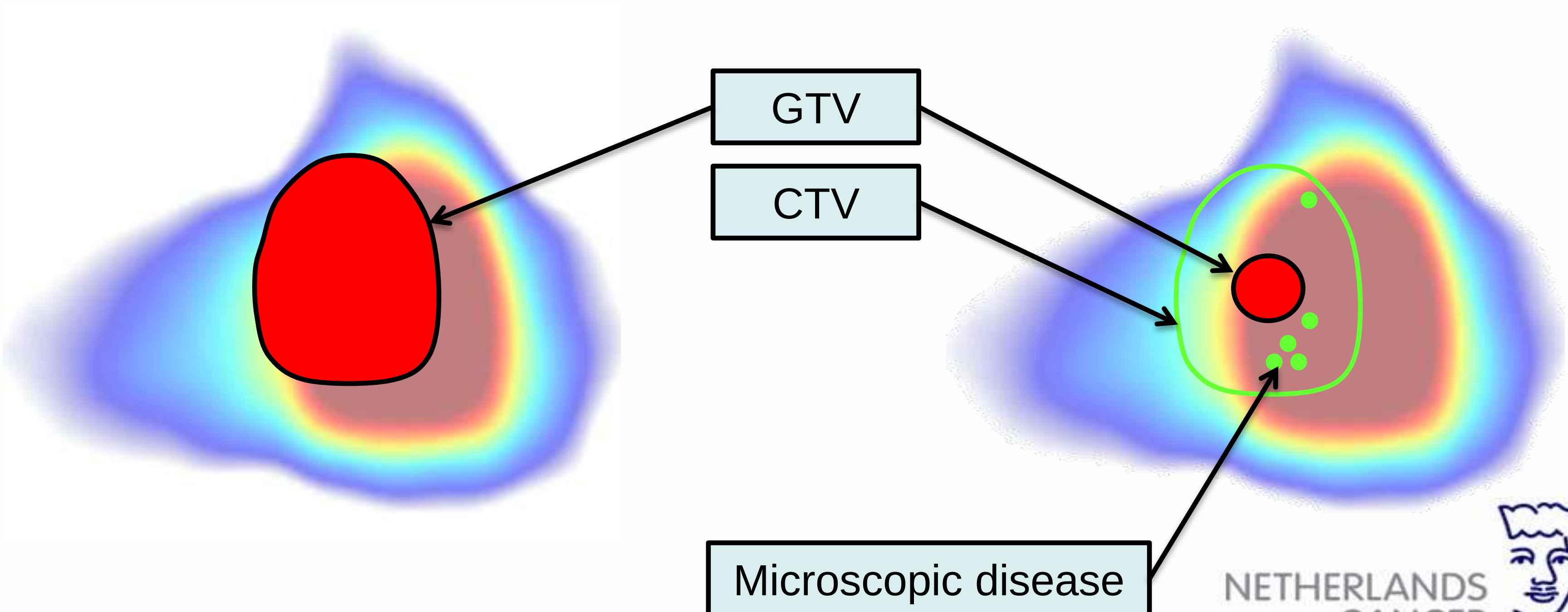
# GTV versus CTV underdosage

Underdosage of GTV will always lead to underdosage of tumor cells

Underdosage of CTV will **not** always lead to underdosage of tumor cells

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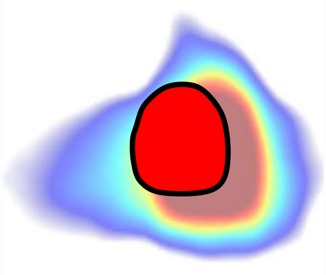
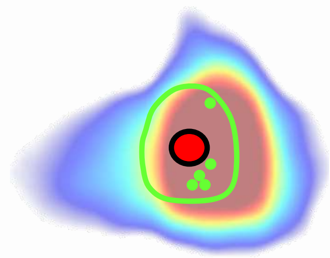
# Keeping things in perspective

- GTV → PTV margin
  - All cells in the GTV are considered to be tumor
  - $P_{underdosage} = P_{geometrical\ miss}$
  - Use margin prescription



- CTV → PTV margin
  - In the CTV there is a probability of tumor cells
  - $P_{underdosage} = P_{geometrical\ miss} \times P_{presence\ of\ tumor\ cells}$
  - Margin can probably be smaller



- Caveat: Tumor cell probability is needed

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# Conclusions

- Systematic errors have different and **larger** dose effects than random errors
- A margin is always necessary. Without the proper margin underdosage will occur
- To determine margins it is important to now the statistics of the geometrical errors
- Since delineation uncertainties are systematic, they will have a large effect on the required margin

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# Deformable Image Registration

Martina Kunze-Busch
Radboud University Medical Center Nijmegen
The Netherlands

Peter Remeijer
Netherlands Cancer Institute
The Netherlands

Radboudumc NKI-AVL The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital ESTRO School

# Overview

- Introduction (M.Kunze-Busch)
- Clinical practice at the AvL (P.Remeijer)

# Available software programs

Features include (among others)

- atlas based auto contouring
- deformable image registration
- dose accumulation

….

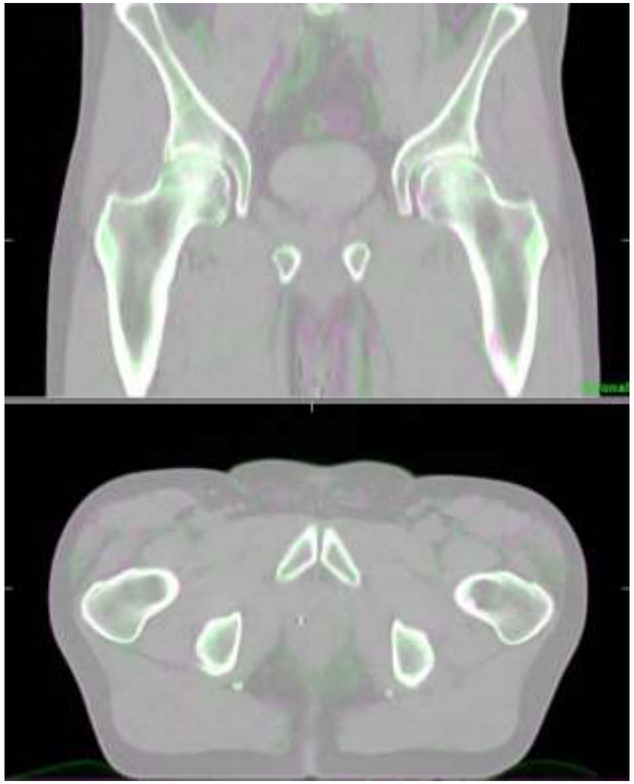
and some treatment planning systems


JUST DO IT.

CAUTION

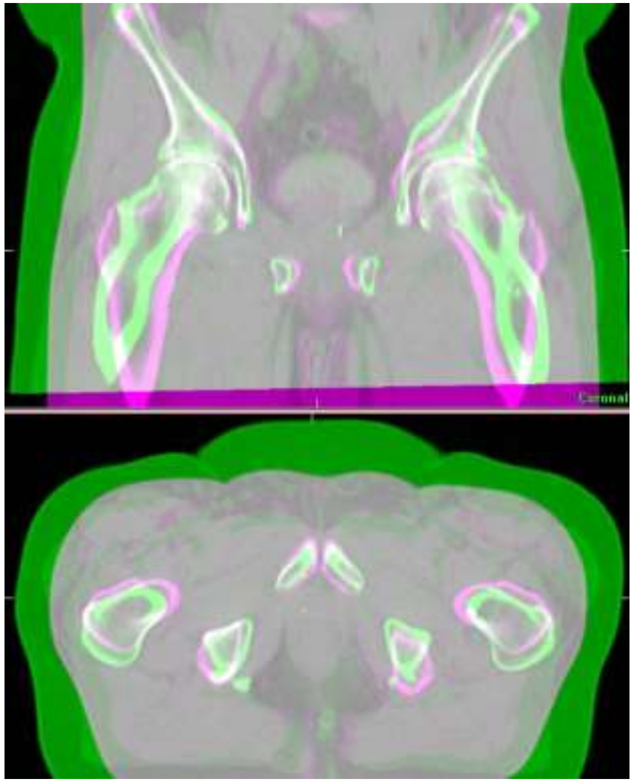
deformable image registration

deformable image registration



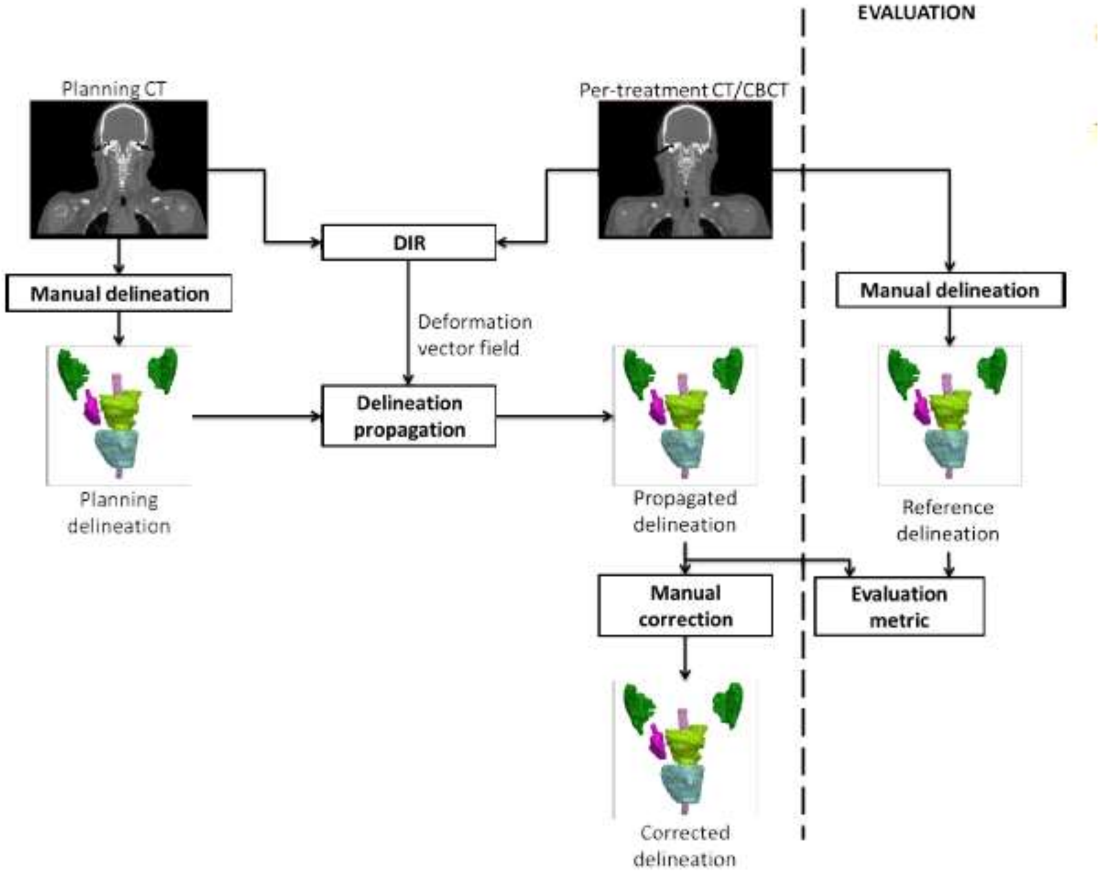
reality

without deformable image registration



# Main applications of DIR in ART

Delineation propagation ✓

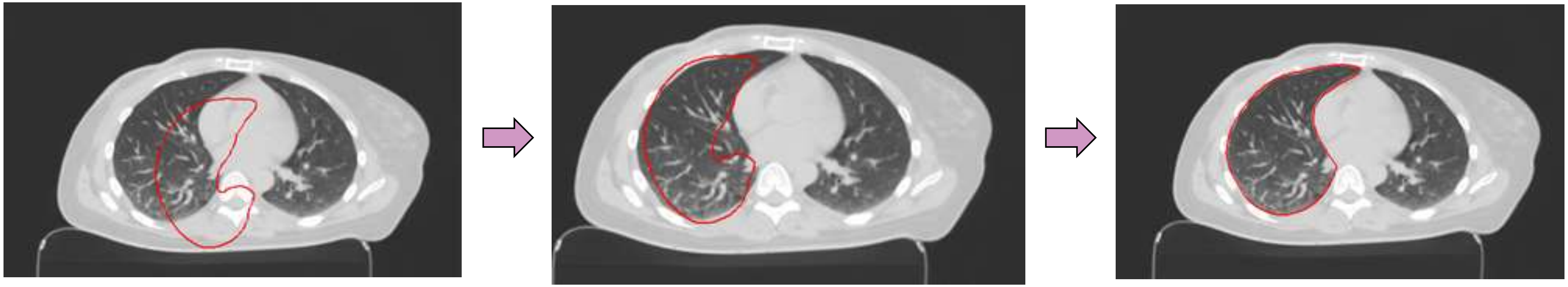



Ref: Simon et al., Conf Proc IEEE Eng Med Biol Soc. 2015

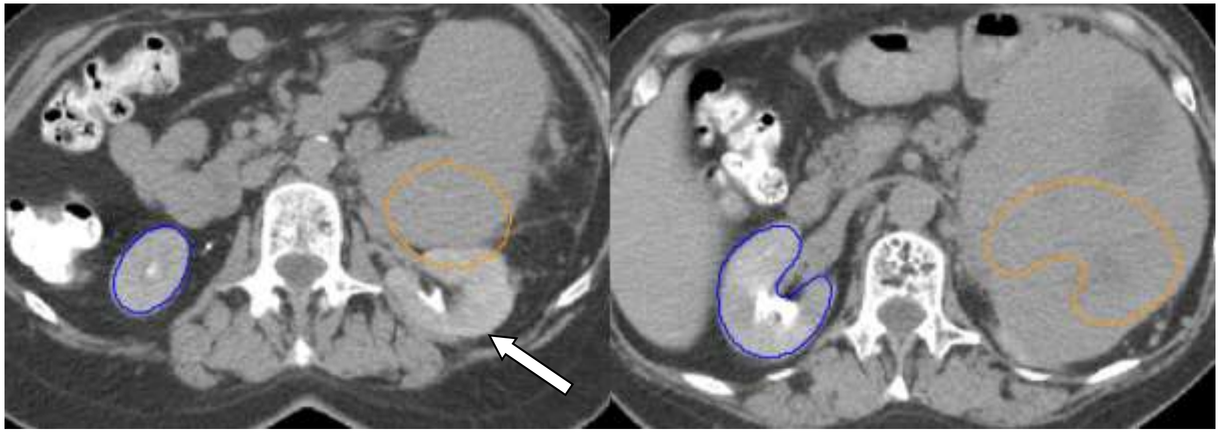
# Atlas based segmentation

Would you tell me, please, which way I ought to go from here?
That depends a good deal on where you want to get to.

Alice and the Cat, "Alice in Wonderland"(1951)

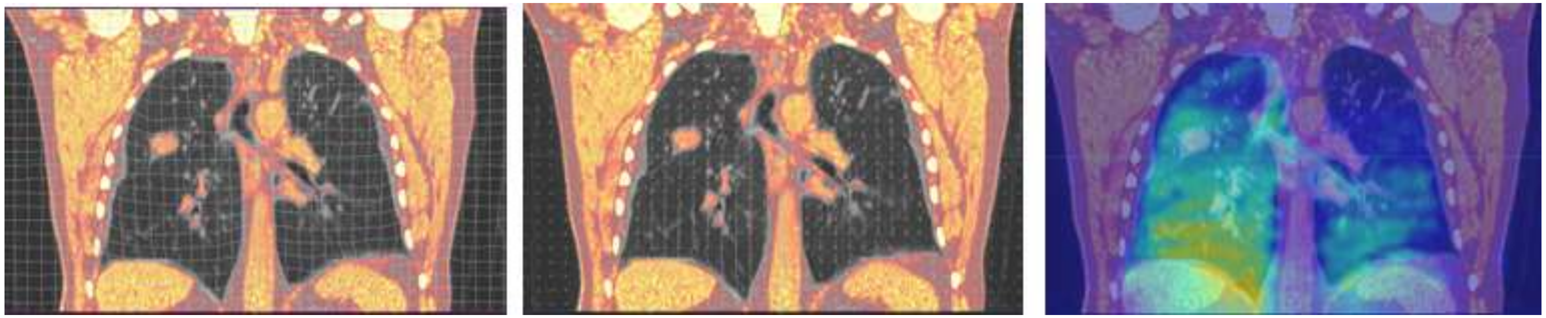


CAUTION



# Evaluation of registration

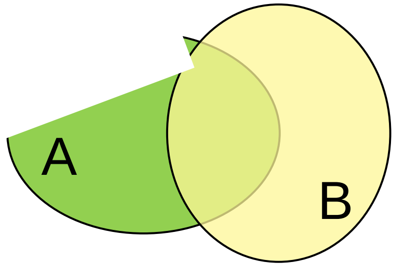
## Visual inspection of deformation field




## Common metrics

- Volume based metric: DICE si

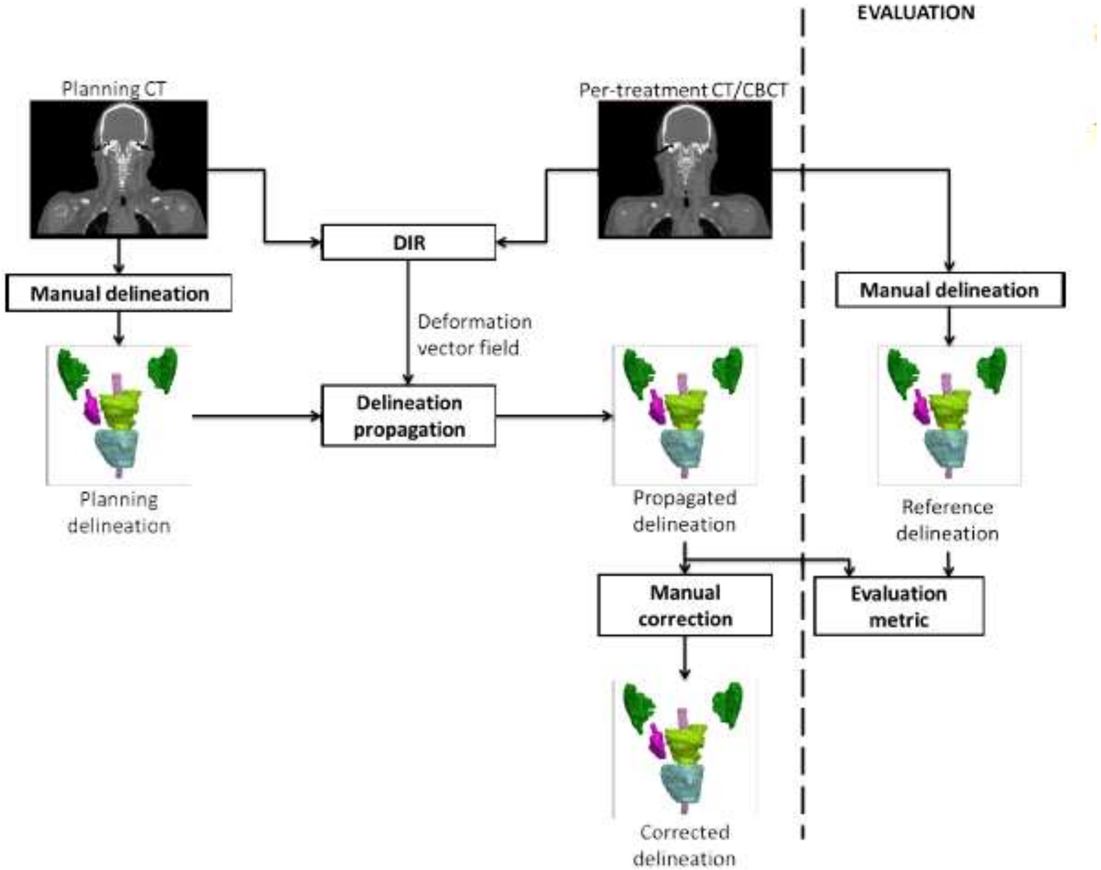
Metrics not a reliable criteria for registration accuracy




- Surface base
usdorff Distance, DTA distance to agreement

# Main applications of DIR in ART

Delineation propagation ✓




Dose accumulation


not yet validated for clinical practice

Ref: Simon et al., Conf Proc IEEE Eng Med Biol Soc. 2015

CAUTION

Dose warping/mapping

warped dose uncertainty
=
spatial error (due to registration) x dose gradient

*Prof. Jean Pouliot*
*AAPM 2014*

active area of research and discussion

IJROBP 2014) Mencarelli et al.
“Ca... applying DIR for tumor ...ve procedures”

Med P...
It is...

...dose along with ...on in adaptive RT

AAPM 2014 Moriya et al.
Study on lung SBRT patients
“commissioning test is essential .... should understand pitfalls of dose warping”

**Validation of dose warping not yet solved !**

“S... be seen between … different alg... that DIR performance should be scru... before application to dose-warping.”

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# Clinical implementation

**Thorough QA of software required !**

Understand how software works

Be aware of the limitations of the algorithms

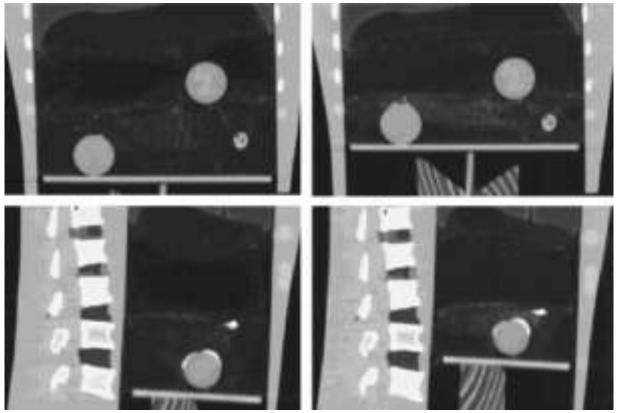
Ask yourself: which accuracy where?

# Physical or digital QA

## Mechanical phantom

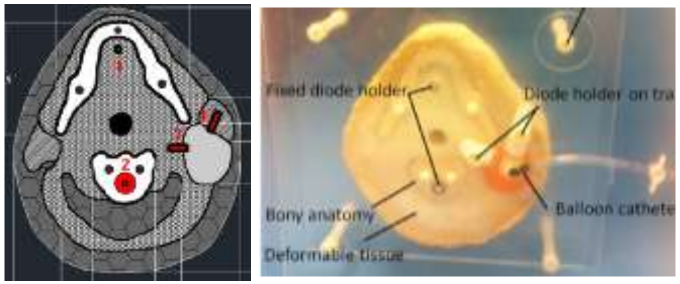
- physical deformable
- in vivo-dosimetry

e.g. lung phantom Univ. of Michigan



Kashani et al., Med Phys 35 (2008)

e.g. deformable H&N phantom Univ. of Calif.




Graves et al., Med Phys 42 (2015)

## Simulation

- artificially deformed real patient images or virtual phantoms

e.g. ImSimQA (commercial software)

## Clinical images

- real patient image data

e.g. - data set from dir-lab/popi…


- replanning CTs or CBCTs

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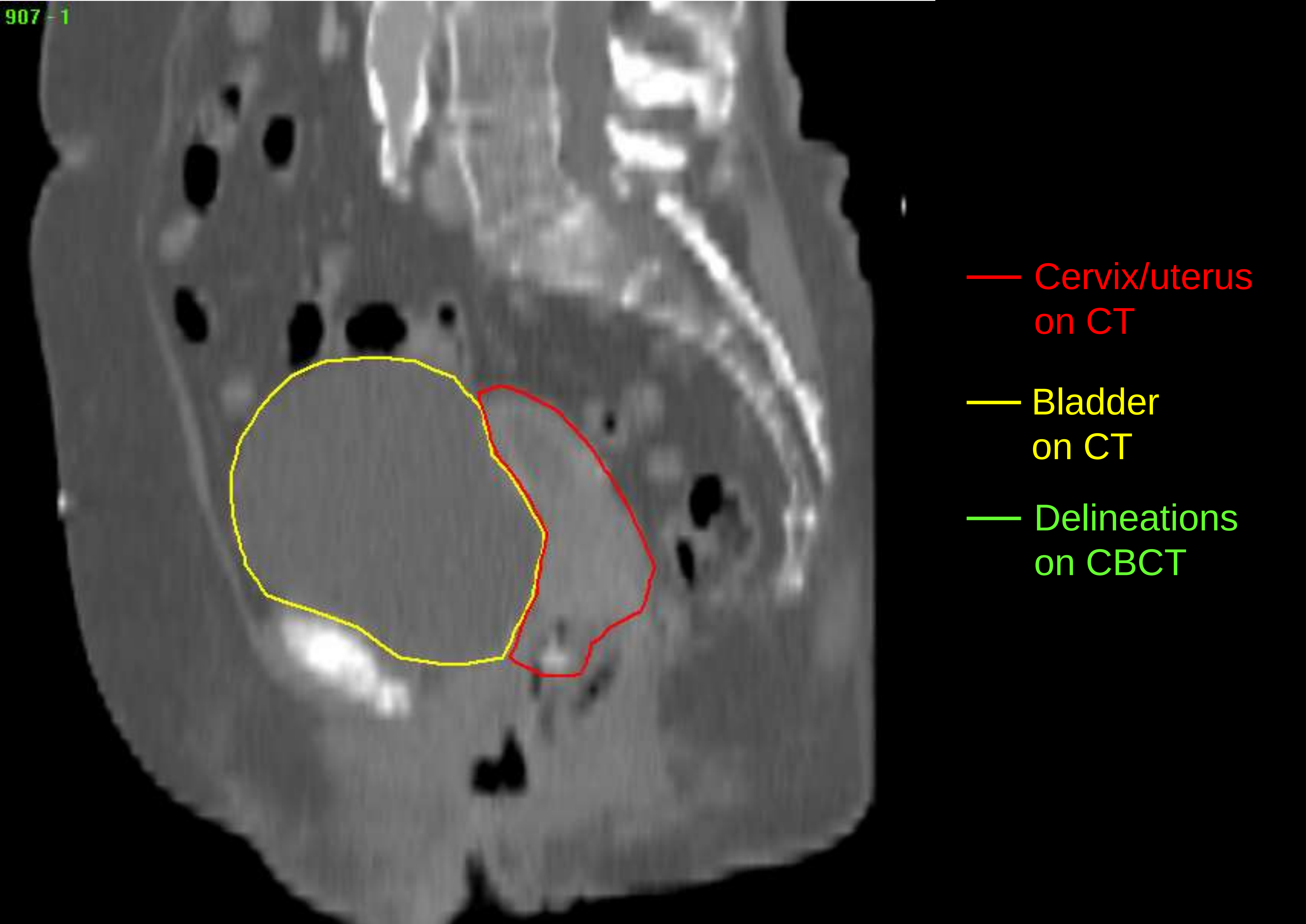
DIR

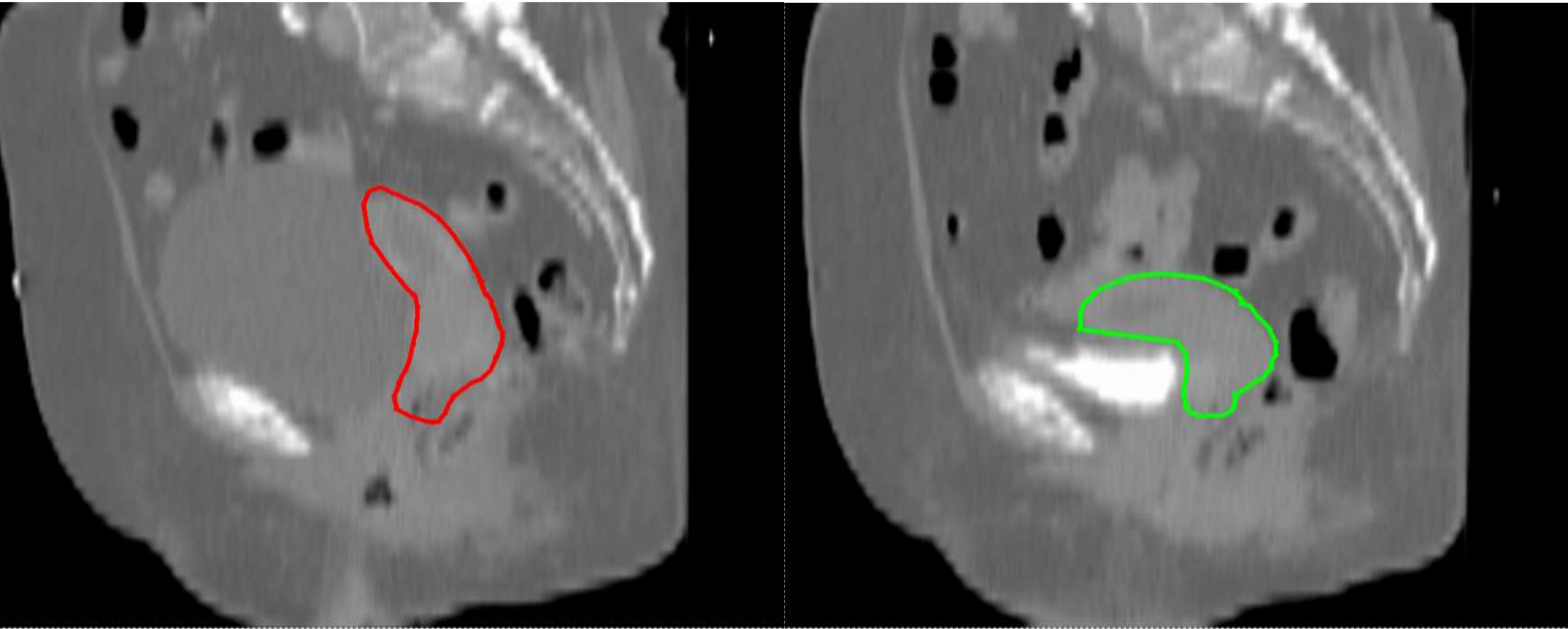
# Clinical practice at the AvL

# Library of plans

- Create a collection of plans
- Select the best fitting plan at treatment, based on CBCT images
- For a library we need N different situations
  - ➢ Usually only one or two situations available
    - ▪ E.g. Empty and full bladder
  - ➢ So how to create intermediate structures?
  - ➢ Deformable registration!


907 - 1
Cervix/uterus on CT
Bladder on CT
Delineations on CBCT

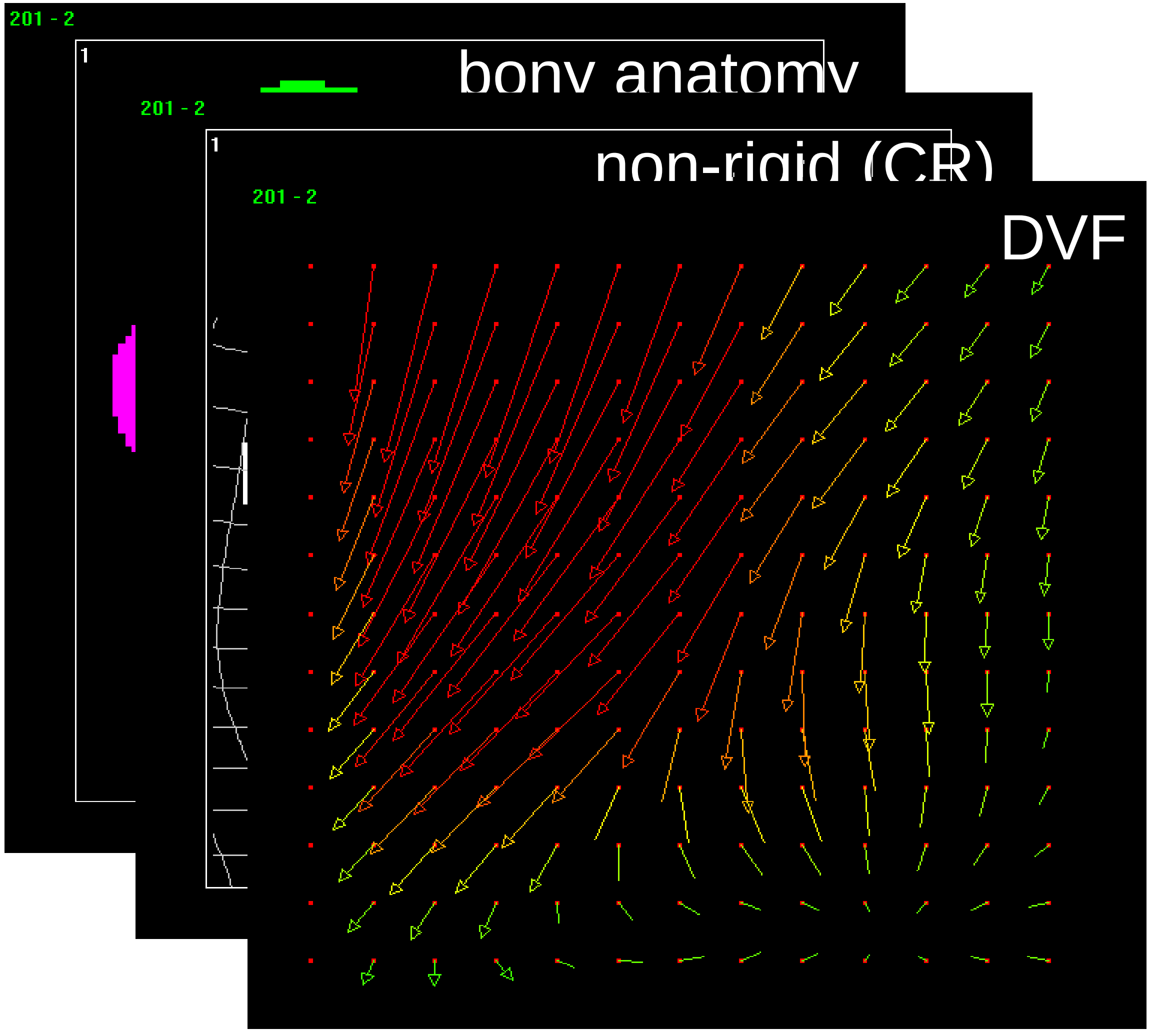
# Full/empty bladder CT



Delineate on full and empty bladder CT

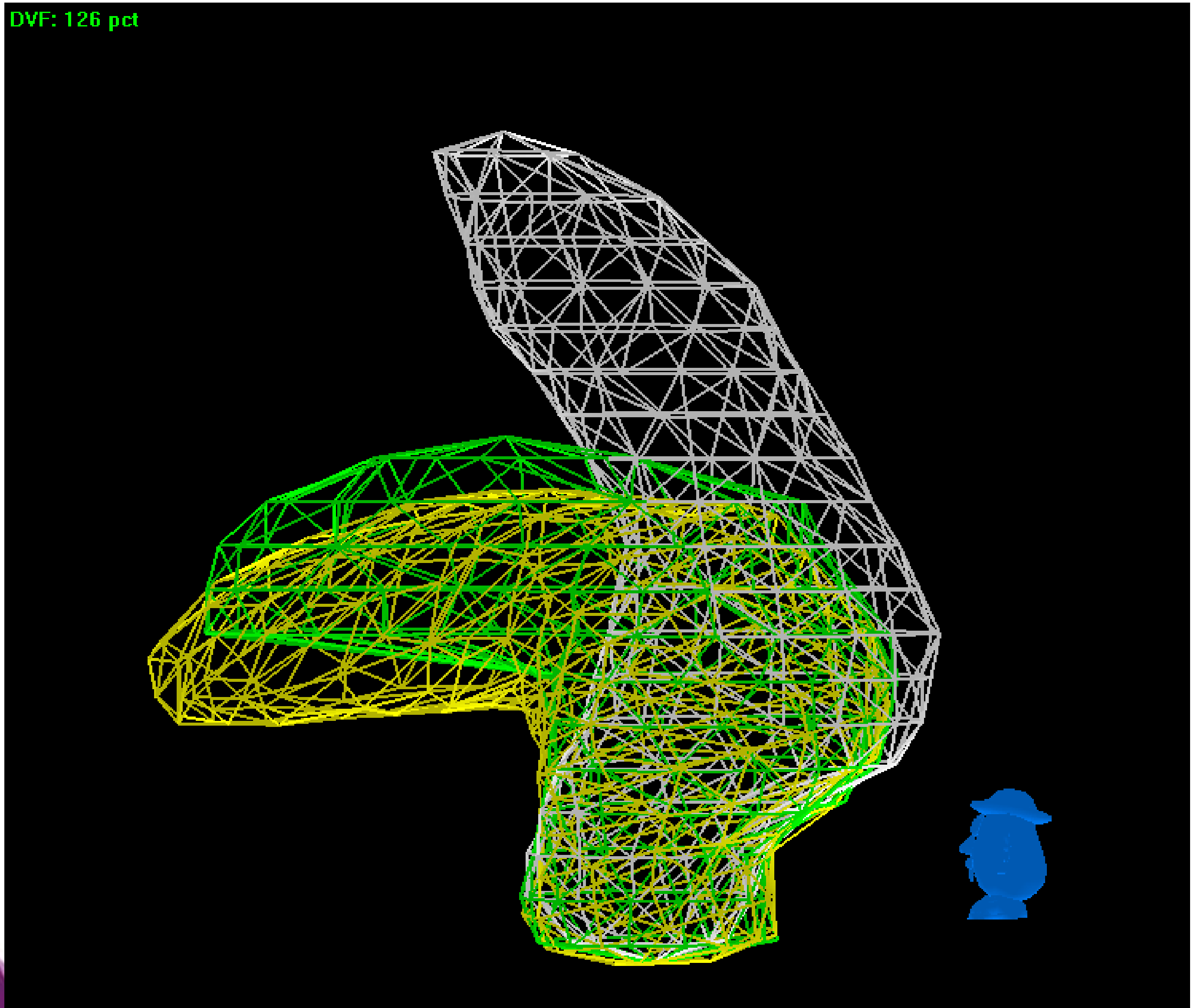
Deform full bladder contour

Generated warp field is model for organ motion




School

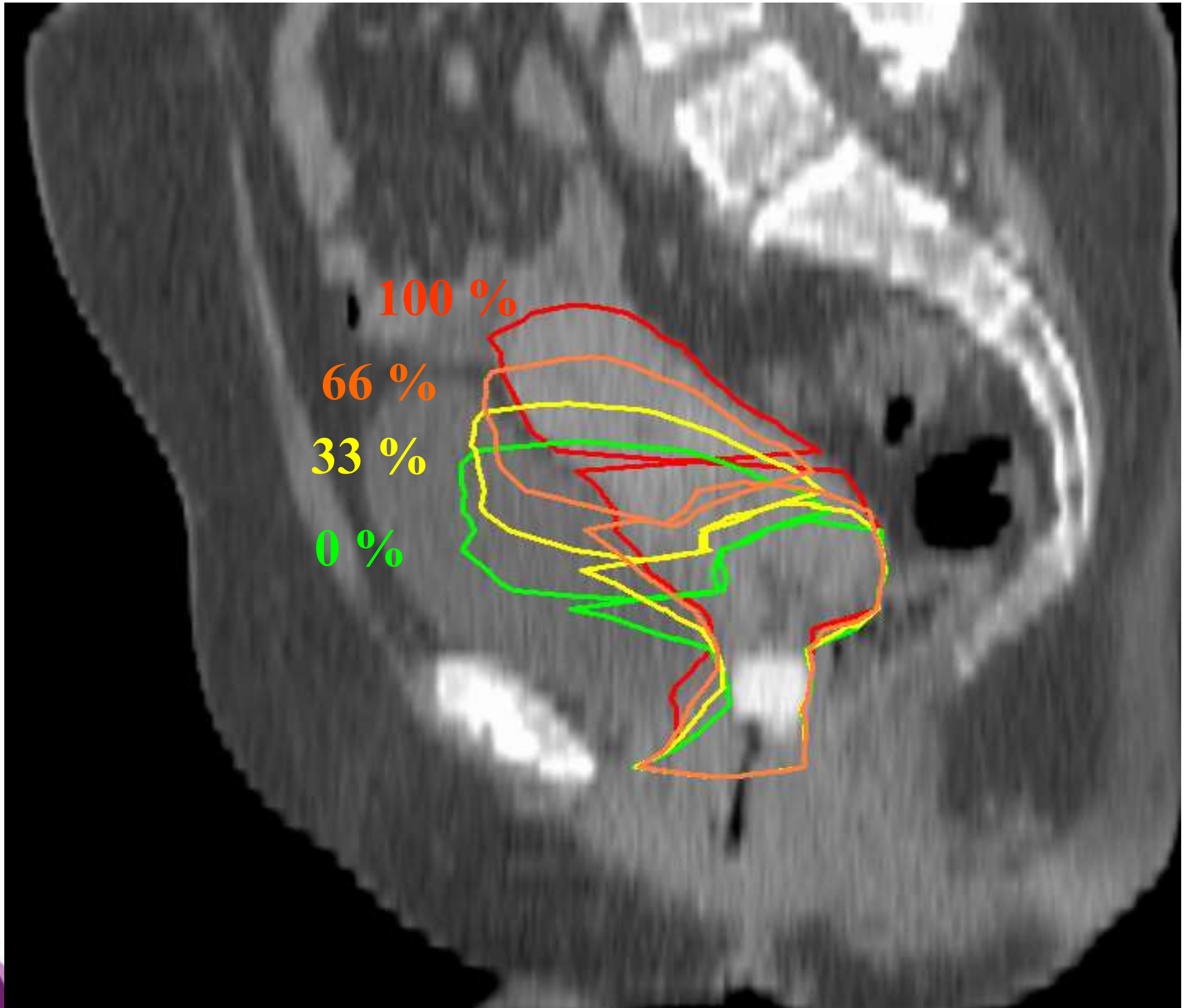
# Uterus motion model




Select 4 bladder fillings based on this model:

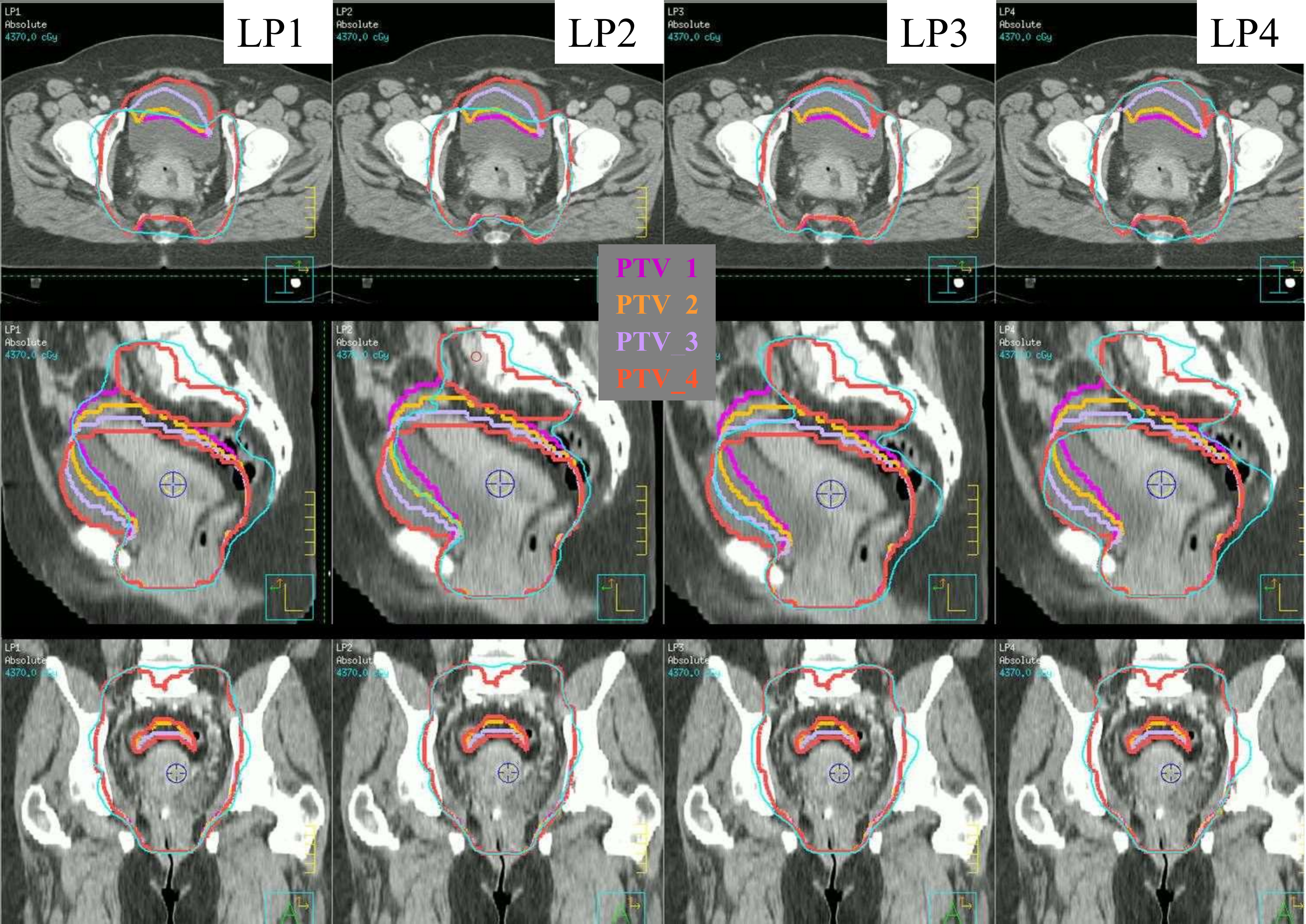
- 0 %
- 33 %
- 66 %
- 100 %

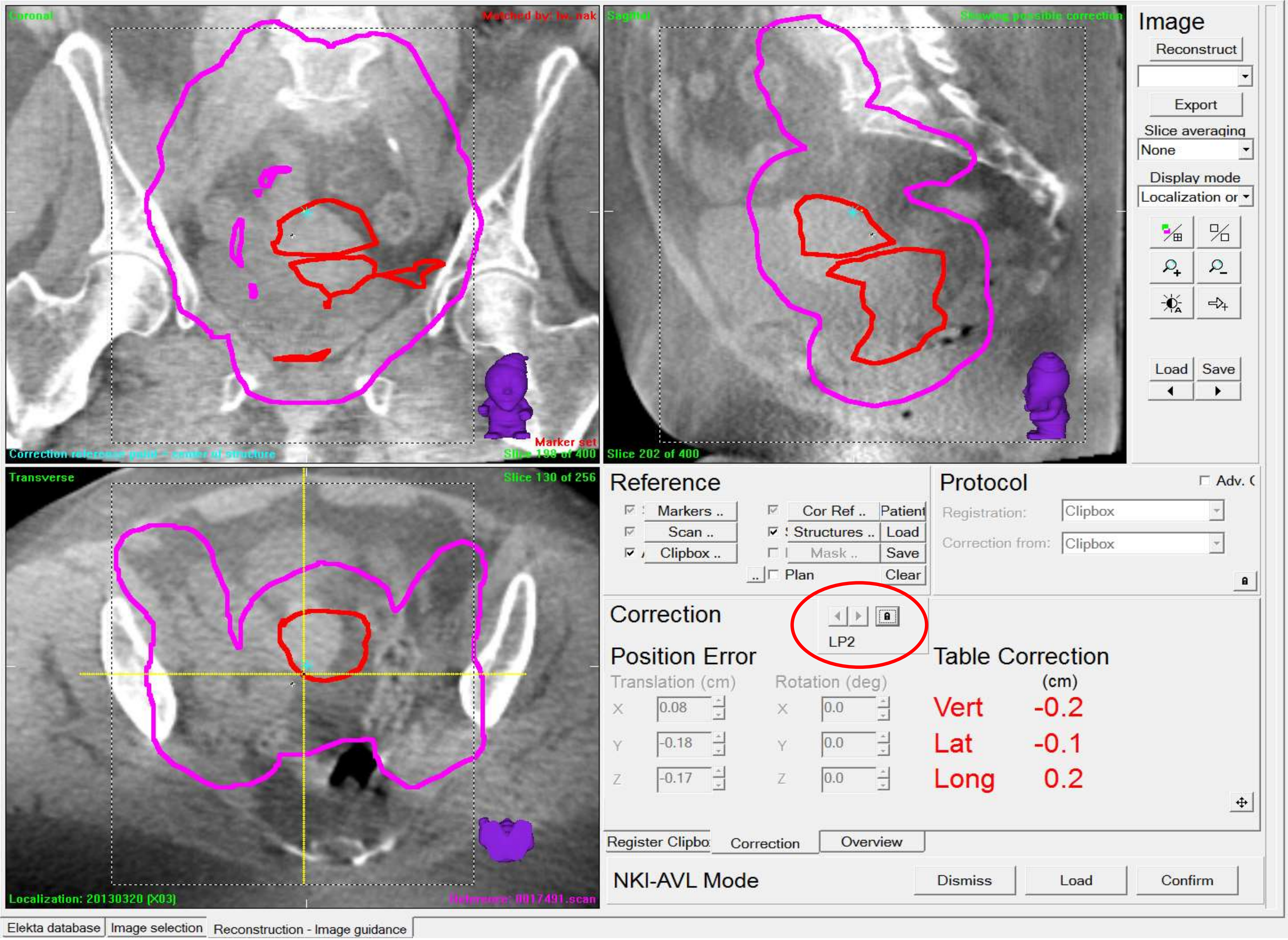
# Generated CTVs




Select 4 bladder fillings based on this model:

- 0 %
- 33 %
- 66 %
- 100 %


LP1
LP2
LP3
LP4
Absolute
4370.0 cGy
PTV_1
PTV_2
PTV_3
PTV_4

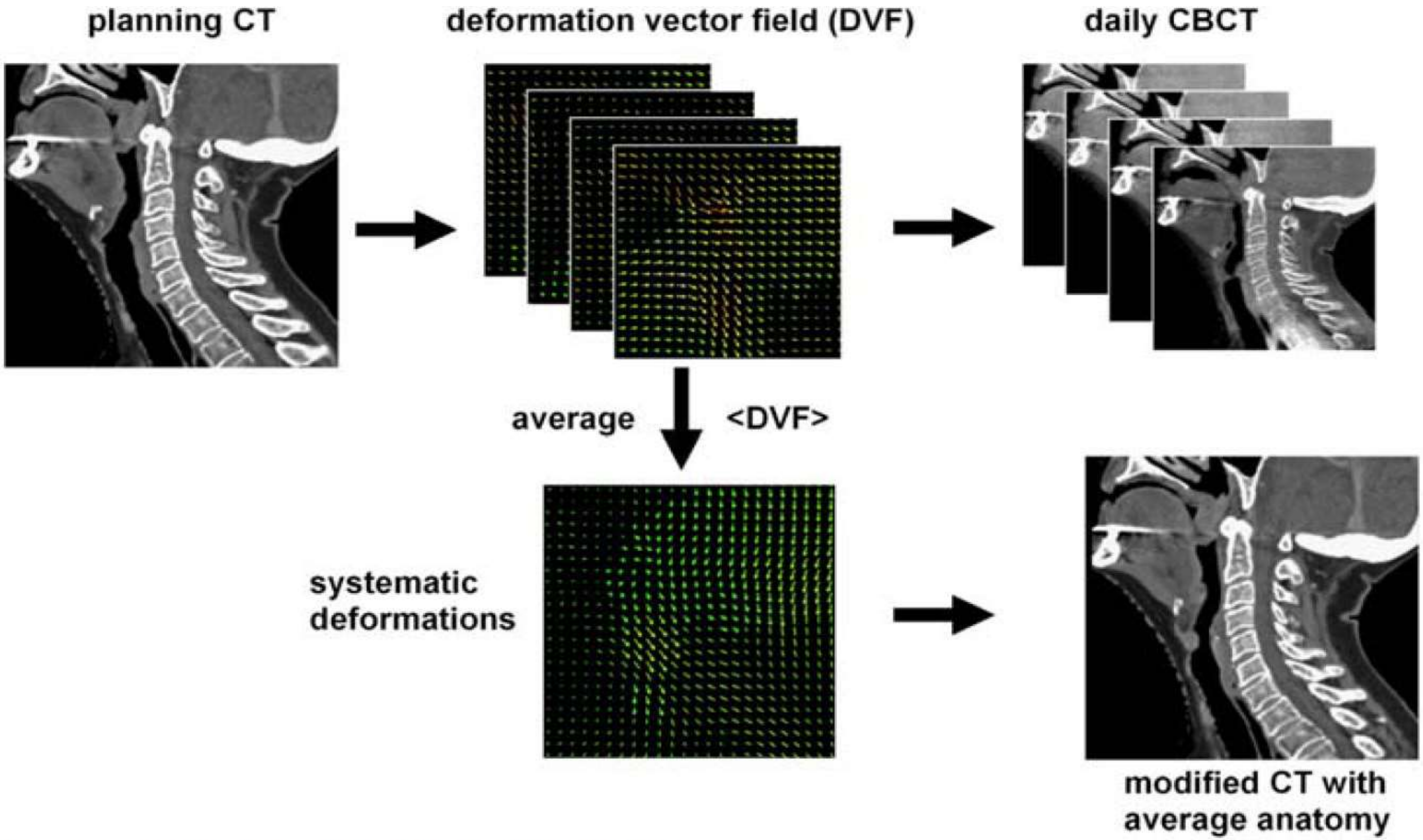



LP1 = full bladder LP4 = empty bladder

Slide Nelly Kager, ESTRO 2014

# Creation of pseudo CT scans

- A ‘deformed’ planning CT scan
- Based on average shape change of patient
- Deformable registration
  - CBCT → CT
  - Average deformation vector fields
  - Use the inverse of this to deform the planning CT




Kranen e.a., Radiotherapy and Oncology 109 (2013) 463-468

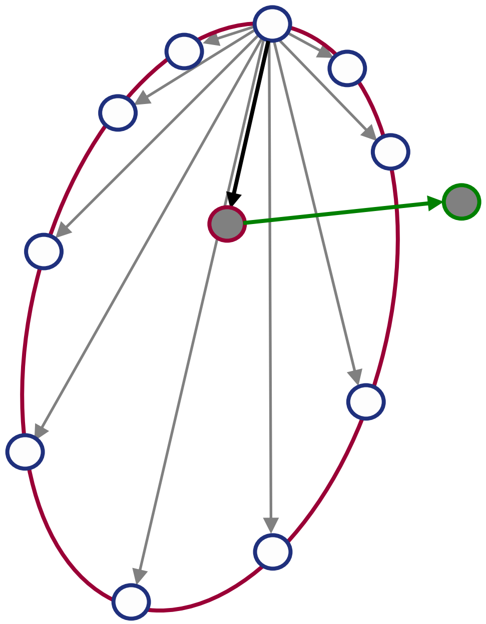
# Mid-position CT scans

- 4D readily available
- How to plan?
- Mid-position is representative of the true average position of the tumor
  - ➢ Small systematic errors
  - ➢ Small margin!
- How do we create this?
  - ➢ Deformable registration!

# 4-D CT

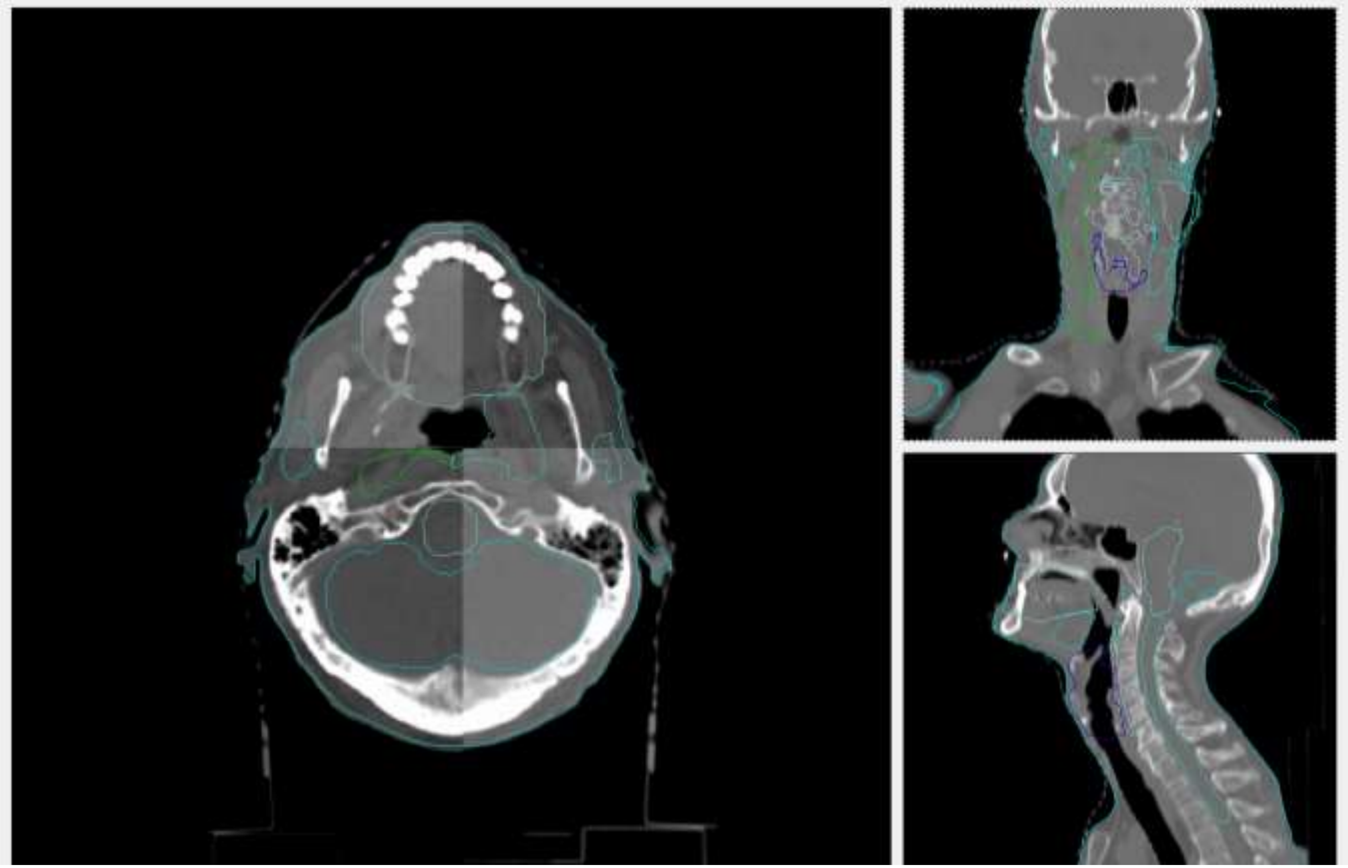
- Register each 4-phase to exhale phase
- Determine average deformation
- Apply inverse of average to get mid-position scan

- Optional:
  - ➢ Deform BH contrast scan to mid-position



# Contour propagation

- Usage
  - Reduce workload by deforming (propagating) delineated structures to match a second scan
  - Validation important!
  - Errors can be on the order of 1-10 mm

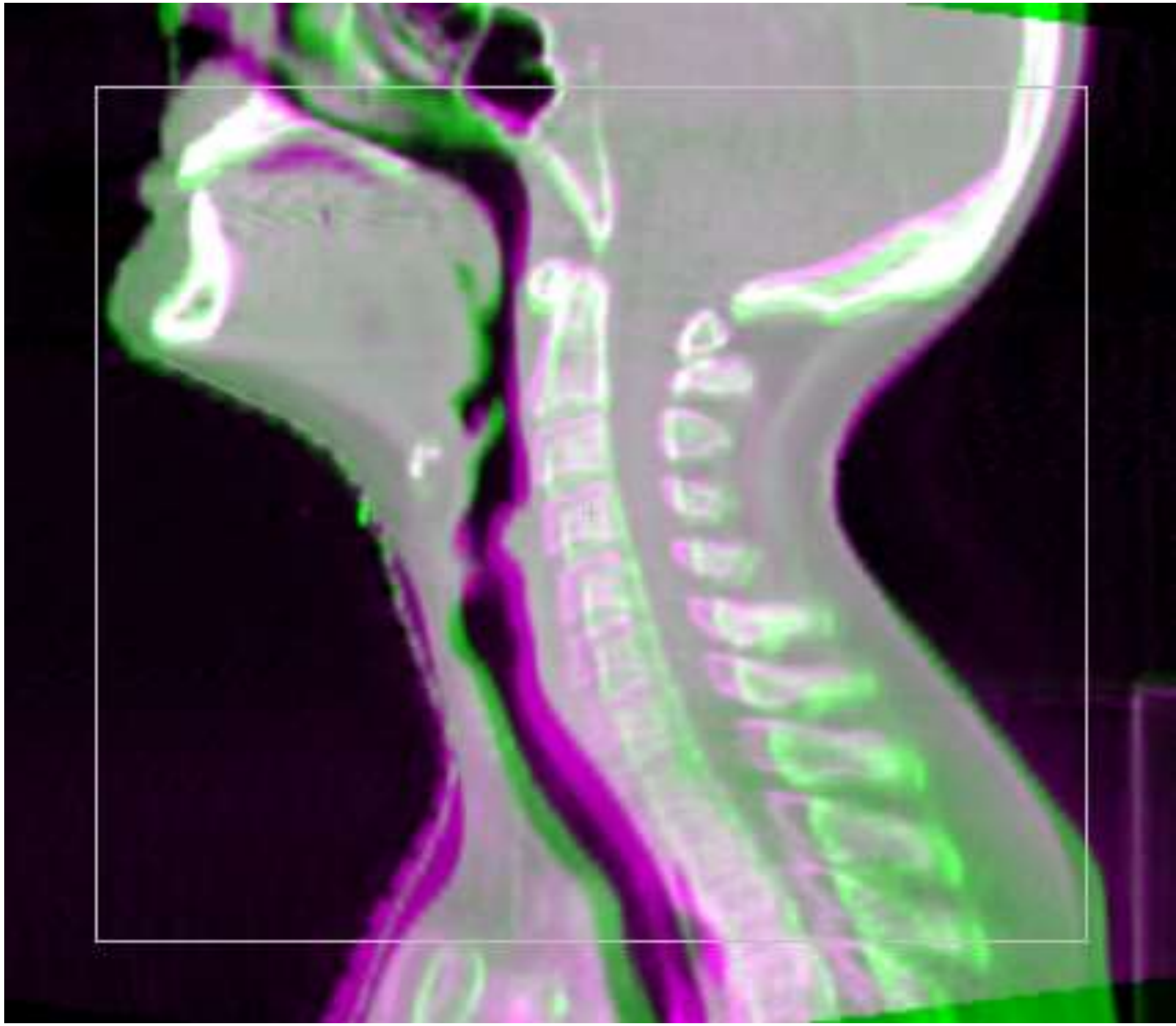


# Head & neck – semi deformable registration

Single ROI, rigid registration

ROI encompasses:

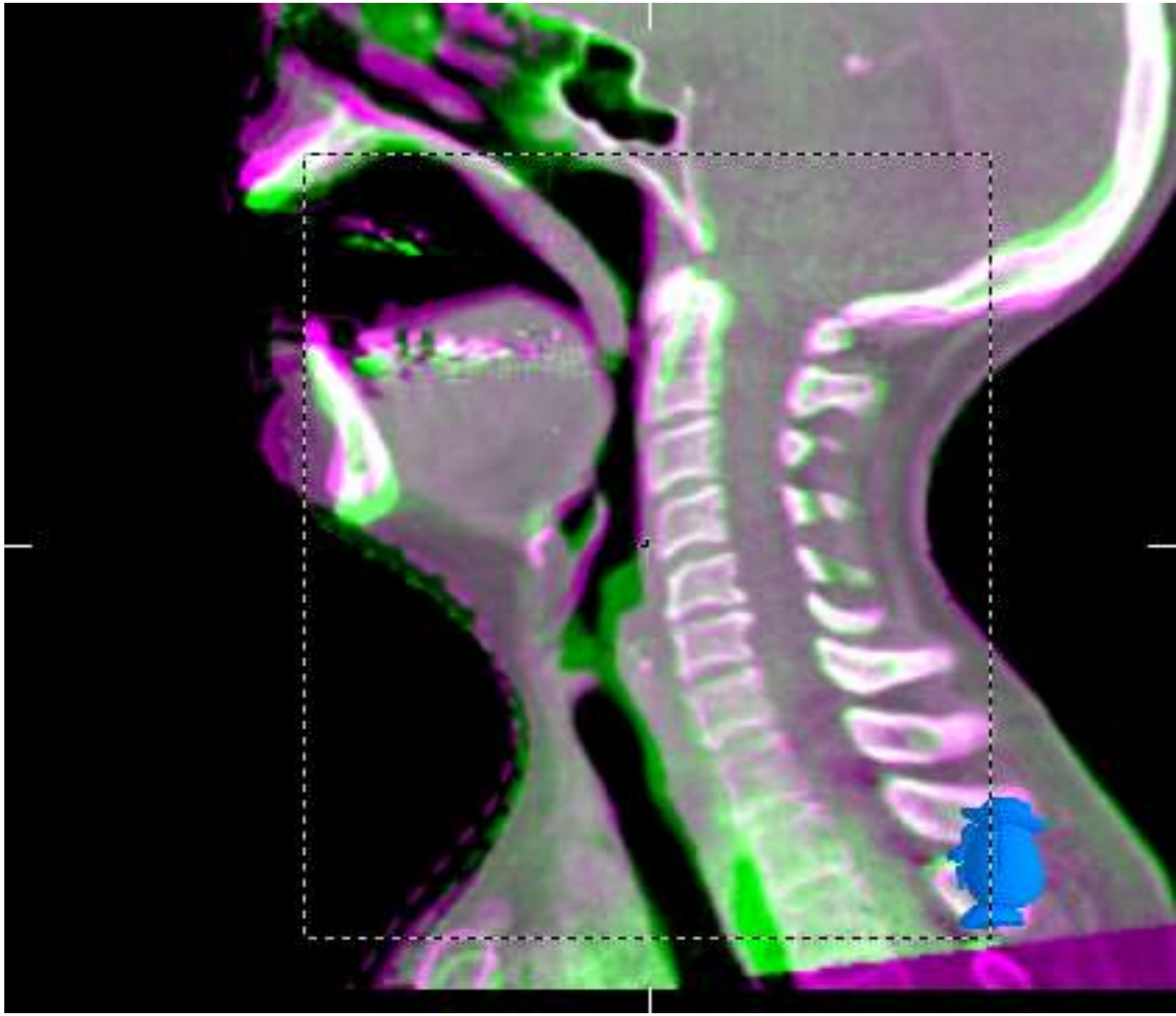
- PTV
- Vertebrae
- Base of skull
- Jaw



Purple: CBCT
Green: planning CT
Overlay: white = match

# Single ROI registration

- Match inaccurate
  - ➢ Misregistration?
  - ➢ Deformation?



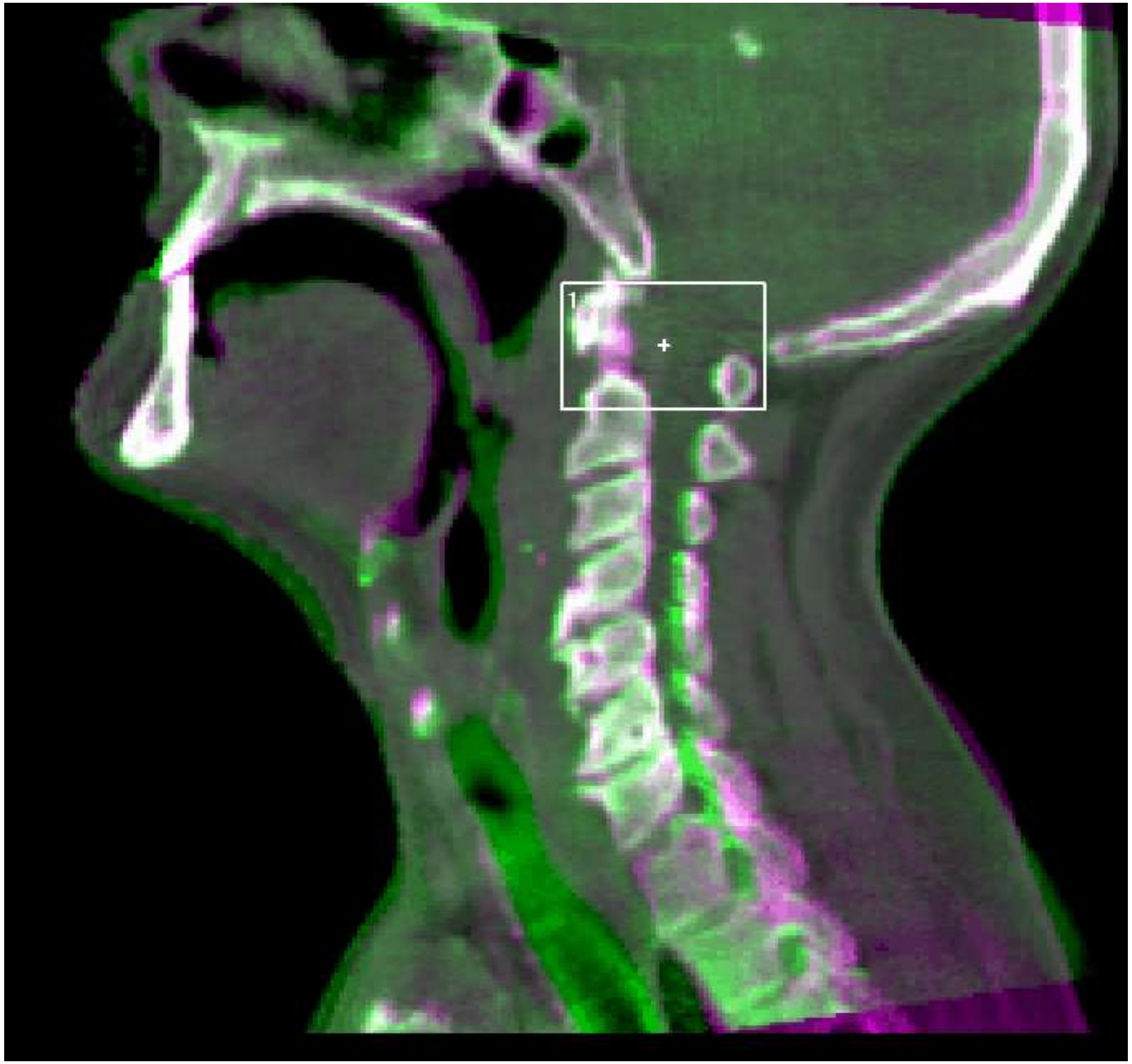
# Use multiple ROIs

Allows:

- Accurate local registration
- Assessment of local setup errors

Still bony anatomy, easy to validate

# Image registration

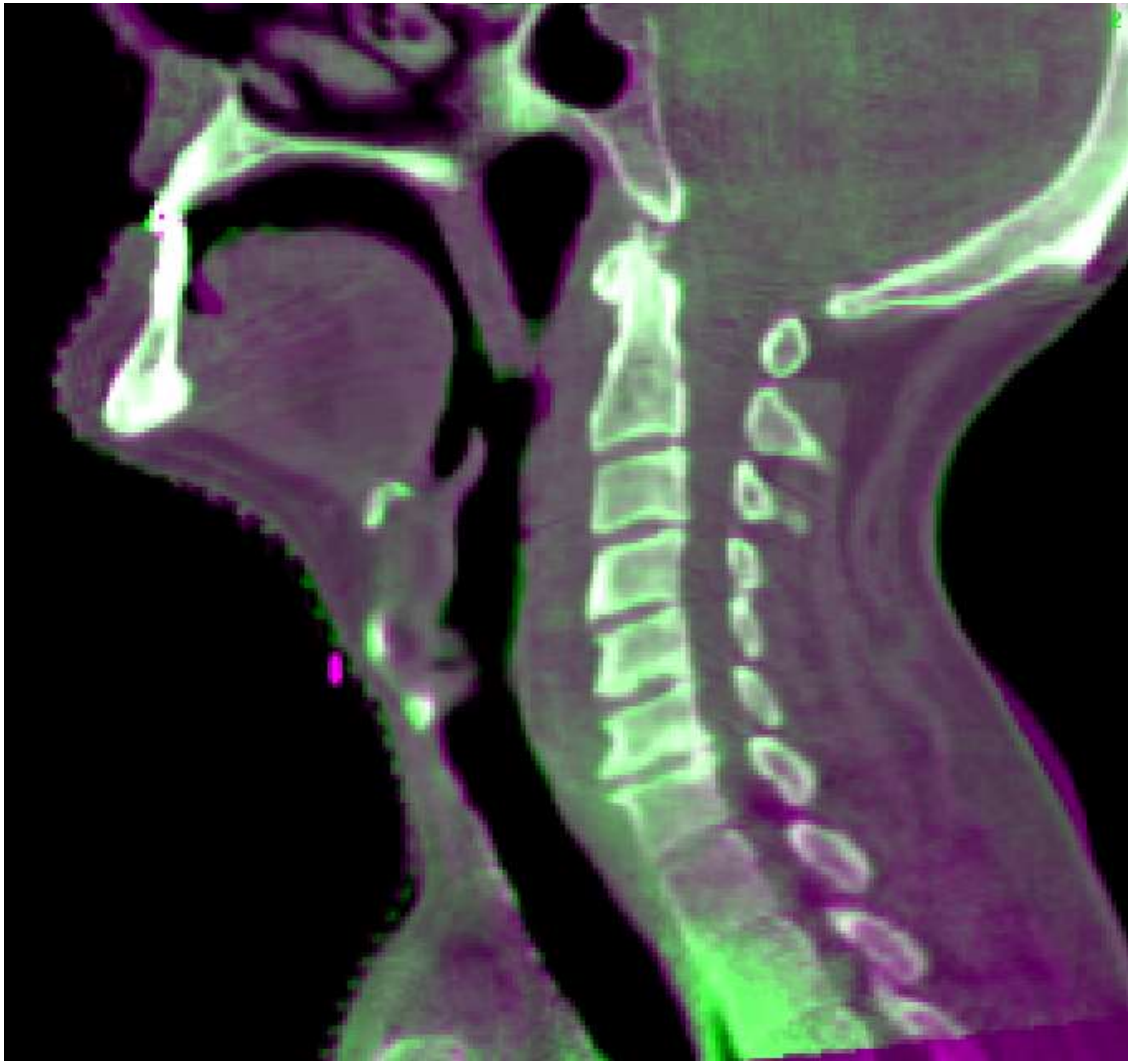



• bony anatomy registration

• Loop over ROIs

Purple: planning CT
Green: CBCT

# Validation of registration

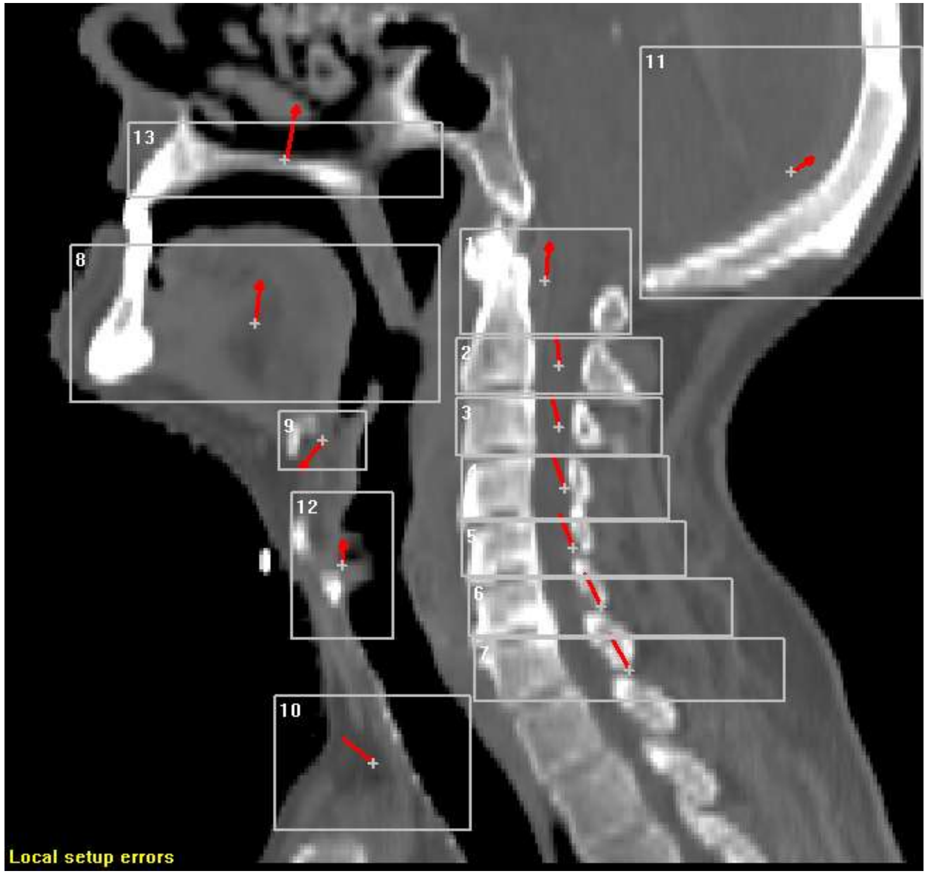


All registrations at once by warping

→Fast

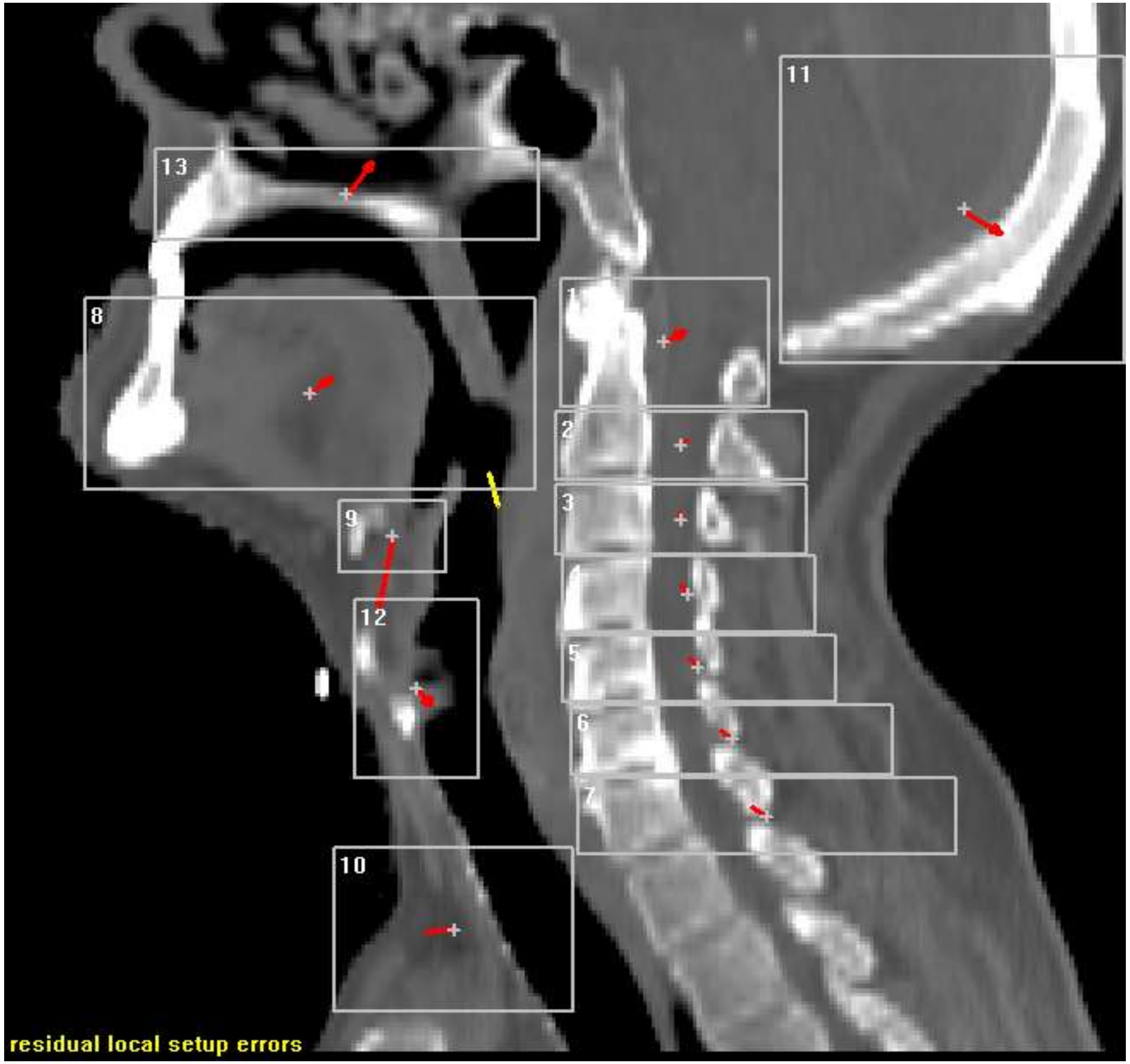
# Corrections

Couch shift: Average of all regions of interest




Correct average

# Corrections




Residual errors and deformations can now be addressed, i.e. by thresholds on movements

# Conclusions

- Deformable image registration is a very powerful tool
- Many applications
- Beware! DIR fixes everything, but is not necessarily anatomically correct
- Validation is important for each application and each treatment site!

ESTRO School

WWW.ESTRO.ORG/SCHOOL

# Image registration

## in Radiation Oncoloy

Martina Kunze-Busch
Radboud University Medical Center Nijmegen
The Netherlands

# Overview

## Image registration

- Definition
- A closer look at the different components/steps
  - geometrical transformation
  - similarity measure
  - optimization algorithm
- Image registration in the RT chain
  - treatment preparation
  - treatment delivery

  *problems/challenges*
- Quantification of organ motion
- Registration accuracy

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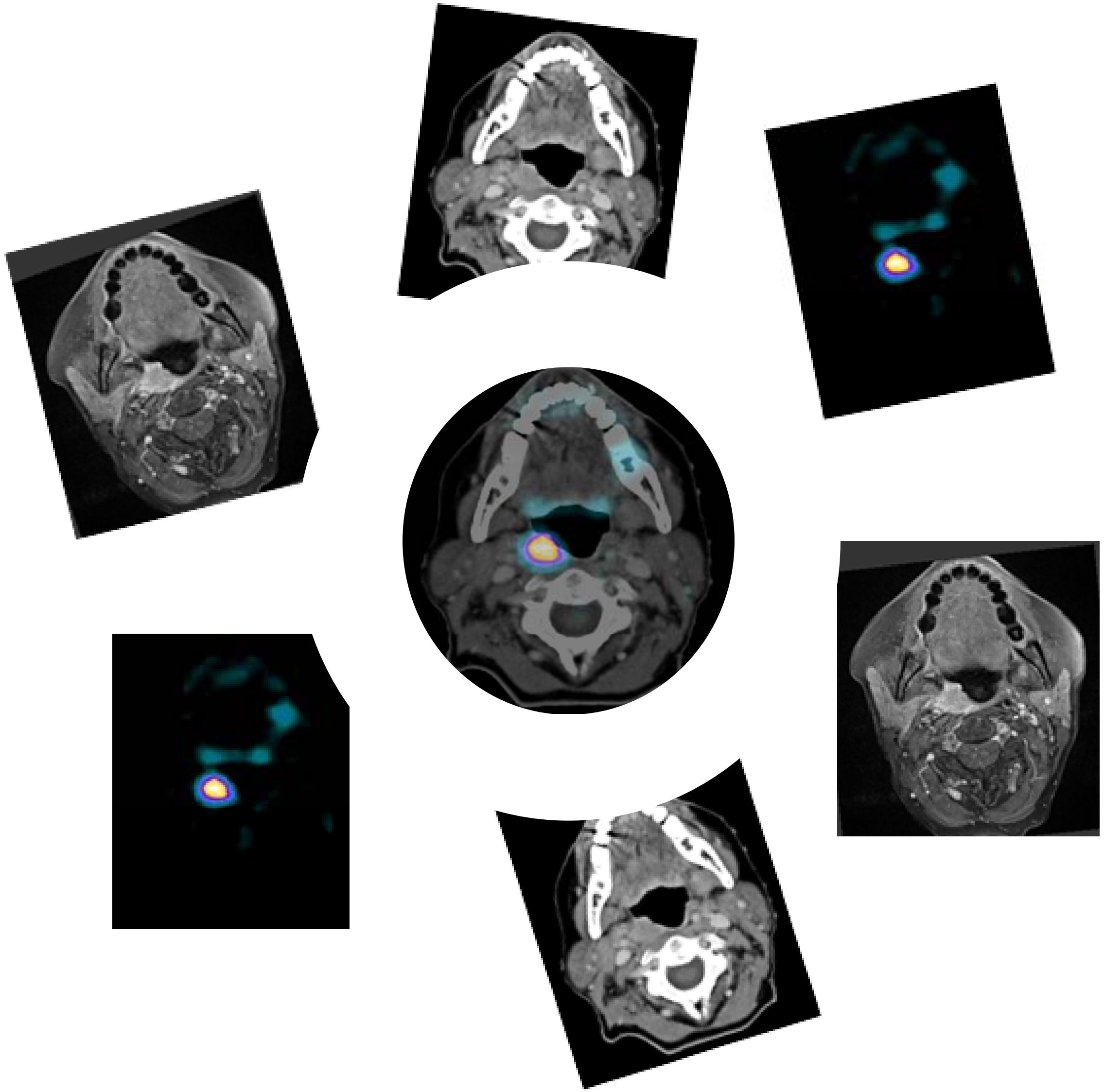

**Image fusion**

Ju click here

# Image registration ↔ image fusion

**Image registration**

spatial alignment/
geometrical transformation T of image

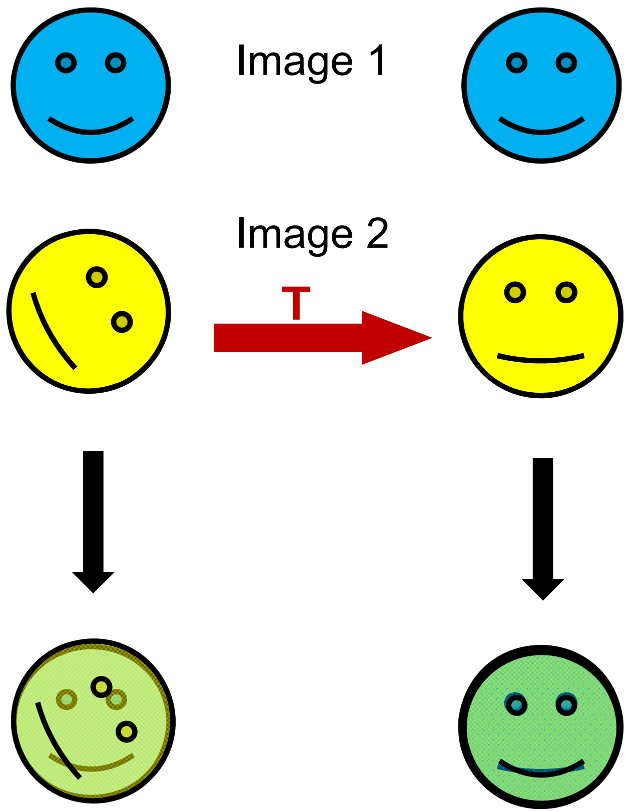


**Image fusion**

integrated display of data

goal of image registration = find geometric **transformation** that **best** aligns two images

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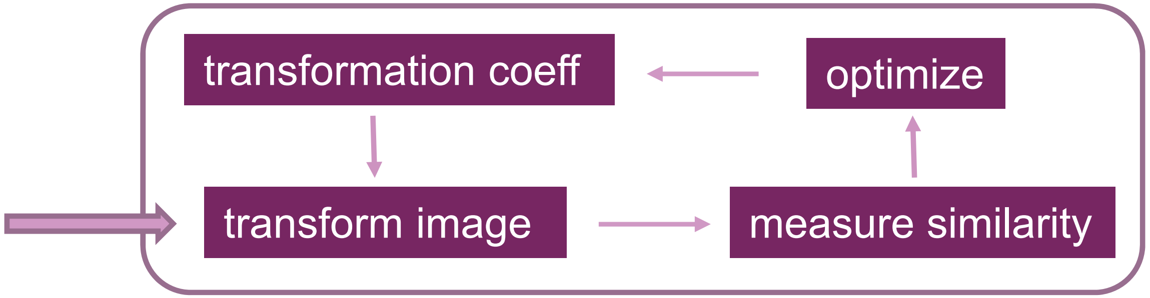
# Image registration

The three core components of image registration:

1. Spatial/geometrical transformation T
2. Similarity measure/cost function
3. Optimization algorithm



# 1. Geometrical transformation T

Image 1

Image 2

- **Rigid**
  - no deformation
  - only translations and rotations are allowed

  (3 rotations, 3 translations → (max) 6 independent parameters)

Image 2

- **Affine**
  - shearing, stretching

  (3 rotations, 3 translations, 3 stretches, 3 shears → (max) 12 parameters)

# 1. Geometrical transformation T

- **Deformable /non-rigid**
  - e.g. elastic
    (milions of parameters!)

Image 2

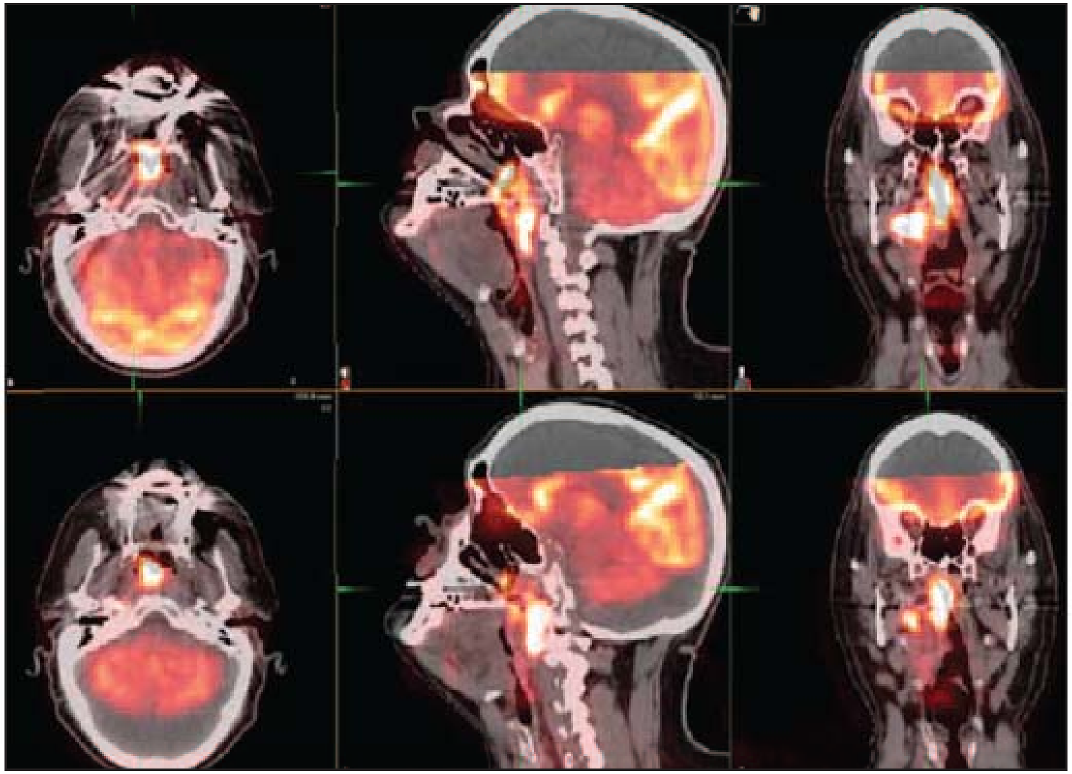
Image 1

# 1. Geometrical transformation T

Example: deformable registration of diagnostic PET and CT

deformable

rigid



Schoenfeld et al, AJR 2012

# 1. Geometrical transformation T

- **Deformable /non-rigid**
  - e.g. elastic
  (**milions** of parameters!)


average errors can be in the range of 1 – 5 mm

**Validation !**

# 2. Similarity measure

Similarity measure quantifies degree of similarity between 2 images

Different methods exist:

- FEATURE – based
- INTENSITY – based  (grey values)
- MODEL – based

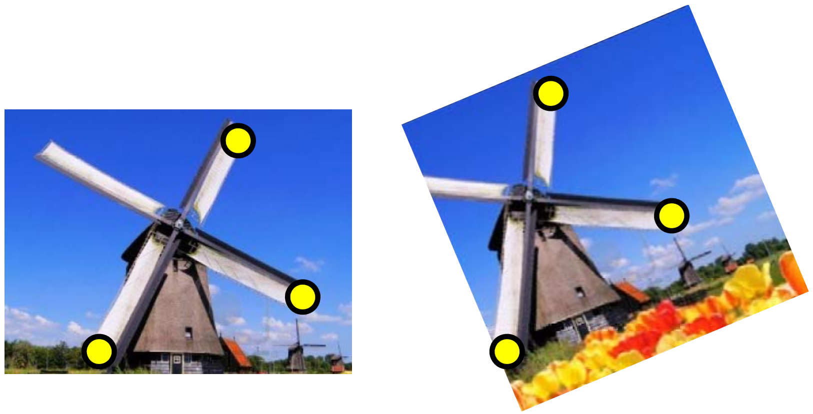
# 2. Similarity measure

## **Feature-based method**

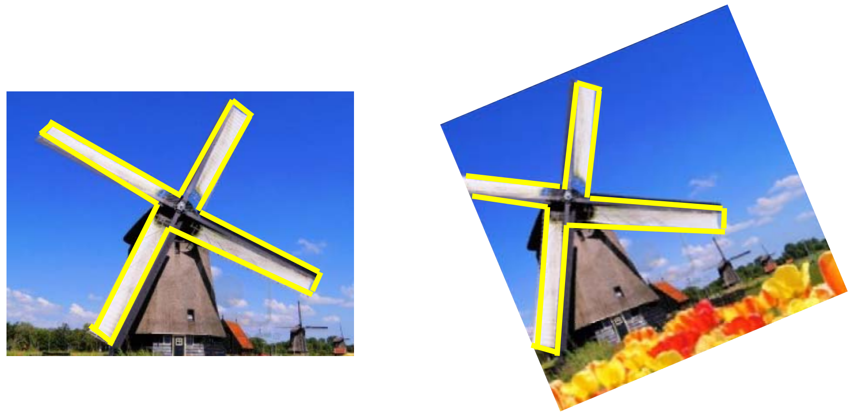
- extract feature from images & evaluate distance between features
- employed when local accuracy is important
- dependent on accuracy of feature extraction

2 types:

**Landmark-based method**



**Segmentation-based method**



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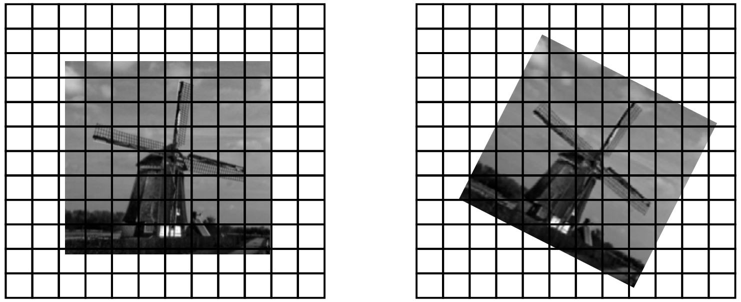
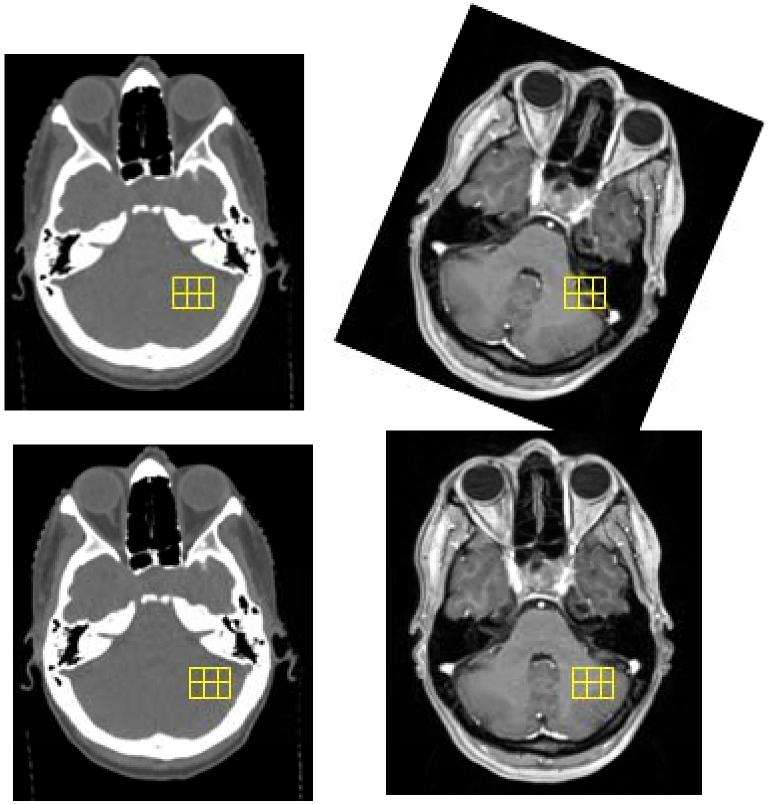
# 2. Similarity measure

**Intensity-based method (grey values)**



- all pixels in overlapping regions are utilized
- does not require detection of geometric features
- time consuming



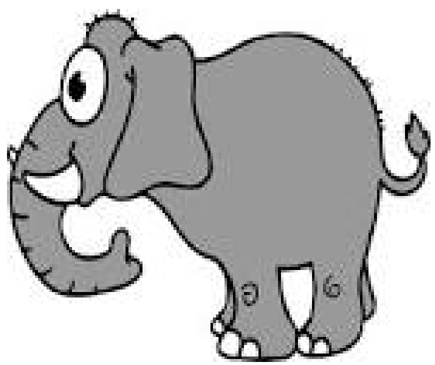
e.g. *mutual information*

# 2. Similarity measure

**Model-based method**

e.g. deformable transformation model for contours

similarity measure + regularization/penalty term (tissue characteristics)



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# 2. Similarity measure/COST FUNTION

description of problem in **mathematical terms**

value of cost function reflects quality of registration: smallest value = best solution

**Example:**

find <u>shortest</u> way to Rome → cost function = Σ path lengths

answer: red

find <u>fastest</u> way to Rome → extra parameter: speed limit

answer: green

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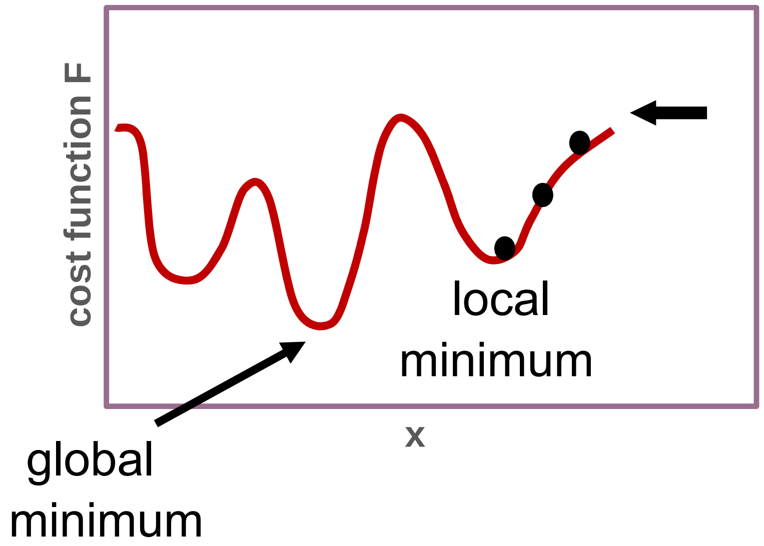
# 3. Optimizer/optimization algorithm

optimizer finds smallest value of cost function (= “optimal” transformation)

example: gradient descent

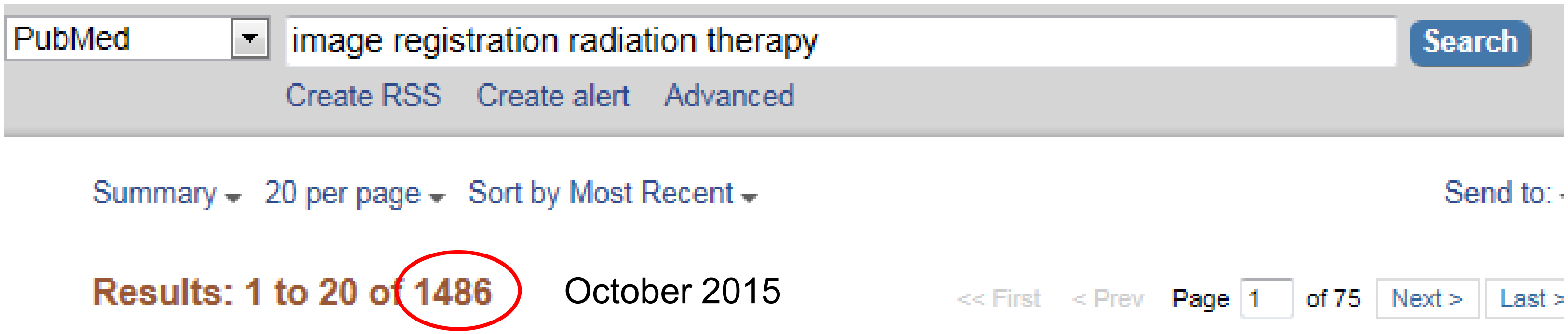





# Image registration in the RT chain

| Initial diagnosis and staging | Preparation/planning (delineation) | Delivery (position verification) | Adaptive RT |
|---|---|---|---|

Quantification of organ motion/ organ motion analysis




October 2015

1 to 20 of 1504

April 2016

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# Image registration in the RT chain

Initial diagnosis and staging

Preparation/planning (delineation)

Delivery (position verification)

Adaptive RT

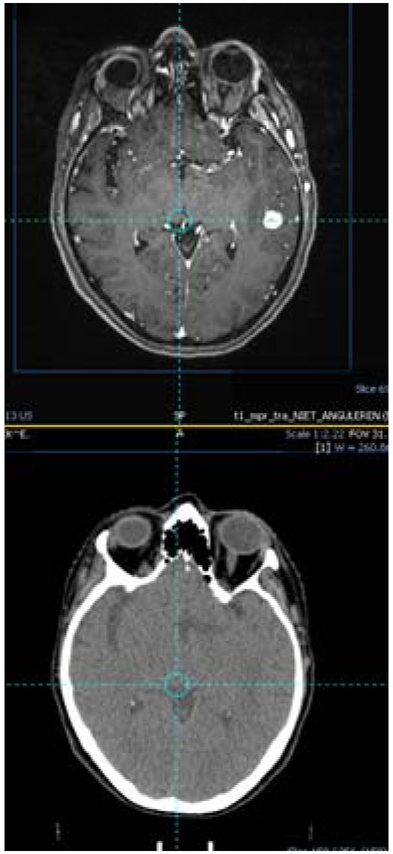
Quantification of organ motion/ organ motion analysis

# Treatment preparation

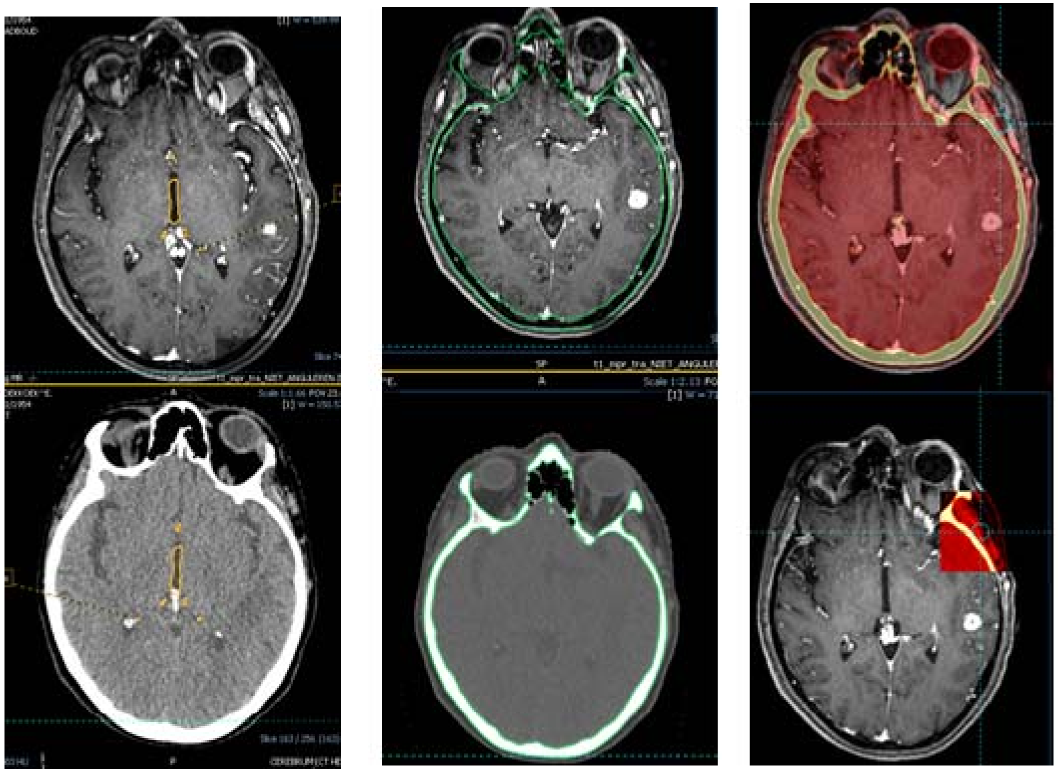
planning CT – diagnostic MRI

MIRADA medical

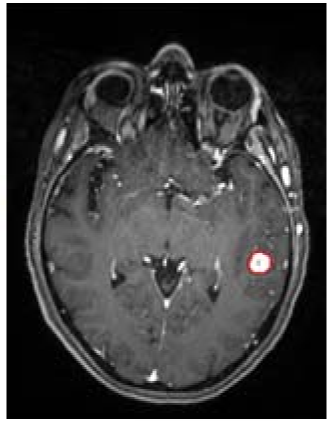
registration



visual check



delineation



# Treatment preparation

**problems/challenges**

- scan artefacts (MRI: geometrical distortions....)
- patient movement / organ motion during scan
  (also possible in hybrid systems)
- different scanning positions in different imaging modalities
- no use of fixation mask in MRI / PET
- different table tops
- ......

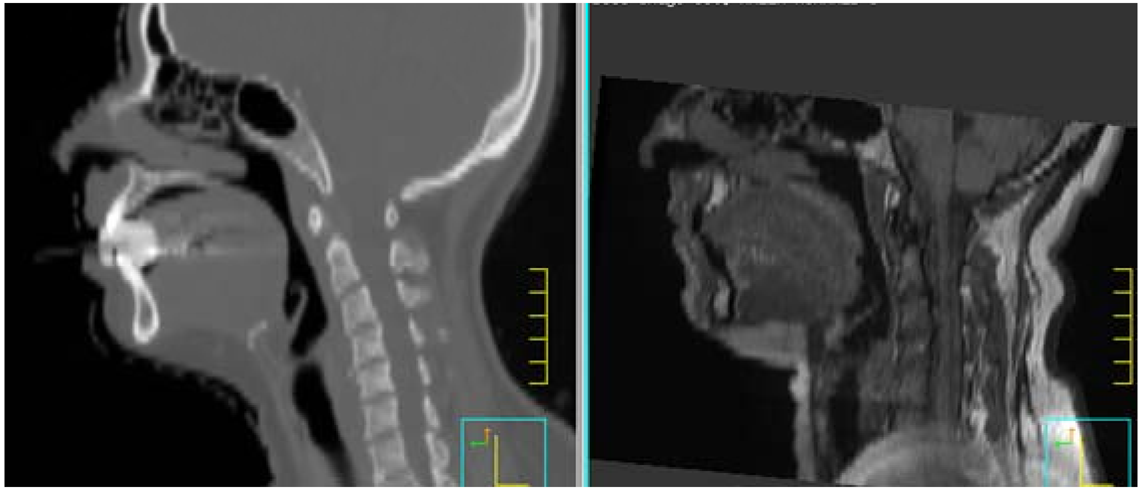
# Treatment preparation

**different scanning position**

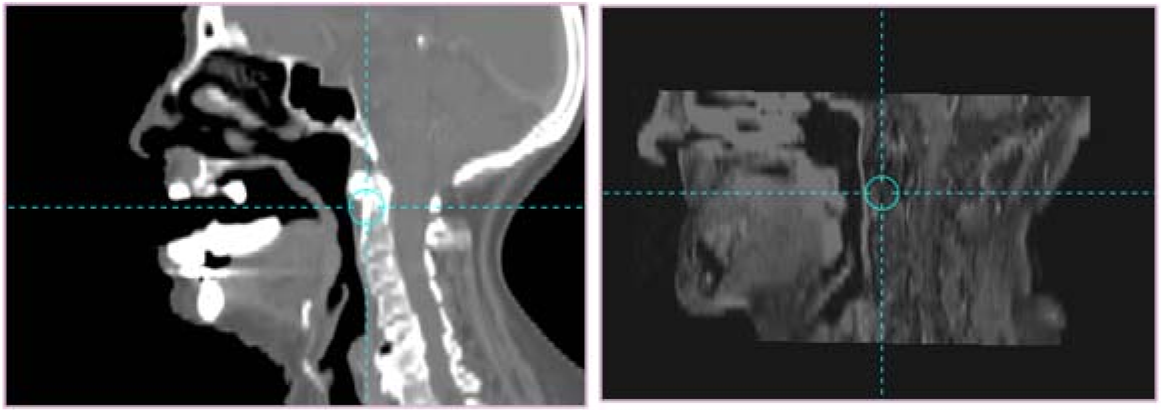
planning CT | diagnostic MRI

no fixation mask on MRI

→ different flexion of neck



mouth open - closed



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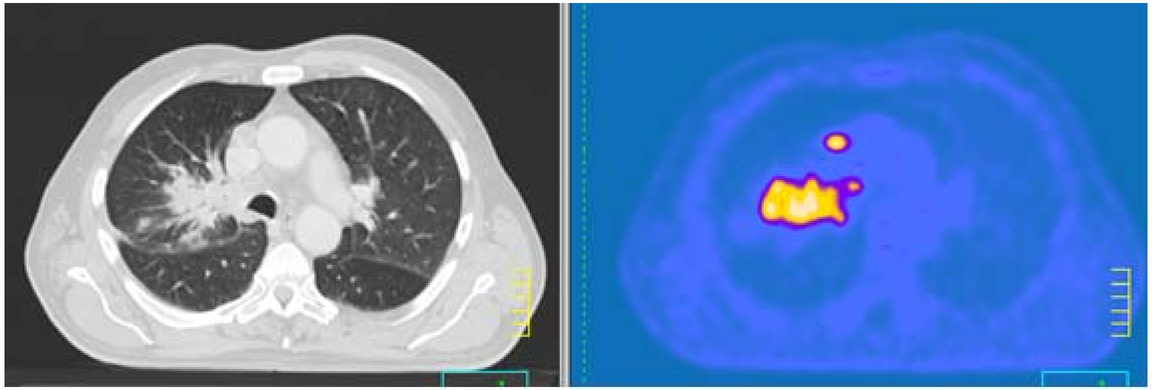
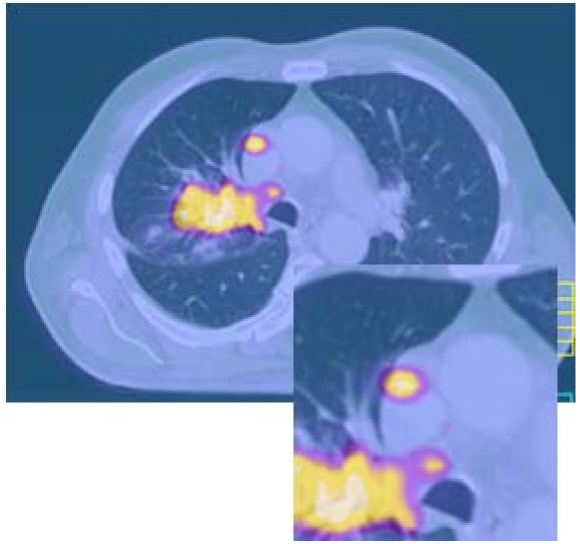
# Treatment preparation

**motion**

Hybrid PET/CT



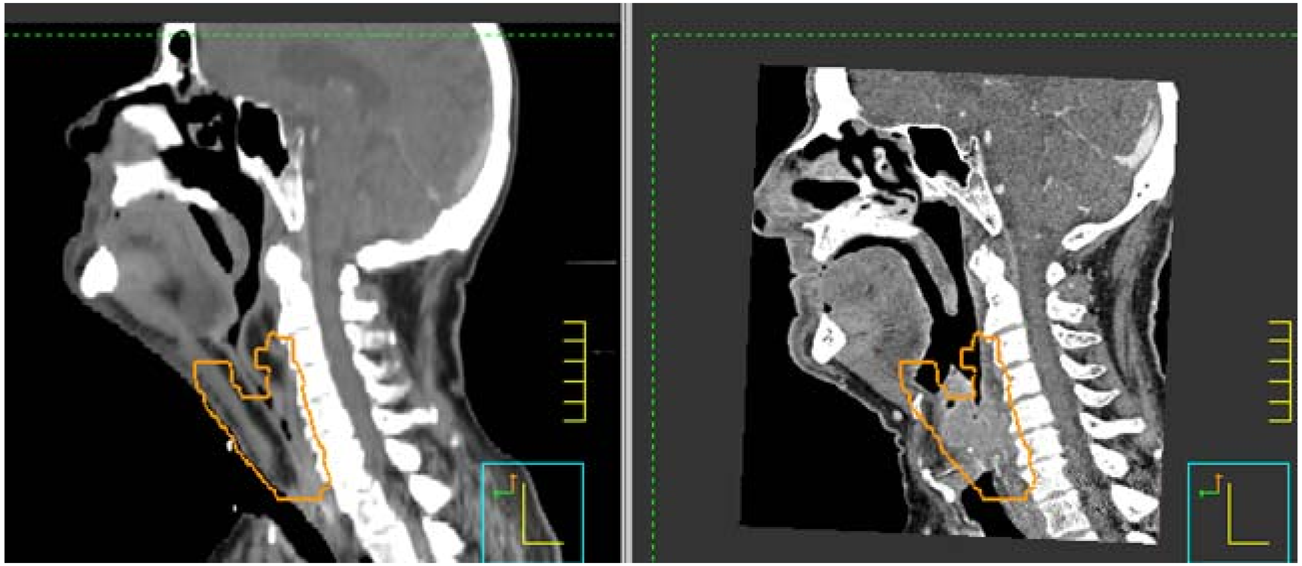
fusion



# Treatment preparation

**scans at different points in time**

planning CT pre-operative diagnostic CT



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# Image registration in the RT chain

| Initial diagnosis and staging | Preparation/Planning (delineation) | Delivery (position verification) | Adaptive RT |
|---|---|---|---|

Quantification of organ motion/ organ motion analysis

# Treatment delivery

**Image guided RT with Cone Beam CT**

alignment of in-room CBCT images
with planning CT images

→ position verification of patient (online/offline protocols)
→ localization of tumor at time of treatment
→ assessment of change in anatomy (tumor size/weight loss or gain)

**Image guided Adaptive Radiotherapy (ART)**

# Treatment delivery

## CT – CBCT: Bone registration

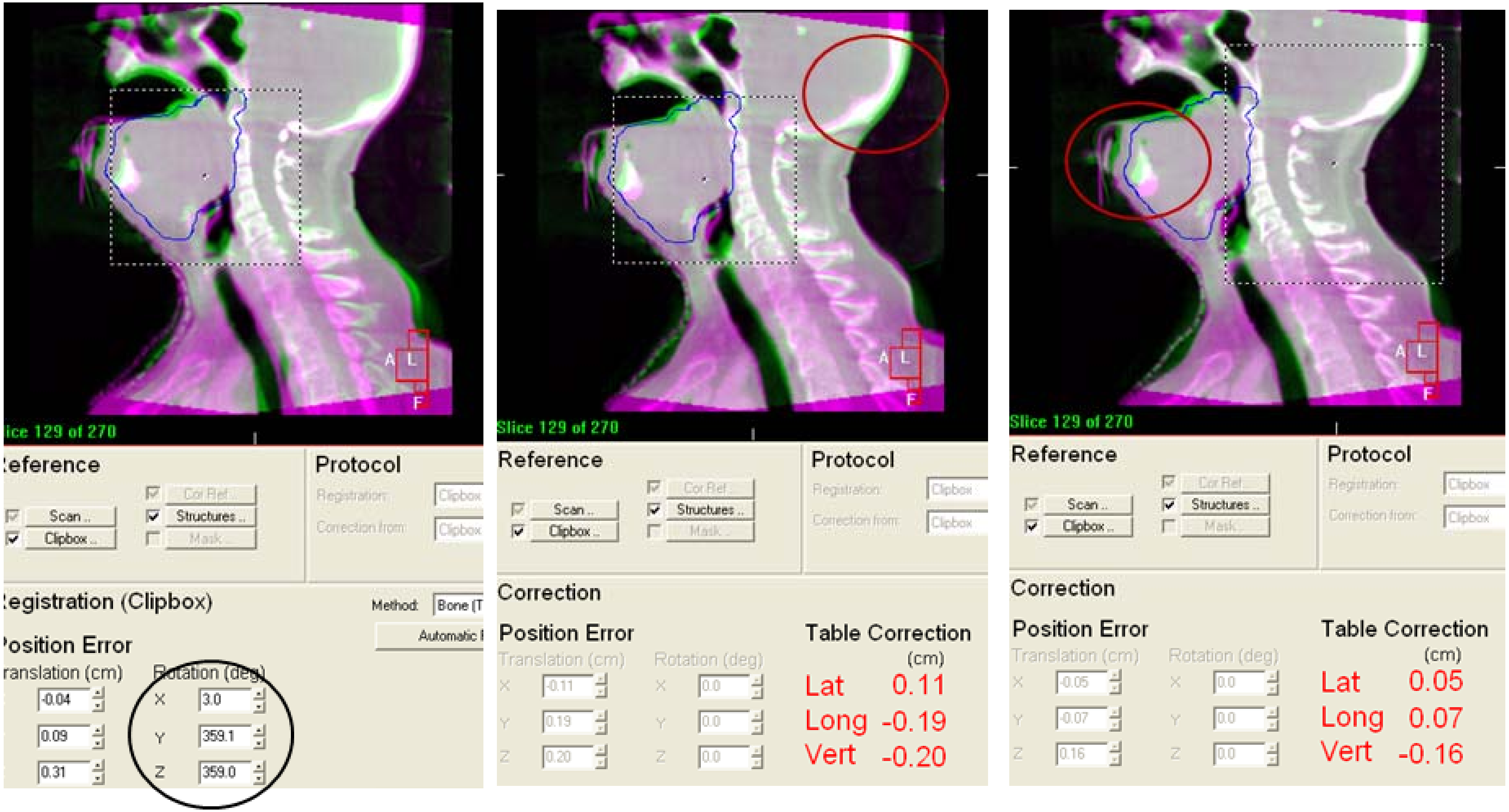

**Planning CT**

**CBCT**

unregistered

# Treatment delivery

## CT – CBCT: Bone registration

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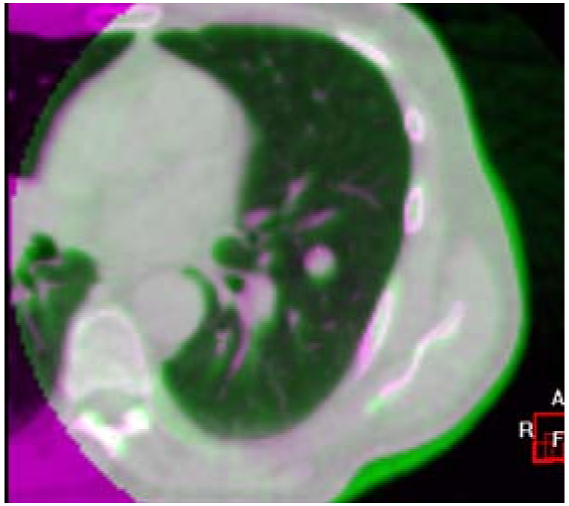
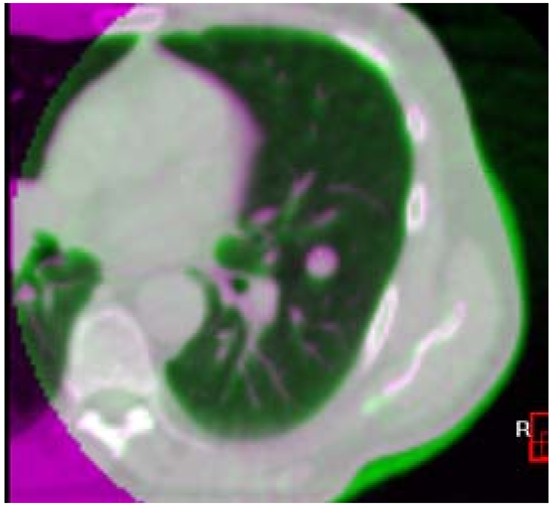
# Treatment delivery

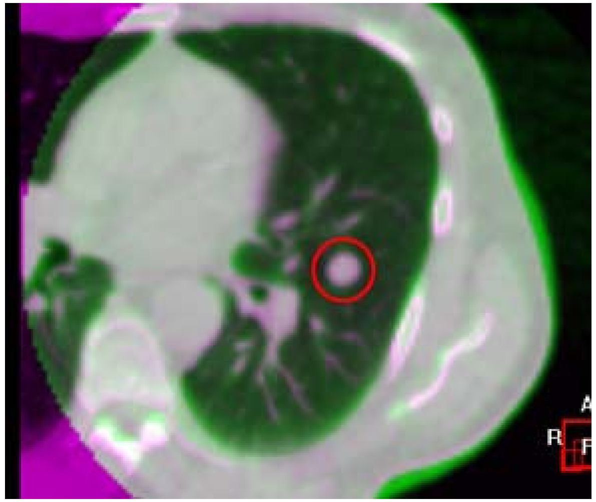
CT – CBCT



unregistered



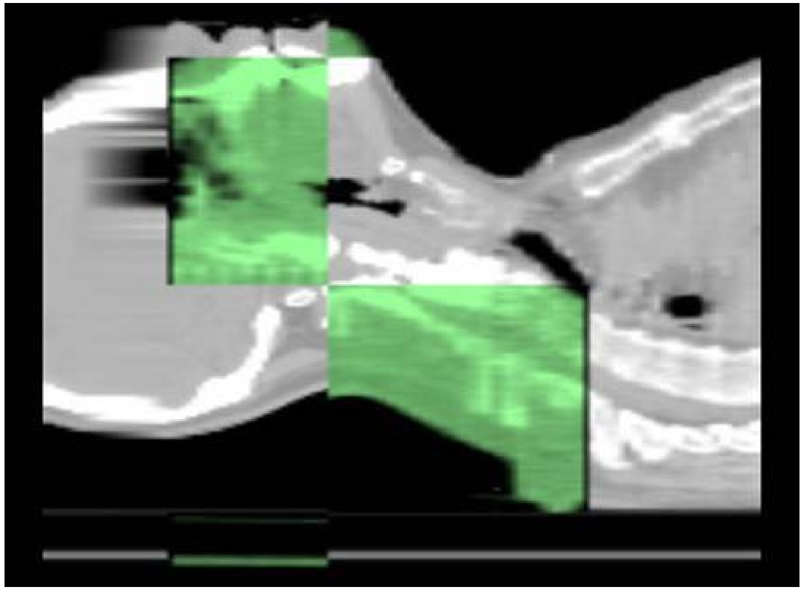
*bone* registration



*grey value* registration

# Treatment delivery

## HI-ART Tomotherapy

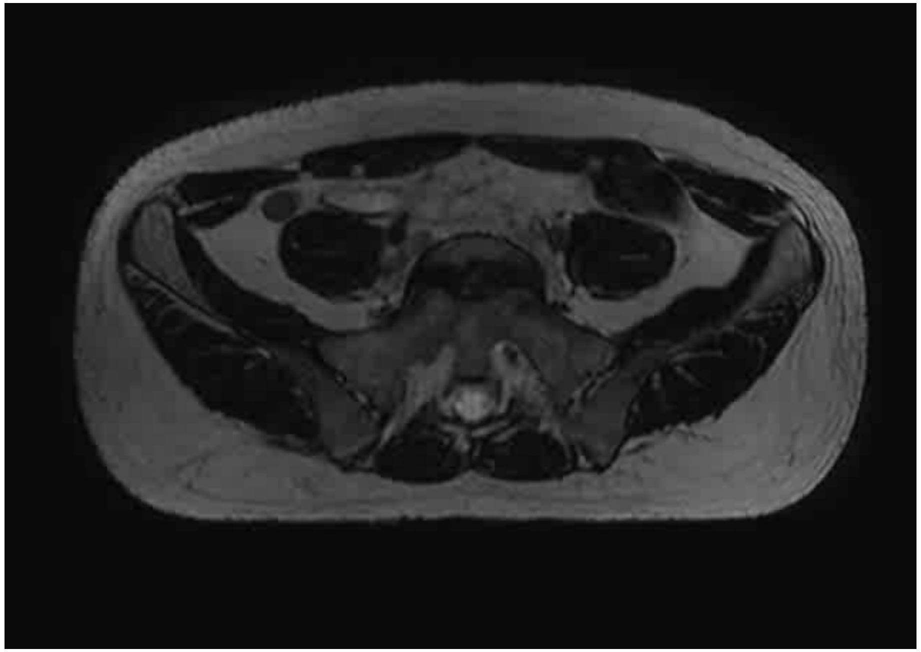


Example of sagittal view of MVCT (green) and kVCT (grey) registration

Yartsev et al. (2007)

# Treatment delivery

Outlook - MR



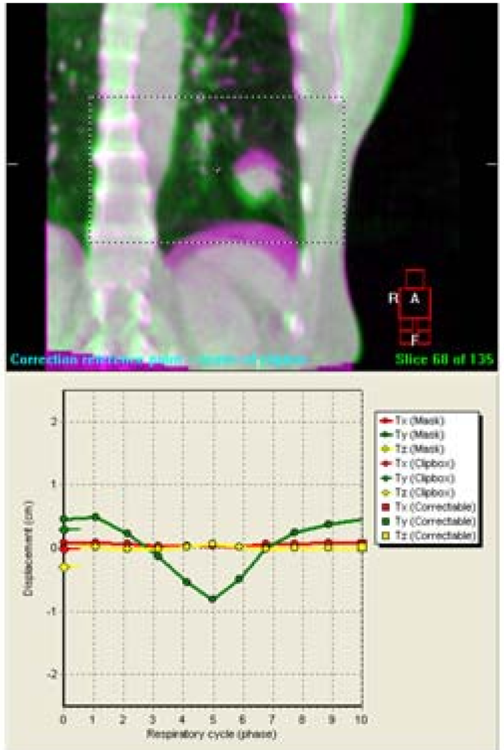
Atlantic **Philips/Elekta**

# Image registration in the RT chain

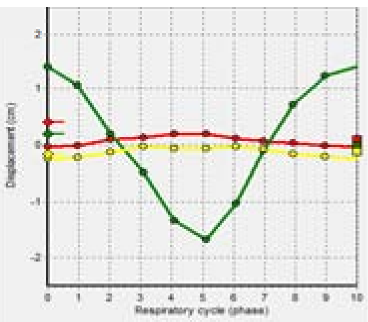
| Initial diagnosis and staging | Preparation/planning (delineation) | Delivery (position verification) | Adaptive RT |
|---|---|---|---|

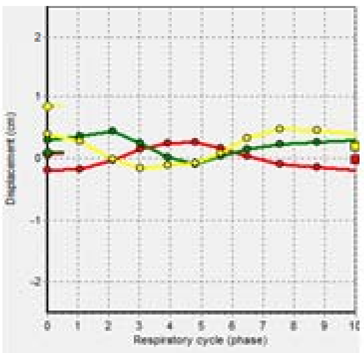
Quantification of organ motion/ organ motion analysis

# Quantification of organ motion




breathing motion:
lung tumor 4D (CB)CT displacement curve




repeat CT

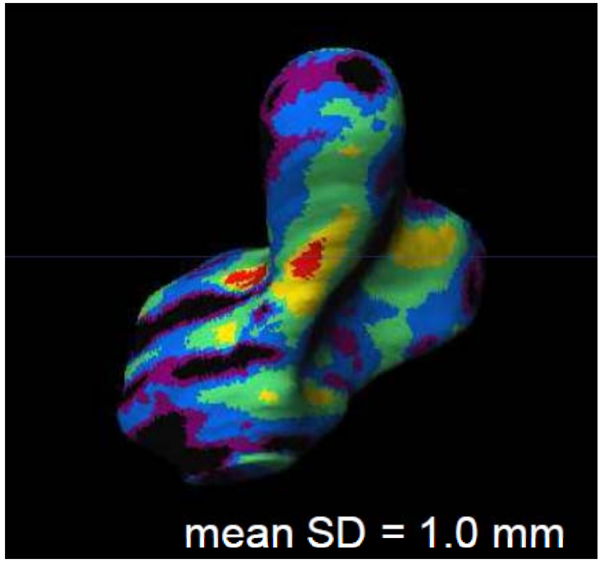
4D CT

4D CBCT

*4D MRI*

# Organ motion analysis

Analysis of prostate motion and deformation
(Deurloo et al IJROBP 2004)




SD (mm)

| 0-0.25 | 0.25-0.75 | 0.75-1.25 | 1.25-1.75 | 1.75-2.25 | 2.25-2.75 |
|---|---|---|---|---|---|

local shape variation displayed in color wash on average GTV

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# Registration accuracy

Impact on margins?

Examples for registration uncertainties:

~ 0.5 mm for cranial **CT-CBCT** registra…
(Sykes et al.,PMB 2009)

≤ 2 mm for cranial **CT-M**…
(Ulin et al., IJROB…

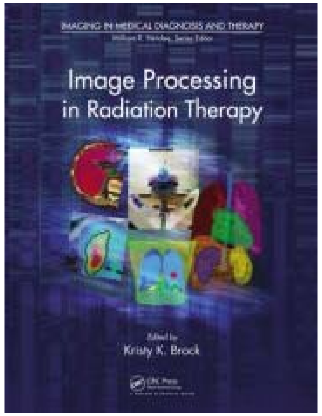
≥ 2 … …al cancer
(D…

~ 2 m… …gistration for prostate
(Nyh… , Radiat. Onc. 2009)

~ 5-7 mm for DIR
(Yeo et al., Med. Phys 2013)

**Dependent on registration method and anatomical site!**

# Some reading material




- Brock (editor) *Image Processing in Radiation Therapy,* CRC Press 2013

- Kessler et al., BJR 2006 *Image registration and data fusion in radiation therapy*

- Brock et al., IJROBP 2010 *Results of a multi-institution deformable registration accuracy study (MIDRAS)*

**Look out for…**

- AAPM TG 132 *Use of image registration and data fusion algorithms and techniques in radiotherapy treatment planning*

Start: 3/9/2006
End: 12/31/2014 (?) for preliminary recommendations: http://amos3.aapm.org/abstracts/pdf/77-22544-313436-90873.pdf

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# Take home message

- Image fusion -
  not as simple as "pushing a button"!

**CAUTION**
Image fusion

- ALWAYS check fusion result to avoid geometric misses

# part 2




"Martina's presentation wasn't so bad. After the third hour, my spirit left my body and went to the beach!"

# DIR

ESTRO School

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

# Anatomy and lymph node drainage in the mediastinum

Esther Troost, MD PhD
Klinik und Poliklinik für Strahlentherapie und Radioonkologie
Universitäts KrebsCentrum (UCC)
esther.troost@uniklinikum-dresden.de

ESTRO course Target Volume Delineation
Barcelona, April 2016

KREBSCENTRUM DRESDEN
(UNIVERSITY CANCER CENTER - UCC)

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

OncoRay
Radiation Research in Oncology

# As promised...

Universitätsklinikum Carl Gustav Carus
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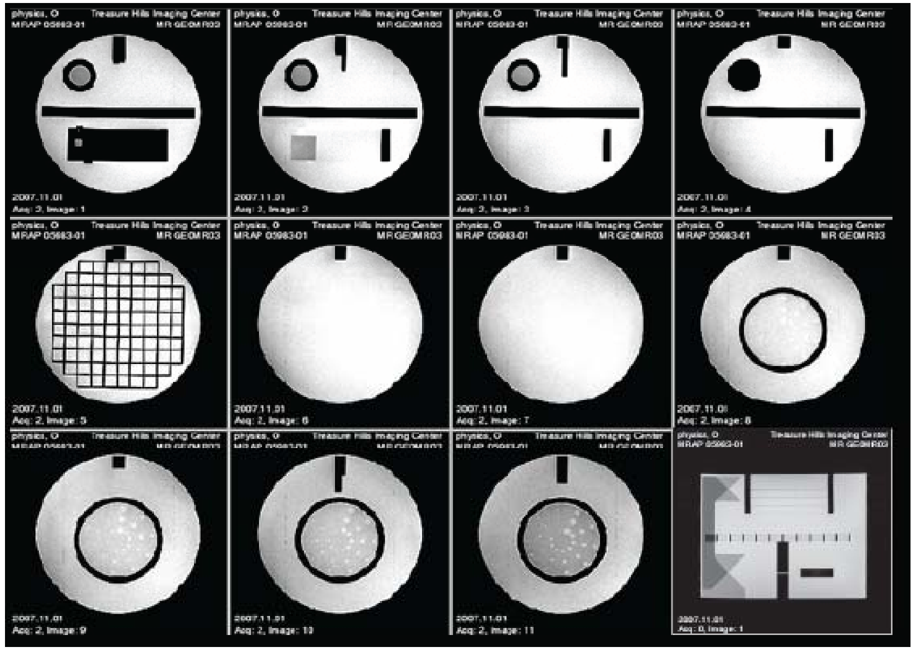
- ACR phantom for MRI quality assurance

*Google.com*

# Content

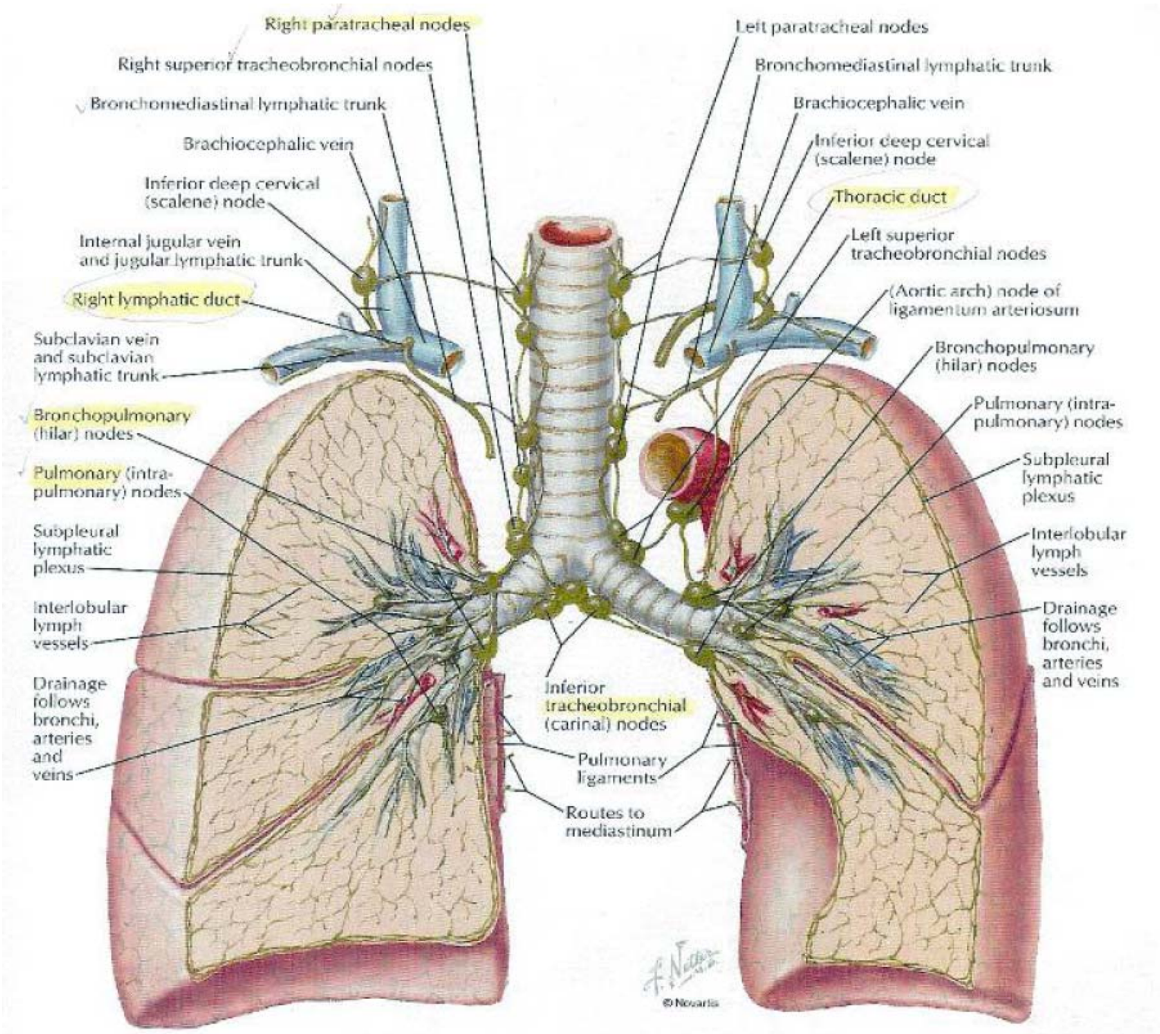


- Lymphatic drainage of the lungs

- N-stage and regional lymph node stations (maps)
  - Naruke
  - Mountain-Dresler map
  - IASLC

- Evaluation of the mediastinal lymph nodes

# Lymphatic drainage of the lungs



# Pattern of mediastinal LN metastases

Universitätsklinikum Carl Gustav Carus
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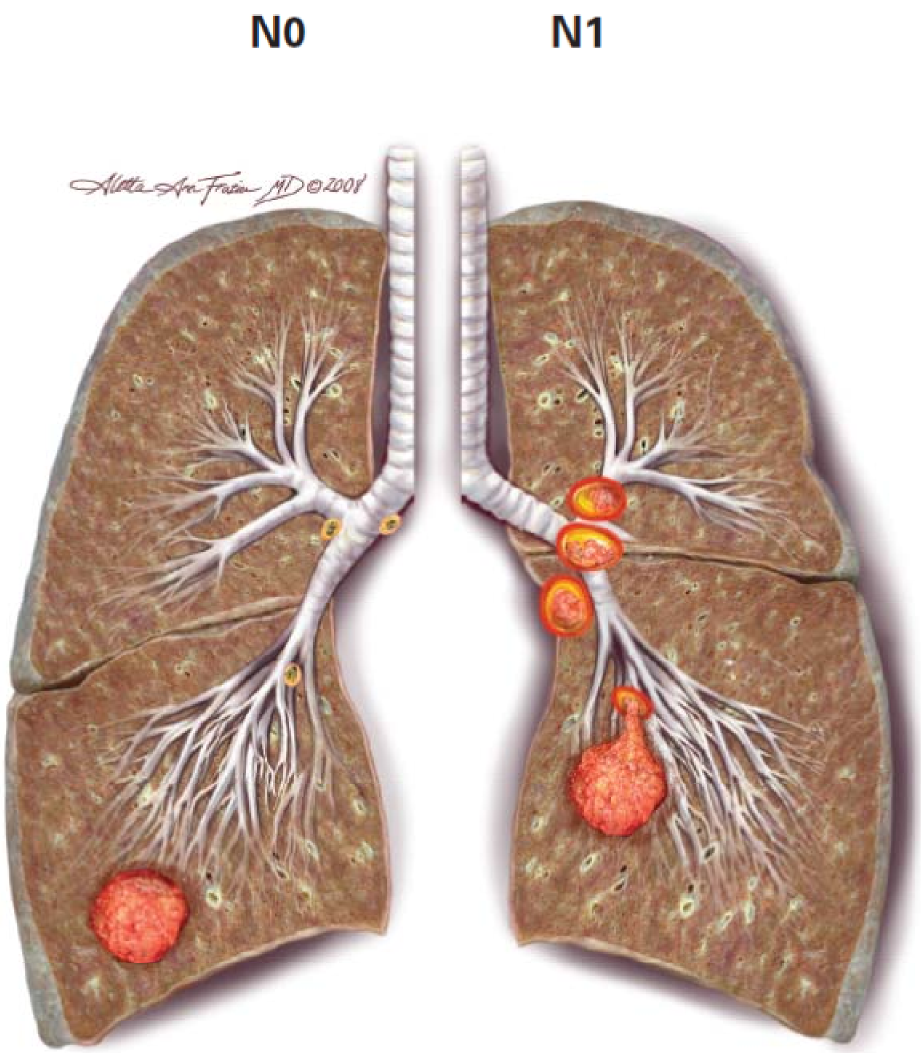
| Nodes | Right upper (N = 113) | Right lower (N = 108) | Left upper (N = 113) | Left lower (N = 68) |
|---|---|---|---|---|
| Tracheobronchial | 16 | 14.3 | | 11.8 |
| Pretracheal | 13.8 | | 6.7 | 14.3 |
| Paratracheal | 15.9 | 11.1 | | |
| Subcarinal | 6.3 | 22.2 | 2.4 | 18.5 |
| Para-aortic | | | 16.7 | |
| Subaortic | | | 15.1 | 19.1 |

Numbers are expressed in %

*Adapted from Ogata and Naruke 1986*

# Nodal stage






NX Regional lymph nodes cannot be assessed

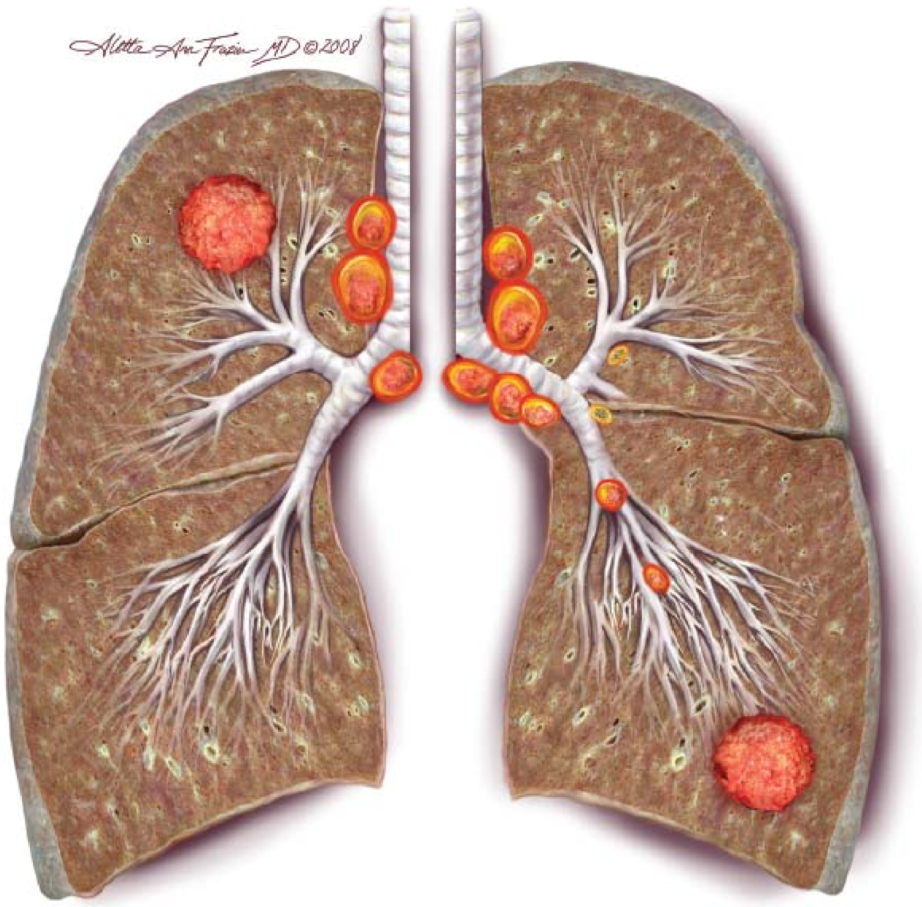
N0 No regional lymph node metastasis

N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intra-pulmonary nodes, including nodal involvement by direct extension

# Nodal stage



N2



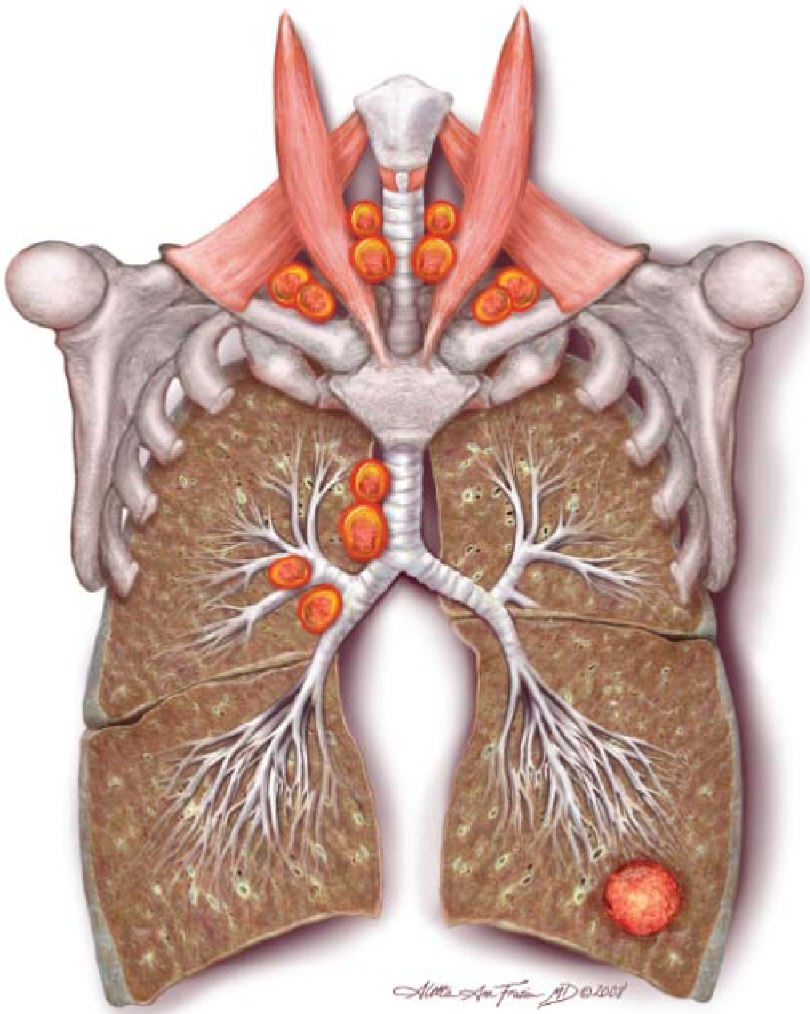

N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)

- including skip metastasis without N1 involvement
- or associated with N1 disease

# Nodal stage



N3



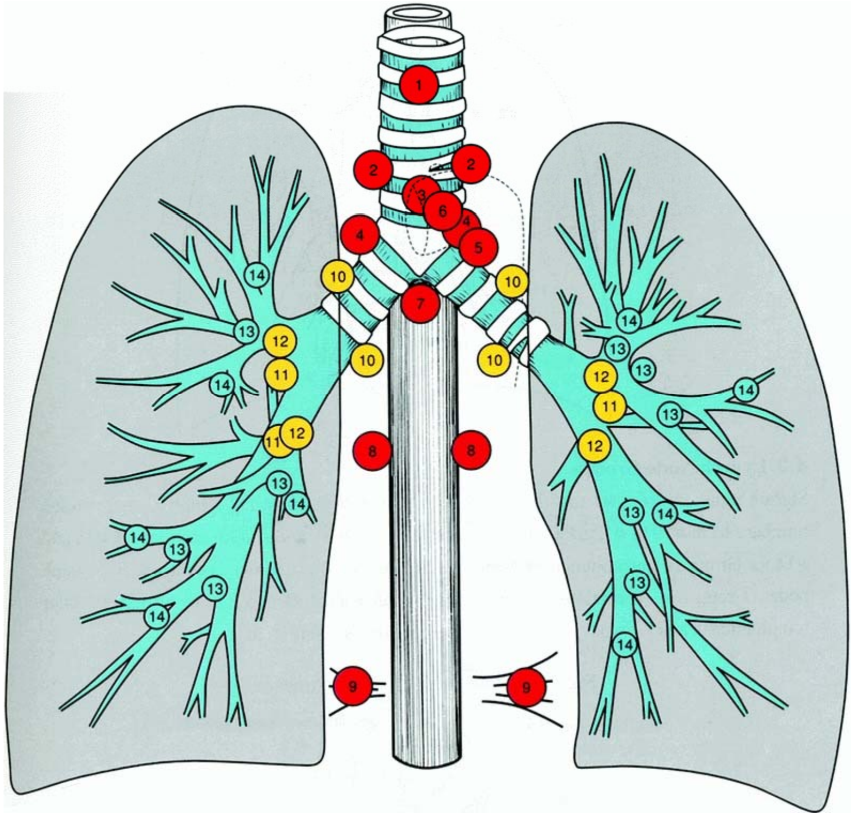

N3 Metastasis to

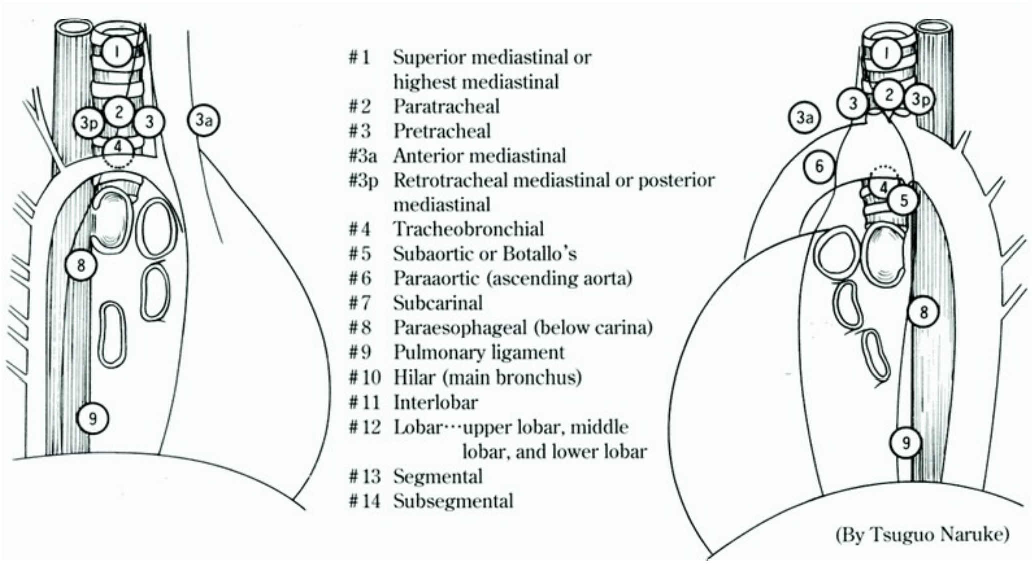
- contralateral mediastinal, contralateral hilar, contralateral scalene or supraclavicular lymph node(s)

- ipsilateral scalene or supraclavicular lymph node(s)

# Regional LN stations: Naruke map

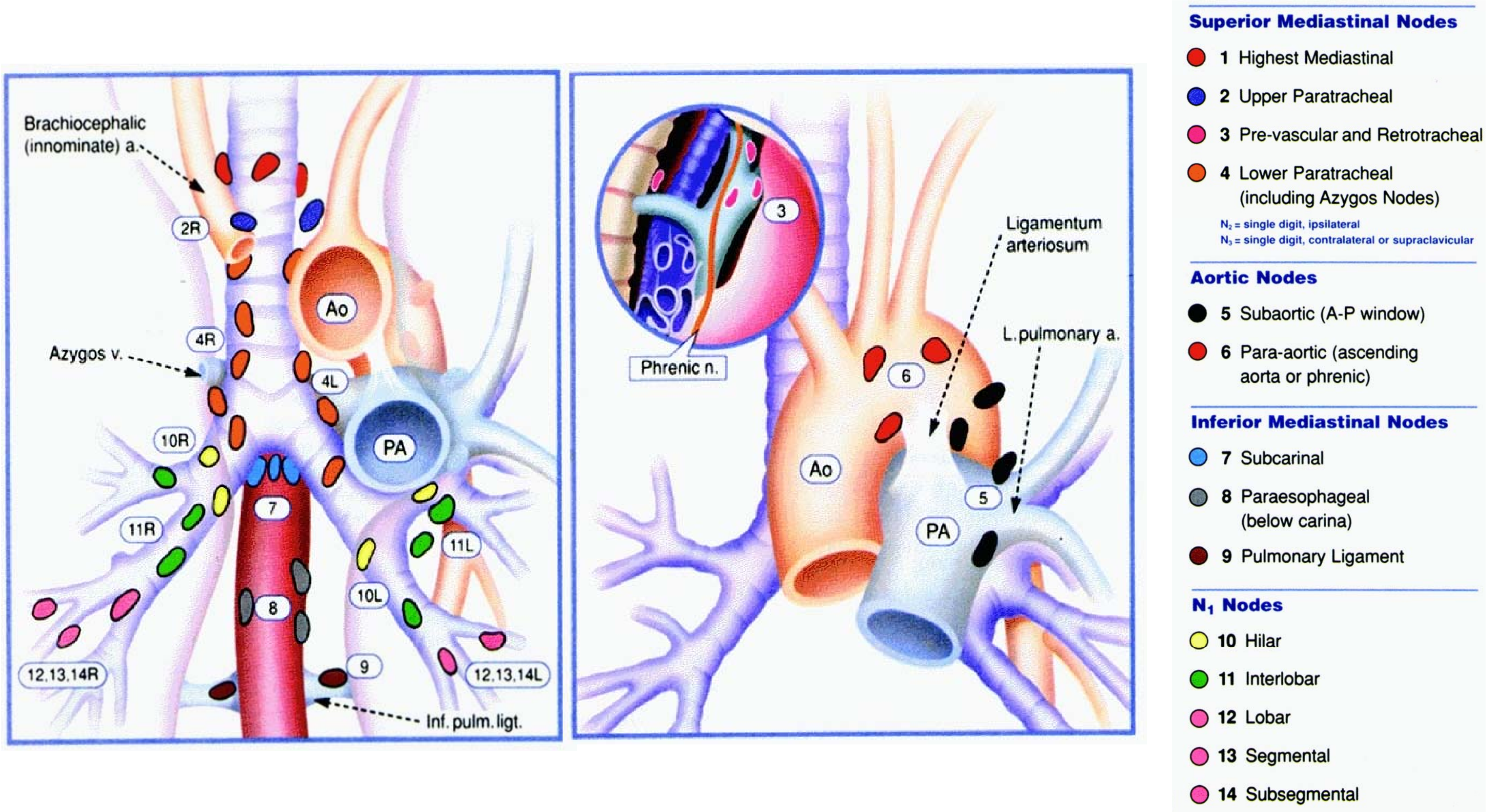







*The Japan Lung Cancer Society. Classification of Lung Cancer, 1st English Ed. Tokyo: Kanehara & Co., 2000*

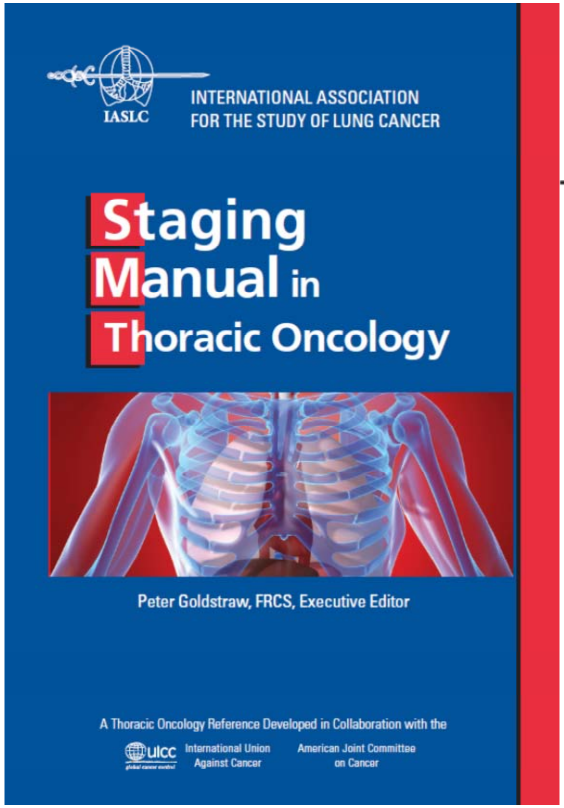
# Regional LN stations: Mountain-Dresler map




*Adapted from Mountain, Dresler Chest 1974*

# UICC 7 classification (2010)






IASLC STAGING COMMITTEE ARTICLE

## The IASLC Lung Cancer Staging Project

*A Proposal for a New International Lymph Node Map in the Forthcoming Seventh Edition of the TNM Classification for Lung Cancer*

*Valerie W. Rusch, MD,* Hisao Asamura, MD,† Hirokazu Watanabe, MD,‡ Dorothy J. Giroux, MS,§ Ramon Rami-Porta, MD,‖ and Peter Goldstraw, MD,¶ on Behalf of the Members of the IASLC Staging Committee*

*Rusch et al J Thorac Oncol 2009*
*IASLC - staging manual in thoracic oncology 2009*

# UICC 6 *versus* 7 classification

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

| $6^{th}$ edition T/M descriptor | Revised T/M descriptor | N0 | N1 | N2 | N3 |
|---|---|---|---|---|---|
| *T1 (≤2cm)* | **T1a** | IA | IIA | IIIA | IIIB |
| *T1 (>2-3cm)* | **T1b** | IA | IIA | IIIA | IIIB |
| *T2 (>3-5 cm)* | **T2a** | IB | **IIA** | IIIA | IIIB |
| *T2 (>5-7cm)* | **T2b** | **IIA** | IIB | IIIA | IIIB |
| *T2 (>7cm)* | **T3** | **IIB** | **IIIA** | IIIA | IIIB |
| *T3 invasion* | **T3** | IIB | IIIA | IIIA | IIIB |
| *T4 (same lobe nodules)* | **T3** | **IIB** | **IIIA** | **IIIA** | IIIB |
| *T4 (extension)* | **T4** | **IIIA** | **IIIA** | IIIB | IIIB |
| *M1 (ipsilateral lung)* | **T4** | **IIIA** | **IIIA** | **IIIB** | **IIIB** |
| *T4 (pleural effusion)* | **M1a** | **IV** | **IV** | **IV** | **IV** |
| *M1 (contralateral lung)* | **M1a** | IV | IV | IV | IV |
| *M1 (distant)* | **M1b** | IV | IV | IV | IV |

*IASLC - staging manual in thoracic oncology 2009*

# UICC 7 classification (2010)



- Detailed nomenclature for the surgical anatomical boundaries of lymph nodes stations

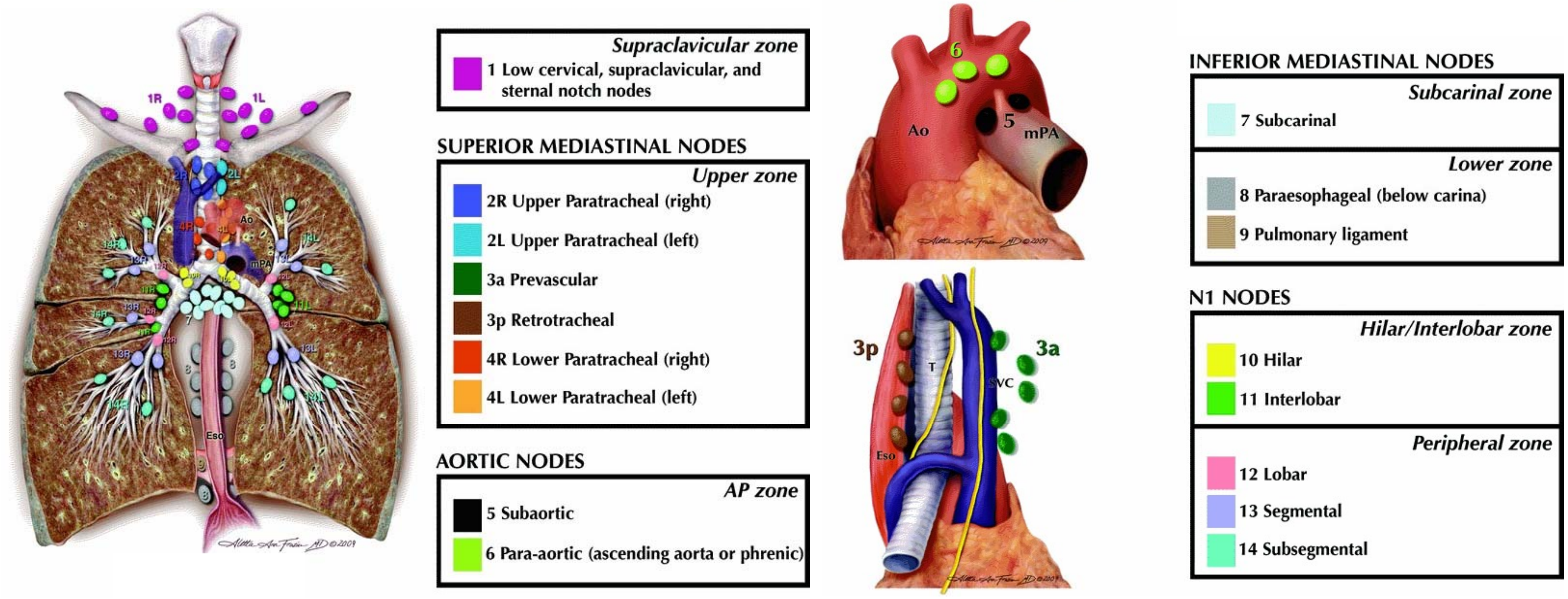
- Most important changes from Mountain-Dresler map
  - Shift of midline to the left of the trachea:
    4R includes pretracheal LN
  - Shift of cranial and caudal boundaries of # 2, 7, 10R, 10 L
  - Might result in some recoding of N1 -> N2

- No of involved zones (single vs multiple)

*Rusch et al J Thorac Oncol 2009*

# UICC 7 classification (2010)

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

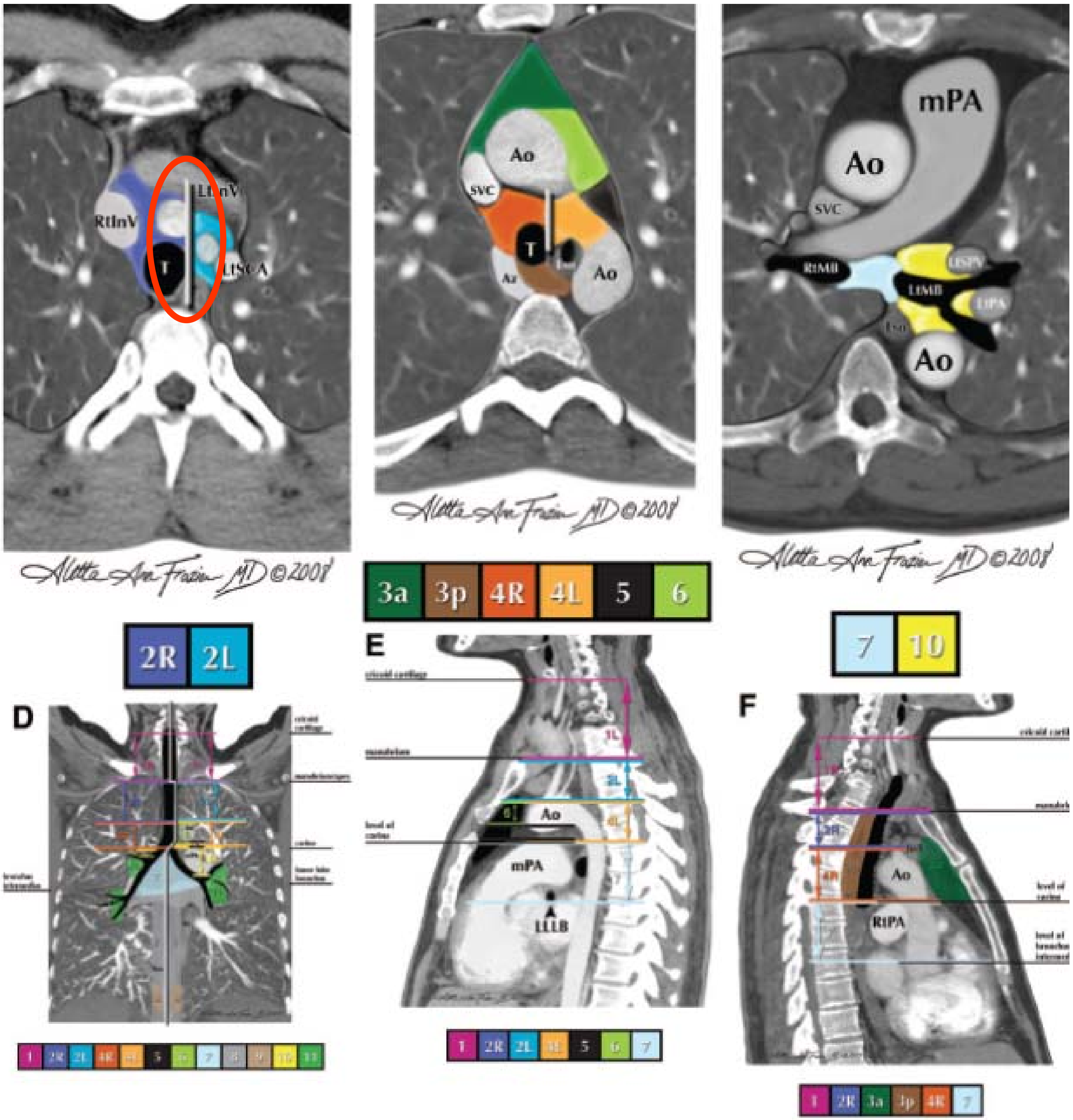



*Rusch et al J Thorac Oncol 2009*

# IASLC Map

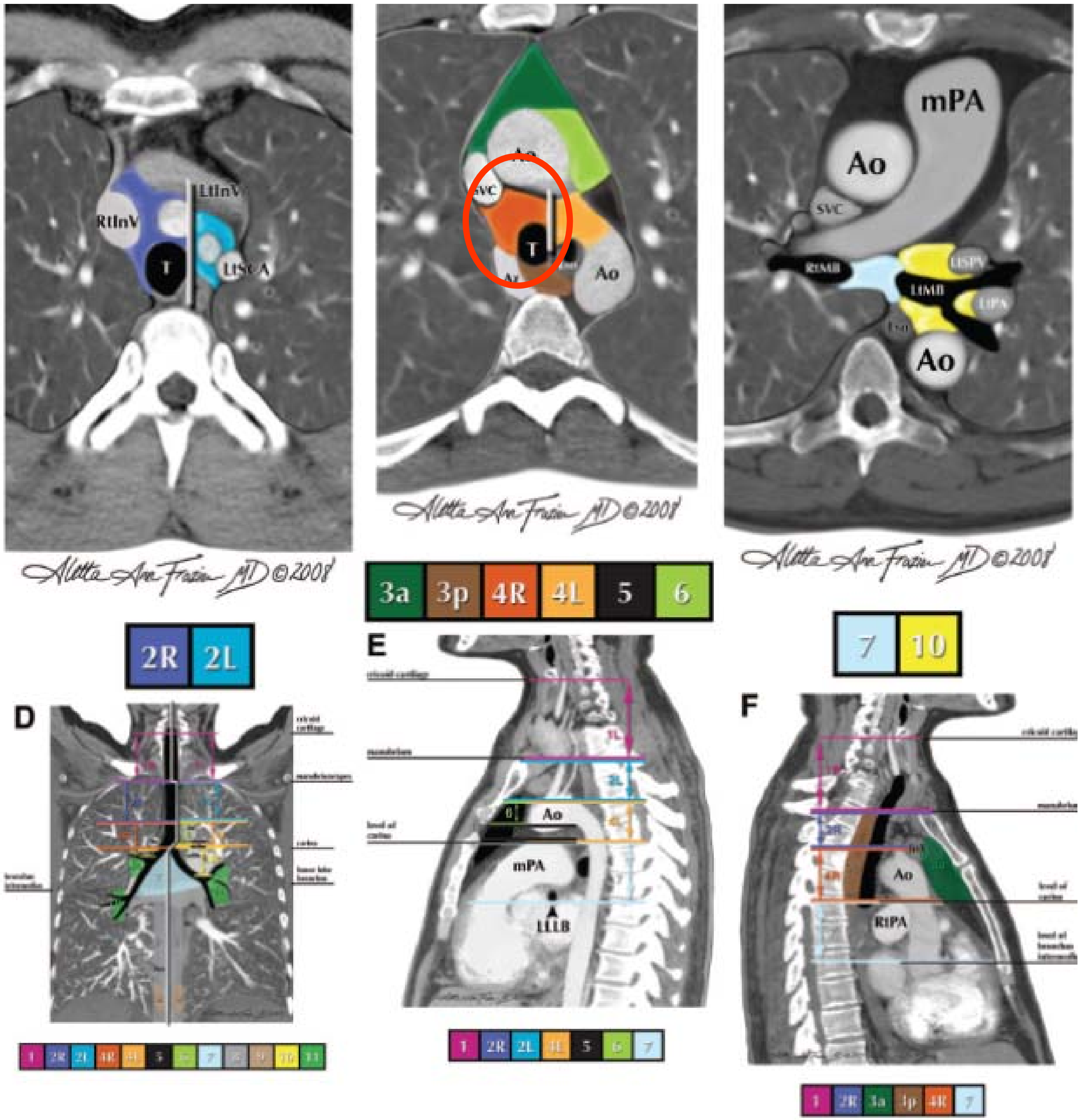
| Station | Definition |
| --- | --- |
| 1 | Upper border: lower margin of cricoid cartilage<br>Lower border: clavicles bilaterally and, in the midline, the upper border of the manubrium, 1R designates right-sided nodes, 1L, left-sided nodes in this region<br>For lymph node station 1, the midline of the trachea serves as the border between 1R and 1L |
| 2 | 2R: Upper border: apex of the right lung and pleural space, and in the midline, the upper border of the manubrium<br>Lower border: intersection of caudal margin of innominate vein with the trachea<br>As for lymph node station 4R, 2R includes nodes extending to the left lateral border of the trachea<br>2L: Upper border: apex of the left lung and pleural space, and in the midline, the upper border of the manubrium<br>Lower border: superior border of the aortic arch |
| 3 | 3a: Prevascular<br>On the right<br>Upper border: apex of chest<br>Lower border: level of carina<br>Anterior border: posterior aspect of sternum<br>Posterior border: anterior border of superior vena cava<br>On the left:<br>Upper border: apex of chest<br>Lower border: level of carina<br>Anterior border: posterior aspect of sternum<br>Posterior border: left carotid artery<br>3p: Retrotracheal<br>Upper border: apex of chest<br>Lower border: carina |
| 4 | 4R: includes right paratracheal nodes, and pretracheal nodes extending to the left lateral border of trachea<br>Upper border: intersection of caudal margin of innominate vein with the trachea<br>Lower border: lower border of azygos vein<br>4L: includes nodes to the left of the left lateral border of the trachea, medial to the ligamentum arteriosum<br>Upper border: upper margin of the aortic arch<br>Lower border: upper rim of the left main pulmonary artery |
| 5 | Subaortic lymph nodes lateral to the ligamentum arteriosum<br>Upper border: the lower border of the aortic arch<br>Lower border: upper rim of the left main pulmonary artery |
| 6 | Lymph nodes anterior and lateral to the ascending aorta and aortic arch<br>Upper border: a line tangential to the upper border of the aortic arch<br>Lower border: the lower border of the aortic arch |
| 7 | Upper border: the carina of the trachea<br>Lower border: the upper border of the lower lobe bronchus on the left; the lower border of the bronchus intermedius on the right |
| 8 | Nodes lying adjacent to the wall of the esophagus and to the right or left of the midline, excluding subcarinal nodes<br>Upper border: the upper border of the lower lobe bronchus on the left; the lower border of the bronchus intermedius on the right<br>Lower border: the diaphragm |
| 9 | Nodes lying within the pulmonary ligament<br>Upper border: the inferior pulmonary vein<br>Lower border: the diaphragm |
| 10 | Includes nodes immediately adjacent to the mainstem bronchus and hilar vessels including the proximal portions of the pulmonary veins and main pulmonary artery<br>Upper border: the lower rim of the azygos vein on the right; upper rim of the pulmonary artery on the left<br>Lower border: interlobar region bilaterally |
| 11 | Between the origin of the lobar bronchi<br>"#11s: between the upper lobe bronchus and bronchus intermedius on the right<br>"#11i: between the middle and lower lobe bronchi on the right |

*Rusch et al J Thorac Oncol 2009*




*Rusch et al J Thorac Oncol 2009*

www.uniklinikum-dresden.de




*Rusch et al J Thorac Oncol 2009*

www.uniklinikum-dresden.de

# Content

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

- Lymphatic drainage of the lungs

- N-stage and regional lymph node stations (maps)
  - Naruke
  - Mountain-Dresler map
  - IASLC

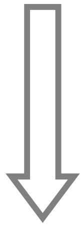
- Evaluation of the mediastinal lymph nodes

# Evaluation of mediastinum

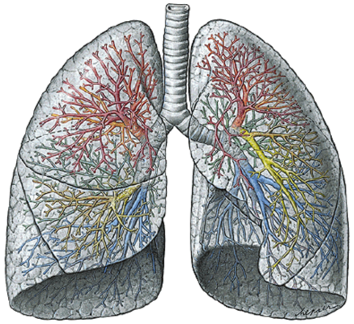


- Mediastinoscopy
- EBUS – TBNA
- EUS – FNA
- PET
- CT

**Invasive**



**Non - invasive**



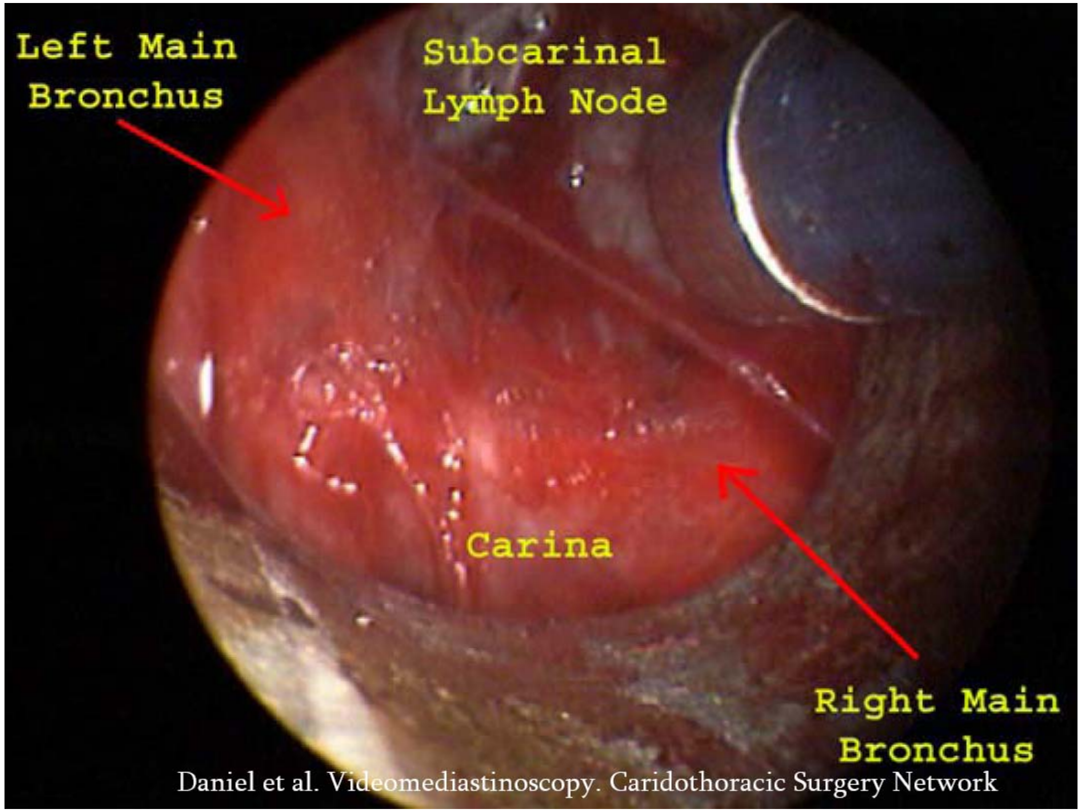
**EBUS-TBNA:** Endo Bronchial Ultrasound Guided – Trans Bronchial Needle Aspiration

**EUS-FNA:** Esophageal Ultrasound Guided – Fine Needle Aspiration

*Herth et al, Eur Respir J 2006*

# Mediastinoscopy

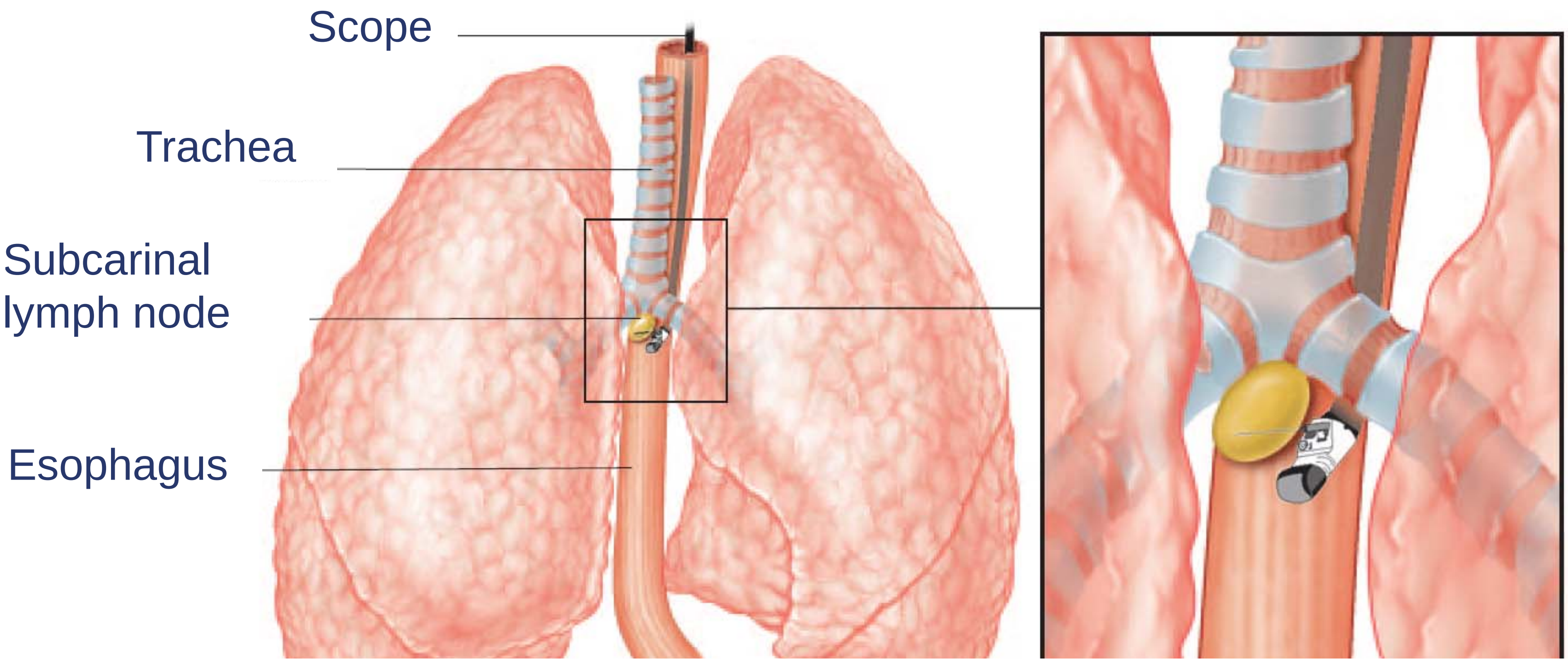





- Sensitivity 76-85%
- Negative PV 82-92%
- Complication rate 5%
  - Pneumothorax
  - Hemorrhage
  - Laryngeal nerve palsy

# Transesophageal ultrasound






Transesophageal ultrasound-guided fine needle aspiration of a subcarinal lymph node. Sensitivity of 78% and specificity of 71%

*Toloza et al, Chest 2003*
*Herth et al, Eur Respir J 2006*

# Transesophageal US-guided FNA

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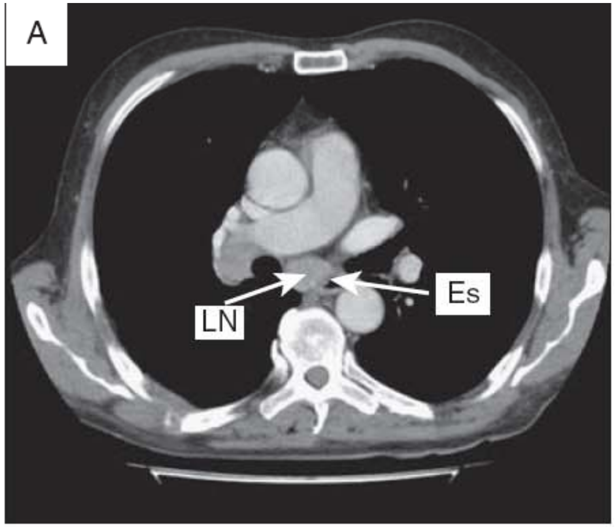
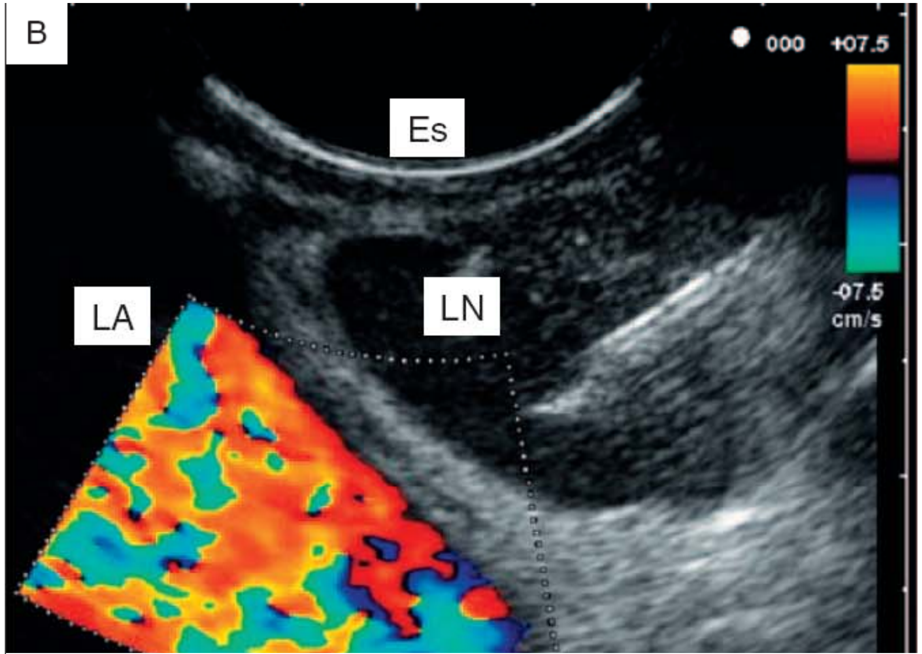
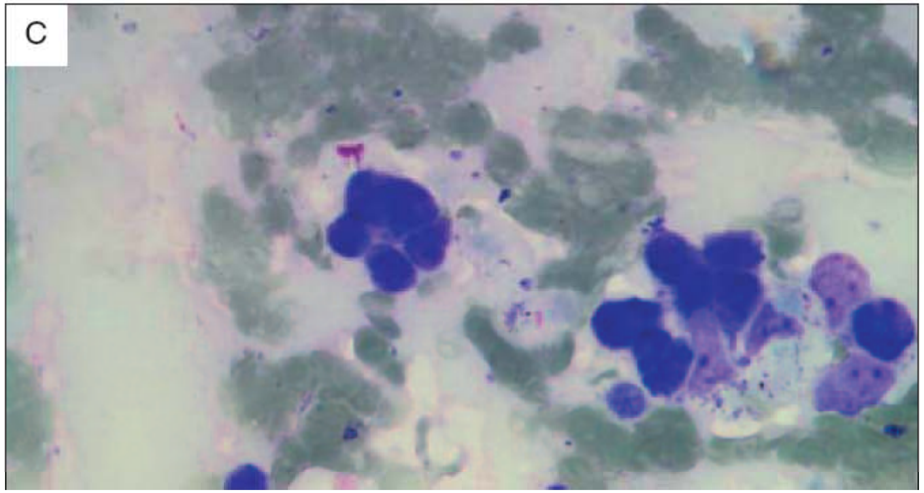


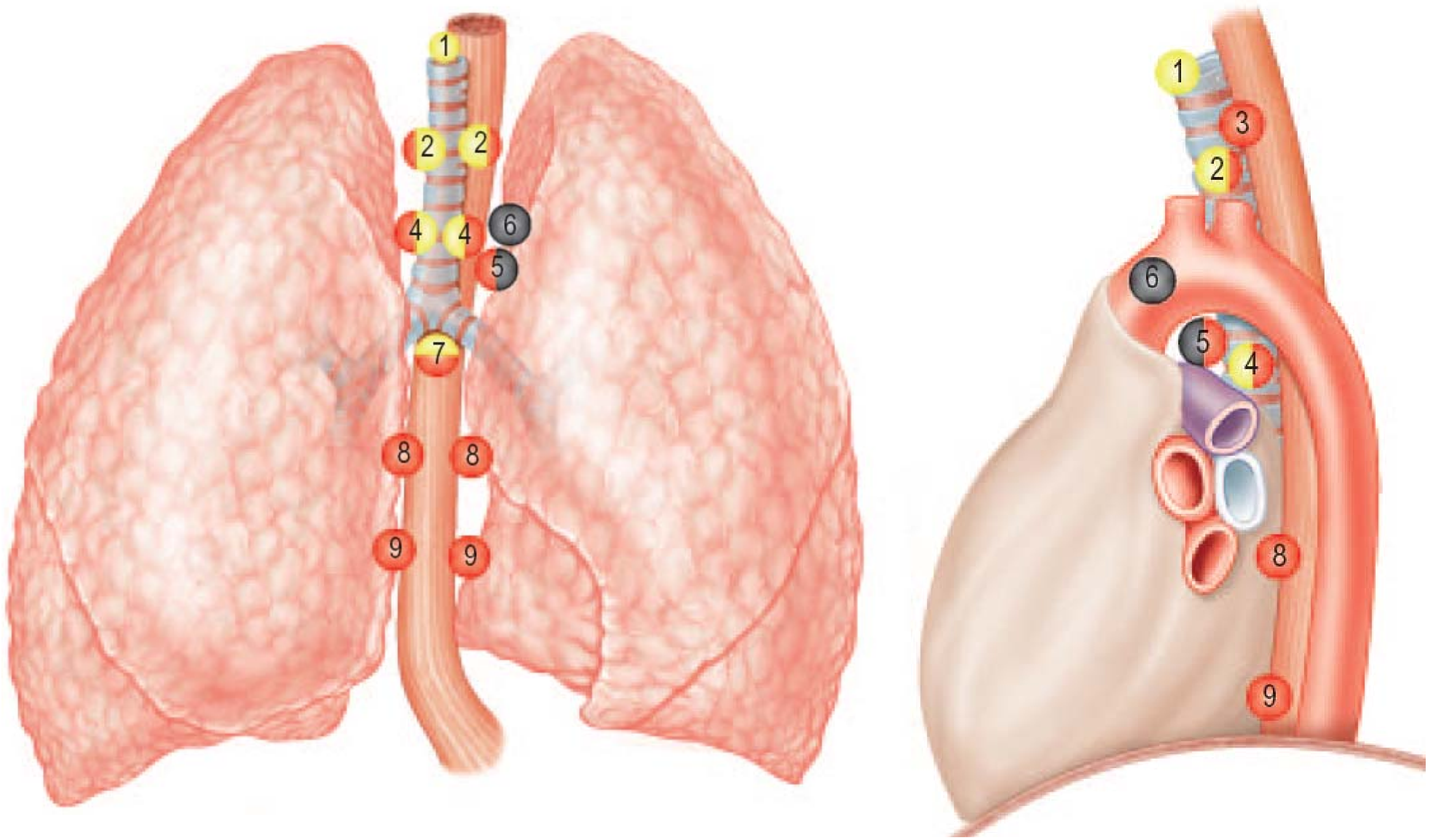

LN: Lymph node
Es: Esophagus
LA: Left Atrium




*Toloza et al, Chest 2003*
*Herth et al, Eur Respir J 2006*

# Reach of staging techniques






EUS - FNA Mediastinoscopy – EBUS / TBNA Mediastinotomy (VATS)

*adapted from Annema et al, JAMA 2005*

# Non-invasive staging: PET-CT



**Review:**

- At least 17 well-documented prospective studies, 3 meta-analyses
- PET more accurate than CT (90% vs 75%)
- Correlation with CT scan improves interpretation
- More reading – see subsequent presentation

| | CT | PET |
|---|---|---|
| Sensitivity | 60% | 79% |
| Specificity | 77% | 91% |

*Dwamena 1999, Fischer 2001, Toloza 2003*

# Non-invasive staging: MRI



- Meta-analysis on value of MRI for staging and RT planning
- N=12 studies eligible

| | PET/CT per-patient basis | | PET/CT per-nodal basis | |
|---|---|---|---|---|
| Meta-analyses | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) |
| Lv YL 2011 | 76 [65-84] | 88 [82-92] | 65 [62-68] | 95 [94-95] |
| Zhao L 2012 | 72 [68-75] | 90 [88-91] | 61 [58-64] | 93 [92-93] |
| Wu Y 2013 | 72 [65-78]* | 91 [86-94]* | 78 [64-87] | 90 [84-94] |
| Wu LM 2012 | 75 [68-81] | 89 [85-91] | - | - |

*Peerlings et al, Radiology in press*

# Take home messages

The optimal nodal target volume determination remains challenging……

- Extensive lymphatic drainage
- Knowledge! of the incidence of lymph node involvement in different lymph node stations in relation to location of primary tumor
- Knowledge! of the anatomy of lymph node stations and boundaries
- Knowledge! of the TNM classification (use the same language as your colleagues!)
- Knowledge! of the reliability of staging procedures


OncoRay – National Center for Radiation Research in Oncology, Dresden

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

# GTV and CTV for lung cancer – Delineation of Organs at Risk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ESTRO course Target Volume Delineation

Barcelona, April 2016

KREBSCENTRUM DRESDEN (UNIVERSITY CANCER CENTER - UCC)

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

OncoRay
Radiation Research in Oncology

# Content



- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk
- Beyond…

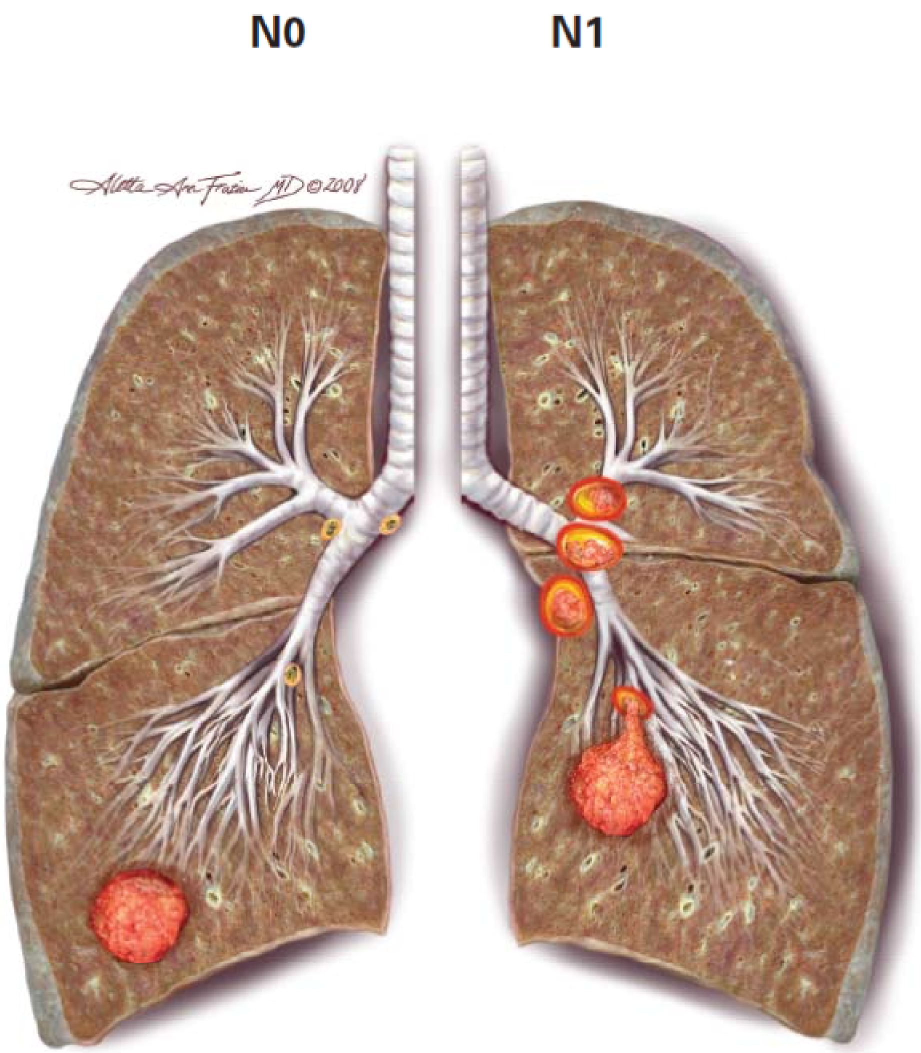
# Content



- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk
- Beyond…

# Nodal stage






NX Regional lymph nodes cannot be assessed

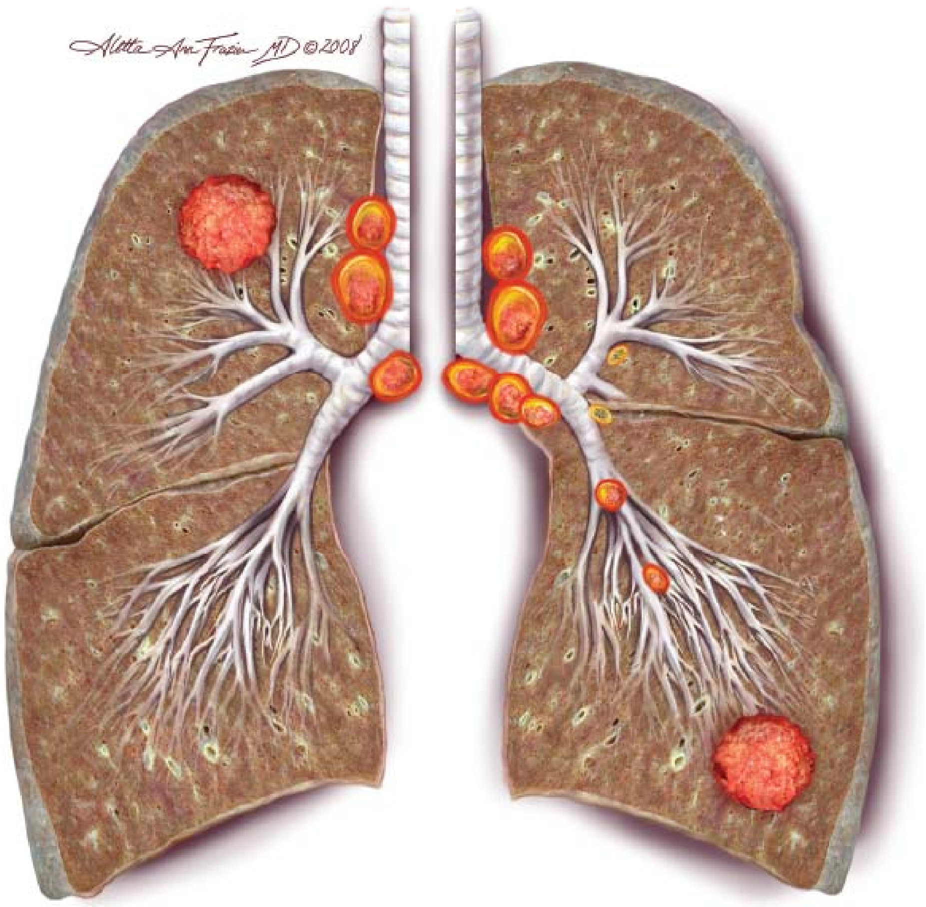
N0 No regional lymph node metastasis

N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intra-pulmonary nodes, including nodal involvement by direct extension

# Nodal stage



**N2**




N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)

- including skip metastasis without N1 involvement
- or associated with N1 disease

# Nodal stage

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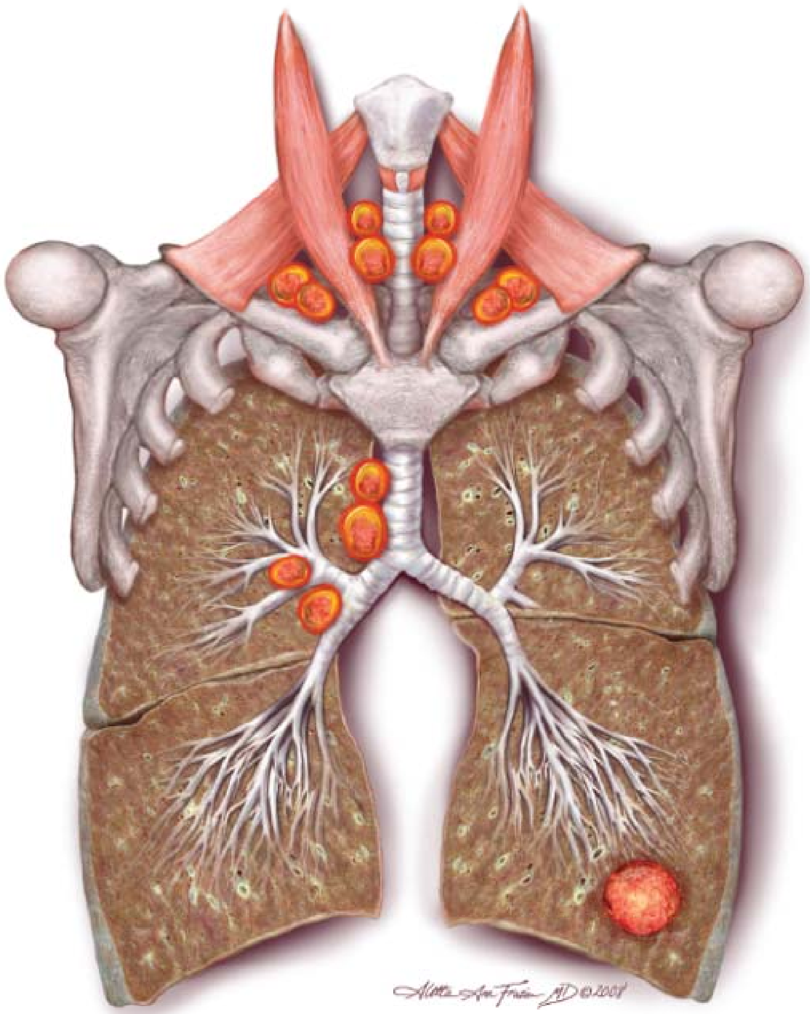
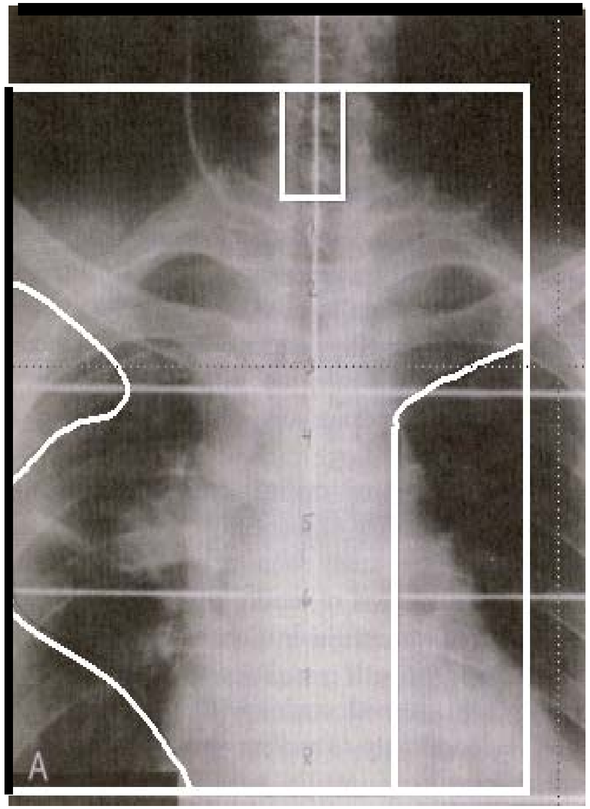
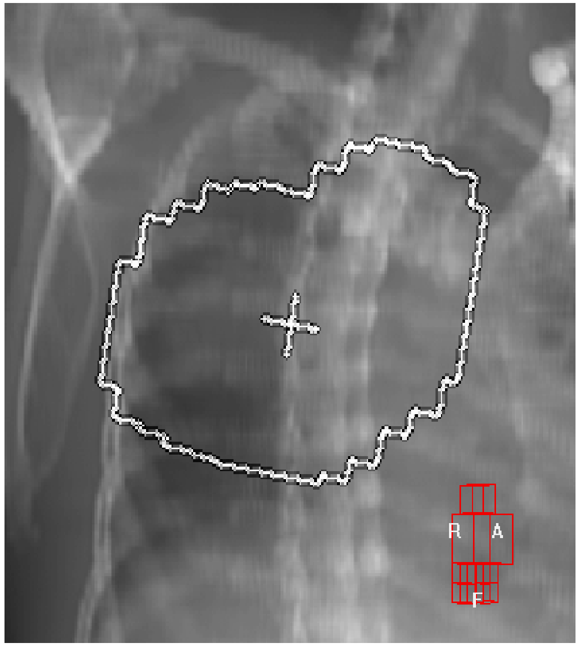



N3 Metastasis to

- contralateral mediastinal, contralateral hilar, contralateral scalene or supraclavicular lymph node(s)
- ipsilateral scalene or supraclavicular lymph node(s)

# Elective versus selective nodal irradiation in NSCLC




**Importance of staging**

CT 1 cm size criterion (short axis)

PET positive lymph nodes

# Elective versus selective nodal irradiation in NSCLC



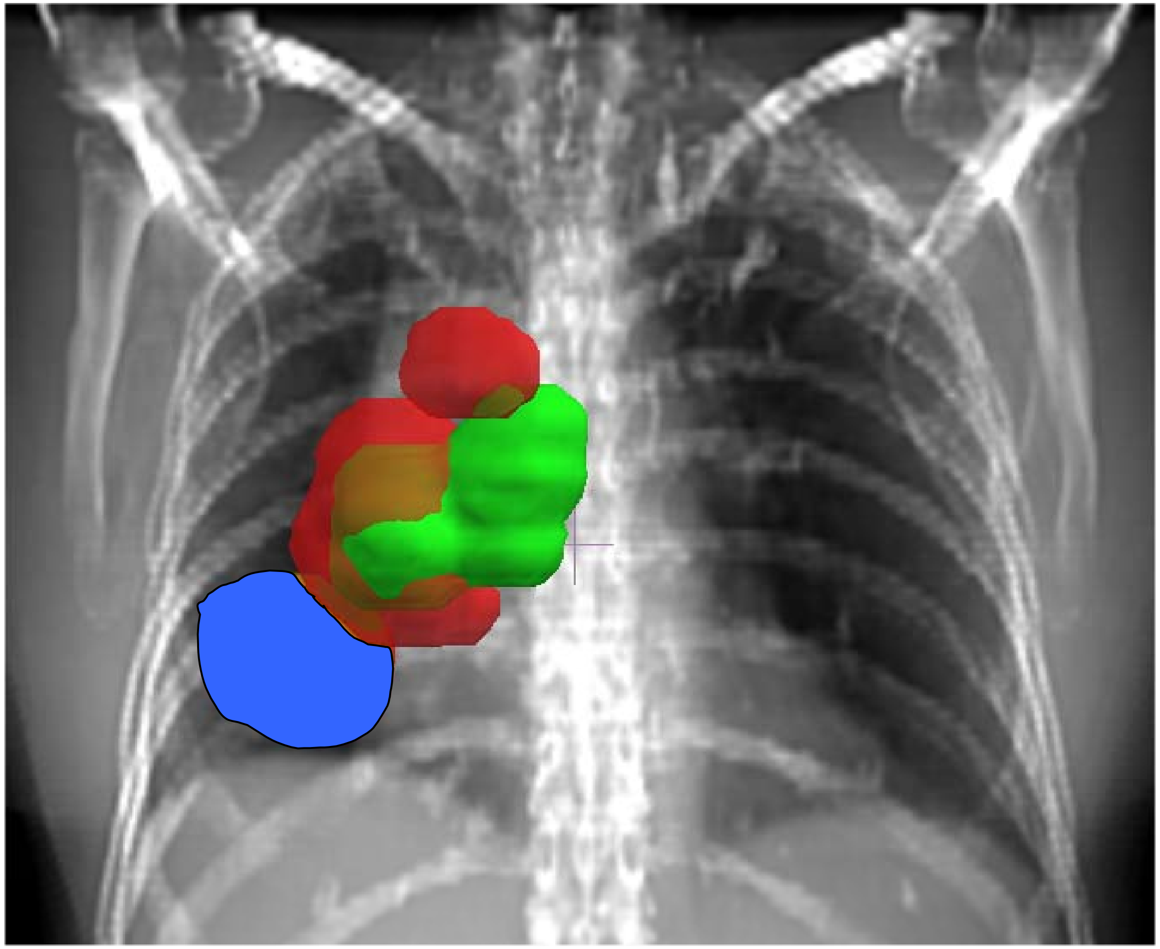
**+ elective**

- Conventional
- False negative rate on CT scan
- Occult micrometastases

**+ selective**

- Toxicity
- Relapses mainly local and distant
- Isolated nodal relapse 0-6%
- Incidental dose in regional lymph nodes

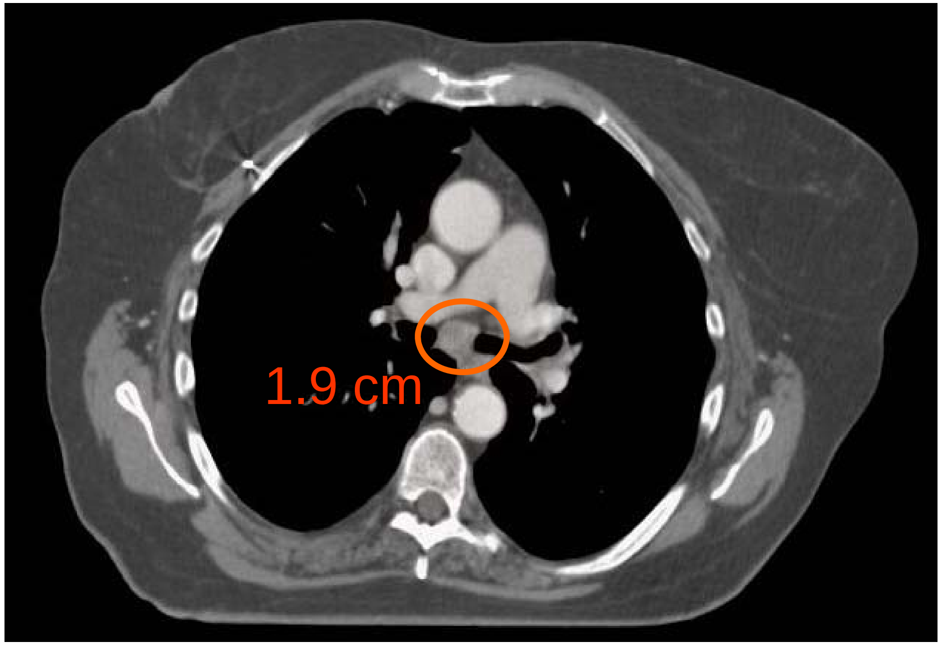
# Selective nodal irradiation in NSCLC: CT or PET?

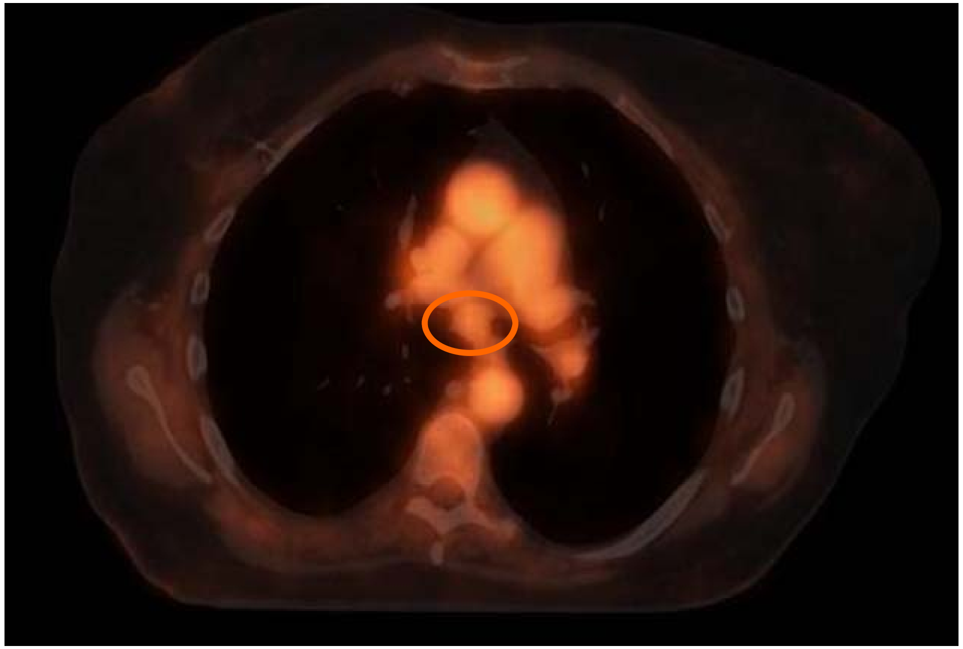


Primary tumour right lower lobe (blue)

Pathological lymph nodes
CT based: red
FDG-PET scan based: green

# Selective nodal irradiation in NSCLC: CT or PET?



CT: lnn station 7 enlarged
cT4**N2**M0

PET: lnn station 7 negative
cT4**N0**M0

# Selective nodal irradiation in NSCLC: FDG-PET-CT based!

- 44 patients NSCLC
- 61.2-64.8 Gy (1.8 Gy BID)
- median FU: 16 months
- Isolated nodal recurrence: 1 patient (2.3%)

- 88 patients NSCLC
- dose-escalation study
- median FU: 16 months
- Isolated nodal recurrence: 2 patients (2.3%)

Selective nodal irradiation based on **PET-CT** is safe in NSCLC

De Ruysscher *et al*., IJROBP 2005
Belderbos *et al*., IJROBP 2006

# Elective versus selective nodal irradiation in NSCLC

| Reference | Number of patients | LN target volume using CT and/or $^{18}$FDG PET | ENI yes/no | ENI dose (Gy) | % isolated LN failure |
|---|---|---|---|---|---|
| Graham M., *et al.*, 1995† | 179 | LN ≥1 cm | No | | 8% |
| Kong FM., *et al.*, 2005* | 106 | LN ≥1 cm (pre-chemotherapy) | No | | 6% |
| Rosenzweig K., *et al.*, 2001* | 171 | LN ≥1.5 cm | No | - | 6.4% |
| Senan S., *et al.*, 2002* | 50 | LN ≥1 cm N2 and T4N0 tumors: ipsilateral hilus included | Yes | 50 | 0 |
| De Ruysscher D., *et al.*, 2005† | 44 | PET + LN only | No | - | 2 % |
| Belderbos J., *et al.*, 2006† | 67 | PET + LN only | No | - | 3 % |
| Rosenzweig K., *et al.*, 2007* | 524 | LN ≥1.5 cm and in 314 patients PET + LN also | No | | 6.1% |

- No proven benefit of ENI in NSCLC
- Selective nodal RT is recommended

Belderbos *et al.*, IJROBP 2008

# Selective nodal irradiation in NSCLC: FDG-PET-CT based in IMRT!

- Validation of concept in IMRT era
- Retrospective study in N=183 NSCLC patients, median FUP 58 mths

- 61.7% suffered from recurrent disease:
  - Isolated nodal recurrence in 2.2% of the patients
  - Local recurrence 11.5%, locoregional recurrence 2.7%, distant metastases only 26.8%, combined failure 18.0%.

- Selective nodal irradiation remains safe in the era of highly conformal RT

Martinussen *et al.*, submitted

# Proposal definition of nodal target volume in NSCLC

**Table 1** Scheme for Defining the Mediastinal GTV for NSCLC

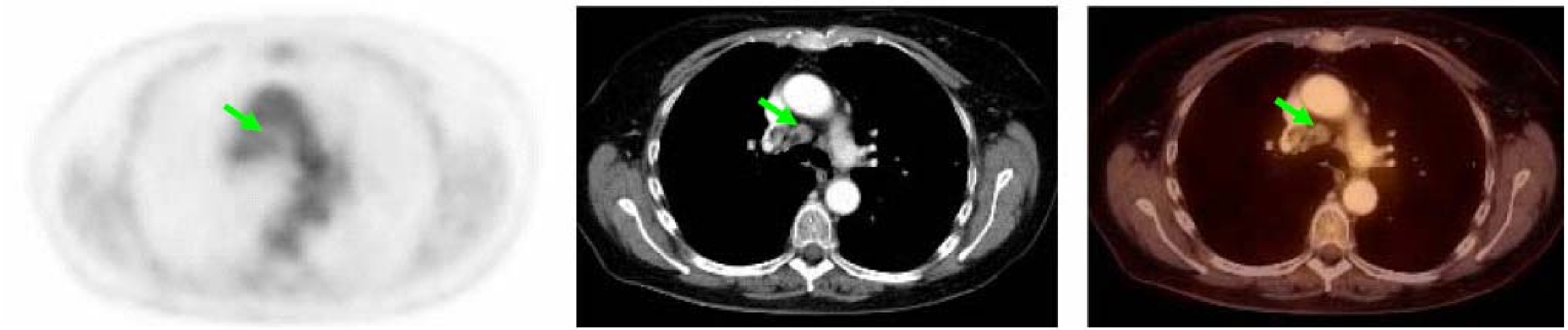
| Nodal Diameter* and PET† | Action |
|---|---|
| <1 cm PET +ve | Include in GTV |
| <1 cm PET −ve | Exclude from GTV |
| >1 cm PET +ve | Include in GTV unless repeated cytology of the node is negative |
| >1 cm PET −ve and where no cytology is available | Include in GTV if primary tumor is PET negative<br>If primary tumor shows PET uptake, exclude node from GTV unless cytologically positive |

*Diameter in short-axis.

†Using a dedicated PET scanner.

Senan *et al.*, Radiother Oncol 2004

# Elective versus selective nodal irradiation in SCLC



- Is selective nodal irradiation save in SCLC?
- If so, CT or PET based?

# Selective nodal irradiation in SCLC: CT based

- 27 patients with SCLC – Limited Disease
- Concurrent chemo-radiotherapy (30 x 1.5 Gy BID)
- Selective nodal irradiation to CT-positive nodes
- Median follow-up 18 months
- 3 patients (11%) developed isolated nodal recurrence in the ipsilateral supraclavicular fossa

Selective nodal irradiation based on **CT** is possibly not safe in SCLC

De Ruysscher *et al.*, Radiother Oncol 2006

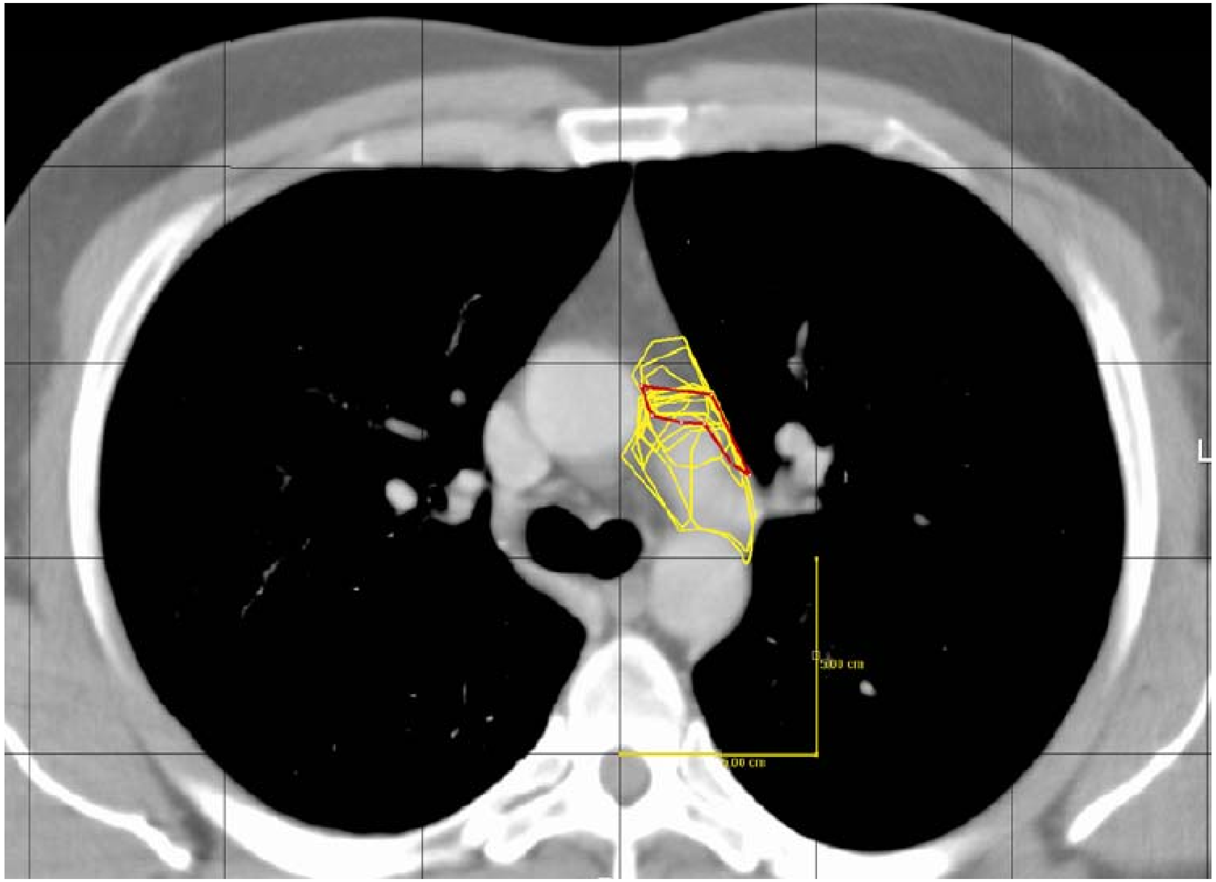
# Selective nodal irradiation in SCLC: FDG-PET based

- 60 patients with SCLC – Limited Disease
- Concurrent chemo-radiotherapy (30 x 1.5 Gy BID)
- Selective nodal irradiation to PET-positive nodes
- Median follow-up 29 months
- 2 patients (3%) developed isolated regional recurrence

Selective nodal irradiation based on **FDG-PET** seems safe in <u>SCLC</u>

Van Loon *et al.*, Int J Radiat Oncol Biol Phys 2010

# Interobserver variation in nodal delineation

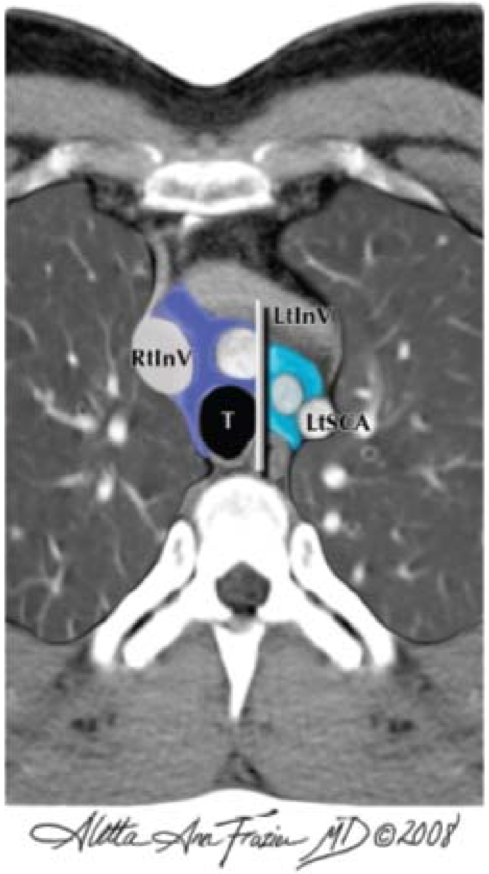


Consensus
Different observers

Kepka *et al.*, Radiother Oncol 2007

# IASCL Nodal Definitions

| Nodal station | Description | Definition |
|---|---|---|
| #1 (Left/Right) | Low cervical, supraclavicular and sternal notch nodes | Upper border: lower margin of cricoid cartilage<br>Lower border: clavicles bilaterally and, in the midline, the upper border of the manubrium #L1 and #R1 limited by the midline of the trachea. |
| #2 (Left/Right) | Upper paratracheal nodes | 2R: Upper border: apex of lung and pleural space and, in the midline, the upper border of the manubrium<br>Lower border: intersection of caudal margin of innominate vein with the trachea<br>2L: Upper border: apex of the lung and pleural space and, in the midline, the upper border of the manubrium<br>Lower border: superior border of the aortic arch<br>As for #4, in #2 the oncologic midline is along the left lateral border of the trachea. |



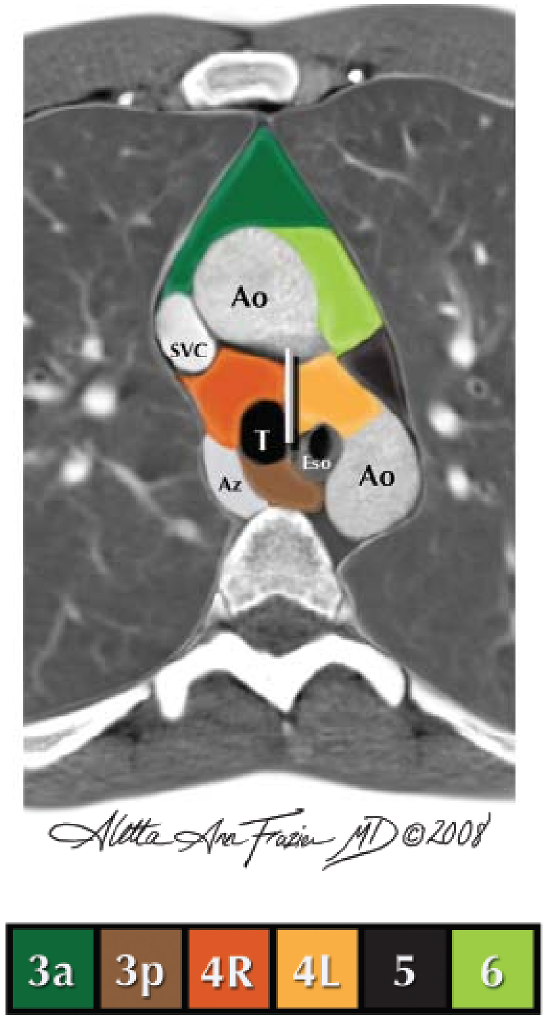


IASCL – staging manual in thoracic oncology 2009

# IASCL Nodal Definitions



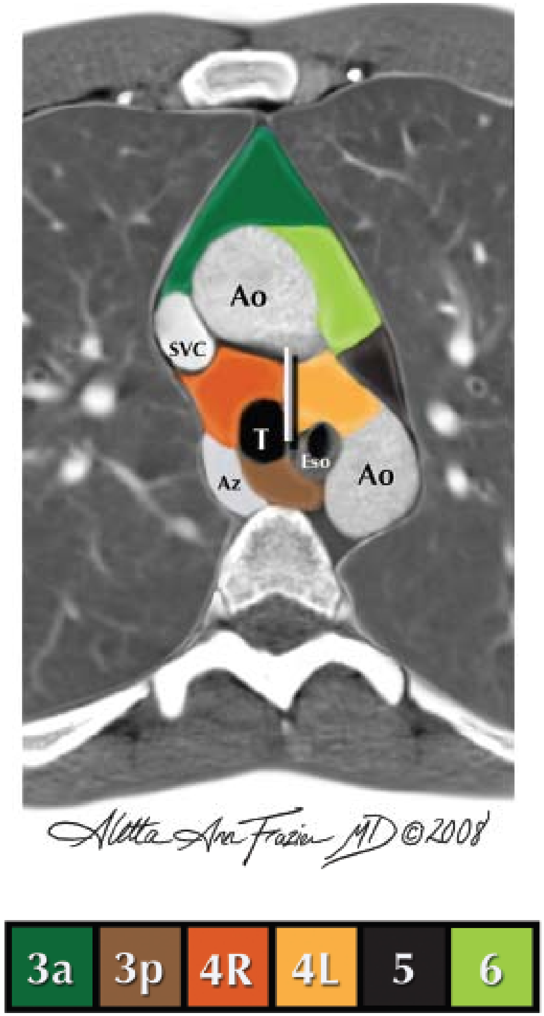
| | | |
|---|---|---|
| #3 | Pre-vascular and retrotracheal nodes | 3a: Prevascular<br>On the right<br>upper border: apex of chest<br>lower border: level of carina<br>anterior border: posterior aspect of sternum<br>posterior border: anterior border of superior vena cava<br>On the left<br>upper border: apex of chest<br>lower border: level of carina<br>anterior border: posterior aspect of sternum<br>posterior border: left carotid artery<br>3p: Retrotracheal<br>upper border: apex of chest<br>lower border: carina |
| #4 (Left/Right) | Lower paratracheal nodes | 4R: includes right paratracheal nodes, and pretracheal nodes extending to the left lateral border of trachea<br>upper border: intersection of caudal margin of innominate vein with the trachea<br>lower border: lower border of azygos vein<br>4L: includes nodes to the left of the left lateral border of the trachea, medial to the ligamentum arteriosum<br>upper border: upper margin of the aortic arch<br>lower border: upper rim of the left main pulmonary artery |




IASCL – staging manual in thoracic oncology 2009

# IASCL Nodal Definitions

| | | |
|---|---|---|
| #5 | Subaortic (aorto-pulmonary window) | Subaortic lymph nodes lateral to the ligamentum arteriosum<br>upper border: the lower border of the aortic arch<br>lower border: upper rim of the left main pulmonary artery |
| #6 | Para-aortic nodes (ascending aorta or phrenic) | Lymph nodes anterior and lateral to the ascending aorta and aortic arch<br>upper border: a line tangential to the upper border of the aortic arch<br>lower border: the lower border of the aortic arch |
| #7 | Subcarinal nodes | upper border: the carina of the trachea<br>lower border: the upper border of the lower lobe bronchus on the left; the lower border of the bronchus intermedius on the right |
| #8 (Left/Right) | Para-esophageal nodes (below carina) | Nodes lying adjacent to the wall of the esophagus and to the right or left of the midline, excluding subcarinal nodes<br>upper border: the upper border of the lower lobe<br>bronchus on the left; the lower border of the bronchus intermedius on the right<br>lower border: the diaphragm |




IASCL – staging manual in thoracic oncology 2009

# IASCL Nodal Definitions

Universitätsklinikum Carl Gustav Carus
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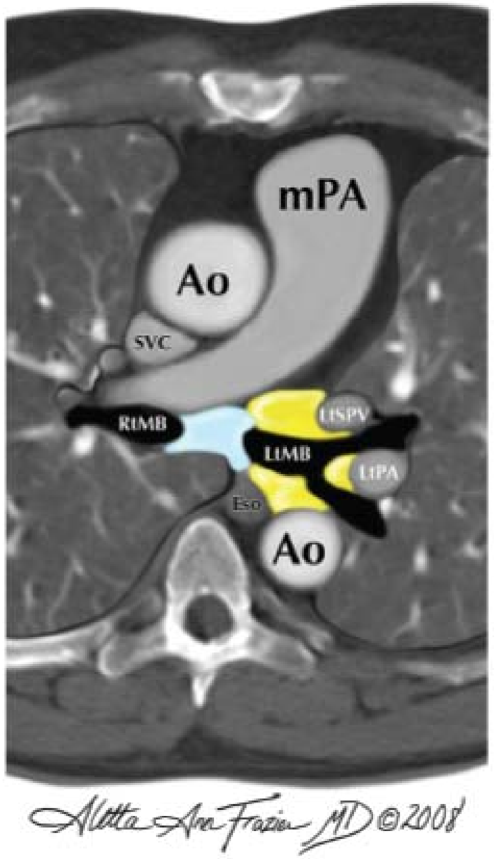
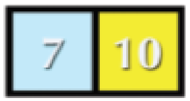
| | | |
|---|---|---|
| #9 (Left/Right) | Pulmonary ligament nodes | Nodes lying within the pulmonary ligament<br>upper border: the inferior pulmonary vein<br>lower border: the diaphragm |
| #10 (Left/Right) | Hilar nodes | Includes nodes immediately adjacent to the mainstem bronchus and hilar vessels including the proximal portions of the pulmonary veins and main pulmonary artery<br>upper border: the lower rim of the azygos vein on the right; upper rim of the pulmonary artery on the left<br>lower border: interlobar region bilaterally |
| #11 | Interlobar nodes | Between the origin of the lobar bronchi<br>*#11s: between the upper lobe bronchus and bronchus intermedius on the right<br>*#11i: between the middle and lower lobe bronchi on the right<br>*optional sub-categories |



# Content



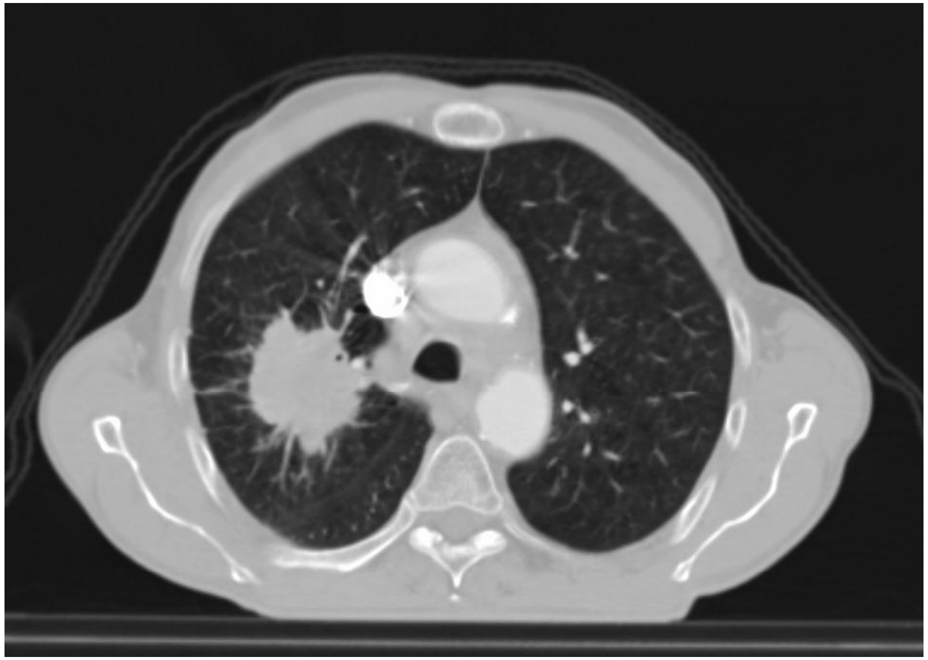
- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk
- Beyond…

# CT



- Window-level setting:
  - lung window for lung interfaces
  - soft tissue window for mediastinal and hilar interfaces

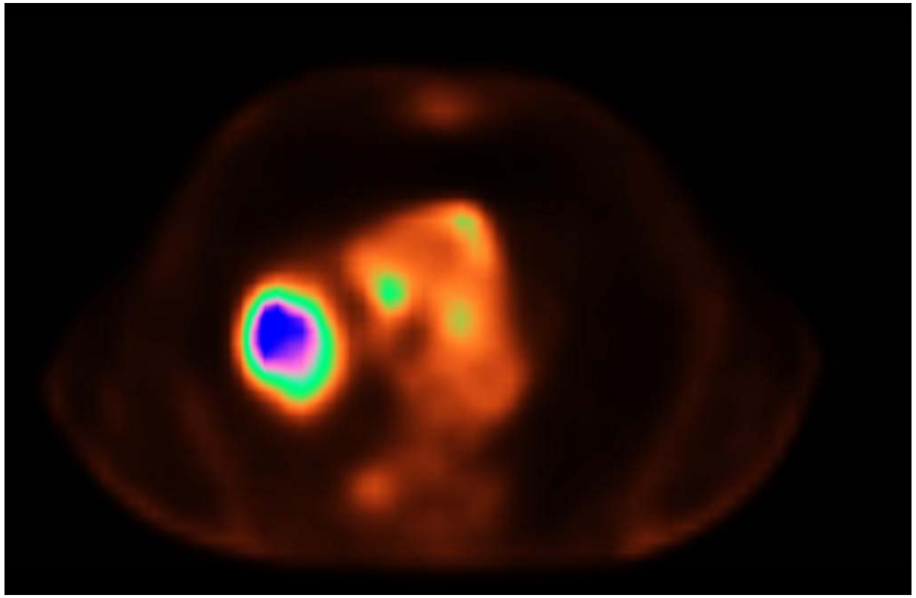
soft tissue window

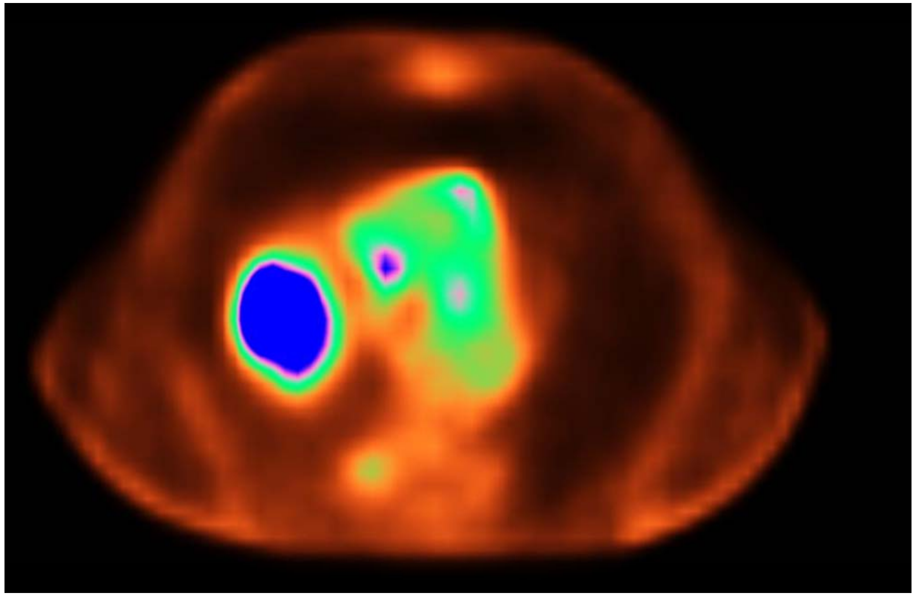


lung window

# PET

- Window-level setting:
  - fixed setting necessary





Same tumor, different settings

Boellaard *et al.*, Eur J Nucl Med Mol Imaging 2010

# CT and PET for GTV



**CT**

- Window-level setting:
  - lung window for lung
  - soft tissue window for mediastinum
- Challenges for RT planning:
  - atelectasis
  - effusion
  - nodal involvement
  - movements

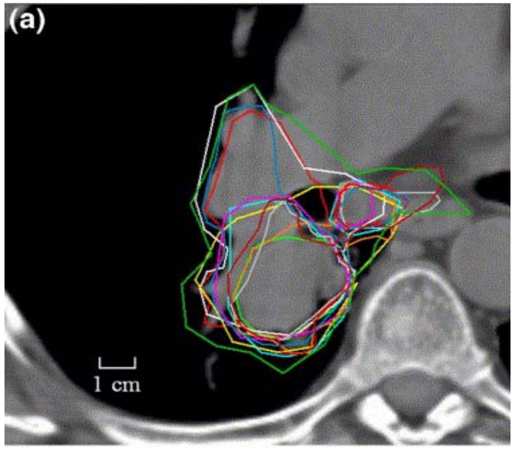
**PET**

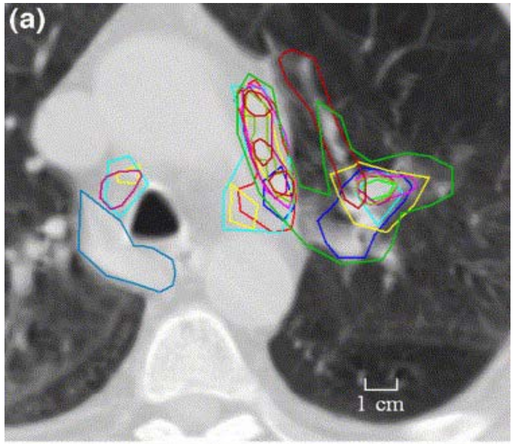
- Window-level setting:
  - fixed setting necessary
- Challenges for RT planning:
  - inflammation
  - border (low resolution)
  - movements

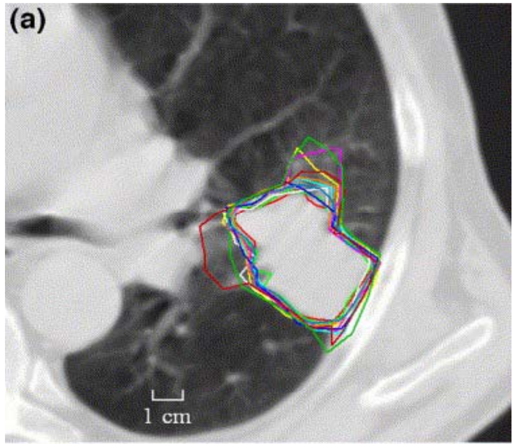
Boellaard *et al.*, Eur J Nucl Med Mol Imaging 2010

# Interobserver variability in delineation






CT: large interobserver variation

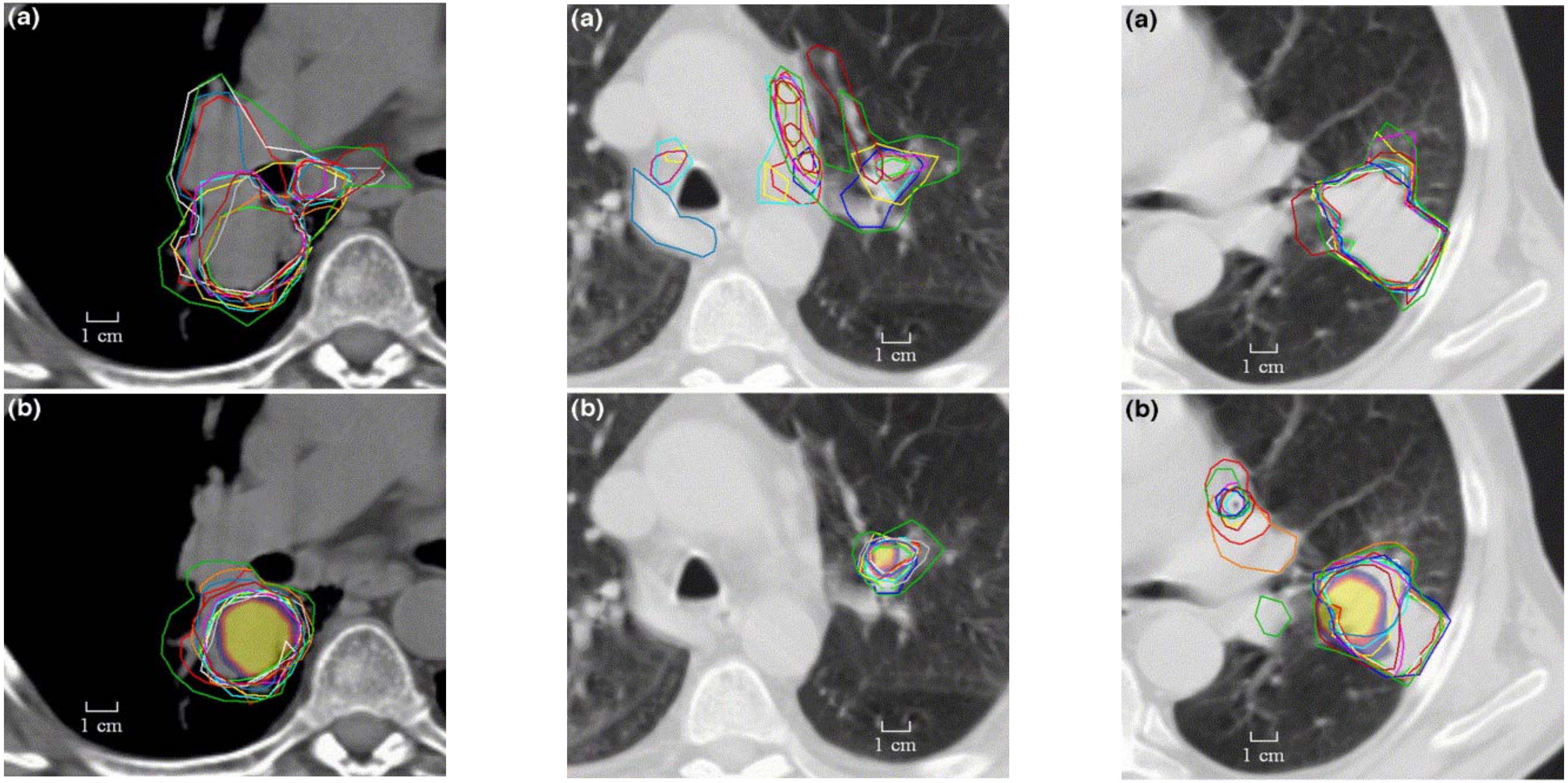
Steenbakkers *et al.*, Int J Radiat Biol Oncol Phys 2006

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

# Interobserver variability in delineation

SD 10.2 mm

SD 5.2 mm



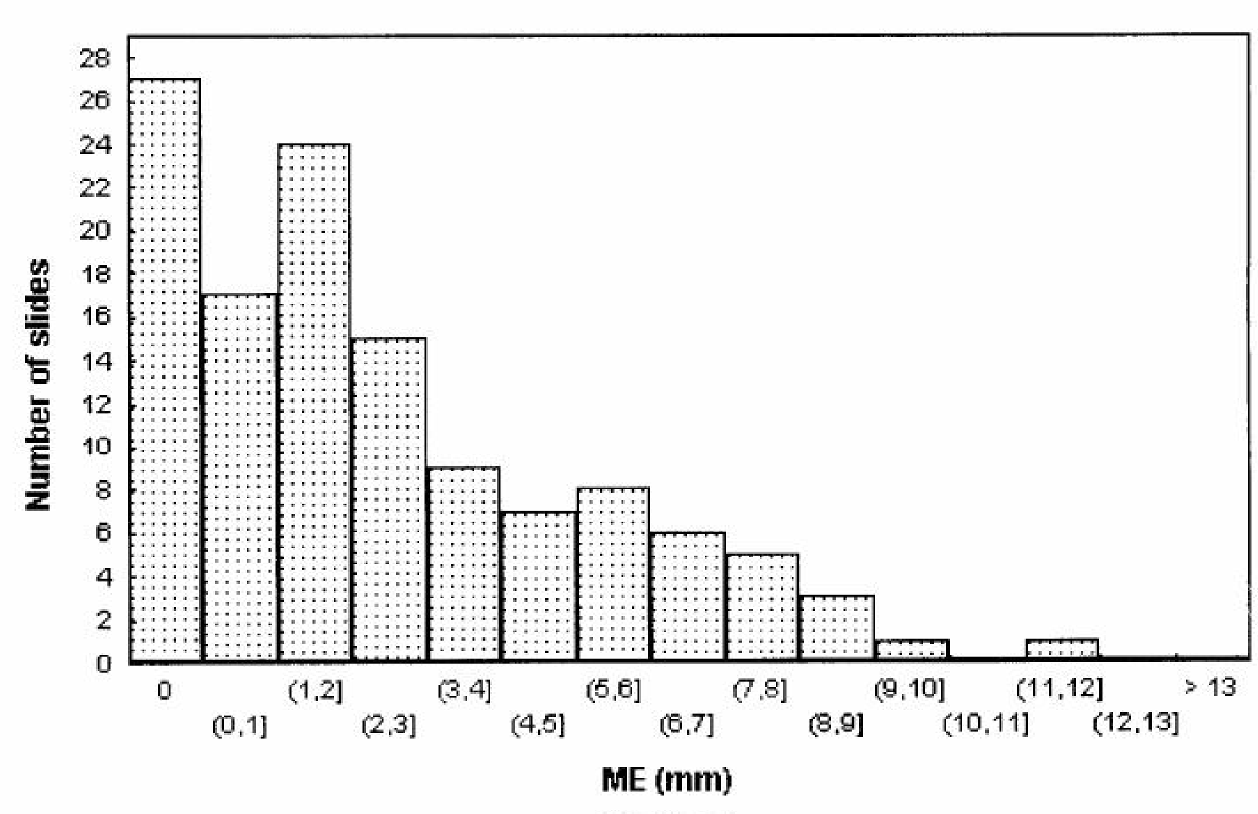

PET: reduced interobserver variation

Steenbakkers *et al.*, Int J Radiat Biol Oncol Phys 2006

# CTV: Imaging vs pathology



- n=70 surgical resection specimens
- quantification of microscopic extension




adenocarcinoma
95% of microscopic extension < 8 mm

Giraud *et al.*, Int J Radiat Biol Oncol Phys 2000

# CTV: Imaging vs pathology

Universitätsklinikum Carl Gustav Carus
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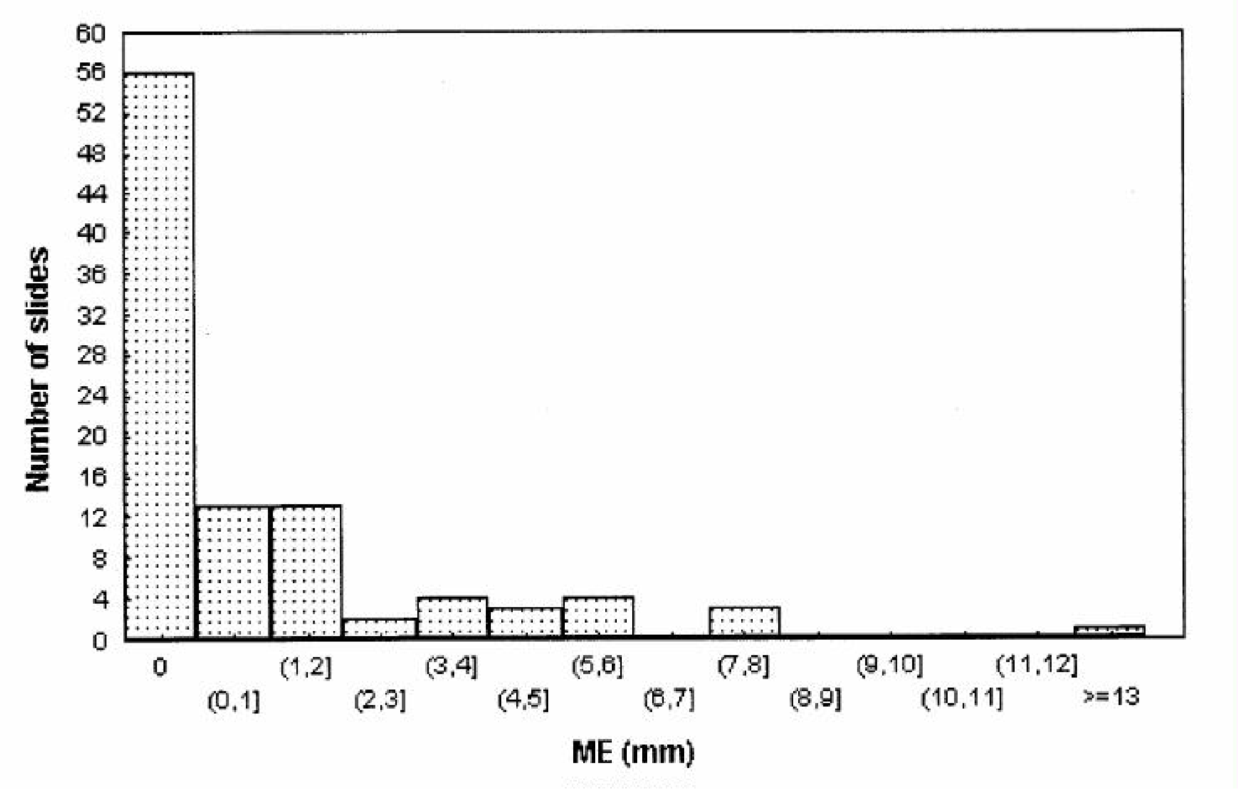
- n=70 surgical resection specimens
- quantification of microscopic extension



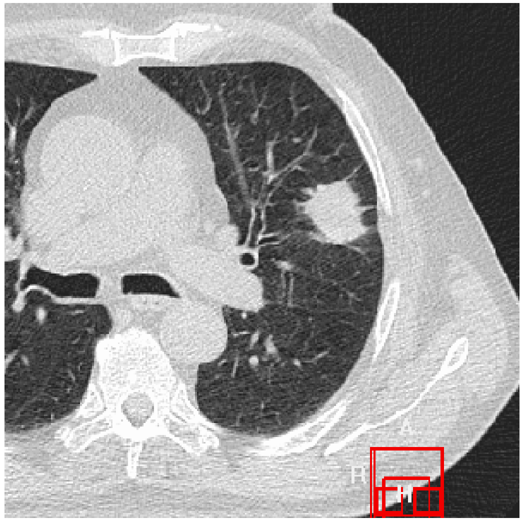

Squamous cell ca
95% of microscopic extension < 6 mm

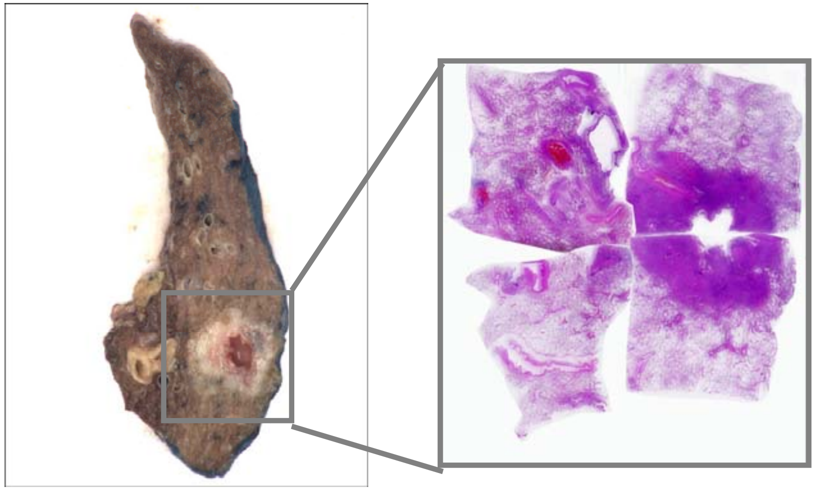
Giraud *et al.*, Int J Radiat Biol Oncol Phys 2000

# CTV: Imaging vs pathology

## Imaging vs pathology

- patients undergoing lobectomy
- Pre-operative imaging
  - High resolution RC-CT
  - (RC-)FDG-PET
- Post-operative imaging
  - Macroscopy
  - Microscopy





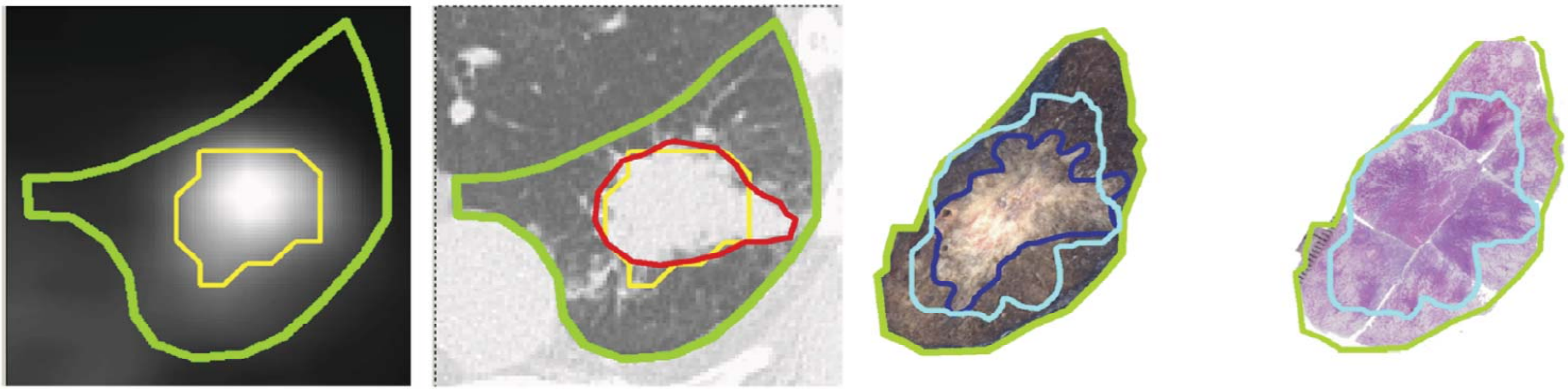
Stroom *et al.*, Int J Radiat Biol Oncol Phys 2007

# CTV: Imaging vs pathology

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

GTV: volume comparison CT – PET - pathology

| | GTVs ($cm^3$) | | | |
|---|---|---|---|---|
| Pt. No. | CT | PET | Pathology | $ME_{max}$ (mm) |
| 1 | 15 | 13 | 6 | 6 |
| 2 | 12 | - | 12 | 5 |
| 3 | 9 | 7 | 4 | 9 |
| 4 | 10 | 7 | 8 | 0 |
| 5 | 23 | 24 | 39 | 3 |



pt # 5

Stroom *et al.*, Int J Radiat Biol Oncol Phys 2007

# Content

- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk

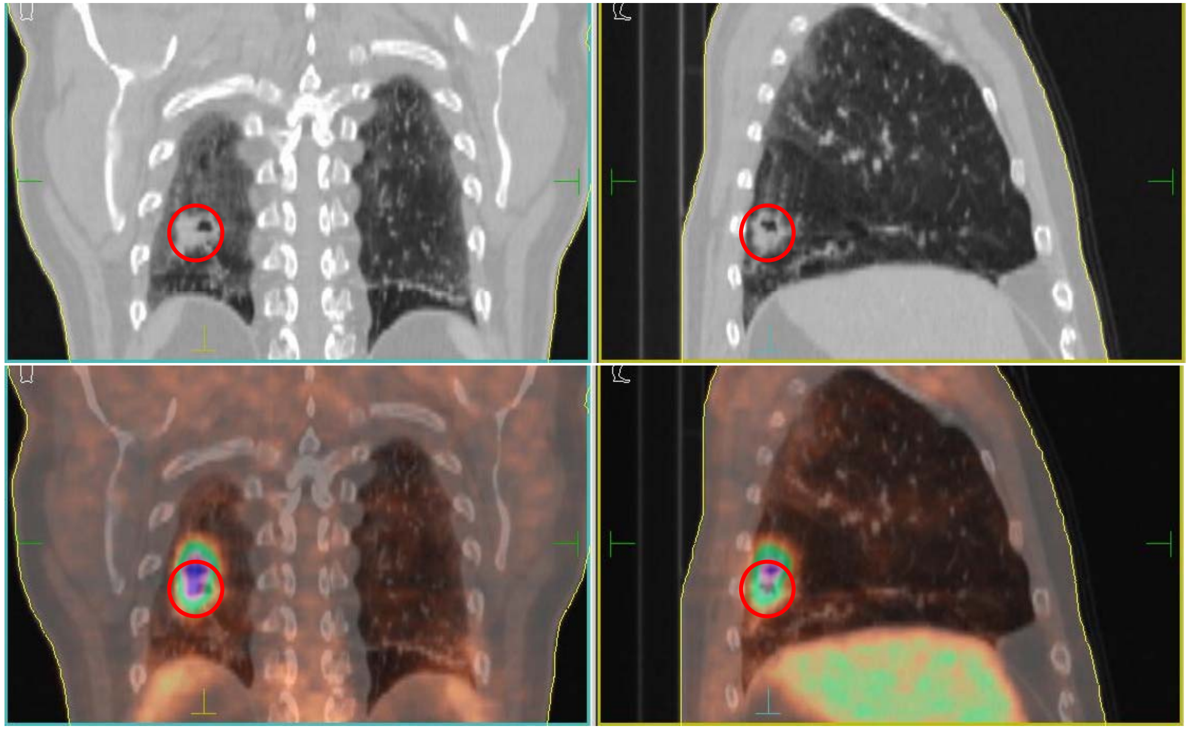
# Respiration-induced imaging artifacts

- One CT scan is not sufficient to delineate the GTV
- Motion should be taken into account:
  - fluoroscopy
  - slow CT
  - 4D CT / midventilation CT

# Respiration-induced imaging artifacts – FDG-PET

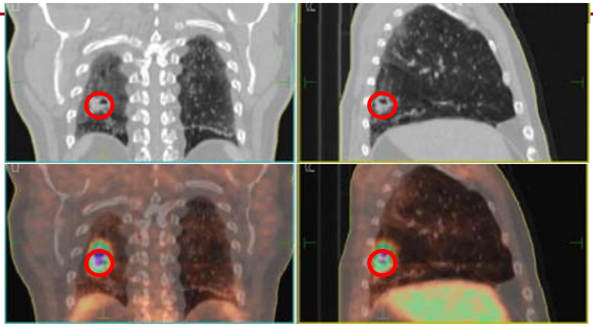
Why respiration correlated PET-CT?

- Motion blurring → Contrast reduction!
- Different acquisition times: PET 2-5 min CT 20-50 sec



# Respiration correlated FDG-PET/CT





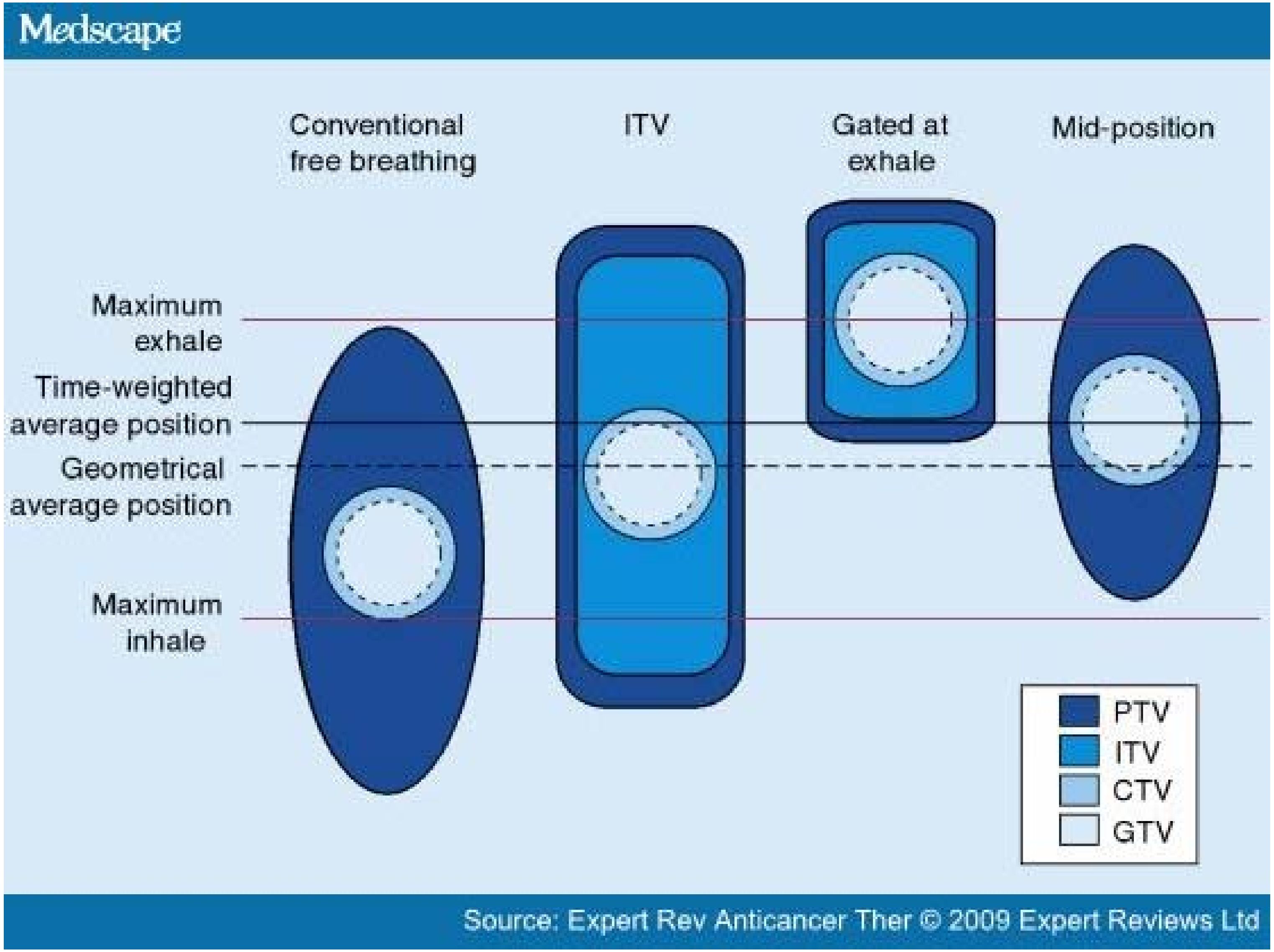
Consequences for GTV delineation:

- Stage I / SABR:
  - Delineation on CT of all (8) phases of the respiratory cycle
  - ITV generated on 3D-FDG-PET is NO surrogate!!
  - Automatically segmented 4D-FDG-PET may provide additional information

- Advanced stage:
  - Delineation of target volume on CT of 3 respiratory phases – i.e., 0%/50%/100% exspiration
  - FDG-PET provides additional information, e.g. Atelectasis.

Troost *et al.*, in preparation

# Different SABR concepts



# Content

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- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk
- Beyond…

# Postoperative irradiation

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- Possibly perform a FDG-PET-CT scan for postoperative staging and treatment planning, especially after adjuvant chemotherapy
- Use surgical report and clips as guidance
- Include the entire surgical bed
- No uniform recommendation on lymph node levels:
  - Only include the involved level?
  - Or 1 adjacent level (cranially and caudally) in the presence of extranodal spread?
  - Take lymphatic drainage into account!

# Content



- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk
- Beyond…

# Organs at risk



- Joint recommendation by RTOG, EORTC, SWOG
- 3D-delination of OARs described
- Lungs, bronchial tree, brachial plexus, spinal cord, oesophagus, ribs

Kong *et al.*, Int J Radiat Oncol Biol Phys 2011

# Importance

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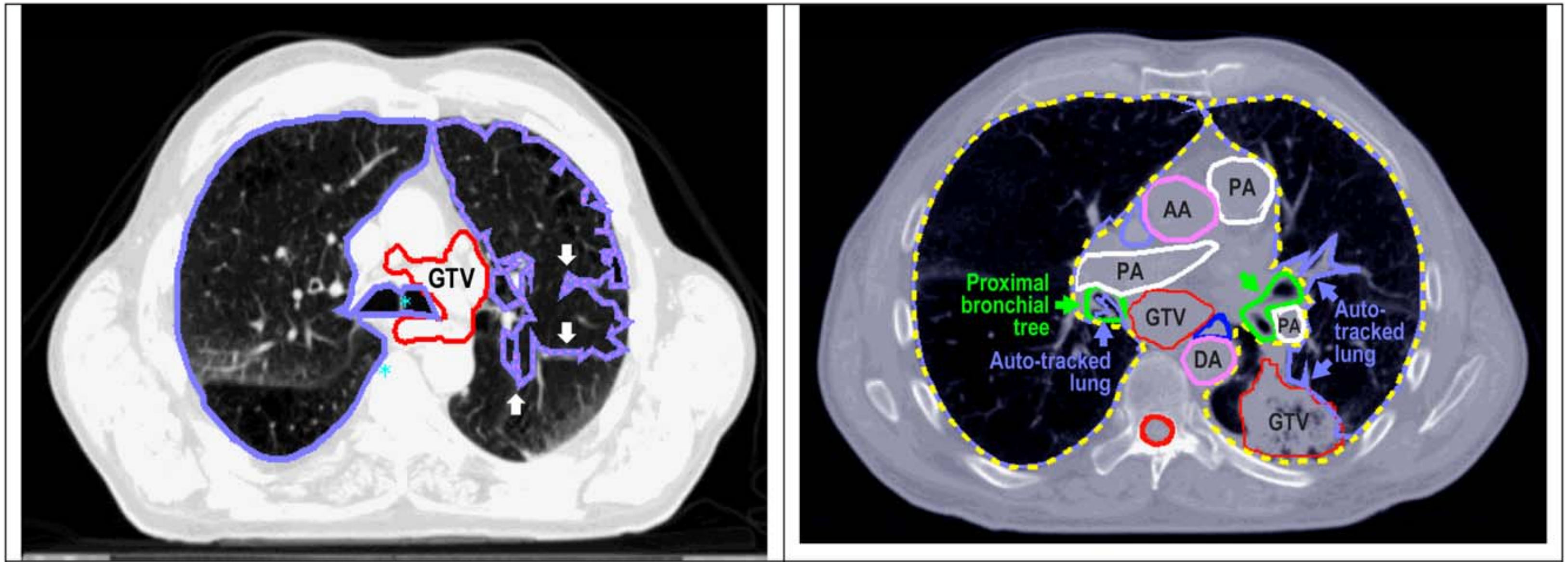
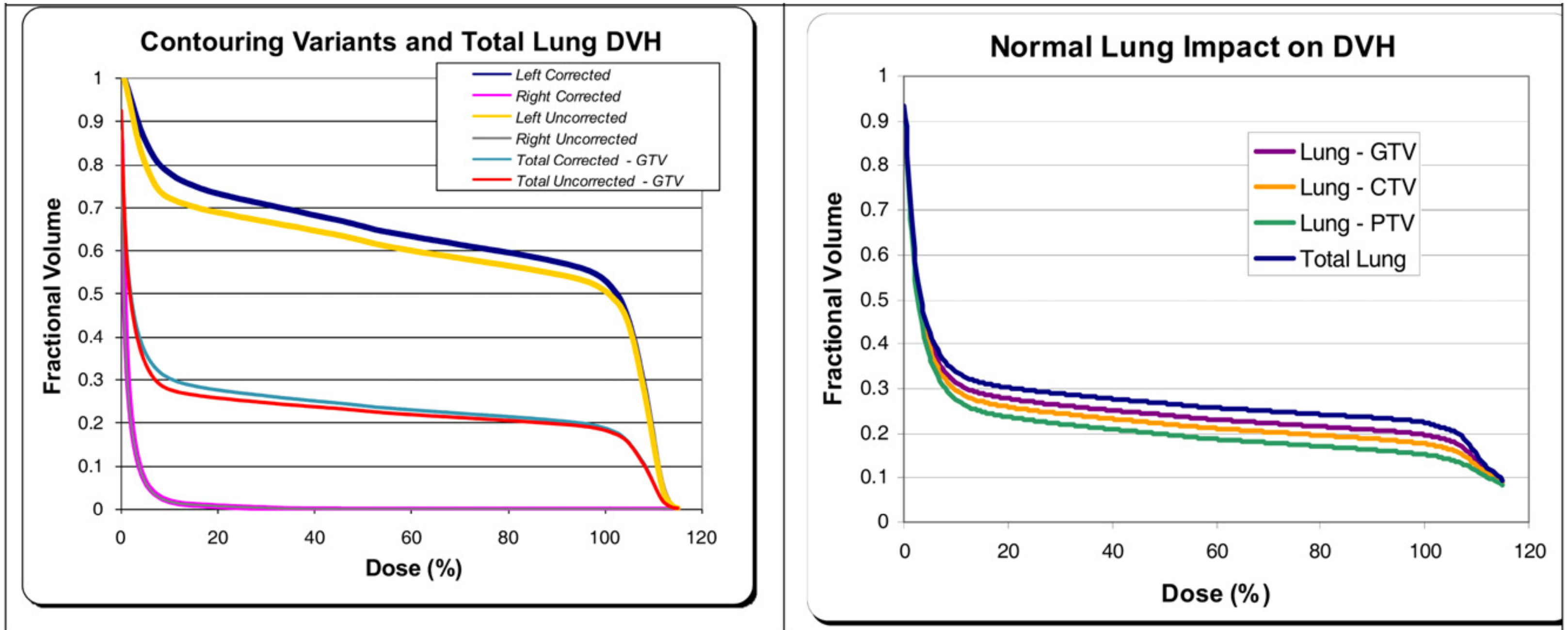



| A: Lung Contour - Autotrack Failure (white arrows) | B: Lung Contour Variants (dashed and solid) |
|---|---|

Kong *et al.*, Int J Radiat Oncol Biol Phys 2011

# Importance



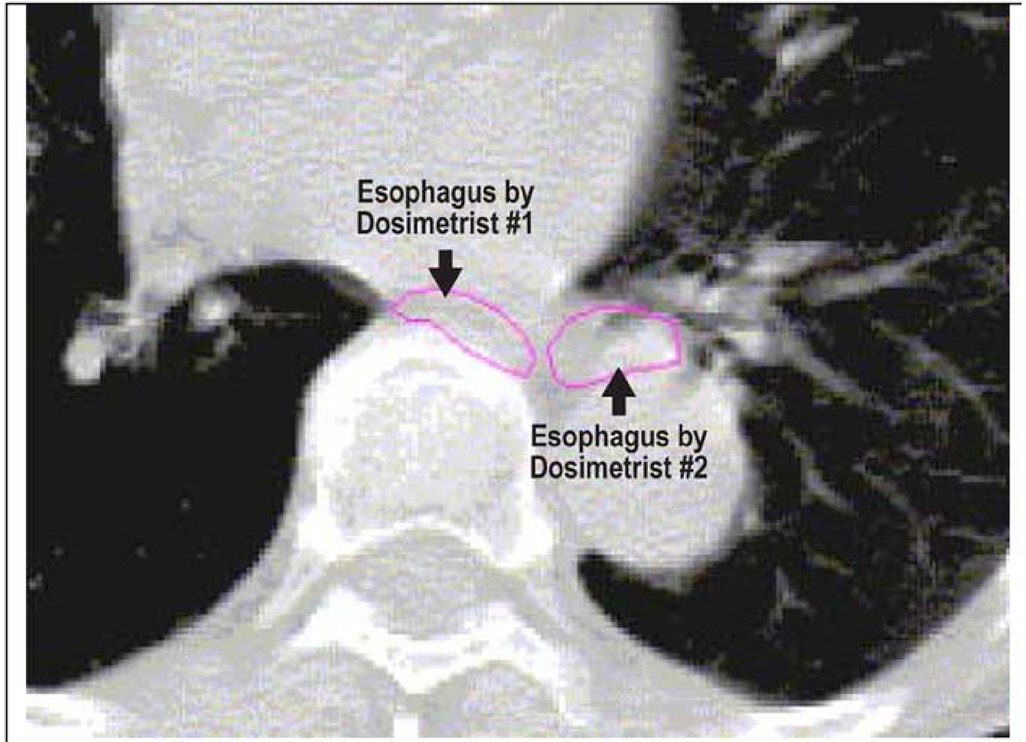



C: Lung DVH differences of contouring variants | D: Lung DVH differences on target consideration

Kong *et al.*, Int J Radiat Oncol Biol Phys 2011

# Variation and motion of OARs



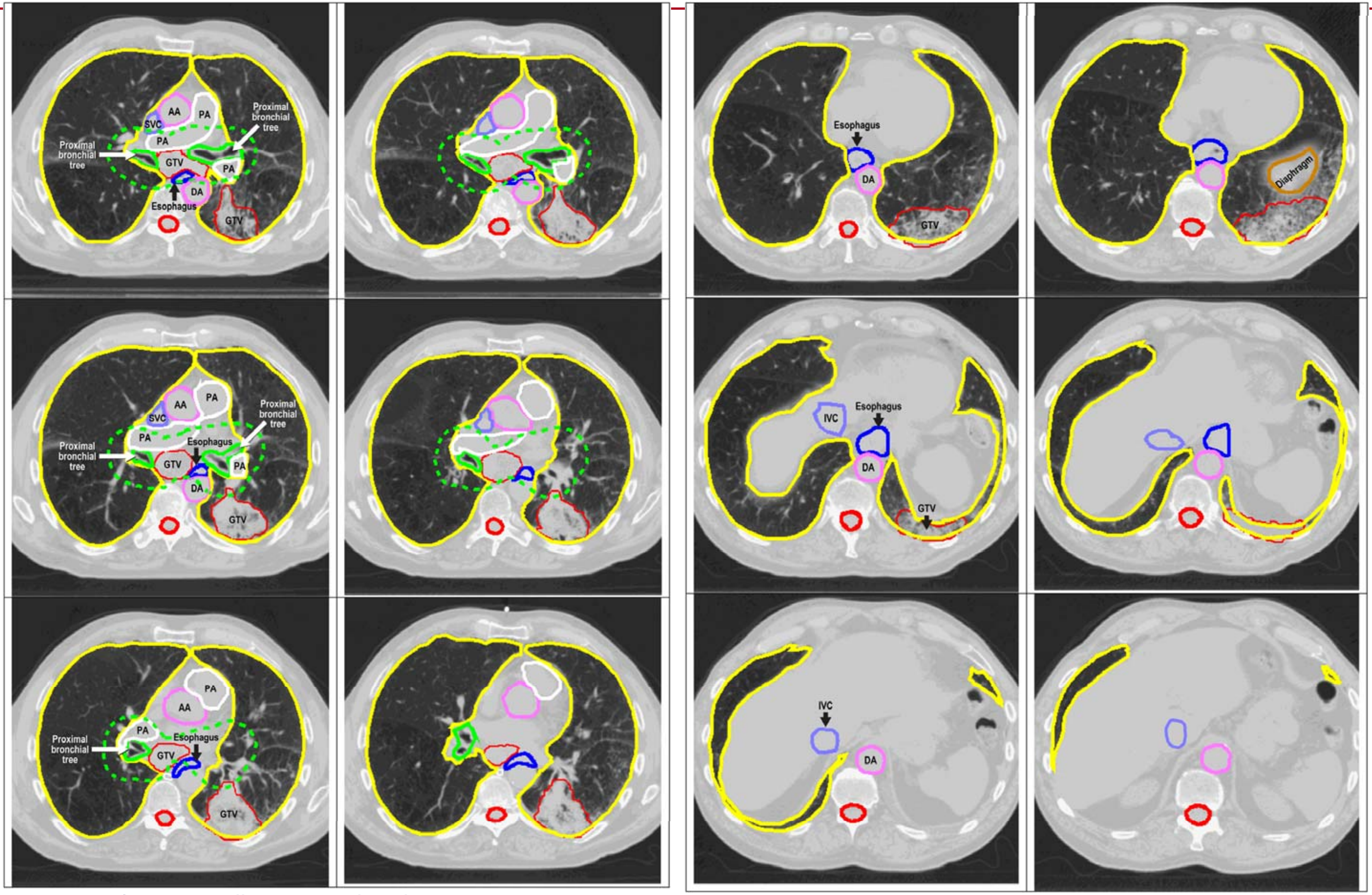



A: Esophagus Contour Variants

Kong *et al.*, Int J Radiat Oncol Biol Phys 2011

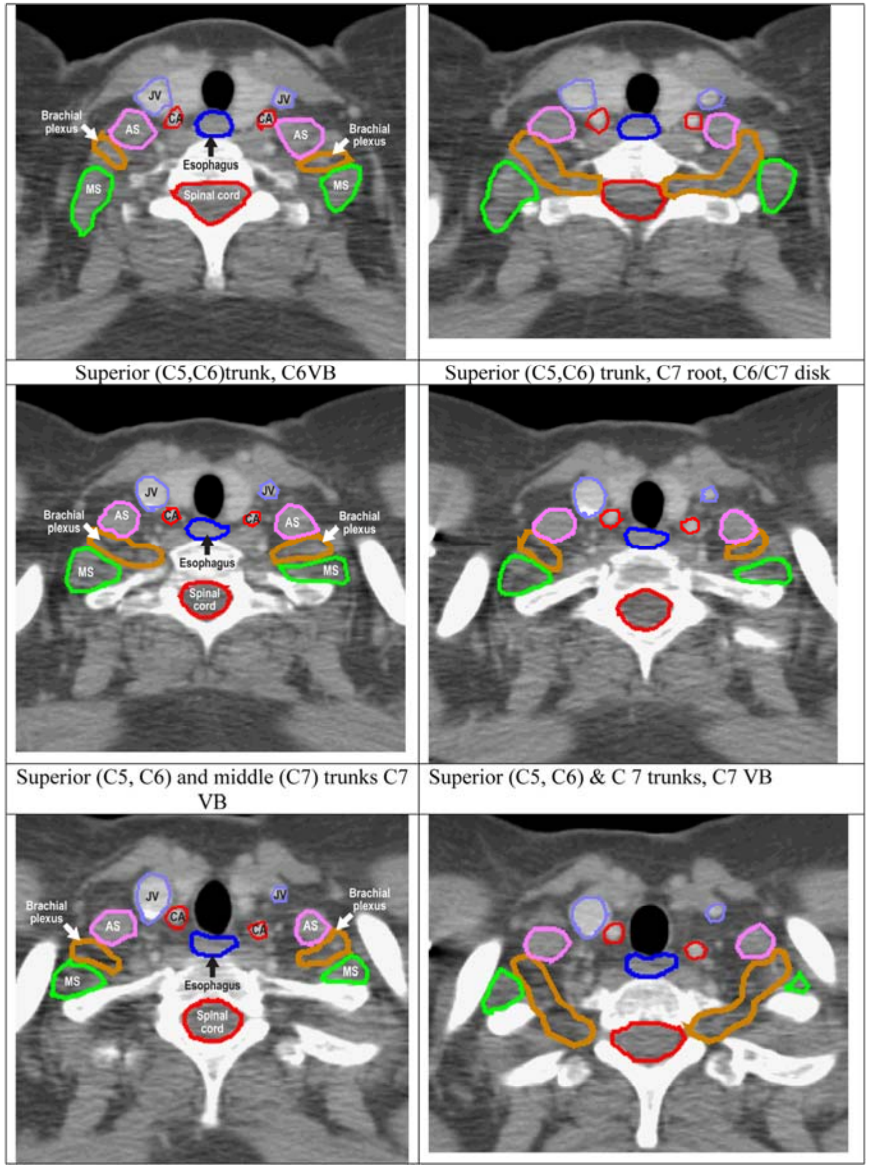
# Thorax






Kong *et al.*, Int J Radiat Oncol Biol Phys 2011

# Brachial plexus




Kong *et al.*, Int J Radiat Oncol Biol Phys 2011

# Content



- Elective nodal irradiation *versus* selective nodal irradiation in NSCLC and SCLC
- Proposal for nodal target volume
- Primary tumor
- SABR
- Postoperative irradiation
- Organs at risk
- Beyond…

# Treatment volume adaptation



Goal: decreased NTCP, increased TCP by increased dose

- Tumor regression 0.6%-2.4% per day, high regression results in poor outcome (in non-adenocarcinoma histology)
- Noticeable tumor regression in 40% of patients (progression in only 1%), which was >25% in 17% of the patients in the fourth week (N=114)
- Tumor shrinkage more pronounced in concurrent as opposed to sequential RCHT (50.1% versus 33.7%, respectively, *p*=0.003)
- Treatment planning studies investigating dose escalation resulted in varying results

Sonke, Belderbos. Sem Radiat Oncol 2011
Brink, *et al*., Radiother Oncol 2014
Zwienen, *et al*. Int J Radiat Oncol Biol Phys 2008
Berkovic, *et al*. Acta Oncol 2015

# First report on ART outcome

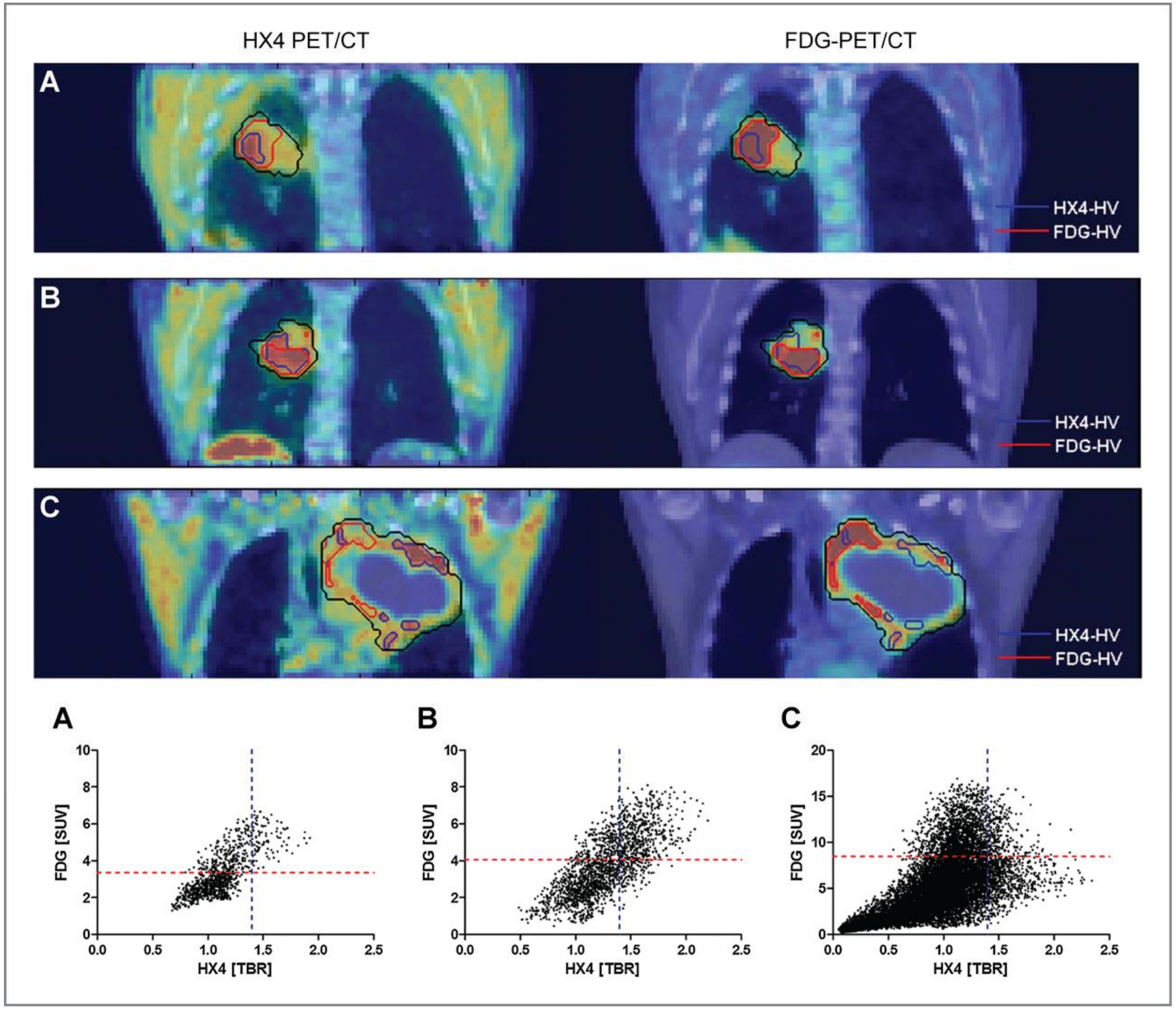


- N=104 (N)SCLC patients, 52 ART with PTV margin 4mm for tumor, 52 bone match with 10mm PTV margin
- Follow-up CT scans obtained 3-monthly
- Median follow-up 16 months (3-35 months), replanning 12 ART-pts
- Locoregional failure 35% ART, 53% in non-ART (*p*=0.05), marginal failure in 1 *versus* 4 patients
- Overall survival: 10 *versus* 8 months
- Severe pneumonitis: 18% *versus* 22% (*p*=0.6)

Tvilum *et al.*, Acta Oncologica 2015

# FDG- *versus* hypoxia-PET






Zegers *et al*. Clin Cancer Res 2014

# Radiation boost strategies

Universitätsklinikum Carl Gustav Carus
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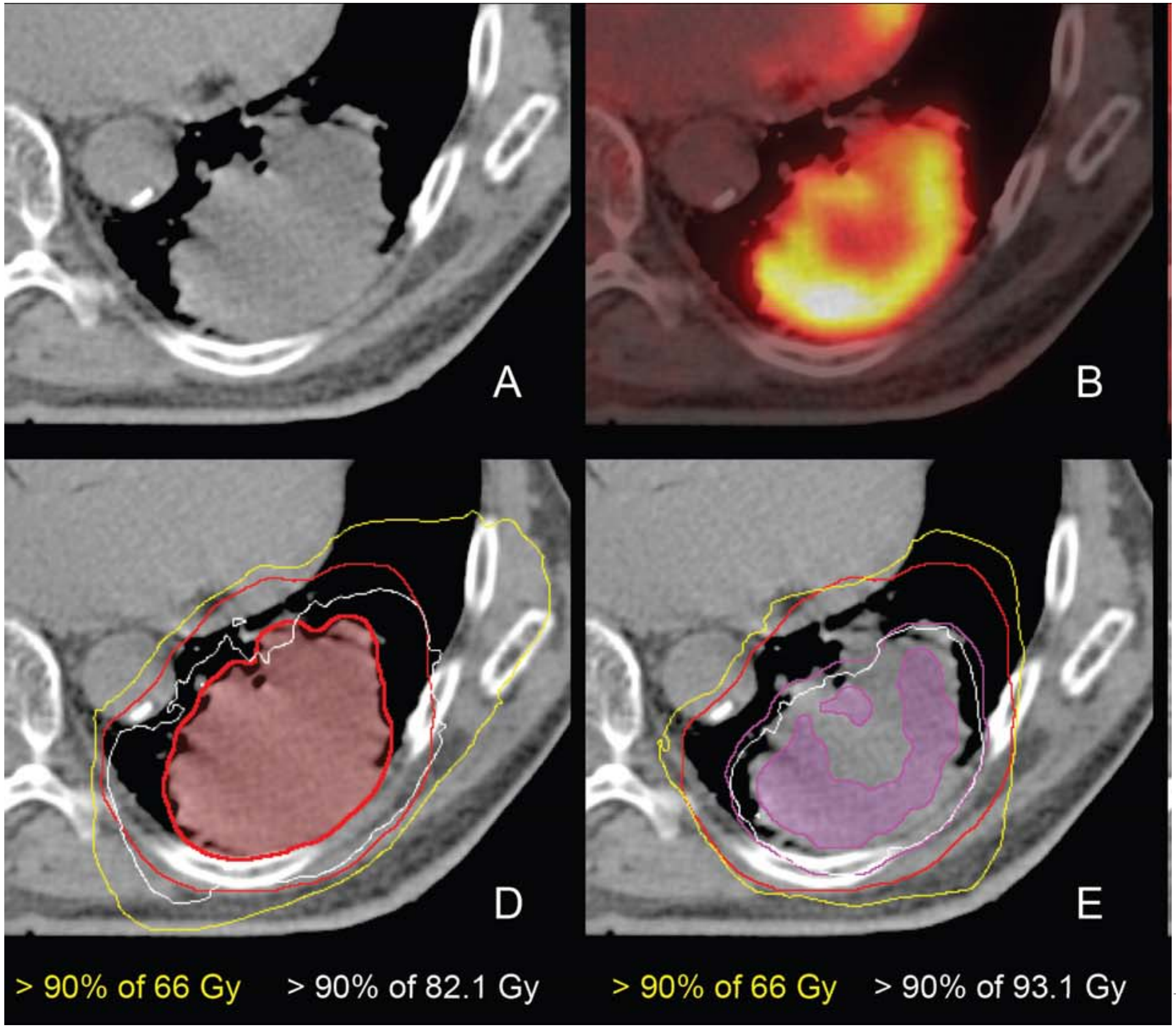
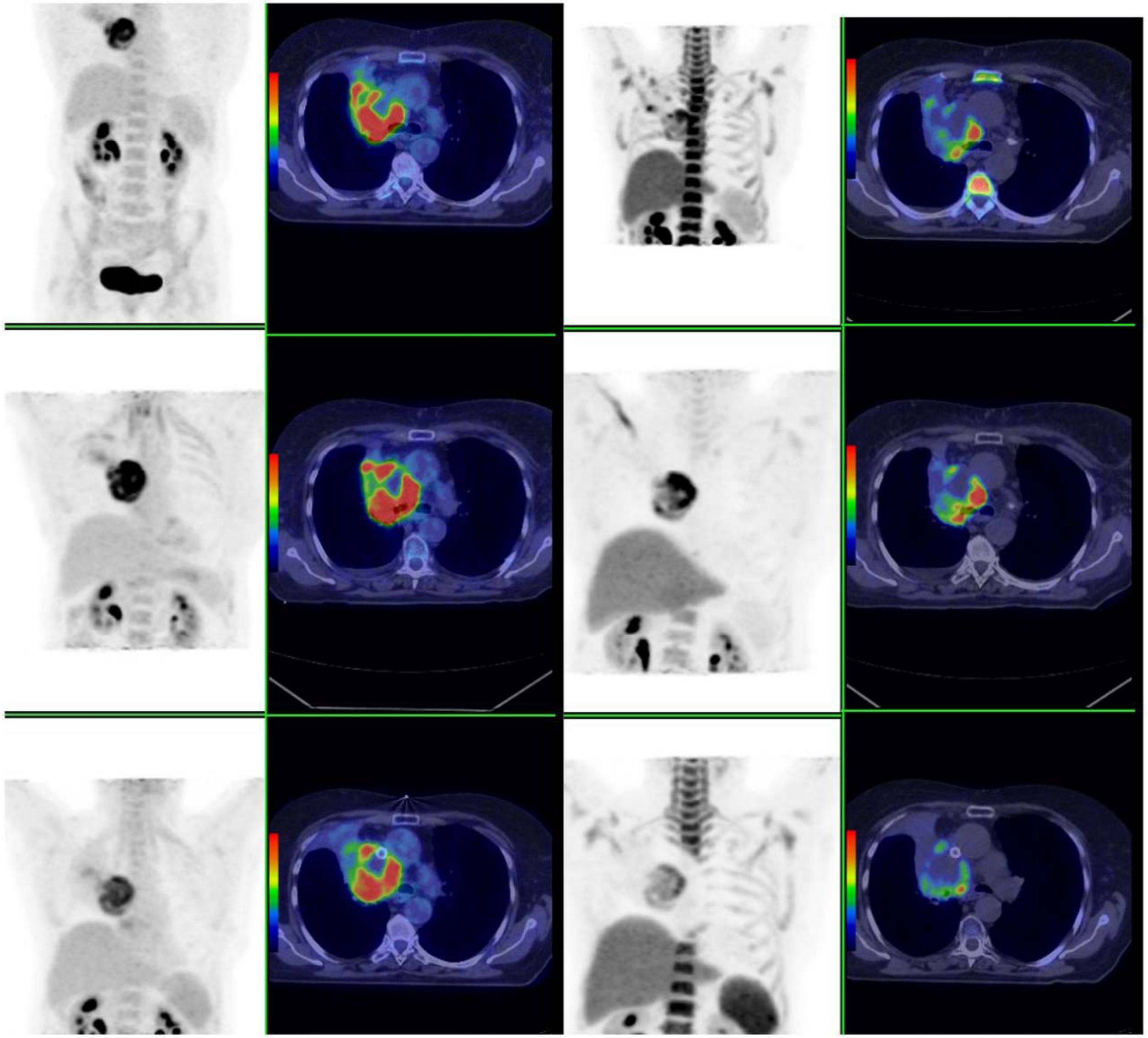


# FLT for early response evaluation



Everitt *et al*. J Nucl Med 2014

# FDG-PET predicts pneumonitis

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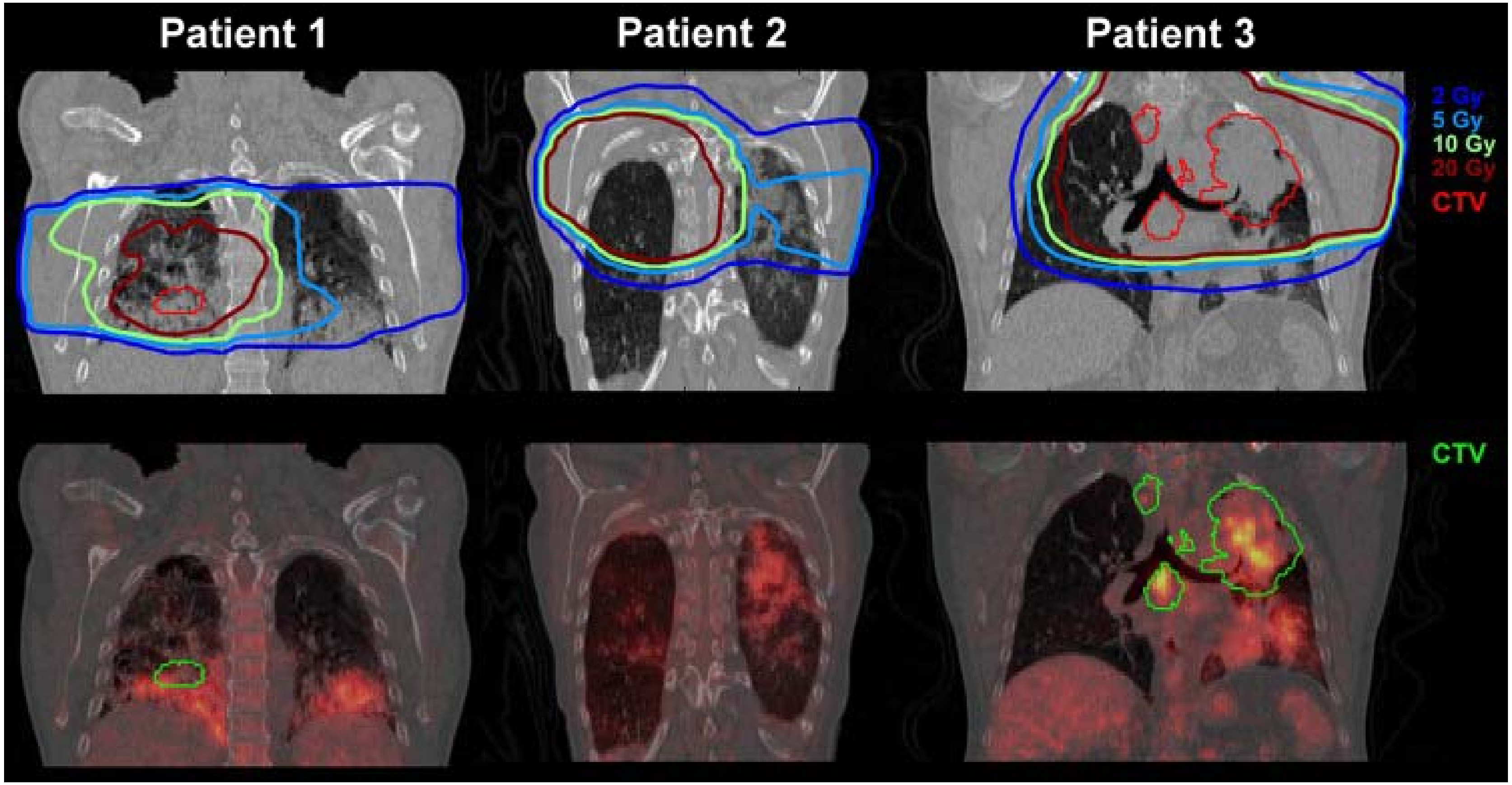


Petit *et al*. Int J Radiat Oncol Biol Phys 2011

# Take home messages



The optimal nodal target volume determination remains challenging……

- Selective nodal irradiation based on non-invasive techniques (CT/PET/EUS) standard of care in many centers → seems safe also in era of highly conformal RT techniques

- Use of IASCL nodal mapping

# Take home messages



- Reduction of interobserver variation in GTV delineation when using combined CT and FDG-PET
- Delineation of EBRT *versus* SABR requires different strategies
- No consensus guidelines on postoperative target volume
- Organs at risk are gaining importance for dose-escalation or re-irradiation

# Further reading

Universitätsklinikum Carl Gustav Carus
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- Konert *et al*., Radiother Oncol 2015;116(1):27-34
- MacManus *et al*., Radiother Oncol 2009;91 (1):85-94
- Grootjans *et al*., Nature Reviews Clinical Oncology 2015;12:395-407

# Thank you for your attention!

# Physics aspects of the lung case

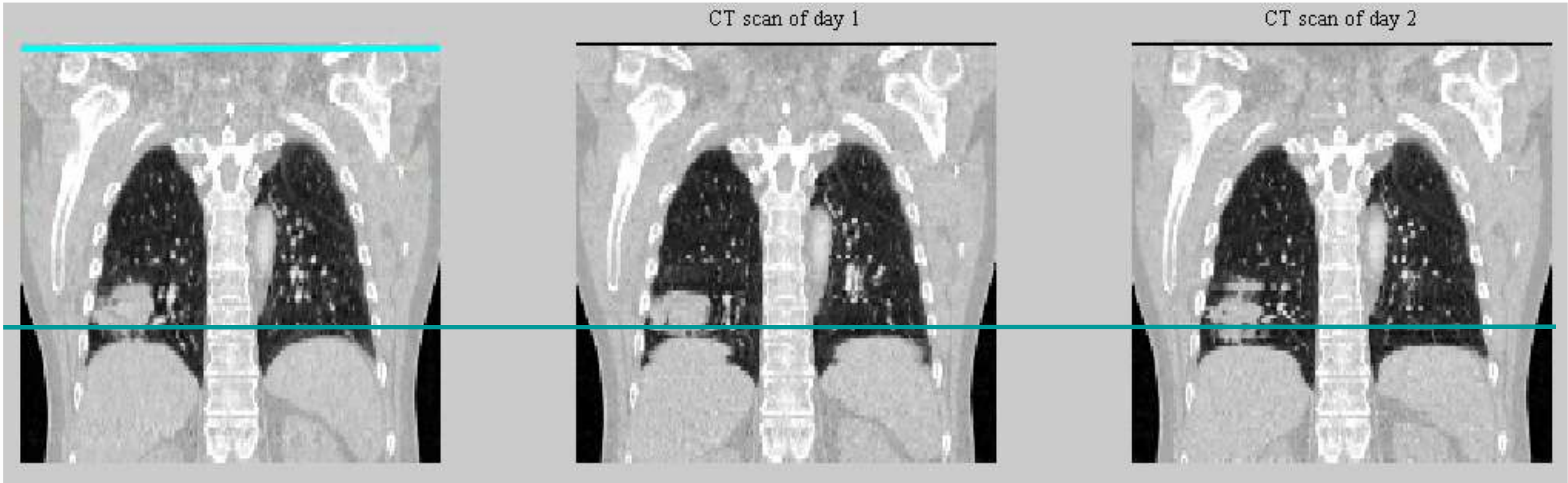
Peter Remeijer

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

# Motion During Imaging

NETHERLANDS
CANCER
INSTITUTE
ANTONI VAN LEEUWENHOEK

# The CT imaging problem

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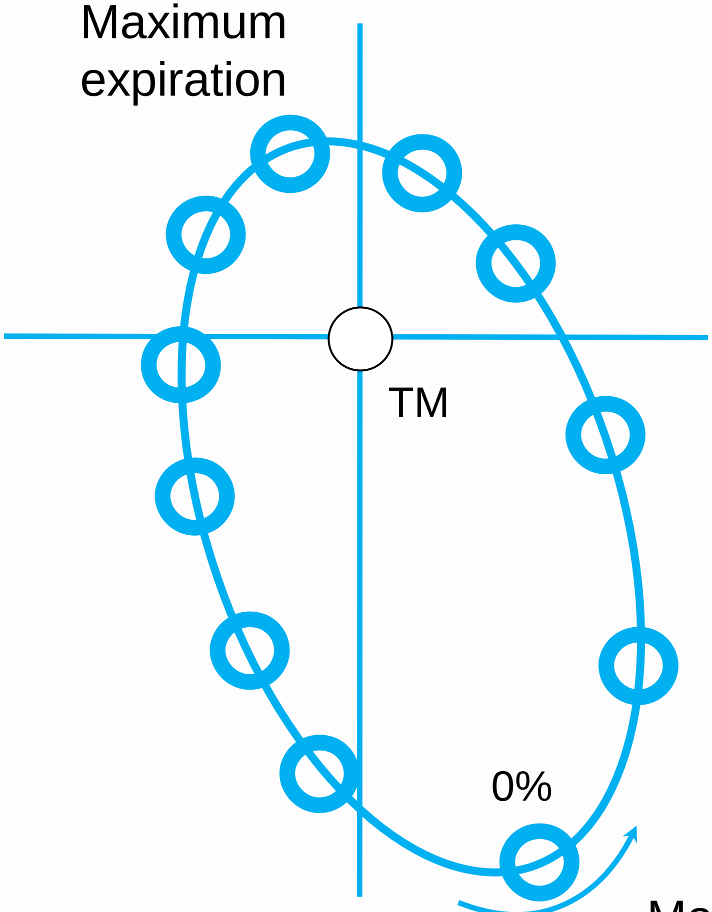
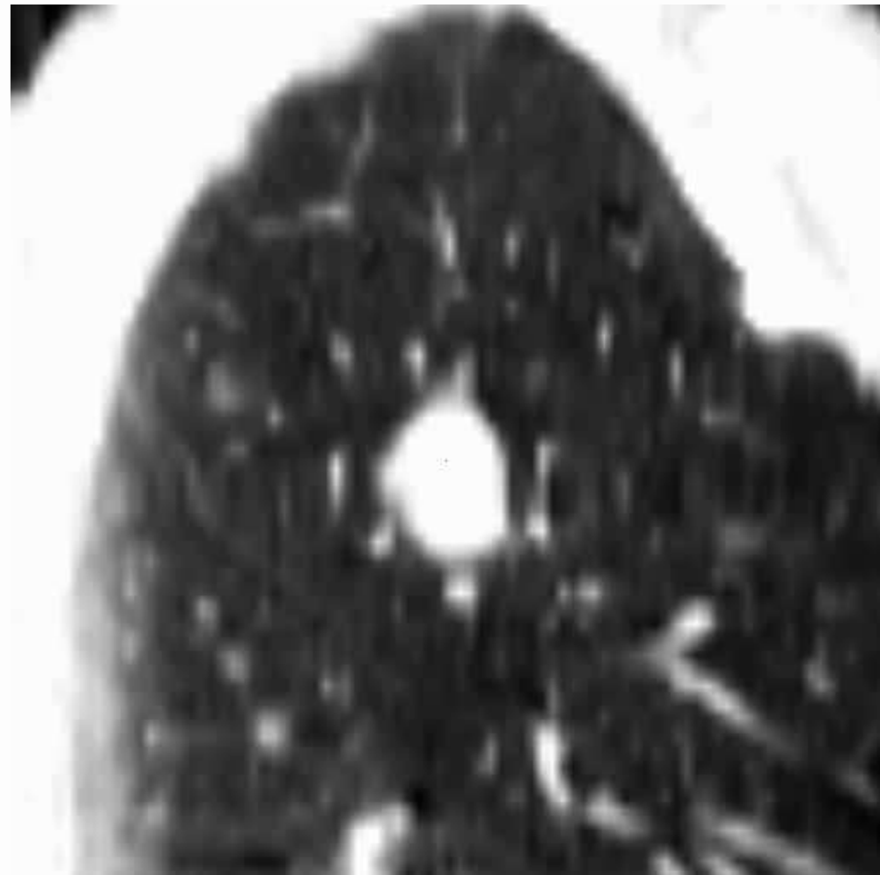
# Mid-ventilation

Selection of a single appropriate CT scan from a 4D scan



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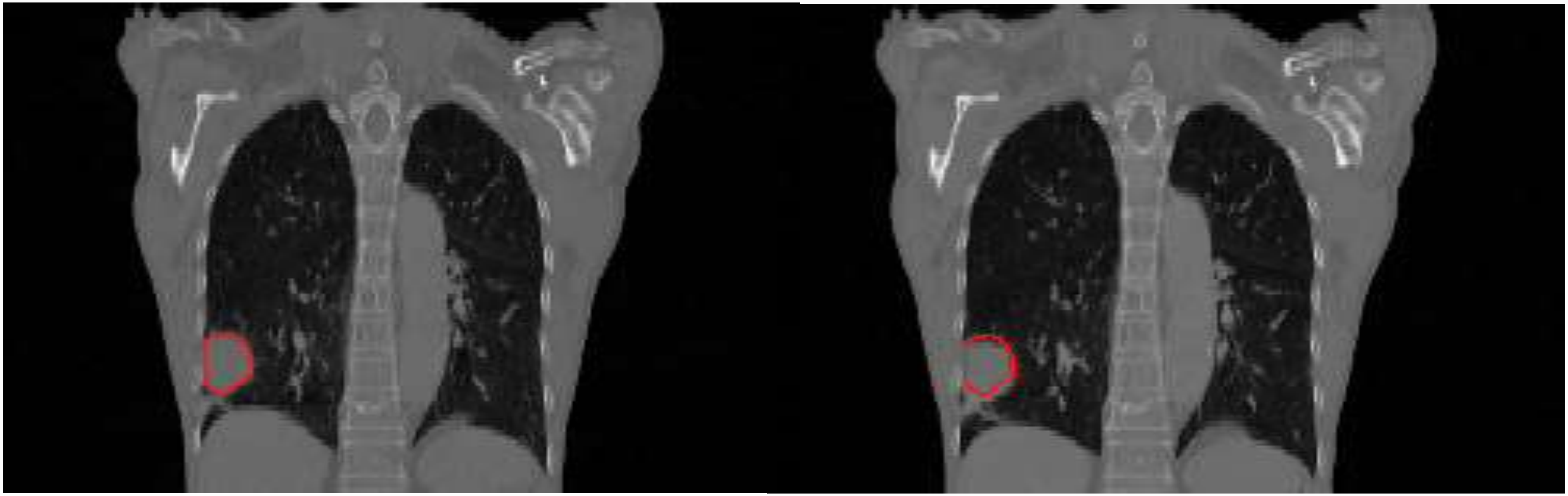
# Mid-ventilation example



## Geometrically most representative 3D scan:

Small geometric error due to hysteresis

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# Image guidance

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CANCER
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# SBRT Lung: Protocol at NKI

- Acquire 4D CT scan
- Select mid-ventilation phase:
  Element of 4D scan closest to mid-position
- Optimize treatment plan on mid-ventilation

*Planning*

- Acquire 4D CBCT
- Bone match →Tumor match
- Apply correction
- Validate correction with 2nd scan
- Contact physician if
  - Shift > 1 cm
  - Anatomical changes

*Treatment*

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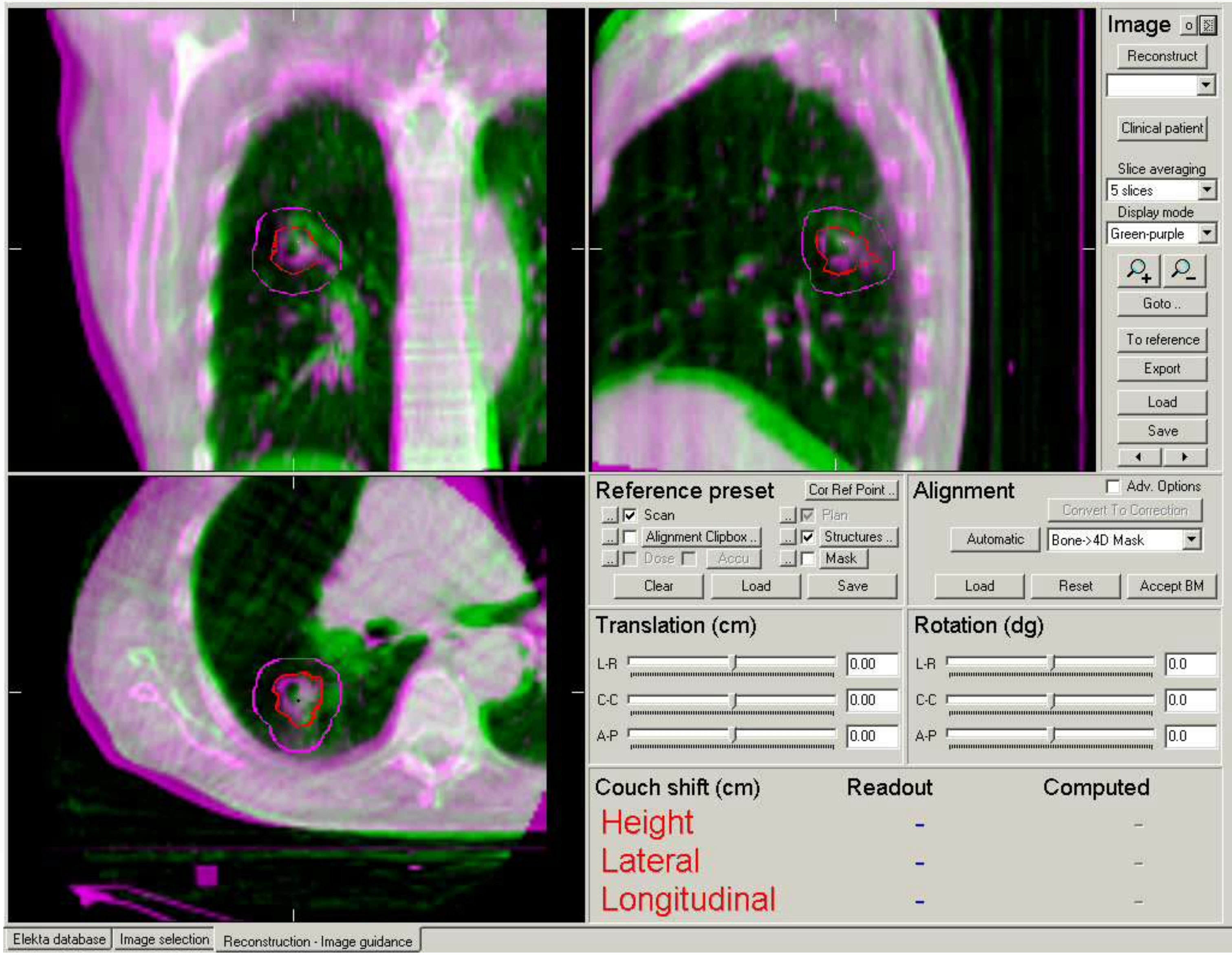
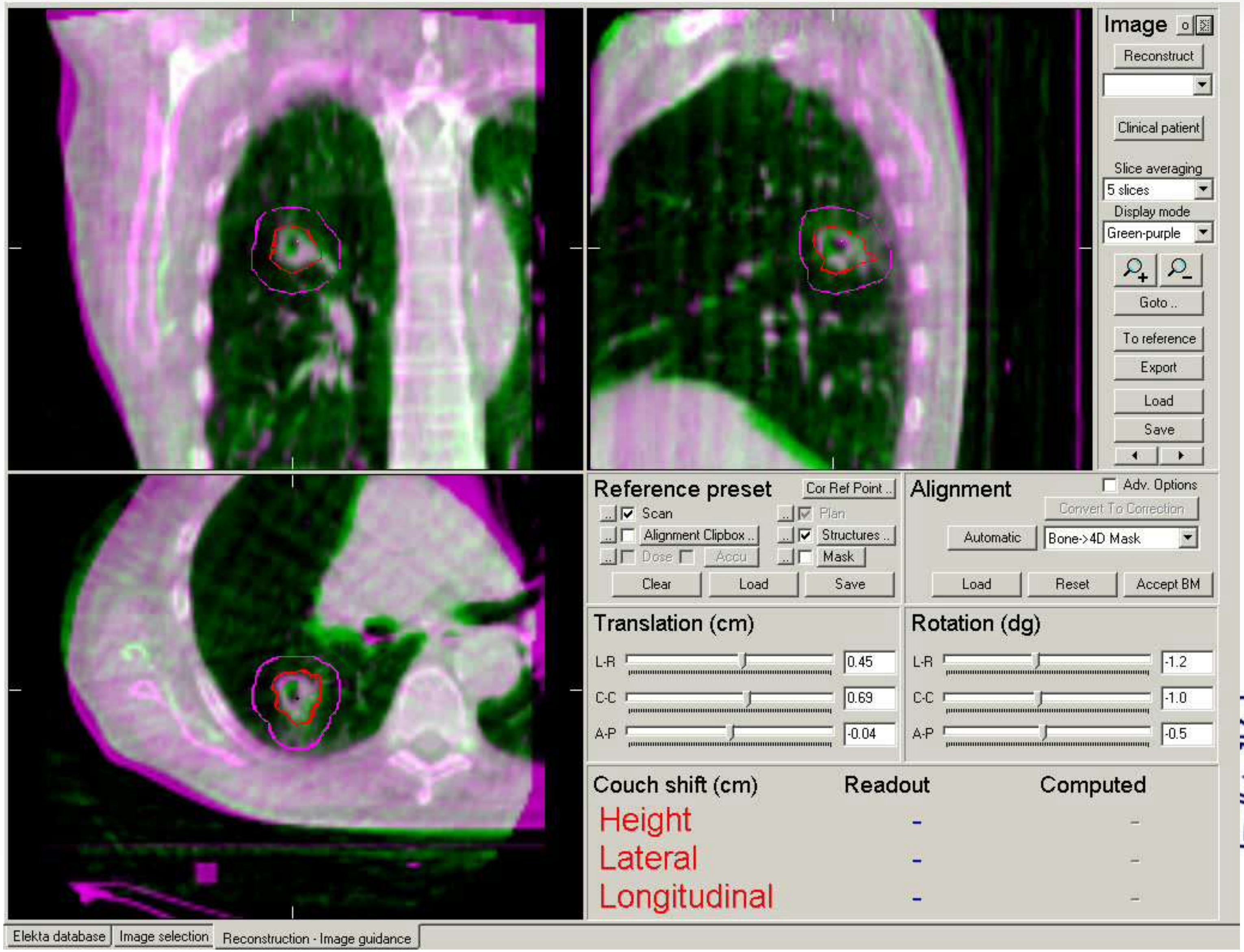
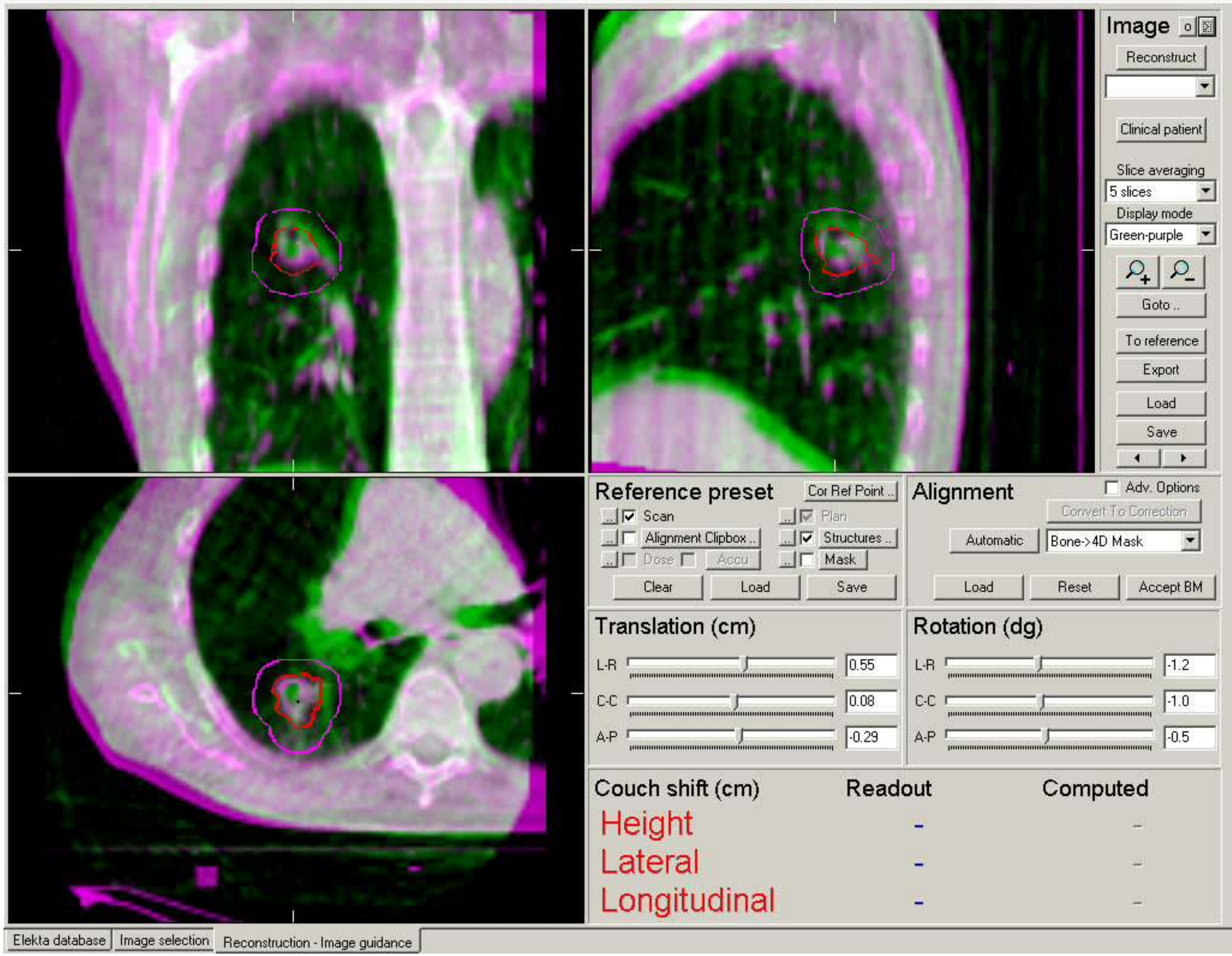
# SBRT lung: first scan (4 min for 4D)



# SBRT lung: matched on bone



# SBRT lung: matched on tumor



# Geometrical Uncertainties

*59 Patients, 3 fractions per patient*

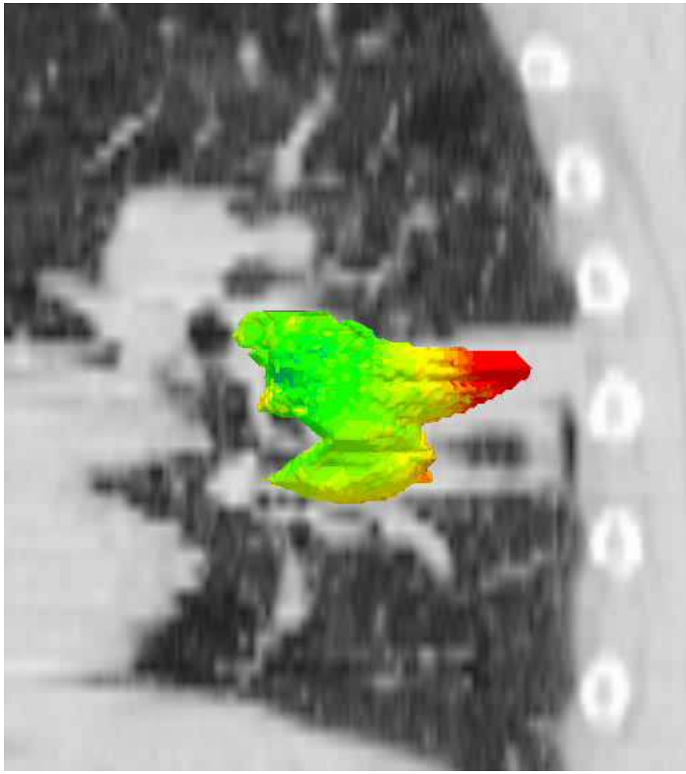
| | | LR (mm) | CC (mm) | AP (mm) |
|---|---|---|---|---|
| Residual Inter-fraction | GM | 0.2 | 0.6 | -0.6 |
| | Σ | 0.8 | 0.8 | 1.0 |
| | σ | 1.1 | 1.1 | 1.4 |
| Intra-fraction | GM | 0.0 | 1.0 | -0.9 |
| | Σ | 1.2 | 1.3 | 1.9 |
| | σ | 1.2 | 1.4 | 1.7 |

# Geometrical Uncertainties

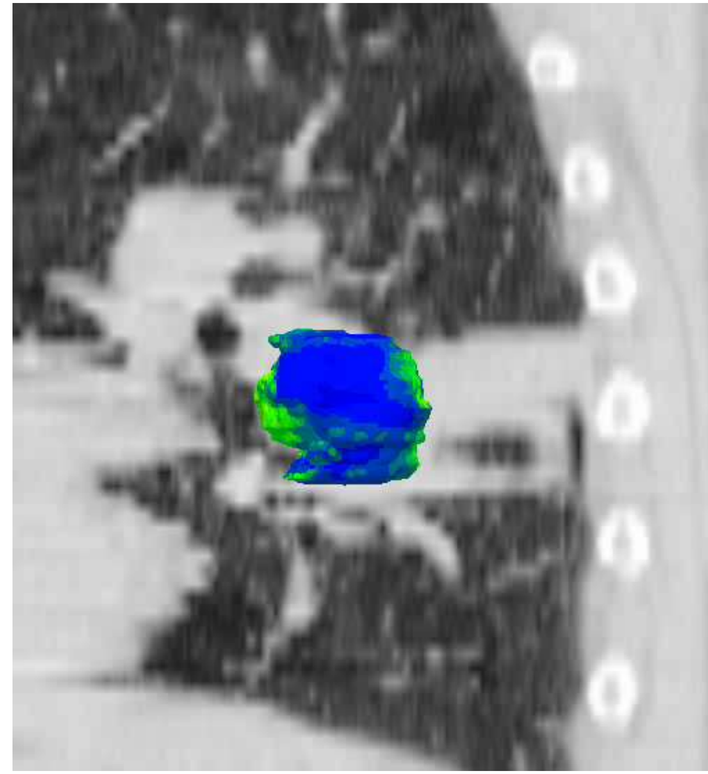
*59 Patients, 3 fractions per patient*

| | | 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 |

# Delineation uncertainties



CT



CT + PET

LOCAL SD (mm)

0 – 1
1 – 2
2 – 3
3 – 4
4 – 5
5 – 6
6 – 7
7 – 8
8 – 9
9 – 10
10 – 11
11 – 12
12 – 13
13 – 14
14 – 15
> 15

# Total margin

- Margins?
  - ITV → Full trajectory of motion
  - ITV will result in large margins
  - But respiratory motion can be regarded as a random error
  - Maybe margin can be smaller ☺

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# Total margin

- Complicated formula…

$$M = 2.5\Sigma + 0.84\sqrt{(\sigma_p^2 + \sigma^2)} - 0.84\sigma_p^2 \neq 2.5\Sigma + 0.7\sigma$$

- But σ is still the sum of all random errors
  - Setup + organ motion ≈ 1.5 mm
  - Breathing ≈ 0.25 * Amplitude

- And Σ the sum of all systematic errors
  - Setup + organ motion ≈ 1.5 mm
  - Delineation variability ≈ 2-3 mm

- Delineation largest contributor

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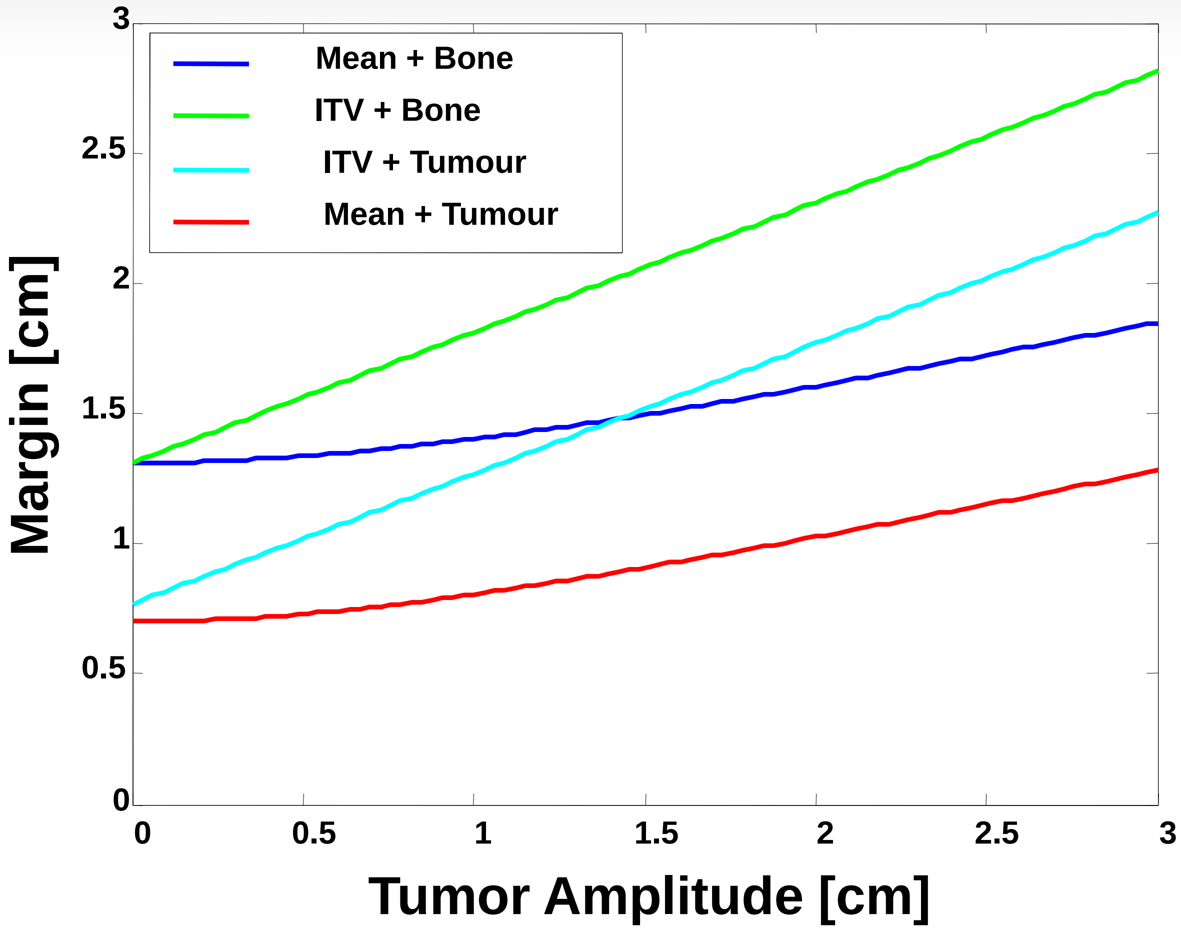
# Total margin




$$M = 2.5\Sigma + 0.84\sqrt{(\sigma_p^2 + \sigma^2)} - 0.84\sigma_p^2 \neq 2.5\Sigma + 0.7\sigma \qquad \sigma_p \approx 6.4 \text{ mm}$$

Assures 80% isodose encompasses GTV 90% of time in lung

# Conclusions

- The mid-ventilation concept leads to smaller margins than the ITV concept, while maintaining coverage
- Systematic baseline shifts of the target can lead to large underdosage
- But this can be well managed with image guidance

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# Solution of clinical lung cancer case


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ESTRO course Target Volume Delineation

Barcelona, April 2016

KREBSCENTRUM DRESDEN (UNIVERSITY CANCER CENTER - UCC)

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

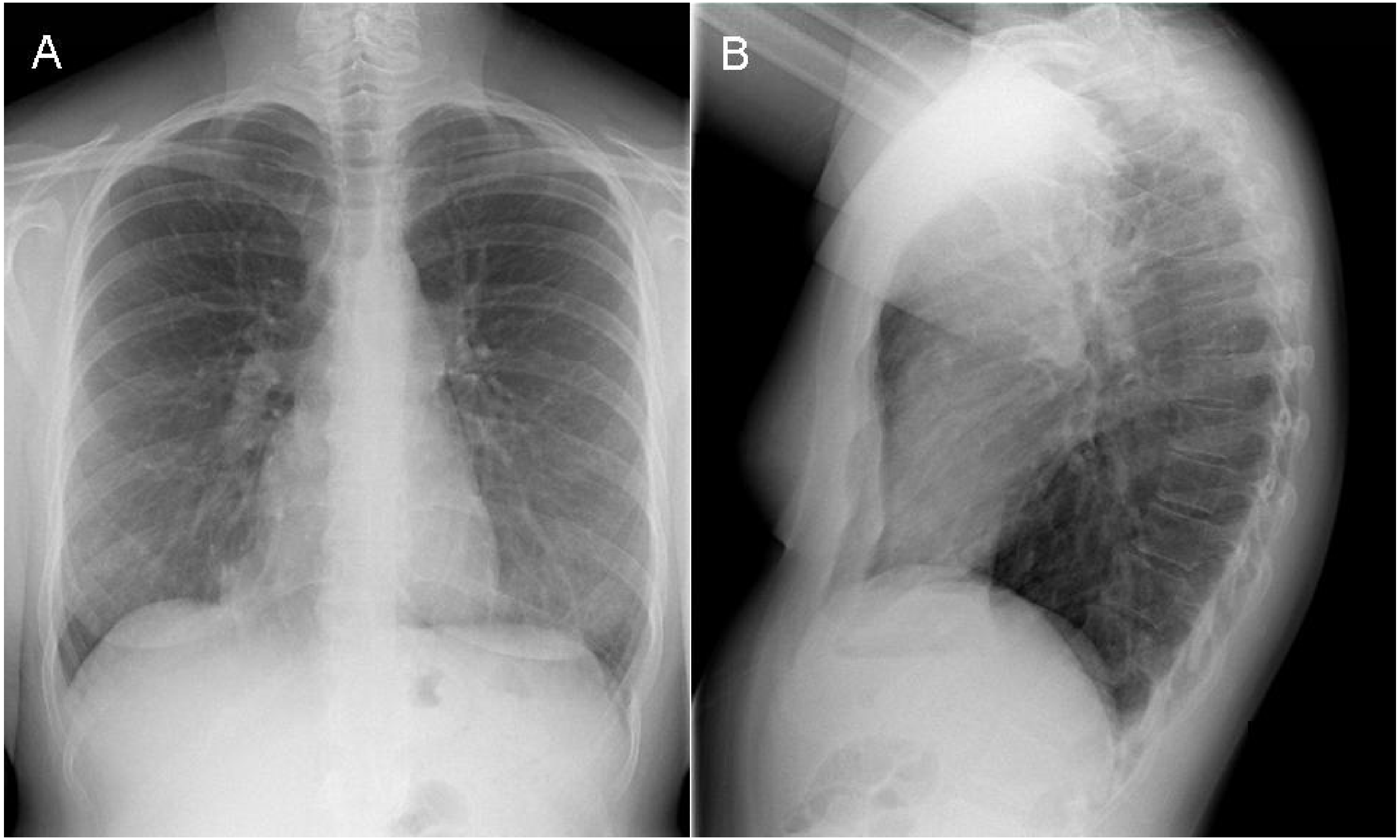
OncoRay Radiation Research in Oncology

# Presentation

- a 58-year old male, active smoker (15 PY)
- **Medical history:**
  polymyalgia reumatica, mesencephalon bleeding, tubular adenomas with dysplasia
  COPD Gold 1
- **Clinical presentation:**
  ECOG performance status = 0,
  no pulmonary complaints, no weight loss
  clinical examination: no abnormalities

# Diagnostic work-up: chest X-ray





# Diagnostic work-up

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- **Bronchoscopy**: mucosal thickening left lower lobe
- **Brush:** non-small cell lung cancer (NOS)

# Diagnostic work-up: FDG-PET/CT

# Diagnostic work-up



- **$^{18}$FDG – PET – CT scan with i.v. contrast :**
  Tumor left lower lobe. Enlarged nodes, PET + in level 4R, 4L and 7; enlarged node left hilar region, PET –. No distant metastases.

- **EBUS:** confirmed positive lymph nodes in level 4R, 4L, 7; not in 10. Invasive adenocarcinoma, EGFR negative.

- **Pulmonary function tests:**
  FEV1 = 2,8 liter (102% of predicted)
  Diffusion capacity = 76% of predicted

# Questions (1)



**Therapy:**
Sequential chemotherapy (3 cycles) and radiotherapy

**Questions**

- What is the tumor stage?

- Would you perform additional invasive procedures?

# Primary tumor stage



| | PRIMARY TUMOR (T) |
|---|---|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Tis | Tis Carcinoma *in situ* |
| T1 | Tumor ≤3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)* |
| T1a | Tumor ≤2 cm in greatest dimension |
| T1b | Tumor > 2 cm but ≤3 cm in greatest dimension |
| T2 | Tumor > 3 cm but ≤7 cm or tumor with any of the following features (T2 tumors with these features are classified T2a if ≤ 5 cm)<br>Involves main bronchus, ≥2 cm distal to the carina<br>Invades visceral pleura (PL1 or PL2)<br>Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung |
| T2a | Tumor > 3 cm but ≤5 cm in greatest dimension |
| T2b | Tumor > 5 cm but ≤7 cm in greatest dimension |
| T3 | Tumor > 7 cm or one that directly invades any of the following: parietal pleural (PL3) chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus (< 2 cm distal to the carina* but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe |
| T4 | Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe |

* The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1a.

# Lymph node stage



**NX.** Regional lymph nodes cannot be assessed

**N0.** No regional lymph node metastasis

**N1.** Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension

**N2.** Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)

**N3.** Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

# Additional procedures: Mediastinoscopy

**Dutch guidelines:**

- a mediastinoscopy needs to be performed in all patients with a NSCLC without distant metastases AND in whom on CT or PET there is evidence for mediastinal lymph node invasion

- no mediastinoscopy needs to be performed if:
  - primary tumor is PET + AND
  - no N1 on PET AND
  - tumor makes no contact with mediastinum AND
  - nodes on CT are < 1 cm (short axis)

# Additional procedures: staging of brain

# Questions (2)

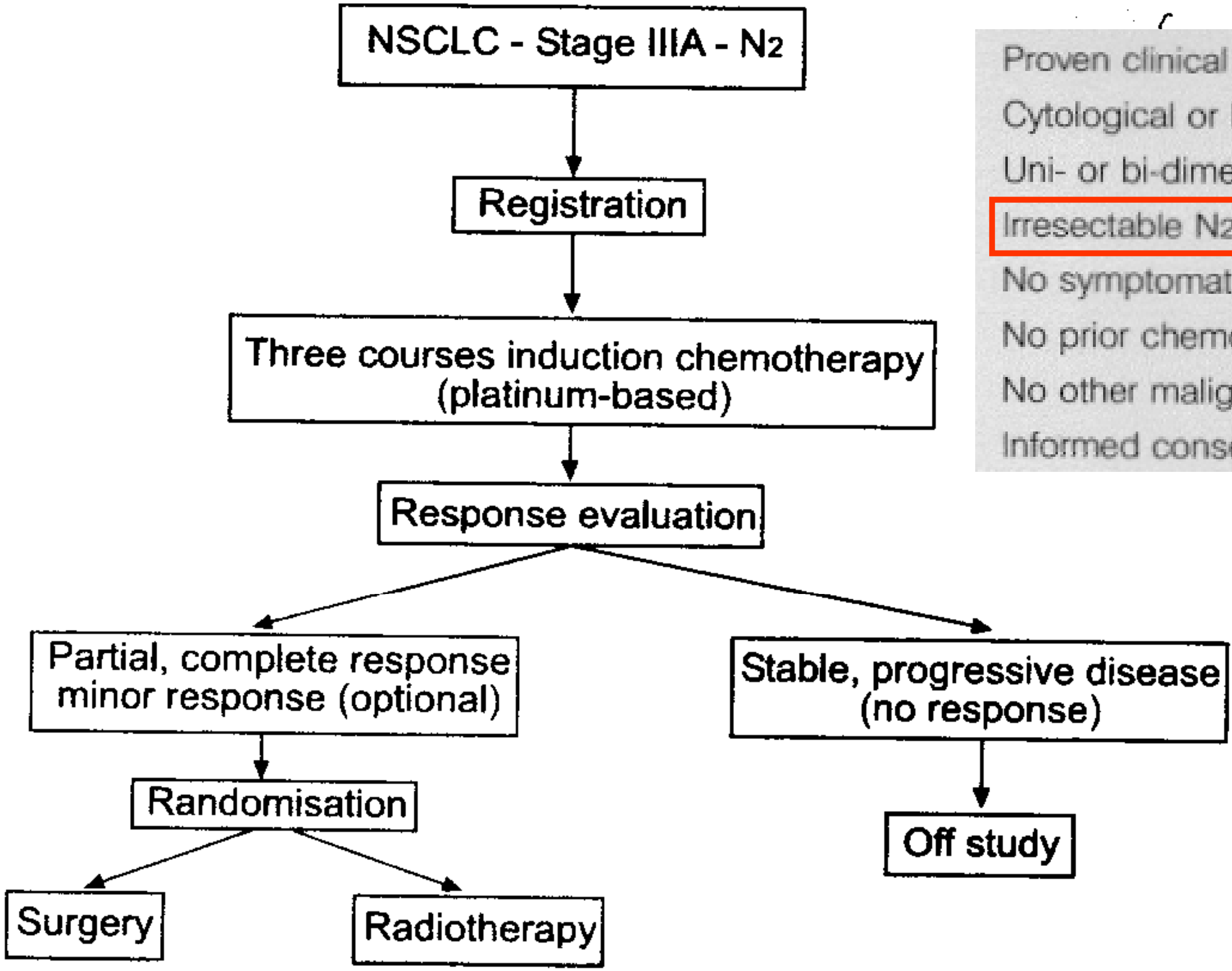


- Would you have proposed a different approach?
  - Surgery?
  - RT alone?
  - Combined CT + RT ?

    Sequential?

    Concurrent?
  - CT + RT + surgery?

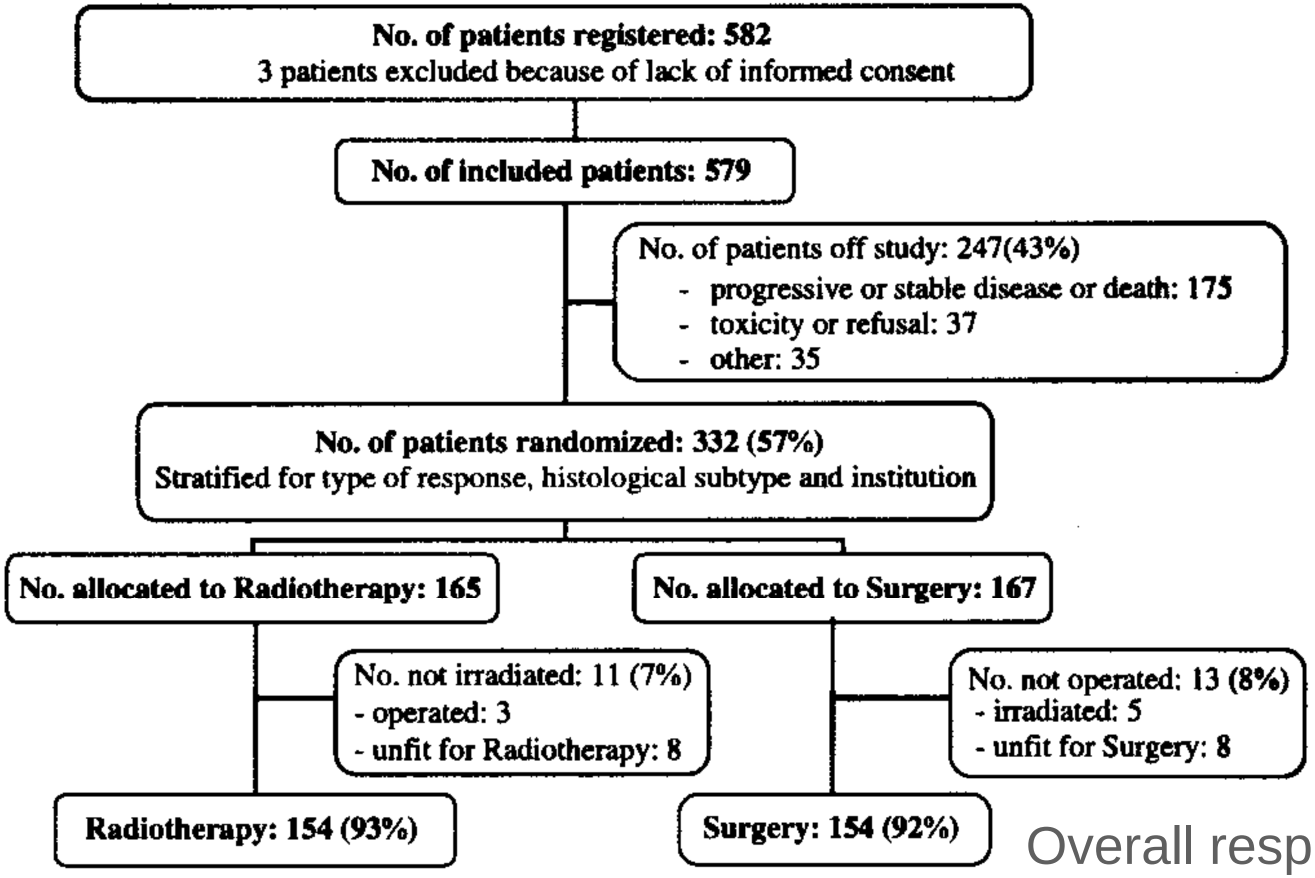
# EORTC 08941




- Proven clinical stage IIIA-nonsmall cell lung cancer
- Cytological or histological proof of N2 disease
- Uni- or bi-dimensional measurable tumour
- Irresectable N2 disease
- No symptomatic central nervous system involvement
- No prior chemotherapy or radiotherapy
- No other malignancies
- Informed consent

# EORTC 08941: Results

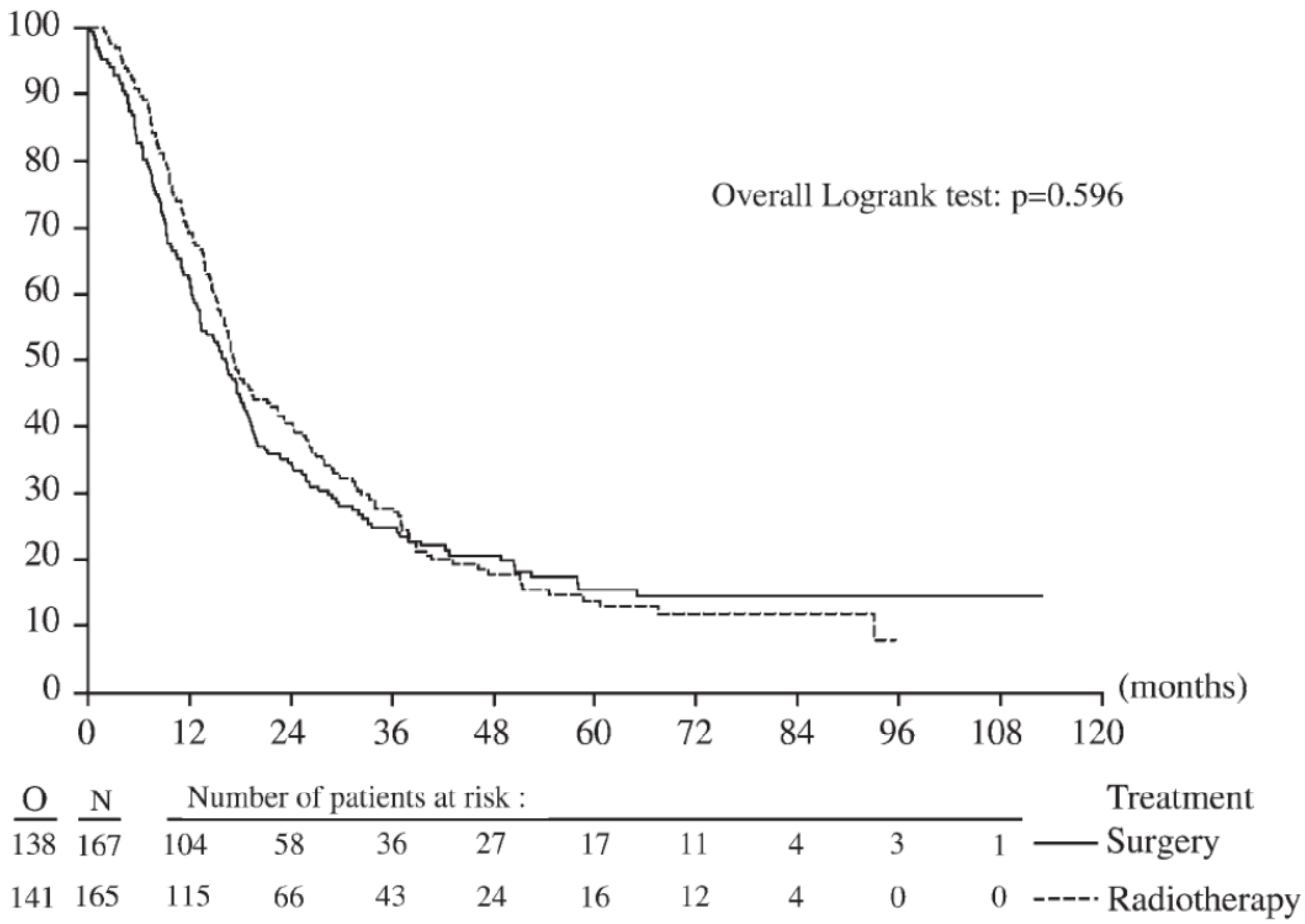





Overall response 61%

# EORTC 08941: Overall survival





# EORTC 08941: Results

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- Irresectable st IIIa-N2: overall prognose after induction chemotherapy+ surgery = induction chemo + radiotherapy.

- However, if induction chemotherapy leads to mediastinal down staging and complete resection (lobectomy): surgery leads to a better local control and prognosis than standard therapy.

# Intergroup 0139/RTOG 9309



## stage IIIA

cispl / etop + RT 45Gy → **surgery** → cispl / etop x 2

versus

cispl / etop + RT 45Gy → **RT 61 Gy** → cispl / etop x 2

**Inclusion criteria:**

- histologically proven N2, T1-3
- potentially resectable
- operable

# Intergroup 0139/RTOG 9309: OS

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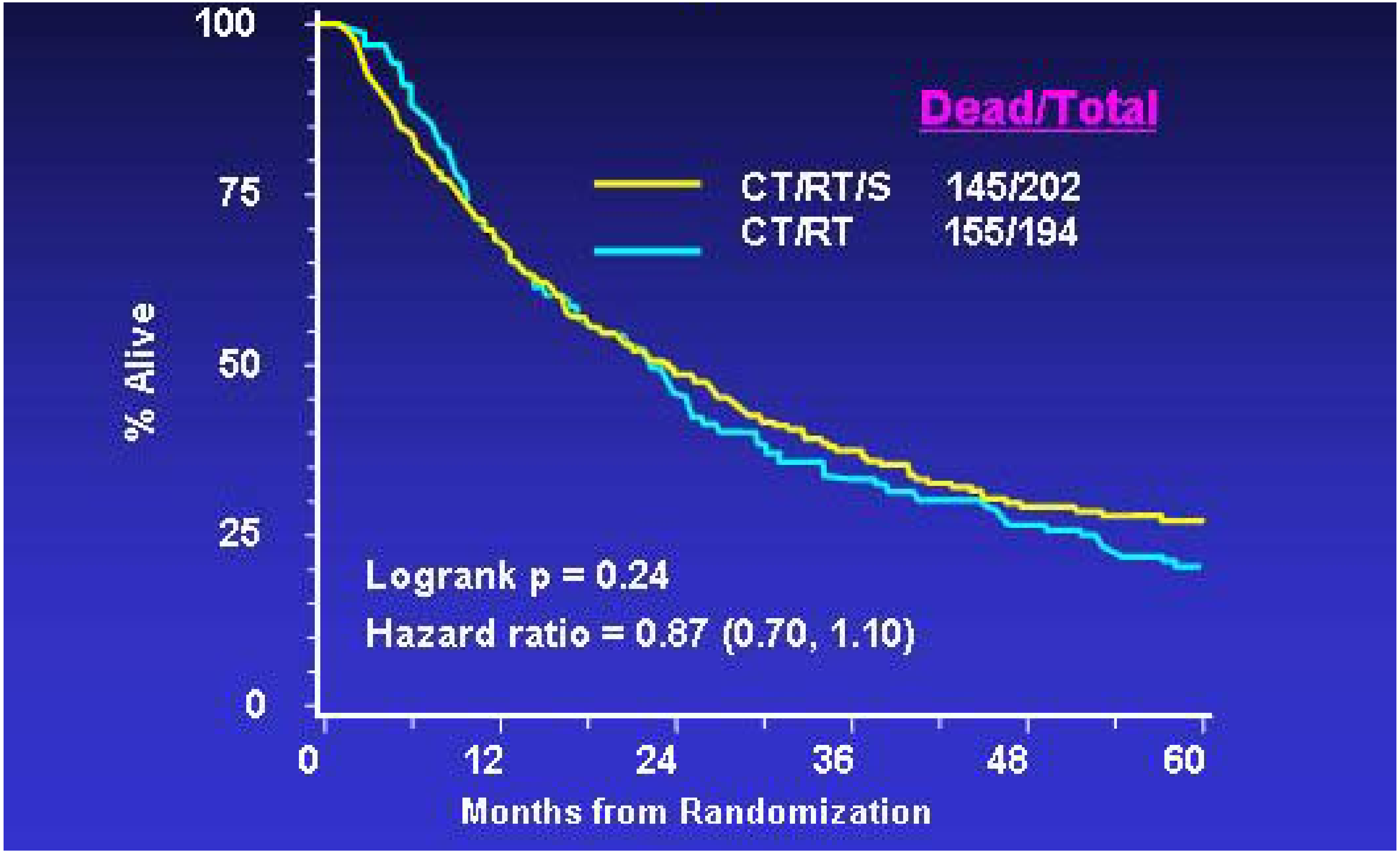
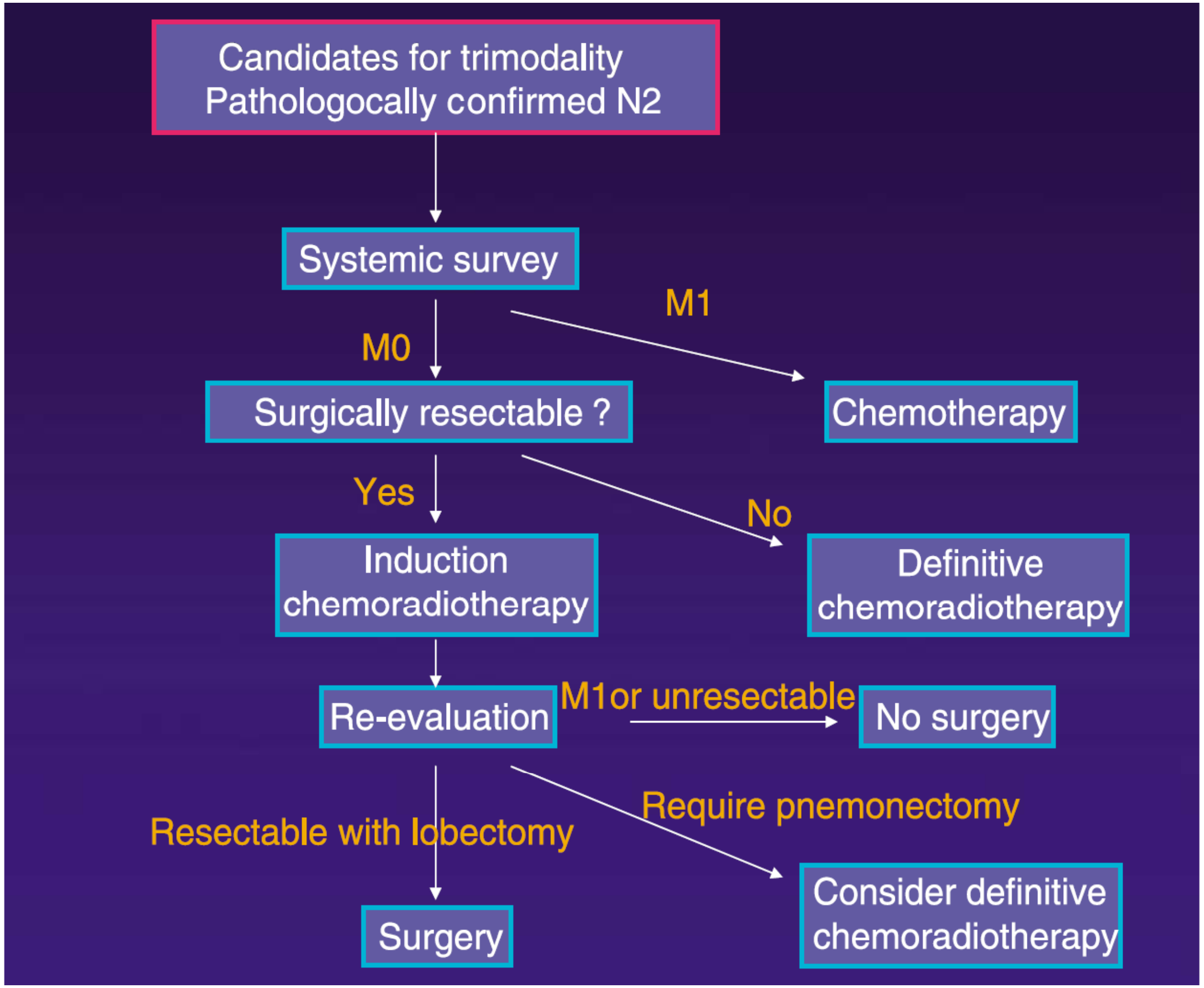


# Management of N2 disease

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

## Trimodality




Kunitoh *et al.*, Br J Cancer 2007

# Treatment approach



- Aupérin (2010) benefit of concurrent radiochemotherapy regarding overall survival (5.7% @ 3 yrs, 4.5% @ 5 yrs)
- Higher treatment-related toxicity
(4% seq vs 18% concurr)
- Which radiation dose would you give?

# Radiation Dose



- Internationally accepted: 60-66 Gy
- What about RTOG 0617 results?

# Questions (3)



- Define and draw the GTV of the primary lung tumor on the CT taking into account the FDG-PET.

# Questions (4)

- Discuss treatment of the mediastinum:
  - elective lymph node irradiation?
  - involved field irradiation?
  - which lymph node areas?

# Questions (5)

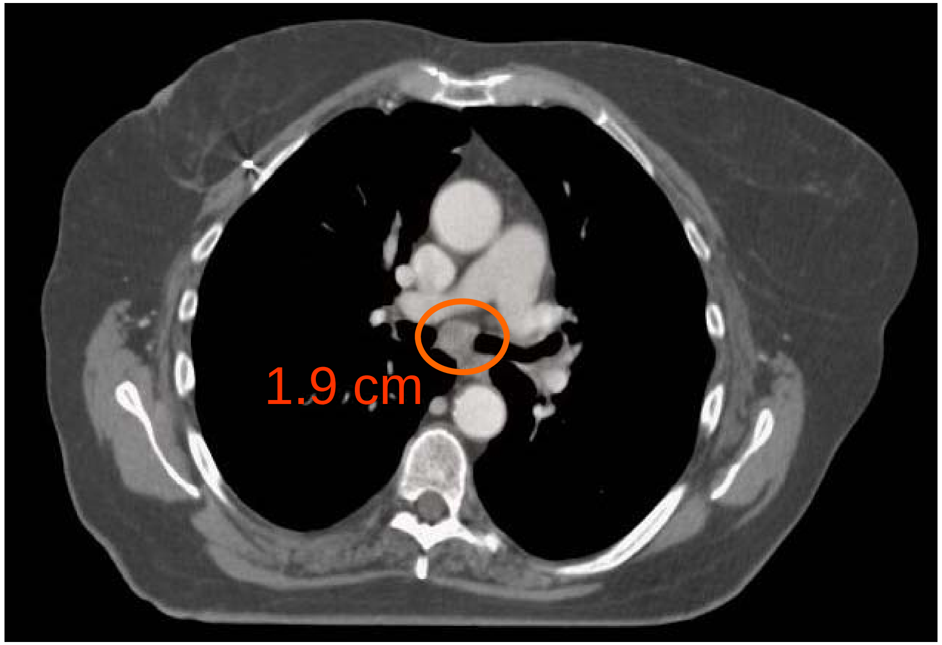


- Define and draw the GTV of the lymph node(s) on the CT taking into account the FDG-PET.

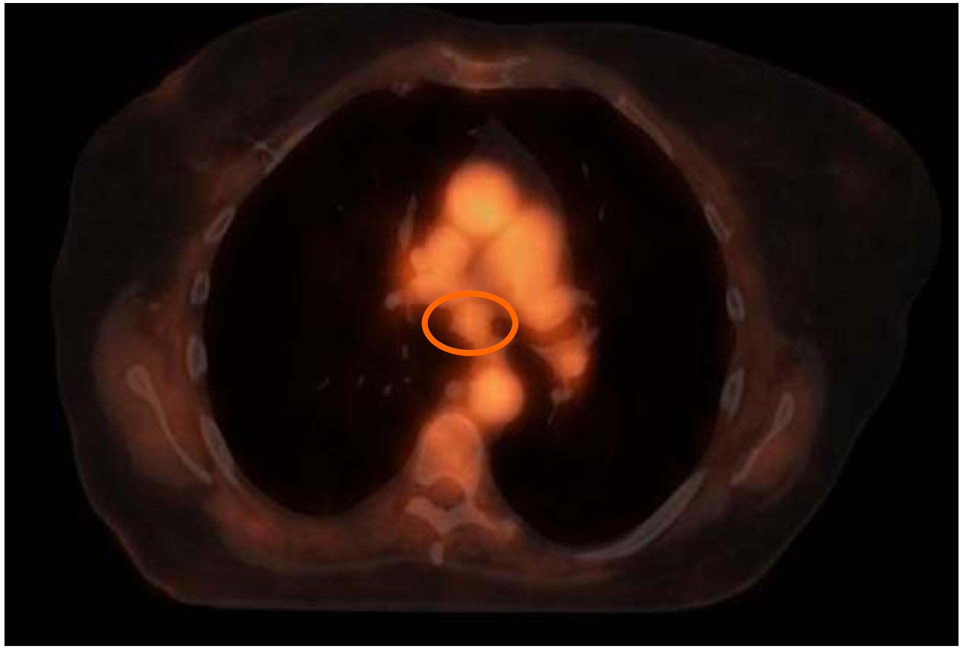
# Questions (6)

- Did the PET information influence your determination of the nodal GTV?

# Selective nodal irradiation in NSCLC: CT or PET?




CT: lnn station 7 enlarged
cT4**N2**M0



PET: lnn station 7 negative
cT4**N0**M0

# Selective nodal irradiation in NSCLC: FDG-PET based!

- 44 patients NSCLC
- 61.2-64.8 Gy (1.8 Gy BID)
- median FU: 16 months
- Isolated nodal recurrence: 1 patient (2.3%)

- 88 patients NSCLC
- dose-escalation study
- median FU: 16 months
- Isolated nodal recurrence: 2 patients (2.3%)

Selective nodal irradiation based on **PET** is safe in NSCLC

De Ruysscher *et al*., IJROBP 2005
Belderbos *et al*., IJROBP 2006

# Questions (6)



- Did the PET information influence your determination of the nodal GTV?

  - 4R: PET+
  - 4L: PET+
  - 7: PET+

  - 10L: PET-

# Questions (7)



- Did the EBUS information influence your determination of the nodal GTV?

# Questions (7)

- Did the EBUS information influence your determination of the nodal GTV?

  – 4R: PET+ and cytol+
  – 4L: PET+ and cytol+
  – 7: PET+ and cytol+

  – 10L: PET- and cytol-

# Questions (8)

Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

- Would you have defined the GTV differently in case of concurrent chemoradiotherapy?

# Questions (9)



- Which margin from GTV to CTV for both the primary tumor as well as for the lymph nodes do you use?
- Do you include additional lymph nodes in the CTV?
- Which margin from CTV to PTV for both the primary tumor and the lymph nodes do you use?

# Thank you for your attention!

OncoRay – National Center for Radiation Research in Oncology, Dresden

# *Anatomy and Lymph Node Drainage. GTV and CTV for Breast. Delineation of OAR in breast cancer*

Dra Meritxell Arenas Prat, MD, PhD
Radiation Oncology Department,
Hospital Universitari Sant Joan de Reus
University Rovira i Virgili, Spain

Hospital Universitari Sant Joan
REUS

*TVD Barcelona*

*10-13 April, 2015*

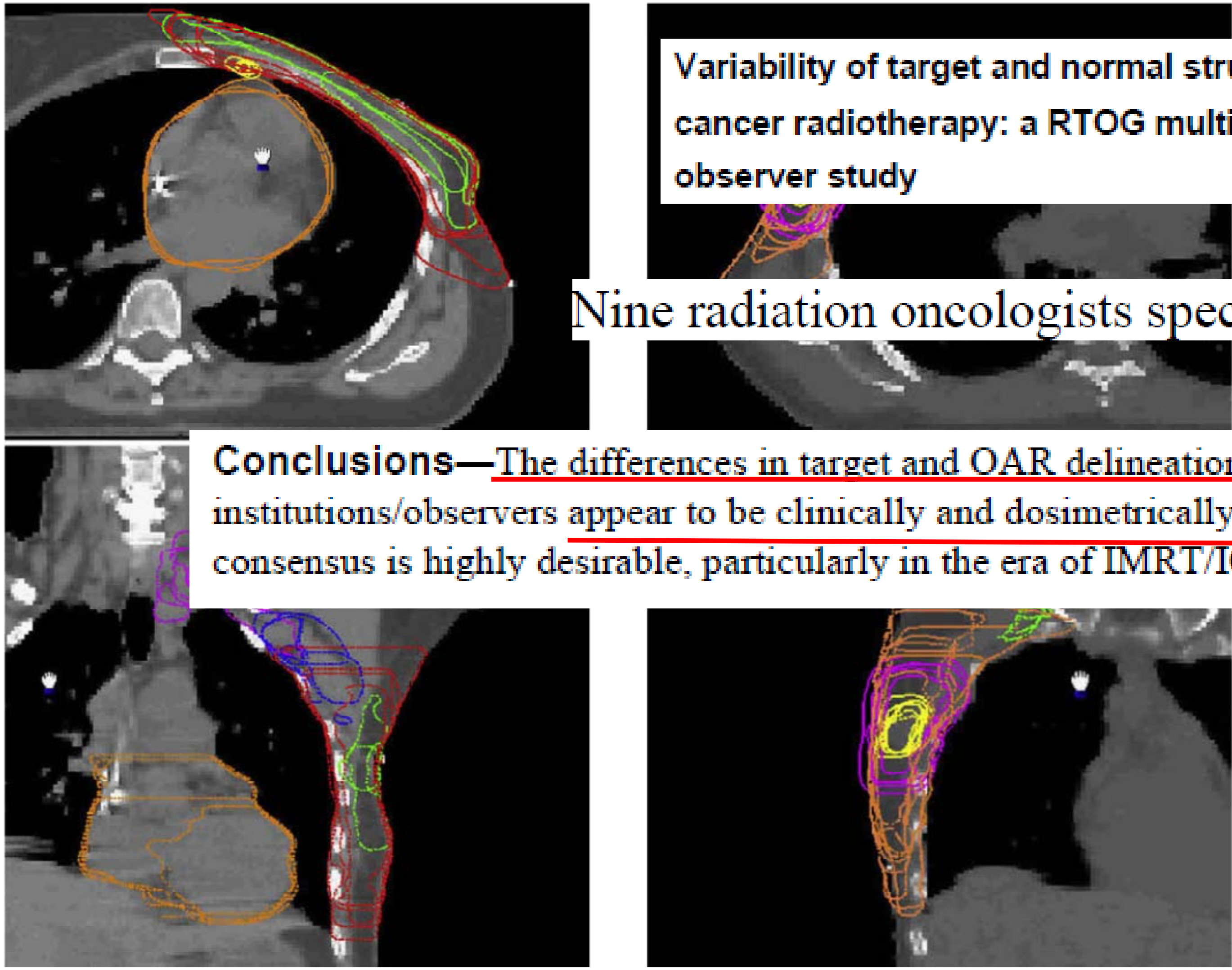
ESTRO School

- **Introduction**
- **Anatomy and lymph node drainage**
- Indications and CTV:
  - Whole Breast
  - Boost
  - Chest wall
  - Regional nodes
    - L4, L3, L2, L1, IM, Rotter
- Organs at risk and constraints
- Margins CTV → PTV     OAR → PRV
- Conclusions

# *WHEN WE CHOOSE RT TREATMENT ....*

- Correct delineation of volumes
- An homogeneous coverage of PTV
- Avoiding organs at risk to reduce acute and late complications

# VOLUME DELINEATION: VARIABILITY!!!



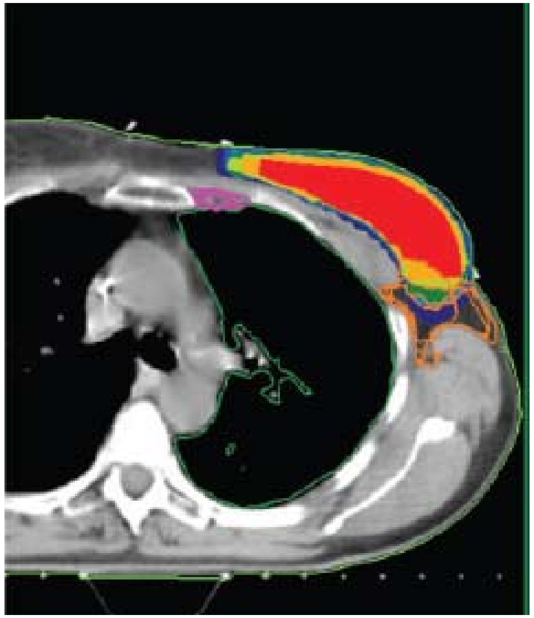
**Variability of target and normal structure delineation for breast-cancer radiotherapy: a RTOG multi-institutional and multi-observer study**

Nine radiation oncologists specializing in breast RT

**Conclusions—**The differences in target and OAR delineation for breast irradiation between institutions/observers appear to be clinically and dosimetrically significant. A systematic consensus is highly desirable, particularly in the era of IMRT/IGRT.

X. Allen Li. Int. J. Radiation Oncology Biol. Phys., Vol. 73, No. 3, pp. 944–951, 2009

# VOLUME DELINEATION: VARIABILITY!!!



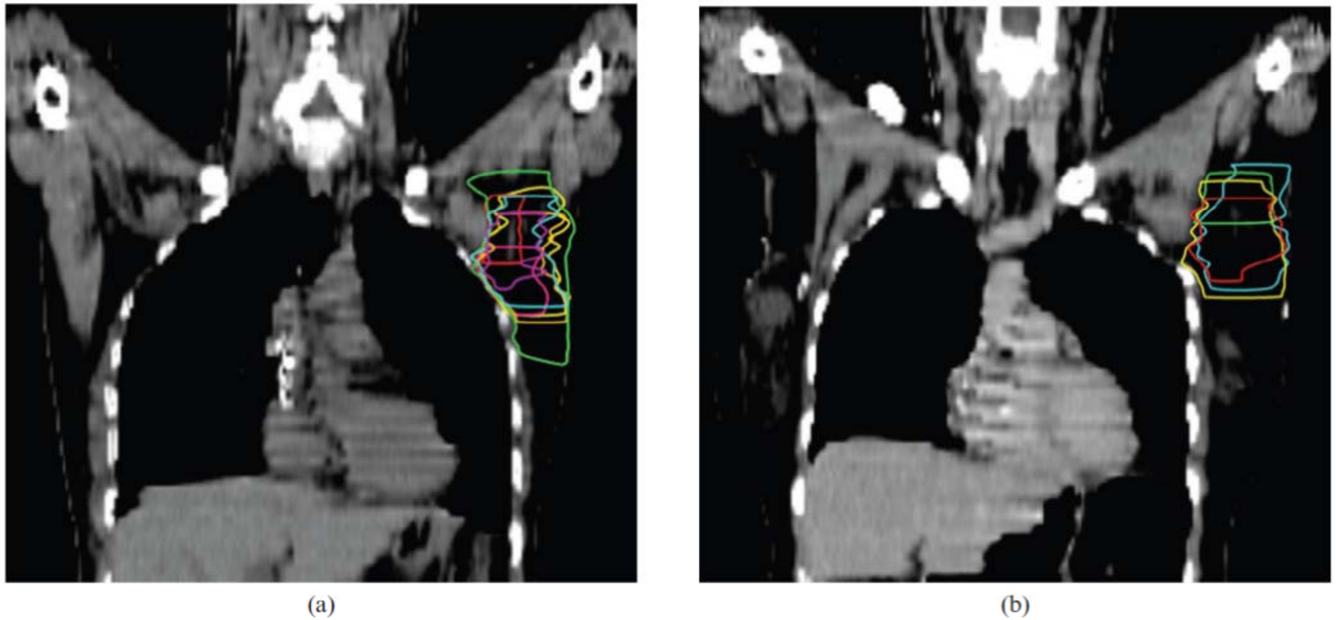



**Figure 3.** Practical example of axillary delineation before and after continuing medical education (CME) and using the simplified practical rules: ''how to delineate the lymph node areas?''. (a) Before training; (b) after training.

It's very important to know the individual anatomy of the patients, their position and the large variability in the depth of nodes

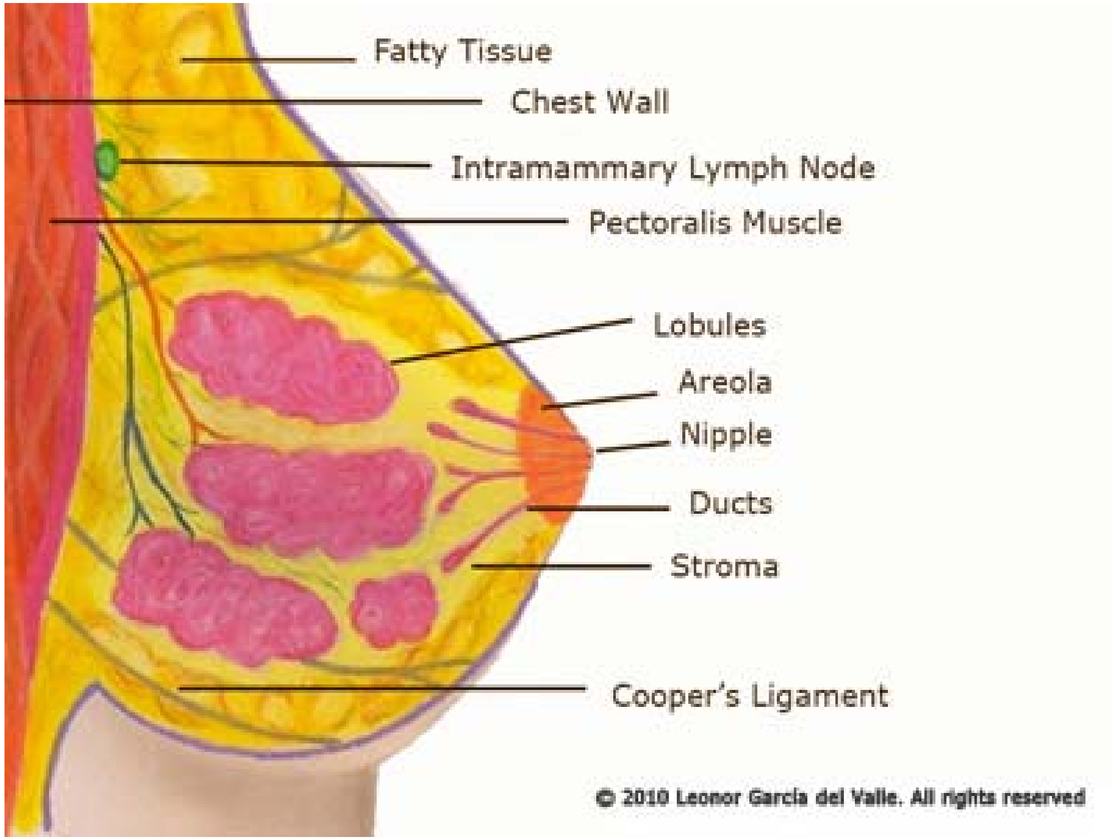
*The British Journal of Radiology, 82* (2009), 595–599

**Anatomical, clinical and radiological delineation of target volumes in breast cancer radiotherapy planning: individual variability, questions and answers**

P CASTRO PENA, MD, Y M KIROVA, MD, F CAMPANA, MD, R DENDALE, MD, M A BOLLET, MD, N FOURNIER-BIDOZ, PhD and A FOURQUET, MD

ESTRO School

# BREAST ANATOMY

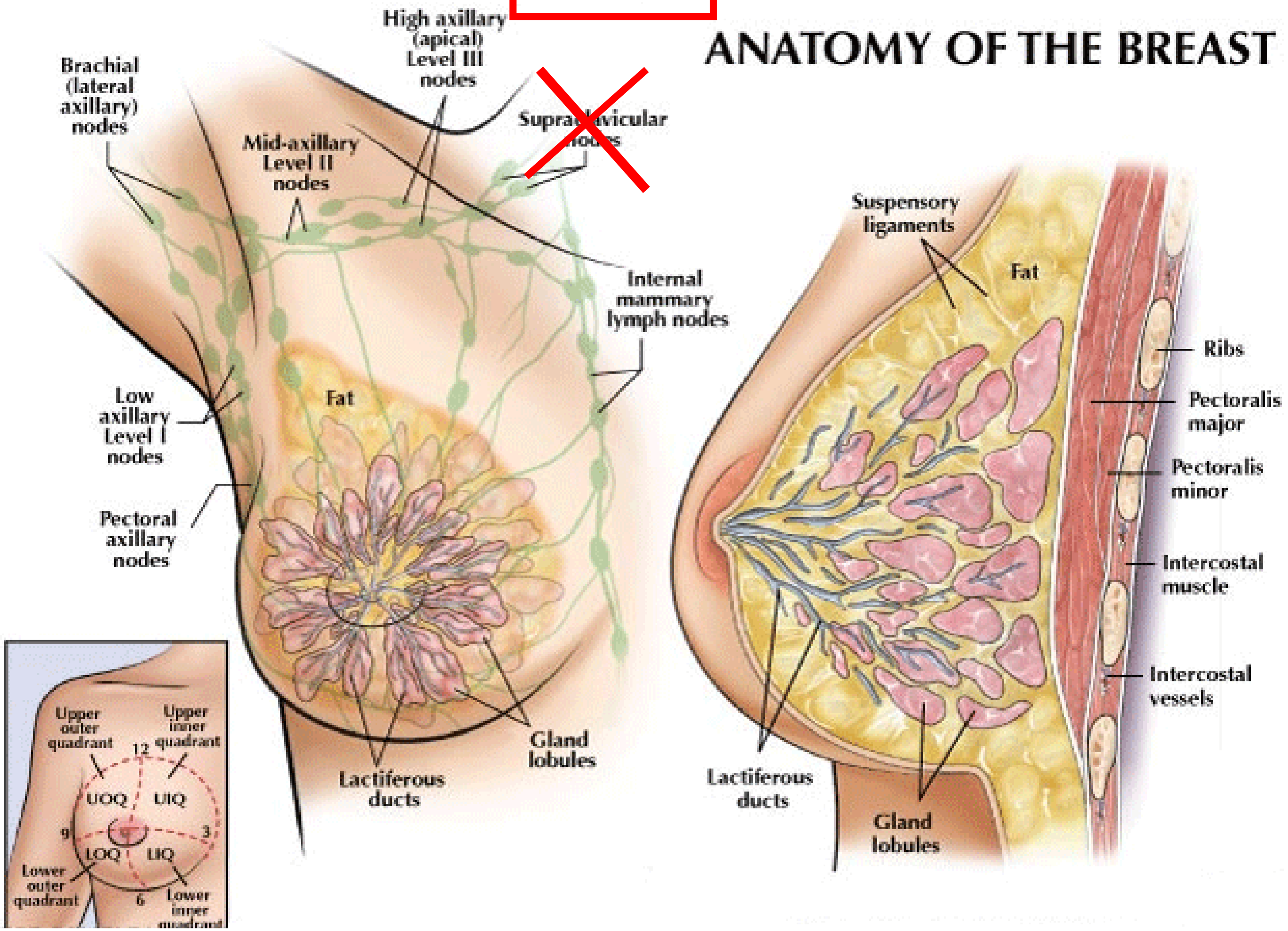



Limits:

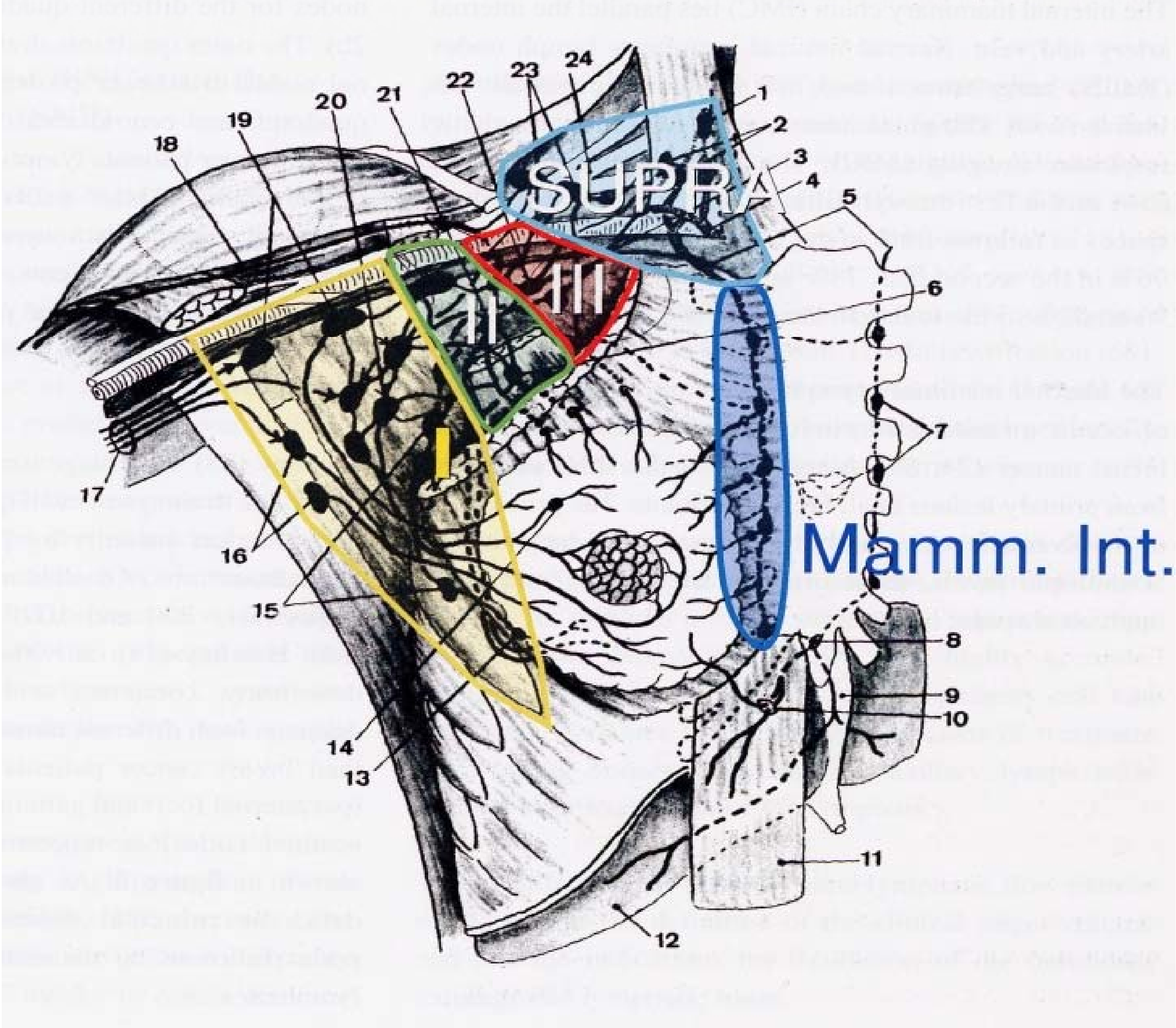
2nd costal arch
6th-7th rib cartilage
Anterior axillary line
Sternal border

# BREAST ANATOMY

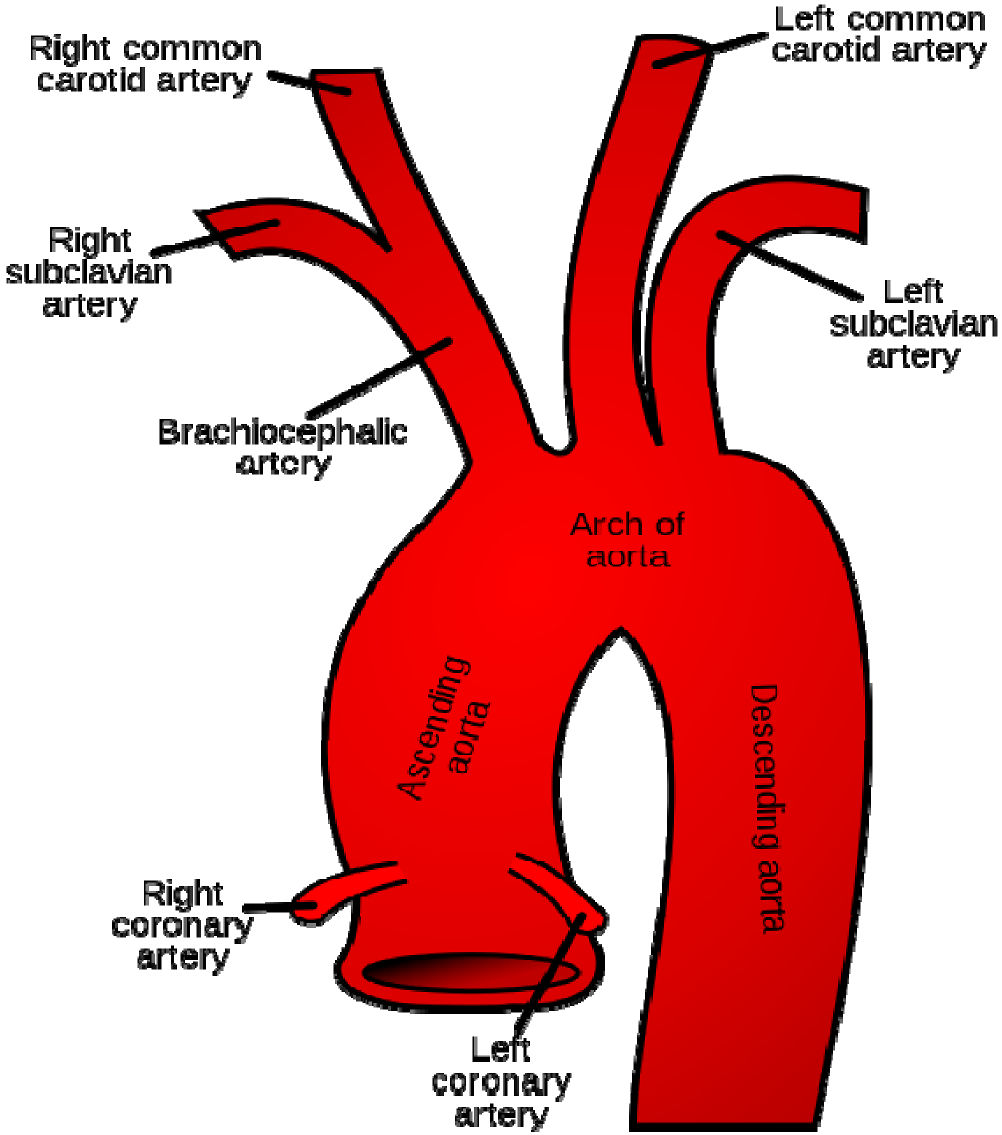
Level 4



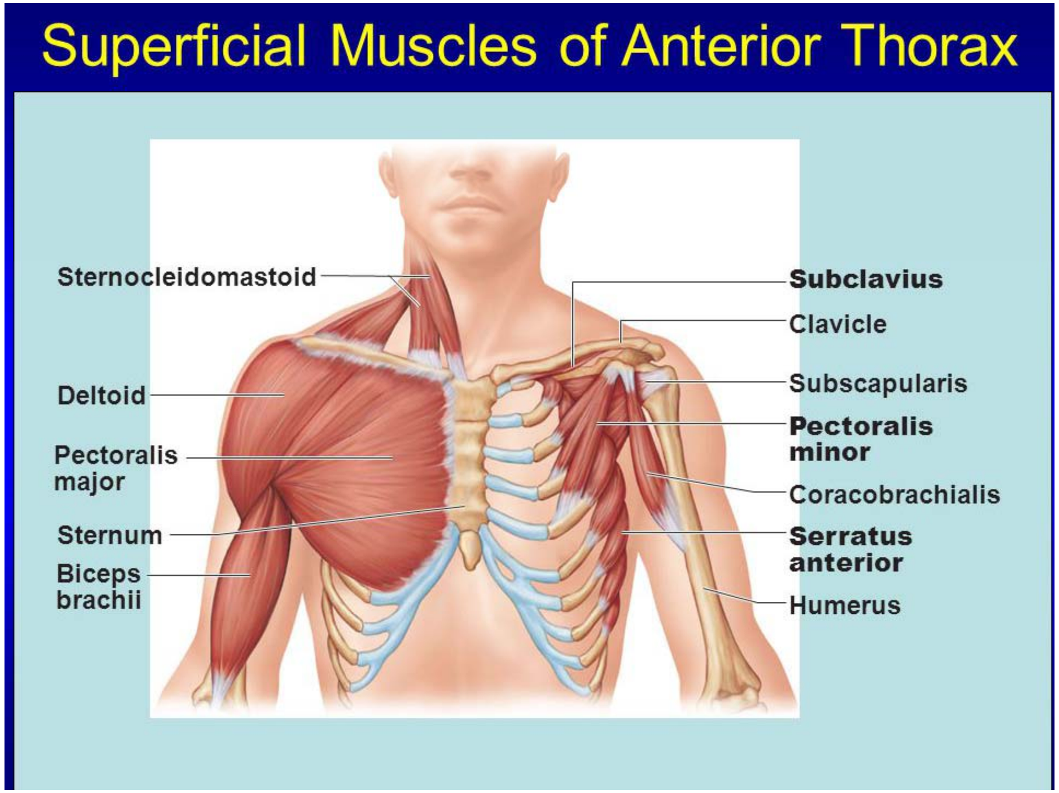
# BREAST ANATOMY

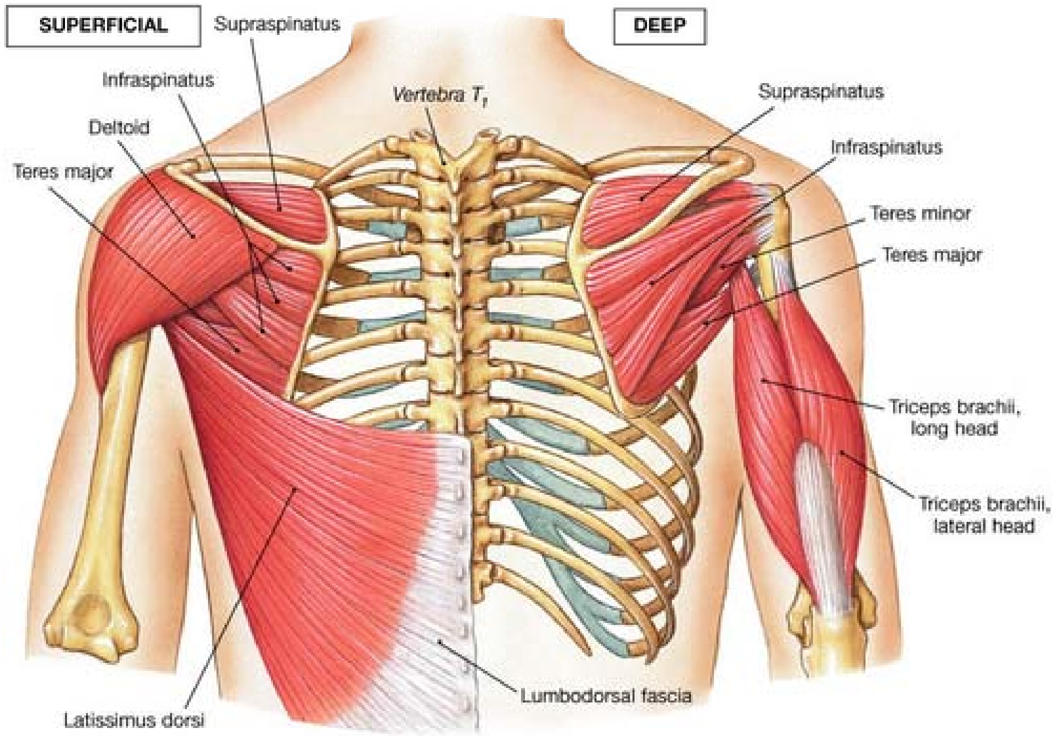


# BREAST ANATOMY



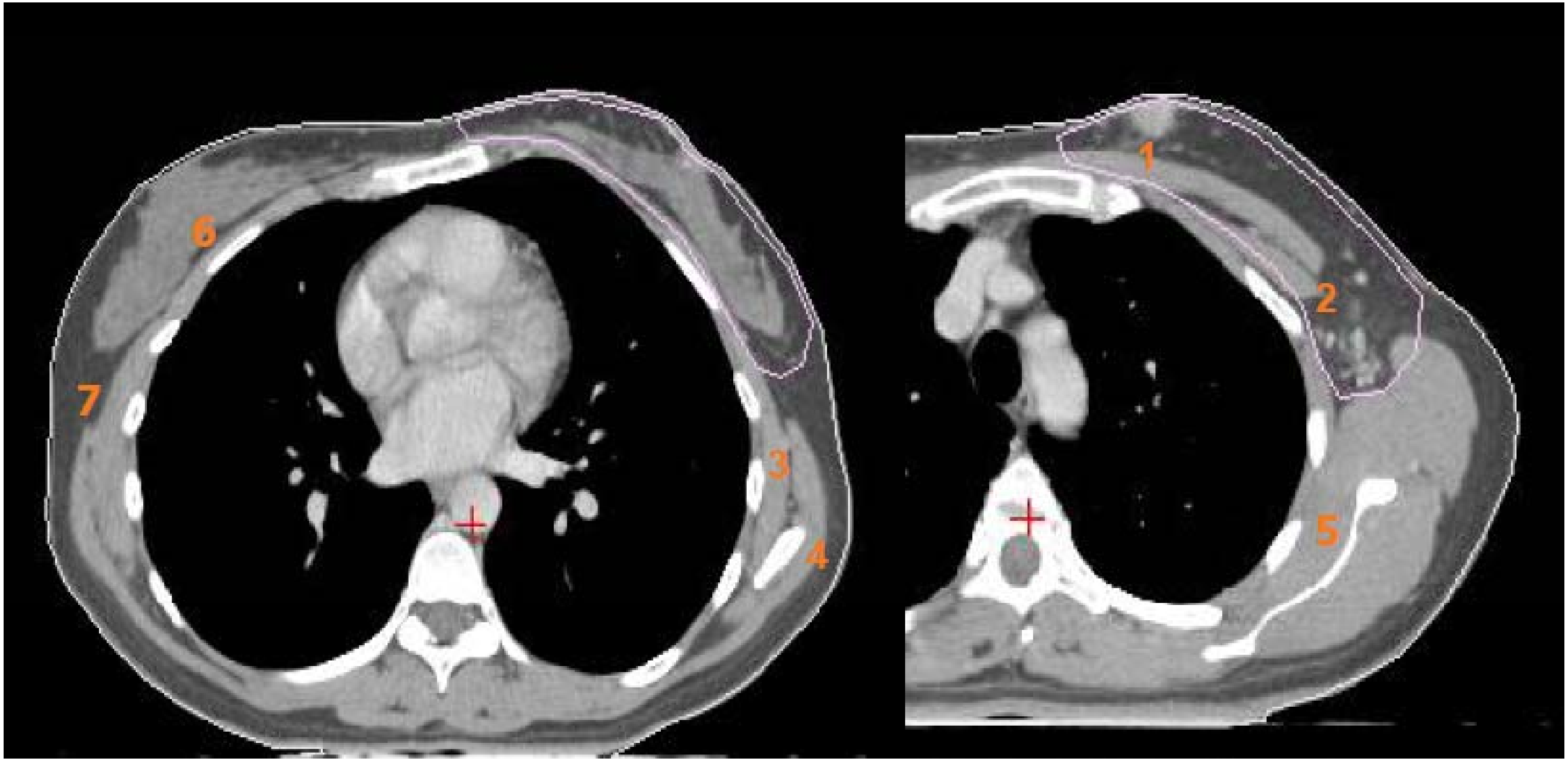
# BREAST ANATOMY




(b) Posterior view

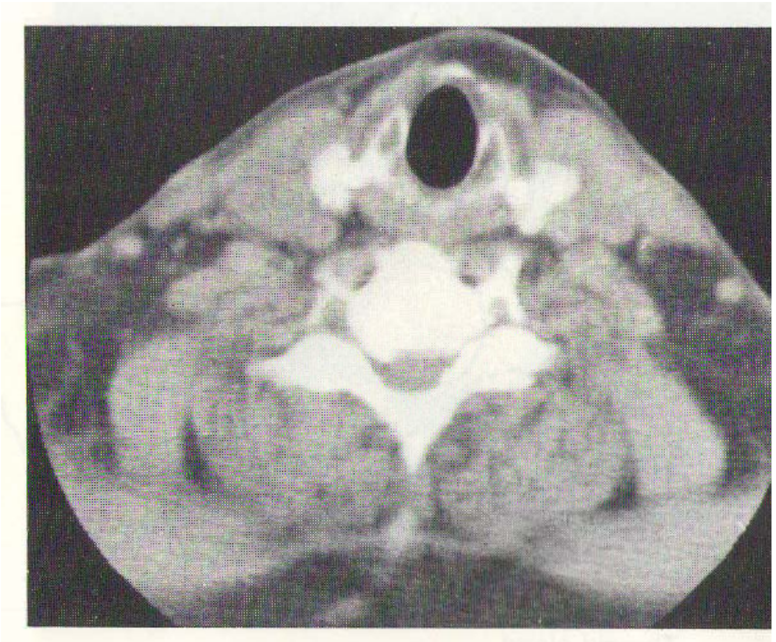
# BREAST ANATOMY

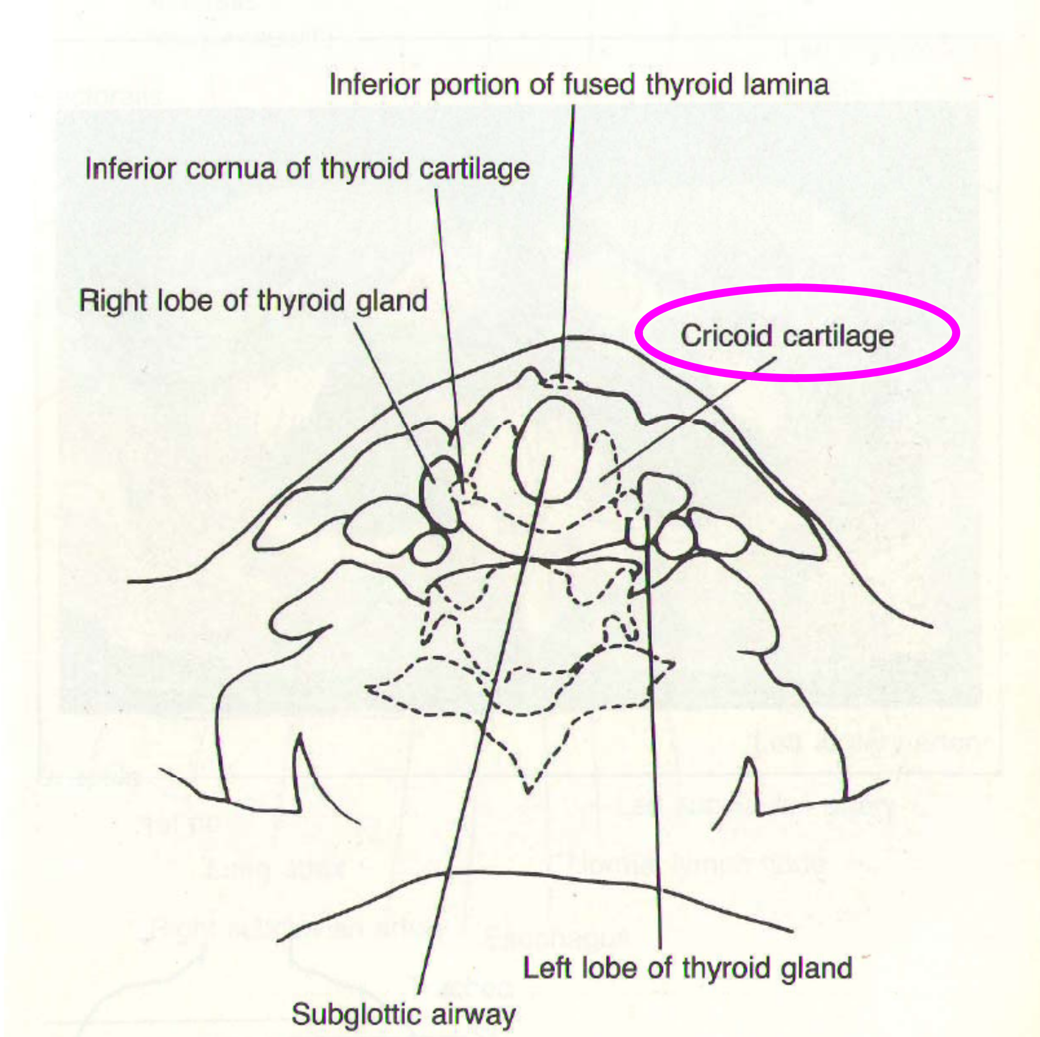



1 pectoralis major. 2 pectoralis minor. 3 serratus anterior.

4 latissimus dorsi. 5 subscapularis. 6 mammary gland. 7 fat

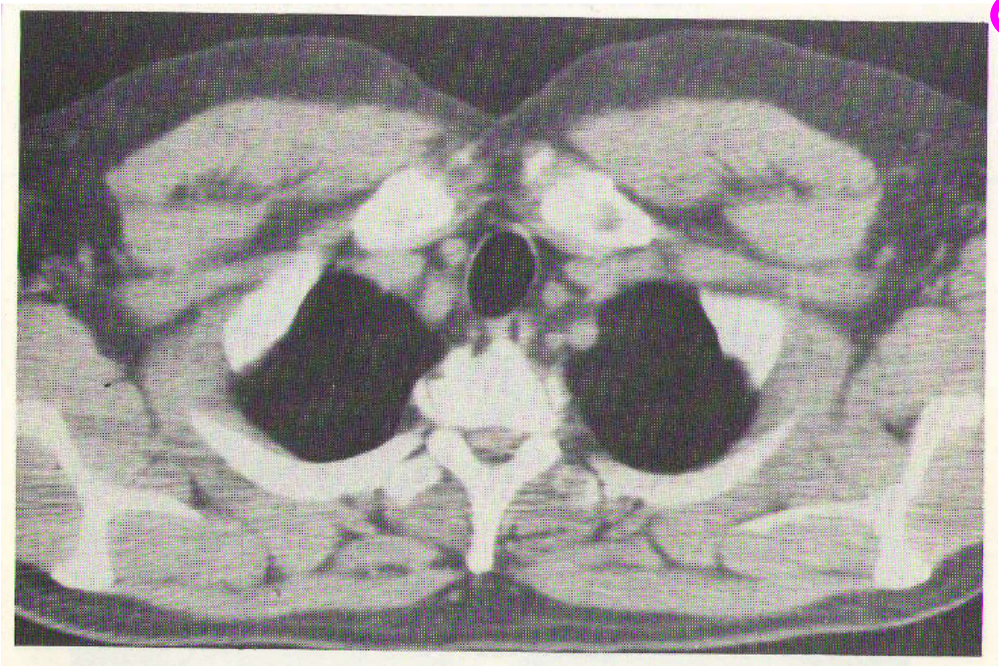
# BREAST ANATOMY

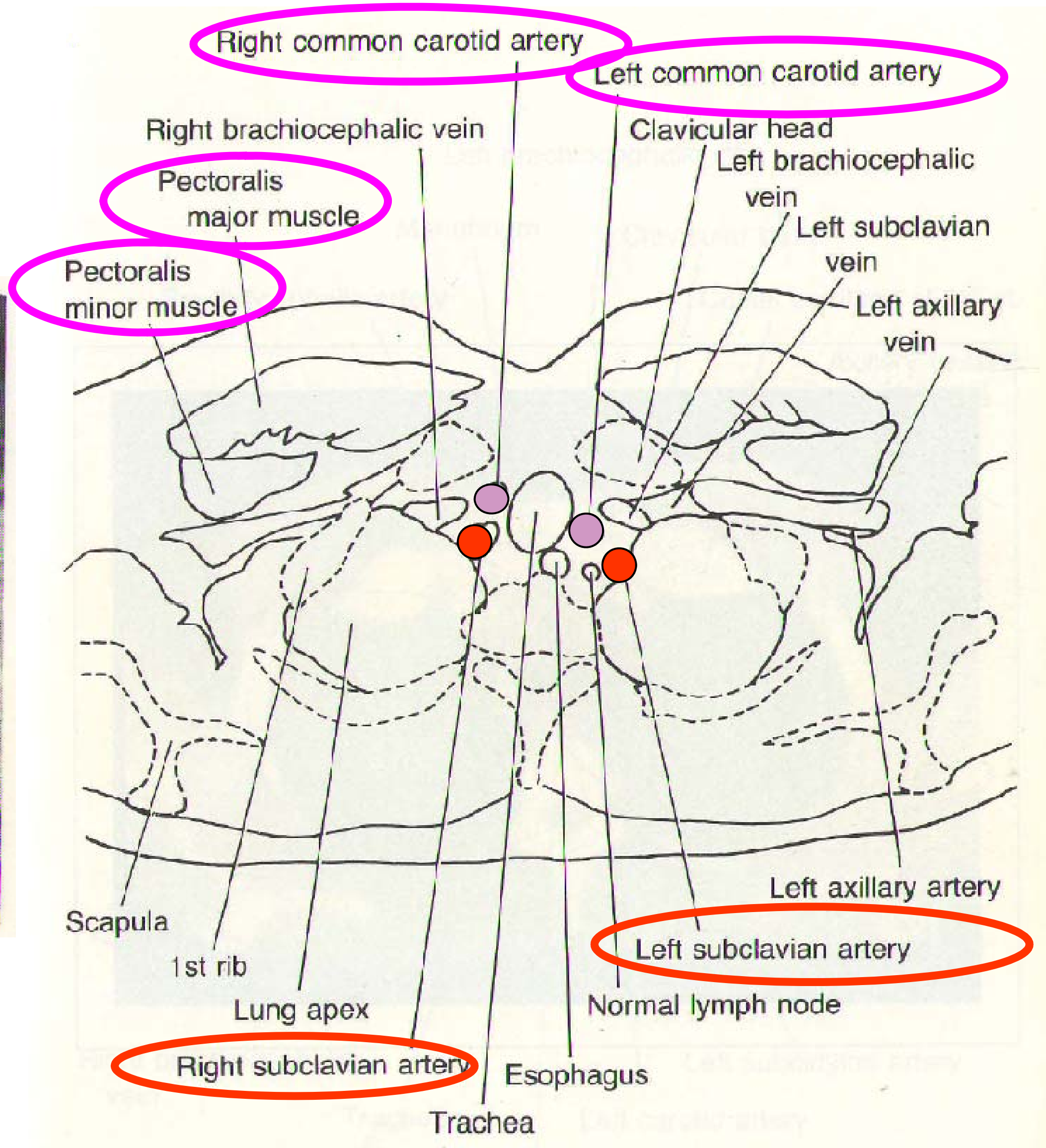





*Pocket Atlas of Normal CT Anatomy. JB Weinstein*

# BREAST ANATOMY






*Pocket Atlas of Normal CT Anatomy. JB Weinstein*

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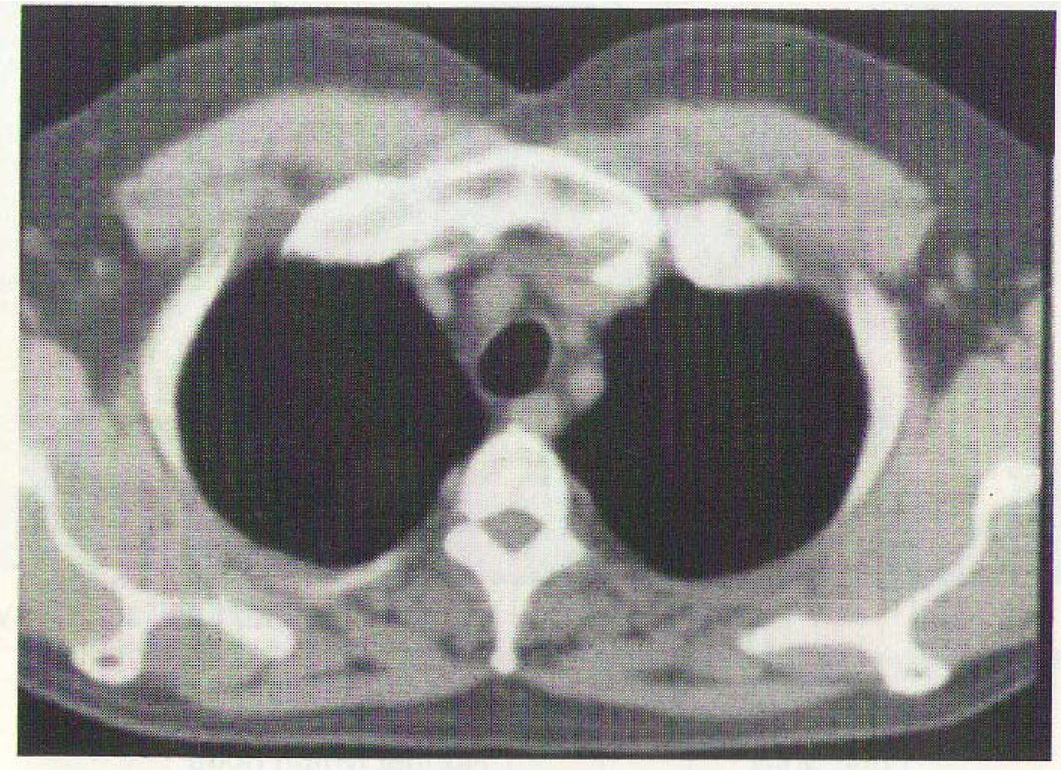
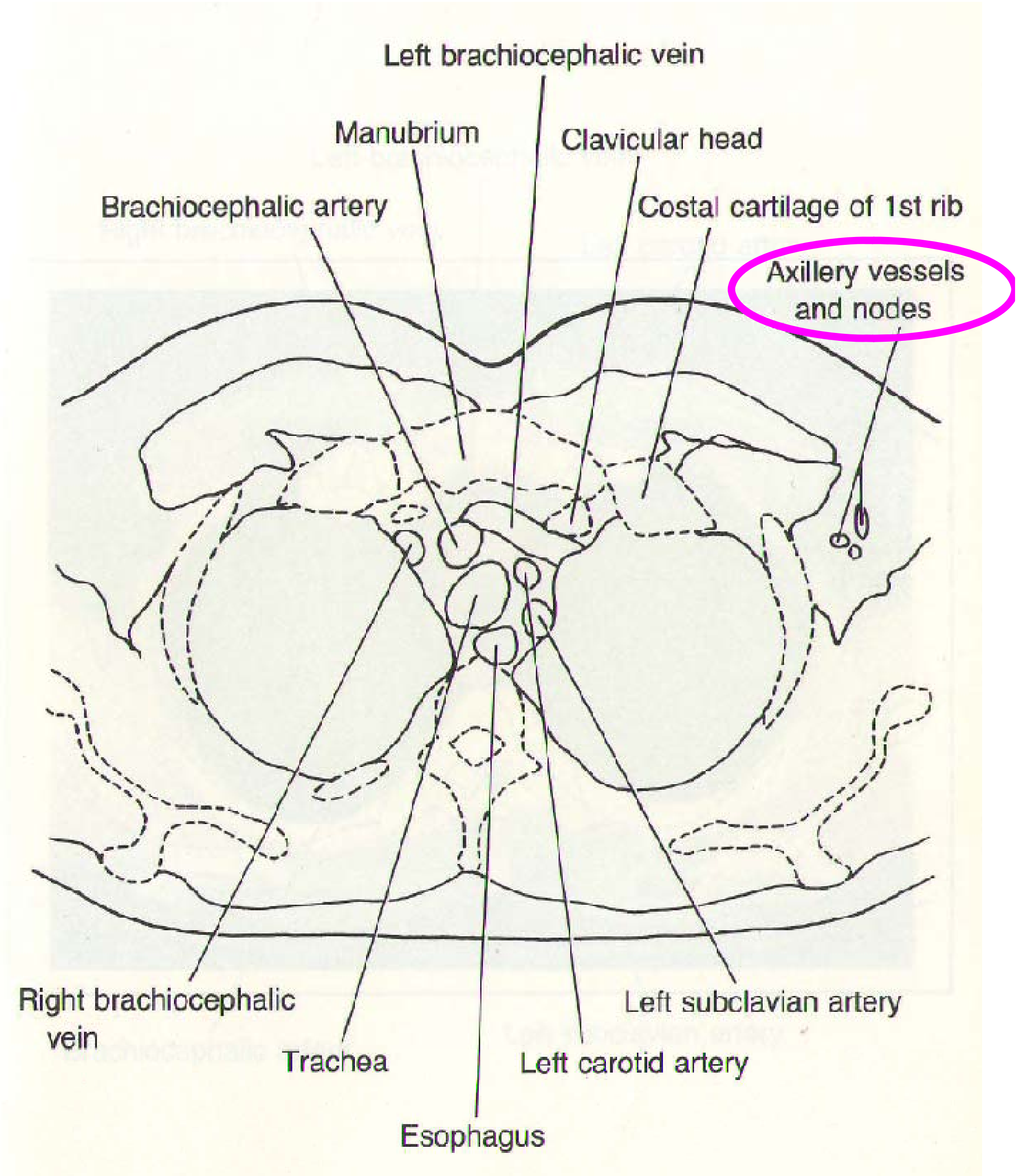
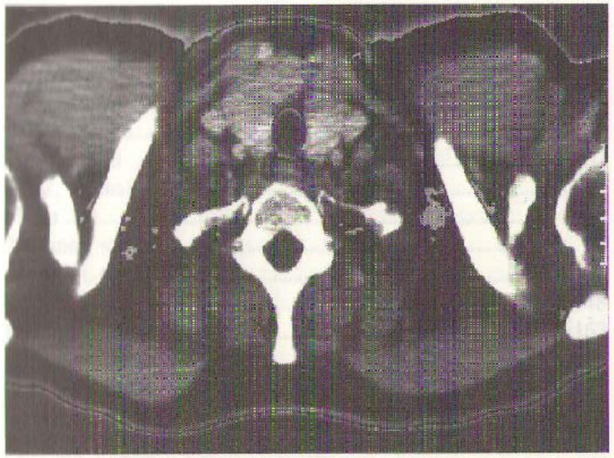


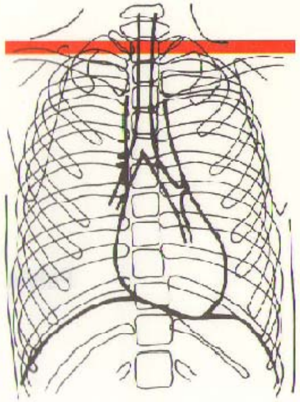


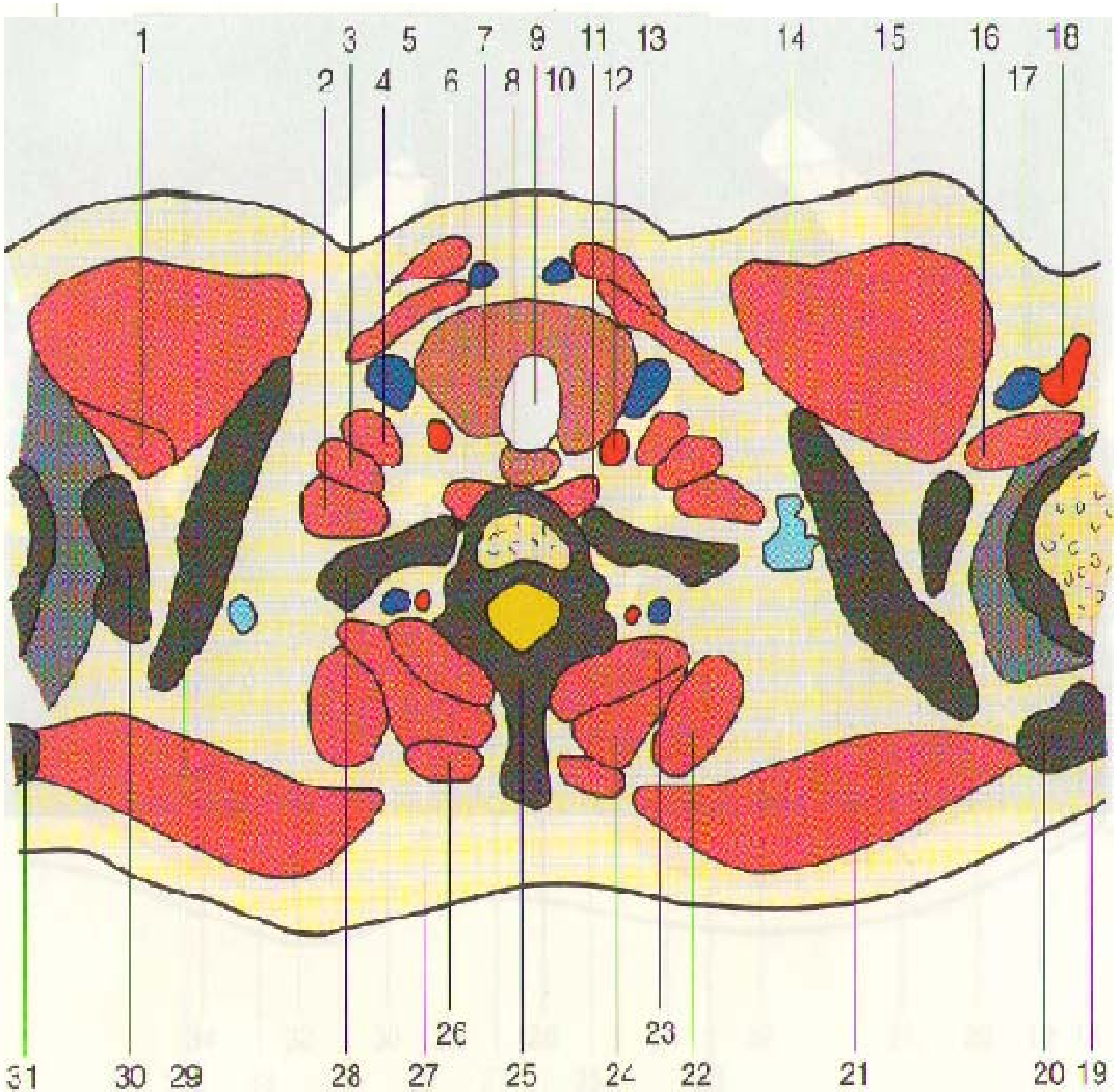

*Pocket Atlas of Normal CT Anatomy. JB Weinstein*

# BREAST ANATOMY



Thyroid gland (7)
Scalene muscles (2-4)
Common carotid artery (12)
Internal Jugular vein (13)



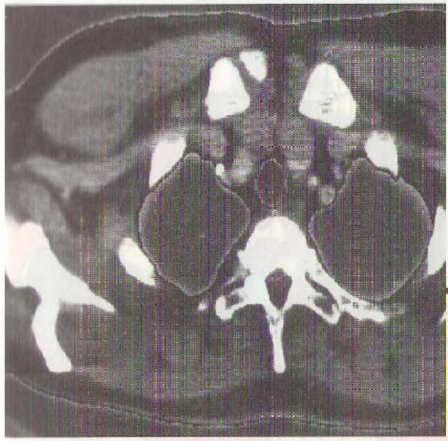


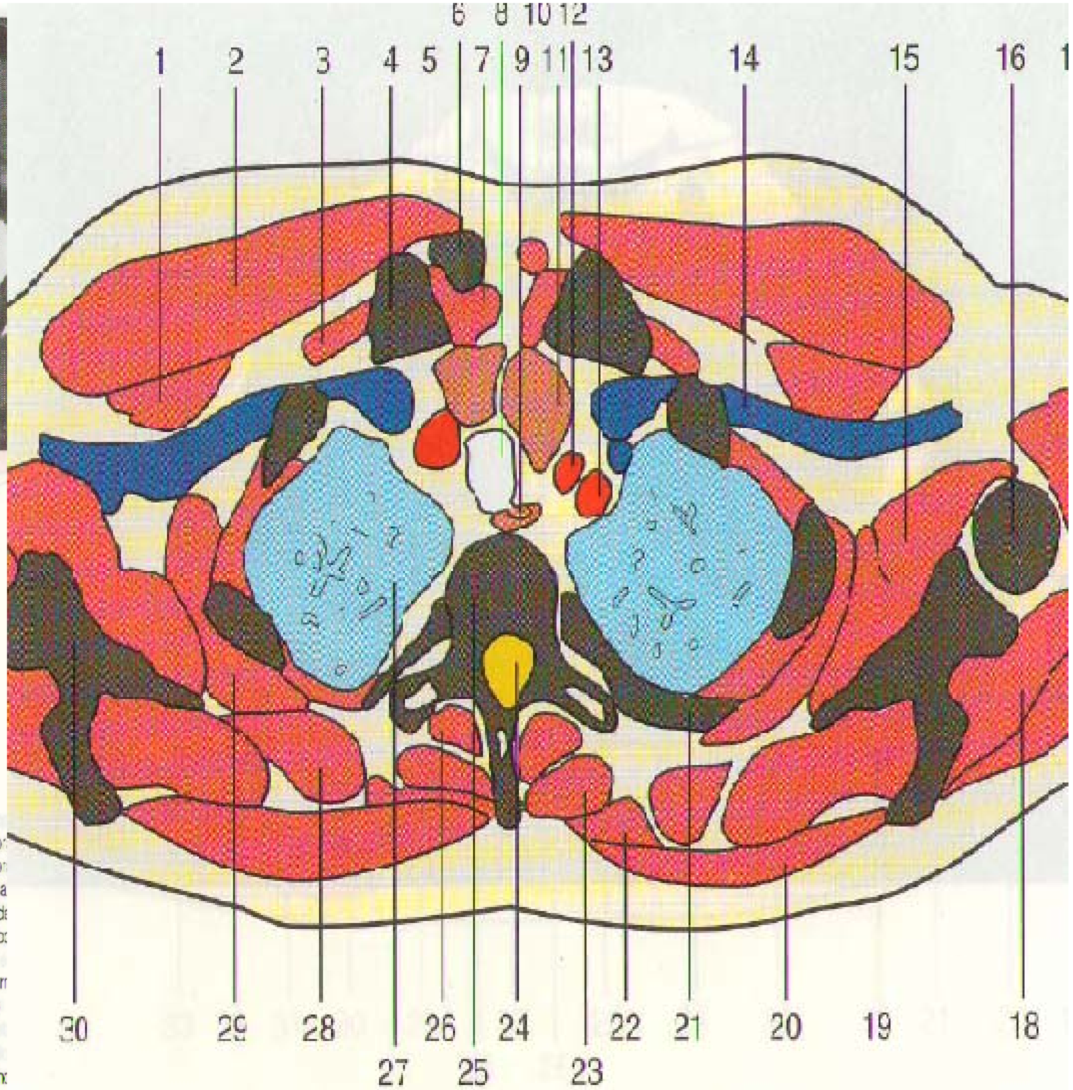

1. Músculo pectoral menor
2. Músculo escaleno posterior
3. Músculo escaleno medio
4. Músculo escaleno anterior
5. Músculo esternohioideo
6. Músculo esternocleidomastoideo
7. Glándula tiroides
8. Esófago
9. Tráquea
10. Vena yugular externa
11. Músculo largo del cuello
12. Arteria carótida común
13. Vena yugular interna
14. Vértice pulmonar
15. Músculo pectoral mayor
16. Músculo subescapular
17. Vena axilar
18. Arteria axilar
19. Húmero (cabeza)

35. Ganglios linfáticos paratraqueales
36. Ganglios linfáticos cervicales anteriores
37. Ganglios linfáticos retrofaríngeos

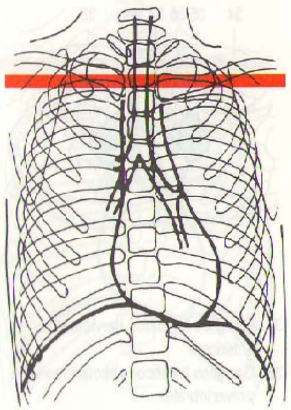
*Atlas CT Anatomy.*
*Torsten B. Möller*

# BREAST ANATOMY






Common carotid artery (12)
Subclavian artery (13)
Subclavian vein (14)
Subescapularis muscle (15)
Pectoralis major muscle (1) and minor (2)



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# BREAST ATLASES CAN HELP US!!!

**Special Report**

Rafael Martinez-Monge, MD
Patrick S. Fernandes, MD
Nilendu Gupta, PhD
Reinhard Gahbauer, MD

Index terms:
Computed tomography (CT), three-dimensional, 99.12917, 99.92
Lymphatic system, 99.12917, 99.92
Special reports
Treatment planning, 99.92

Radiology 1999; 211:815–828

Abbreviations:
CTV = clinical target volume
GTV = gross tumor volume
3D = three-dimensional

## Cross-sectional Nodal Atlas: A Tool for the Definition of Clinical Target Volumes in Three-dimensional Radiation Therapy Planning[1]

Virtual three-dimensional clinical target volume definition requires the identification of areas suspected of containing microscopic disease (frequently related to nodal stations) on a set of computed tomographic (CT) images, rather than the traditional approach based on anatomic landmarks. This atlas displays the clinically relevant nodal stations and their correlation with normal lymphatic pathways on a set of CT images.

**1999**

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 61, No. 2, pp. 358–364, 2005
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Printed in the USA. All rights reserved
0360-3016/05/$–see front matter

doi:10.1016/j.ijrobp.2004.06.006

**CLINICAL INVESTIGATION** **Breast**

## AXILLARY LYMPH NODE DOSE WITH TANGENTIAL BREAST IRRADIATION

Daniel R. Reed, D.O.,* Skyler Karen Lindsley, M.D.,* Gary N. Mann, M.D.,[†] Mary Austin-Seymour, M.D.,* Tammy Korssjoen, C.M.D.,* Benjamin O. Anderson, M.D.,[†] and Roger Moe, M.D.[†]

*Departments of Radiation Oncology and [†]Surgery, University of Washington Medical Center, Seattle, WA

**2000**

## Target Volume Definition and Target Conformal Irradiation Technique for Breast Cancer Patients

Ion Christian Kiricuta, Uwe Götz, Franz Schwab, Martin Fehn and Heinz Helmut Neumann

Acta Oncologica Vol. 39, No. 3, pp. 429–436, 2000

**2000**

**Radiation Oncology**

Chika N. Madu, BS
Douglas J. Quint, MD
Daniel P. Normolle, PhD
Robin B. Marsh, CMD
Edwin Y. Wang, MD
Lori J. Pierce, MD

Index terms:
Breast neoplasms, 00.32
Breast neoplasms, therapeutic radiology, 00.125
Lymphatic system, CT, 997.12912, 997.92
Lymphatic system, therapeutic radiology, 997.33, 997.92
Treatment planning

Published online before print 10.1148/radiol.2212010247
Radiology 2001; 221:333–339

## Definition of the Supraclavicular and Infraclavicular Nodes: Implications for Three-dimensional CT-based Conformal Radiation Therapy[1]

**PURPOSE:** To delineate with computed tomography (CT) the anatomic regions containing the supraclavicular (SCV) and infraclavicular (IFV) nodal groups, to define the course of the brachial plexus, to estimate the actual radiation dose received by

**2001**

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ELSEVIER

Radiotherapy and Oncology 71 (2004) 287–295

RADIOTHERAPY & ONCOLOGY

www.elsevier.com/locate/radonline

Loco-regional conformal radiotherapy of the breast: delineation of the regional lymph node clinical target volumes in treatment position

Ivessa M. Dijkema[a,*], Pieter Hofman[a], Cornelis P.J. Raaijmakers[a], Jan J. Lagendijk[a], Jan J. Battermann[a], Berend Hillen[b]

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[b]Department of Functional Anatomy, University Medical Centre Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

Received 22 January 2003; received in revised form 14 February 2004; accepted 26 February 2004

2004

SIMULACIÓN VIRTUAL

Y

RADIOTERAPIA CONFORMADA 3D

Guía práctica para la delimitación de volúmenes

Hospital Ramón y Cajal

CAPITULO 10

**TUMORES DE MAMA**

Sonsoles Sancho, Ángel Montero, Sofía Córdoba

*The British Journal of Radiology, 83* (2010), 683–686

Simplified rules for everyday delineation of lymph node areas for breast cancer radiotherapy

[1]Y M KIROVA, MD, [1]P CASTRO PENA, MD, [1]R DENDALE, MD, [2]V SERVOIS, MD, [1]M A BOLLET, MD, [1]N FOURNIER-BIDOZ, PhD, [1]F CAMPANA, MD and [1]A FOURQUET, MD

2010

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Original article

A simplified CT-based definition of the supraclavicular and infraclavicular nodal volumes in breast cancer

*Règles de délinéation simplifiées des volumes ganglionnaires sus- et sous-claviculaires dans le traitement des cancers du sein*

I. Atean[a,*,b], Y. Pointreau[a,c], L. Ouldamer[c,d], C. Monghal[e], A. Bougnoux[a], G. Bera[a], I. Barillot[a,c]

Cancer/Radiothérapie 17 (2013) 39–43

***Nodes***

**2013**

*Acta Oncologica*, 2013; 52: 703–710

informa healthcare

ORIGINAL ARTICLE: ACTA ONCOLOGICA JUBILEE ARTICLE

**Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer: National guidelines and contouring atlas by the Danish Breast Cancer Cooperative Group**

METTE H. NIELSEN[1], MARTIN BERG[2], ANDERS N. PEDERSEN[3], KAREN ANDERSEN[4],

***Breast and Nodes***

**DBCG**

**2013**

http://www.dbcg.dk/PDF%20Filer/DBCG_CT_contouring_Atlas.pdf

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https://www.abro-bvro.be/index.php?option=com_attachments&task=download&id=105

Radiotherapy and Oncology 114 (2015) 11–16

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Guidelines

## Vessel based delineation guidelines for the elective lymph node regions in breast cancer radiation therapy – PROCAB guidelines

Karolien Verhoeven[a,*], Caroline Weltens[a], Vincent Remouchamps[b], Khalil Mahjoubi[b], Liv Veldeman[c], Benoit Lengele[d], Eszter Hortobagyi[a], Carine Kirkove[d]

[a] University Hospitals Leuven/KU Leuven; [b] Clinique Sainte Elisabeth (AMPR), Namur; [c] Ghent University Hospital; and [d] Catholic University of Louvain, Brussels, Belgium

**Nodes**

**PROCAB**

**2015**

**Nodes** **2015**

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation

## Delineation of Supraclavicular Target Volumes in Breast Cancer Radiation Therapy

Lindsay C. Brown, MD,* Felix E. Diehn, MD,† Judy C. Boughey, MD,‡ Stephanie K. Childs, MD,* Sean S. Park, MD, PhD,* Elizabeth S. Yan, MD,* Ivy A. Petersen, MD,* and Robert W. Mutter, MD*

Departments of *Radiation Oncology, †Radiology, and ‡Surgery, Mayo Clinic, Rochester, Minnesota

Received Sep 8, 2014, and in revised form Jan 6, 2015. Accepted for publication Feb 12, 2015.

## Supraclavicular and infraclavicular lymph node delineation in breast cancer patients: a proposal deriving from a comparative study

Francesca Cucciarelli[1], Youlia M. Kirova[2], Isabella Palumbo[3], Cynthia Aristei[3]

Tumori 2015; 00(00): 000-000

DOI: 10.5301/tj.5000330

ORIGINAL RESEARCH ARTICLE

**2015**

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**Breast and Nodes**

2015

Radiotherapy and Oncology 114 (2015) 3–10

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

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]

2016

Radiotherapy and Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Letter to the Editor

**ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1**[☆]

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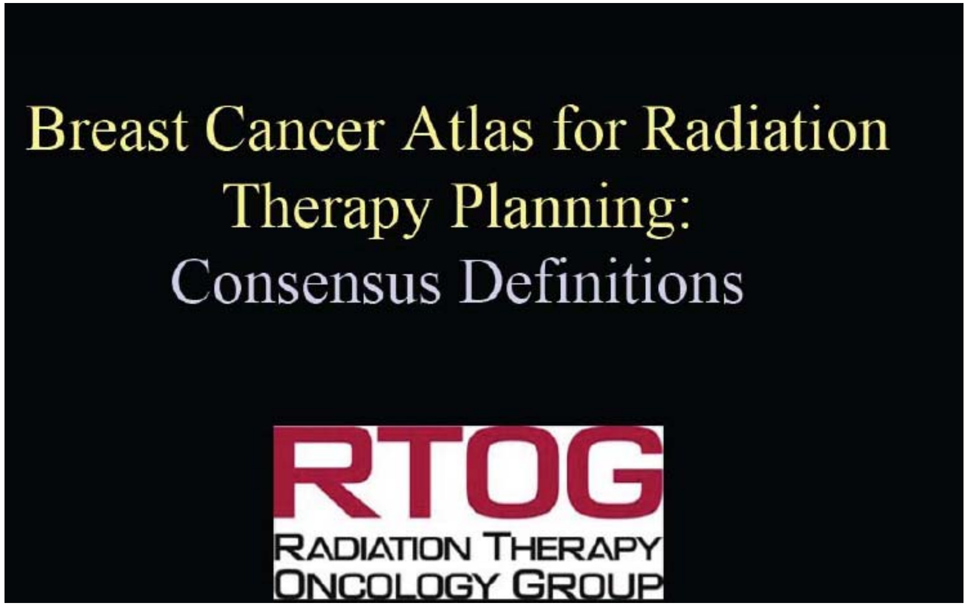
**RTOG**

**2015**




***Breast and Nodes***


International Journal of Radiation Oncology biology • physics

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BRIEF REPORT

## RTOG Chest Wall Contouring Guidelines for Post-Mastectomy Radiation Therapy: Is It Evidence-Based?

CrossMark


John A. Vargo, MD, and Sushil Beriwal, MD

*Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania*



Received Aug 12, 2014, and in revised form Feb 2, 2015. Accepted for publication Mar 2, 2015.


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# Volumes can be treated with RT

- Whole breast. Boost to lumpectomy. Partial Breast irradiation
- Chest wall
- Regional Nodes:
  - L4 (SC), L3, L2, L1
  - Internal Mammary (IM)
  - Rotter Nodes

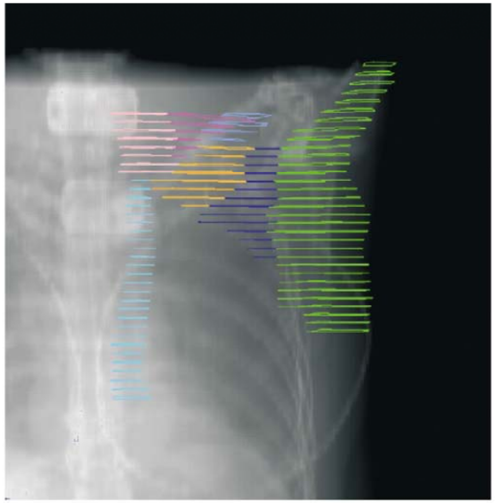
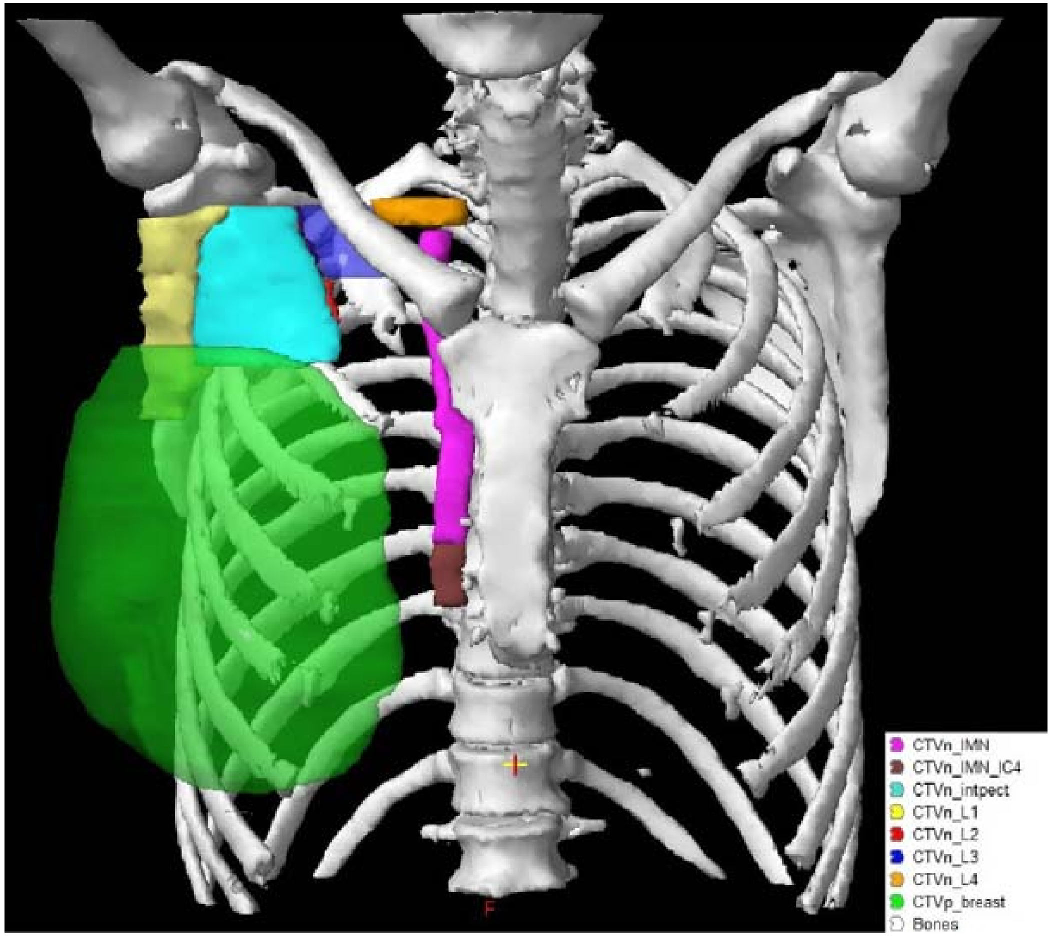


Fig. 3. Digitally reconstructed radiograph (DRR) of CT-images with regional LN CTVs (except for the interpectoral LN CTV) (CT-images from same patient as in Fig. 2).

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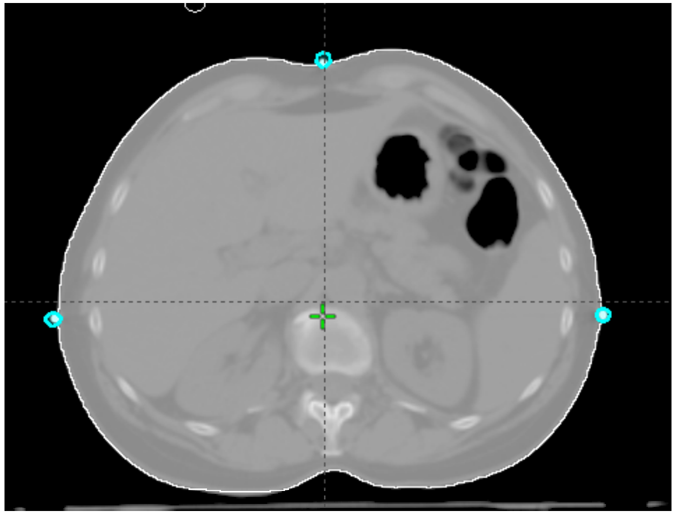

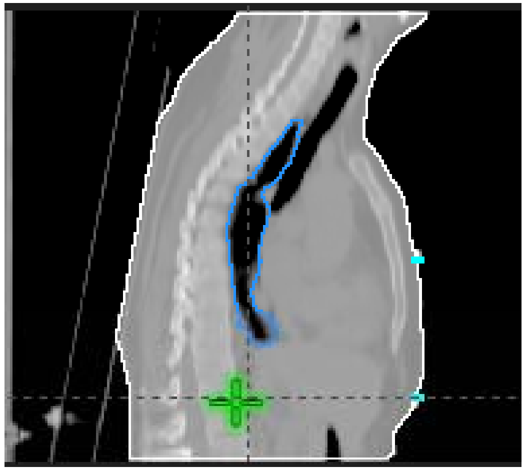

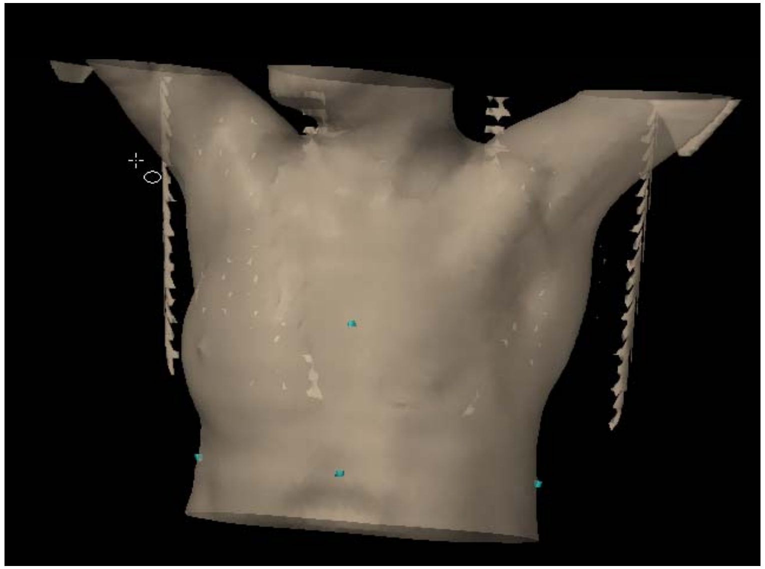

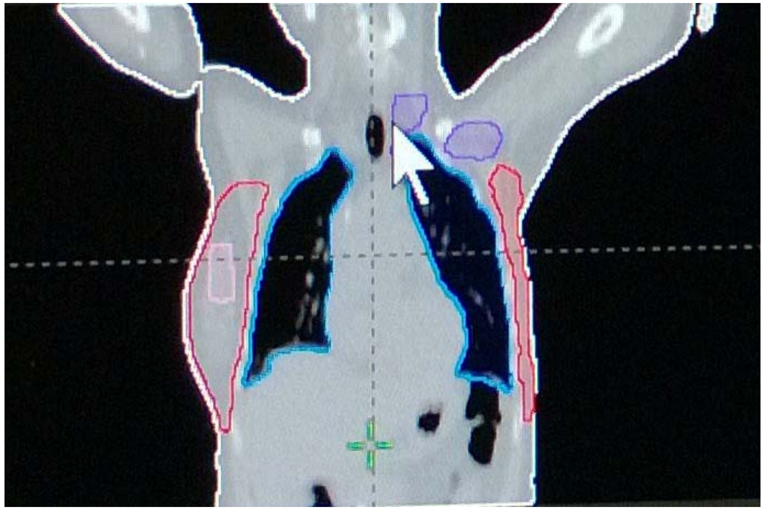

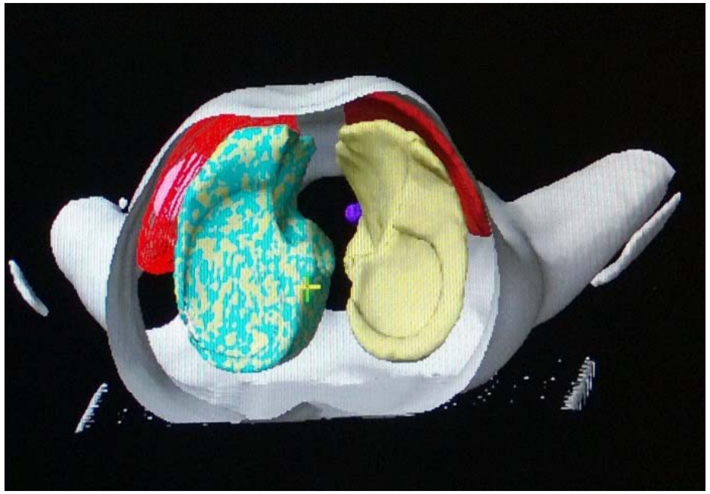

- Introduction

- **Indications and CTV:**
  - **Whole Breast**
  - Boost
  - Chest wall
  - Regional nodes
    - L4, L3, L2, L1, IM, Rotter

- Organs at risk and constraints

- Margins CTV → PTV      OAR → PRV

- Conclusions

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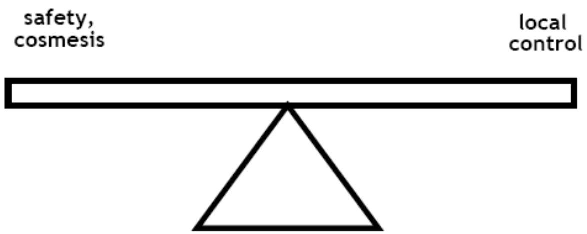
# BREAST CTV: INDICATIONS

- RT after breast conserving surgery is indicated for "all" cases

- Conserving surgery and RT is equivalent to a mastectomy in terms of DFS in stages I-II

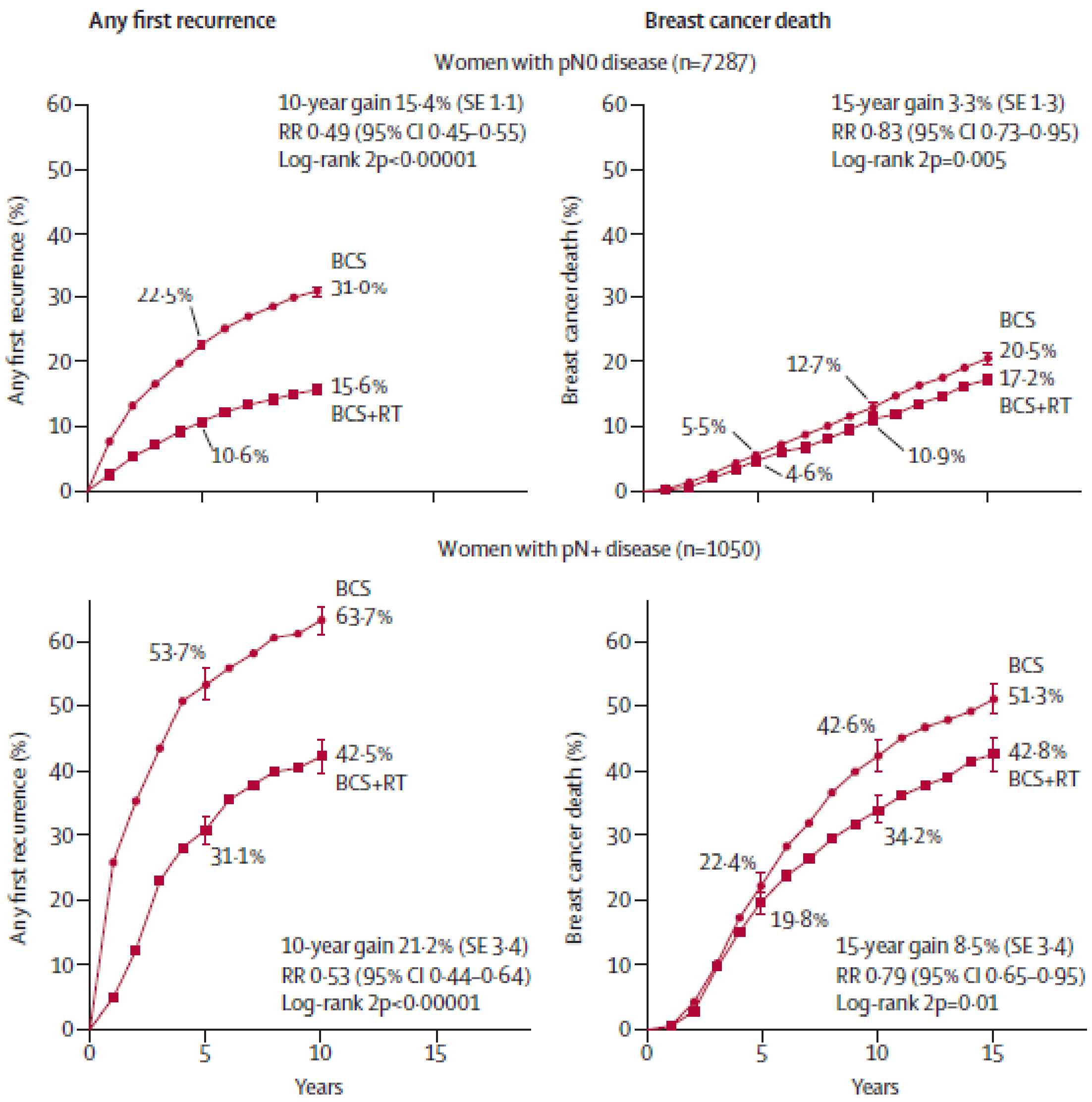
- The aim is:
  - ↓ local relapse
  - ↑ DFS
  - Minimum side effects (lung, heart, skin)
  - Good cosmetic results



# Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials

*Lancet* 2011; 378: 1707–16

*Early Breast Cancer Trialists' Collaborative Group (EBCTCG)**




Reduces **recurrence** 31% to 15.4% (N- (7287 pts)) and 63.7% to 42.5% (N+ (1050 pts))

- 10 year gain **15,7% (N-) and 21,2% (N+)**

Reduces breast cancer **mortality** of 20.5% to 17.2% (N-) and 51.3% to 42.8% (N+)

- 15 year gain **3.3% (N-) and 8.5% (N+)**

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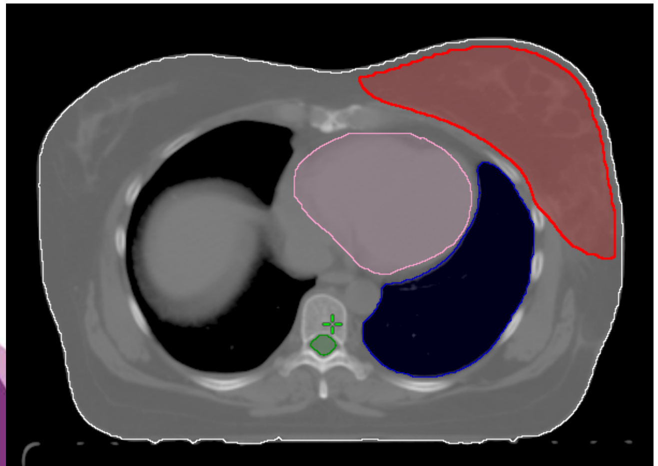
# BREAST CTV

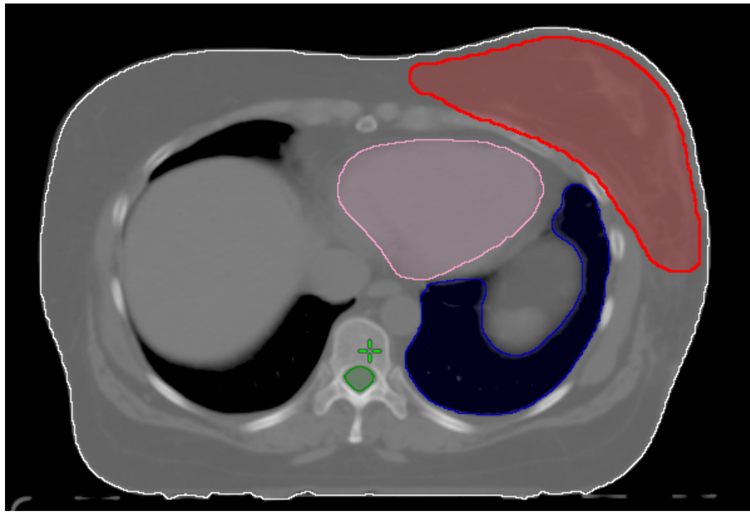
After conserving surgery, CTV of the entire breast should be considered (unless the patient is a candidate for partial breast irradiation)

It may be useful to mark the scar

It may be useful to mark lateral, lower and upper limits



Volume between the pectoralis major and 5 mm below the skin



*Cranial*

Clinical Reference + Second rib insertion[a]

RTOG

Residual breast CTVp_breast

Upper border of palpable/ visible breast tissue: maximally up to the inferior edge of the sterno-clavicular joint

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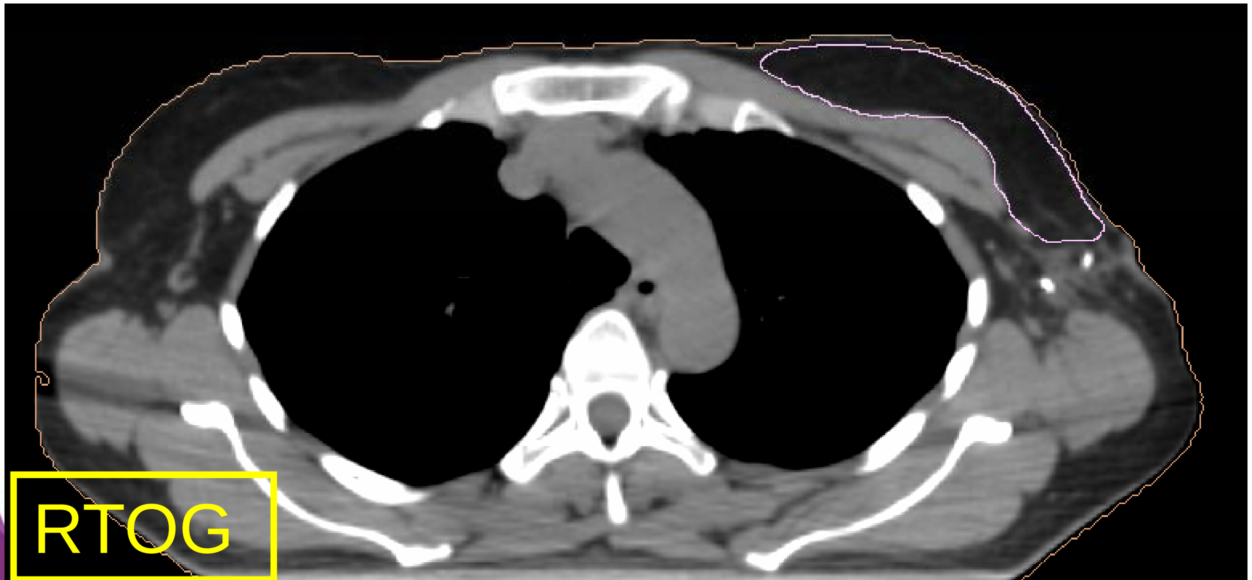
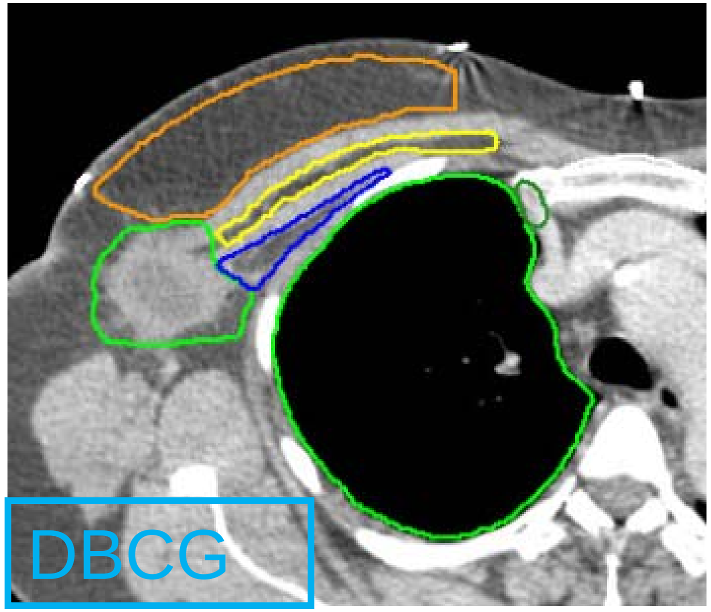
Maximal to the caudal edge of the sterno-clavicular-junction

DBCG

The cranial boundary is highly variable and depends on the size of the breast and its ptosis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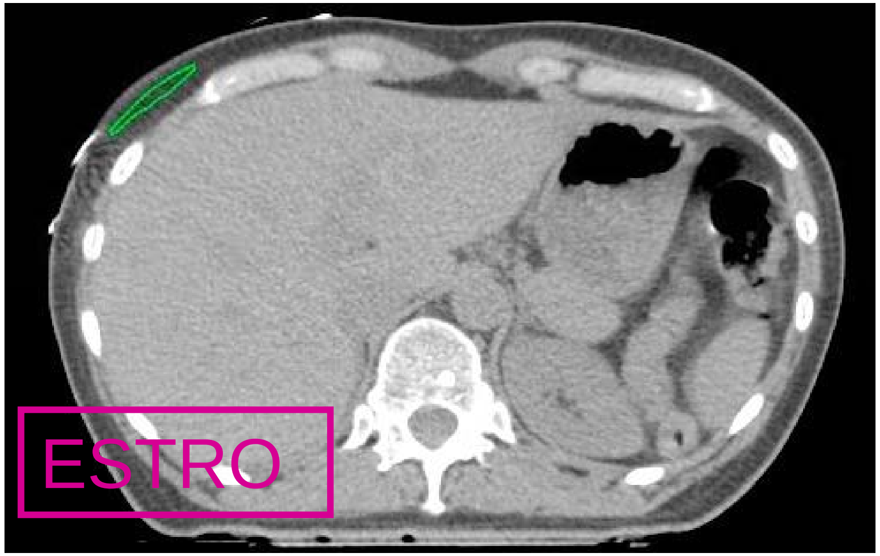
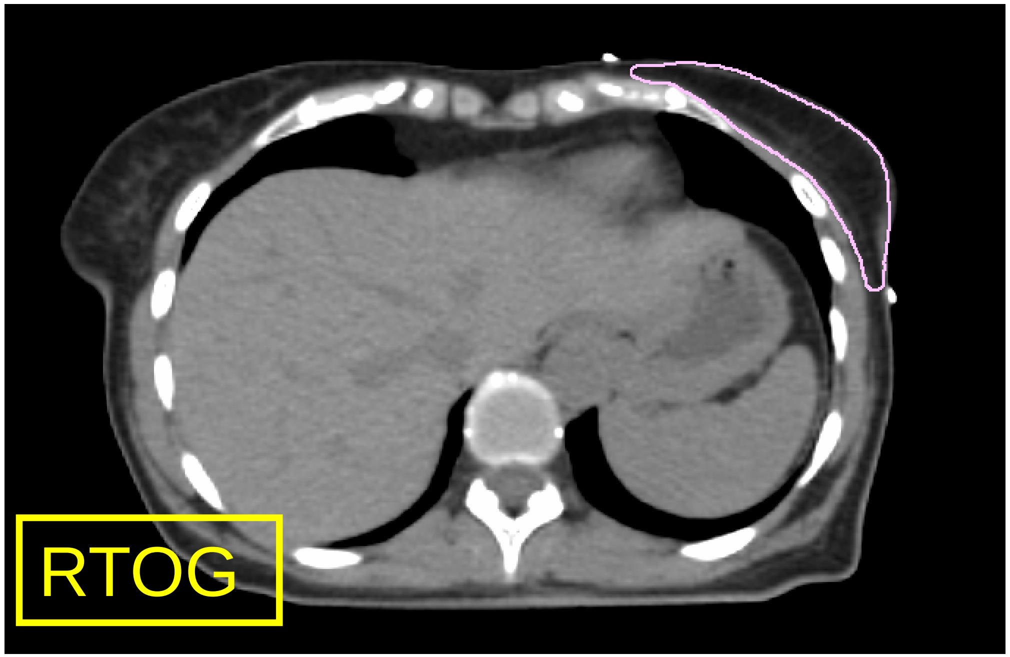
*Caudal*

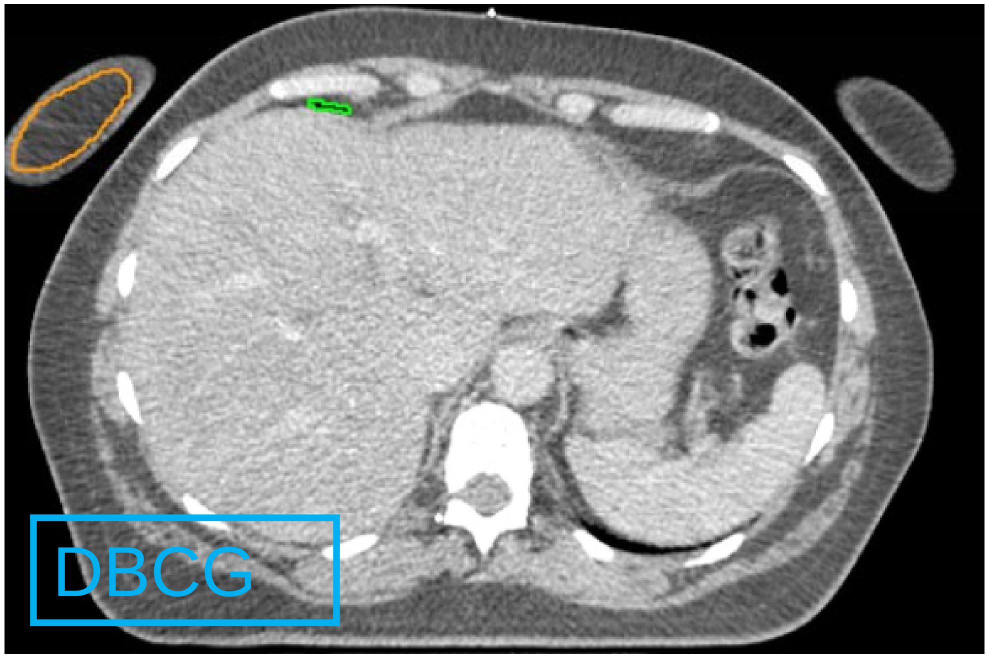
Clinical reference + loss of CT apparent breast

Most caudal CT slice with visible breast

The intermammary sulcus



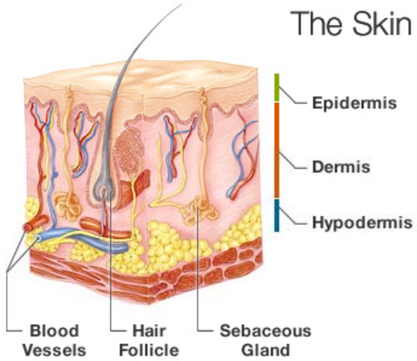



Anterior

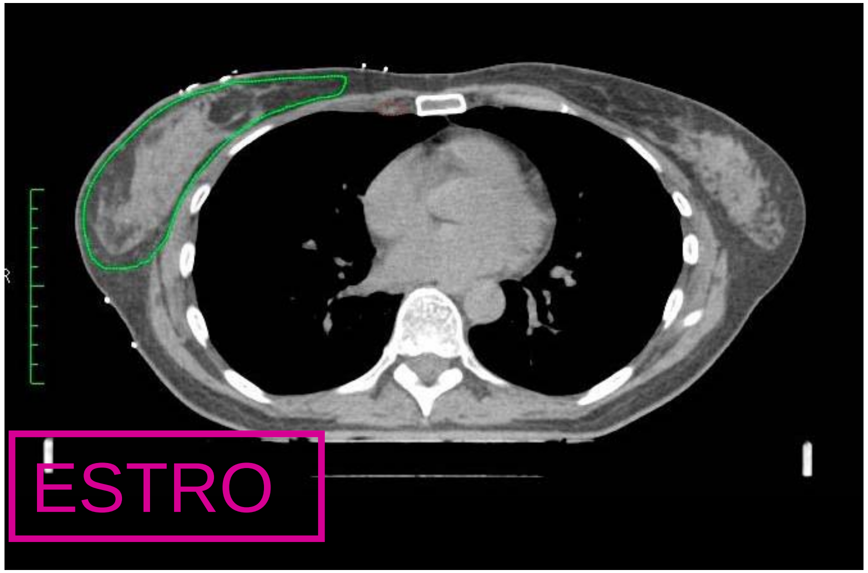
Skin

5 mm under skin surface

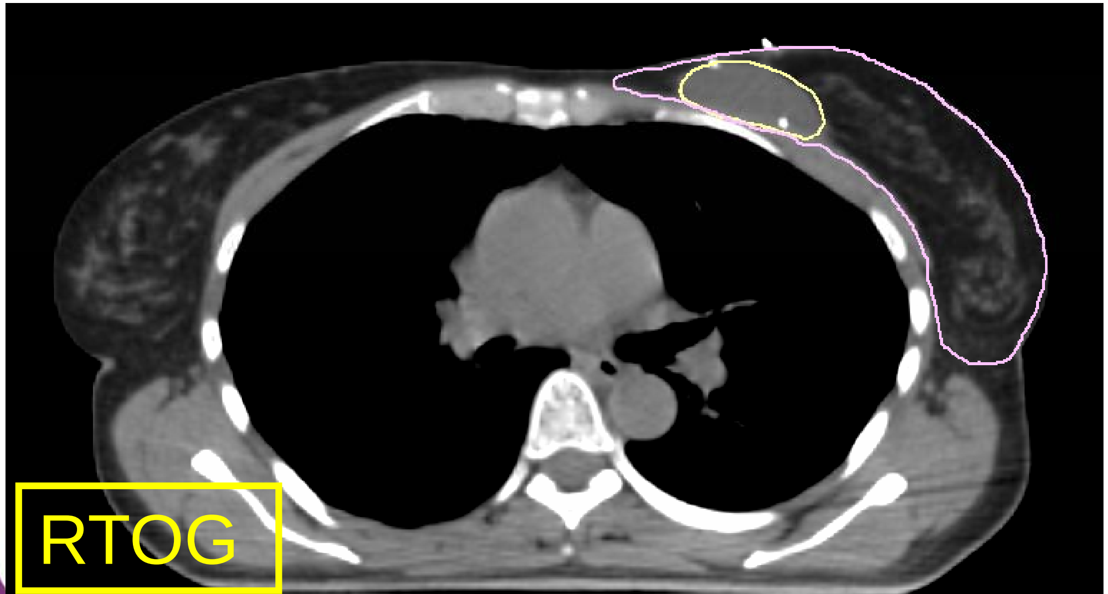
5 mm below the skin

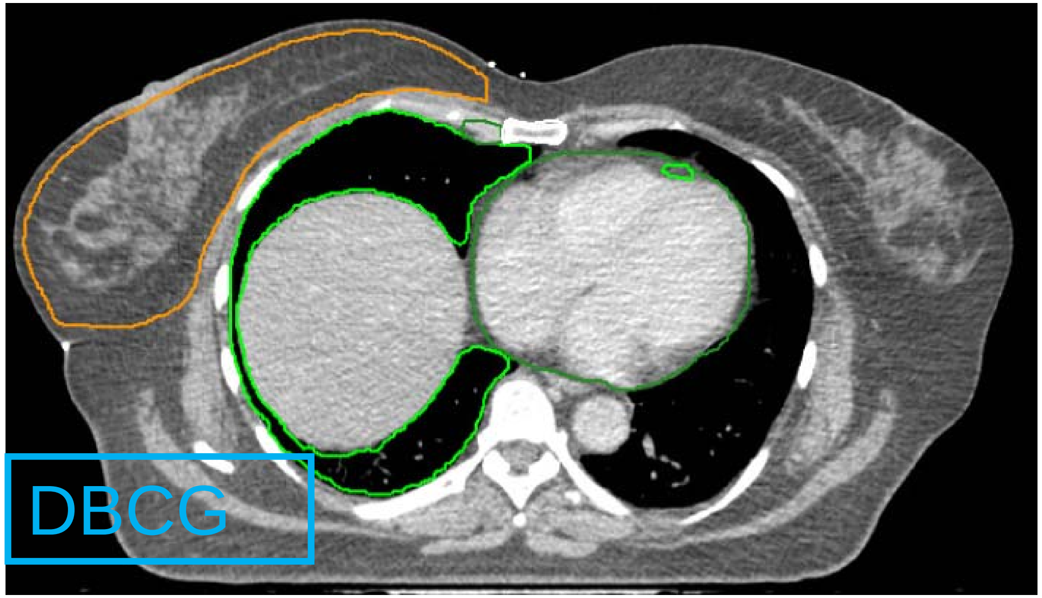



Creating an automatic internal contour can be helpful




RTOG: Skin
ESTRO, DBCG: 5 mm under the skin

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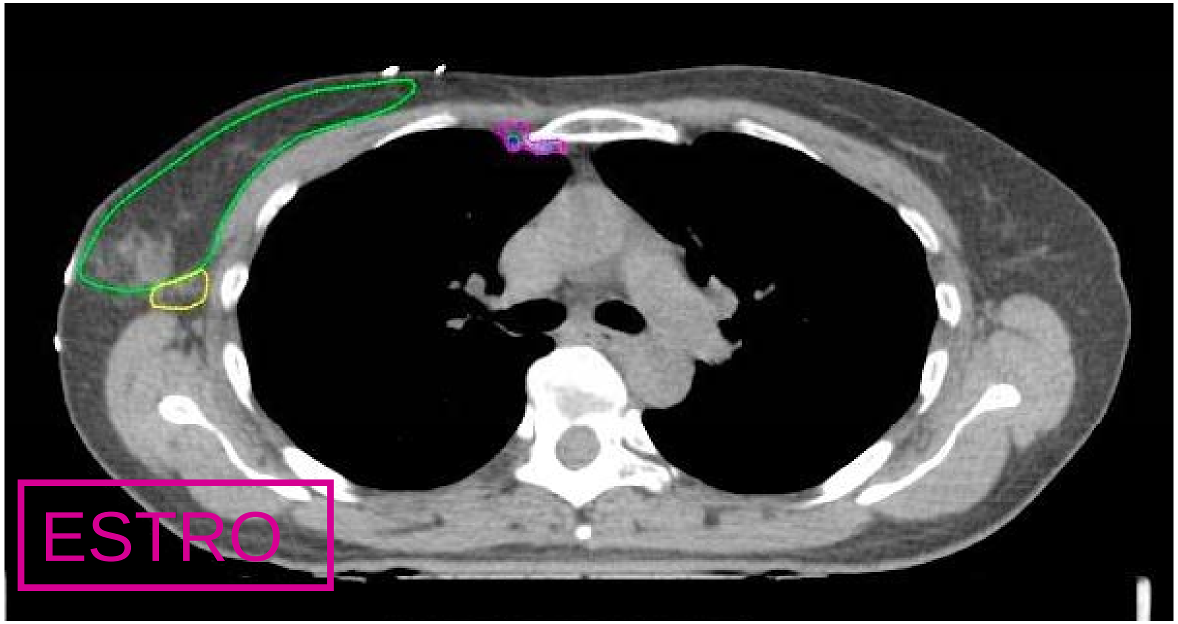
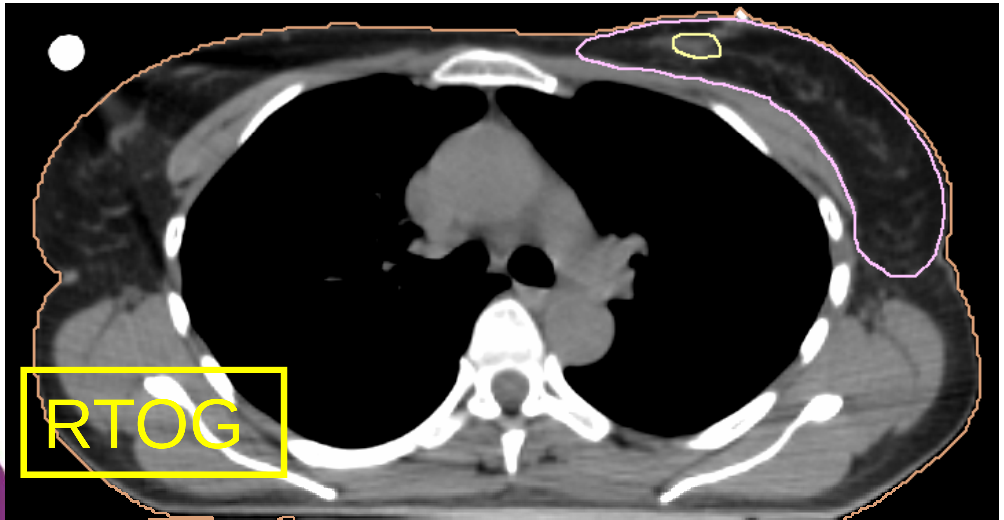
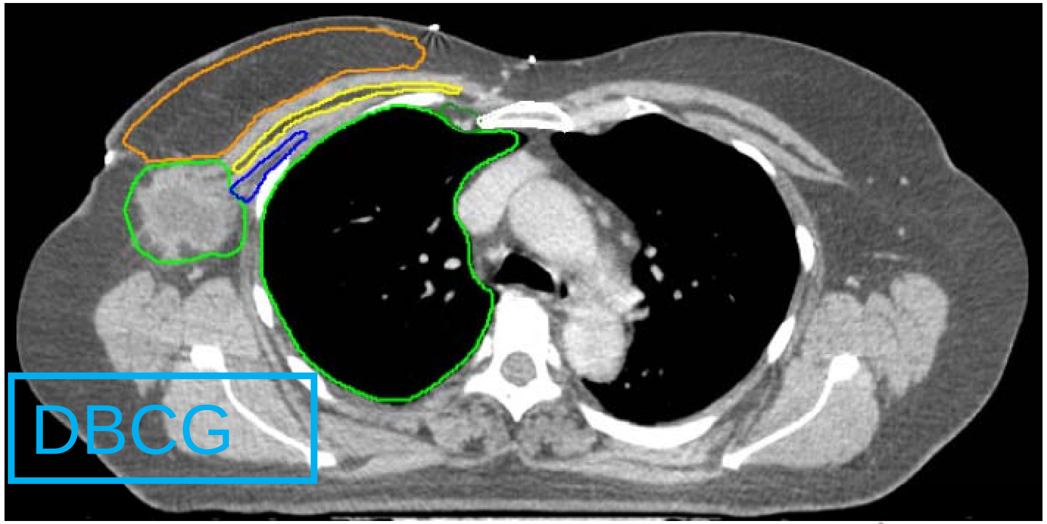
| *Posterior* | |
|---|---|
| Excludes pectoralis muscles, chestwall muscles, ribs | Major pectoral muscle or costae and intercostal muscles where no muscle |

M. pectoralis major

Some authors recommend including part of the pectoralis major because sometimes there are deep extensions of the breast parenchyma that penetrate the surface portion of it



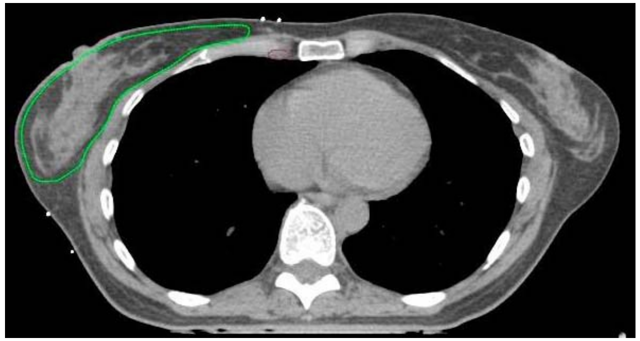
**Lateral**

Clinical Reference + mid axillary line typically, excludes latissimus (Lat.) dorsi m. b

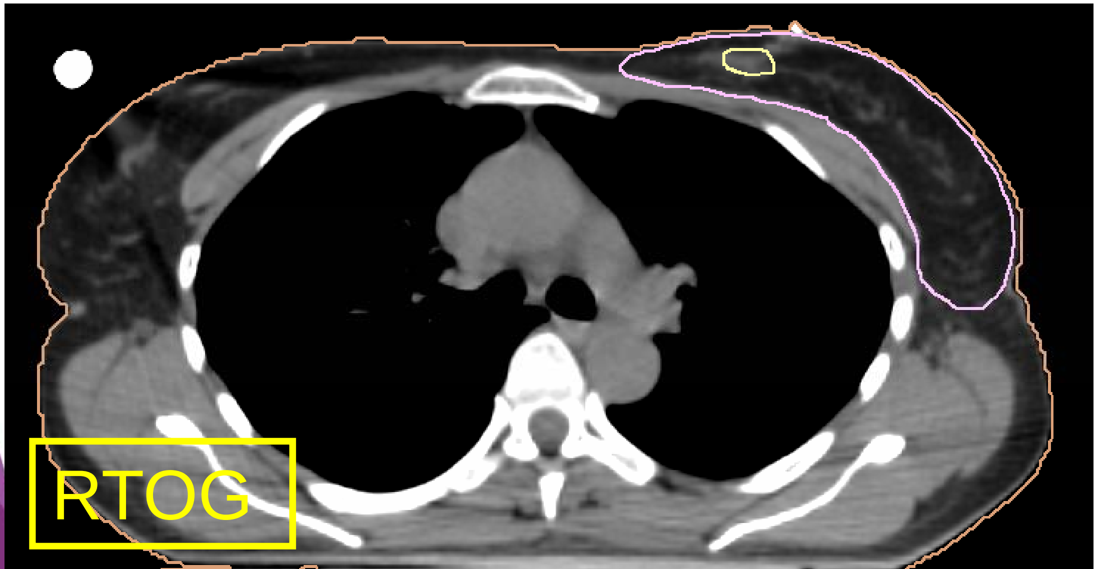
Lateral breast fold; anterior to the lateral thoracic artery

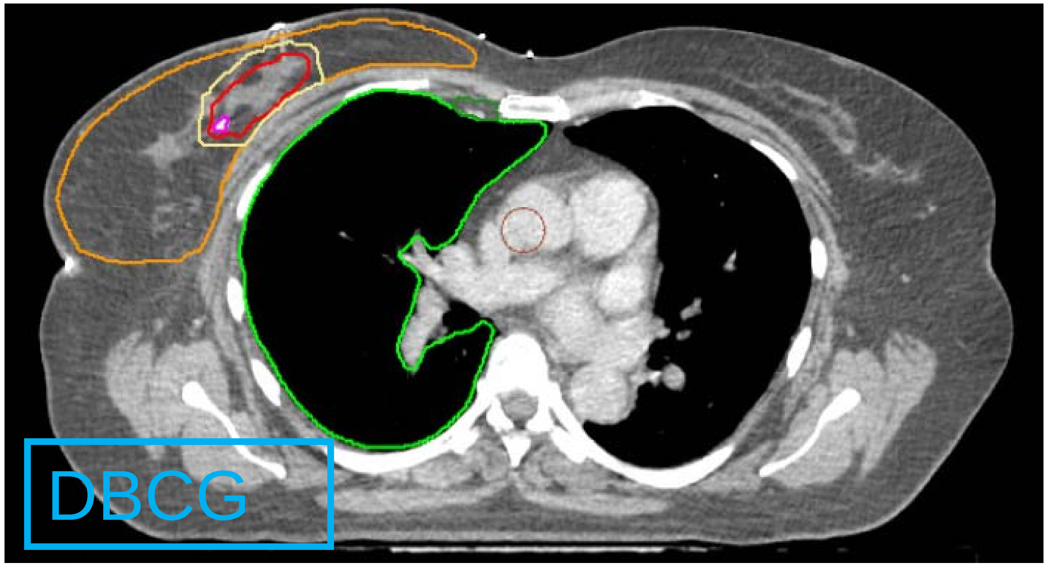
The axillary vessels (branches from the lateral thoracic vessel)

The lateral boundary is highly variable and it depends on the size of the breast and its ptosis



ESTRO



Letter to the Editor

Radiotherapy and Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

# ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1 ☆


## Lateral border of CTVp_breast

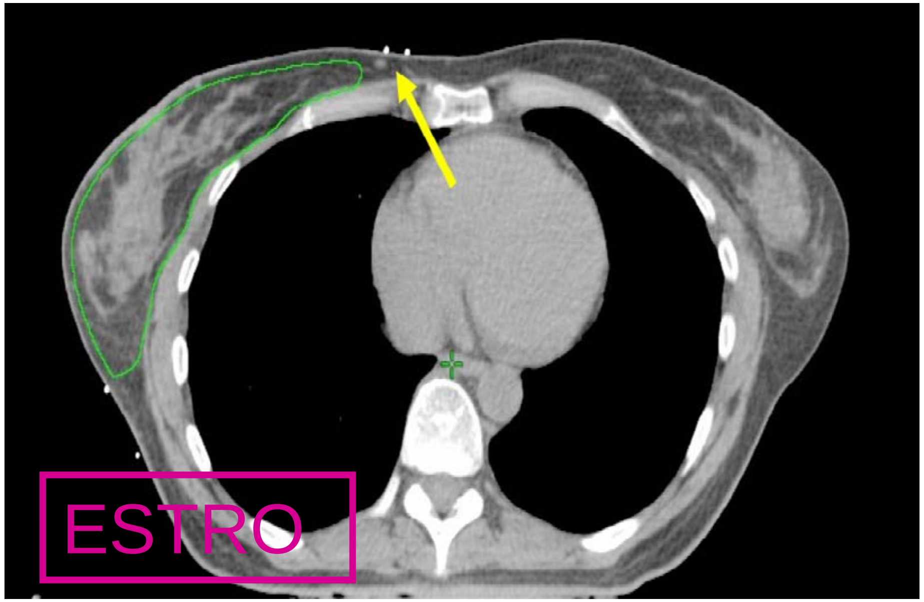
The thoracic vessels at the lateral border of the breast can be a helpful guide to define the lateral border of the CTVp_breast. However, it is not always necessary to delineate the CTVp_breast that far lateral. In patients with clearly visible glandular breast tissue, it is recommended to include the glandular tissue and not necessarily extend the volume lateral upto the thoracic vessels (Fig. 1C).

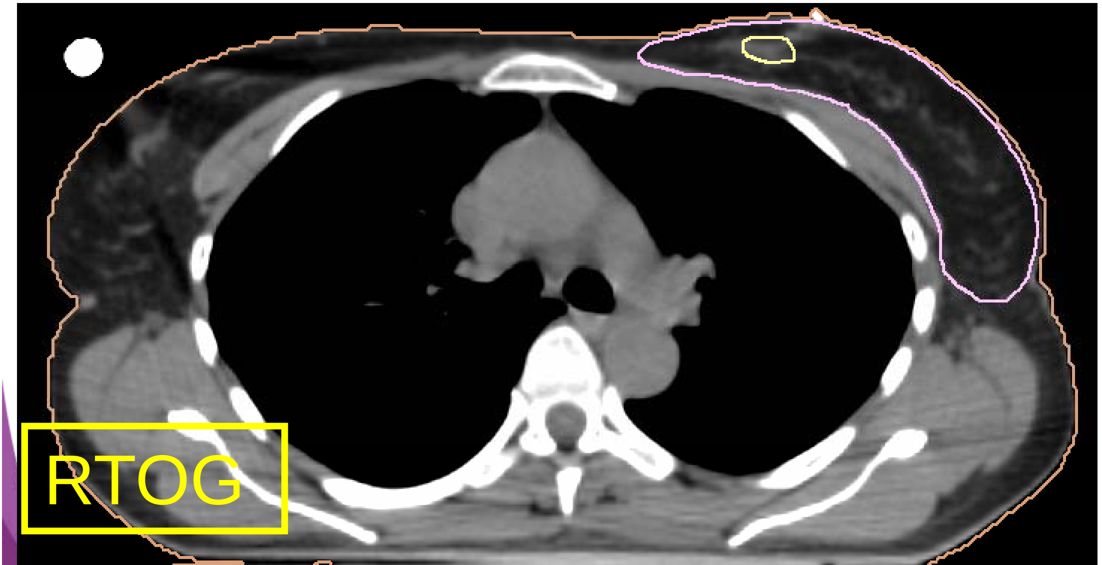
*Medial*

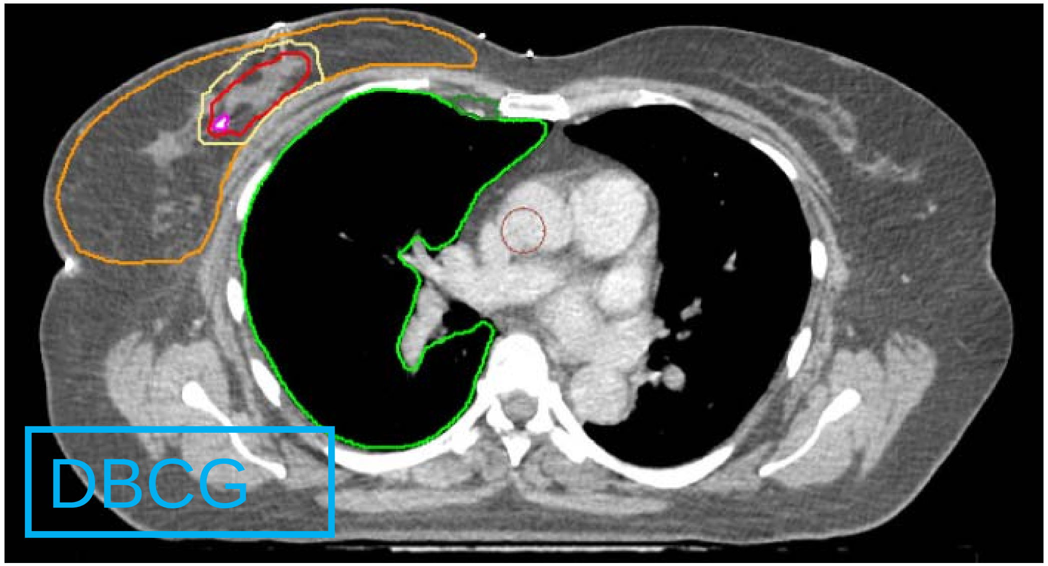
Sternal-rib junction [c]

Lateral to the medial perforating mammarian vessels; maximally to the edge of the sternal bone

Maximal to the ipsilateral edge of sternum



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- Margins CTV → PTV    OAR → PRV
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# BOOST CTV: INDICATIONS

Boost treatment to the tumour bed reduces local relapse at all ages, but it has no impact on the OS

2 randomized trials confirm this:

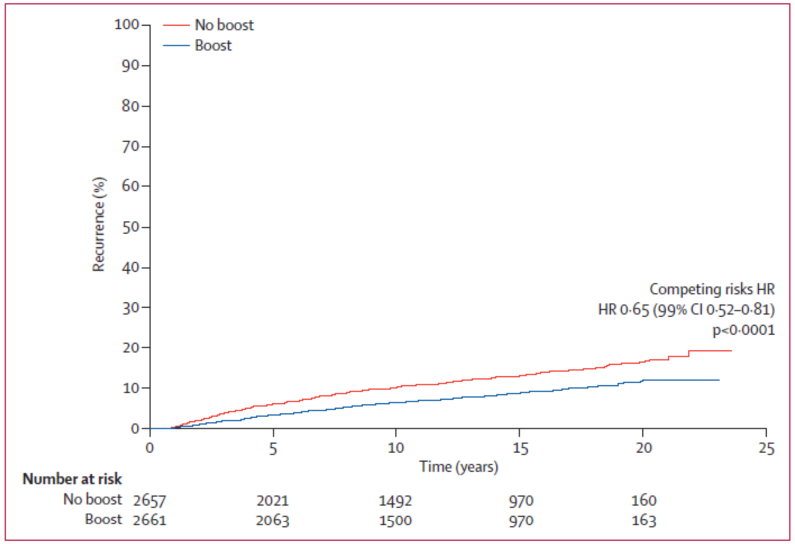
*Lyon trial*
*EORTC trial*

# ± Boost – EORTC Trial

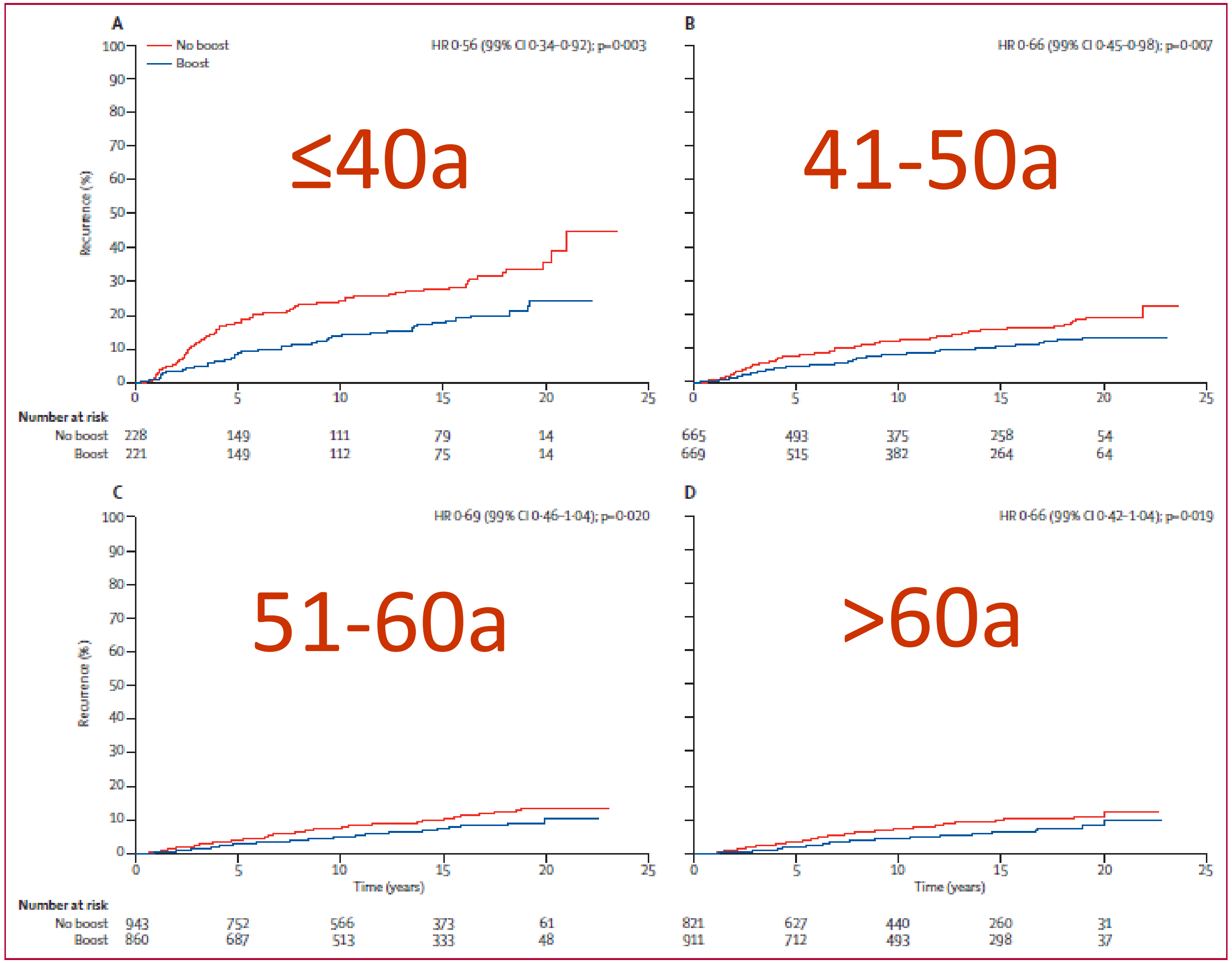
## *Bartelink H, Lancet Oncol 2015; 16:47-56*

## *Follow up: 20y*

## N = 4.318




| Age | Gain (LR) |
|---|---|
| **≤40** | **11.6%** |
| 41-50 | 5.9% |
| 51-60 | 2.9% |
| >60 | 3% |

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# BOOST CTV

- It might be useful to mark the scar
- Surgical clips
- Imaging studies before surgery (Mx, MRI ..)
- Seroma or surgical clips should be included when they are present
- Oncoplastic surgery??? (Surgical clips!)

# BOOST CTV

USE OF PRE-OPERATIVE CT IN COMBINATION WITH SURGICAL CLIPS IMPROVES LOCALIZATION OF THE TUMOUR BED

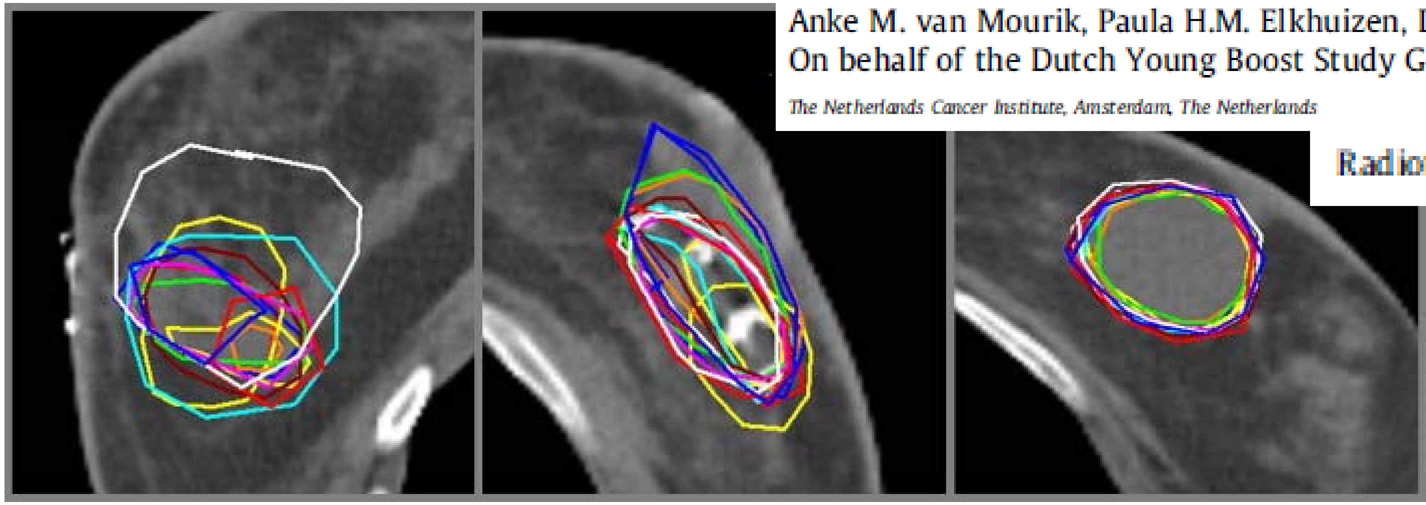
Good communication is ESSENTIAL between radiation oncologists, surgeons, pathologists and radiologists and could help to reduce interobserver differences

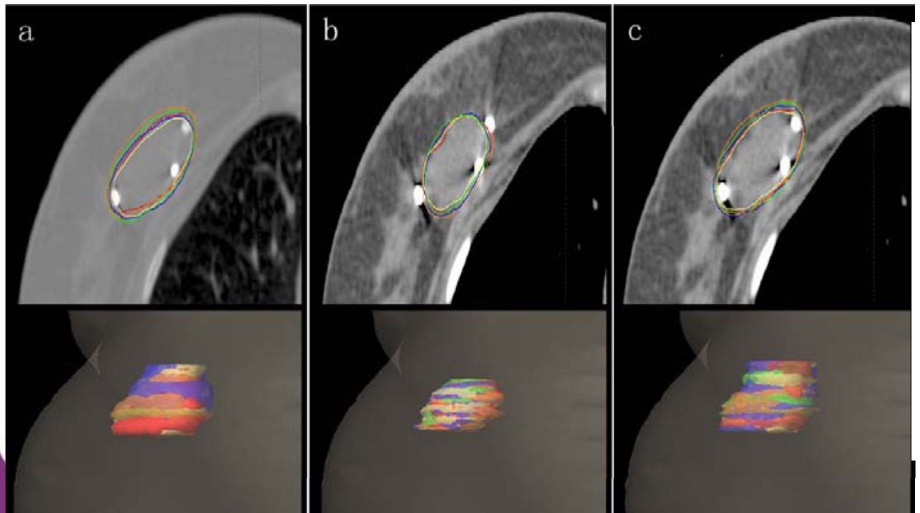
# BOOST CTV

Multiinstitutional study on target volume delineation variation in breast radiotherapy in the presence of guidelines

Anke M. van Mourik, Paula H.M. Elkhuizen, Danny Minkema, Joop C. Duppen,
On behalf of the Dutch Young Boost Study Group[1], Corine van Vliet-Vroegindeweij *
The Netherlands Cancer Institute, Amsterdam, The Netherlands

Radiotherapy and Oncology 94 (2010) 286–291






Guo et al. Radiation Oncology (2015) 10:66
DOI 10.1186/s13014-015-0370-3

RADIATION ONCOLOGY

RESEARCH Open Access

Interobserver variability in the delineation of the tumour bed using seroma and surgical clips based on 4DCT scan for external-beam partial breast irradiation

Bing Guo[1,2], Jianbin Li[1*], Wei Wang[1], Min Xu[1], Qian Shao[1], Yingjie Zhang[1], Chaoqian Liang[1] and Yanluan Guo[1,2]

**Conclusions:** When the SCS was 3 ~ 5 points and the number of surgical clips was ≥5, interobserver variability was minimal for the delineation of the tumour bed based on seroma.

**Figure 1 Single CT slice and volumetric image of one patient with delineated $TB_C$ (a), $TB_S$ (b) and $TB_{C+S}$ (c) of all 5 observers.** $TB_C$, the TB delineated based on clips; $TB_S$, the TB delineated based on the seroma; $TB_{C+S}$, the TB delineated based on both seroma and clips.

# BOOST CTV

Radiotherapy and Oncology 106 (2013) 231–235

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ELSEVIER

10) 286–291

Tumor localization and dose planning

Tumour bed delineation for partial breast/breast boost radiotherapy: What is the optimal number of implanted markers?

Anna M. Kirby[a,*], Rajesh Jena[b], Emma J. Harris[c], Phil M. Evans[c], Clare Crowley[a], Deborah L. Gregory[b], Charlotte E. Coles[b]

[a]*Royal Marsden NHS Foundation Trust, Sutton;* [b]*Cambridge University Hospitals NHS Foundation Trust;* [c]*Institute of Cancer Research, Sutton, UK*

- They compare tumor bed volumes delineated using 6, 5, 1 and 0 clips.
- 5 implanted markers (one deep and four radial) are likely to be adequate assuming the addition of a standard 10-15 mm boost CTV margin.

# BOOST CTV

Radiotherapy and Oncology 103 (2012) 178–182

## Reducing interobserver variation of boost-CTV delineation in breast conserving radiation therapy using a pre-operative CT and delineation guidelines ☆

Liesbeth J. Boersma [a,*,1], Tomas Janssen [b,1], Paula H.M. Elkhuizen [b], Philip Poortmans [d], Maurice van der Sangen [c], Astrid N. Scholten [e], Bianca Hanbeukers [a], Joop C. Duppen [b], Coen Hurkmans [c], Corine van Vliet [b]

*Conclusion:* Use of a Preop-CT in BCT results in a modest but statistically significant reduction in interobserver variation of the boost-CTV delineations and in a significant reduction in the boost-CTV volume.

den Hartogh *et al. Radiation Oncology* 2014, 9:63
http://www.ro-journal.com/content/9/1/63

RADIATION ONCOLOGY

RESEARCH Open Access

## MRI and CT imaging for preoperative target volume delineation in breast-conserving therapy

Mariska D den Hartogh[1*], Marielle EP Philippens[1], Iris E van Dam[1], Catharina E Kleynen[1], Robbert JHA Tersteeg[1], Ruud M Pijnappel[2], Alexis NTJ Kotte[1], Helena M Verkooijen[1,2], Maurice AAJ van den Bosch[2], Marco van Vulpen[1], Bram van Asselen[1] and HJG Desirée van den Bongard[1]

**Figure 1** MRI patient setup in radiotherapy supine position.

- Introduction

- **Indications and CTV:**
  - Whole Breast
  - Boost
  - **Chest wall**
  - Regional nodes
    - L4, L3, L2, L1, IM, Rotter

- Organs at risk and constraints

- Margins CTV → PTV      OAR → PRV

- Conclusions

# CHEST WALL AND LYMPH NODES RT. INDICATIONS

- Tumours > 5 cm (T3) ***RT chest wall + L4-L3***
- Invasion of the skin or chest wall (T4) ***RT chest wall + L4-L3***
- Positive margins ***RT chest wall +/- L4-L3***
- Chest wall recurrence ***RT chest wall + L4-L3***
- Positive nodes ***RT chest wall + L4-L3***
- No or inadequate lymphadenectomy (≤ 6-10 nodes) ***RT chest wall + L4-L3***
- SN (+) (Macrometastases) without lymphadenectomy ***RT chest wall + L4-L3***

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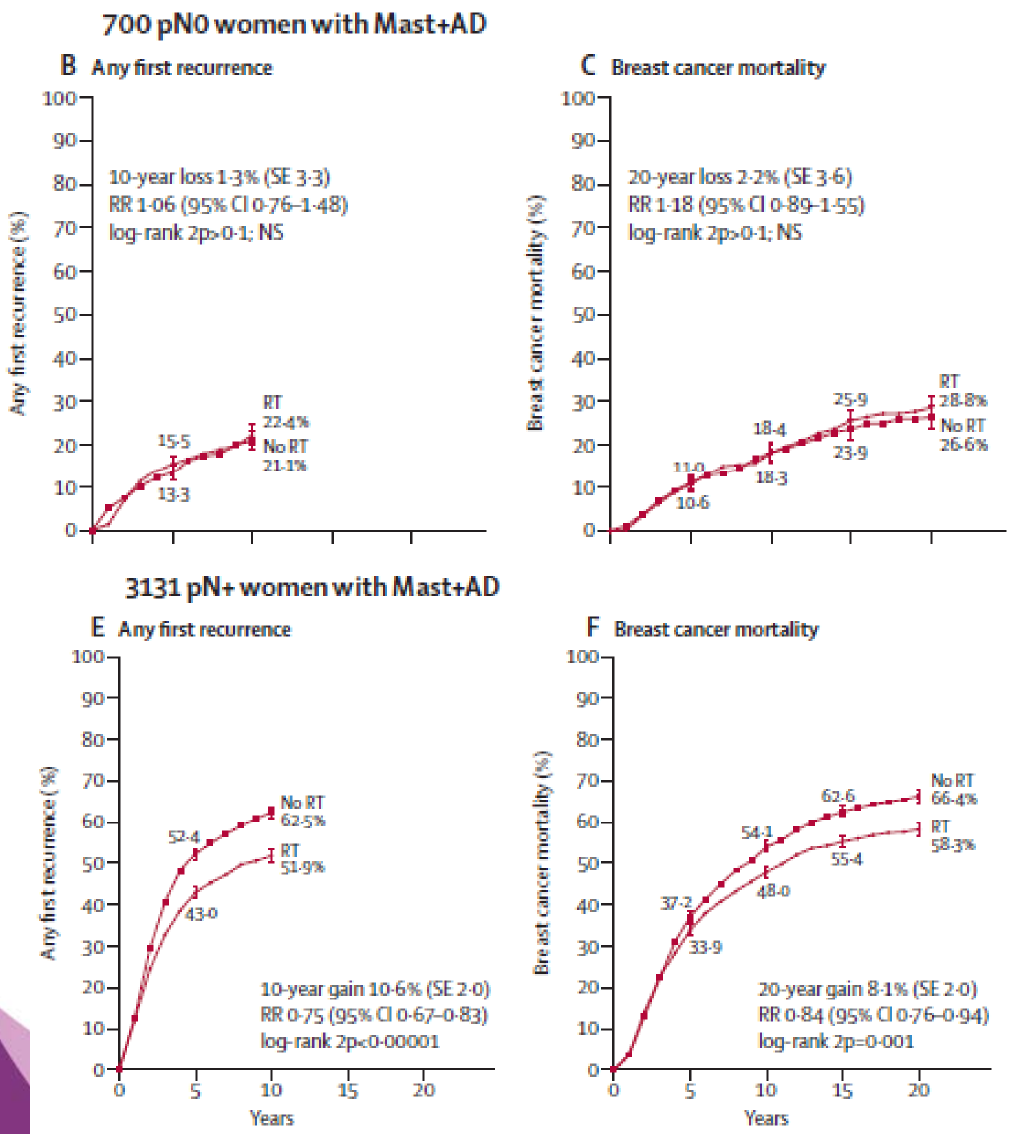
# Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials

Lancet 2014; 383: 2127–35

EBCTCG (Early Breast Cancer Trialists' Collaborative Group)*




Reduces **<u>recurrence</u>**

(Node (-) (700 pts)

(Node (+) (3131 pts)

- 10 year gain **1.3% (N-) and 10.6% (N+)**

Reduces breast cancer **<u>mortality</u>**

- 20 year gain **2.2% (N-) and 8.1% (N+)**

ONE BREAST CANCER DEATH IS AVOIDED FOR EVERY FOUR LOCAL RECURRENCES AVOIDED

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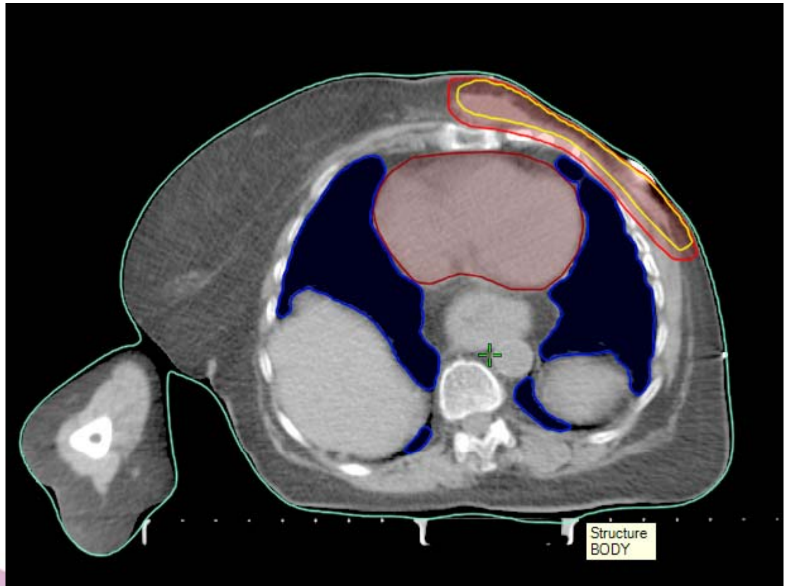
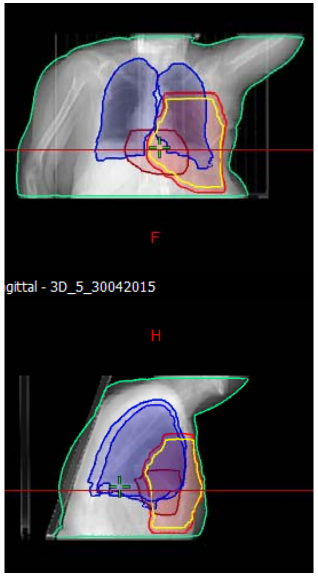
# CHEST WALL CTV

It might be useful to mark the scar

It might be useful to mark the medial, lateral and inferior limit (reference: contralateral breast)

Include all the scar whenever possible

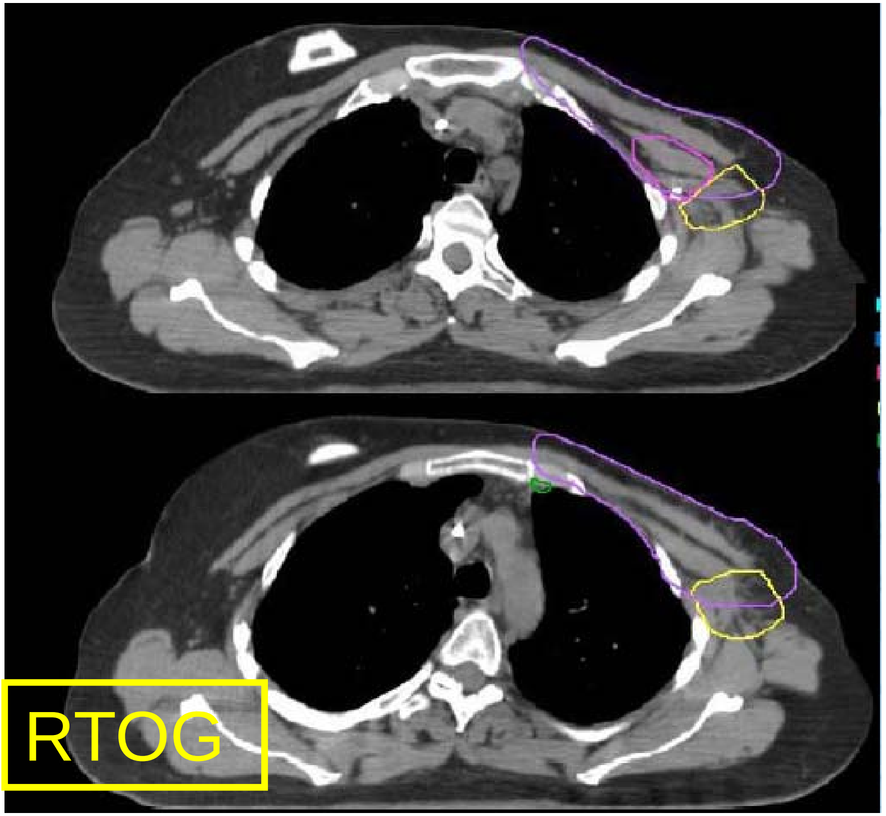


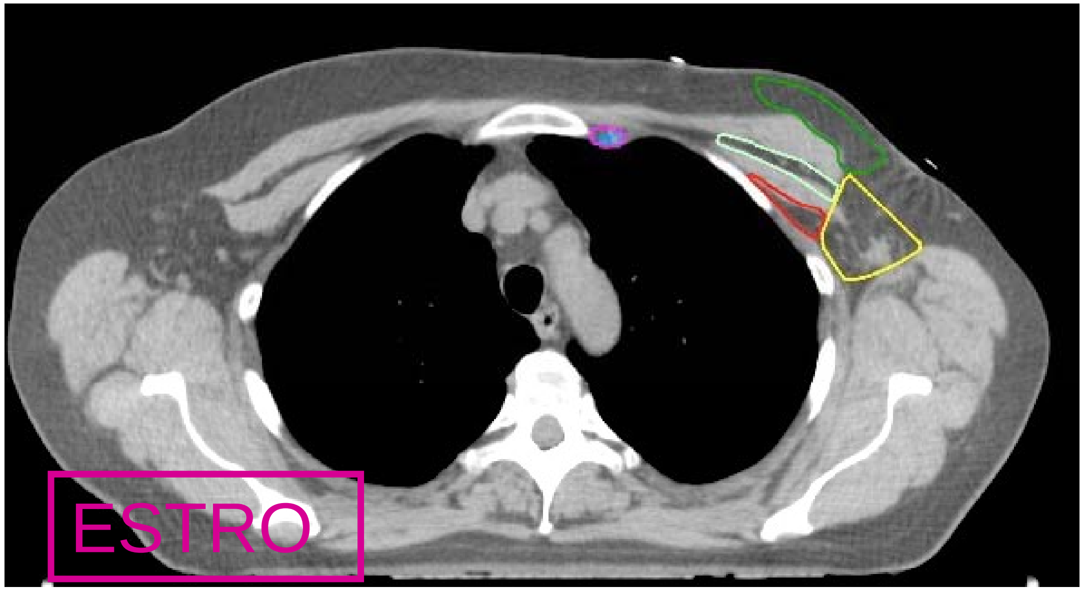



Craneal

Caudal border of the clavicle head

Guided by palpable/visible signs; if appropriate guided by the contralateral breast; maximally up to the inferior edge of the sterno-clavicular joint




Equal to a CTV-breast guided by the contralateral breast

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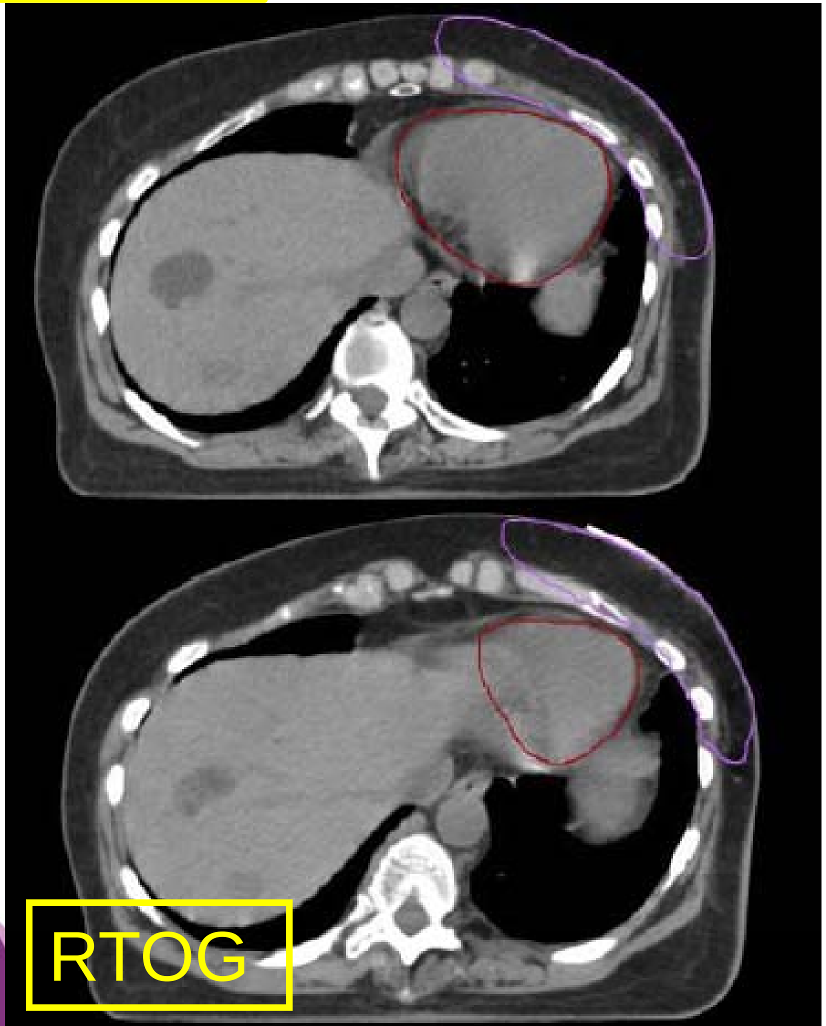
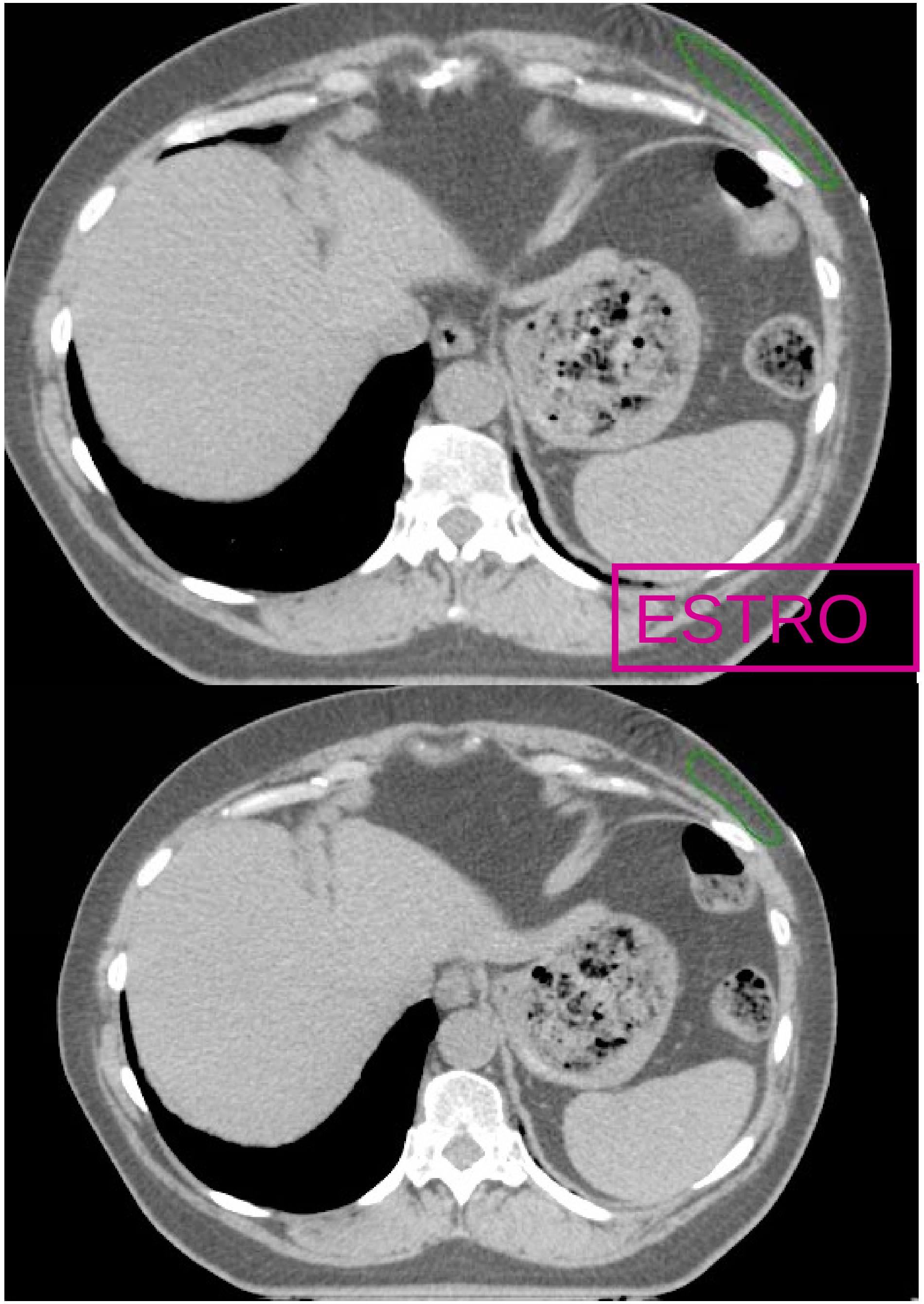
**Caudal**

Clinical reference+ loss of CT apparent contralateral breast

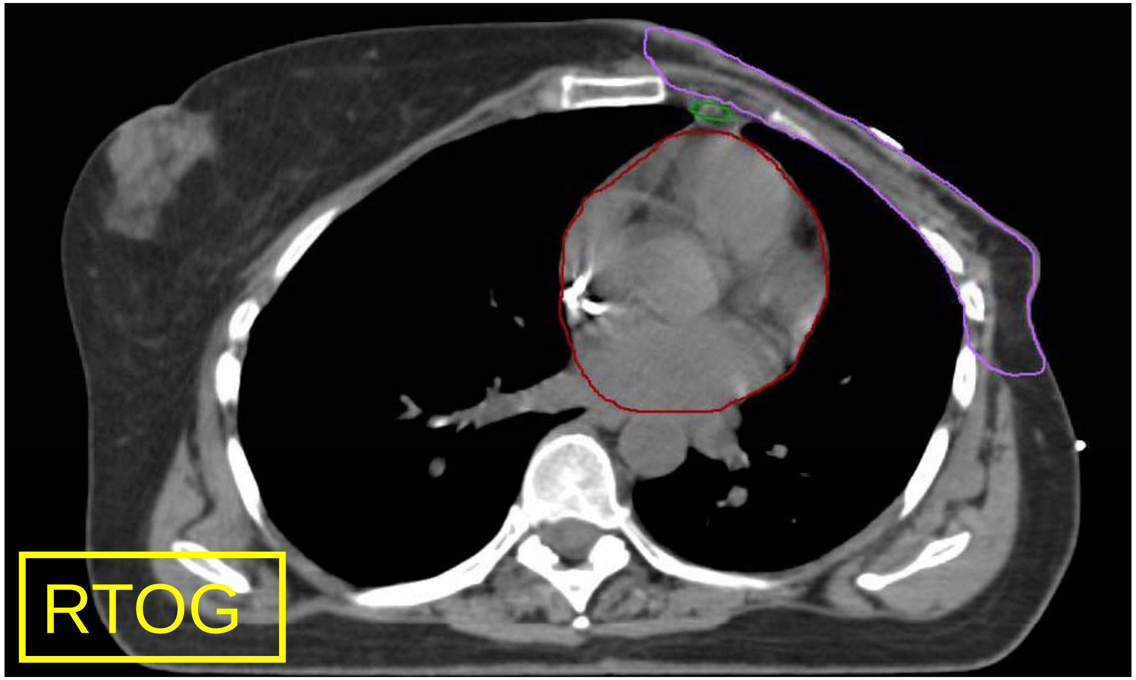
Guided by palpable/visible signs; if appropriate guided by the contralateral breast

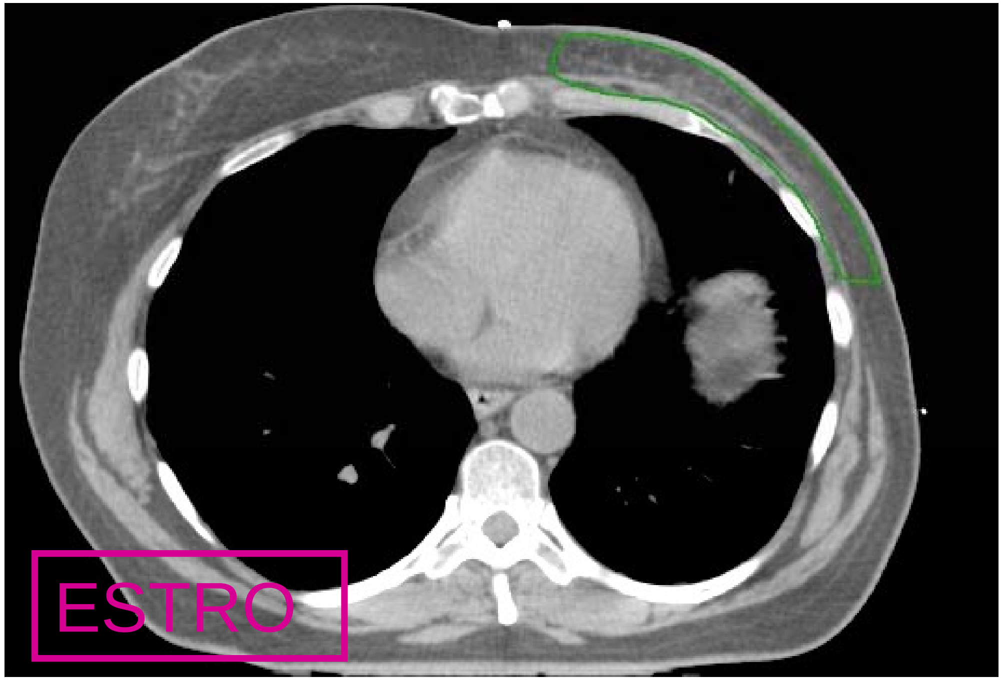


5 mm under skin surface

In case of a thin thoracic wall, omission of the first 5 mm under the skin may result in no CTV at all. In that case, the CTV should be extended into the skin and a bolus should be used



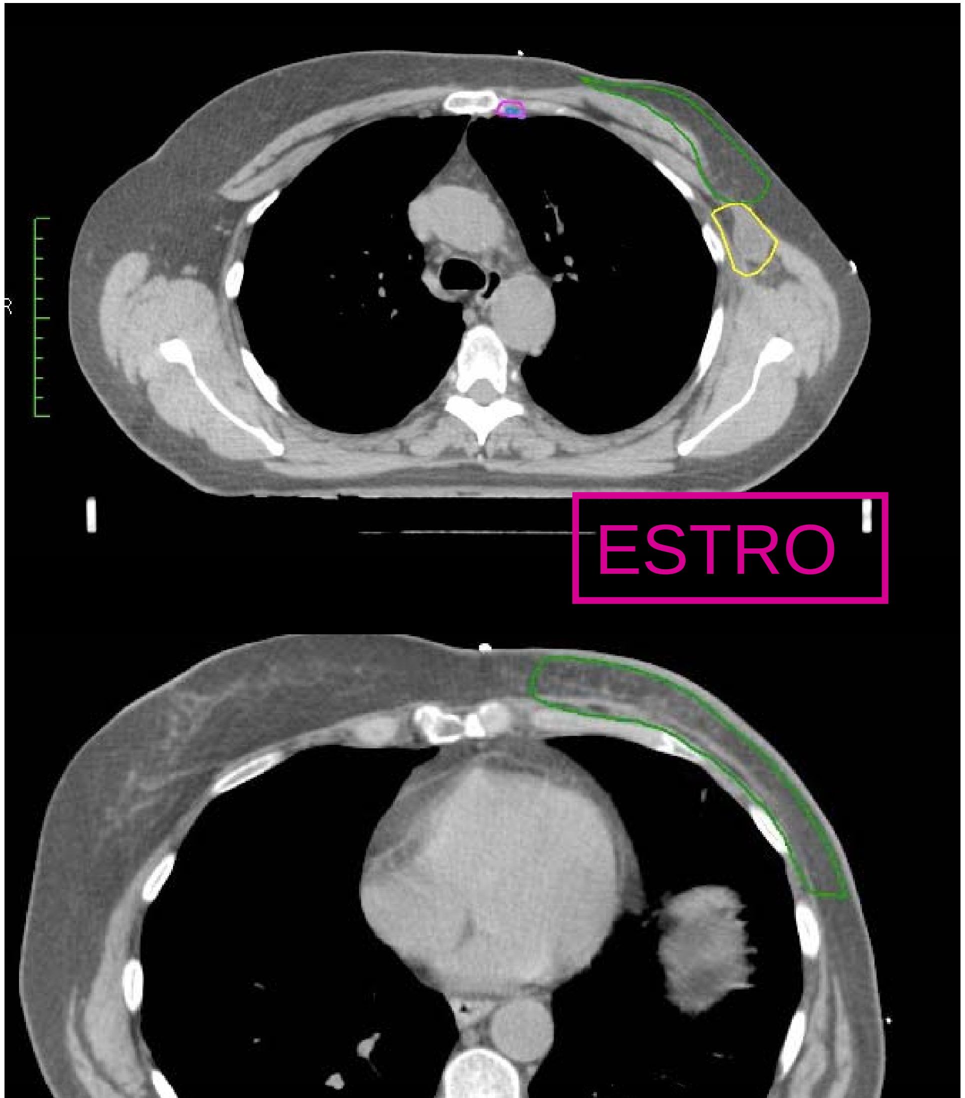

RTOG: Skin
ESTRO: 5 mm under the skin

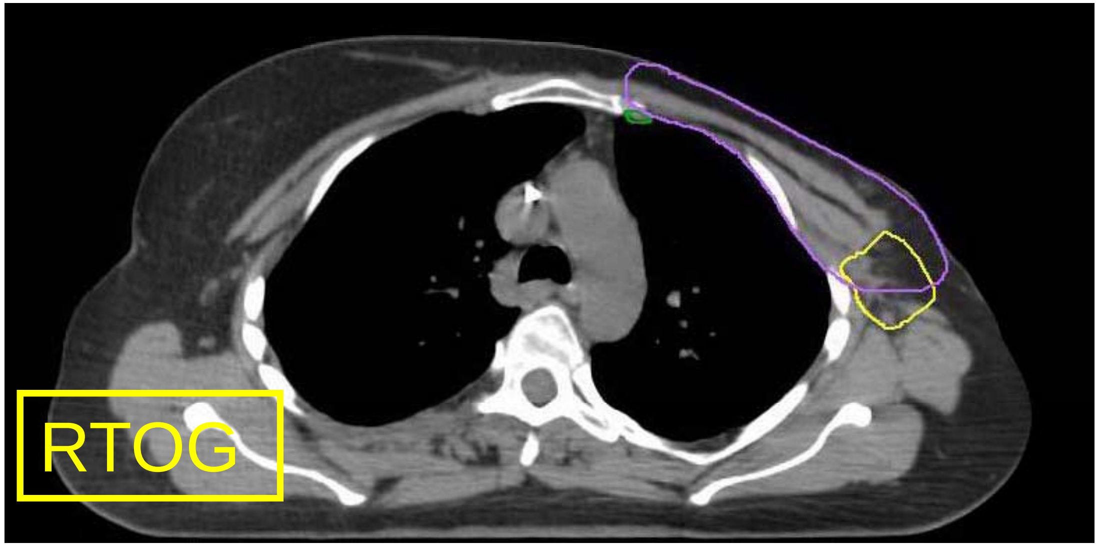
The deep fascia and the pectoralis are anatomical barriers.

**Posterior**

Rib-pleural interface. (Includes pectoralis muscles, chestwall muscles, ribs)

Major pectoral muscle or costae and intercostal muscles where no muscle




ESTRO recommendations do not include the pectoralis muscles, the chestwall muscles or the ribs

# RTOG published some studies about RTOG atlas in September 2015 Red Journal

International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

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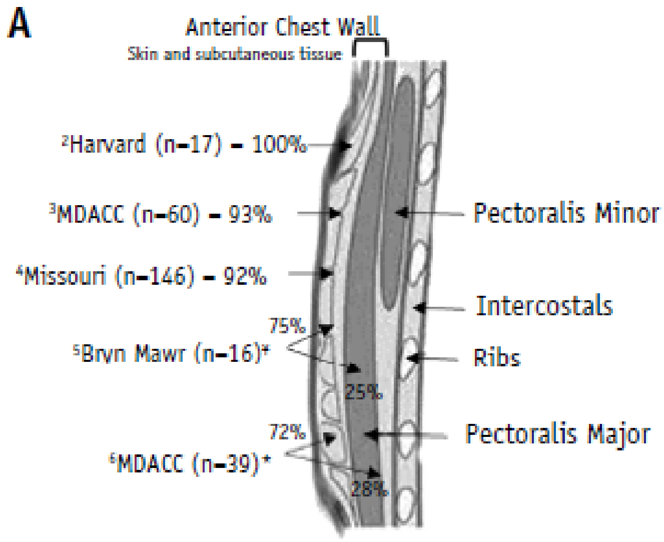
BRIEF REPORT

## RTOG Chest Wall Contouring Guidelines for Post-Mastectomy Radiation Therapy: Is It Evidence-Based?

**John A. Vargo, MD, and Sushil Beriwal, MD**

*Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania*

Received Aug 12, 2014, and in revised form Feb 2, 2015. Accepted for publication Mar 2, 2015.




They recommend changing posterior boundary of chest wall CTV: Subcutaneous tissue and pectoralis musculature may be warranted. Not including ribs and intercostal muscles.

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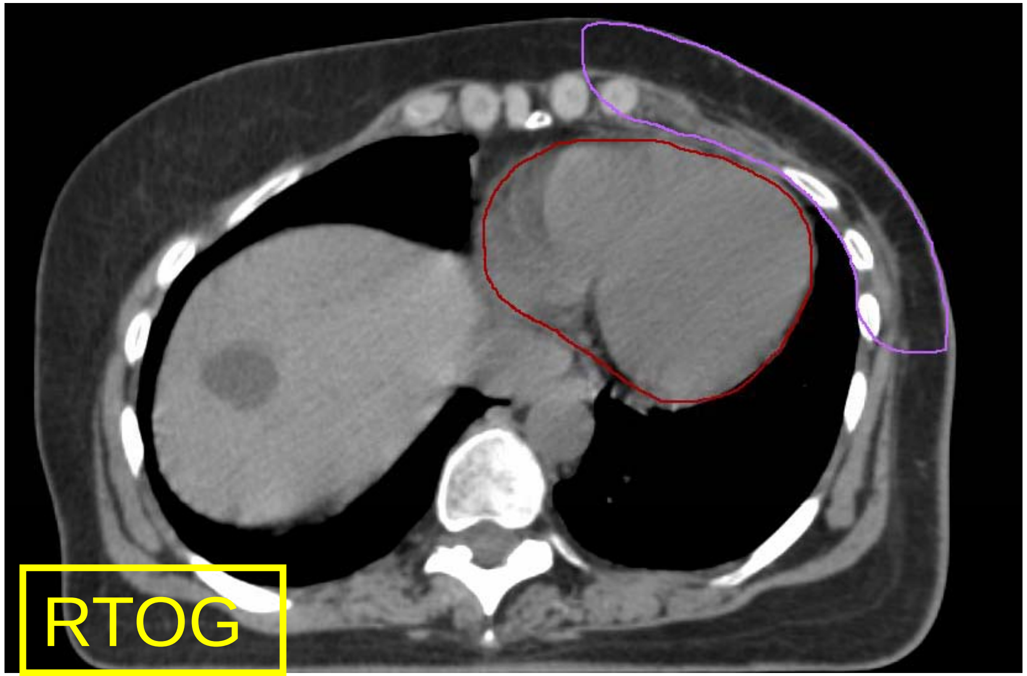
Medial

Sternal-rib junction [b]

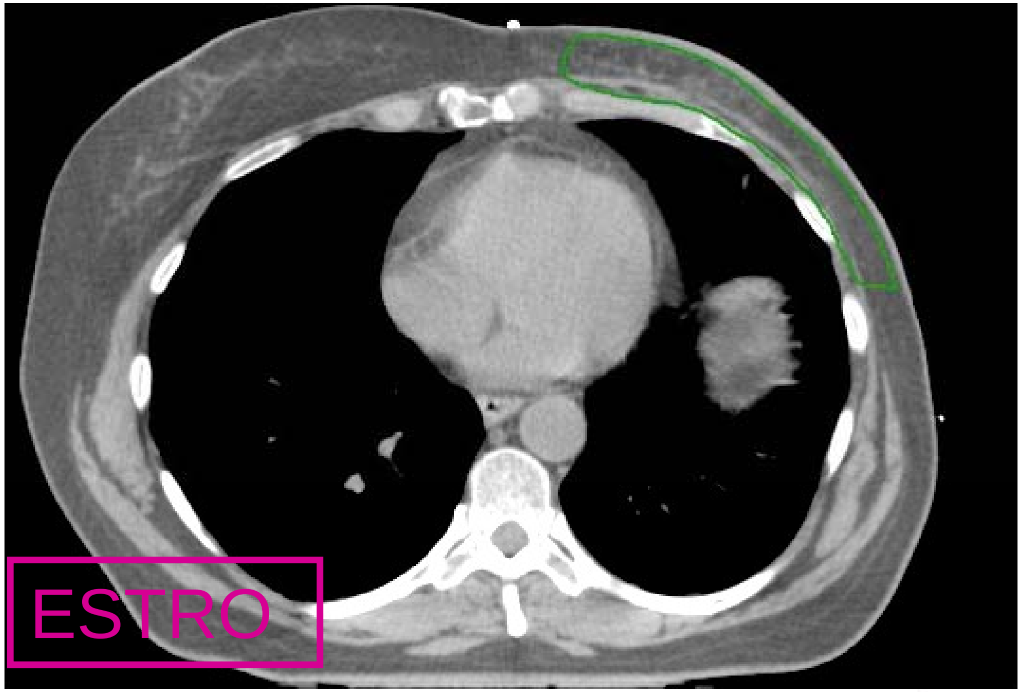
Guided by palpable/visible signs; if appropriate guided by the contralateral breast



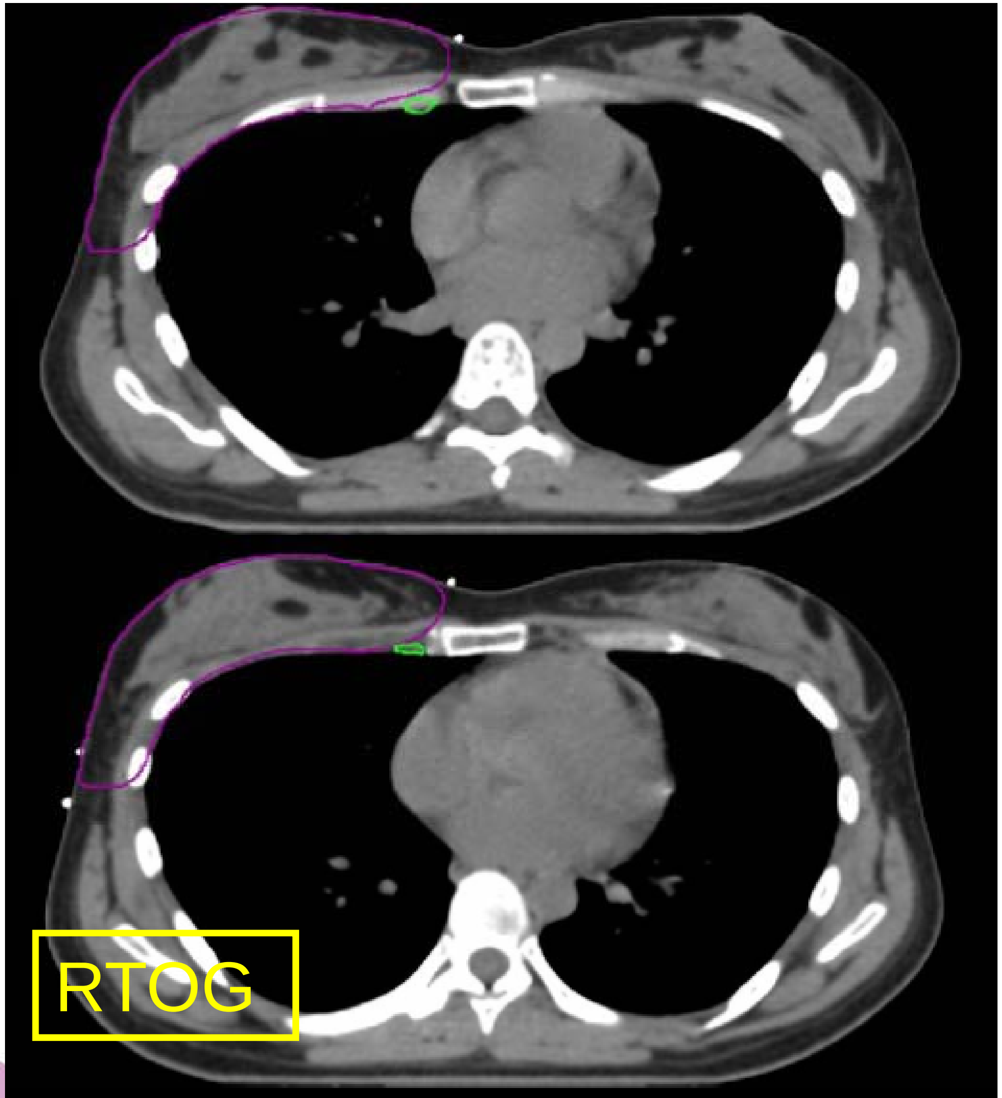

Lateral

Clinical Reference/ mid axillary line typically, excludes lattismus dorsi m [a]

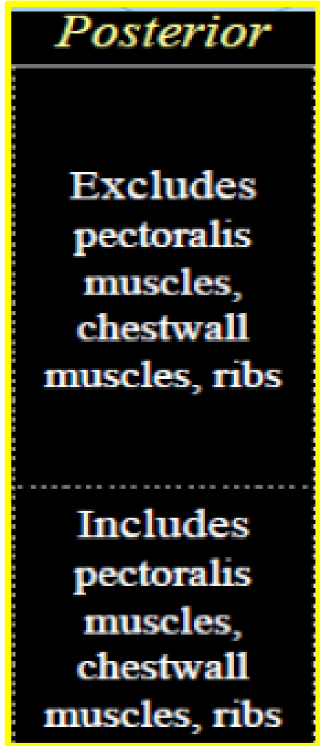
Guided by palpable/visible signs; if appropriate guided by the contralateral breast. Usually anterior to the mid-axillary line



# CTV: CONSERVATIVE SURGERY AFTER PRIMARY SYSTEMIC TREATMENT




Only one difference

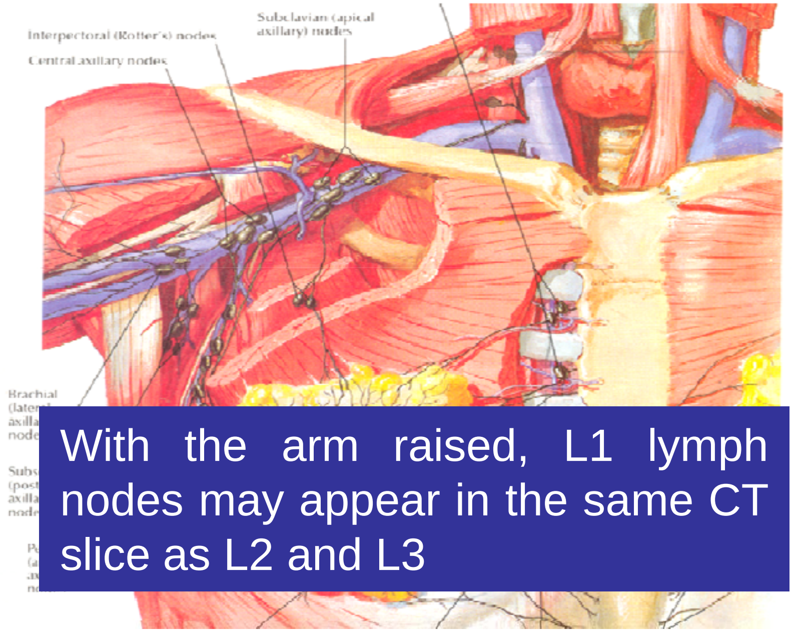



ESTRO School

- Introduction
- **Indications and CTV:**
  - Whole Breast
  - Boost
  - Chest wall
  - **Regional nodes**
    - **L4, L3, L2, L1, IM, Rotter**
- Organs at risk and constraints
- Margins CTV → PTV  OAR → PRV
- Conclusions

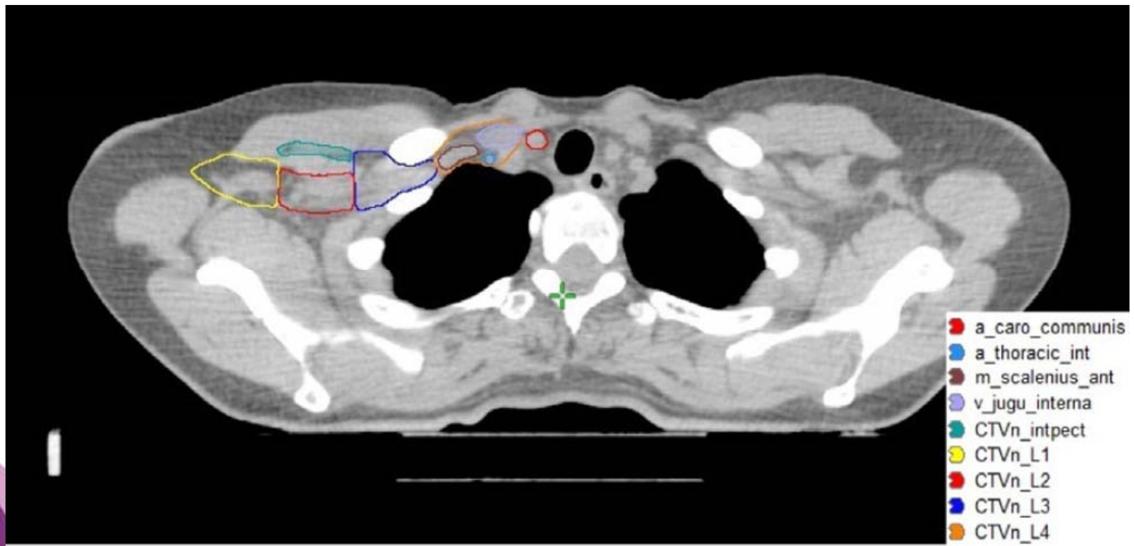
# REGIONAL NODES

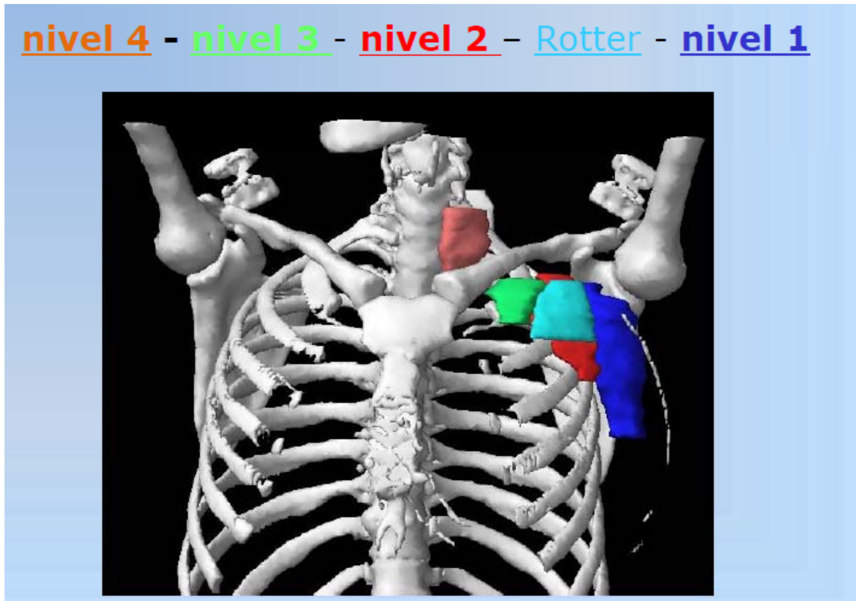
**L4**: or supraclavicular
**L3** or infraclavicular: above pectoral muscles
**L2**: posterior to pectoralis minor
**L1**: caudally to pectoralis major
**IM**
**Rotter**: between pectoralis major and minor




With the arm raised, L1 lymph nodes may appear in the same CT slice as L2 and L3

***A lymph node is typically a 5 mm margin around the veins***




School

# CTV L4-L3: INDICATIONS

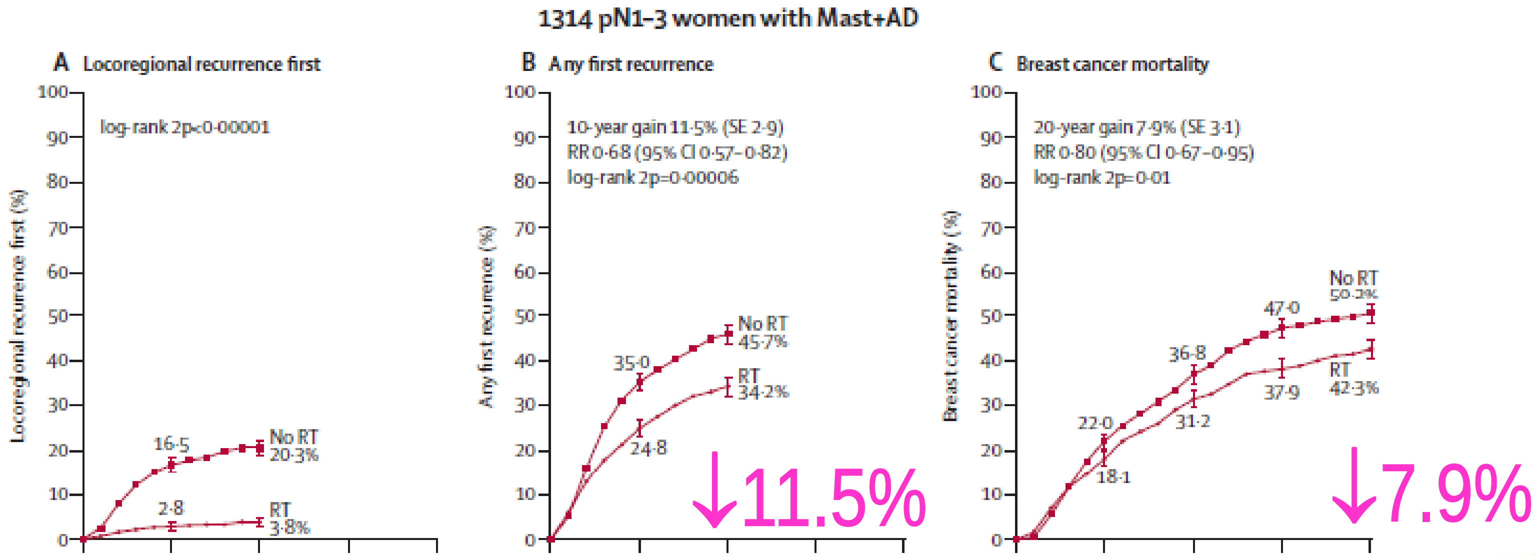
- Tumours > 5 cm (T3)
- Invasion of the skin or chest wall (T4)
- Positive nodes
- No or inadequate lymphadenectomy ($\leq$ 6-10 nodes)
- SN (+) (Macrometastases) without lymphadenectomy

# CTV L4-L3: 1-3 N+: INDICATIONS

The results are PENDING for these randomized trials :

- RTOG 9915 (SWOG)
- EORTC (SUPREMO – Selective Use of Postoperative Radiotherapy After Mastectomy): In this trial, apart from randomize 1-3 N(+) patients, pT2 pN0 with grade 3 and/or vasculo-lymphatic invasion were also randomized.
- NCI CTG
- French study

**EBCTG META-ANALYSIS: POSITIVE RESULTS OF SURVIVAL 1-3 N+**



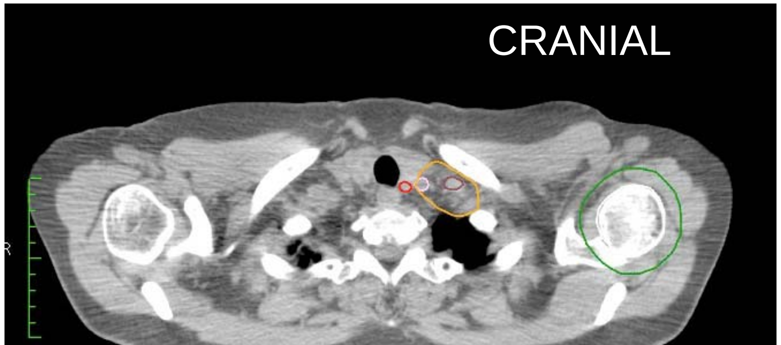
# Postmastectomy radiation in breast cancer with one to three involved lymph nodes: ending the debate

www.thelancet.com **Vol 383 June 21, 2014**

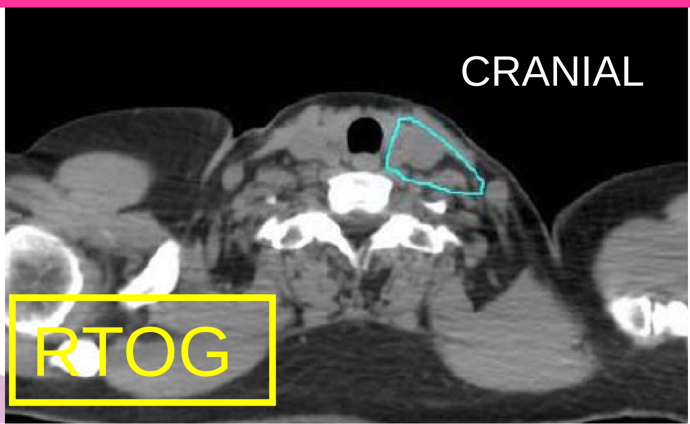
*Philip Poortmans*
Department of Radiation Oncology, Institute Verbeeten, Tilburg, LA 5000, Netherlands
poortmans.ph@bvi.nl

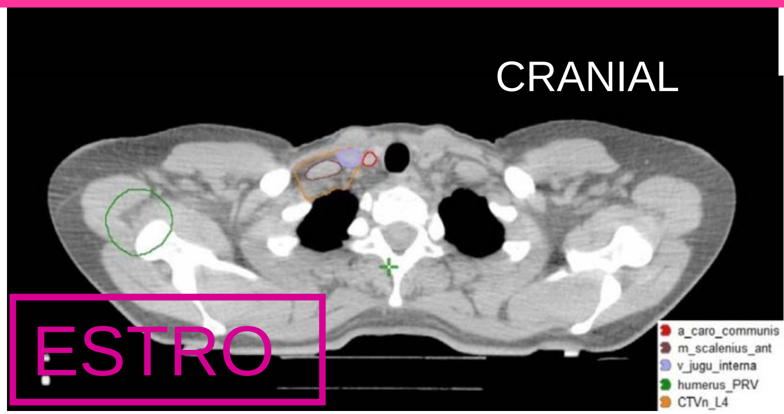
The results of this EBCTCG meta-analysis clearly confirm that postmastectomy radiotherapy should be considered equally for patients with one to three involved axillary lymph nodes as it should be for patients with four or more affected axillary lymph nodes. The same considerations concerning regional radiotherapy also seem to be valid for patients treated with breast-conserving therapy.[1,2] Here, the addition of regional radiotherapy to whole breast irradiation adds less to the burden of treatment to the patient, on the condition that long-term toxic effects can be avoided with modern radiotherapy techniques.

| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Supra-clavicular | Caudal to the cricoid cartilage | Junction of brachioceph.-axillary vns./ caudal edge clavicle head [a] | Sternocleido mastoid (SCM) muscle (m.) | Anterior aspect of the scalene m. | Cranial: lateral edge of SCM m. Caudal: junction 1st rib-clavicle | Excludes thyroid and trachea |
| Lymph node level 4 CTVn_L4 | Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein) | Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of CTVn_IMN | Sternocleidomastoid muscle, dorsal edge of the clavicle | Pleura | Includes the anterior scalene muscles and connects to the medial border of CTVn_L3 | Including the jugular vein without margin; excluding the thyroid gland and the common carotid artery |


ESTRO recommends lowering the cranial limit (cranial of subclavian vein)

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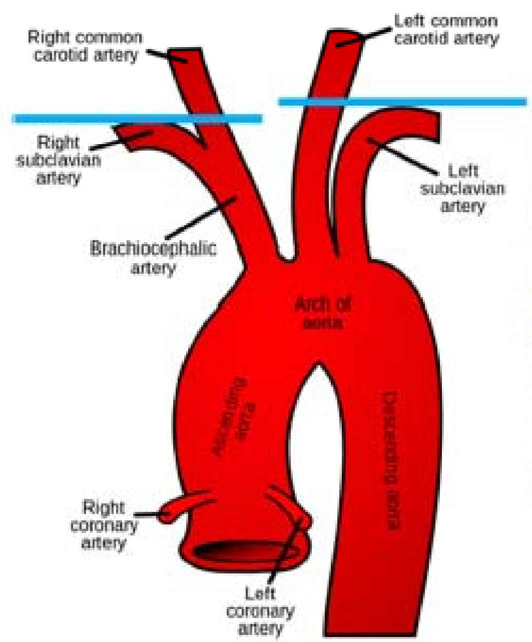
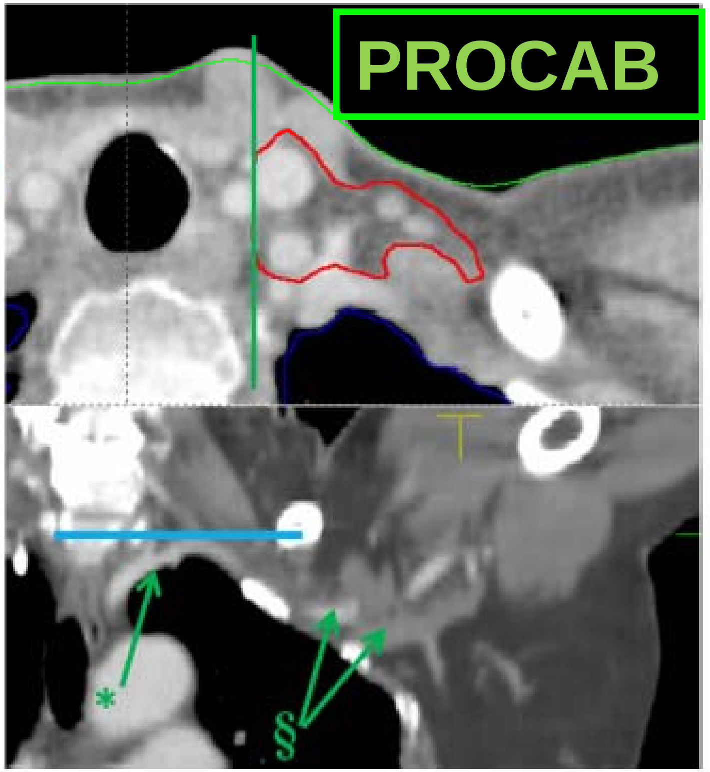
| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Level IV CTVn_L4 | Cranial edge of the subclavian A. arch | 5 mm caudal of the junction of the subclavian and the internal jugular vein | *Cranially: dorsal surface of the SCM *Caudally: the infrahyoid muscle (strap muscles) and clavicle | *Cranially: ventral edge of the subclavian artery *Caudally: lung | *Cranially: lateral border of the anterior scalene m. *Caudally: joining CTVn_L3, excluding the subclavian A. | The medial edge of the internal jugular vein, without any margin medially, excluding the carotid A. and thyroid gland |

*DBCG guidelines*

| | | | | | | |
|---|---|---|---|---|---|---|
| Lymph node level 4 CTVn_L4 | Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein) | Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of CTVn_IMN | Sternocleidomastoid muscle, dorsal edge of the clavicle | Pleura | Includes the anterior scalene muscles and connects to the medial border of CTVn_L3 | Including the jugular vein without margin; excluding the thyroid gland and the common carotid artery |

PROCAB guidelines



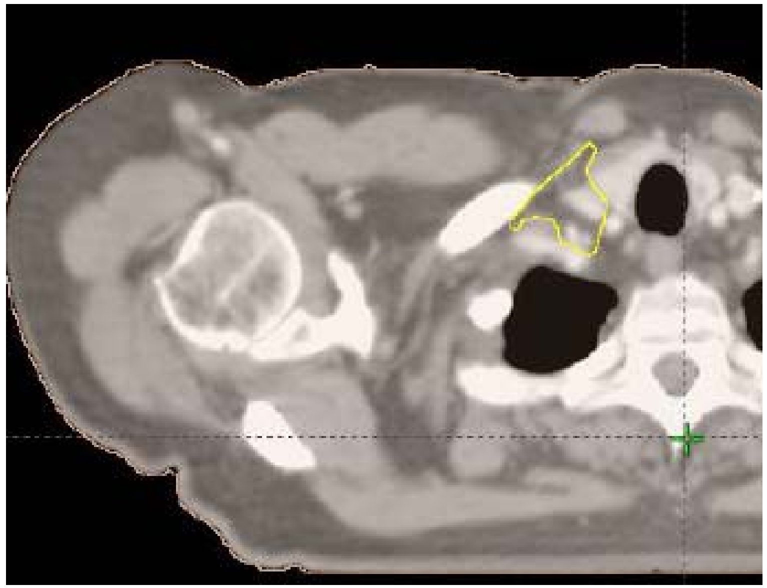



Fig. 2. The cranial border of level 4 or the supraclavicular region. *Subclavian artery arch. §Axillary artery and vein.

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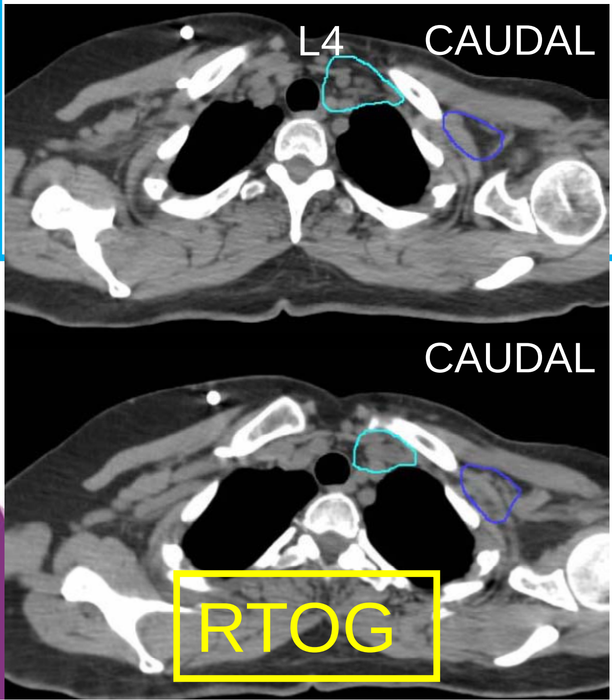
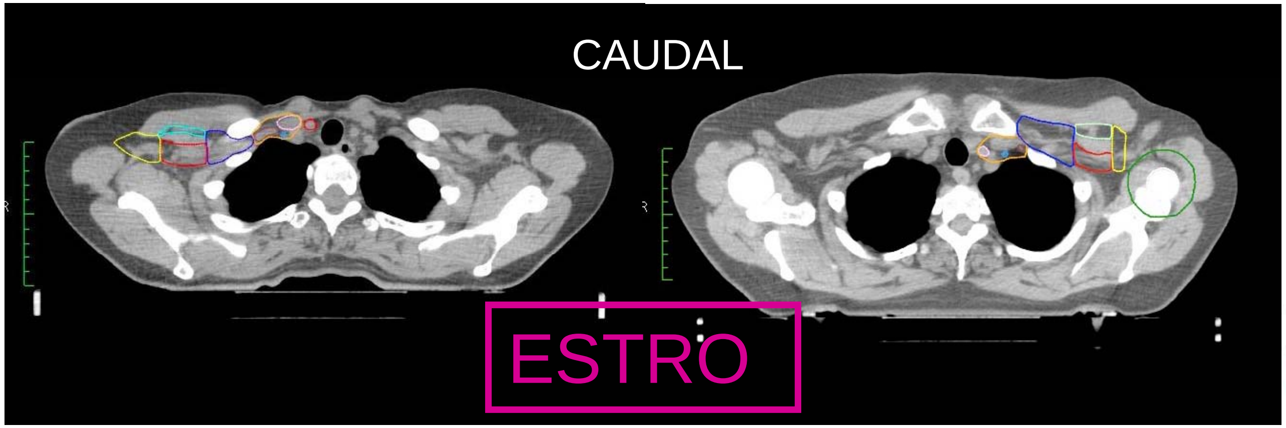
| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Supra-clavicular | Caudal to the cricoid cartilage | Junction of brachioceph.-axillary vns./ caudal edge clavicle head [a] | Sternocleido mastoid (SCM) muscle (m.) | Anterior aspect of the scalene m. | Cranial: lateral edge of SCM m. Caudal: junction 1st rib-clavicle | Excludes thyroid and trachea |
| Lymph node level 4 CTVn_L4 | Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein) | Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of CTVn_IMN | Sternocleidomastoid muscle, dorsal edge of the clavicle | Pleura | Includes the anterior scalene muscles and connects to the medial border of CTVn_L3 | Including the jugular vein without margin; excluding the thyroid gland and the common carotid artery |
| Periclavicular | Caudal edge of cricoid cartilage | Cranial border of level II and III (lateral). Cranial edge of the sterno-clavicular-junction (medial) | Dorsal surface of m. sternomastoideus, dorsal surface of clavicle, 5 mm below skin | In front of the clavicle, behind a. carotis interna, in front of m. scalenus ant, m. scalenus med, m. omo-hyoideus and m. levator scapulae | Medial edge of m. pectoralis minor, clavicle | Medial edge of a. carotis interna and v. jugularis interna |

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# Letter to the Editor

Radiotherapy and Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

## ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1 ☆

### Caudal part of CTVn_L4

In the consensus guideline a link is given to an atlas with patients treated for left-sided and right-sided breast cancer, respectively. In both cases the caudal border of CTVn_L4 has now been modified a few slices more caudal to fully include the Subclavian vein, which is positioned caudal and ventral to the Subclavian artery (Figs. 1A and 1B). New links are provided to the corrected atlases (links…).

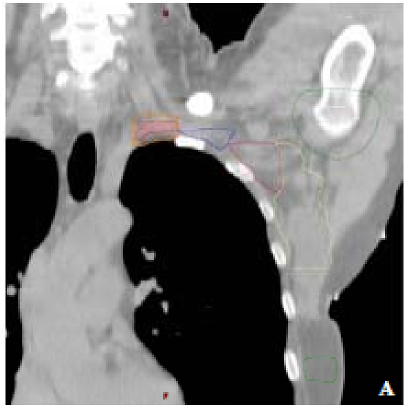


**Fig. 1A.** CTVn_L4 including the Subclavian artery highlighted in red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

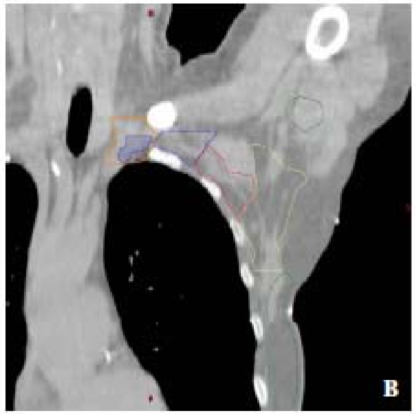


**Fig. 1B.** CTVn_L4 including the Subclavian vein highlighted in blue (positioned slightly more caudal and ventral to the Subclavian artery). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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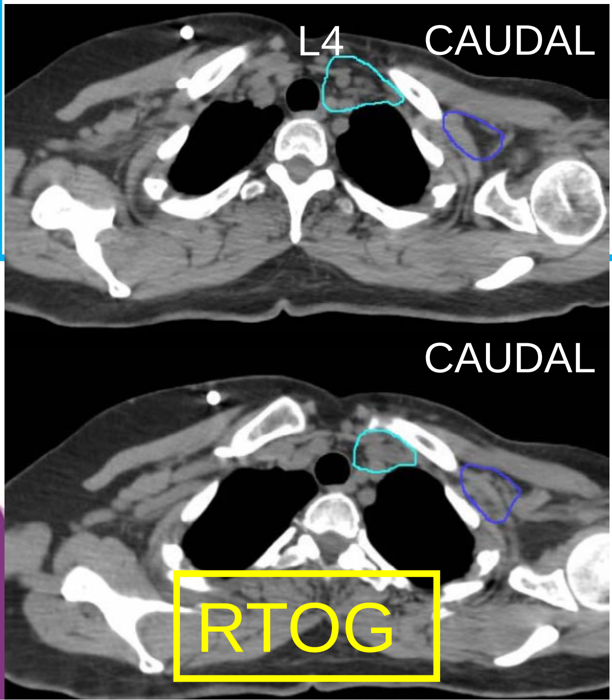
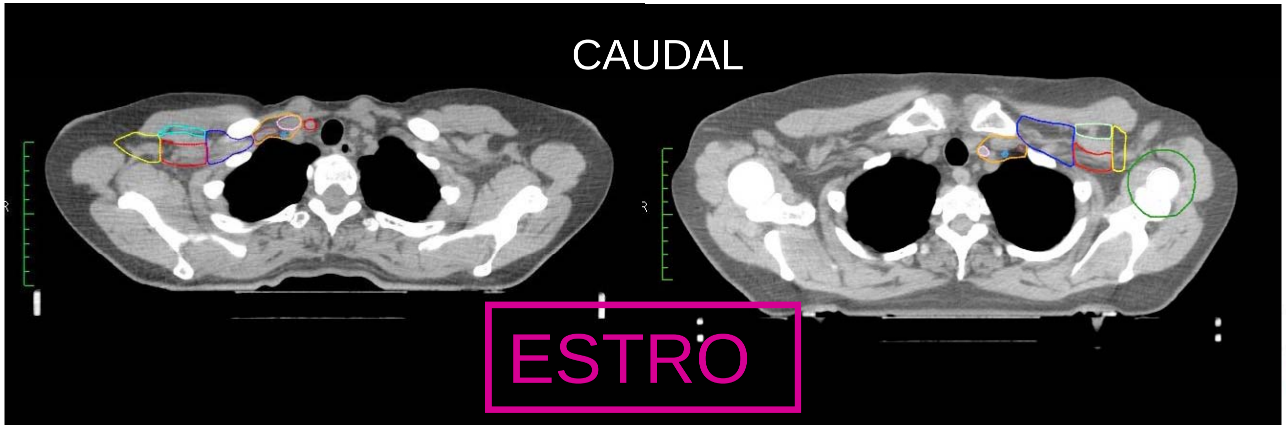
| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Supra-clavicular | Caudal to the cricoid cartilage | Junction of brachioceph.-axillary vns./ caudal edge clavicle head [a] | Sternocleido mastoid (SCM) muscle (m.) | Anterior aspect of the scalene m. | Cranial: lateral edge of SCM m. Caudal: junction 1st rib-clavicle | Excludes thyroid and trachea |
| Lymph node level 4 CTVn_L4 | Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein) | Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of CTVn_IMN | Sternocleidomastoid muscle, dorsal edge of the clavicle | Pleura | Includes the anterior scalene muscles and connects to the medial border of CTVn_L3 | Including the jugular vein without margin; excluding the thyroid gland and the common carotid artery |
| Periclavicular | Caudal edge of cricoid cartilage | Cranial border of level II and III (lateral). Cranial edge of the sterno-clavicular-junction (medial) | Dorsal surface of m. sternomastoideus, dorsal surface of clavicle, 5 mm below skin | In front of the clavicle, behind a. carotis interna, in front of m. scalenus ant, m. scalenus med, m. omo-hyoideus and m. levator scapulae | Medial edge of m. pectoralis minor, clavicle | Medial edge of a. carotis interna and v. jugularis interna |

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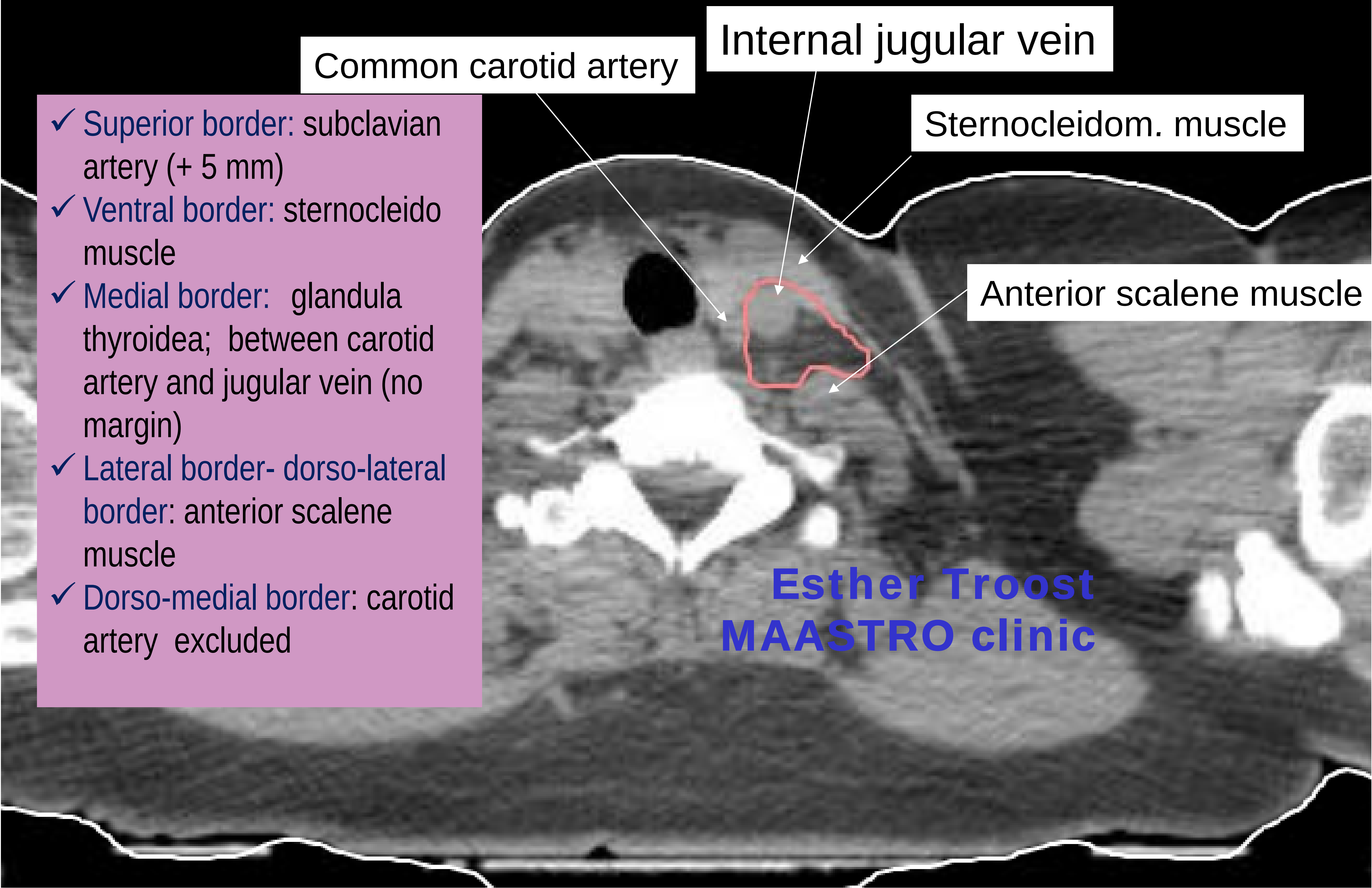
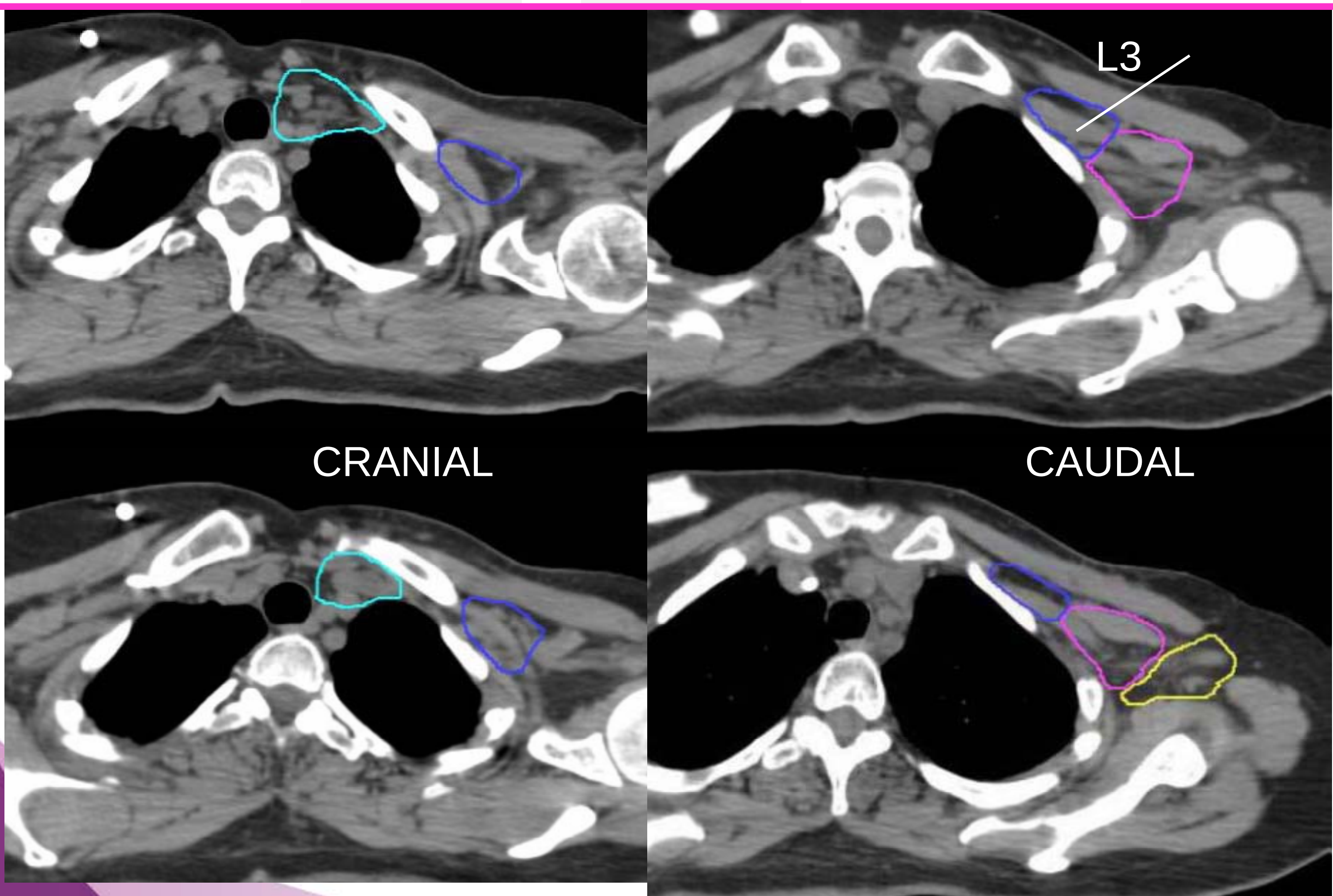
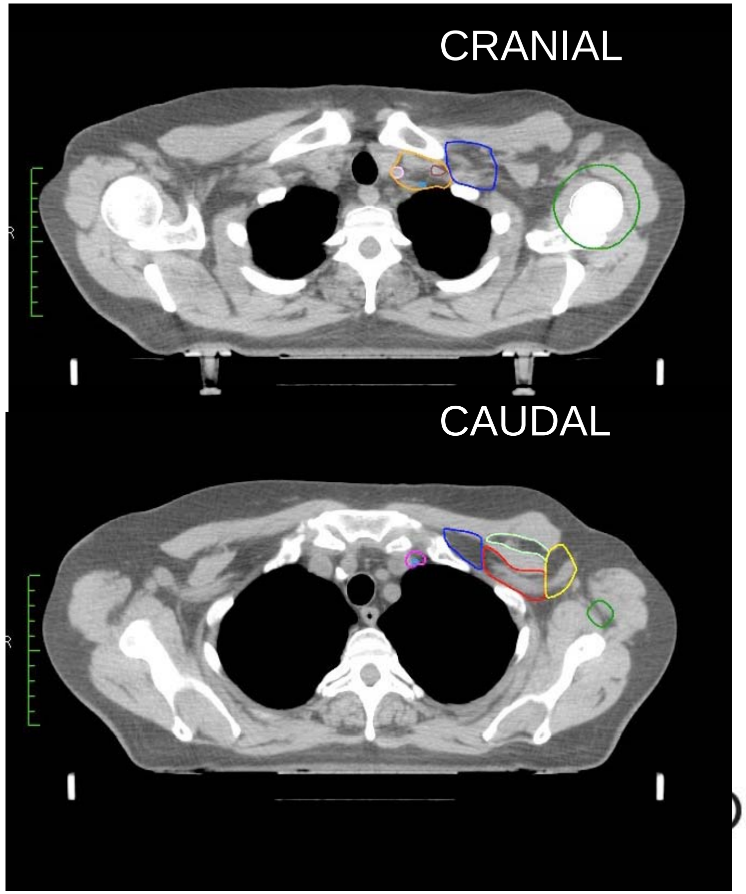
# Delineation of CTVn_L4 – supraclavicular lymph node area




- ✓ Superior border: subclavian artery (+ 5 mm)
- ✓ Ventral border: sternocleido muscle
- ✓ Medial border: glandula thyroidea; between carotid artery and jugular vein (no margin)
- ✓ Lateral border- dorso-lateral border: anterior scalene muscle
- ✓ Dorso-medial border: carotid artery excluded

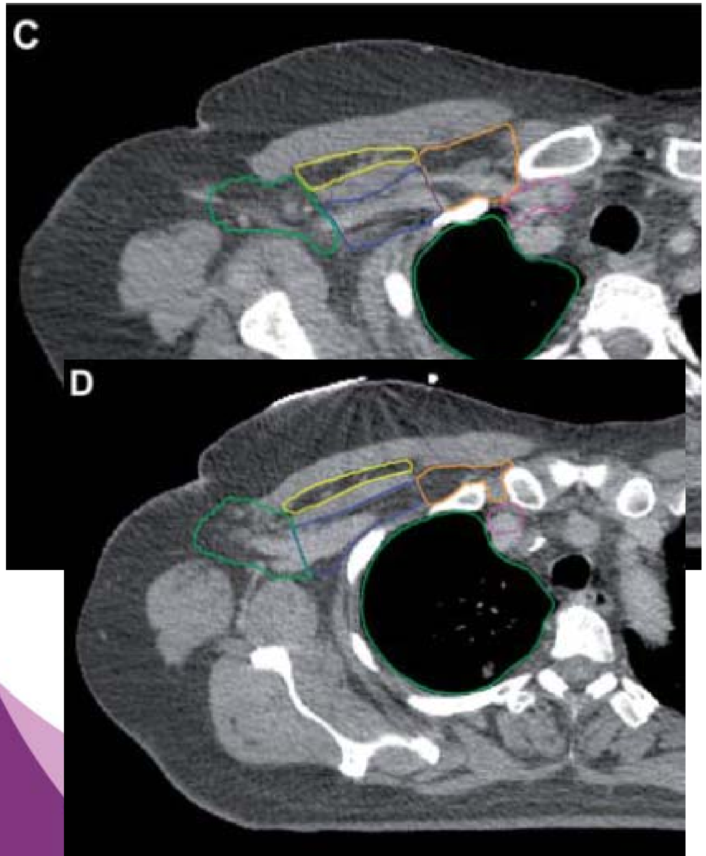
| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Axilla-level III | Pec. Minor m. insert on cricoid CORACOID | Axillary vessels cross medial edge of Pec. Minor m. d. | Posterior surface Pec. Major m. | Ribs and intercostal muscles | Medial border of Pec. Minor m. | Thoracic inlet |
| Axilla level 3 CTVn_L3 | Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein) | 5 mm caudal to the subclavian vein. If appropriate: top of surgical ALND | Major pectoral muscle | Up to 5 mm dorsal of subclavian vein or to costae and intercostal muscles | Medial side of the minor pectoral muscle | Junction of subclavian and internal jugular veins – >level 4 |

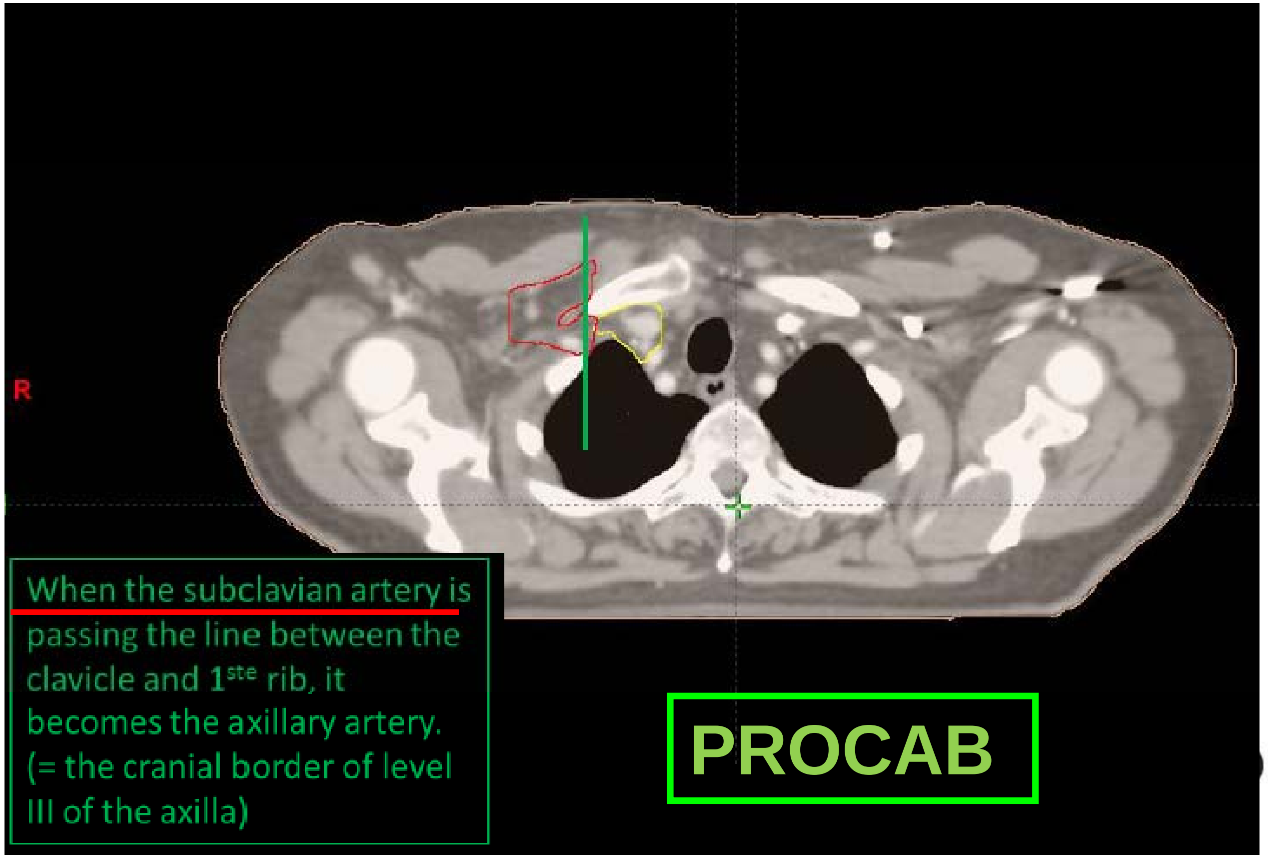


DCBG guidelines for delineation of CTV of breast and CTVs of the regional lymph node regions

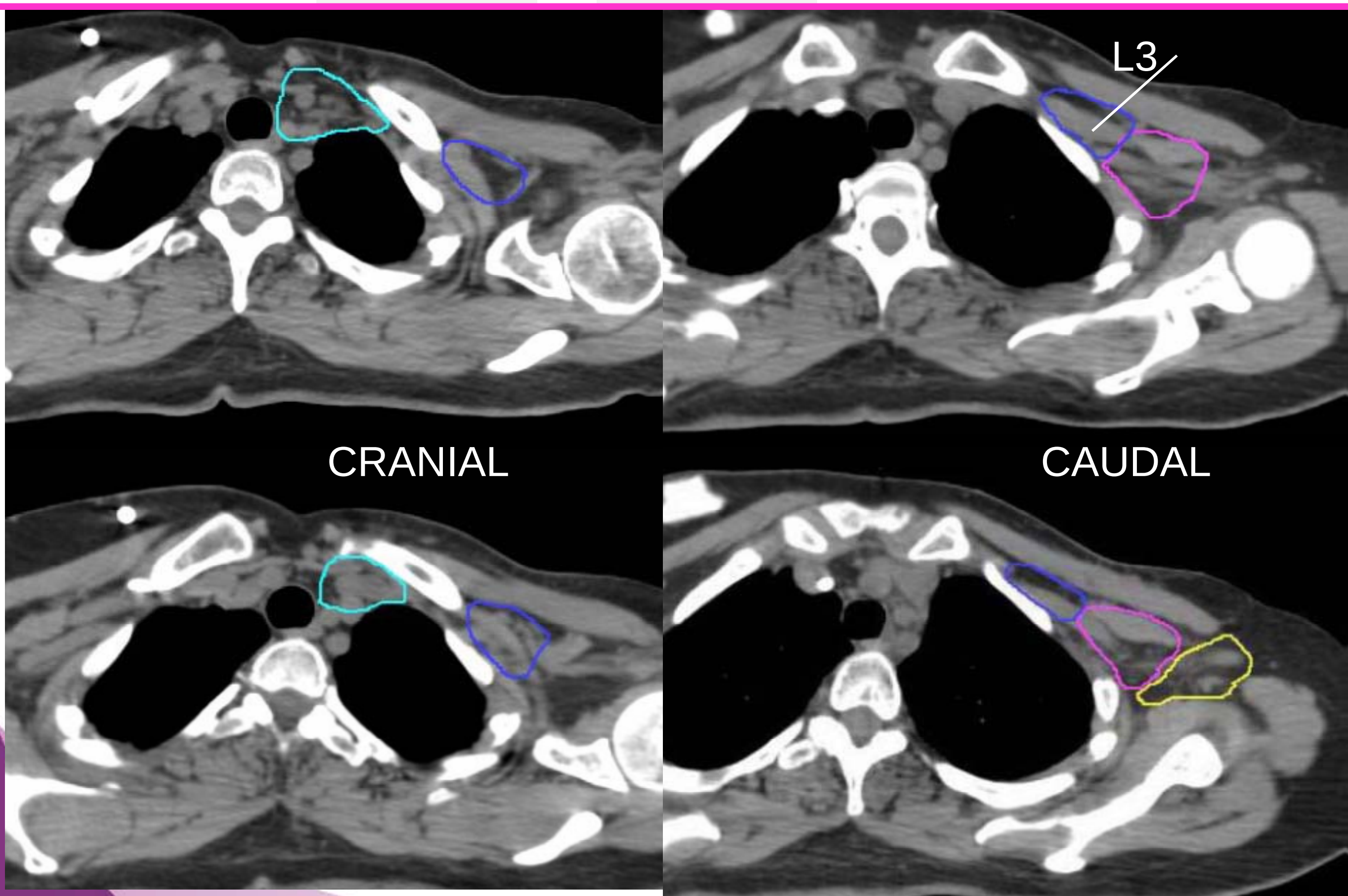
| LN region | cranial | caudal | ventral | dorsal | lateral | medial |
|---|---|---|---|---|---|---|
| Level III *DBCG guidelines* | 5 mm cranial to the axillary vessels | 1 cm caudal to the axillary vessels | Dorsal surface of m. pectoralis major | Chest wall, 5 mm dorsal of the axillary and subclavian vessels | Medial border of m. pectoralis minor | Clavicle |
| Level III of the axilla CTVn_L3 PROCAB guidelines | When the subclavian A. exits the thorax (crosses the vertical line between the clavicle and the first rib) and becomes the axillary A. | 5 mm below the axillary vein when it crosses the medial border of the pectoralis minor m. | Posterior surface of the pectoralis major m. and the clavicle | Ribs and intercostal muscles. Try to exclude the brachial plexus if visible | Medial border of the pectoralis minor m. | Clavicle and/or lateral border of CTVn_L4 |

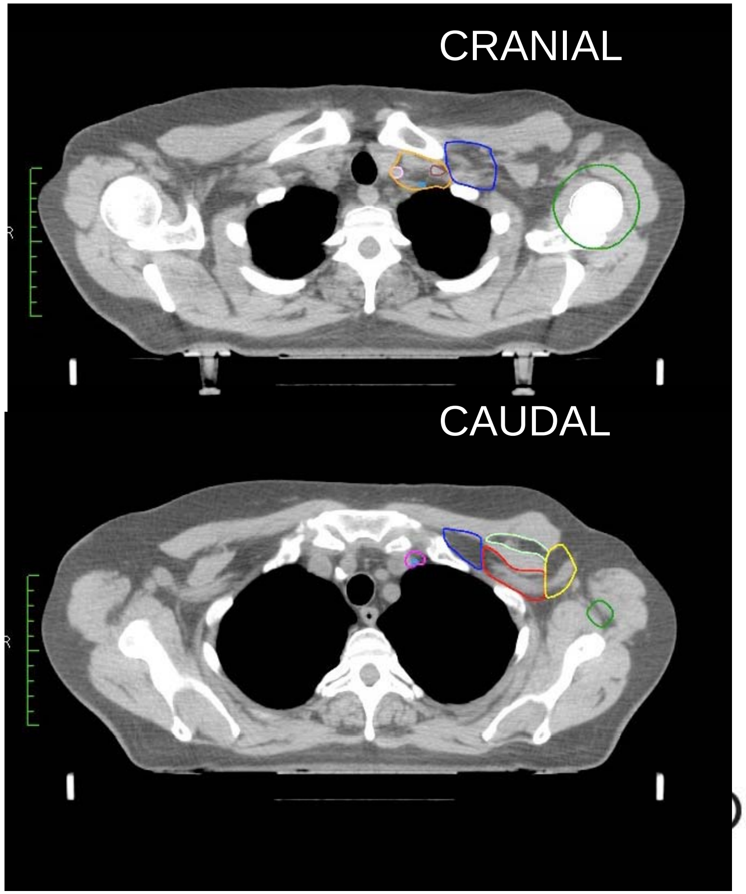


| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Axilla-level III | Pec. Minor m. insert on cricoid CORACOID | Axillary vessels cross medial edge of Pec. Minor m. d. | Posterior surface Pec. Major m. | Ribs and intercostal muscles | Medial border of Pec. Minor m. | Thoracic inlet |

| | | | | | | |
|---|---|---|---|---|---|---|
| Axilla level 3 CTVn_L3 | Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein) | 5 mm caudal to the subclavian vein. If appropriate: top of surgical ALND | Major pectoral muscle | Up to 5 mm dorsal of subclavian vein or to costae and intercostal muscles | Medial side of the minor pectoral muscle | Junction of subclavian and internal jugular veins – >level 4 |



# *CTV L2-L1: INDICATIONS*

- No or inadequate lymphadenectomy (L) **RT L4-L3-L2-L1**
- Bulky nodal disease
- SN (+) (Macrometastases) without lymphadenectomy

**AMAROS Trial (EORTC)** (Adjuvant Management of the Axilla Radiotherapy of Surgery) is comparing L vs axillary RT with SN (+).

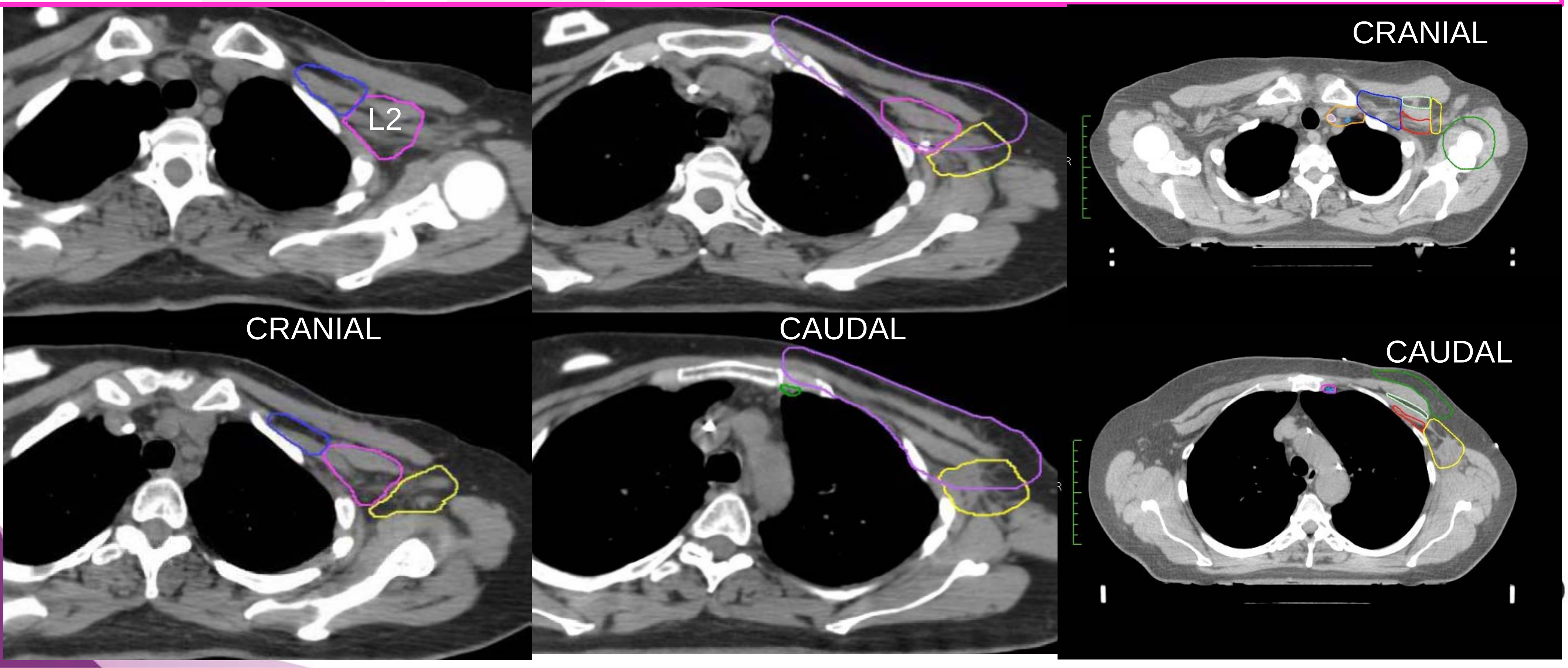
**RT L4-L3-L2-L1**

(Micrometastases: no RT)

**AMAROS** Donker 2014 Lancet Oncol

Including 4800 patients demonstrated that axillary RT is as effective as axillary surgery with less morbidity at 5 year follow-up.

| | Cranial | Caudal | Anterior | Posterior | Lateral | Medial |
|---|---|---|---|---|---|---|
| Axilla-level II | Axillary vessels cross medial edge of Pec. Minor m. | Axillary vessels cross lateral edge of Pec. Minor m. [c] | Anterior surface Pec. Minor m. | Ribs and intercostal muscles | Lateral border of Pec. Minor m. | Medial border of Pec. Minor m. |
| Axilla level 2 CTVn_L2 | Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein) | The caudal border of the minor pectoral muscle. If appropriate: top of surgical ALND | Minor pectoral muscle | Up to 5 mm dorsal of axillary vein or to costae and intercostal muscles | Lateral edge of minor pectoral muscle | Medial edge of minor pectoral muscle |



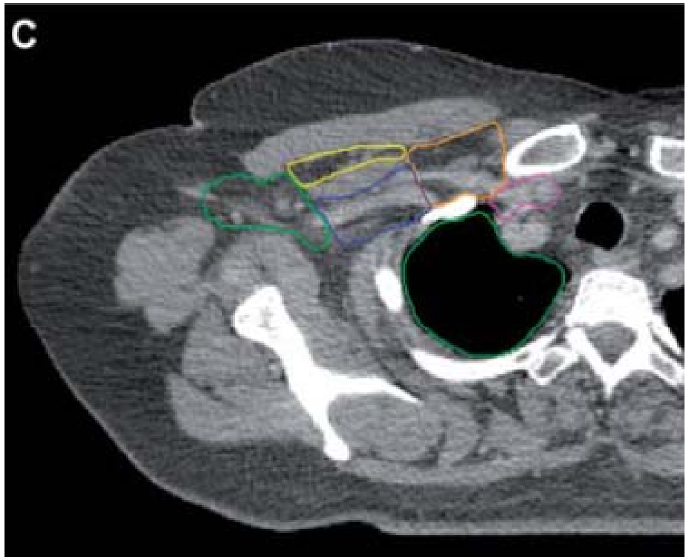
DCBG guidelines for delineation of CTV of breast and CTVs of the regional lymph node regions

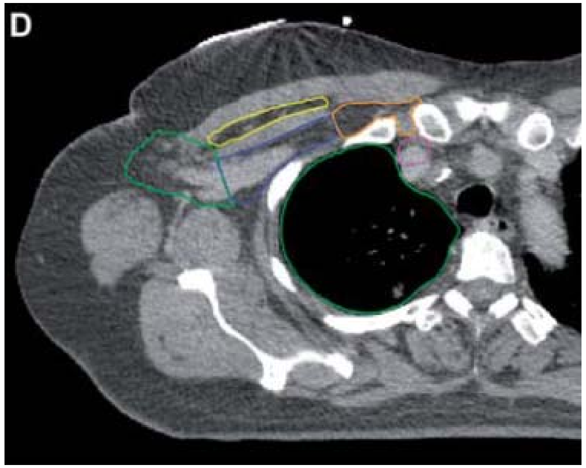
| LN region | cranial | caudal | ventral | dorsal | lateral | medial |
|---|---|---|---|---|---|---|
| Level II | 5 mm cranial to the axillary vessels | Caudal edge of m. pectoralis minor | Dorsal surface of m. pectoralis minor | Chest wall, 5 mm dorsal of the axillary vessels | Lateral border of m. pectoralis minor | Medial border of m. pectoralis minor |

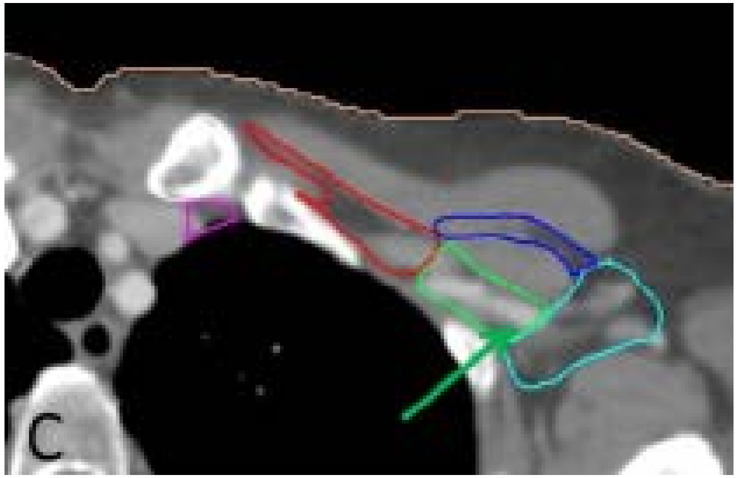
*DBCG guidelines*

| | | | | | | |
|---|---|---|---|---|---|---|
| Level II of the axilla CTVn_L2 | When the axillary A. crosses the medial edge of the pectoralis minor m. | 5 mm below the axillary vein when it crosses the lateral border of the pectoralis minor m. | Dorsal surface of the pectoralis minor m. | visible Ribs and intercostal muscles | Lateral border of the pectoralis minor m. | Medial border of the pectoralis minor m. |

PROCAB guidelines

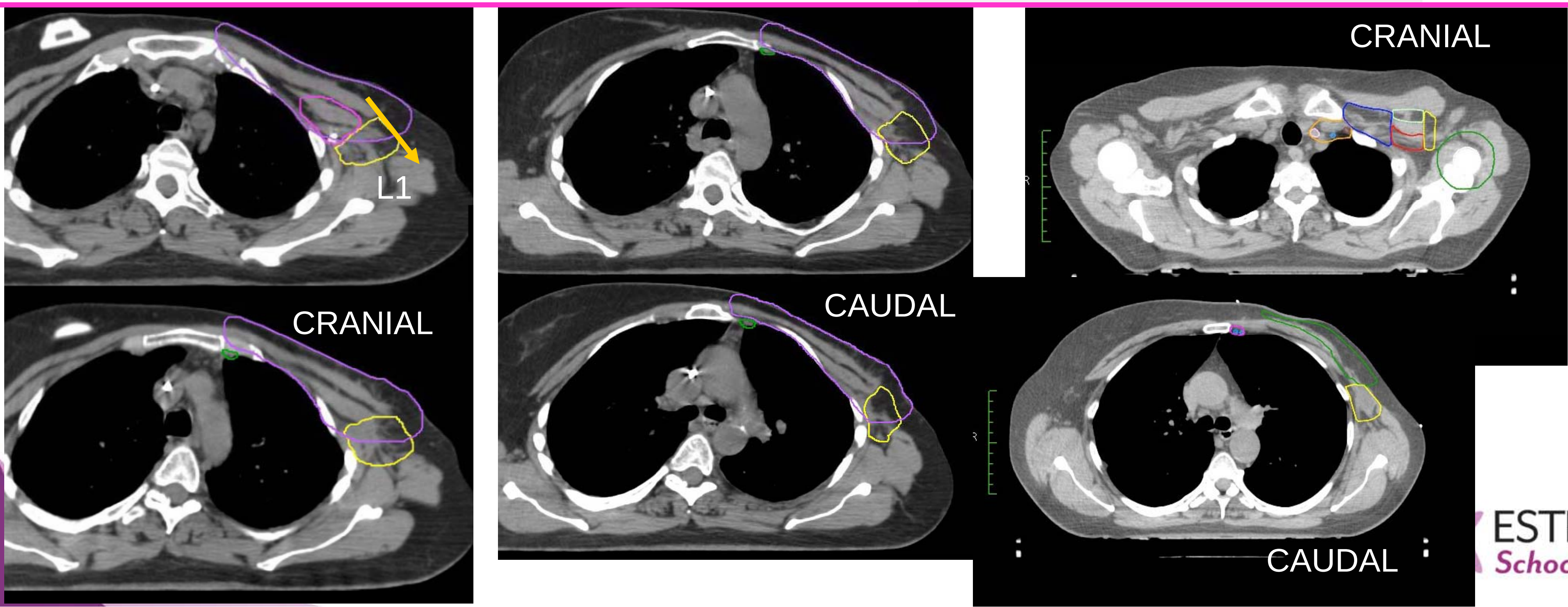


| | *Cranial* | *Caudal* | *Anterior* | *Posterior* | *Lateral* | *Medial* |
|---|---|---|---|---|---|---|
| Axilla-Level I | Axillary vessels cross lateral edge of Pec. Minor m. | Pectoralis (Pec.) major muscle insert into ribs [b] | Plane defined by: anterior surface of Pec. Maj. m. and Lat. Dorsi m. | Anterior surface of subscapularis m. | Medial border of lat. dorsi m. | Lateral border of Pec. minor m. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Axilla level 1 CTVn_L1 | 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 | To the level of rib 4 – 5, taking also into account the visible effects of the sentinel lymph node biopsy | Pectoralis major & minor muscles | Cranially up to the thoraco-dorsal vessels, and more caudally up to an imaginary line between the anterior edge of the latissimus dorsi muscle and the intercostal muscles | Cranially up to an imaginary line between the major pectoral and deltoid muscles, and further caudal up to a line between the major pectoral and latissimus dorsi muscles | Level 2, the interpectoral level and the thoracic wall |



2016

# Letter to the Editor

Radiotherapy and Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

## ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1 ☆

### Dose to CTVn_L1

In the consensus guideline a planning risk volume (PRV) around the humeral head is advised to help dose planning so that the resulting field edge (i.e. the 50% isodose line) follows the humeral head. This may cause a need for compromise on dose coverage of the lateral part of CTVn_L1 and sometimes also of CTVn_L2, which

viously used, which can be avoided by defining the PRV around the humeral head. Fig. 1D illustrates suggestions for RT planning

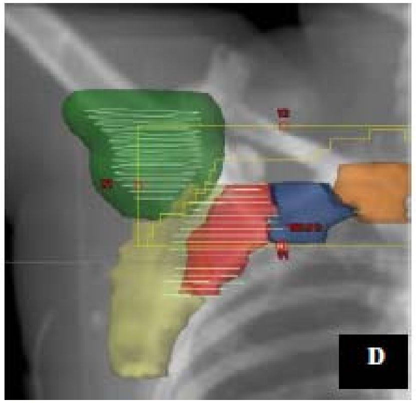



Fig. 1D. Position of field edge in a patient where CTVn_L1 is not included in the RT fields.

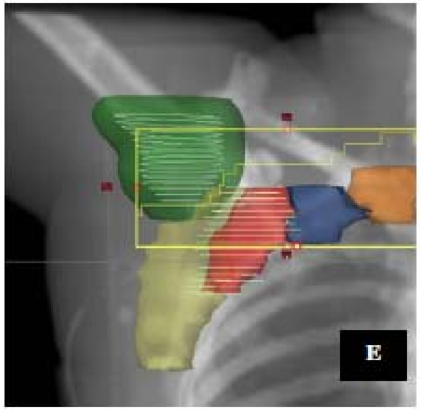



Fig. 1E. Position of field edge in a patient where CTVn_L1 is included in the RT fields with a compromise to shield the humeral head.

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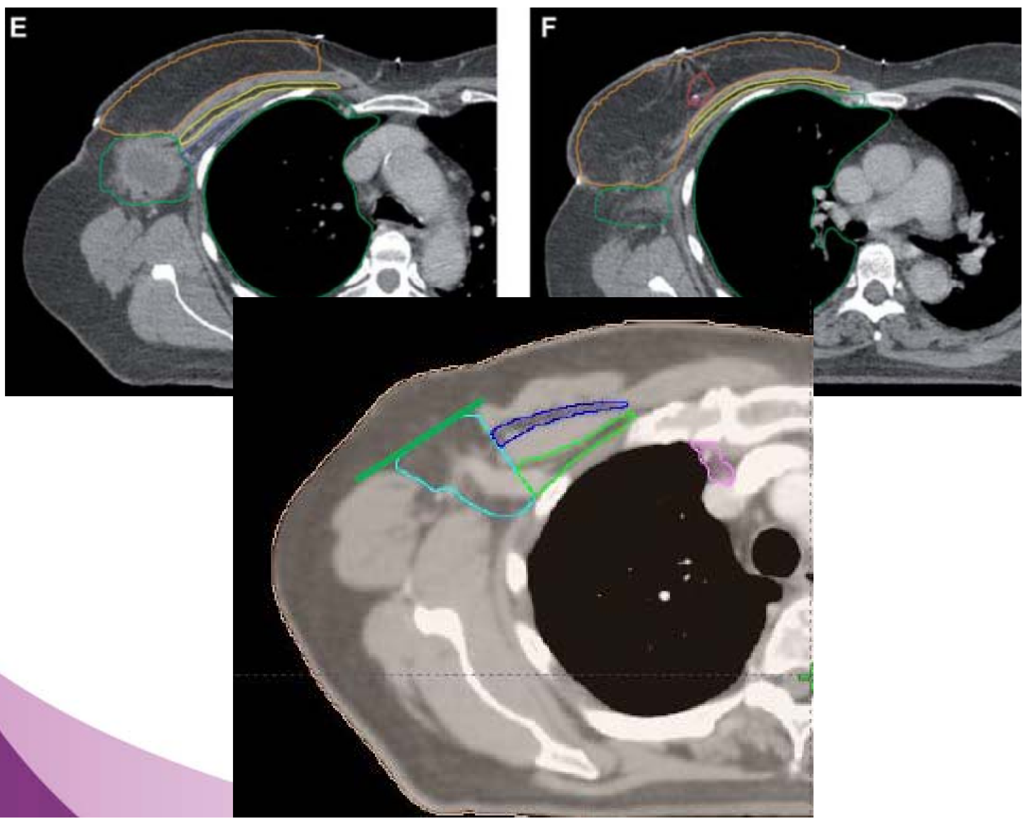
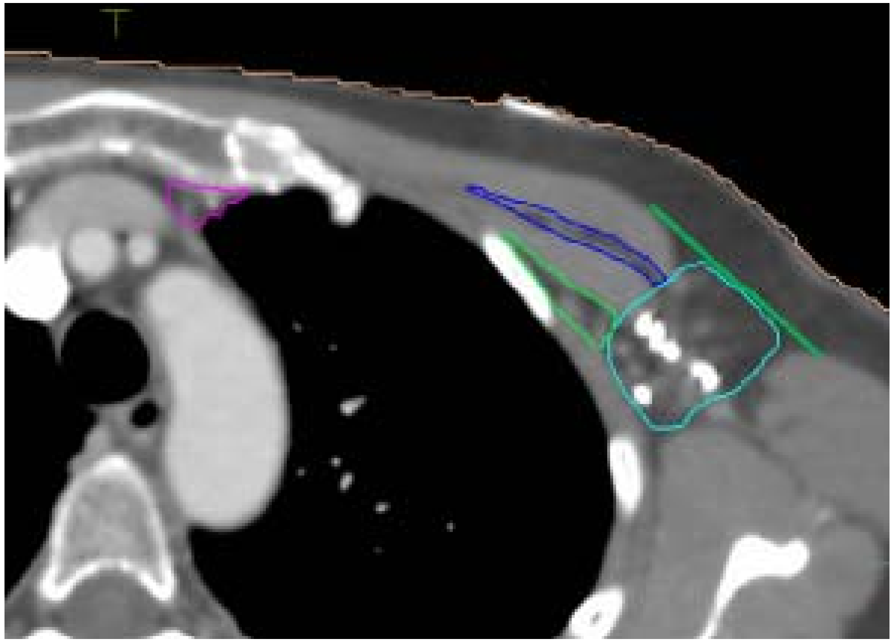
DCBG guidelines for delineation of CTV of breast and CTVs of the regional lymph node regions

| LN region | cranial | caudal | ventral | dorsal | lateral | medial |
|---|---|---|---|---|---|---|
| Level I *DBCG guidelines* | 1 cm below caput humeri | Free edge of m. pectoralis major including seroma | 5 mm below the skin | M. latissimus dorsi, 5 mm dorsal of the axillary vessels | Maximal to 5 mm below the skin | CTV-breast, lateral border of m. pectoralis minor, m. biceps brachii |
| Level I of the axilla CTVn_L1 PROCAB guidelines | The top of the axillary artery where it crosses the lateral edge of the pectoralis minor muscle or 5 mm above the axillary vein, including clips and seroma | Around 4th–5th rib and guided by the clips and/or seroma if present | Not external to the 'imaginary' line between the anterior surface of pectoralis major muscle and latero-anterior border of the deltoid muscle (cranially) and the latissimus dorsi muscle (caudally), but include seroma and/or clips | Lateral border of the pectoralis major and minor muscle and the thoracic wall | Up to the 'imaginary line' connecting the anterior border of the subscapular m and the anterior border of the deltoid or latissimus dorsi muscle, so excluding the subscapular vessels | |



# *CTV IM: INDICATIONS*

- Controversy
- IN FAVOR: ↓ LR

  *Freedman / Gustave-Roussy / Veronessi / Host*
- AGAINST: No ↓ LR, fibrosis, cardiotoxicity

  *Fowble / Obedian*

RT IM if SN (+) (histologically confirmed) in IM

Locally advanced disease, medial tumour with positive axillary nodes

**Trials: EORTC 22922 /** Canadian **NCIC MA20**

Budach et al. Radiation Oncology (2015) 10:258
DOI 10.1186/s13014-015-0568-4
Radiation Oncology

RESEARCH Open Access

Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update

Wilfried Budach[1*], Edwin Bölke[1], Kai Kammers[2], Peter Arne Gerber[3], Carolin Nestle-Krämling[4] and Christiane Matuschek[1]

Budach et al. Radiation Oncology 2013, 8:267
http://www.ro-journal.com/content/8/1/267
RADIATION ONCOLOGY

RESEARCH Open Access

Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials

Wilfried Budach[1*], Kai Kammers[2], Edwin Boelke[1] and Christiane Matuschek[1]

# *EORTC, MA.20, French*

**Meta-analysis concludes that RT to IM and SC statistically improve DFS and OS in I-III stages of BC.**

**Overall, it has to recommend including IM in locally advanced tumours.**

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2015;373:317-27.
DOI: 10.1056/NEJMoa1415369

ORIGINAL ARTICLE

# Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

P.M. Poortmans, S. Collette, C. Kirkove, E. Van Limbergen, V. Budach, H. Struikmans, L. Collette, A. Fourquet, P. Maingon, M. Valli, K. De Winter, S. Marnitz, I. Barillot, L. Scandolaro, E. Vonk, C. Rodenhuis, H. Marsiglia, N. Weidner, G. van Tienhoven, C. Glanzmann, A. Kuten, R. Arriagada, H. Bartelink, and W. Van den Bogaert, for the EORTC Radiation Oncology and Breast Cancer Groups*

4004 patients

Randomized between RT IMC and Medial SC nodes or no RT.

PATIENTS

From July 1996 through January 2004, a total of 4004 patients were enrolled at 46 institutions in 13 countries. Eligibility criteria included unilateral histologically confirmed breast adenocarcinoma of stage I, II, or III with a centrally or medially located primary tumor, irrespective of axillary involvement, or an externally located tumor with axillary involvement. Eligible patients had undergone mastectomy or breast-conserving surgery and axillary dissection. During the last years of the trial, patients were eligible if they had undergone a sentinel-node biopsy followed by an axillary dissection in the case of a positive node.

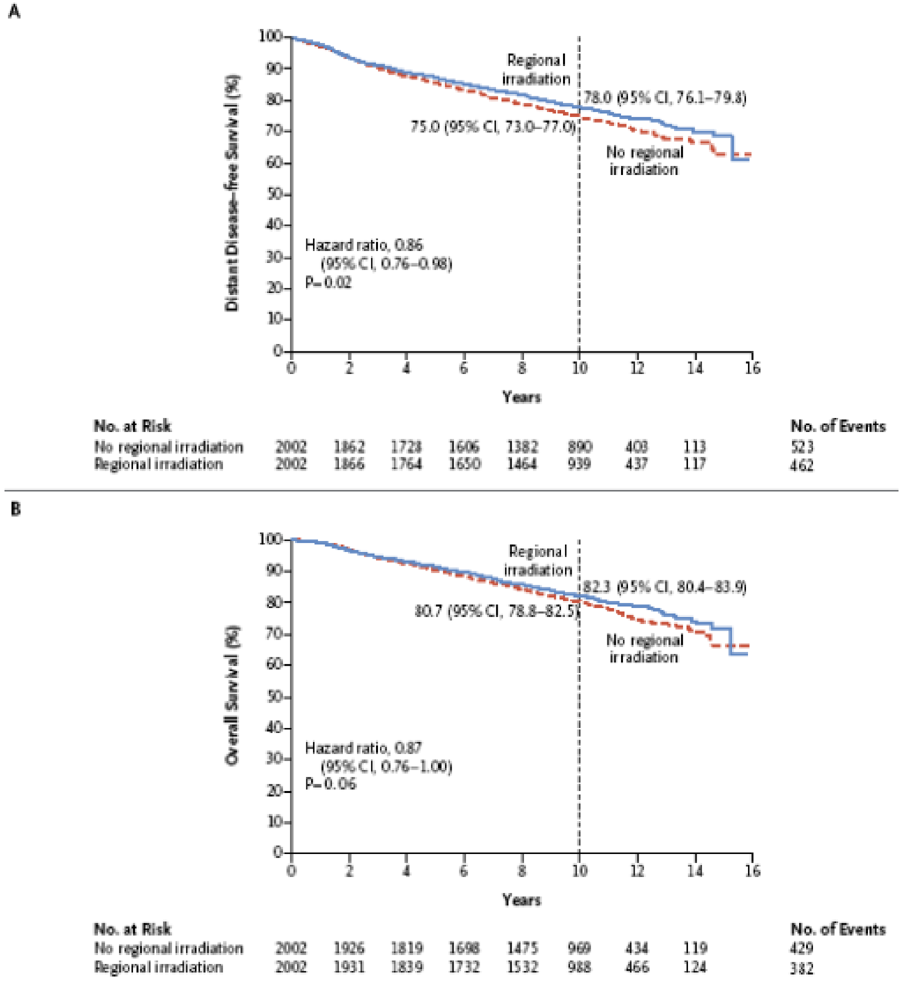



**Figure 2. Distant Disease-free and Overall Survival.**
Kaplan–Meier curves for survival free from distant disease (Panel A) and overall survival (Panel B) are shown.

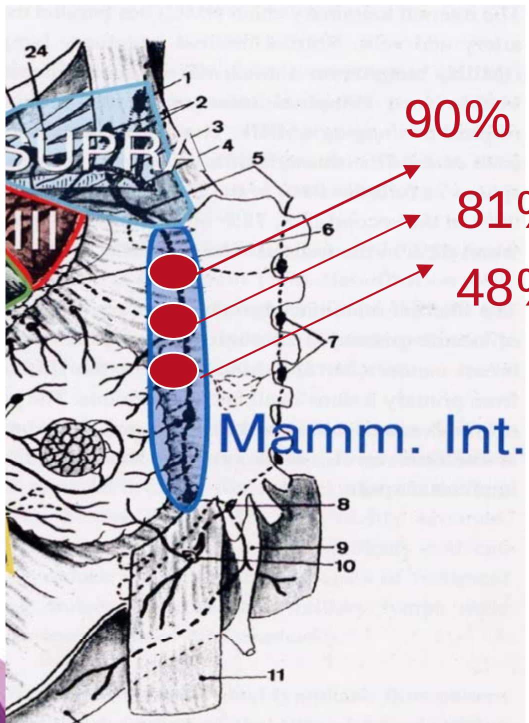
## CONCLUSIONS

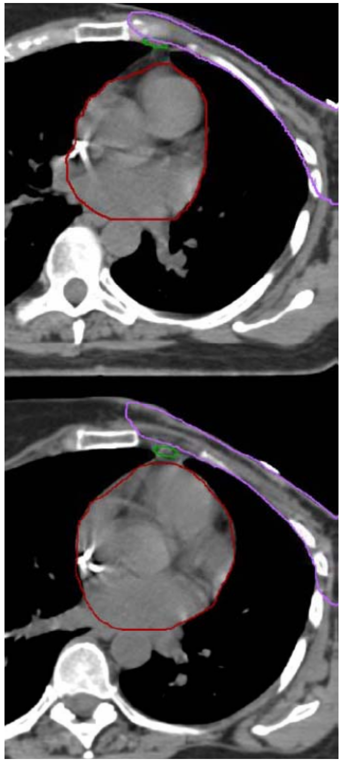
In patients with early-stage breast cancer, irradiation of the regional nodes had a marginal effect on overall survival. Disease-free survival and distant disease-free survival were improved, and breast-cancer mortality was reduced. (Funded by Fonds

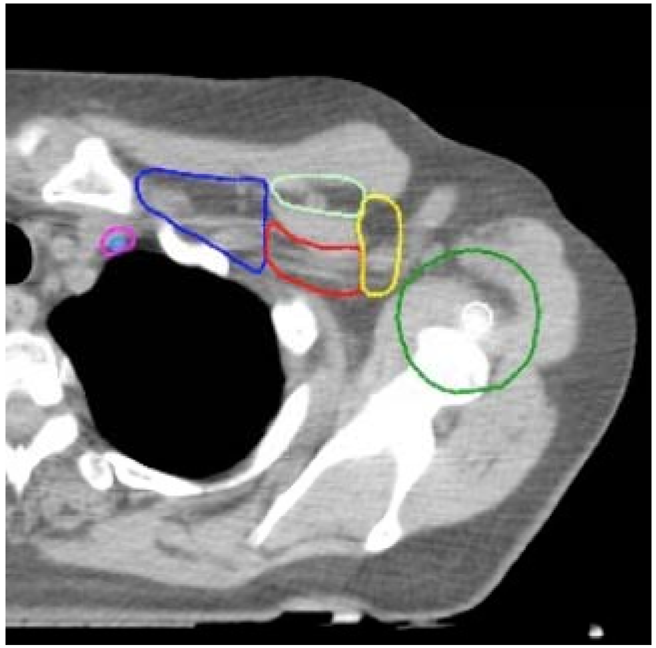
| | *Cranial* | *Caudal* | *Anterior* | *Posterior* | *Lateral* | *Medial* |
|---|---|---|---|---|---|---|
| Internal mammary | Superior aspect of the medial 1st rib. | Cranial aspect of the 4th rib | e. | e. | e. | e. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Internal mammary chain CTVn_IMN | Caudal limit of CTVn_L4 | Cranial side of the 4th rib (in selected cases 5th rib, see text) | Ventral limit of the vascular area | Pleura | 5 mm from the internal mammary vein (artery in cranial part up to and including first intercostal space) | 5 mm from the internal mammary vein (artery in cranial part up to and including first intercostal space) |

Most IMN in first 3-4 intercostal spaces





2016

# Letter to the Editor

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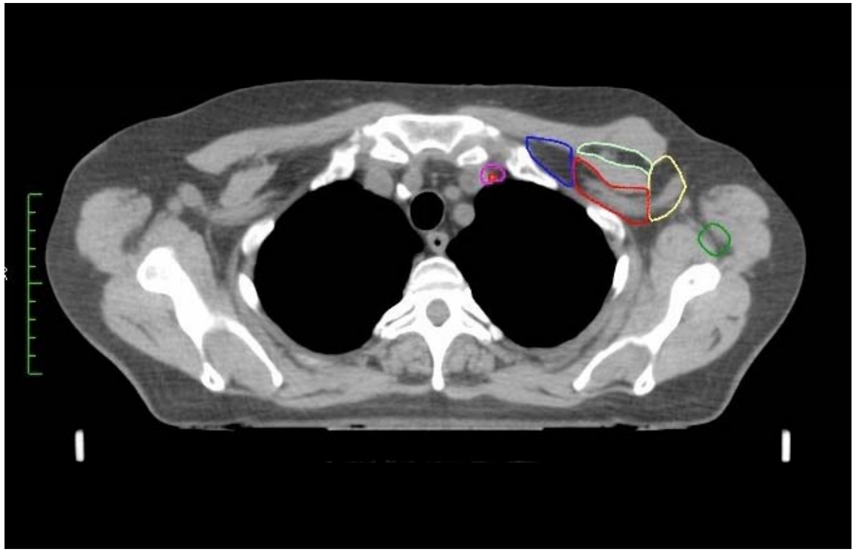
## ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1 ☆

### Lateral border of CTVn_IMN

Since lymph nodes are positioned equally frequent medial and lateral to the internal mammary vessels, the definition of CTVn_IMN is modified to include both the internal mammary vein and artery with 5 mm margin (Table 1) [2,3].



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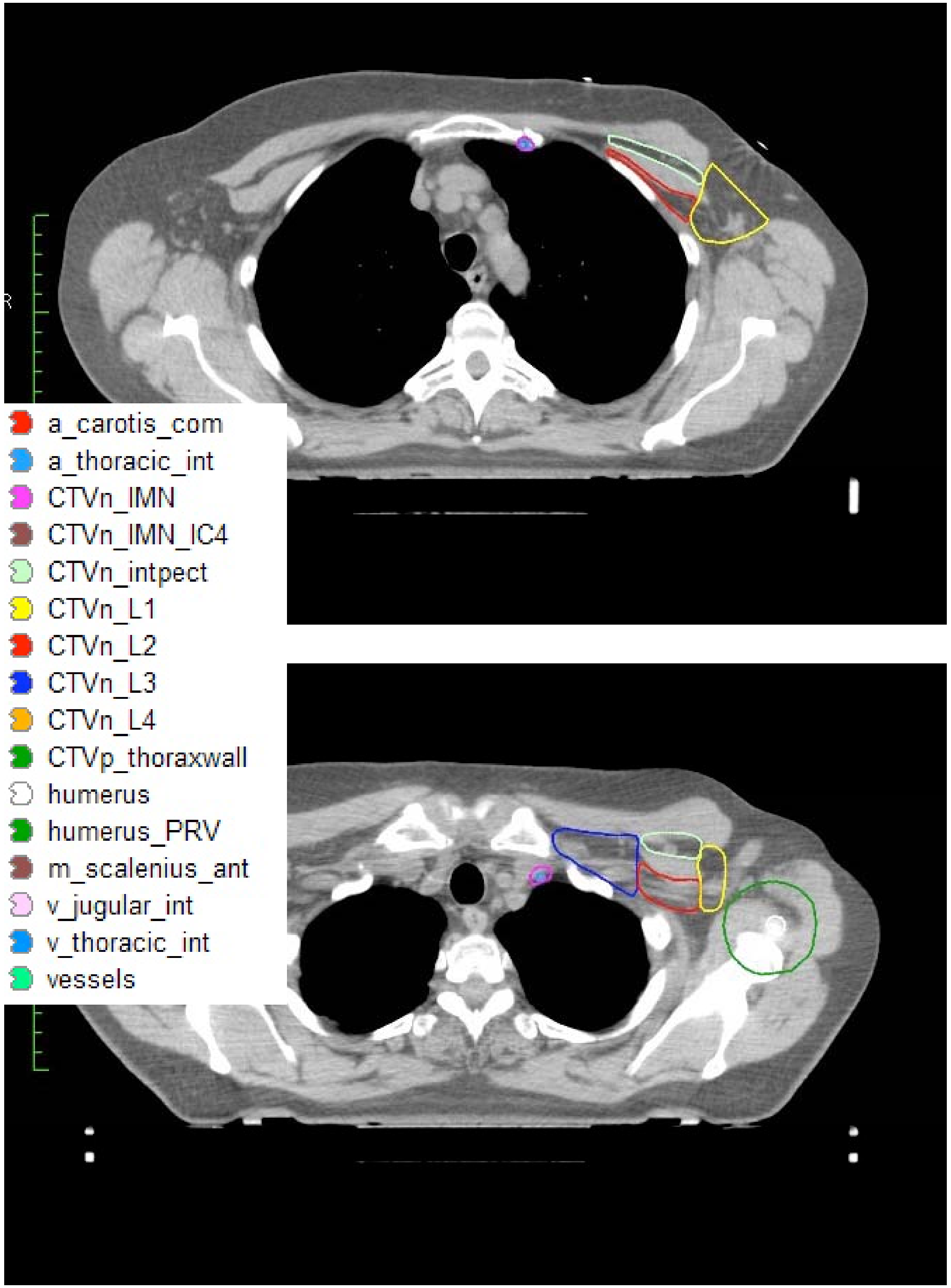
| Interpectoral nodes CTVn_interpectoralis | |
|---|---|
| Cranial | Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein) |
| Caudal | Level 2's caudal limit |
| Ventral | Major pectoral muscle |
| Dorsal | Minor pectoral muscle |
| Medial | Medial edge of minor pectoral muscle |
| Lateral | Lateral edge of minor pectoral muscle |




Interpectoral or Rotter lymph nodes: between pectoral major and minor

- Introduction

- Indications and CTV:
  - Whole Breast
  - Boost
  - Chest wall
  - Regional nodal
    - L4, L3, L2, L1, IM, Rotter

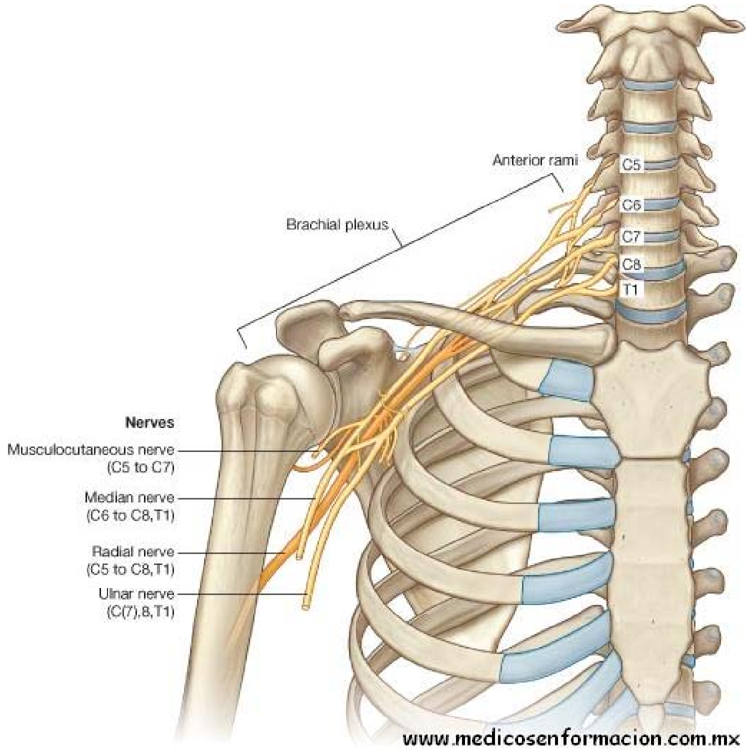
- **Organs at risk and constraints**

- Margins CTV → PTV    OAR → PRV

- Conclusions

# ORGANS AT RISK

- Lung
- Heart
- Contralateral breast
- Skin
- Humeral heads
- Spinal Cord
- Thyroid
- Brachial plexus

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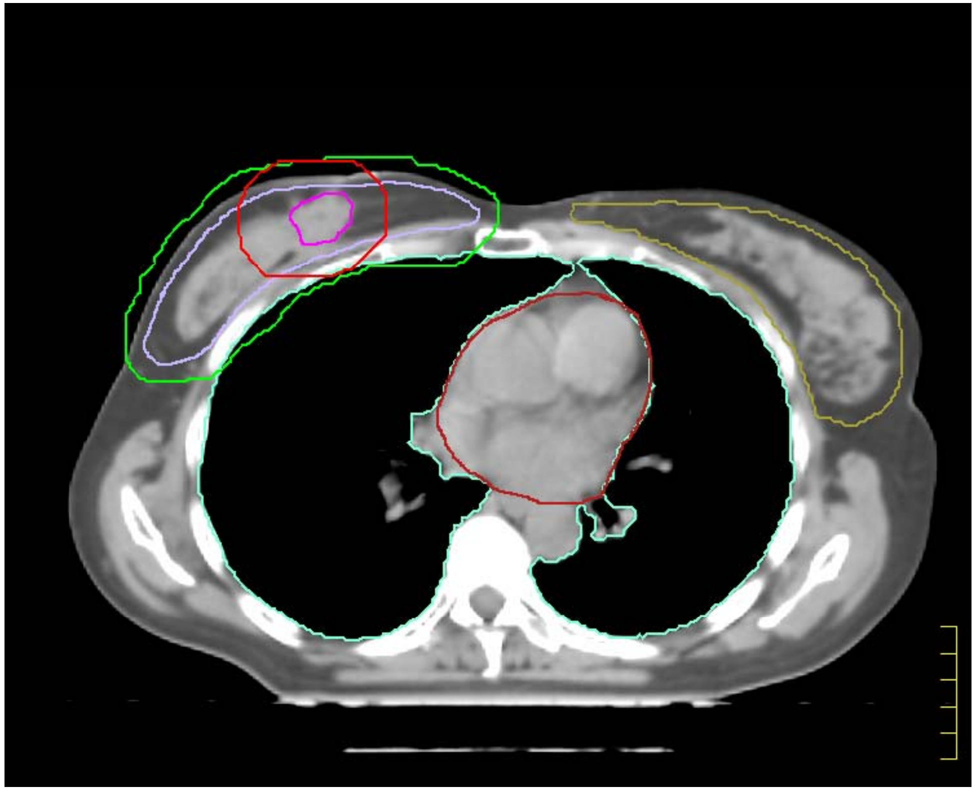
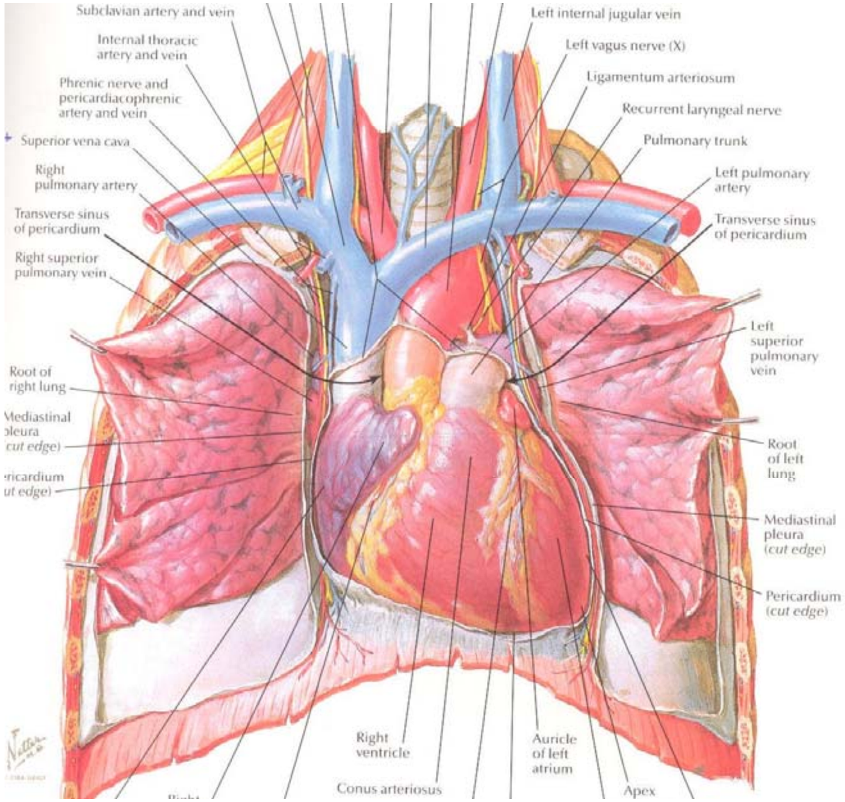
# *LUNG*

- Automatic delineation
- Both lungs should be evaluated as a single organ
- Pulmonary hila and trachea should be excluded



# HEART

- It begins below the left pulmonary artery
- The first cavity that you see is usually the left atrium
- Lower limit: peak myocardial
- The whole heart should be contoured apart from the pericardium
- The left anterior descending coronary artery should be outlined, if possible
- Pulmonary artery trunk, ascending aorta and superior vein cava should be excluded

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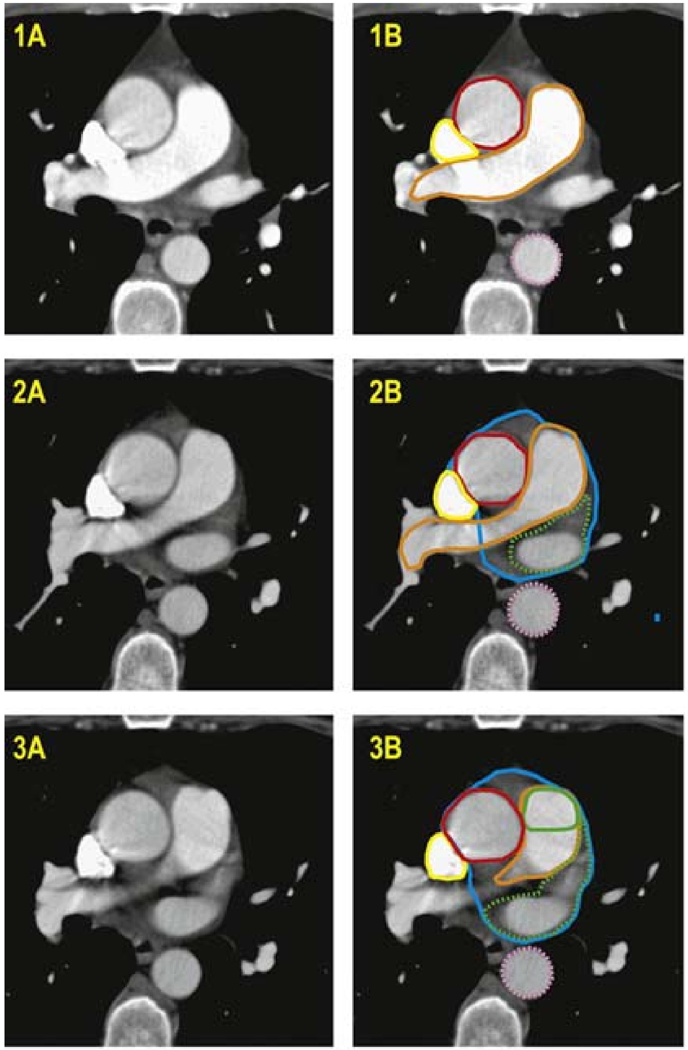
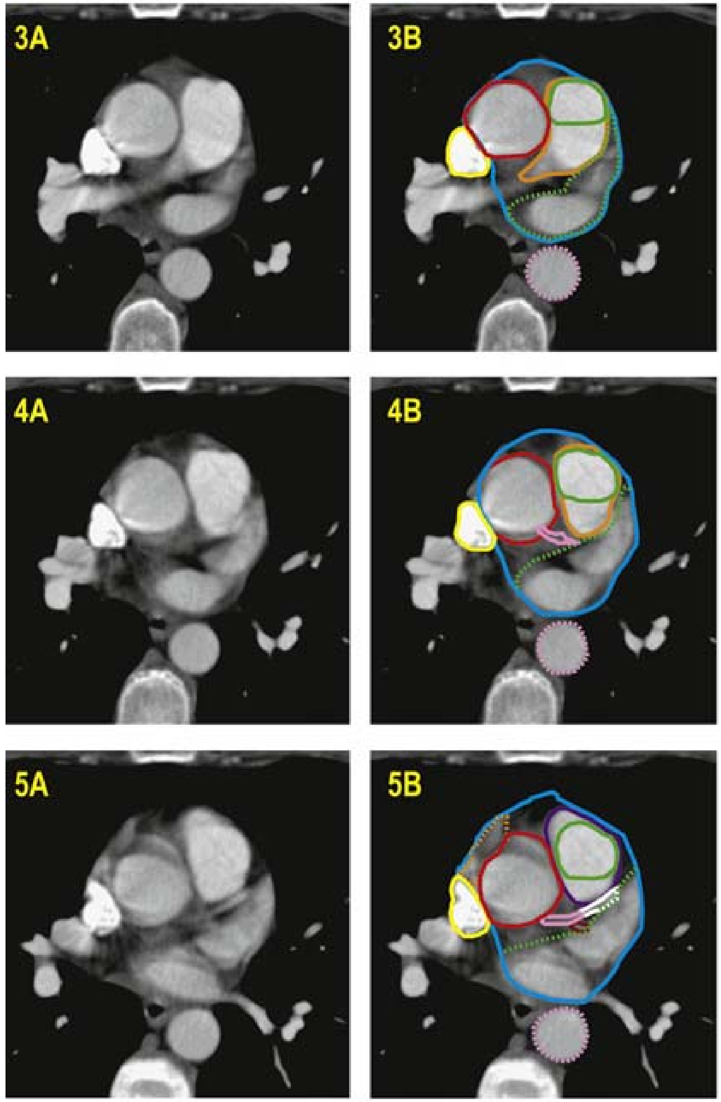



## University of Michigan Medical Center

**KEY**

- Heart
- Right atrium
- Left atrium
- Right ventricle
- Left ventricle
- Pulmonary artery
- Superior vena cava
- Descending aorta
- Ascending aorta
- Aortic valve
- Pulmonic valve
- Mitral valve
- Tricuspid valve
- Left main coronary artery
- Left anterior descending artery
- Left circumflex
- Right coronary artery
- AV node




*Int J Radiat Oncol Biol Phys.* 2011 January 1; 79(1): 10–18. doi:10.1016/j.ijrobp.2009.10.058.

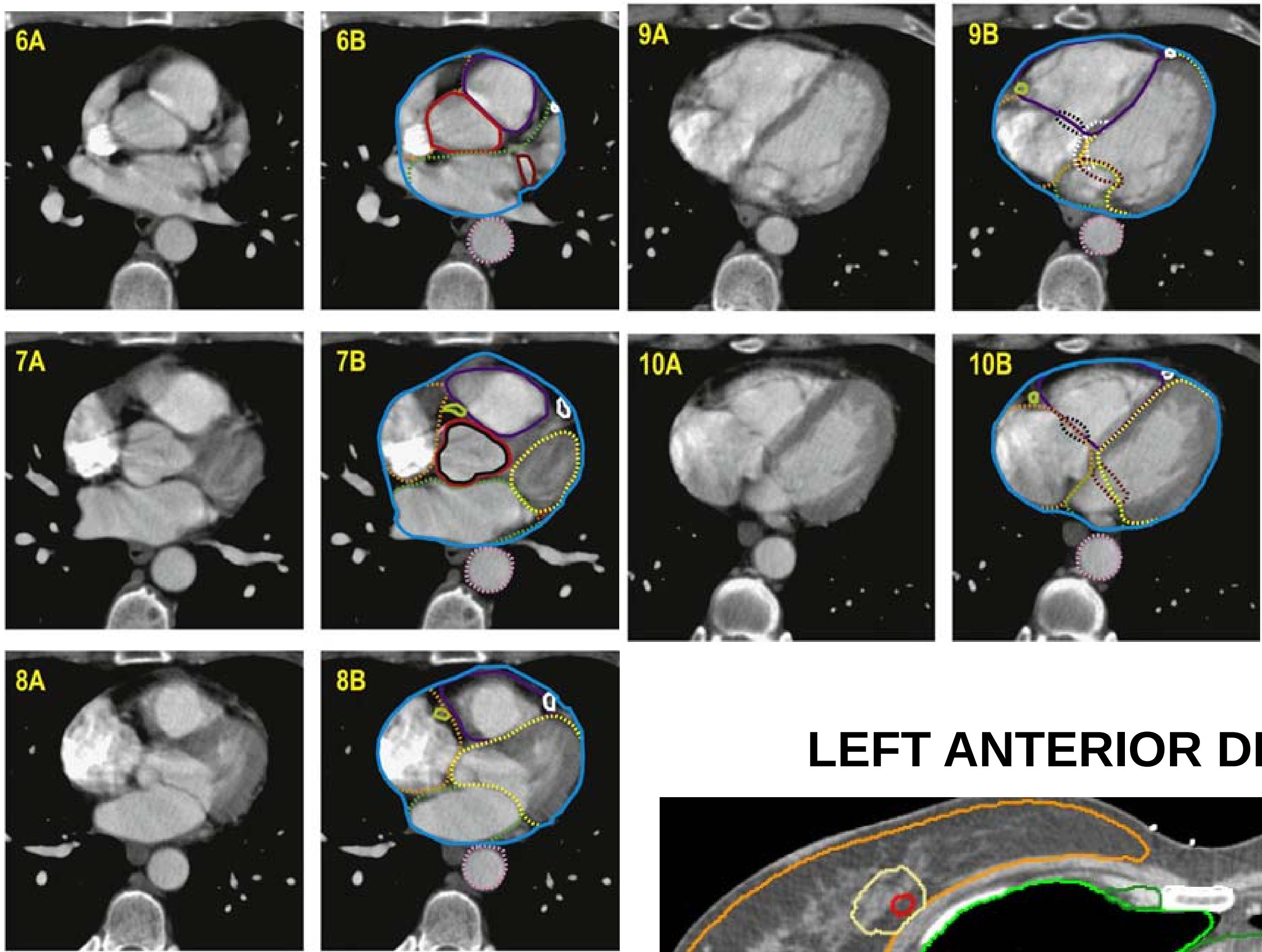
**Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer**

Mary Feng, M.D.[1], Jean M. Moran, Ph.D.[1], Todd Koelling, M.D.[2], Aamer Chughtai, M.D.[3], June L. Chan, M.D.[1], Laura Freedman, M.D.[1], James A. Hayman, M.D.[1], Reshma Jagsi, M.D., D. Phil.[1], Shruti Jolly, M.D.[1], Janice Larouere, M.D.[1], Julie Soriano, M.D.[1], Robin Marsh, C.M.D.[1], and Lori J. Pierce, M.D.[1]

[1] Department of Radiation Oncology, University of Michigan Medical Center

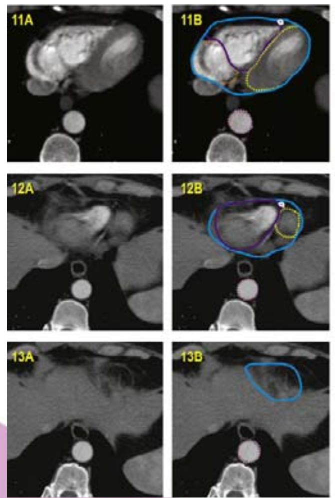
# First LEFT ATRIUM

# LEFT ANTERIOR DESCENDING ARTERY

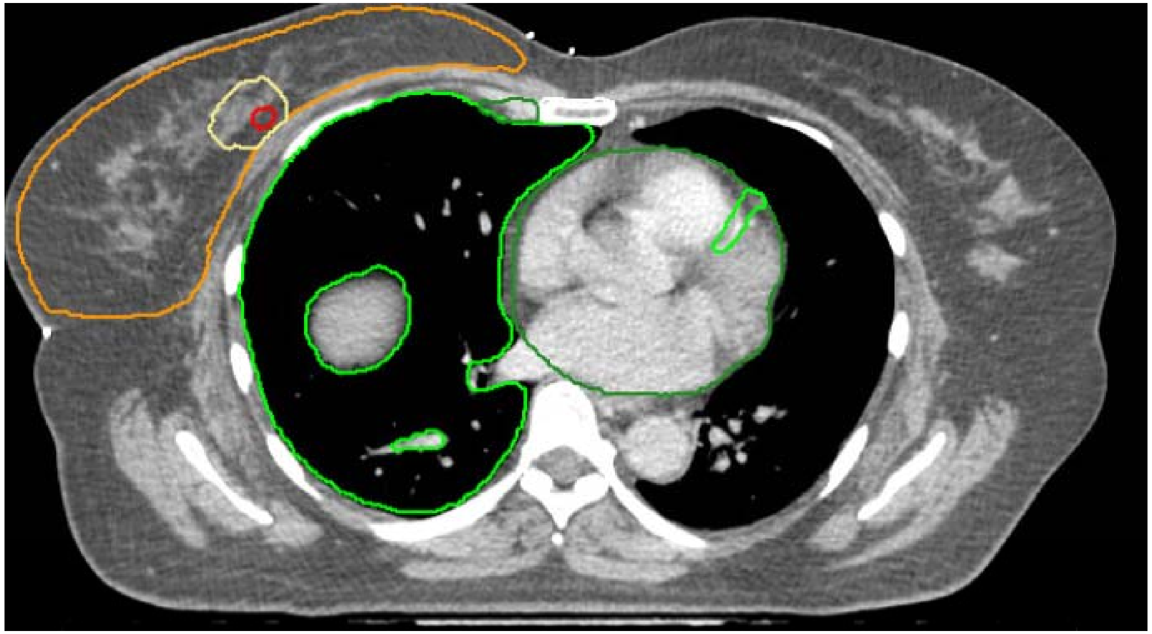



KEY

- Heart
- Right atrium
- Left atrium
- Right ventricle
- Left ventricle
- Pulmonary artery
- Superior vena cava
- Descending aorta
- Ascending aorta
- Aortic valve
- Pulmonic valve
- Mitral valve
- Tricuspid valve
- Left main coronary artery
- Left anterior descending artery
- Left circumflex
- Right coronary artery
- AV node




# LEFT ANTERIOR DESCENDING ARTERY



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# BRACHIAL PLEXUS

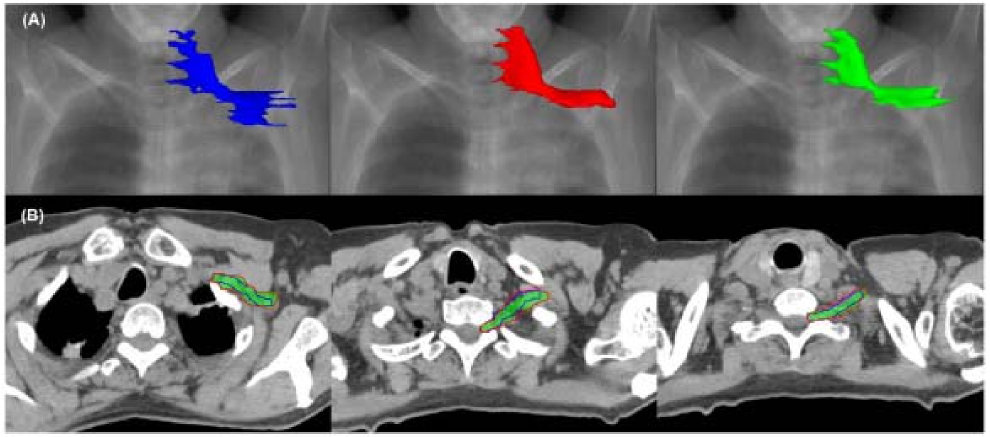
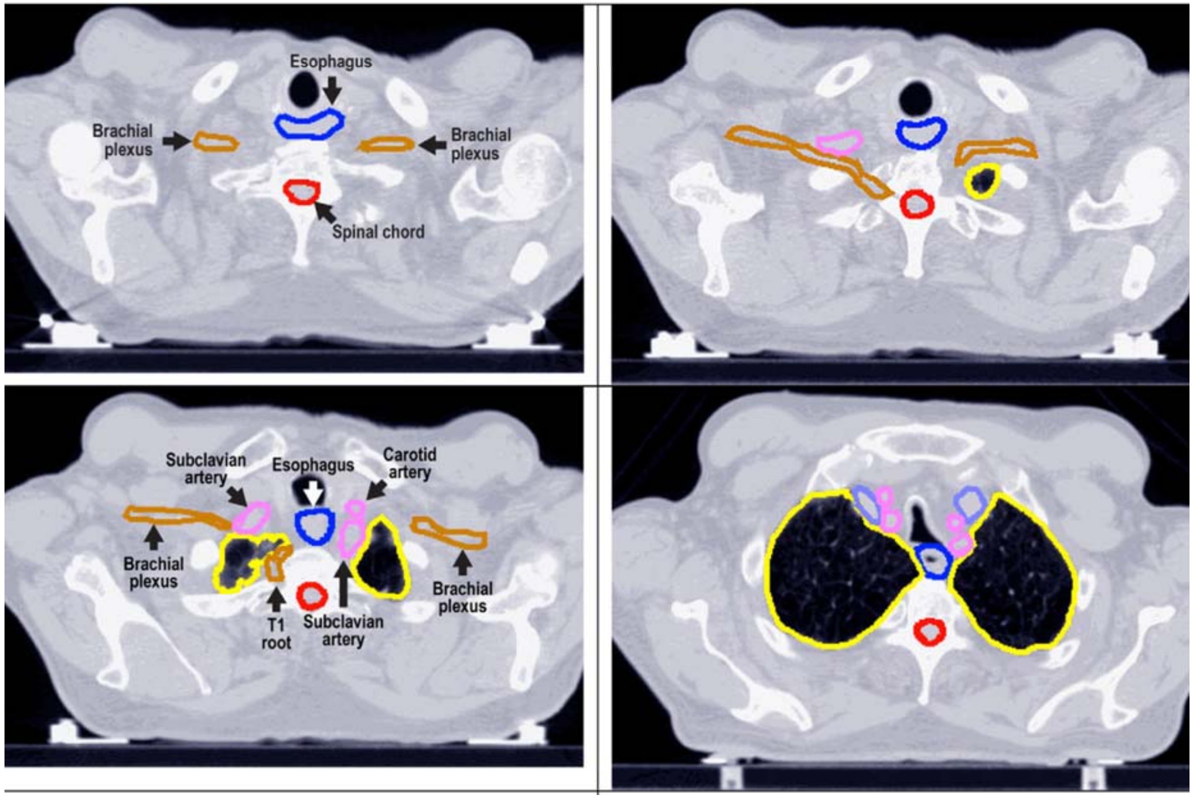



**Figure 2.**
Comparison of manual (blue), auto-segmented (red), and modified (green) contours in the (A) 3D surface view and (B) 2D axial slice view.




*Int J Radiat Oncol Biol Phys*. 2011 December 1; 81(5): 1442–1457. doi:10.1016/j.ijrobp.2010.07.1977.

*Pract Radiat Oncol*. 2013 October 1; 3(4): . doi:10.1016/j.prro.2013.01.002.

## Automatic contouring of brachial plexus using a multi-atlas approach for lung cancer radiotherapy

Jinzhong Yang, Ph.D.[1], Arya Amini, M.D.[2,3], Ryan Williamson, B.S.[1], Lifei Zhang, Ph.D.[1], Yongbin Zhang, M.S.[1], Ritsuko Komaki, M.D.[3], Zhongxing Liao, M.D.[3], James Cox, M.D.[3], James Welsh, M.D.[3], Laurence Court, Ph.D.[1], and Lei Dong, Ph.D.[1,4]

## 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 W. Hurkmans, Ph.D.[‖], Robert Timmerman, M.D.[#], Andrea Bezjak, M.D.[**], Jeffrey D. Bradley, M.D.[††], Benjamin Movsas, M.D.[‡‡], Lon Marsh, C.M.D.[*], Paul Okunieff, M.D.[§§], Hak Choy, M.D.[#], and Walter J. Curran Jr., M.D.[¶¶]

# CONSTRAINTS (Our Department)

Total volume of both ***lungs*** taken together V20<30%
Ipsilateral lung V20<20-25%, mean dose <15Gy
Contralateral lung V10<10% mean dose <5Gy

***Heart*** V20<10%, V25<10%, V45<30%, V50<20%

***Contralateral breast*** V10<10% mean dose <5Gy

***Humerus and ribcage*** maximum dose 50Gy

***Brachyal plexus*** maximum dose 60Gy

***Thyroid*** maximum dose 45Gy

***Spinal cord*** maximum dose 46Gy

Other: QUANTEC

- Introduction
- Indications and CTV:
  - Whole Breast
  - Boost. Partial Breast Irradiation
  - Chestwall
  - Regional nodal
    - L4, L3, L2, L1, IM, Rotter
- Organs at risk and constraints
- **Margins CTV → PTV OAR → PRV**
- Conclusions

5 mm

# CTV → PTV (Planning Target Volume)
# OAR → PRV (Planning Organs at Risk Volume)

ICRU (International Comission on Radiation Units and Mesuraments) 50 and 62

CTV margin for creating PTV:
- geometrical errors
- internal motion of CTV
- treatment technique (beam orientation)
- intra and interfractional errors (patient fixation, daily setup errors)

OAR margin for creating PRV: movements of the OAR due to the change in size and setup uncertainities

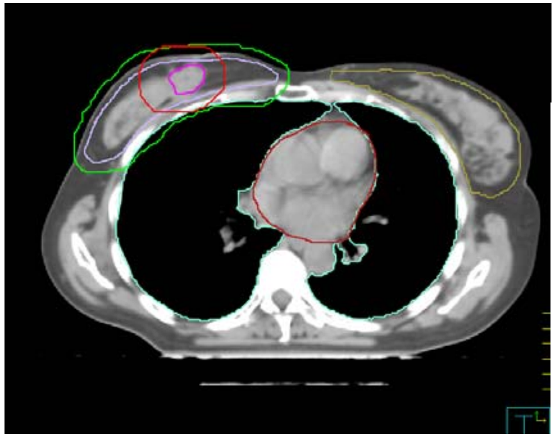
5 mm

# CTV → PTV (Planning Target Volume)
# OAR → PRV (Planning Organs at Risk Volume)

The recommended CTV margin to create PTV is at least 5 mm.

But, PTV outside skin can't be used for dosimetric calculations (air, outside the body ...). Typical solutions:

1. To crop PTV by 3 mm (without reaching the skin) but treatment planning carried out with 2-3 cm
2. To create PTV outside the body (margin for breathing) without croping → An additional "cropped" PTV volume will then be needed for normalization purposes and DVH analysis



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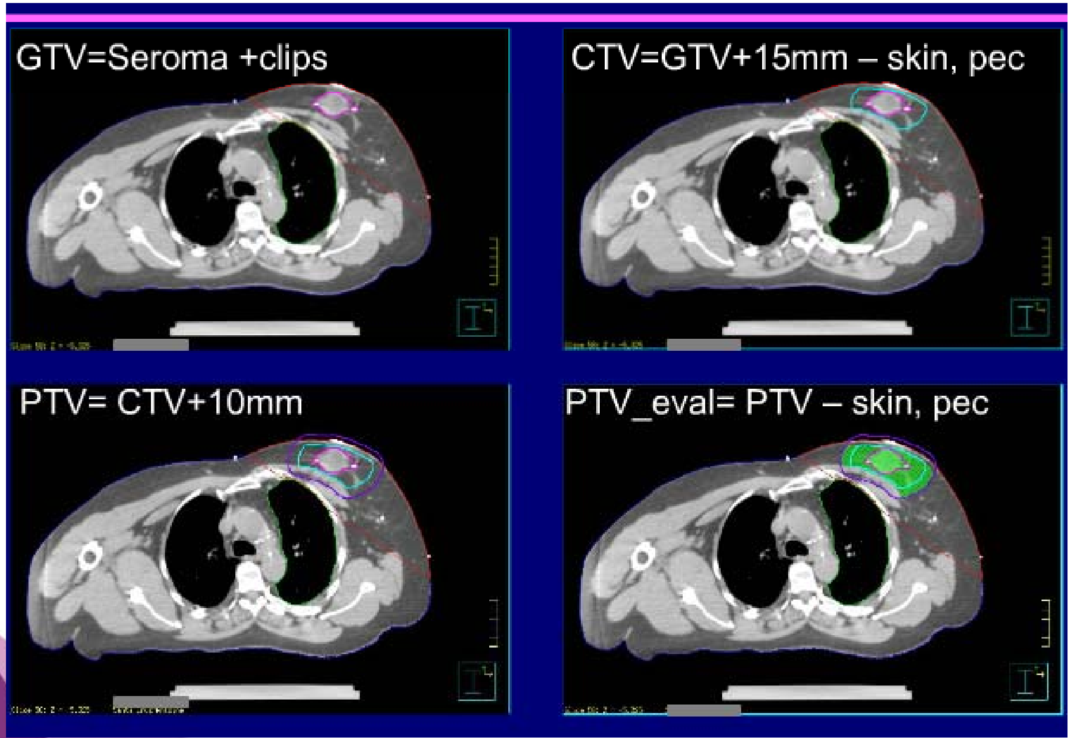
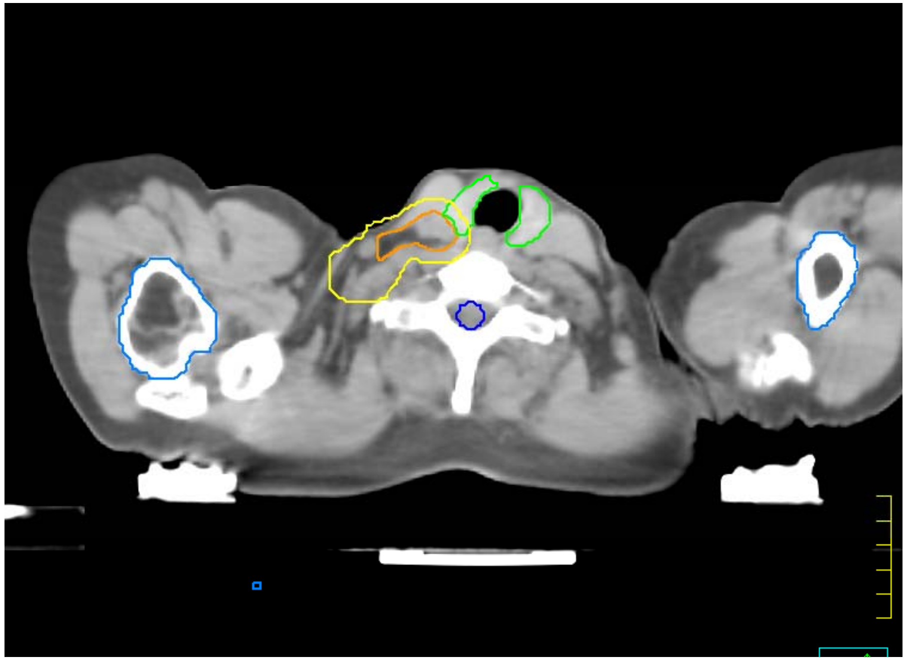
5 mm

# CTV → PTV (Planning Target Volume)
# OAR → PRV (Planning Organs at Risk Volume)

PTV Breast 5 mm, skin 3-5 mm
PTV Boost 5 – 10 mm, skin 3-5 mm
PTV Chest wall 5 mm, skin 0-5 mm
PTV Nodes 5 mm
PRV 5 mm

Avoid the lungs



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- Introduction
- Indications and CTV:
  - Whole Breast
  - Boost
  - Chest wall
  - Regional nodes
    - L4, L3, L2, L1, IM, Rotter
- Organs at risk and constraints
- Margins CTV → PTV     OAR → PRV
- **Conclusions**

# CONCLUSIONS

- Irradiation of breast cancer involves a variety of clinical situations and individualized treatment for each patient should be designed

- We need clear criteria for PTV and OAR delineation. There are several guidelines (RTOG, DCBCG, PROCAB, ESTRO) to help us to delineate CTV in breast cancer

- We need adequate positioning, immobilization and verification systems

<u>Proper volumes delineation is CRUCIAL</u>

# QUICK GUIDE

**Breast or chest wall:**

**CRANIAL:** Clinical reference, maximally up to inferior edge sterno-clavicular joint

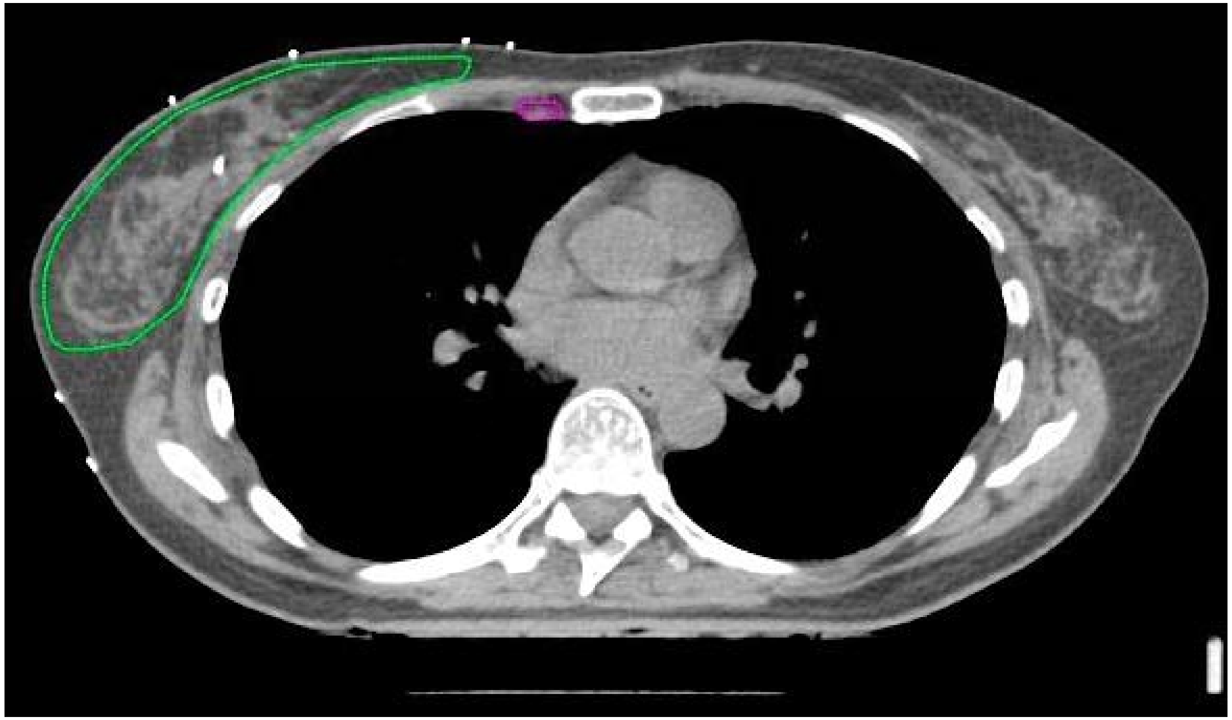
**CAUDAL:** Breast end (chest wall: guided by contralateral breast)

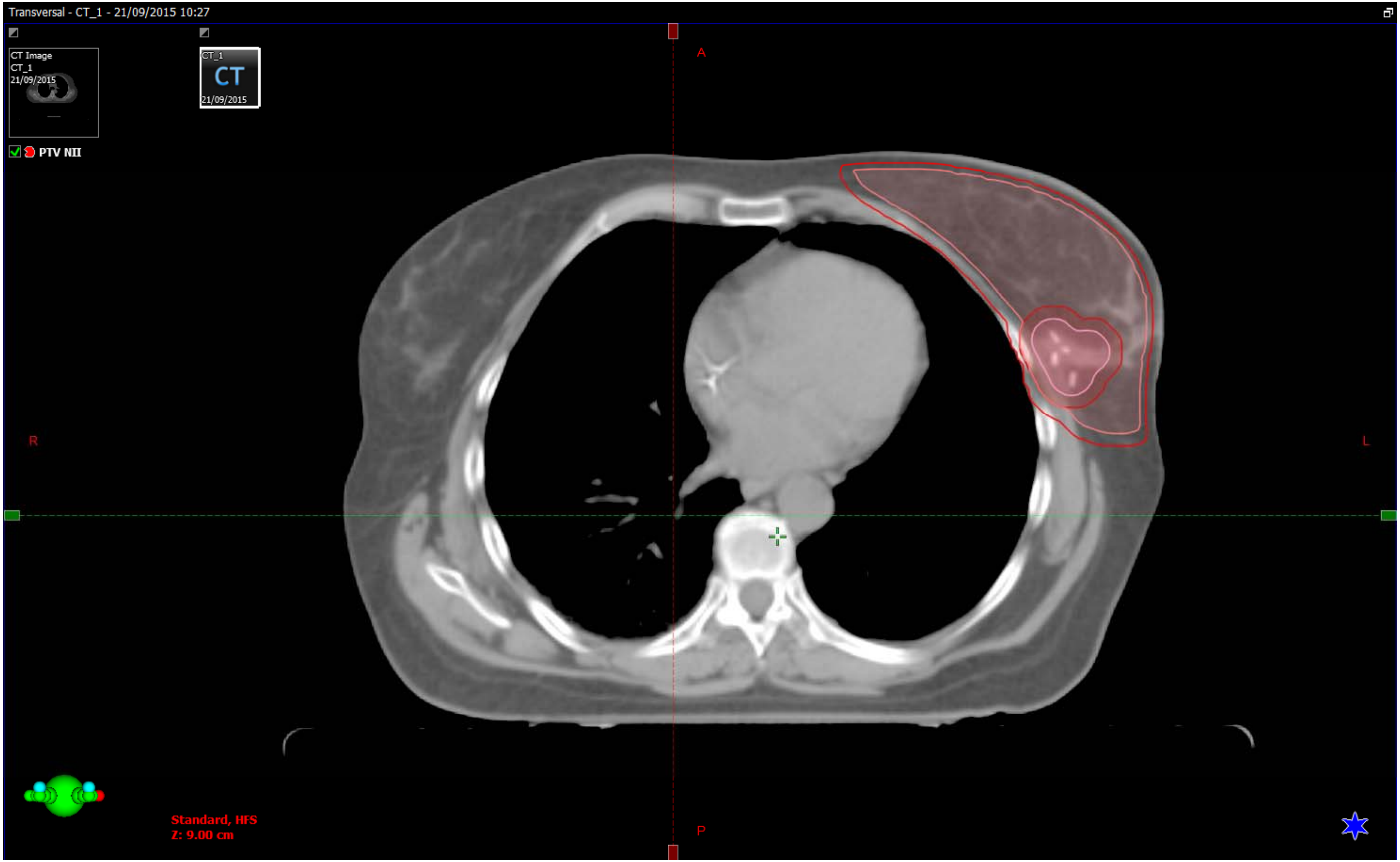
**ANT:** 5 mm skin or skin (RTOG)

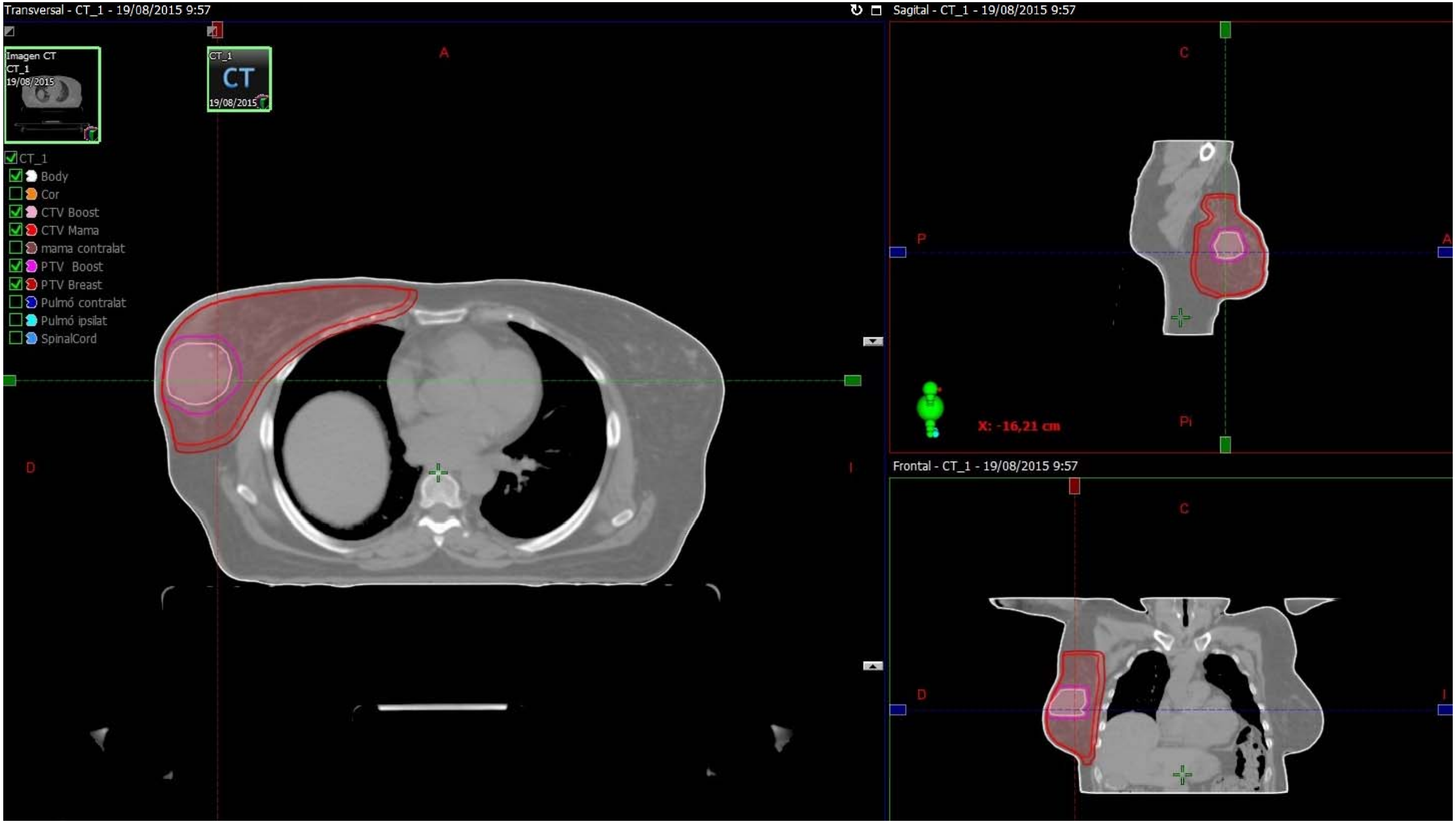
**POST:** Pectoral M, intercostal muscle or ribs, or include both (Chest Wall) (RTOG)

**LAT:** Clinical reference, anterior to the lateral thoracic artery

**MEDIAL:** Sternal-rib junction




Transversal - CT_1 - 21/09/2015 10:27
CT Image
CT_1
21/09/2015
CT_1
CT
21/09/2015
PTV NII
A
R
L
P
Standard, HFS
Z: 9.00 cm

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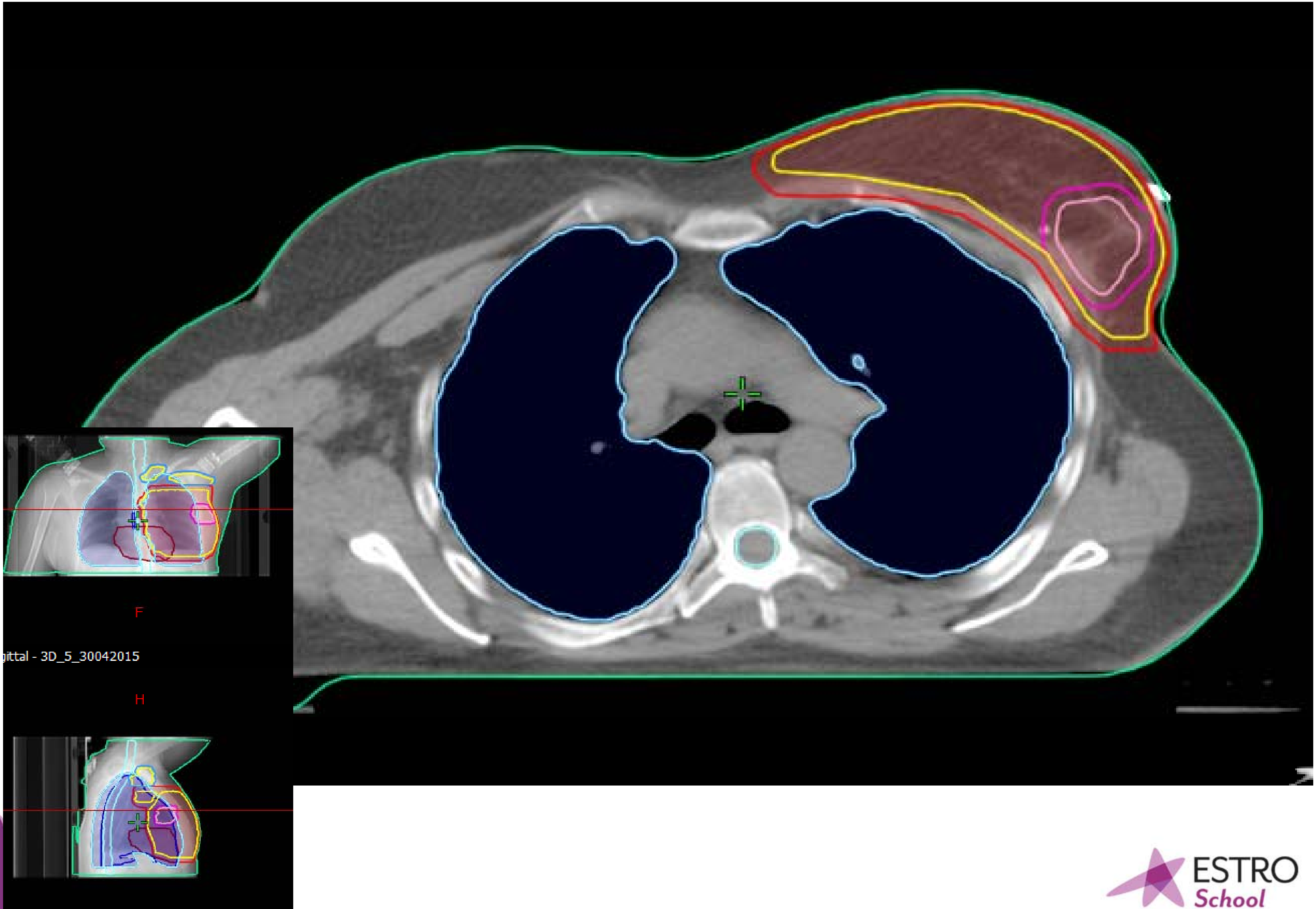
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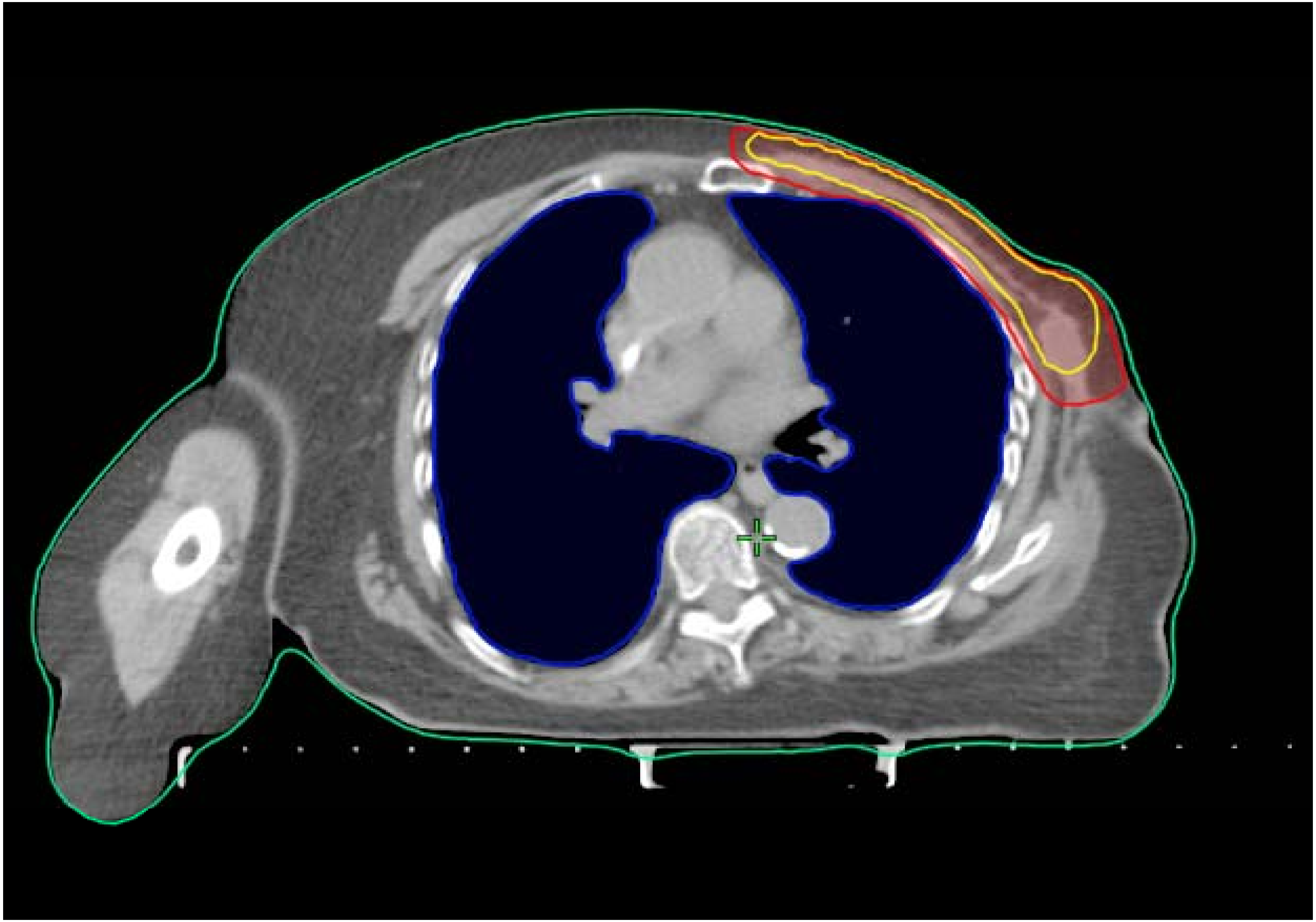
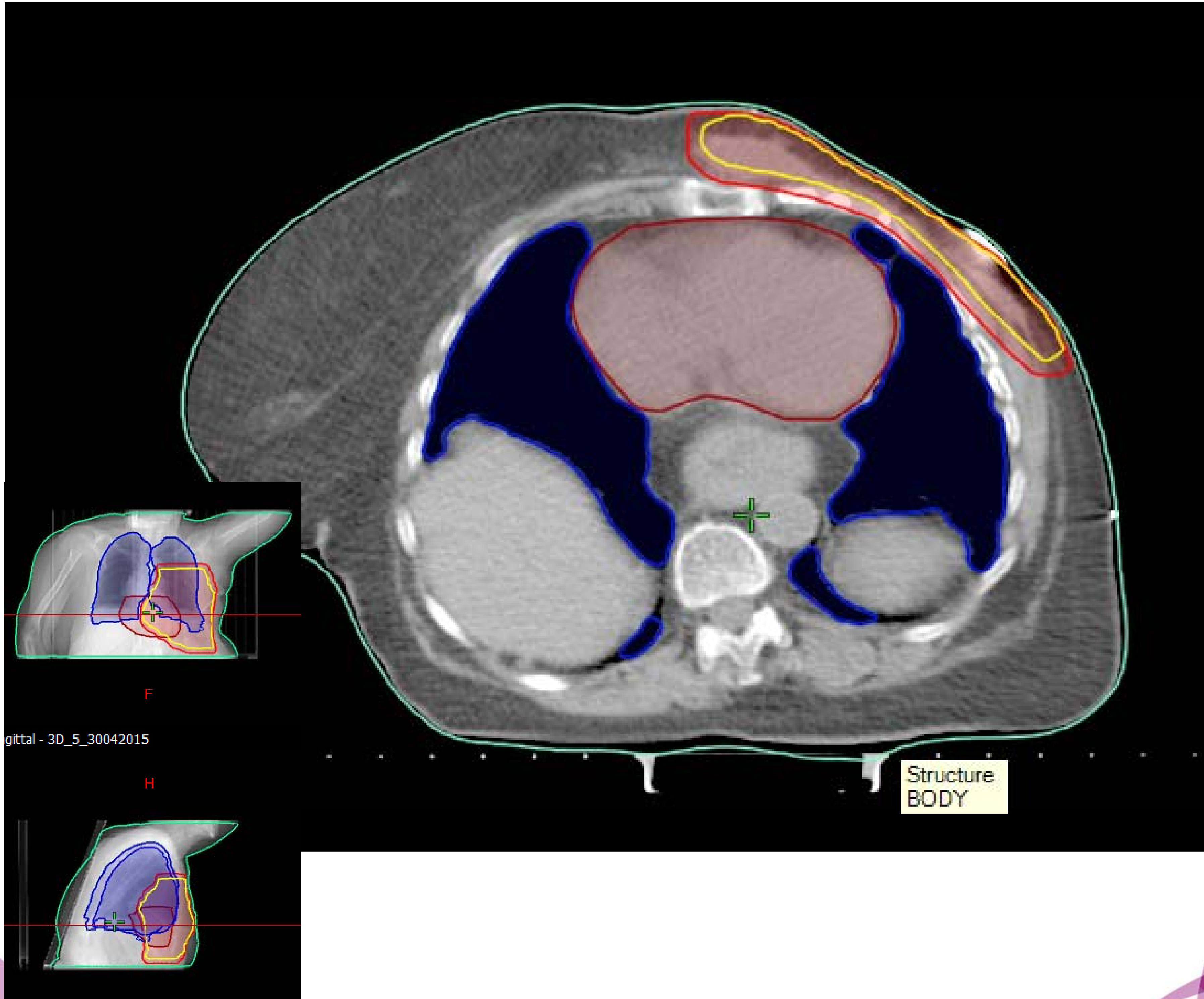
gittal - 3D_5_30042015
H

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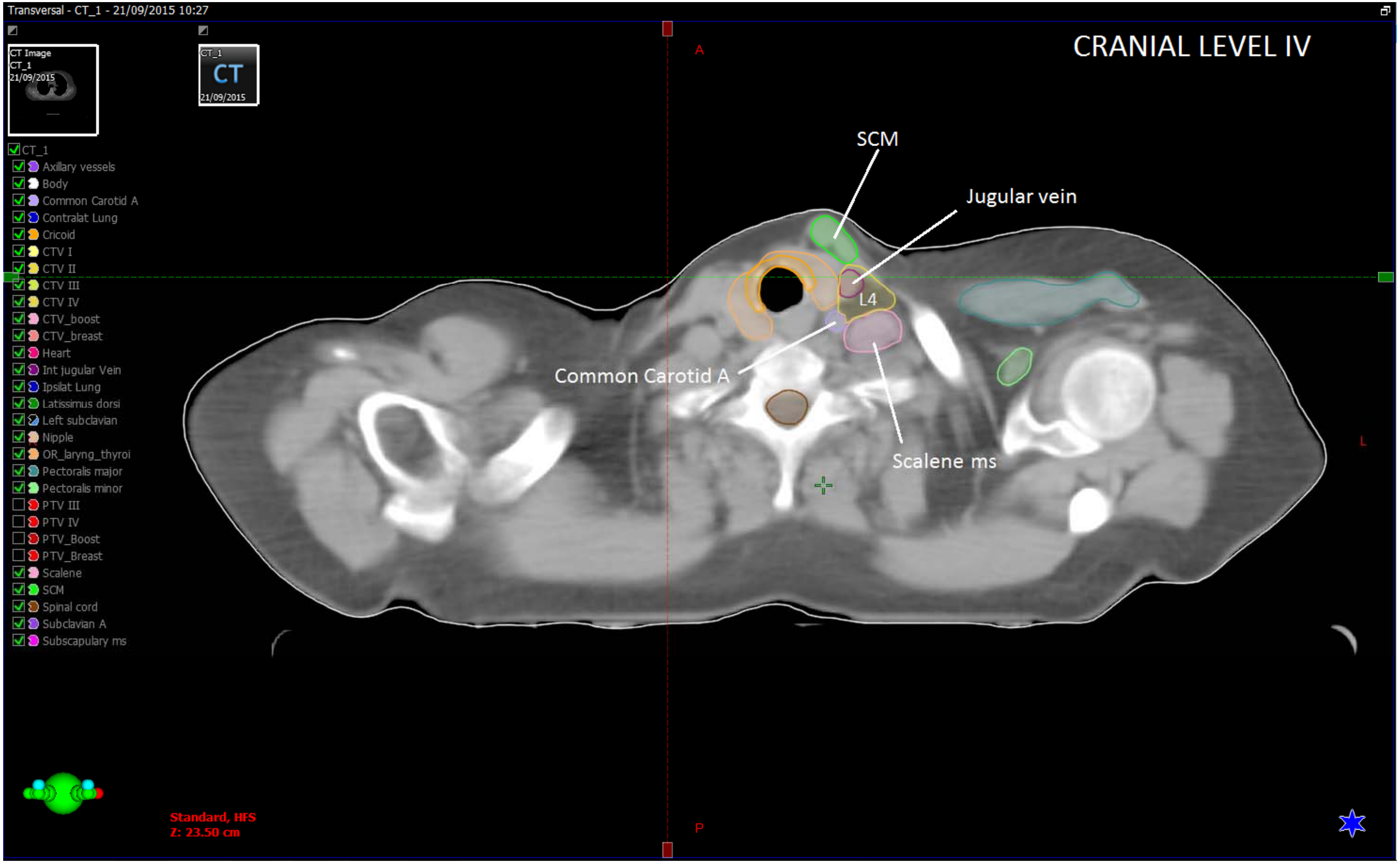
gittal - 3D_5_30042015
H
Structure
BODY

# QUICK GUIDE

## L4:

**CRANIAL:** Cranial subclavian artery or caudal cricoid (RTOG)
**CAUDAL:** 5 mm subclavian vein or caudal edge clavicle head (RTOG)
**ANT:** SCM muscle
**POST:** Scalene muscle
**LAT:** Lateral edge of SCM or junction 1st rib-clavicle
**MEDIAL:** Include: jugular vein. Exclude: common cartotid artery, thyroid

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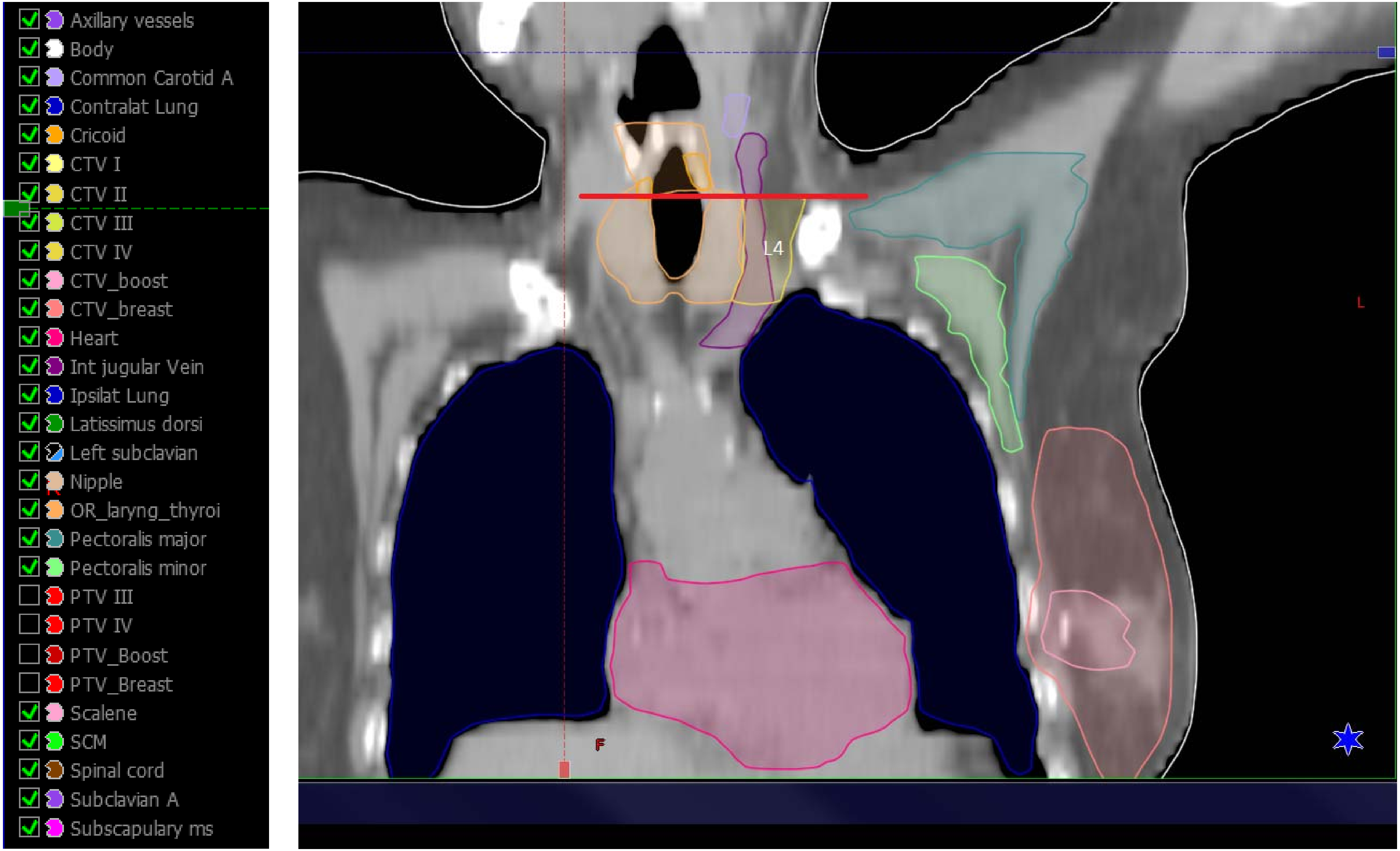


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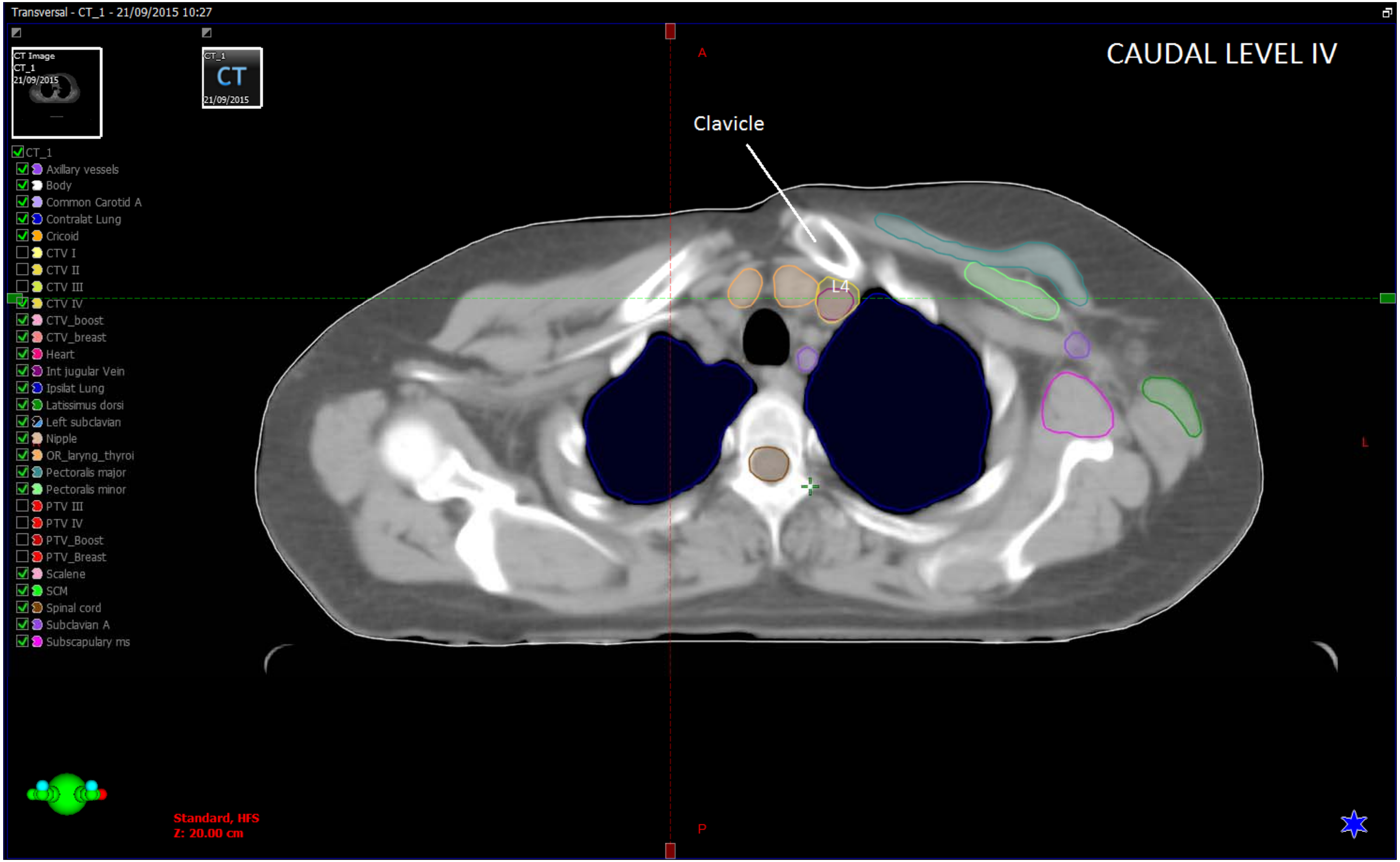


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# QUICK GUIDE

## L3: above pectoralis muscles

**CRANIAL:** Cranial subclavian artery or pectoral minor insert on coracoid (RTOG).
Where the subclavian artery passes the line between clavicle-1st rib (PROCAB)

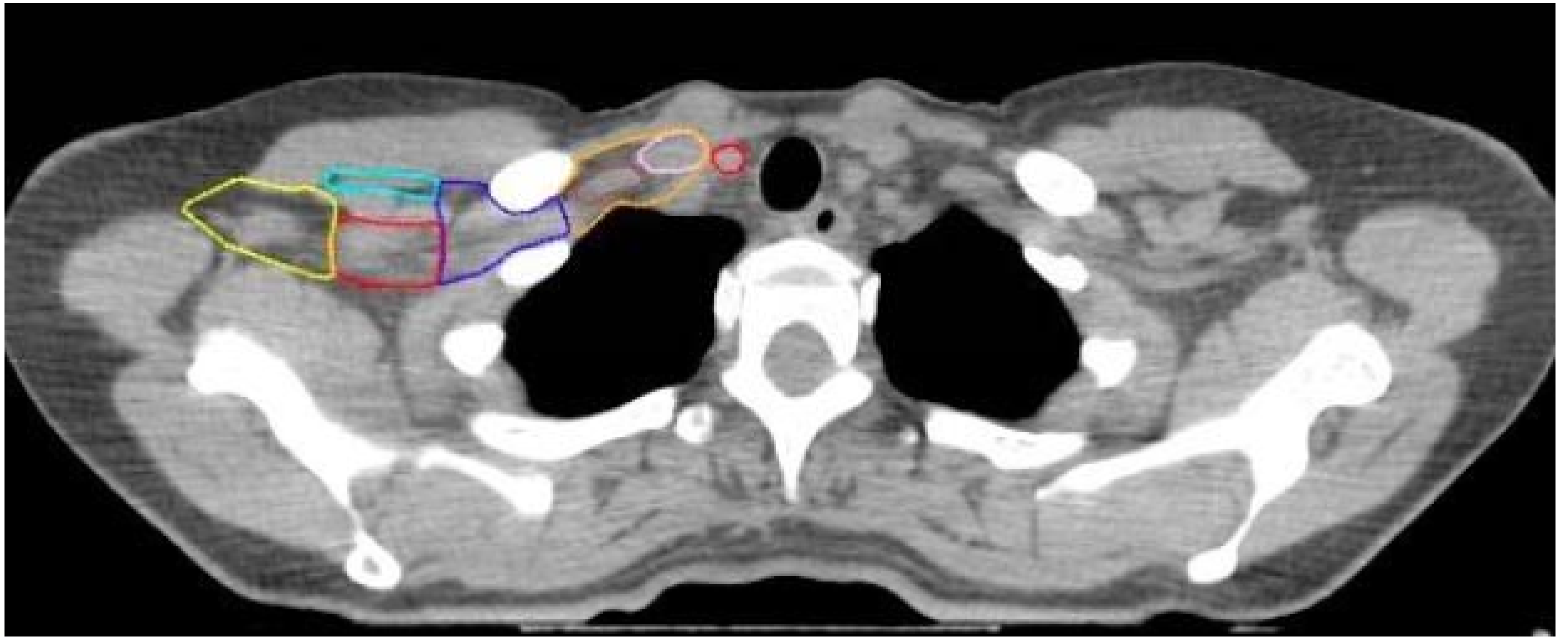
**CAUDAL:** Where the axillary vessels cross the medial edge of pectoral minor

**ANT:** Pectoralis major

**POST:** Ribs and intercostal muscles

**LAT:** Medial border pectoral minor

**MEDIAL:** The junction of subclavian and internal jugular veins



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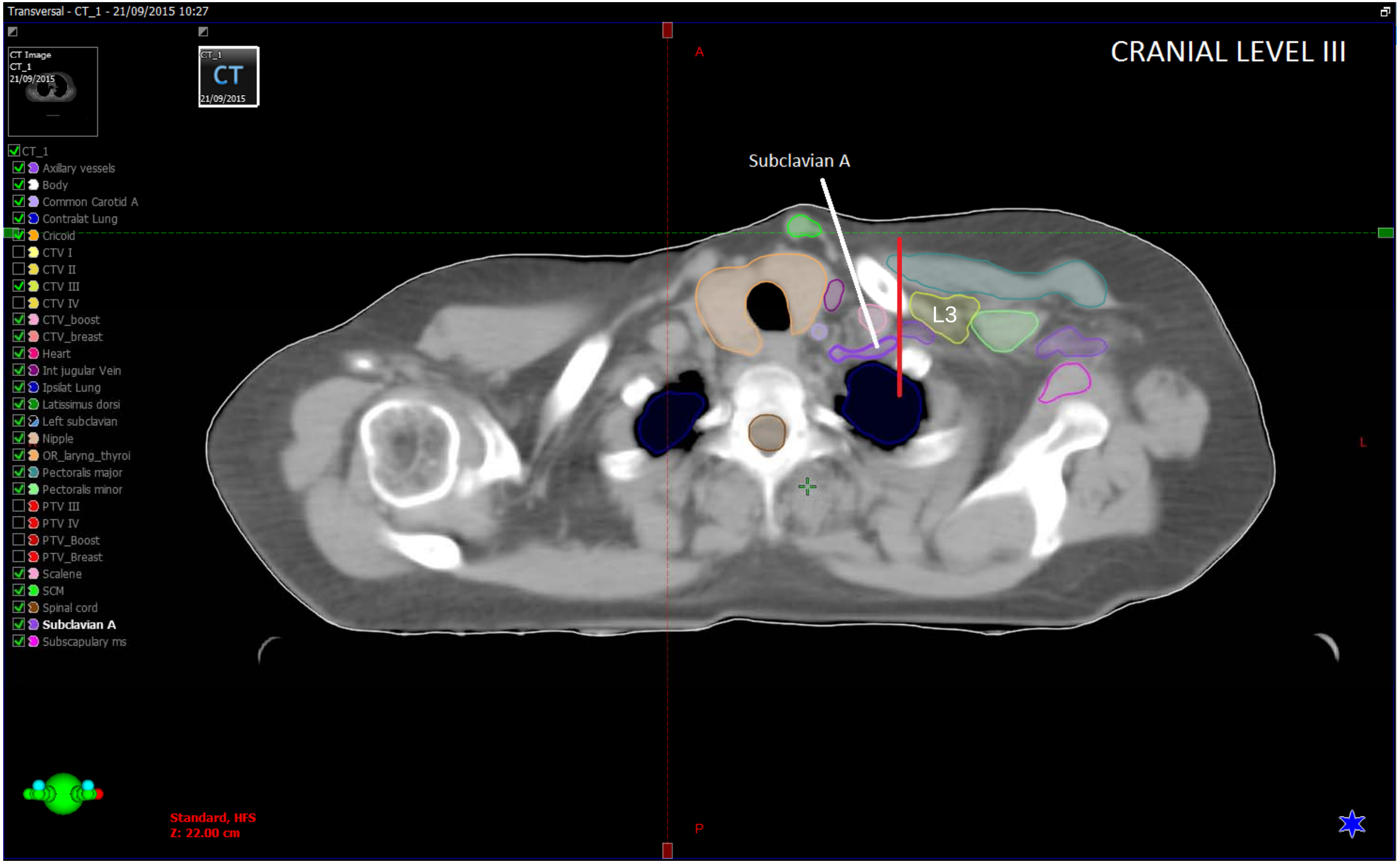
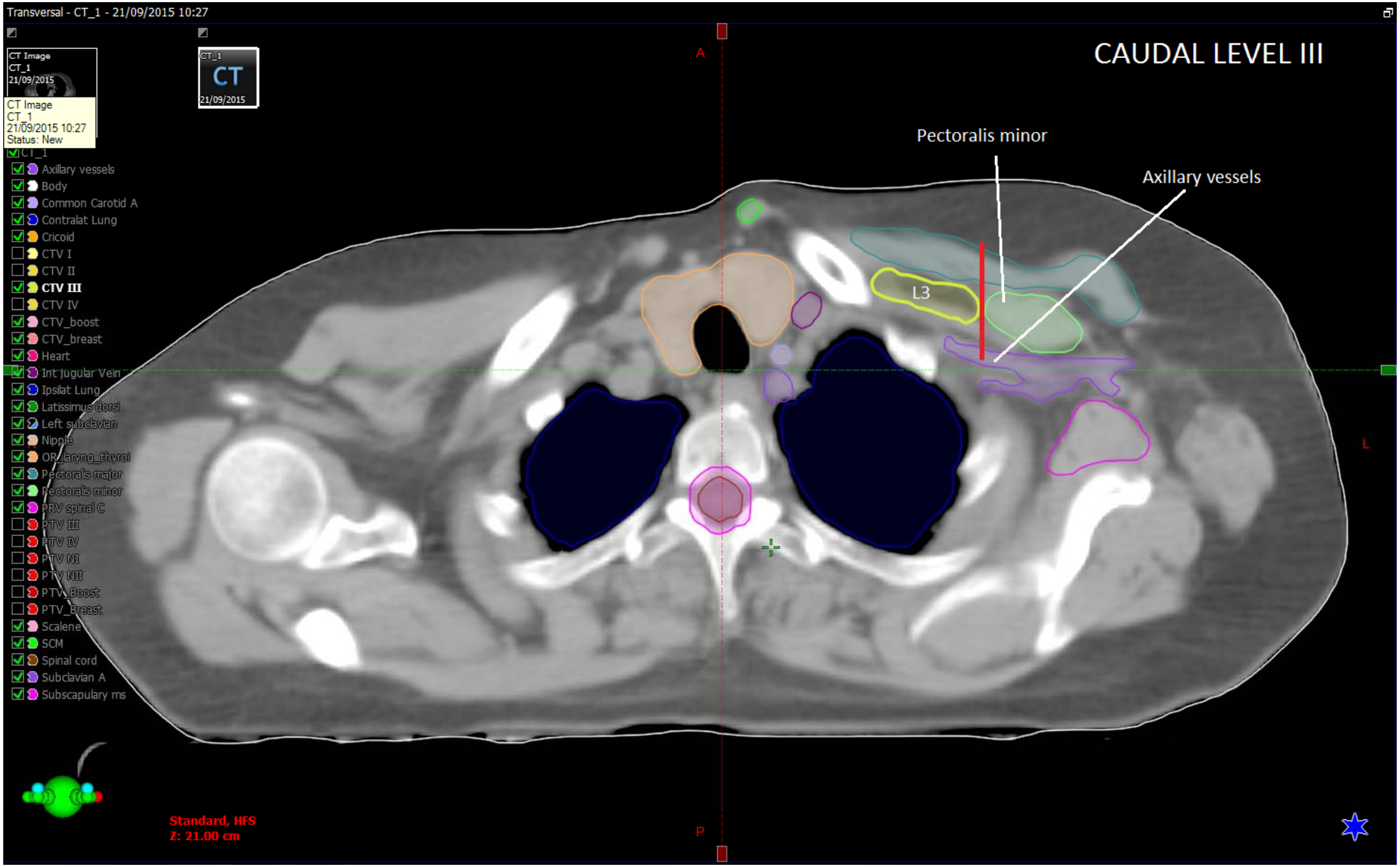


Transversal - CT_1 - 21/09/2015 10:27
CRANIAL LEVEL III
CT Image
CT_1
21/09/2015
CT_1
CT
21/09/2015
CT_1
Axillary vessels
Body
Common Carotid A
Contralat Lung
Cricoid
CTV I
CTV II
CTV III
CTV IV
CTV_boost
CTV_breast
Heart
Int jugular Vein
Ipsilat Lung
Latissimus dorsi
Left subclavian
Nipple
OR_laryng_thyroi
Pectoralis major
Pectoralis minor
PTV III
PTV IV
PTV_Boost
PTV_Breast
Scalene
SCM
Spinal cord
Subclavian A
Subscapulary ms
Subclavian A
L3
A
P
L
Standard, HFS
Z: 22.00 cm

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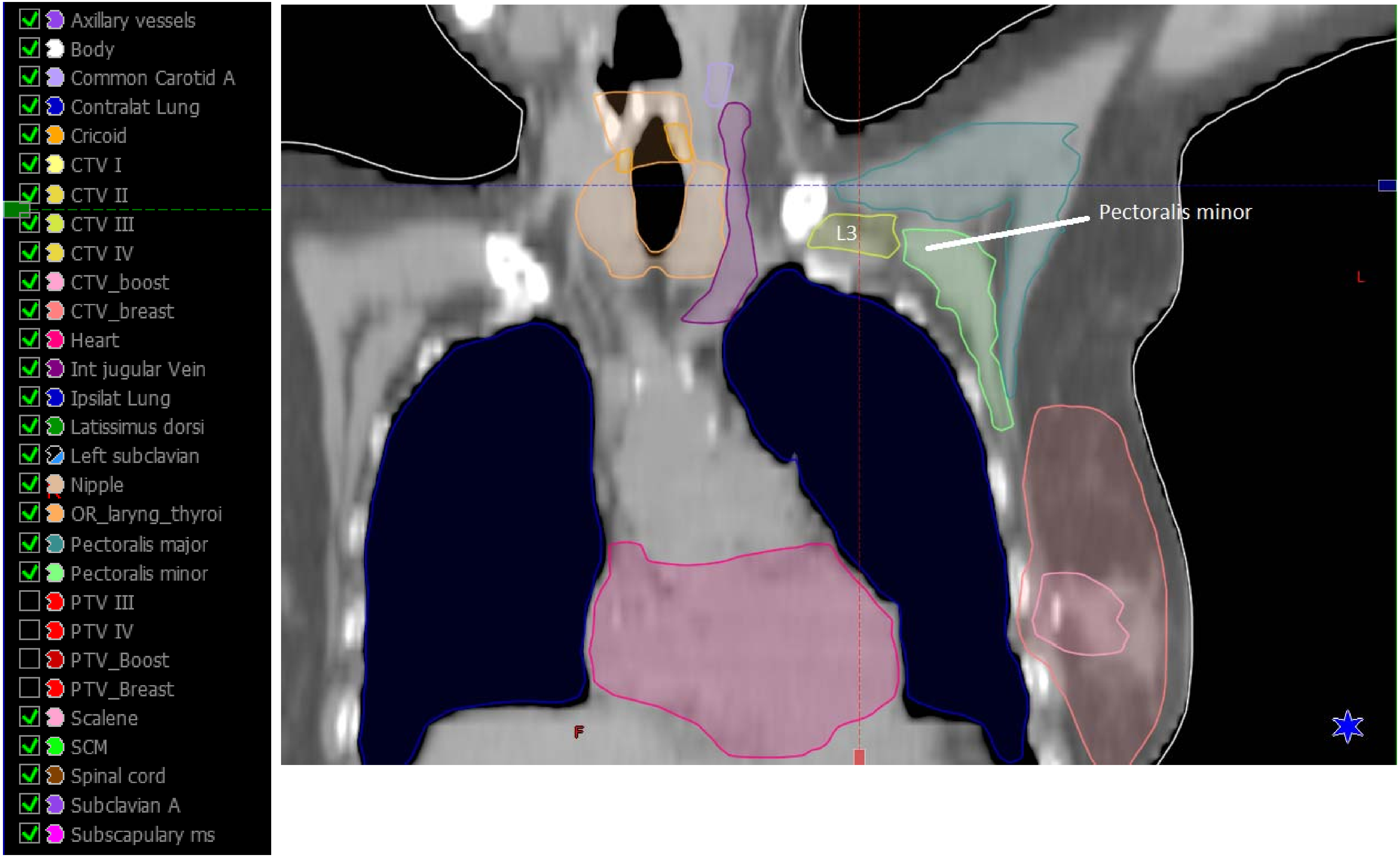
Axillary vessels
Body
Common Carotid A
Contralat Lung
Cricoid
CTV I
CTV II
CTV III
CTV IV
CTV_boost
CTV_breast
Heart
Int jugular Vein
Ipsilat Lung
Latissimus dorsi
Left subclavian
Nipple
OR_laryng_thyroi
Pectoralis major
Pectoralis minor
PTV III
PTV IV
PTV_Boost
PTV_Breast
Scalene
SCM
Spinal cord
Subclavian A
Subscapulary ms
L3
Pectoralis minor
L
F

# QUICK GUIDE

## L2: posterior to pectoral minor muscle

**CRANIAL:** Where the axillary vessels cross the medial edge of pectoral minor
**CAUDAL:** Caudal border pectoral minor
**ANT:** Pectoralis minor
**POST:** Ribs and intercostal muscles
**LAT:** Lateral border pectoral m
**MEDIAL:** Medial border pectoral m

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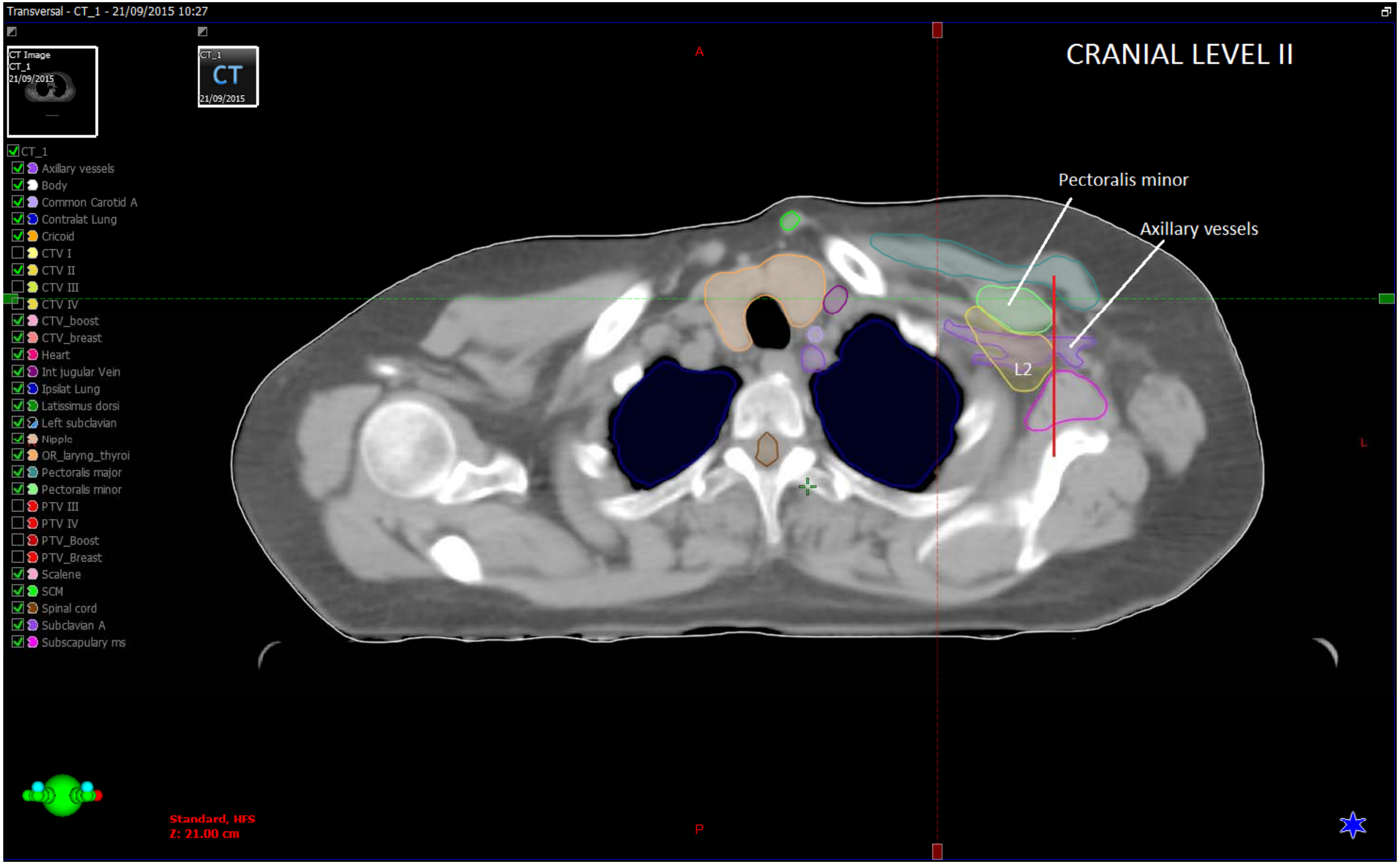
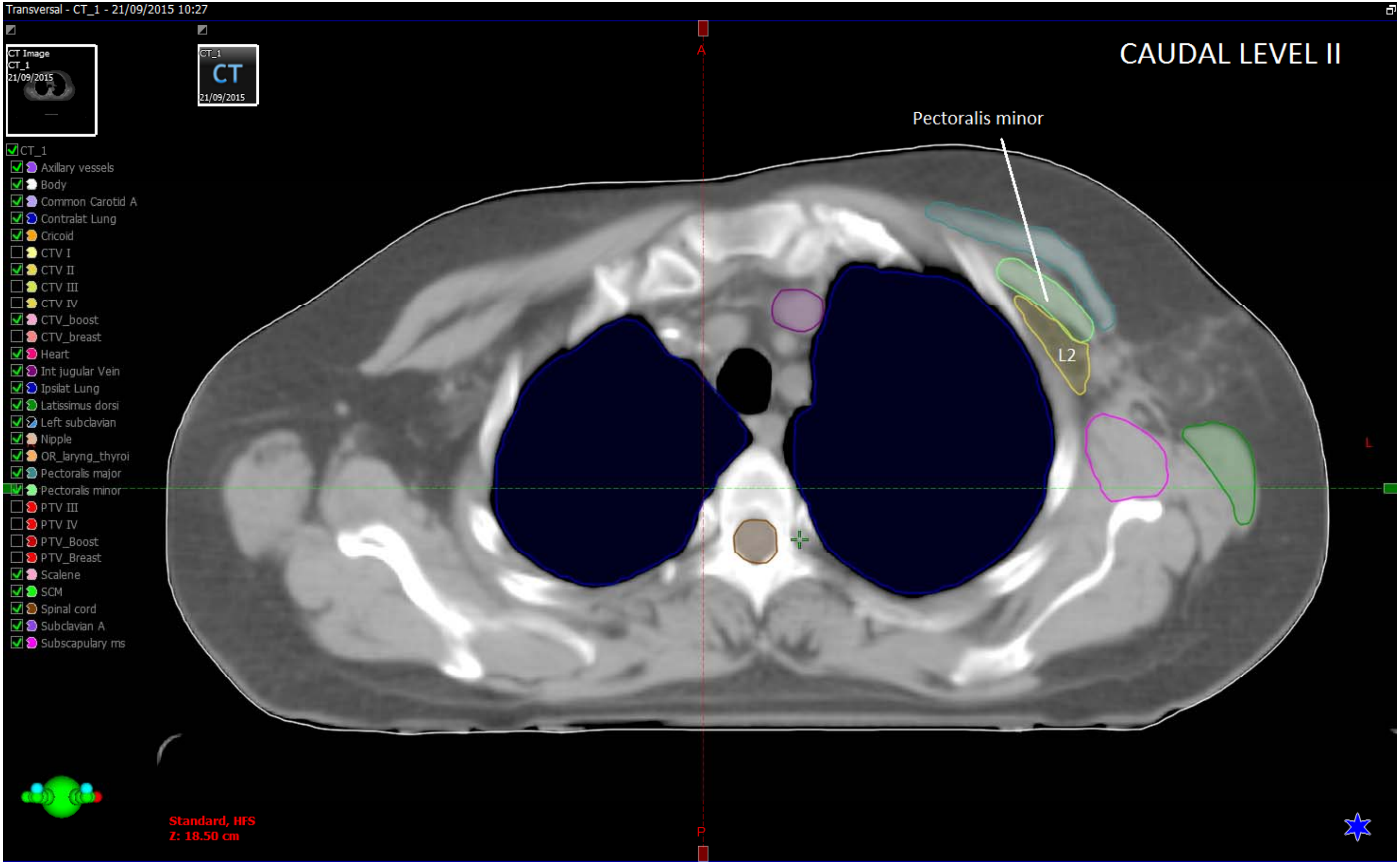


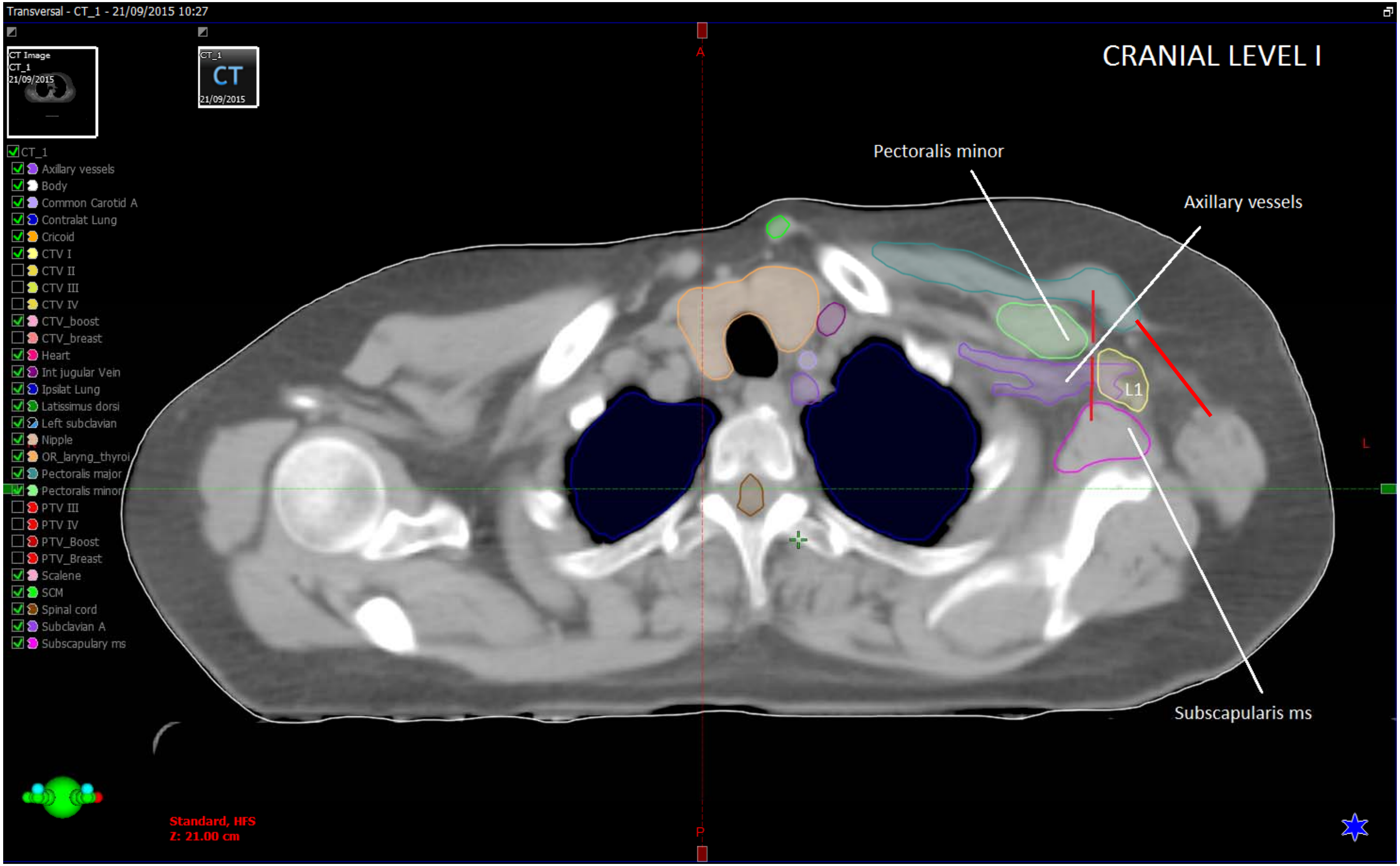
Transversal - CT_1 - 21/09/2015 10:27
CRANIAL LEVEL II
CT_1
Axillary vessels
Body
Common Carotid A
Contralat Lung
Cricoid
CTV I
CTV II
CTV III
CTV IV
CTV_boost
CTV_breast
Heart
Int jugular Vein
Ipsilat Lung
Latissimus dorsi
Left subclavian
Nipple
OR_laryng_thyroi
Pectoralis major
Pectoralis minor
PTV III
PTV IV
PTV_Boost
PTV_Breast
Scalene
SCM
Spinal cord
Subclavian A
Subscapulary ms
Pectoralis minor
Axillary vessels
L2
A
P
L
Standard, HFS
Z: 21.00 cm


Transversal - CT_1 - 21/09/2015 10:27
CAUDAL LEVEL II
Pectoralis minor
L2
CT Image
CT_1
21/09/2015
CT
CT_1
Axillary vessels
Body
Common Carotid A
Contralat Lung
Cricoid
CTV I
CTV II
CTV III
CTV IV
CTV_boost
CTV_breast
Heart
Int jugular Vein
Ipsilat Lung
Latissimus dorsi
Left subclavian
Nipple
OR_laryng_thyroi
Pectoralis major
Pectoralis minor
PTV III
PTV IV
PTV_Boost
PTV_Breast
Scalene
SCM
Spinal cord
Subclavian A
Subscapulary ms
A
P
L
Standard, HFS
Z: 18.50 cm

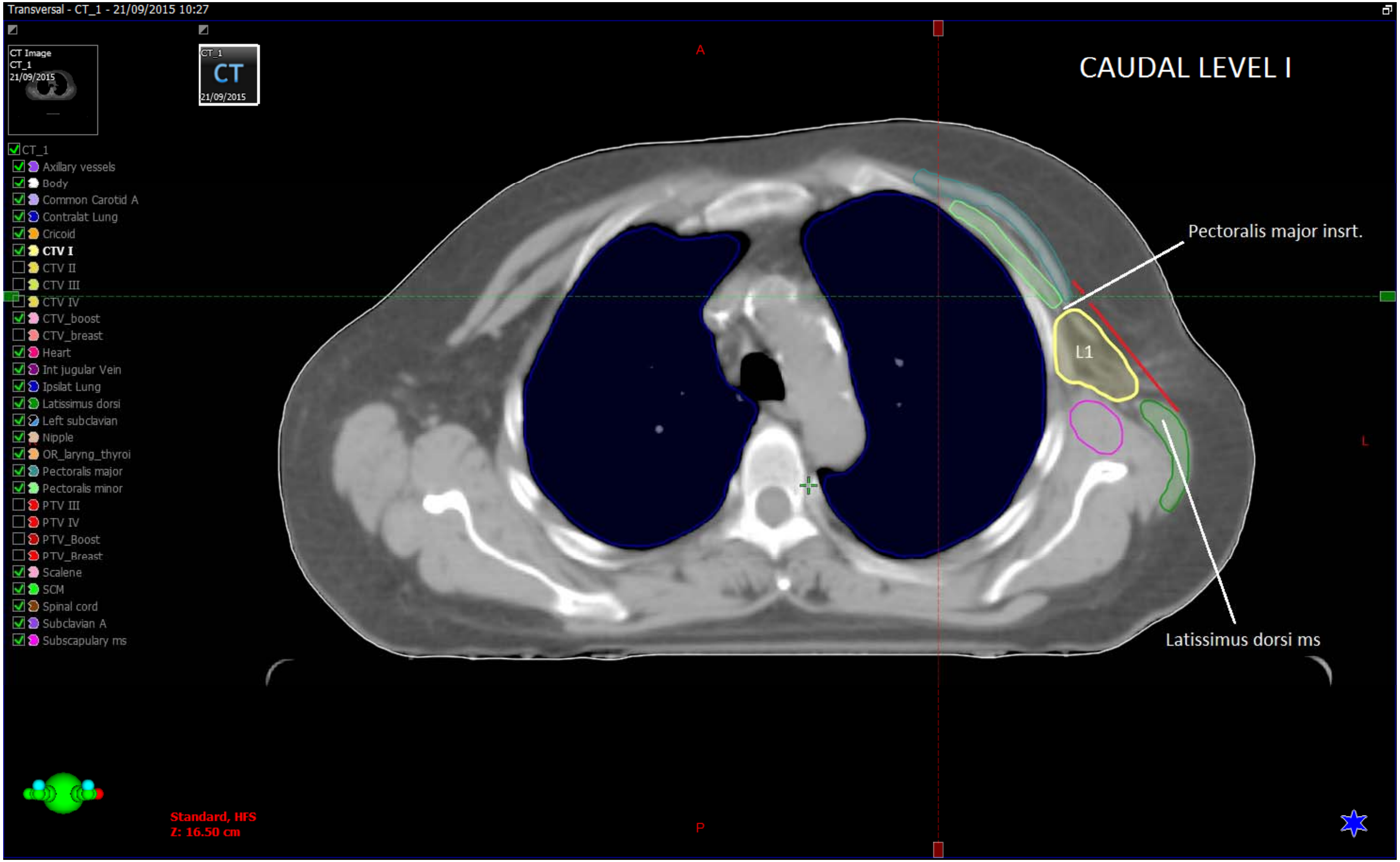
# QUICK GUIDE

## L1: caudally to pectoralis major

**CRANIAL:** Where the axillary vessels cross lateral edge of pectoral minor
**CAUDAL:** Pectoral major insert into ribs
**ANT:** Pectoralis major and minor
**POST:** Subscapularis muscle
**LAT:** Imaginary line between pectoral major and deltoid / latissiumus dorsi
**MEDIAL:** Lateral border pectoral minor



Transversal - CT_1 - 21/09/2015 10:27
CRANIAL LEVEL I
CT Image
CT_1
21/09/2015
CT_1
CT
21/09/2015
CT_1
Axillary vessels
Body
Common Carotid A
Contralat Lung
Cricoid
CTV I
CTV II
CTV III
CTV IV
CTV_boost
CTV_breast
Heart
Int jugular Vein
Ipsilat Lung
Latissimus dorsi
Left subclavian
Nipple
OR_laryng_thyroi
Pectoralis major
Pectoralis minor
PTV III
PTV IV
PTV_Boost
PTV_Breast
Scalene
SCM
Spinal cord
Subclavian A
Subscapulary ms
Pectoralis minor
Axillary vessels
L1
Subscapularis ms
Standard, HFS
Z: 21.00 cm

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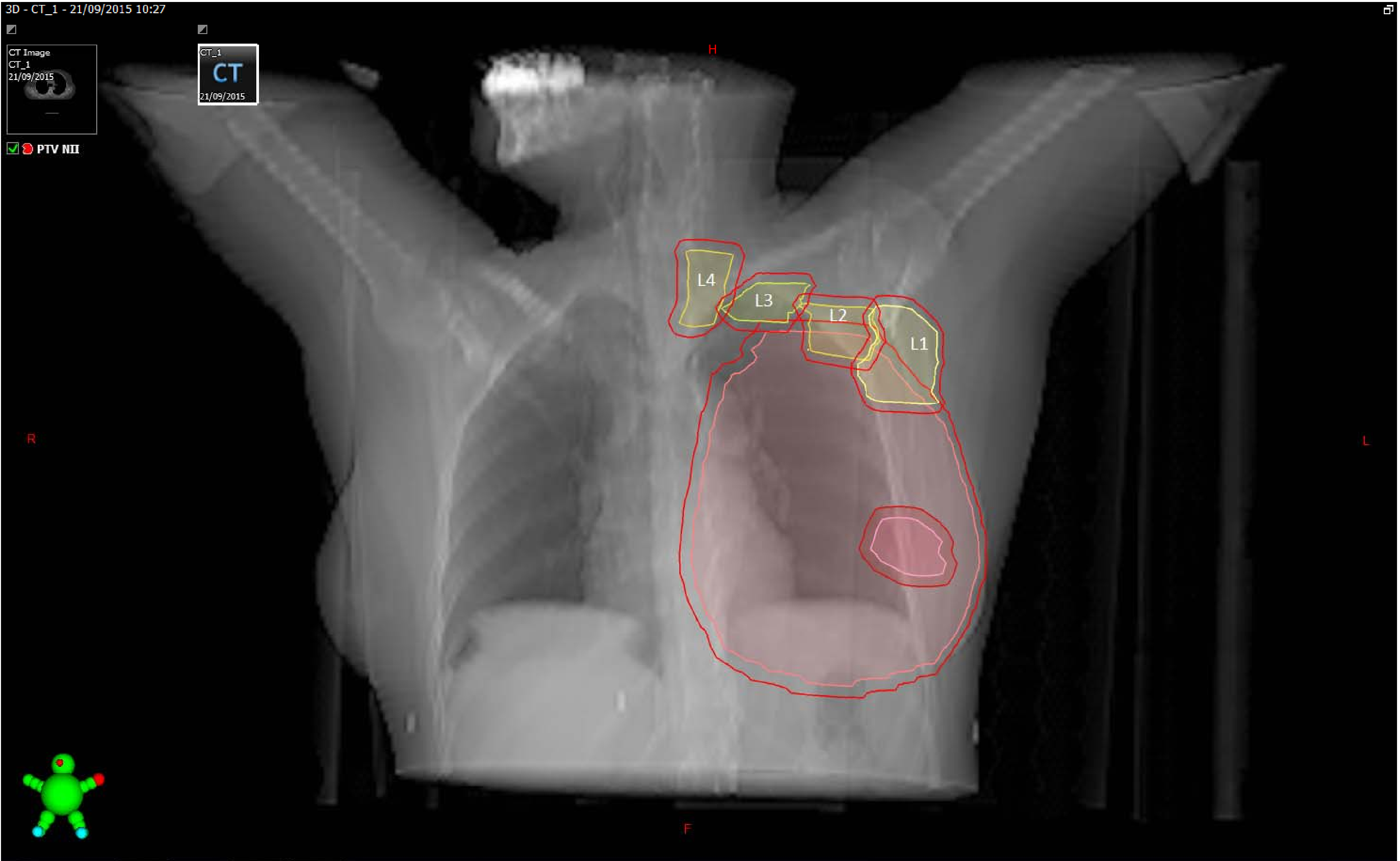
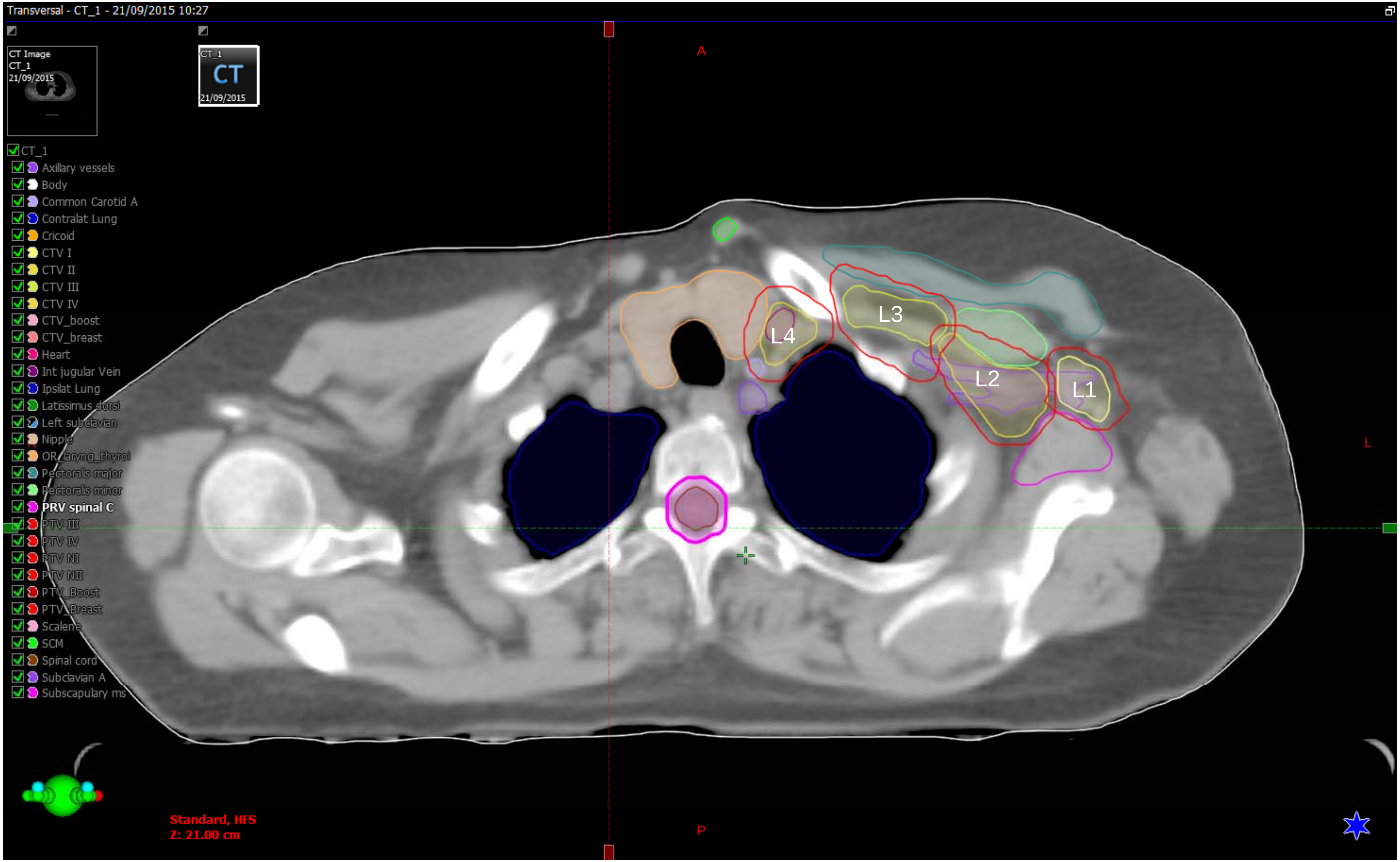
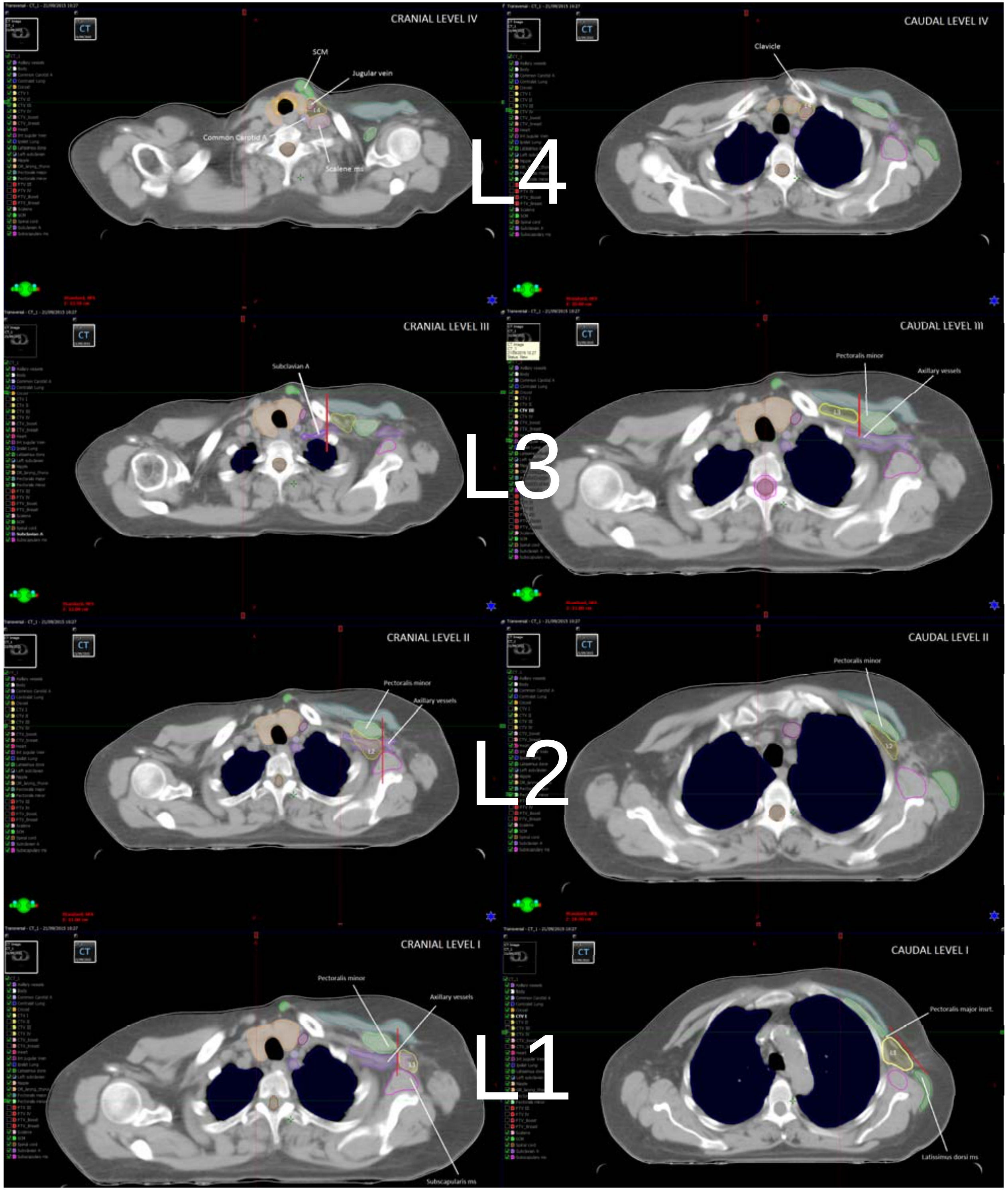


3D - CT_1 - 21/09/2015 10:27
CT Image
CT_1
21/09/2015
CT_1
CT
21/09/2015
PTV NII
H
R
L
F
L4
L3
L2
L1



Transversal - CT_1 - 21/09/2015 10:27
CT Image
CT_1
21/09/2015
CT_1
CT
21/09/2015
A
CT_1
Axillary vessels
Body
Common Carotid A
Contralat Lung
Cricoid
CTV I
CTV II
CTV III
CTV IV
CTV_boost
CTV_breast
Heart
Int jugular Vein
Ipsilat Lung
Latissimus dorsi
Left subclavian
Nipple
OR_laryng_thyroi
Pectoralis major
Pectoralis minor
PRV spinal C
PTV III
PTV IV
PTV NI
PTV NII
PTV_Boost
PTV_Breast
Scalene
SCM
Spinal cord
Subclavian A
Subscapulary ms
L4
L3
L2
L1
L
Standard, HFS
Z: 21.00 cm
P

CRANIAL




CAUDAL

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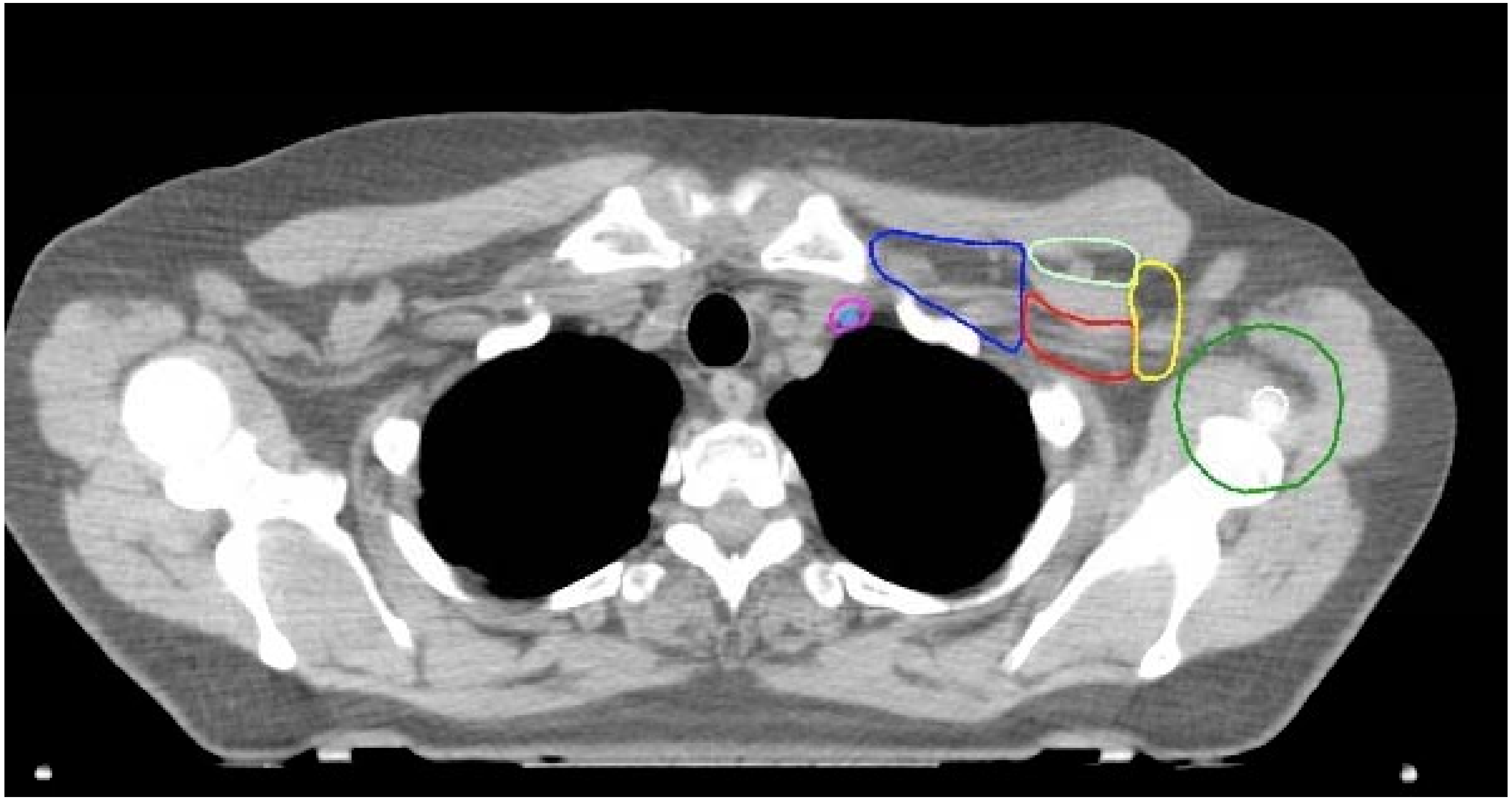
# *QUICK GUIDE*

**IMN:** First 3-4 intercostal spaces

**Rotter Nodes:** Between pectoral M and m



Pocket Atlas of Normal CT Anatomy

DBCG Counturing atlas pdf
PROCAB Counturing atlas pdf
ESTRO Counturing atlas pdf
RTOG Counturing atlas pdf

EXAMPLES OF CTV AND PTV BREAST CANCER (Our Department)

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*Philip Poortmans*
*.....*

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**Gràcies!**

*Target Volume Determination -*
*From Imaging to Margins*
*ESTRO*
*Barcelona 2016*

# Anatomy and Lymph Node Drainage for Gynaecological Cancer

Dr Sarah Swift

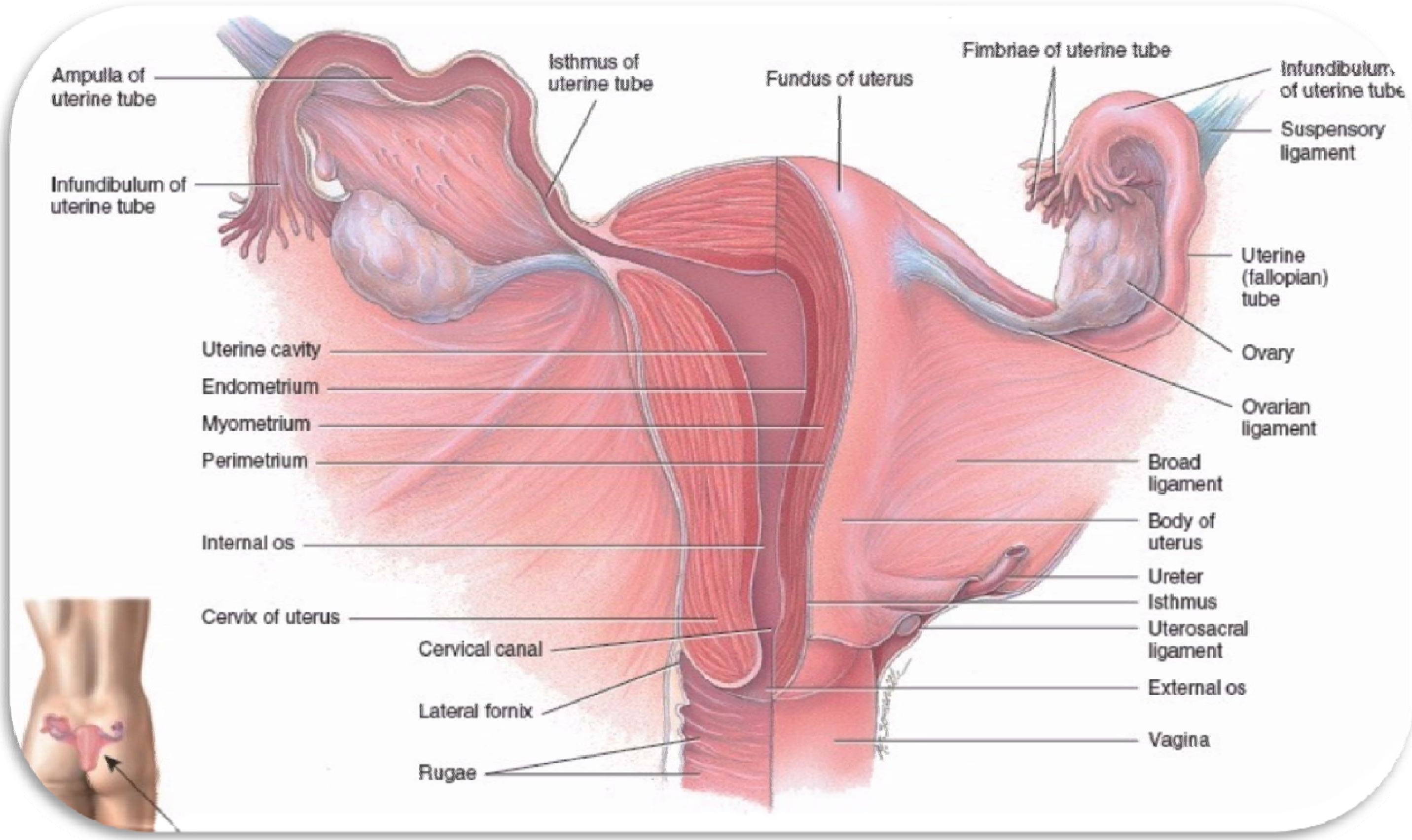
St James's University Hospital

Leeds, UK

Imaging Techniques for Cervix and Endometrial Cancer

Normal & Tumour anatomy

Lymph Node Drainage



# Cervix Cancer

# MRI and Cervix Cancer

- Established evidence base for the use of MRI
- Provides sufficient information for management decision making
- Revised FIGO staging – influenced by imaging findings

- Accuracy
- Subak et al. Obstet Gynaecol 1995

- Cost effective
- Hricak et al. Radiology 1996

# Cervix Cancer

- Traditionally ….
- FIGO Staging System based on clinical examination
- Introduced in 1928
- 8 revisions since 1950
- Most recently 2009

- Inaccurate
- Clinical staging errors in up to 25% of Stage I and II disease
- Up to 67% in Stage II – IV disease
- Underestimation in 25 – 67%
- Overestimation in 2%

# FIGO Staging 2009

| | |
|---|---|
| Stage I | The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded) |
| IA | Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≤5 mm and largest extension ≥7 mm |
| IA1 | Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm |
| IA2 | Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm |
| IB | Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA * |
| IB1 | Clinically visible lesion ≤4.0 cm in greatest dimension |
| IB2 | Clinically visible lesion >4.0 cm in greatest dimension |
| Stage II | Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina |
| IIA | Without parametrial invasion |
| IIA1 | Clinically visible lesion ≤4.0 cm in greatest dimension |
| IIA2 | Clinically visible lesion >4 cm in greatest dimension |
| IIB | With obvious parametrial invasion |
| Stage III | The tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney ** |
| IIIA | Tumor involves lower third of the vagina, with no extension to the pelvic wall |
| IIIB | Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney |
| Stage IV | The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV |
| IVA | Spread of the growth to adjacent organs |
| IVB | Spread to distant organs |

Stage I Tumour confined to cervix

*IA* Micro invasive

*IB* Clinically invasive

Stage II tumour extension beyond cervix but not to pelvic sidewall

*IIA* involvement of upper 2/3rds of vagina

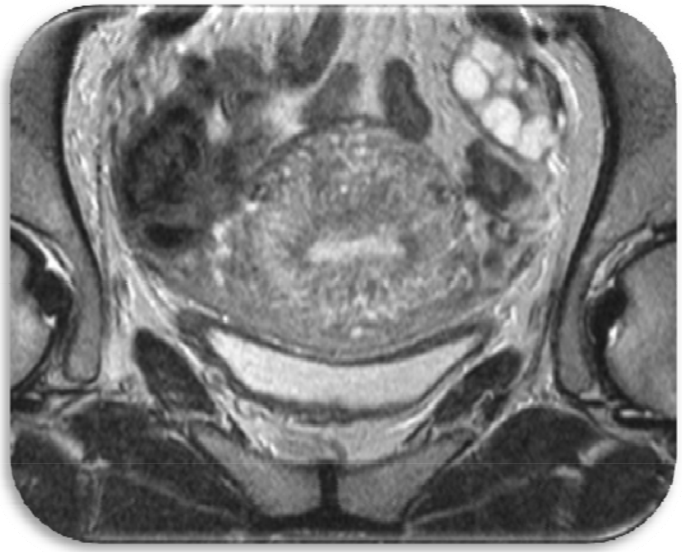
*IIB* parametrial invasion

# FIGO Staging 2009

- Examination under anaesthesia, cystoscopy, sigmoidoscopy and IVP are optional and no longer mandatory
- MRI / CT scanning with tumour size and parametrial involvement should be recorded
- Does not include nodal disease

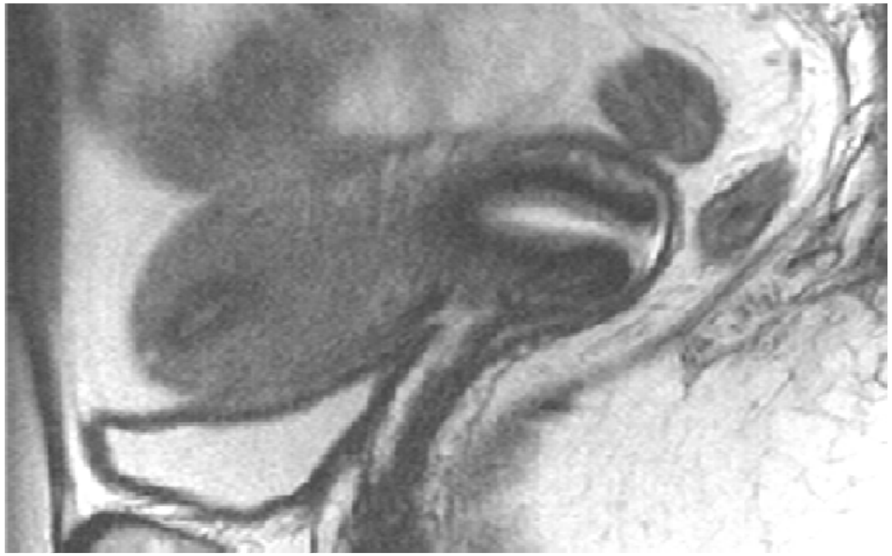
# Uterine Zonal Anatomy on T2 MRI

- **Inner high signal intensity stripe**
- **Low signal intensity junctional zone**
- **Intermediate signal intensity myometrium**



# Cervical Zonal Anatomy on T2 MRI

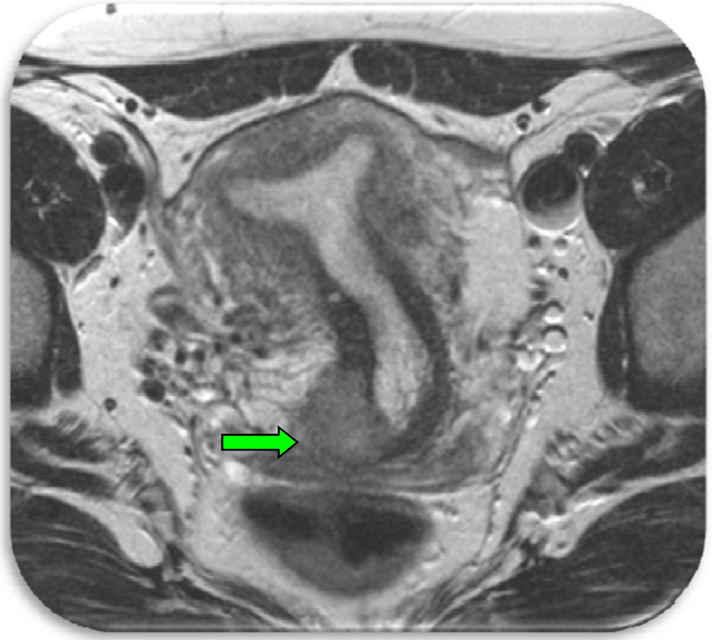
- **Central high signal intensity endocervical canal**
- **Intermediate signal cervical mucosa**
- **Low signal fibrous stroma**
- **Intermediate signal intensity myometrium**

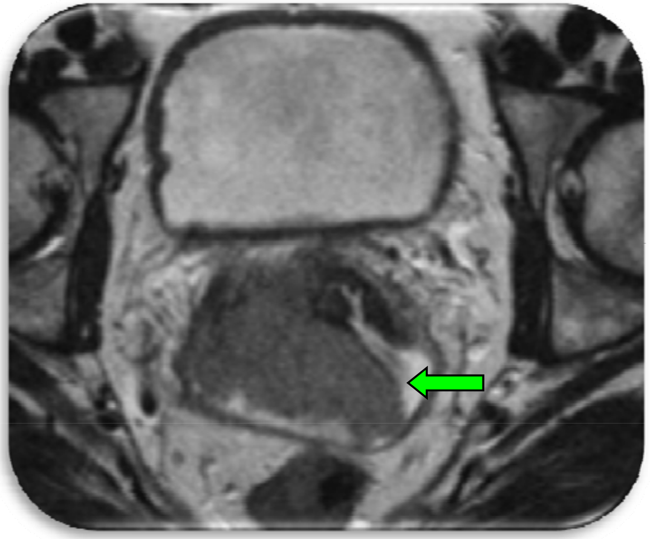


# Uterine Cervix on MRI

•Increased fibrous tissue in the cervical stroma causes it to be ***lower*** signal than myometrium

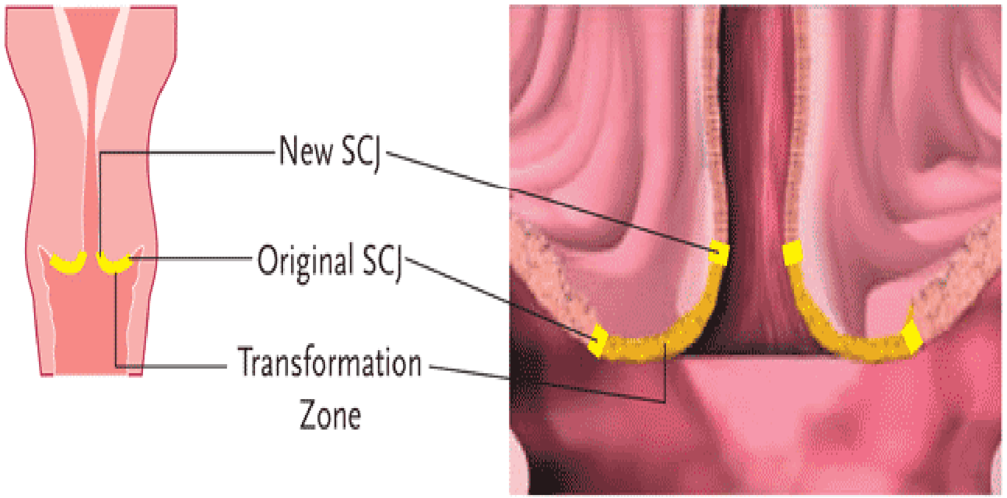
•Tumour appears as ***increased*** signal intensity material replacing the low signal cervical stroma

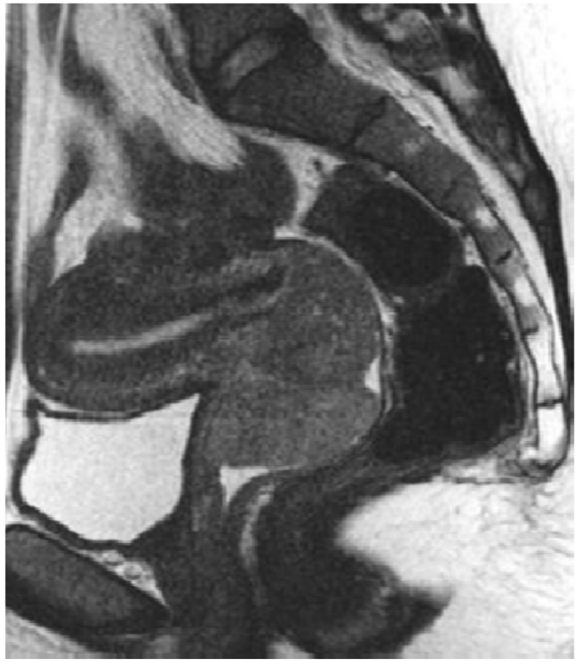




•Squamous cervical tumours occur at the squamo-columnar junction.

**•In premenopausal women this is at the level of the ectocervix and consequently tumours may be exophytic**

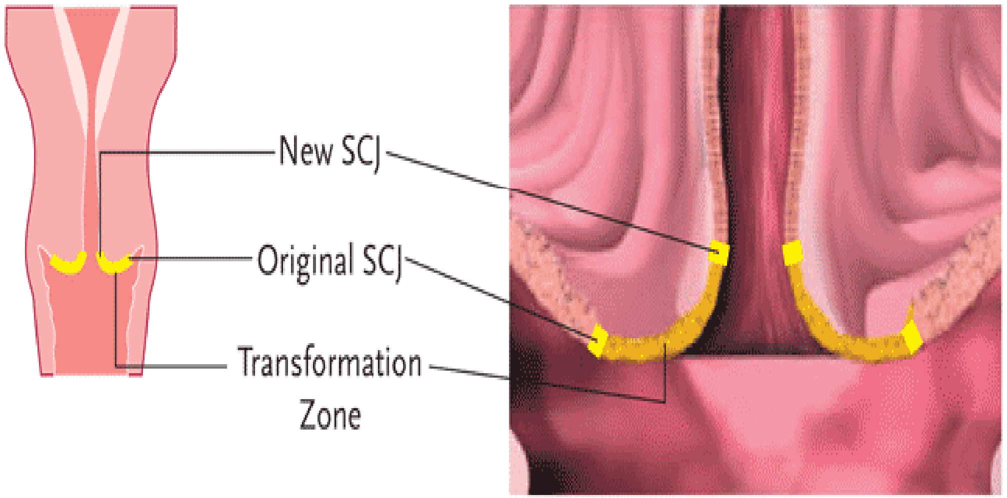


• **In post menopausal women the junction migrates up the endocervical canal**

• Tumours grow superiorly into the uterine body

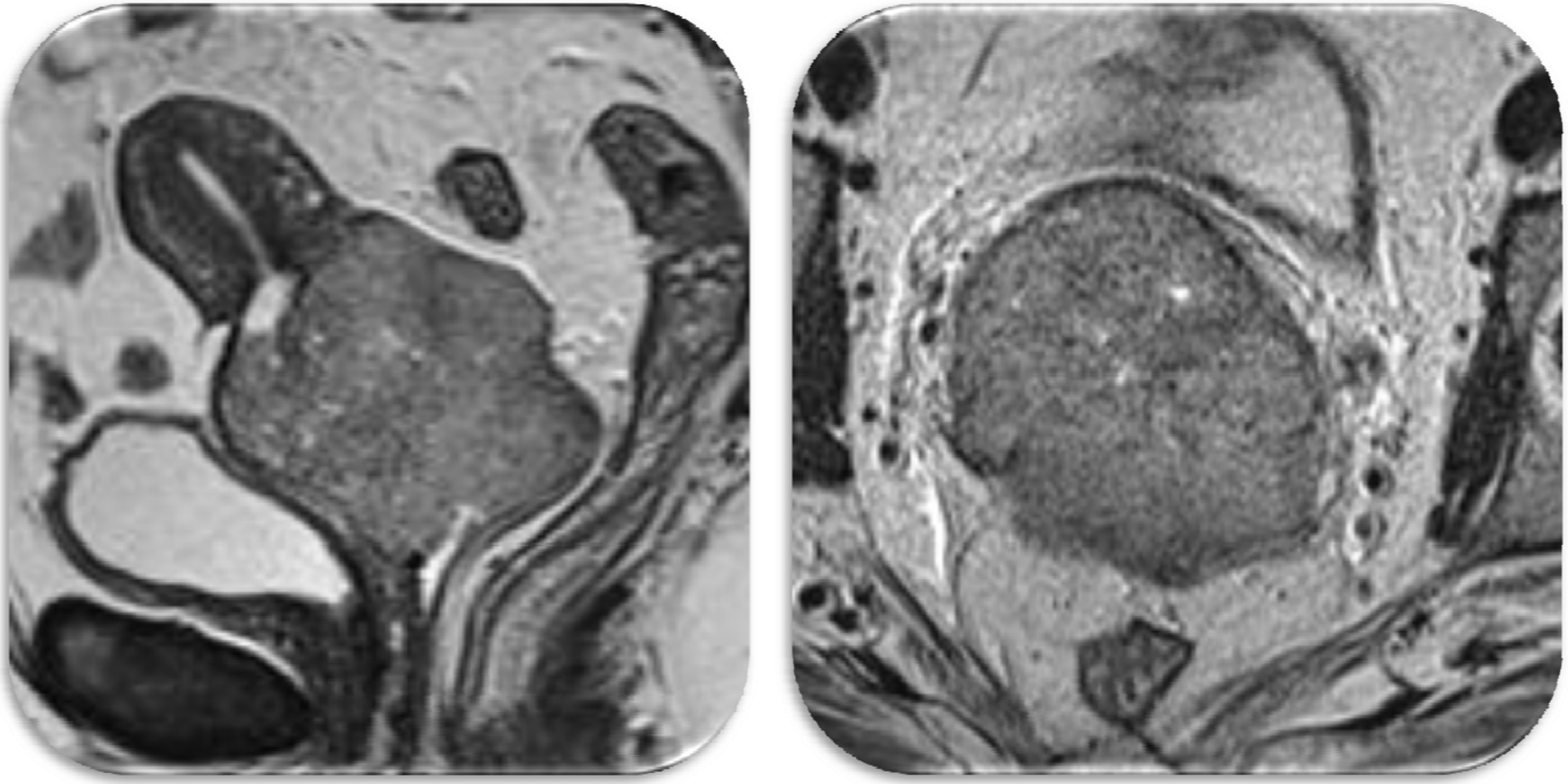
• Obstruction of the endometrial cavity may occur




•MRI is the only imaging technique that can give an accurate measurement of tumour length and volume

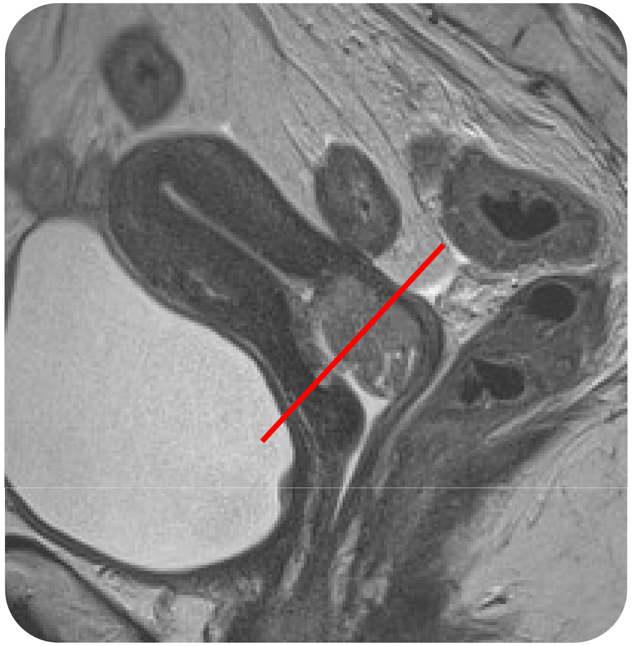
•Tumour volume is an independent poor prognostic factor

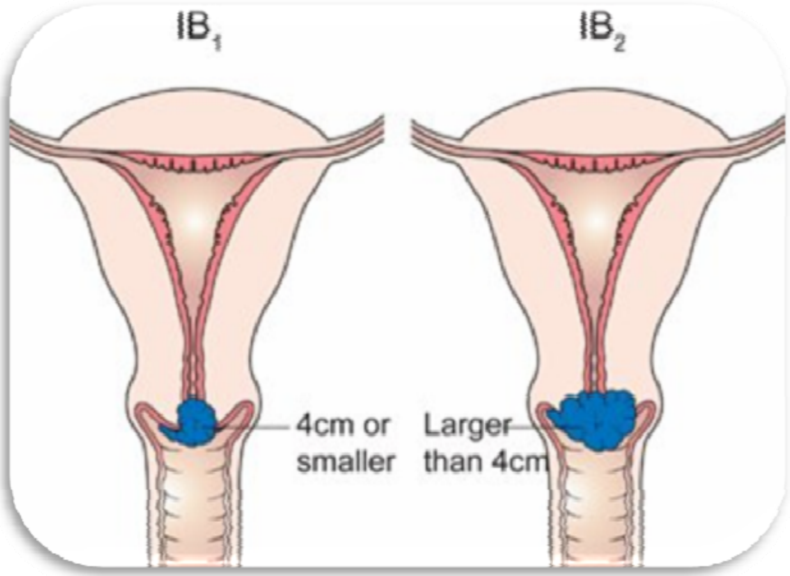
•Craniocaudal dimension important for brachytherapy planning

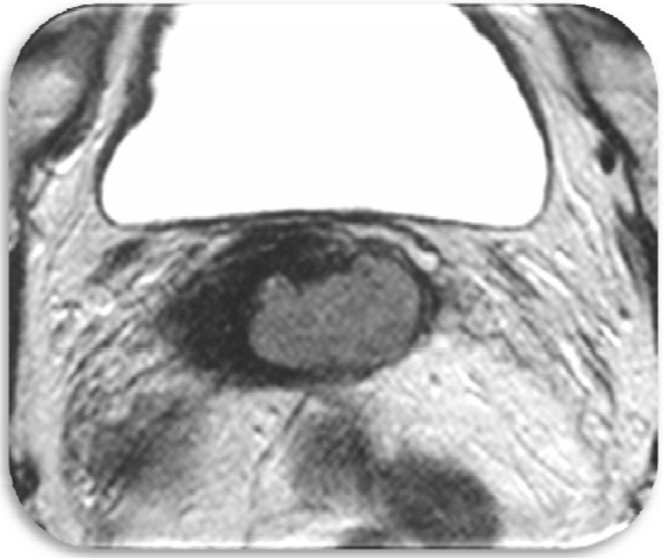


# Stage 1B Cervix Cancer

- Confined to cervix
- Intermediate signal tumour against low signal stroma
- Intact low signal intensity stromal ring



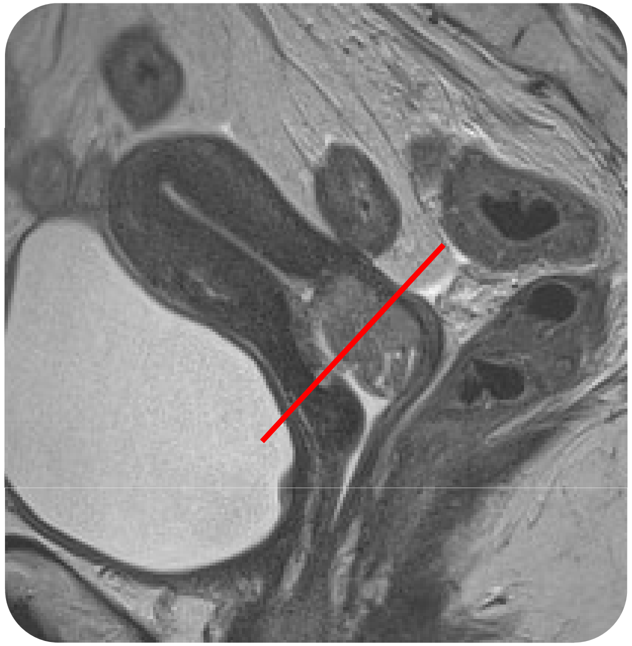


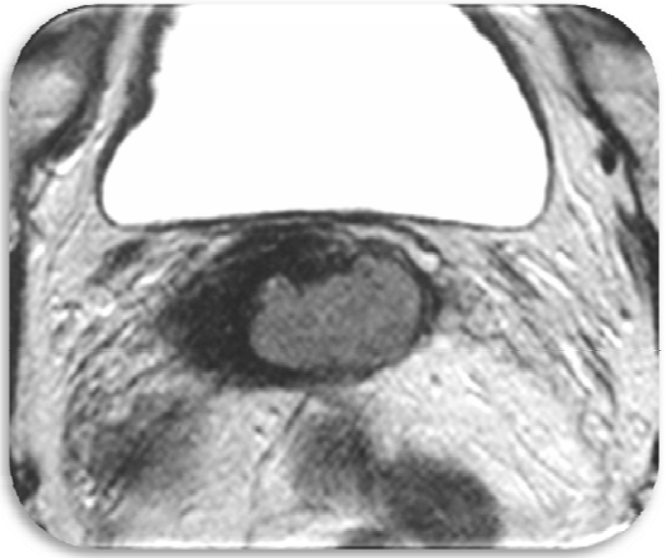



# Stage 1B Cervix Cancer

- Confined to cervix
- Intermediate signal tumour against low signal stroma
- Intact low signal intensity stromal ring
- Intact stromal ring has a high (95%) negative predictive value for parametrial invasion

(Subek LL et al, 1995)



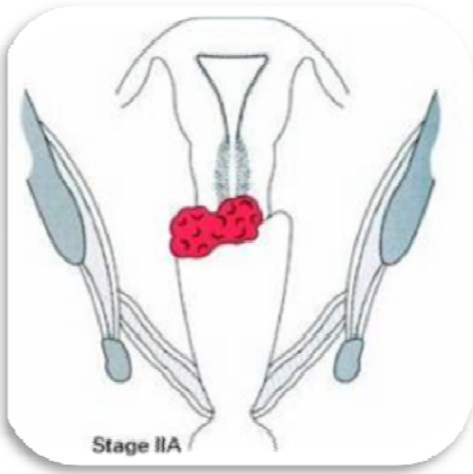


# Bulky Stage IB disease

- Cervix stromal ring remains intact

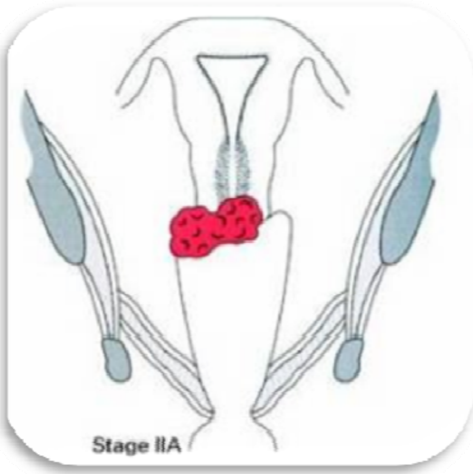
# Stage IIA disease

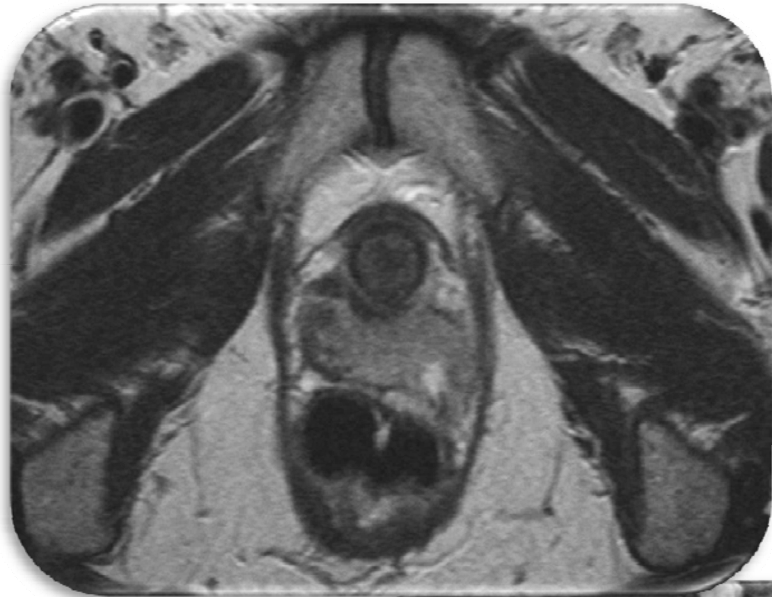
- Involvement of the upper 2/3rds of the vagina




# Stage IIA disease

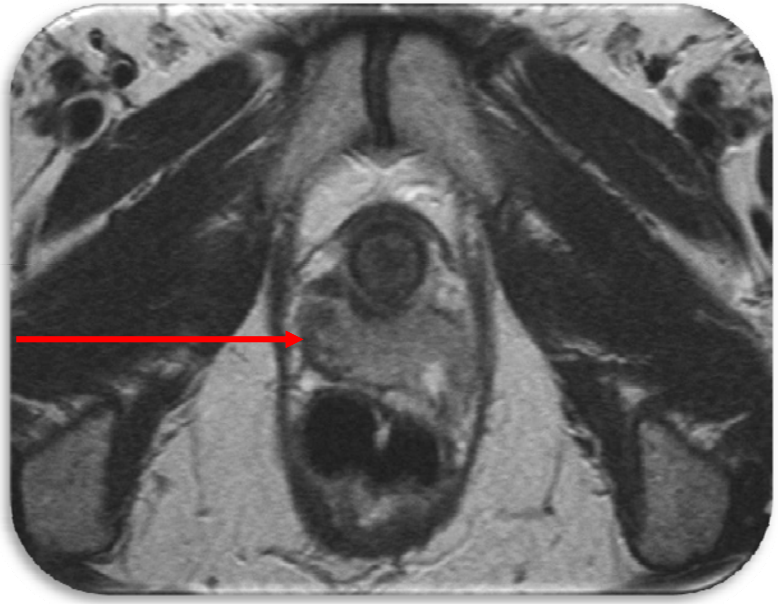
- Involvement of the upper 2/3rds of the vagina



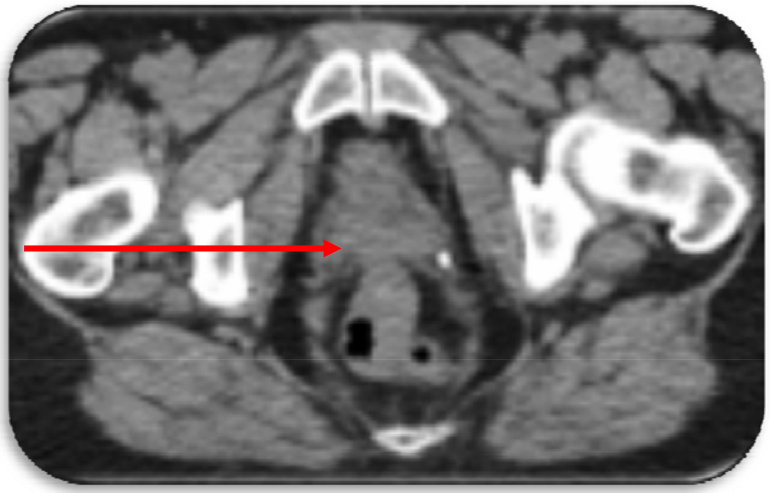



# Stage IIA disease

- MRI not as good as clinical assessment for evaluating vaginal disease



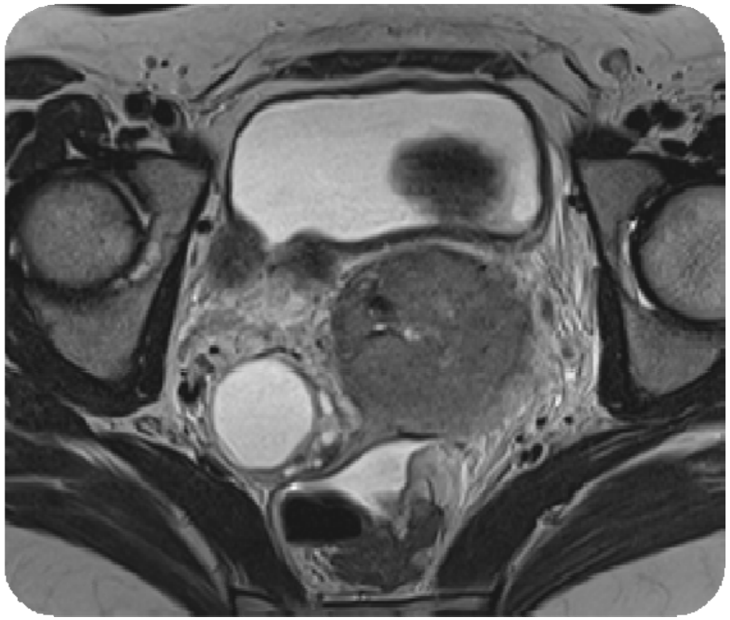
- Difficult to see on planning CT

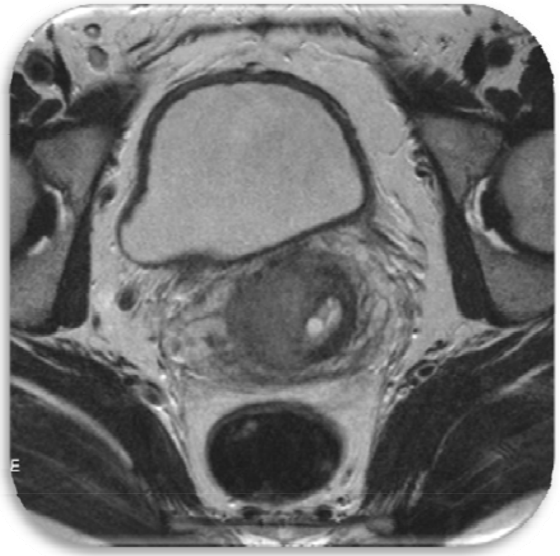


# Stage IIB disease

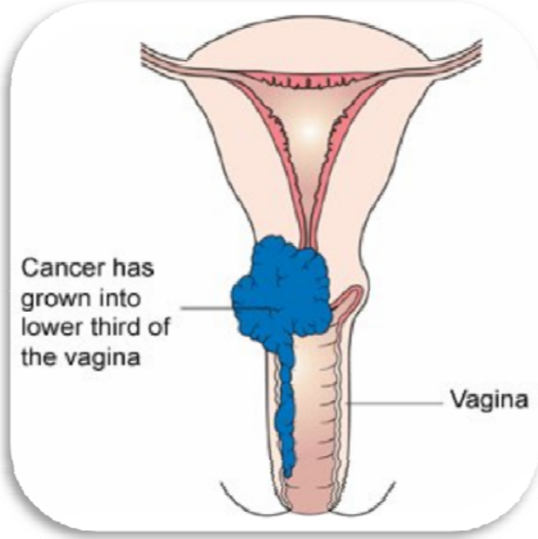
- Deficient stromal ring

•Tumour extending into parametrium



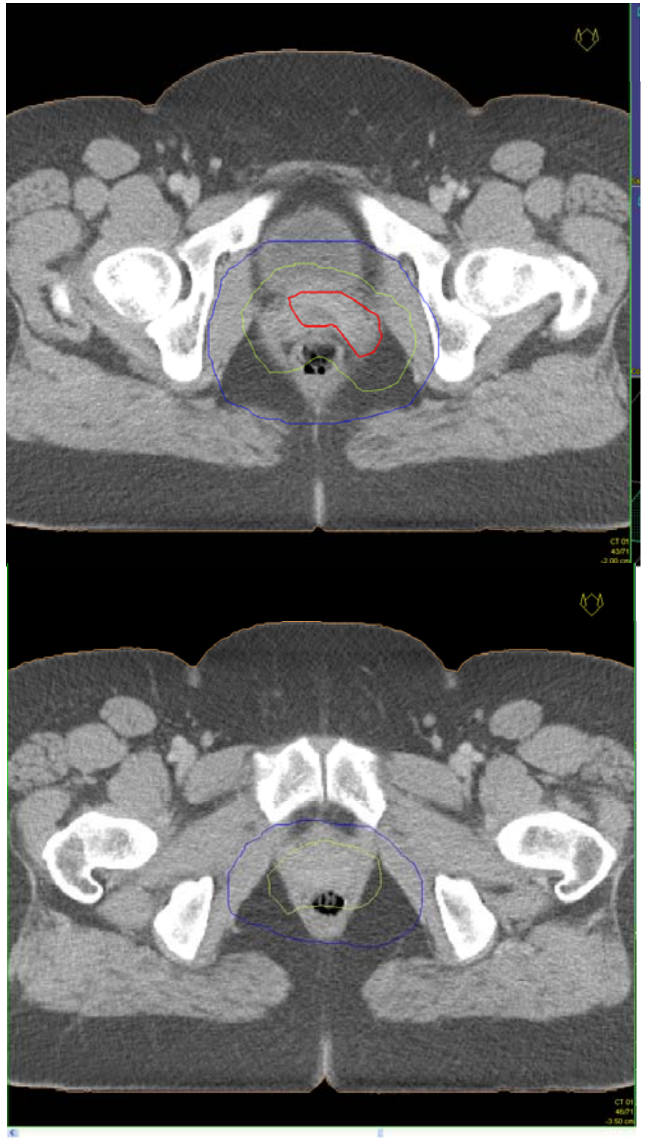


# Stage IIIA – lower vagina

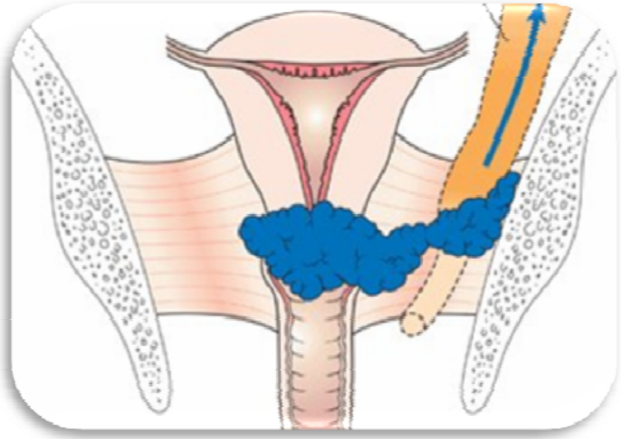


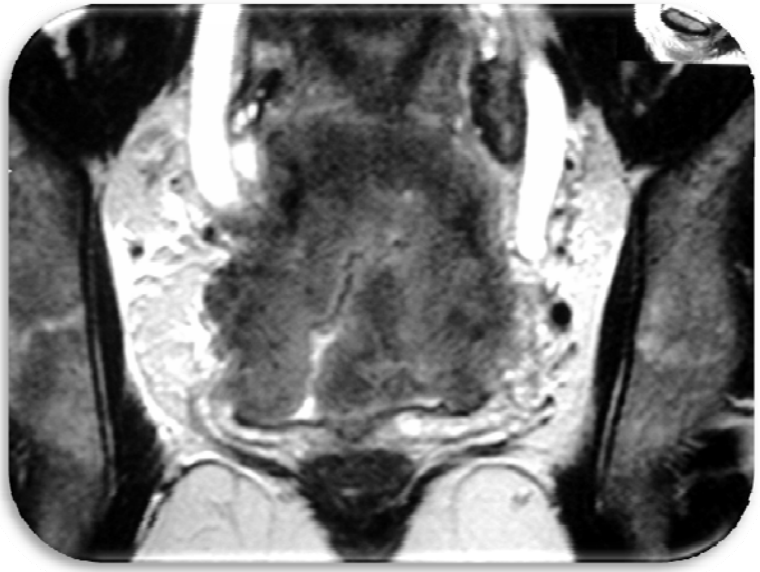

# Stage IIIA disease

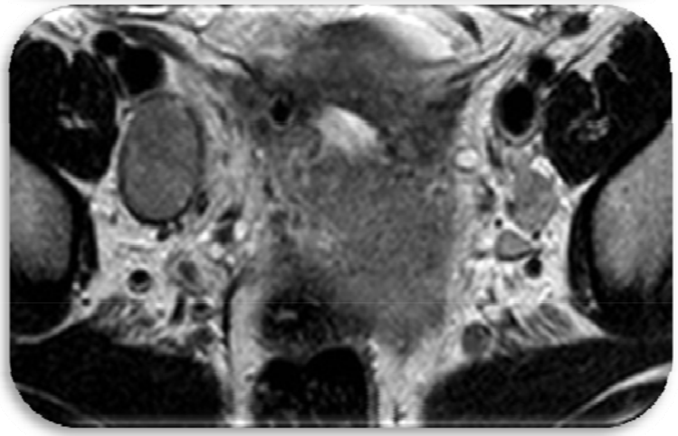
- What is the inferior extent of the tumour?
- Affect the radiotherapy volumes
- Nodal coverage

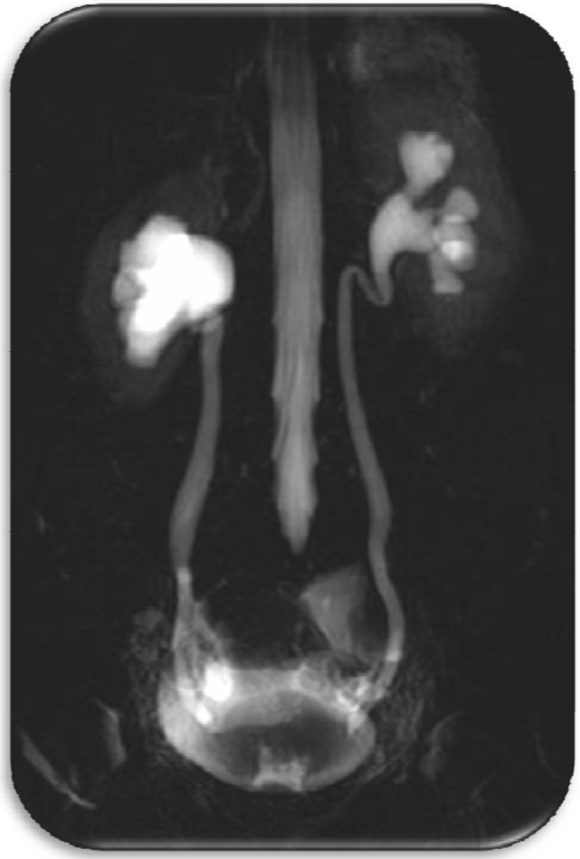


# Stage IIIB – hydronephrosis / extension to the pelvic sidewall

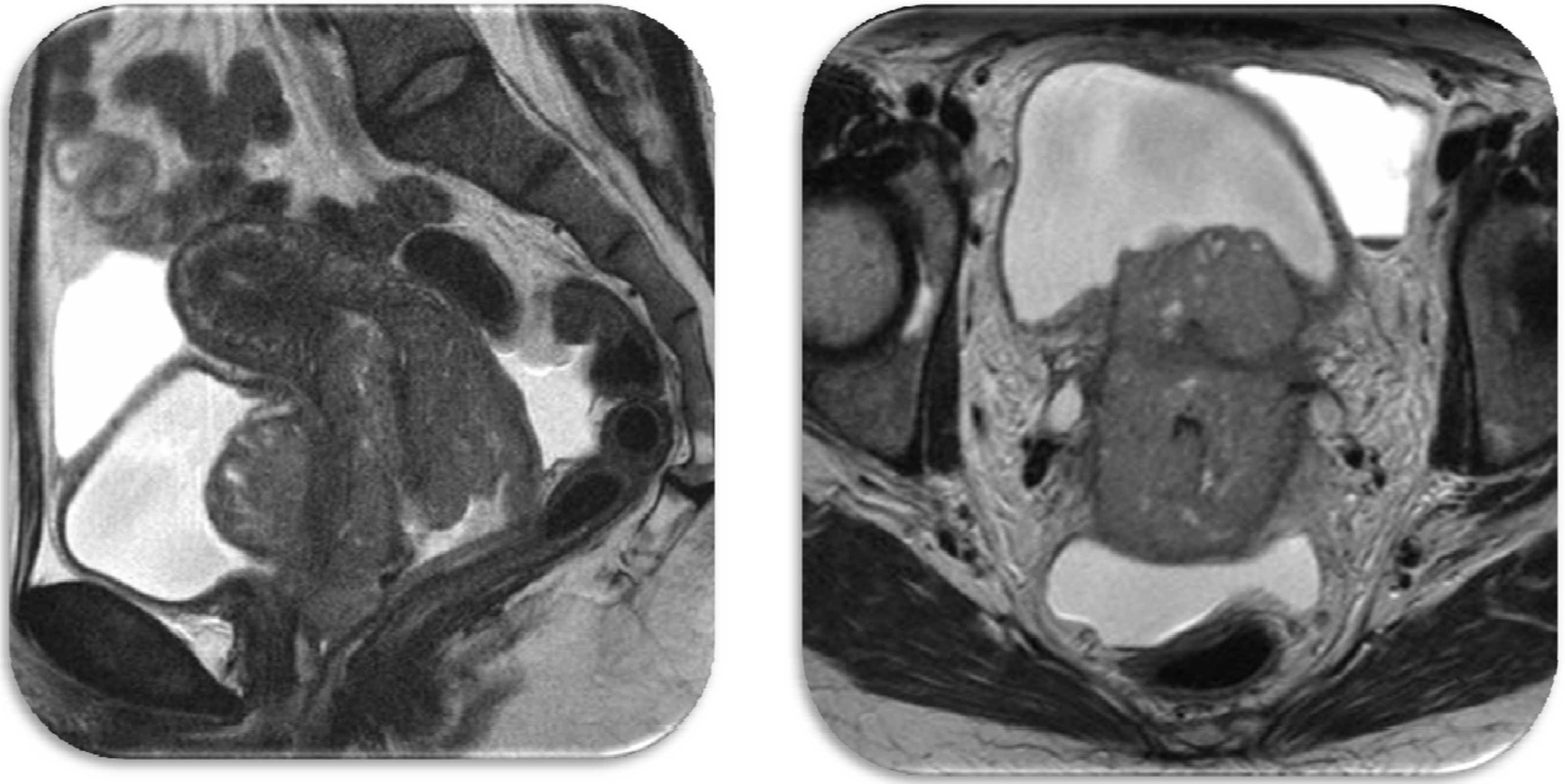






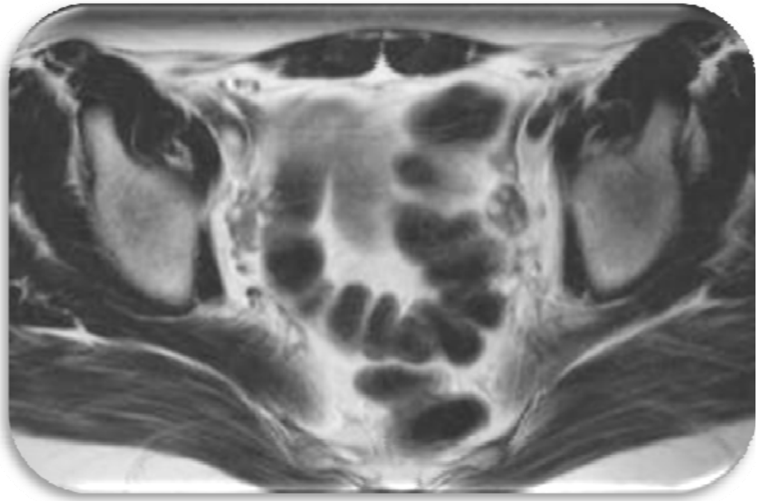


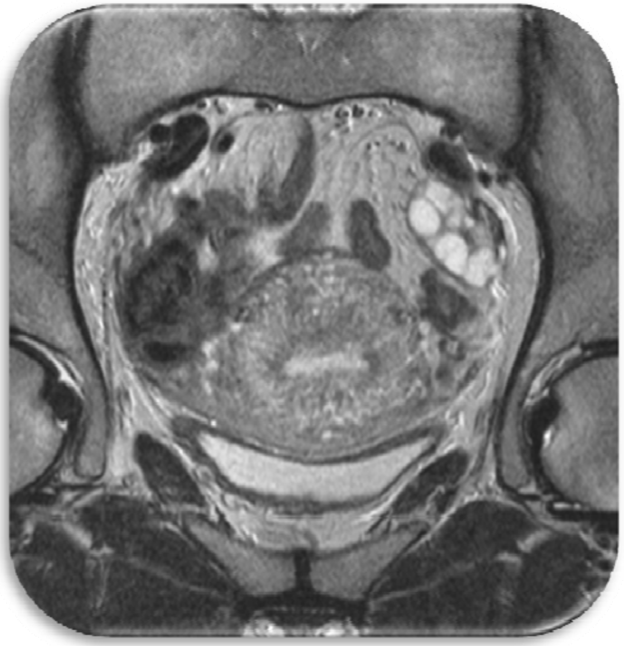
# Stage IV disease



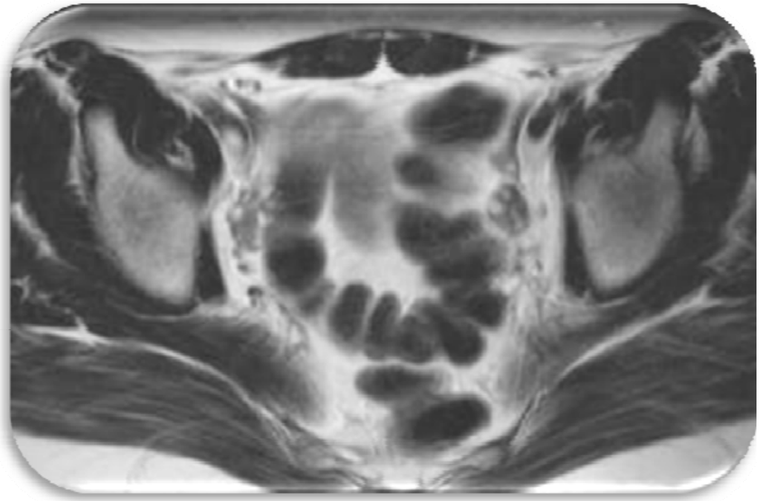
Tumour extending through the bladder wall and mucosa into the lumen

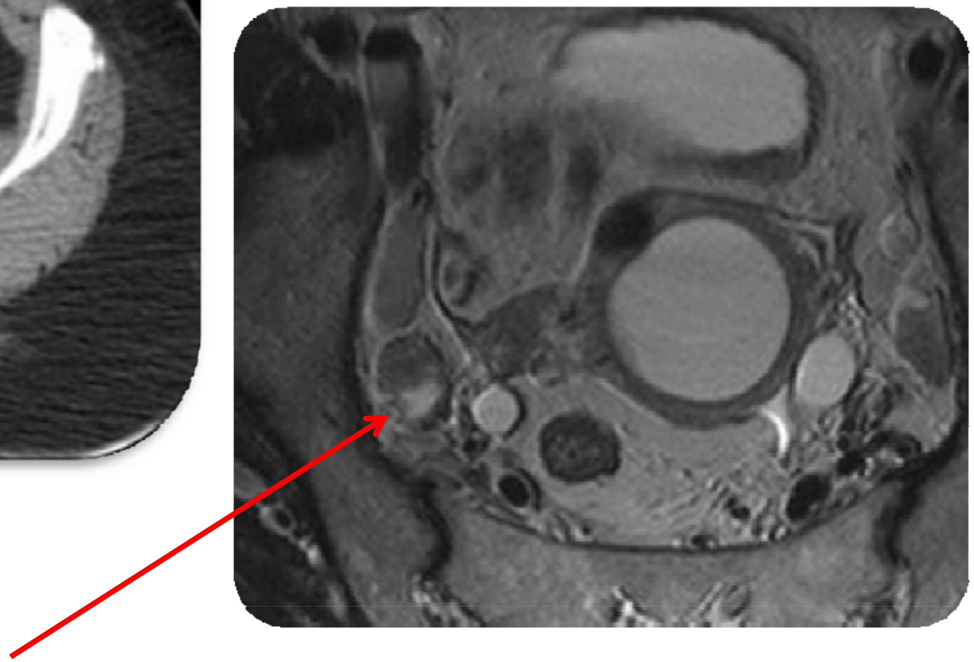
# Ovaries….



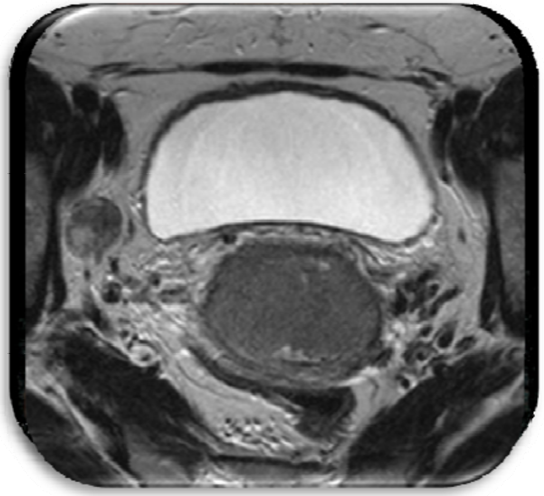


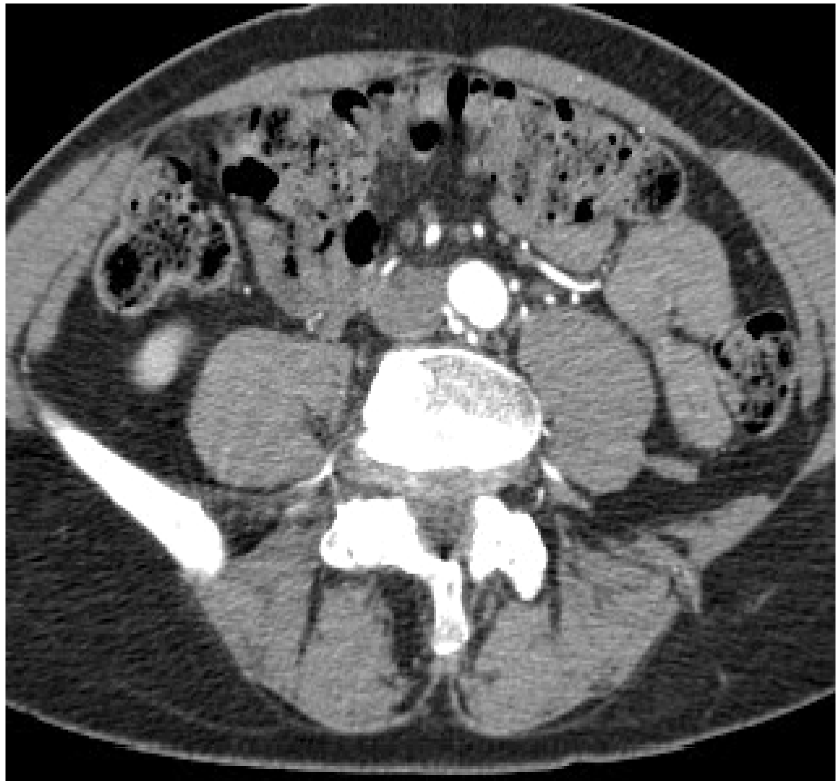
Do not confuse with Lymph Nodes





# Nodal disease in Gynae Cancer



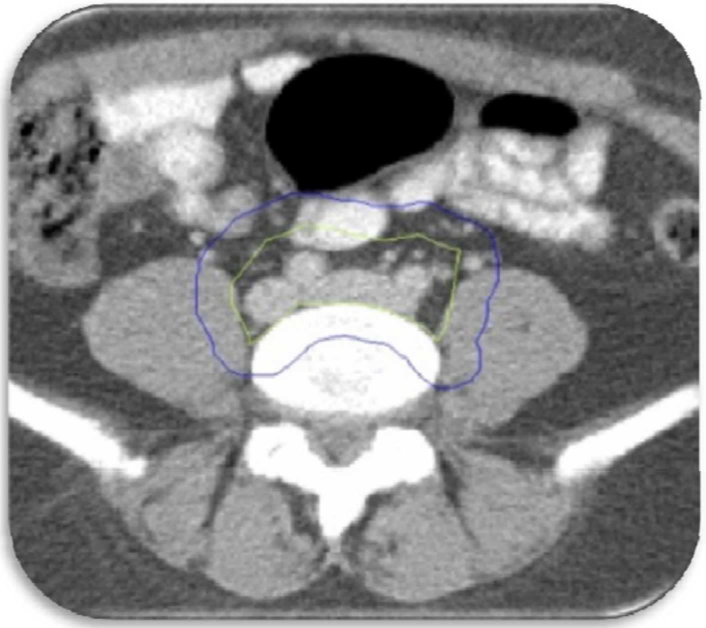


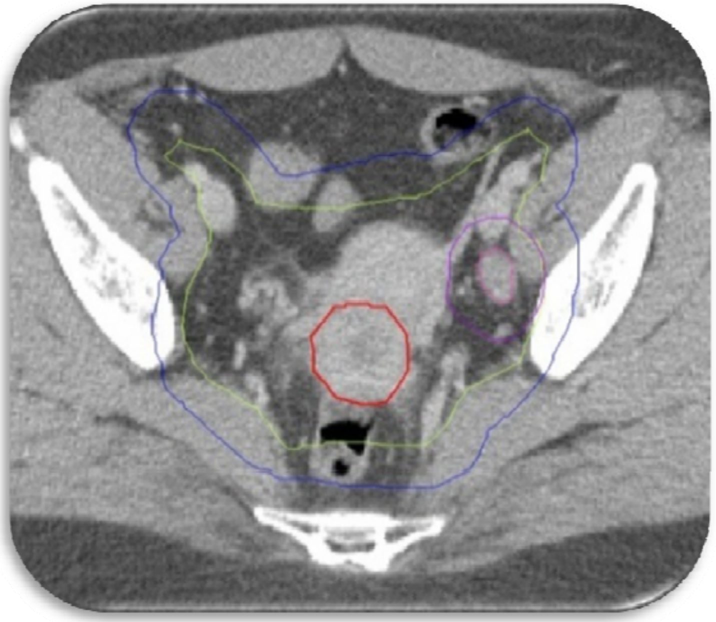
Within the pelvis, cervical cancer spreads first to parametrial nodes, then to obturator, internal and external iliac nodes.

In more advanced disease, common iliac and para-aortic nodes may be involved.

Although not incorporated in the FIGO staging system, presence of lymph node metastases has significant prognostic and treatment consequences.

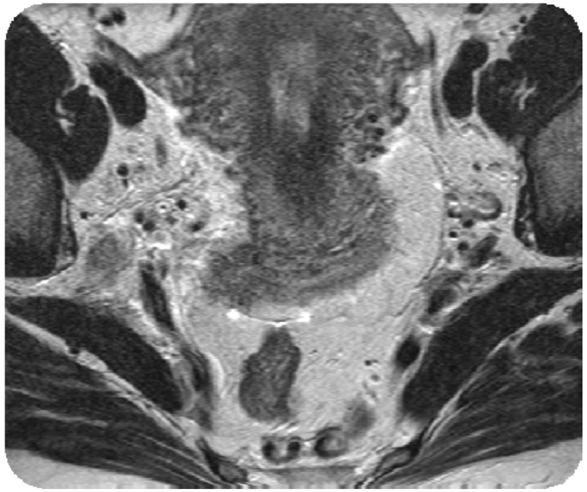
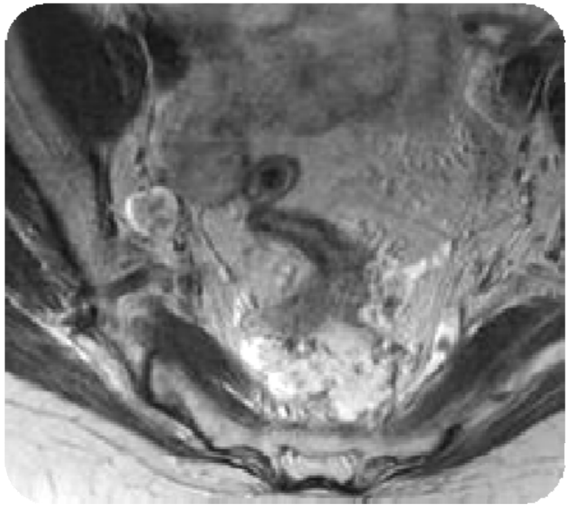
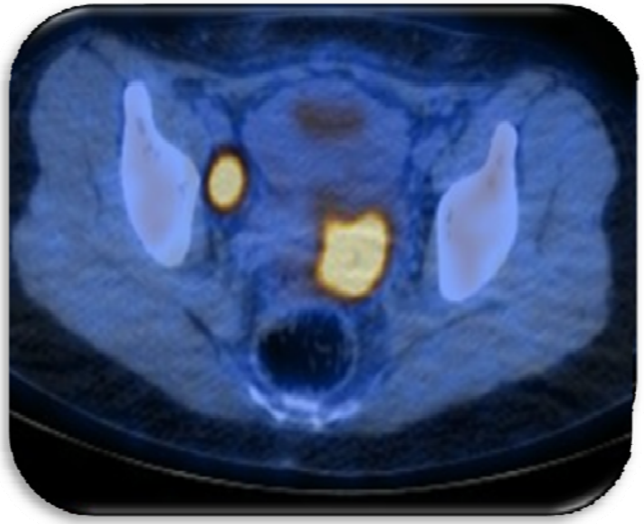
The 5-year survival for node positive patients is 39-54% compared with 67-92% in patients without nodal involvement .



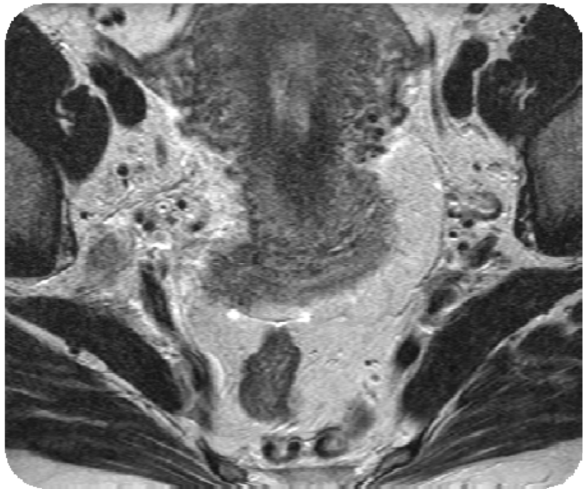


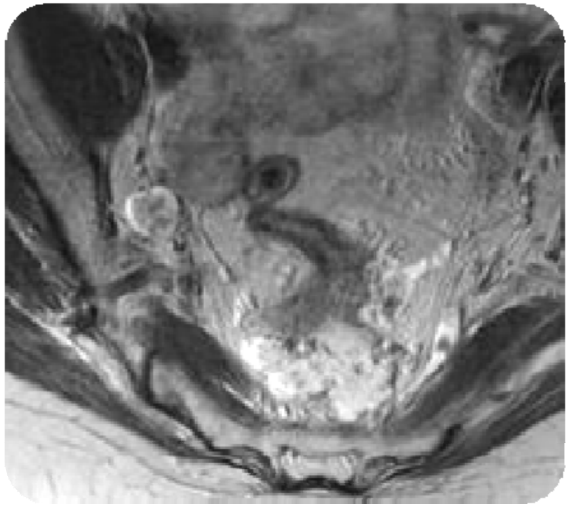
In early stage tumour, nodal involvement is important as it excludes curative surgery changing management to non surgical treatment

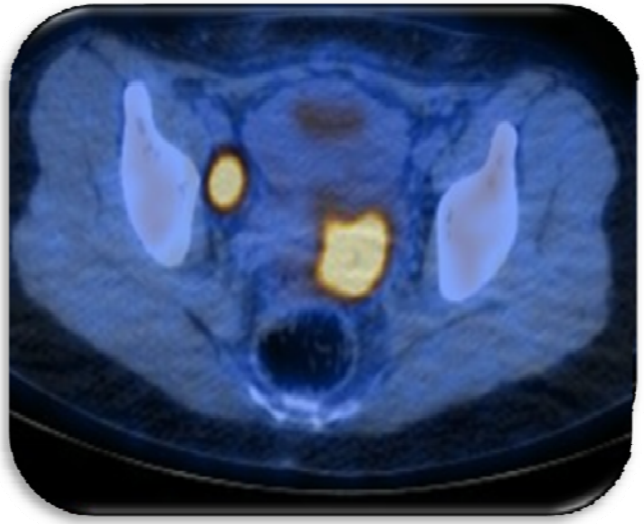
In advanced disease, detection of para-aortic nodes is important for planning the extent of the radiation field.

- Limitations to nodal assessment with all imaging techniques
- Size criteria
- Consistency and outline
- Inability to identify metastatic disease in normal sized nodes

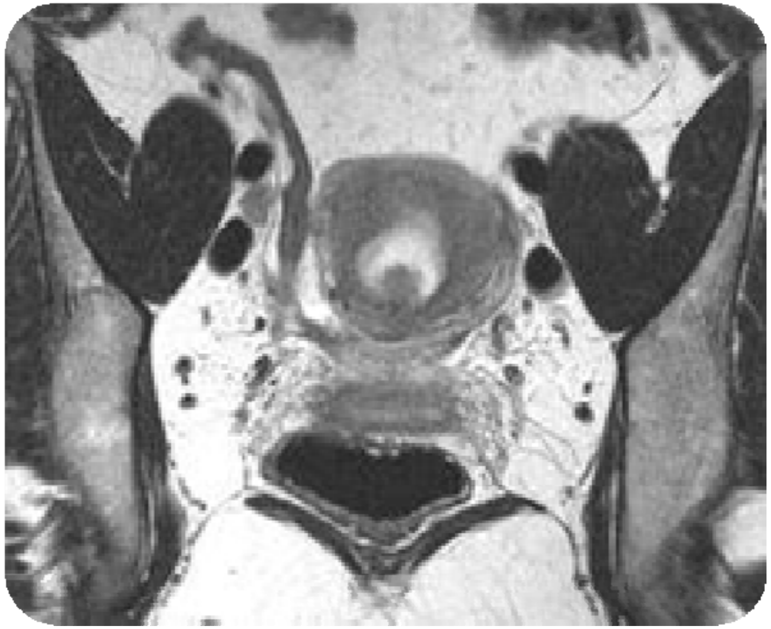


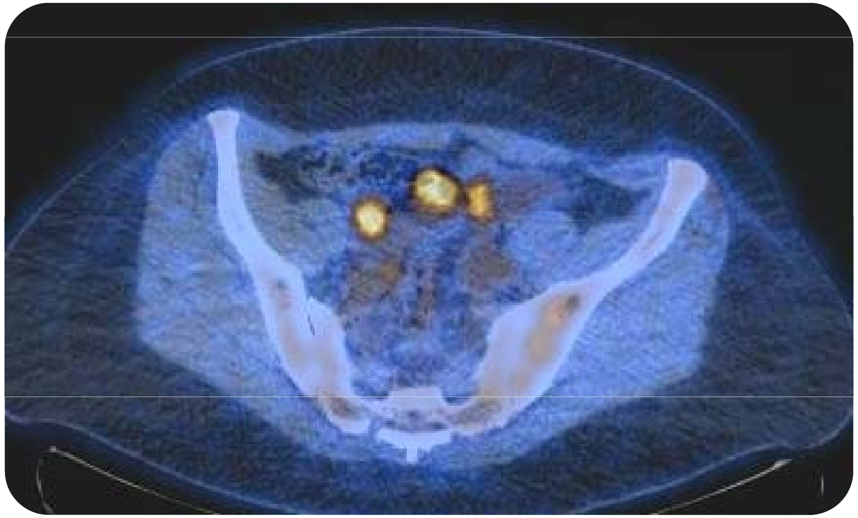




- **PET CT high sensitivity for detecting nodal disease in > Stage IB2 disease**
- **Positive predictive value high enough to modify treatment strategy**

Rose et al J Clin Onc 1999
Naragyan et al J Int Gynecol Oncol 2001





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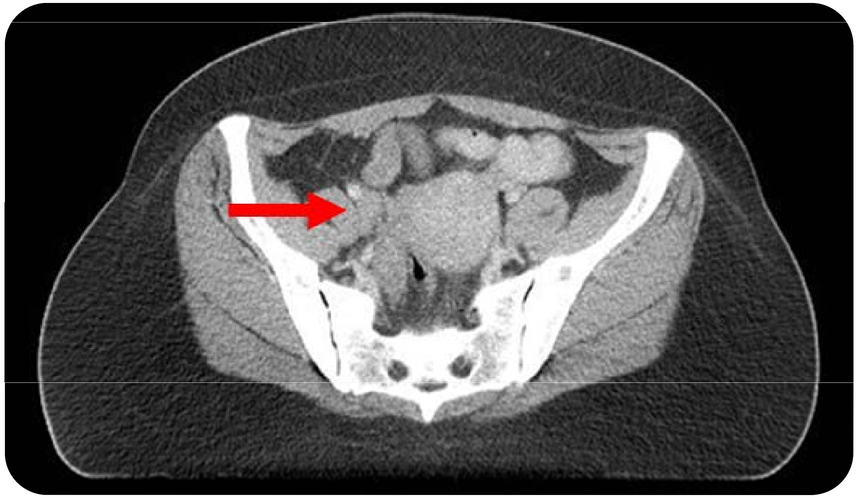

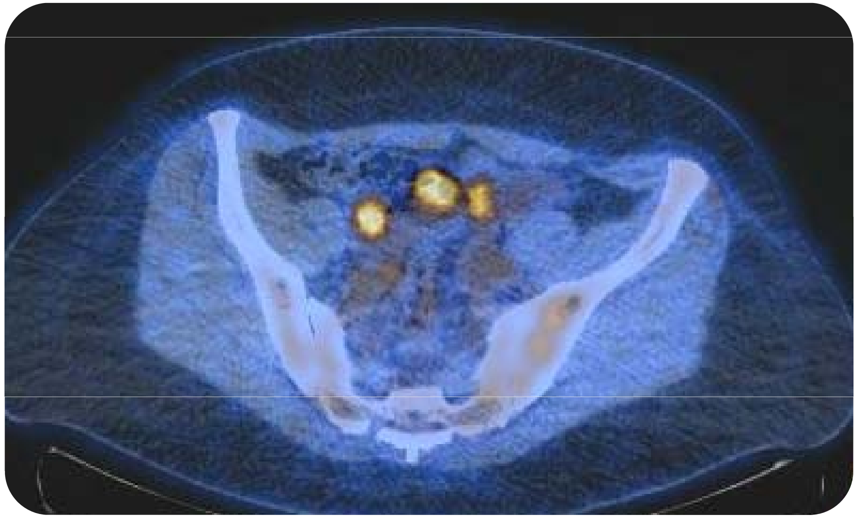

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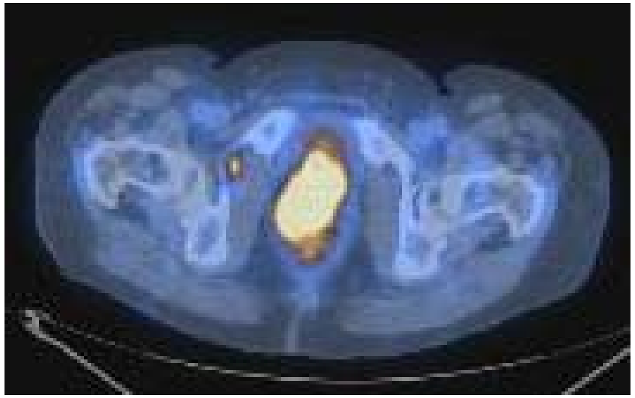 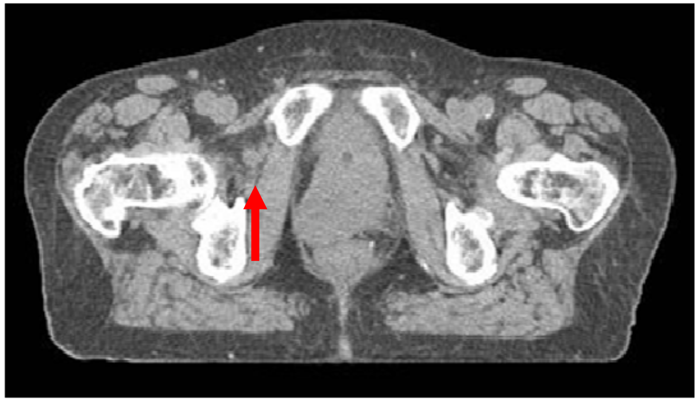 

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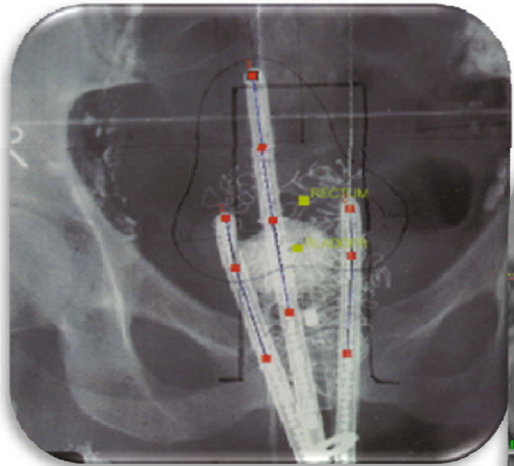
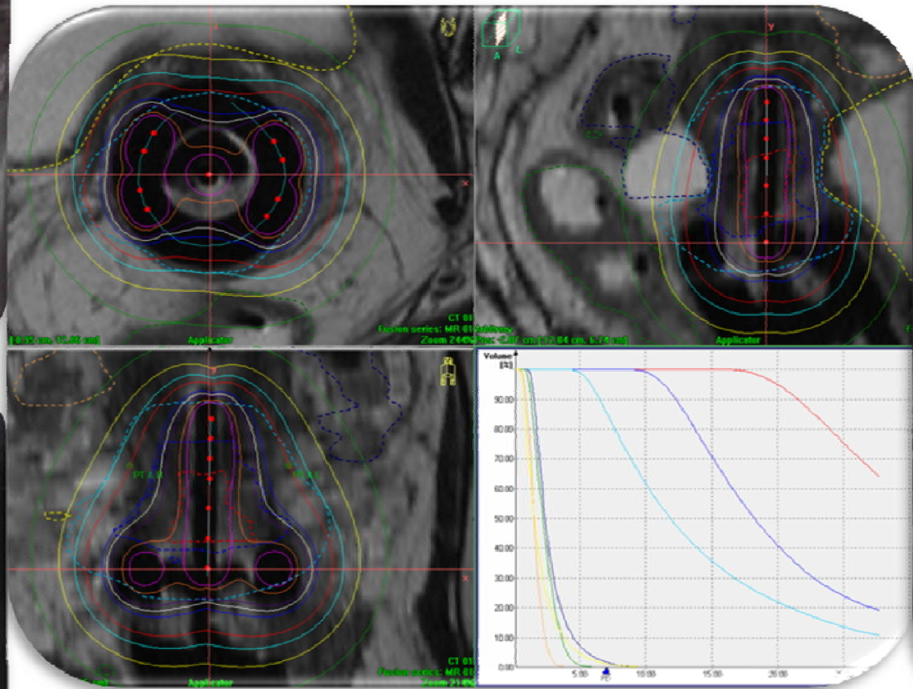
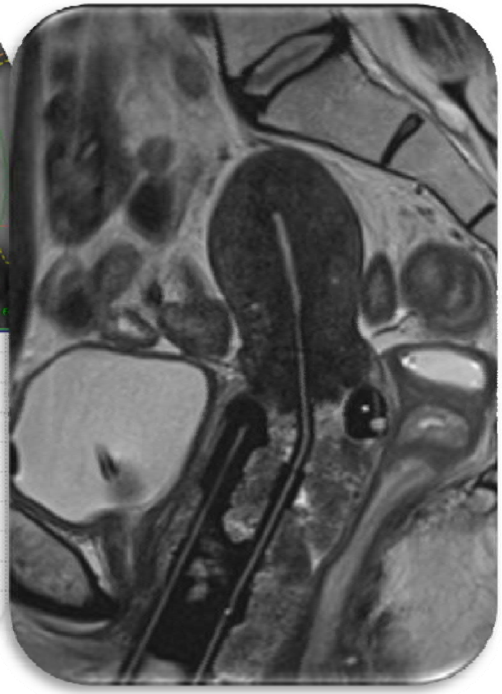
# Imaging for brachytherapy

# Imaging for brachytherapy



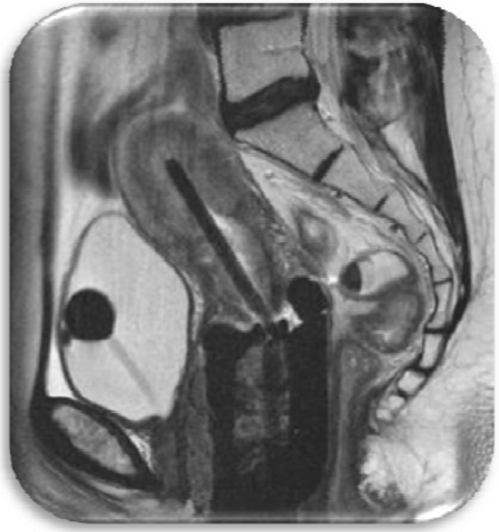


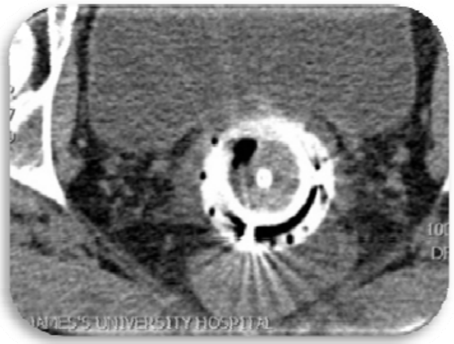


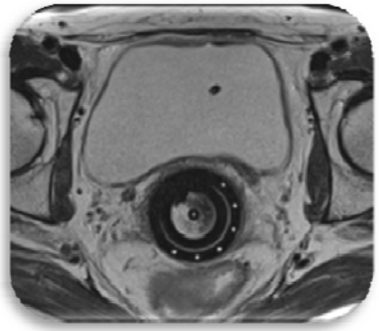


# Imaging for Brachytherapy

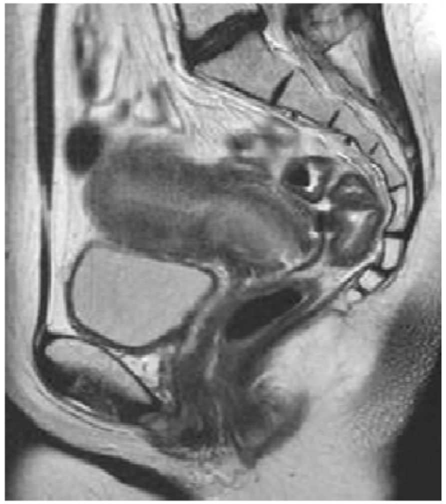
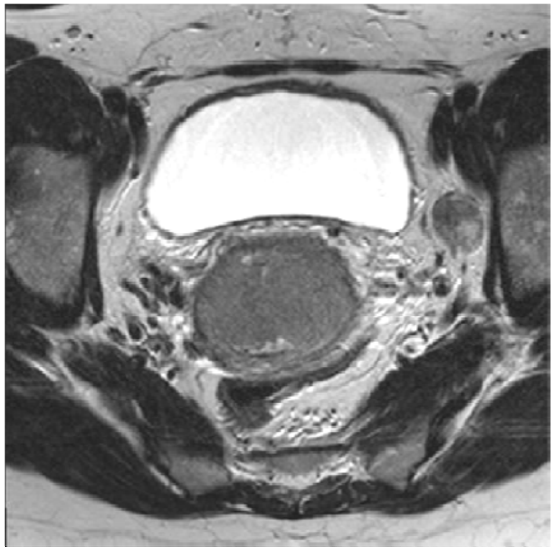
- **MRI compatible brachytherapy applicators**
- **Use MR Imaging for delineation of visible GTV**
- **'High risk' CTV**



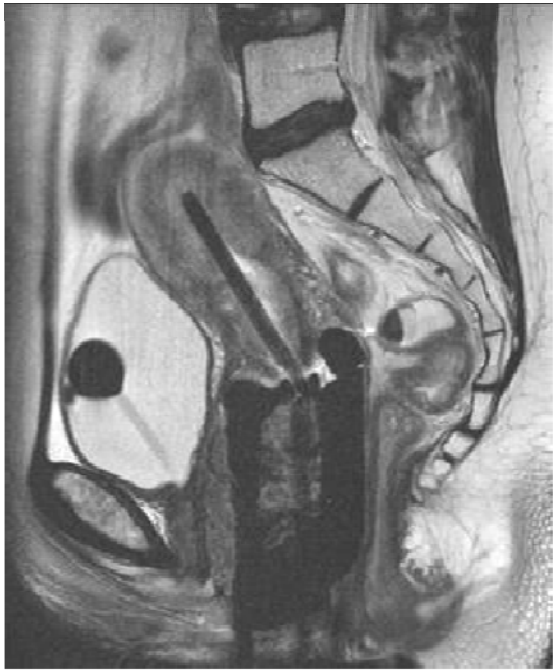




# Imaging for brachytherapy


# Imaging for brachytherapy



ESTRO School

WWW.ESTRO.ORG/SCHOOL

# Target volume definition in brachytherapy for cervical and prostate cancer

**Ángeles Rovirosa**

**Radiation Oncology Dpt.**
**Hospital Clínic i Universitari, Barcelona**

International Journal of
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EDITORIAL

# Curative Radiation Therapy for Locally Advanced Cervical Cancer: Brachytherapy Is NOT Optional

Kari Tanderup, PhD,[*,†] Patricia J. Eifel, MD,[‡] Catheryn M. Yashar, MD,[§] Richard Pötter, MD,[‖] and Perry W. Grigsby, MD[*]

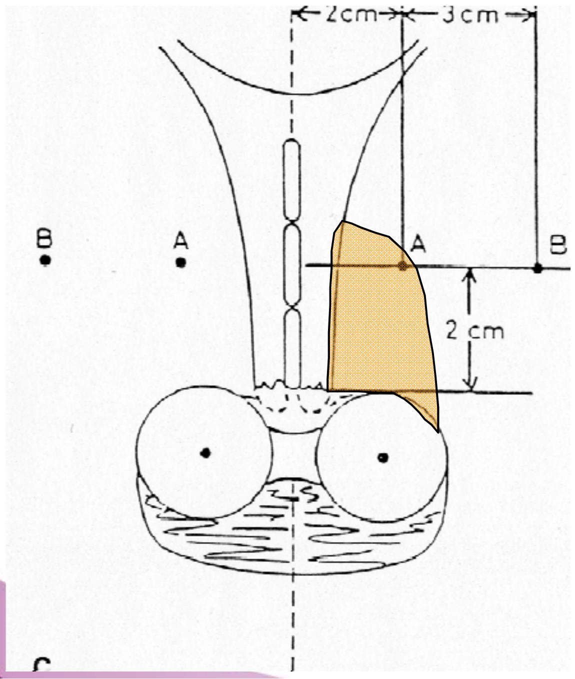
*Department of Radiation Oncology, Washington University School of Medicine, St. Louis, Missouri; †Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; ‡Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; §Department of Radiation Oncology, University of California, San Diego, La Jolla, California; and ‖Department of Radiotherapy and Oncology, Comprehensive Cancer Center and Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University of Vienna, Vienna, Austria

# Cervical cancer: TVD Brachy

**1903 Radium: Empirical dose prescription.**

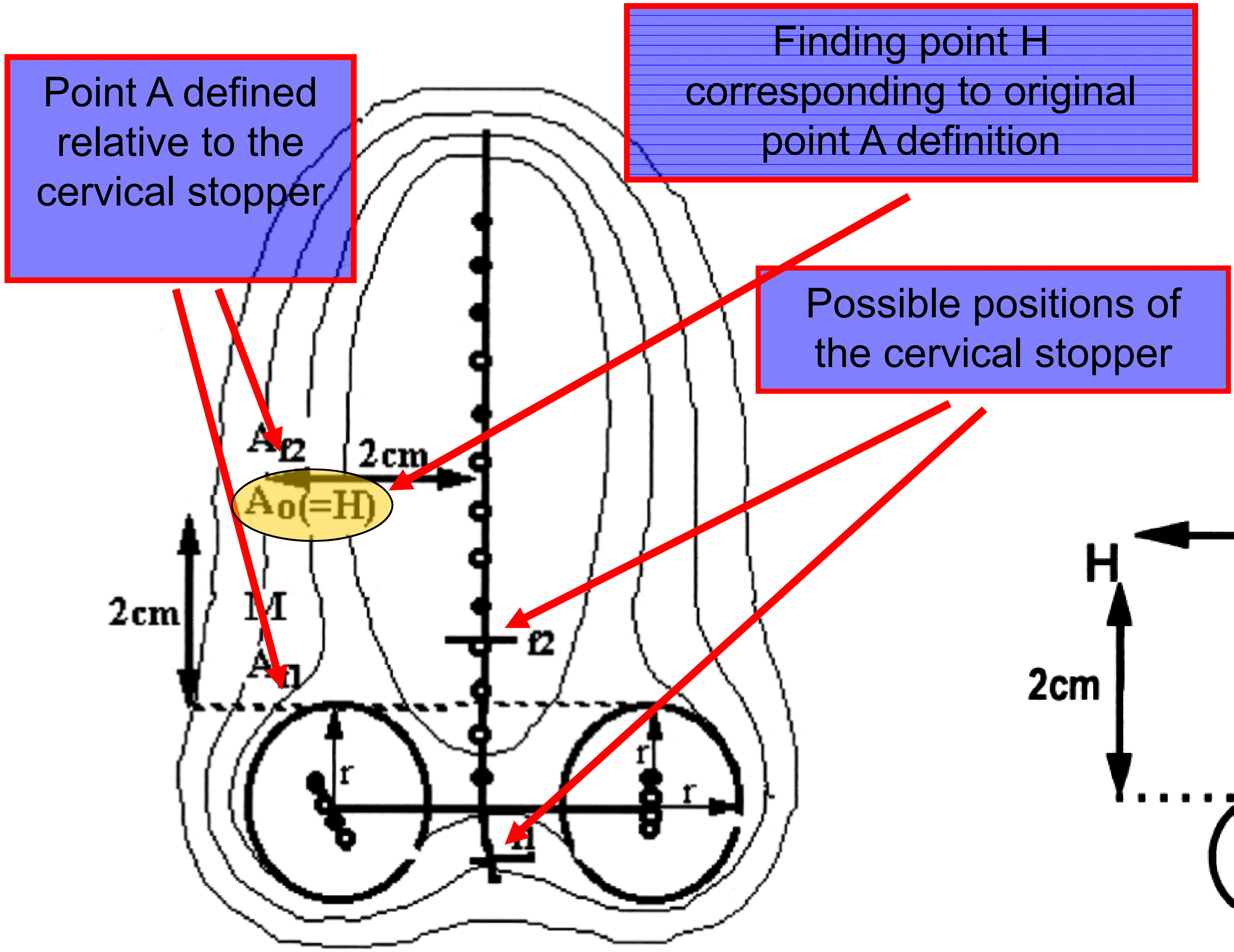
**Lack of:** 1) knowledge about biological effects of radiation
on normal tissue and tumor.
2) Understanding about dose, dose distribution
and treatment duration.

**Paris, Manchester and Stockholm systems.**

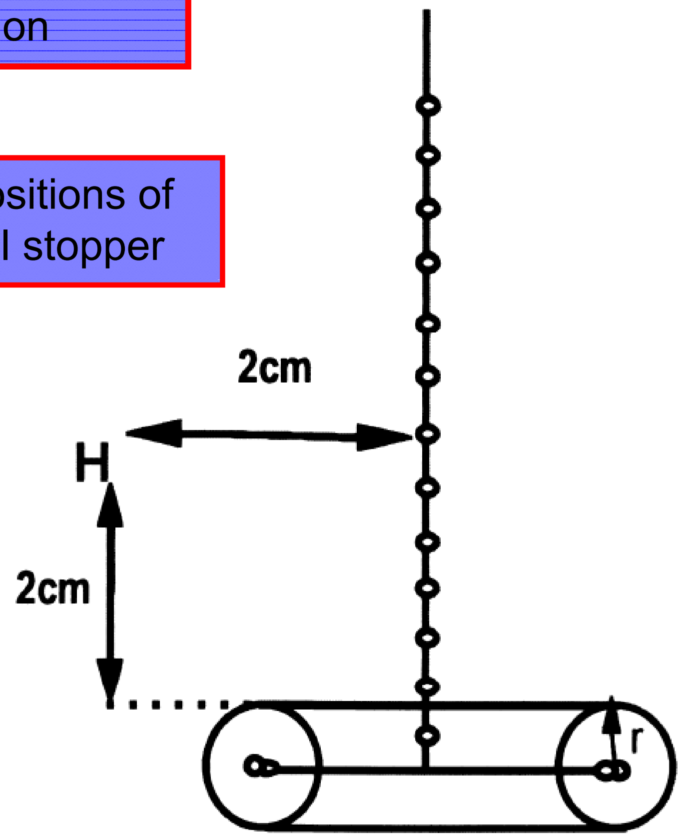



1. Inconsistent and varied definitions
2. Inconsistent and varied scoring and reporting systems
3. Volume was ignored

## The American Brachytherapy Society recommendations for HDR brachytherapy for carcinoma of the cervix

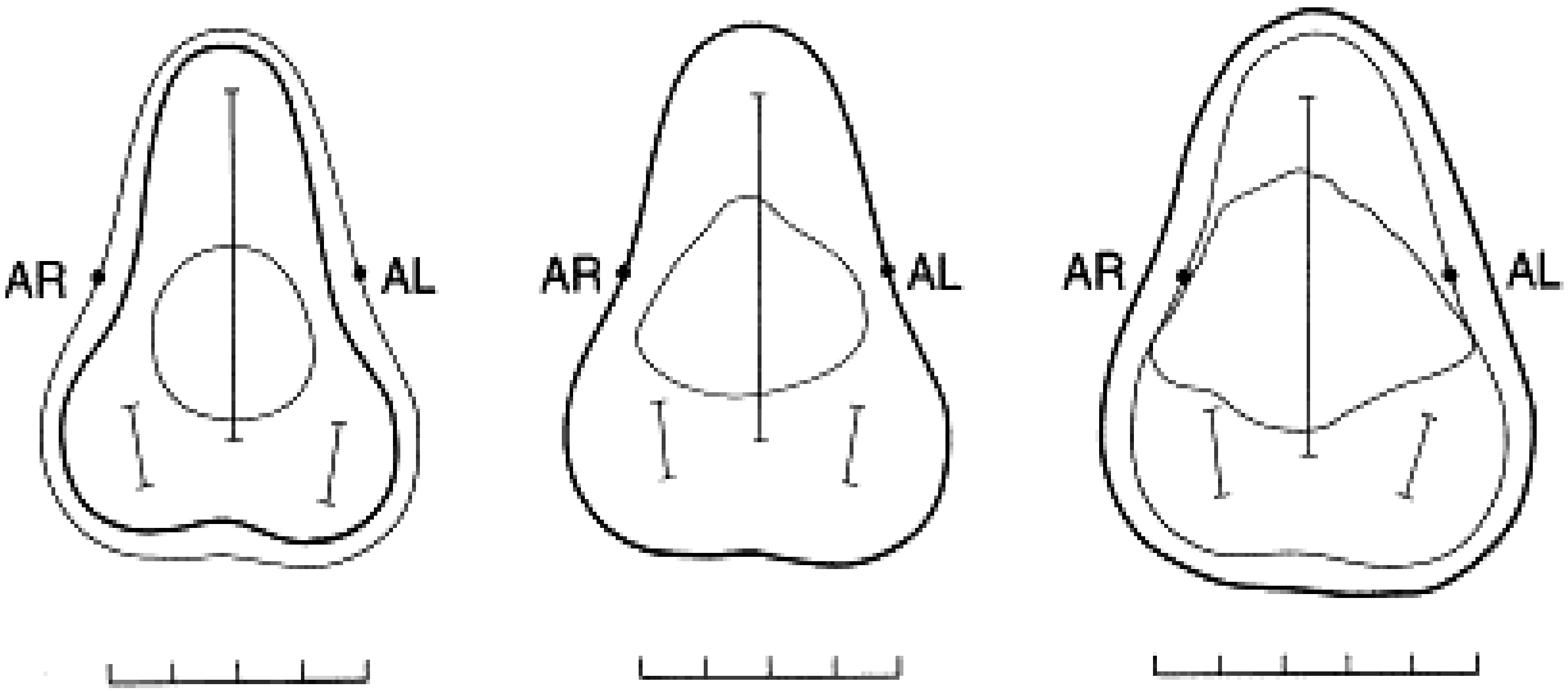



Tandem & ovoids




Tandem & ring

Nag S. et al. Int. J. Radiation Oncology Biol. Phys.,48, 201–211, 2000

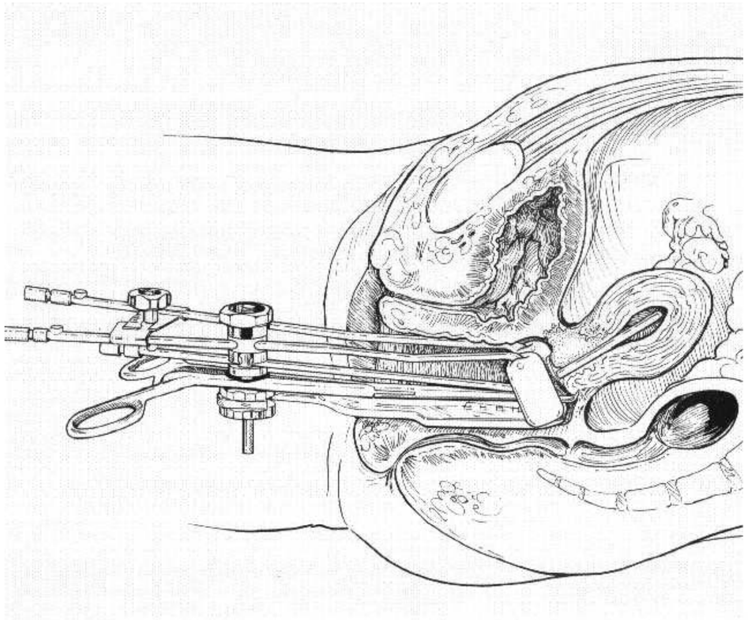


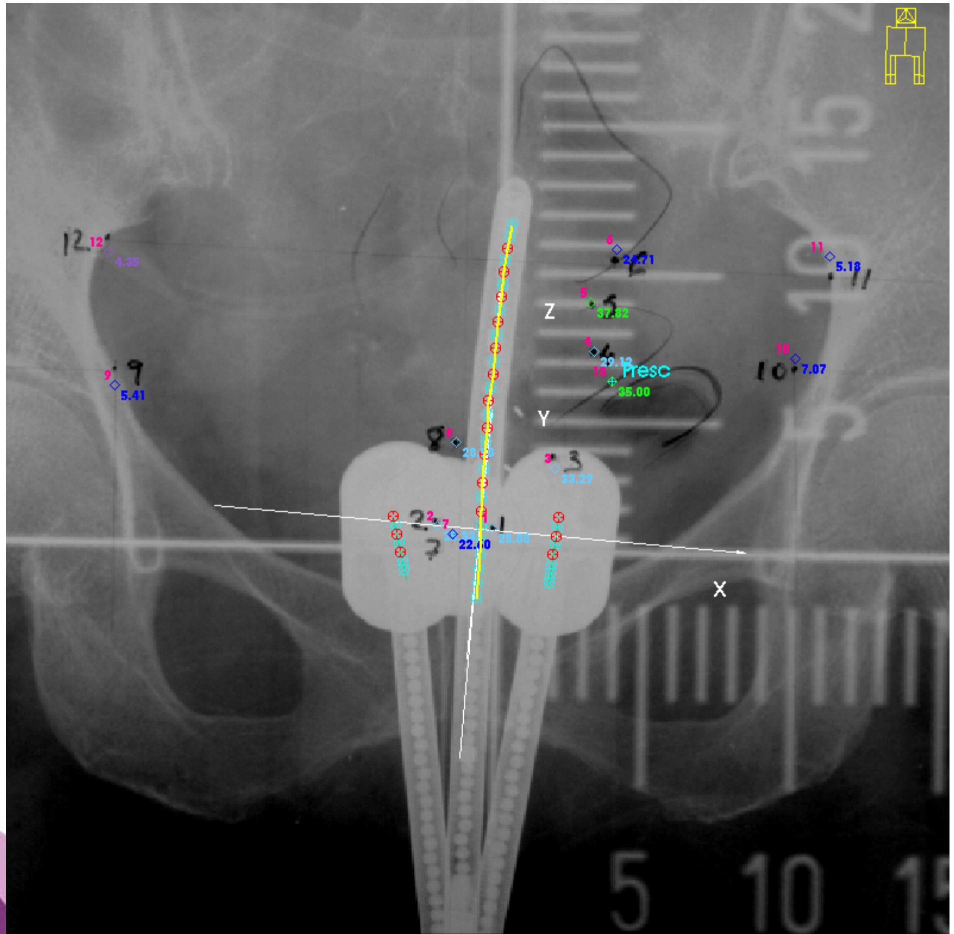

Tumor width 25 mm
Small pear
TRAK 3.04 cGy (LDR) at 1m
2.43 cGy (HDR) at 1m
Width Ref. Volume 52 mm
60 Gy Ref. Volume 59 cm³
Point A: 45 Gy LDR
36 Gy (6x6 Gy) HDR

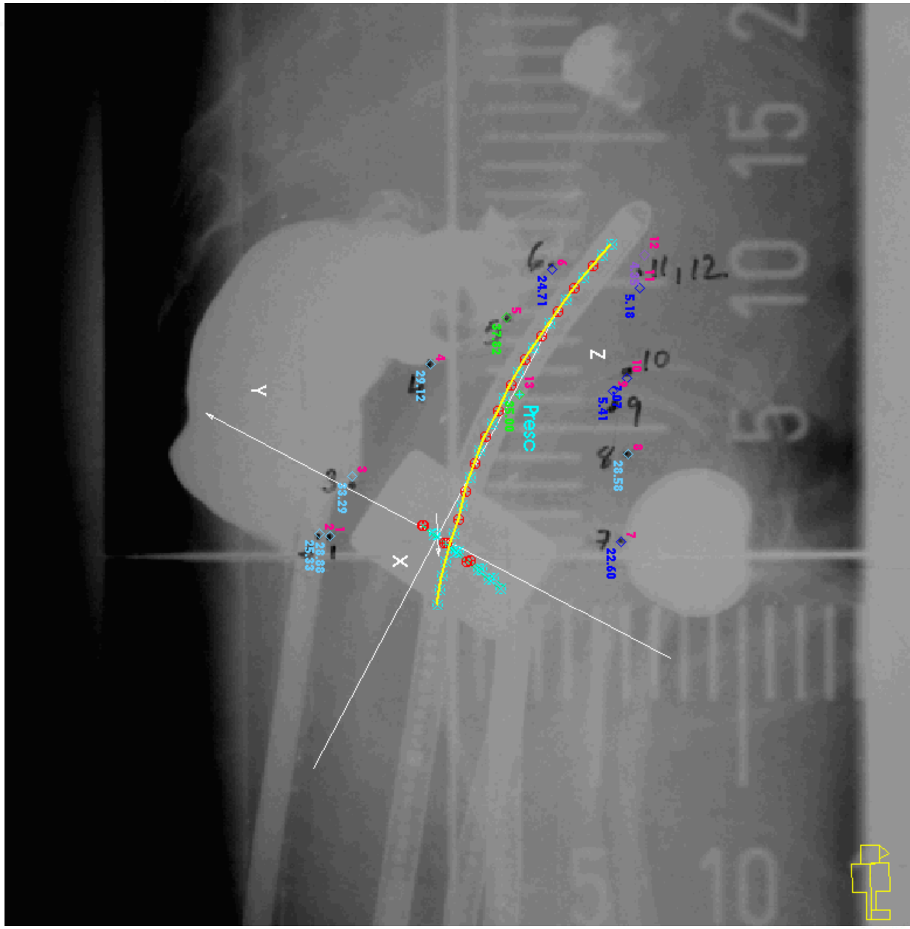
Tumor width 35 mm
Medium pear
TRAK 4.04 cGy (LDR) at 1m
2.83 cGy (HDR) at1m
Width Ref. Volume 59 mm
60 Gy Ref. Volume 89 cm³
Point A: 60 Gy LDR
42 Gy (6x7 Gy) HDR

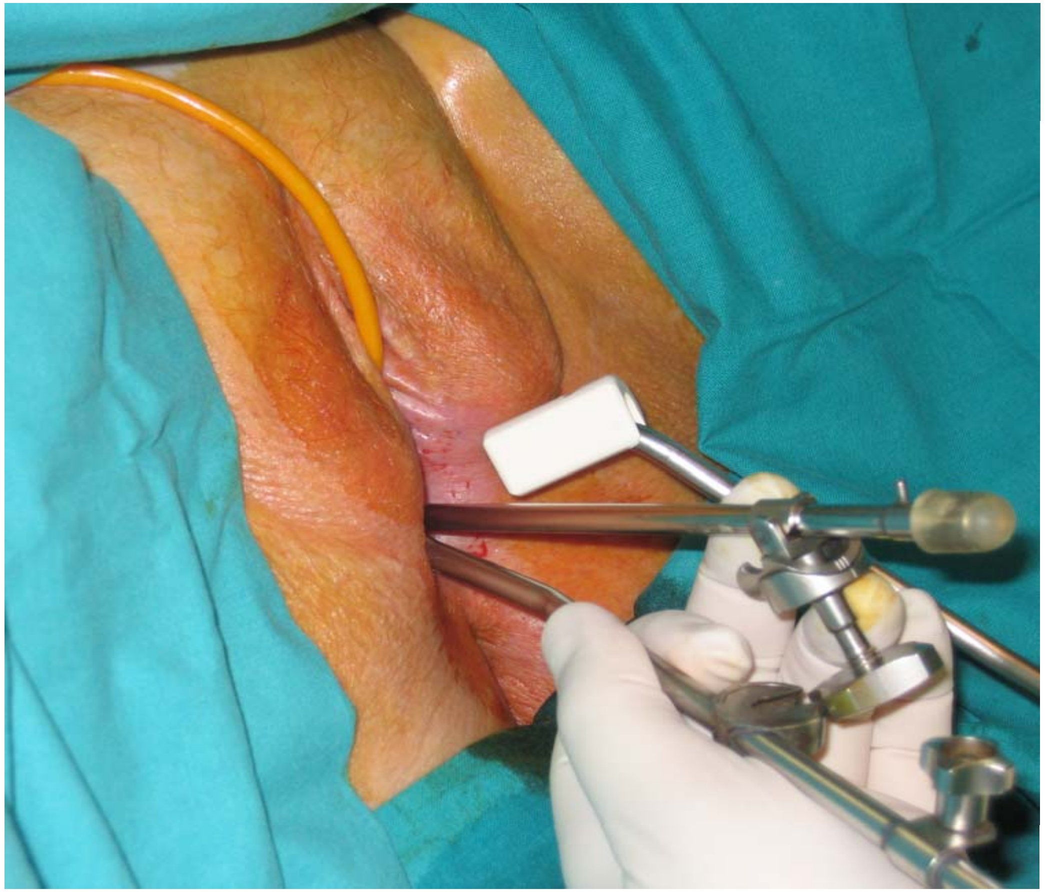
Tumor width 50 mm
Large pear
TRAK 5.72 cGy (LDR) at 1m
3.23 cGy (HDR) at 1m
Width Ref. Volume 67 mm
60 Gy Ref. Volume 145 cm³
Point A: 84.5 Gy LDR
48 Gy (6x8 Gy) HDR

# 2D planning








X-ray (2D)

- GOOD implant reconstruction and spatial resolution
- BETTER OAR position determination in regards to implant
- LESS anatomical information on OAR volumes

CT (3D)

- GOOD implant reconstruction and spatial resolution
- BETTER anatomical information on OAR volumes and doses

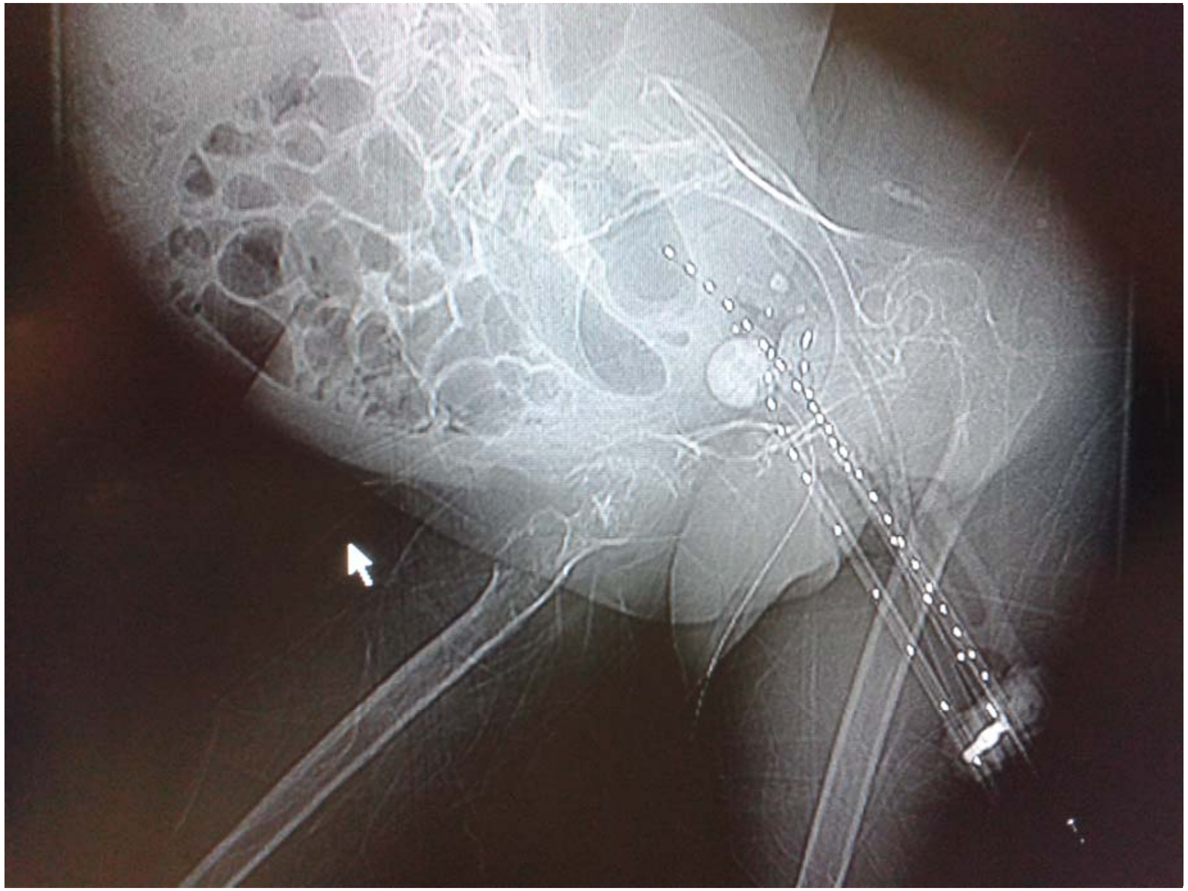
# PREVIOUS GOLD KEYS FOR TVD AND PLANNING

Precise clinical examination before EBI and brachy.

MR before EBI and brachy.

Correct implant (US guided) and implant geometry


H. CLINIC - BARCELONA -
10:08:32 Lu 20/12/2010
SIEMENS
Renal
30 dB
3.6 MHz
CD 60 dB
Persist 3
Contorno 1
R/V 3
Mapa F
Matiz 1
MI: 0.7
D = 9.6mm
14cm
19pps
Medición
TB: BDistance
Distancia
%Estenosis
Longitud trazo
Volumen
Area
Vol de flujo
Angulo
Relación A/B
Posición MDA



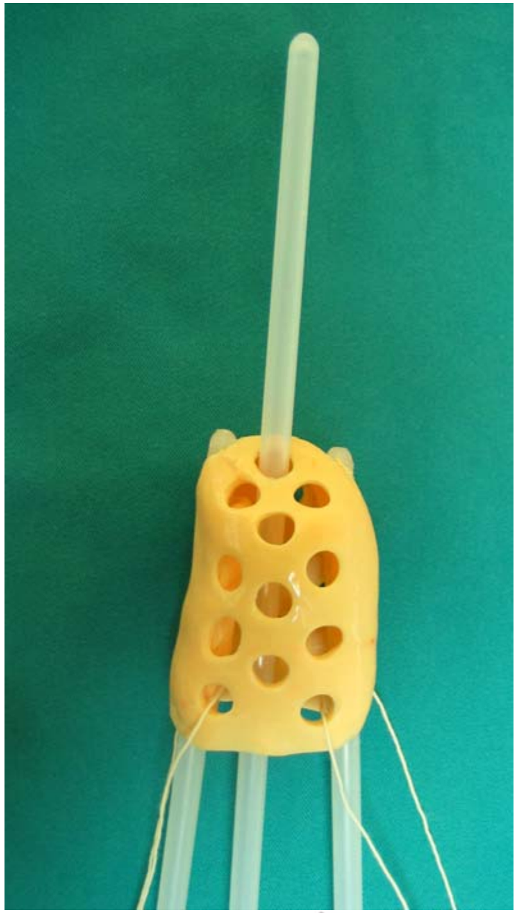
# Brachytherapy as a 3D conformal technique

Viewing of target volume and other relevant anatomical structures

Calculation of 3D dose distributions

Display and evaluation of dose distributions

And the use of dose-volume histograms



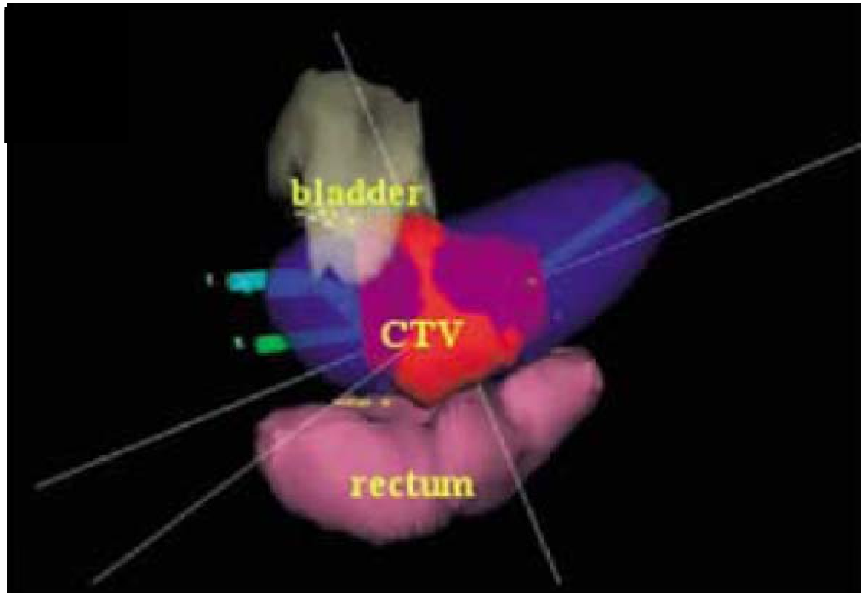
# Comparison of point A plan with 3D plan

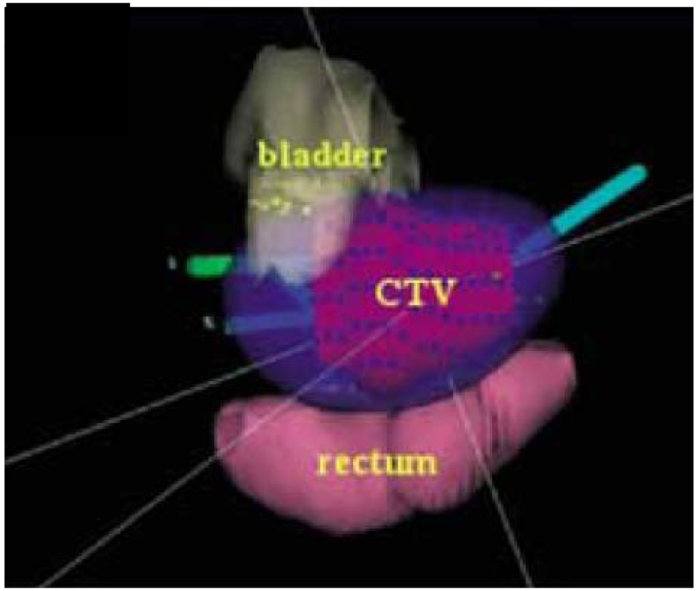
Large CTV

not fully encompassed by 100% isodose line prescribed to point A

Conventional planning

3D planning




Kyung Wan Shin.. et al. Int. J. Radiation Oncology Biol. Phys., 64, 197–204, 2006

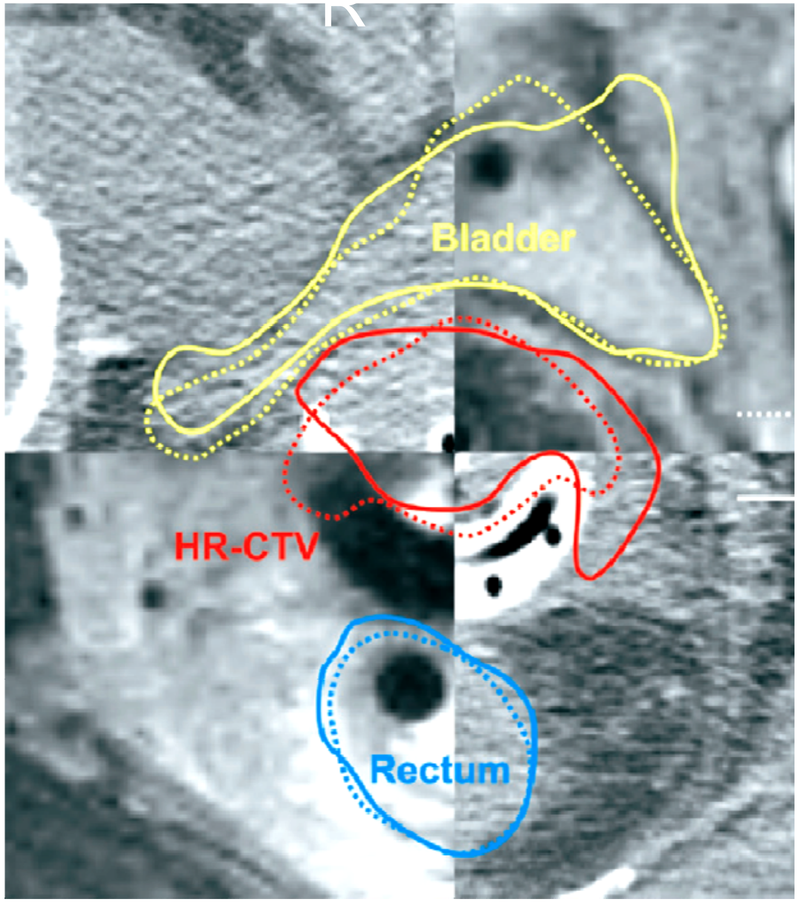
# CT versus MR

## MR: BETTER CONTRAST RESOLUTION OF SOFT TISSUES

•Outer rectum contours overlap nicely

•Bladder contours show only slight deviations

•The high-risk clinical target volume contour highlights the difference in lateral extension seen between CT and MR-imaging and reveals difficulty in accurately assessing the lateral dimension.




Viswanathan A.N... et al., Int. J. Radiation Oncology Biol. Phys., 68, 491–498, 2007

# CT versus MR

| Parameter | IR-$CTV_{MRI}$ | IR-$CTV_{CTStd}$ |
|---|---|---|
| Height (cm) | 7.1 ± 2.5 | 6.1 ± 1.3 |
| Width at Point A (cm) | 6.7 ± 1.1 | 8.1 ± 0.9 ($p = 0.01$)* |
| Thickness at Point A (cm) | 5.3 ± 1.3 | 4.8 ± 0.9 |
| Volume ($cm^3$) | 115.1 ± 46.9 | 117.9 ± 45.7 |
| $V_{100}$ (%) | 75 ± 10 | 71 ± 15 |
| $D_{100}$ (Gy) | 3.0 ± 0.8 | 2.2 ± 0.5 ($p = 0.01$)* |
| $D_{90}$ (Gy) | 5.6 ± 1.0 | 4.6 ± 1.2 ($p = 0.02$)* |

Viswanathan A.N... et al., Int. J. Radiation Oncology Biol. Phys., 68, 491–498, 2007

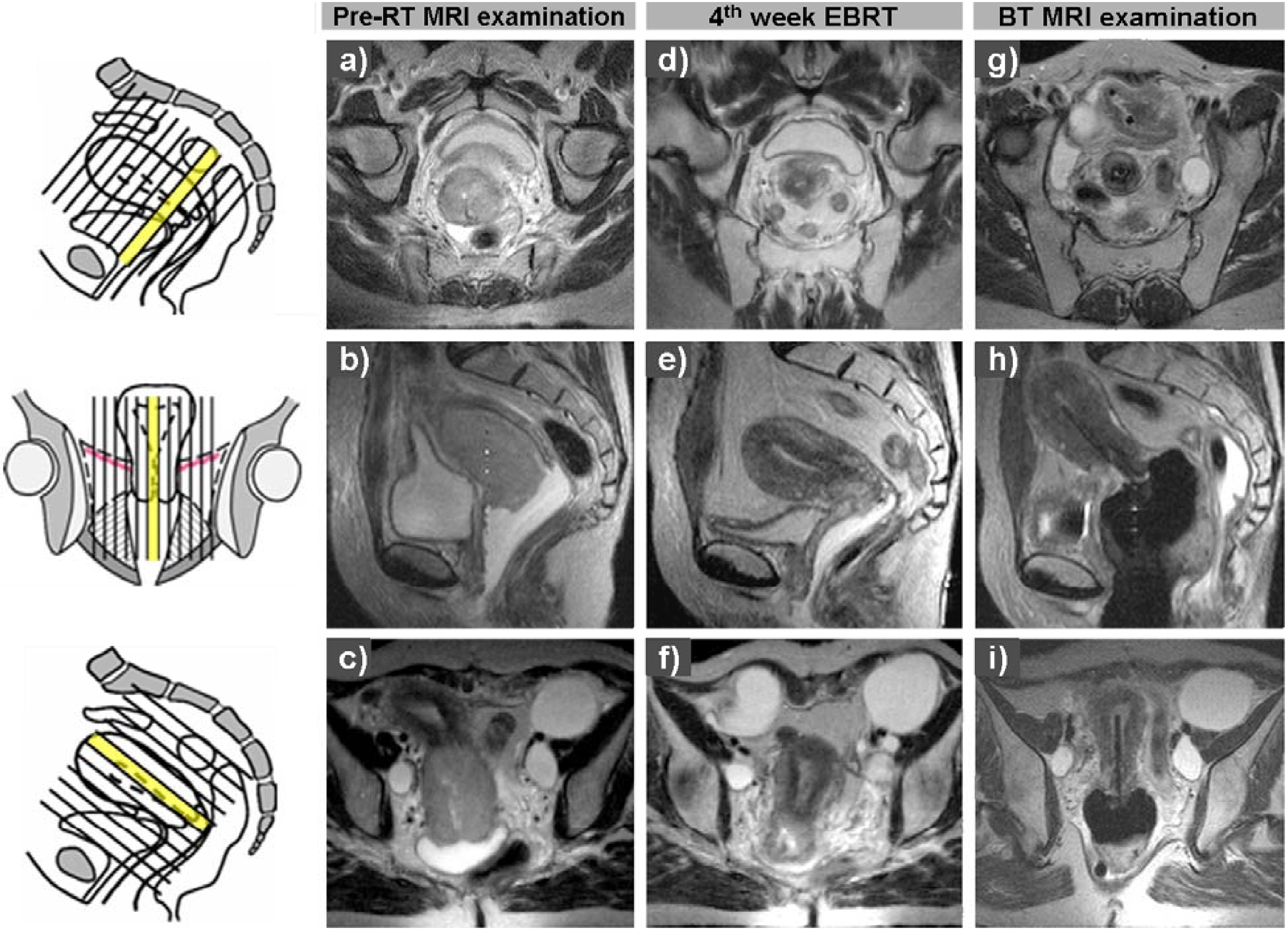
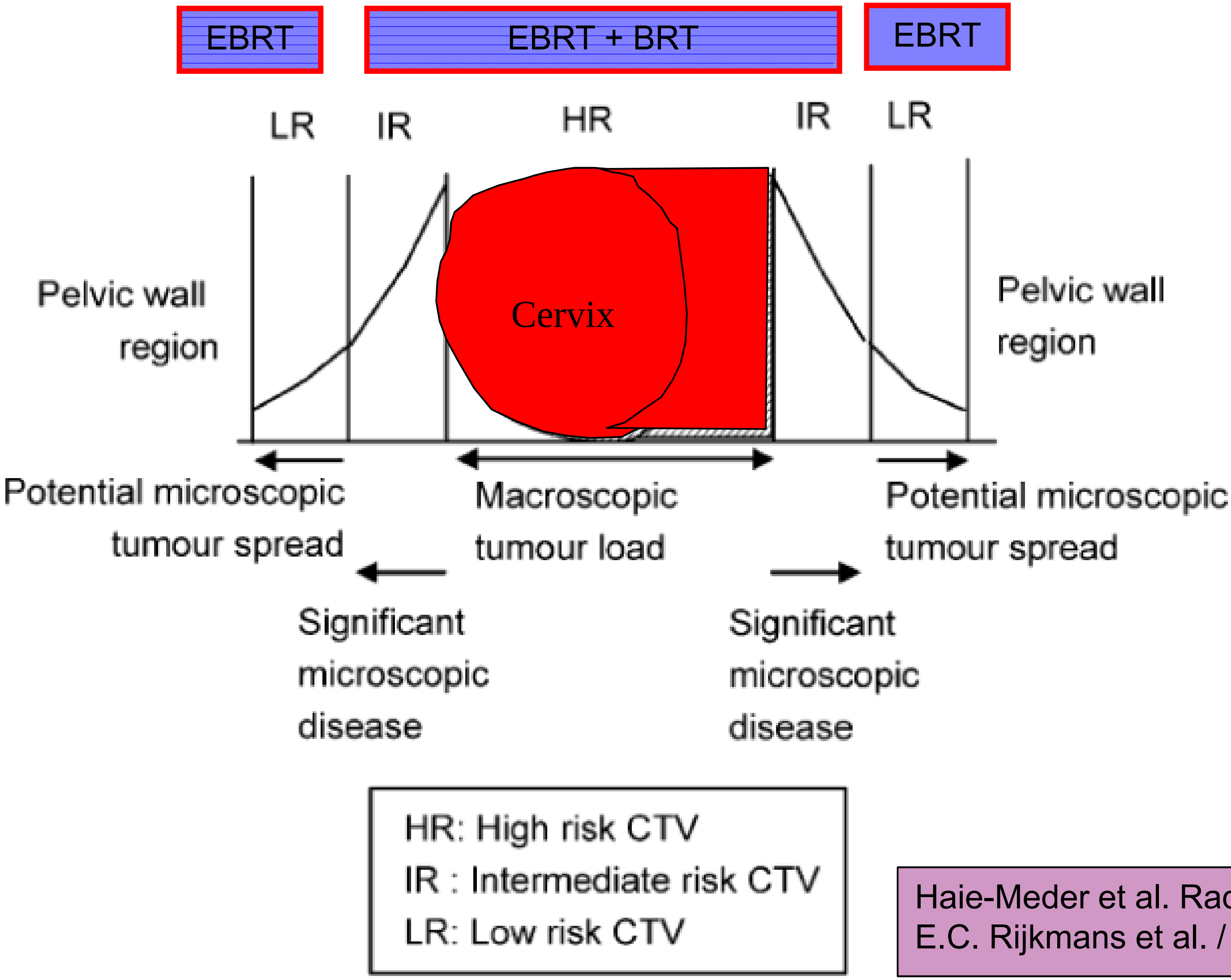



Image acquisition: Imaging parameters: technique (e.g. spin echo (SE), fast spin echo (FSE), turbo spin echo (TSE)), repetition times (TR), echo times (TE), field of view (FOV) and matrix of data collection

# Three different target volumes according to cancer cell density




**The standard brachytherapy dose schedule for HDR was 21 Gy in 3 fractions of 7 Gy, in the CBT period specified at point A.**

**IGBT period: specified at the 100% isodose around the HR-CTV, aiming at a total EQD2 dose of 80–85 Gy to 90% of HR-CTV (D90 HR-CTV).**

**In some patients a fourth fraction, resulting in a total BT dose of 28 Gy was necessary to achieve an adequate dose to the HR-CTV. In a few patients with significant comorbidities, a schedule of 17 Gy HDR in 2 fractions of 8.5 Gy was used.**

Haie-Meder et al. Radiotherapy and Oncology 2005; 74:235-24.
E.C. Rijkmans et al. / Gynecologic Oncology 2014:135; 231–238

# GEC-ESTRO Recommendations

MR T2

GTV, HR-CTV, IR-CTV

D90 D100 V100

High Dose Volumes

V150 V200

OAR

0.1, 1, 2, 5, 10 cc

*Potter, RO 2006*

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]

*Haide-Meder RO 2005*

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group☆ (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV

Christine Haie-Meder[a,*], Richard Pötter[b], Erik Van Limbergen[c], Edith Briot[a], Marisol De Brabandere[c], Johannes Dimopoulos[b], Isabelle Dumas[a], Taran Paulsen Hellebust[d], Christian Kirisits[b], Stefan Lang[b], Sabine Muschitz[b], Juliana Nevinson[e], An Nulens[c], Peter Petrow[f], Natascha Wachter-Gerstner[b]

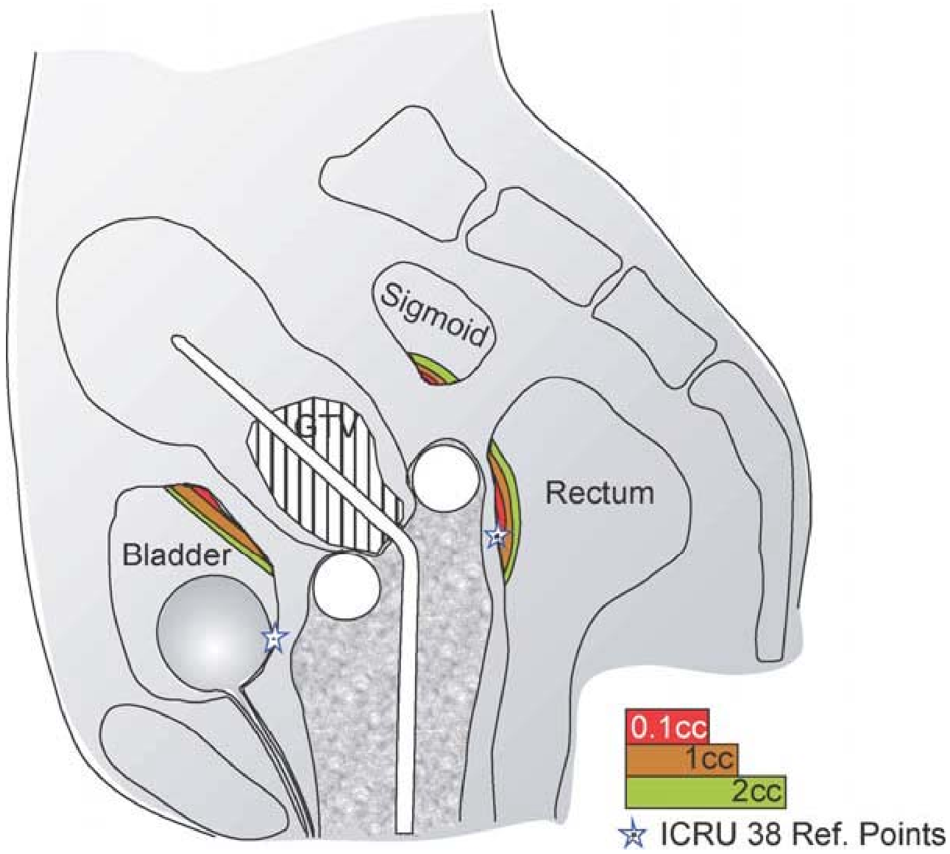
# GEC-ESTRO Recommendations

Cumulative dose volume histograms (DVH) are recommended for evaluation of the complex dose heterogeneity.

DVH parameters for GTV, HR CTV and IR CTV are the minimum dose delivered to 90 and 100% of the respective volume: D90, D100. The volume, which is enclosed by 150 or 200% of the prescribed dose (V150, V200), is recommended for overall assessment of high dose volumes. V100 is recommended for quality assessment only within a given treatment schedule.

For Organs at Risk (OAR) the minimum dose in the most irradiated tissue volume is recommended for reporting: 0.1, 1, and 2 cm3; optional 5 and 10 cm3. Underlying assumptions are: full dose of external beam therapy in the volume of interest, identical location during fractionated BT, contiguous volumes and contouring of organ walls for O2 cm3.

Dose values are reported as absorbed dose and also taking into account different dose rates. The linear-quadratic radiobiological model—equivalent dose (EQD2)—is applied for brachytherapy and is also used for calculating dose from external beam therapy. This formalism allows systematic assessment within one patient




Potter R. Radiotherapy and Oncology 2006; 78: 67–77

# GTV, HR-CTV and IR-CTV DELINEATION

**GTV:** Macroscopic tumour extension at time of brachytherapy in the cervix/ corpus, parametria, vagina, bladder and rectum using high signal intensity mass(es) (FSE, T2 MR).

**HR-CTV:** includes GTV, whole cervix, and presumed extracervical tumour extension.
Pathologic residual tissue(s) as defined by palpable indurations and /or grey zones in parametria, uterine corpus, vagina or rectum and bladder are included.
No safety margins are added.

**IR-CTV:** IR-CTV encompasses HR-CTV with a safety margin of 5 to15 mm.
The amount of safety margin is chosen according to tumour size, location, potential tumour spread, tumour regression and treatment strategy

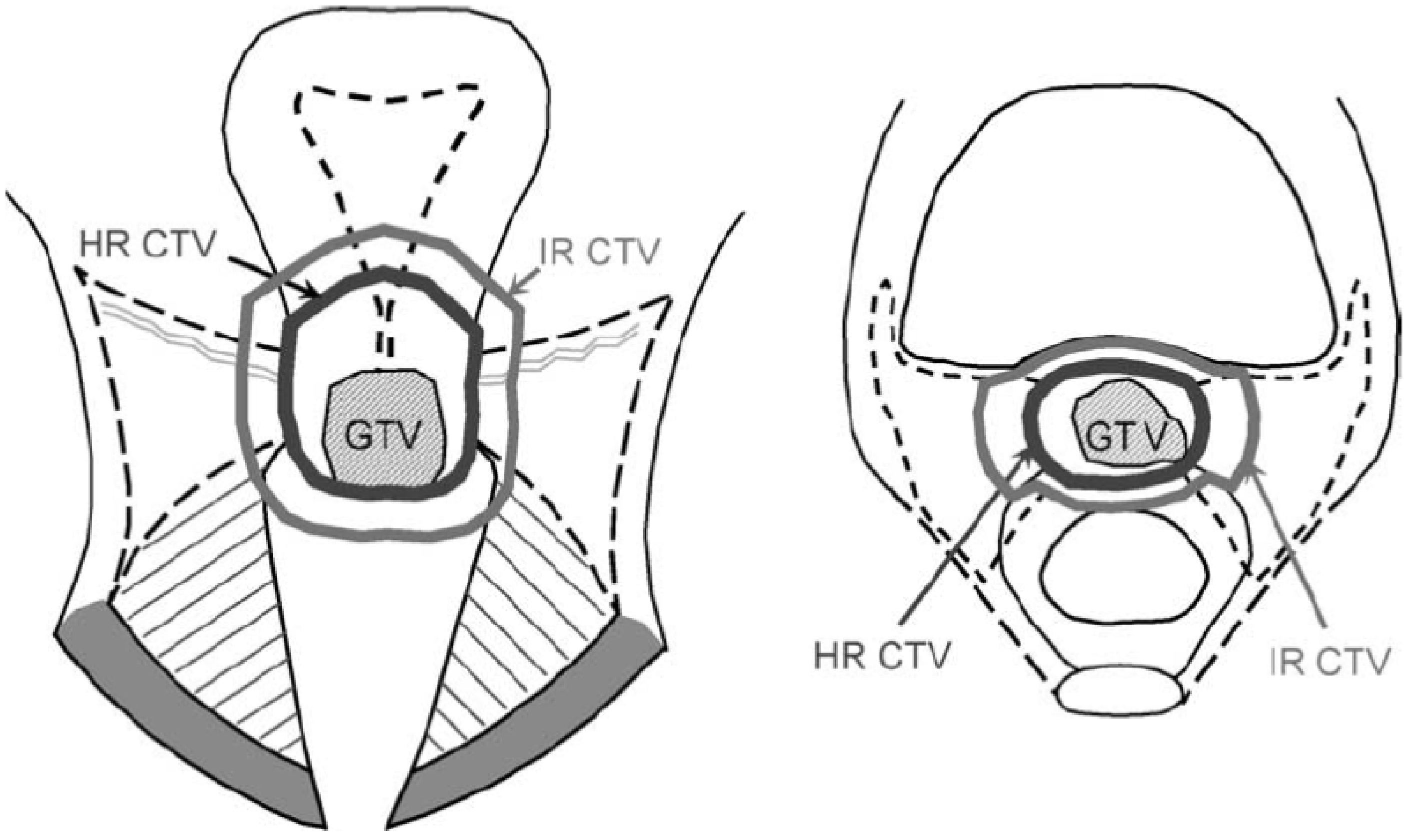
# OAR CONTOURING

**Rectum, bladder and sigmoid must be systematically delineated using the outer contour for delineation.**

**These organs at risk can readily be seen on CT and MR. MR delineation seems to be slightly easier (and more accurate?).**

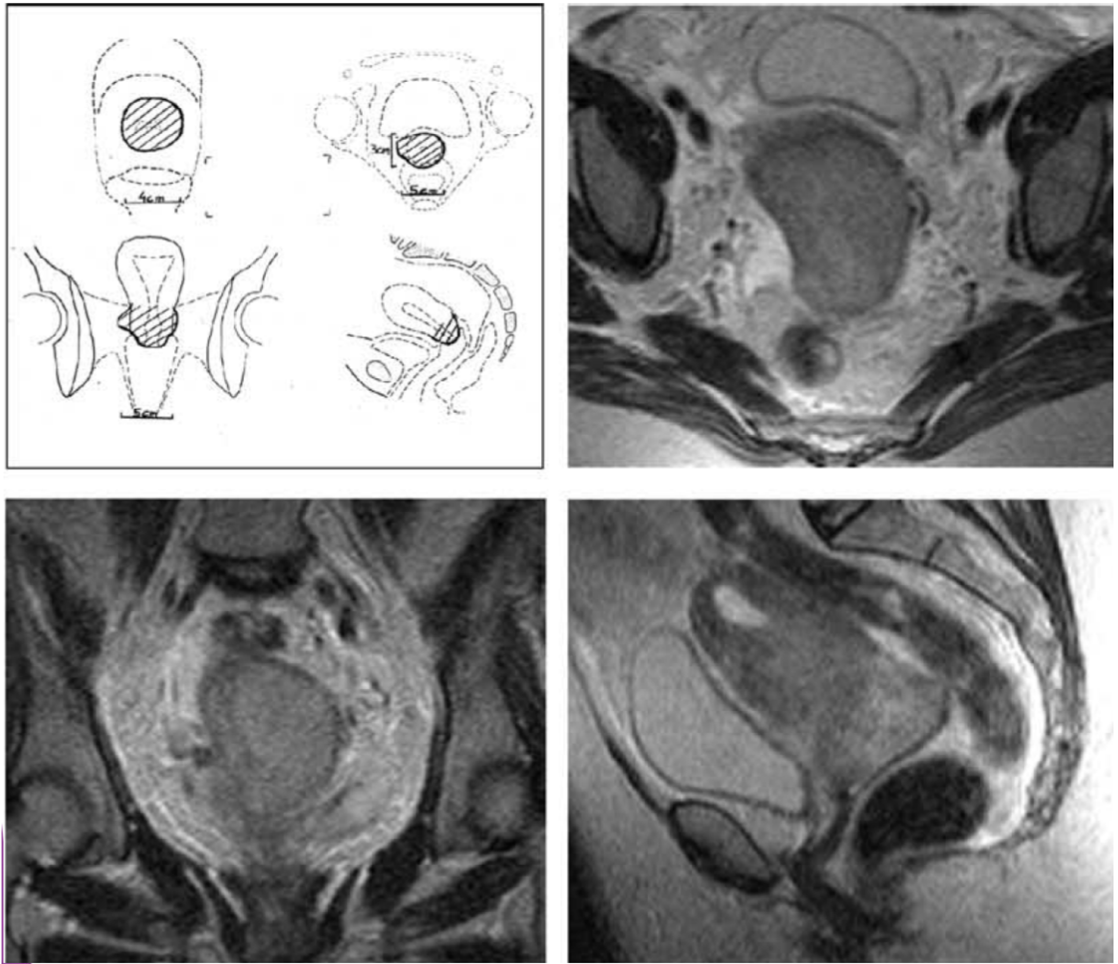
**Delineation of the outer contour permits a reliable estimation of the dose actually delivered to 2 and 5cc of the wall of the organ exposed to a high dose.**

# Schematic diagram for cervix cancer, limited disease, with GTV, high risk CTV and intermediate risk CTV

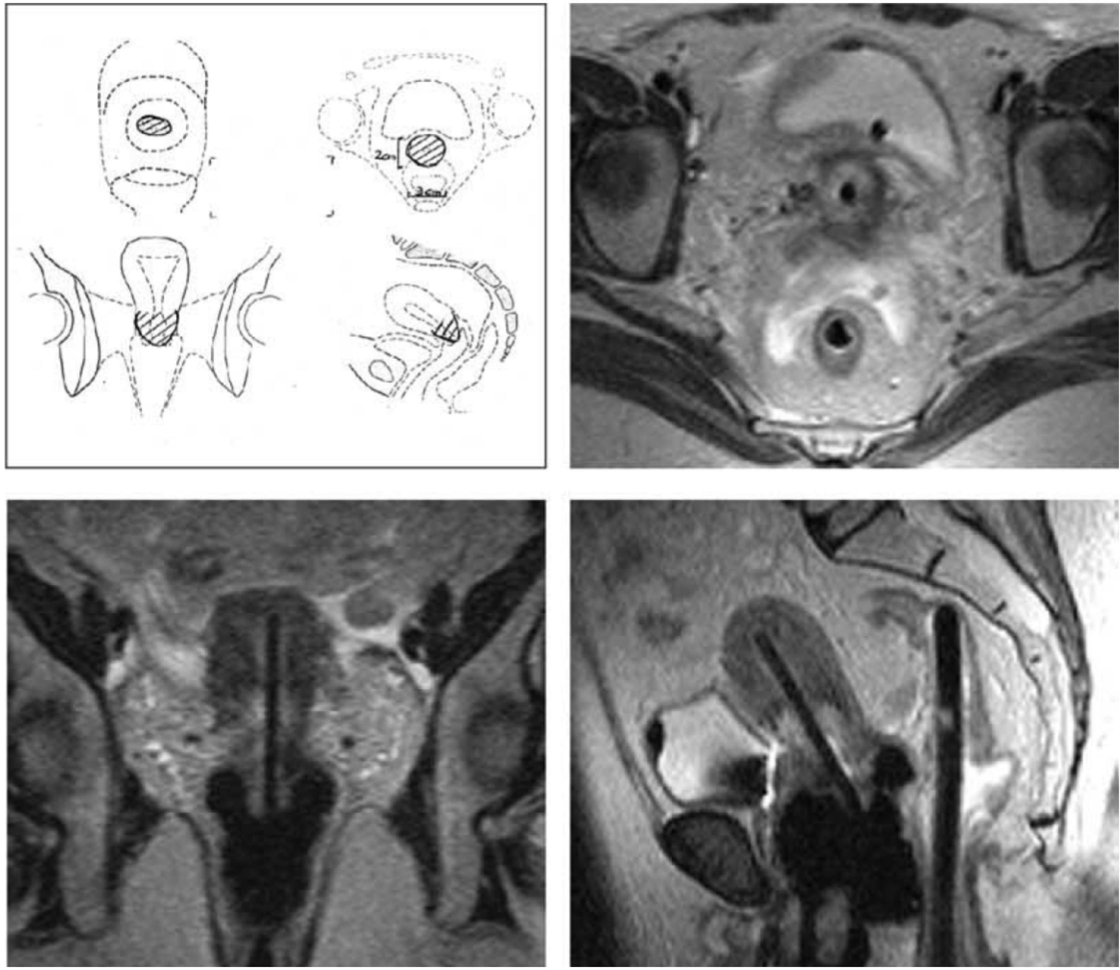



Haie-Meder C. et al., Radiotherapy and Oncology 74 (2005) 235–24

# Findings at diagnosis and at time of brachytherapy stage IIB: right proximal parametrial infiltration



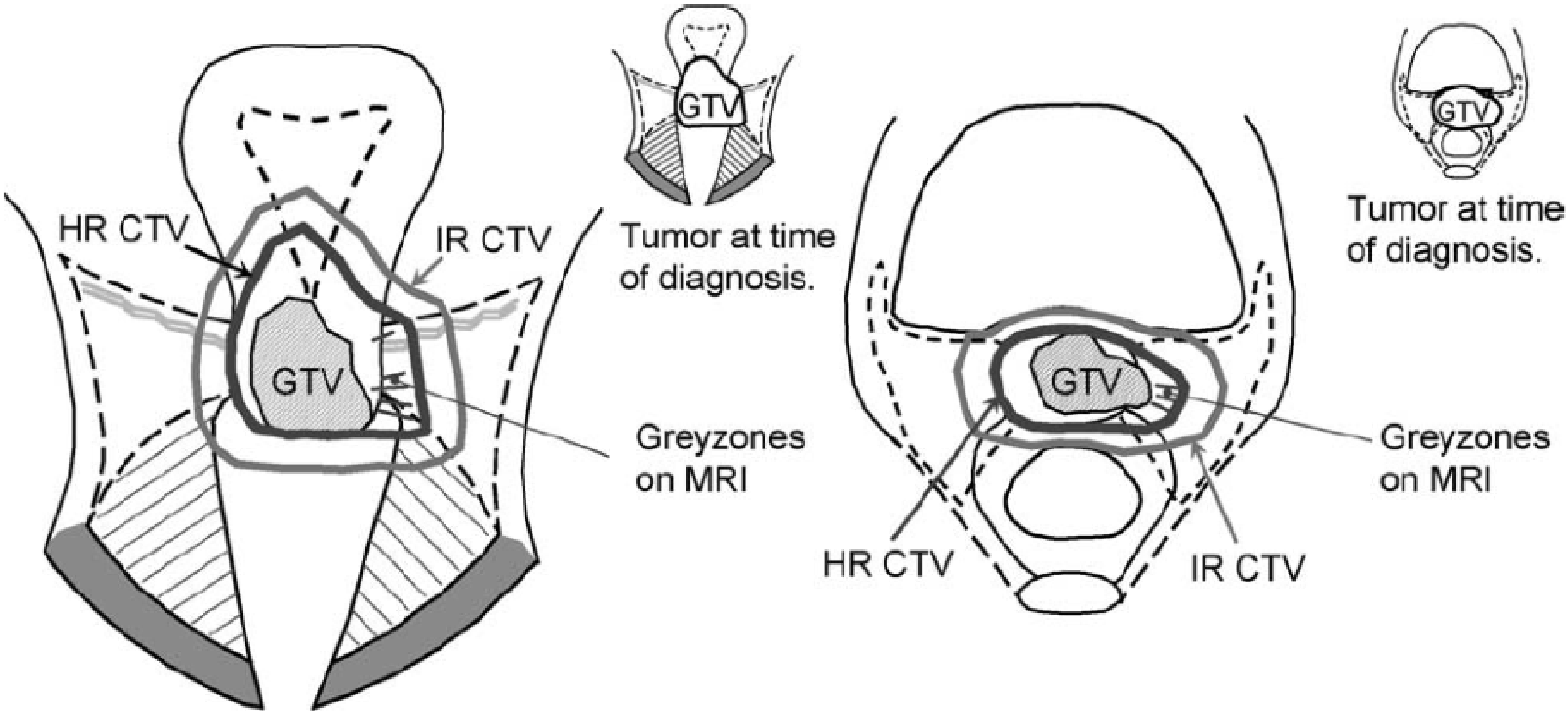
at diagnosis



at the time of brachytherapy

Haie-Meder C. et al., Radiotherapy and Oncology 74 (2005) 235–24

# Schematic diagram for cervix cancer, extensive disease, with GTV, high risk CTV and intermediate risk CTV




Haie-Meder C. et al., Radiotherapy and Oncology 74 (2005) 235–24

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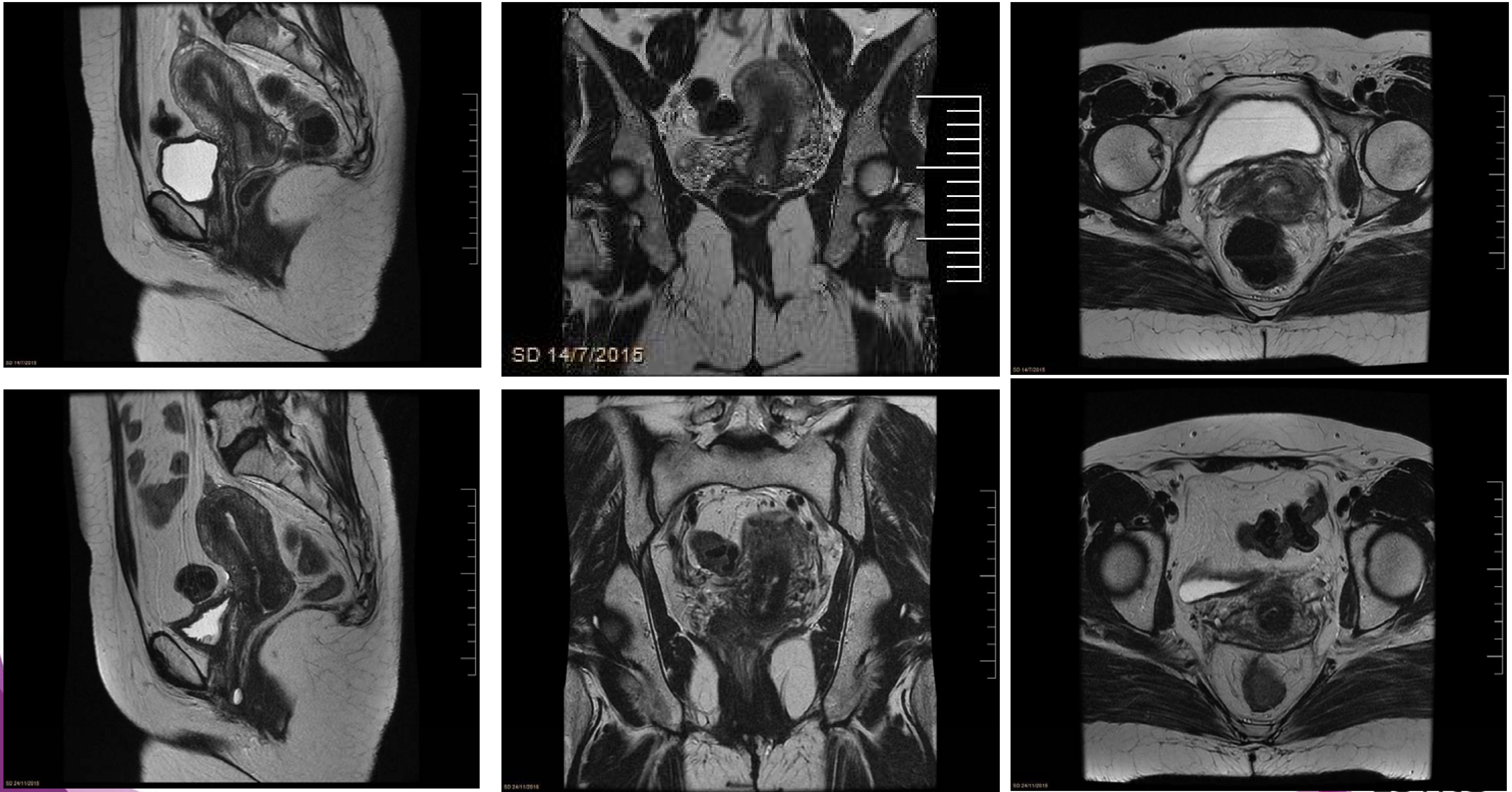
# MR CONTOURING

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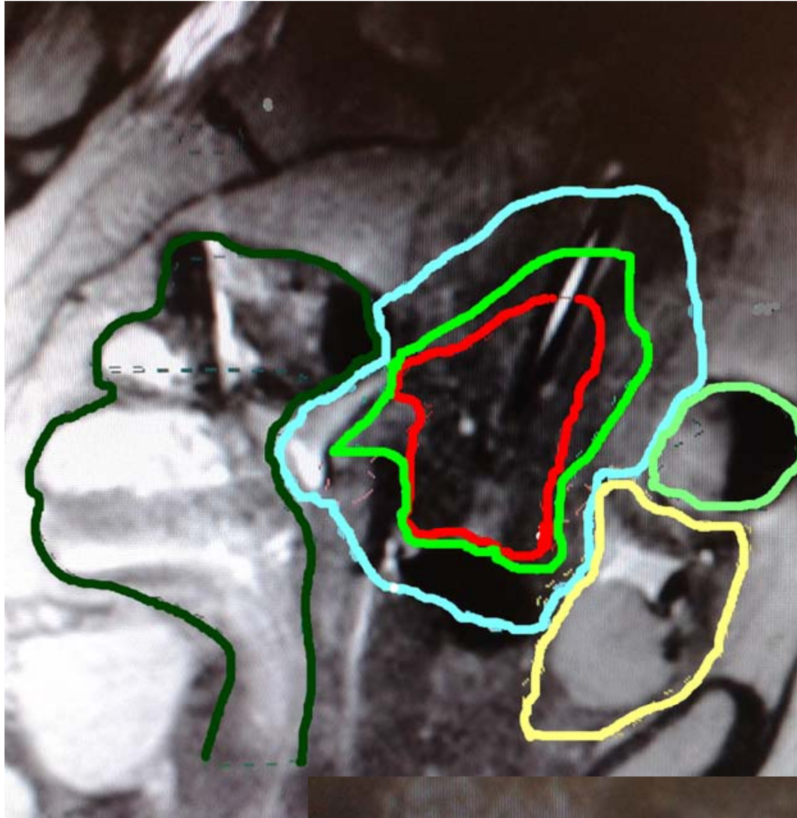
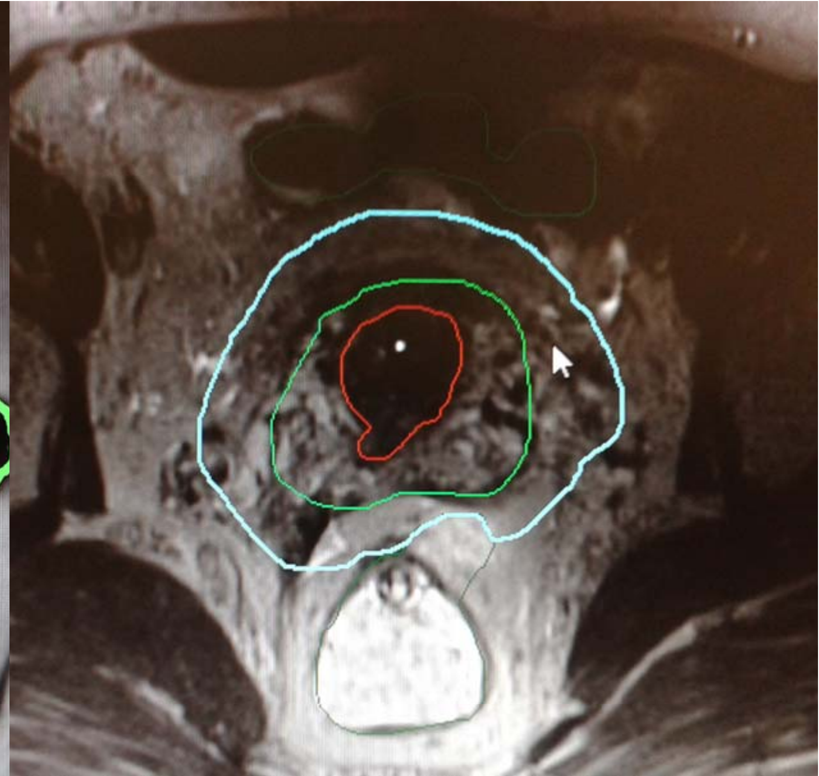
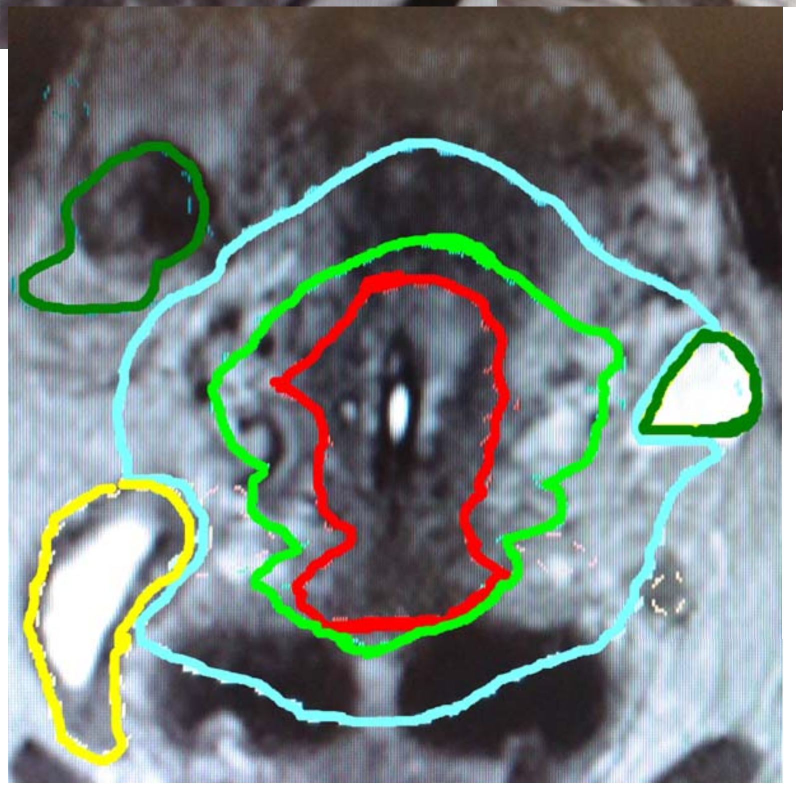
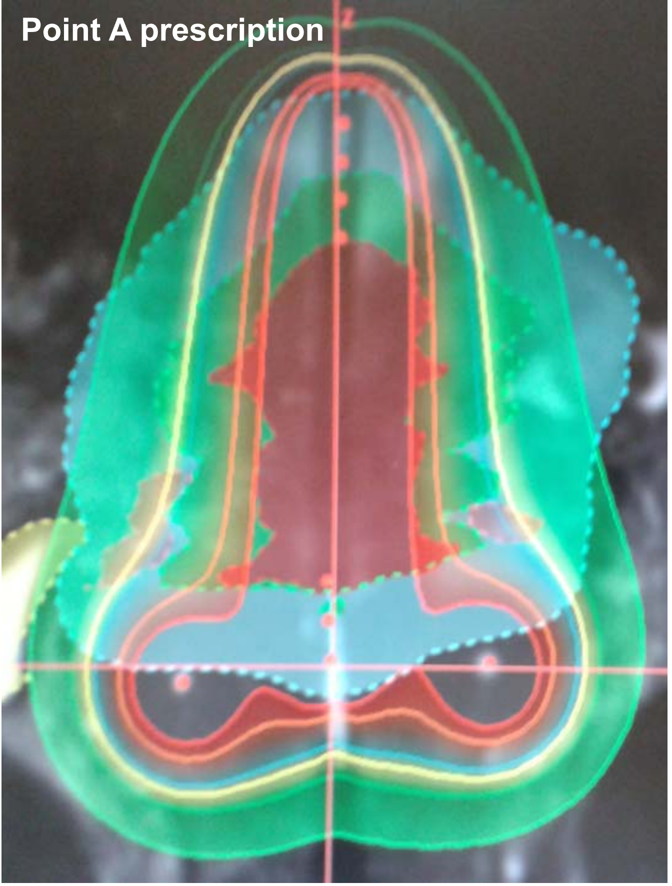
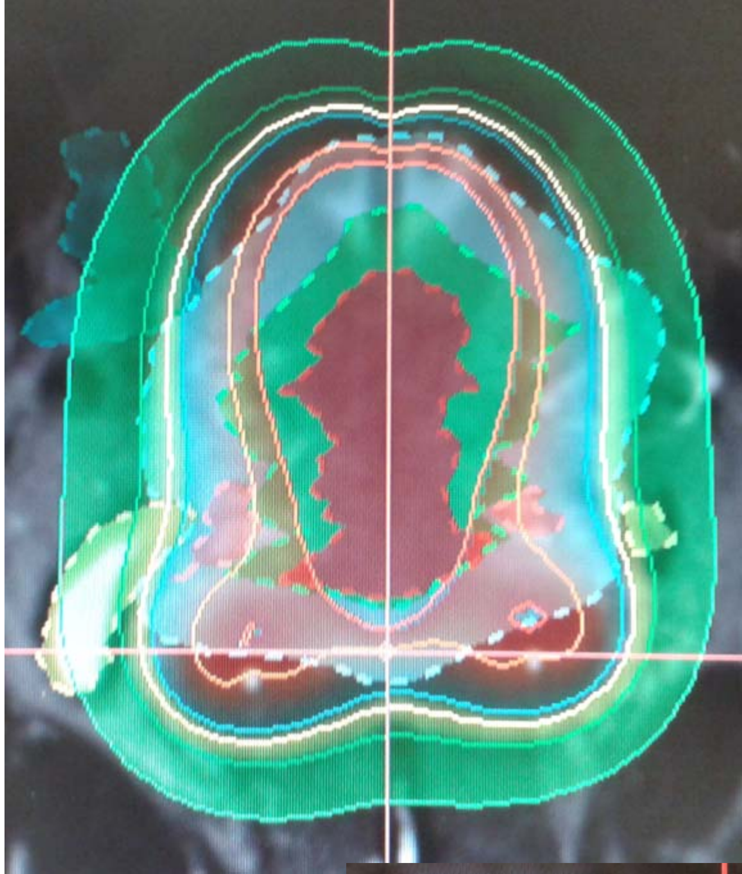
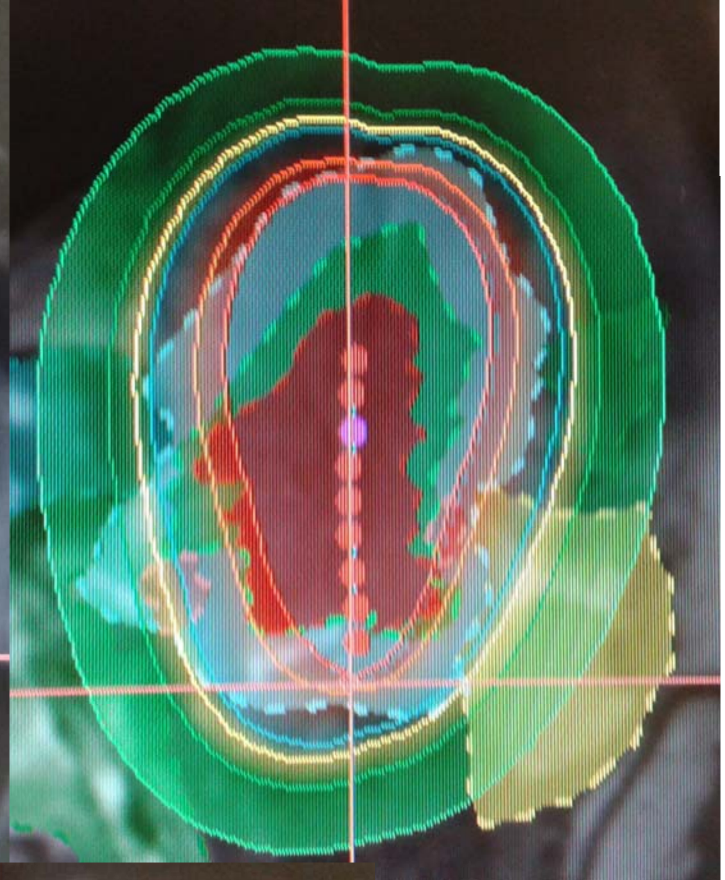
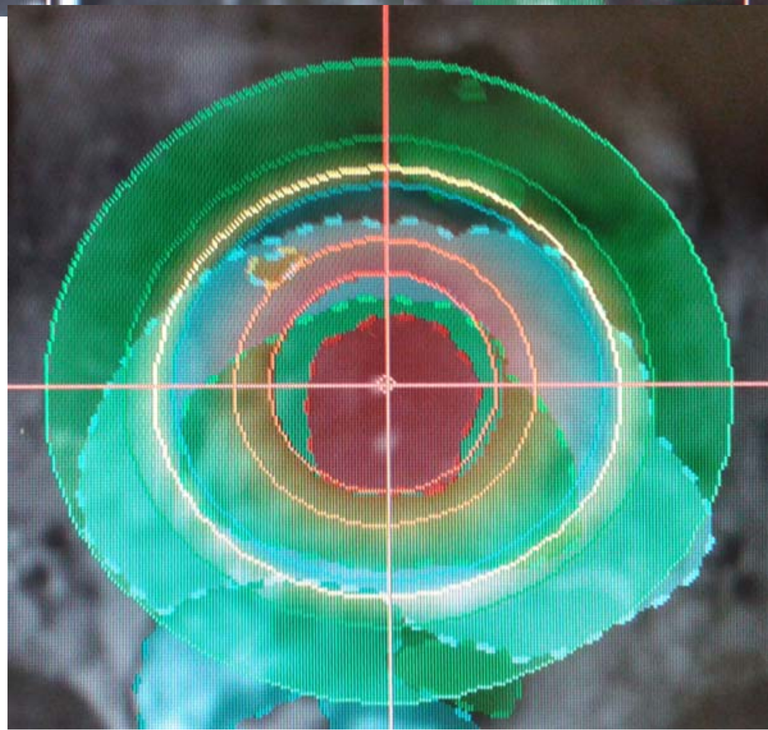





Point A prescription







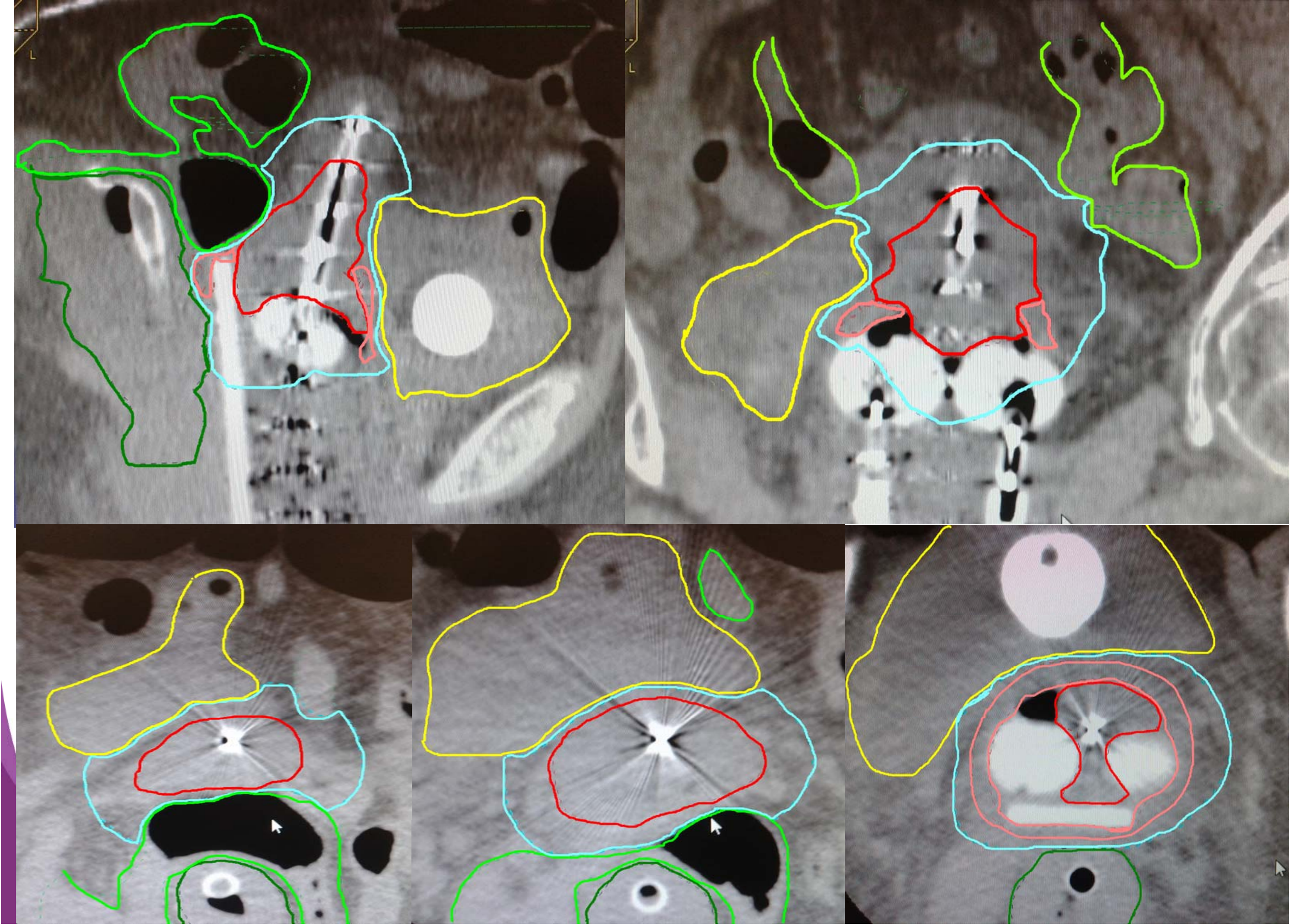
# CT CONTOURING

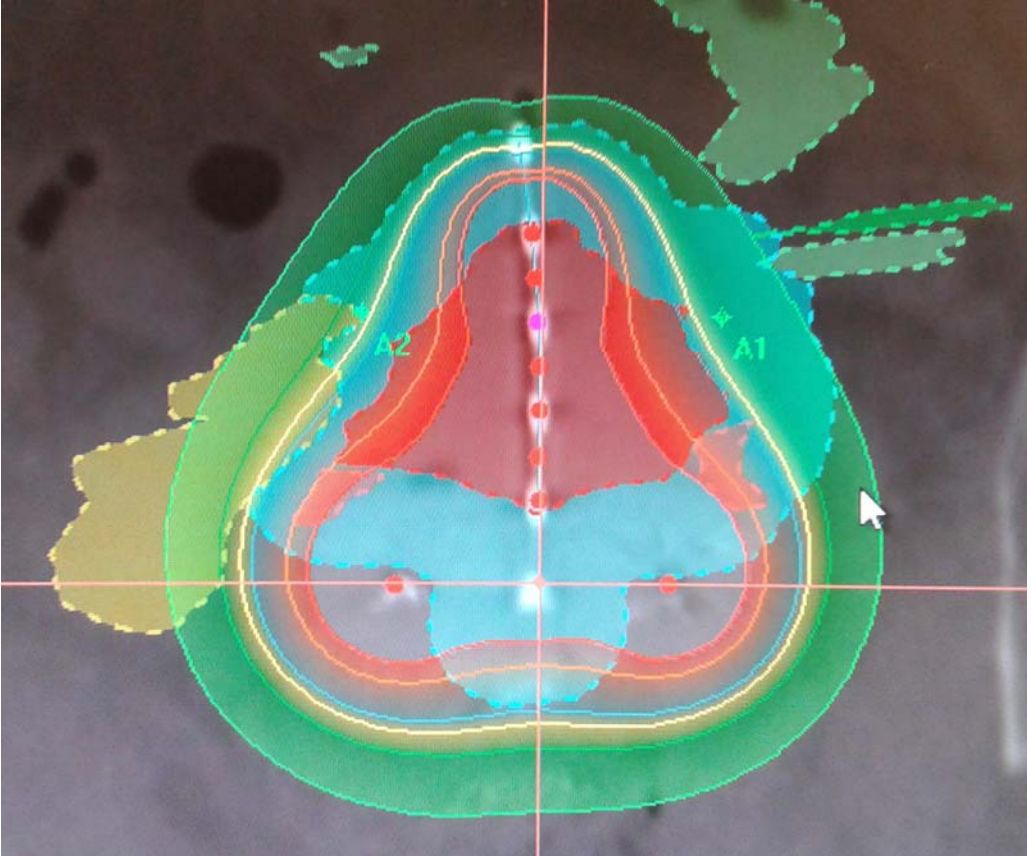
- For CT-based treatment planning, the width of the cervix and any parametrial extension should be contoured as the HR-CTV.

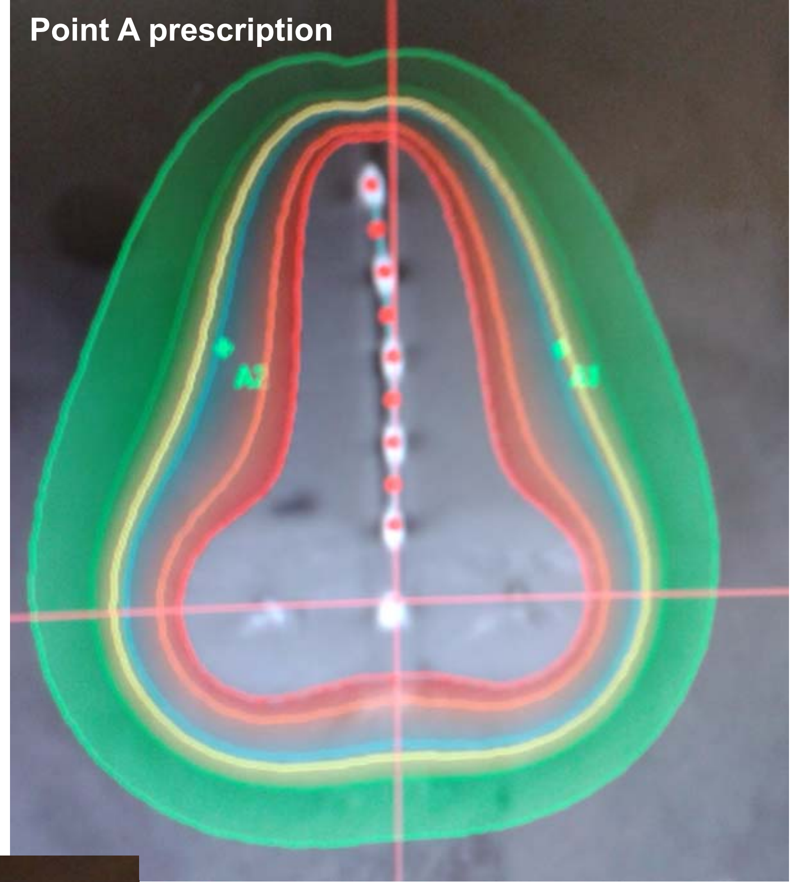
- The superior border of the cervix should extend at least 1 cm above the uterine vessels identified by intravenous contrast or the location where the uterus begins to enlarge.

- If CT anatomy does not permit identification of the cervix, a height of approximately 3 cm should be contoured for the cervix, with the caveat for CT-planned cases that the entire length of the tandem should be treated, as precise determination of the superior extent of disease is not feasible.

- OAR should be contoured including the bladder, rectum, and sigmoid.




A2
A1


Point A prescription
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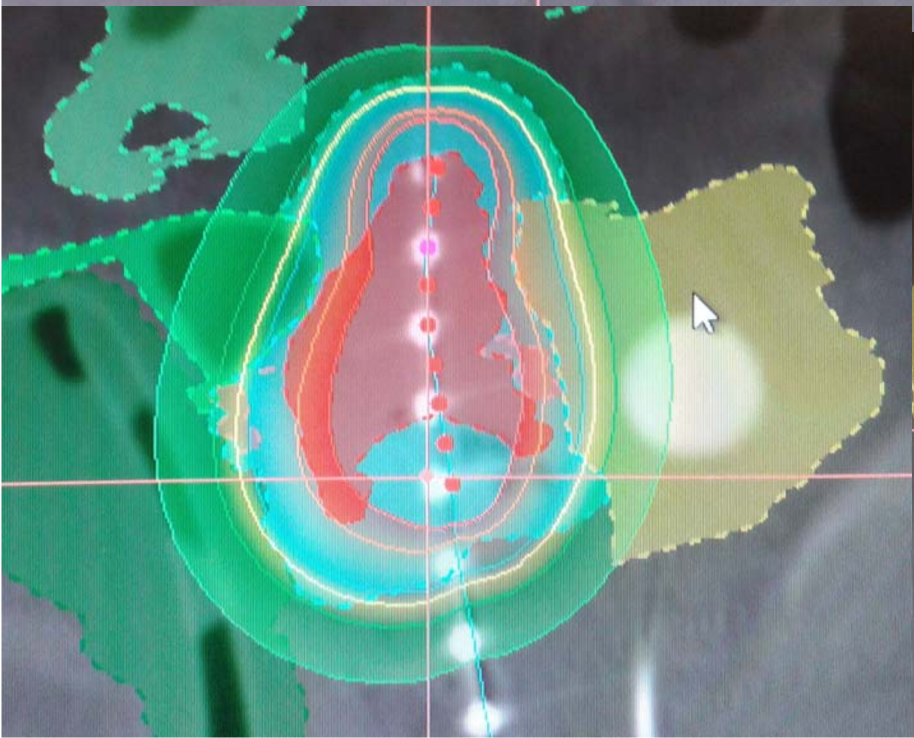

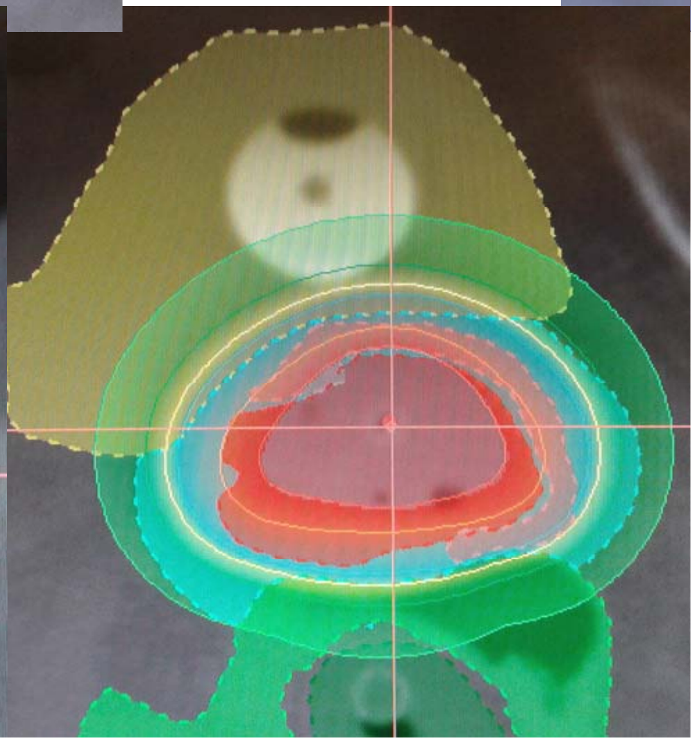

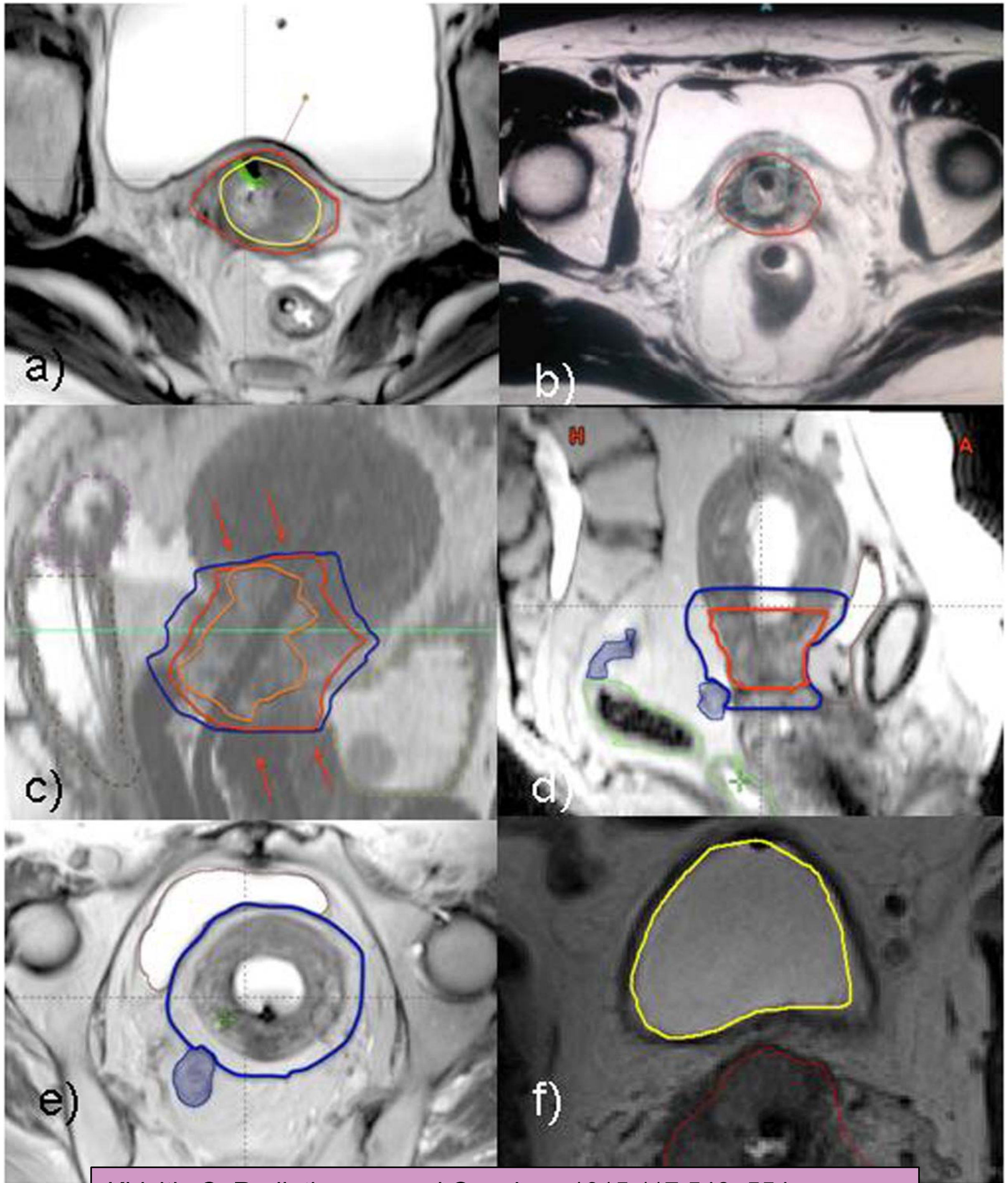


Kirisitis C. Radiotherapy and Oncology 1015;117:548–554

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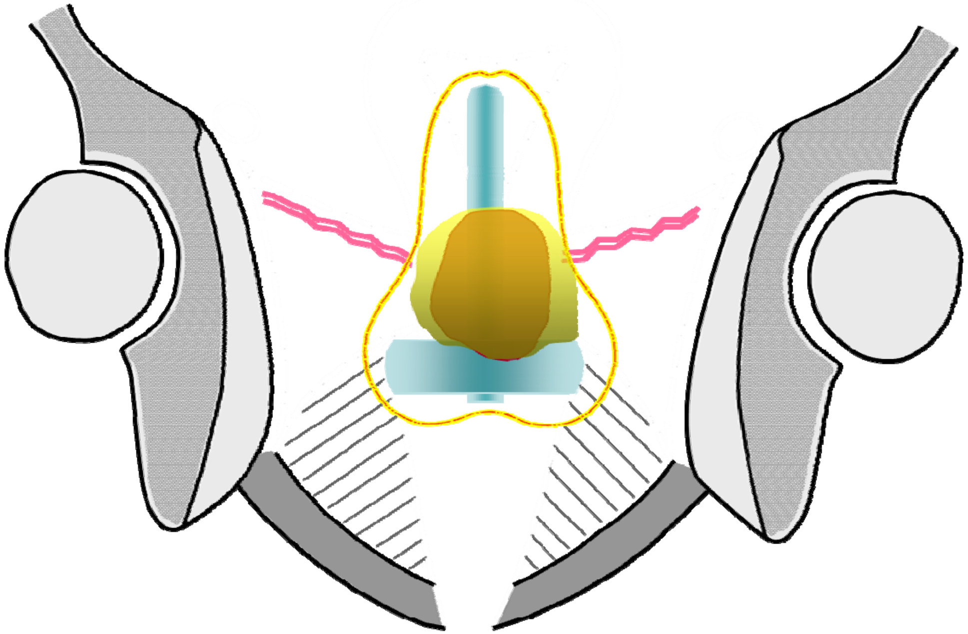
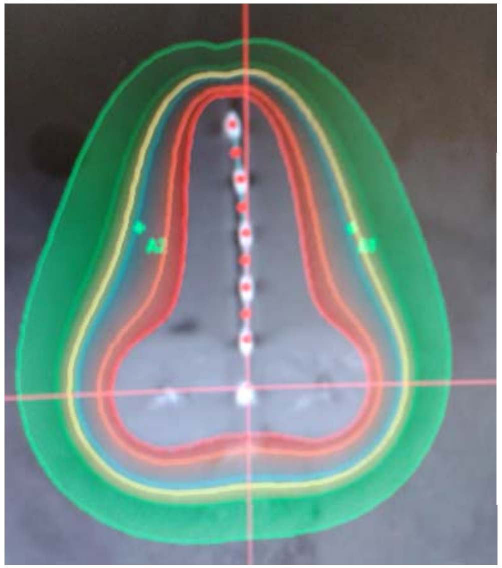
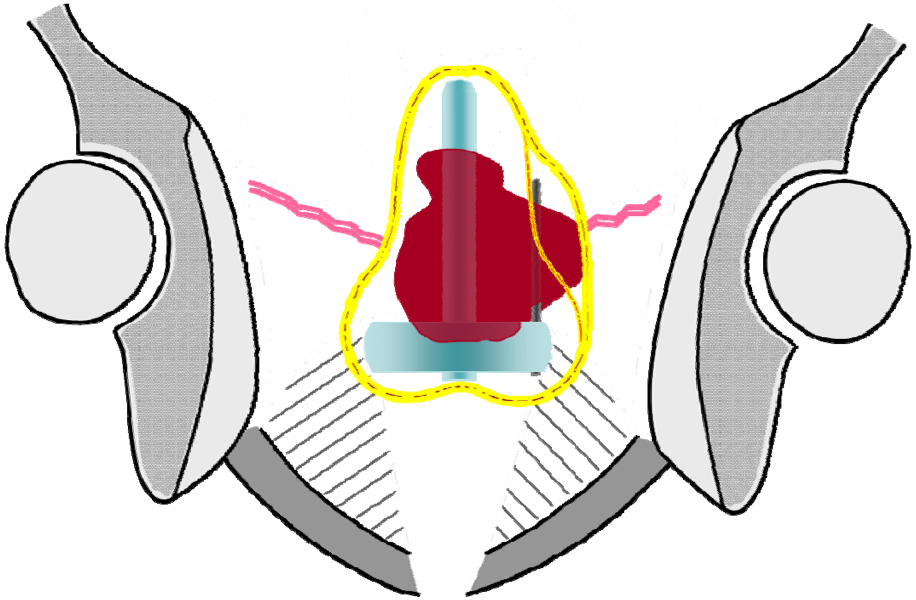
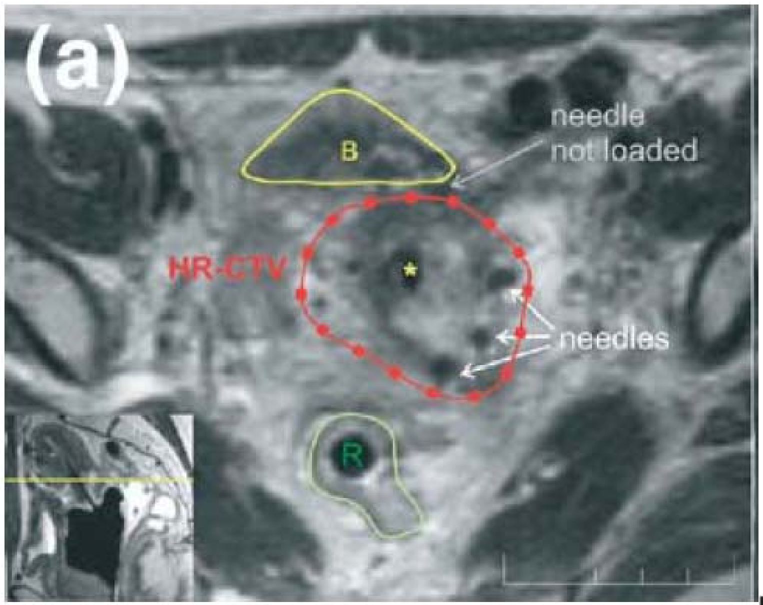
## Pattern of tumor regression I, II





## Pattern of tumor regression III



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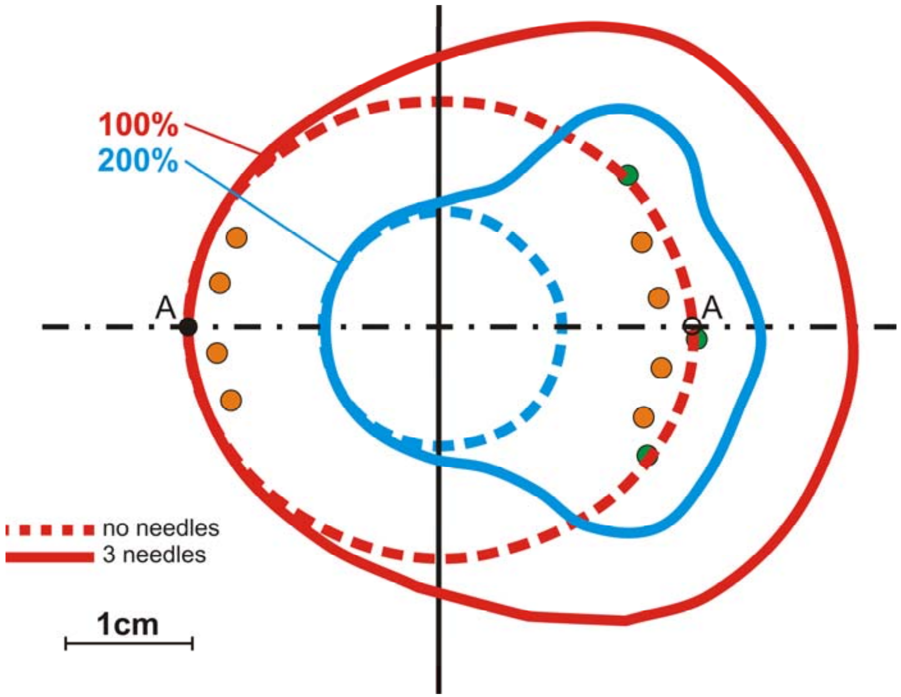
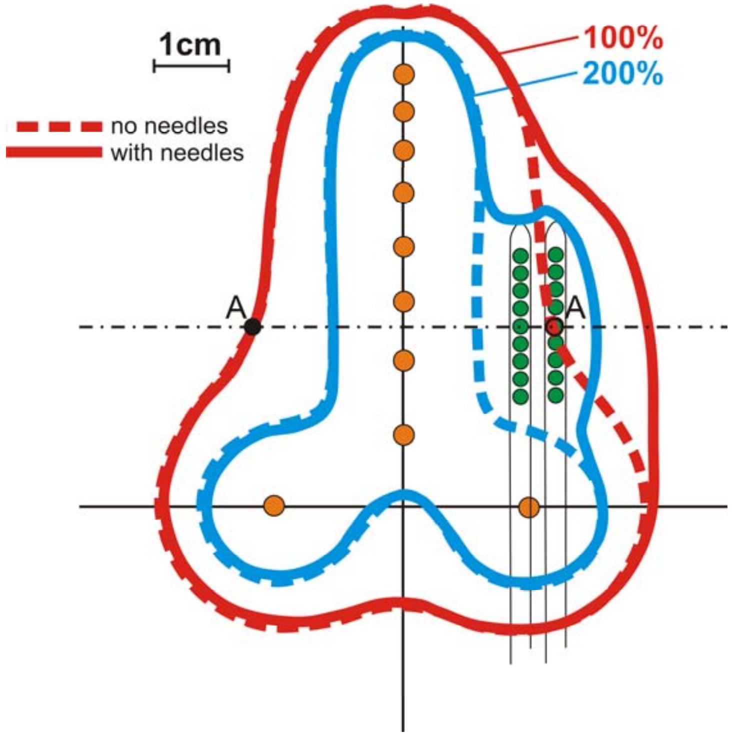
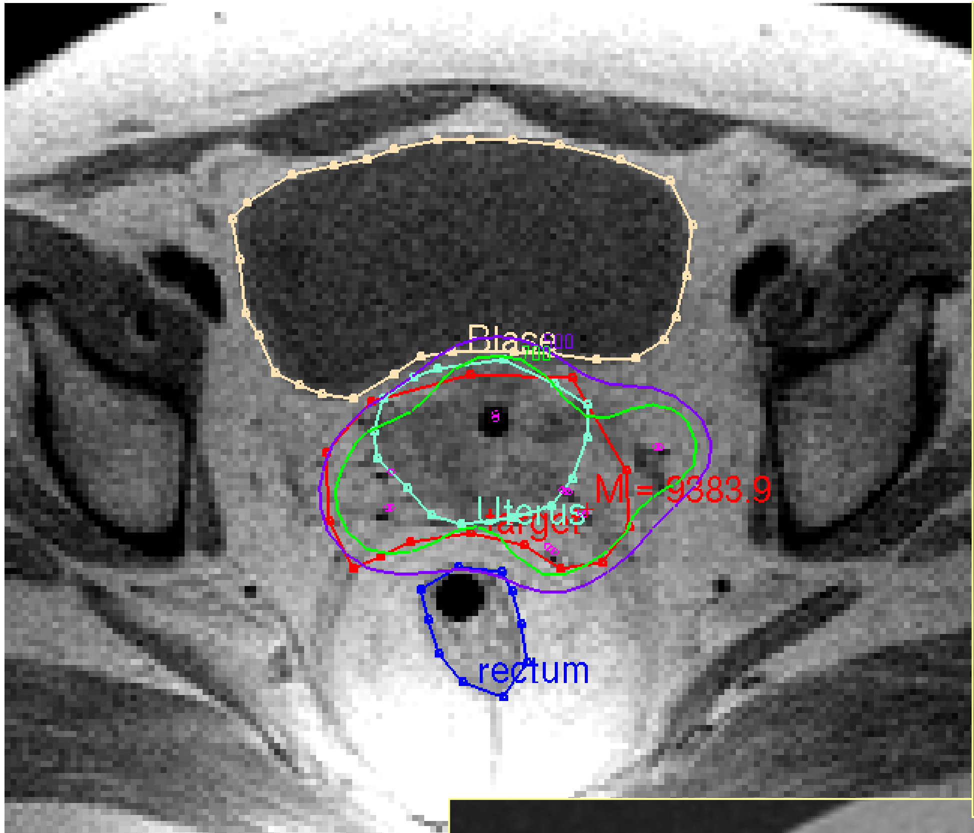
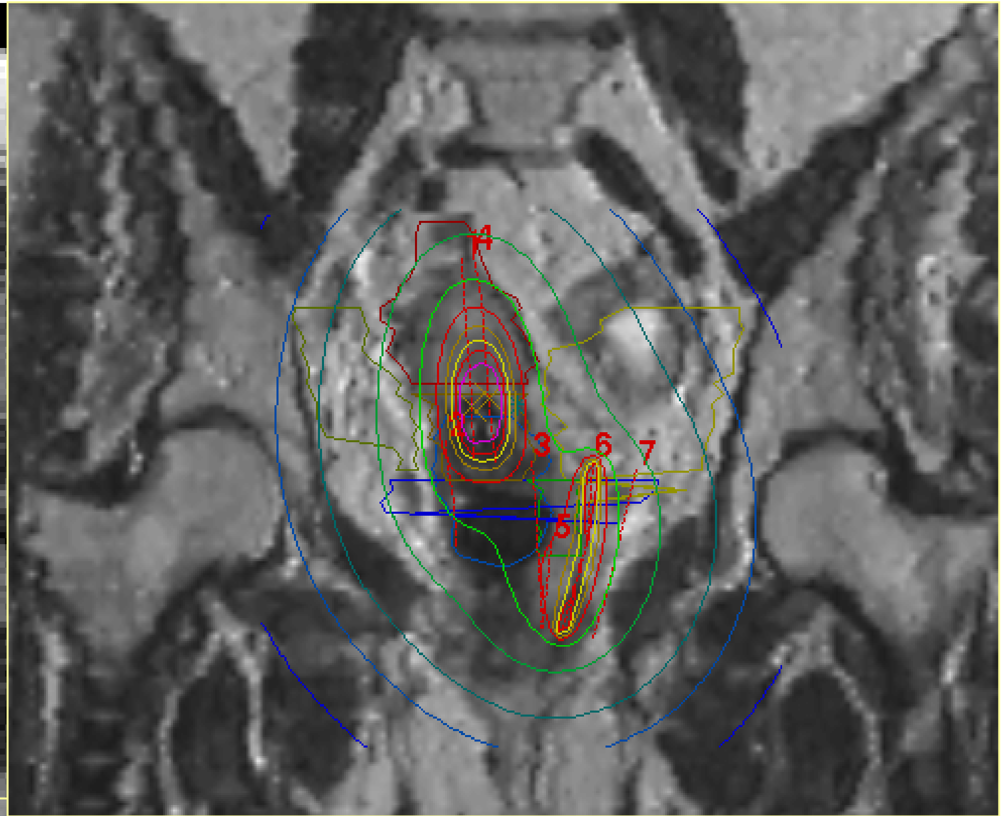
# Asymmetric dose distribution




Courtesy of AKH Wien


Blase
Uterus
MI = 9383.9
rectum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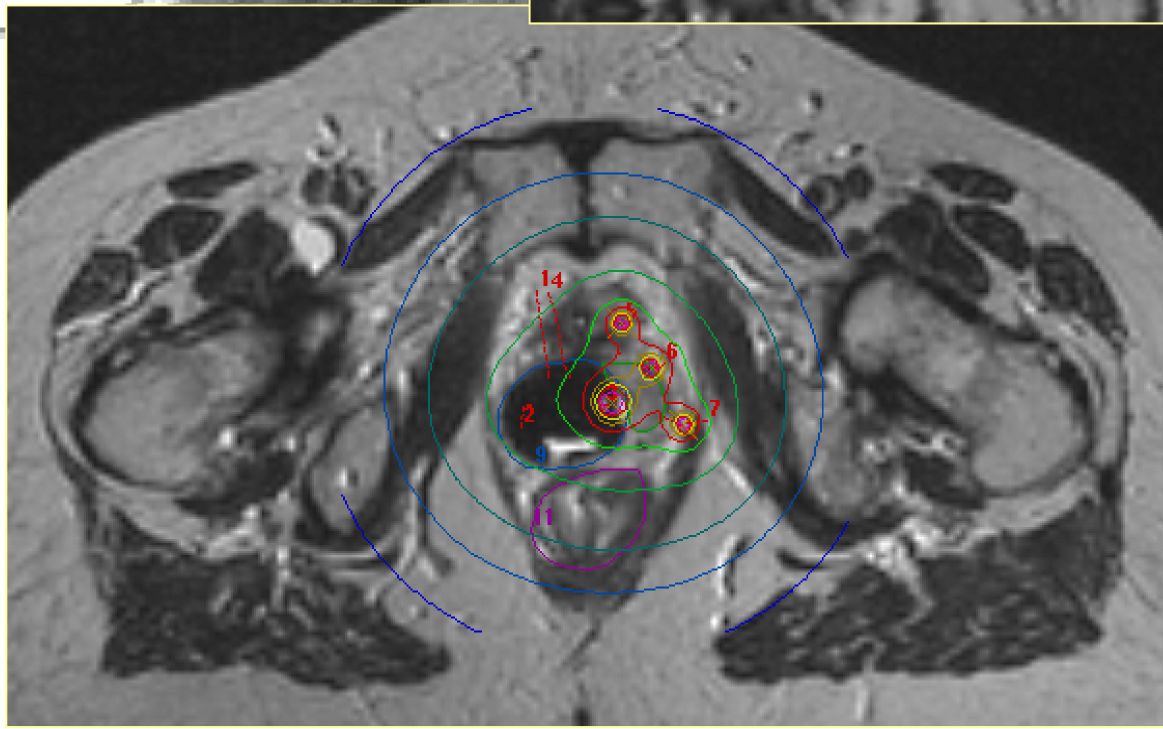
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Clinical Investigation

# Value of Magnetic Resonance Imaging Without or With Applicator in Place for Target Definition in Cervix Cancer Brachytherapy

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*[*]Department of Radiotherapy, Comprehensive Cancer Center, and [†]Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University of Vienna, Vienna, Austria; [‡]Department of Radiation Oncology, Gran Canaria University Hospital, Las Palmas de Gran Canaria, Spain; [§]Institute of Physics and Technology, Tomsk Polytechnic University, Tomsk Oblast, Russia; and [‖]Department of Clinical Oncology, Medical University of Alexandria, Alexandria, Egypt*

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**Summary**

Pretreatment magnetic resonance imaging shows a substantial impact on computed tomography-based contouring for cervix cancer brachytherapy, especially in cases with limited parametrial disease.

**Purpose:** To define, in the setting of cervical cancer, to what extent information from additional pretreatment magnetic resonance imaging (MRI) without the brachytherapy applicator improves conformity of CT-based high-risk clinical target volume ($CTV_{HR}$) contours, compared with the MRI for various tumor stages (International Federation of Gynecology and Obstetrics [FIGO] stages I-IVA).

**Methods and Materials:** The $CTV_{HR}$ was contoured in 39 patients with cervical cancer (FIGO stages I-IVA) (*1*) on CT images based on clinical information ($CTV_{HR}$-$CT_{Clinical}$) alone; and (*2*) using an additional MRI before brachytherapy, without the applicator ($CTV_{HR}$-$CT_{pre\text{-}BT\ MRI}$). The CT contours were compared with reference contours on MRI with the applicator in place ($CTV_{HR}$-$MRI_{ref}$). Width, height, thickness, volumes, and topography were analyzed.

**Results:** The CT-$MRI_{ref}$ differences hardly varied in stage I tumors (n=8). In limited-volume stage IIB and IIIB tumors (n=19), $CTV_{HR}$-$CT_{pre\text{-}BT\ MRI}$−$MRI_{ref}$ volume differences (2.6 $cm^3$ [IIB], 7.3 $cm^3$ [IIIB]) were superior to $CTV_{HR}$-$CT_{Clinical}$−$MRI_{ref}$ (11.8 $cm^3$ [IIB], 22.9 $cm^3$ [IIIB]), owing to significant improvement of height and width ($P$<.05). In advanced disease (n=12), improved agreement with MR volume, width, and height was achieved for $CTV_{HR}$-$CT_{pre\text{-}BT\ MRI}$. In 5 of 12 cases, $MRI_{ref}$ contours were partly missed on CT.

**Conclusions:** Pre-BT MRI helps to define $CTV_{HR}$ before BT implantation appropriately, if only CT images with the applicator in place are available for BT planning. Significant improvement is achievable in limited-volume stage IIB and IIIB tumors. In more advanced disease (extensive IIB to IVA), improvement of conformity is possible but may be associated with geographic misses. Limited impact on precision of $CTV_{HR}$-CT is expected in stage IB tumors. 

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Brachytherapy of cervical cancer

# Clinical outcome of protocol based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer

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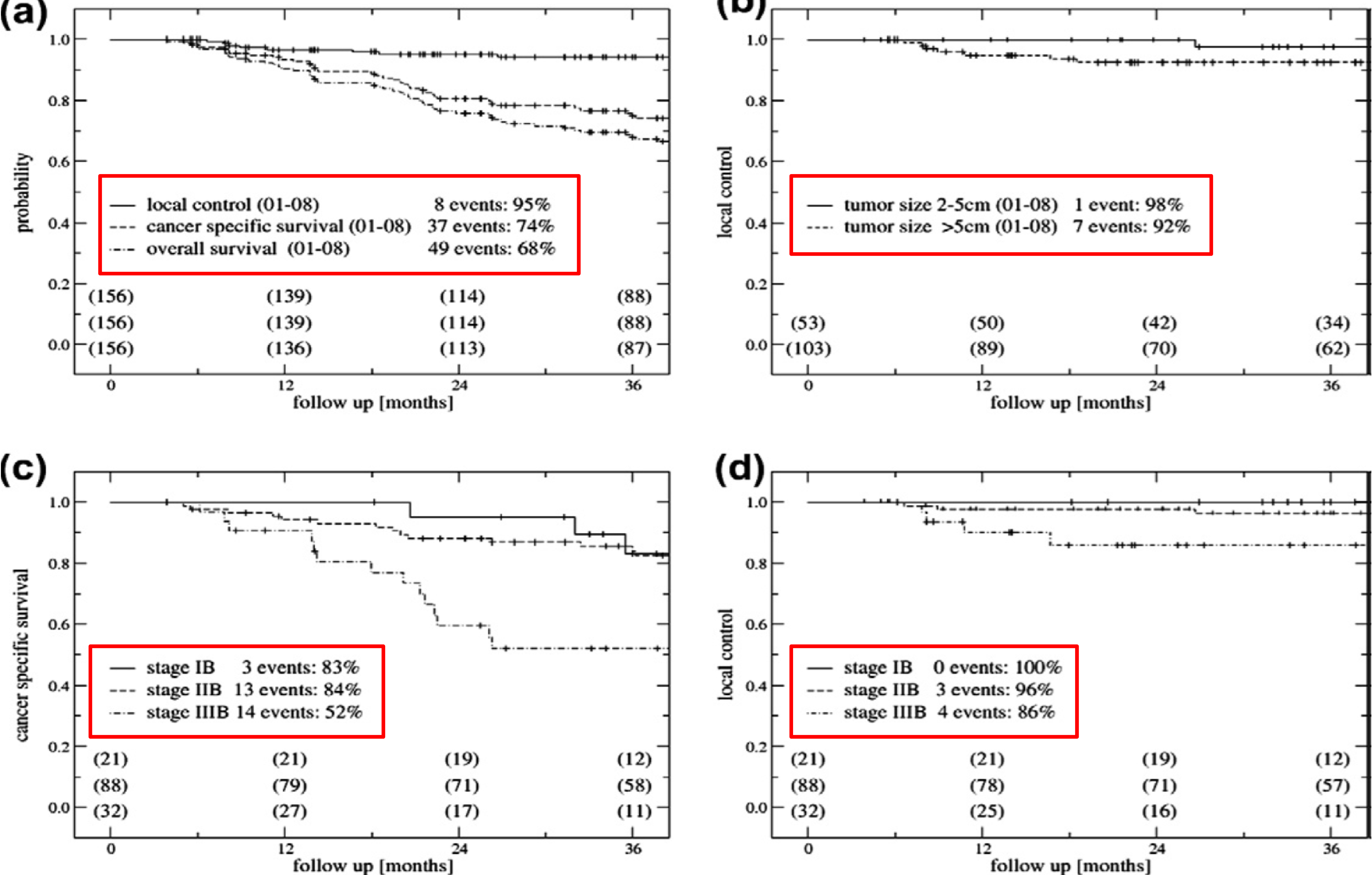
ABSTRACT

*Background:* To analyse the overall clinical outcome and benefits by applying protocol based image guided adaptive brachytherapy combined with 3D conformal external beam radiotherapy (EBRT) ± chemotherapy (ChT).
*Methods:* Treatment schedule was EBRT with 45–50.4 Gy ± concomitant cisplatin chemotherapy plus 4 × 7 Gy High Dose Rate (HDR) brachytherapy. Patients were treated in the "protocol period" (2001–2008) with the prospective application of the High Risk CTV concept (D90) and dose volume constraints for organs at risk including biological modelling. Dose volume adaptation was performed with the aim of dose escalation in large tumours (prescribed D90 > 85 Gy), often with inserting additional interstitial needles. Dose volume constraints ($D_{2cc}$) were 70–75 Gy for rectum and sigmoid and 90 Gy for bladder.
Late morbidity was prospectively scored, using LENT/SOMA Score. Disease outcome and treatment related late morbidity were evaluated and compared using actuarial analysis.
*Findings:* One hundred and fifty-six consecutive patients (median age 58 years) with cervix cancer FIGO stages IB–IVA were treated with definitive radiotherapy in curative intent. Histology was squamous cell cancer in 134 patients (86%), tumour size was >5 cm in 103 patients (66%), lymph node involvement in 75 patients (48%). Median follow-up was 42 months for all patients.
Interstitial techniques were used in addition to intracavitary brachytherapy in 69/156 (44%) patients. Total prescribed mean dose (D90) was 93 ± 13 Gy, $D_{2cc}$ 86 ± 17 Gy for bladder, 65 ± 9 Gy for rectum and 64 ± 9 Gy for sigmoid.
Complete remission was achieved in 151/156 patients (97%). Overall local control at 3 years was 95%; 98% for tumours 2–5 cm, and 92% for tumours >5 cm ($p$ = 0.04), 100% for IB, 96% for IIB, 86% for IIIB. Cancer specific survival at 3 years was overall 74%, 83% for tumours 2–5 cm, 70% for tumours >5 cm, 83% for IB, 84% for IIB, 52% for IIIB. Overall survival at 3 years was in total 68%, 72% for tumours 2–5 cm, 65% for tumours >5 cm, 74% for IB, 78% for IIB, 45% for IIIB.
In regard to late morbidity in total 188 grade 1 + 2 and 11 grade 3 + 4 late events were observed in 143 patients. G1 + 2/G3 + 4 events for bladder were $n$ = 32/3, for rectum $n$ = 14/5, for bowel (including sigmoid) $n$ = 3/0, for vagina $n$ = 128/2, respectively.
*Interpretation:* 3D conformal radiotherapy ± chemotherapy plus image (MRI) guided adaptive intracavitary brachytherapy including needle insertion in advanced disease results in local control rates of 95–100% at 3 years in limited/favourable (IB/IIB) and 85–90% in large/poor response (IIB/III/IV) cervix cancer patients associated with a moderate rate of treatment related morbidity. Compared to the historical Vienna series there is relative reduction in pelvic recurrence by 65–70% and reduction in major morbidity. The local control improvement seems to have impact on CSS and OS. Prospective clinical multi-centre studies are mandatory to evaluate these challenging mono-institutional findings.

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ESTRO School

# Probability of G2–G4 side effects according to dose levels

Dose volume Probability of EQD2 for G2–G4 side effects (Gy) for the incidence rates shown (95% CI)

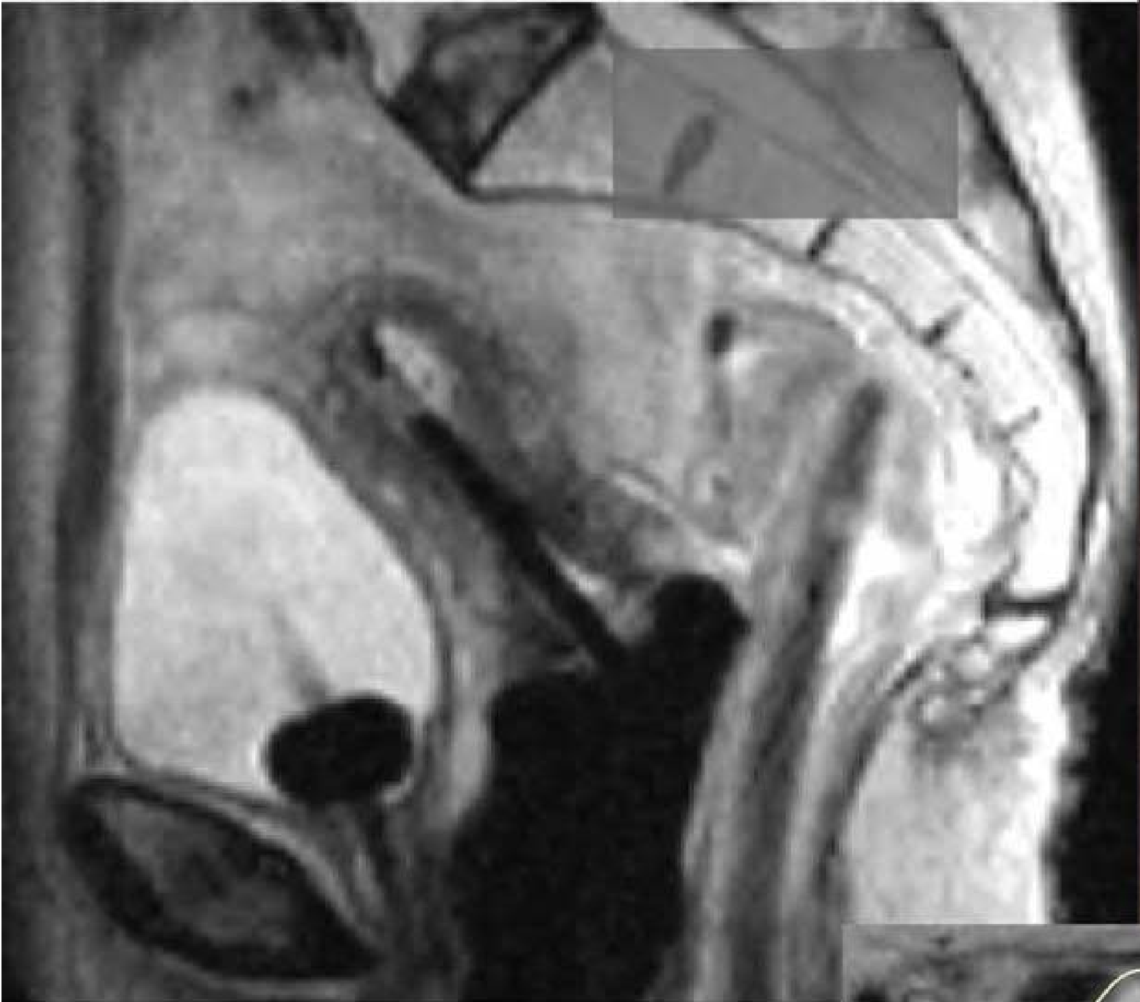
| | 5% | 10% | 20% | p value |
|---|---|---|---|---|
| **Rectum** | | | | |
| D2cc | 67 (30–79) | 78 (66–110) | 90 (78–171) | 0.0178 |
| D1cc | 71 (0-89) | 87 (69–209) | 104 (87–443) | 0.0352 |
| D0.1cc | 83 | 132 | 186 | 0.1364 |
| **Bladder** | | | | |
| D2cc | 70 (0-95) | 101 (29–137) | 134 (110–371) | 0.0274 |
| D1cc | 71 (0–107) | 116 (17–169) | 164 (129–498) | 0.0268 |
| D0.1cc | 61*(0–155) | 178 (0–368) | 305 (213–2126) | 0.0369 |

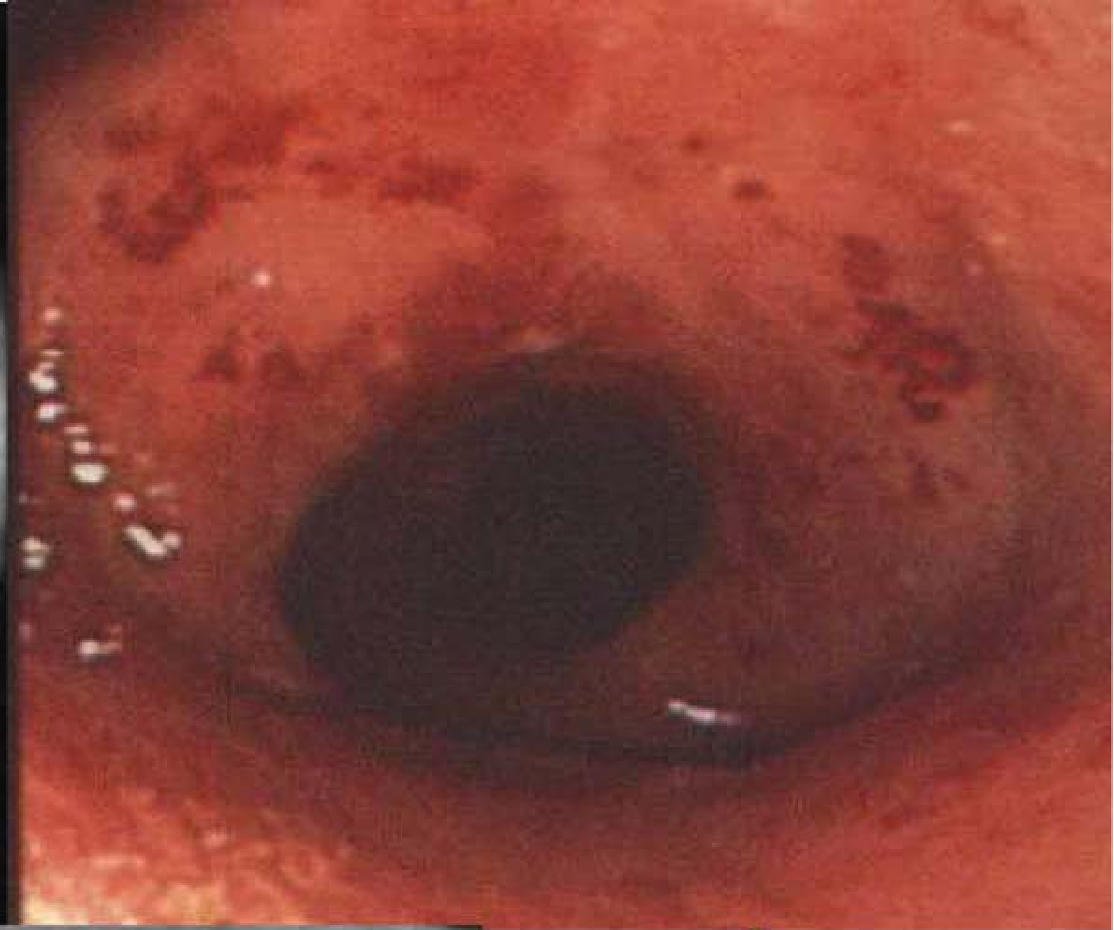
**Rectum** (Topographic changes with DVH parameters)**:**
Telangiectasia: corresponded to the $2cm^3$ high-dose rectal volume.
Ulcerations: limited to the small high-dose volumes of $0.1cm^3$ at the anterior rectal wall segment.

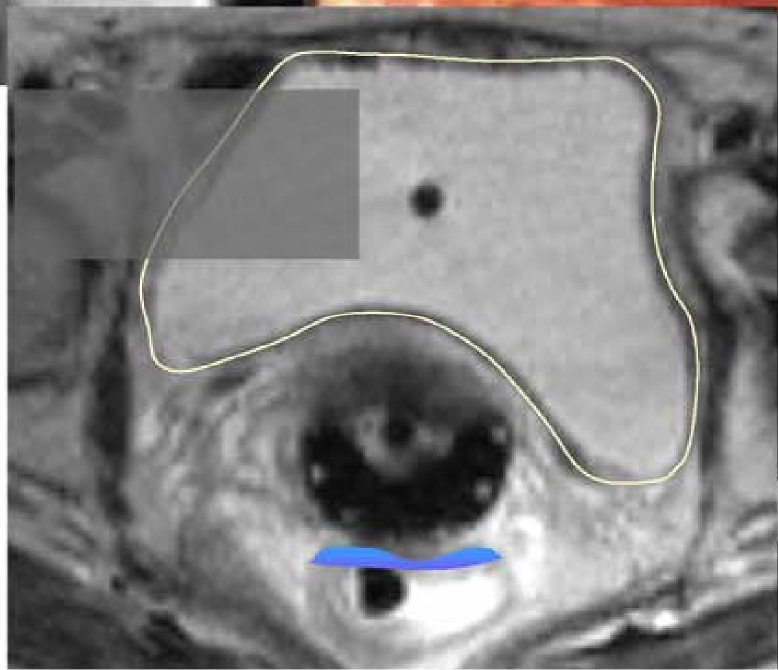
**Bladder:** The 5% incidence is observed at dose ranges from 60 to 70 Gy, independently of the DVH parameter.
In contrast, as in the rectum, the doses for 10% and 20% complication rates are clearly dependent on the DVH parameter and increase with decreasing volume. This confirms that the 3D dose-volume parameters describe the dose effect in the urinary bladder very well.

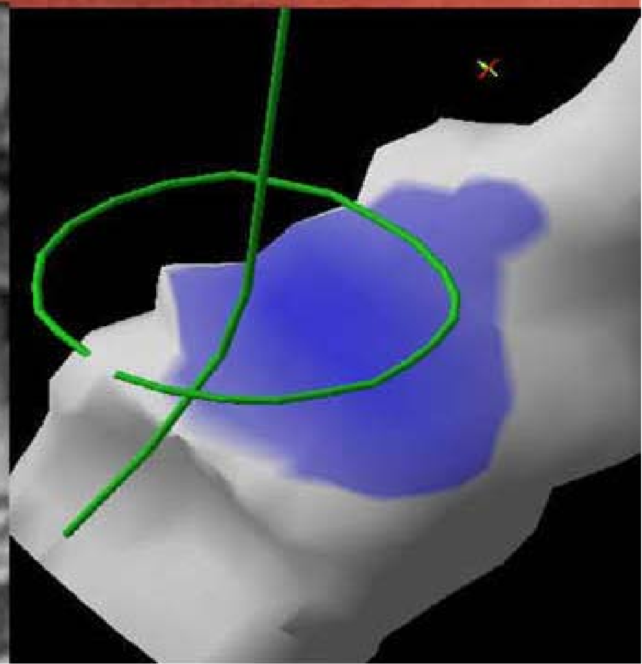
**Sigmoid, colon:** When the commonly used institutional dose constraints for OARs are not fulfilled, the expected risk of side effects can be estimated based on the dose response curves. Useful limits for D2 cc to the sigmoid and rectum not including the contents (70-75 Gy)

P. Georg et al Int. J. Radiation Oncology Biol. Phys., 2012; 82(2): 653–657









Total DVH parameters (calculated taking into account all 4 fractions)
D2cc= 75 Gy EQD2
D1cc= 82 Gy EQD2
D0.1cc= 103 Gy EQD2

EQD2>90 Gy in 0.1cc was associated With ulceration and fistula.

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Clinical Investigation

# Image Guided Cervical Brachytherapy: 2014 Survey of the American Brachytherapy Society

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Linda P. Cho, BA,[‡] Beth Erickson, MD,[§] Christina Small, MPH,[||]
William Small, Jr, MD,[†] and Akila N. Viswanathan, MD, MPH[‡]

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Received Jul 21, 2015

**Summary**

The American Brachytherapy Society conducted a survey of image guided cervical brachytherapy practices in the United States in 2007, which showed that most physicians used computed tomography (CT) for planning and used a point-based system only for target-dose prescription. We present the updated results of a 2014 practice pattern survey showing that, compared with 2007, it seems that significantly more physicians are using CT and magnetic

**Purpose:** To provide an update of the 2007 American brachytherapy survey on image-based brachytherapy, which showed that in the setting of treatment planning for gynecologic brachytherapy, although computed tomography (CT) was often used for treatment planning, most brachytherapists used point A for dose specification.

**Methods and Materials:** A 45-question electronic survey on cervical cancer brachytherapy practice patterns was sent to all American Brachytherapy Society members and additional radiation oncologists and physicists based in the United States between January and September 2014. Responses from the 2007 survey and the present survey were compared using the $\chi^2$ test.

**Results:** There were 370 respondents. Of those, only respondents, not in training, who treat more than 1 cervical cancer patient per year and practice in the United States, were included in the analysis (219). For dose specification to the target (cervix and tumor), 95% always use CT, and 34% always use MRI. However, 46% use point A only for dose specification to the target. There was a lot of variation in parameters used for dose evaluation of target volume and normal tissues. Compared with the 2007 survey, use of MRI has increased from 2% to 34% ($P<.0001$) for dose specification to the target. Use of volume-based dose delineation to the target has increased from 14% to 52% ($P<.0001$).

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Original article

# Transrectal ultrasound for image-guided adaptive brachytherapy in cervix cancer – An alternative to MRI for target definition?

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A B S T R A C T

*Purpose:* To compare the maximum high risk clinical target volume ($CTV_{HR}$) dimensions and image quality between magnetic resonance imaging (MRI), transrectal ultrasound (TRUS) and computed tomography (CT) in image guided adaptive brachytherapy (IGABT) of locally advanced cervical cancer.

*Material and methods:* All patients with locally advanced cervical cancer treated with radiochemotherapy and IGABT between 09/2012-05/2013 were included in this study. T2-weighted MRI (1.5 tesla), TRUS and CT were performed before ($MRI_{preBT}$, $TRUS_{preBT}$) and/or after ($MRI_{BT}$, $TRUS_{BT}$ and $CT_{BT}$) insertion of the applicator. 3D TRUS image acquisition was done with a customized US stepper device and software. The HR CTV was defined on 3D image sequences acquired with different imaging modalities by one blinded observer, in accordance to the GEC-ESTRO recommendations for MRI-based target volume delineation, as the complete cervical mass including the tumour, any suspicious areas of parametrial involvement and the normal cervical stroma. Maximum HR CTV width and thickness were measured on transversal planes. Image quality was classified using the following scoring system: Grade 0: not depicted, Grade 1: inability to discriminate, margin not recognizable, Grade 2: fair discrimination, margin indistinct, Grade 3: excellent discrimination, margin distinct. Descriptive statistics, mean differences between the groups, with $MRI_{BT}$ as reference, and a paired *t*-test were calculated.

*Results:* Images from 19 patients (FIGO IB: 3, IIB: 9, IIIB: 5, IVB: 2) were available for analysis. The mean difference in maximum HR CTV width of $TRUS_{BT}$, $TRUS_{preBT}$, $MRI_{preBT}$, $CT_{BT}$ to $MRI_{BT}$ was 0.0 mm ± 4.7 (n.s.), −1.1 mm ± 5.6 (n.s.), 0.7 mm ± 6.4 (n.s.) and 13.8 mm ± 6.7 ($p < 0.001$). The mean difference in maximum HR CTV thickness of $TRUS_{BT}$, $TRUS_{preBT}$, $MRI_{preBT}$, $CT_{BT}$ to $MRI_{BT}$ was -3.4 mm ± 5.9 ($p = 0.037$), −3.4 mm ± 4.2 ($p < 0.001$), 2.0 mm ± 6.1 (n.s.) and 13.9 mm ± 6.3 ($p < 0.001$). Mean scores of image quality of the target volume was 2.9 for $TRUS_{preBT}$, 2.3 for $TRUS_{BT}$, 2.9 for $MRI_{preBT}$, 2.7 for $MRI_{BT}$ and 2.1 for $CT_{BT}$.

*Conclusion:* For the assessment of the HR CTV in IGABT of cervical cancer, TRUS is within the intraobserver variability of MRI. TRUS is superior to CT as it yields systematically smaller deviations from MRI, with good to excellent image quality. Small differences of TRUS HR CTV thickness are likely related to differences in image slice orientation and compression of the cervix by the TRUS probe before insertion of the brachytherapy applicator.

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Image guided brachytherapy

# Adaptive image guided brachytherapy for cervical cancer: A combined MRI-/CT-planning technique with MRI only at first fraction

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MRI-based brachytherapy

ABSTRACT

*Purpose:* To investigate and test the feasibility of adaptive 3D image based BT planning for cervix cancer patients in settings with limited access to MRI, using a combination of MRI for the first BT fraction and planning of subsequent fractions on CT.

*Material and methods:* For 20 patients treated with EBRT and HDR BT with tandem/ring applicators two sets of treatment plans were compared. Scenario one is based on the "gold standard" with individual MRI-based treatment plans (applicator reconstruction, target contouring and dose optimization) for two BT applications with two fractions each. Scenario two is based on one initial MRI acquisition with an applicator in place for the planning of the two fractions of the first BT application and reuse of the target contour delineated on MRI for subsequent planning of the second application on CT. Transfer of the target from MRI of the first application to the CT of the second one was accomplished by use of an automatic applicator-based image registration procedure. Individual dose optimization of the second BT application was based on the transferred MRI target volume and OAR structures delineated on CT.

*Material and methods:* DVH parameters were calculated for transferred target structures (virtual dose from MRI/CT plan) and CT-based OAR.

*Material and methods:* The quality of the MRI/CT combination method was investigated by evaluating the CT-based dose distributions on MRI-based target and OAR contours of the same application (real dose from MRI/CT plan).

*Results:* The mean difference between the MRI based target volumes (HR $CTV_{MRI2}$) and the structures transferred from MRI to CT (HR $CTV_{CT2}$) was $-1.7 \pm 6.6$ cm$^3$ ($-2.9 \pm 20.4$%) with a median of $-0.7$ cm$^3$.

*Results:* The mean difference between the virtual and the real total D90, based on the MRI/CT combination technique was $-1.5 \pm 4.3$ Gy EQD2. This indicates a small systematic underestimation of the real D90.

*Conclusions:* A combination of MRI for first fraction and subsequent CT based planning is feasible and easy when automatic applicator-based image registration and target transfer are technically available. The results show striking similarity to fully MRI-based planning in cases of small tumours and intracavitary applications, both in terms of HR CTV coverage and respecting of OAR dose limits. For larger tumours and complex applications, as well as situations with unfavourable OAR topography, especially for the sigmoid, MRI based adaptive BT planning remains the superior method.

 Radiotherapy and Oncology 107 (2013) 75–81

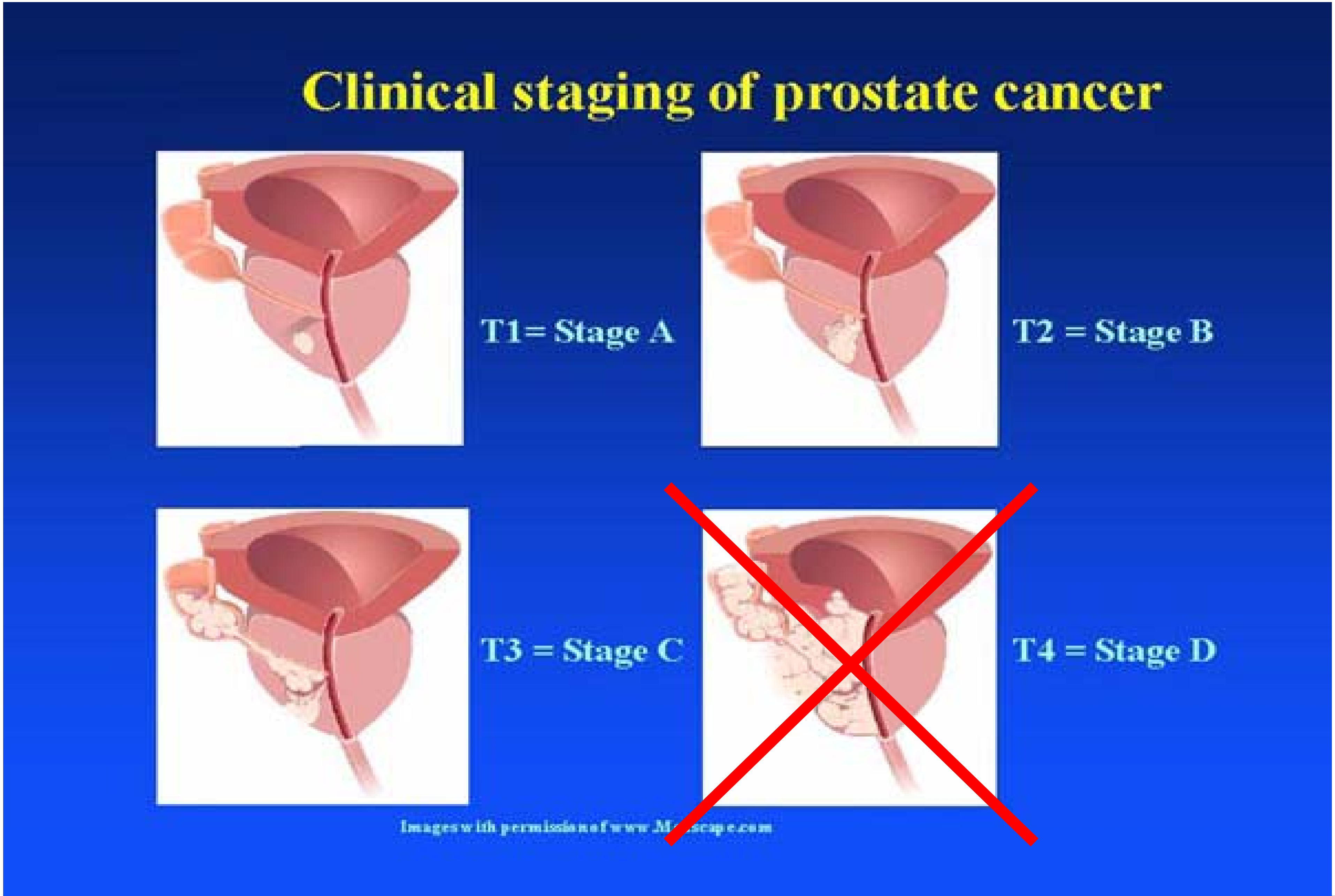
# FINALLY……

- A significant learning period is needed to fully understand all the different aspects of this complex procedure.

- However, 3D image-based brachytherapy is expected to become a practical clinical strategy which will be comparable in its complexity with the most advanced external beam therapy techniques such as intensity-modulated radiotherapy, stereotactic radiotherapy, and 4D-adaptive radiotherapy

Additional human resources are required to provide a 3-D HDR brachytherapy service, owing to the additional complexity in imaging and treatment planning. The IAEA has developed a tool to estimate staffing levels in radiotherapy practice which will soon be published. If 200 patients per year are to be treated with 3-D brachytherapy, then the number of radiation oncologists dedicated to brachytherapy needs to increase by 0.8 full-time equivalent (FTE) compared with a 2-D service managing the same number of patients. Similarly, the number of medical physicists needs to increase by 0.5 FTE and radiation oncology nurses by 0.3 FTE.

# PROSTATE: TVD BRACHY



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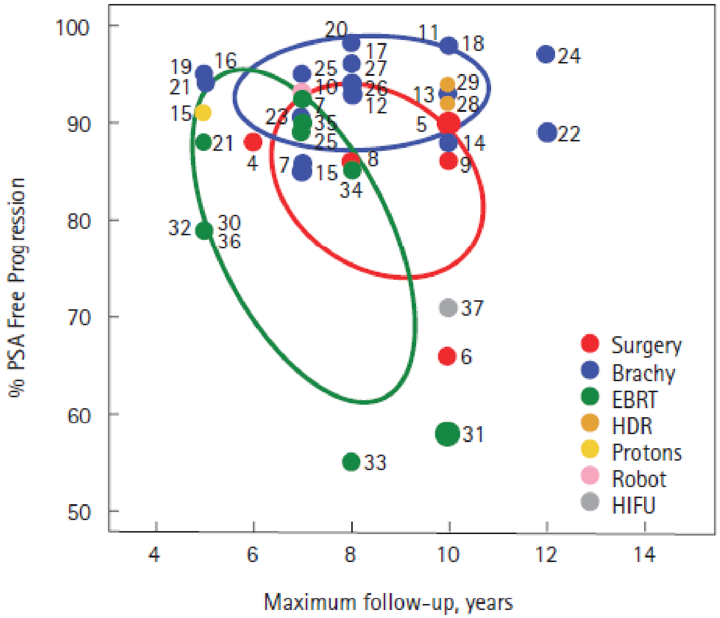
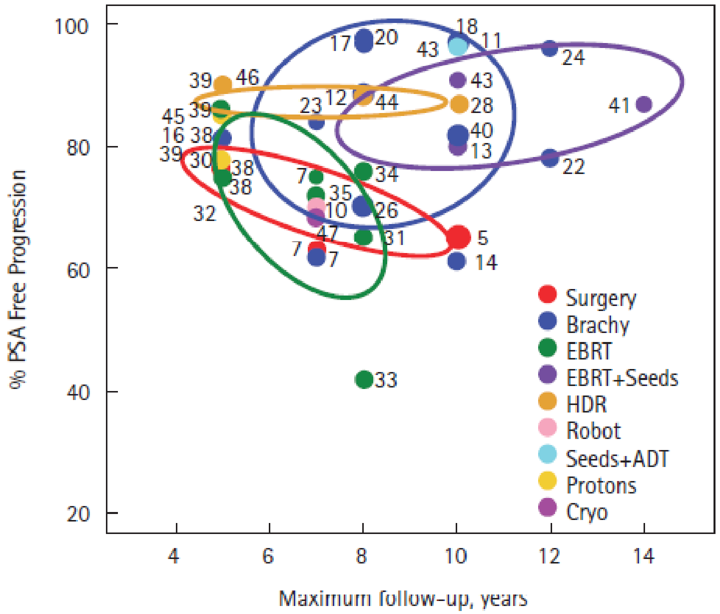
# Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group

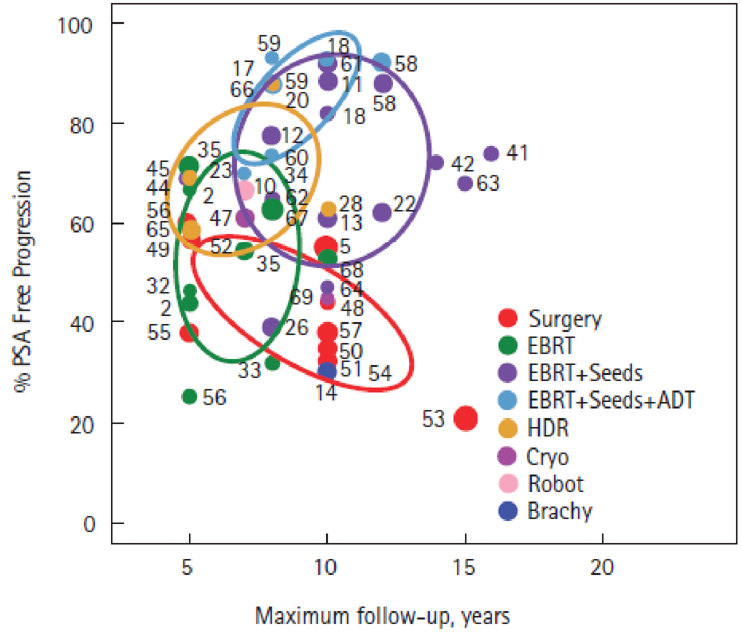
## Low risk




## Intermediate risk




## High risk




Grimm et al. B J U I 2 01 2, 109 (Suppl. 1):22-9

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# RECOMMENDATIONS ABS/GEC-ESTRO

Contents lists available at SciVerse ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

GEC/ESTRO recommendations

## GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: An update

Peter J. Hoskin[a,*,1], Alessandro Colombo[b,1], Ann Henry[c,1], Peter Niehoff[d,1], Taran Paulsen Hellebust[e,1], Frank-Andre Siebert[f,1], Gyorgy Kovacs[g,1]

Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 2, pp. 335–341, 2011

0360-3016/$ - see front matter
doi:10.1016/j.ijrobp.2010.08.045

ASTRO GUIDELINE

## AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) AND AMERICAN COLLEGE OF RADIOLOGY (ACR) PRACTICE GUIDELINE FOR THE TRANSPERINEAL PERMANENT BRACHYTHERAPY OF PROSTATE CANCER

Seth A. Rosenthal, M.D.,* Nathan H. J. Bittner, M.D., M.S.,[†] David C. Beyer, M.D.,[‡] D. Jeffrey Demanes, M.D.,[§] Brian J. Goldsmith, M.D.,* Eric M. Horwitz, M.D.,[¶] Geoffrey S. Ibbott, Ph.D.,[‖] W. Robert Lee, M.D.,[#] Subir Nag, M.D.,** W. Warren Suh, M.D.,[††] and Louis Potters, M.D.[‡‡]

Radiotherapy and Oncology 83 (2007) 3–10
www.thegreenjournal.com

*Guidelines prostate brachytherapy*

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

Carl Salembier[a], Pablo Lavagnini[b], Philippe Nickers[c], Paola Mangili[d], Alex Rijnders[a], Alfredo Polo[e], Jack Venselaar[f], Peter Hoskin[g,*], on behalf of the PROBATE group of GEC ESTRO

[a]Department of Radiation Oncology, Europe Hospitals, Brussels, Belgium, [b]Department of Radiation Oncology, MultiMedica Institute, Milan, Italy, [c]Department of Radiation Oncology, Domaine Universitaire du Sart Tilman, Liège, Belgium, [d]Department of Medical Physics, IRCCS, S-Raffaele, Milan, Italy, [e]Department of Radiation Oncology, Catalan Institute of Oncology, Barcelona, Spain, [f]Department of Radiotherapy, Dr B. Verbeeten Institute, Tilburg, The Netherlands, [g]Mount Vernon Cancer Centre, Northwood, UK

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Radiotherapy and Oncology 74 (2005) 137–148
RADIOTHERAPY & ONCOLOGY
JOURNAL OF THE EUROPEAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY
www.elsevier.com/locate/radonline

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

György Kovács[a,*], Richard Pötter[b], Tillmann Loch[c], Josef Hammer[d], Inger-Karine Kolkman-Deurloo[e], Jean J.M.C.H. de la Rosette[f], Hagen Bertermann[g]

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# GEC-ESTRO indications

## Inclusion criteria.

- Most low risk patients undergoing seeds brachy or surgery but HDR is possible.
- HDR is more frequently indicated after EBI (high risk and ECE)
- Stages T1b-T3b .
- Any Gleason score.
- Any PSA level.

## Exclusion Criteria

- TURP within the previous 3-6 months
- Maximum urinary flow rate < 10 ml/s
- IPSS greater than 20
- Pubic arch interference
- Lithotomy or anesthesia not possible
- Rectal fistula
- Direct contact between applicators and rectal mucosa

# POTENTIAL EXCLUSION CRITERIA

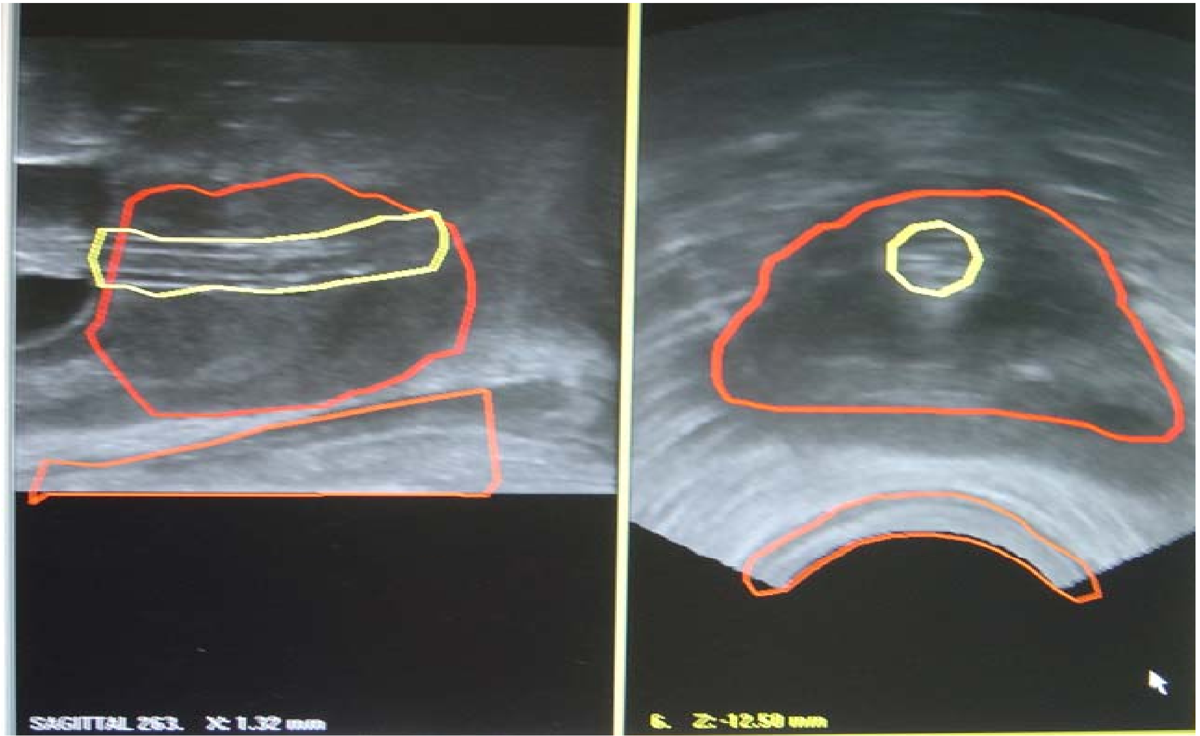
- Prostate volume > 60cc (consider androgen deprivation)
- Unacceptable operative risk
- Poor anatomy which leads to a suboptimal implant
- Positive lymph nodes and M1+
- Pubic arch interference
- Large median lobe (limited excision should be considered)
- Seminal vesicle infiltration
- Large or poorly healed TURP
- Significant obstructive uropathy
- T3 stage
- And Infiltration of the external sphincter of the bladder neck

# Pre-treatment studies

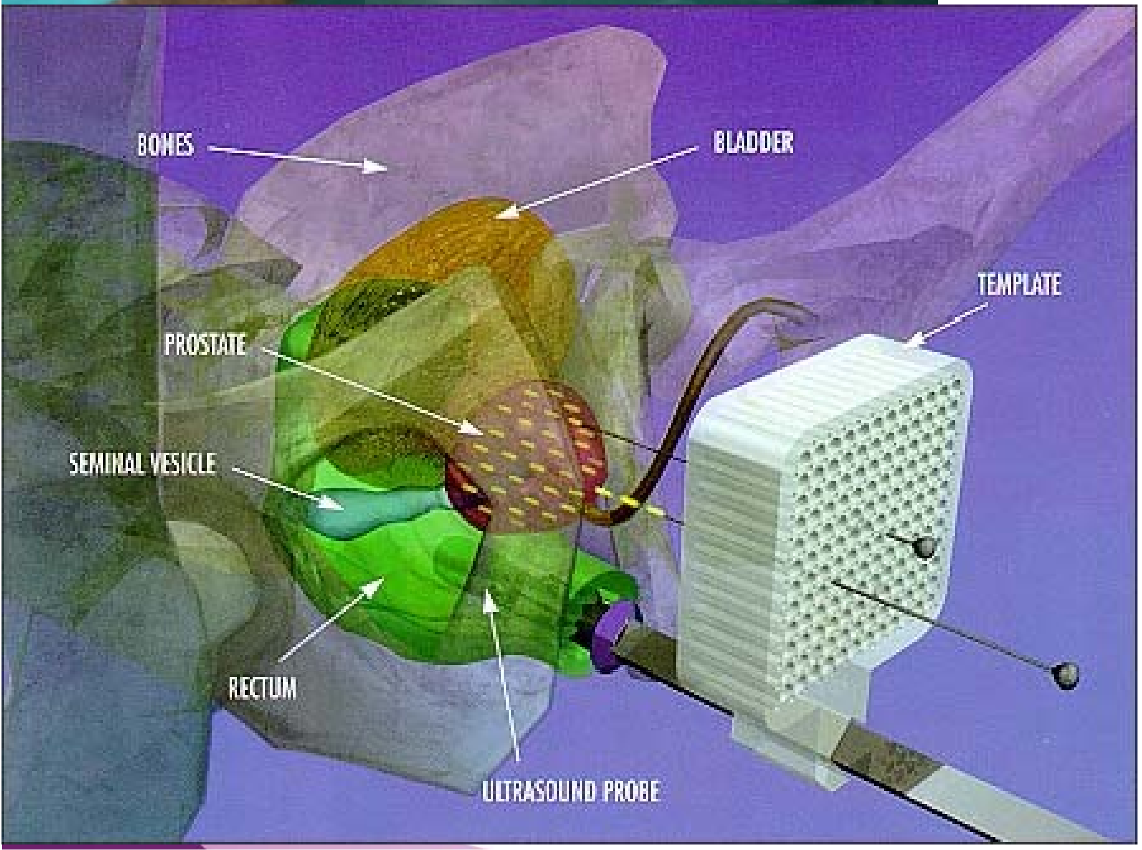
- Digital rectal examination
- PSA level
- TRUS and biopsy
- Bone scan: Gleason score 7(4+3) , PSA greater than 20 ng/ml.
- MR in intermediate and high risk patients.
- CT for pelvic and paraaortic lymph nodes. Choline PET and/or laparoscopic surgical sampling in equivocal cases.
- IPSS or AUA symptom scores.
- Urinary flow tests.
- Index of erectile function scale

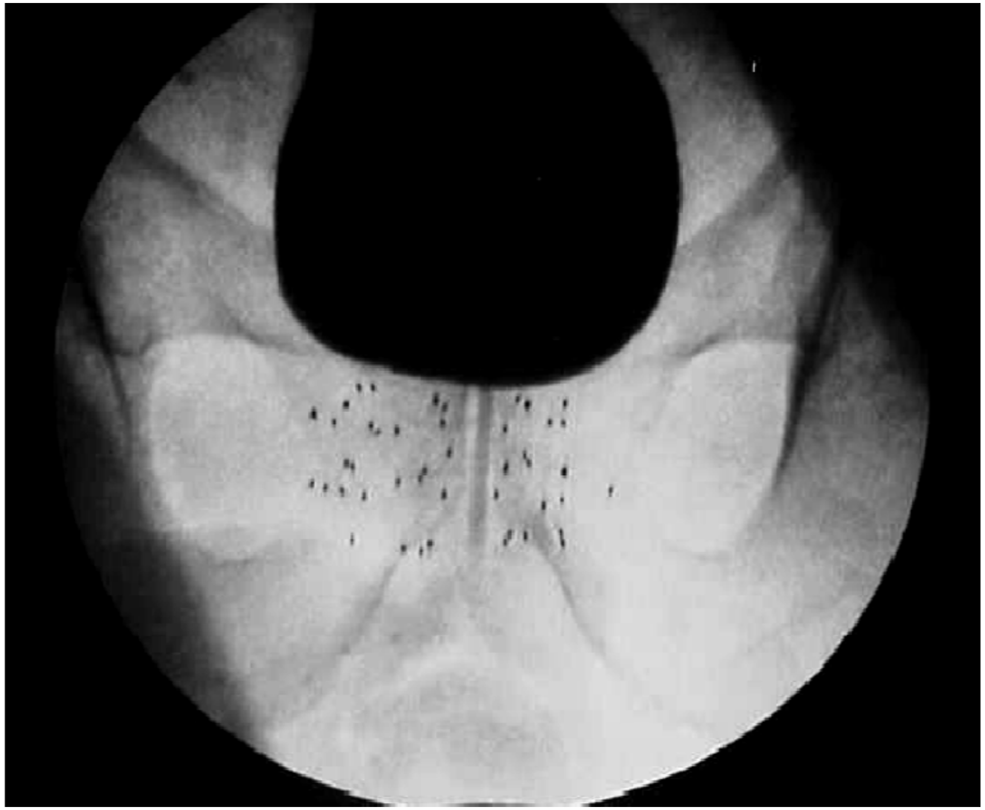
# OAR delimitation

- Prostatic urethra: a 10 mm urinary catheter should be contoured with aereated gel inside to avoid distension of the urethra. Delineation of the outer contour should be from the prostatic base to 5-10 mm below the prostatic apex.
- Rectum: contouring of the outer wall is the minimum requirement. Contouring of the inner and outer walls is more correct for analysis of late damage.
- Penile bulb and Neurovascular bundles: remains under study.



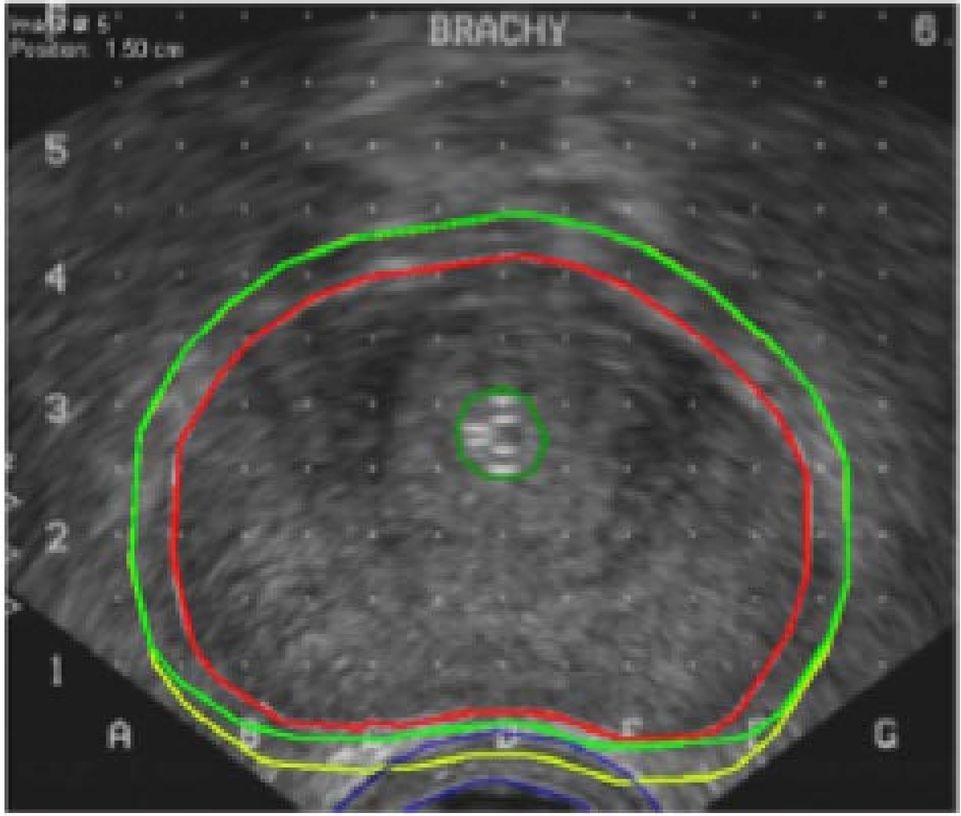
# CONTOURING PERMANENT IMPLANTS



## Intra-operative planning:

1) Contouring for Pre-planning
2) Real time planning




## Contouring:

Every 3-5 mm for contouring
From the base to the apex with a 3 mm margin (not posteriorly)

**To justify the 3mm margin:**

PARTIN tables: 10% extracapsular penetration
Studies by Davis BJ (Cancer 1999),
the 96% extracapsular extension ≤ 3mm in patients with good prognosis

- **GTV** is usually not considered (may be defined using the information from previous diagnostic images.
- **CTV**: Volume that contains GTV and includes all sublinical malignant diseases at a certain probability level: Prostate + 3mm.
- **CTV= PTV**: Prostate + 3 mm.
- T3: CTV corresponds to the visible contour of the prostate including visible extension due to extracapsular growth + 3mm.

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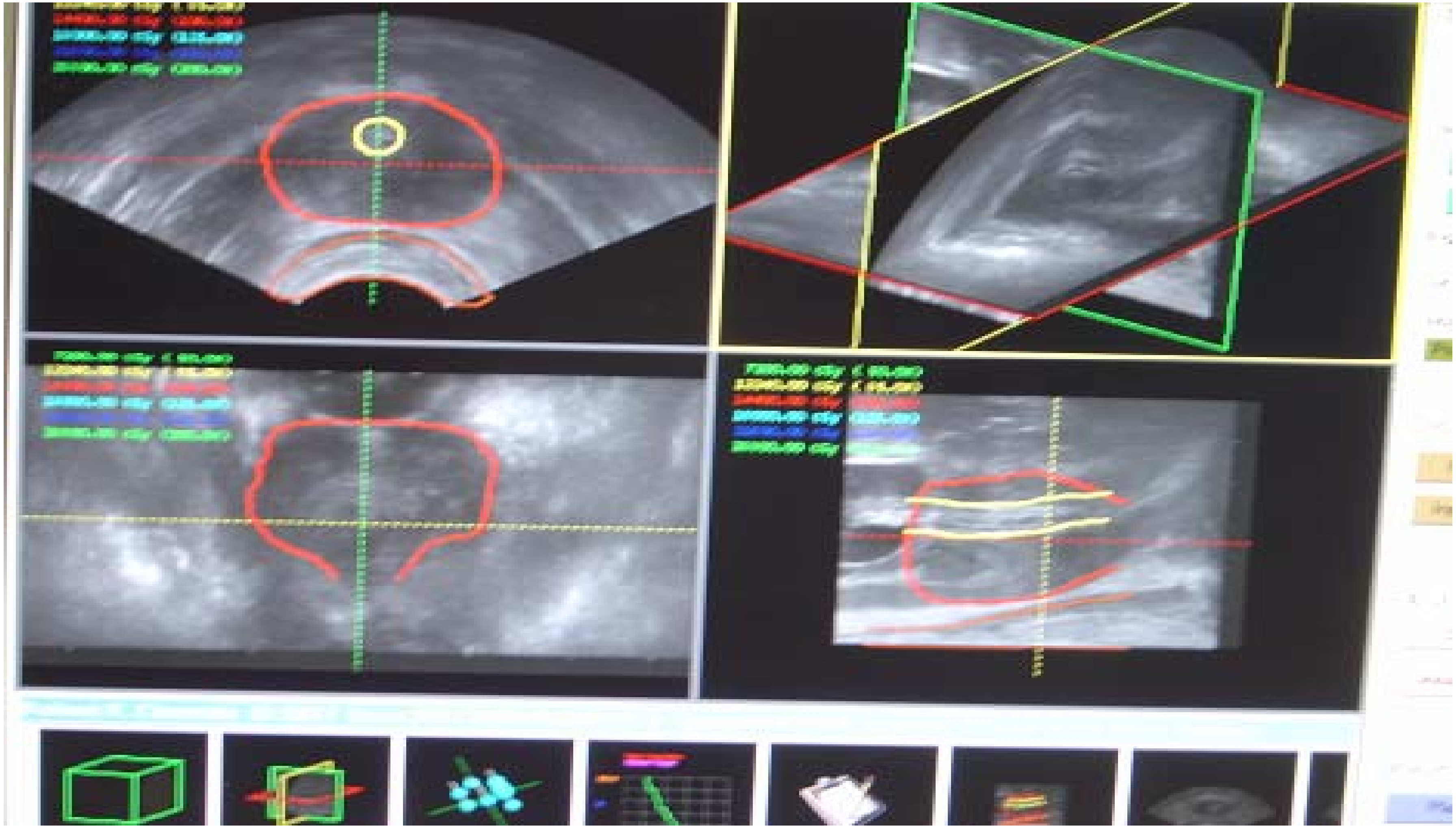

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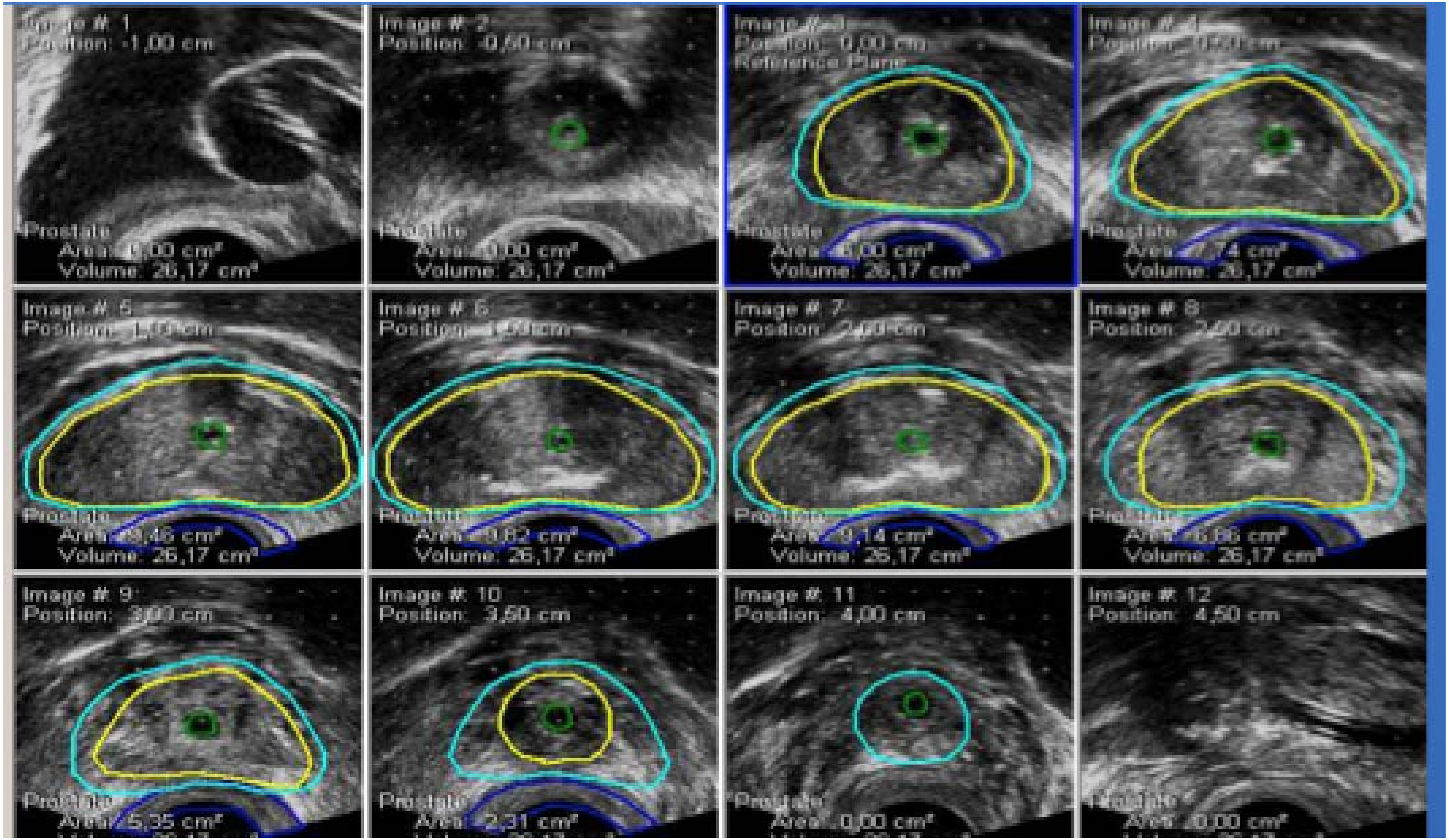


IVO Courtesy

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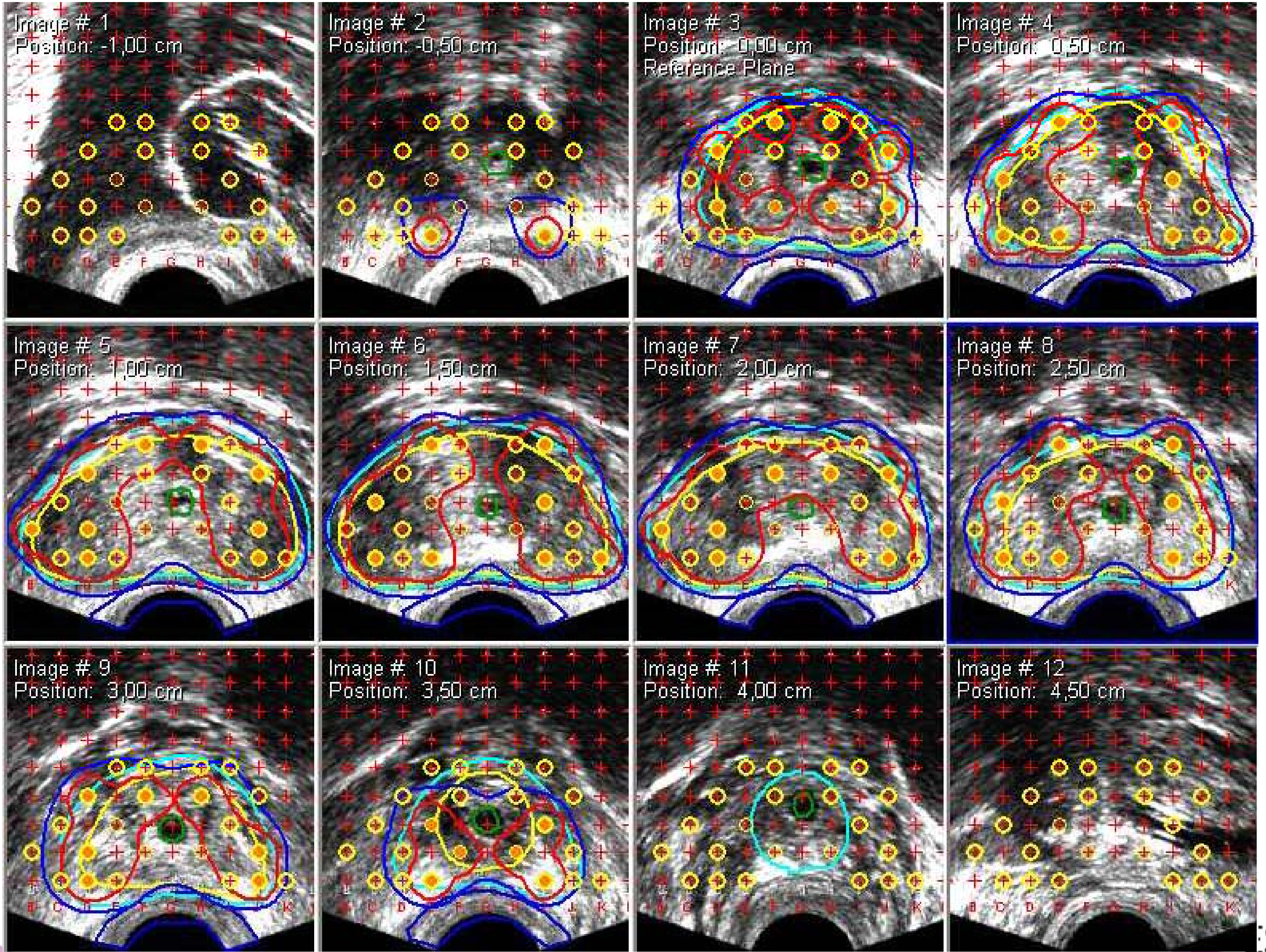


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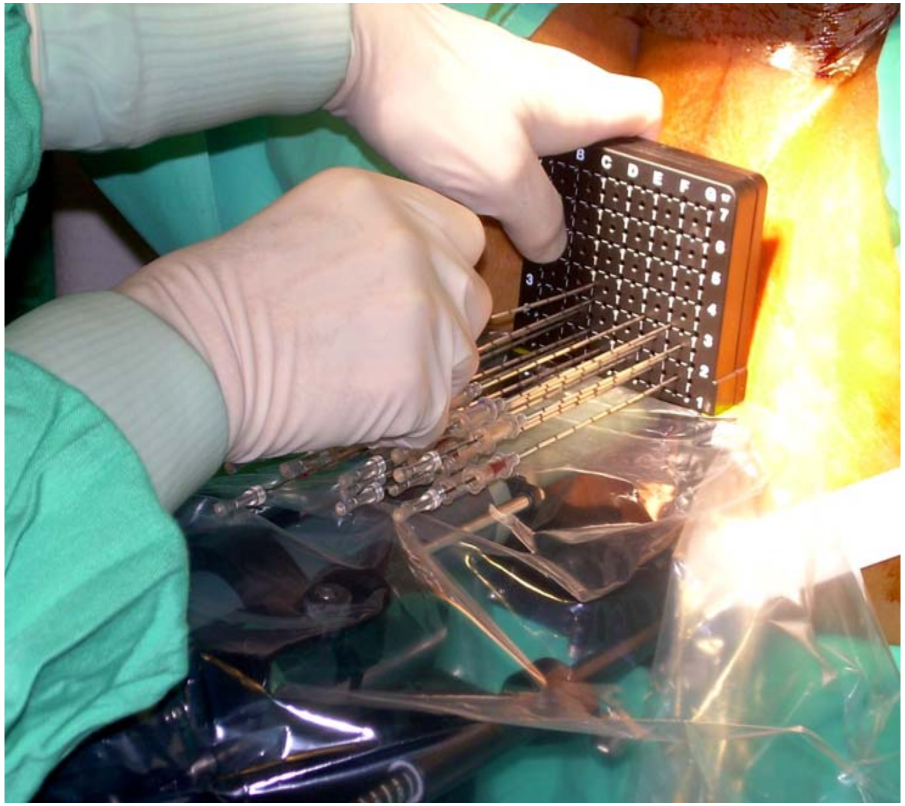
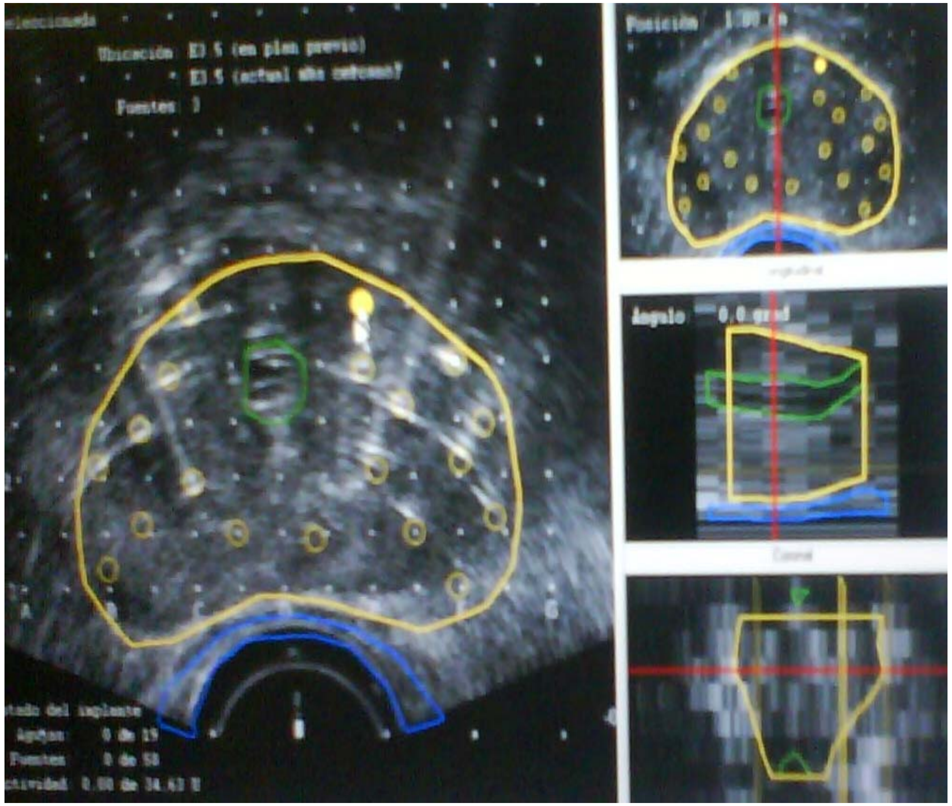
# HDR BRACHY PROSTATE CONTOURING





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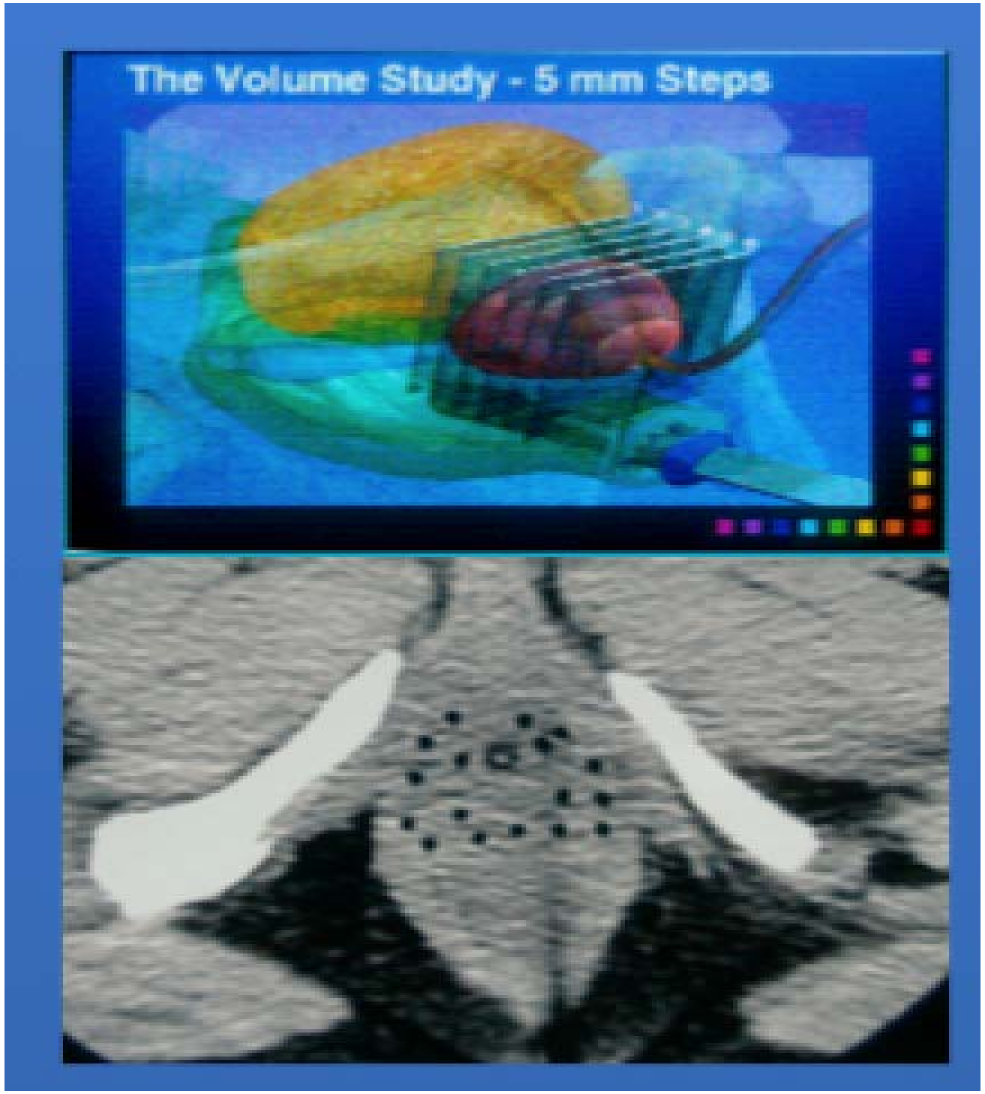
# CT, MR or US PLANNING



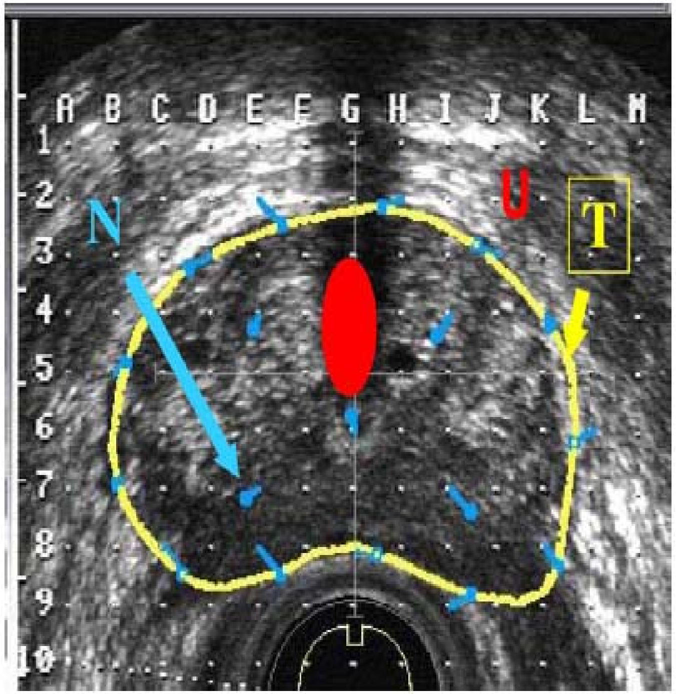

CT: Every 3 mm slices from the base to the template.

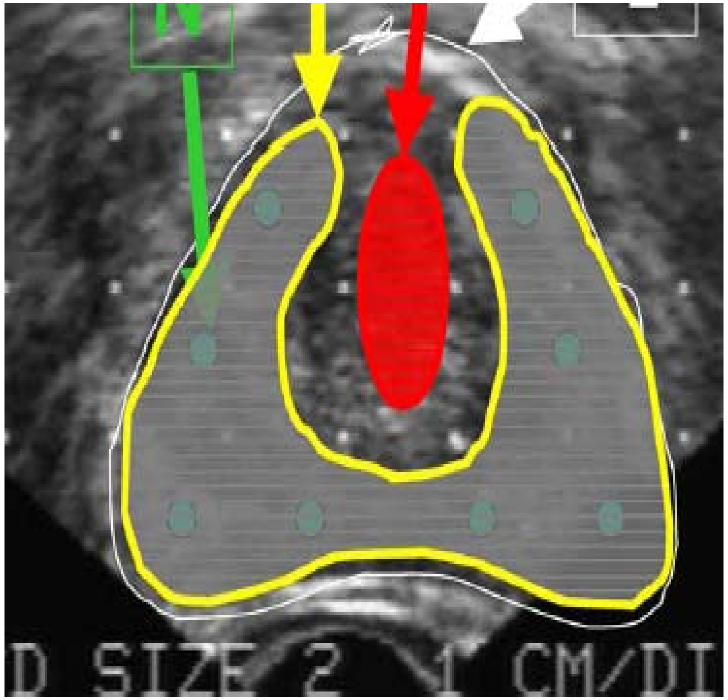
T2 MR provides optimal anatomical definition but T1 provides more accurate catheter reconstruction.

Image fusion may be used to maximize information from different imaging modalities.

Delimitations of the prostate and OARs should be included.

# REAL TIME PLANNING (US)



Different subvolumes of interests are considered

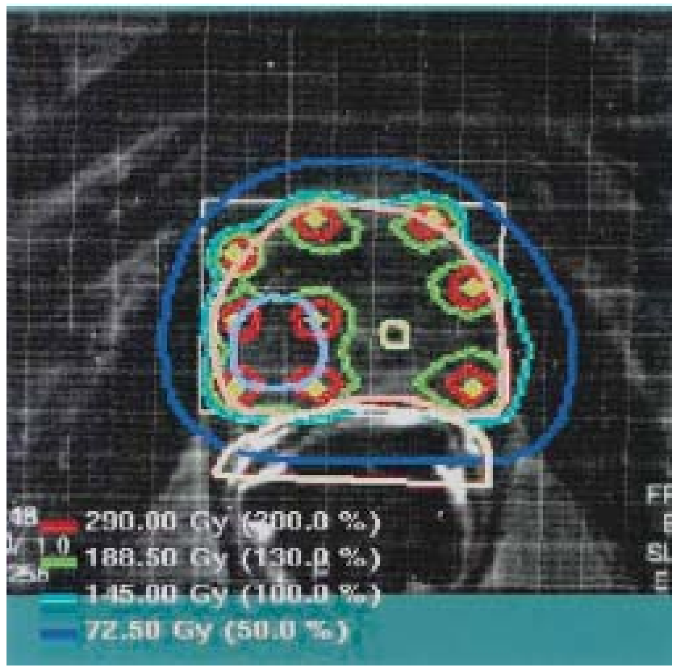
CTV1: **Peripheral zone (main tumour burden: in yellow)**

CTV2: **Macroscopic tumour shown in red**

CTV3…..

CTV: **prostate capsule plus any EPE or seminal vesicle involvement. CTV margins are constrained posteriorly to the anterior rectal wall and superiorly to the bladder base.**

PTV: **should be considered as a CTV expansion accounting for uncertainties like catheter tracking and image registration.**



# Parameter reporting

- **External beam dose**
- **Implant technique, number of catheters**
- **TRACK Pattern dwell time for each applicator**
- **CTV: D90, V100; V150, V200**
- **PTV (if defined): D90, V100, V150, V200**
- **Organs at risk: rectum: D0.1cc, D2cc.**
- **Urethra: D0.1cc, D10, D30**

**In general for CTV:**

- **V100 ≥ 95%**
- **D90 > 100%**
- **V150 15% CTV**
- **V200 5% CTV**

**OARs:**

**$RD_2cm^3 \leq$ 75% prescribed dose**

**$UD_1cm^3 \leq$ 120% prescribed dose**

# FINALLY….

- When indicated,  BT in prostate cancer is a safe technique with proven results.
- BT in prostate cancer requires adequate volume delimitation of the prostate and extraprostatic extension, if present.
- Real time planning needs a good working team and…
- Accurate planning provides similar results to surgery

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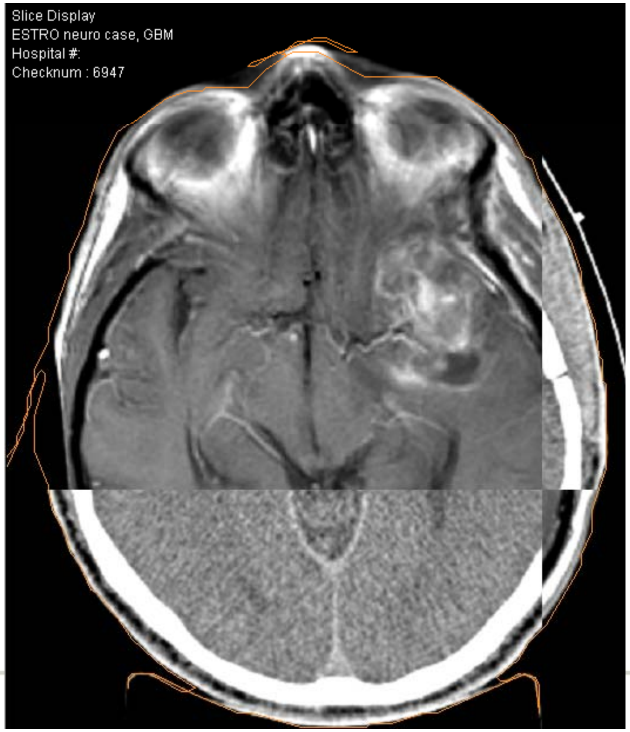
# CNS case solution

## Glioblastoma




***ESTRO Course***
***Barcelona 2016***

# CNS case

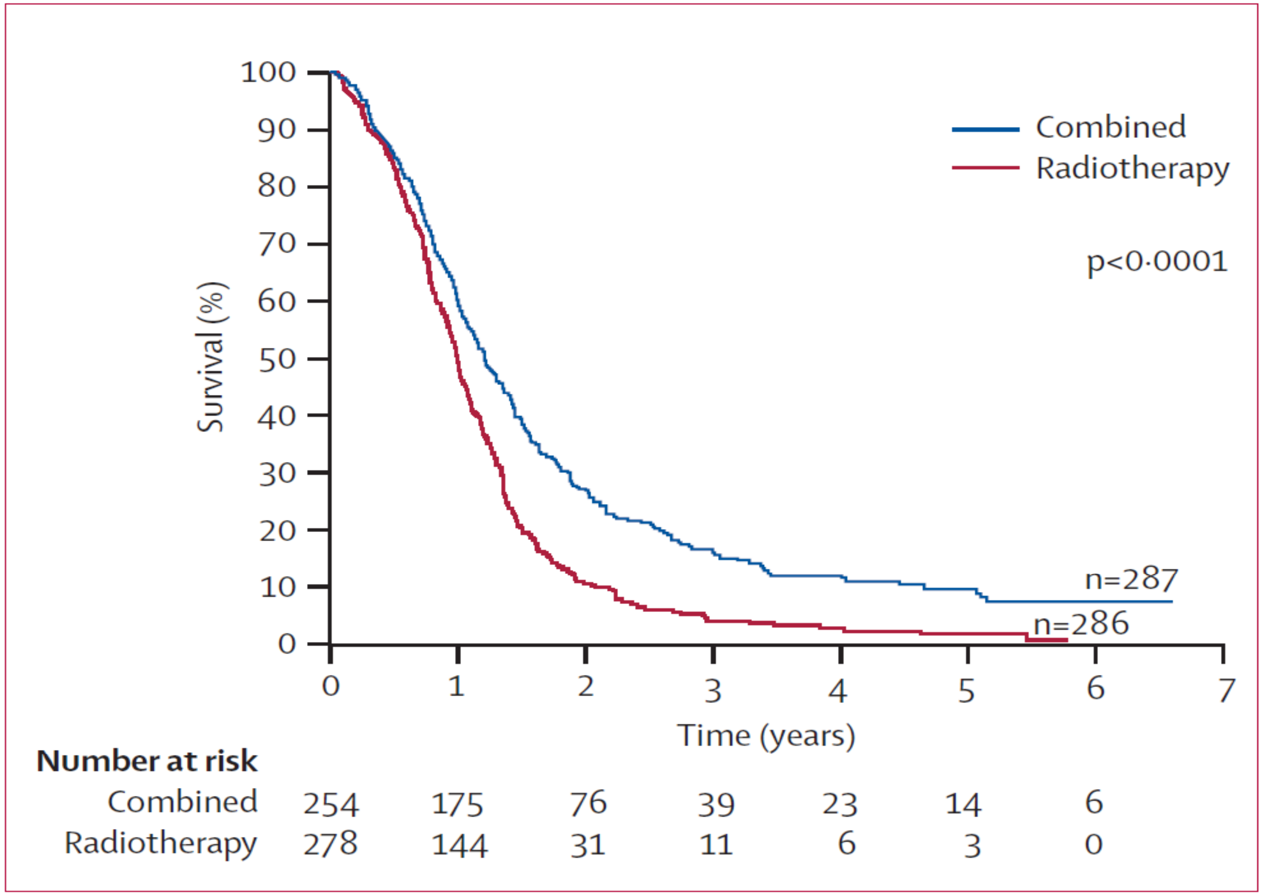
- Man aged 52
- Seizures, for 3 months

- Craniotomy - temporal lobectomy and debulking
- Histology – glioblastoma
- MGMT - unmethylated

- Radical radiotherapy (+ temozolomide):
  - positioning & immobilisation
  - beam energy
  - treatment approach – CRT or IMRT

# Chemo + RT for GBM

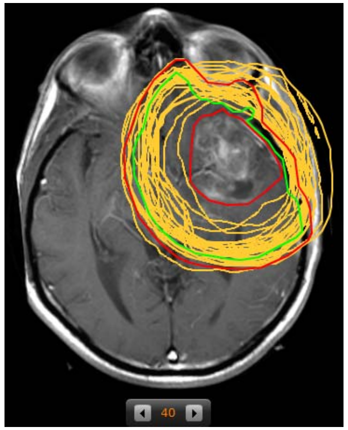
- Stupp et al. *Lancet Oncol* 2009; 10: 459–66
- ~ 20% 3 year survival ~10% 5 year survival



# CNS case

- GTV outlining
- What CTV margin?
  - Edit CTV?
- What PTV margin?
- What are the critical normal tissues?
- RT dose and fractionation

# CNS case

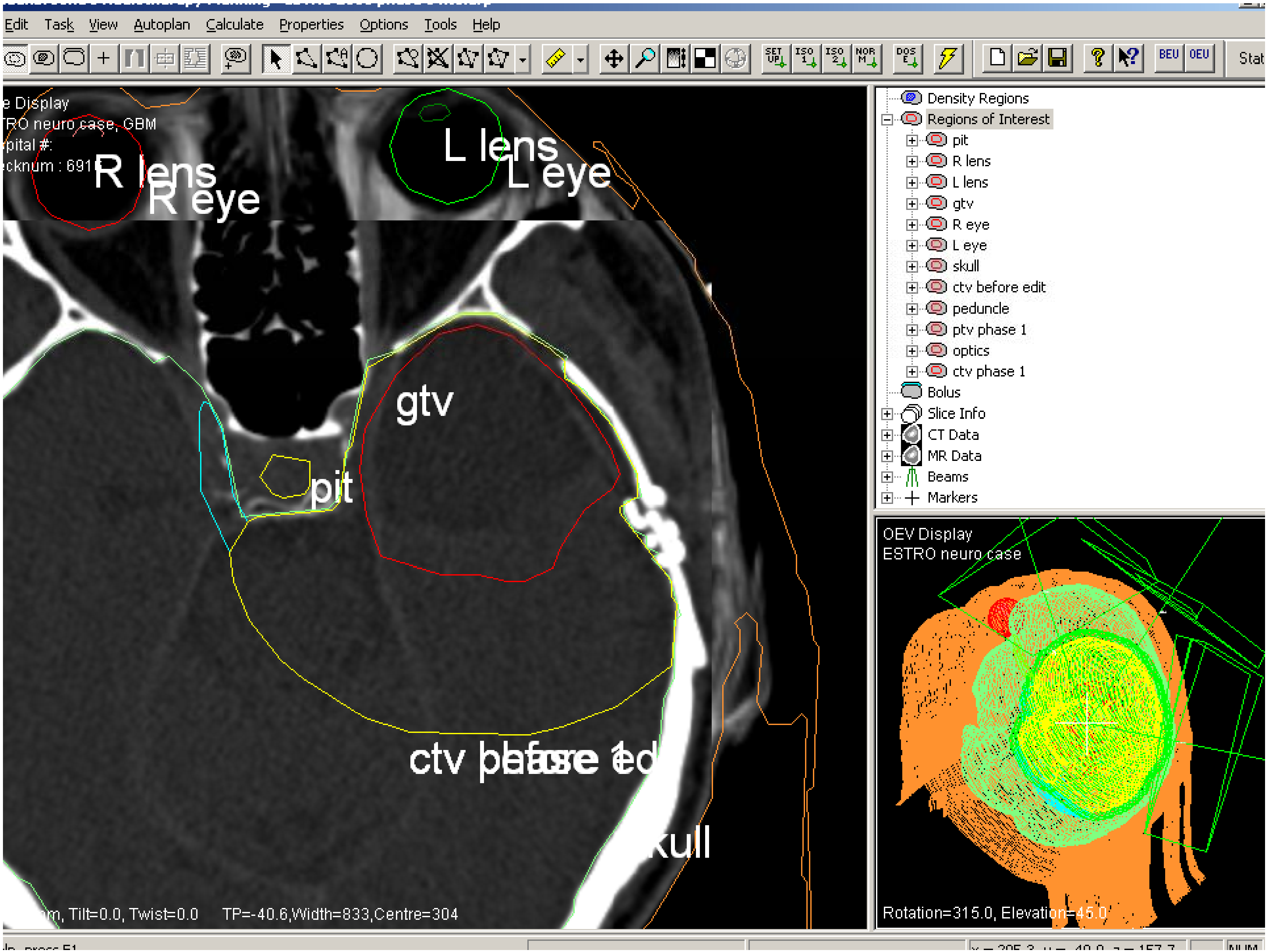



- Review of imaging

- Individual and group outlining

# Review of outlining

- Both CT and MRI useful – CT for bone + skull base
- Don’t worry too much about *every* margin – if large CTV margin is to be added
- Distinguish which margins are important and which are not
- In the end, we want the CTV to be correct



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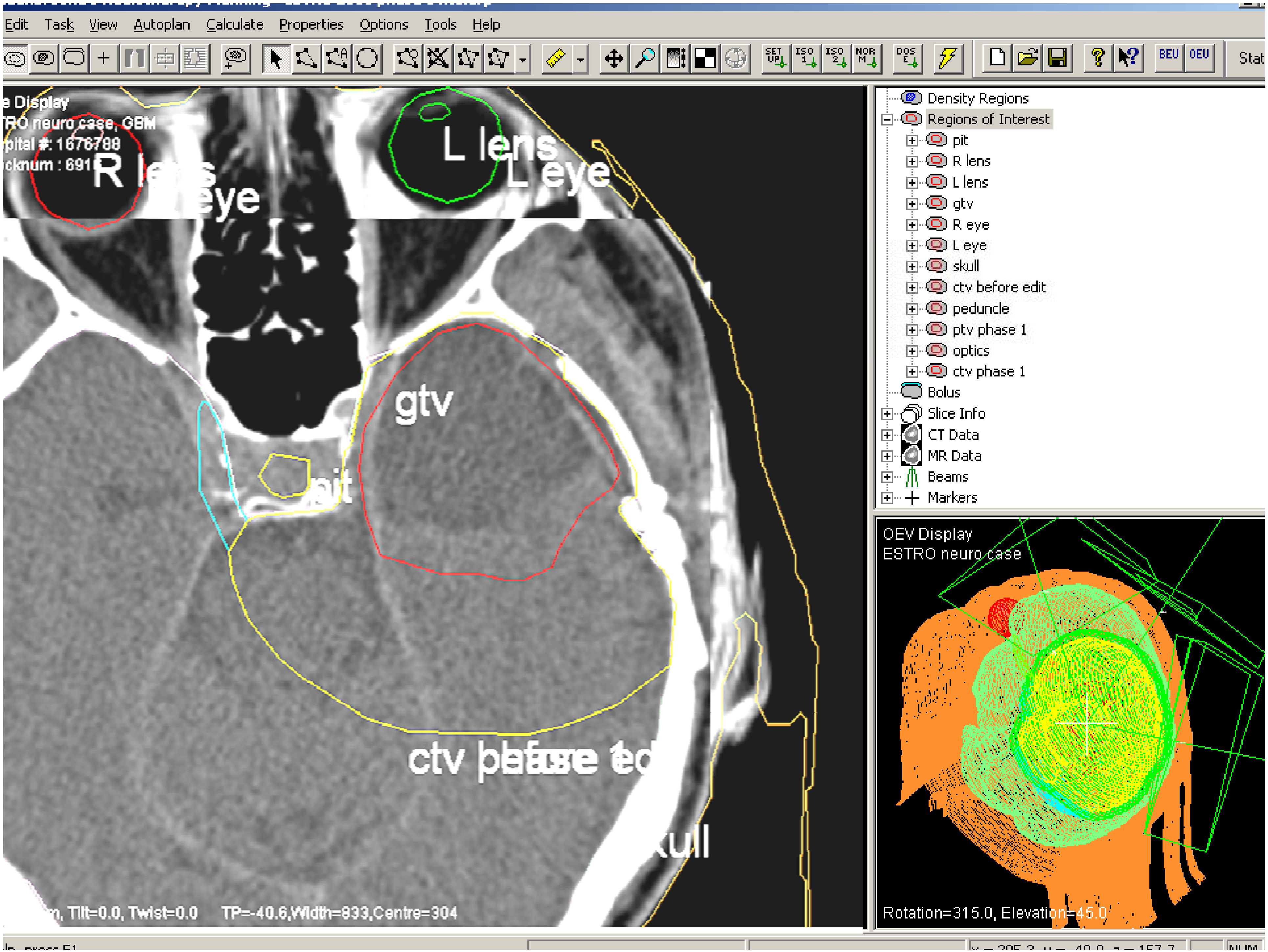
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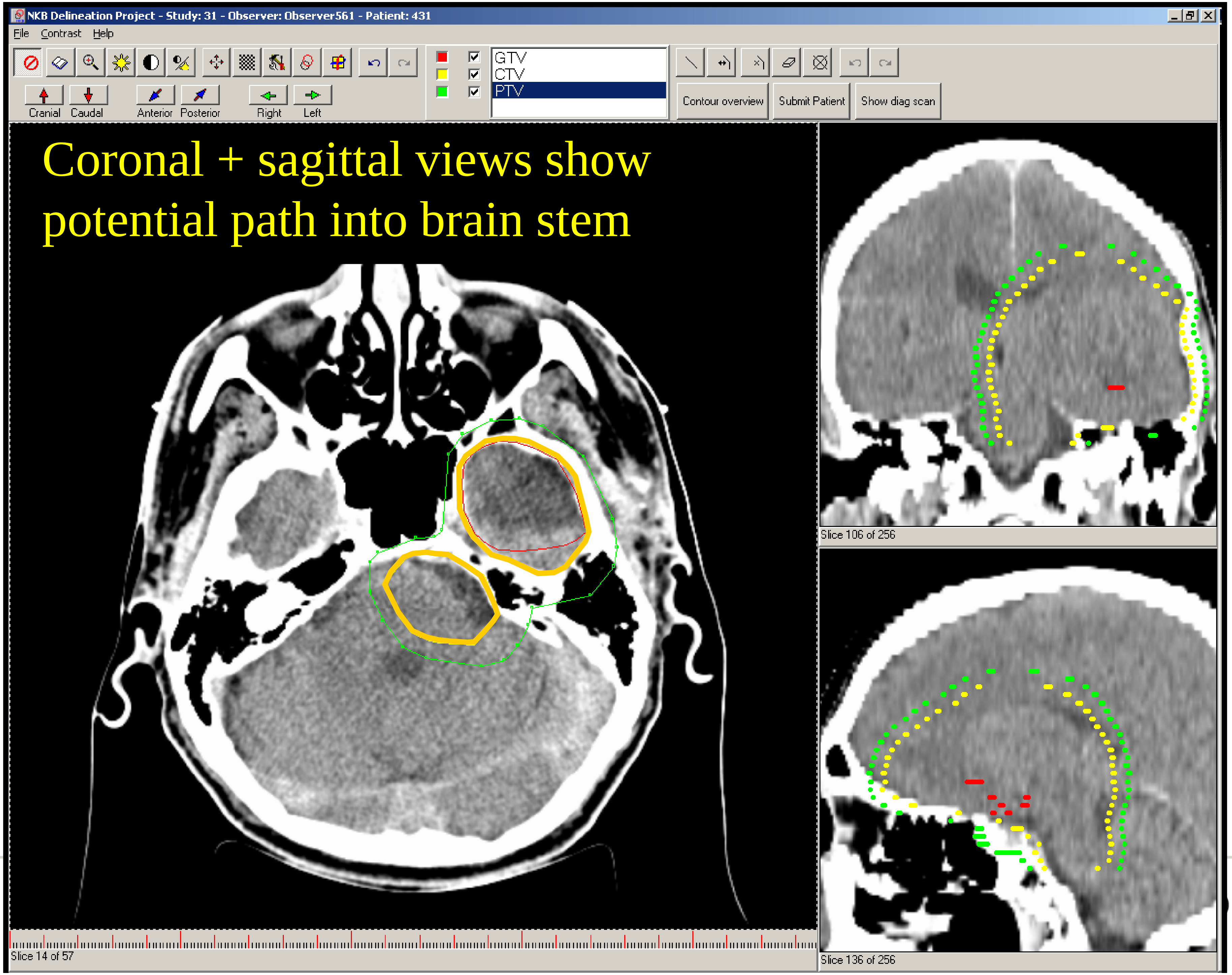
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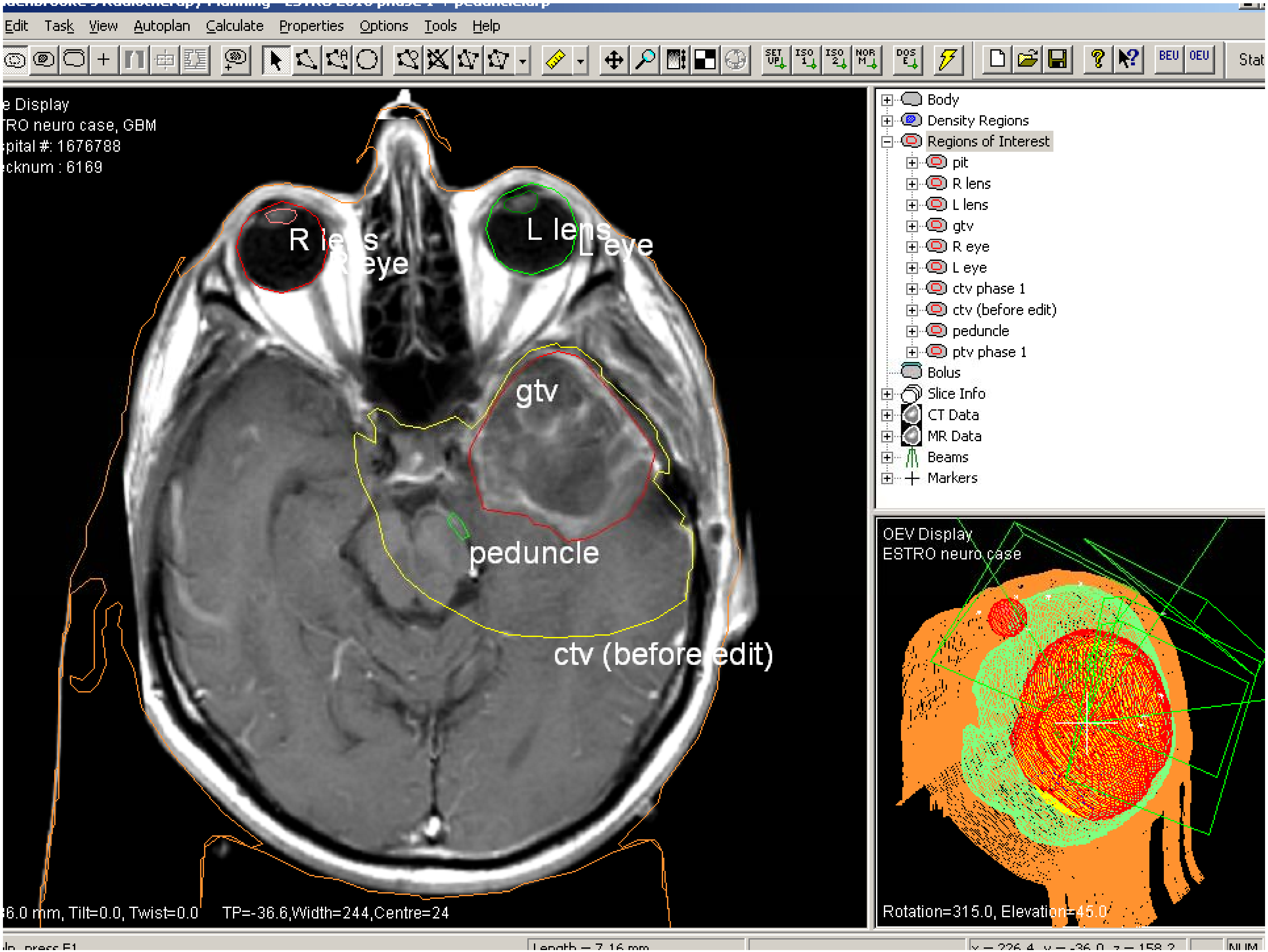

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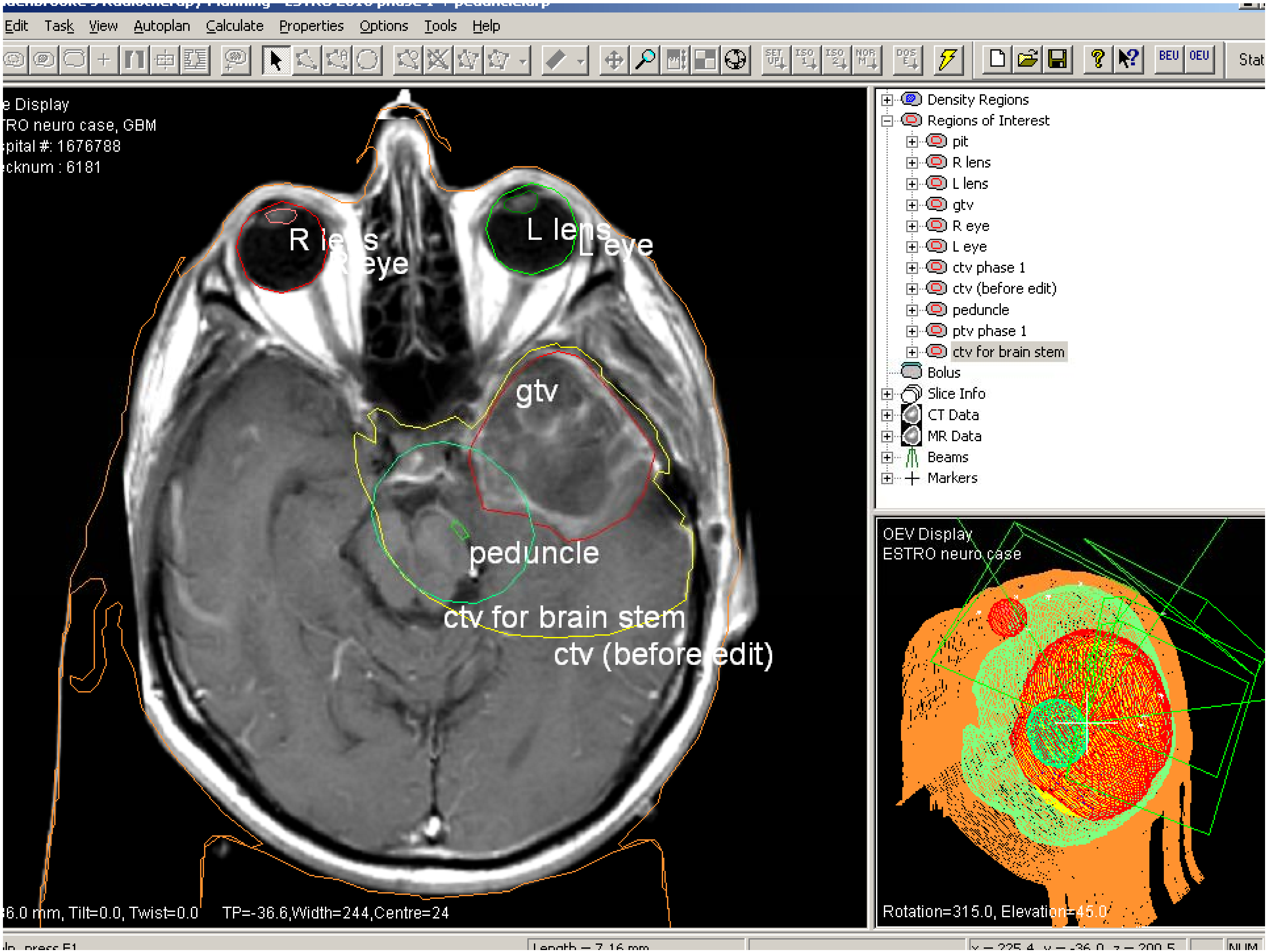
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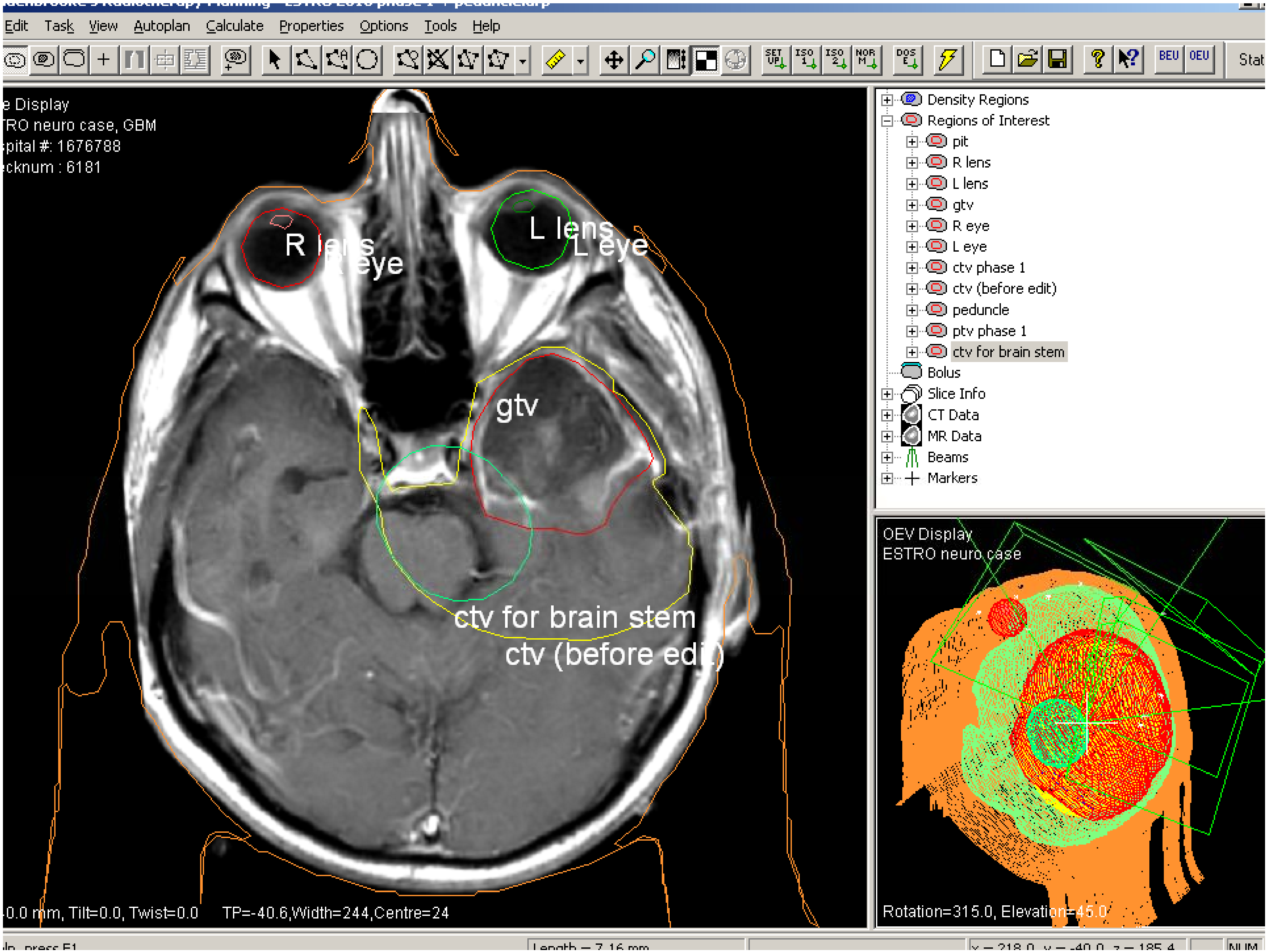

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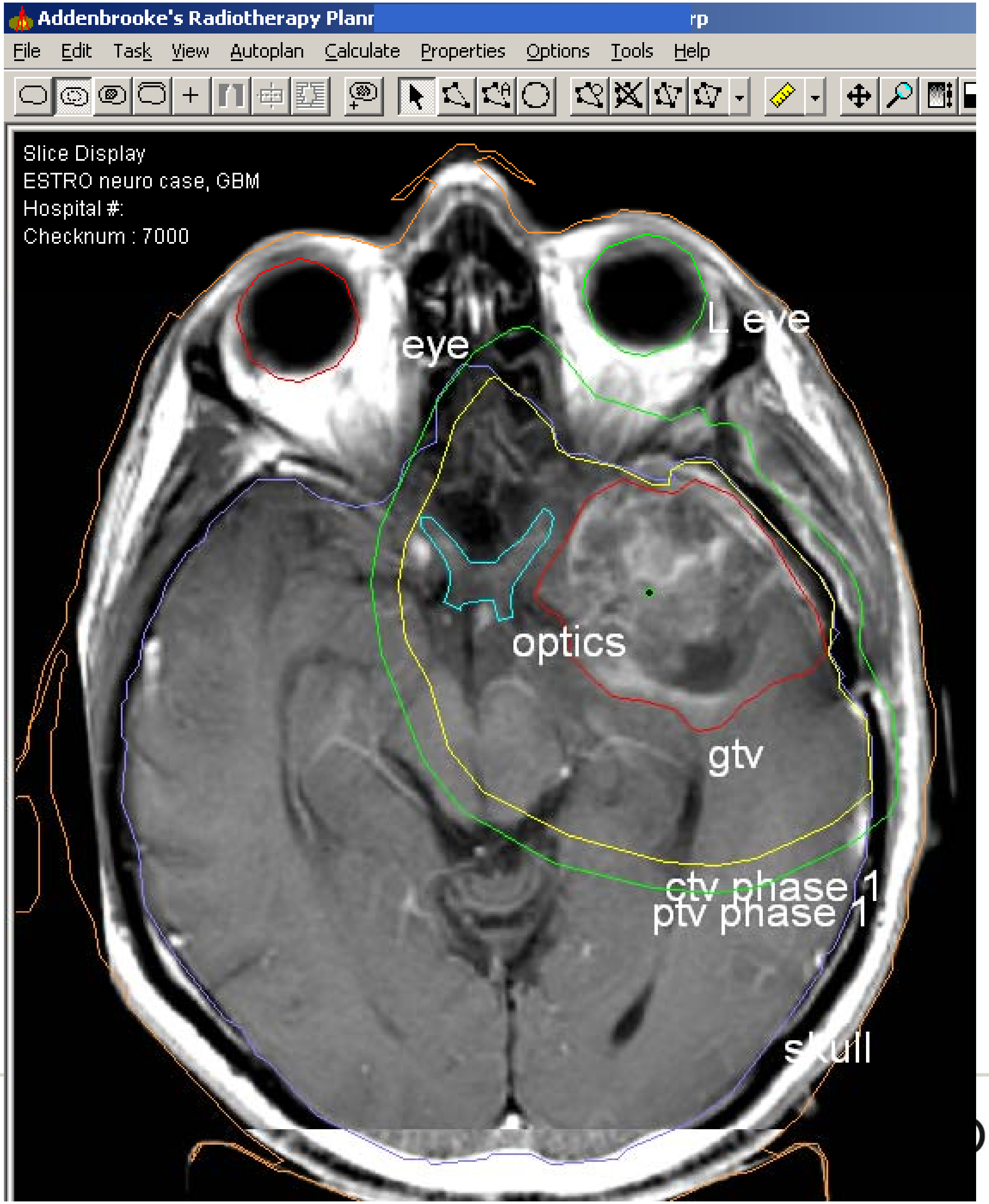
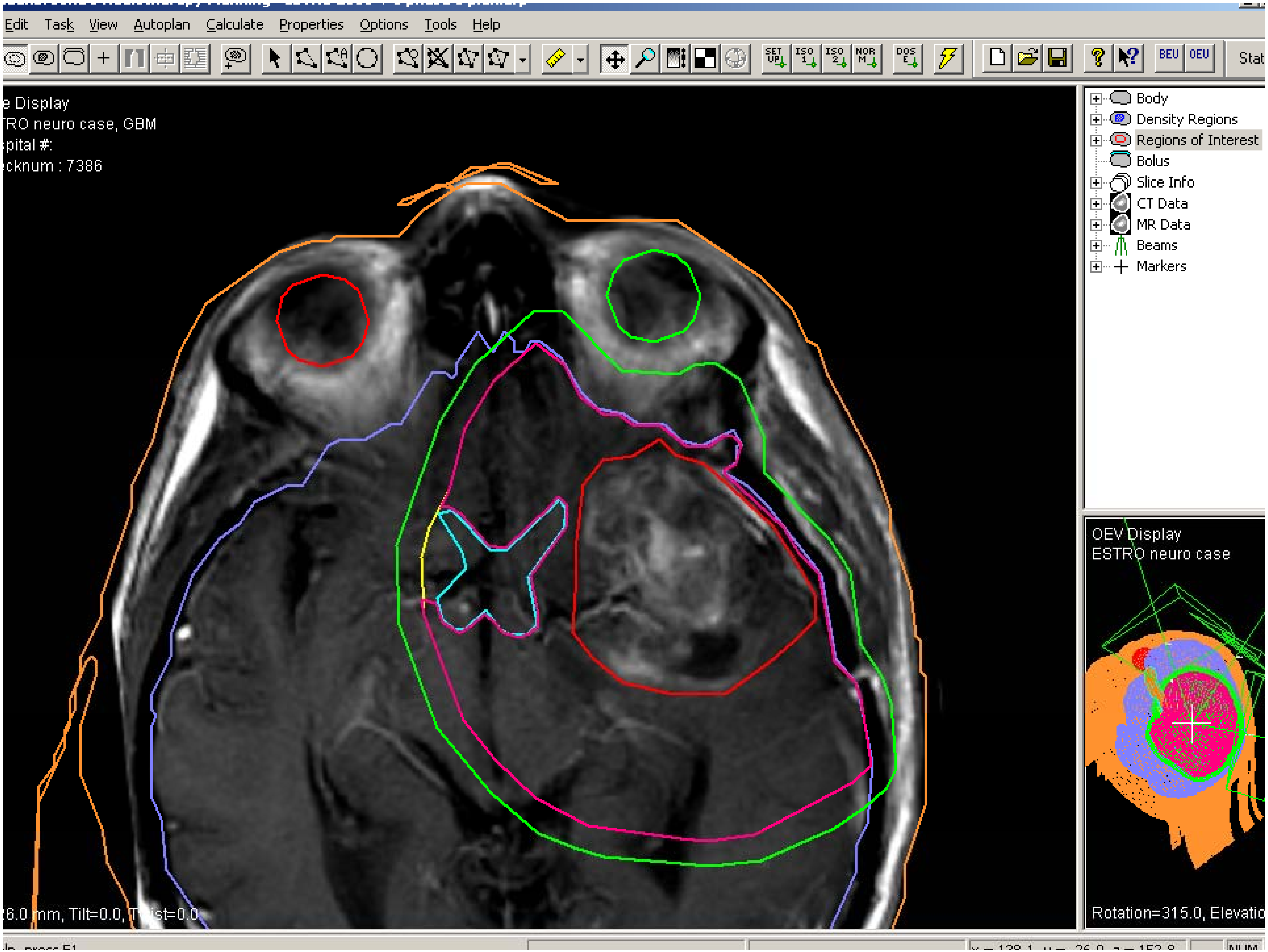
# CNS case

- Optic pathway - OAR

- Optic chiasm

- ? Dose-limiting
- ? Context

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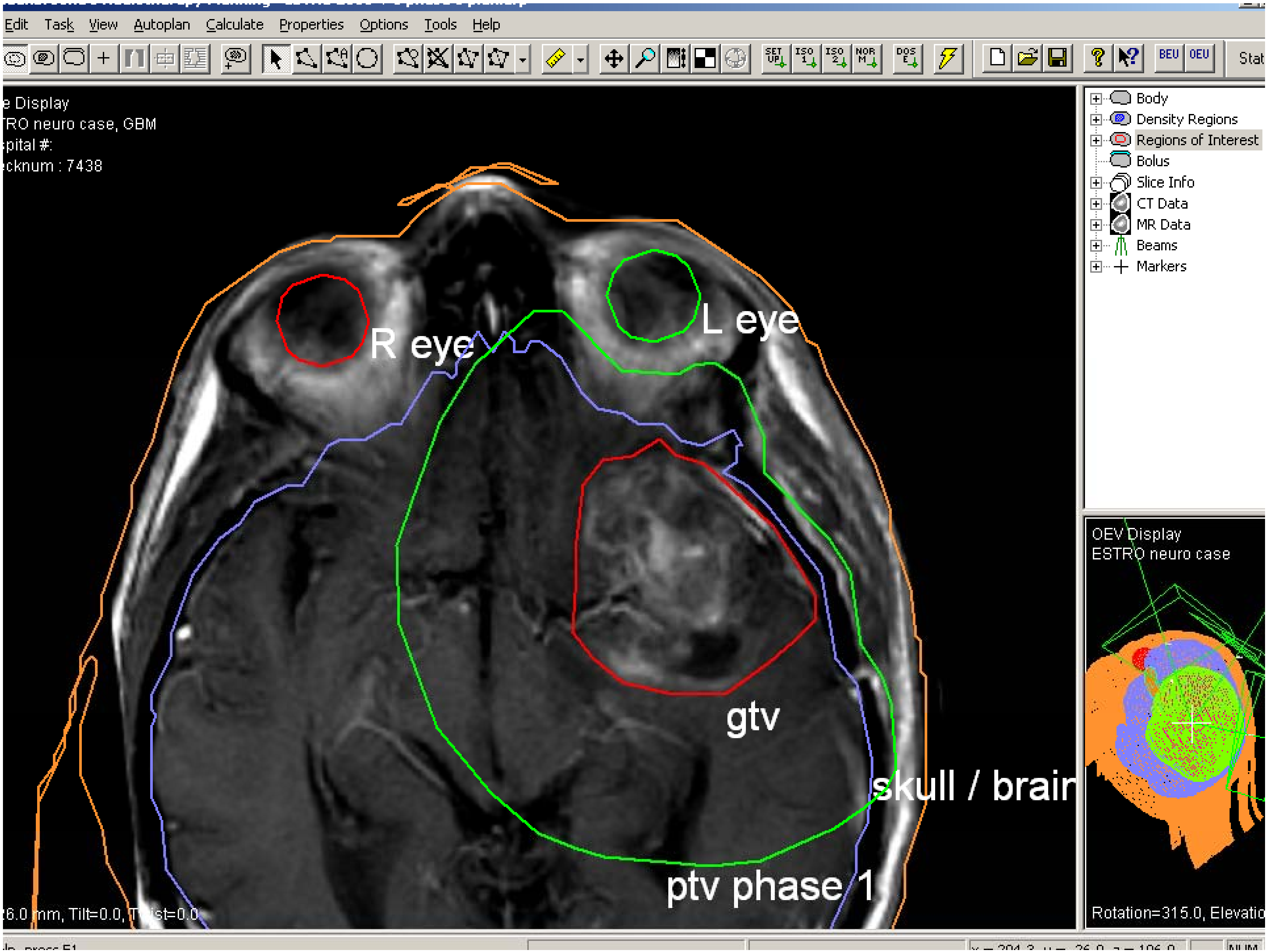

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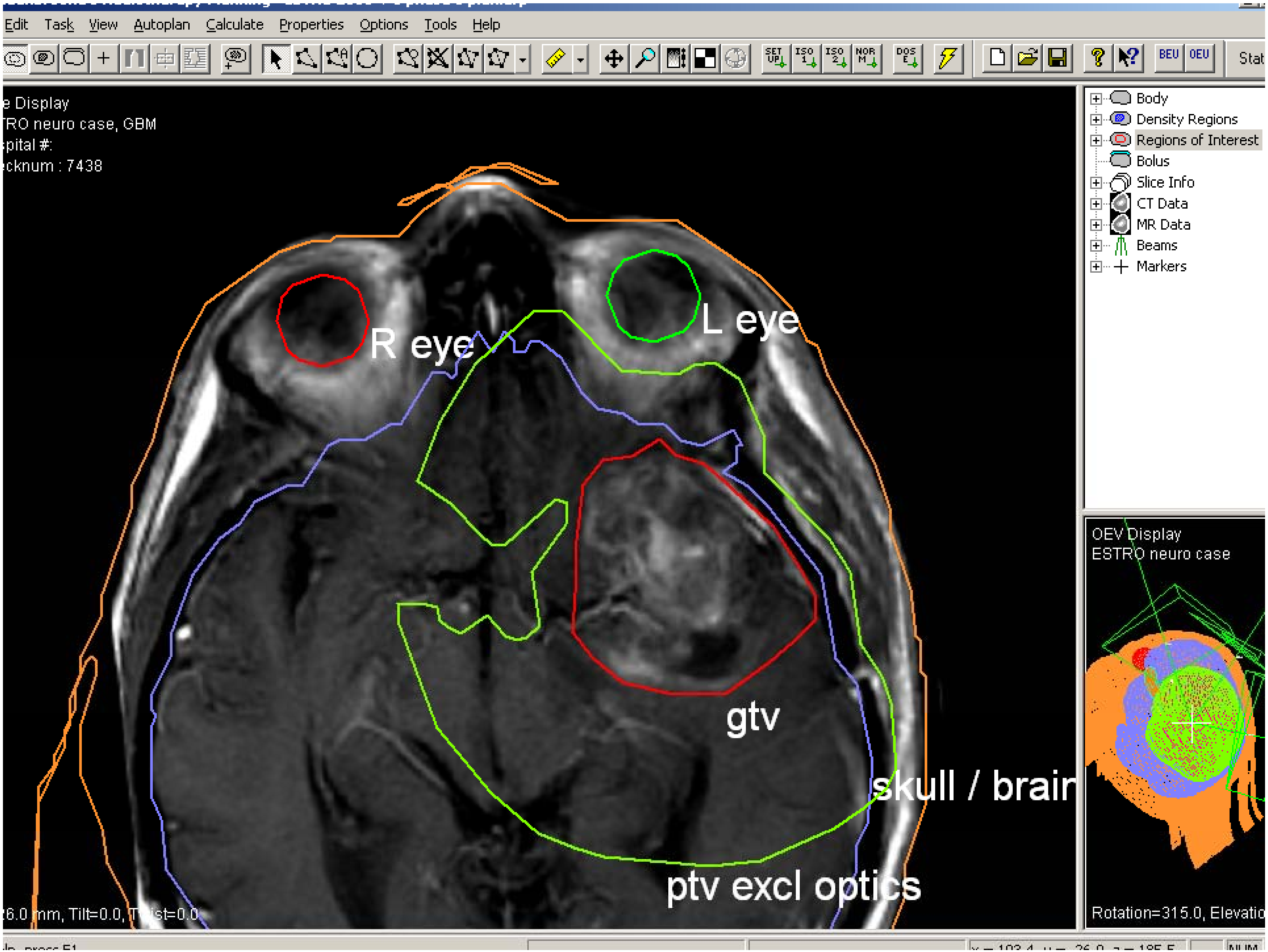

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CT Data
MR Data
Beams
Markers
R eye
L eye
gtv
skull / brain
ptv excl optics
OEV Display
ESTRO neuro case
Rotation=315.0, Elevatio
6.0 mm, Tilt=0.0, Twist=0.0

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WWW.ESTRO.ORG/SCHOOL

# Inter-observer variation in target volume delineation

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Department of Radiation Oncology
The Netherlands Cancer Institute

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

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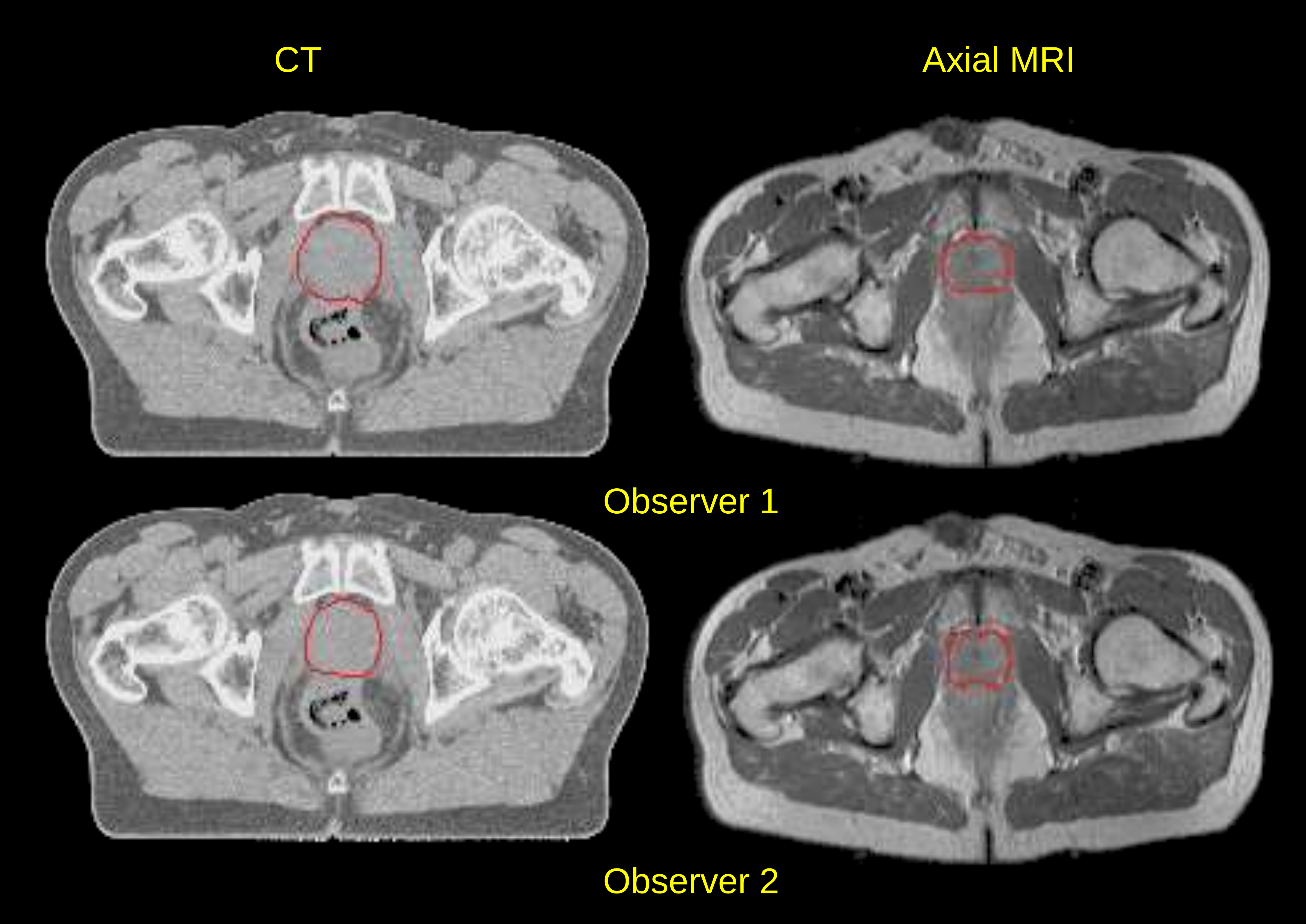
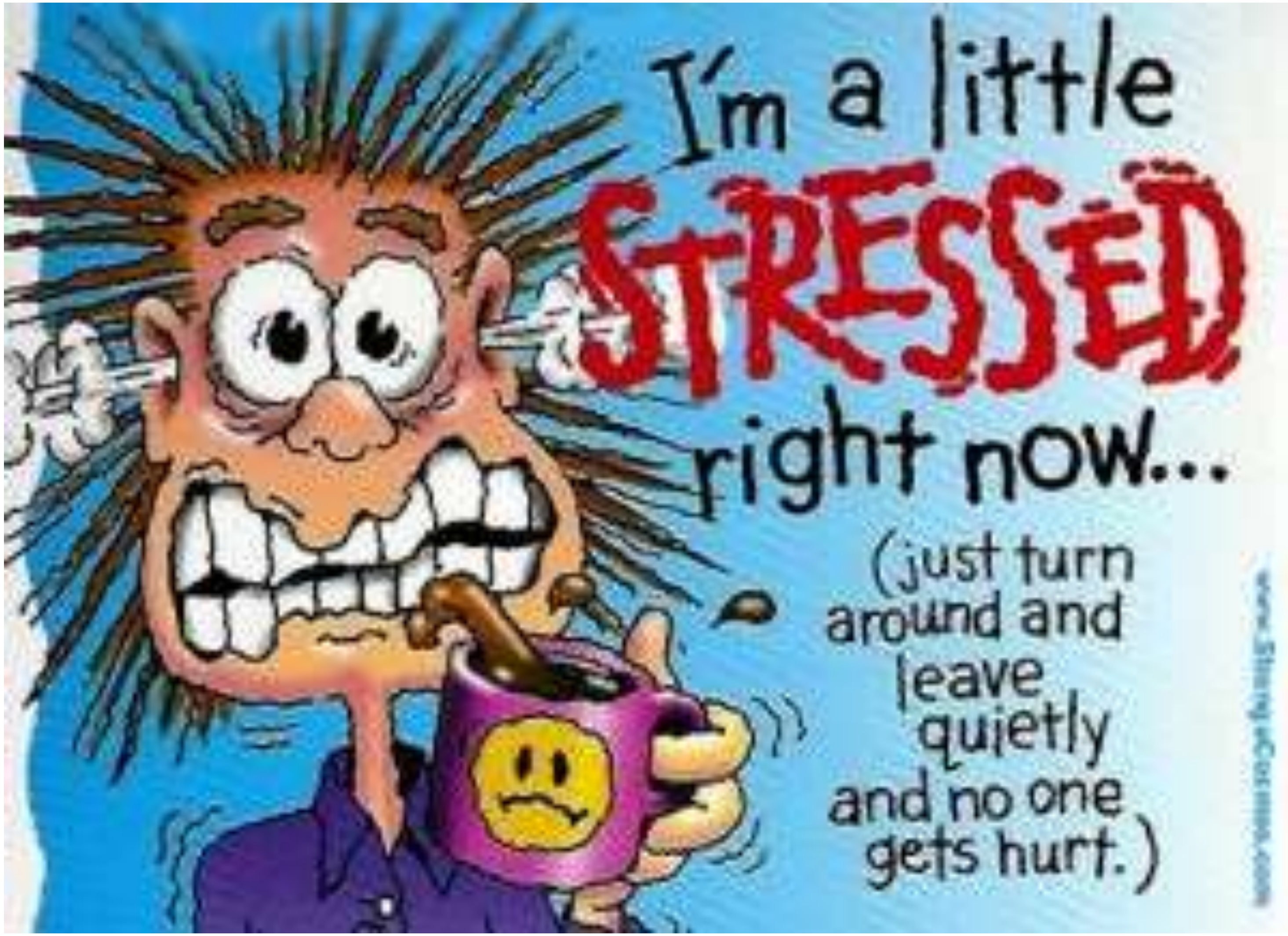

CT
Axial MRI
Observer 1
Observer 2

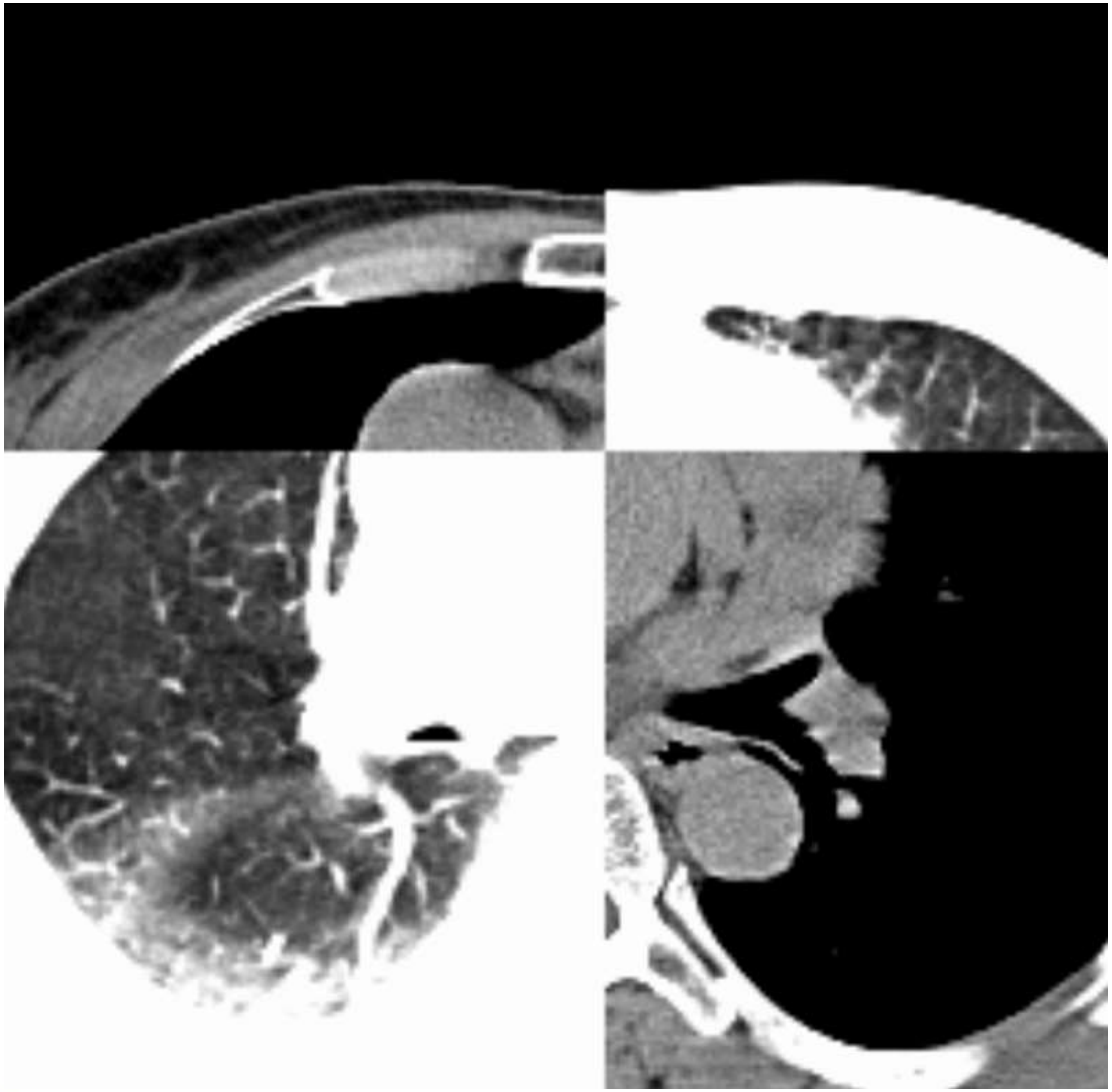
# What influences delineation uncertainty?

# Lack of coffee…..

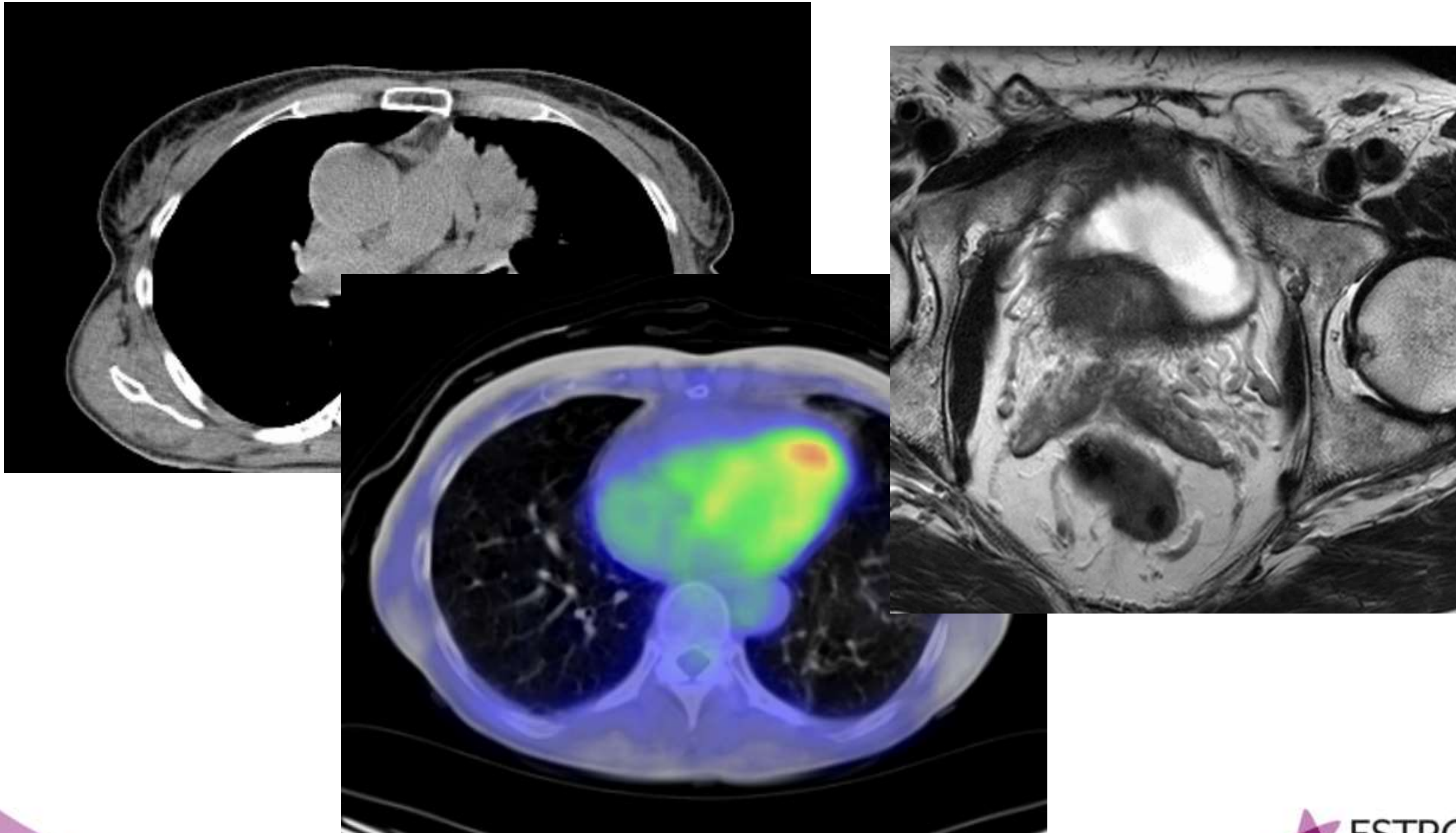
# … or too much coffee



# Level/window



# Modalities



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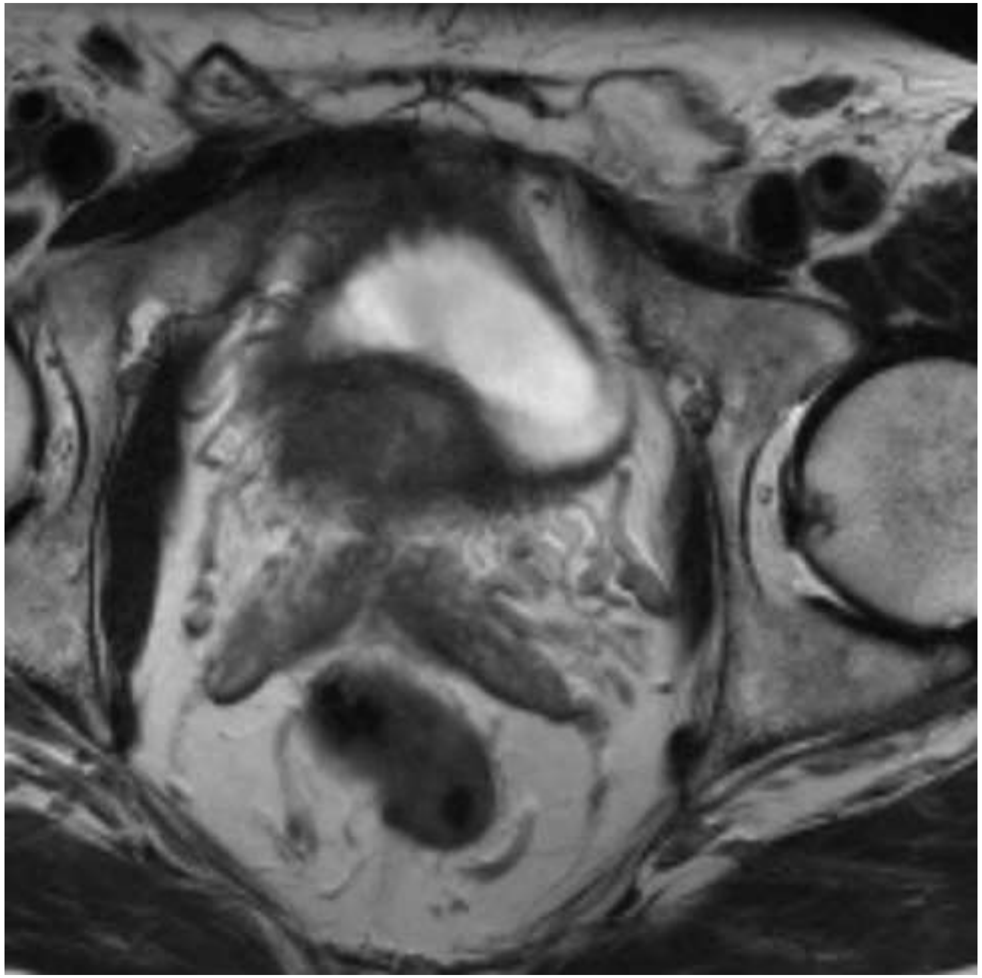
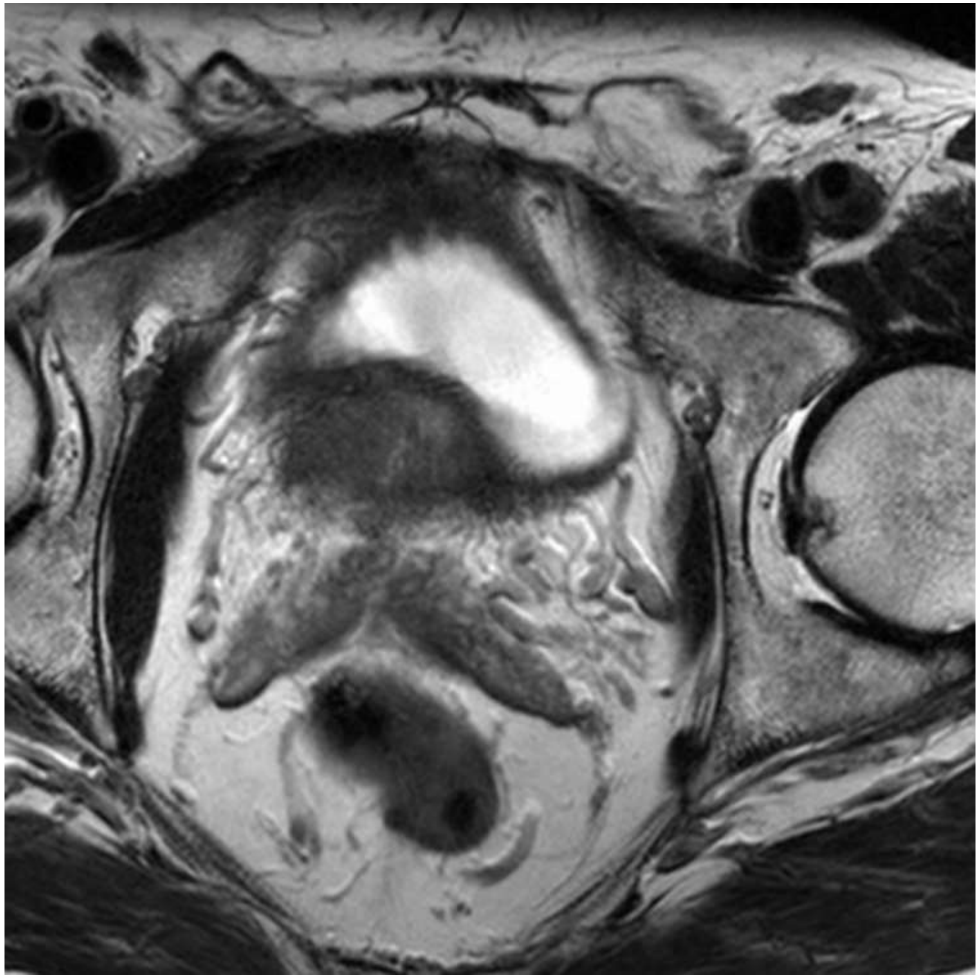
# Resolution

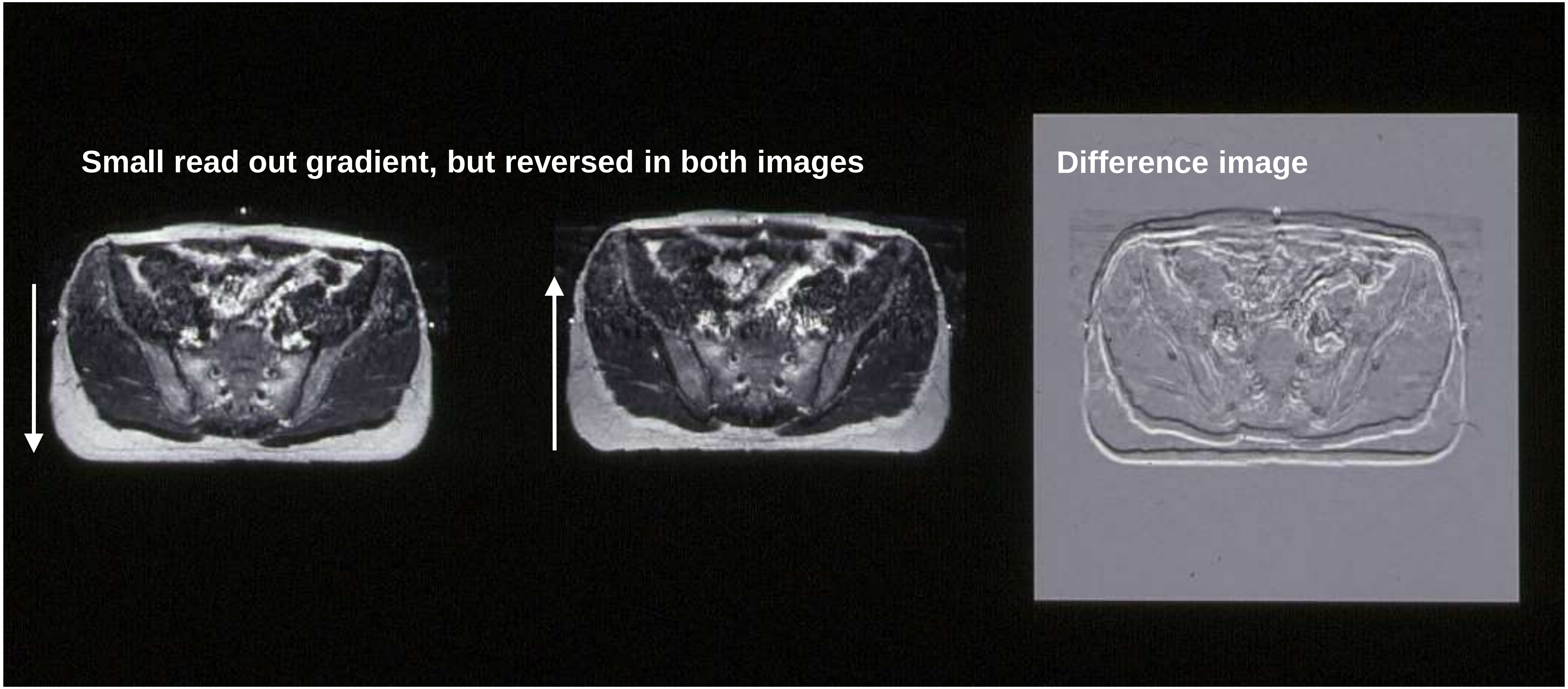


1 mm  pixel size



0.4 mm  pixel size

# MRI artifacts can cause invisible geometrical errors!




What you see is not always what you get

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

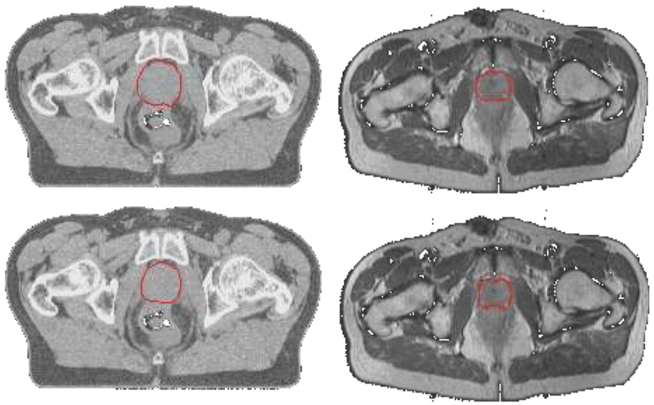
Anything can be deformed in anything else…
But is it true?

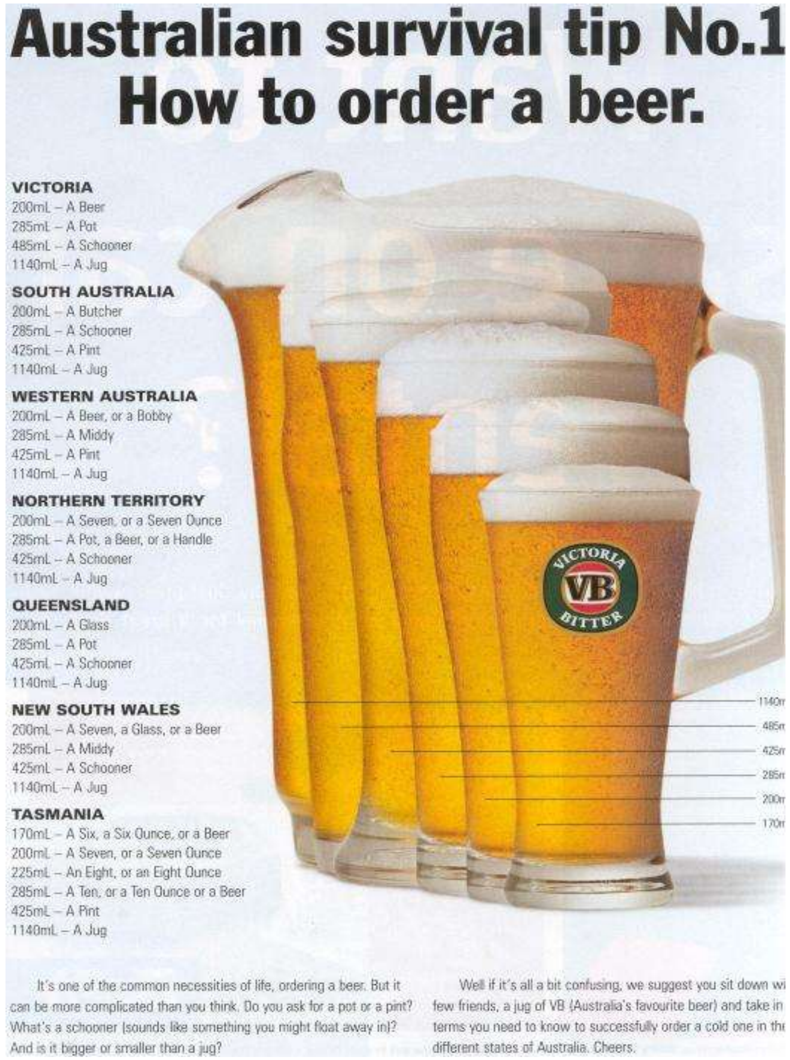
# Why is this so important?

- Purely systematic error source
- Effectively shifts the dose distribution for ALL fractions
- Margin = 2.5 x SD of the errors
- E.g. 4 mm SD → 1 cm margin!

# How to analyze?

- Volumes?



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# How to analyze: Volumes?

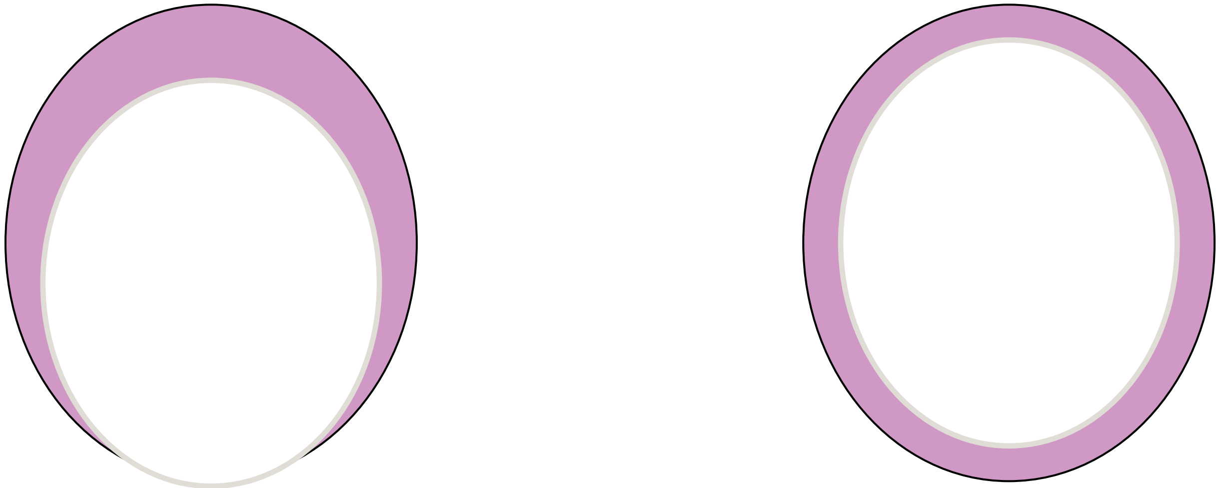
- Volumes?
- Often used: DICE index

- DICE Index = $\frac{2 * \text{common volume}}{\text{Volume 1} + \text{Volume 2}}$

- No common volume: Index = 0
- Volumes identical: Index = 1

# How to analyze: Volumes?

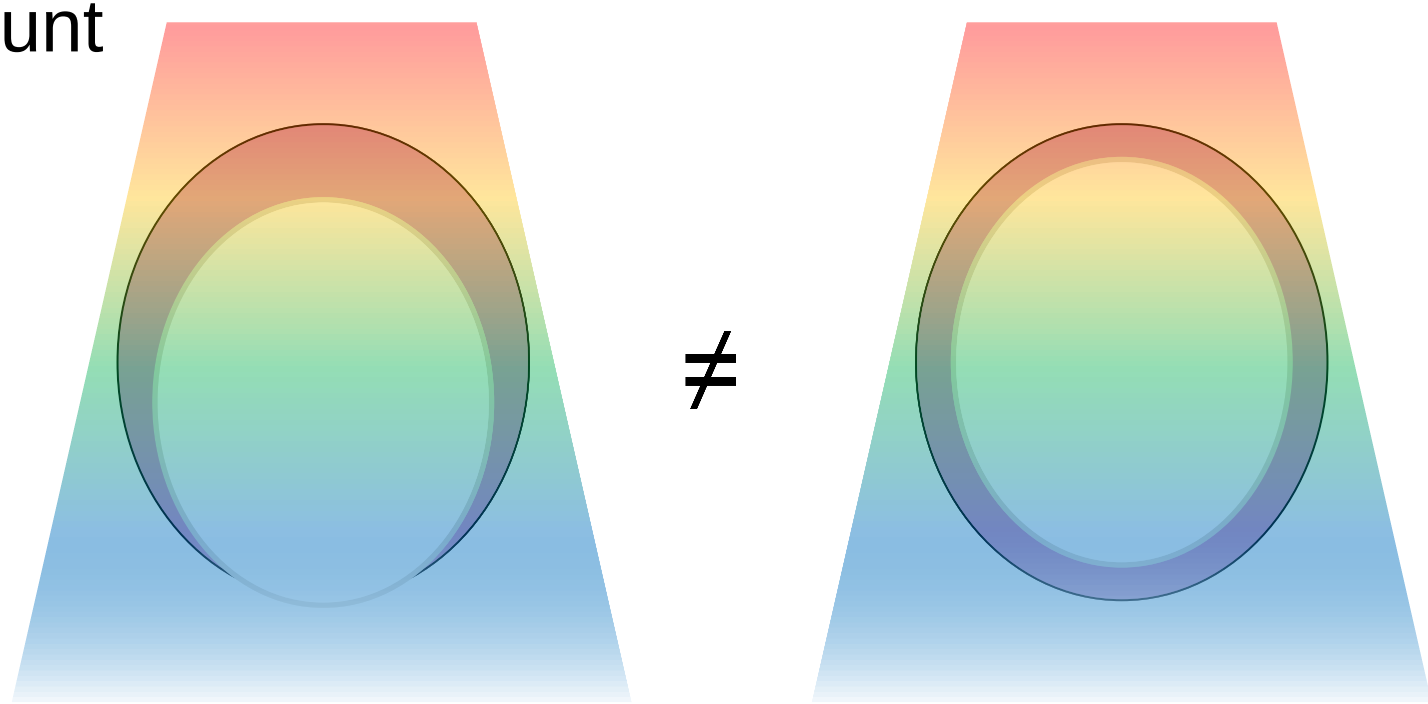
- Problem: Left and right have the same volume difference!
- DICE index the same for both situations
- Clinically this may have a completely different impact



→ DICE is mainly a <u>qualitative</u> comparison tool

# How to analyze?

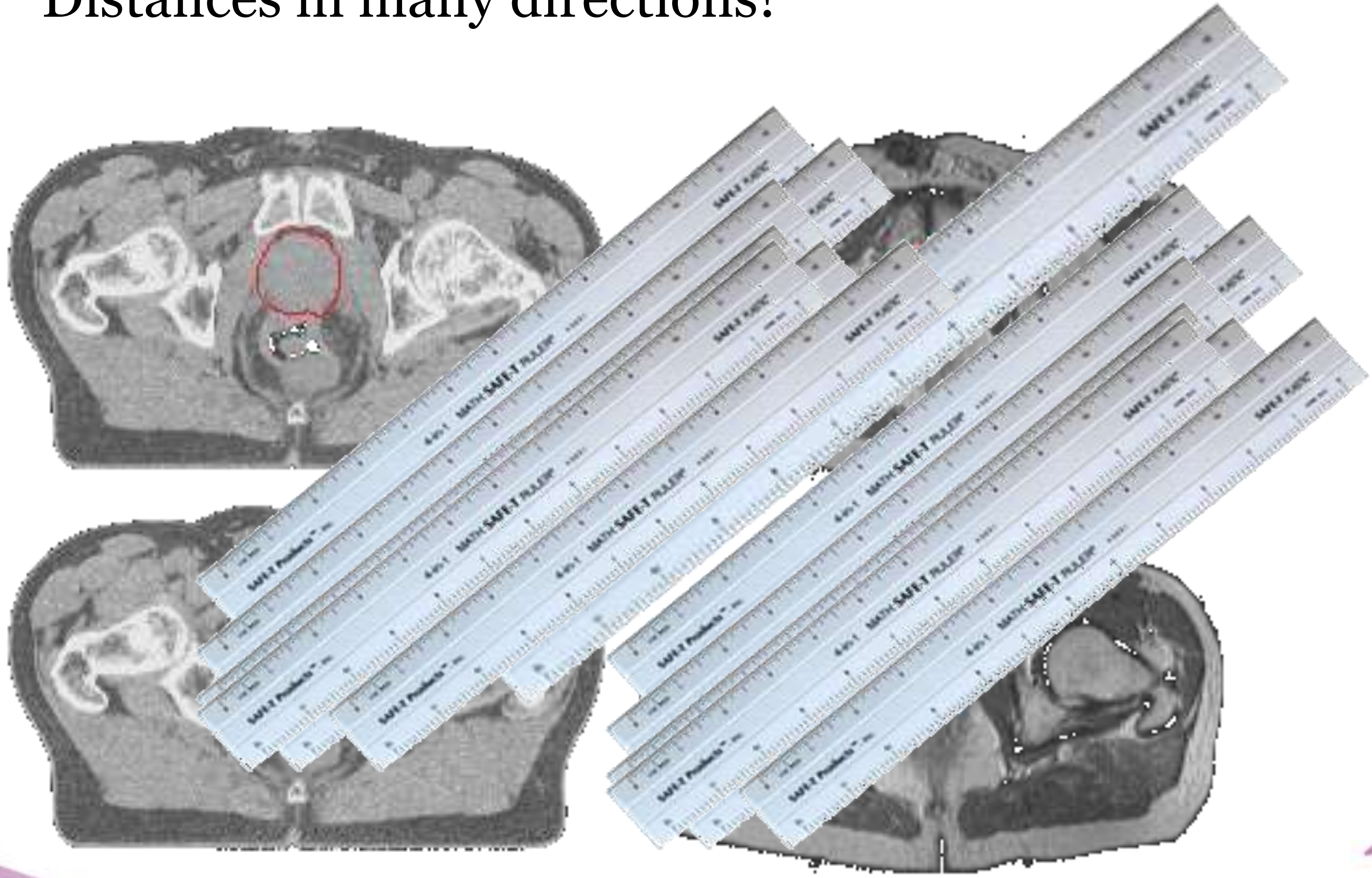
- Dose?
- E.g. evaluate DVHs of different structures
- Better, because spatial information is taken into account



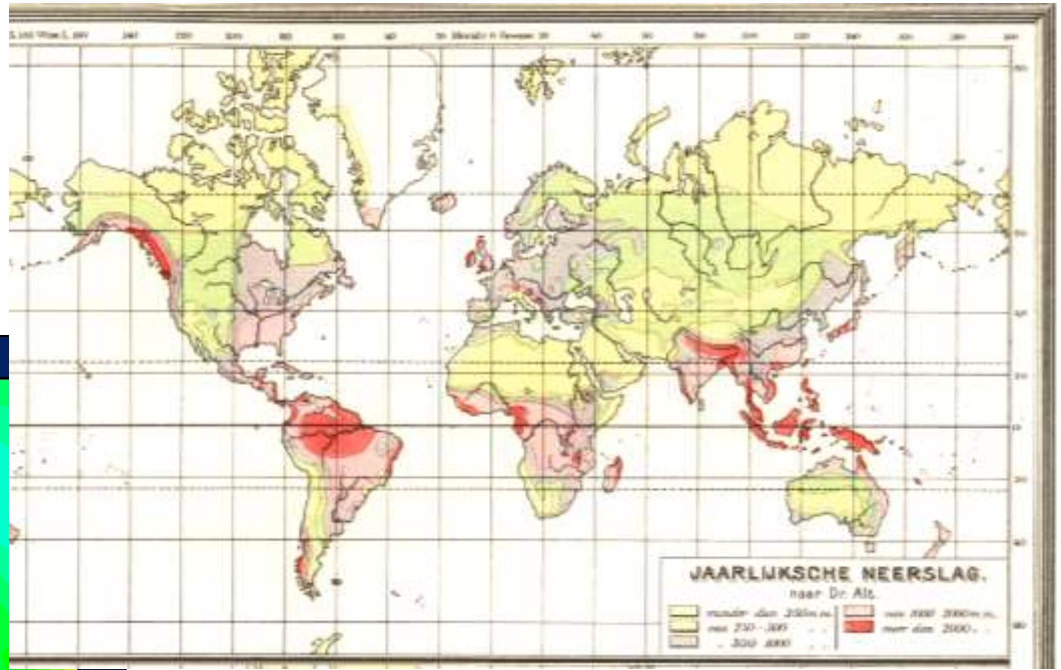

- Still no information on <u>where</u> the difference is

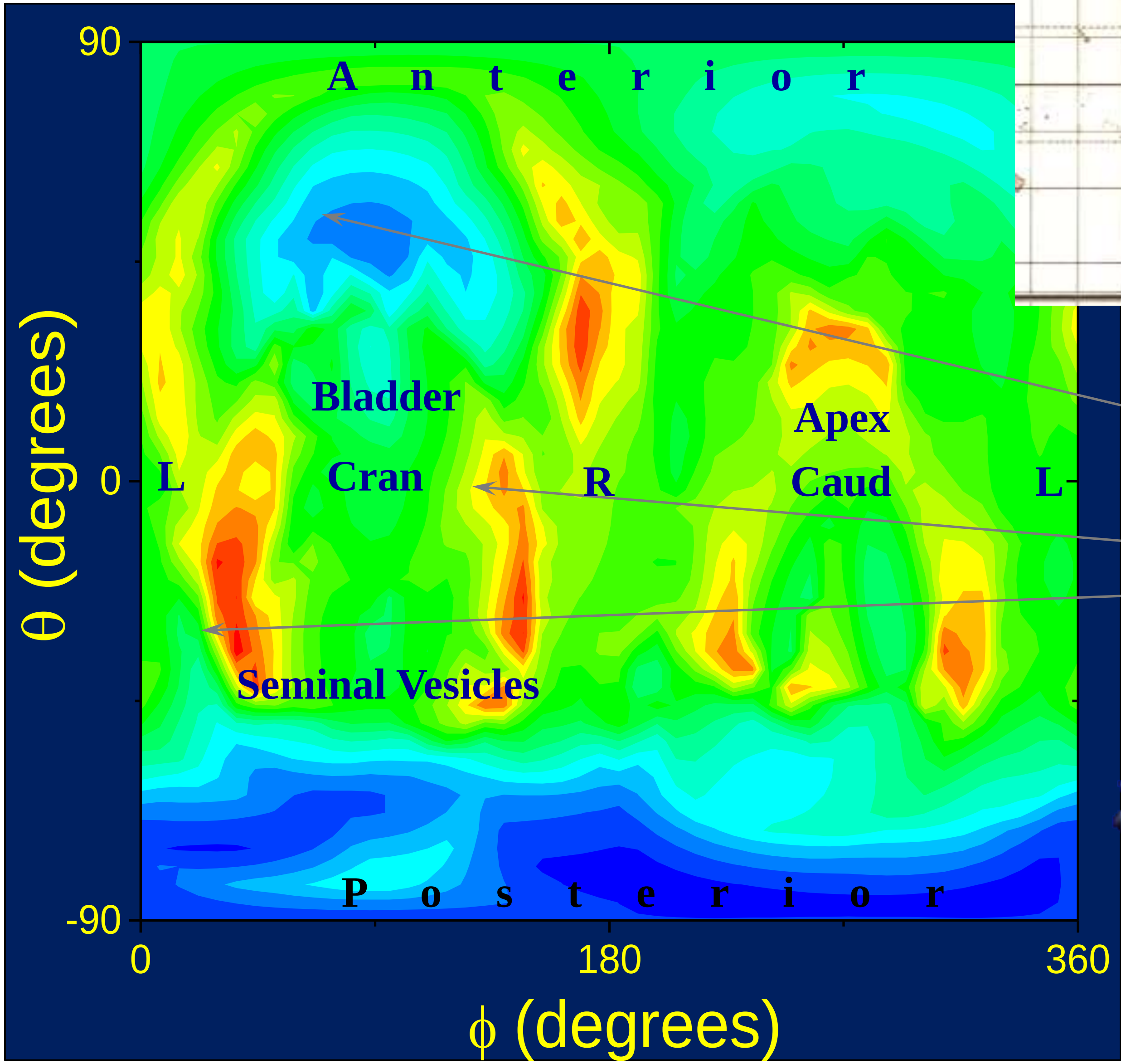
# How to analyze?

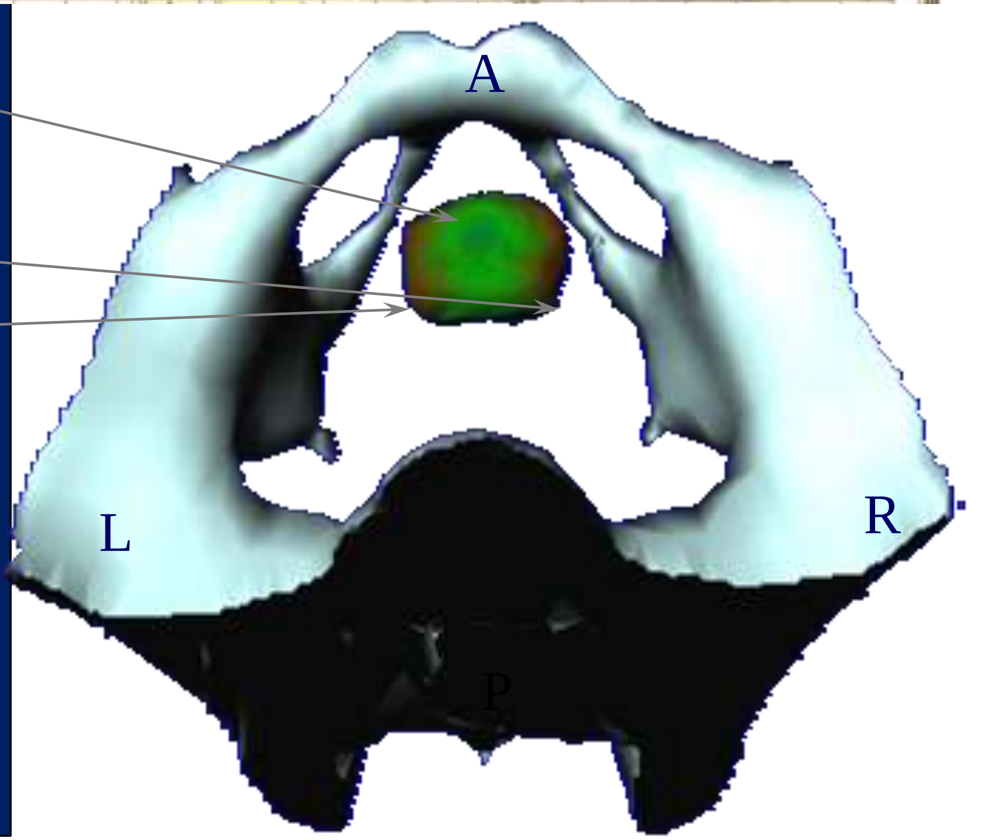
- Volumes?
- Dose?
- Distances in many directions!



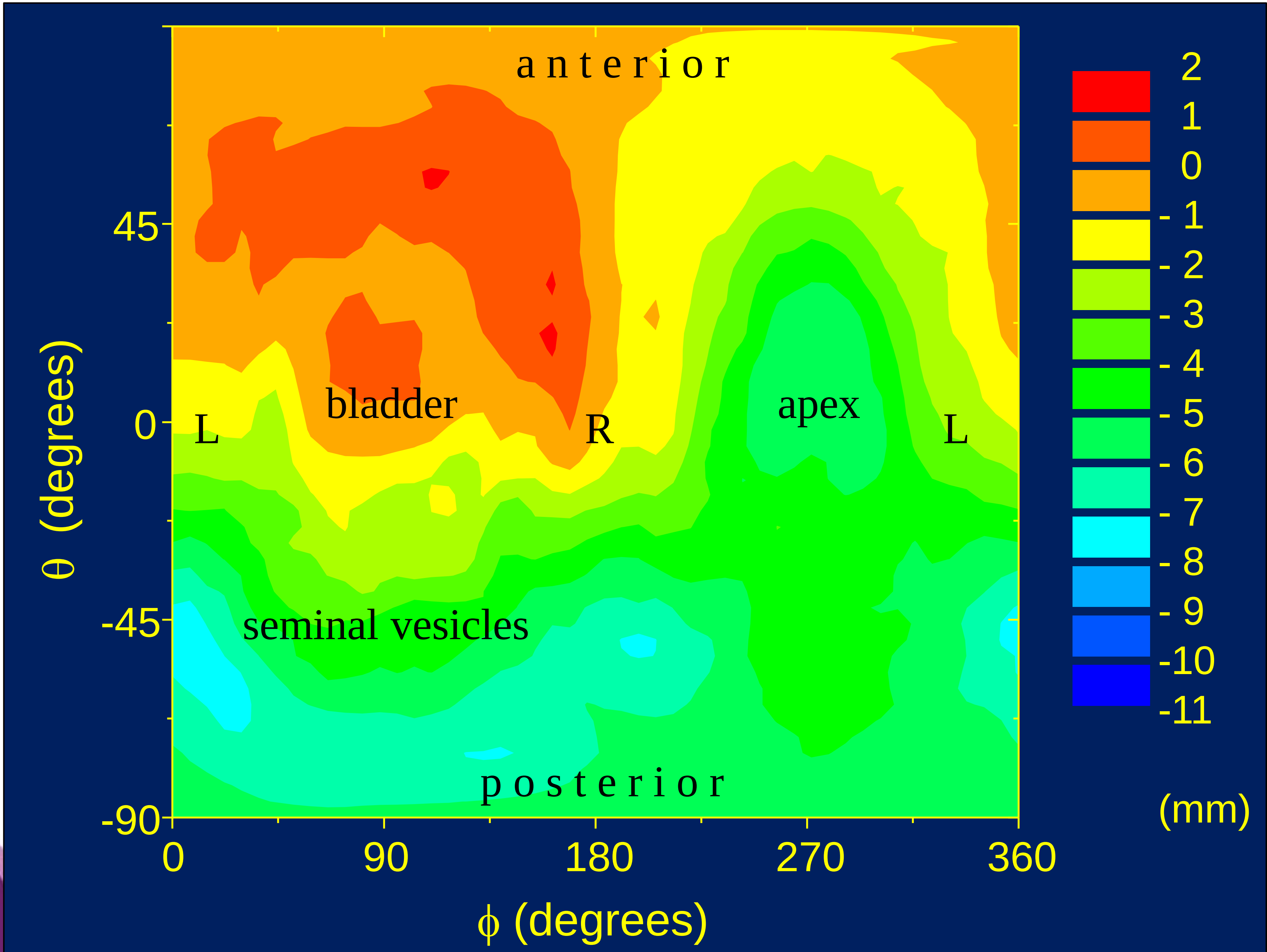
# Distance maps



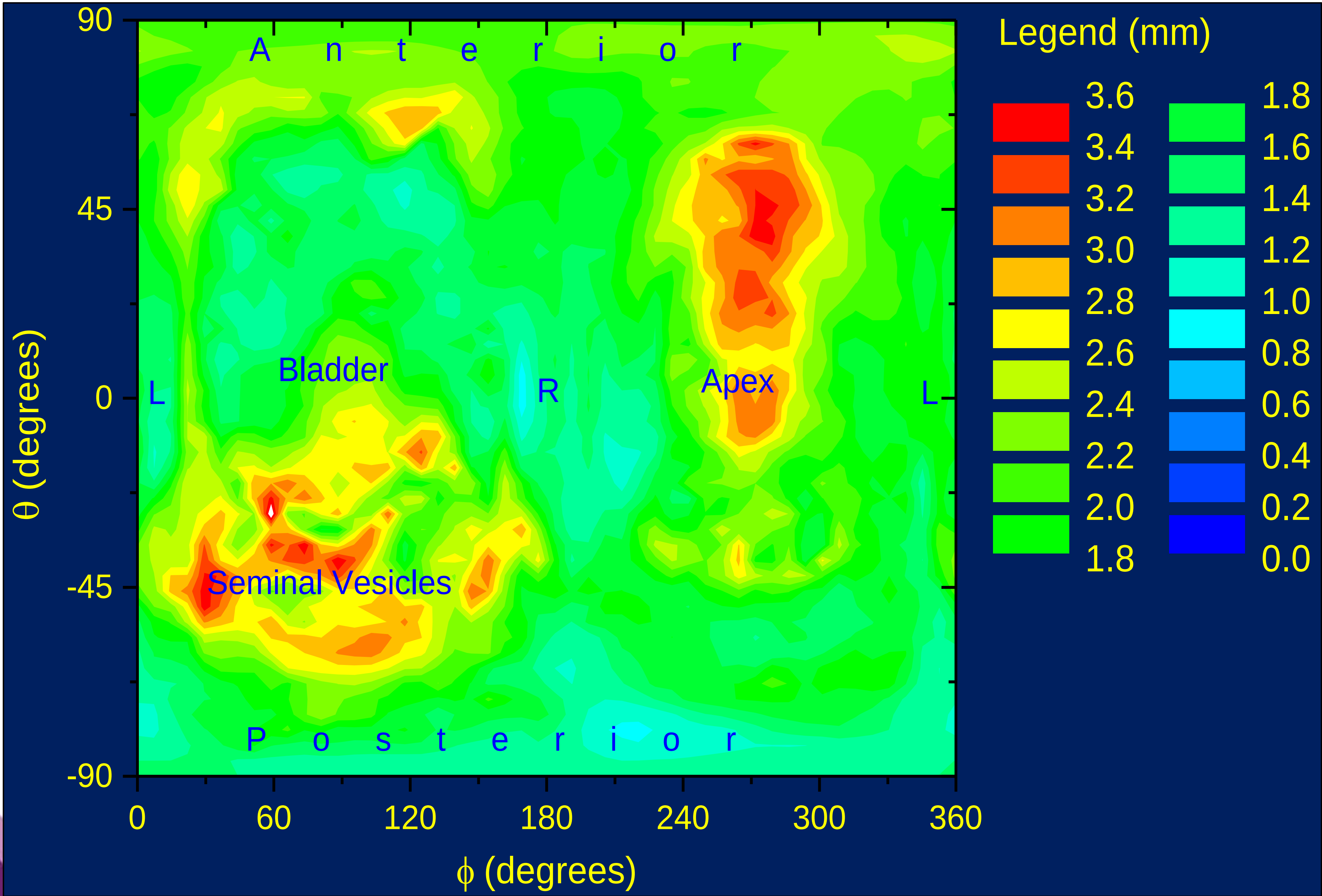



# Systematic modality difference (axial MRI - CT)



# Overall observer variation in CT (SD)

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# What next?

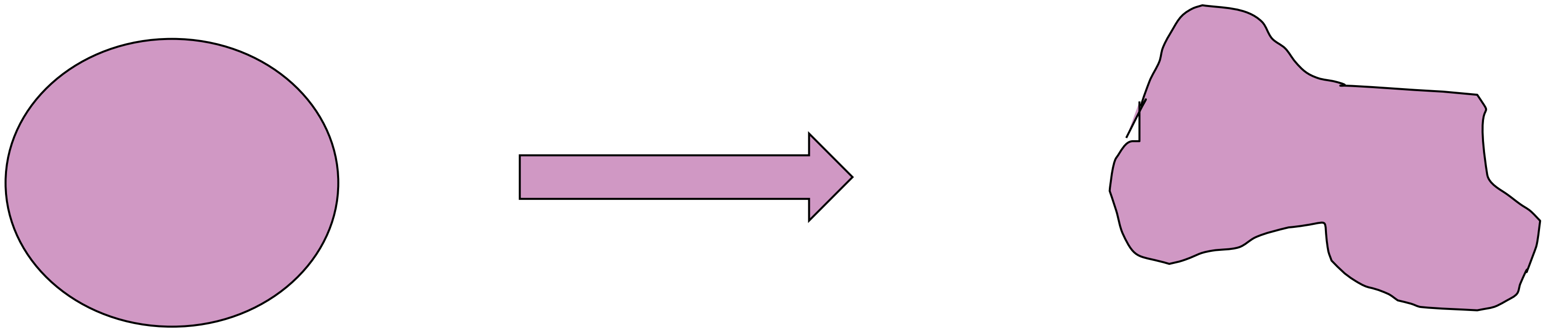
- Improve delineation uncertainty by
  - ➢ Inclusion of more modalities – Quantify improvements
  - ➢ Clear protocols

- To quantify improvements → Extend model to measure more complex structures

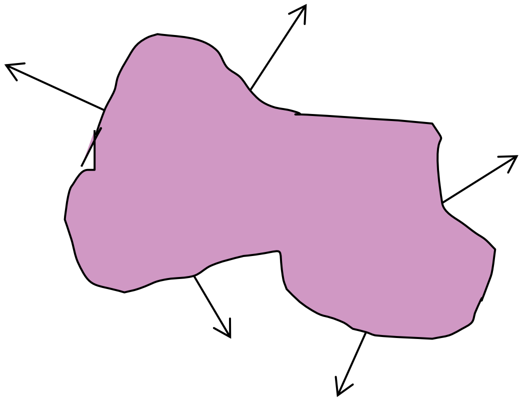
- To determine protocols → See <u>how</u> the doctors are delineating

# What next?

- Measure complex structures



- Measure normal to the surface instead of using polar coordinates (=measurement from one central point)

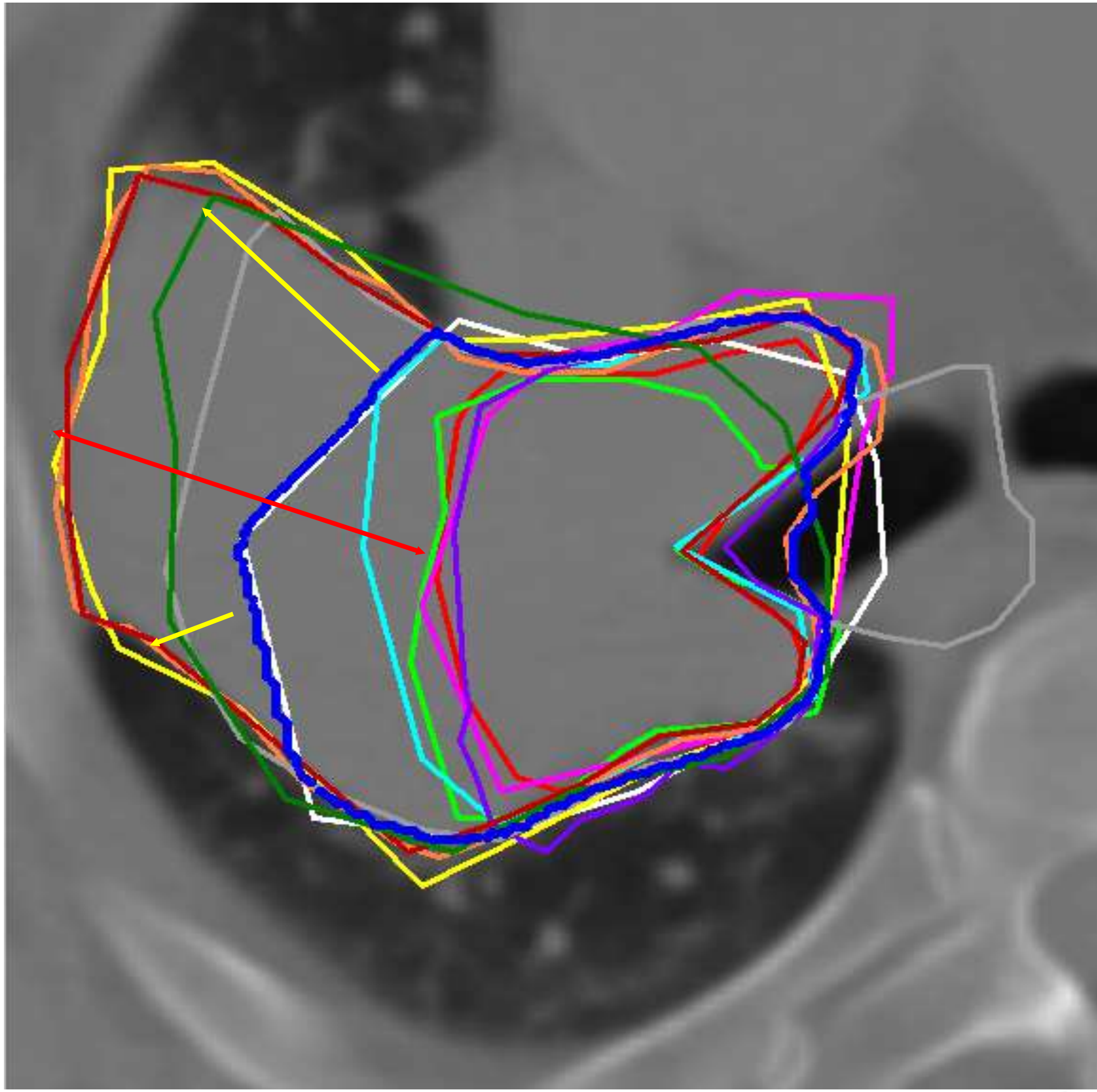


# Geometrical analysis in 3-D

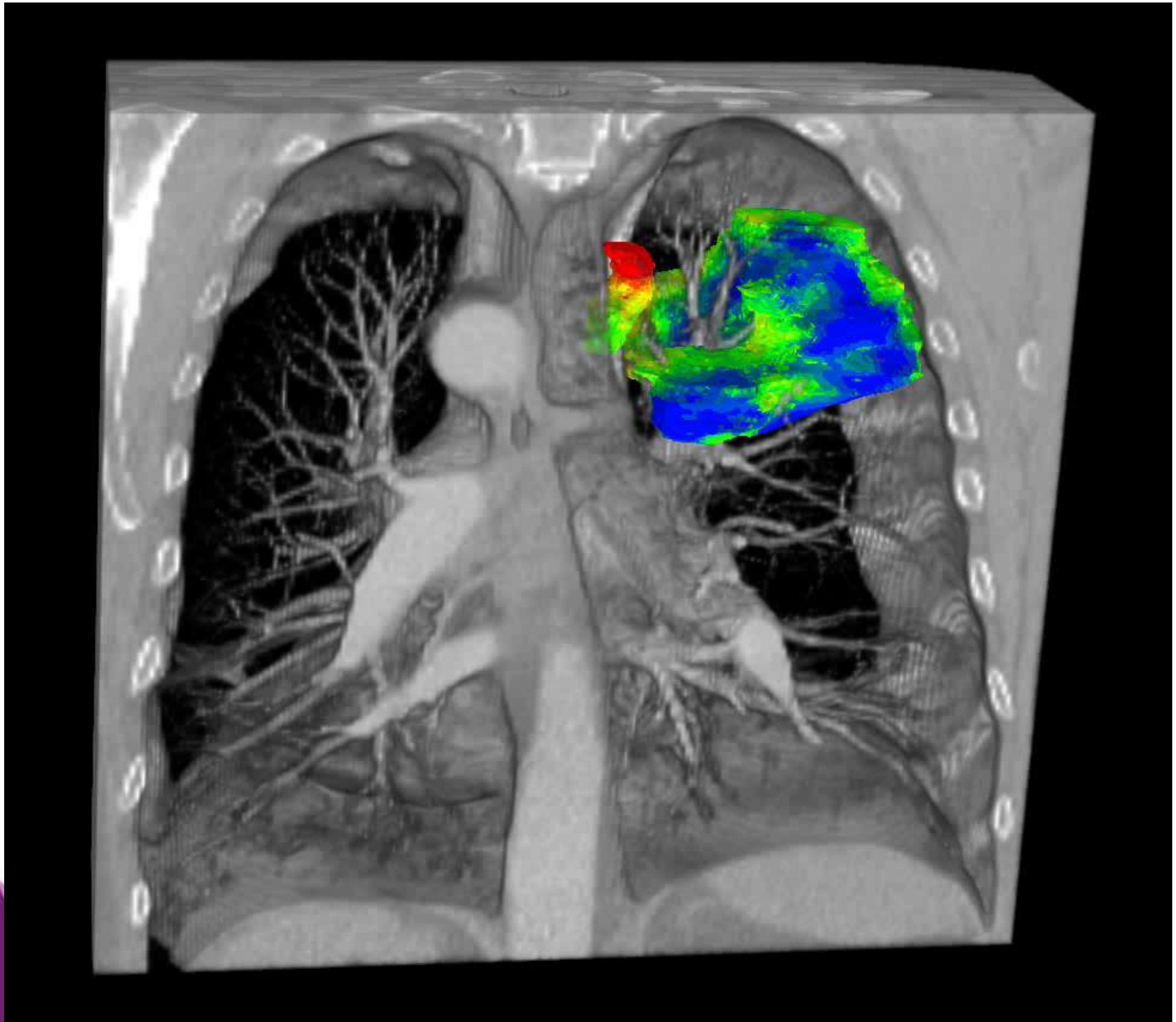
Median Surface

Distance measured

Local SD



# Geometrical analysis in 3-D



LOCAL SD (mm)

0 – 1
1 – 2
2 – 3
3 – 4
4 – 5
5 – 6
6 – 7
7 – 8
8 – 9
9 – 10
10 – 11
11 – 12
12 – 13
13 – 14
14 – 15
> 15

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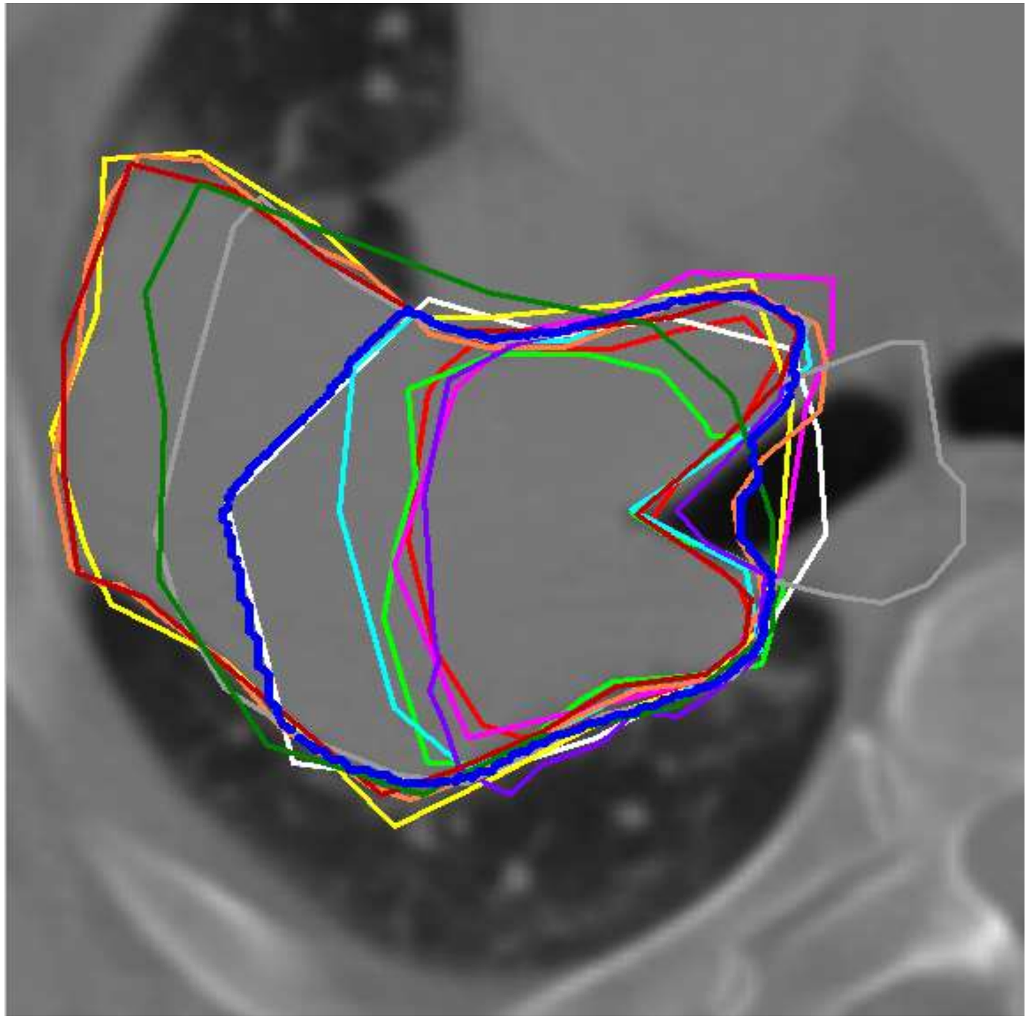
# What are the doctors doing?



Big brother… ☻

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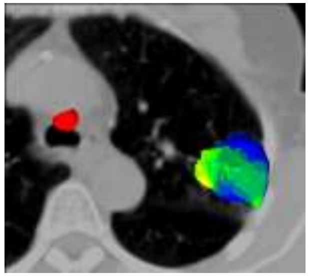
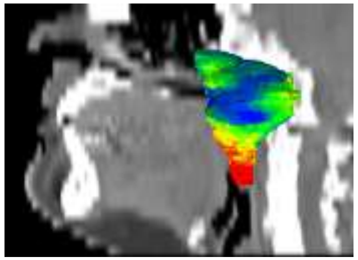
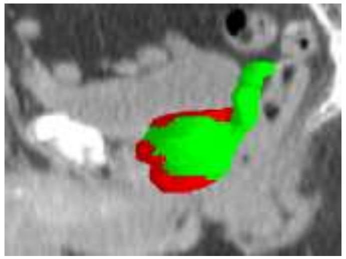
# Target volume delineation

More sites were investigated

- Lung  11 radiation oncologists
- H&N  10 radiation oncologists
- Prostate  13 radiation oncologists

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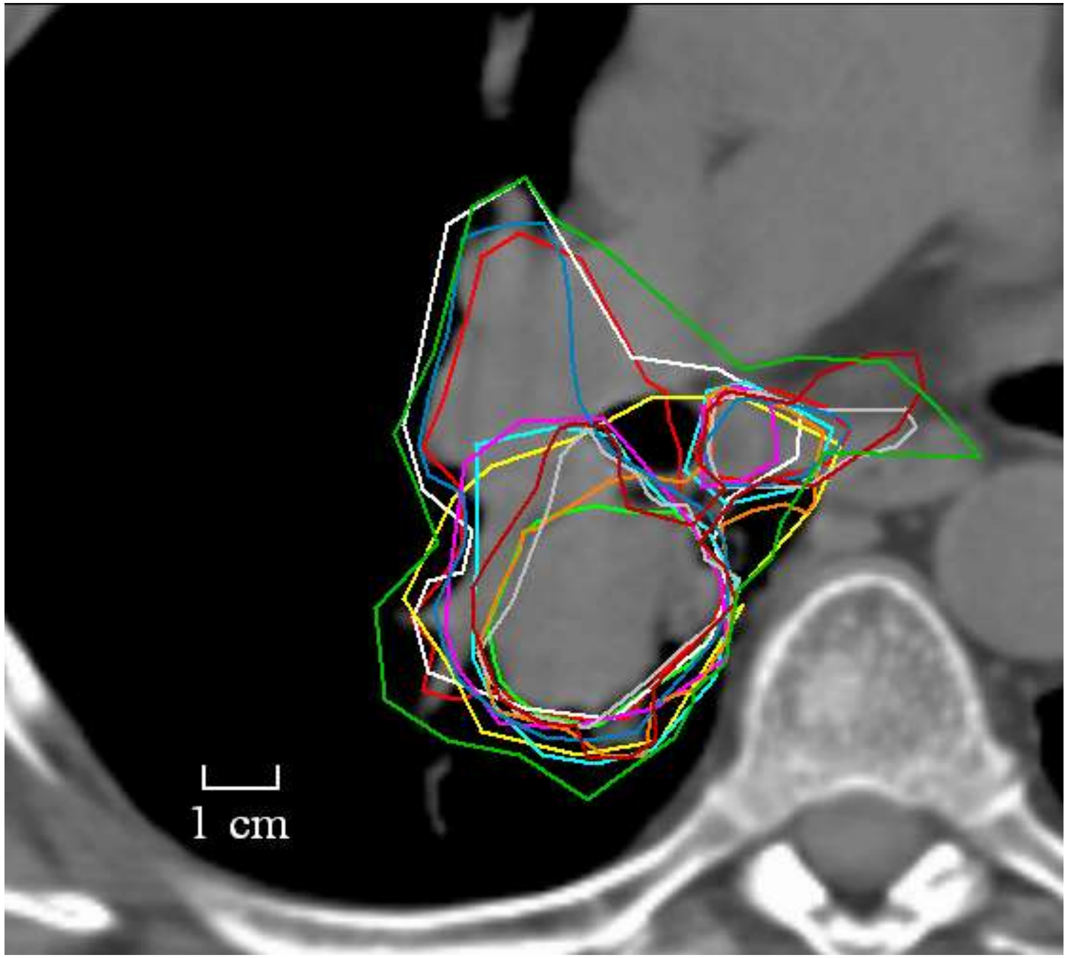
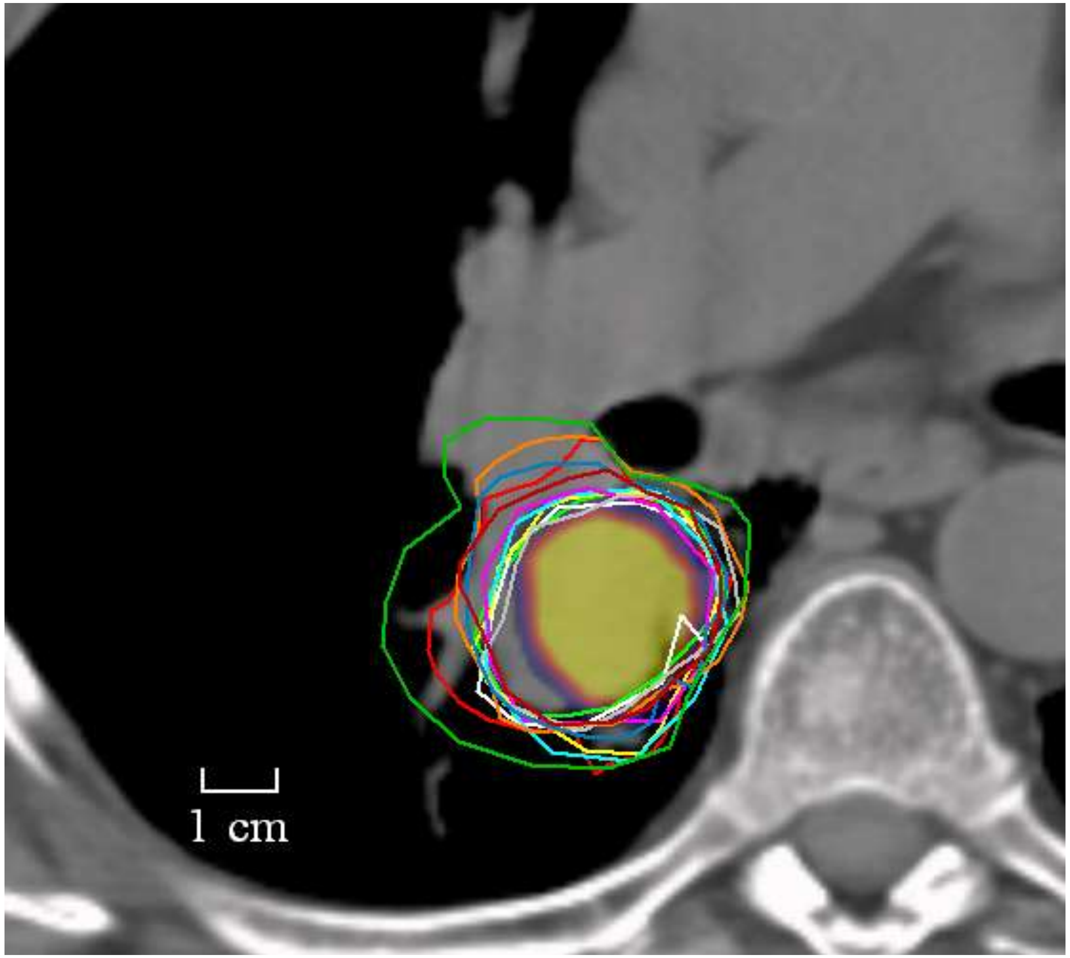
Some examples......

# Lung




CT

SD 10.2 mm




CT + PET

SD 4.2 mm

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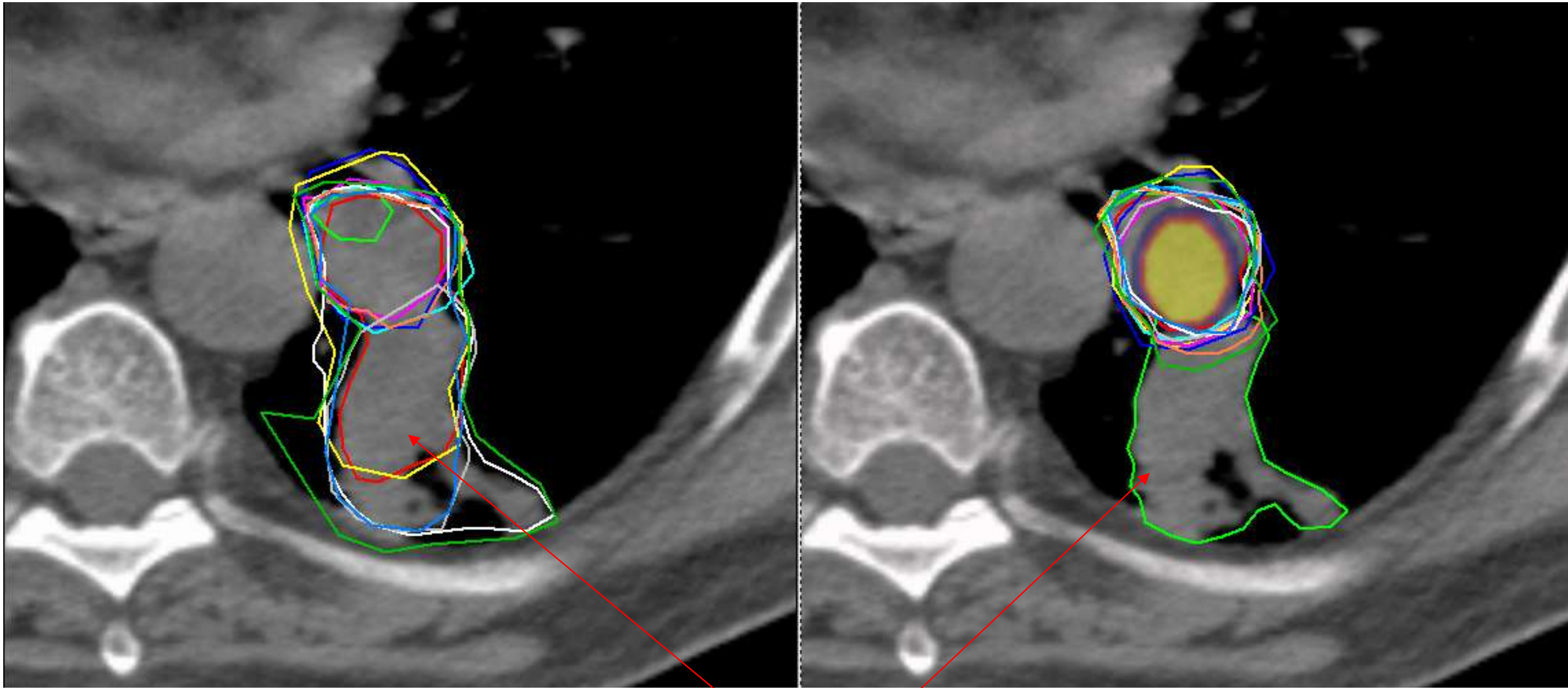
# Lung



CT

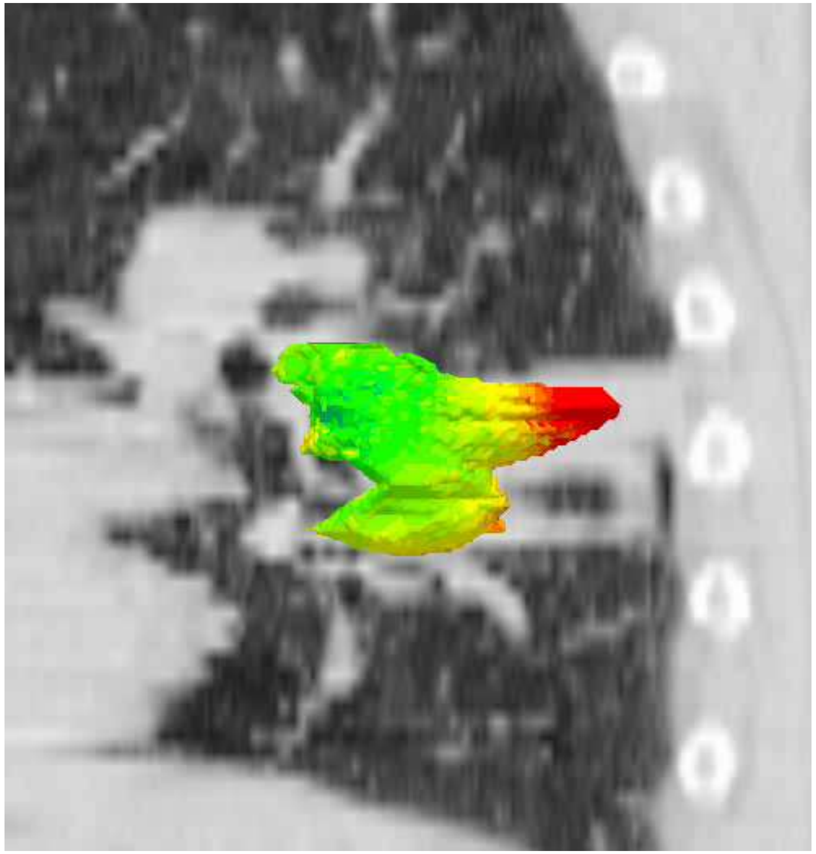
SD 10.9 mm

Atelectasis?

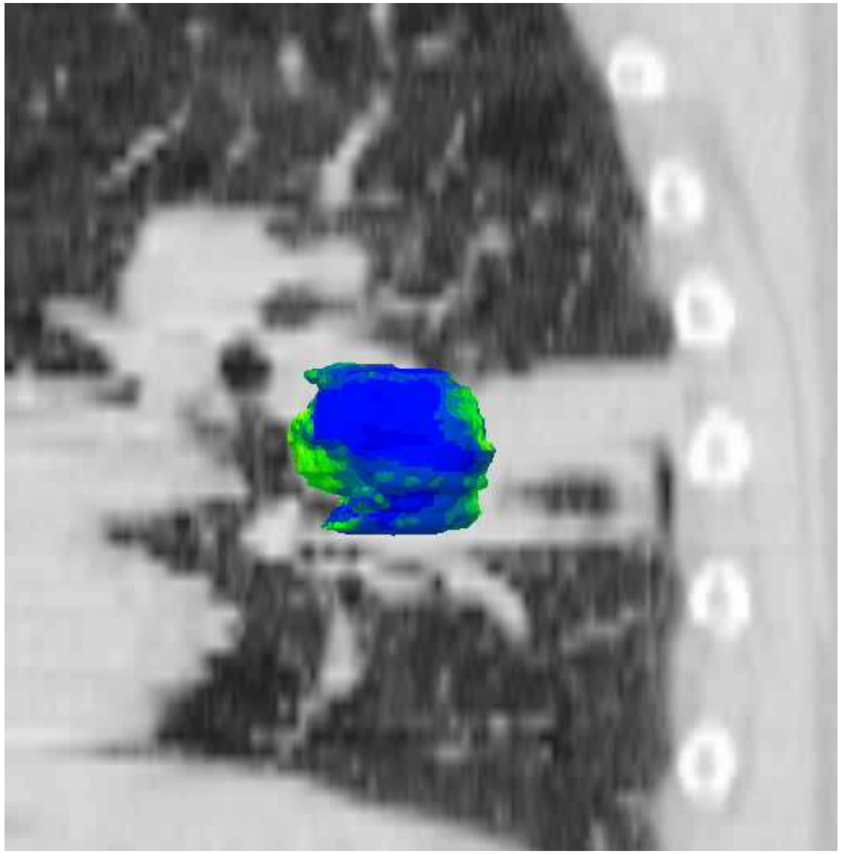
CT+PET

SD 3.5 mm

# Lung



CT



CT + PET

| LOCAL SD (mm) | | | | |
| --- | --- | --- | --- | --- |
| | 0 – 1 | 4 – 5 | 8 – 9 | 12 – 13 |
| | 1 – 2 | 5 – 6 | 9 – 10 | 13 – 14 |
| | 2 – 3 | 6 – 7 | 10 – 11 | 14 – 15 |
| | 3 – 4 | 7 – 8 | 11 – 12 | > 15 |

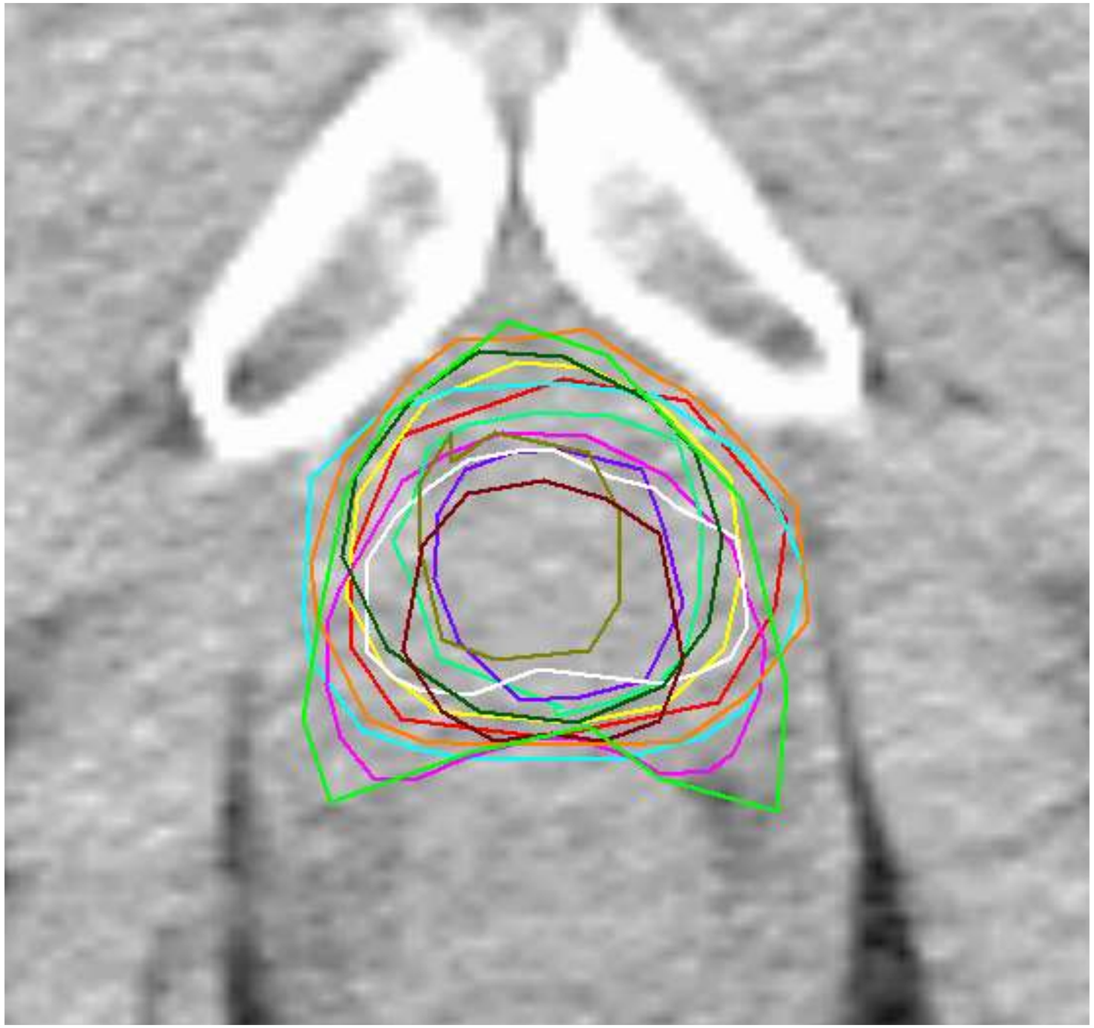
# "Big Brother"

- Mean del. time: CT 16 min; CT-PET 12 min — $p < 0.001$ paired students T-test

- Corrections

| Region | CT (corr / cm²) | CT-PET (corr / cm²) |
|---|---|---|
| Tumor – lung | 4.2 | 3.1 |
| Tumor – chest wall | 5.0 | 3.8 |
| Tumor – mediastinum | 4.1 | 3.4 |
| Lymph nodes | 4.9 | **5.4** |
| Tumor – atelectasis | 2.4 | 1.9 |
| | | |
| Total | **4.0** | **3.2** |
| | | |
| Total # corrections | **9416** | **6144** |

# Prostate case

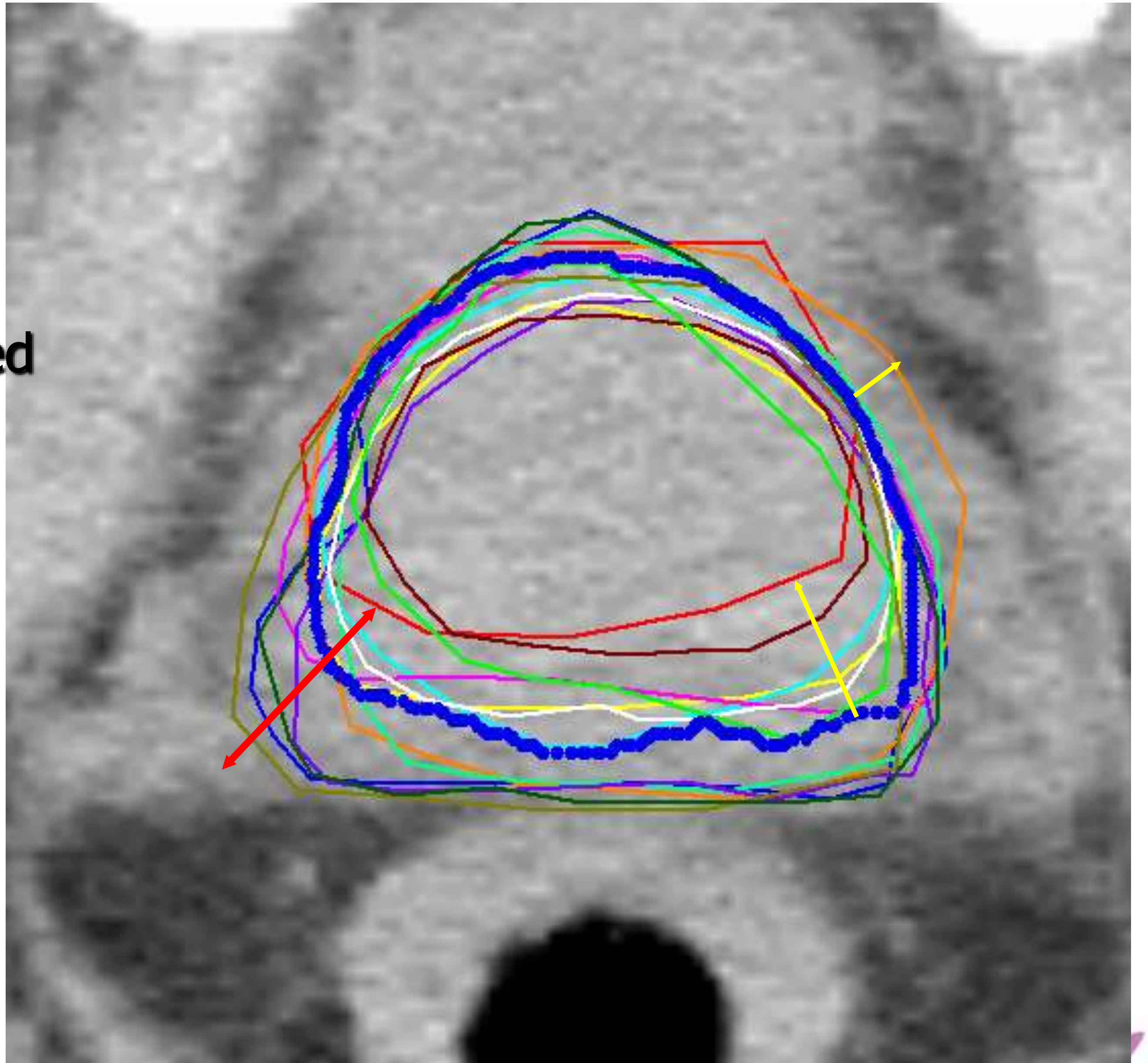


# 3-D median surface with local SD

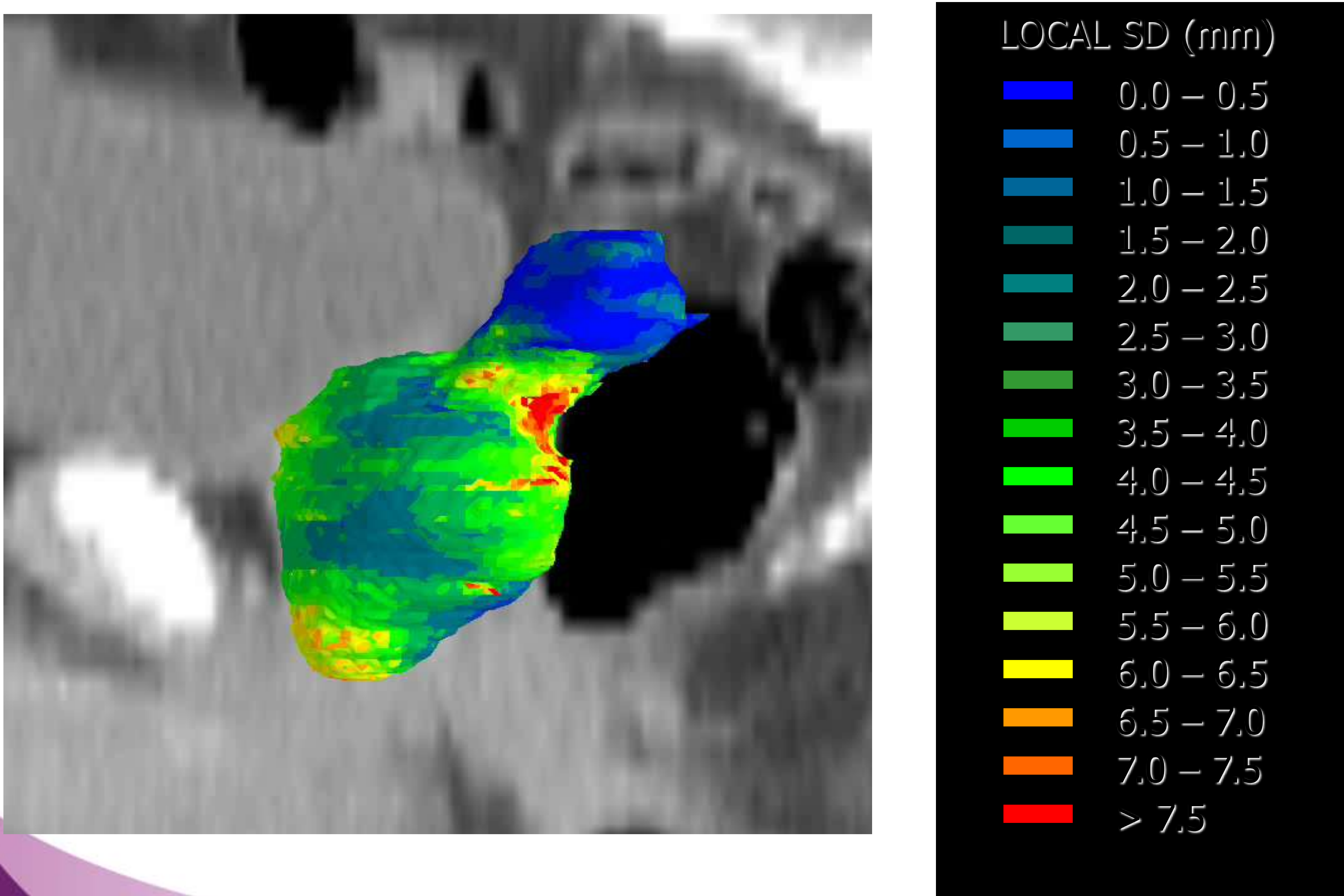
Median Surface

Distance measured

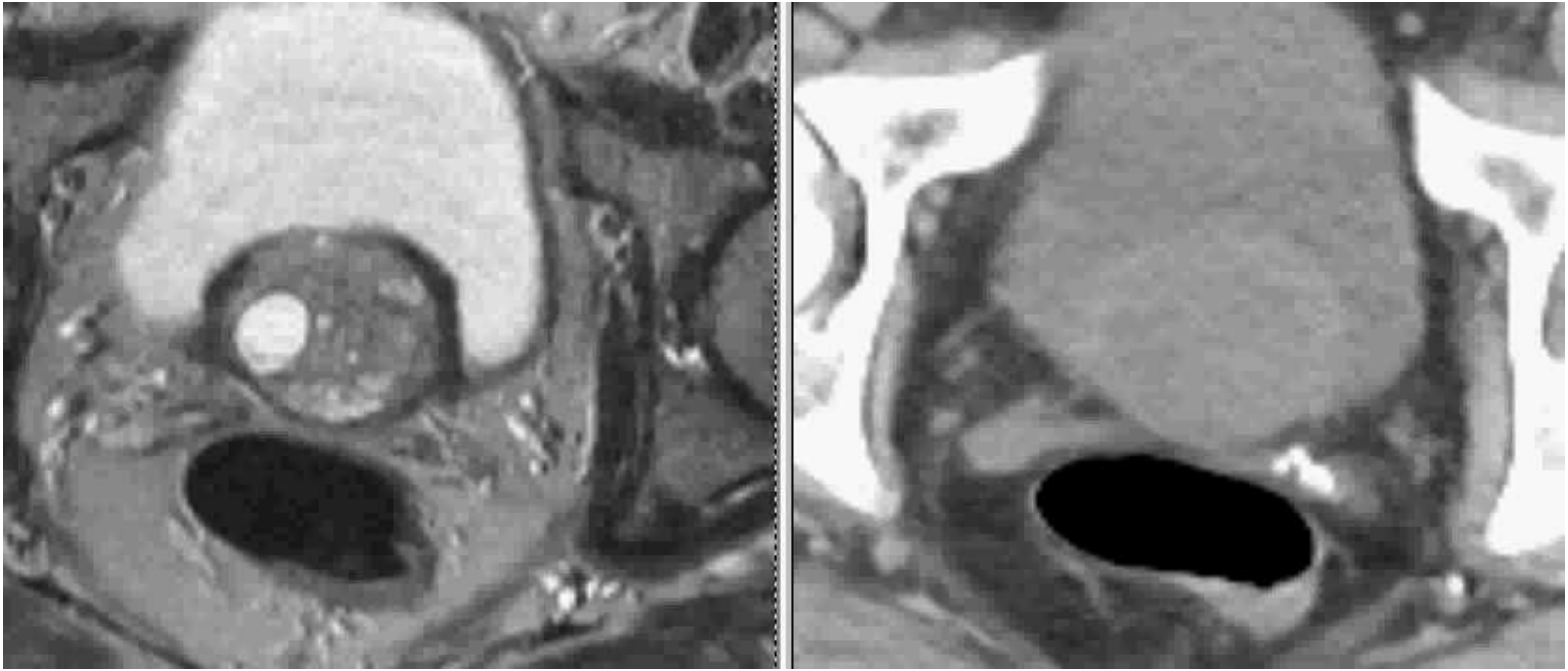
Local SD



# 3-D median surface with local SD

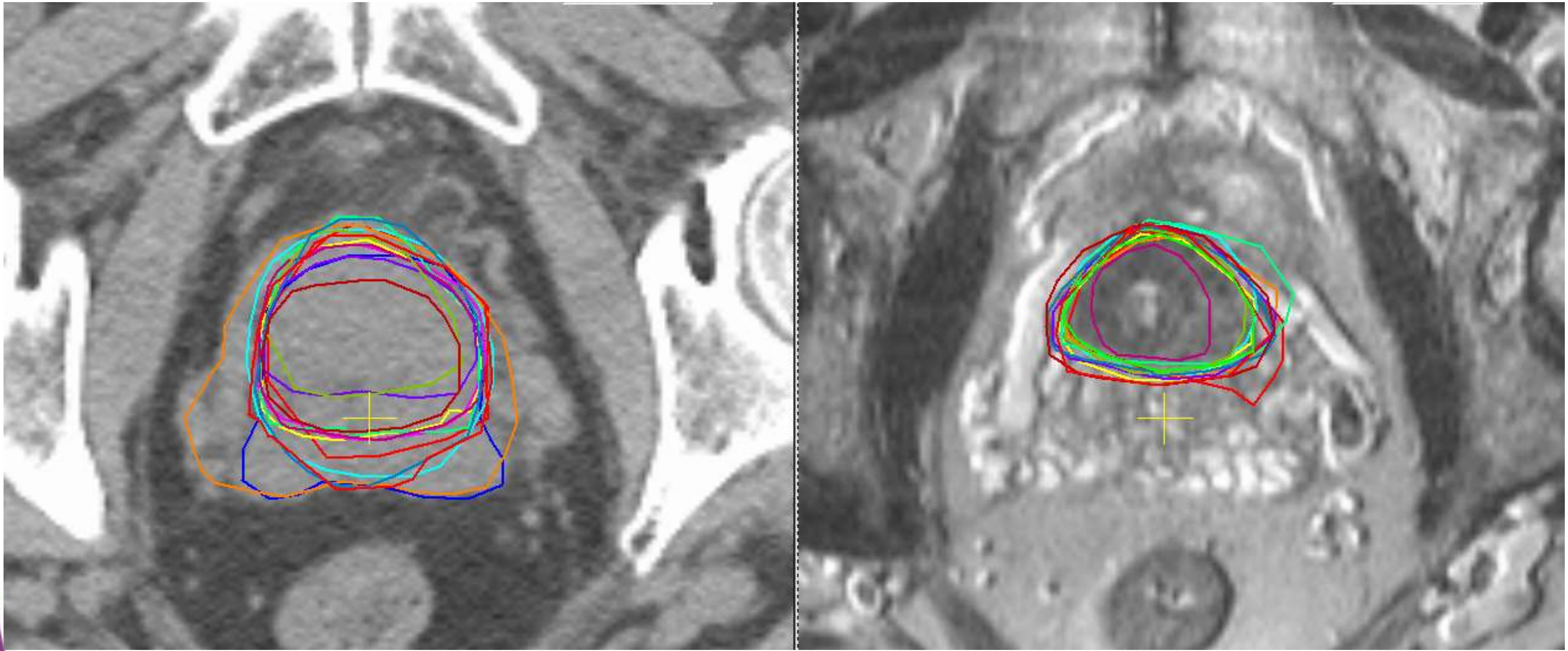


Use diffferent imaging modalities



Matched MRI – CT

# Prostate



CT

SD 3.0 mm

CT + MRI

SD 2.8 mm

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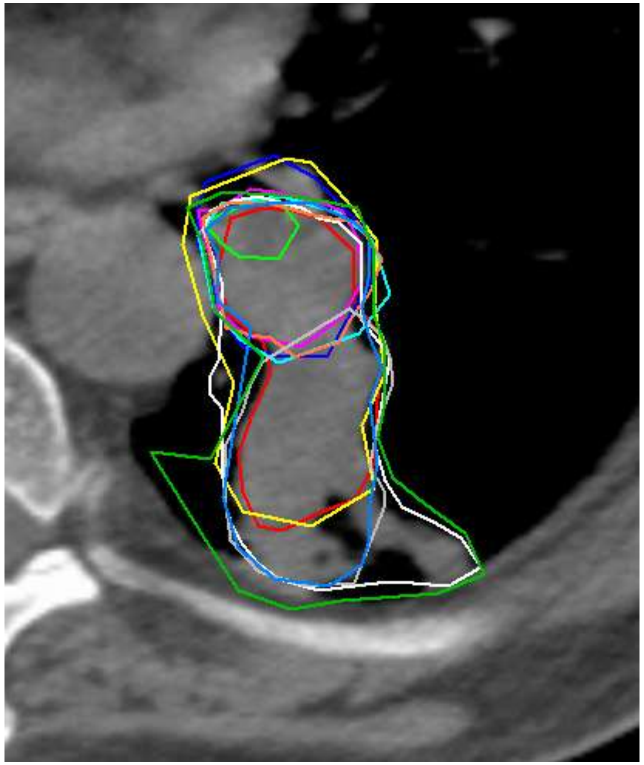
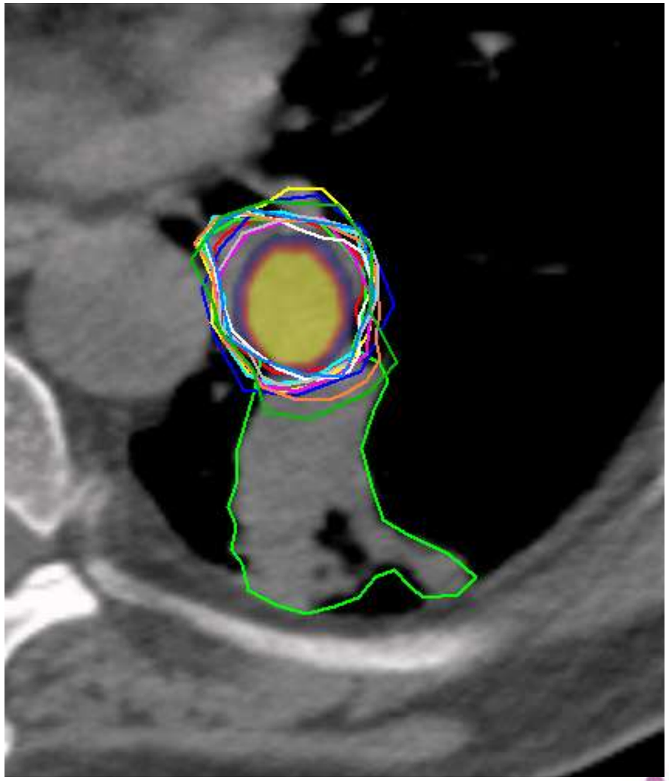
# So do we need margins for delineation uncertainties?

- Yes and no
- If it is genuine uncertainty → Yes
- If it is a protocol related difference → No





# Margins for delineation uncertainties

- But: The standard recipe may not apply….

- Assumes translations only and rigid structures

- Delineations are often biased towards larger volumes
  - Areas with poor tumor definition are included to ensure coverage of the target
  - The better the imaging, the smaller this bias will be

- What is the golden standard?

# Conclusions

- Many factors influence the delineation accuracy
- To quantify, a full 3-D analysis (in cms) is needed
- Benefits of different modalities, protocols can then be validated
- Because it's a systematic deviation, the effect on the treatment is large
- However, incorporation into a margin is not always trivial


DuBouillon

Target Volume Determination

From Imaging to Margins

Barcelona 10-13 April 2016

# GTV and CTV for Rectal Cancer and Anal cancer

**Maria Antonietta Gambacorta**

Radiotherapy Department

Università Cattolica del Sacro Cuore

Rome Italy

# after 2000 randomized trials

| Trial | Pre ERT | Winner |
|---|---|---|
| German trial | Pre RT+ vs Post RT | Pre RT |

| Trial | Short ERT | Winner |
|---|---|---|
| Duch Trial | SC RT+TME vs TME | SC RT |
| MRC C07 | SC RT+TME vs TME | SC RT |

| Trial | Long ERT | Winner |
|---|---|---|
| EORTC 22921 | LC RT vs C-RT | C-RT |
| FFCD 9203 | LC RT vs C-RT | C-RT |
| Scandinavian | LC RT vs C-RT | C-RT |

| Trial | Short vs Long | Winner |
|---|---|---|
| Polish Trial | SC RT vs C-RT | = |
| TROG Trial | SC RT vs C-RT | C-RT |

# after 2000 randomized trials

Trial | Short ERT | Winner

# SURVIVAL

no improvement

Duch Trial — SC RT+T

MRC CR07 — SC RT+T

# Local control

improvement

Trial | Long ERT | Winner

# Acute Toxicity

increased

EORTC 22921 — LC RT vs C-RT — C-RT

FFCD 9203 — LC RT vs C-RT — C-RT

Polish Trial — SC RT vs C-RT — =

TROG Trial

Scandinavian — LC RT vs C-RT — C-RT

# CTV: what to include

1. GTV
2. MESORECTM and PRESACRAL SPACE
3. LATERAL NODES
4. Sphincter Complex & Inguinal Nodes

# CTV in rectal cancer

**Surgery targets**

**Tumor (GTV)**

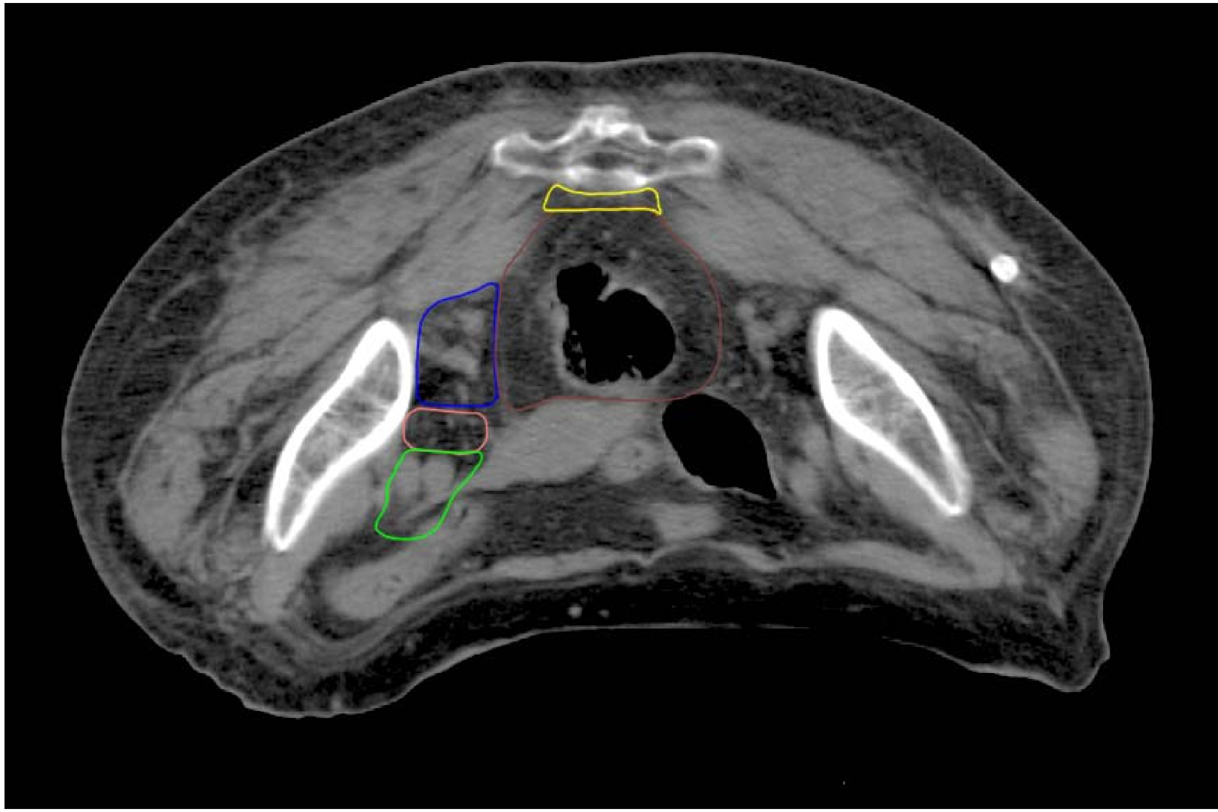
**Mesorectum**

**Not surgery targets**

**Mesorectal fascia**

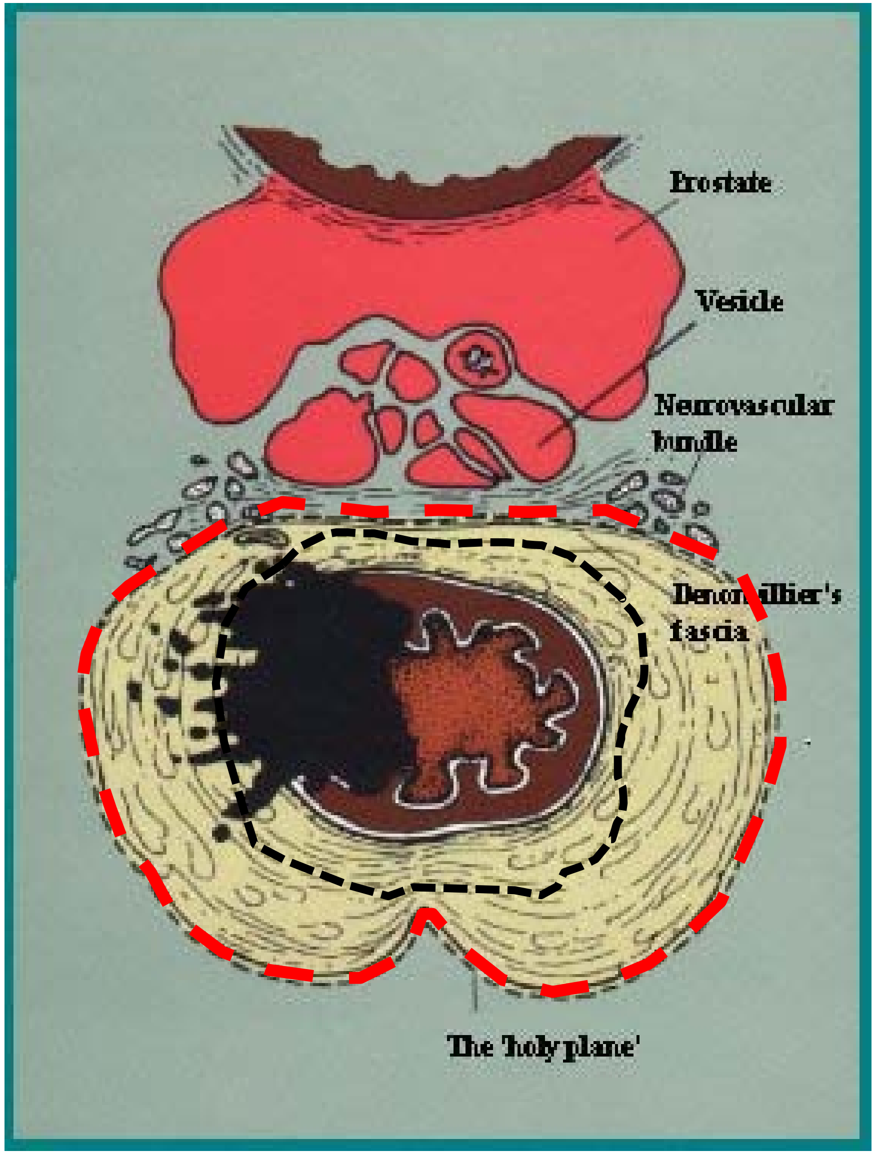
**Presacral region**

**Lateral lymphnodes**



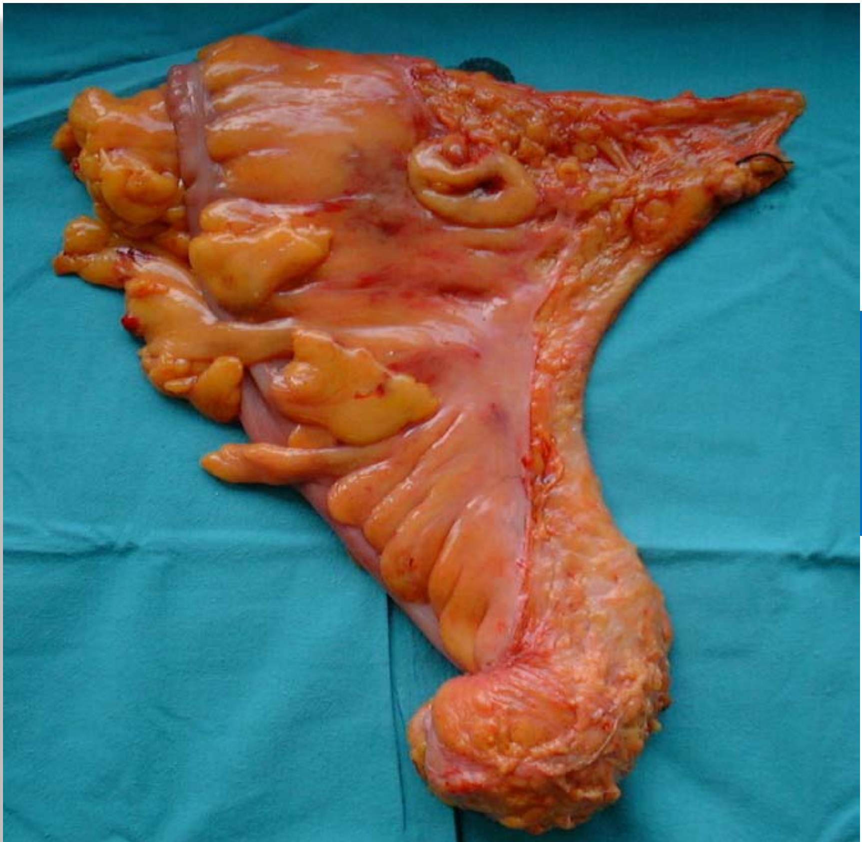
# TME clinical target

**"…en bloc removal of the rectum together with the mesorectal fat column"**



# TME clinical target

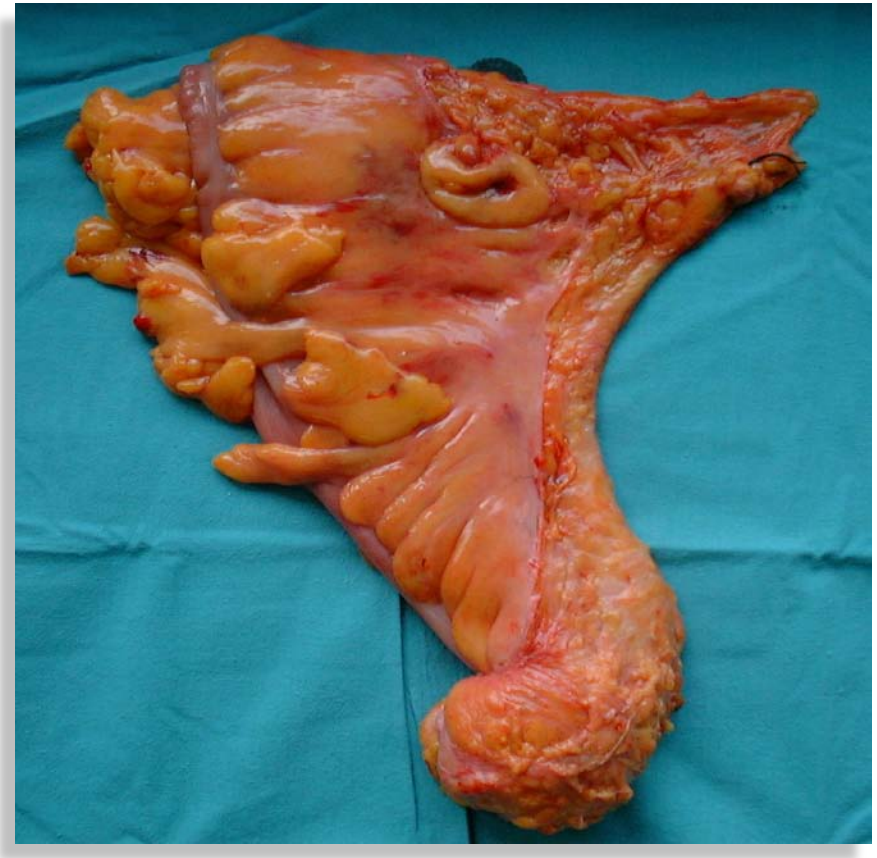
**removed**



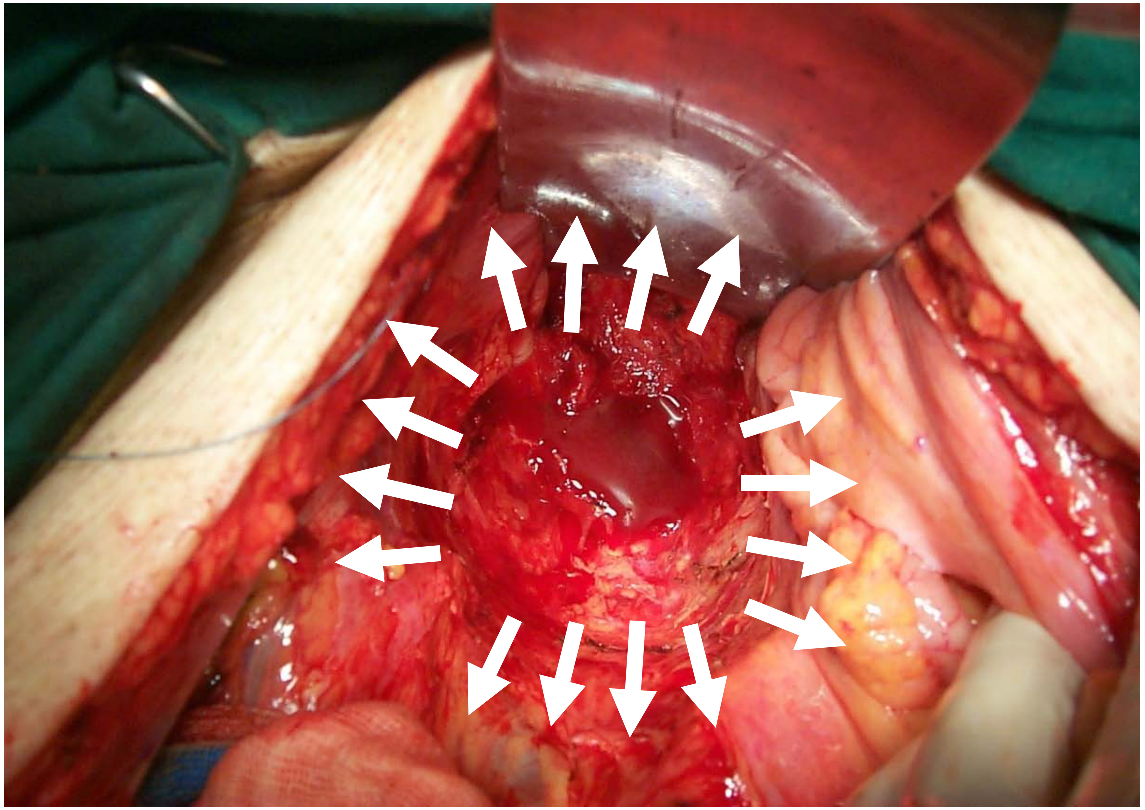
- **TUMOR: GTV**
- **MESORECTUM: Nodes**

# TME clinical target

**removed**

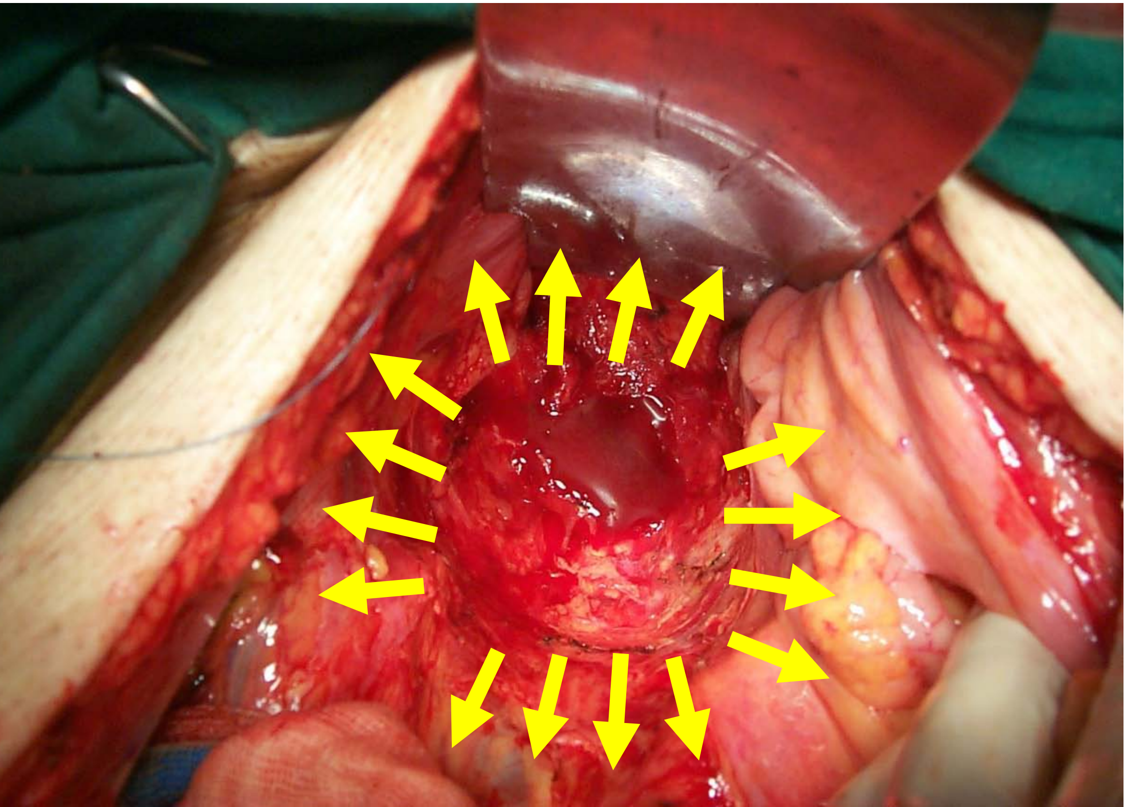


**left**



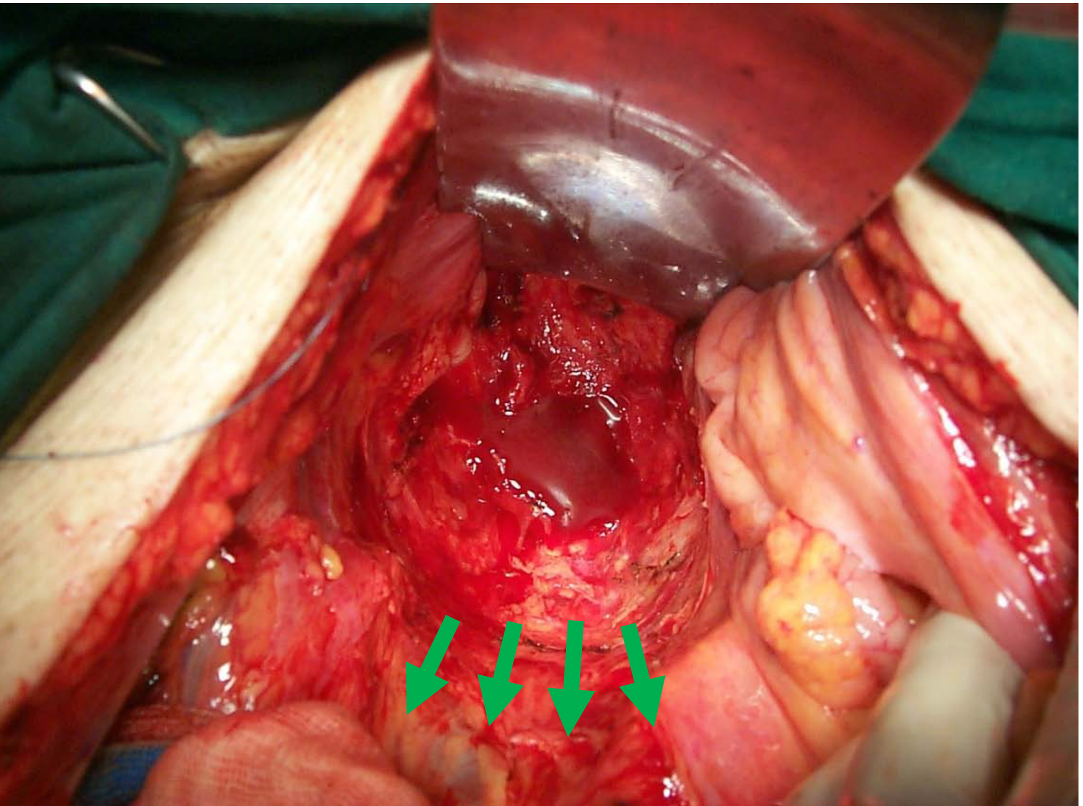
# Not surgical targets

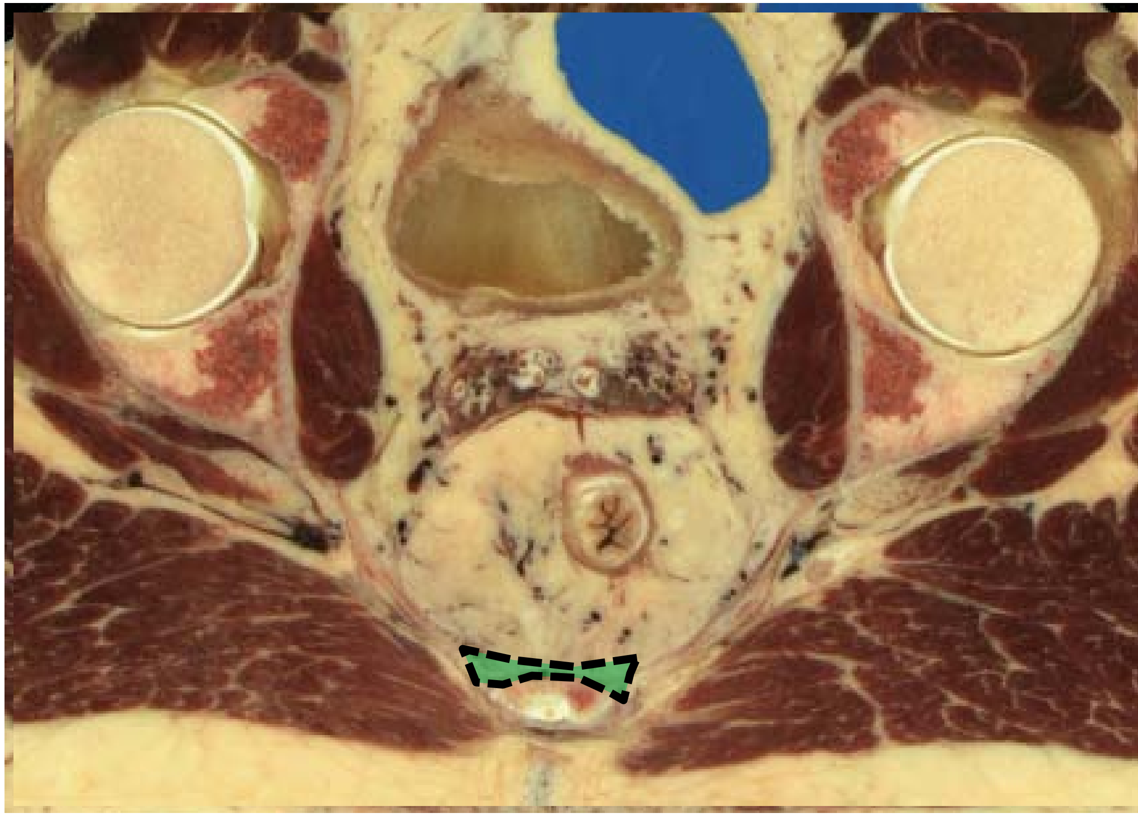
## Mesorectal fascia



# Not surgical targets

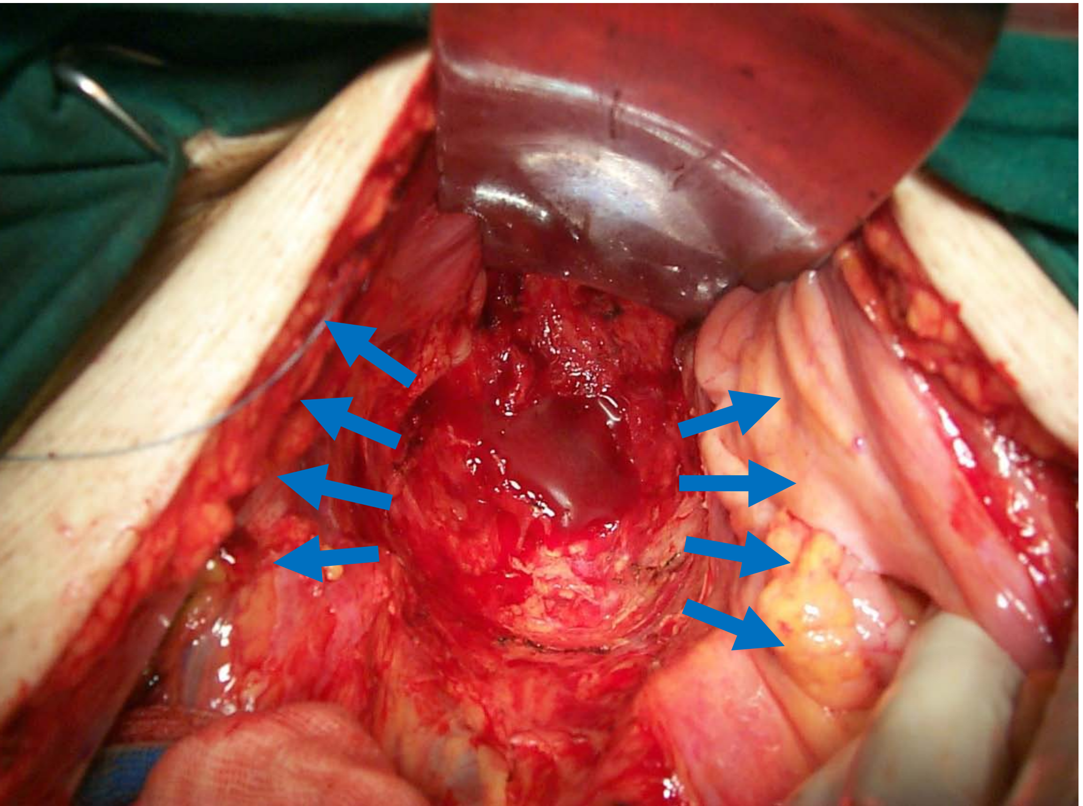
## Presacral Space





# Not surgical targets

## Lateral Spaces Nodes

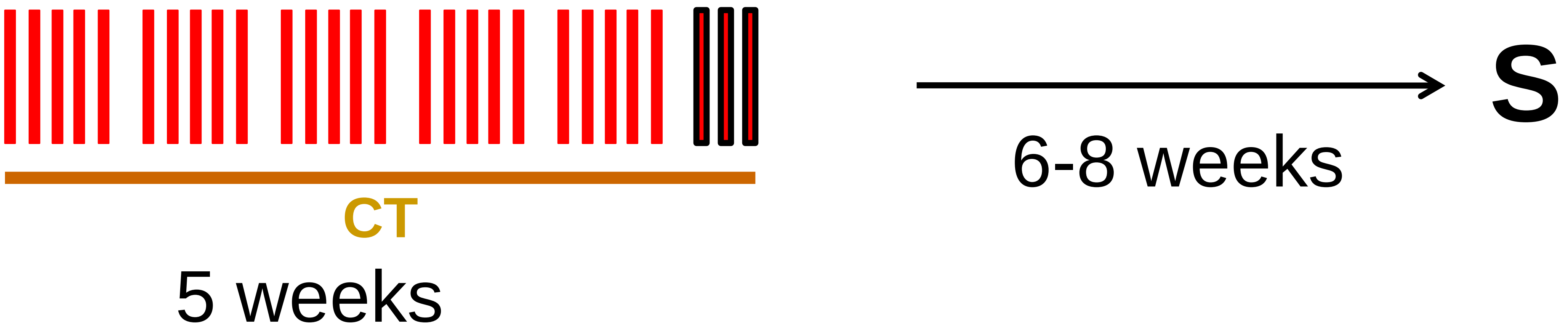


# GTV: the tumor

**GTV: removed by surgery**

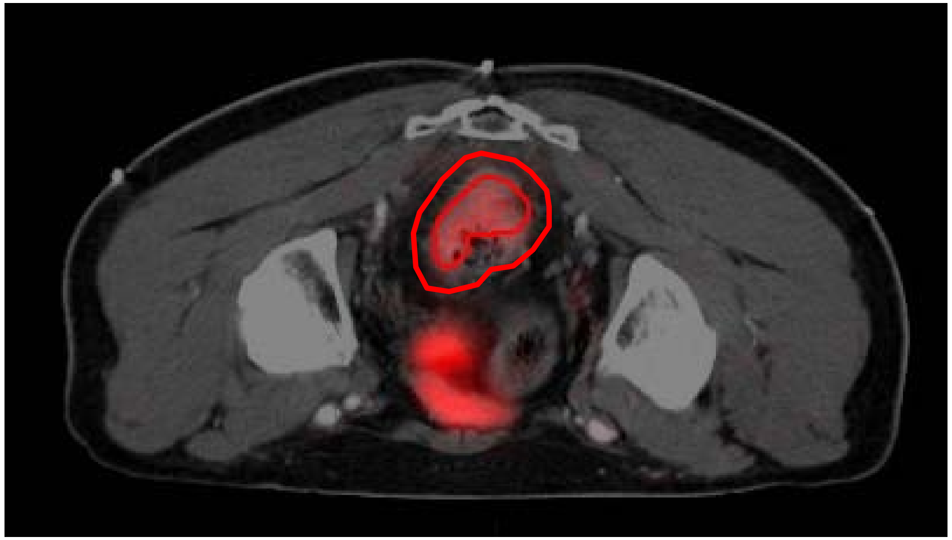
**Long course RT-CT and delayed surgery**

**Boost: Local control; shrinkage/regression**

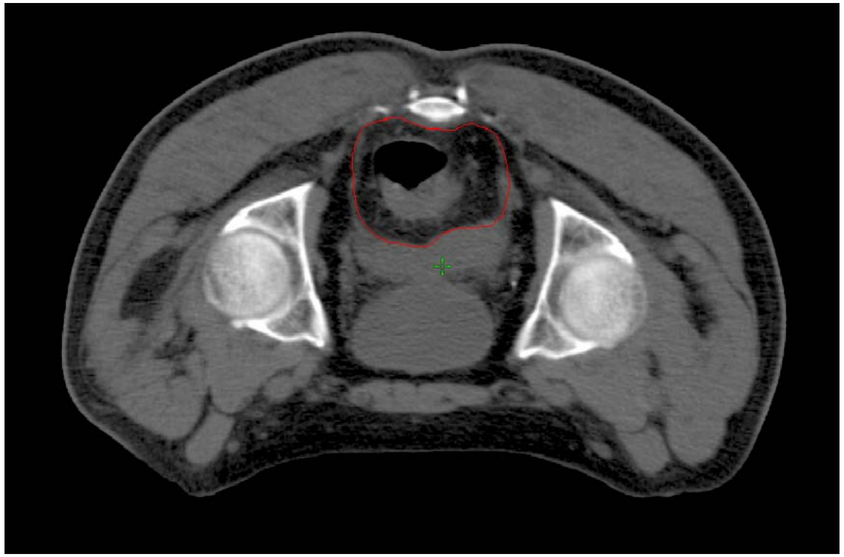


# CTV1: the tumor + margin

**No consensus! No Guideliens!**



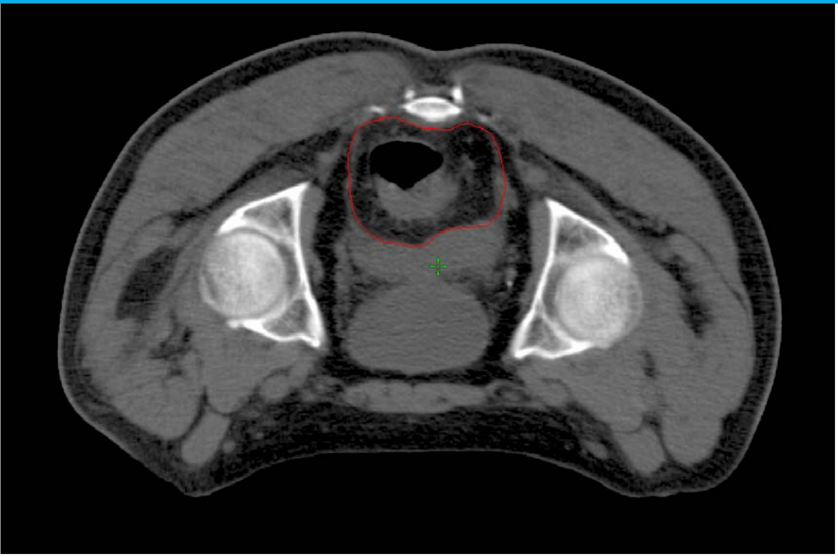
GTV + margin

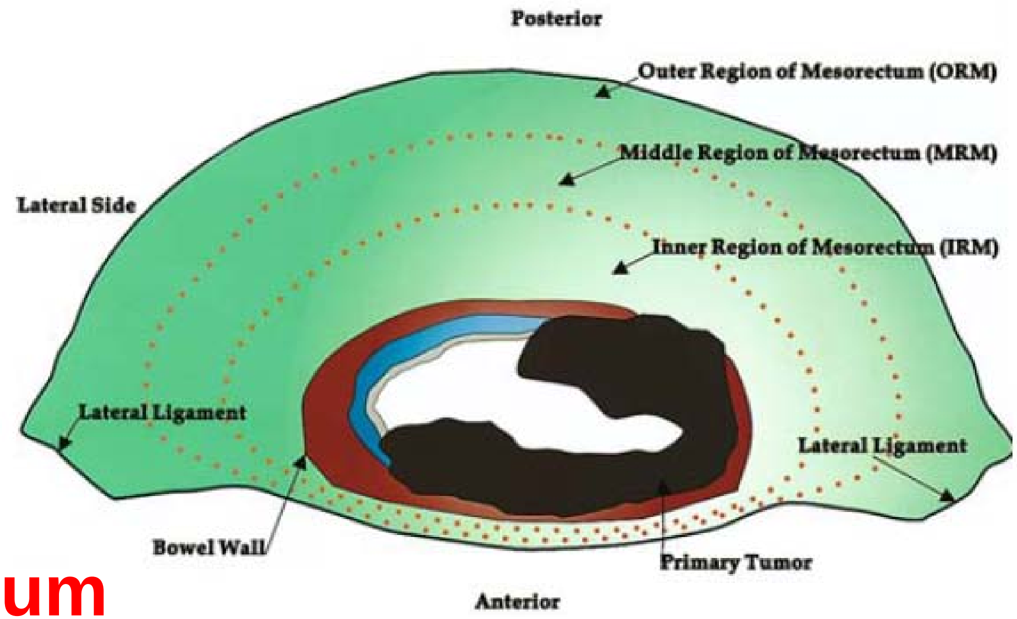


GTV + corresponding mesorectum

*Myerson et al IJROBP 2009*

# CTV1: the tumor + margin






**GTV + corresponding mesorectum**

**Microscopic** tumor deposits in the Mesorectum: **38%**

**Outer** Region of the Mesorectum: **25%**

**Distal tumor deposits** in the mesorectal fat **3 cm** from the cancer: **6.5%**

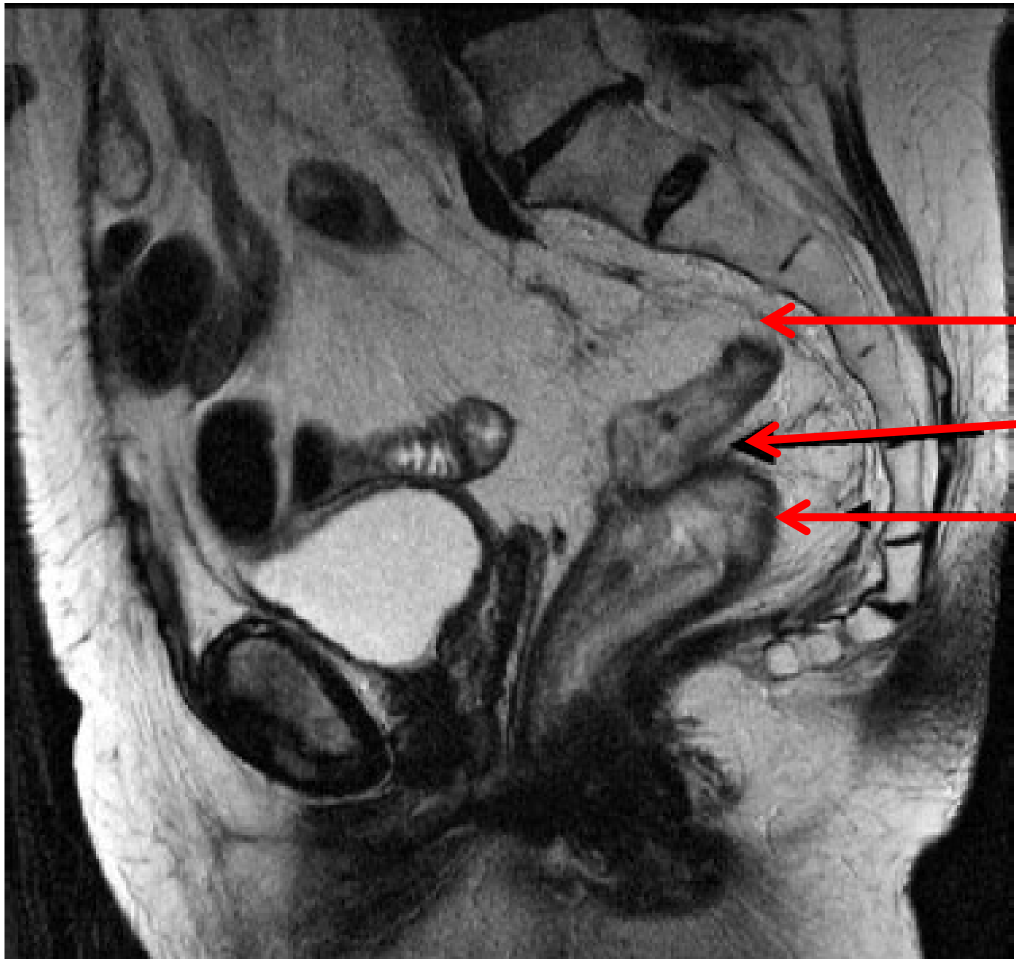
**Prevent target missing related to movement (ITV)**

*Myerson et al IJROBP 2009*

*Wang et al. Int J Colorectal dis 2005*

# CTV2: mesorectum

**Removed by TME**



**Residual distal mesorectal fat**

in **50%** of patients who

underwent **TME**

*Kusters et al. EJCO 2010*
*Syc et al IJROBP 2006*

# CTV2: mesorectum

## RT-TME decrease anastomotic LR

Subsites of local recurrence.

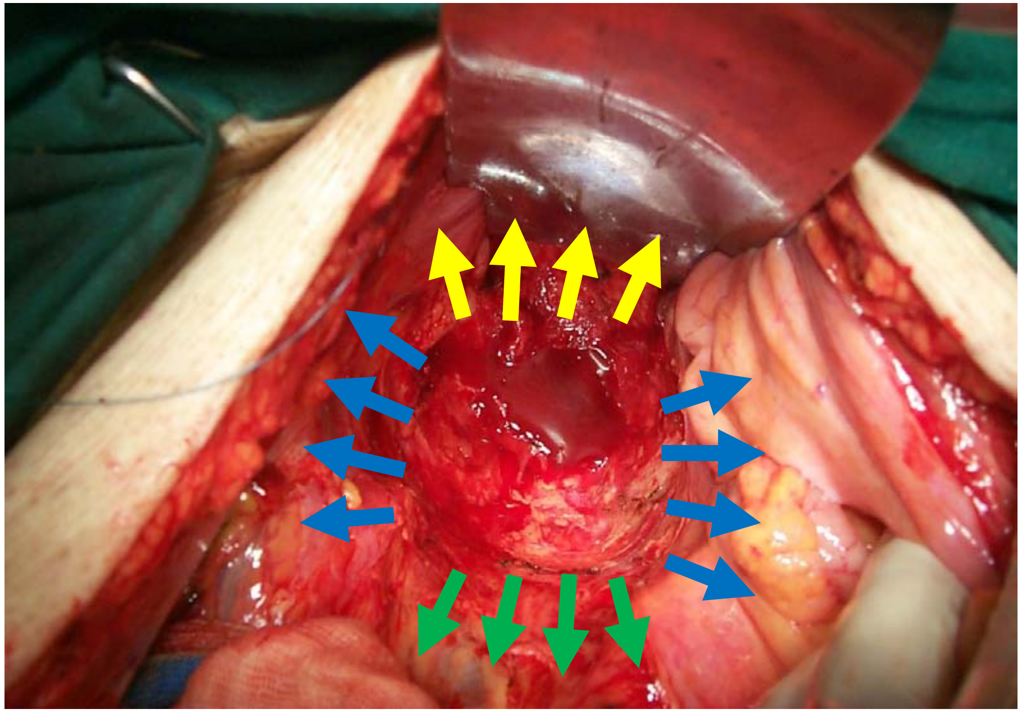
| | RT + ($n = 713$) | RT − ($n = 704$) |
|---|---|---|
| Presacral | 15 (2.0) | 25 (3.6) |
| Lateral | 9 (1.1) | 14 (1.9) |
| Anterior | 6 (0.7) | 14 (1.9) |
| Anastomosis | → 5 (0.7) | → 19 (2.7) |
| Perineum | 0 (0) | 4 (0.6) |
| Unknown | 1 (0.1) | 2 (0.3) |
| TOTAL | 36 (4.6) | 78 (11.0) |

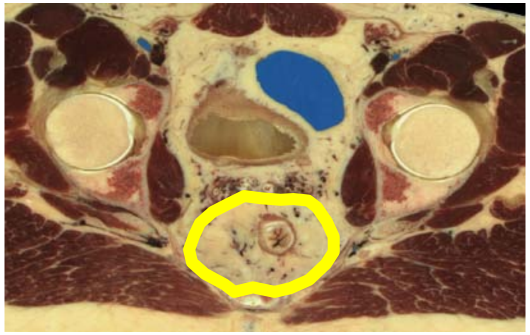
Values in parenthesis are 5-year LR-rates, by competing risks analysis.

**Anastomotic LR** had residual mesorectum

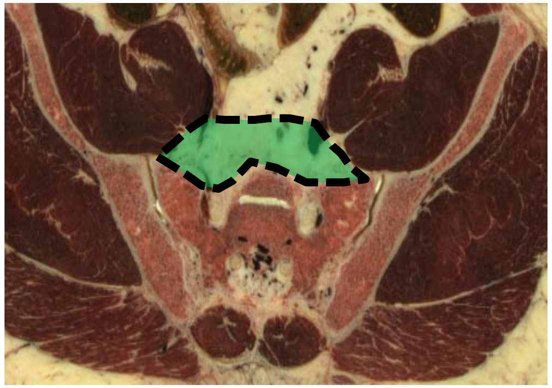
*Kusters et al. EJCO 2010*

# Not surgical targets

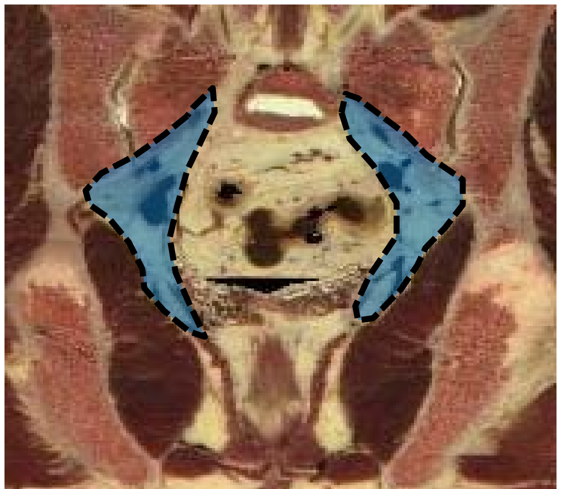




Mesorectal Fascia

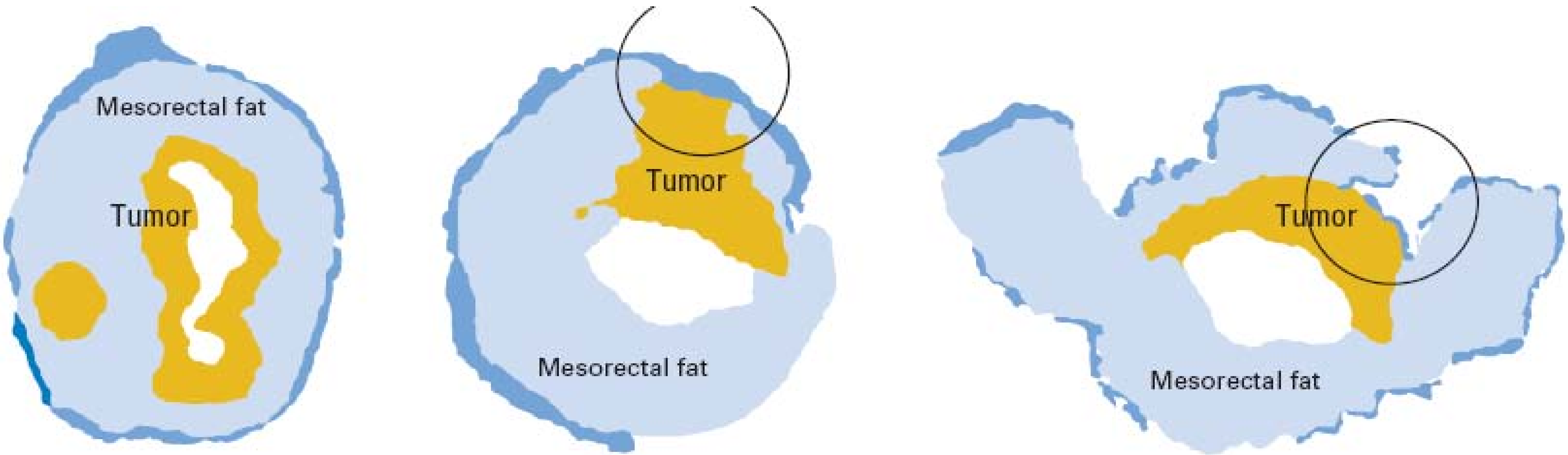


Prescral Space



Lateral Nodes

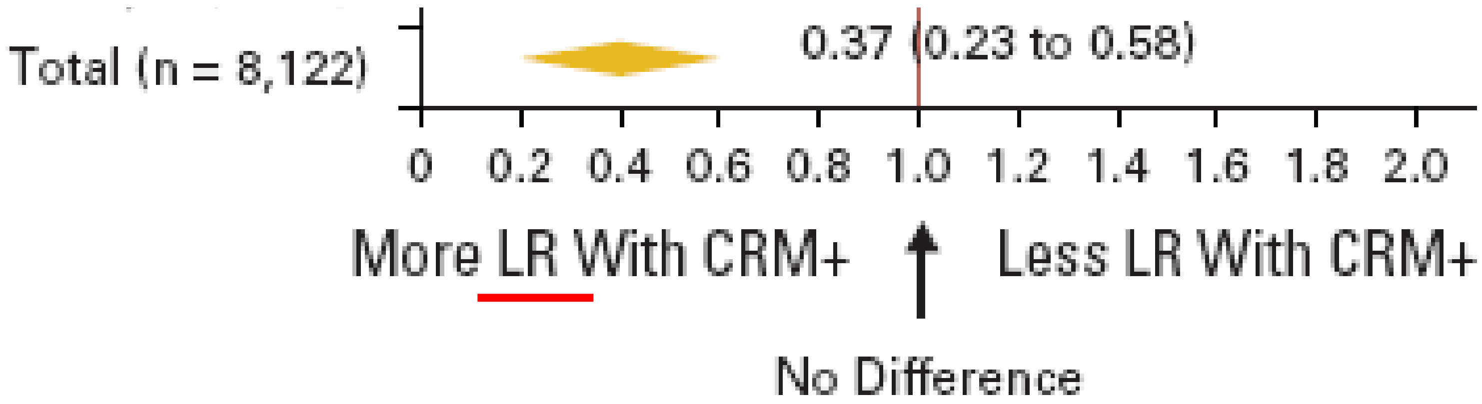
# Mesorectal Fascia

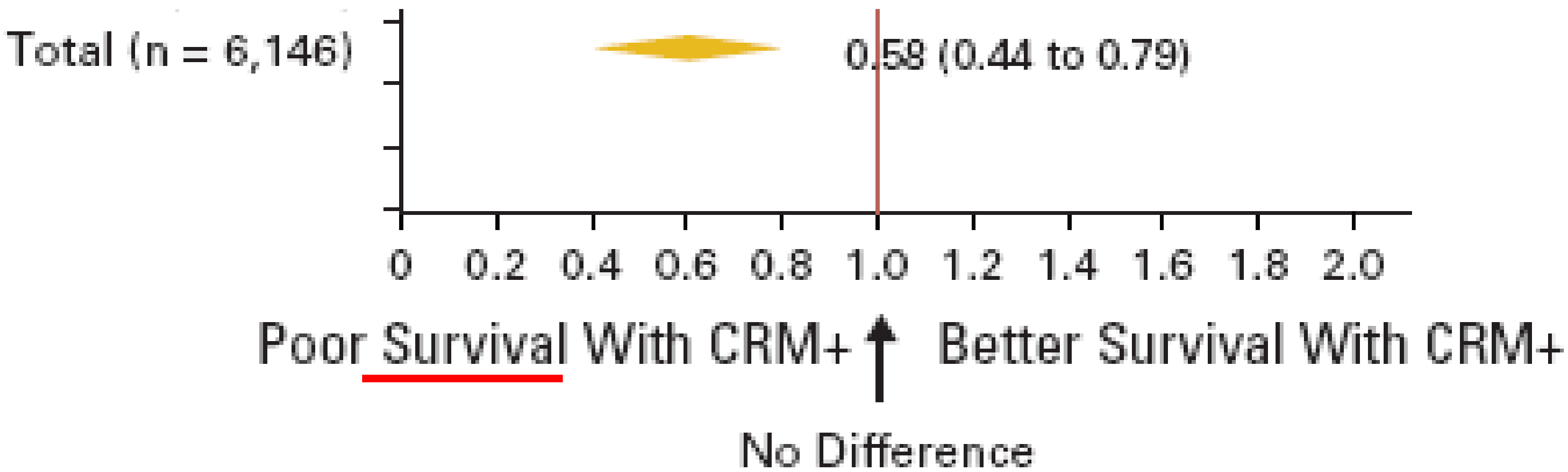



## Circurferential Resection Margin

*Naagtegaal et al. JCO 2009*

# CRM and Oucomes

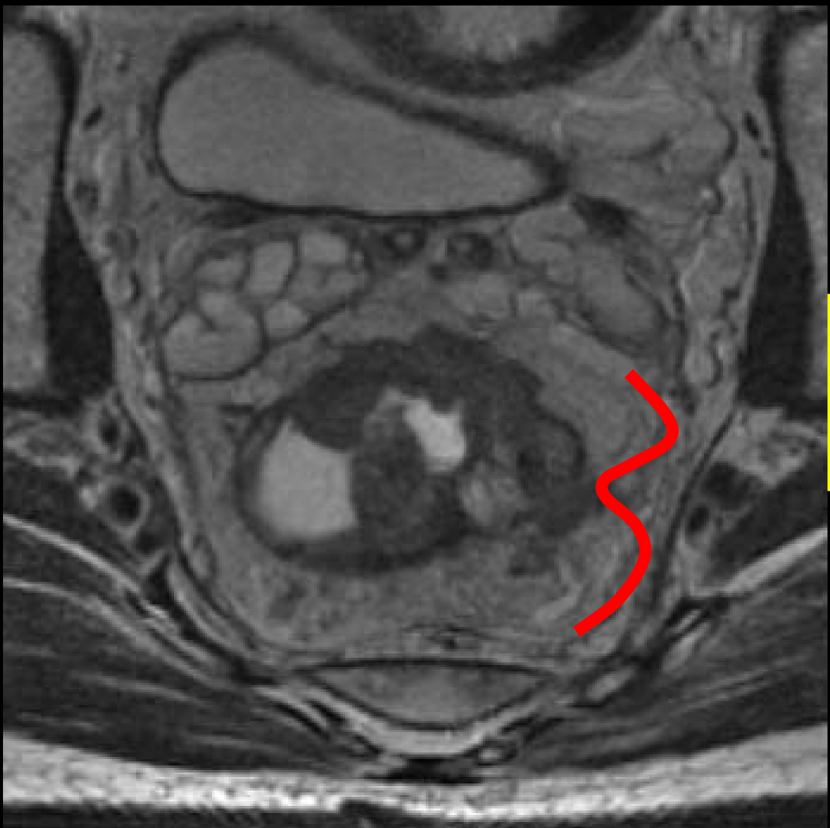



*Naagtegaal et al. JCO 2009*

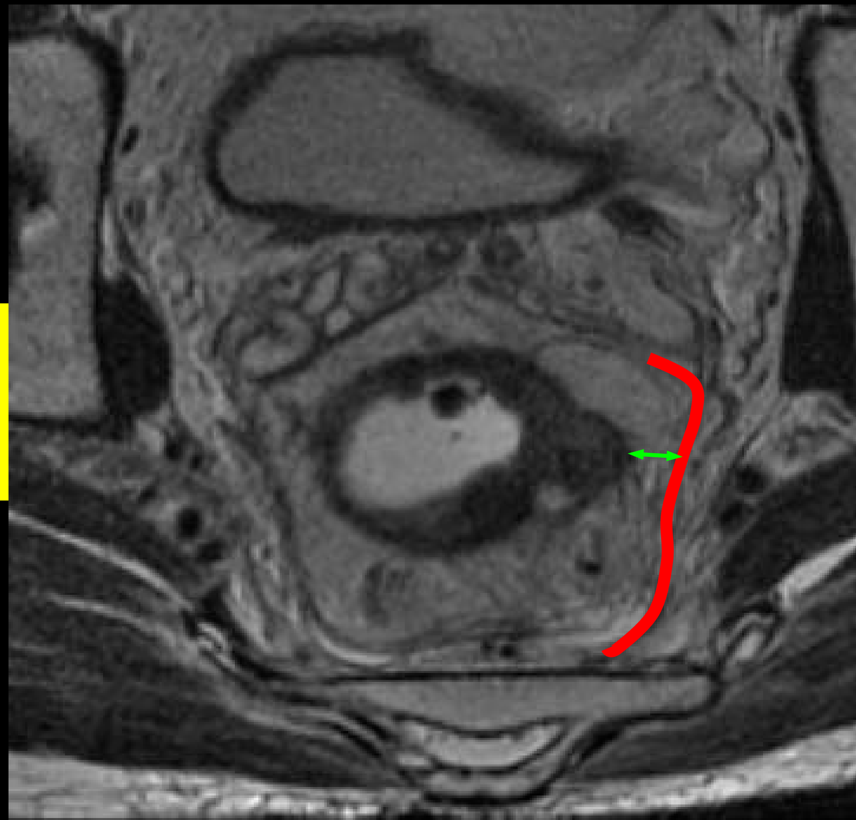
# Mesorectal Fascia by treatment

**preradiation**



**LC-CRT**

**postradiation**



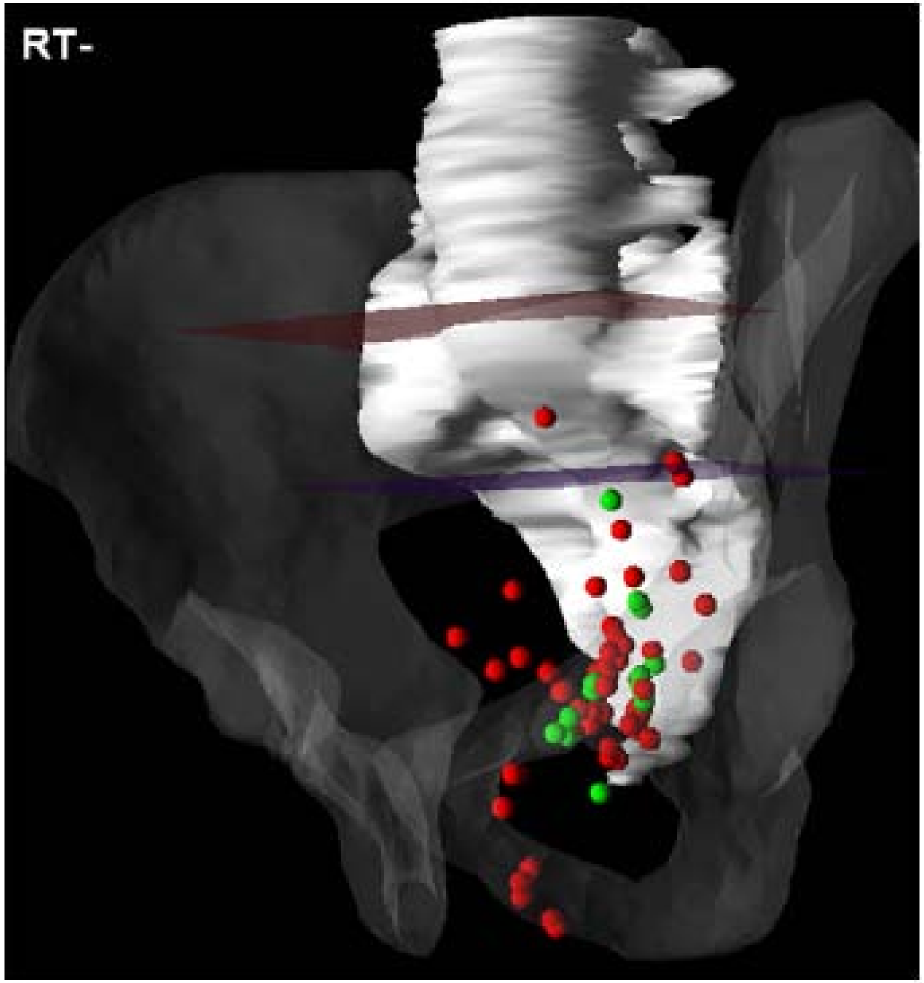
# CRM by treatment

| | Preop **Short RT** | Preop **Long RTCH** |
|---|---|---|
| **pCRM+** | **13 %** | **4 %** |

p = 0.017

Bujko K et al, Radioth Oncol 2006

# Presacral Space




**The majority of RL in the**

**posterior lower 2/3**

**of the pelvis**

*Nijkamp et al IJROBP 2011*
*Hruby et al. IJROBP 2003*

# Presacral Space

Subsites of local recurrence.

| | RT + ($n$ = 713) | RT − ($n$ = 704) |
|---|---|---|
| Presacral | 15 (2.0) | 25 (3.6) |
| Lateral | 9 (1.1) | 14 (1.9) |
| Anterior | 6 (0.7) | 14 (1.9) |
| Anastomosis | 5 (0.7) | 19 (2.7) |
| Perineum | 0 (0) | 4 (0.6) |
| Unknown | 1 (0.1) | 2 (0.3) |
| TOTAL | 36 (4.6) | 78 (11.0) |

Values in parenthesis are 5-year LR-rates, by competing risks analysis.
RT = preoperative radiotherapy.

*Kusters et al EJCO 2010*

# Why…if presacral space is

- **the easiest plane of dissection during surgery**
- **always in radiotherapy fiels**
- **boosted region (ERT/IORT)**
- **no lymphatic tissue in presacral area**

*Kusters et al BJS 2010*

# Presacral and Lateral space

The authors hypothesized that, when mobilizing the rectum during surgical excision, lymph fluid and tumour cells flow into the lateral lymph node system. As this lateral lymph tissue is left behind in a standard TME and partly damaged during sharp dissection of the lateral ligament, one would expect the basins to start leaking after the procedure. This lymph fluid, collected presacrally in a seroma, might give rise to local tumour recurrence.

*Kusters et al BJS 2010*

# Lateral Spaces

**5 yrs OS** when N+ extra-mesorectal: **~40%**

**Positive LLN in surgical series: ~15 %**

- T stage and location
- Grading
- N+mesorectal

*Kusters et al Ann Surg 2009*

# Lateral Spaces

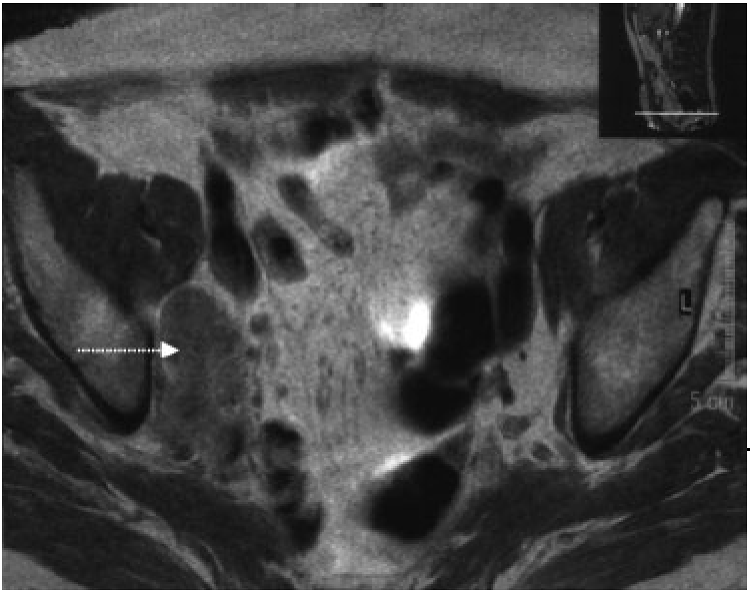
## Radioterapy vs Surgery (LLND*)

same results with less side effects (sexual & urinary)

*Lateral Lymph Node Dissection

*Kusters et al Ann Surg 2009*

# Lateral Spaces

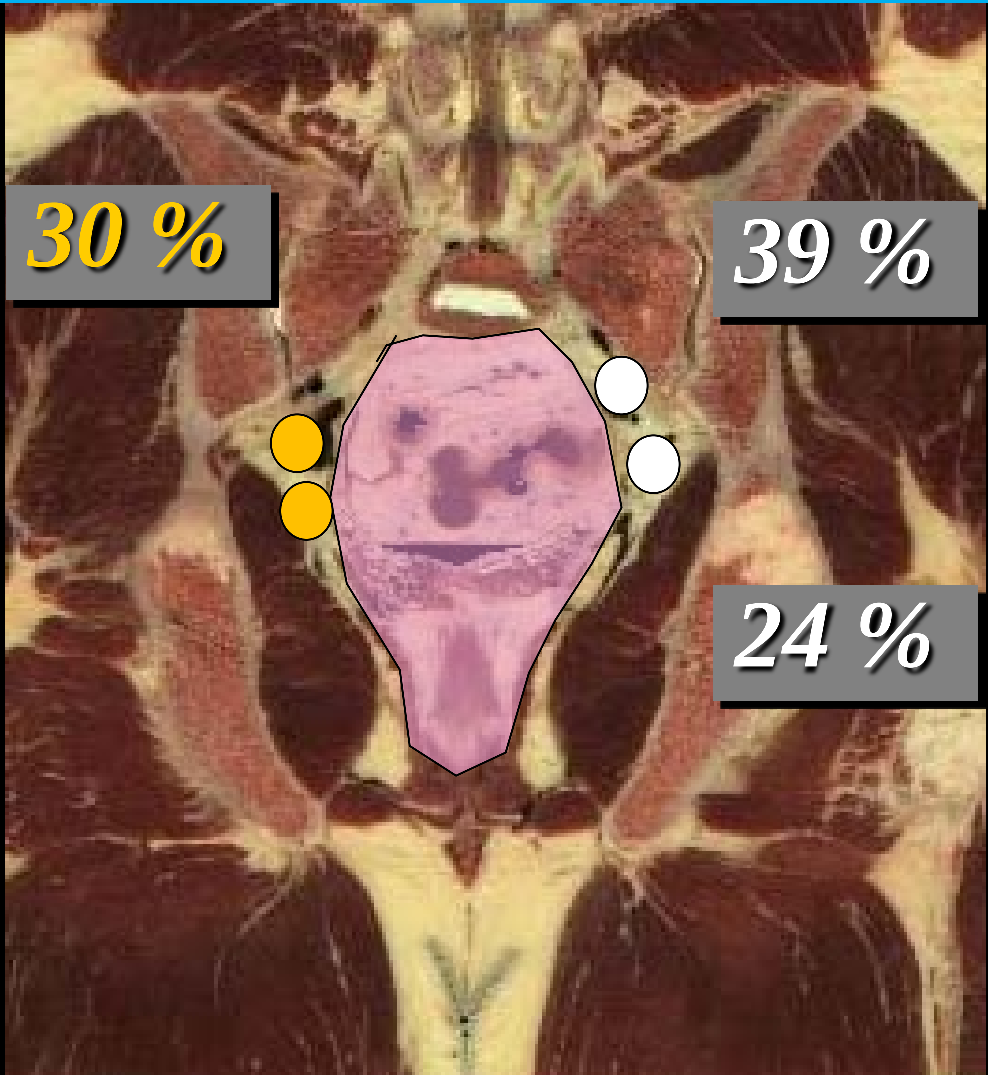


## Relapses in the lateral spaces in radiological series: <5%

| Primary tumor level (cm) | RT | Patients (n) | TME | Visible mesorectal fat | Anastomotic | Presacral midline | Presacral asymmetric | Pelvic wall: Medial | Pelvic wall: Lateral | Pelvic floor |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Recurrent tumor location | | | | | |
| 0–5 | All | 39 | 38 | 8 | 7 | 14 | 12 | 7 | 4 | 19 |
| | No | 13 | 13 | 3 | 2 | 3 | 7 | 1 | 1 | 7 |
| | Yes | 26 | 25 | 5 | 5 | 11 | 5 | 6 | 3 | 12 |
| 6–10 | All | 20 | 18 | 13 | 10 | 9 | 5 | 5 | 2 | 1 |
| | No | 11 | 10 | 6 | 4 | 4 | 4 | 2 | 2 | 0 |
| | Yes | 9 | 8 | 7 | 6 | 5 | 1 | 3 | 0 | 1 |
| 11–15 | All | 24 | 16 | 21 | 16 | 4 | 3 | 5 | 0 | 1 |
| | No | 15 | 8 | 13 | 11 | 2 | 2 | 2 | 0 | 1 |
| | Yes | 9 | 8 | 8 | 5 | 2 | 1 | 3 | 0 | 0 |

*Syc et al IJROBP 2008*

# Lateral Spaces




***Tumor location***

***≤ 5 cm to dentate line***

***< peritoneal reflection***

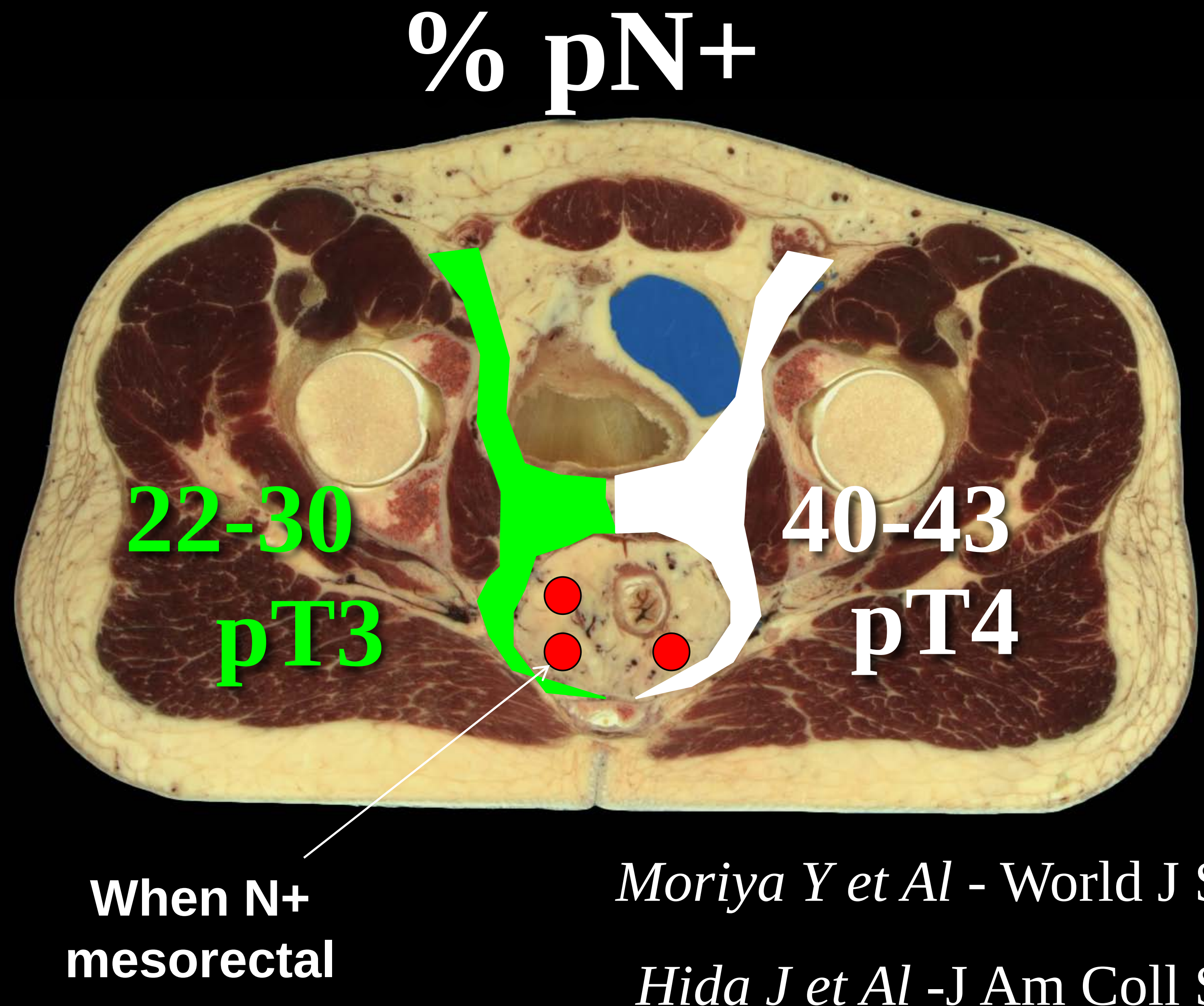
***Diameter of rectal tumor***

***> 3 cm***

*Takahashi T et Al* – Dis Colon Rectum -2000

*Steup WH et Al* – Eur J Cancer - 2002

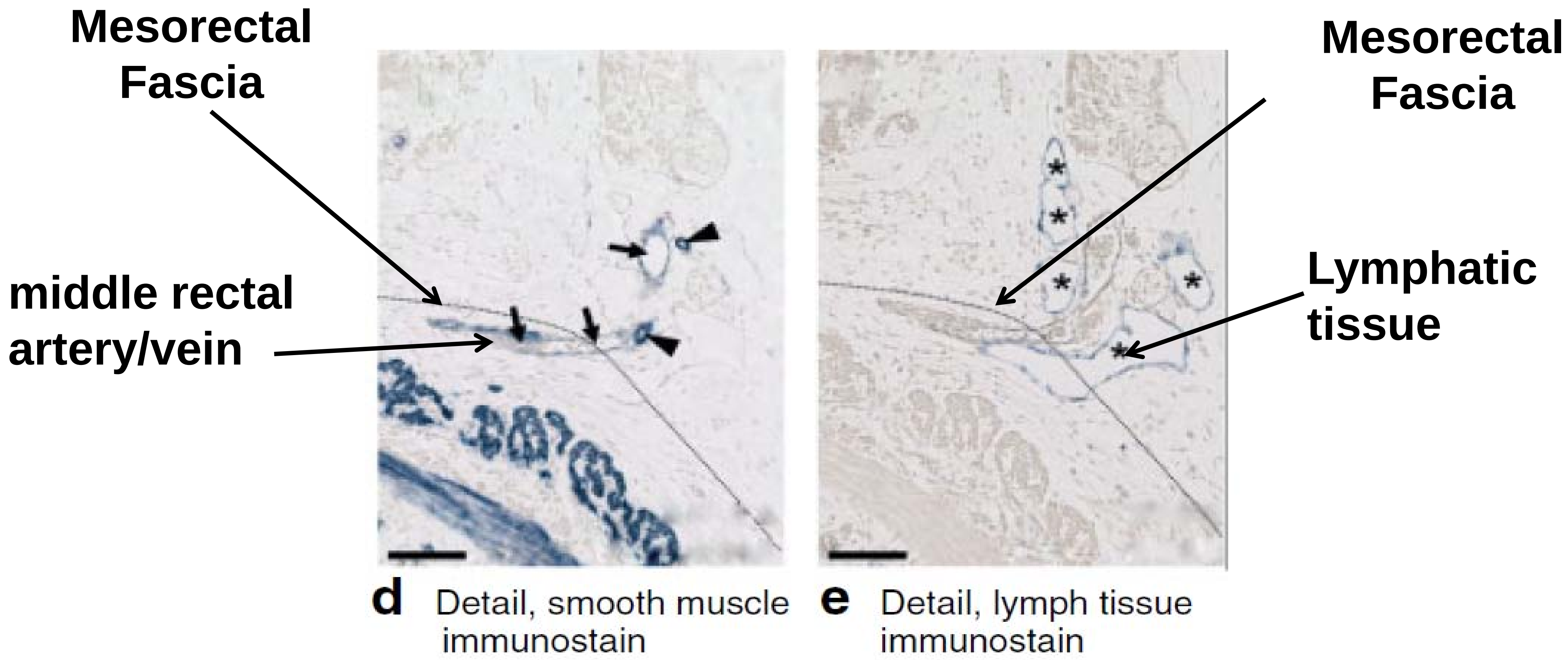
# Lateral Space




*Moriya Y et Al* - World J Surg - 1997

*Hida J et Al* -J Am Coll Surg - 1997

# Lateral Spaces

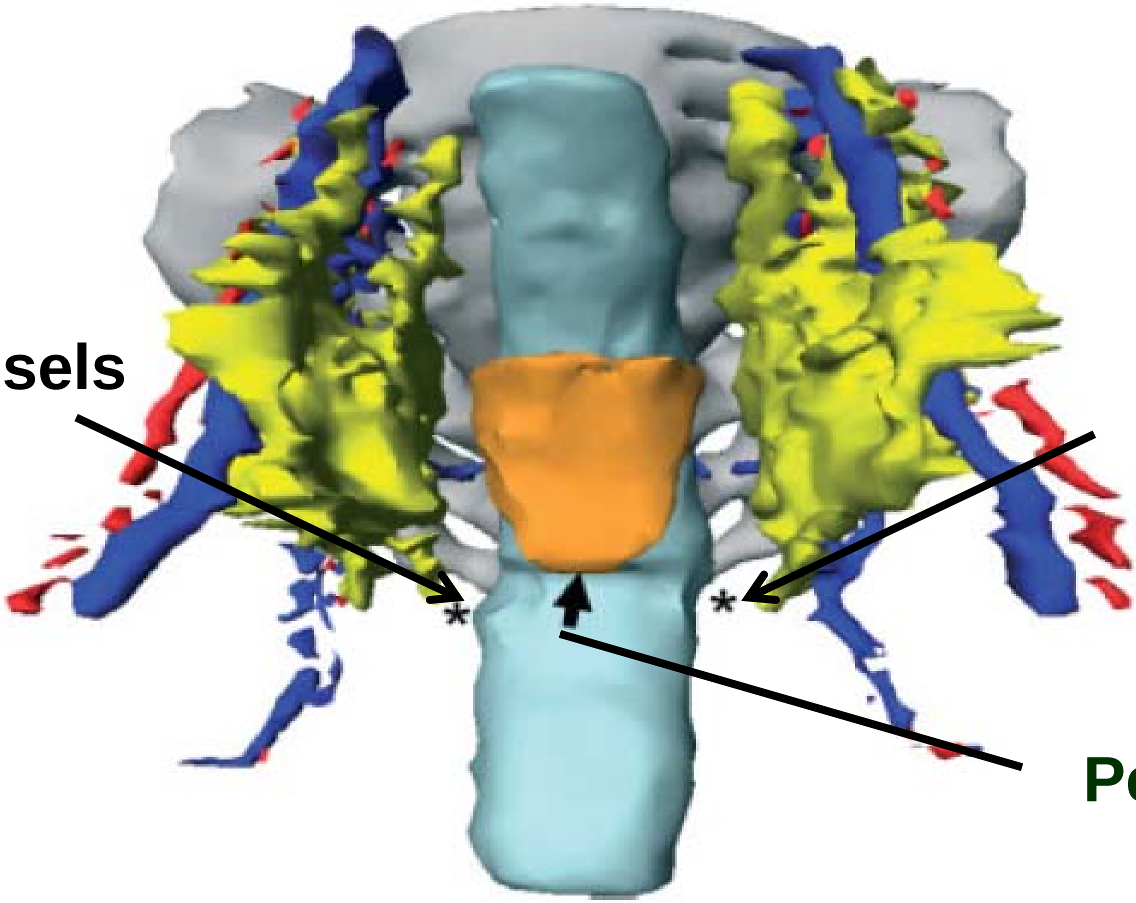



“The middle rectal artery/veins entered the mesorectum below the peritoneal reflection[···]. Vessels were accompained by lymph tissue.”

*Kusters et al BJS 2010*

# Lateral Spaces

middle rectal artery/vein + lymphatic vessels



middle rectal artery/vein + lymphatic vessels

Peritoneal Reflection

*Kusters et al BJS 2010*

# Delineation guidelines

**Good consensus in subsites to be included in the Rectal Cancer CTV**

**Low consensus in subsites boundaries**

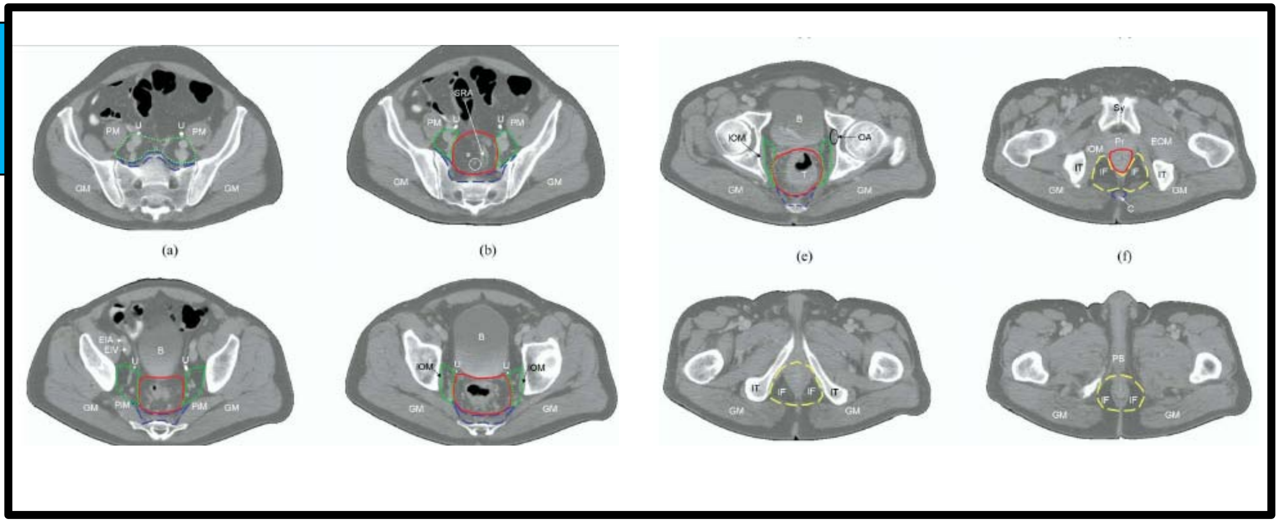
**DIFFERENT DELINEATION GUIDELINES!**

## European

**Revision of literature for LR**

**ANATOMICAL SUBSITES**

**No consensus for boudaries**



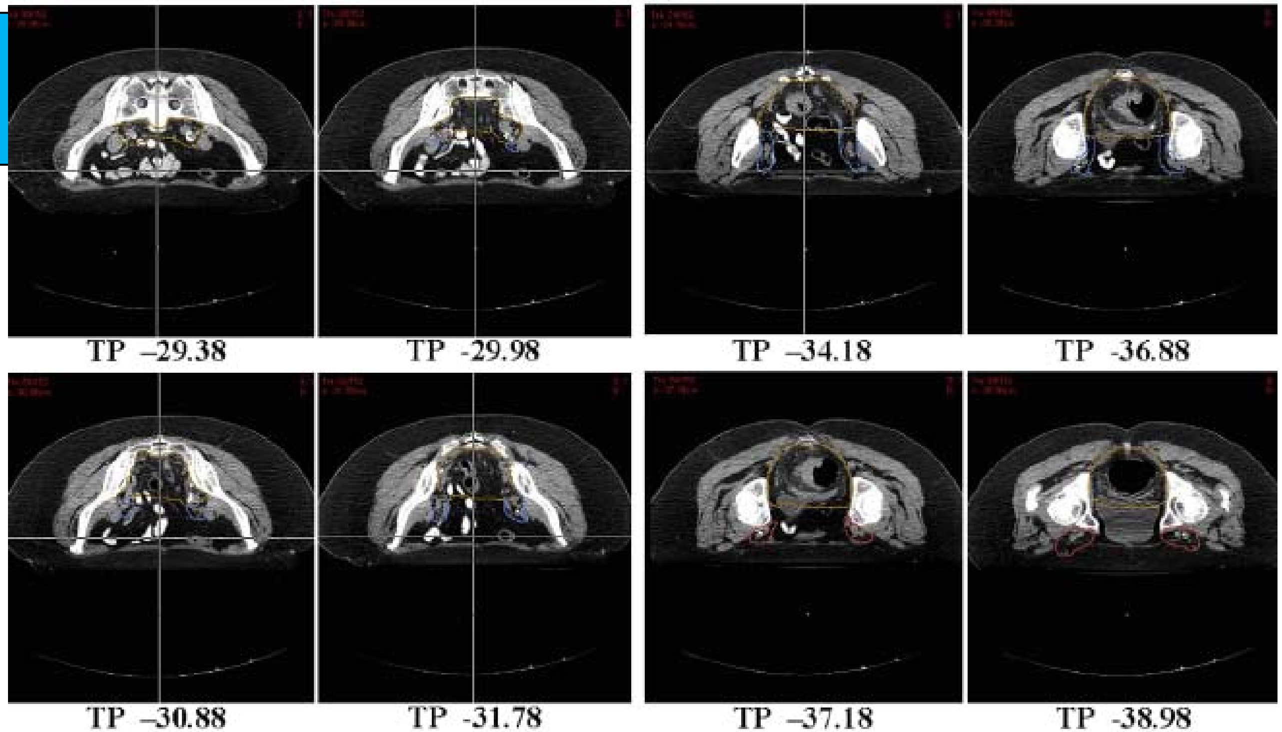
*Roels S et al. IJROBP 2006*

## US

**No literature revision**

**RT CTVs**

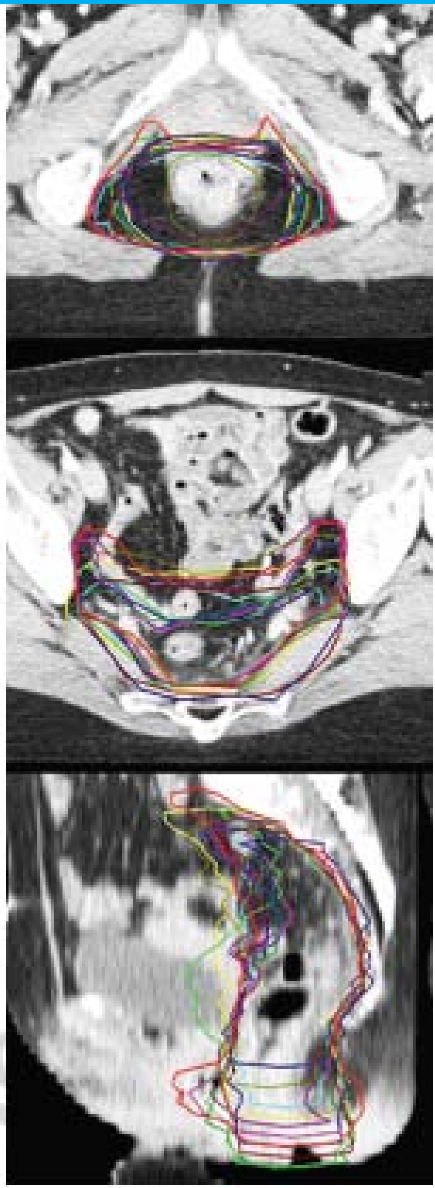
**EXPERT consensus**




*Myerson RJ et al. IJROBP 2008*

# Delineation guidelines

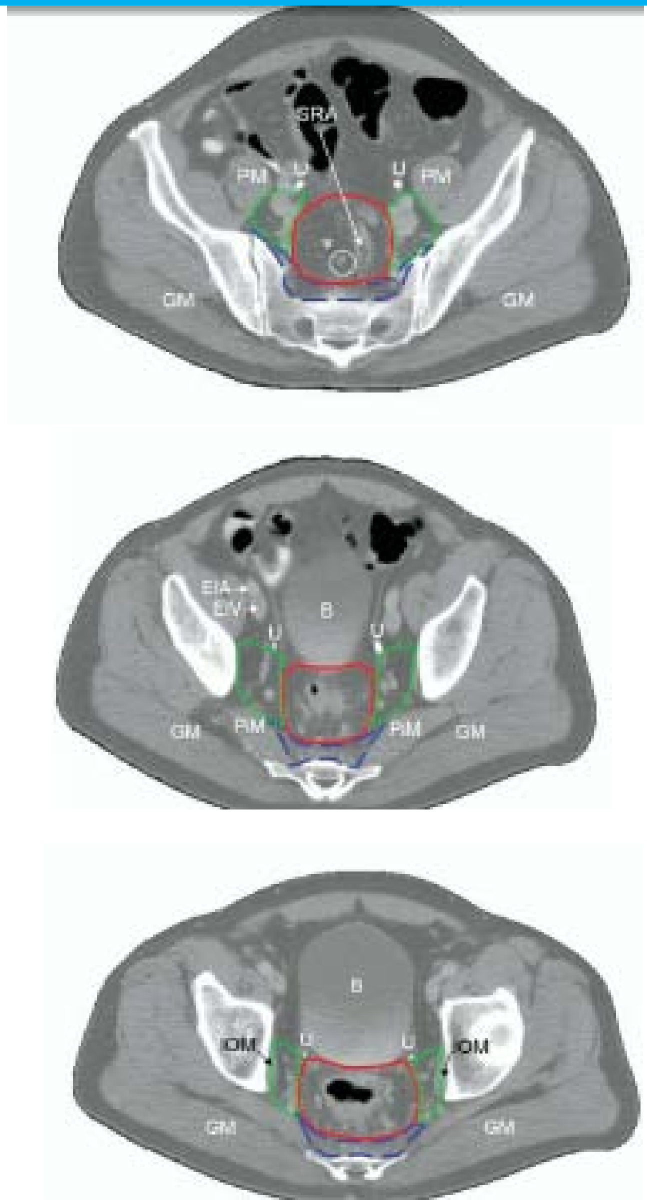
**NO**



**YES**

*Nijkamp J et al. Multidisciplinary Magement of Rectal Cancer 2012*

# Mesorectum: delineation guidelines

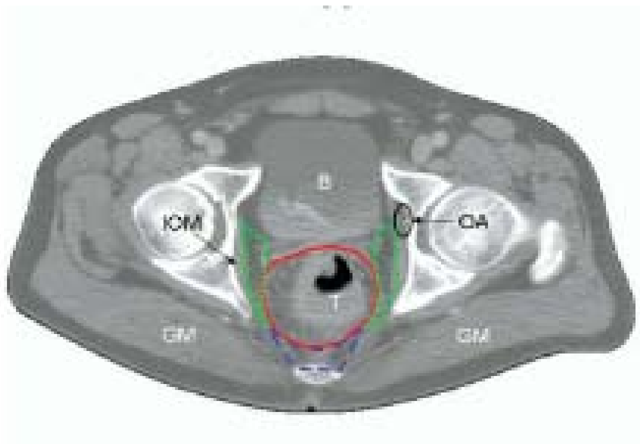



**SUPERIOR**
**bifurcation of the IMA** into the sigmoid artery and the upper rectal artery

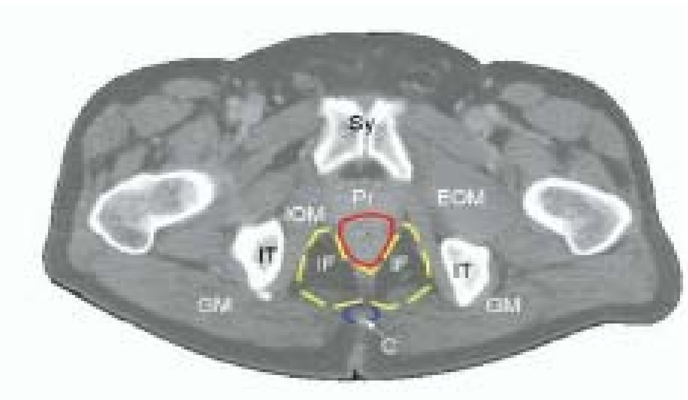
**ANTERIOR**
Denonvillier **fascia**,recto-vaginal septum; anterior **pelvic organs**

*Roels et al IJROBP 2006*

# Mesorectum: delineation guidelines



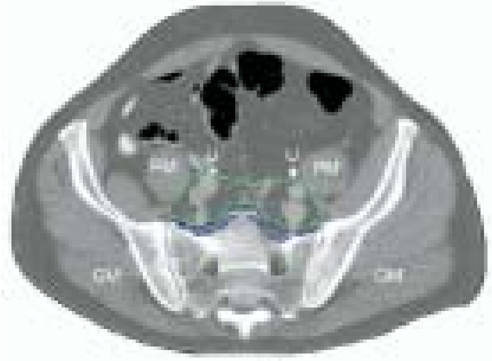

**LATERAL**
Mesorectal fascia



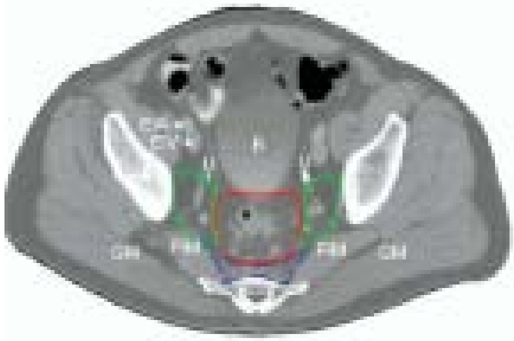

**INFERIOR**
Inserction of the levator ani muscle into the rectal wall

*Roels et al IJROBP 2006*

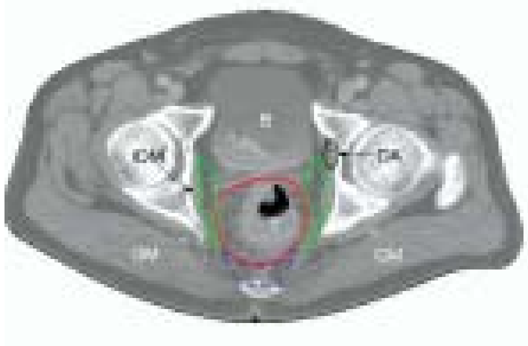
# Presacral: delineation guidelines



(a)



(c)



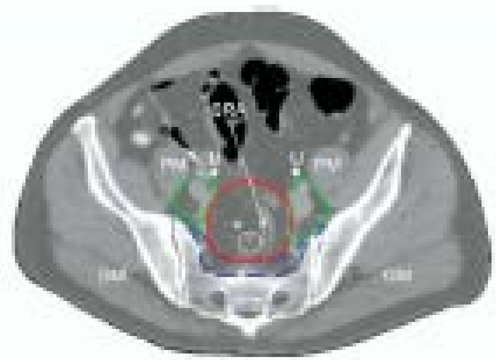
**SUPERIOR**
Sacral promontory

**POSTERIOR**
Sacrum

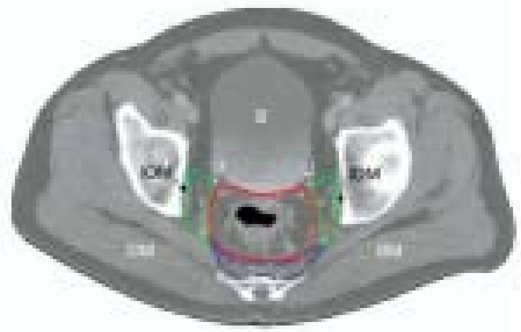
**ANTERIOR**
Mesorectum or 1 cm ventral to the sacrum

**INFERIOR**
Coccyx

**LATERAL**
Lateral borders of the Sacrum



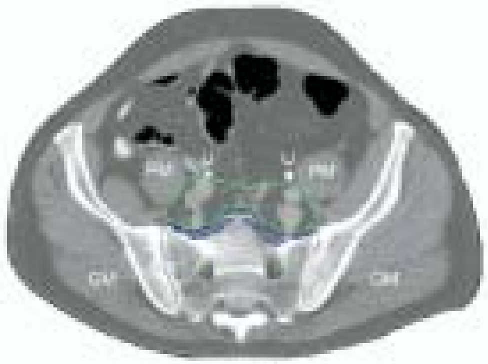
(b)



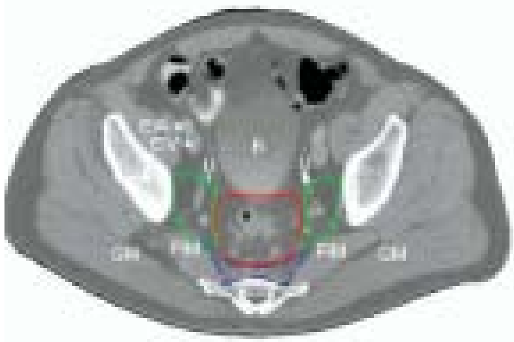
(d)

*Roels et al IJROBP 2006*

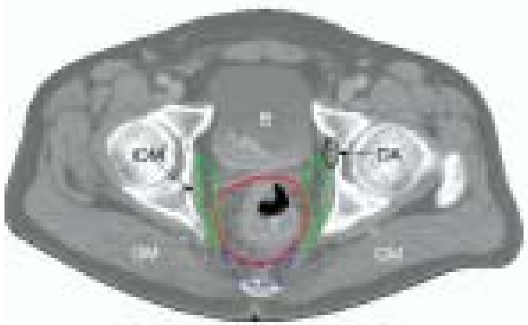
# Lateral spaces: delineation guidelines



(a)



(c)



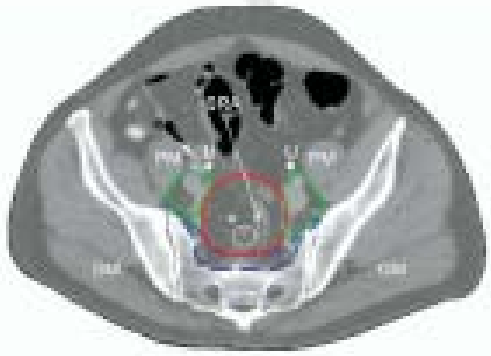
**SUPERIOR**
Bifurcation of iliac vessels

**POSTERIOR**
Sacro-iliac joints

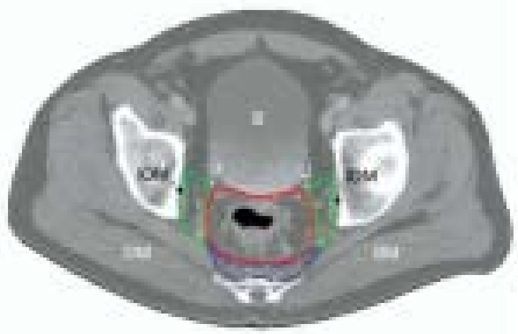
**ANTERIOR**
ureter

**INFERIOR**
Where the obt artery enters in the obt canal

**LATERAL**
Psoas; ischium; piriform; intern ob; levator ani muscles



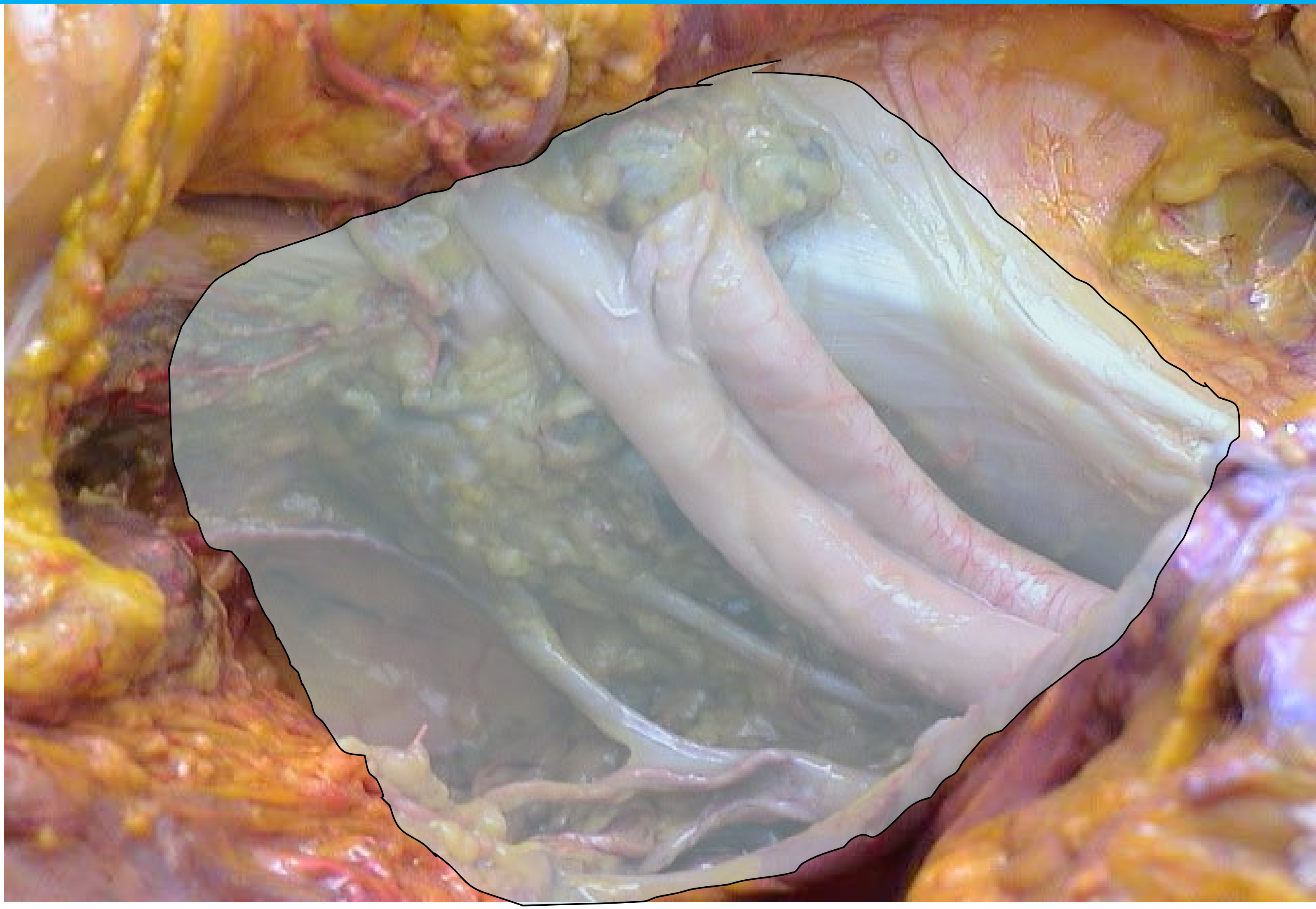
(b)



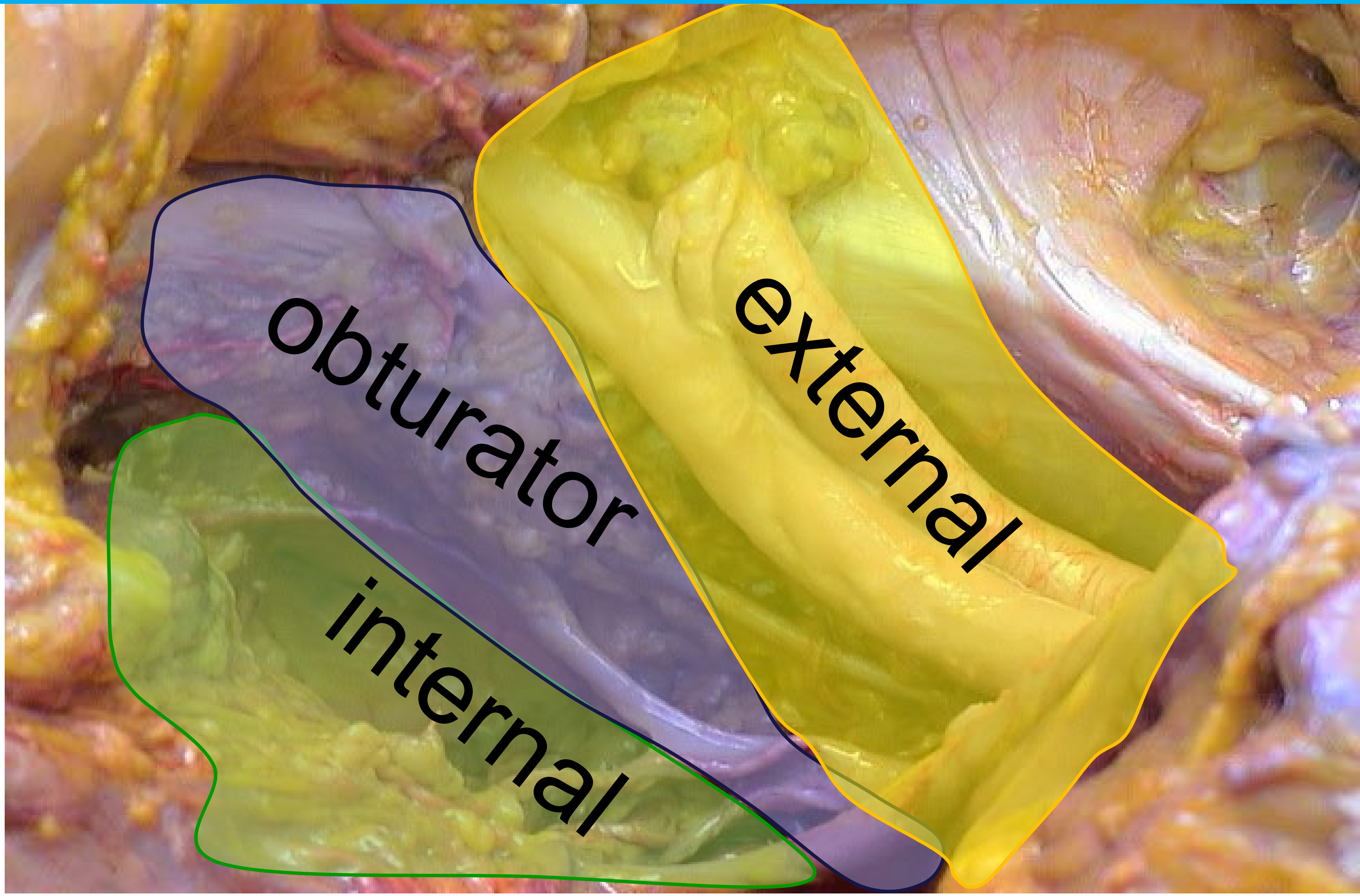
(d)

*Roels et al IJROBP 2006*

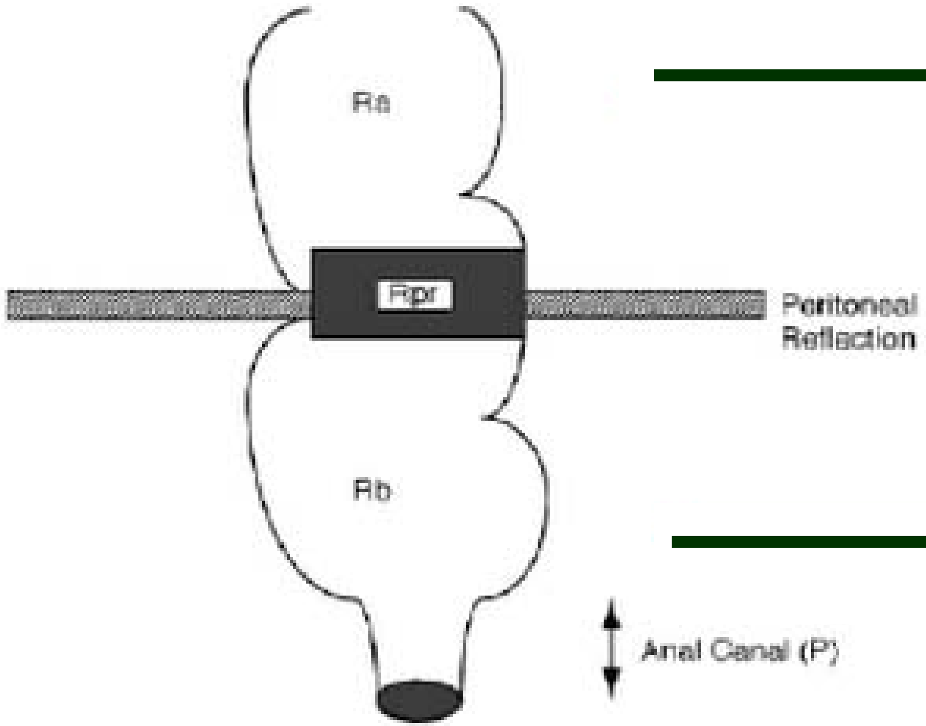
# Lateral Spaces



# Lateral Spaces



# Obturator nodes




0% (0/133)

3% (3/99)

9% (33/373)

*Steup et al EJC 2002*

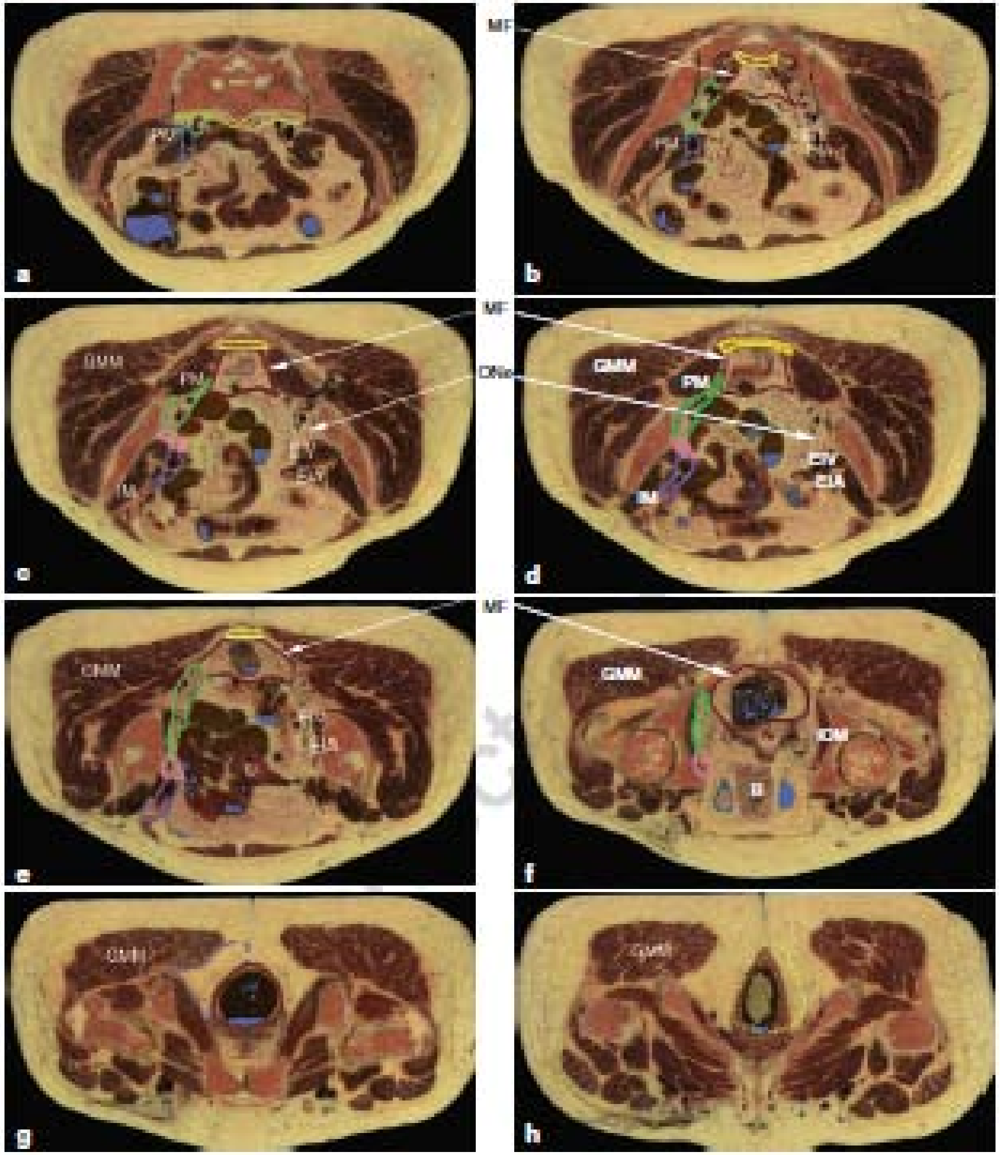
# External iliac nodes

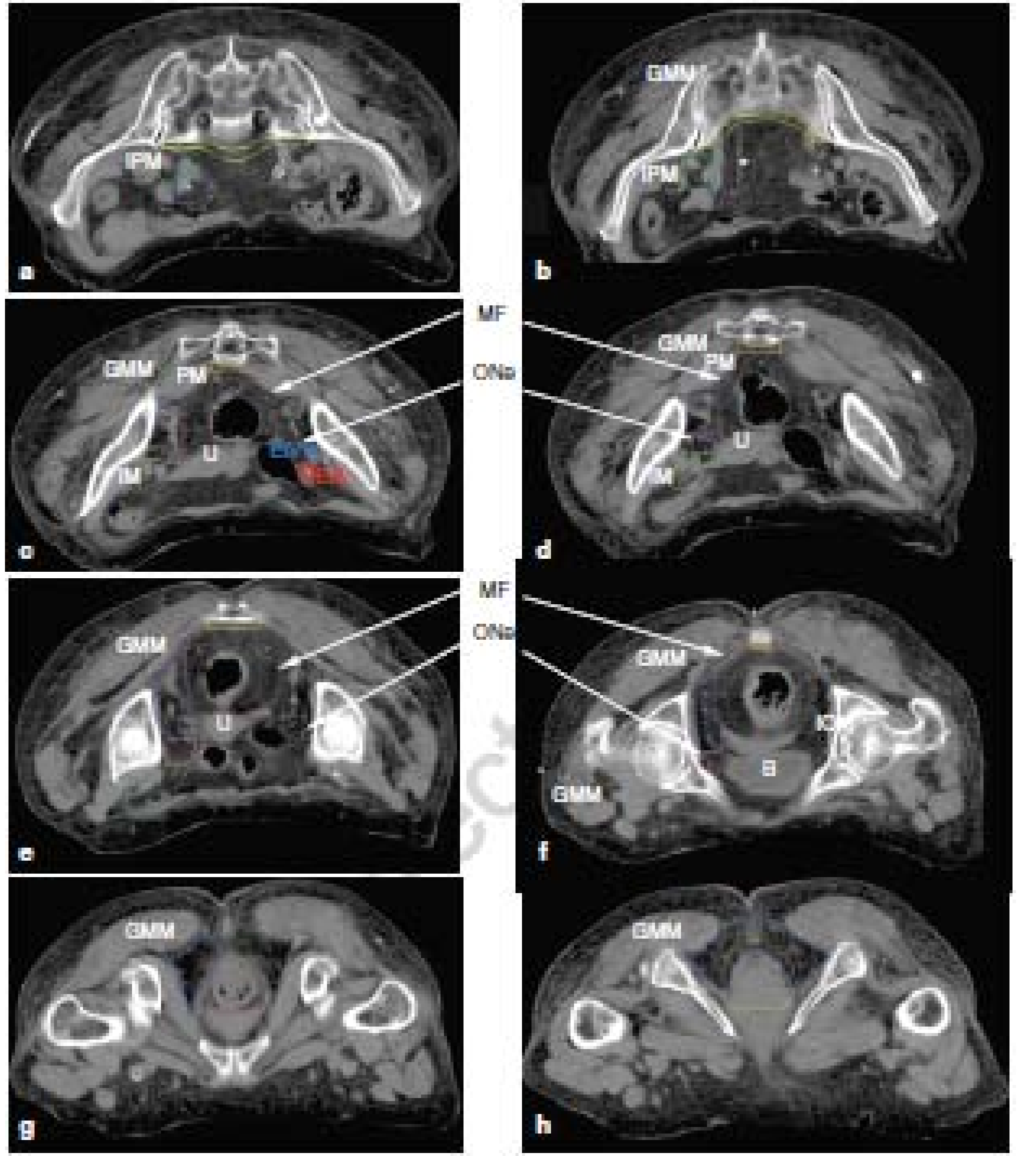
- RL very rare in EIN: **4%**
- **When positive nodes: 9%**
- Found in **low seated tumors:**
- **APR vs LAR = 5% vs 3%**

Usually NOT included in the CTV, unless invasion of anterior organ

**LOW CONSENSUS**

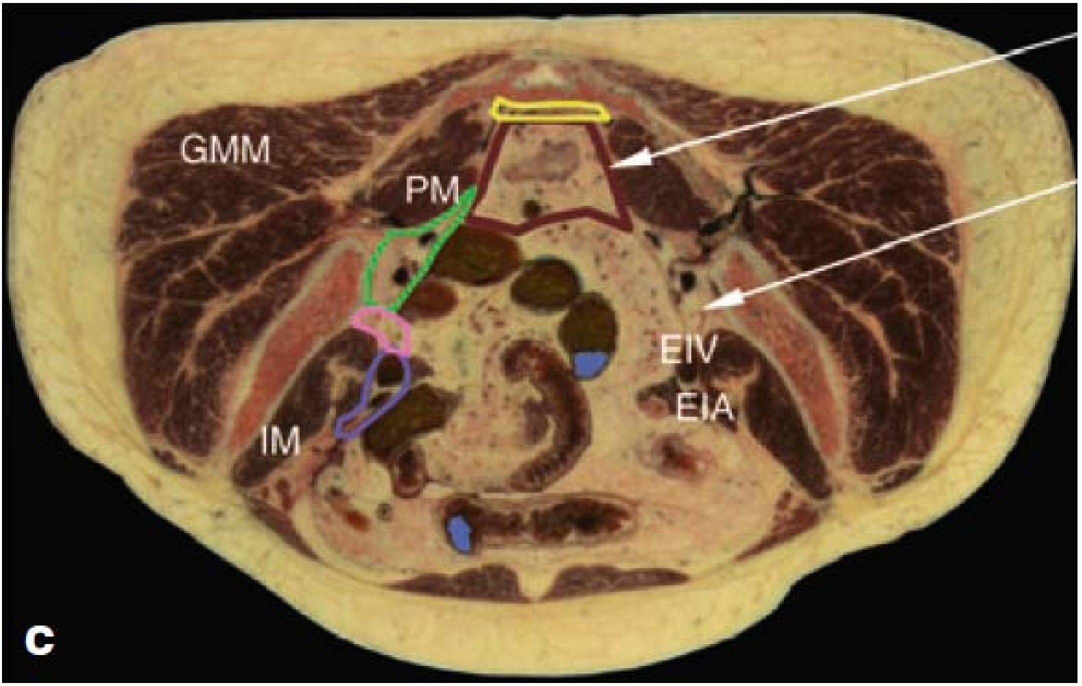
# Delineation guidelines

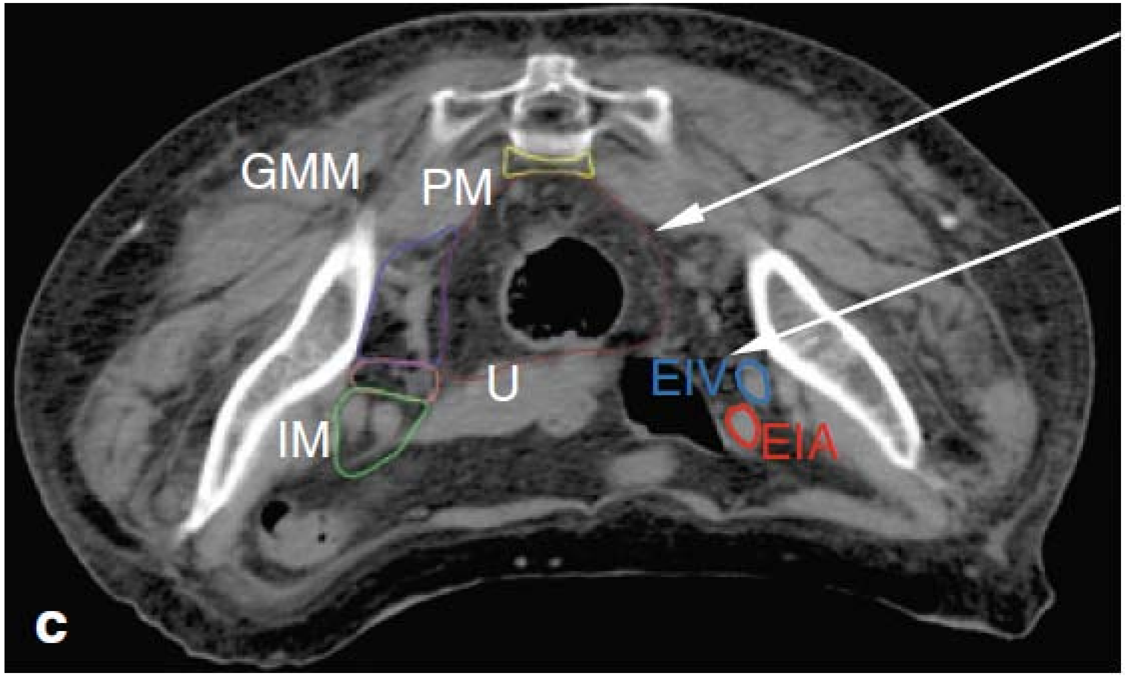



*Gambacorta MA et al. Multidisciplinary Magement of Rectal Cancer*

# Delineation guidelines




*Gambacorta MA et al. Multidisciplinary Magement of Rectal Cancer*

# CTV modulation

| | Presaral space | Mesorectum | Internal iliac nodes | Obturator nodes | Extrenal iliac nodes | sphincter complex | ischiorectal fossae |
|---|---|---|---|---|---|---|---|
| cT3 mid-low (below the peritoneal reflection) | + | + | + | | | + (when sphincter infiltration) | + (when direct tumor infiltration) |
| Any cT with massive positive internal iliac nodes | + | + | + | + | | + (when sphincter infiltration) | + (when direct tumor infiltration) |
| Any cT with massive positive obturator nodes nodes | + | + | + | + | + | + (when sphincter infiltration) | + (when direct tumor infiltration) |
| cT4 with for anterior pelvic organ | + | + | + | + | + | + (when sphincter infiltration) | + (when direct tumor infiltration) |

*Gambacorta et al. Multidisciplinary Magement of Rectal Cancer 2012*

| | Presaral space | Mesorectum | Internal iliac nodes | Obturator nodes | Extrenal iliac nodes | sphincter complex | ischiorectal fossae |
|---|---|---|---|---|---|---|---|
| cT3 mid-low (below the peritoneal reflection) | + | + | + | | | | |
| Any cT with massive positive internal iliac nodes | + | + | + | | | | |
| Any cT with massive positive obturator nodes nodes | + | + | + | | | | |
| cT4 with for anterior pelvic organ | + | + | + | | | | |

*Gambacorta et al. Multidisciplinary Magement of Rectal Cancer 2012*

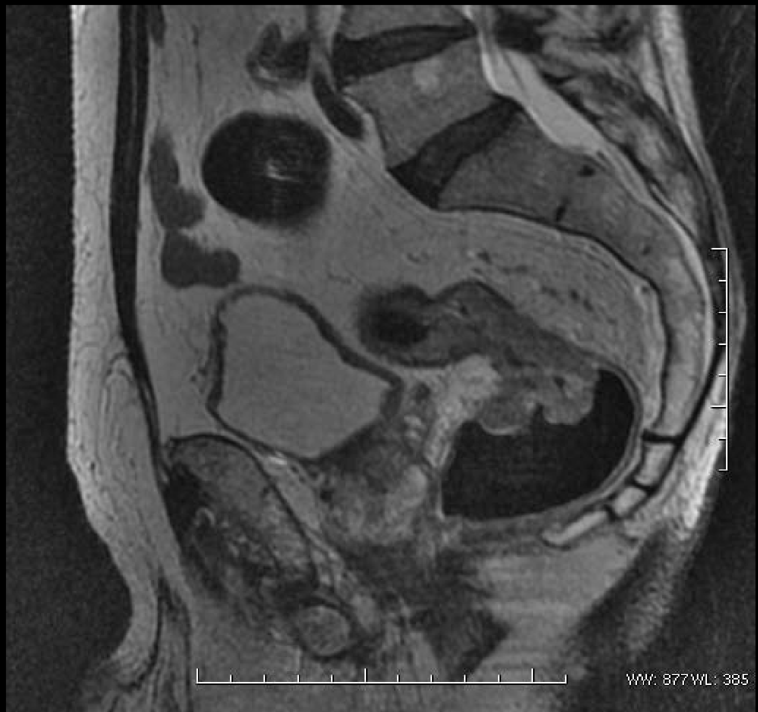
| | Presaral space | Mesorectum | Internal iliac nodes | Obturator nodes | Extrenal iliac nodes | sphincter complex | ischiorectal fossae |
|---|---|---|---|---|---|---|---|
| cT3 mid-low (below the peritoneal reflection) | + | + | + | | | | |
| Any cT with massive positive internal iliac nodes | + | + | + | + | | | |
| Any cT with massive positive obturator nodes nodes | + | + | + | + | | | |
| cT4 with for anterior pelvic organ | + | + | + | + | | | |

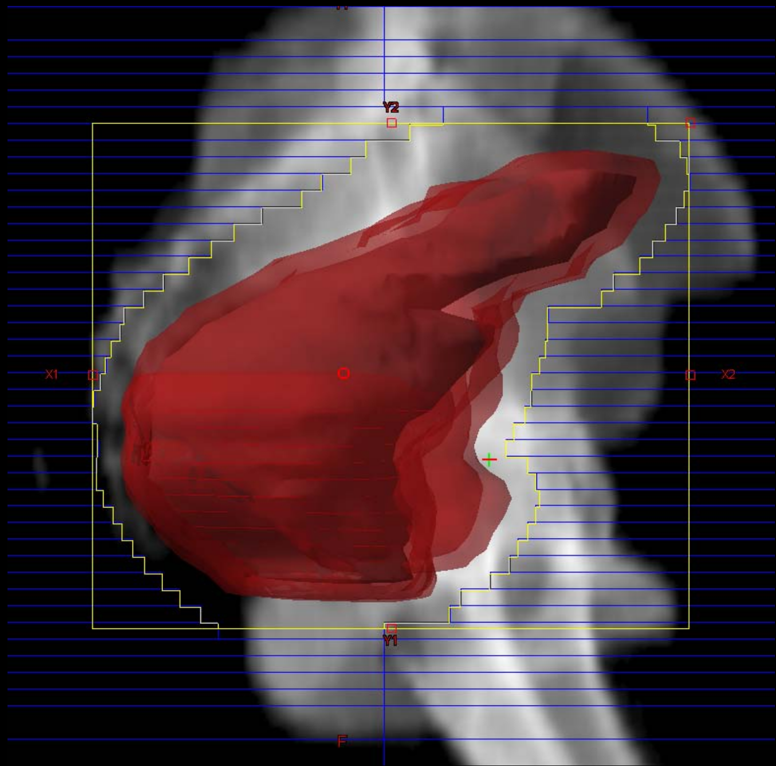
*Gambacorta et al. Multidisciplinary Magement of Rectal Cancer 2012*

| | Presaral space | Mesorectum | Internal iliac nodes | Obturator nodes | Extrenal iliac nodes | sphincter complex | ischiorectal fossae |
|---|---|---|---|---|---|---|---|
| cT3 mid-low (below the peritoneal reflection) | + | + | + | | | | |
| Any cT with massive positive internal iliac nodes | + | + | + | + | | | |
| Any cT with massive positive obturator nodes nodes | + | + | + | + | + | | |
| cT4 with for anterior pelvic organ | + | + | + | + | + | | |

*Gambacorta MA et al. Multidisciplinary Magement of Rectal Cancer*

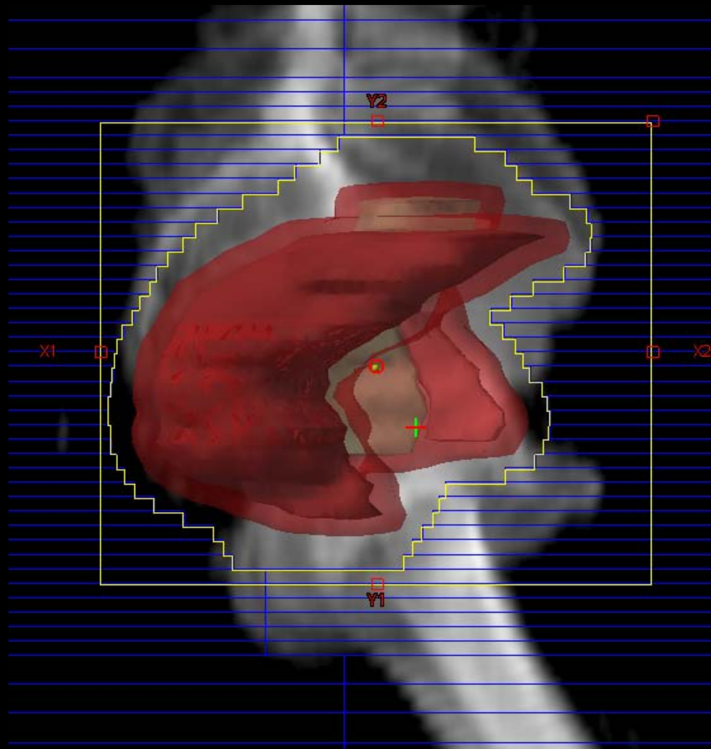
# CTV modulation




**Mid tumor above the PR**

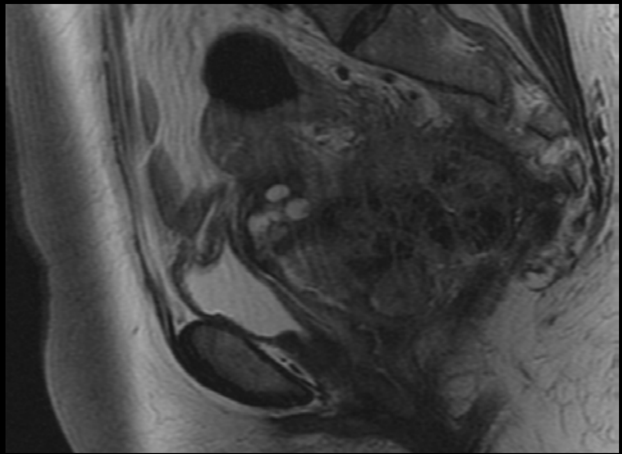
# CTV modulation

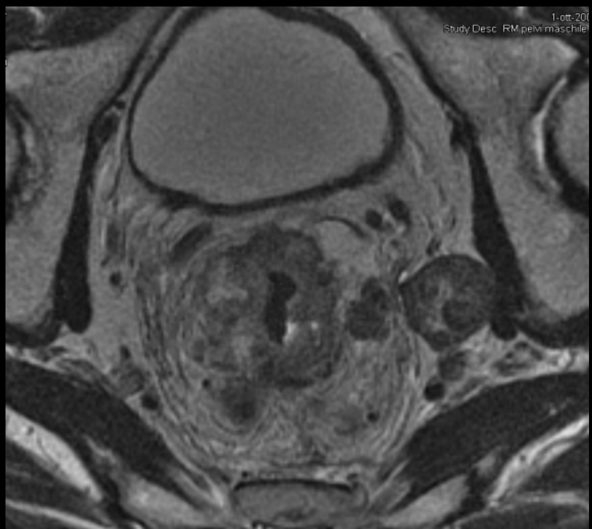



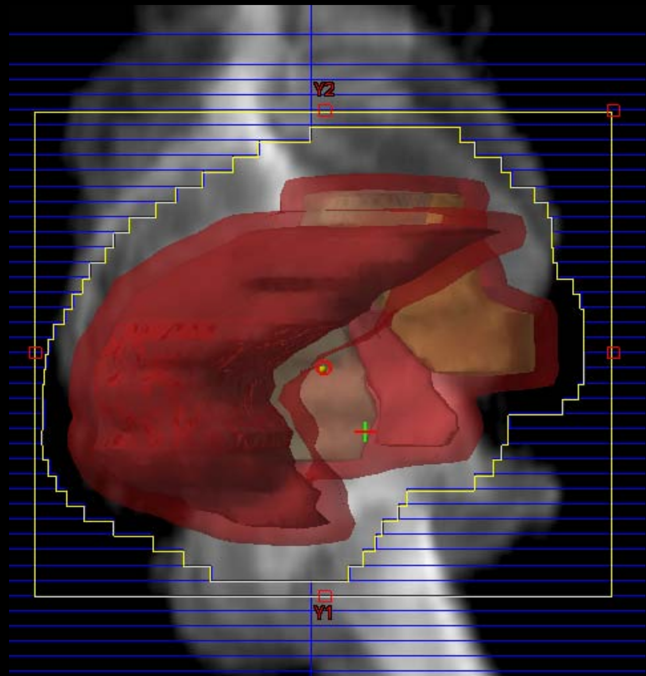

**low tumor below the PR**

*Gambacorta MA et al. Multidisciplinary Magement of Rectal Cancer 2012*

# CTV modulation








**cT4 invading anterior organ or N+ in the lateral space**

*Gambacorta MA et al. Multidisciplinary Magement of Rectal Cancer 2012*

# Inferior pelvic subsite
## (anal sphincter and ischiorectal fossae)

- **IPS** has a risk of **LR: 4%,**
- low seated tumors **(<6 cm** from the AV): **8%**
- after APR: **11%**

## Rules for inclusion in the CTV

**Anal sphincter:**

**INCLUDE** when INFILTRATED and when APR is planned

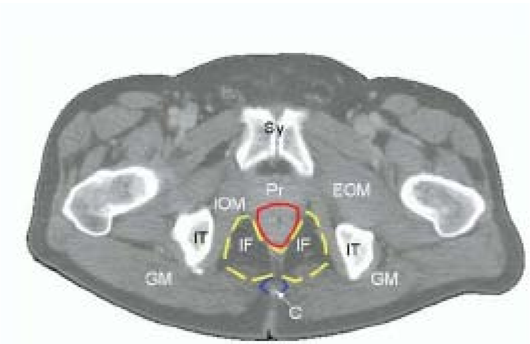
**EXCLUDE** when SPHINCTER PRESERVATION is planned

**IR fossa:**

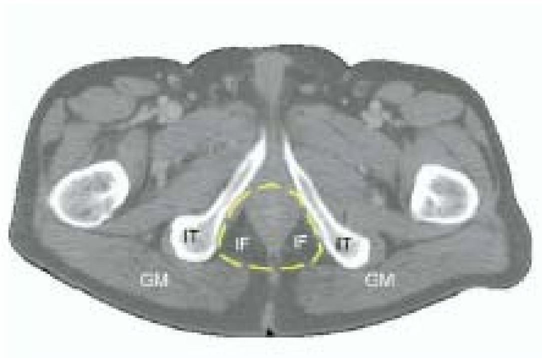
**INCLUDE** only in case of direct infiltration

*Joye I and Haustermas K et al IJROBP 2014* *Roels et al IJROBP 2006*

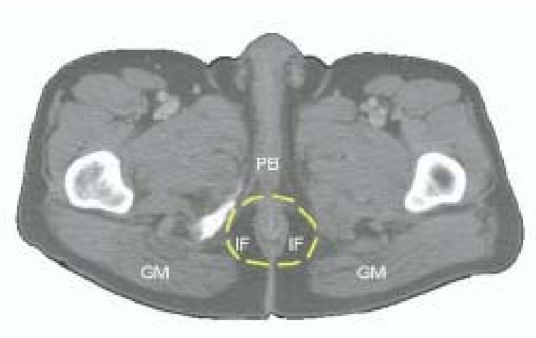
# Inferior pelvic subsite




**LATERAL**
internal obturator muscles,
ischial tuberosities




**POSTERIOR**
coccix gluteal muscles




**ANTERIOR**
penile bulb

*Roels et al IJROBP 2006*

# CTV modulation

| | Presaral space | Mesorectum | Internal iliac nodes | Obturator nodes | Extrenal iliac nodes | sphincter complex | ischiorectal fossae |
|---|---|---|---|---|---|---|---|
| cT3 high (above the peritoneal reflection) | + | + | + | | | | |
| cT3 mid-low (below the peritoneal reflection) | + | + | + | + | | + (when sphincter infiltration) | + (when direct tumor infiltration) |
| Any cT with massive positive internal iliac nodes | + | + | + | + | | + (when sphincter infiltration) | + (when direct tumor infiltration) |
| Any cT with massive positive obturator nodes nodes | + | + | + | + | + | + (when sphincter infiltration) | + (when direct tumor infiltration) |
| cT4 with for anterior pelvic organ | + | + | + | + | + | + (when sphincter infiltration) | + (when direct tumor infiltration) |

*Gambacorta et al. Multidisciplinary Magement of Rectal Cancer 2012*

# Inguinal nodes

RL very rare in IN: **1%**

Found in **low seated tumors**

Usually included in the CTV, in RC invading the **anus, lower third of the vagina**.

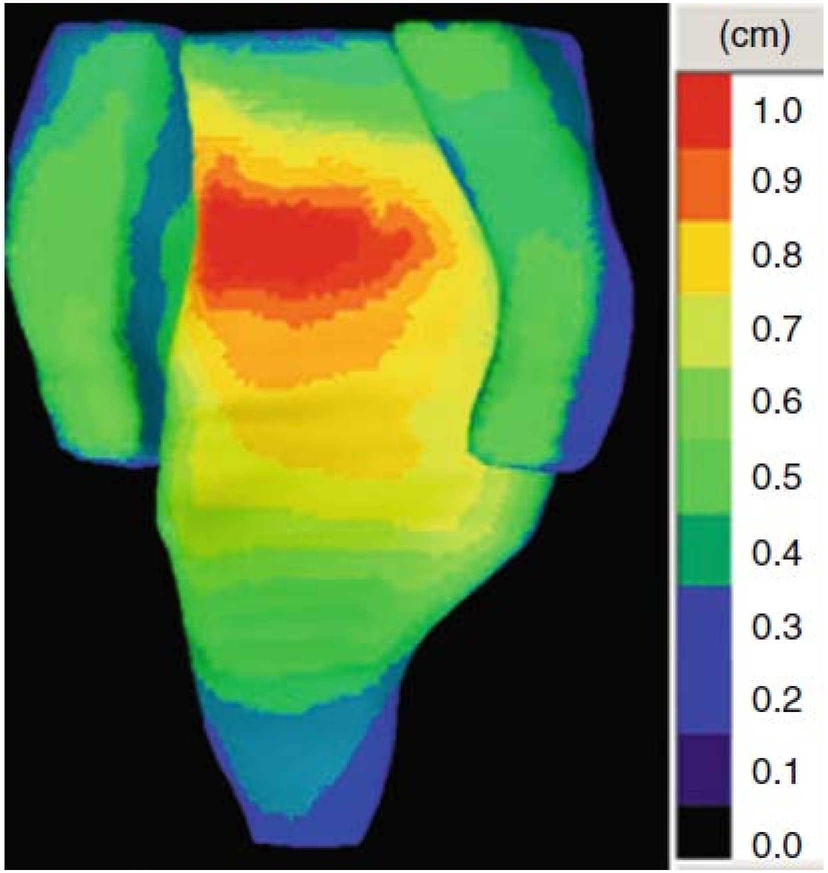
**LOW CONSENSUS**

*Roels et al IJROBP 2006*

*Myerson et al IJROBP 2009*

# PTV definition

## Shape variation




## Set-up

**Prone** up to **0.24 cm** left-right direction

**Supine < 0.1 cm**

Pts are more stable!

*Nijkamp J et al. Radiother Oncol 2009*

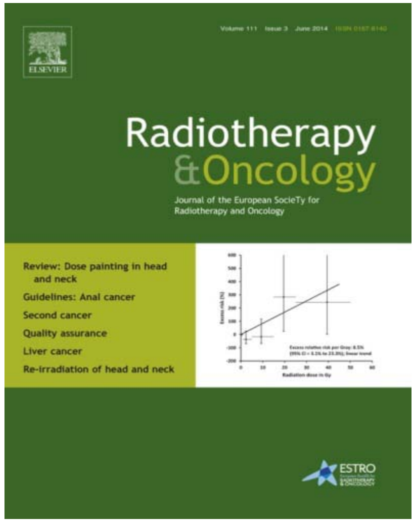
# To summarize

- Refer to **GUIDELINES** to reduce variability
- **Modulate CTV** according to T stage and T location
- Account for **CTV shape variations:** ant-sup mesorectum
- **SET-UP:**

  **Prone position** + belly board + full bladder: (less SB) in **3D**

  **Supine position**: (MORE STABLE) in **IMRT**

# ANAL CANCER




*Radiotherapy and Oncology* June 2014 111(3):330–339,

clinical practice guidelines

*Annals of Oncology* 00: 1–11, 2014
doi:10.1093/annonc/mdu159


## Anal cancer: ESMO-ESSO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

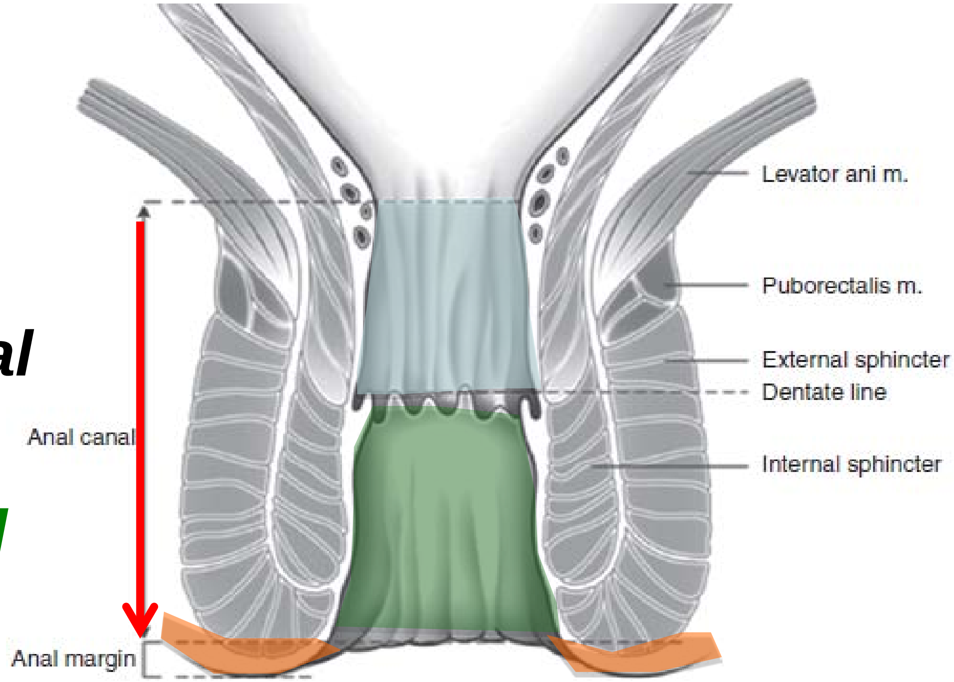
R. Glynne-Jones[1], P. J. Nilsson[2], C. Aschele[3], V. Goh[4], D. Peiffert[5], A. Cervantes[6] & D. Arnold[7]*

[1]Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, Middlesex, UK; [2]Department of Molecular Medicine and Surgery, Karolinska Institutet and Center for Surgical Gastroenterology, Karolinska University Hospital, Stockholm, Sweden; [3]Medical Oncology and Hematology, Felettino Hospital, La Spezia, Italy; [4]Division of Imaging Sciences and Biomedical Engineering, King's College London, London, UK; [5] Department of Radiotherapy, Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France; [6]Department of Hematology and Medical Oncology, INCLIVA, University of Valencia, Valencia, Spain; [7]Klinik für Tumorbiologie, Freiburg, Germany

**The anal canal extends from the anorectal junction to the anal margin**

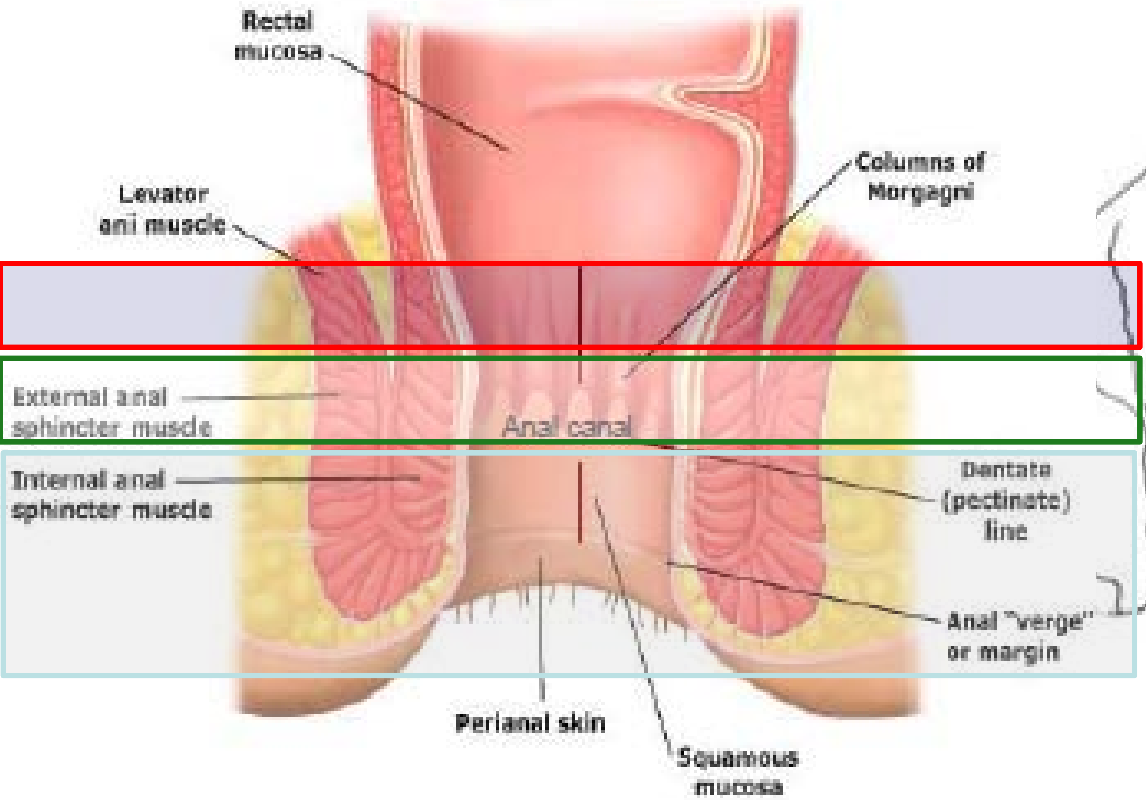
***The columnar, or cylindric, epithelium of the rectum extends to about 1 cm above the dentate line where the anal transitional zone begins.***

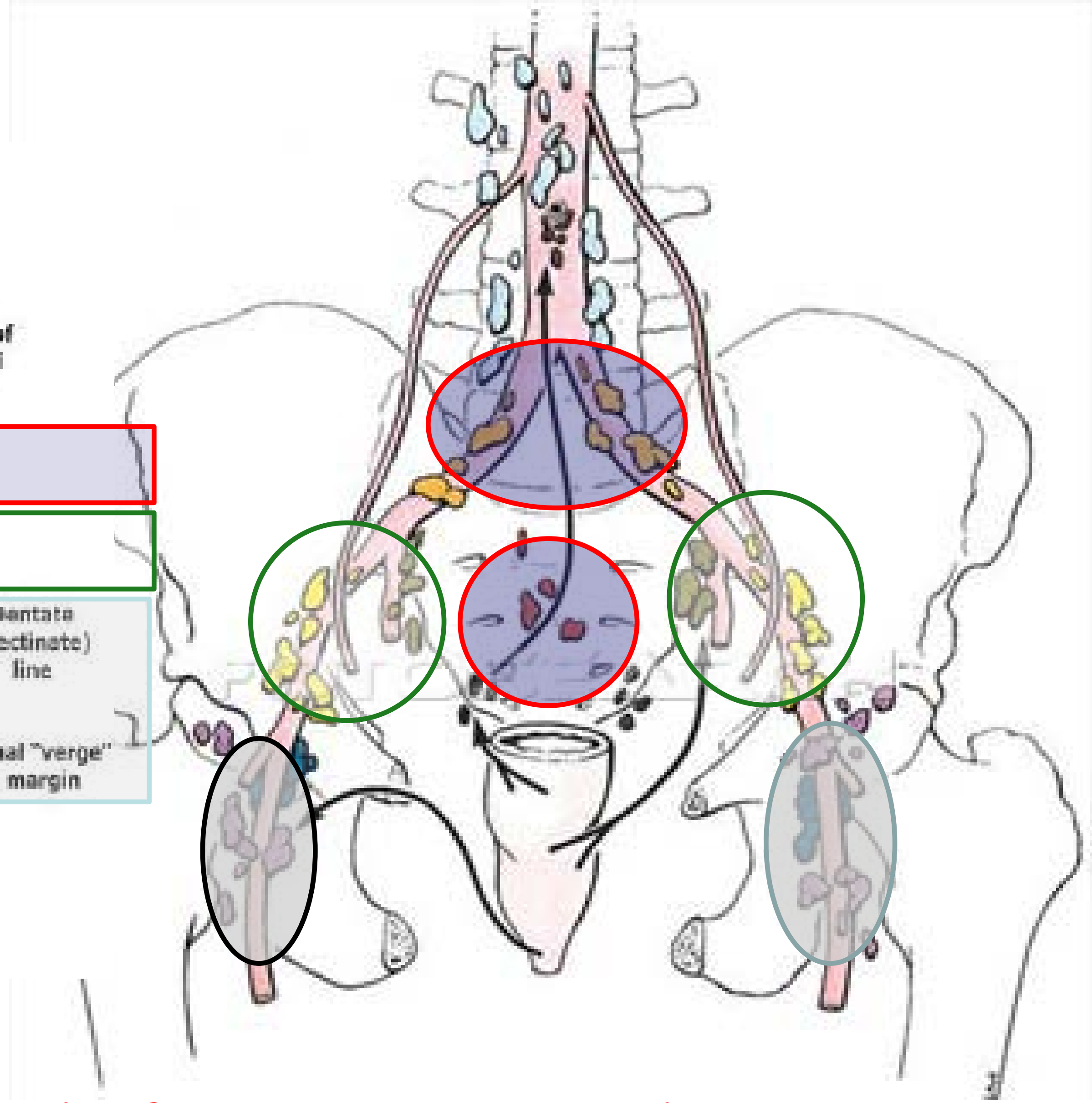
***Below the dentate line the epithelium is all squamous.***




***The anal margin is the pigmented skin immediately surrounding the anal orifice, extending laterally to a radius of approximately 5 cm.***

# LYMPHATIC PATHWAYS



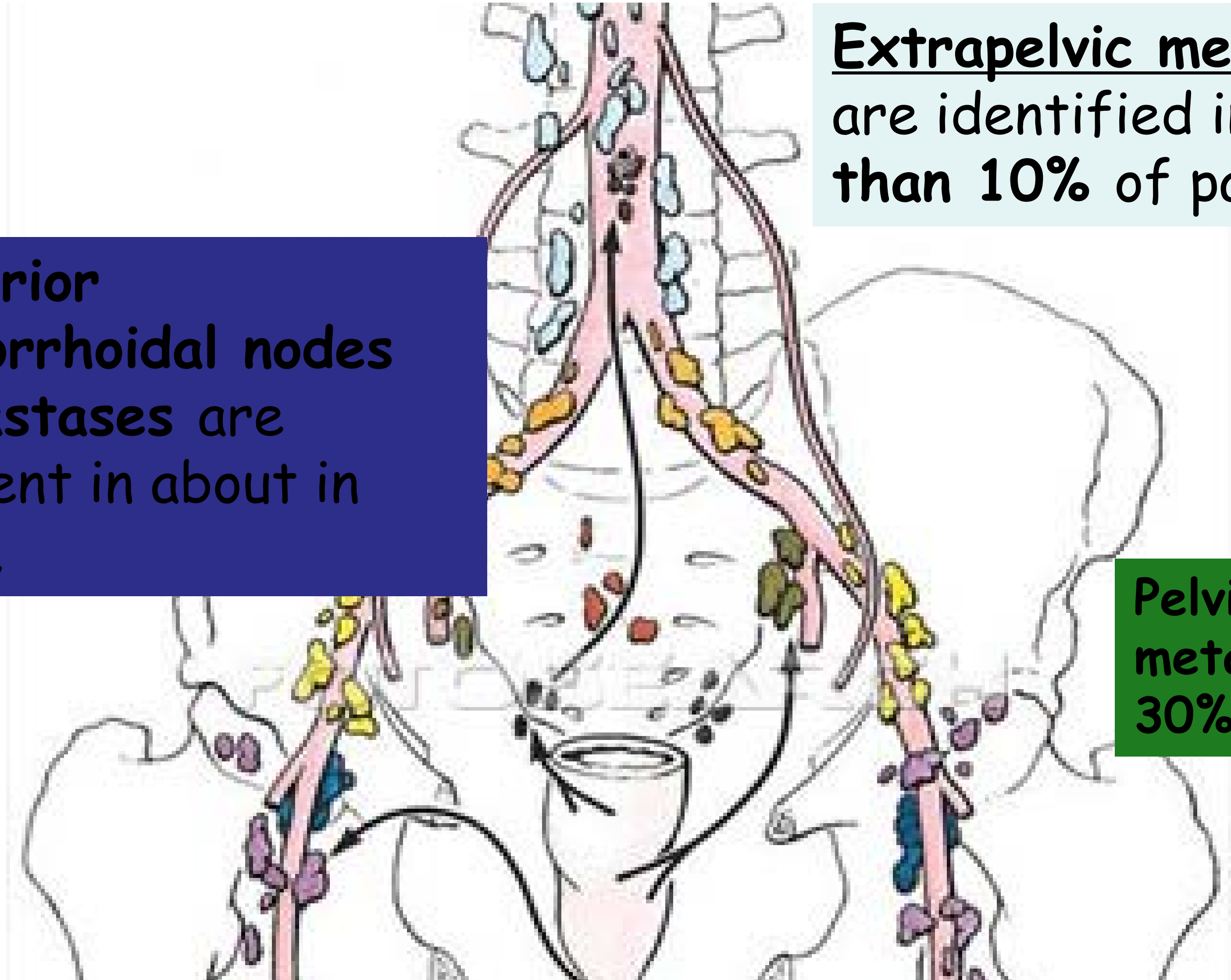



Perirectal, superior hemorroidal and inferior mesenteric nodes

Internal pudendal, hypogastric and obturator nodes

Inguinal, femoral and external iliac nodes

The overall risk of **regional nodal involvement** at diagnosis is about **25%.**



**Extrapelvic metastases** are identified in **fewer than 10%** of patients.

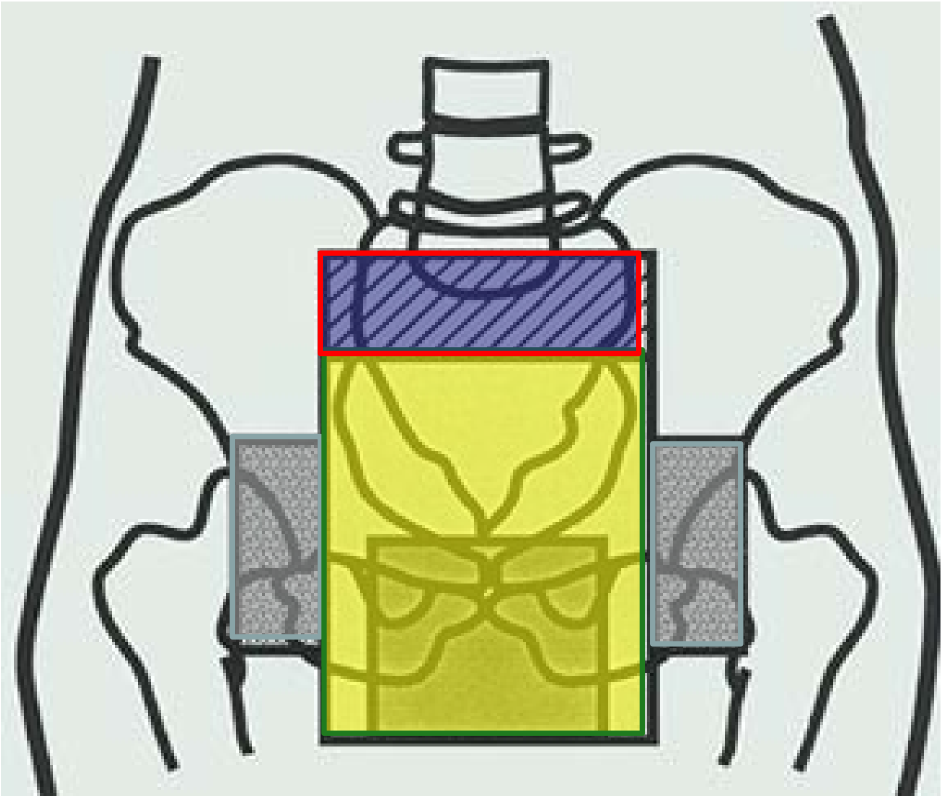
**Superior hemorrhoidal nodes metastases** are present in about in **25%,**

**Pelvic nodes metastases** in **30%**

**Inguinal metastases are clinically detectable in up to 20% of patients at initial diagnosis and are present subclinically in a further 10% to 20%.**

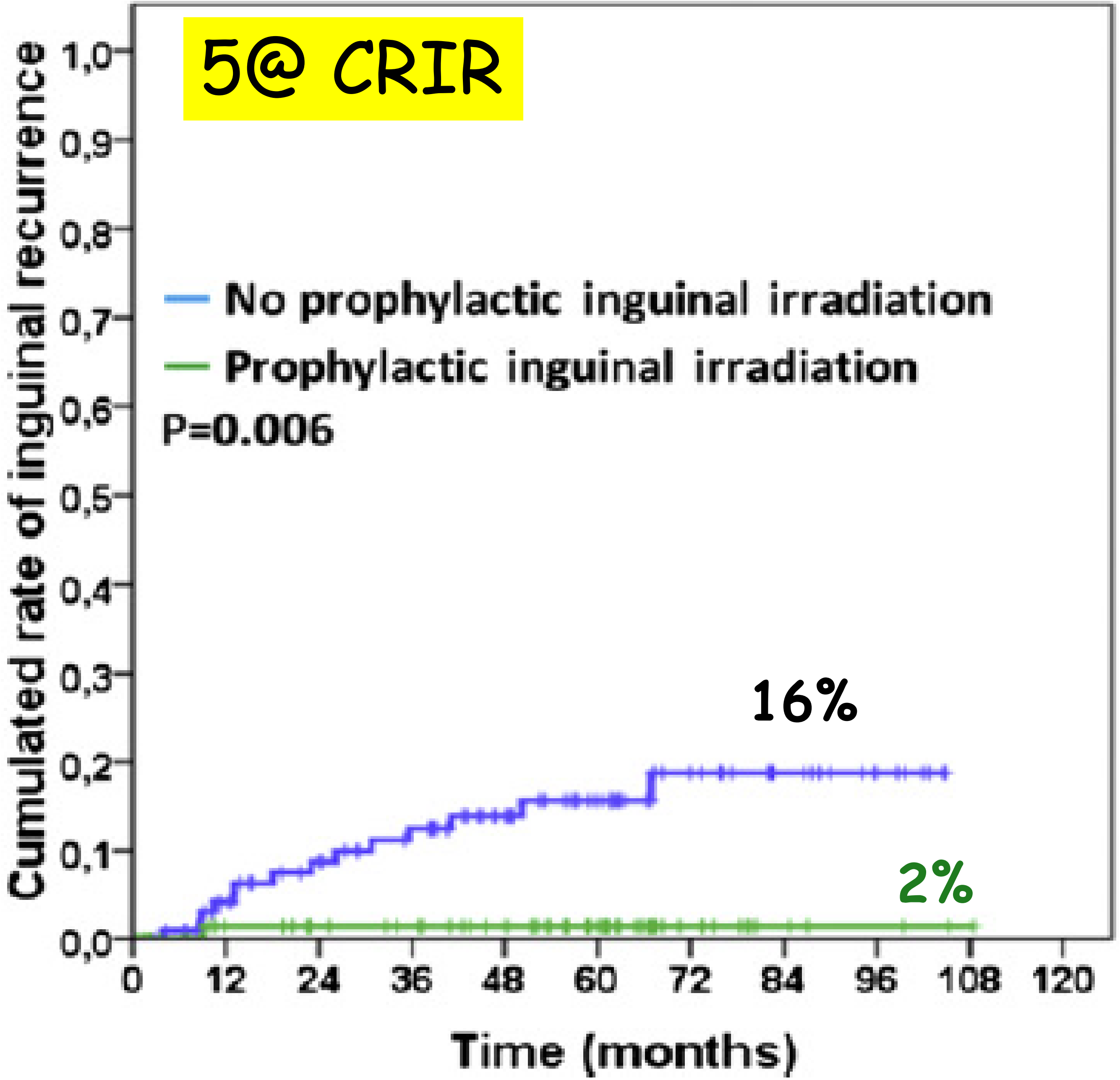
The finding in surgical series of histopathologically verified metastases in the **pararectal and internal iliac nodes in up to 30%** and in **inguinal nodes in up to 20%** has encouraged most centers to irradiate these node groups electively.

**As a result,**
**planning target volumes**
**may be extensive.**



Only well-differentiated squamous cell cancers $\leq$2 cm in size situated in the distal canal appear to have a risk of nodal metastases <5%.

# PROPHYLACTIC INGUINAL IRRADIATION




In the PII group 5-year CRIR was significantly lower (p= 0.006)

In the PII group, no Grade >2 toxicity of the lower extremity was observed

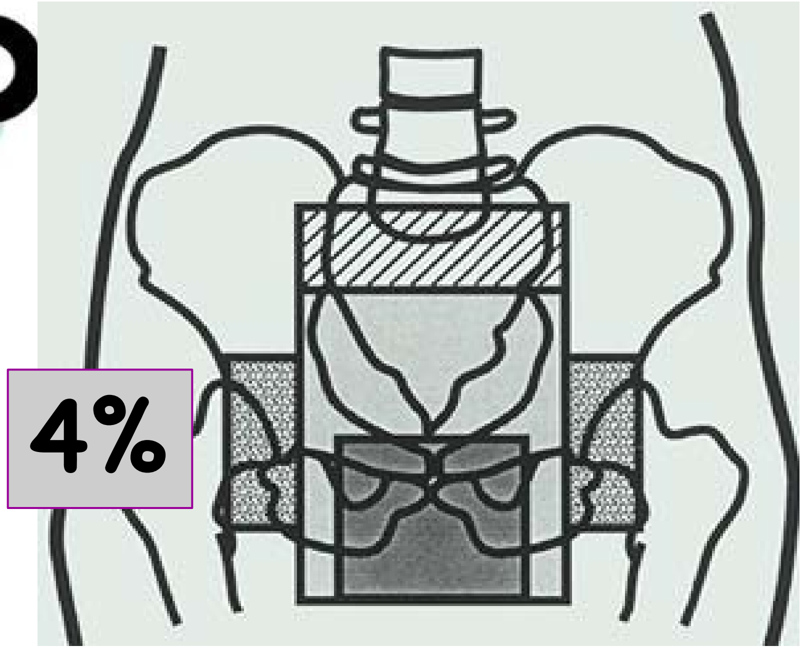
In the no PII group, the 5-year CRIR was 12% and 30% for T1-T2 and T3-T4 respectively (p = 0.02).

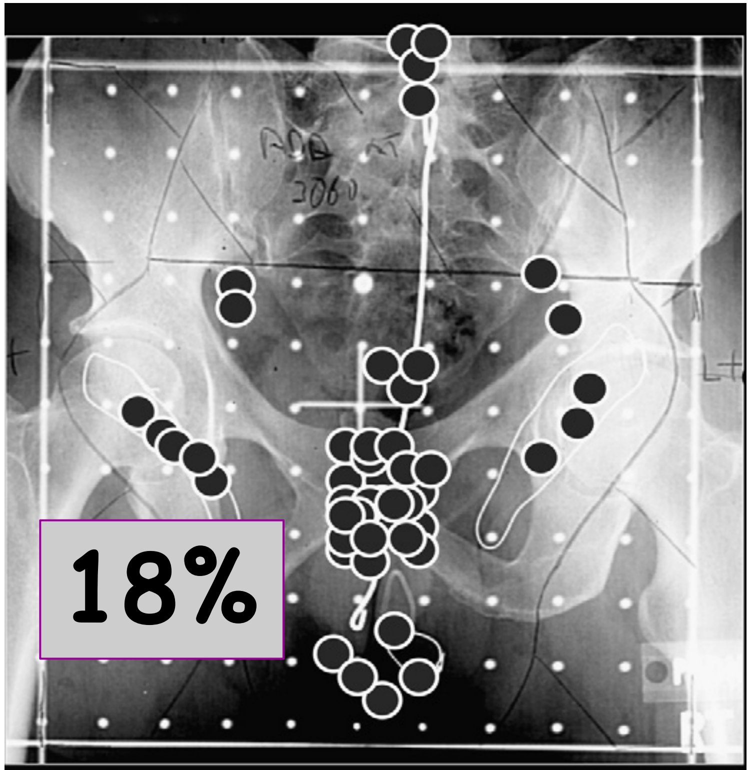
In the PII group, the 5-year CRIR was not different in T1-2 vs T3-4 (0% vs 3%)

PII didn't affect OS and DFS

C. ORTHOLAN et al. Int. J. Radiation Oncology Biol. Phys., 2012

# Critical issues: inguinal nodes

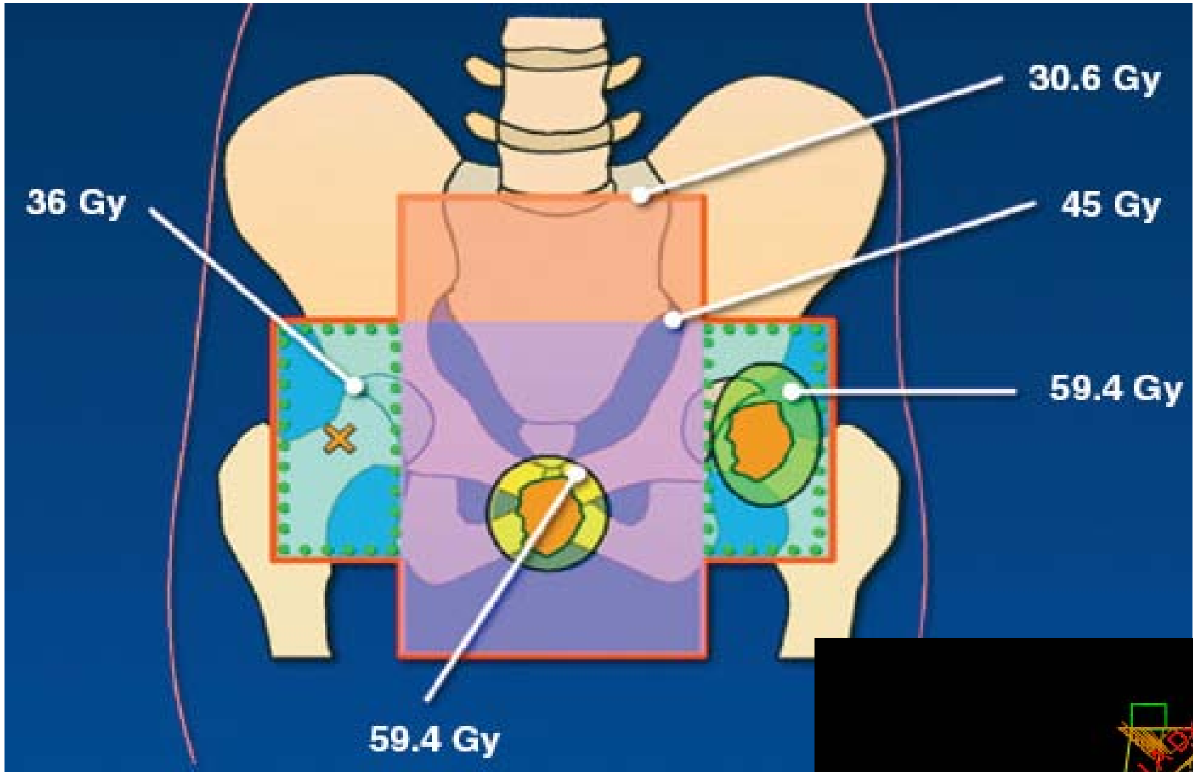


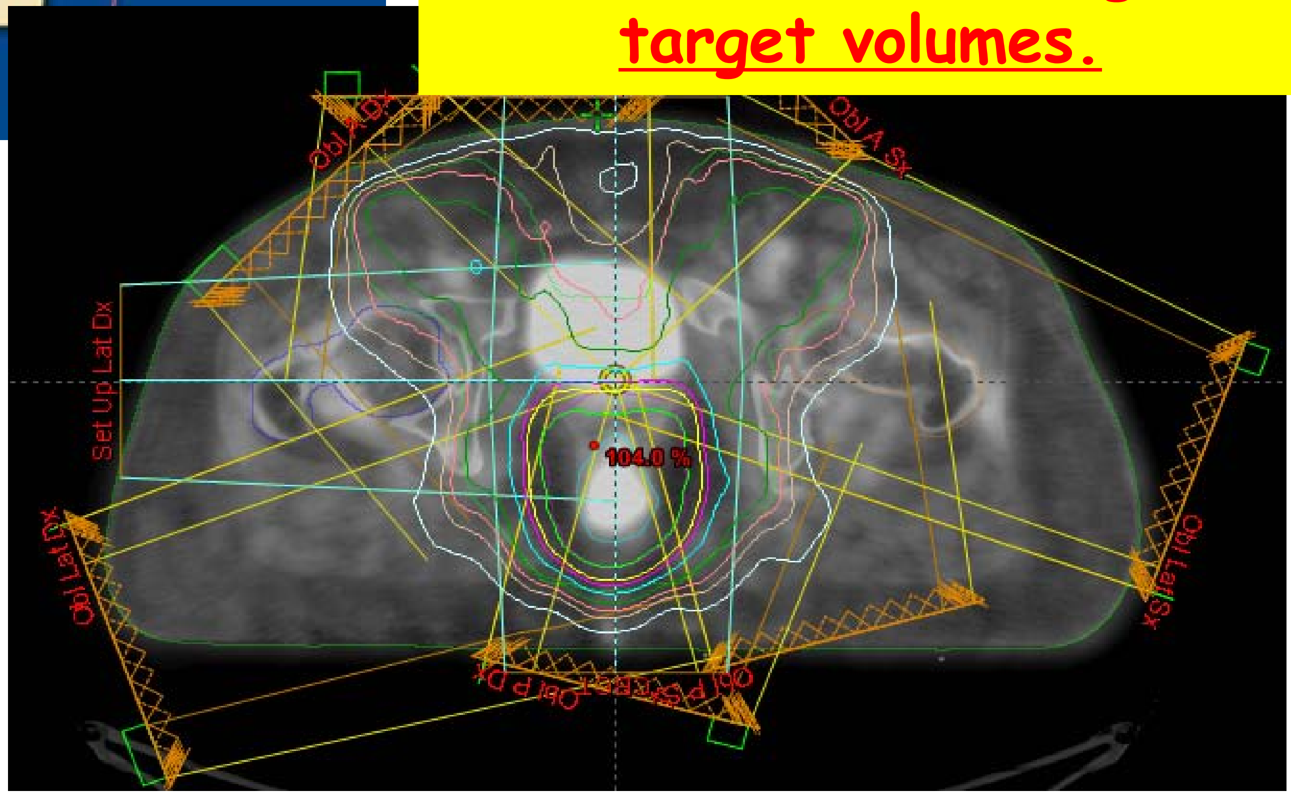

This difference may be related to the higher dose delivered to **involved inguinal nodes** in study of Das P. et al (**55 Gy**) vs the prescribed dose to the inguinal nodes in all inguinal failures in the study of Wright et al. was **45 Gy**.

J. L. Wright et al, Int. J. Radiation Oncology Biol. Phys. 2010

P. Das et al, Int. J. Radiation Oncology Biol. Phys. 2007

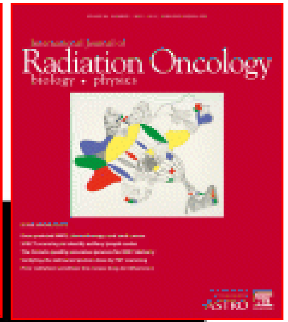



With the advent of CT-planning
and conformal radiation techniques including **IMRT**, comes the **prerequisite** for **accurate and consistent contouring of target volumes.**

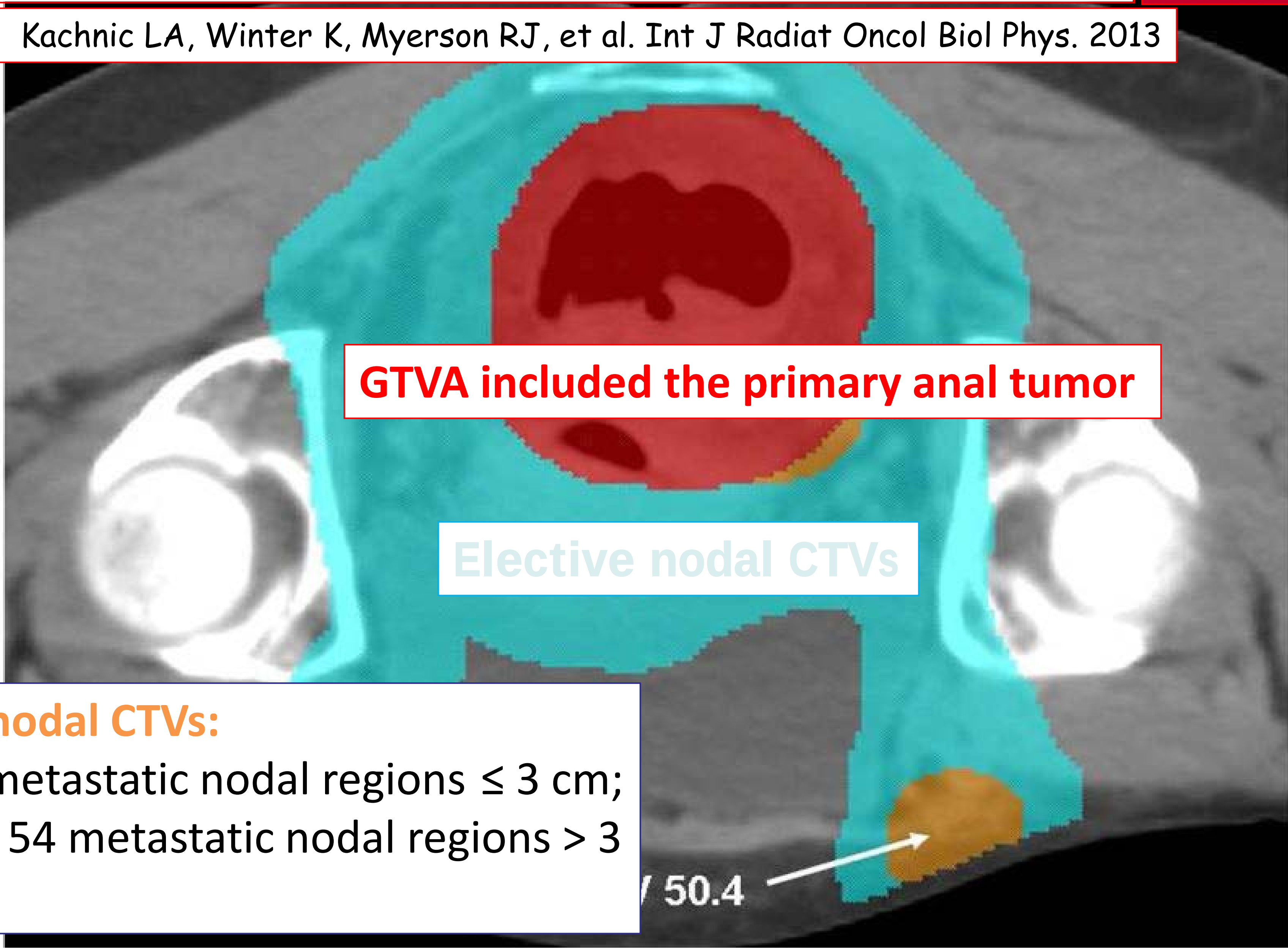


Clinical Investigation: Gastrointestinal Cancer

# RTOG 0529: A Phase 2 Evaluation of Dose-Painted Intensity Modulated Radiation Therapy in Combination With 5-Fluorouracil and Mitomycin-C for the Reduction of Acute Morbidity in Carcinoma of the Anal Canal




Kachnic LA, Winter K, Myerson RJ, et al. Int J Radiat Oncol Biol Phys. 2013




GTVA included the primary anal tumor

Elective nodal CTVs

**Involved nodal CTVs:**
CTVN 50 metastatic nodal regions ≤ 3 cm; and CTVN 54 metastatic nodal regions > 3 cm.

Clinical Investigation: Gastrointestinal Cancer

# RTOG 0529: A Phase 2 Evaluation of Dose-Painted Intensity Modulated Radiation Therapy in Combination With 5-Fluorouracil and Mitomycin-C for the Reduction of Acute Morbidity in Carcinoma of the Anal Canal


Kachnic LA, Winter K, Myerson RJ, et al. Int J Radiat Oncol Biol Phys. 2013

## Radiation Planning Quality Assurance

Of the 52 DP-I … n initial
submission, 46 … assed. Incorrect
investigator co … ), miscontouring
of elective nod … 33%, iliac
nodal groups 3 … el 60%, large
bowel 45%). E … ption and
normal tissue … ent for tumor
dosing, and 39 … femoral head
coverage. On … cerning target
dosing, and on … nvestigators
who did not at … s considered
reproducible i…

### Incorrect contouring (81%)

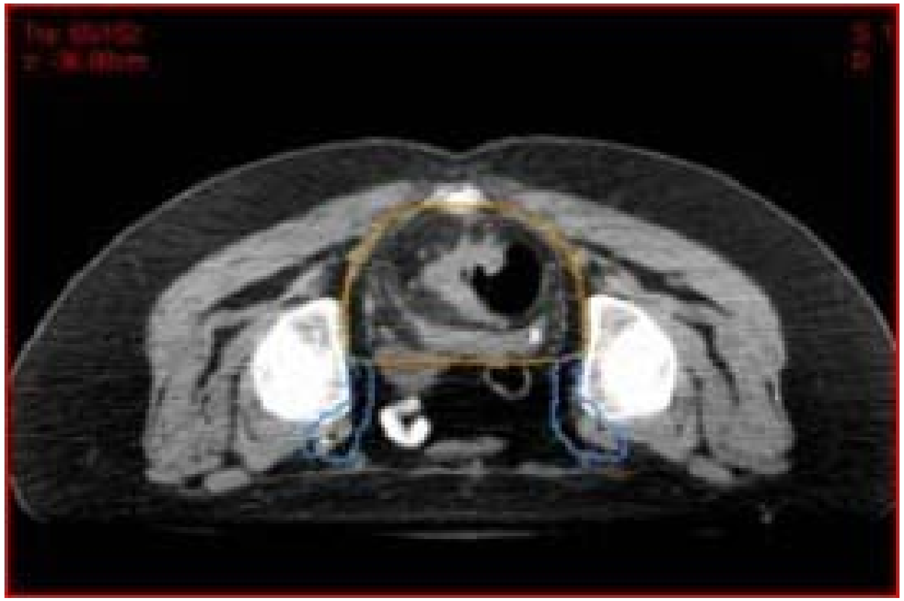
| | |
|---|---|
| **GTV:** | **21%** |
| **CTV elective N:** | |
| Mesorectum | 55% |
| Presacrum | 43% |
| Inguinal fossa | 33% |
| Iliac nodes | 31% |

CLINICAL INVESTIGATION Rectum

ELECTIVE CLINICAL TARGET VOLUMES FOR CONFORMAL THERAPY IN ANORECTAL CANCER: A RADIATION THERAPY ONCOLOGY GROUP CONSENSUS PANEL CONTOURING ATLAS


# Elective nodal CTVs

CTVA: internal iliac, pre-sacral, peri-rectal.
CTVB: external iliac nodal region
CTVC: inguinal nodal region



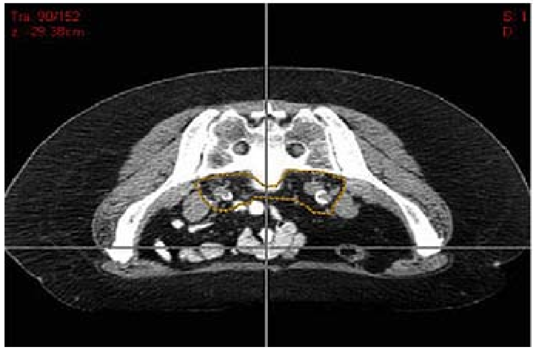
LIMITATIONS:
•no clear definition of the different anatomical boundaries

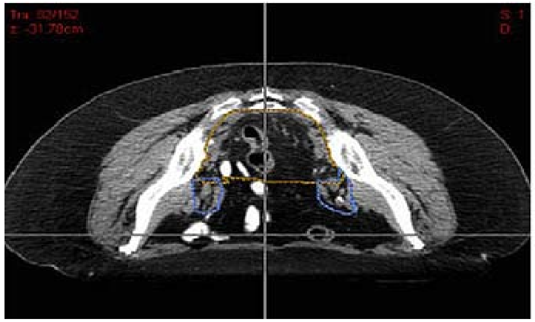
Myerson RJ, Garofalo MC, El Naqa I, et al. Int J Radiat Oncol Biol Phys. 2009

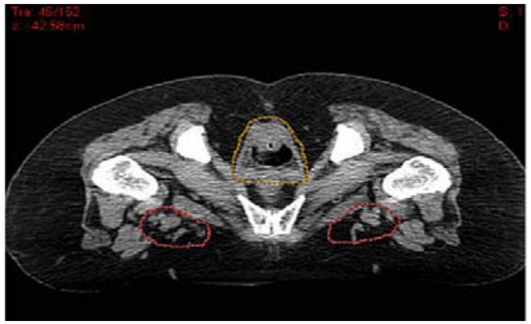
**CLINICAL INVESTIGATION** Rectum

ELECTIVE CLINICAL TARGET VOLUMES FOR CONFORMAL THERAPY IN ANORECTAL CANCER: A RADIATION THERAPY ONCOLOGY GROUP CONSENSUS PANEL CONTOURING ATLAS


# CTVA: internal iliac, pre-sacral, peri-rectal







**Cranial:**

- Bifurcation of the common iliac vessels into external/internal iliacs (bony landmark: sacral promontory)
- Recto-sigmoid junction

**Anterior:**

- 1 cm anterior to the sacrum
- Perirectal fascia
- 1 cm into the bladder
- Pelvic organs

sup → inf

**Lateral and posterior:**

- Pelvic side-wall muscles or bones

**Caudal:**

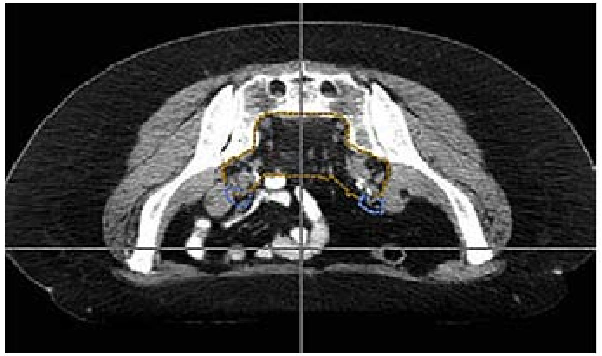
Anal canal + 2 cm around, the anal verge
Anal skin involved + 2 cm beyond

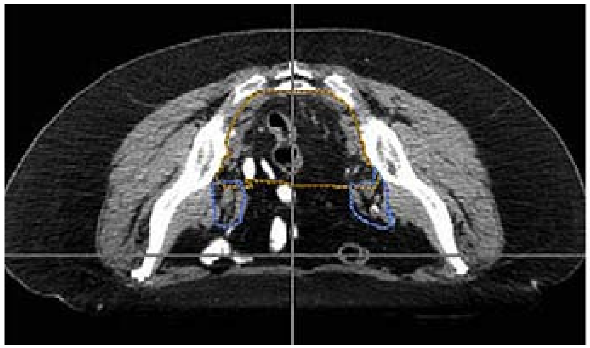
Myerson RJ, Garofalo MC, El Naqa I, et al. Int J Radiat Oncol Biol Phys. 2009

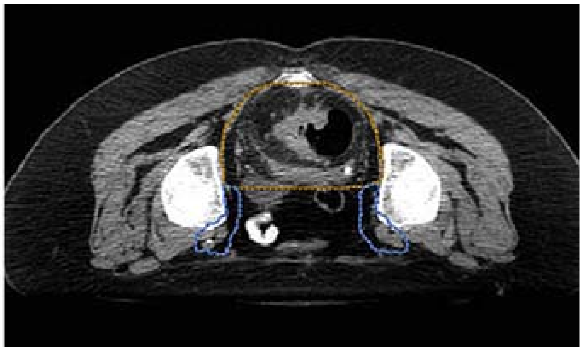
**CLINICAL INVESTIGATION** Rectum

**ELECTIVE CLINICAL TARGET VOLUMES FOR CONFORMAL THERAPY IN ANORECTAL CANCER: A RADIATION THERAPY ONCOLOGY GROUP CONSENSUS PANEL CONTOURING ATLAS**


# CTVB: external iliac nodal region







**Cranial:**

Bifurcation of the common iliac vessels into external/internal iliacs

(bony landmark: sacral promontory)

**Anterior-medial:**

0.7-0.8 cm around the vessels

≥1 cm antero-laterally in case of small vessels or nodes are identified in this area

**Lateral:**

Muscles and pelvic bones

**Posterior:**

CTVA

**Caudal:**

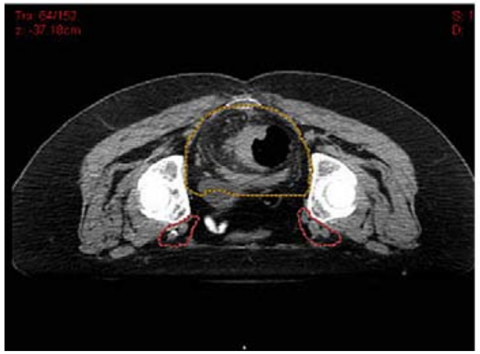
caudad edge of internal obturator vessels (bony landmark: upper edge of the superior rami pubic)

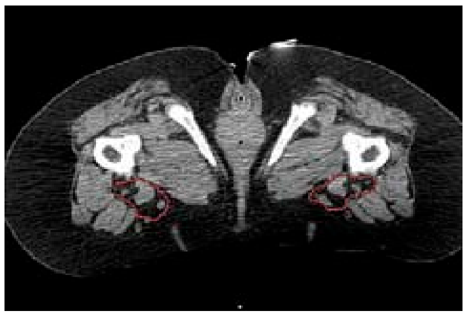
Myerson RJ, Garofalo MC, El Naqa I, et al. Int J Radiat Oncol Biol Phys. 2009

**CLINICAL INVESTIGATION** **Rectum**

**ELECTIVE CLINICAL TARGET VOLUMES FOR CONFORMAL THERAPY IN ANORECTAL CANCER: A RADIATION THERAPY ONCOLOGY GROUP CONSENSUS PANEL CONTOURING ATLAS**


# CTVC: inguinal nodal region





**Cranial:**

caudad edge of internal obturator vessels (bony landmark: upper edge of the superior rami pubic)

**Caudal:**

2 cm below the saphenous-femural junction

**Margin around the vessels:**

The inguinal femural region should be contoured as a compartment with any identified nodes (expecially in the lateral inguinal region) included

**IF AUTOMATED EXPANSION ARE USED, THE CTV SHOULD BE TRIMMED OFF UNINVOLVED BONE AND MUSCLES**

Myerson RJ, Garofalo MC, El Naqa I, et al. Int J Radiat Oncol Biol Phys. 2009

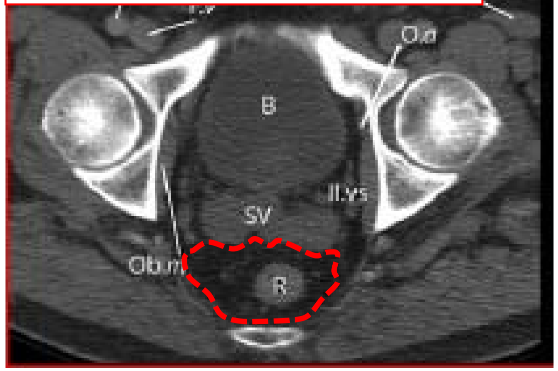
Clinical Investigation: Gastrointestinal Cancer

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

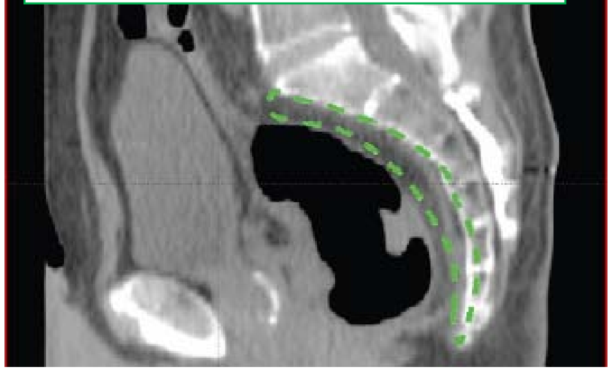

M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

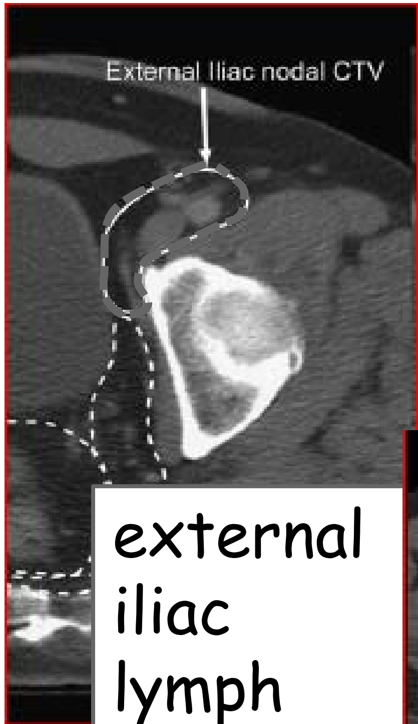
## ELECTIVE NODAL VOLUMES

mesorectum

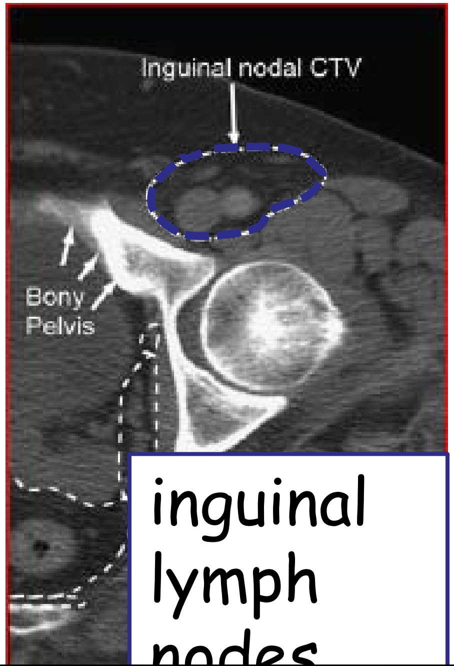



presacral space



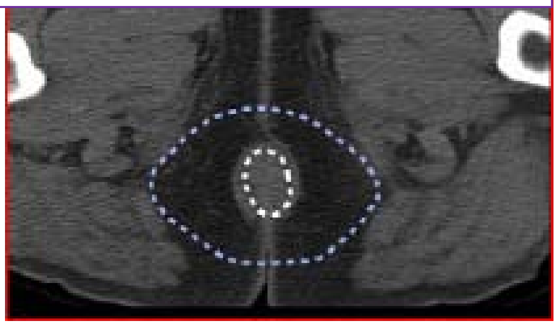



external iliac lymph nodes

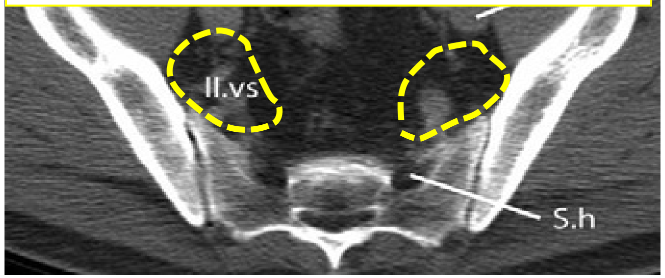


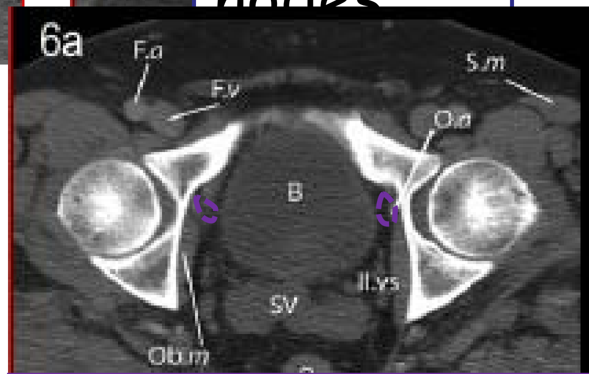

inguinal lymph nodes

ischiorectal fossa



internal iliac lymph nodes

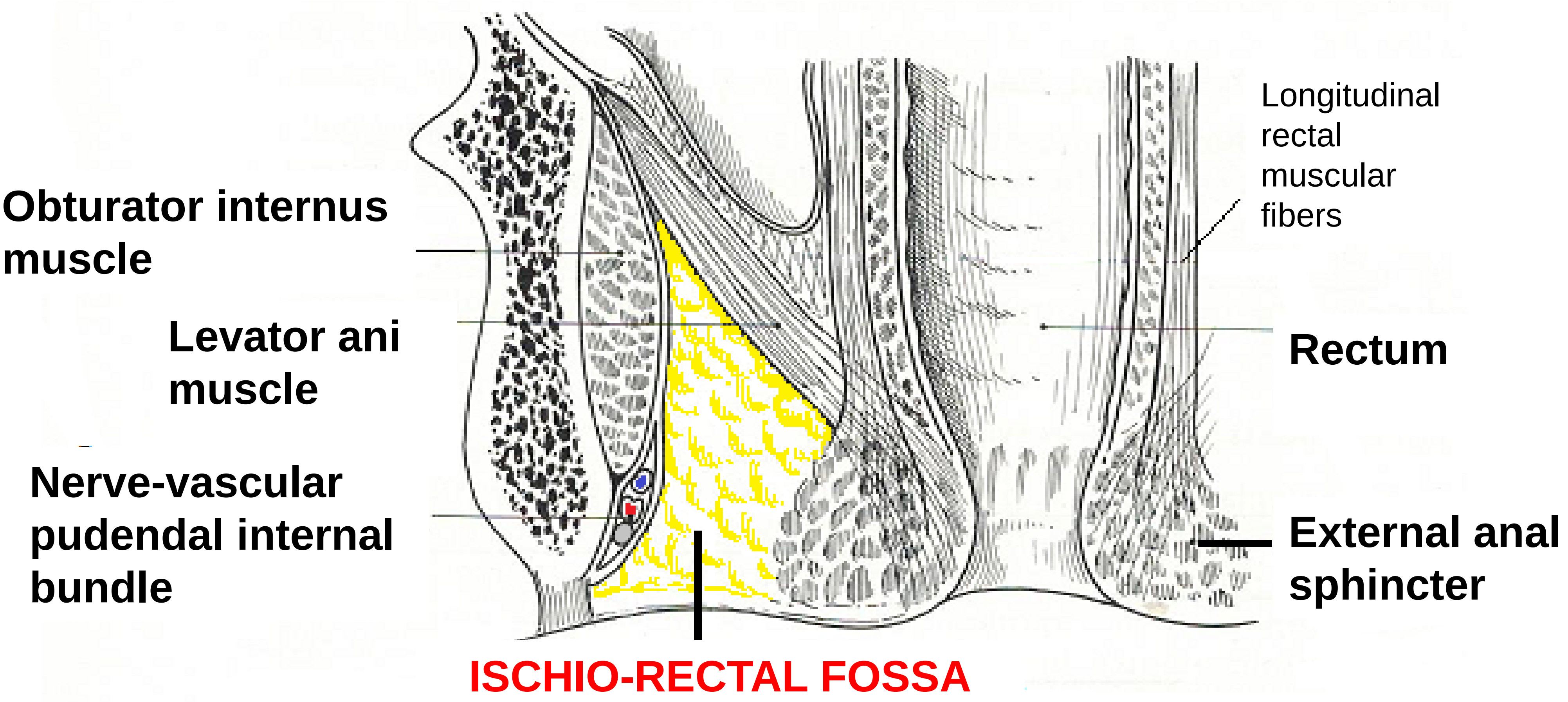



obturator lymph nodes

CTV borders for individual nodal groups

# ISCHIORECTAL FOSSA



# ISCHIORECTAL FOSSA

Cranial = levator ani, gluteus maximus, and obturator internus

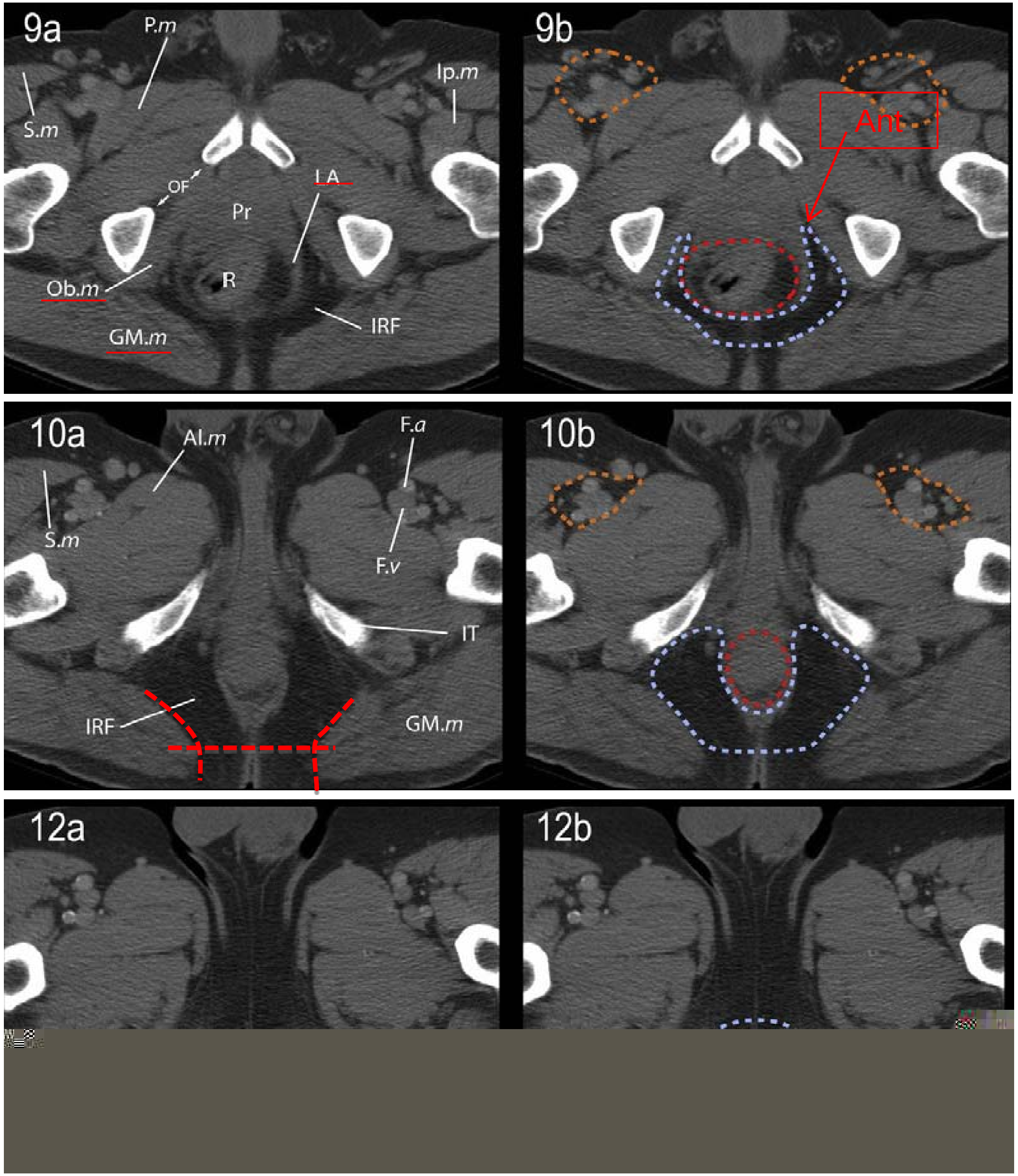
Anterior = at the level where the obturator internus muscle, levator ani, and anal sphincter muscles fuse.

.

Posterior = a transverse plane joining the anterior edge of the medial walls of the gluteus maximus muscle.

Lateral =, obturator internus, ischial tuberosity and gluteus maximus muscles

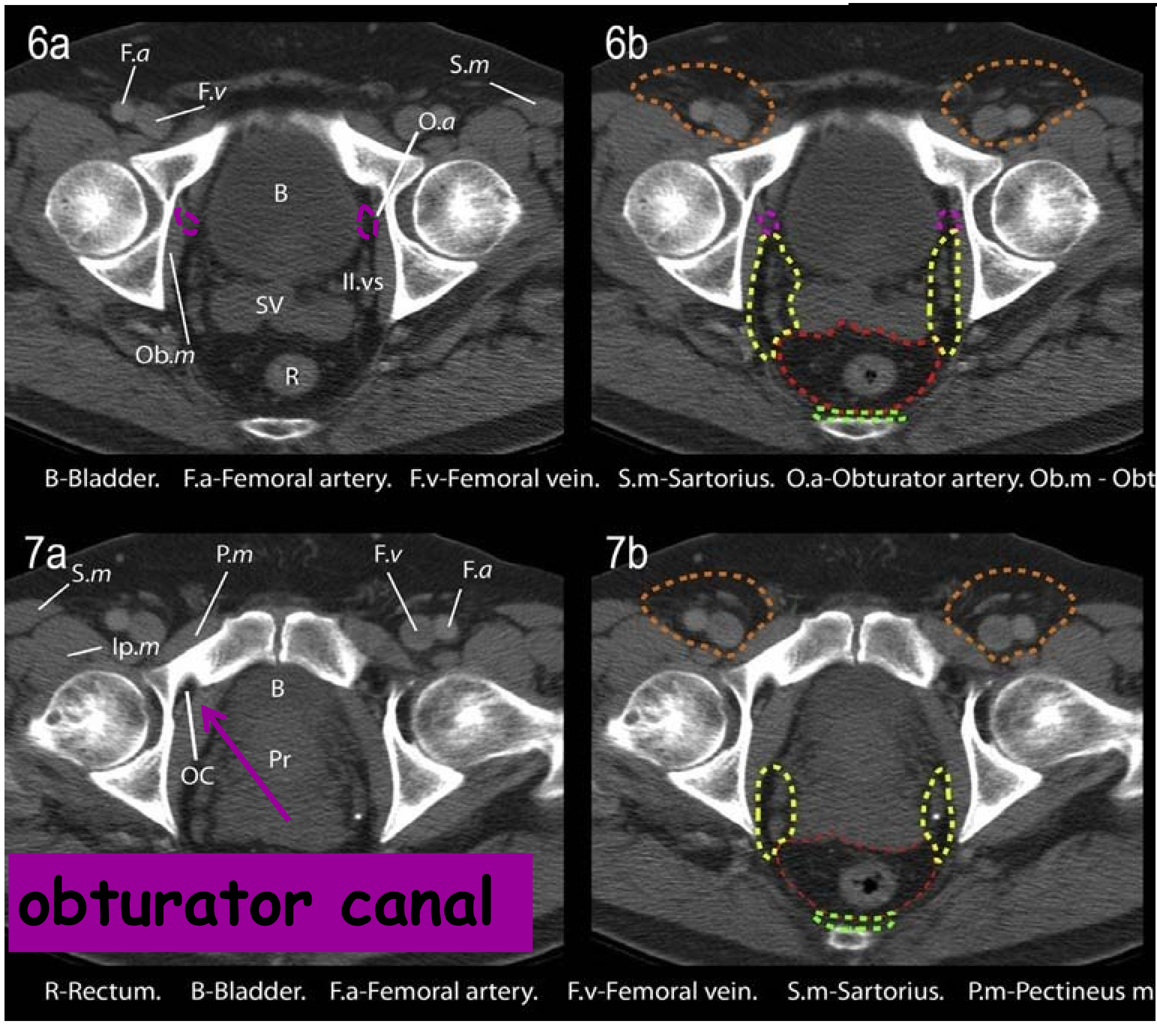
Caudal =at the level of the anal verge




M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

# OBTURATOR LYMPH NODES

Along the obturator artery, a branch of the internal iliac artery that usually starts at the level of the acetabulum, and exits via the obturator canal.




Cranial = 3 to 5 mm cranial to the obturator canal where the obturator artery is sometimes visible.

Caudal =The obturator canal,where the obturator artery has exited the pelvis.

Anterior = The anterior extent of the obturator internus muscle.

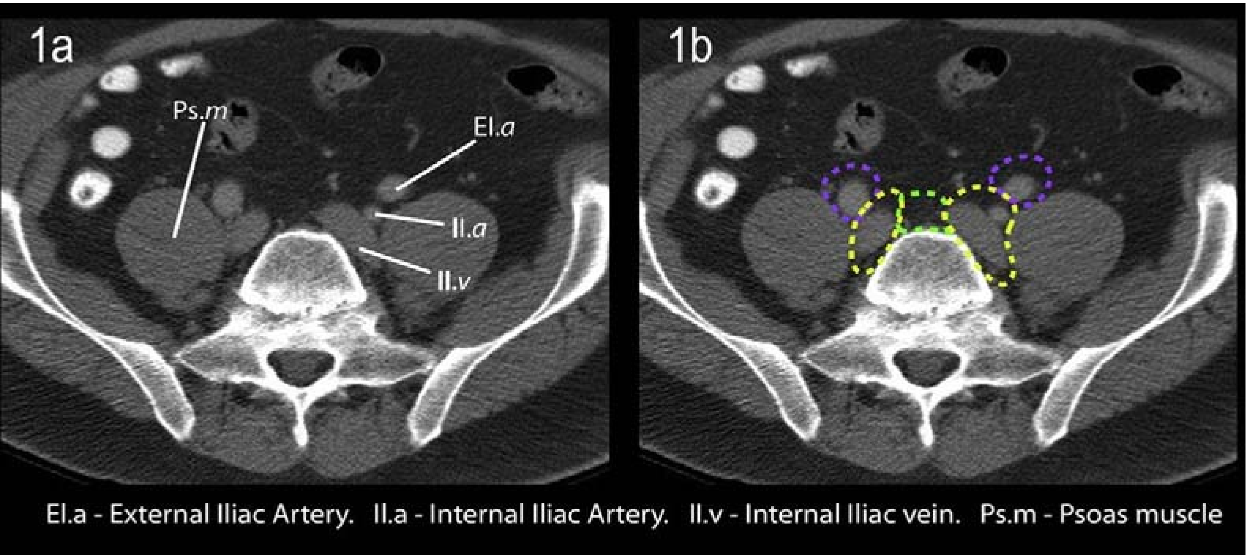
Posterior = The internal iliac lymph node group.

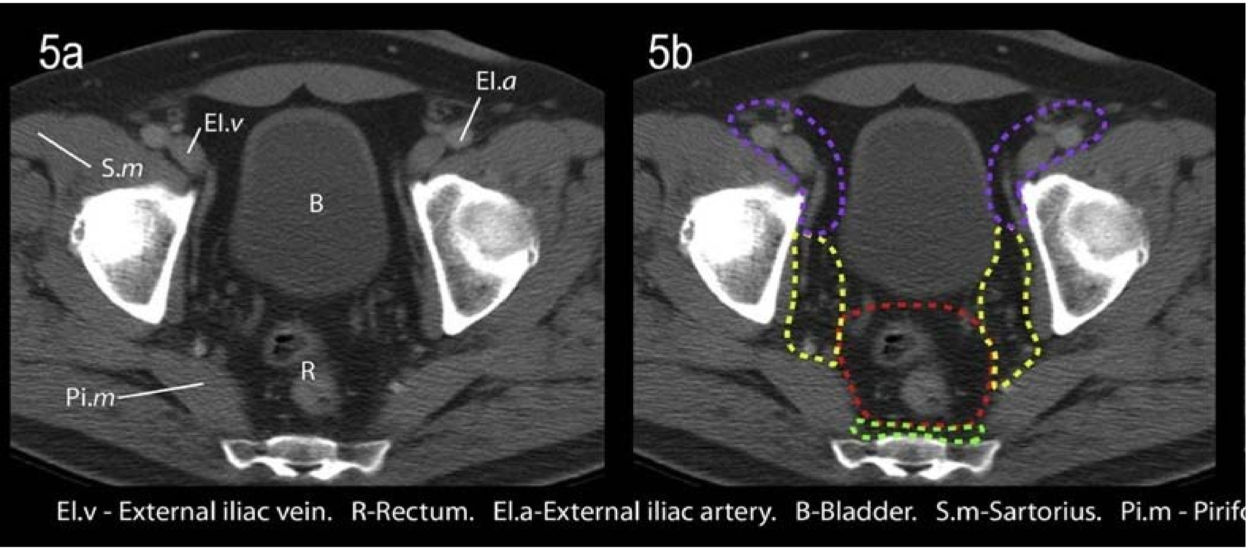
Lateral = The obturator internus muscle.

Medial = The bladder.

M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

# EXTERNAL ILIAC LYMPH NODES




<u>Cranial</u> = Bifurcation of the common iliac artery into the external and internal iliac arteries.

<u>Lateral</u> =The iliopsoas muscle

<u>Medially</u> = the bladder or a 7-mm margin around the vessels

<u>Anterior</u> = A 7-mm margin anterior to the external iliac vessels, 1.5 cm antero-laterally along the iliopsoas muscle to include the antero-lateral nodes

<u>Posterior</u> = The internal iliac lymph node group

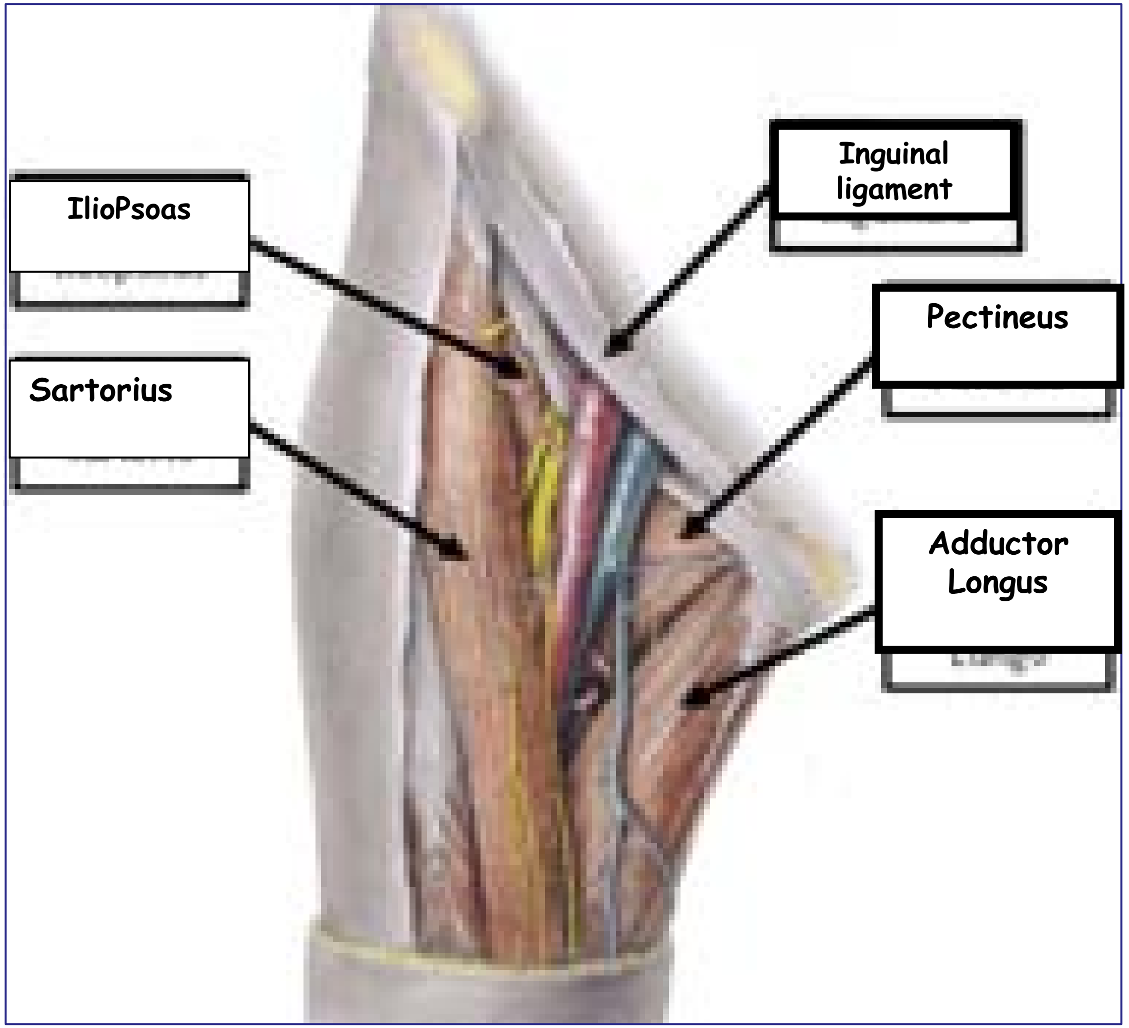
<u>Caudal</u> =The level where the external iliac vessels are still located within the bony pelvis before continuing as the femoral. This transition usually occurs between the <u>acetabulum's roof and the superior pubic rami</u>


M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

Taylor A et al. Clin Oncol (R Coll Radiol). 2007

# INGUINAL LYMPH NODES

- Is an area bounded posteriorly by triangle formed by ilio-psoas, pectineus and abductor longus muscles
- At least a margin of 1-2 cm around the vessels antero-laterally should be added
- Superficial and deep nodes and any visible node or lymphcoeles outside the folowing boundaries should be included

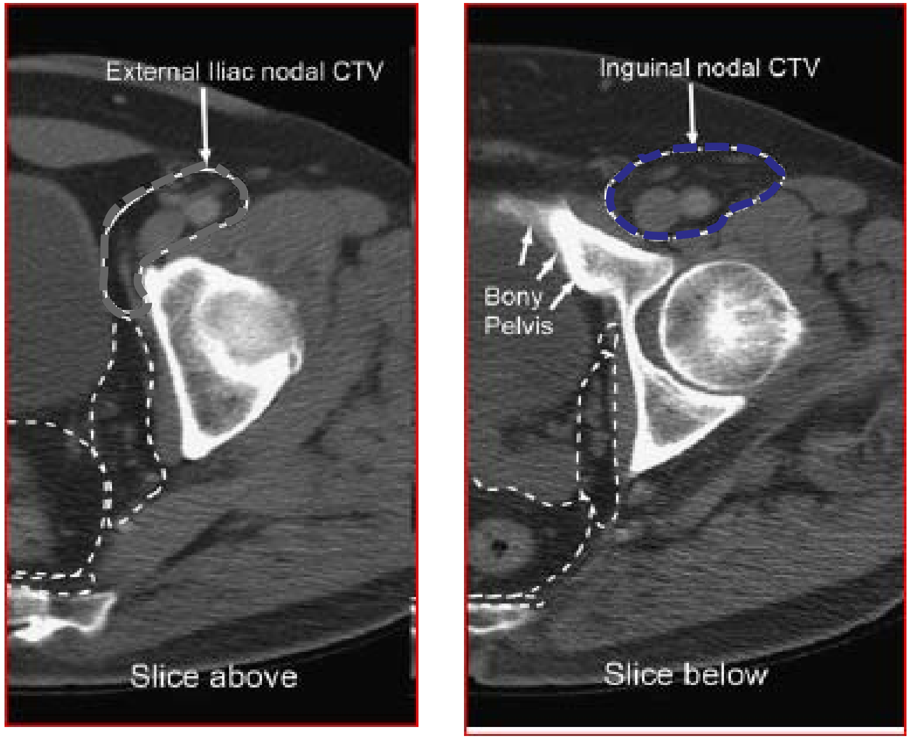



Taylor A et al. Clin Oncol (R Coll Radiol). 2007

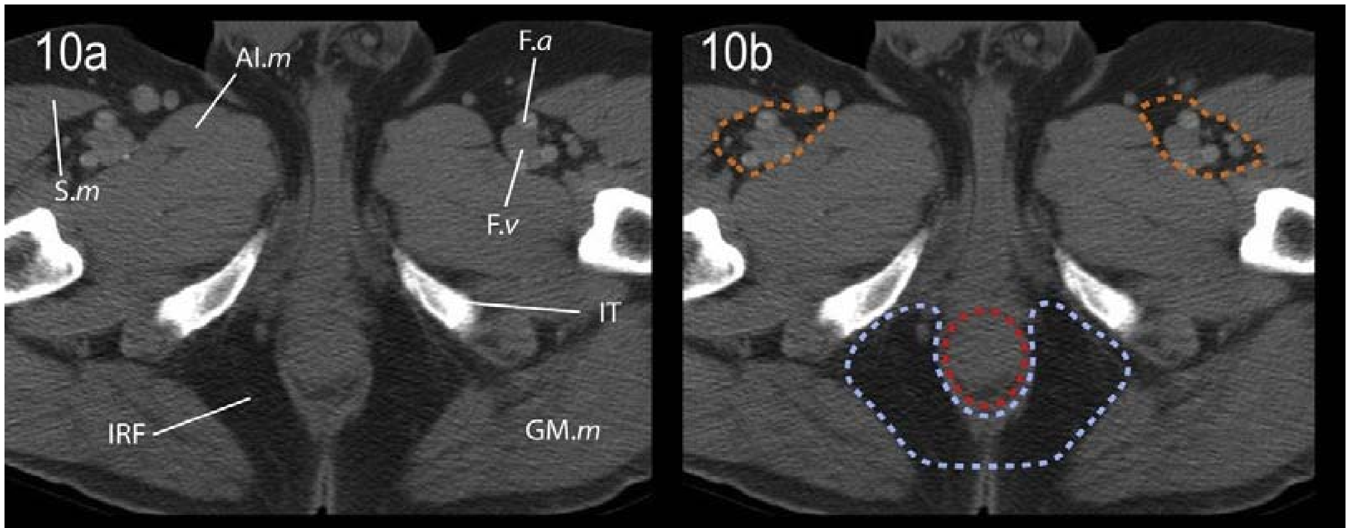
M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

# INGUINAL LYMPH NODES

Cranial =The level where the external iliac artery leaves the bony pelvis to become the femoral artery (acetabulum roof and superior pubic rami)




Caudal = lower edge of the ischial tuberosities

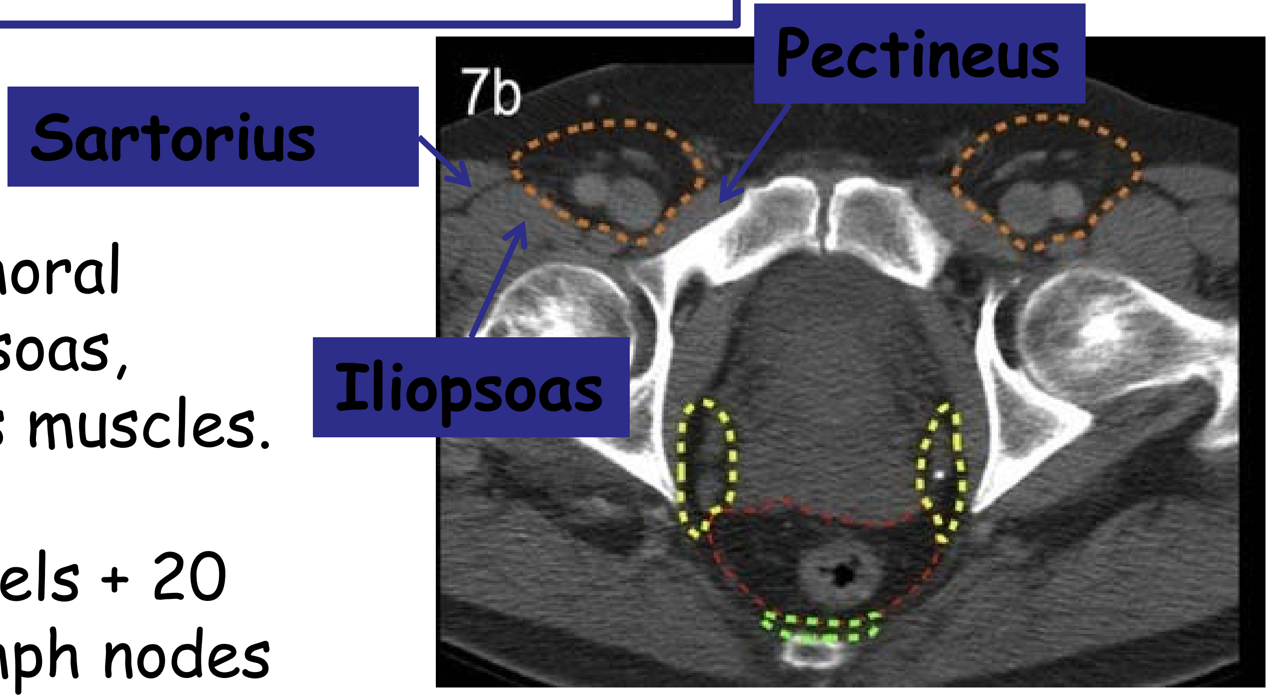



A-Anal canal. Sp.m-Sphincter muscles. IRF-Ischiorectal fossa. F.a-femoral artery. F.v-Femoral vein

Taylor A et al. Clin Oncol (R Coll Radiol). 2007

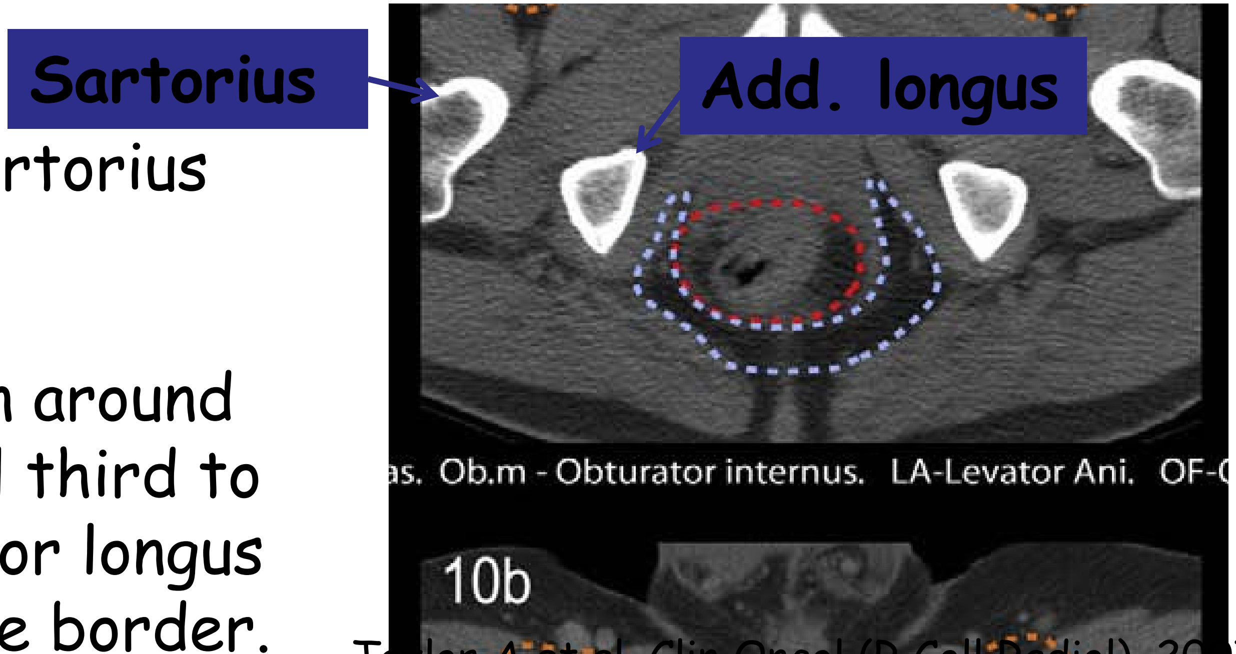
M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

# INGUINAL LYMPH NODES




Posterior =The bed of the femoral triangle is formed by the iliopsoas, pectineus, and adductor longus muscles.

Anterior = on the inguinal vessels + 20 mm, inclusive of any visible lymph nodes or lymphocoeles



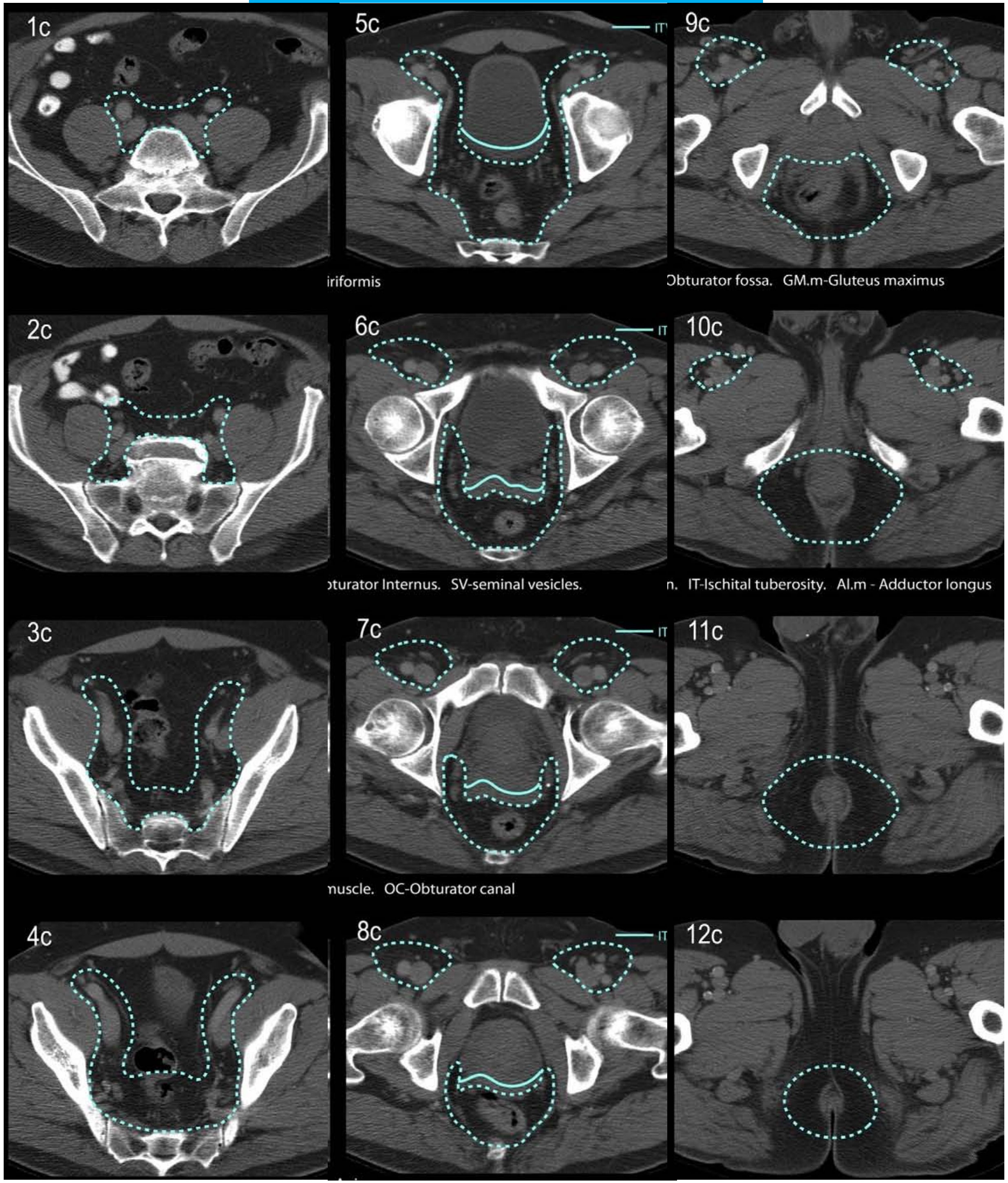

Lateral = The medial edge of sartorius or iliopsoas

Medial = A 10- to 20-mm margin around the femoral vessels. The medial third to half of the pectineus or adductor longus muscle serves as an approximate border.

Taylor A et al. Clin Oncol (R Coll Radiol). 2007

M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

# CTV COMBINED



Clinical Investigation: Gastrointestinal Cancer

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

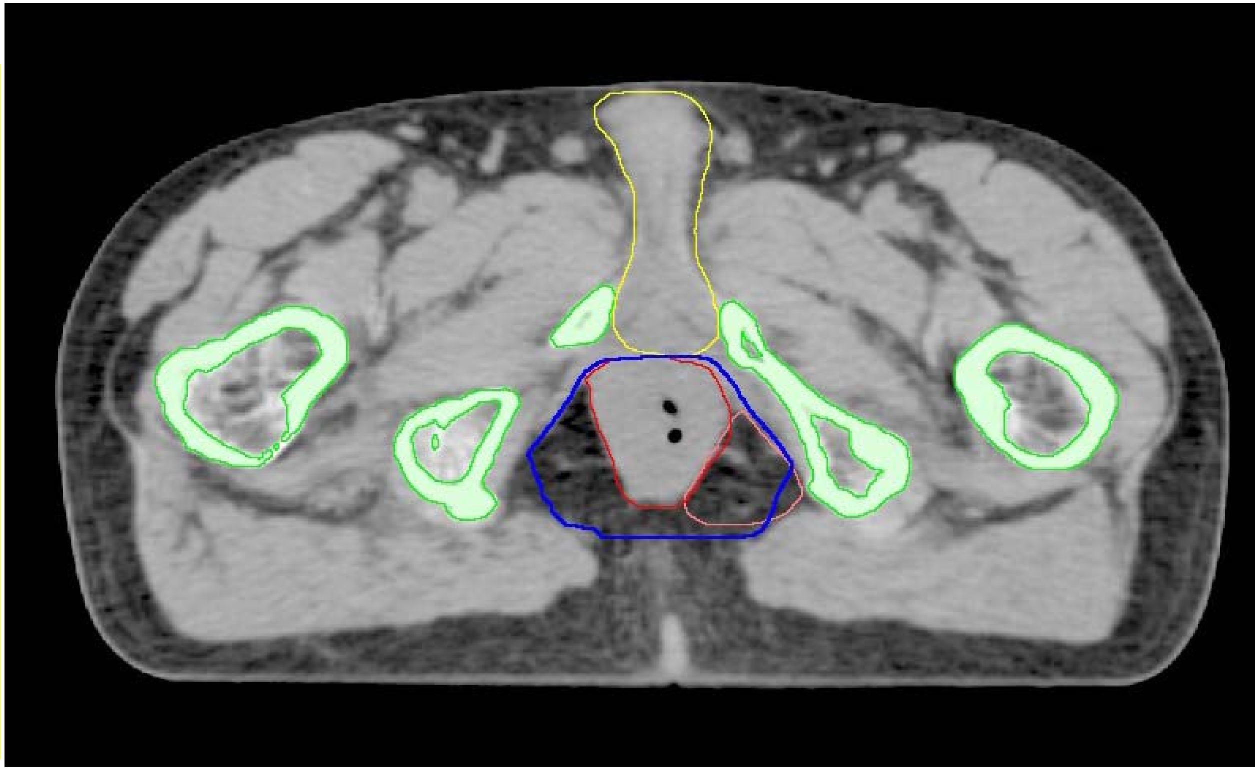

M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012

## CLINICAL TARGET VOLUME FOR GROSS DISEASE

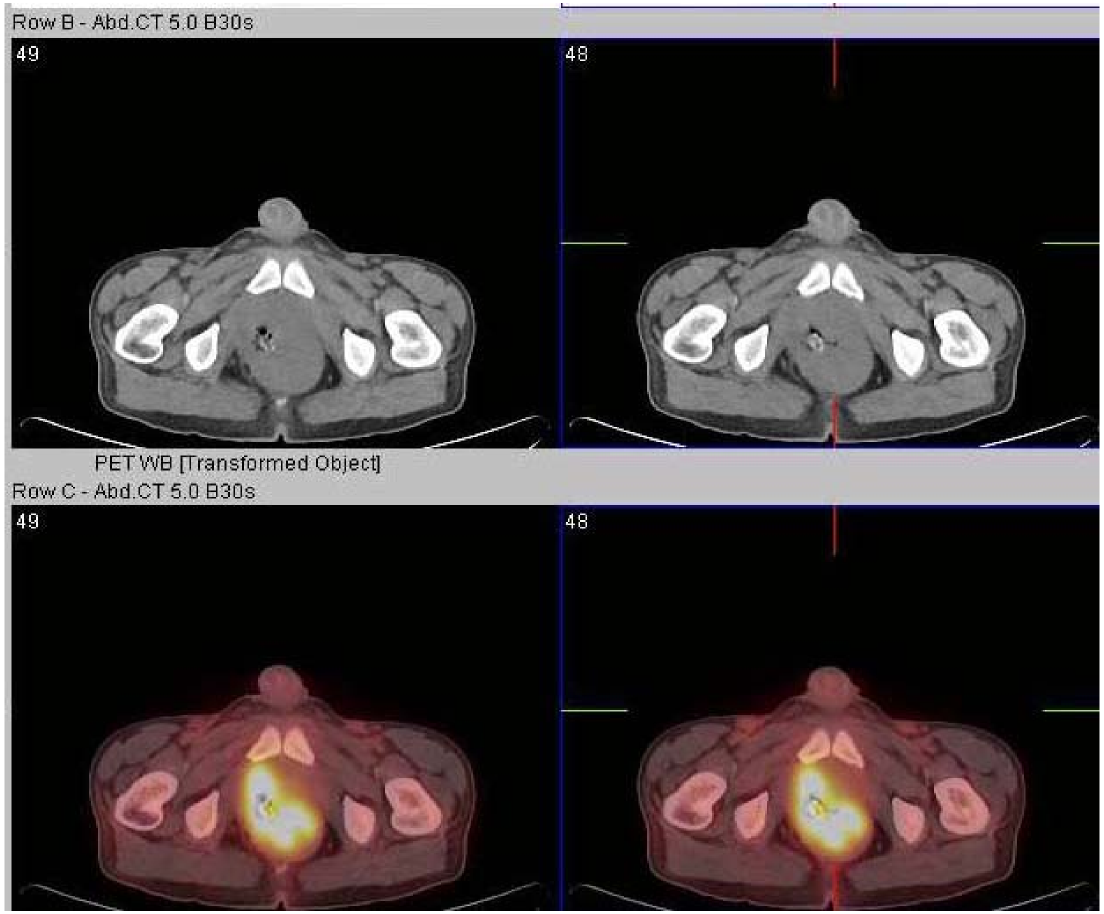
## PRIMARY TUMOR

**CTV-T**

- GTV
- entire **anal canal**
- internal and external **sphinter**
- **20 mm** isotropic margin, while respecting anatomical boudaries



M. Ng, et al. (AGITG) Int J Radiation Oncol Biol Phys, 2012




For very **advanced anal** or rectal cancers, extending through the mesorectum or the levators, the group's recommendation is to add ~2 cm margin up to bone wherever the cancer extends beyond the usual compartments.

**An MRI and/or PET/CT scan is strongly recommended in such cases.**

Myerson RJ, Garofalo MC, El Naqa I, et al. Int J Radiat Oncol Biol Phys. 2009

Clinical Investigation: Gastrointestinal Cancer

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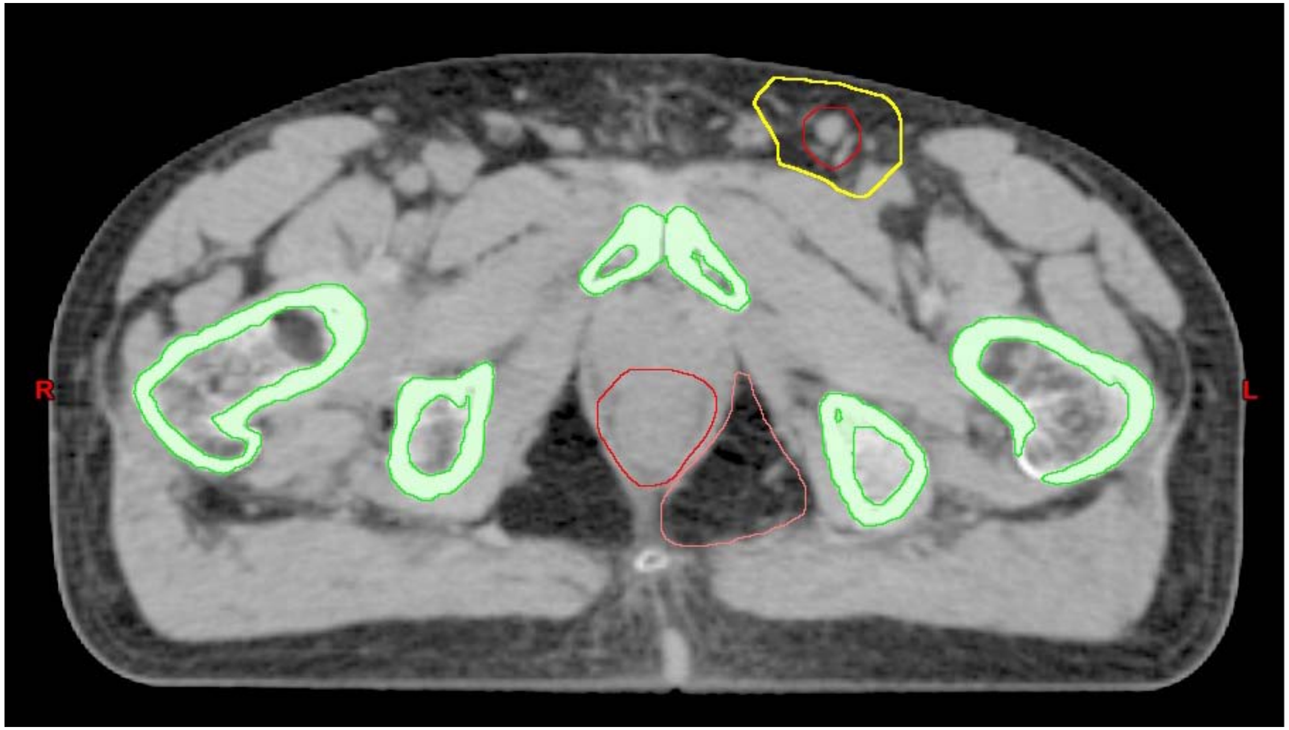
## CLINICAL TARGET VOLUME FOR GROSS DISEASE

## INVOLVED NODE(S)

**CTV-N**
**Involved nodes** + **10-20 mm** ispotropic margin, respecting anatomical boundaries.

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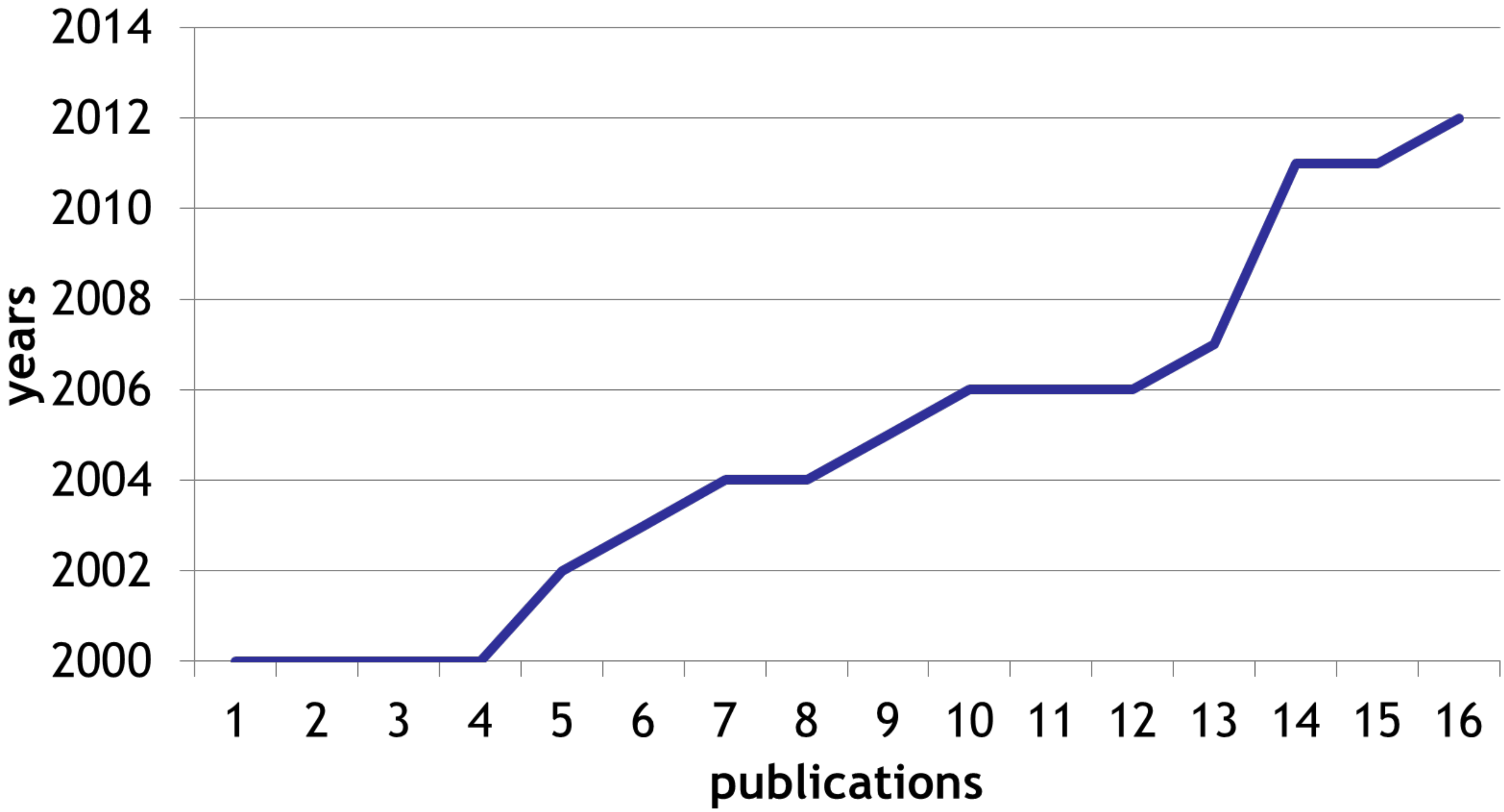
# PTV

- An isotropic 10-mm expansion is recommended on CTVs to generate PTVs.

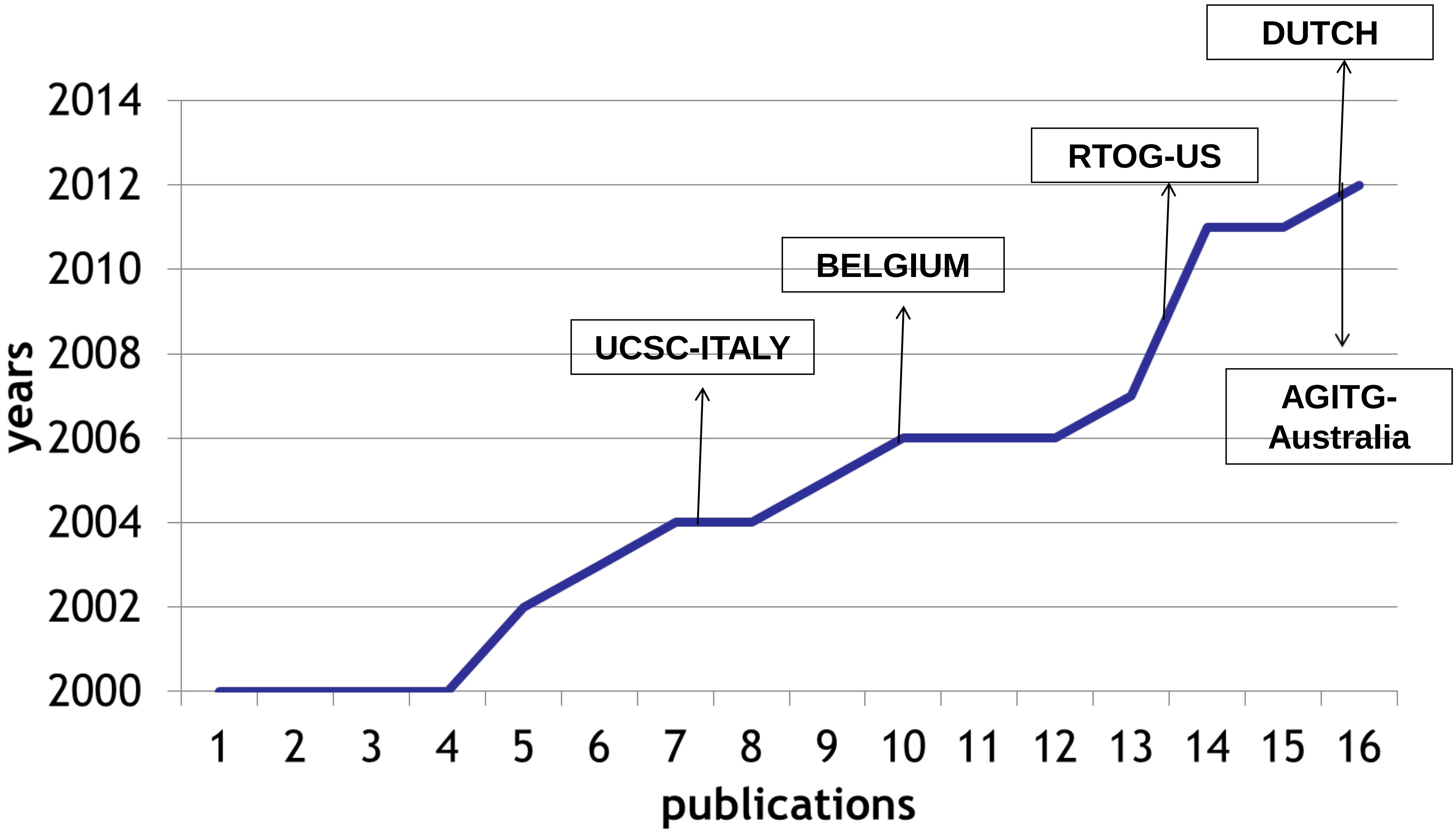
- Daily image guidance is recommended for IMRT, especially prone patients, which may allow CTVePTV margin reduction to 5- to 7-mm.

# Rectal cancer guidelines: what is going on...

# Pelvis Delineation Guidelines



# Pelvis Delineation Guidelines




DUTCH
RTOG-US
BELGIUM
UCSC-ITALY
AGITG-
Australia

# Rectal Cancer Delineation Guidelines
# AGREEMENT and DISAGREEMENT

| GUIDELINE | METHOD | TUMOR SITE | T-stage | IMAGING | POSITION | SUBSITES | RECOMMENDATIONS |
|---|---|---|---|---|---|---|---|
| **BELGIUM 2006-2015** | Site of recurrence **Expert review** | Rectum | none | CT-MR | Supine | yes | yes |
| **RTOG-USA 2009** | Delineation comnparison **Consensus** | Ano-Rectum | cT3N2 | CT | Prone | CTV | yes |
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# Elective Nodes Atlas

| GUIDELINES | subsites | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Mesorectum | Presacral space | SC and IRF | Lateral nodes | Intiernal iliac nodes | Obturator nodes | External iliac nodes | Inguinal nodes |
| BELGIUM | + | + | + | + | Lateral nodes | Lateral nodes | - | - |
| RTOG-USA | CTVA | CTVA | CTVA | CTVA CTVB | CTVA | CTVA | CTVB | CTVC |
| AGITG-Australia | + | + | + | Internal-obturator-external nodes | + | + | + | + |
| DUTCH 2012 | + | + | Mesorectum | Internal-obturator nodes | + | + | + | - |
| UCSC Italy | + | + | + | Internal-obturator-external nodes | + | + | + | - |

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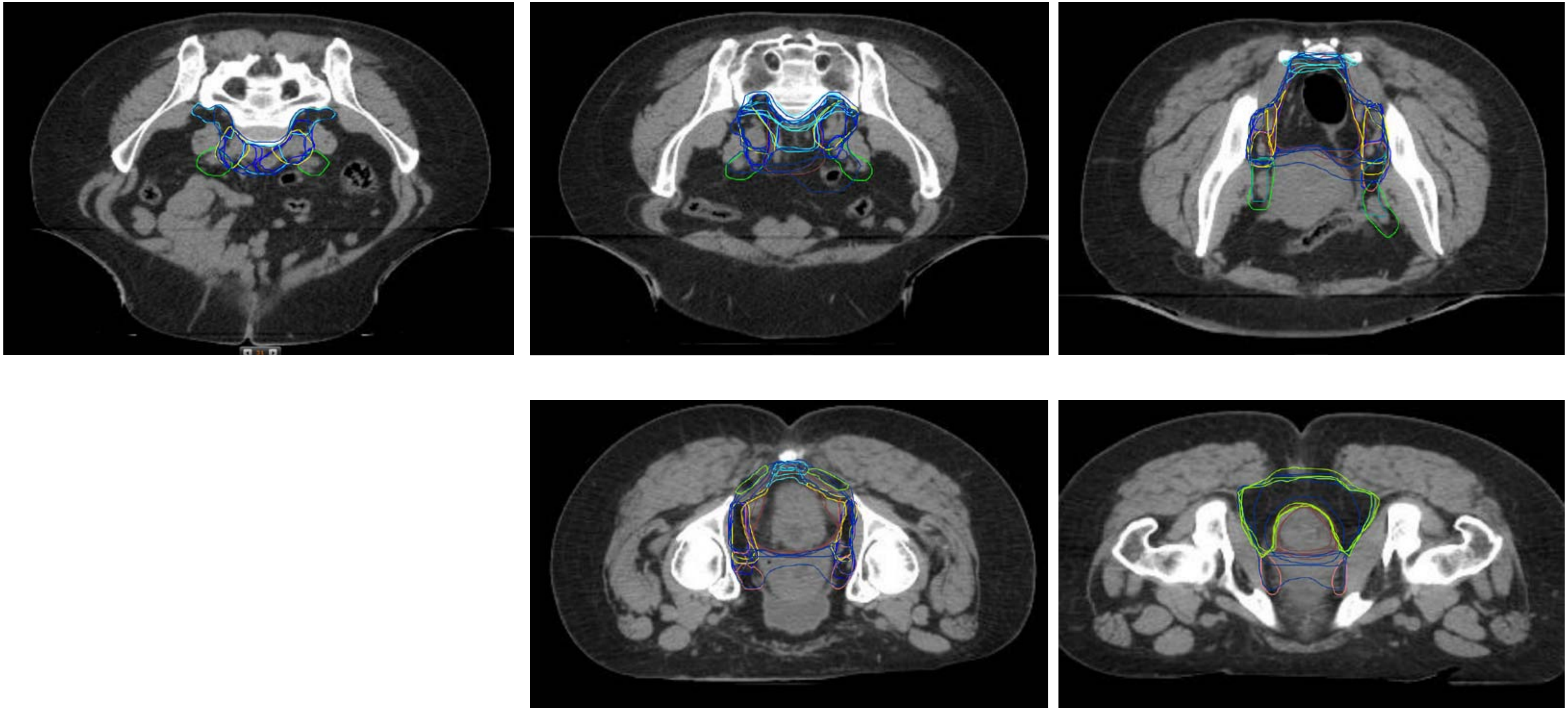
# Experts delineation according different GL



Differences in CTV definition
Difference in boundaries

**ESTRO**

**ASTRO- AGITG-EORTC**

**Multi-Society Guidelines Working Group**

# AIM of the project:

to generate

**COMMON DELINEATION**

**GUIDELINES** in **RECTAL CANCER**

# THE PROCESS OF AGREEMENT

1. EXPERTS IN RECTAL CANCER WHO PUBLISHED GUIDELINES (ESTRO, ASTRO, TROG, EORTC)
2. SUMMARY OF PUBLISHED GUIDELINES
3. SELETION OF CASES: 7 most common presentation
4. DELINEATIONS on FALCON PLATFORM according to different GL
5. LIVE MEETING

   AGREEMENT OF SUBSITES: PS, M, LLN, EIN, IN, SC, IRF

   AGREEMENT OF SUBSITES TO INCLUDE IN THE CTV ACCORDING TO T
6. RE-DELINEATION of cases according to new GUIDELINES
7. ATLAS of 7 ‘tipical cases’ on FALCON
8. PRESENTATION at ESTRO meeting in Turin
9. Accepted for publication on GREEN JOURNAL

# SELECTED CASES

- cT3 MRF - mid rectum
- cT3 MRF - low rectum
- cT3 MRF +
- cT4 with anterior pelvic organ infiltration
- cT4with infiltration of the anal canal
- cT4 N2 with extramesorectal lymphnode
- cT4 with external anal sphincter infitration and IRF

# Remaining issues

Motion

Margin from CTV to PTV

Margin for rectum

# Organ motion

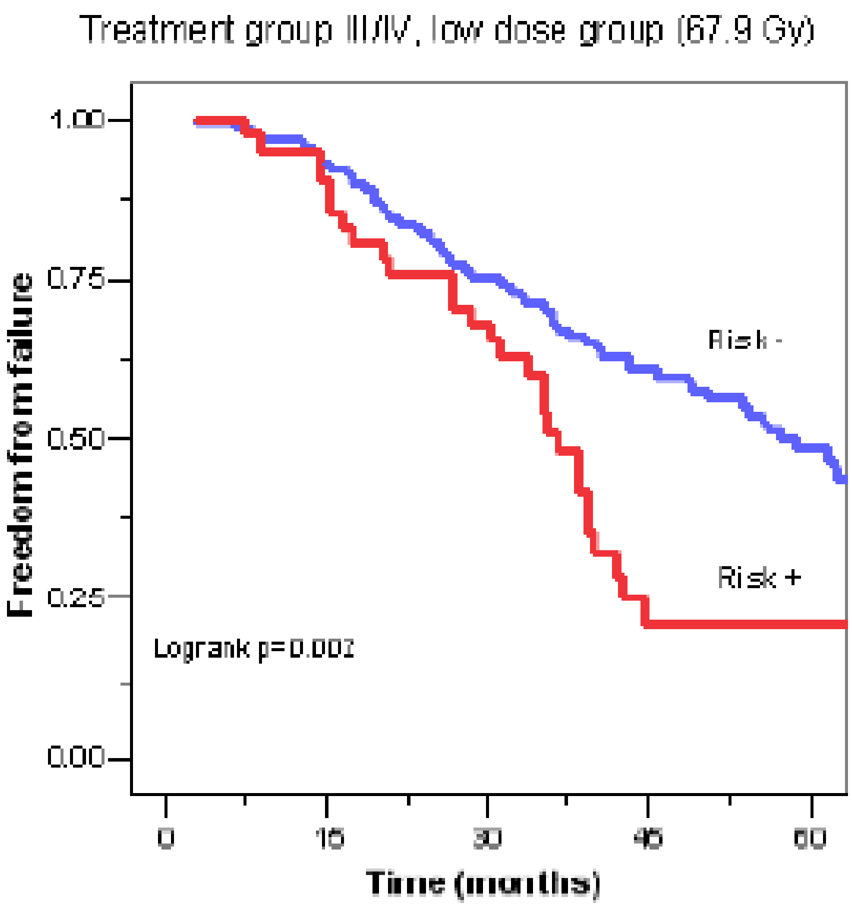
During planning CT → systematic error
During treatment → random error

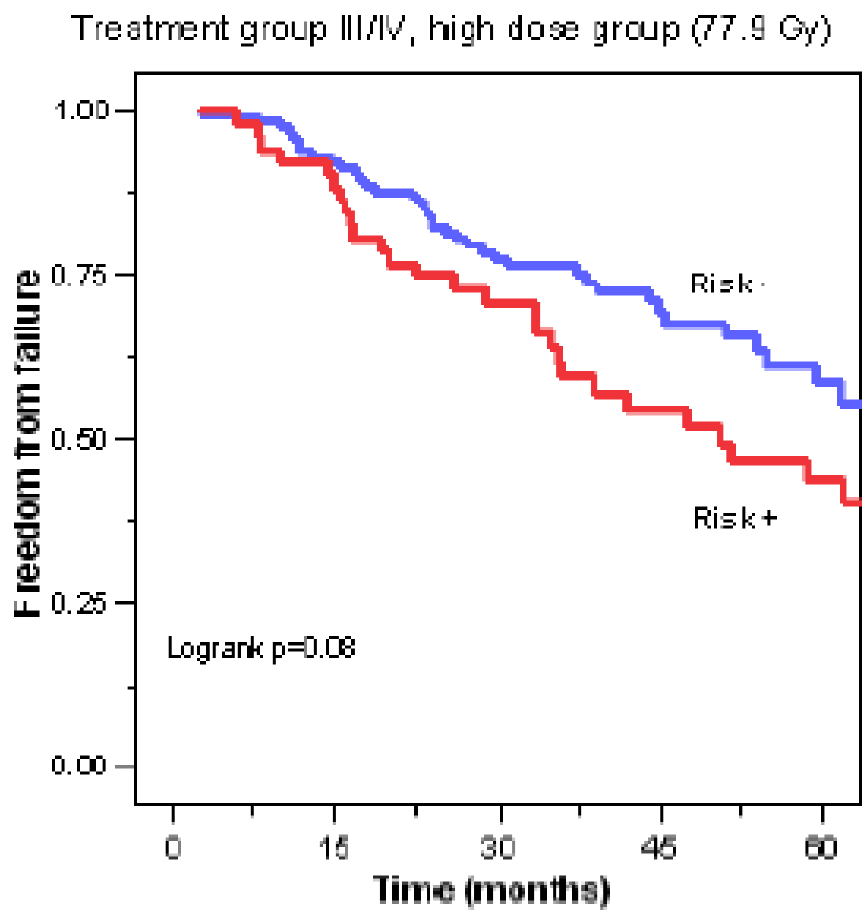
3 mm SD

# Margin CTV to PTV: 2.5Σ + 0.7 σ

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| all in cm | systematic errors | squared | random errors | squared | | | |
| | Σ | | σ | | | | |
| delineation | 1 | 1.00 | 0 | 0.00 | | | |
| organ motion | 4 | 16.00 | 4 | 16.00 | | | |
| setup error | 3 | 9.00 | 3 | 9.00 | | | |
| | | | | | | | |
| total error | 5.10 | 26.00 | 5.00 | 25.00 | | | |
| | times 2.5 | | times 0.7 | | | | |
| | | | | | | | |
| error margin | 12.75 | | 3.50 | | | | |
| | | | | | | | |
| total CTV-PTV margin | | 16.25 | | | | | |
| | | | | | | | |
| | | | | | | | |

# Motion is important: effect of rectal filling on outcome in Dutch prostate cancer trial (660 patients)




**Risk+ = Full rectum at planning**

# Margin for rectum (PRV) ?

- Planned rectum differs from treated rectum
- In 50% of the cases organ motion moves rectum closer during treatment →Higher dose
- In 50% of the cases organ motion moves rectum away during treatment → Lower dose

<u>On average the planning system predicts the rectum dose correctly</u>

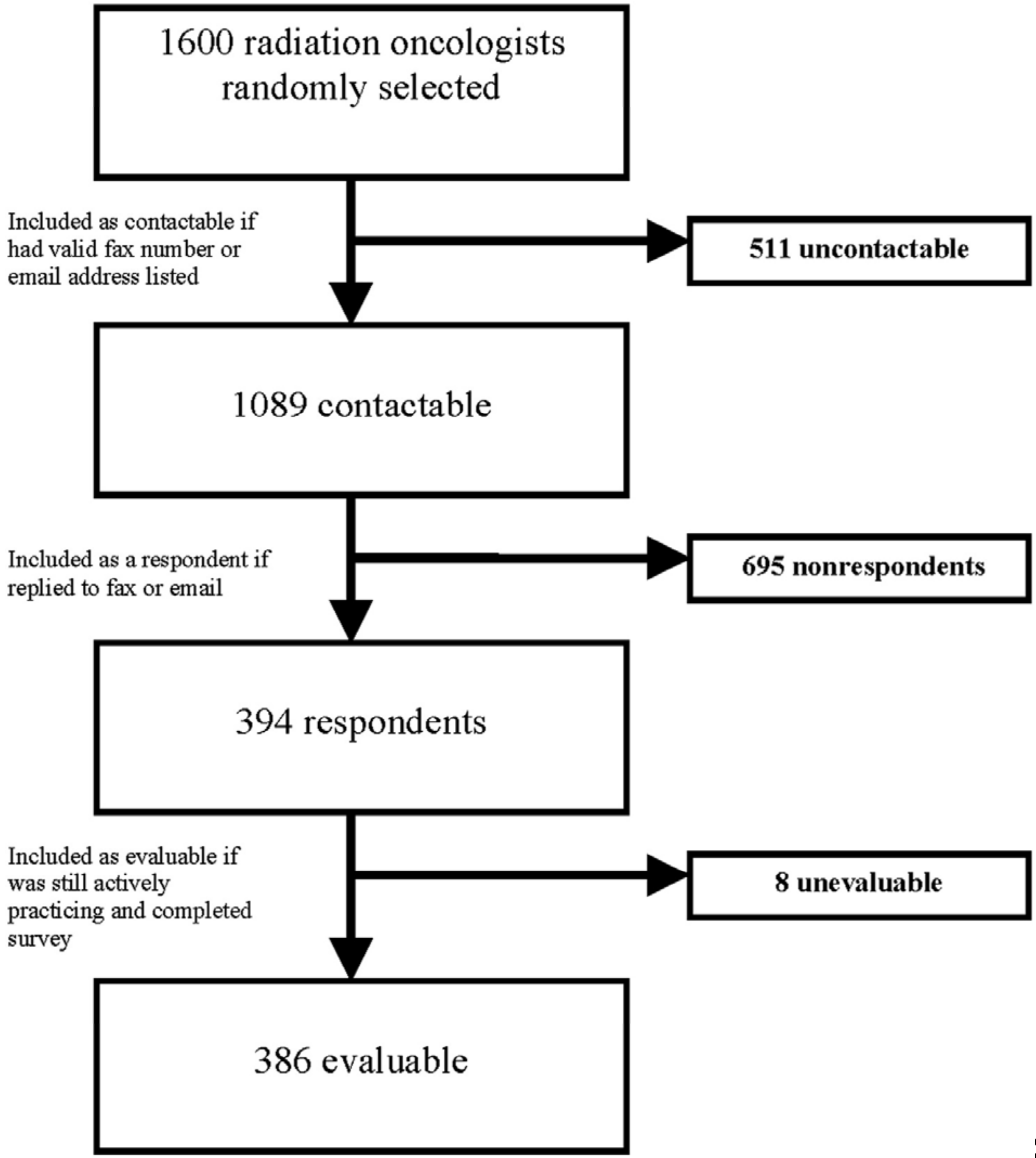
- Therefore no PRV margin is needed

# Sequence of events

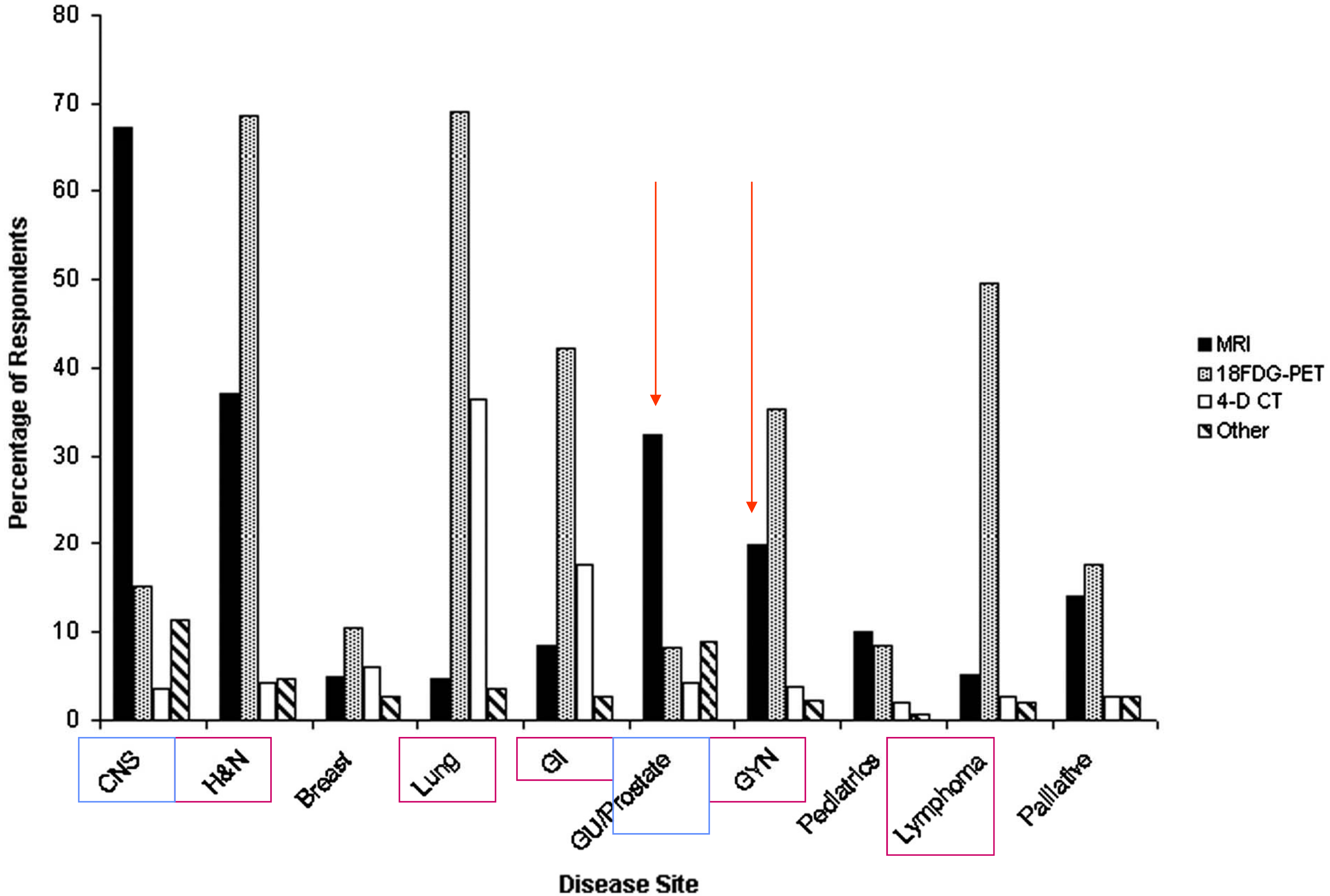
1. Discussion of questions (Vincent)
2. Anatomy (Brendan)
   1. CT alone
   2. CT+MR
   3. Questions by VK to BC
3. Slice by slice disc (All)
   1. Individuals
   2. Groups
   3. Vincent/Brendan
4. Remaining questions? (Vincent)
5. PTV / Physics

# Advanced imaging for target delineation, treatment planning & IGRT.

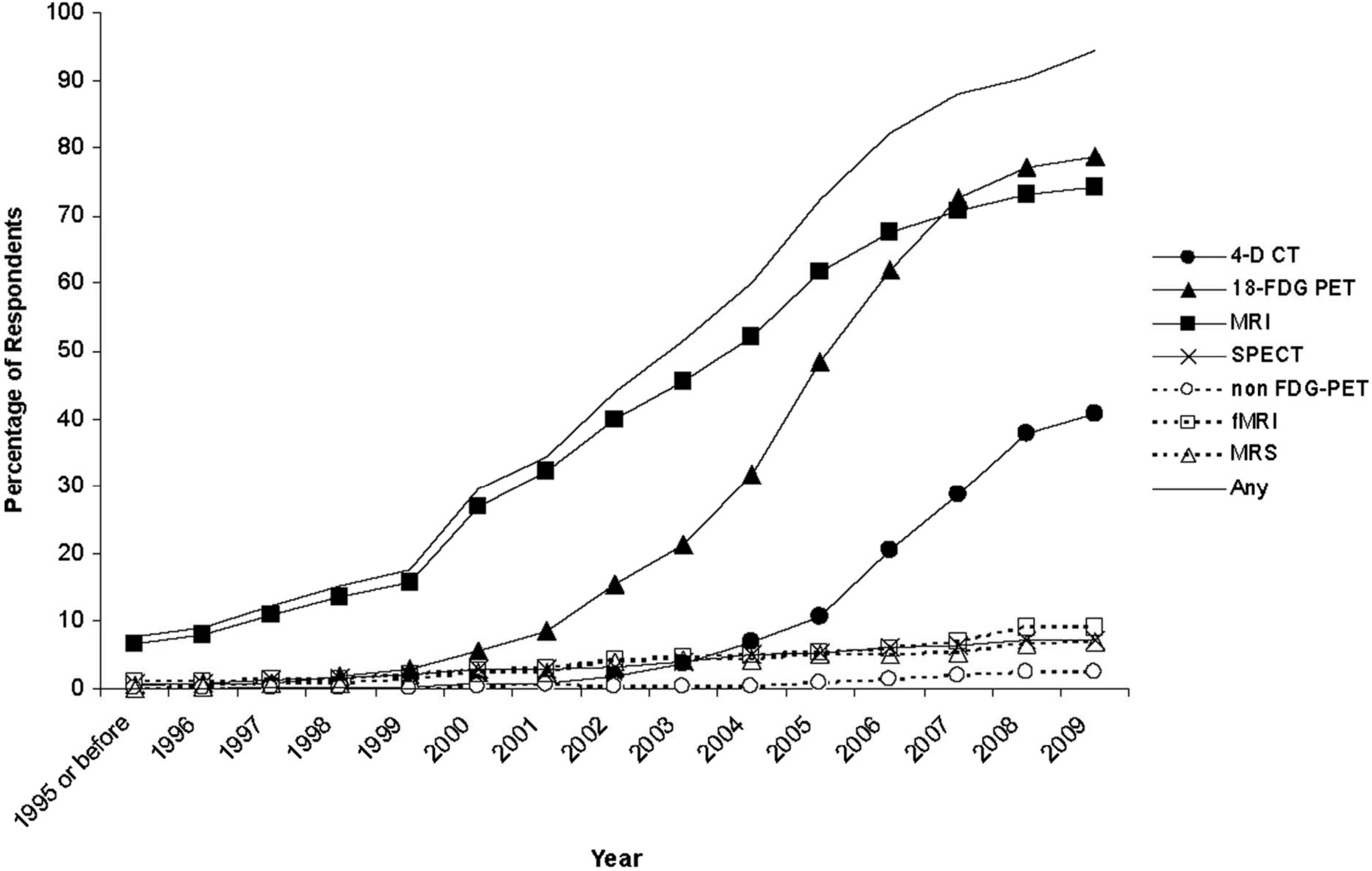
Gert De Meerleer
M.D., Ph.D.
Radiation Oncology
Gent University Hospital
Belgium




Simpson et al, 2009

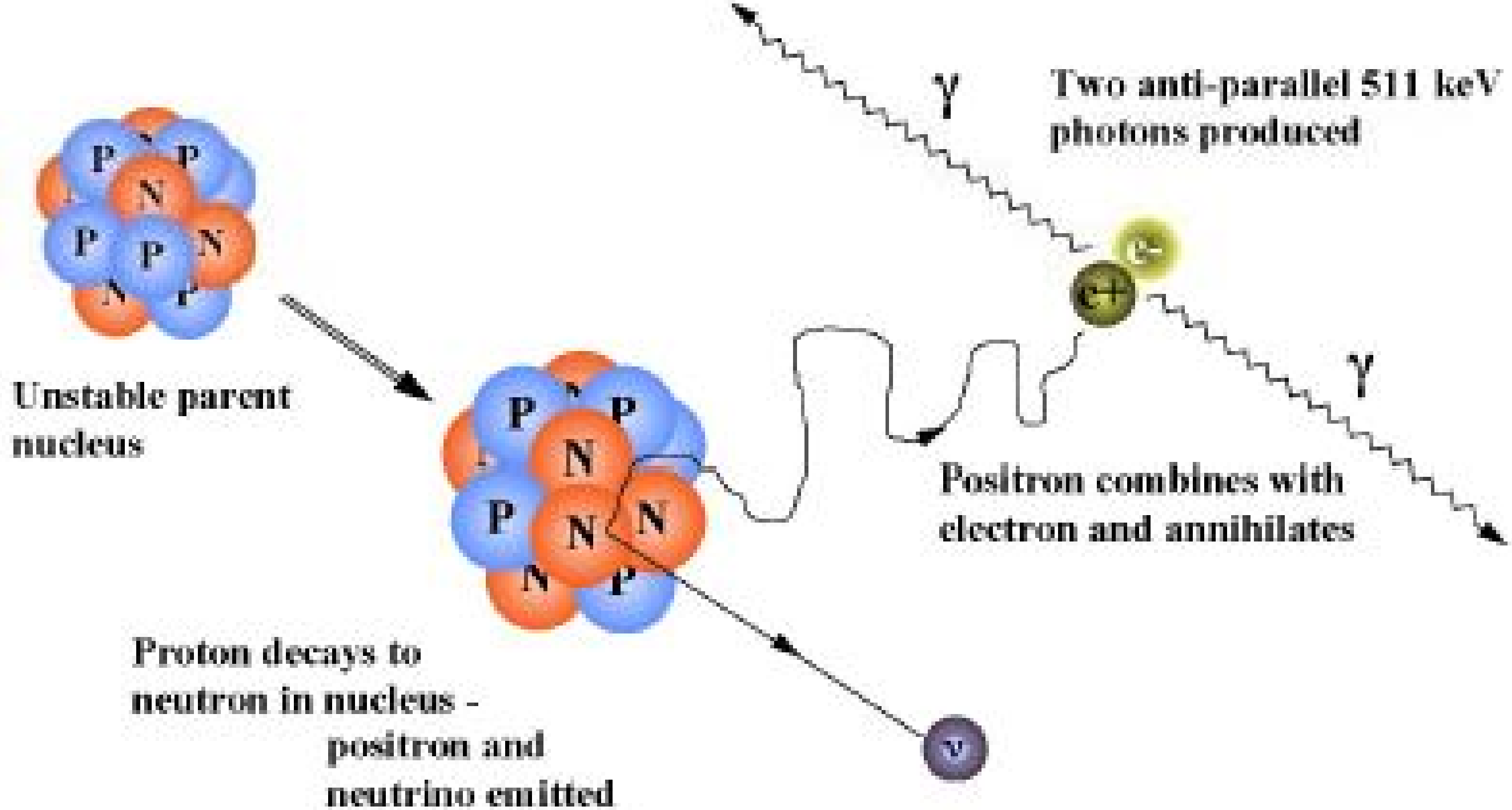


80
70
60
50
40
30
20
10
0
Percentage of Respondents
CNS
H&N
Breast
Lung
GI
GU/Prostate
GYN
Pediatrics
Lymphoma
Palliative
Disease Site
MRI
18FDG-PET
4-D CT
Other

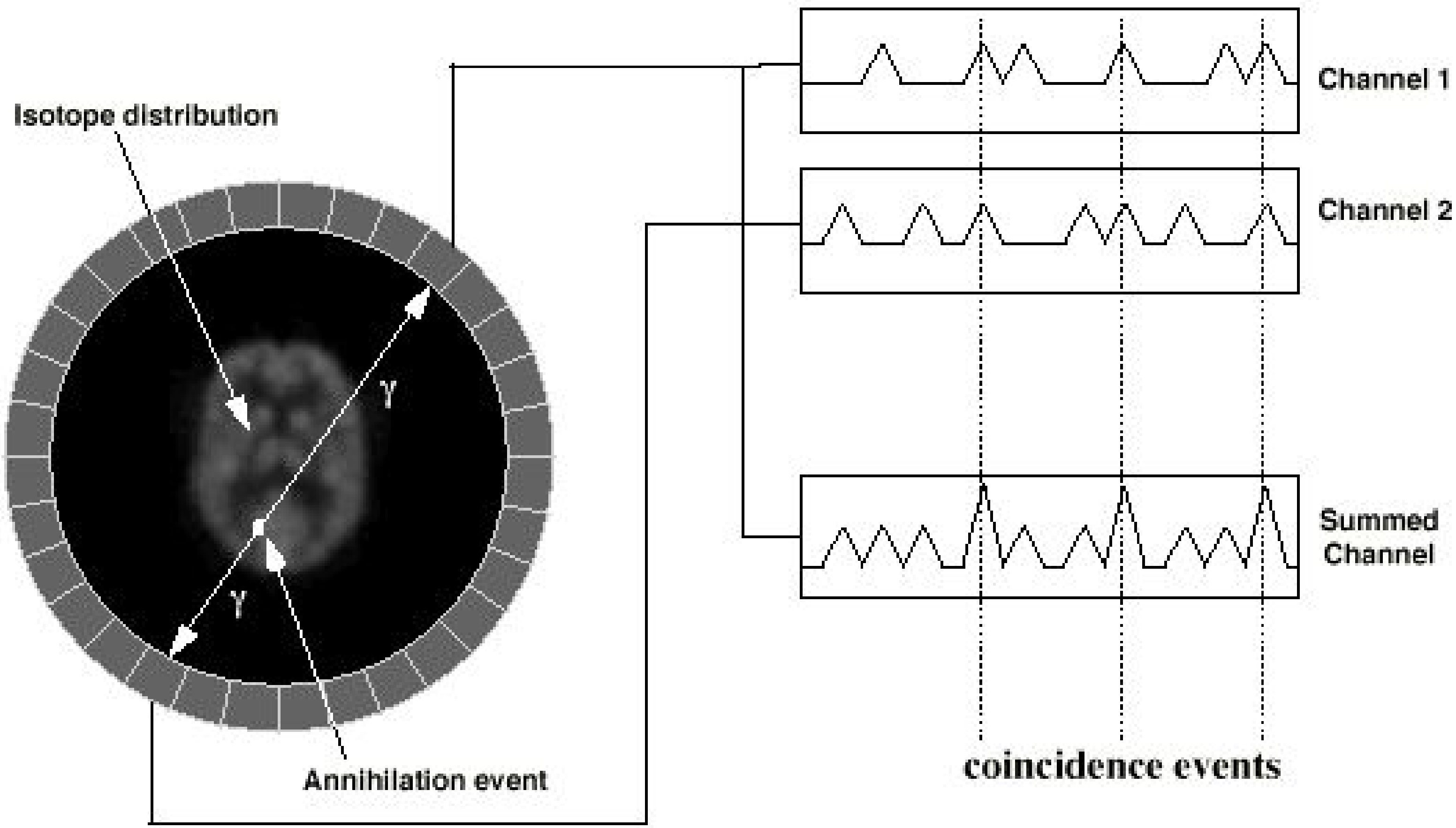


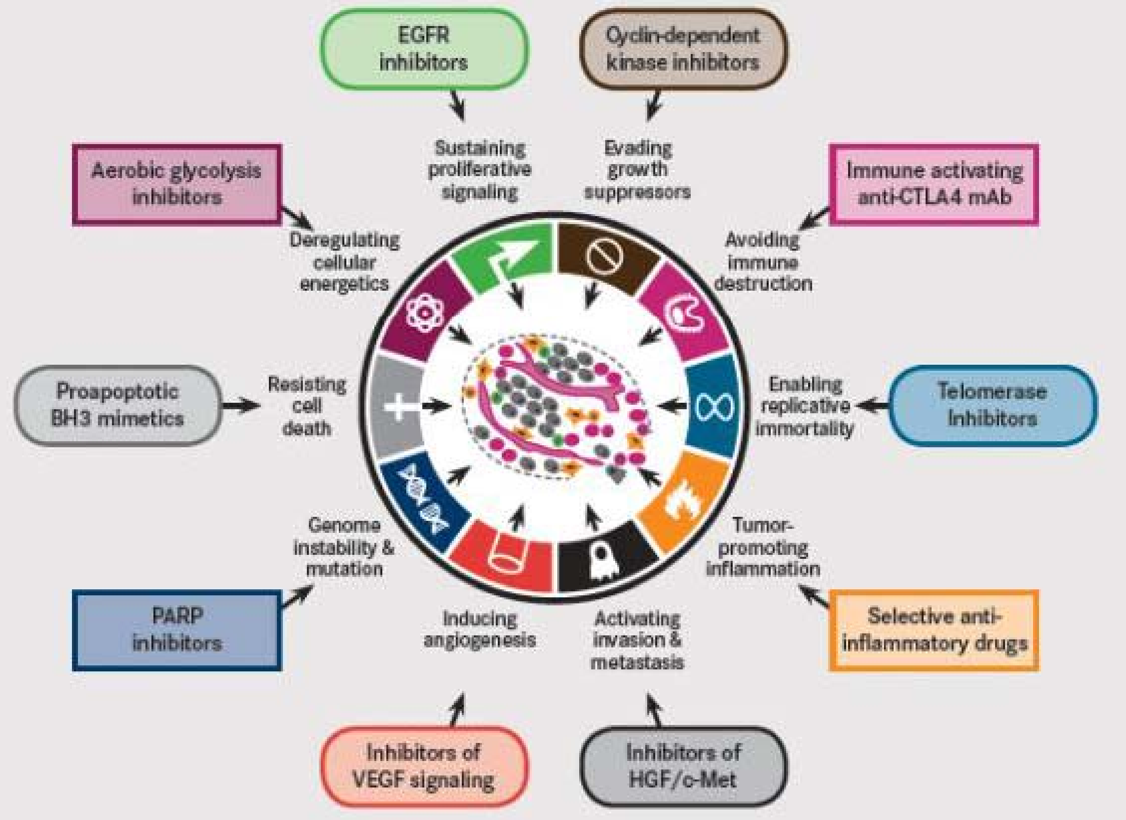
100
90
80
70
60
50
40
30
20
10
0
Percentage of Respondents
1995 or before
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
Year
4-D CT
18-FDG PET
MRI
SPECT
non FDG-PET
fMRI
MRS
Any


GV



Unstable parent nucleus
Proton decays to neutron in nucleus - positron and neutrino emitted
Positron combines with electron and annihilates
Two anti-parallel 511 keV photons produced
γ
γ
e+
e-
ν
P
N

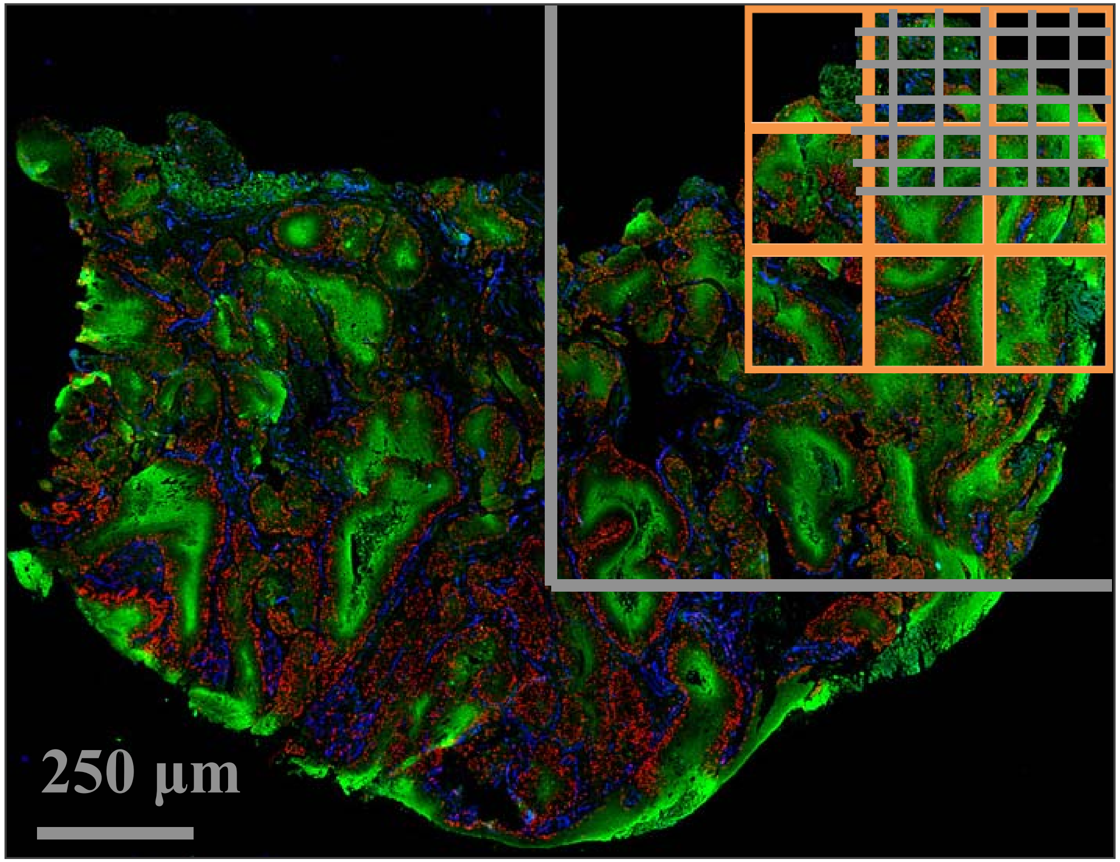

Isotope distribution
γ
γ
Annihilation event
Channel 1
Channel 2
Summed Channel
coincidence events




This figure illustrates some of the many approaches employed in developing therapeutics targeted to the known and emerging hallmarks of cancer.

EGFR indicates epidermal growth factor receptor; CTLA4, cytotoxic T lymphocyte-associated antigen 4; mAb, monoclonal antibody; HGF, hepatocyte growth factor; VEGF, vascular endothelial growth factor; PARP, poly-(ADP ribose) polymerase.

Source: Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*. 2011; 144:646-674. Reprinted with permission.




**Autoradiography**
**(50 µm)**

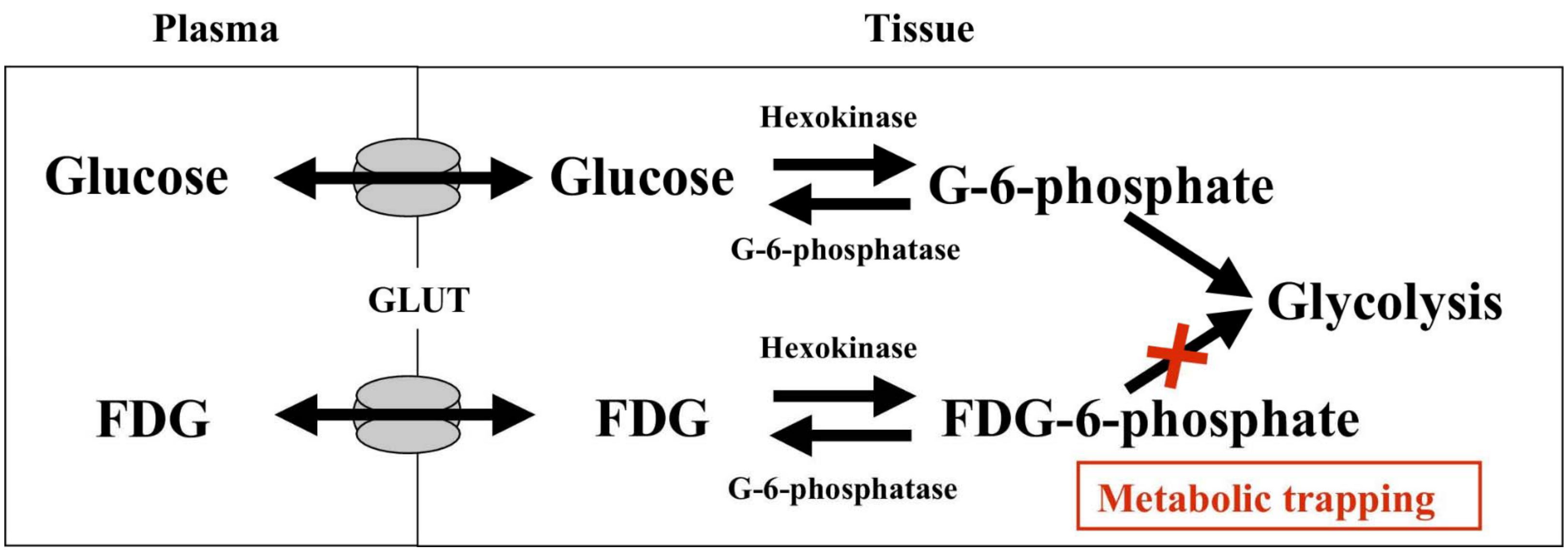
**microPET**
**(1.5 mm)**

**PET**
**(5-7 mm)**

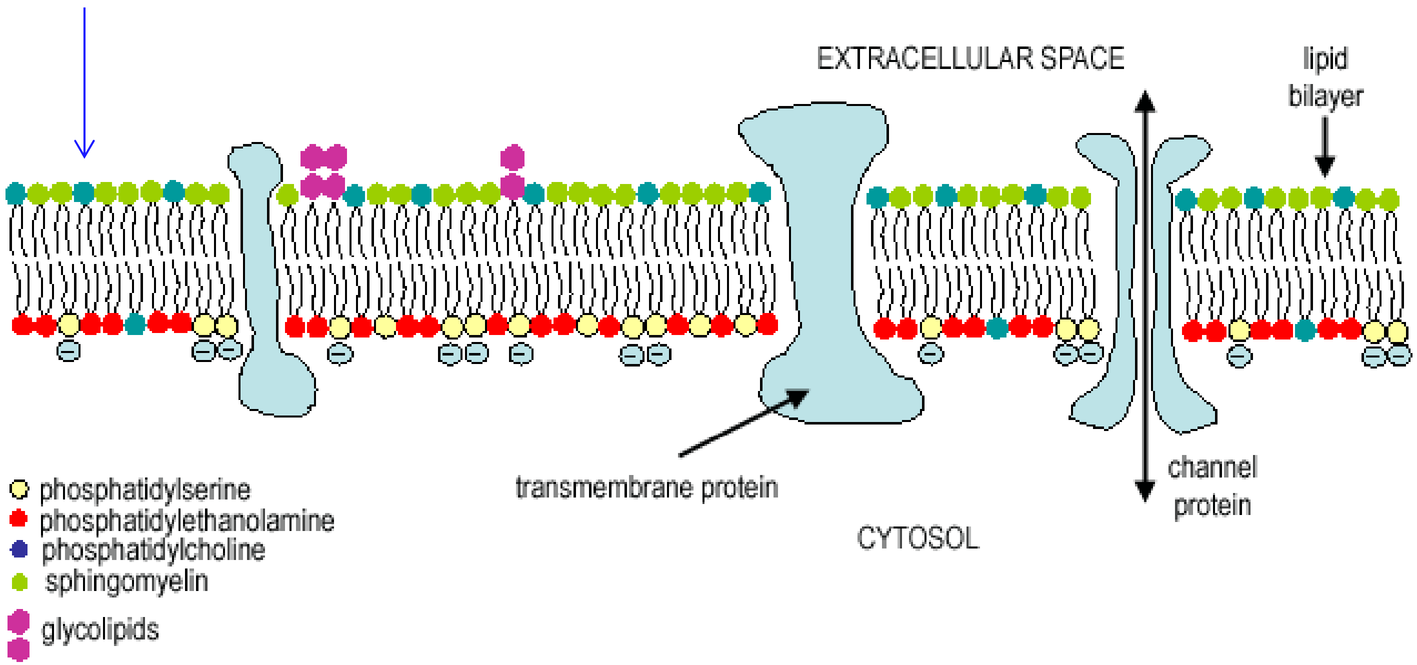
# Some famous PET tracers

| Radio-pharmaceutical | Depicted parameter | Possible RT-application | Clinically relevant neoplasms | Evidence for diagnostic value | Use in/state of evaluation for RT planning |
|---|---|---|---|---|---|
| FDG | Glucose metabolism | Tumour delineation | For example, lung cancer Head and neck cancer Esophageal Ca Lymphomas | Given for various tumours in staging and restaging | Probable, ongoing randomized clinical studies |
| AA | Protein metabolism | Tumour delineation | Primary and recurrent brain tumours | Given for brain tumours in staging and restaging | Probable, ongoing randomized clinical studies |
| MISO | Hypoxia | Hypoxic subvolume | HNC (SCC), NSCLC, Glioma, others | Under evaluation | Promising, practical implication not yet defined |

- $^{18}$F-FDG
  - most commonly used for various tumour types
  - based on increased uptake in tumour cells showing increased glucose metabolism
  - “Metabolic trapping”



- $^{11}C$-choline – $^{18}F$-choline
  - marker of cell membrane turnover
  - based on increased phospholipid synthesis in tumour cells showing upregulation of choline kinase

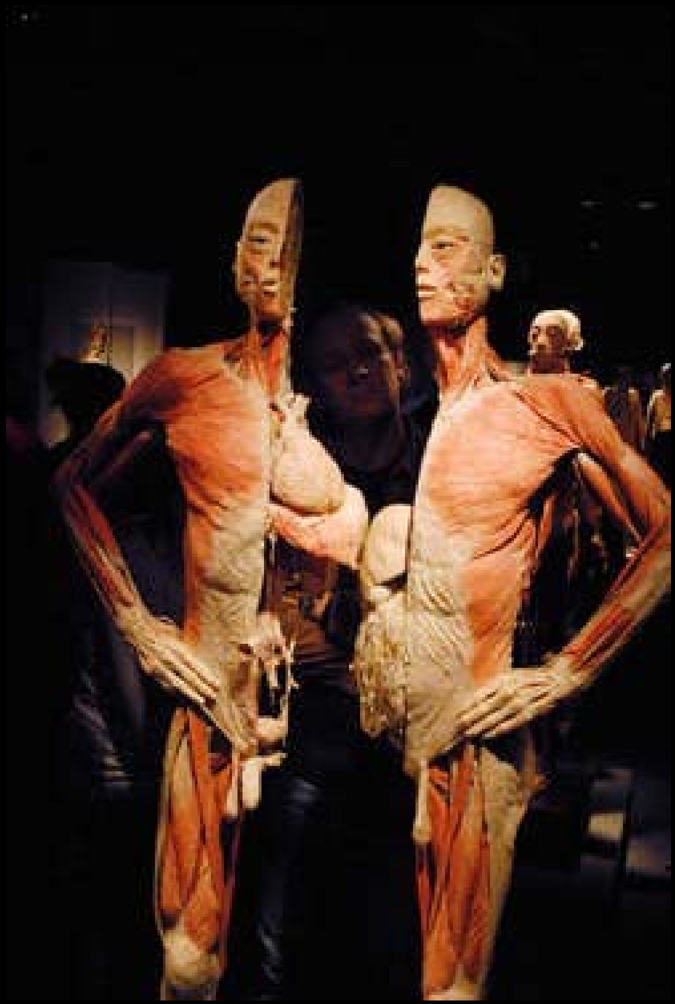


- $^{11}C$-methionine
  - marker of proteine synthesis (essential AA)
  - based on increased cellular proliferation in tumour cells showing increased amino acid transport
  - > brain tumors

- $^{18}F$-MISO / $^{18}F$-HX4 / $^{18}F$-AZA
  - nitroimidazoles, markers of tumor cell hypoxia
  - based on reduction of marker and accumulation under hypoxic conditions
  - > head-and-neck, (N)SCLC

- $^{11}C$-acetate
  - marker of lipid metabolism
  - based on increased fatty acid synthesis in tumour cells showing overexpression of fatty acid synthase
  - very similar to $^{11}C$-choline (also few urinary excretion)

- $^{68}Ga$-PSMA
  - Glycoprotein with enzymatic function (NAAG to glutamate & NAA)
  - marker of lipid metabolism
  - based on increased fatty acid synthesis in tumour cells showing overexpression of fatty acid synthase



BRAIN

H & N

LUNG

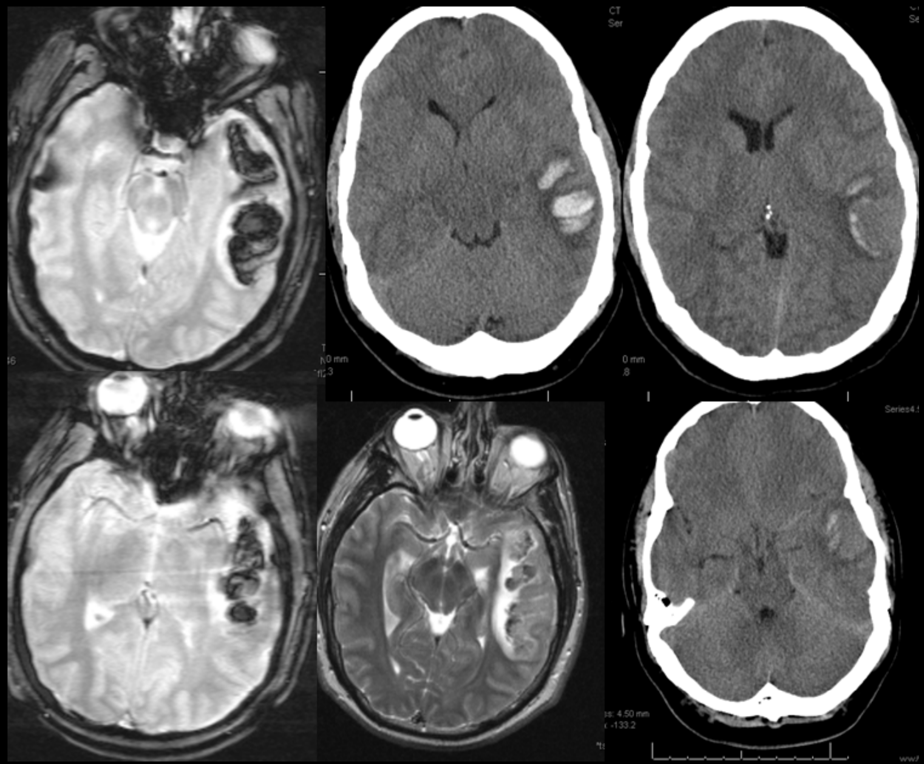
GYN

PROSTATE

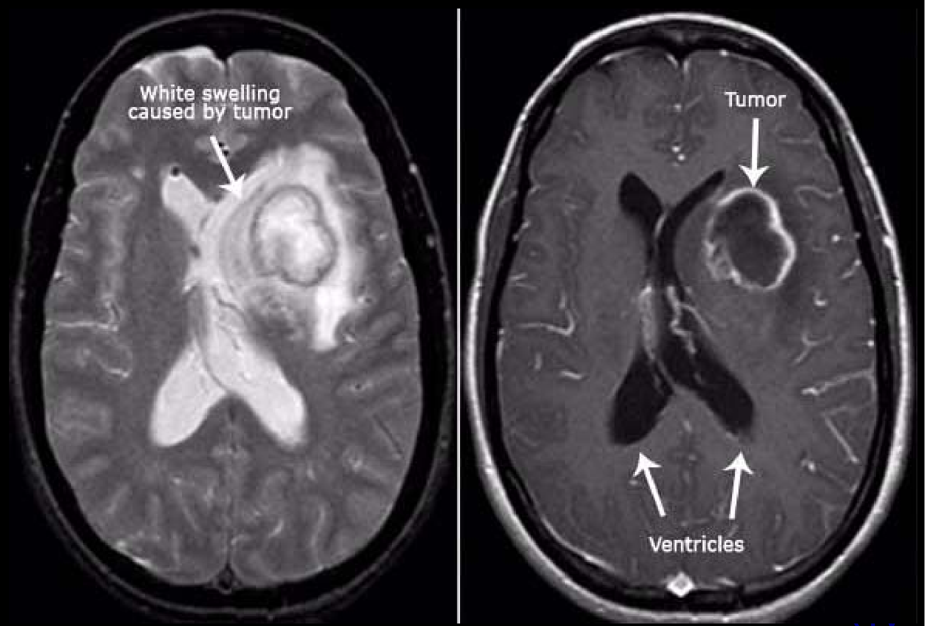
RECTUM

GV

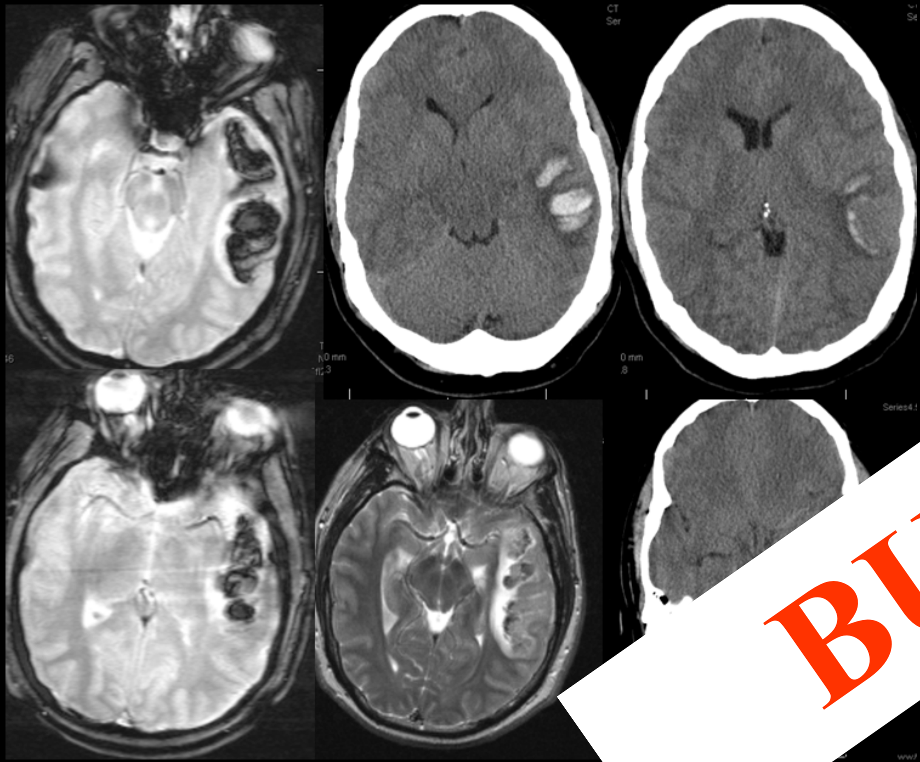
# BRAIN



Advantage MR unequivocal

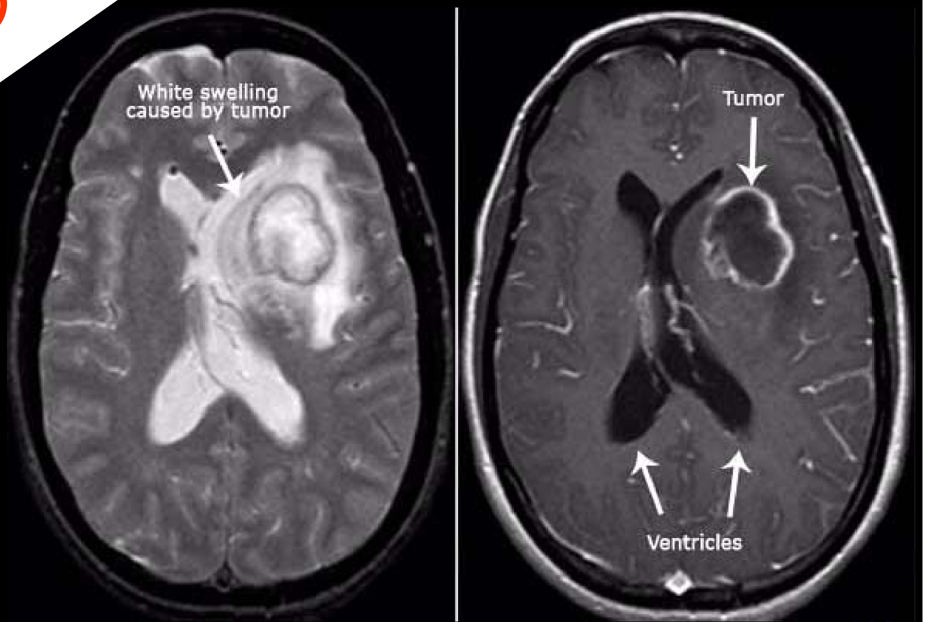


# BRAIN



Advantage MR unequivocal

**BUT**

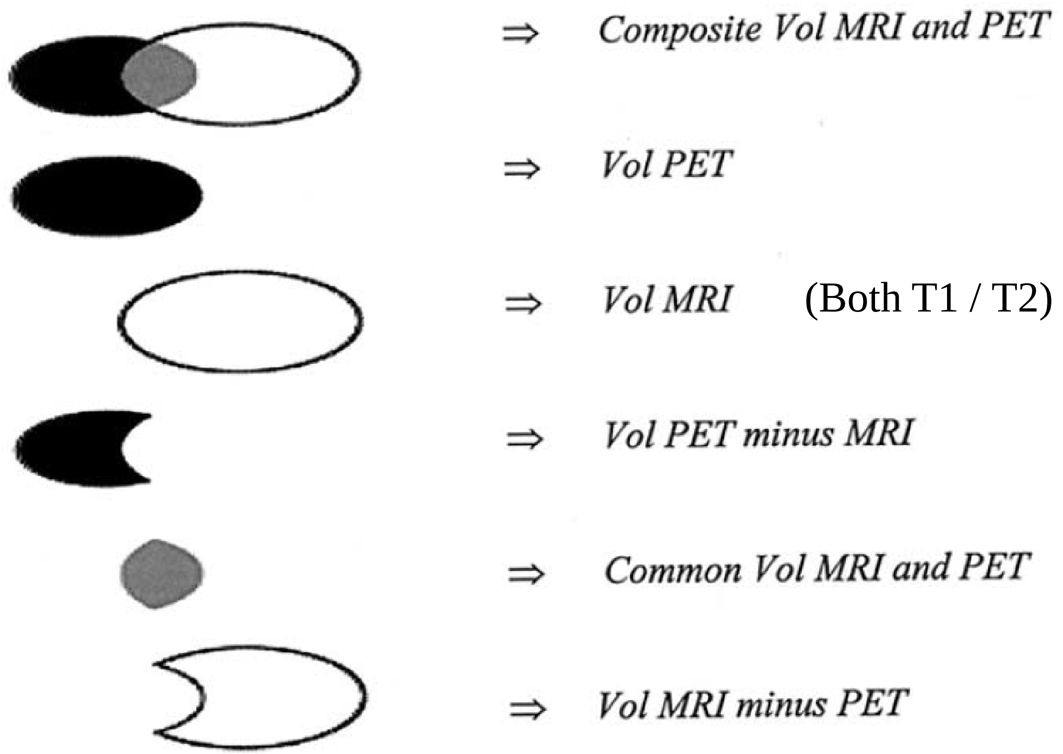


# BRAIN


Edema can be treatment related

# L-(METHYL-11C) METHIONINE POSITRON EMISSION TOMOGRAPHY FOR TARGET DELINEATION IN RESECTED HIGH-GRADE GLIOMAS BEFORE RADIOTHERAPY

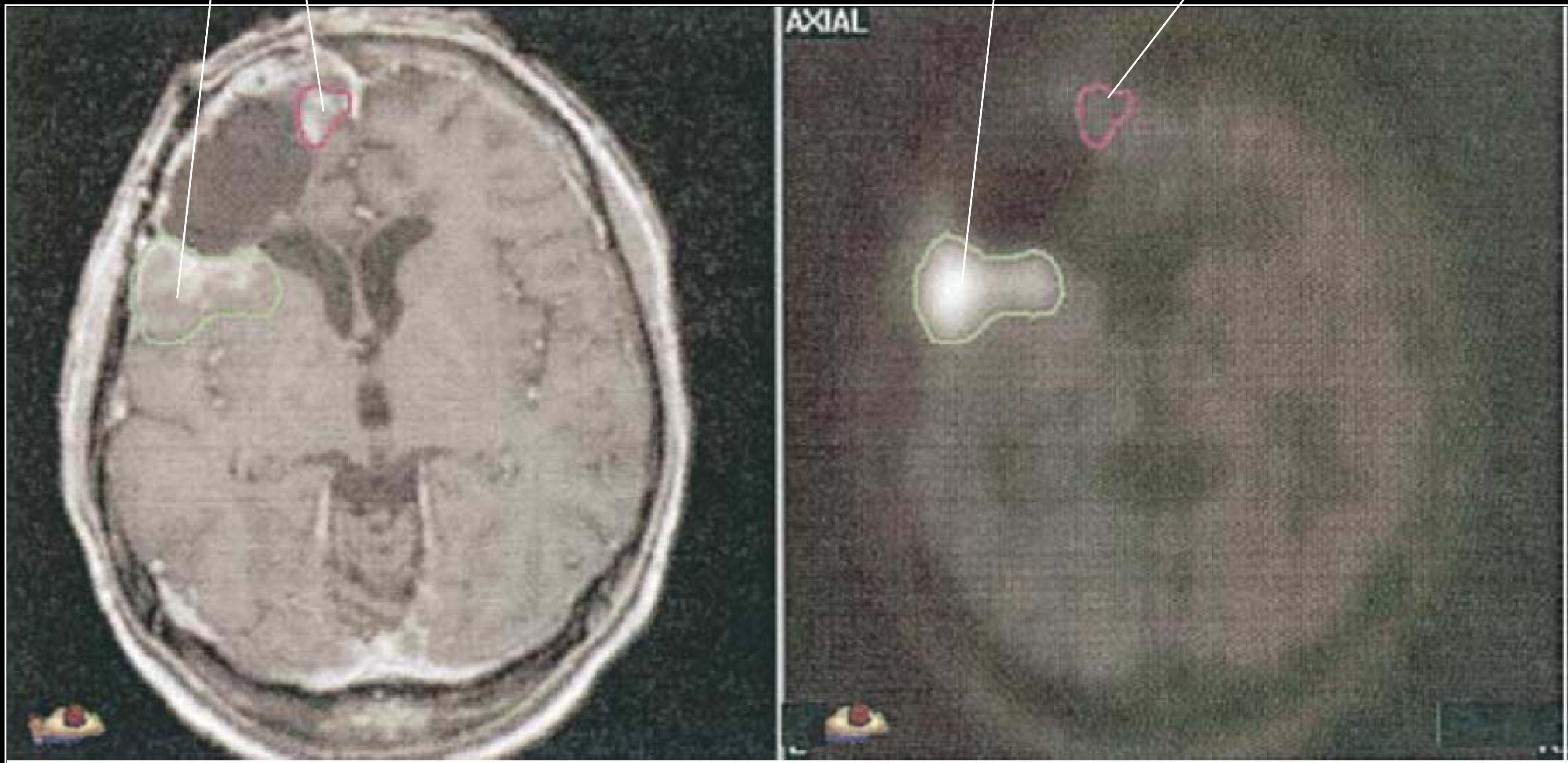

Anca-Ligia Grosu, M.D.,* Wolfgang A. Weber, M.D.,† Eva Riedel, M.D.,* Branislav Jeremic, M.D.,* Carsten Nieder, M.D.,* Martina Franz,* Hartmut Gumprecht, M.D., Ruprecht Jaeger, M.D.,§ Markus Schwaiger, M.D.,† and Michael Molls, M.D.*

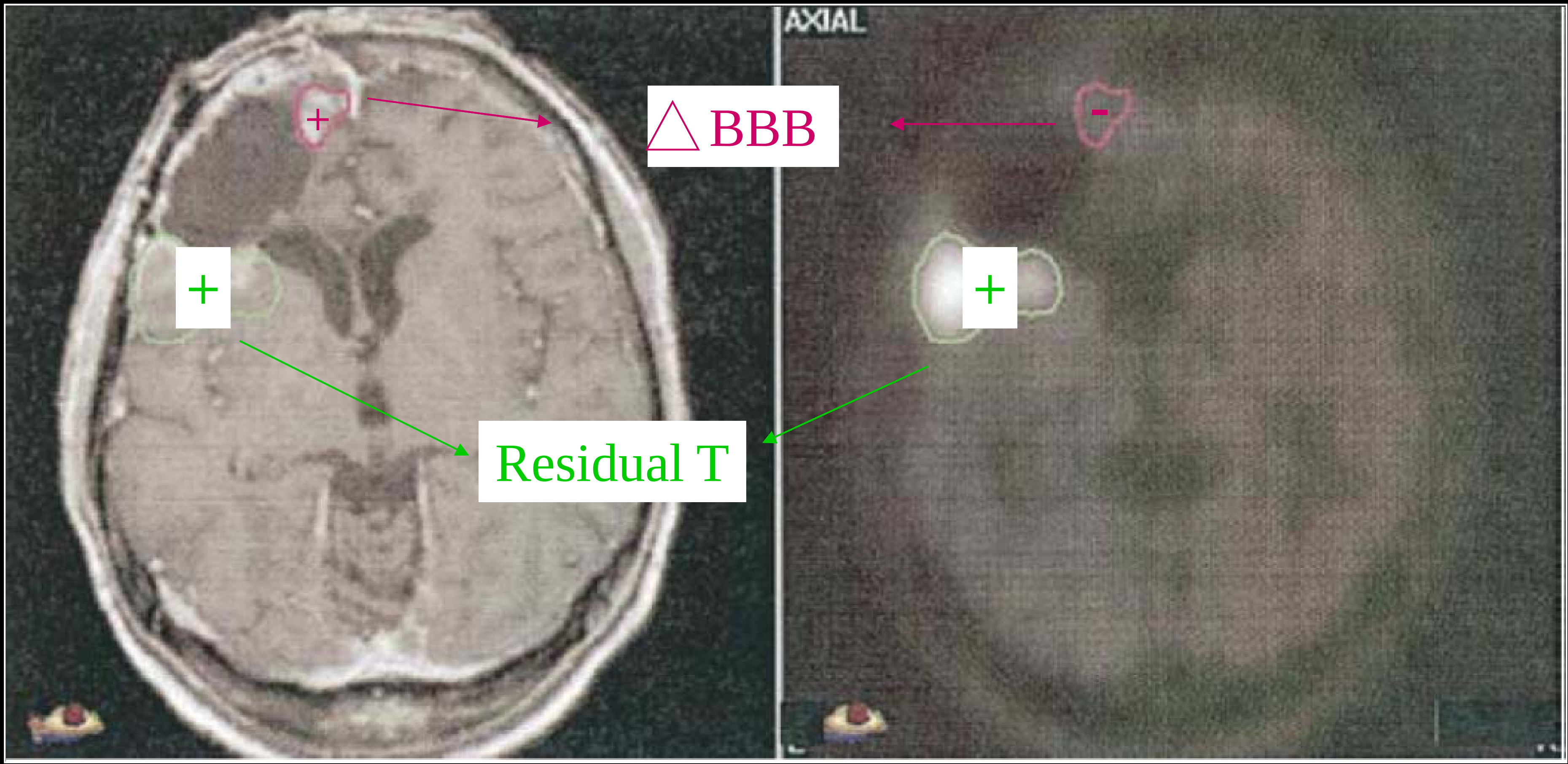



T1 MR1 MET-PET

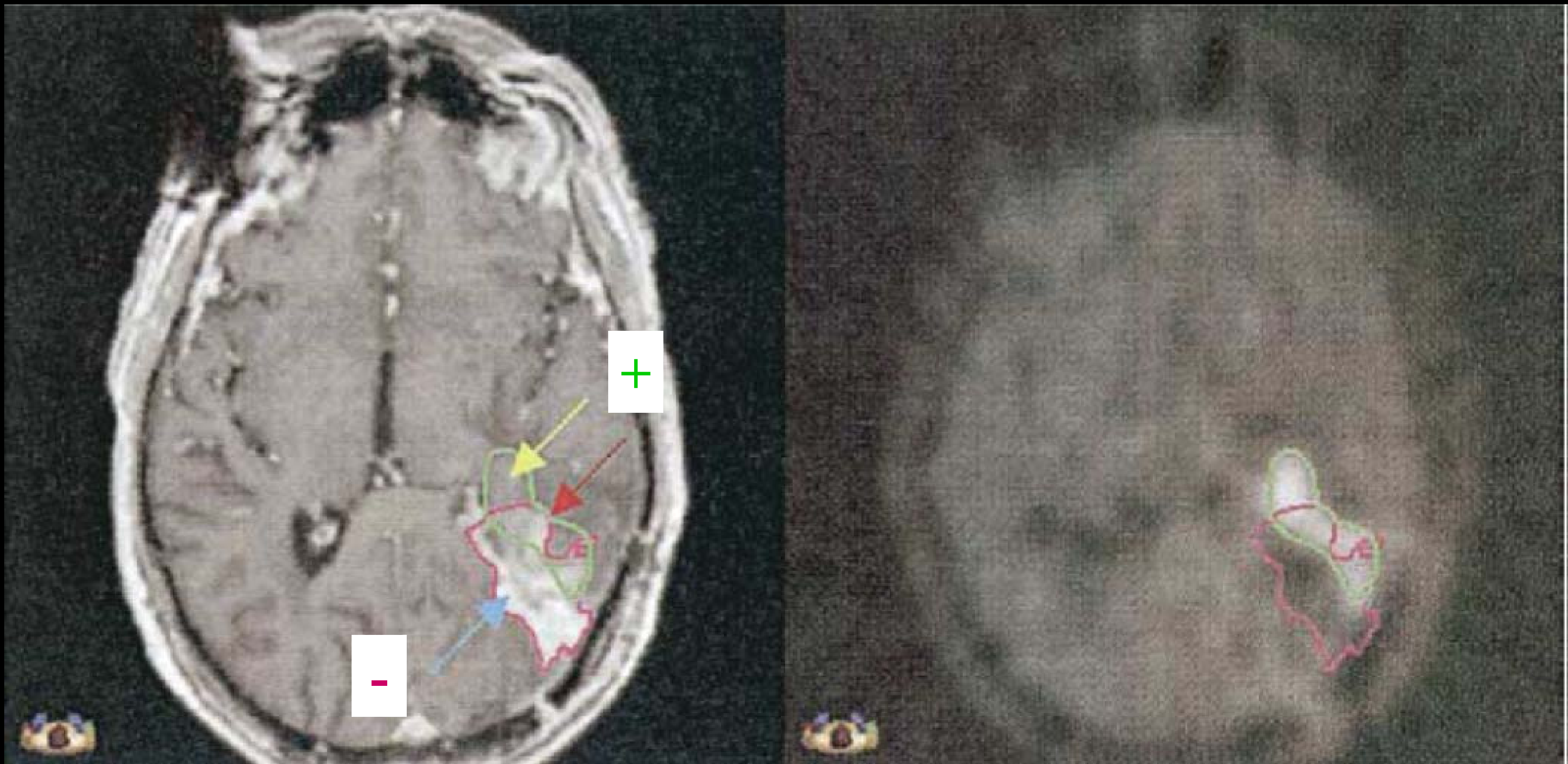
Gd enhancement

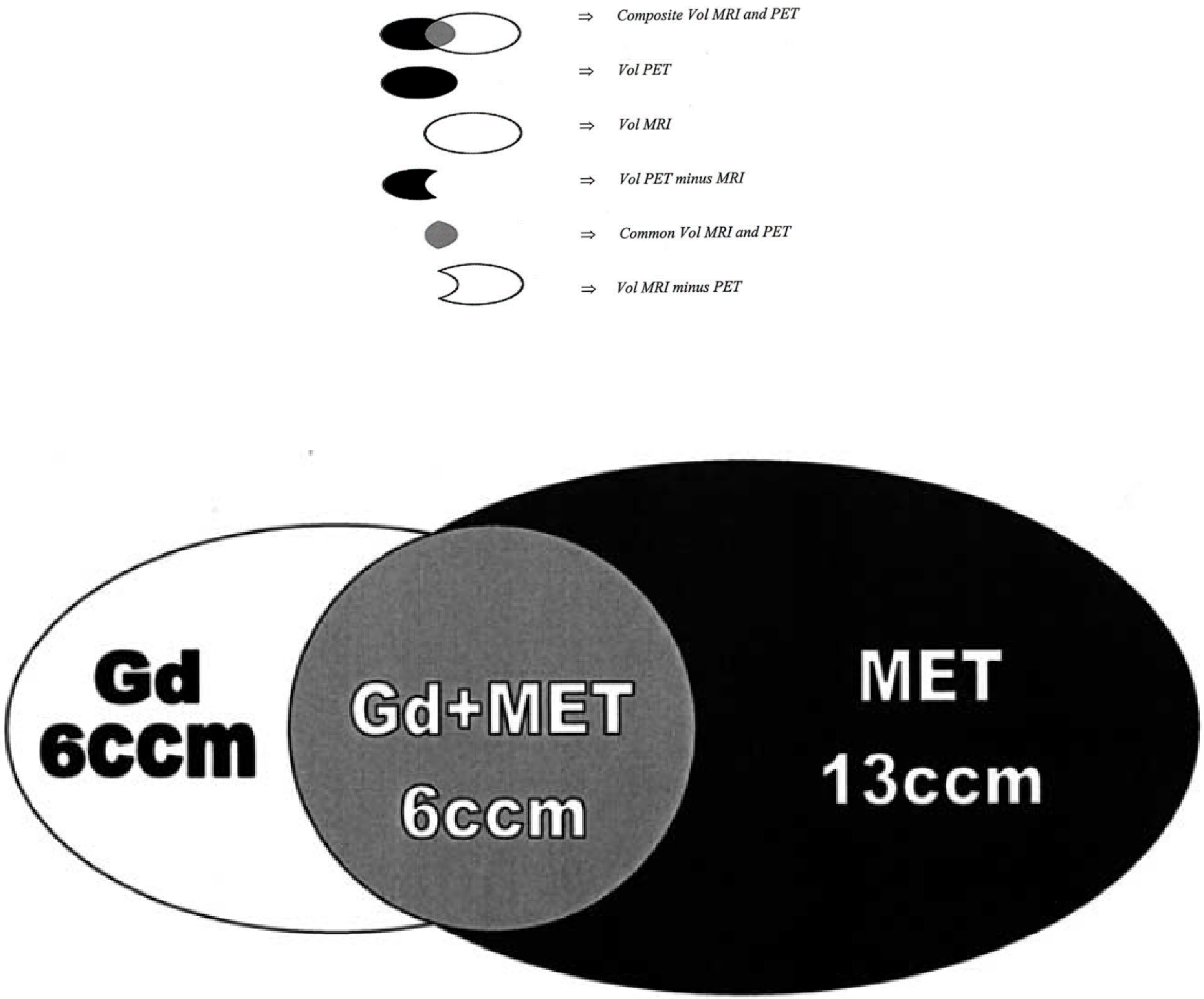
MET uptake No MET uptake





AXIAL
△ BBB
+
-
+
+
Residual T

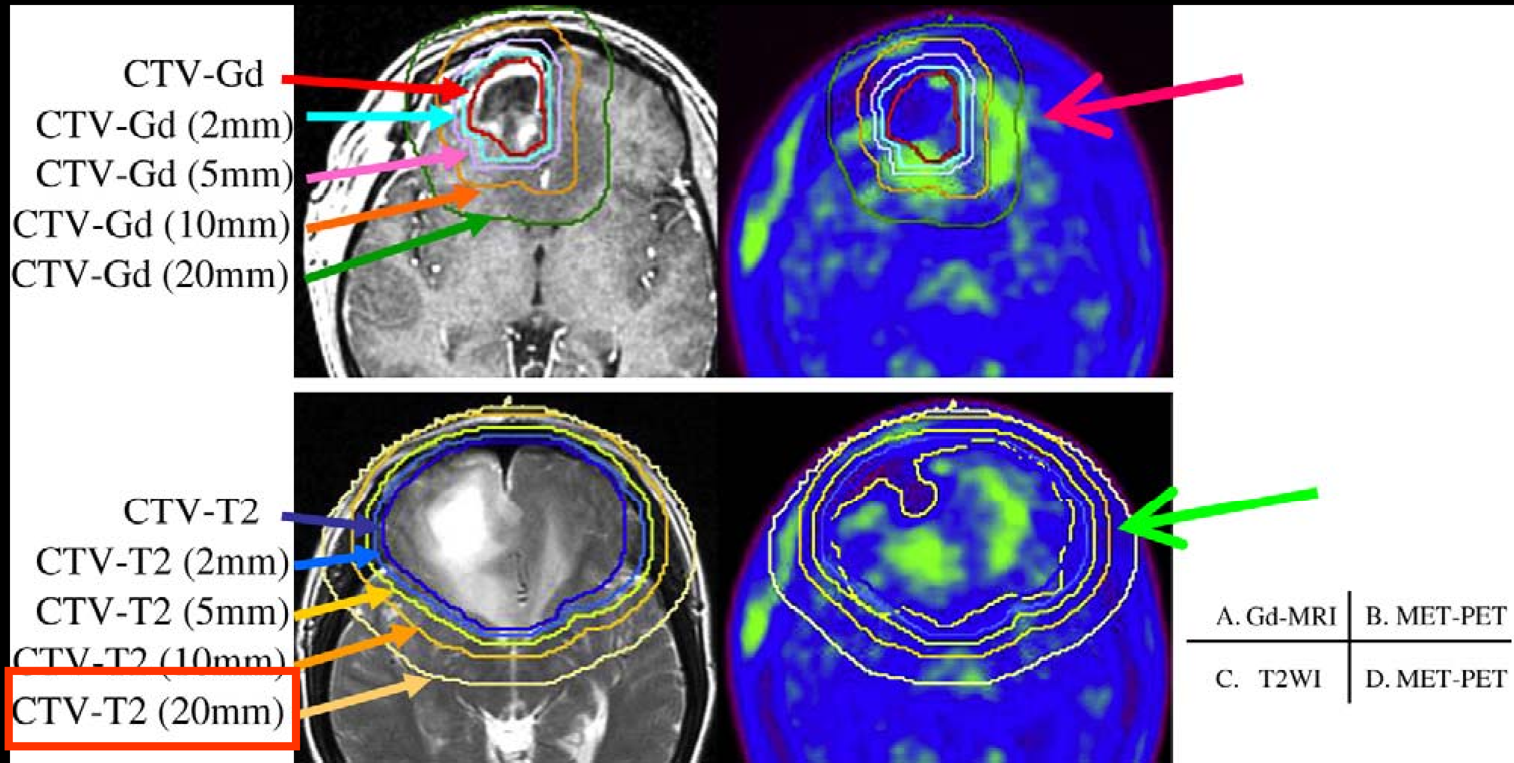



⇒ Composite Vol MRI and PET
⇒ Vol PET
⇒ Vol MRI
⇒ Vol PET minus MRI
⇒ Common Vol MRI and PET
⇒ Vol MRI minus PET
Gd
6ccm
Gd+MET
6ccm
MET
13ccm

MR vs. MET-PET

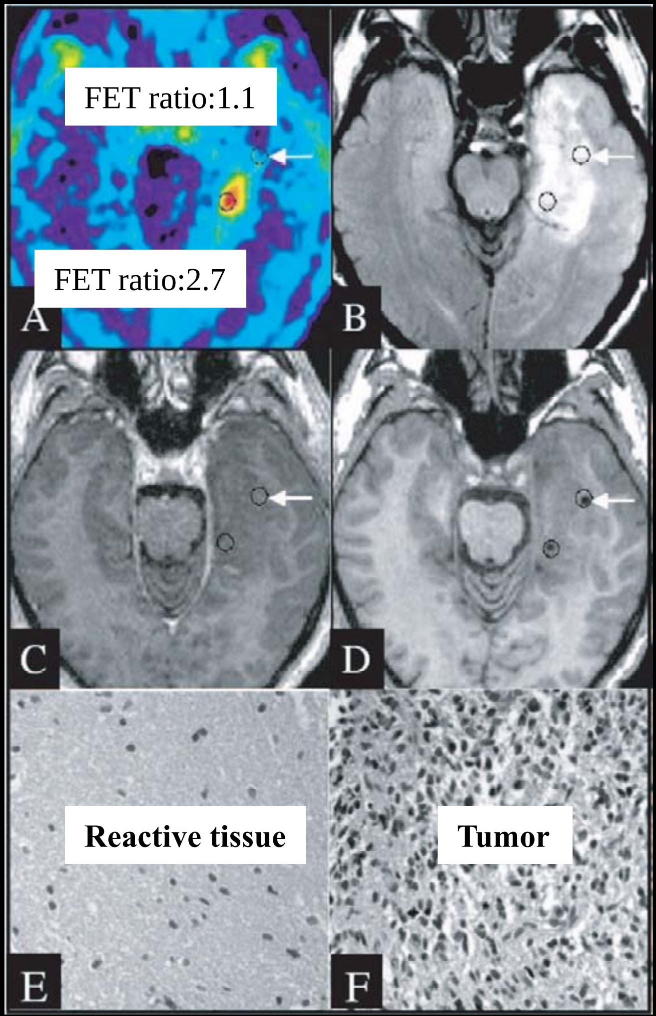
+: total extent of associated pathological changes
preferred: Gd contrast

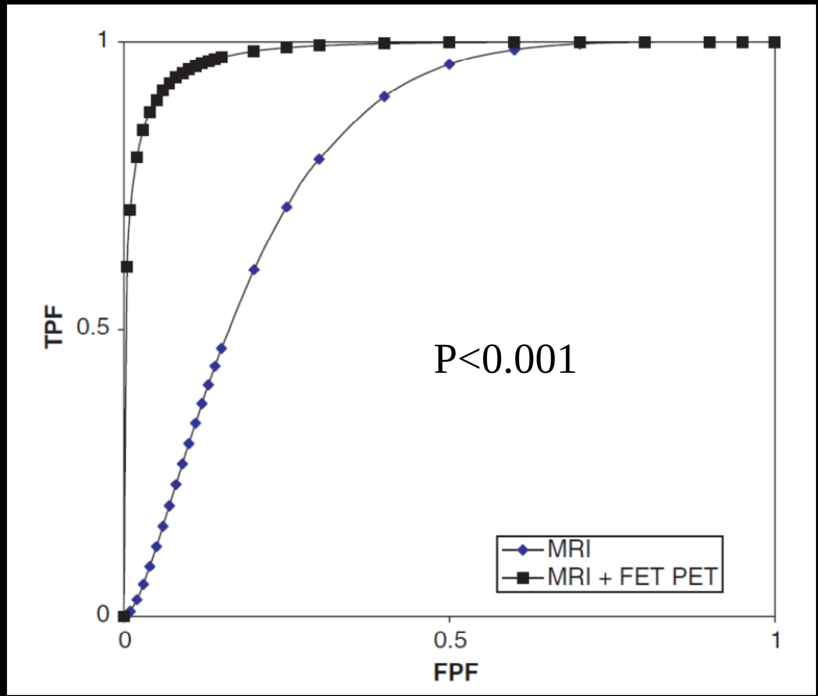
+: extent of viable tumor
methionine



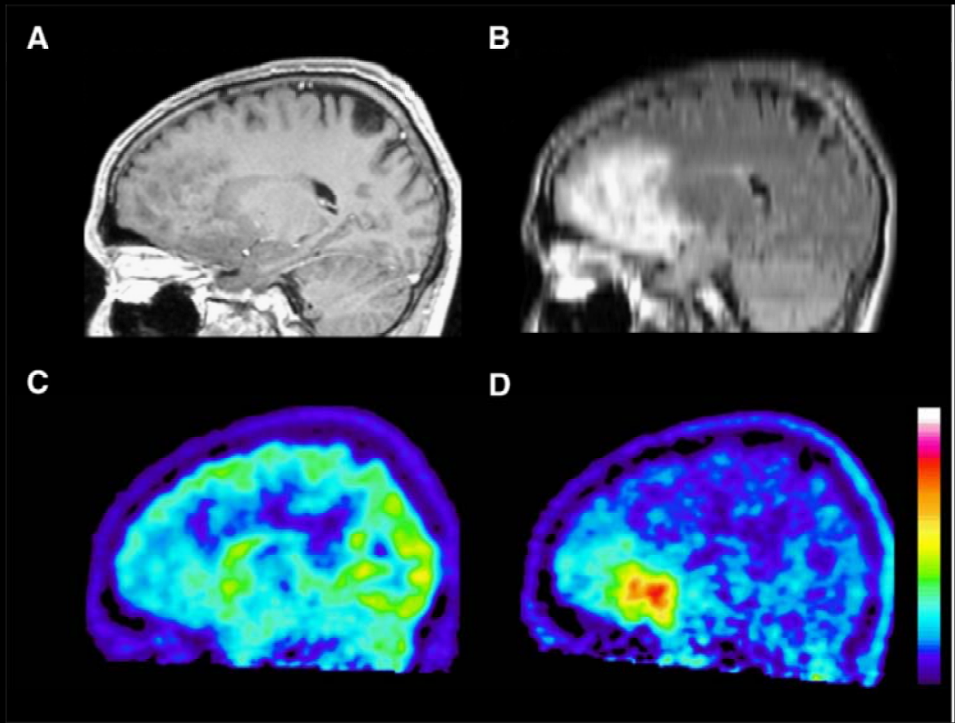
# Other PET tracers

## FET-PET



# FET-PET vs. FDG-PET




FDG-PET FET-PET

N=43 glioma patients (LGG / HGG)

- FET: uptake in 37 patients
- FDG: uptake in 15 patients

- FET: ok for delineation in all
- FDG: problem: gray matter!

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Available online at www.sciencedirect.com
ScienceDirect
Nuclear Medicine and Biology 36 (2009) 779–787
NUCLEAR MEDICINE AND BIOLOGY
www.elsevier.com/locate/nucmedbio

Comparison of $^{18}$F-FET and $^{18}$F-FDG PET in brain tumors

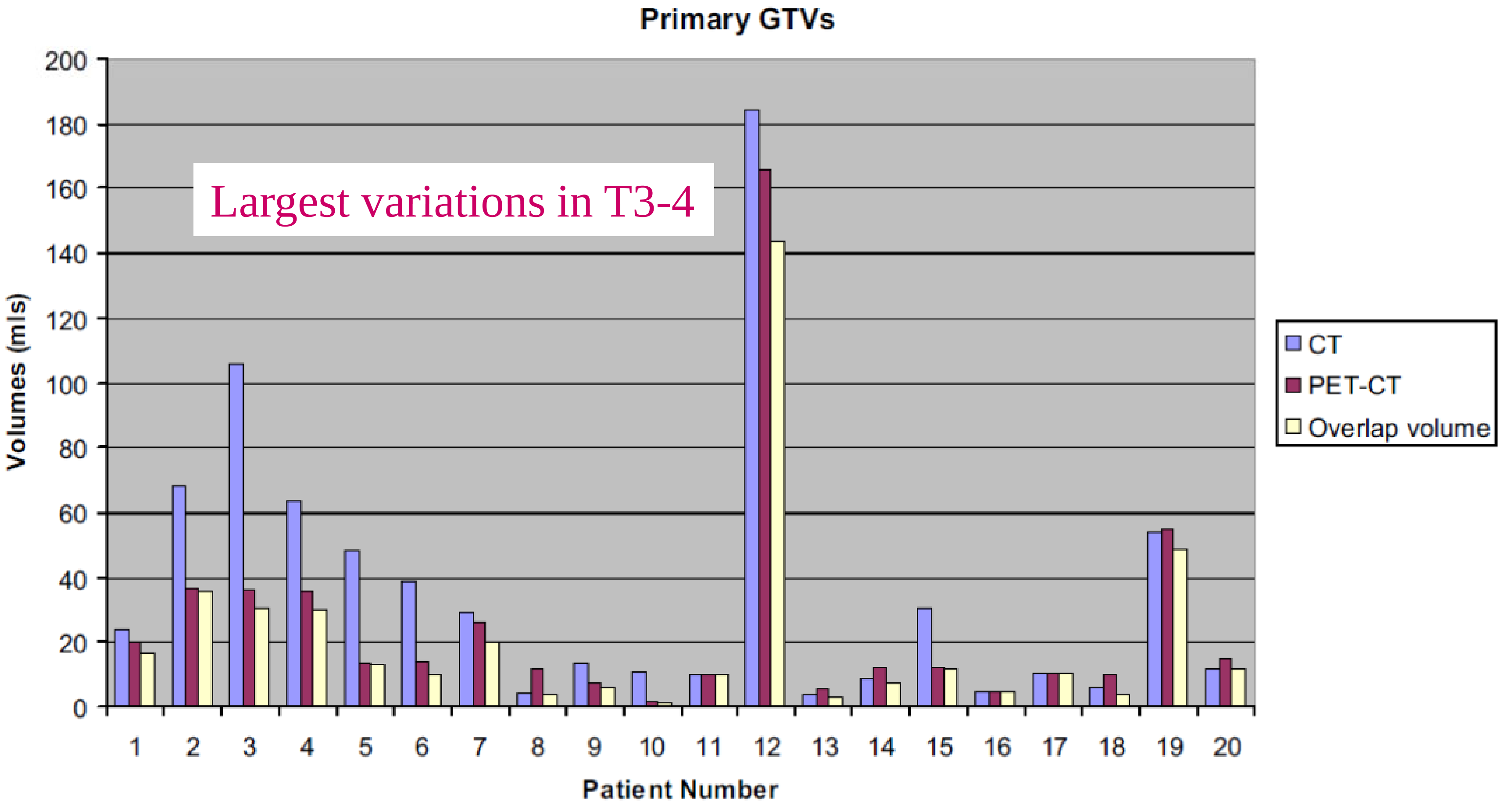
Dirk Pauleit[a], Gabriele Stoffels[a], Ansgar Bachofner[b], Frank W. Floeth[c], Michael Sabel[c], Hans Herzog[a], Lutz Tellmann[a], Paul Jansen[d], Guido Reifenberger[e], Kurt Hamacher[a], Heinz H. Coenen[a], Karl-Josef Langen[a,*]

# Other PET tracers

# HEAD & NECK

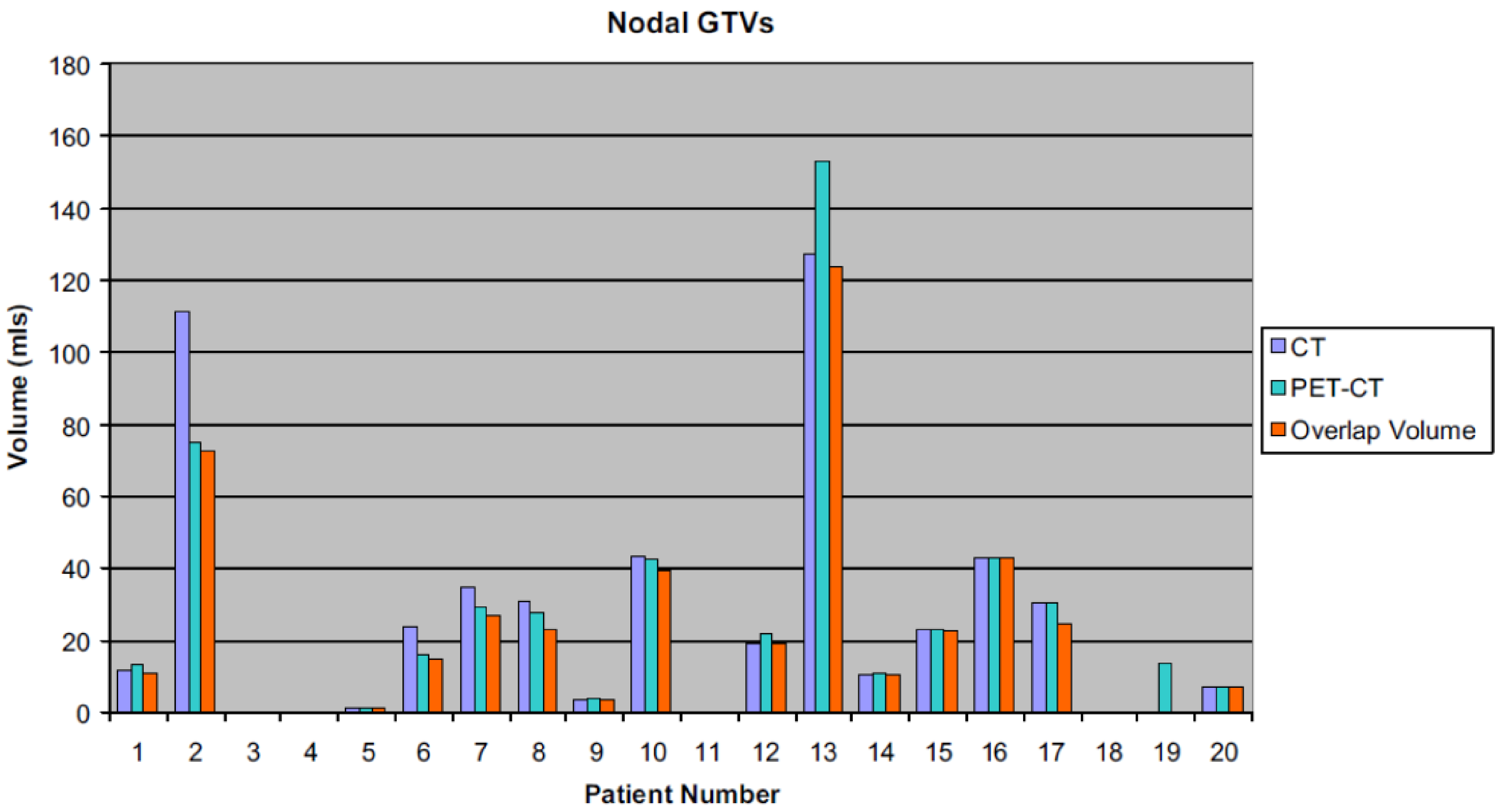
FDG PET-CT: does it holds its promise?

# Oropharyngeal cancer: Delineations ~ imaging tool




Chatterjee 2012

# Oropharyngeal cancer: Delineations ~ imaging tool




Chatterjee 2012

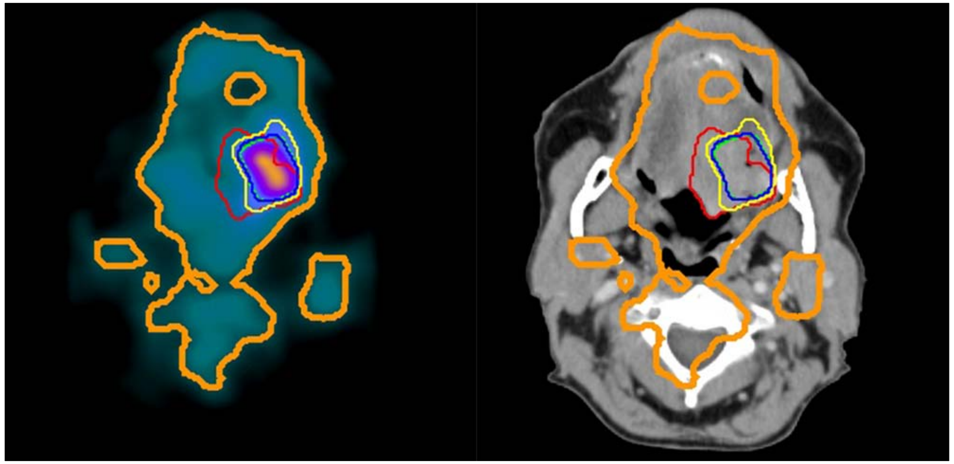
# PET segmentation tools

**Available methods**

- Visual / manual
- SUV (different versions)
- % of tumor activity
- % of background activity
- Ratio tumor - background
- Advanced algorithms

**This choice is not trivial !**

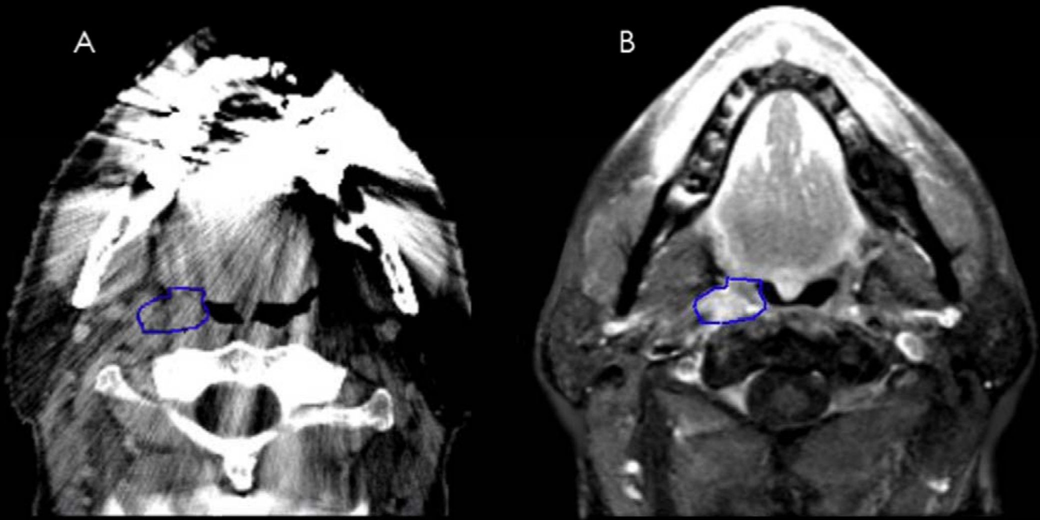
- Fixed SUV is not suitable
- Volume depends on method
- Inter-observer variation
- Insufficient validation

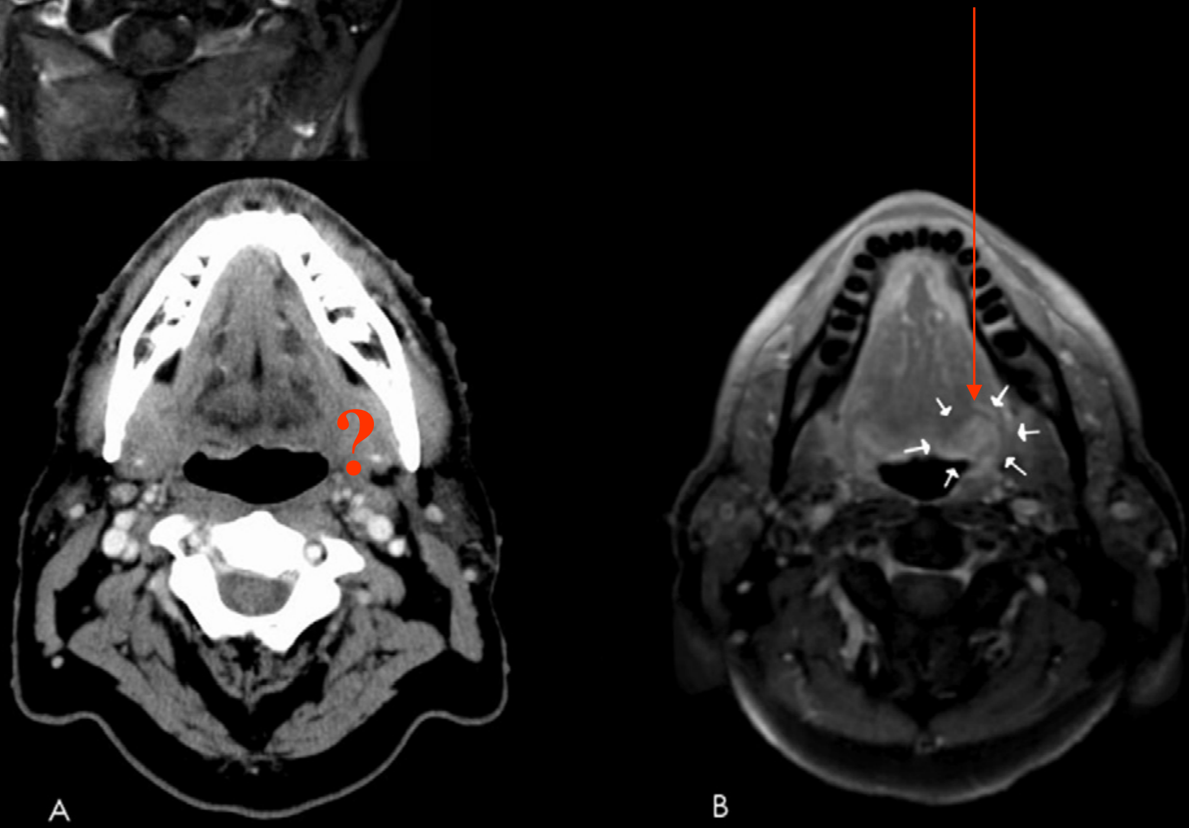


**Choose and standardize a method in your center!**

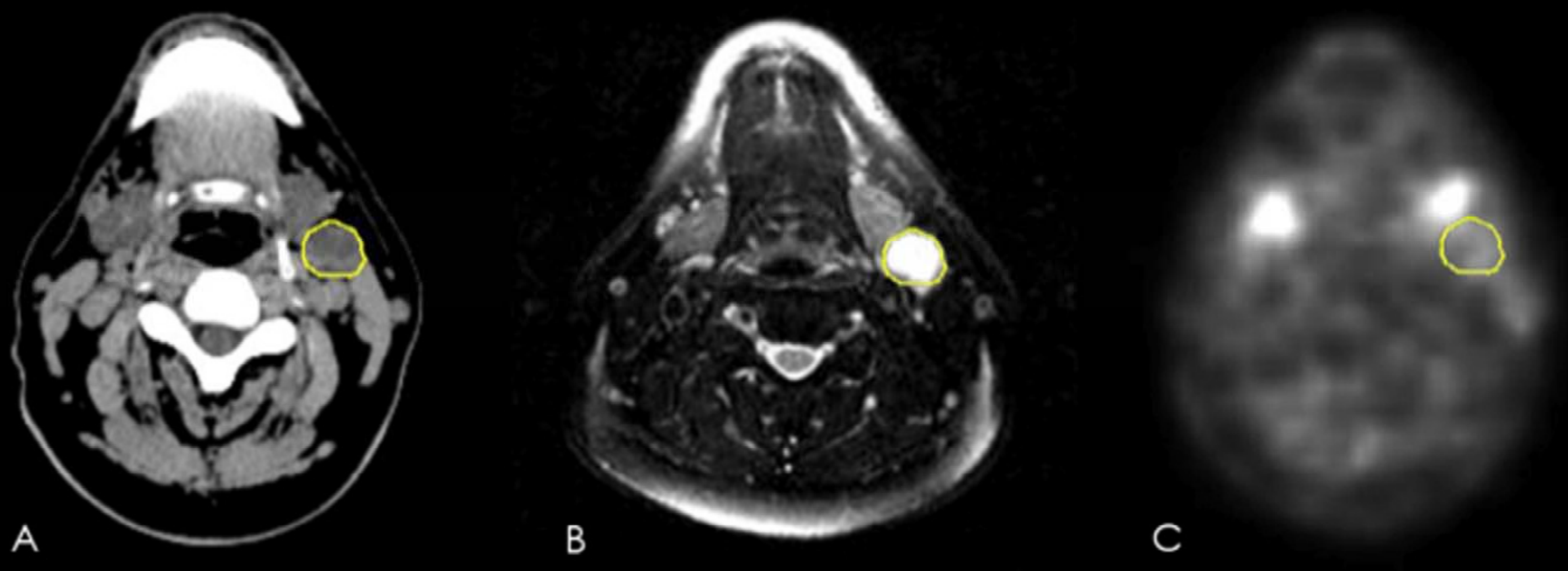
Schinagl 2007

# IS THERE a ROLE for MRI?



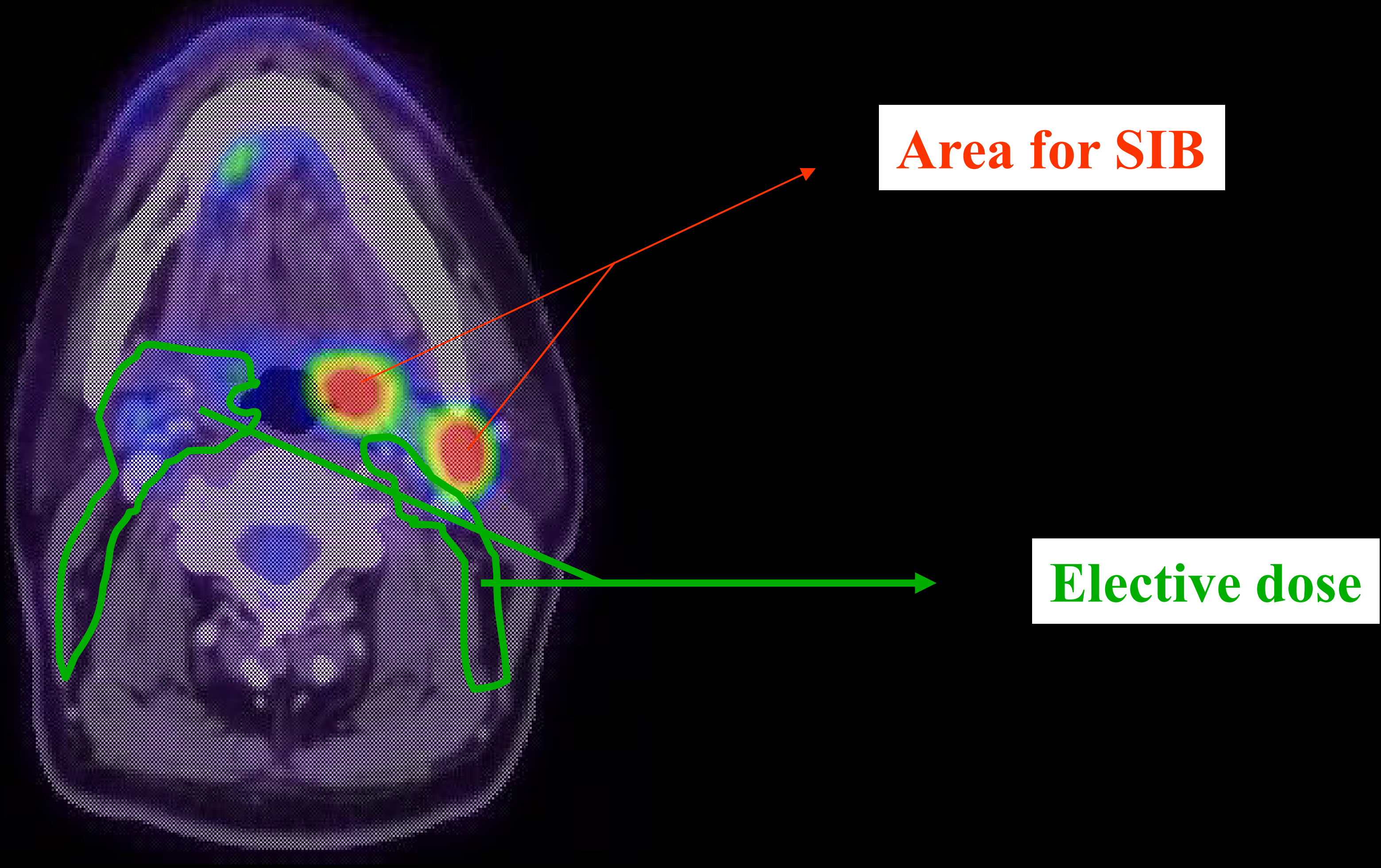
# IS PET-CT the HOLY GRALE?




Problem: 30-50% of PET N0 contains tumor cells (AP)!

(Thiagarajan et al. 2011)

# POSSIBLE IMPLICATIONS IN TP



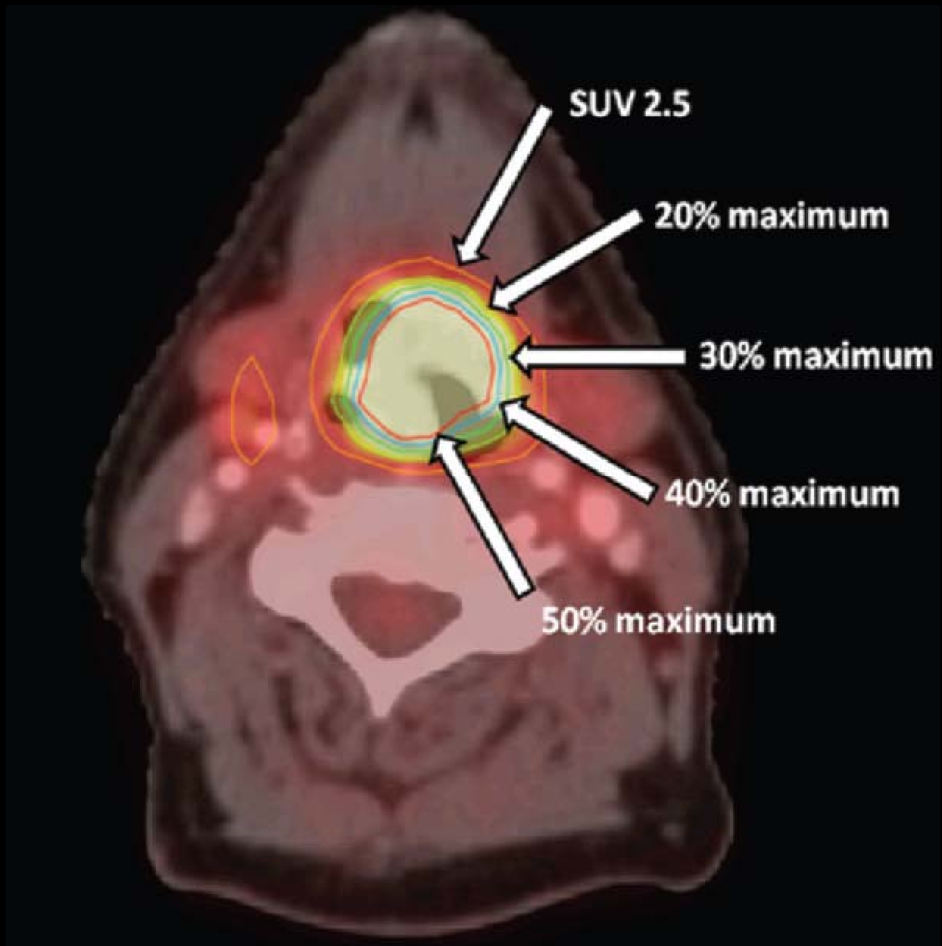
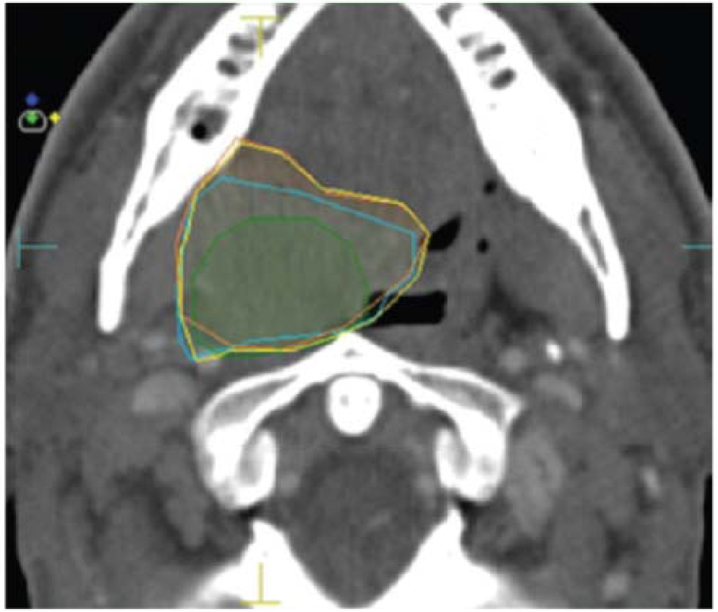
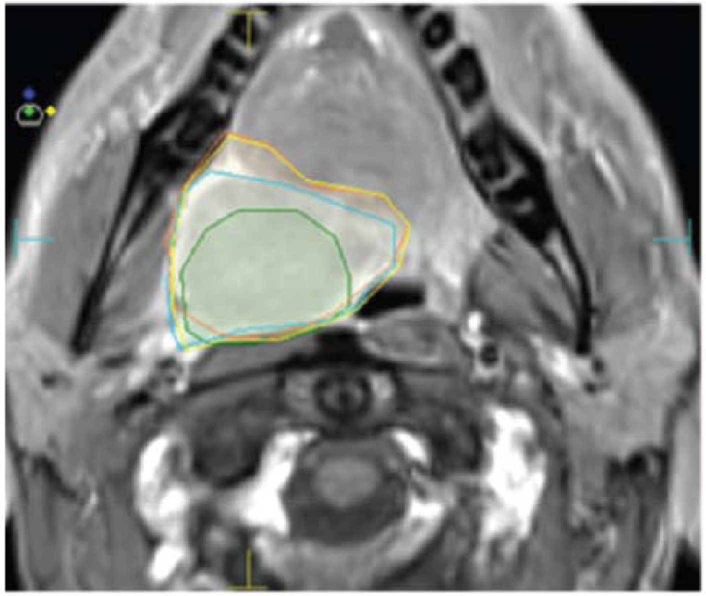

SUV 2.5
20% maximum
30% maximum
40% maximum
50% maximum

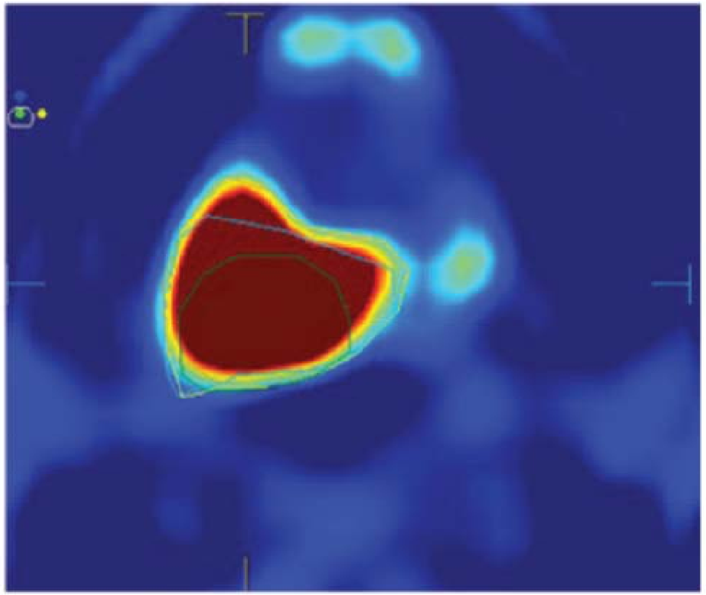
**Figure 4.** SCC in the right tonsil (T3N0M0) of a 65-year-old man. **(a, b)** Axial CT image obtained for radiation therapy planning **(a)** and deformably coregistered axial T1-weighted MR image **(b)** show GTVs generated independently from each image data set. Deformable coregistration of **b** with **a** was performed by using the same diagnostic software as in Figure 2. **(c)** Axial FDG PET image shows a composite of the GTVs that was contoured manually at image interpretation. Contour lines are color coded to show the imaging modality on which they are based (green = CT, blue = MR imaging, orange = PET).



a.

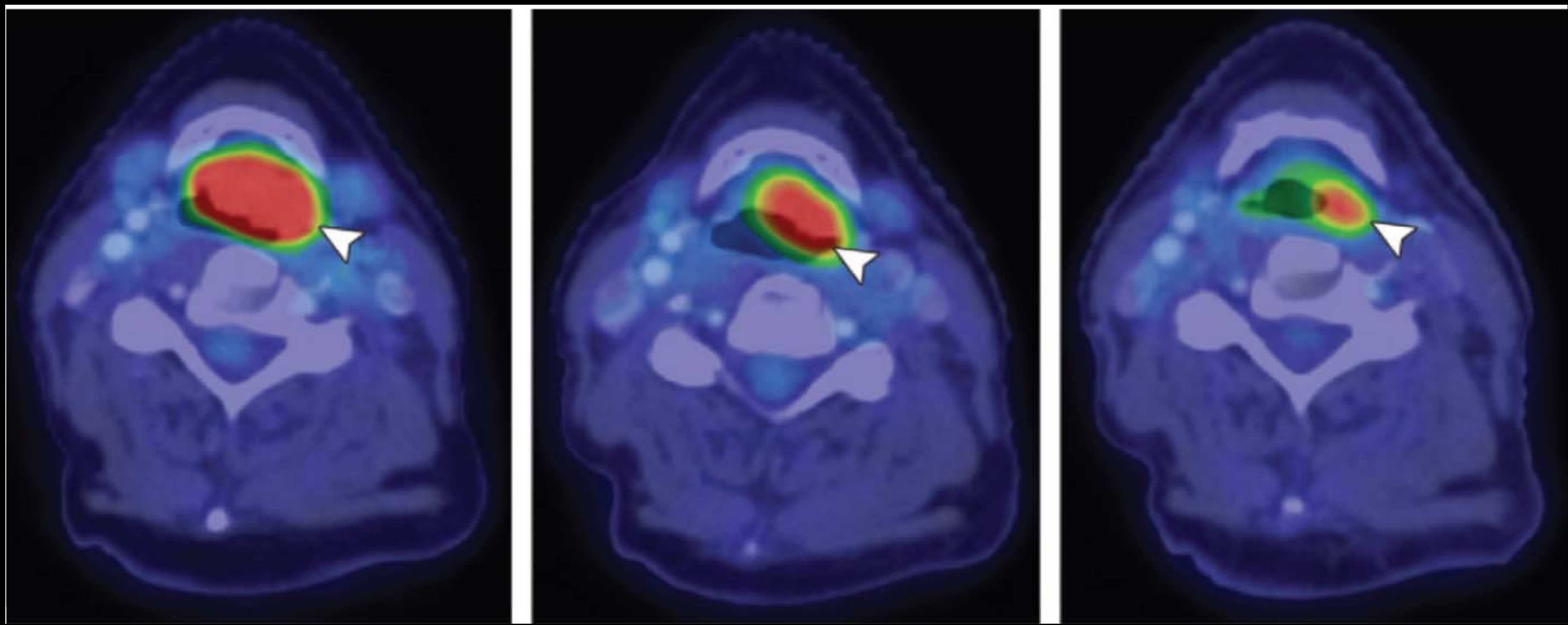


b.



c.

GV



GV

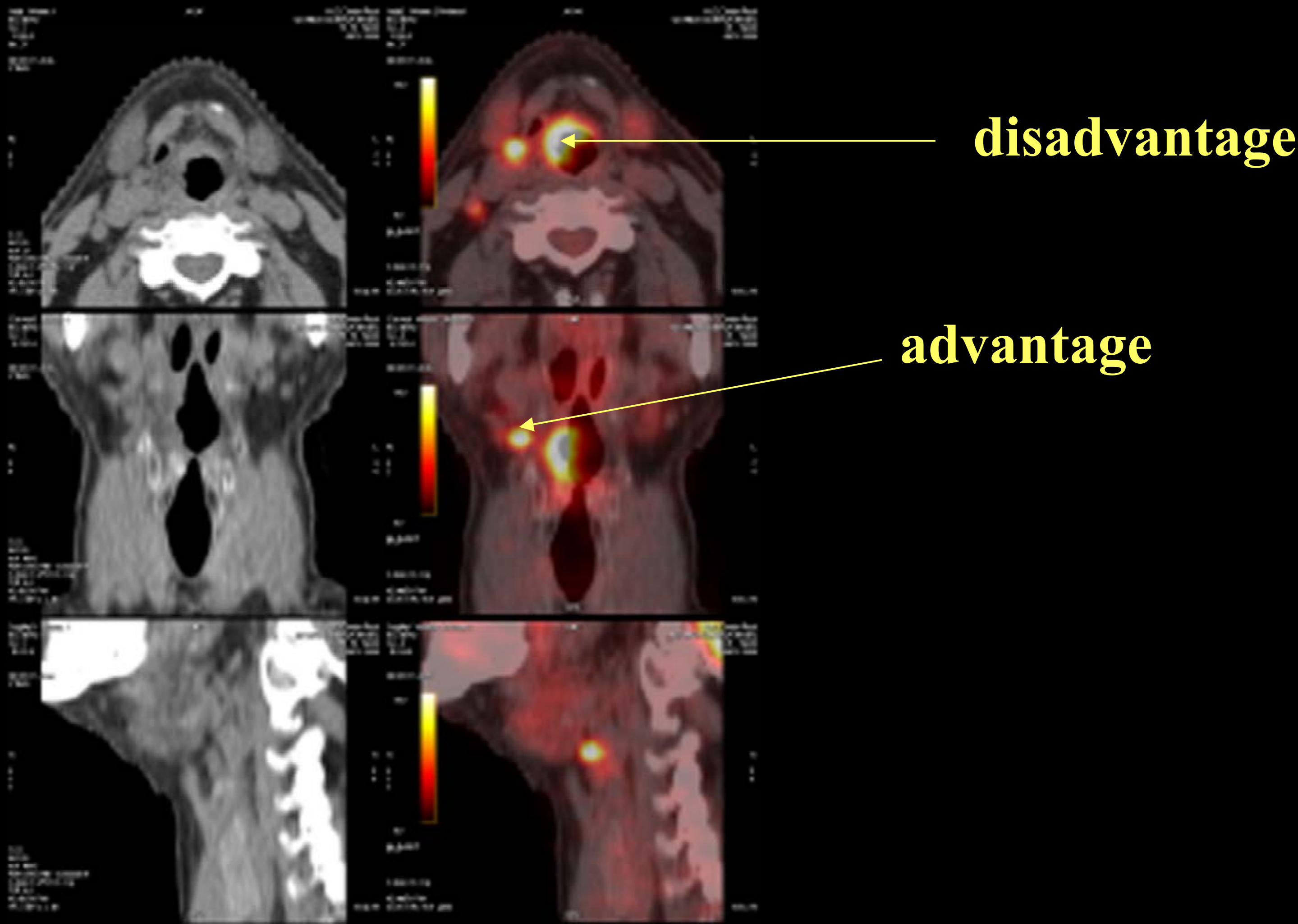
# A critical note …

## Is Image Registration of Fluorodeoxyglucose–Positron Emission Tomography/Computed Tomography for Head-and-Neck Cancer Treatment Planning Necessary?

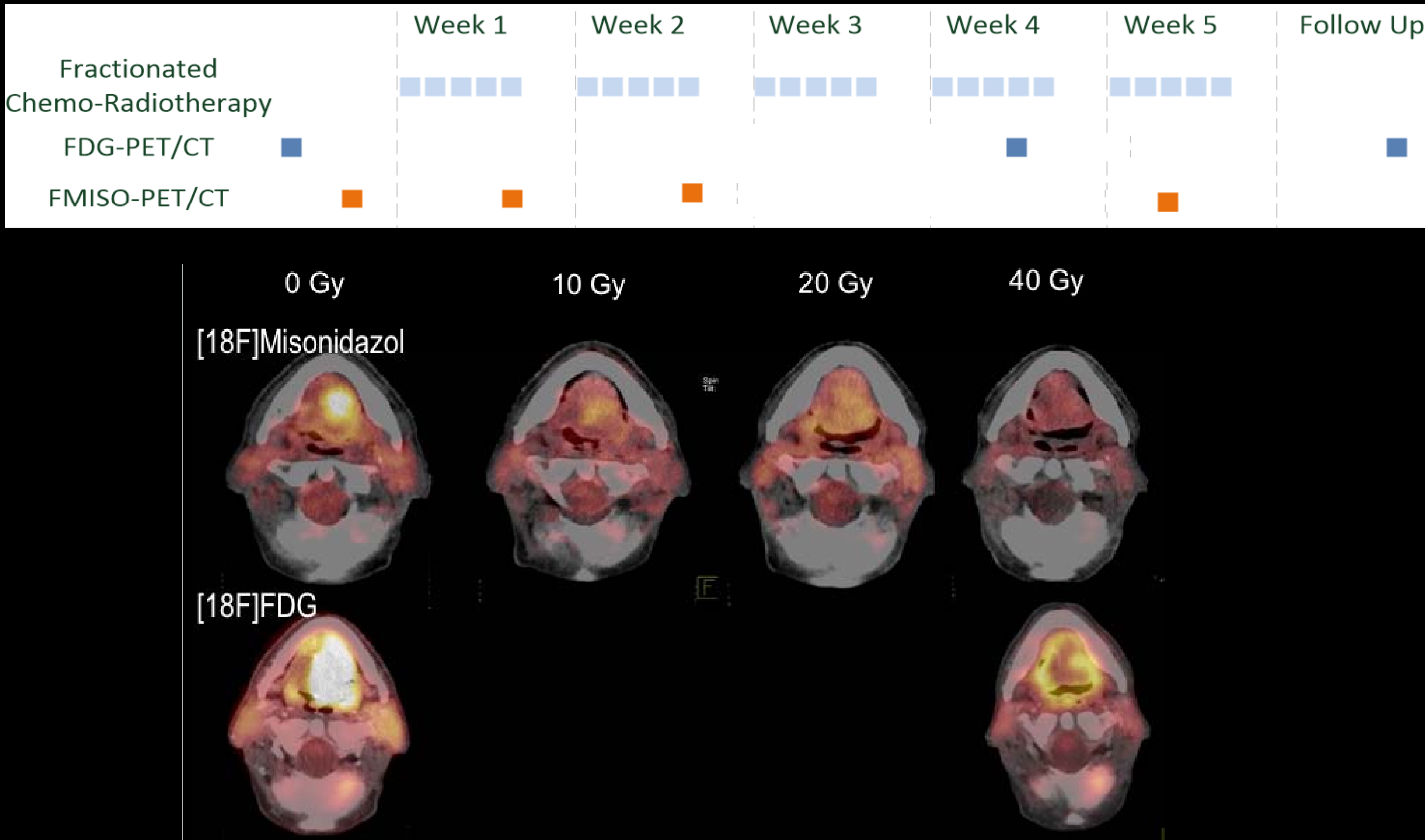
David Fried, B.S.,[*] Michael Lawrence, Ph.D.,[*] Amir H. Khandani, M.D.,[†]
Julian Rosenman, M.D., Ph.D.,[*,‡] Tim Cullip, M.S.,[*] and Bhishamjit S. Chera, M.D.[*,‡]

**Conclusions:** PET and CT-defined tumor volumes received similar RT doses despite having less than complete overlap and the inaccuracies of image registration. LRF correlated with both CT and PET-defined volumes. The dosimetry for PET- and/or CT-based tumor volumes was not significantly inferior in patients with LRF. CT-based delineation alone may be sufficient for treatment planning in patients with HNSCC. Image registration of FDG-PET may not be necessary. 

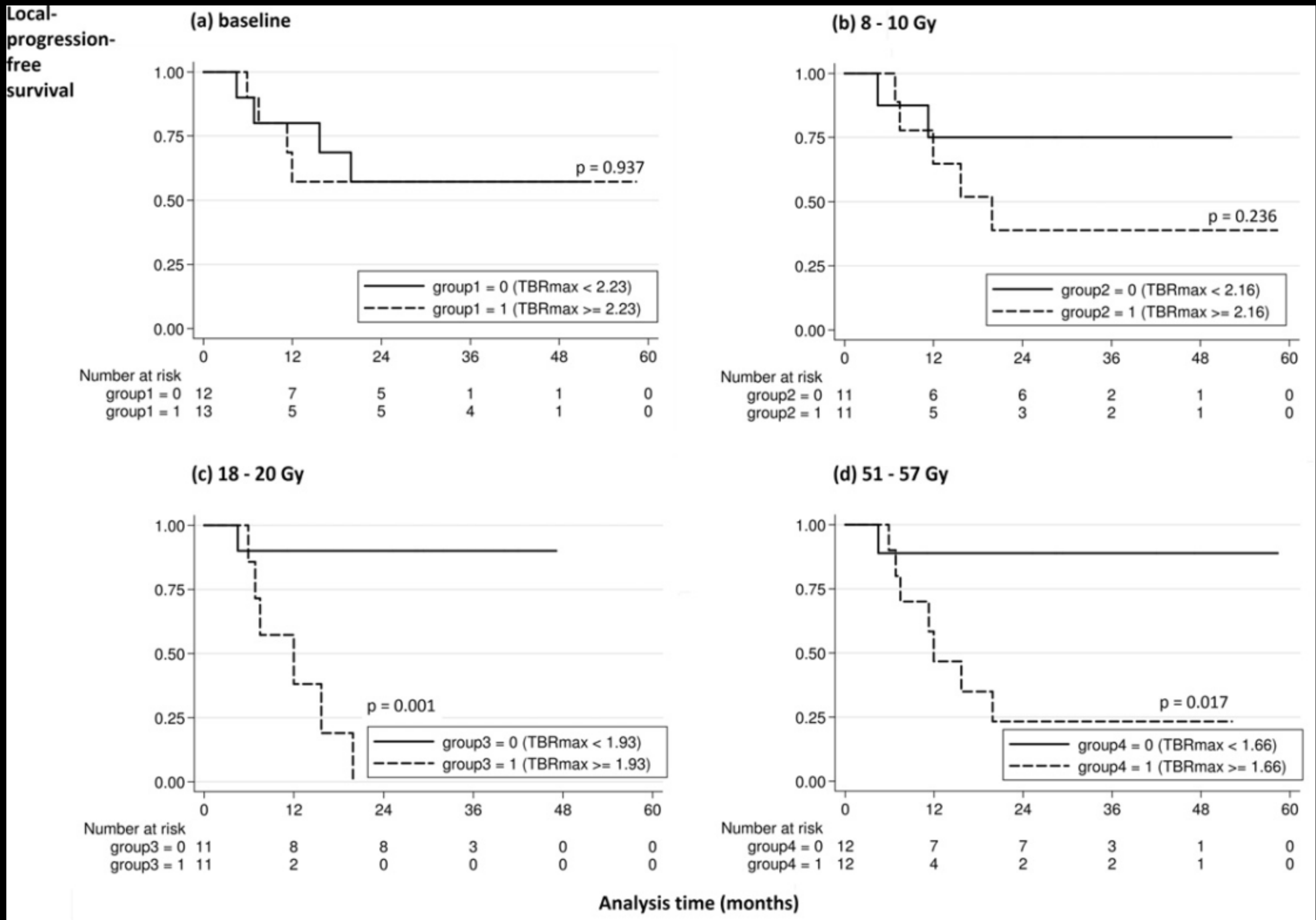
IJROBP 2012




GV

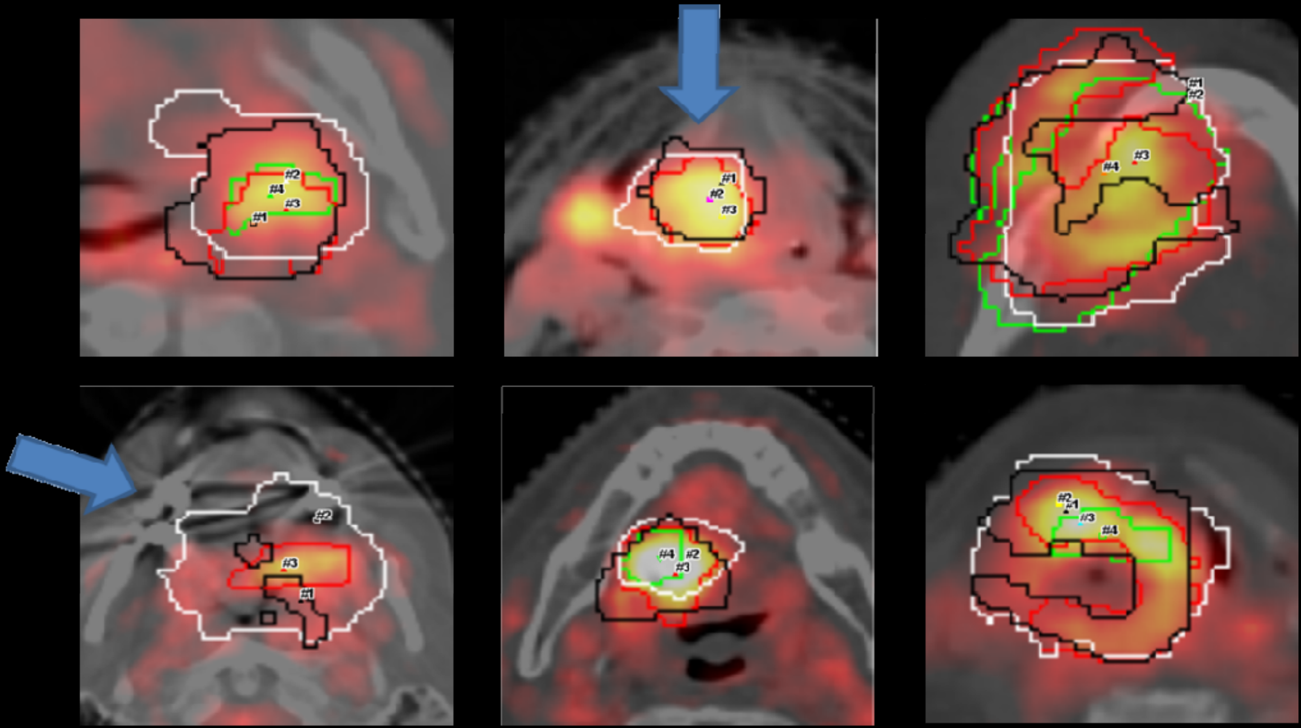

Week 1
Week 2
Week 3
Week 4
Week 5
Follow Up
Fractionated Chemo-Radiotherapy
FDG-PET/CT
FMISO-PET/CT
0 Gy
10 Gy
20 Gy
40 Gy
[18F]Misonidazol
[18F]FDG

Zips 2012



Local-progression-free survival
(a) baseline
p = 0.937
group1 = 0 (TBRmax < 2.23)
group1 = 1 (TBRmax >= 2.23)
Number at risk
group1 = 0 12 7 5 1 1 0
group1 = 1 13 5 5 4 1 0
(b) 8 - 10 Gy
p = 0.236
group2 = 0 (TBRmax < 2.16)
group2 = 1 (TBRmax >= 2.16)
Number at risk
group2 = 0 11 6 6 2 1 0
group2 = 1 11 5 3 2 1 0
(c) 18 - 20 Gy
p = 0.001
group3 = 0 (TBRmax < 1.93)
group3 = 1 (TBRmax >= 1.93)
Number at risk
group3 = 0 11 8 8 3 0 0
group3 = 1 11 2 0 0 0 0
(d) 51 - 57 Gy
p = 0.017
group4 = 0 (TBRmax < 1.66)
group4 = 1 (TBRmax >= 1.66)
Number at risk
group4 = 0 12 7 7 3 1 0
group4 = 1 12 4 2 2 1 0
Analysis time (months)


Zips 2012



FMISO1black, FMISO2 white, FMISO3 red, FMISO4 green; 6 patients contoured by one observer

# FMISO-hypoxic volume changes during the course of RCHT

GV

# LUNG CANCER

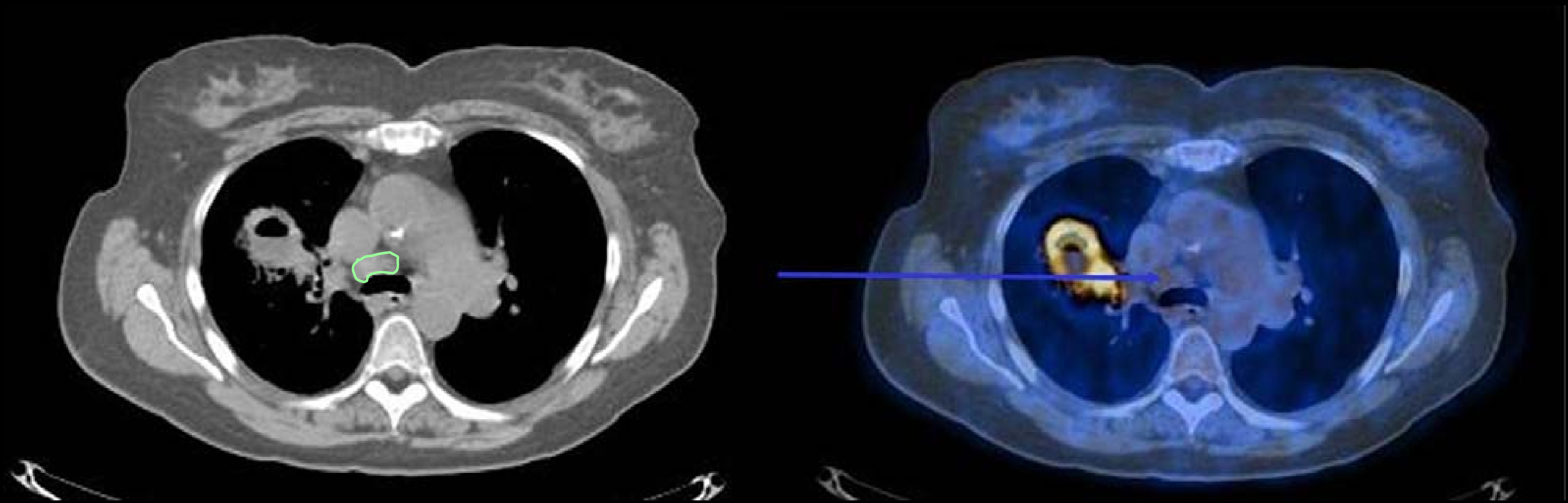
# PET can change staging & delineation

**N=167**

| Pre-PET stage | No. of patients | No. with metastasis | % |
|---|---|---|---|
| Stage IA | 21 | 0 | 0 |
| Stage IB | 18 | 3 | 17 |
| All Stage I | 39 | 3 | 8 |
| Stage IIA | 6 | 1 | 17 |
| Stage IIB | 22 | 4 | 18 |
| All Stage II | 28 | 5 | 18 |
| Stage IIIA | 62 | 16 | 26 |
| Stage IIIB | 38 | 8 | 21 |
| All Stage III | 100 | 24 | 24 |

**MacManus 2001**

# PET can change staging & delineation



PET -: APD confirmed

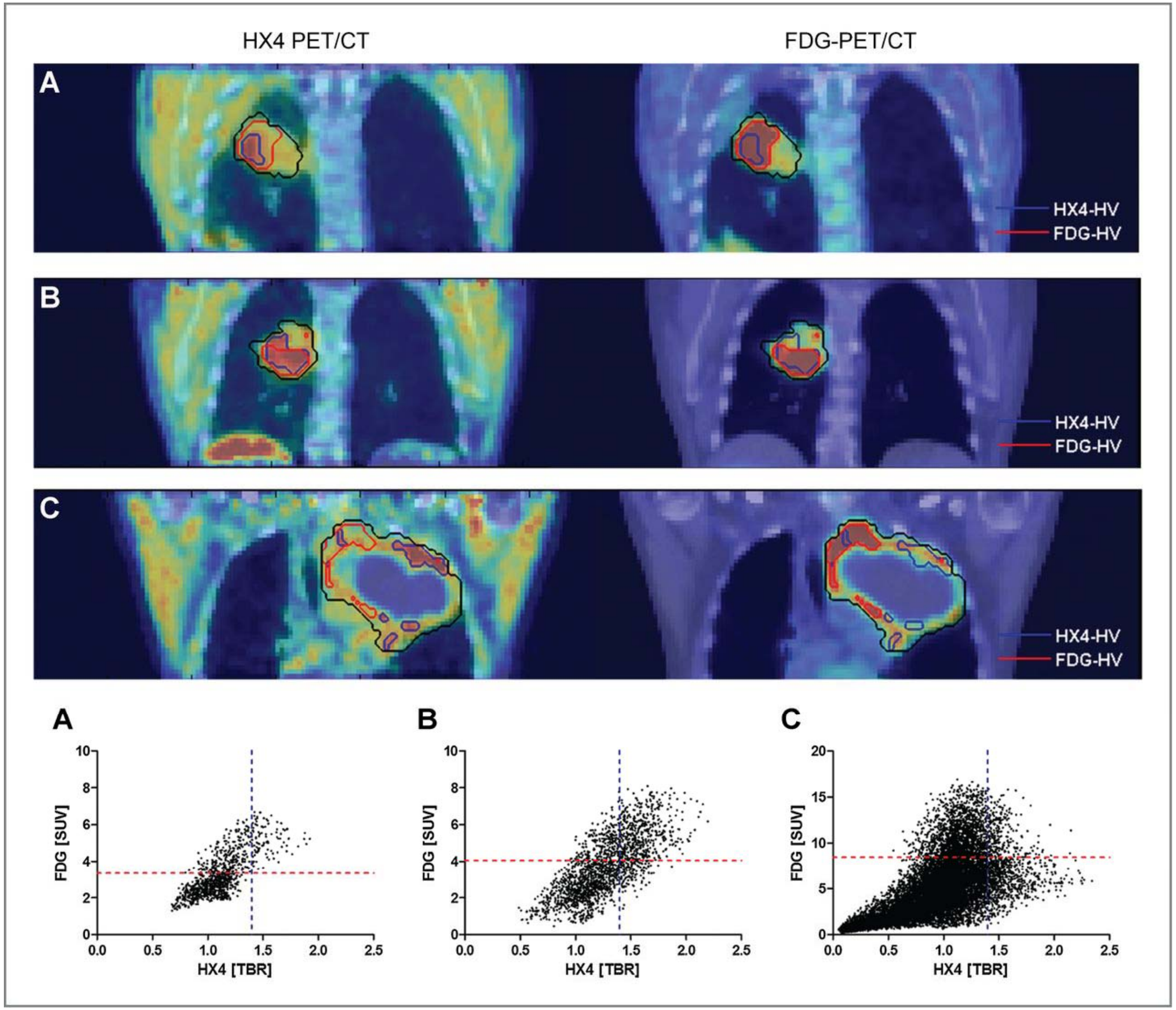
| Pt. No. | CT scan | PET scan | Pathologic examination |
|---|---|---|---|
| 1 | 0 | 0 | 0 |
| 2 | 0 | 2 | 2 |
| 3 | 0 | 2 | 2 |
| 4 | 0 | 0 | 2 |
| 5 | 0 | 0 | 1 |
| 6 | 0 | 0 | 2 |
| 7 | 2 | 2 | 0 |
| 8 | 2 | 2 | 2 |
| 9 | 0 | 0 | 1 |
| 10 | 0 | 0 | 0 |
| 11 | 2 | 2 | 2 |
| 12 | 0 | 0 | 0 |
| 13 | 0 | 0 | 0 |
| 14 | 1 | 2 | 2 |
| 15 | 0 | 0 | 0 |
| 16 | 0 | 0 | 0 |
| 17 | 0 | 0 | 2 |
| 18 | 0 | 0 | 0 |
| 19 | 1 | 1 | 0 |
| 20 | 0 | 0 | 1 |
| 21 | 0 | 0 | 0 |
| 22 | 0 | 0 | 0 |
| 23 | 2 | 1 | 1 |
| 24 | 0 | 0 | 0 |
| 25 | 0 | 0 | 0 |
| 26 | 0 | 1 | 1 |
| 27 | 3 | 3 | 2 |
| 28 | 2 | 0 | 1 |
| 29 | 2 | 0 | 0 |
| 30 | 0 | 0 | 0 |
| 31 | 1 | 0 | 0 |
| 32 | 0 | 0 | 1 |

**32 patients**

**Changes in TN stage between CT and PET:**
**- For T: n=6**
**- For N: n=9**

**APD confirmation in 7 N:**
**- 3 higher N (red)**
**- 4 lower N (green)**

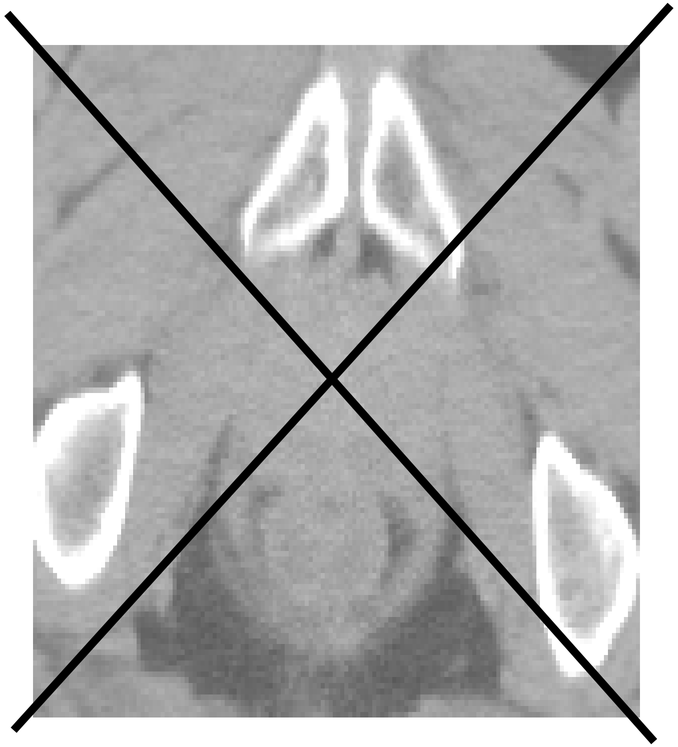
**Faria et al. 2008**




Zegers et al. 2014

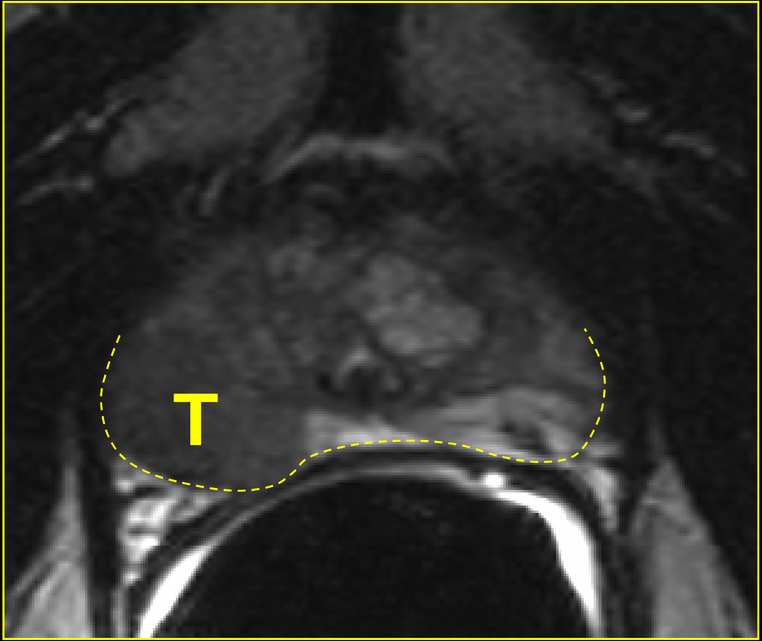
# PROSTATE CANCER

# Imaging of T



# Prostate Cancer Staging

## Extracapsular Tumor Spread

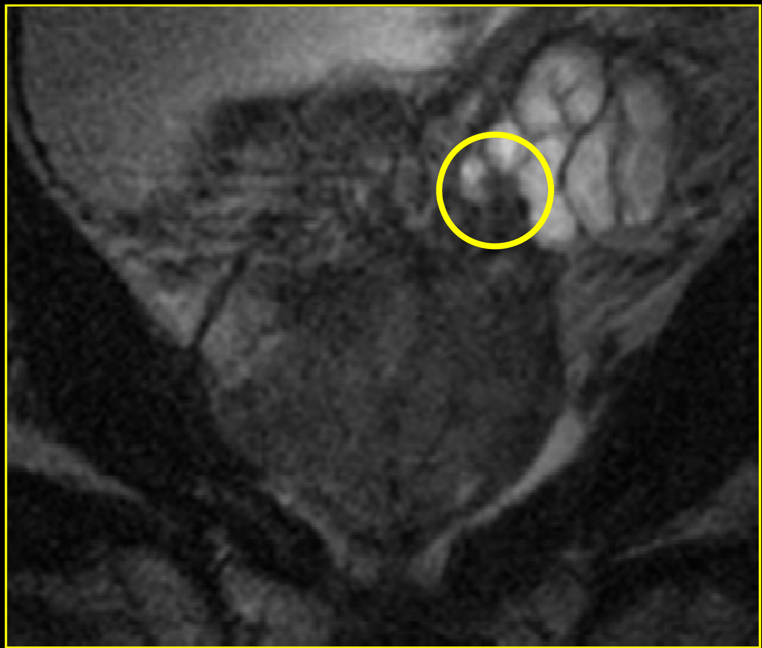


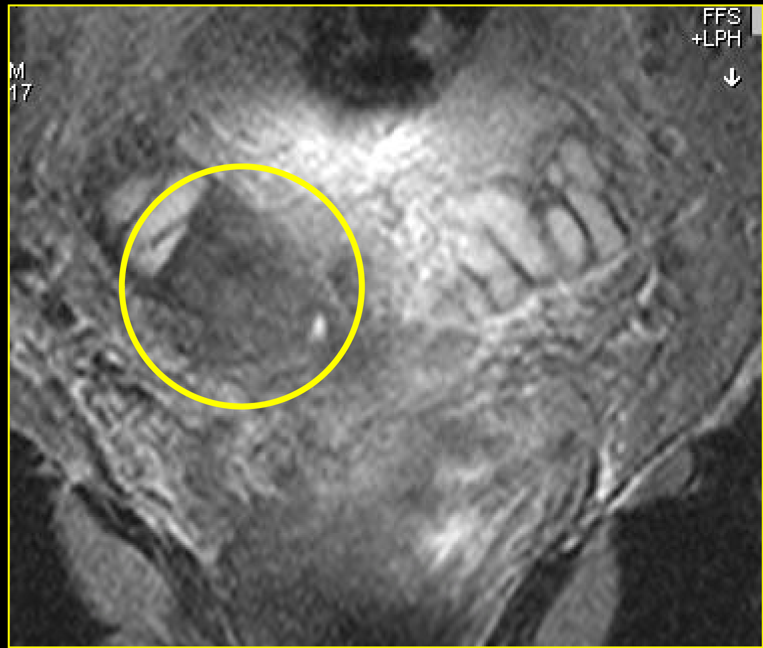

Capsular penetration = irregular capsular bulge OR infiltration of periprostatic fat OR neurovascular bundle asymmetry

GV

# Prostate Cancer Staging

## Seminal Vesicle Involvement






Seminal vesicle invasion =
abnormally low signal intensity within lumen/
focal thickening of seminal vesicle wall

# MRI and its role in prognosis

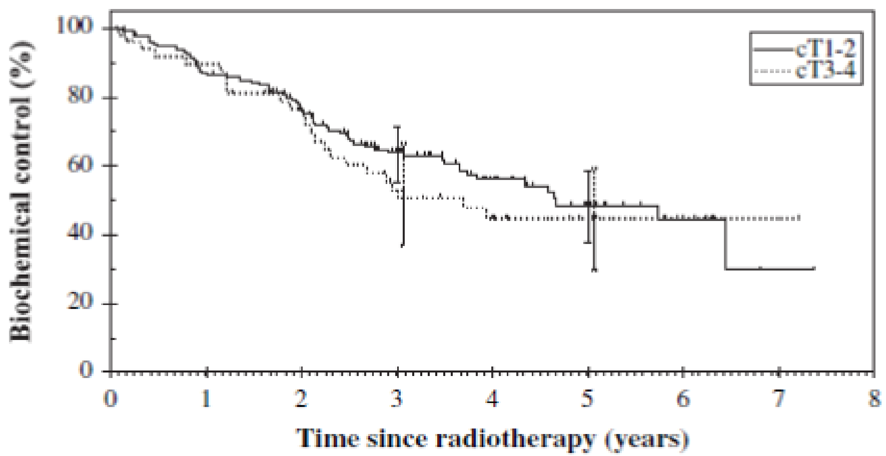



Fig. 1 – Biochemical control by clinical T stage.

**Jackson et al. 2005; Clin Oncol: 167-71.**

**Cellini et al, IJROBP 2002; 53:595-599: 12/12 local failures in the prostate.**

**Speight et al. 2007; JCO: 62-69.**

# Dynamic Contrast-Enhanced MRI

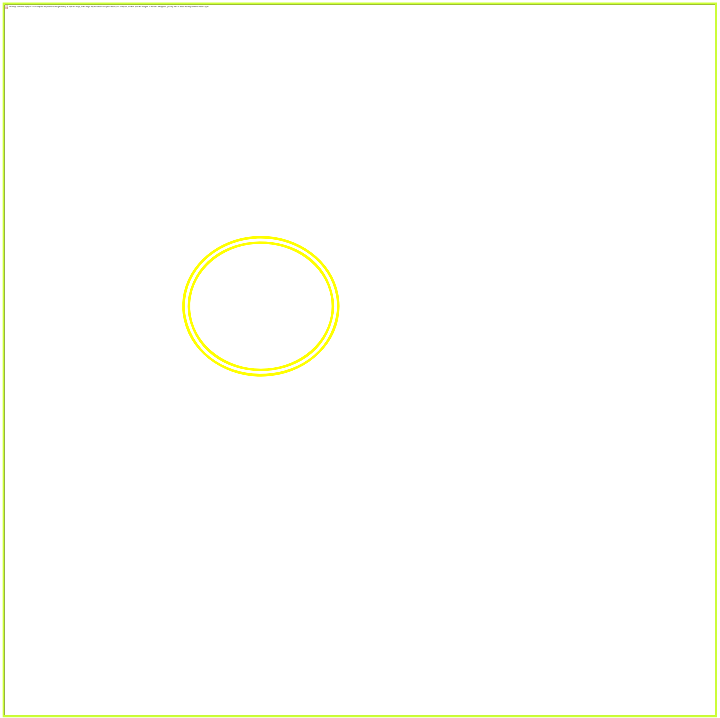
## Assessment of Angiogenesis

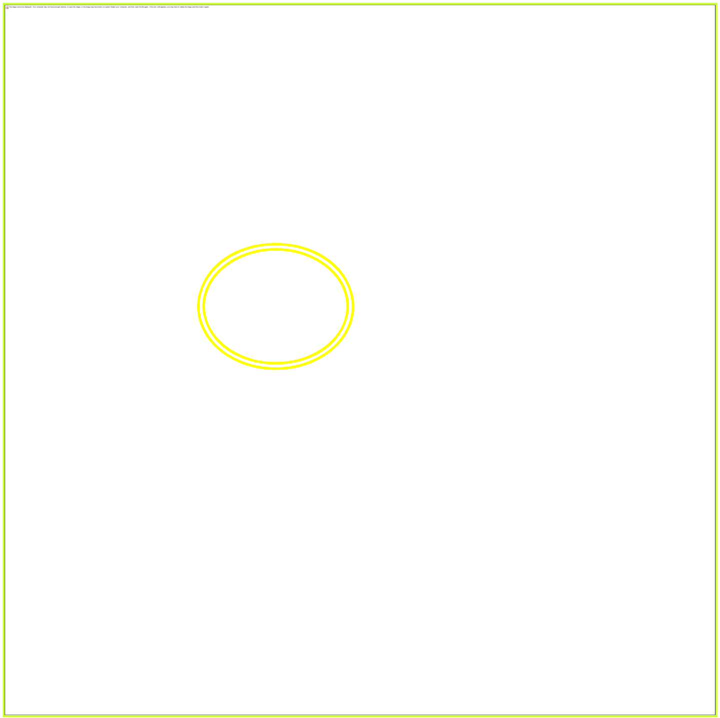
| Lesion Morphology | Enhancement |
|---|---|
| Angiogenic Factors | Increased in- en efflux<br>Expanded extracellular space<br>Increased extravasation |
| Growth of existing vessels<br>De novo angiogenesis | |
| Abnormal configuration: AV-shunts and defective endothelium | Earlier onset of enhancement<br>Increased slope |

# Prostate cancer diagnosis with dCE

GV

# Diffusion Weighted Imaging

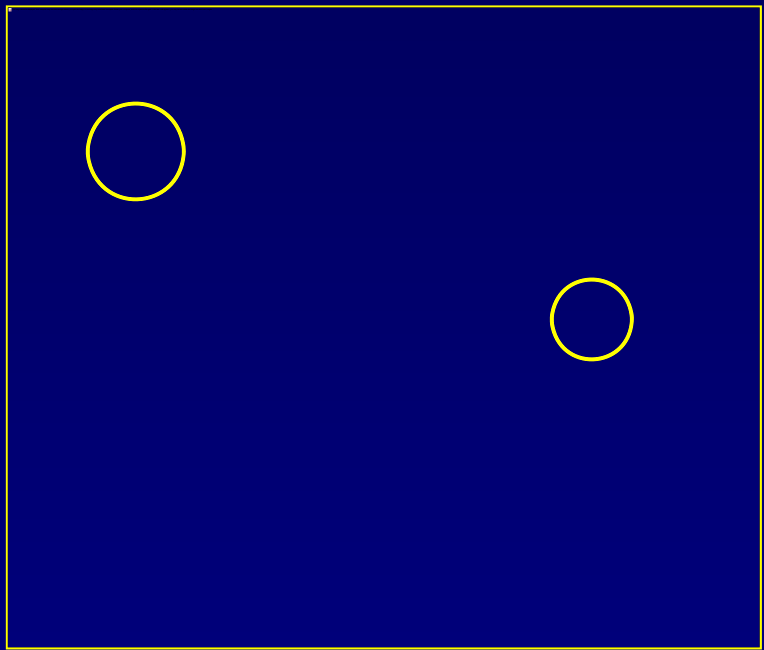


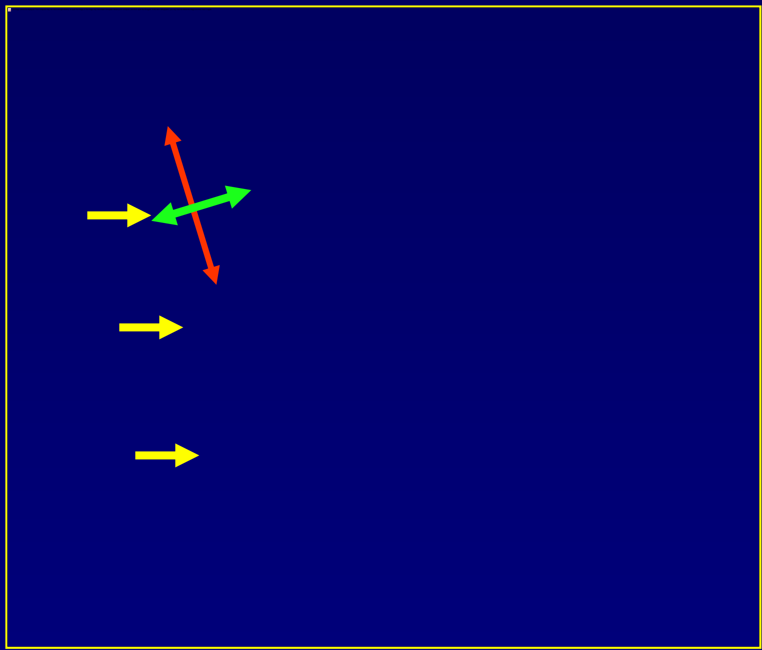


# Imaging of N

# Prostate Cancer Staging

## Lymphatic Spread





Lymph Node Staging

Oval node > 10 mm

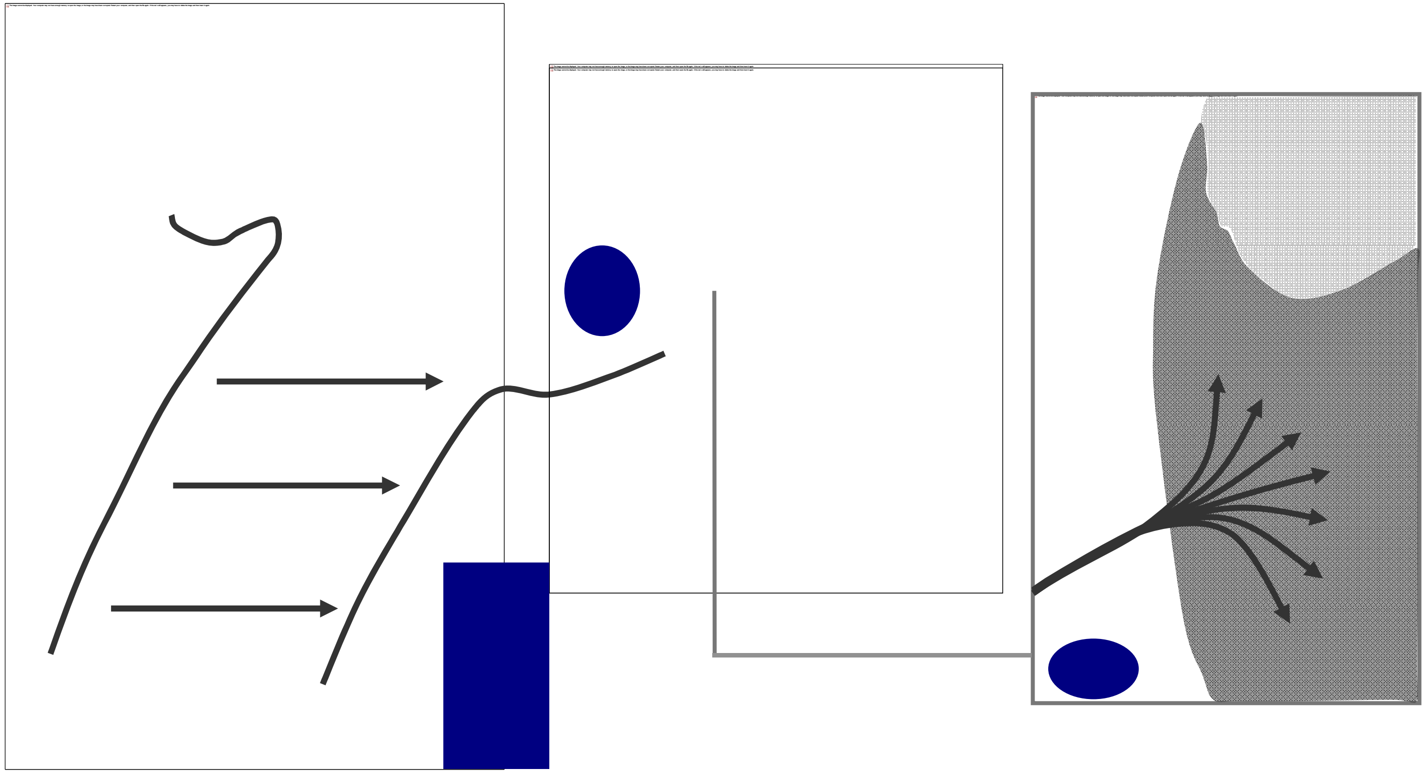
Round node > 8 mm

# IV injection of USPIO
# (“ultra small particles of iron oxide”)

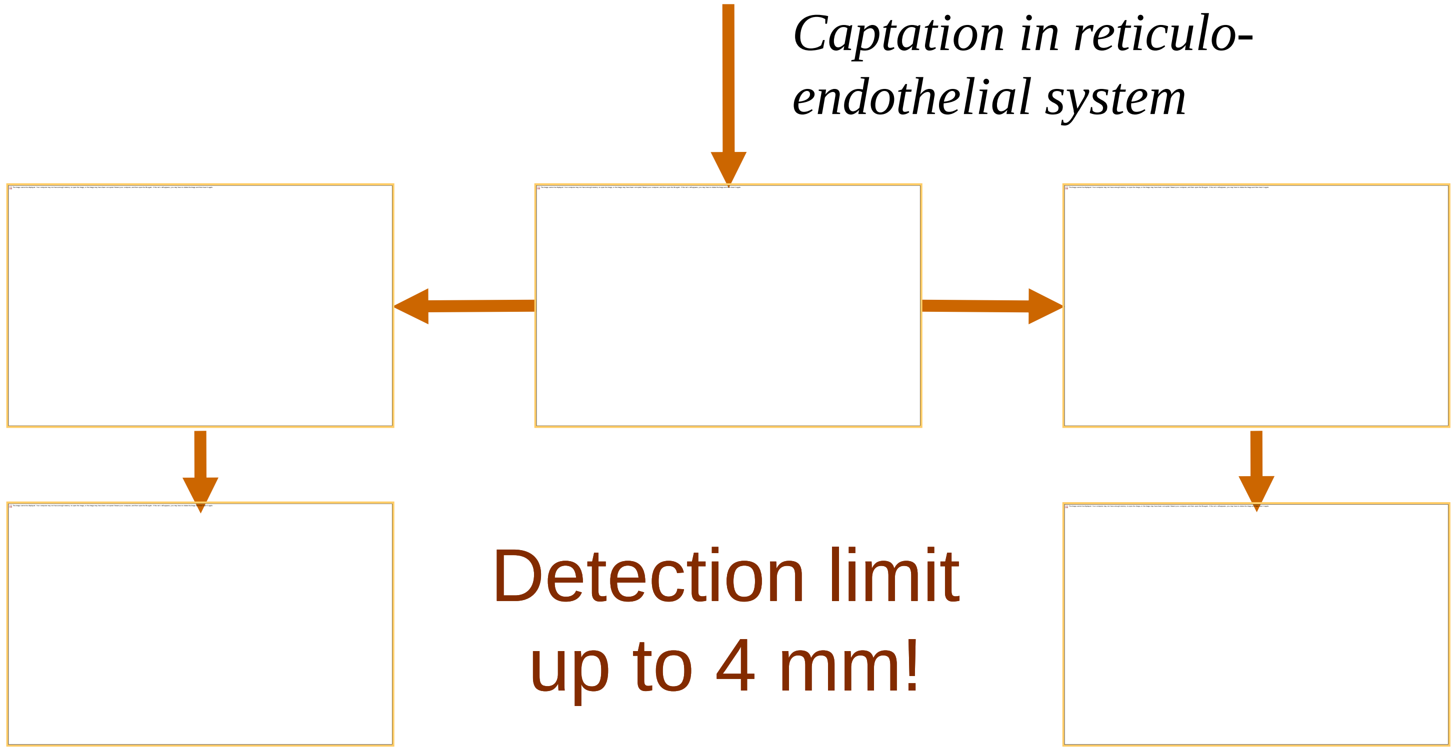
Nanoparticles
Ferumoxtran-10
Sinerem®
Combidex®

21 nm

# IV injection of USPIO
# (“ultra small particles of iron oxide”)



# IV injection of USPIO
# (“ultra small particles of iron oxide”)



- The eternal “promise”: PET

?

# Can imaging help?

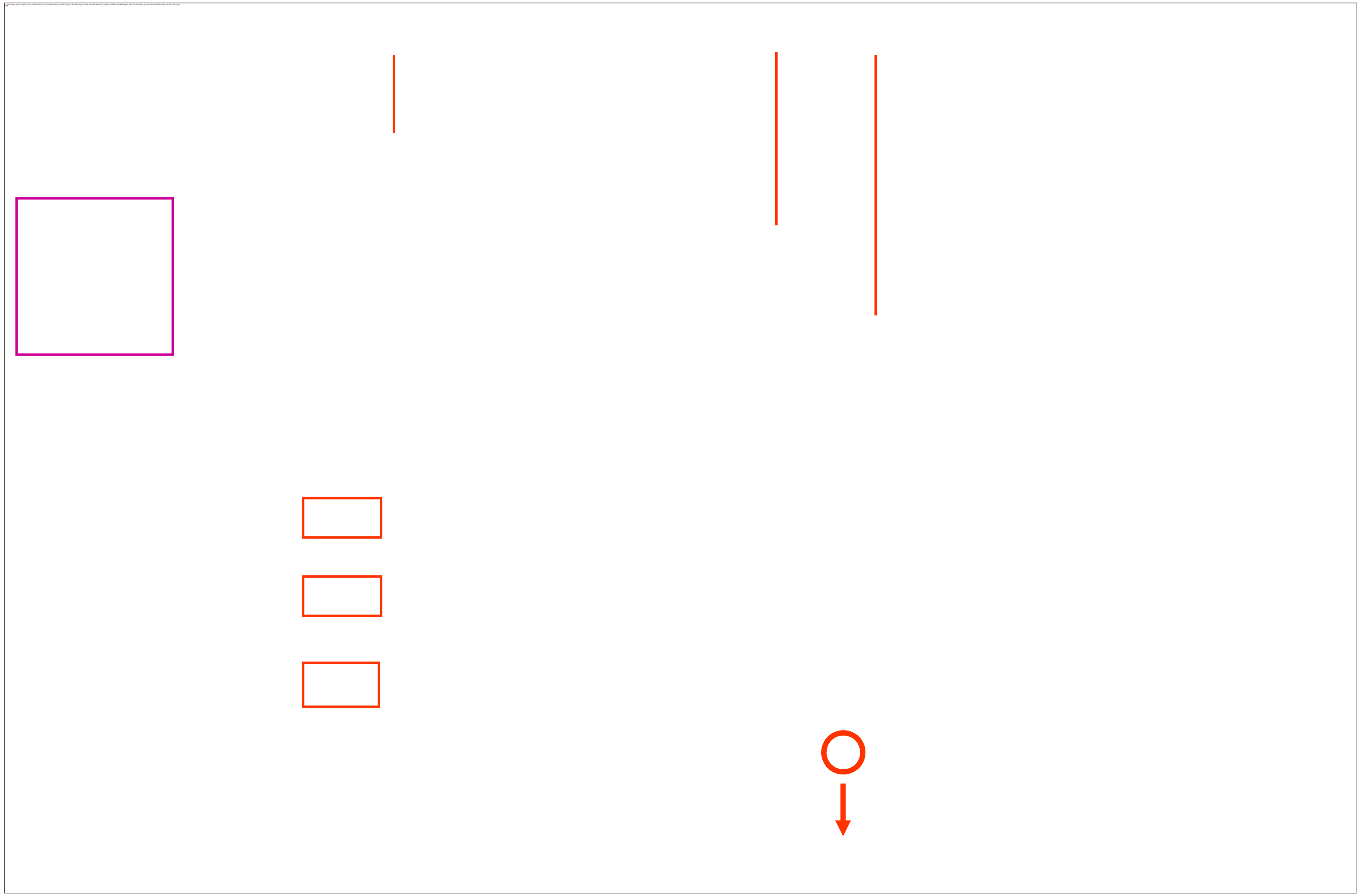
**n=36; 10-35% Partin**
**pN+: 47%**

## Choline Pet CT

**Detection rate for macro LN: 18%**

## DWI

**Detection rate for macro LN: 35%**





Giovacchini et al. Eur J Nucl Med Mol Imaging 2010; 37: 1106-1116.

## 11 C-choline PET and local relapse

## 11 C-choline PET and lymph node relapse

GV

# Patients with PSA recurrence after radical prostatectomy

**N=47**
**All underwent MRL**
**Aim: search for abberant nodes**

Meijer et al. IJROBP

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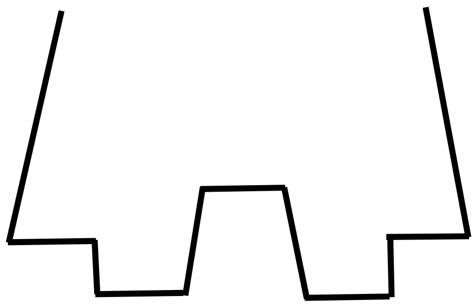

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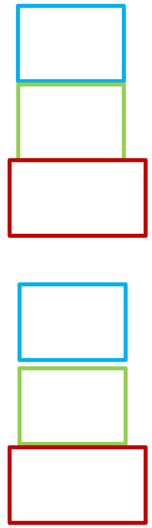
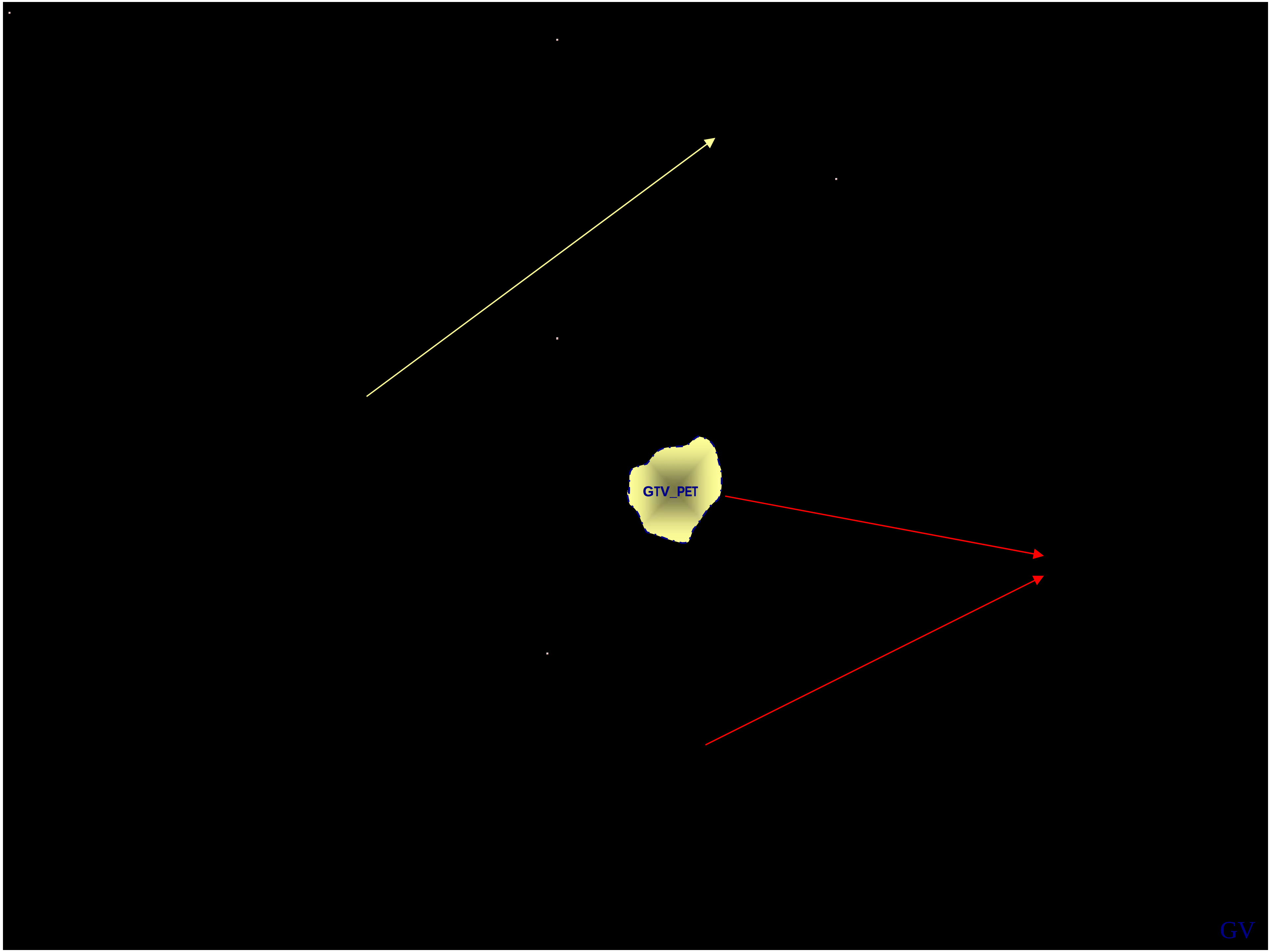
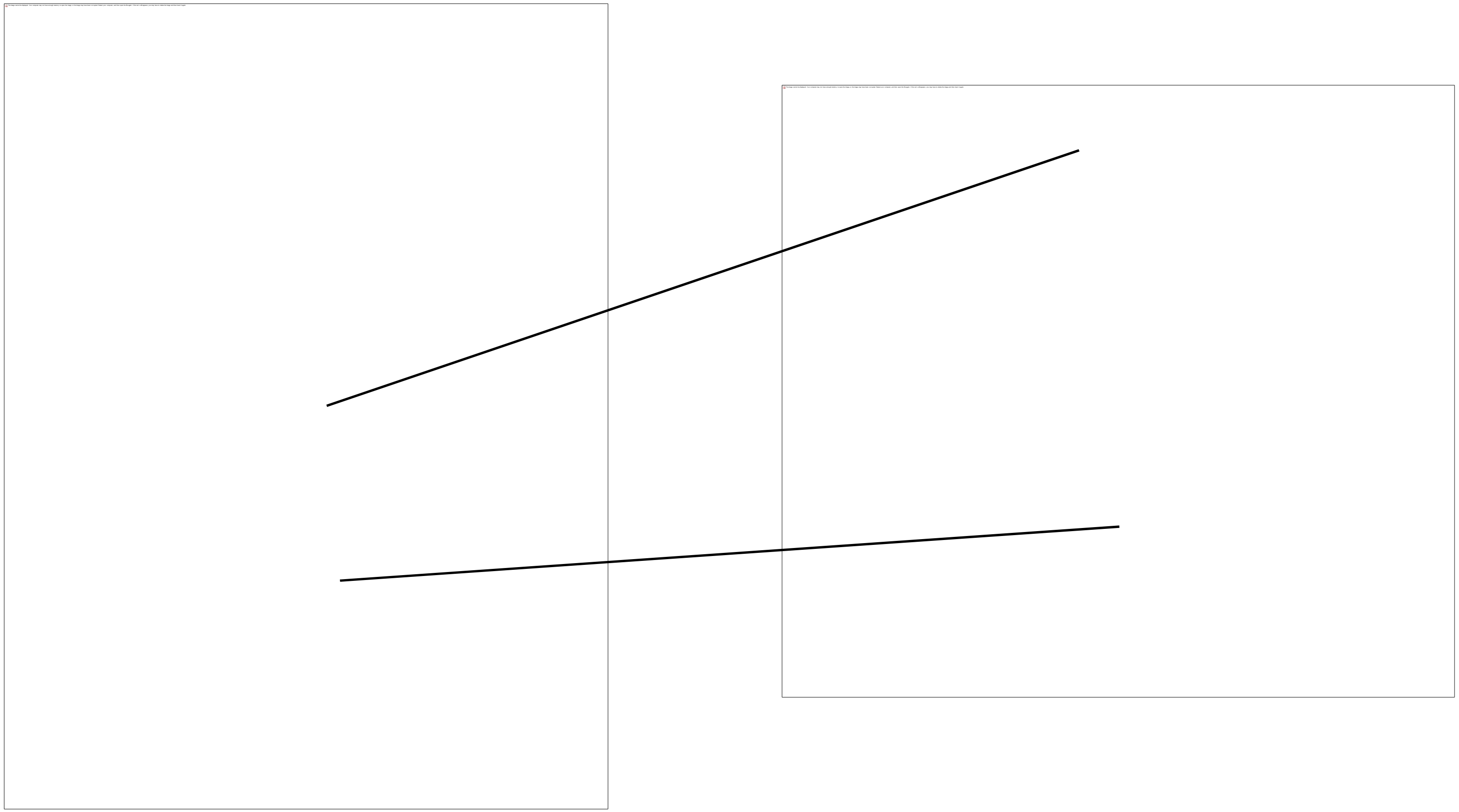


# Change in treatment in 30%

# CERVIX CANCER


GTV_PET
GV

# Pre – treatment investigations: magnetic resonance very useful



# sagital view of dose distribution

# RECTAL CANCER

The image cannot be displayed. Your computer may not have enough memory to open the image, or the image may have been corrupted. Restart your computer, and then open the file again. If the red x still appears, you may have to delete the image and then insert it again.

The image cannot be displayed. Your computer may not have enough memory to open the image, or the image may have been corrupted. Restart your computer, and then open the file again. If the red x still appears, you may have to delete the image and then insert it again.

**Union**

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**Intersection**

# MRI

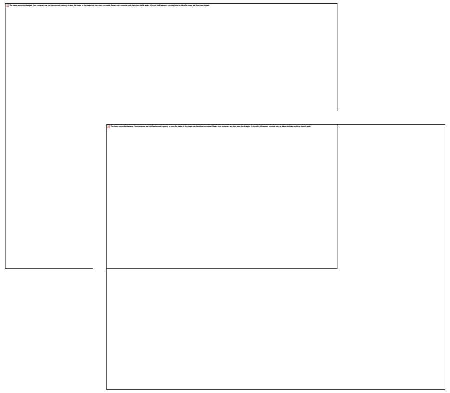
# PET

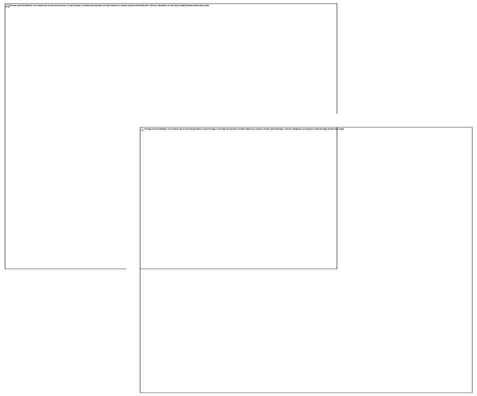
# THM

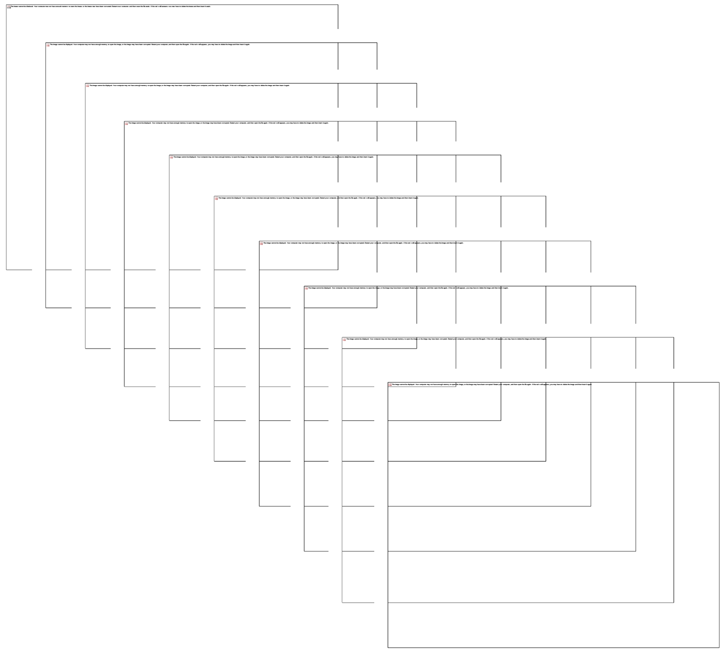
- Both MRI and PET improved target delineation
- MRI: use preferentially in:
    - cervix
    - rectum
    - prostate (prim)
    - brain / H&N if combined with PET

- PET: use preferentially in:
    - brain (no FDG), but combine with MRI
    - H&N (FDG / MISO)
    - prostate (no prim setting, choline in relapse, postop)
    - lung
    - rectum (sorry for limited data)
    - esophagus (?), pancreas (?)

# Words of caution







| Modality | Repeats |
|---|---|
| ▪ Planning CT / MR | 1 – 2 |
| ▪ Additional PET | 1 |
| ▪ Radiation treatment | 25 – 50 |

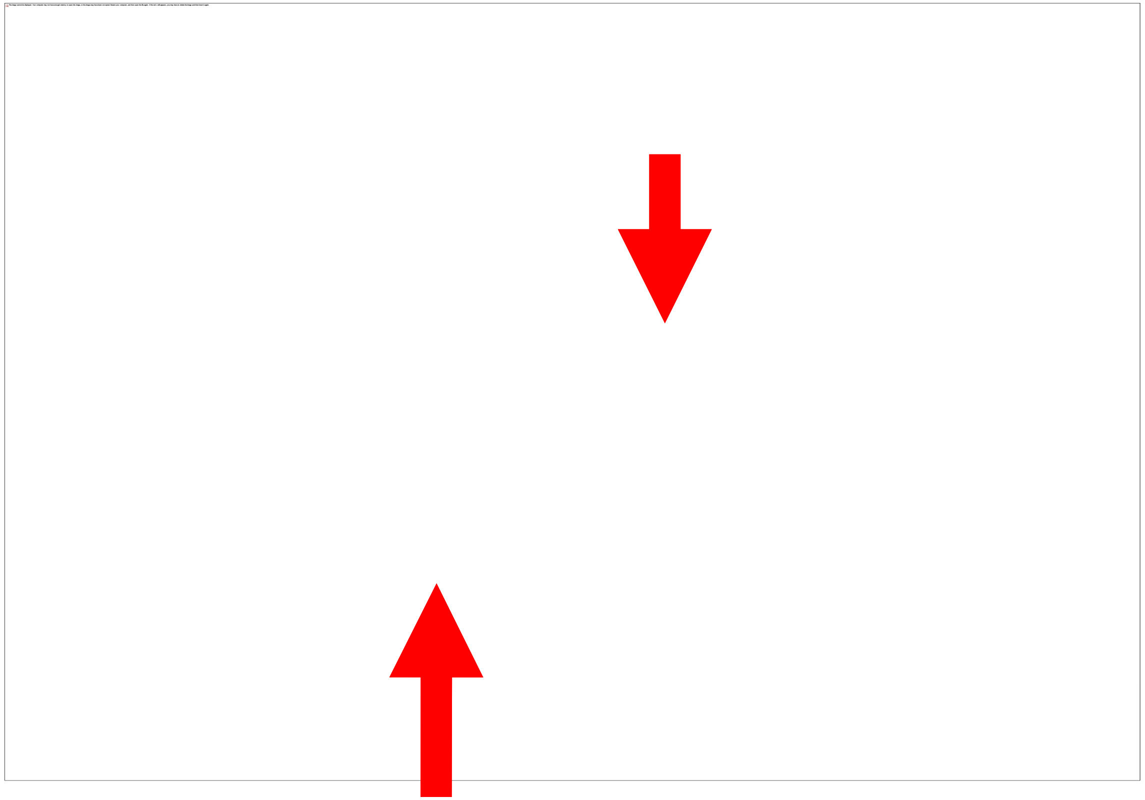
# Words of caution



The image cannot be displayed. Your computer may not have enough memory to open the image, or the image may have been corrupted. Restart your computer, and then open the file again. If the red x still appears, you may have to delete the image and then insert it again.

The image cannot be displayed. Your computer may not have enough memory to open the image, or the image may have been corrupted. Restart your computer, and then open the file again. If the red x still appears, you may have to delete the image and then insert it again.

# Words of caution



**Recommendations**

- **Accept a learning curve for patient positioning**
- **Collaborate with radiotherapy department staff**
- **Train a dedicated PET planning staff**

# Words of caution

- **PET resEARch 4 Life (EARL)**
- **Developed in 2010 by the EANM**

- **Until july 2014, 96 centers had their PET-CT scanners accredited.**

**Aims:**

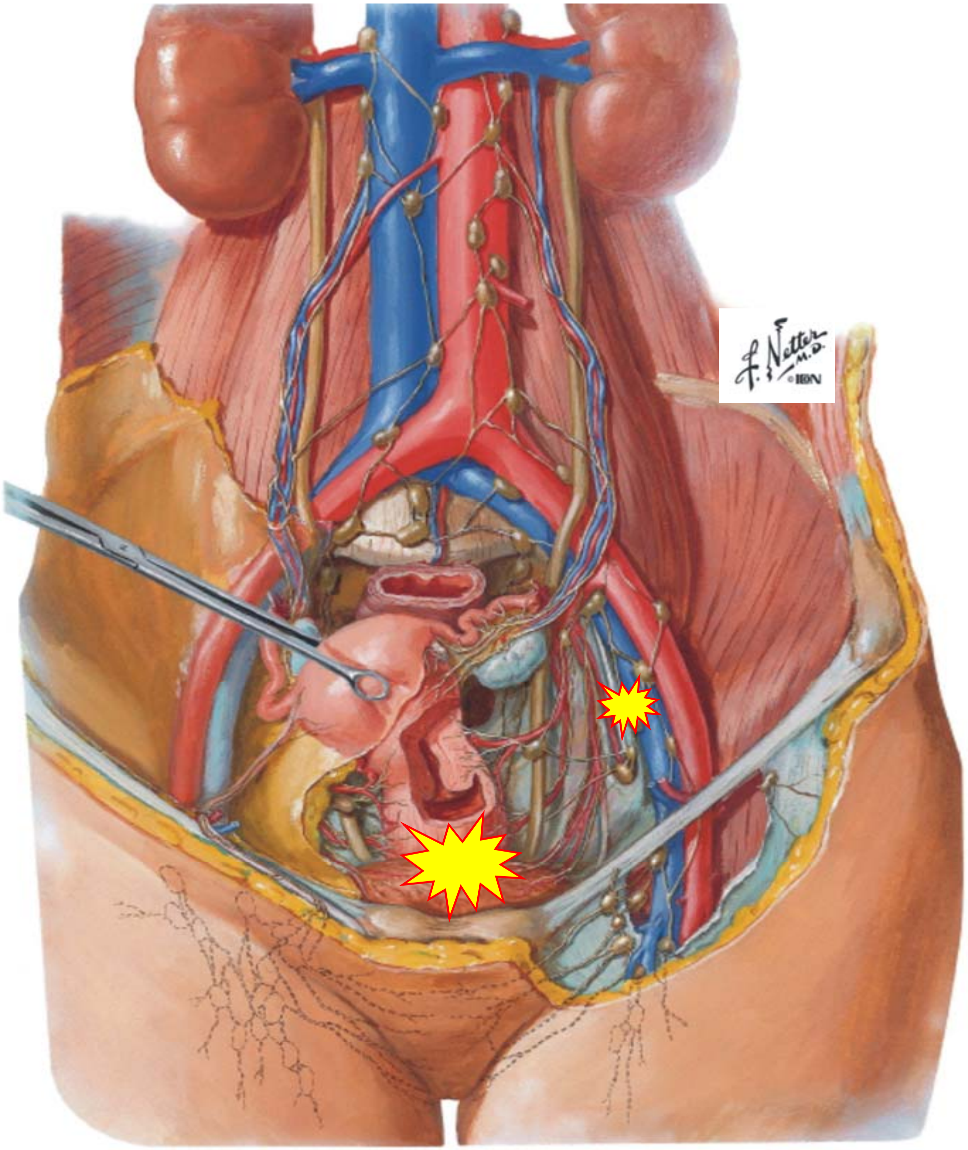
- **Independent quality control by experts in the field of imaging;**
- **Comparable scanner output between centers, harmonisation of acquisition and interpretation of FDG-PET/CT scans;**
- **Accurate, reproducible und quantitative assessment;**
- **Quality certificate of accredited EARL-users.**

# Words of caution

- **Quality assurance of anatomical and functional MR imaging**

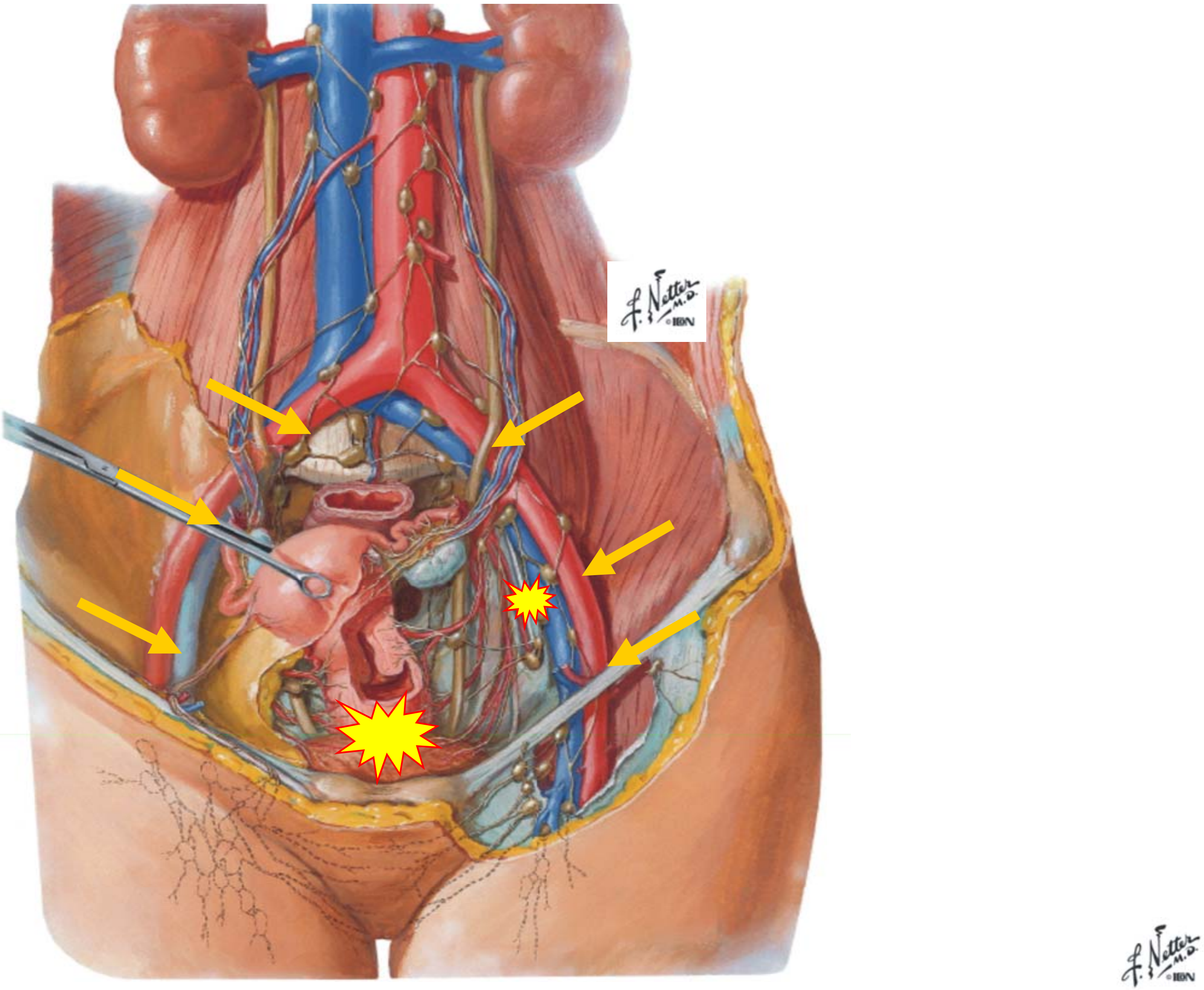
# TVD for cervical cancer: primary setting

# Target volume : defined by "risk of relapse"



Interactive atlas of human anatomy

# Target volume : defined by “risk of relapse”



Interactive atlas of human anatomy

Gross tumor volume

Correct TVD starts with **optimal** imaging

combine morphological and biological imaging

## Correct TVD starts with **optimal** imaging

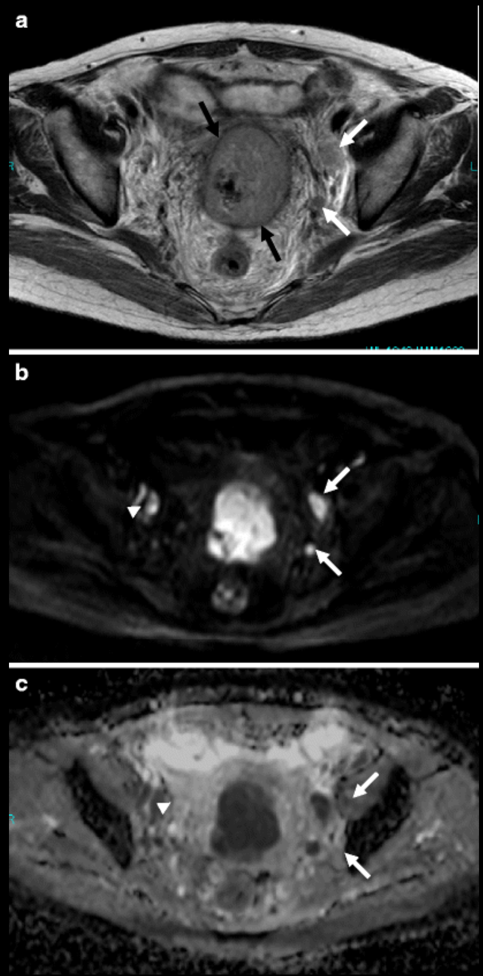
combine morphological and biological imaging

T2w MRI
- T-staging

# Correct TVD starts with **optimal** imaging

combine morphological and biological imaging

T2w MRI
- T-staging

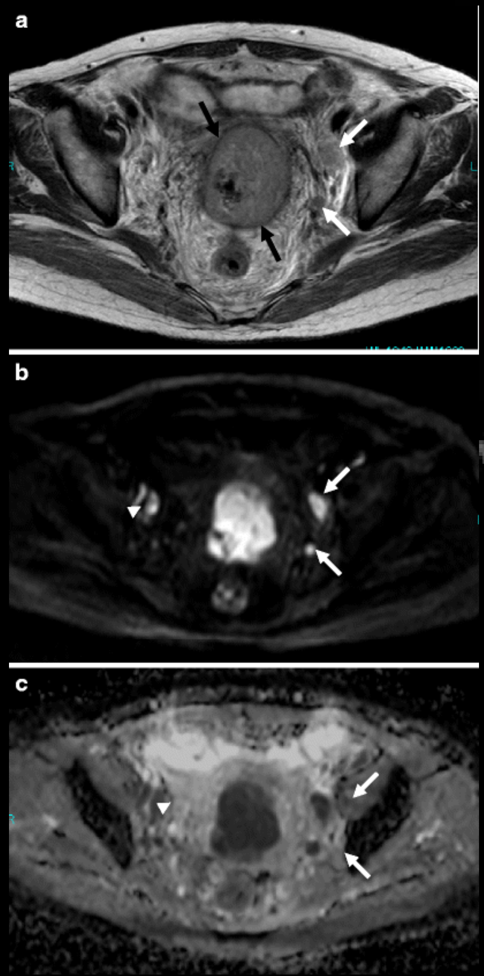



DWI MRI
- T & N-staging

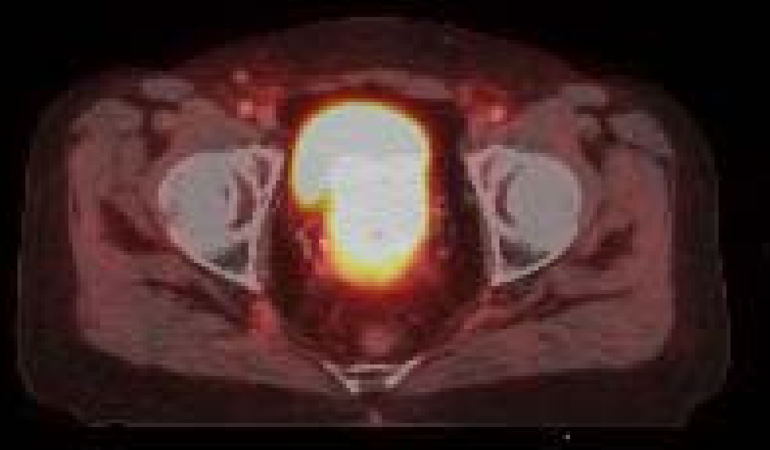
# Correct TVD starts with **optimal** imaging

combine morphological and biological imaging

T2w MRI
- T-staging



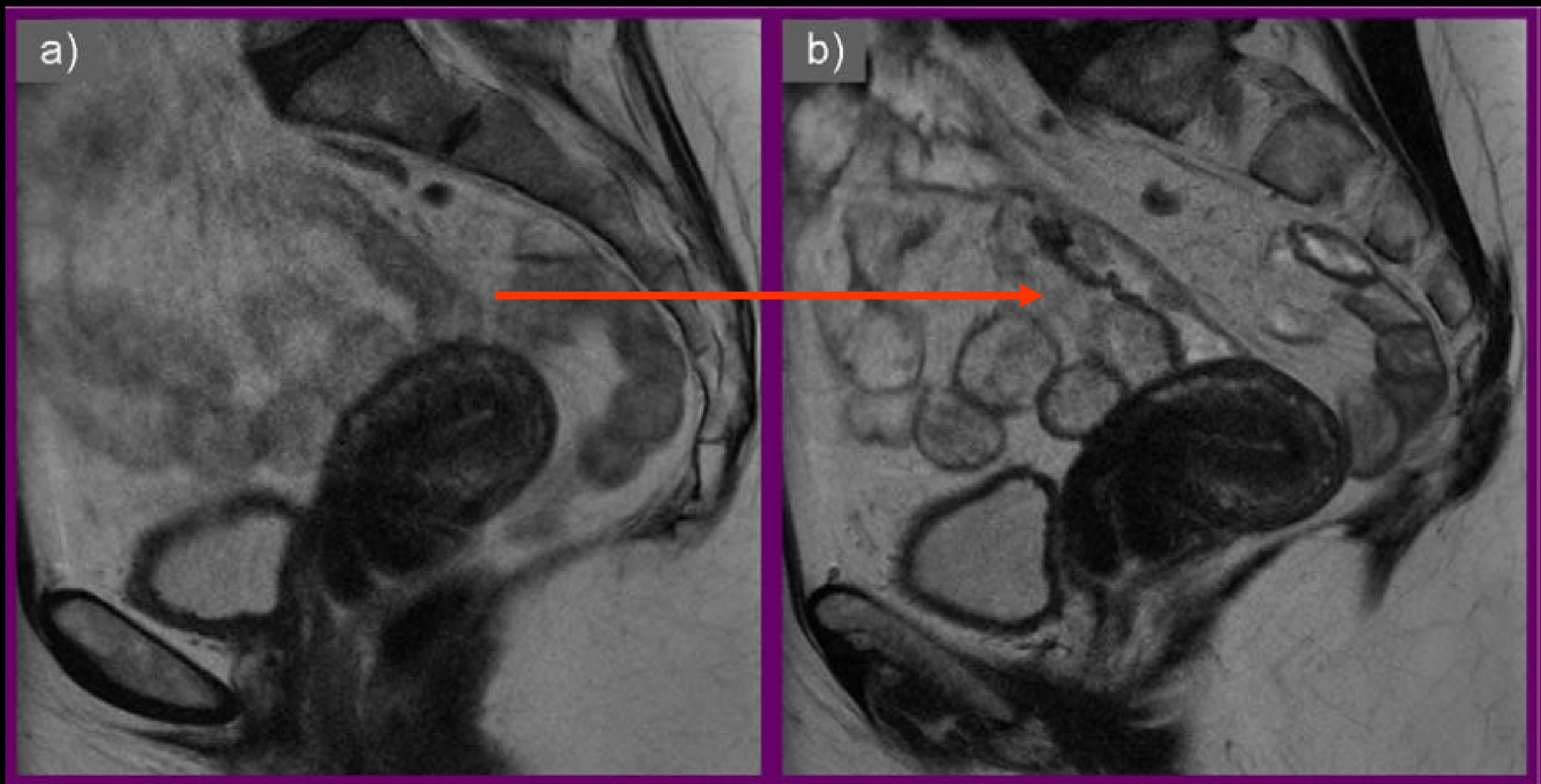

DWI MRI
- T & N-staging



18 FDG PET-CT:
- Primary tumor
- Lymph nodes
  - high sensitivity
  - high specificity

## Magnetic resonance: recommendations from GEC-ESTRO

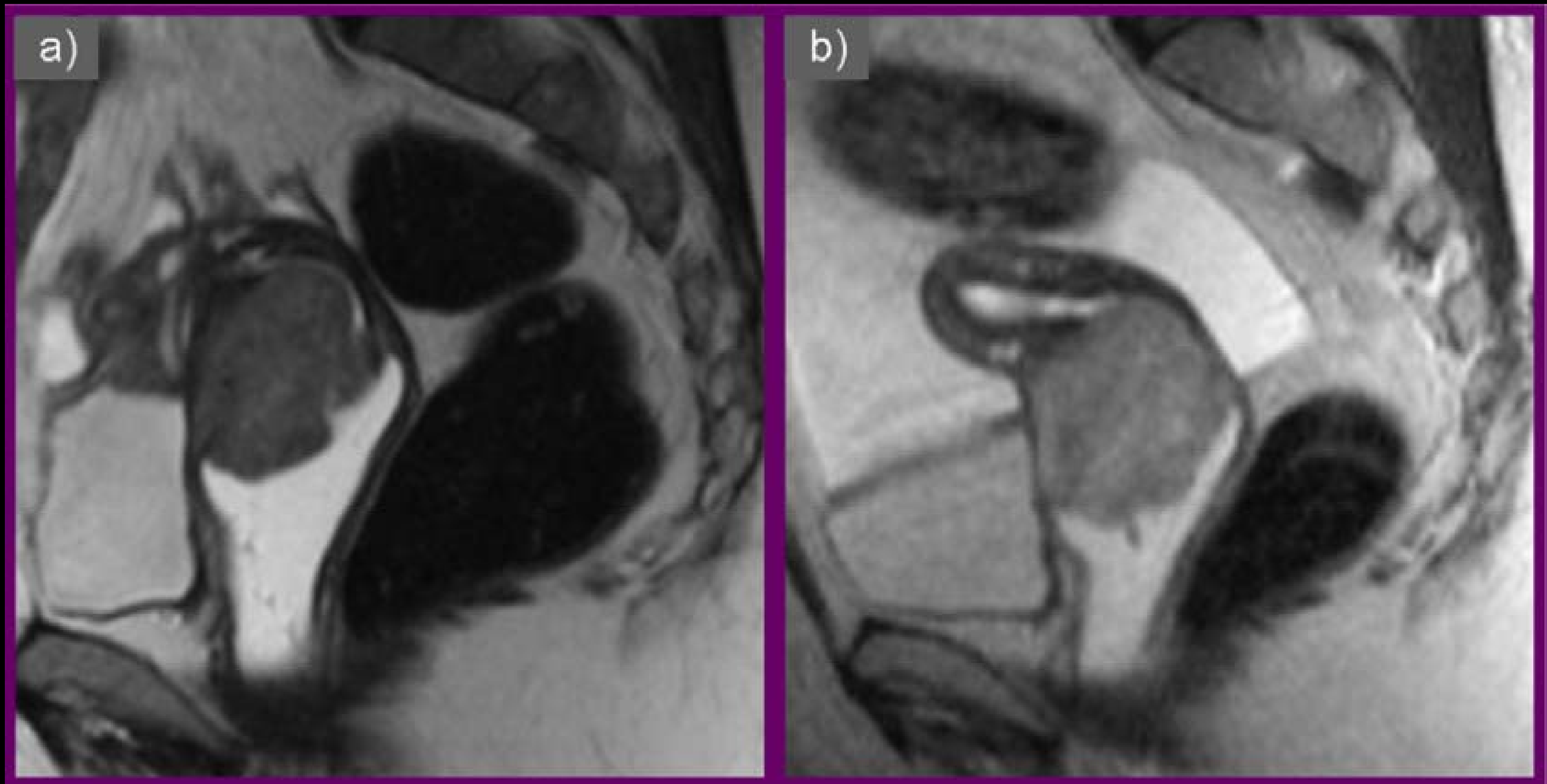
Spasmolytic agent (IV / IM)



# Importance of field strength

1.5 Tesla

0.2 Tesla

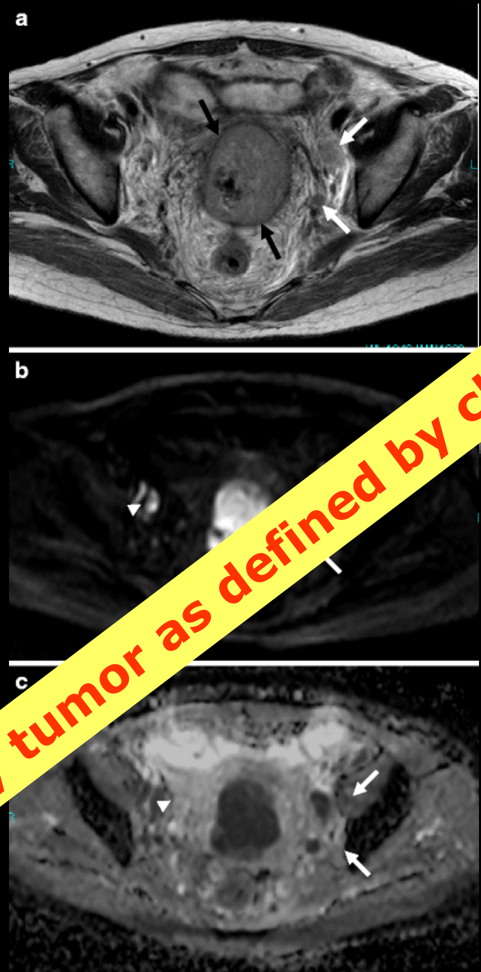


## Correct TVD starts with **optimal** imaging

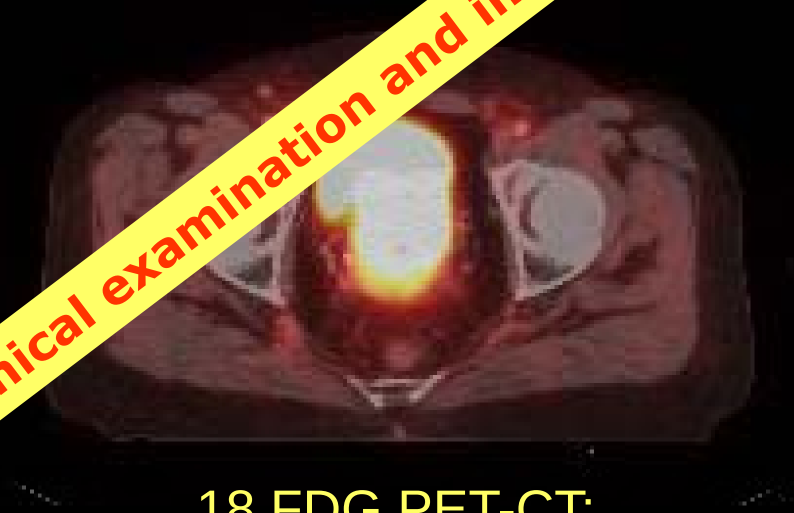
combine morphological and biological imaging

**GTV: primary tumor as defined by clinical examination and imaging**

T2w MRI
- T-staging

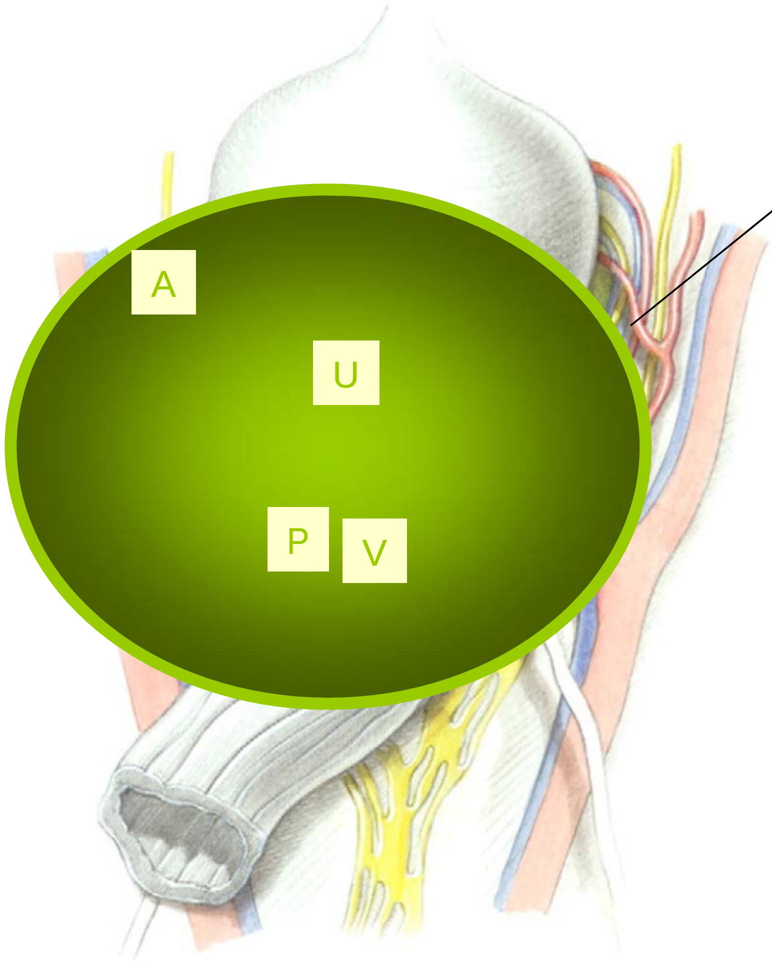



DWI MRI
- T & N-staging



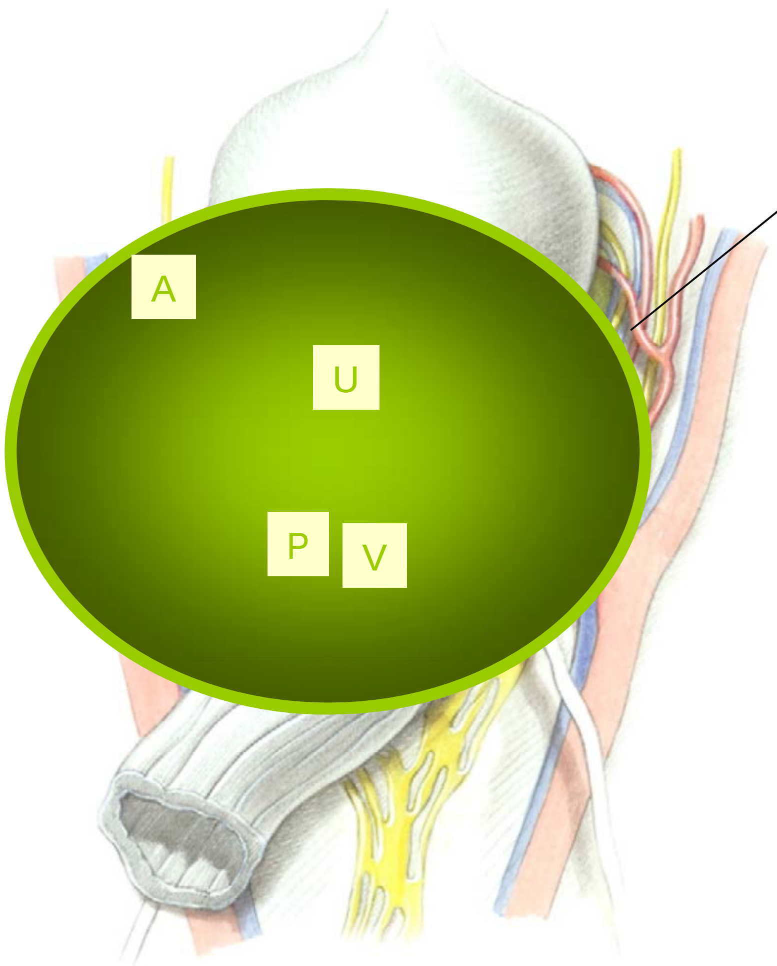
18 FDG PET-CT:
- Primary tumor
- Lymph nodes
    - high sensitivity
    - high specificity

# Clinical target volume



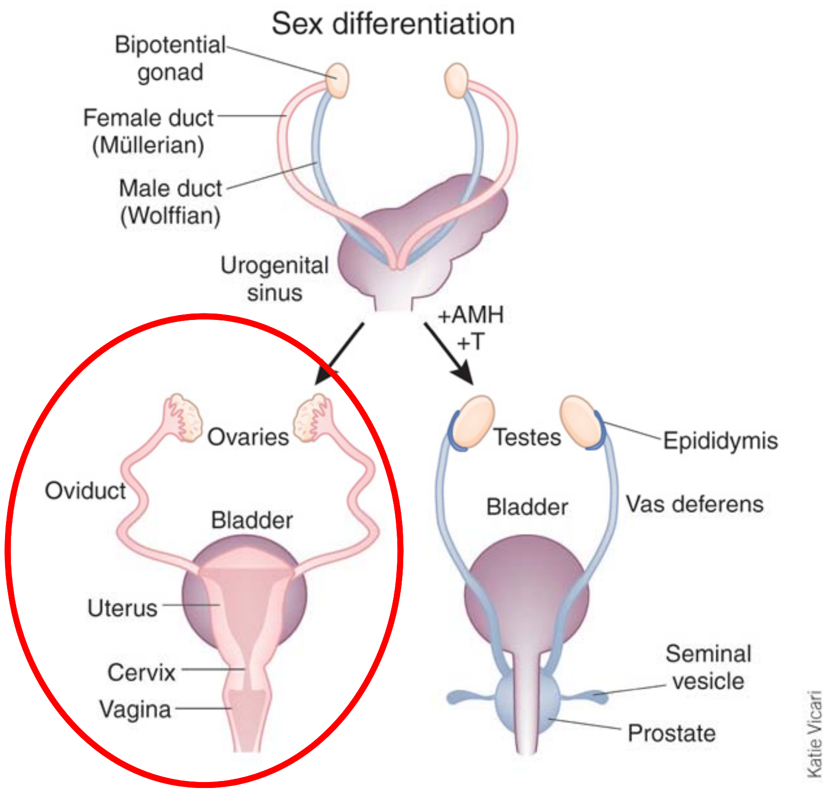

## Uterovaginal compartiment

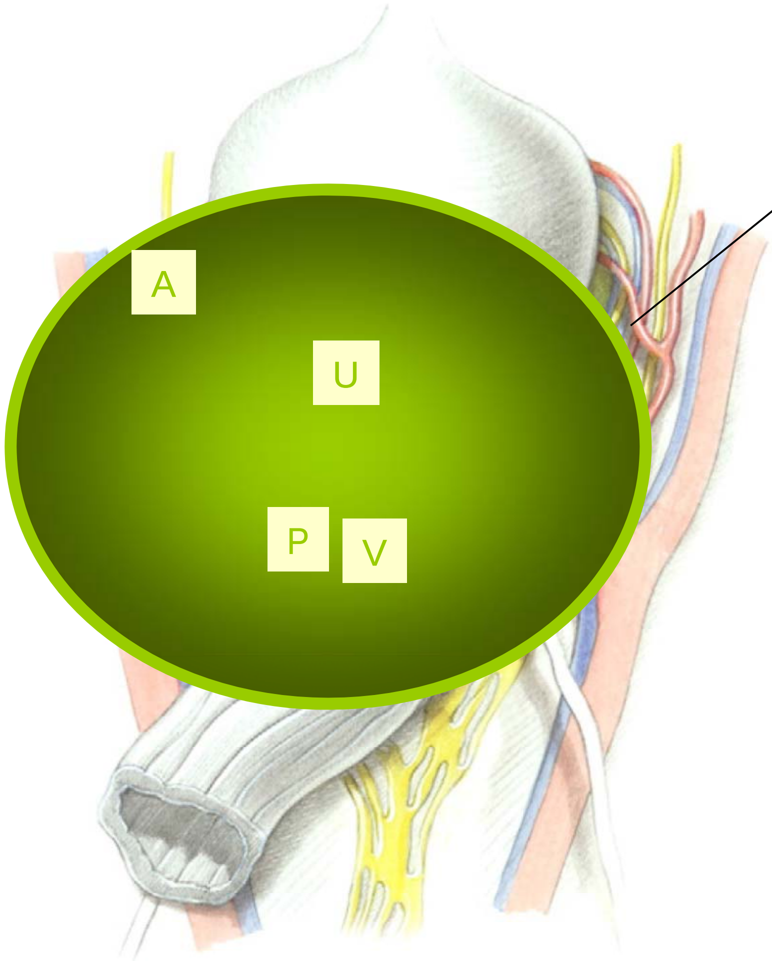
Product of differentiation of the Müllerian canal




Uterovaginal compartiment

Product of differentiation of the Müllerian canal



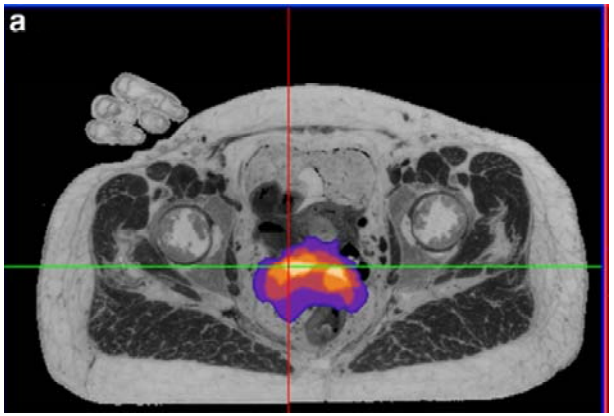


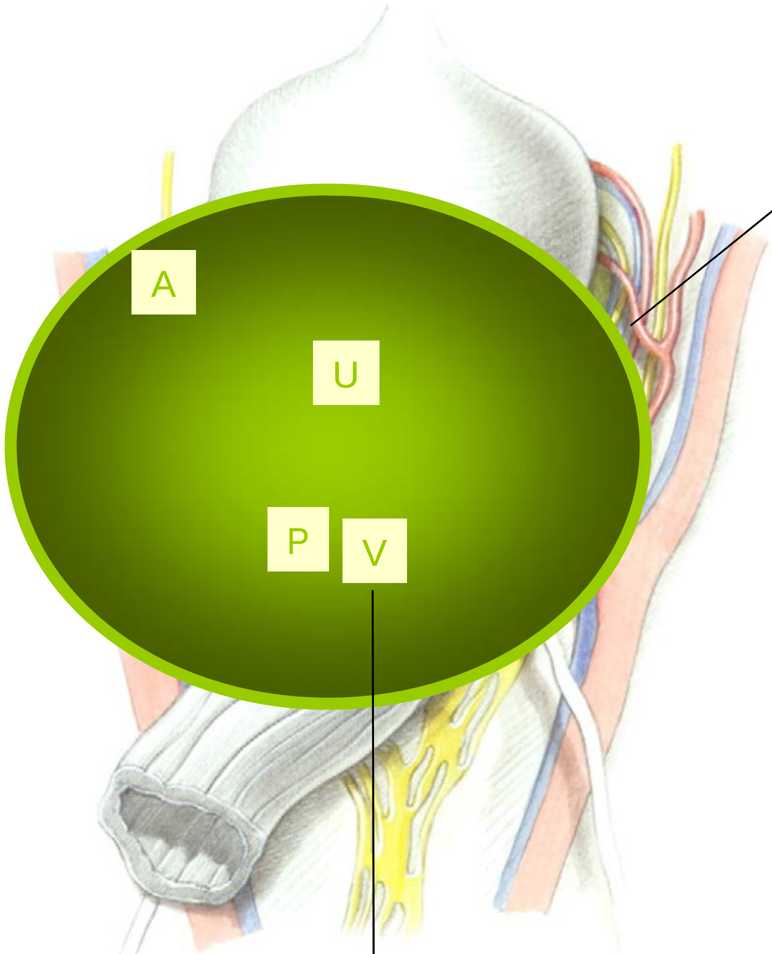

Uterovaginal compartiment

Product of differentiation of the Müllerian canal

+ GTV

CTV






Uterovaginal compartiment

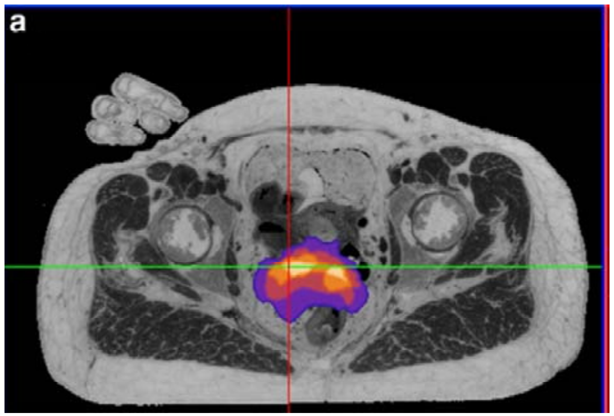
Product of differentiation of the Müllerian canal

+ GTV

CTV

Upper 1/3 when no macro invasion

if macro invasion: + 2 cm



# Pelvic lymph nodes delineation

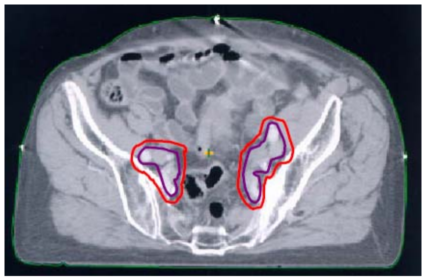
## CTV definition-lymph nodes

**MAPPING PELVIC LYMPH NODES: GUIDELINES FOR DELINEATION IN INTENSITY-MODULATED RADIOTHERAPY**

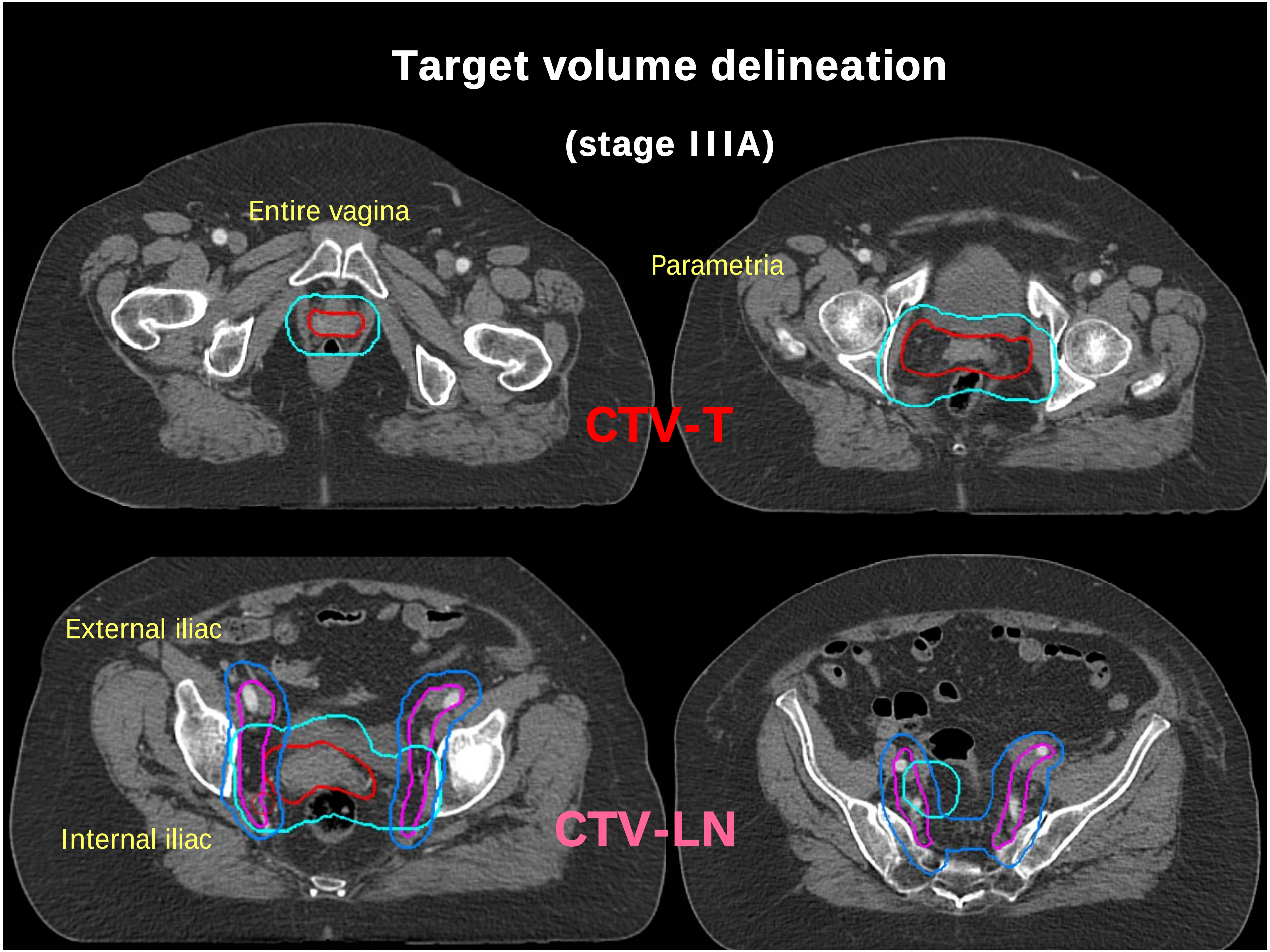
External-internal iliac nodes | common iliac nodes | Para-aortic nodes

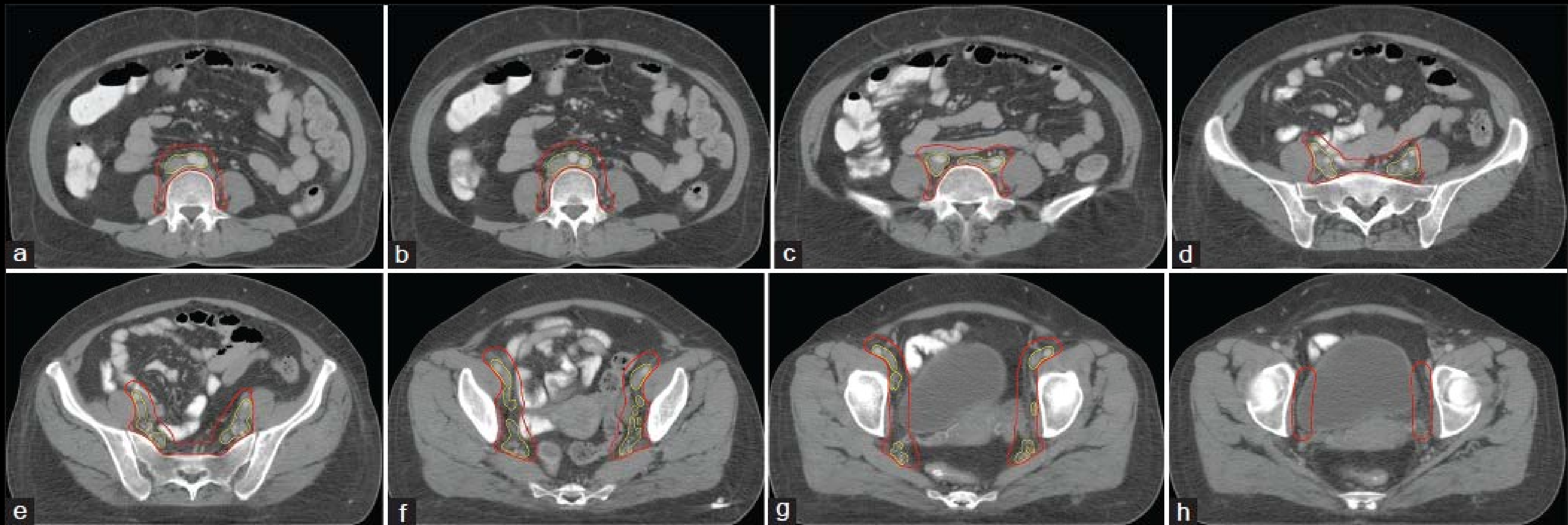
*Small W IJROBP 2008*

**CTV LN delineation**
= Vessels + 7 mm

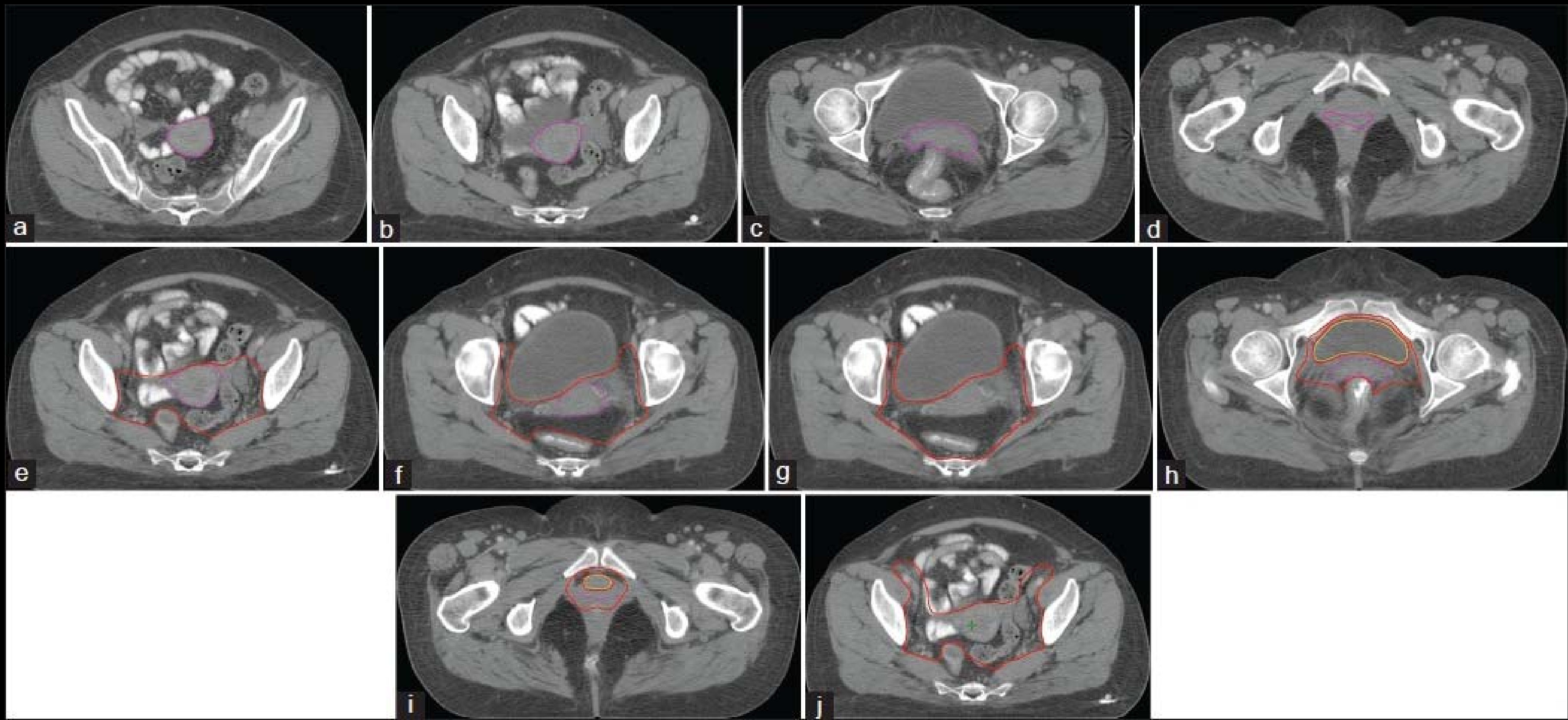


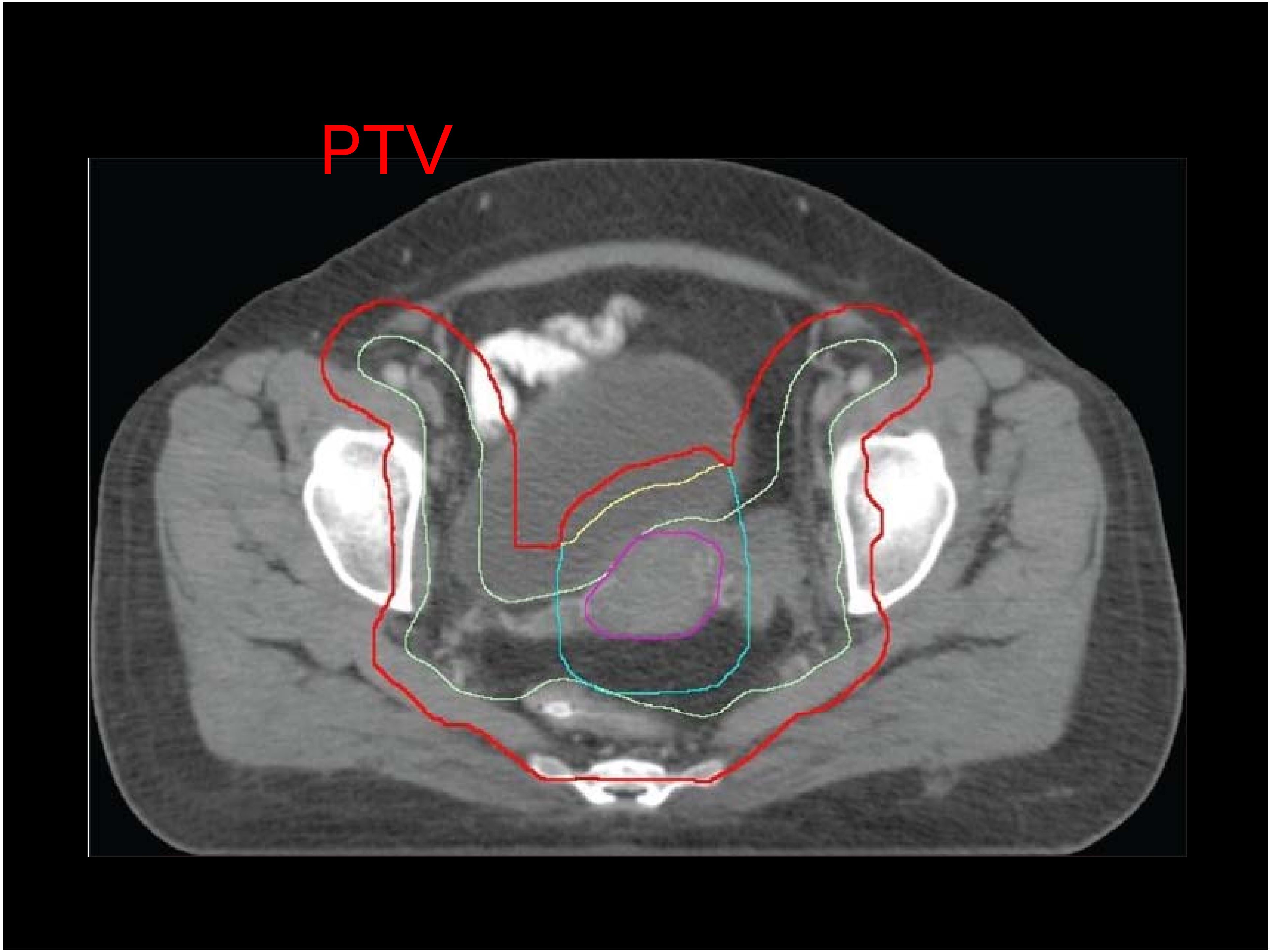
*I. Barillot*


Target volume delineation
(stage IIIA)
Entire vagina
Parametria
CTV-T
External iliac
Internal iliac
CTV-LN

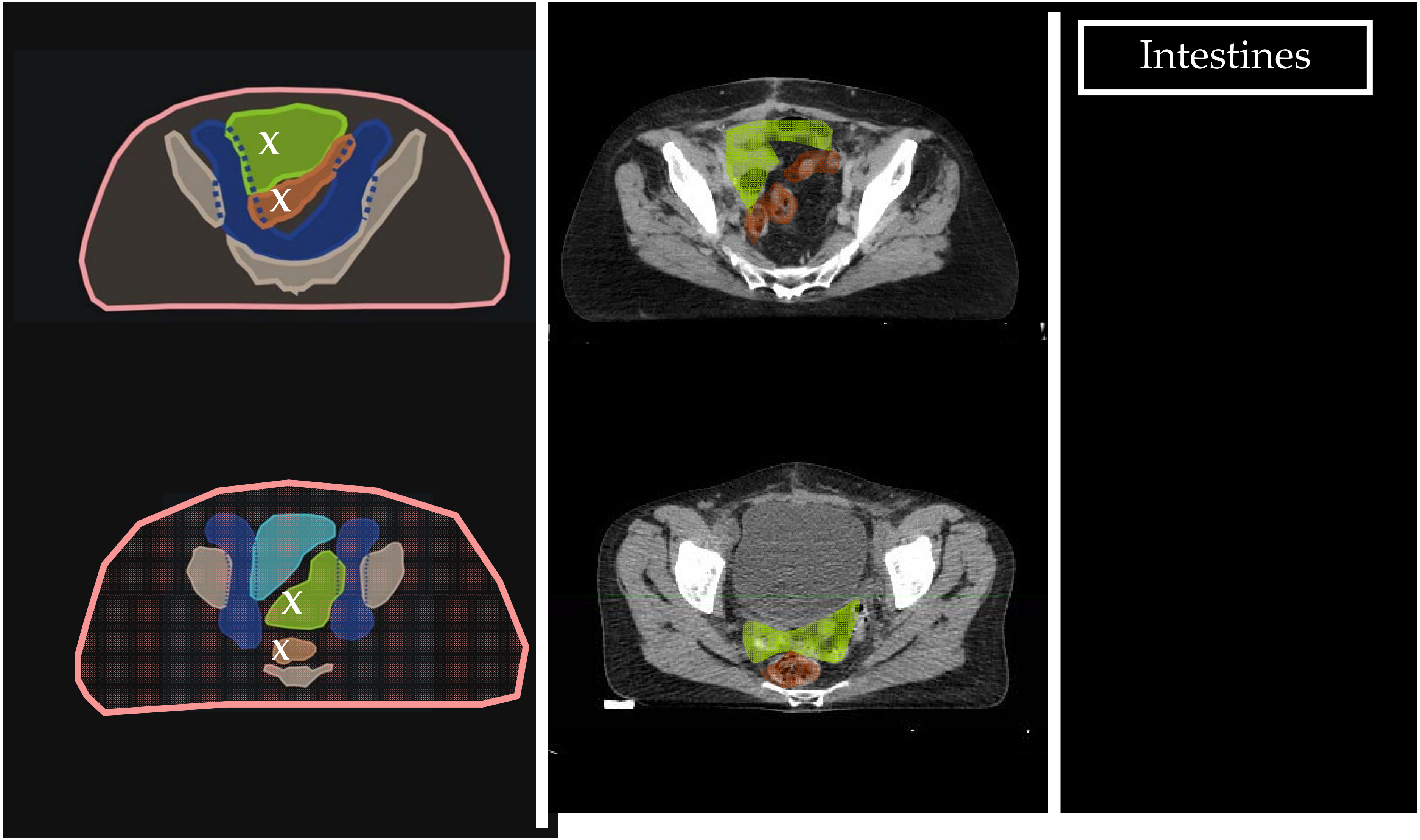



S2-S3

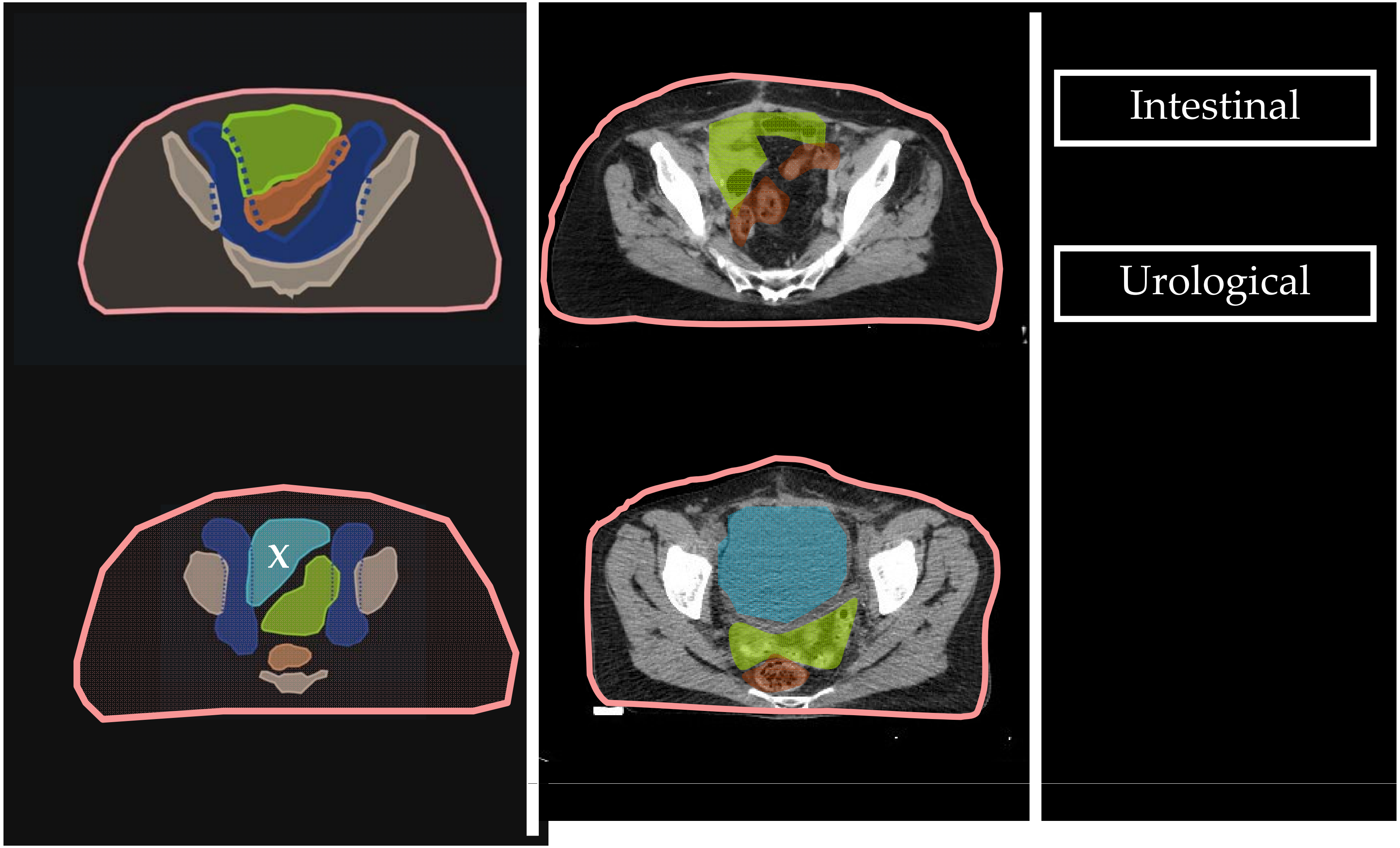

a
b
c
d
e
f
g
h
i
j


PTV

# Major issue: healthy tissue



# Major issue: healthy tissue



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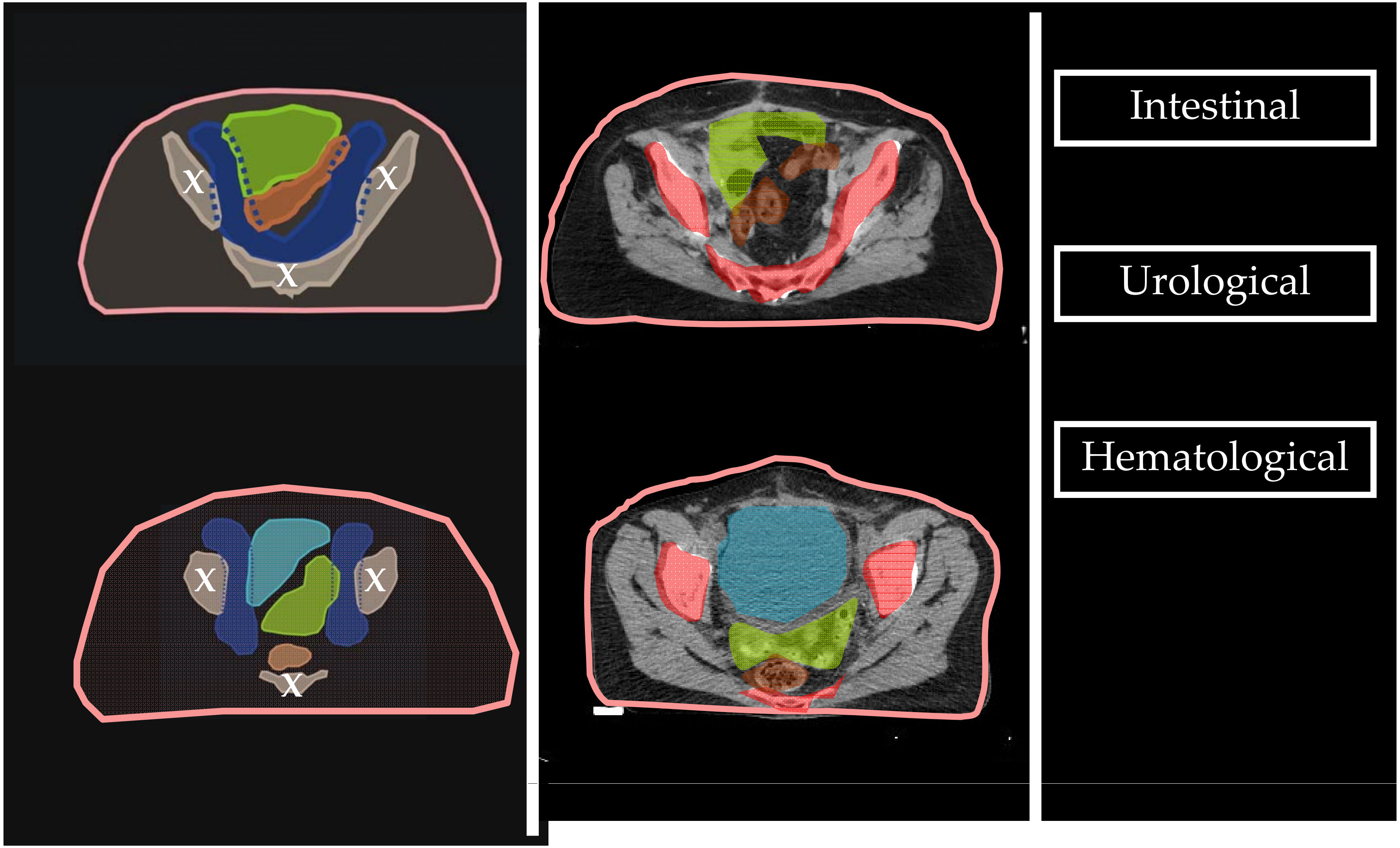
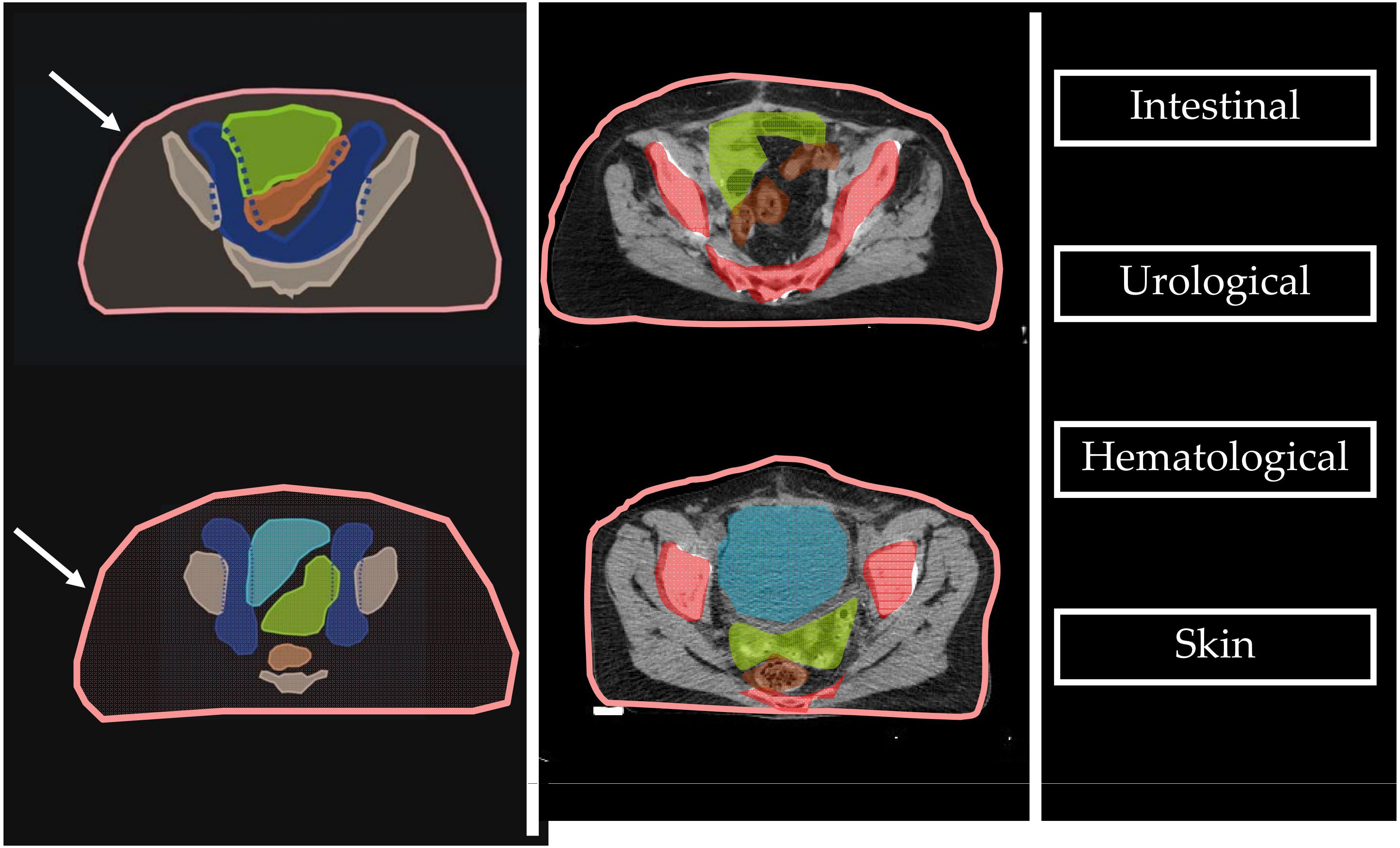
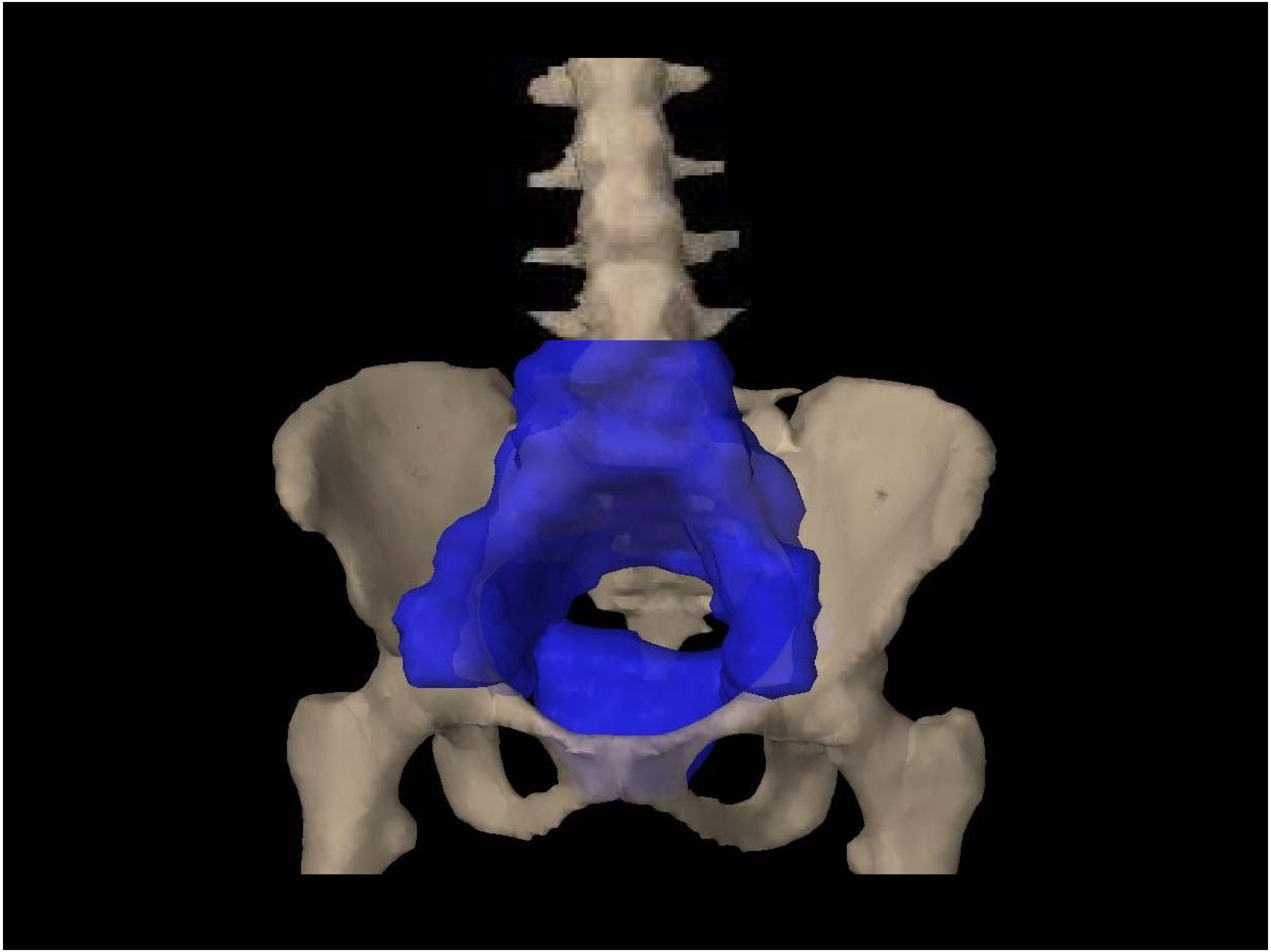


# Major issue: healthy tissue





# PTV margins??

Int. J. Radiation Oncology Biol. Phys., Vol. 80, No. 1, pp. 273–280, 2011

0360-3016/$–see front matter

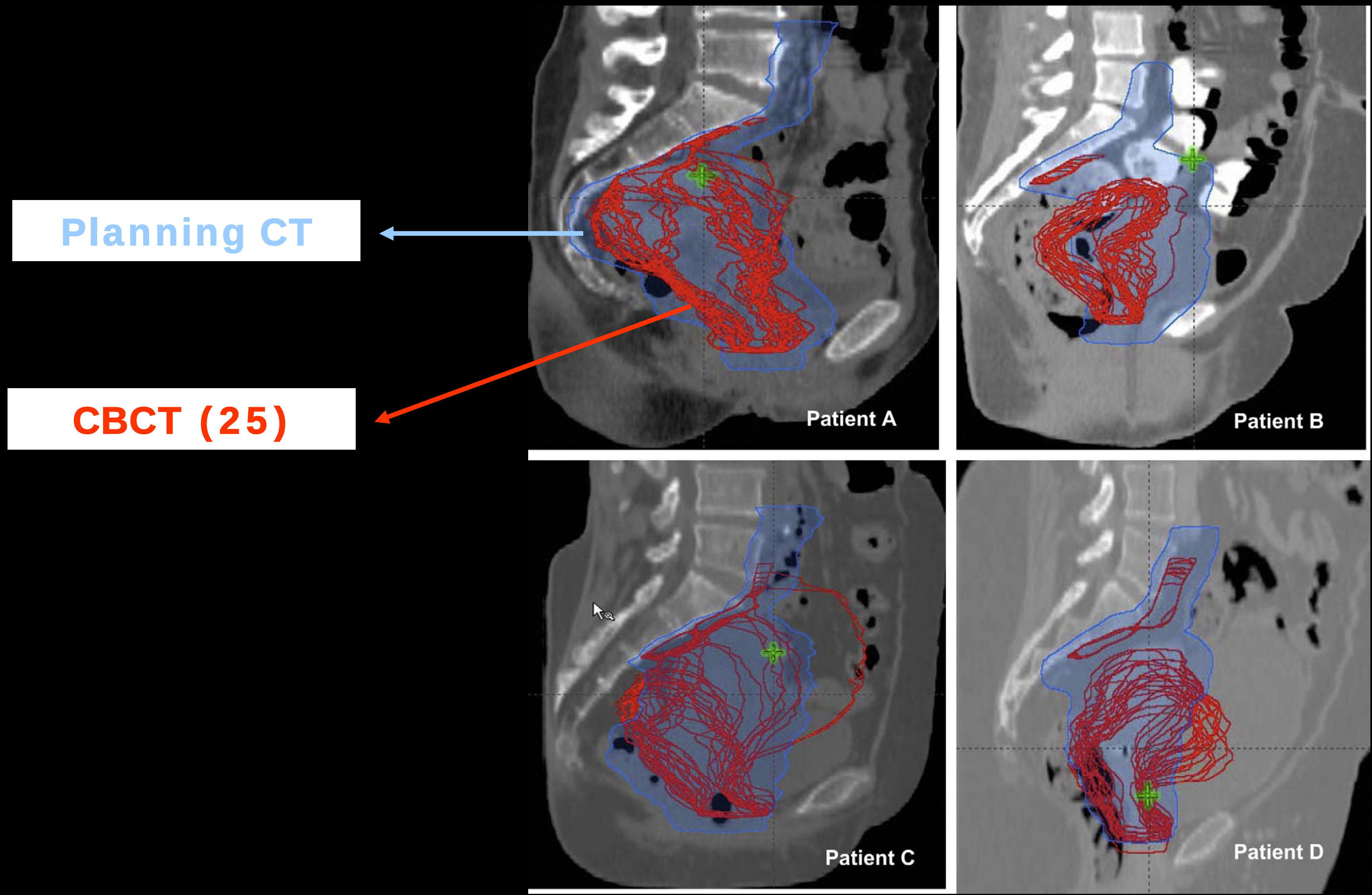
ELSEVIER

doi:10.1016/j.ijrobp.2010.06.003

**PHYSICS CONTRIBUTION**

## DAILY ONLINE CONE BEAM COMPUTED TOMOGRAPHY TO ASSESS INTERFRACTIONAL MOTION IN PATIENTS WITH INTACT CERVICAL CANCER

Neelam Tyagi, Ph.D., John H. Lewis, M.S., Catheryn M. Yashar, M.D.,
Daniel Vo, Steve B. Jiang, Ph.D., Arno J. Mundt, M.D., and Loren K. Mell, M.D.


Planning CT
CBCT (25)
Patient A
Patient B
Patient C
Patient D

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 80, No. 1, pp. 273–280, 2011

0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2010.06.003

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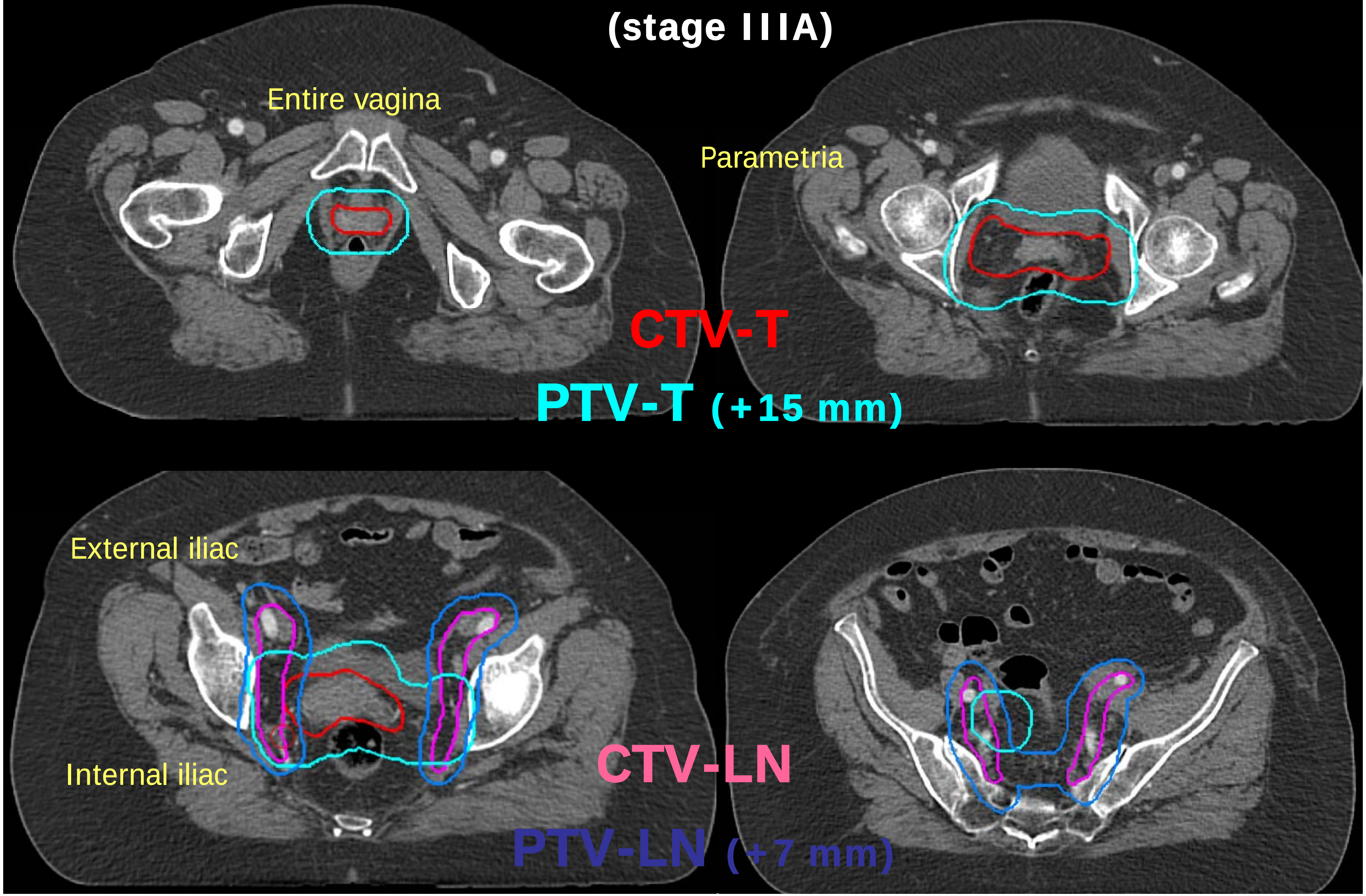
| | | | | Mean % of fractions missing (range) | |
|---|---|---|---|---|---|
| Margin (mm) | Mean % of fractions missing (range) | Mean volume missed (cc) (range) | % of mean volume missed (range) | Cervical region | Fundus region |
| 0 | 100 (100–100) | 45 (15–112) | 10 (3–28) | 95 (75–100) | 100 (100–100) |
| 3 | 99 (92–100) | 25 (10–84) | 6 (2–21) | 80 (54–100) | 89 (33–100) |
| 5 | 95 (73–100) | 20 (5–72) | 4 (1–18) | 65 (25–100) | 84 (5–100) |
| 7 | 87 (54–100) | 14 (0–62) | 3 (0–16) | 50 (0–100) | 70 (0–100) |
| 10 | 59 (0–100) | 9 (0–46) | 2 (0–12) | 36 (0–100) | 54 (0–96) |
| 15 | 32 (0–100) | 4 (0–21) | 1 (0–5) | 19 (0–100) | 22 (0–73) |
| 20 | 19 (0–100) | 2 (0–8) | 0 (0–2) | 11 (0–88) | 11 (0–58) |
| 25 | 14 (0–83) | 1 (0–4) | 0 (0–1) | 7 (0–59) | 7 (0–33) |
| 30 | 7 (0–33) | 0 (0–2) | 0 (0–0) | 1 (0–6) | 4 (0–17) |
| 35 | 2 (0–13) | 0 (0–1) | 0 (0–0) | 0 (0–0) | 2 (0–13) |

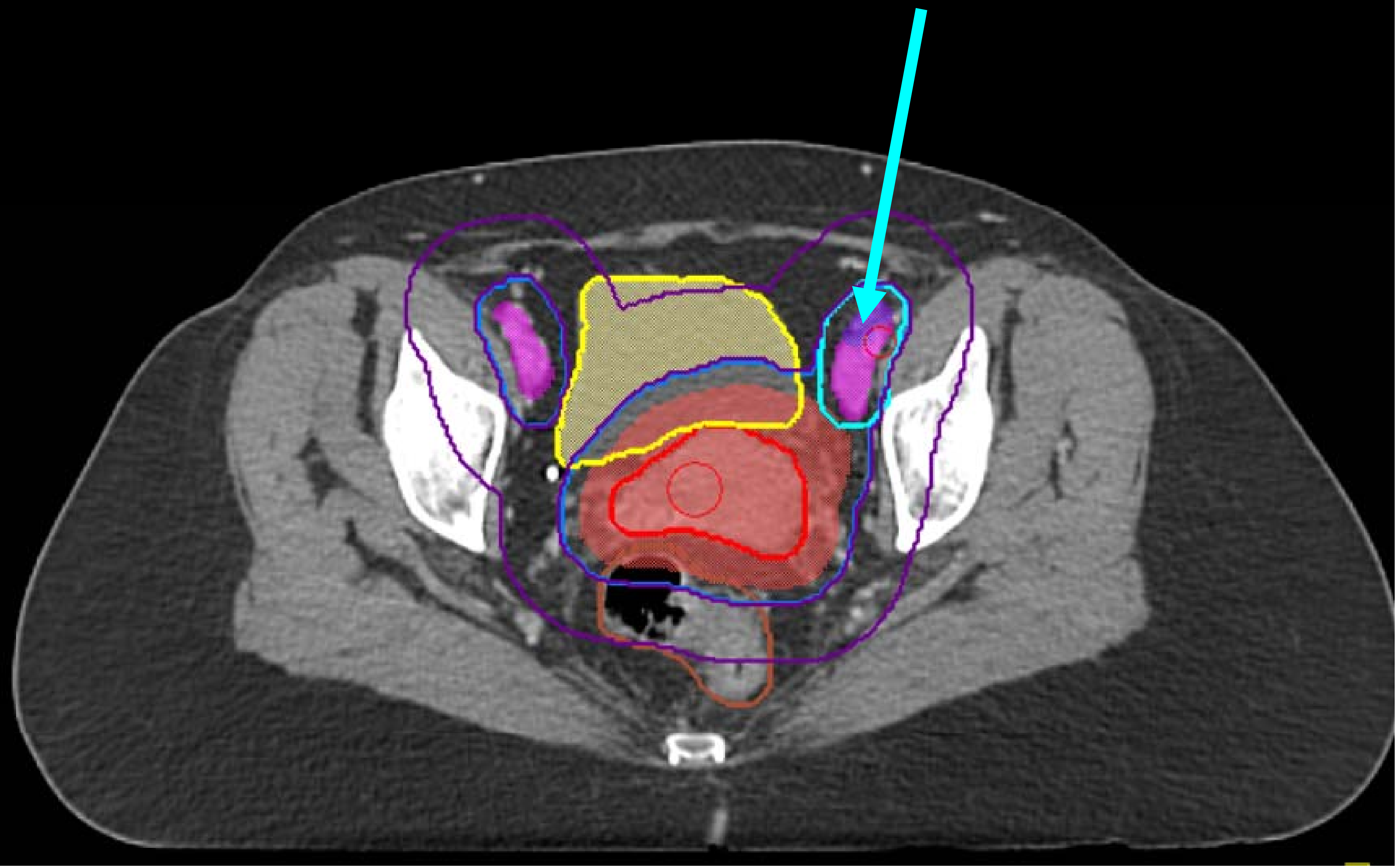
# Target volume delineation

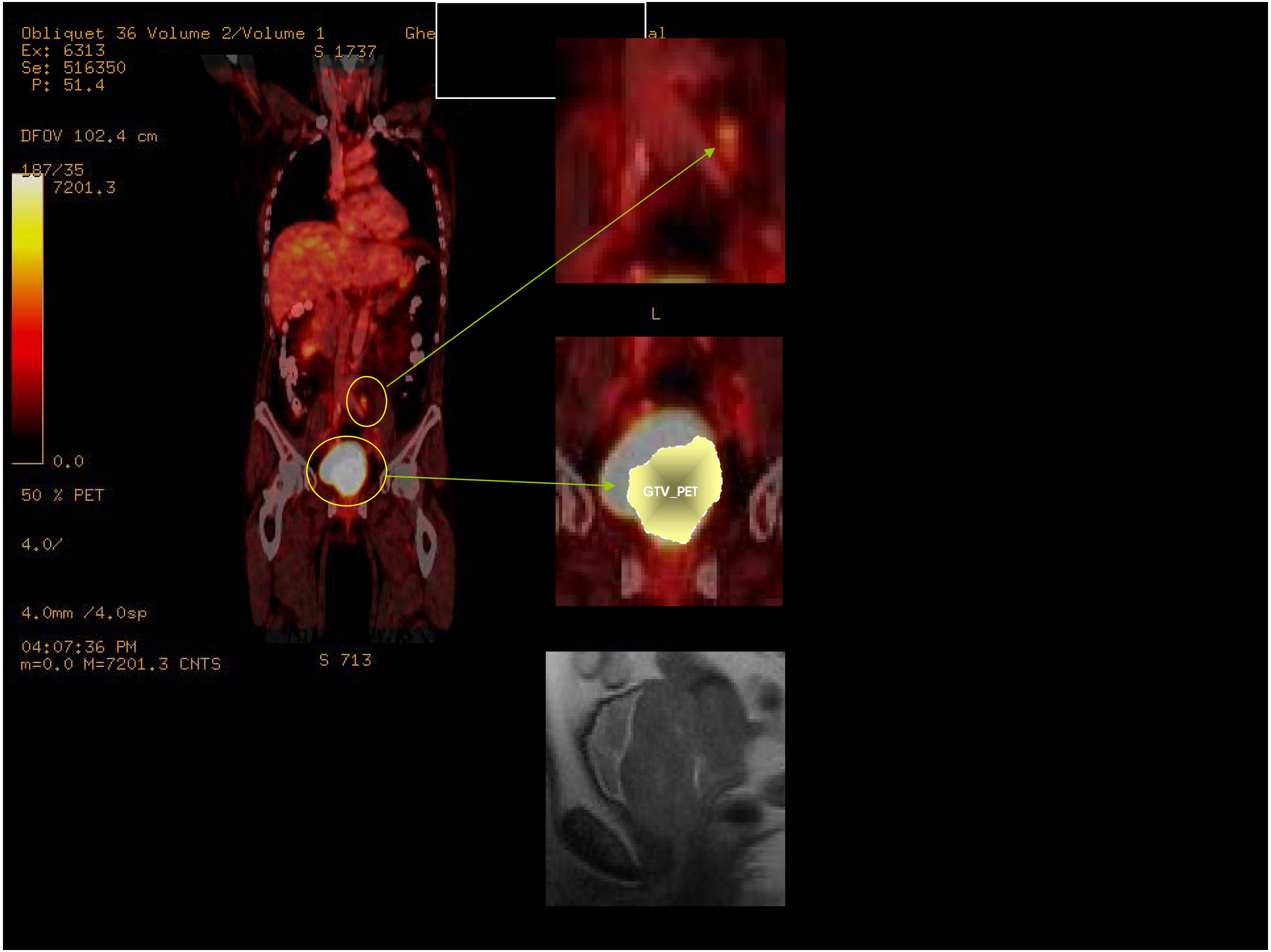
(stage IIIA)

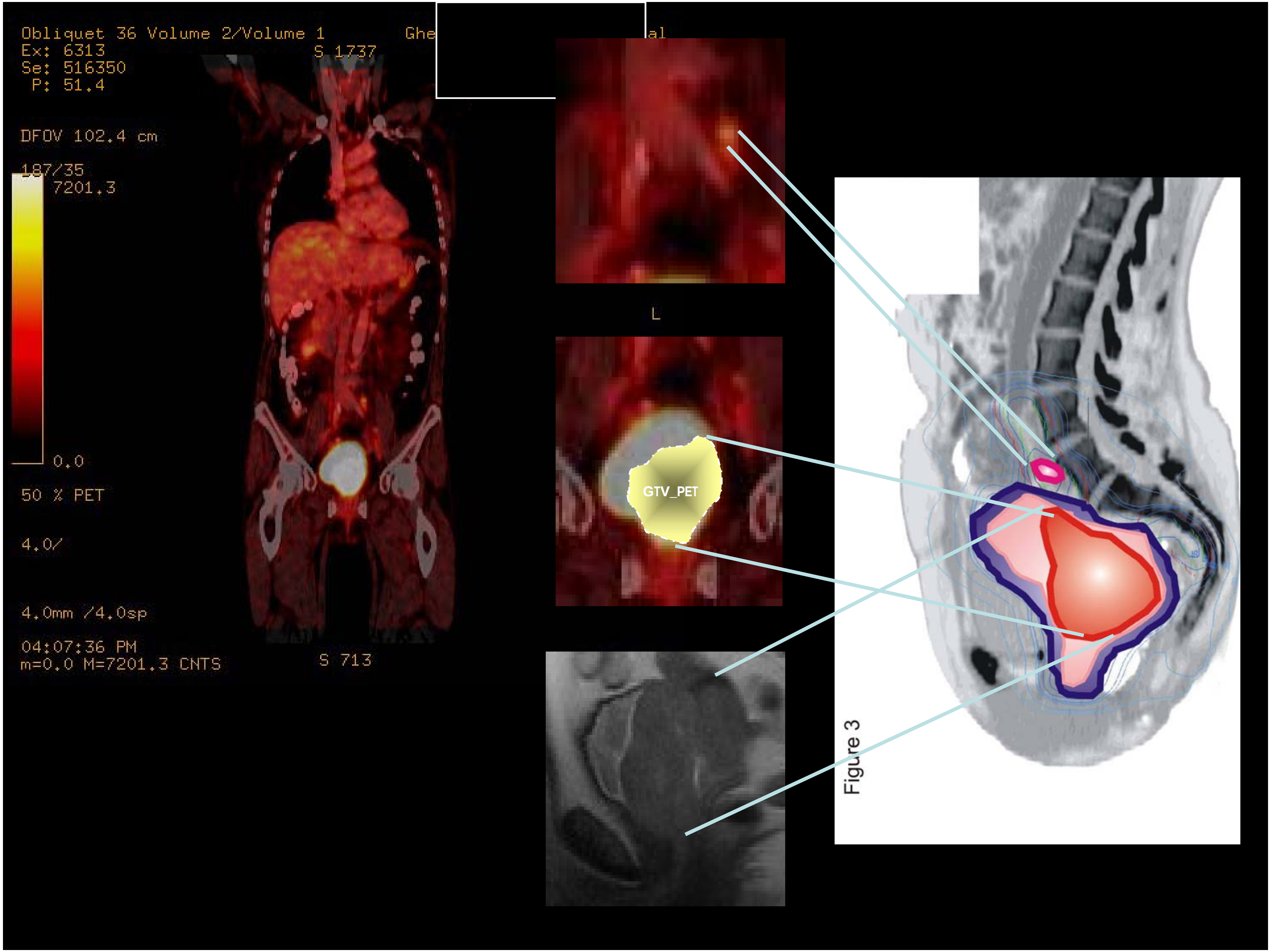


# Target volume delineation

**(stage IIB +left external iliac LN)**

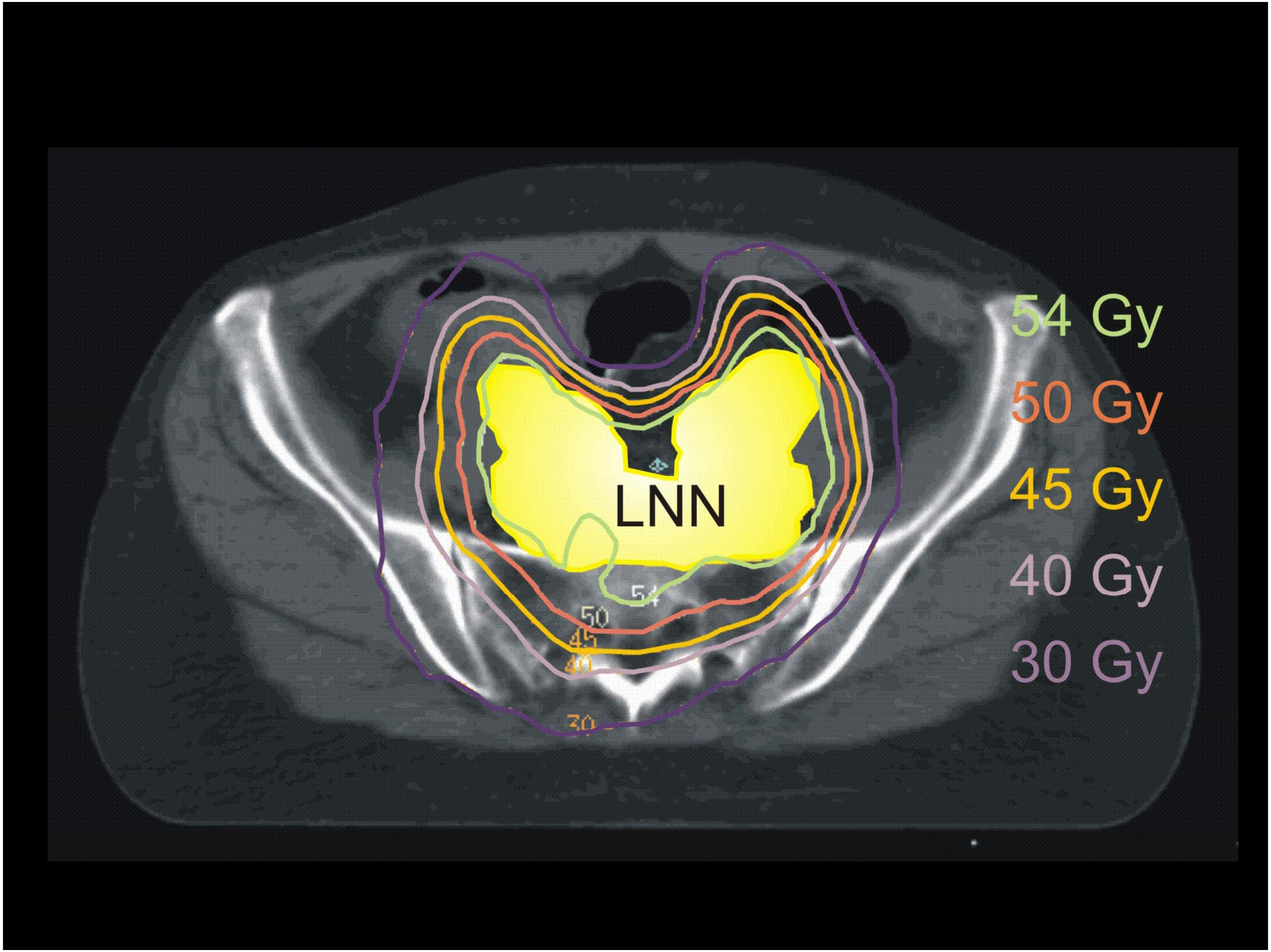



Obliquet 36 Volume 2/Volume 1
Ghe[redacted]al
Ex: 6313
S 1737
Se: 516350
P: 51.4
DFOV 102.4 cm
187/35
7201.3
0.0
50 % PET
4.0/
4.0mm /4.0sp
04:07:36 PM
m=0.0 M=7201.3 CNTS
S 713
L
GTV_PET

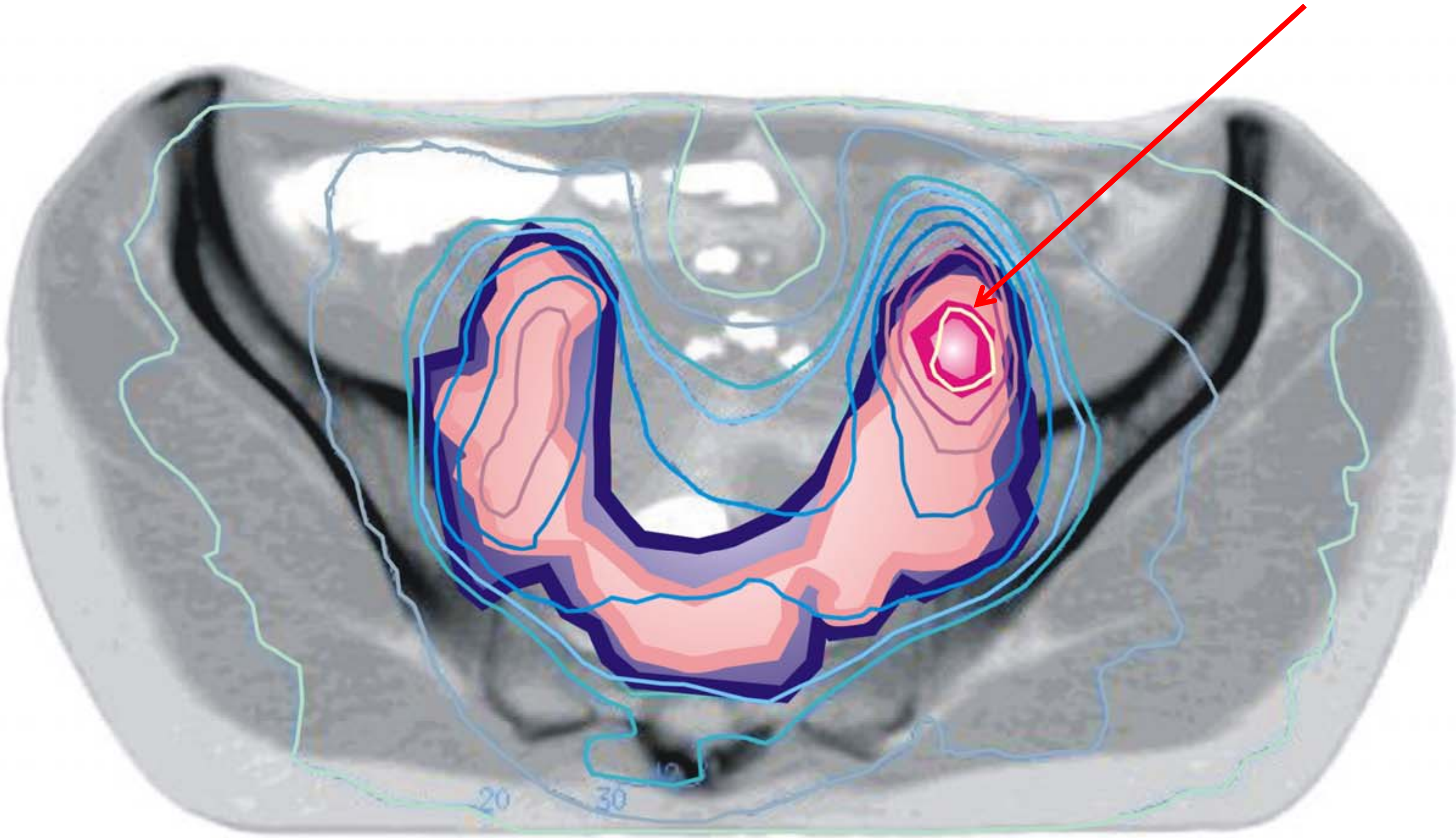


Obliquet 36 Volume 2/Volume 1
Ex: 6313
S 1737
Se: 516350
P: 51.4
DFOV 102.4 cm
187/35
7201.3
0.0
50 % PET
4.0/
4.0mm /4.0sp
04:07:36 PM
m=0.0 M=7201.3 CNTS
S 713
L
GTV_PET

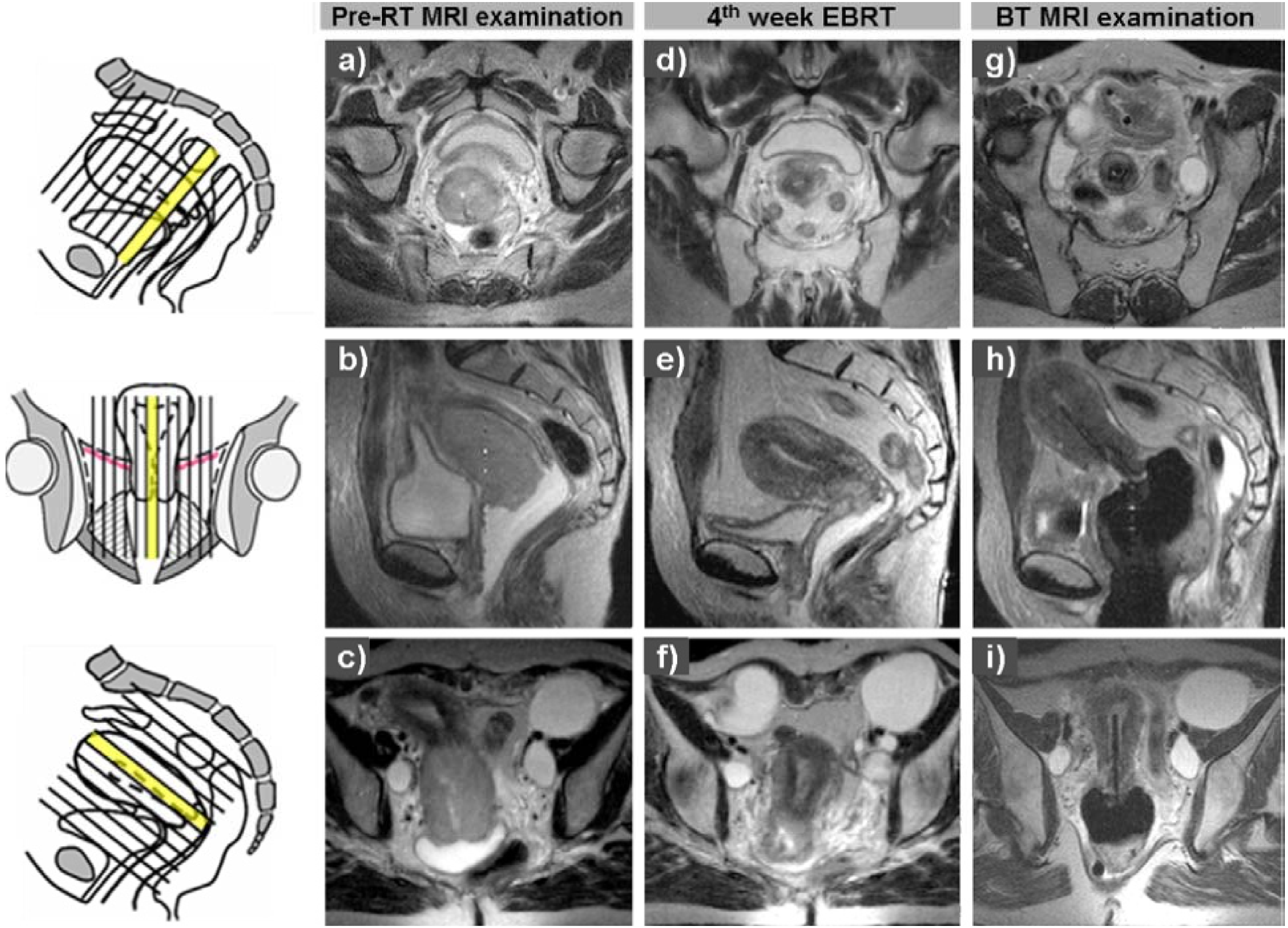

Figure 3



LNN
54
50
45
40
30
54 Gy
50 Gy
45 Gy
40 Gy
30 Gy



20
30



Pre-RT MRI examination
4th week EBRT
BT MRI examination
a)
d)
g)
b)
e)
h)
c)
f)
i)

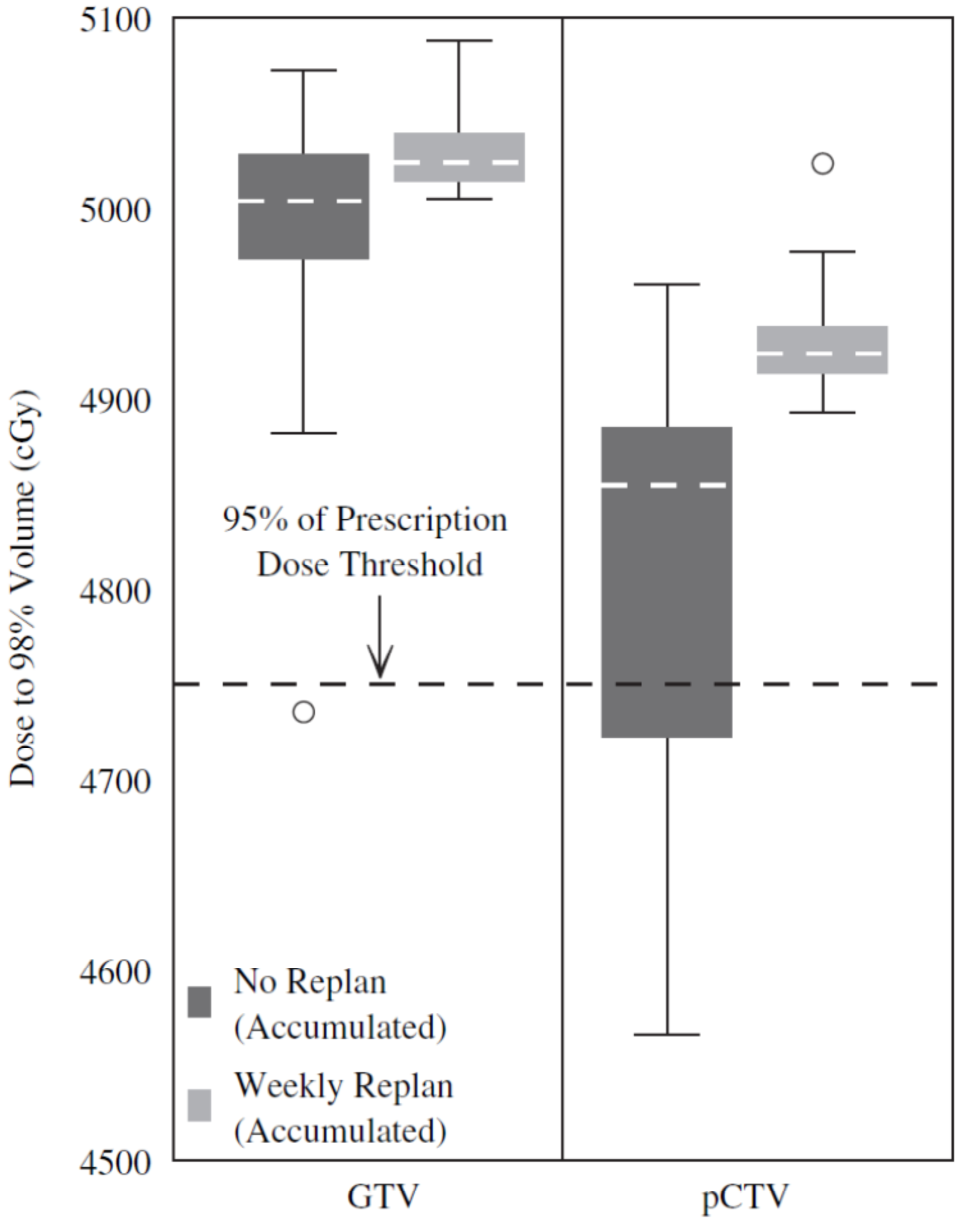
# Primary setting

# Weekly MR-based re-planning

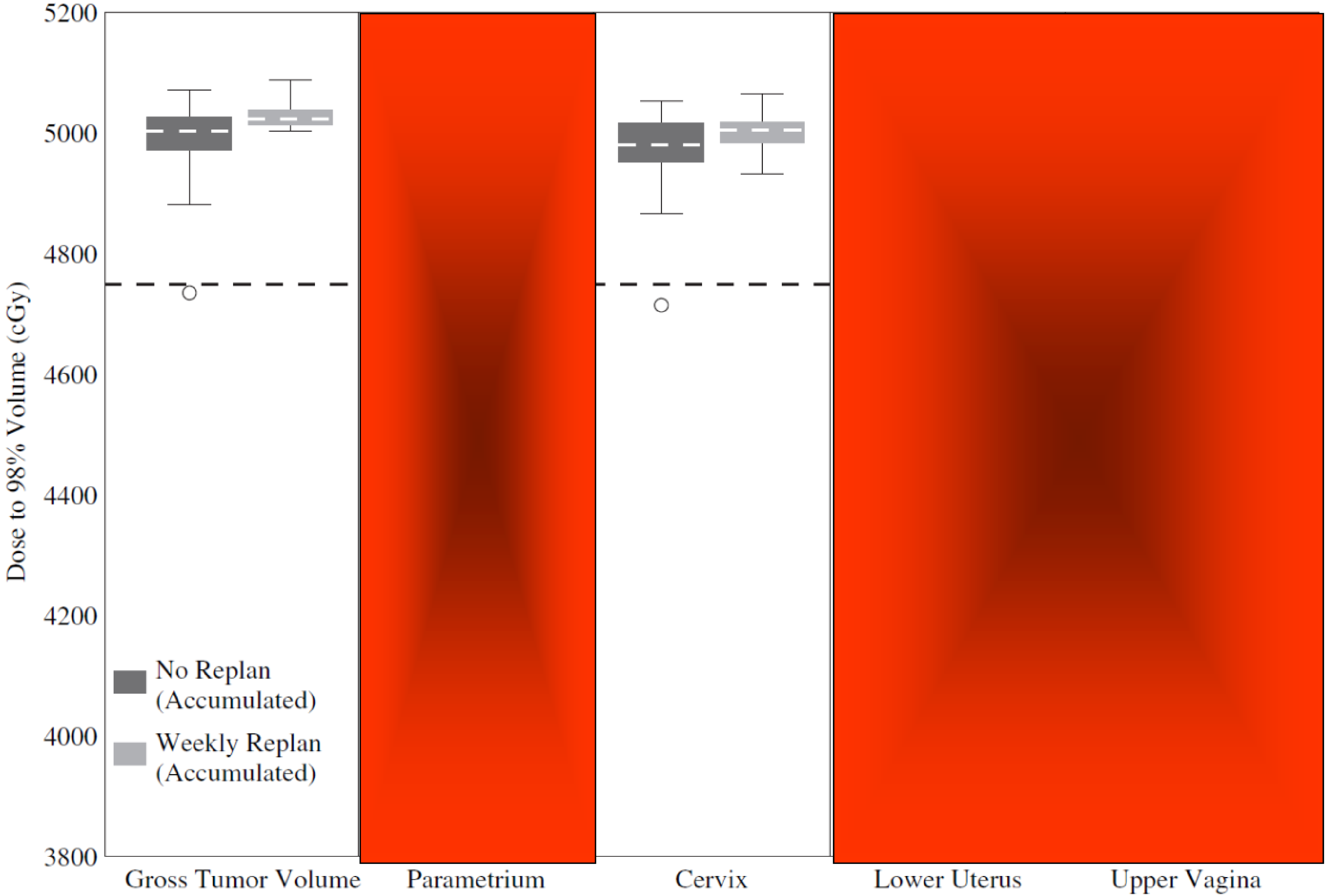
## AUTOMATED WEEKLY REPLANNING FOR INTENSITY-MODULATED RADIOTHERAPY OF CERVIX CANCER

JAMES STEWART, M.A.SC.,* KAREN LIM, M.B.B.S.,*† VALERIE KELLY, M.SC.,*† JASON XIE, M.SC.,* KRISTY K. BROCK, PH.D.,*†‡ JOANNE MOSELEY, B.MATH.,* YOUNG-BIN CHO, PH.D.,*† ANTHONY FYLES, M.D.,*† ANNA LUNDIN, M.SC.,§ HENRIK REHBINDER, PH.D.,§ JOHAN LÖF, PH.D.,§ DAVID JAFFRAY, PH.D.,*‡ AND MICHAEL MILOSEVIC, M.D., FRCPC.*†

**IJROBP 2010: 78: 350-8**



5100
5000
4900
4800
4700
4600
4500
Dose to 98% Volume (cGy)
95% of Prescription
Dose Threshold
No Replan
(Accumulated)
Weekly Replan
(Accumulated)
GTV
pCTV



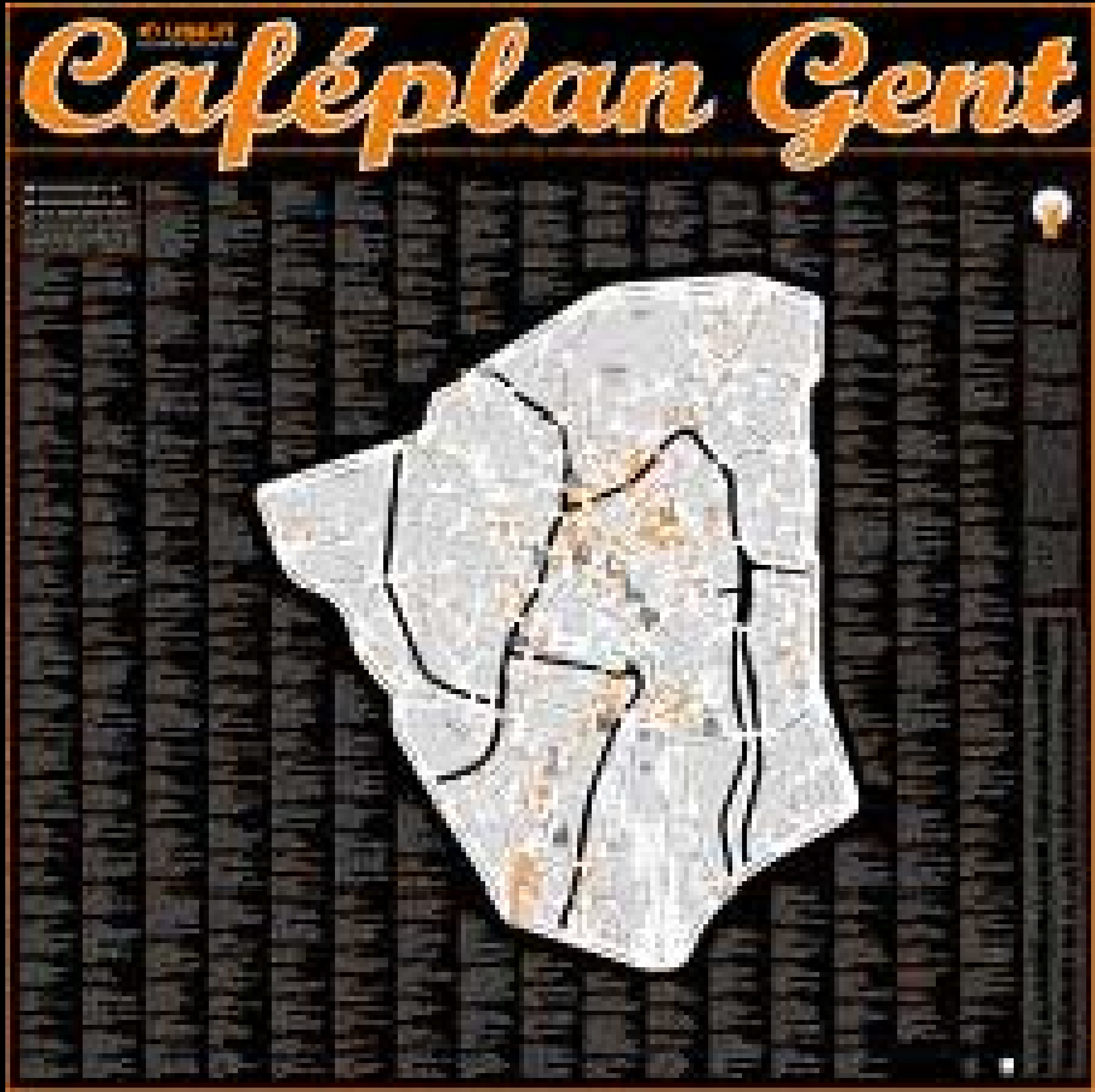
5200
5000
4800
4600
4400
4200
4000
3800
Dose to 98% Volume (cGy)
No Replan (Accumulated)
Weekly Replan (Accumulated)
Gross Tumor Volume
Parametrium
Cervix
Lower Uterus
Upper Vagina

## Take home messages:

- Use modern (incl. biological) imaging

- Delineate positive LN separately

- Adaptive planning might be near future


Caféplan Gent

# CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR INTENSITY-MODULATED PELVIC RADIOTHERAPY IN POSTOPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER

William Small, Jr., M.D.,* Loren K. Mell, M.D.,† Penny Anderson, M.D.,‡
Carien Creutzberg, M.D.,§ Jennifer De Los Santos, M.D.,¶ David Gaffney, M.D., Ph.D.,‖
Anuja Jhingran, M.D.,# Lorraine Portelance, M.D.,** Tracey Schefter, M.D.,††
Revathy Iyer, M.D.,‡‡ Mahesh Varia, M.D.,§§ Kathryn Winter, M.S.,¶¶ and Arno J. Mundt, M.D.‖‖

| Target site | Definition |
|---|---|
| Common iliac lymph nodes | From 7 mm below L4–L5 interspace to level of bifurcation of common iliac arteries into external and internal iliac arteries |
| External iliac lymph nodes | From level of bifurcation of common iliac artery into external artery to level of superior aspect of femoral head where it becomes femoral artery |
| Internal iliac lymph nodes | From level of bifurcation of common iliac artery into internal artery, along its branches (obturator, hypogastric) terminating in paravaginal tissues at level of vaginal cuff |
| Upper vagina | Vaginal cuff and 3 cm of vagina inferior to cuff |
| Parametrial/paravaginal tissue | From vaginal cuff to medial edge of internal obturator muscle/ischial ramus on each side |
| Presacral lymph nodes* | Lymph node region anterior to S1and S2 region |

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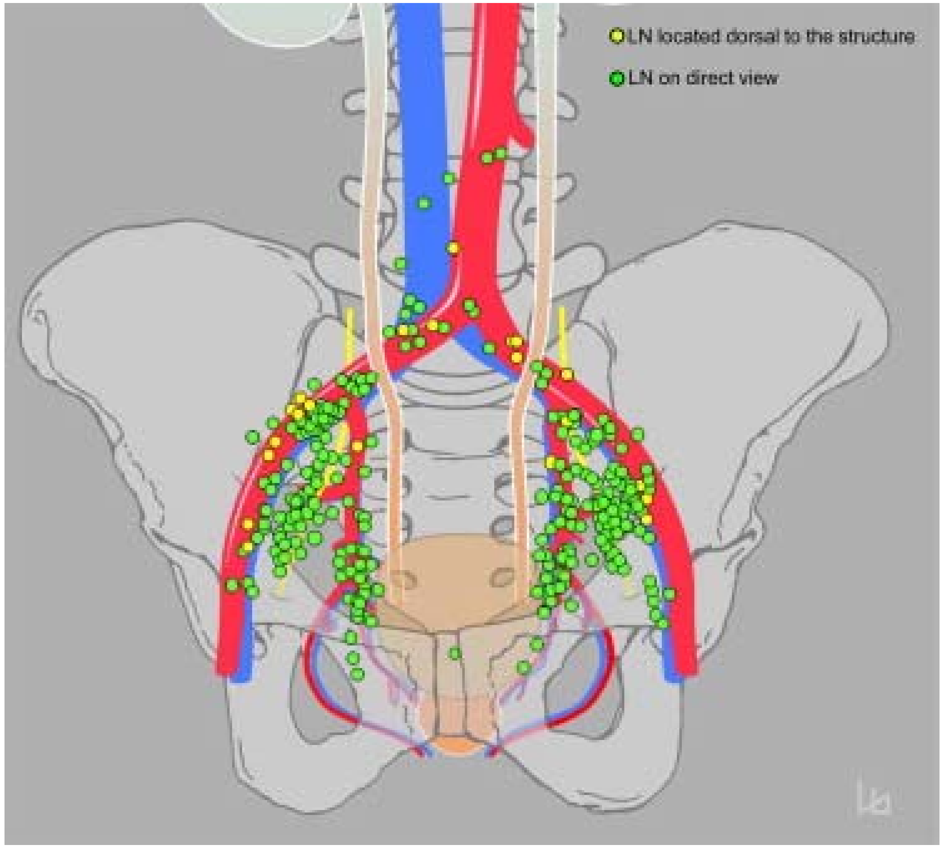
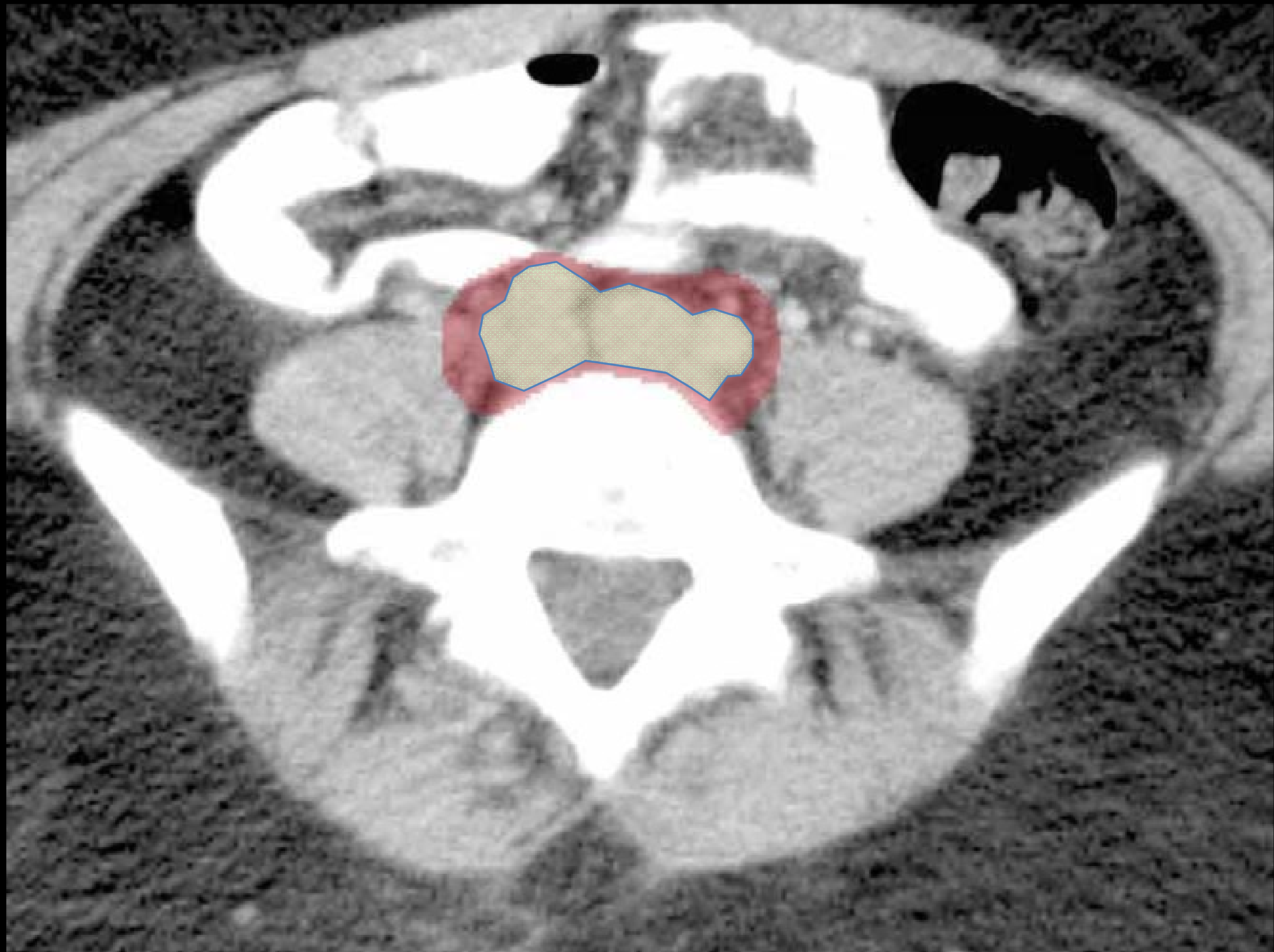
| Upper vagina | Vaginal cuff and 3 cm of vagina inferior to cuff |
| Parametrial/paravaginal tissue | From vaginal cuff to medial edge of internal obturator muscle/ischial ramus on each side |
| Presacral lymph nodes* | Lymph node region anterior to S1and S2 region |

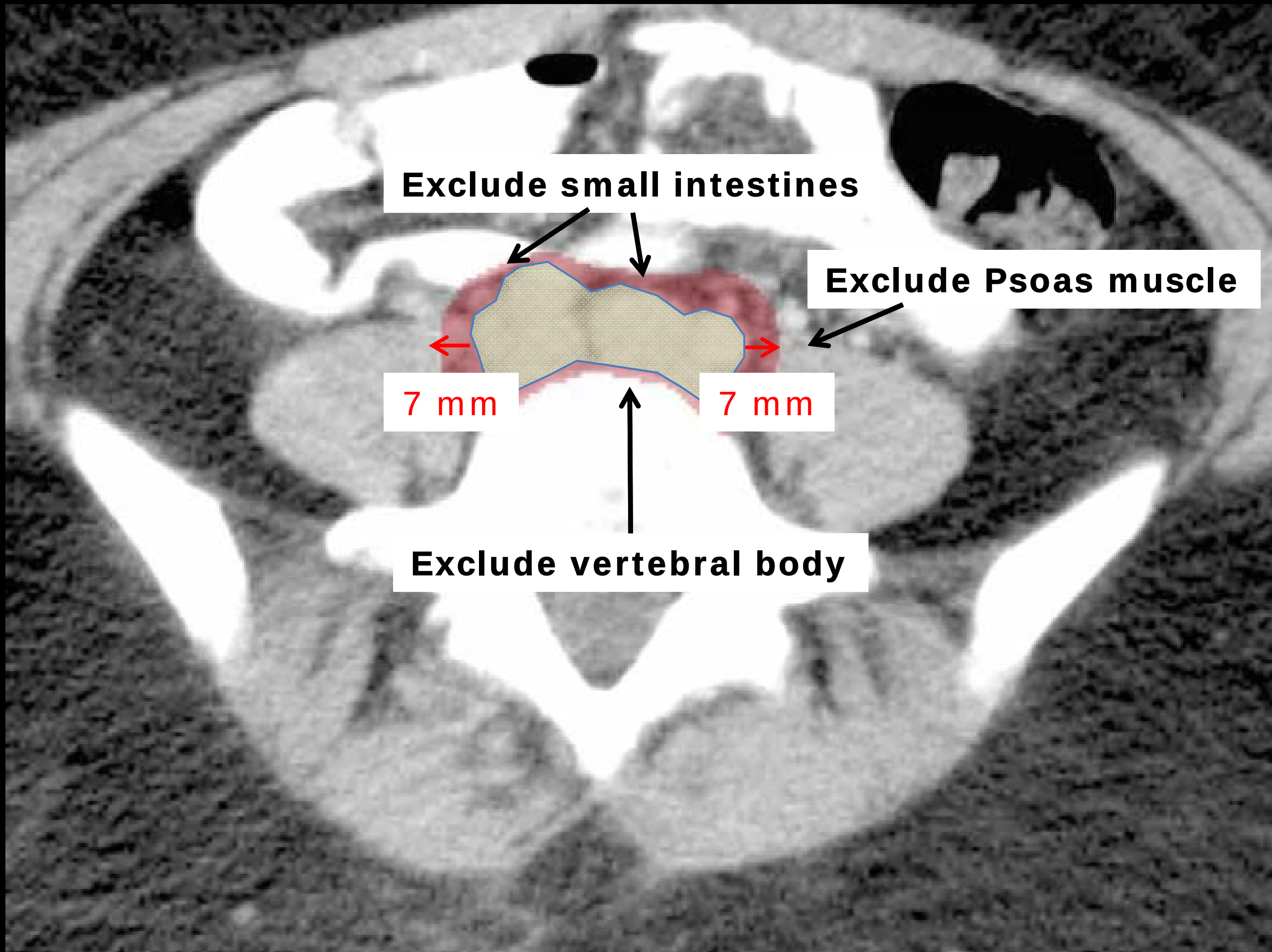


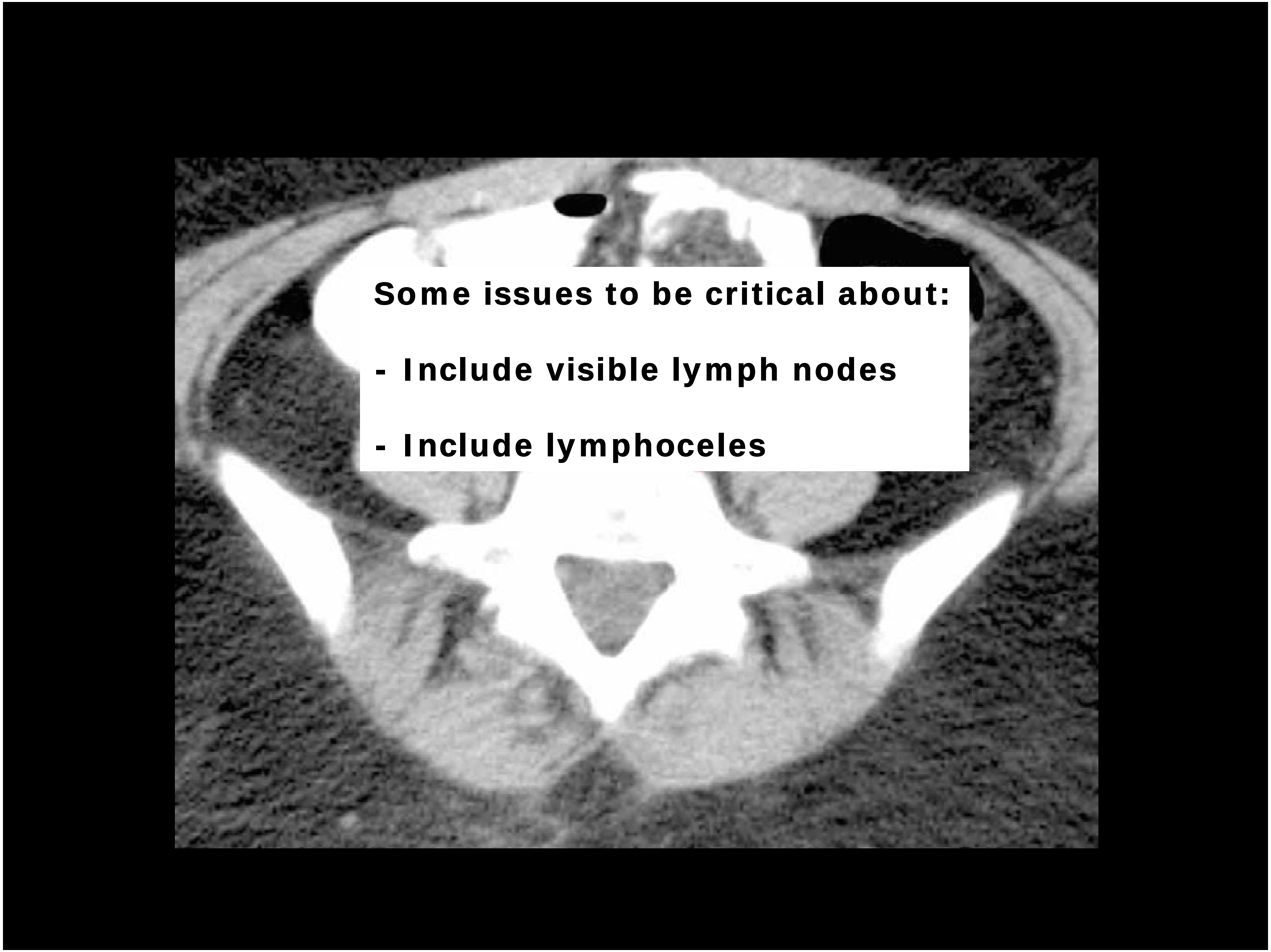
# Upper CTV: aortic bifurcation

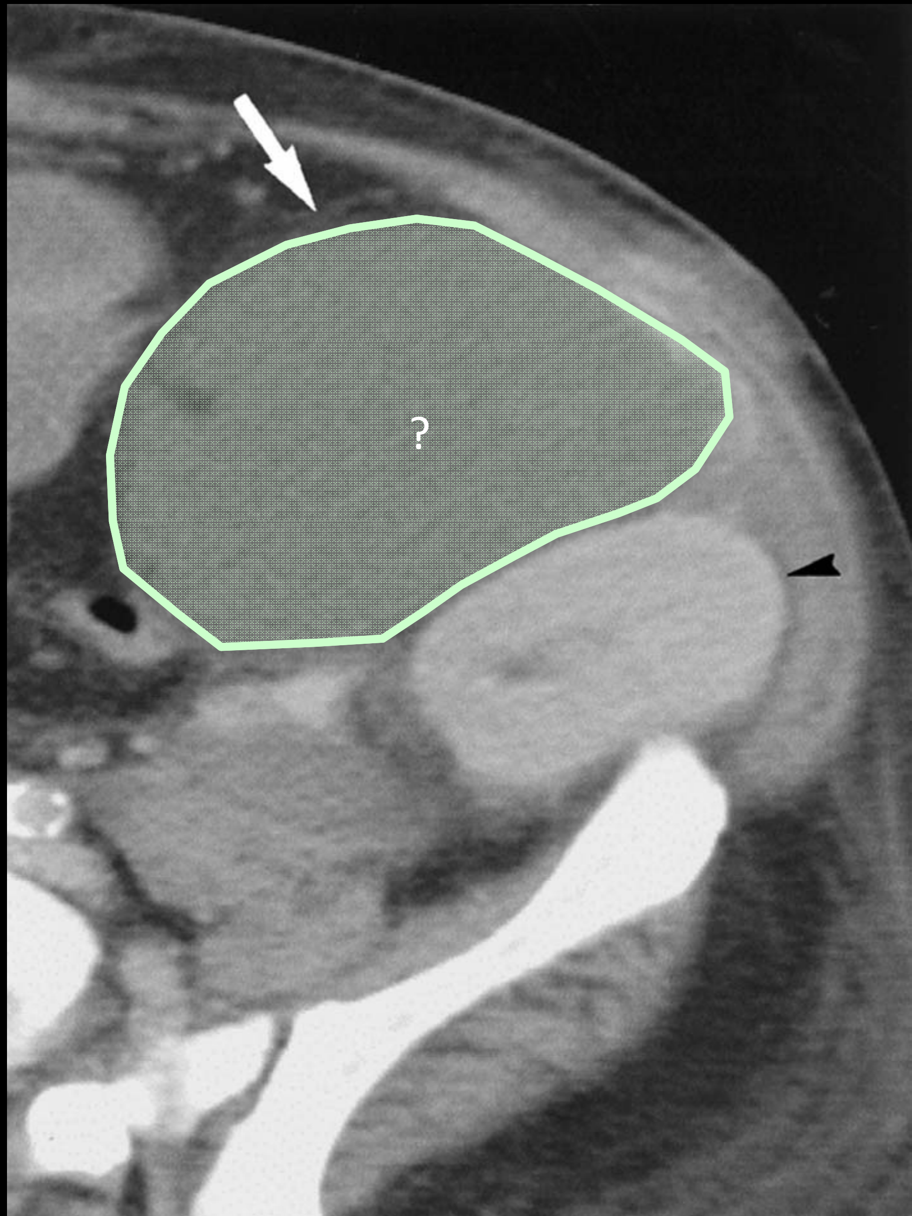


# Upper CTV: aortic bifurcation

# Upper CTV: aortic bifurcation

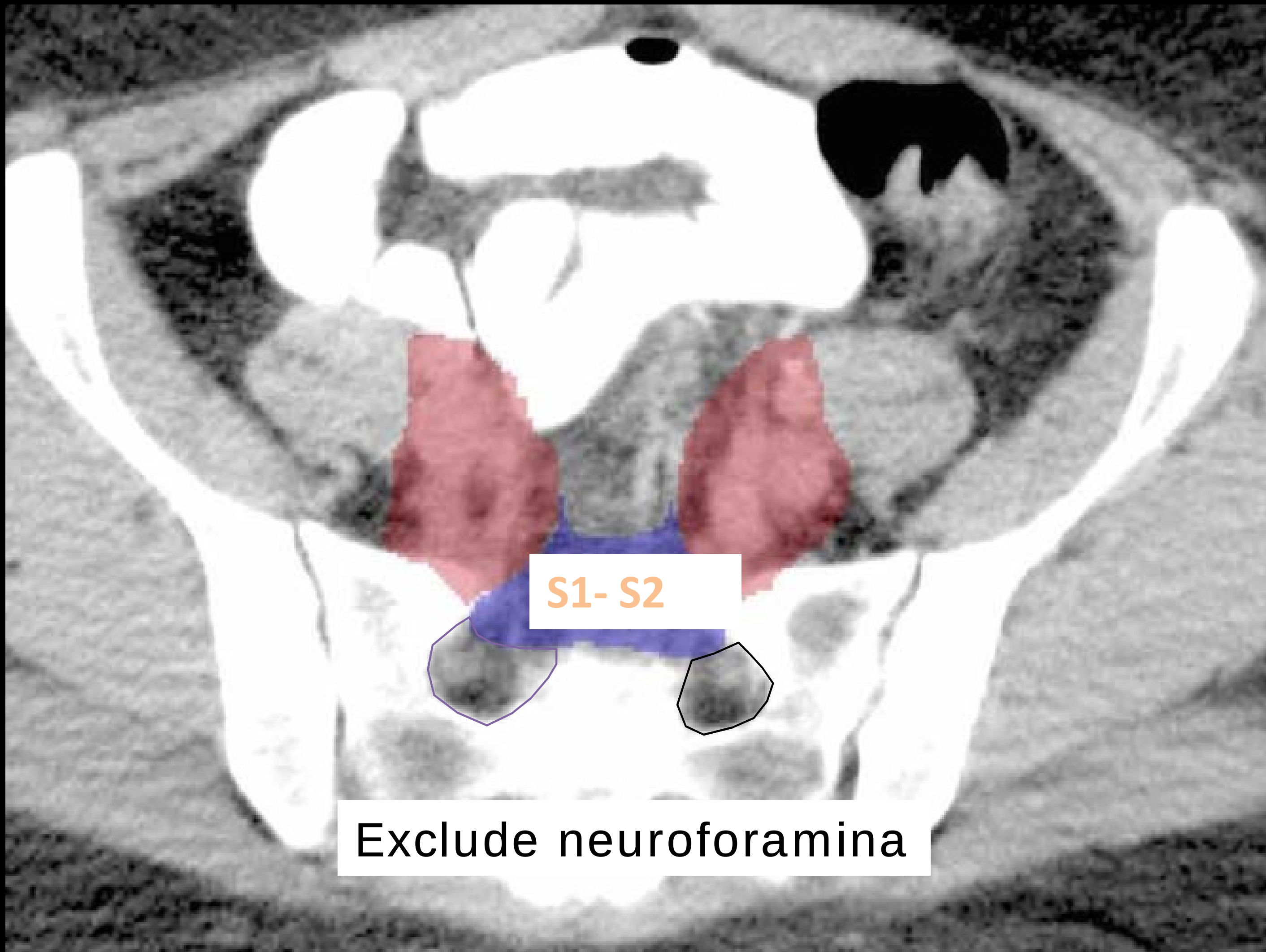



Some issues to be critical about:
- Include visible lymph nodes
- Include lymphoceles

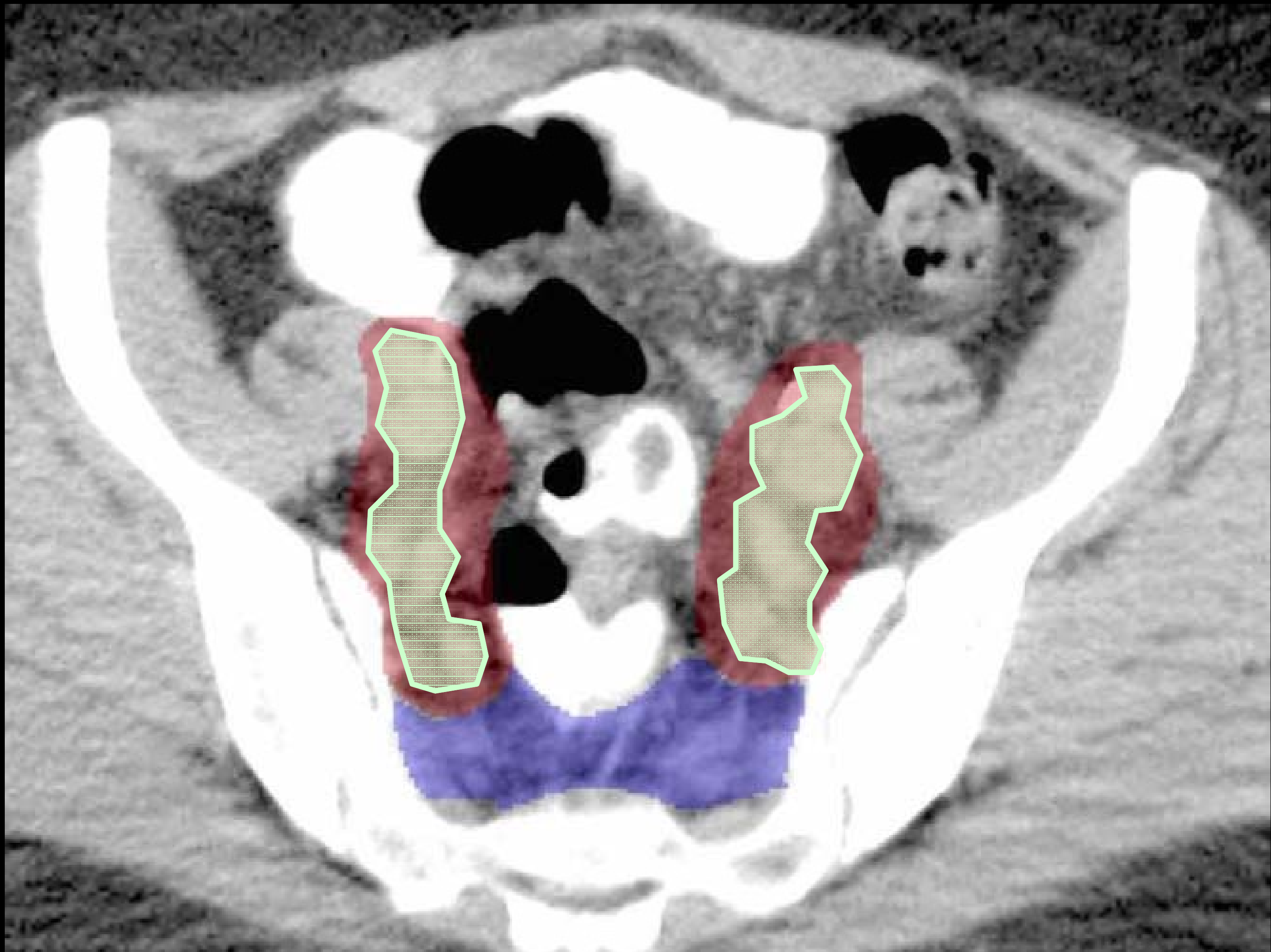


# Upper CTV: common iliac vessels – presacral region

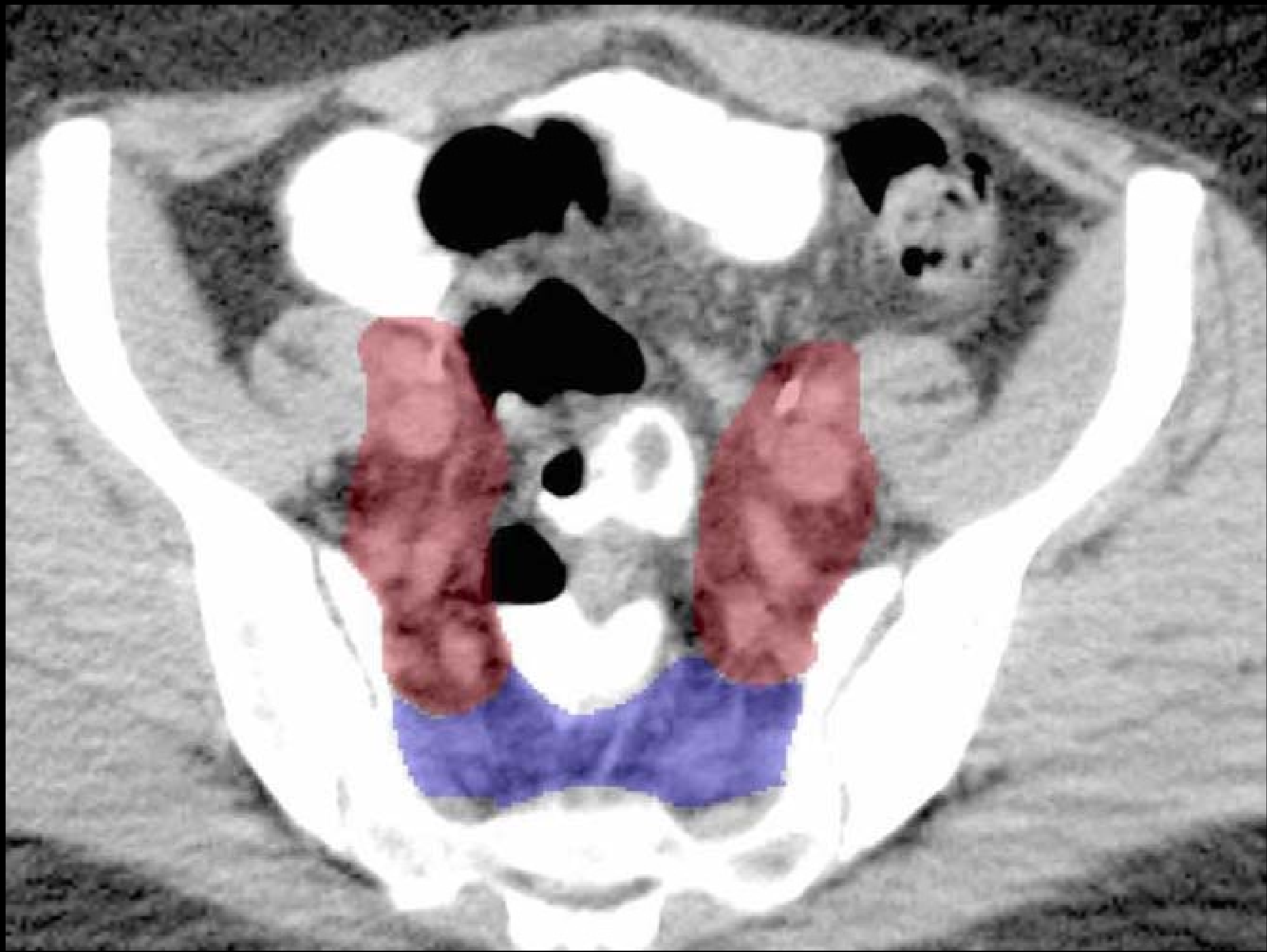
# Upper CTV: common iliac vessels – presacral region



# Middle CTV: internal/external iliac vessels– presacral region

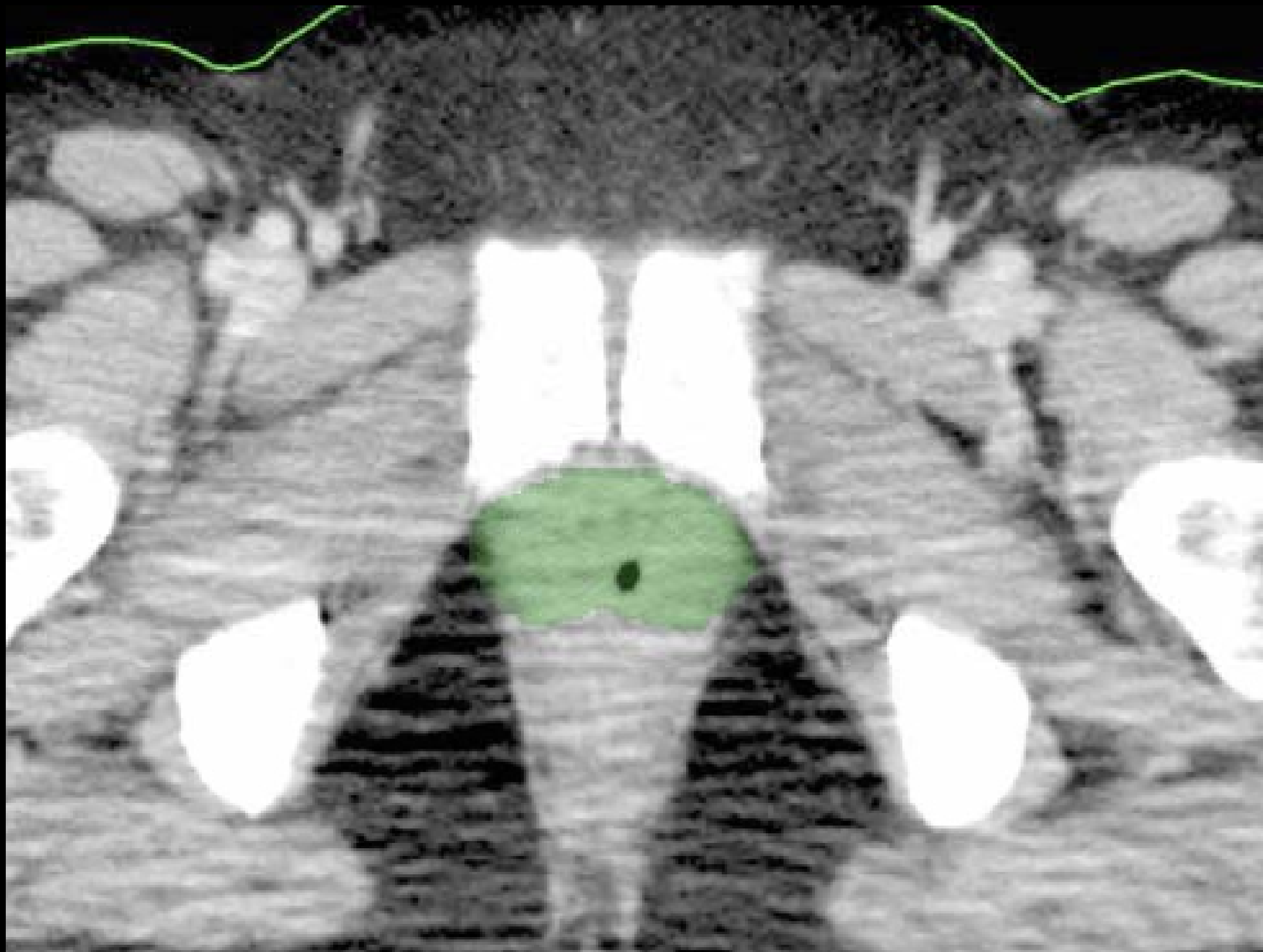


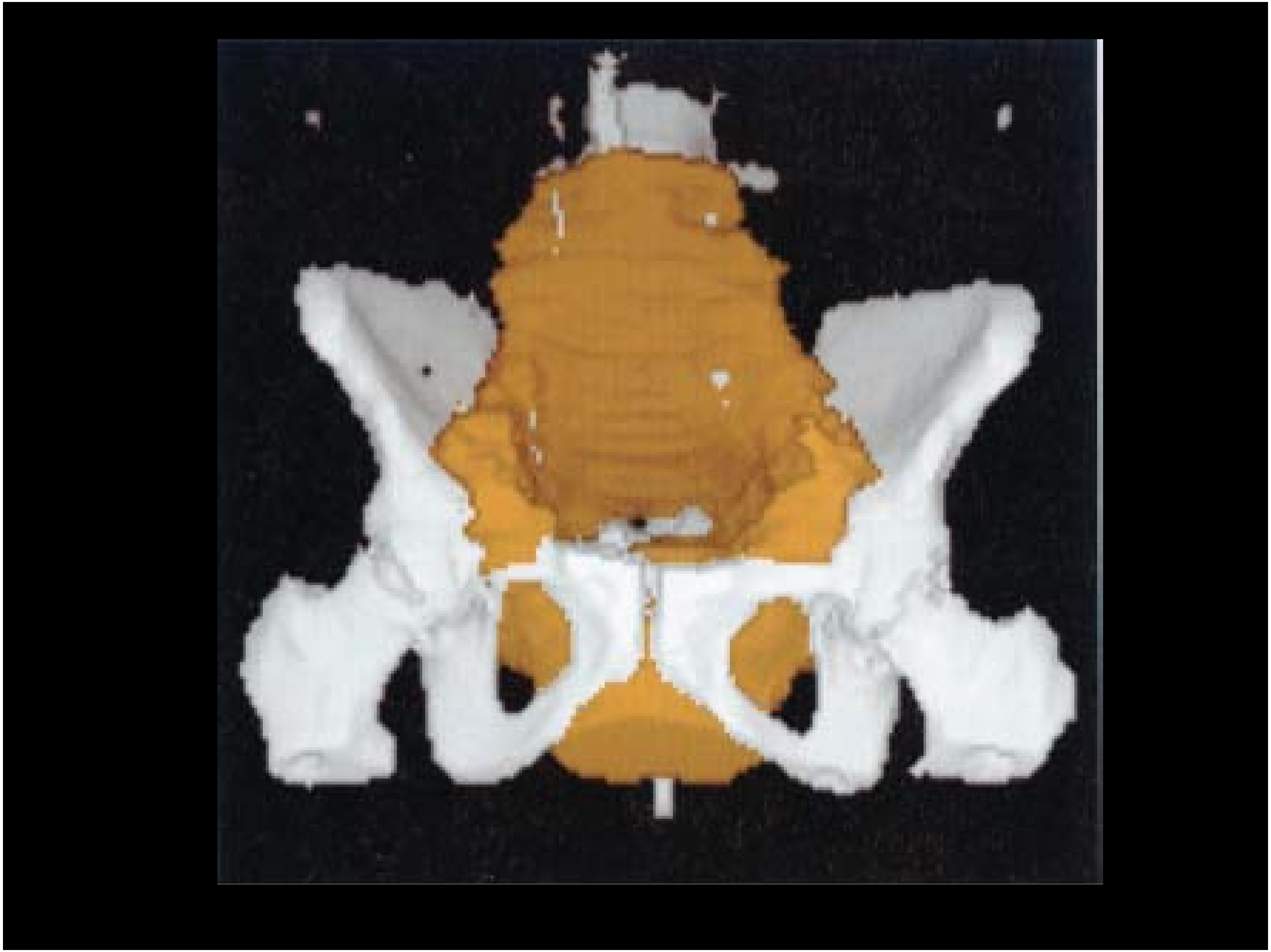
Middle CTV: internal/external iliac vessels– presacral region



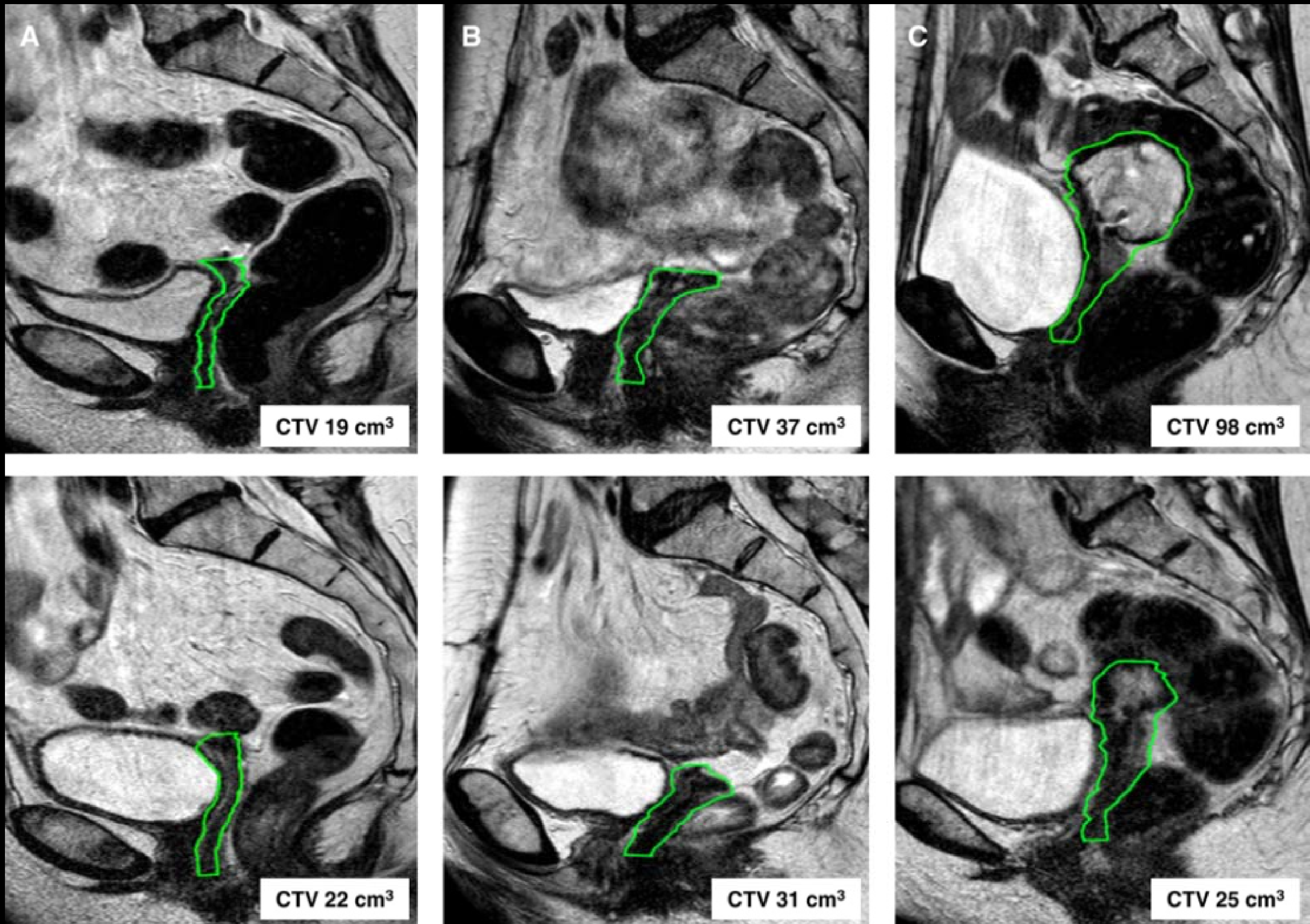
# Parametrial / Vaginal CTV

## Vaginal CTV





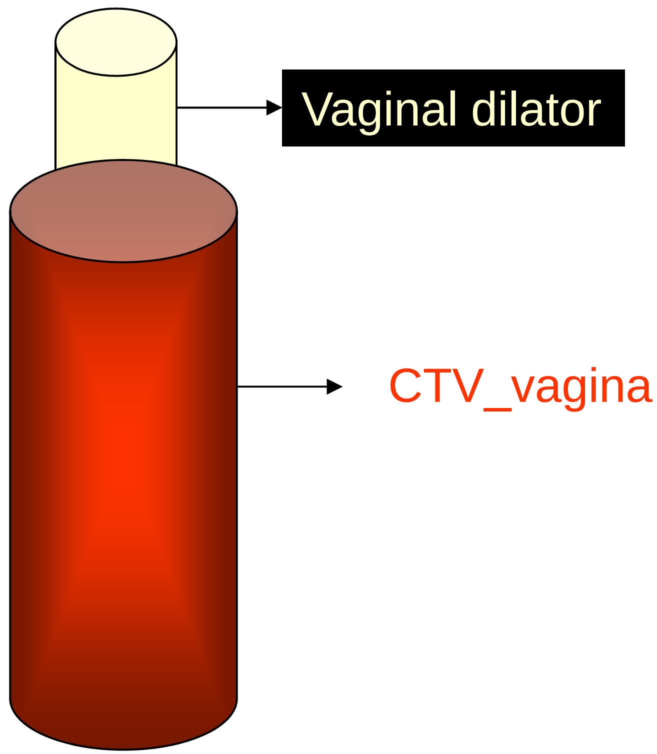
# Postoperative setting: heterogeneous situation

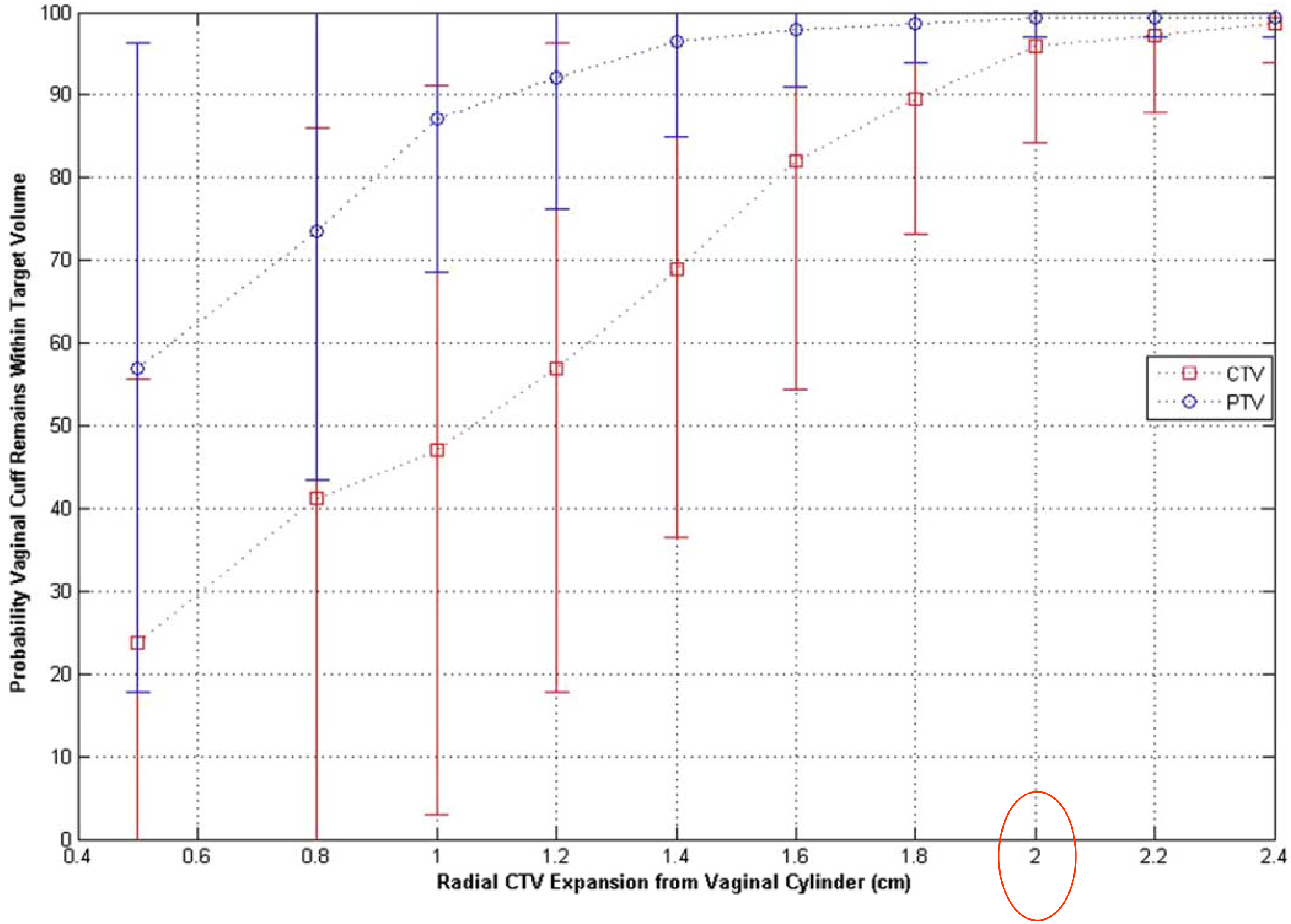


# Vaginal cuff marker

# MAGNITUDE OF INTERFRACTIONAL VAGINAL CUFF MOVEMENT: IMPLICATIONS FOR EXTERNAL IRRADIATION

Daniel J. Ma, M.D.,* Martha Michaletz-Lorenz, M.S.,† S. Murty Goddu, Ph.D., and Perry W. Grigsby, M.D.*‡§



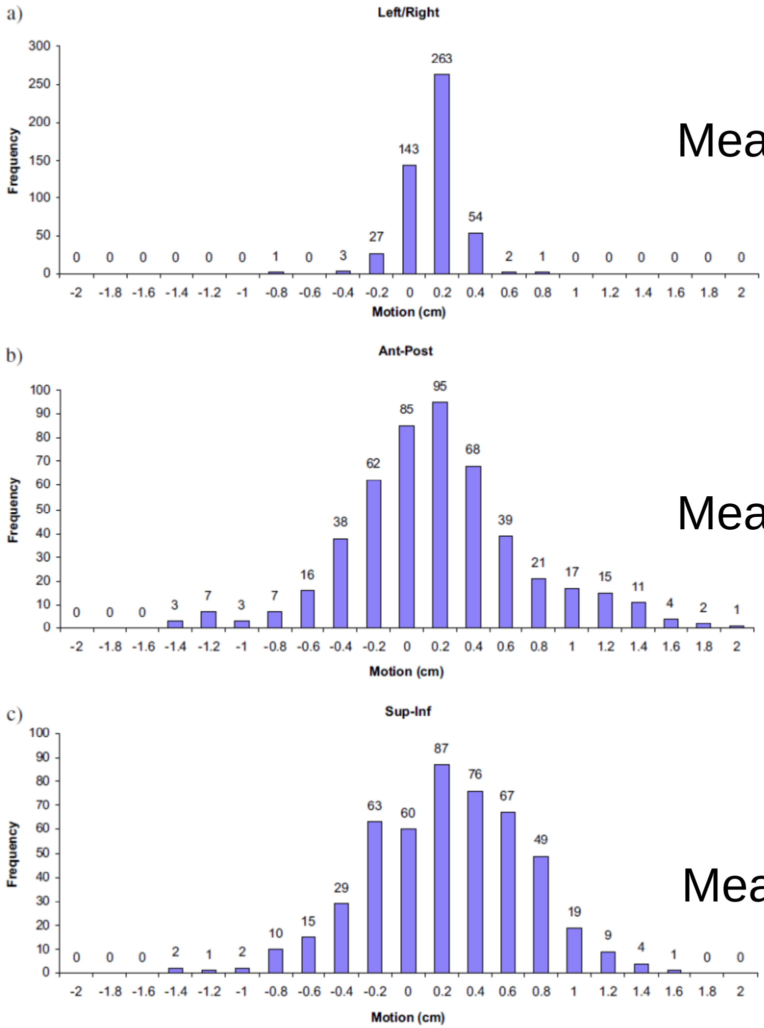


Probability Vaginal Cuff Remains Within Target Volume
Radial CTV Expansion from Vaginal Cylinder (cm)
CTV
PTV
0
10
20
30
40
50
60
70
80
90
100
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
2.2
2.4

# ASSESSMENT OF ORGAN MOTION IN POSTOPERATIVE ENDOMETRIAL AND CERVICAL CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY

ELEANOR E. R. HARRIS, M.D., KUJTIM LATIFI, M.S., CHAD RUSTHOVEN, B.S., KEN JAVEDAN, PH.D., AND KENNETH FORSTER, PH.D.

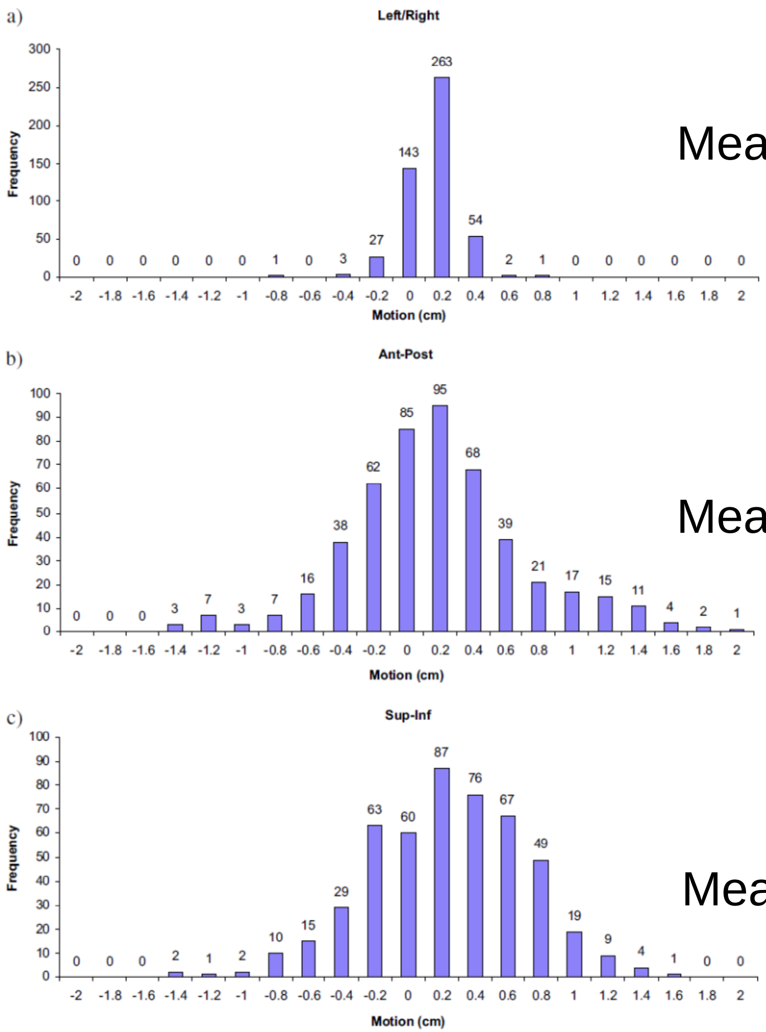
- Daily CBCT
- Vaginal wall organ motion
- n=22
- upper vaginal ½, expanded with 10mm
- 3 fiducial markers, COM




Mean LR motion 1.2 mm

Mean AP motion 4.0 mm

Mean SI motion 4.0 mm




Mean LR motion 1.2 mm

Mean AP motion 4.0 mm

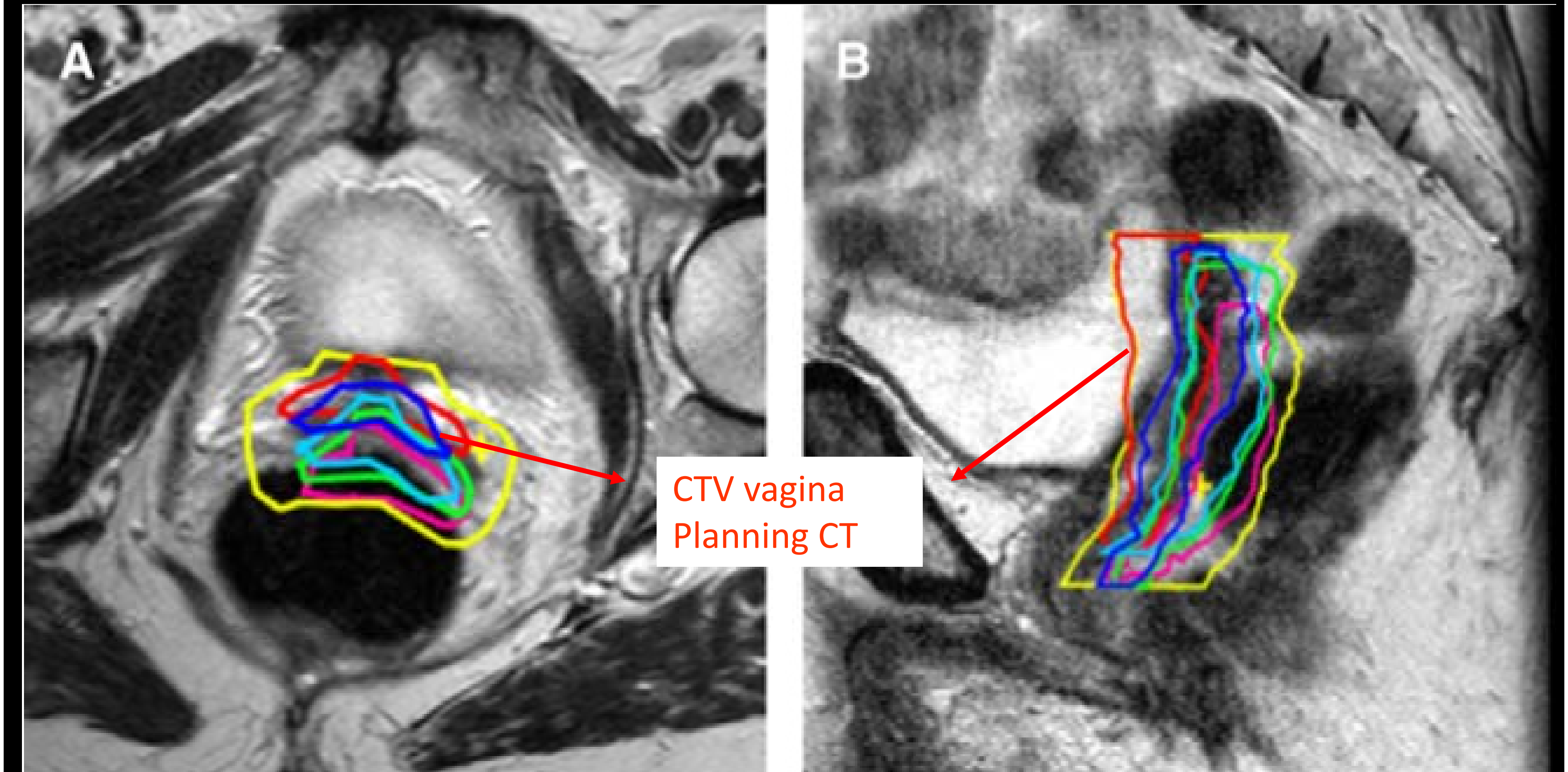
Mean SI motion 4.0 mm

<u>To ensure 95% coverage</u>:

- LR: 3.1 mm needed
- AP: 12.1 mm needed
- SI: 9.5 mm needed

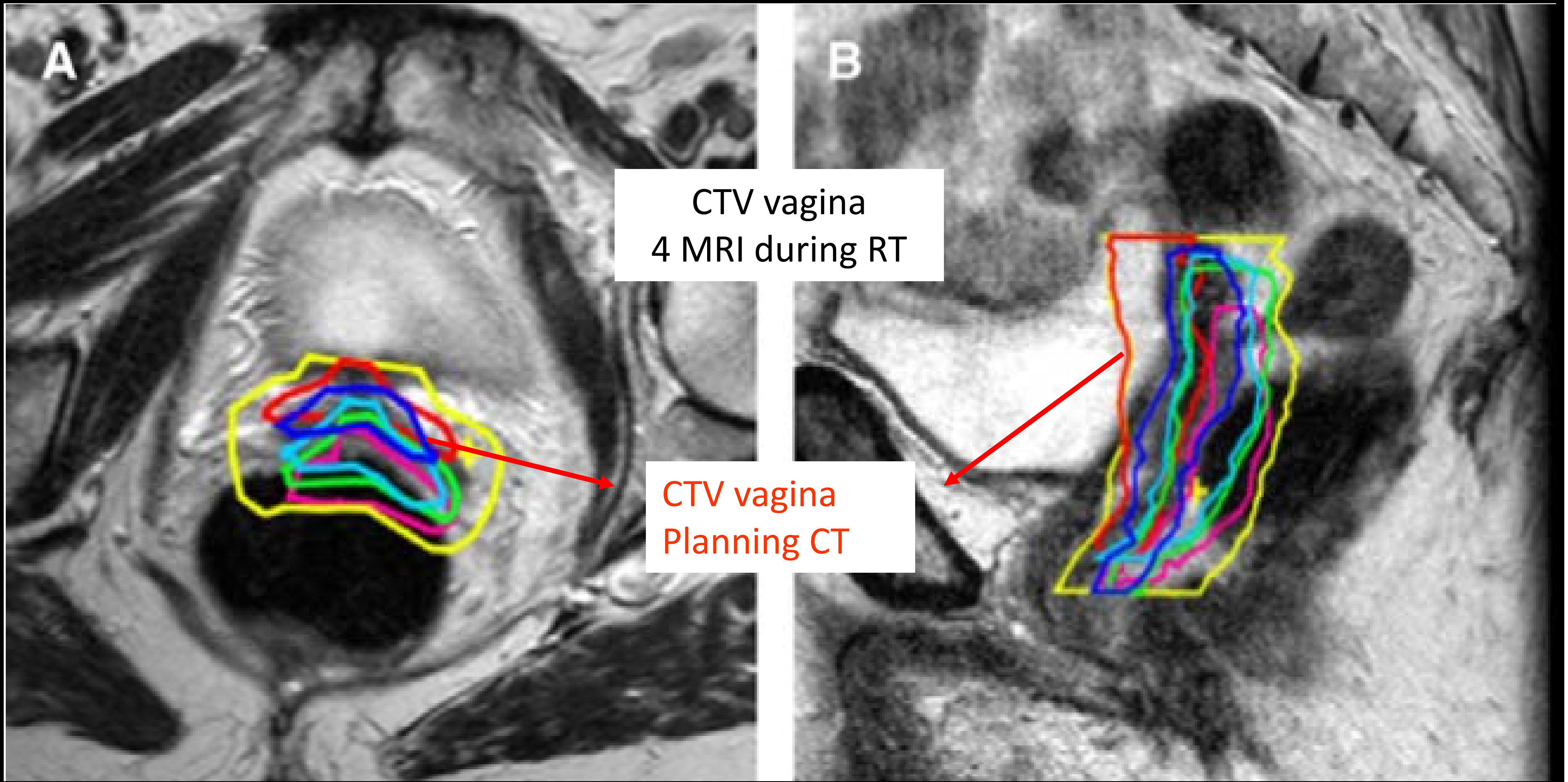
<u>Total motion (COM): 15.7 mm</u>

# Homogeneous margins?



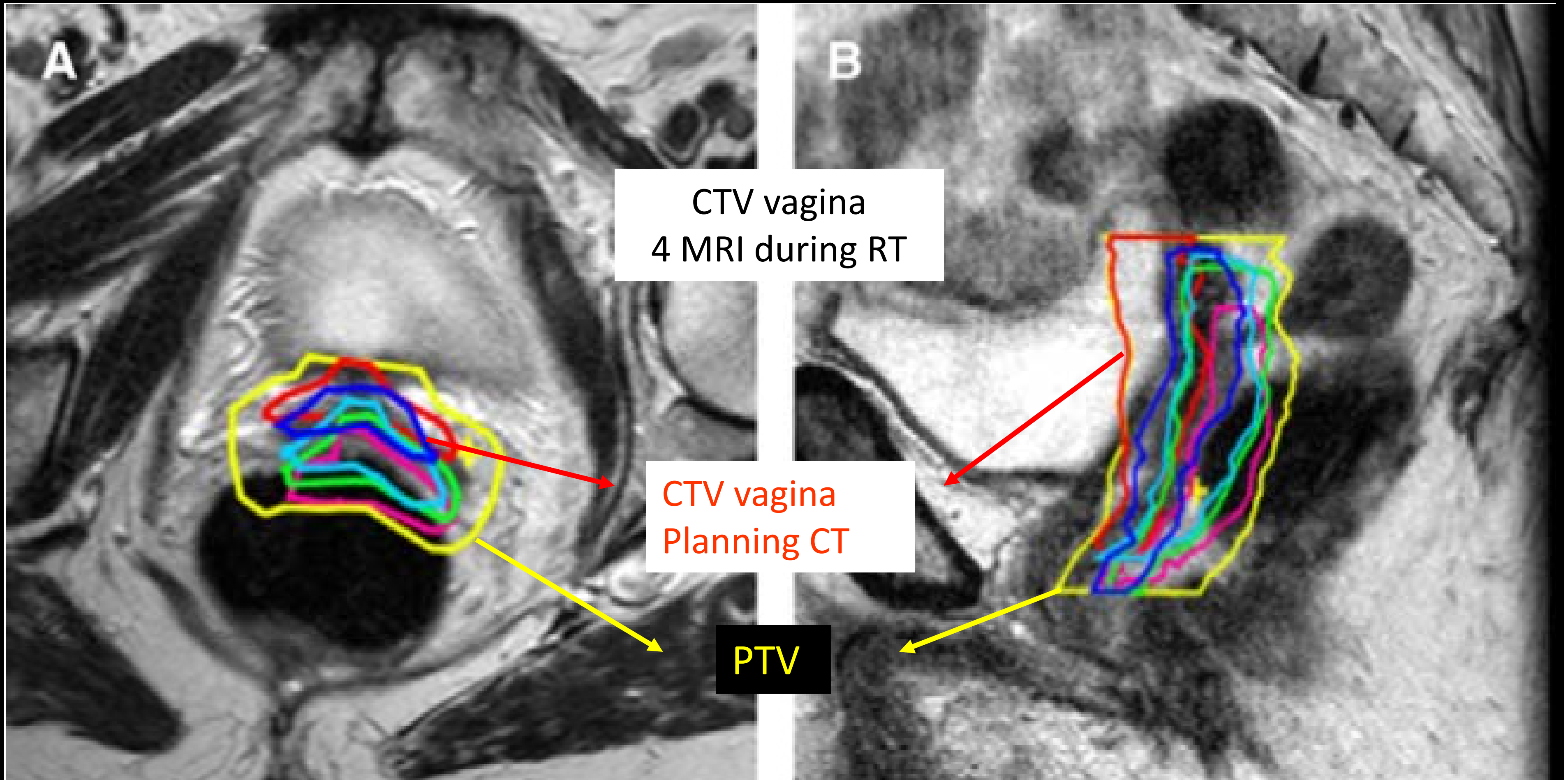

Jürgenliemk-Schulz et al. R&O; 2011;98:

# Homogeneous margins?




Jürgenliemk-Schulz et al. R&O; 2011;98:

# Homogeneous margins?




Jürgenliemk-Schulz et al. R&O; 2011;98:

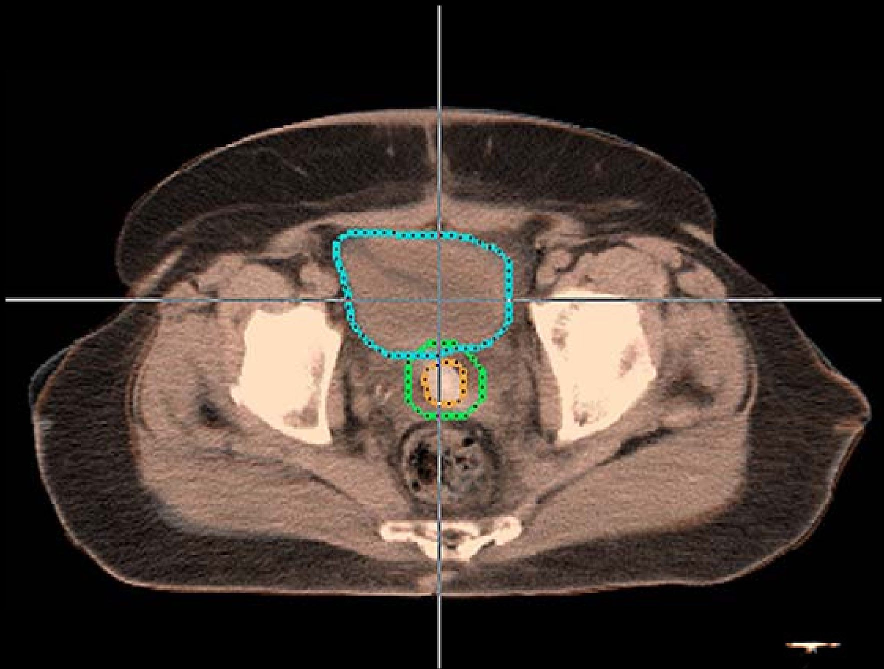
## Suggested margins:

To encompass 90% of the vaginal volumes:
- AP; 19 mm
- LR: 11 mm
- S(I): 15 mm

To encompass 95% of the vaginal volumes:
- AP: 23 mm
- LR: 18 mm
- S(I): 15 mm

Jürgenliemk-Schulz et al. R&O; 2011;98: 244-8.

# What NOT to do!



(a)

(b)

## Take home messages:

Lymph nodes are similar to prostate LN areas

! Inguinal nodes are not part of the CTV, except in particular cases ...

Margins of >15 mm to ensure sufficient coverage of vaginal volumes

## Point of discussion (future?)

PALN??


TICKETS