ESTRO teaching course on

Image-guided and Adaptive Radiotherapy in Clinical Practice

2016

Madrid

<u>**Teaching staff:**</u>

Marianne Aznar (MA), Denmark (Course Director)
Coen Rasch (CR), The Netherlands (Course Director)

Gilles Crehange (GC), France
Rianne de Jong (RdJ),The Netherlands
Andrew Hope (AH), Canada
Helen McNair (HmN), United Kingdom
Uwe Oelfke (UO), United Kingdom
Jan-Jakob Sonke (JJS), The Netherlands
Marcel van Herk (MvH), The Netherlands

Guest lecturer Parag Parikh (PP), USA

SCIENTIFIC PROGRAMME

SUNDAY	23 October	Introduction to IGRT and adaptive

13.00 – 13.10	Welcome and general introduction	CR/MA
13.10 – 14.10	**Entry Exam**	
14.10 – 14.45	IGRT – a physician's perspective	CR
14.45 – 14.55	Discussion	
14.55 – 15.25	*Coffee break*	
15.25 – 16.00	IGRT – a physicist's perspective	MA
16.00 – 16.10	Discussion	
16.10 – 16.45	IGRT- an RTT's perspective	RdJ
16.45 – 16.55	Discussion	
17h00	Visit to the Radiotherapy Department of **Hospital Universitario Puerta de Hierro Majadahonda**	

MONDAY	24 October	IGRT strategies in clinical practice

08.30 – 09.10	Technology: Planar imaging, MV and kV	MA
09.10 – 09.20	Discussion	
09.20 – 10.05	Technology: kV-CBCT, in-room kV CT + MV-CT	UO
10.05 – 10.15	Discussion	
10.15 – 10.45	*Coffee break*	
10.45 – 11.30	Clinical prostate	GC
11.30 – 11.40	Discussion	
11.40 – 12.20	Errors and margins	MvH
12.20 – 12.30	Discussion	
12.30 – 13.30	*Lunch*	
13.30 – 14.10	Corrective strategies: online versus offline	JJS
14.10 – 14.20	Discussion	
14.20 – 15.00	How do offline versus online strategies influence your margin	MvH
15.00 – 15.45	Prostate: registration issues	RdJ/HmN
15.45 – 16.15	*Coffee Break*	
16.15 – 17.00	Technology: non-ionising solutions	UO
19.30	**Social Event: Westin Palace**	

TUESDAY	25 October	MR linac/ Targets with respiratory motion

Chairperson: H. McNair

8.30– 9.15	MR linac technical considerations	UO
9.15 – 10.00	MR guided RT clinical expectations	PP
10.00 – 10.30	*Coffee break*	
10.30 – 11.00	MR guided RT for pelvic tumors	PP
11.00 – 11.10	Discussion	
11.10 – 12.00	Imaging in the 4th dimension	JJS
12.00 – 12.45	Technology: 4D-IGRT	MA
12.45 – 13.45	*Lunch*	
13.45 – 14.45	Clinical lung/breast	AH/MA
14.45 – 15.30	Registration issues lung/breast	RdJ/HmN
15.30 – 16.00	*Coffee break*	
16.00 – 17.00	Break-up sessions (3) - Physics: QA/commissioning of IGRT and motion monitoring systems (Plaza de Armas) - RTT: 4D including breath hold (Prisma) - Clinicians: delineation in the presence of respiration (Barcelona)	

WEDNESDAY	26 October	Focus on adaptation

8.30 – 10.00	IGRT/adaptive for gynae/bladder/rectum	GC/UO
10.00 – 10.30	*Coffee break*	
10.30 – 11.15	Registration issues; choosing from a library of plans	RdJ /HmN
11.15 – 12.15	Uncertainties in image registration and contour propagation	MvH
12.30 – 13.30	*Lunch*	
13.30 – 14.30	IGRT for CNS and Head and neck	CR/MvH
14.30- 15.00	*Coffee break*	
15.00 – 15.45	Adaptive strategies for Head and Neck and Lung	CR
15.45 – 16.45	Break- out sessions on Adaptive Radiotherapy - Physics (Plaza de Armas) - RTT (Prisma) - Clinical (Barcelona)	

THURSDAY	27 October	Perspectives for advanced IGRT/adaptation

08: 30 – 9:15	Problems and procedures and safety	HmN
09.15 – 10.05	Radiosurgery and SBRT: from frame to frameless	AH
10.05– 10.35	*Coffee break*	
10.35 – 11.05	Patient preparation and positioning	RdJ
11.05 – 11.50	IGRT and adaptive for Protons therapy	JJS
11.50 – 12.50	Round-up + EXIT EXAM	The Faculty
12.50 – 13.00	Handing out of certificates of attendance	

IGRT -
A Physician's Perspective

Coen Rasch

AMC, Amsterdam

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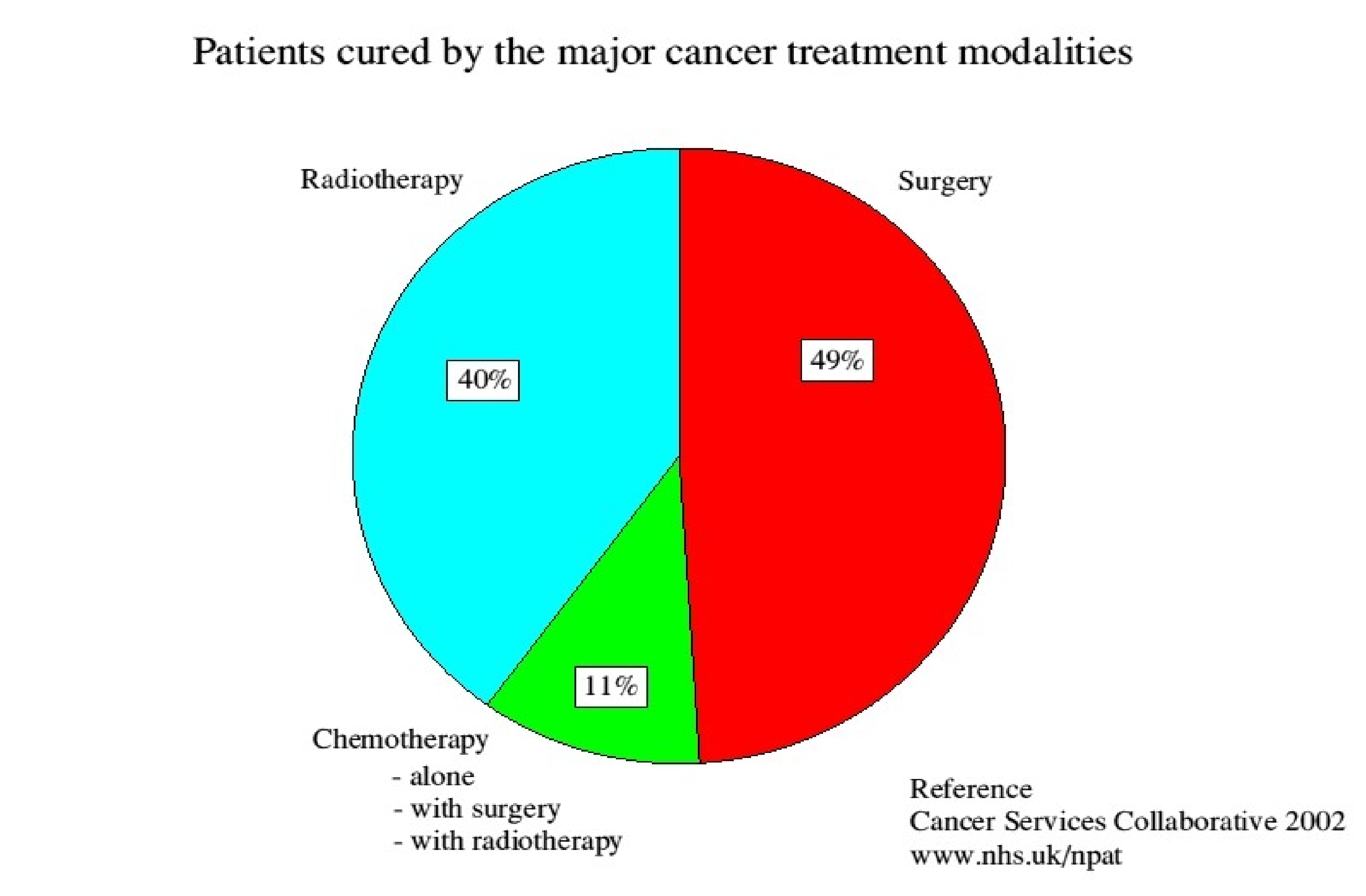
Cancer Cure: Treatment Modality



Radiotherapy & Patient Outcomes

- Increase in XRT use
  - 32% (1992) to 47% (2003)
  - Curative intent ≈ 54%
  - XRT alone ≈ 20%

- Cost of XRT ≈ 6% of all cancer costs

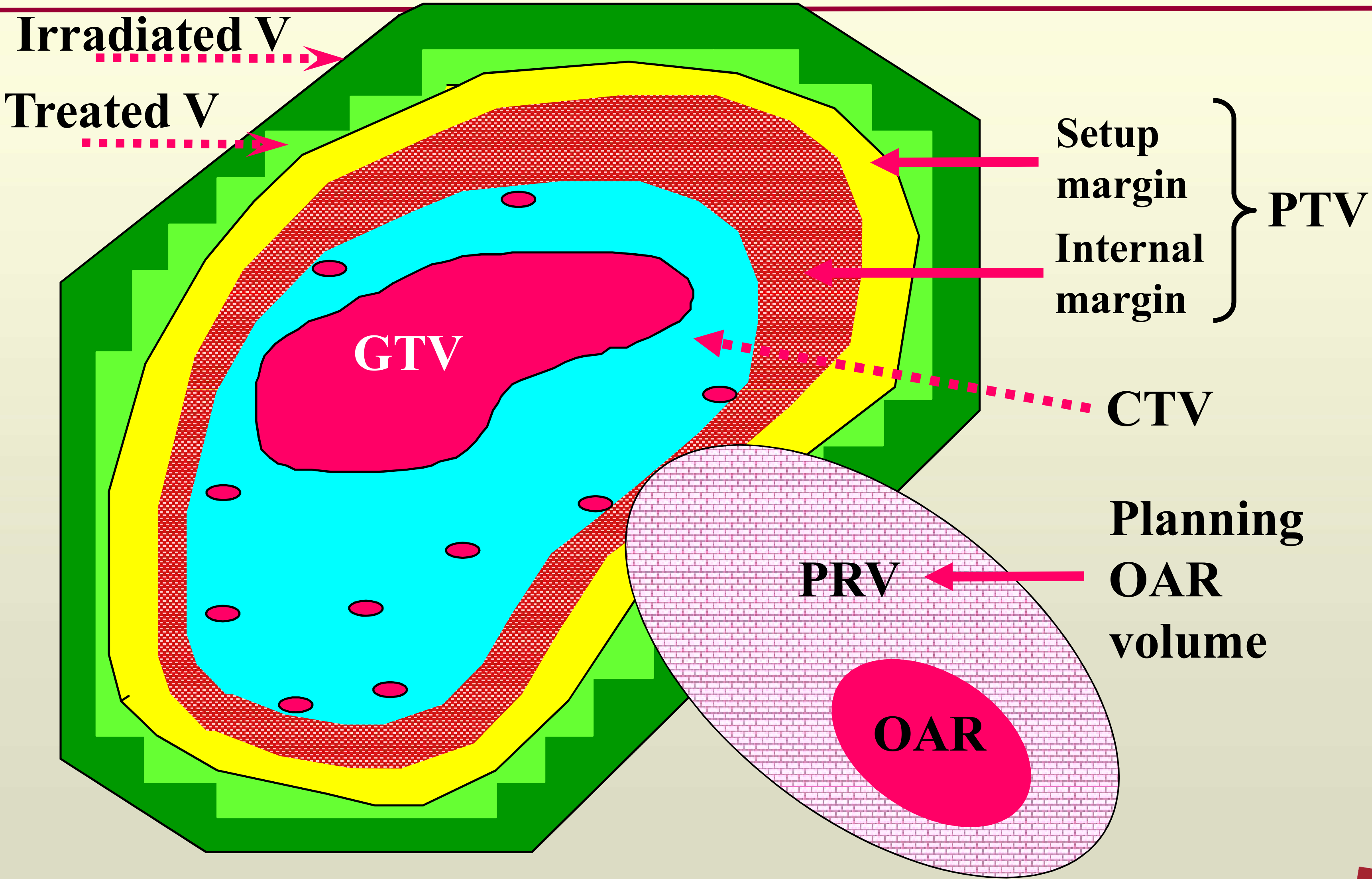
SBU II: Swedish Council on Technology Assessment in Health Care 2003

Definition of IGRT

- IGRT aims at reducing geometrical uncertainty by evaluating the patient geometry at treatment and either altering the patient position or adapting the treatment plan with respect to anatomical changes that occur during the radiotherapy treatment course.

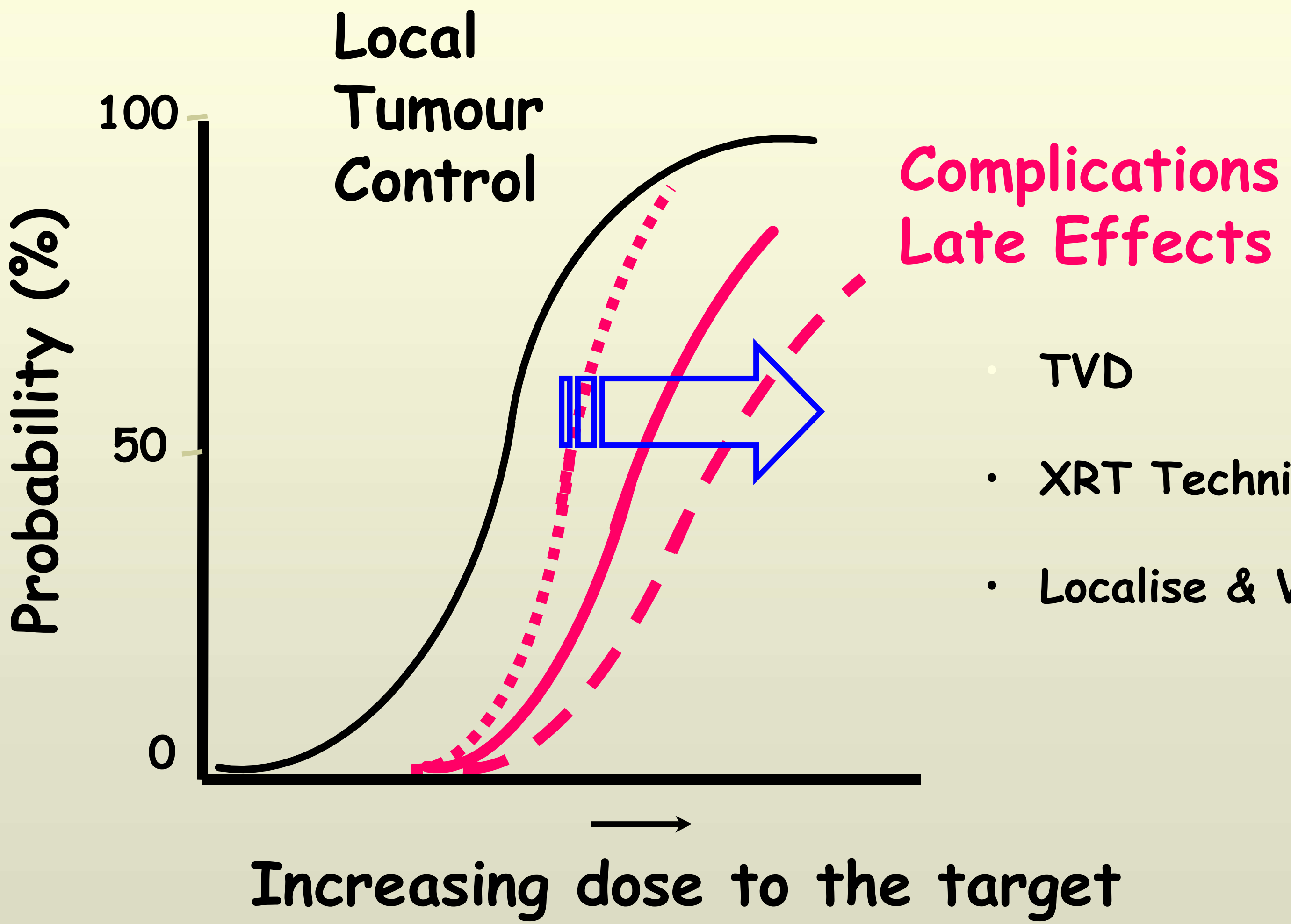
- Estro EIR report: Korreman et al 2010

ICRU 62 Planning Volumes



Khoo. Chap 53. Treatment of Cancer, Ed 5: Price, Sikora, Illidge 2008

Increase the Therapeutic Ratio



- TVD
- XRT Techniques
- Localise & Verify

Smaller margins matter

D. Verellen

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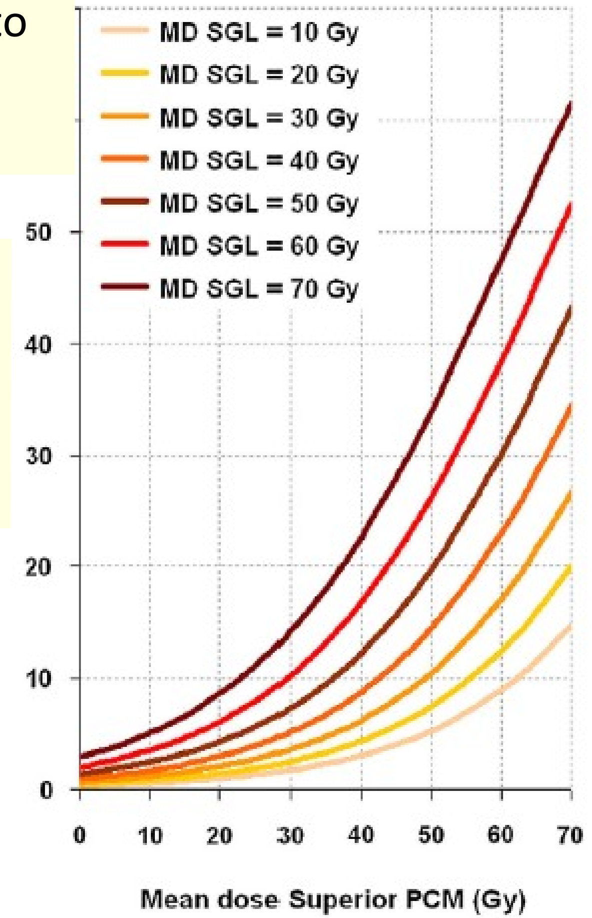
Size matters: NTCP modeling

- Christianen et al
- Prospective analysis, 354 patients
- RTOG/EORTC and QoL HN35 questionnaire
- 6 months
- Head and Neck Cancer

Complication rate depends on dose to the whole functional chain

Mean dose to supraglottic larynx →

NTCP ->



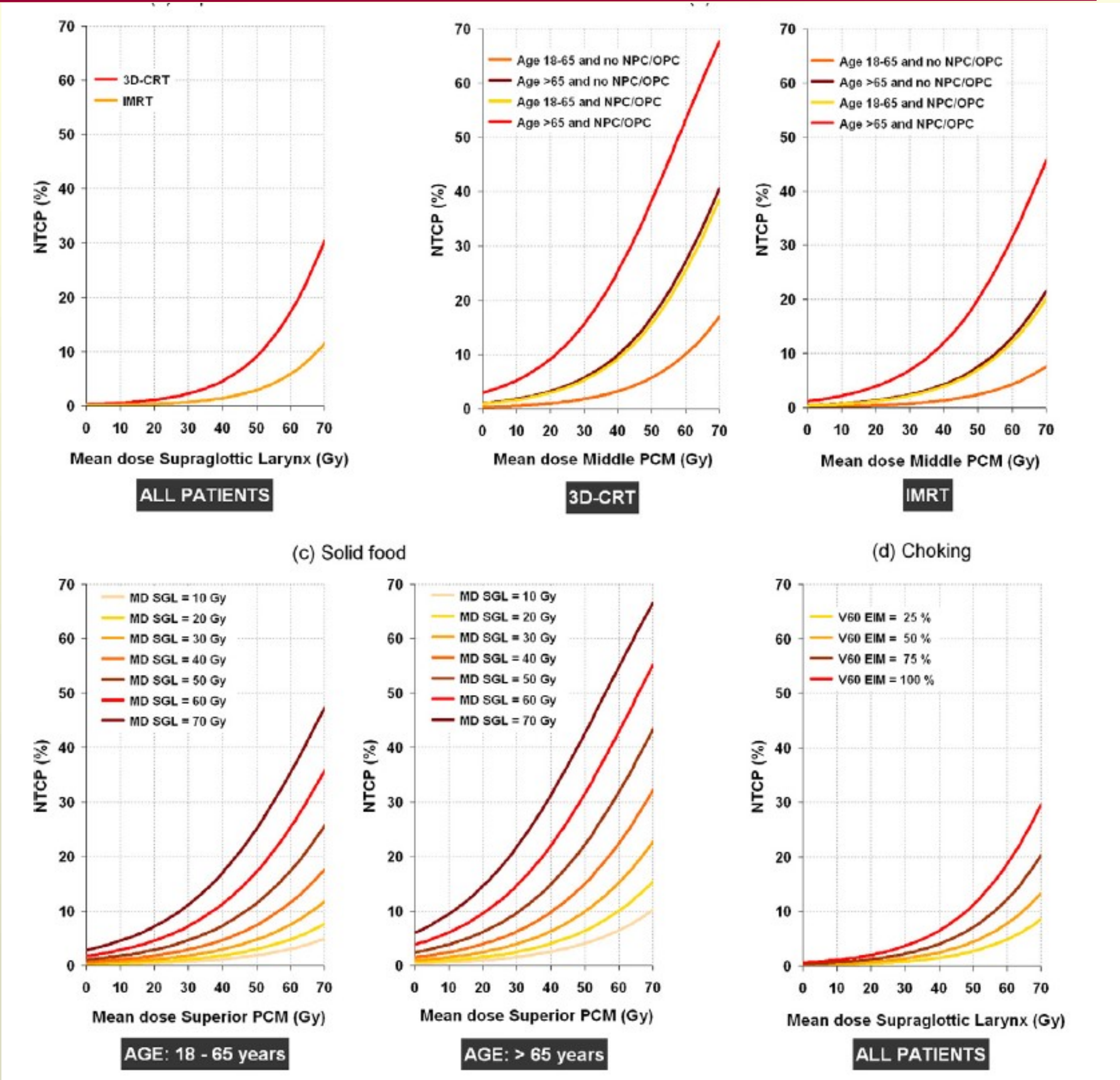
Christianen et al 2012

Mean dose to Pharyngeal Constrictor Muscle →

$$\mathrm{NCTP} = (1 + e^{-S})^{-1}, \text{in which}$$

$S = -6.09 + (\text{mean dose PCM superior} \times 0.057) + (\text{mean dose supra-glottic larynx} \times 0.037)$.

NPC is Nasopharynx
OPC is Oropharynx



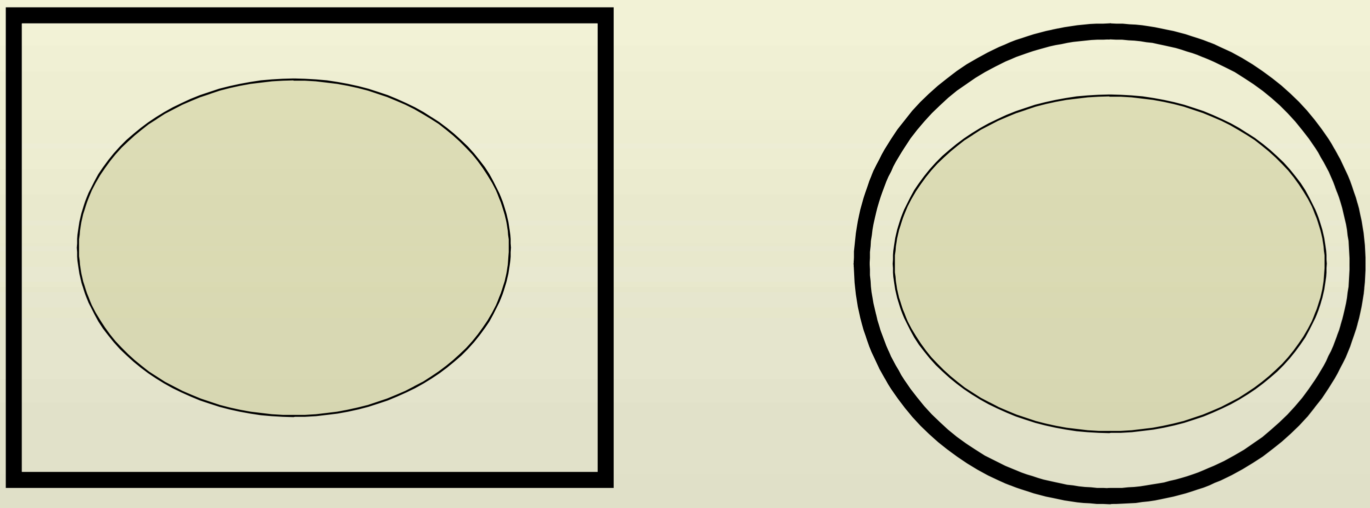
Christianen et al 2012

- So, There is clinical evidence, in this case packed in a model, that less irradiated volume means less damage.

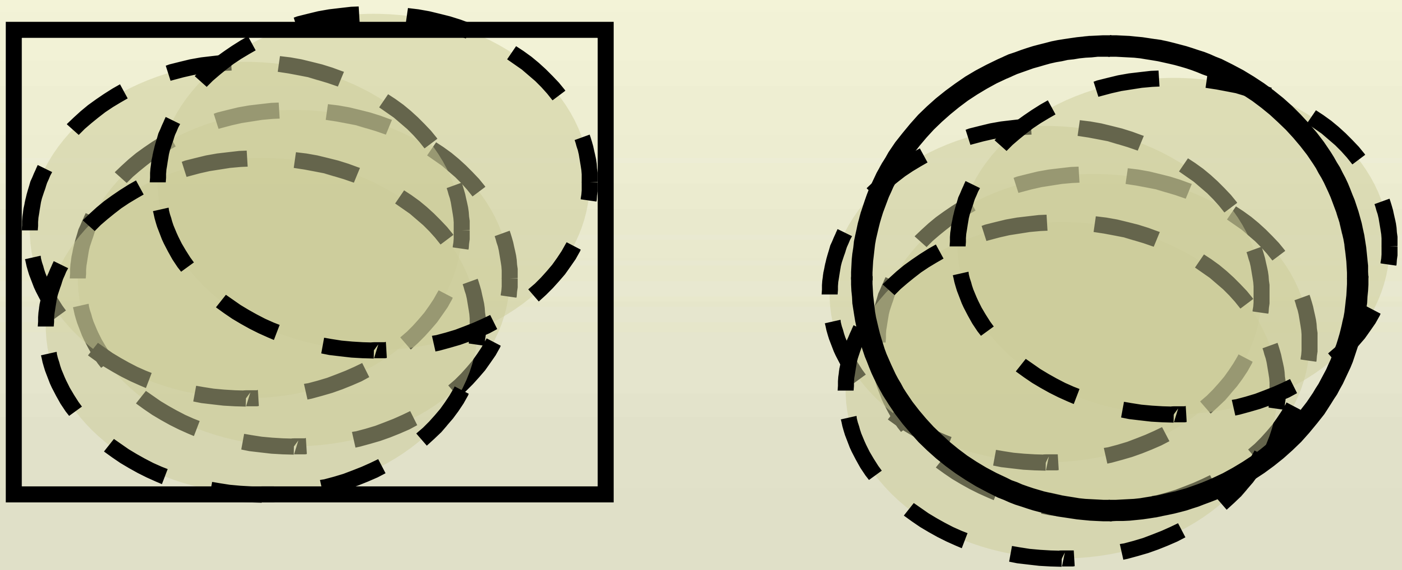
Less irradiated volume means effectively a closer dose distribution

- Tighter dose distribution requires more knowledge on where the target is

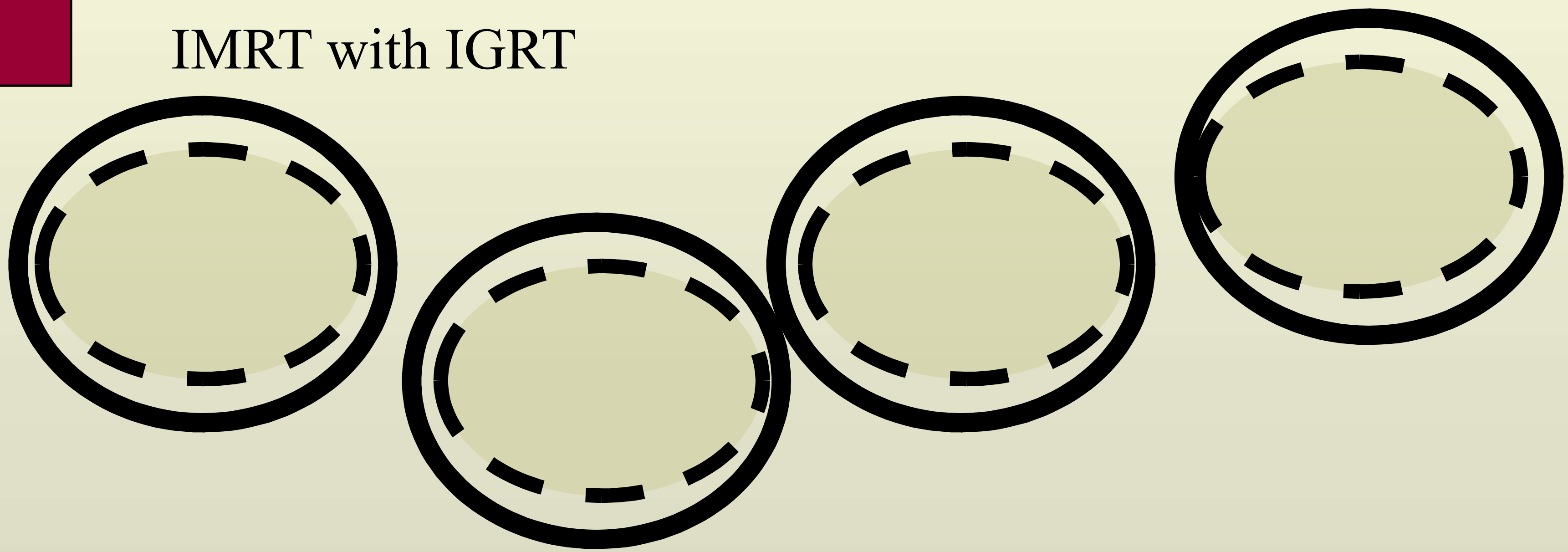
Box technique IMRT



Box technique IMRT



IMRT with IGRT



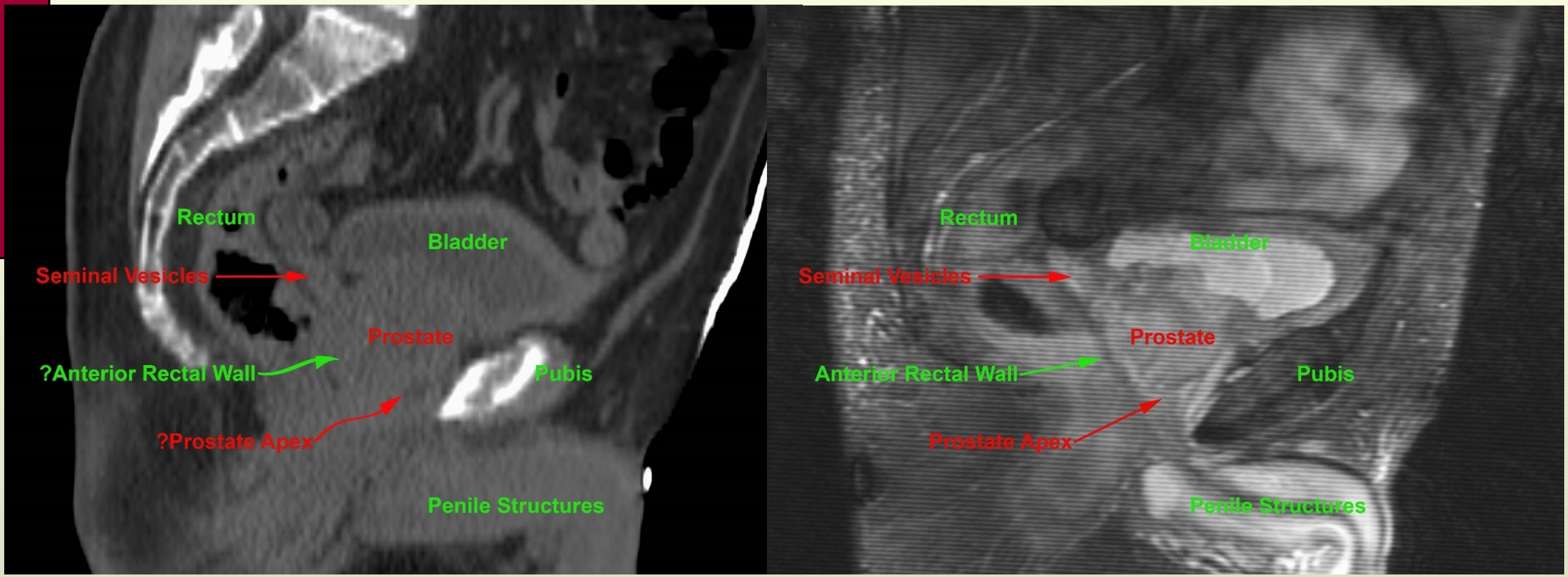
Radiotherapy

Defining GTV/CTV

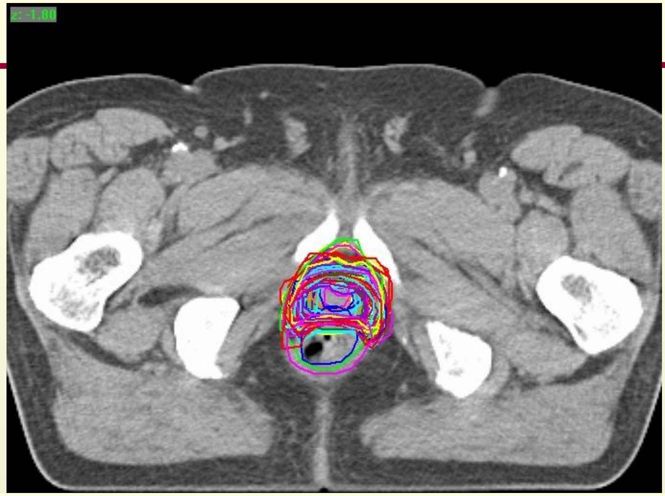
- A weak link getting more important also because of tighter dose distribution

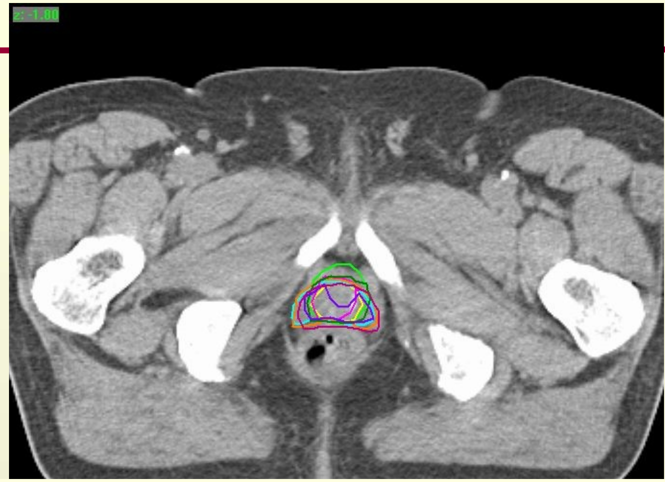
Prostate Cancer XRT: Imaging

Issues in Target Volume Determination

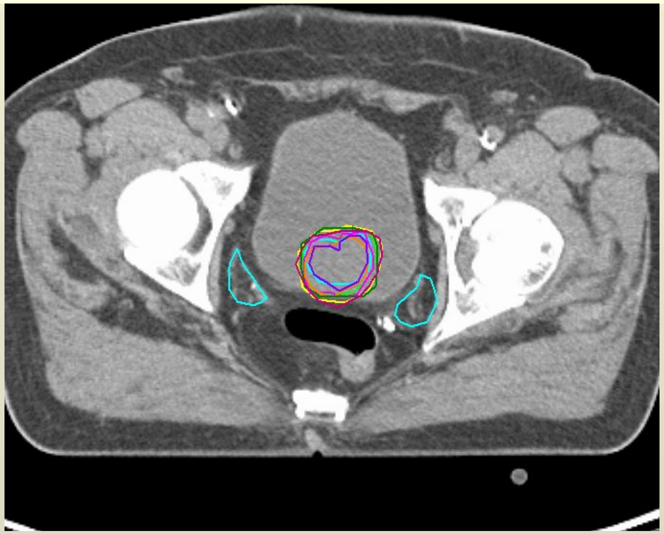


The Greatest Uncertainty: TVD





63y, PC, iPSA=15 ng/ml, Gleason 3+4, T2cN0M0



Students (N≈196): ESTRO TVD Course 2007: Turkey

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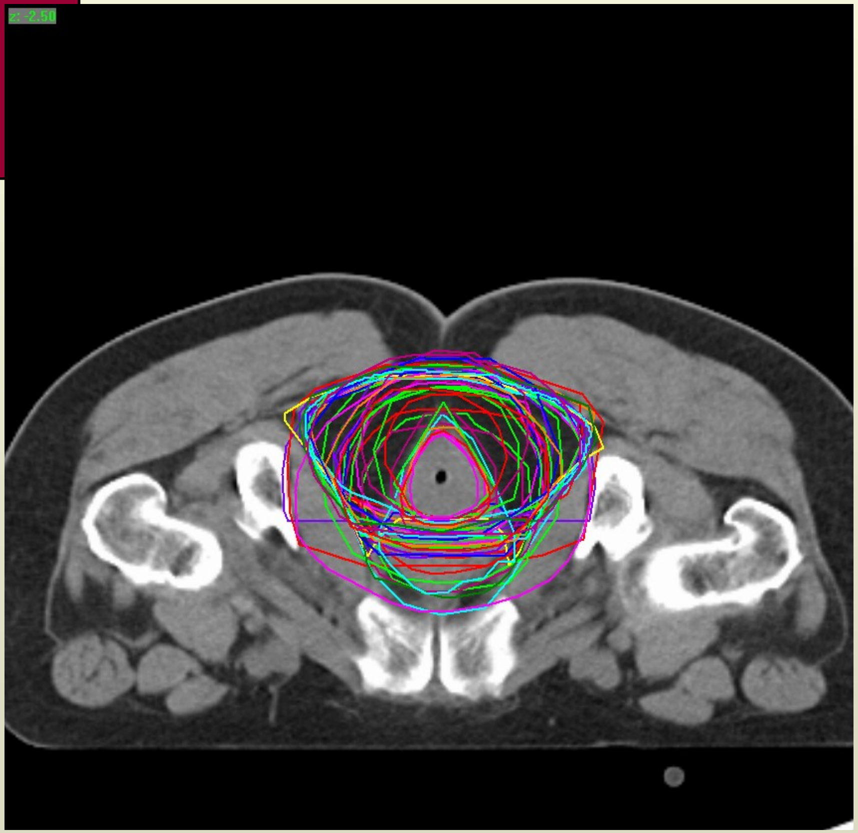
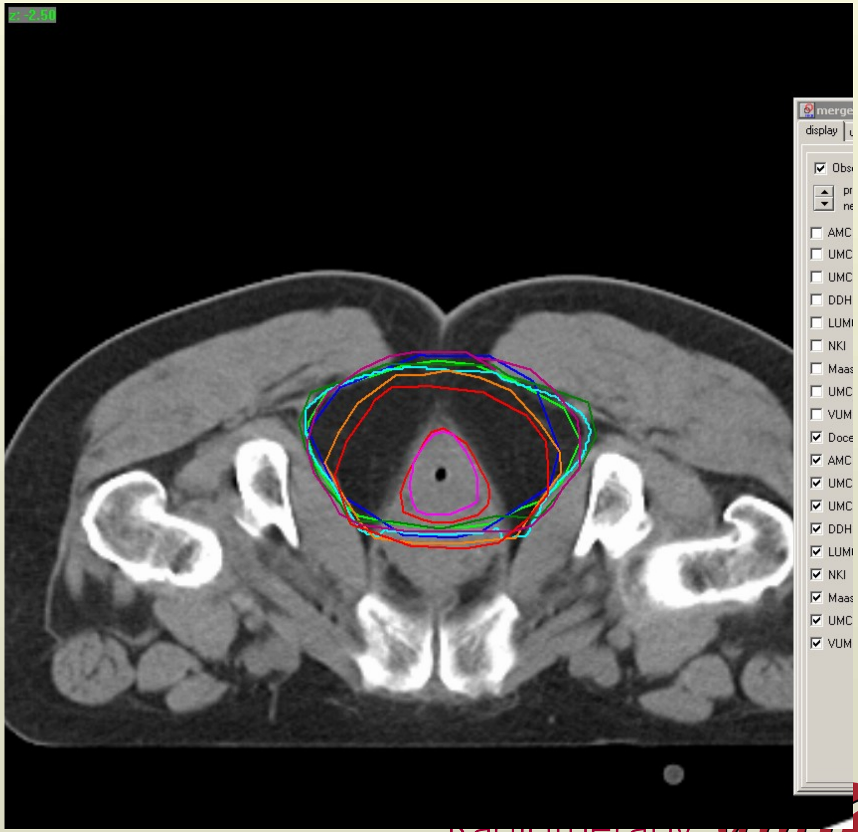
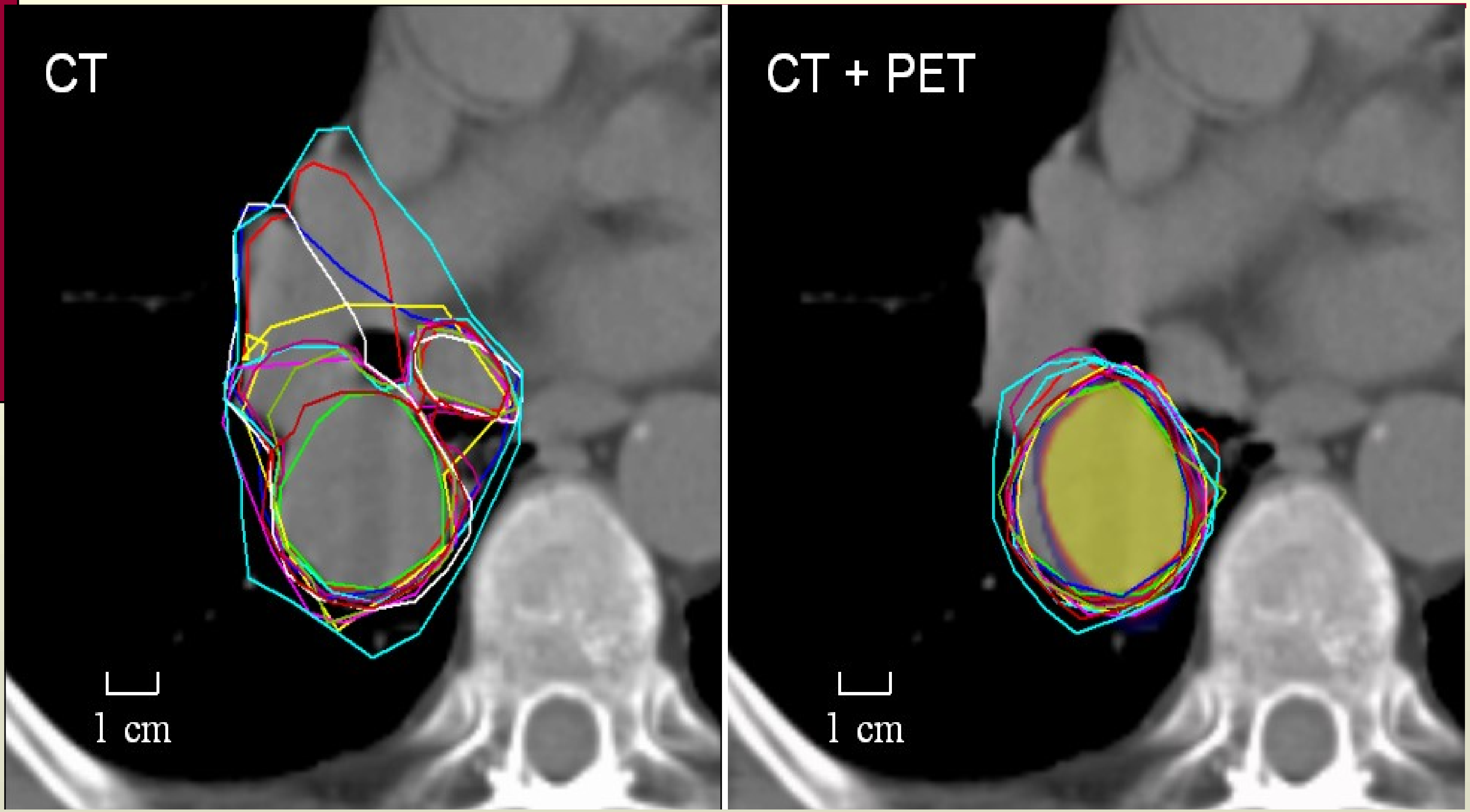
Rectum Target delineation





Radiotherapy

Lung target delineation



Average SD: 10 mm

Average SD: 4 mm

Steenbakkers et al 2005

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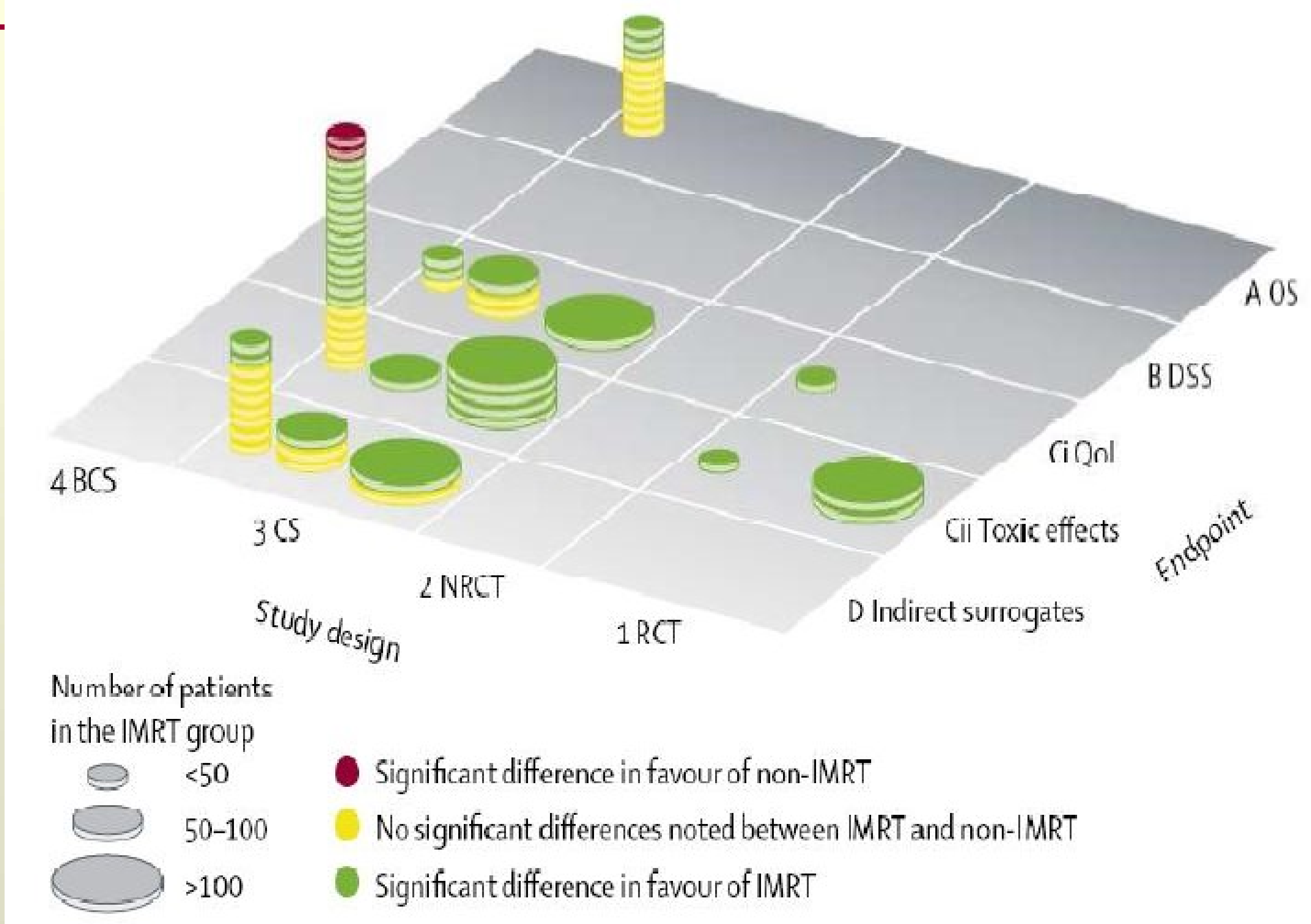
Clinical benefit

- What is the evidence of IMRT over conformal?

Is there Clinical Benefit of IMRT > CFRT?



C/most benefit in toxic effects or surrogates

Veldeman et al LO 2008

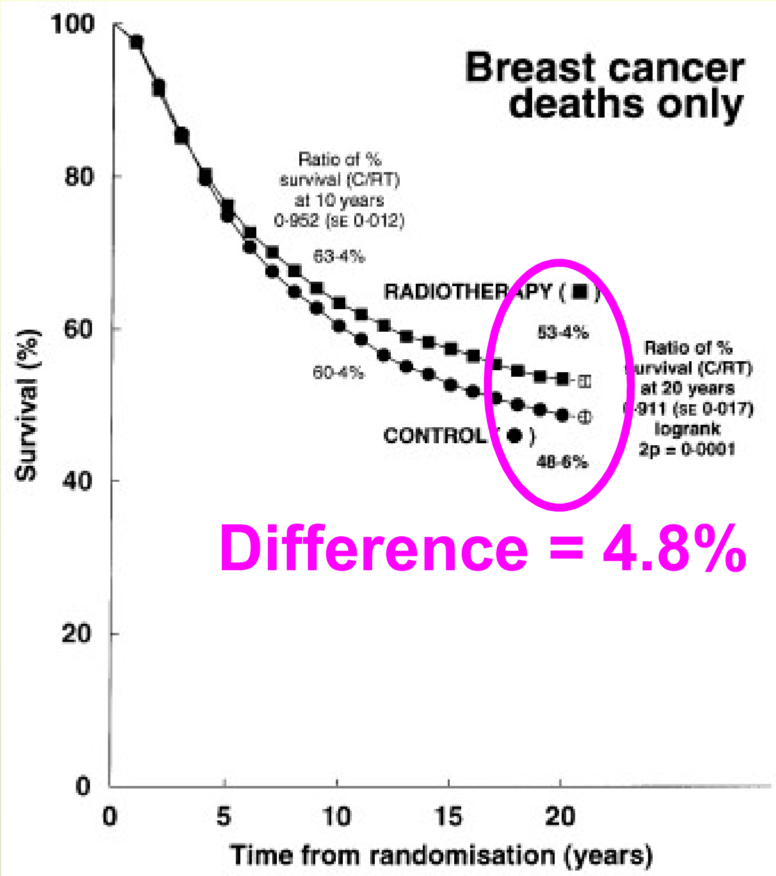
Breast Cancer

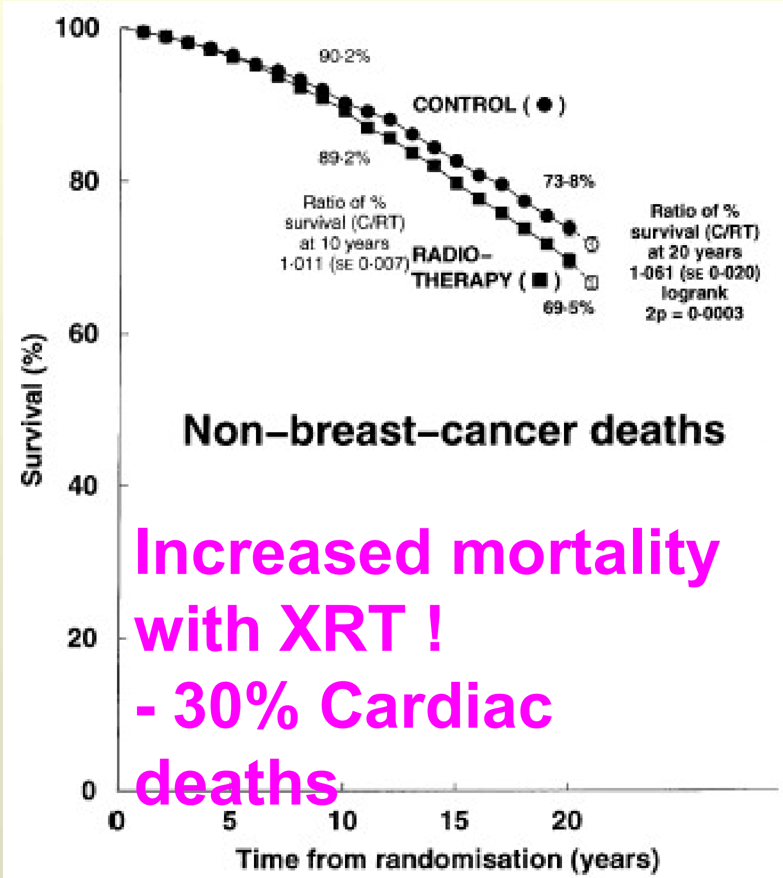
- Chest wall radiotherapy induces cure but at the cost of more heart diseases

Early Breast Cancer: S ± XRT meta-analysis

Total: 40 Prosp. Rand. Trials, N ≈ 20,000 (50% had N+ve disease),

XRT treating breast/chest wall, SCF, AX, IM regions





EBCT Collaborative Group. Lancet 2000

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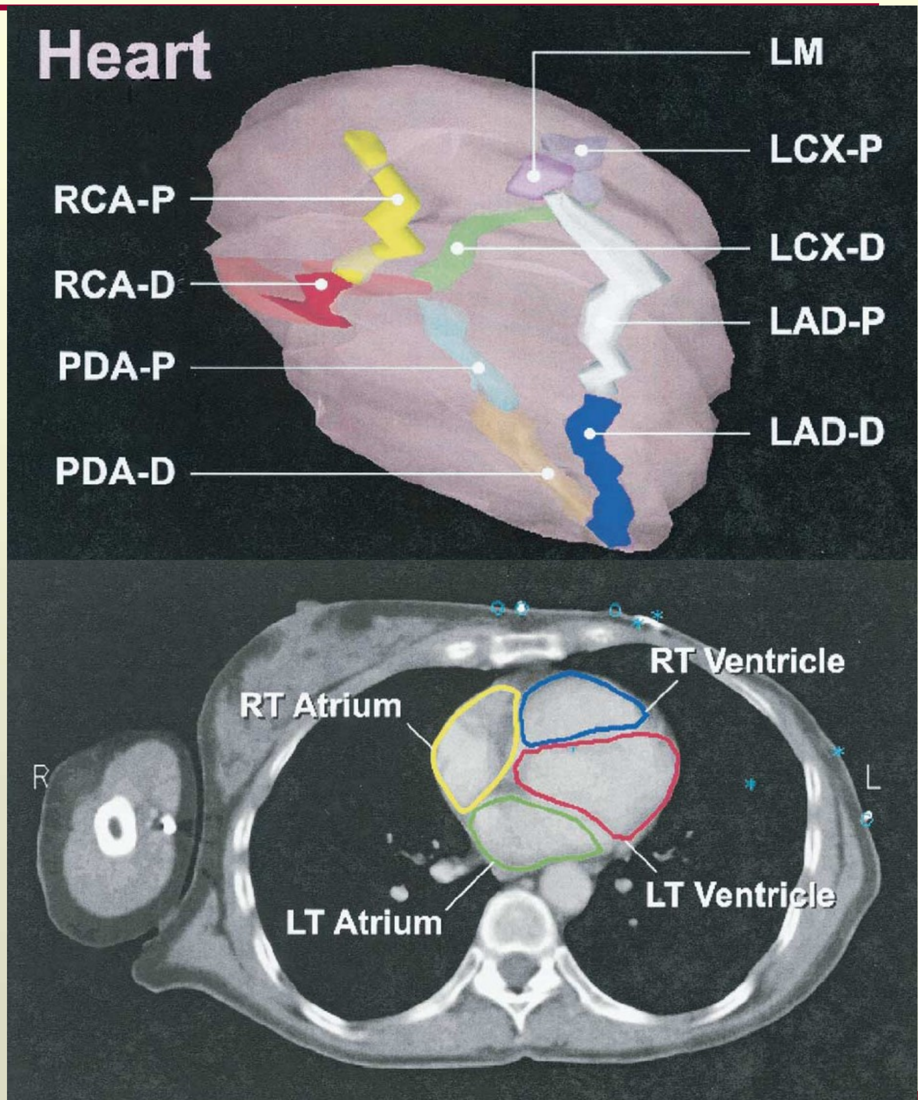
Breast XRT: Reducing Cardiac Dose

Methods:

1. Elevated Arm Position
2. Cardiac Shielding
3. CFRT / IMRT
4. Breath hold
    1. Deep Inspiration
5. ABC
    1. Gated /Gating
6. Real-time Tracking

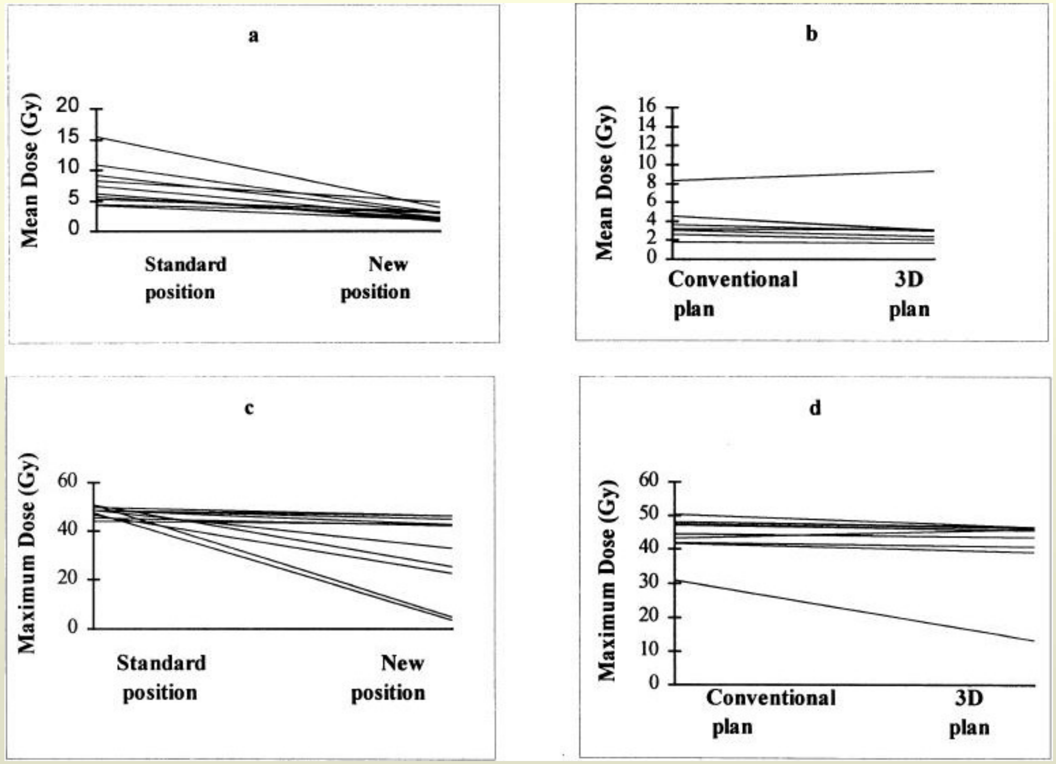


Krueger IJROBP 2004

Breast XRT: Reducing Cardiac Dose with Elevated arm position versus @90 degrees

Methods

- Elevated Arm
  - Arm above head vs arm at 90º
  - Mean cardiac dose reduced by 60%



Canney et al BJR 1999

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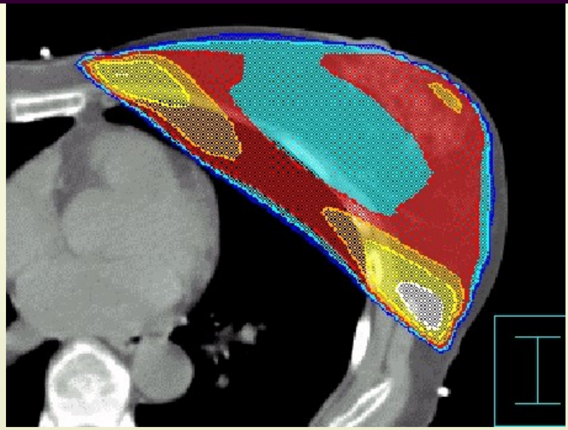
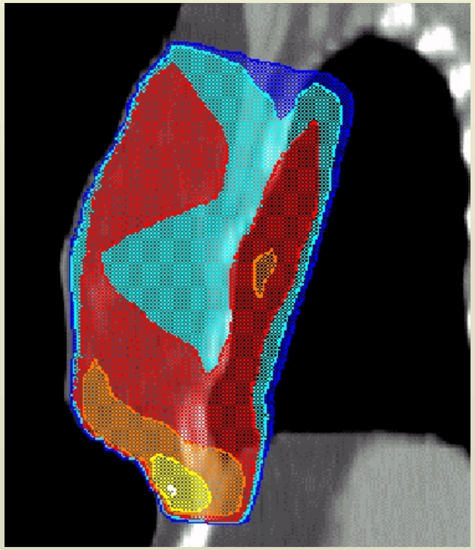
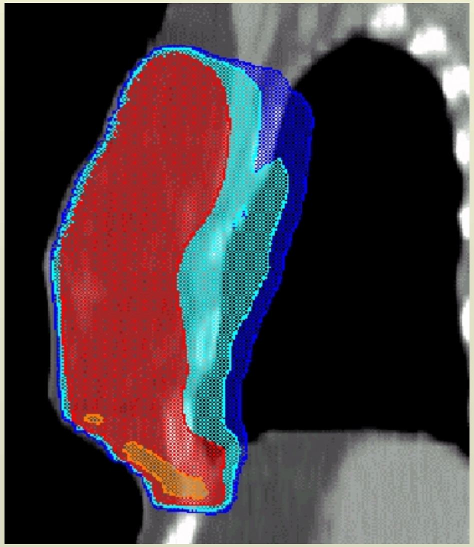
Breast: Reducing cardiac dose
Standard RT vs IMRT

Wedges (Lung Correction)





IMRT



Courtesy: A Martinez

115%, 110%, 105%, 100%, 95%, 90%

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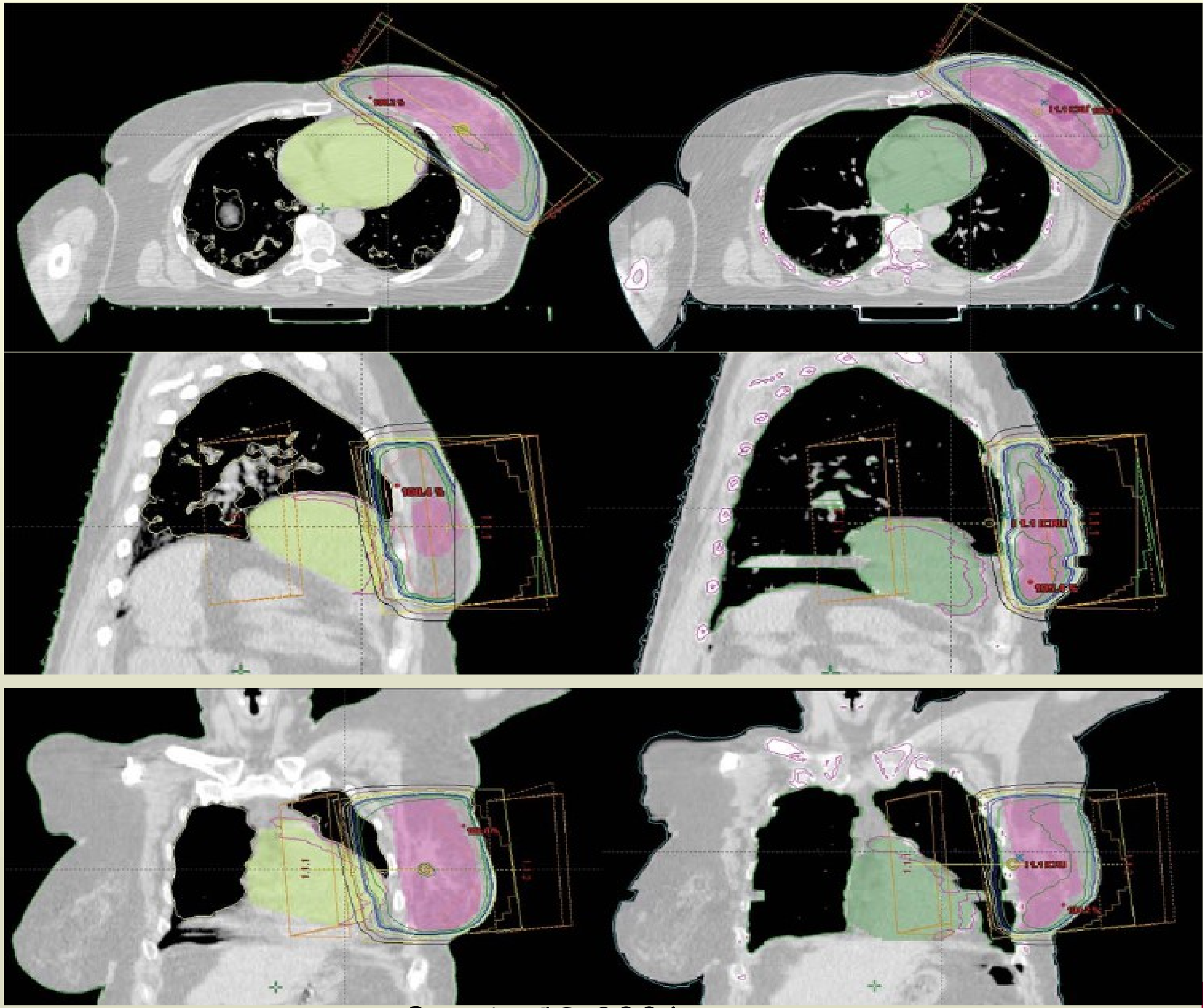
Breast Reducing cardiac dose: normal breathing versus Breathhold



Beavis CO 2006

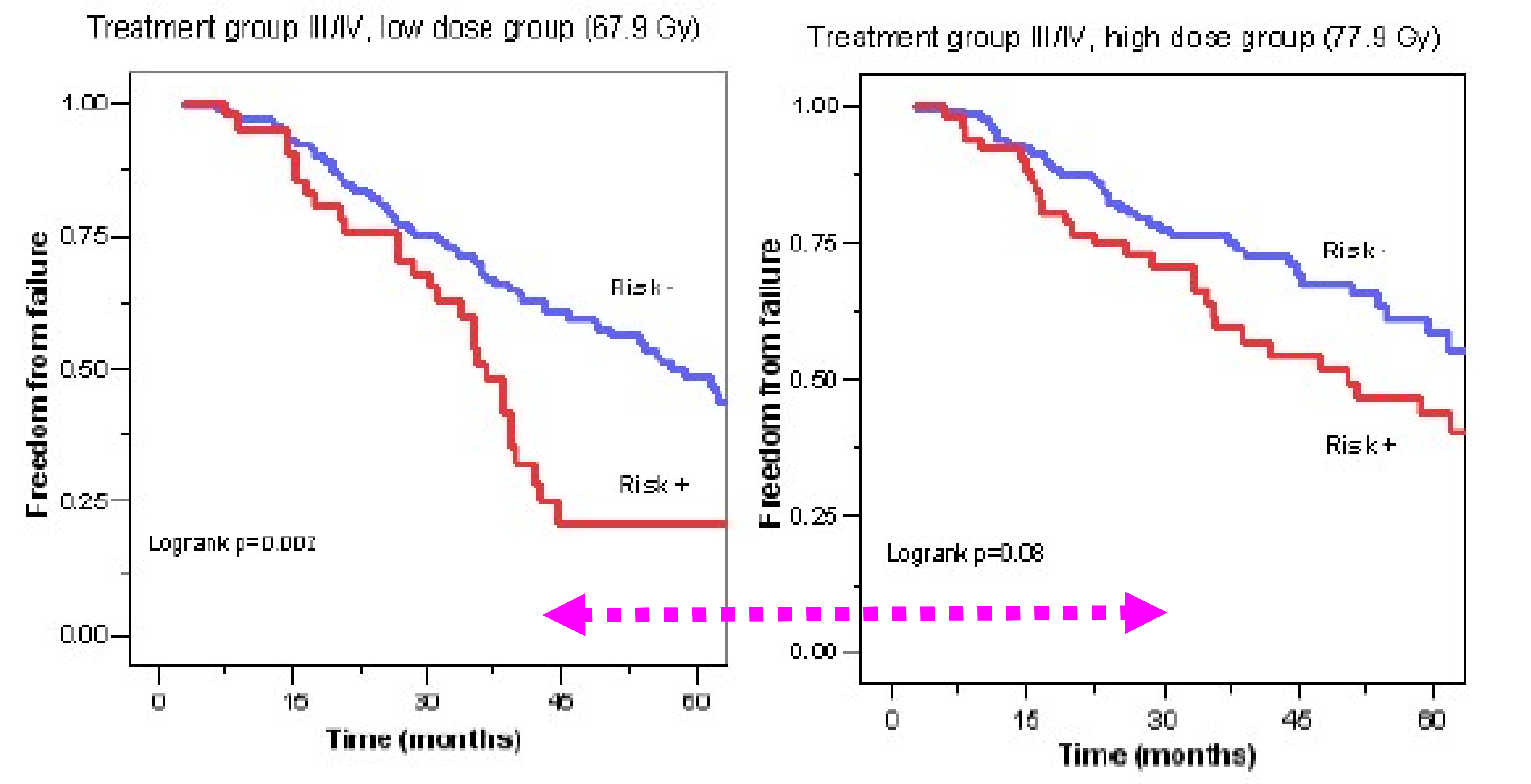
py

Prostate Cancer IMRT without IGRT

- Smaller margins are needed to reduce rectal toxicity and are at the same time dangerous because the posterior edge of the prostate is close to the rectum.
  - Initial full rectum gives rise to more recurrences

PC: Impact of Organ Displacement

(CKTO 96-10: N = 660 patients)



Risk+: initial full rectum, later diarrhoea

Heemsbergen et al, IJROBP 2006

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Prostate Cancer IMRT <u>with</u> IGRT

- Smaller margins are needed to reduce rectal toxicity and are at the same time dangerous because the posterior edge of the prostate is close to the rectum.
  - More recurrences with zero margin and markers:

More biochemical prostate recurrences with zero margins and fiducials

- Engels, 2008
  - Prostate cancer
  - 213 patients with daily bony setup, 25 patients with daily marker setup.
  - Risk factors for recurrence:
    - Distended rectum at start
    - Daily marker setup

Thoughts

- If IGRT is not level I proven better than IMRT (if that can be considered Level I) shoud we be using it?

Thoughts

- If IGRT is not level I proven better than IMRT should we be using it?
  - Quality assurance?

Thoughts

- If IGRT is not level I proven better than IMRT shoud we be using it?
  - Quality assurance?
  - If you can have better vision with glasses do you need to prove that you are a better driver in order to be allowed to use them?

Thoughts

- If IGRT is not level I proven better than IMRT shoud we be using it?
  - Quality assurance?
  - If you can have better vision with glasses do you need to prove that you are a better driver?

  - Nevertheless: **reducing margins** will need clinical proof, Similar when from conformal to IMRT (Eisbruch, Heemsbergen) we will enter an era where marginal misses due to better technology comes on our doorstep. This is bad for the individual patient but can be good for the group provided you close the feedback loop.

Thank You

Head and Neck

Radiotherapy

Is IMRT safe ?

- 133 patients
- Stage I (1), II (6), III (26), IV (95)
- Contralateral neck negative but at high risk
- Bilateral irradiation 50 + 20-30 Gy
- FU 32 months

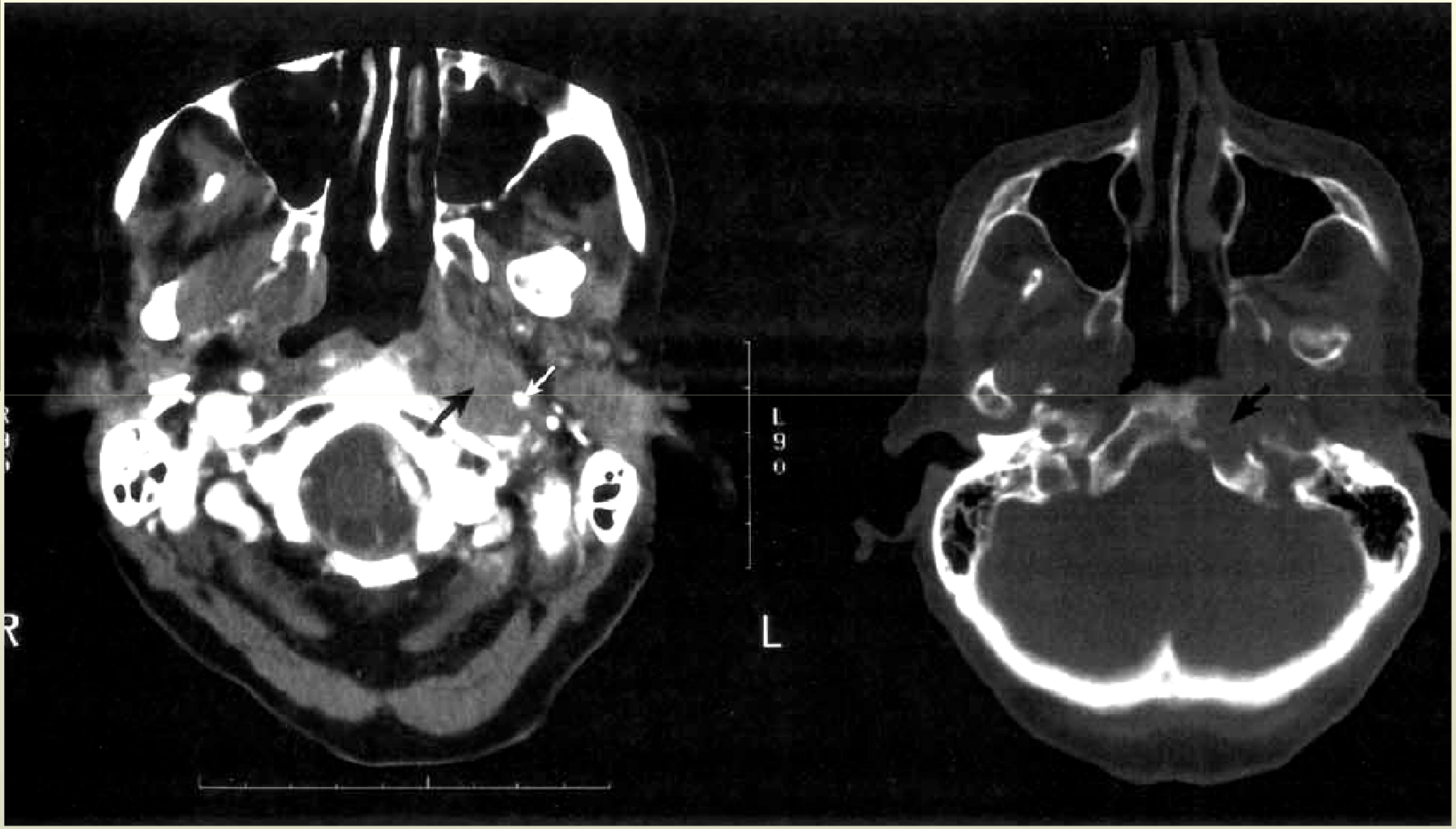
•Eisbruch et al IJROBP 2003

Is IMRT safe ?

- 21 (16 %) loco-regional recurrence
- 17 in field, 4 marginal
- No recurrences contralateral cranial to the SD nodes
- Three (marginal) Retropharyngeal node recurrences therefore target area extended to the level of C1 retropharyngeal
- 82% of cases contralateral dose to the parotid below 26 Gy

•Eisbruch et al IJROBP 2003

Is IMRT safe ?



•Eisbruch et al IJROBP 2003

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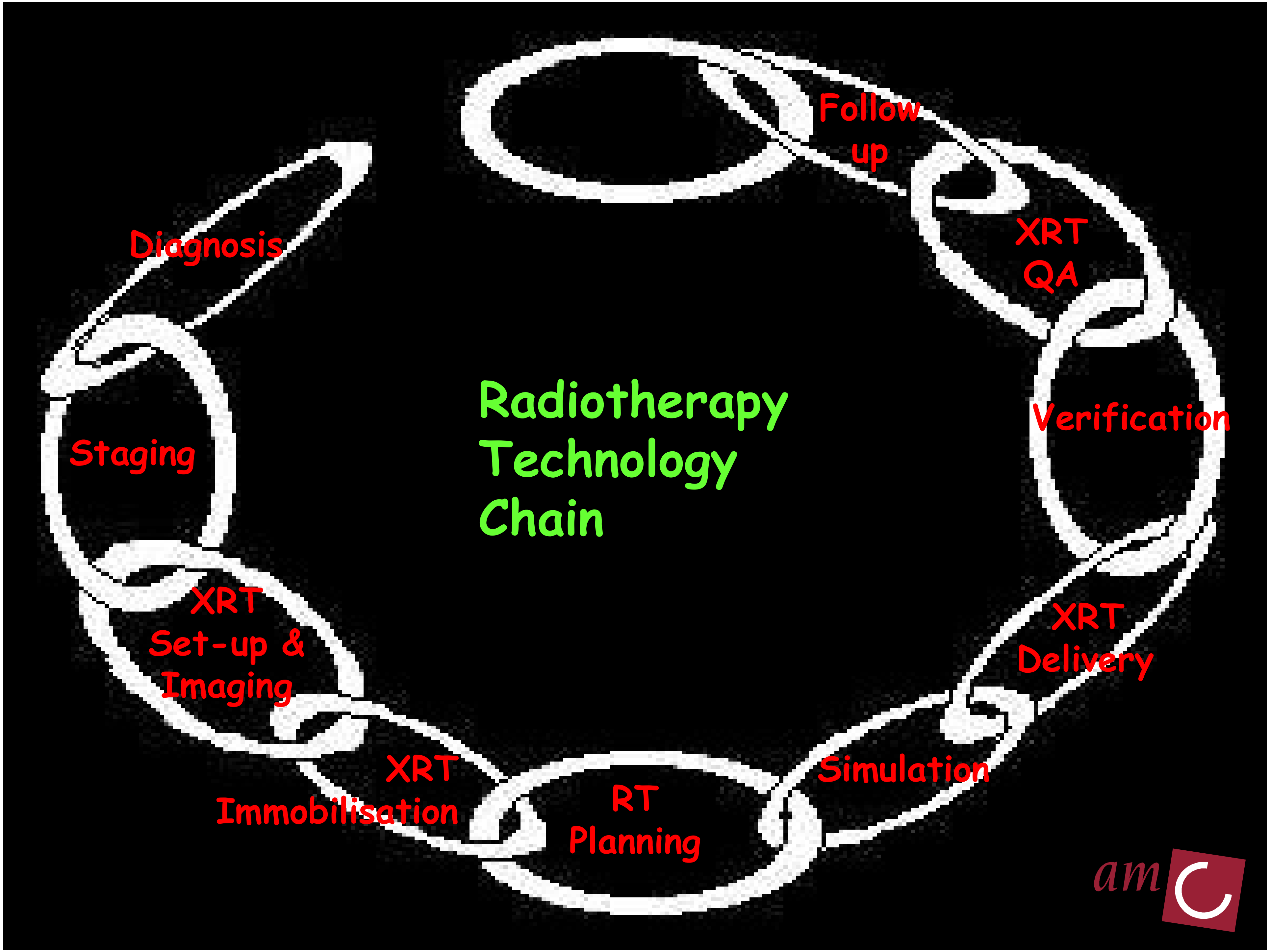
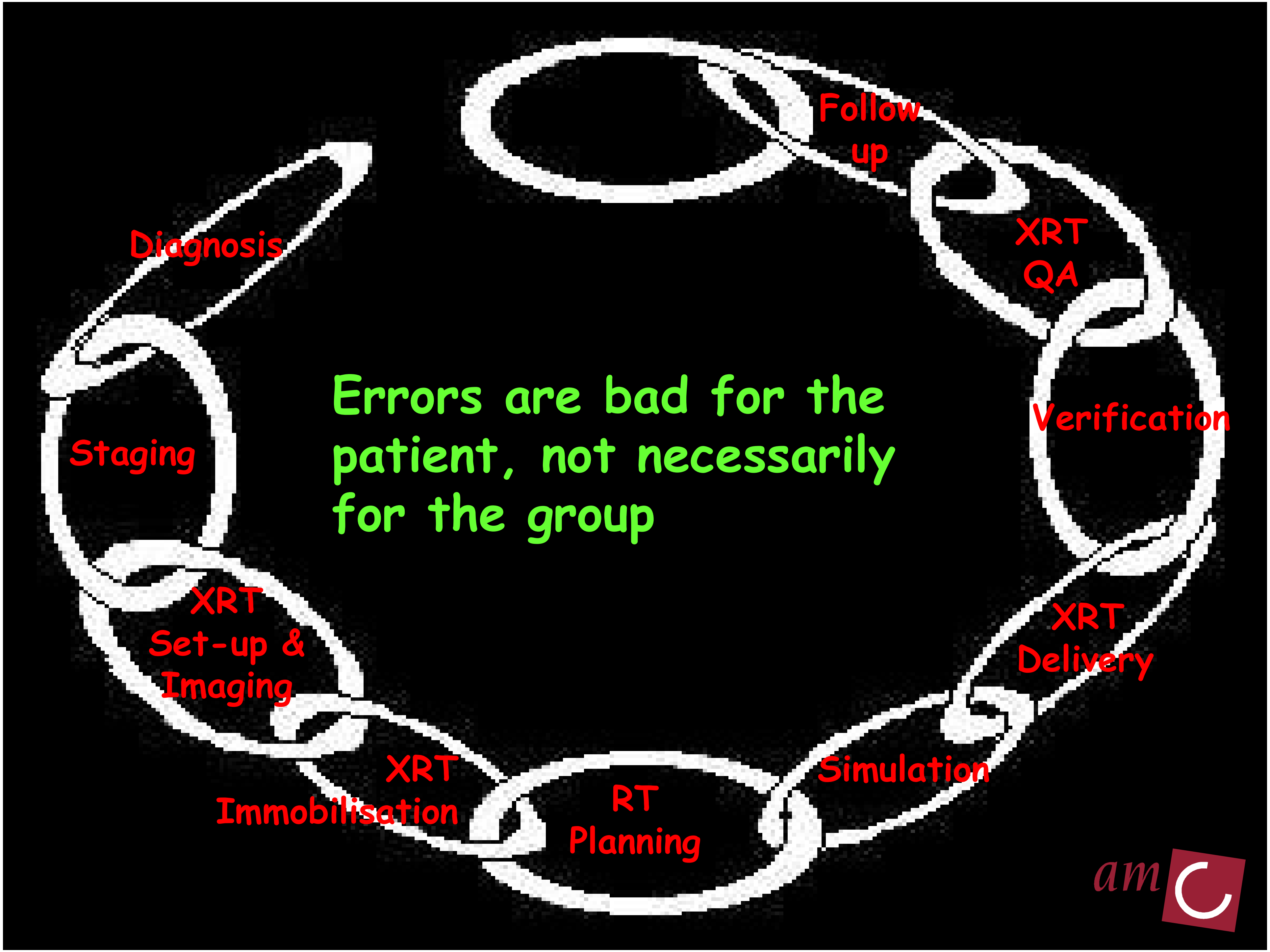
Is IMRT safe ?

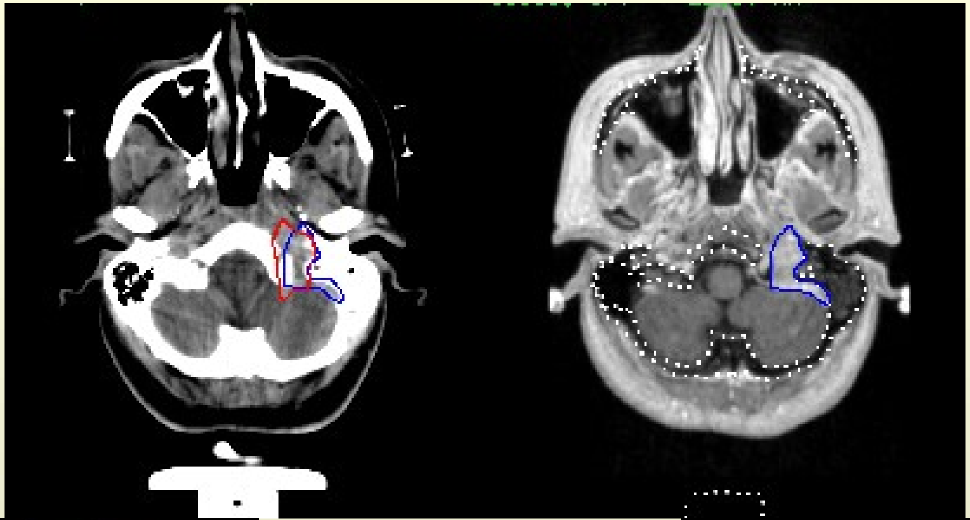
•Eisbruch et al IJROBP 2003


Radiotherapy
Technology
Chain
Diagnosis
Staging
XRT
Set-up &
Imaging
XRT
Immobilisation
RT
Planning
Simulation
XRT
Delivery
Verification
XRT
QA
Follow
up
amc

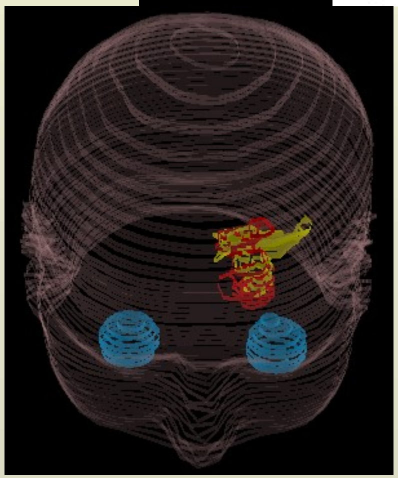

Errors are bad for the patient, not necessarily for the group
Follow up
XRT QA
Verification
XRT Delivery
Simulation
RT Planning
XRT Immobilisation
XRT Set-up & Imaging
Staging
Diagnosis
amc

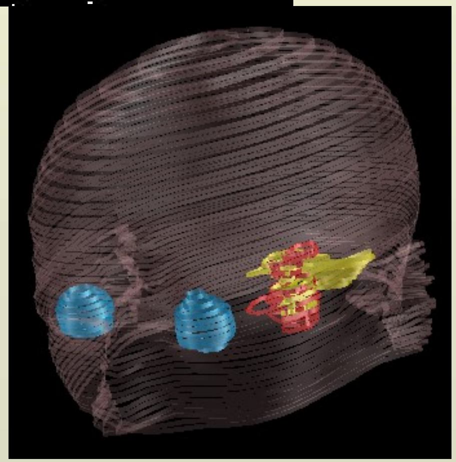
CT vs MRI comparison
Base of Skull Meningiomas

CT-defined CTV (red)



MRI-defined CTV (blue)





Red outlines = CT & Yellow outlines = MRI

Khoo et al IJROBP 2000

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Treatment Uncertainties or Errors

- Therapy Uncertainties or Errors
  - Systematic (Σ)
  - Random (σ)
- For adequate coverage of the CTV
  - approximately $2.5\ \Sigma + 0.7\ \sigma$
  - *van Herk et al IJROBP 2002*
- For adequate OARs margin
  - approximately $1.3\ \Sigma + 0.5\ \sigma$
  - *McKenzie et al RO 2002*

Palliation in one-stop shop

- Single fraction / hypofractionation
- On-line strategy (CBCT) for spinal bone mets
- Time < 30 min (position, image, plan, treat)

- Adv: improved accuracy, convenience & ?outcome and/or QOL

Letourneau et al, IJROBP, 2007

IMRT & IGRT: My Logic

- IMRT
  - Dosimetric advantage
- IGRT
  - Enables us to address temporal spatial uncertainties in treatment delivery
  - 4D reliability and accuracy
  - Smaller margins
- IMRT + IGRT
  - Logical
- Any XRT + IGRT
  - Also logical and worthwhile
  - Need to rationalise potential benefit

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IGRT: General Approach

- Determine what the ‘uncertainty’ is
  - Site and/or patient
- Define the ‘uncertainty’
  - Observe
  - Understand
  - Measure
- Modify the ‘uncertainty’
  - Reduce
  - Avoid or Eliminate
  - Account or Adapt

IGRT: ‘Simple’ Practice

- ‘Gradual’ changes in anatomy & shape
  - Changes over weeks eg weight loss in H&N patients
  - Adapt XRT plans
  - E.g. Adapt treatment to shrinking parotid gland/tumor
- ‘Daily’ changes eg organ filling or emptying
  - Eg bladder and rectum causing displacement or deformation, head and neck flexibility
  - Adjust treatment position ± adaptation
  - Use surrogates of target position or direct organ/target visualisation
- ‘Fast’ changes or rapid moving targets
  - Eg lung XRT with respiration
  - Prevent base line shift (gradual), Track or gate XRT or freeze the ‘motion’

What drives progress?

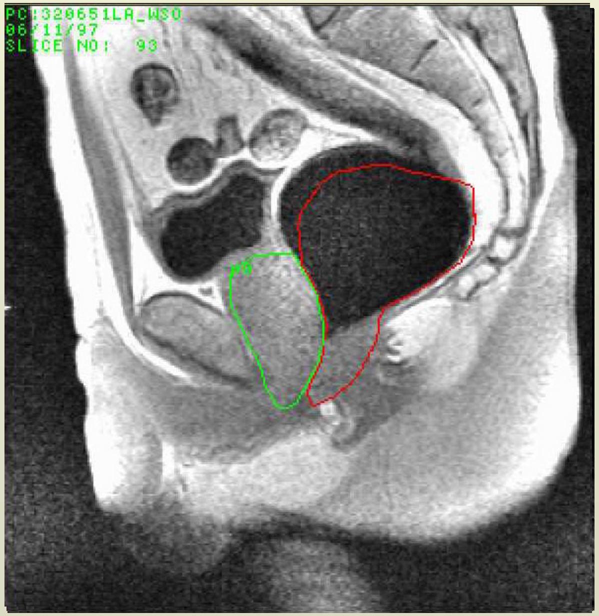
Clinical rationale & gain should 'drive' Technology

And not Technology 'driving' Rationale or Practice

Prostate XRT: 4D Issues

Planning scan

Subsequent scan

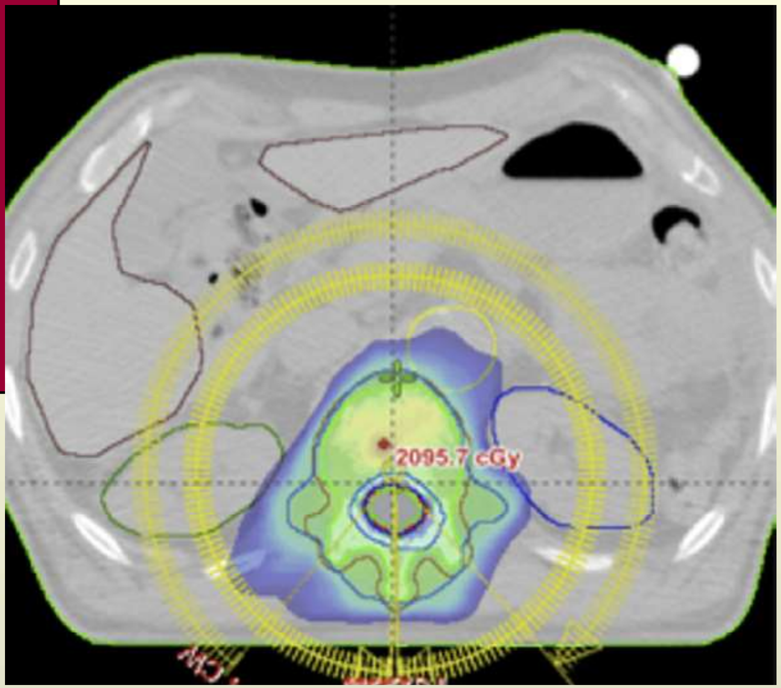


Khoo et al BJC 1998

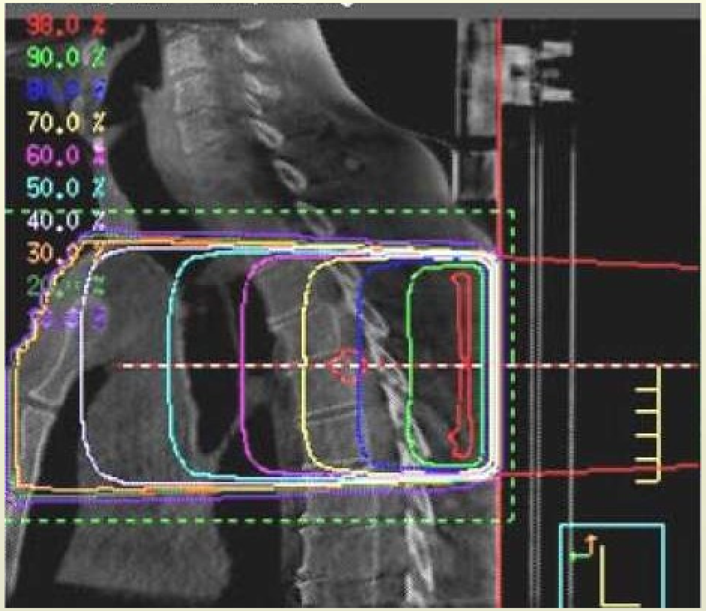
IGRT for palliation

- Over the top or not?

Stereotactic radiation for bone metastases?

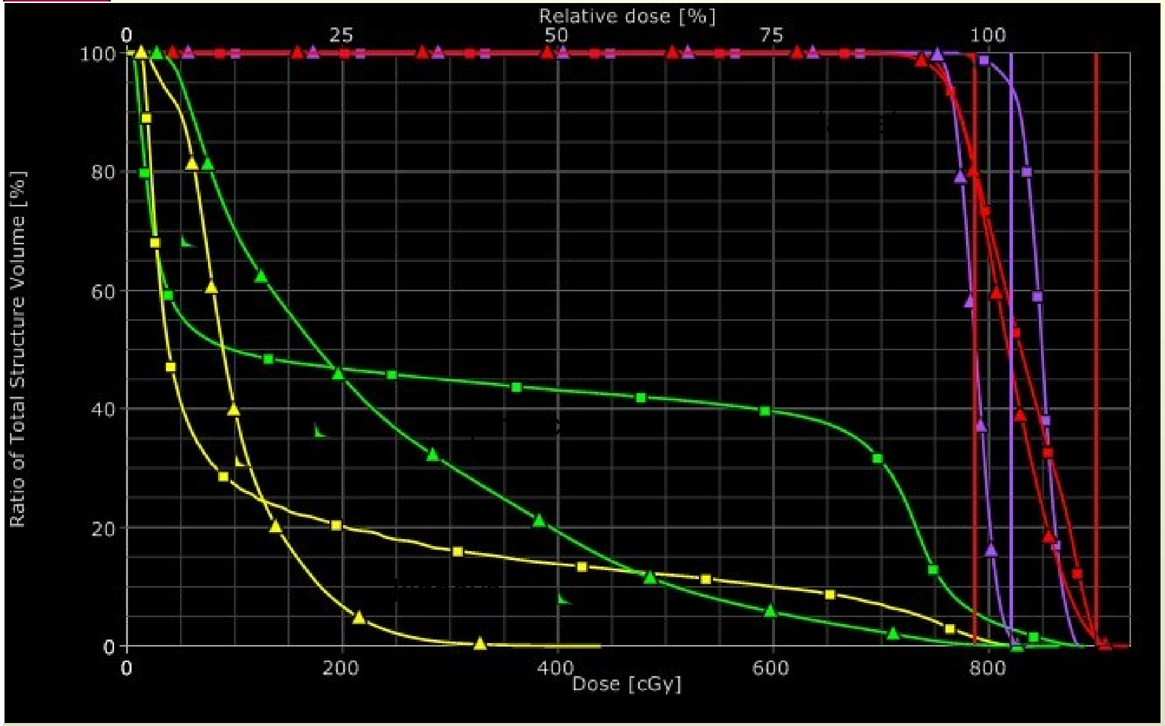


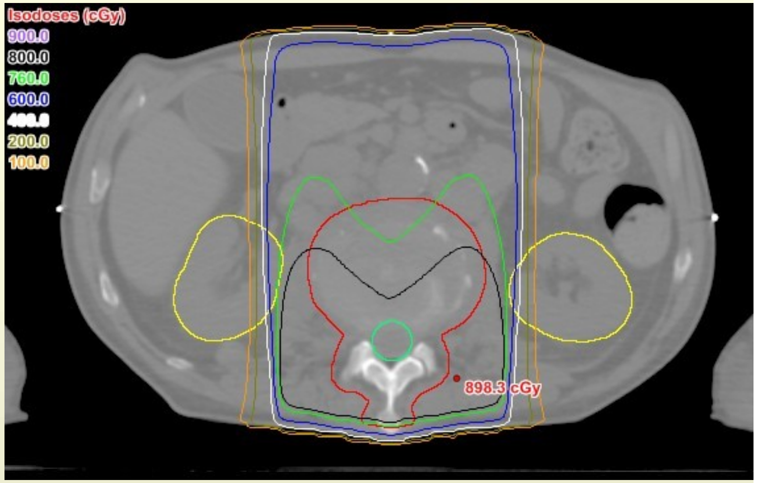
Stereotactic, two ARCs
Dahele 2011

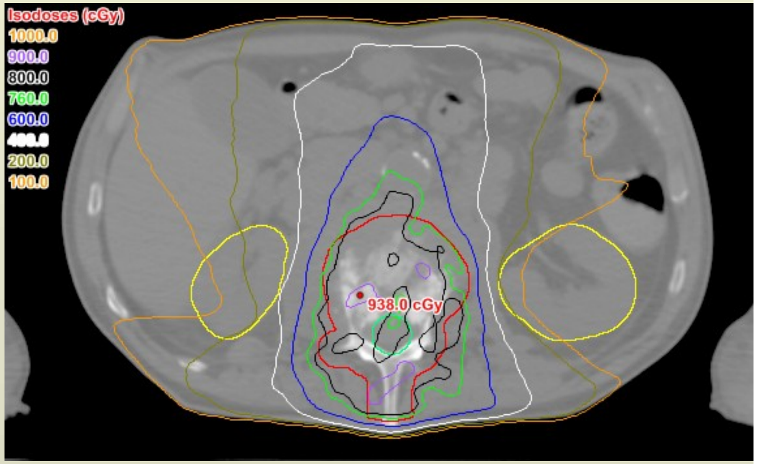


Single PA field
Letourneau 2007

3 Vertebrae, AP-PA versus 1 arc 8 Gy







- Beam-on time:

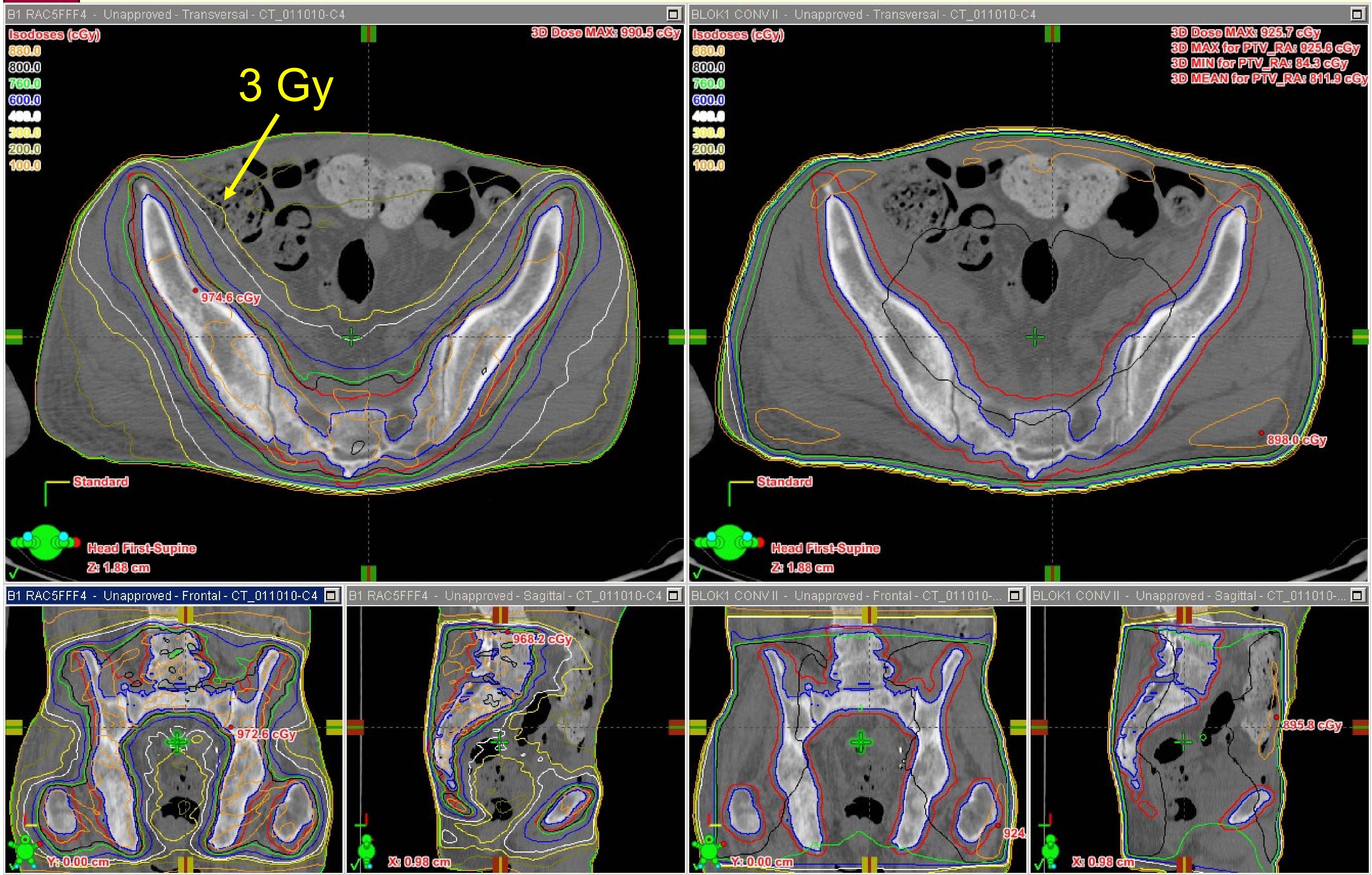
  FFF: 1.24 min, FF: 2.34 min

Courtesy W. Verbakel VuMC

Radiotherapy amc

RArc versus conventional 8Gy

Courtesy W. Verbakel VuMC



ESTRO School

WWW.ESTRO.ORG/SCHOOL

IGRT/ART: a physicist's point of view

Marianne Aznar
Dept of Oncology, Rigshospitalet
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Outline

- A short history of IGRT technology
- Margins
- Adaptive Radiotherapy
- Exposure from imaging: some considerations

A LITTLE TECHNOLOGICAL HISTORY ...

IGRT is not a new (or even “recent”) idea

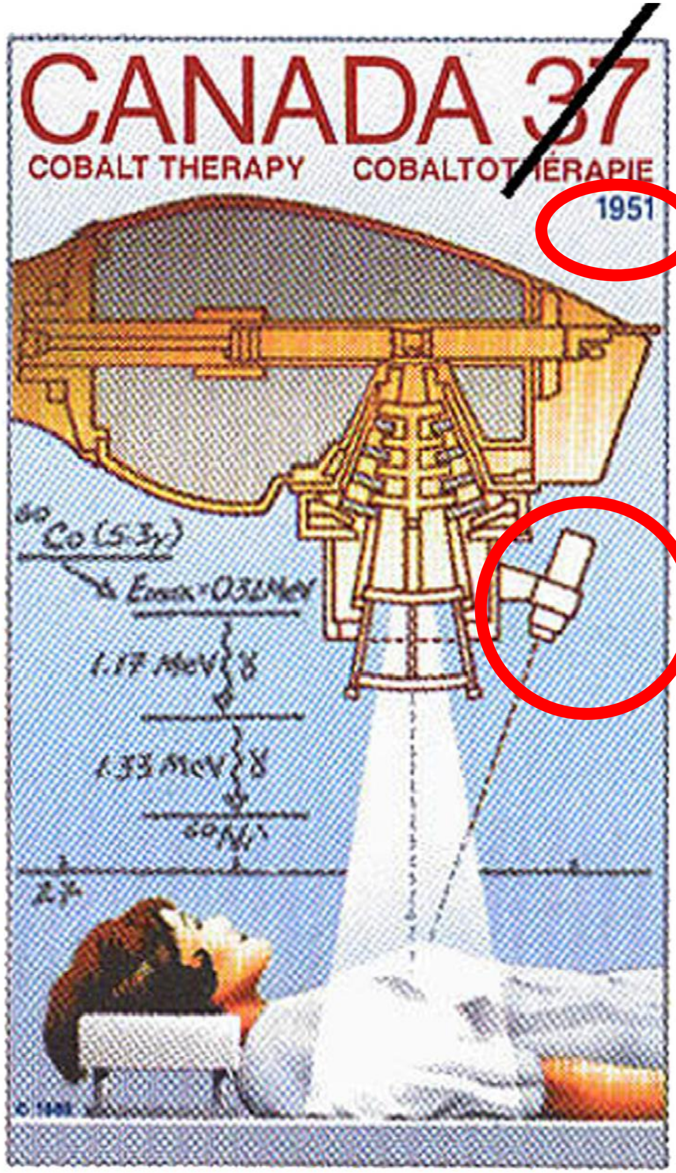

Fig. 1. Cobalt Therapy, 1951, issued 1988, 37 cents, 2003. Note the illustration of a positioning device mounted to the head of the machine that most likely refers to the X-ray systems reported in the literature by Johns, Cunningham and Holloway at that time [31,30]. (© Canada Post Corporation (1988). Reproduced with Permission).

Verellen et al RO 2008

The first “Cobalt Bomb”
London, Ontario

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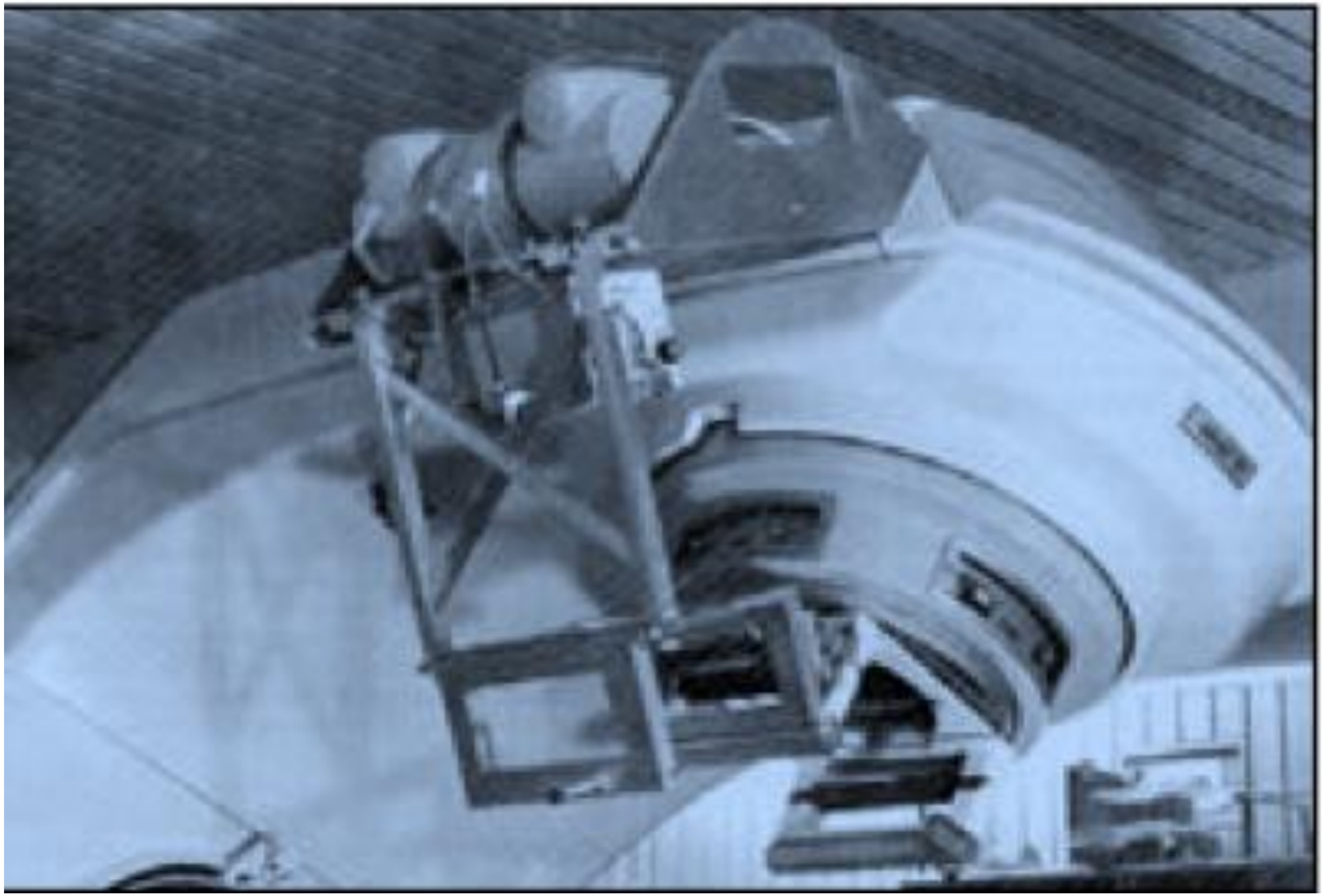
The idea didn't quite catch on for a few decades…



With a few exceptions: here, Biggs et al IJROBP 1985

Why the lack of adoption ?

- Poor image quality (low film sensitivity, size of the Cobalt source)

- “Home made” systems in pioneer academic centers never reached other RT facilities

Conventional RT and simulation

- At the end of previous century, patient set-up and the determination of treatment beams was mainly guided by using a **treatment simulator and drawing skin marks** on the patient's surface, consequently used to position the patient with respect to the treatment machine

- only **35% of the radiotherapy centres were using a simulator** for target localization in the treatment planning process in 1983, and only 47% had access to this equipment in 1986

Chu *et al*, IJROBP 1989.

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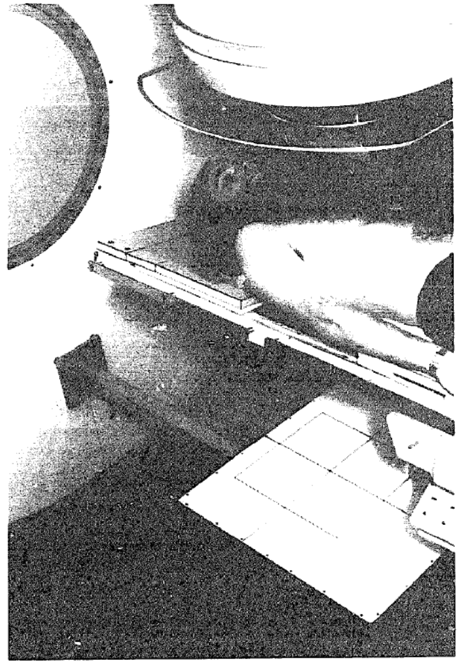
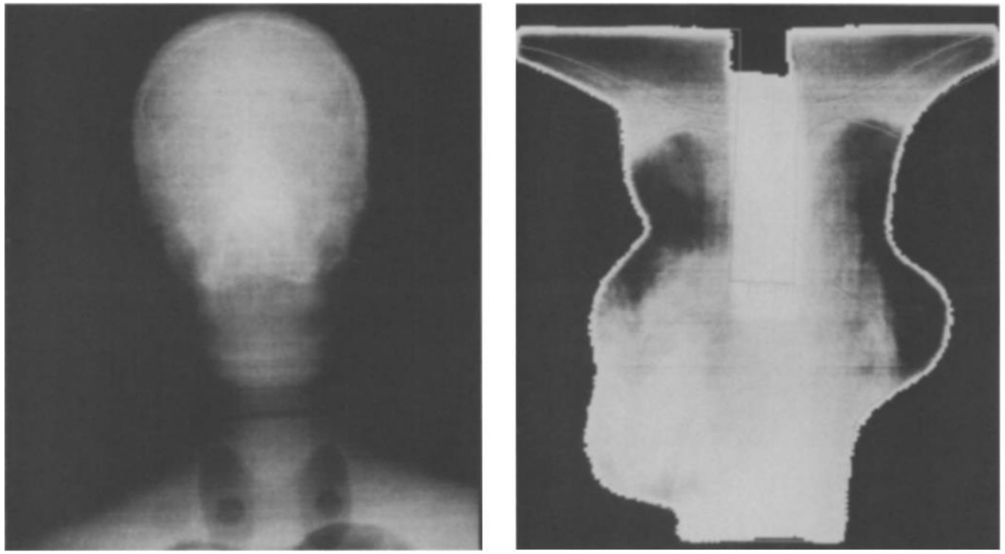
”simulator films” and ”portal films”

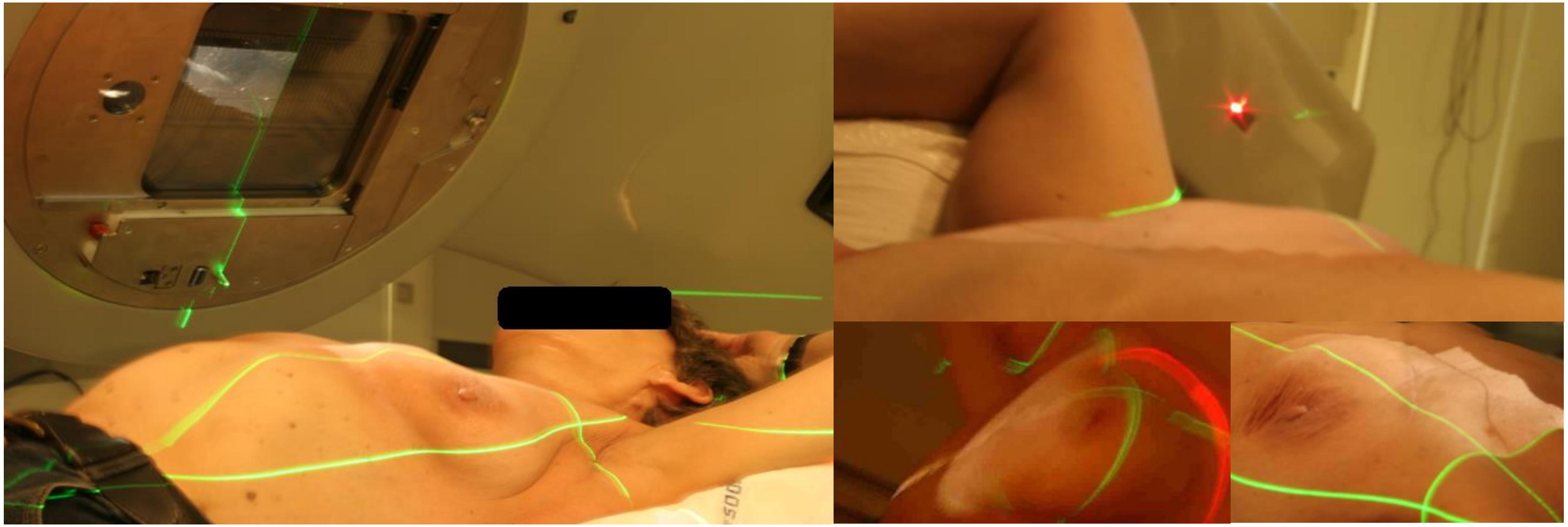
Van Herk et al, RO 1988





Lam et al, BJR 1986

In practice:
One portal film on first treatment day
Then tatoo/light field check ?



- Avoided gross errors, but arguably didn't improve accuracy much

With the exception of a few early studies:

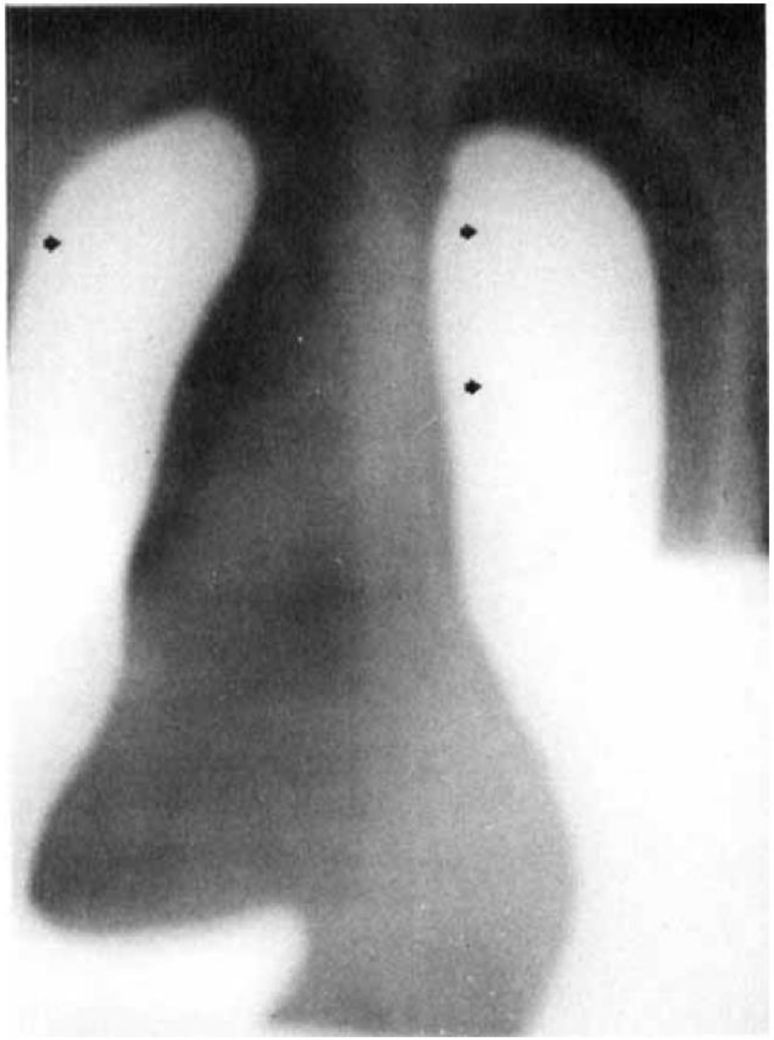


FIG. 4. Mediastinal localization error. Posterior pulmonary shield encroaches upon the soft tissues of the mediastinum.

- Marks et al 1976
- Daily films for Hodgkin Lymphoma patients
- Comfortable immobilization is a must (or 16% error incidence)
- Errors can be due to (1) movement of the patient and (2) movement of external land- marks in relation to internal anatomy.

- Stopped using films after the study !
- *“Perhaps, daily treatment films should be required in cases in which a precise treatment setup is necessary”*

Then came the EPIDs… Significant time and workflow improvement !

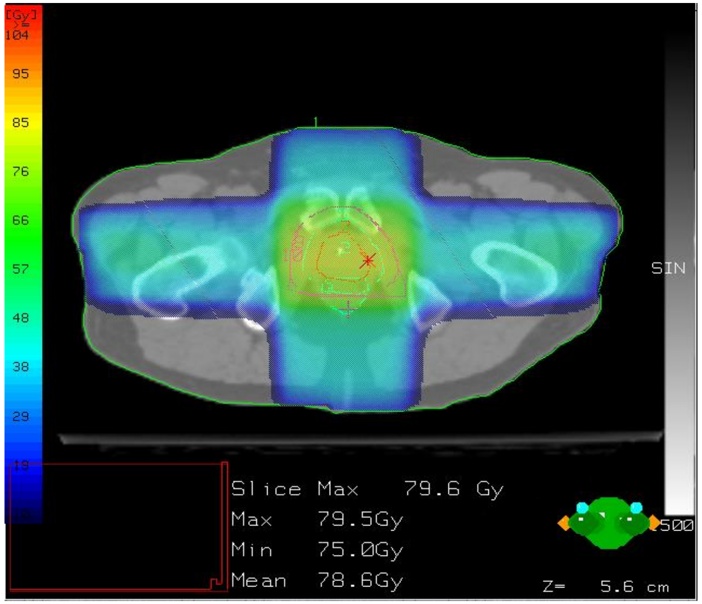
1980ies: Introduction of “offline” approaches and subsequent margin recipes

1990ies: software tools necessary for quantitative image analysis

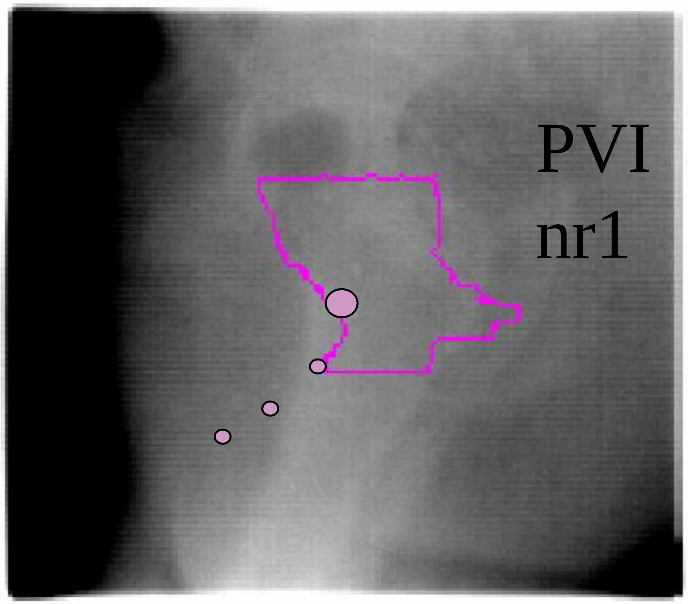
- Real “democratization” of IGRT

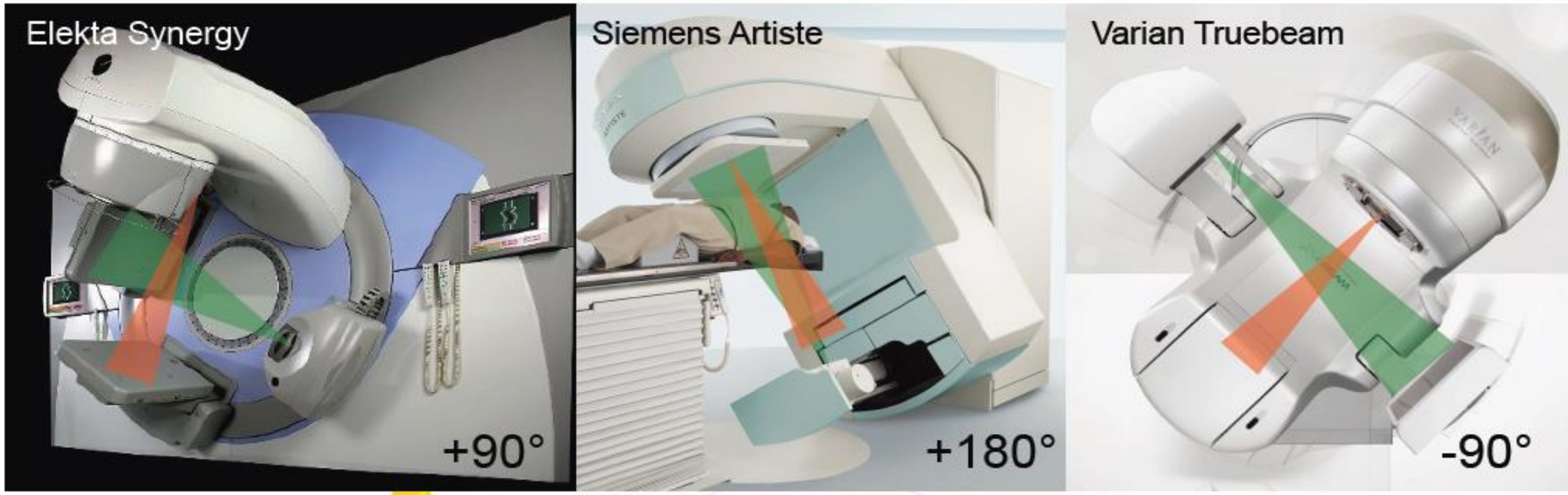
Still, it was hard (impossible!) to see the target

- I 2 fields with catheter; 2Gy x 3 (GTV1)
- II 4 fields 2 Gy x 2 (prostate w. small margin, PTV1a)
- III 4 fields 2 Gy x 8 (prostate w. margin, PTV1b)
- IV 4 fields 2 Gy x 25 (prostate + ves. semin. + margin)
  - Total dose to GTV1: 76 Gy

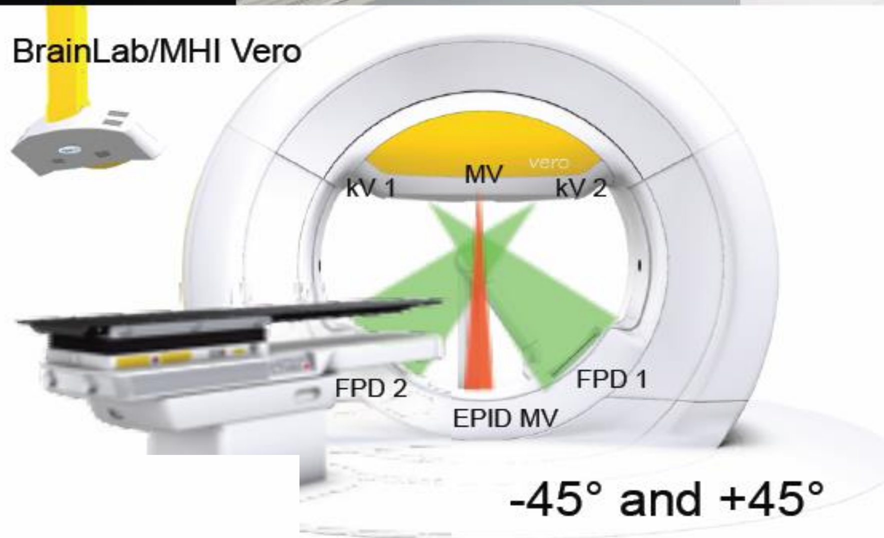


The "Finsen frame"





Elekta Synergy
+90°
Siemens Artiste
+180°
Varian Truebeam
-90°



BrainLab/MHI Vero
kV 1
MV
kV 2
FPD 2
FPD 1
EPID MV
-45° and +45°

kV imaging

Availability of IGRT to day

- 50 centers in the UK
- 26 had kV IGRT capacity on 1 or more machine(s) but only 23 were using it
- Expected to increase to 43 within the coming years
- In contrast, **every center had IMRT capacity**

Mayles , Clin Onc 2010

Table 8
Reasons for lack of progress with image-guided radiotherapy. The reasons are listed in order of the number of centres indicating that the reason was relevant to them.

	An issue	Main reason	In top three
Lack of equipment capability	40	30	33
Lack of machine time	23	2	16
Radiographer availability	17	0	14
Lack of funding	17	3	11
Physicist availability	14	3	10
Time for training	8	0	4
Clinical oncologist availability	7	2	4
Dosimetrist availability	7	0	3
Concerns about dose	1	0	0
Number of respondents for this column	47	40	40

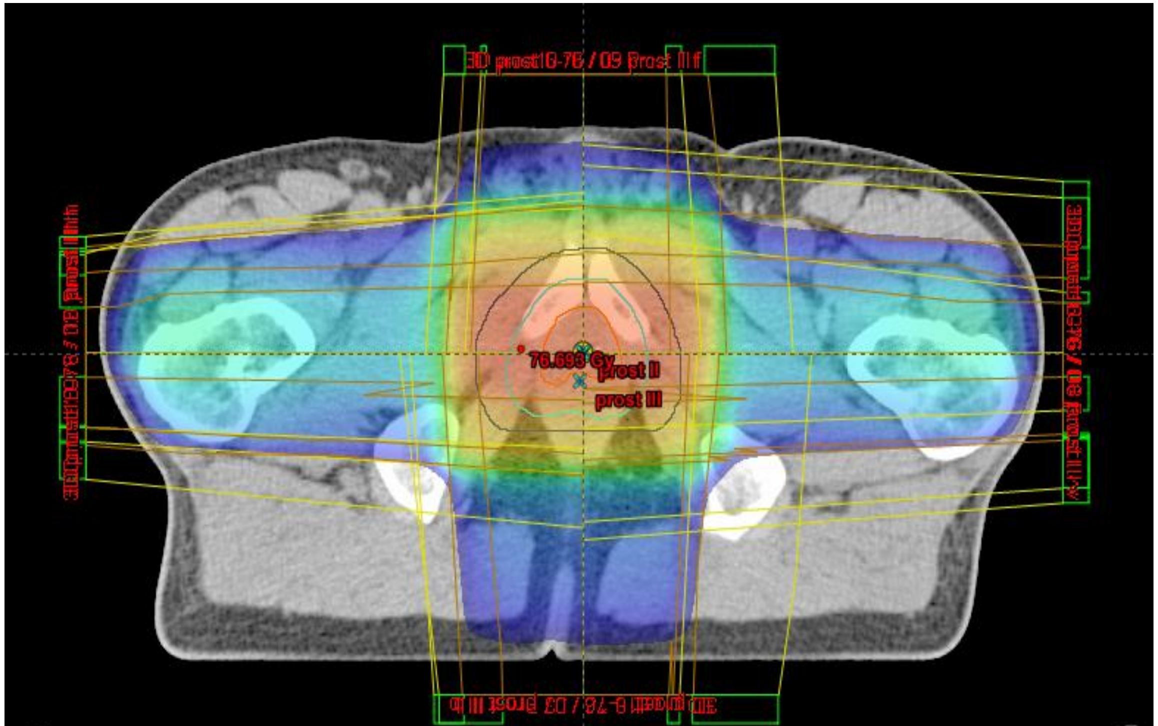
IGRT can be ressource-intensive

- Acquire/commission the equipment
- Verify/calibrate on a regular basis
- Design imaging protocols for different patient groups (what kind of images, how often)

- Acquire the images + online verification
- Offline verification
- Multi-disciplinary review if recurring problems

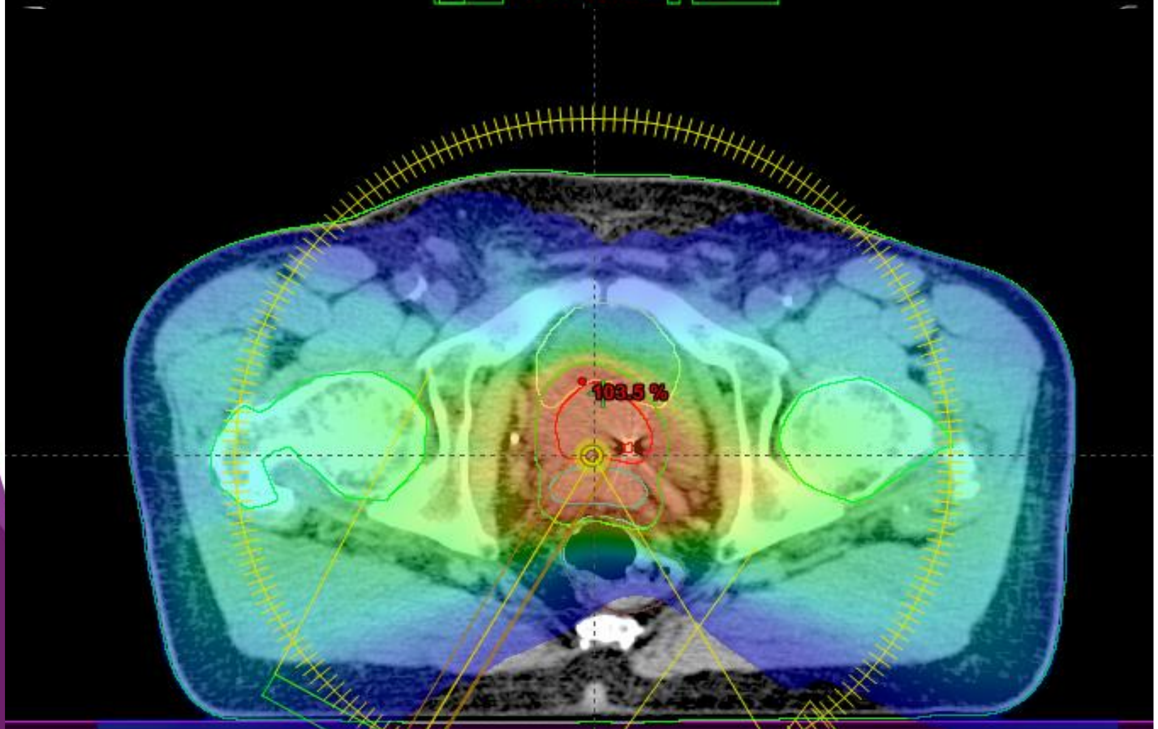
- When applicable: calculation of average shift

IGRT AND IMRT



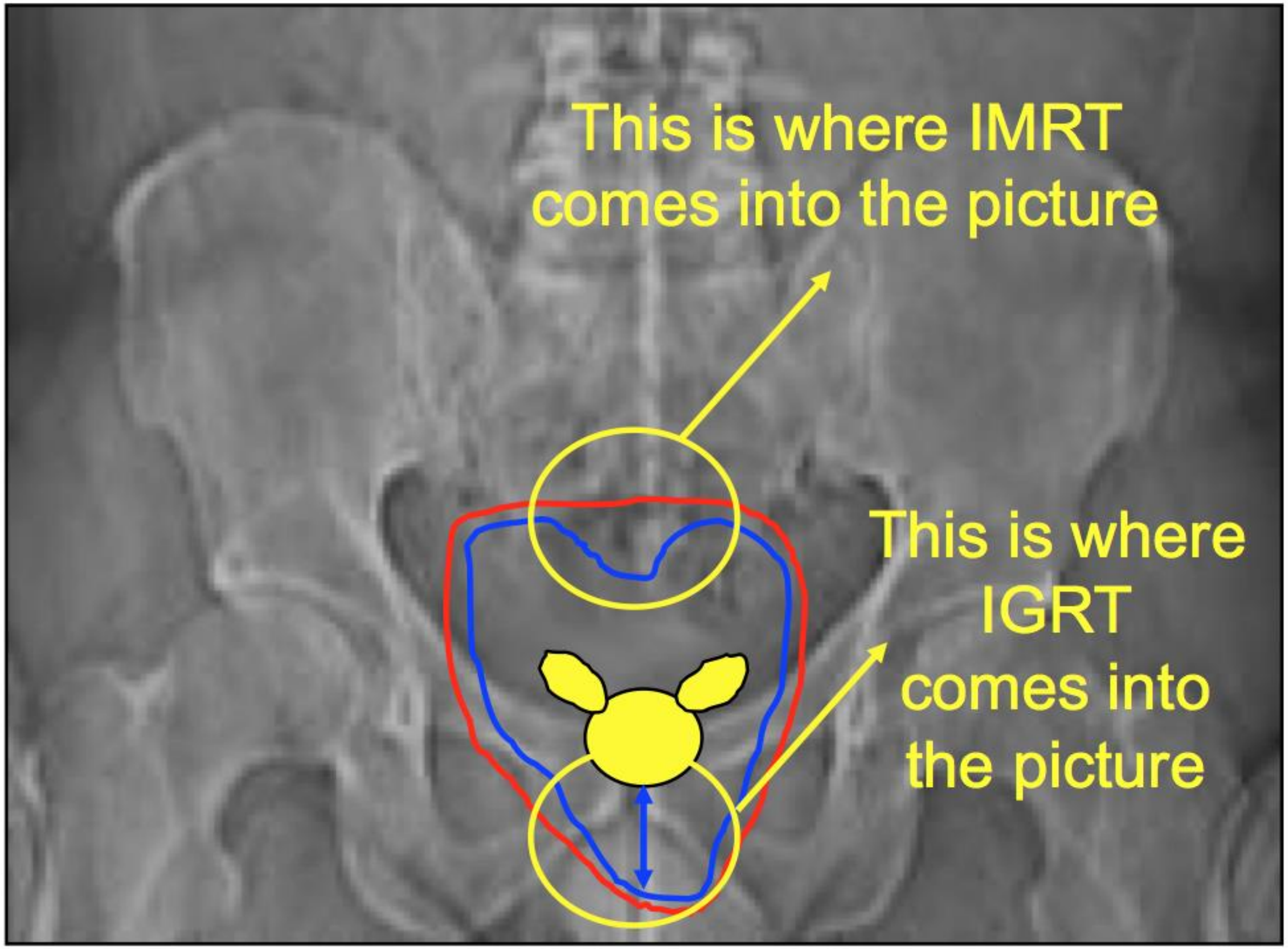
“conventional” therapy

- **Large fields**
- **The large amount of healthy tissue in the field prohibited the use of high doses**



- **More fields**
- **Smaller amount of healthy tissue in the field**
- **Opened the door to dose escalation**
- **Prostate cancer: 60 Gy to 80 Gy**

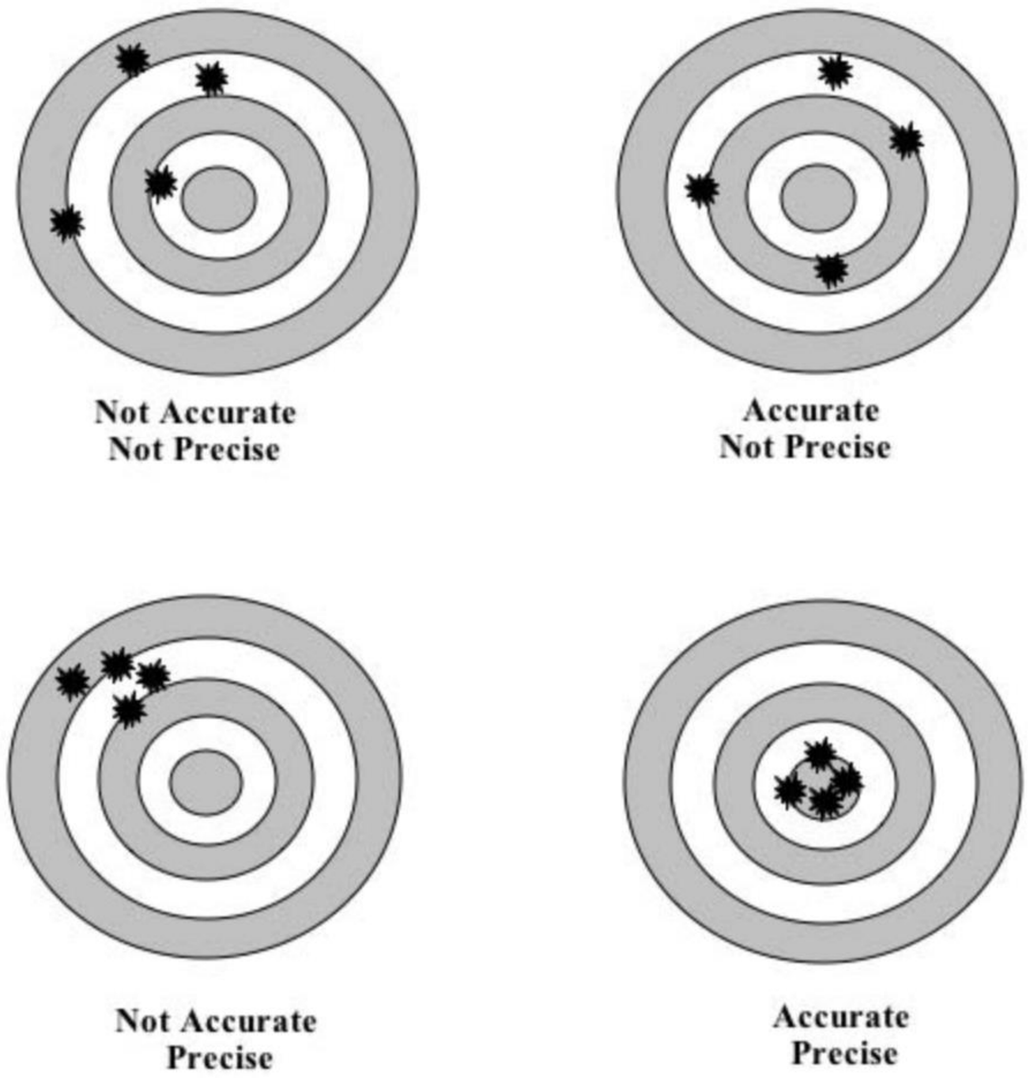
“Dose sculpting” vs “margin reduction”



Set up Margin
+
Internal Margin

Irradiated Volume

“we are at increased risk of missing very precisely” J. Rosenman



IMRT without IGRT ?

Shift of purpose:

PATIENT VS TARGET (AND OAR) POSITIONING

Positioning the patient… vs positioning the tumour

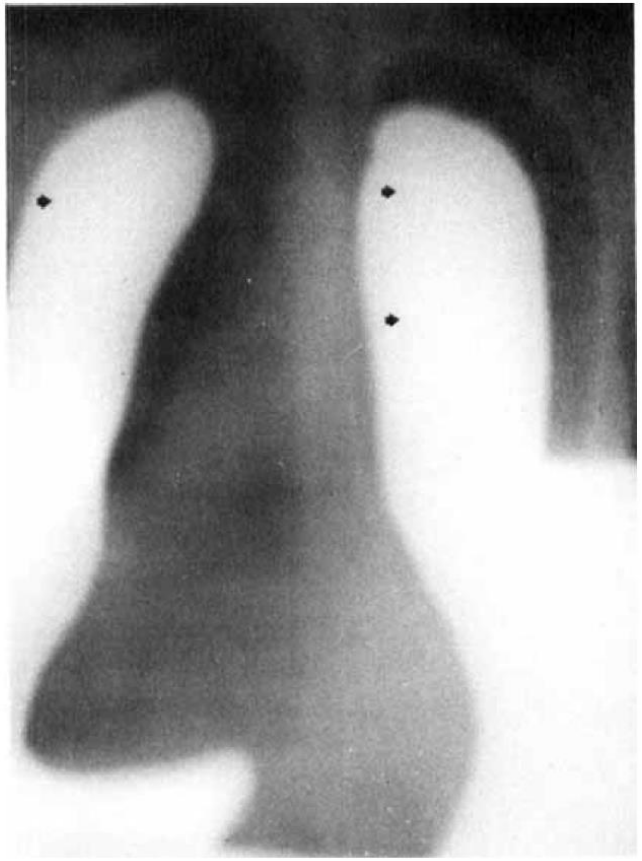
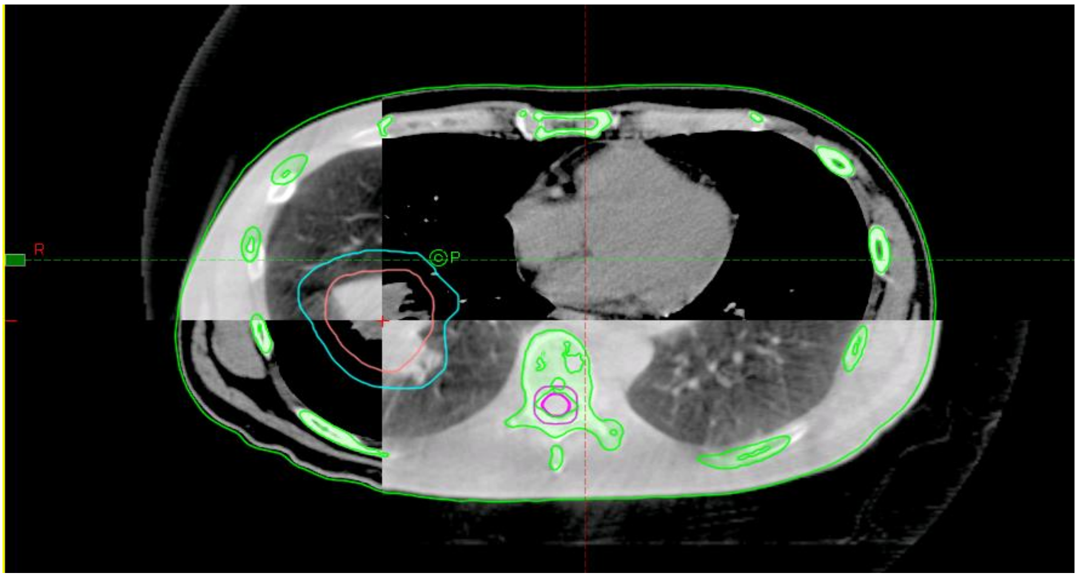
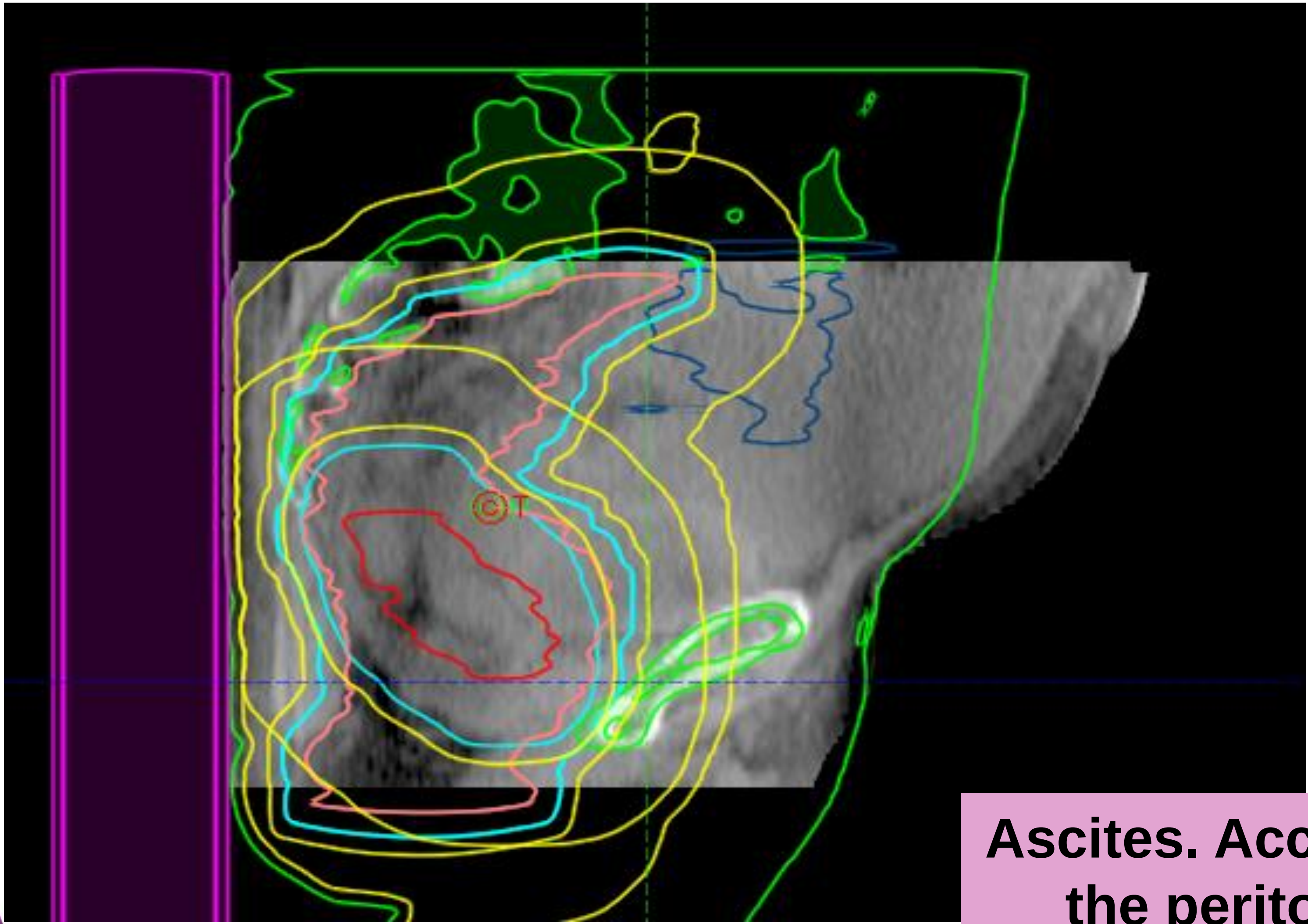


FIG. 4. Mediastinal localization error. Posterior pulmonary shield encroaches upon the soft tissues of the mediastinum.

CBCT



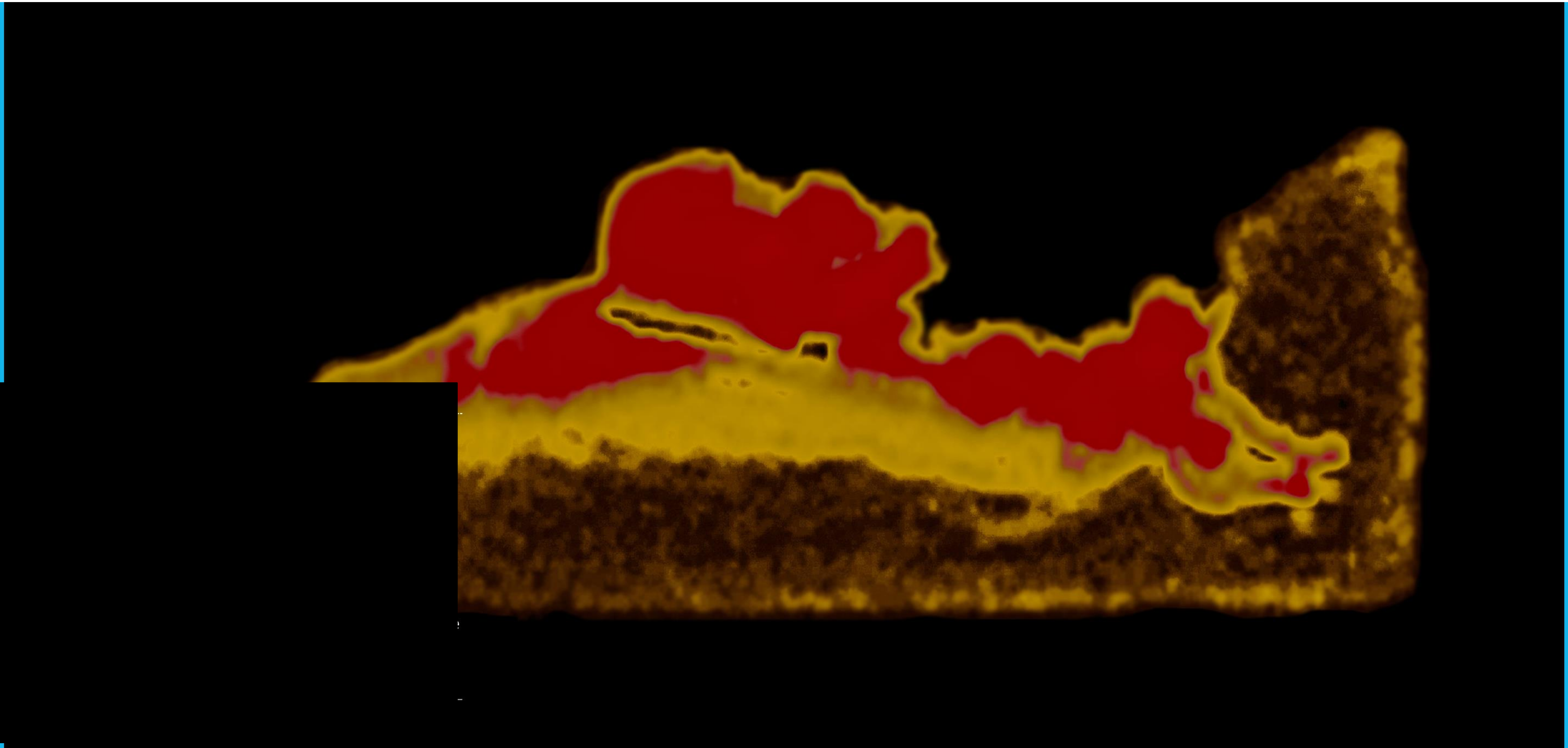
Even with improved image quality: don't expect the machine to think for you !



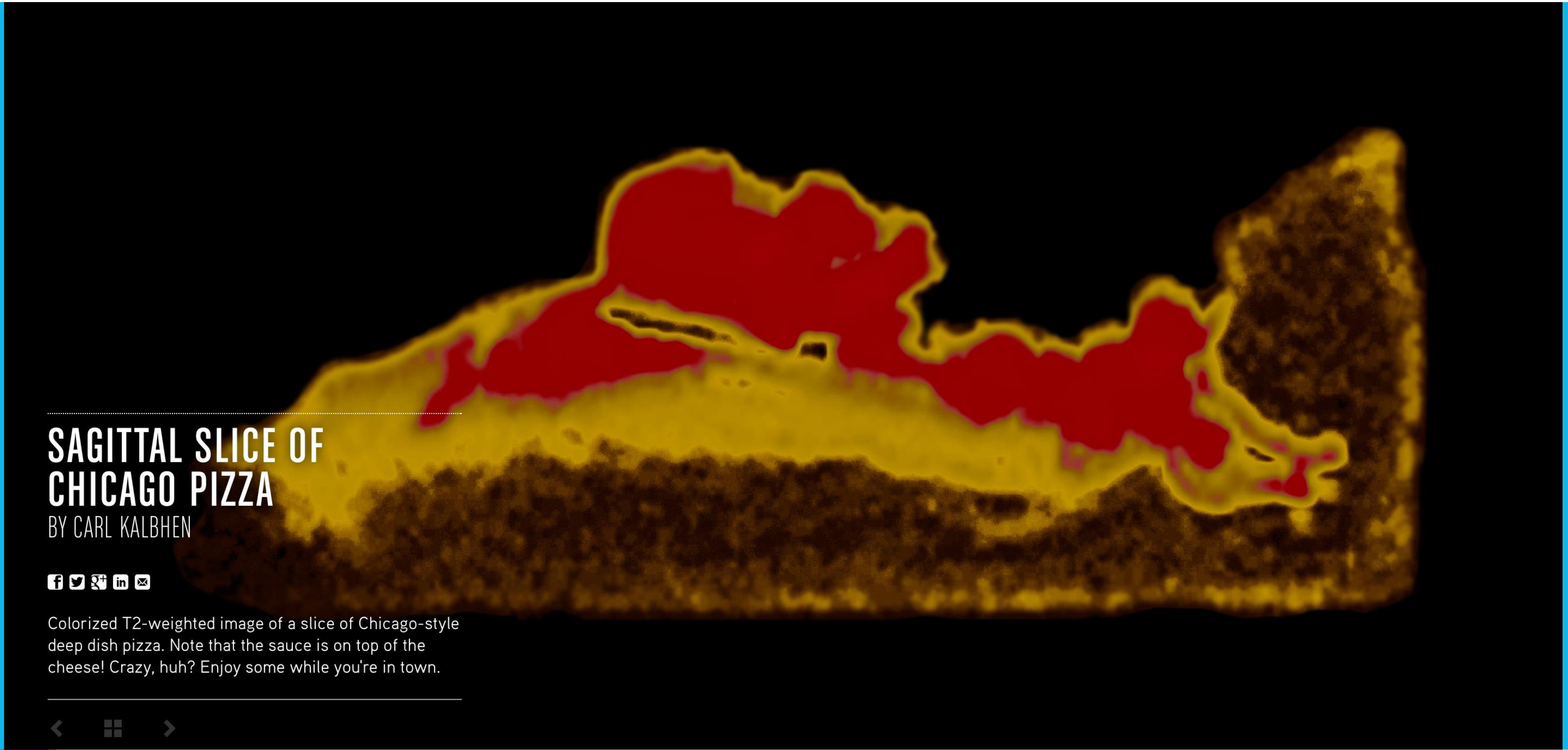
Courtesy of Lotte S Fog, Rigshospitalet

Ascites. Accumulation of fluid in the peritoneal cavity. Dose distribution affected.

Expect the unexpected !



Expect the unexpected !



THE JOY OF MARGINS !

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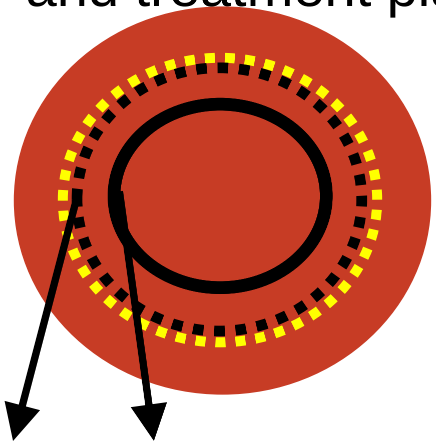
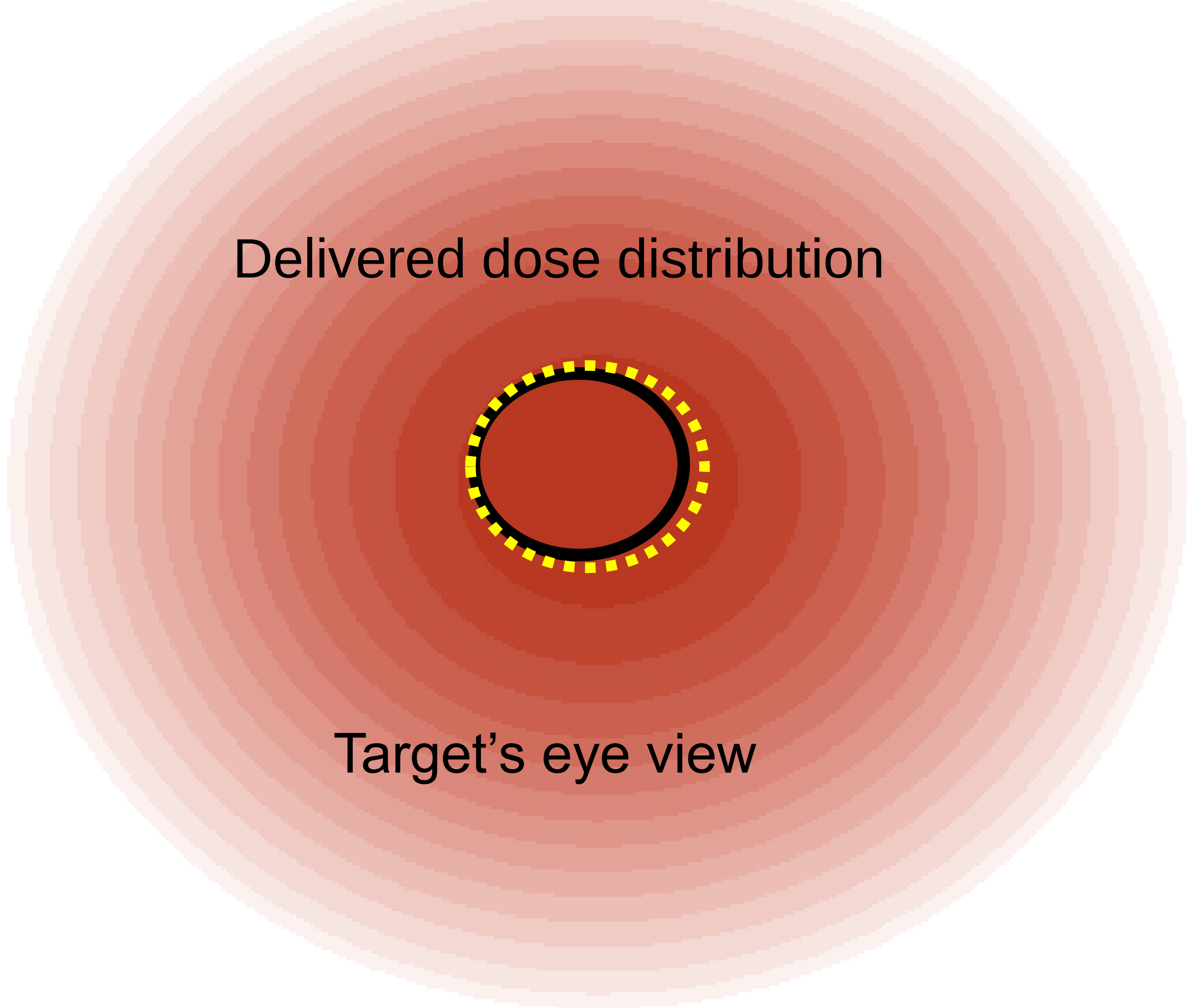
CT and treatment plan

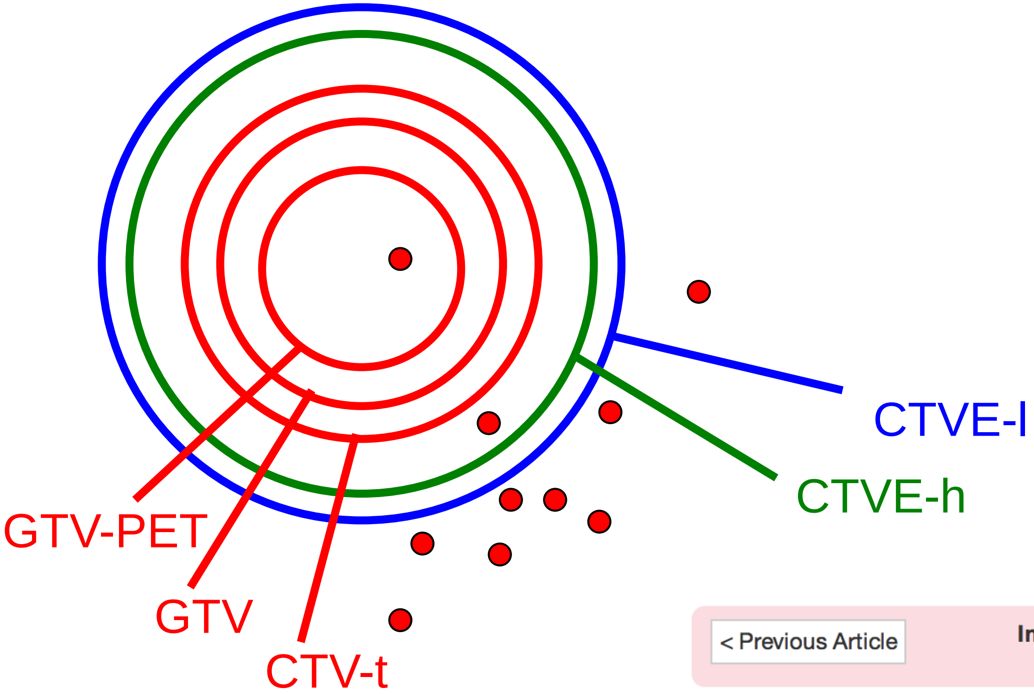


CTV to PTV margin

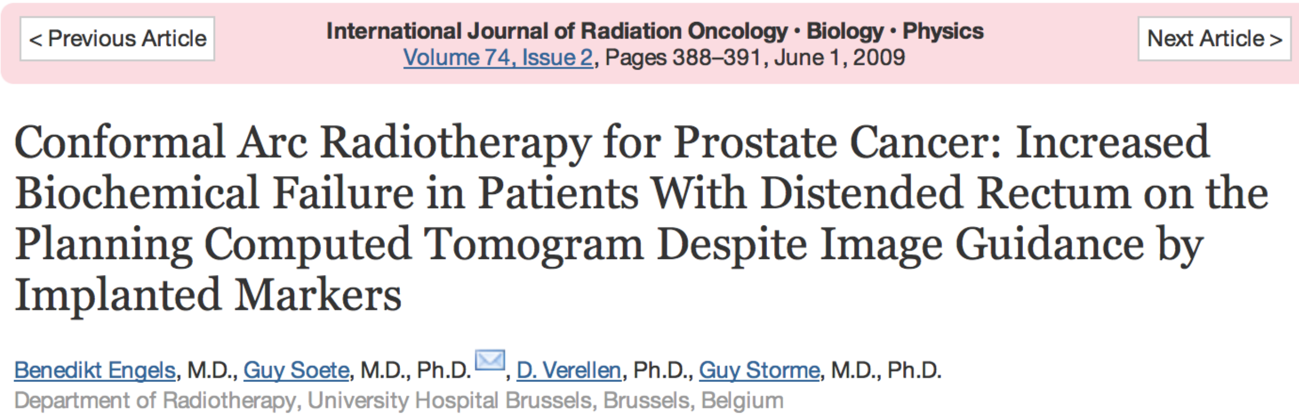


$$M = 2.5\ \Sigma_{tot} + 1.64\ (\sigma_{tot} - \sigma_p)$$

The proof is in the pudding:



Margins too small:
- Marginal recurrences



< Previous Article

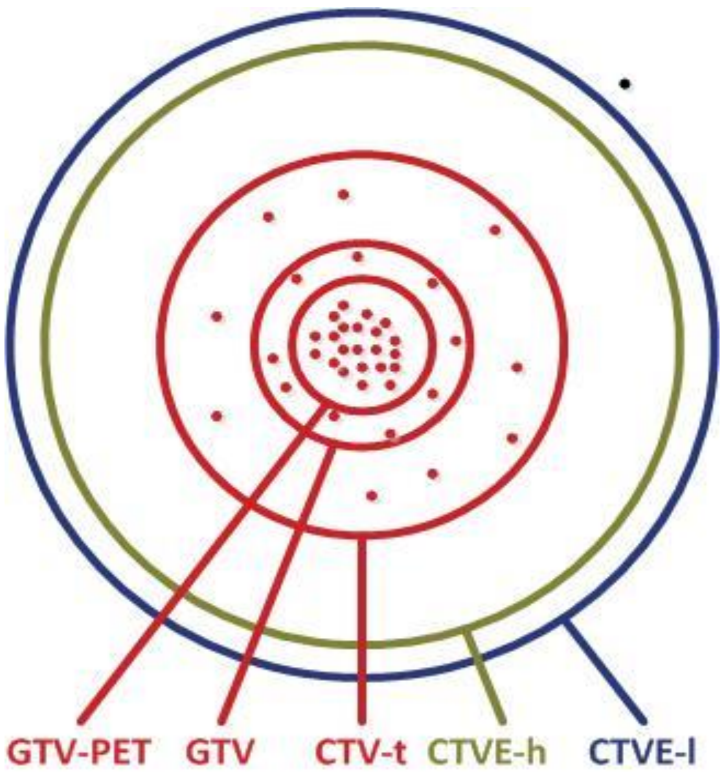
International Journal of Radiation Oncology • Biology • Physics
Volume 74, Issue 2, Pages 388–391, June 1, 2009

Next Article >

Conformal Arc Radiotherapy for Prostate Cancer: Increased Biochemical Failure in Patients With Distended Rectum on the Planning Computed Tomogram Despite Image Guidance by Implanted Markers

Benedikt Engels, M.D., Guy Soete, M.D., Ph.D., D. Verellen, Ph.D., Guy Storme, M.D., Ph.D.
Department of Radiotherapy, University Hospital Brussels, Brussels, Belgium

The proof is in the pudding:



Due et al R&O 2014

Margins too large ??

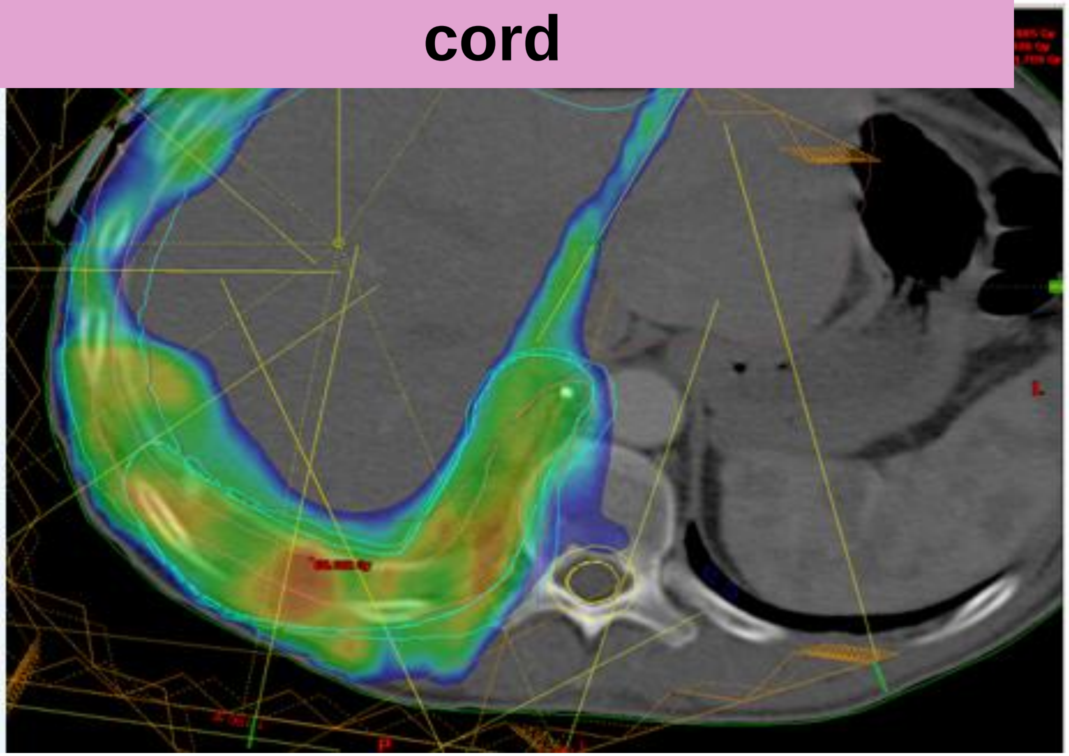
- No (few) marginal recurrence
- Might limit dose escalation and lead to in-field recurrence

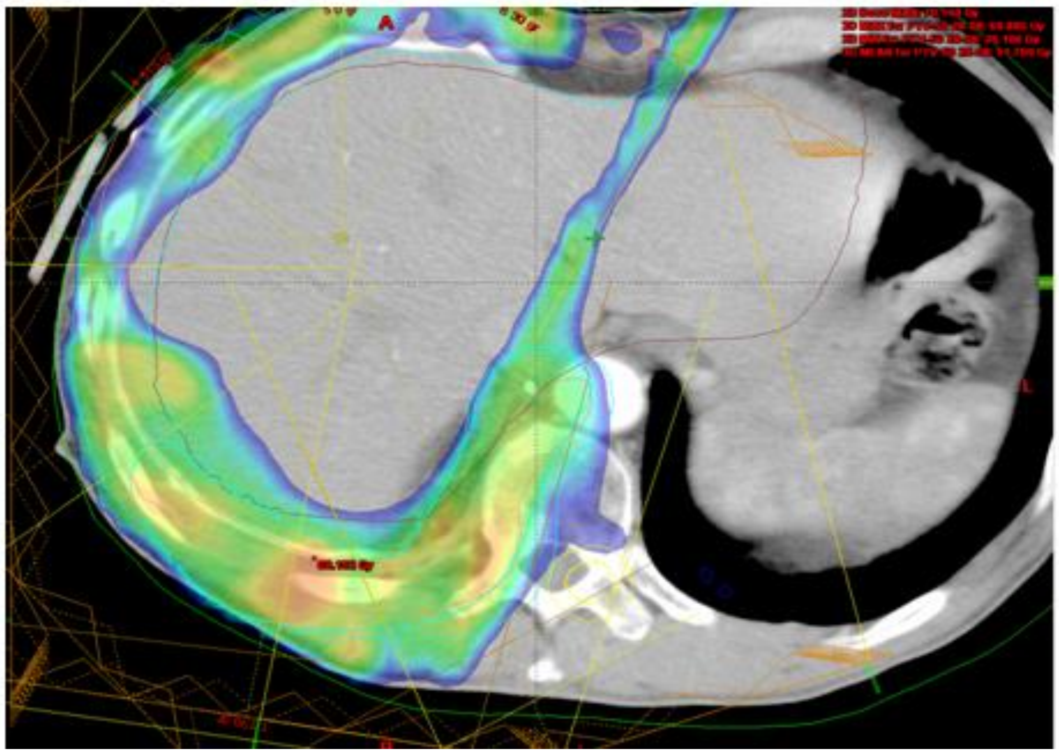
A new attempt at reducing margins

ADAPTIVE RADIOTHERAPY

Things we might not have seen without IGRT…

Mesothelioma patient. Weight loss = increased dose to spinal cord





Courtesy of Lotte S Fog, Rigshospitalet

Re-scanning vs replanning

- New scan, same fixation
- To check that the dose distribution is still acceptable
- Can be planned (e.g. half way through treatment) or ad hoc
- Replace by CBCT recalculation ?

- New fixation?
- New contouring?
- New plan ?
- Hot topic, but limited data on the actual clinical benefits
- New uncertainties can be introduced

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Two main challenges…

- **Identify patients who are likely to benefit**
- **Implement with a sustainable use of resources**

The myth of the "zero margin"

- Contouring uncertainties
- Algorithms (calculation, registration, etc…)
- Patient position
- Tumour position
- Intra fraction motion
- Changes in internal anatomy (weight loss, distance between targets, target and OARs)
- Etc…

Margins can not converge to zero

Conclusion (1)

- The technology has come a long way: we have many tools!
    - ➢ the challenge is to develop/introduce an IGRT approach adapted to the department's philosophy

- We need to be smart about how we use them (and this takes time!)
    - ➢ Where do you get the most "bang for your buck" in terms of ressources, dose, etc..

Conclusion (2)

- IGRT is a requirement (and arguably more important than) IMRT, SIB, SBRT, CBRT, ART, RA, VMAT, …

- We need to keep pushing the manufacturers to include the tools that we are missing

With thanks to:

- Dirk Verellen
- Lotte Fog and Mirjana Josipovic

RTT's Perspective on IGRT

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Madrid 2016

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Contents

Introduction

AvL:

- 9 + 2 linacs (Elekta) all equipped with portal imaging device
- 9/11 Cone-beam CT (Elekta)
- 4 RTT’s per treatment machine
- 120 RTT’s:
  - in-service or full time trained
  - 1 year of further education in department specific protocols and working instructions

Introduction

AMC:

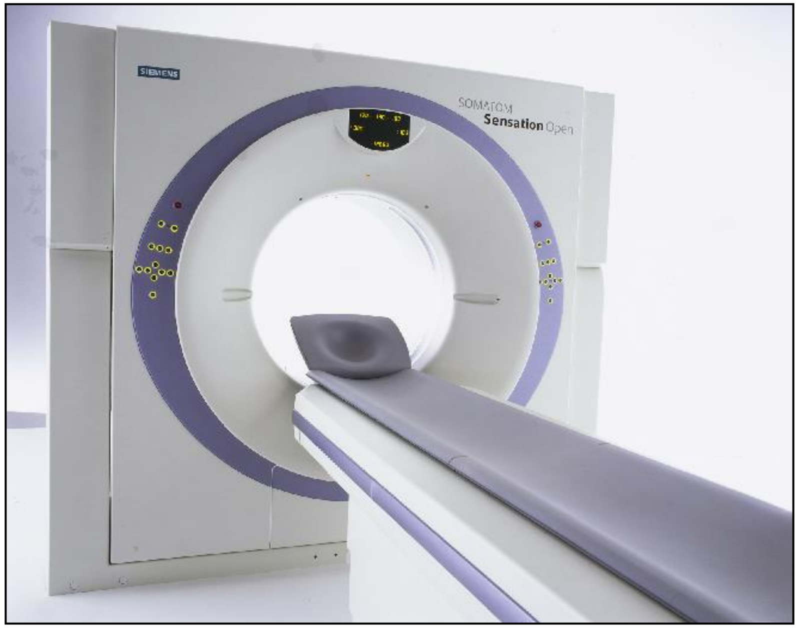
- 4 + 2 linacs (Elekta) all equipped with portal imaging device
- All Cone-beam CT (Elekta)
- 3 RTT's per treatment machine
- 60 RTT's:
  - in-service or full time trained
  - 1 year of further education in department specific protocols and working instructions

Introduction

Changes over the last years

Simulation:

from fluoroscopy to CT



2 D

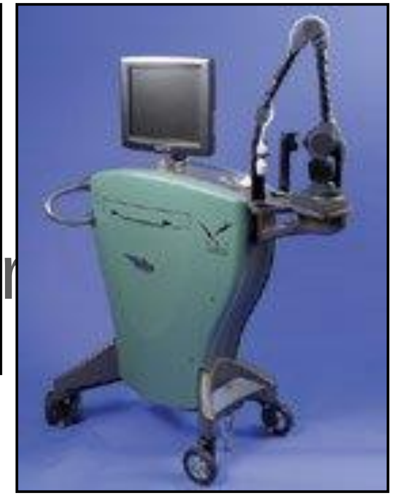
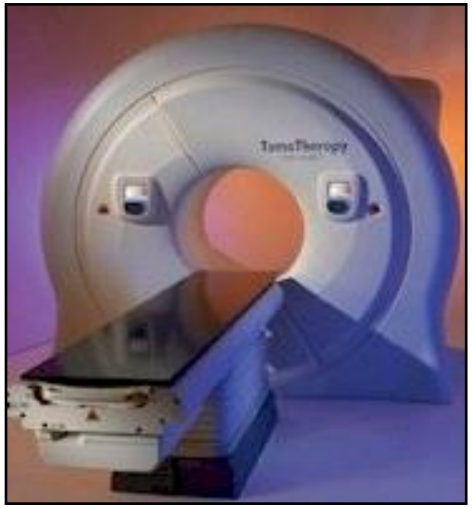
3 D

Introduction

Treatment machine:

From patient set-up with skin marks to additional patient set-up verification

- Portal imaging (2D MV)
- Kilo voltage imaging (3D kV)

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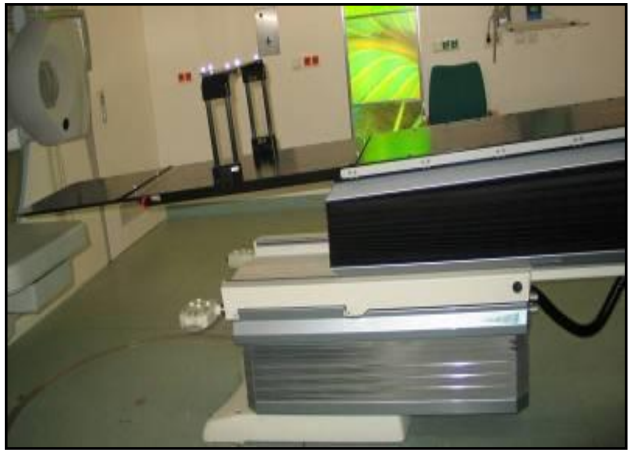
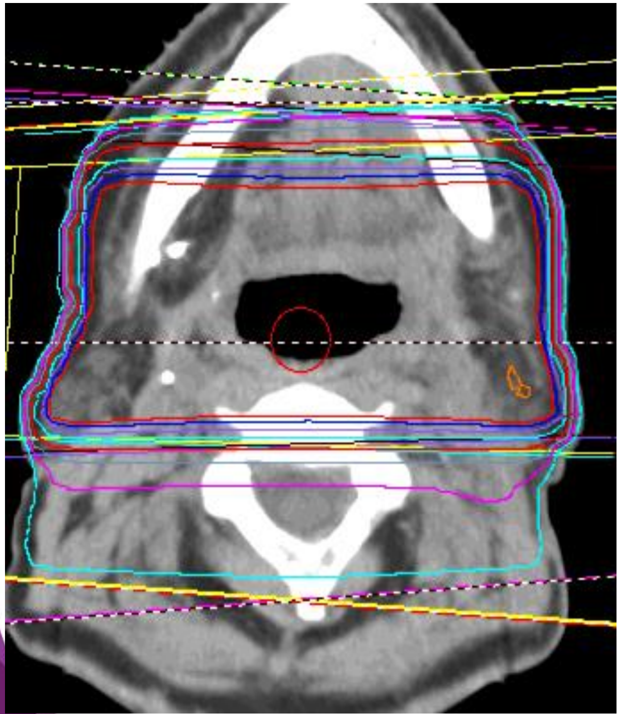
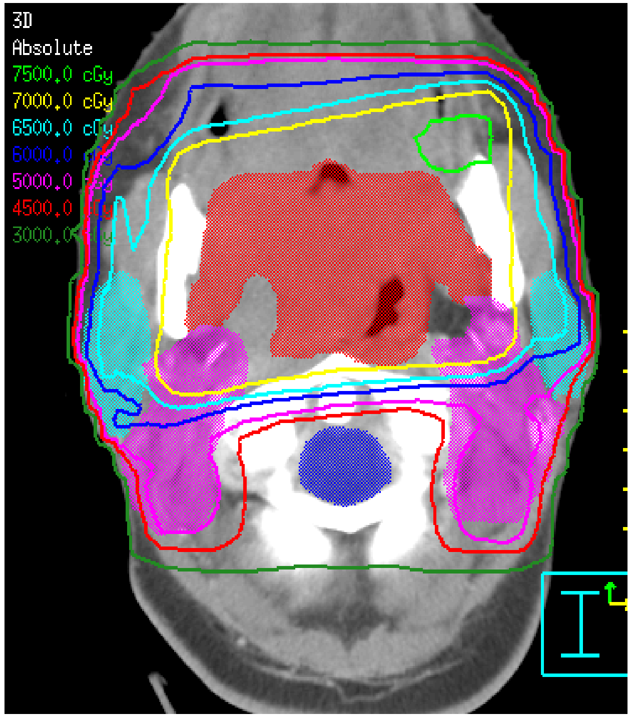


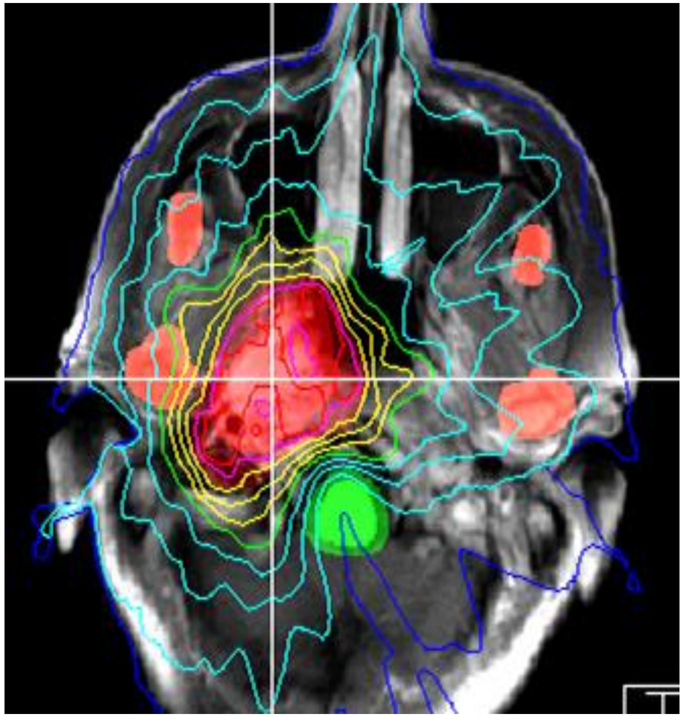

Introduction

Treatment planning:

from conventional to conformal to IMRT & arc therapy







Starting IGRT

Portal Imaging

AvL

In routine clinical use since 1987

RTT's responsibilities:

Acquisition of portal images

Registration of portal images

Evaluation of portal images

Execute decision rules off-line and on-line protocols

Portal Imaging

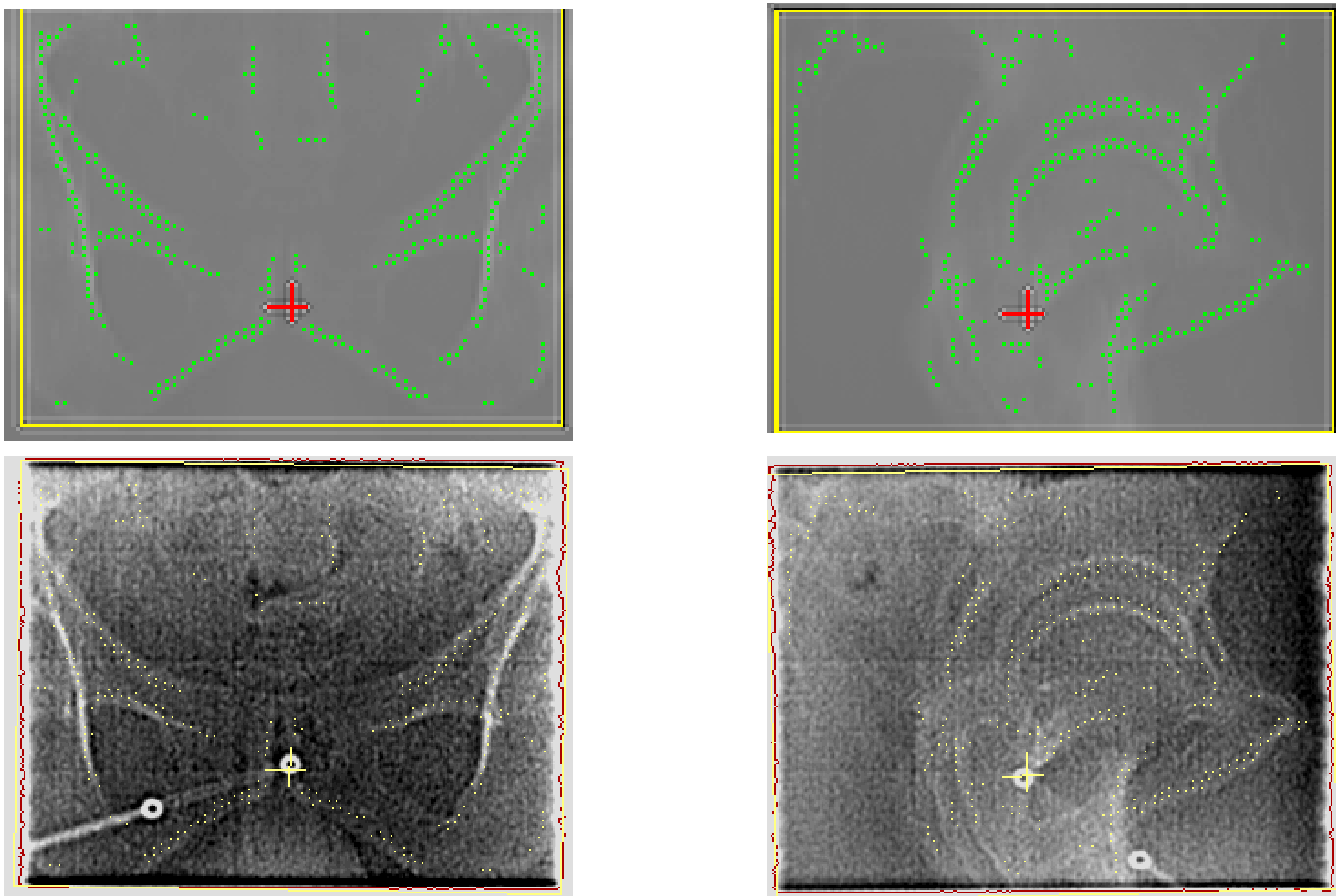
2 RTT's:

Training and education

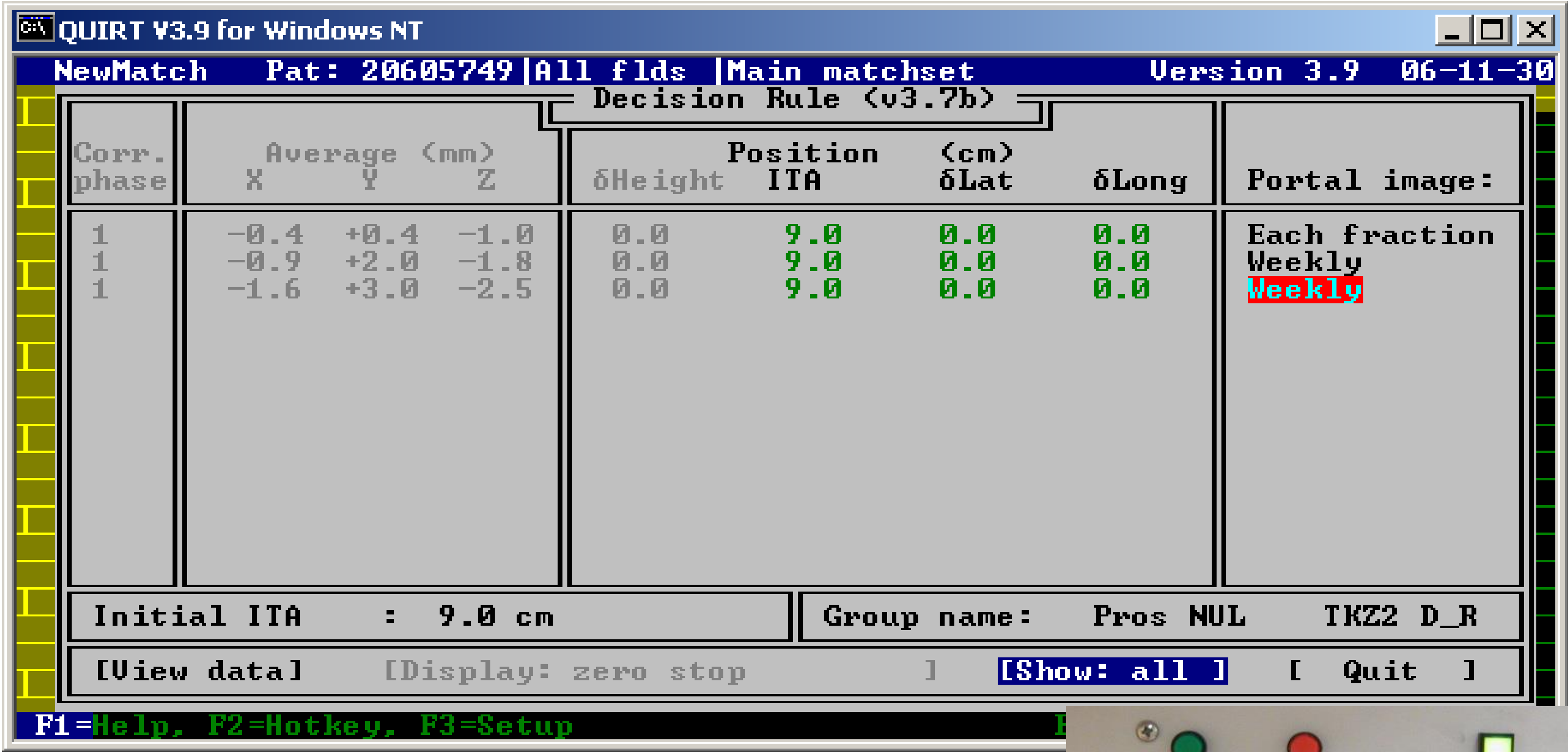
Manuals and protocols

Follow-up and quality assurance

Portal Imaging



Portal Imaging



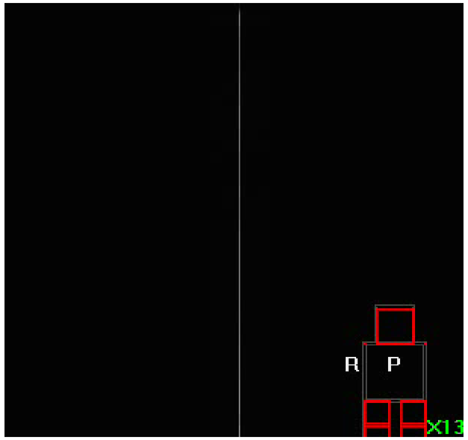
Implementing CBCT

June 2003:

- 4 RTT's
- 2 Physicists
- Patient program in the morning
- CBCT in the afternoon
- 8 months of validation

Implementing CBCT: validation of the system

3D match



Cross validation

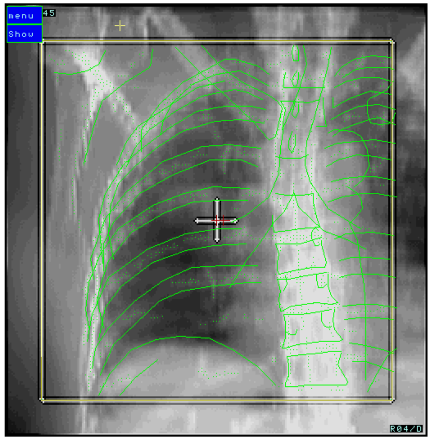
Planning CT

same ?

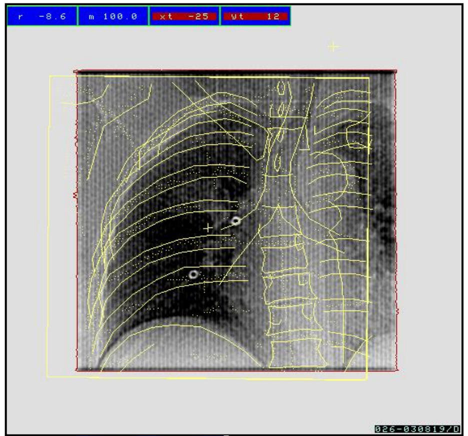
Cone beam CT

DRR +Template

MV image

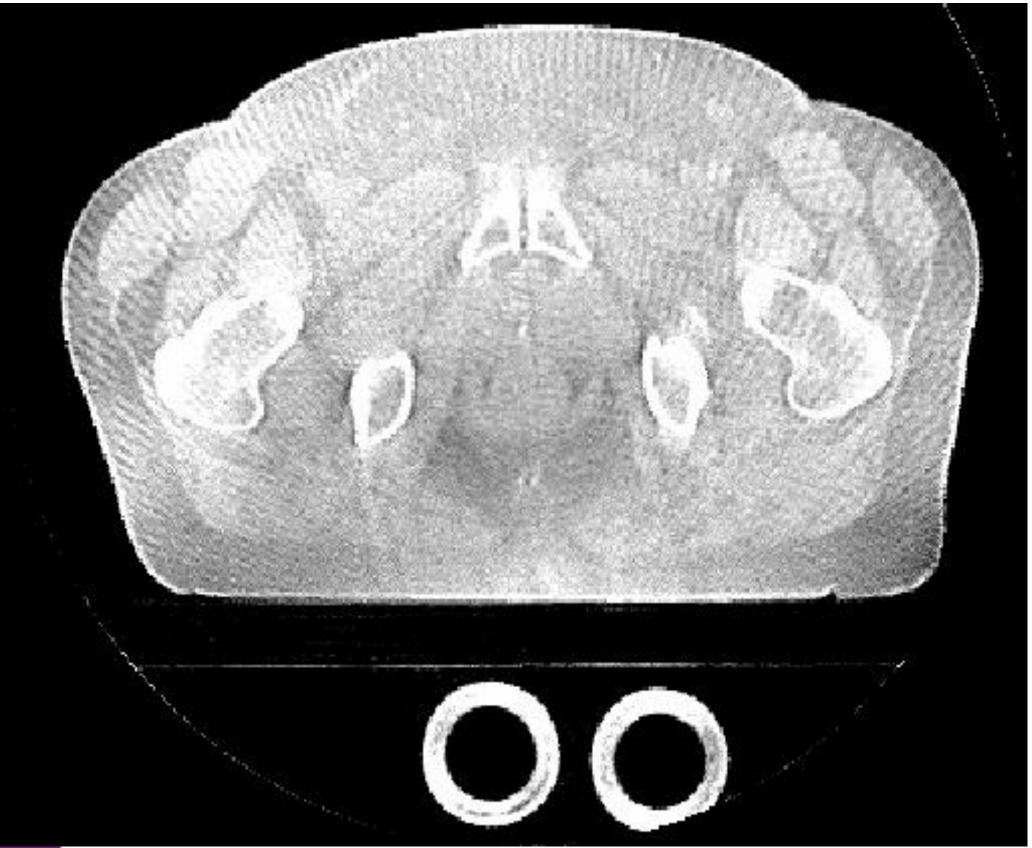


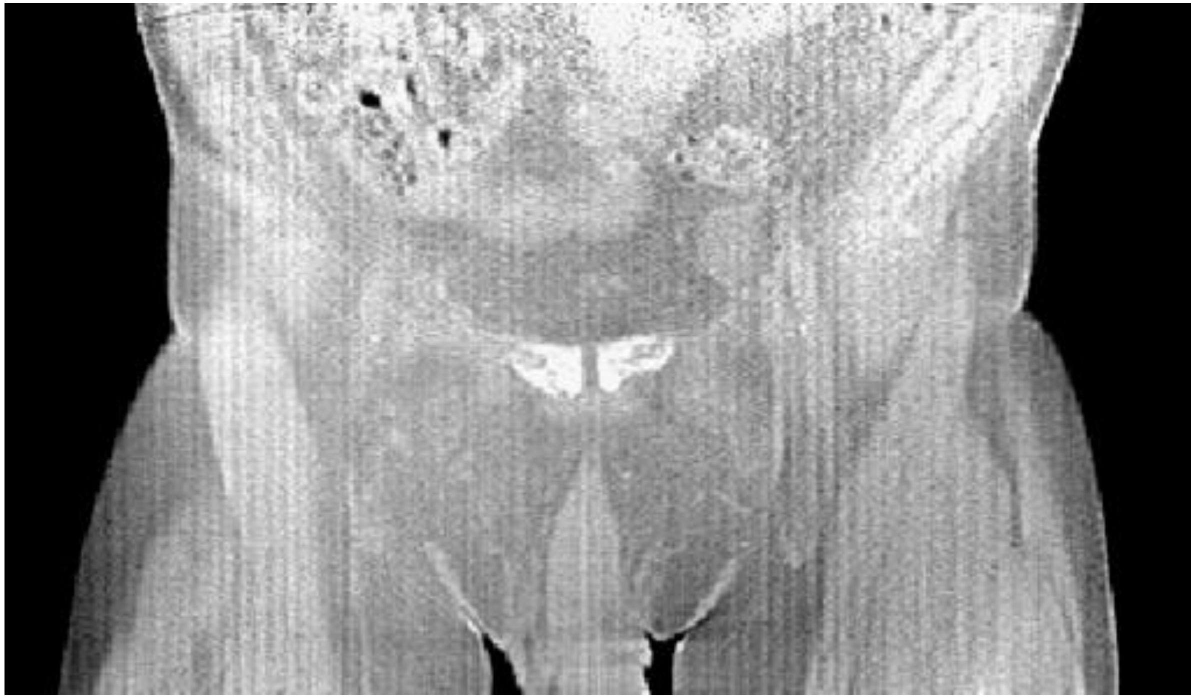
2 x 2D match AP/LAT



Implementing CBCT: designing imaging presets

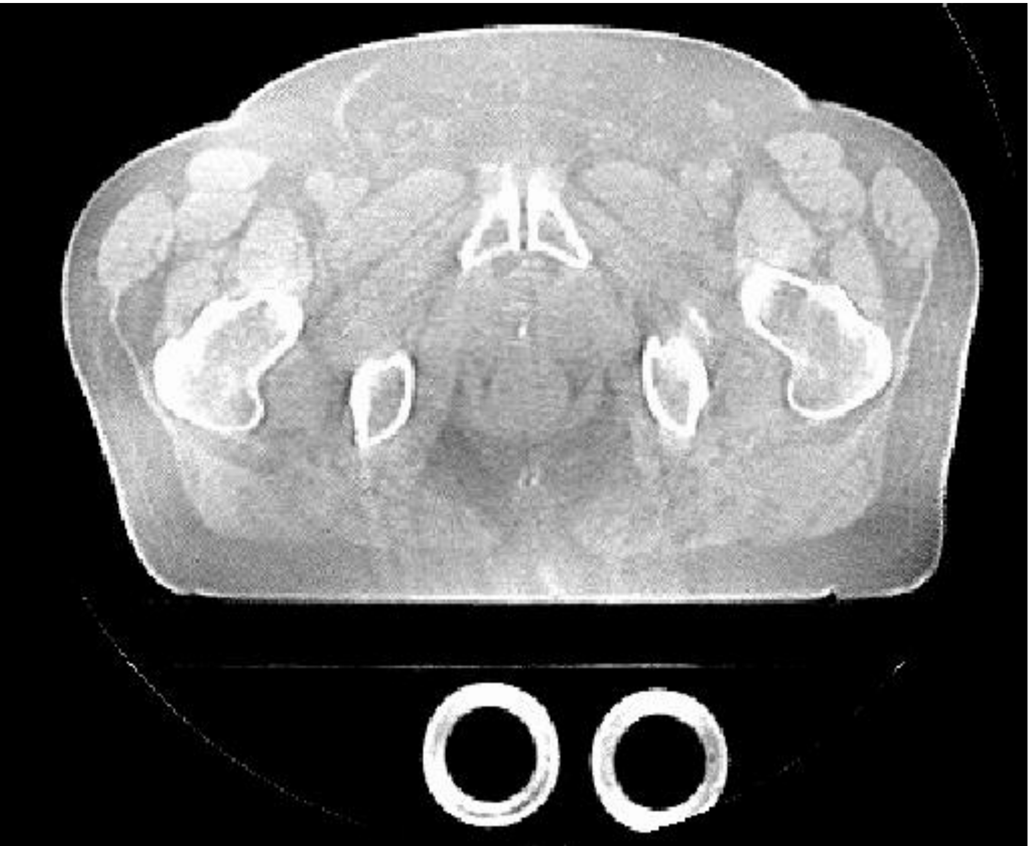
320 Projections 1.5 - 3 cGy





Implementing CBCT: validation of the system

640 Projections 1.5 - 3 cGy



Implementing CBCT: role of RTT

- Understanding basic physics and technical aspects of new imaging modality
  - IQ: artefacts
- Implementing in daily workflow
  - Protocols, manuals and working instructions
- Setting up training program for RTT's

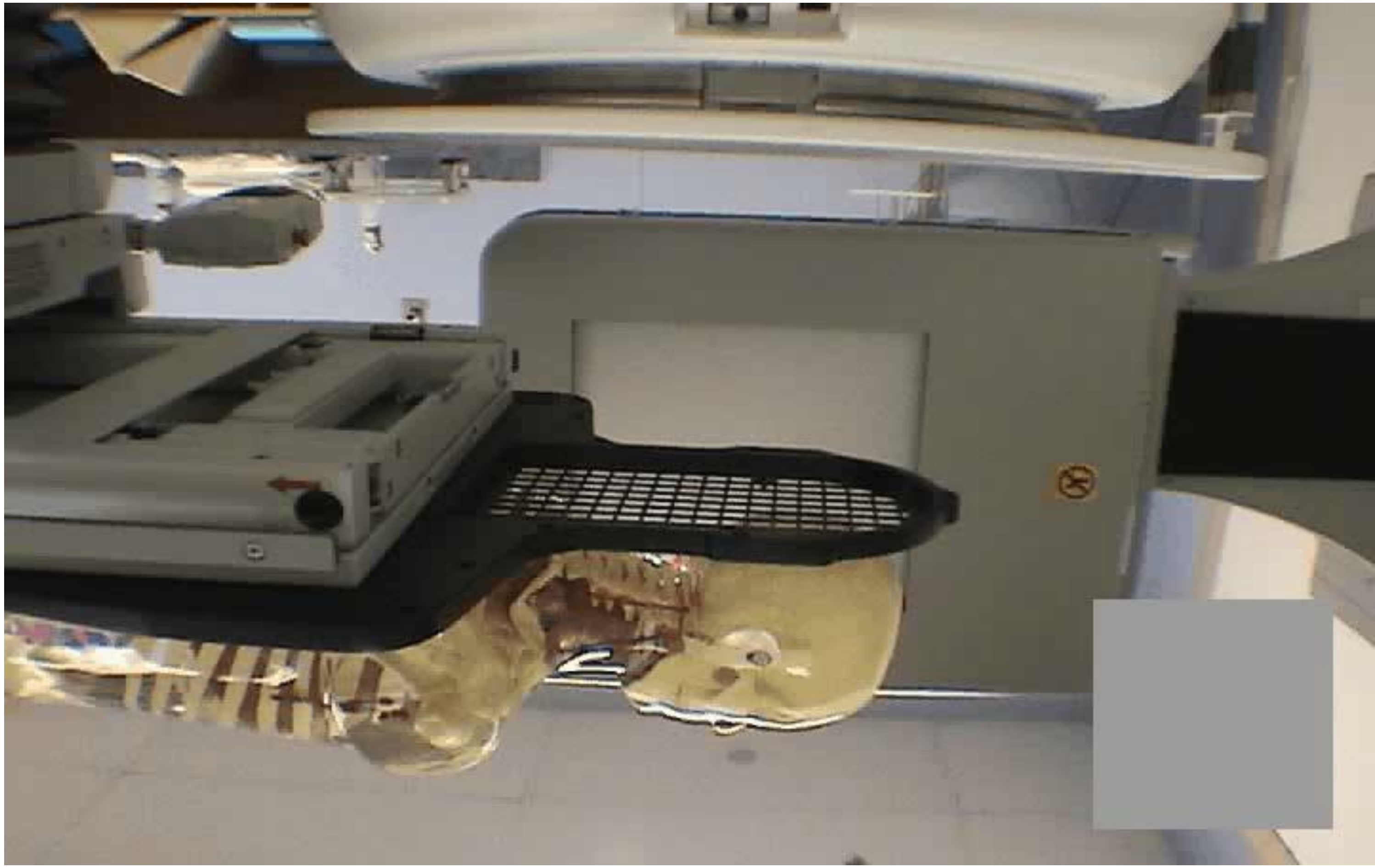
Starting clinical use of CBCT

RTT's responsibilities:

- Acquisition of CBCT
- Registration bony anatomy (CBCT)
- Evaluation registration (CBCT)
- Evaluation of treatment !
- Execute decision rules off-line and on-line protocols

→ Same as portal imaging and a bit extra

Clinical daily routine



Courtesy to Doug Moseley (PMH) Jan-Jakob Sonke (AvL)

Princess Margaret Hospital

amc NKI-AVL

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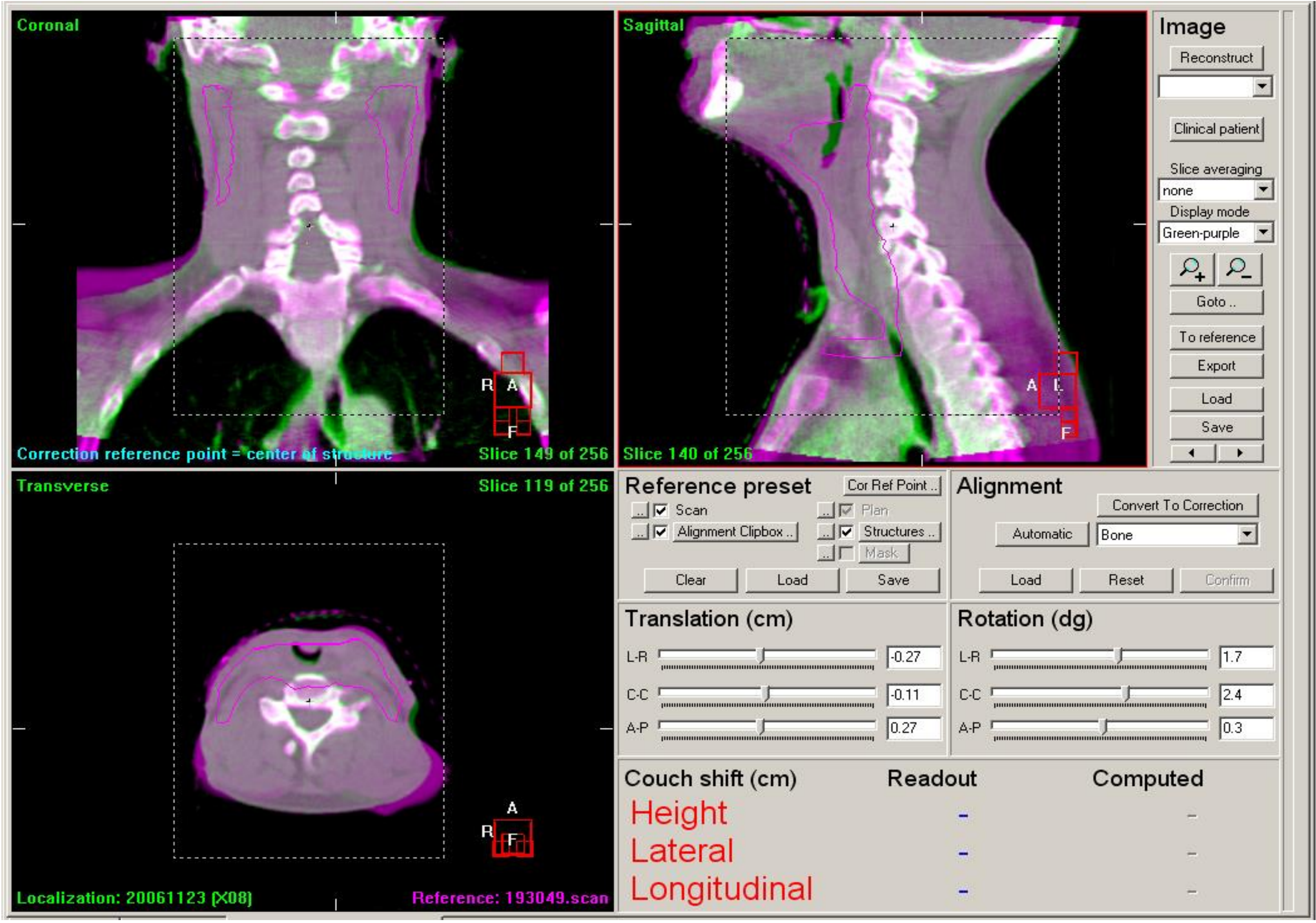
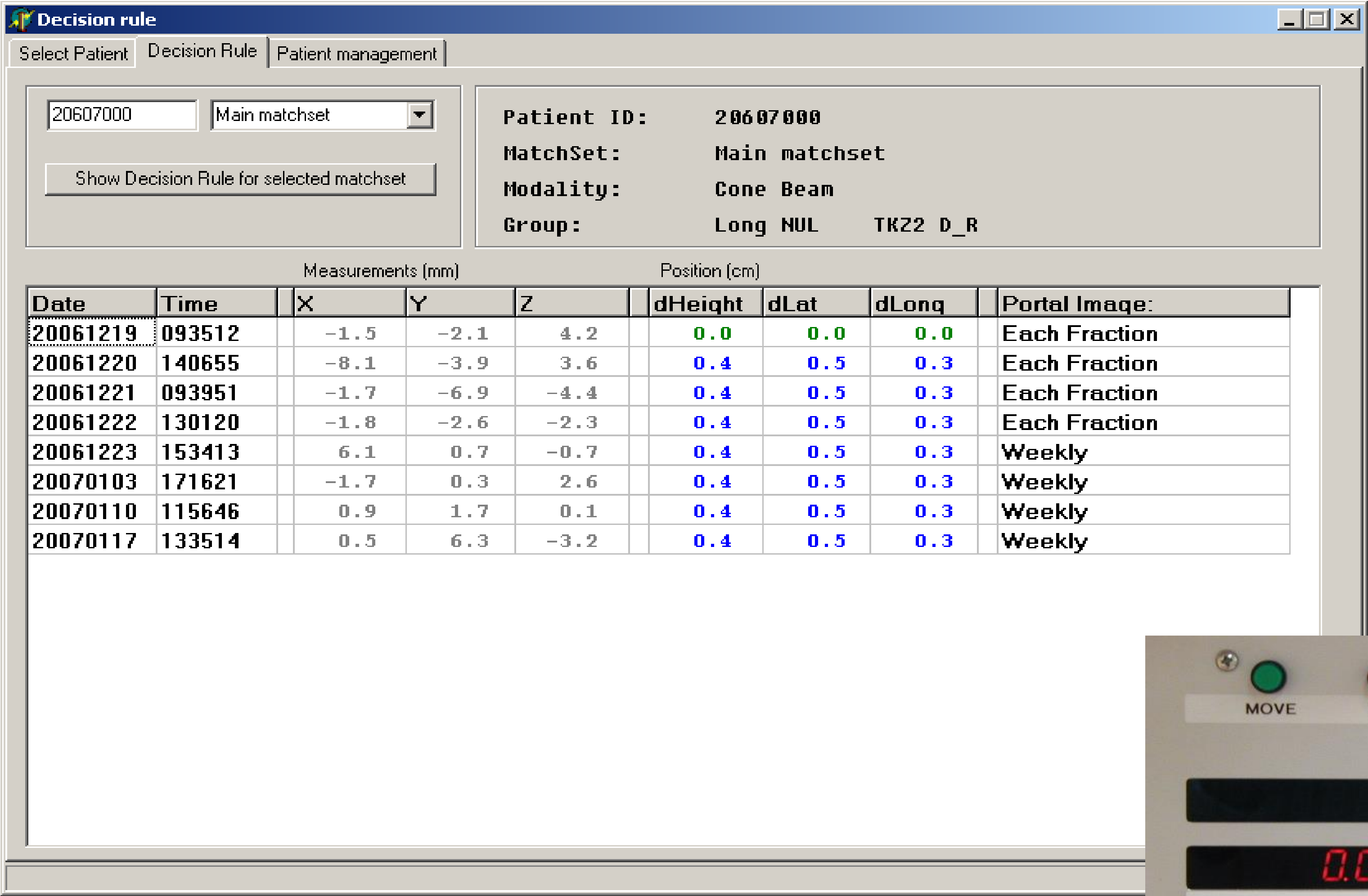
Clinical daily routine



Automatic registration CBCT scan

KV imaging



Decision rule

Select Patient | Decision Rule | Patient management

20607000 | Main matchset

Show Decision Rule for selected matchset

Patient ID: 20607000
MatchSet: Main matchset
Modality: Cone Beam
Group: Long NUL TKZ2 D_R

		Measurements (mm)			Position (cm)			
Date	Time	X	Y	Z	dHeight	dLat	dLong	Portal Image:
20061219	093512	-1.5	-2.1	4.2	0.0	0.0	0.0	Each Fraction
20061220	140655	-8.1	-3.9	3.6	0.4	0.5	0.3	Each Fraction
20061221	093951	-1.7	-6.9	-4.4	0.4	0.5	0.3	Each Fraction
20061222	130120	-1.8	-2.6	-2.3	0.4	0.5	0.3	Each Fraction
20061223	153413	6.1	0.7	-0.7	0.4	0.5	0.3	Weekly
20070103	171621	-1.7	0.3	2.6	0.4	0.5	0.3	Weekly
20070110	115646	0.9	1.7	0.1	0.4	0.5	0.3	Weekly
20070117	133514	0.5	6.3	-3.2	0.4	0.5	0.3	Weekly

Starting clinical use of CBCT

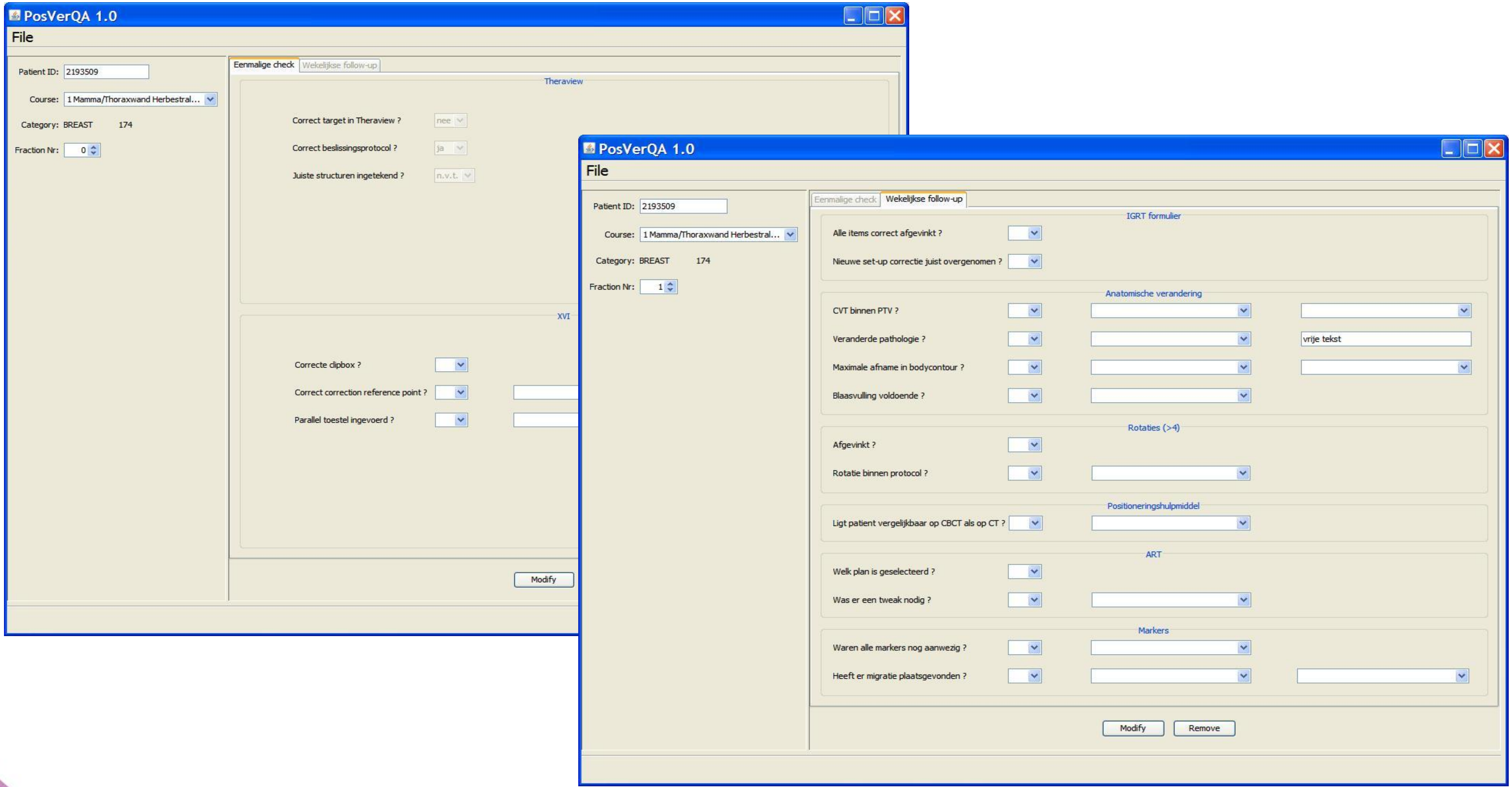
5 RTT's:

- **Track, check patients**
- First contact of changes occur
- Training and education
- Manuals and protocols
- Data collection

@AMC:

- *All linacs equipped with CBCT*
- *All protocols with CBCT*
- *~90% protocols online*

Track & check patients



Starting clinical use of CBCT

5 RTT’s:

- Track, check patients
- **First contact of changes occur**
- Training and education
- Manuals and protocols
- Data collection

Anatomical Changes

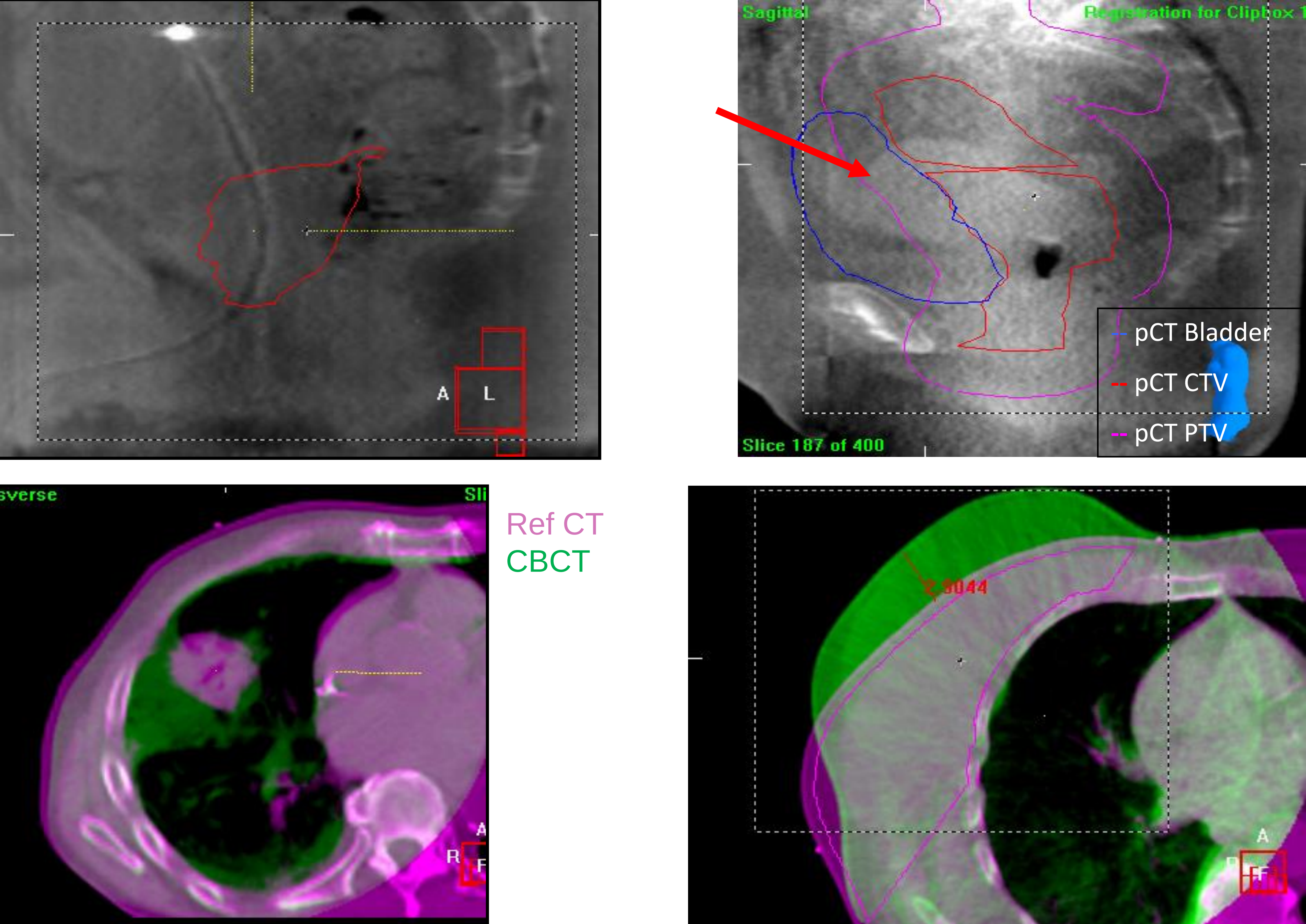
RTT should be trained in:

Recognizing patient changes/anatomical changes that have an influence on radiation treatment: Target coverage and/or dose distribution

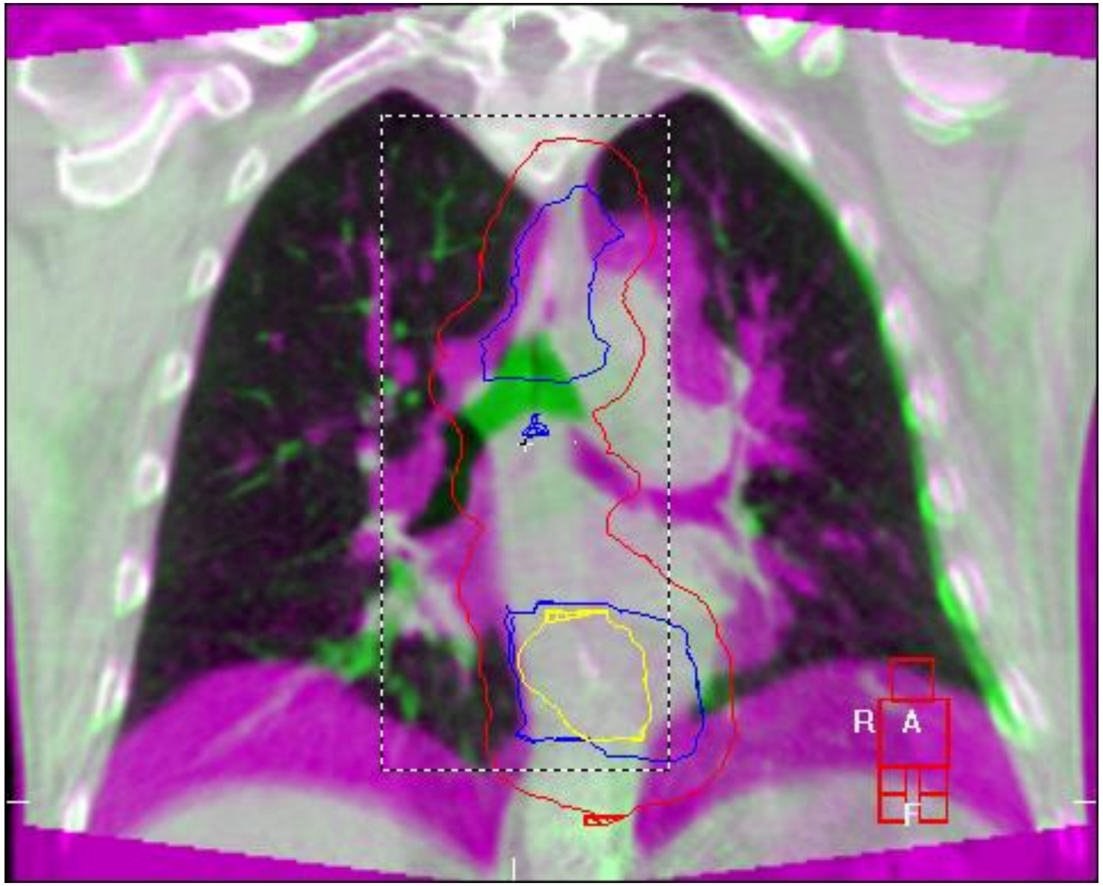
&

RTT should have:

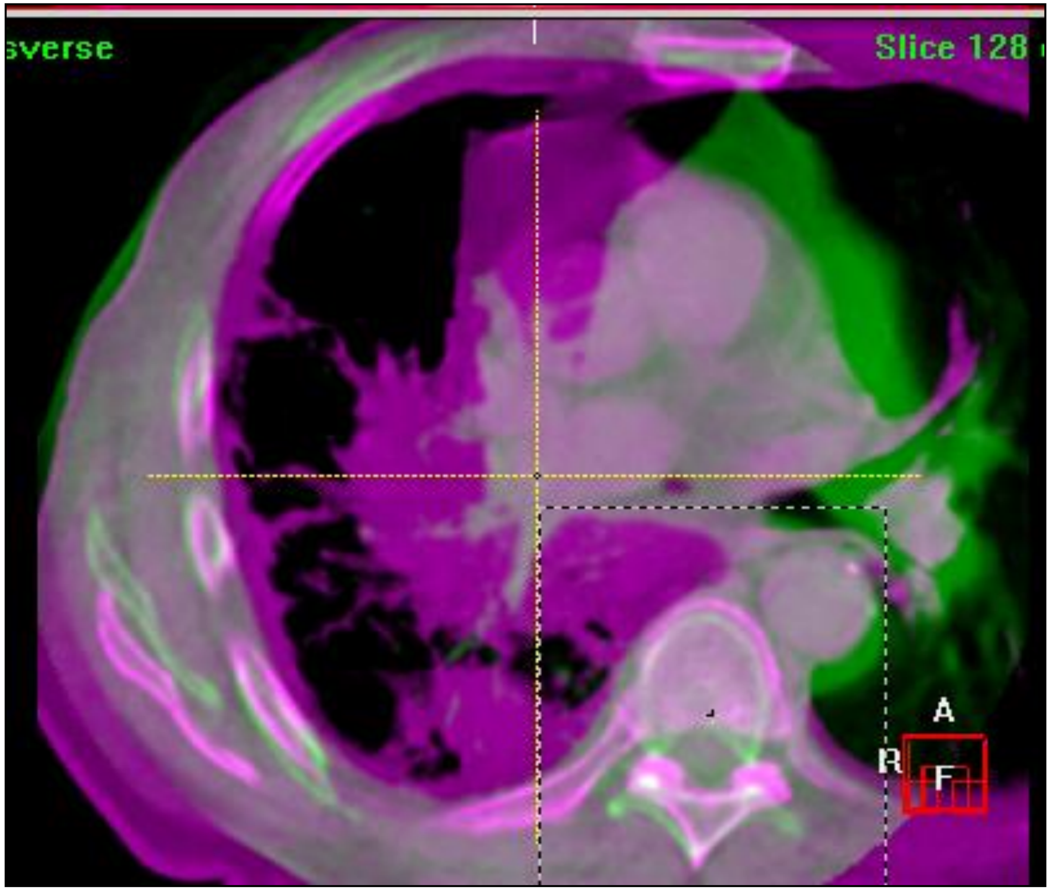
a management system for anatomical changes that flag the changes that may need intervention of some sort.


A
L
Sagittal
Slice 187 of 400
pCT Bladder
pCT CTV
pCT PTV
Ref CT
CBCT
A
R
F

oesophagus

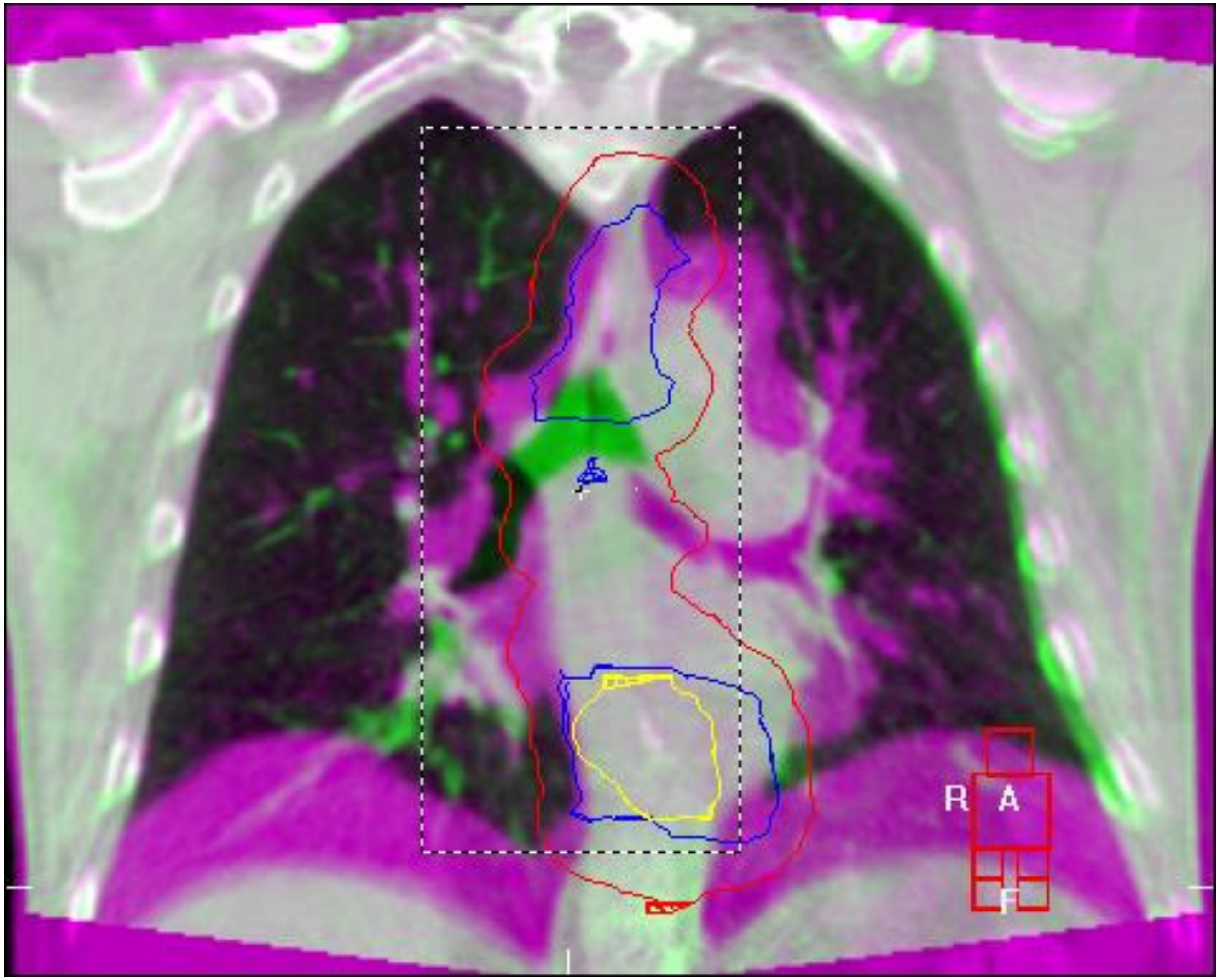


Lung/mediastinum



Purple = Planning CT scan

Green = CBCT scan


R A
F

Anatomical Changes

The important questions:

1: Is the target volume (CTV or GTV) within PTV?

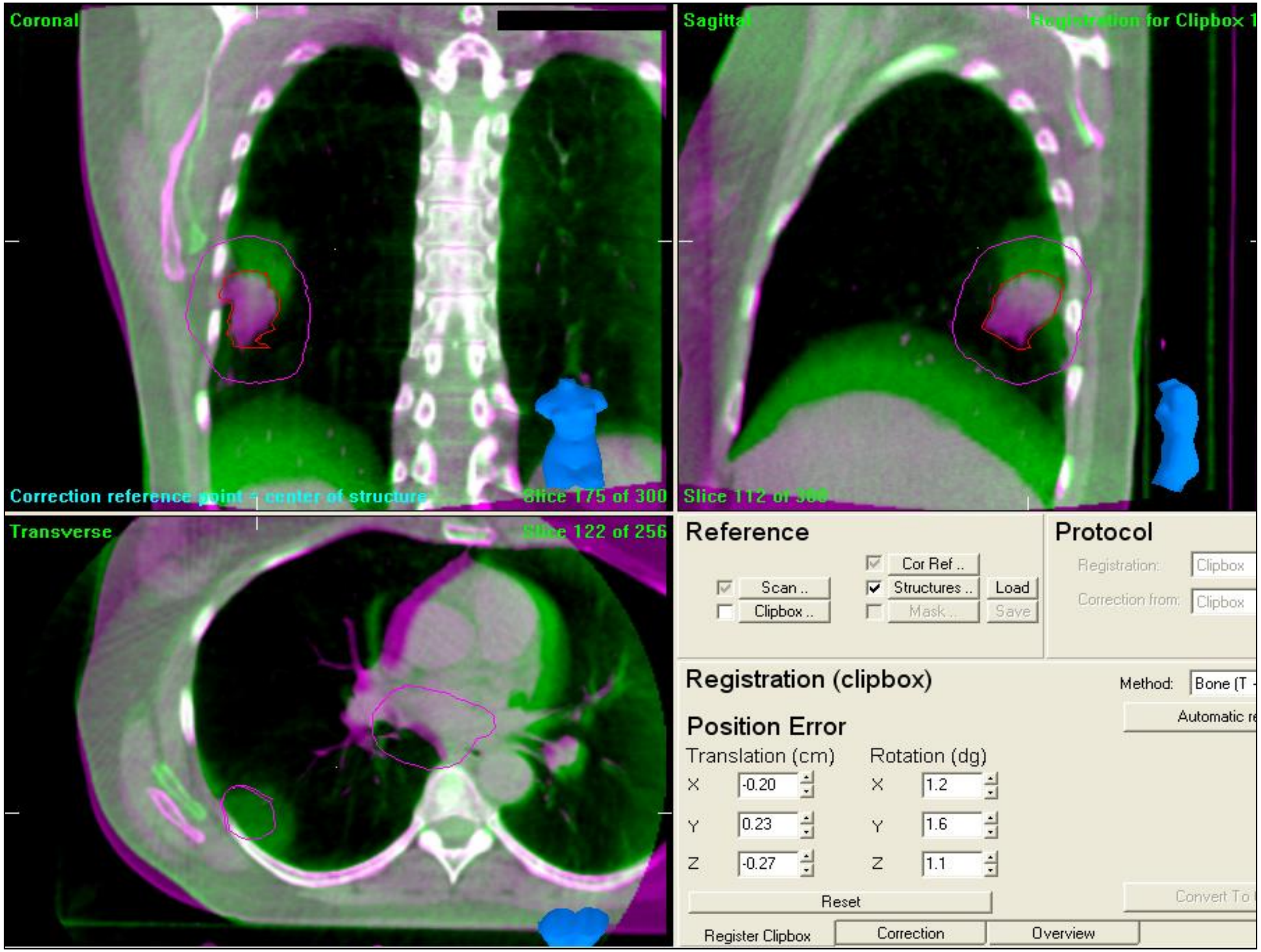
2: Is the dose distribution compromised?

Green	Level green, no action needed.
Yellow	Level yellow, the radiation oncologist is notified by email, but no response is required to continue treatment.
Orange	Level orange, the treating radiation oncologist (or back-up colleague) is informed by email and a response is required before the next fraction.
Red	Level red changes, the radiation oncologist must be consulted immediately before the treatment fraction is allowed to be delivered.

ANTONI VAN LEEUWENHOEK
NEDERLANDS KANKER INSTITUUT

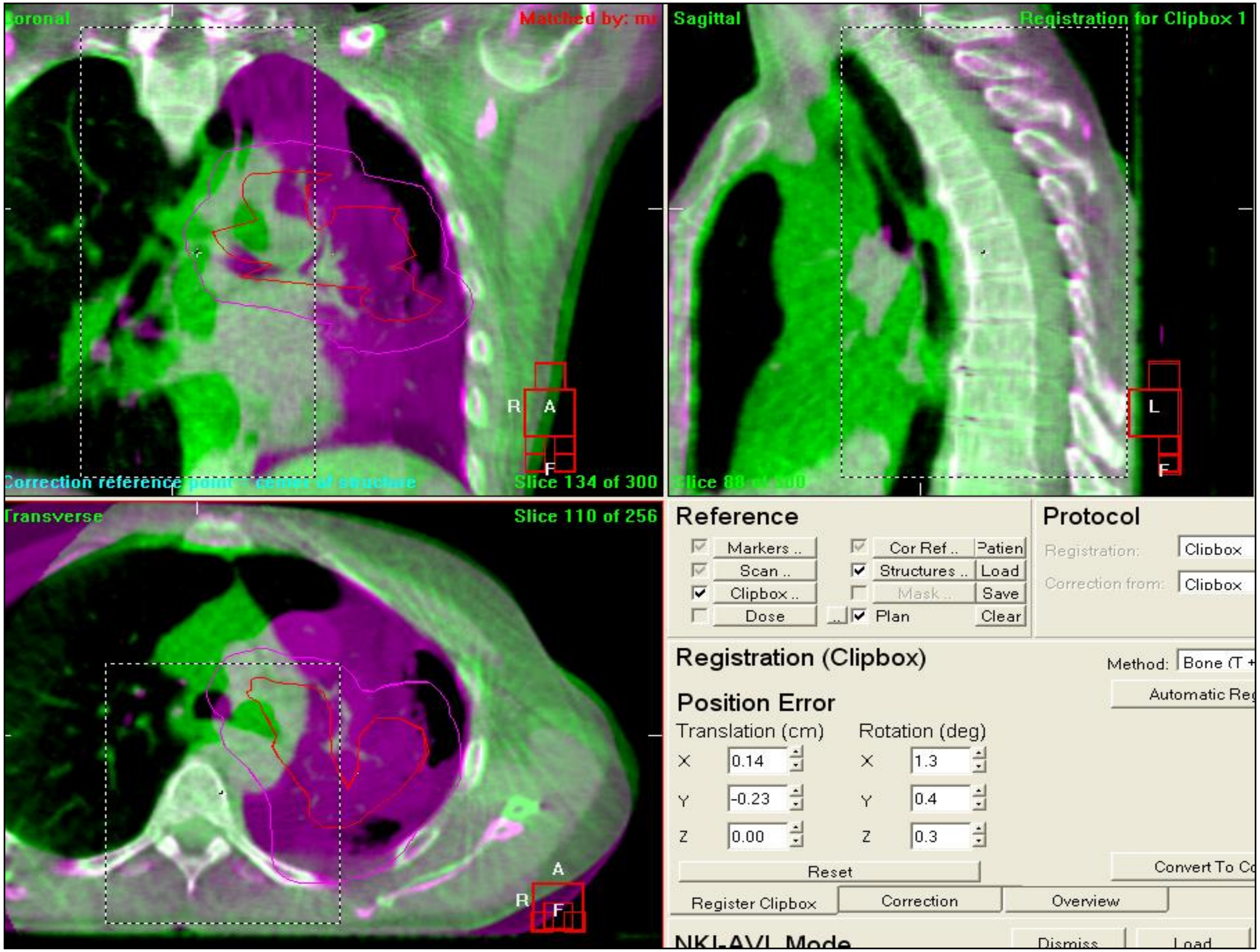
http://www.avl.nl/media/291805/xvi_engelse_protocols_16_7_2014
Kwint Radiother Oncol 2014

Level 1 Tumor shift



GTV is not within PTV

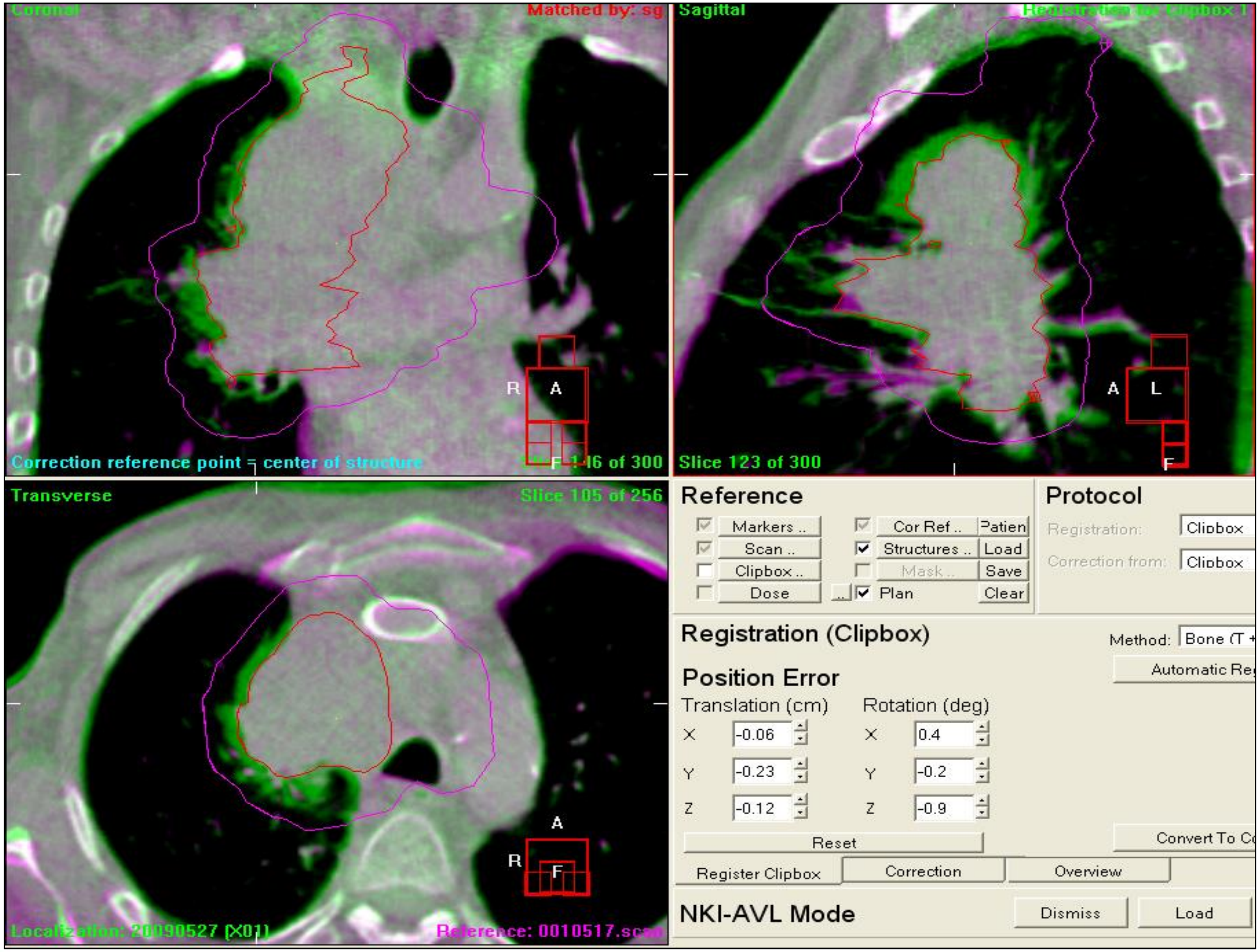
Level 1 Atelectasis resolved



GTV is not within PTV

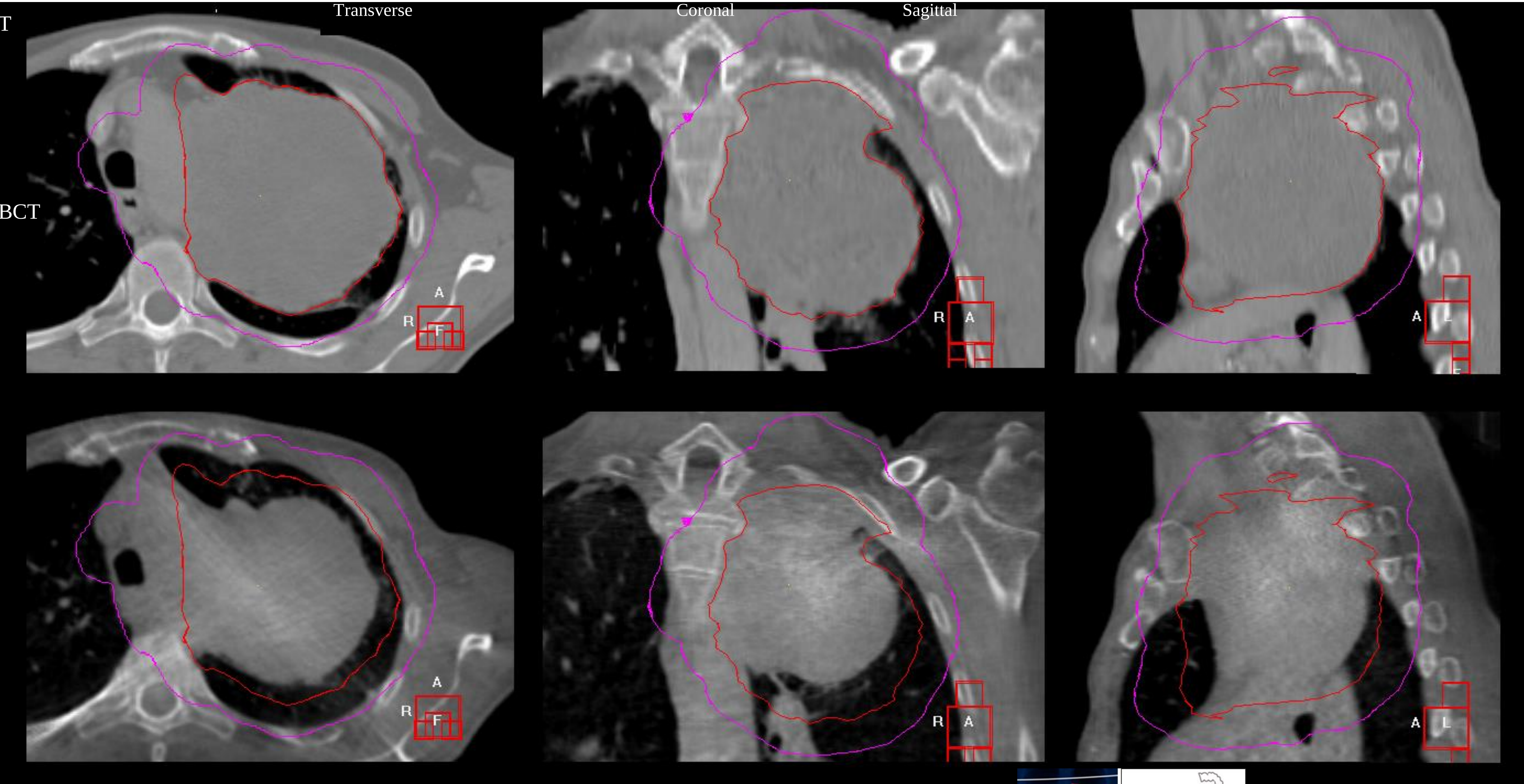
Dose distribution is compromised

Level 2 Tumour growth



GTV is within PTV

Level 3 Tumor regression



Anatomical Changes

Protocol Anatomische Veranderingen

IGART bellen

- Vóór start RT
  - Toename/afname atelectase > 1 cm
  - GTV en/of CTV buiten PTV
- Uiterlijk volgende dag
  - Milde doelgebied progressie
  - Alle veranderingen > 1 cm, denk aan:
    - Doelgebied veranderingen (zoals progressie of regressie)
    - Baseline shift
    - Overige onvoorziene omstandigheden
  - Bij contourveranderingen
    - > 0.5 cm t.h.v SIB gebied bij mamma elektronen SIB
    - > 1 cm kno, mamma en extremiteiten
    - > 2 cm overige locaties

13-10-2016

IGART

Or keep it very simple:

Contact the IGRT-group when

- GTV is outside of PTV
- Anatomical changes > 1 cm

2x year: per site meeting with physicists, radiation oncologists and RTT to discuss images

Communication with physicians?

Clinical use of CBCT

5 RTT's:

- Track, check patients
- First contact of changes occur
- **Training and education**
- Manuals and protocols
- Data collection

Clinical use of CBCT

3 lectures (1h)

- Theraview: Portal imaging system and decision rule management system
- geometrical errors & correction strategies
- CBCT incl artefacts, image quality

1 Workshop (2h) in registration and image evaluation

Clinical use of CBCT

5 RTT's:

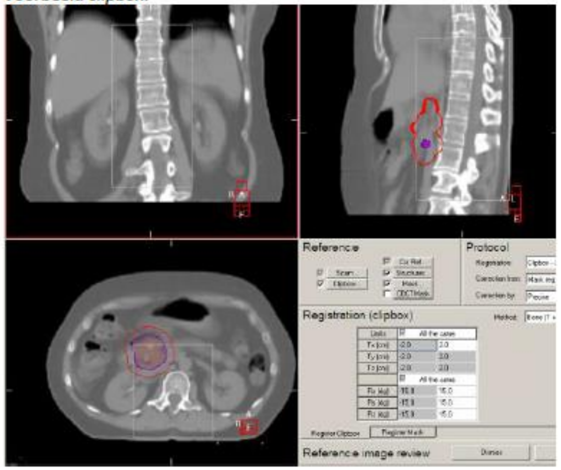
- Track, check patients
- First contact of changes occur
- Training and education
- **Manuals and protocols**
- Data collection

4.3 Pancreas

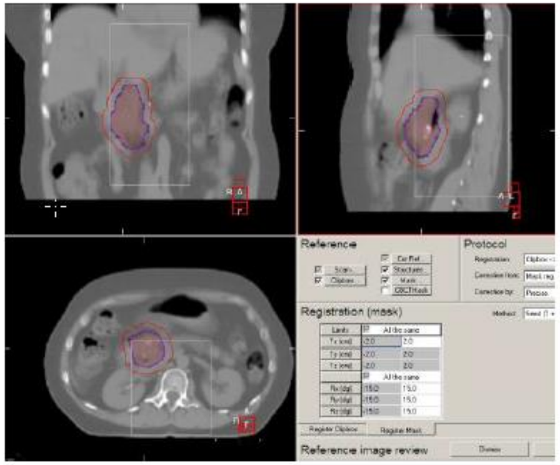
Invoer

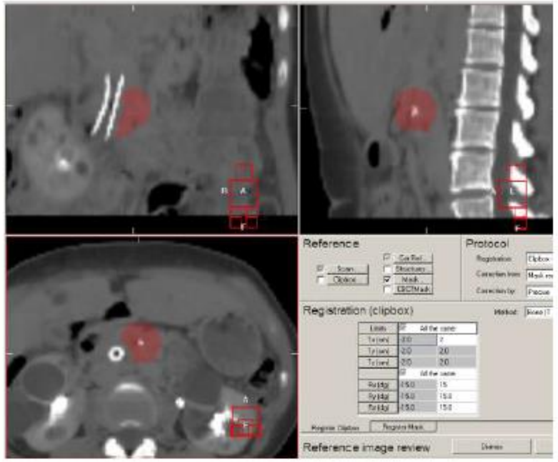
MATCH PARAMETERS		SCAN PARAMETERS	
Structures	GTV, ITV, PTV	**Preset selection**	A1 – A3
Correction ref point	PTV	**Rotatie**	-180° → 180°
Registration	Dual registration	**Gantry speed**	Normaal
Method	Clipbox : Bone (T + R) Mask : Seed/Greyvalue (T + R)	**Detectorstand**	M
Registr. Clipbox	1,0 cm, 4°	**Filter**	F1
Registr. Mask	0,1 cm, 4°	**Collimator**	M20

Voorbeeld clipbox:



- De clipbox omvat de wervels, gebruik in cranio-caudale richting het hele FOV.





Het masker wordt gemaakt van de structuur 'ITV' zonder marge. Zie uitleg voor het maken van het masker de IGART Handleiding op KWADRAET. Wanneer de patiënt ook een stent heeft dan via de optie 'empty' zelf een masker maken van alleen de markers.

Uitvoer

Wanneer er minder dan 3 markers geïmplanteerd zijn kan het algoritme moeite hebben met het definiëren van de rotaties. Voorbereiden als automatische match, maar in de praktijk zal dit een manual match worden waarbij de rotaties van de botmatch worden gebruikt.
Korte dikke stents zijn niet altijd betrouwbaar, is uit eigen onderzoek gebleken. Deze kunnen nog wel eens van vorm veranderen en/of 'uitzakken', *fig1*. Let daarom na de match ook altijd op omgevende structuren zoals de positie van de nieren en/of de leverrand.
Mocht de automatische stentmatch niet lukken dan kan er manual gematcht worden vanaf de botmatch. IGART zal deze manuele match uitvoeren en indien mogelijk overdragen aan het toestel met een werkinstructie, te vinden in het tabblad IGART in de navigator in Mosaiq. Indien de manuele match niet overdraagbaar is zal deze patiënt door IGART gematcht worden.

Fig1. Let op verschil in positie van stent tov markers, en vormverandering van de stent.

Stent week 1

stent week 4

Clinical use of CBCT

5 RTT's:

- Track, check patients
- First contact of changes occur
- Training and education
- Manuals and protocols
- **Data collection**

→ These RTT's also work in the clinic

Implementing IG&ART

Research department → Clinic

Multi disciplinary group to implement, research and evaluate IGRT protocols:

- Physicists
- Physicians
- RTT's
- Software developers
- Post-docs/PhD students

Introducing IGRT

RTT **:**

Evaluation of bulk of data: for example

- Inter fraction set up variability
- Intra fraction stability
- Organ motion or deformation
- Testing new (software) tools

Designing (logistics of) new protocols

Training and education in house

Protocols and manuals

Clinic!

Implementing IG&ART

AvL

9 + 2 linacs:

4 teams

2 dedicated RTT / team

1 focus treatment site / team

AMC

6 linacs, 2 teams

Daily Clinical Routine

Quality Assurance

Performed by the RTT:

Daily: (15 minutes timeslot)

Laser alignment

MV Isocenter

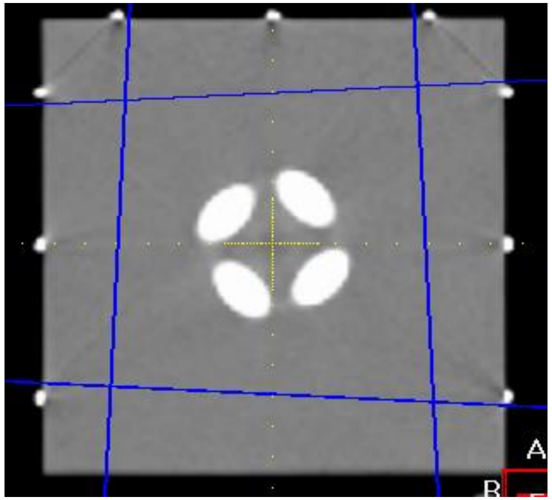
Light field of linac

kV Isocenter

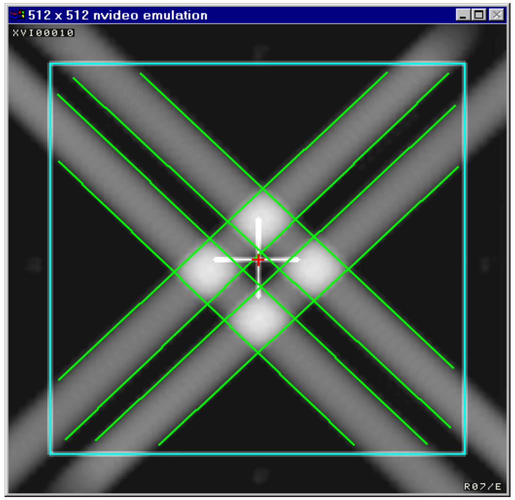
Additional:

MV dosimetry: 2 per week

kV dosimetry: 1 a month

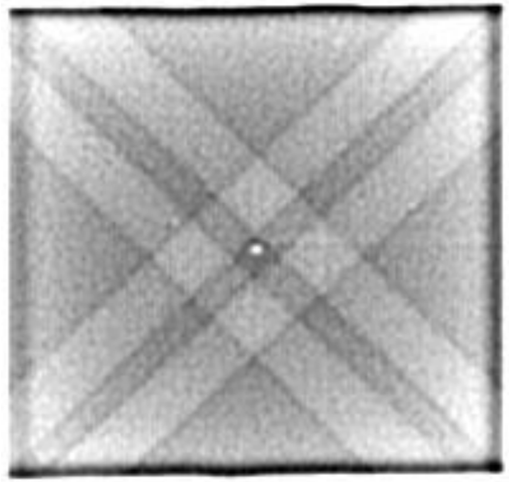


Reference scan



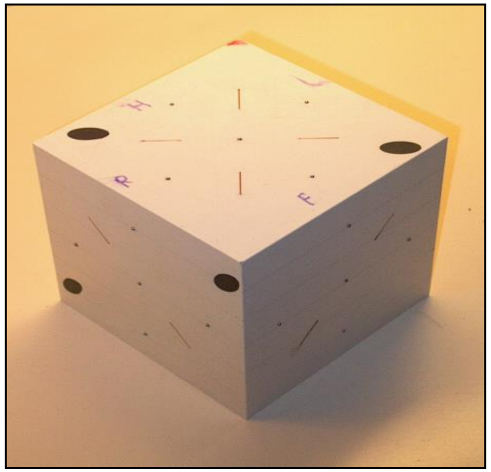
DRR

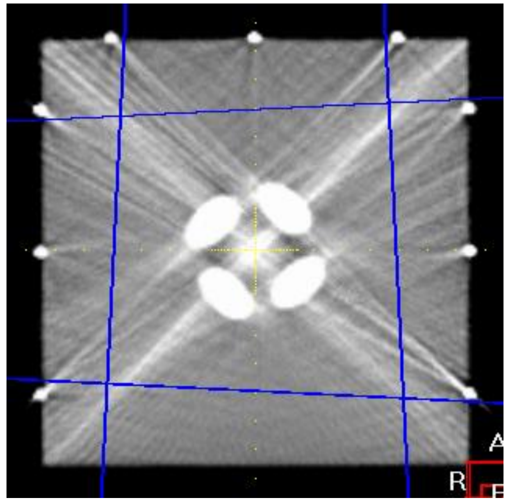
Match



MV image

Match



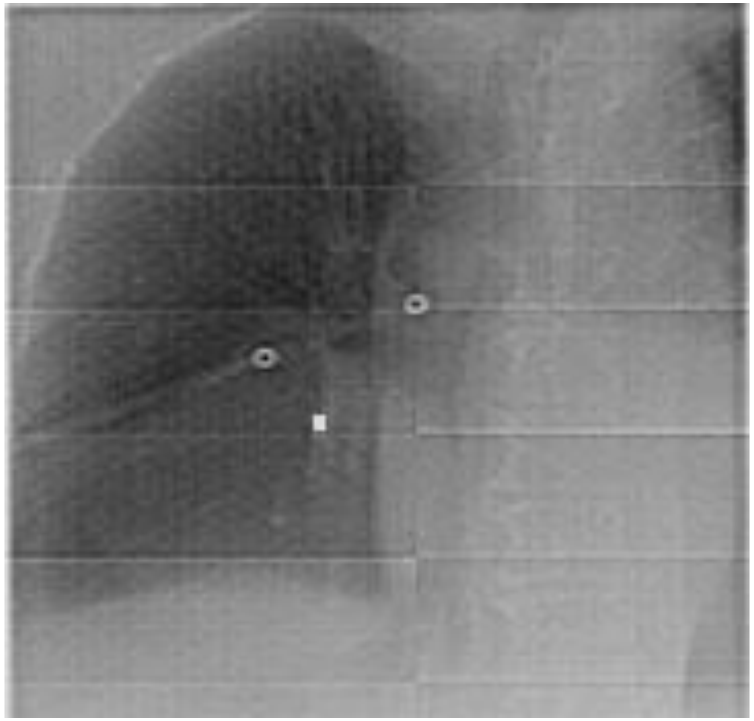


CBCT scan

Patient Support

Support patients and their relatives and friends:

During RT in RTT's working area for support and transparency



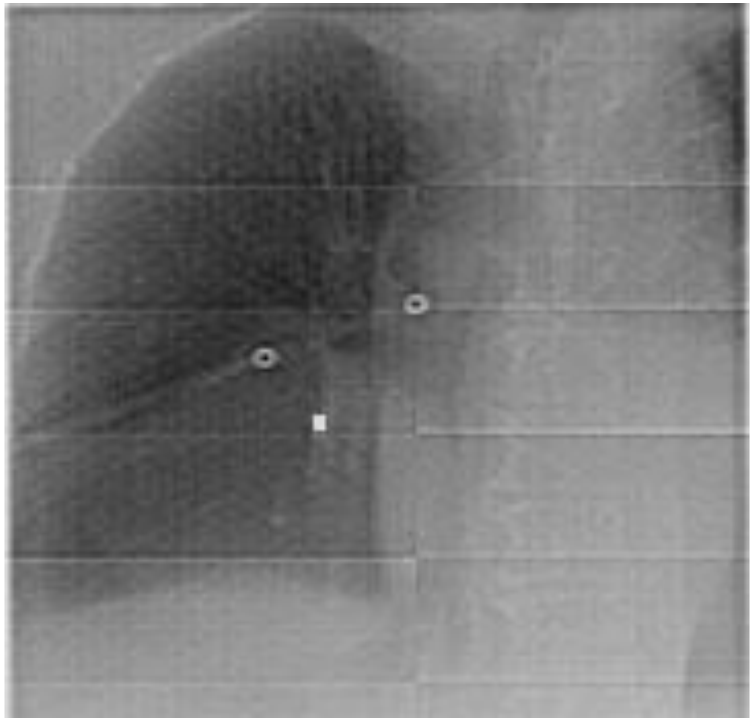
Portal image

CBCT image

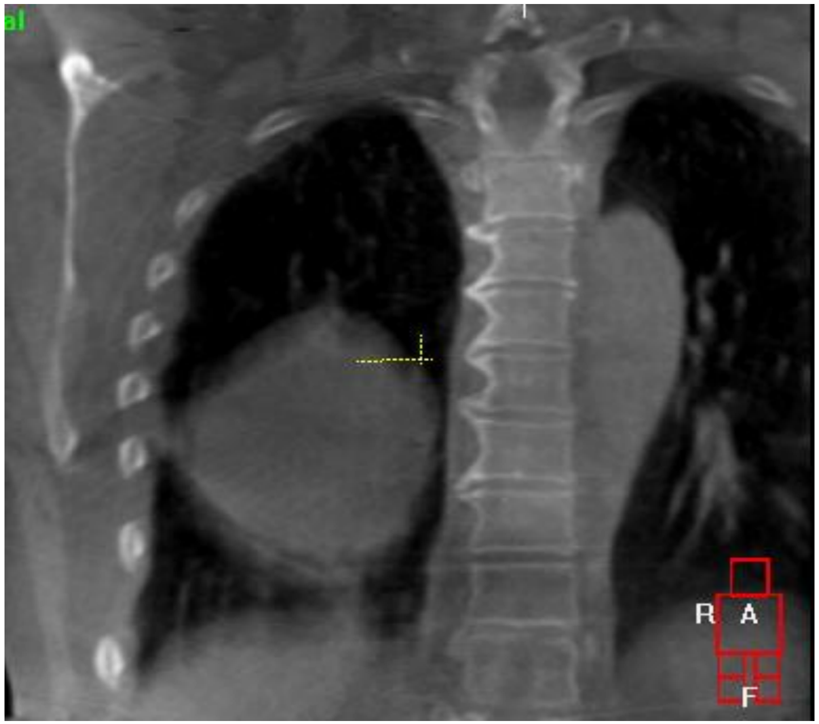
Patient Support

Support patients and their relatives and friends:

During RT in RTT's working area for support and transparency



Portal image



CBCT image

Time Slots

Time-slot **patient treatment preparation :**

Same for all imaging protocols:

Radiotherapy management (mosaiq): treatment and scanning

Imaging modality (CBCT): registration

Decision rules management

Time Slots at the linac

Time-slot for patient treatment delivery

Learning curve:

1. **Add 5 minutes compared to portal imaging, same protocol.**
2. Approx. same time introduction IMRT, adding more time because of more gantry angles and segments
3. Development of new soft tissue IGRT protocols, nothing to compare with.
4. Using rotational treatment is reducing beam delivery time.

Time Slots at the linac

Time-slot for patient treatment delivery

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Time Slots at the linac

Time-slot for patient treatment delivery

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4. **Using rotational treatment is reducing beam delivery time.**

Protocols

Typical Protocol

Steps of IGRT on the treatment machine using CBCT

1. Green-purple overview: entire FOV visible
2. Registration in 6 DoF
3. Evaluation of registration, did the algorithm work?
4. Evaluation of anatomy:
   - GTV/CTV within PTV?
   - no anatomical changes compromising dose distribution?
   - Rotations within threshold?
5. Evaluation of the correction

Fr.	Datum	PTV?		Rotatie		(cm)	(cm)
		JA	NEE	<4°	≥4°		
1		☐	☐	☐	☐		
2		☐	☐	☐	☐		
3		☐	☐	☐	☐		
4		☐	☐	☐	☐		
5		☐	☐	☐	☐		

Modern IGRT Protocols

Lung:	4D dual registration
Bladder:	Library of plans

IGRT 4D dual registration Lung

Hypo fractionated lung, 3x 18 Gy, On-line tumor match

Aligning the patient

First pre-treatment CBCT scan

Registration

Correction with automatic table shift

Second pre-treatment CBCT scan

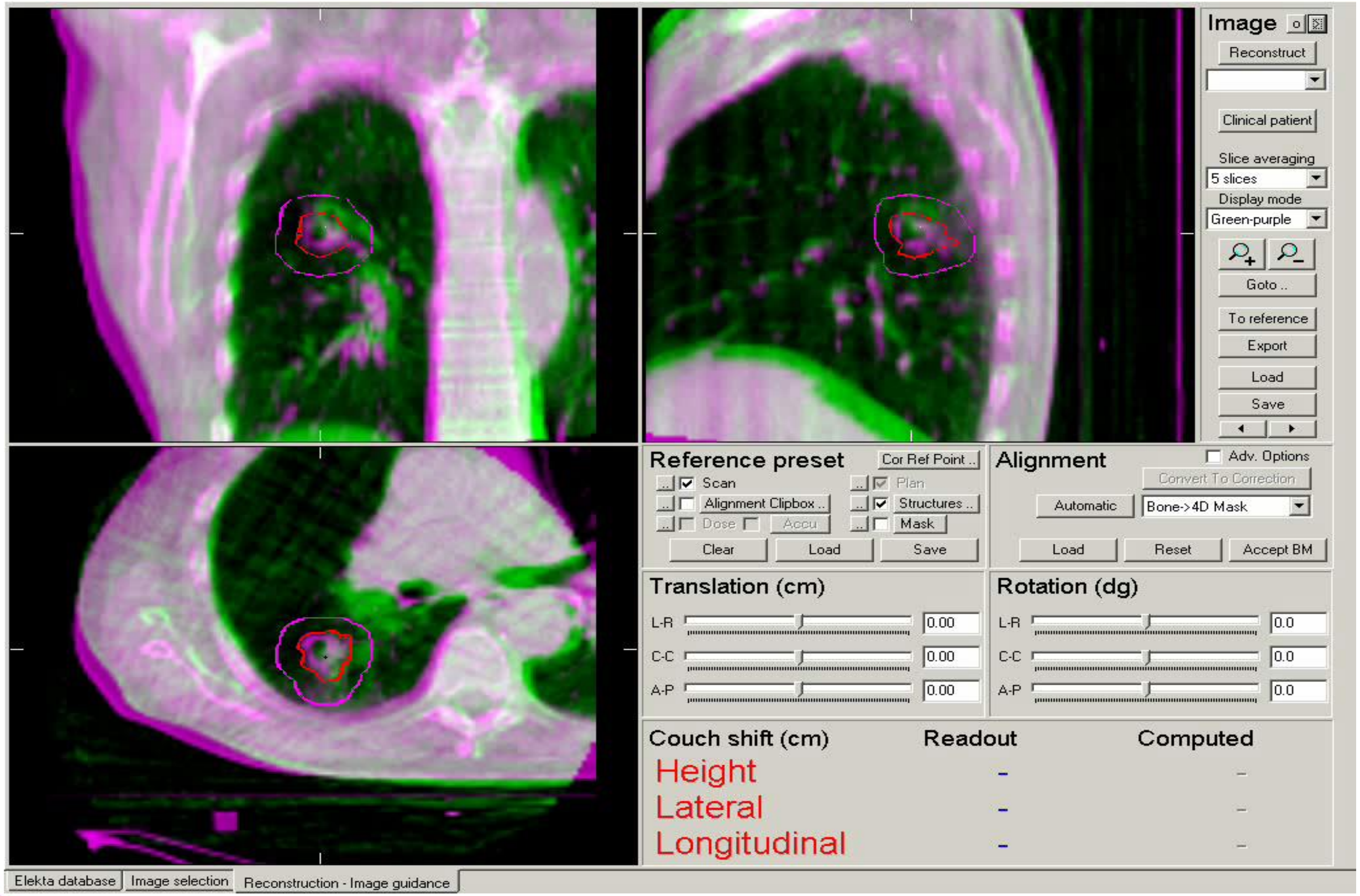
Evaluation CBCT scan

Beam delivery arc therapy

Post treatment CBCT scan

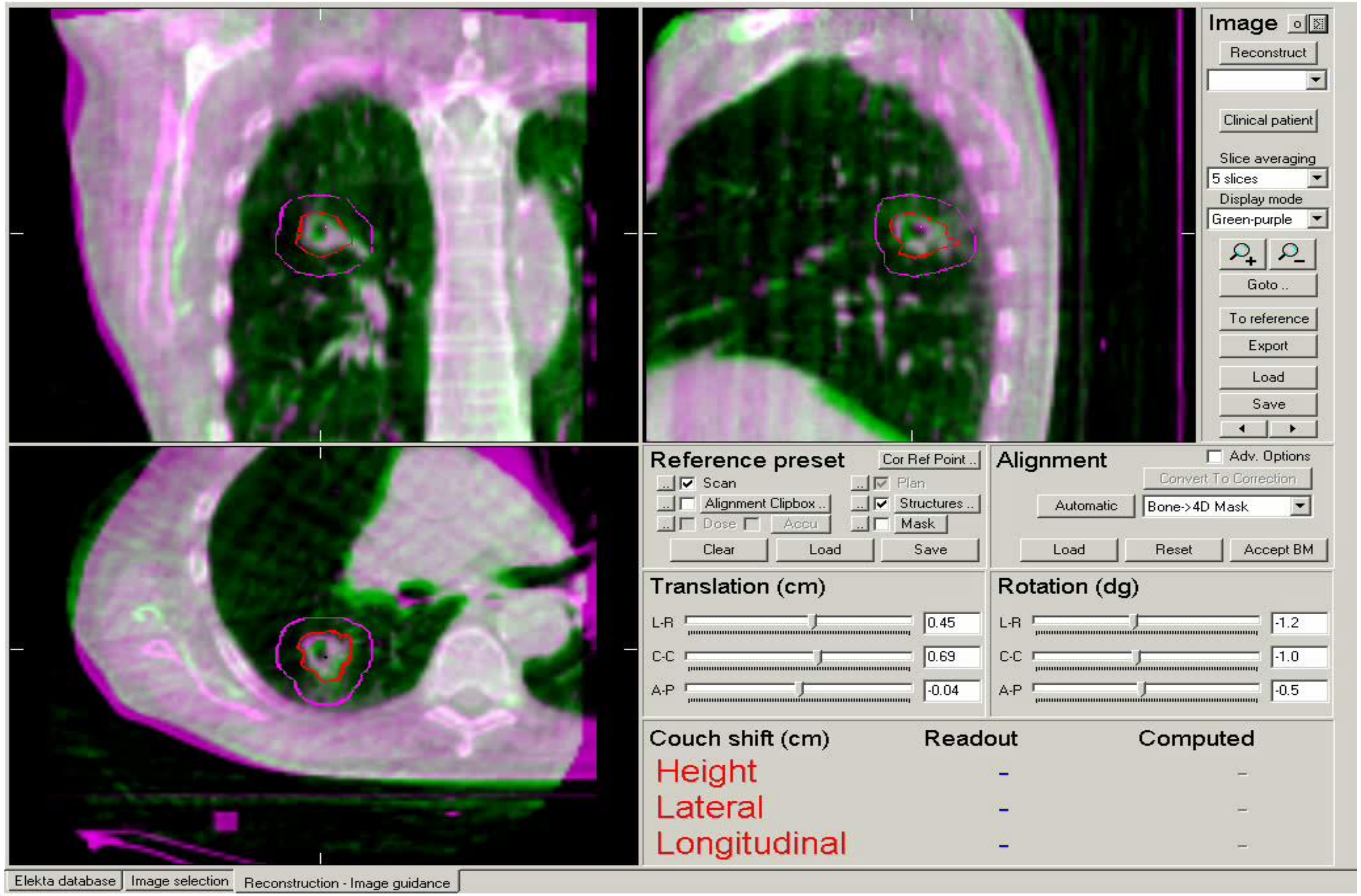
Timeslot of 30 minutes

IGRT 4D dual registration Lung



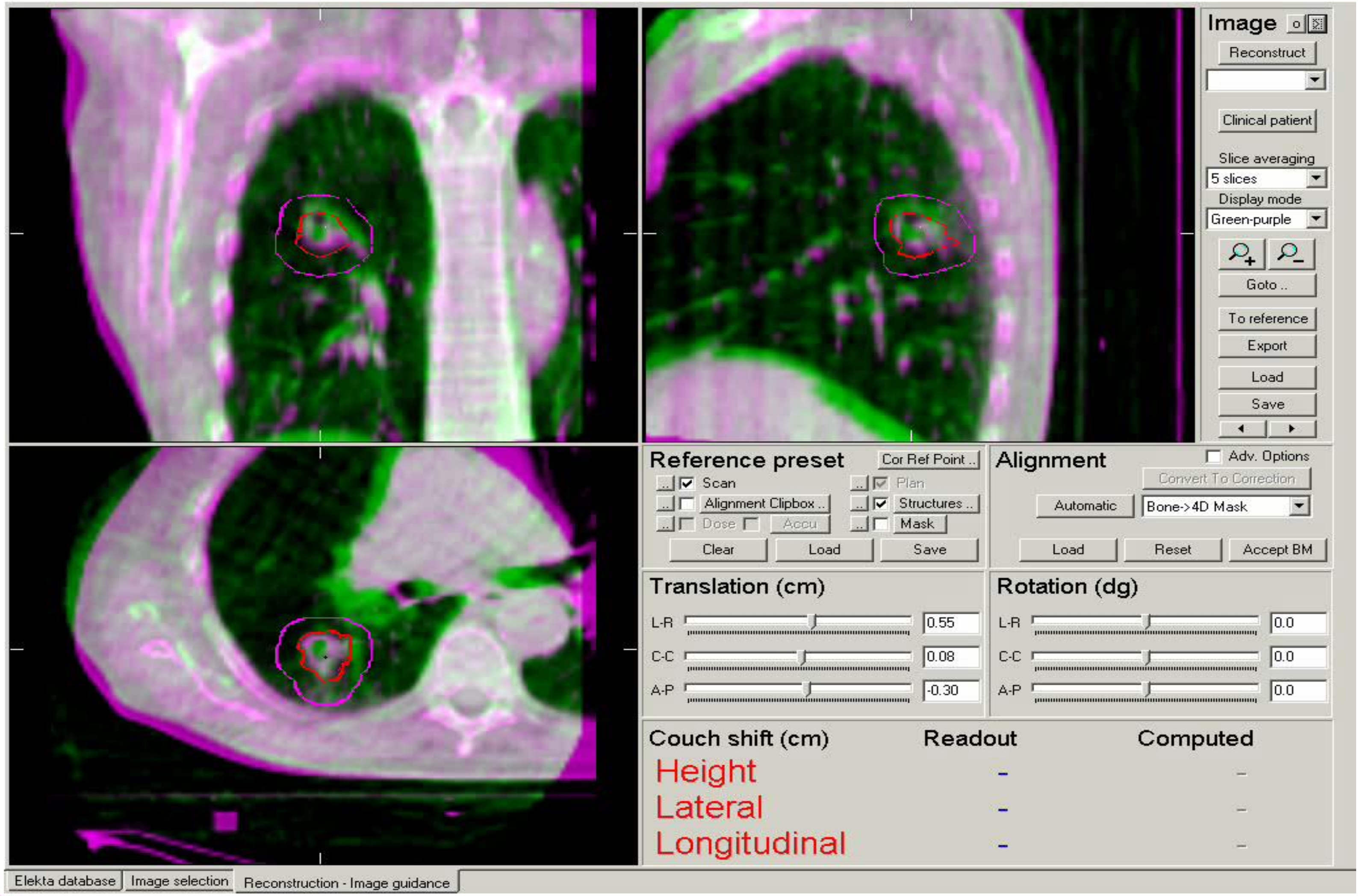
first scan

IGRT 4D dual registration Lung



matched on bone

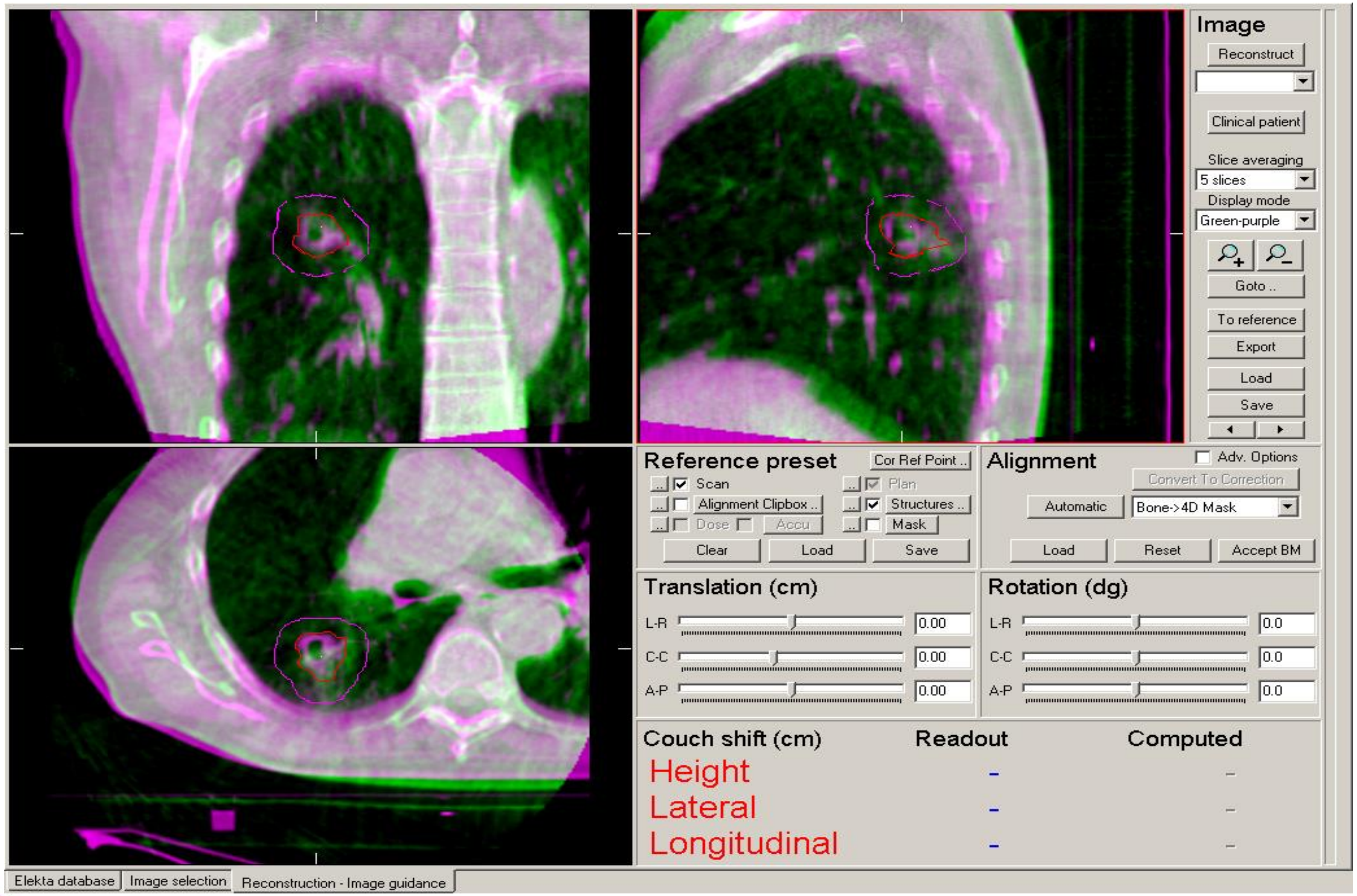
IGRT 4D dual registration Lung



matched on tumor

Critical structure avoidance

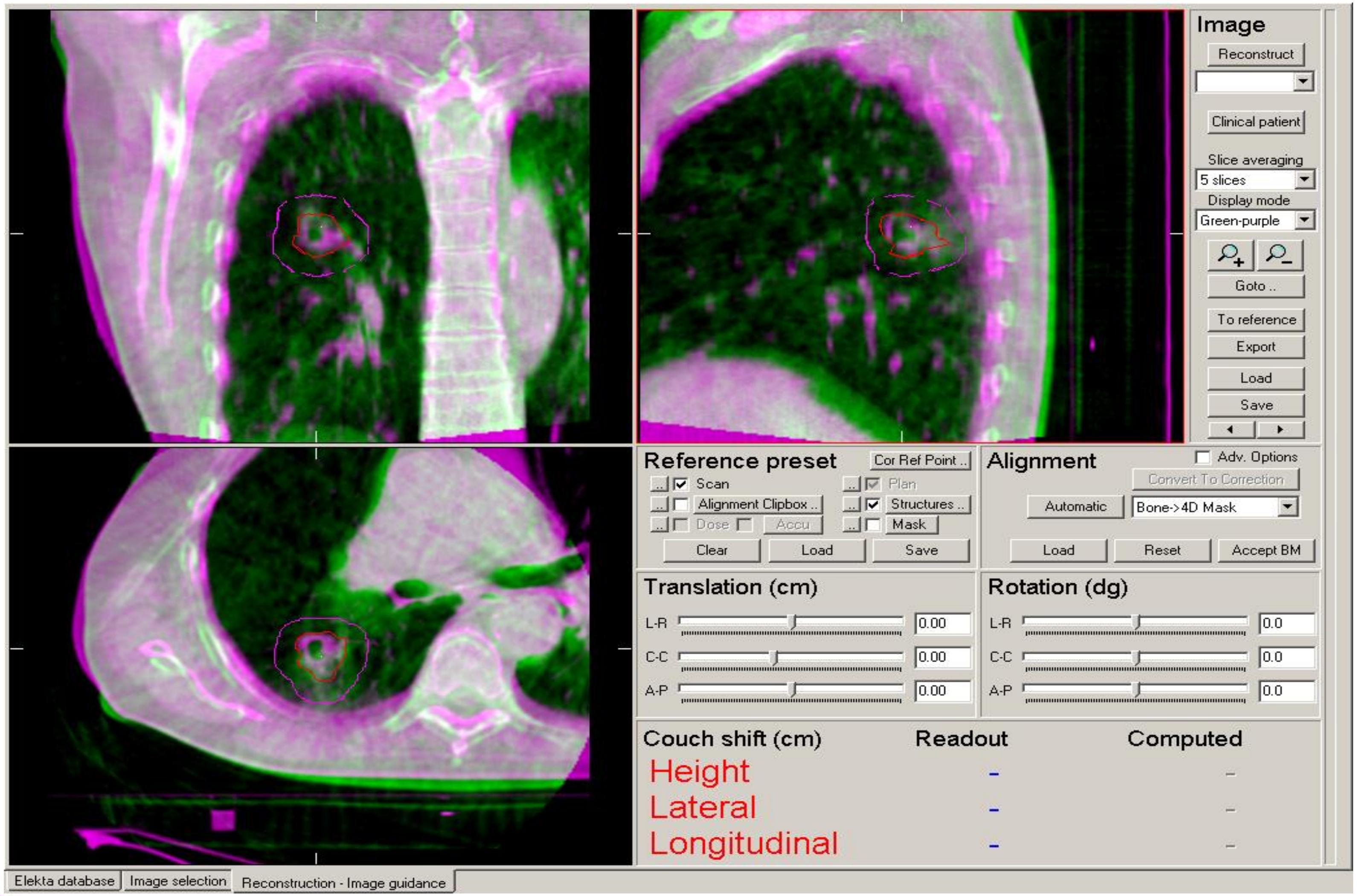
IGRT 4D dual registration Lung



prior to treatment

interfraction

IGRT 4D dual registration Lung



after treatment

Intra fraction

Stereotaxie - Long

Patiëntnummer:	
Patiëntnaam:	
Course:	2
Max. baselineshift R (cm):	0,5
Advies voor CB H1 bij FFF:	Geen FFF

Gegevens opslaan

Initialen laboranten:	lwr
Datum:	12 oktober 2016

NB1: BOTMATCH EN TUMORMATCH VOOR CO
NB2: TUMOR MATCHEN ZONDER ROTATIES (G
Indien tumorvector Tv kleiner of gelijk is aan 0,25 c

Moment	CBCT	Clipbox (T&R) (cm)			Mask (T) (cm)			Correctable (cm)			Baselineshift R (cm)	Tumorvector Tv (cm)
		X	Y	Z	X	Y	Z	X	Y	Z		
Vooraf	V1	-0,05	0,18	0,05	-0,03	0,26	0,05	-0,03	0,26	0,05	0,08	0,27
Vooraf	V2	-0,02	-0,05	-0,04	0,02	0,02	-0,01	0,02	0,02	-0,01	0,09	0,03
Vooraf	V3											
Vooraf	V4											
Vooraf	V5											
Halverwege	H1											
Halverwege	H2											
Halverwege	H3											
Halverwege	H4											
Halverwege	H5											
Eind	N1	-0,03	-0,04	-0,02	-0,05	0,04	-0,03	-0,05	0,04	-0,03	0,08	0,07

	X
H1tumor-Ref	
N1tumor-Ref	-0,07

Overview

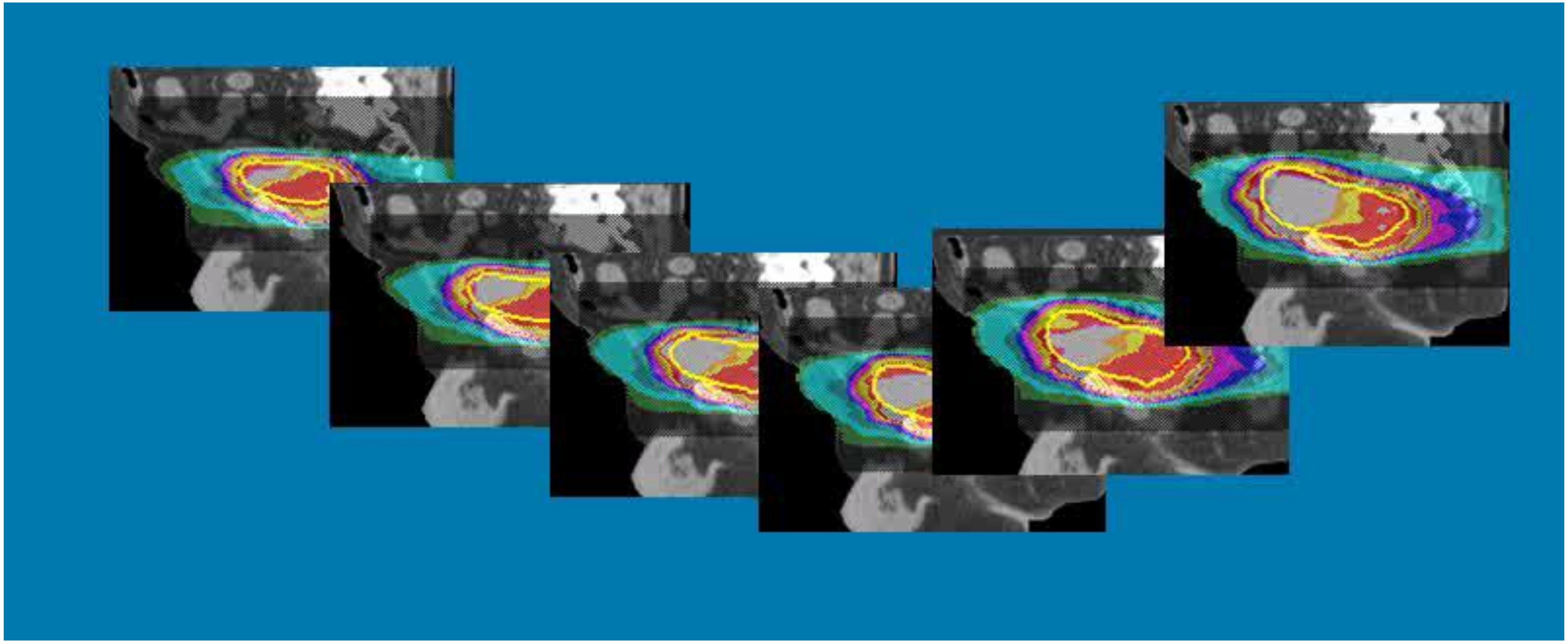
Current analysis data

	Tx (cm)	Ty (cm)	Tz (cm)	Rx (deg)	Ry (deg)	Rz (deg)
Clipbox	-0.24	0.23	-0.16	2.8	0.2	0.2
Mask	-0.18	-0.63	0.72	2.8	0.2	0.2
Correctable	-0.18	-0.58	0.72	0.0	0.0	0.0

Let op!
Rotaties moeten gelijk zijn!

ART: plan selection

Dealing with daily volume changes



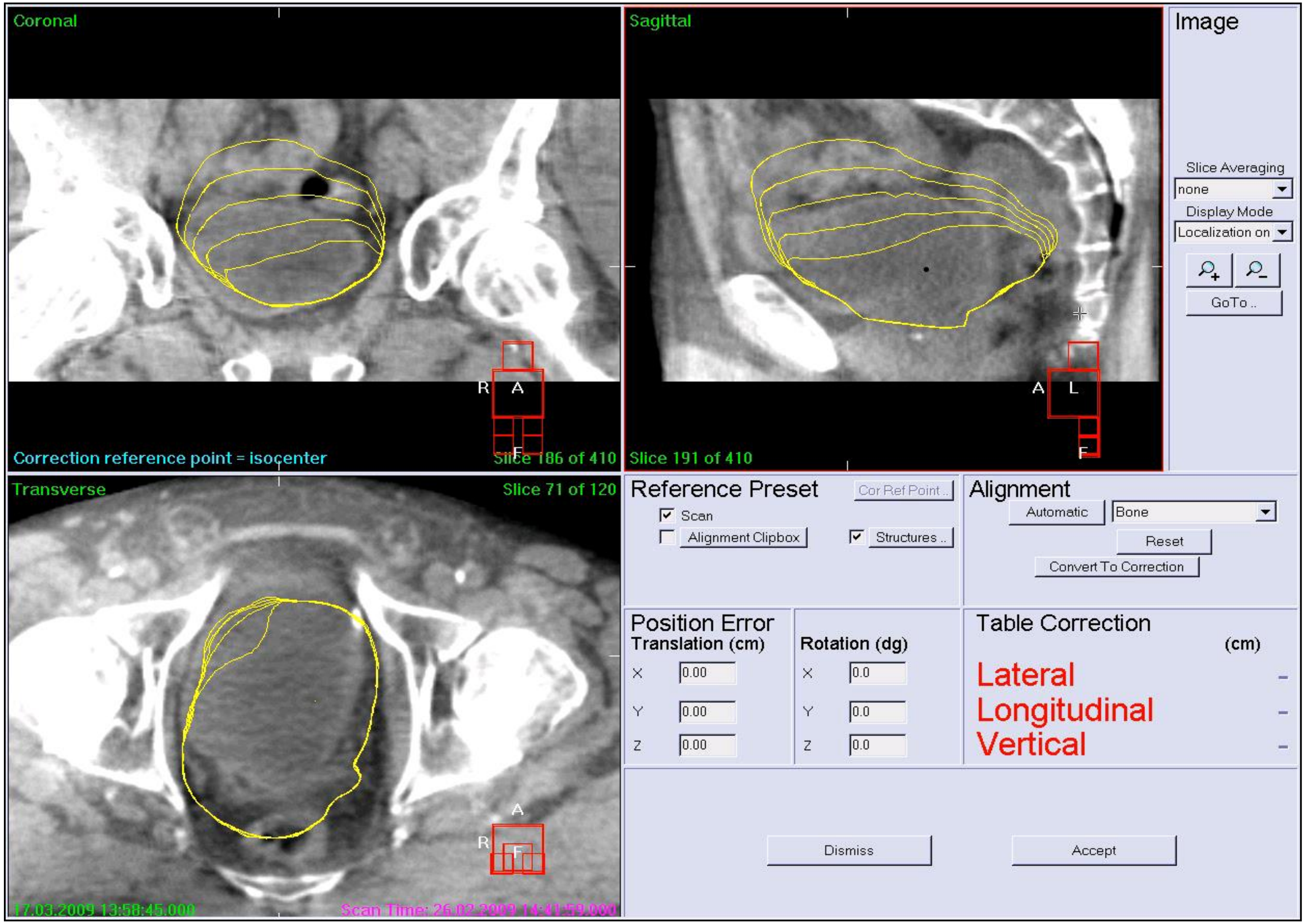
Courtesy Danny Schuring,
Catharina Ziekenhuis, Einhoven

Treatment Procedure

- Lipiodol demarcation of tumor by urologist
- Full & empty bladder CT scan
- Instructions to ensure full bladder
  - Good hydration prior to treatment
  - Empty bladder 1 hr before treatment
  - Drink 2 – 3 glasses
  - Continuous steering during treatment
- Cone-beam CT at start of treatment
- Selection of “plan of the day” based on bladder filling

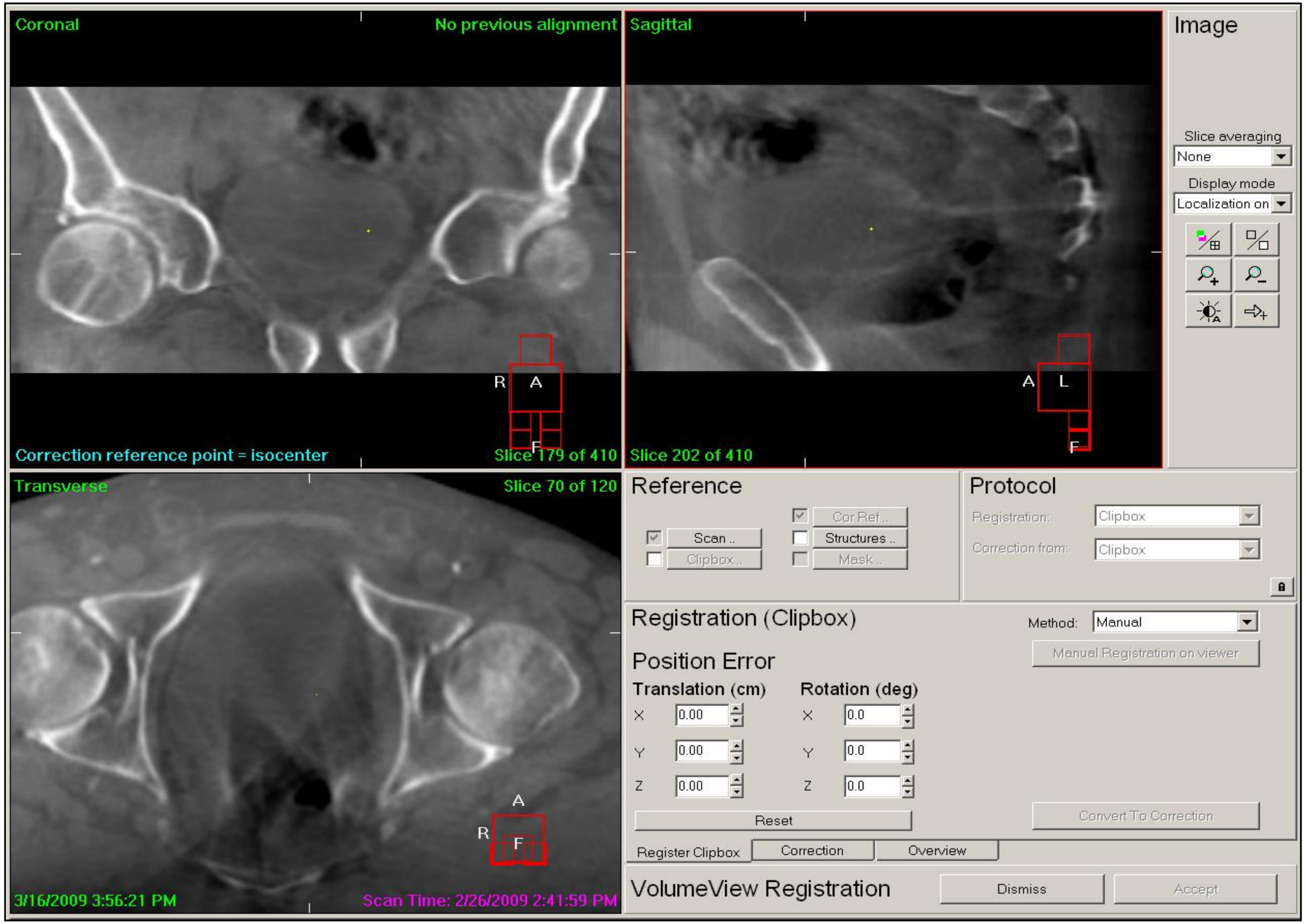
Courtesy Danny Schuring

Matching Procedure



Courtesy Danny Schuring

XVI quality



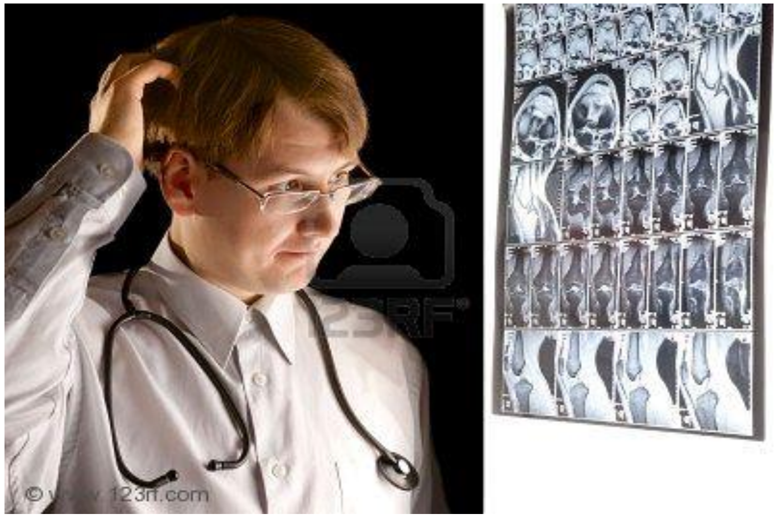
Courtesy Danny Schuring

Daily plan selection

- Daily plan selection at linac

  ⇓

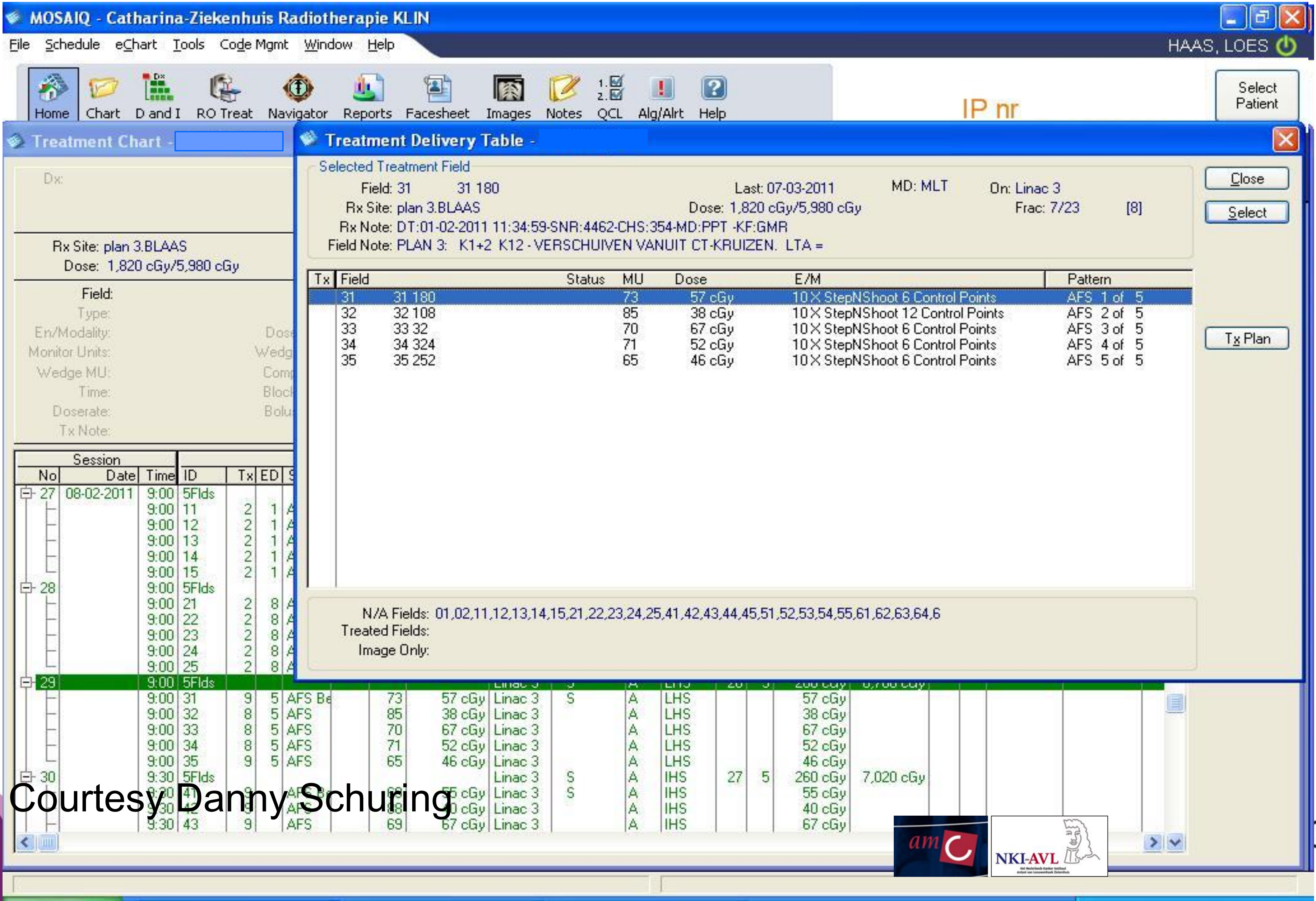
  Shift in responsibilities!



- Current practice: selection by physicist or specialized technologist

Courtesy Danny Schuring

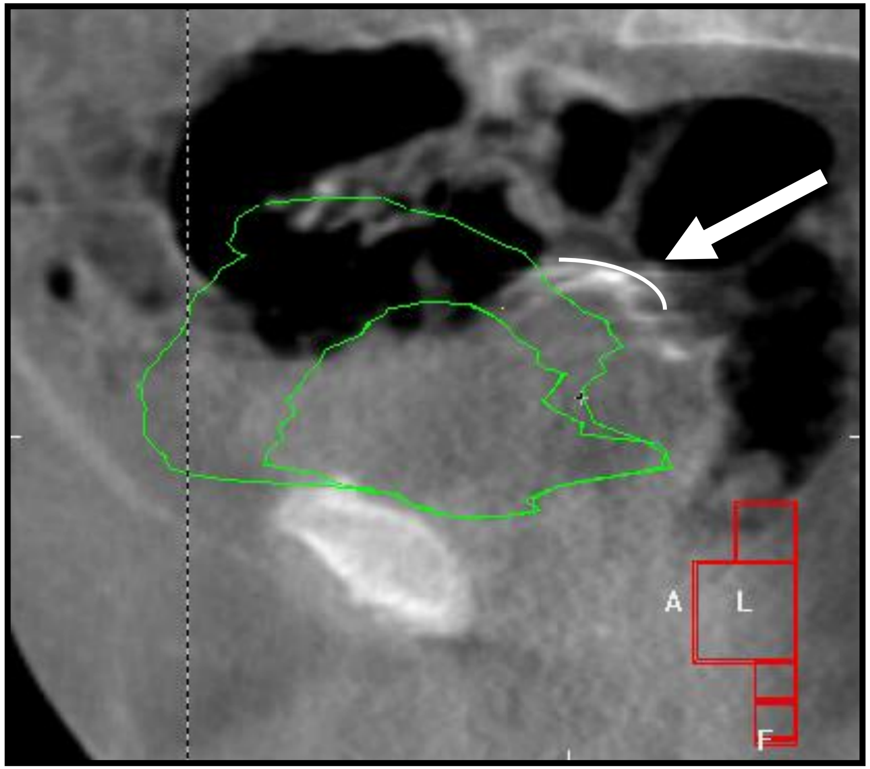
Plan selection in Mosaiq



Courtesy Danny Schuring

3 van de 18 scans:

Groen: Bladder 0%, 100%



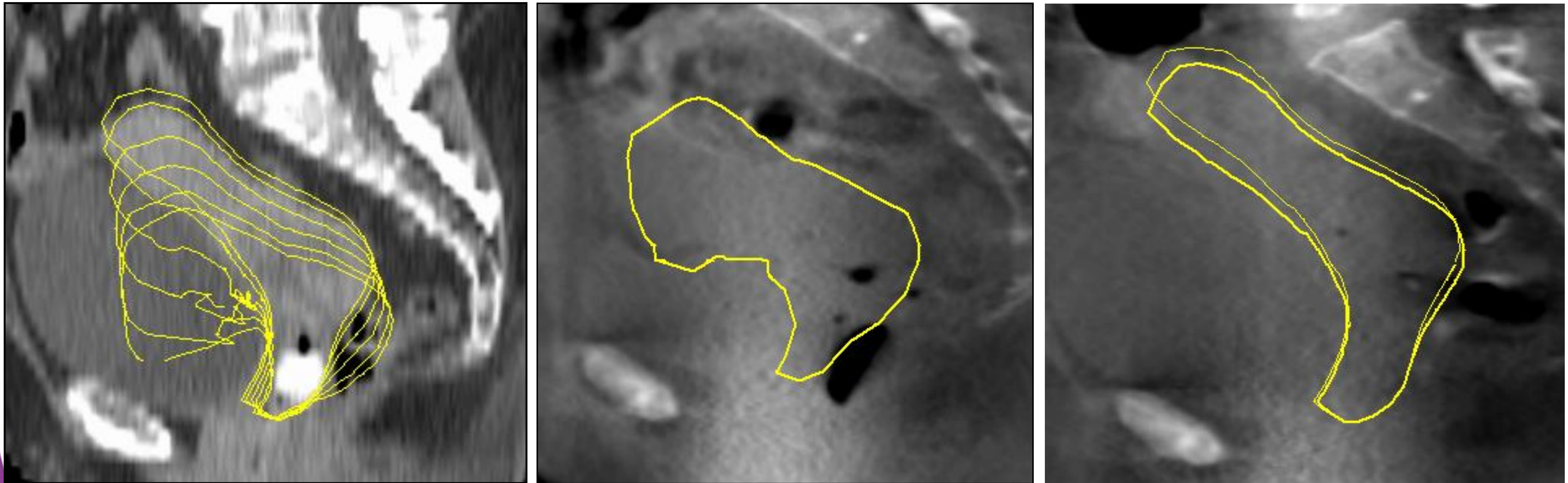
Observer Study selection of plans for Cervix patients

Design of the study

1. First measurement
2. Workshop
3. Second measurement

- 5 patients, 23 scans
- Per patient 6 structures
- 9 Observers:
  - 5 RTTs working treatment machine
  - 2 imaging RTTs
  - 2 IGART RTTs

Observer Study selection of plans for Cervix patients



Observer Study selection of plans for Cervix patients

First measurement **77.1%**, second **84.7%** agreement

Workshop very usefull:

Both RTT's and Radiation Oncologist gained trust that they all see the same things although there is not an 100% agreement.

There is more variation than just the variation captured with full & empty bladder CT scan! **rectum, small bowel, heamorrage, tumor shrinkage**

Treatment & Imaging Cervix Selection of Plans

Procedure imaging:

1. Registration of bony anatomy
2. Selection of plan in XVI with structure overlay
3. Check if markers (vagina) are within PTV.

- Big brother software checks correct plan: Do Mosaiq and XVI agree?
- Big brother software checks that not more than 1 plan is treated.

Evaluation of Cervix Selection of Plans

1x a week by the imaging RTT's and/or physician

- Was the correct plan selected?
- Is the target volume moving as predicted in de pre-treatment full and empty bladder CT scans?
- Is the predicted movement still valid? (regression)

Protocol started in 1 team, with only RTT's that participated in the workshop and observer study.

Demo database for practice for new RTT's

De Jong et al. Radiother Oncol. 2016
Plan selection strategy for rectum cancer patients – inter observer study

Who is doing What in Radiation Therapy?

Survey

Questionnaires to participants of ESTRO course on “IGRT in clinical practice” in 2006-2010:

48 hospitals

19 countries

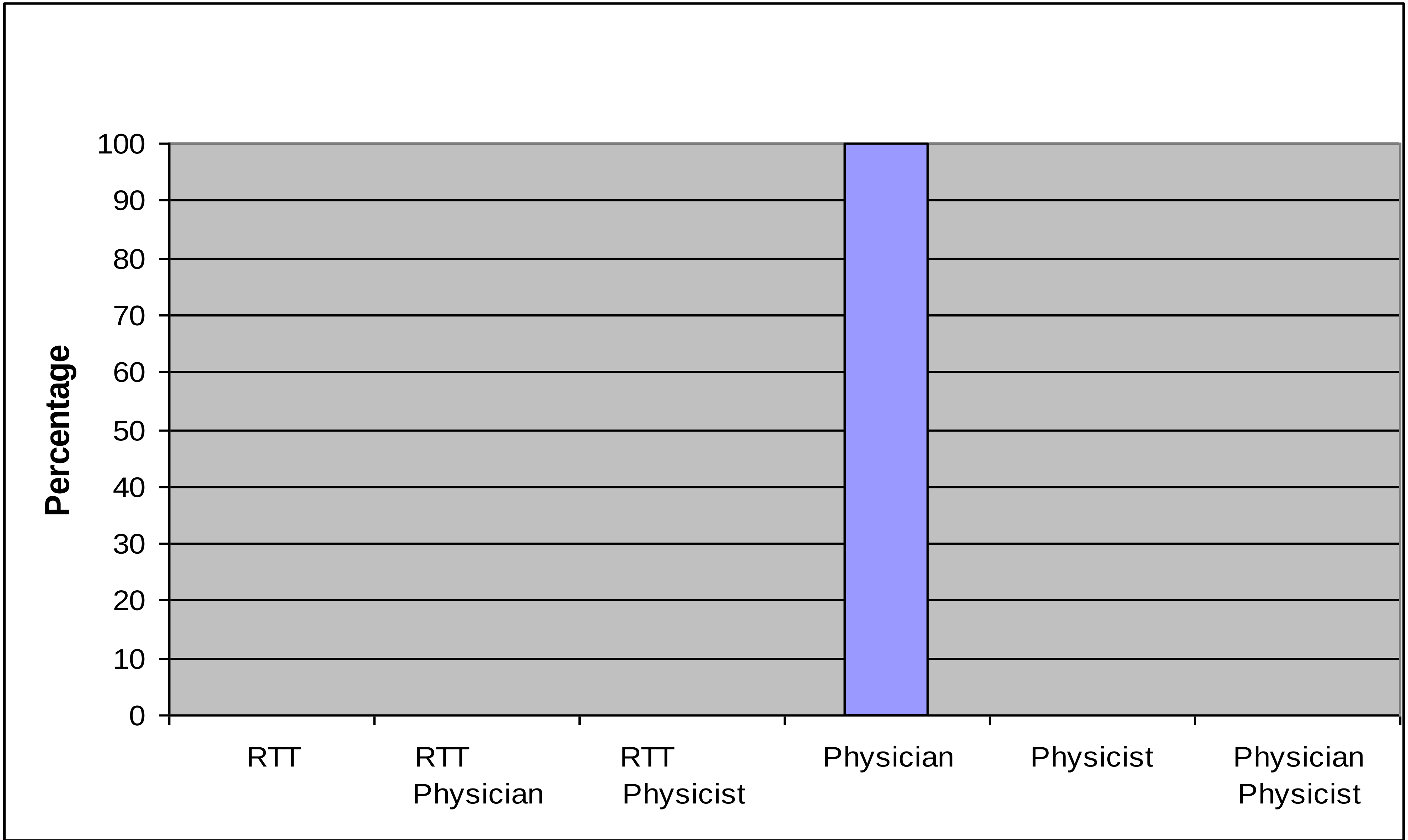
Survey

1. Indication/Design of Radiation Treatment
2. Pre treatment imaging: CT/simulation
3. Delineation
4. Treatment Planning
5. Treatment
6. Image Guidance/Adaptation treatment

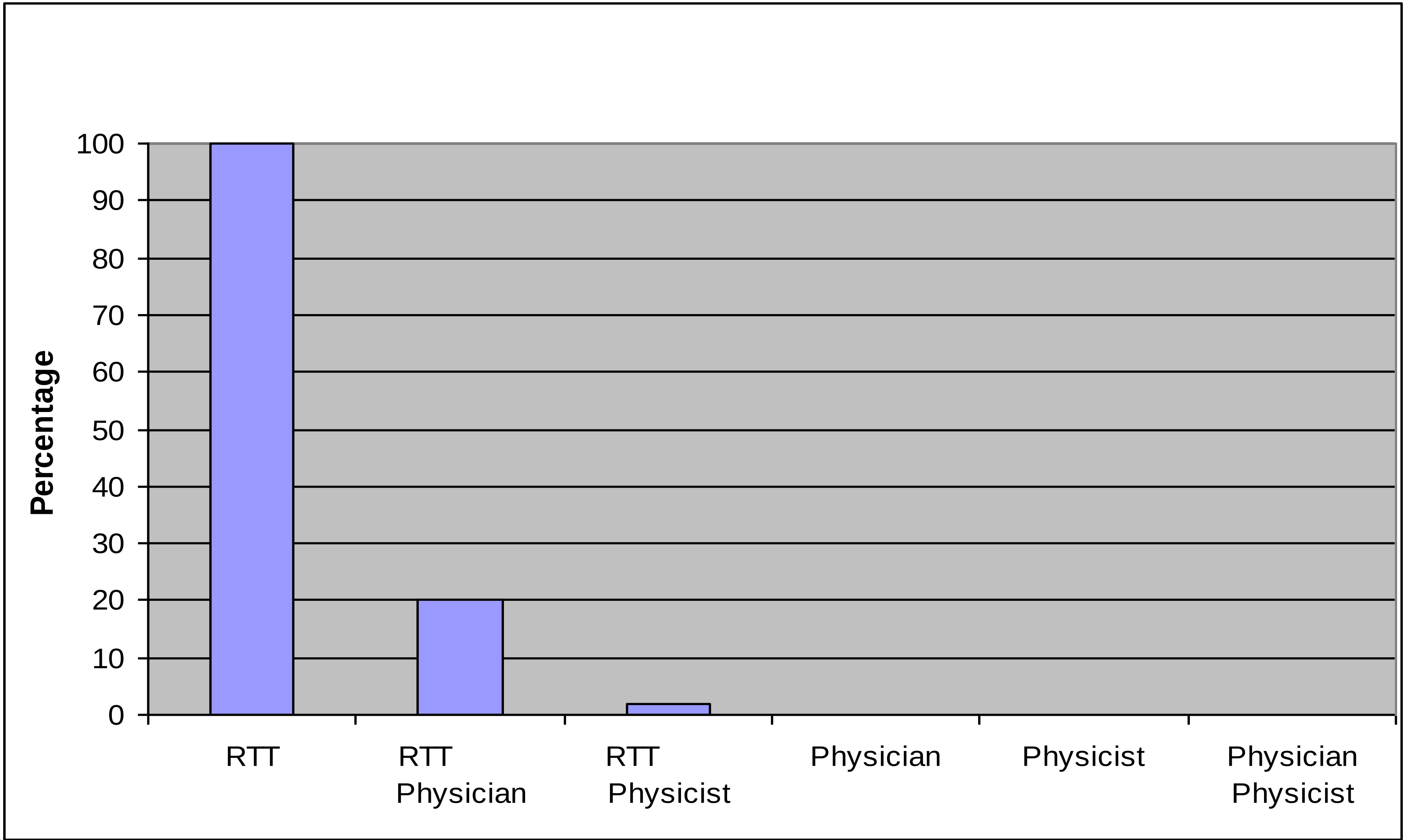
→

- Radiation Therapy Technicians (RTT)
- Physicians
- Physicists

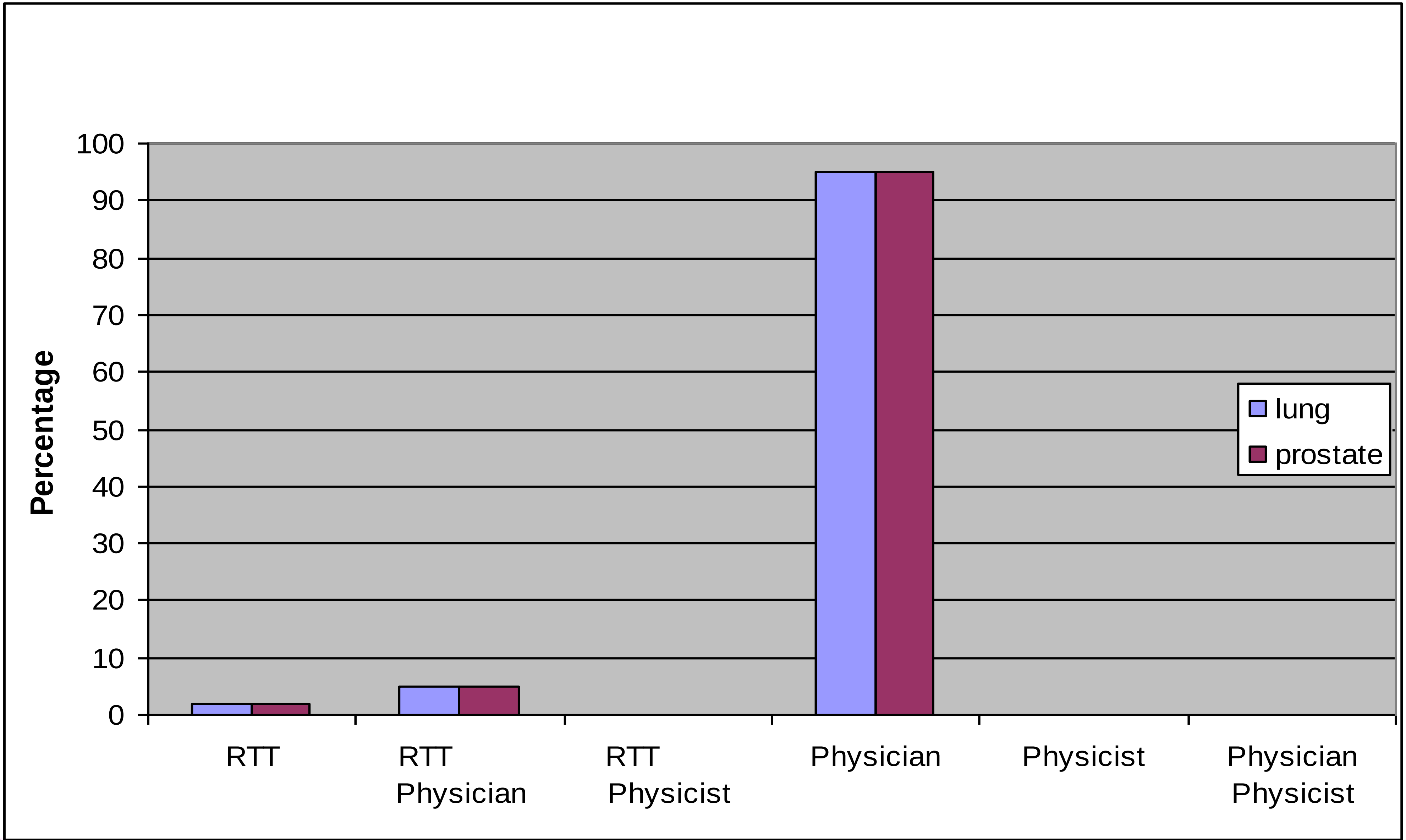
1. Indication of treatment



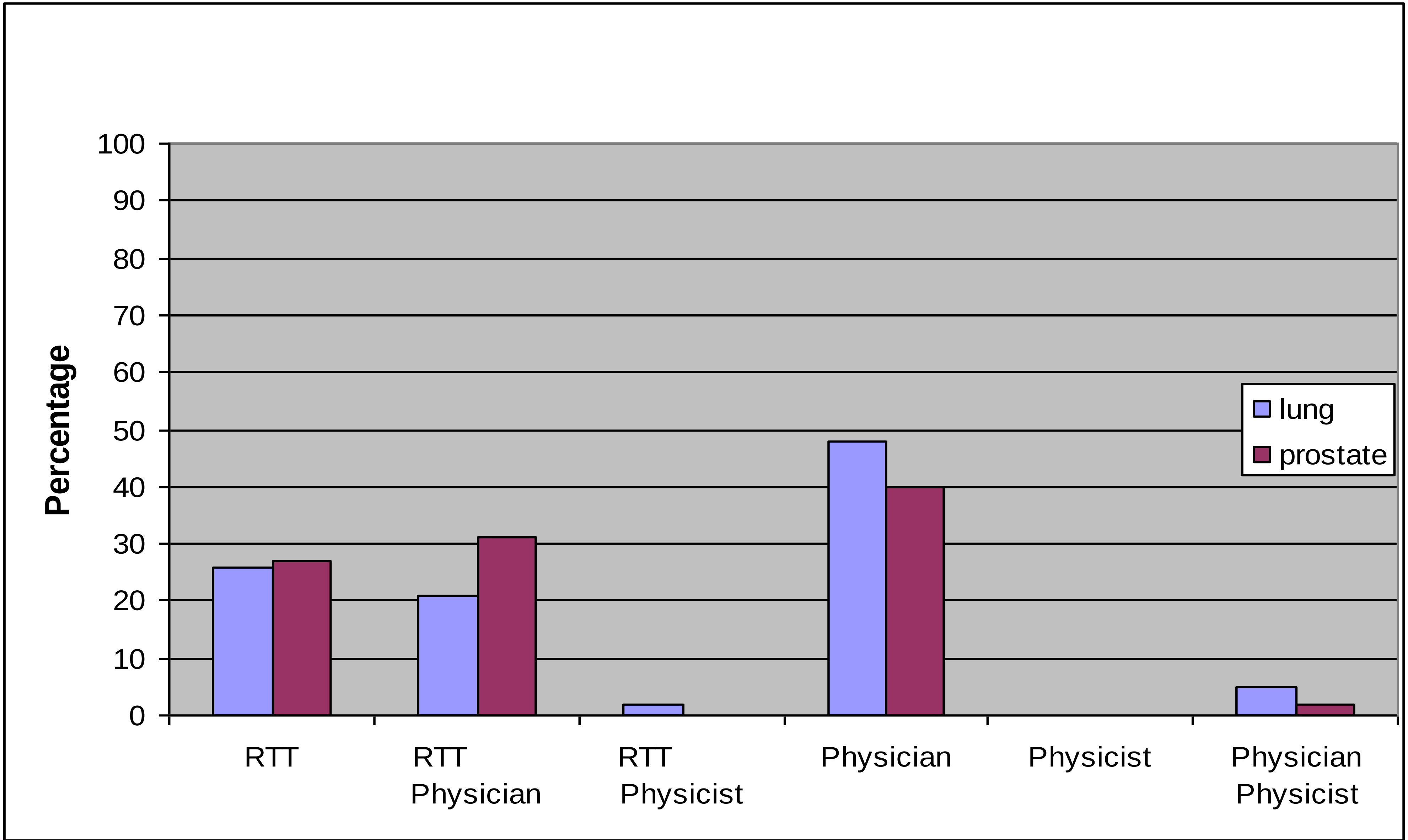
2. Pre-treatment Imaging



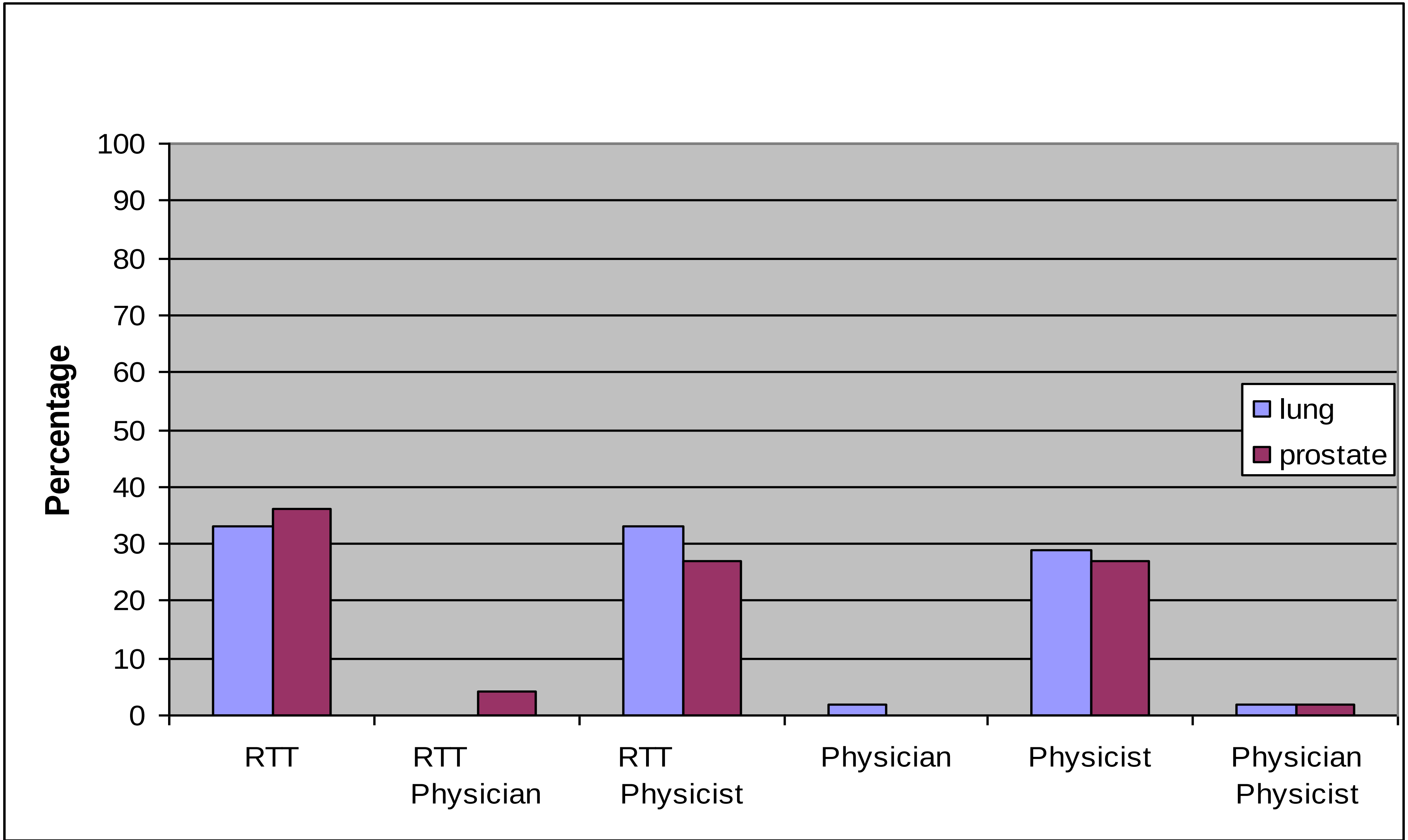
3. Delineation: Target Volume



3. Delineation: Organs at Risk

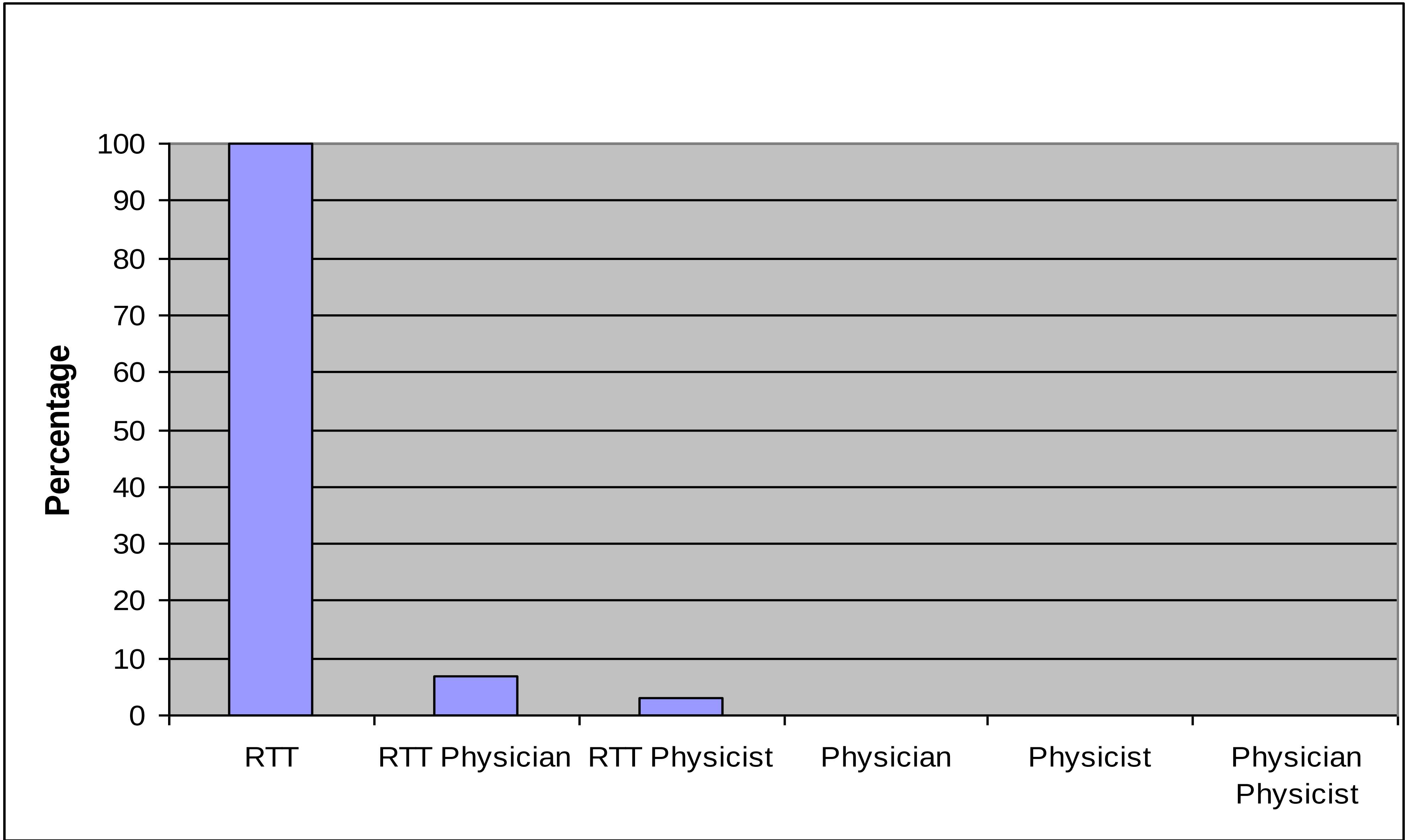


4. Treatment Planning

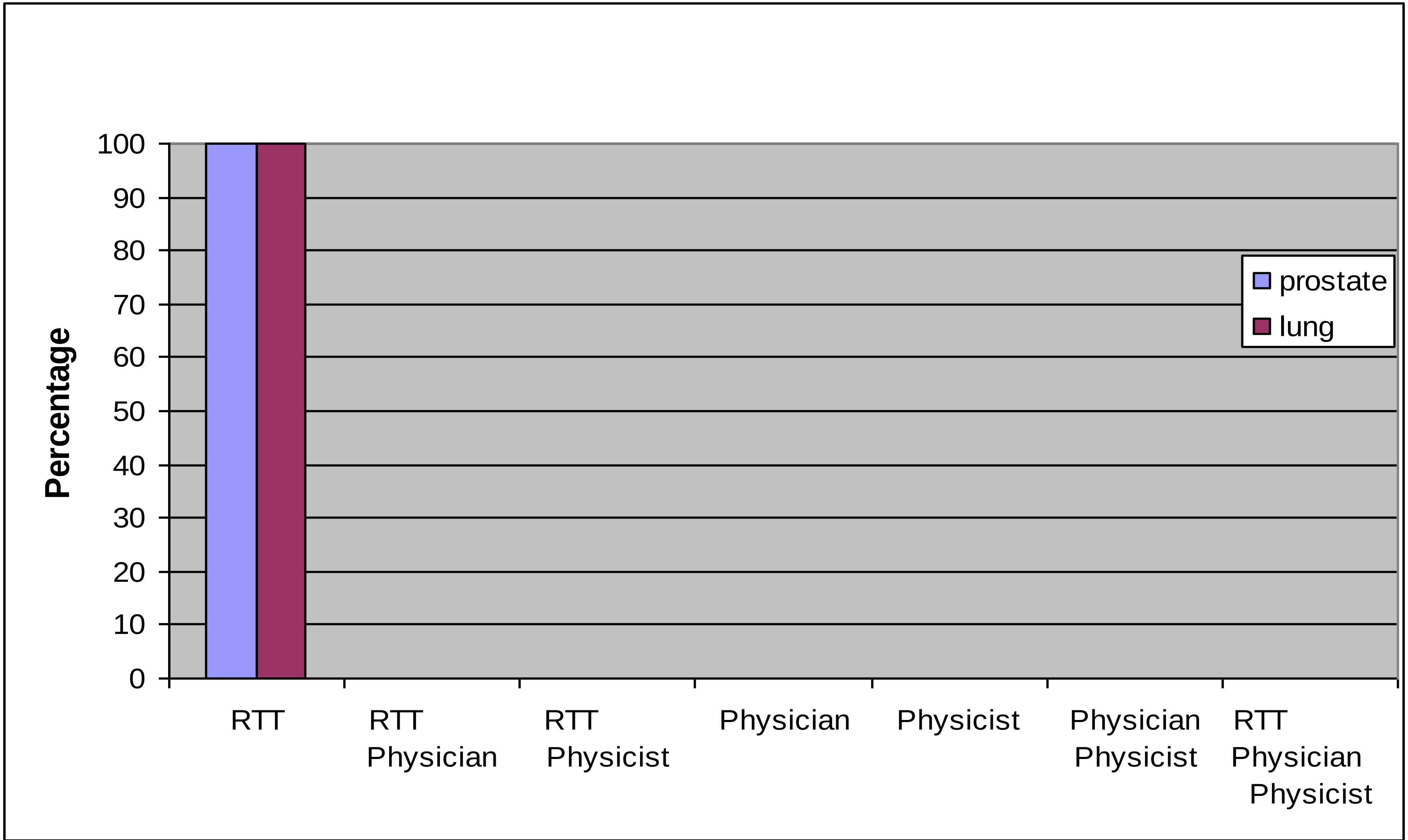


RTT: supervised and/or accepted by physician or physicist

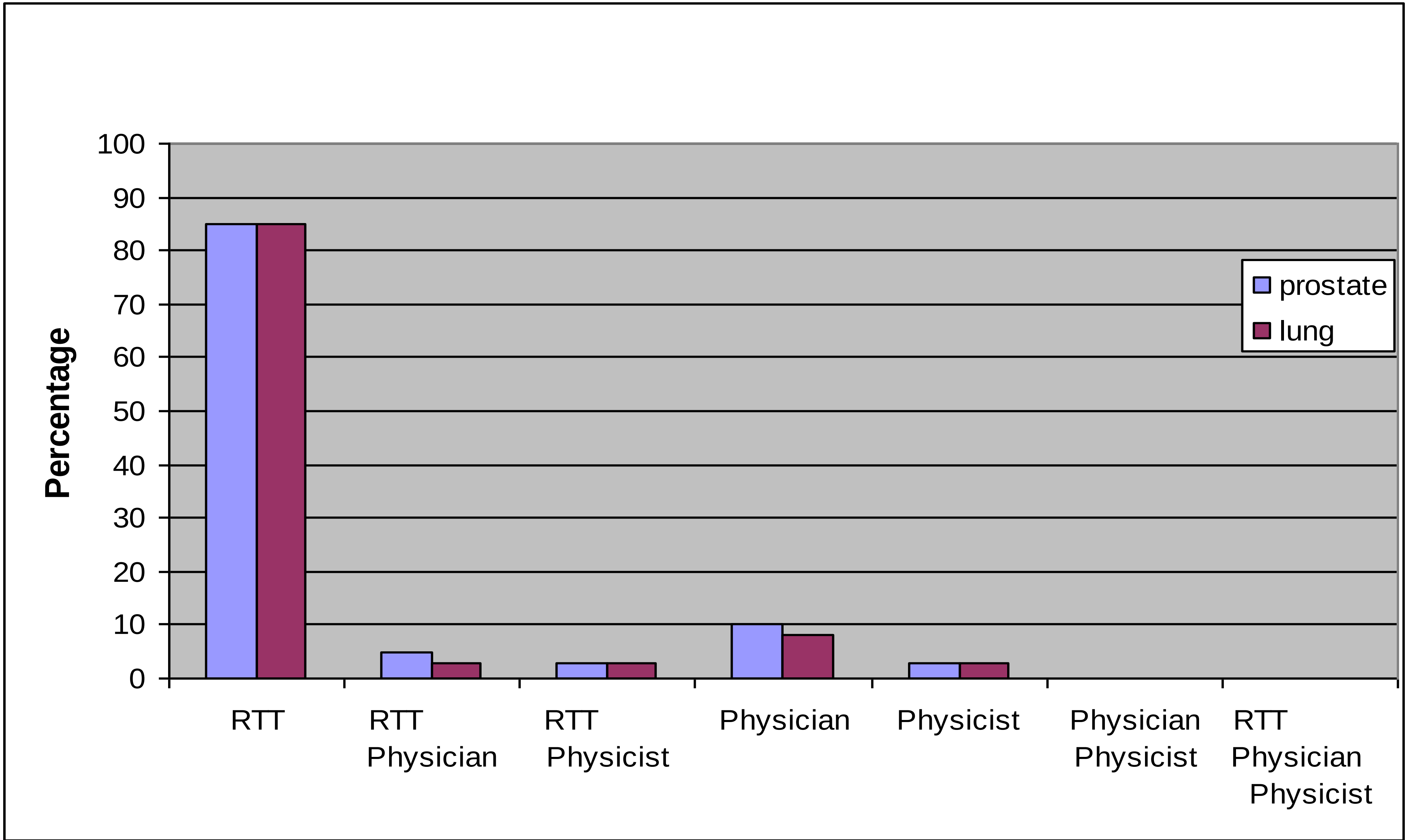
5. Treatment Delivery



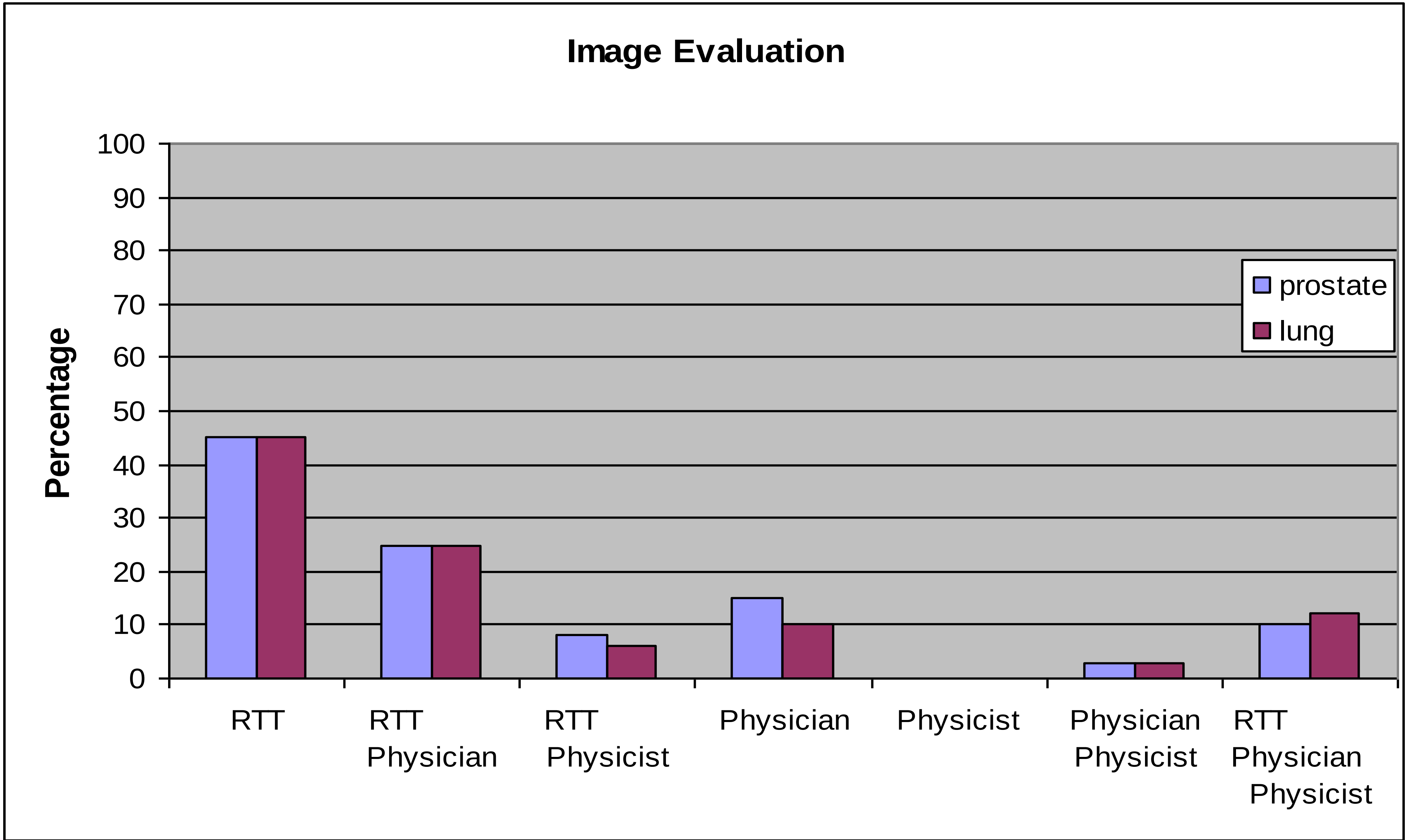
6a. Image Guidance: Acquisition



6b. Image Guidance: Registration



6c. Image Guidance: Evaluation



Who is doing what?

Conclusion: Largest differences in ***Treatment Planning*** and ***Image Guidance***.

Why? What are the **variables** in the different departments that could have an influence on these differences?

- RTT – education / training
- Department size
- Resources per treatment machine
- IGRT modalities
- *Culture / History*
- *Money*

RTT training / Education

Majority:

- 3 years of classroom combined with clinical intern hours

  → bachelor degree

Also:

- 2 or 4 years of classroom combined with clinical intern hours

  → bachelor degree

- 3 years of nursing school with bachelor degree with additional theoretical or clinical RTT training ~1 year.

RTT training / Education

Majority:

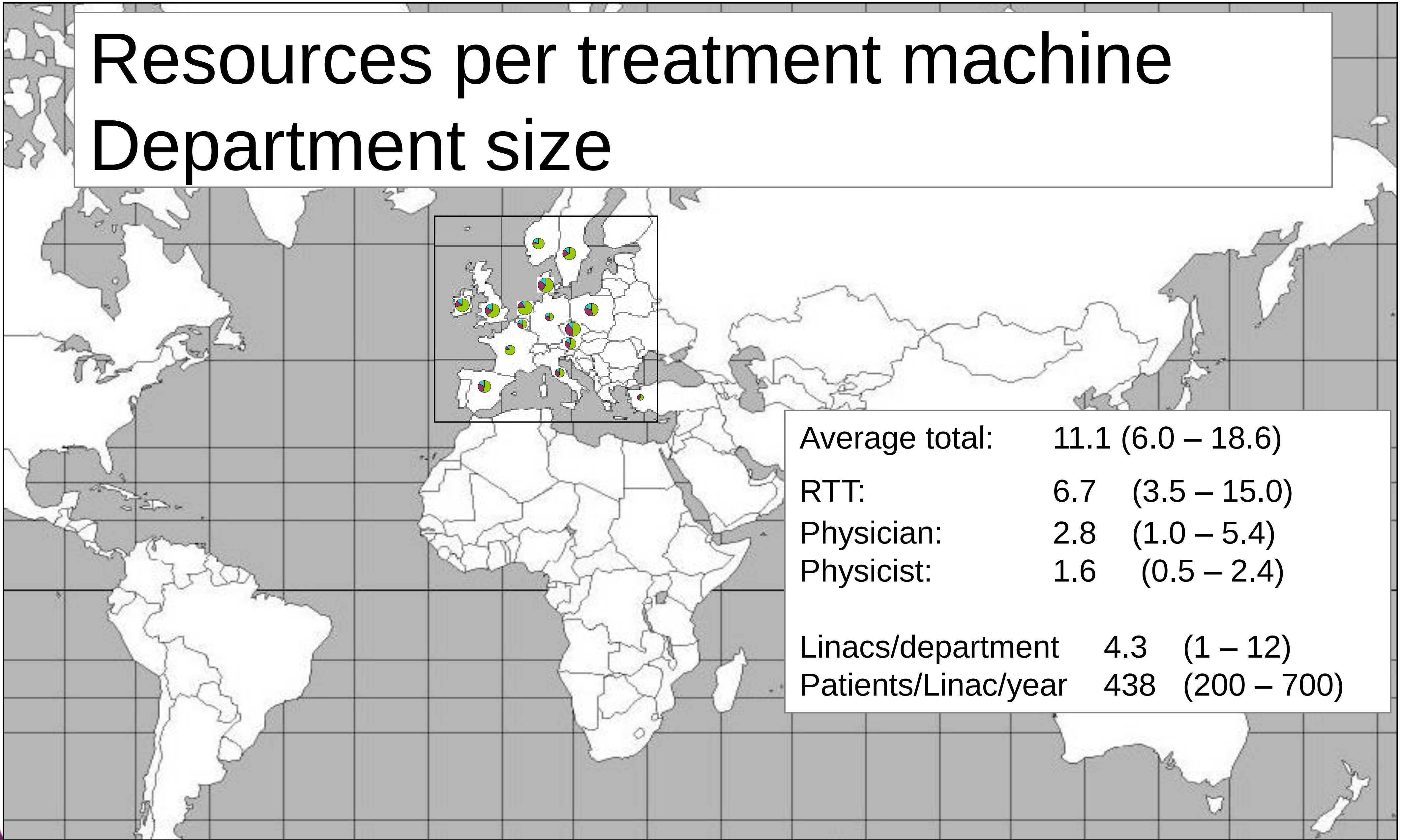
- 3 years of classroom combined with clinical intern hours
  → bachelor degree

Does not correlate

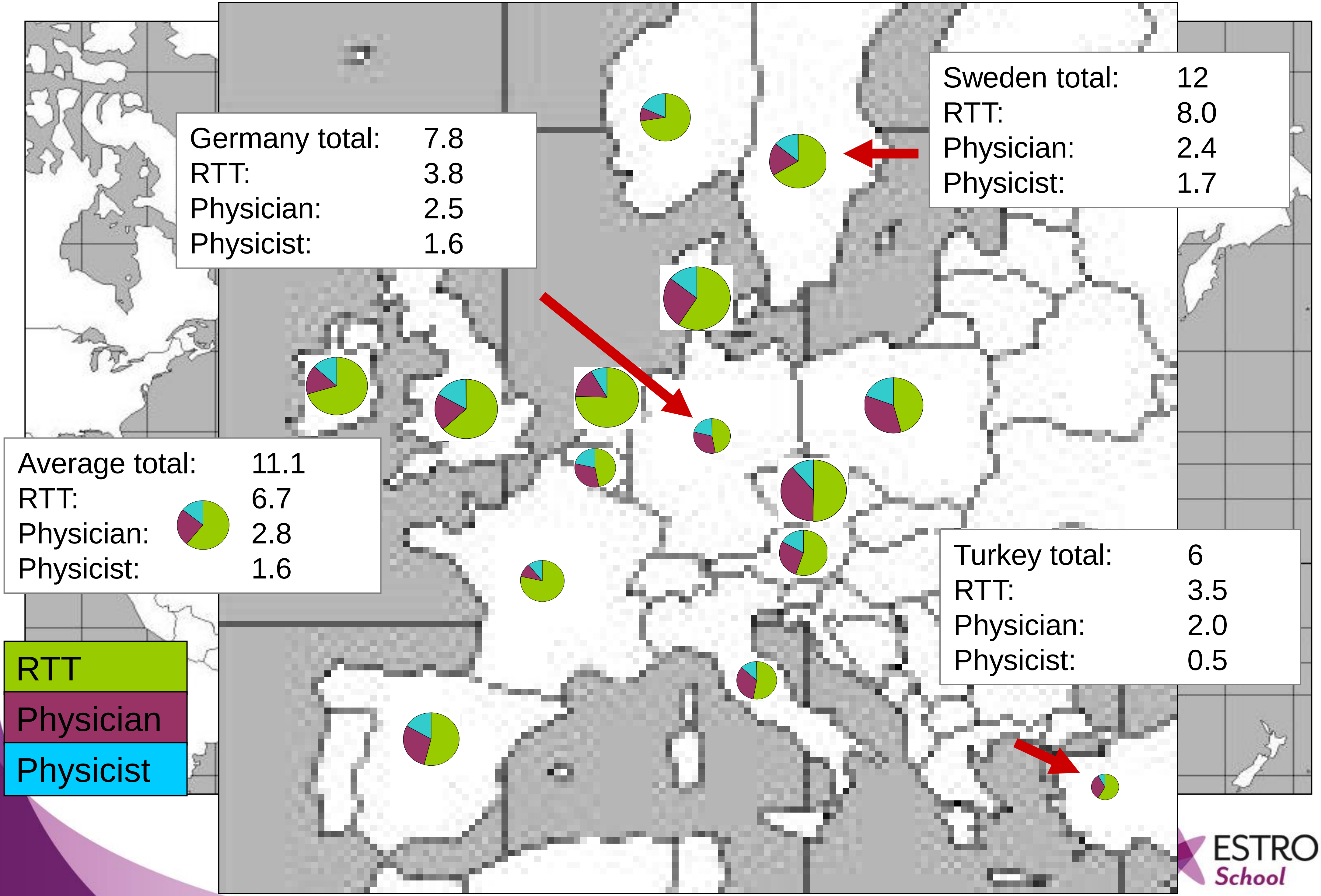
Also:

- 2 or 4 years of classroom combined with clinical intern hours
  → bachelor degree
- 3 years of nursing school with bachelor degree with additional theoretical or clinical RTT training ~1 year.

Resources per treatment machine
Department size



Average total:	11.1	(6.0 – 18.6)
RTT:	6.7	(3.5 – 15.0)
Physician:	2.8	(1.0 – 5.4)
Physicist:	1.6	(0.5 – 2.4)
Linacs/department	4.3	(1 – 12)
Patients/Linac/year	438	(200 – 700)



Germany total: 7.8
RTT: 3.8
Physician: 2.5
Physicist: 1.6
Sweden total: 12
RTT: 8.0
Physician: 2.4
Physicist: 1.7
Average total: 11.1
RTT: 6.7
Physician: 2.8
Physicist: 1.6
Turkey total: 6
RTT: 3.5
Physician: 2.0
Physicist: 0.5
RTT
Physician
Physicist
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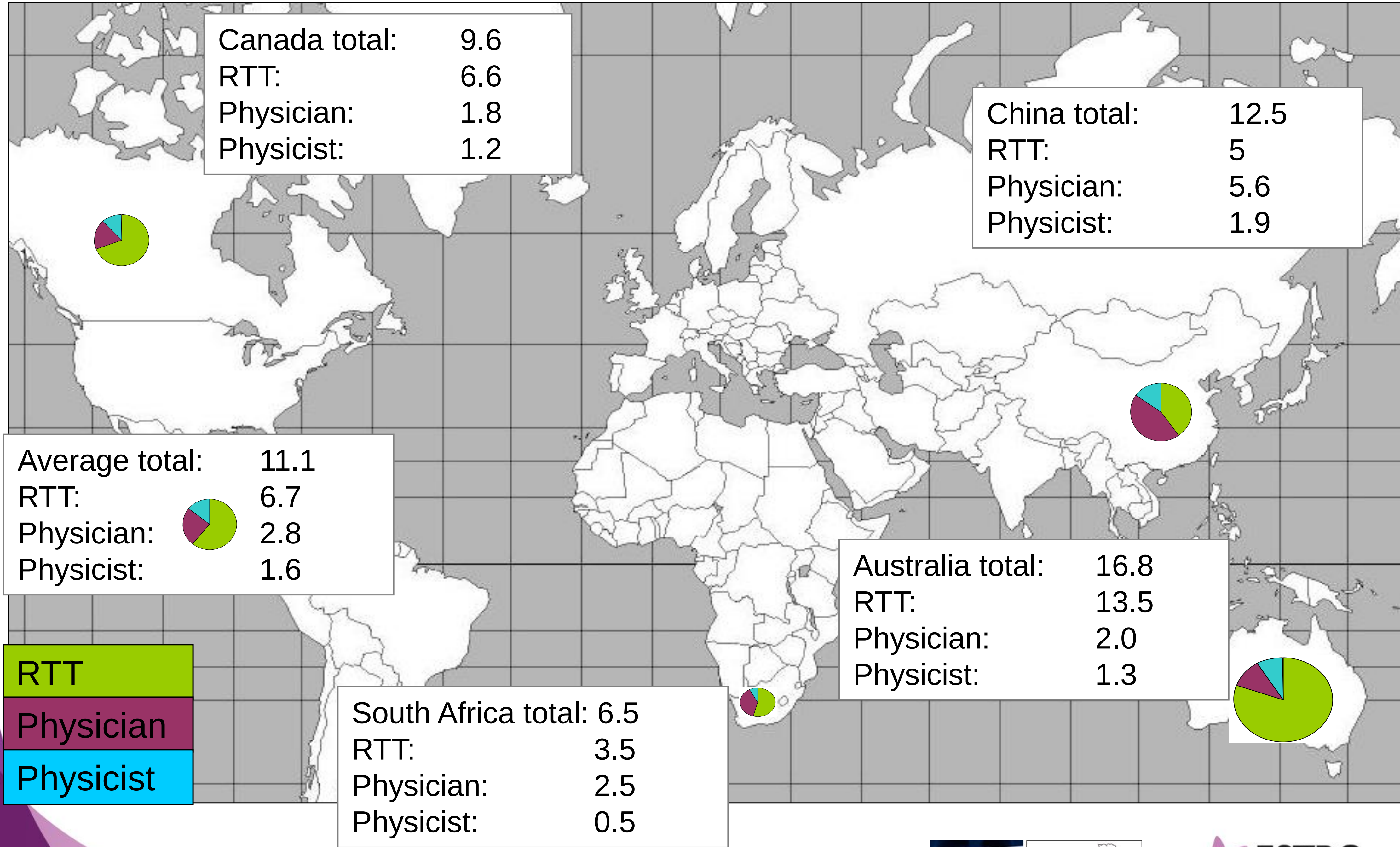
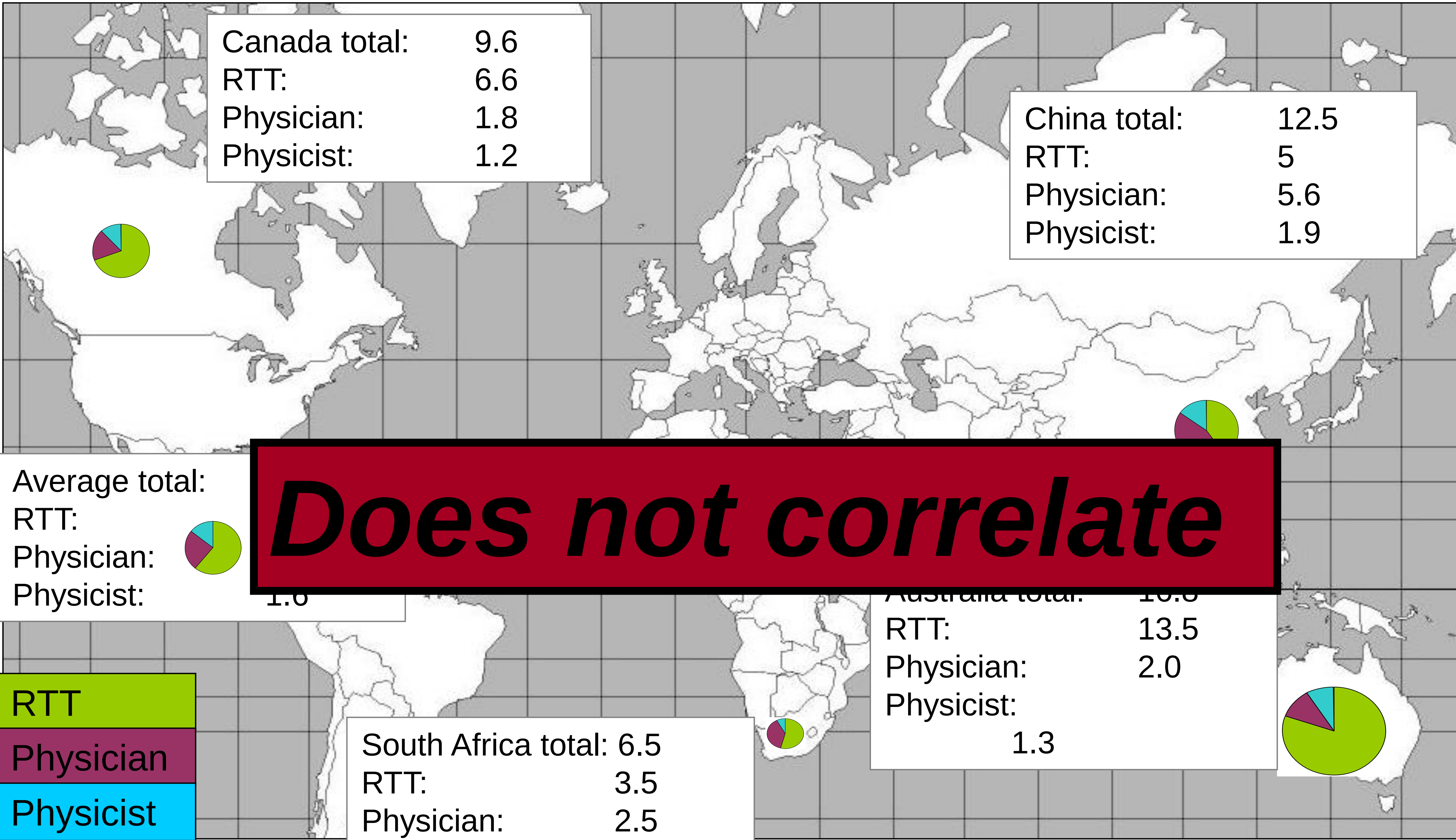

Canada total: 9.6
RTT: 6.6
Physician: 1.8
Physicist: 1.2
China total: 12.5
RTT: 5
Physician: 5.6
Physicist: 1.9
Average total: 11.1
RTT: 6.7
Physician: 2.8
Physicist: 1.6
Australia total: 16.8
RTT: 13.5
Physician: 2.0
Physicist: 1.3
South Africa total: 6.5
RTT: 3.5
Physician: 2.5
Physicist: 0.5
RTT
Physician
Physicist



Canada total: 9.6
RTT: 6.6
Physician: 1.8
Physicist: 1.2

China total: 12.5
RTT: 5
Physician: 5.6
Physicist: 1.9

Average total:
RTT:
Physician:
Physicist:

Does not correlate

RTT: 13.5
Physician: 2.0
Physicist: 1.3

South Africa total: 6.5
RTT: 3.5
Physician: 2.5
Physicist: 0.5

RTT
Physician
Physicist

IGRT

IGRT Modalities:

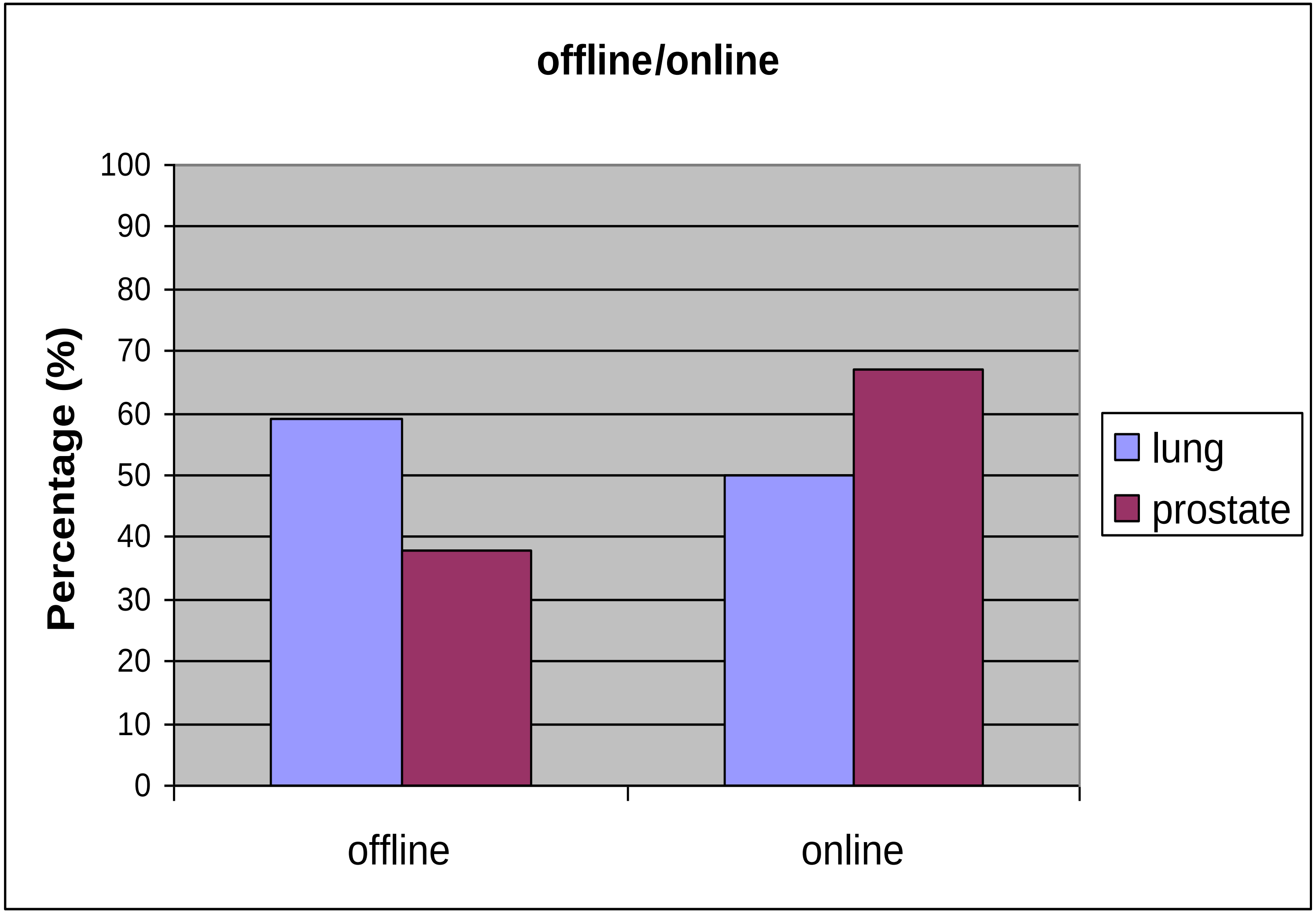
2D Portal Images	79%
2D kV Images	6%
kV Conebeam CT	66%
MV Conebeam CT	17%

IGRT protocols are:

➢ **Tumor site specific**	**100%**
➢ Patient specific	18%
➢ Physician specific	2%

IGRT

2D Portal Images	69%
kV Conebeam CT	67%
MV Conebeam CT	18%



Summary: Who is doing what?

Large variation between departments in:

- Amount of resources per linac
- Their distribution in different disciplines:
  - ➢ Treatment planning
  - ➢ IGRT evaluation

Some Variables

- RTT training and education
- Department size
- Resources per treatment machine
- IGRT Modalities
      » Culture – History

Not decisive

Opportunity:
Might consider different solutions?

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Summary

IGRT is a multi disciplinary approach

IGRT has opened the field of RT for RTT's:

1. RTT's should be responsible for IGRT at the treatment machine
    - Registration & evaluation images
    - Training & education / Quality assurance
    - First assessment of anatomical / relevant changes
2. Research, development and implementation of IGRT

“patient preparation and positioning”:

Even with IGRT, setting up the patient remains **very** important!

Questions & Discussion

m.a.j.dejong@amc.uva.nl

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WWW.ESTRO.ORG/SCHOOL

Planar imaging: MV and kV

Marianne Aznar PhD,
Risgshopitalet, Copenhagen

With thanks to: Dirk Verellen, Stine Korreman

Outline

EPIDs

Planar kV imaging systems

- Gantry-mounted
- Floor/ceiling mounted

Issues adressed:

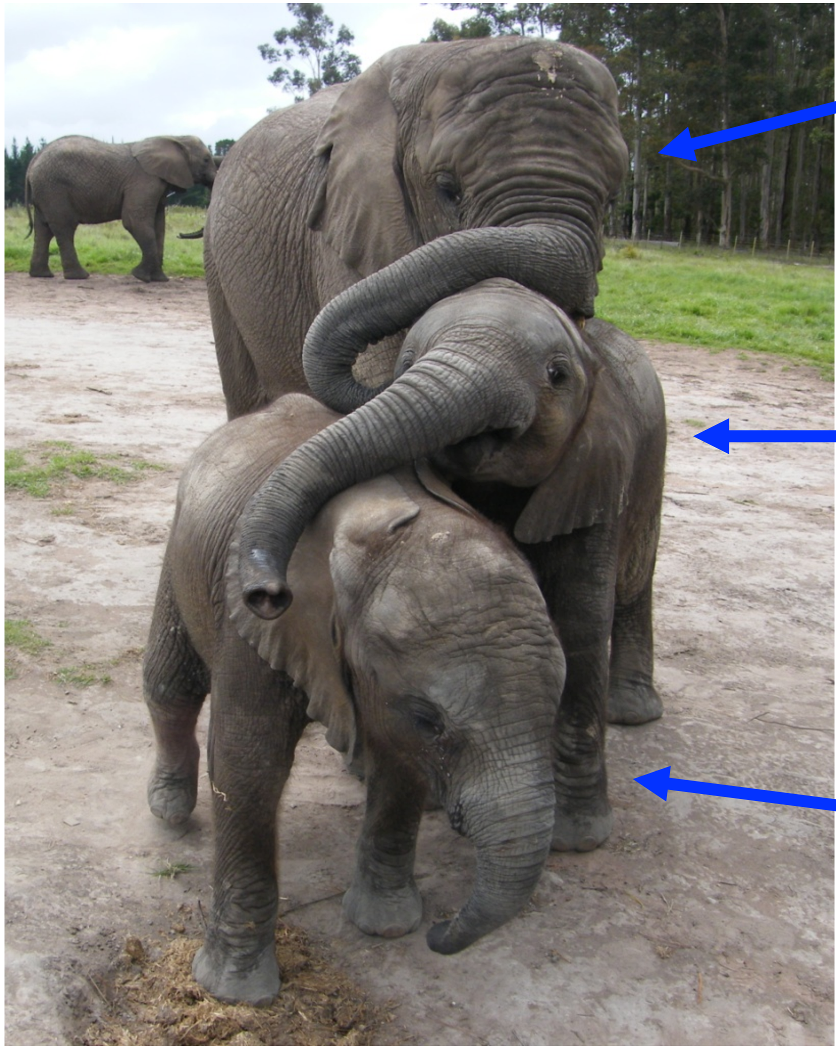
Basic principles; pros and cons

Alignment and calibration; QA issues

Intrafraction monitoring

Example of clinical strategy

Let's adress the elephants in the room…



Is MV portal imaging still relevant today?

Is planar kV imaging still relevant today?

What about 5-10 years from now?

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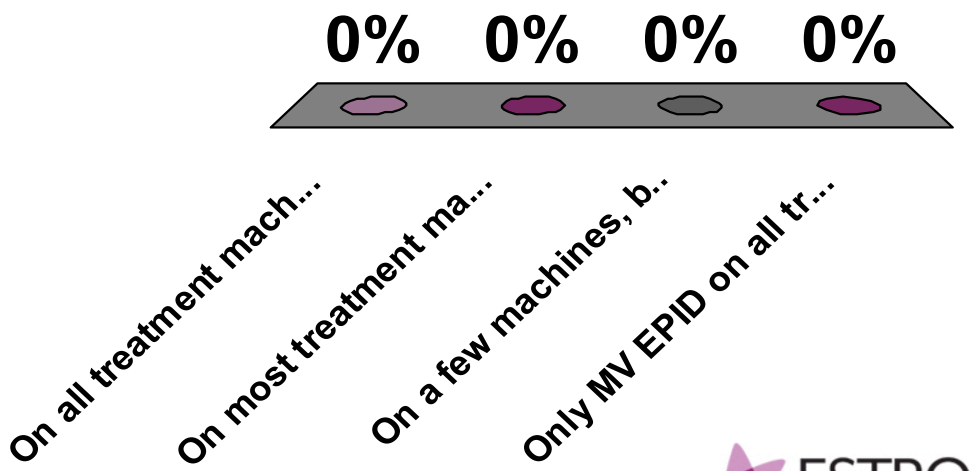
MV vs kV capabilities: in your institution, do you have kV imaging capabilities:

A. On all treatment machines

B. On most treatment machines

C. On a few machines, but mostly MV

D. Only MV EPID on all treatment units



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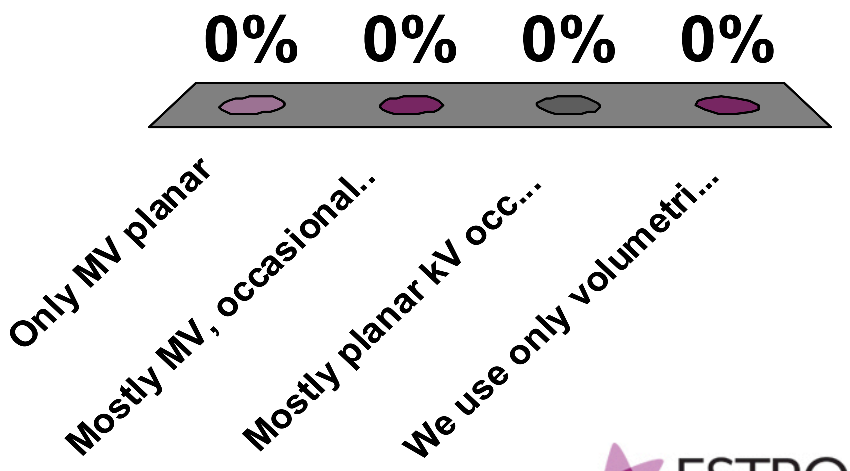
MV vs kV usage: which type of planar imaging do you use ?

A. Only MV planar

B. Mostly MV, occasionally planar kV

C. Mostly planar kV occasionally MV

D. We use only volumetric imaging



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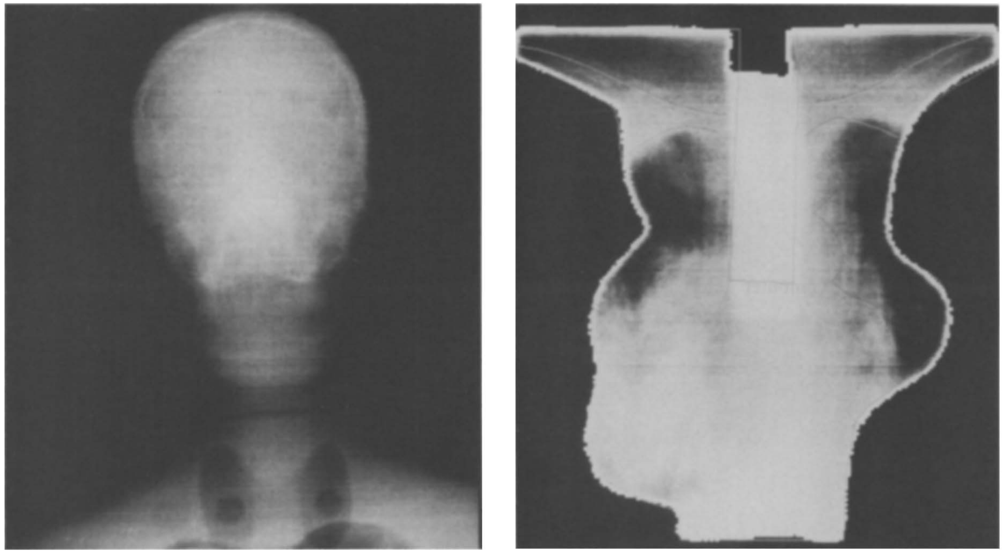
EPIDs: basic principles

Why EPIDs ?

Ca 25 years of experience



Lam et al, BJR 1986

Van Herk et al, RO 1988

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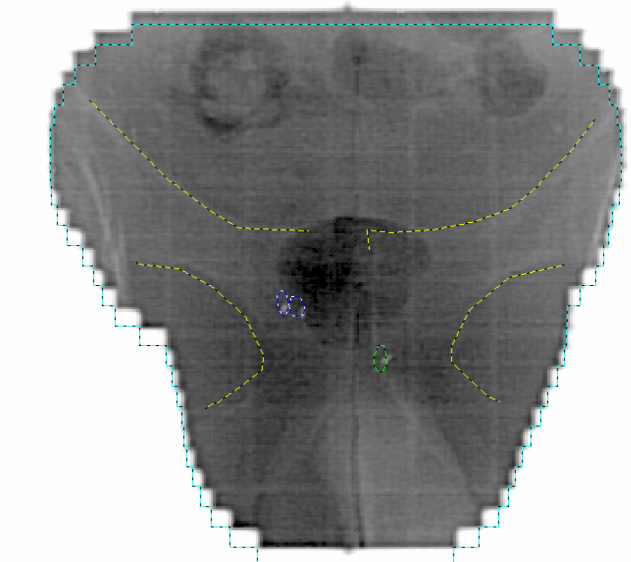
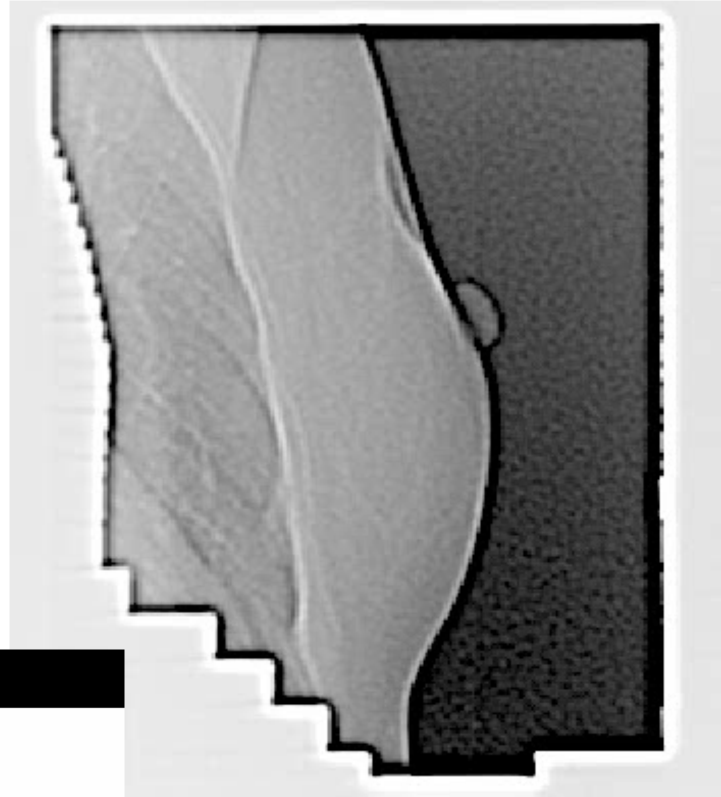
Why EPIDs ?

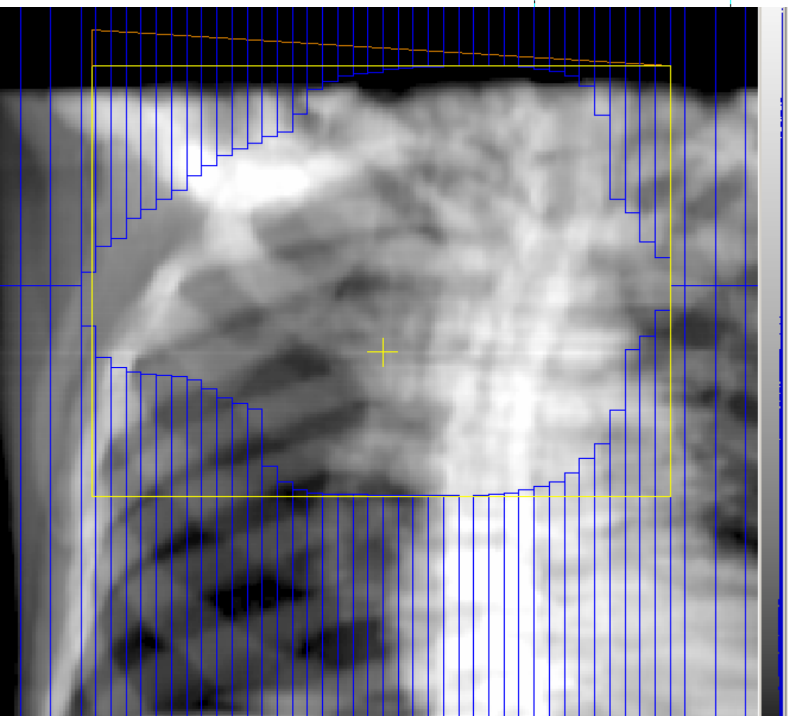
Now widely available

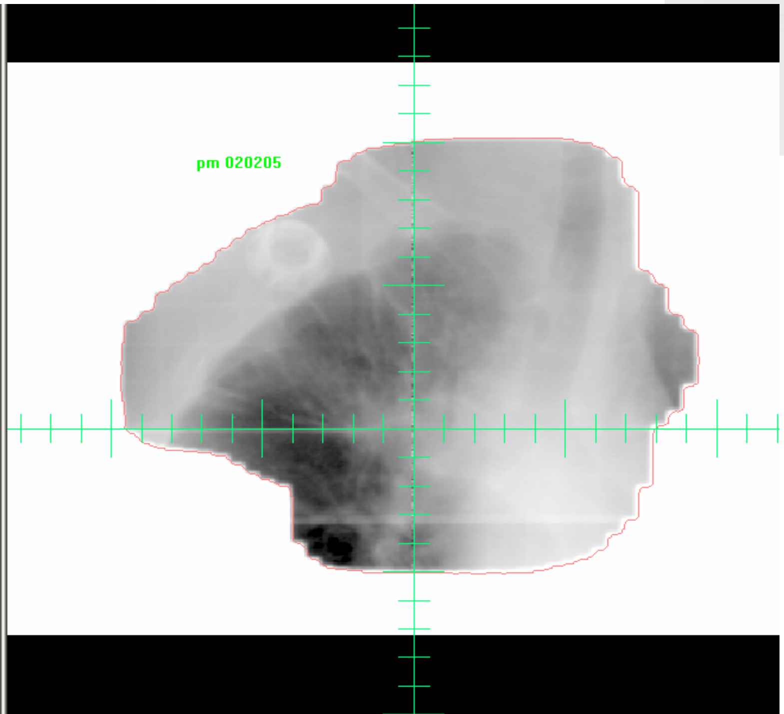
Why EPIDs?

Field images









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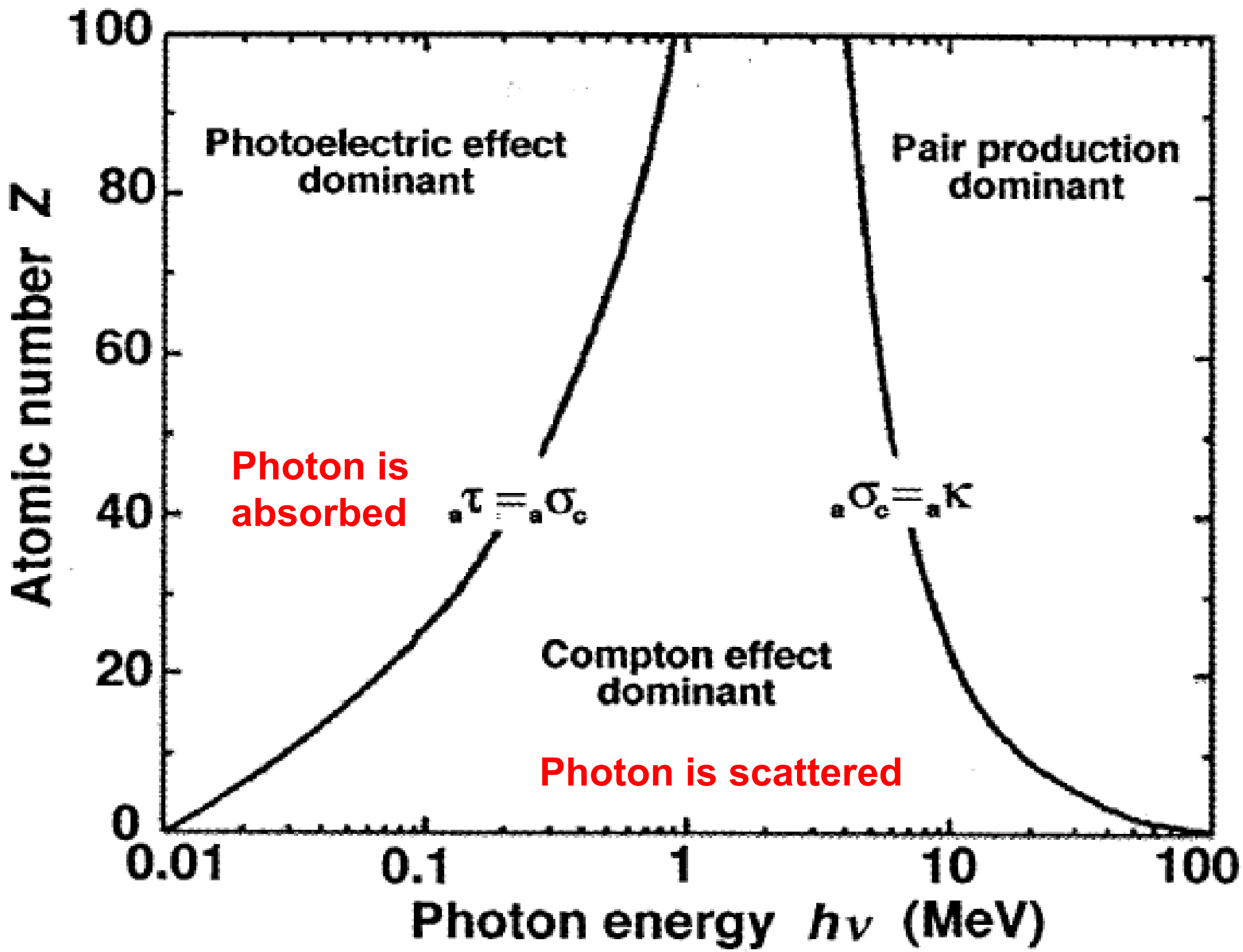
Main challenge: low contrast
(some easy breakfast time physics ☺)



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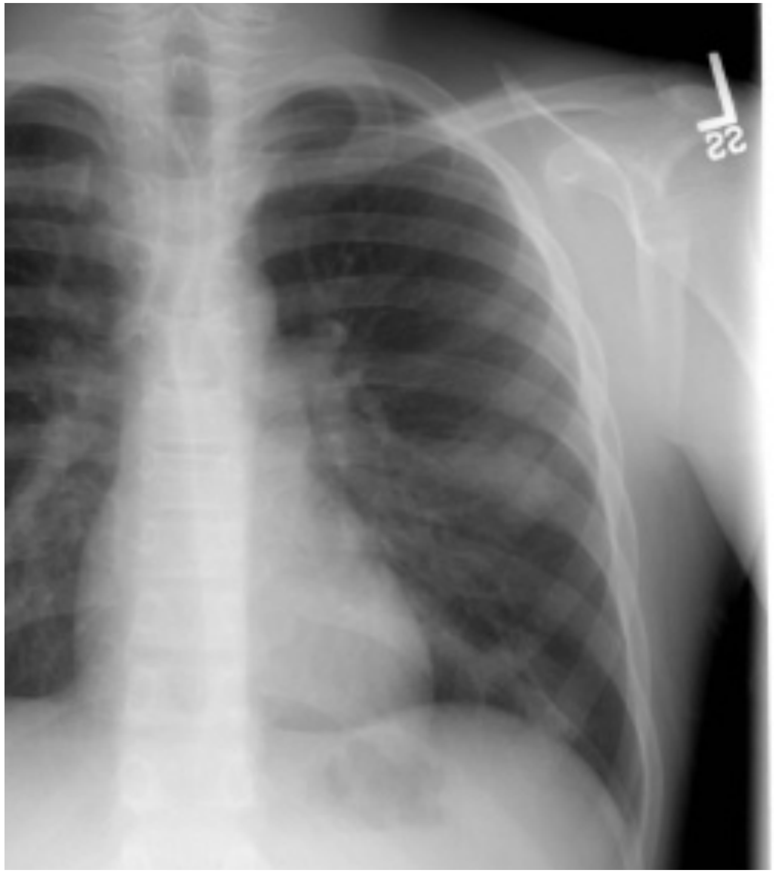
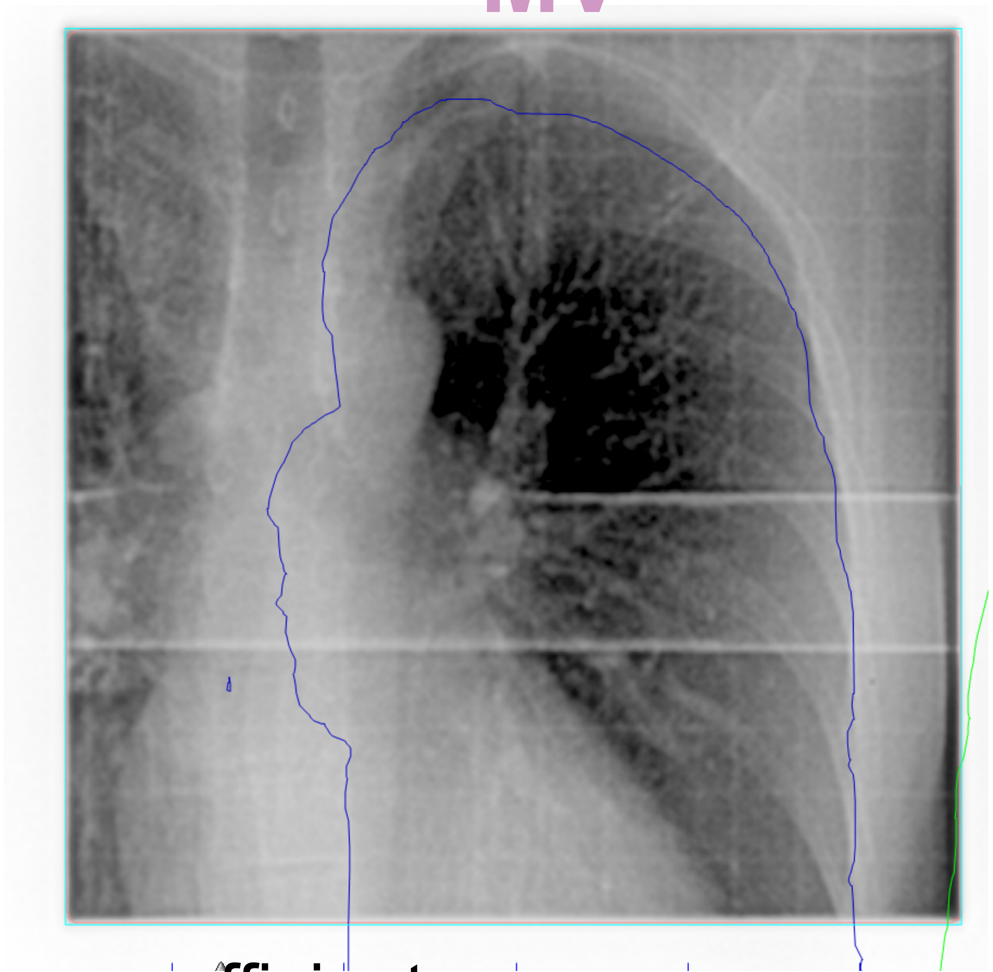
kV



MV



Mass energy absorption coefficient

$\sigma/\rho \sim Z^{3-\ 3.8}$

$\sigma/\rho \sim Z^{0}$

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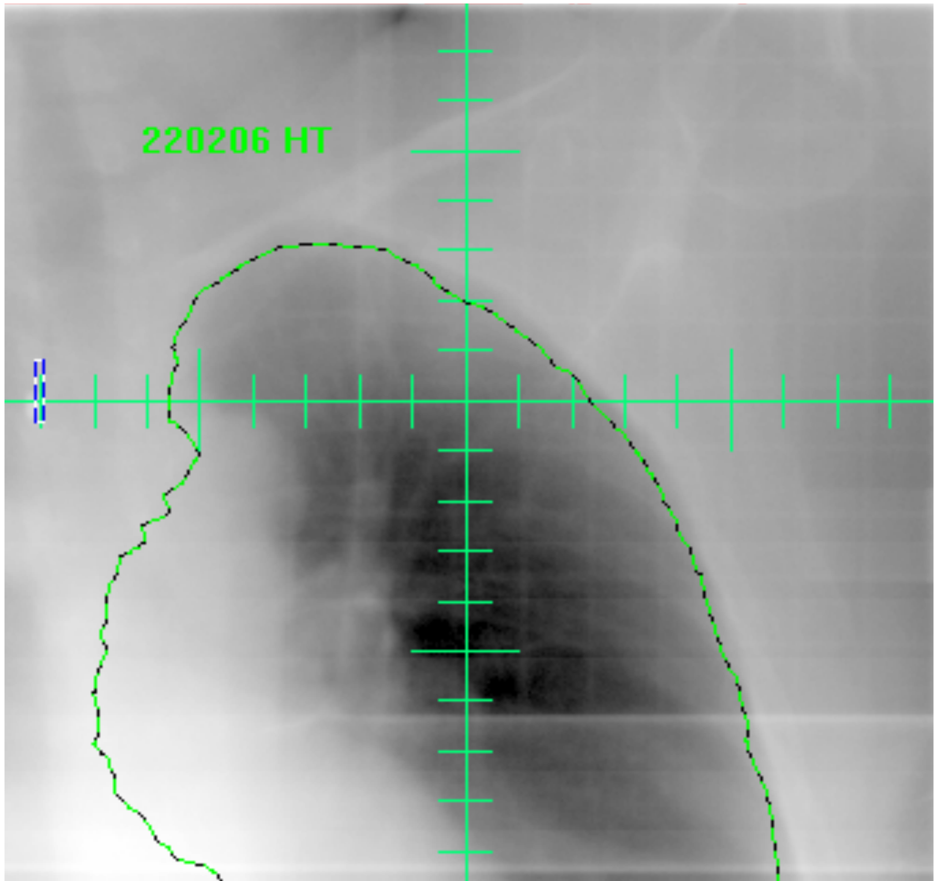
EPID- orthogonal images:
give all translational displacements



EPIDs: Pros and cons

Isocentric alignment: the imaging beam is the treatment beam (obs: gravity)

The imaging dose to the patient can be easily calculated in the TPS

Verifies the field outline with respect to the patient anatomy

Can use the EPID for transmission (in vivo) dosimetry

Monoscopic: needs several angles for 3D positioning information

Considerable dose for large FOV images outside the target volume (1 to 5 MU per image)

Low contrast (bony structures or markers)

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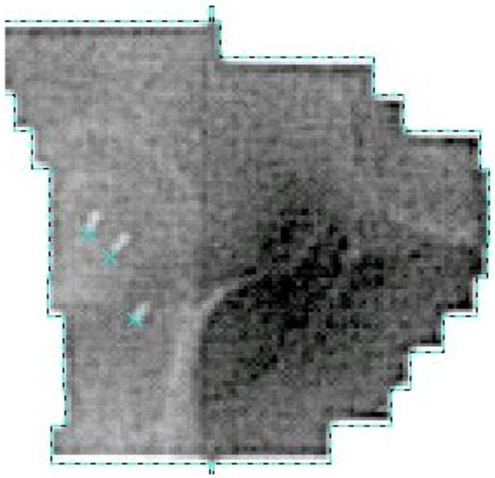
EPIDs: intrafraction monitoring

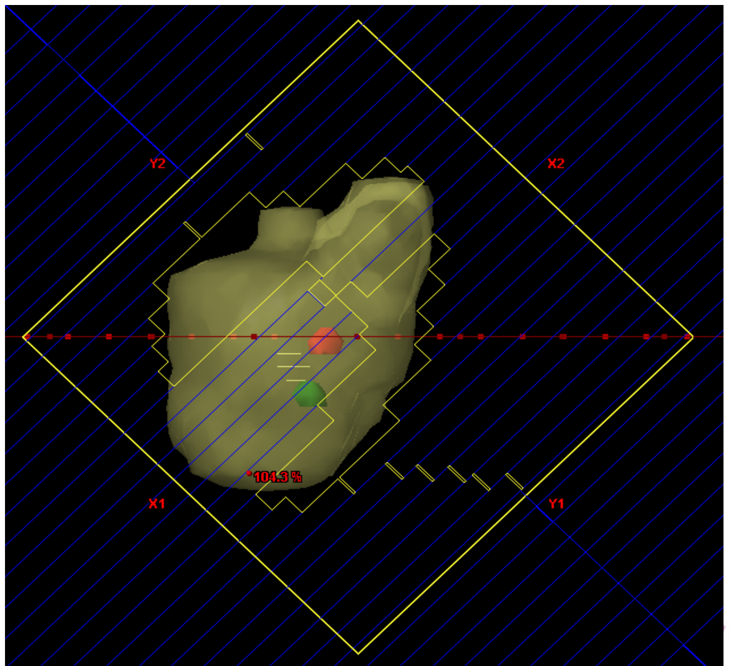
Is it possible to do intrafraction monitoring with EPIDs ?

Tracking internal fiducials

- Fiducials are visible with MV in Beams-Eye-View with EPID in cine mode
- Structures in the Beams-Eye-View can be used for image correlation analysis



•Advantage: least dose
•Pitfall: restricted to 3D-CRT



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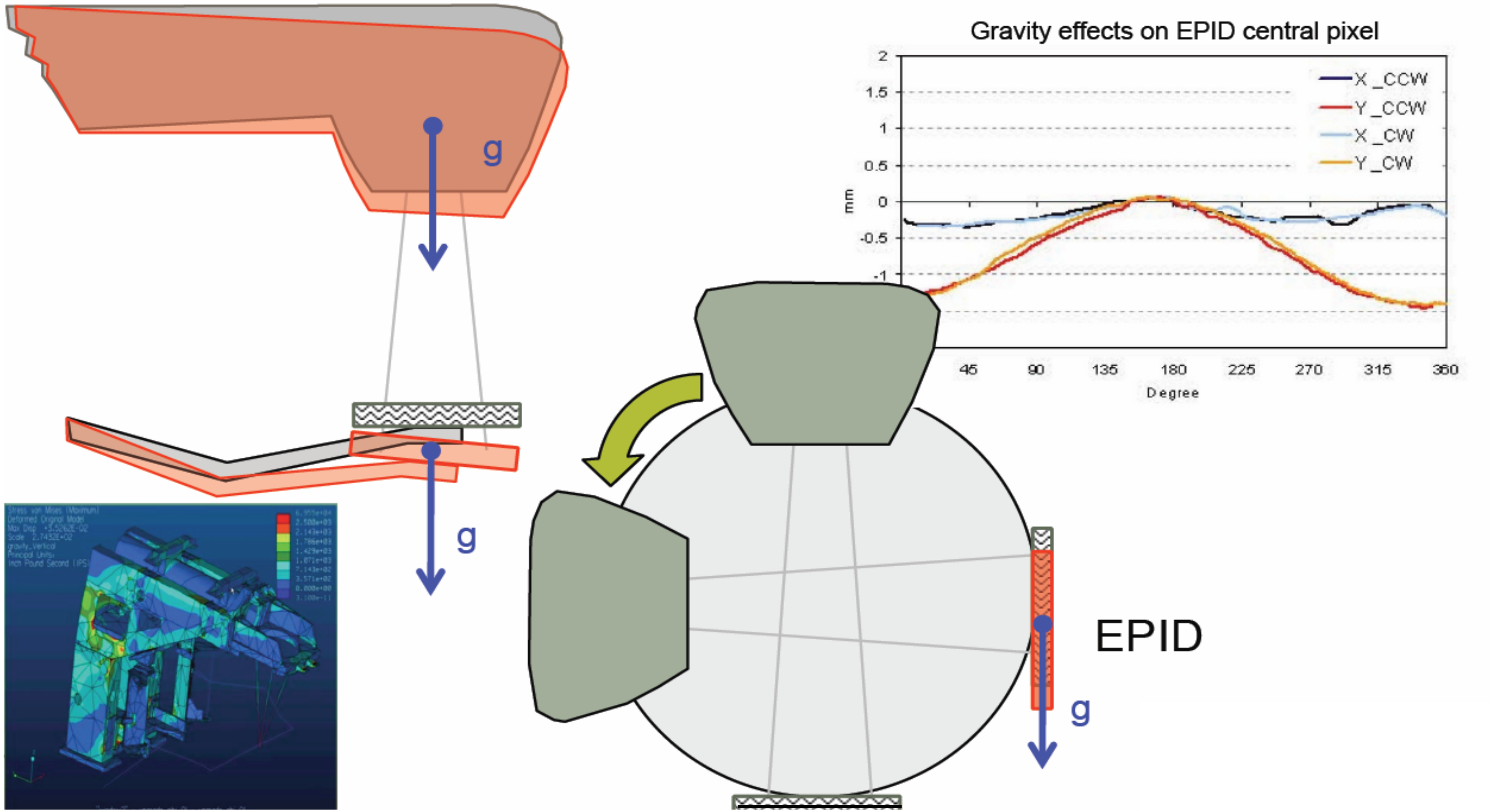
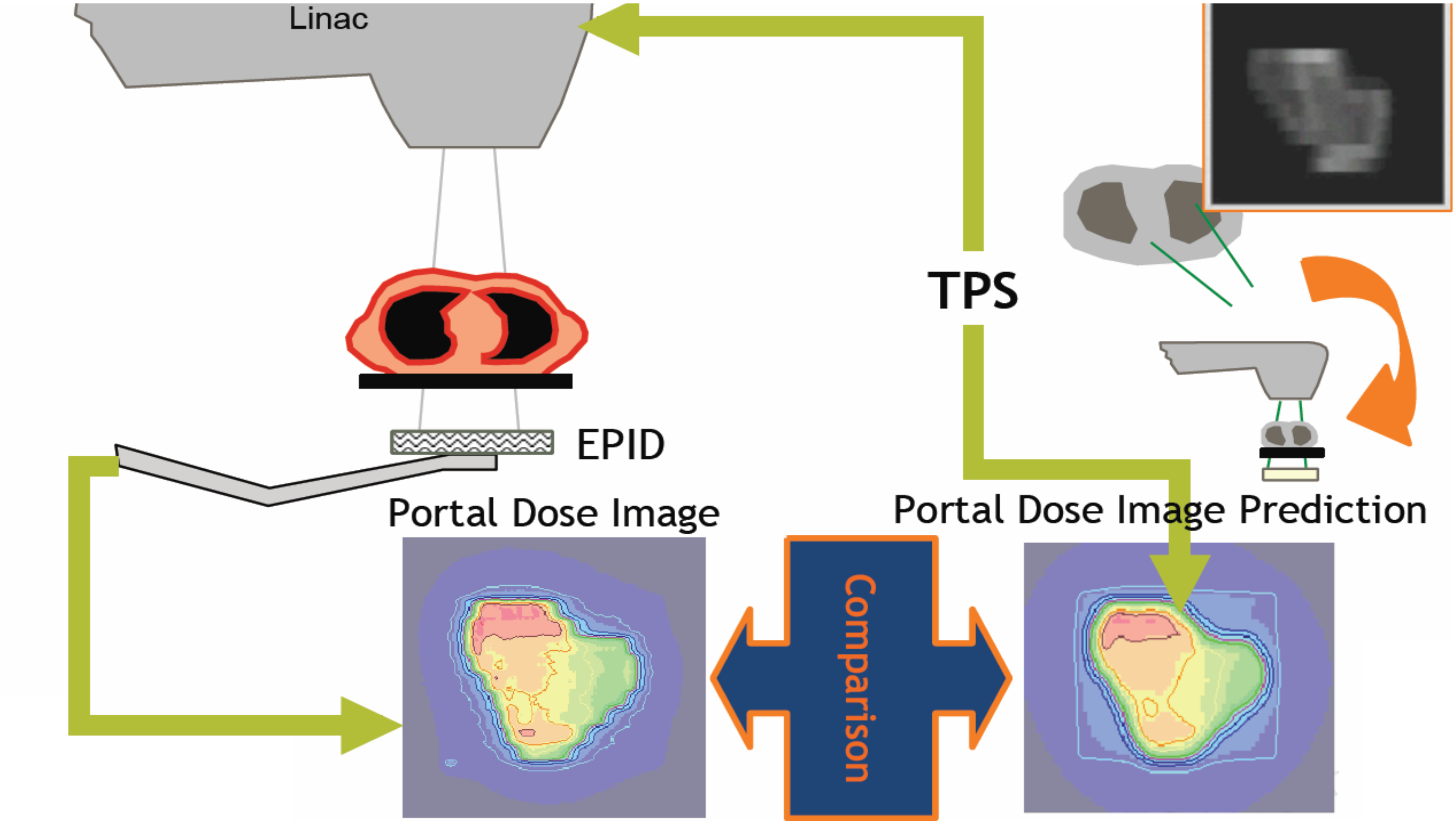
EPIDs: QA

QA /calibration for EPIDs



Non-imaging uses: portal dosimetry



•With/without phantom or patient
•commercial and non-commercial solutions

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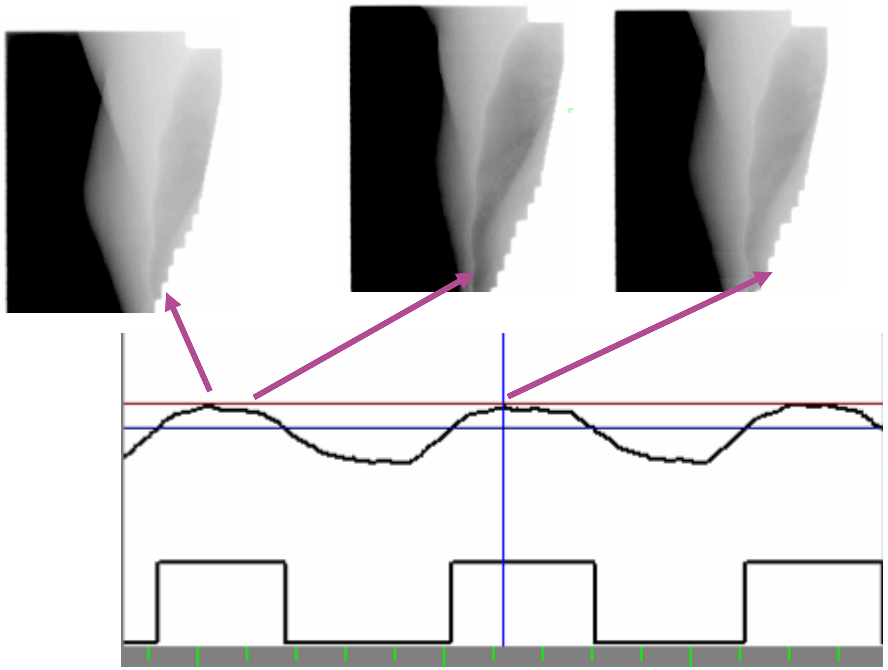
EPIDs: example of clinical strategy

EPIDs at Rigshospitalet

- 13 linacs in total
- 3 without kV imaging (EPID-based set-up of palliative treatments; some breast patients)
- On other machines: ”beam’s eye view” checks (gating window with cine EPID)



Let's adress the elephants in the room…

Is MV portal imaging still relevant today?

Yes but…

- ➢Less and less for set-up imaging purposes
- ➢Unlikely that it will be the best solution for intrafraction monitoring
- ➢Possibly increasing use for QA, transmission dosimetry, etc..

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Why planar kV?

- Better contrast (vs EPID)
- Lower dose (vs EPID)
- Speed of acquisition (stereoscopic vs CBCT)
- Experience (transferrable from EPID)

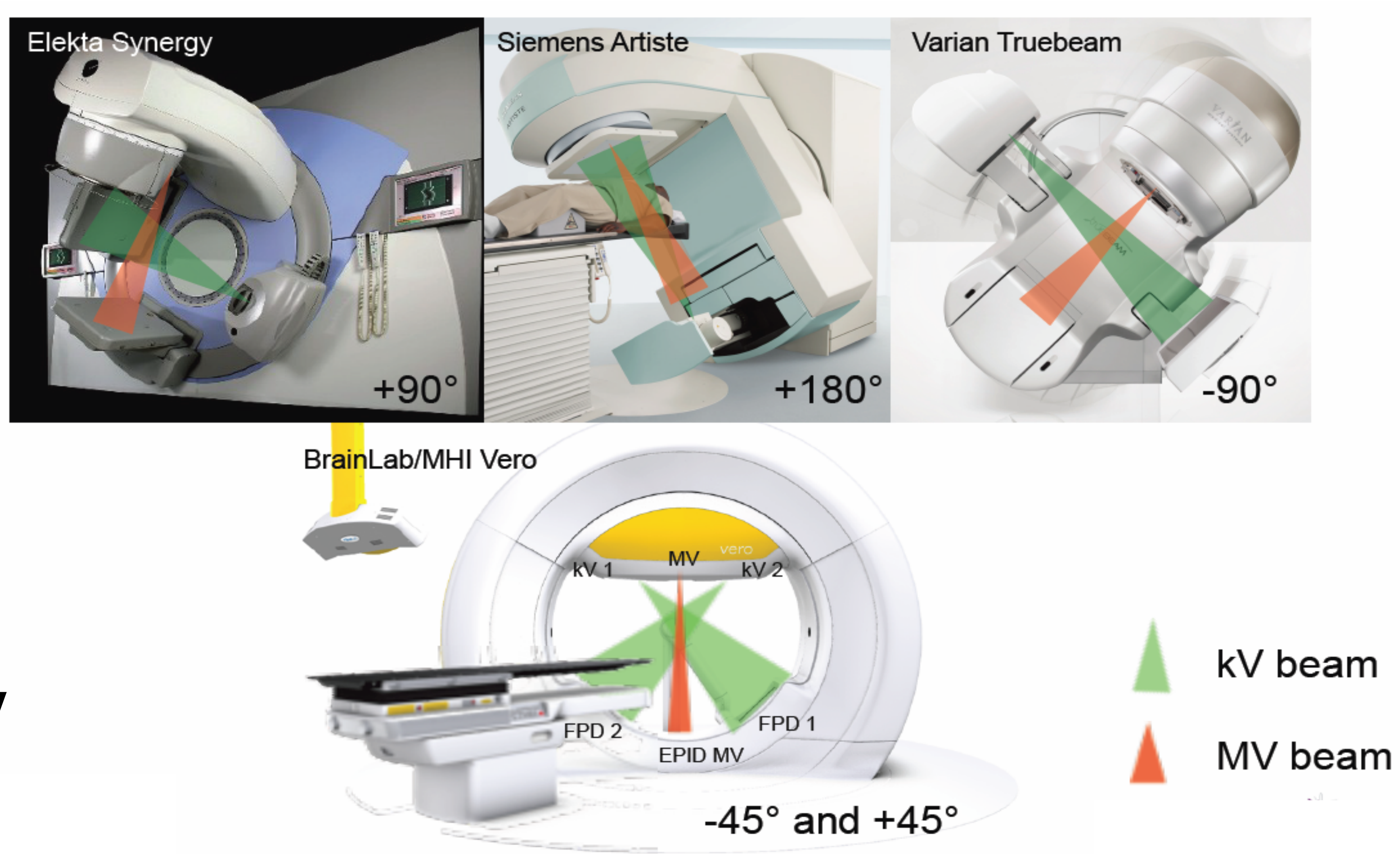
- Gantry-mounted vs floor/ceiling-mounted

Gantry-mounted kV: basic principles

Gantry-mounted systems

1x kV

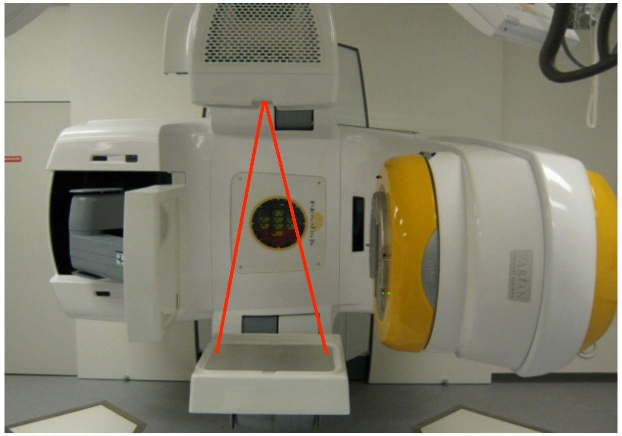
2 x kV



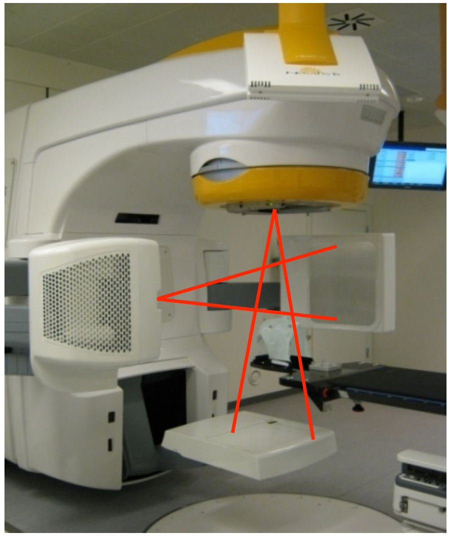
Gantry-mounted kV workflow: monoscopic

Option 1:
kV-kV

+



Option 2:
kV-MV



Advantages
- Isocentric
- CBCT acquisition

Limitations
- Monoscopic
- Geometrical distortions with rotation

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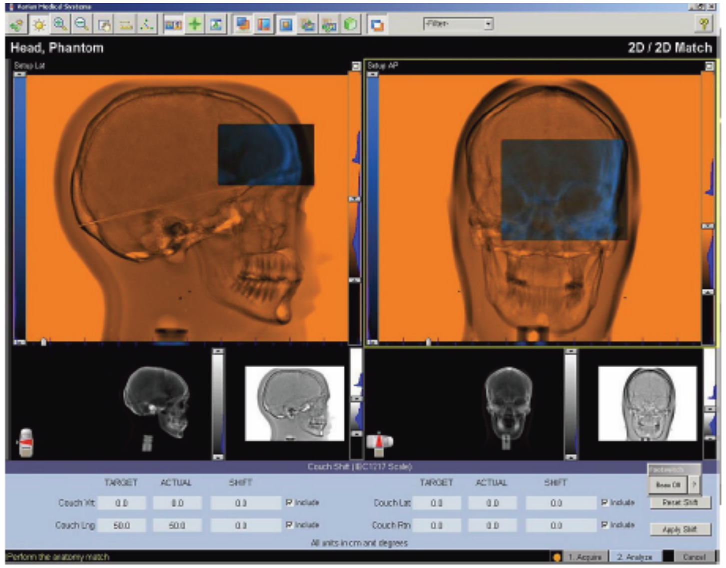
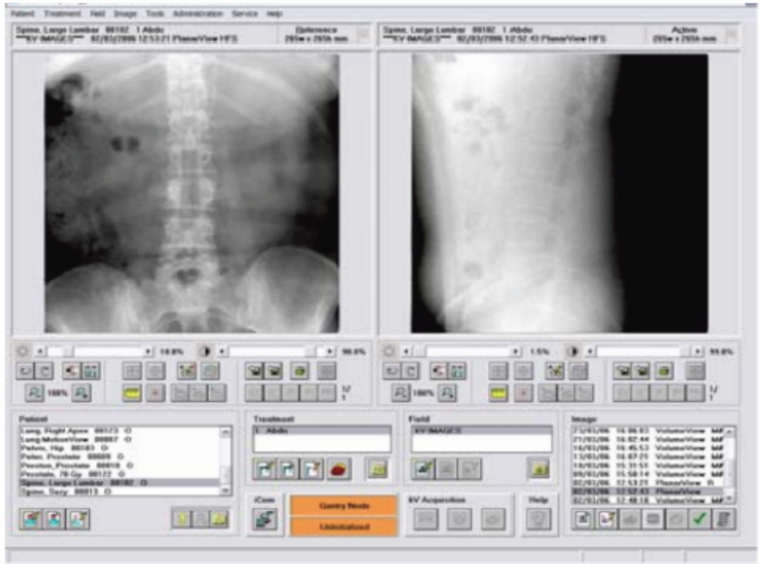
On-Board Imager (Varian)

Synergy PlanarView (Elekta)





30 x 40 cm flat panel

Pixel size 0.39 mm

15 frames/second rate

kV source 0.4 mm focal spot, 40-125 kVp

Robotic arms to position FPD and source

41 x 41 cm flat panel

Pixel size 0.4 mm

15 frames /sec rate

kV source 0.4 mm focal spot, 70-150 kVp

Manual positioning of FPD and source

Gantry-mounted kV: Pros and cons

Improved image quality

Low dose

Can acquire images at any angle

Possibility for volumetric imaging

<u>Intrafraction monitoring?</u>

Relatively poor soft tissue contrast (bone / marker match);

Monoscopic: needs several angles for 3D positioning information

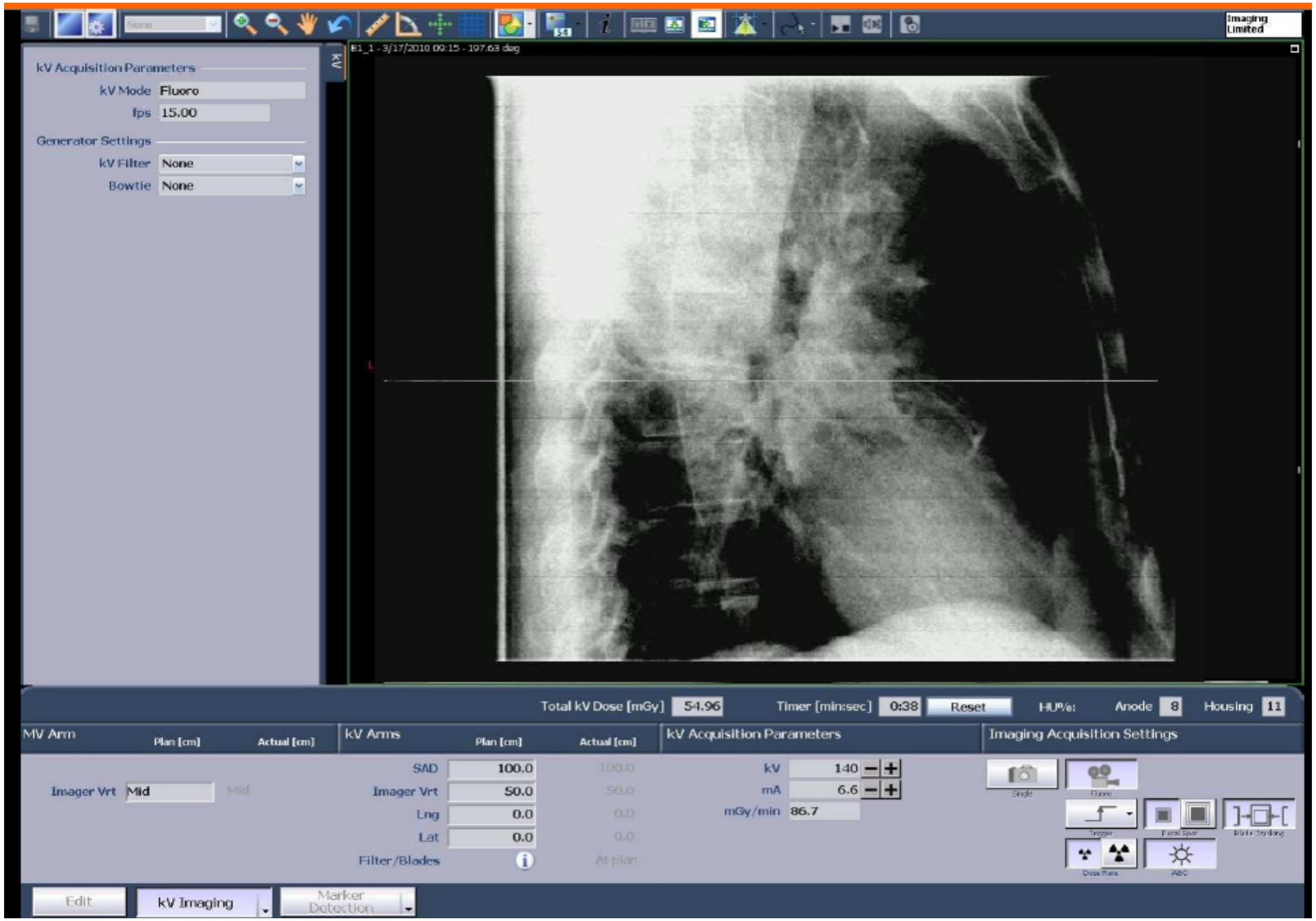
Potential collision with different couch angles (and very lateral targets?)

Inexact coincidence of kV and MV isocentre

<u>Intrafraction monitoring?</u>

Gantry-mounted kV: intrafraction monitoring

kV fluoroscopic imaging: pre- or during treatment



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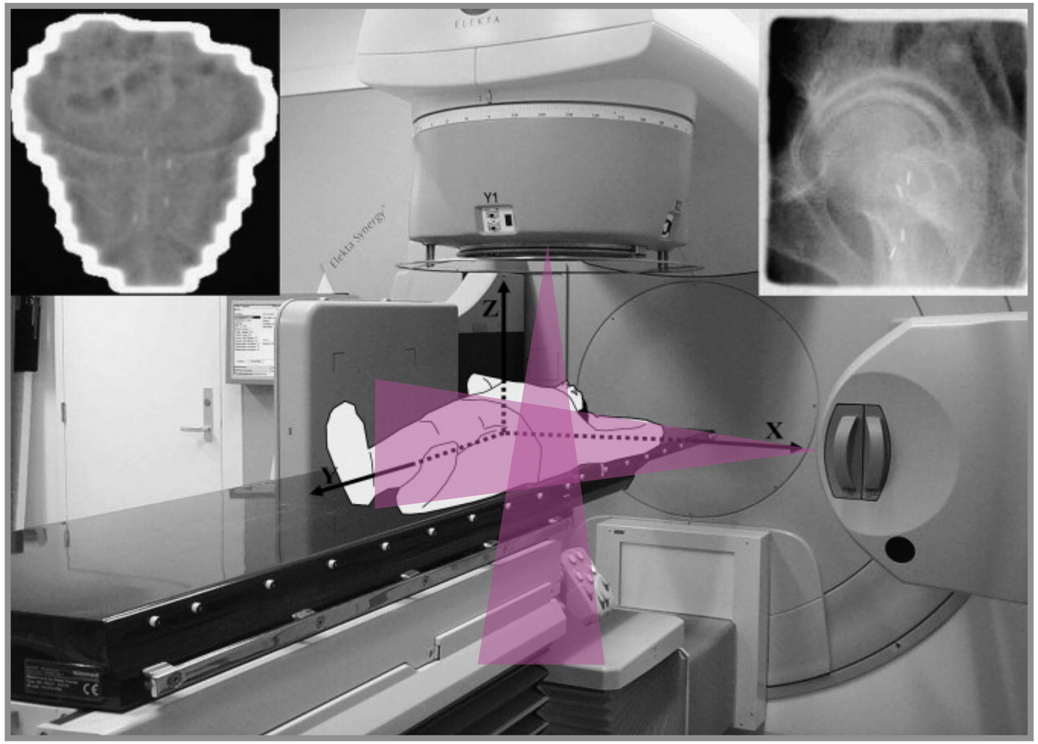
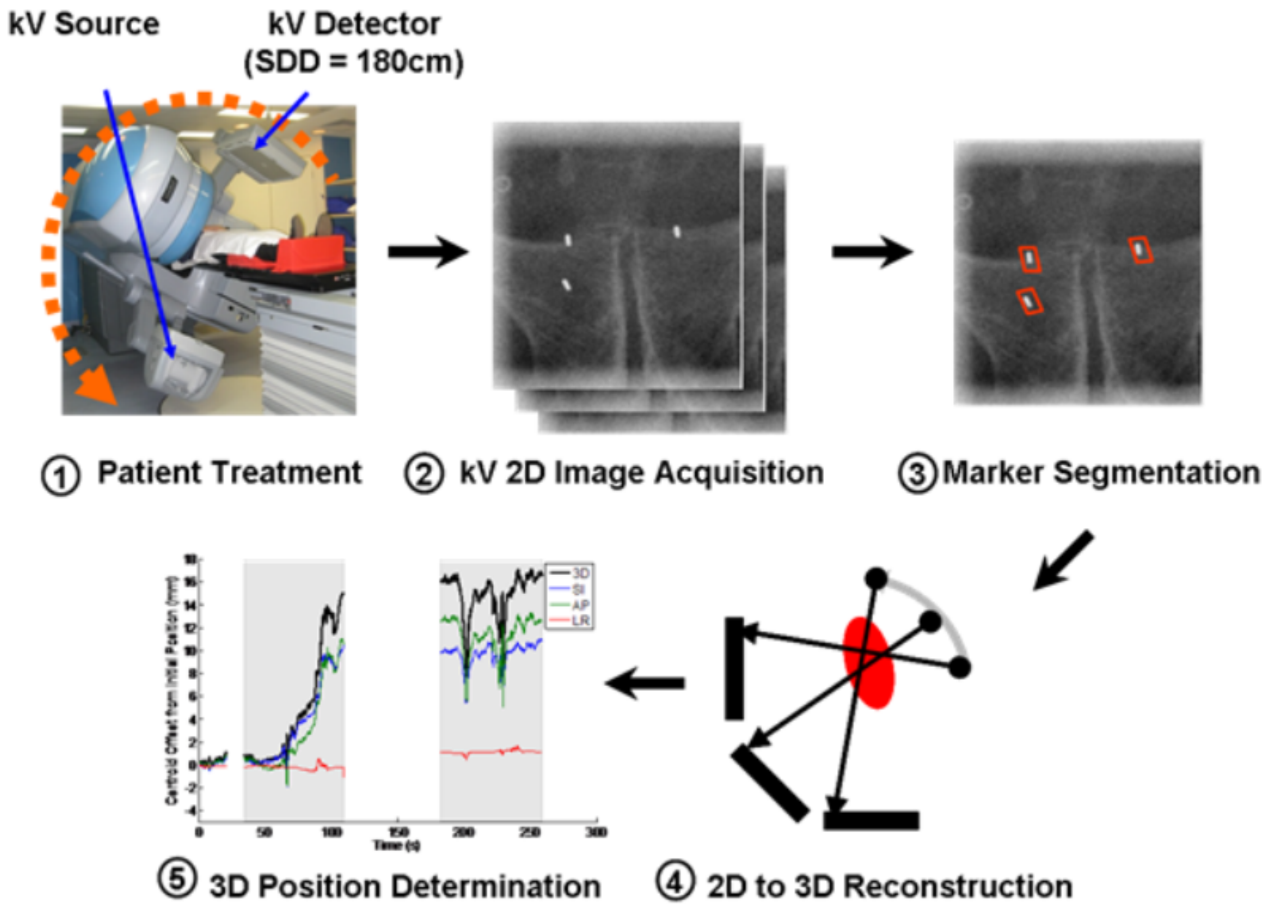
Inter + Intrafraction management on Conventional LINAC

- Dual MV/kV imaging
- Quick extraction of markers
- Automated correction by couch
- Residual error < 1 mm in < 1 min added treatment time
- Also compensating intra-fraction motion



Mutanga TF et al. Stereographic targeting in prostate radiotherapy: speed and precision by daily automatic positioning corrections using kilovoltage/megavoltage image pairs. IJROBP 2008

Inter + Intrafraction management on Conventional LINAC

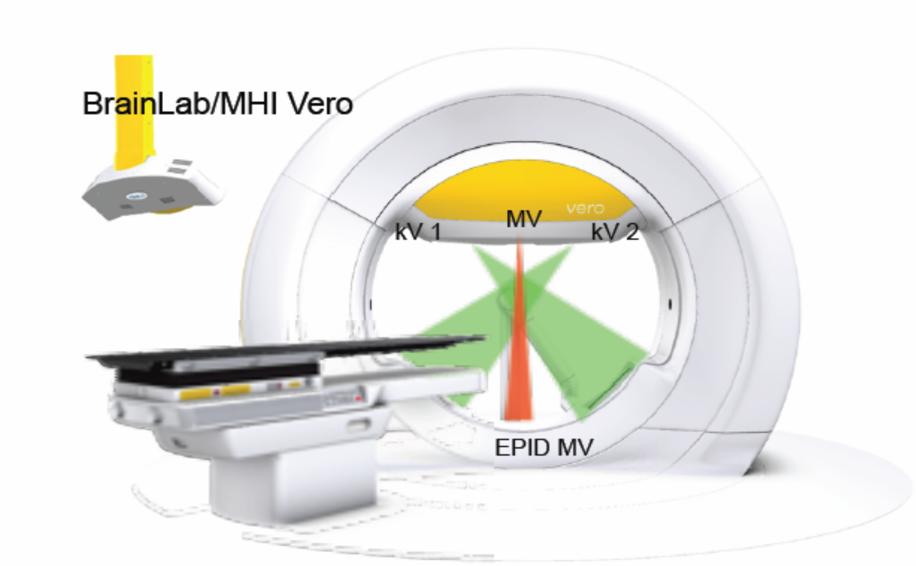


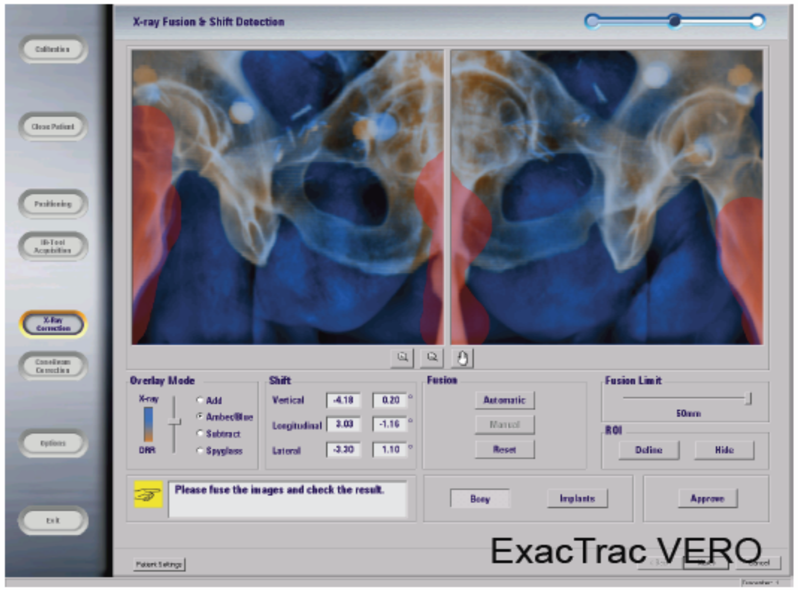
The clinical process workflow for Kilovoltage Intrafraction Monitoring gating.

Kilovoltage Intrafraction monitoring gating

Press release from sydney.edu.au, first patient treated sept 2014

”O-ring” gantry systems





Specifications
•2 times 30x40cm flat panel aSi (PaxScan 4030CB)
•Pixel size 0.39mm, 1024x768 matrix
•15 frames/sec rate
•kV source, 0.4mm focal spot, 40-125kVp
•kVs and FPB **fixed rigidly** to the O-ring gantry

GANTRY (deg)	RING (deg)	Measured deviation X(mm)	Y(mm)
270	0	-0.2	0.0
0	0	0.0	0.2
90	0	0.2	0.0
180	0	0.2	0.2
180	20	0.0	0.2
90	20	0.2	0.2
0	20	0.0	0.2
270	20	-0.2	0.0
270	340	-0.2	0.0
0	340	0.0	0.2
90	340	0.2	0.0
180	340	0.2	0.0

MV-kV isocenter
Coincidence < 0.2mm

Universitair Ziekenhuis Brussel
Vrije Universiteit Brussel

• Designed for intrafraction monitoring

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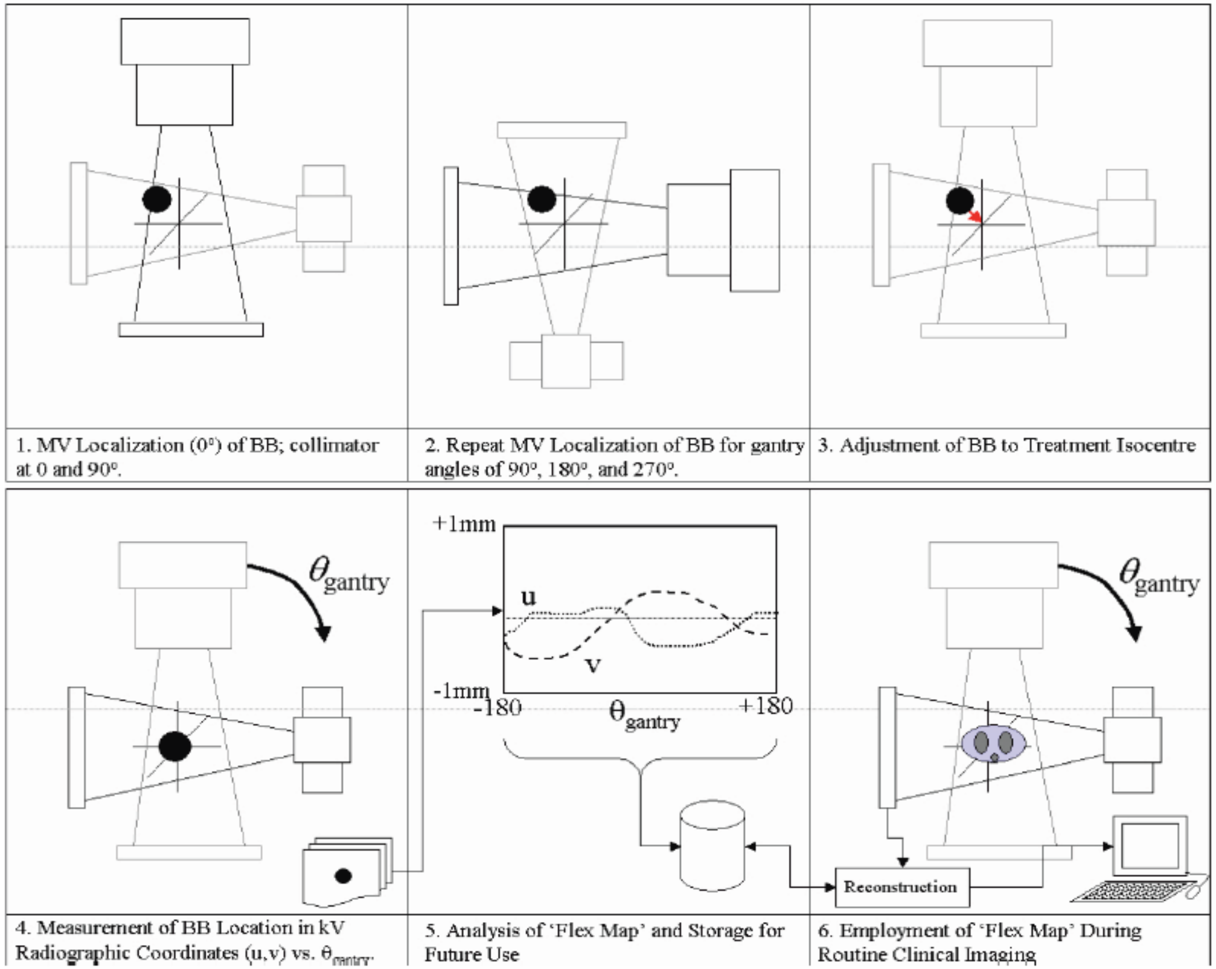
Gantry-mounted kV: QA

kV, gantry-mounted: Isocenter calibration



- ”gantry-mounted” does not guarantee the same isocenter as the treatment beam
- Geometric calibration to compensate for mechanical distortions (Flex Maps)
- good long-term stability

Bissonette JP, Princess Margaret Hospital, Canada

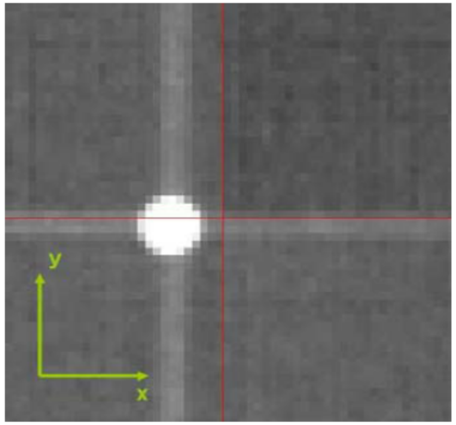
Disagreement between kV and MV isocenter at different gantry angles (cube isocenter phantom)

Table 3: Mean difference in position of the BB in kV images and MV images at different gantry orientations, n = 5.

Projection	Gantry/kVS orientation	Mean disagreement [mm] $\lvert\Delta x\rvert \pm 1\sigma$	$\lvert\Delta y\rvert \pm 1\sigma$
AP	0°	1.3 ± 0.1	1.5 ± 0.1
LR	90°	1.8 ± 0.1	1.3 ± 0.1
PA	180°	0.8 ± 0.1	1.5 ± 0.2
RL	270°	0.4 ± 0.1	1.6 ± 0.1

Milos Djordejvic ”evaluation of geometric accuracy and image quality of an OBI”, MSc thesis, Karolinska

X transverse
Y longitudinal



kV, gantry-mounted: Isocenter calibration

example of calibration tool

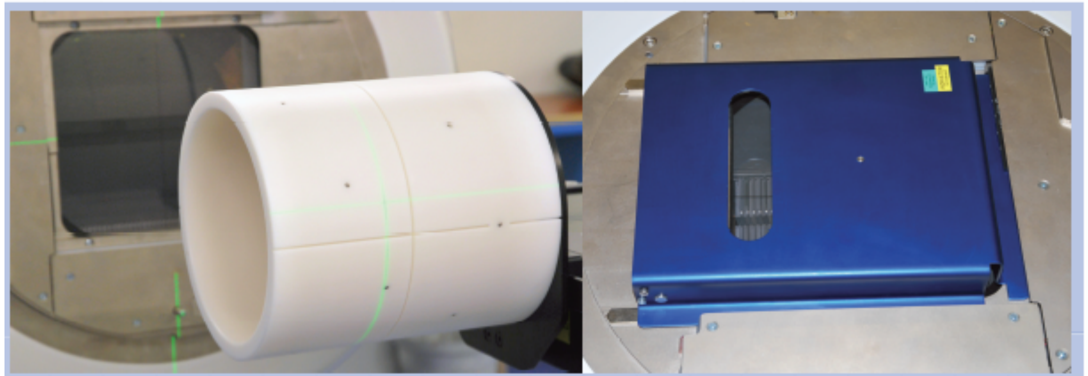


Figure 1: The BB phantom (left) and the collimator insert (right)

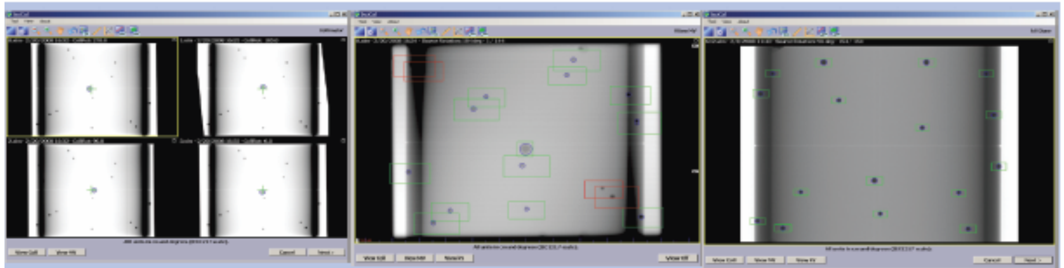


Figure 2: Left-to-right: Images of rotated MV collimator; MV image during gantry rotation ; kV images during gantry rotation. Cross correlation algorithms automatically detect the BB locations.

Jeung et al, ESTRO 2010
IsoCal, Varian Medical Systems

- 16 BBs, 4mm, should overlap when imaged
- Collimator insert, with a pin to determine MV central axis
- Automatic imager correction while the gantry is turning
- About 15 min for calibration procedure

Gantry-mounted kV : example of clinical strategy

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Gantry-mounted kV strategy at Rigshospitalet

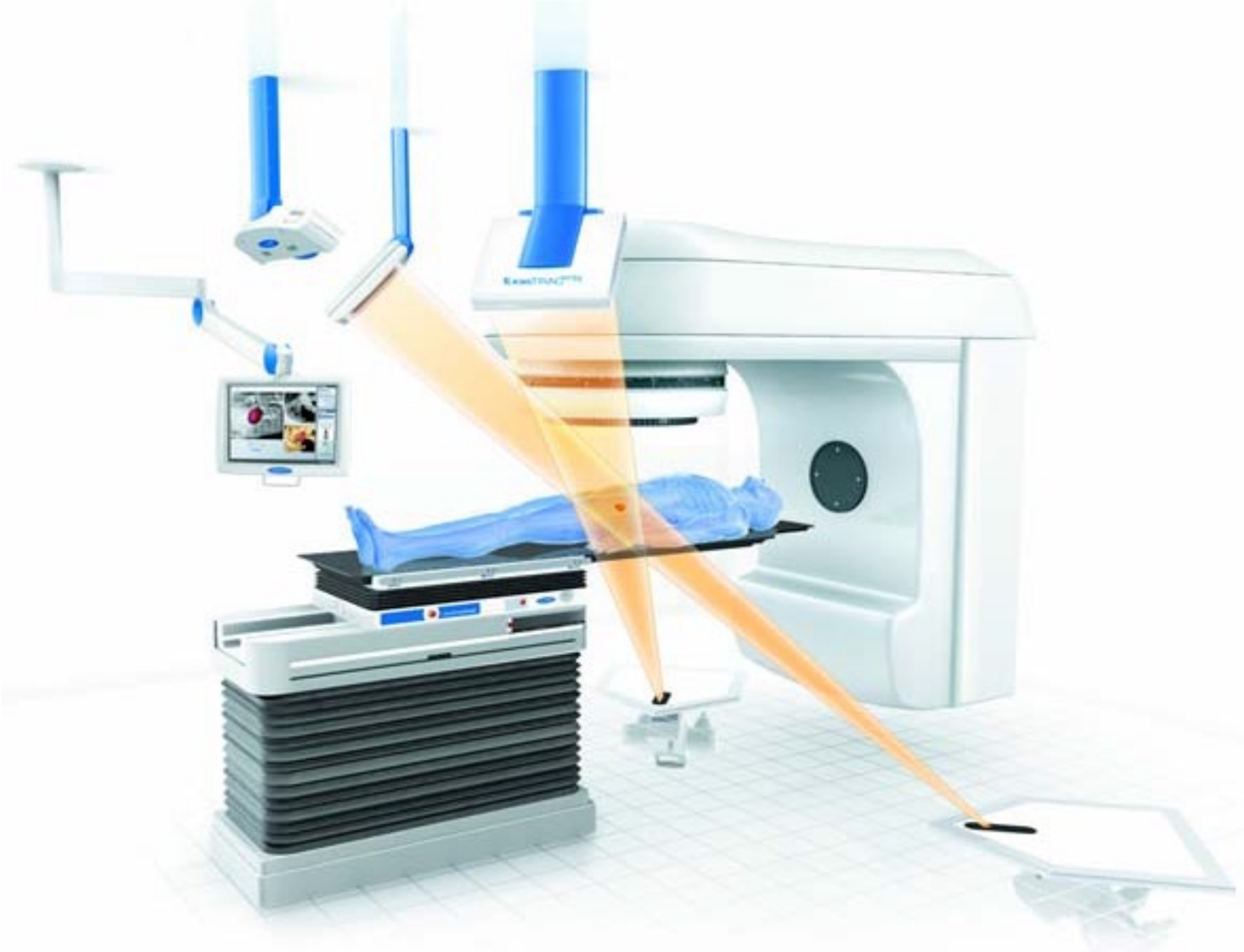
10/13 linacs have OBI capabilities

OBI images are used:

- When bony anatomy is a good surrogate (breast + regional nodes; mediastinal lymphoma)
- With gated treatments (left-sided breast)
- When dose is a concern (same + pediatrics)
- When the potential of CBCT hasn't been evaluated yet (palliative)
- And…. As a back-up when problems with CBCT!

Floor/ceiling-mounted kV: basic principles

Ceiling/floor mounted kV



Exactrac, Brainlab

Specifications
•20cmx20cm flat-panel aSi imagers;
•spatial resolution 0.39 mm with 512x512 matrix
• max 150 kVp
•x-ray system + optical tracking system

CyberKnife
Accuray, Inc.

• 20cmx20cm or 40cmx40cm flat-panel aSi imagers;

• resolution 0.4 mm at 512x512 pixels

•150 kVp X-ray sources Toshiba (separate power supplies)

•Designed for intrafraction monitoring:

  - •Works integrated with tracking software for a number of tumour sites (includes an optical marker system for respiratory tumour tracking)

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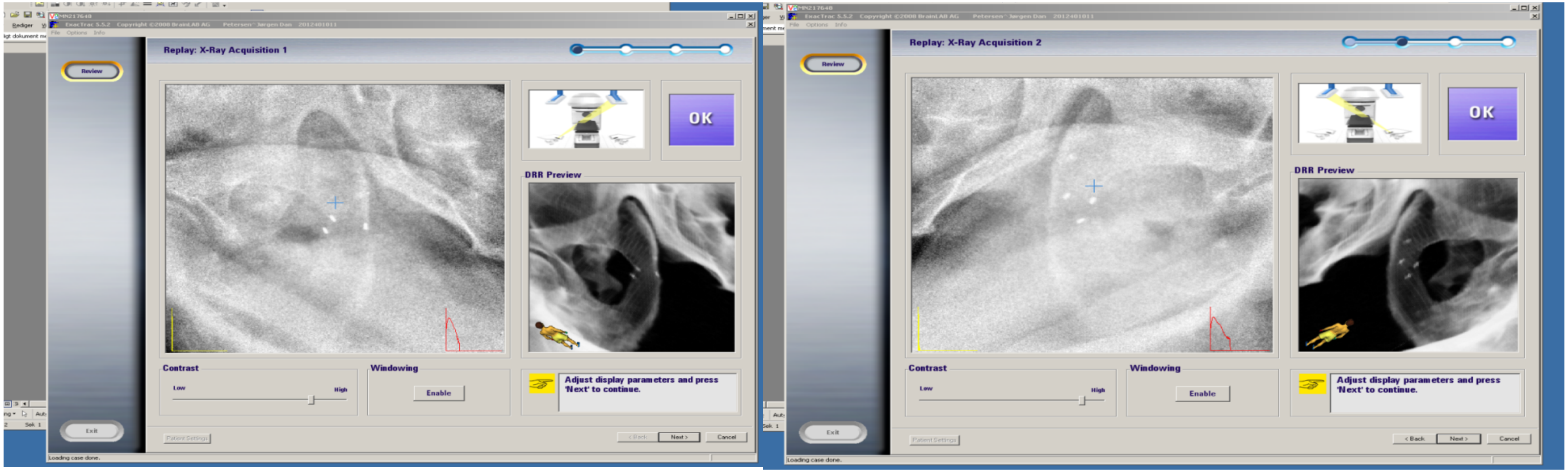
Main challenge: image interpretation !

Prostate: Planar oblique angle stereoscopic imaging with implanted markers



- This implies a certain reliance on the automatic fusion software
- Images should still be reviewed

Floor/ceiling mounted kV: Pros and cons

Stereoscopic: very fast acquisition

Very low dose?

Fixed system: high stability

Independent from MV source: intrafraction monitoring

Oblique images: interpretation?

Bone/marker match

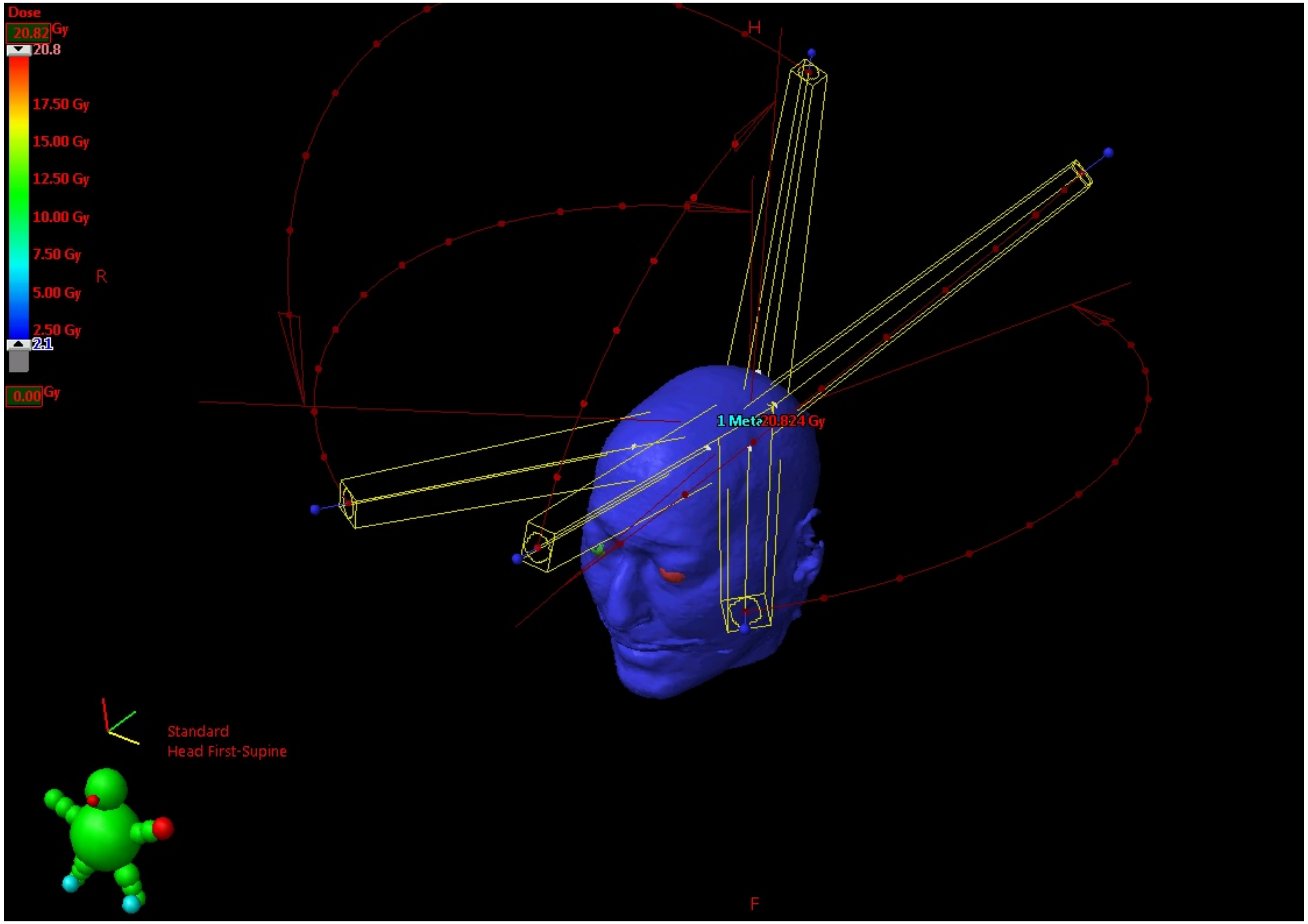
At some angles, the gantry can block the beam

No CBCT possibility

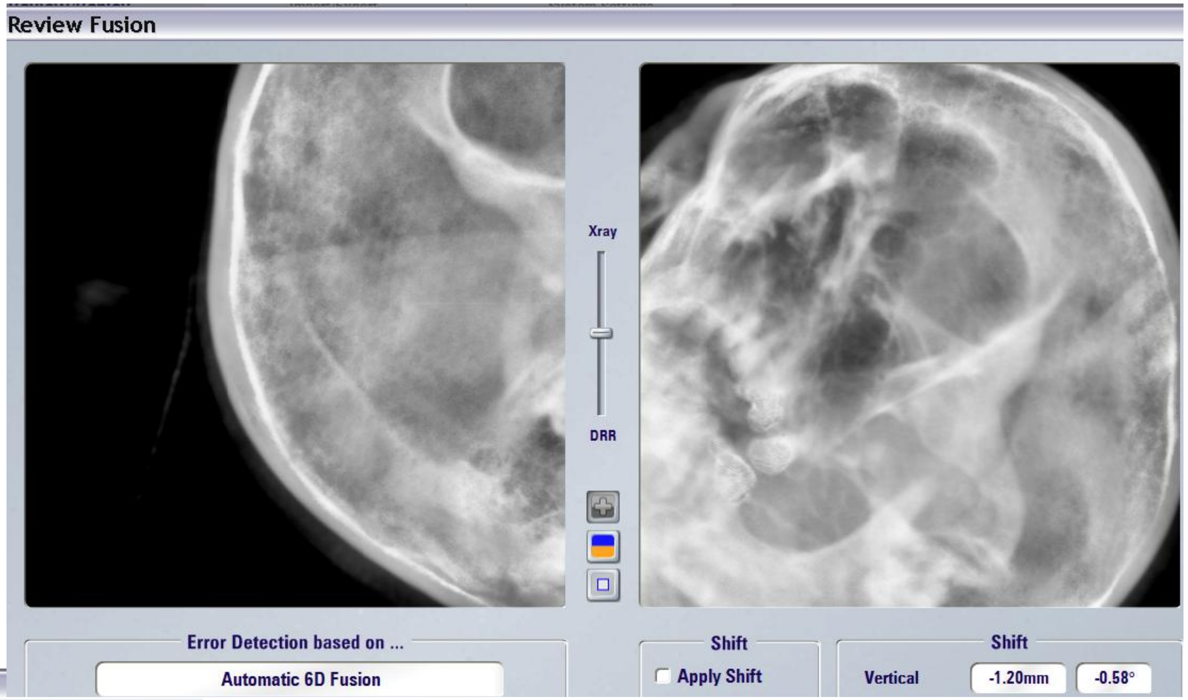
Frequent calibrations necessary to check alignment of kV and MV isocentres

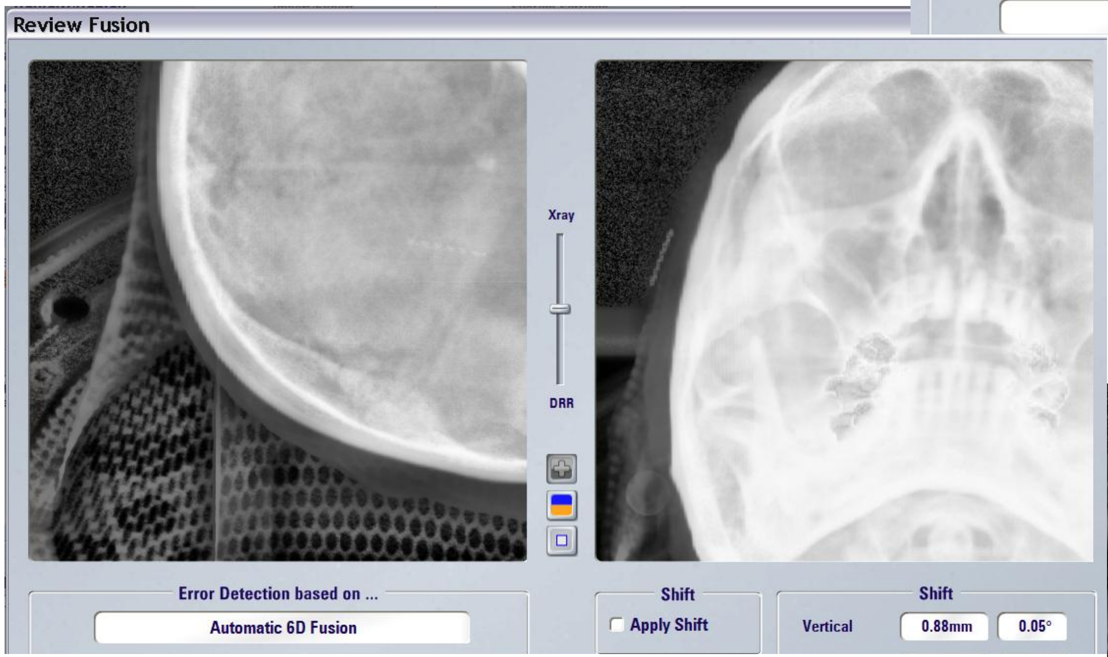
Floor/ceiling-mounted kV: intrafraction monitoring

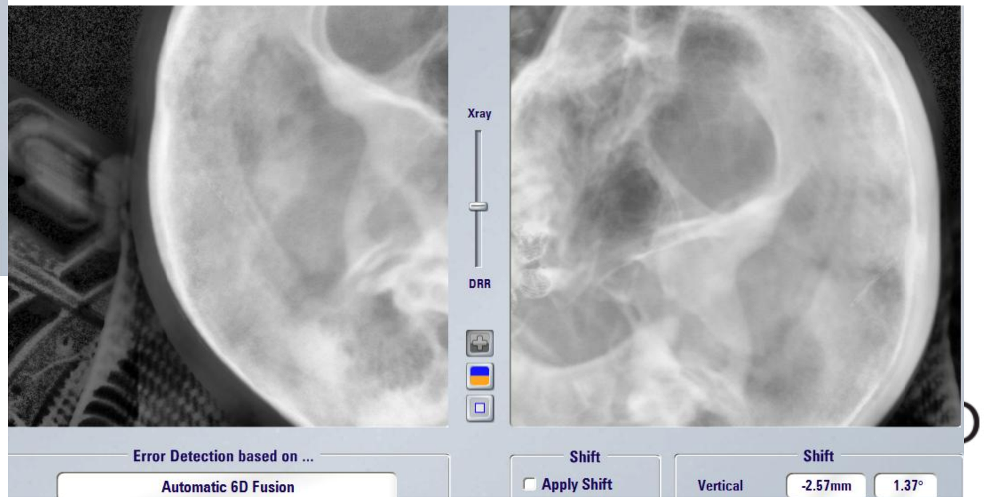
Intrafraction monitoring with stereoscopic kV: example of clinical application: Brain SRT



- 1 mm tolerance
- Image (and re-position) after every new couch angle
- Automatic fusion with visual review

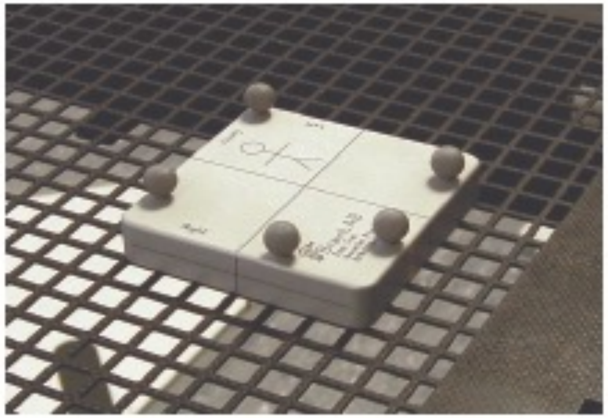


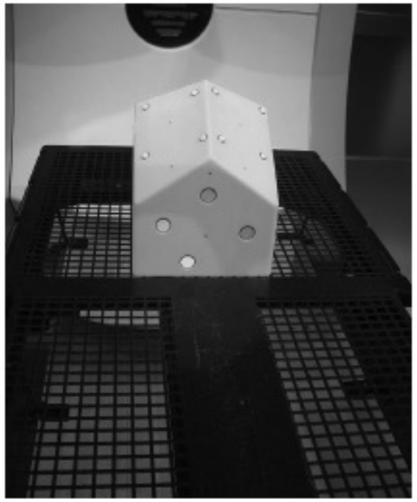




Floor/ceiling-mounted kV: QA

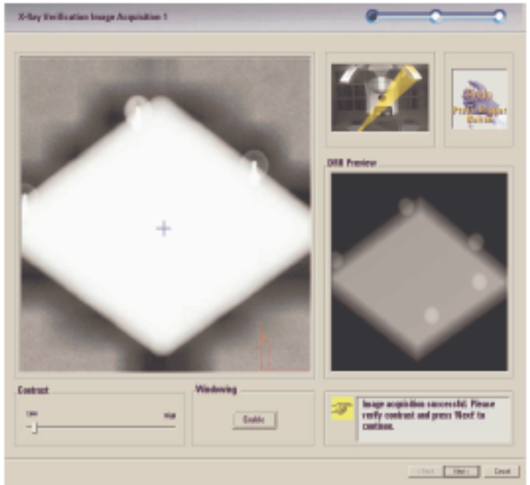
Example of alignment QA: ExacTrac

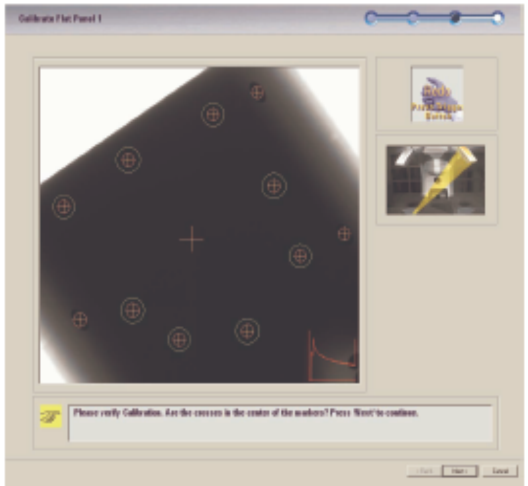




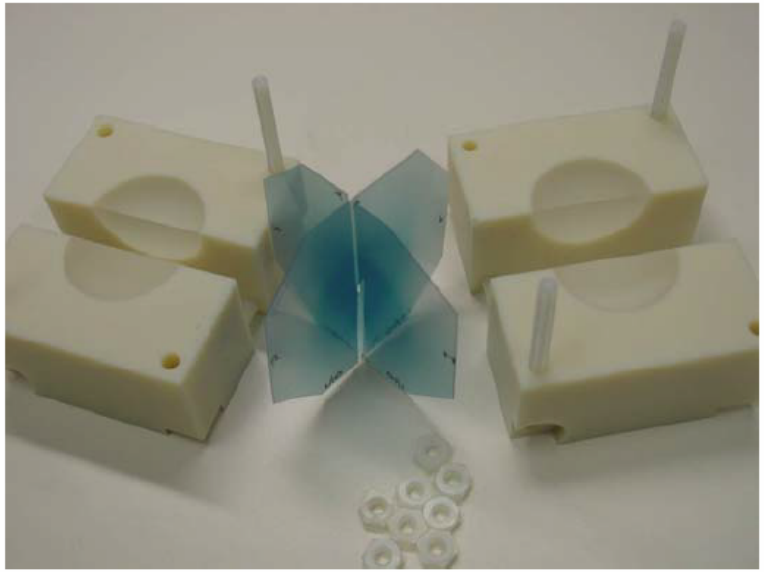
3 steps:

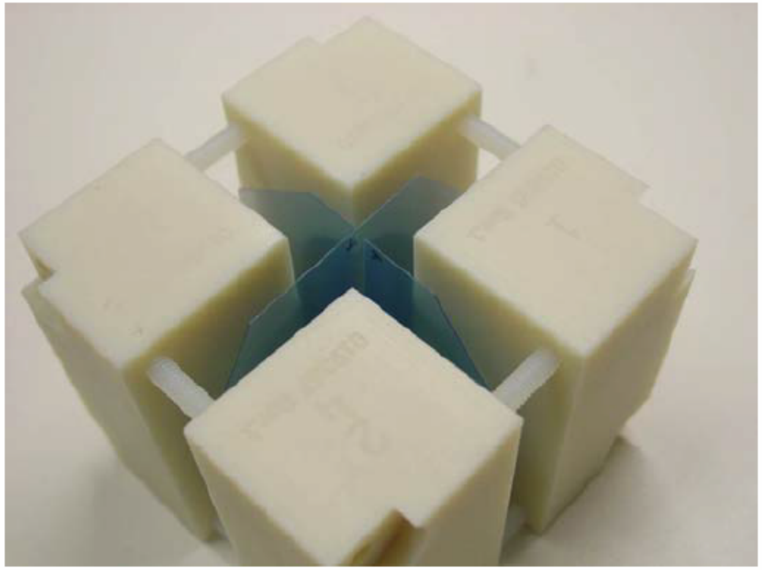
•Infrared isocenter to lasers
•Infrared to kV x-ray isocenter
•kV to MV isocenter





Cyberknife: ”end to end test”





QA tool to check the alignment of robot coordinate system and image guidance system

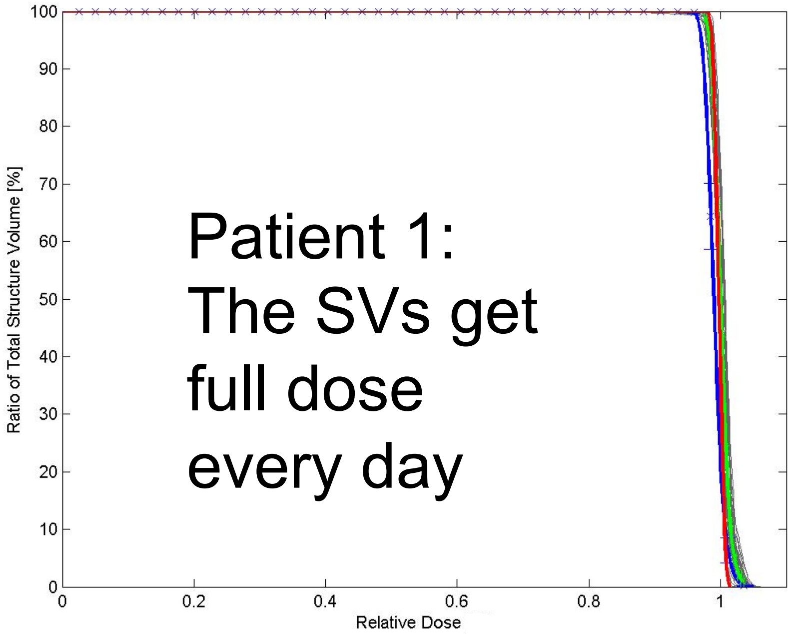
Floor/ceiling-mounted kV: example of clinical strategy

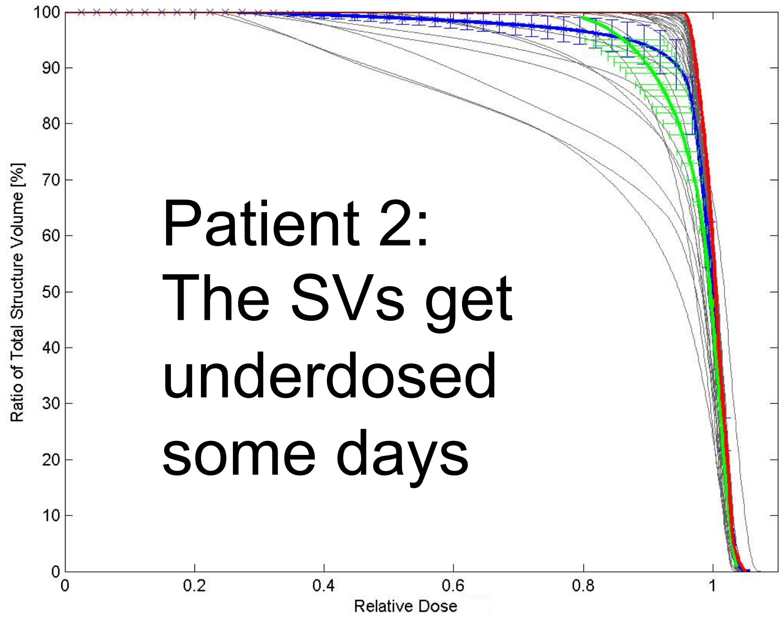
Floor/ceiling mounted kV strategy at Rigshospitalet

- 10/13 linacs have Exactrac capabilities
- Exactrac images are used:
  - When speed is important (palliative; prostate), simultaneous acquisition
  - In between non-coplanar beams (brain)
  - *When dose is a concern (breast-whole)*
  - When 6D position correction is desirable (brain)
    - Integration with Brainlab 6D couch

- When markers are available (prostate; breast-boost)

One note of caution about markers





- DVH of seminal vesicles after marker match on planar kV, recalculated on daily CBC
- Don't forget markers are <u>surrogates</u> and always wonder <u>what</u> they are good surrogates <u>of</u>

Let’s adress the elephants in the room…

Is MV portal imaging still relevant today?

Is kV planar imaging still relevant today?

Yes

- speed
- dose
- enables intrafraction monitoring

-easily compatible with gating, etc…

-But be aware of what you (don’t) see

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Let’s adress the elephants in the room…

Is MV portal imaging still relevant today?

Is planar imaging still relevant today?

What about 5-10 years from now?

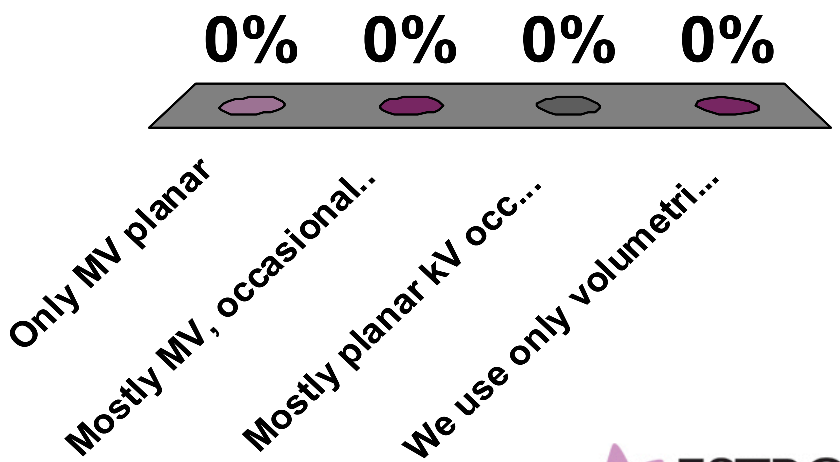
If you had unlimited resources (time/equipment), what do you think you would use?

A. Only CBCT

B. Mostly CBCT, but I still see some use for planar imaging

C. Mostly planar kV, CBCT only where a real benefit is demonstrated

D. I'm not sure, actually !



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Thinking beyond image quality

- **Workflow/ expertise issue**

The opinion of the faculty:

- **Where do you get the most "bang for your buck" out of 3D imaging?**
  - ➢ **Most: lung**
  - ➢ **Least: breast*/prostate***
- **Where is it easiest to start?**
  - ➢ **Breast/prostate**

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Conclusion

Planar imaging is widely available, and provides an excellent set-up/monitoring strategy when a match on markers or bony anatomy is possible/desired

It is an interesting option for intrafraction monitoring

It has clear advantage in terms of speed (especially stereoscopic systems) and, possibly, dose

Don't throw away your MV imager just yet: potential for "beam's eye view" and as a dosimetry tool

Trend towards increasing use of volumetric imaging

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WWW.ESTRO.ORG/SCHOOL

kV-cone beam CT/In-room kV-CT

MV CT

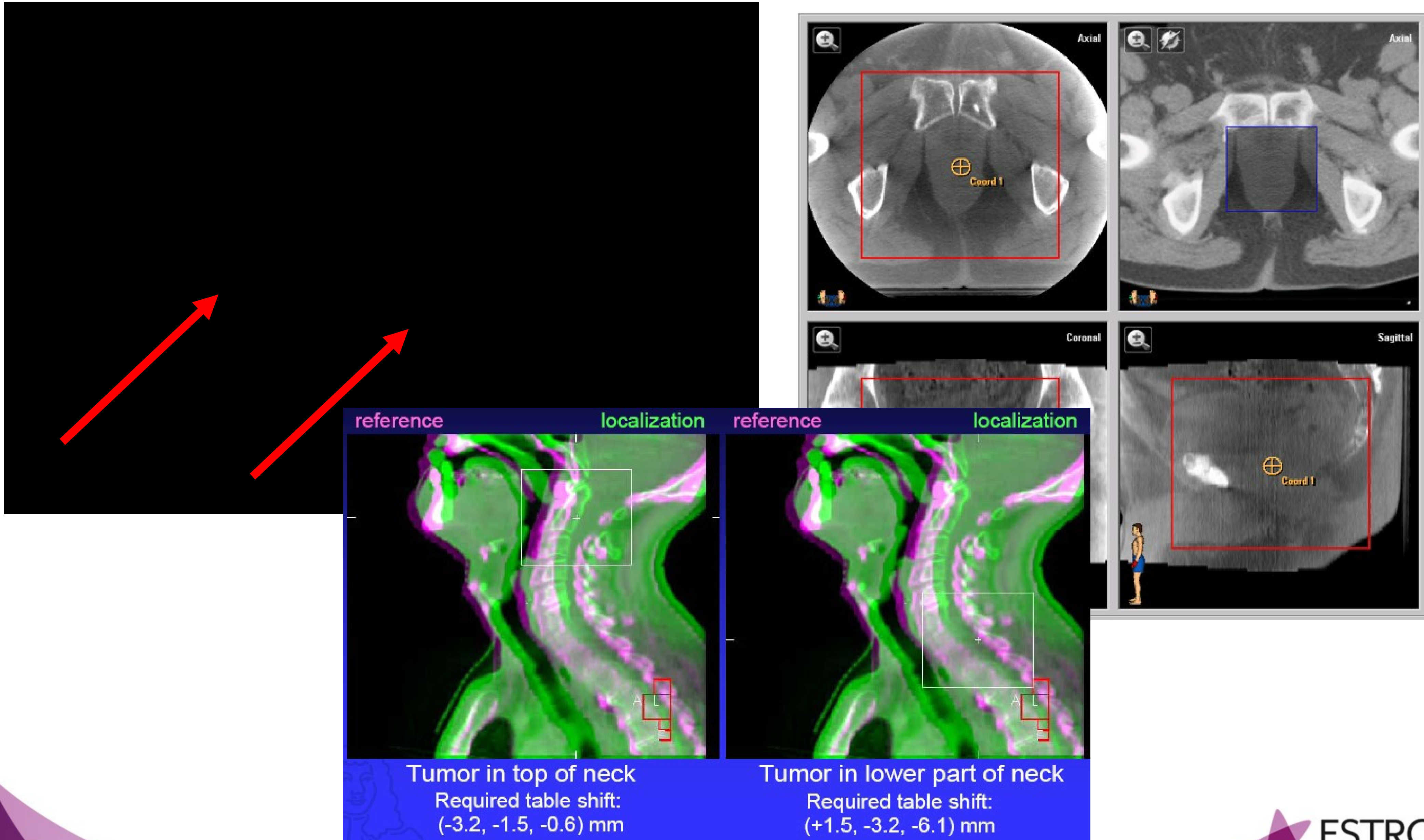
Uwe Oelfke

ICR/ RMH London
Joint Department of Physics
uwe.oelfke@icr.ac.uk

Why volumetric imaging for IGRT?

- 3D definition of anatomy (volumetric imaging) in the treatment room
- CT with full FOV and adequate e^--density quantification for dose calculation
- CT images are widely accepted and familiar with radiation oncologists (delineation target and OAR)
- Single modality when compared with planning CT

Why volumetric imaging for IGRT?



Courtesy of M. van Herk & J-J Sonke

Generic Features

kV vs MV

Fan Beam vs Cone Beam

Volumetric imaging systems for IGRT

CT

CBCT

kV

MV

kV vs MV - Contrast

Attenuation Process	Mass coeff. dependence		
Raleigh scattering	Z		
Photo-electric effect	Z^3	⇨	kV
Compton scattering	(only e^- density)	⇨	MV
Pair production	Z^2		

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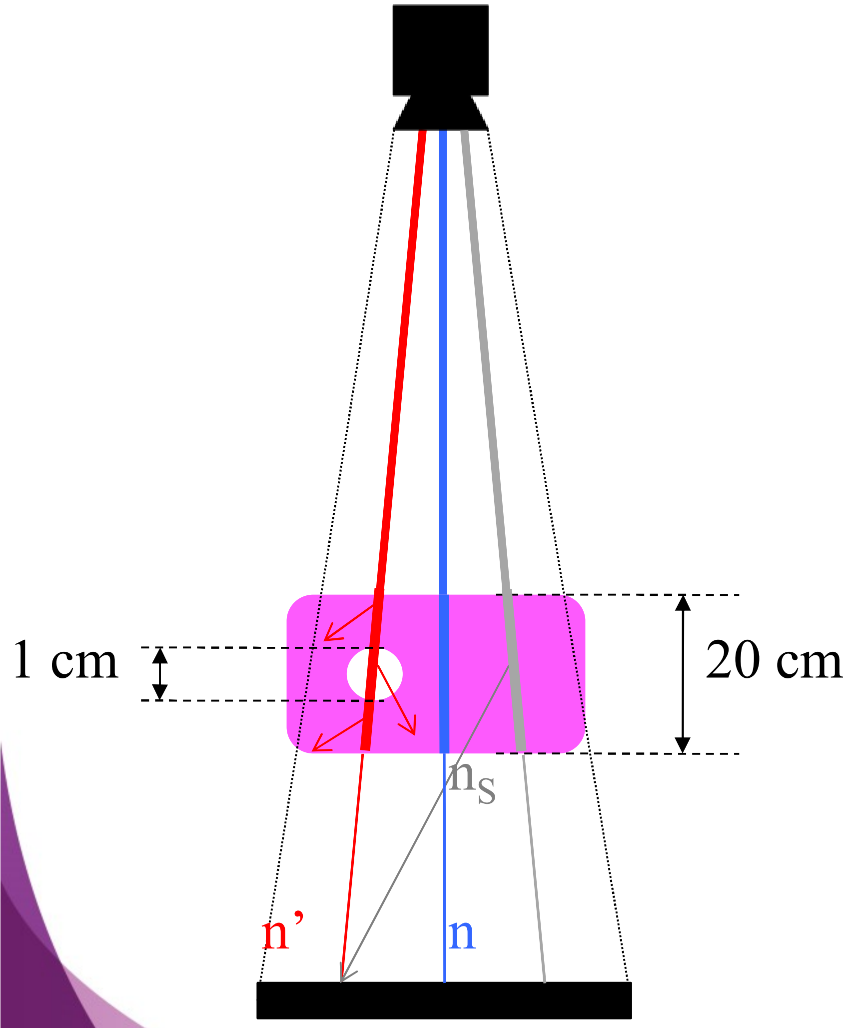
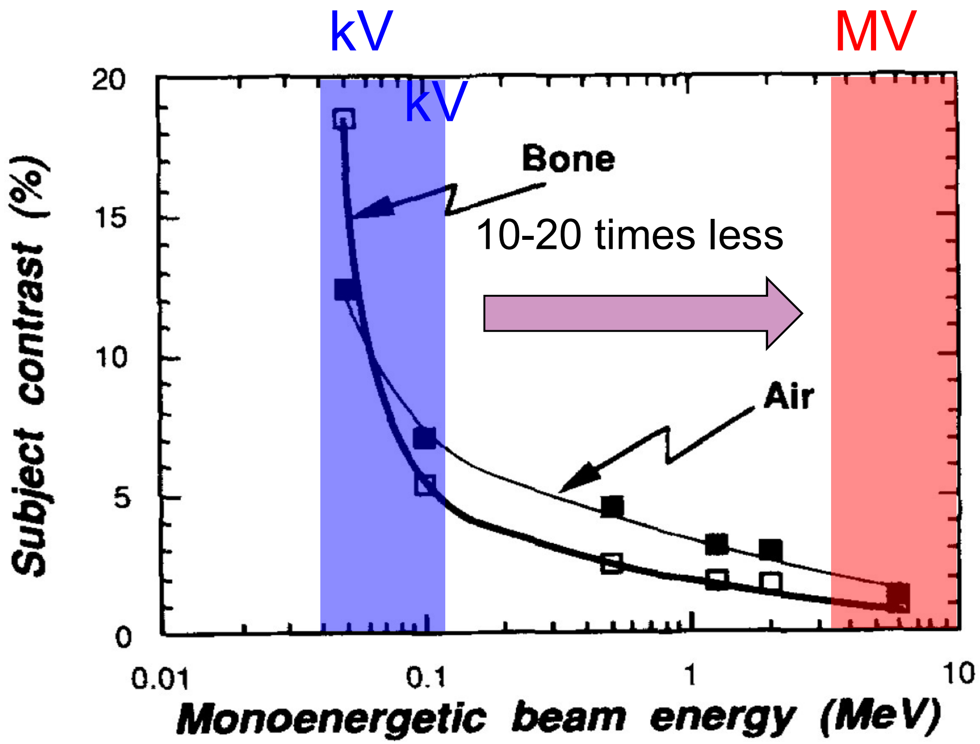
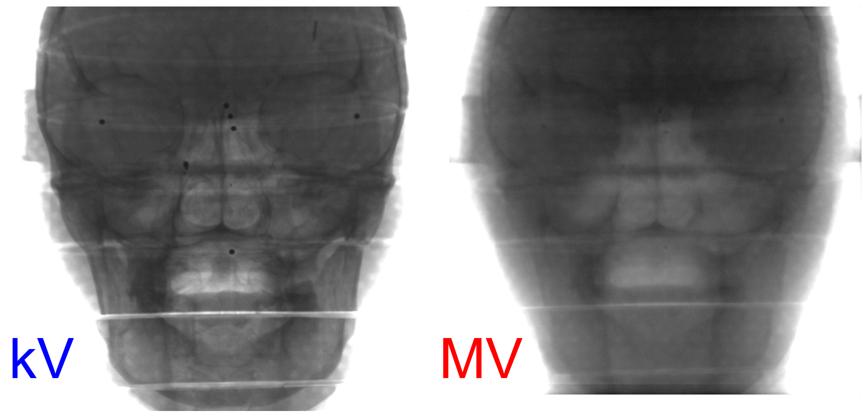
kV vs MV - Contrast

"Impact of imaging beam spectrum on image quality"





Energy	S
50 kV	18.5 %
1.25 MV	1.8 %
2.00 MV	1.4 %
6.00 MV	1.0 %

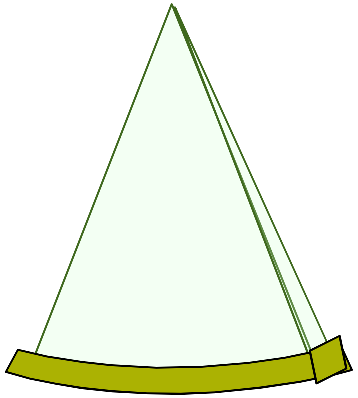


A. Boyer et al. Med. Phys 1992;19(1)

Volumetric IGRT systems: Fan Beam vs. Cone Beam

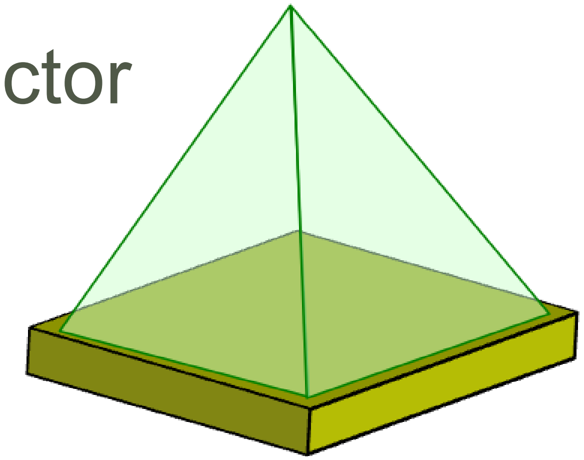
➔ Fan beam systems:

- Fan beam / linear detector array
- In room kV CT
- Helical Tomotherapy: MV CT



➔ Cone beam systems:

- Open beam / large area flat panel detector
- MV CBCT
- kV CBCT



Fan beam CT vs. Cone beam CT

(same radiation quality)

Advantages of FBCT:

- Efficient, ‘optimized’ detectors
  - Ionisation chambers, ultra-fast ceramics
  - Detectors are shielded against scattered radiation
- Reduced scatter (imaging a smaller volume per rotation)
- Faster gantry rotation

→ FBCT Image quality > CBCT Image quality

X-ray based IGRT technologies

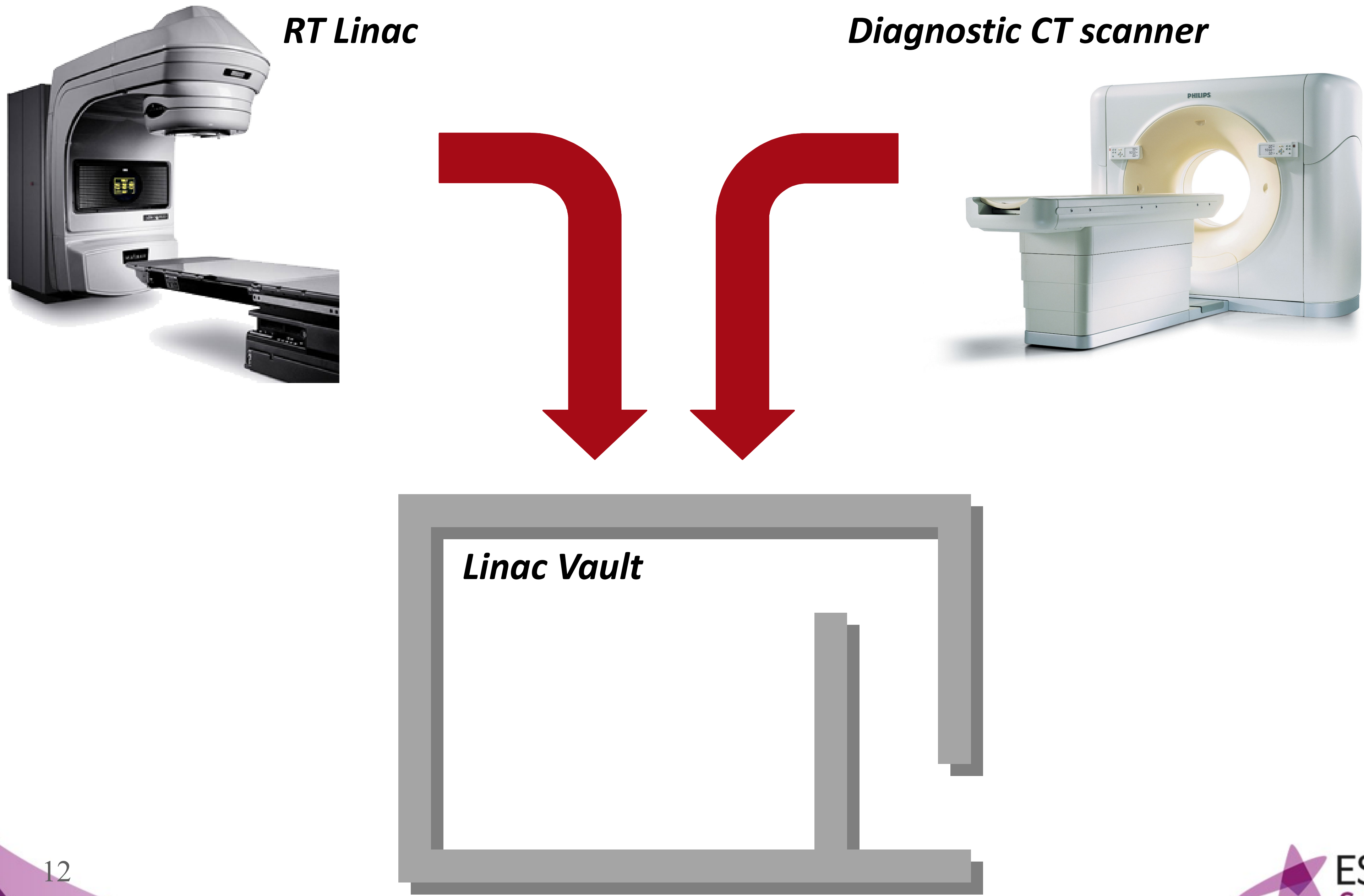
TABLE I. Commercially available CT-based IGRT systems.

Make and model		Elekta XVI	Varian On-Board Imager	Siemens Artiste	TomoTherapy	Siemens Primatom
Imaging configuration		kV-CBCT	kV-CBCT	MV-CBCT	MVCT	kVCT-on rails
Field of view		50 × 50 × 25.6	45 × 45 × 17	40 × 40 × 27.4	40 cm	50 cm
Correction method	Translation	Automatic couch motion	Automatic couch motion	Automatic couch motion	Automatic in 2 directions	Manual couch motion
	Rotation	Optional	None	None	Optional	Optional
Geometric accuracy		Submillimeter	Submillimeter	Submillimeter	Submillimeter	Submillimeter
Dose (cGy)		0.1–3.5	0.2–2.0	3–10	0.7–3.0	0.05–1
Image acquisition and reconstruction time		2 min	1.5 min	1.5 min	5 s per slice	3 s per sec

Bisonette et al. AAPM TG 179

Medical Physics, Vol. 39, No. 4, April 2012

Linac + CT (in the same room)= In-room CT IGRT?



In-room CT-on-rails setup

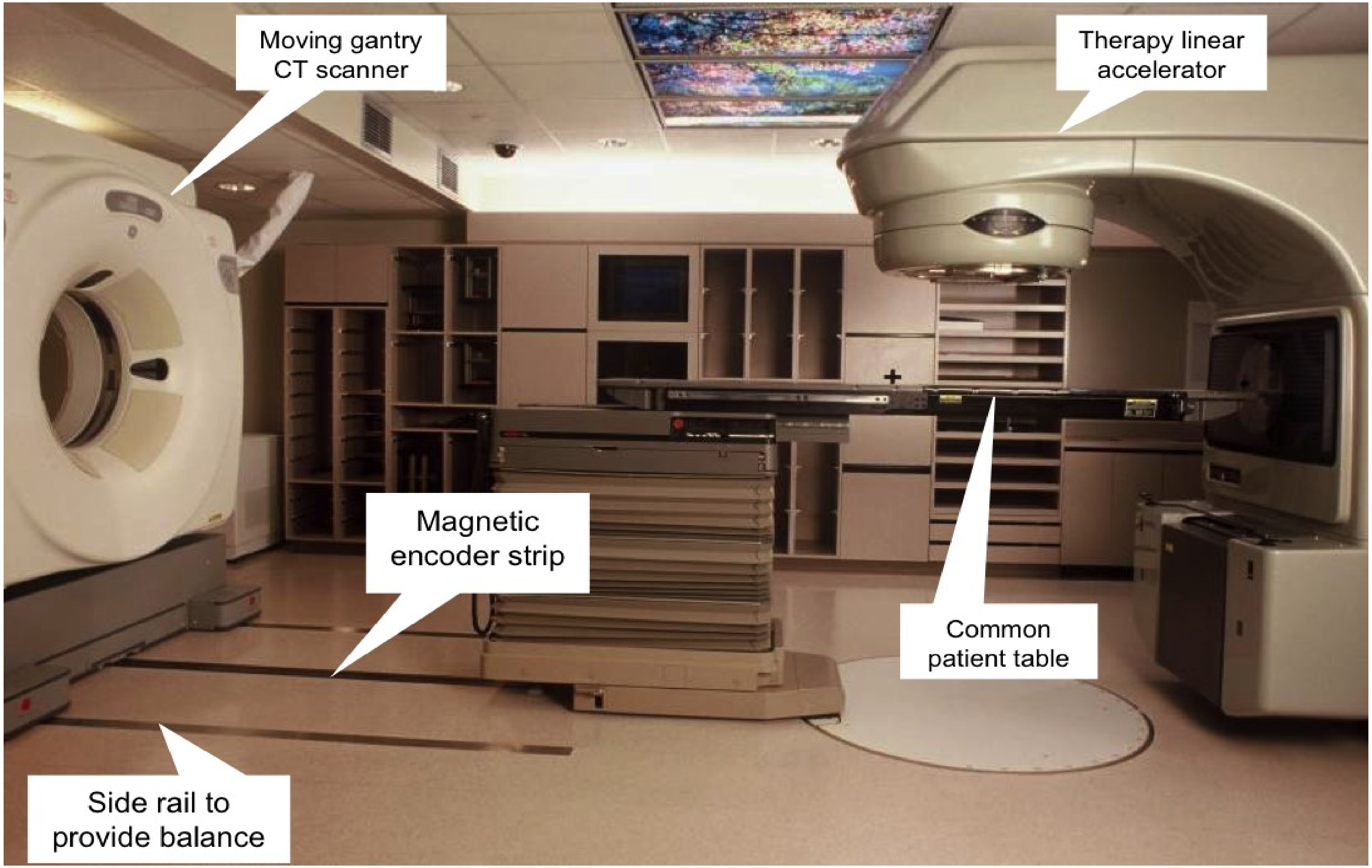
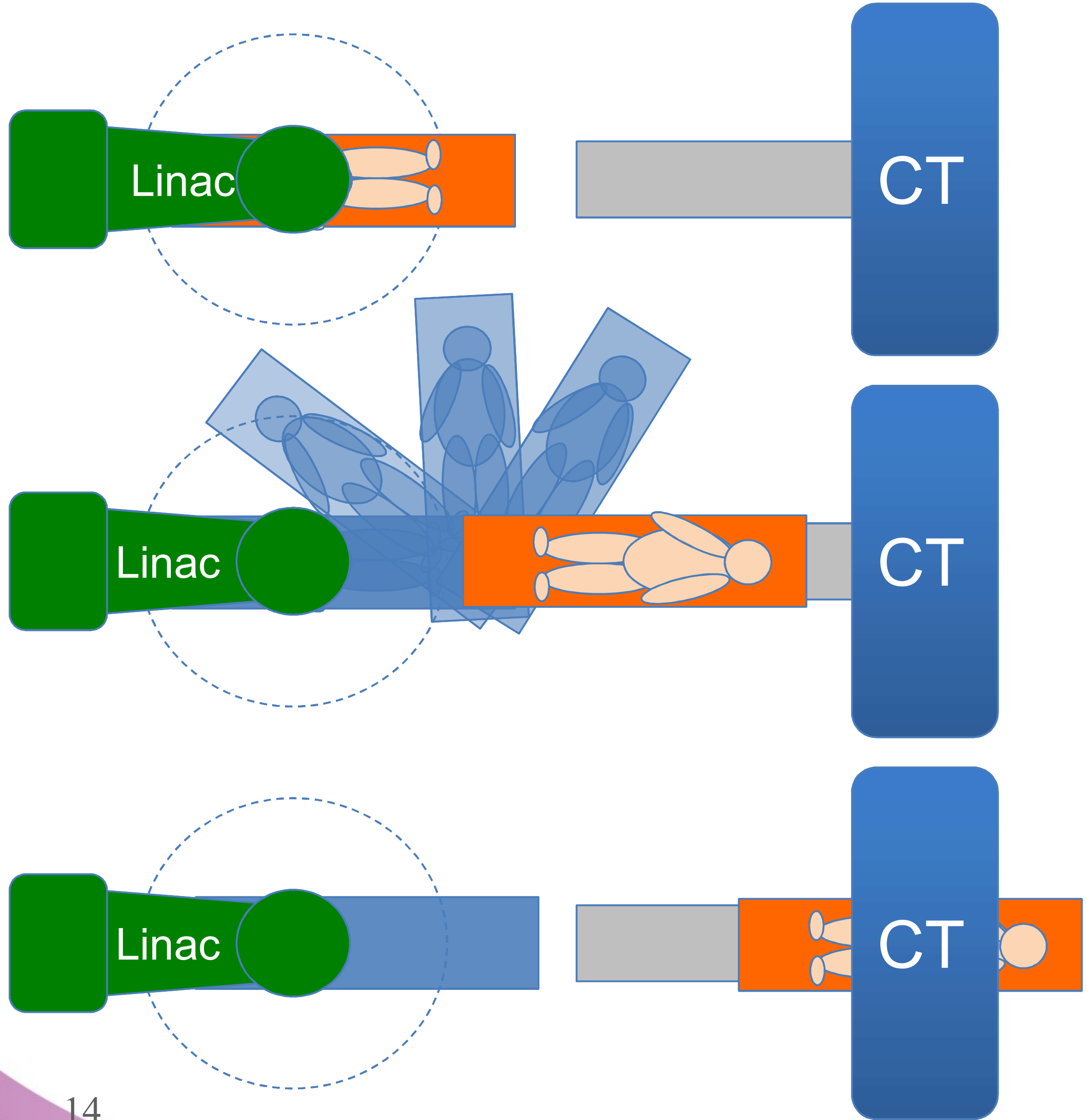


Figure 4. A CT-on-Rails system combining a GE Smart Gantry CT scanner and a Varian 2100EX linear accelerator was installed at the M.D. Anderson Cancer Center. After rotating the couch 180 degrees, a patient can receive a CT scan while in the immobilized treatment position just prior to the start of radiation treatment.

In-room CT setup



Initial setup on linac

Transportation Patient to the CT

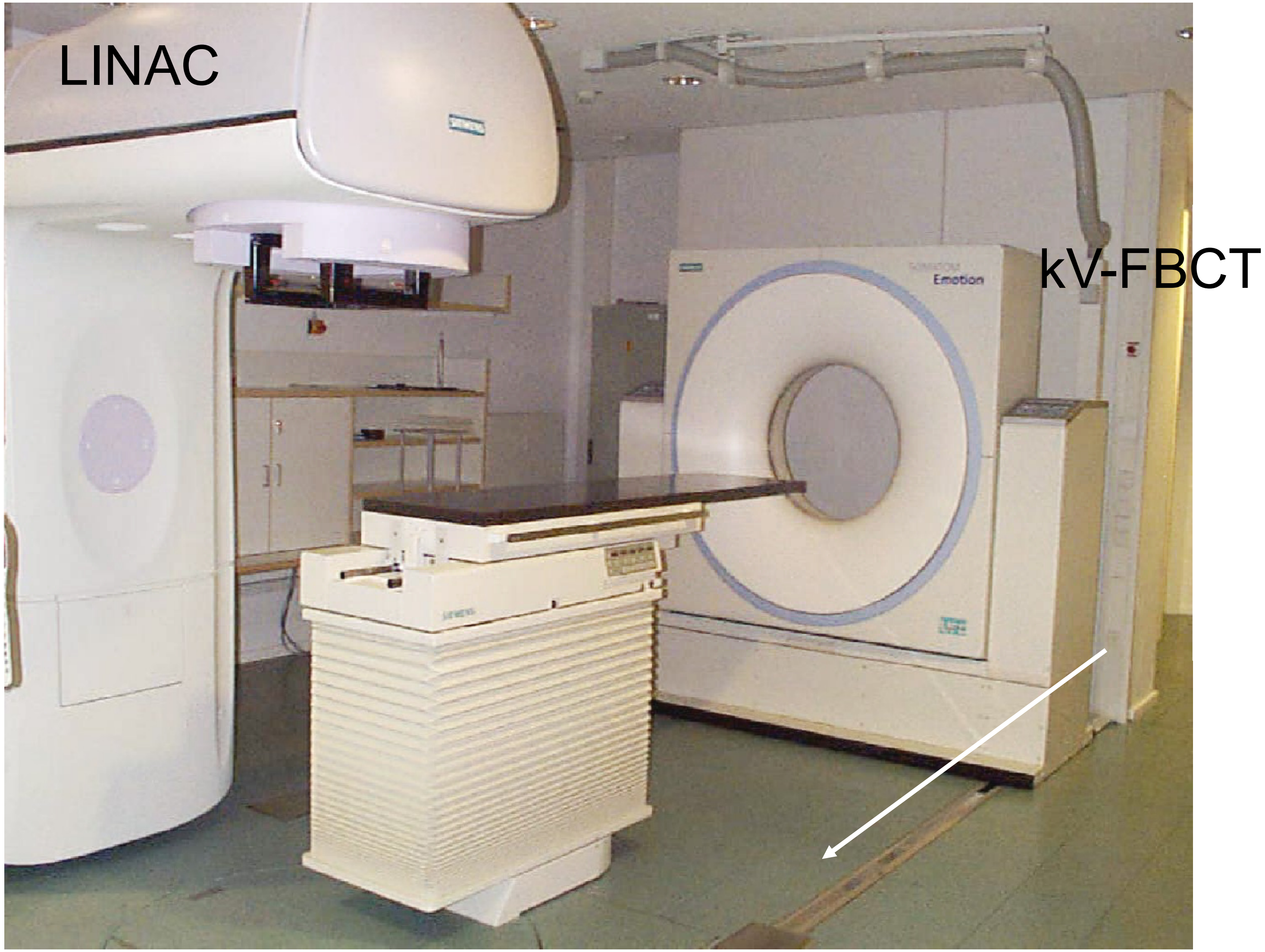
CT image acquisition

Image fusion, Calculation shifts

Transportation Patient back to the linac

Apply shift corrections, start treatment

In-room kV-CT PRIMATOM



Patient positioning with CT-on rails

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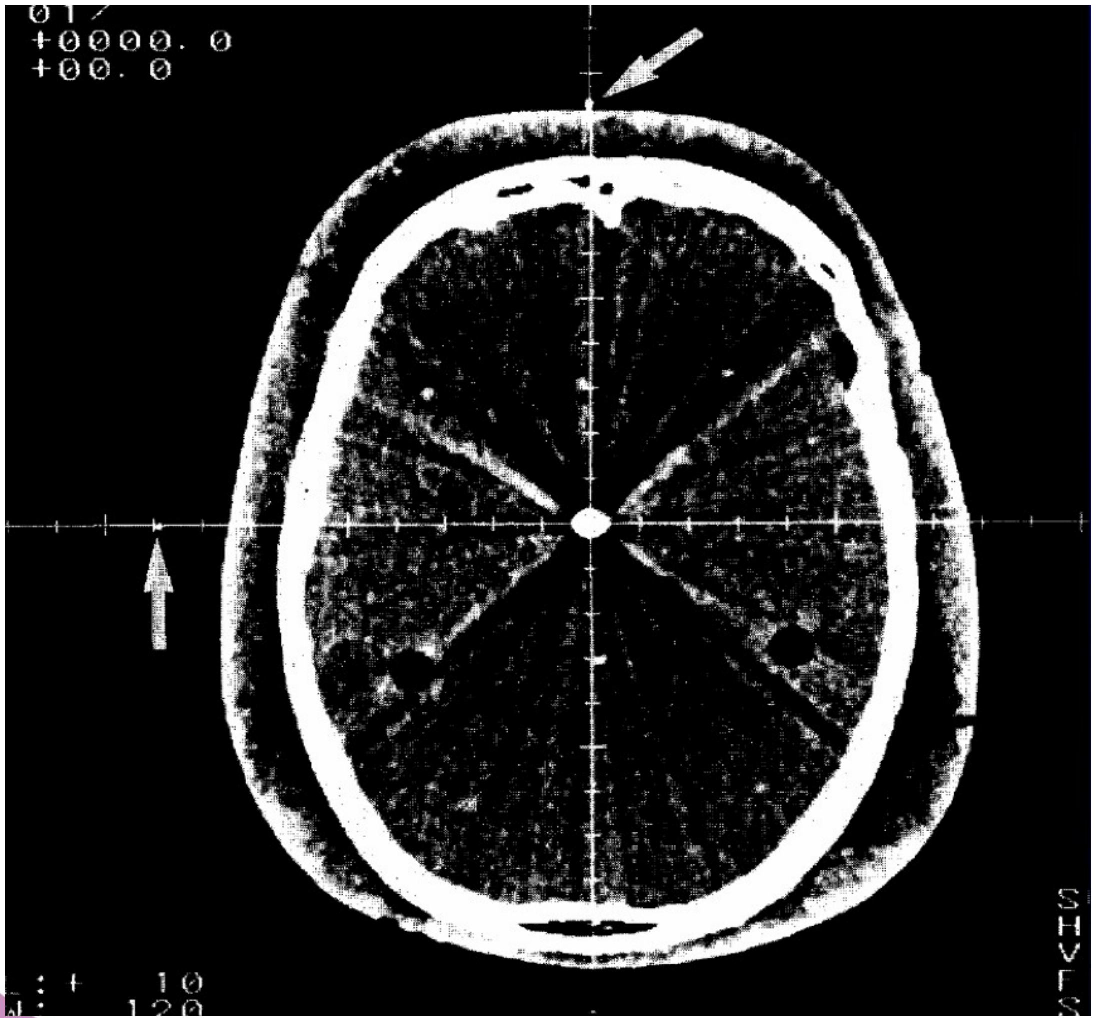
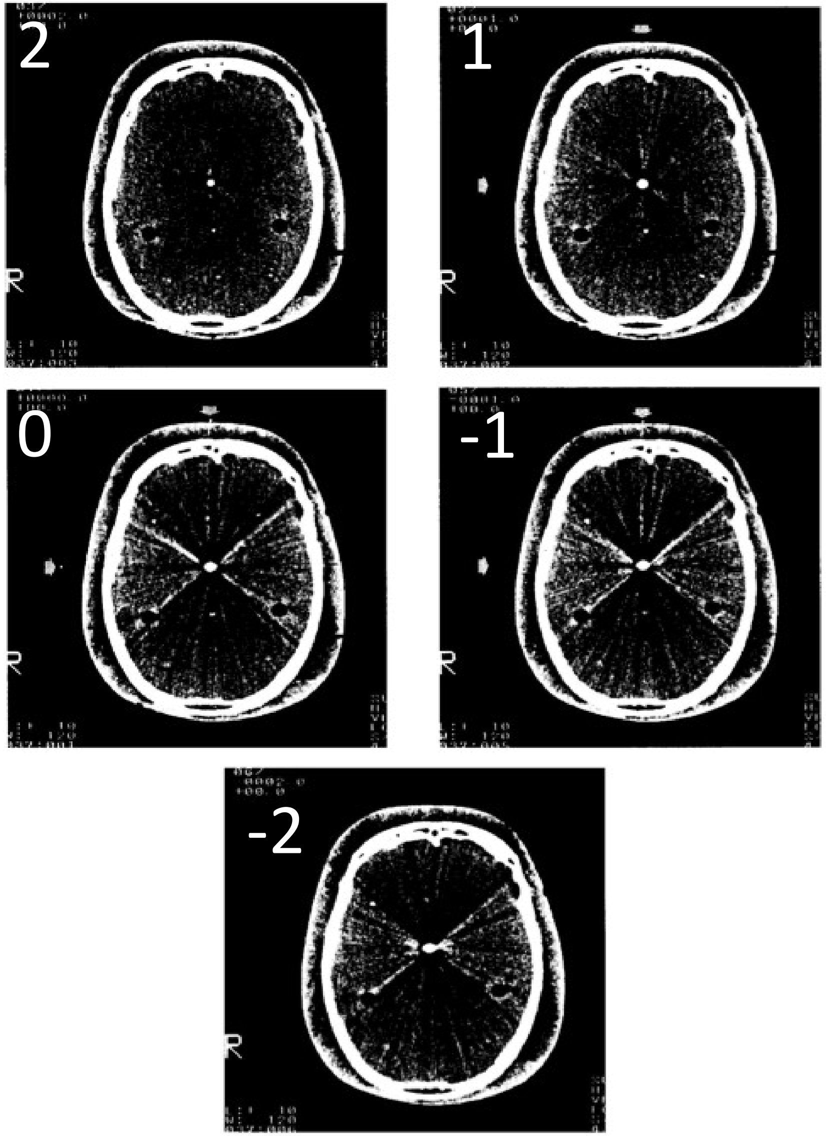
In-room CT setup

Common Linac-CT isocenter verification





Uematsu et al. 1996.

In-room CT

- Features
  - Diagnostic image quality (single-slice, multi-slice helical CT, 4D)
  - Short scanning times
  - Large FOV 50 -70 cm diameter
  - Isocenter calibration of the image has to be done
    - Stereotactic frame
    - Surface markers
  - Patient has to be moved

In-room CT

- ‚Diagnostic' image quality
  - Easy registration with planning CT, alignment of GTV
  - Reliable Hounsfield-units
    - Adaptive planning, re-planning
- Imaging doses
  - 2 – 10 mSv/Scan
  - well suited for adaptive planning, re-planning

In-room CT imaging dose

CT-guided treatments

– Multiple, repeated imaging

- 42 fractions for prostate treatments

– Low CT dose becomes a concern

Head & Neck

Scout:120kV,20mA

- HelicalScan

– 3mm thickness – 1.0 pitch
– 120kV, 110mA

Prostate

Scout:120kV,80mA

- HelicalScan

– 3mm thickness – 1.5 pitch
– 120kV, 200mA

One film = 6 - 8 MU
- Two orthogonal films each week,8 weeks of treatment, assuming no repeat films.

– 96-128MU~**100cGy**

- Typical prescription for prostate=7560cGy
- Typical prescription for head&neck=7000 cGy

~ 1.3% of prescription dose for prostate

~ 1.4% for prescription dose for head&neck

CT dose:
~2 cGy x 42 = **~84 cGy**

Dong et al.

MV Based Imaging

➔ General principles:

- Advantage: The actual treatment beam is used for imaging, therefore it provides direct geometric information concerning alignment of treatment beam and target
- Disadvantage: MV-based image quality will always be inferior to kV-based.

Advantages of MV tomography IGRT

- ➔ Actual treatment beam used for imaging
  - Direct geometric alignment
  - Beam has been modeled in TPS and concomitant IGRT dose can *"easily"* be incorporated into dose calculation.
- ➔ 3D volumetric imaging, no surrogates required.
- ➔ CT-CT registration, similar information
- ➔ Registration of dose distribution and anatomy possible
- ➔ No high-Z artifacts
- ➔ MV-CT usable for dose calculation and dose reconstruction

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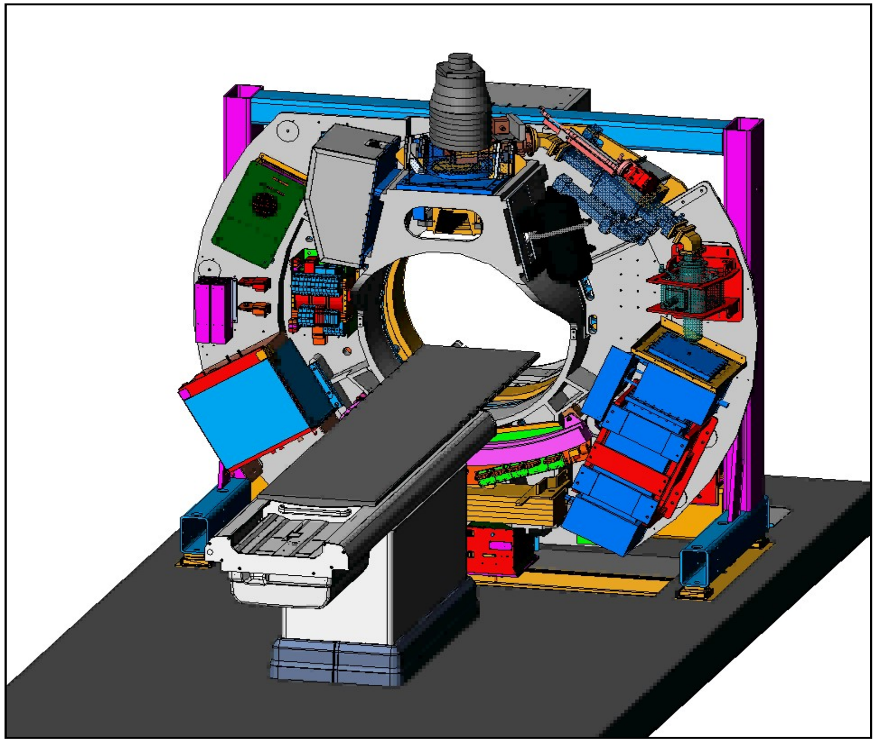
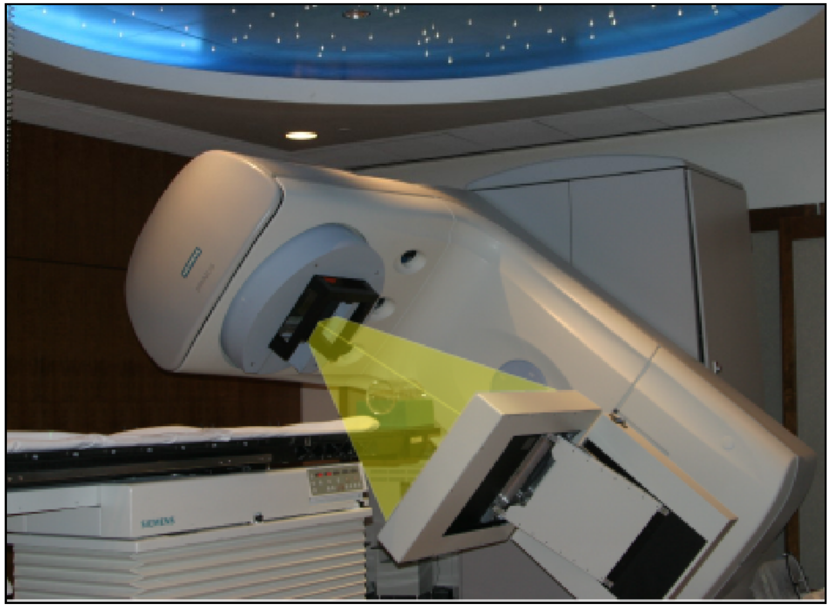
Same* beam used for imaging and treatment





- ➔ Alignment and calibration of system straightforward (identical beam axis, identical isocenter)
- ➔ Potential for dose reconstruction based on transmission measurements using CT-of-the-day

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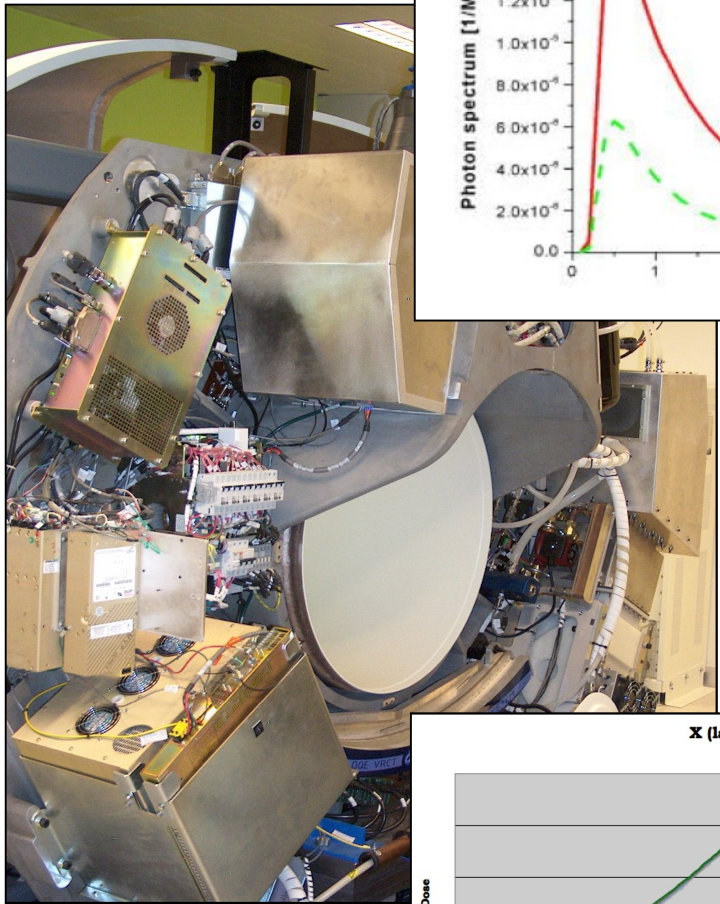
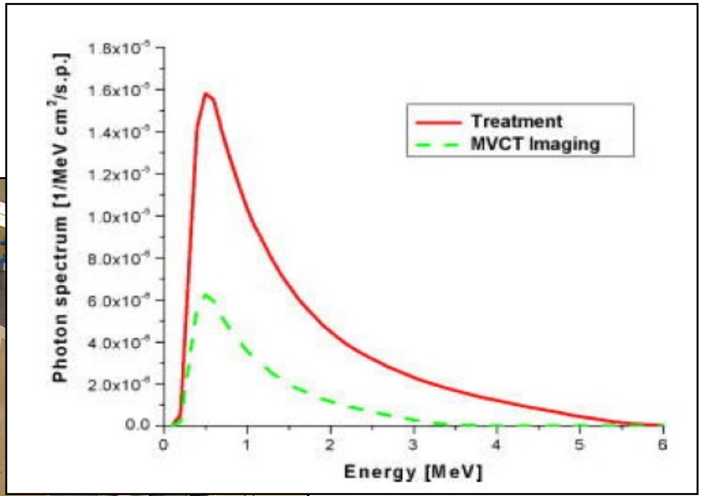
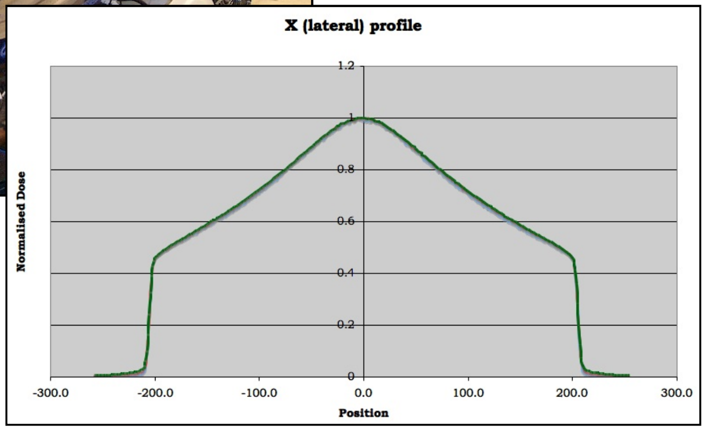
* … not really the same…

MV CT: Characteristics







- Fan beam:
  - "de-tuned" treatment beam from 6MV to 3.5MV
- Lowered dose rate:
  - from 899 cGy/min to 11 cGy/min
- Xe-detectors (640 channels)
- Beam design requires less filtering (**no bow tie filter!**)

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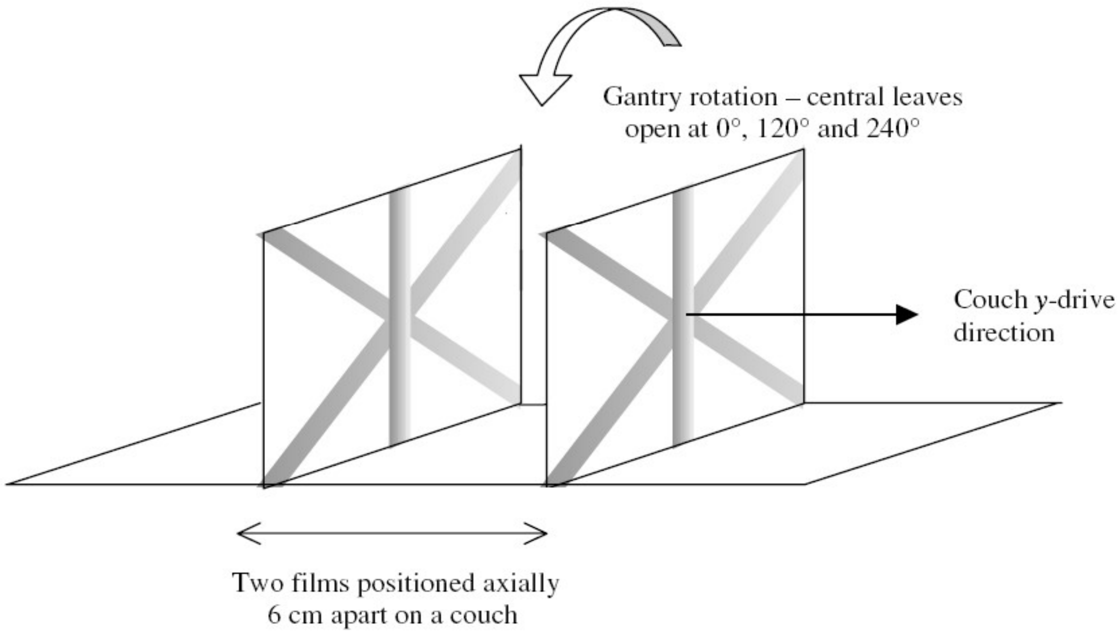
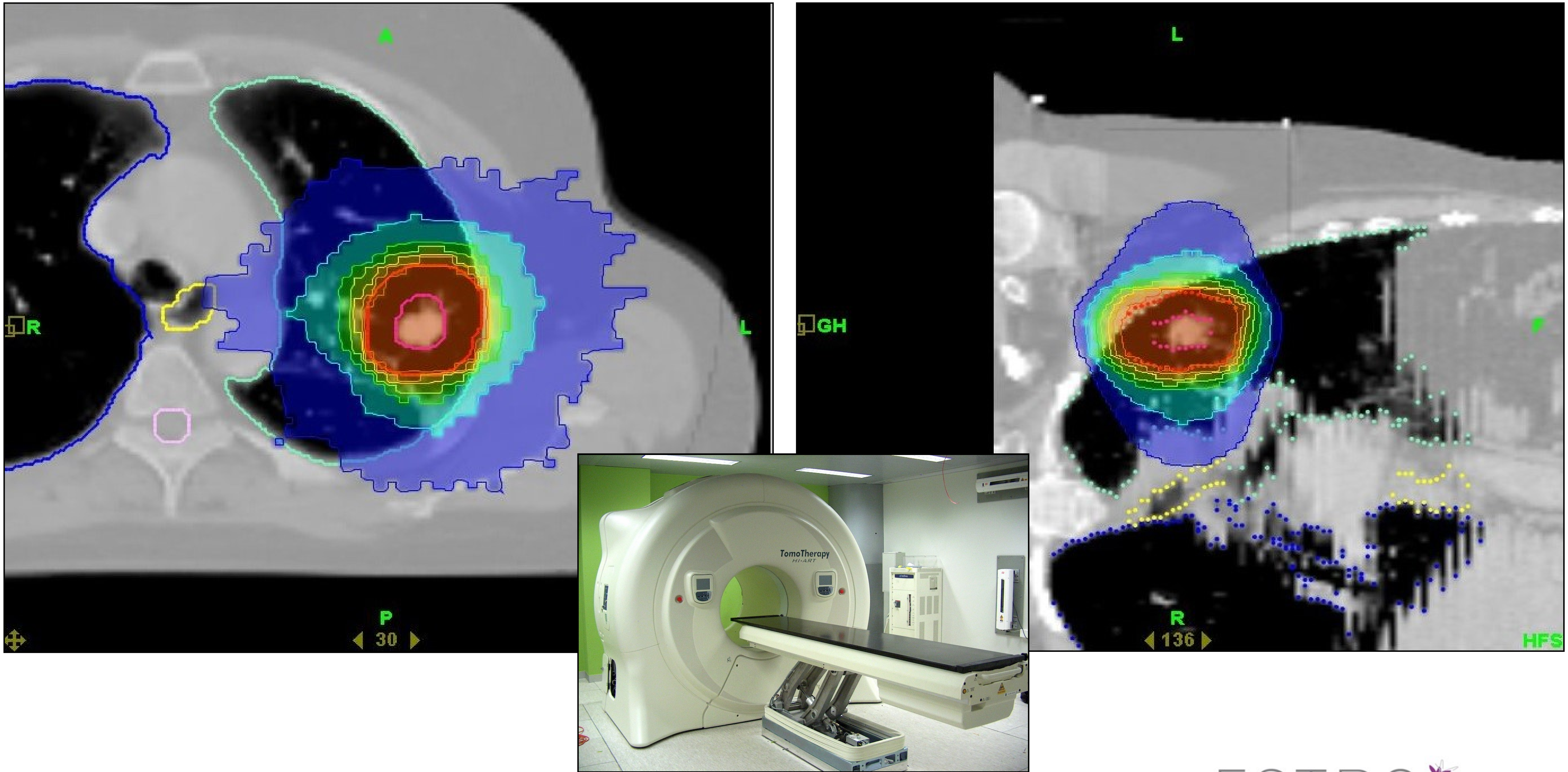
Helical tomotherapy: QA MV CT

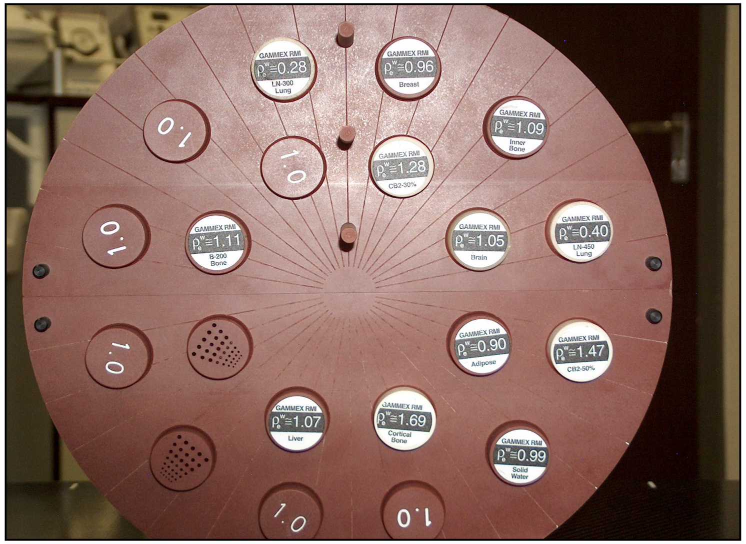
- As the imaging system and delivery system are identical, the QA for the MV CT is integrated in the general QA of the entire system.
- Some examples:
  - Couch translation and gantry rotation synchronization:

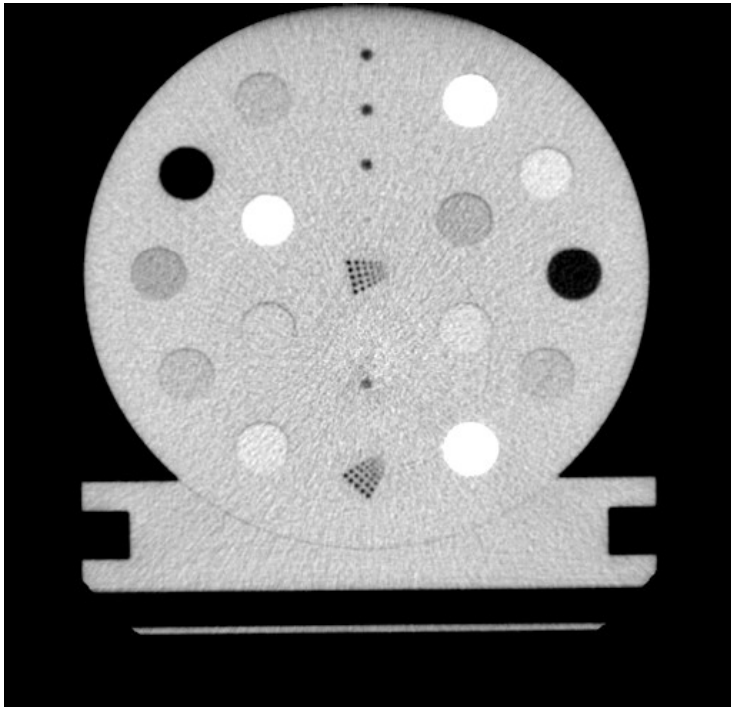


MVCT (dose based positioning)



MV CT: for dose calculation





- HU-to-electron density conversion can be used for dose calculation
- No high-Z artifacts (advantage for target delineation and dose calculation in presence of prosthesis)
- FOV: 400 mm diameter, but MV and kV set can be merged using the appropriate correlation tables

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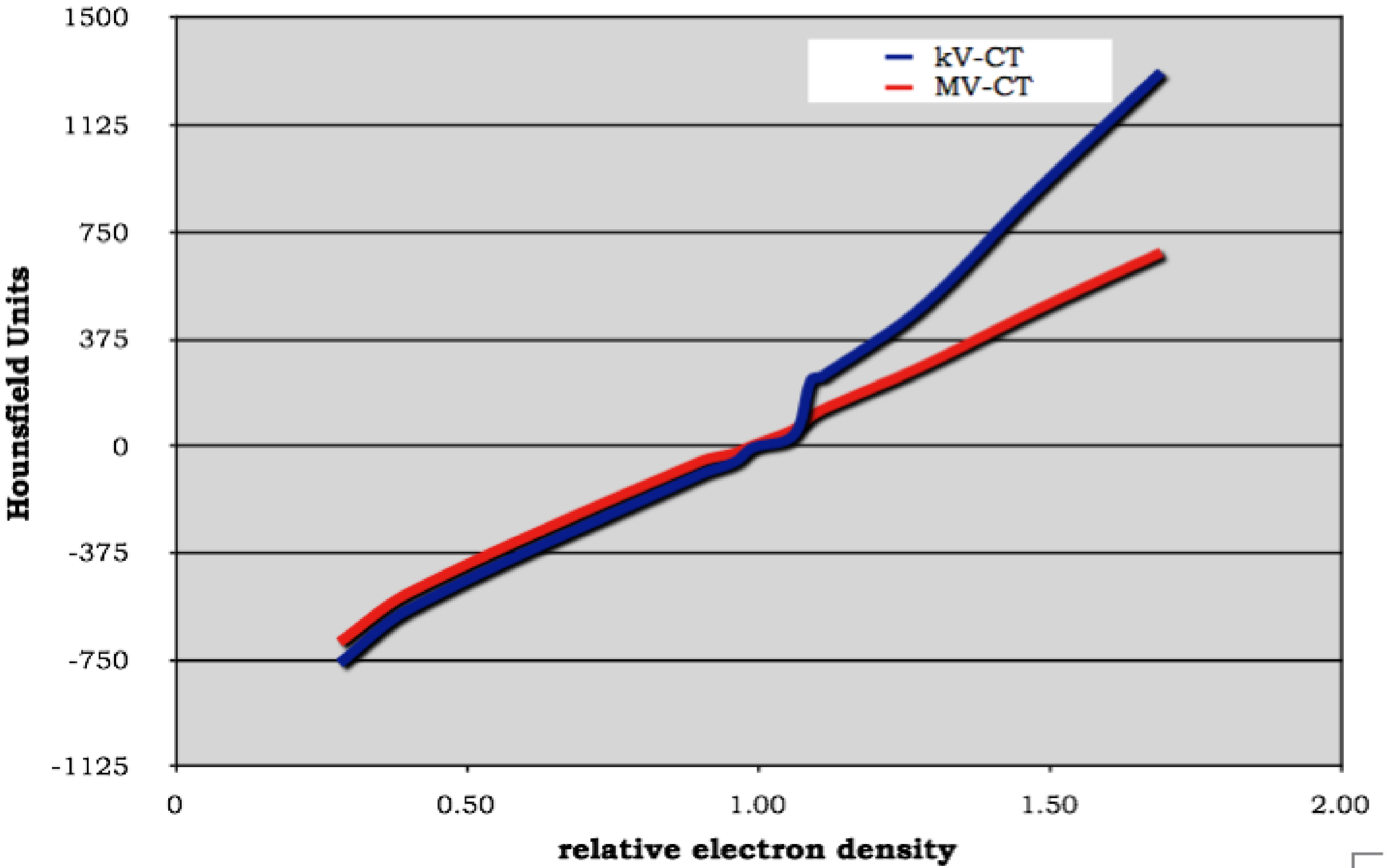
MV CT: for dose calculation



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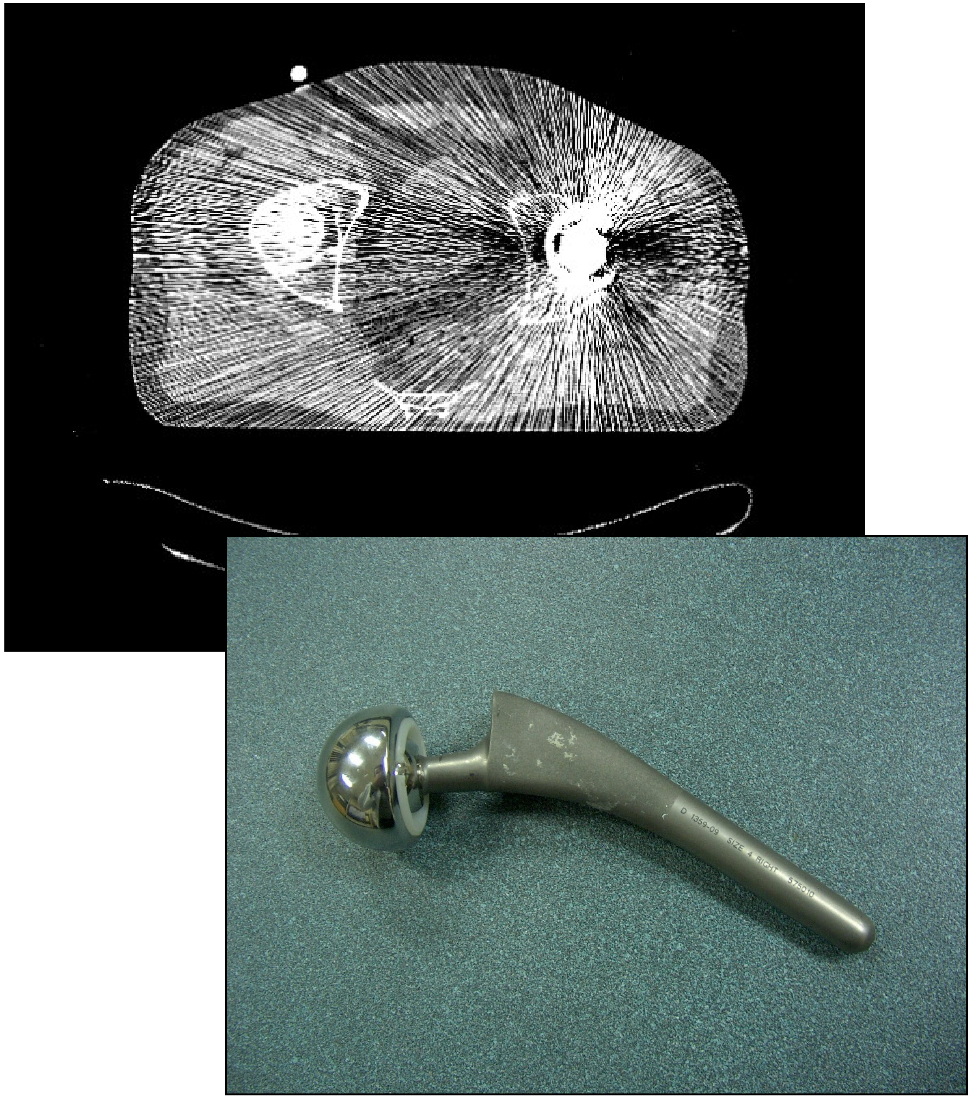
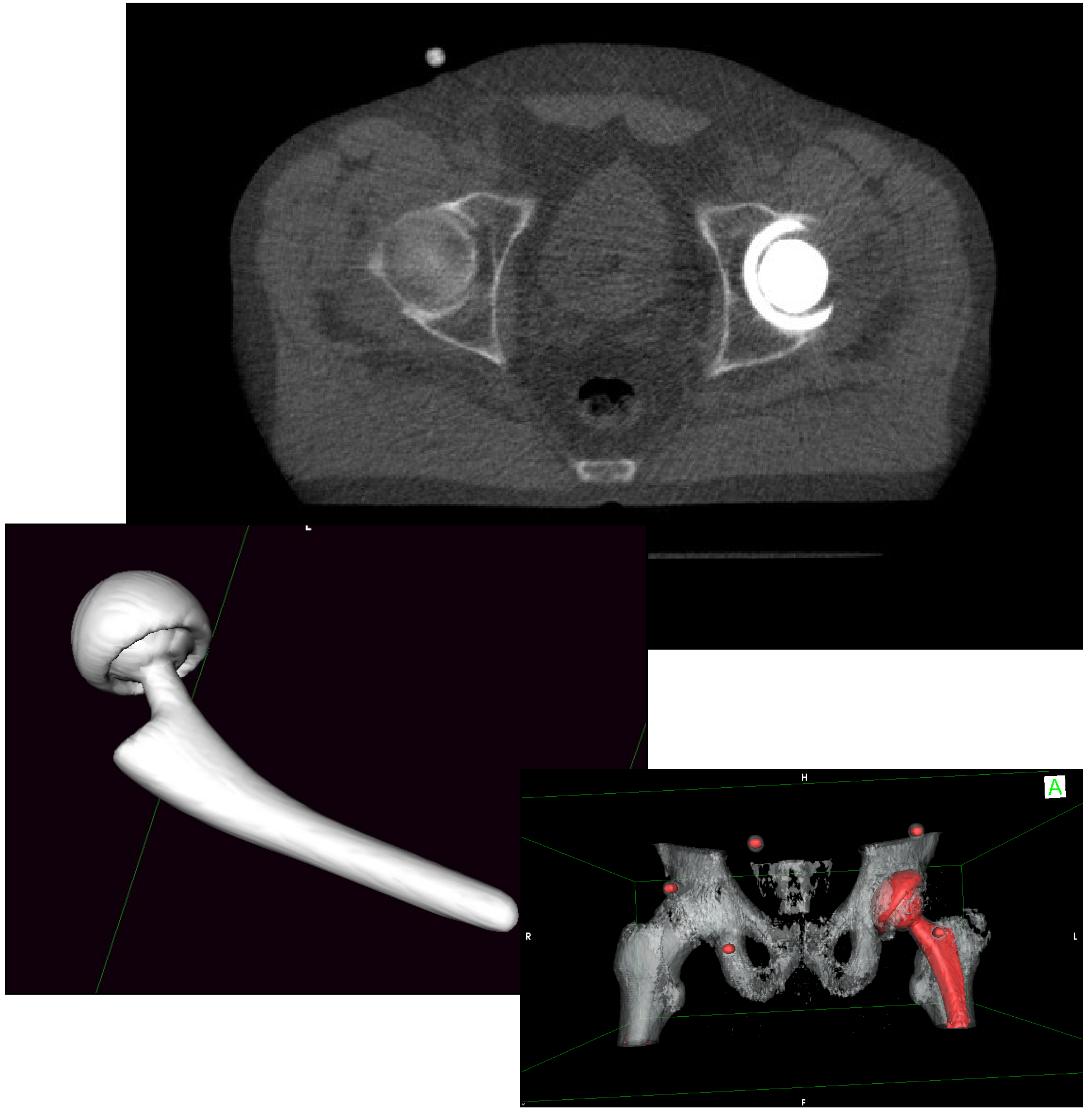
MV CT: for dose calculation

Hip prosthesis : kVCT



Hip prosthesis : MVCT



Conclusion: MVCT/MV CBCT

- Geometric accuracy:
  - MV CT: Mechanical rigidity of the system minimizes geometrical uncertainties.
  - MV CBCT: Geometrical uncertainties are quantified and included in projection matrices and filtered back projection algorithm.
- Image quality:
  - Adequate for all systems
  - MV CT and CBCT ready to be used for dose calculations
- Patient dose:
  - Depends on what you ask for.

Conclusion: MVCT/MV CBCT

➔ MV-CBCT and MV-CT present some interesting features for IGRT:

- Same beam is used for imaging and treatment
- Potential for dose reconstruction
- Volumetric imaging

➔ Difficult to use for monitoring of intra-fraction organ motion

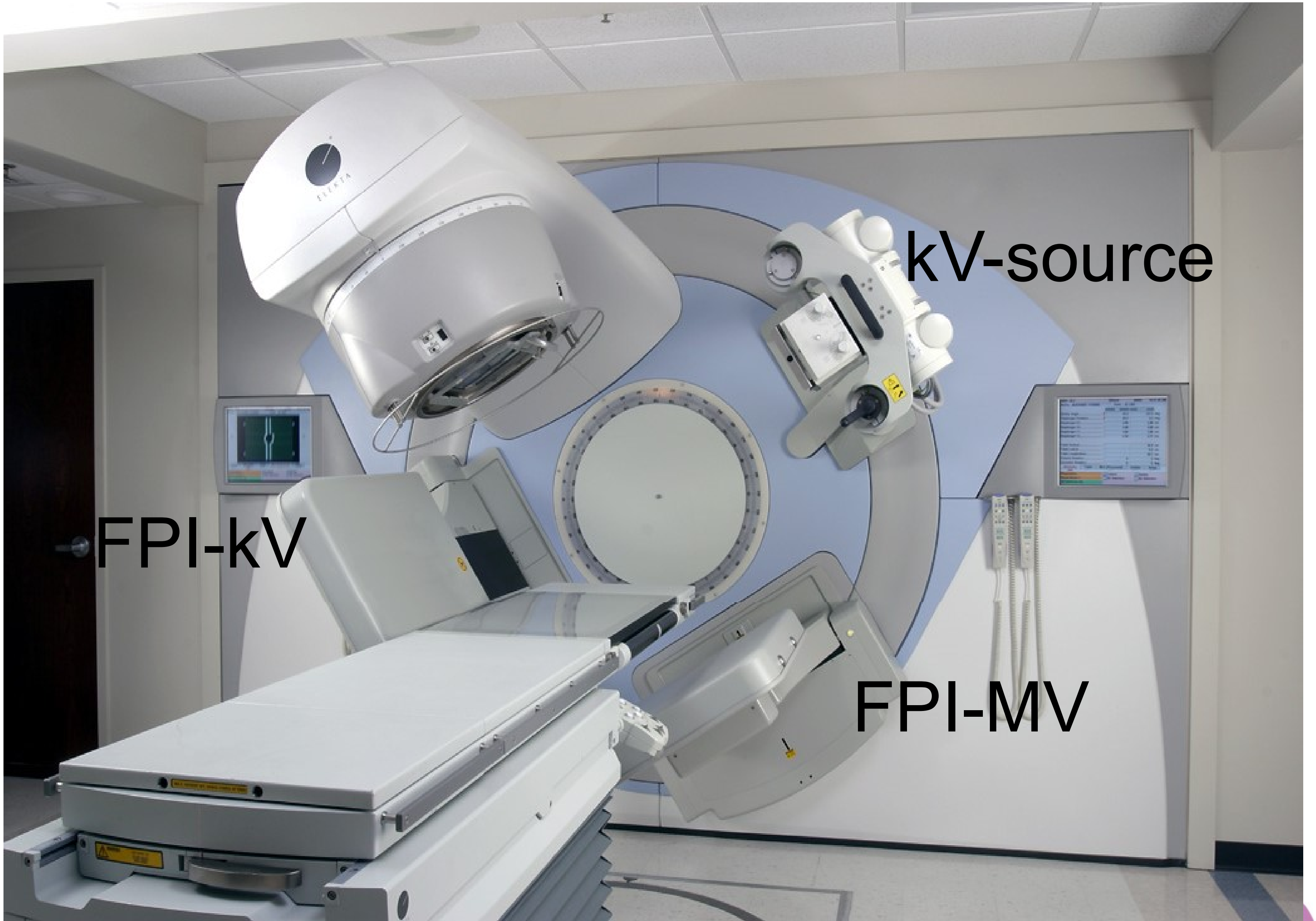
Linac-integrated Cone Beam CT

- kV-Cone Beam CT
  - Linac integrated Hardware
    - kV-x-ray source
    - FPI Detector
  - Geometry
    - 90° angle between imaging- and treatment beam
    - 180° angle between imaging and treatment beam (only very few systems ....)

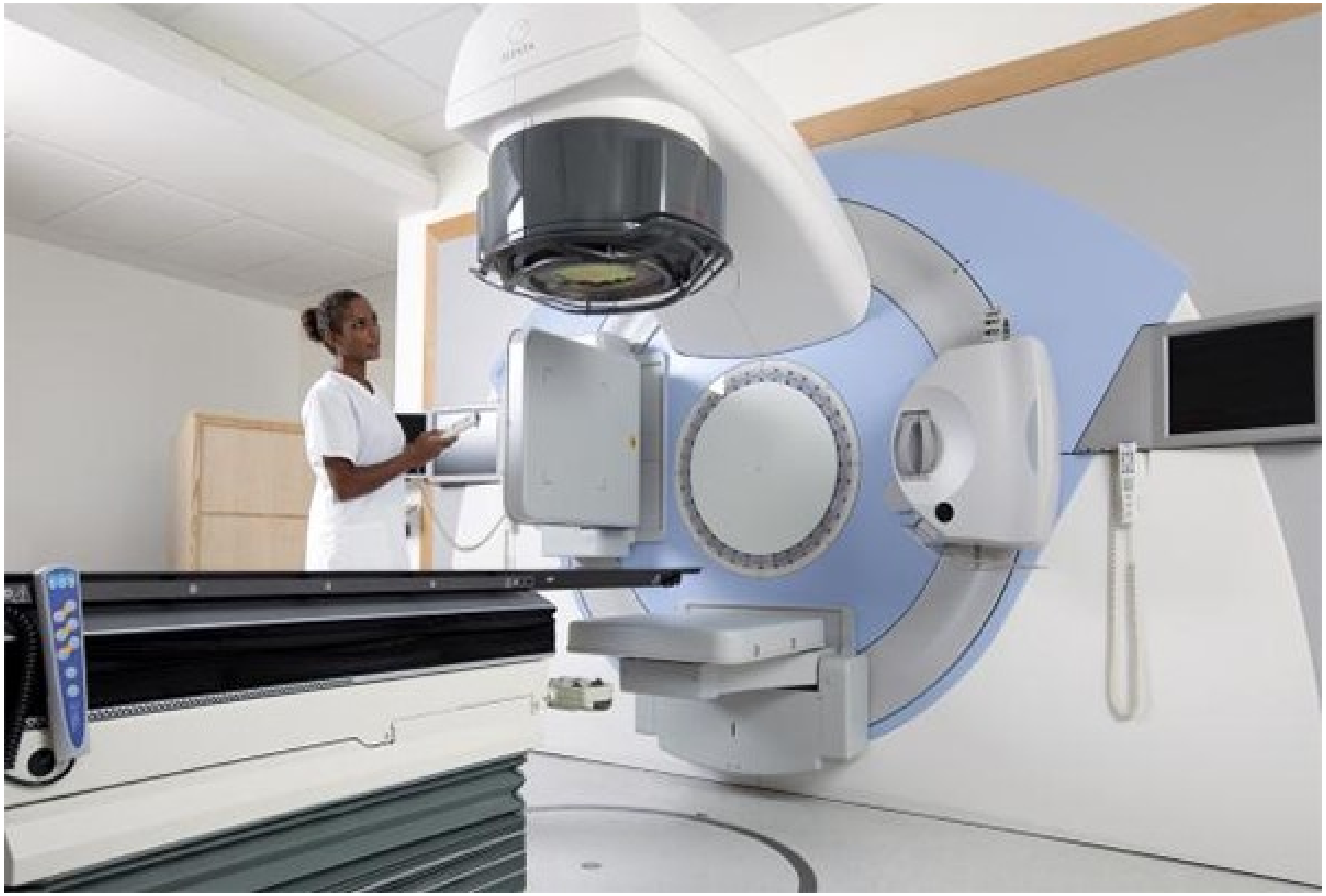
Prototype: Elekta Synergy

Courtesy of B. Groh

Elekta - Synergy



ELEKTA Aguility



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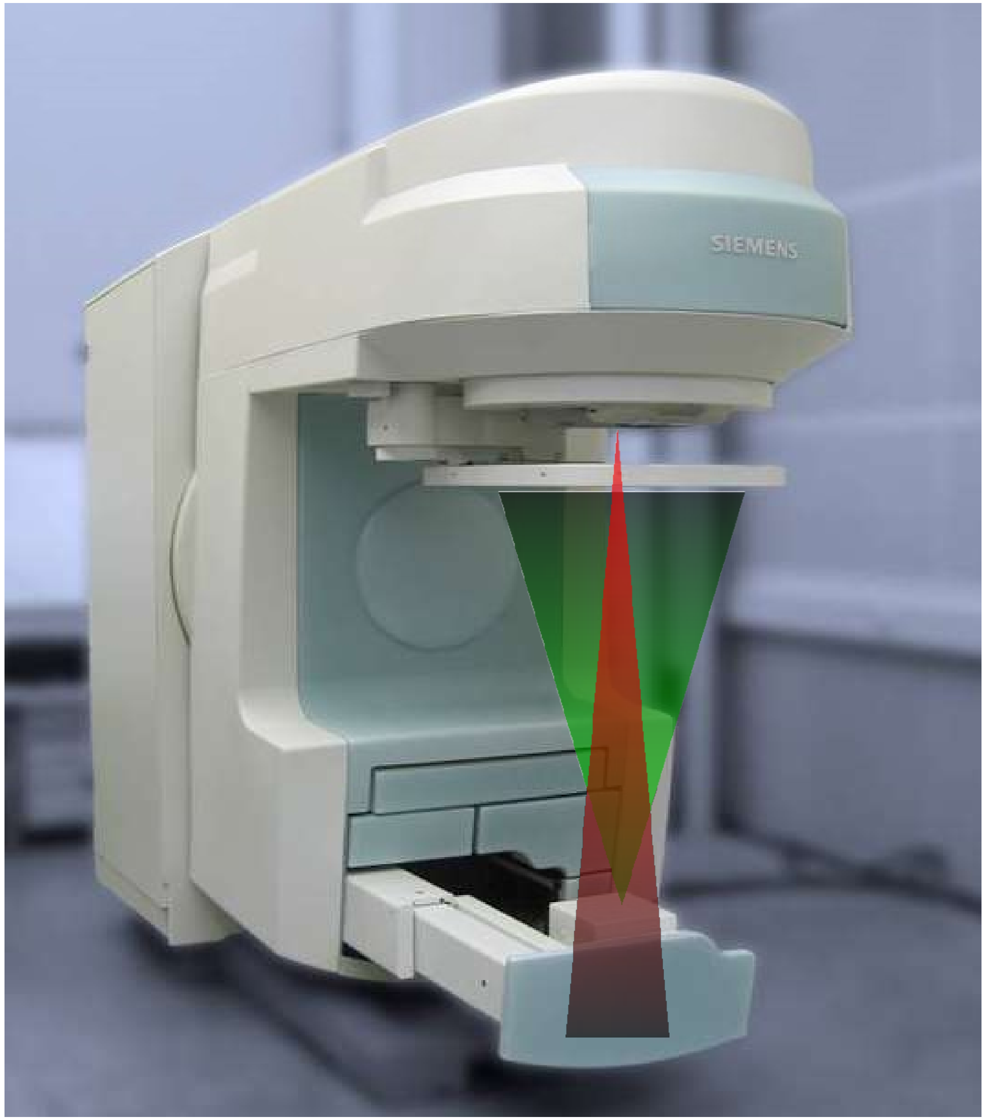
VARIAN TRUEBEAM

Artiste Linac



- External beam (photon) radiotherapy
- MLC with 160 leafs
- Prototype system
  - + kV inline imaging
  - + Gating
  - + kV CBCT

Scanning modes

- Short scan: 180° + (fan-beam angle) gantry rotation
  - 220 – 440 frames (e.g. head and neck)

- Full scan: 360° gantry rotation
  - 360 – 720 frames (e.g. prostate, extended FOV)

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CBCT: limited FOV shifted detector

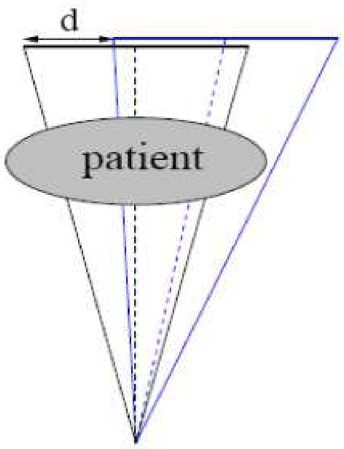
Original FOV: 27 cm

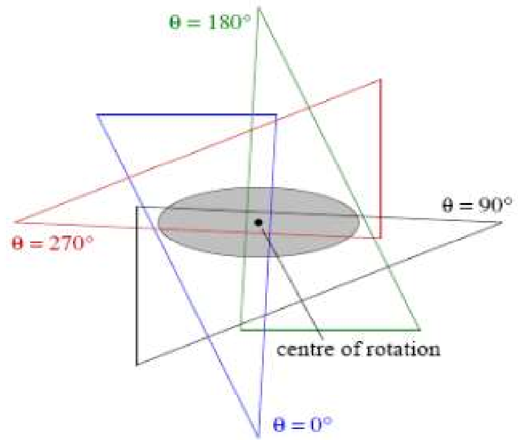
Shifted detect.: 48 cm

detector shift

Method: detector offset

- Approach to enlarge the FOV: lateral shift of the FPI

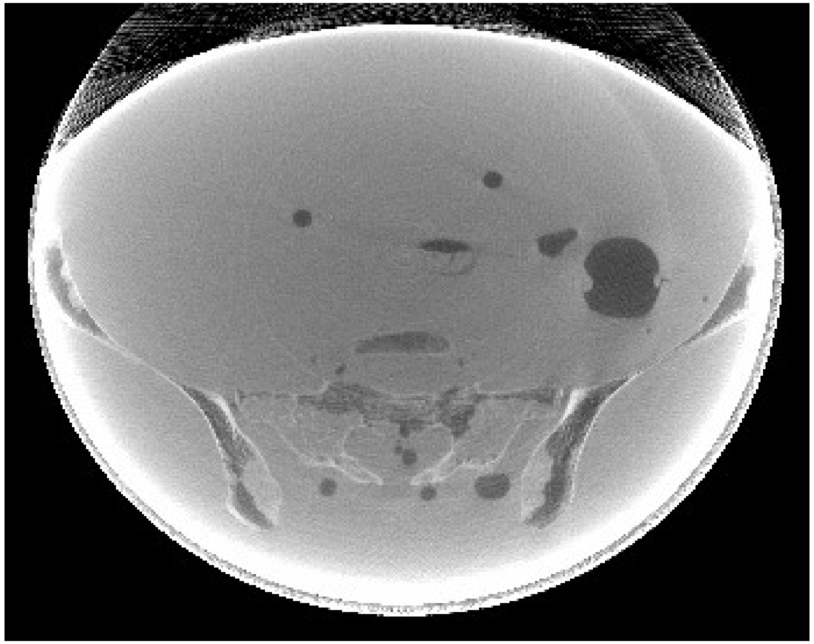




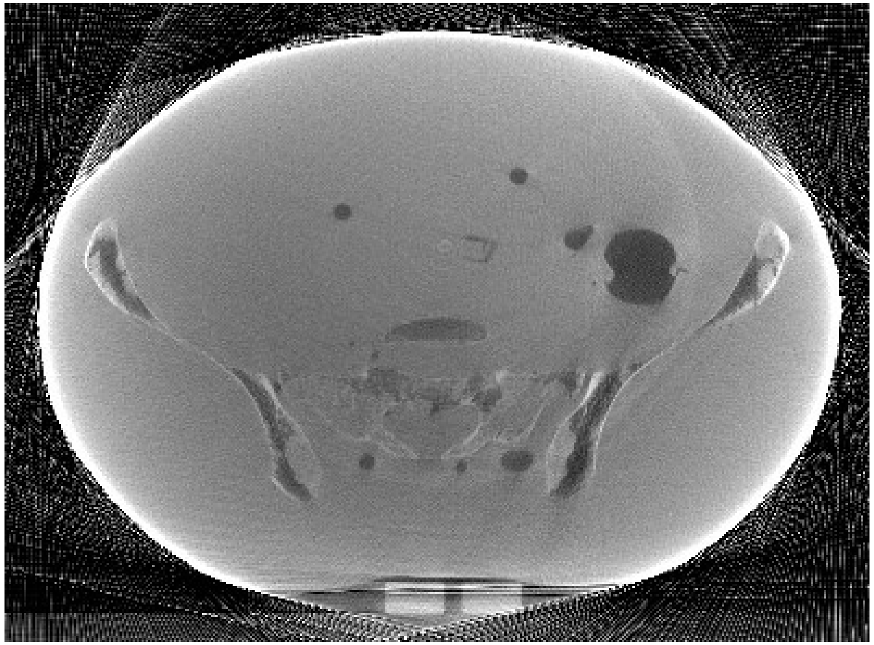
⇒ adaptation of the image reconstruction algorithm required:

Extended FOV

- FOV extension clearly visible
- Truncation artefacts reduced



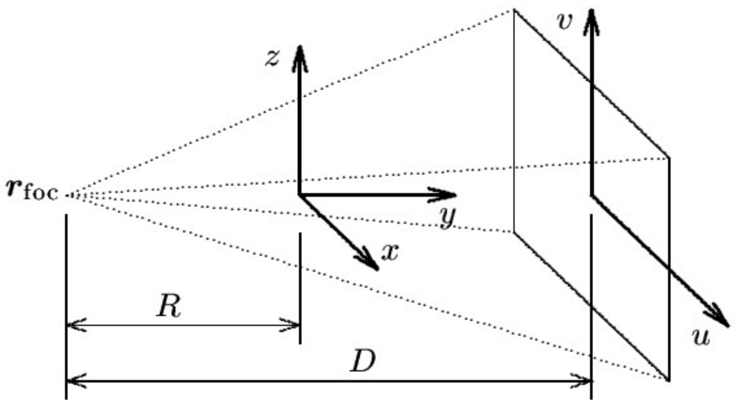
Centered detector



8 cm offset

Ideal imaging geometry

- Ideal projection geometry can be calculated given
  - ➢projection angle
  - ➢distances D (source-to-detector) and R (source-to-isocentre)



⇒ 3x4 projection matrix to map 2D detector (u,v) to (fixed) 3D patient (x,y,z) coordinate system

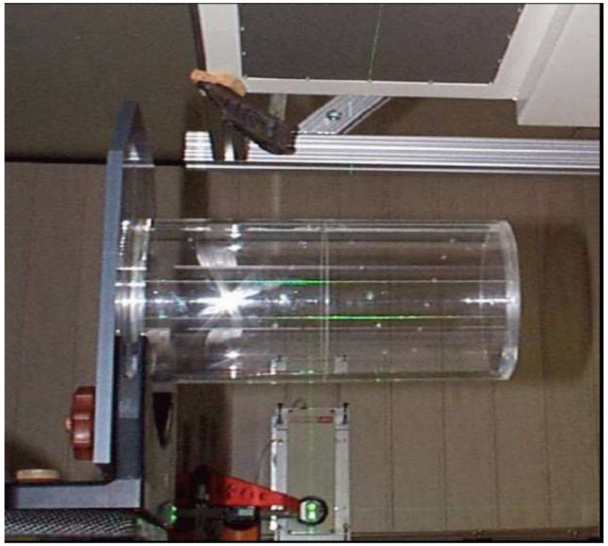
$$\lambda \begin{pmatrix} u_k \\ v_k \\ 1 \end{pmatrix} = \begin{pmatrix} p_{11} & p_{12} & p_{13} & p_{14} \\ p_{21} & p_{22} & p_{23} & p_{24} \\ p_{31} & p_{32} & p_{33} & p_{34} \end{pmatrix} \begin{pmatrix} x_k \\ y_k \\ z_k \\ 1 \end{pmatrix}$$

⇒ used for voxel-driven backprojection

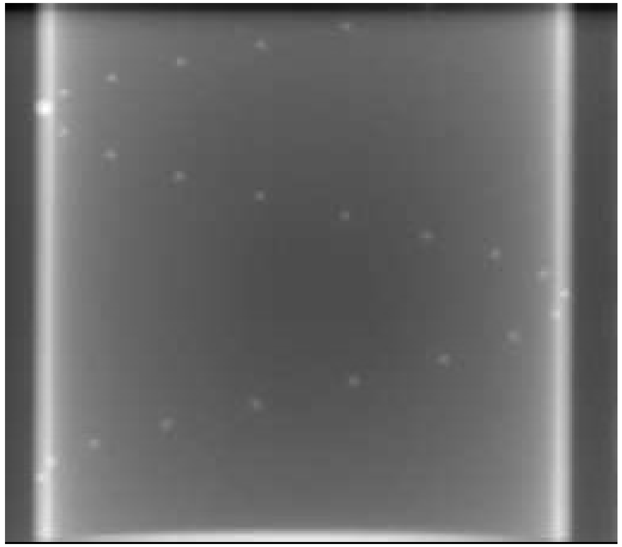
Non-ideal projection geometry

- Real world: projection geometry is non-ideal due to gravitational sag of the imaging hardware
  $\Rightarrow$ determine projection matrix experimentally:

calibration phantom



alignment at the isocentre

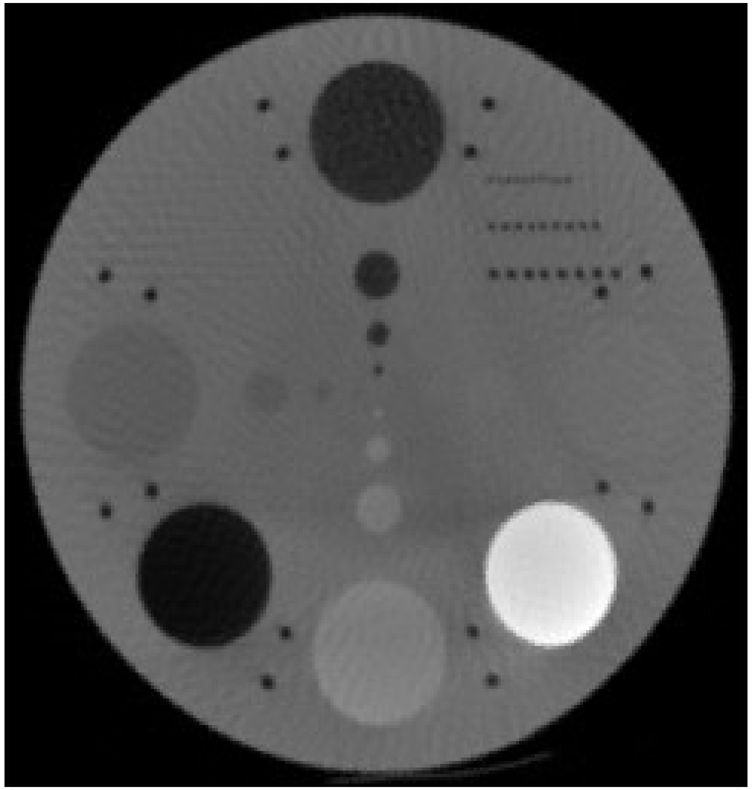


sample projection

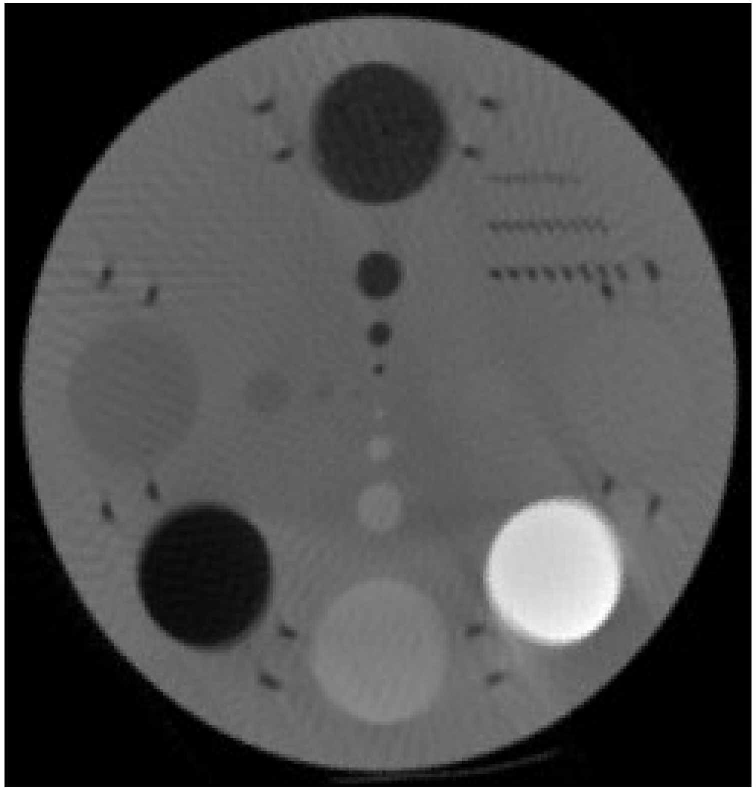
Geometrical calibration

Contrast/resolution phantom

calibrated



Not calibrated



QA Issues

Quality assurance for image-guided radiation therapy utilizing CT-based technologies: A report of the AAPM TG-179

Medical Physics, Vol. 39, No. 4, April 2012

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Initial application of a geometric QA tool for integrated MV and kV imaging systems on three image guided radiotherapy systems

W. Mao et al. 2335 Med. Phys. 38 (5), May 2011

TABLE I. Summary of nominal geometric parameters of imaging systems. SDD is the source-detector distance.

Linac	Energy	SDD (mm)	Detectors: Pixel size (mm)	Detectors: Dimensions
Trilogy	MV	1500	0.784	512 × 384
	kV	1500	0.392	1024 × 768
SynergyS	MV	1600	0.4	1024 × 1024
	kV	1536	0.8	512 × 512
Vero	MV	2212	0.4	1024 × 1024
	kV	1876	0.4	1024 × 1024

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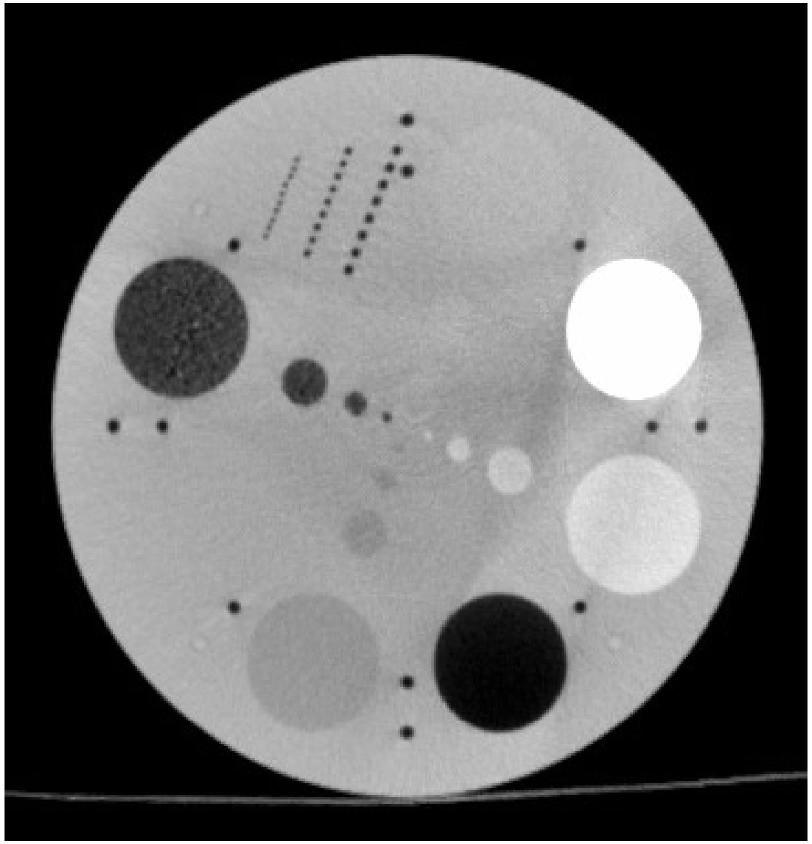
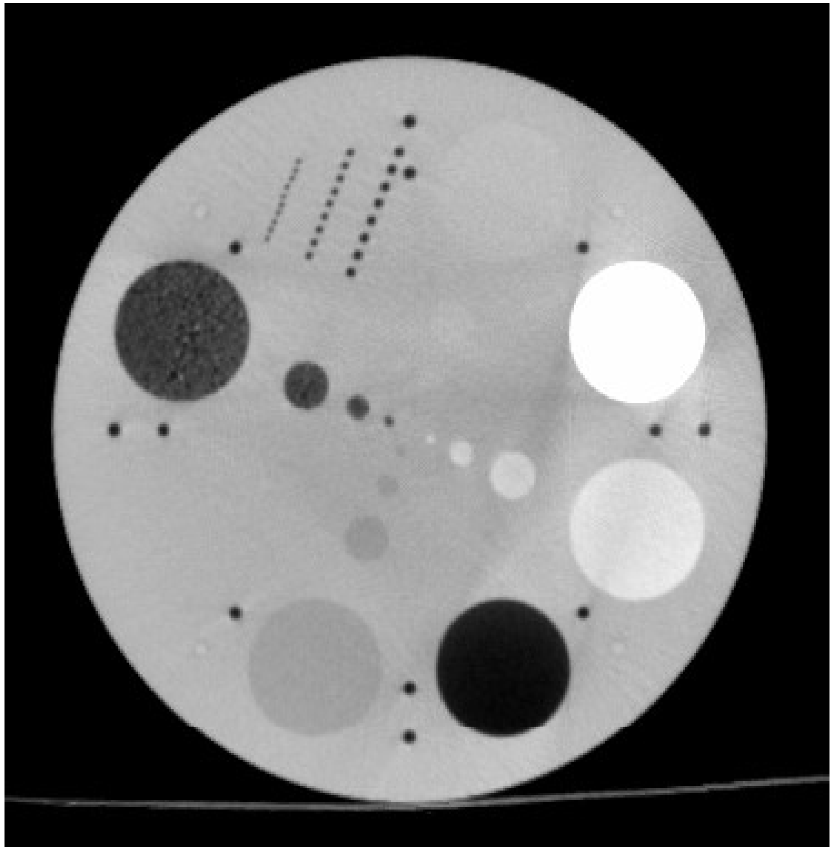
Image Quality and Imaging Dose

- Images: examples
- Images: artifacts
- Images: doses

kV-CBCT: Contrast phantom



1cGy

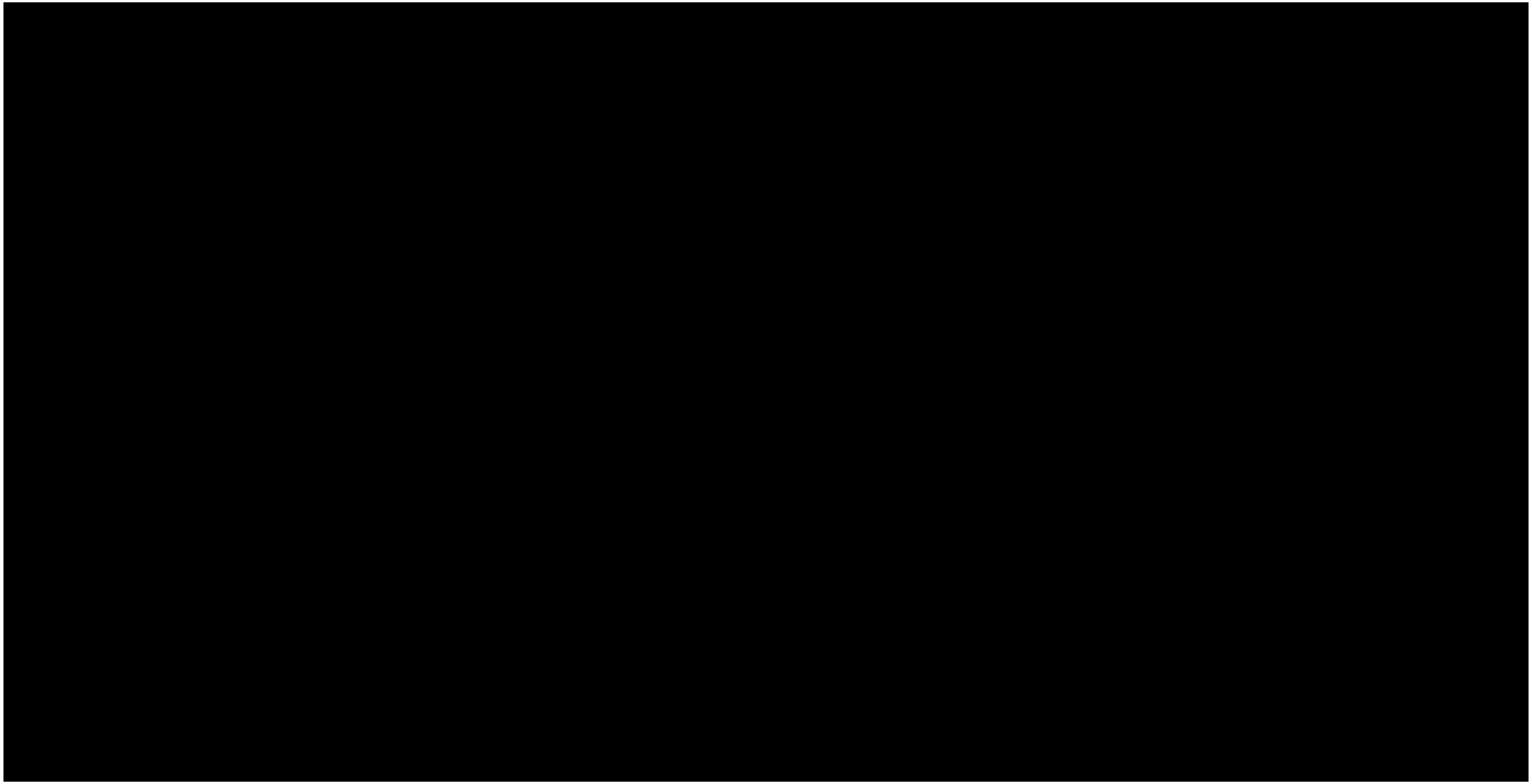


2cGy

440 projections over 220 degrees

Estimated dose at the isocenter

Cone beam CT @ LINAC

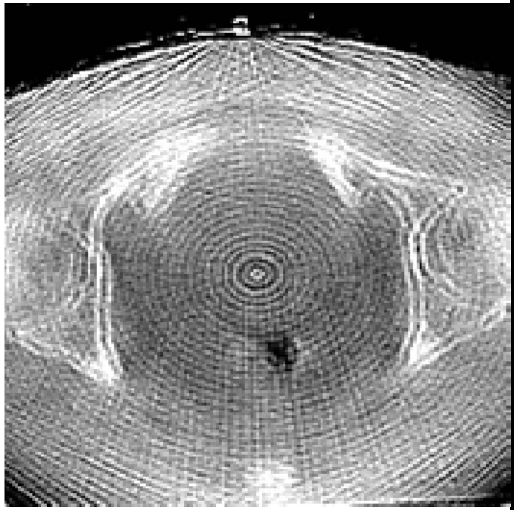


Planning CT

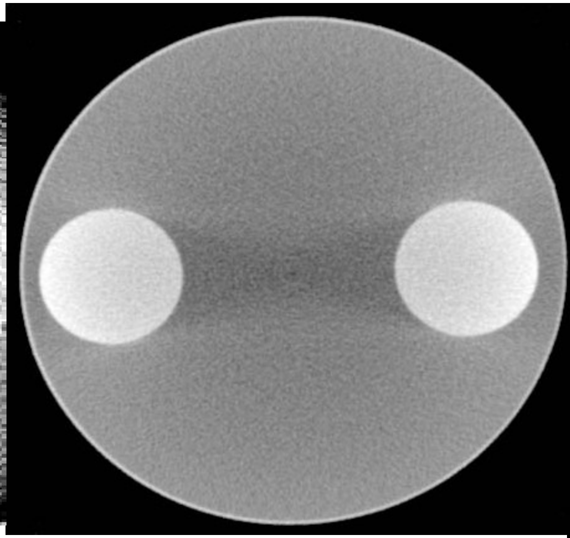
Cone beam CT @Linac

Image Artifacts

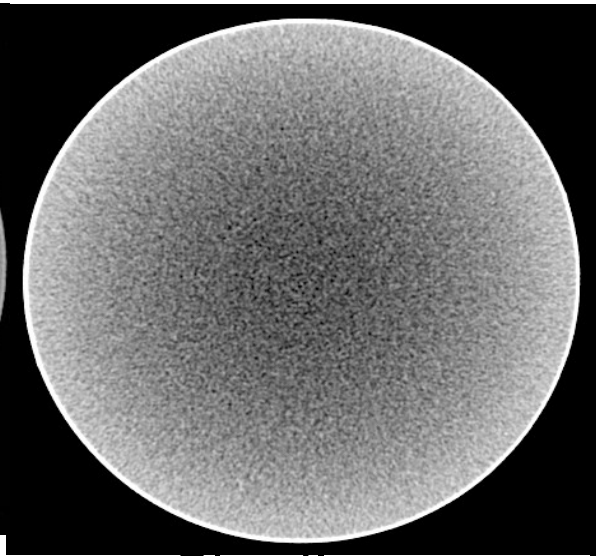
Courtesy of Jeffrey Siewerdsen



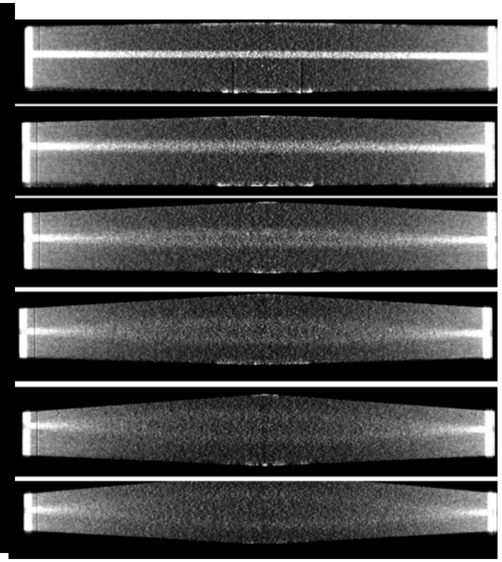
Rings & flex



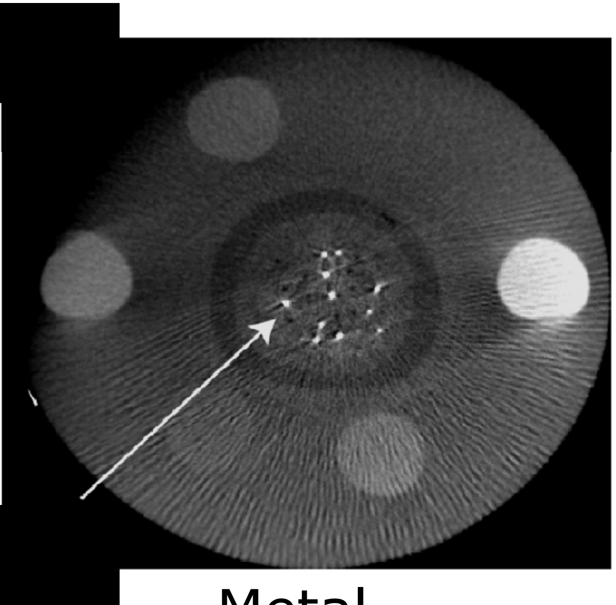
Streaks



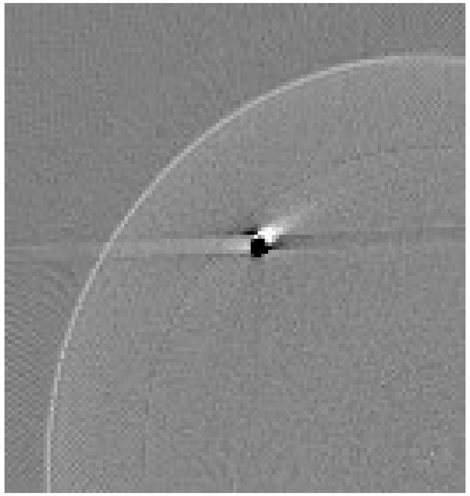
Shading



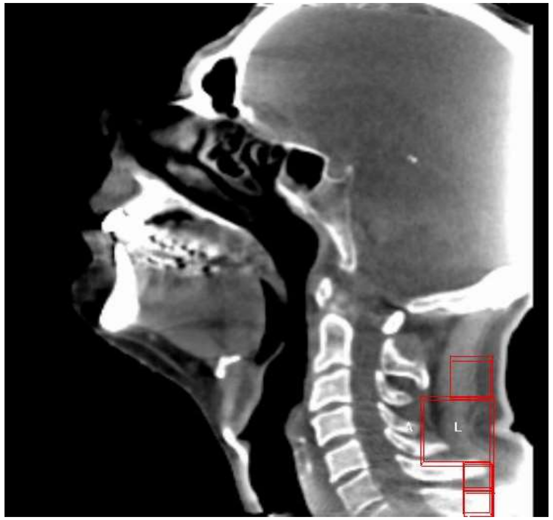
de Frise



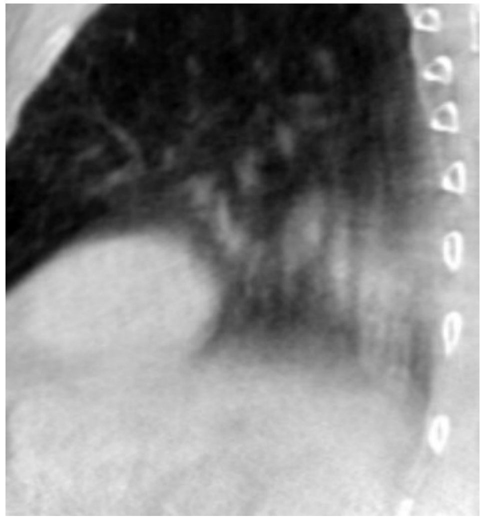
Metal



Lag

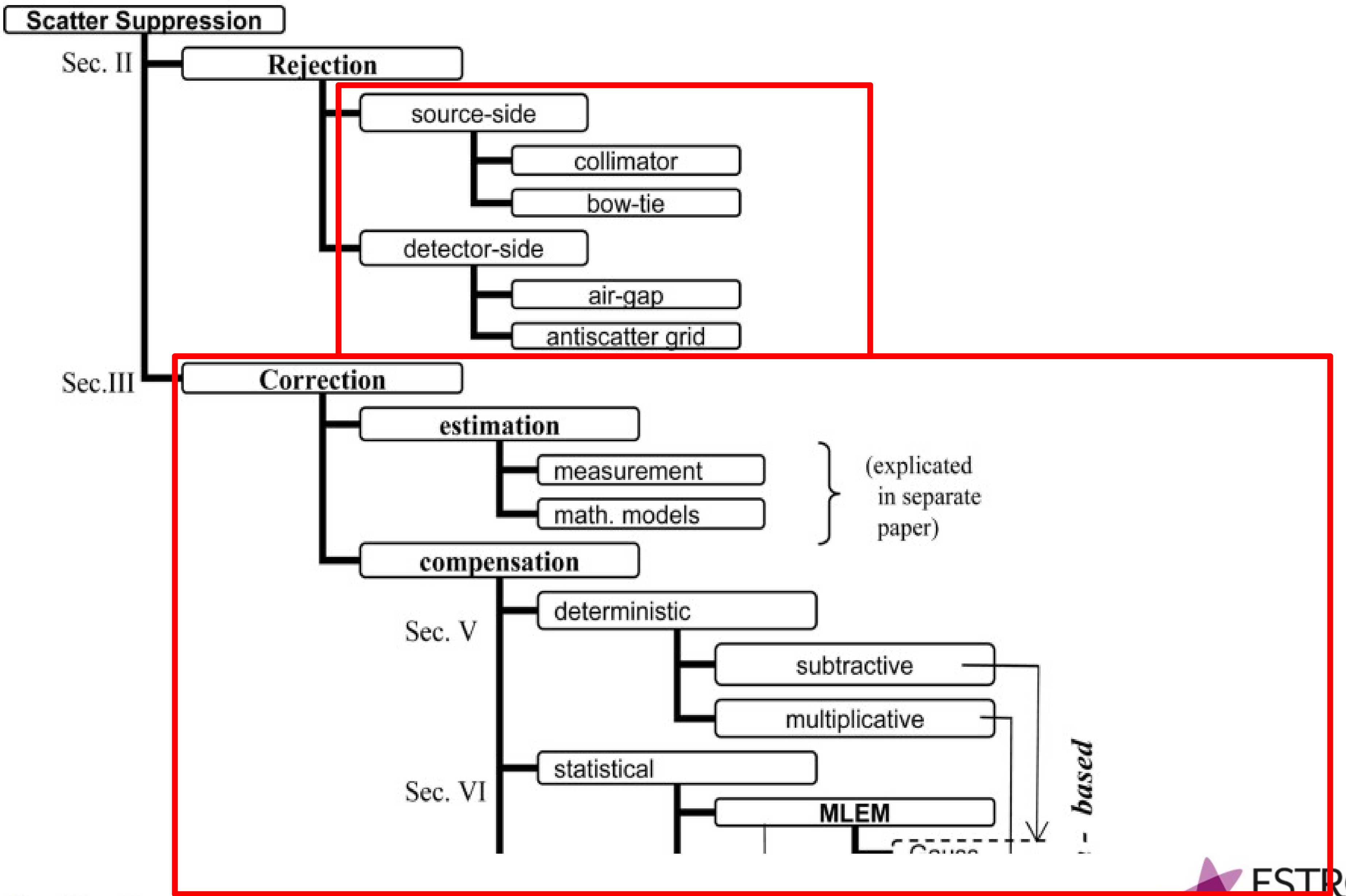


Truncation



Motion

Scatter suppression for CBCT - CT



Ernst-Peter Rührnschopf[a] and Klaus Klingenbeck
Siemens AG, Healthcare Sector, Imaging & Therapy Division, Forchheim, Germany

Medical Physics, Vol. 38, No. 7, July 2011

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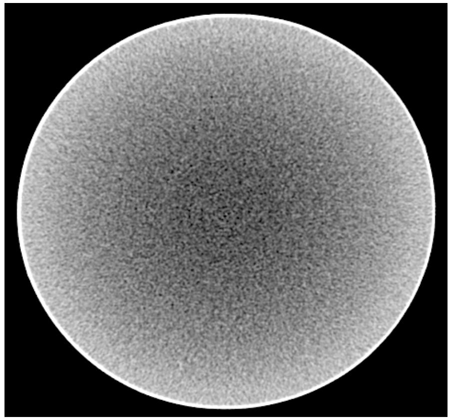
Scatter: Reduction/Correction



Water Phantom: Cupping Artifact

Scatter rejection

Hardware: Anti-scatter grid, Bow-tie filter

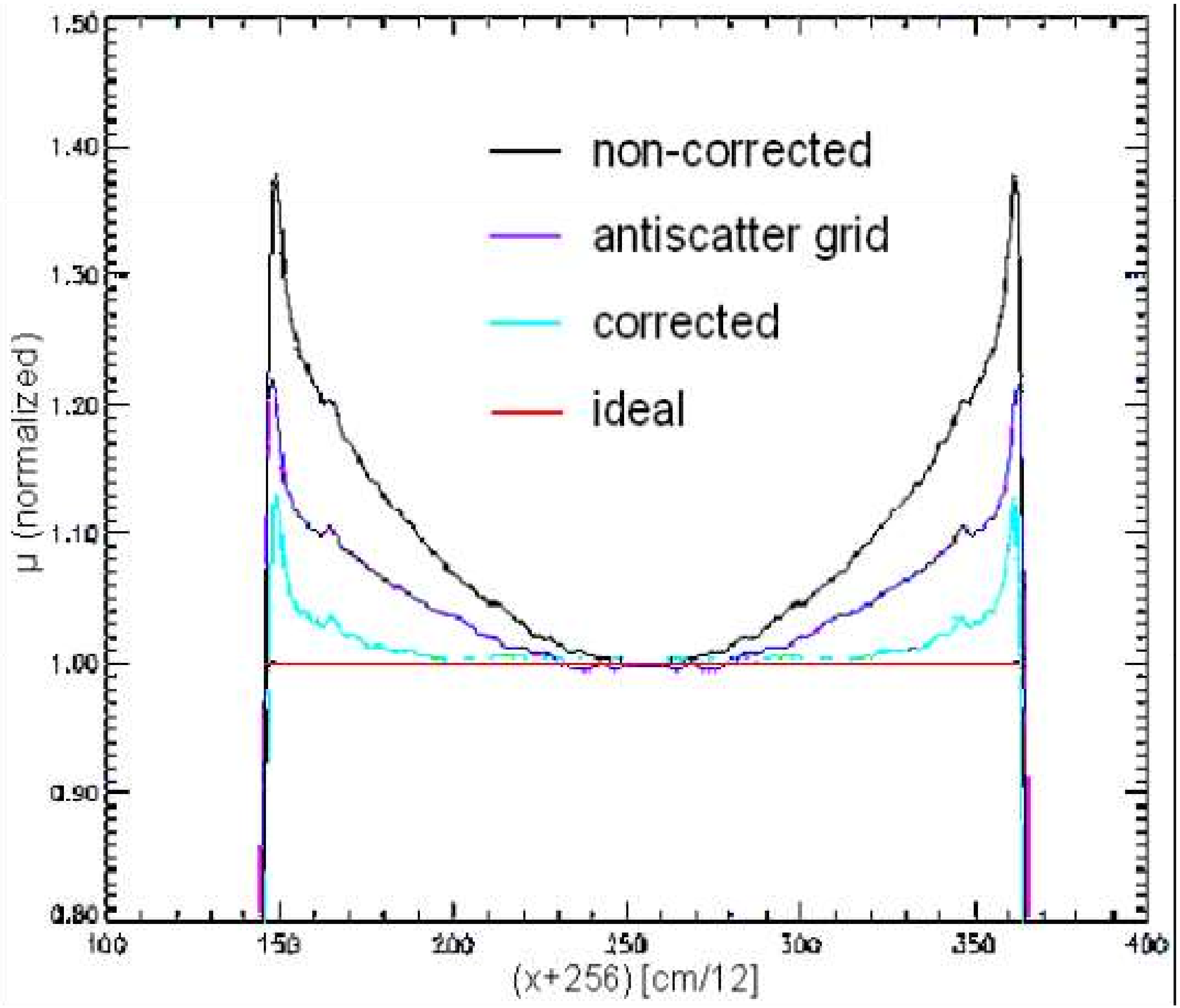
Scatter reduction

Software: Scatter correction algorithms

iterativ, heuristic …

closely related to Hounsfield calibration of CBCTs

Scatter – Cuping Artifact



Bow tie filters

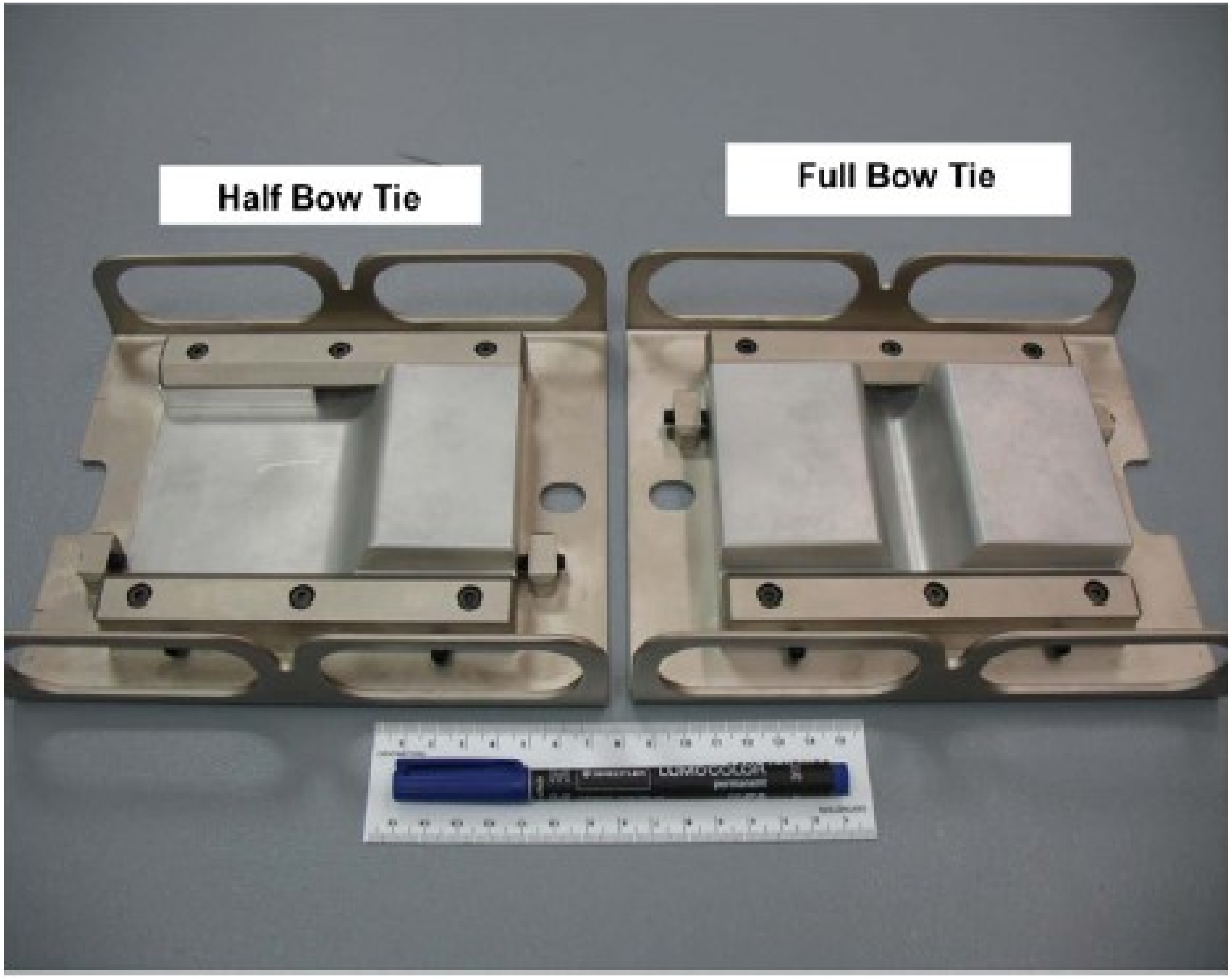
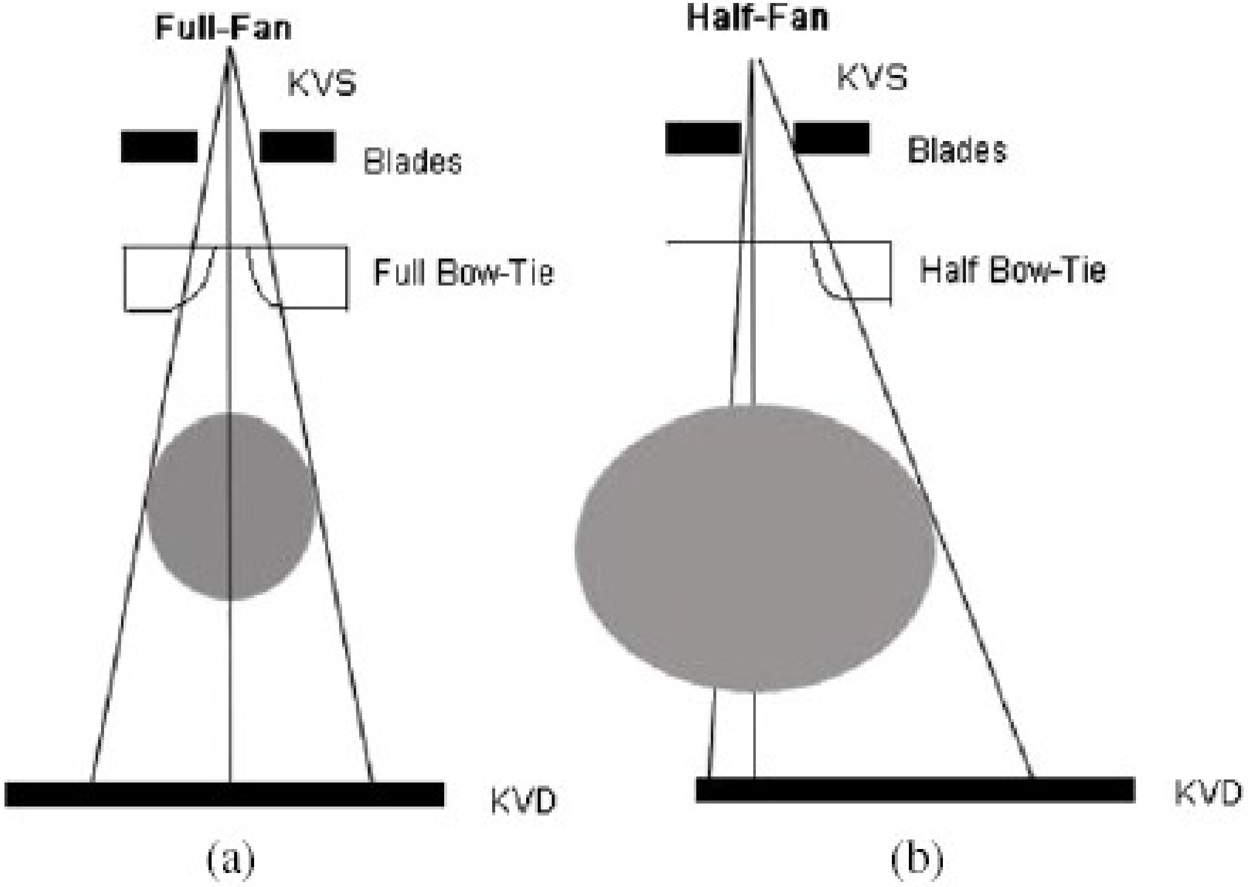


Figure 2. A photo showing the two types of bow tie filters: half bow tie (left) and full bow tie (right).

Ding et al. PMB 52 (2007), 1595 ff



Wen et al. Phys. Med. Biol. **52** (2007) 2267–2276

Imaging doses

<u>Range of measured/published doses</u>

- Head & Neck
  - 1 – 2 cGy (330 – 360 frames)

- Prostate
  - 4 – 7 cGy (640 – 720 frames)

Measured doses

DKFZ 30 cm diameter cylindrical
water phantom

	dose calibration factors	
	peripheral [mGy/As]	central [mGy/As]
80 kV	22	16
120 kV	70	52

	Dose (central) (cGy)	Dose (periph.) (cGy)
DKFZ/SMS	1.7	2.3
Synergy*	1.6	2.3

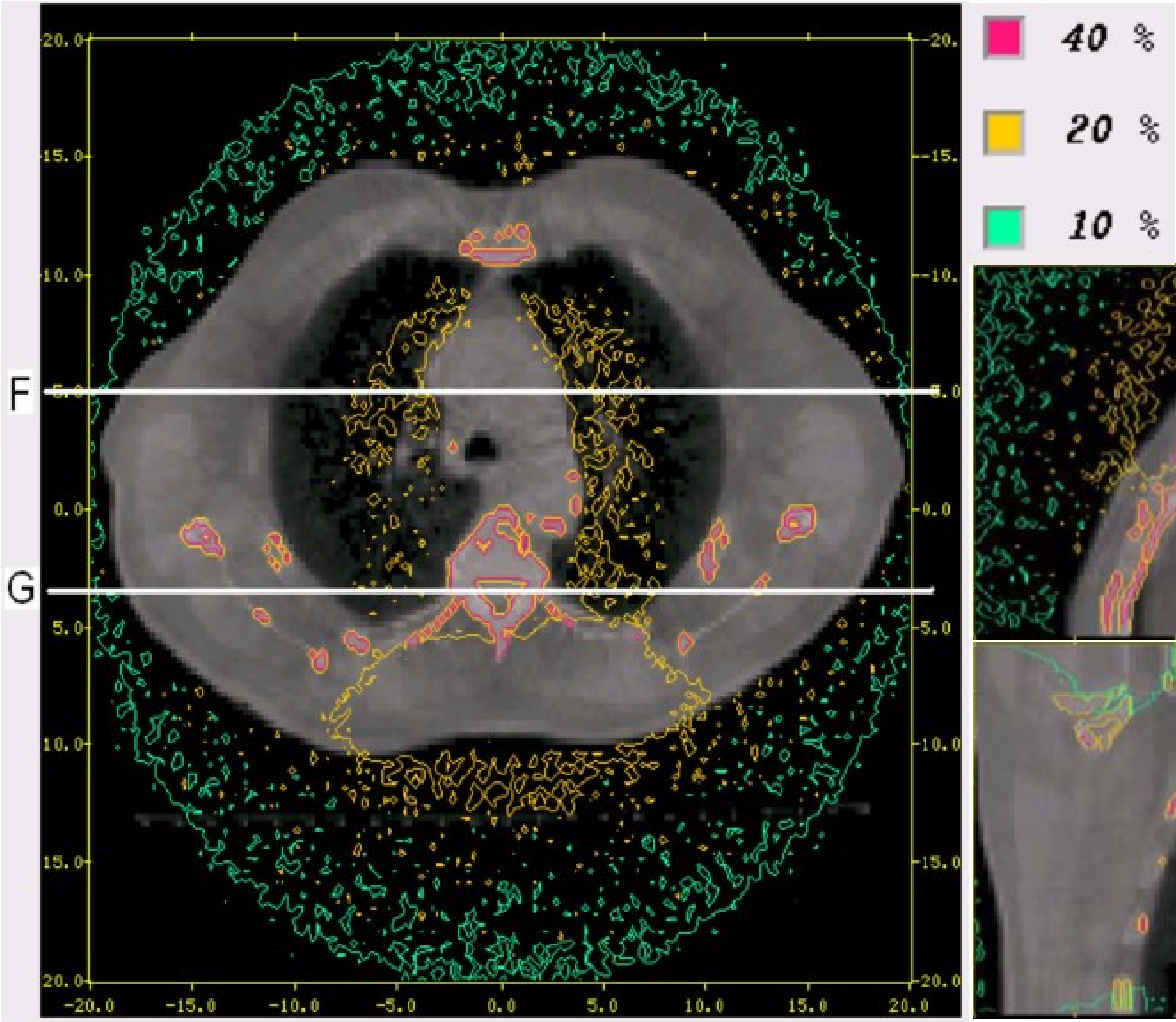
*M. K. Islam, T. G. Purdie, B. D. Norrlinger, H. Alasti, D. J. Moseley, M. B. Sharpe, J. H. Siewerdsen, and D. A. Jaffray, “Patient dose from kilovoltage cone beam computed tomography imaging in radiation therapy”, Med. Phys. 33(6), 1573-1582, 2006.

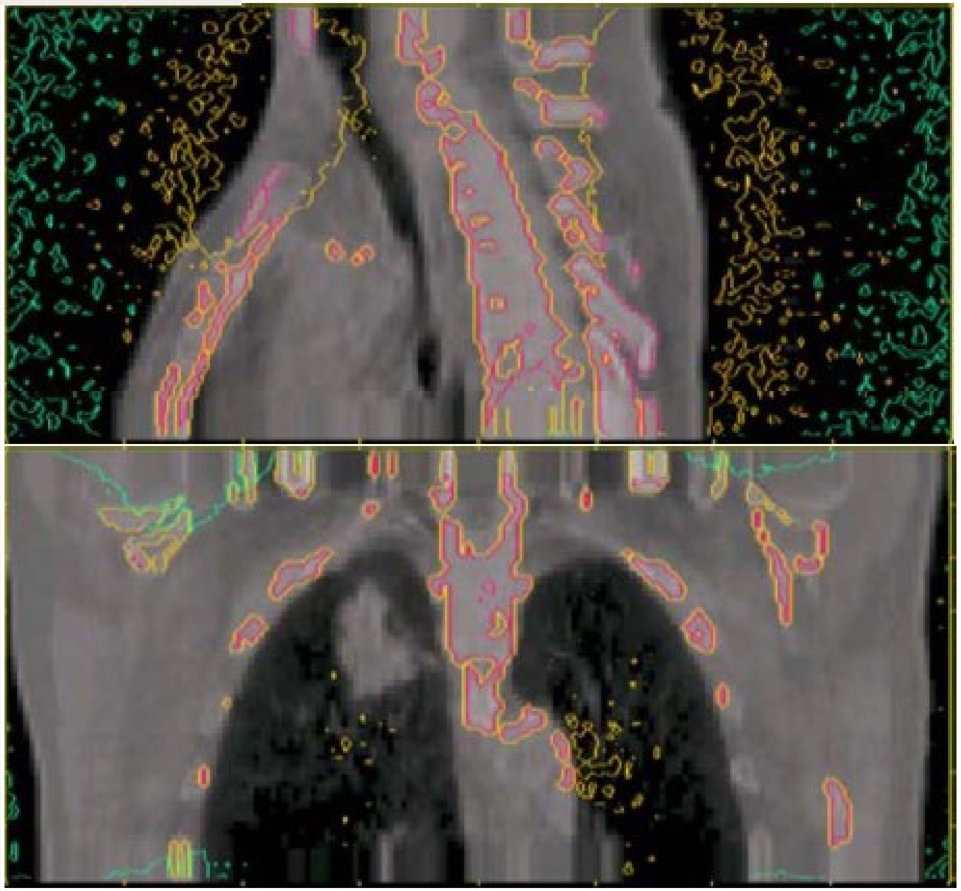
Imaging dose to patient anatomy

- MC simulation of imaging dose (VARIAN, OBI)
  - ➢ Full scan: 125 kVp, 80 mA, 25 ms
  - ➢ Low dose scan: 125 kVp, 40 mA, 10ms
- Anatomies:
  - ➢ Head & neck
  - ➢ Chest-lung
  - ➢ Pelvis

Ding et al.,Medical Physics, Vol. 35, No. 3,p 1135 ff, March 2008

Lung-Chest





(a)

Ding et al.,Medical Physics, Vol. 35, No. 3,p 1135 ff, March 2008

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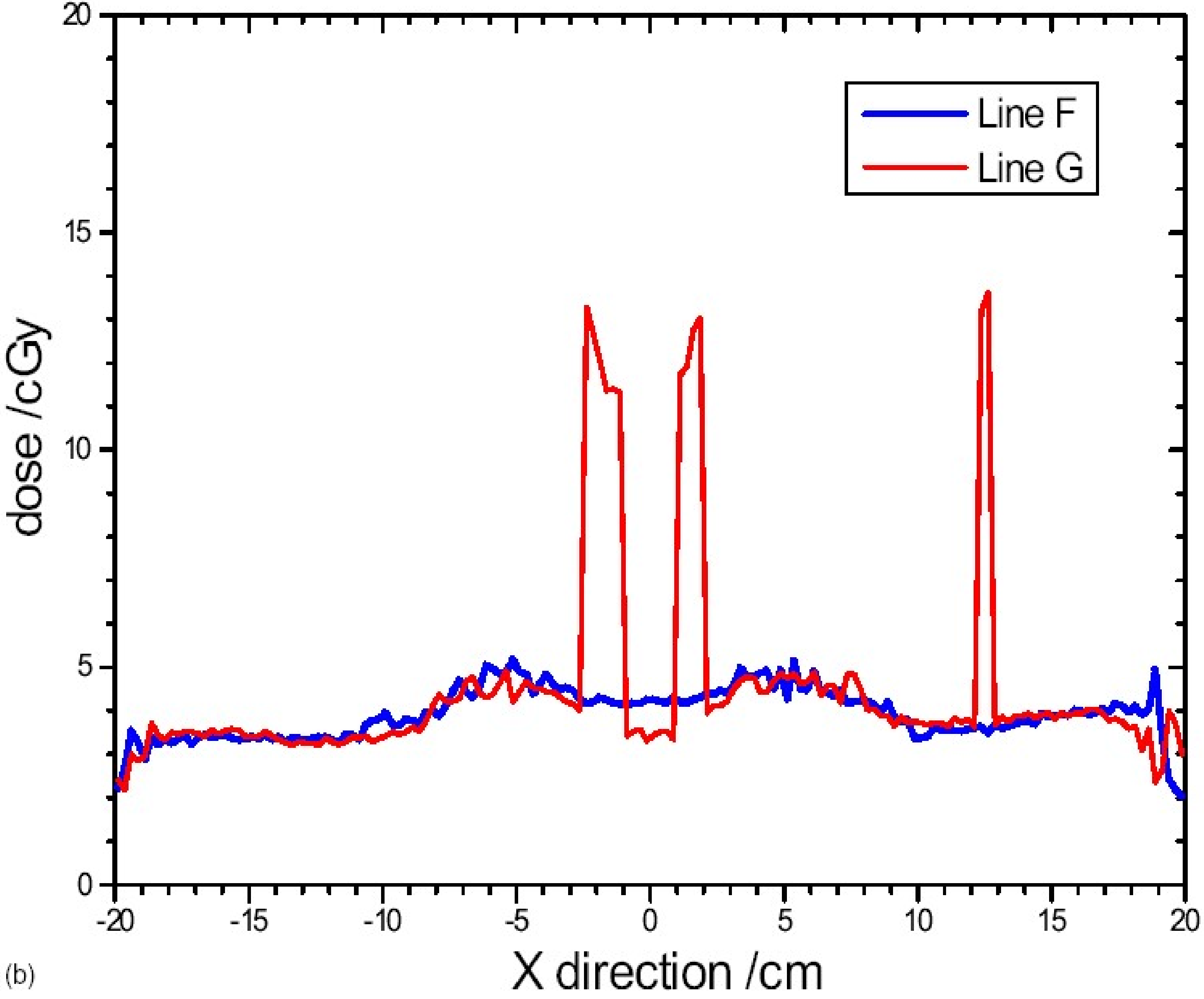

Line F
Line G
dose /cGy
X direction /cm
20
15
10
5
0
-20
-15
-10
-5
0
5
10
15
20
(b)

TABLE I. Monte Carlo calculated dose to different organs in a typical patient CBCT scan in clinical default half-fan mode settings.

Dose to organs (cGy)	Head and neck scan	Chest scan	Pelvis scan	Prostate scan
Skin	6–12	4–6	3–6	3–6
Soft tissue	4–7	4–6	3–8	4–7
Eye	8		⋯	⋯
Brain	4–5			⋯
Spinal cord	3–5	3–4	⋯	⋯
Lung	⋯	4–5	⋯	⋯
Prostate	⋯	⋯	⋯	4
Ovary	⋯	⋯	4	
Bone	23–27	10–15	8–22	8–20

Ding et al.,Medical Physics, Vol. 35, No. 3,p 1135 ff, March 2008

Imaging dose kV-CBCT

- Dose depends on geometry patient thickness etc.
- Published measured doses cover a spectrum of ranges
- CBCT needs more dose for same image quality than diagnostic CT (noise from scatter)

Reference

The management of imaging dose during image-guided radiotherapy: Report of the AAPM Task Group 75

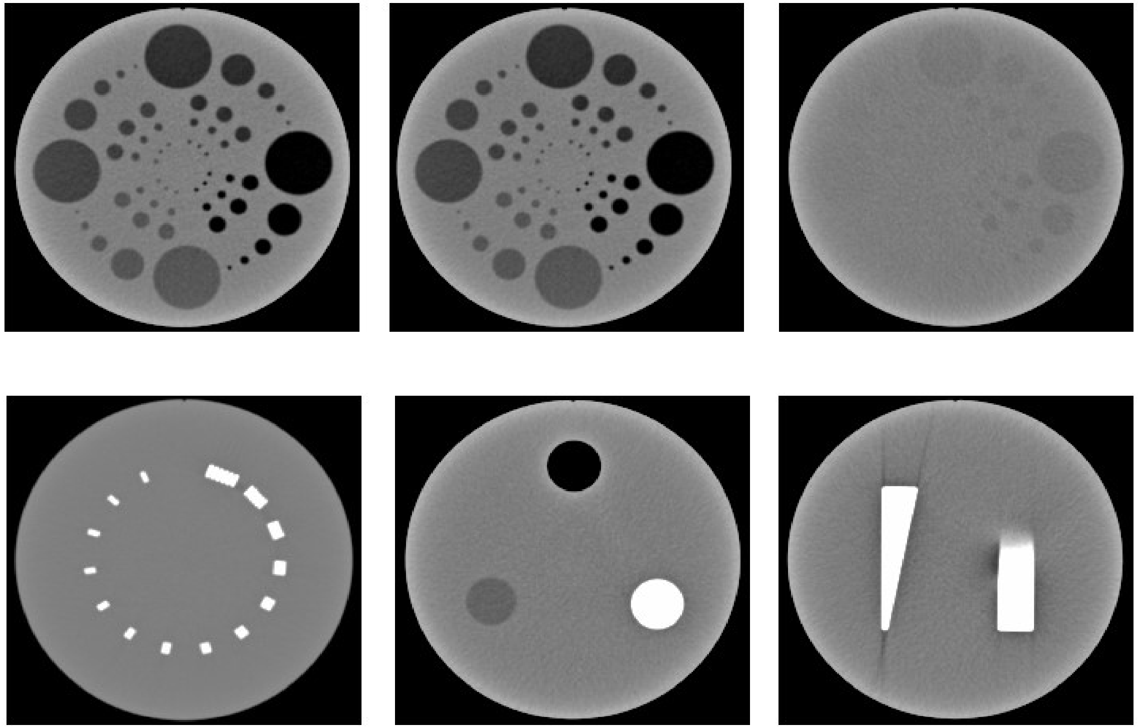
Med. Phys. 34 (10), October 2007 0094-2405/2007/34(10)/4041

In room 3D-imaging…MV/kV

- kV CBCT (cone beam, electron energy: 70 -140 keV,FPI)
- In room kV-CT (Spiral CT (fan), 60 -140 KeV, ion-chamber)
- MV – CBCT (Cone beam, 6 MeV,FPI)
- MV-CT (Fan beam, tomo, 3.5 MeV,FPI)
- IBL (‚inline kView‘, conebeam, 3.5 MeV, C-target,FPI)

Siemens Cone beam phantom

Contrast slices I,II,III,



spatial resolution slice, noise & scaling slice, MTF slice

The Siemens ConeBeam Phantom V2.5. From left to right: Contrast slice I (inserts have CT-numbers -200 HU, -120 HU, -90 HU, -60HU relative to the basic material, which has 35HU at 120 keV), Contrast slice II (-45 HU, -30 HU, -25 HU, -20 HU), Contrast slice III (-15 HU, -10 HU, -5 HU, -3 HU), Spatial resolution slice, Noise and scaling slice, MTF slice. (Images were acquired with the Siemens Primatom scanner.)

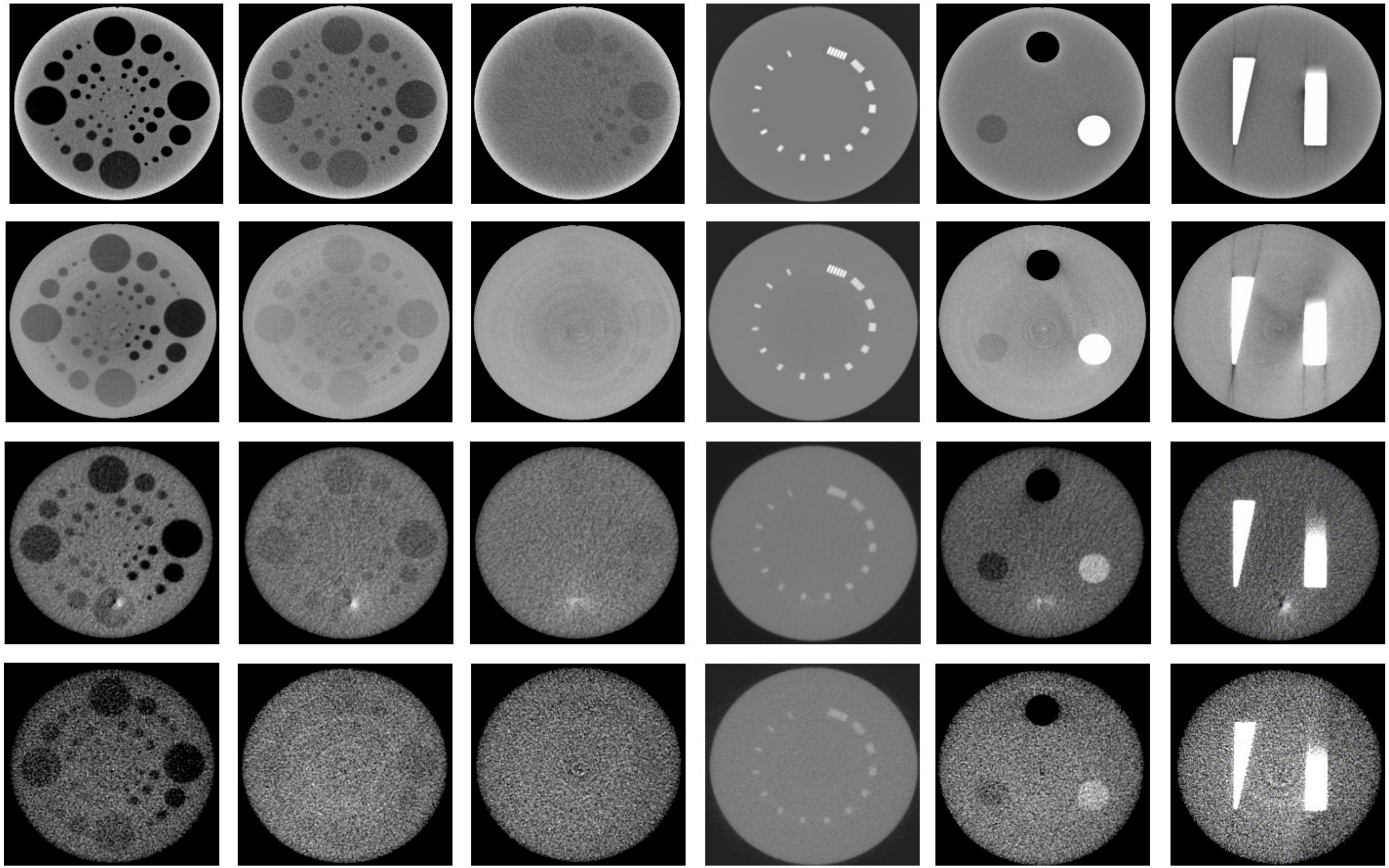
Example: Image quality and dose

Primatom
1.5cGy

kVCT
1.5cGy

MV CT
1.5cGy

MV- CBCT
8cGy



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IGRT strategies in clinical practice : prostate cancer

Pr Gilles Créhange, MD, PhD

Department of Radiation oncology, Centre Georges François Leclerc, Dijon, France

Medical Imaging Group, Laboratory of Electronics, Computer Science and Imaging, (Le2I), CNRS 6306, University of Burgundy

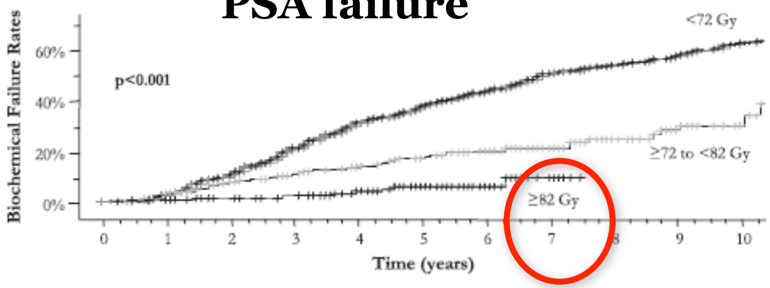
Issues that must be adressed

1. Why we do IGRT in prostate cancer?
2. Contours
3. Interfraction mvts
4. How to manage the rectum?
5. Intrafraction mvts
6. Is there a better IGRT protocol?
7. Room for IG Adaptive RT (IGART)?
8. Concomitant nodal radiotherapy
9. IGRT in the postop setting

Why we do IGRT in prostate cancer?

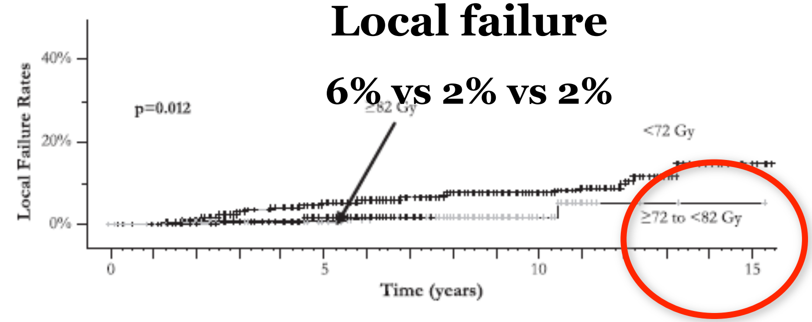
Why IGRT?

PSA failure



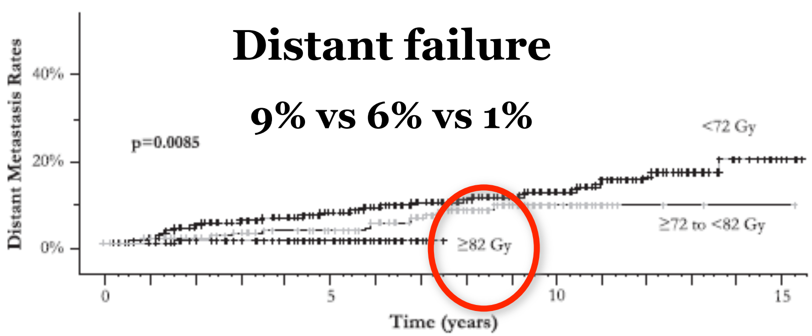
Local failure

6% vs 2% vs 2%

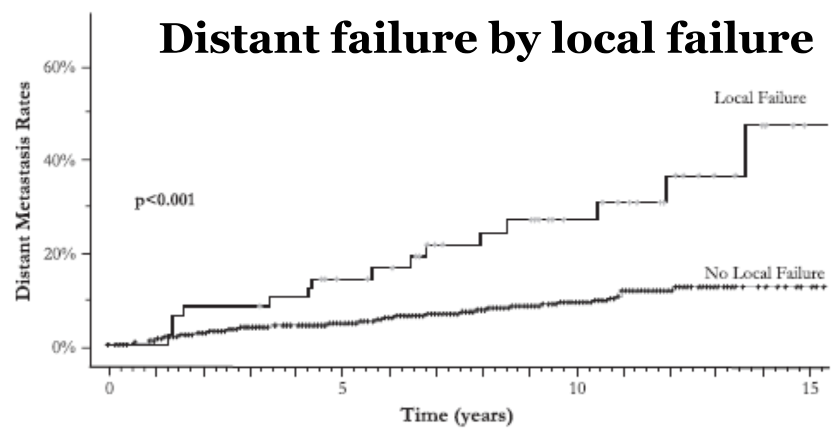


Distant failure

9% vs 6% vs 1%



Distant failure by local failure



Kupelian P. IJROBP 2008;71:16-22

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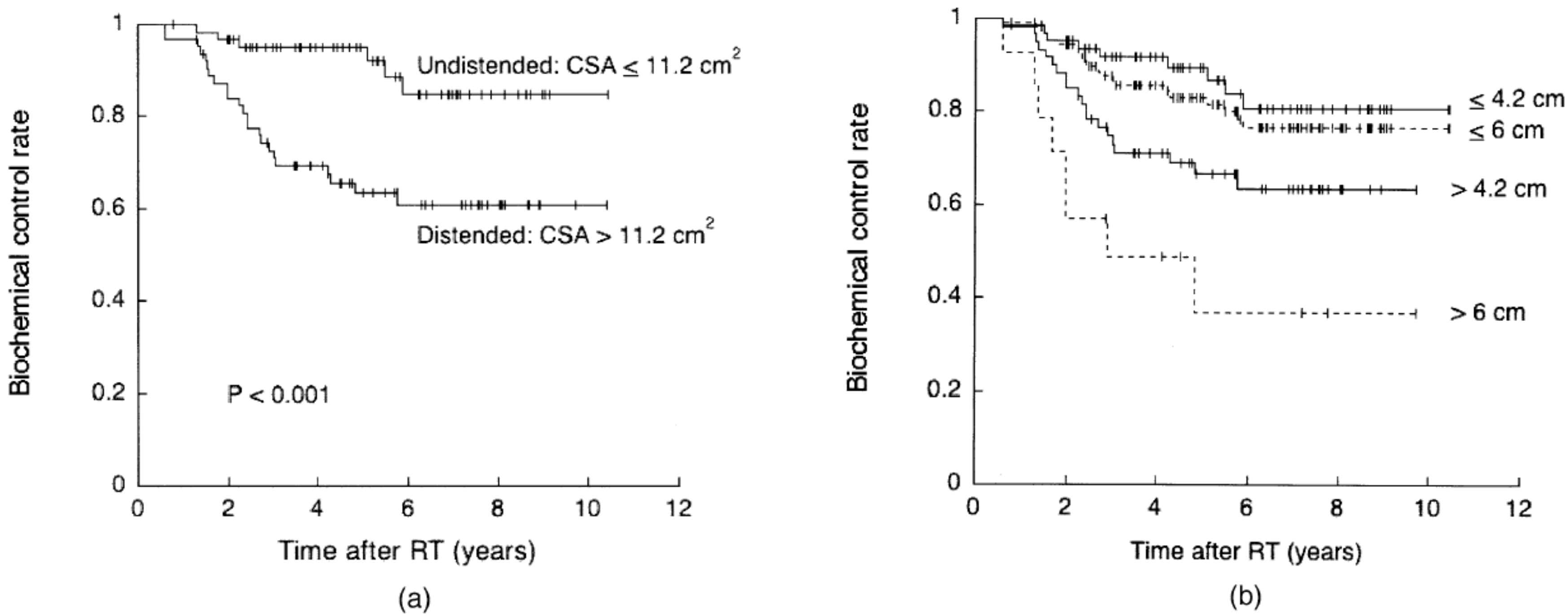
Dose escalation in 3D-CRT and late toxicity

	GI	GU
MDACC 70Gy 78Gy	13%(10-y) 26% G2+ (10-y)	8% (10-y) 13% (10-y)
MRC RT 01 64Gy 74Gy	24%(5-y) 33% (5-y)	8% (5-y) 11% (5-y)
CVKO 9610 68Gy 78Gy	27%(5-y) 32% (5-y)	41% (5-y) 39% (5-y)
PROG 70.2Gy 79.2CGE	8% (5-y) 10% (5-y)	18% (5-y) 20% (5-y)

Rectal distension and Local control



MDACC trial: De Crevoisier R et al. IJROBP 2005

Also,

Dutch trial: Heemsbergen WD IJROBP 2007

UZ Brussels: Engels B IJROBP 2008

Int. J. Radiation Oncology Biol. Phys., Vol. 62, No. 4, pp. 965–973, 2005

0360-3016/05/$–see front matter

doi:10.1016/j.ijrobp.2004.11.032

This report by De Crevoiser *et al.* (1) is essentially a "proof of principle" that what might otherwise be considered an insignificant finding (distended rectum) in the planning process could have a profound impact on outcome. This observation causes me to pause and ask what other otherwise "insignificant little things" might also have a profound impact on outcome. Yes, the "devil is in the details," and there are many details in the treatment planning process for localized prostate cancer. These investigators are to be applauded for their work. More studies are needed to confirm these findings, as well as to address other factors that might affect outcome. Einstein said ". . . not all things that can be counted count and not all things that count can be counted." As researchers, we must count what we can and hope that that counts. These investigators have done just that.

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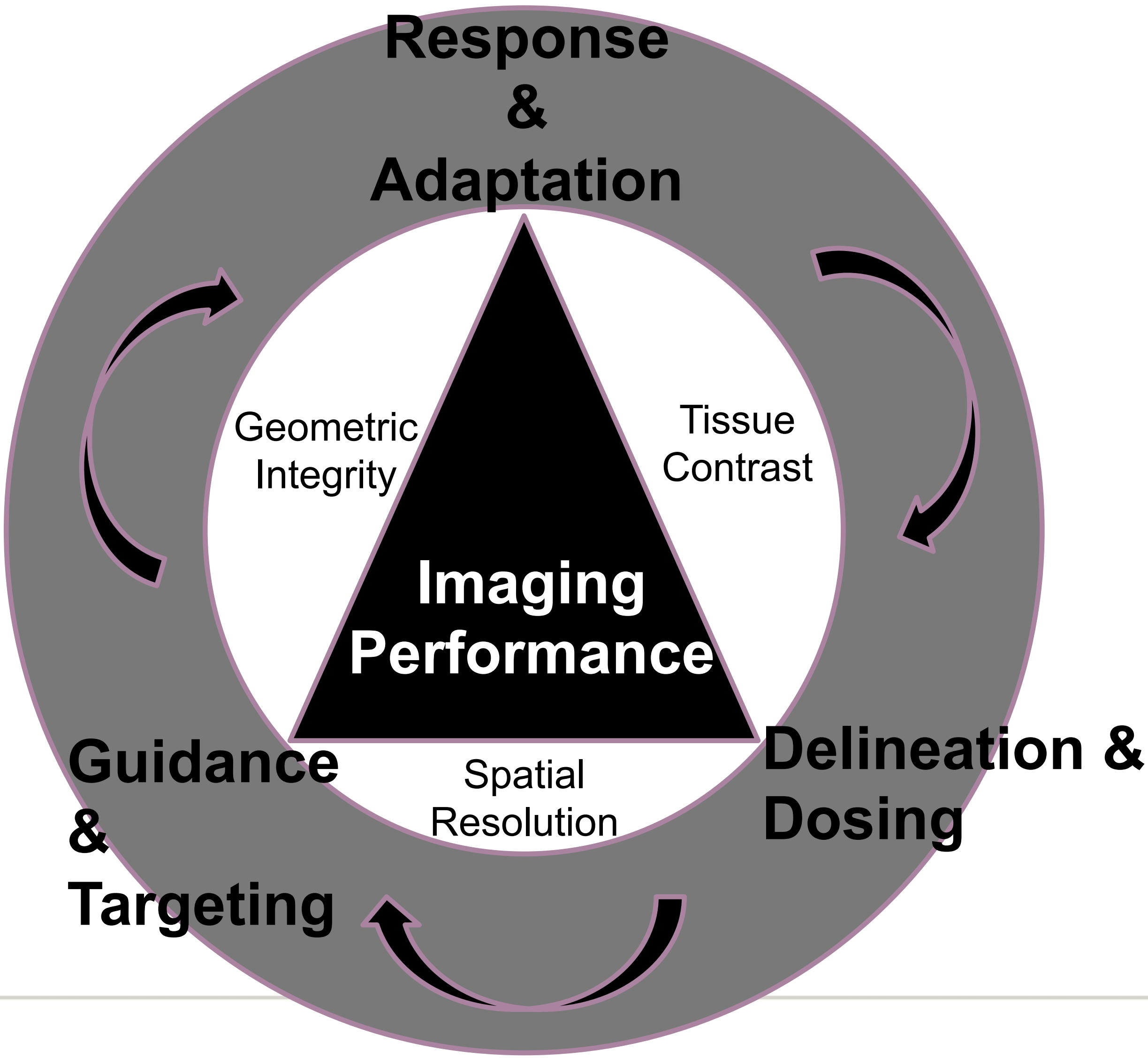
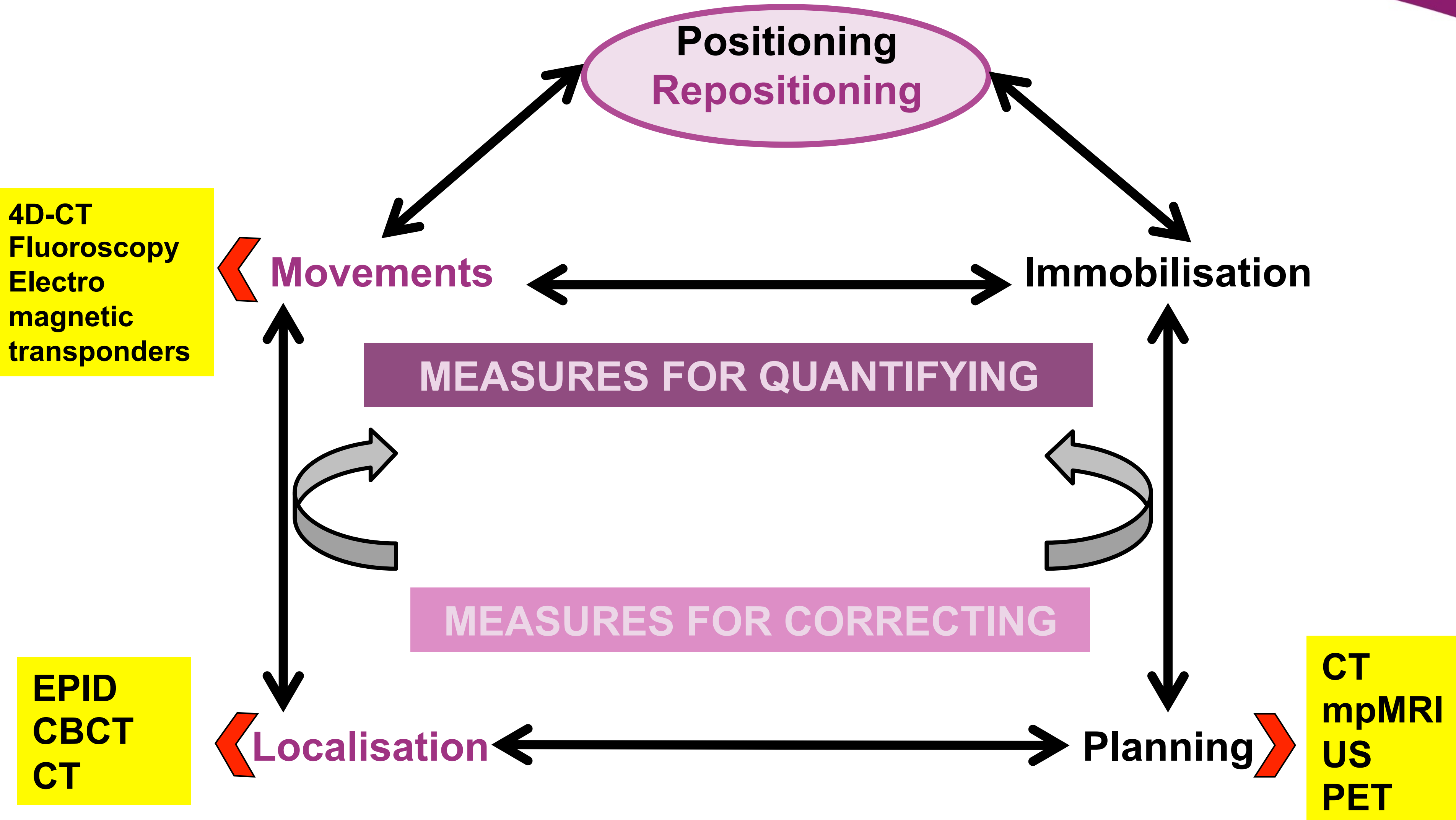
« Multimodality » Image-guided RT



Adapted from Menard C and Dawson L, Oncologist 2010

Multistep imaging for real-time accuracy



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

Special commentary

Fr … nd?

[a]Department of Medic… …nter, New York, NY, USA

but that these will take some time to complete. As the capabilities of IGRT improve, it will provide the tools to better understand treatment uncertainties and allow a re-examination of the present practice regarding the expansion of GTV into the CTV, ITV and PTV, the limitations of which are well known. We are uncertain about the tumor extension from what is visible radiologically, so we enlarge GTV to CTV. To account for organ motion, we further enlarge CTV to ITV and to account for set-up error, we cover the ITV with the PTV. Given such practice, it simply makes no sense to use IGRT to assure that the PTV is within the each radiation field, each and every day during a course of conventional fractionated radiotherapy.

What is of potential, after validating its capabilities, is that IGRT will allow us to refine our definition of the target volume. We suggest the concept of image-guided target volume (IGTV or PTV_{IG}), which is CTV plus a margin to account for residual set-up uncertainty and organ motion when 'image-guidance' is used during radiation delivery. It is most likely that IGTV is smaller than the corresponding PTV, which would translate to reduced dose to normal tissues, allowing dose escalation and improving local control. Viewed in this perspective, IGRT is a continuation of the progress we experienced with 3DCRT and IMRT, processes that permit increased tumor dose while keeping normal tissue toxicity at bay. As was performed for 3DCRT and IMRT, clinical trials

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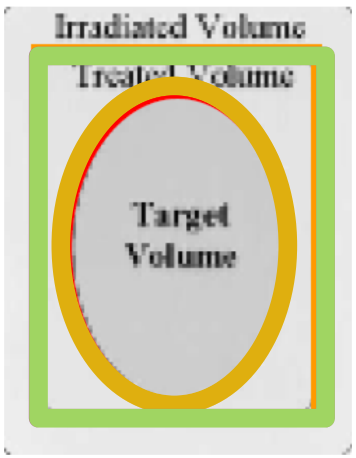
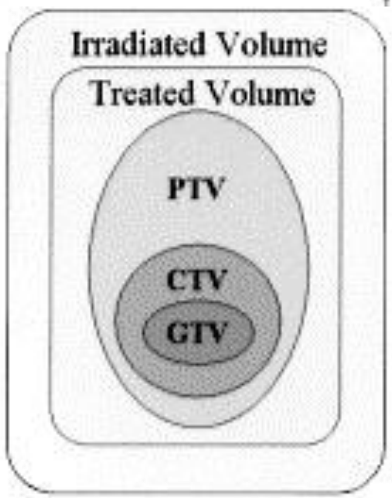
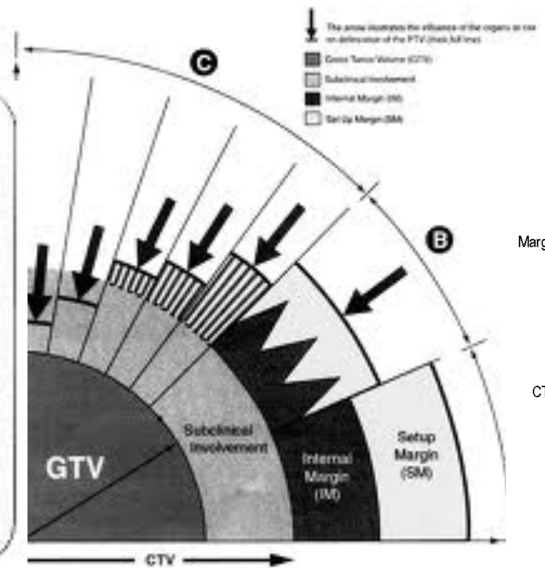
ICRU 62 and IGRT



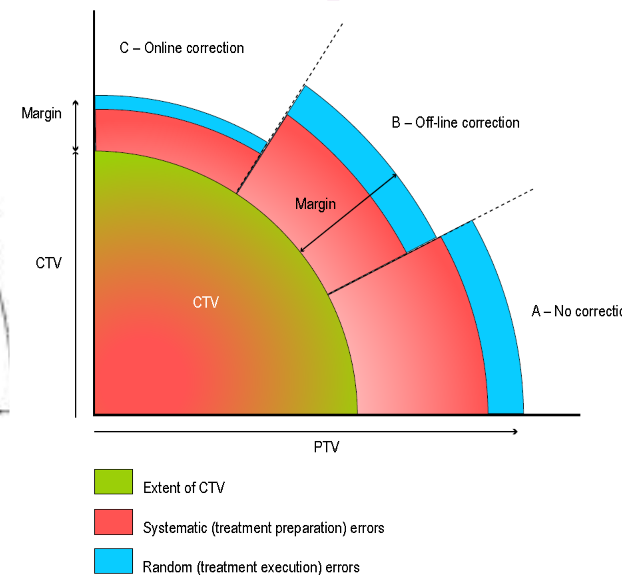
ICRU 29



ICRU 50

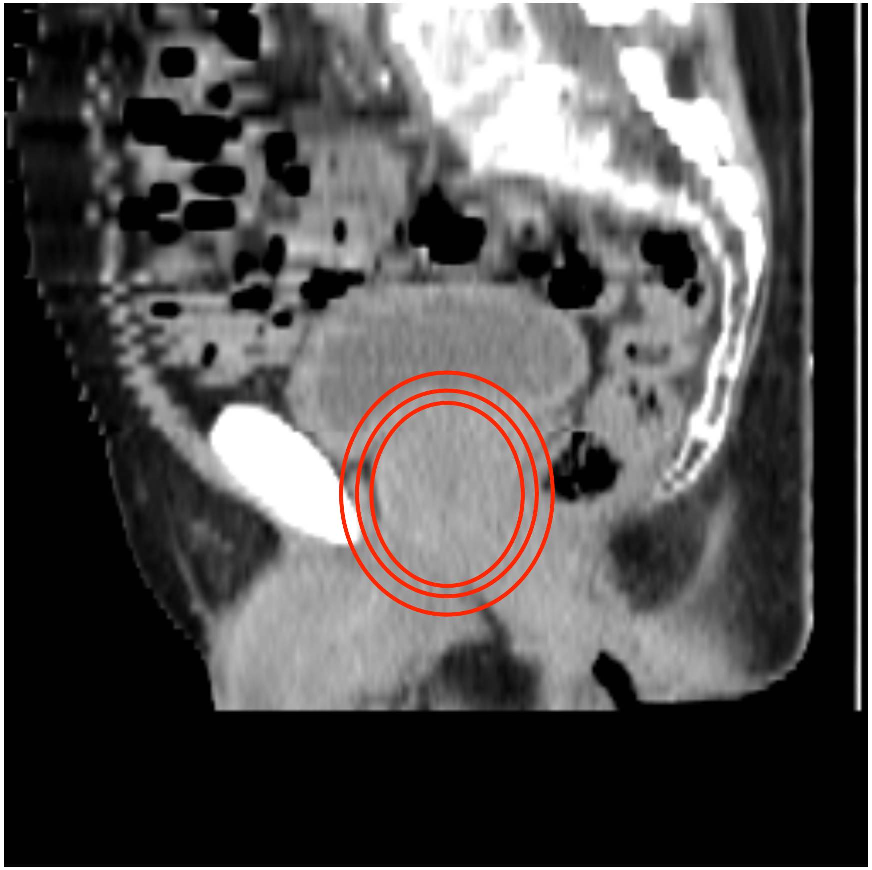


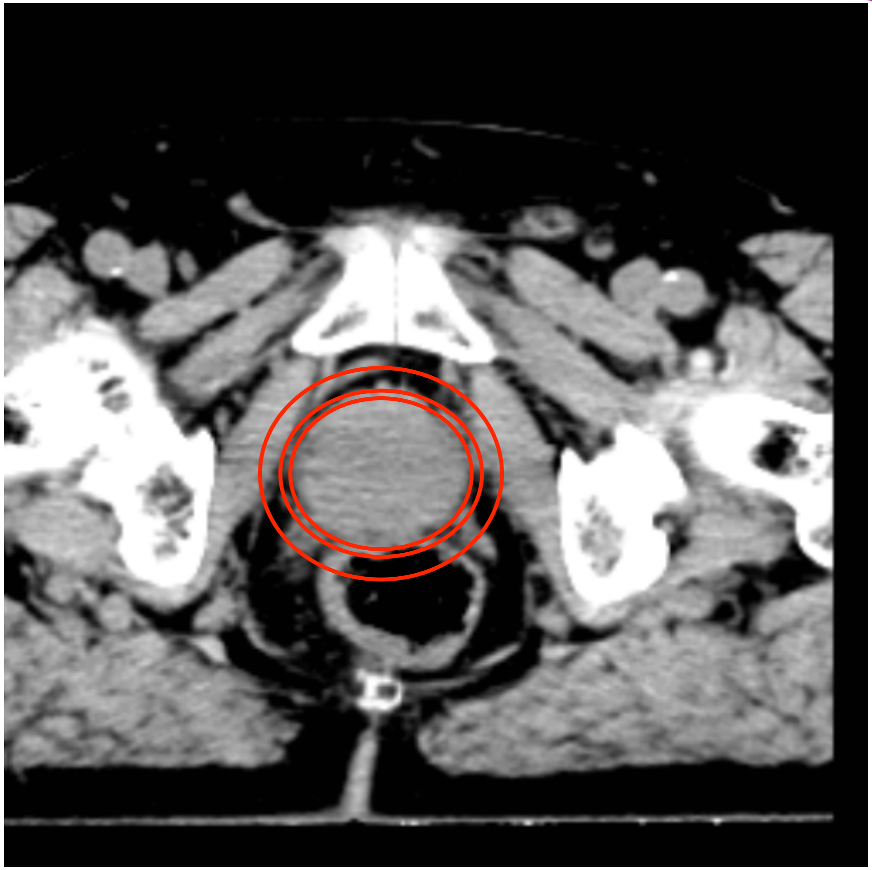
ICRU 62



ICRU 62 and IGRT

Why each mm counts in large amount?





Prostate vol : 50 cm^3

PTV = 1cm → PTV vol = 90 cm^3
PTV = 0.5cm → PTV vol = 68 cm^3
PTV = 0.1cm → PTV vol = 53 cm^3

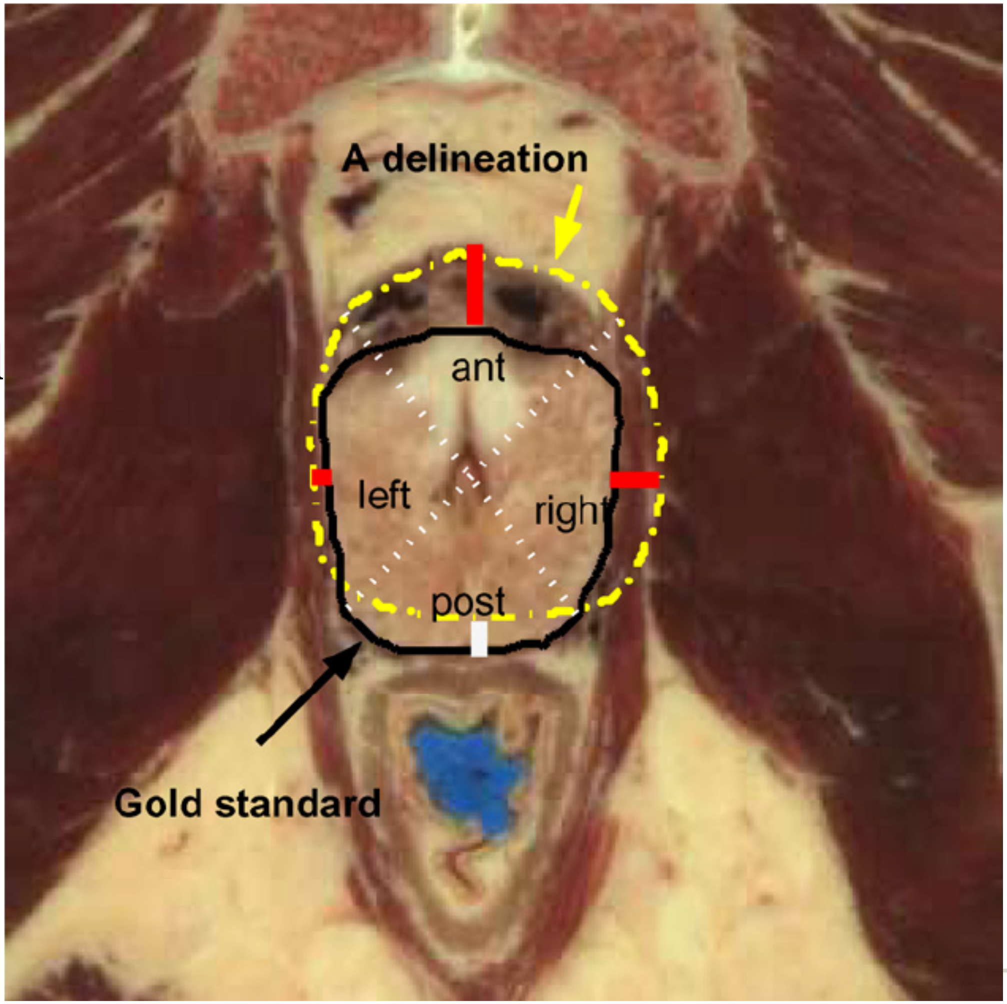
A 5mm margin = **Volume X 35%**

A 10mm margin = **Volume X 80%**

Prostate volume/contours : which standard imaging for reference?

(a) Anatomical image of pelvic region

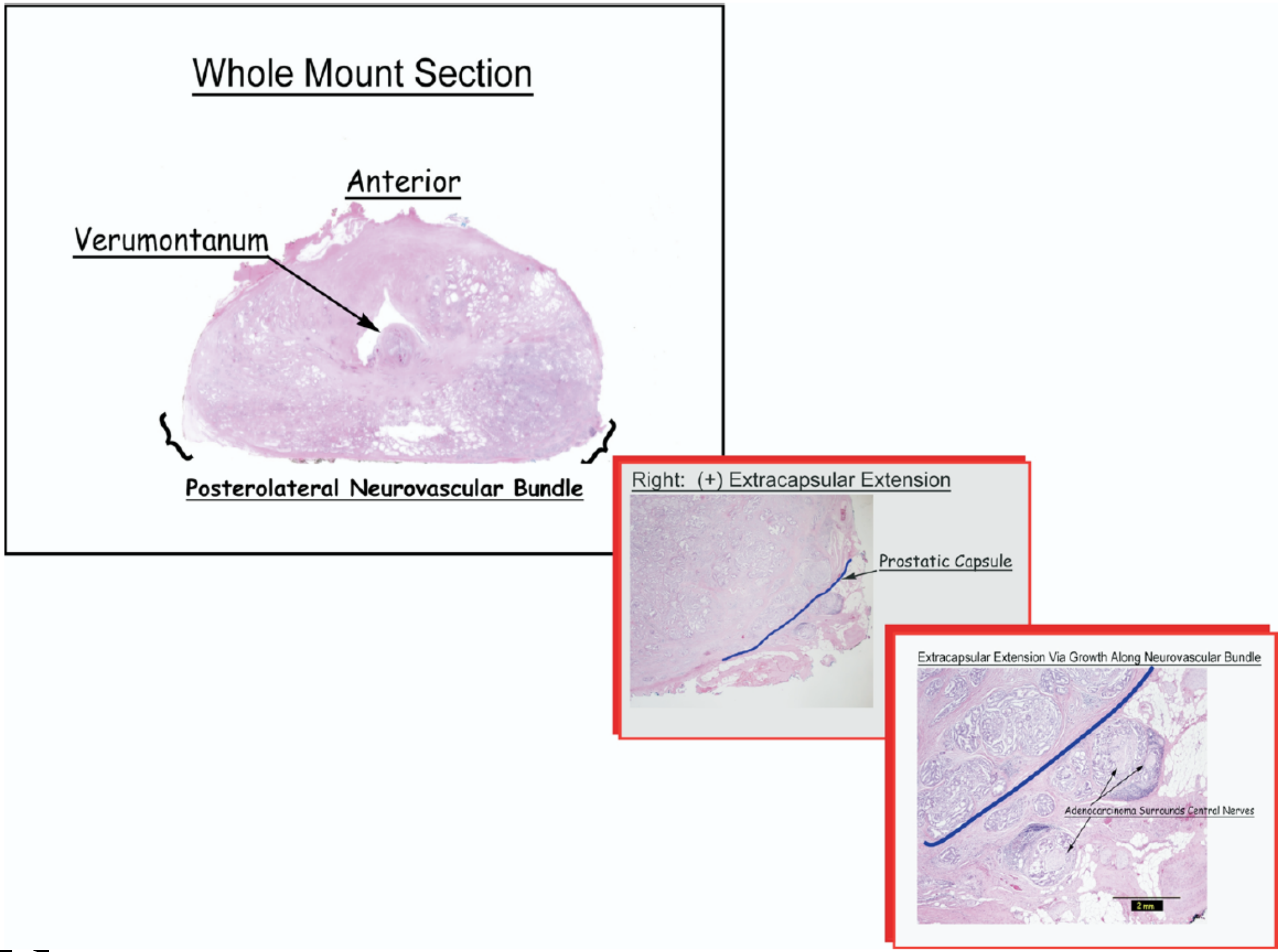
(b) Corresponding CT image



Gao Z et al., Radiother Oncol 2007

Prostate=GTV=CTV?

- WBH (n= 371)
- PSA > 10 ng/mL
- and GS ≥ 7
- 20% ECE
- **4-5mm post and lat**

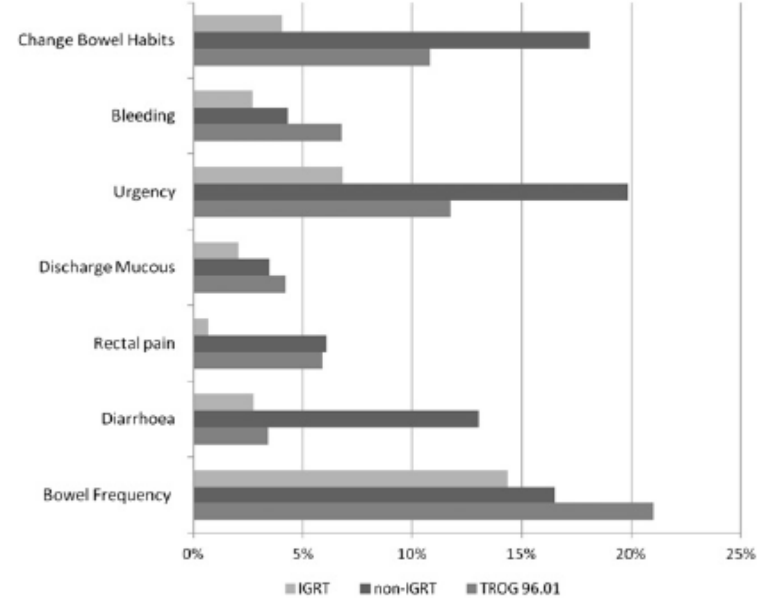


Chao KK et al., IJROBP 2006

IGRT and smaller margins

Margins		Range (cm)		
	Margin	non-IGRT	IGRT	*P* value
CTV1-PTV1	Posterior	0.7-1	0.5-0.7	
	Other	1-1.5	0.7-1.2	
CTV2-PTV2	Posterior	0.7-1	0.5-0.7	
	Other	1	0.6-1	

Volumes		Mean (cm^3) non-IGRT	IGRT	*P* value
CTV1	Prostate + proximal SV	52.6	52.7	.96
CTV2	Prostate only	45.1	39.5	.27
PTV1	CTV1 + margin	173.2	154.4	.018
PTV2	CTV2 + margin	137.4	117.6	.043



Dose and volume	Median (IQR) non-IGRT	IGRT	*P*
Absolute rectal volume irradiated			
Within 50 Gy isodose	21.9 (15.4-31)	20.4 (14.6-28.4)	.669
60 Gy isodose	9.6 (5.7-15.9)	14.8 (9.9-21.2)	.0001
70 Gy isodose	3.8 (0-14.9)	6.3 (3.1-9.8)	.0001
Percentage of rectal volume			
Within 50 Gy isodose	43.6 (34.8-53.8)	49.9 (39.1-59.1)	.007
60 Gy isodose	30 (22.3-36.6)	36.6 (22.3-46.3)	.0001
70 Gy isodose	8.5 (0-15)	17.3 (8.3-25.7)	.0001
	n = Exceeding tolerance (%) non-IGRT	IGRT	*P*
QUANTEC constraints			
V50 <50%	38 (32.5)	72 (49)	.008
V60 <35%	34 (29.1)	79 (53.7)	.0001
V70 <20%	16 (13.7)	57 (38.8)	.0001

Singh J, IJROBP 2012

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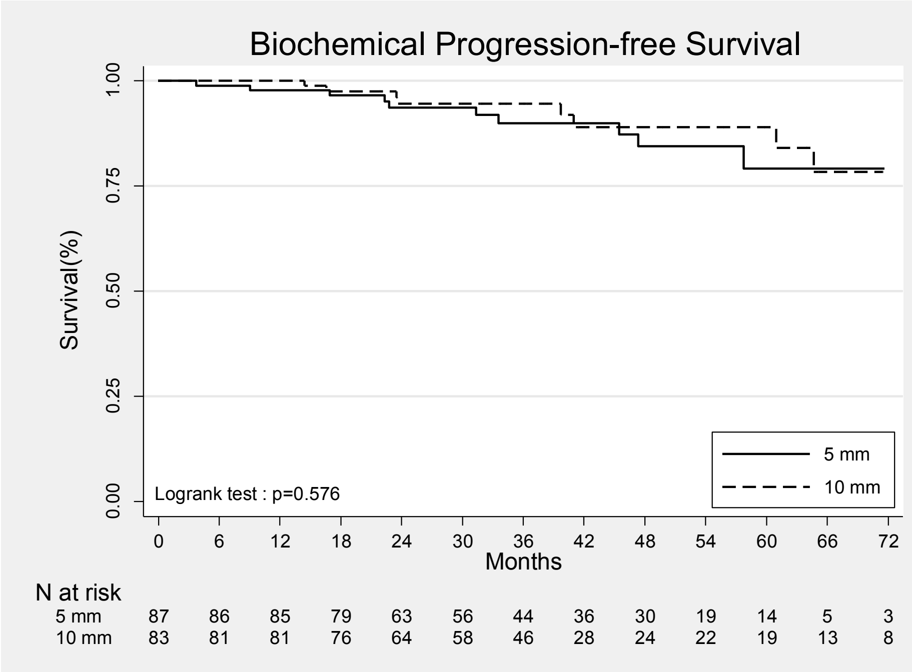
Daily IG-IMRT and reduced PTV margin in clinical practice

- 2001-2007
- Daily IG-IMRT
- Median dose 78 Gy (74-78Gy @ 2Gy/fx)
- 165 pts
- PTV margin10mm (n= 78) vs. 5mm (n= 87)
- Median FU = 39 months
- <u>GI : G2 = 1.2% (5mm) vs. 2.6% (10mm) , p = NS</u>
- NoG3+

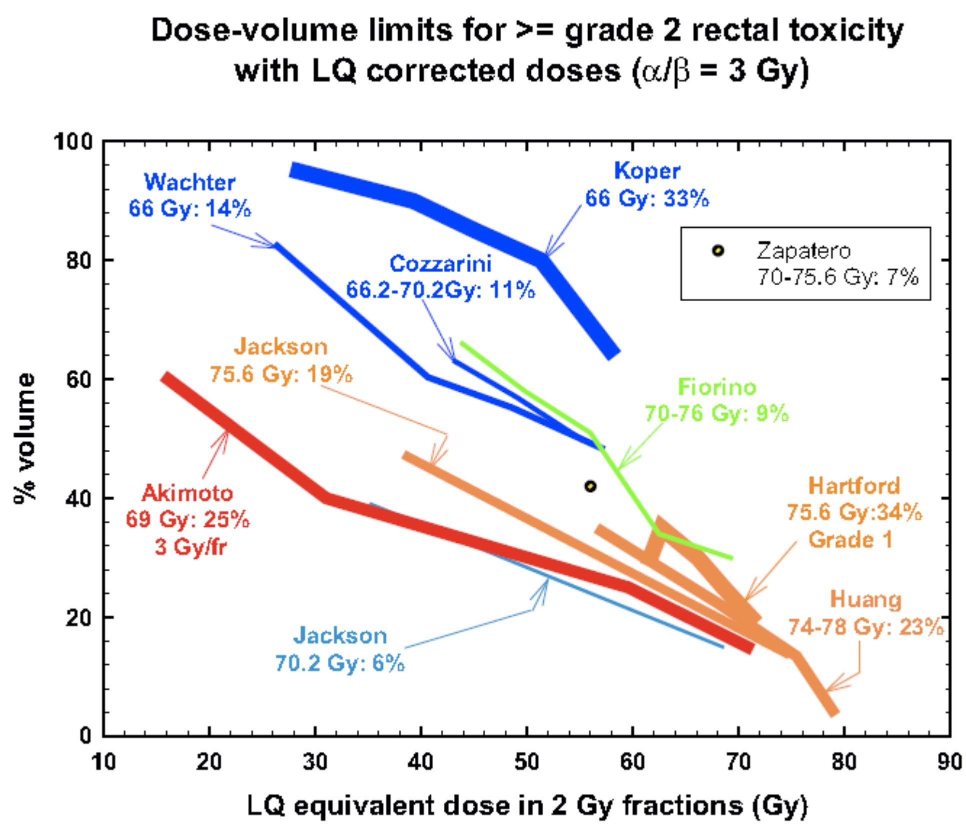


Créhange G. et al., Radiother Oncol 2012

QUANTEC Guidelines : from 3D-RT…

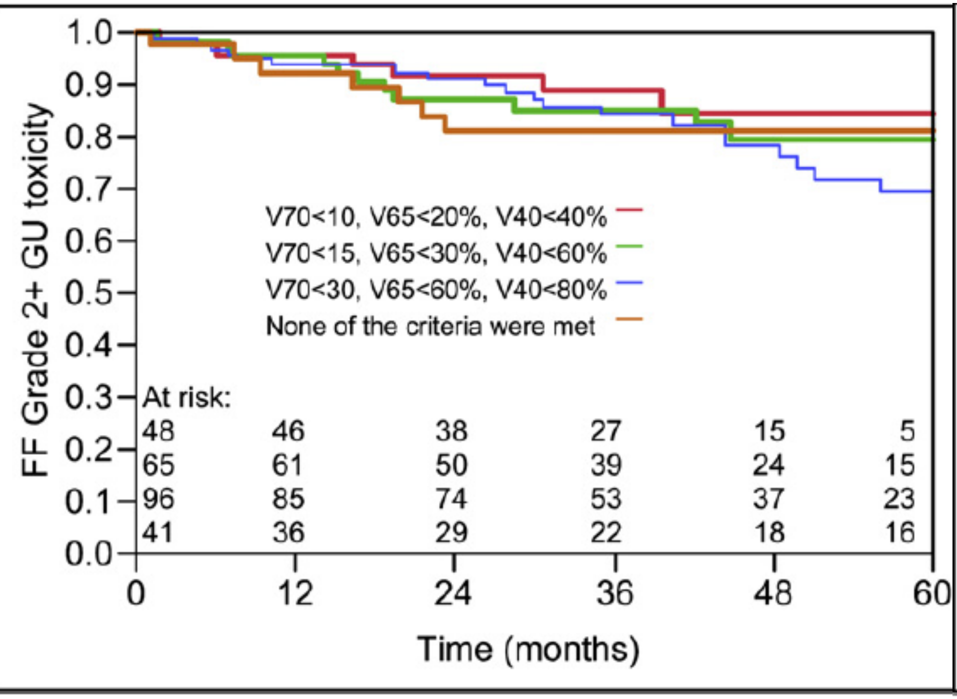
- **Rectal constraints**
- Conventional fractionation (≤78Gy)

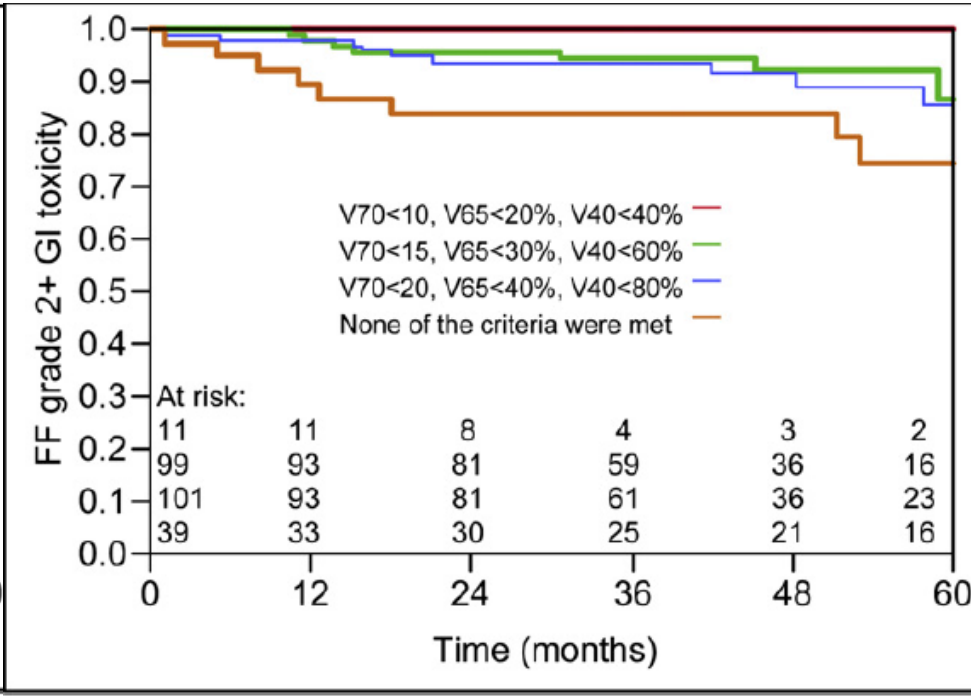
- V50 < 50%,
- V60 < 35%,
- V65 < 25%,
- V70 < 20%,
- V75 <15%.



Michalski J et al., IJROBP 2010

QUANTEC Guidelines : …to IMRT?





GU, p=0.77

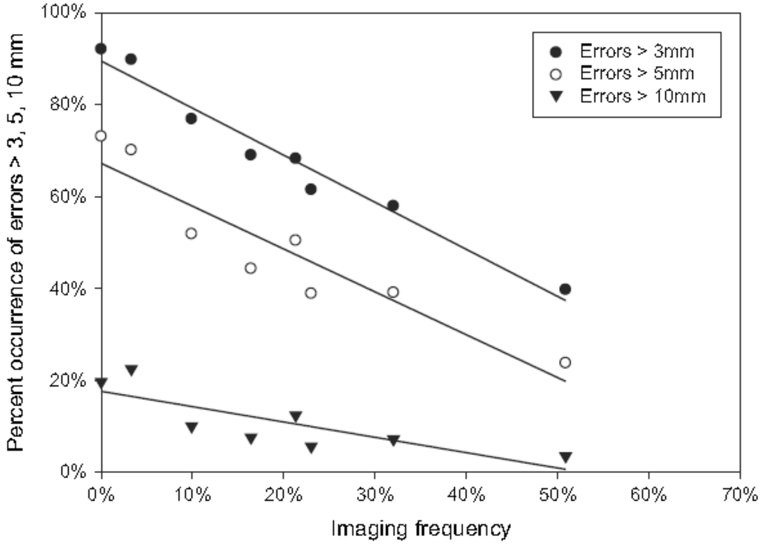
GI, p=0.13

Pederson A et al., IJROBP 2012

Interfraction mvts and imaging frequency

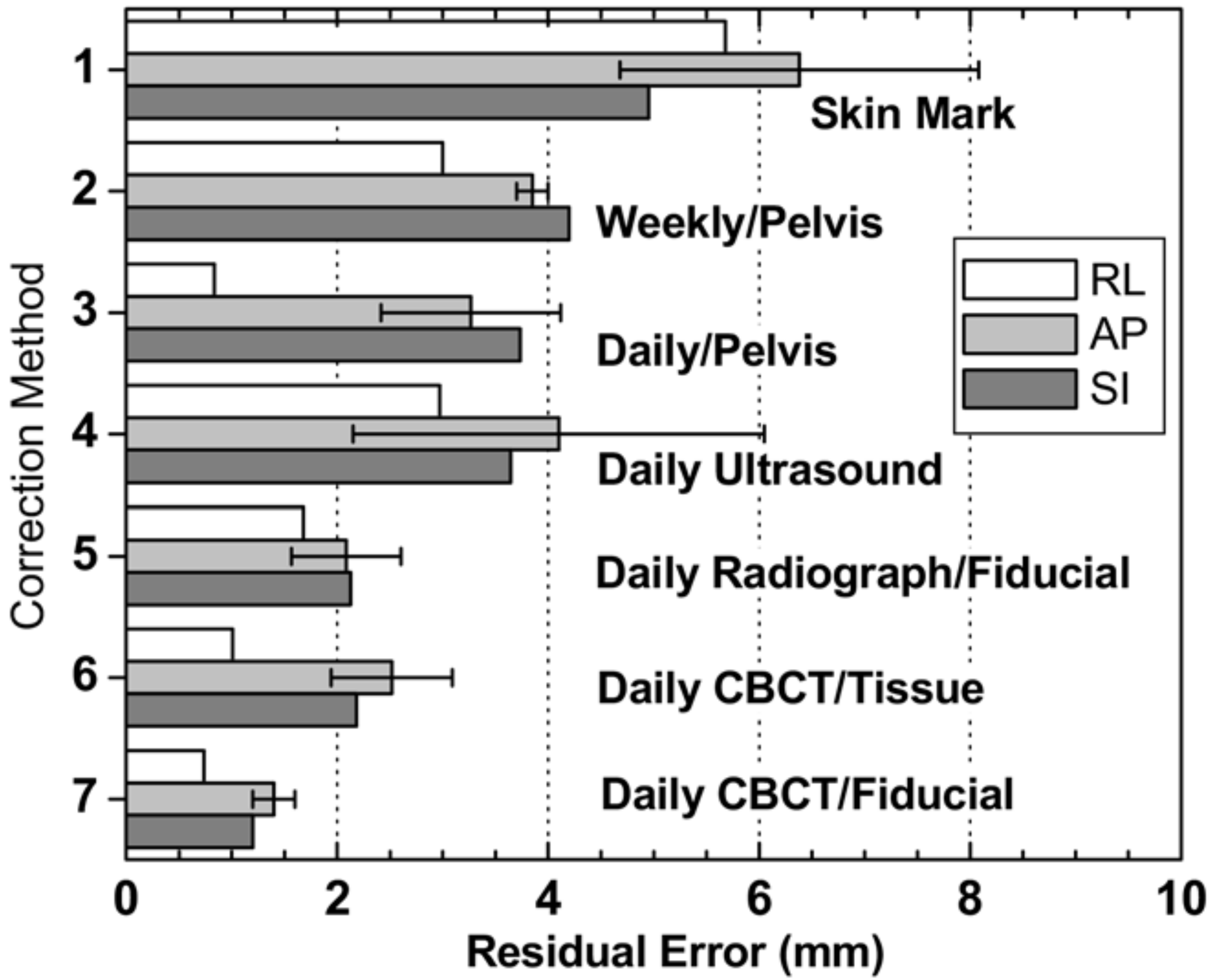
IGRT : Imaging frequency?

Scenario	IG (%)	AP M	AP Σ	AP σ	Lateral M	Lateral Σ	Lateral σ	SI M	SI Σ	SI σ
Skin marks	0	0.1	3.8	3.4	1.6	2.9	3.7	−0.5	3.3	2.4
D1 + correct	3	0.8	4.5	3.4	−0.4	4.5	3.7	−0.1	2.0	2.4
D1-D3 Mean+correct	10	0.8	2.9	3.3	−0.2	2.8	3.6	0.0	1.4	2.4
D1-D5 Mean+correct	16	0.6	2.6	3.3	−0.3	2.3	3.6	0.0	1.4	2.4
D1-D7 Mean+correct	23	0.5	2.3	3.3	−0.2	1.8	3.6	−0.1	1.3	2.5
Weekly	21	−0.1	1.8	4.4	−0.4	1.8	4.8	0.2	1.4	3.3
D1-D5 then Weekly	32	0.3	1.8	3.8	−0.3	2.2	4.1	0.1	1.2	2.9
Daily	50	0.5	1.8	3.5	−0.5	1.6	3.8	0.0	0.8	2.2



Kupelian PA, IJROBP 2008

ESTRO School



Mageras GS, Mechalakos J, Semin Radiat Oncol 2007

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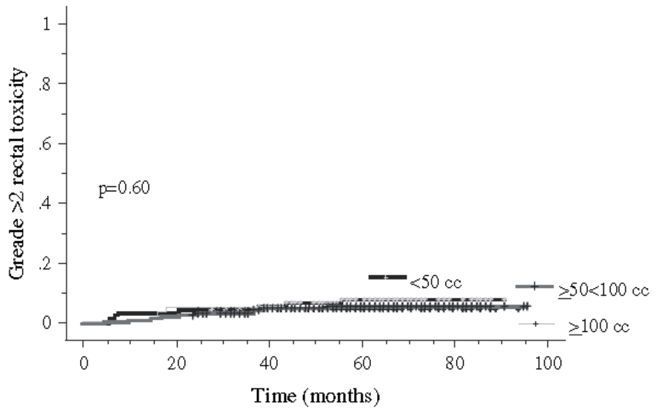
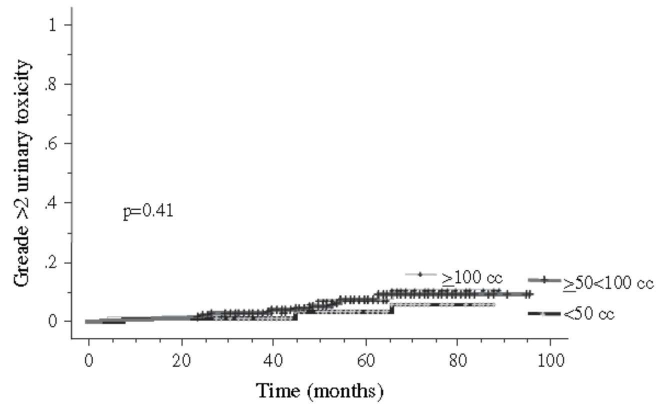
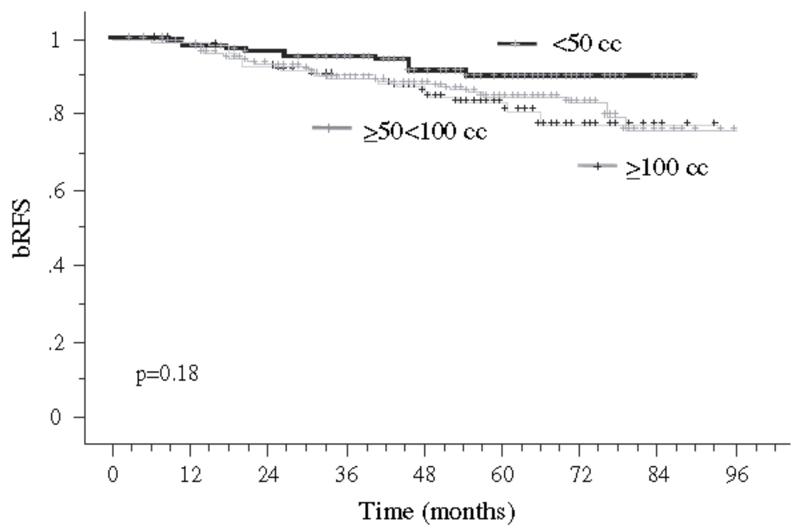
How to manage the rectum?

Rectal distension no matters w/ IGRT?

- n= 488 IMRT patients
- No bowel preparation (planning + daily ttt)







Kupelian P, IJROBP 2008

Rectal behavior

18 pts, daily MVCT = 540 MVCT

Enema 1H before planning CT

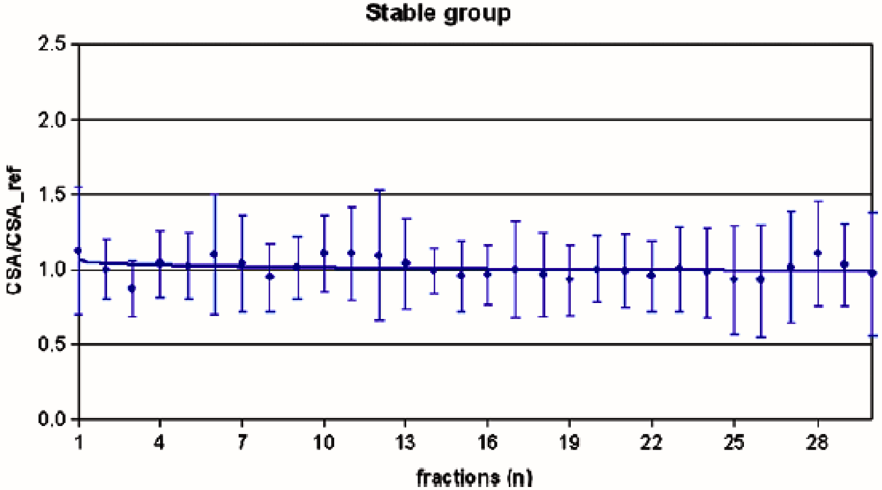
Empty bladder 1H before and then drink 500 mL

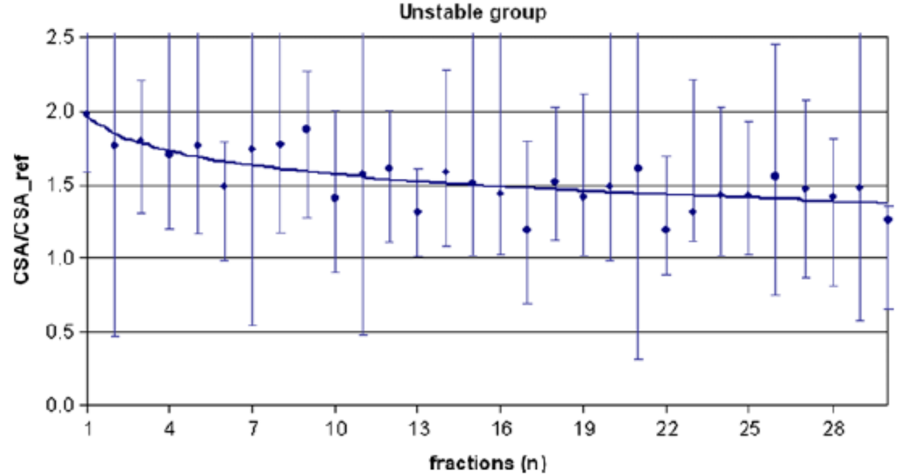
MVCT matched with planning CT on bony anatomy

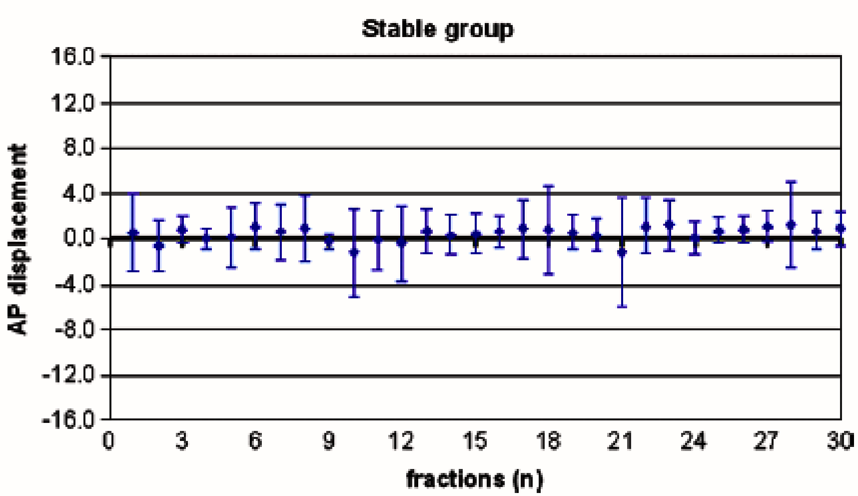
AP displacements measured for mid P

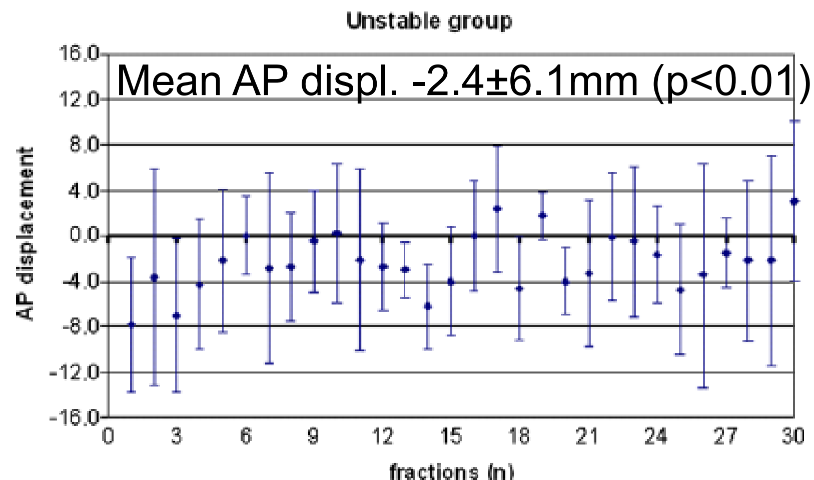
Engels B, UZ Brussels Radiother Oncol 2009

Rectal behavior









→ Risk of geographical miss

Engels B, UZ Brussels RO 2009

Unstable rectum :
Which 'daily' solution could account for mobile gas?

<u>First solution:</u>

Larger PTV margin

- Larger amount of surrounding tissue irradiated
- Lower dose escalation 72-74Gy?
- Dose in the air

<u>Second solution:</u>

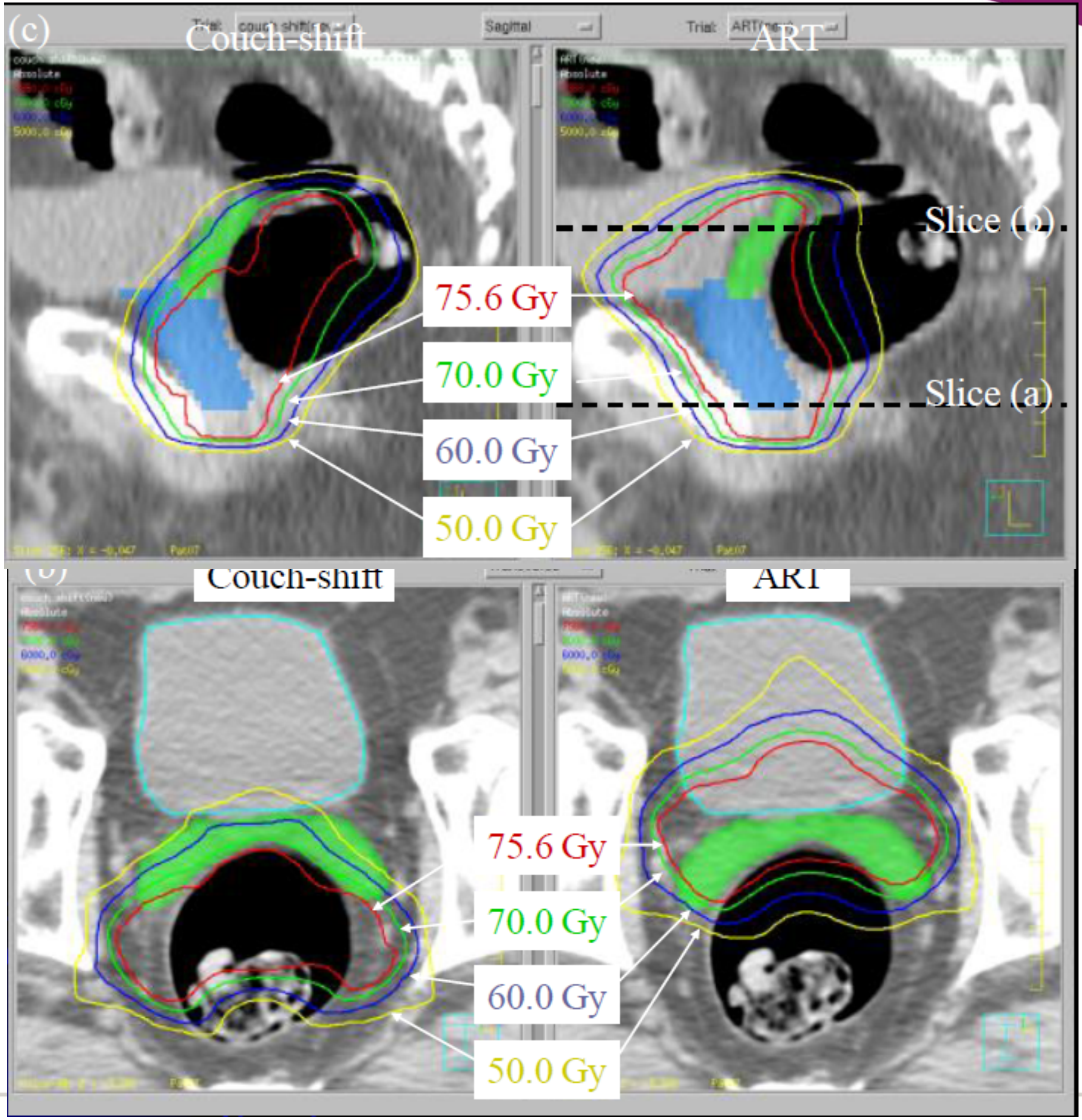
Same dose prescription

- Daily enema
- Dose distribution related to gas

<u>Third solution:</u>

IG-Adaptive IMRT

- Time consuming
- High workload



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Off-line adaptive RT and rectal distension (WBH)

N= 962

GTV=CTV (+/- 2cm SV)

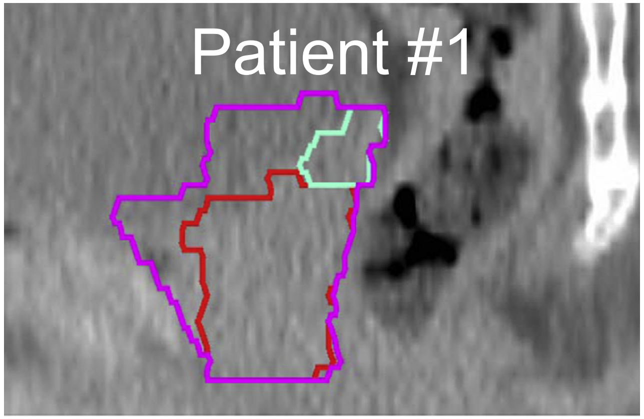
No diet modification, laxatives, or rectal enemas were used

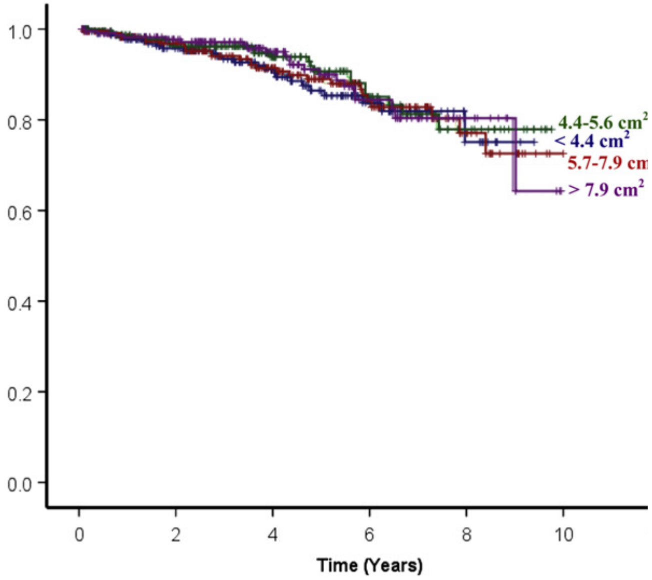
3DCRT plan for 9 fractions (PTV 1cm isotropic)

Prostate ITV based on planning CT + 4CBCT

Late G≥2 and G3 = 21% and 3%

No impact of RV on both late tox and BC





Park S. et al., IJROBP 2012

Intrafraction mvts

Intrafraction motion

Negligeable (Langen KM IJROBP 2001)

BUT...

1. Amplitude of motion increases with elapsed time
(Ghilezan M, IJROBP 2004)

How much time between daily image and treatment is acceptable?

2. Correlated with rectal filling

Diet advices and mild laxatives may help :
2-fold reduction of the SD for P motion
(Nijkamp J IJROBP 2008)

Smaller margin and intra-fraction mvts

Prostate tracking (Calypso)

31 pts (1045 séances)

Simulation of the prostate position at :

10'', 15'', 20'', 30'', 45'', 60'', 90'', 120'', 180'' et 240'' with respect to the reference P position.

PTV margin: Dose distribution and P position

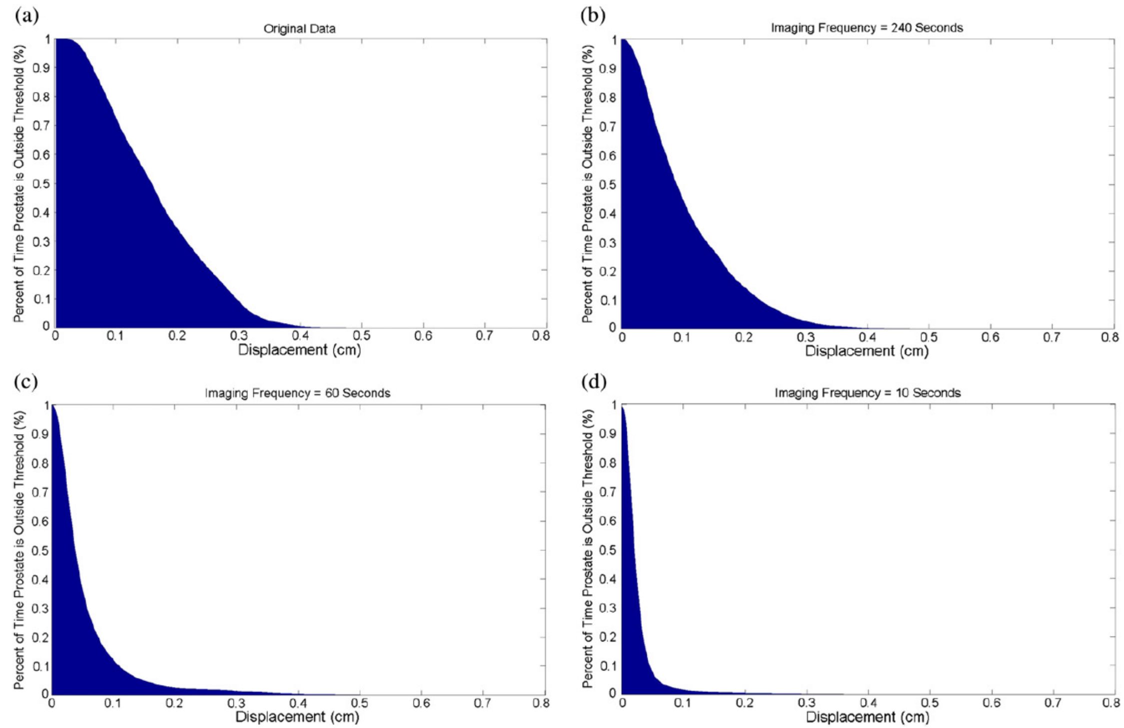


Fig. 2. Percentage of time (y axis) during the selected fraction the prostate spent displaced farther than a given distance (x axis) for no repositioning (a) and repositioning every 4 minutes (b), 1 minute (c), and 10 seconds (d).

Curtis W et al., IJROBP 2013

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Is there a better IGRT imaging protocol?

Is there a better IGRT protocol?

Feature	EPI	X-ray	kV CT	MV CT	US	MRI
No radiation exposure for image acquisition	---	-	---	---	+	+
Soft tissue imaging	-	-	++	+	+	+++
No need for implanted markers	-	-	+	+	+	+
Integrated and fast; suitable for daily use	+	+	+	+	+	+
No organ displacement due to image acquisition	+	+	+	+	-	+
Deals with intrafraction motion	-	+	-	-	-	++

Implanted gold markers

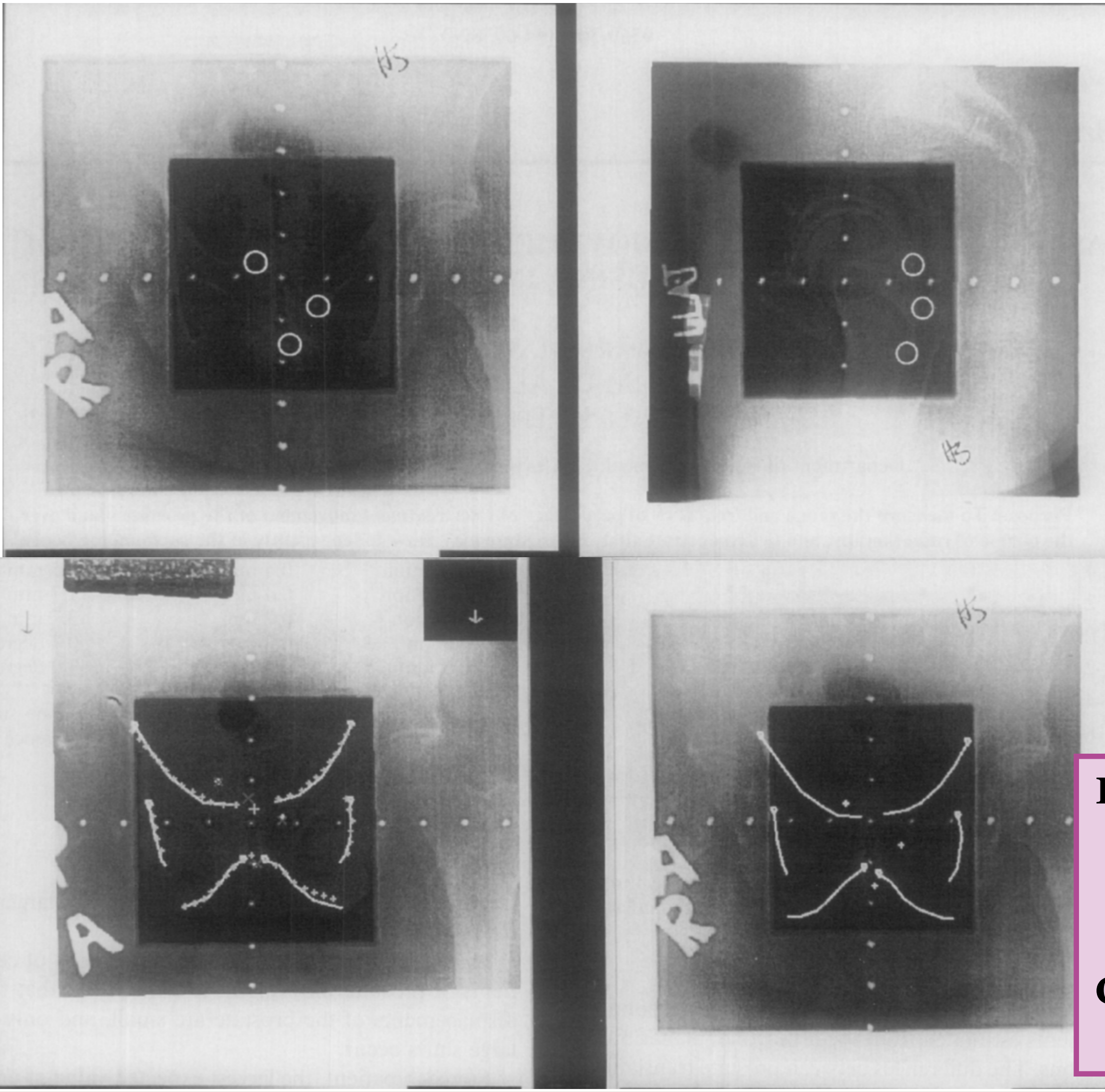

Table 1. Measured prostate motion

Component of motion	Uncertainty in measurement	Maximum expected motion ($p = 0.05$)
AP translation	0.4 mm	4.5 mm
LR translation	0.4 mm	1.7 mm
IS translation	0.2 mm	3.7 mm
AP rotation	0.2 degrees	0.7 degrees
LR rotation	0.7 degrees	3.2 degrees

Table 3. Margins needed for 95% geometric coverage of the prostate

Direction	Repositioning by bony anatomy	Repositioning by prostate markers
AP	6 mm	3 mm
LR	5 mm	3 mm
IS	4 mm	3 mm

Pros : accuracy, easier, low inter-observer variability, , RTT-friendly, Fully or semi- to fully automated, No contouring, Tracking with fluoroscopy

Cons : trauma, off-line, surrogacy for prostate position, pelvis?

Balter JM, IJROBP 1995

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CALCIFICATIONS ARE POTENTIAL SURROGATES FOR PROSTATE LOCALIZATION IN IMAGE-GUIDED RADIOTHERAPY

Grace G. Zeng, Ph.D.,* Tom S. McGowan, M.D.,*† Tessa M. Larsen, B.Sc.,* Lisa M. Bruce, B.Sc.,* Natasha K. Moran, B.Sc.,* Jonathan R. Tsao, M.D.,* and Miller S. MacPherson, Ph.D.*‡

*Carlo Fidani Peel Cancer Center, the Credit Valley Hospital, Mississauga, ON, Canada; †Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada; ‡Princess Margaret Hospital, University Health Network, Toronto, ON, Canada

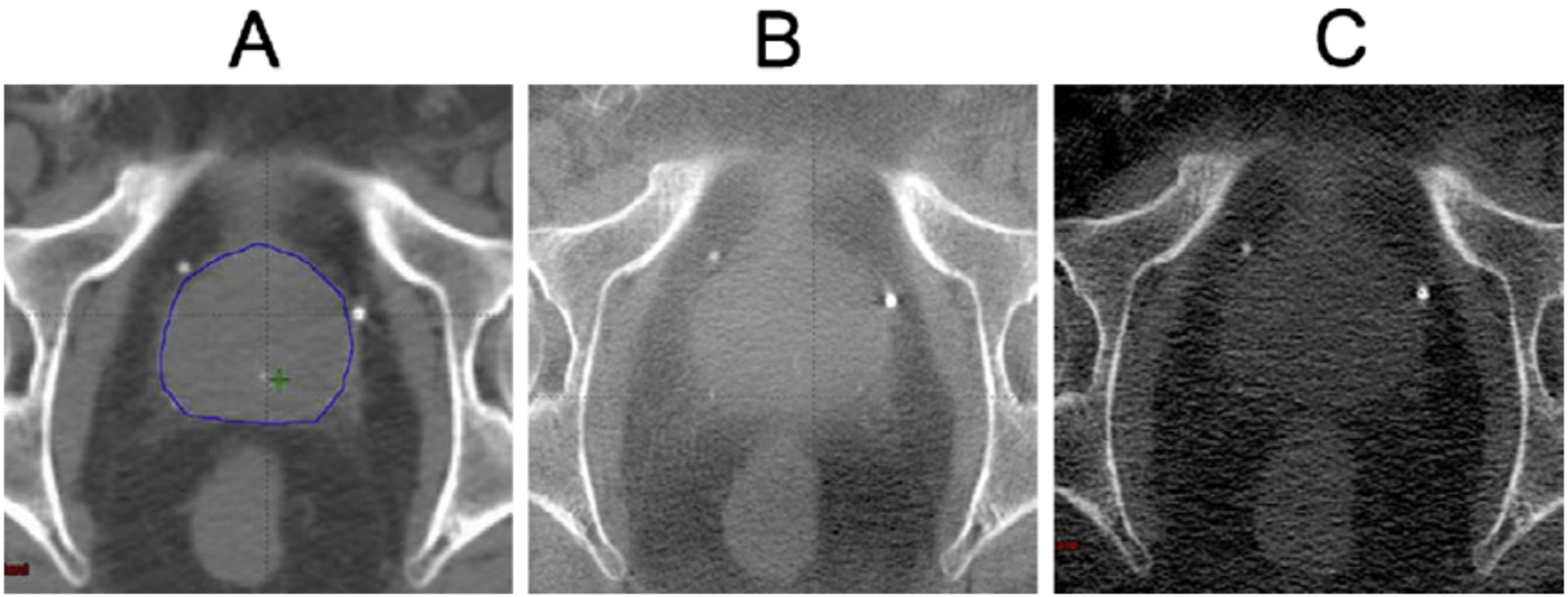
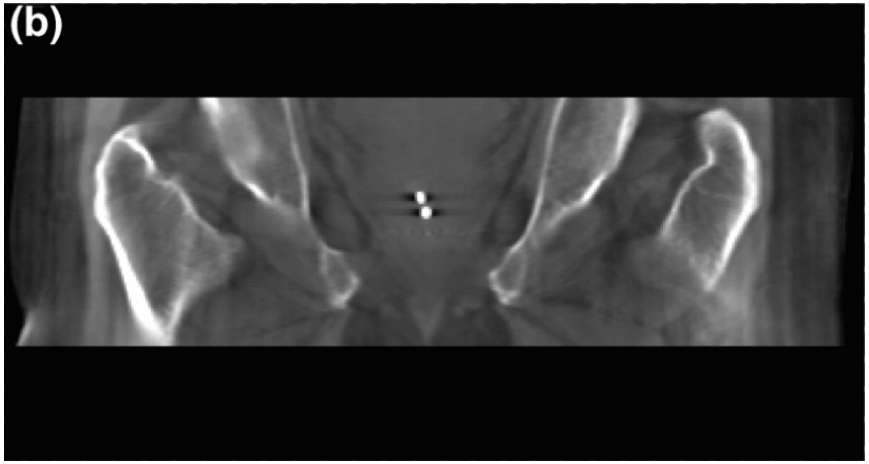


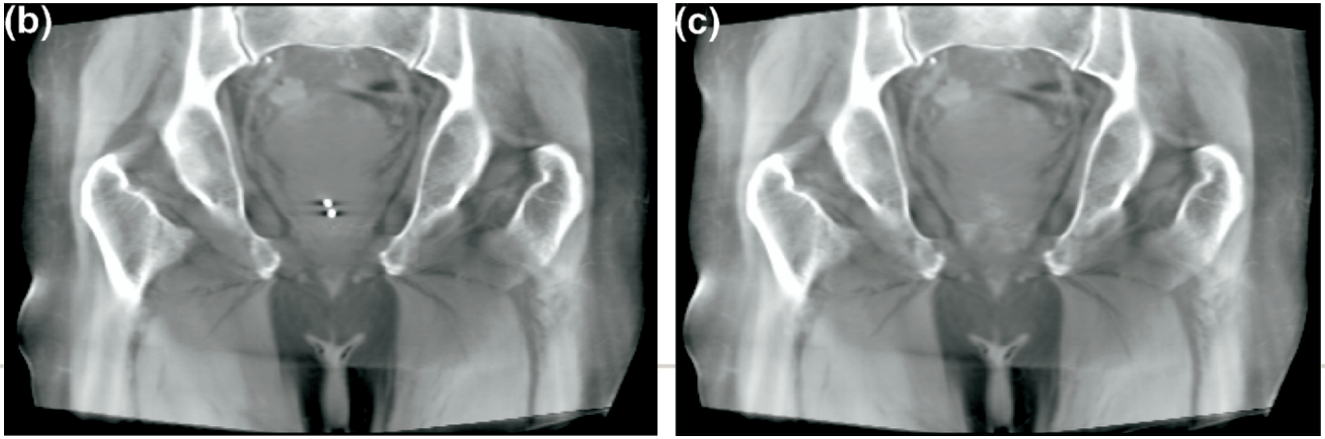
Fig. 2. Calcifications shown on (A) planning computed tomography (CT) scan, (B) cone-beam CT scan with standard dose, and (C) cone-beam CT scan with low dose. Blue line indicates prostate contour drawn on planning CT scan.

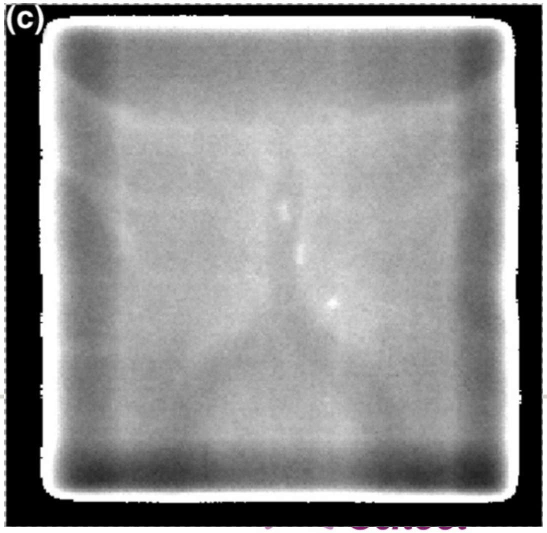
Cone beam kV CT :
FM vs soft tissues

N = 15 (256 CT)

PTV = 10 mm (7 mm en AR)







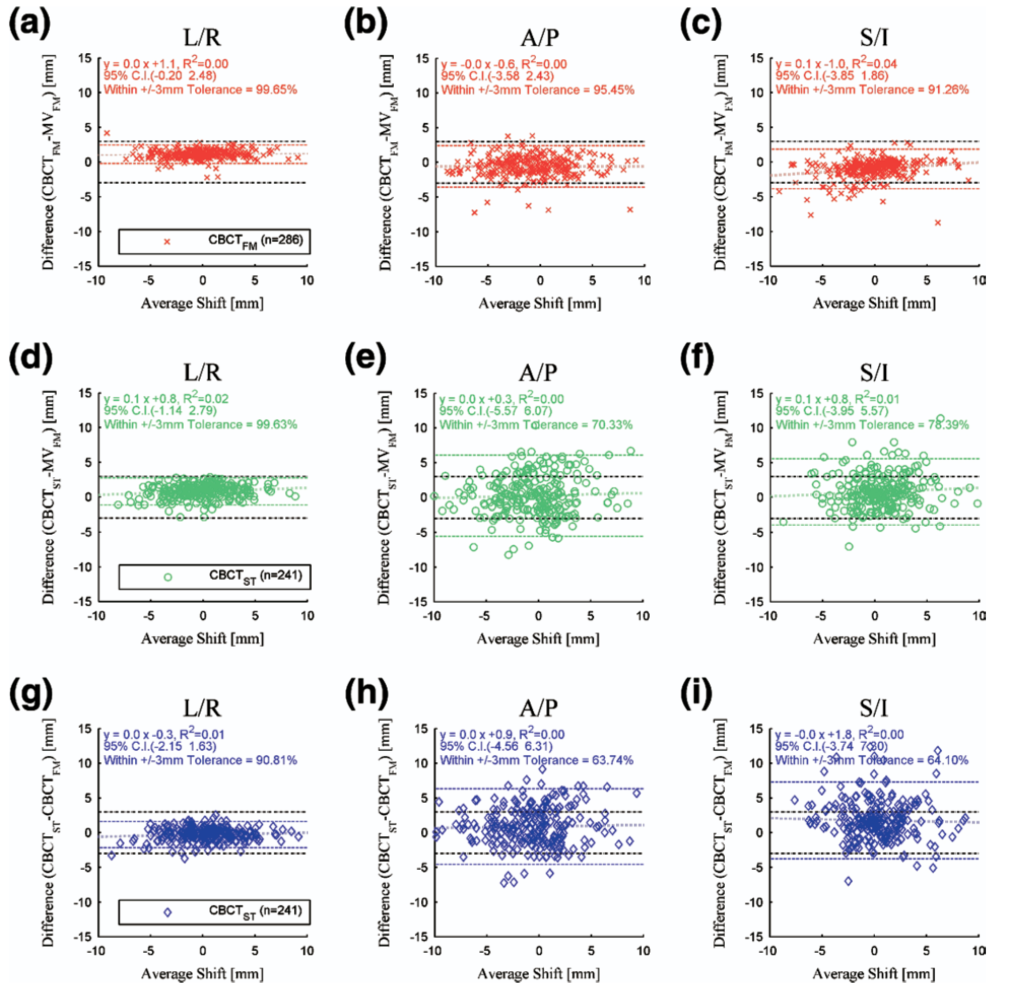
Moseley DJ, IJROBP 2007

Impact on repositioning

Differences $CBCT_{FM}$ - MV_{FM}

Differences $CBCT_{ST}$ - MV_{FM}

Differences $CBCT_{ST}$ - $CBCT_{FM}$



LR	91%	LR r^2 0.90
AP	64%	AP r^2 0.55
SI	64%	SI r^2 0.41

Moseley DJ, IJROBP 2007

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Radiation oncologist vs. RTT (w/ and w/o FM)?

MV CT : 3 patients (112 CTs)

Methods for aligning: FM, anatomy, contours

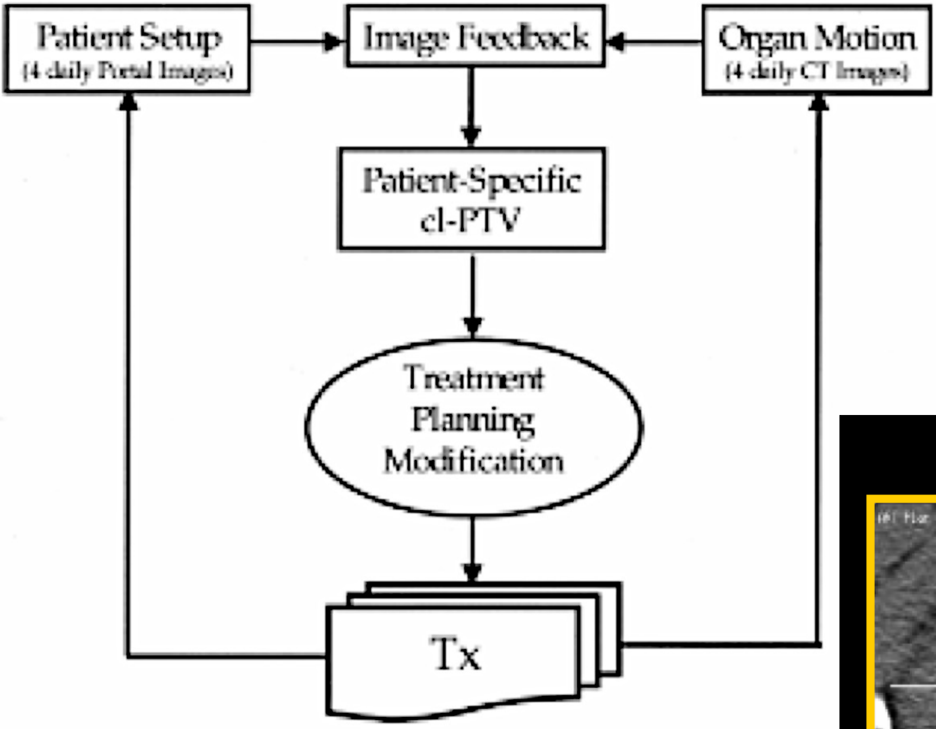
Radiation oncologist vs RTT

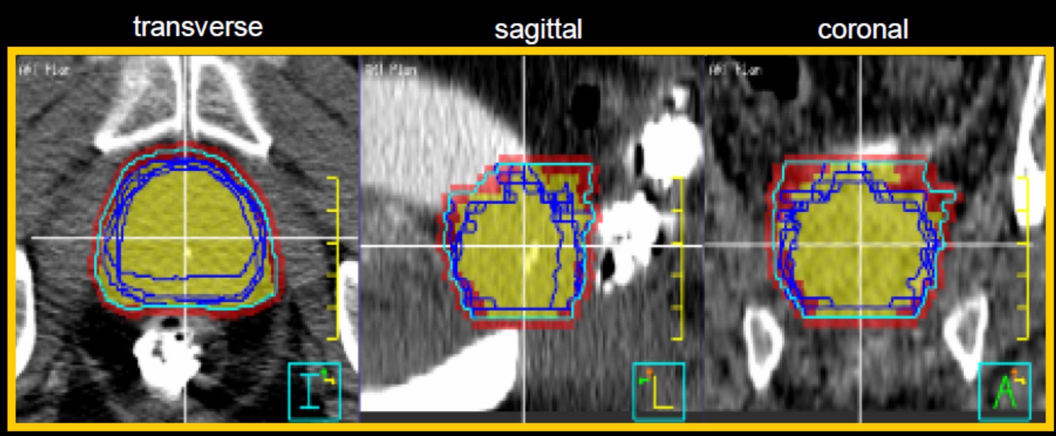
	Difference ≥ 5 mm		
	FM	Contours	Anatomy
A / P	1%	5%	17%
S / I	2%	10%	31%
Lat	1%	0%	3%

Langen et al., IJROBP 2005

Room for IG Adaptive RT (IGART)?

Off-line Adaptive RT (ART)

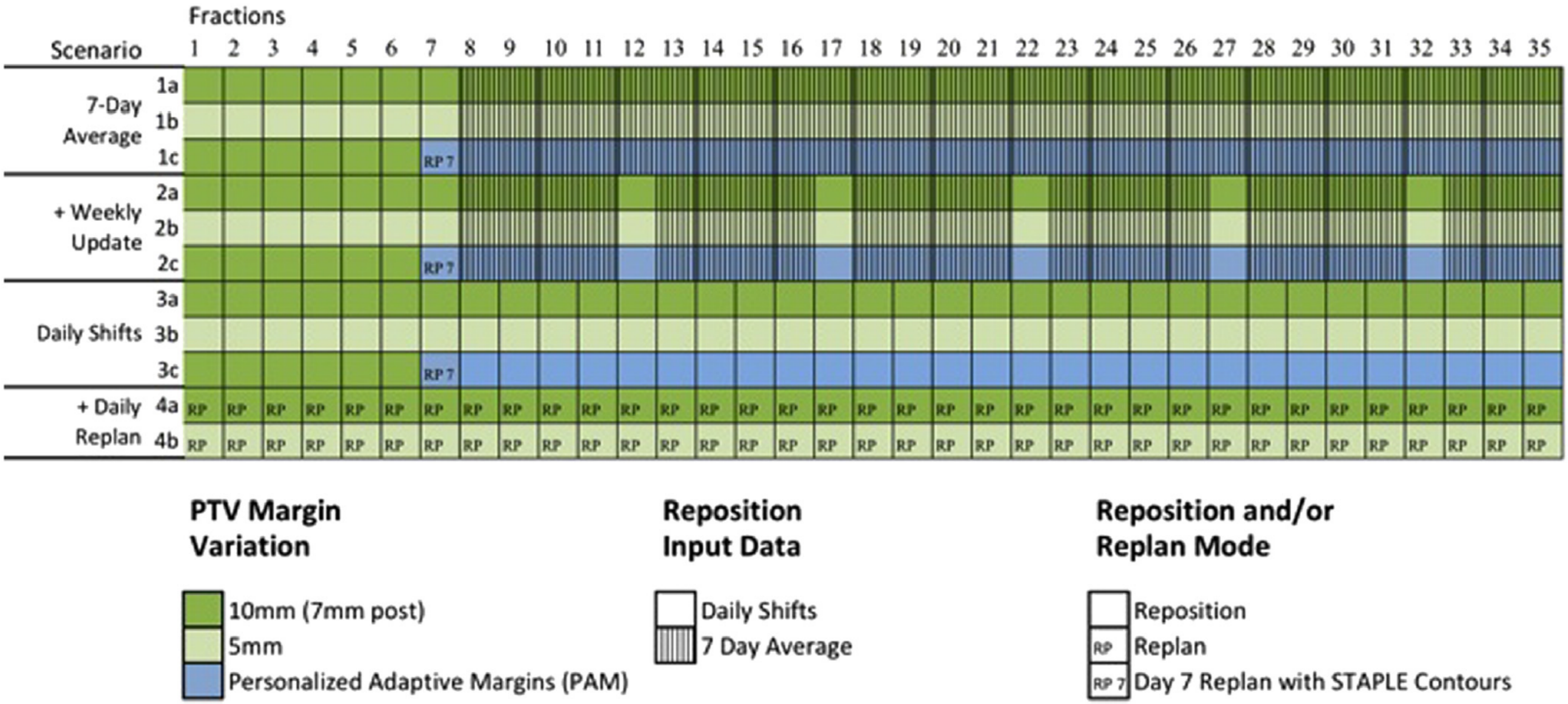




Initial CTV + 4 CTVs = ITV

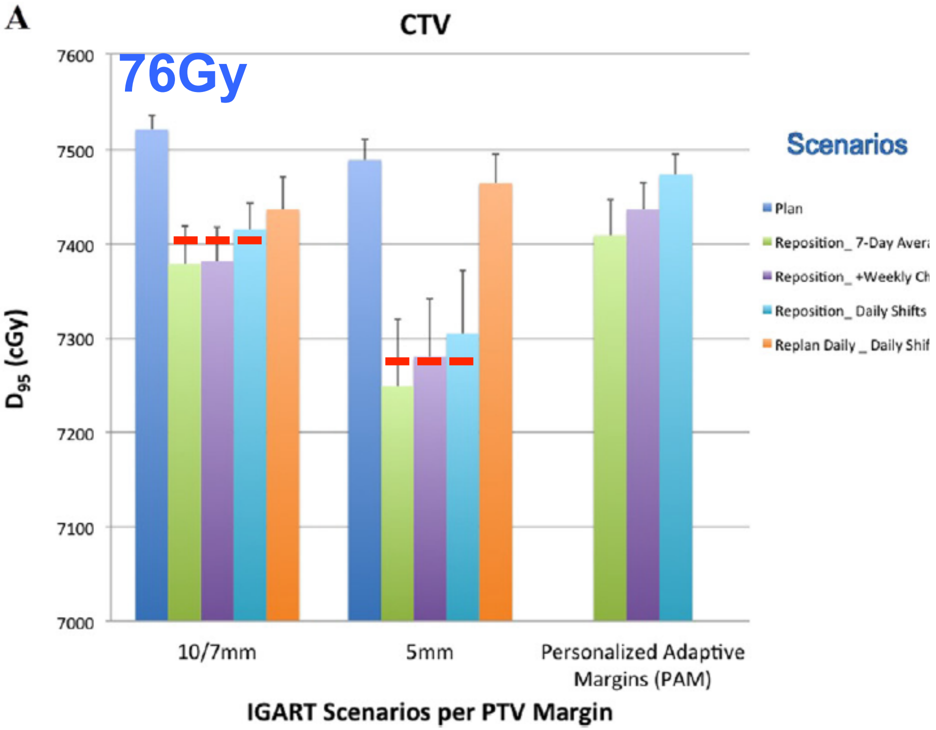
ITV + Random Setup Error of Bones = cl-PTV

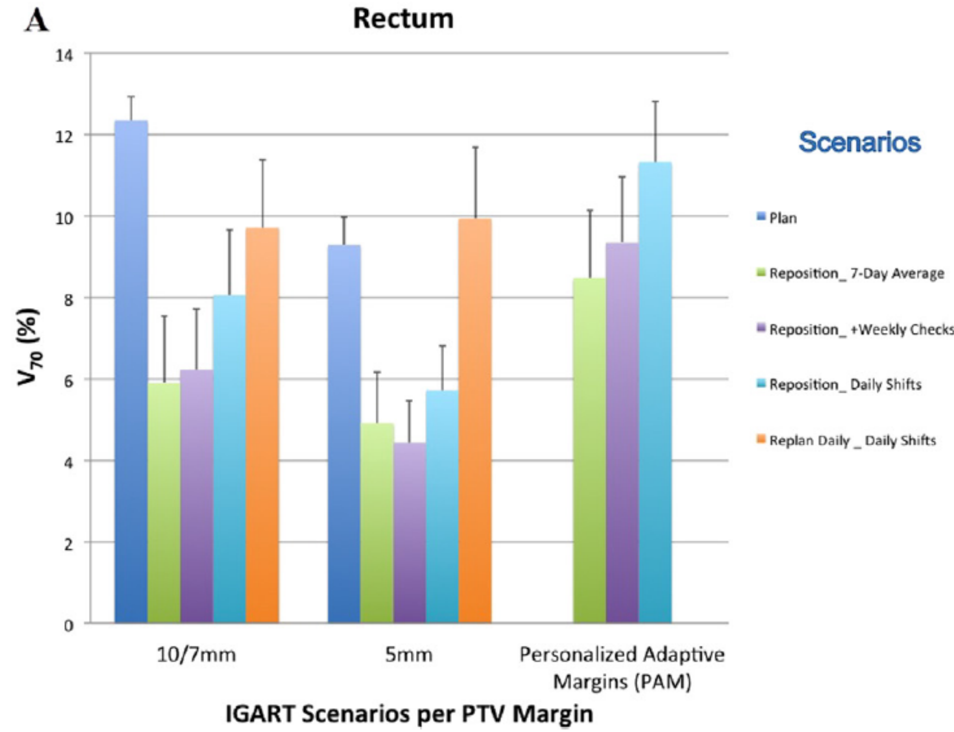
Daily IGRT vs Off-line IGART vs On-line IGART



Battista JJ, IJROBP 2014

Daily IGRT vs Off-line IGART vs On-line IGART





With smaller PTV margin, D95 to CTV drops to 73Gy (without daily on-line replan)

Battista JJ, IJROBP 2014

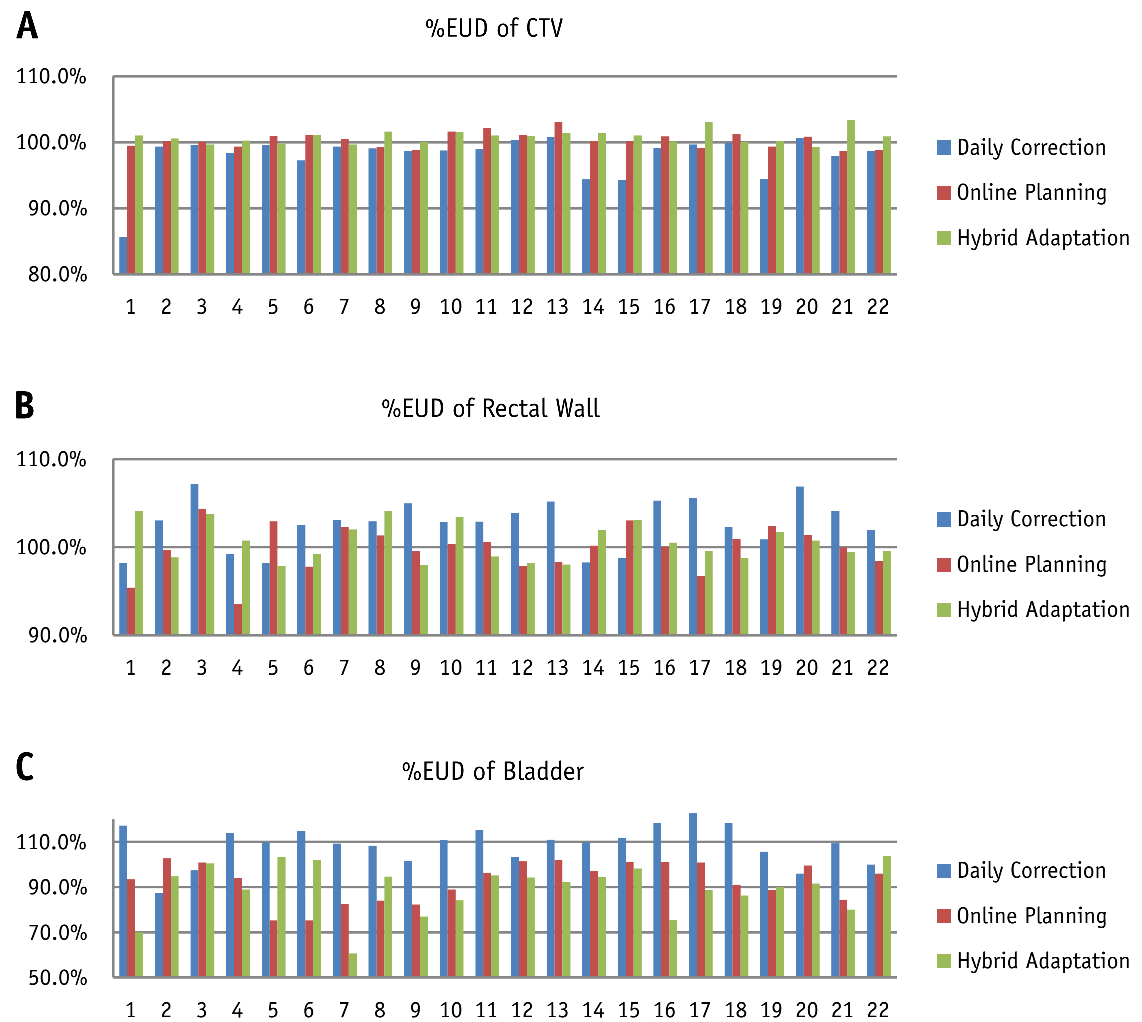
Online/Offline adaptation

3 strategies:

1. Daily online repositioning

2. Daily online replaning

3. Hybrid adaptation : Cumulative dose distribution on 5 post CBCT



Qin A, Yan D IJROBP 2015

Concomitant nodal radiotherapy

Whole Pelvic nodal RT and prostate IGRT : unsolvable?

Which target for repositioning? (independent motion) ↳ TRADE-OFF

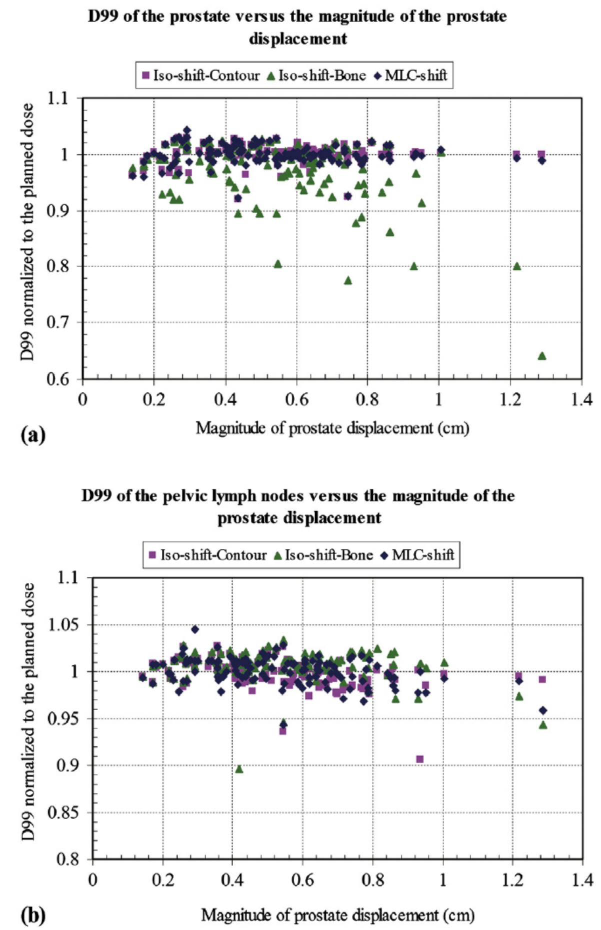
<u>If you want to spare more bowels from a large volume?</u>
A wider margin around the prostate and a smaller margin around the nodes are required

<u>If you want to spare more rectum from a high dose?</u>
A smaller margin around the prostate and a wider margin around the nodes are required

If the target is : Prostate (Mobile)
☞0 cm prostate shift resulted in an underdosage of pelvic nodes by **14%**±6%

If the target is : Pelvis (Less mobile)
☞1 cm prostate shift resulted in an average decrease of **14%** in D95%

☞ Isoshift bone = 30% prostate missed!



Hwang AB, Med Phys 2012
Ferjani S, IJROBP 2014

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WPRT and MAP-IGRT vs. MLC tracking

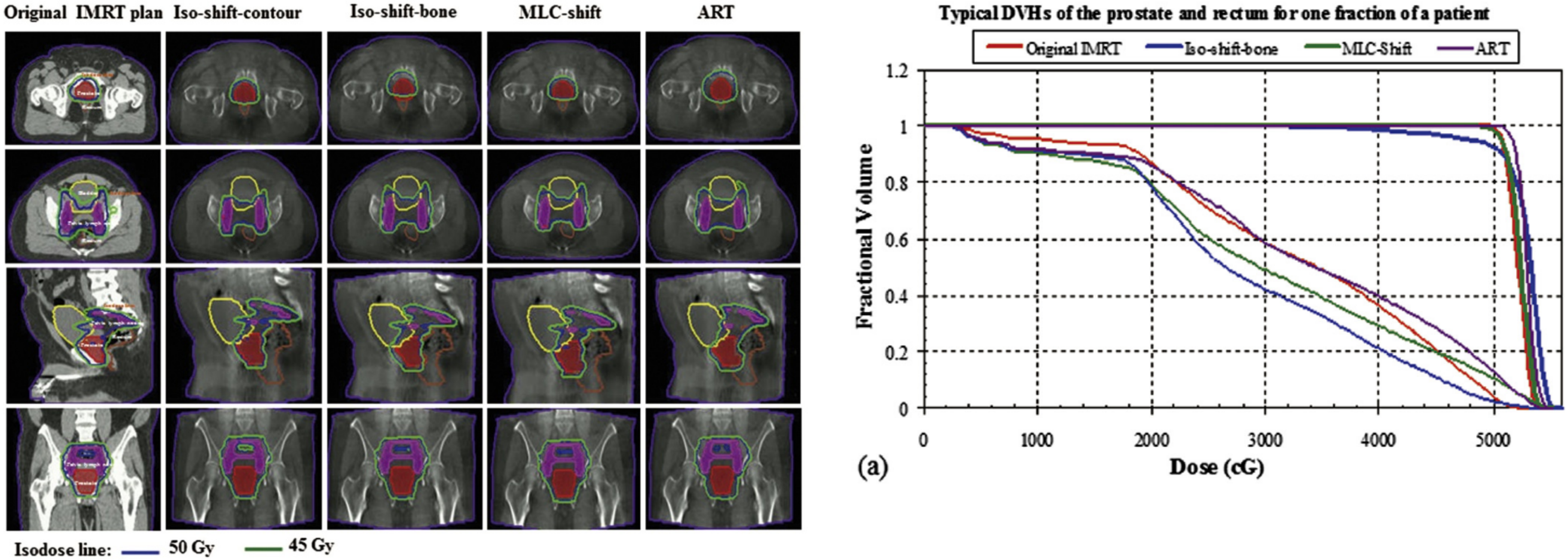

Table 1 Percentage of 124 fractions having D99 of the prostate and PLN greater than 97% of the prescription dose, 97% of the original planned D99, or 97% of ART planned D99 in isoshift (contour and pelvic bones), MLC shift, and ART plans

	Isoshift contour method (%)		Isoshift bone method (%)		MLC shift method (%)		Adaptive planning method (%)	
	Prostate	PLN	Prostate	PLN	Prostate	PLN	Prostate	PLN
D99 > 97% of prescription dose	97.6	98.4	73.4	98.4	98.8	98.4	98.6	100
D99 >97% of original IMRT D99	94.4	98.4	70.2	97.6	96.8	98.4	98.6	99.2
D99 >97% of adaptive method	93.6	96.8	67.7	95.2	93.51	94.4		

Ferjani S, IJROBP 2014

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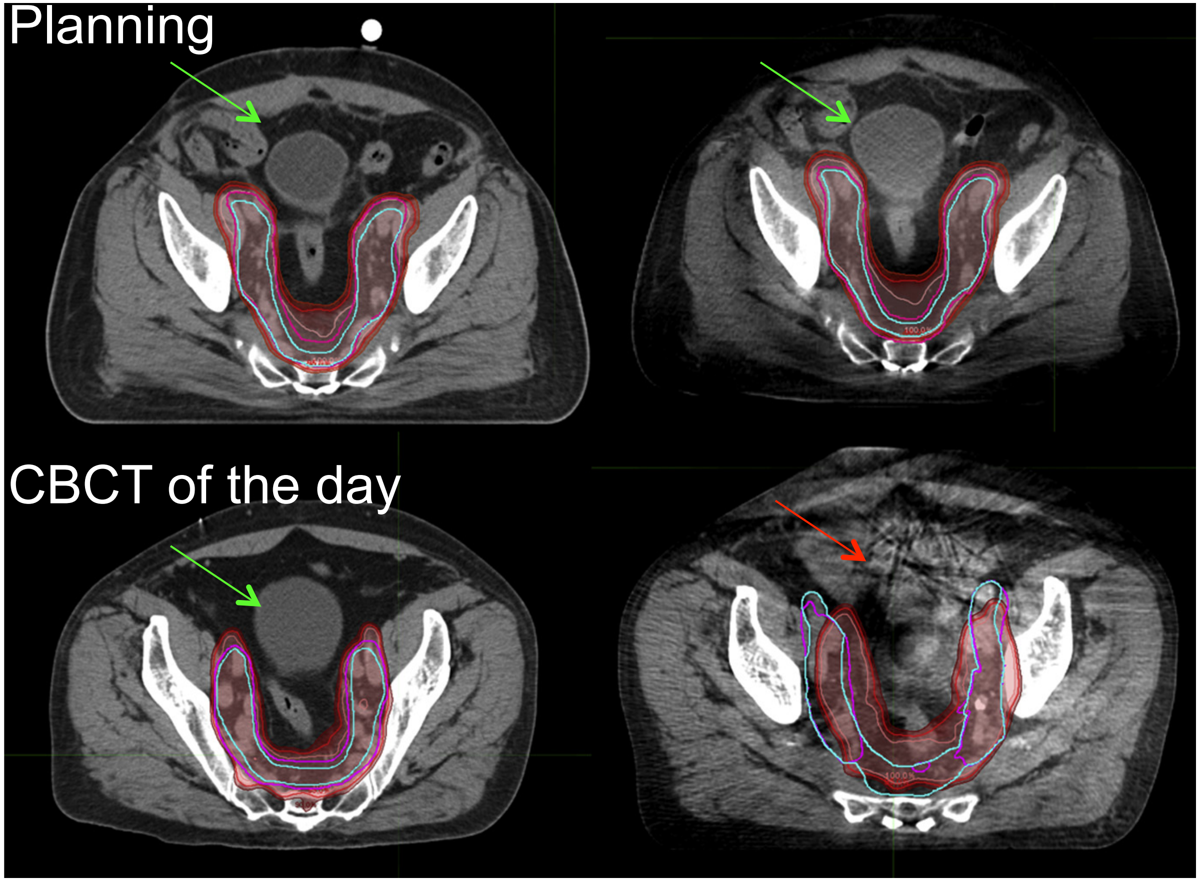
Pelvic nodal dosing and bladder filling?



Patient 1 **Patient 2**

Inadequate nodal coverage if :

☞SI shift on the prostate >5mm
☞Or variation of bladder height >18%

3 SOLUTIONS:

1. Enforcing strict bladder filling

2. Larger nodal PTV margins

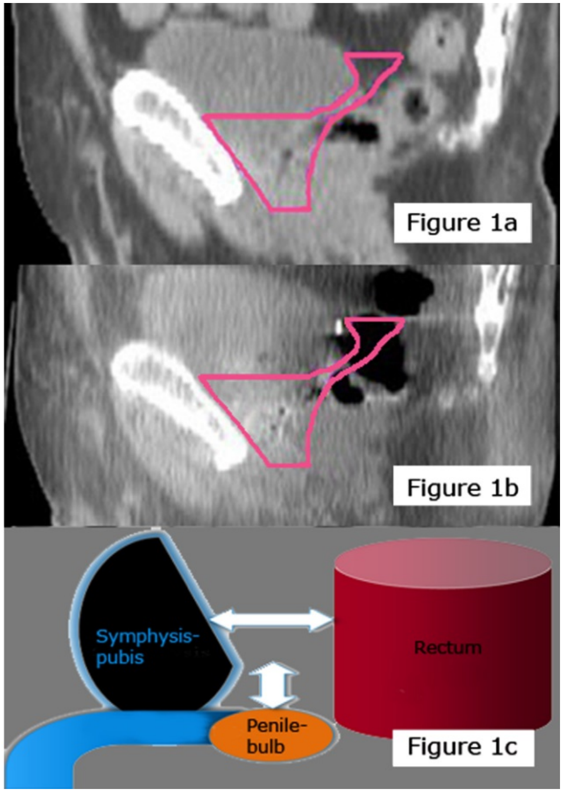
3. Daily online replan or library of plans

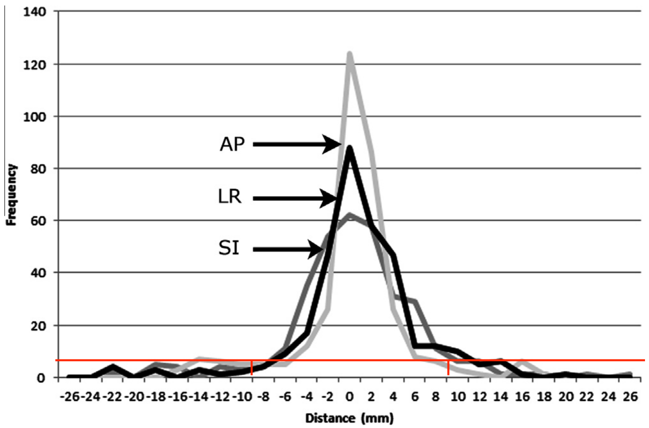
Kishan A, IJROBP 2015

Postoperative IGRT

Post operative margins

- 547 daily CBCT from 15 pts





Variable	M (mm)	Σ (mm)	σ (mm)	PTV margin (mm)
Total error (Ti)				
Anteroposterior	1.74	2.65	2.25	8.19
Left–right	1.45	2.69	1.99	8.12
Superoinferior	−0.51	2.00	1.49	6.04
Bony misalignment (Bi)				
Anteroposterior	−0.45	2.60	1.77	7.74
Left–right	1.46	2.66	1.88	7.96
Superoinferior	−1.09	1.83	1.24	5.43
Prostate bed motion (Pi)				
Anteroposterior	2.19	2.50	2.32	7.88
Left–right	0.01	0.44	0.99	1.78
Superoinferior	0.58	0.92	1.38	3.27

Ost P, IJROBP 2011
Gill S, Radiother Oncol 2013

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

Special commentary

From IM … and?

[a]Department of Medical Physics, ar … Center, New York, NY, USA

For simplicity, an ideal IGRT system should have three essential elements: (1) 3D volumetrics of soft tissues including tumors, (2) efficient acquisition and comparison of the 3D volumetrics, and (3) an efficacious process for clinically meaningful intervention. Clearly, 'clinically meaningful intervention' is the most important goal, the raison d'être of IGRT. In contrast to this simple definition and well-defined goal, many other aspects of IGRT are anything but simple or clear, and there is much uncertainty and debate regarding many topics, e.g. 2D vs 3D, kilovoltage vs megavoltage, the use of markers, and how to minimize the effect of respiration on treatment uncertainties. So, amidst the frenzied activities in the commercial exhibit halls of ESTRO and ASTRO, it is prudent to take stock of the clinical issues, and then match the technology to them.

Proponents of IGRT generally adopt the axiomatic, apple-pie and motherhood argument that IGRT can reduce set-up error and account for organ motion, and therefore will improve treatment outcome. Axiom aside, the question is what will be the real benefit, balanced against cost. Of the two, cost is the easier one to calculate. Quantification of benefit will be much more difficult, but certainly essential both for evidence-based medicine, and in terms of medico-economics, may be needed in some countries for reimbursement. Unfortunately the latter issue, in addition to perception and competition for patients, may dictate how quickly IGRT becomes popular, appropriately or inappropriately.

Leaving the issue of strict economics aside, the more relevant question for this discussion is the quantification of benefit. The most pertinent metric is treatment outcome,

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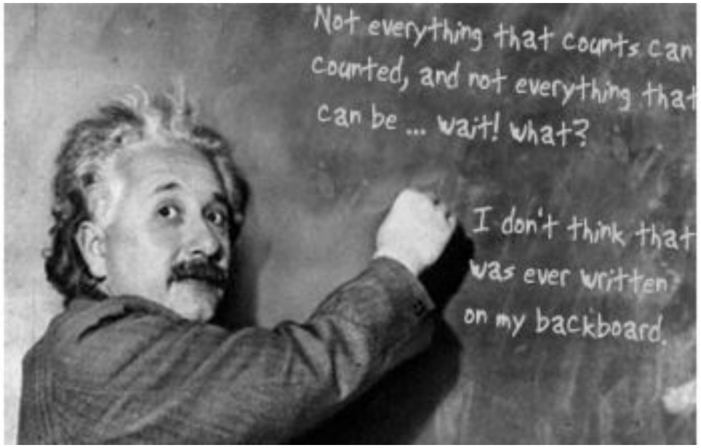
CONCLUSION : Where do we stand?

Attributes	Outcomes	Results
Technical performance	Set-up error	Can be quantified and minimized
	Intra-fraction organ motion	Can be quantified. Correction is investigational
	Inter-fraction organ motion	Can be quantified and corrected
Feasibility	Patient compliance	Fair
	Learning curve	Steep
	Cost	Expensive
Safety	Acute AE/Toxicity	**Significant reduction**
	Late AE/Toxicity	Data not mature
Clinical efficacy	Surrogate outcomes -Biochemical control	No robust data yet **Adaptive> daily IGRT???**
	Secondary outcomes -DFS -QOL	**Significant positive impact on QOL**
	Primary outcomes -DSS -OS	No robust data yet

«…Not everything that can be counted counts.
Not everything that counts can be counted…»

(A.Einstein, 1879-1955)



Uncertainties and margins in image guided radiotherapy

Marcel van Herk

On behalf of the image guidance groups

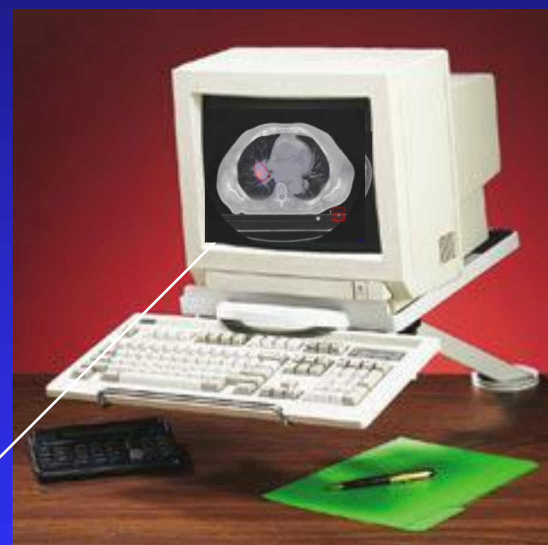
University of Manchester,
Christie NHS trust, Manchester UK

(prior at the Netherlands Cancer Institute, Amsterdam)

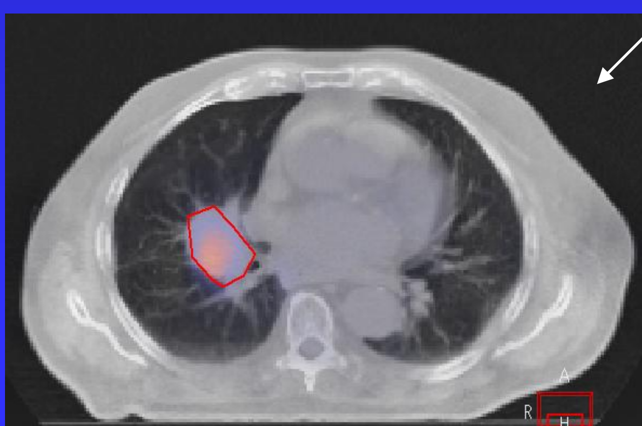
Classic radiotherapy procedure

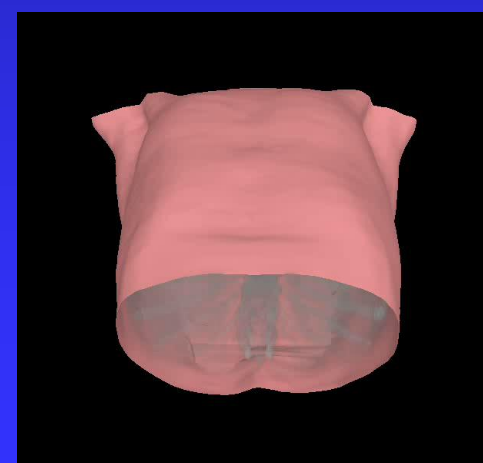
Tattoo, align and scan patient

Align patient on machine on tattoos and treat (many days)



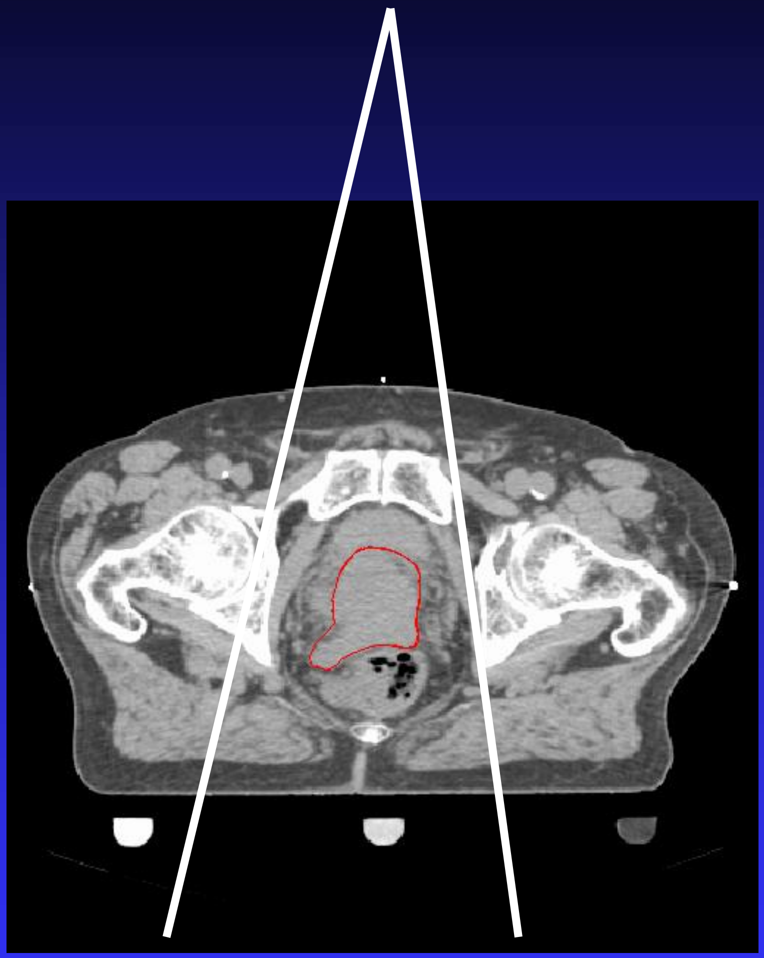
Draw target and plan treatment on RTP



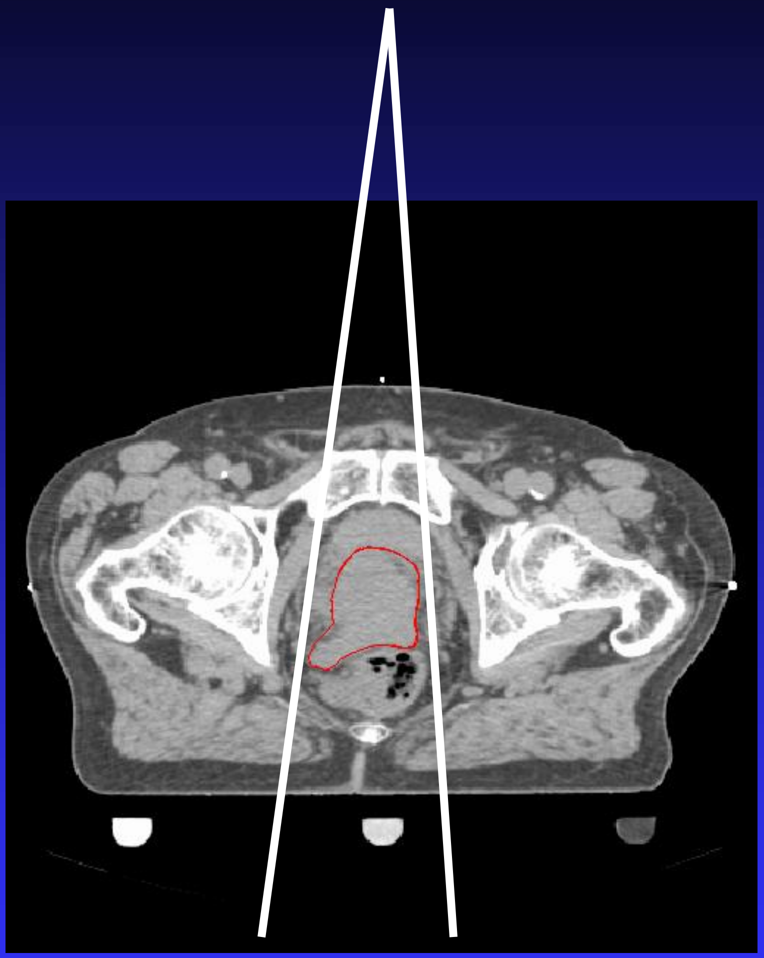


In principle this procedure should be accurate but …

Patients move !



1. Use large margins, irradiating too much healthy tissues



2. Use small margins, and risk missing the target

3. Or: use image guided radiotherapy

Nomenclature

- Gross error: mistakes, transcription errors, software faults:
  - must be caught by QA, not in this lecture

- Error: difference between planned measurand and its true value during treatment, however small

  - Uncertainty: unpredictable errors– quantified by standard deviations

  - Variation: predictable or periodic errors– quantified by amplitude or standard deviations

EPID dosimetry QA to catch gross errors: used for almost all patients at NKI

EPID movie

Reconstructed EPID dose (VMAT case)

per frame

cumulative

-140° 140°

Precision: within few %, enough to catch gross errors

Mans et al, 2010

Gross errors detected in NKI

TABLE I. Errors detected by means of EPID dosimetry from the clinical introduction to July 2009, grouped by (a) treatment site and (b) error type.

(a) Site	Clinical introduction	No. of patients	No. of errors
Prostate	02–2005	1018	2
Rectum	07–2006	602	4
Head-and-neck	06–2007	543	4
Breast	01–2008	1319	2
Lung	01–2008	454	2
Others	01–2008	401	3
	Total	**4337**	**17**

(b) Error type	No. of errors
Patient anatomy	7
Plan transfer	4
Suboptimally tuned TPS parameter	2
Accidental plan modification	2
Failed delivery	1
Dosimetrically undeliverable plan	1
Total	**17**

0.4% of treatments show a gross error (>10% dose)

9 out of 17 errors would not have been detected pre-treatment !!

Mans et al, 2010

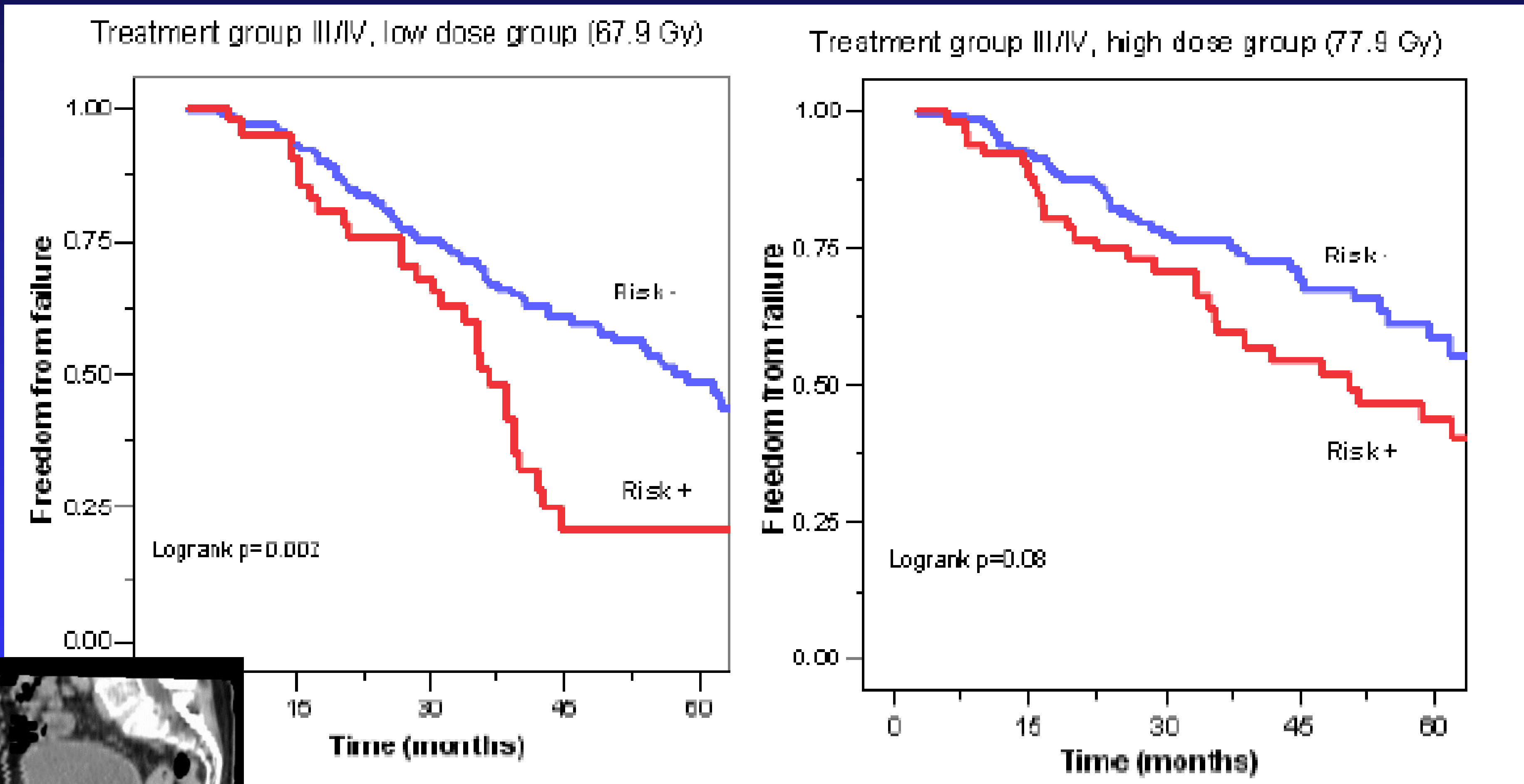
What happens in the other 99.6% ?

- There are many small unavoidable errors (mm size) in all steps of radiotherapy
  - In some cases many of these small errors point in the same direction
  - I.e., in some patients large (cm) errors occur(ed)
- This is not a fault, this is purely statistics
- What effect does this have on treatment?
  - We do not really know!

Motion counts? Prostate trial data (1996)

N=185 (42 risk+)

N=168 (52 risk+)



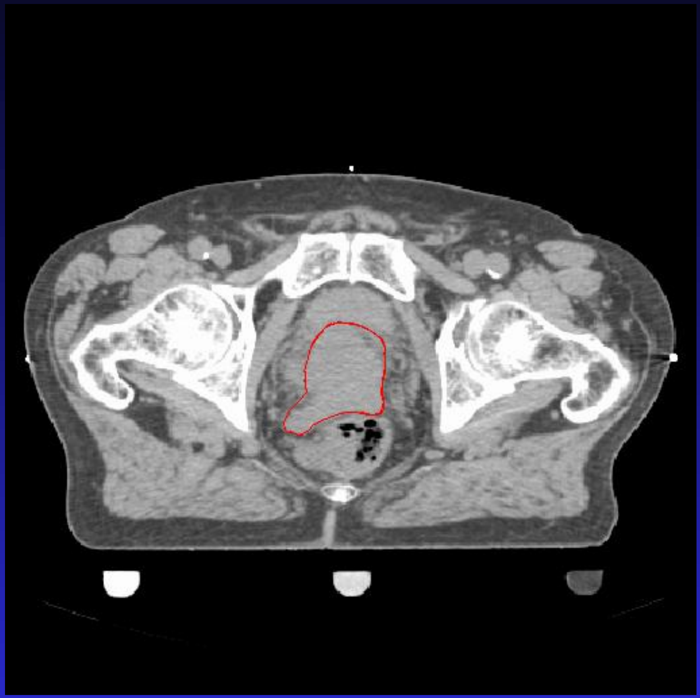
Risk+: initial full rectum, later diarrhea

Heemsbergen et al, IJROBP 2007

Did you do a good job planning the treatment?

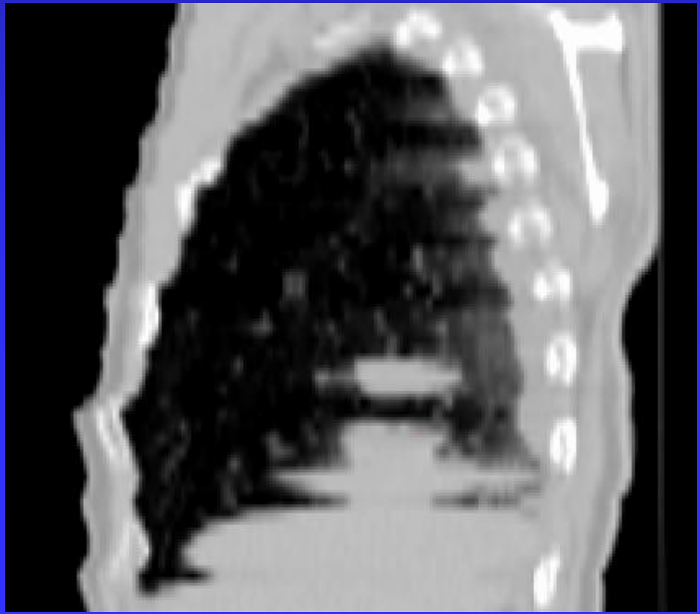
Imaging errors

- CT scan is just a random snapshot of a changing patient
  - Organ motion and setup error are frozen in arbitrary position

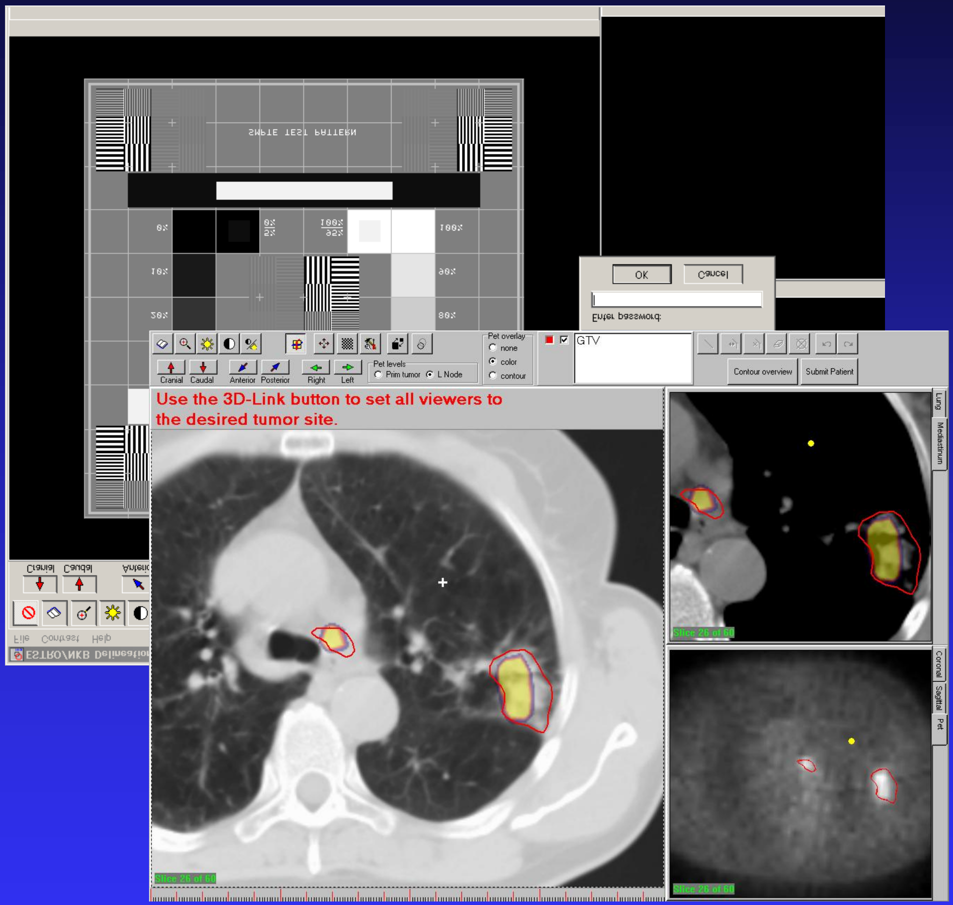


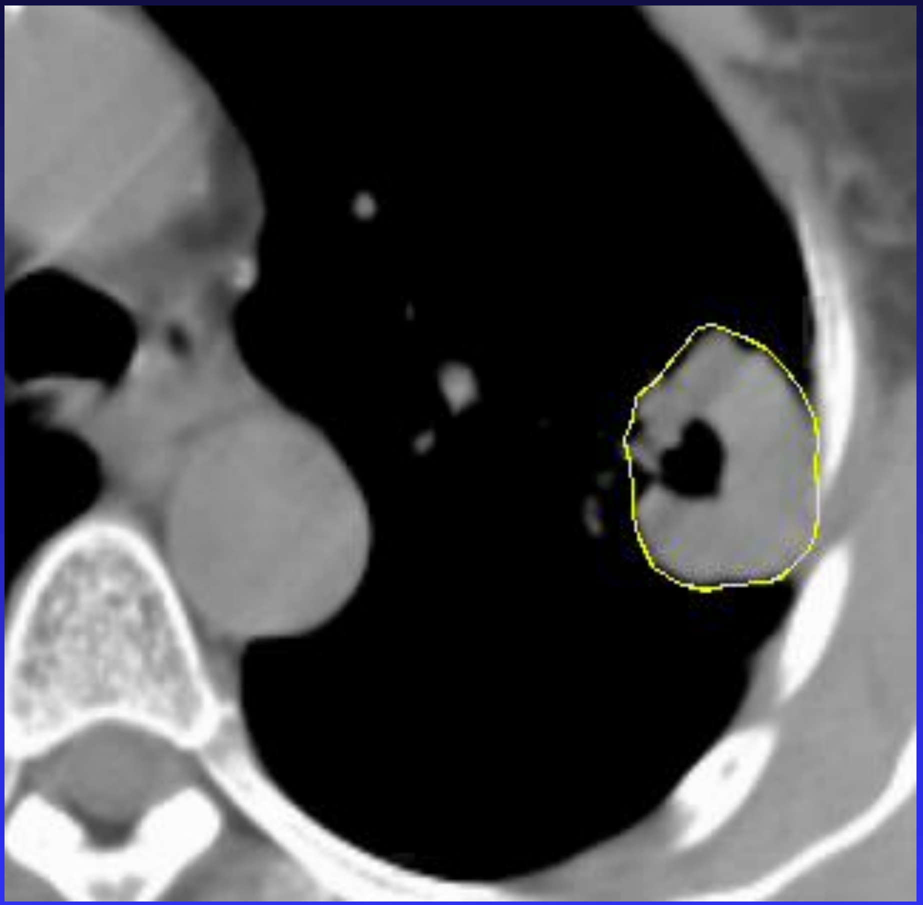
- Interference between motion and imaging distorts image contents

- The beams will be pointed to the target in this image → systematic error !



Main planning error: GTV/CTV delineation

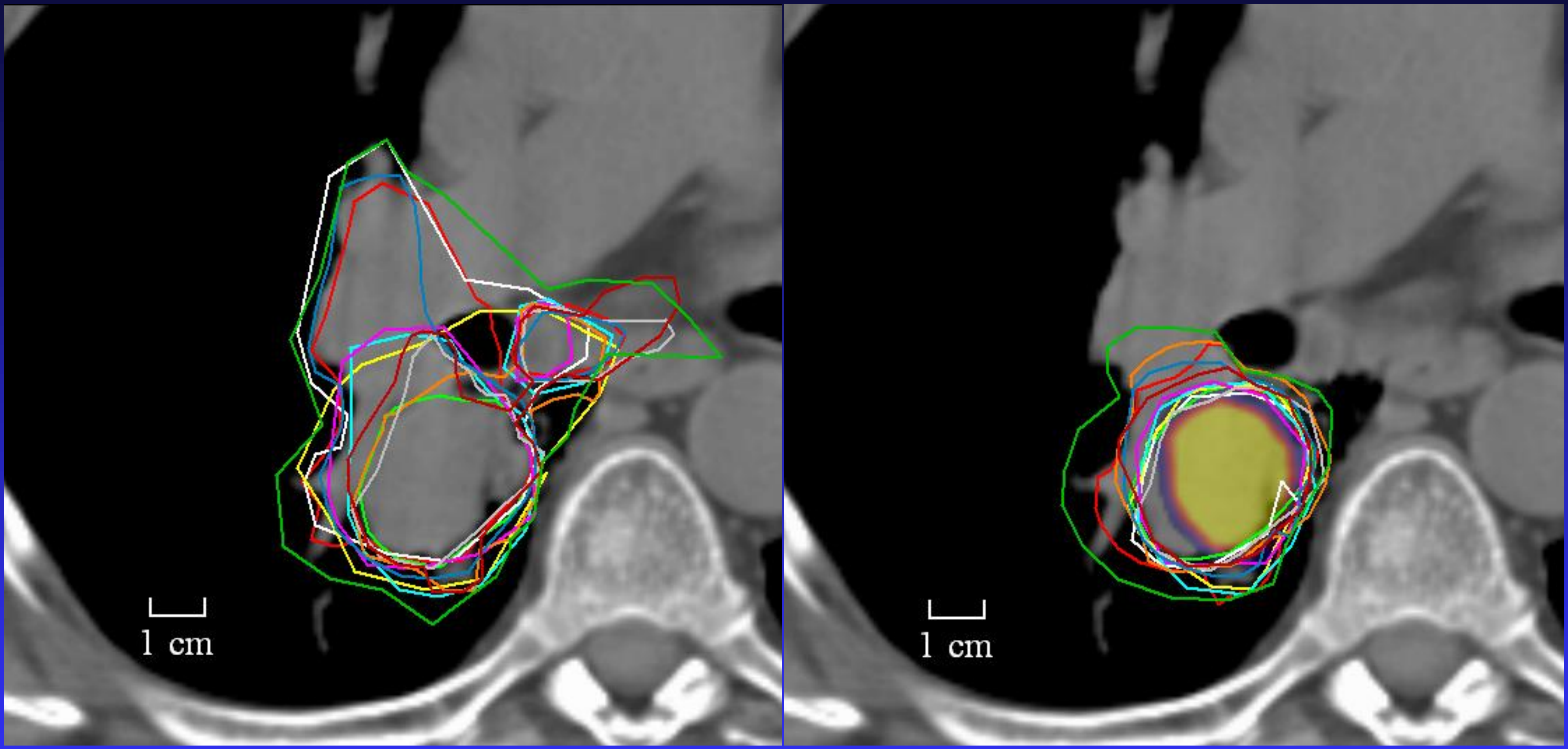




- 11 observers from 5 institutions, 22 patients
- newly developed delineation software (runs from CD)
- delineation on CT + (one year later) CT+PET

Steenbakkers et al, IJROBP 2005

Delineation variation: CT versus CT + PET



CT (T_2N_2)

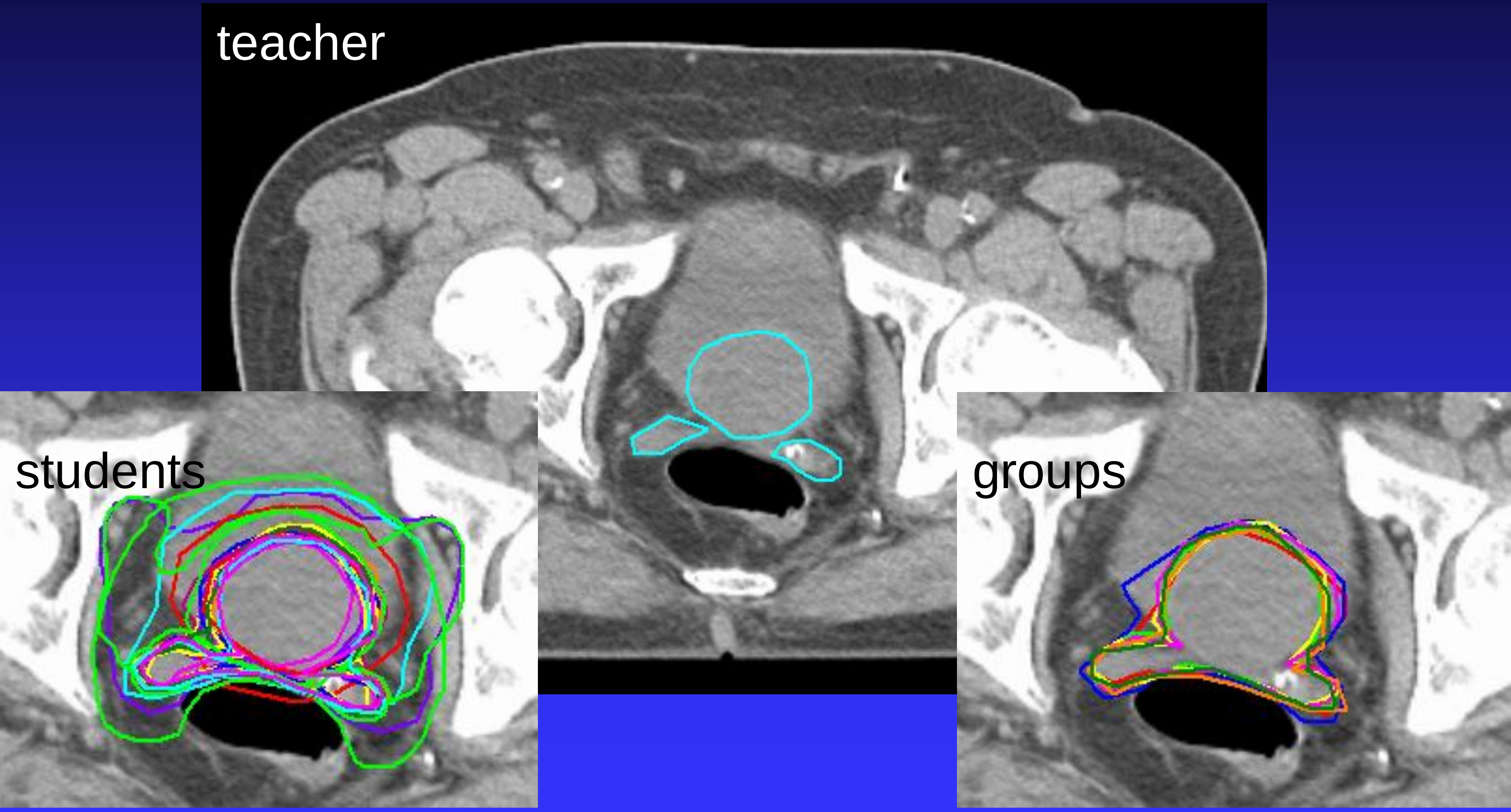
SD 7.5 mm

CT + PET (T_2N_1)

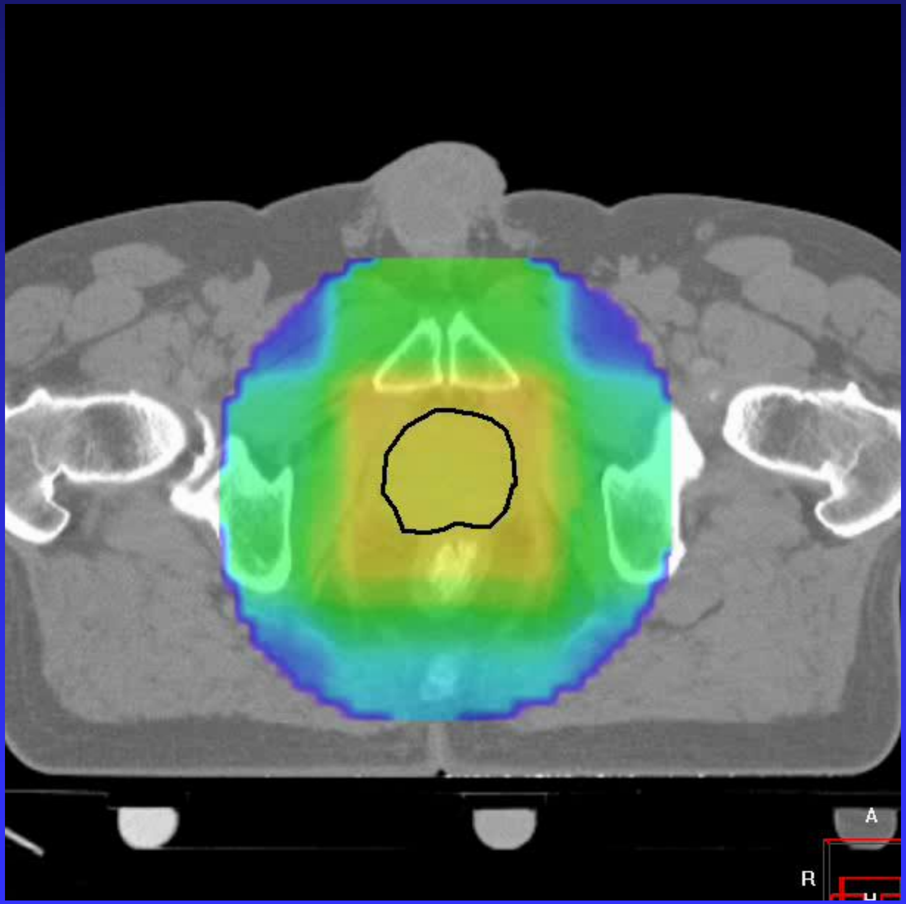
SD 3.5 mm

The beams will be pointed to the target the physician draws !

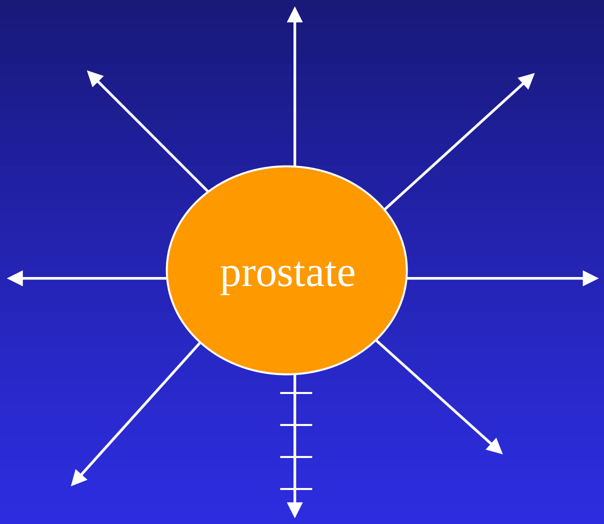
Effect of training



CTV: is dose <u>outside</u> the prostate related with outcome?
→ detect disease spread in historical data of high risk prostate cancer patients



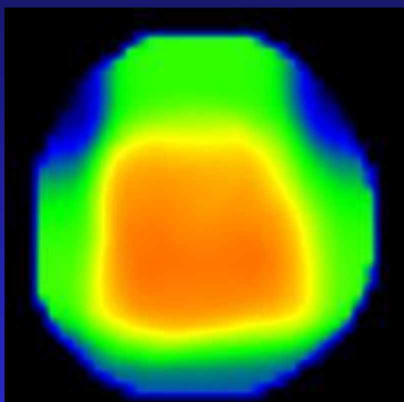
Mapping of planned dose cubes
to standard patient



Dose differences due to:

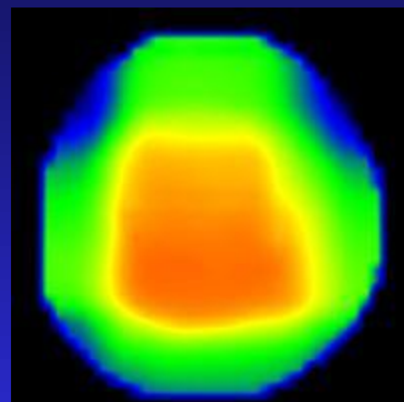
- randomization
- anatomy
- technique

Estimate pattern of spread from response to incidental dose in clinical trial data (high risk prostate patients)



PSA controls

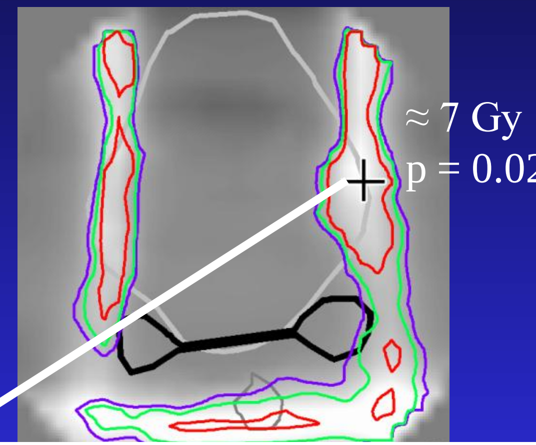
\-

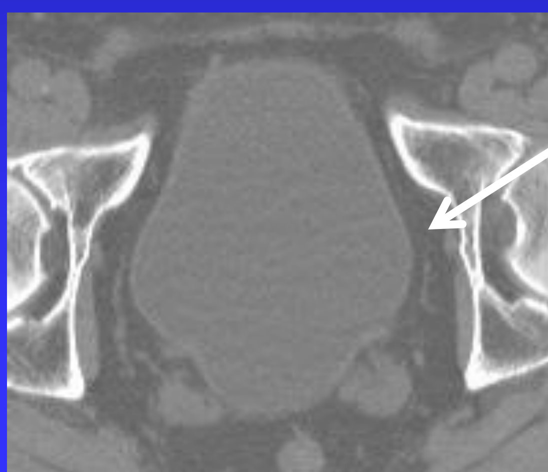


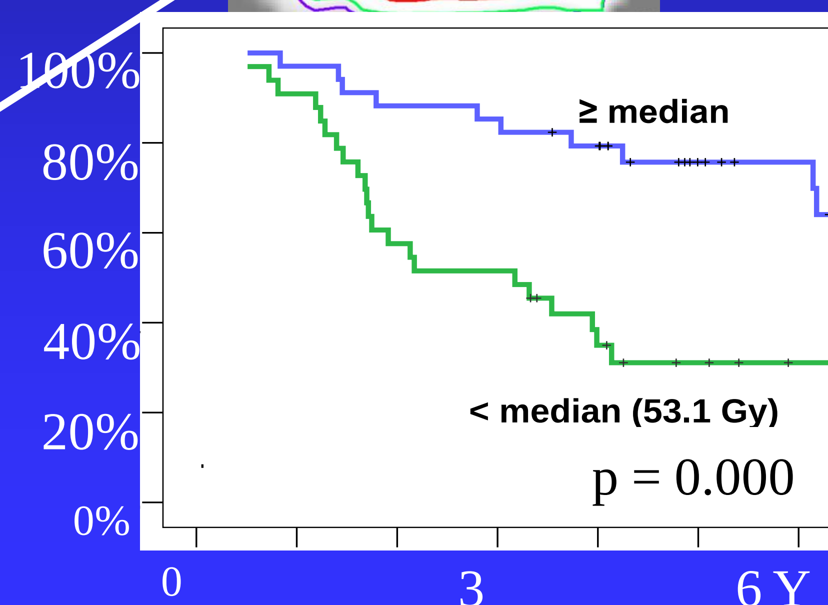
PSA failures

=

Average dose no failures – average dose failures







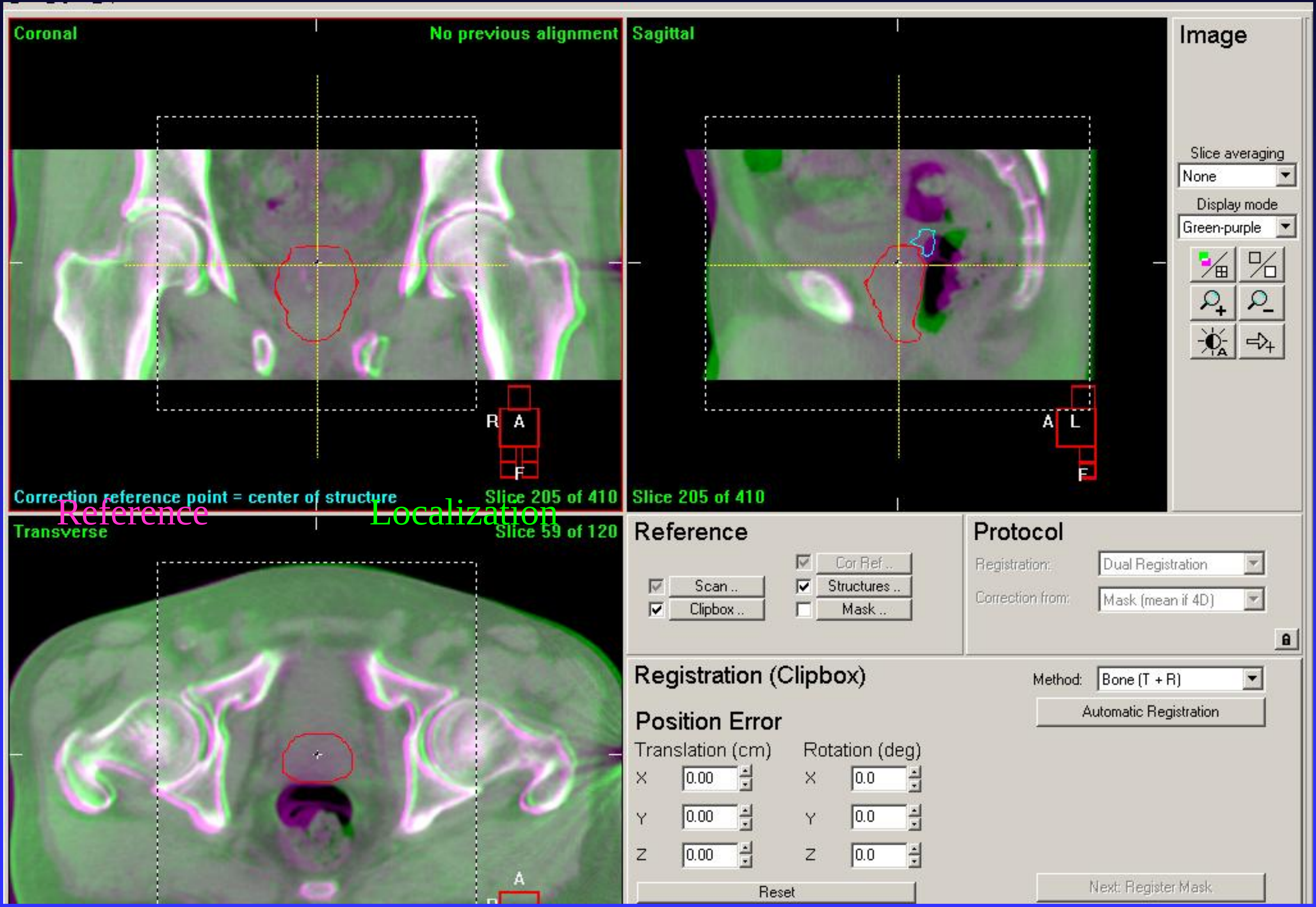
Witte et al, IJROBP2009; Chen et al, ICCR2010

Main errors in image guided RT

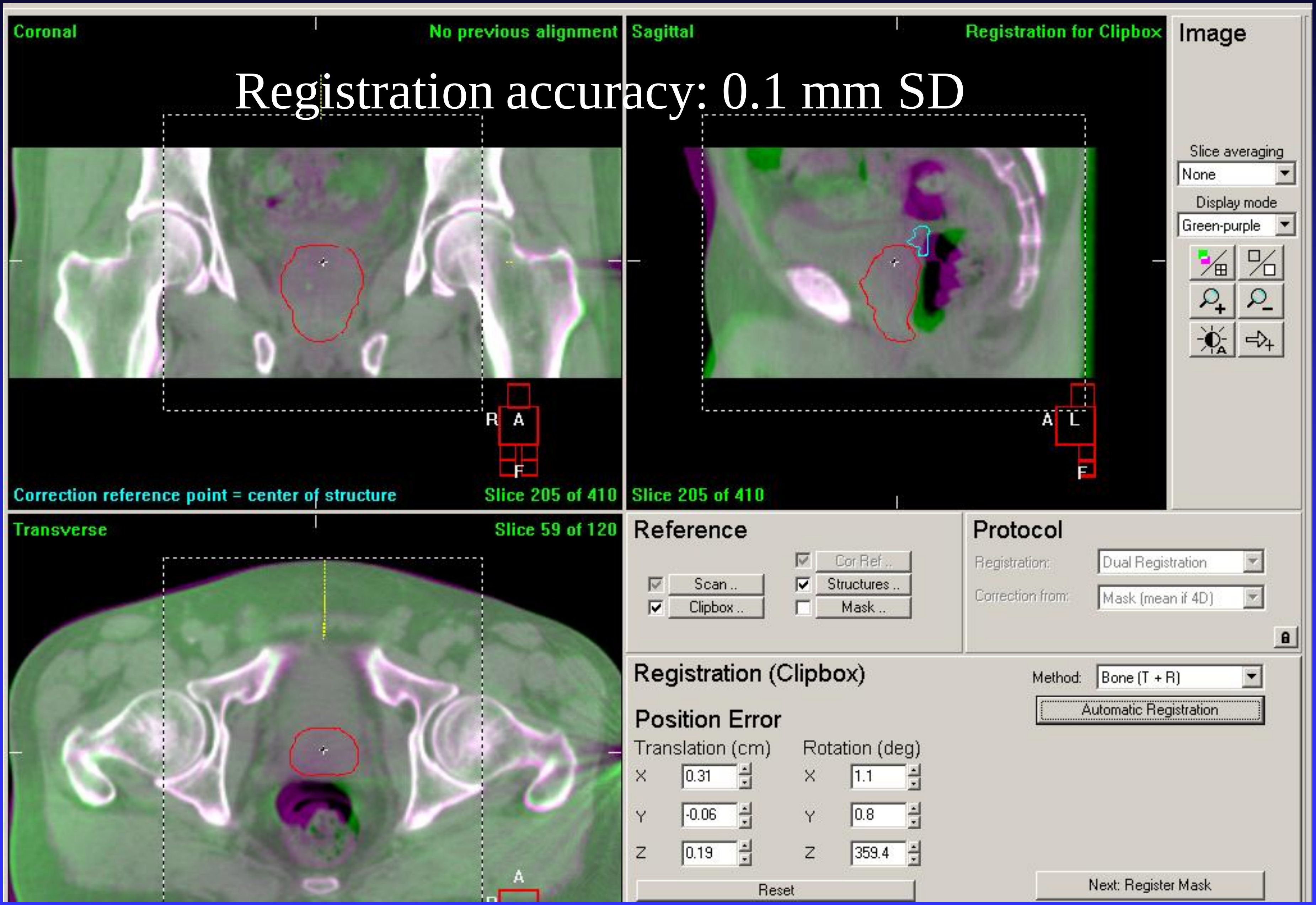
- Imaging (planning CT) and planning (delineation) errors
  - Systematic error not solved by image guidance
- Observer errors in image guidance
  - Random and systematic
- Short-term (intra-fraction) motion
  - Random and systematic
- Inadequacy of surrogate for tumor position
- Machine calibration

Are you an accurate observer ?

IGRT software: automatic bone localization



IGRT software: automatic bone localization



Does the tumor move after imaging ?

Short-term prostate motion (1 h)

Data courtesy of Jaffray and Gilhezan, Beaumont

Home > Vol 16, No 2 (2015) > **Tong**

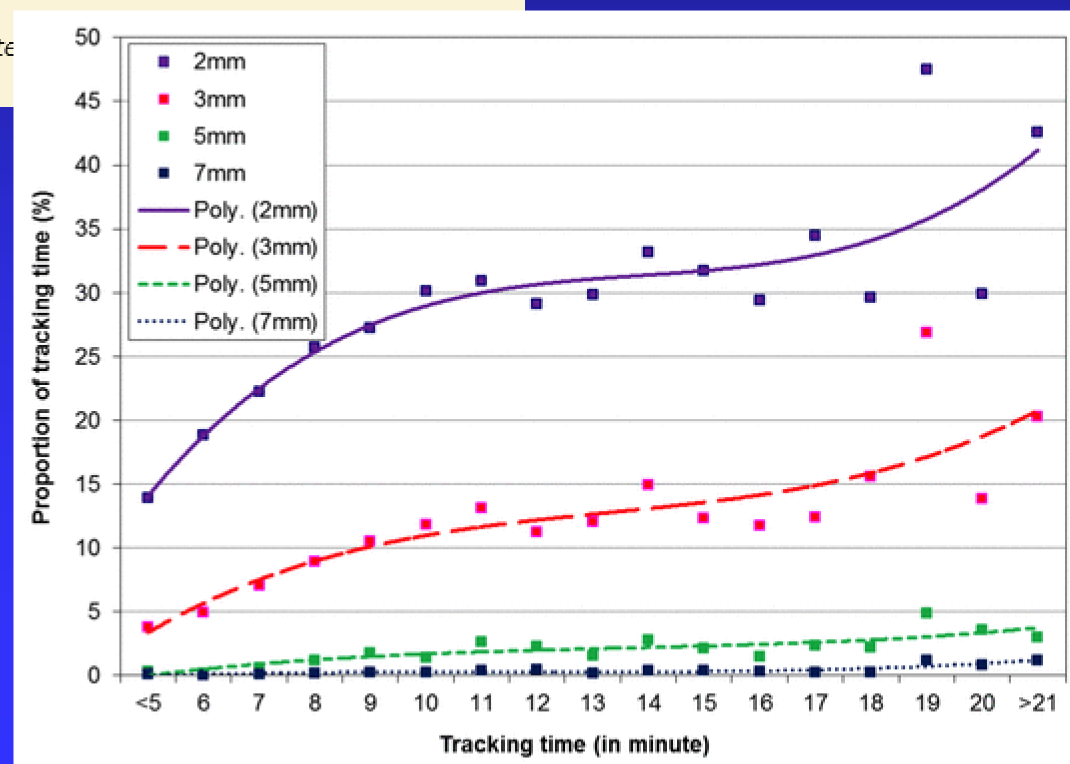
Intrafractional prostate motion during external beam radiotherapy monitored by a real-time target localization system

Xu Tong [1], Xiaoming Chen [2], Jinsheng Li [2], Qianqian Xu [1], Mu-han Lin [2], Lili Chen [2], Robert A. Price [2], Chang-Ming Ma [2,a]

Radiation Oncology Department,[1] Third-Affiliated Hospital of Qiqihar Medical University, Qiqihar, China

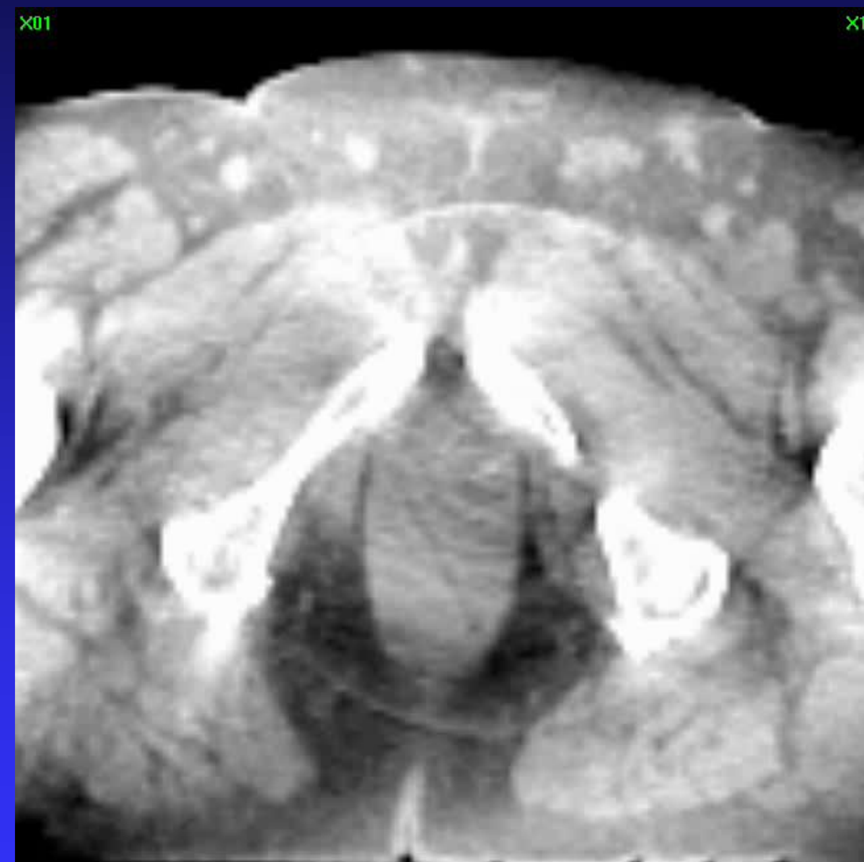
Radiation Oncology Department,[2] Fox Chase Cancer Cente

Charlie.ma@fccc.edu



Main problem for any prostate IGRT: moving gas

Projection images

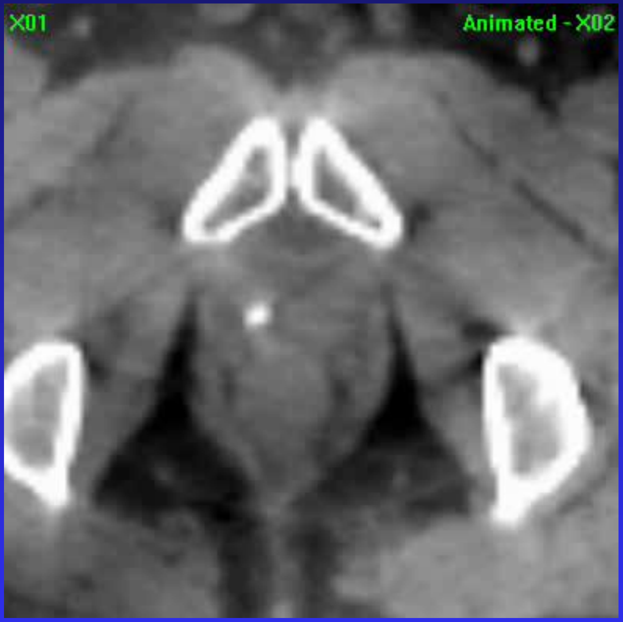


cone-beam CT scan

Moving gas reduces image quality *and* introduces short term motion

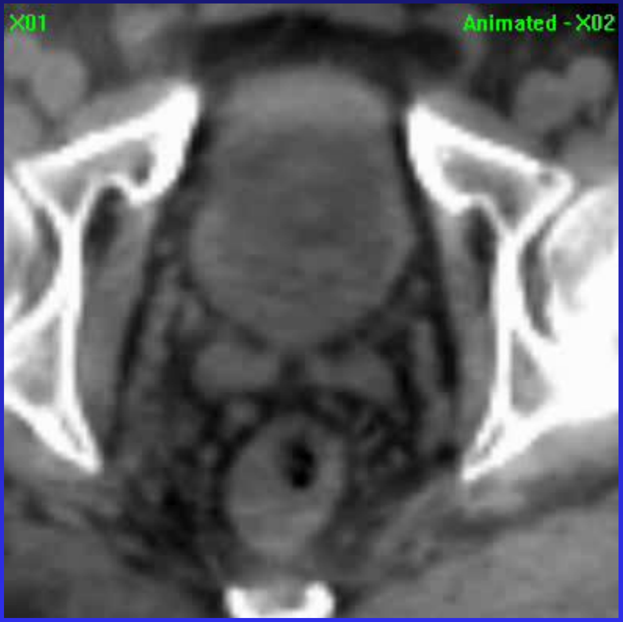
Are you using a good surrogate for the tumor position?

Are markers perfect ?



Apex

Base



Sem. Vesicles

→ +/-1 cm margin required

Best: combine markers
with low dose CBCT ?

van der Wielen, IJROBP 2008
Smitsmans, IJROBP 2010

What should the margin be ?

Analysis of motion
(random and systematic errors)

	patient 1	patient 2	patient 3	patient 4
fraction 1	0.5	0.0	0.2	0.7
fraction 2	0.6	-0.5	0.3	0.2
fraction 3	0.9	0.2	0.2	-0.4
fraction 4	1.3	-1.1	0.3	-0.1
mean	0.8	-0.4	0.3	0.1
sd	0.3	0.6	0.1	0.5

mean =M
SD = Σ
RMS = σ

Intra-fraction
0.0
0.3
0.4
0.1
0.3
Mean = 0.2
RMS of SD = σ_f

M = group systematic error (equipment)

Σ = standard deviation of the systematic (preparation) error

{ σ = standard deviation of the random (execution) error

σf = standard deviation of the intra-fraction motion

van Herk et al, Sem Rad Onc 2004

Definitions (sloppy)

- CTV: Clinical Target Volume
  The region that needs to be treated (visible plus suspected tumor)

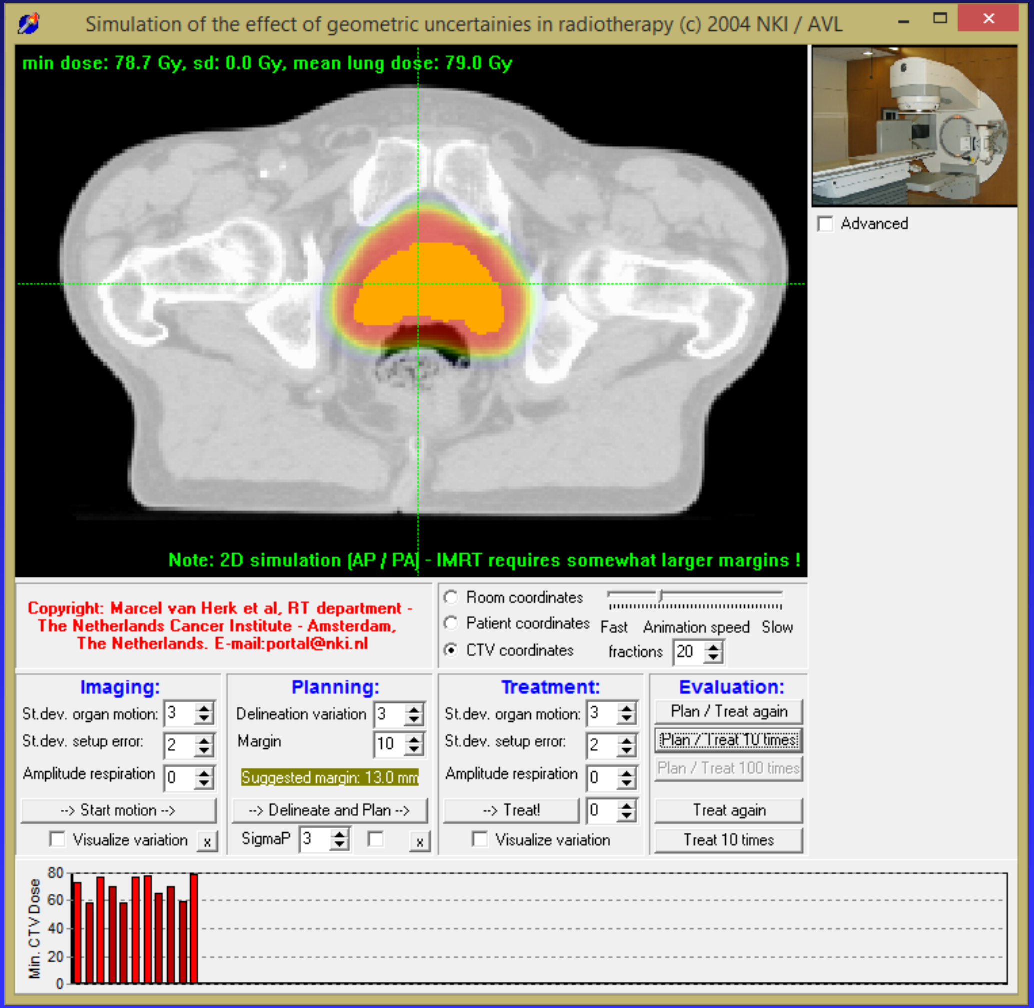
- PTV: Planning Target Volume
  The region that is given a high dose to allow for errors in the position of the CTV

- PTV margin: distance between CTV and PTV

- Don’t even think of using an ITV! (SD adds quadratically)

Demonstration – errors in RT

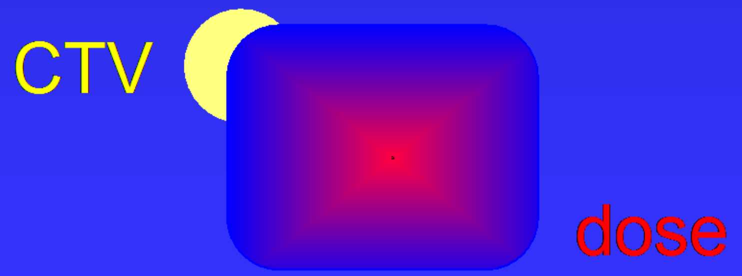
- Margin between CTV and PTV: 10 mm
- Errors:
  - Setup error:
    - 2 mm SD (x, y)
  - Organ motion:
    - 3 mm SD (x, y)
  - Delineation error:
    3 mm SD



What is the effect of geometrical errors on the CTV dose ?

Treatment execution (random) errors blur the dose distribution

Preparation (systematic) errors shift the dose distribution

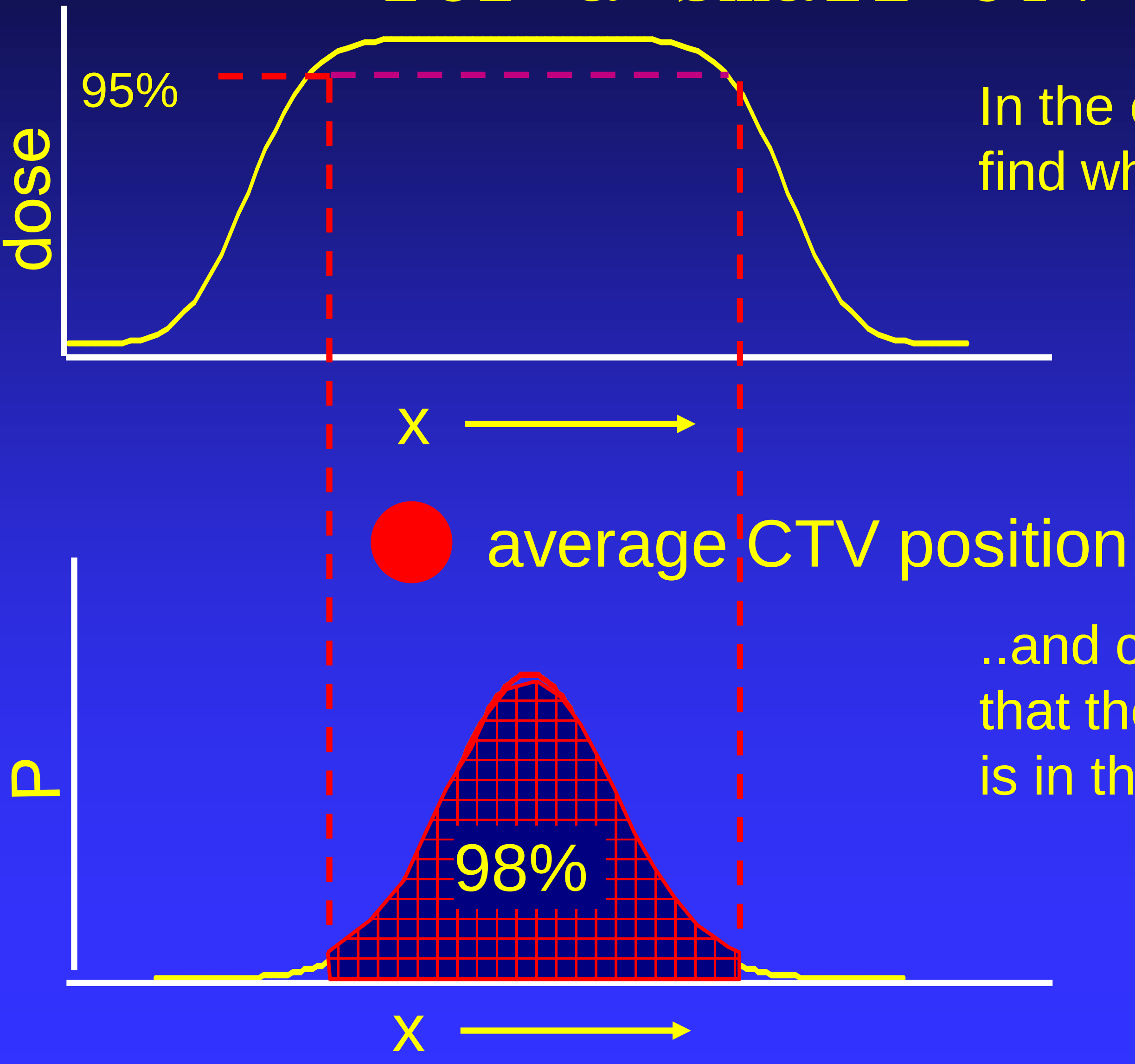


Analysis of CTV dose probability

- Blur planned dose distribution *with all execution (random) errors* to estimate the cumulative dose distribution

- For a given *dose* level:
  - Find region of space where the cumulative dose exceeds the given level
  - Compute *probability* that the CTV is in this region

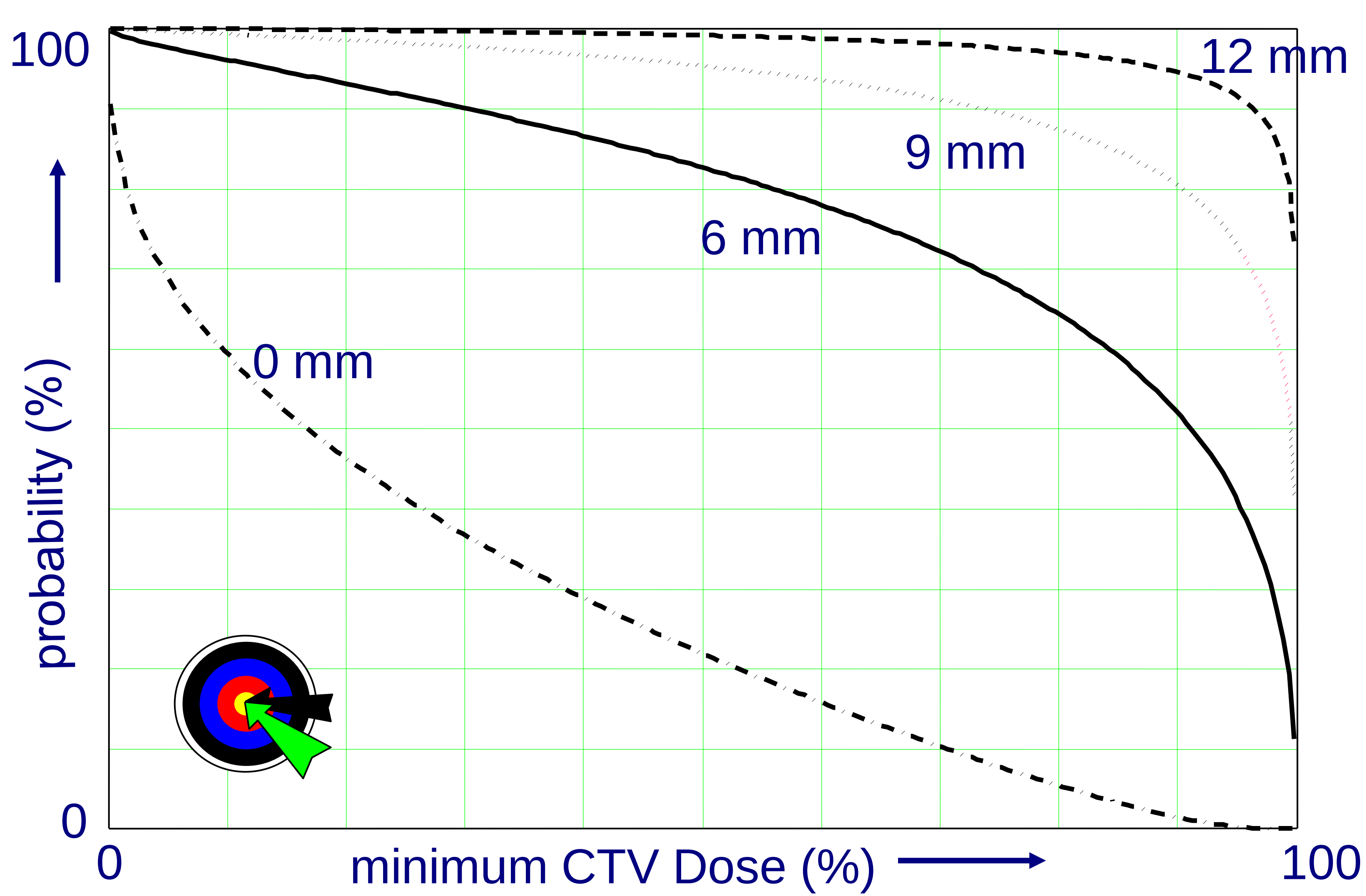
Computation of the dose probability for a small CTV in 1D



In the cumulative (blurred) dose, find where the dose > 95%

..and compute the probability that the average CTV position is in this area

What should the margin be ?



How to choose the PTV margin

- Express required CTV dose for a specified fraction of patients. For example: 90% of the patients must get a minimum CTV dose of 95% or more

- Add first margin so that 90% of the preparation (systematic) errors are covered

- Add margin for penumbra and execution (random) variation so that CTV + first margin lies within the 95% isodose

Simplified PTV margin recipe for dose – probability

To cover the CTV for 90% of the patients with the 95% isodose (analytical solution) :

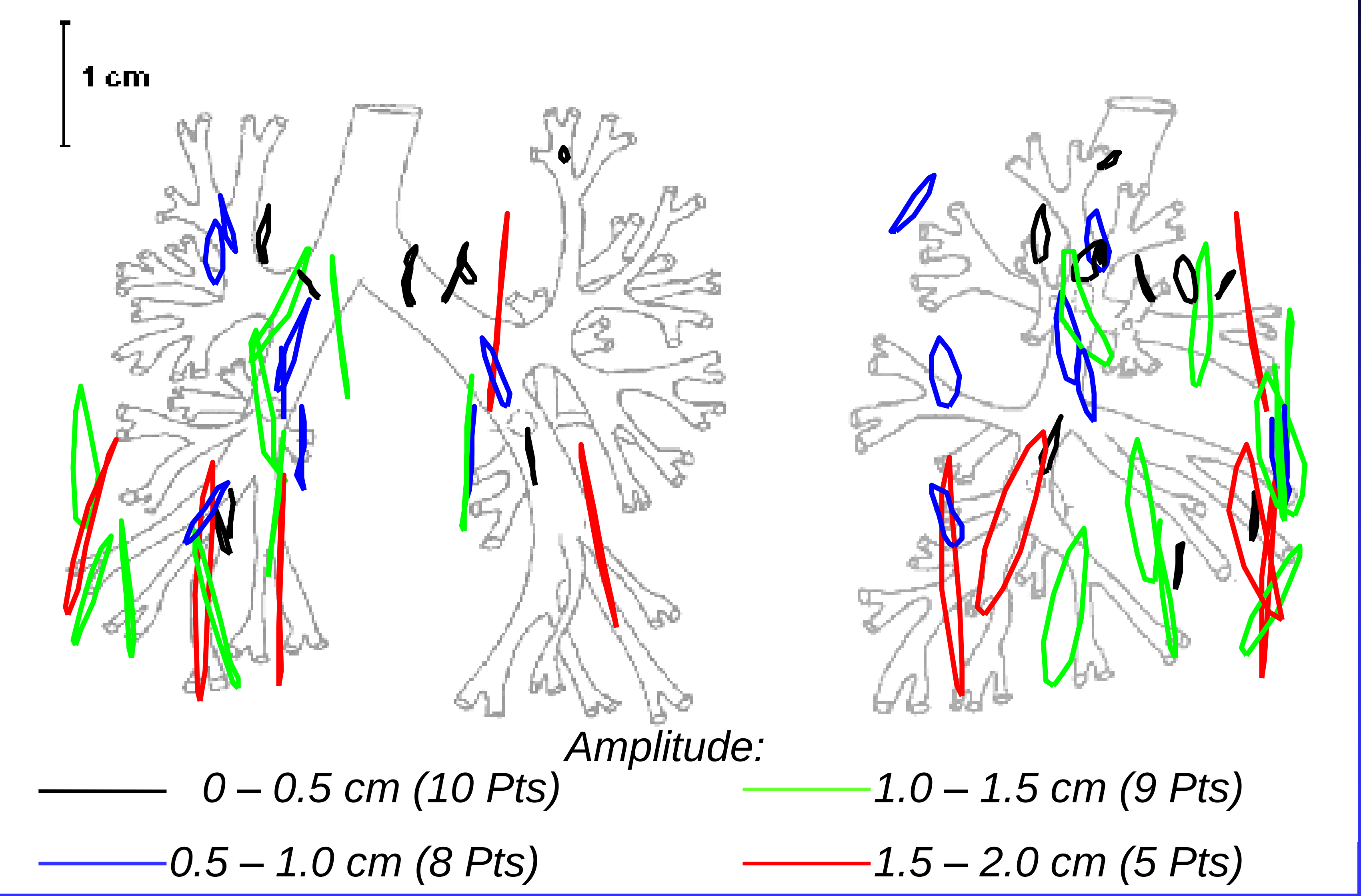
PTV margin = 2.5 Σ + 0.7 σ

Σ = quadratic sum of SD of all preparation (systematic) errors
σ = quadratic sum of SD of all execution (random) errors

(van Herk et al, IJROBP 47: 1121-1135, 2000)

*For a big CTV with smooth shape, penumbra 5 mm

What about respiration ?



SD = 0.35 peak-peak

Jan-Jakob Sonke et al, IJROBP 2007

Computing margins

Error (SD)		Lung classic
Imaging snapshot setup	Σ	4 mm
Imaging snapshot organ	Σ	3 mm
Imaging snapshot respiration	Σ	A=10 mm → 3.3 mm
Delineation	Σ	4 mm
Treatment setup	σ	4 mm
Treatment organ motion	σ	3 mm
Treatment respiration	σ	A=10 mm → 3.3 mm
Margin *M*		22 mm

$$M \approx 2.5\Sigma + 0.7\sigma$$

$$2.5 \cdot \sqrt{4^2 + 3^2 + 3.3^2 + 4^2} + 0.7 \cdot \sqrt{4^2 + 3^2 + 3.3^2} = 22.202$$

van Herk et al IJROBP 2000

2.5Σ + 0.7σ is a simplification

- Dose gradients ('penumbra' = σ_p) shallower in lung → smaller margins for random errors

$$M = 2.5\Sigma + 1.64\sqrt{(\sigma_p^2 + \sigma^2)} - 1.64\sigma_p$$

- Number of fractions is small in hypofractionation
  - BUT: beam on time is very long → respiration only causes dose blurring

- Dose prescription at 80% instead of 95%

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

Margins in lung hypo (3 x 18 Gy)

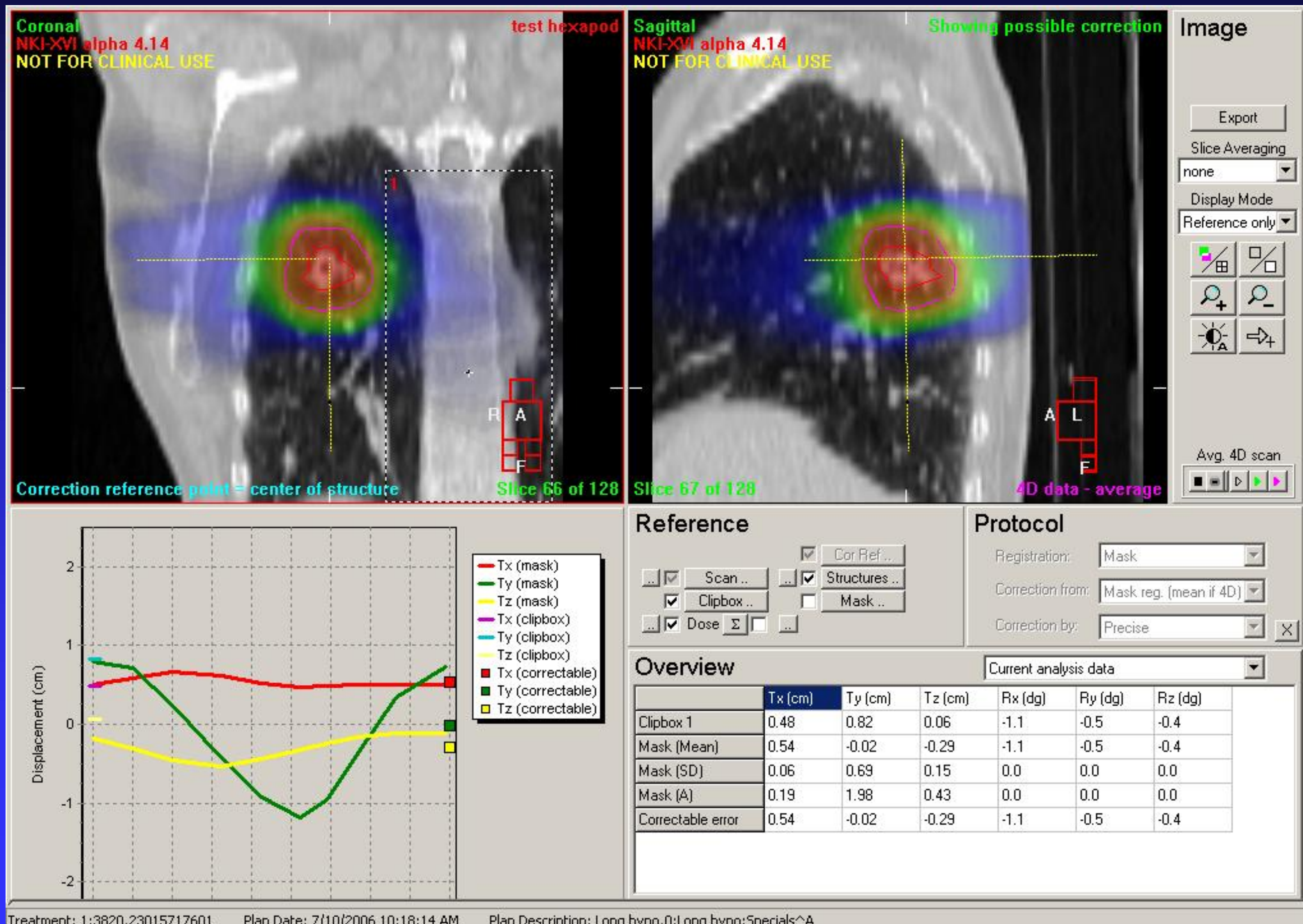
	Systematic	Random
Delineation	2 mm SD	-
Registration/couch shift	1.5 mm SD	1.5 mm SD
Intra-fraction motion	1.5 mm SD	1.5 mm SD
Total	3 mm SD	2.2 mm SD
Margin A=10 mm	7 mm +	0 mm
Margin A=20 mm	7 mm +	2 mm

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

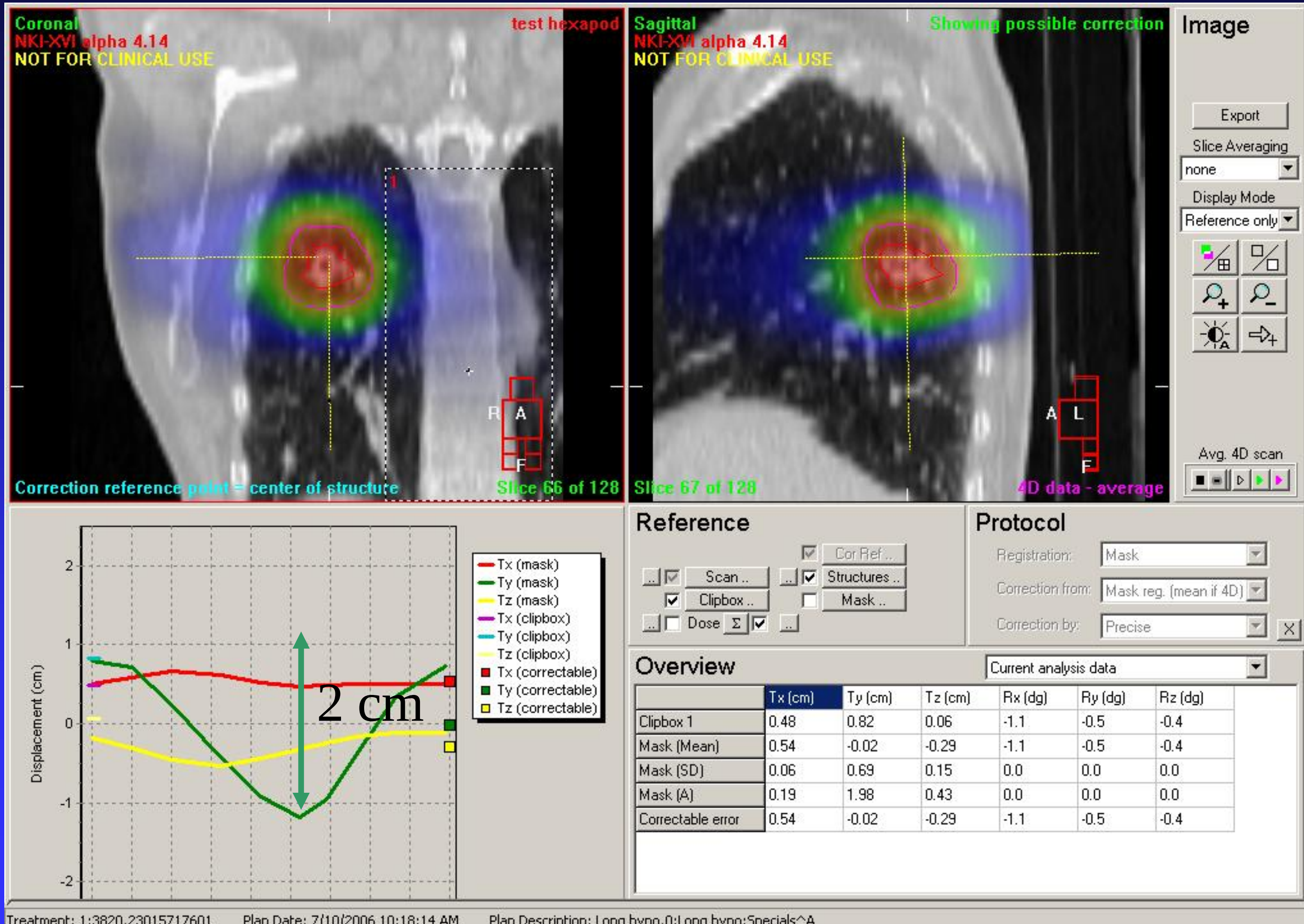
$$\sigma_p \approx 7.8 \text{ mm}$$

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

Planned dose distribution: hypofractionated lung treatment 3x18 Gy



Realized dose distribution with daily IGRT on tumor (no gating)

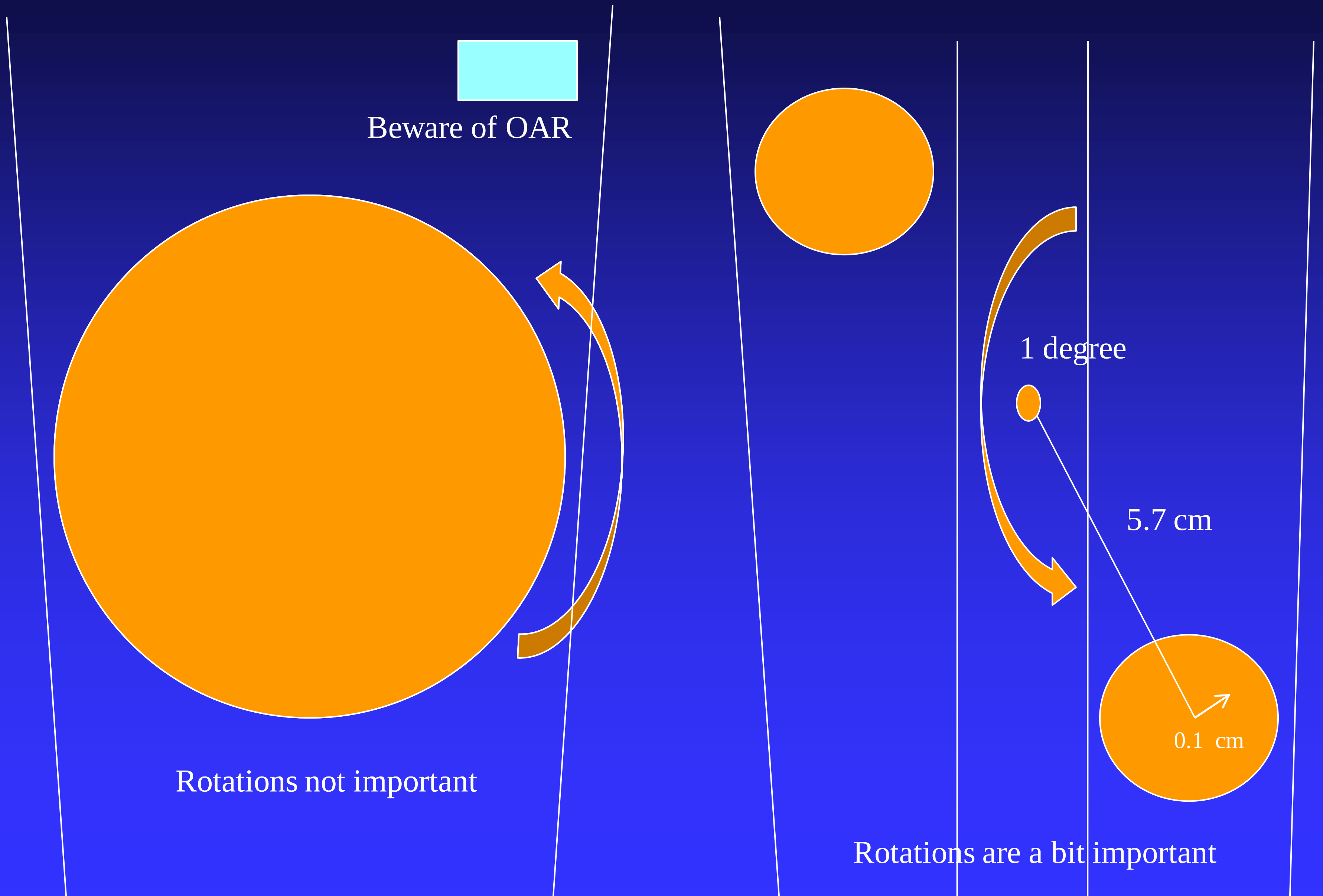


9 mm margin is adequate even with 2 cm intrafraction motion

Where is the ITV ?

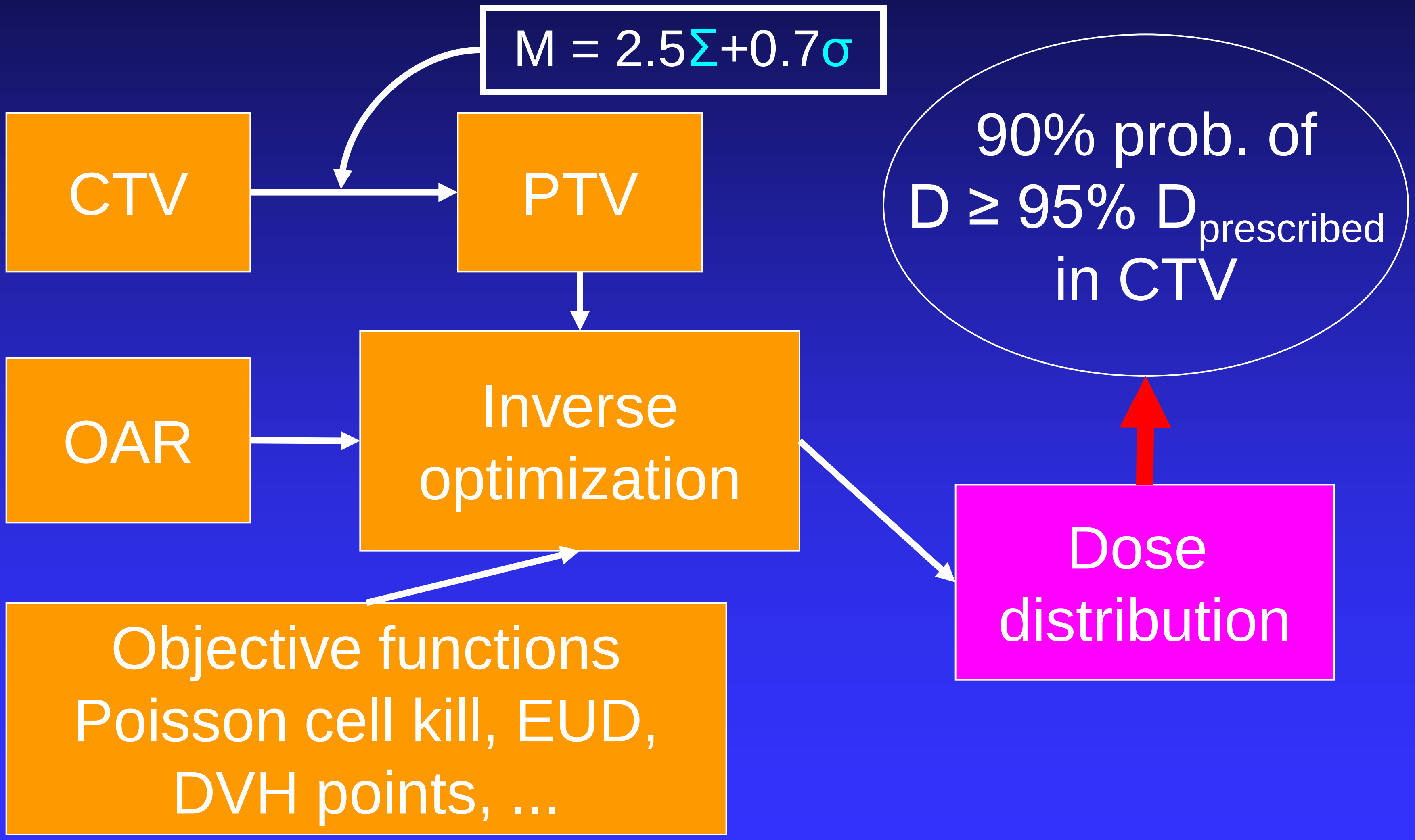
Respiration motion causes a little dose blurring that is easily compensated with a very small margin

What about rotations ?



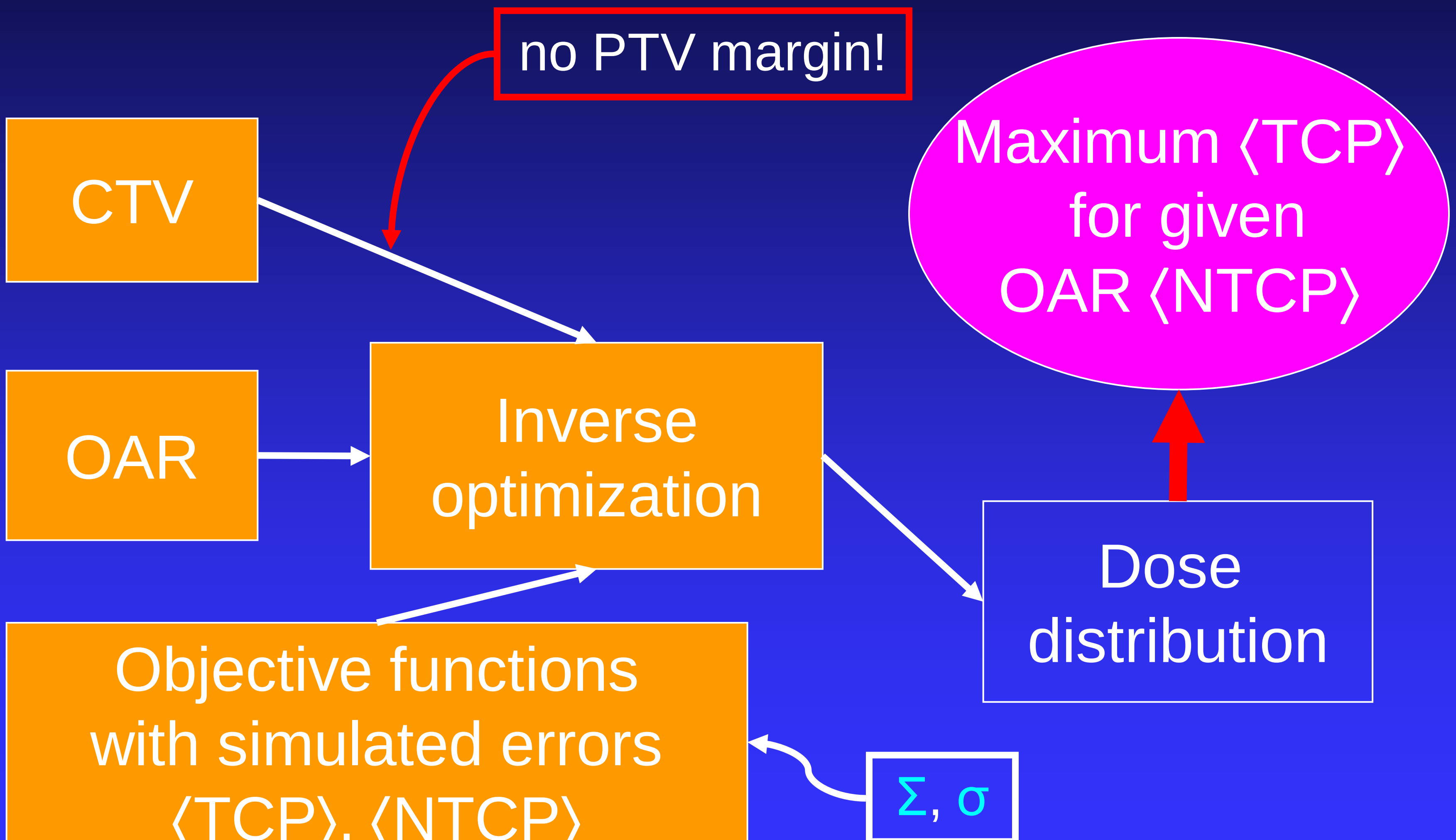
Future developments

Uncertainty management: Conventional IMRT planning with margin



Witte et al, IJROBP 2007

Uncertainty management: Probabilistic biological IMRT planning without margin



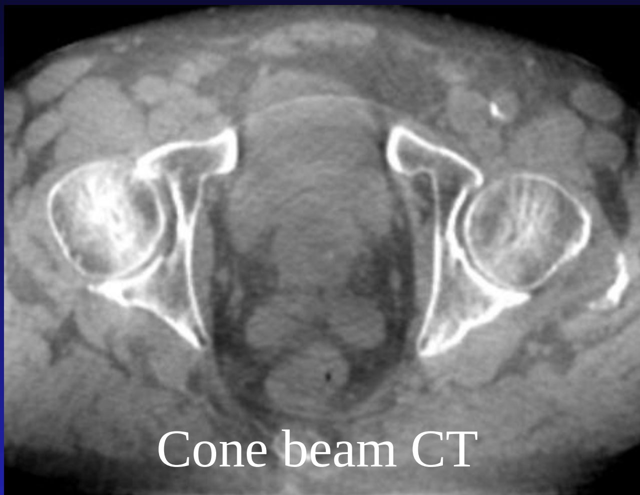
Witte et al, IJROBP 2007
Bohoslavsky et al, IJROBP 2013

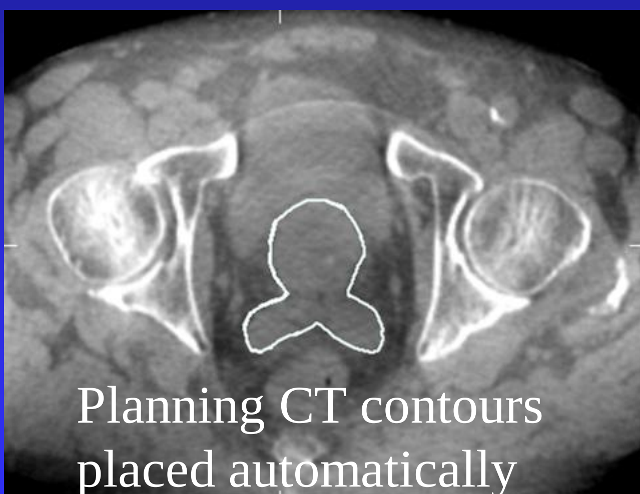
Conclusions

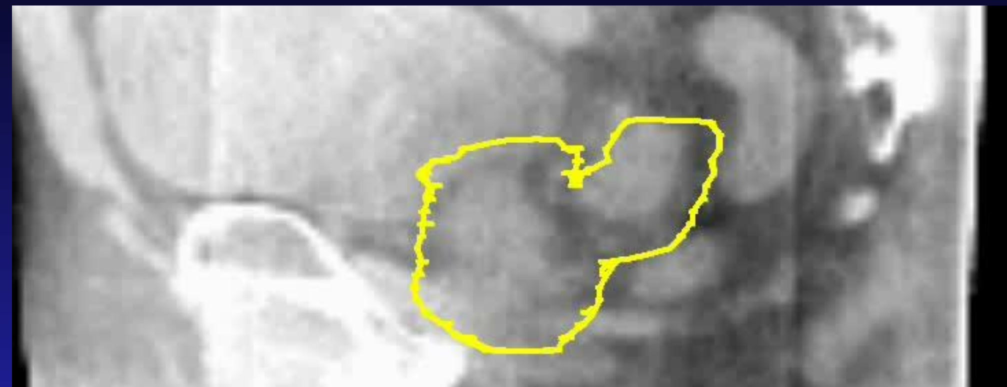
- There are many error sources in radiotherapy, determine what they are in your department
- Focus on correcting remaining systematic errors
  - Do not forget the doctor's error – delineation, and CTV
- IGRT does not eliminate all errors; carefully consider the margins to be used
- IGRT introduces some new errors and makes old errors more important (where is the CTV?)
- Margin recipes assume that you know ALL ERRORS … USE AT YOUR OWN RISK

Thank you for your attention!

Automatic prostate localization in CBCT (30 s)







10 CBCT scans: automatic bone match

10 CBCT scans: automatic prostate match
help line (GTV+3.6 mm)

Observer error:
(calcifications)

	LR (mm)	CC (mm)	AP (mm)
Mean	0.2	-0.4	-0.9
SD	1.0	2.4	2.3

Smitsmans *et al.*, IJROBP 2004, 2005

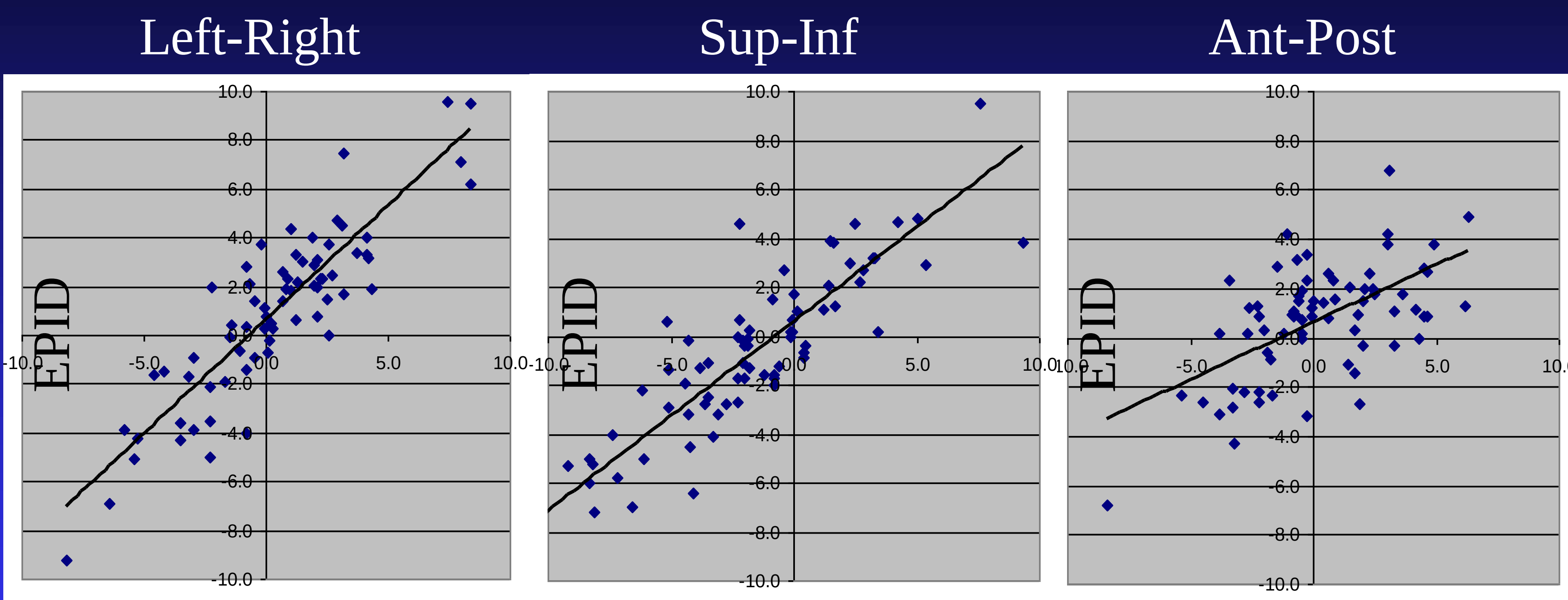
Image Guided Radiotherapy

Increase precision by imaging target and/or healthy tissues just prior to treatment

Image guidance does not solve all geometrical uncertainties and variations *and introduces new ones*

- Let's look at geometrical errors in RT
  - Imaging errors
  - Planning errors
  - Treatment errors
  - Image guidance errors

Correlation CBCT – EPID for lung



Setup error measured with cone beam CT

Slope: 0.81 .. 1.06 0.66 .. 0.88 0.30 .. 0.66 (95% CI)

Observer error in CBCT is negligible → large observer error in EPID such as a clear under-estimation of AP shift (lung)

Borst et al, IJROBP 2007

Errors and margins in image guided radiation therapy

Marcel van Herk[1], David Jaffray[2], Anja Betgen[3], Peter Remeijer[3], Jan-Jakob Sonke[3], Roel Steenbakkers[3], Monique Smitsmans[3], Marnix Witte[3] and Joos Lebesque[3]

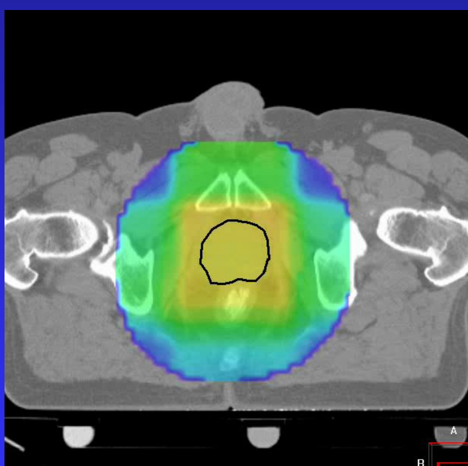
[1]University of Manchester, Institute for Cancer Sciences

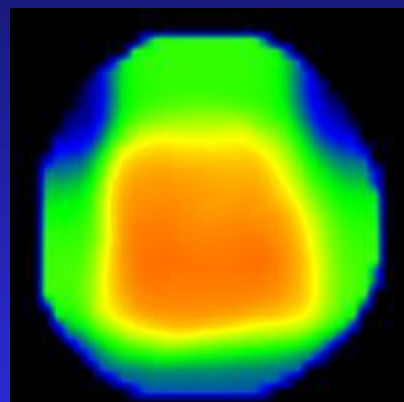
[2]Princess Margaret Hospital, Toronto, Canada

[3]Netherlands Cancer Institute, Amsterdam, The Netherlands

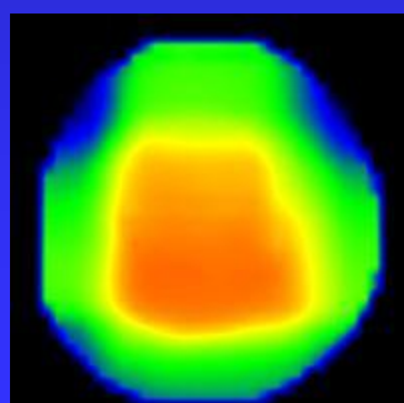
Parts of this work were sponsored by the Dutch Cancer Foundation, NIH and Elekta Oncology Systems

Clickers: where did we find the largest dose difference for high risk patients?





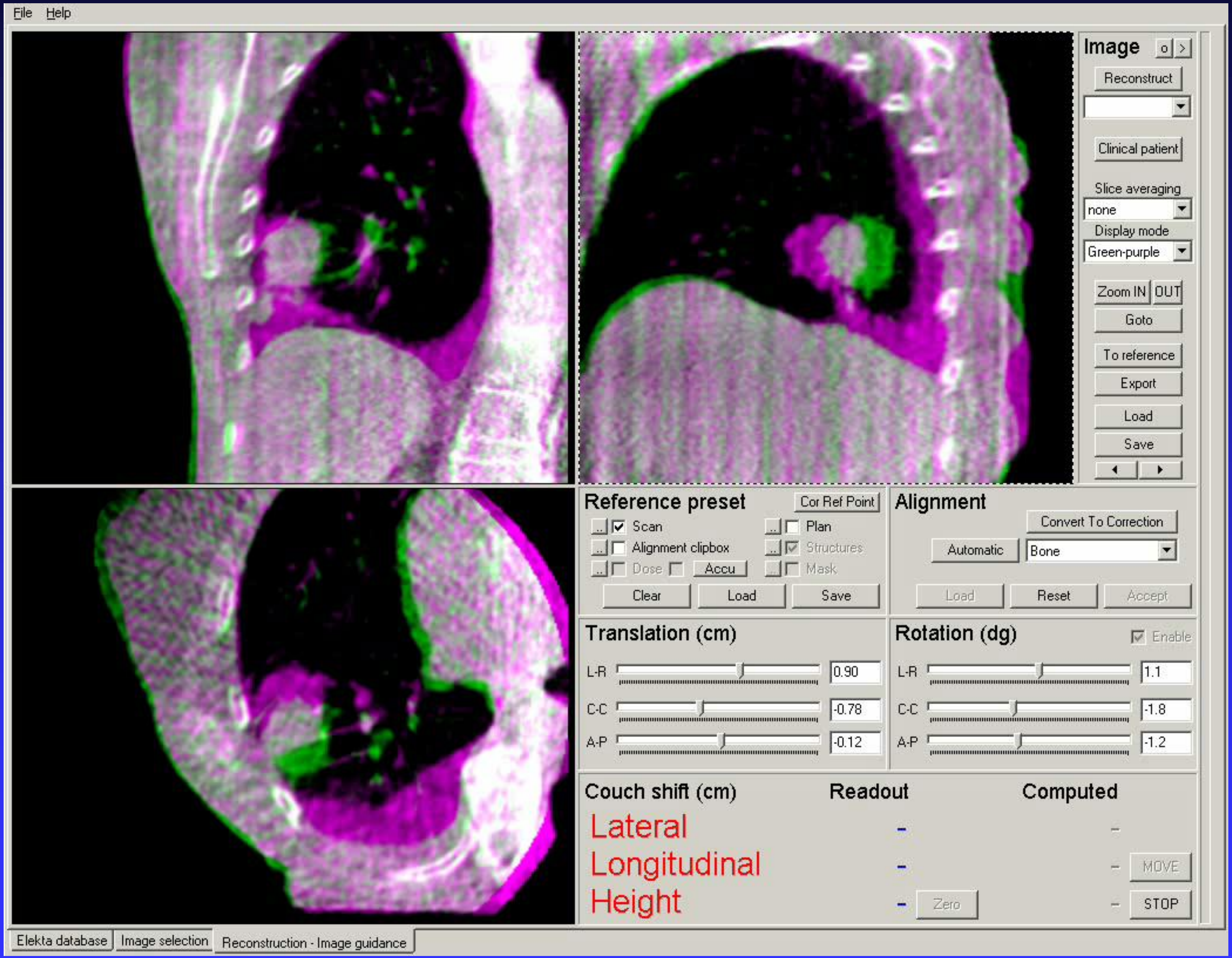
Controls/failures



Where was the largest dose difference observed?

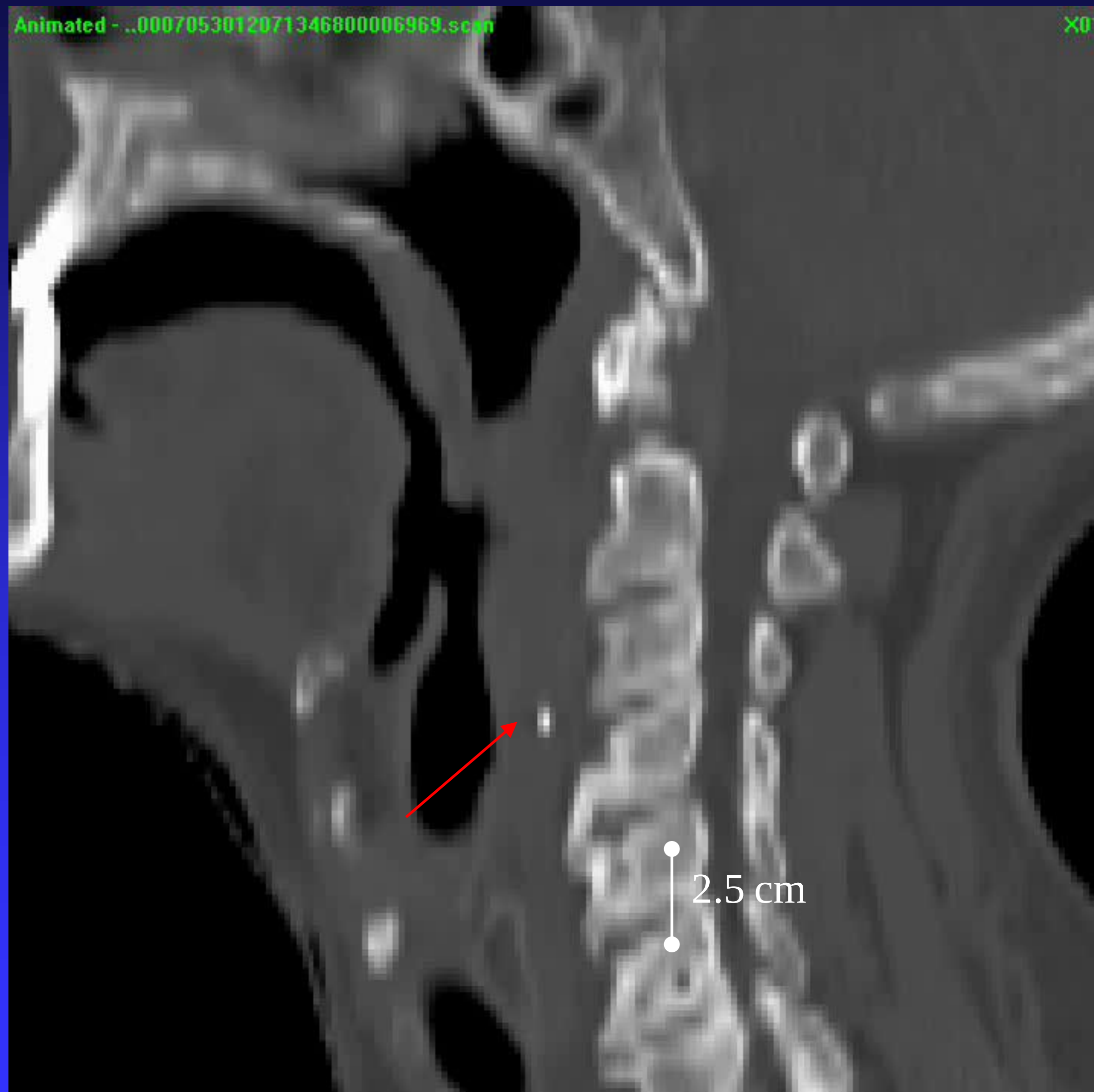
1) Inside the prostate
2) On the border of the prostate
3) Within 2 cm of the prostate
4) Within 4 cm of the prostate

Baseline motion: 4D scans taken within one week and matched on bone, displayed in same phase



Imagine treating this patient with gating and a small margin, without 4D cone-beam CT!

Is the surrogate appropriate?



Motion of tumor boundary relative to bony anatomy

Intra-fraction patient motion (bone) negligible – examples:

- 6 bladder cancer patients, 35 x 2 CBCT scans
- 10 minutes between post- and pre-scan

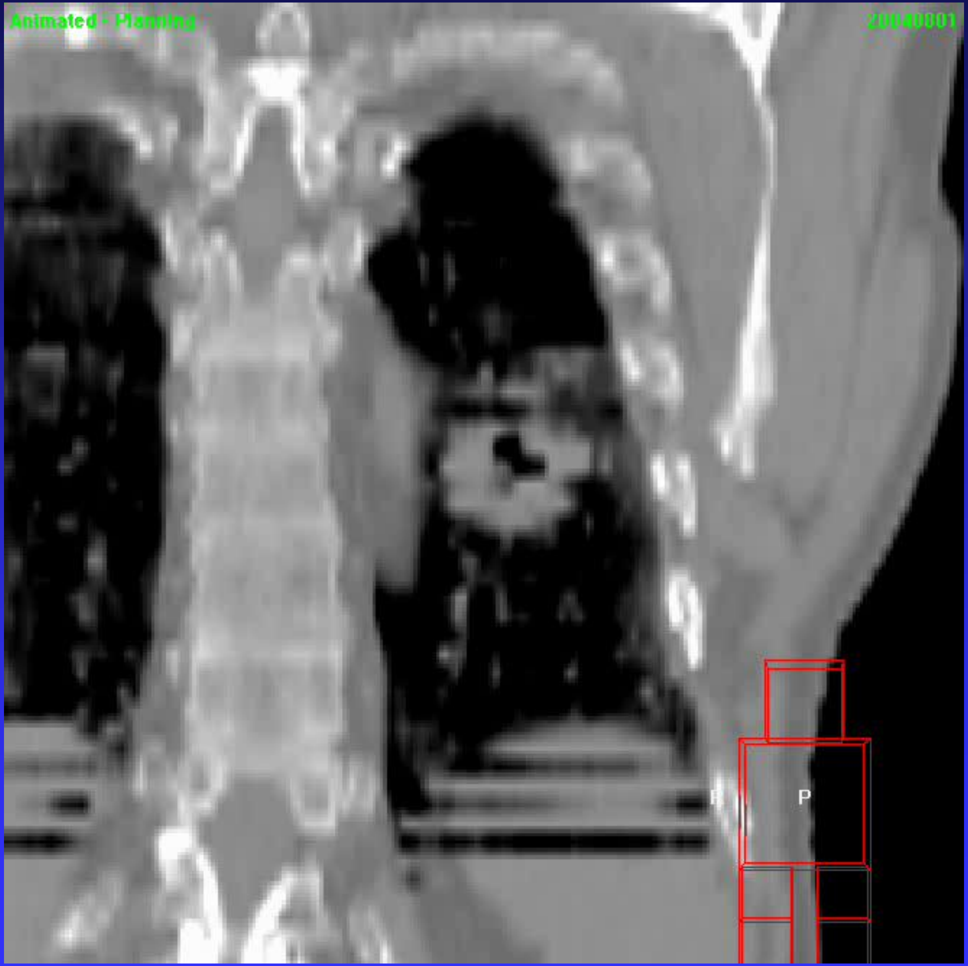
	left-right (mm)		**cranio-caudal (mm)**		**anterior-posterior (mm)**	
	mean	SD	mean	SD	mean	SD
post-pre	0	0.4	0	0.3	-0.1	0.5

- Brain SRS (2 x 25 pats):

	LR Thermo:	LR PET:	CC Thermo:	CC PET:	AP Thermo:	AP PET:
Translations (mm):						
M	**0.2**	**-0.1**	**0.1**	**0.2**	**-0.2**	**-0.2**
SD	**0.6**	**0.7**	**0.3**	**0.3**	**0.3**	**0.3**
Rotations (in °):						
M	**0.1**	**0.0**	**-0.1**	**0.1**	**0.1**	**-0.0**
SD	**0.2**	**0.3**	**0.7**	**0.5**	**0.4**	**0.4**

This is what IGRT solves: setup errors - measured with CBCT at NKI

Elekta Synergy system

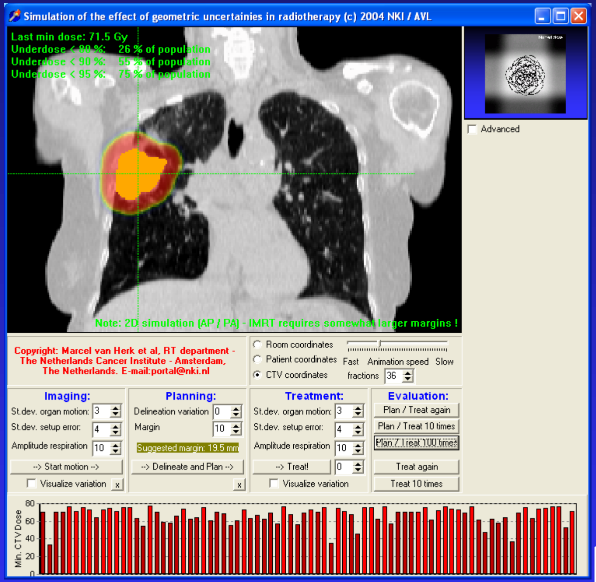


Bony setup error: 3 mm SD

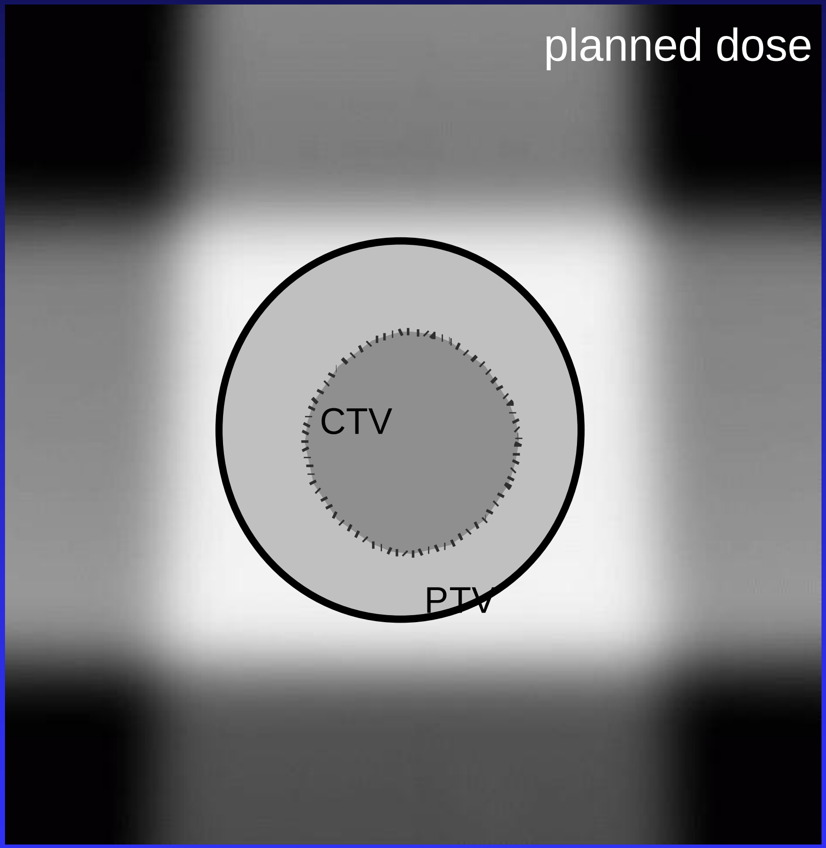
Van Herk et al EPI 2K4, Borst et al, IJROBP 2007

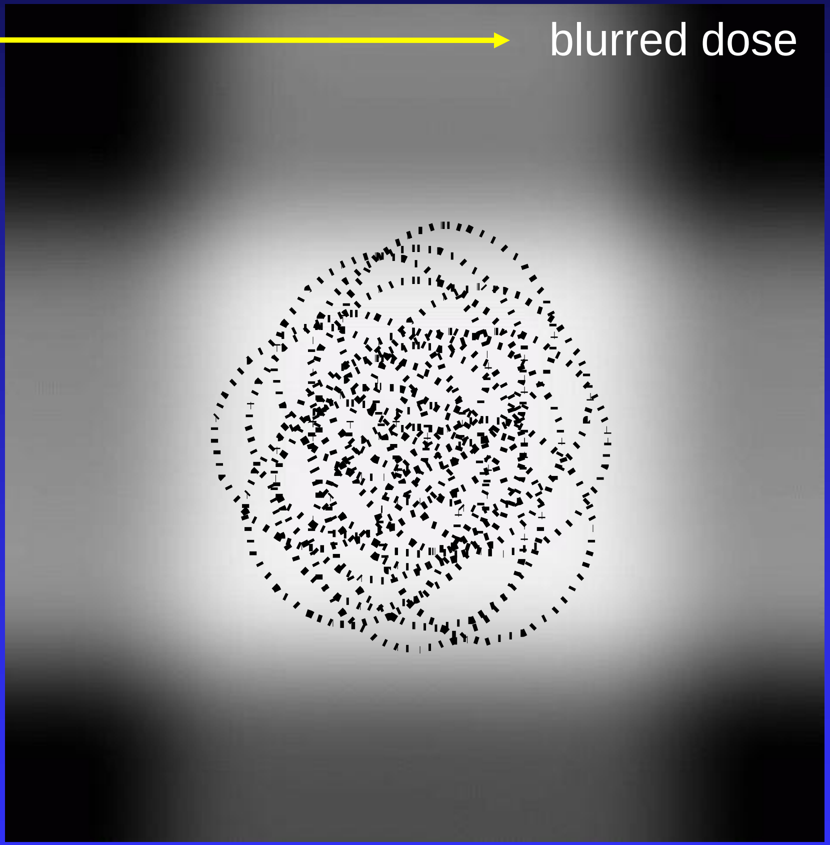
Clickers: if we would gate the beam during treatment (eliminating respiratory movement) how much can the margin be reduced to keep 90% of patients treated correctly ?

1. By 1 cm
2. By 5 mm
3. By 1 mm
4. By 0 mm



Incorporation of remaining geometrical errors in radiotherapy planning





Wrong - compute DVH
and TCP for PTV

Correct - blur for random
and test all systematic errors

Clickers

- Ask question
- Discuss scores
- Try to convince your neighbour
- Ask question again
- Let representatives explain which answer is right

- Do this 4 times per lecture

Todo

- Break 4 times with interactive clicker discussion
- Make excel file with sheets for excel session
- Lung margin calculation
- Errors
  - Delineation: (range – outliers) / 3
  - Organ motion: show data/laila repeat CT simplified
  - Setup error analysis
    - Without correction
    - With correction NAL, daily
  - Intrafraction error analysis
- Worksheet prostate, lung (too early?)

Breakout sessions

```
function solve(f, x)
  local steps, range = 30, 3
  for i=0, steps do
    y = f(-6+range*i/steps)
    if y>x then
      return -6+range*(i-1)/steps -
           (y - x                       ) /
          ((y - f(-6+range*(i-1)/steps))*steps)
    end
  end
end

-- create plot area
if p==nil then
  p = graph.plot('Simulation of the effect of random errors in RT')
  p:show()
end

sigma_penumbra = 0.64
sigma_random   = 0.00
dose_presc     = 0.83

sigma_total = math.sqrt(sigma_penumbra*sigma_penumbra + sigma_random*sigma_random)
f0 = |v| num.integ(|t|randist.gaussian_pdf(t, sigma_penumbra), v-5, v+5)
f  = |v| num.integ(|t|randist.gaussian_pdf(t, sigma_total   ), v-5, v+5)
print('margin (cm) =', solve(f, dose_presc)-solve(f0, dose_presc))

require('mobdebug').off()
local ln2 = graph.fxline(f, -8, 8, 100)
--p:clear()
p:addline(ln2, 'blue')
p:addline(graph.fxline(|v|dose_presc, -10, 10), 'red')
require('mobdebug').on()
```

Breakout sessions

```
function mean(A)
  local a = 0
  for i=1, #A do
    for j=1, #A[i] do
      a = a + A:get(i, j)
    end
  end
  return a / (#A * #A[1])
end

function sd(A)
  local a = 0
  local m = mean(A)
  for i=1, #A do
    for j=1, #A[i] do
      a = a + (A:get(i, j)-m)^2
    end
  end
  return math.sqrt(a / (#A * #A[1]))
end

trace = matrix.new(1, 360, |i,j| math.sin(j/57.0)^6)
graph.fiplot(|i| trace[1][i], 1, 360)
print(sd(trace))
```

Correction Strategies and Adaptive Radiotherapy

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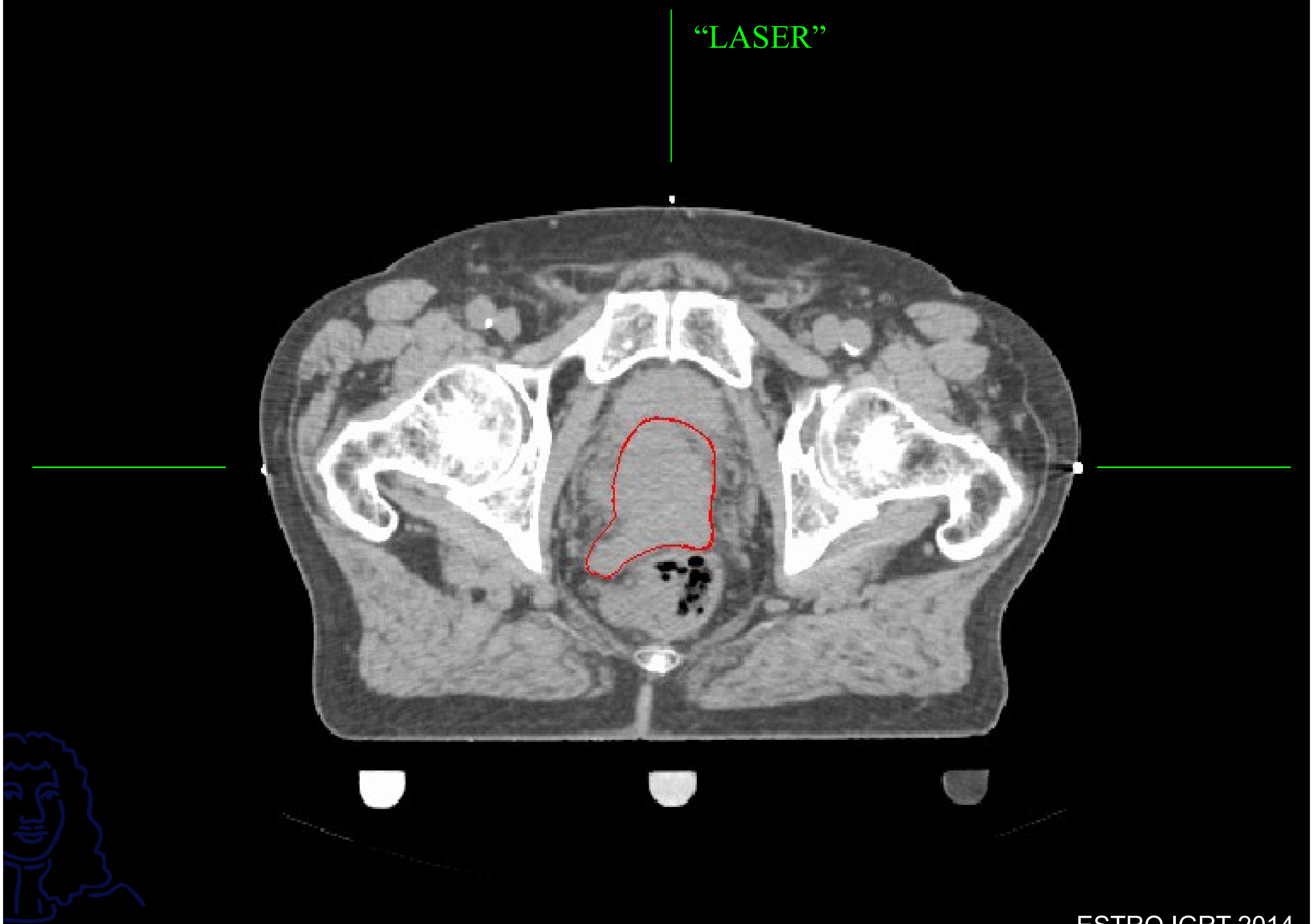
NKI-AVL
Het Nederlands Kanker Instituut
Antoni van Leeuwenhoek Ziekenhuis

ESTRO IGRT 2014

Outline

- Introduction
- Correction Protocols
- Advanced Correction Strategies
- Adaptive Radiotherapy


"LASER"

The radiotherapy chain

Patient →

Patient

1 x

- CT room
- Lasers
- Skin markers
- Images
- Bone
- Tumor
- Delineation
- Margin
- Planned beam

Patient data

35 x

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

- Beam
- Accelerator
- Treatment room

17 steps with a lot of room for errors

Portal imaging

	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

Image guided RT (on tumor)

1 x

- CT room
- Lasers
- Skin markers
- Images
- Bone
- Tumor
- Delineation
- Margin
- Planned beam

35 x

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

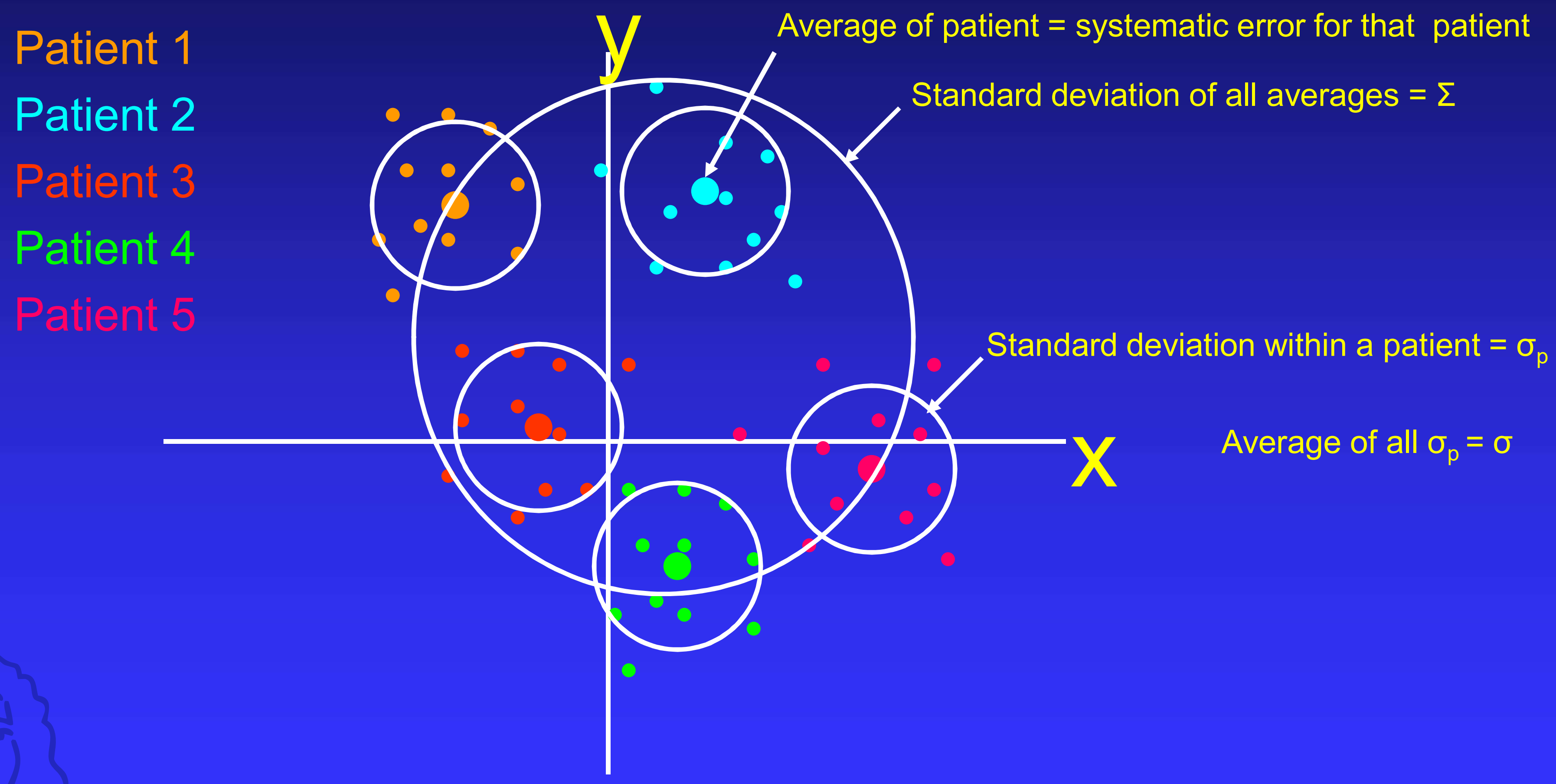
Patient →

Patient

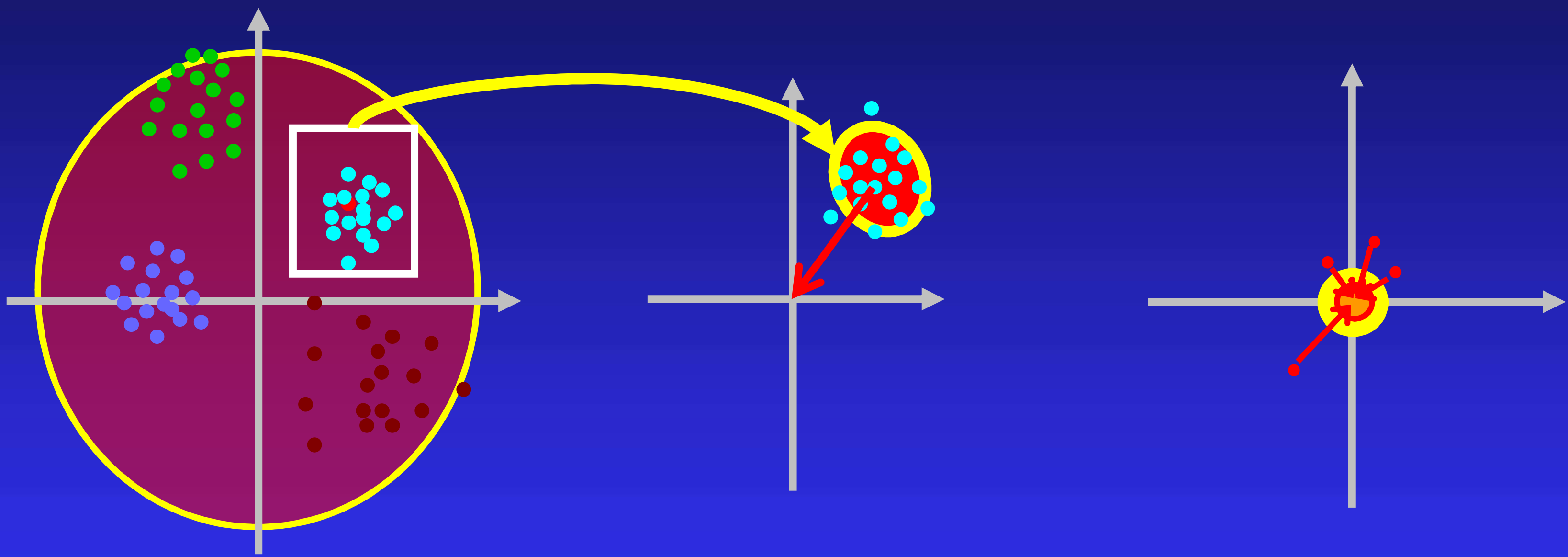
Patient data

17 steps with a lot of room for errors

Systematic and random errors



Variation Management vs Target Margin



No Corrections

Population only
Large Margins

Off-line corrections

Data: k < N
Considerable margin reduction

On-line correction

Data: N
Further Margin reduction

Courtesy to Di Yan, WBH

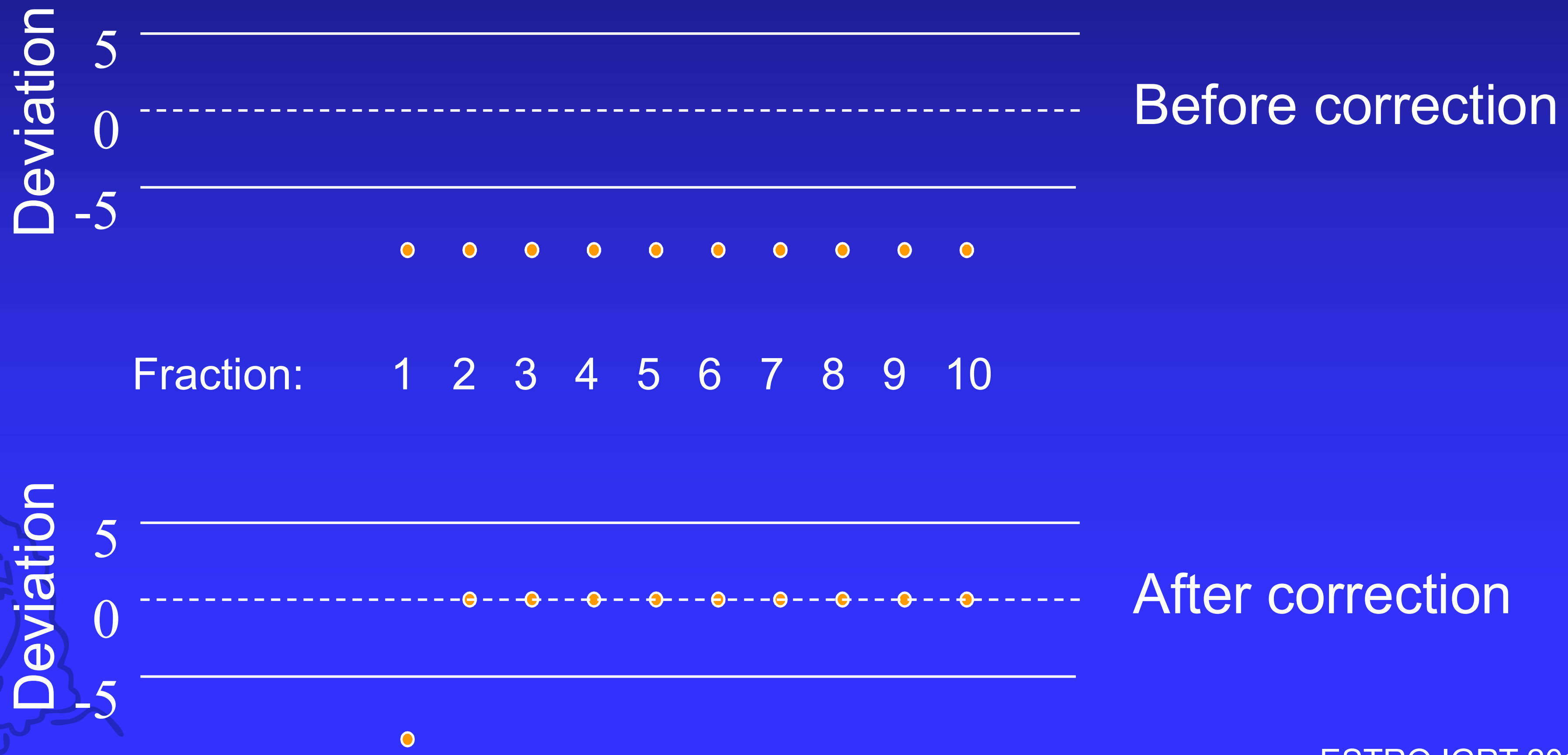
Correction Protocols

Correction protocols

- No corrections (monitoring)
  - Aimed at determining accuracy of clinical practice
- Ad-hoc corrections
  - Not recommended
- Off-line correction protocols
  - Aimed at correcting inter-treatment/systematic errors
  - SAL, NAL, etc
- On-line correction protocols
  - Aimed at correcting day to day variations

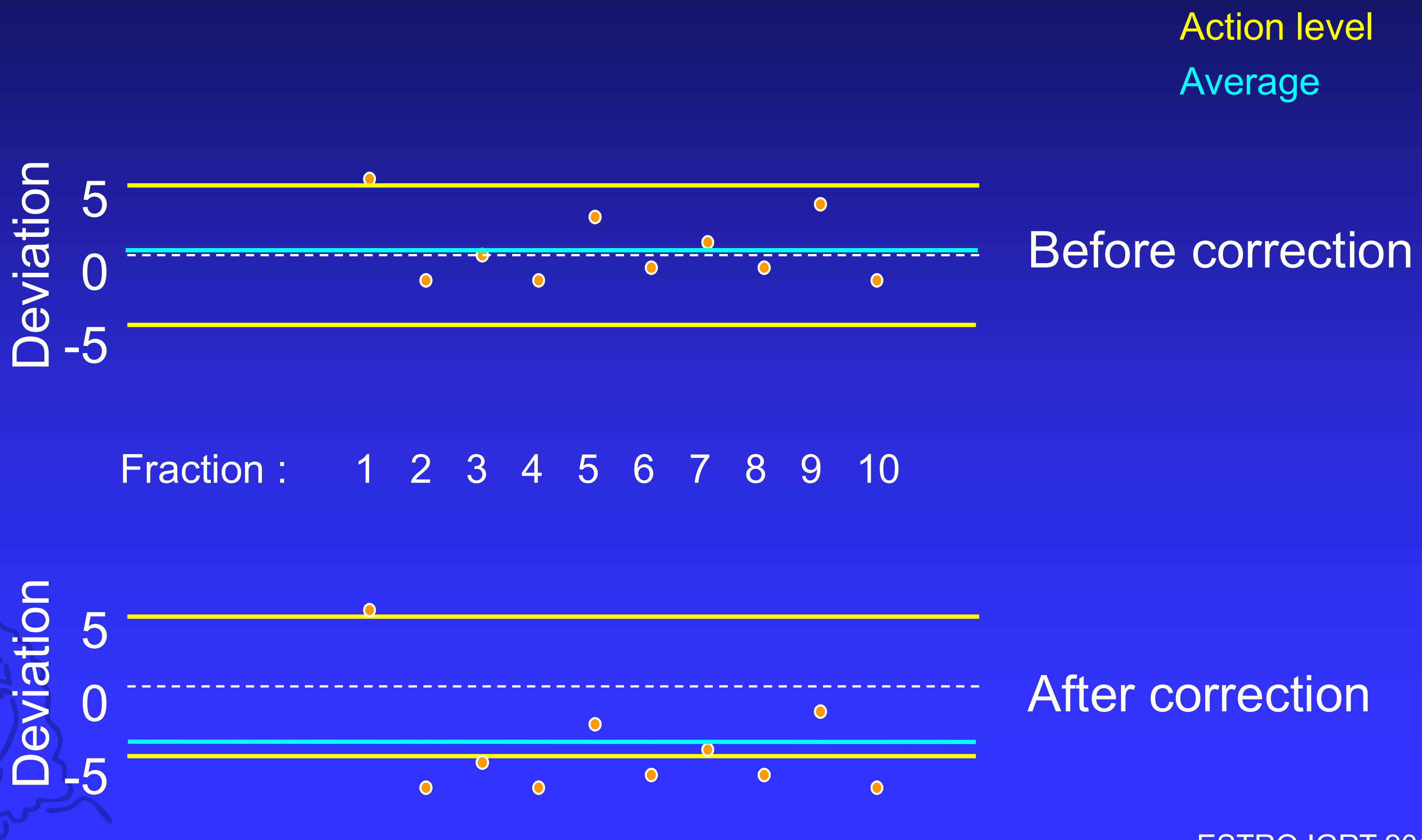
Ad-hoc correction protocol

- No day-to-day (random) variation



Ad-hoc correction protocol

- Normal day-to-day variation



Shrinking action level protocol (SAL)

Start; $N = 1$

Correct next fraction

Measure deviation

$N = N + 1$

Is average deviation larger than $\alpha/\sqrt{N}$?

Yes

No

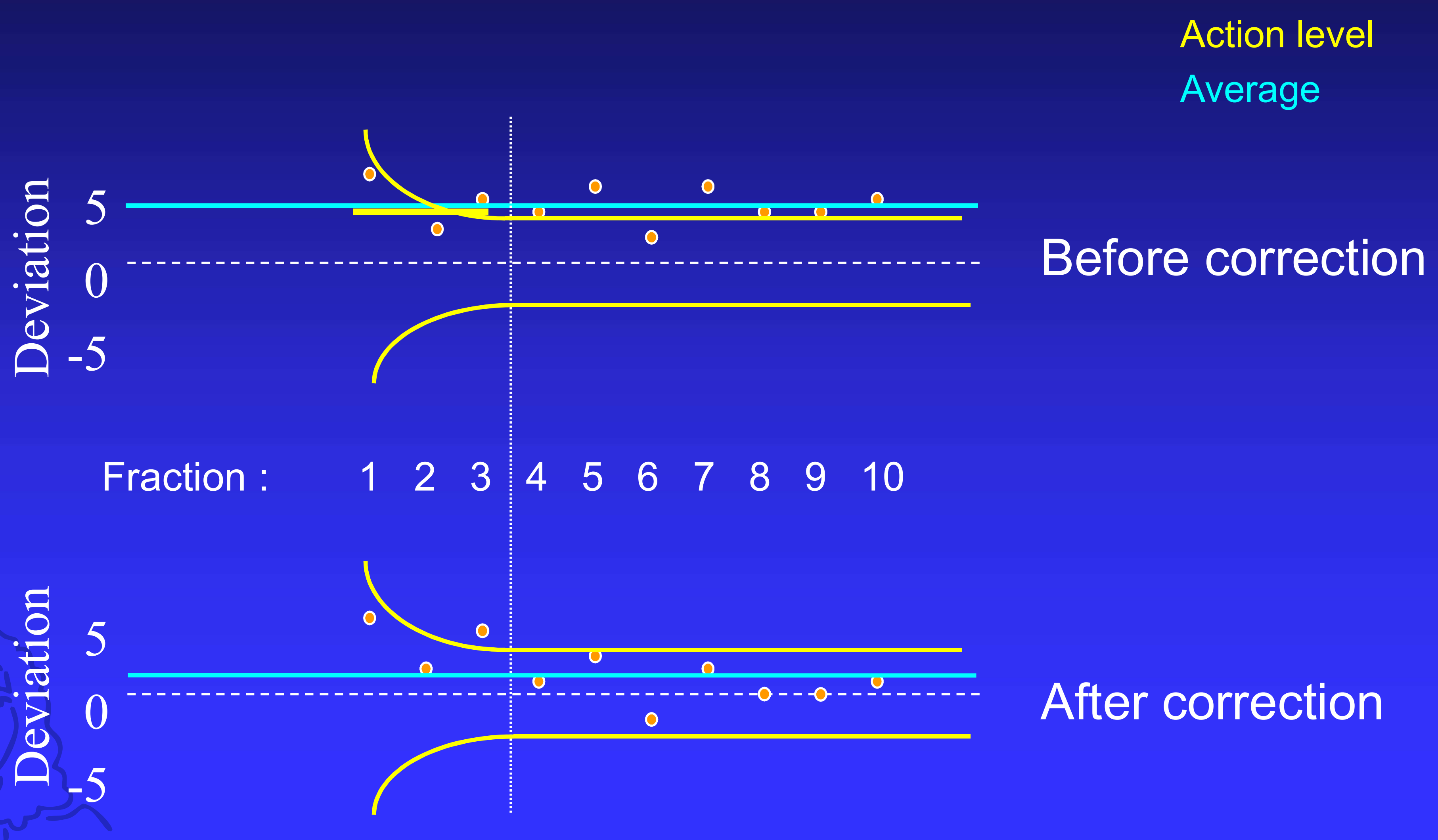
Is N smaller than N_{max} ?

Yes

No

Stop daily – start weekly measurements

SAL protocol

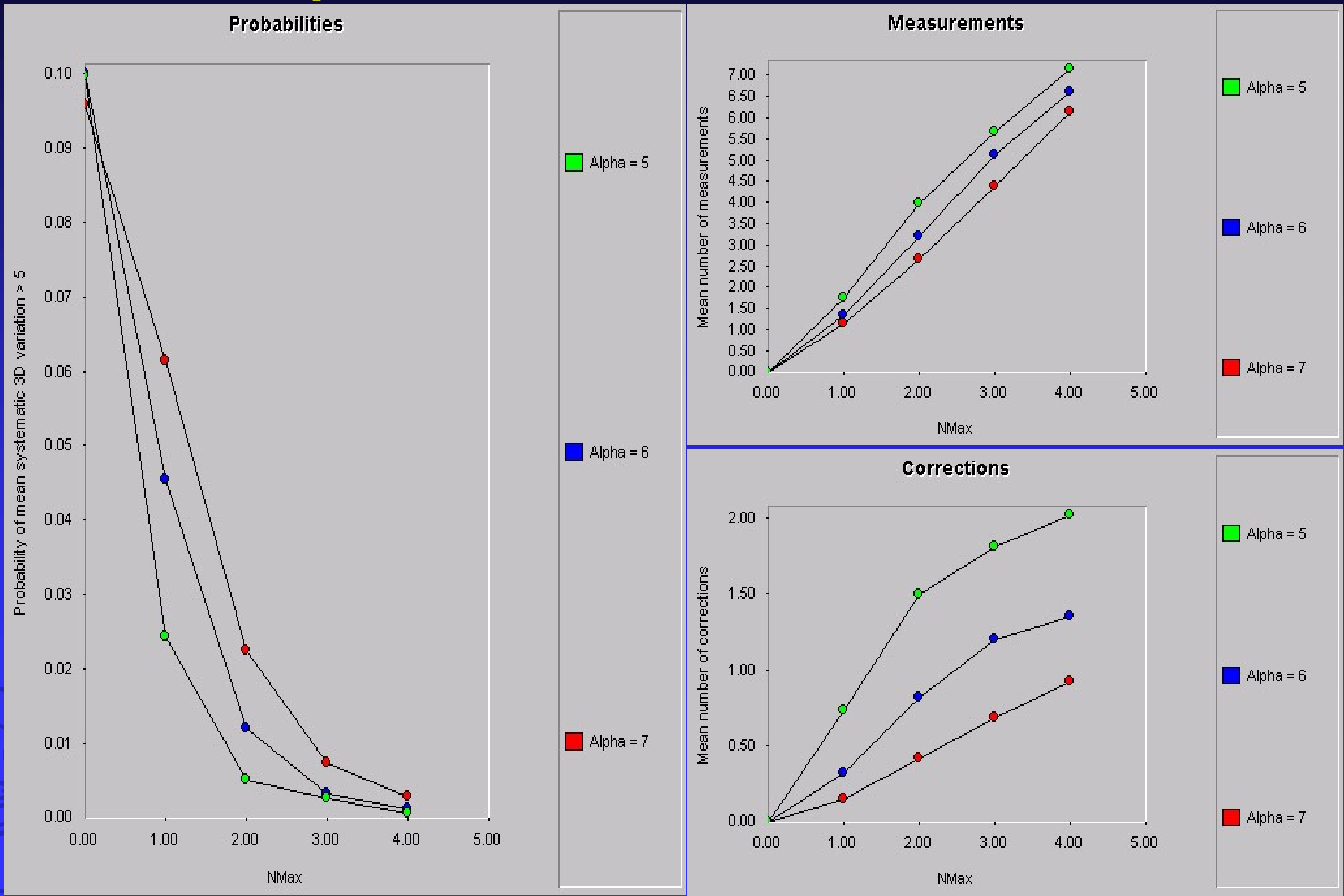


How to choose α and N_{max} ?

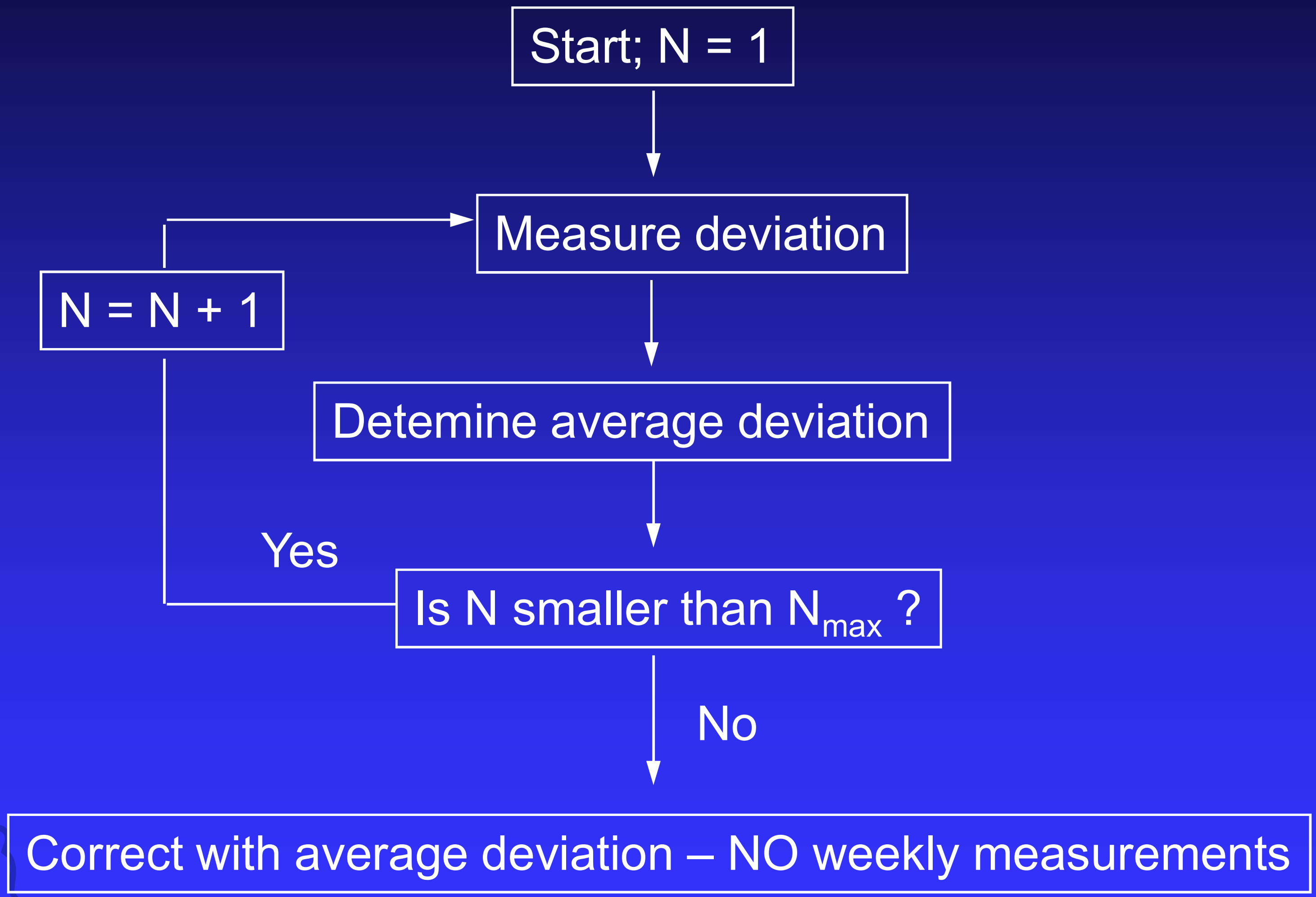
- Analytical computation not possible

$\Rightarrow$ Simulations: Apply Decision Rule on large number of ‘virtual’ patients

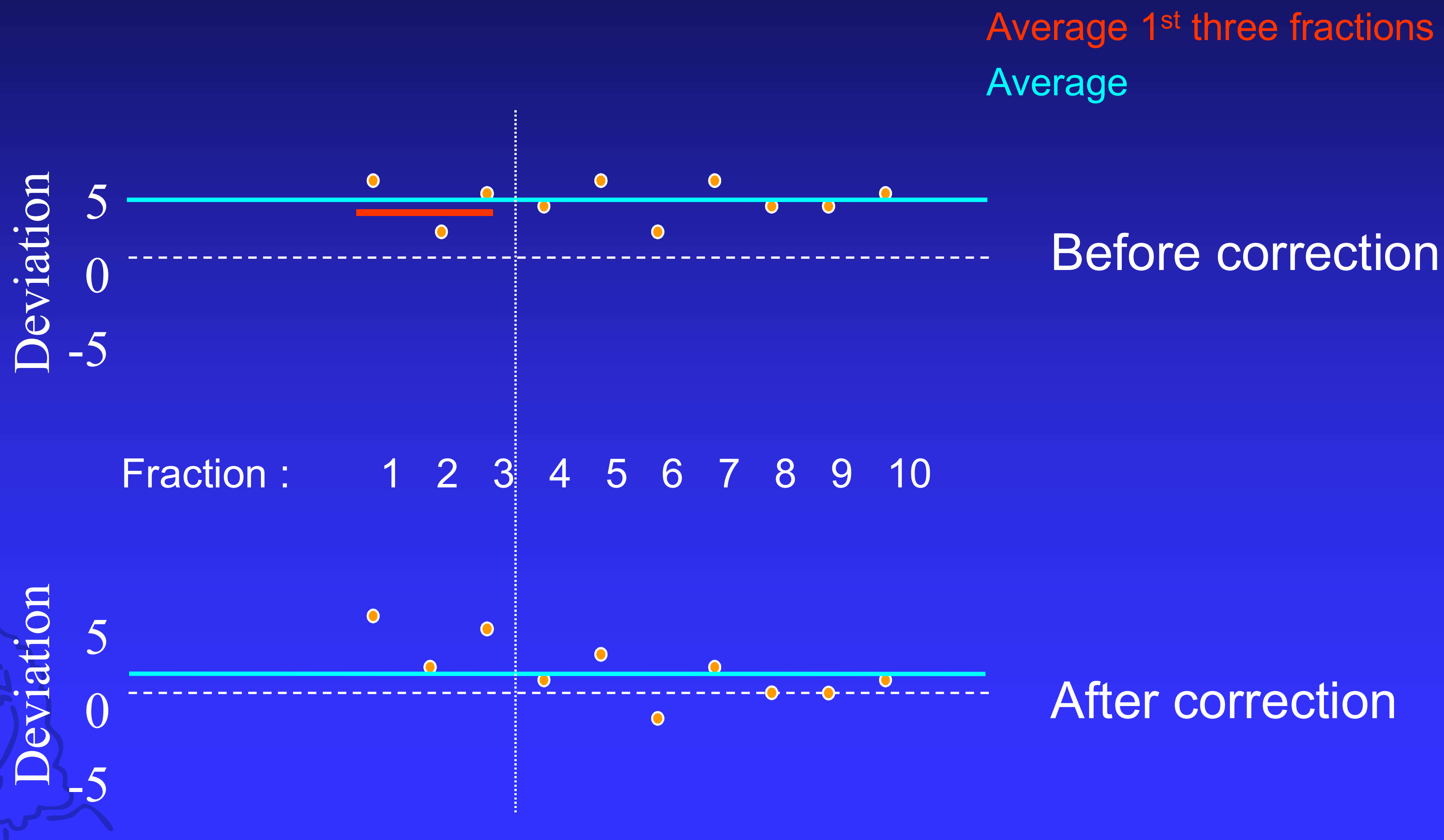
Example of simulation



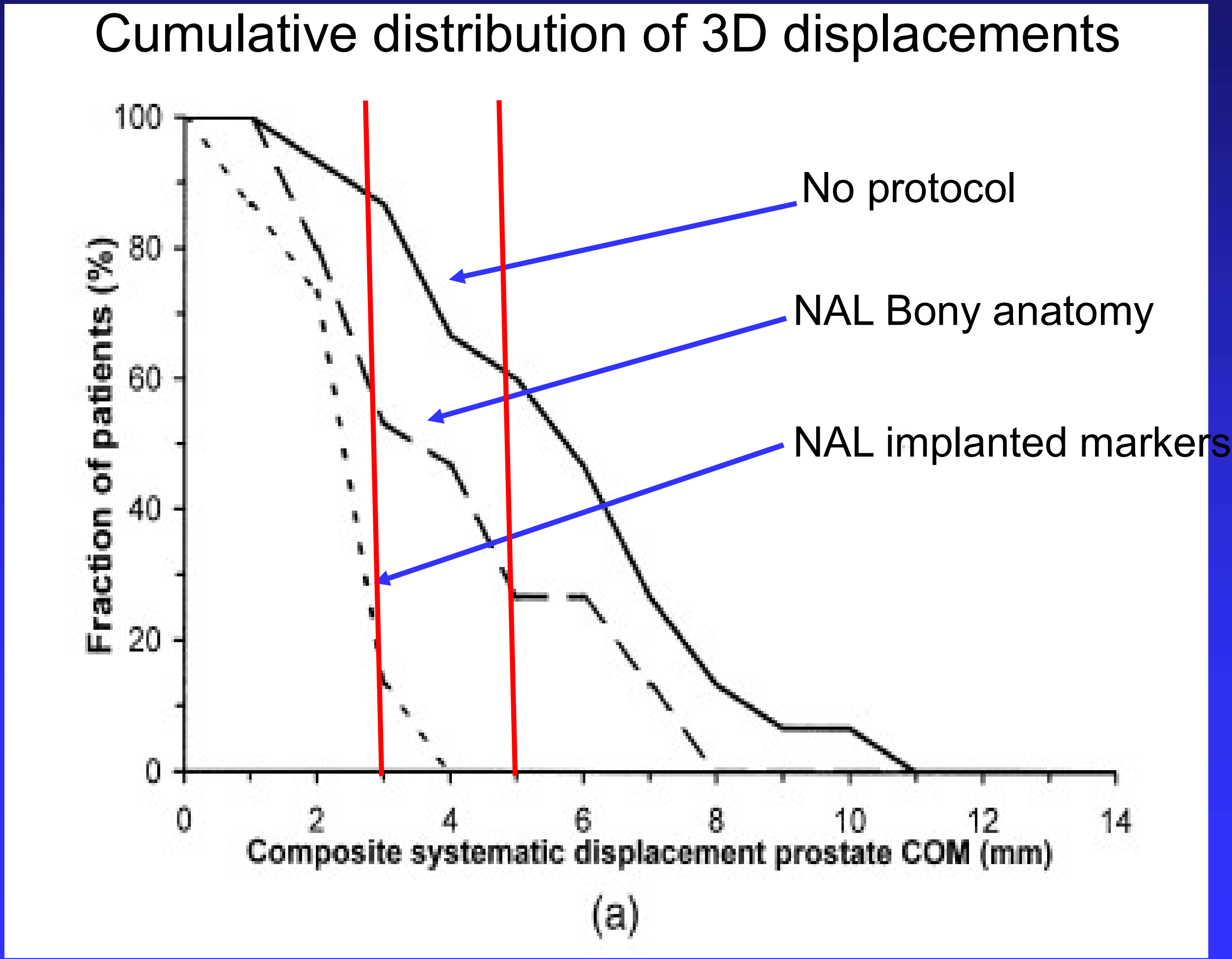
No action level protocol (NAL)



NAL protocol



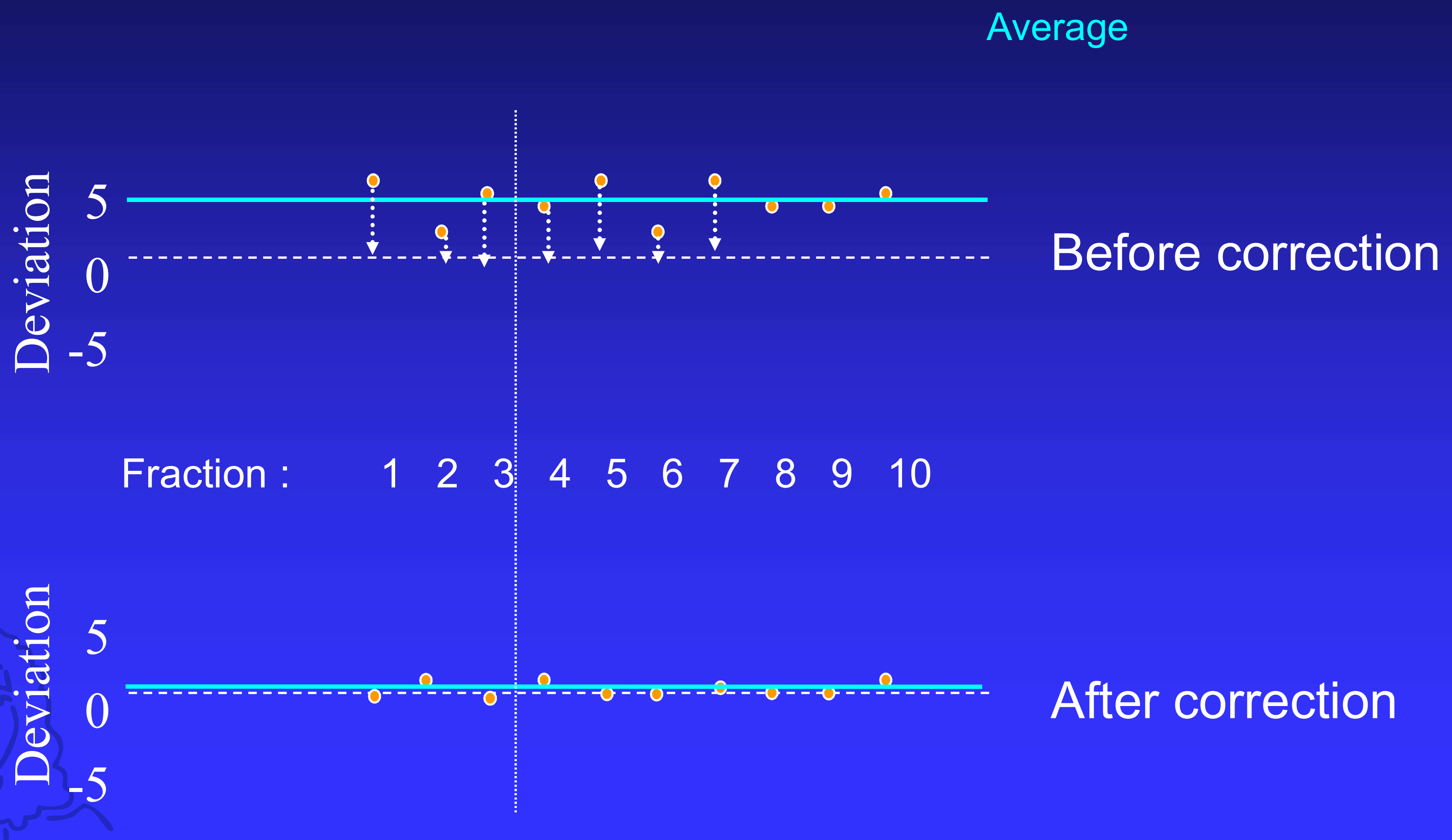
Benefit of the NAL protocol



*H.C. de Boer et al., Int J RO Biol Phys 2005, 61:969-983

Retrospective analysis of patient data

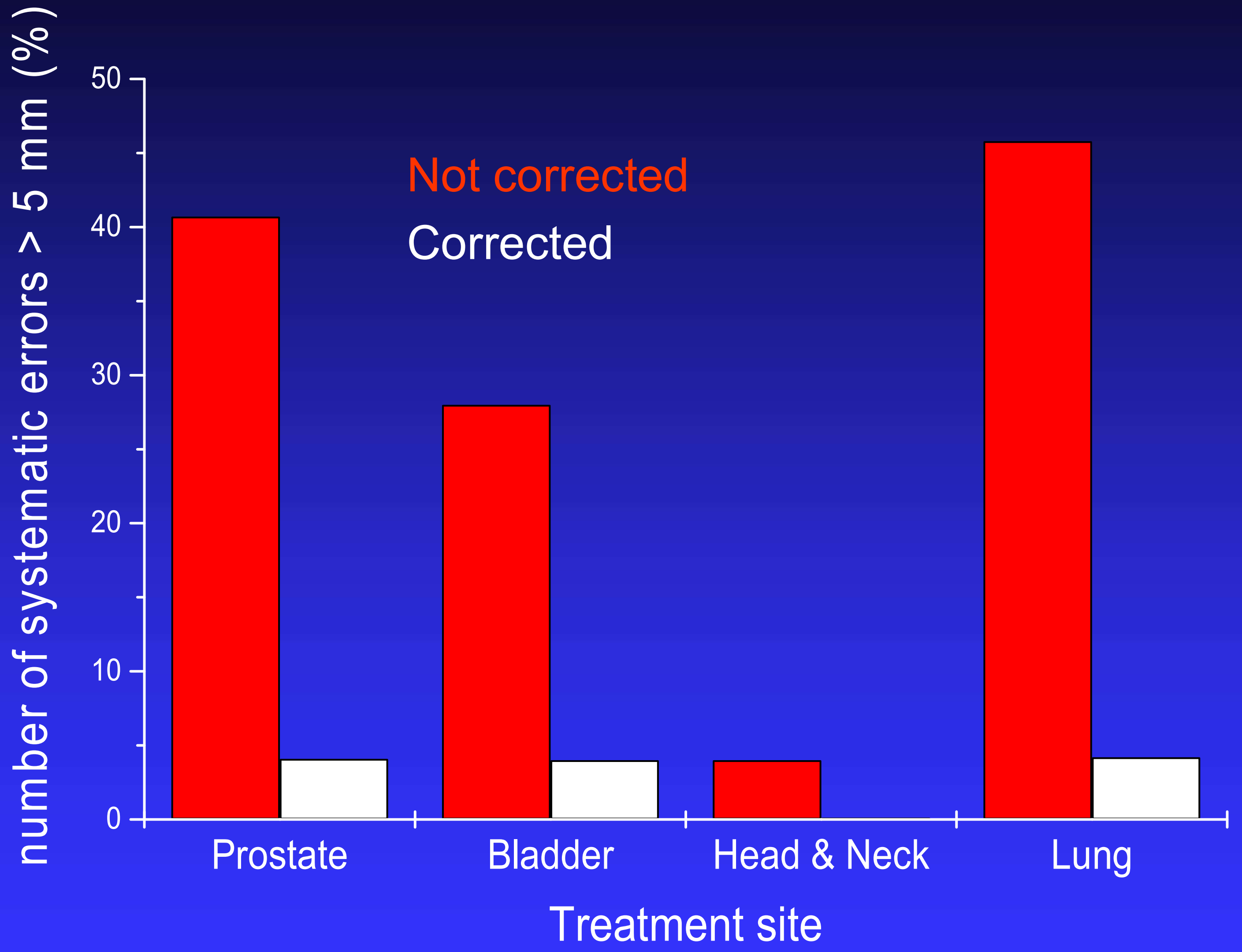
Online protocol



Setup correction protocol at NKI

- Shrinking action level protocol
- Parameters α and N_{max} optimized per patient group
- Weekly imaging after a number of uncorrected fractions

Offline corrections



Margin Example

		No Correction
Setup	Σ	3 mm
	σ	3 mm
Organ	Σ	4 mm
	σ	4 mm
Breathing	A	15 mm
	a	15 mm
Margin		**23 mm**

Margin Example

		No Correction	Offline Bone
Setup	Σ	3 mm	0 mm
	σ	3 mm	3 mm
Organ	Σ	4 mm	4 mm
	σ	4 mm	4 mm
Breathing	A	15 mm	15 mm
	a	15 mm	15 mm
Margin		**23 mm**	**21 mm**

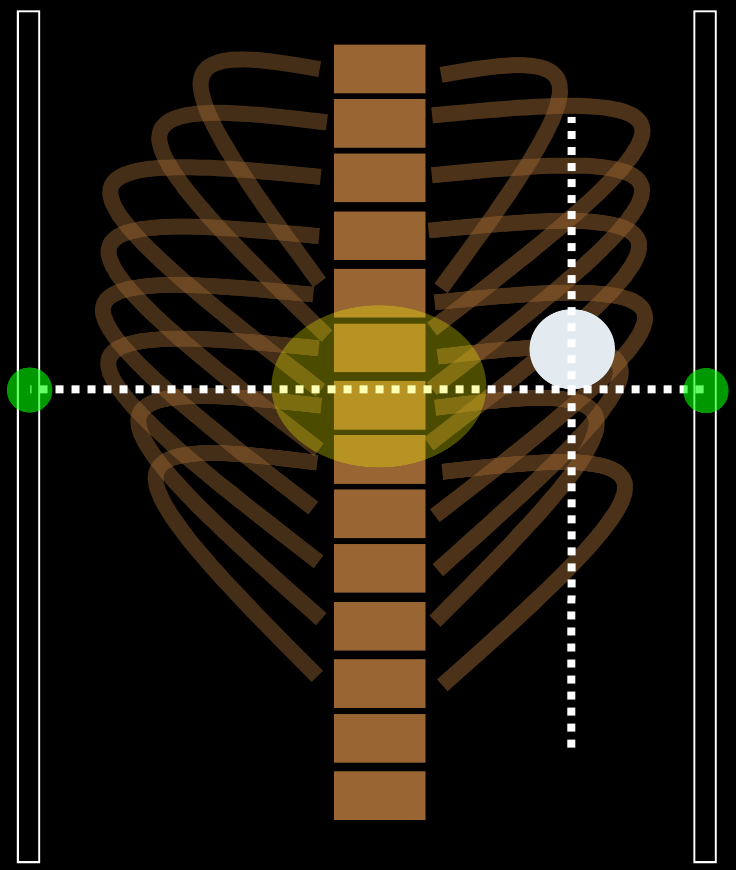
Margin Example

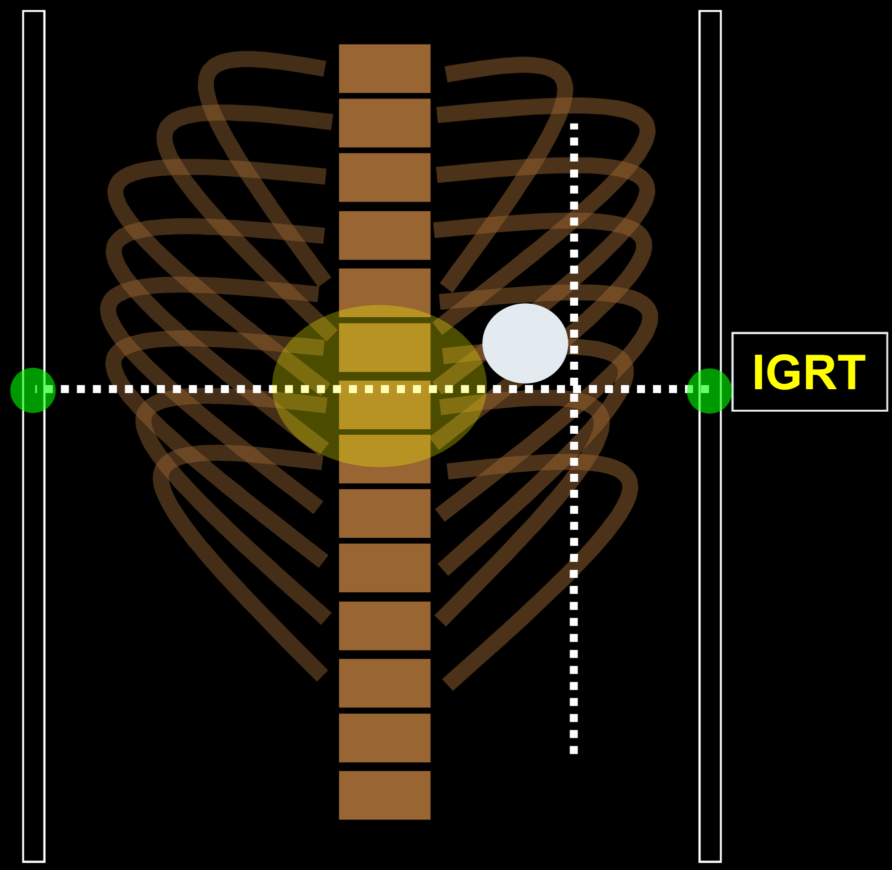
		No Correction	Offline Bone	Online Soft-tissue
Setup	Σ	3 mm	0 mm	0 mm
	σ	3 mm	3 mm	0 mm
Organ	Σ	4 mm	4 mm	1 mm
	σ	4 mm	4 mm	2 mm
Breathing	A	15 mm	15 mm	0 mm
	a	15 mm	15 mm	15 mm
Margin		**23 mm**	**21 mm**	**6 mm**

‘Small Errors’

		No Correction	Offline Bone	Online Soft-tissue
Setup	Σ	3 mm	0 mm	0 mm
	σ	3 mm	3 mm	0 mm
Organ	Σ	4 mm	4 mm	1 mm
	σ	4 mm	4 mm	2 mm
Breathing	A	15 mm	15 mm	0 mm
	a	15 mm	15 mm	15 mm
Delineation	Σ	**2 mm**	**2 mm**	**2 mm**
Margin		**24 mm**	**22 mm**	**9 mm**

Internal target position variability – base line shift



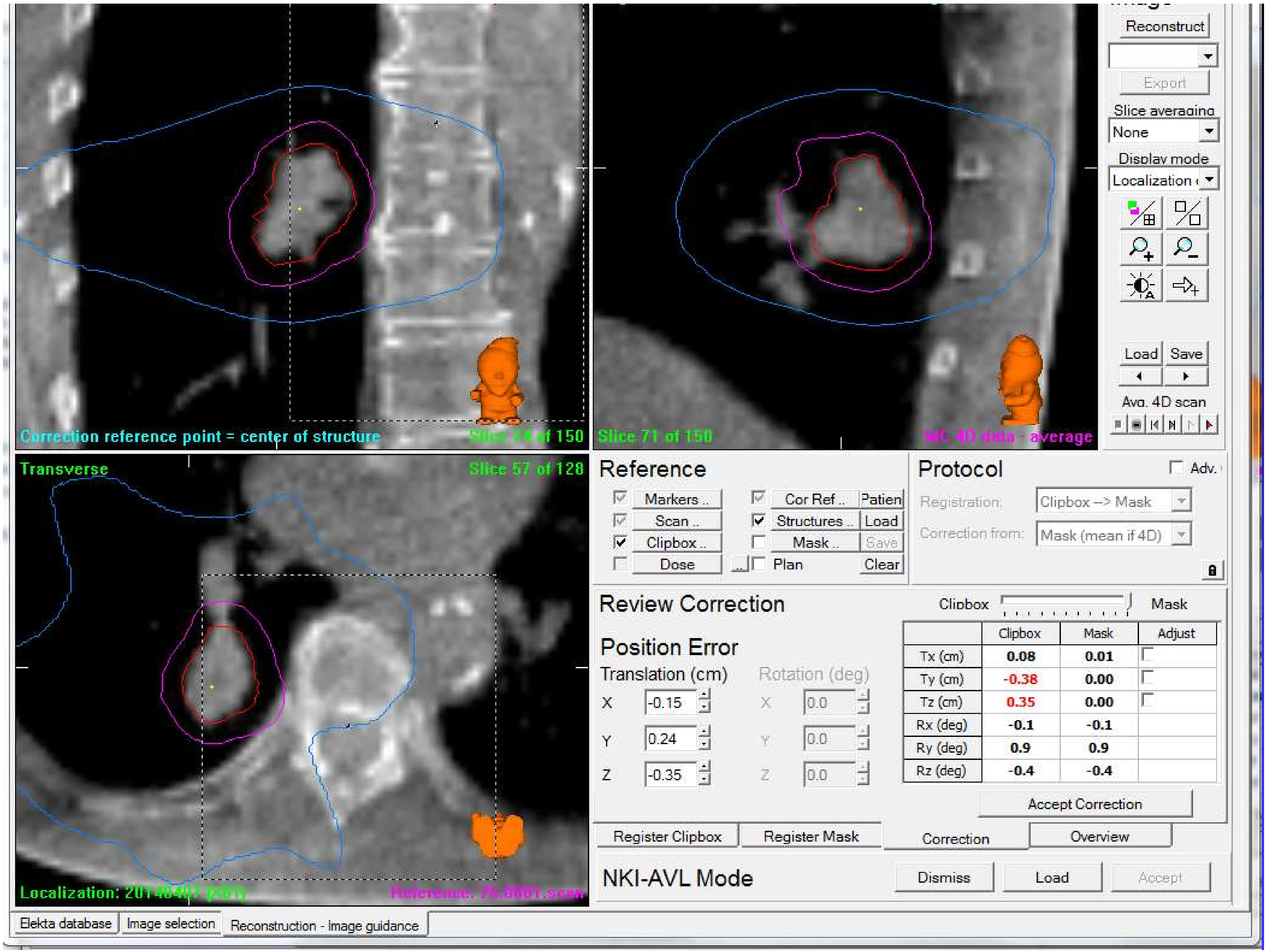


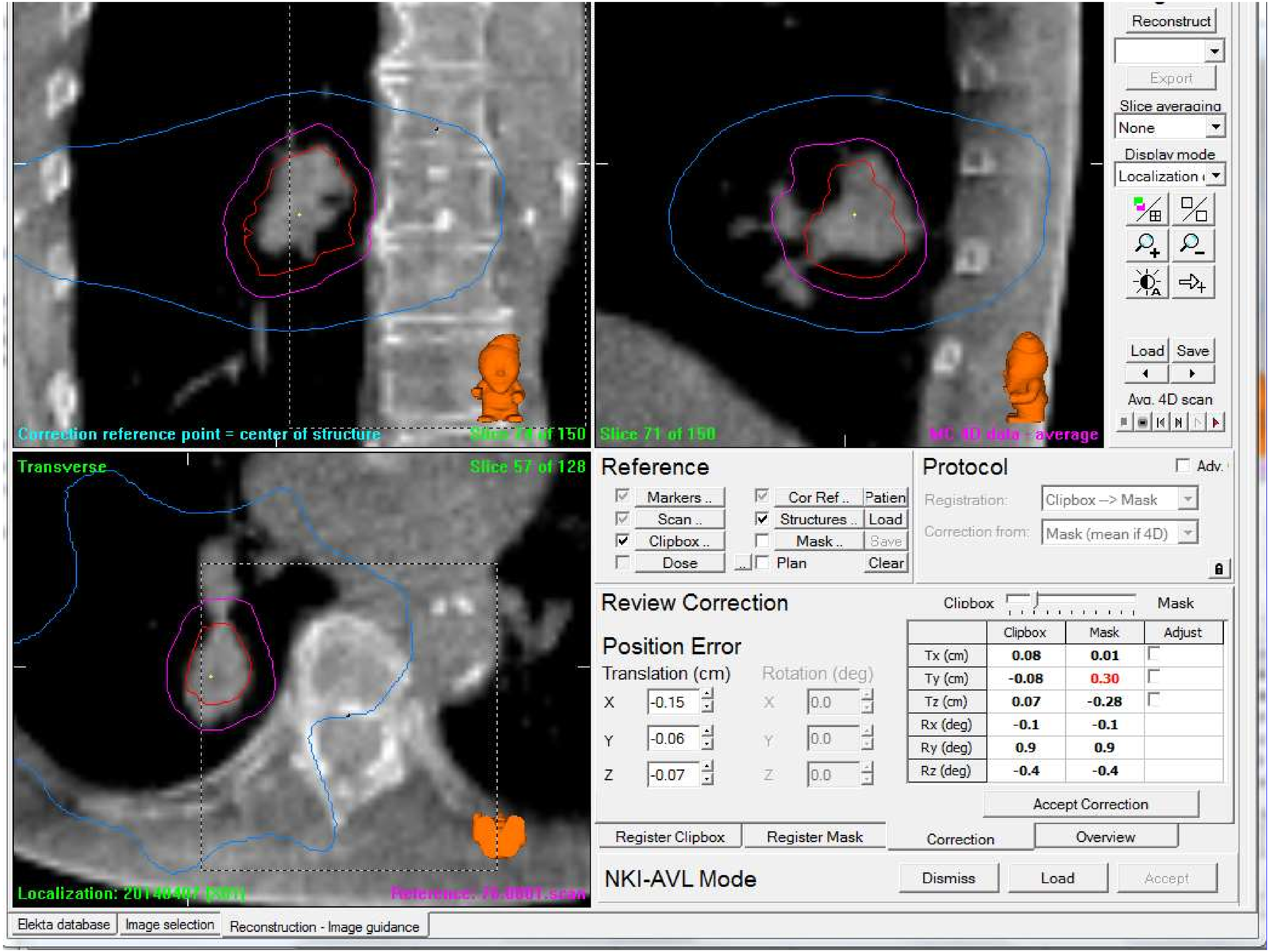
Planning:

Definition of stereotactic isocentre

Treatment:

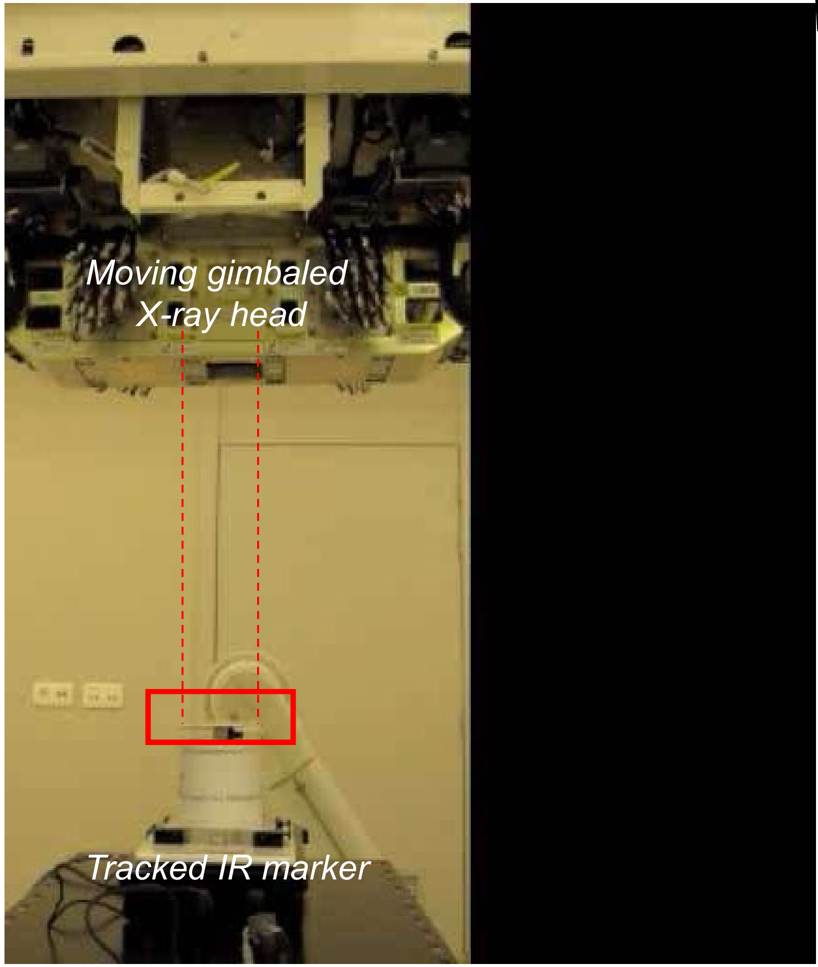
Stereotactic positioning

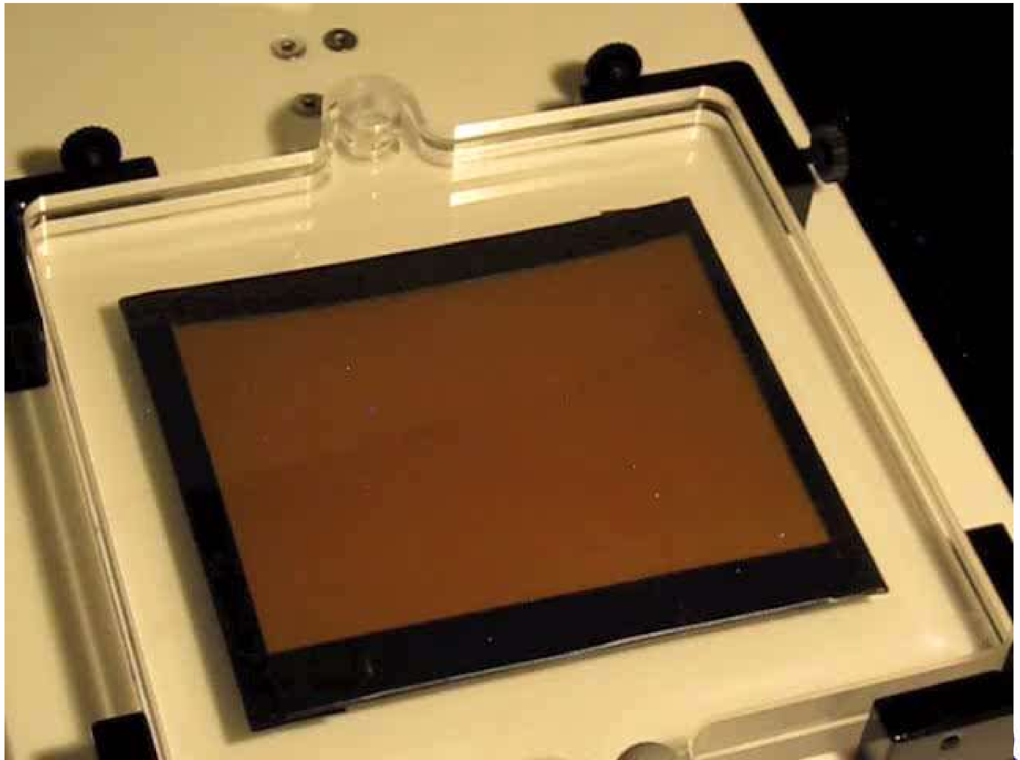

Reconstruct
Export
Slice averaging
None
Display mode
Localization
Load
Save
Avg. 4D scan
Correction reference point = center of structure
Slice 71 of 150
Transverse
Slice 57 of 128
Reference
Markers ..
Scan ..
Clipbox ..
Dose
Cor Ref ..
Structures ..
Mask ..
Plan
Patien
Load
Save
Clear
Protocol
Adv.
Registration:
Clipbox --> Mask
Correction from:
Mask (mean if 4D)
Review Correction
Clipbox
Mask
Position Error
Translation (cm)
Rotation (deg)
X -0.15
Y 0.24
Z -0.35
X 0.0
Y 0.0
Z 0.0
Clipbox Mask Adjust
Tx (cm) 0.08 0.01
Ty (cm) -0.38 0.00
Tz (cm) 0.35 0.00
Rx (deg) -0.1 -0.1
Ry (deg) 0.9 0.9
Rz (deg) -0.4 -0.4
Accept Correction
Register Clipbox
Register Mask
Correction
Overview
NKI-AVL Mode
Dismiss
Load
Accept
Elekta database
Image selection
Reconstruction - Image guidance


Reconstruct
Export
Slice averaging
None
Display mode
Localization
Load
Save
Avg. 4D scan
Correction reference point = center of structure
Slice 71 of 150
Transverse
Slice 57 of 128
Reference
Markers ..
Scan ..
Clipbox ..
Dose
Cor Ref ..
Patien
Structures ..
Load
Mask ..
Save
Plan
Clear
Protocol
Adv.
Registration:
Clipbox --> Mask
Correction from:
Mask (mean if 4D)
Review Correction
Clipbox
Mask
Position Error
Translation (cm)
Rotation (deg)
X -0.15
Y -0.06
Z -0.07
X 0.0
Y 0.0
Z 0.0
	Clipbox	Mask	Adjust
Tx (cm)	0.08	0.01	
Ty (cm)	-0.08	0.30	
Tz (cm)	0.07	-0.28	
Rx (deg)	-0.1	-0.1	
Ry (deg)	0.9	0.9	
Rz (deg)	-0.4	-0.4	
Accept Correction
Register Clipbox
Register Mask
Correction
Overview
NKI-AVL Mode
Dismiss
Load
Accept
Elekta database
Image selection
Reconstruction - Image guidance

Tracking

Writing "UZB" with the 6 MV beam in a moving GafChromic film with gimbals pan/tilt movements





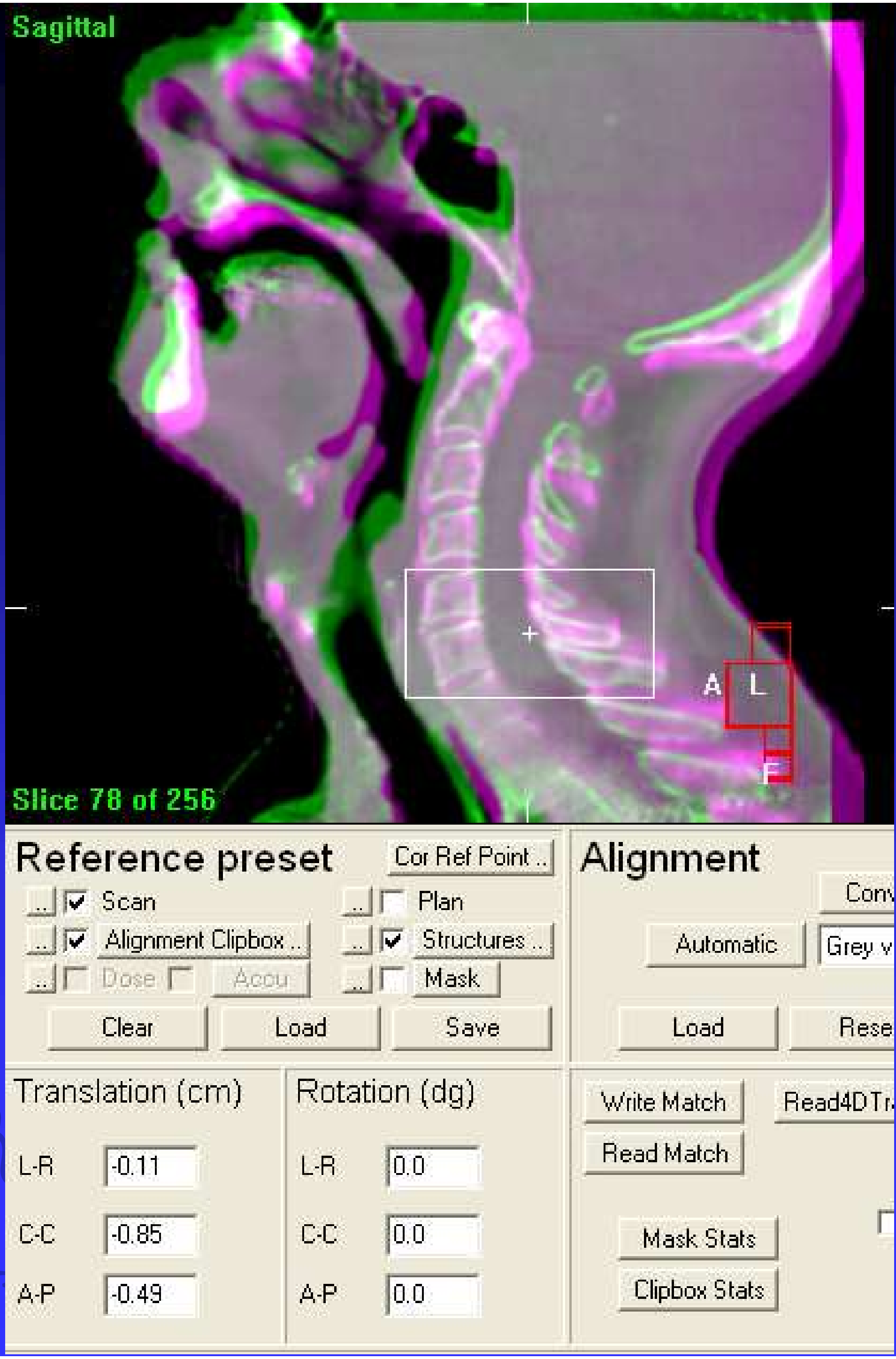
(3x FFW)

CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

VERO system UZ Brussel, 2010

Courtesy of Tom Depuydt

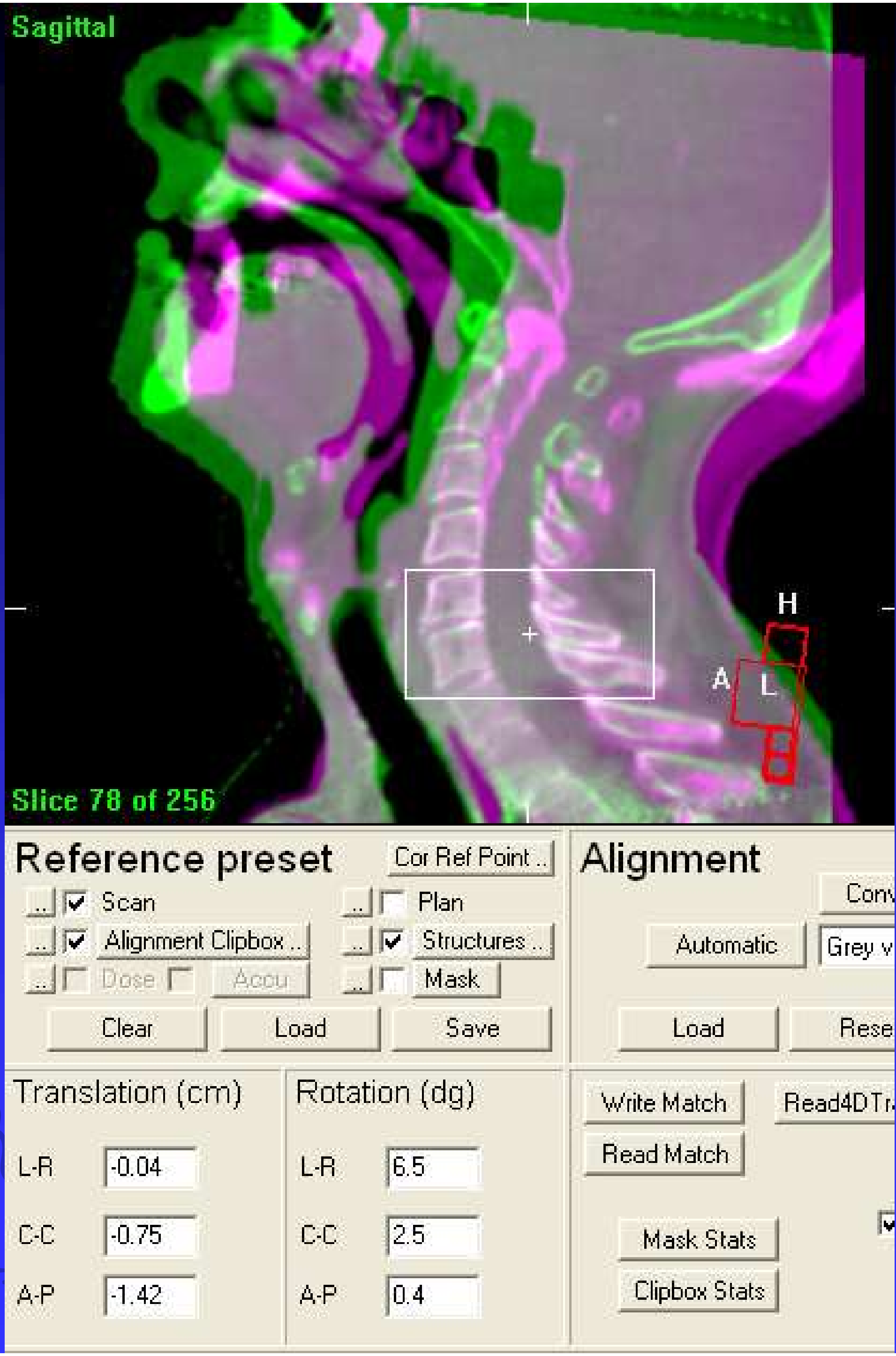
Correcting for Rotations



Automatic matching on region of interest *without* rotations

reference
localization

Automatic matching on region of interest *with* rotations



reference
localization

Rotations (bone) measured with CBCT (°): SD (|max|)

Head & neck (55 scans) [big clipbox]	LR	1.1	(2.6)
	CC	1.0	(3.3)
	AP	1.0	(3.2)
Pelvis (554 scans)	LR	1.6	(9.7)
	CC	0.8	(3.8)
	AP	0.5	(3.7)
Lung (274 scans)	LR	1.1	(5.3)
	CC	1.2	(3.6)
	AP	1.5	(4.7)

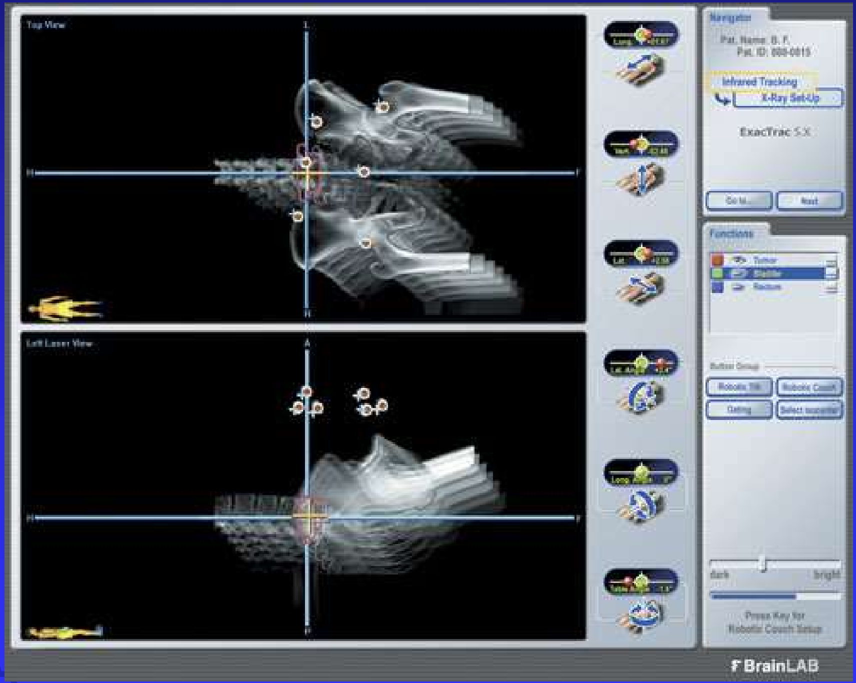
Tilt and roll couches

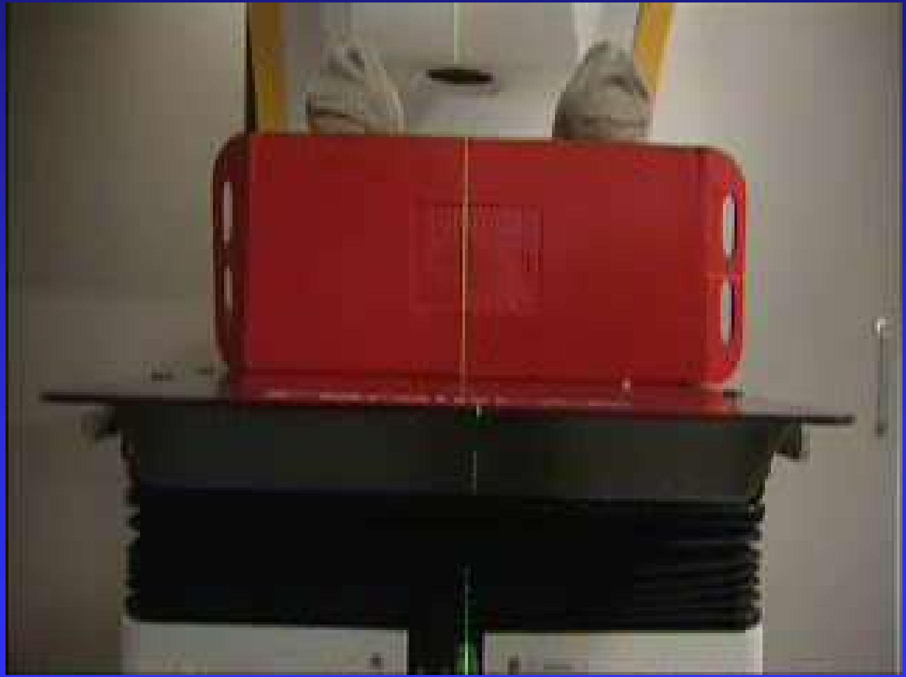
- Hornick DC, Litzenberg DW, Lam KL, Balter JM, Hetrick J, Ten Haken RK.
  - A tilt and roll device for automated correction of rotational setup errors. Med Phys. 1998 Sep;25(9):1739-40.

- Abandoned because of patient comfort:
  - More than 3 degrees rotation impossible
  - Is this a relevant angle to correct?

6 degrees of freedom couch

Stine Korreman





Literature

- Guckenberger et al. *Precision of image-guided radiotherapy (IGRT) in six degrees of freedom and limitations in clinical practice.* Strahlenther Onkol. 2007 Jun;183(6):307-13

  → Reported 0.6 mm compensating translation per degree rotation for non-immobilized patients

- Linthout et al. *Assessment of secondary patient motion induced by automated couch movement during on-line 6 dimensional repositioning in prostate cancer treatment.* Radiother Oncol. 2007 May;83(2):168-74.

  → Reported negligible secondary motion, but did not correlate the motion to the amount of rotation

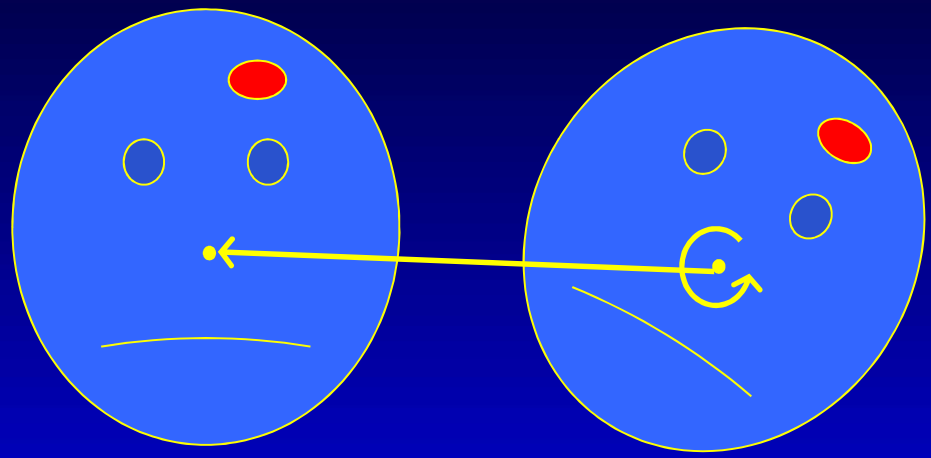
Smart ignoring of rotations

- Cone beam CT image guidance provides more detail about patient setup than currently can be corrected
- The solution is to make correction an optimization process: i.e., perform correction such that best CTV coverage is obtained
- For correcting rotations with just a couch shift, this is equivalent to optimizing one point: the correction reference point

Registration procedure

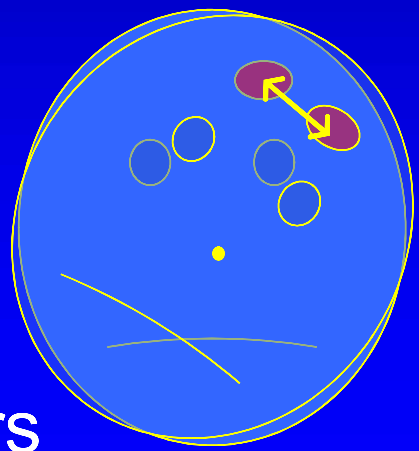
Registration

- Bony anatomy
- Translations and rotations
- Very accurate



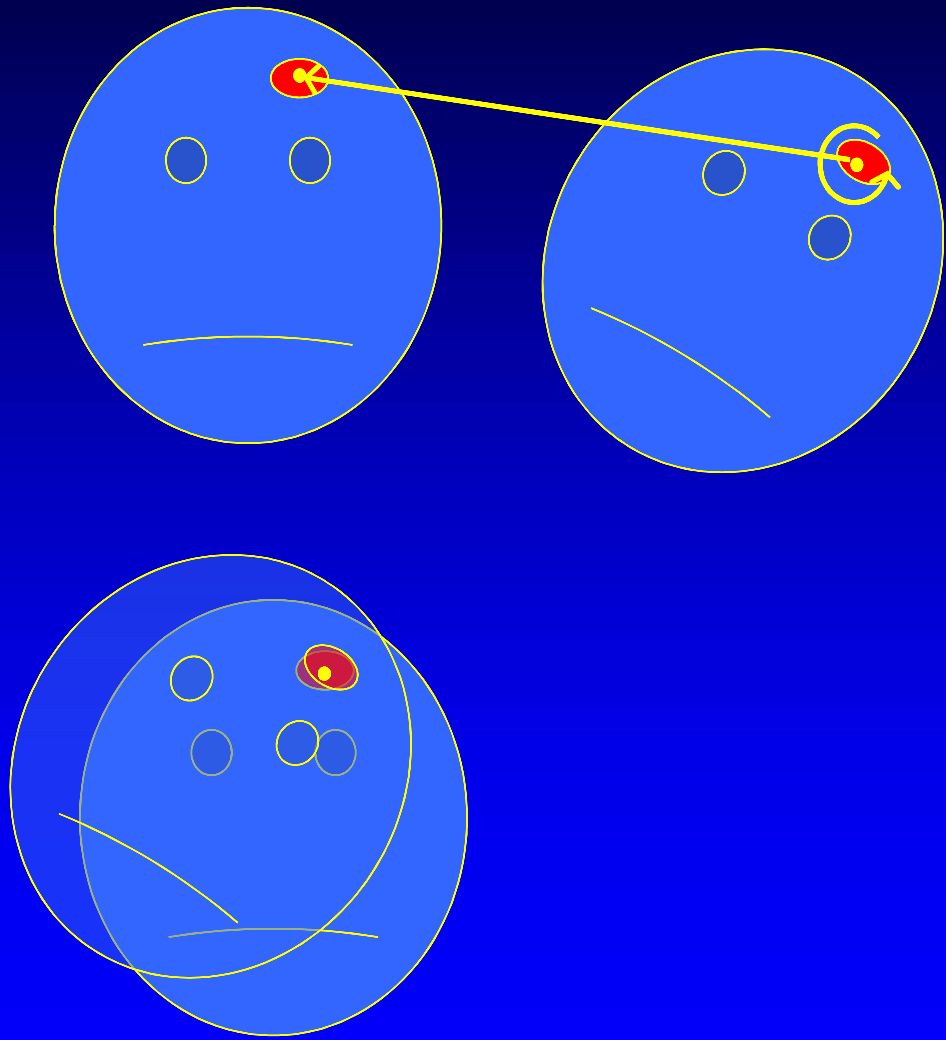
Correction

- Only translations
- Potentially large errors



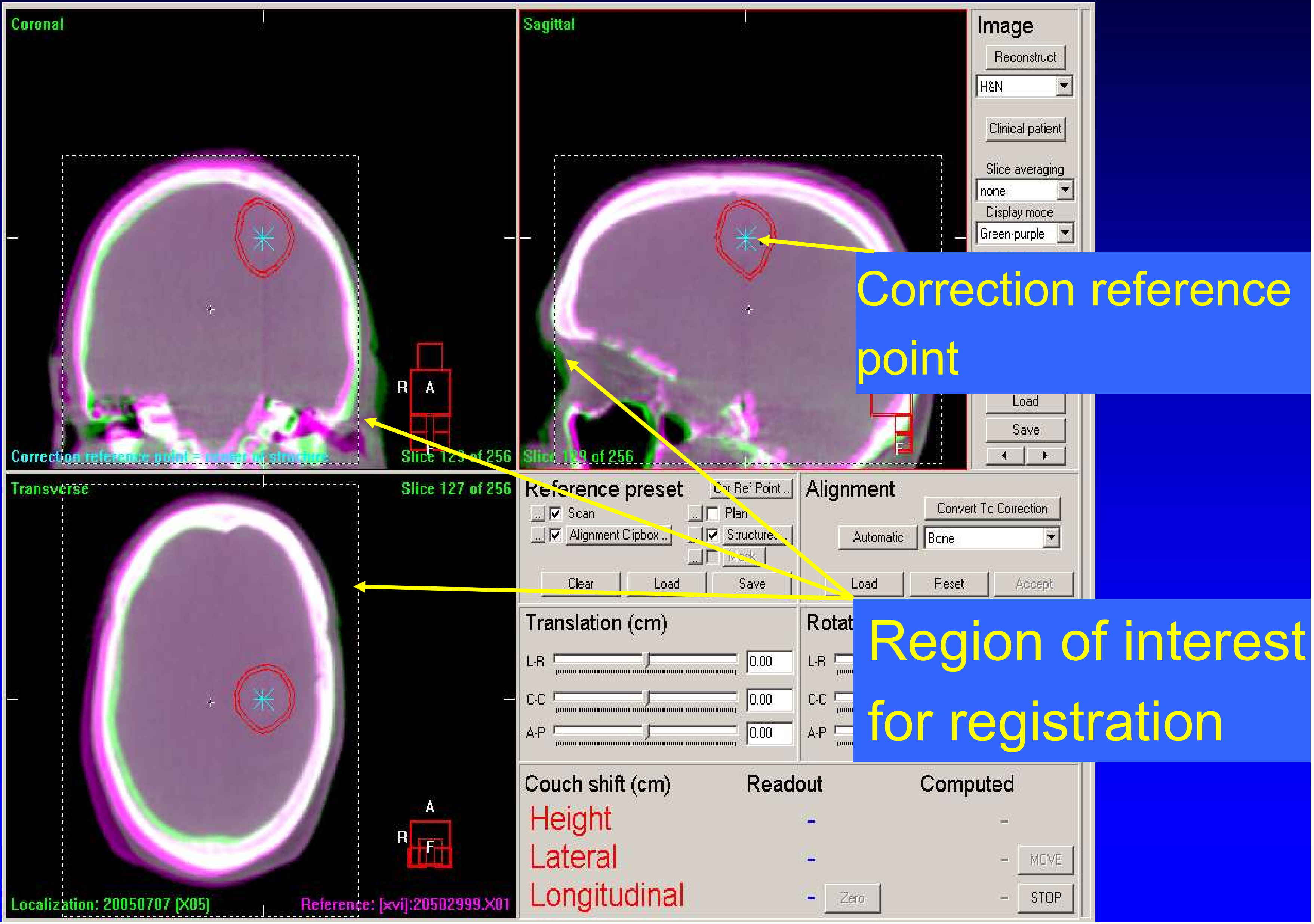
Registration procedure – Rotational errors

Registration
- Bony anatomy
- Redefine center of rotation (correction reference point)

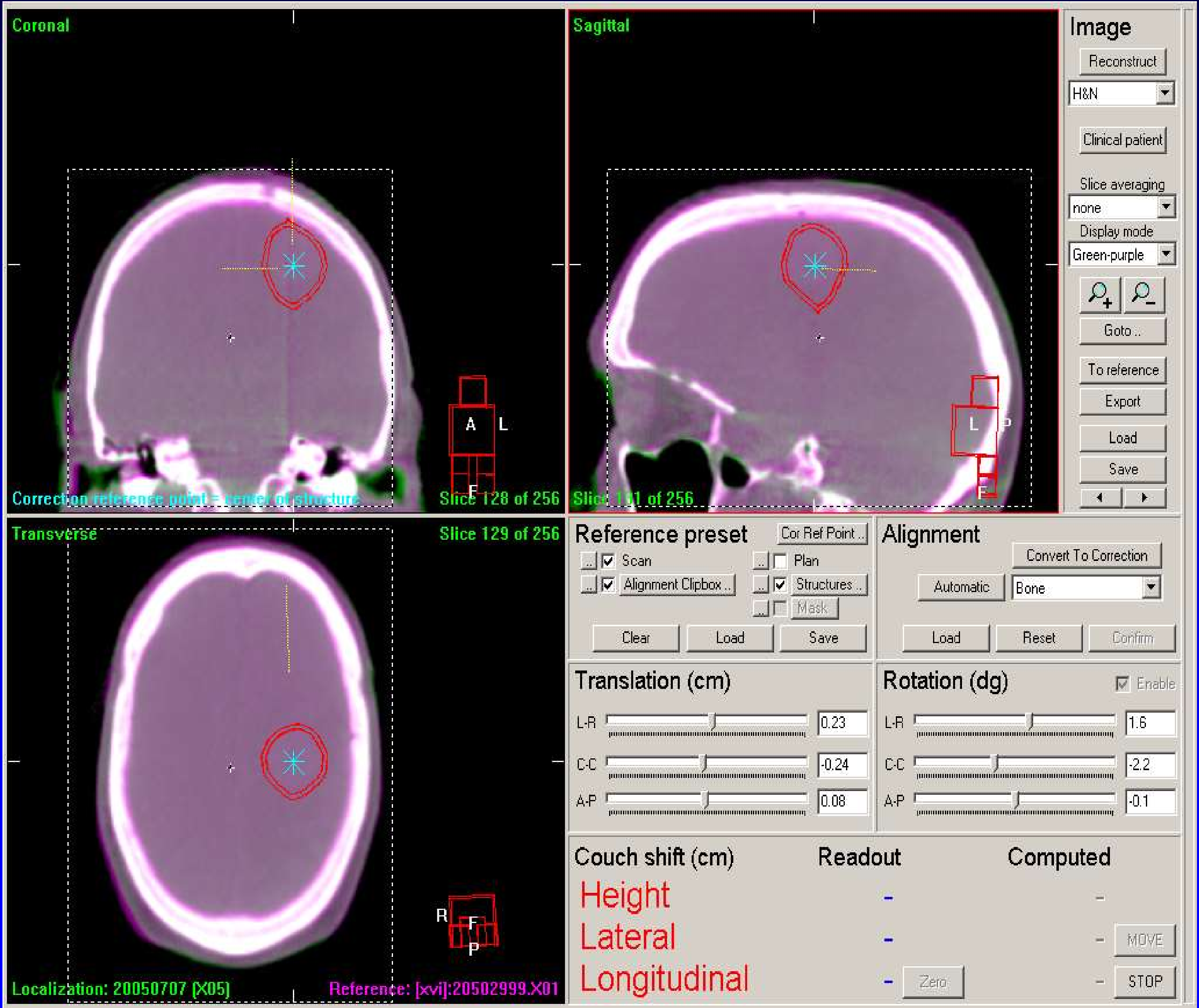


Correction
- Only translations
- Rotational errors are small close to rotation center

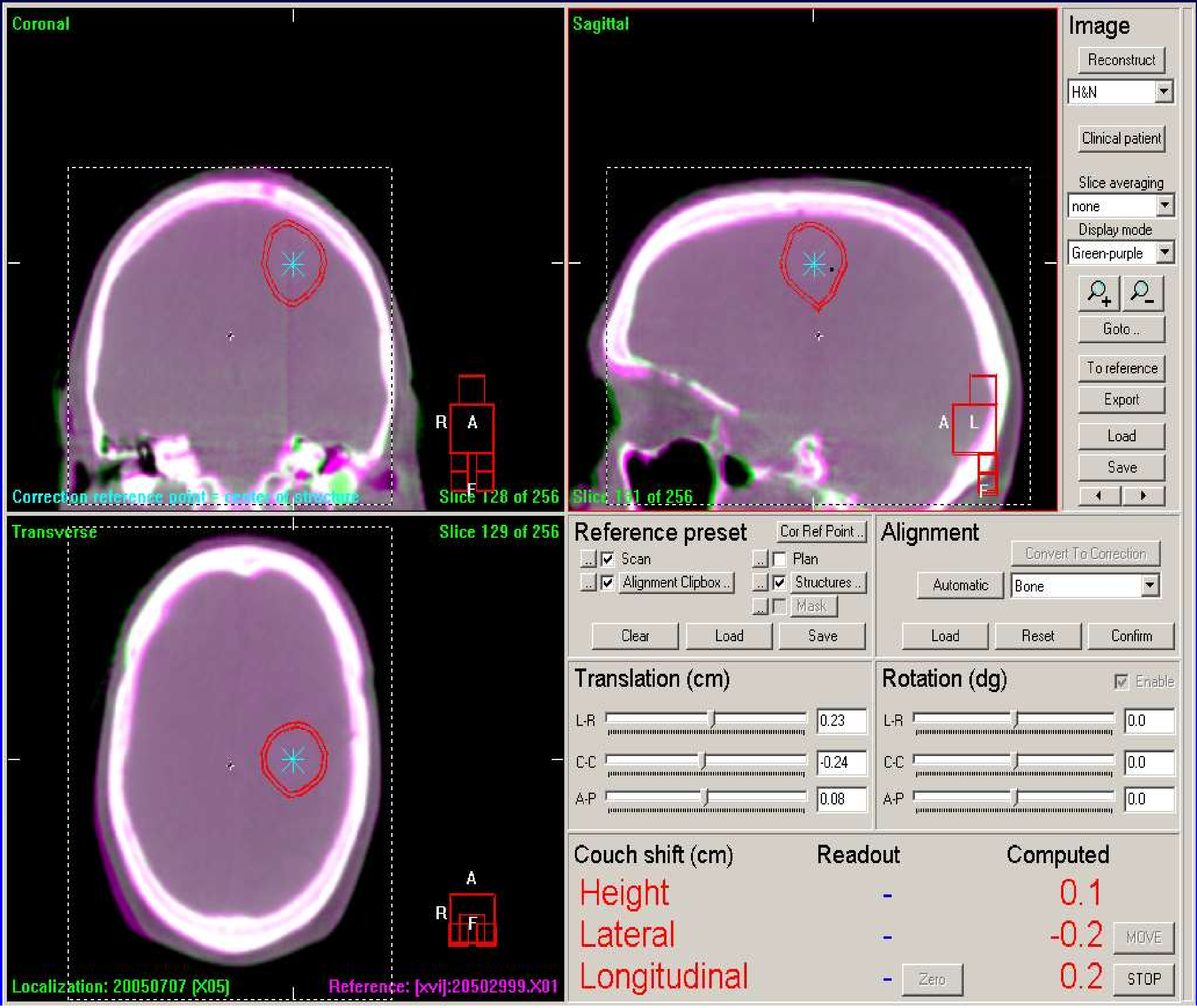
Registration procedure – not matched



Registration procedure – matched

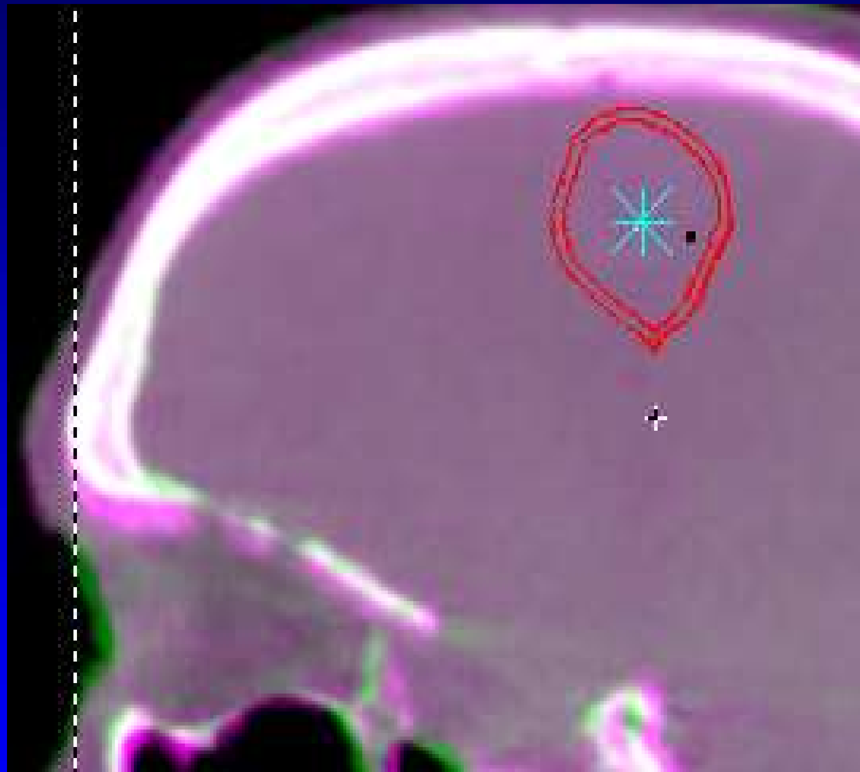


Registration procedure – rotations removed



Registration procedure – Rotational errors

Match including rotations

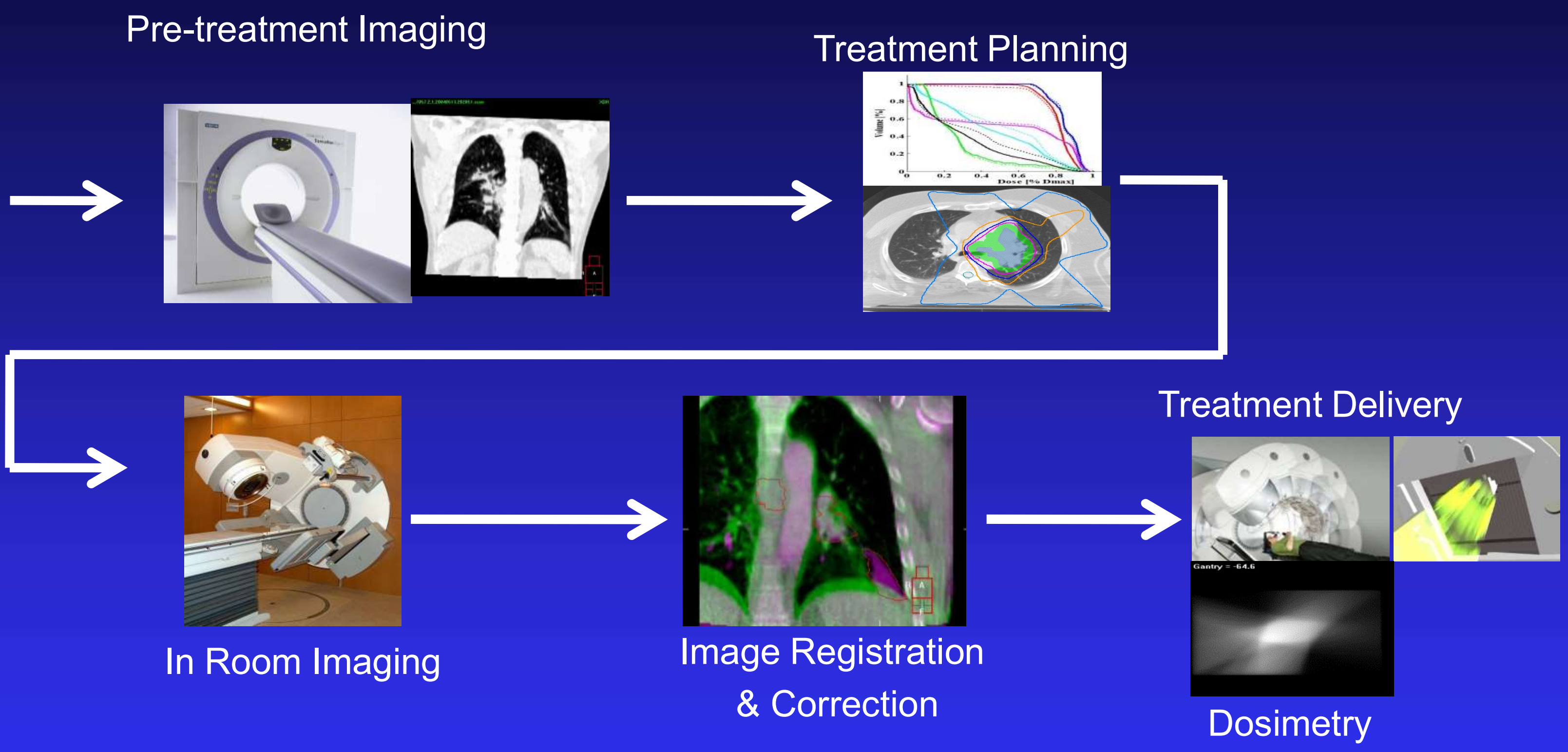


Match without rotations

Difference between translation part of registration and correction (mm) - lung

	LR	CC	AP
Mean	0.1	0.0	0.1
SD	0.6	0.7	0.9
Range	-2.5 .. 2.0	-2.1 .. 3.4	-2.3 .. 5.9

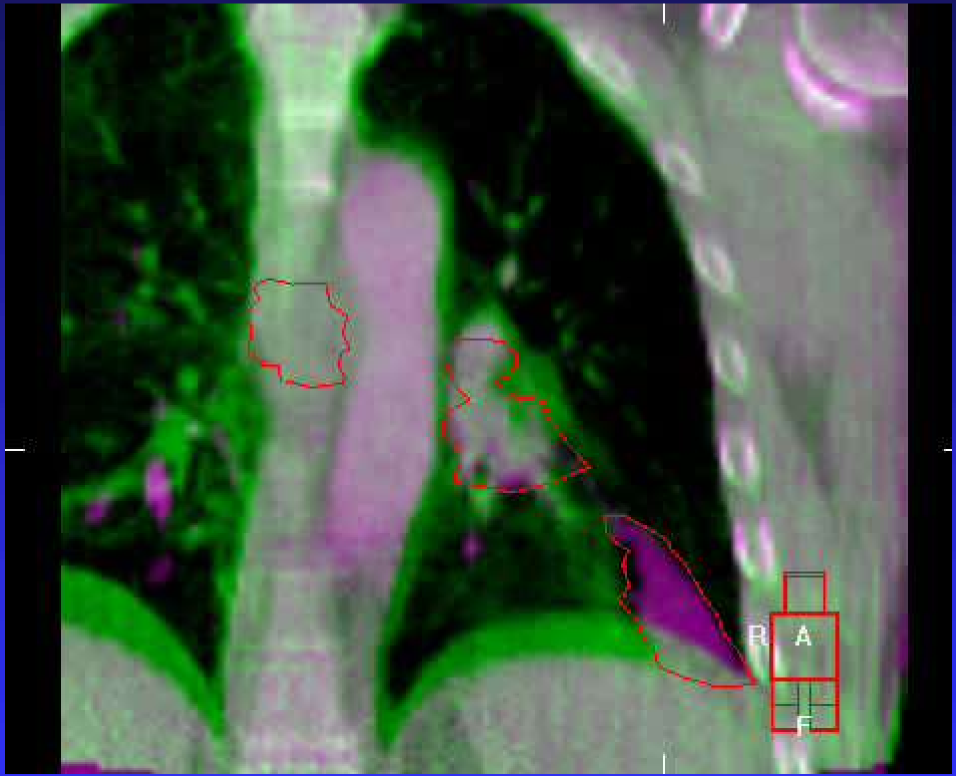
The modern radiotherapy process

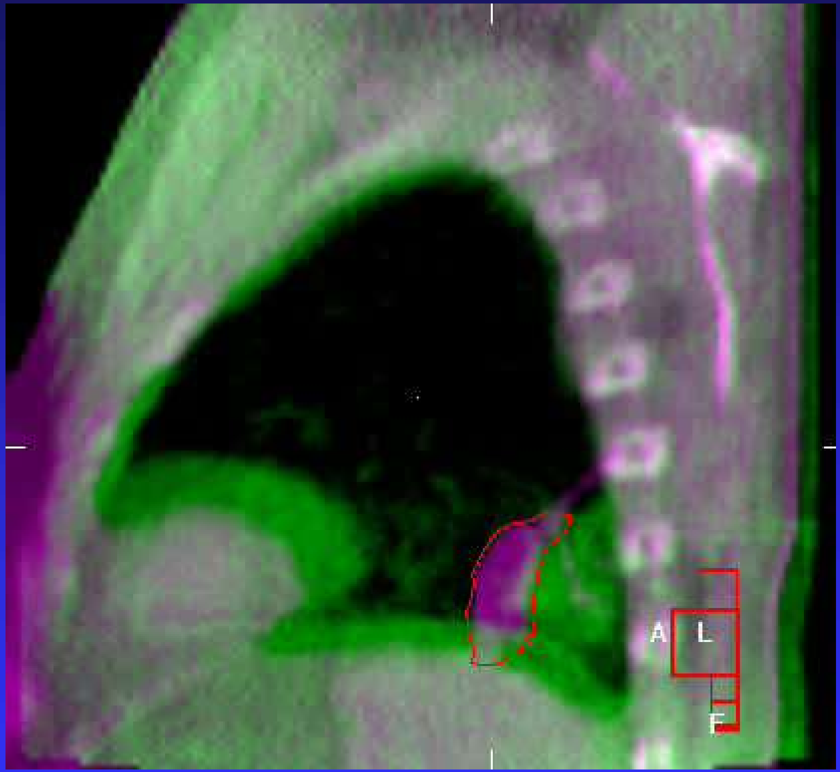


Very high accuracy achieved

Are all problems now solved ?

Differential Motion





No couch correction can solve this problem

Adaptive Radiotherapy

The Start of Adaptive Radiotherapy

IJROBP 1997; 38: 197-206

- *Physics Contribution*

ADAPTIVE MODIFICATION OF TREATMENT PLANNING TO MINIMIZE THE DELETERIOUS EFFECTS OF TREATMENT SETUP ERRORS

DI YAN, D.SC.,* JOHN WONG, PH.D.,* FRANK VICINI, M.D.,* JEFF MICHALSKI, M.D.†
CHENG PAN, PH.D.,* ARTHUR FRAZIER, M.D.,* ERIC HORWITZ, M.D.*
AND ALVARO MARTINEZ, M.D., F.A.C.R.*

In this study, a new approach, called adaptive radiation therapy (ART), is introduced to minimize the deleterious effects of setup variation on each individual patient.

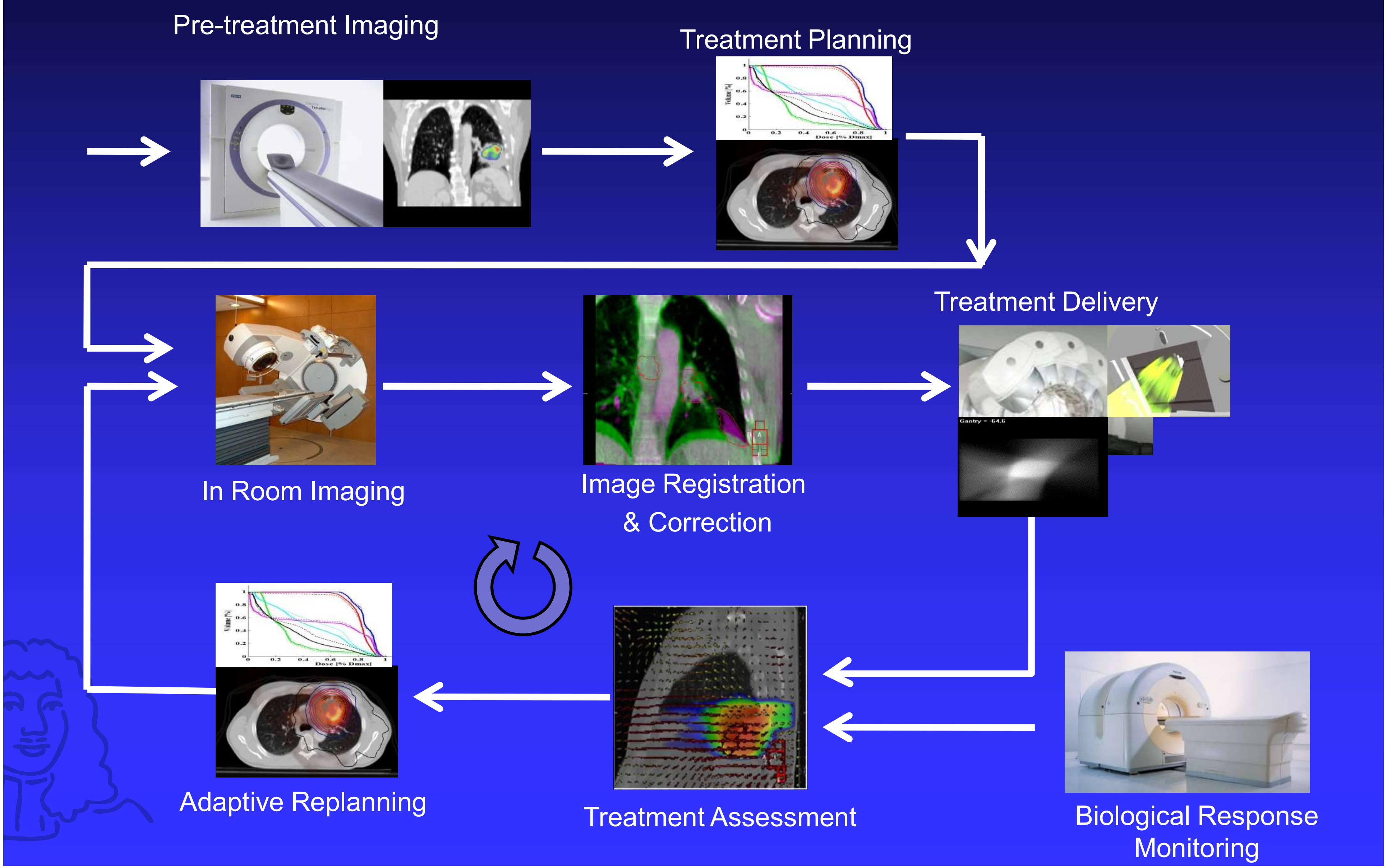
Adaptive Radiotherapy

Seminars in Radiation Oncology, 2005

The adaptive radiotherapy technique aims to customize each patient's treatment plan to patient-specific variation by evaluating and characterizing the systematic and random variations through image feedback and including them in adaptive planning.

Adaptive radiotherapy will become a new treatment standard.

The Adaptive Replanning Process



PTV Margins assure target coverage

- Most popular formulation is **2.5Σ** + **0.7σ,** where:
  - Σ is the standard deviation of systematic uncertainty
  - σ is the standard deviation of random uncertainty

van Herk et al, IJROBP 2000;47:1121-1135

ART Strategies

Patient-specific PTV

- Constructed with repeated imaging.
- Based on the first few days of treatment.
- Adapt the plan once using MLC beam apertures to correct margins and systematic error.
- No on-line interventions.

Yan et al PMB 42 (1997) 123–132
D.Yan, D. Lockman et al, IJROBP 48, 289–302, 2000
Martinez, Yan et al IJROBP 50, 1226–1234, 2001
D. Brabbins et al, IJROBP 61. 400–408, 2005
Nuver et al IJROBP 67(5); 1559-67 (2007)

Hugo et al Radioth & Oncol 78 (2006) 326–331

Adapt Dose Distribution

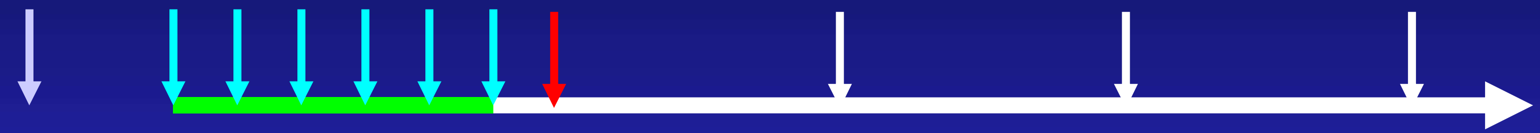
- Imaging feedback to assess dose in moving and deforming organs.
- “4D” patient models.
  - Relate target/organ segmentations
  - Track deforming organs
  - Accumulate fraction doses
  - Evaluate dose delivered: to date, current fraction, anticipated “trajectory”.

J Löf et al, PMB 43 (1998) 1605–1628
Birkner M et al, Med Phys. 2003 30(10):2822-31
Rehbinder et al, Med Phys. 2004 31(12):3363-71

Adaptive Radiotherapy

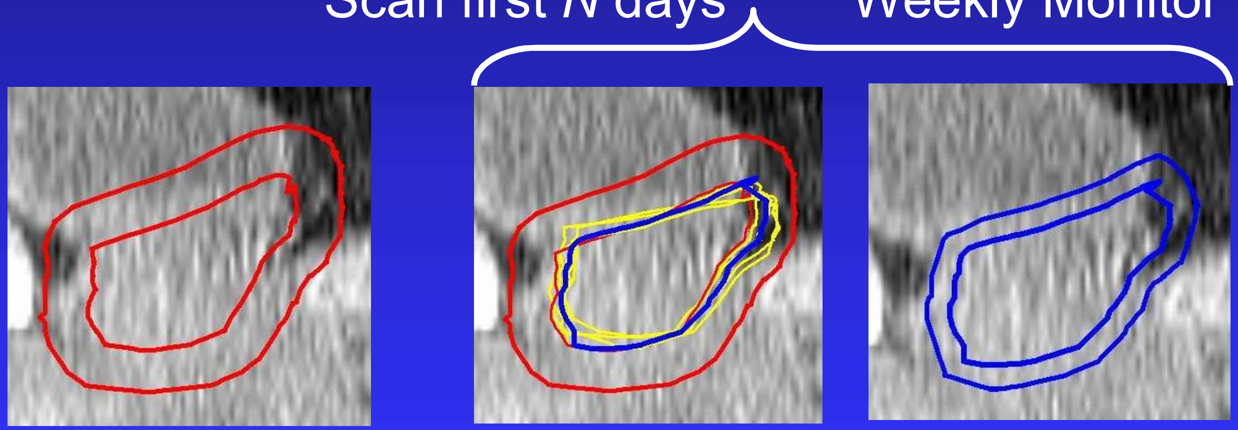
Initial treatment plan

Adapt treatment plan



Scan first *N* days

Weekly Monitor treatment



10 mm PTV margin

AVG CTV

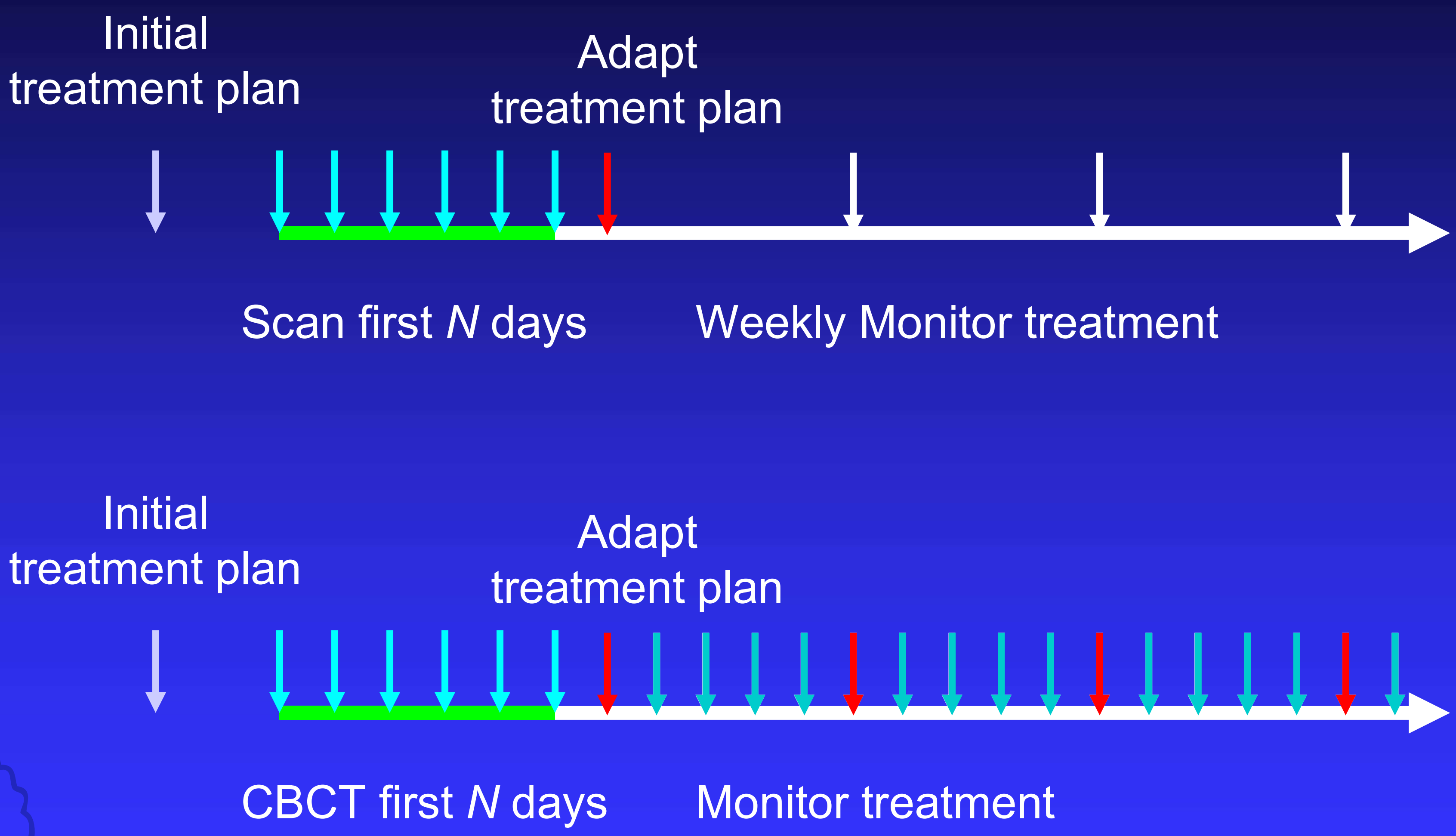
7 mm PTV

Group-specific ART strategy

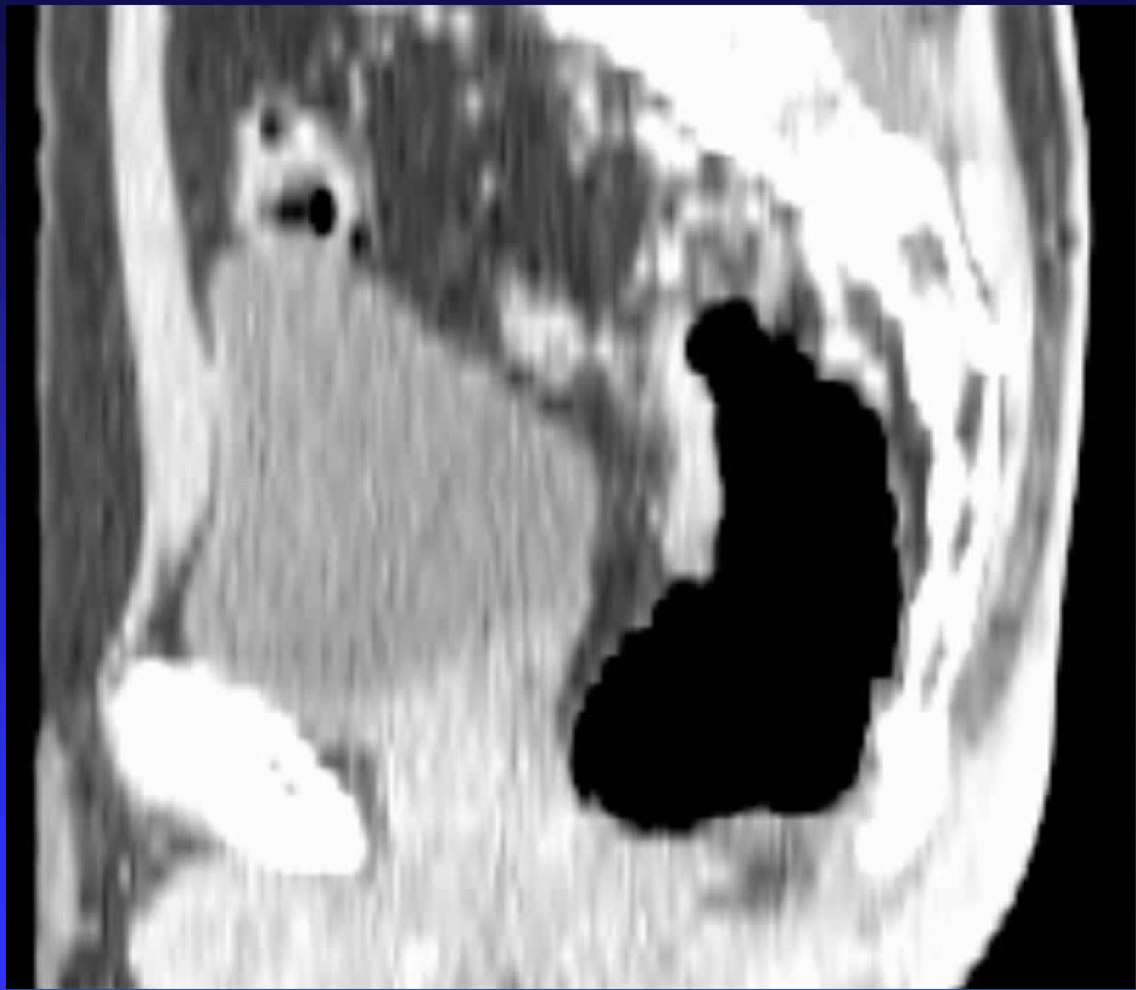
ADAPTIVE RADIOTHERAPY FOR PROSTATE CANCER USING KILOVOLTAGE CONE-BEAM COMPUTED TOMOGRAPHY: FIRST CLINICAL RESULTS

JASPER NIJKAMP, M.SC., FLORIS J. POS, M.D., PH.D., TONNIS T. NUVER, PH.D., RIANNE DE JONG, R.T.T., PETER REMEIJER, PH.D., JAN-JAKOB SONKE, PH.D., AND JOOS V. LEBESQUE, M.D., PH.D.

Adaptive Radiotherapy

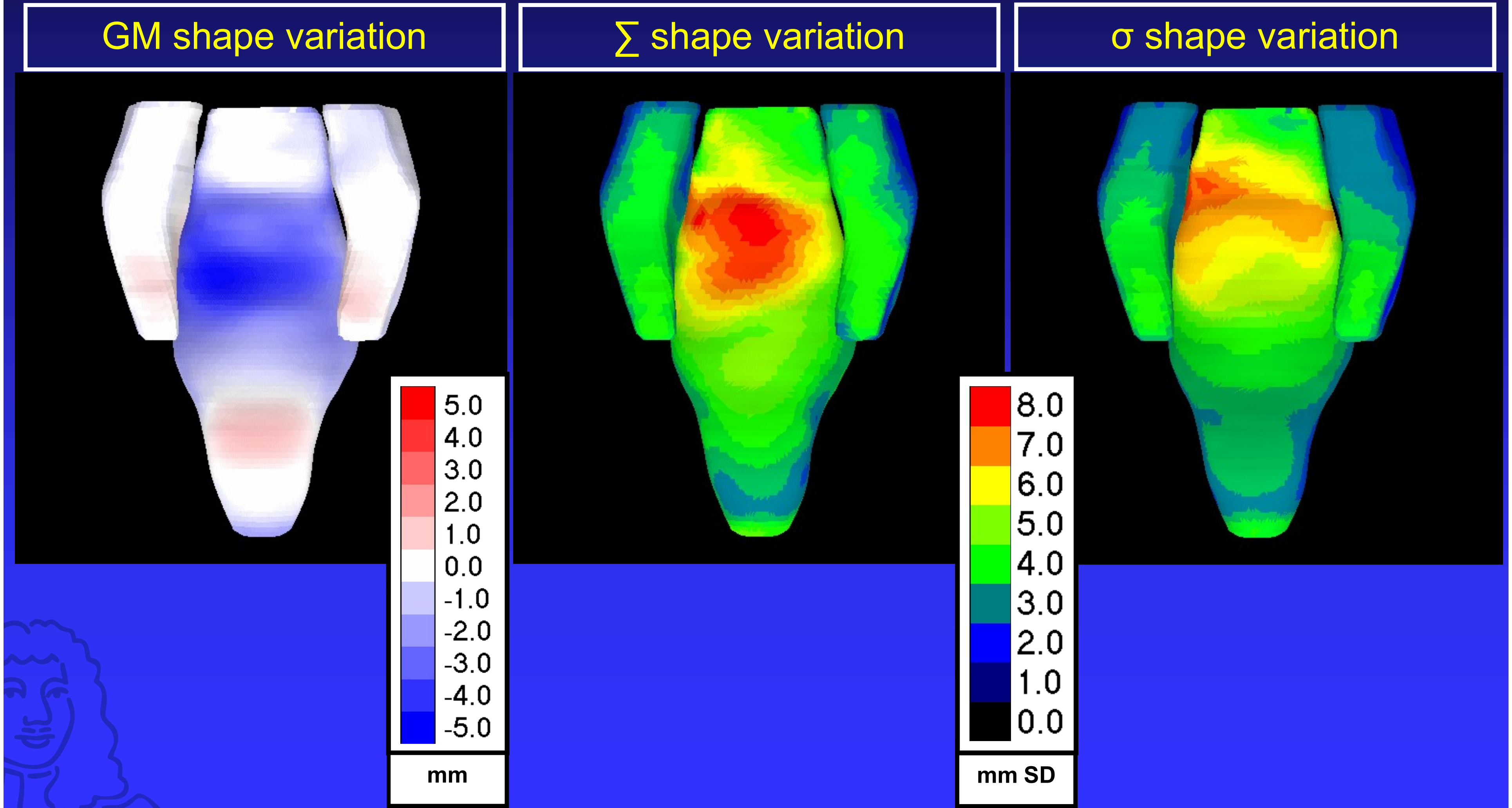


Day-to-day variation

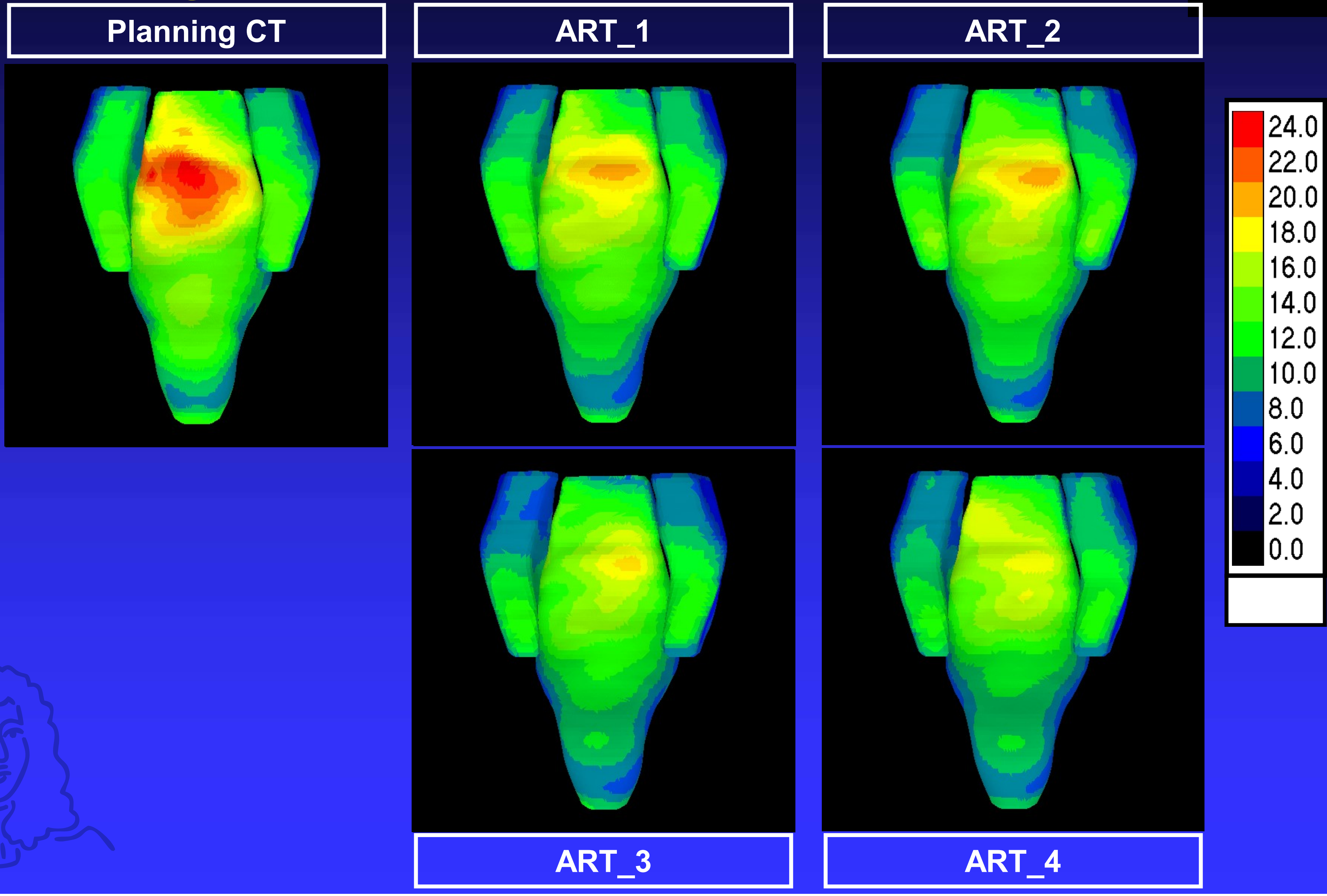


Series of a planning CT and 9 repeat CT scans during 25 x 2 Gy treatment (sagittal view)

Geometrical Uncertainties



Margin estimation

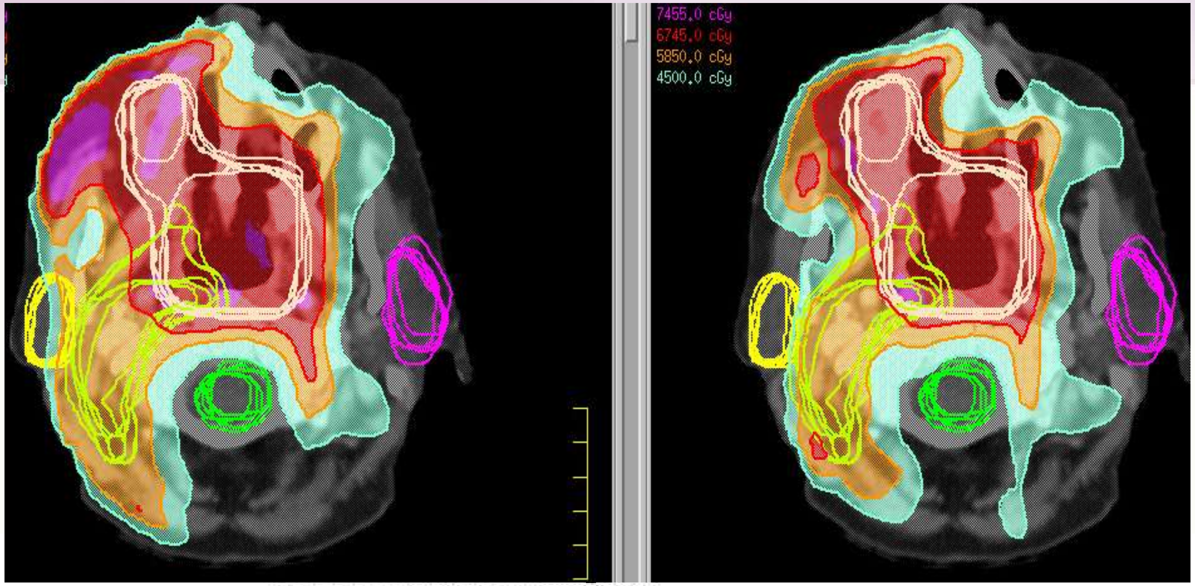


Adaptive Inverse Planning Optimization

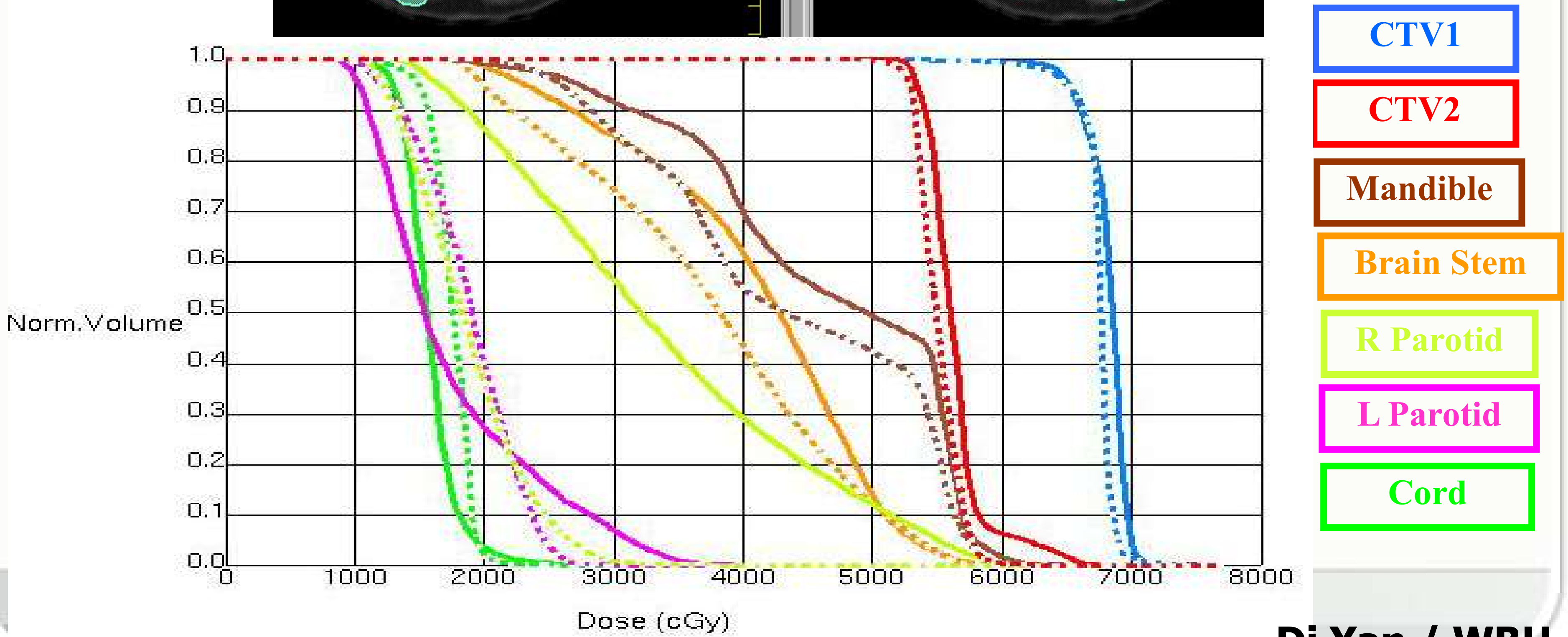
Adaptive Inverse Planning Optimization

- Self-tuning: Obtain the "true optimal" once the identified variation process (*pdf*) converges to the real one
- Self-learning: Utilize the "estimated treatment dose/volume parameters" to automatically modify the constrains in the adaptive inverse planning optimization

Conventional Inverse Plan: 5mm CTV-to-PTV margin. Solid lines in DVH

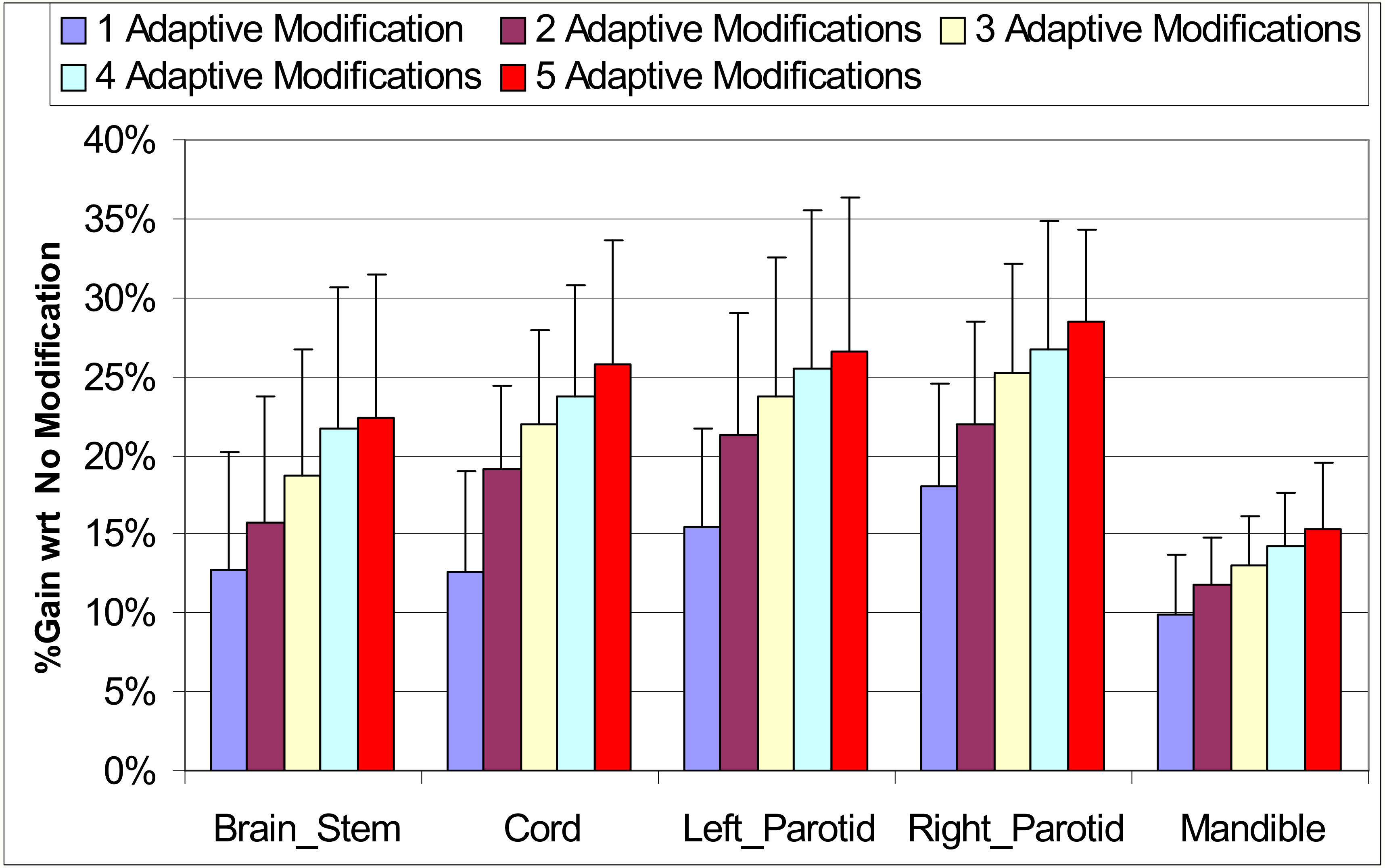


Adaptive Inverse Plan: one modify after the 2nd week. Dash lines in DVH



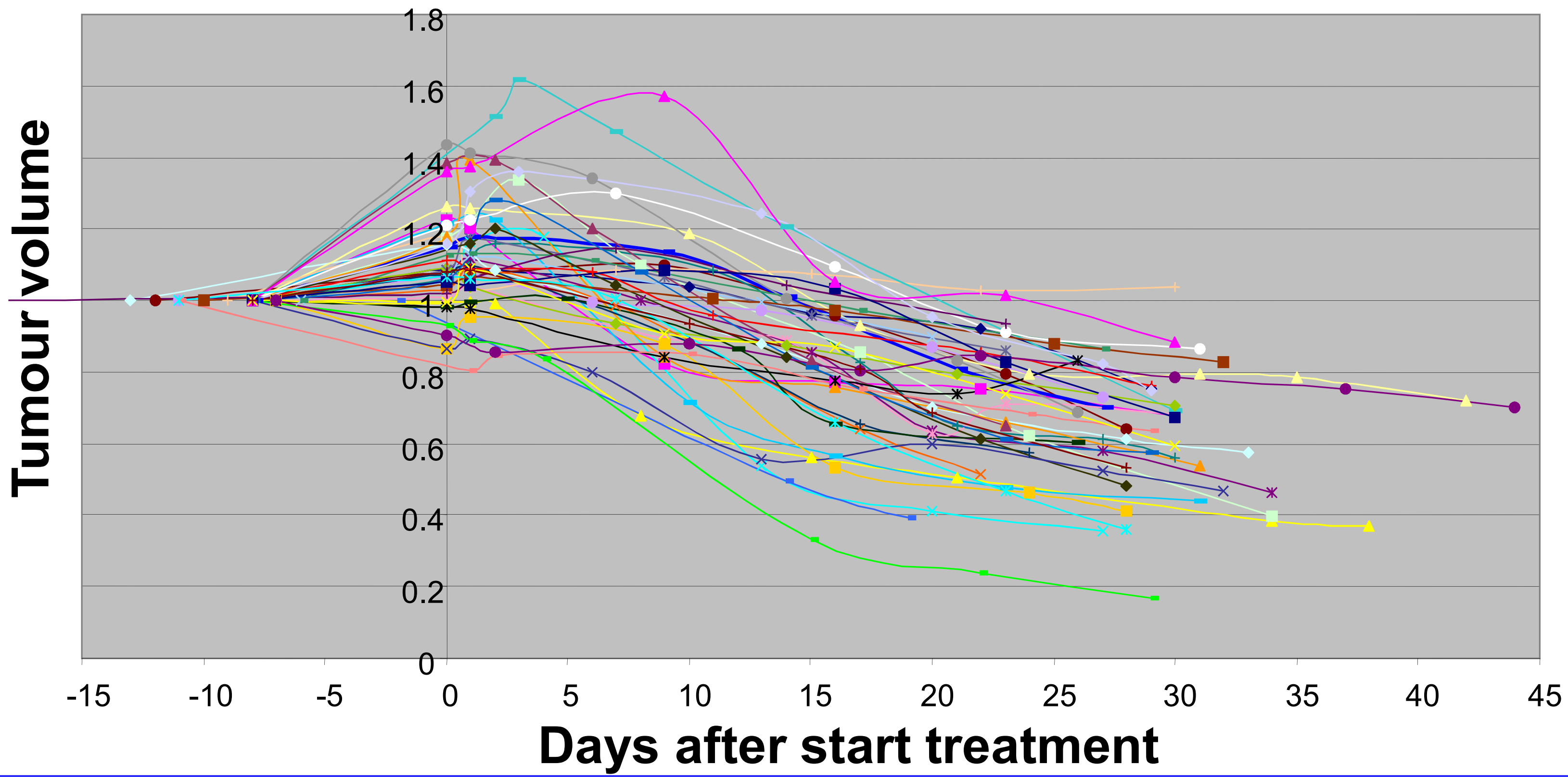
Di Yan / WBH

Weekly Adaptive Modification

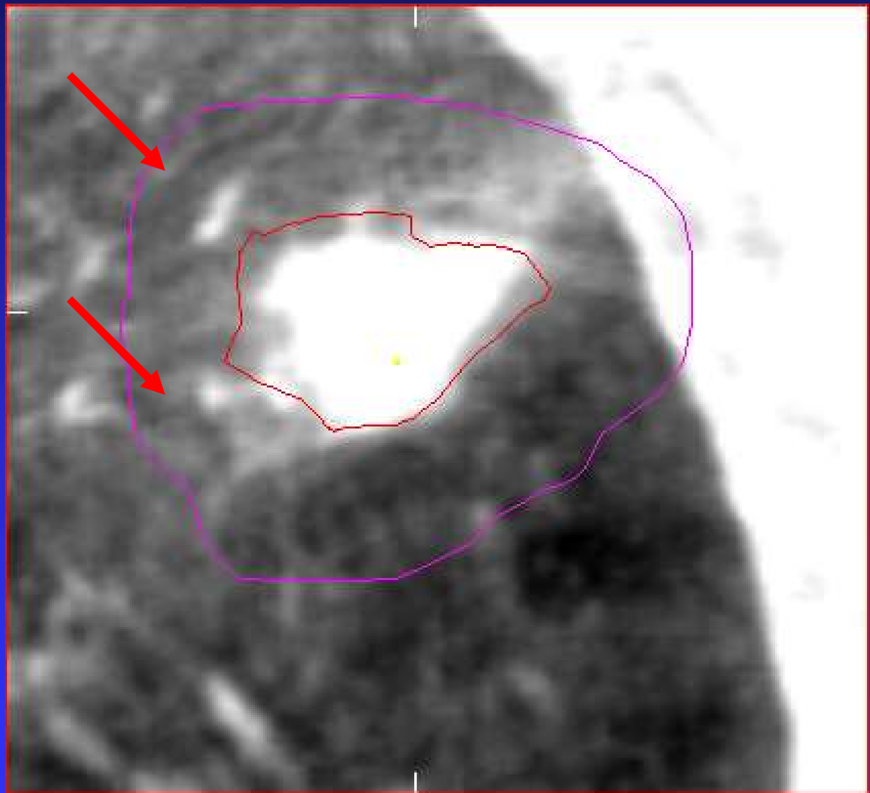


Di Yan / WBH

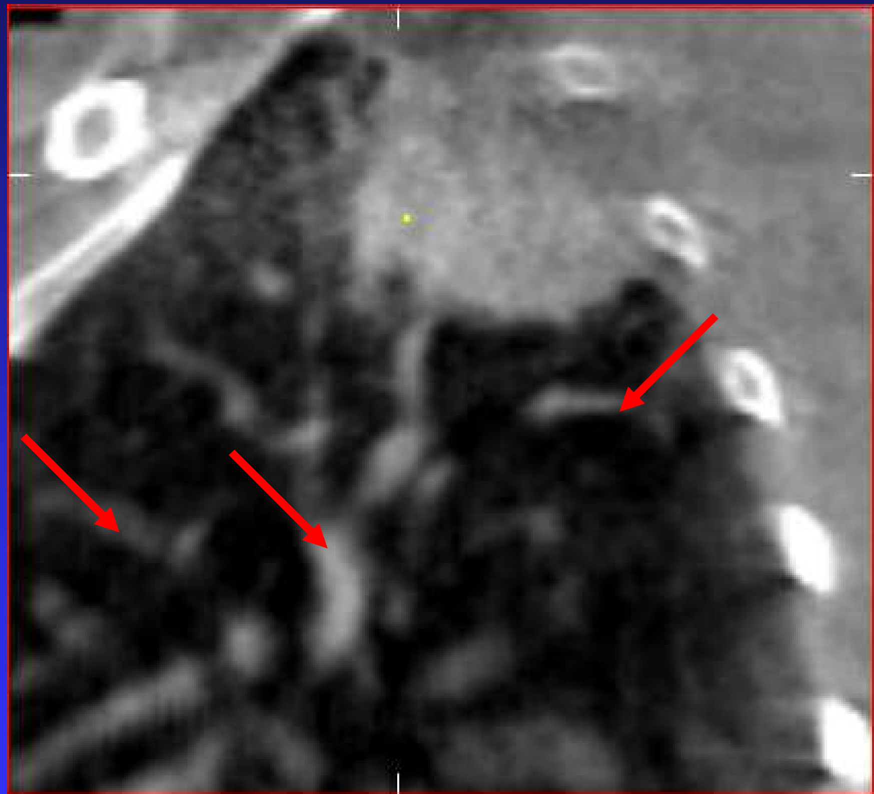
Volume change in 58 patients with regression



Modes of Tumor Regression



38%

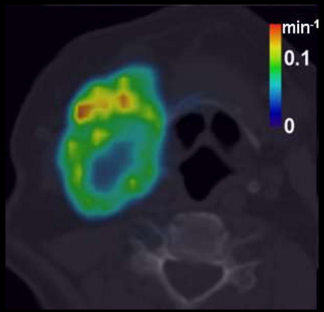


44%

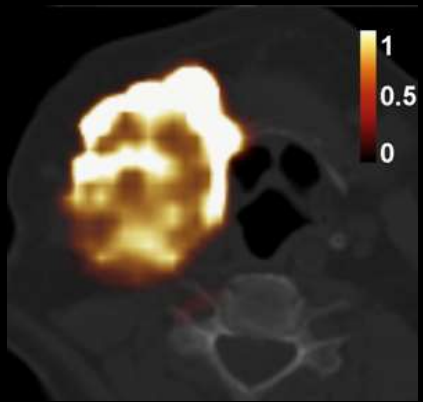
18% combined effect

Applications – dose painting

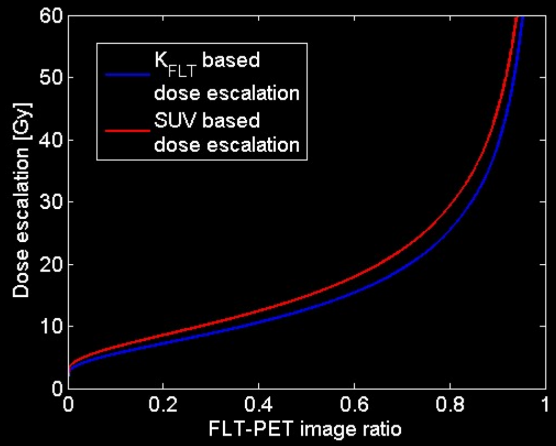
Pre-treatment

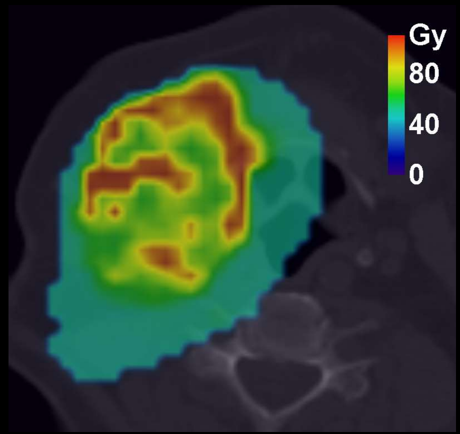


Treatment response

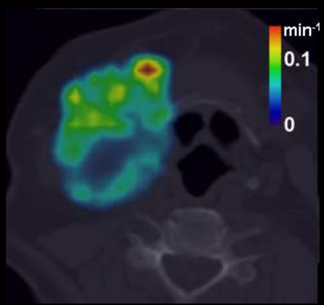


Prescription function





Mid-treatment



Robert Jeraj / UW

What can we detect ?

Tissue Dislocations

- Patient/Target Setup-Errors
- Interfractional organ motion
- Intrafraction organ motion

Tissue Deformations

- Interfractional organ deformations
- Tumor Shrinkage/Growth
- Tissue Swelling
- Weight-Loss/Gain of the Patient

Trends

What can we not detect?

- Remaining Uncertainties
  - Target Delineation Uncertainties
  - Uncertainty of the IGRT procedure

Appropriate Margins

Conclusions

- Systematic errors are most important for the margin
- Offline protocols can reduce the systematic errors effectively
- ART: Systematic improvement of treatment plan based on imaging information
- Development of clinical ART is one of the major tasks for future IGRT

Thanks to

- Stine Korreman
- Uwe Oelfke
- Tom Depuijdt
- Marcel van Herk
- Robert Jeraj
- Di Yan
- Wouter Vogel
- Mike Sharpe
- Peter Remeijer

Adaptive workshop

Helen McNair

Royal Marsden NHS Foundation Trust and Institute of Cancer Research

Rianne de Jong

Academic Medical Centre, Amsterdam

The ROYAL MARSDEN
NHS Foundation Trust

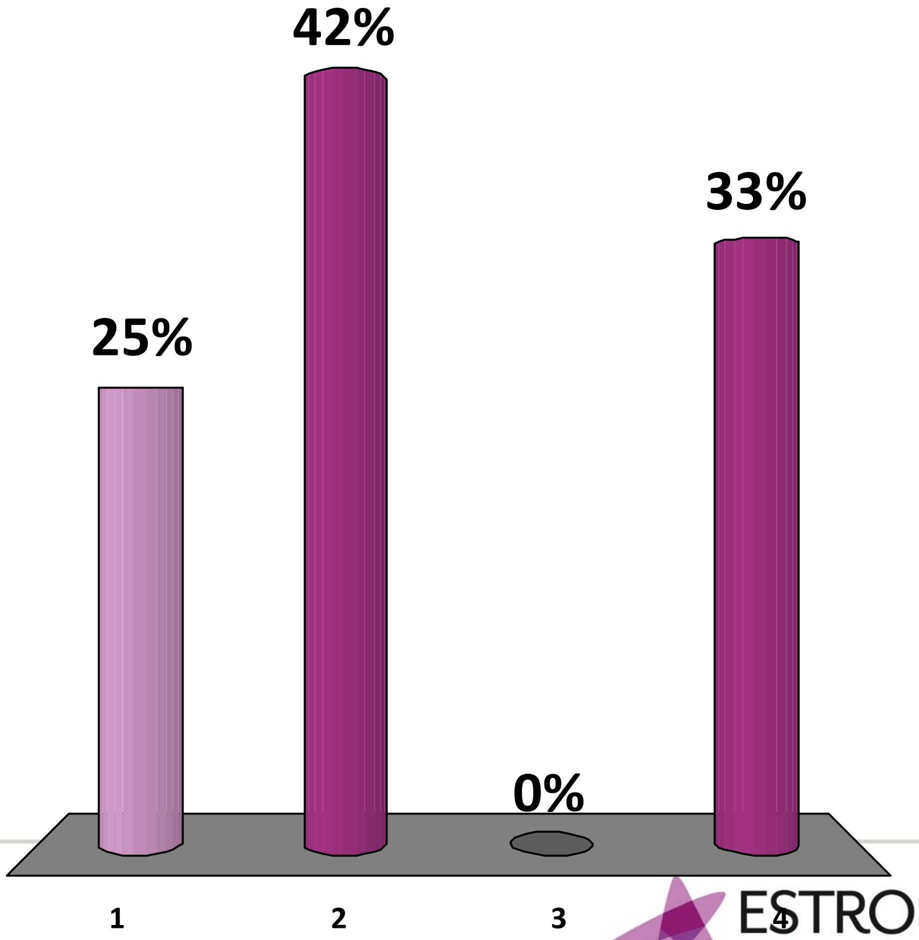
ICR The Institute of Cancer Research

ESTRO School

November 2014

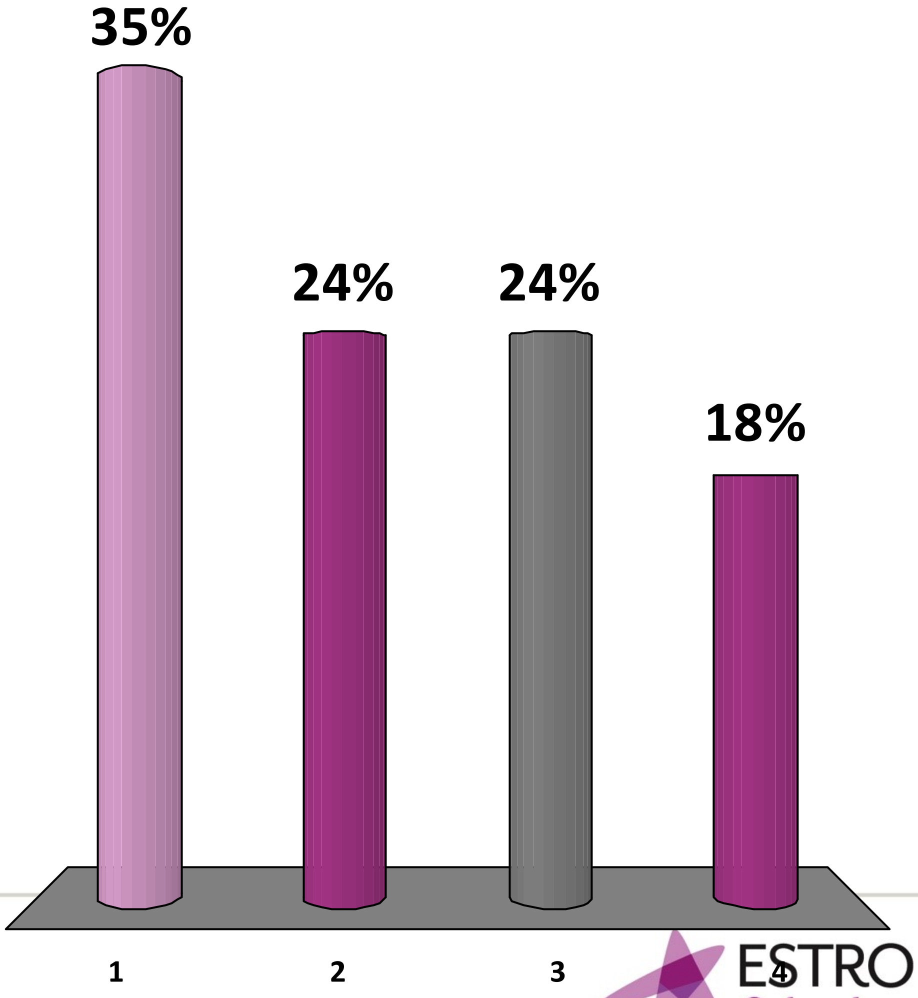
Plan of the day-are you using

1. Bladder
2. Cervix
3. Rectum
4. More than 1 of the above



Plan of the day-are you implementing/want to

1. Bladder
2. Cervix
3. Rectum
4. More than 1 of the above



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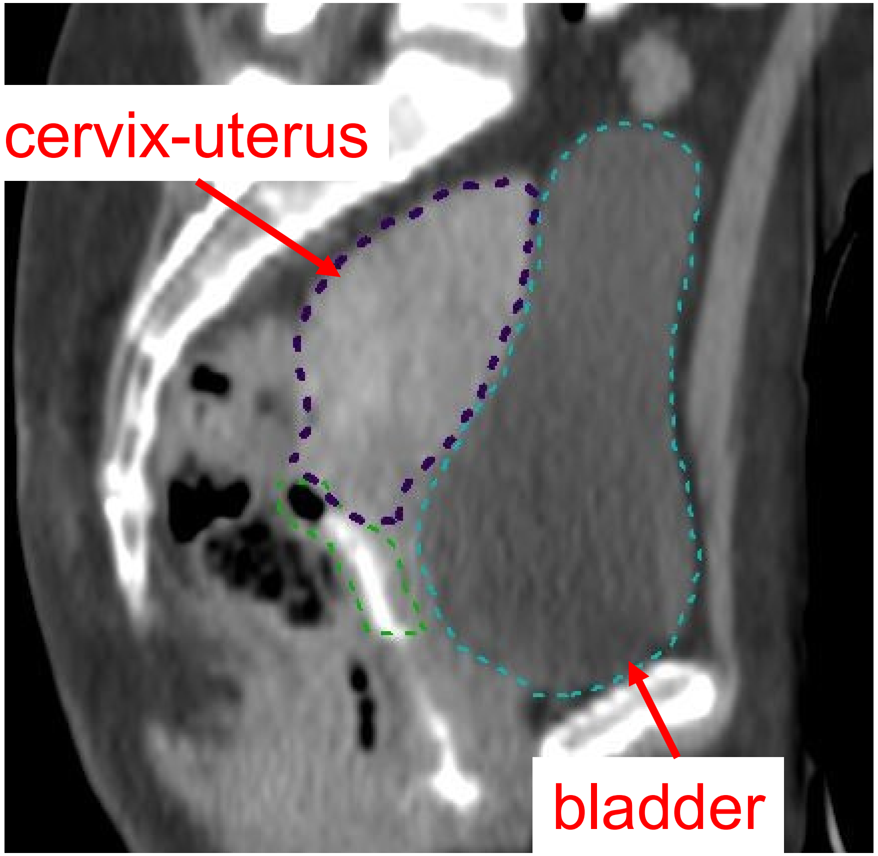
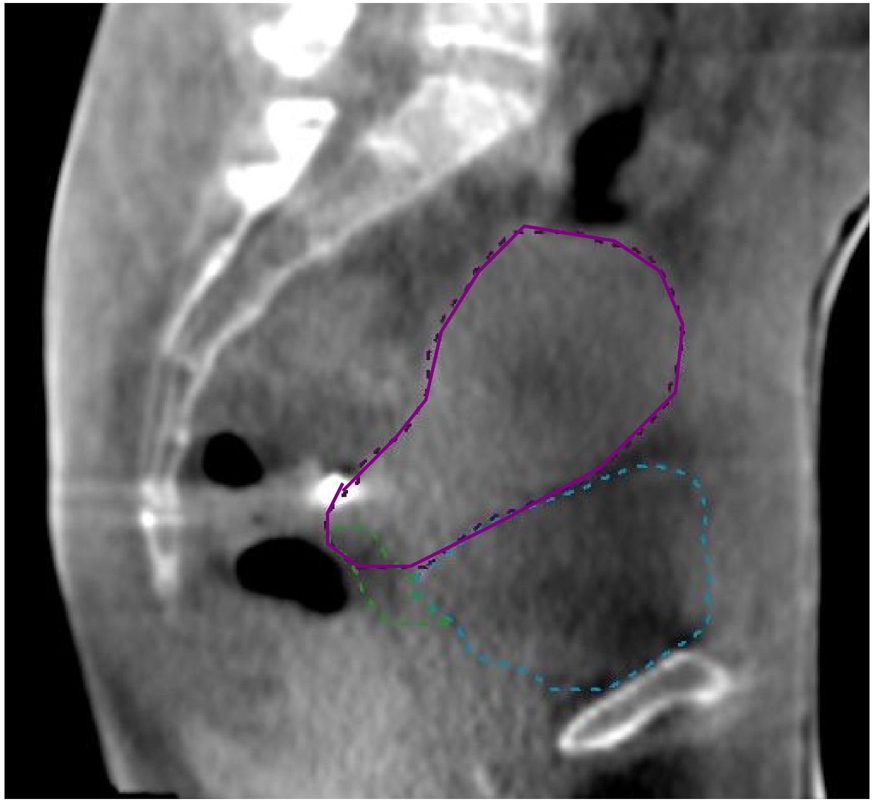
Tumour sites

Planning CT



Conebeam CT



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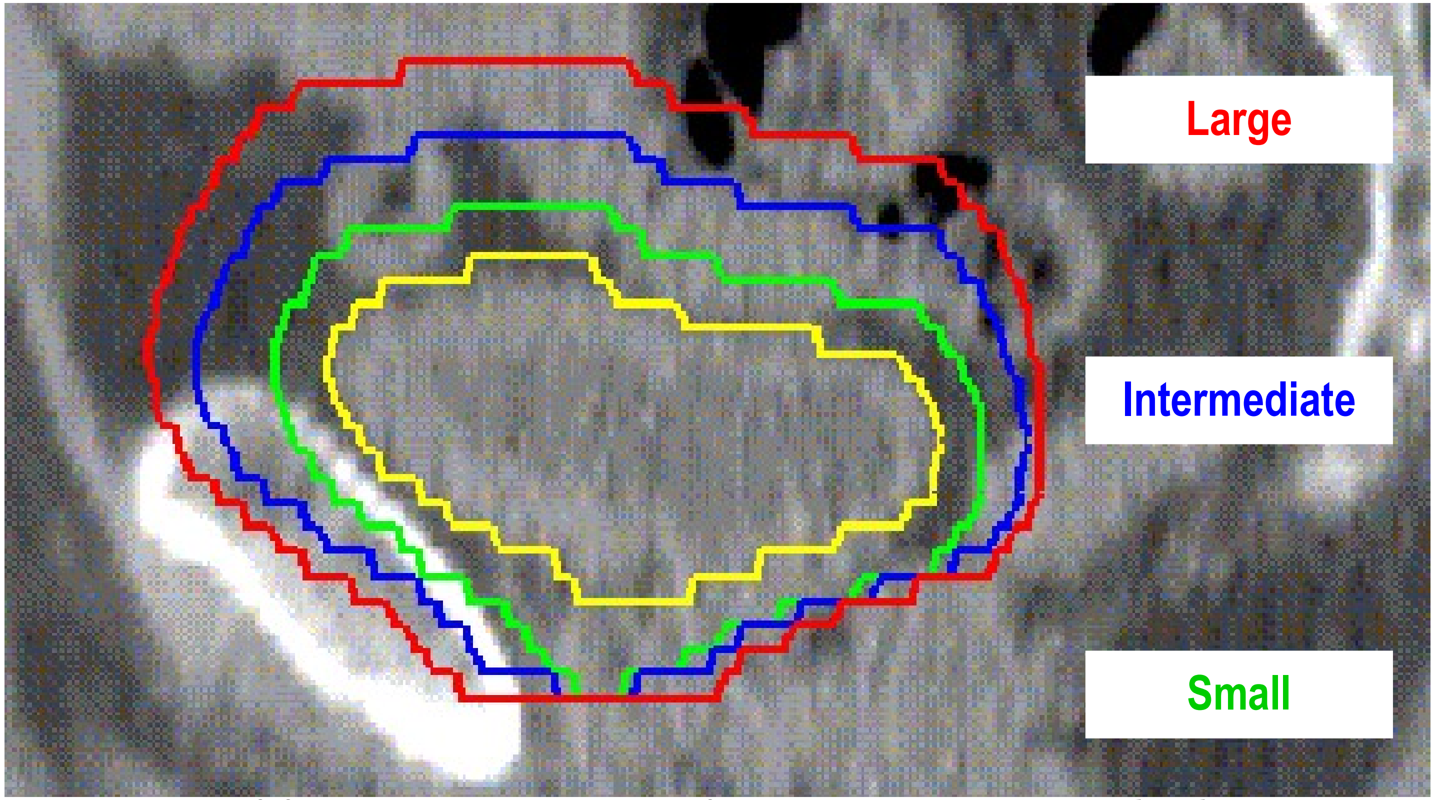
Adaptive-predictive organ localisation



51% of fractions in 10 out of 15 patients required adaptive

73% fractions delivered correctly using adaptive

Remaining 27% improved coverage

Lalondrelle , IJROBP, 2011

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Plan of the day

PTV small

PTV medium

PTV large

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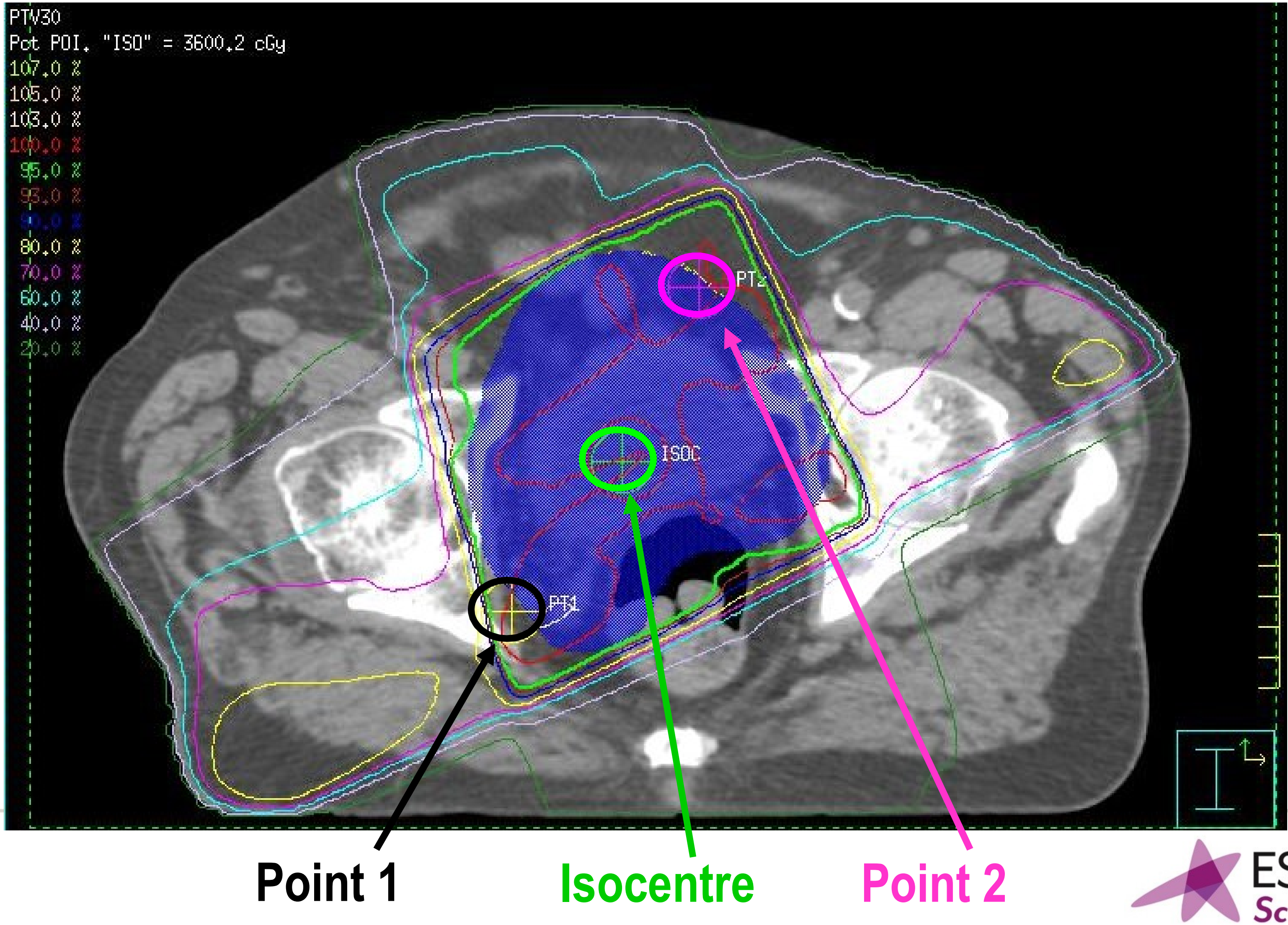
Treatment delivery-plan of day



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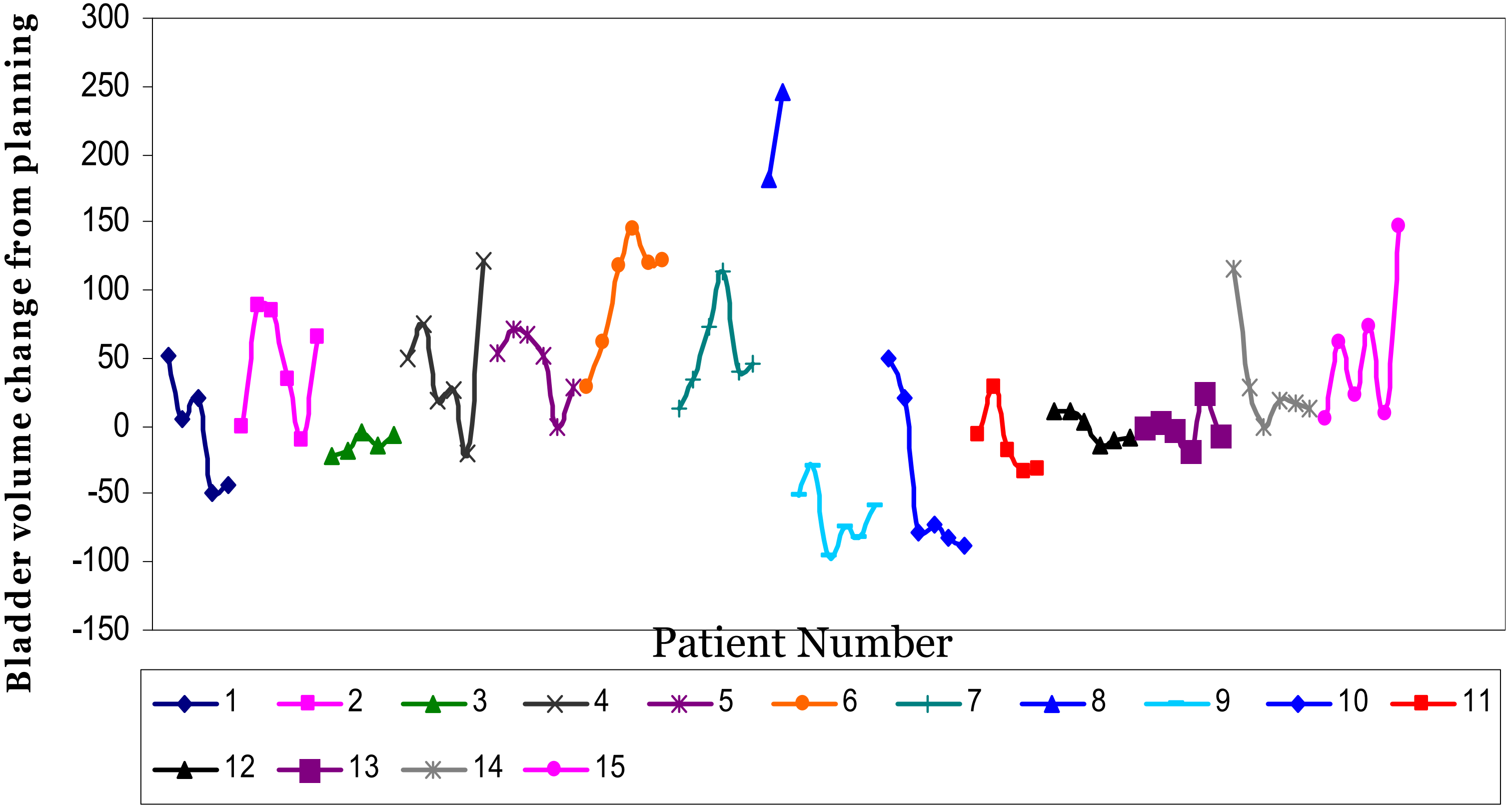
Registration issues

Representative reference image

Empty bladder

Full bladder

Interfraction volume variation



No predictive factors

Lalondrelle , IJROBP, 2011

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Registration issues

Consistent PTV selection between observers

No PTV is suitable- too large

No PTV is suitable – too small

Registration issues

Consistent PTV selection between observers

No PTV is suitable- too large

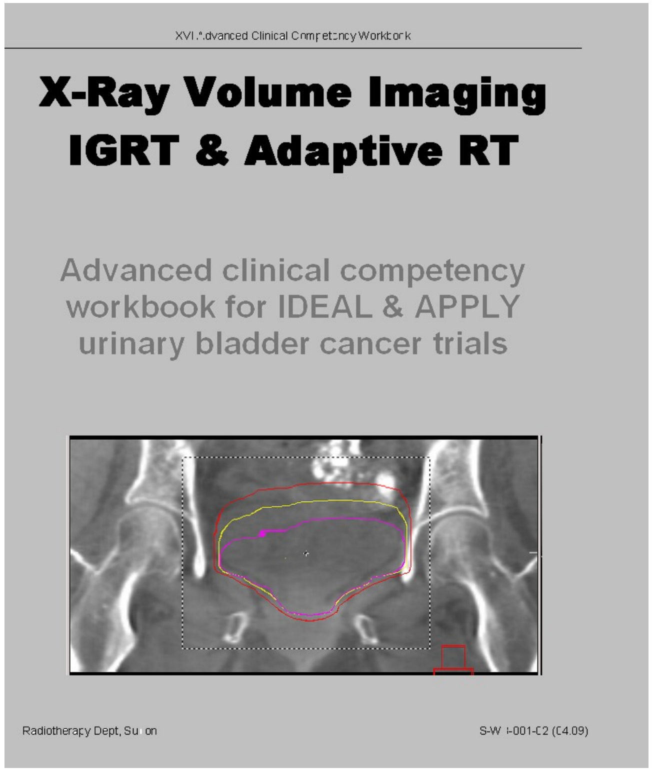
No PTV is suitable – too small

Training

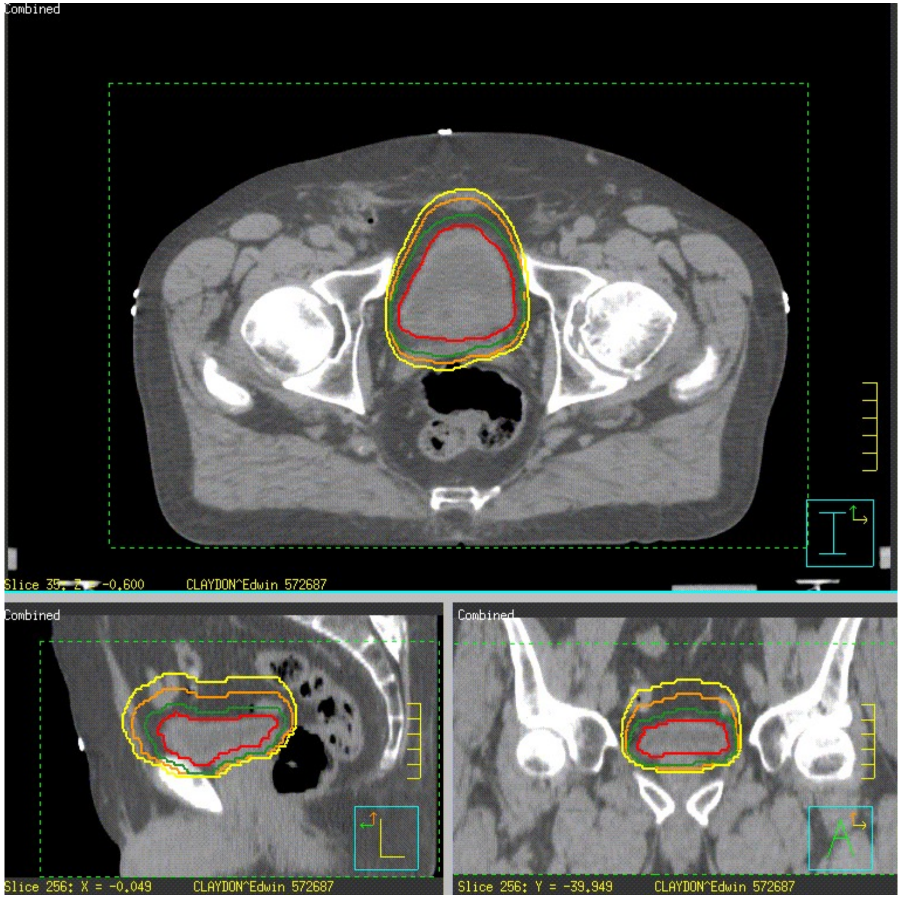
Anatomy teaching provided by University & clinicians

Normal/abnormal pelvic pathology

Complete competency workbook



Training-Bladder



12 radiographers

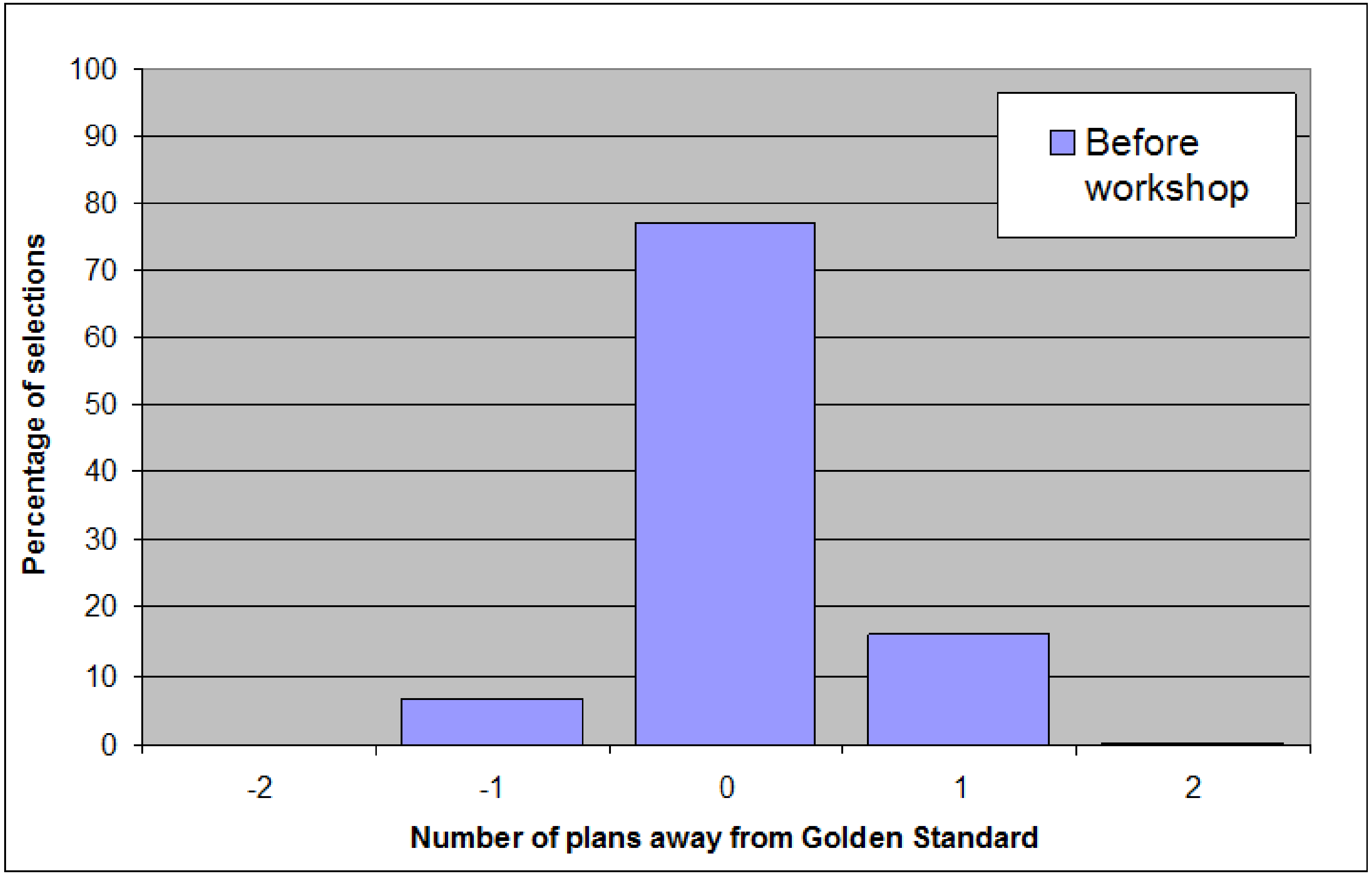
2 clinicians

Mean concordance 76%

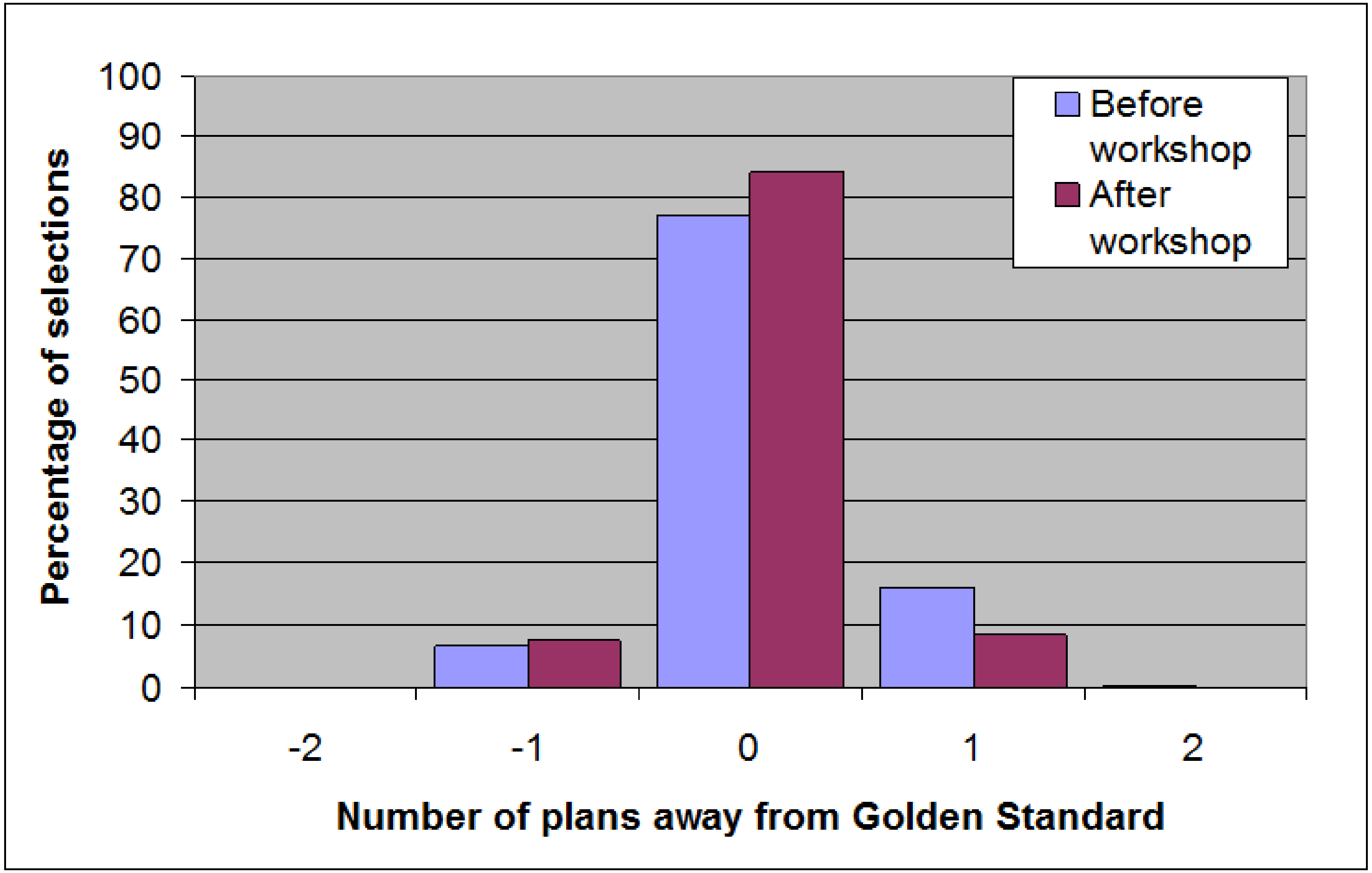
Matching/ set up: 2 min 28s

Plan selection: 1 min 24s

Training- cervix



Training-cervix



Volume selection

On-line by 2 trained observers

CBCT → Set-up correction → Volume selection → Treatment 6Gy → CBCT

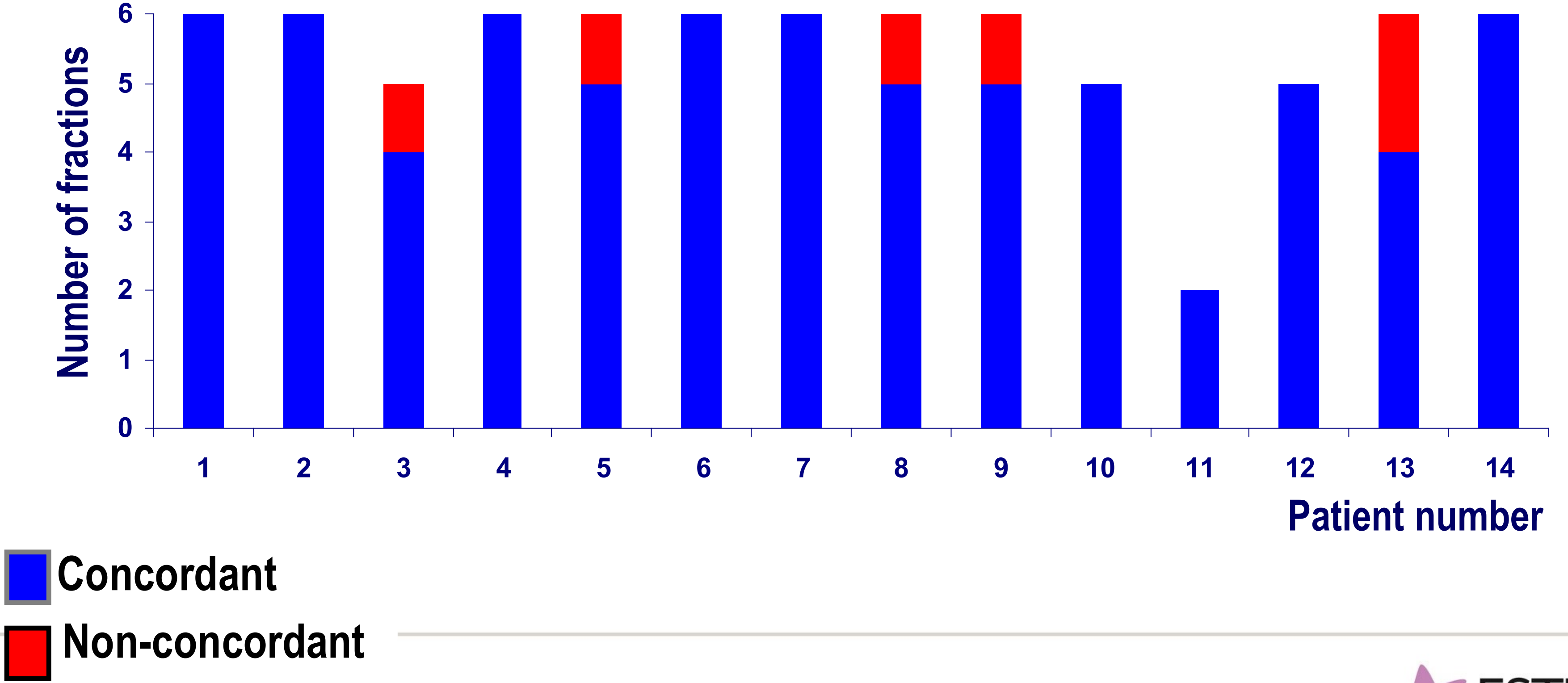
Off-line by independent blinded observer

CBCT → Bony match → Volume selection

Courtesy of Fiona McDonald

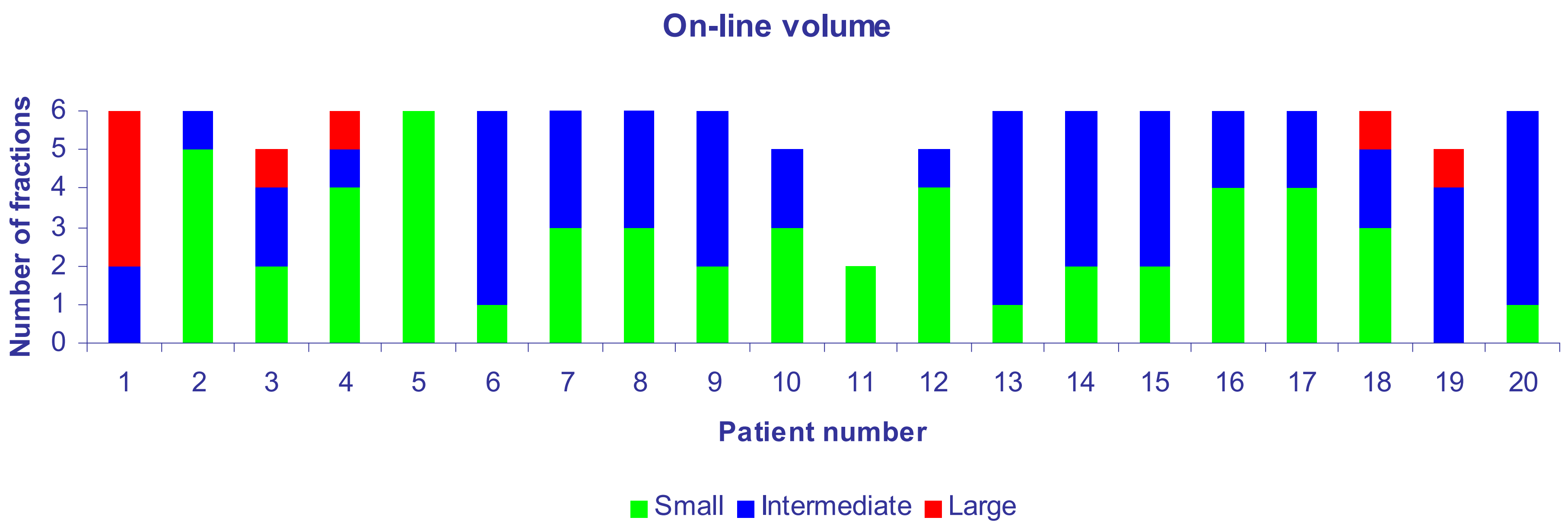
Volume selection

Concordance rate 92% **(71/77#)**



Courtesy of Fiona McDonald

On-line volume



139 RT fractions assessed

•68 (49%) small, 63 (45%) medium and 8 (6%) large selected

•3 (12%) same plan throughout the course

•Manual isocentre shift in 15 fractions (10%)

•1 fraction CTV considered too large for the large plan

National Trial

HYBRID

62 patients with **pT2-T4a N0 M0** bladder carcinoma unsuitable for standard daily radiotherapy

↓

Due to receive six 6Gy fractions of radiotherapy delivered weekly (total dose: 36Gy over 6 weeks)

↓

RANDOMISE

1:1

↓

Group 1: STANDARD PLANNING (CONTROL)	**Group 2:** ADAPTIVE PLANNING (EXPERIMENTAL)

↓

Follow up

- Weekly on treatment
- 4 weeks after last treatment
- **3 months after last treatment**
- 6, 12 and 24 months

Endpoints

HYBRID

Primary endpoint

•Acute non-genitourinary grade 3 or greater toxicity (up to 3 months following treatment completion)

Secondary endpoints

•Local disease control rate at 3 months
•Control rate of presenting symptoms
•Patient reported outcomes
•Late toxicity
•Time to local disease progression
•Overall survival
•Proportion of fractions benefiting from adaptive planning
•Appropriate identification and correction of fractions requiring adaptive planning

Planning CT

Patient preparation

Advise no drinking 30min prior to scanning

Void immediately before planning CT

Encourage rectal emptying

Local rectal preparation protocols permissible (micro enemas etc.)

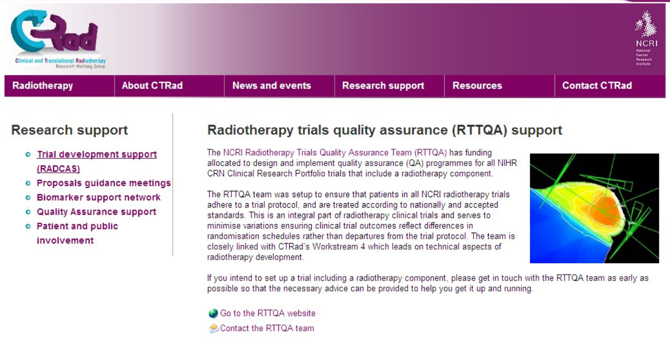
Patient positioning

CT scanning

Slice thickness ≤3mm

Scan at least 4cm above bladder dome and 2cm below ischial tuberosities

RTTQA IGRT Credentialing programme


Radiotherapy | About CTRad | News and events | Research support | Resources | Contact CTRad

Research support

- Trial development support (RADCAS)
- Proposals guidance meetings
- Biomarker support network
- Quality Assurance support
- Patient and public involvement

Radiotherapy trials quality assurance (RTTQA) support

The NCRI Radiotherapy Trials Quality Assurance Team (RTTQA) has funding allocated to design and implement quality assurance (QA) programmes for all NIHR CRN Clinical Research Portfolio trials that include a radiotherapy component.

The RTTQA team was setup to ensure that patients in all NCRI radiotherapy trials adhere to a trial protocol, and are treated according to nationally and accepted standards. This is an integral part of radiotherapy clinical trials and serves to minimise variations ensuring clinical trial outcomes reflect differences in randomisation schedules rather than departures from the trial protocol. The team is closely linked with CTRad's Workstream 4 which leads on technical aspects of radiotherapy development.

If you intend to set up a trial including a radiotherapy component, please get in touch with the RTTQA team as early as possible so that the necessary advice can be provided to help you get it up and running.

Go to the RTTQA website
Contact the RTTQA team

Evidence of in-house IGRT training programme (bladder)

HYBRID specific training programme

IGRT independent review cases: this acts as competency assessment

Verification of electronic data transfer: CBCT and registration objects

IGRT site visit: during first patient's treatment. Review process/decision making

RTT QA for plan selection

Remote access to Elekta/Varian databases

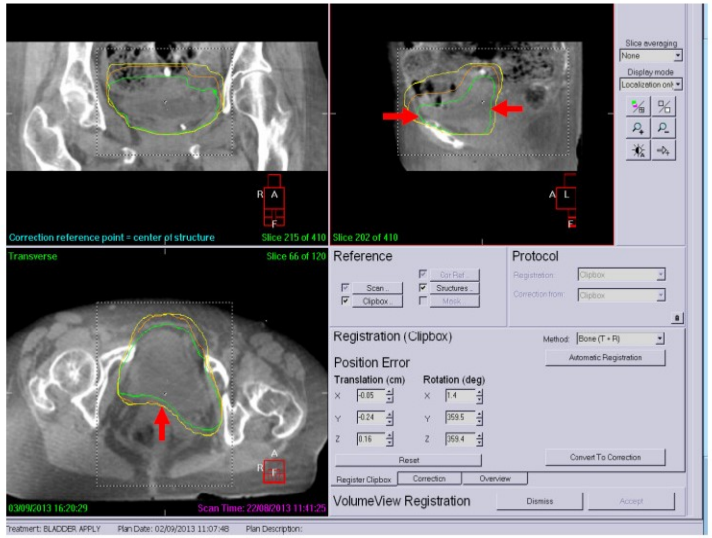
5 patients, 6 CBCT each

Patient 1: step by step process of how plan selected

Patient 2-3: practice with answers provided

Patient 4-5:test cases

Figure 1: Axial, sagittal and coronal view of PTVsmall (green), PTVmedium (orange) and PTV large (yellow) with arrows highlighting where the bladder is close to the boundary of PTVsmall.



- Remove PTV small as it does not incorporate the bladder volume and a margin of 3mm in the anterior-posterior dimension (Figure2).

51 Staff assessed, 9 centres

Maintenance of competency

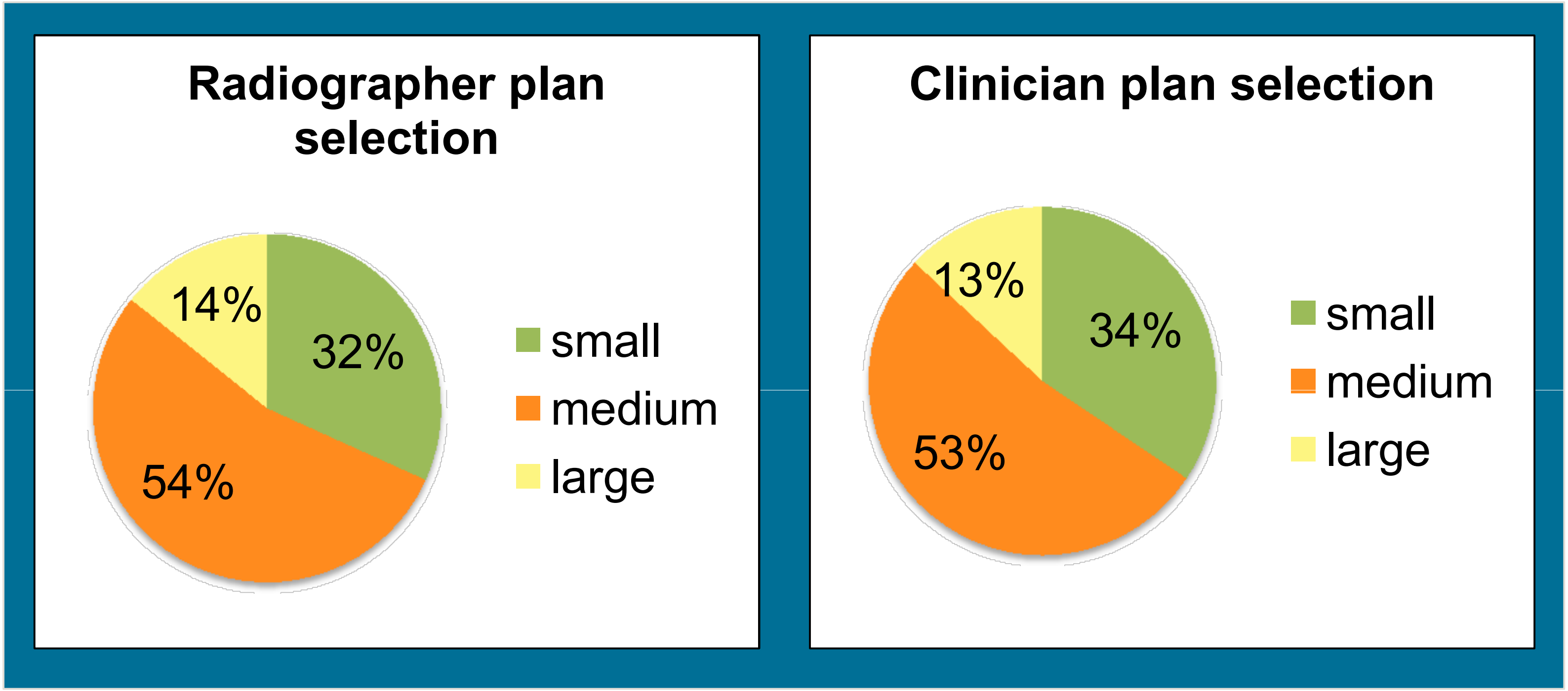
Advanced competency assessment record of
practise in adaptive bladder radiotherapy for bladder cancer

A maximum of 2 scans per patient, should be recorded as part of the competency assessment.

Date	Relevant Experience	Outcome / Reflection
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	

Maintenance of competency

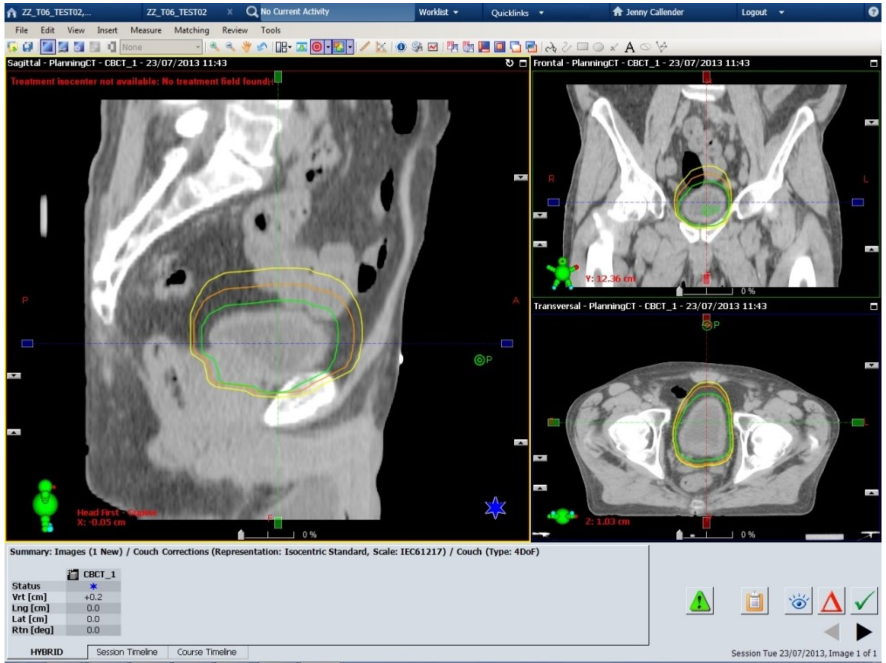
16 radiographers trained
Audit 3 years after

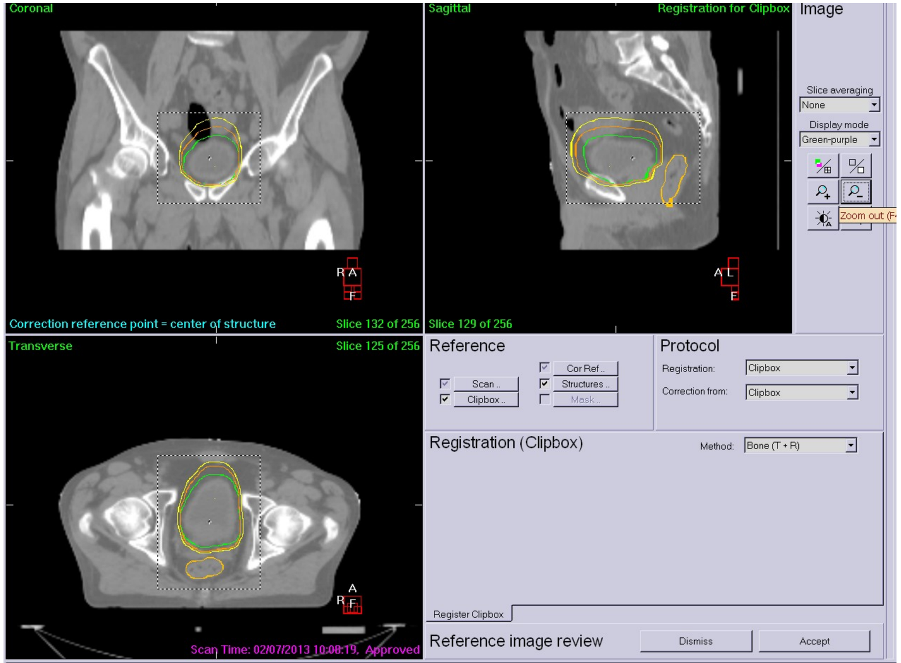


125 CBCTs (63 pre; 62 post radiotherapy) were evaluated
Concordance of plan selection was 92% (58/63)

Registration-guidelines

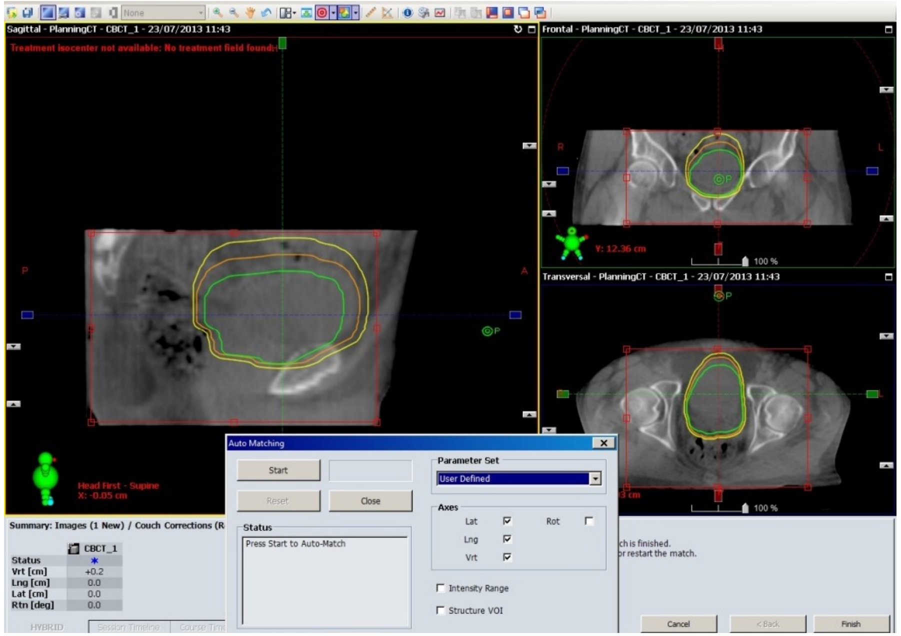
Assess reference image

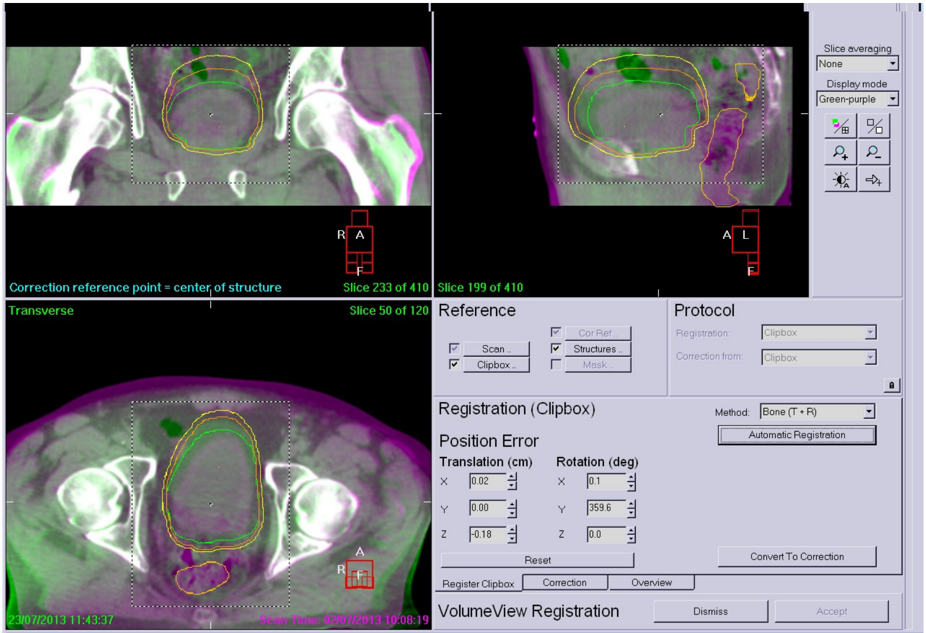




Registration-standard process

Contrast and Bone registration





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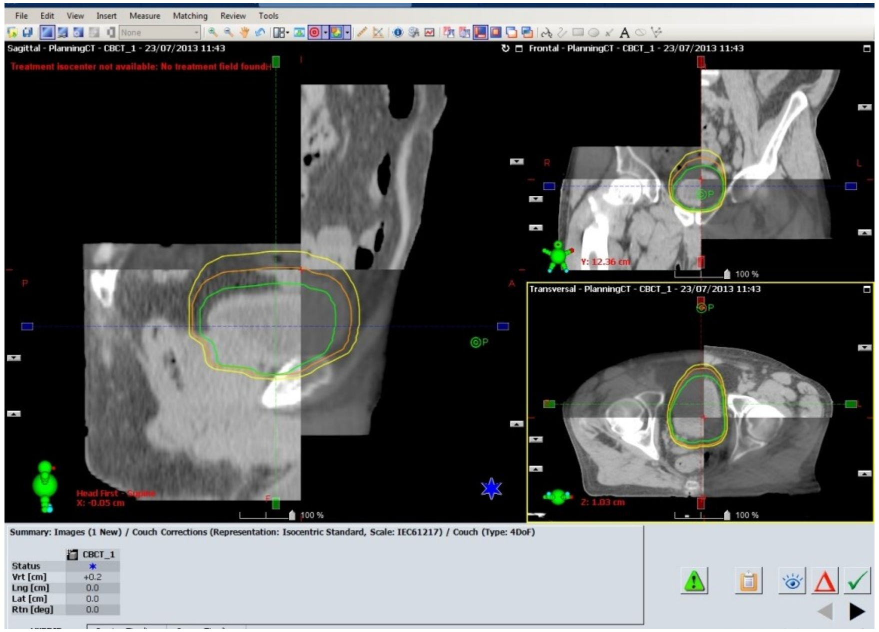
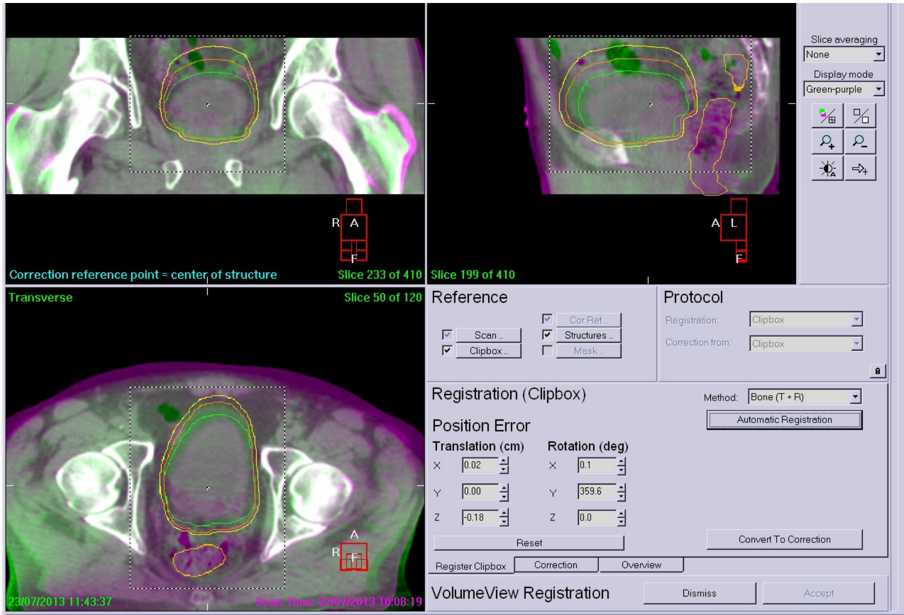
Registration-guidelines

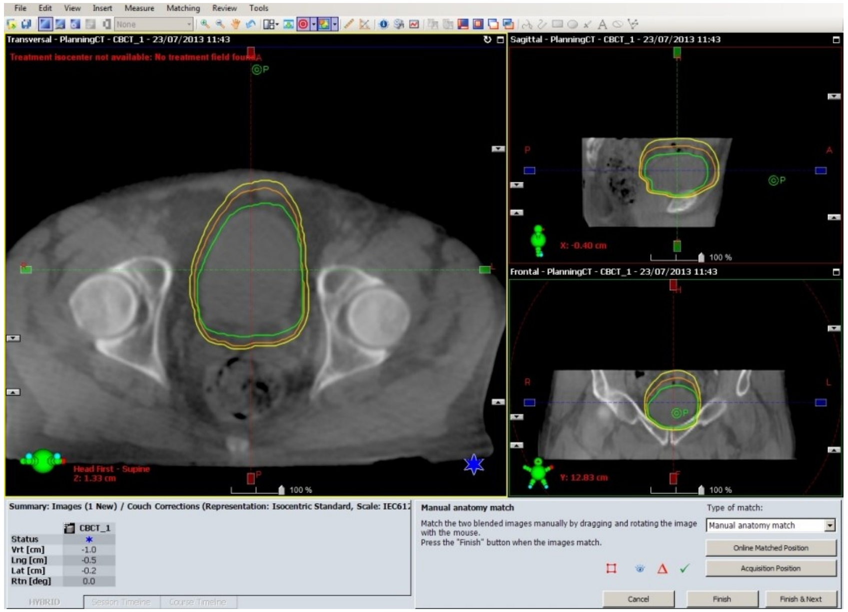
Check match

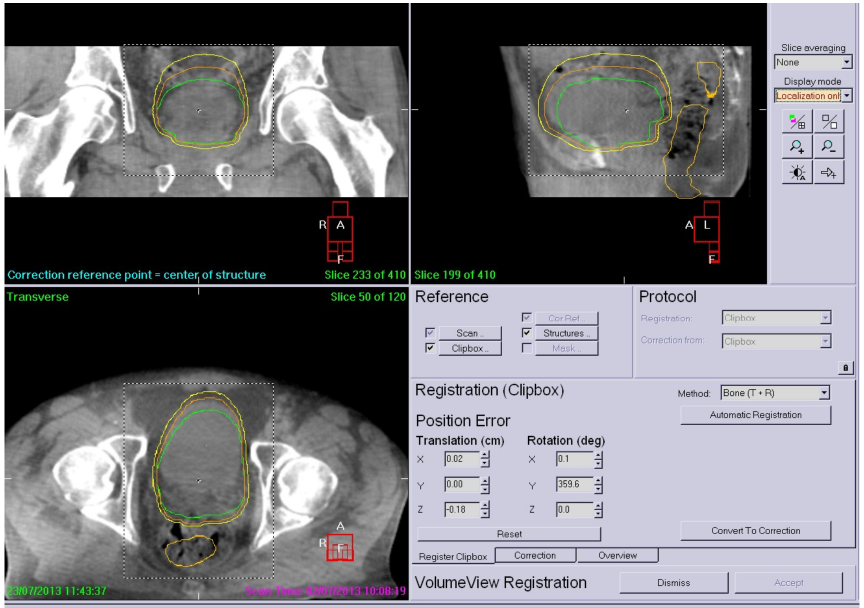




Registration-guidelines

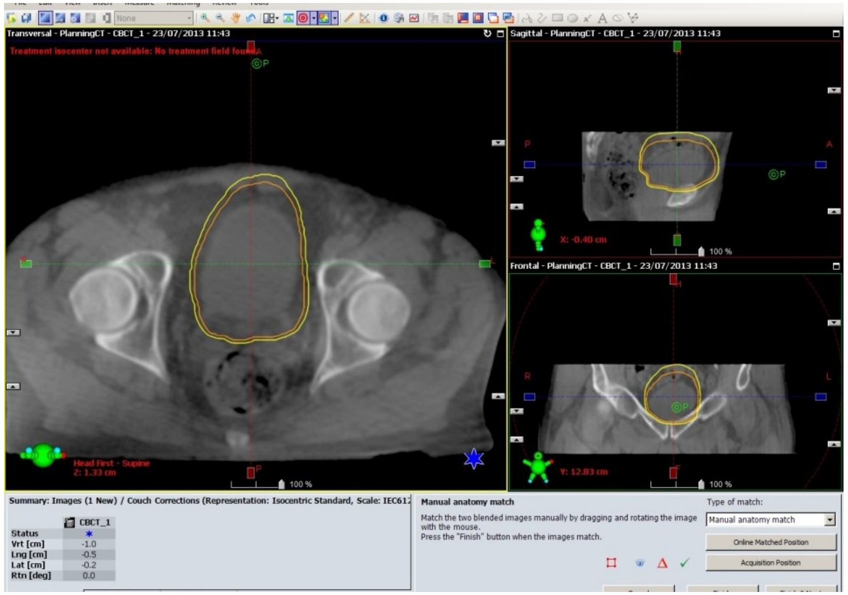
Quick gross assessment

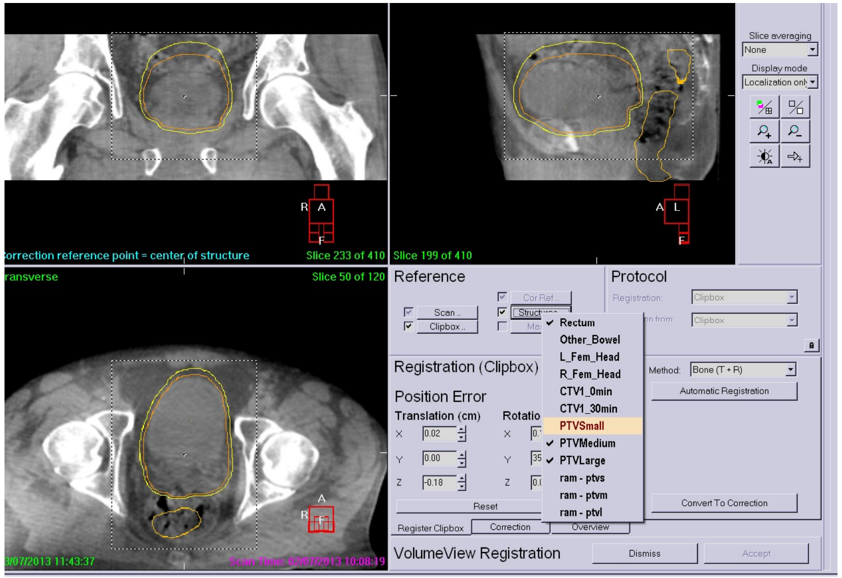




Registration-guidelines

Assess next plans





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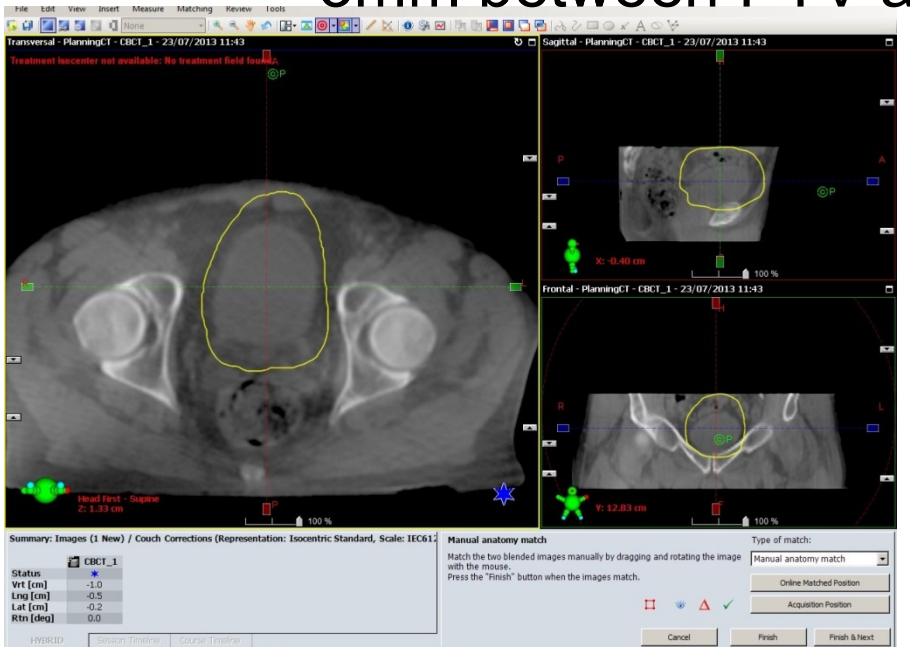
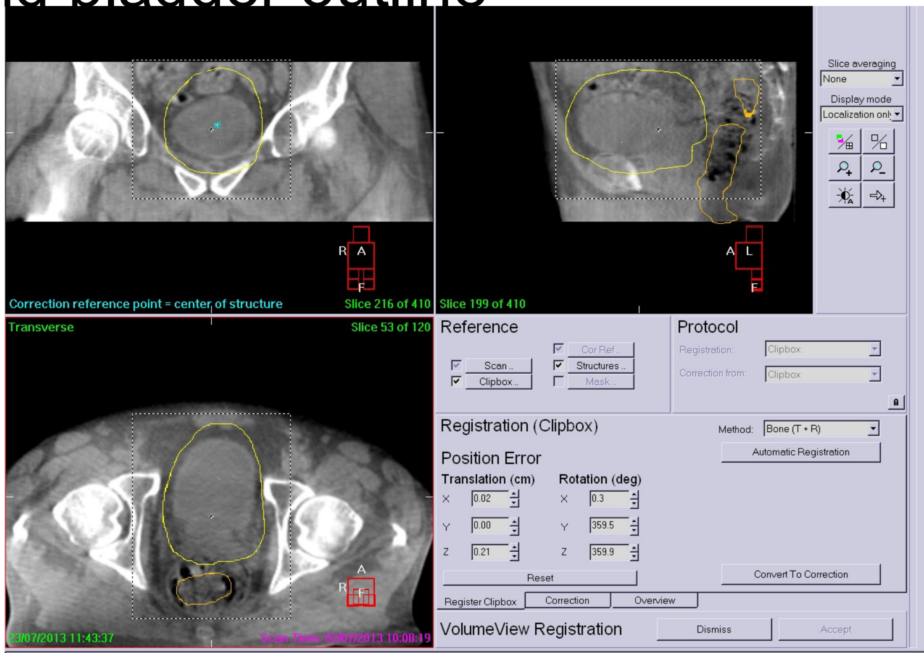
Registration-guidelines

Manual adjustment

3mm between PTV and bladder outline

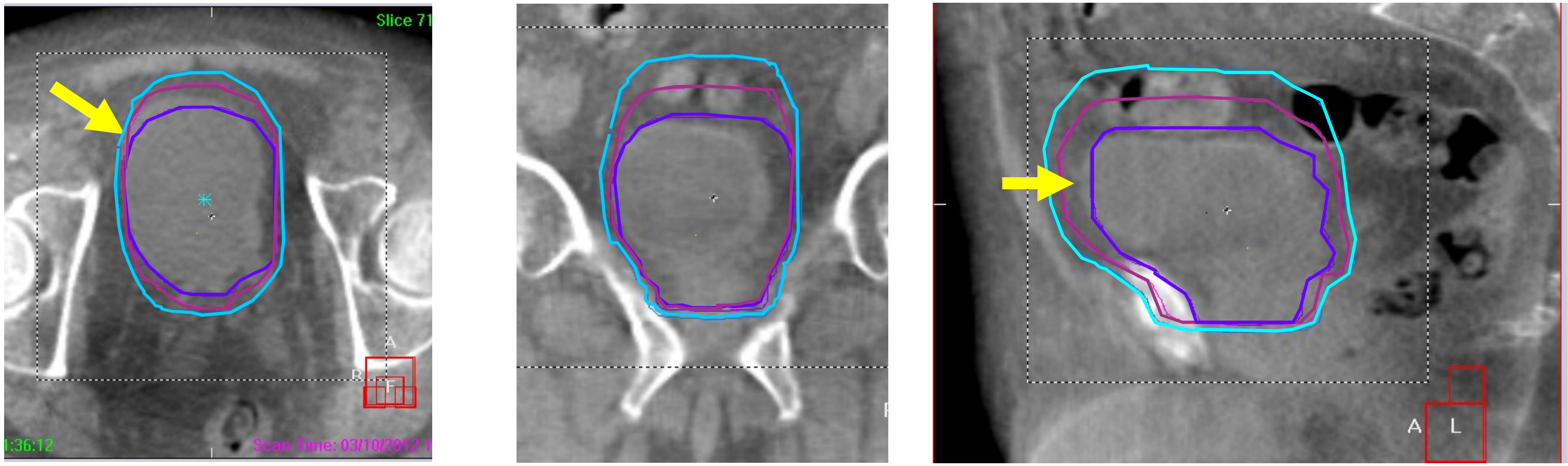




ESTRO School

Case 1

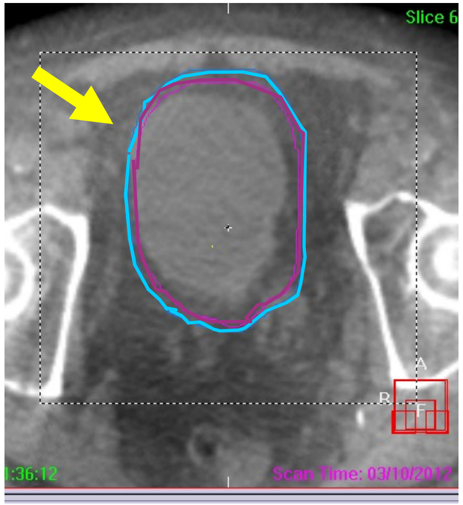
Gross assessment

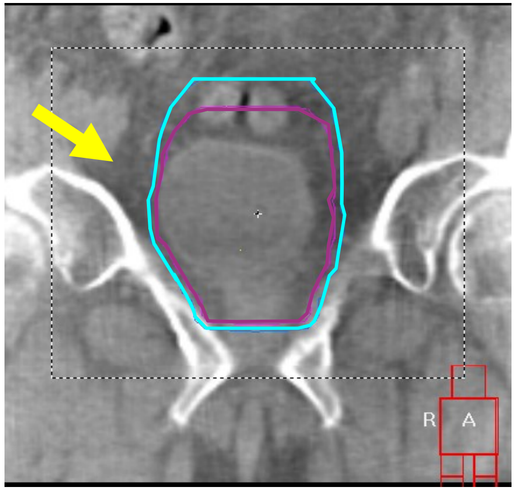


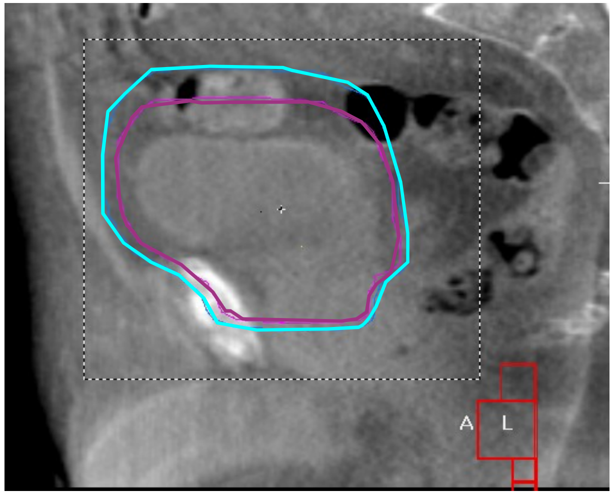
Small too small

Case 1

View all images/slices



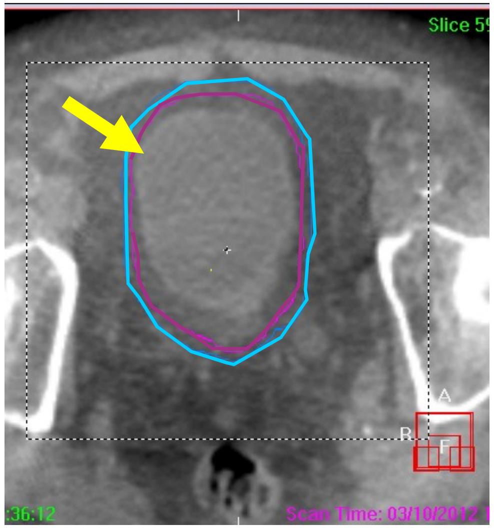


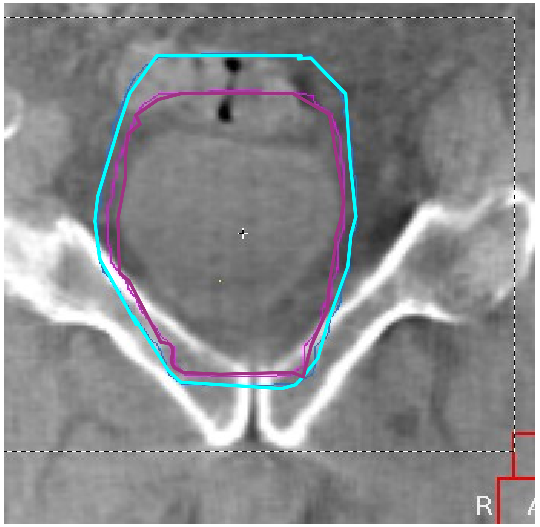


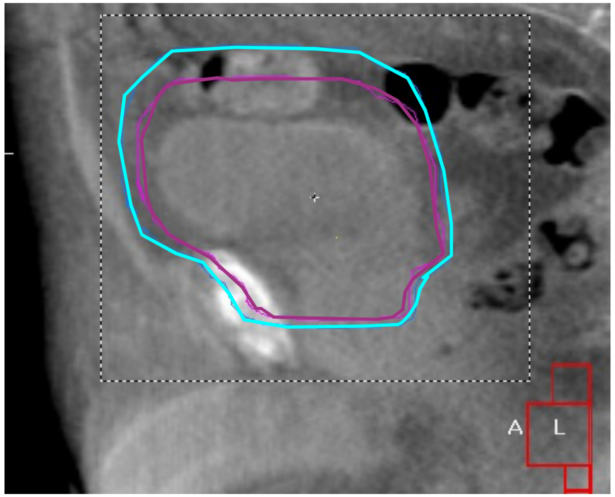
Needs right left shift

Case 1

Shift Right-left

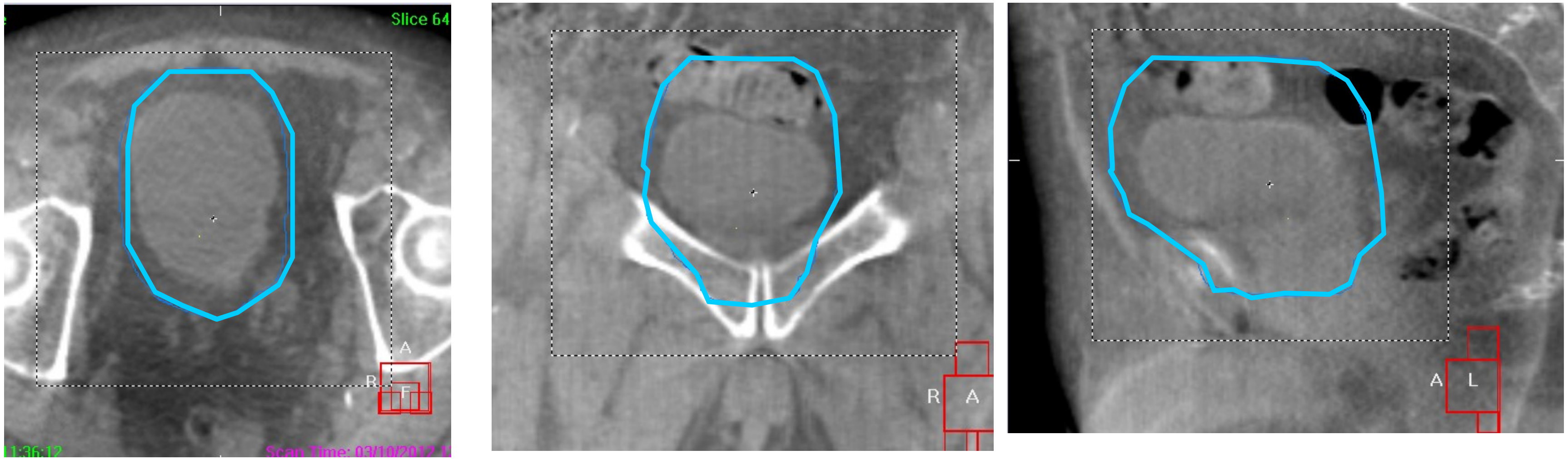






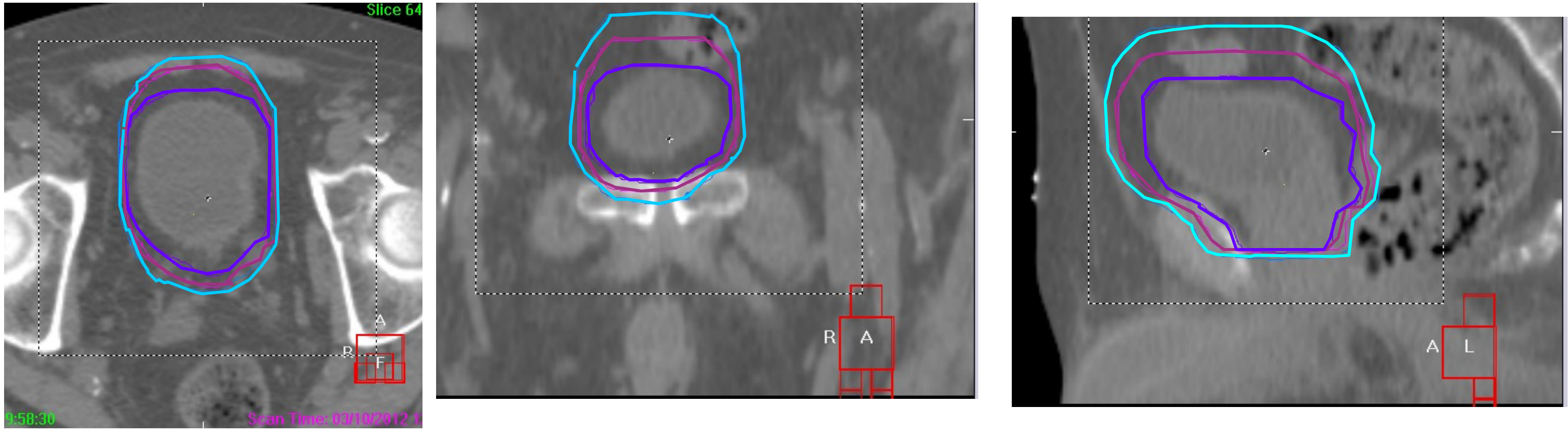
Medium still too tight

Case 1



Select large

Case 2



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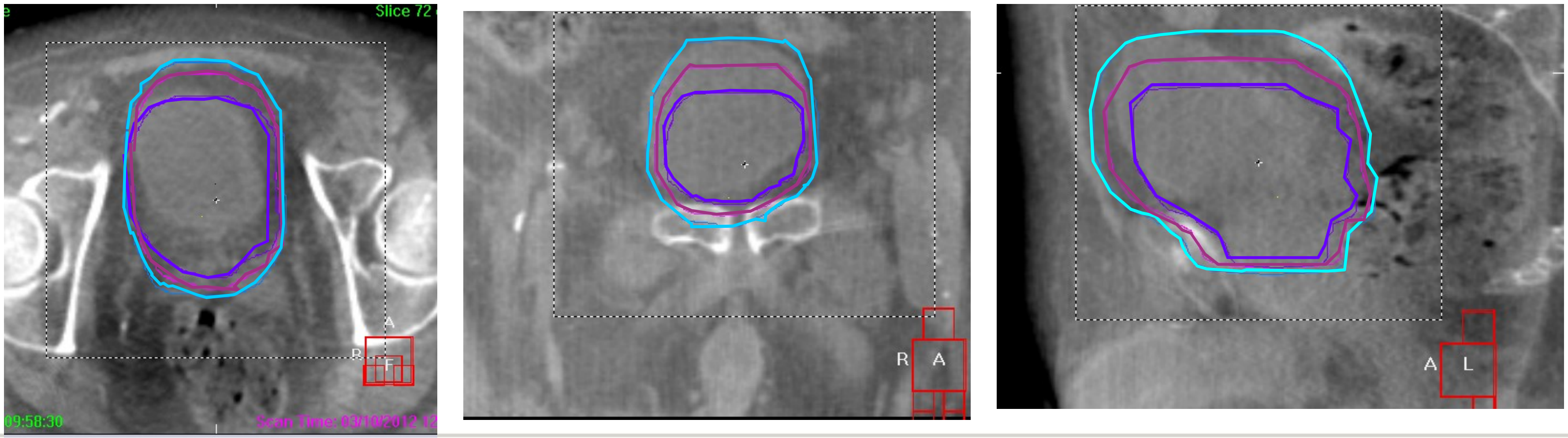


Treatment image

ESTRO School

Turning point question

Which choice is best

1. Small
2. Medium
3. Large
4. Shift
5. None

Registration issues

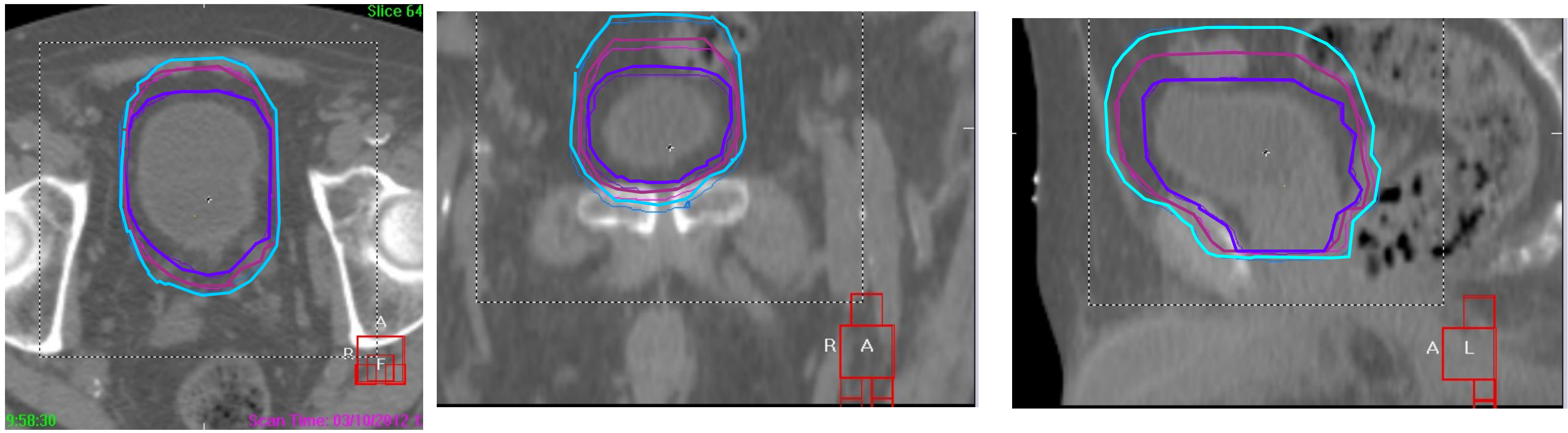
Consistent PTV selection between observers

No PTV is suitable- too large

No PTV is suitable – too small

Case 2

Too large- empty bladder



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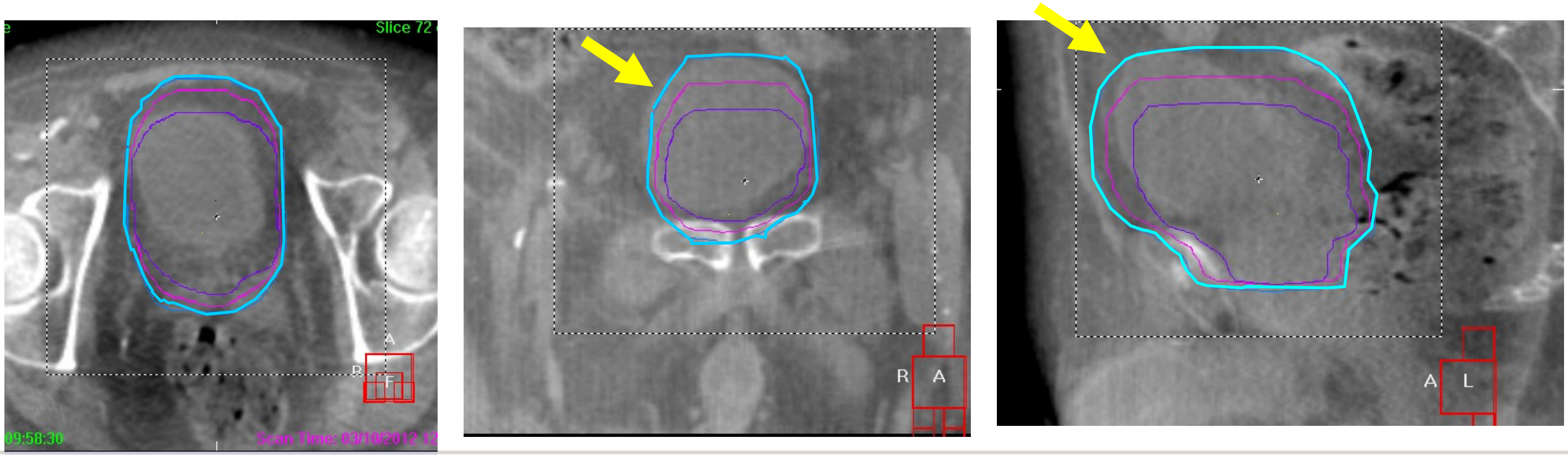


Treatment image

ESTRO School

Significant shape change

Bladder too big

No plan provides appropriate coverage

Shape change due to bladder overfilled

Shape change due to rectal filling (flatus/faeces)

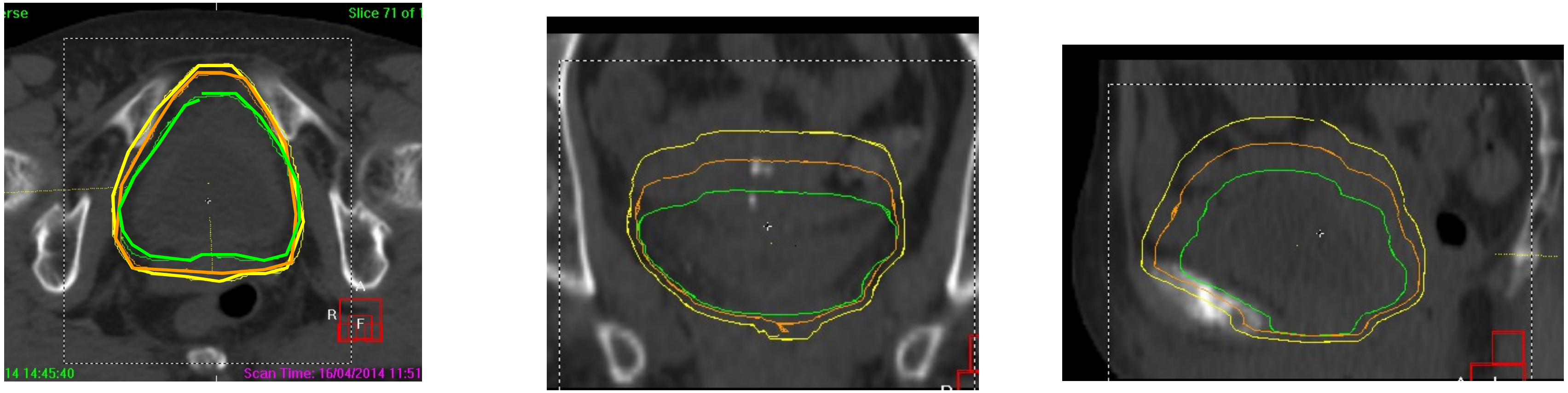
Remove patient from couch, void bladder, repeat drinking protocol but review

i) volume of fluid drank and or

ii) reducing time to image acquisition (<30mins),

iii) ensure appropriate clinical assessment is made and that patient is not developing toxicity necessitating intervention and preventing from appropriate voiding

Case 3



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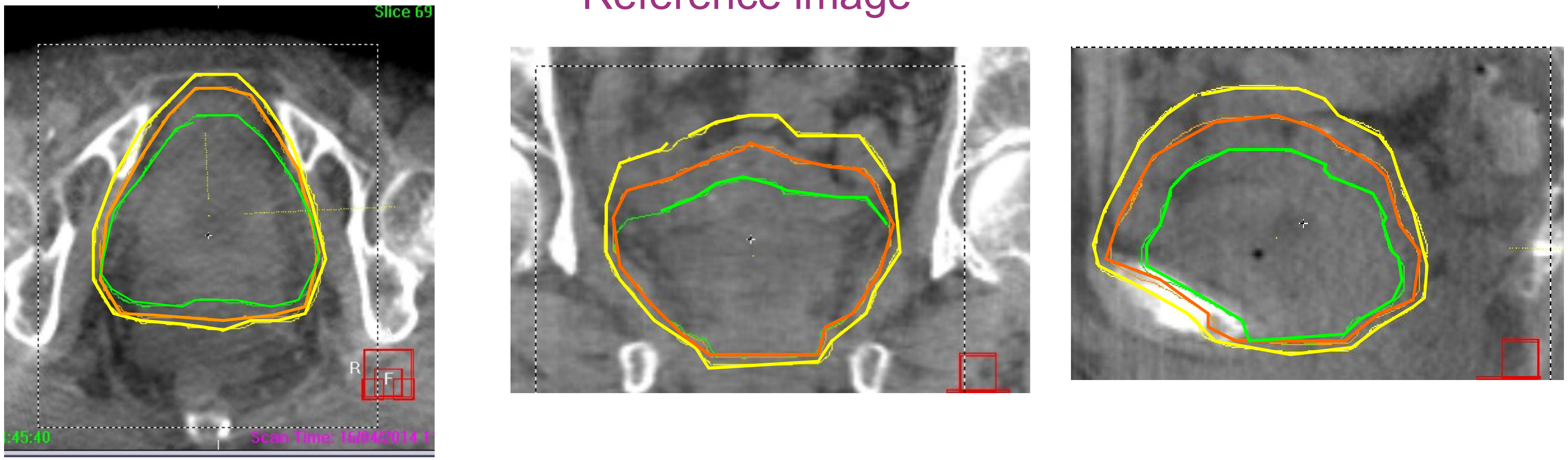


Treatment image

Which choice is best

1. Small

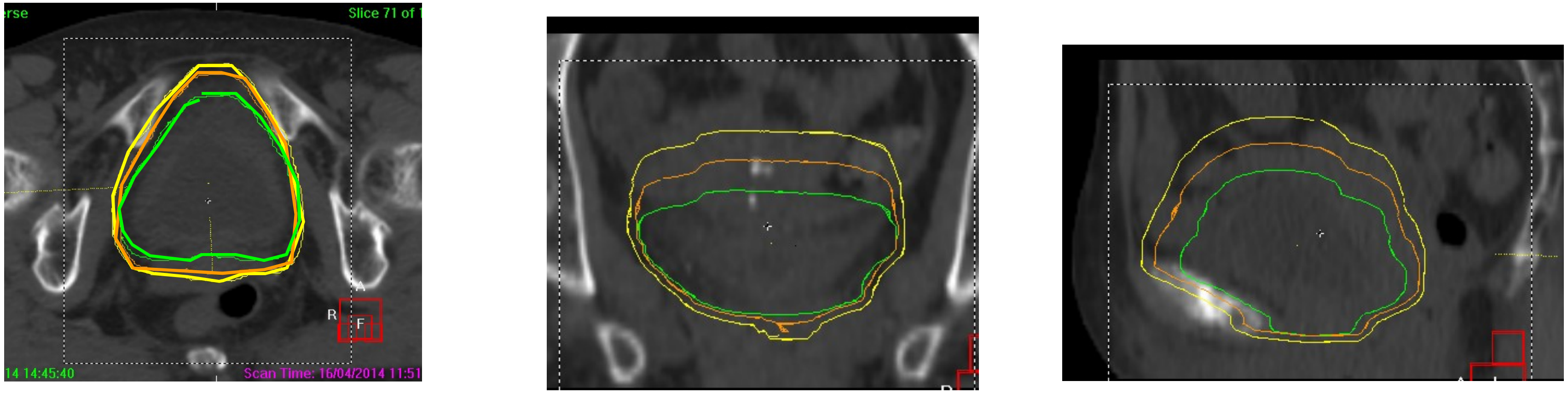
2.Medium

3.Large

4.Shift

5.None

Case 3-Small



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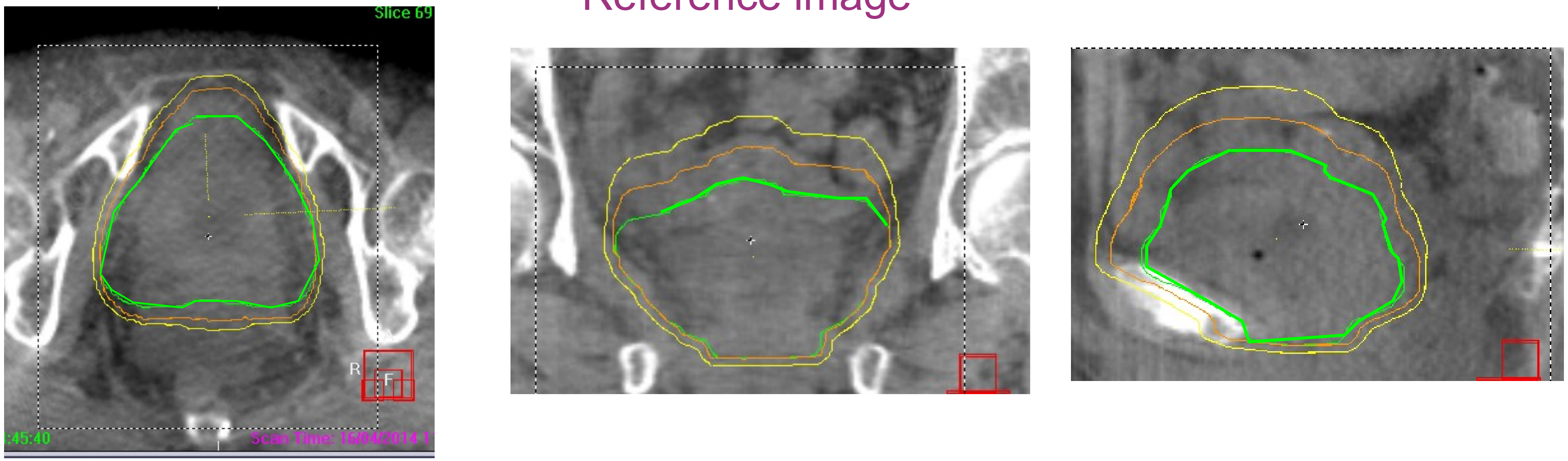


Treatment image

Registration issues

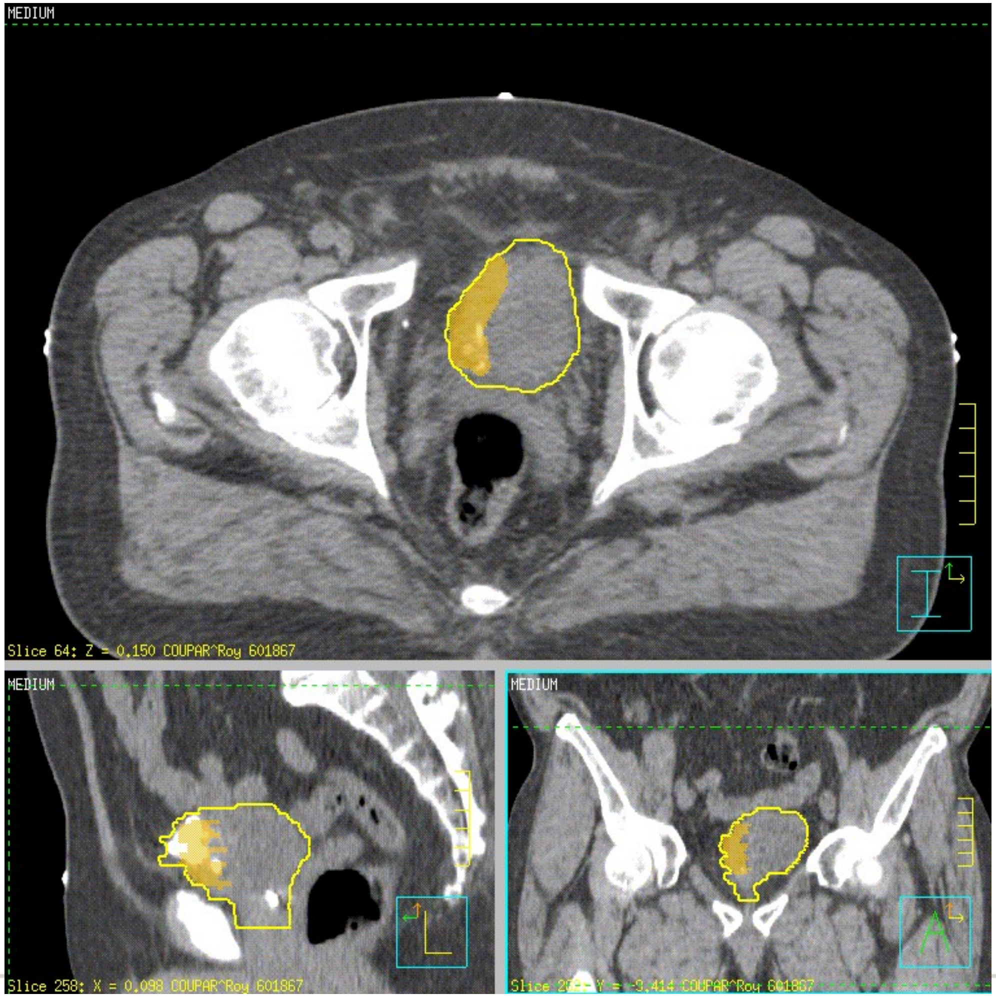
Consistent PTV selection between observers

No PTV is suitable- too large

Small

Replan of systematically smaller ?

Plan of the day – Full bladder



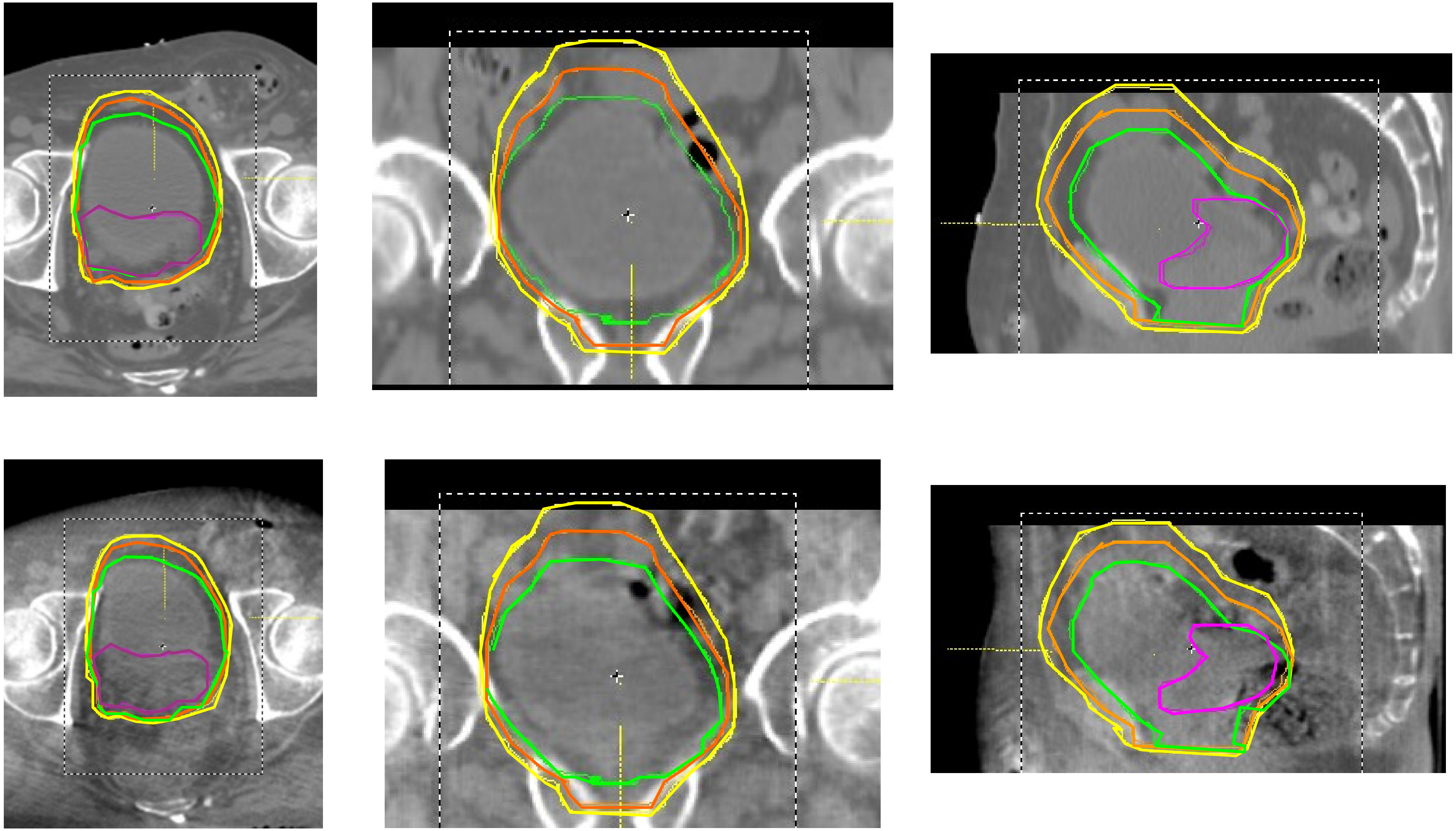
Partially' full bladder

30 and 60 min scans after emptying + 350mls of fluid

Concomitant boost

Plan of the day – Full bladder

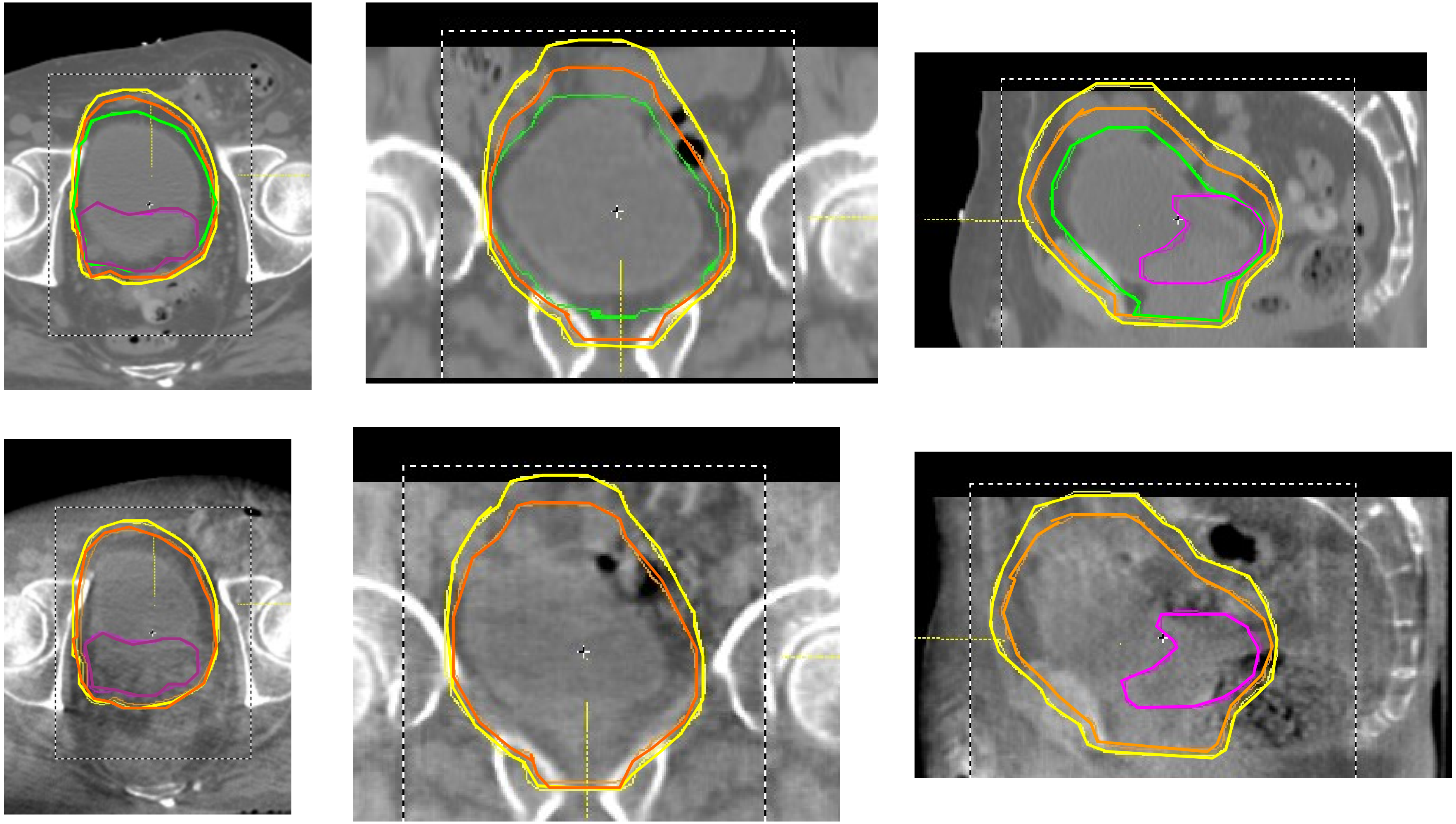
Which outline is not good?



Goss assessment – which outline is NOT good

1. Small
2. Medium
3. Large
4. Shift
5. None

Plan of the day – Reject small



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Which choice is best

1. Small

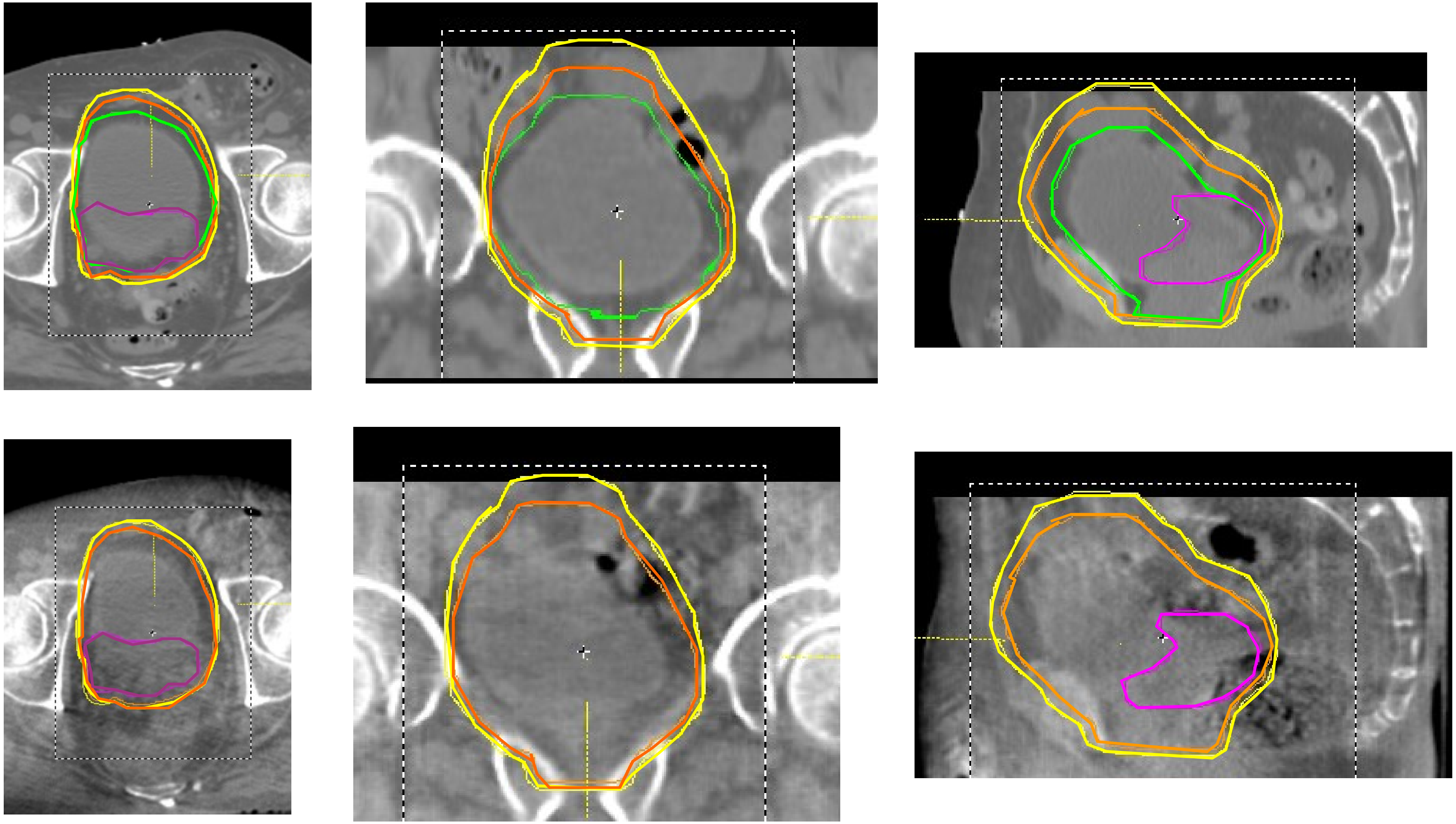
2.Medium

3.Large

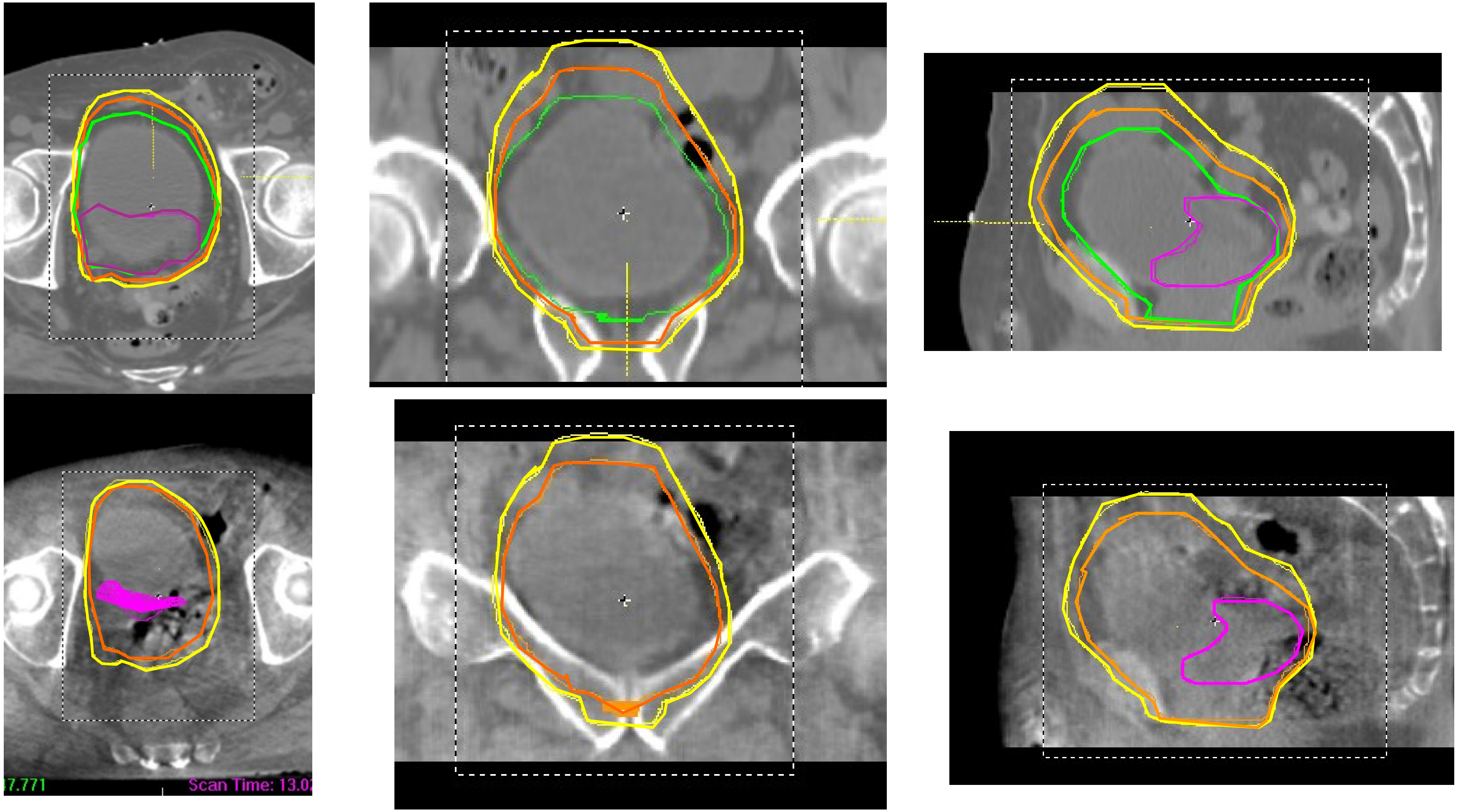
4.Shift

5.None

Plan of the day – Shift



Plan of the day – check

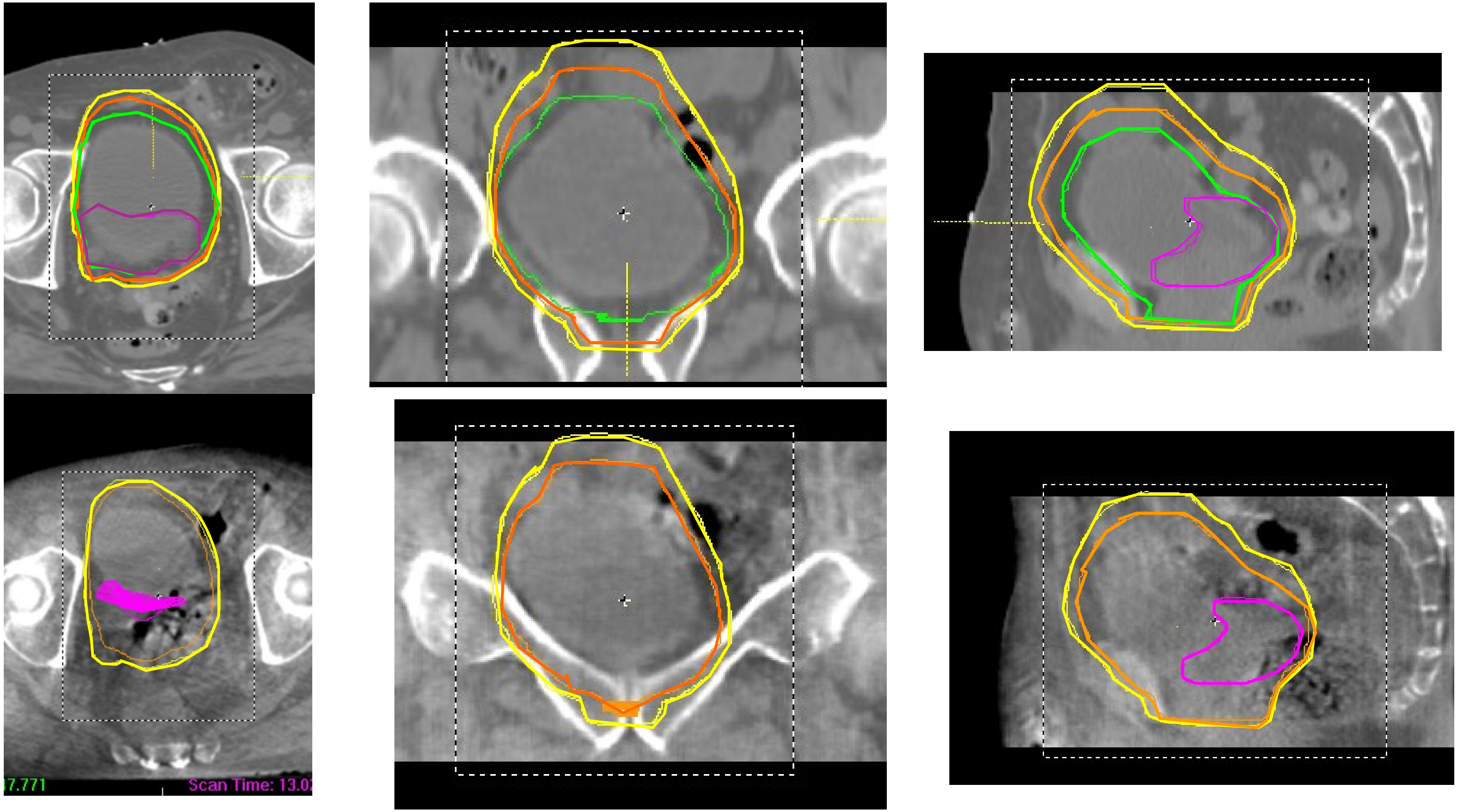


Turning point question

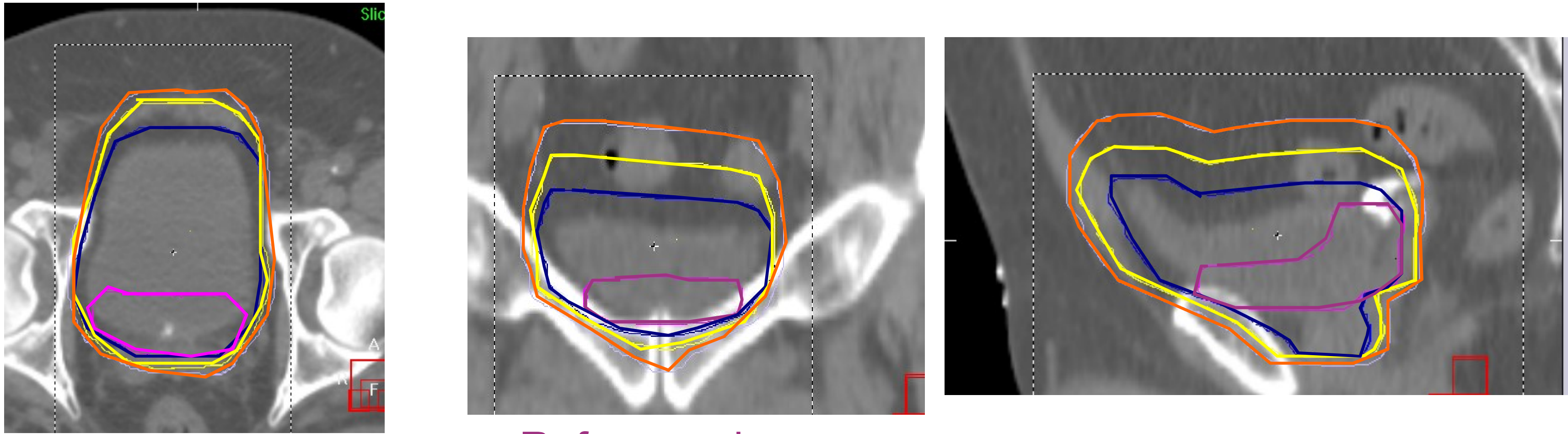
Which choice is best

1. Small
2. Medium
3. Large
4. Shift
5. None

Plan of the day – check



Case 5



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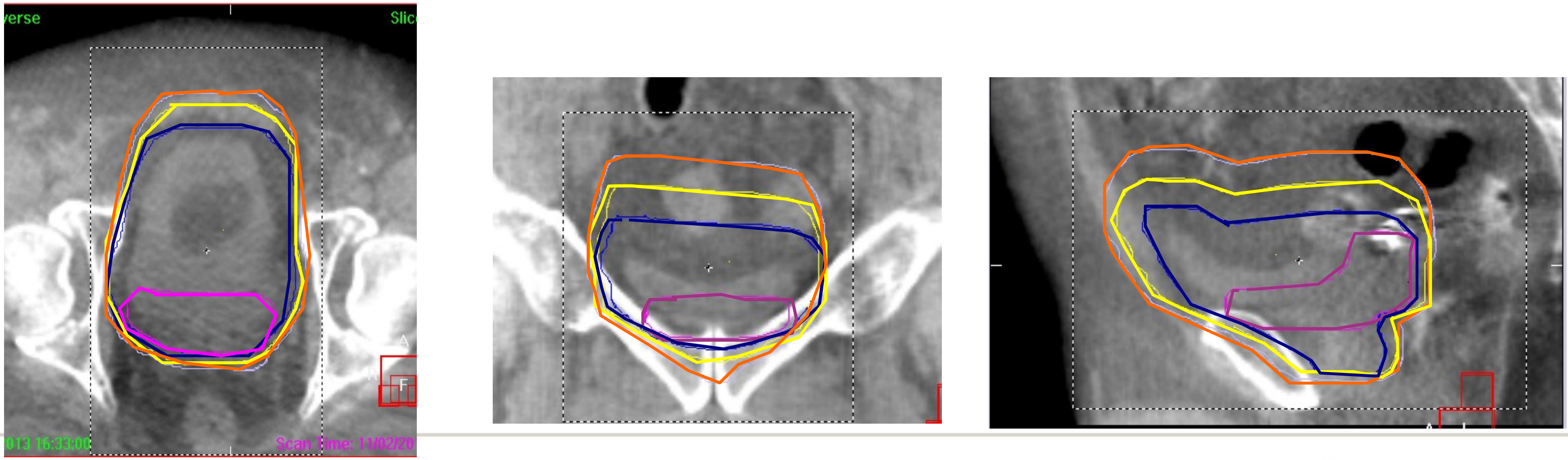


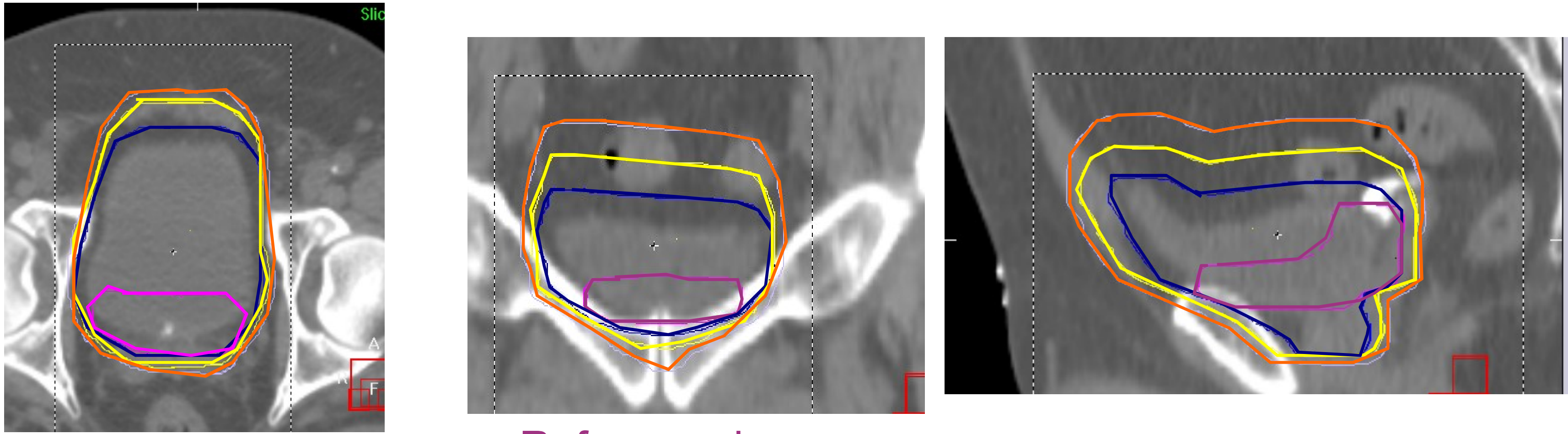
Treatment image

Turning point question

Which outline is best

1. Small
2. Medium
3. Large
4. Shift
5. None

Case 5



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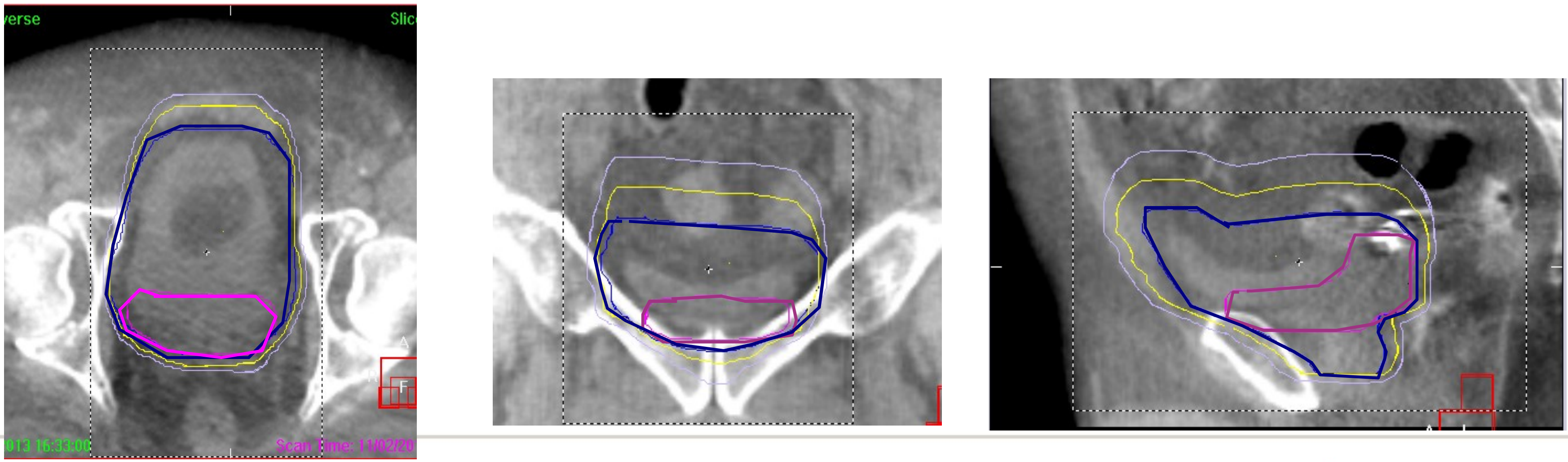


Treatment image

ESTRO School

Significant shape change

Bladder too small

↓

Small plan provides appropriate coverage of bladder but normal tissue sparing from high dose region compromised

↓

Appropriate to consider treatment with small plan

↓

Requires clinical review prior to next fraction.
Assessment :-
i) general hydration status
ii) development of urinary toxicity requiring intervention (preventing from appropriate holding)
iii) increasing time to image acquisition>30mins and, or
iv) increasing volume of fluids in drinking protocol

Registration issues

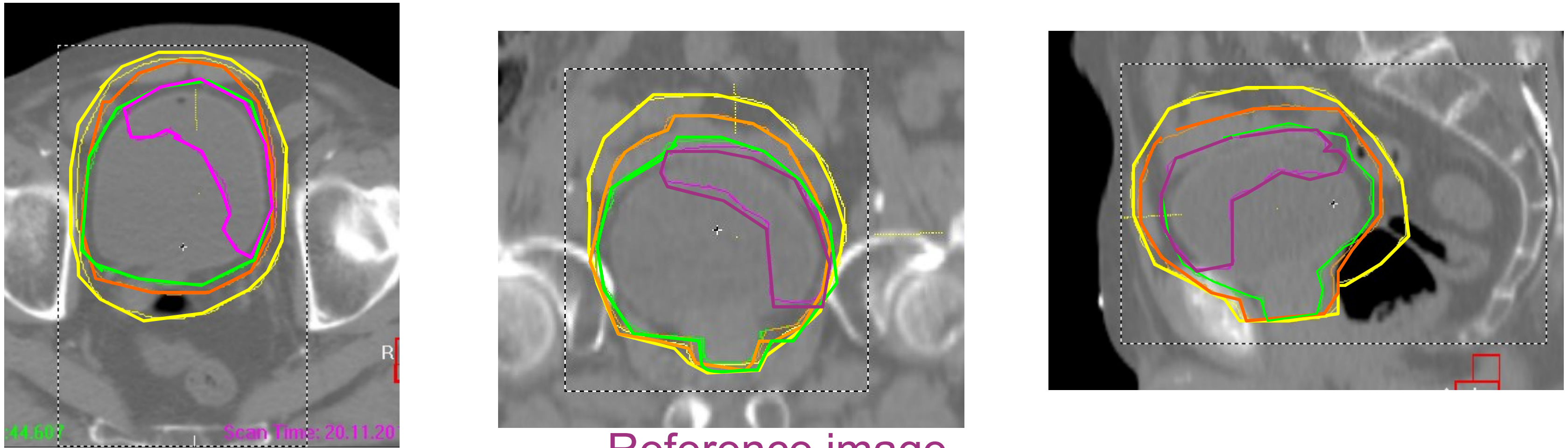
Consistent PTV selection between observers

No PTV is suitable- too large

No PTV is suitable – too small

Replan of systematically smaller ??

Case 6



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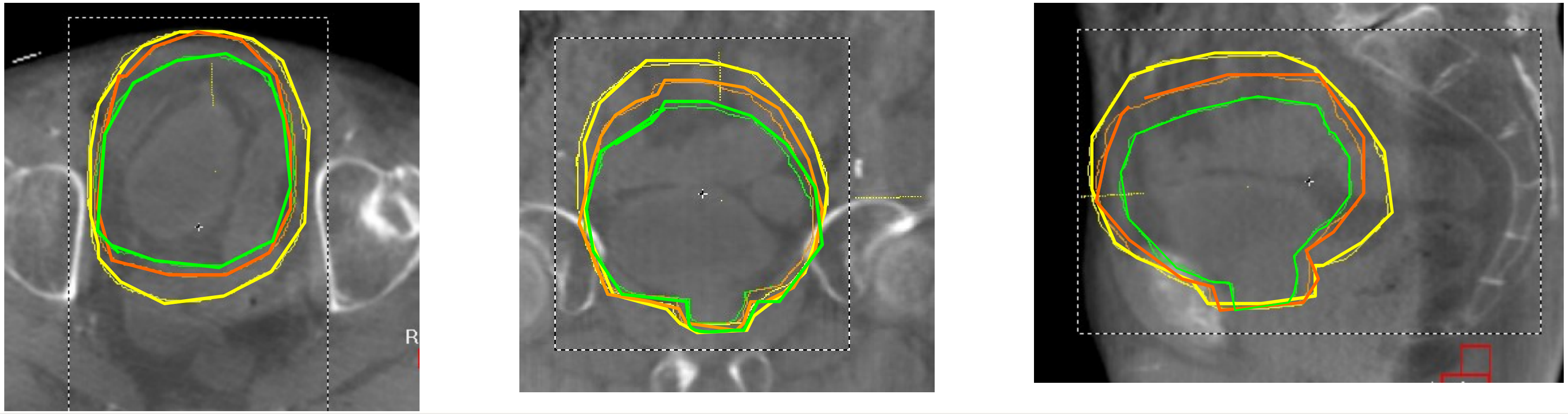
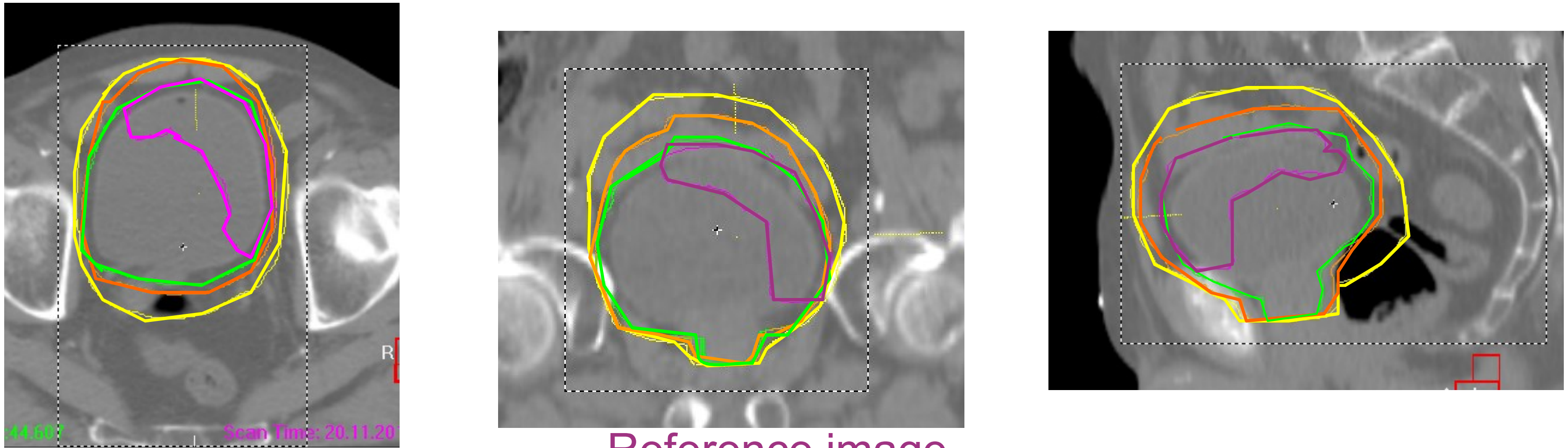


Treatment image

Case 6



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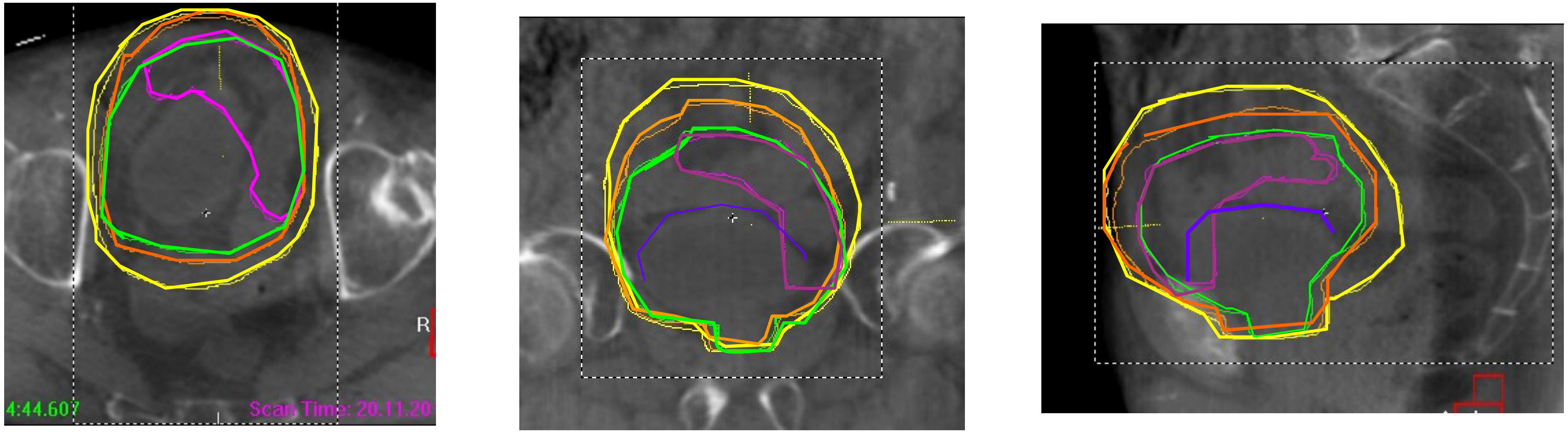


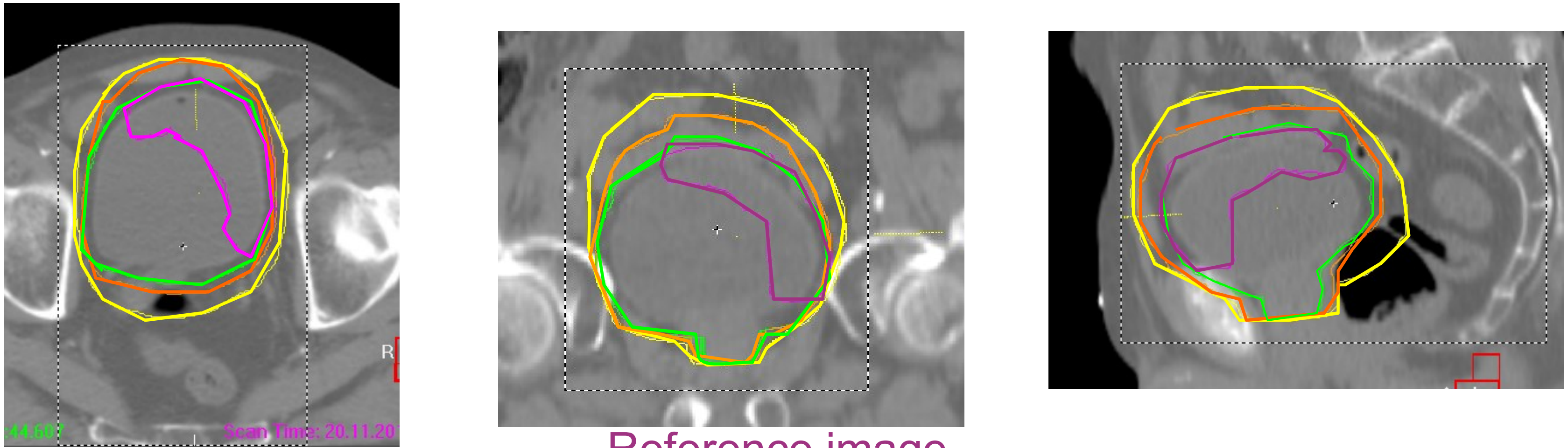
Treatment image

Turning point question

Which choice is best

1. Small
2. Medium
3. Large
4. Shift
5. None

Case 6-bowel boost!



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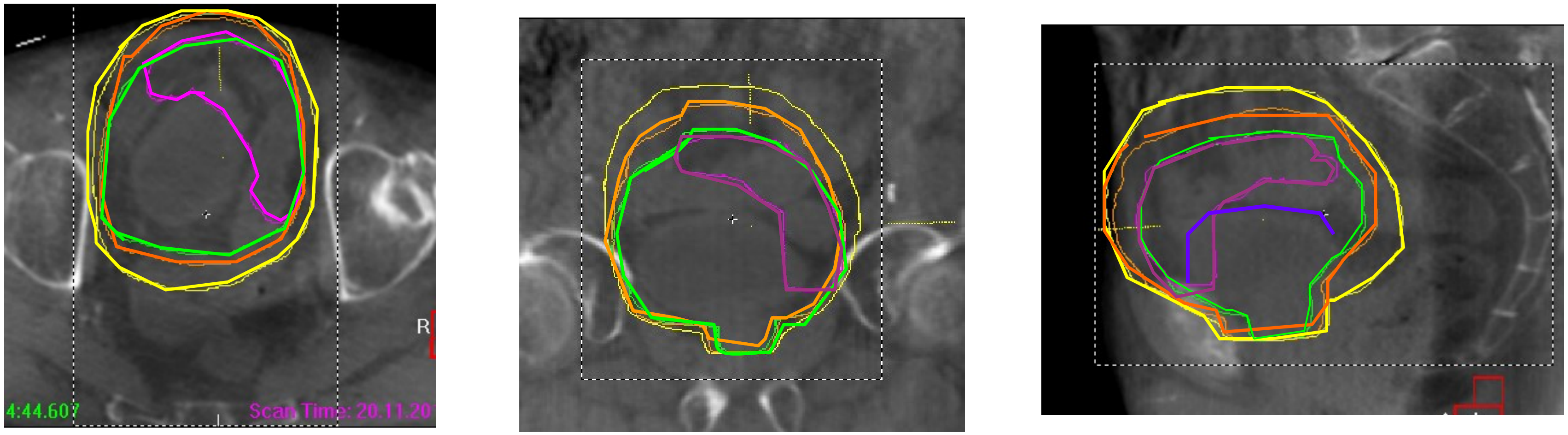


Treatment image

ESTRO School

Turning point question

Action

1. Treat
2. Shift and treat
3. Ask patient to drink more
4. Ask patient to get off bed and drink more
5. Adjust drinking protocol for tomorrow

Significant shape change

Bladder too small

↓

Small plan provides appropriate coverage of bladder but normal tissue sparing from high dose region compromised

↓

Appropriate to consider treatment with small plan

↓

Requires clinical review prior to next fraction.
Assessment :-
i) general hydration status
ii) development of urinary toxicity requiring intervention (preventing from appropriate holding)
iii) increasing time to image acquisition>30mins and, or
iv) increasing volume of fluids in drinking protocol

Significant shape change

Bladder too small

↓

Small plan provides appropriate coverage of bladder but normal tissue sparing from high dose region compromised

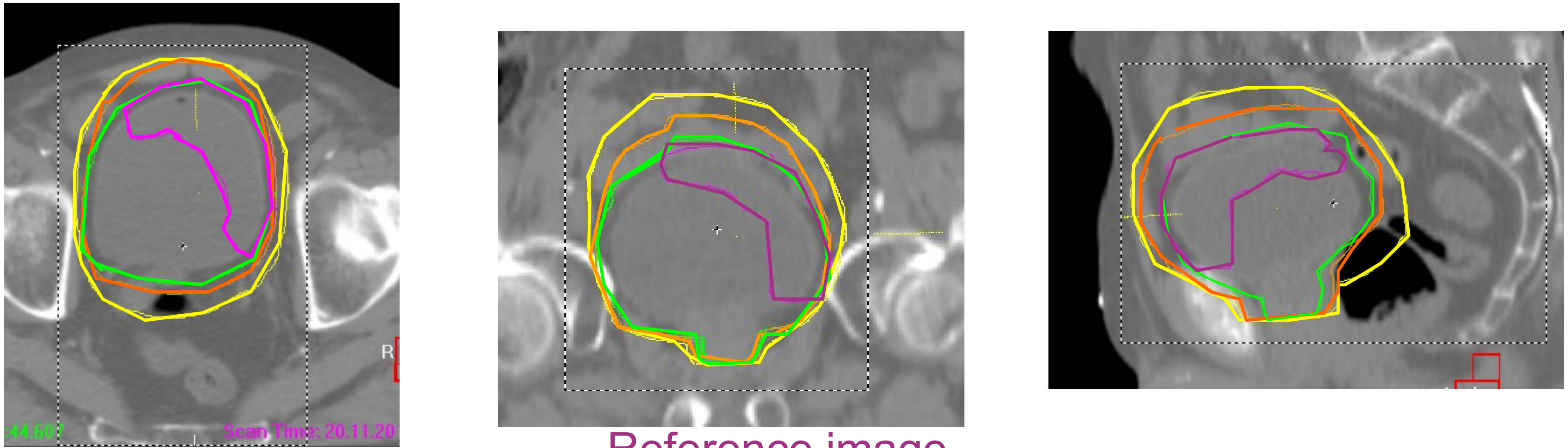
↓

Appropriate to consider treatment with small plan

↓

Requires clinical review prior to next fraction.
Assessment :-
i) general hydration status
ii) development of urinary toxicity requiring intervention (preventing from appropriate holding)
iii) increasing time to image acquisition>30mins and, or
iv) increasing volume of fluids in drinking protocol

Case 6 – extra drinking-40mins + more water



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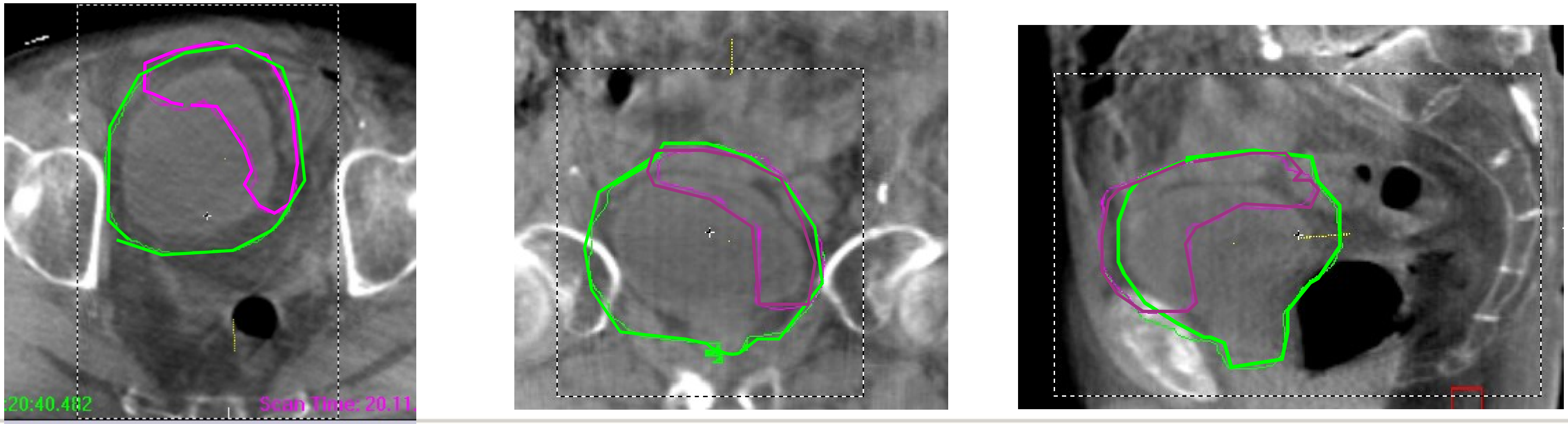

Treatment image

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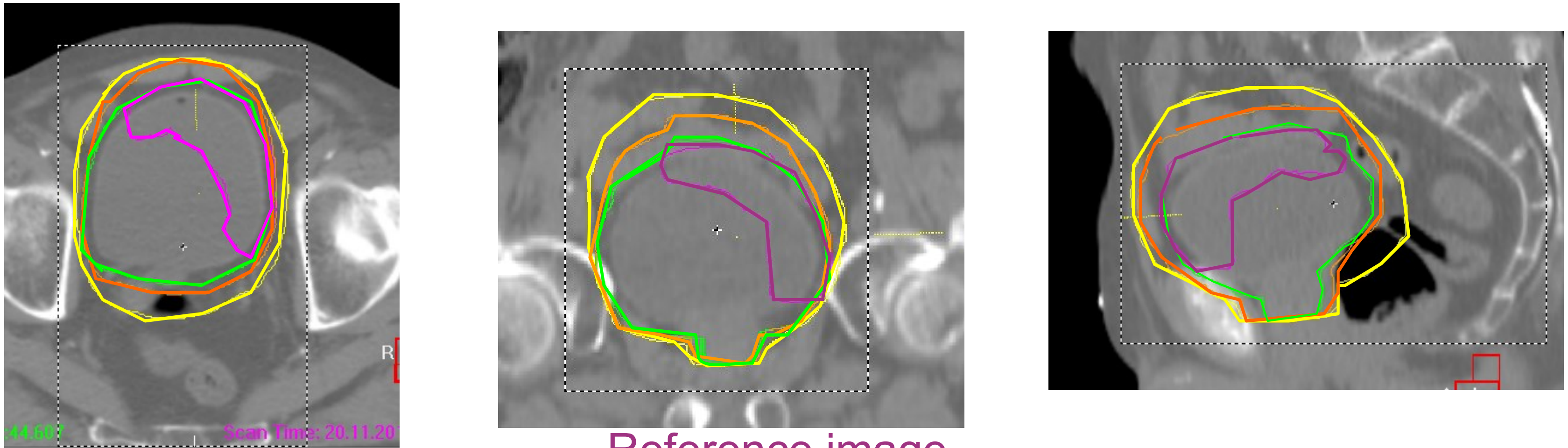
Case 6 (Day 2)- bony match



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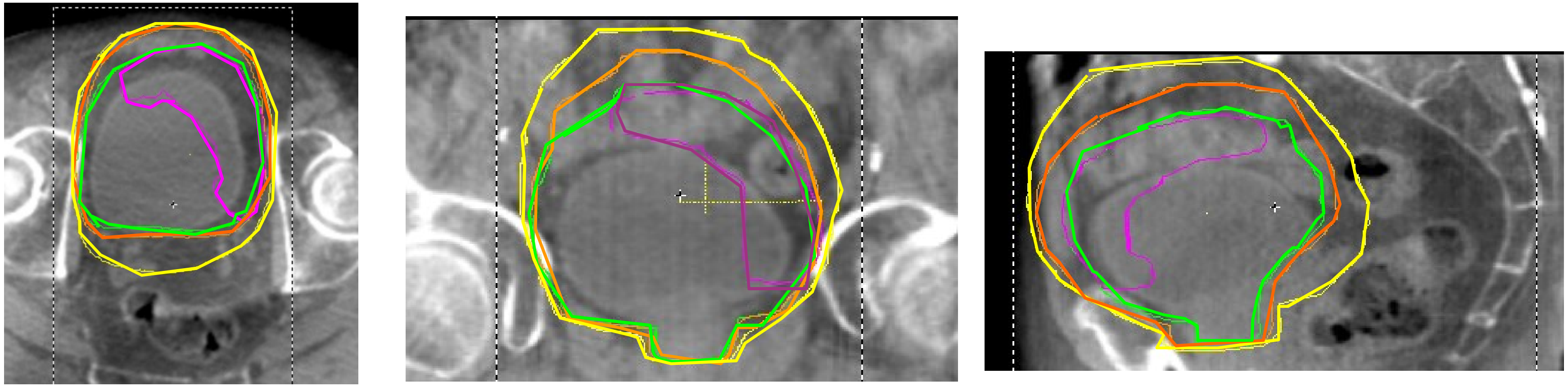
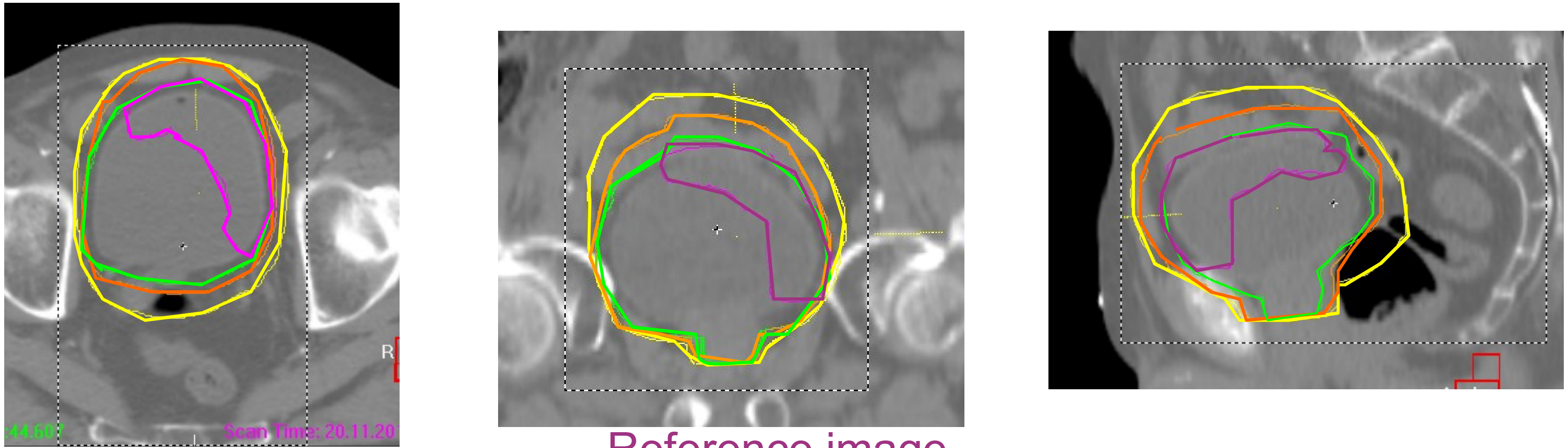


Treatment image

Case 6 - soft tissue adjustment



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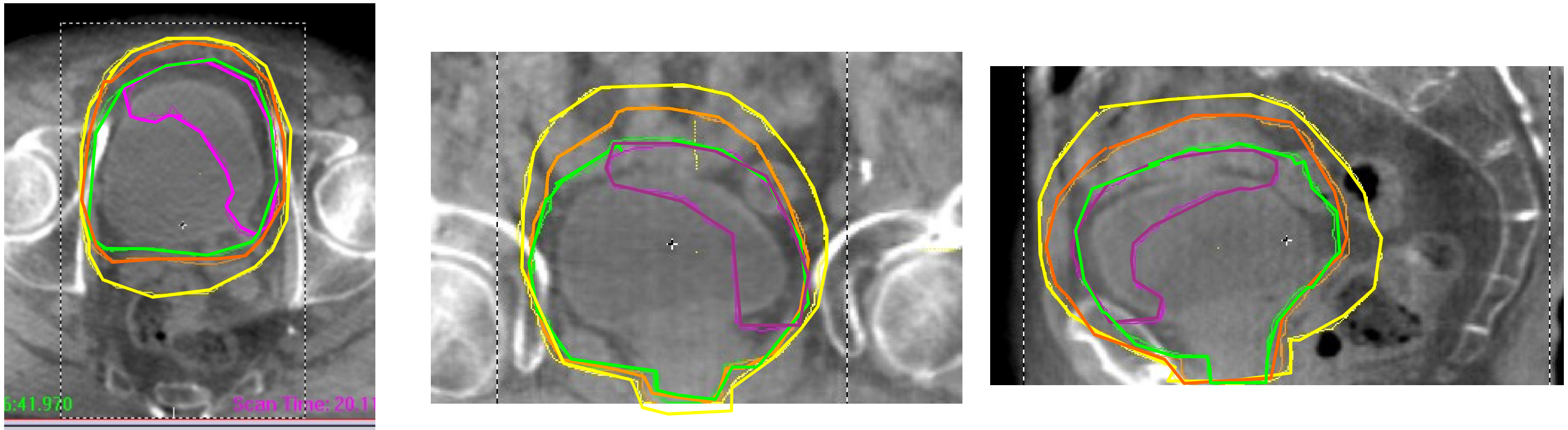
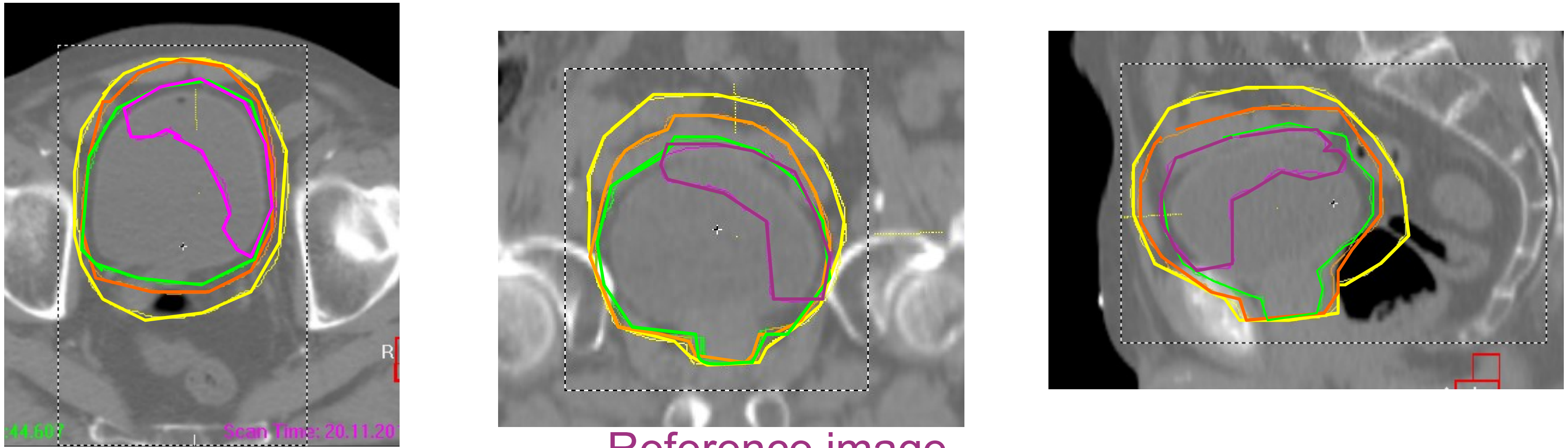


Treatment image

Check coverage



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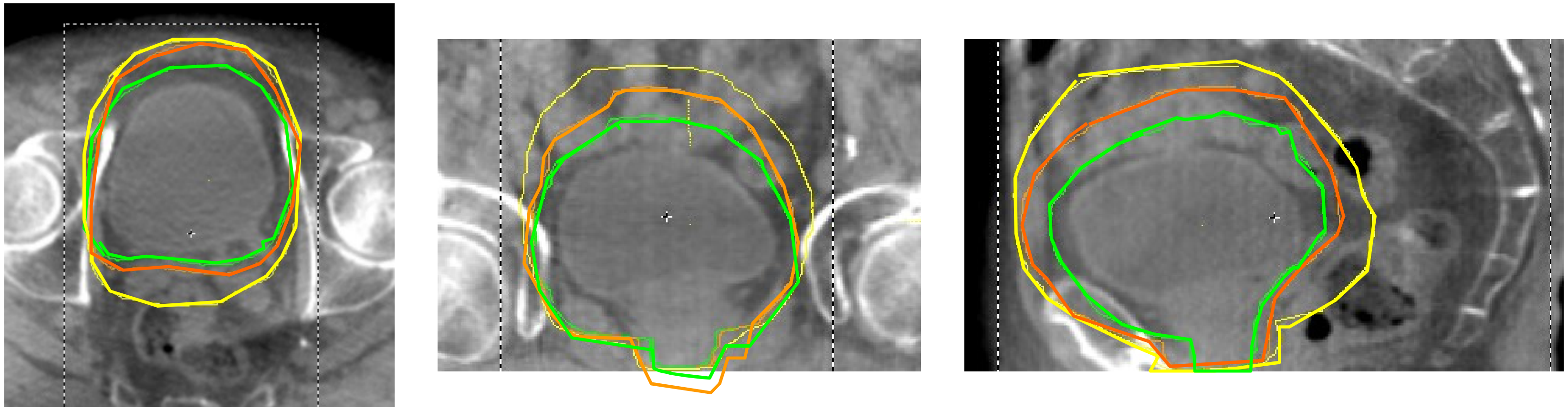
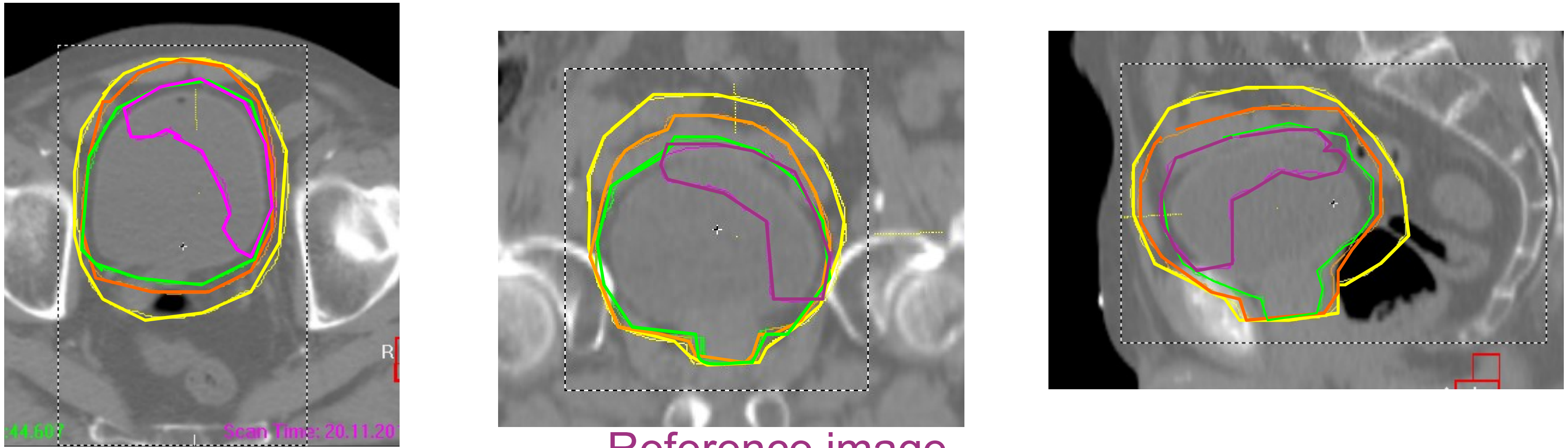


Treatment image

ESTRO School

Check coverage



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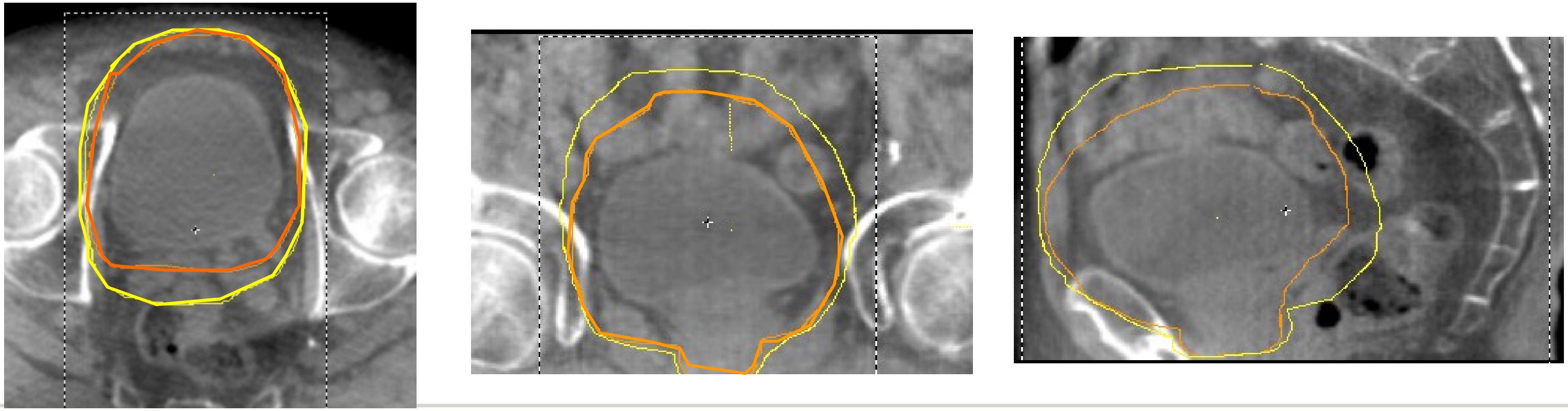
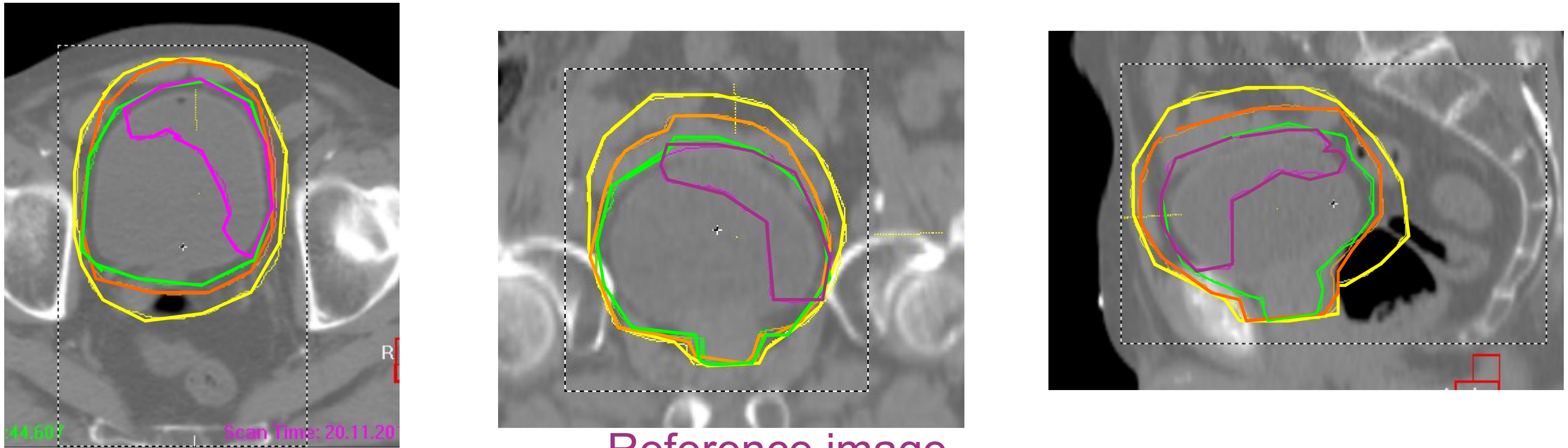


Treatment image

Check boost



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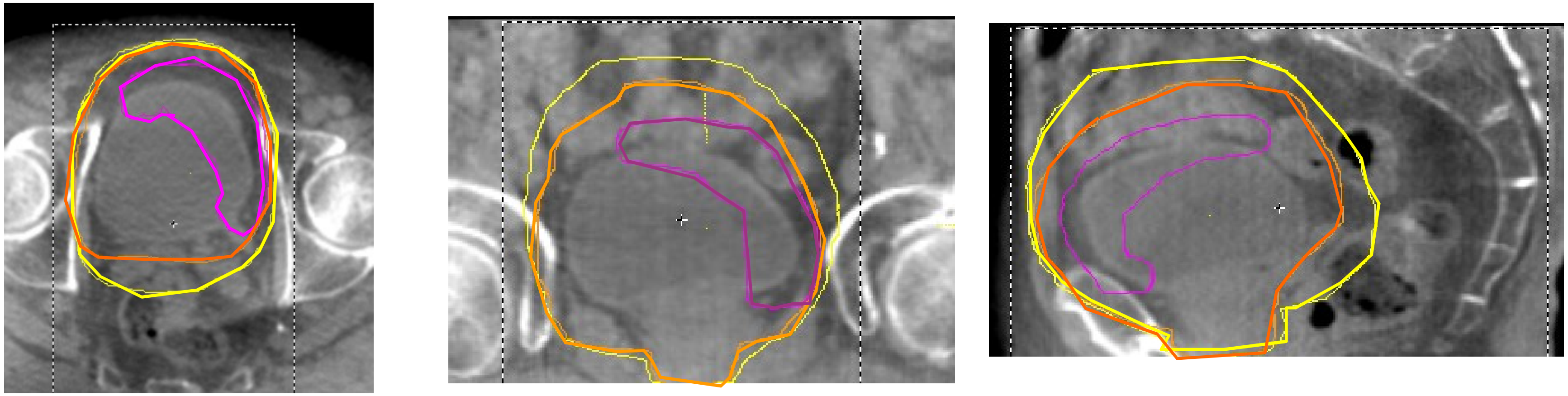
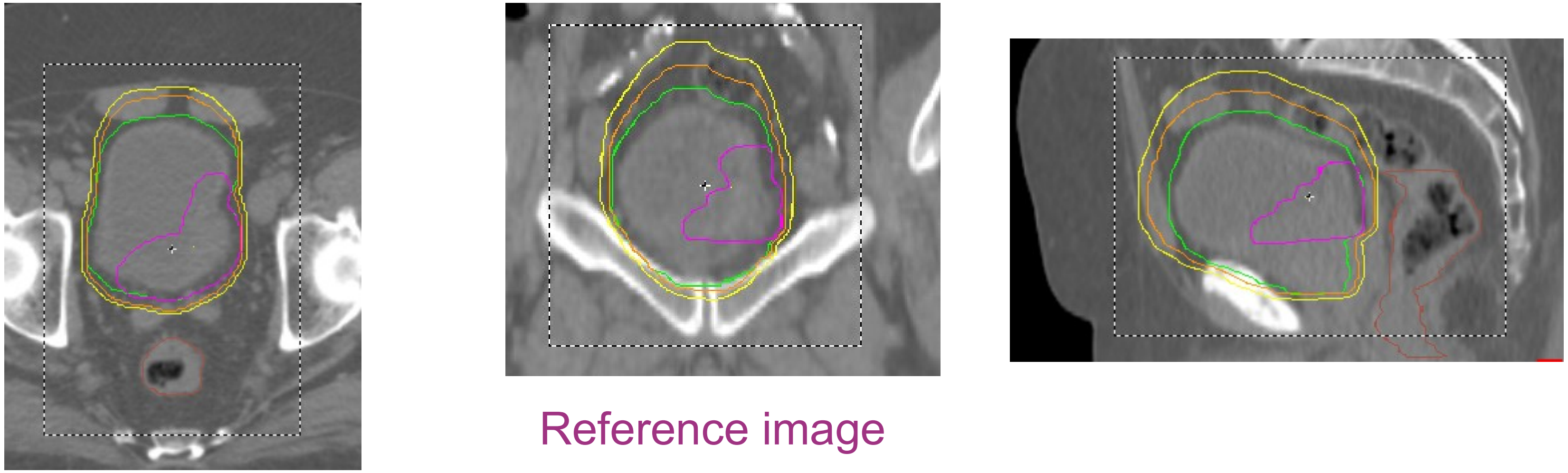


Treatment image

ESTRO School

Case 7 - gas



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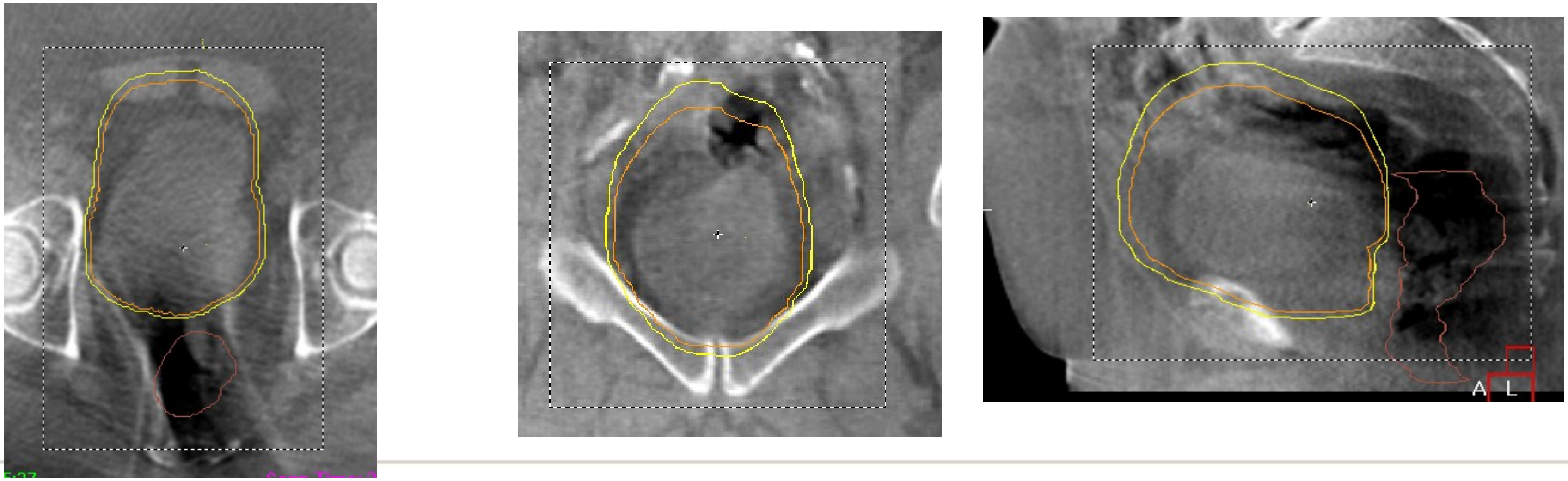


Treatment image

Significant shape change

Bladder too big

↓

No plan provides appropriate coverage

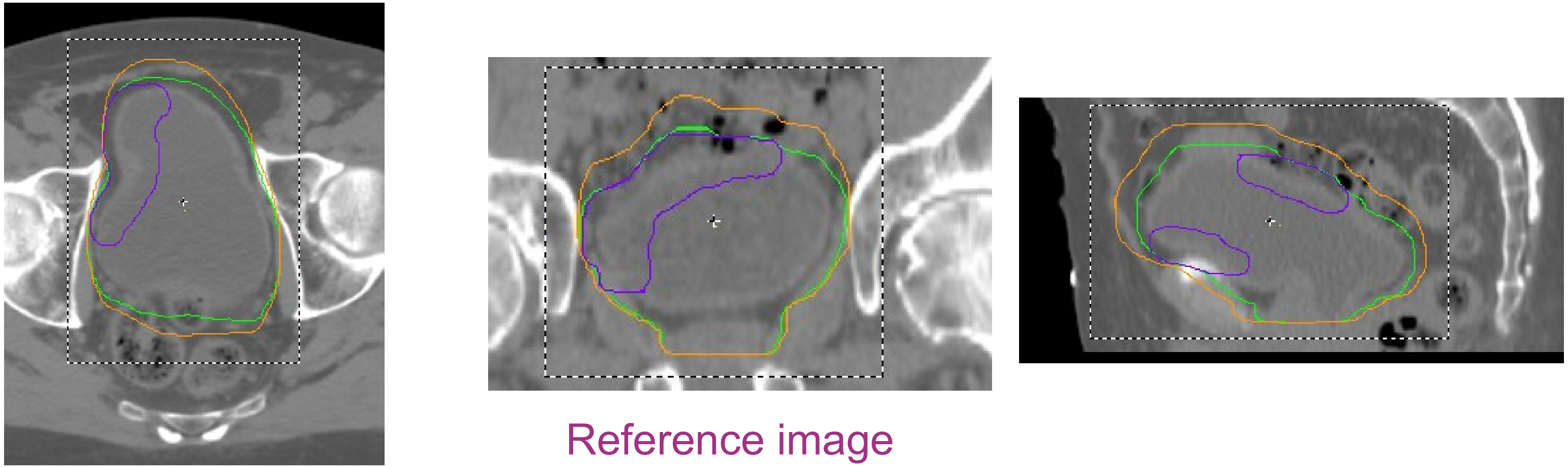
↓

Shape change due to rectal filling (flatus/faeces)

↓

Remove patient from couch, empty bowel (and bladder), repeat drinking protocol but consider clinical review prior to next fraction to determine whether laxative or suppositories indicated

Case 8 - unusual



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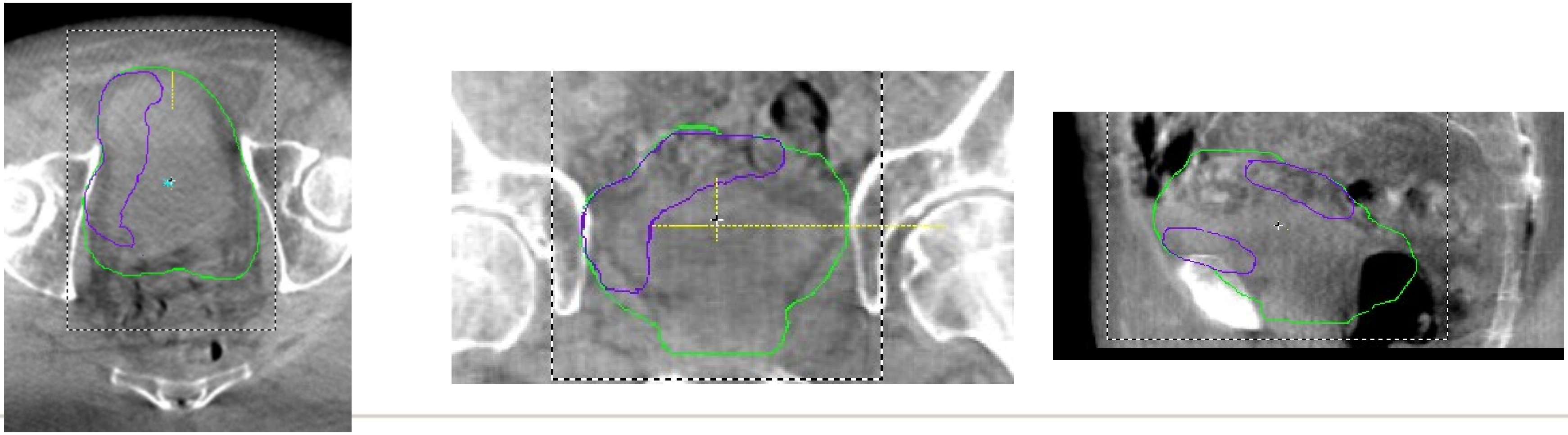
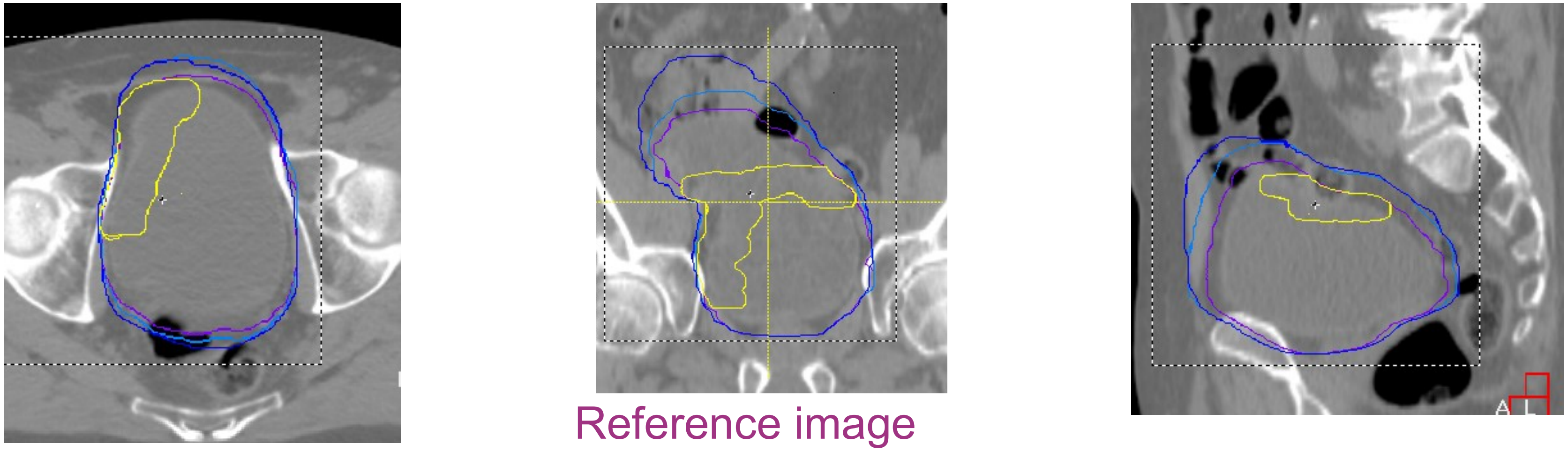


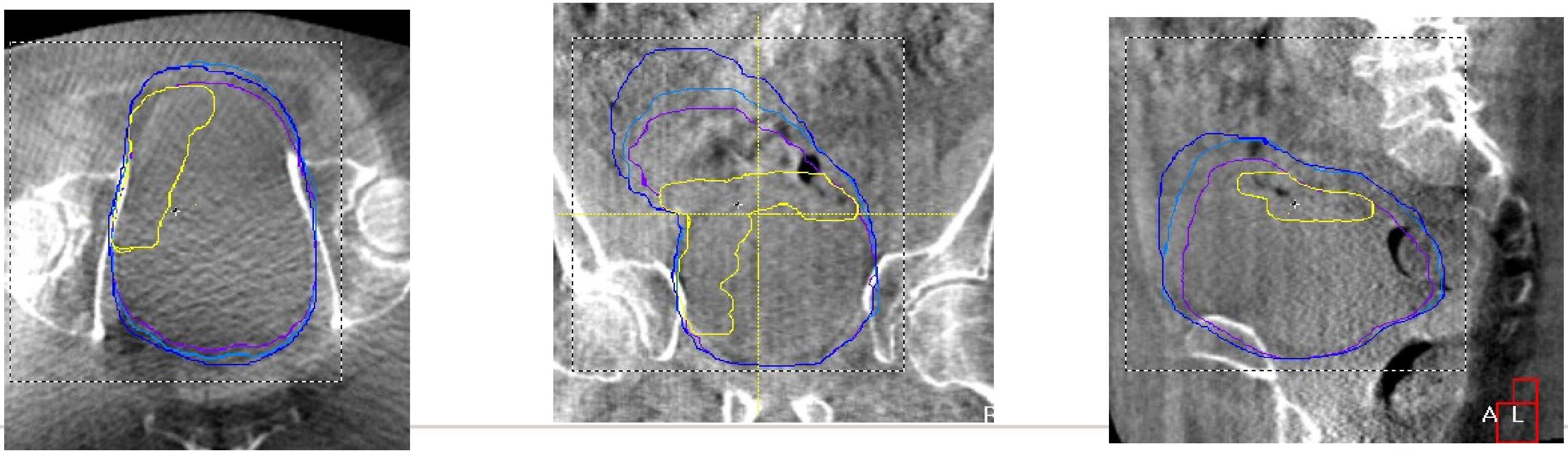
Treatment image

ESTRO School

Case 8- unusual

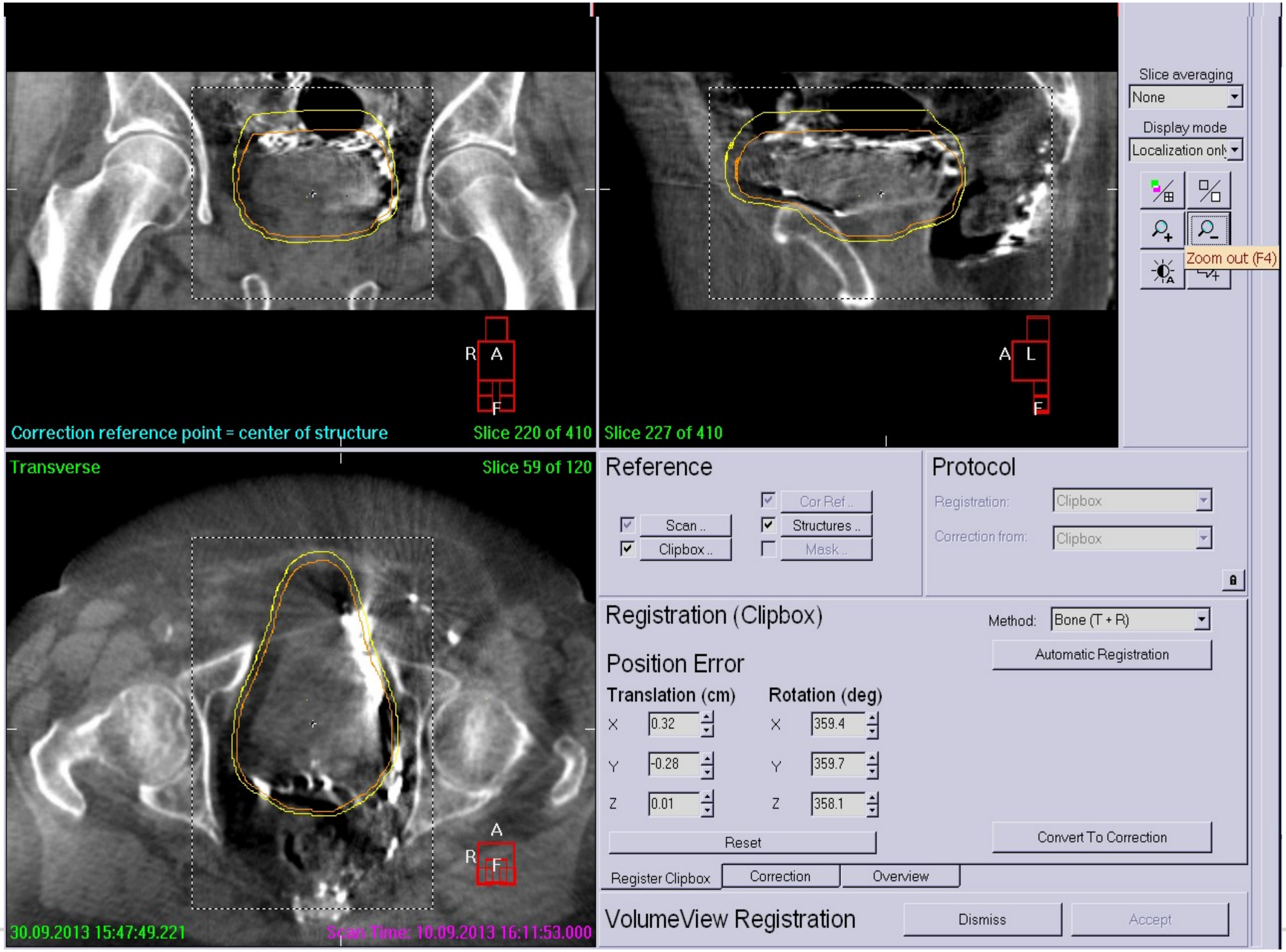


Reference image



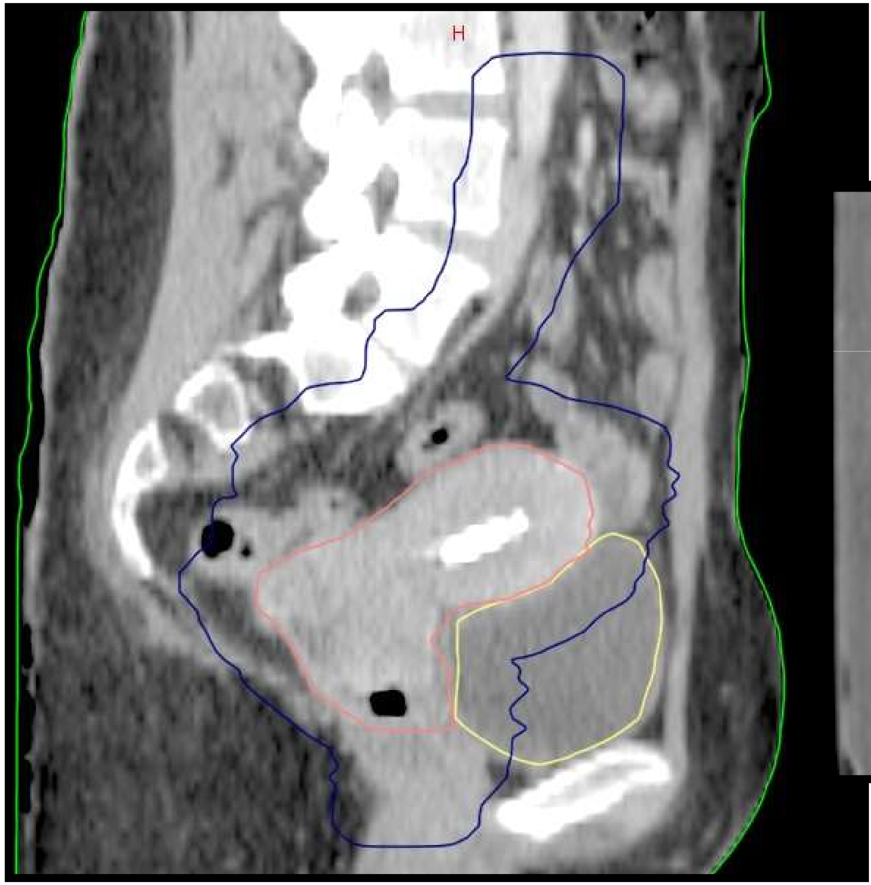
Treatment image

Case 9- boost and contrast?

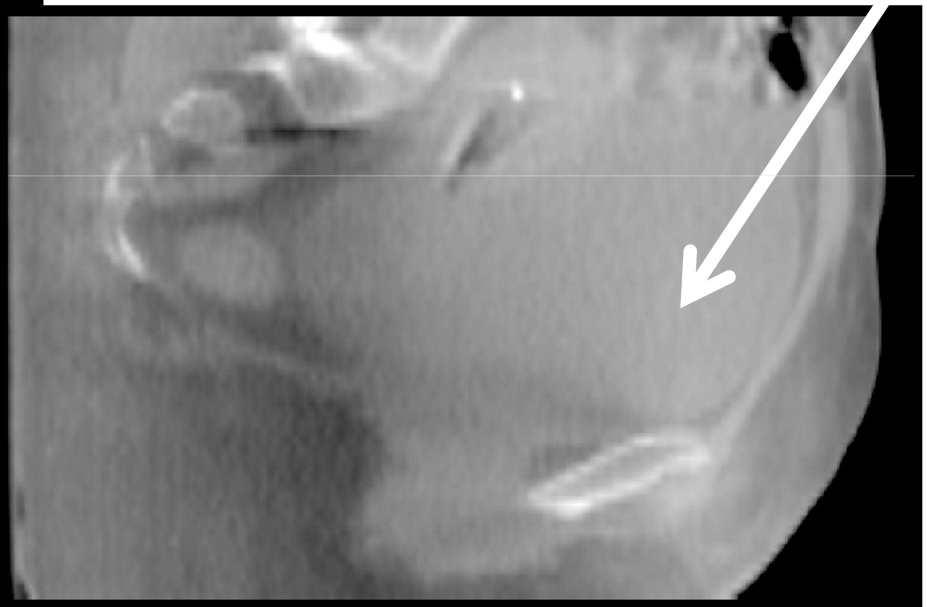


CERVIX

Clinical Example 1 – Bladder

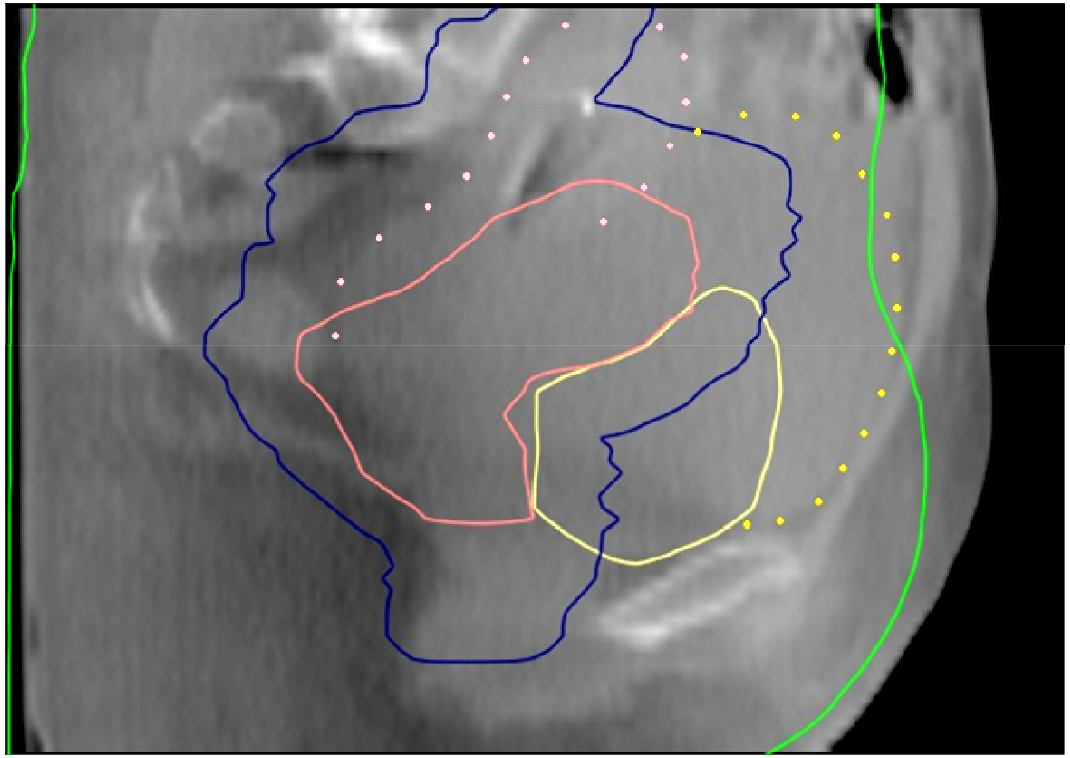


Is there a problem?



Slide courtesy of Sophie Alexander

Clinical Example 1 – Bladder



Bladder significantly bigger than planned.

Displacing uterus superiorly.

Why?

Chemotherapy day.

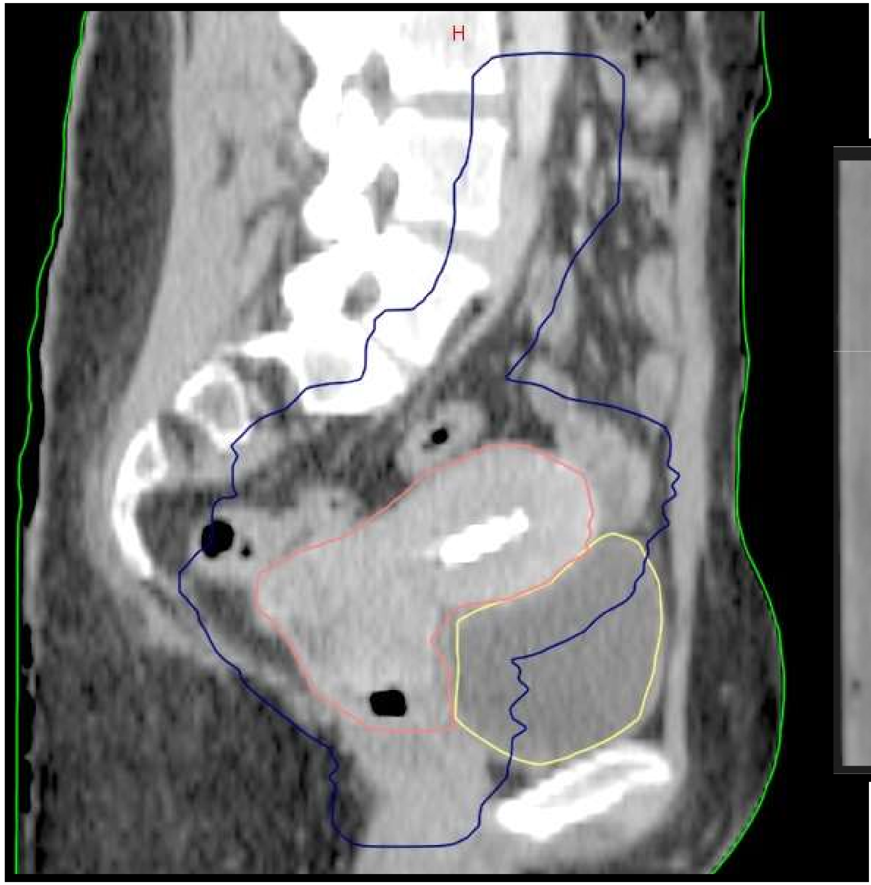
Incorrect drinking instructions.

Poor patient compliance.

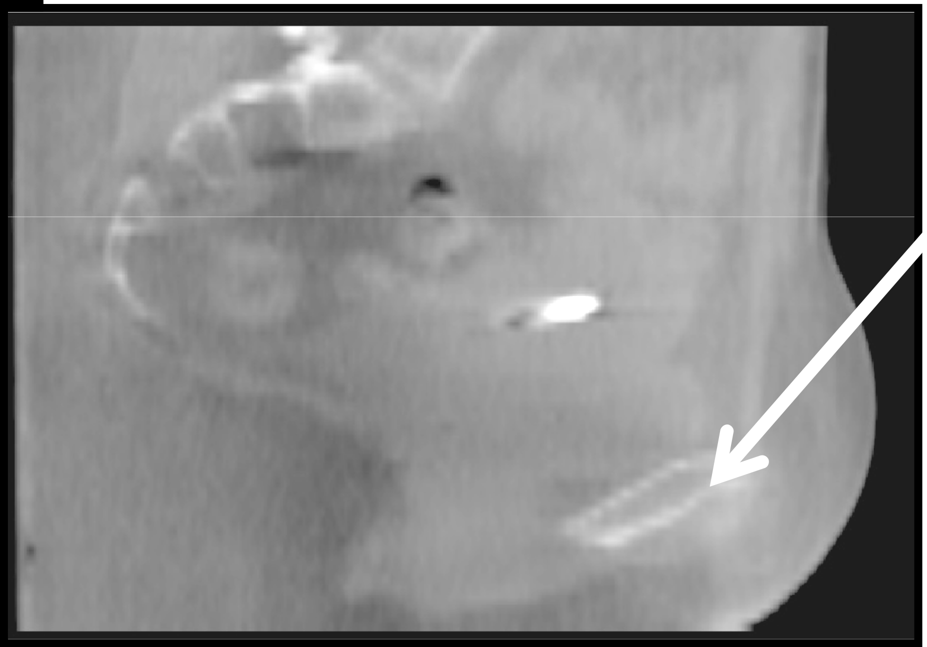
Treatment delay.

Slide courtesy of Sophie Alexander

Clinical Example 2 - Bladder

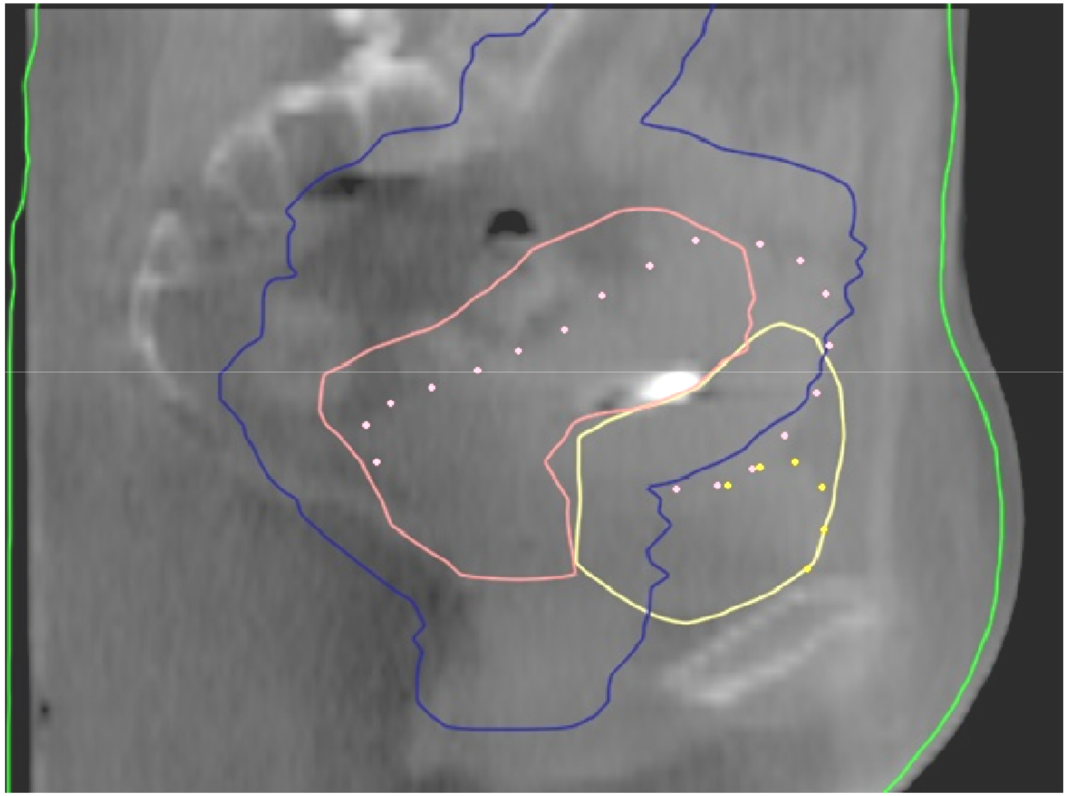


Same patient – different problem



Slide courtesy of Sophie Alexander

Clinical Example 2 - Bladder



PTV coverage sub-optimal.

Why?

Incorrect drinking instructions.

Poor patient compliance.

Wait time too short.

Dehydration

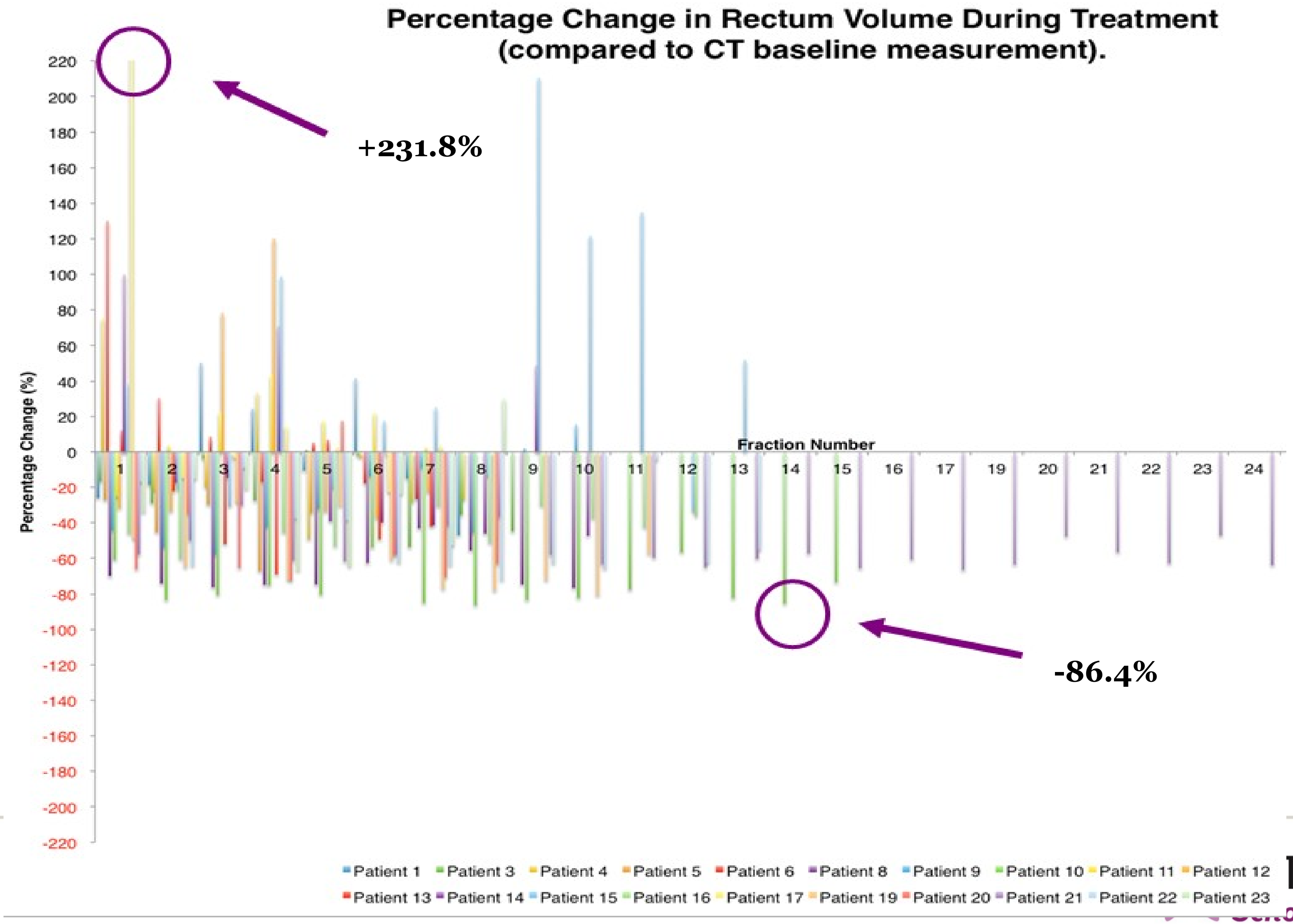
Treatment related bladder toxicity.

Reduced bladder capacity.

[redacted]

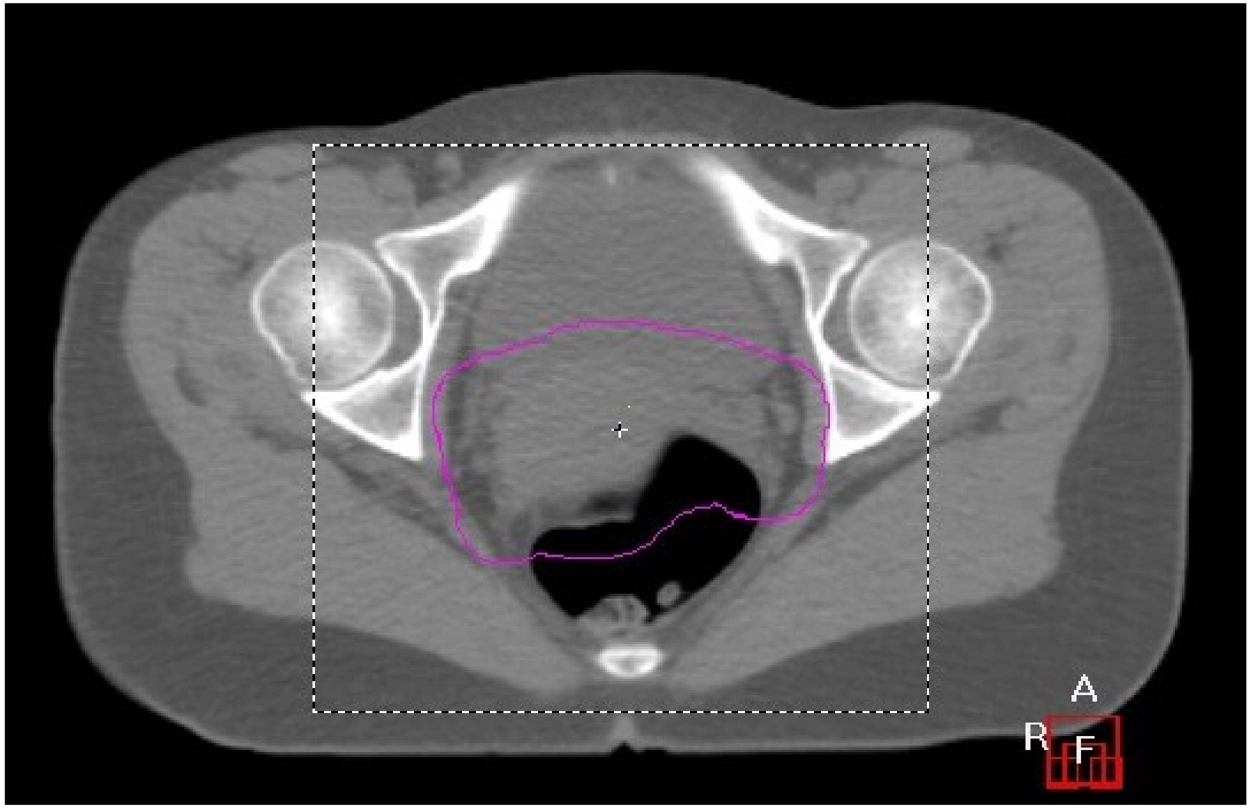
Slide courtesy of Sophie Alexander

Rectal Motion / Variability



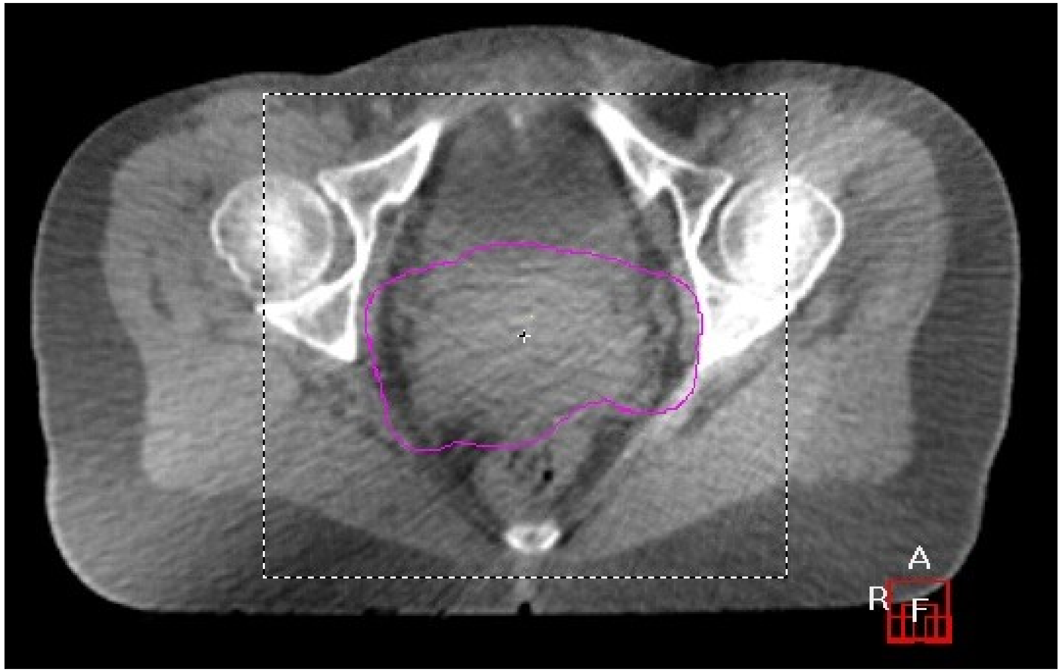
Clinical Example 4 - Rectum

From this planning CT what potential set-up issue may be encountered during their radiotherapy course?



Slide courtesy of Sophie Alexander

Clinical Example 4 - Rectum



Reduced rectal volume.

No gas on CBCT.

Cervix displaced posteriorly.

CTV anatomy just covered by the PTV contour.

No margin for intra-fractional motion.

Slide courtesy of Sophie Alexander

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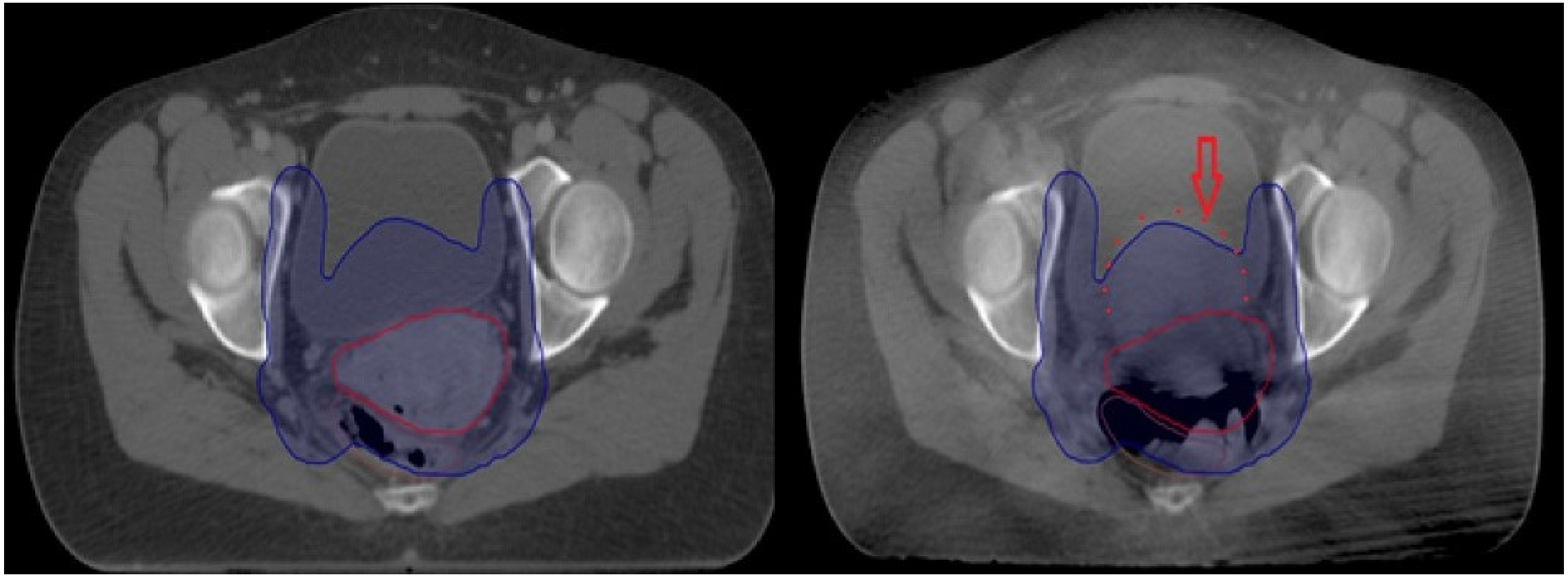
Clinical Example 5 - Rectum



Increased rectal volume on CBCT.
Rectum distension due to Gas.
Treatment toxicity?
Pushing cervix anteriorly – out of PTV contour.

Uterine and Cervix Motion

Evidence that the cervix and uterus as well as the pelvic OARs are highly mobile and naturally prone to positional and volumetric changes.

Uterus moves more than the cervix, they can move independently of each other and their position can be influenced by the adjacent OARs (Jadon et al, 2014).

Author	Mean cervix motion mm			Mean uterus motion mm		
	Anterior (A) Posterior (P)	Superior (S) Inferior (I)	Left (L) Right (R)	Anterior (A) Posterior (P)	Superior (S) Inferior (I)	Left (L) Right (R)
Taylor & Powell (2008)	2.7(±4.4)	4.1(±2.8)	0.3(±0.8)	7.0(±9.0)	7.1(±6.8)	0.8(±1.3)
Wang et al (2012)	7.9(±6.8)	3.8(±4.0)	3.9(±4.0)	14.2(±10.5)	9.5(±6.6)	6.5(±4.8)

Slide courtesy of Sophie Alexander

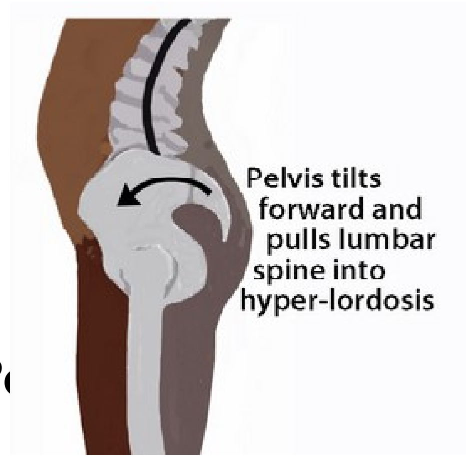
Rotation - Pitch

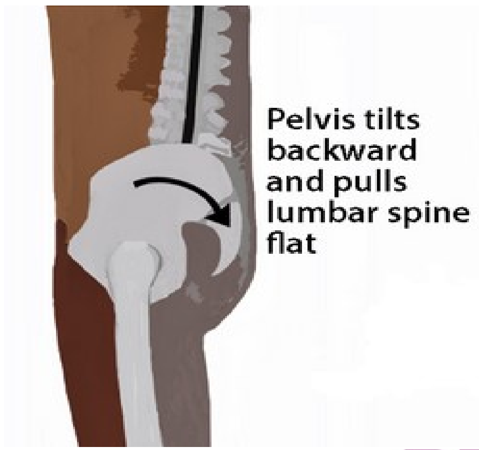
Pelvic tilt can be; anterior or posterior.

Affects lumber spine position.

L-spine position is important as the iliac lymph nodes follow the L5-L4 vertebra.

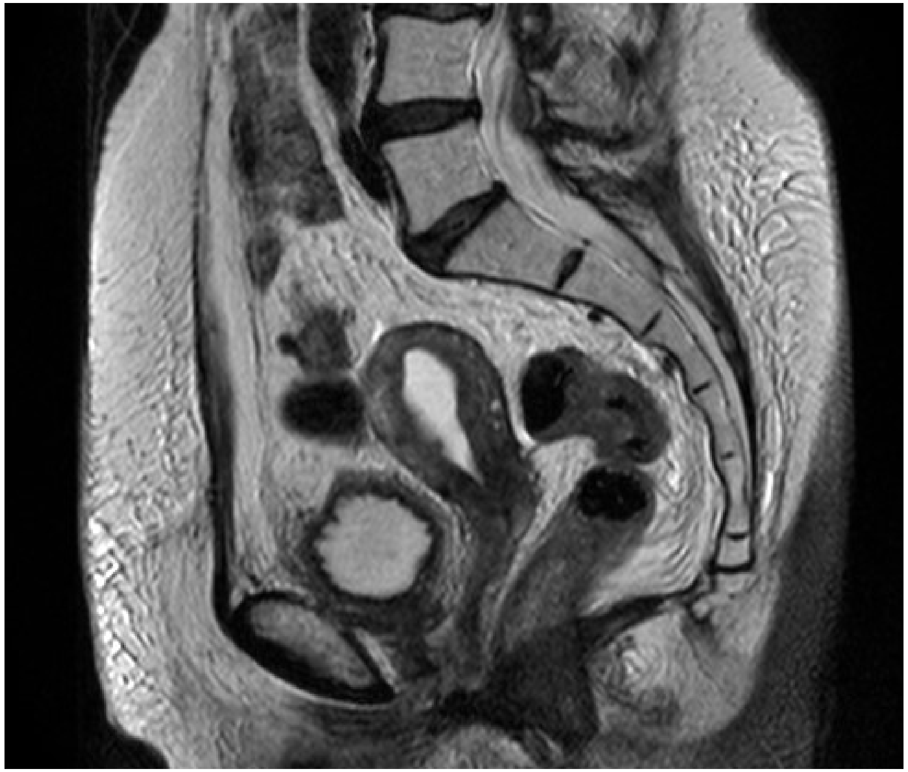
Anterior Pelvic Tilt



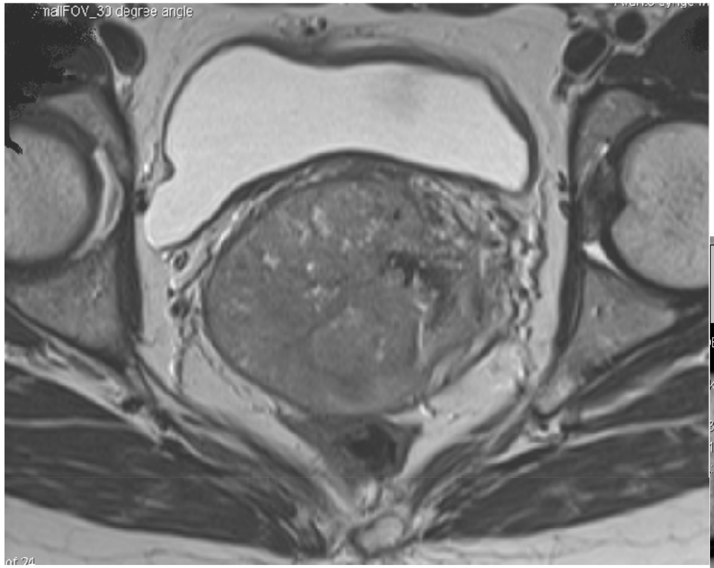


Slide courtesy of Sophie Alexander

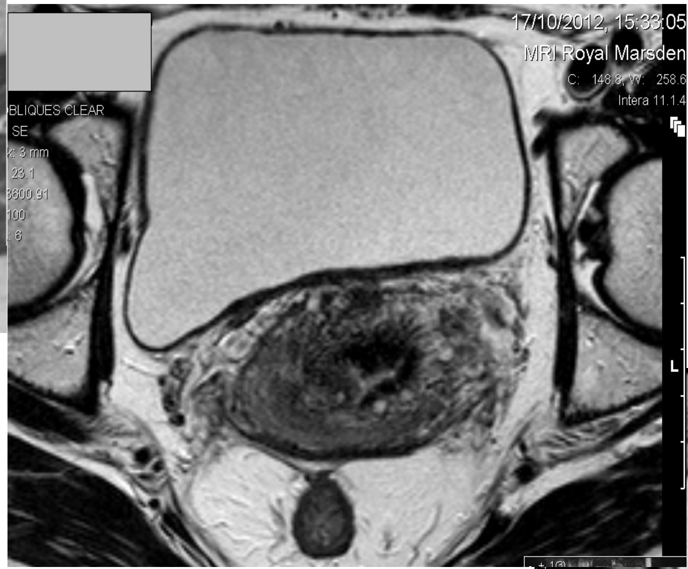
Tumour Regression or Progression



Target Volume Change

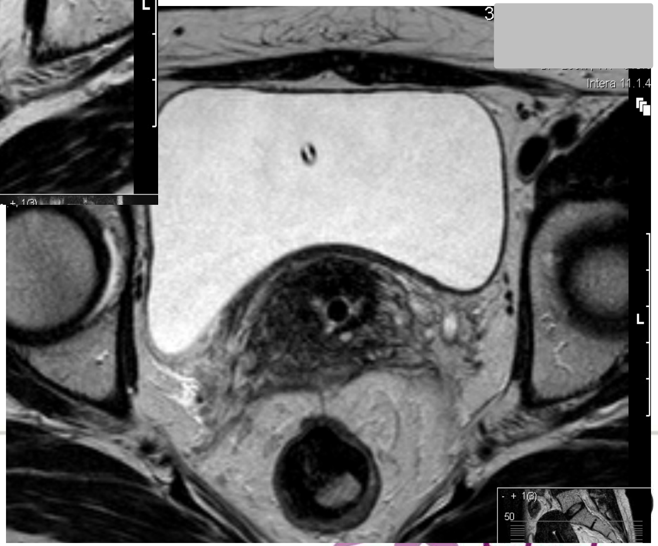


PRE RT



Week 4

Week 6



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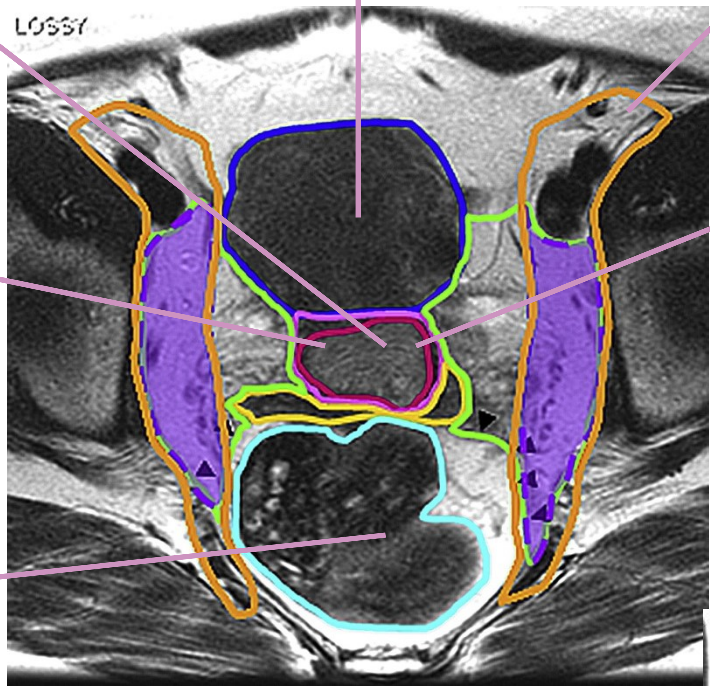
Key Problems in Radiotherapy Delivery for Cervix Cancer

Variable bladder filling

Volume delineation on CT

Nodal motion independent to target

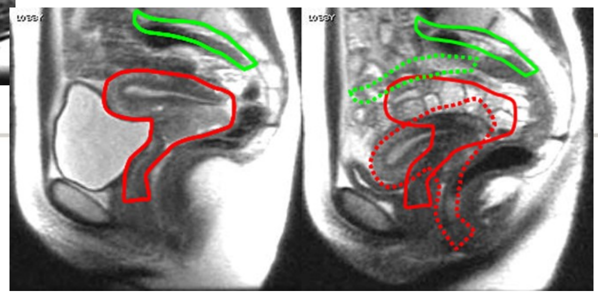


Target regression

Target Motion

Extended fields subject to rotational set up error

Rectal volume changes



Online CBCT Soft Tissue Imaging Competency Programme

CERVIX CBCT ASSESSMENT SHEET

STUDY LETTER: ………………………… IMAGE NUMBER: …………………………………

PITCH
RED= >4°

AMBER= 3-4°

GREEN= <3°

BLADDER VOLUME
RED=UNDER OR OVER FULL– PROBABLE CAUSE OF INADEQUATE PTV COVERAGE.

AMBER= UNDER OR OVER FULL – NOT AFFECTING PTV COVERAGE.

GREEN= SIMILAR TO PLANNED VOLUME.

BODY CONTOUR
RED= ≥1CM AT ALL FIELD ENTRY POINTS.

AMBER= CHANGE ≥1CM AT 1 POINT.

GREEN= <1CM CHANGE

RECTAL VOLUME
RED= UNDER OR OVER FULL- PROBABLE CAUSE OF INADEQUATE PTV COVERAGE.

AMBER= UNDER OR OVER FULL- NOT AFFECTING PTV COVERAGE.

GREEN= SIMILAR TO PLANNED VOLUME.

PTV COVERAGE
RED= PTV CONTOUR NOT COVERING TARGET.

AMBER= TARGET AT EDGE OF PTV CONTOUR.

GREEN= ≥3mm MARGIN AROUND TARGET.

DECISION (PLEASE SELECT ALL THAT APPLY)

☐NO ACTION	☐REPEAT CBCT ☐REVIEW BOWEL PREPARATION ☐DRINKING INSTRUCTIONS/ QUANTITY ☐REVIEW TATTOO ALIGNMENT ☐TAKE FSDs AT FIELD ENTRY POINTS	☐SEEK ADVICE BEFORE NEXT # ☐SEEK ADVICE IF INTERVENTION FAILS ***(E.G. DR, SUPERINTENDENT, PHYSICS)***
COMMENTS……………………………………………………………………… …………………………………………………………………………… …………………………………………………………………		

Slide courtesy of Sophie Alexander

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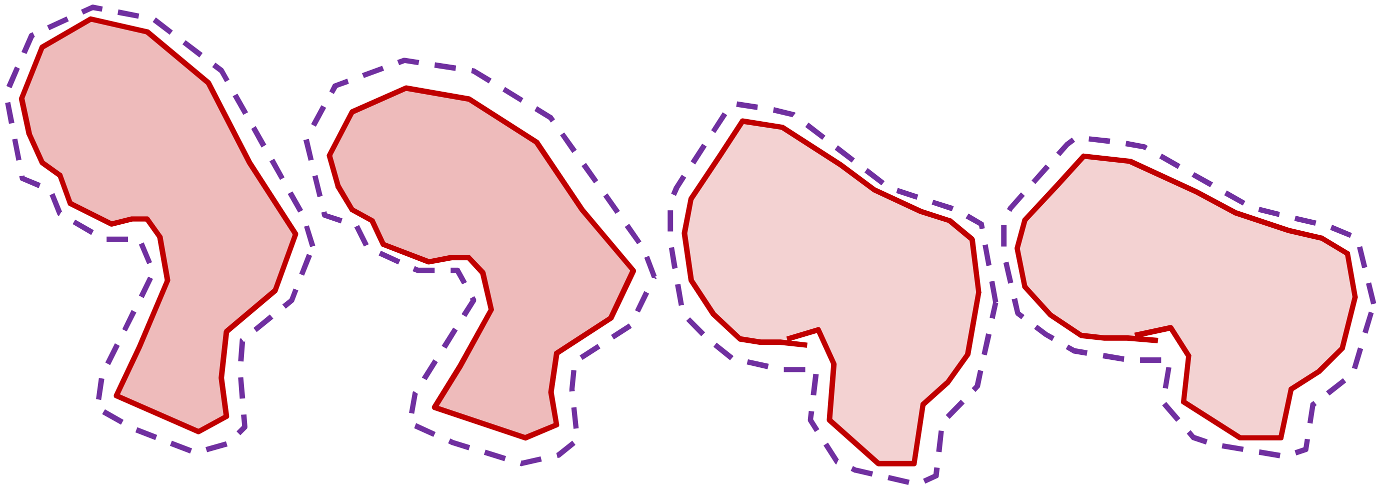
Cervix Library of Plans NKI

Pre-treatment: - Automatic interpolation CTVs

PTV margins *- Expansion to PTVs*



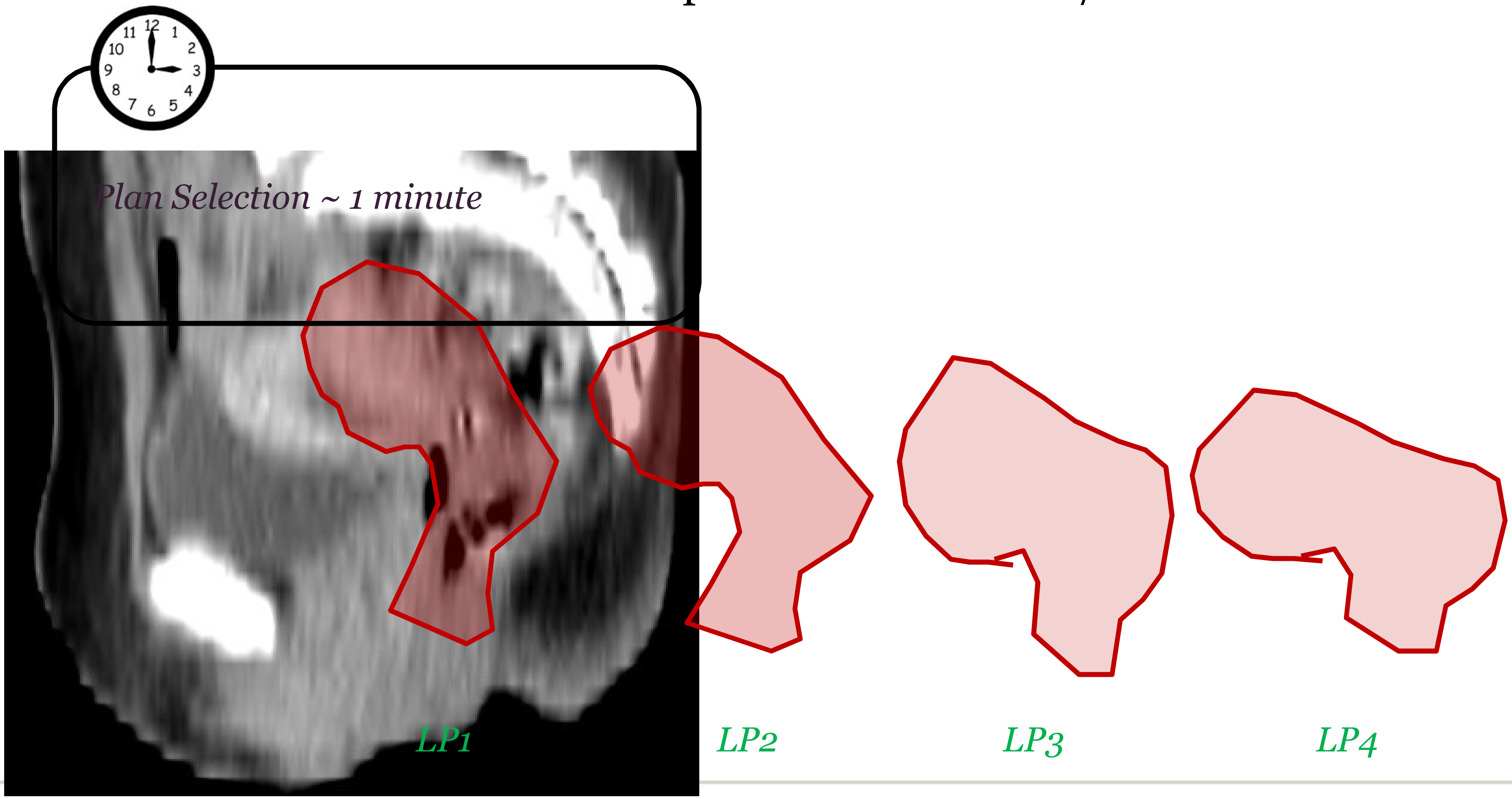
LP1 *LP2* *LP3* *LP4*

Full *Empty*

Courtesy B. Van Triest, NKI

Cervix Library of Plans NKI

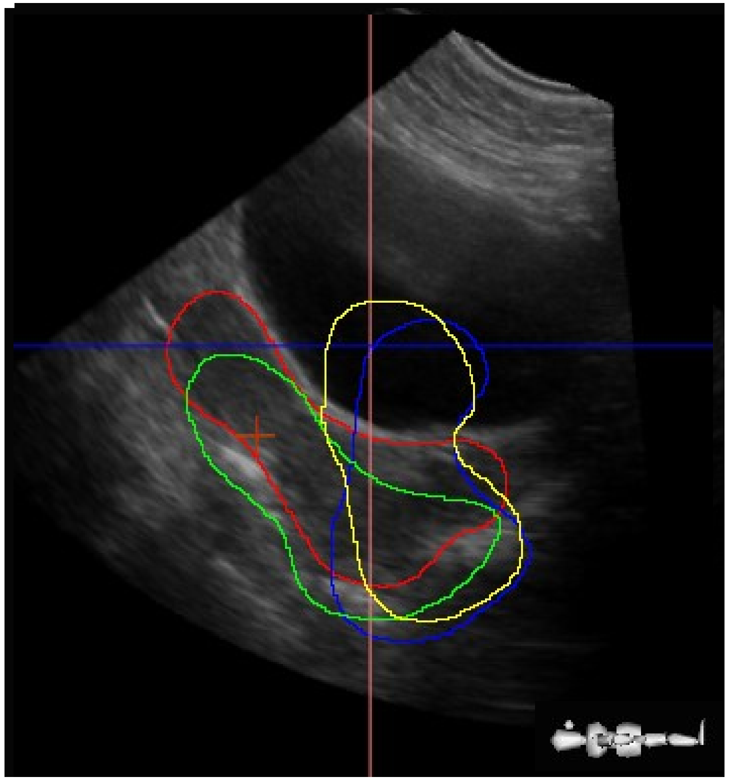
Pre-beam: - Select most suitable plan based on CBCT/MRI



Full *Courtesy B. Van Triest, NKI* *Empty*

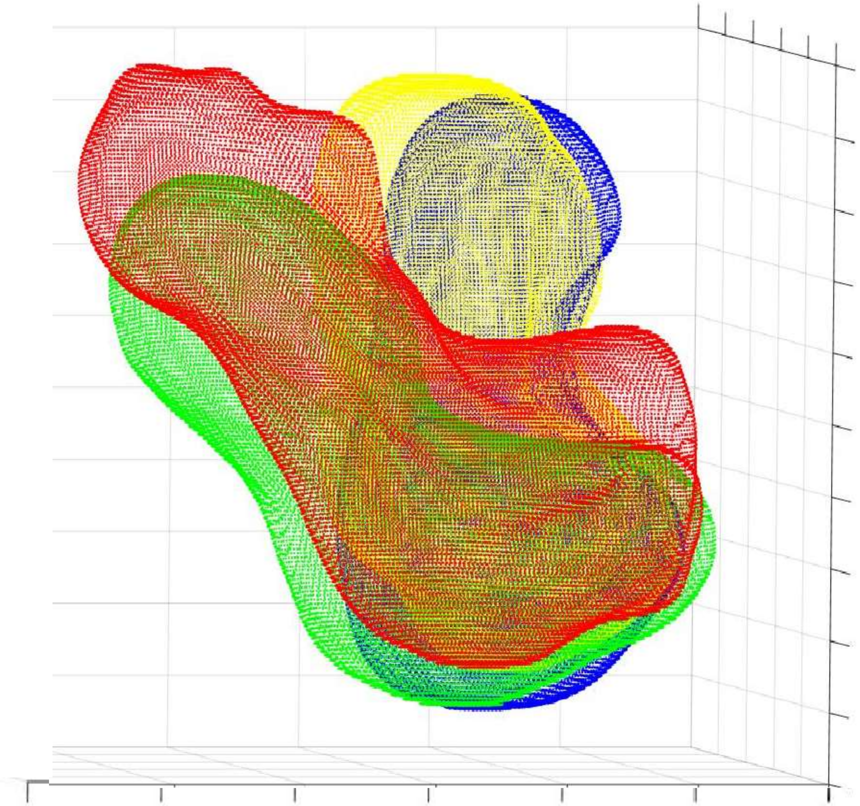
Uterus visualized during treatment with transabdominal ultrasound (US)

Superimposition of manual contours



Example US image frame

(Elekta Clarity® soft tissue imaging system)

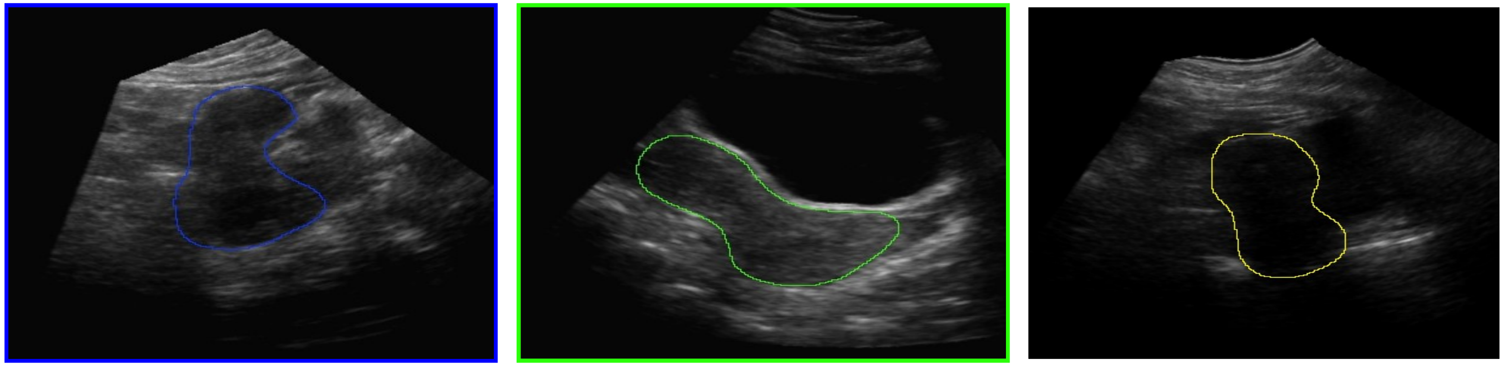


Corresponding 3D manual segmentation

Courtesy of Sarah Mason

Ultrasound-guided radiotherapy

Tailor treatment according to US image of the day



- *Soft tissue-based couch shift*
- *Library of plans (plan of the day)*
- *Adapt plan to match patient anatomy*

Accurate online segmentation needed

Ongoing work:

Developing a automatic segmentation algorithm for transabdominal US!

Slide courtesy of Sarah Mason

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More Registration issues

Tolerance for movement   for example >1cm

Re plan if systematically smaller

Bladder and nodes

Training for selection

Guidelines for selection

Acknowledgements

Academic urology unit

Prostate

Helen McNair

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Rianne de Jong

Academic Medical Centre, Amsterdam

The ROYAL MARSDEN
NHS Foundation Trust

ICR The Institute of Cancer Research

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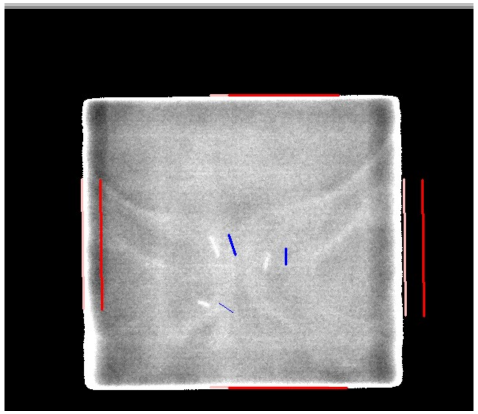
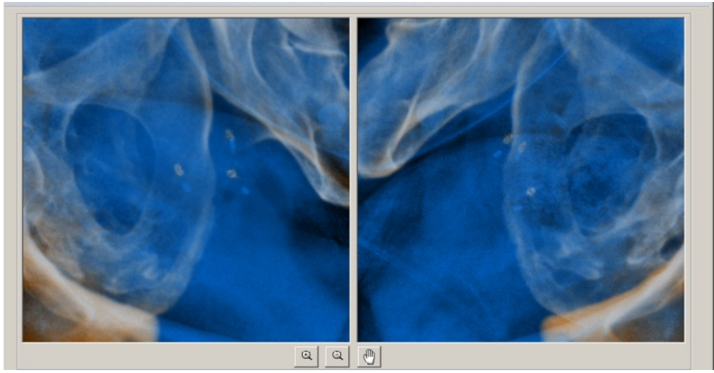
November 2014

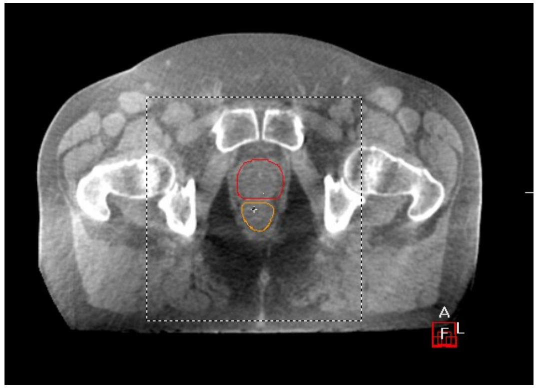
Methods of registration



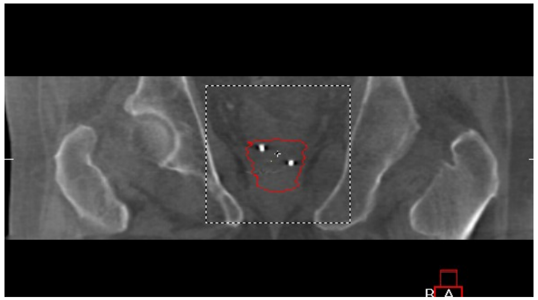
MV & markers



kV & markers



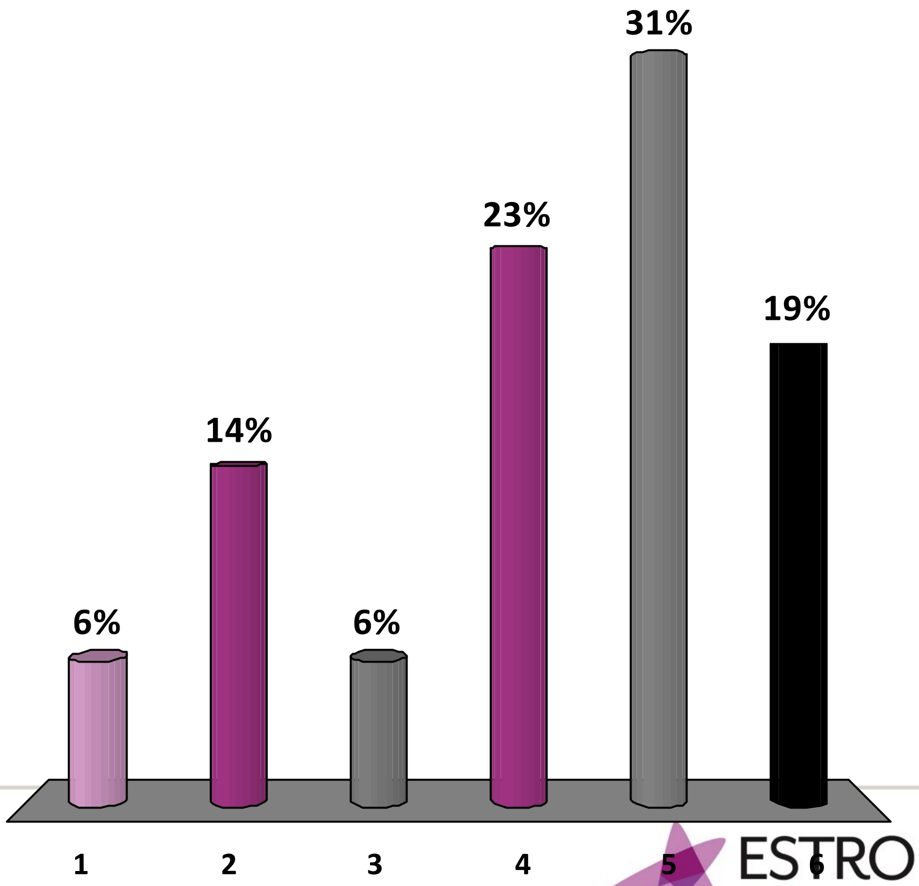
CBCT



CBCT & markers

Which method do you use?

1. MV imaging
2. MV imaging and markers
3. KV planar imaging
4. KV planar imaging and markers
5. 3D soft tissue imaging
6. 3D soft tissue imaging and markers



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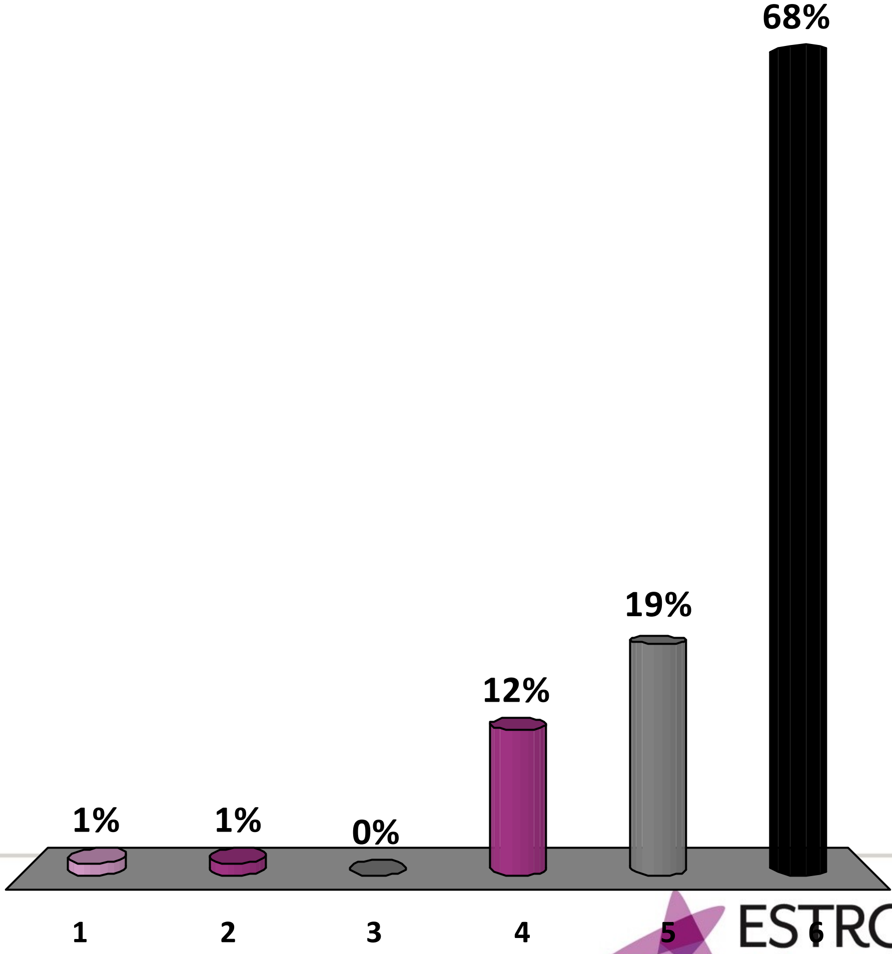
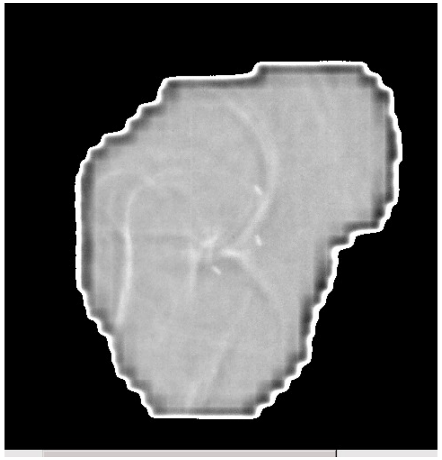
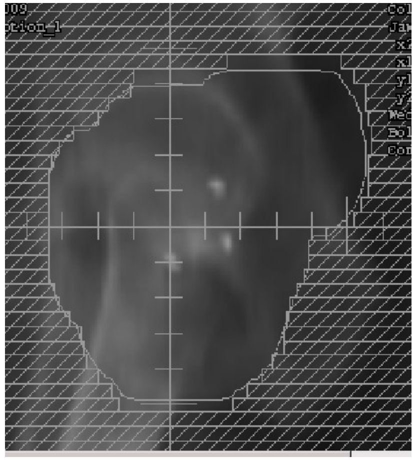
Which method would you prefer to use?

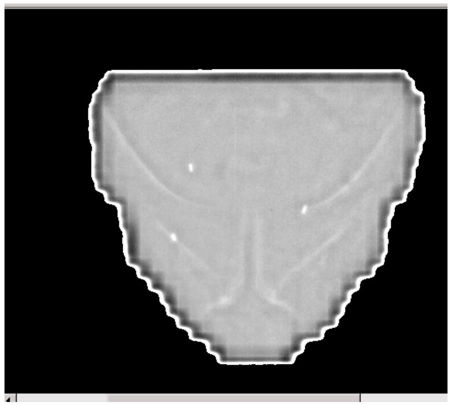
1. MV imaging
2. MV imaging and markers
3. KV planar imaging
4. KV planar imaging and markers
5. 3D soft tissue imaging
6. 3D soft tissue imaging and markers

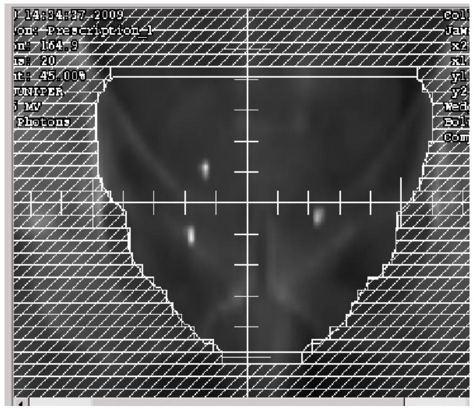


MV Marker registration

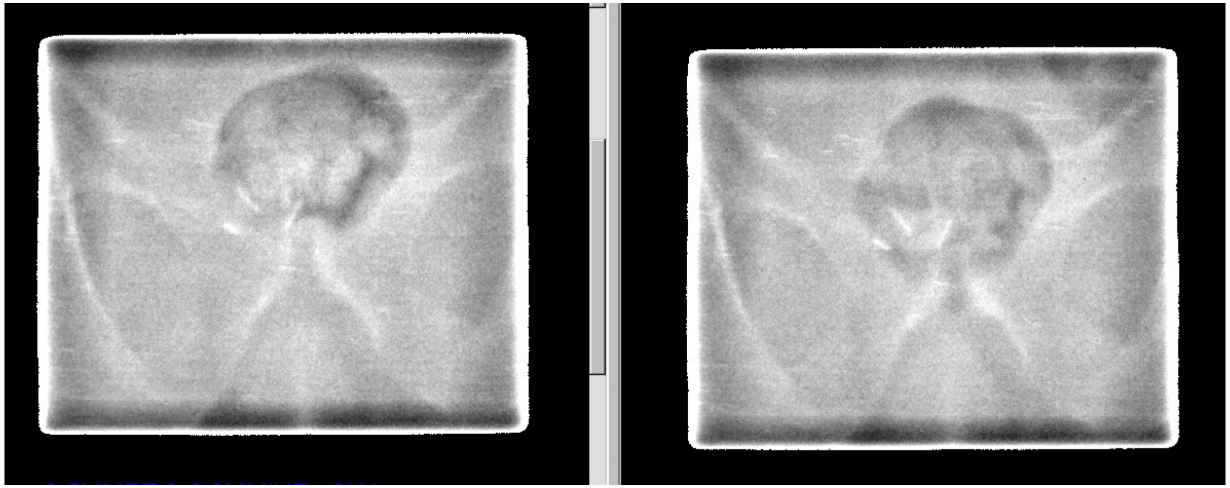


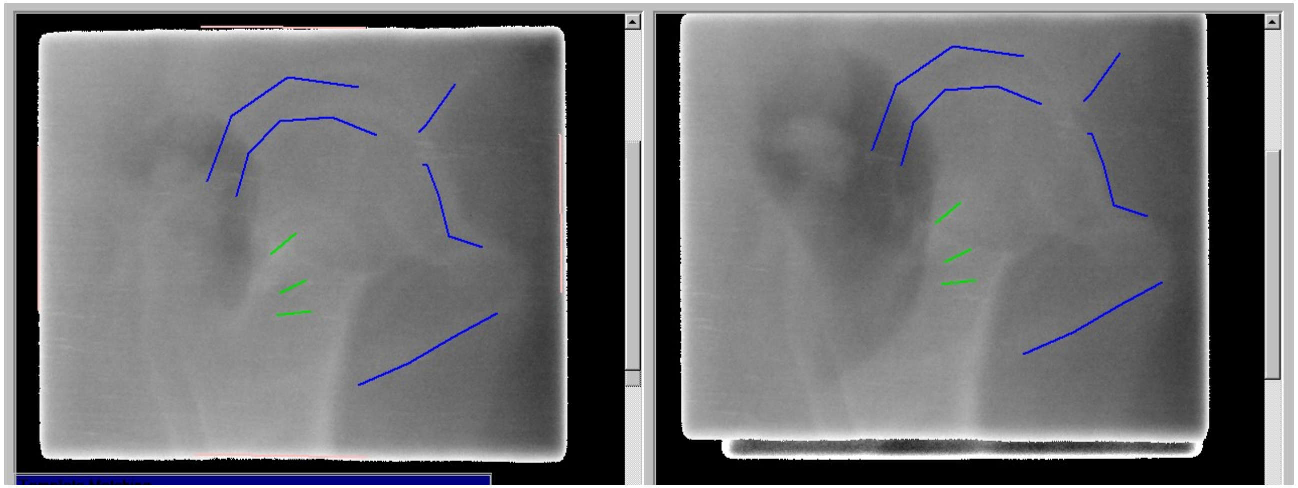




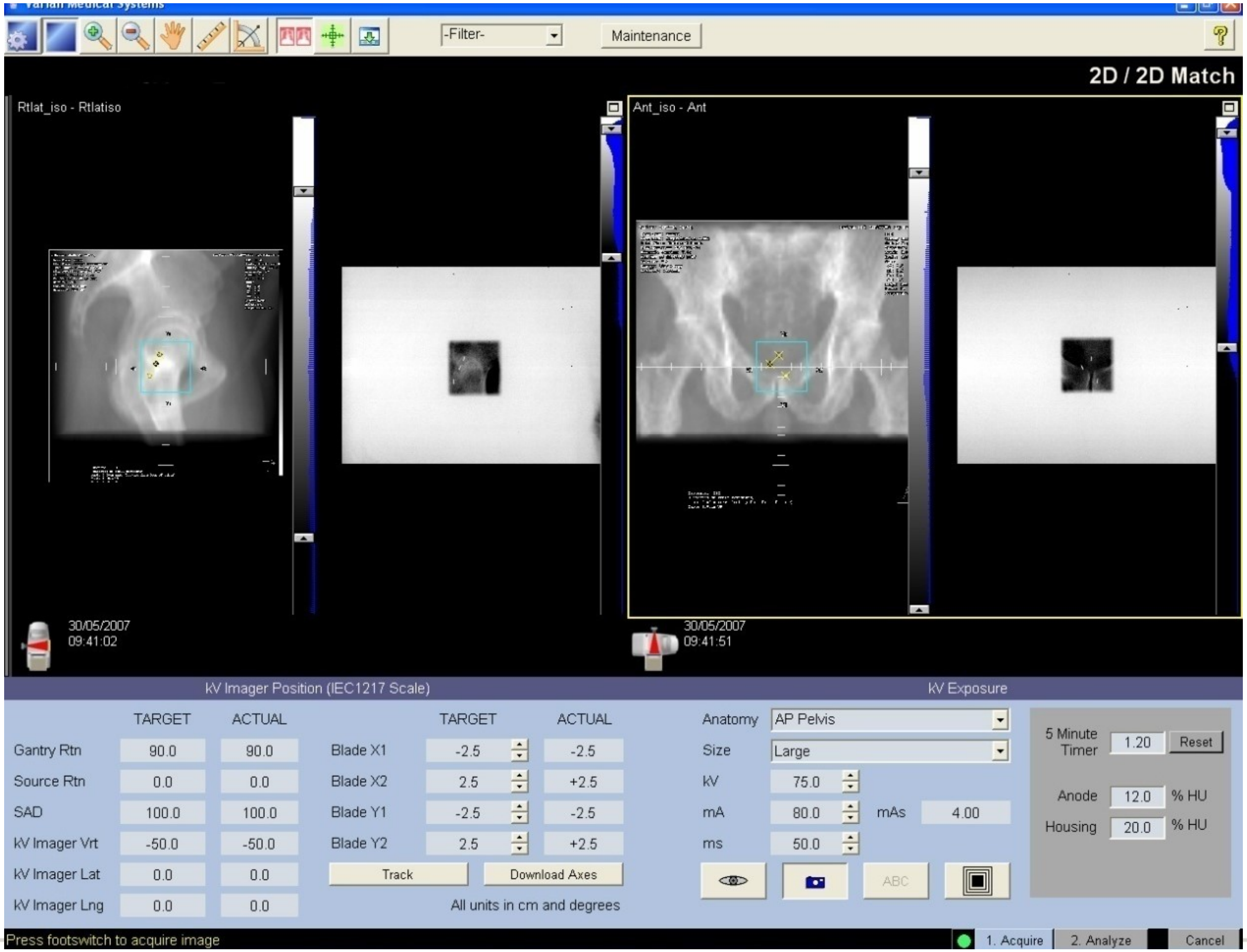


MV Marker registration

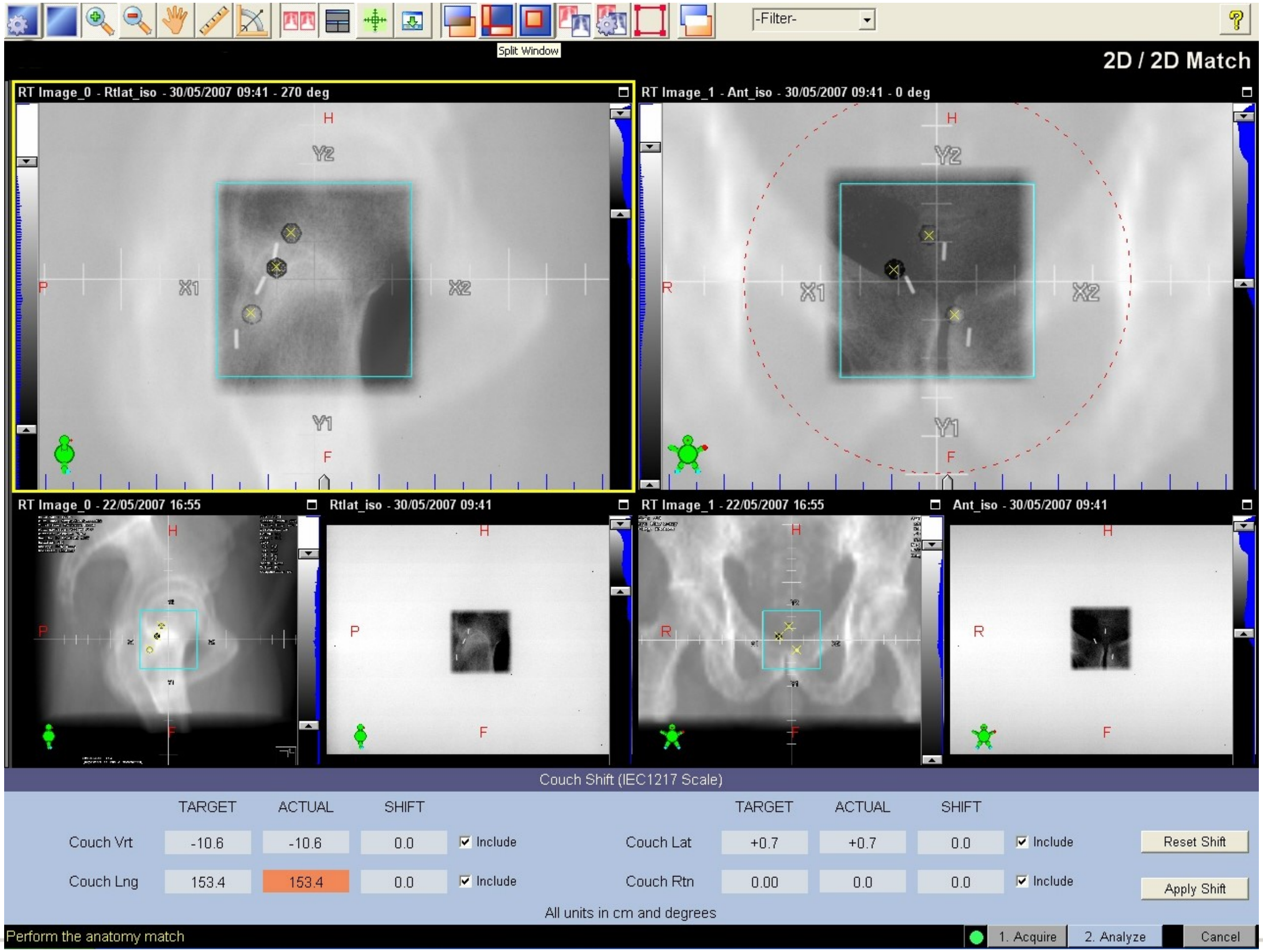




Marker registration - 2D/2D match facility

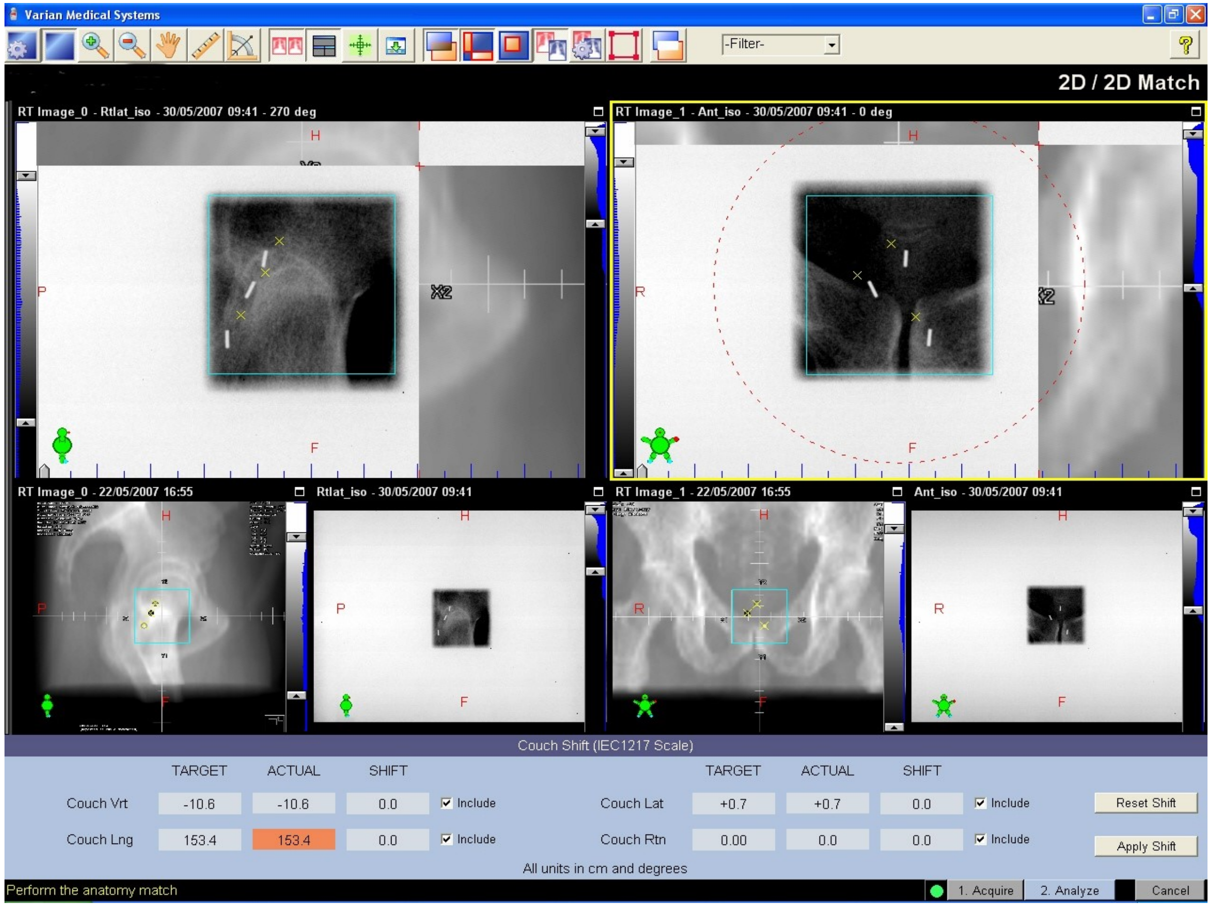


Marker registration – Image blend



Marker registration – Image Analysis

Objective (template match)



observers	RL (%)	SI (%)	AP (%)
Off line (3) v on line (2)	100	99.1	99.3
Off line (3)	100	100	99.7

Deegan et al Journal of Medical Imaging and Radiation Oncology 2013

Marker registration – Apply couch corrections

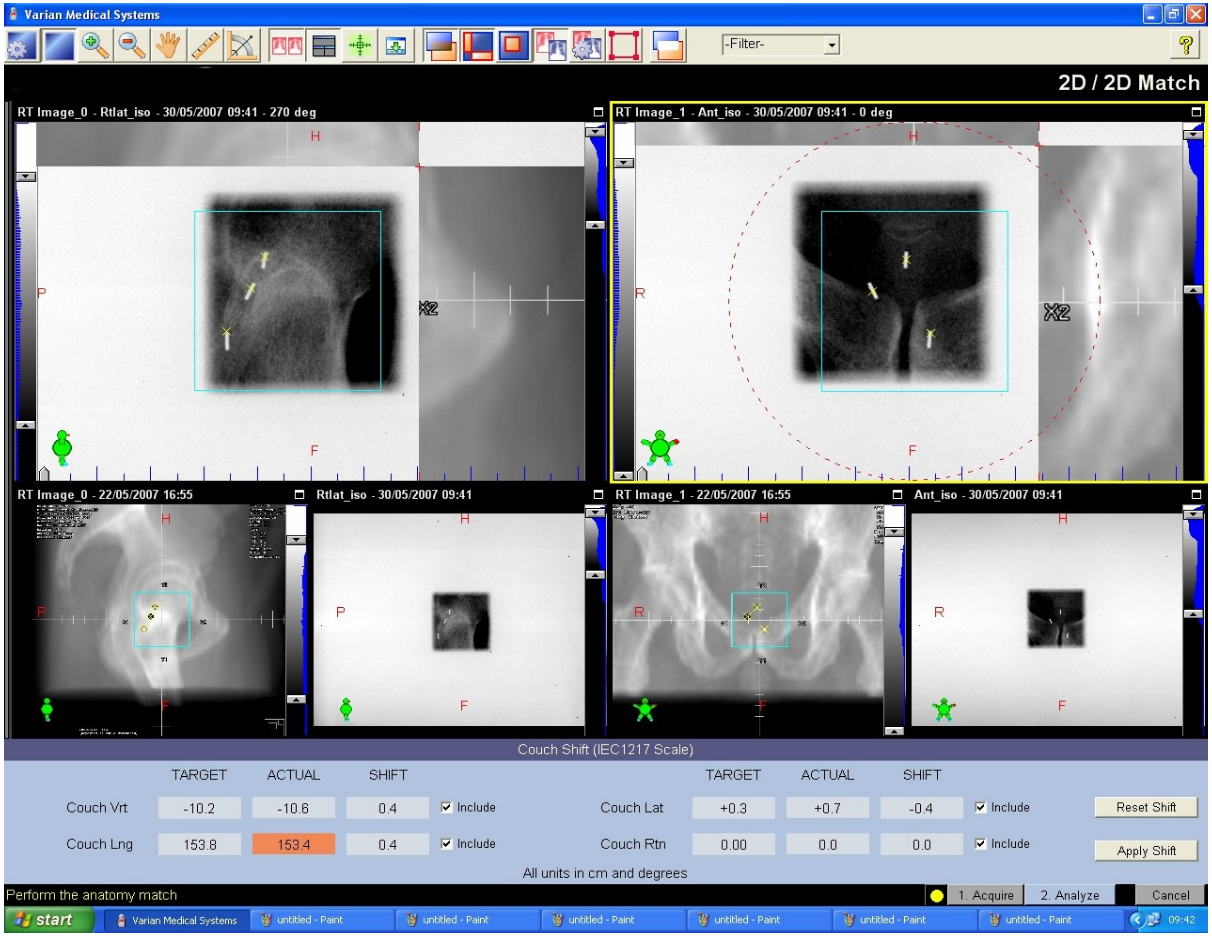


Image acquisition and analysis- 10 patients in-room timings (pre-VMAT)

Range 10.12 – 22.15 mins

Mean 14.36 mins, SD 1.95 mins

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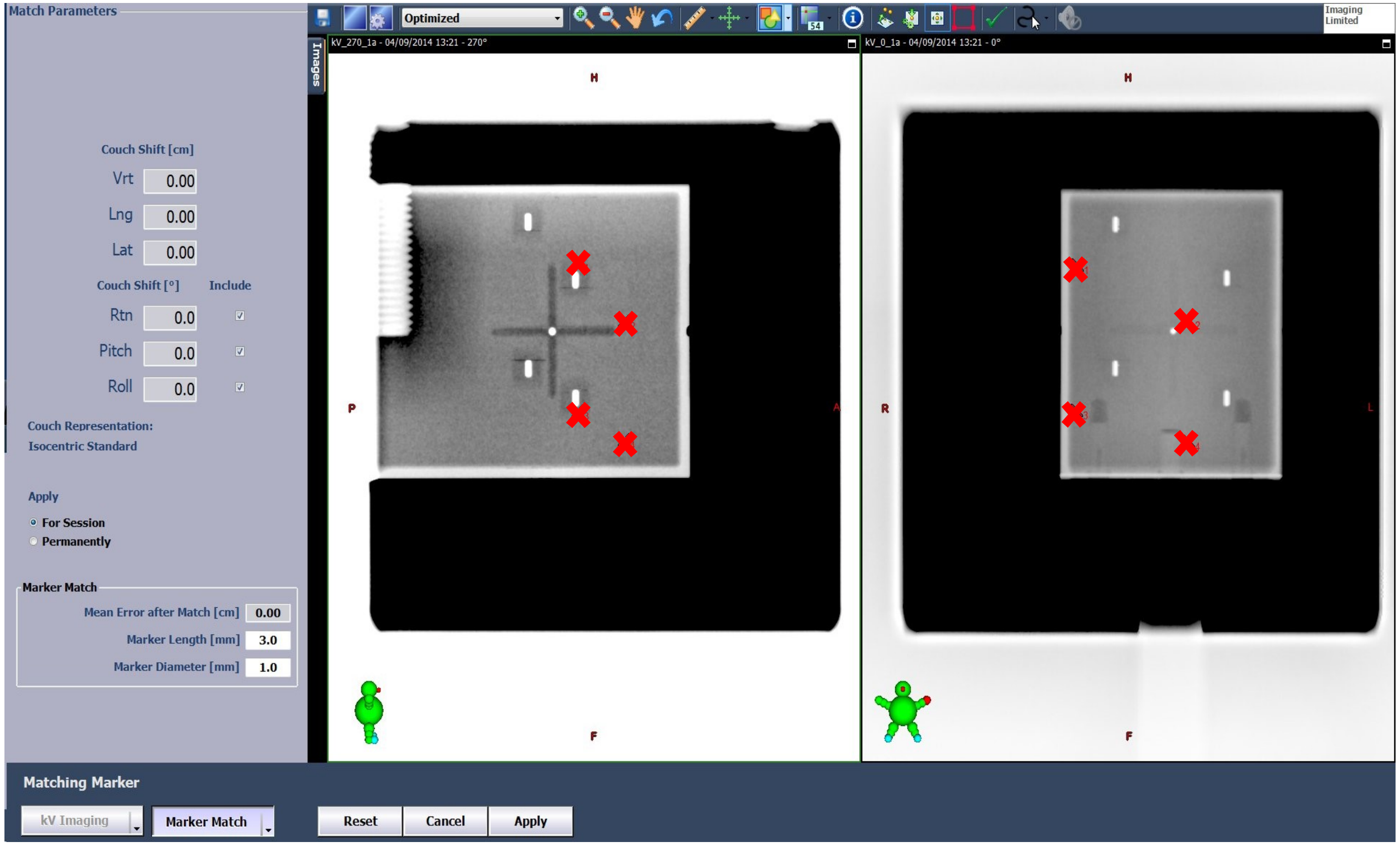
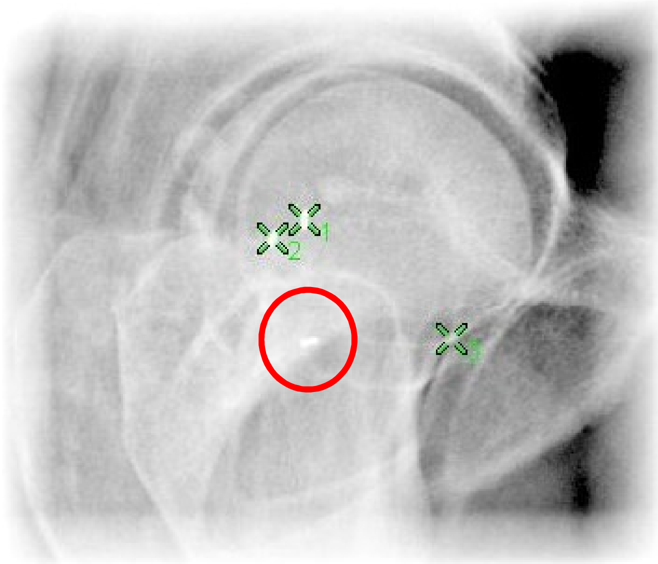
kV Marker registration –marker match

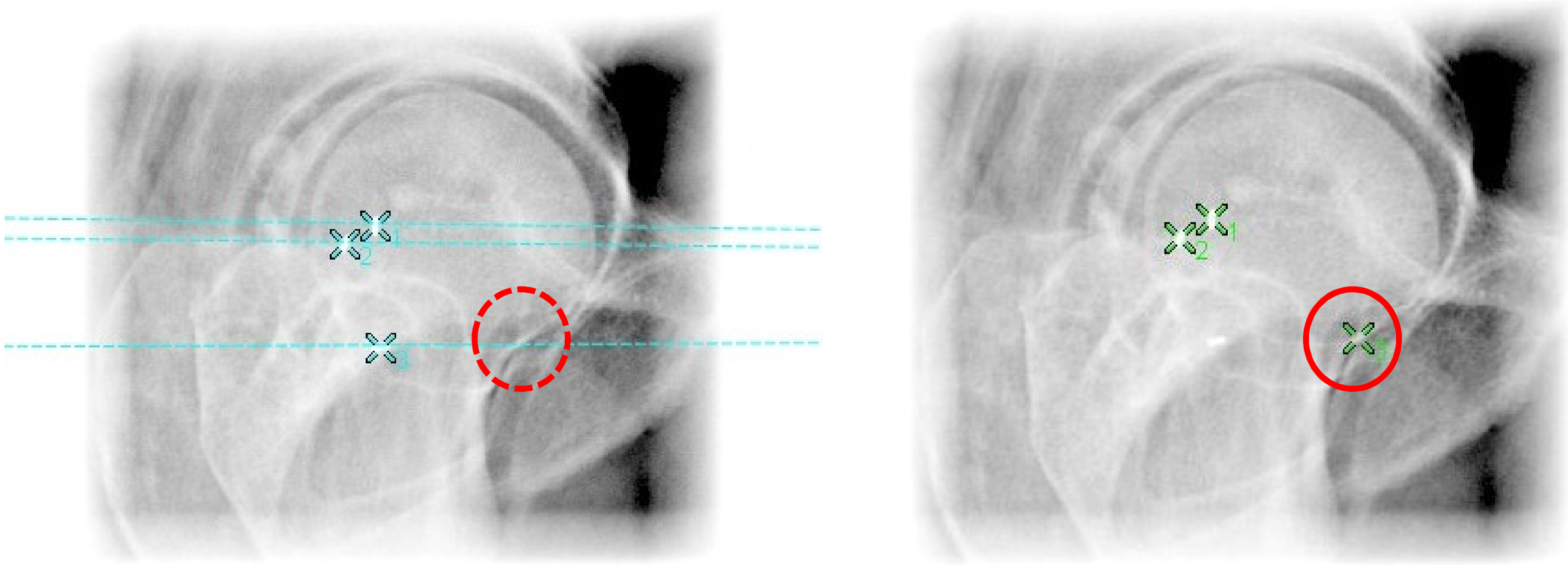


Eclipse – identify seeds from CT data set

Automatic marker match

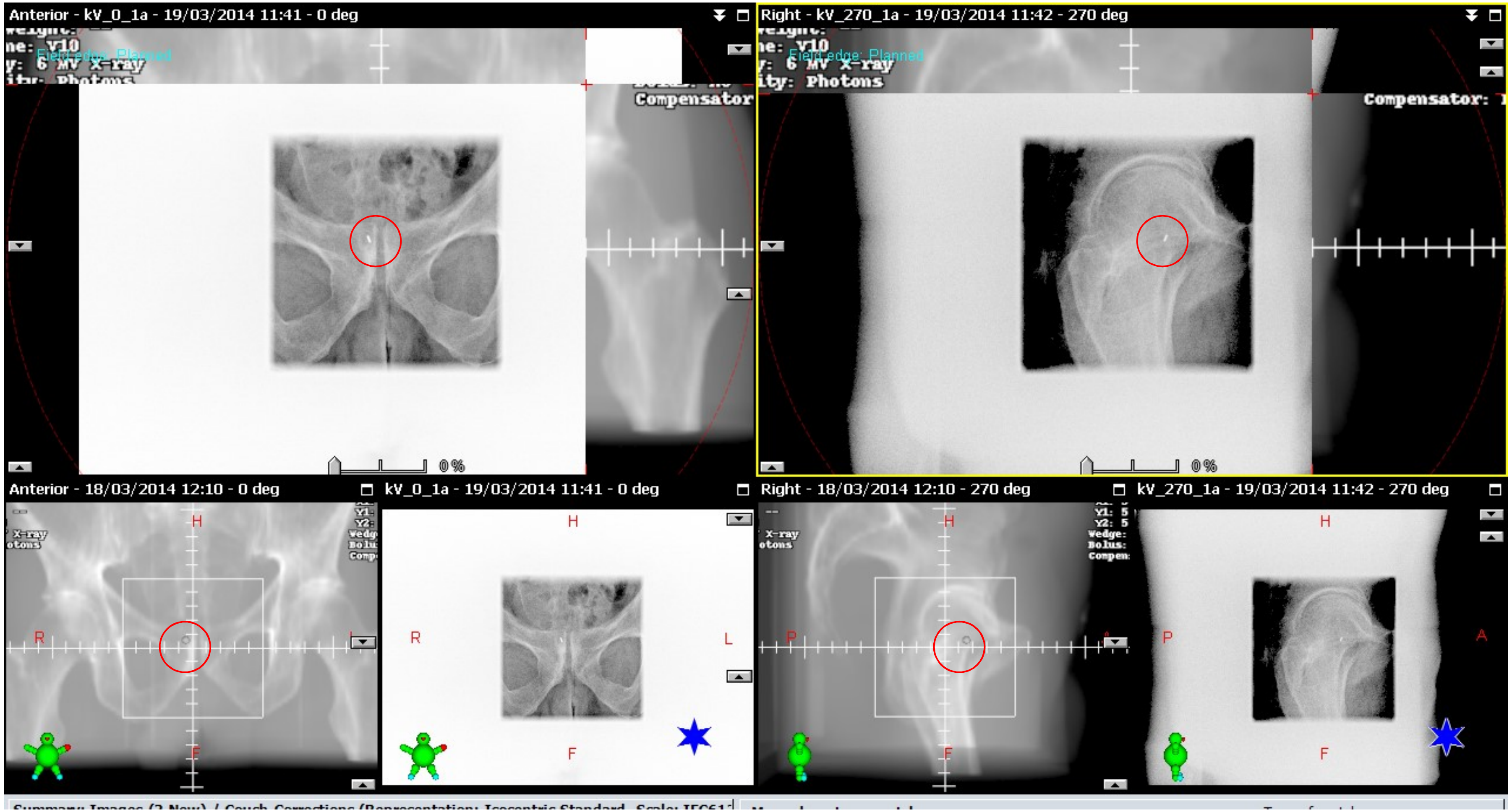


Automatic marker match

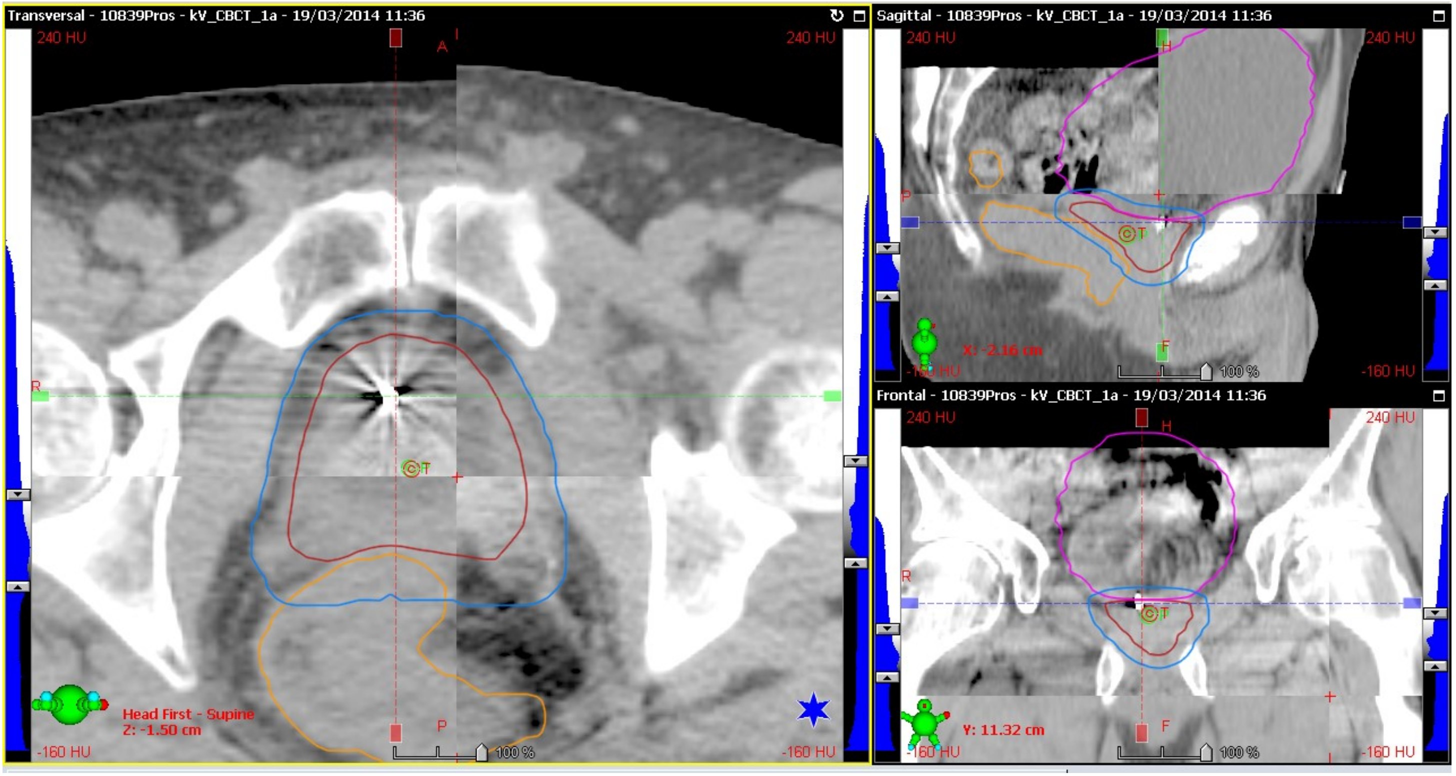


Manual adjustment of one seed

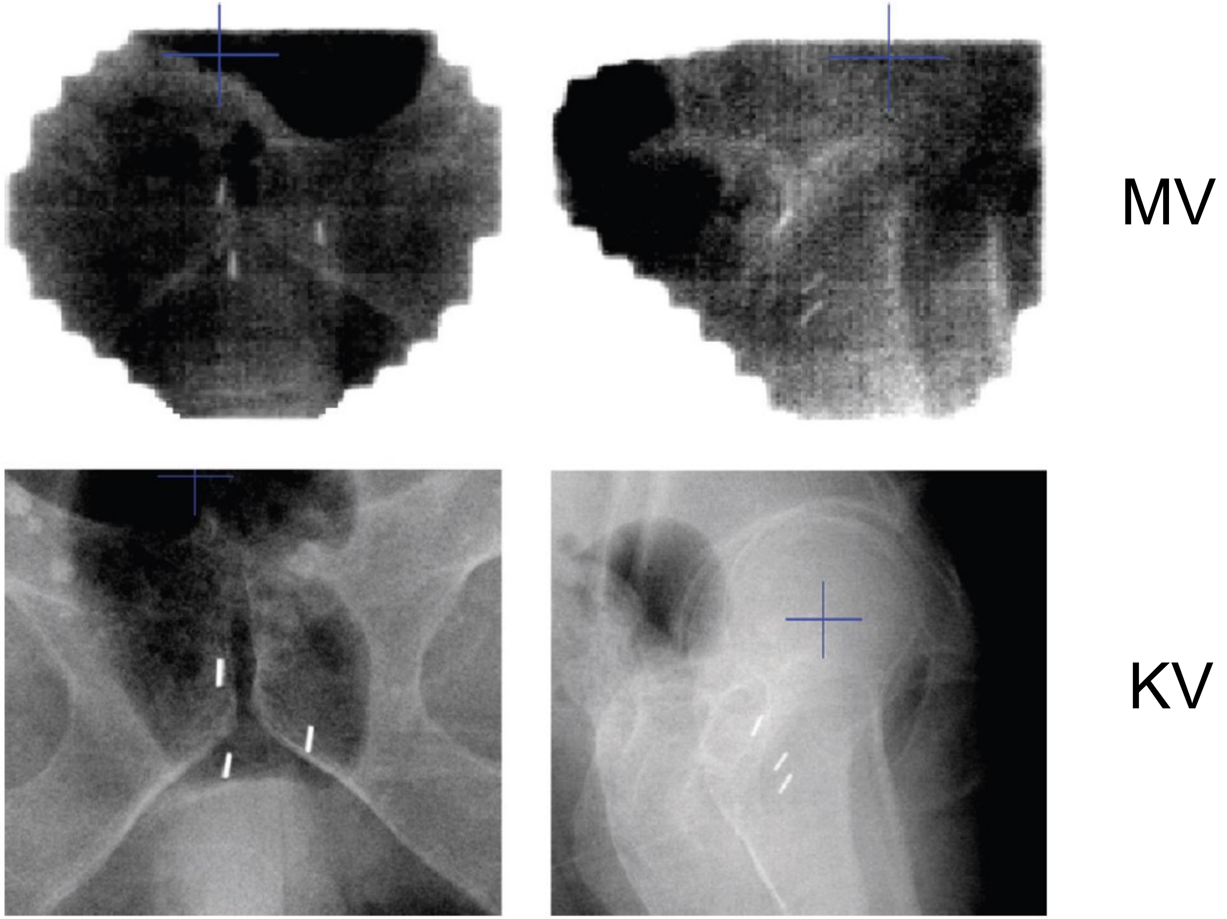
Registration issues –Lost seed(s)



Registration issues –Lost seed(s)



Comparison of systems



Example of MVI and EPI in same patient

Gill, 2012 BJR

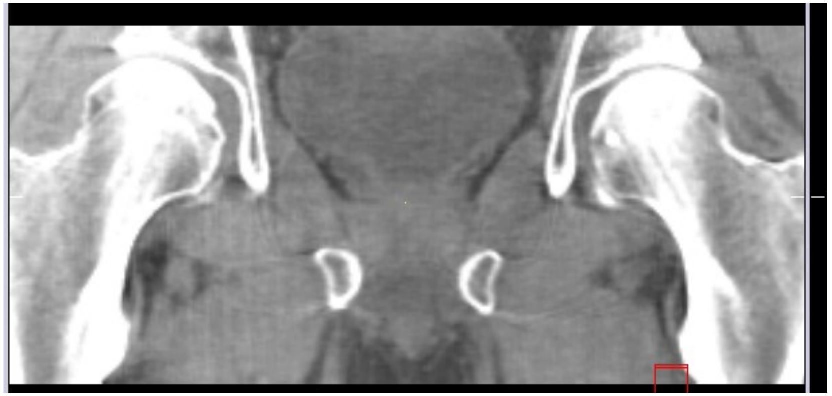
Comparison of systems

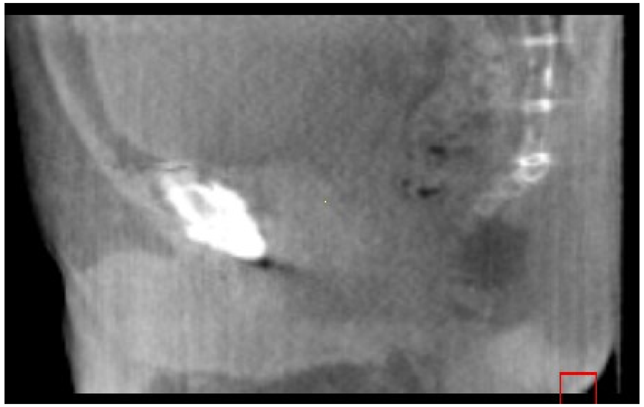
	Right Left (%)	Superior Inferior (%)	Anterior Posterior (%)
Proportion of displacements <3mm - KVI	62	56	45
Proportion of displacements <3mm - MVI	76	66	68
Proportion of displacements <5mm - KVI	88	79	74
Proportion of displacements <5mm - MVI	90	84	84

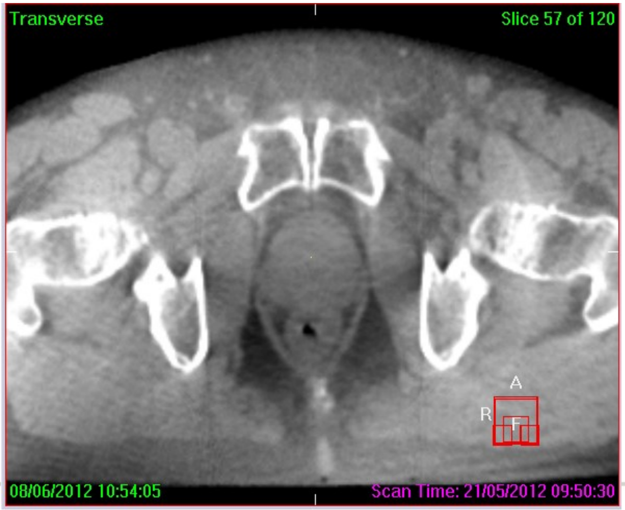
3 mm action level - 27% more shifts on KVI than on EPI; ($p = 0.0001$)

Gill, 2012 BJR

3D imaging

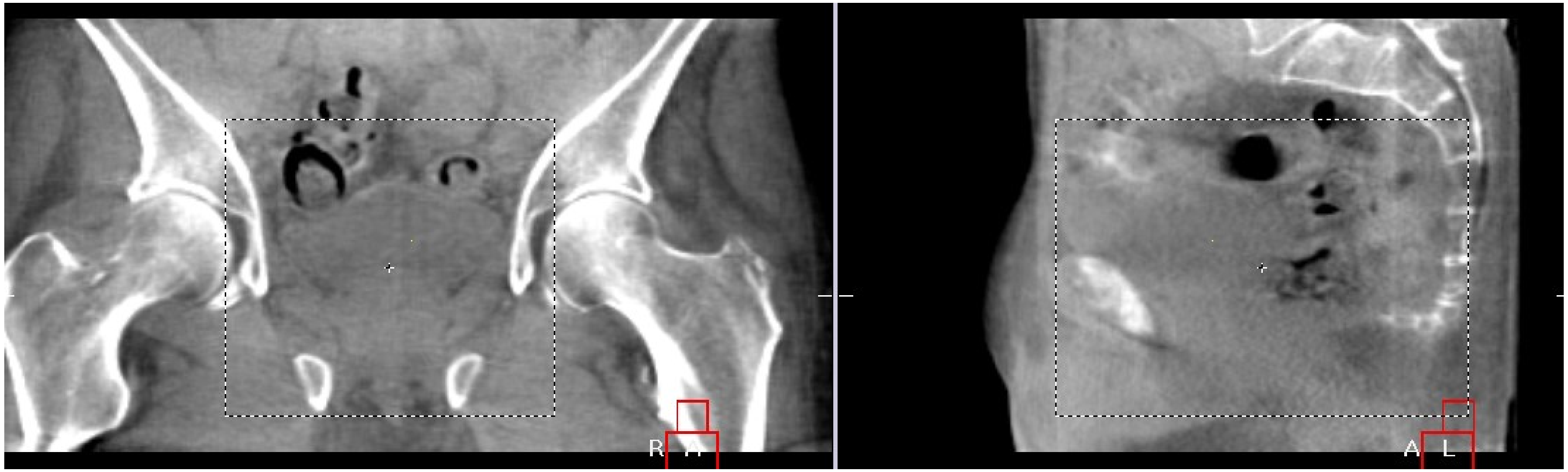


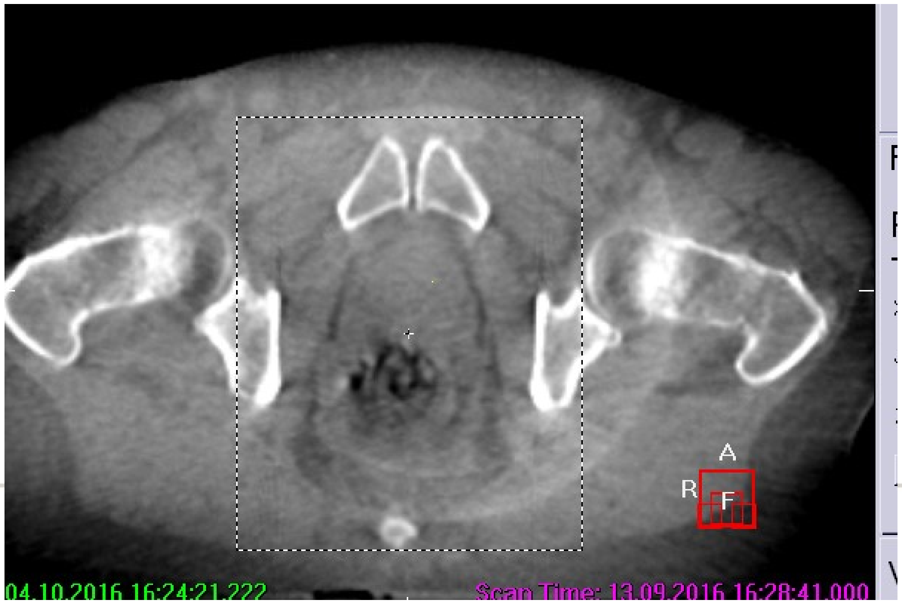




1664mAs
650 frames

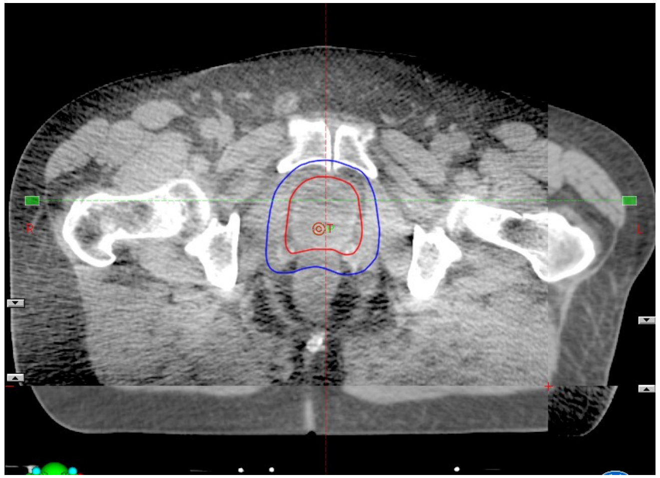
3D imaging

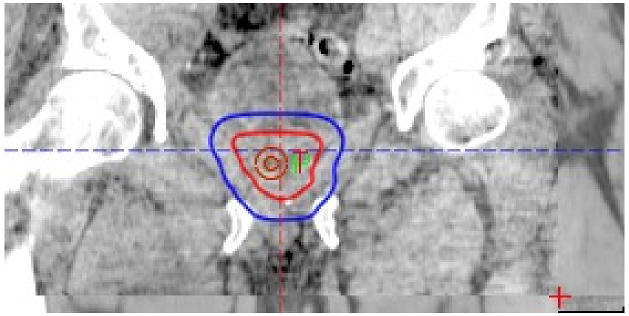


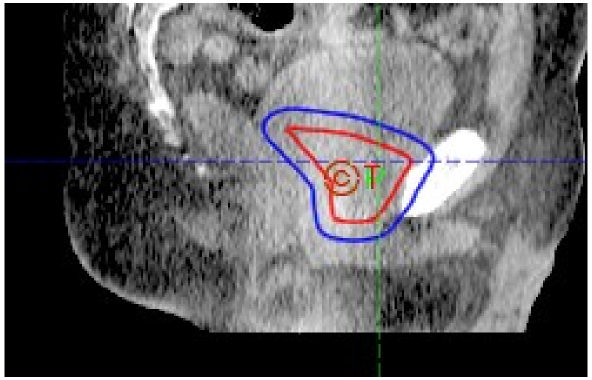


Elekta- fast scan
1047 mAs
409 frames

3D imaging



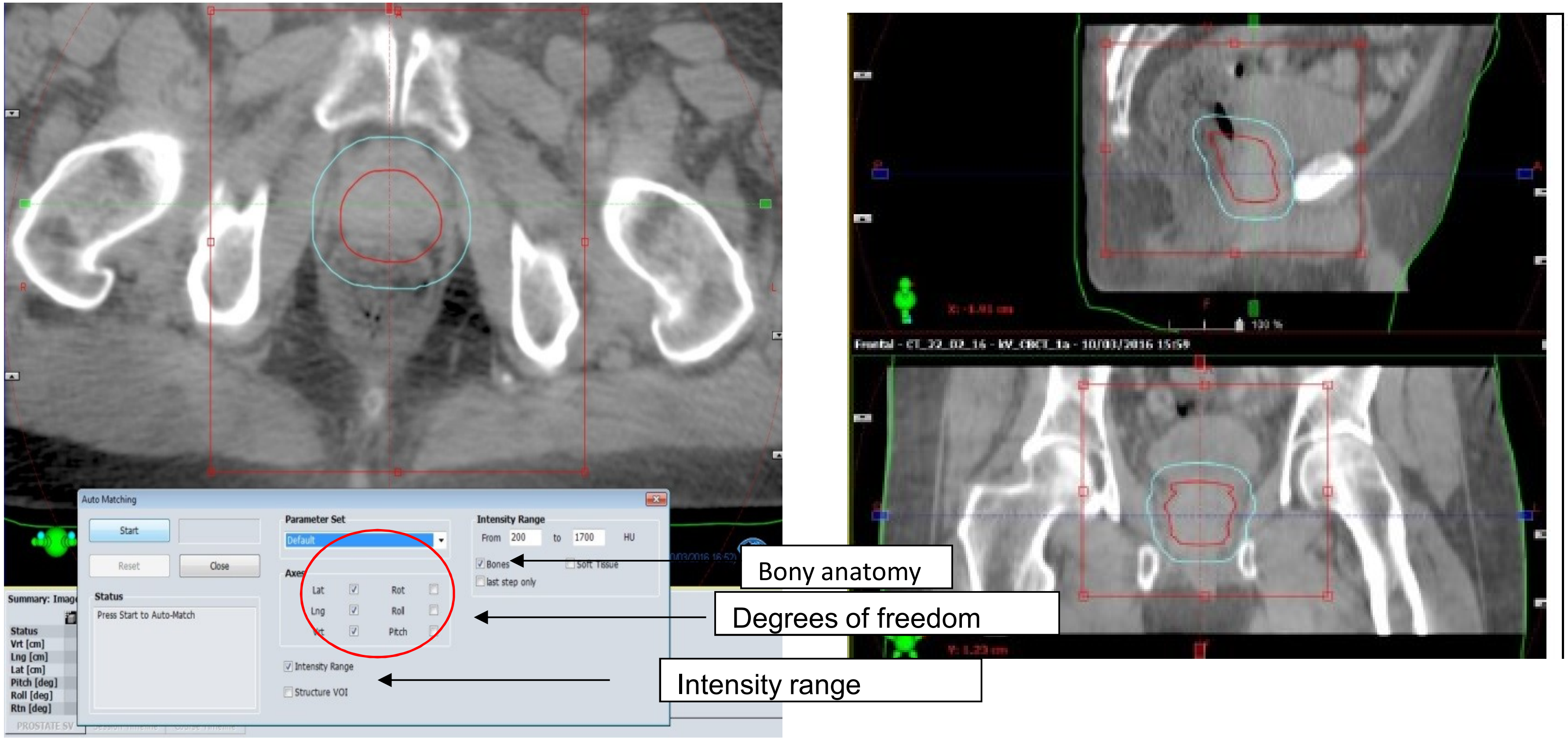




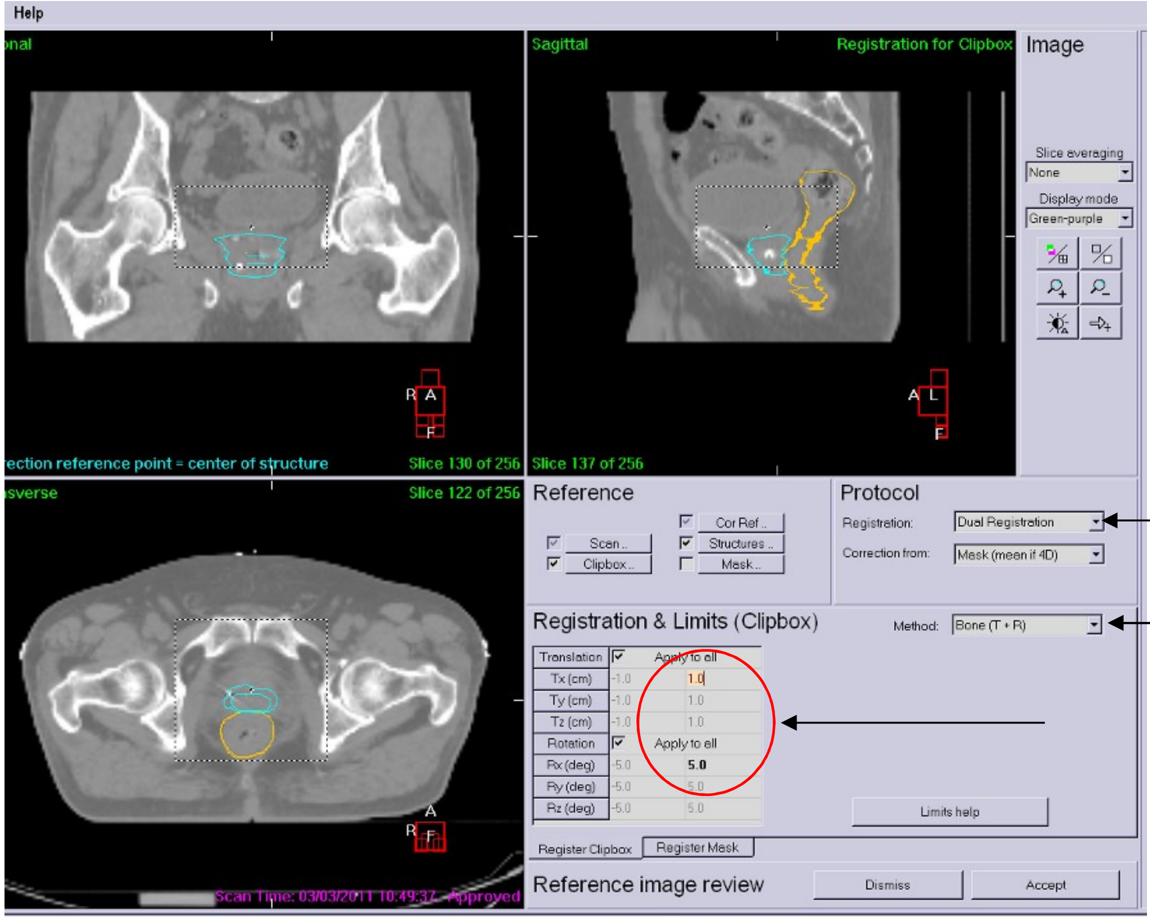
Medium Pelvis 125kV 1044 mAs
Large Pelvis 125kV 1314 mAs

True beam, 125kV 680 mAs

3D prostate registration- 1. Patient position



3D prostate registration- 1. Patient position

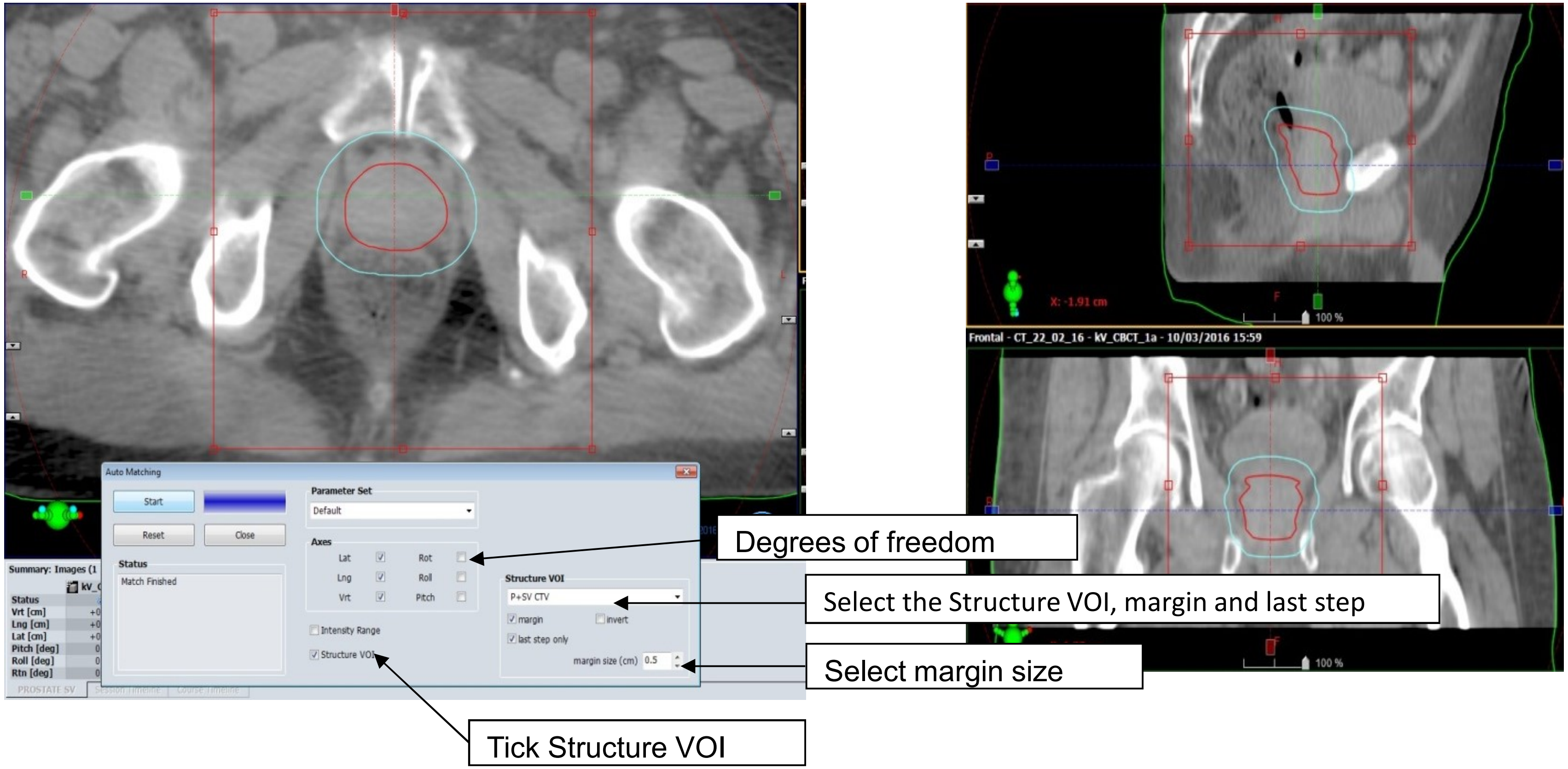


Dual registration

Bony anatomy

Limits set

3D prostate registration- 2. Prostate position



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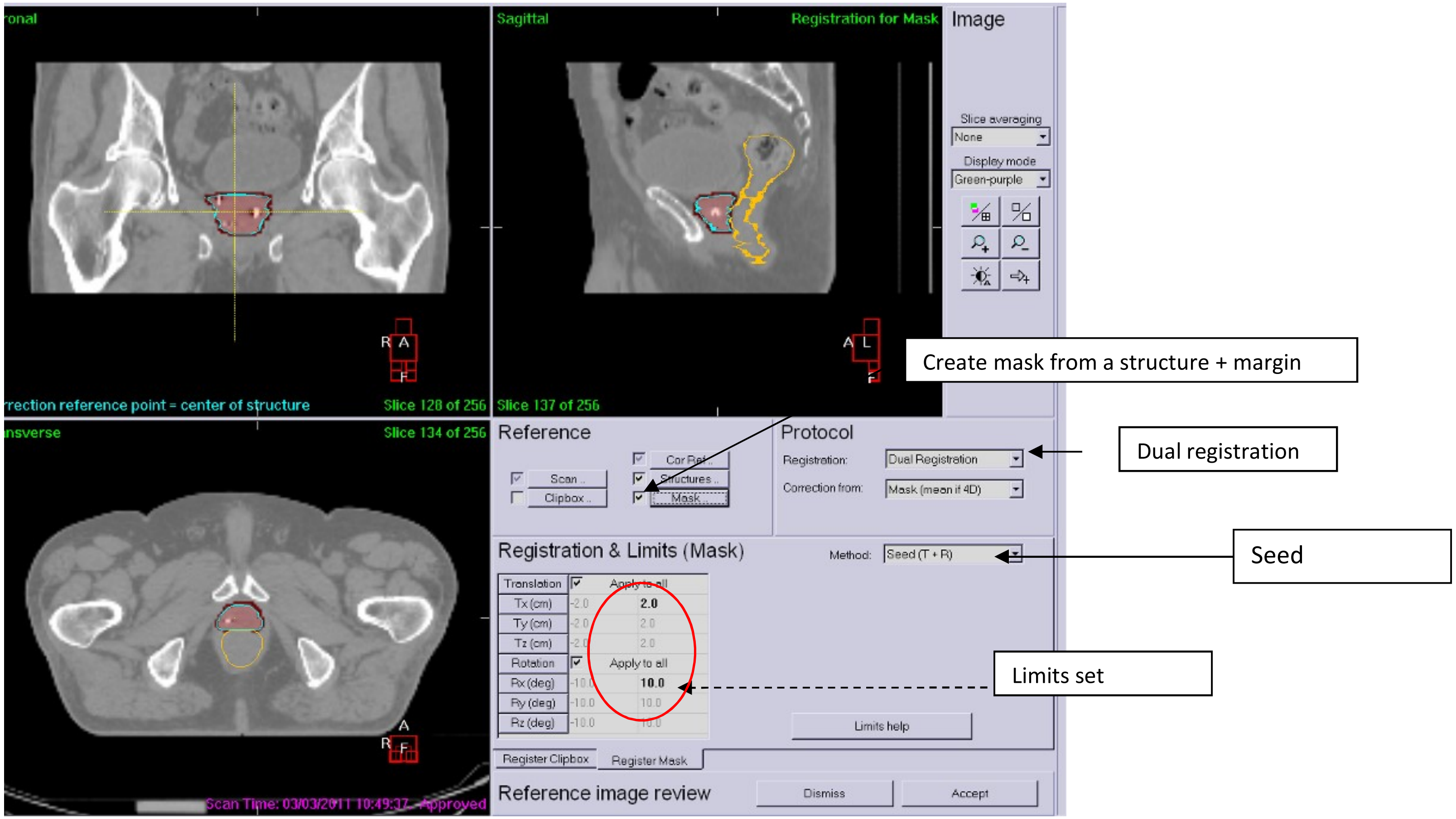
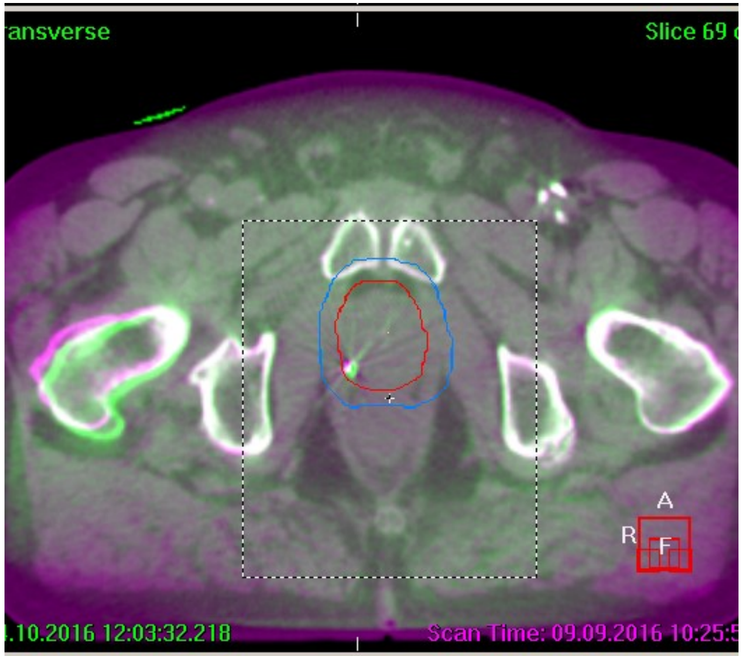
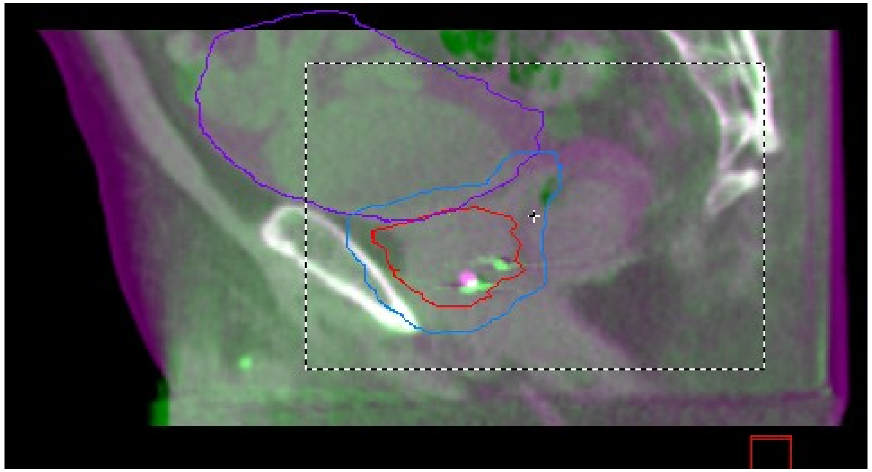
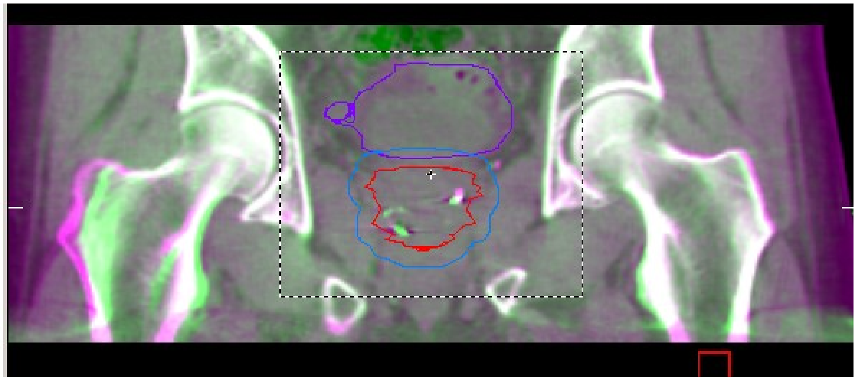
3D prostate registration- 2. Prostate position



3D prostate registration- 1.patient position

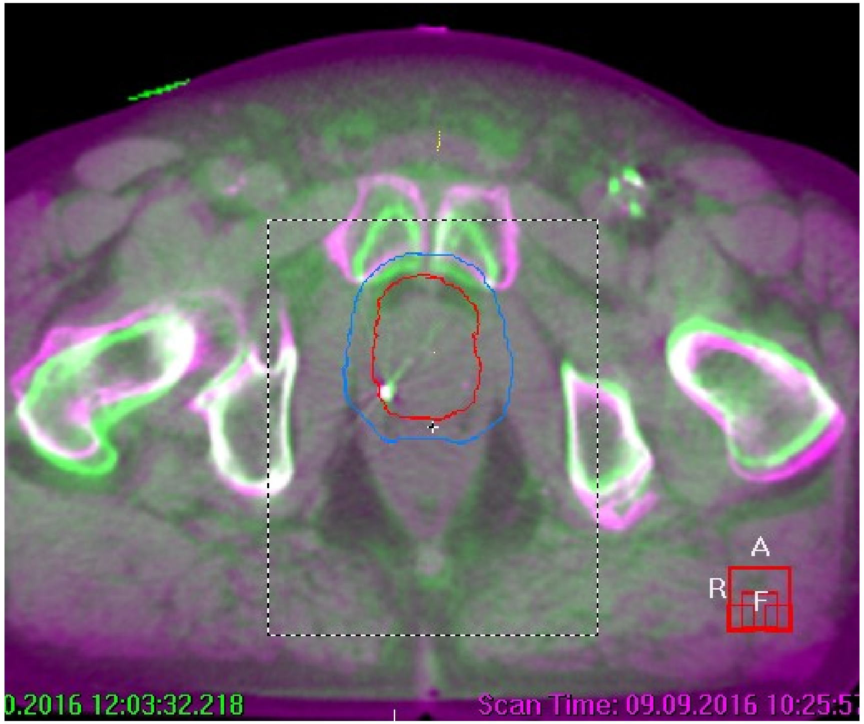


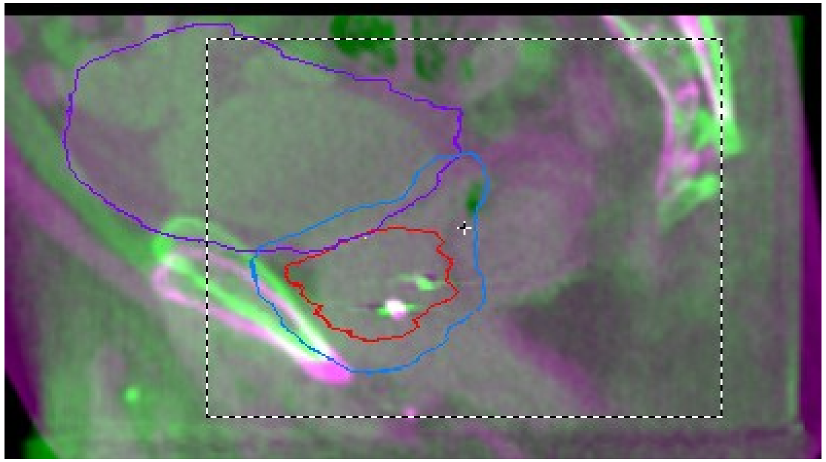


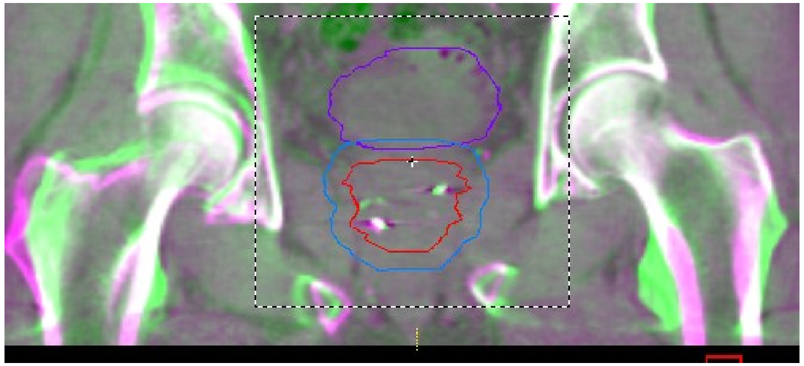


Bone registration

3D prostate registration- 2.prostate position

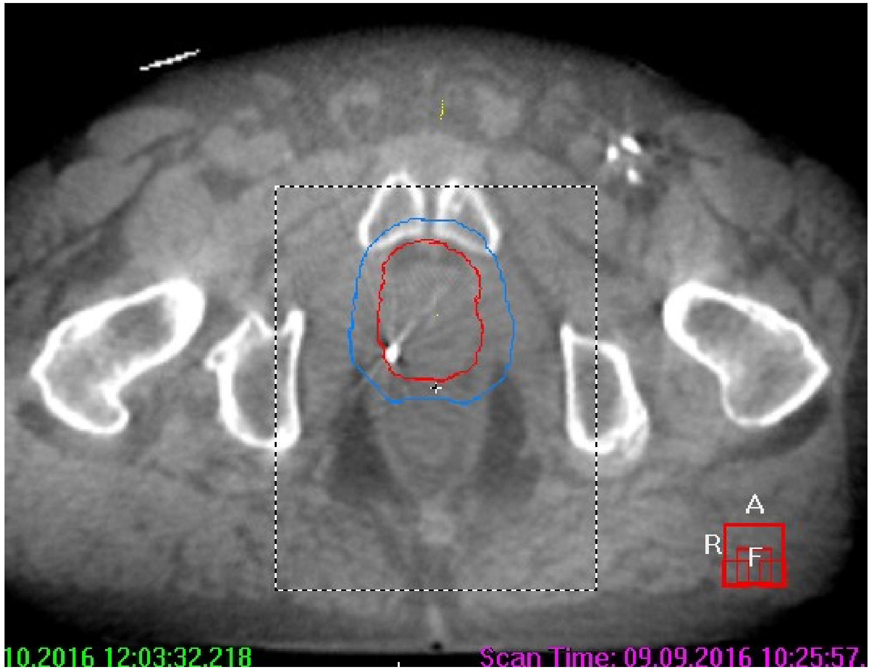


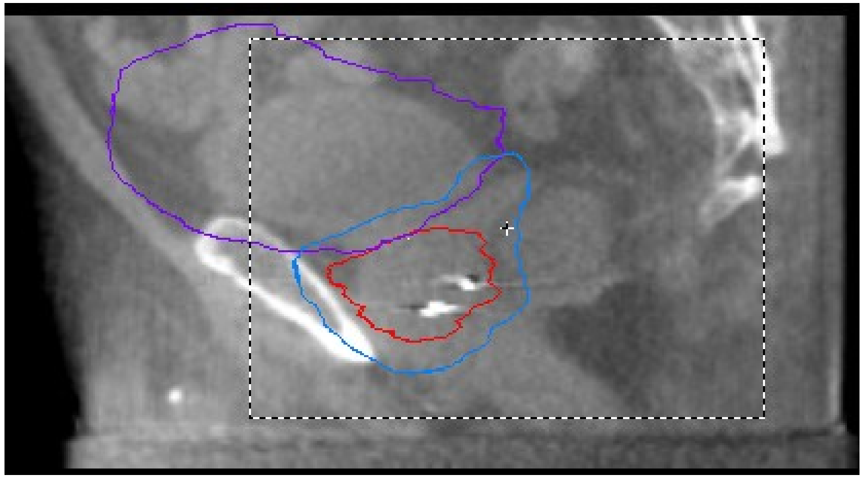


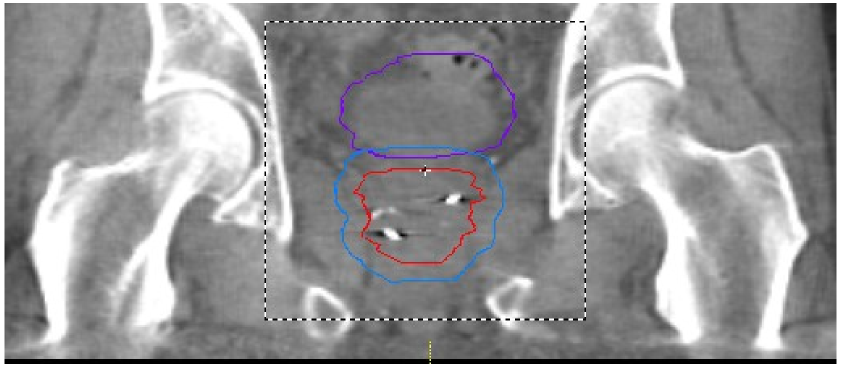


Prostate registration-6 degrees of freedom

3D prostate registration- 2.prostate position

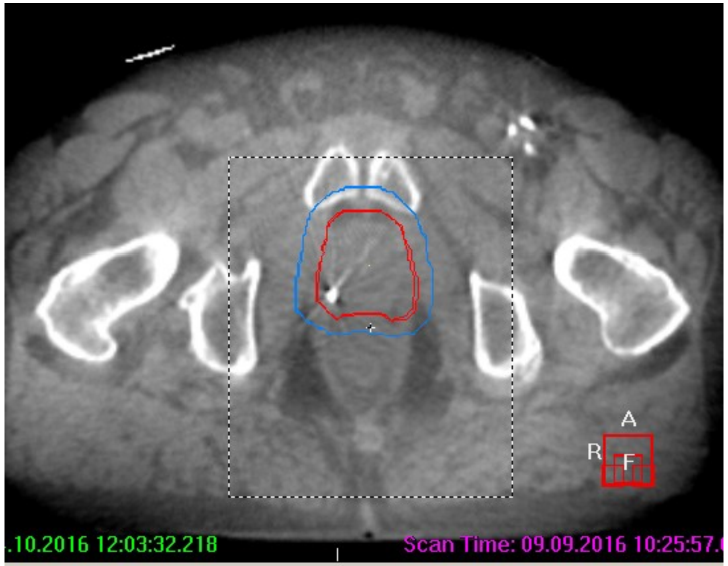


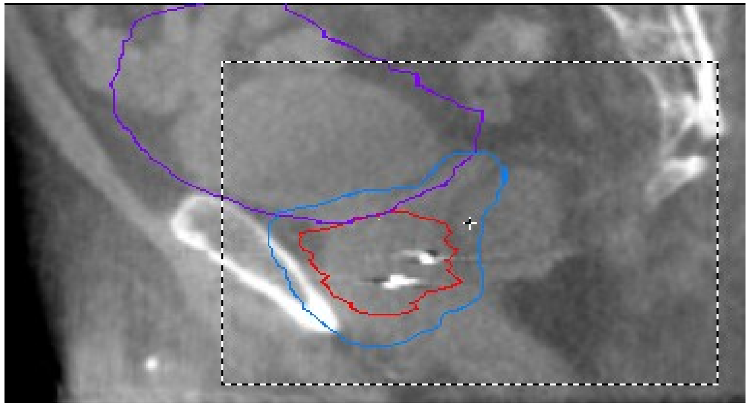


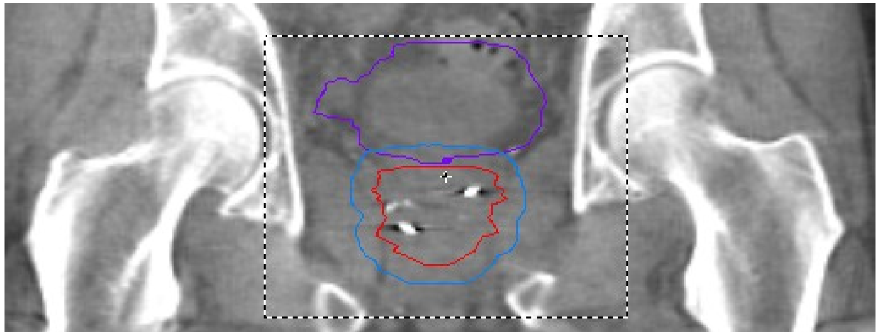


Prostate registration-6 degrees of freedom

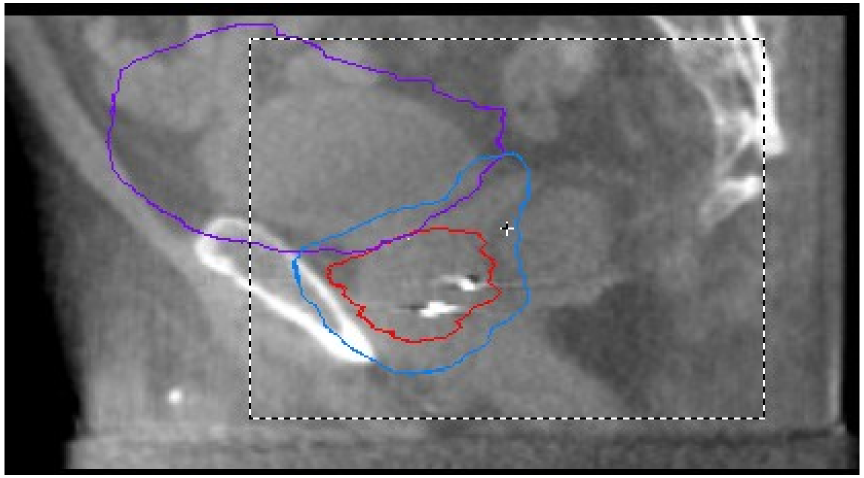
3D prostate registration- 2.prostate position



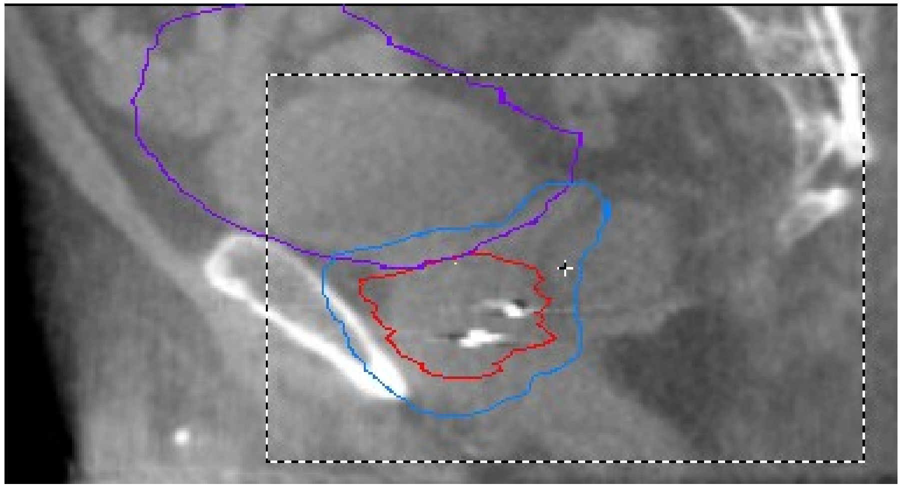




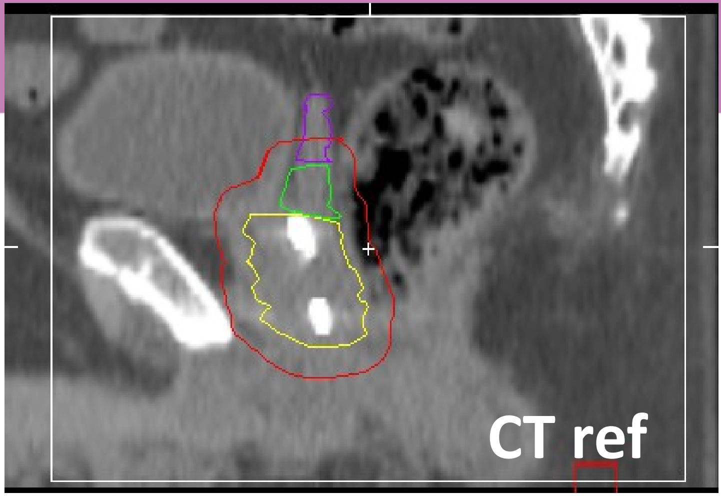
Prostate registration-3 degrees of freedom

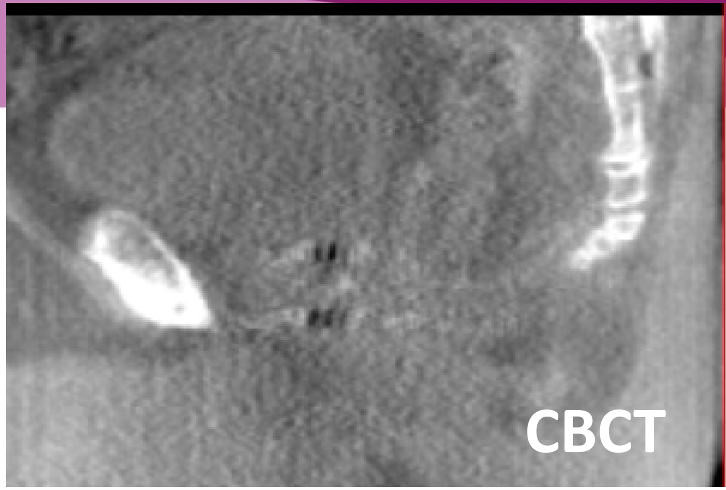


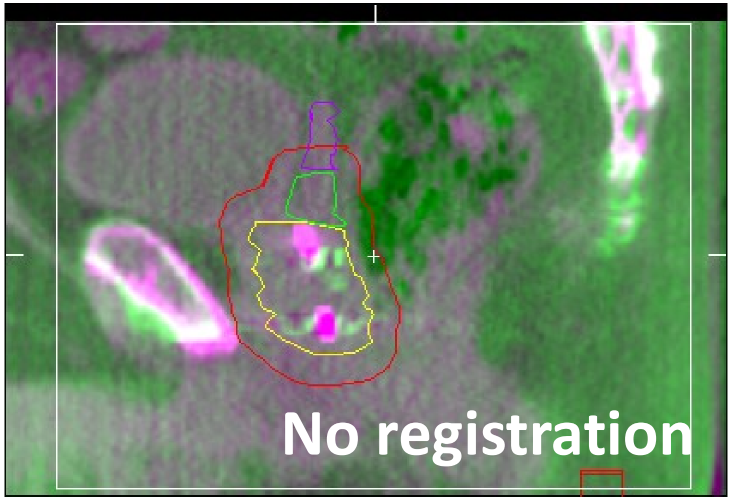
6 degrees



3 degrees







Full rectum on CT planning scan (CT ref)

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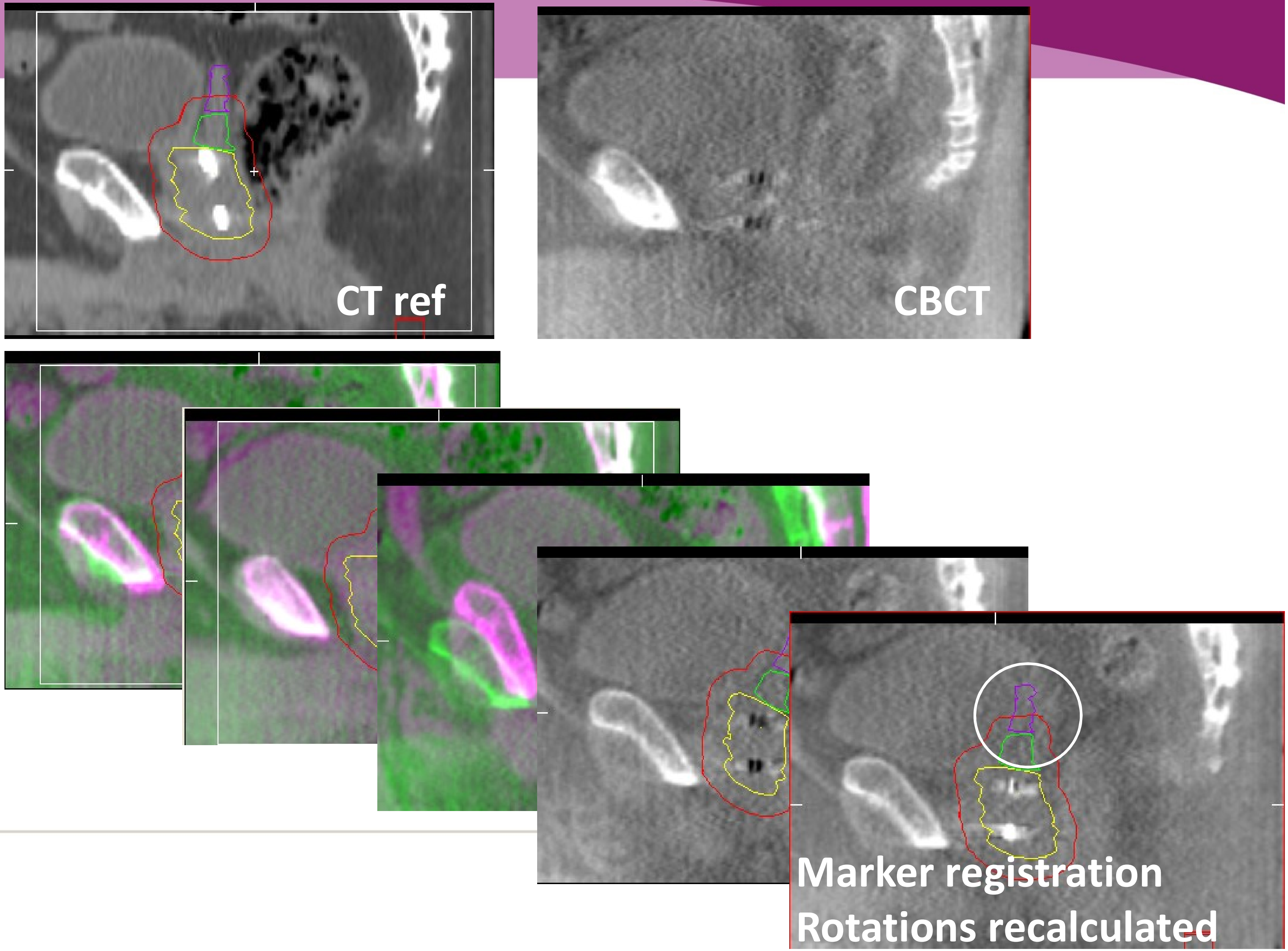
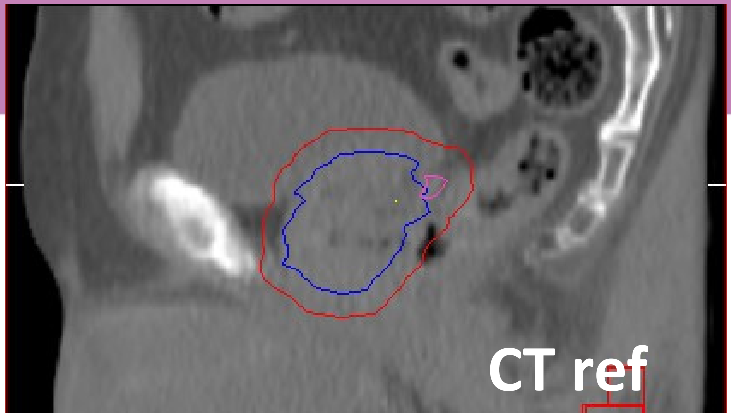
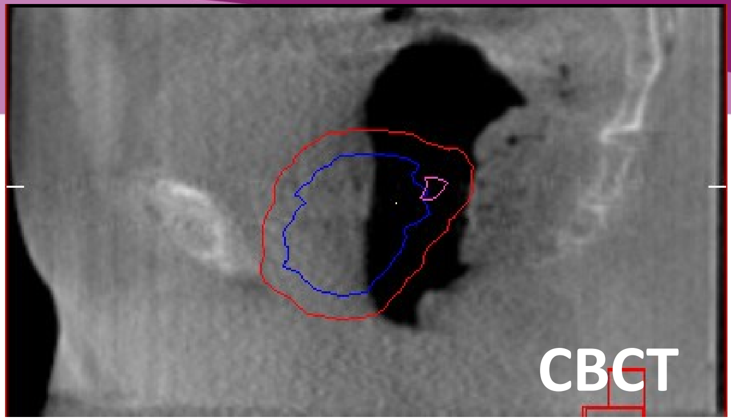
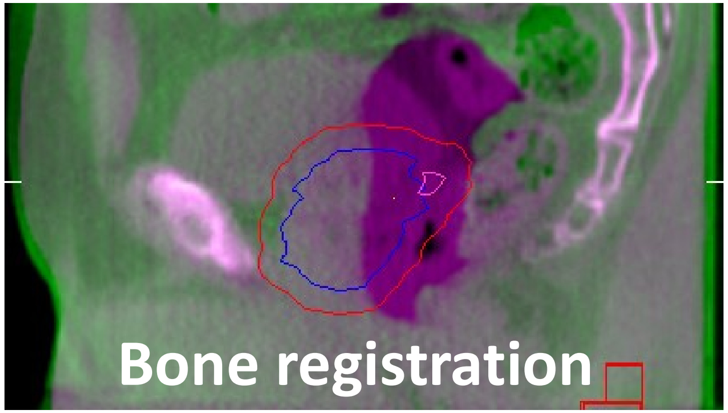
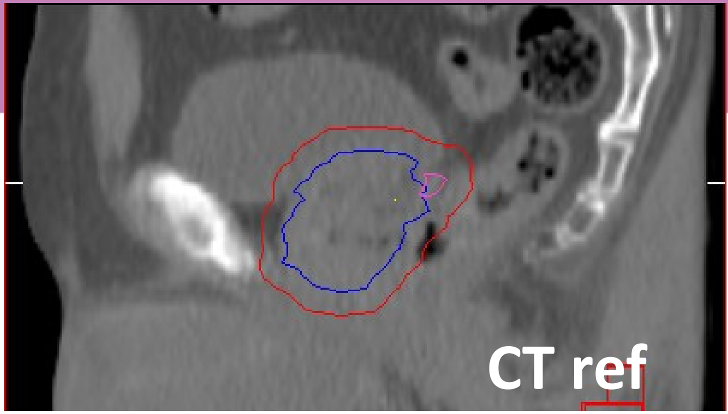

CT ref
CBCT
Marker registration
Rotations recalculated

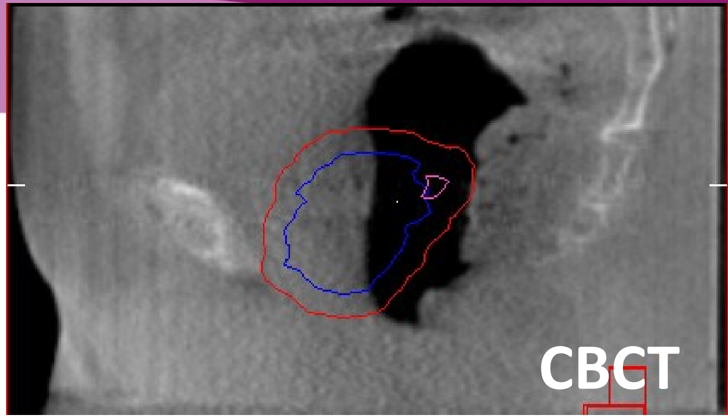


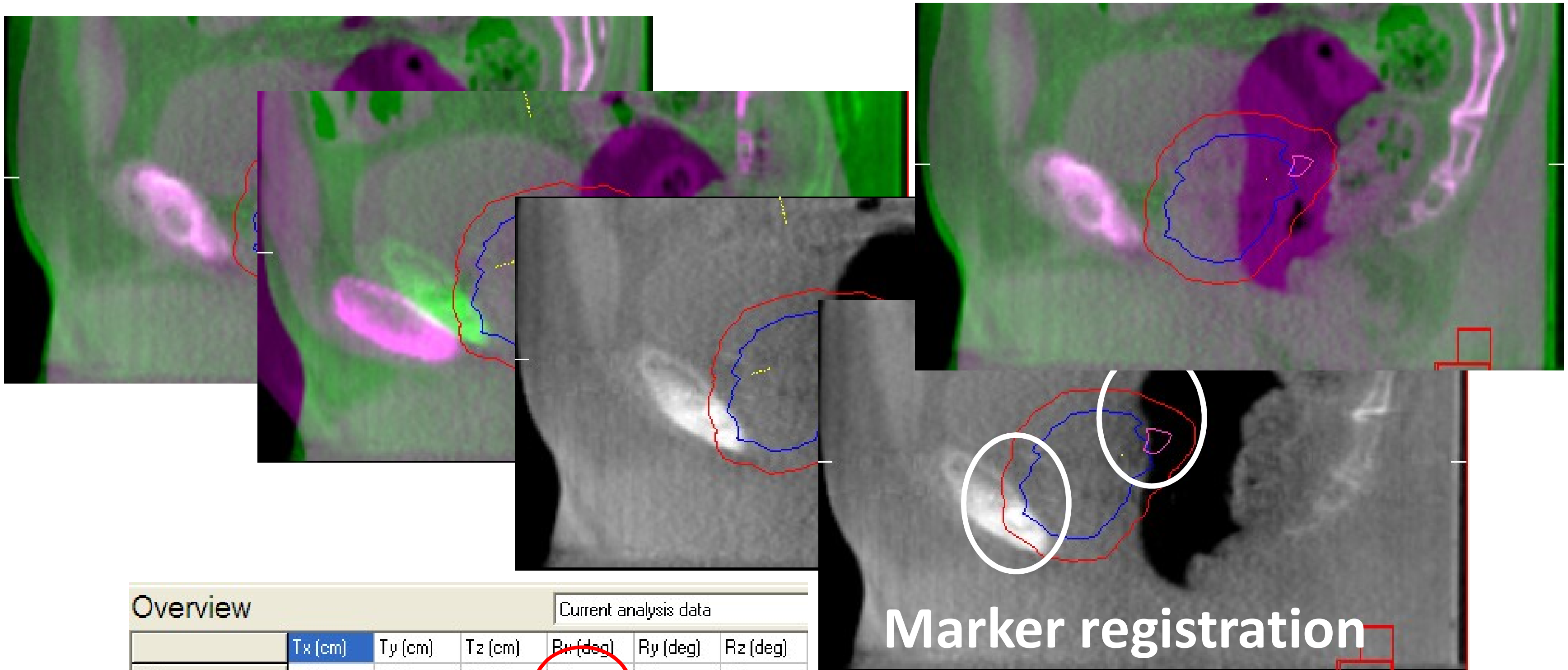




Empty rectum on CT planning scan (CT ref)







Overview

Current analysis data

	Tx (cm)	Ty (cm)	Tz (cm)	Rx (deg)	Ry (deg)	Rz (deg)
Clipbox	0.34	0.30	-0.03	1.2	0.0	0.1
Mask	0.36	1.00	1.67	345.2	9.3	1.2
Correctable	0.34	1.03	1.67	0.0	0.0	0.0

Marker registration rotations recalculated

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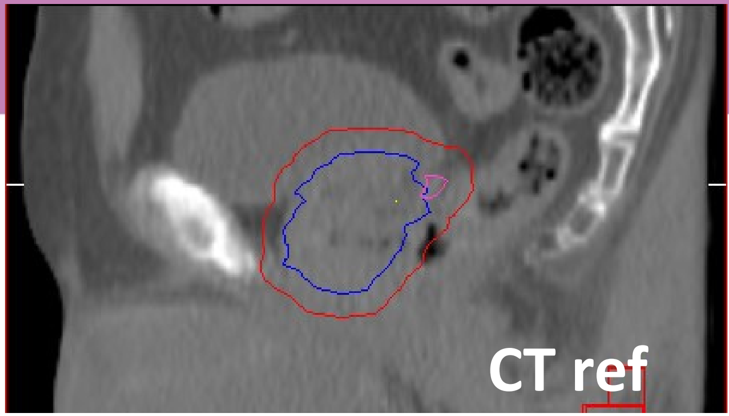
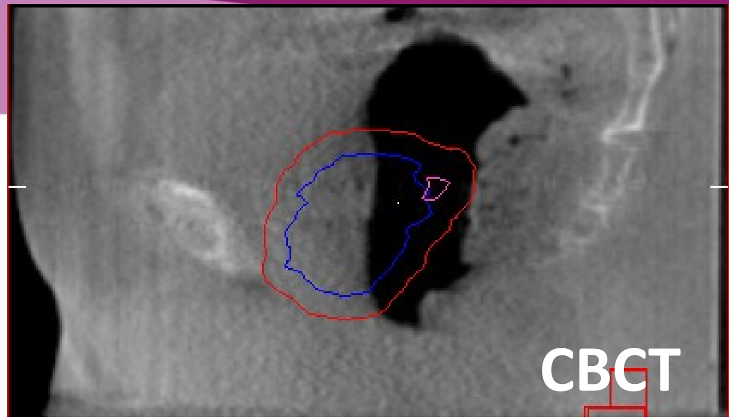
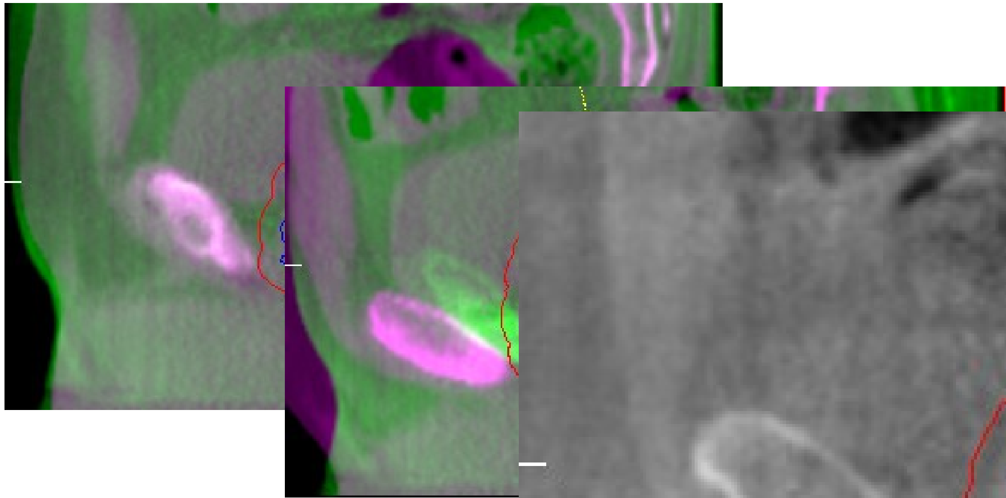






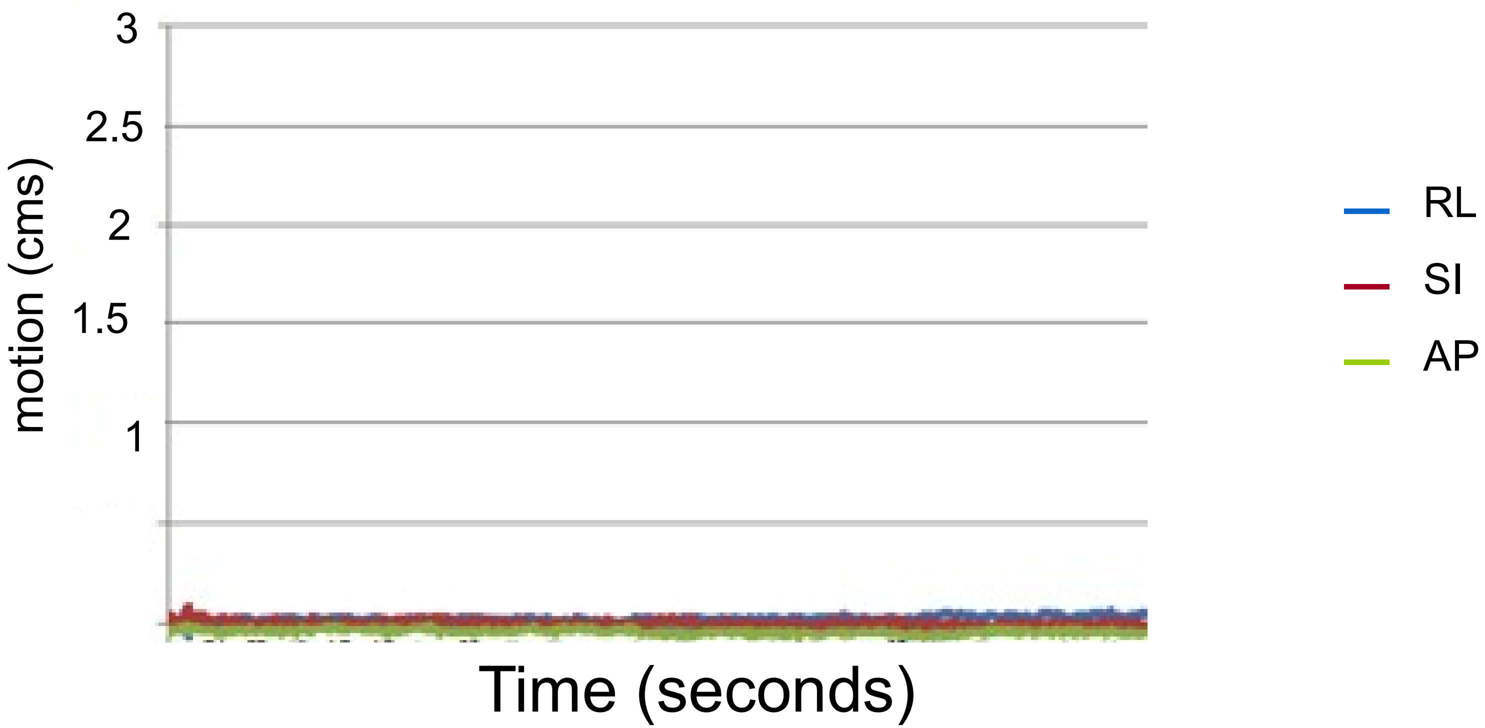
Overview

	Tx (cm)	Ty (cm)
Clipbox	0.34	0.30
Mask	0.36	1.00
Correctable	0.34	1.03

School

Pelvic floor muscle activation

"Ask patient to cough or to lift and squeeze inside as if they are trying to hold back urine"

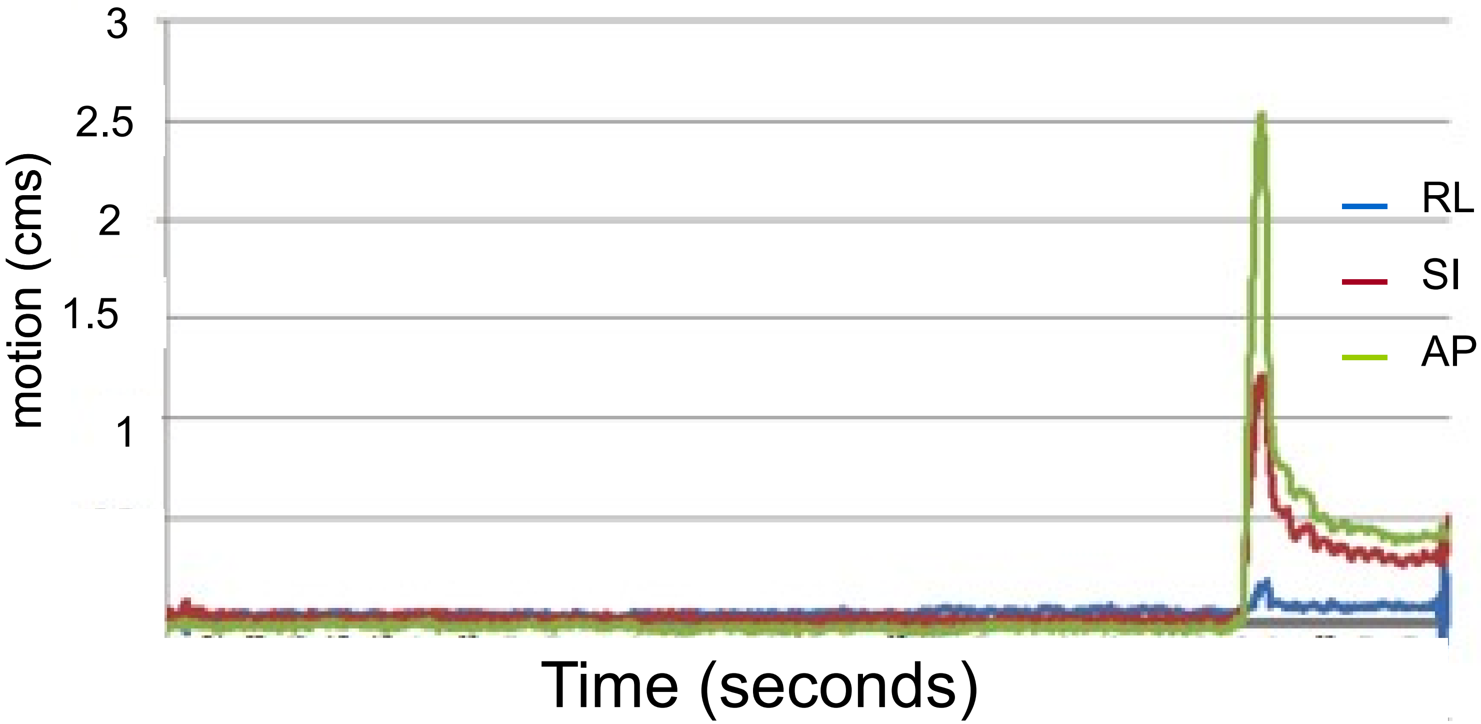


Calypso trace

Courtesy of Julia Murray , RMH & ICR

Pelvic floor muscle activation

"Ask patient to cough or to lift and squeeze inside as if they are trying to hold back urine"



Calypso trace

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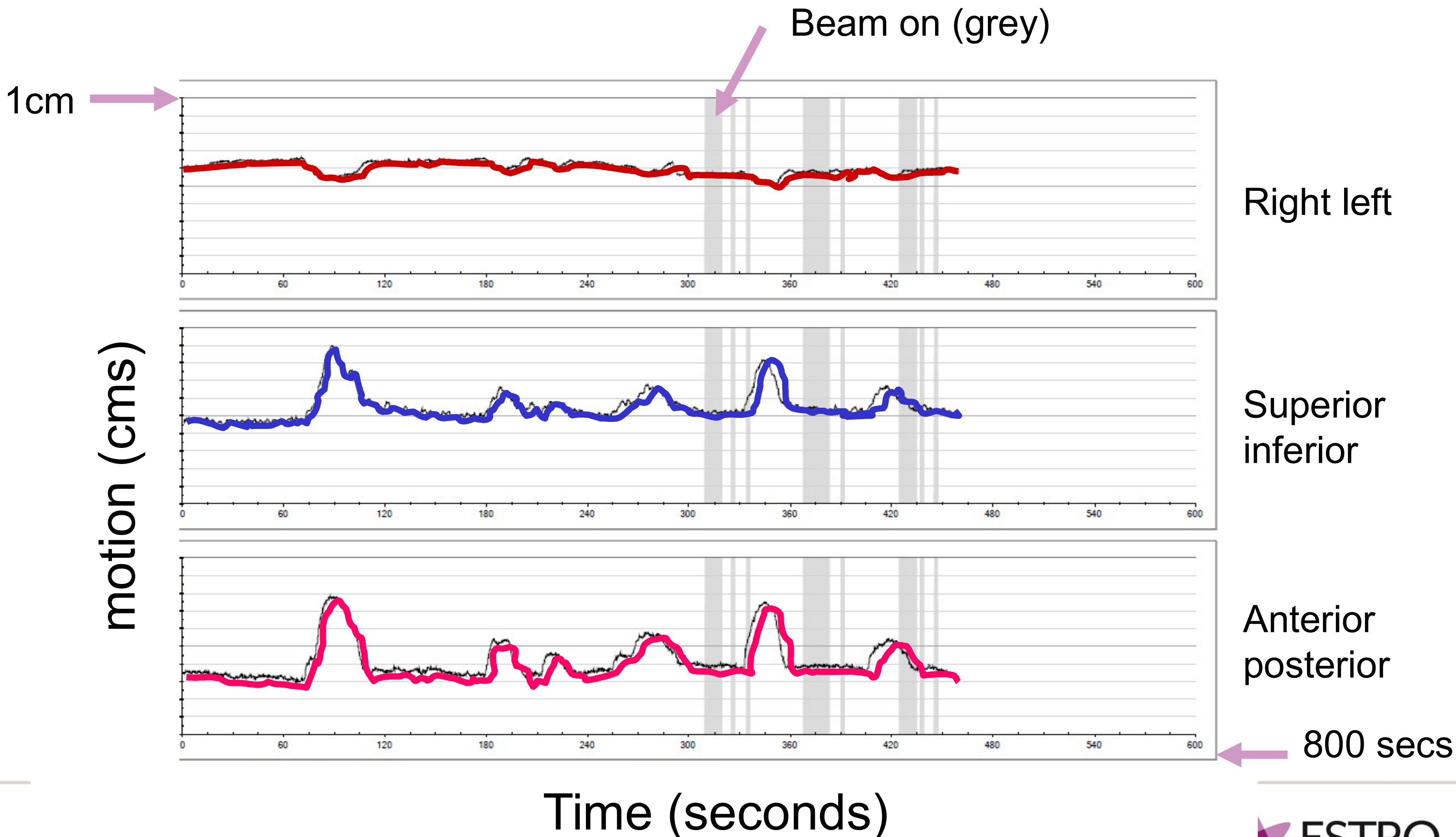
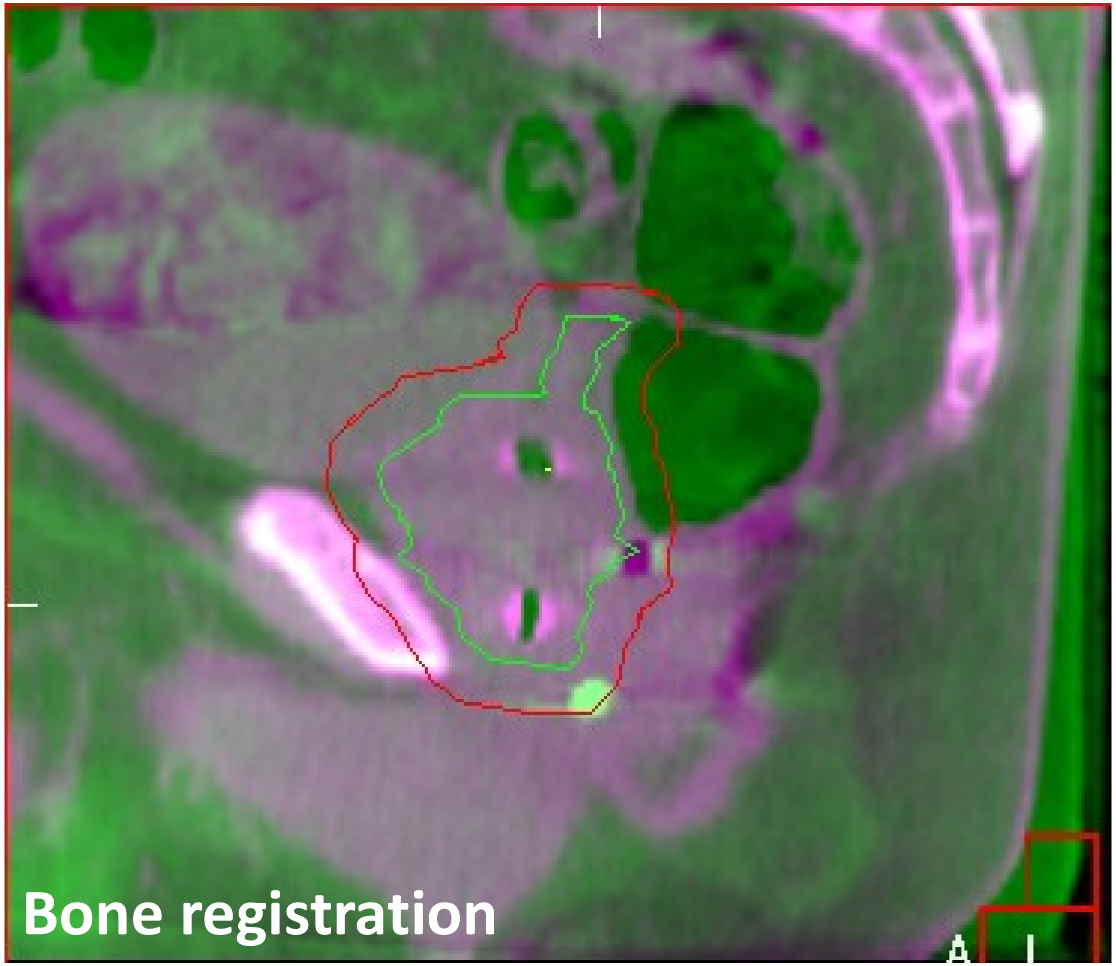
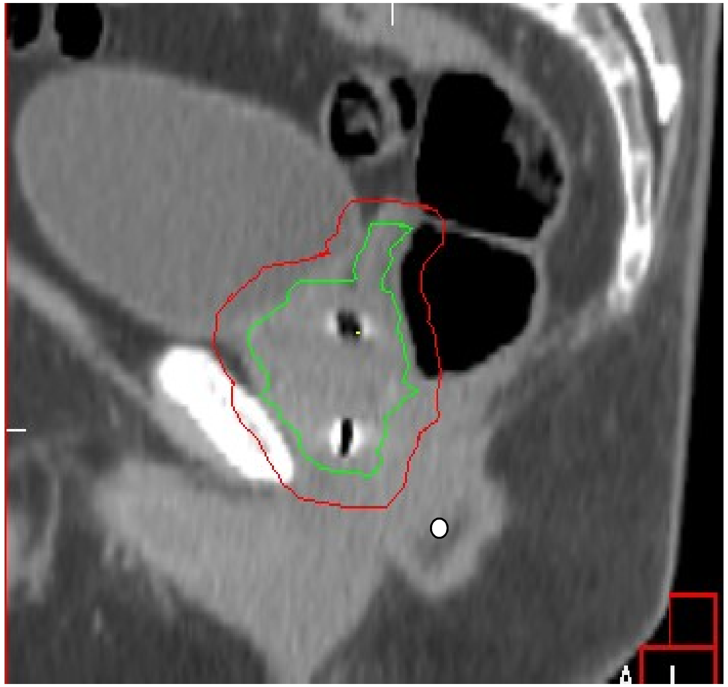
Pelvic floor muscle activation



Muscular tension



Muscular tension



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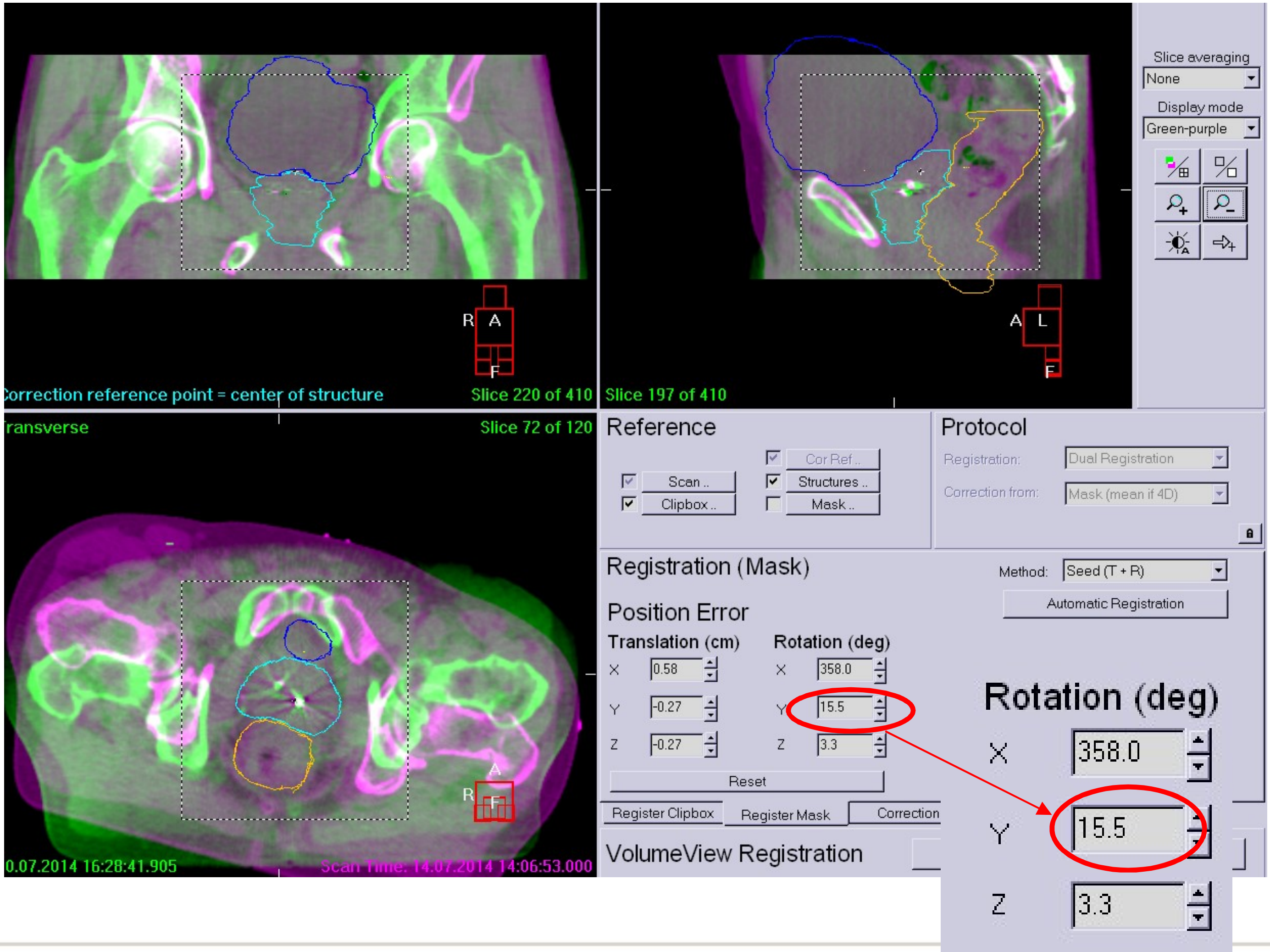
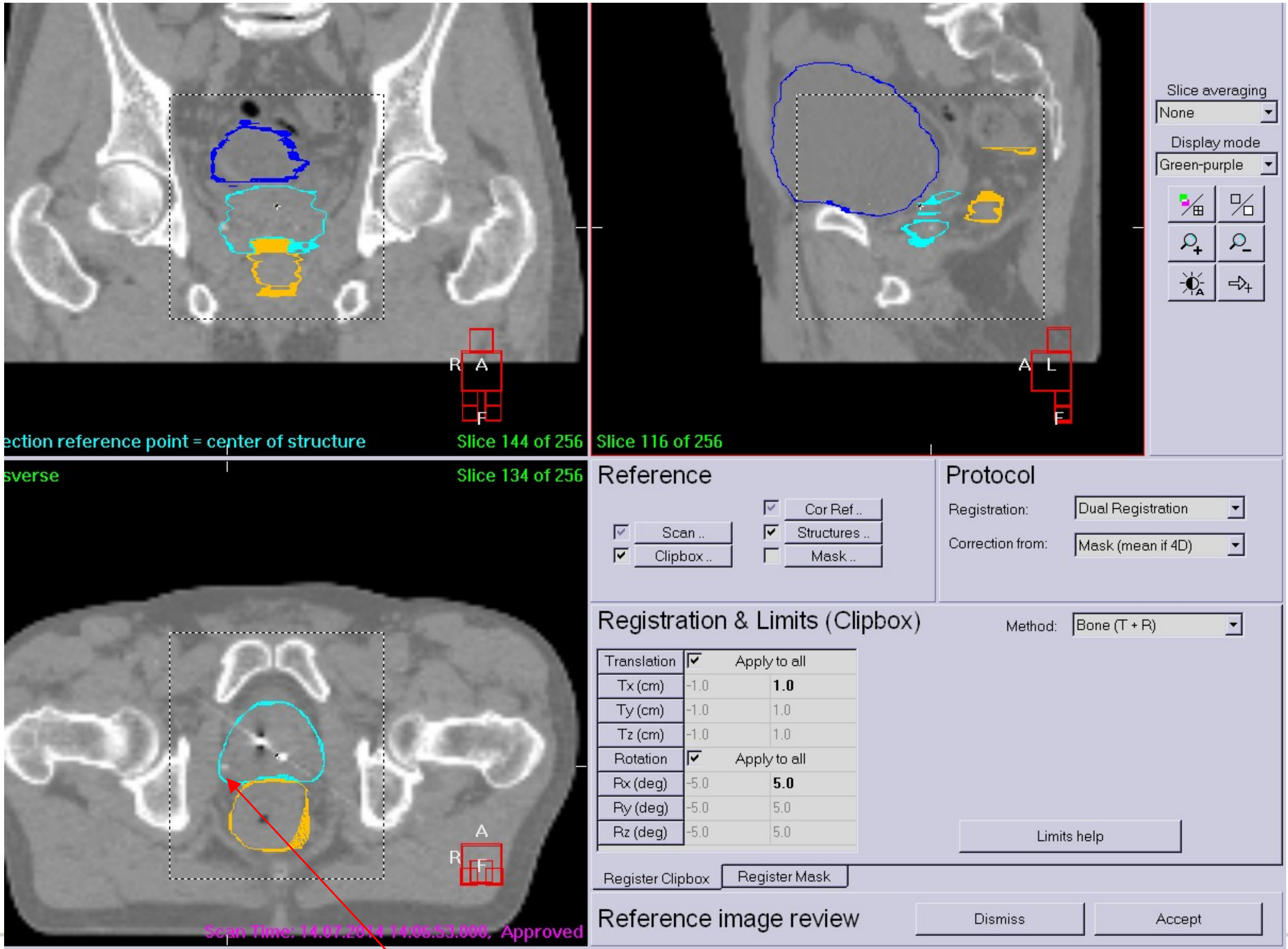
Rotations – check why?

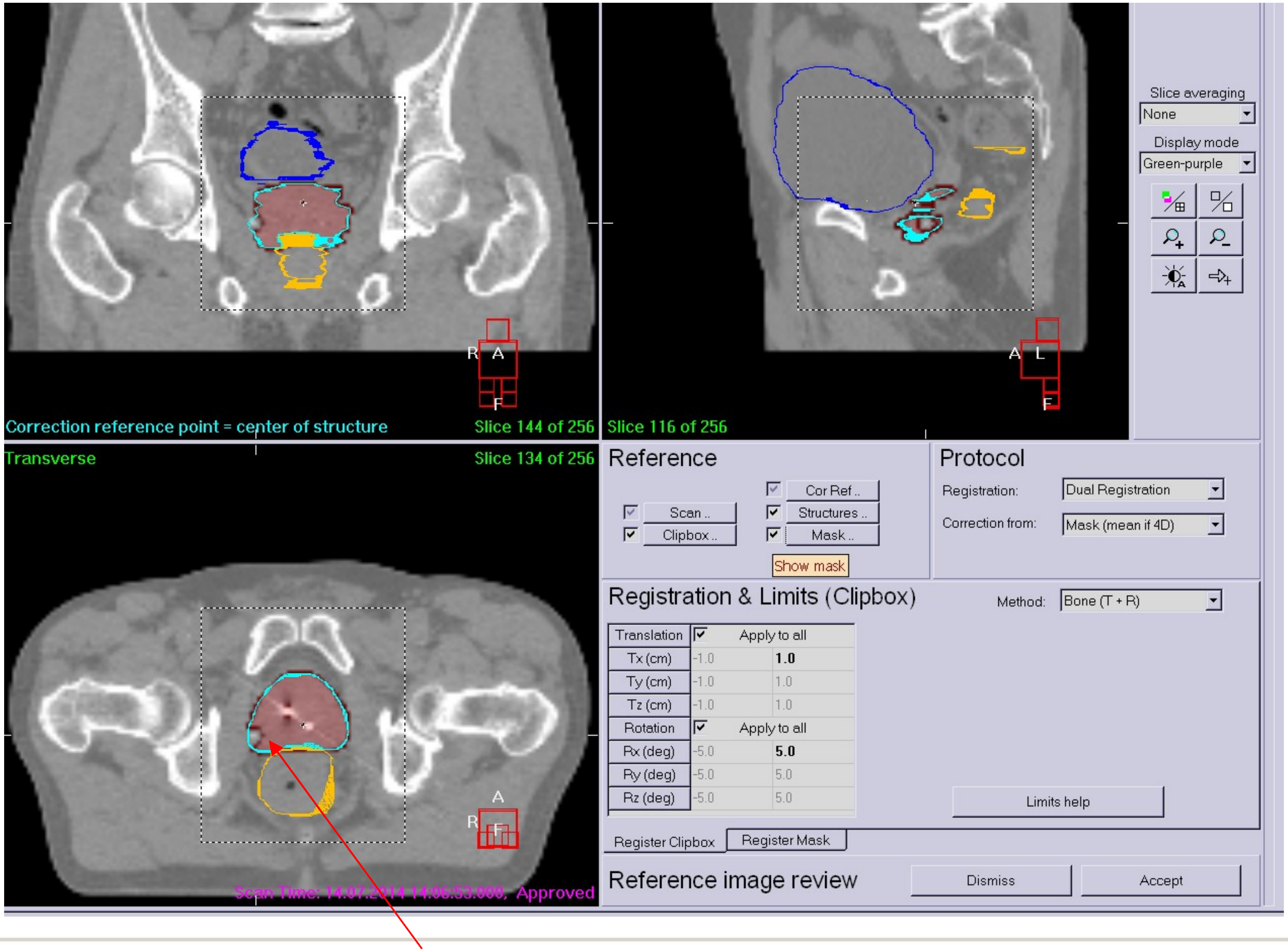


Rotations – check why?



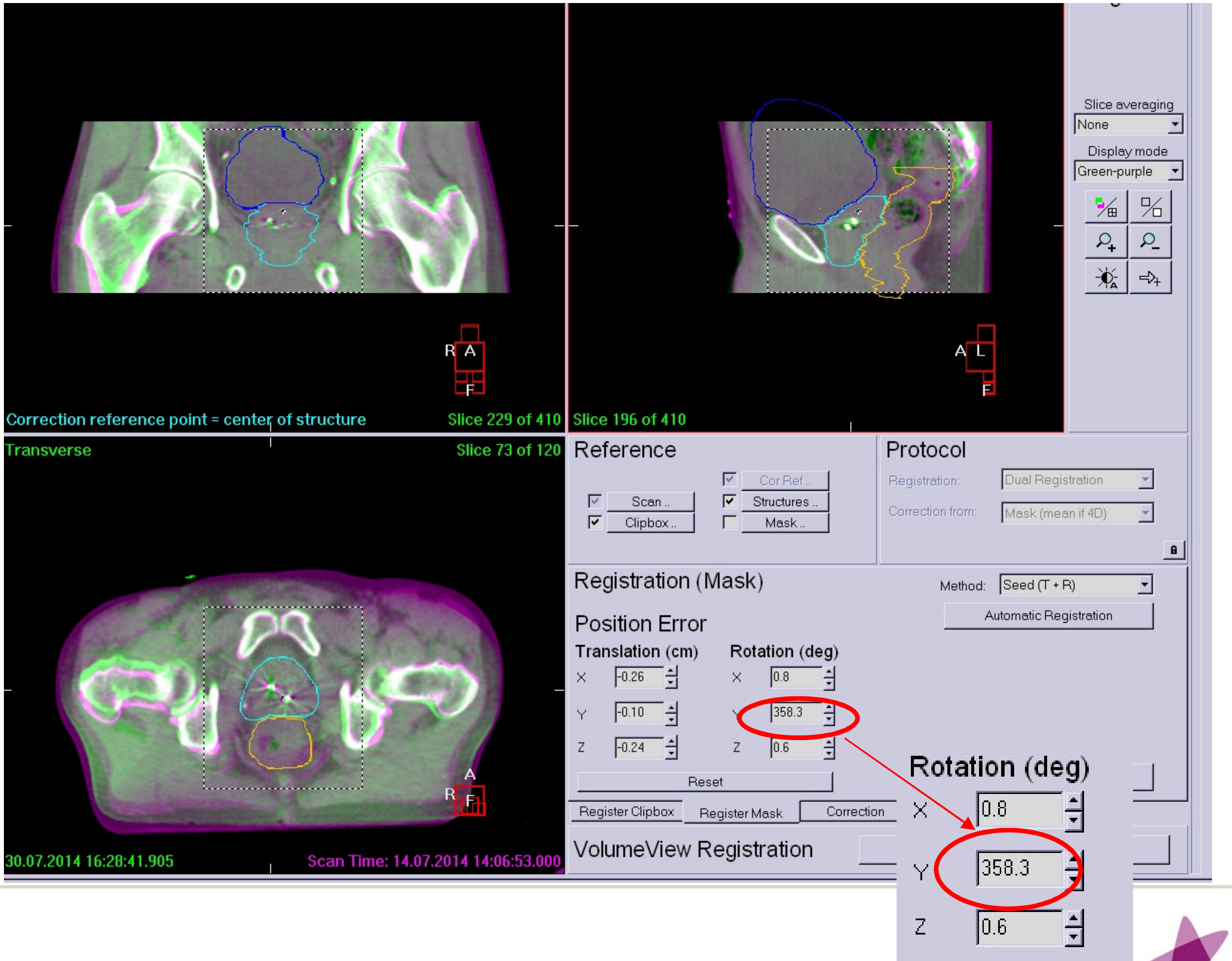
Calcification in the reference image

Rotations – check why?



Erased

Rotations – check why?



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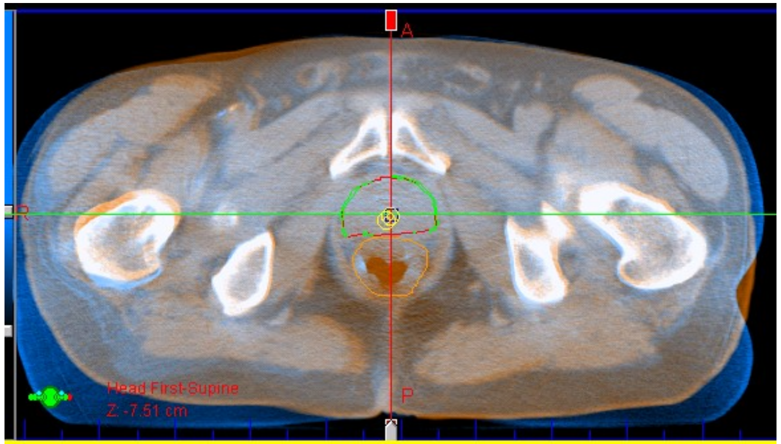
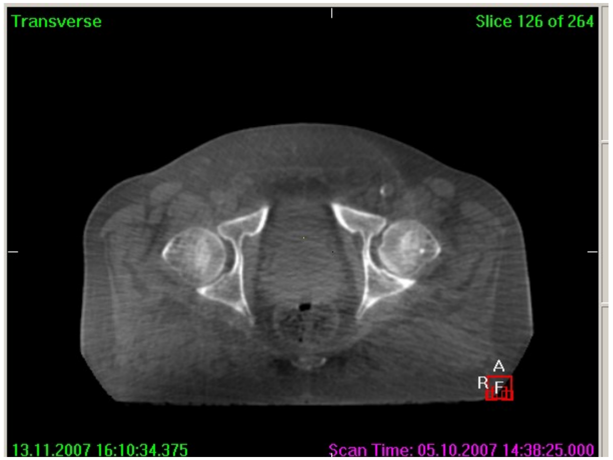
Comparison of systems

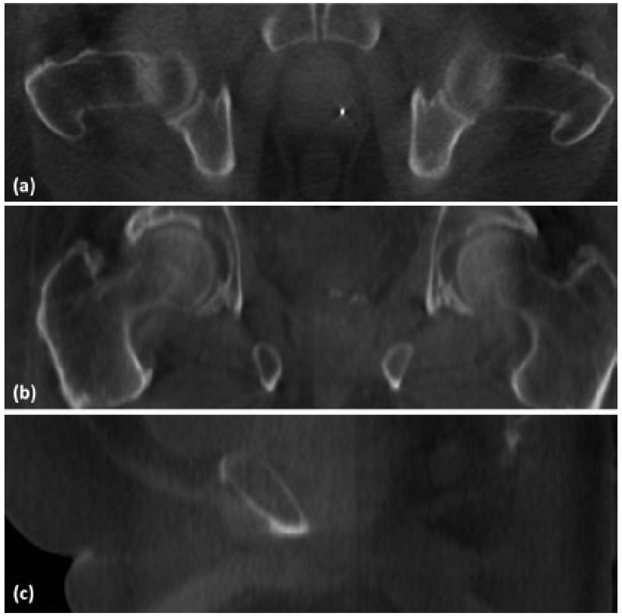




Modality	MV	CBCT Fiducial markers	CBCT Soft tissue
Largest source of uncertainty	Marker localisation	Intrafraction motion	Inter observer variability

Moseley 2007 IJROBP

Comparison of systems



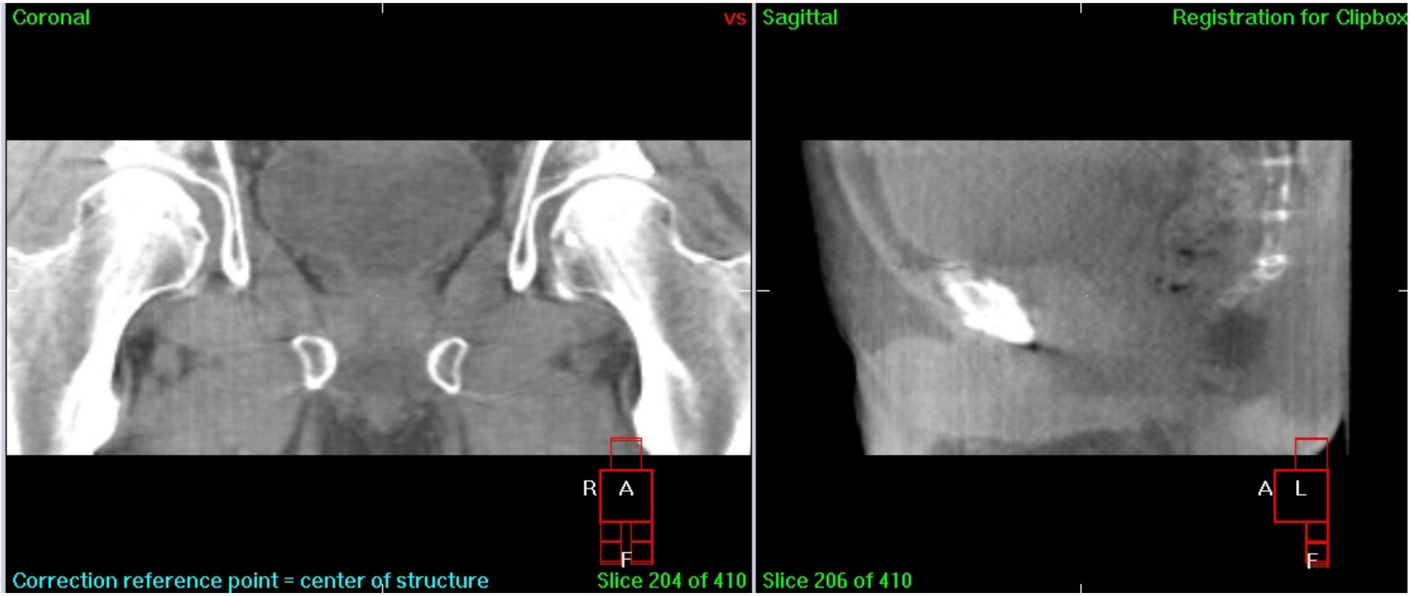
Seeds
0.9 × 3.0 mm, CIVCO

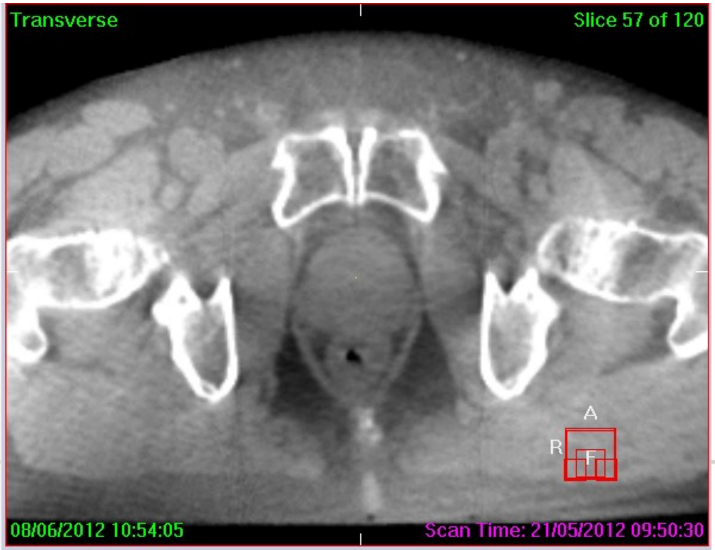
OBI
half fan
half bow-tie filter
360 degree gantry rotation
Reconstruction:512 × 512 resolution; 2mm slice thickness

95% Limits of agreement 3 observers	Right left (mm)	Superior Inferior (mm)	Anterior Posterior (mm)
CBCT fiducial markers	<2mm	<2mm	<2mm
CBCT soft tissue	<3mm	<3mm	<3mm
Average CBCT Fiducial markers compared CBCT Soft tissue	-1.6 to 2.5	-4.9 to 2.6	-4.7 to 1.9

Deegan 2014, Journal of Medical Imaging and Radiation Oncology

Soft tissue matching – no markers





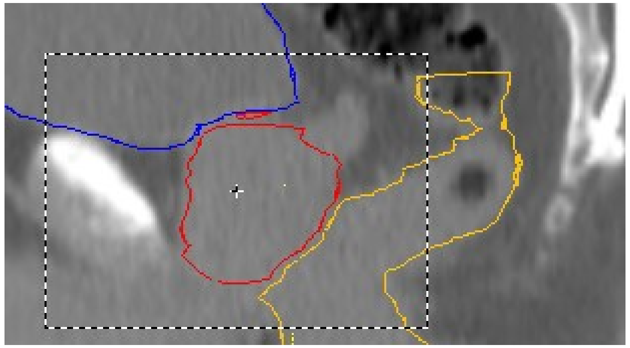
Inter observer errors – evaluate

(CT definition = 5-6mm)*

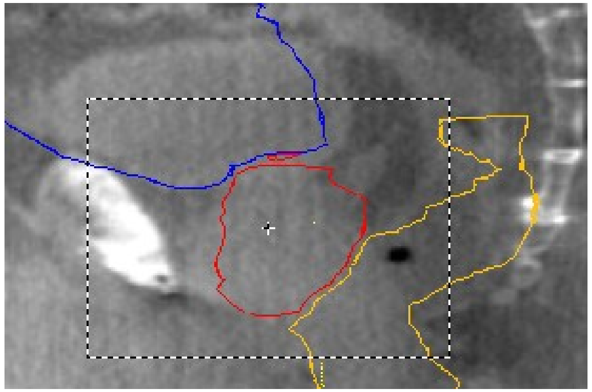
Gain organ motion information

* Roach M, 1996; Kagawa K, 1997

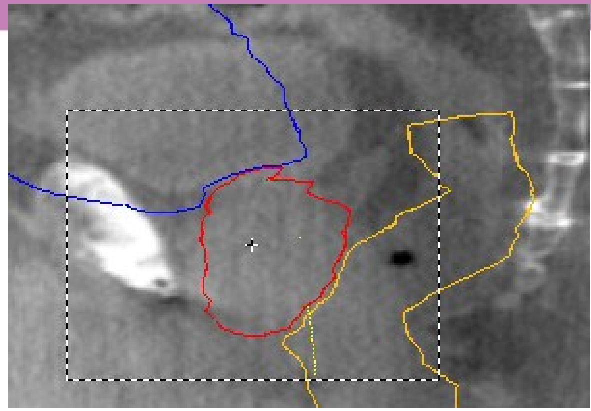
Difference between observers



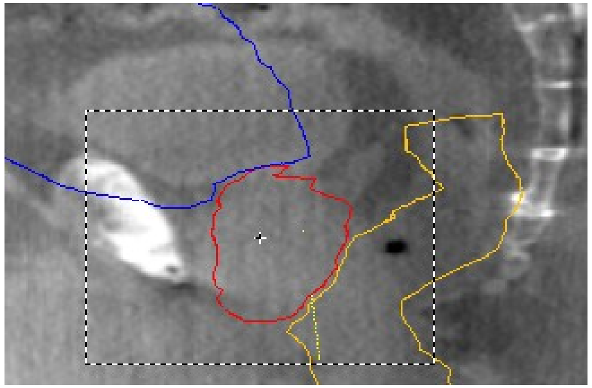
Reference



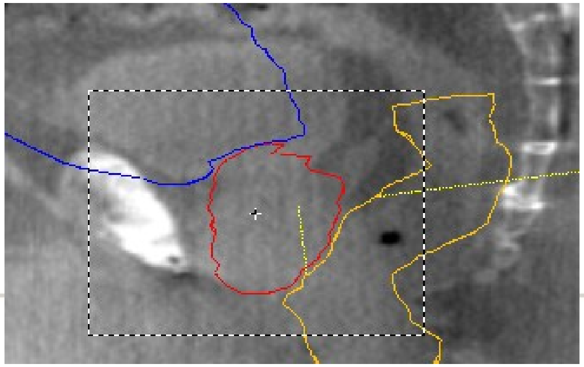
Automatic
SI= -0.43
AP=-0.78



OBS1
SI= -0.88
AP=-0.80

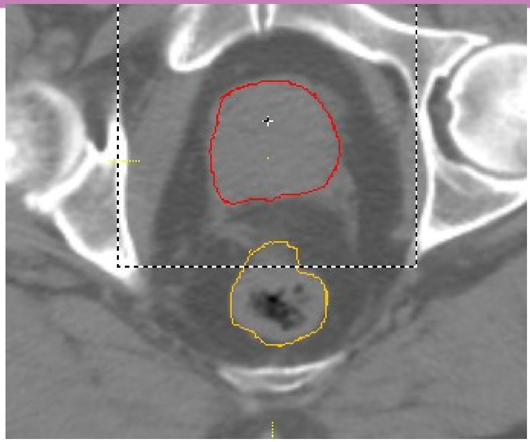


OBS2
SI= -0.98
AP= -0.89



OBS3
SI= -0.48
AP=-0.80

Difference between observers



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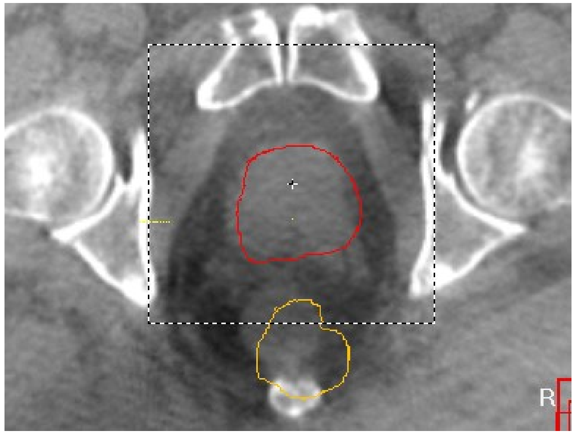
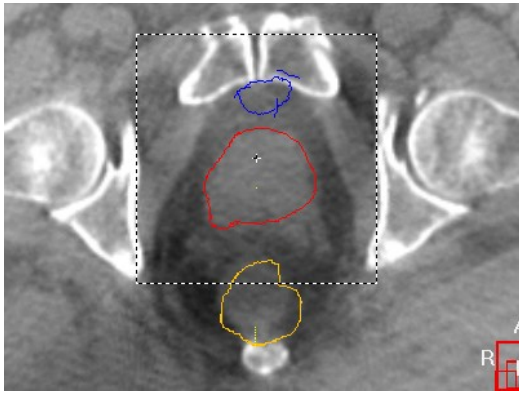
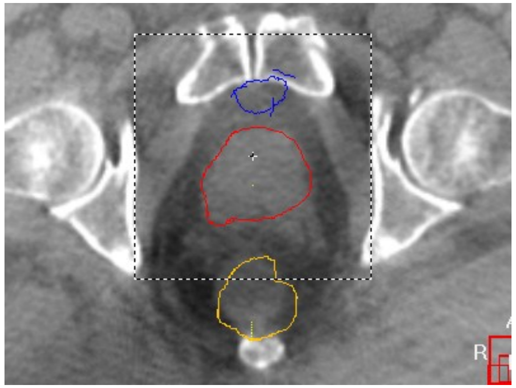


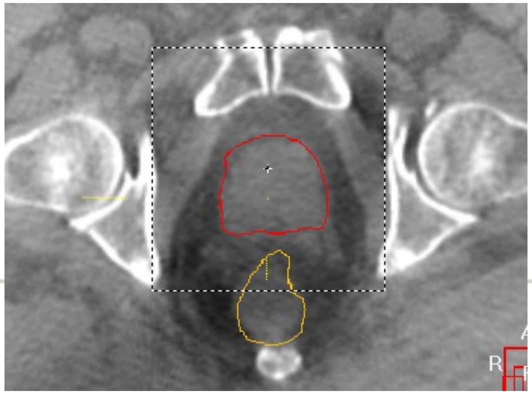
Automatic
RL= -0.53
AP=-0.78



OBS1
RL=-0.54
AP=-0.80



OBS2
RL=- 0.54
AP=-0.89



OBS3
RL=-0.64
AP=-0.80

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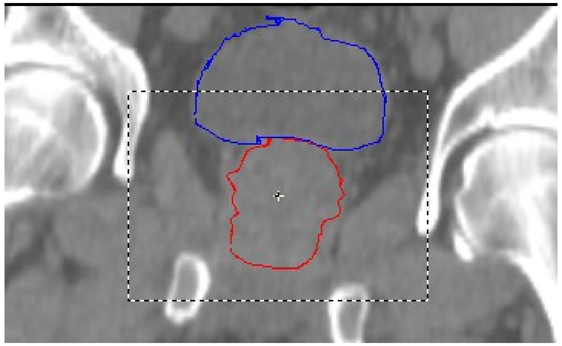
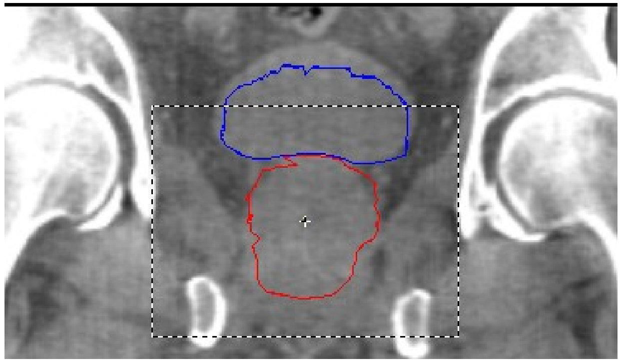
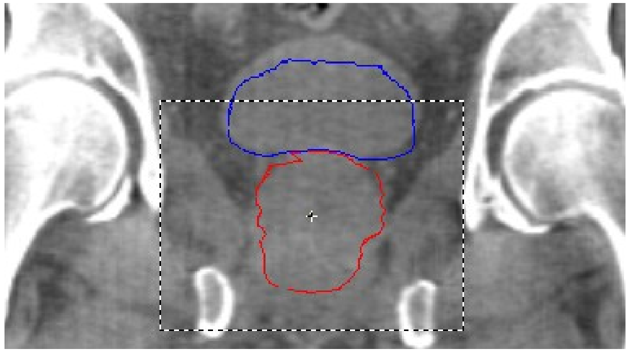
Difference between observers



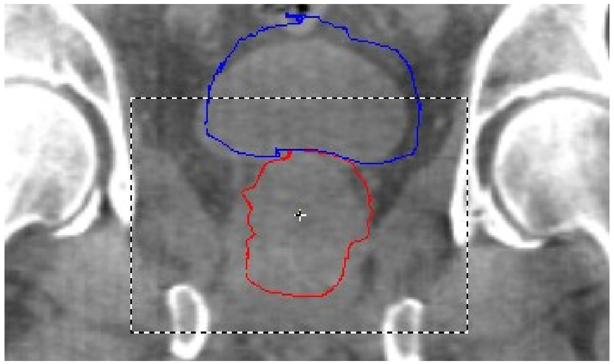
Reference



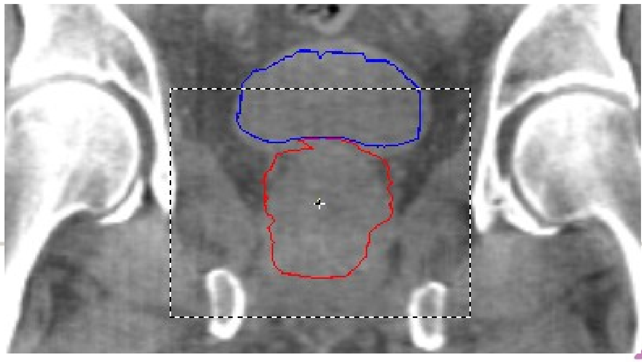
OBS1
RL= -0.54
SI= -0.88



OBS2
RL = -0.54
SI= -0.98



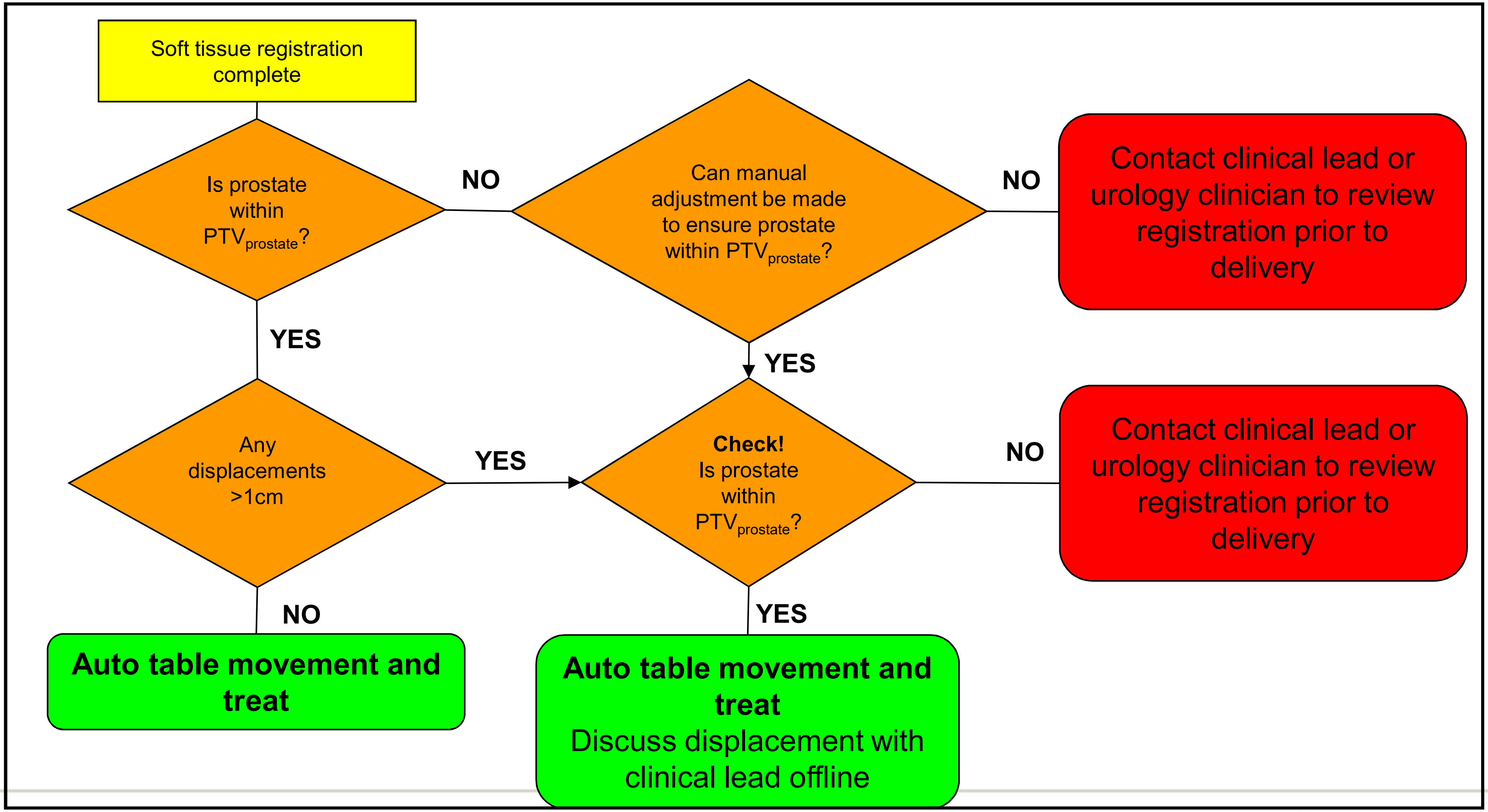
Automatic
RL= -0.53
SI= -0.43



OBS3
RL= -0.64
SI = -0.48

Online decision making soft tissue matching
Prostate +/- Seminal Vesicles only

NB All operators must have completed competency assessment (S-WB-019) to carry out prostate soft tissue matching. It may be necessary for the clinical lead or urology clinician to review imaging offline.



Courtesy of Steven Landeg, RMH

Offline decision making soft tissue matching
Prostate +/- Seminal Vesicles only

NB All operators must have completed competency assessment (S-WB-019) to carry out prostate soft tissue matching. It may be necessary for clinical lead or urology clinician to review imaging offline.

Review rectum and bladder status

Is rectum ≥50% different from planning scan? (see example Figure 1)

YES → Discuss with patient and check correct used of rectal preparation (as per J-CH-059). Record rectal status on S-RT-083-02.

NO → Record ‘**Rectal status ‘good**’ on log S-RT-083-02

Is bladder under-filled?

YES → Encourage hydration and record **‘under-filled bladder’** on XVI log S-RT-083-02.

NO → Record **‘Bladder status good**’ on XVI log S-RT-083-02

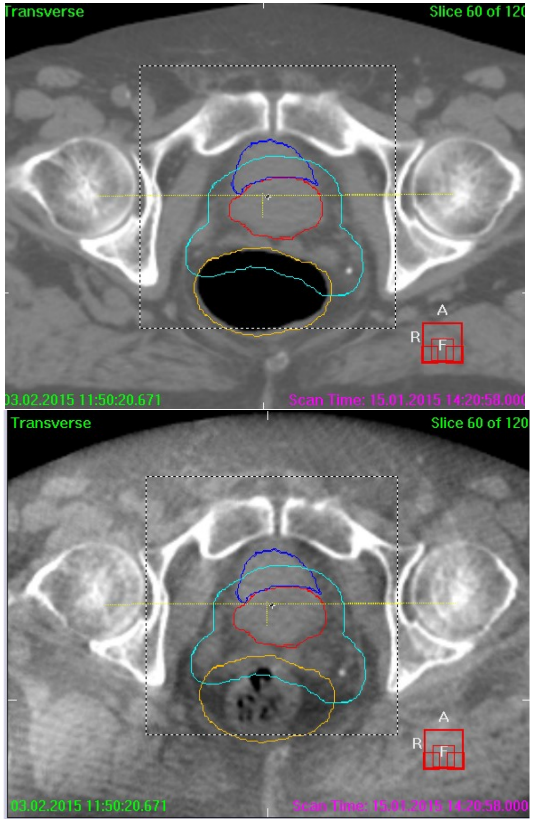


Figure 1: Planning scan (top) showing large gas filled rectum. CBCT (bottom) showing smaller, stool filled rectum on treatment (~50% smaller).

Courtesy of Steven Landeg, RMH

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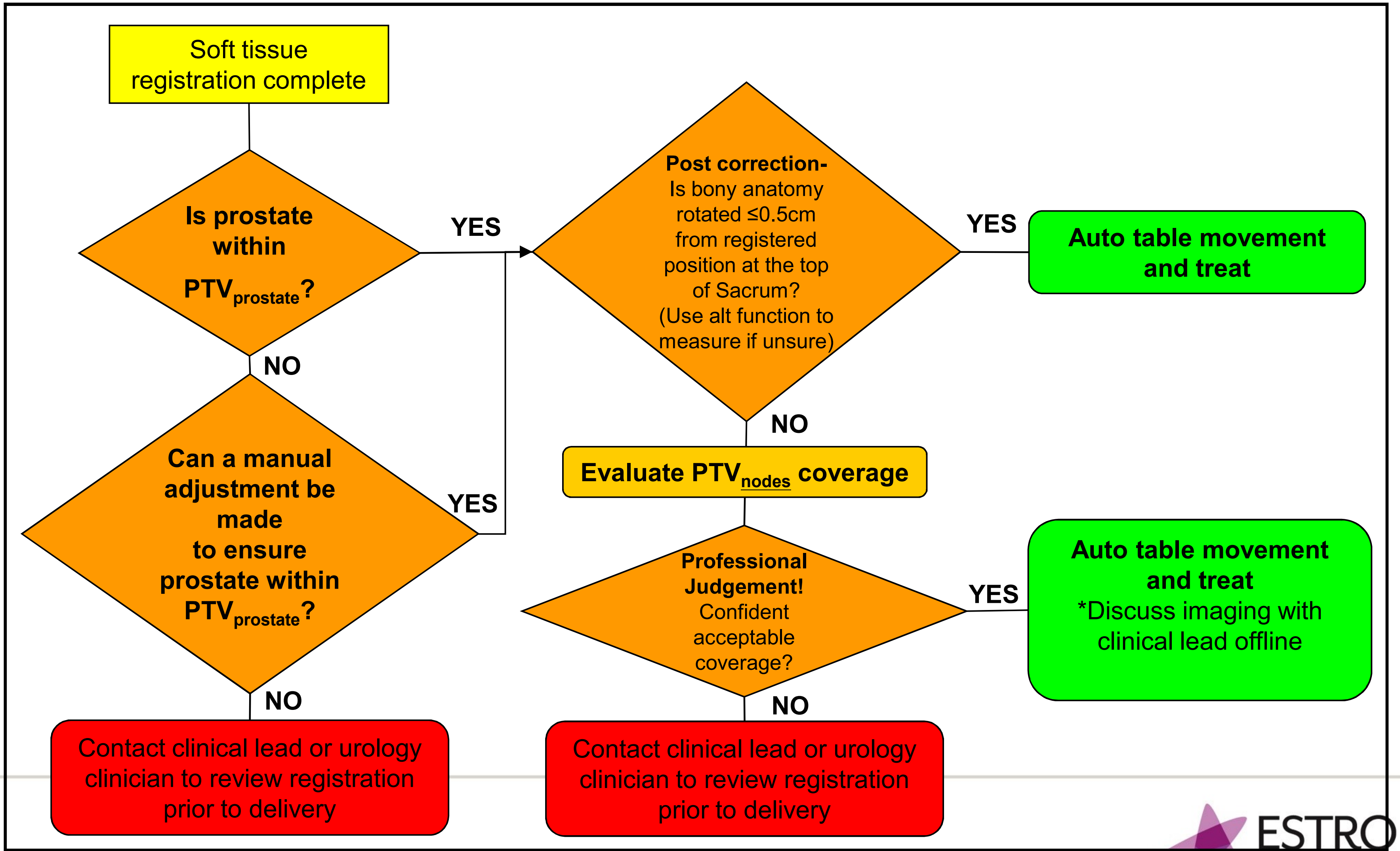
Online decision making for CBCT verification
Prostate and nodes

NB All operators must have completed competency assessment (S-WB-019) to carry out prostate soft tissue matching. It may be necessary for the clinical lead or urology clinician to review imaging offline.



Courtesy of Steven Landeg, RMH

Offline decision making for CBCT verification
Prostate and nodes

NB All operators must have completed competency assessment (S-WB-019) to carry out prostate soft tissue matching. It may be necessary for clinical lead or urology clinician to review imaging offline.

Review rectum and bladder status

Is rectum ≥50% different from planning scan?

- **YES** → Discuss with patient and check correct used of rectal preparation (as per J-CH-059). Record rectal status on S-RT-083-02.
- **NO** → Record ‘**Rectal status ‘good**’ on log S-RT-083-02

Is bladder over or under-filled?

- **YES** → **Under-filled:** Encourage hydration.

  Over-filled: Discuss bladder preparation (J-CH-053-02) with patient. If consistently over-filled discuss with clinical team.

  Record **‘under** *or* **over-filled bladder’** on XVI log S-RT-083-02.
- **NO** → Record ‘**Bladder status good**’ on XVI log S-RT-083-02

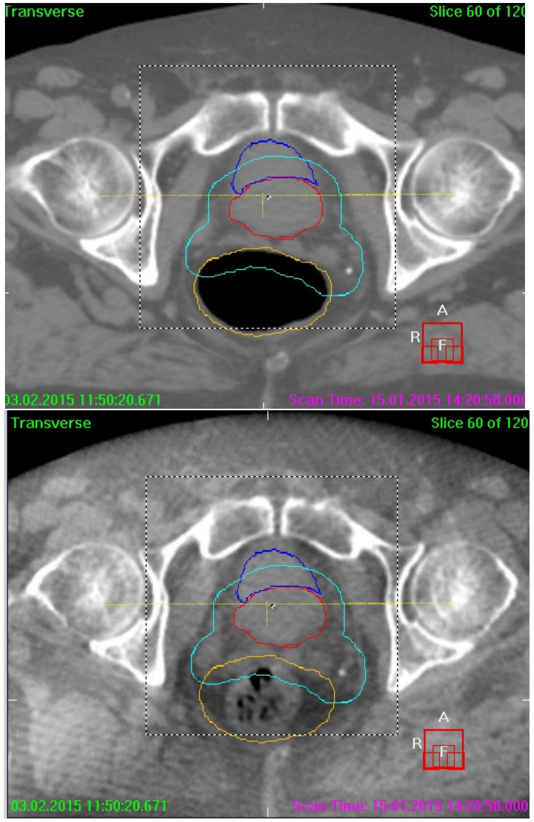


Figure 1: Planning scan (top) showing large gas filled rectum. CBCT (bottom) showing smaller, stool filled rectum on treatment (~50% smaller).

Courtesy of Steven Landeg, RMH

Summary

	Advantages	Disadvantages
Markers and MV	Image while treating	May not be visible No information regarding soft tissue anatomy
Markers and KV	Quick Objective	No information regarding soft tissue anatomy Not representative of deformation
3D (markers)	Soft tissue anatomical information Objective	Increase time Artefacts
3D (no markers)	Soft tissue anatomical information	Increase time Inter observer error

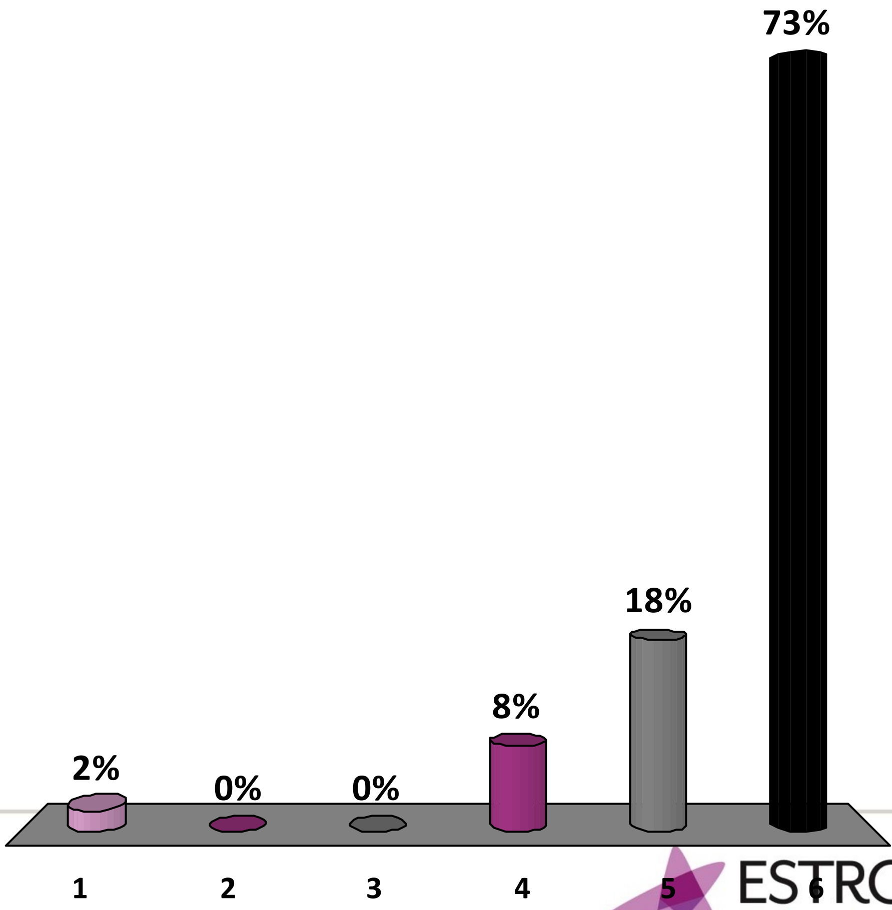
Summary

Know limitations

Work within limitations

Which method would you prefer to use?

1. MV imaging
2. MV imaging and markers
3. KV planar imaging
4. KV planar imaging and markers
5. 3D soft tissue imaging
6. 3D soft tissue imaging and markers



Acknowledgements

Angela Baker -

Sophie Alexander

Steven Landeg

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WWW.ESTRO.ORG/SCHOOL

Non radiographic IGRT techniques for in-room target localisation

Uwe Oelfke

ICR/ RMH London
Joint Department of Physics
uwe.oelfke@icr.ac.uk

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Outline

- Non-radiographic solutions
  - Surface based (optical scanners)
  - Ultrasound
  - RF transponders
  - In-room MRI

Reducing margins: immobilization?

- Immobilization devices:
  - Help maintain a reproducible position during treatment
  - Might be used as external reference system for positioning

- Immobilization devices ≠ target localization
  - Useless for motion management
  - Patient comfort might be more efficient in practice

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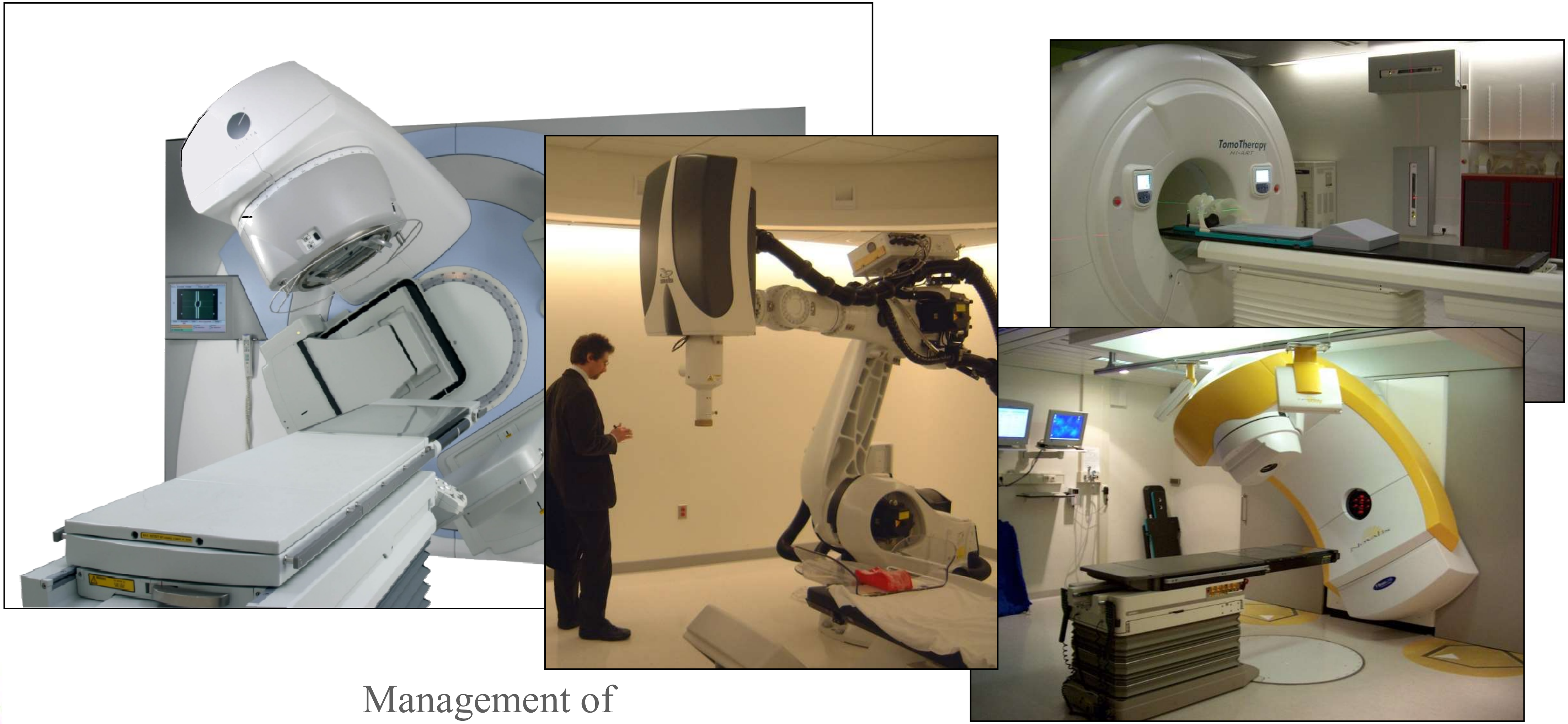
… image-guidance (IGRT)



Management of

- Inter-fraction geometric uncertainties
- Intra-fraction geometric uncertainties

Real-time tracking - CyberKnife

Internal/external marker correlation

Model building

Courtesy of Accuray, Inc.

Models:

Linear

Elliptical

Polynomial

Model updated by use of online kV images

IGRT and Imaging dose…

	Dose / acquisition	Patient dose for a 78Gy treatment (2Gy fractions)
MV Electronic Portal Imaging Device	**~ 30 mSv** (3 MU, isocenter dose)*	2340 mSv
MV cone beam CT	**~ 20-90 mSv** (0.005 MU/°, isocenter dose)***	1950 mSv
Stereoscopic kV-imaging	**~ 0.51 mSv** (surface dose)*	40 mSv (400 mSv, gating)
kV cone beam CT	**~ 50 mSv** (surface dose)**	1950 mSv
MV CT (TomoTherapy)	**~ 20 mSv** (isocenter dose)*	780 mSv

* Dose measurements at UZ Brussel

** D. Jaffray 2006

*** J. Pouliot 2006

Patient dose due to IGRT

- Difficult to synthesize a complete picture of the patient's exposure:

  - Imaging modalities range from **planar portal images** to fluoroscopy to **CT-based solutions**.
  - Procedures can be as simple as acquiring **single set-up images** or as complex as assessment of **intra-fraction target tracking**.
  - Patient dose can be concentrated on the **skin** (planar kV x-ray imaging) or distributes throughout the anatomical **volume** of interest (CT-based)
  - High **image quality** versus **necessary information** has an impact on settings and dose

Patient dose due to IGRT

- Should be managed case-by-case:
  - ➢ IGRT SRS for a 15 year old patient with AVM

    $\neq$

  - ➢ IGRT for a 70 year old patient with prostate ca
- The management of imaging dose during image-guided radiotherapy: Report of the AAPM Task Group 75 (Med Phys 2007; 34(10): 4041-4063

Non-radiografic IGRT

- Monitoring the patient surface
- Ultrasound
- RF-frequency
- MRI-in the treatment room

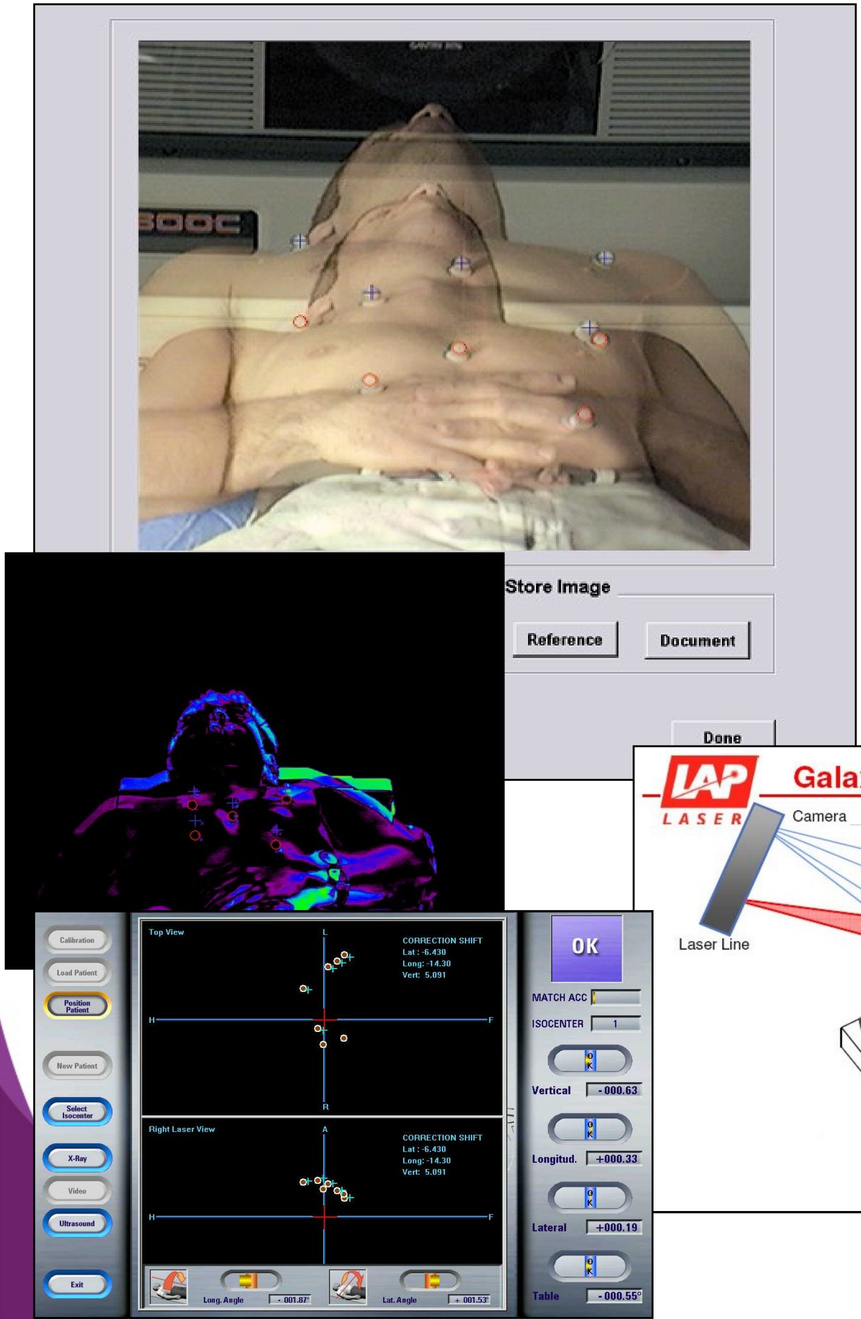
Objectives:

Automatic accurate target postioning

Real time monitoring of target movements

NO extra dose

Patient surfaces..detection, monitoring

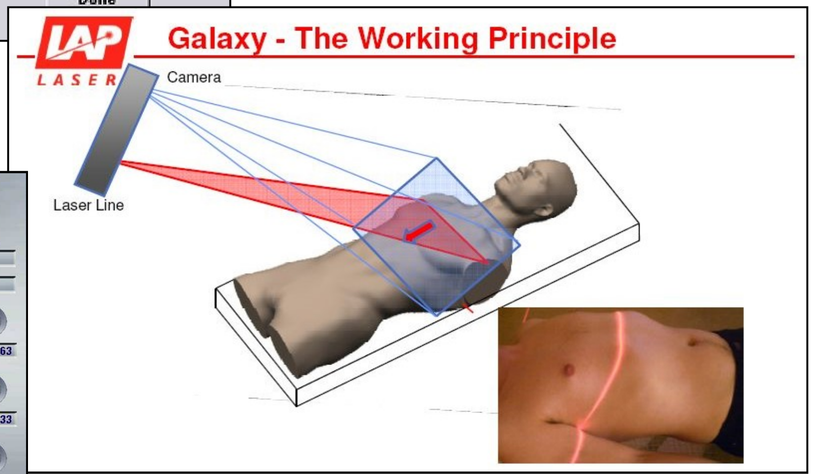


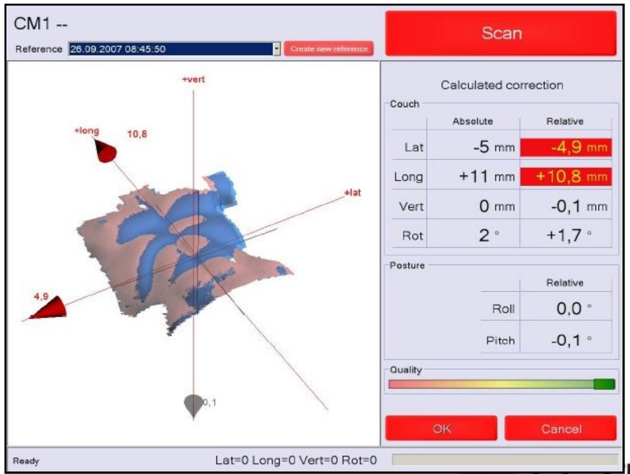
Optically-guided or video-based systems

Image-based and have potential to fully automate the positioning process

High precision positioning of the skin NOT internal structures

Increases efficiency but NOT efficacy





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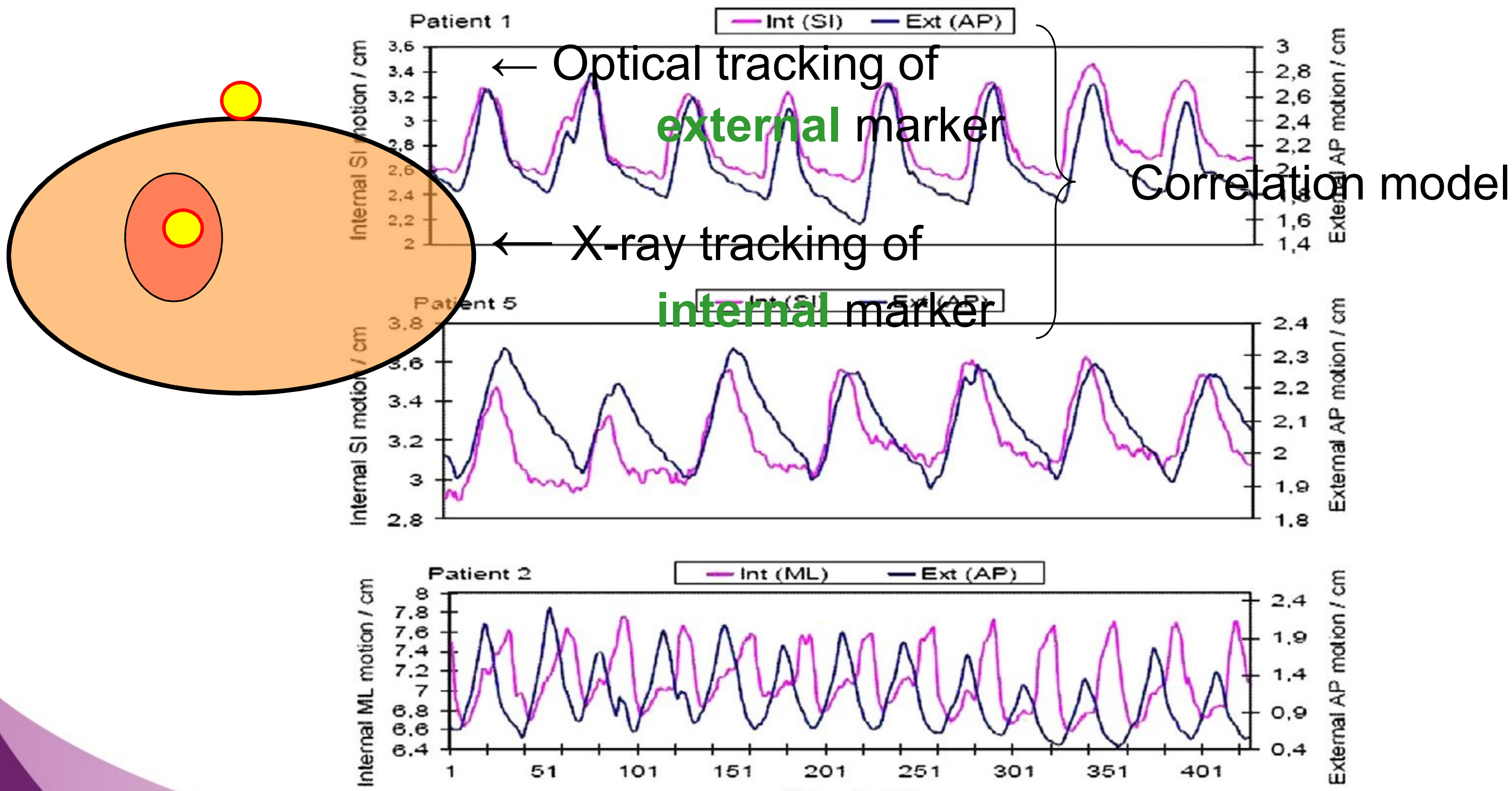
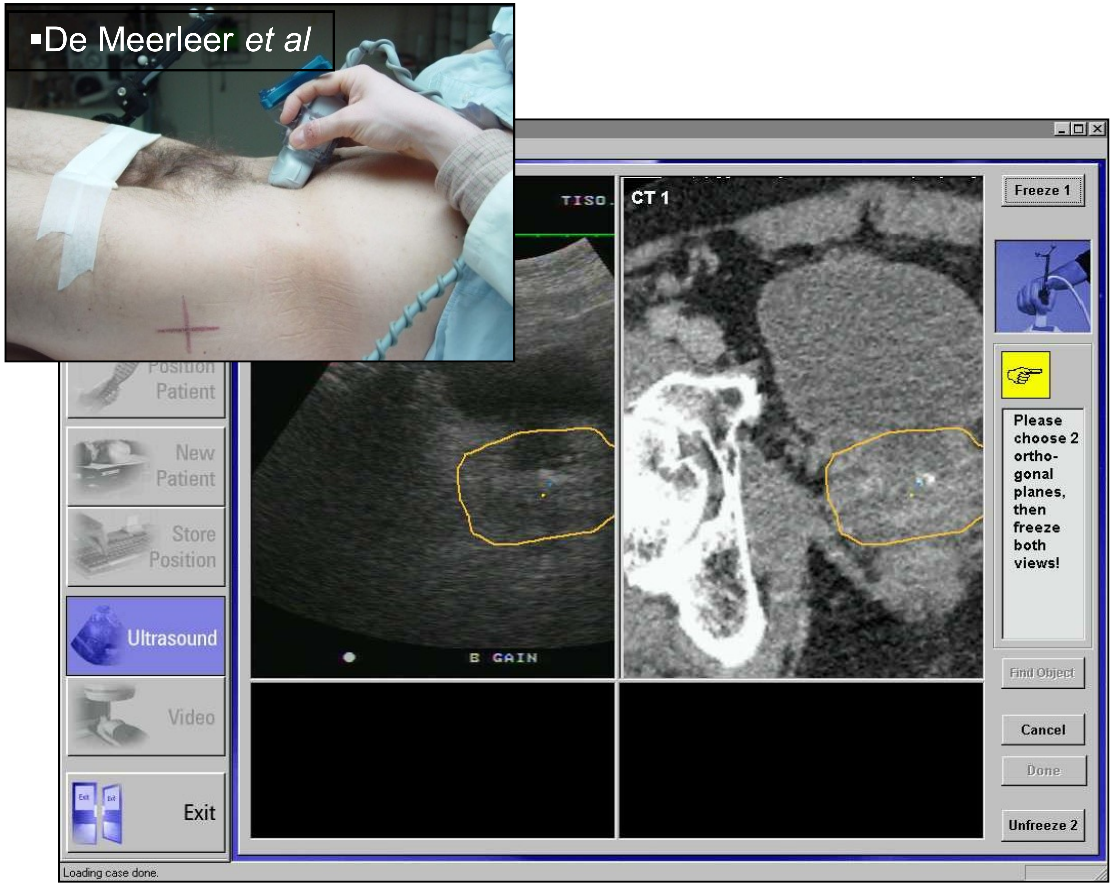
Limitations of surrogate technology



Korreman (2008)

Ultrasound



No surrogate required (soft tissue visualization)

Marker vs US:

– Remaining random error same magnitude as with initial set-up

– CT-contour ≠ US-structure

– Important inter-user variability

Van den Heuvel *et al*, Med.Phys. 2003; 30

Langen *et al*, IJROBP 2003; 57

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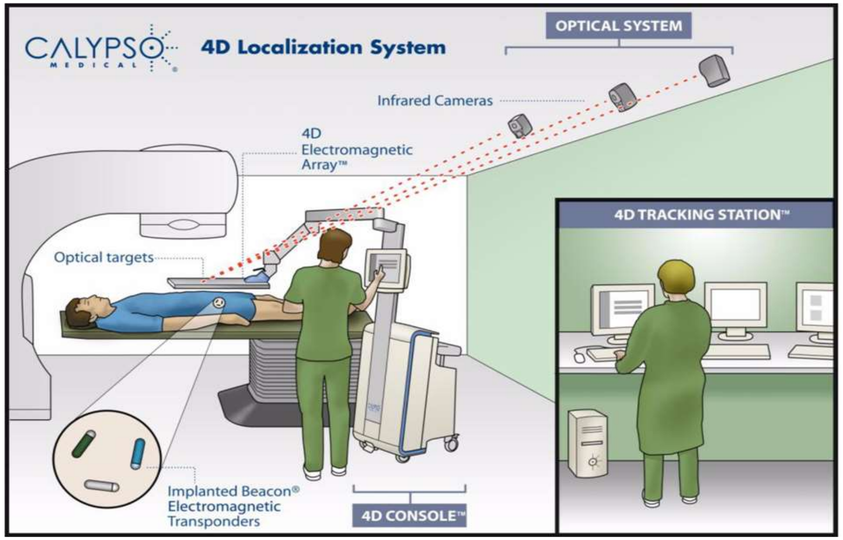
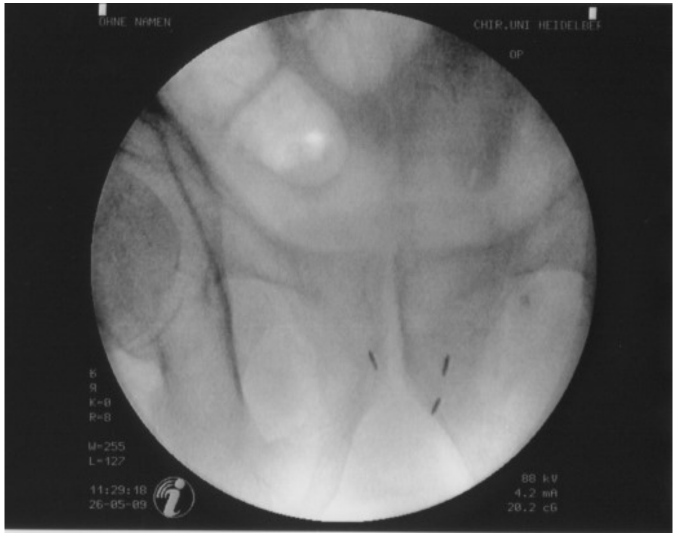
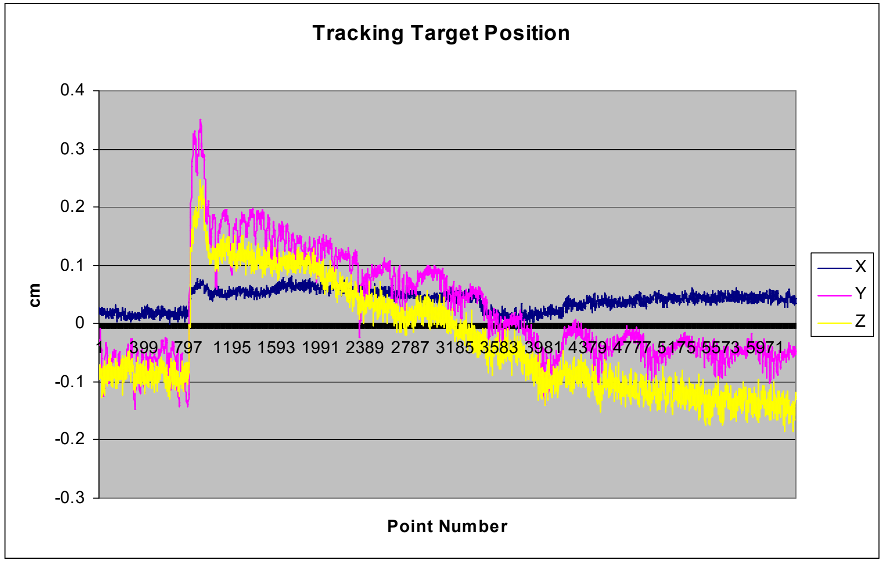
Internal Surrogat: Calypso System

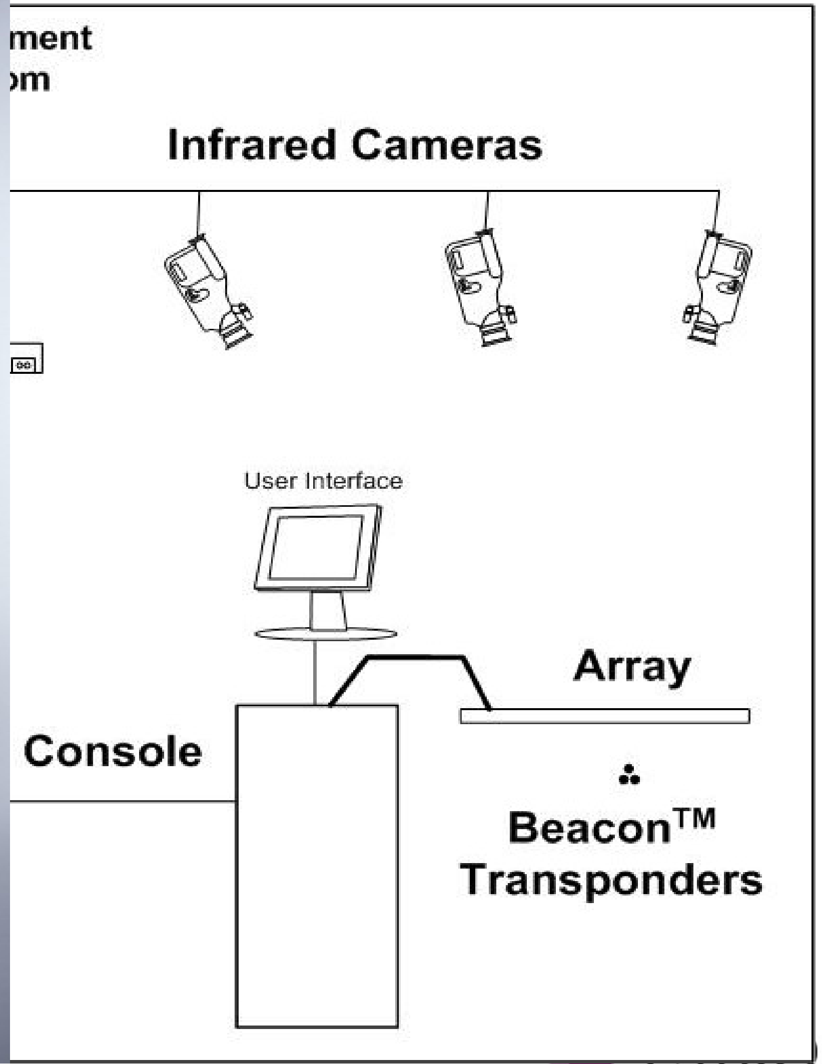




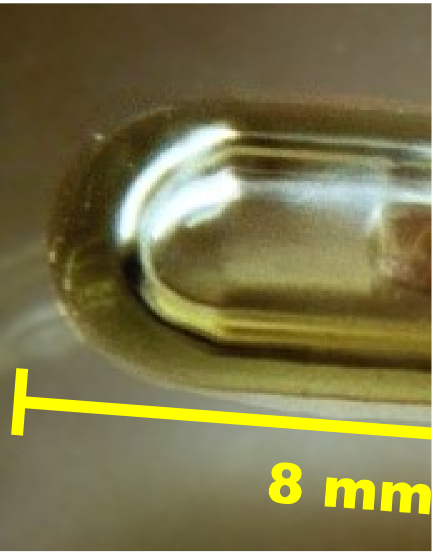


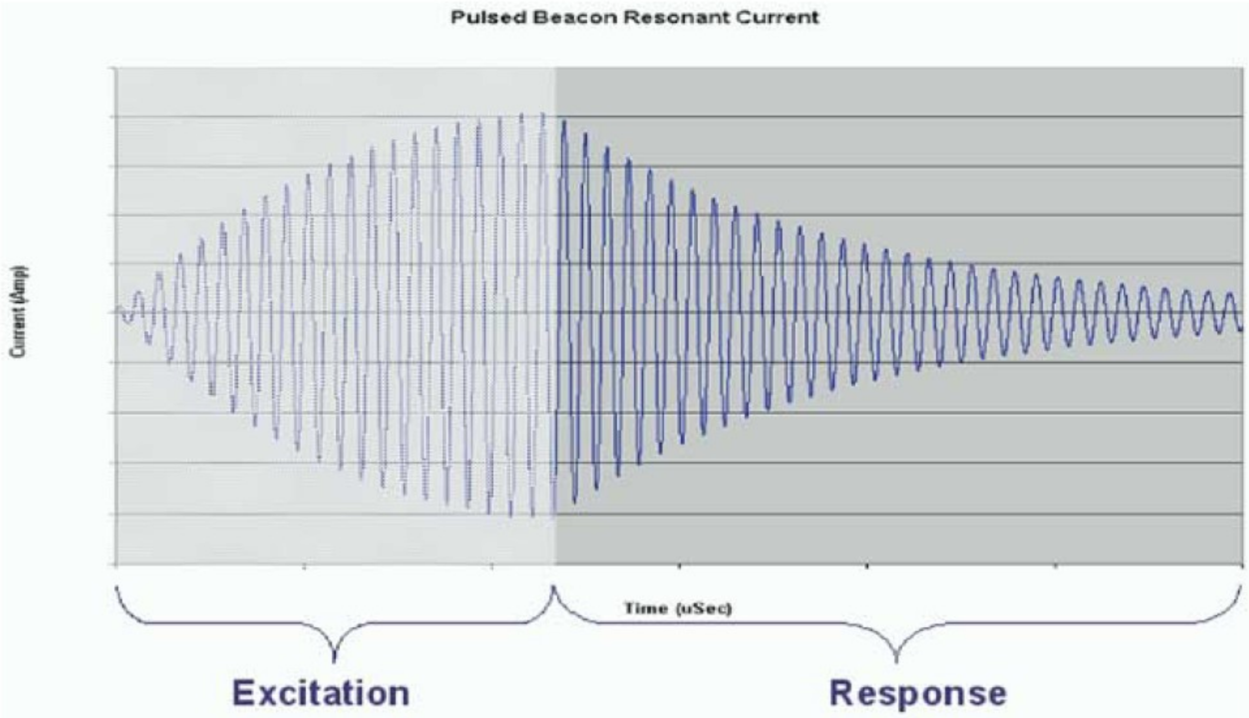
RF Transponder – Calypso system

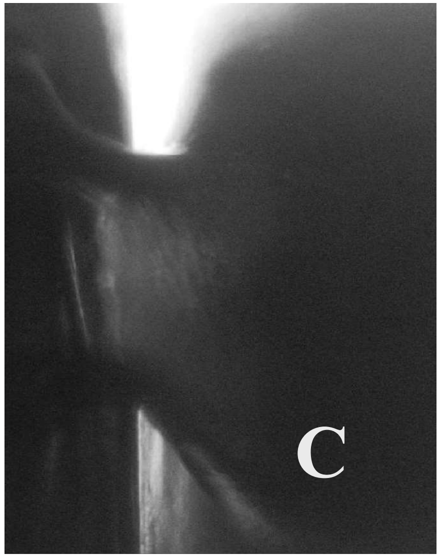
1. **Beacon transponders**
2. **Magnetic array**
3. **Console**
4. **Infrared su**
5. **Tracking st**



Beacon transponder





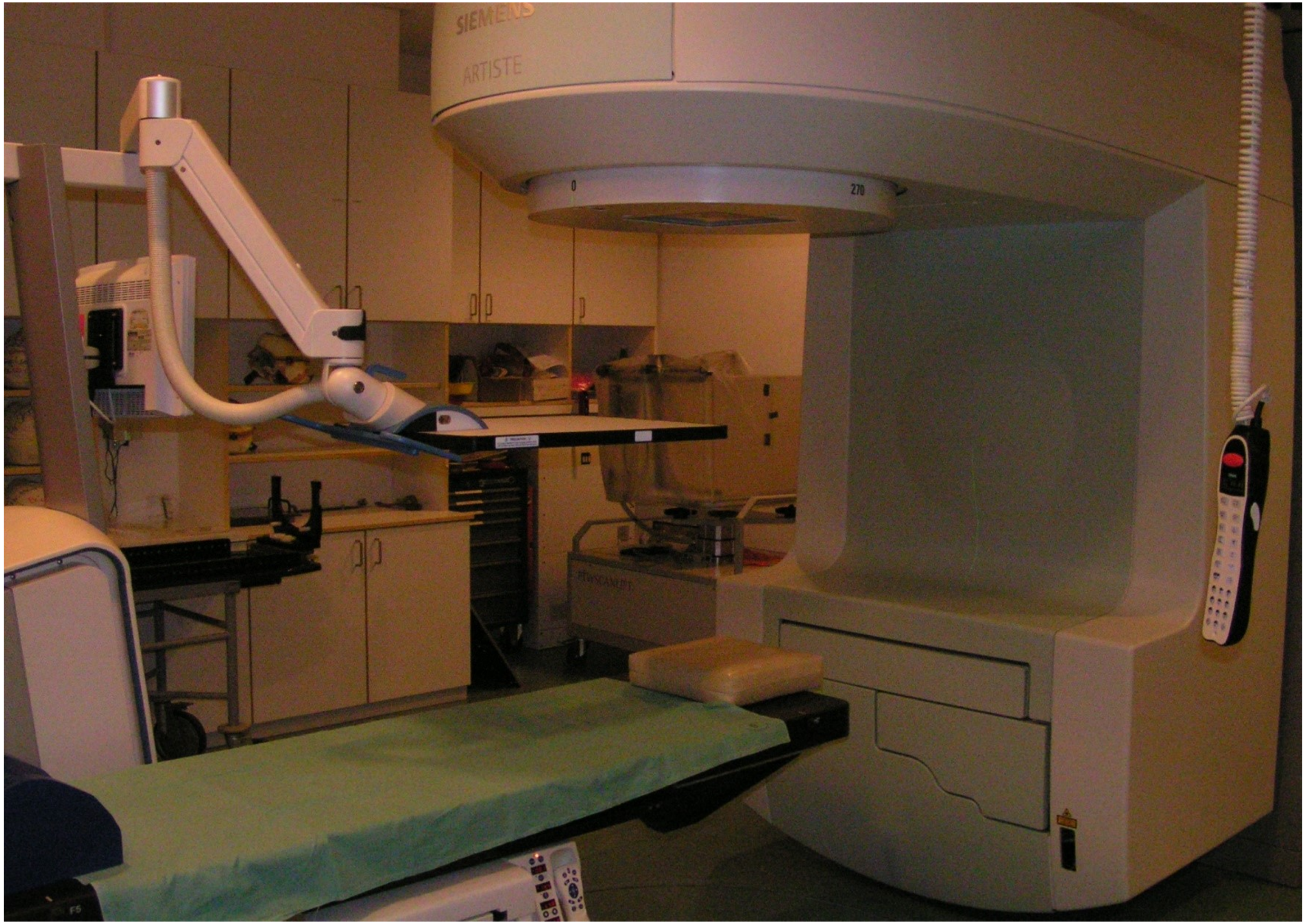


Mit Hilfe von Dr. Anne Nies

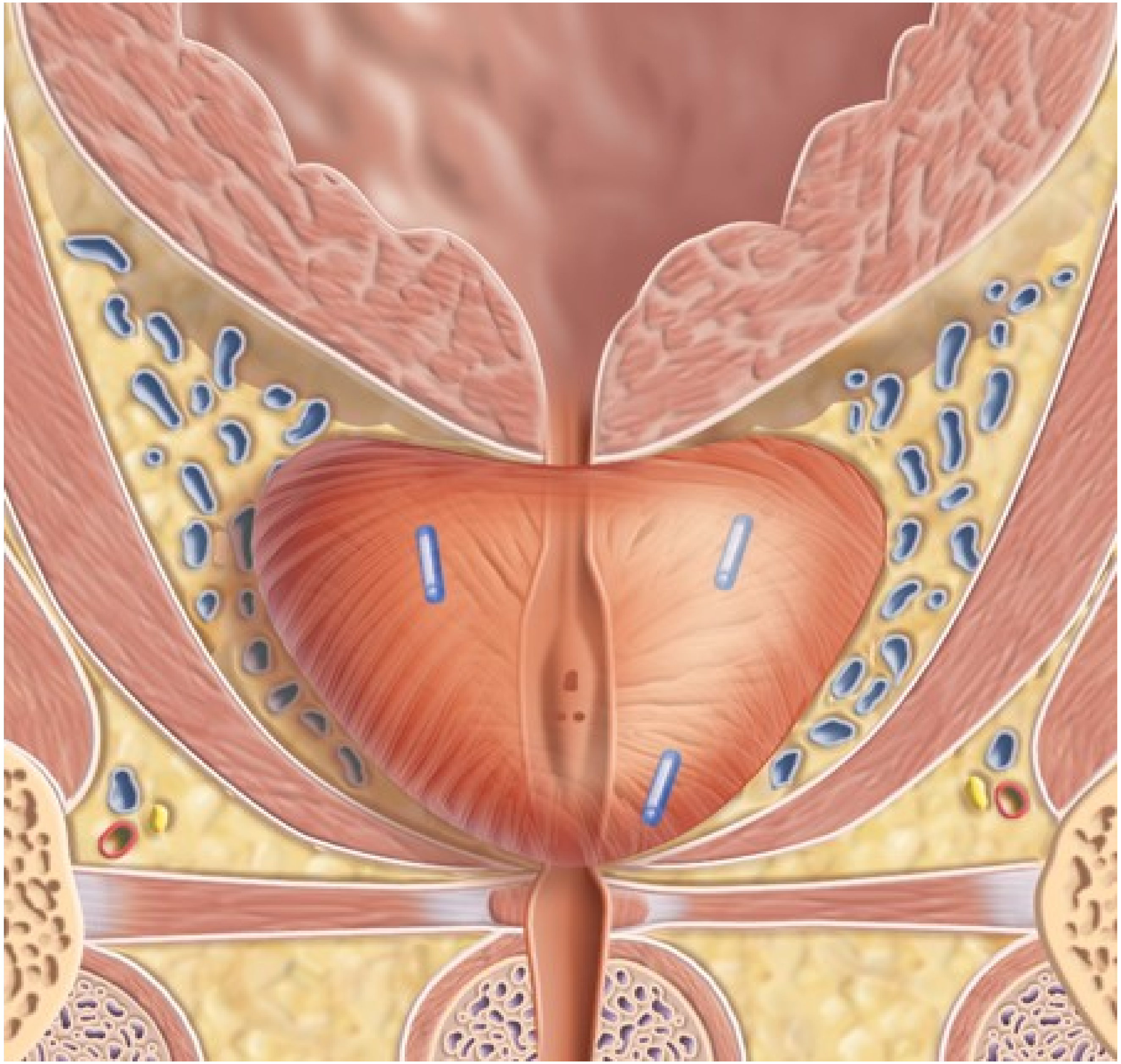
LC(R) resonant circuit: energized via inductive coupling

Tunable parameters: resonant frequency, quality factor (inv. damping)

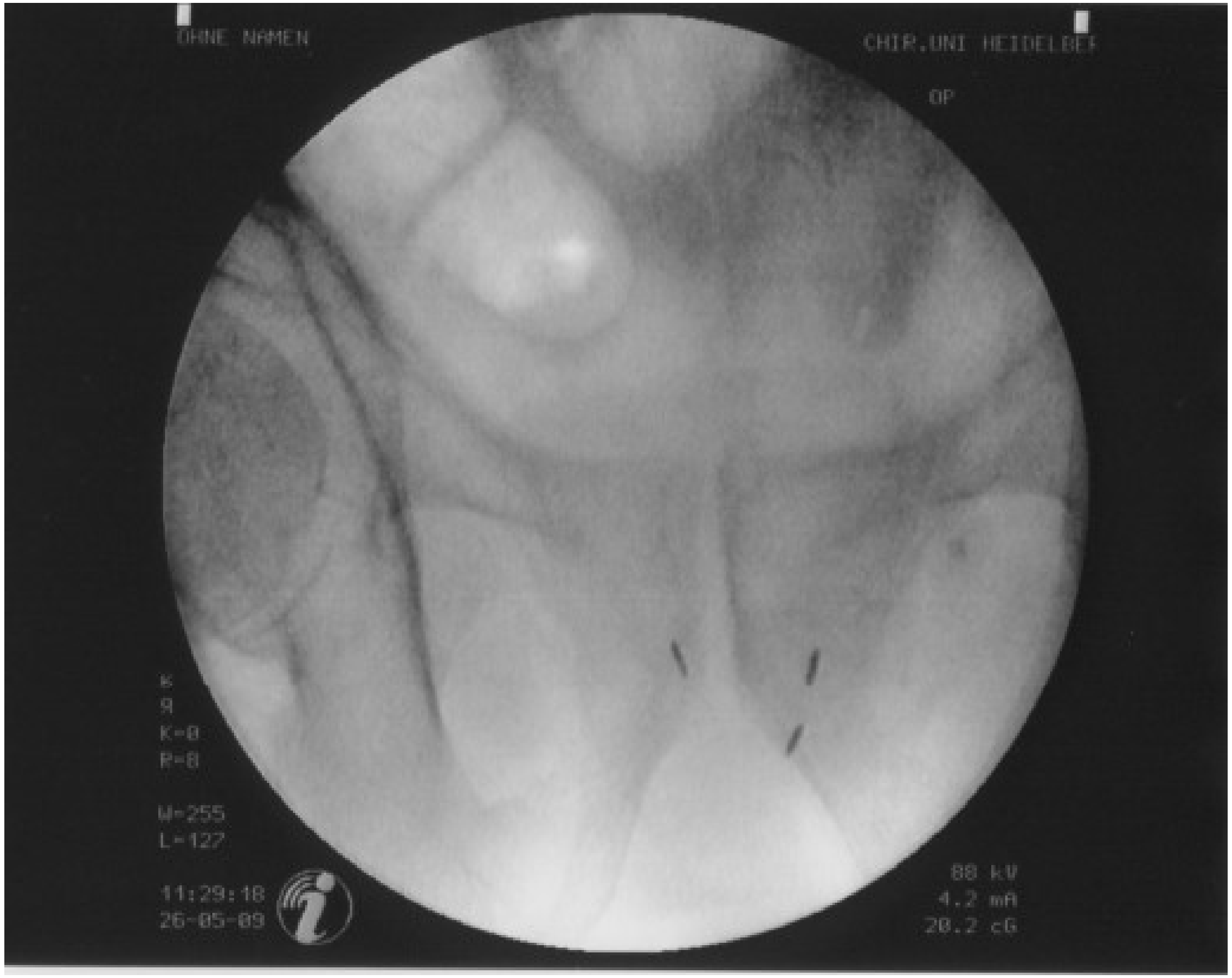
$$L = N^2 \frac{\mu_0 \mu_r A}{l} \qquad f_0 = \frac{1}{2\pi\sqrt{LC}} \qquad Q\ factor = \frac{1}{R}\sqrt{\frac{L}{C}}$$


SIEMENS
ARTISTE
0
270

Intrafractional motion: prostate



Clinical application of Calypso at DKFZ & Univ. Clinic HD



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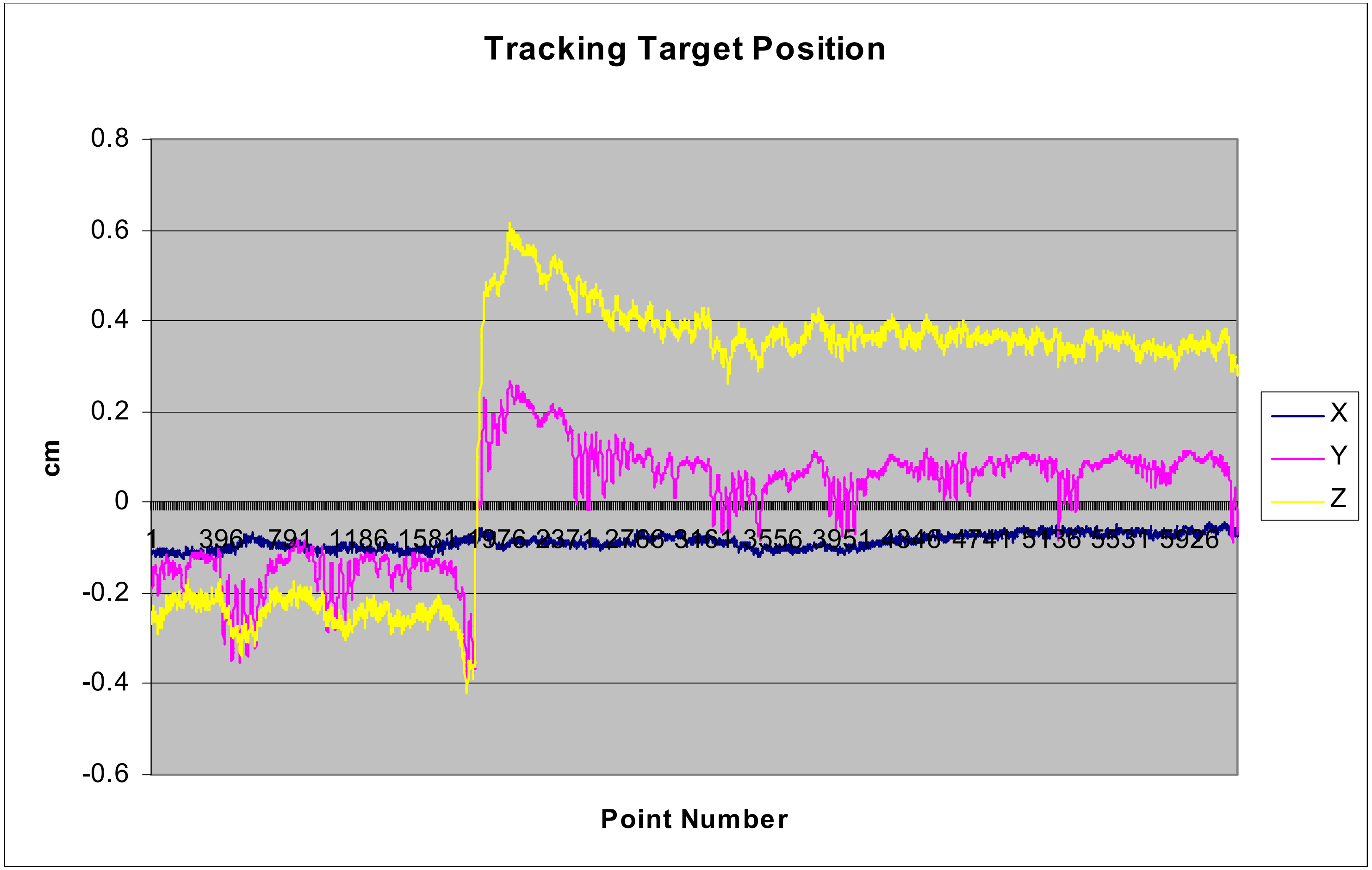
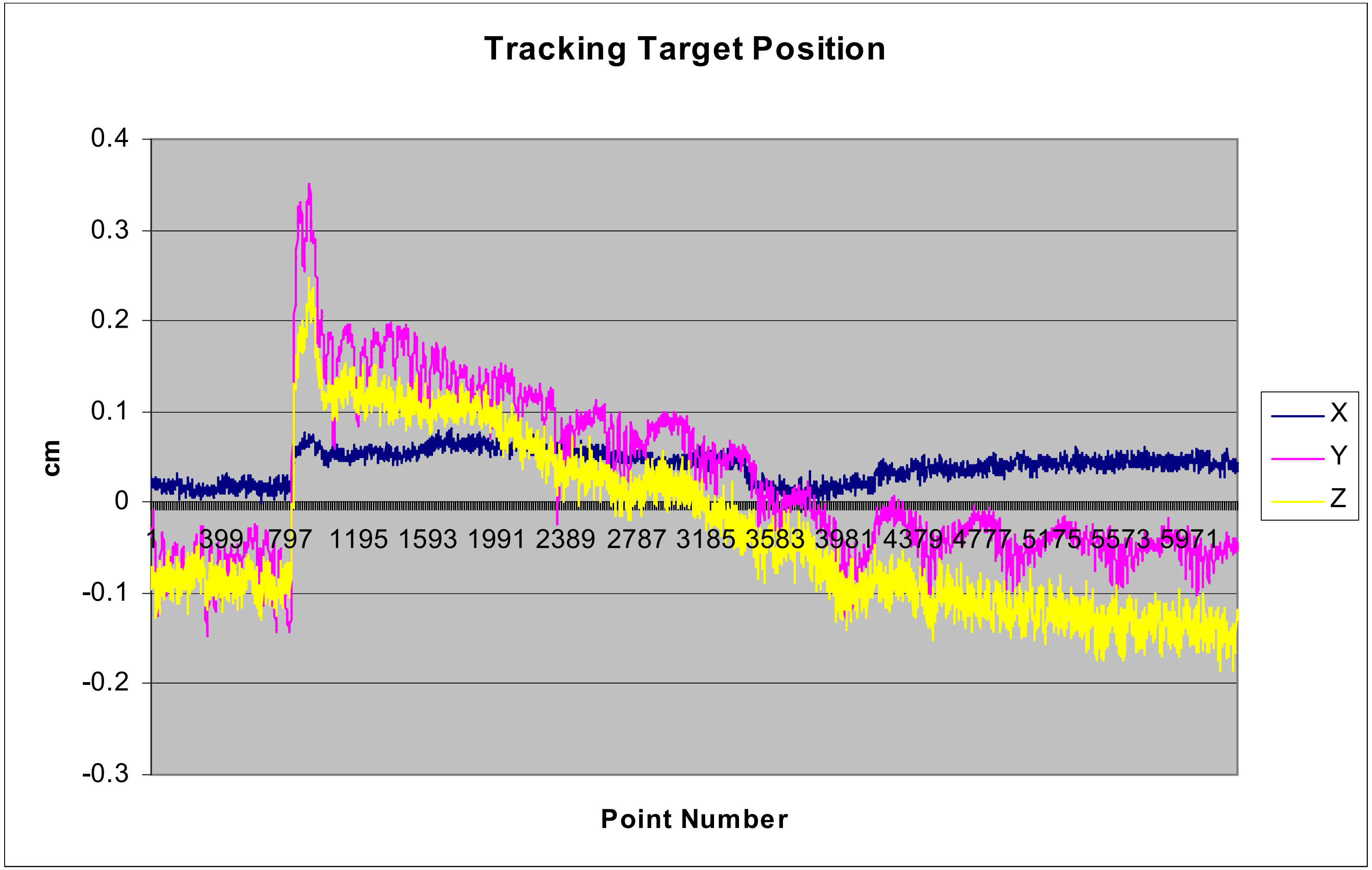
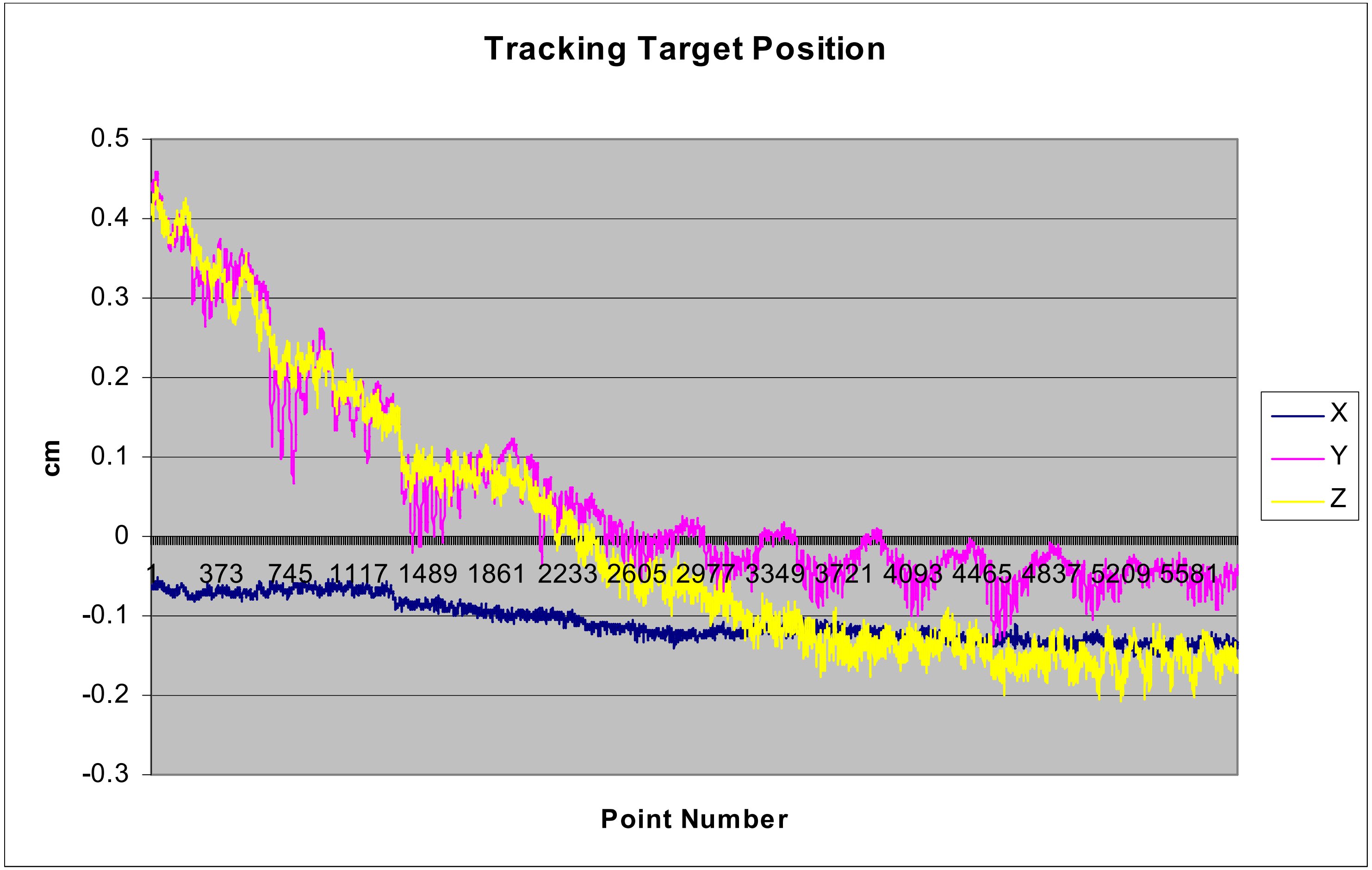
Unpredictable intrafraction organ motion: prostate



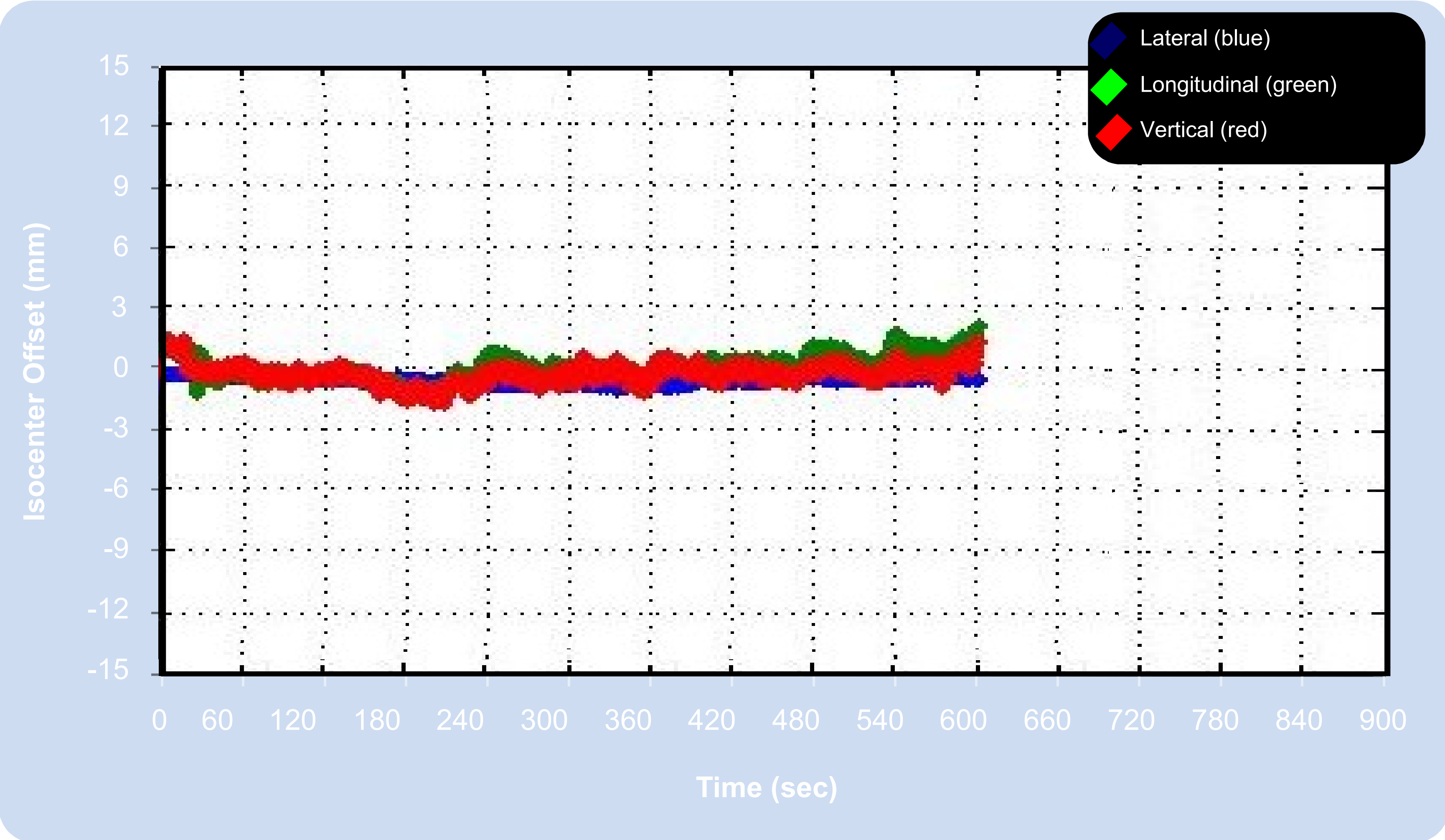


Tracking Target Position
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
cm
1
399
797
1195
1593
1991
2389
2787
3185
3583
3981
4379
4777
5175
5573
5971
Point Number
X
Y
Z

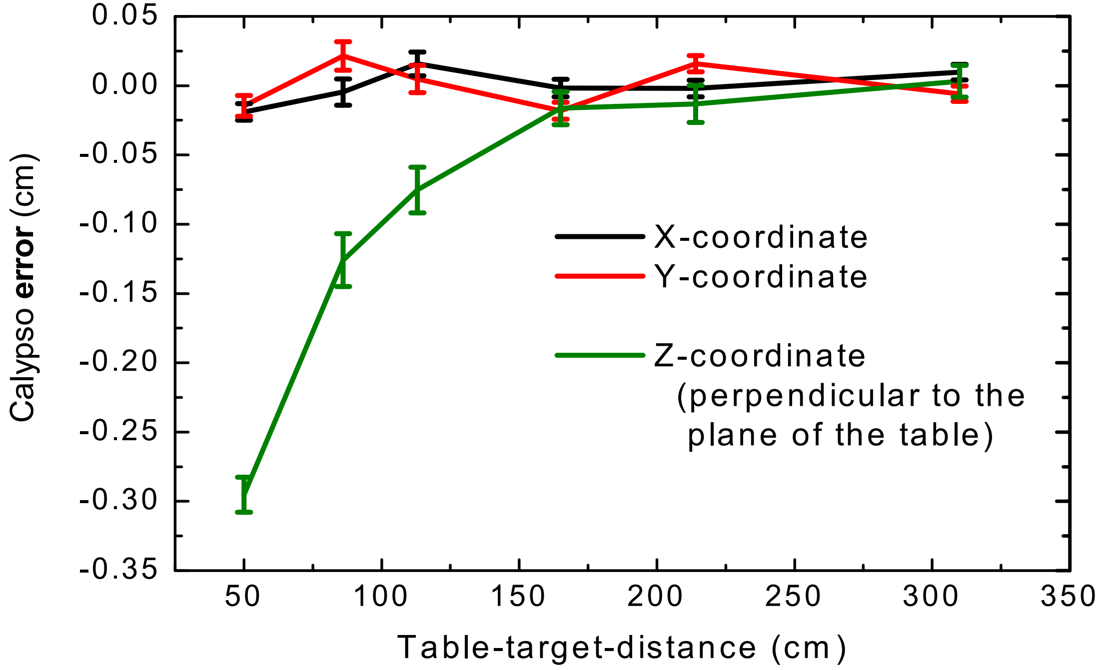


Tracking Target Position
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
cm
1 373 745 1117 1489 1861 2233 2605 2977 3349 3721 4093 4465 4837 5209 5581
Point Number
X
Y
Z

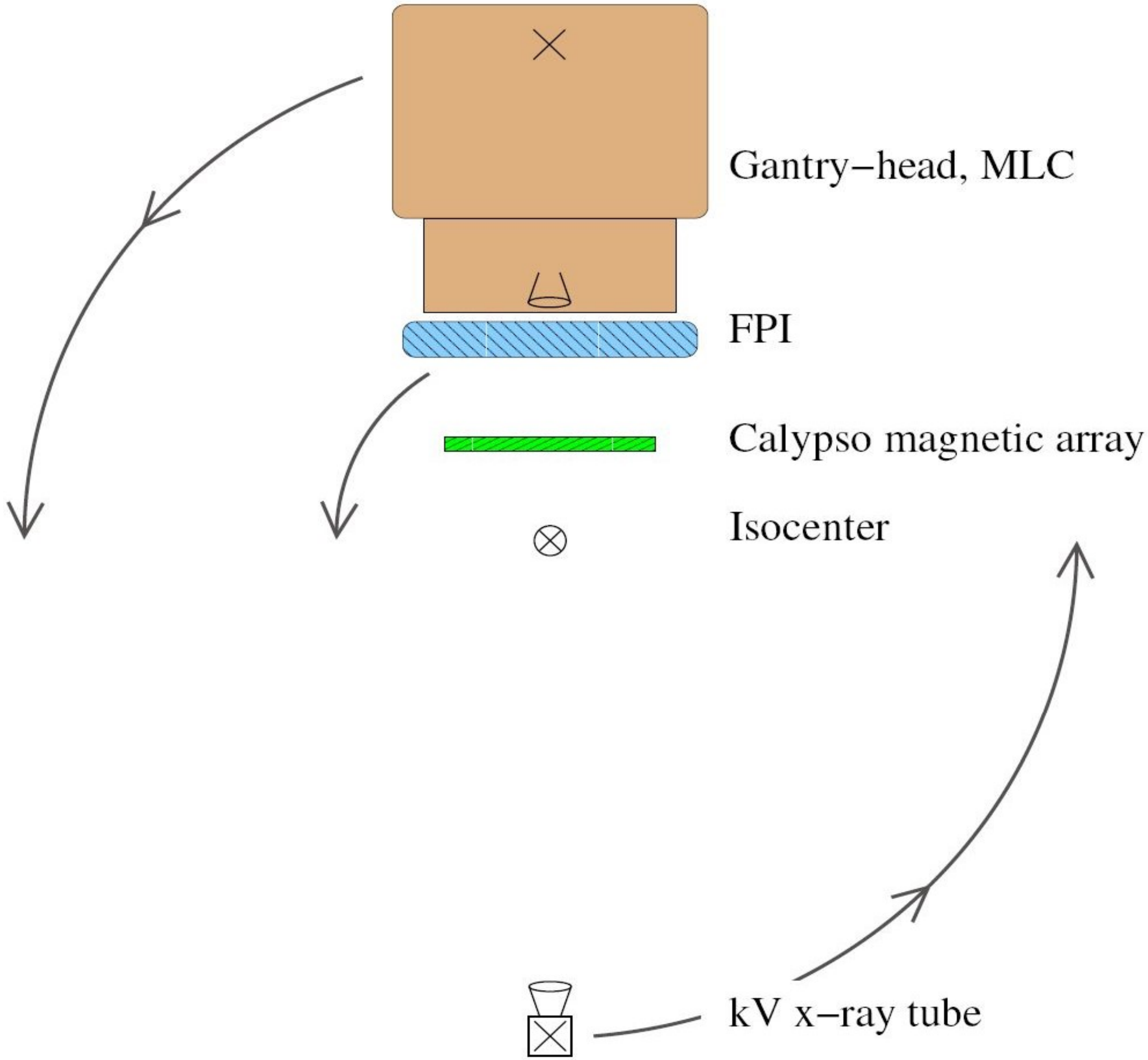
Same Patient, 39 Fractions



Compatibility testing: TD-D carbon table top



Linac compatibility



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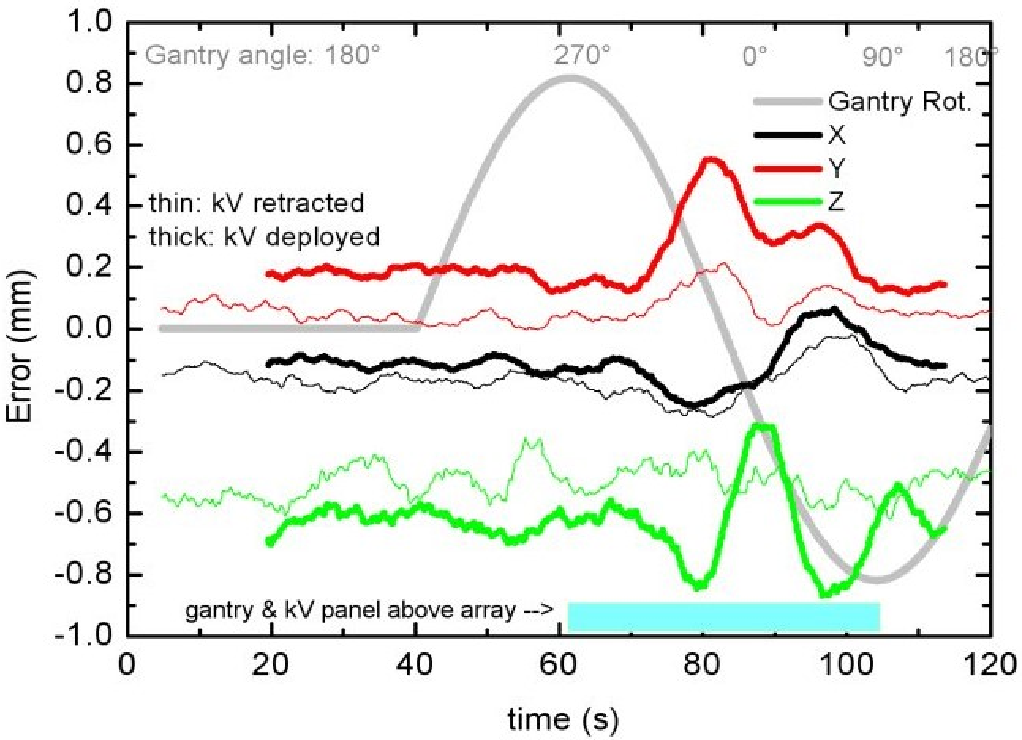
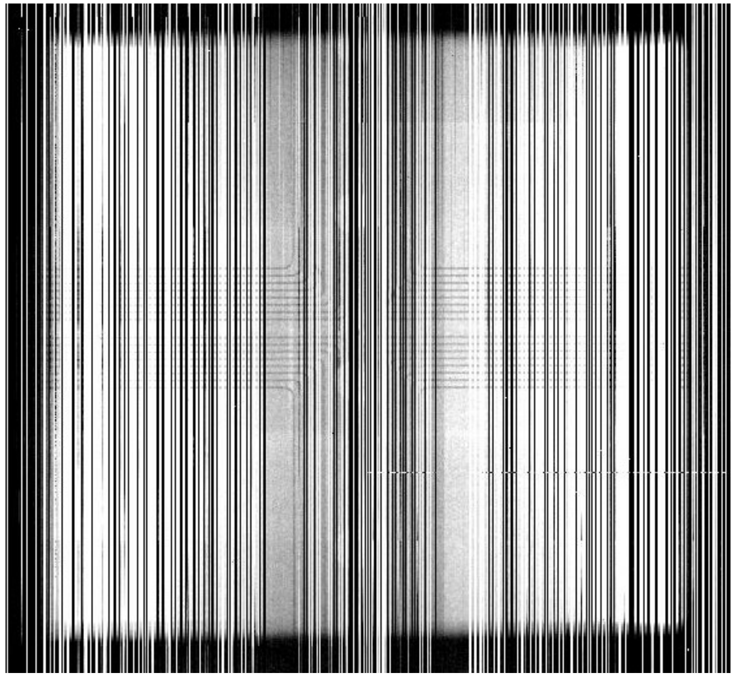
System interference



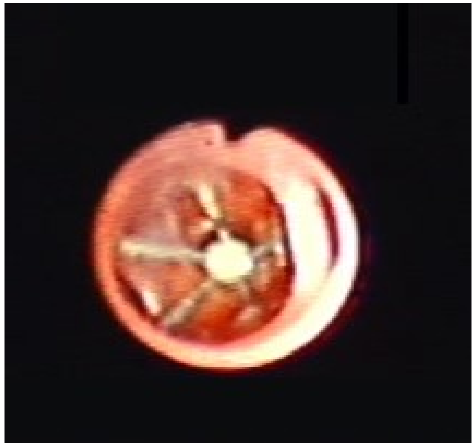
Imaging panel interferes with Calypso system



Calypso system interferes with imaging panel

The Anchored Beacon Transponder

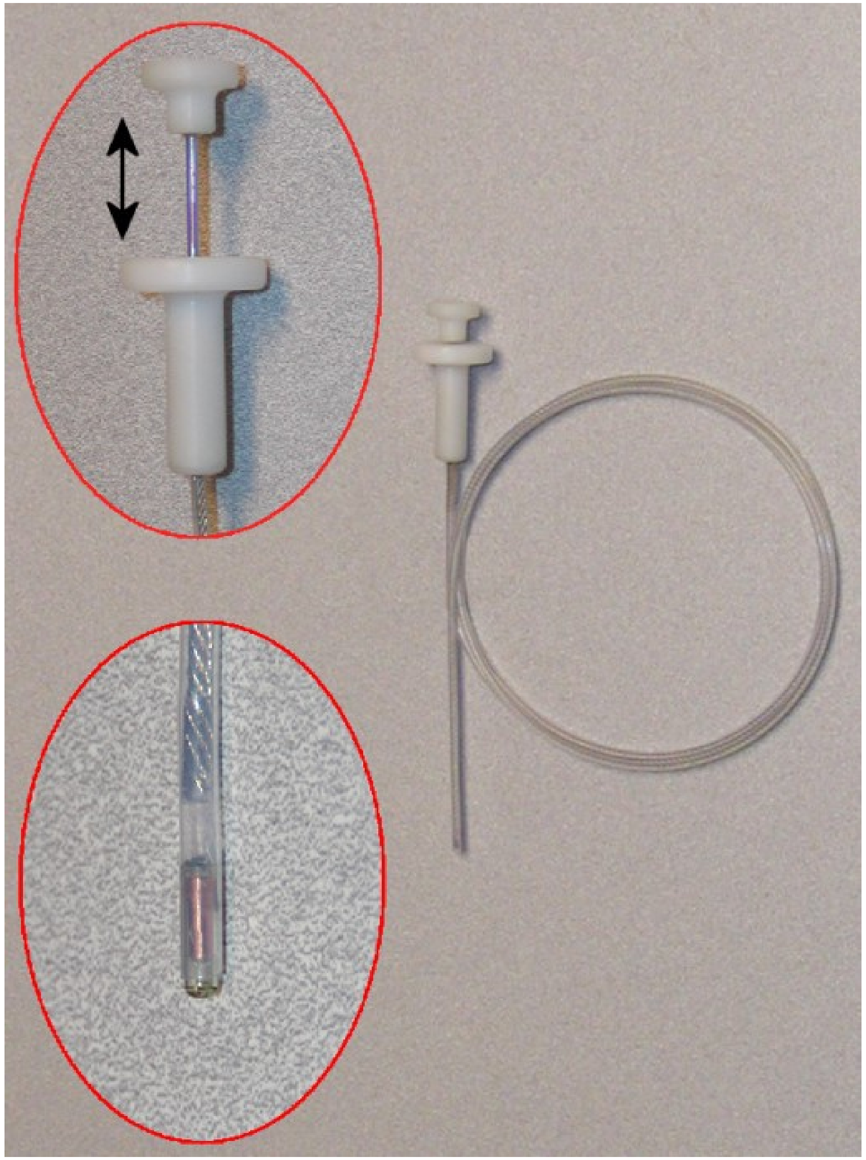
- Implanted in airways within or near the tumor
- Aimed at airways with diameter of approximately 2.5 mm or smaller
- Designed for bronchoscopic implantation



The anchored Beacon transponder is work in progress.

Implantation Procedure

- Custom, dedicated, pre-loaded delivery catheter
- Fluoroscopic guidance
- Optional superDimension® guidance



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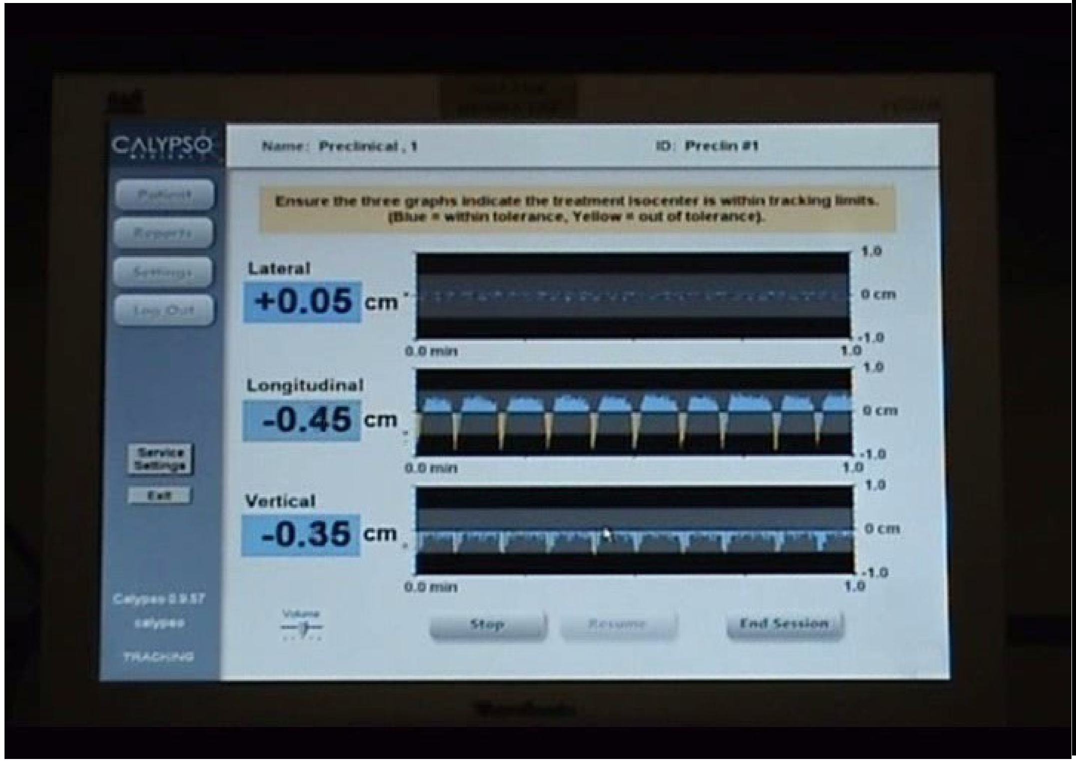
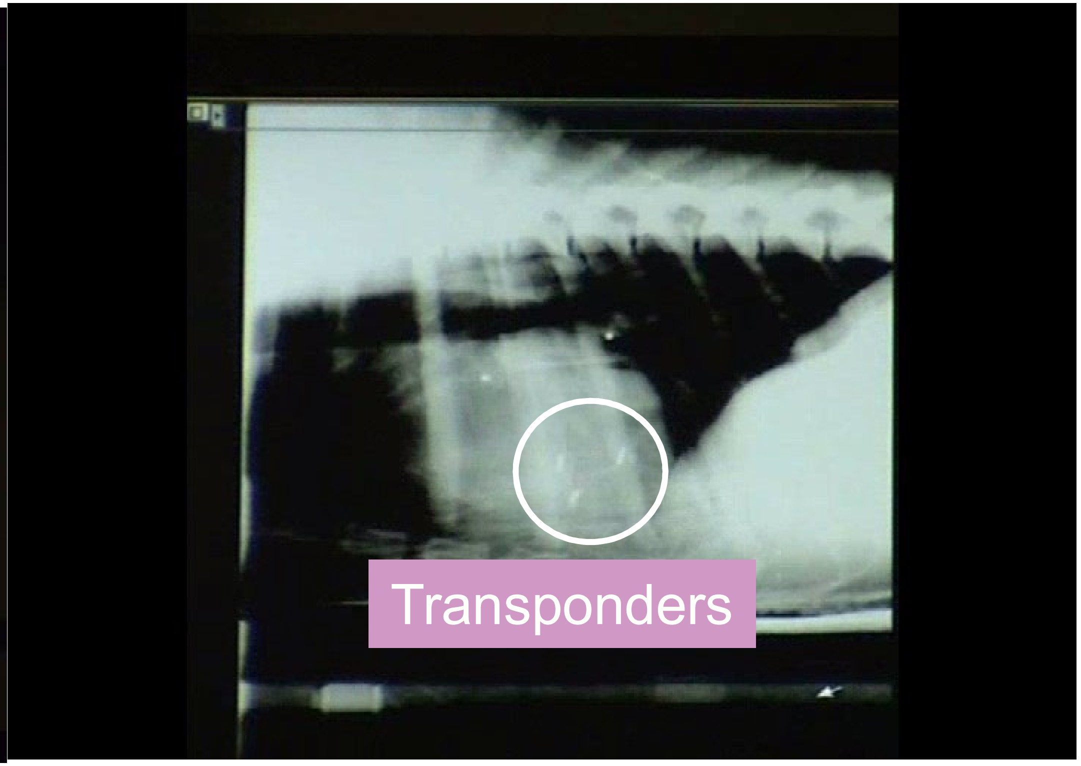
Preclinical In-vivo Lung Tracking

- Real-time, non-ionizing, objective lung tracking demonstration



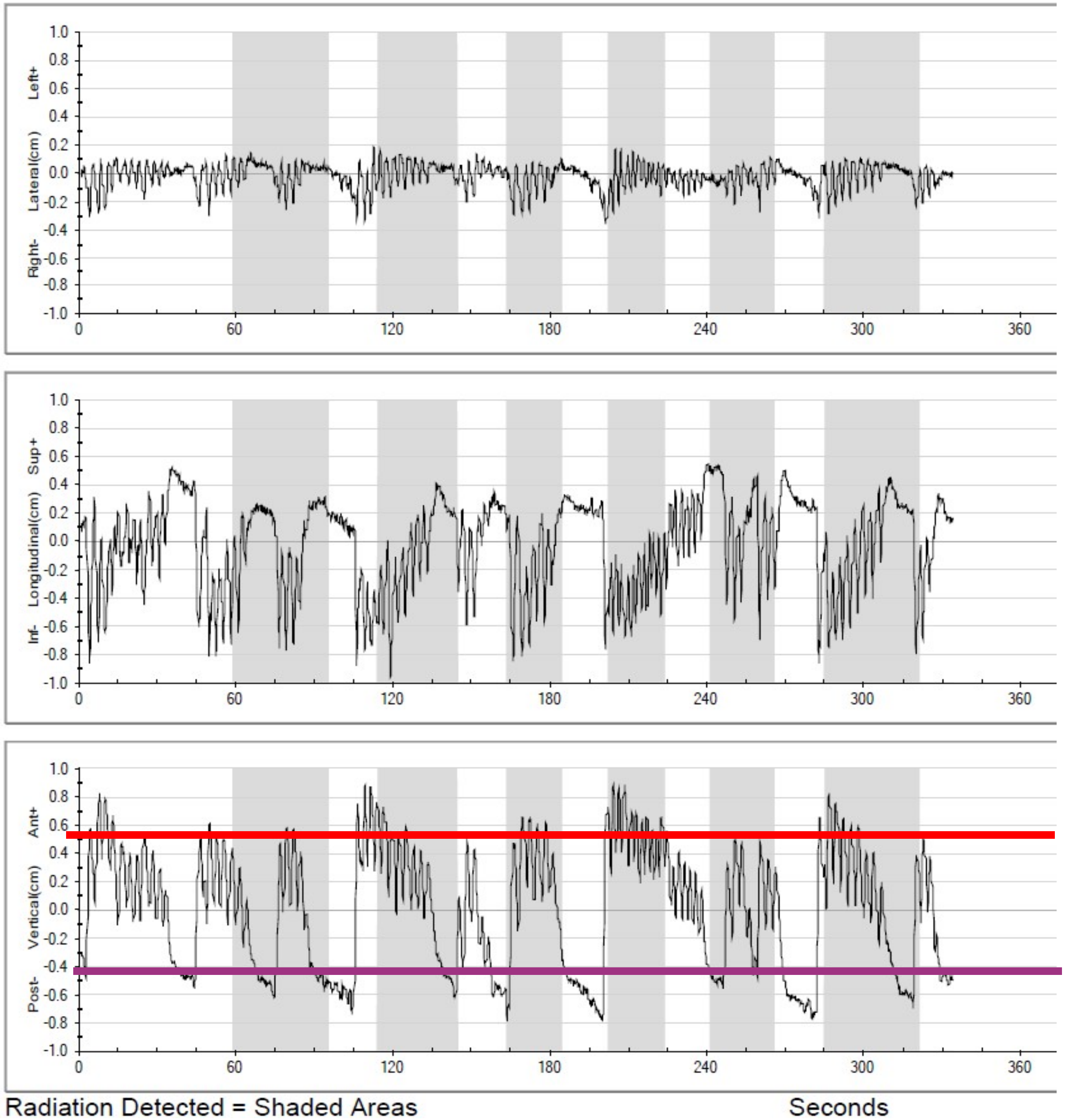
Calypso Tracking Station



Fluoroscopy View

Fraction 1

Baseline shift ?



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Summary

- RF localization using implanted transponders is feasible
- This system has shown the potential to provide rapid positioning based on transponder location
- Intra-treatment monitoring is possible, and early studies show the potential value for detecting large transient shifts, as well as slower trends in position variation

Courtesy of J. Balter

In-room MR Guidance

Patient in treatment position:

No imaging dose
MR enhanced soft tissue contrast

Real time imaging
Functional/biological imaging

4 Technical Approaches

MR on rails (IMRIS)

MR + rotating LINAC (Philips/Elekta, Utrecht))

Rotating MR/LINAC (Edmonton)

Cobalt sources/MR (ViewRay)
Linac/MR (ViewRay)

MR on rails

patient positioning

shielding of rooms

decoupling of MR and linac

no real time imaging at treatment

first installation PMH (2014)

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Challenge: Image Quality - MRI on rails

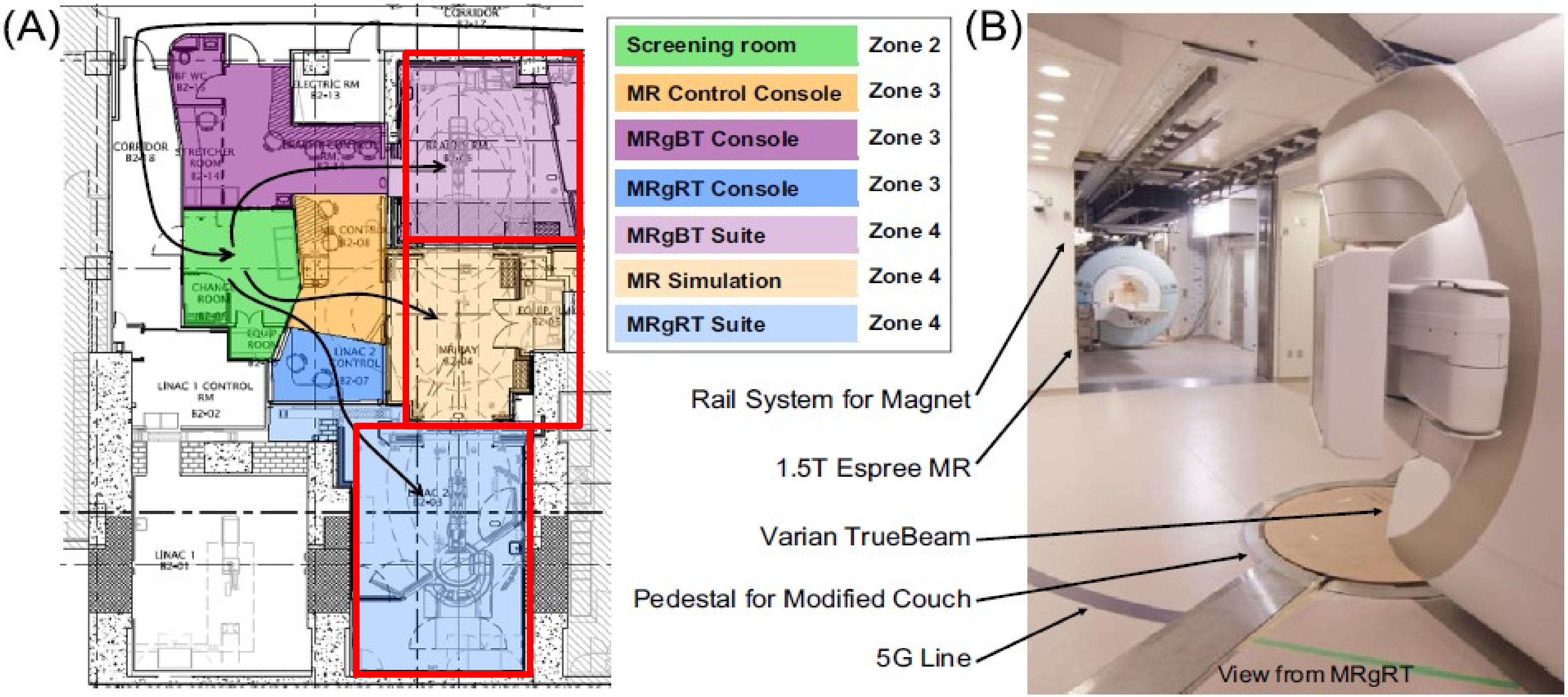
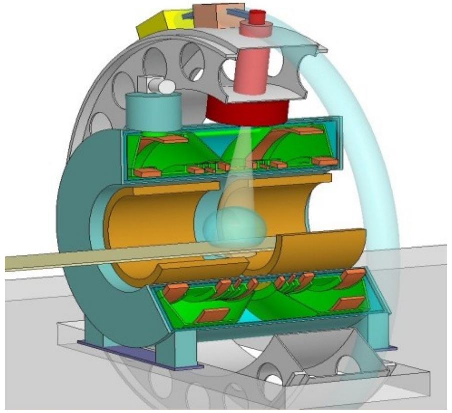


Figure (A) Floor plan and safety zones of the MR-guided RT facility at the Princess Margaret Cancer Centre showing brachytherapy, imaging, and external-beam RT suites. (B) Photograph of the accelerator and MR scanner in the facility. The magnet is advanced on the rail system into the MRgRT suite, and the patient is positioned via a modified treatment couch. At nearest approach, the magnet to linear accelerator isocenter distance is 3.1 m.

Jaffray et al. Seminars in Radiation Oncology
http://dx.doi.org/10.1016/j.semradonc.2014.02.012

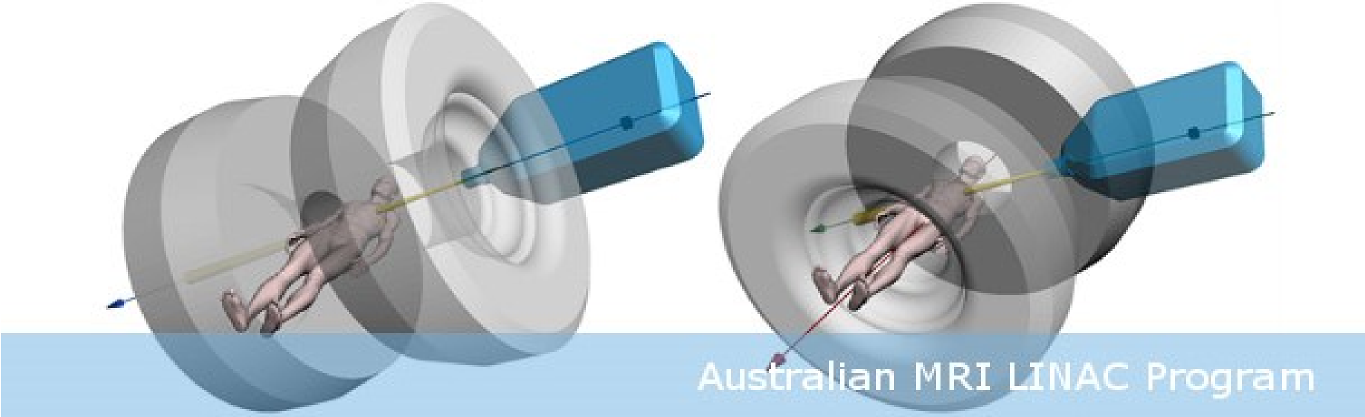
IGRT: Magnetic Resonance imaging

- Integrated devices



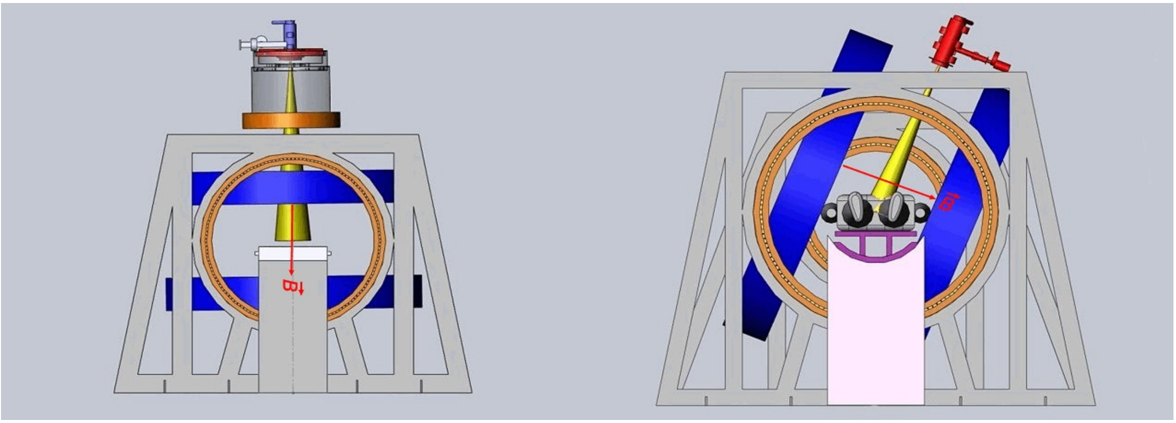
Utrect

Courtesy of Bas Raaymakers



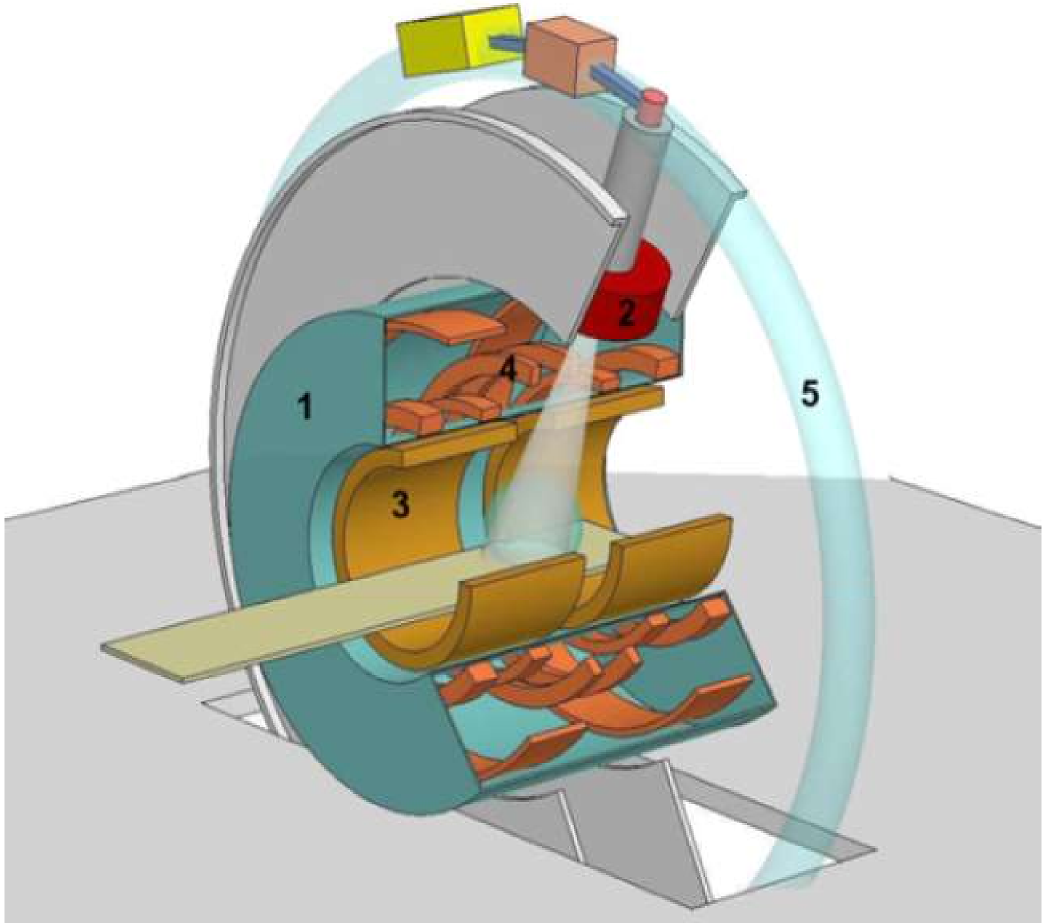
Sydney (Paul Keall)

Renaissance Viewray



Alberta (B. Fallone)

MR-LINAC (Utrecht)



Lagendijk JJ, et al. Radiotherapy and Oncology 86 (2008) 25–29

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Specifications MRI accelerator

1.5 T diagnostic MRI

6 MV linac

Continuous rotation
Both directions

10 RPM

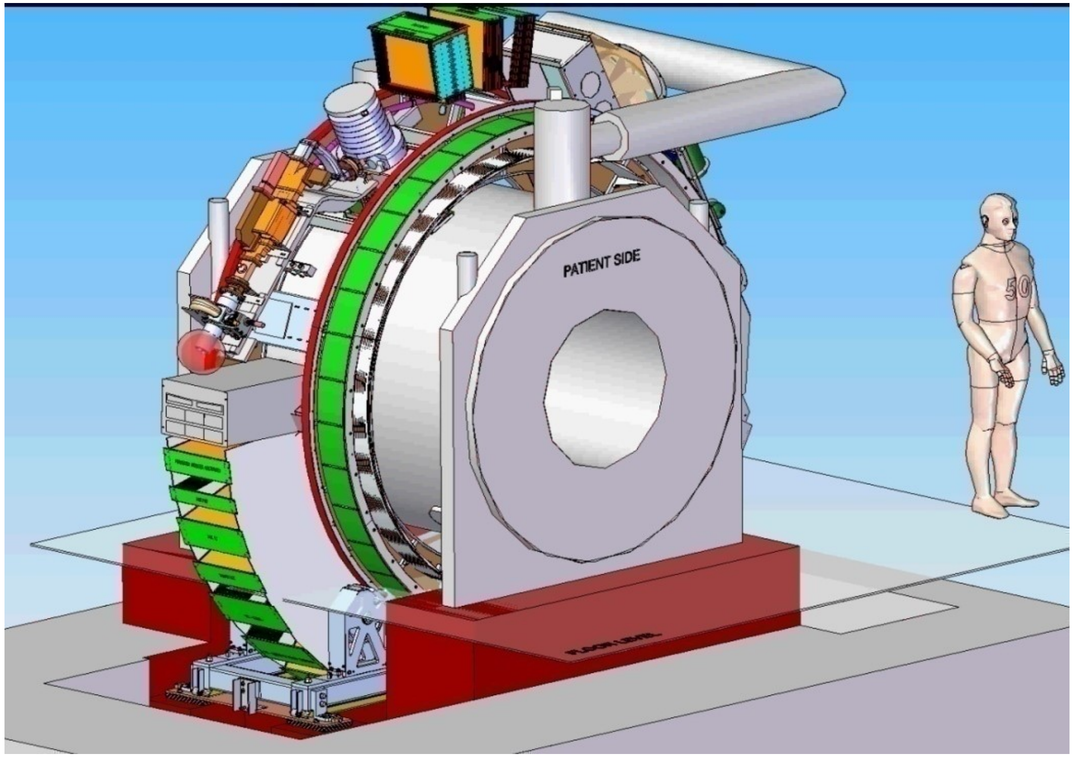
0.1 degree accuracy

1 mm spherical volume as target

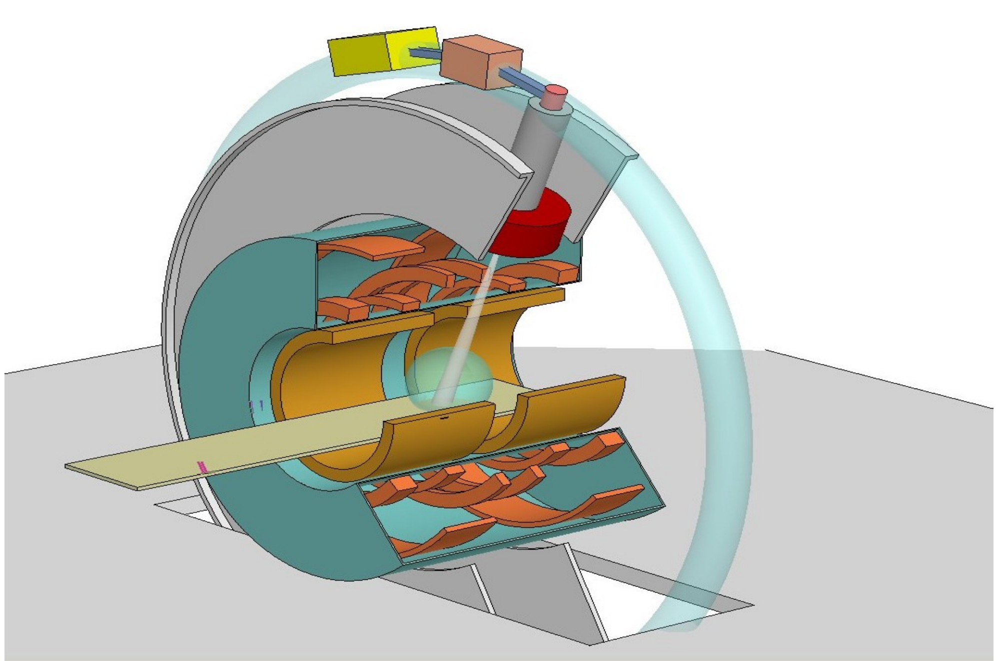
MLC Field size 24x56 cm2
7 mm leaves at isoc

Installation started April 2014

Courtesy of Bas Raaymakers

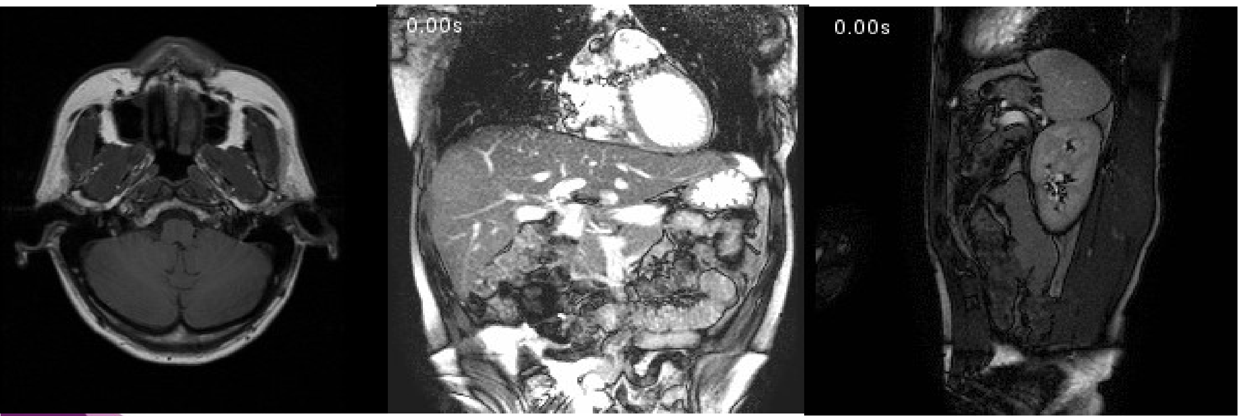


1.5 T MRI accelerator: Simultaneous beam on and MRI

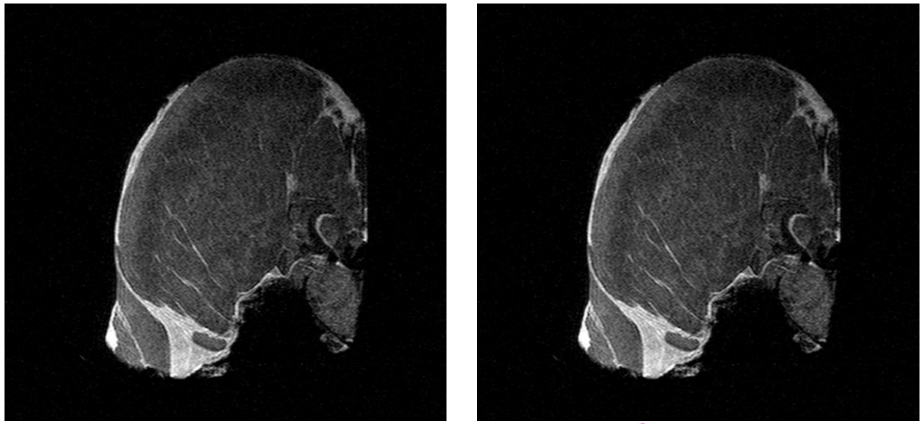


Artist impression

Prototype MRI accelerator



1.5 T diagnostic MRI quality



No impact of beam on MRI

Courtesy of Bas Raaymakers

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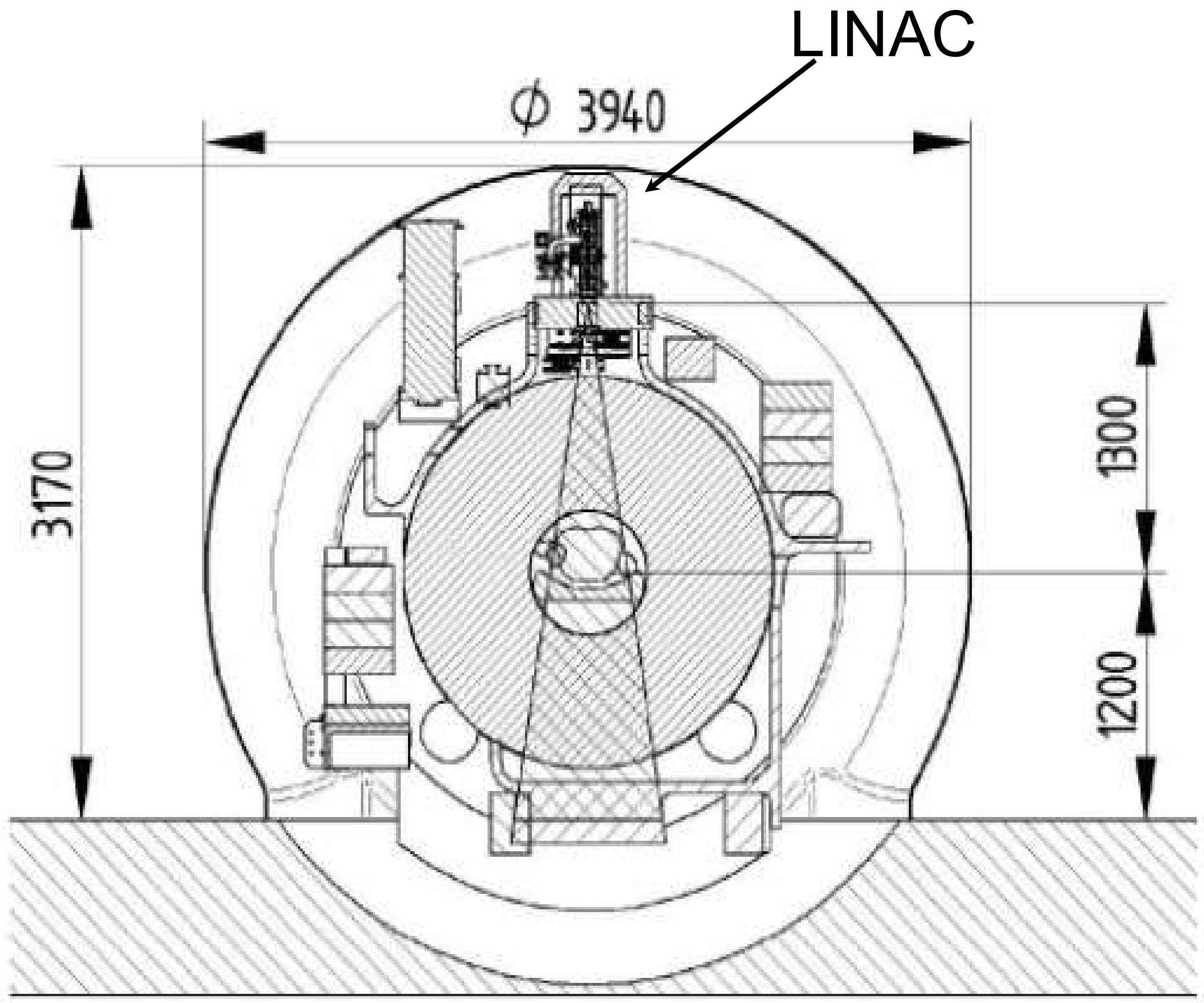
Design treatment to deal with breathing related motion

irregular breathing von Hippel Lindau kidney tumour

Courtesy of Bas Raaymakers

MR-LINAC



B. Raaymaakers,UMC Utrecht

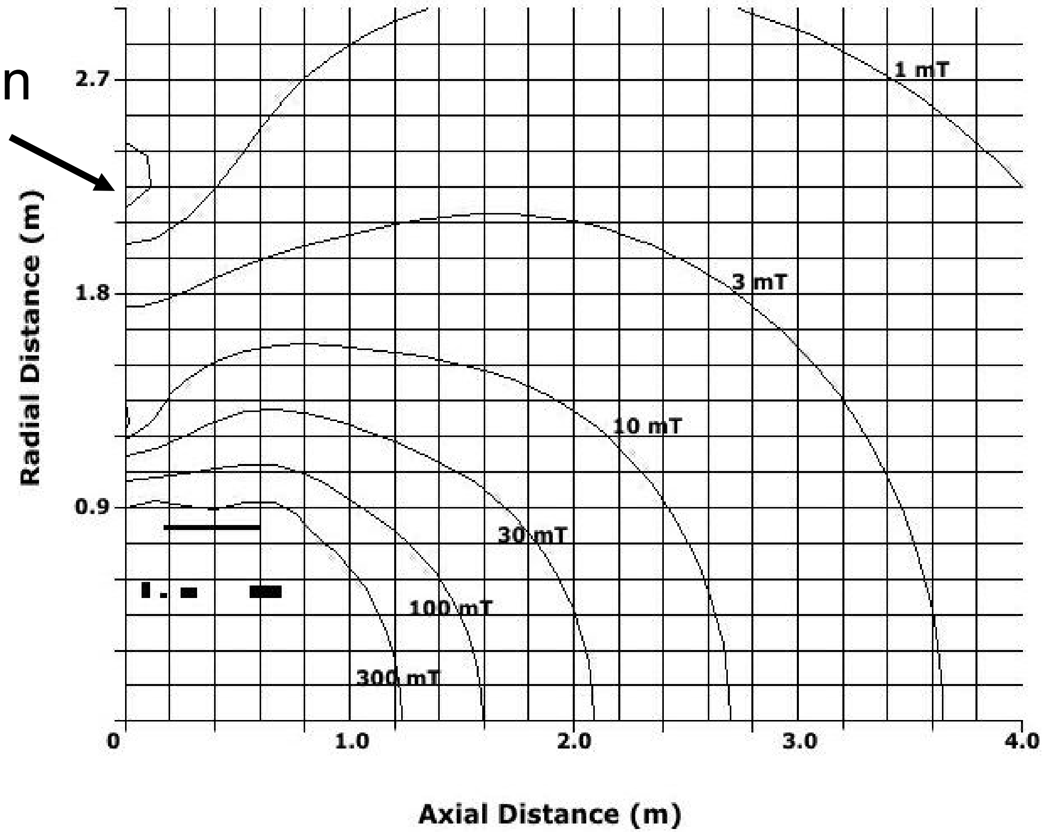
Technical Challenges

- Magnetic interference between MRT and LINAC
  - ➢ B-field of MRT disturbs operation of LINAC
  - ➢ Magnetization of moving LINAC components
    ⇨ image artefacts (modulation of 1.5 T)
- Dose deposition kernels @ 1.5 T
- Aim: Uncompromised quality of images <u>and</u> delivered dose (beam characteristics)

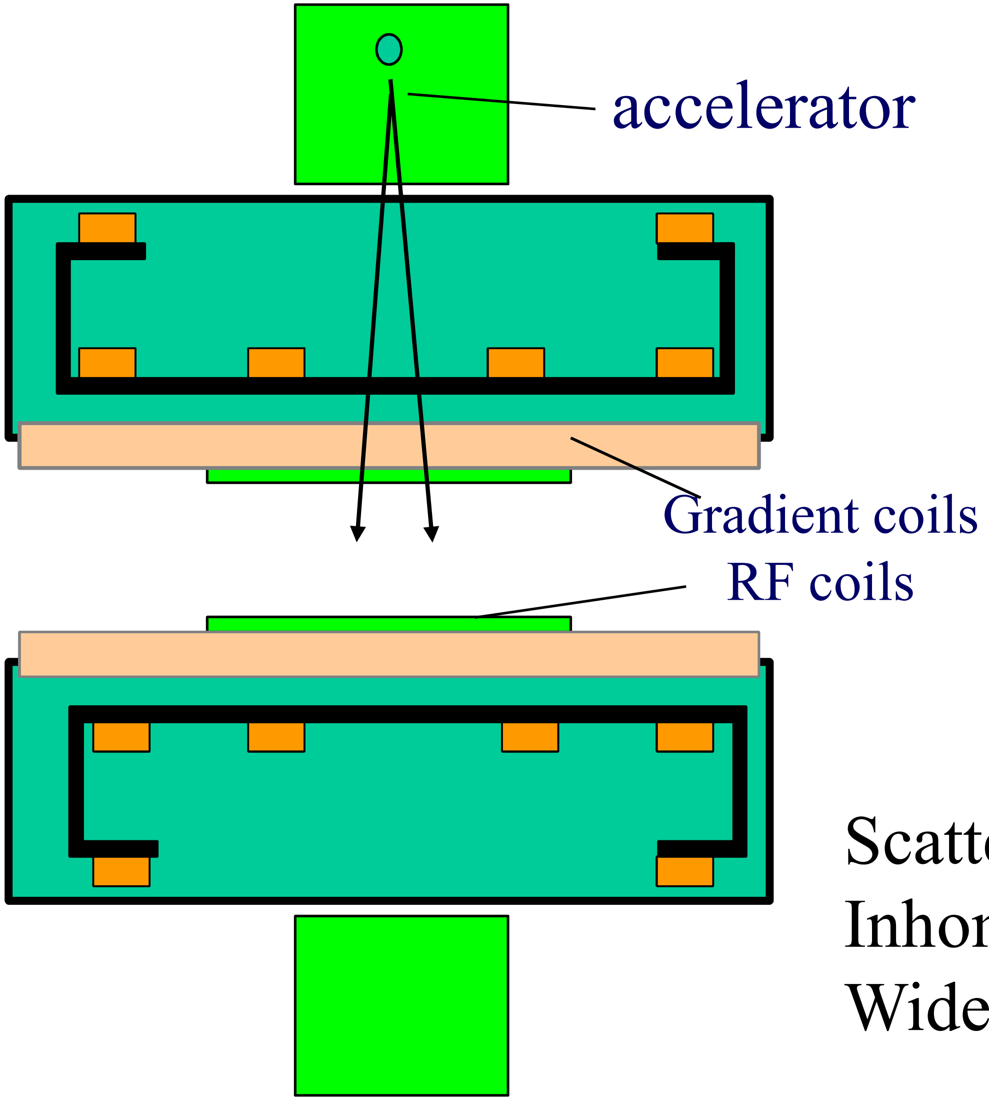
Undisturbed Operation of LINAC

- Active Shielding of 1.5 T MRT field
  - ➢ Minimising interference by dcreasing B @ LINAC
    B < 1 mT, mid-plane magnet

Location of e-gun



Transmission of treatment beam



Scatter
Inhomogeneous absorption
Widened penumbra

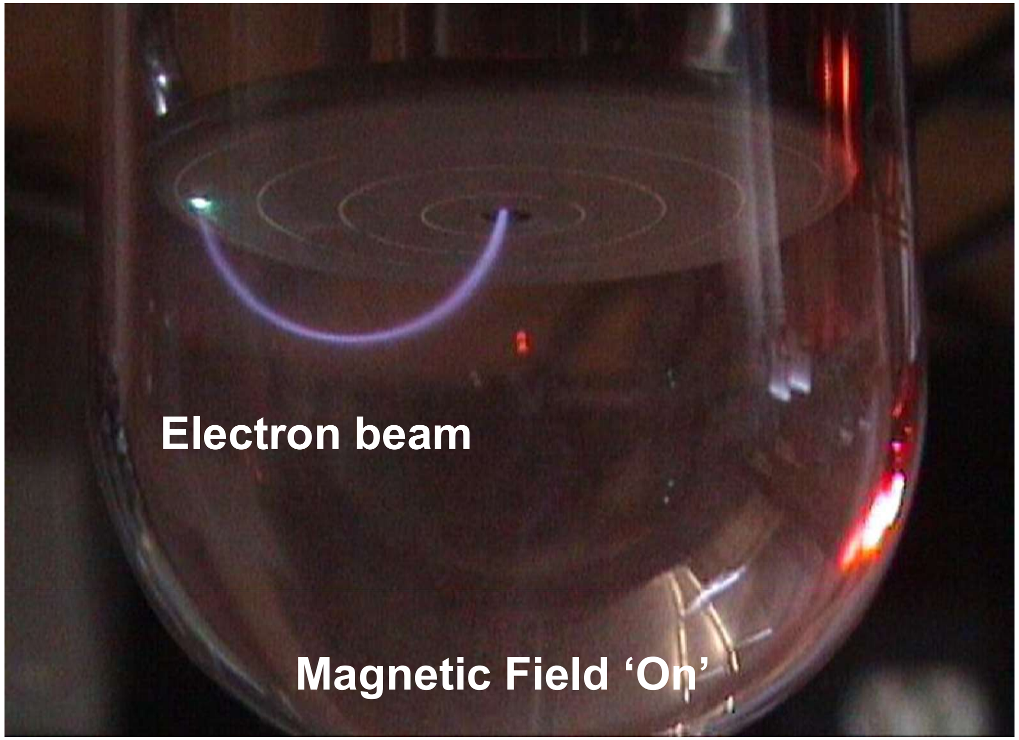
B. Raaymaakers,UMC Utrecht

Dose Calculation/Optimisation/Dosimetry

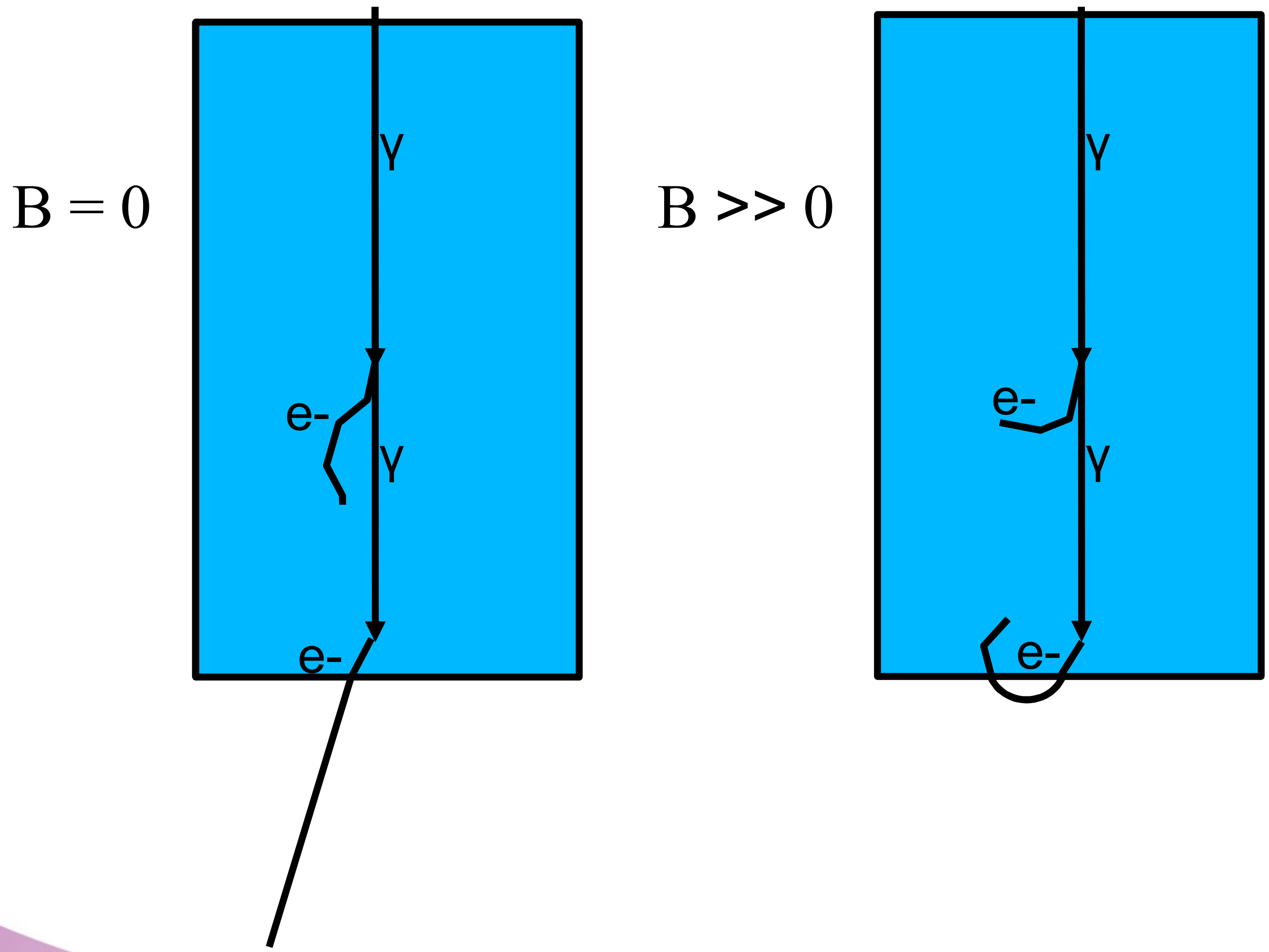
- Dose calculation/Dosimetry @ 1.5T or 3T
  - Lorentz force on secondary electrons
  - Electron return effect (ERE)
  - Response of dosimeters is changing

Development of Accurate and Reliable Dosimetry

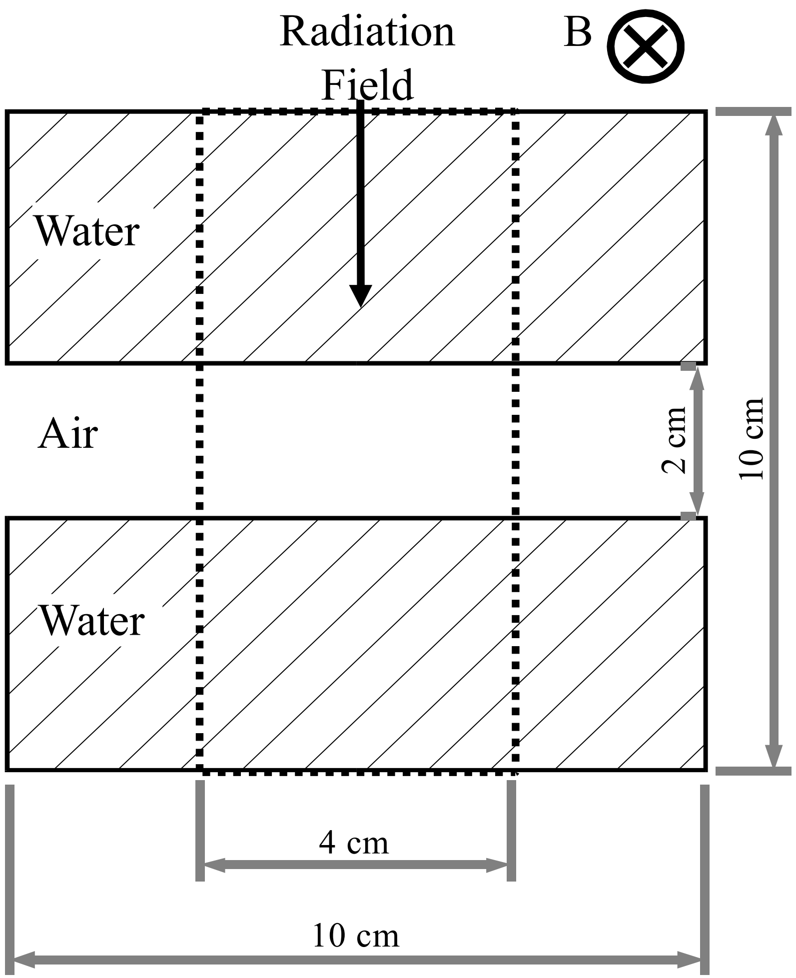
Electrons in a magnetic field

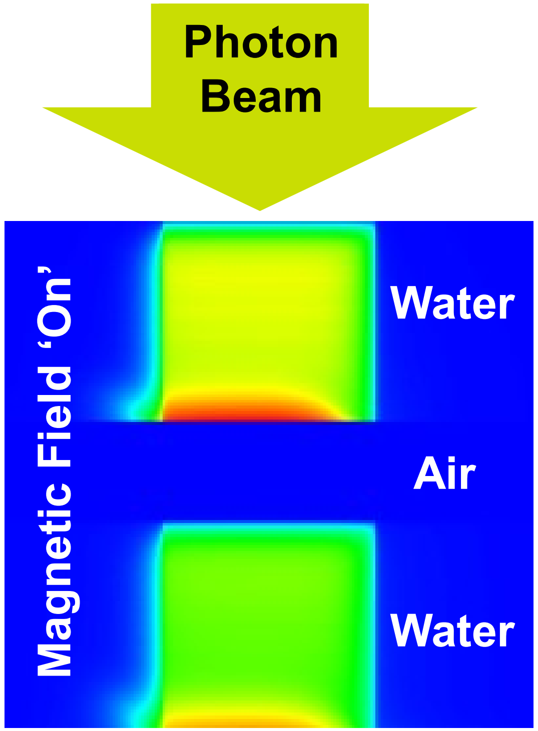


Electron return effect



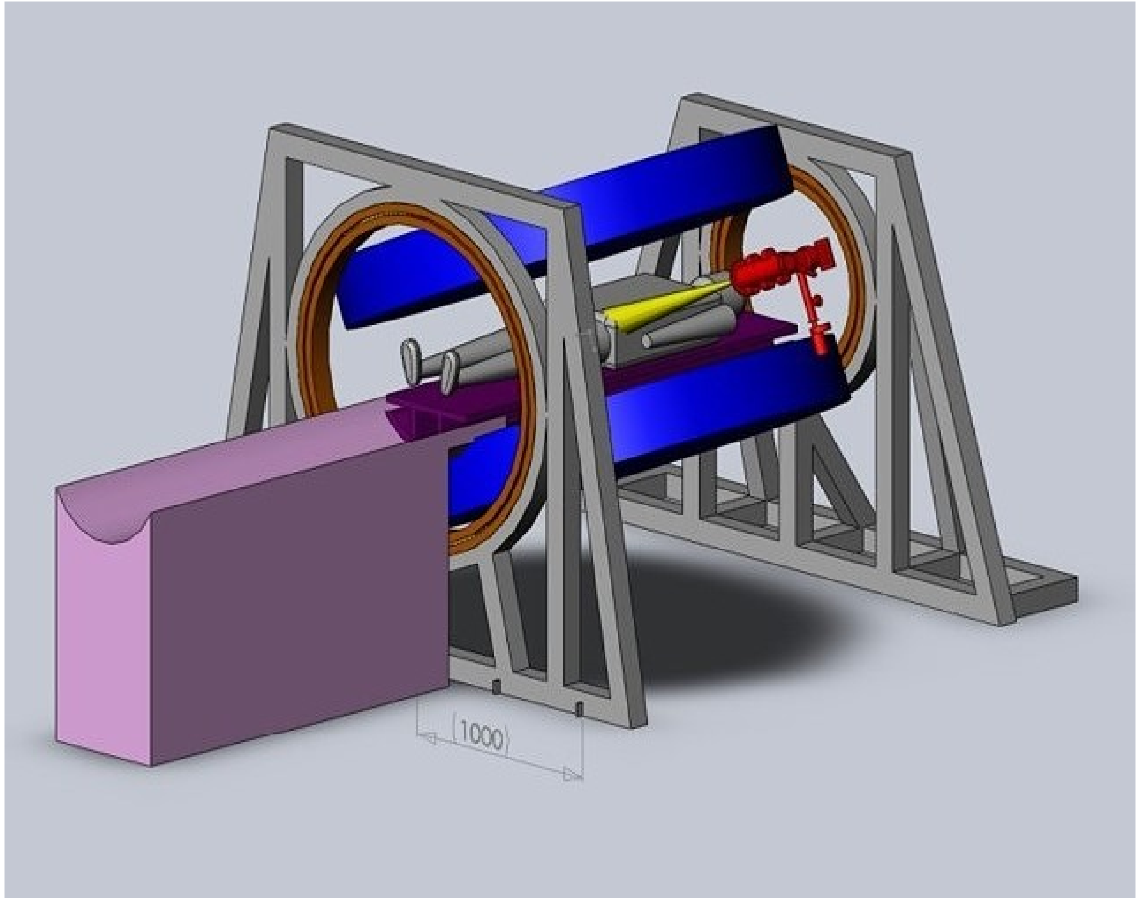
ERE at air gap





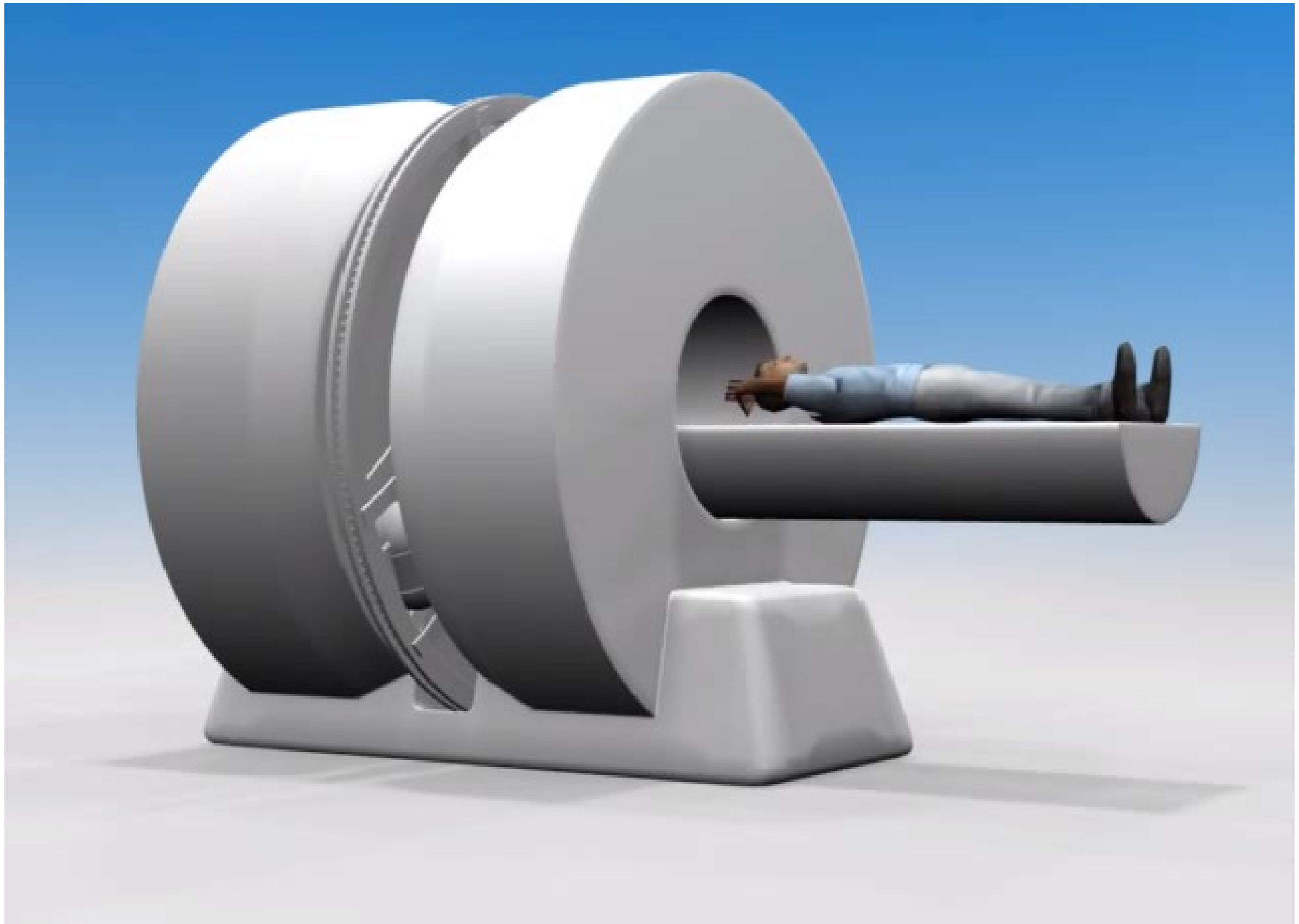
Impact of electron 'bending' on dosimetry

Rotating MR/LINAC (Edmonton)



M. Lamey, et al. Phys Med Biol 55(4), 995-1006 (2010).

MRI + Cobalt RT - ViewRay



Renaissance System (ViewRay)

Online ART using MRI guidance

MRIdian from ViewRay:

- 3D MRI acquisition
- Deformable registration to transfer contours onto current MRI
- Manual review of contours
- Re-optimization of treatment plan on current MRI (no dose accumulation)
- Independent Monte Carlo calculation to verify treatment plan

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MRI/Co ViewRay

<u>Technical Configuration</u>

Split MR magnet 0,3 T

3 Co sources,

3 MLCs

Why ^{60}Co?

Linac and MRI don't match:

RF for acceleration

RF for imaging

Why 0.3 T?

High field causes a loss of spatial integrity

High field is more sensitive to electron return effect

MRIdian Linac: Therapy System

- Magnetic & RF shielding eliminating all Linac-MRI interference & preserves compact design
- Pulse transformer, magnetron, port circulator, gun driver, & linac shielded on gantry
- 6 MV FFF S-band inline standing-wave side-coupled cavity linac - <1 Gauss from gun to just before target
- 27.3 cm x 27.3 cm double-focused MLC with jaw-spec shielding, minimum 2 mm x 4mm field size, full over travel and inter-digitation
- multi-isocenter delivery at 90 cm SAD Conformal or IMRT or both with single-button push plan delivery

Seeing is Believing – The MR Linac Project

MR Linac at ICR / RMH: Timeline

Planning permission

17/12/2014

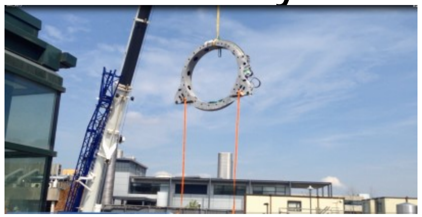
Ground breaking

1/03/2015

Constructio
n completed

03/2016

Gantry



07/05/2016

Magnet

04/06/201
6

RF Cage

11/07/201
6

Setting to work

12/09/201
6


RADIATION
CONTROLLED
AREA

Conclusions

- Some of these developments are not mainstream solutions now, but some of them one may have the potential to become a major player in the long run .

- There are interesting and new developments, just be aware of the limitations and pitfalls, as well as the advantages.

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ICR The Institute of Cancer Research

CANCER RESEARCH UK

in partnership with
The ROYAL MARSDEN
NHS Foundation Trust

MRIgRT: implications for treatment planning and delivery

U. Oelfke



Division of Radiotherapy & Imaging
uwe.oelfke@icr.ac.uk

Making the discoveries that defeat cancer

Real-time tracking - CyberKnife

Internal/external marker correlation

Model building

Courtesy of Accuray, Inc.

Models:

Linear

Elliptical

Polynomial

Model updated by use of online kV images

Disclaimer

- ICR/RMH is a member of the Elekta Atlantic Research Consortium

Treatment Devices: Overview

Institution	Radiation Source	B field strength	Magnet Type	Beam-field orientation (with respect to the treatment beam)
Princess Margaret Hospital	Standard Linac	1.5T	Closed	NA
Viewray	^{60}Co	0.35T	Split	Perpendicular
Viewray	6MV x-rays	0.35 T	Split	Perpendicular
Australian MRI-Linac	6MV x-rays	1.0T	Split	Inline and perpendicular
University of Alberta	6MV x-rays	0.2T & 0.5T	Split	Inline and perpendicular
Elekta/Philips	7MV x-rays	1.5T	Closed	Perpendicular

Seeing is Believing – The MR Linac Project

ATLANTIC.

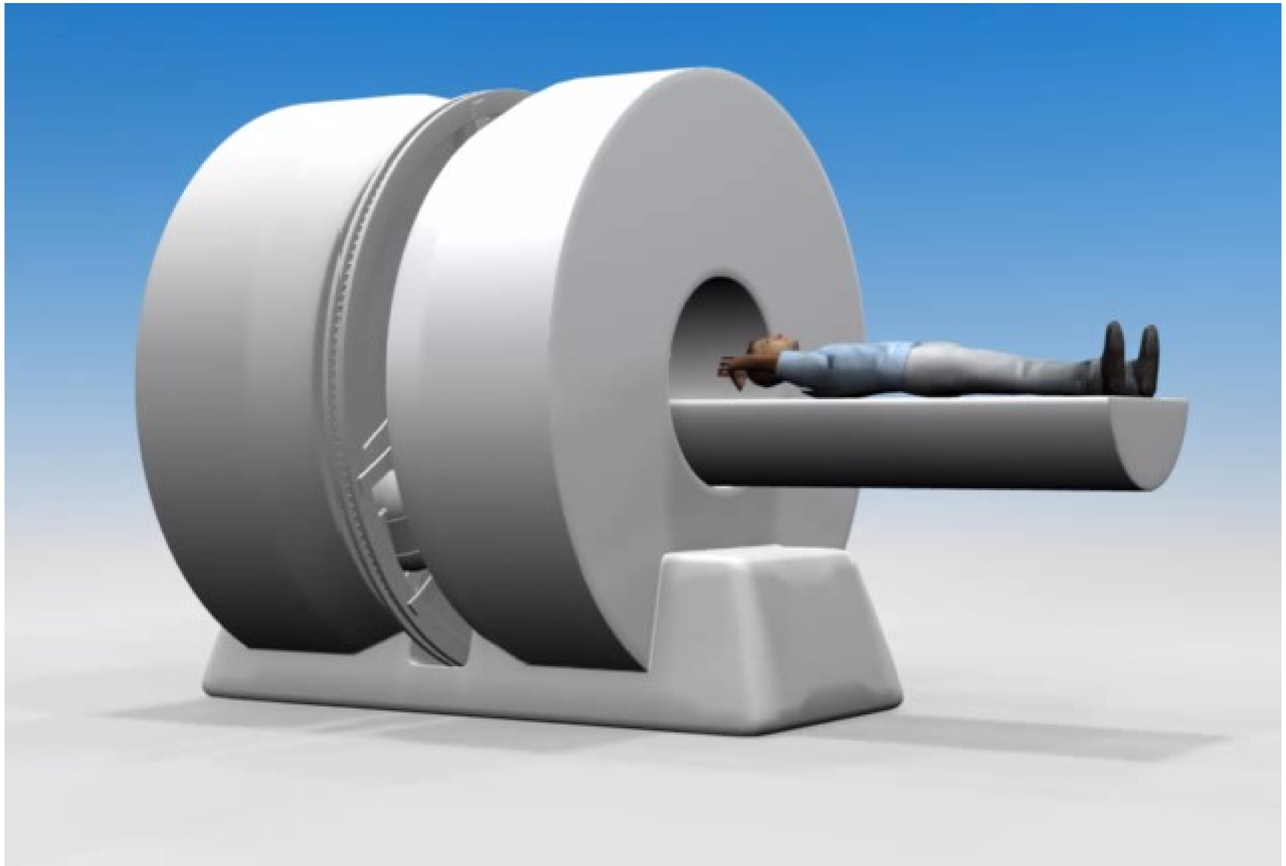
CONSORTIUM

DISCOVER

COLLABORATE

INNOVATE

MRI + Cobalt RT - ViewRay



Renaissance System (ViewRay)

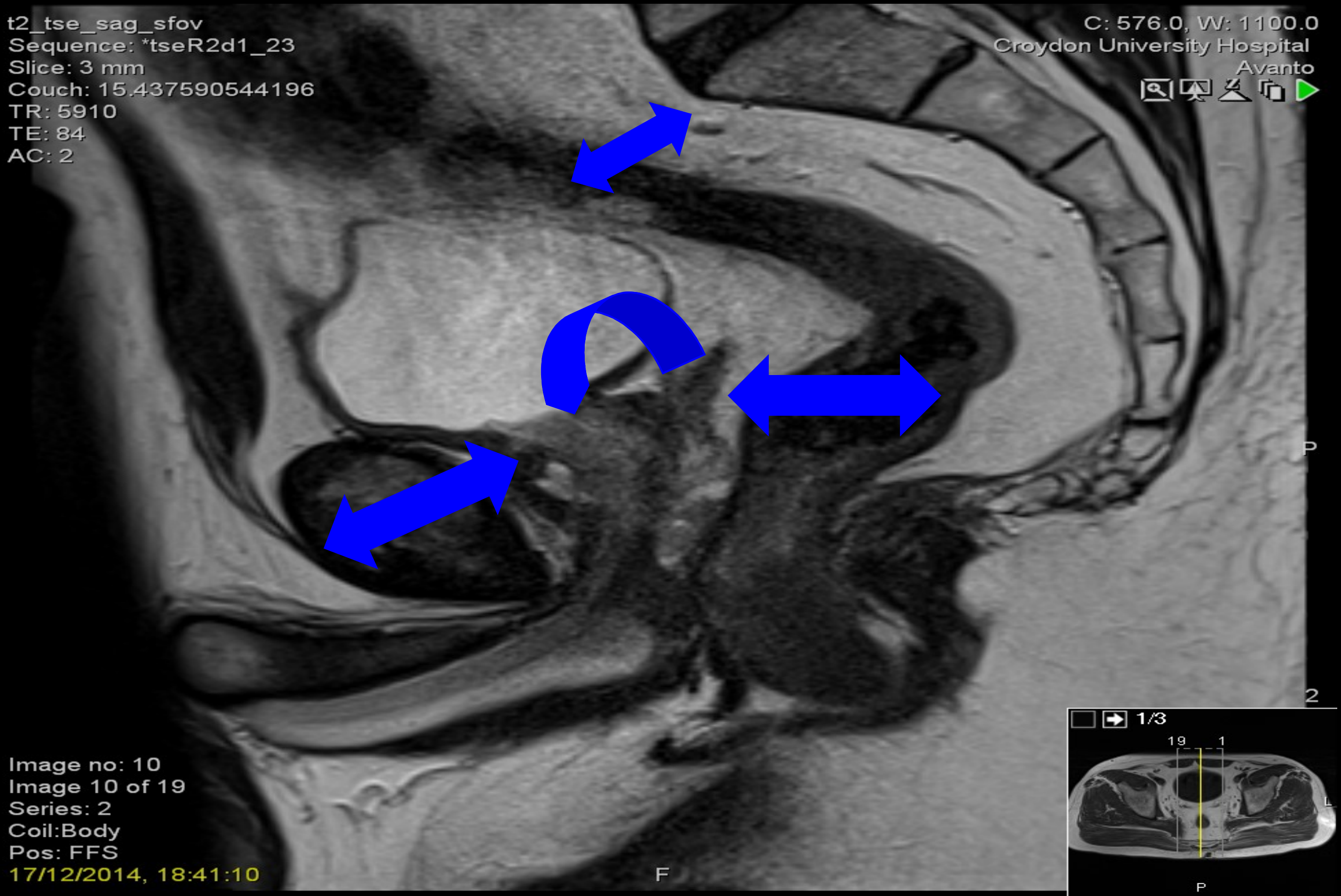
Impact on treatment planning

- ❑ Improved Soft tissue contrast
- ❑ Calibration of MR images for dose calculations
- ❑ Influence of the treatment geometry
- ❑ Influence of the magnetic field

Impact on treatment planning

- ❑ Improved Soft tissue contrast
  - ❑ Reduction of geometrical uncertainties → margin reduction
  - ❑ Enabling high precision RT technqiues
  - ❑ Enabling enhanced automation of segmentation and treatment planning
  - ❑ Enabling advanced adaptive dose delivery/planning concepts

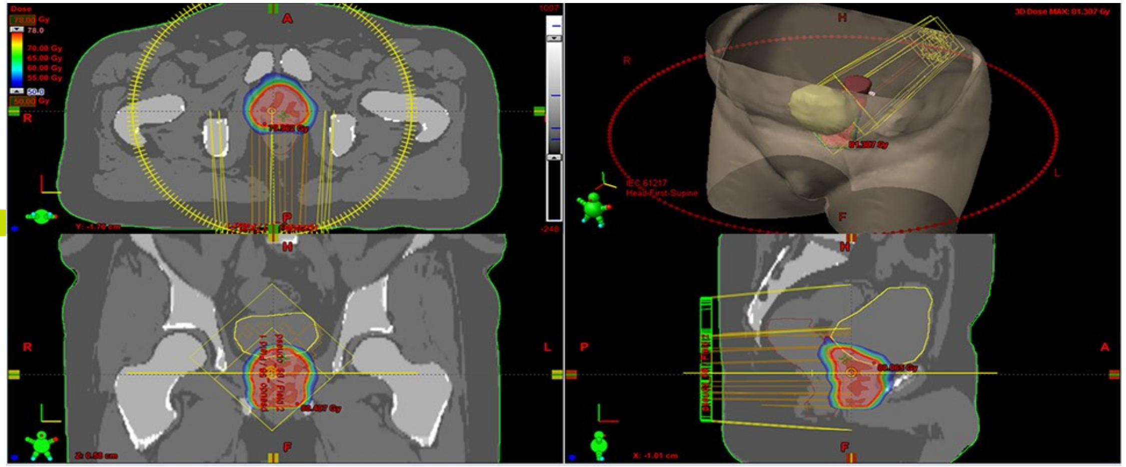
- Adaptive re-planning – plan of the day



Impact on treatment planning

- ❑ Calibration of MR images for dose calculations
  - ❑ Many, many good approaches → MR only
  - ❑ Challenges are tumour site specific
  - ❑ Effects of errors are mostly ‘small’

MRCAT and autoplanning



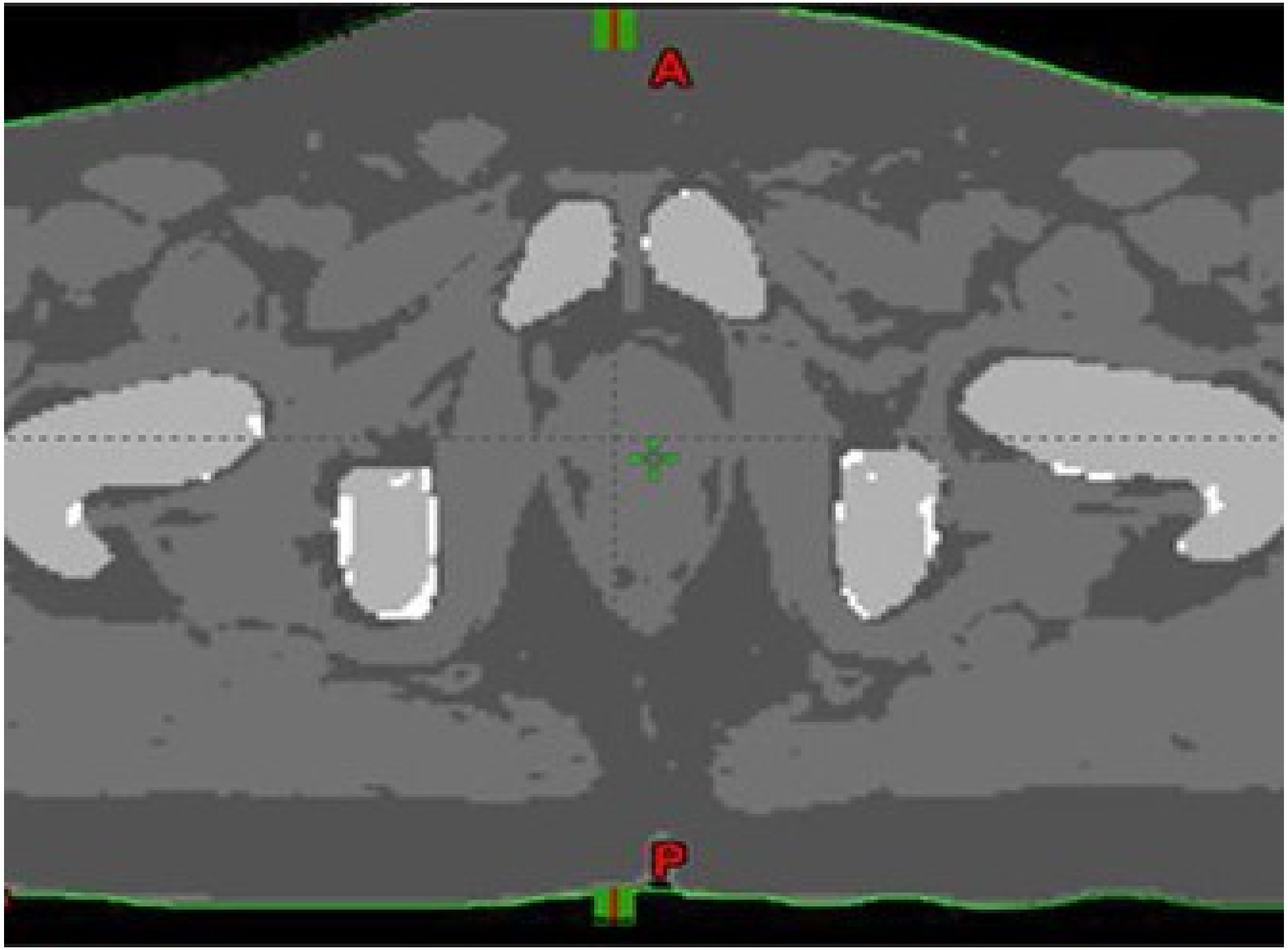
1. MRCAT installation
    develop mDIXON scanning sequence
    comparison with CT based plans

2. Autoplanning assessment
    assessment of autoplanning IMRT/ VMAT with CT based plans

3. Assessment of utility of MRCAT DRR and volumetric images for treatment verification

MRCAT Philips

3D density maps based on MR imaging



Impact on treatment planning

- ❑ Influence of the treatment geometry
  - ❑ Increased leaf width of the MLCs (Elekta/Philips)
    - 7mm, 10 mm depends on clinical indication, slightly reduced conformity
  - ❑ Reduced dose rate

Impact on treatment planning

- ❑ Improved Soft tissue contrast
- ❑ Calibration of MR images for dose calculations
- ❑ Influence of the treatment geometry
- ❑ Influence of the magnetic field

ERE ….electron rotation effect…

Challenge: Magnetic Field of the MR

Lorentz force: Electrons trajectories are affected by the magnetic field of the magnet

$$\vec{F} = q\,(\vec{v} \times \vec{B}) - \mathrm{S}\,\frac{\vec{v}}{v}$$

q: Electron charge

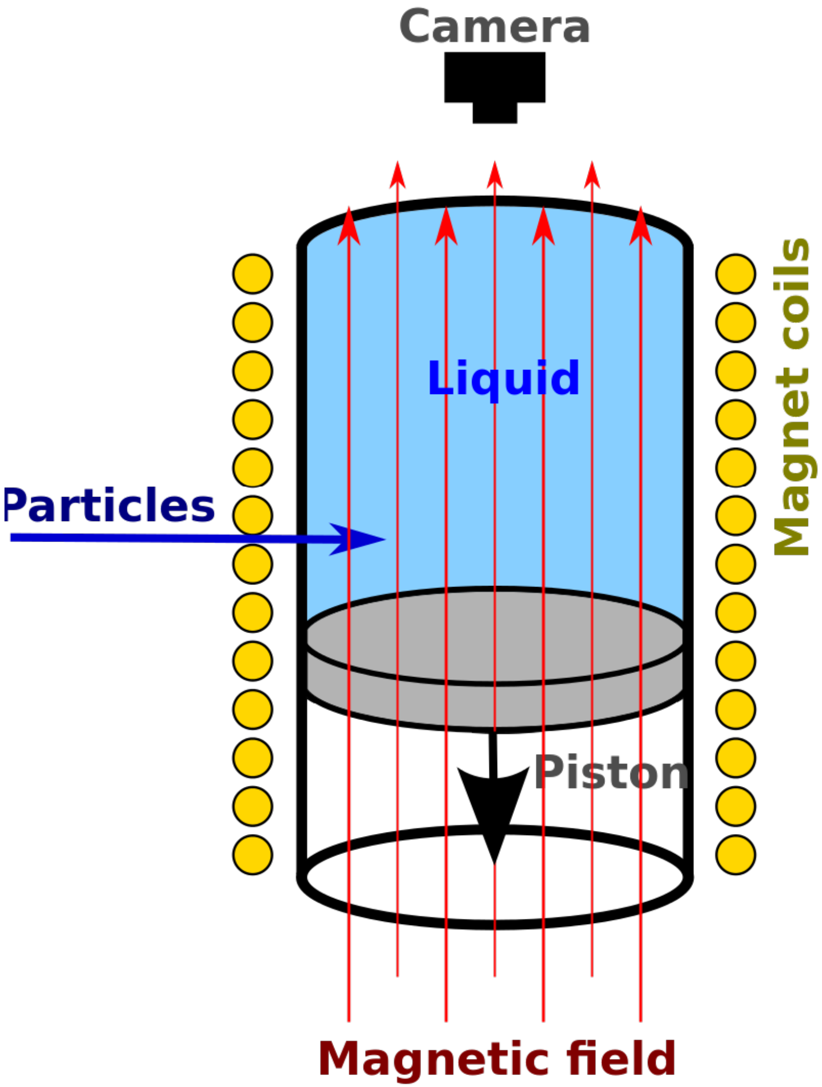
$\vec{B}$: Magnetic field

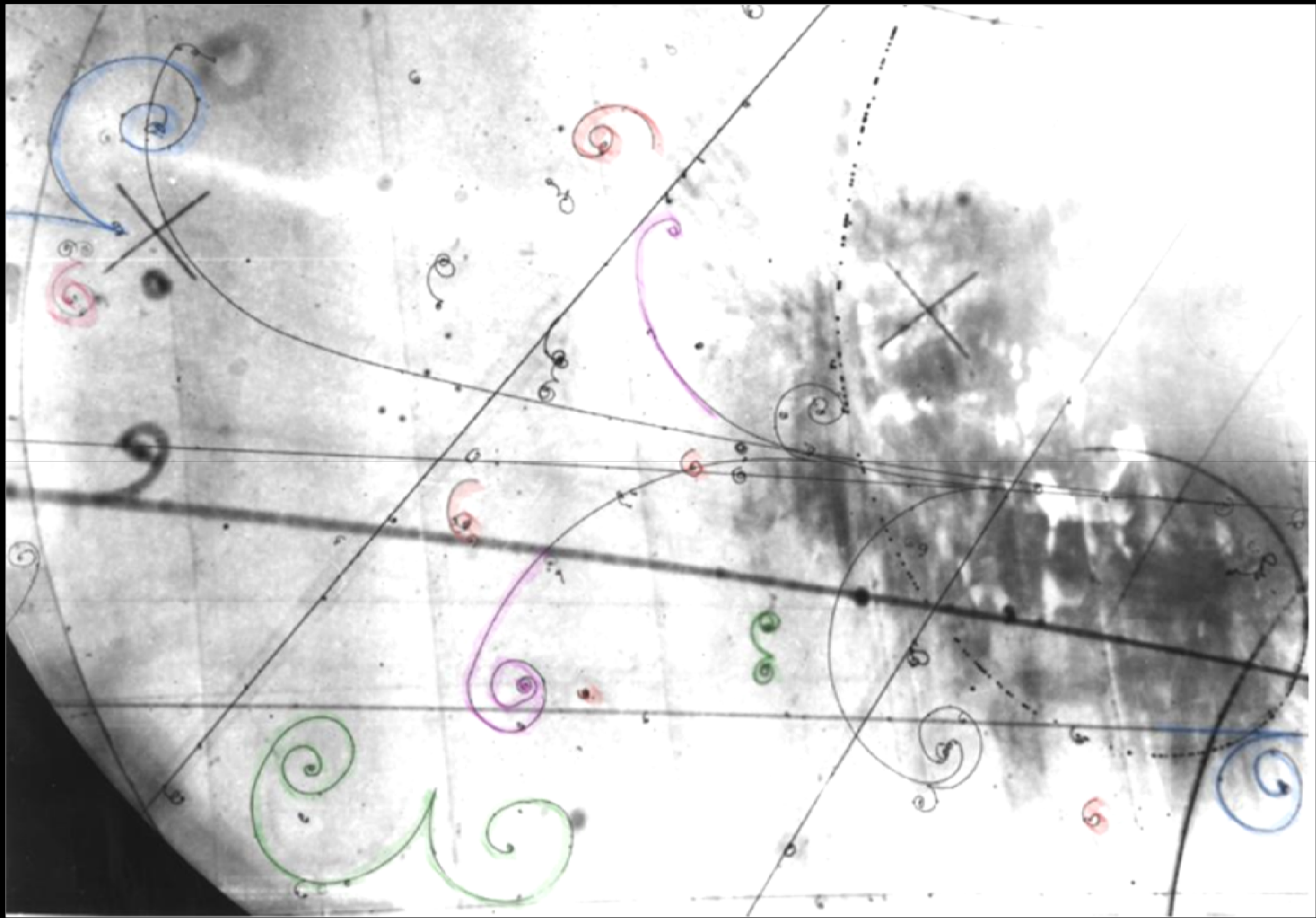
$\vec{v}$: Electron speed

$\vec{E}$: Electric field

S: Stopping Power

Visualisation of particle tracks: Bubble chamber





Larmor frequency and radius

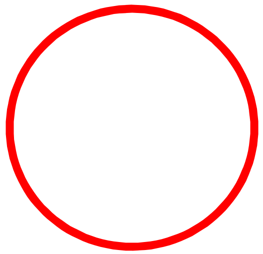
$$\omega = \frac{q\ B}{m} = 1.76\ *\ 10^{11}\left(\frac{1}{s\ T}\right)$$

$$\mathrm{R} = \frac{v_{perp}}{\omega} = 1.7\ \mathrm{mm}\ \frac{\beta_{perp}}{\sqrt{1-\beta^2}}\left(\frac{1}{B\ (T)}\right)$$

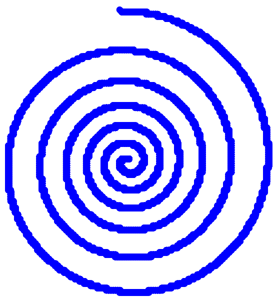
Impact of the electron energy, magnetic field and electron density

E_k kinetic energy (MeV) , electron density — range (mm)

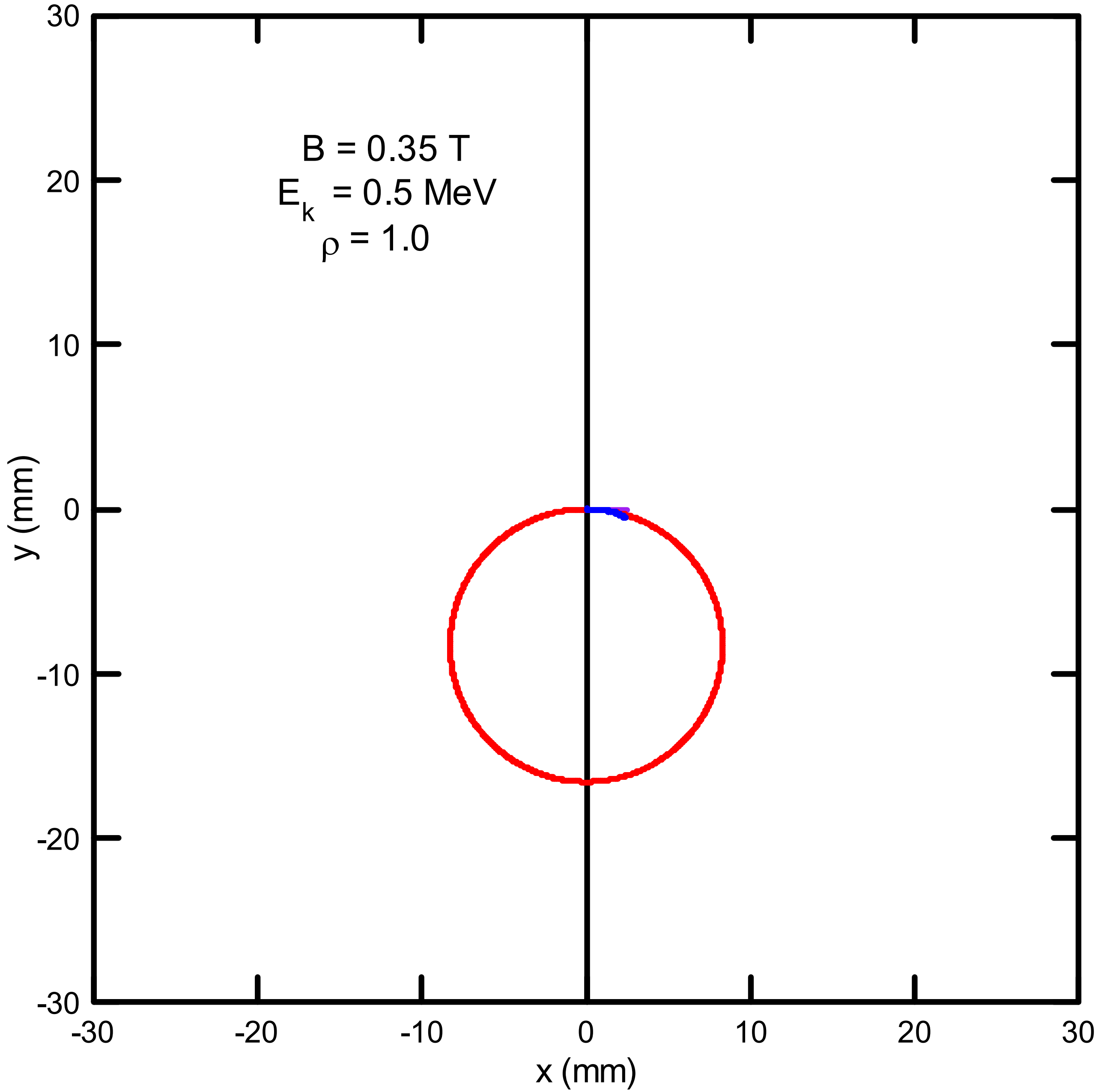
E_k , B magnetic field (Tesla)

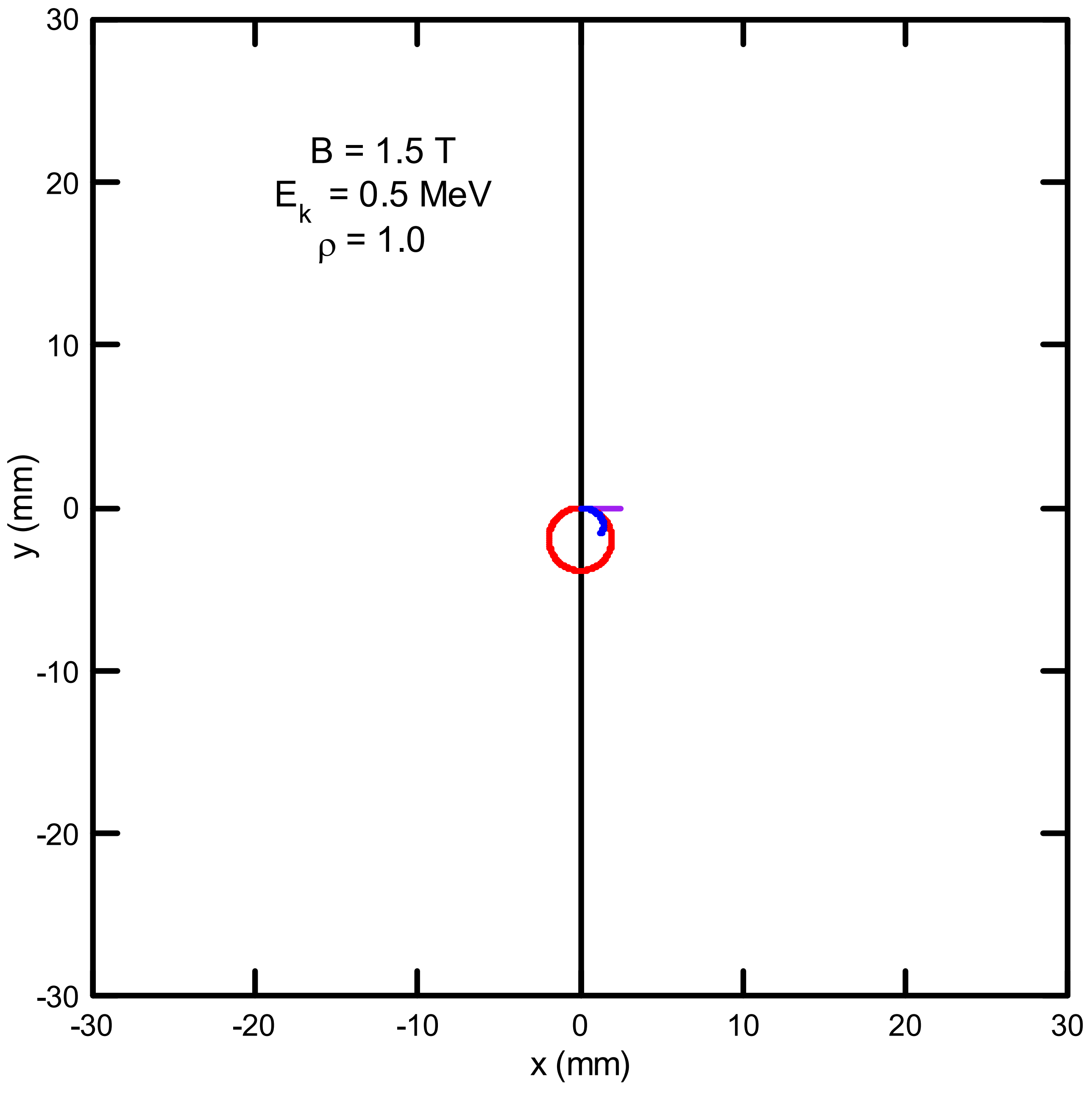


E_k , B magnetic field (Tesla), electron density



i) Impact of increasing magnetic field

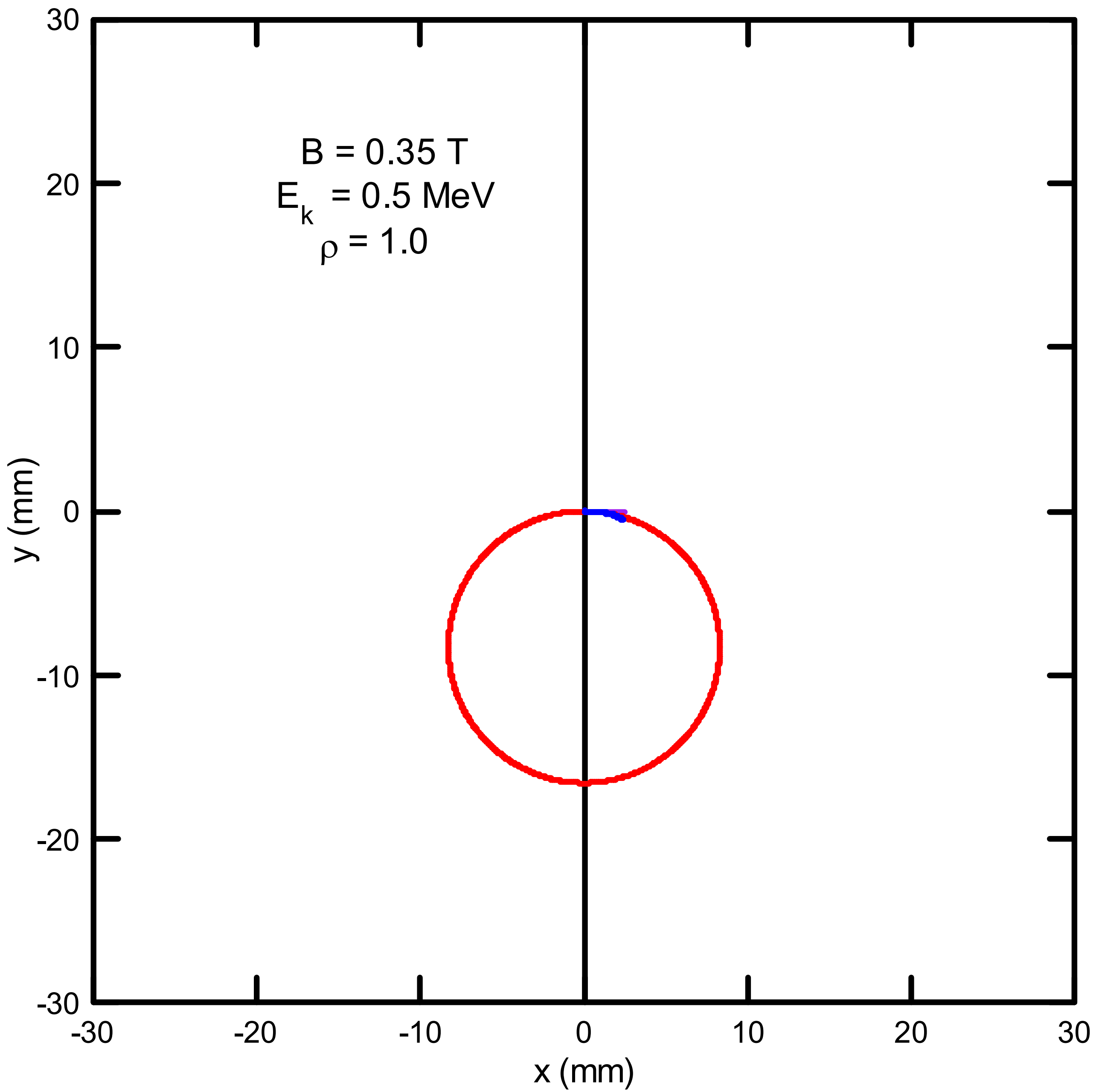

B = 0.35 T
E_k = 0.5 MeV
ρ = 1.0
30
20
10
0
-10
-20
-30
y (mm)
-30
-20
-10
0
10
20
30
x (mm)


B = 1.5 T
E k = 0.5 MeV
ρ = 1.0
30
20
10
0
-10
-20
-30
y (mm)
-30
-20
-10
0
10
20
30
x (mm)

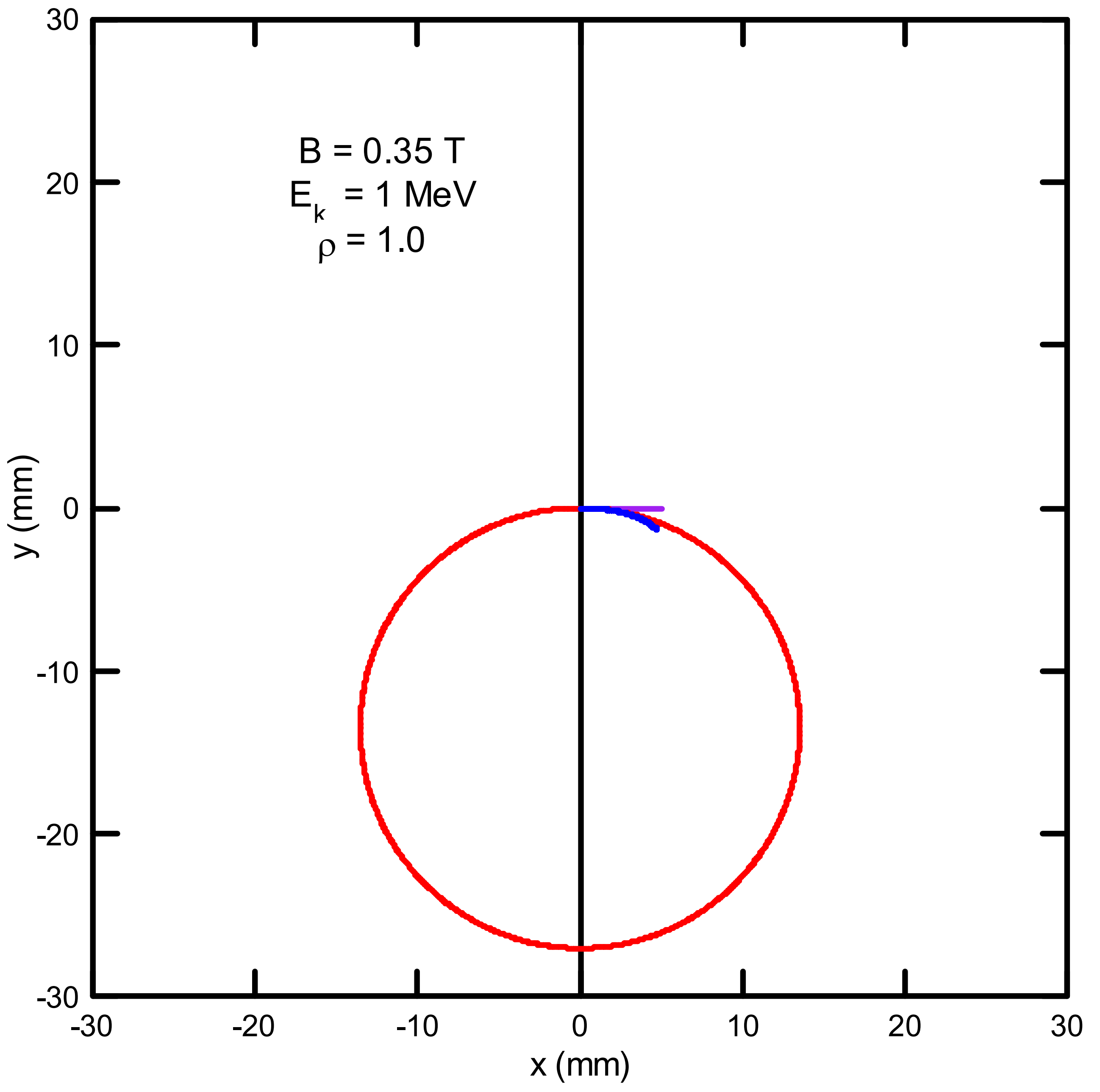
Consequences: Increasing magnetic field strength

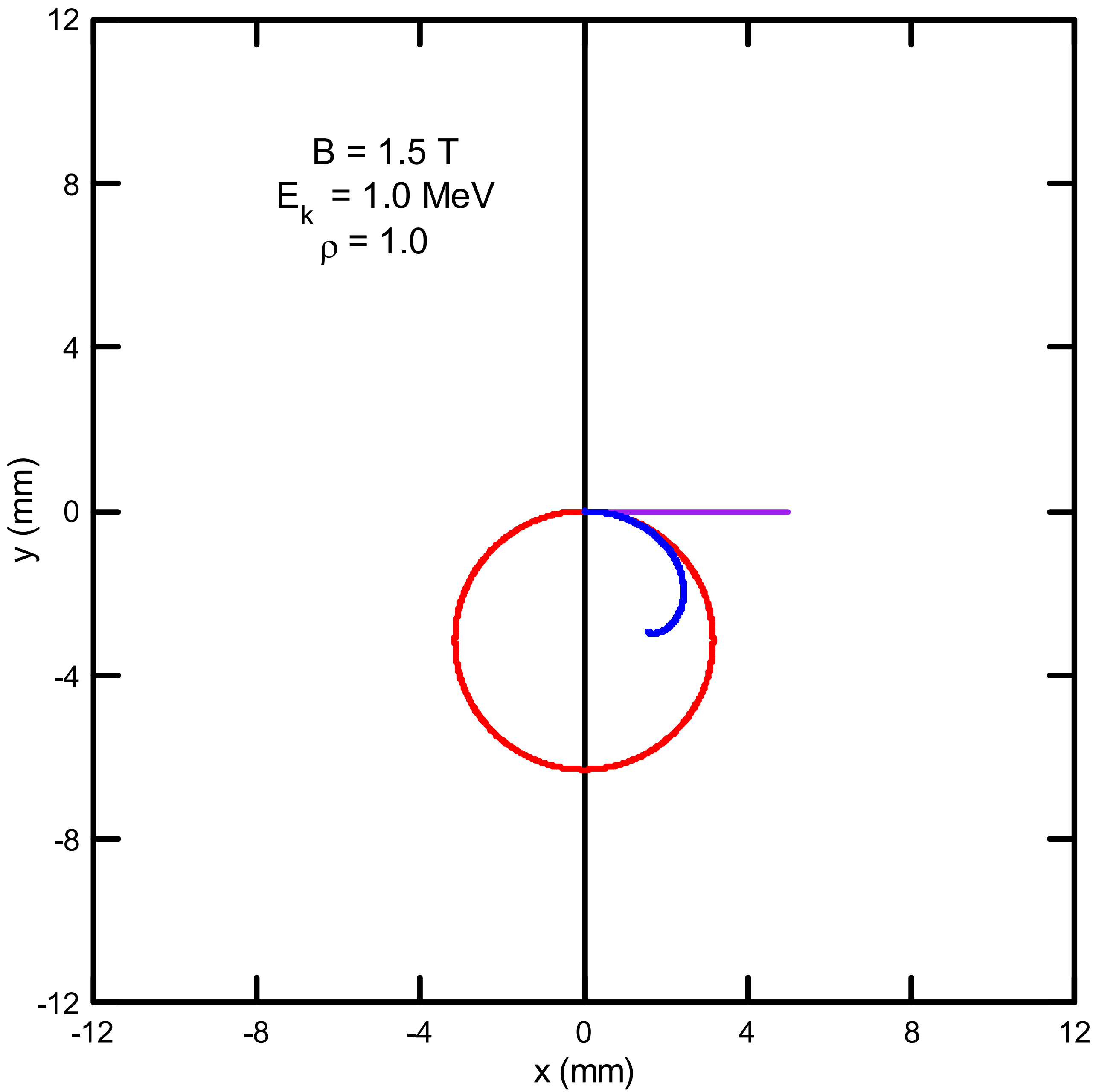
- Range stays constant
- Radius of trajectory decreases
- Dose dislocation/concentration increases
- Reduced build-up effect

ii) Impact of the kinetic energy



B = 0.35 T
E_k = 0.5 MeV
ρ = 1.0
y (mm)
x (mm)
30
20
10
0
-10
-20
-30

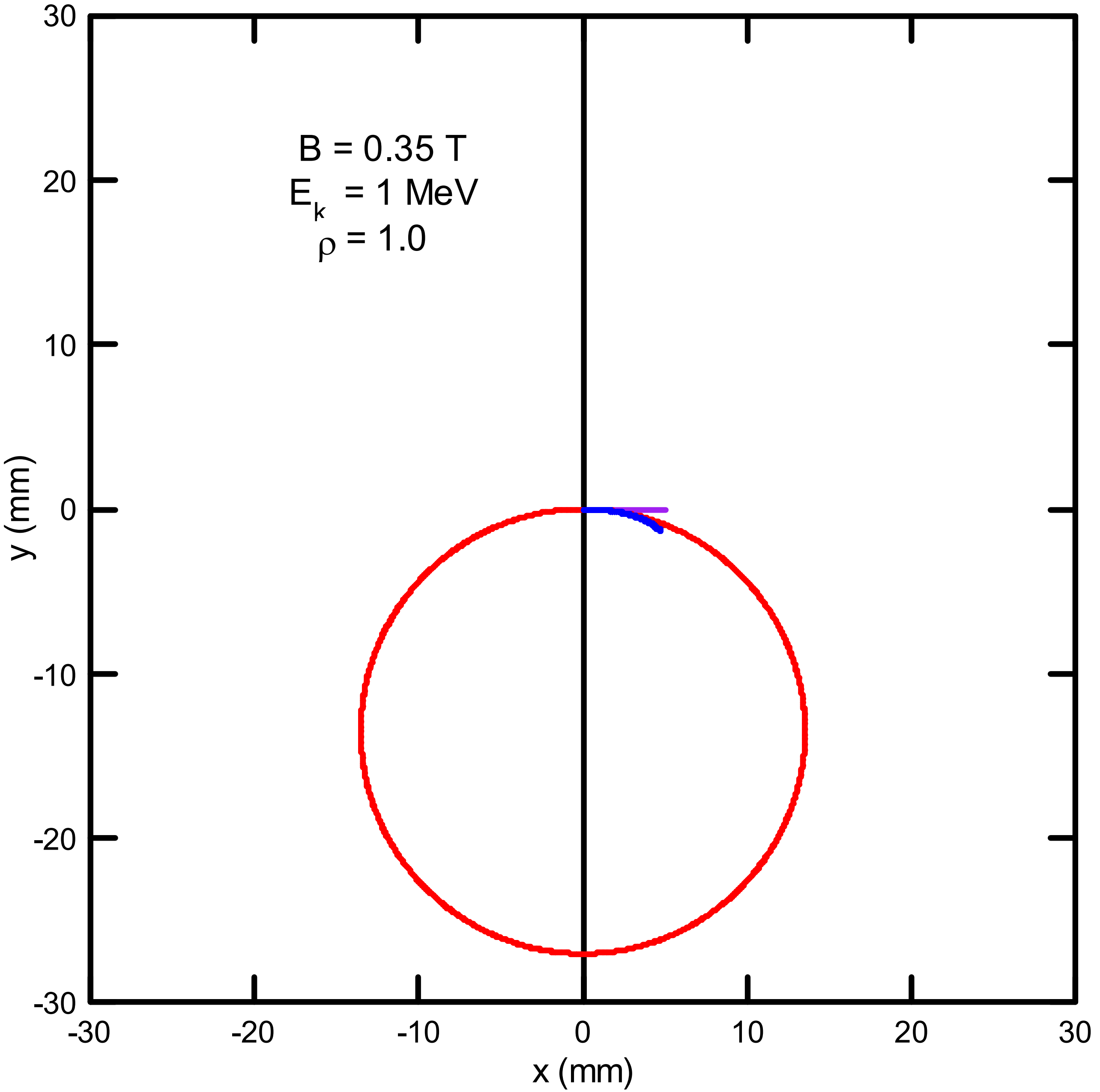

B = 0.35 T
E_k = 1 MeV
ρ = 1.0
30
20
10
0
-10
-20
-30
y (mm)
-30
-20
-10
0
10
20
30
x (mm)


B = 1.5 T
E_k = 1.0 MeV
ρ = 1.0
y (mm)
x (mm)
12
8
4
0
-4
-8
-12
-12
-8
-4
0
4
8
12

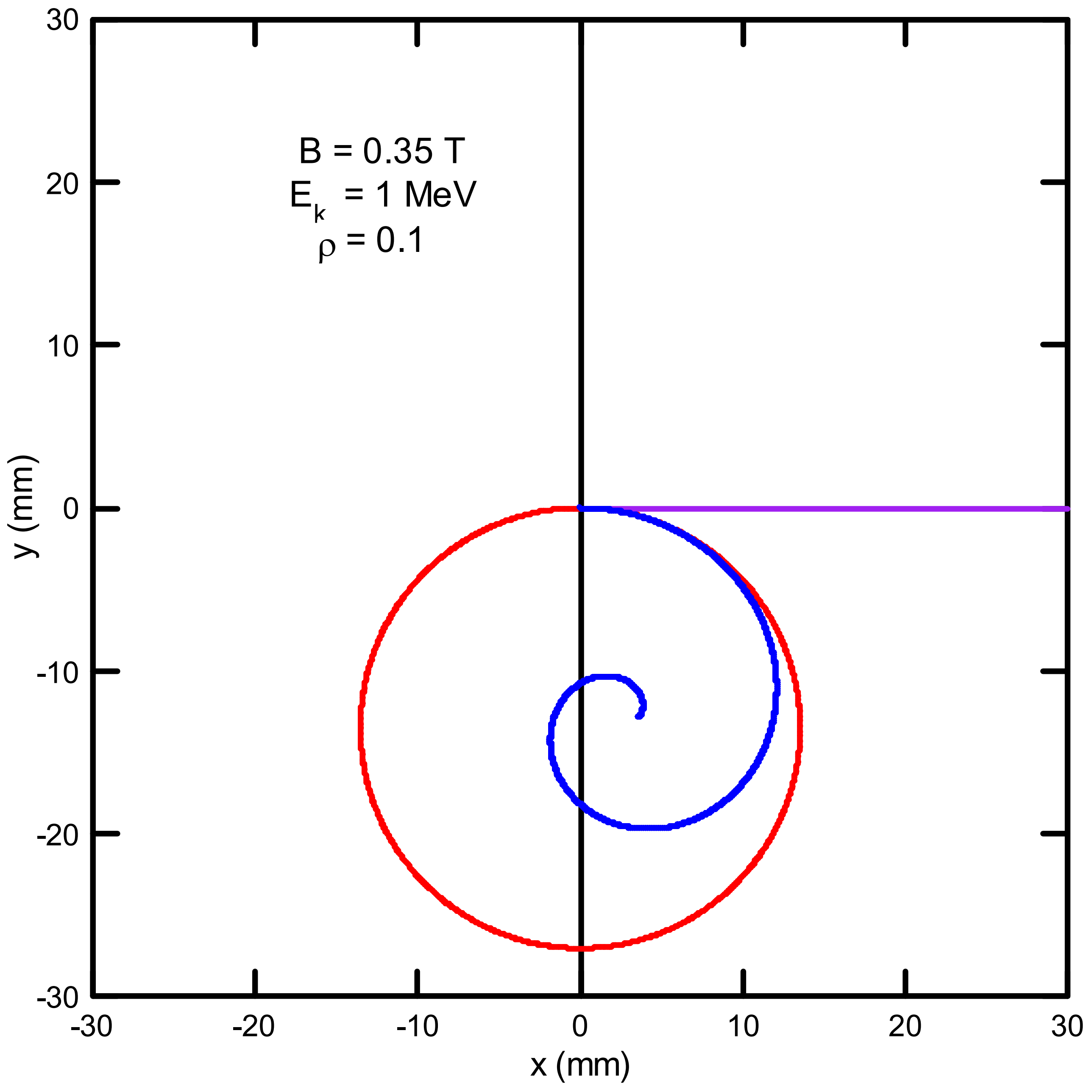
Consequences: Increased kinetic energy

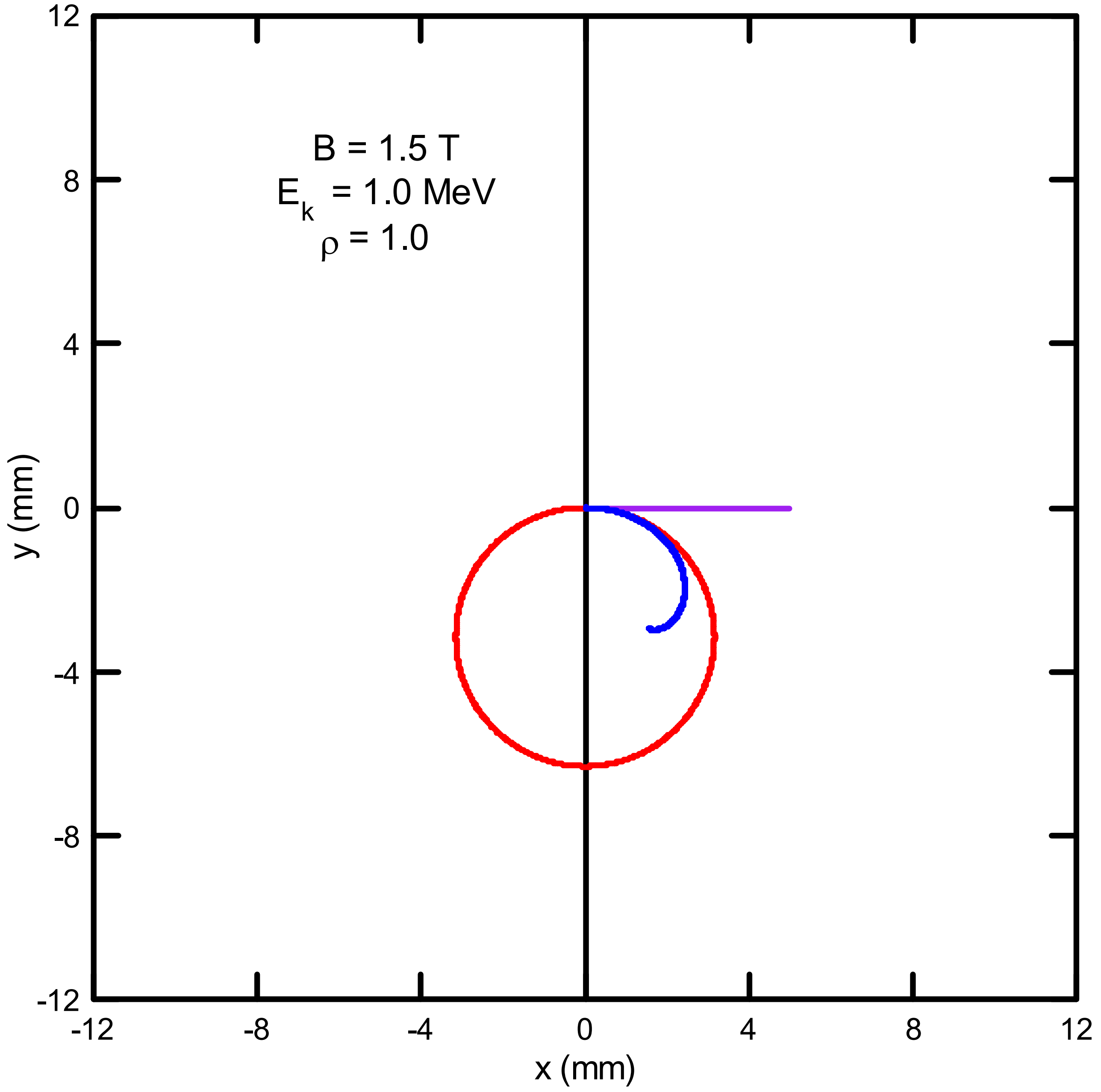
- Range increases
- Radius of trajectory increases
- Dose dislocation increases
- Reduced build-up effect

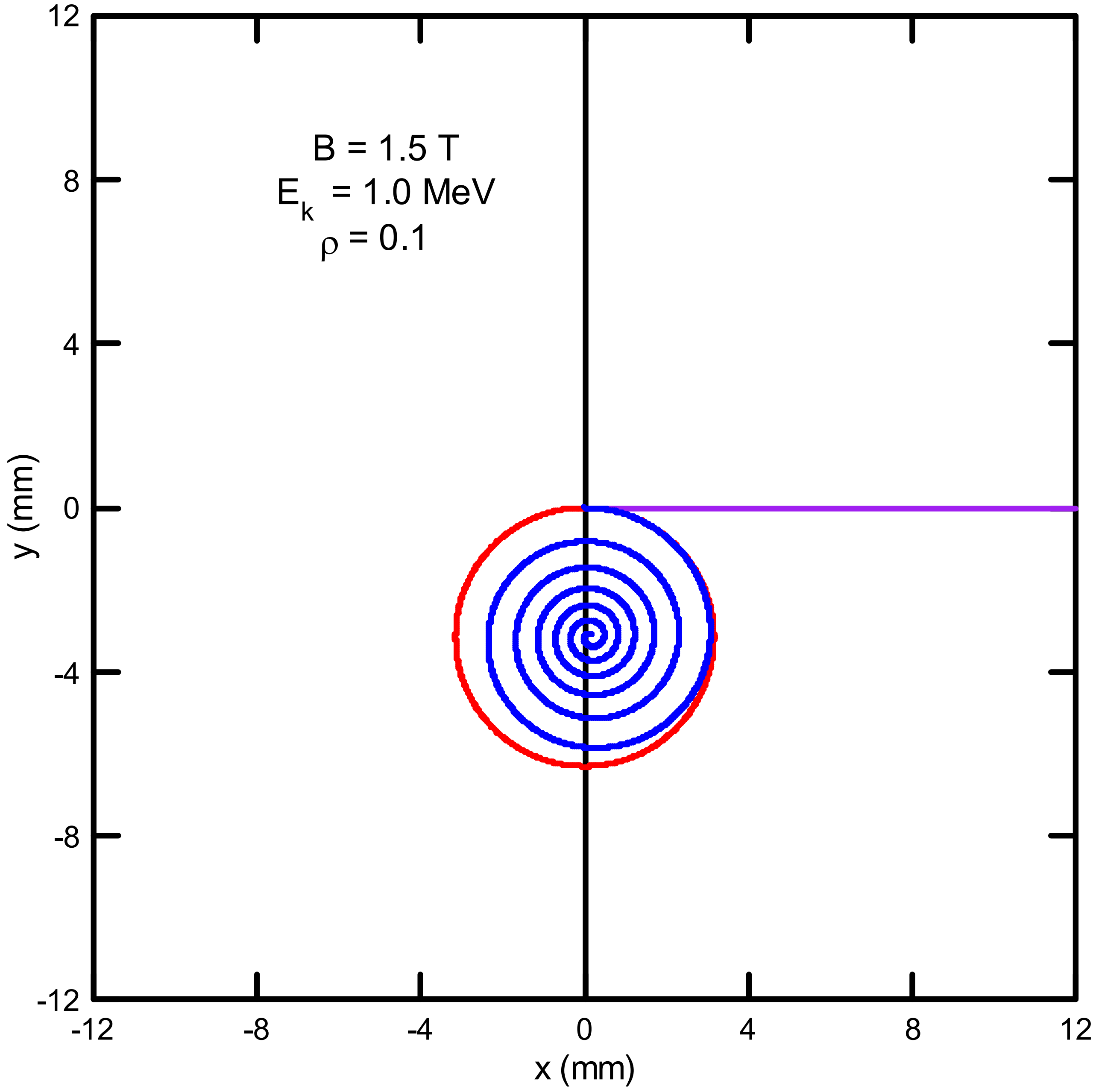
iii) Impact of the electron density

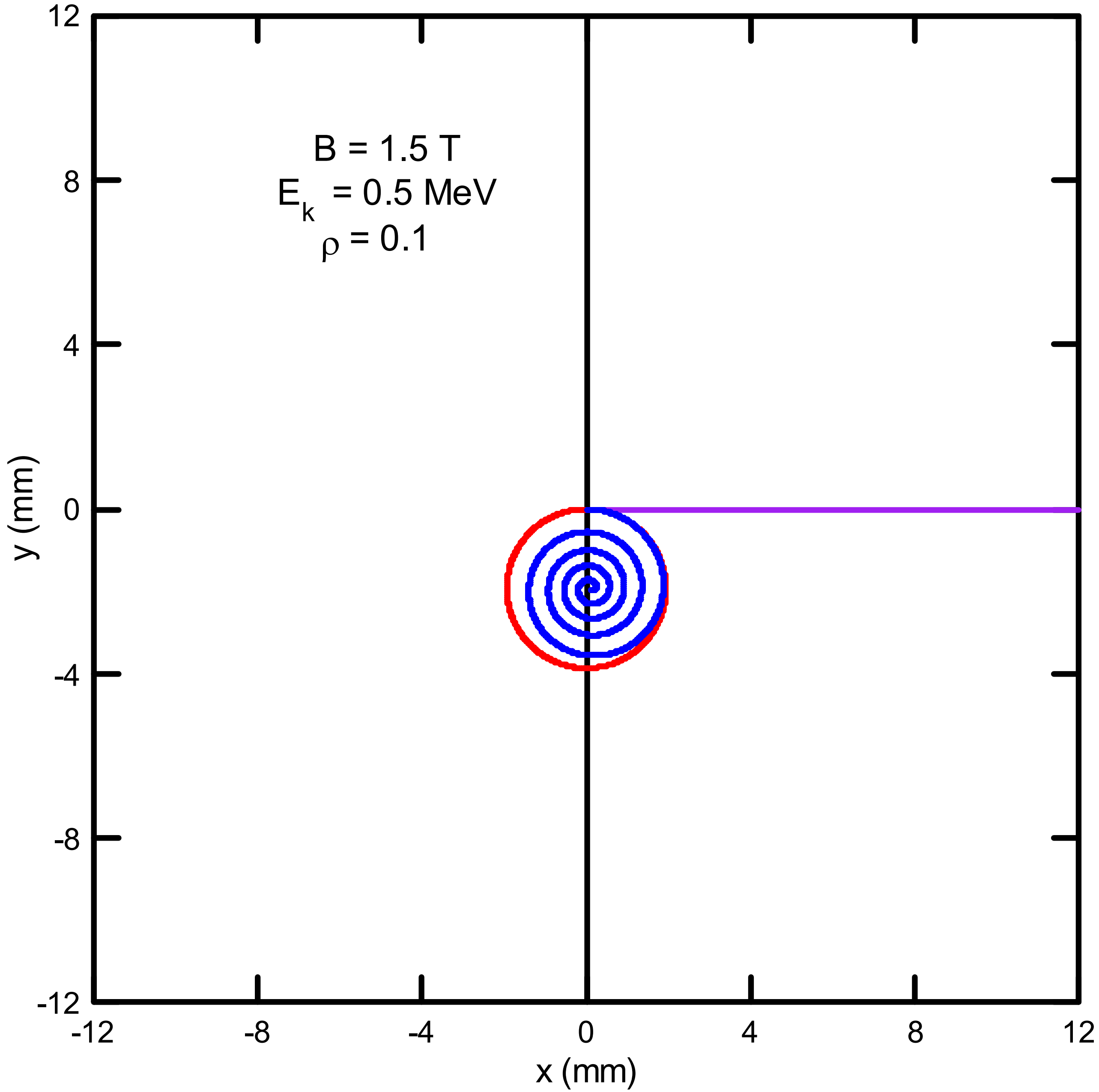


B = 0.35 T
E_k = 1 MeV
ρ = 1.0
y (mm)
x (mm)
30
20
10
0
-10
-20
-30


B = 0.35 T
E_k = 1 MeV
ρ = 0.1
30
20
10
0
-10
-20
-30
y (mm)
-30
-20
-10
0
10
20
30
x (mm)


B = 1.5 T
E$_k$ = 1.0 MeV
ρ = 1.0
y (mm)
x (mm)
12
8
4
0
-4
-8
-12
-12
-8
-4
0
4
8
12


B = 1.5 T
E_k = 1.0 MeV
ρ = 0.1
y (mm)
x (mm)
12
8
4
0
-4
-8
-12
-12
-8
-4
0
4
8
12



B = 1.5 T
E$_k$ = 0.5 MeV
ρ = 0.1
y (mm)
x (mm)
12
8
4
0
-4
-8
-12

Consequences: Decreased electron density

- Range increases
- Radius stays constant
- Dose dislocation/concentration increases
- Reduced build-up effect
- The most ‘dramatic’ effect

Point spread kernels as a function of the magnetic field strength

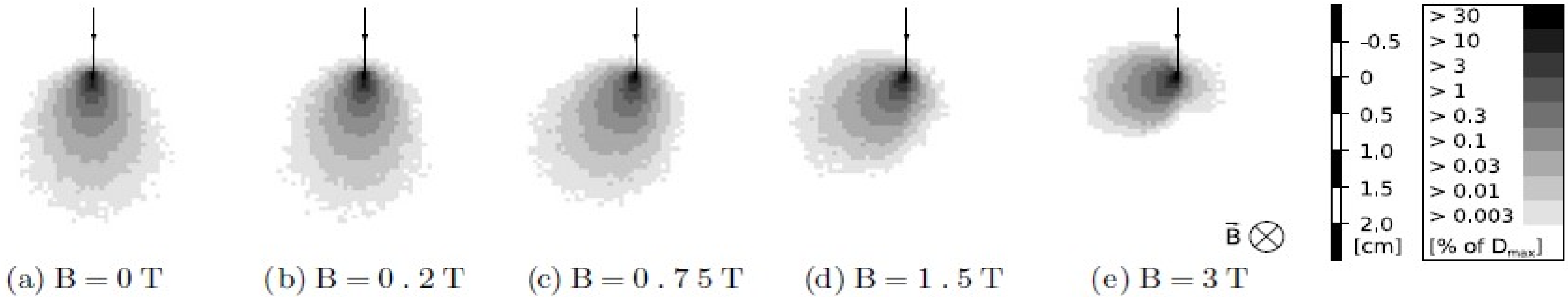


Figure 2. Monte Carlo calculated pointspread kernels for secondary electrons, depending on the magnetic field strength *B*. Logarithmic grey value scaling is used. Primary photons are simulated with a realistic 6 MV linear accelerator energy spectrum.

From Raaymakers et al. PMB 53:909-923(2008)

Electron Return Effect (ERE) at tissue air boundaries

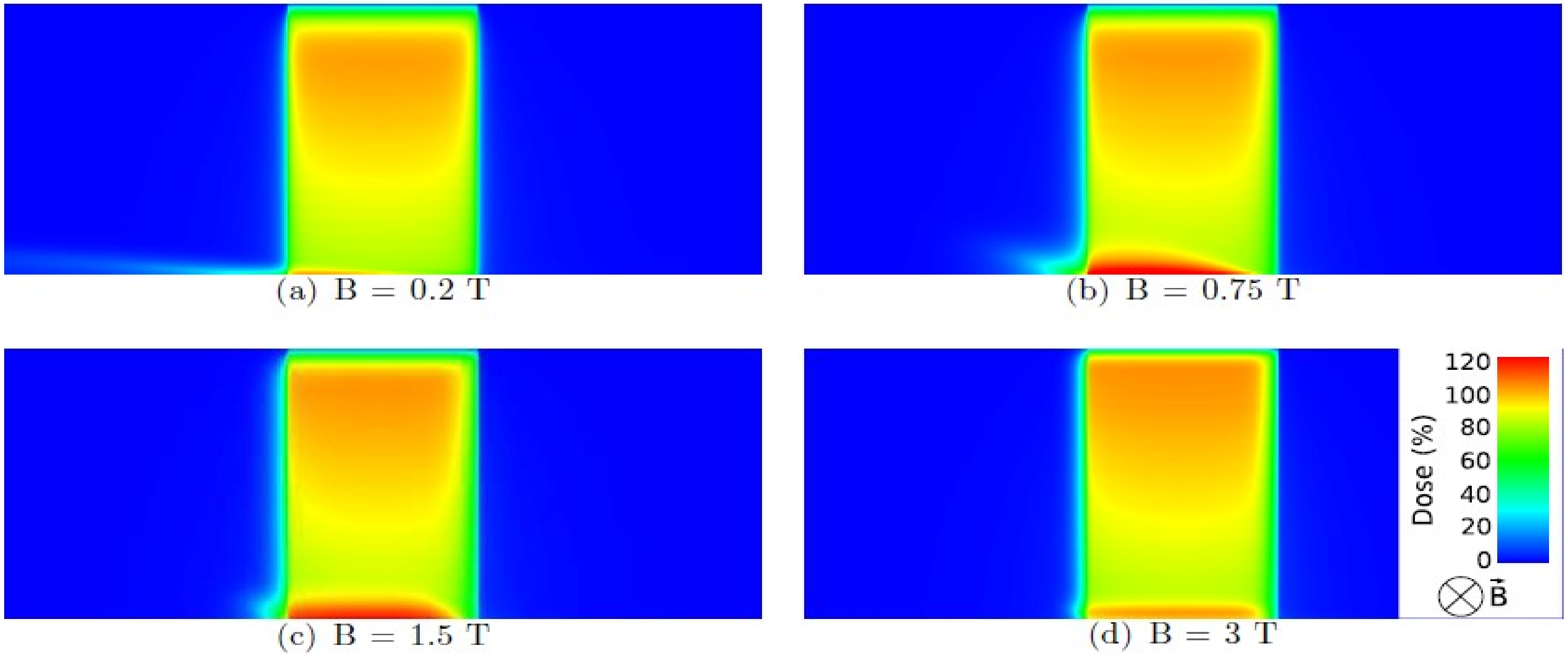


Figure 4. Dose distributions for a 5 × 5 cm^2 6 MV photon beam at the indicated magnetic field strengths.

From Raaymakers et al. PMB 53:909-923(2008)

Comparative Treatment Planning Impact of ERE in lung

Study design

4DCT data of nine stage I lung cancer patients

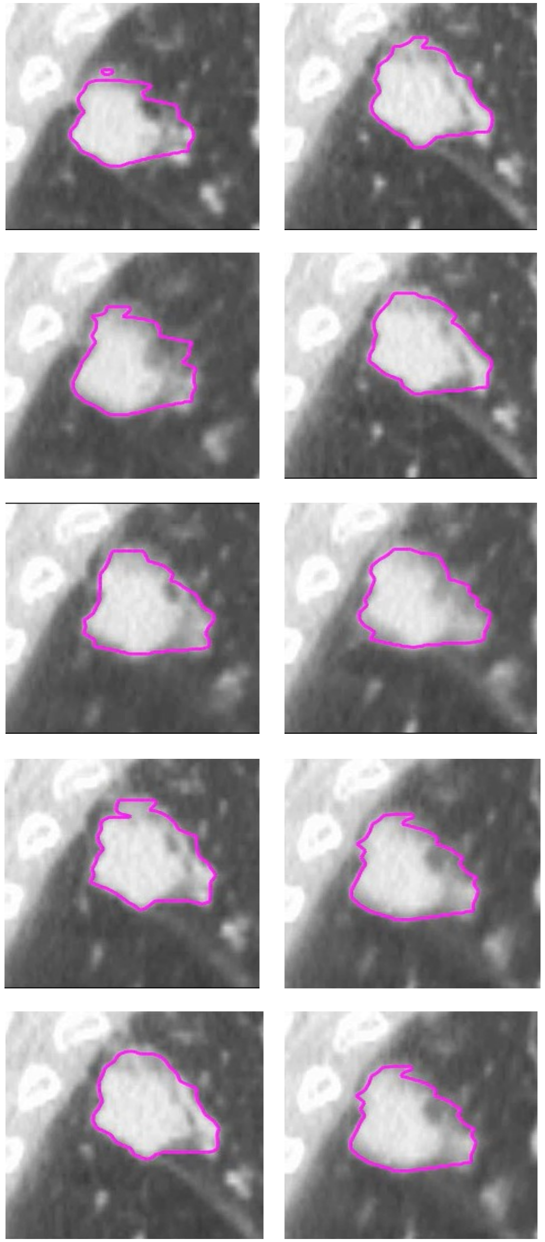
↓

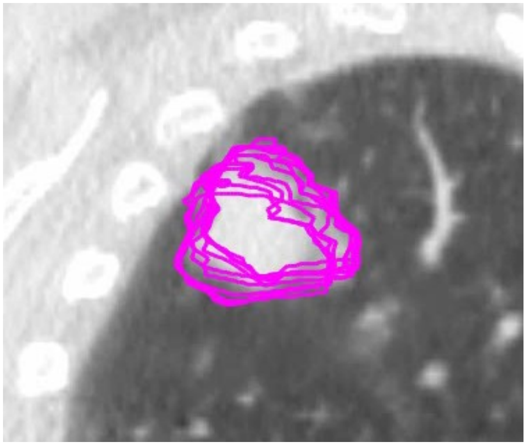
Contouring

- Design of treatment plan using ITV approach without magnetic field
- Design of treatment plan using MTV approach without magnetic field
- Design of treatment plan using MTV approach with 1.5T magnetic field
- Design of treatment plan using ITV approach with 1.5T magnetic field

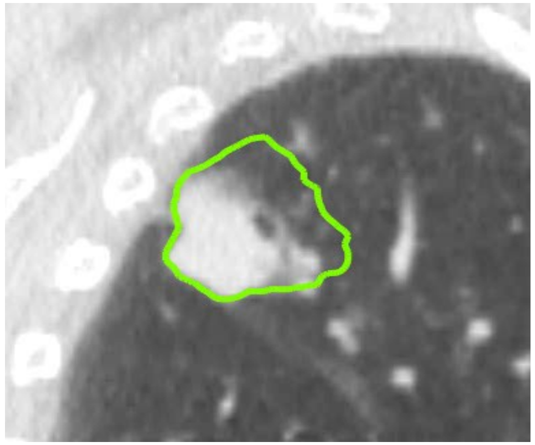
Menten et al., Radiotherapy and Oncology 2016

ITV vs MTV concept

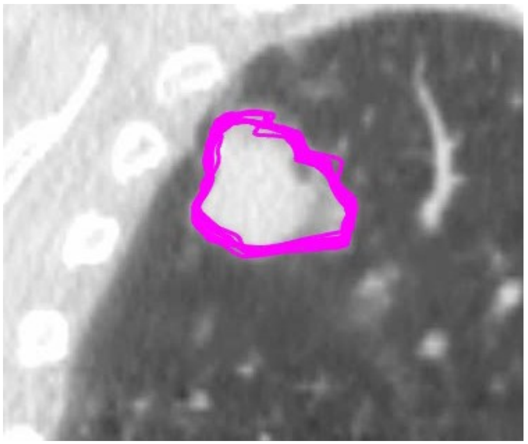




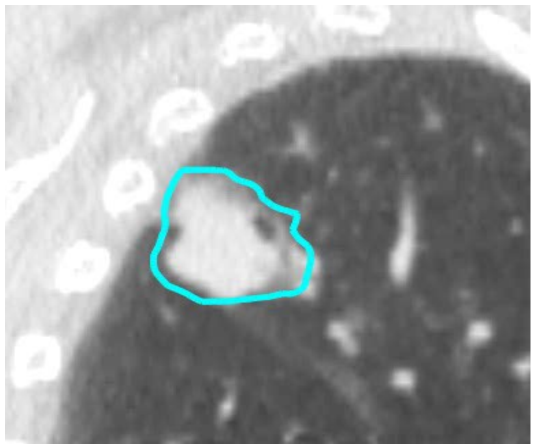
Overlay of all CTVs



Unified maximum =
Internal Target Volume (ITV)



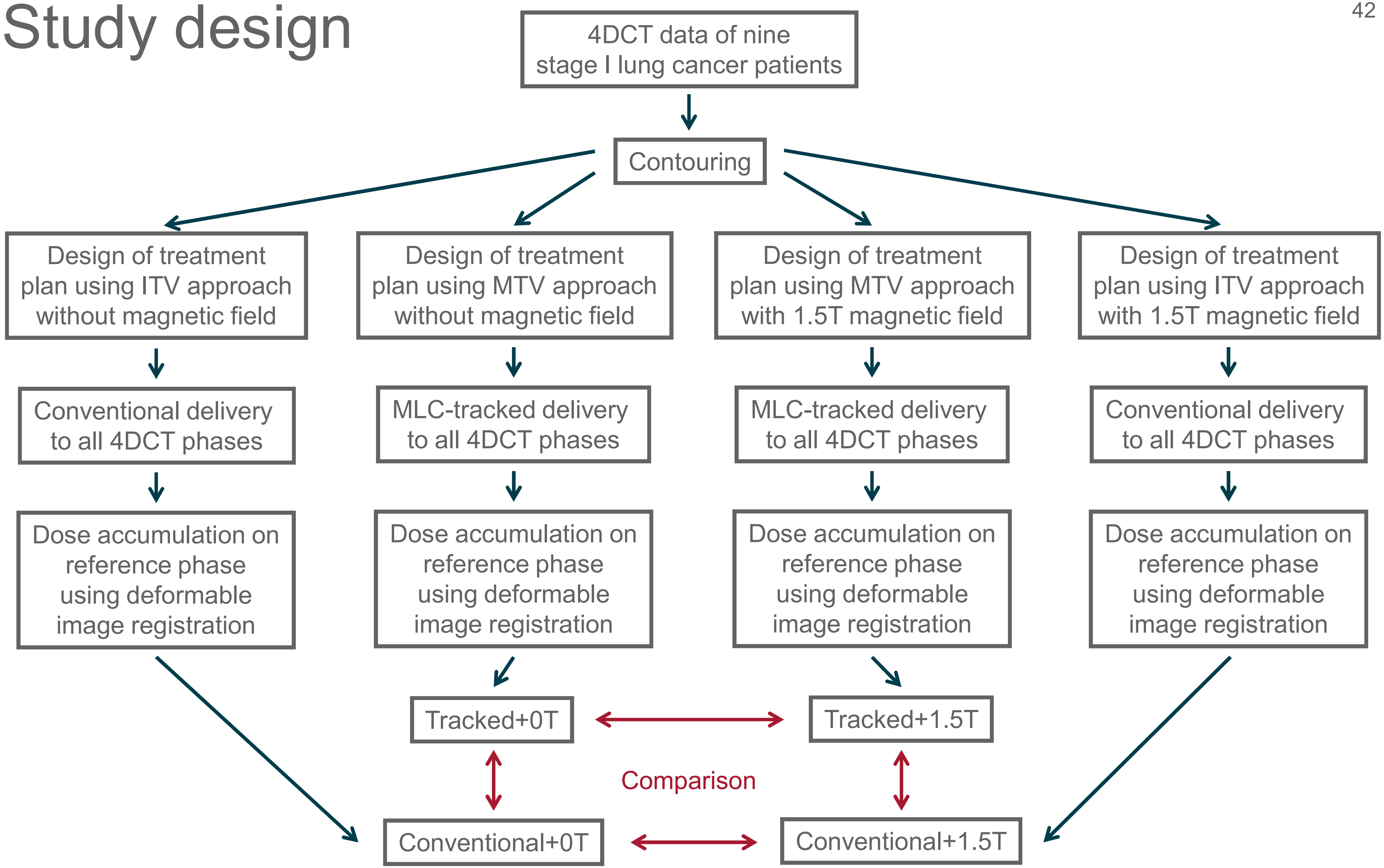
Overlay of all rigidly aligned CTVs



Unified maximum =
Motion Target Volume (MTV)

Kamerling and Fast et al., AAPM 2015

Study design



Menten et al., submitted to Radiotherapy and Oncology

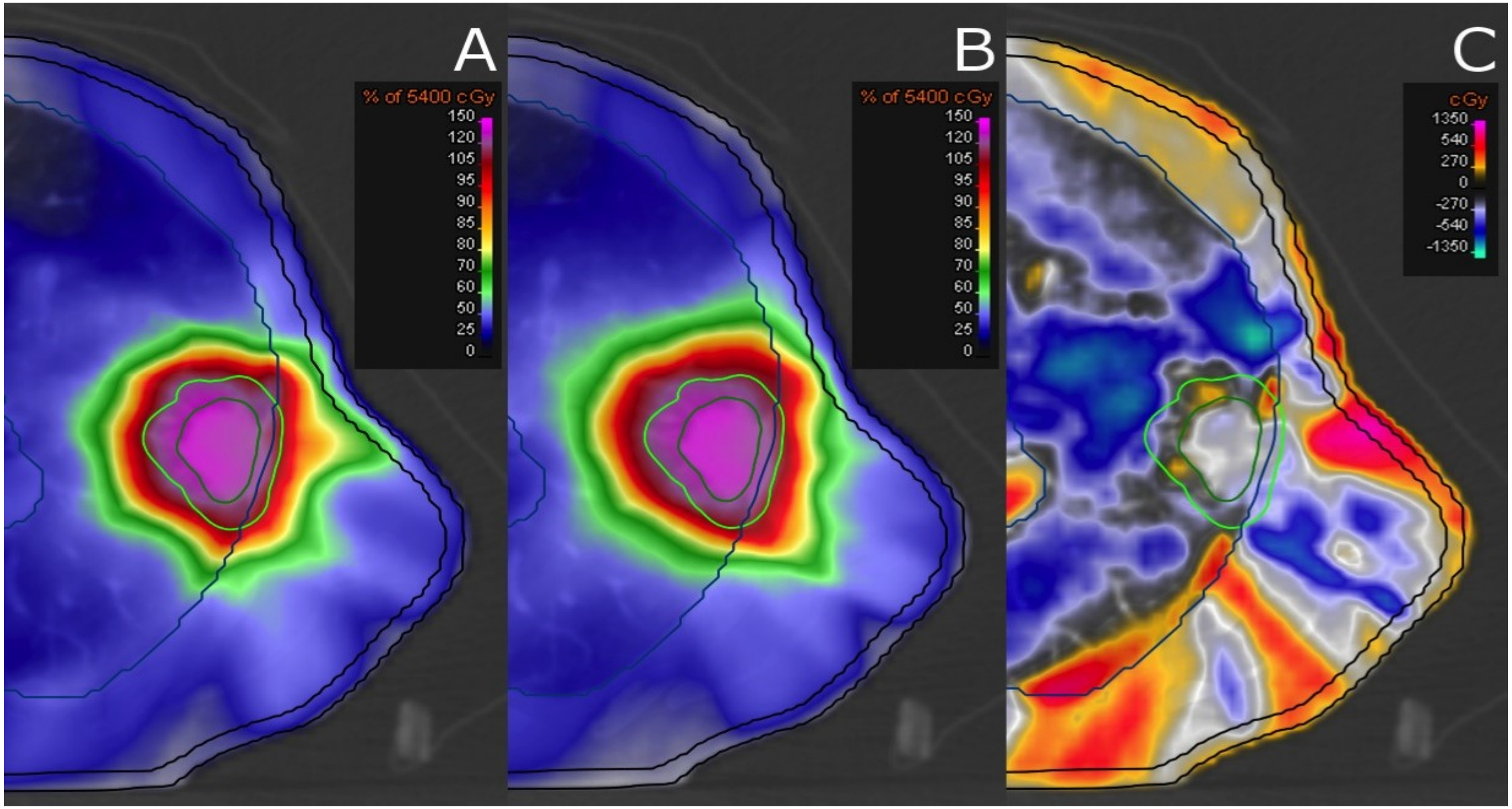
Results: effect of magnetic field

	Effect of 1.5 T magnetic field during			
	conventional delivery		tracked delivery	
	Difference	p-value	Difference	p-value
GTV - $D_{98\%}$ [Gy]	-0.83 ± 0.91	0.03	-0.92 ± 0.76	0.0065
Skin - $D_{2\%}$ [Gy]	$+1.29 \pm 0.52$	< 0.0001	$+1.38 \pm 0.55$	< 0.0001
Lungs - D_{mean} [Gy]	-0.09 ± 0.17	0.14	-0.15 ± 0.21	0.06
Integral deposited energy [J]	$+0.09 \pm 1.17$	0.84	-0.01 ± 1.72	0.99
Great vessels - $D_{2\%}$ [Gy]	$+0.75 \pm 1.58$	0.19	-0.05 ± 1.73	0.91
Oesophagus - $D_{2\%}$ [Gy]	-0.58 ± 1.34	0.23	-1.15 ± 2.15	0.15
Proximal airways - $D_{2\%}$ [Gy]	-0.06 ± 0.90	0.83	-0.87 ± 1.85	0.20
Ribs - $D_{2\%}$ [Gy]	-0.57 ± 0.87	0.08	-0.63 ± 1.39	0.21
Skin - D_{mean} [Gy]	$+0.10 \pm 0.03$	< 0.0001	$+0.09 \pm 0.03$	< 0.0001
Spinal cord - $D_{2\%}$ [Gy]	-0.50 ± 1.84	0.44	-0.11 ± 0.33	0.81

Despite the increase in skin dose and decrease in dose to the GTV, the target prescription was exceeded in all treatments and they were deemed clinically acceptable with regard to normal tissue exposure

Menten et al., submitted to Radiotherapy and Oncology

Results: effect of magnetic field



With magnetic field | Without magnetic field | Local difference

Menten et al., Radiotherapy and Oncology 2016

Conclusions

- When accounting for the magnetic field during treatment planning, it is possible to design clinically acceptable lung SBRT treatments

Impact on treatment delivery

- Inter-fraction treatment adaptation
- Real time adaptive radiation therapy

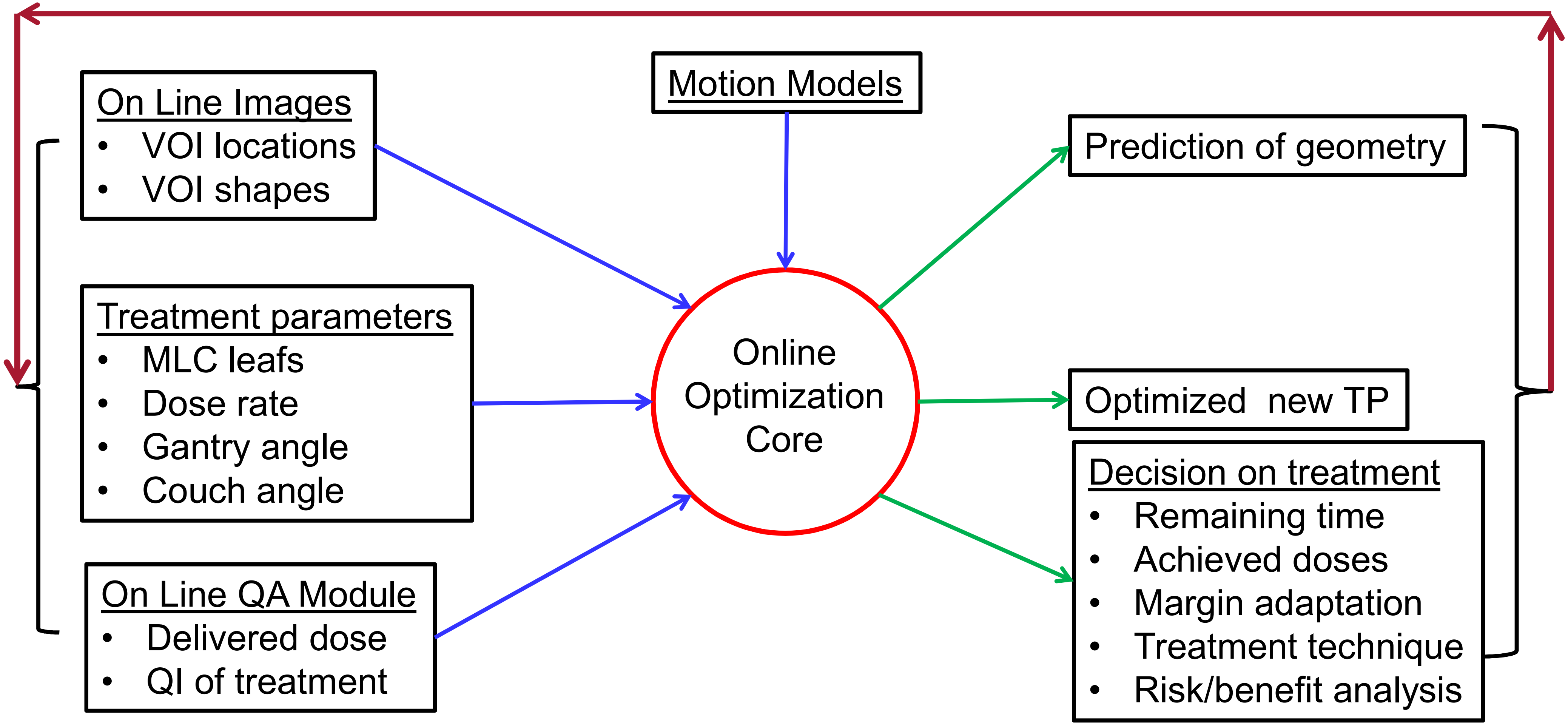
The Task: Treating what we see

Patient scheduled for 5-20 minute treatment

????

- Optimal treatment for the anatomy observed at this time
- Not the anatomy we once have observed
- Original Plan is almost certainly not optimal

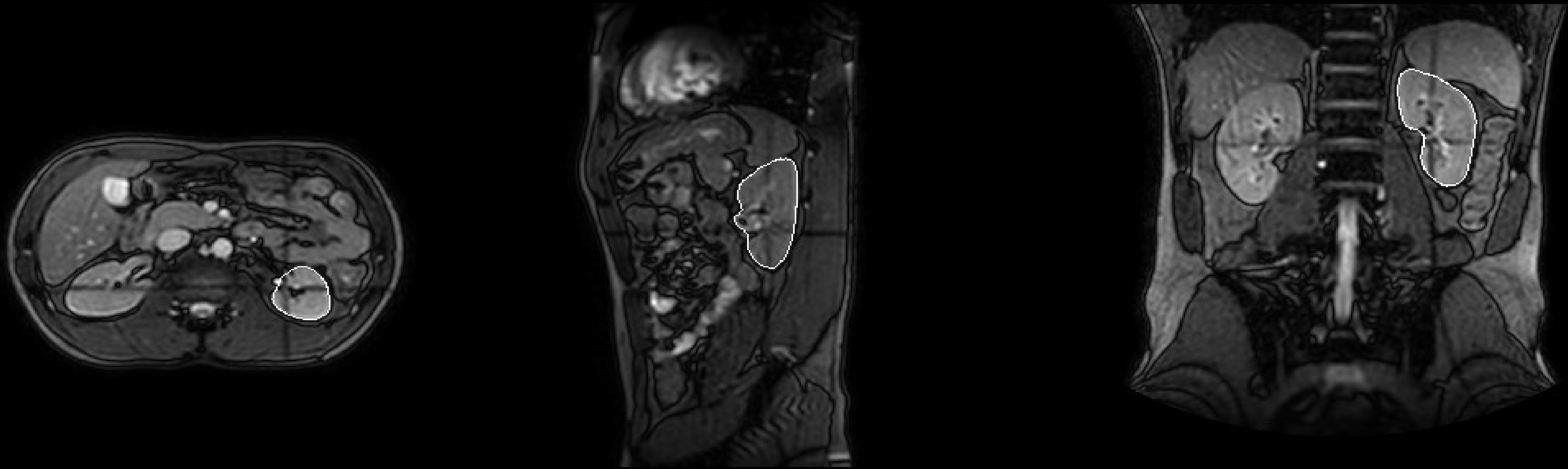
Online adaptation
(5 – 15 mins)



Challenges

- Speed of software components
  - Dose calculation/updates
  - VOI segmentation/registration
  - Risk/benefit analysis
  - Treatment time as constraint to dynamic adaptation
  - Decision making….
- Reliable automation of processes
- On-line image quality/speed of image acquisition
  - X – ray imaging vs. MRI

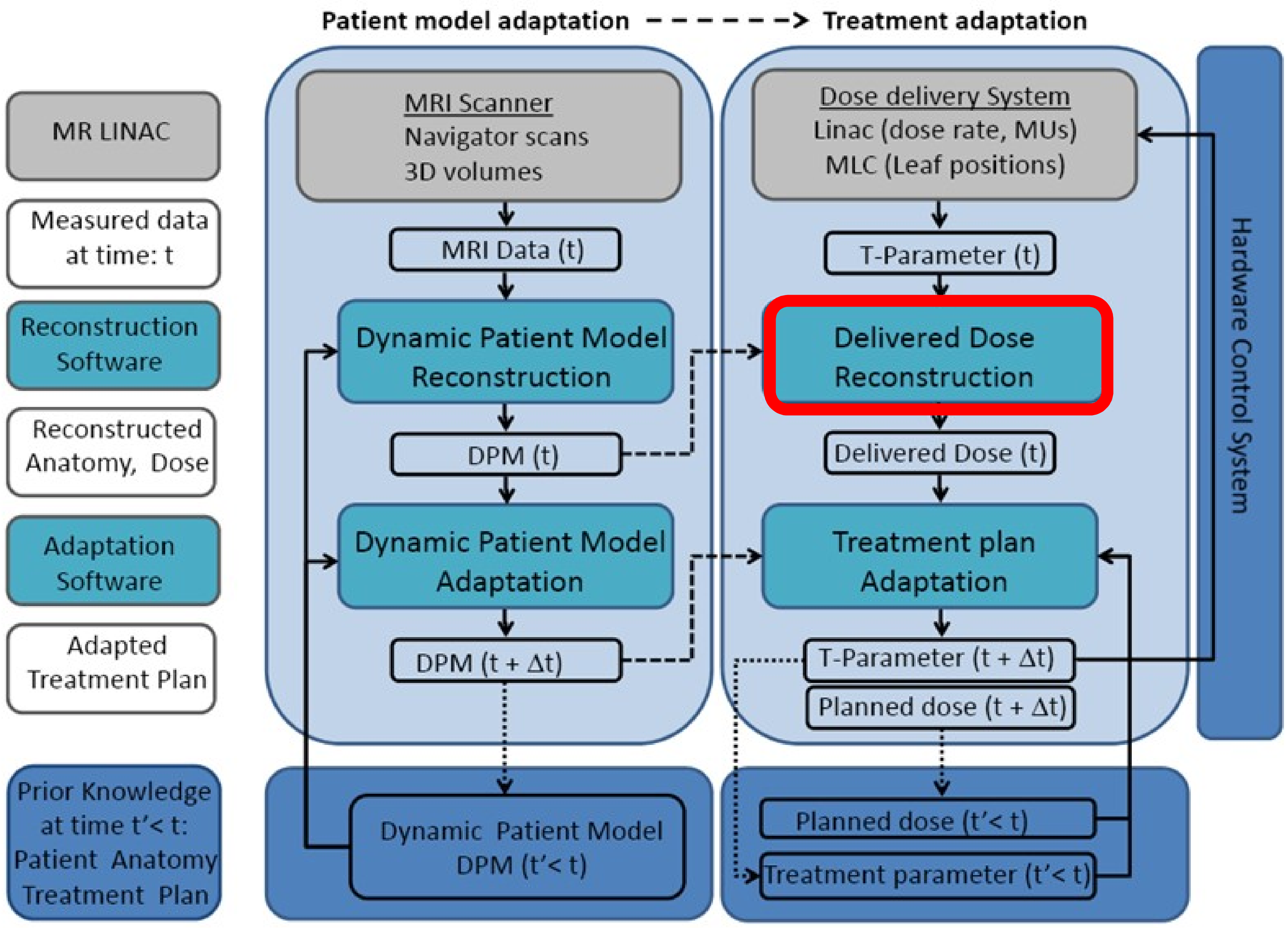
Atlantic pilot system: Image and detect anatomy in real time



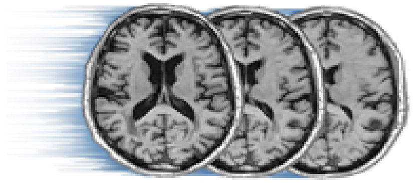
Alternating axial, coronal and sagittal slices acquired and processed in 200 ms

Courtesy of Elekta / Philips

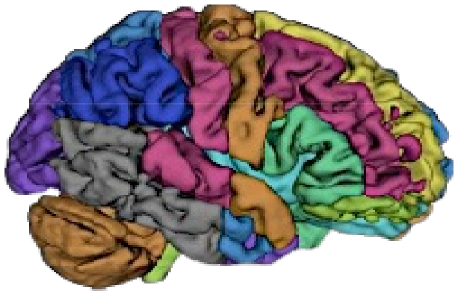
Real-time therapy adaptation



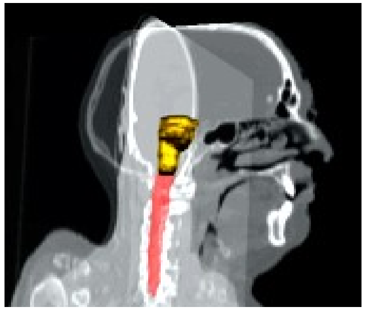
NiftyReg



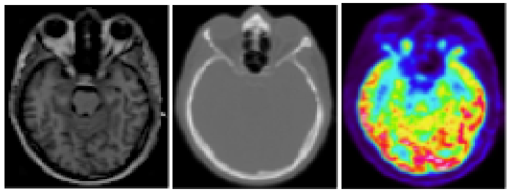
- Open-source tools for efficient image registration
- Used in various applications



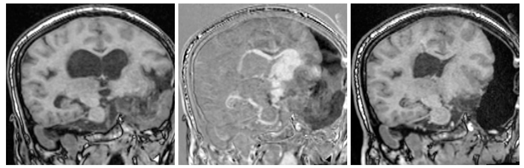
Neuroimaging



Oncology / radiotherapy

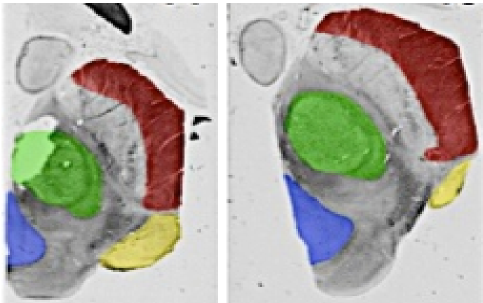


PET/MRI + pCT

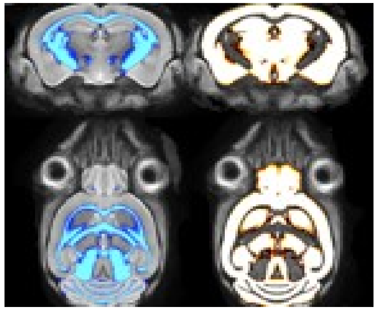


Interventional MRI

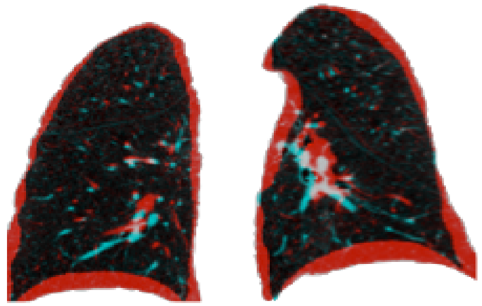
Cardiac imaging



Histology

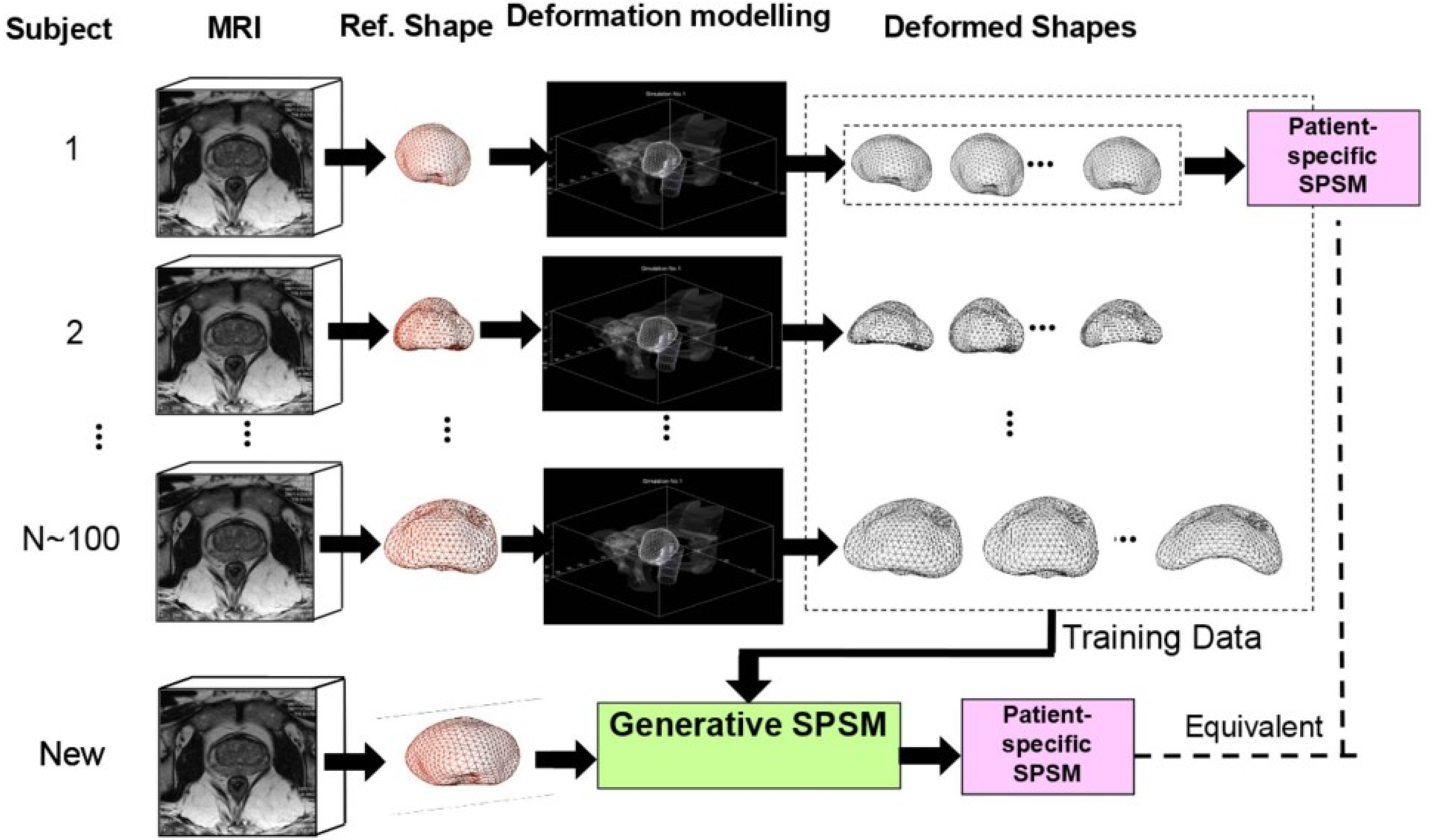


Small animal imaging

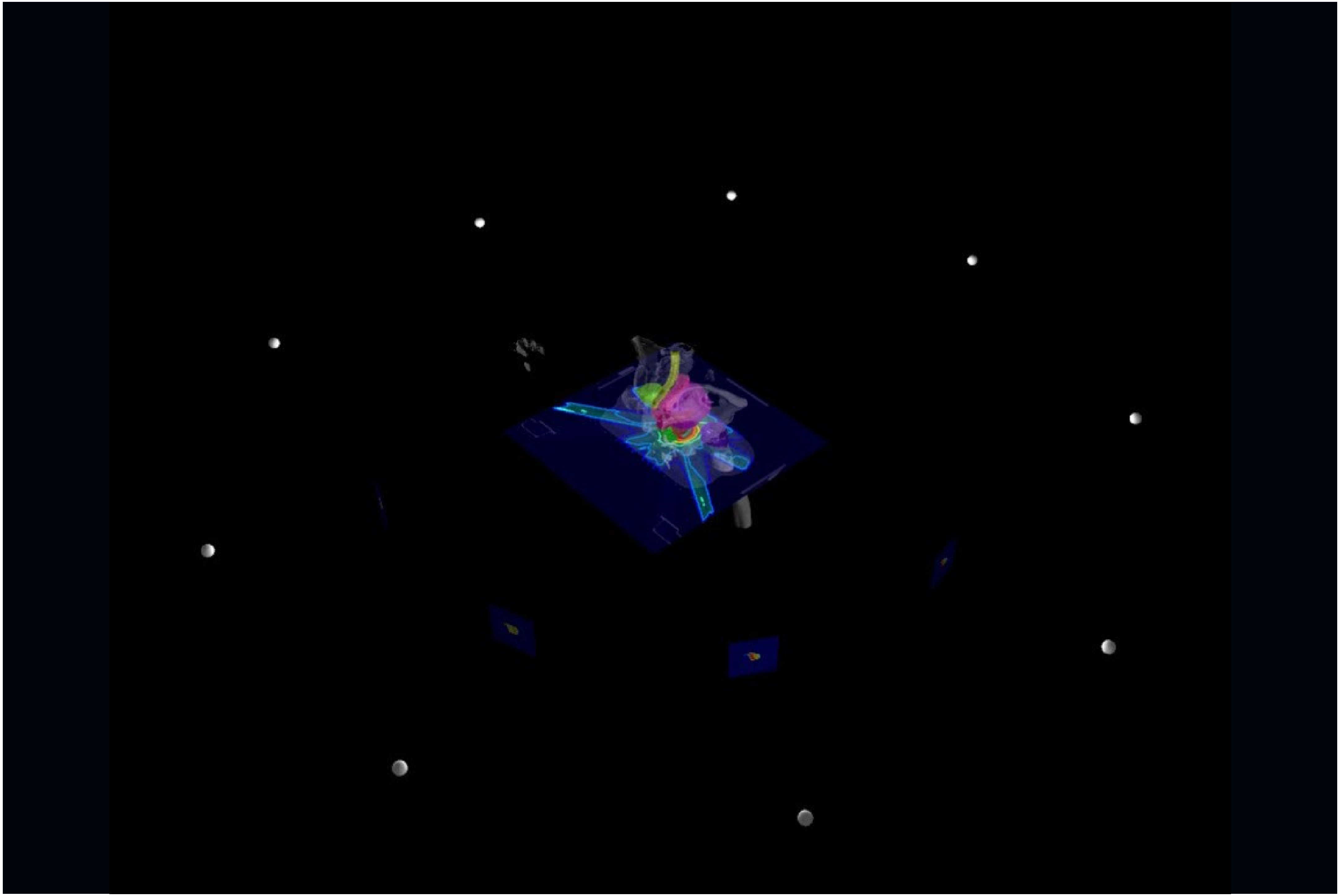


Motion modeling

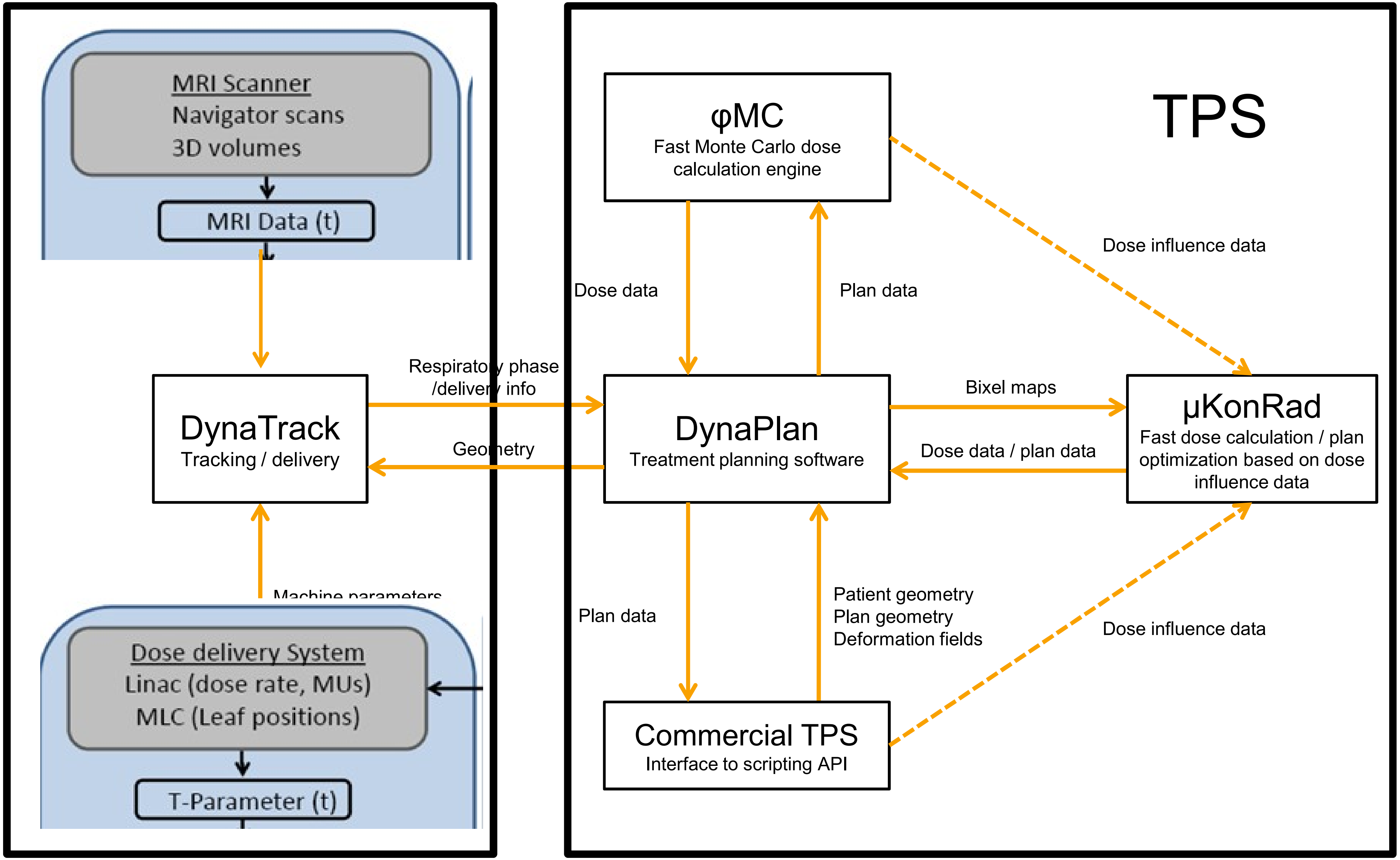
Automatic generation of deformable organ models



Hu et al. Medical Image Analysis, 2012



Research RT software platform at ICR



Real time dose reconstruction for tumour tracking

Prior Knowledge:

•Dynamic Patient Model - 4D-CT

•Pre-calculated Dose Influence Data for 'all' potential tumour positions (200-1300MB dose influence data per beam (generated by Commercial TPS)

Real time dose reconstruction for tumour tracking

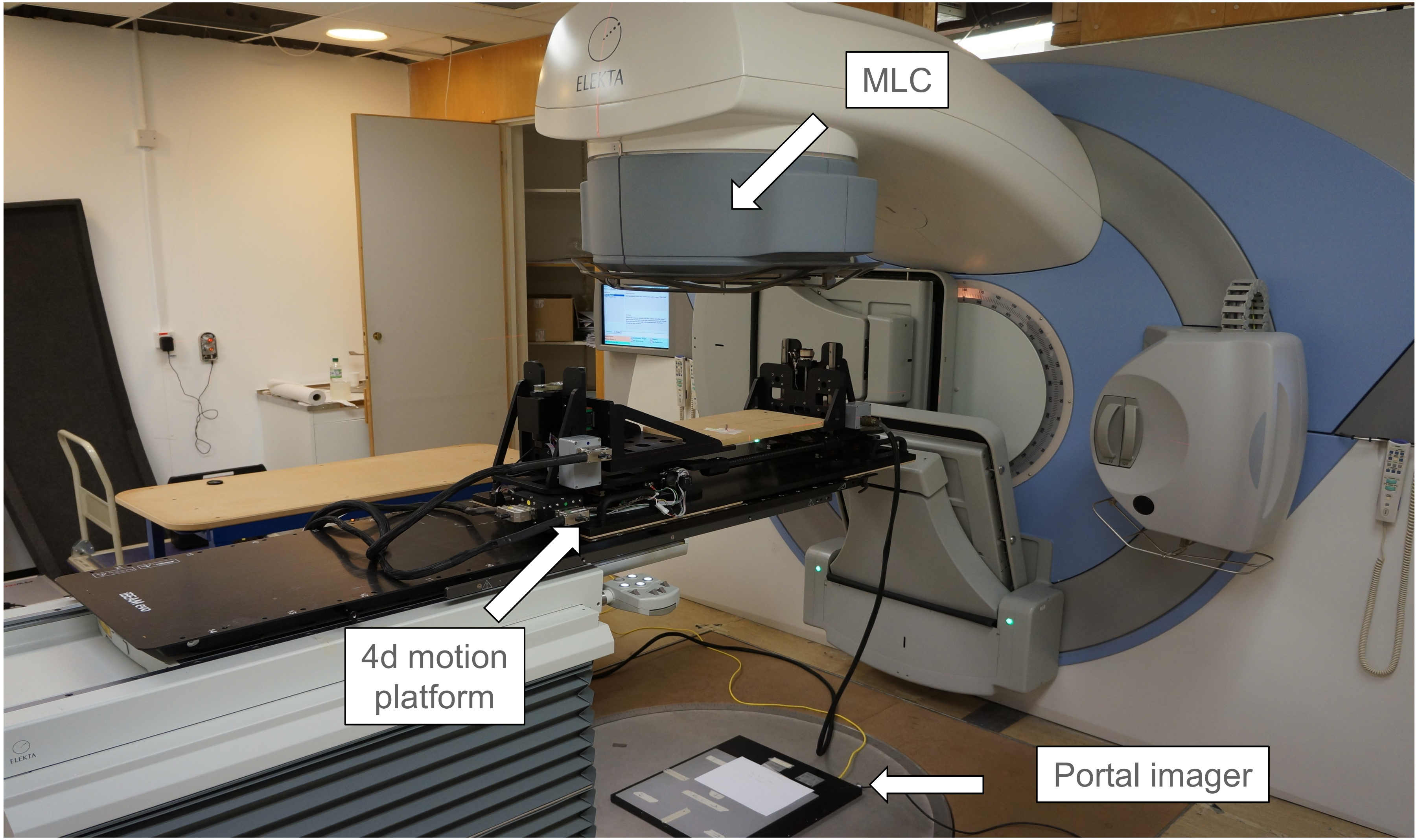
‘Experiment’:

- Interface between tracking tool and Elekta Synergy linac / Agility MLC
- Network communication between tracking tool and research TPS
- Simulated Target positions (every 20ms)
- Adapted MLC positions (every 40ms)

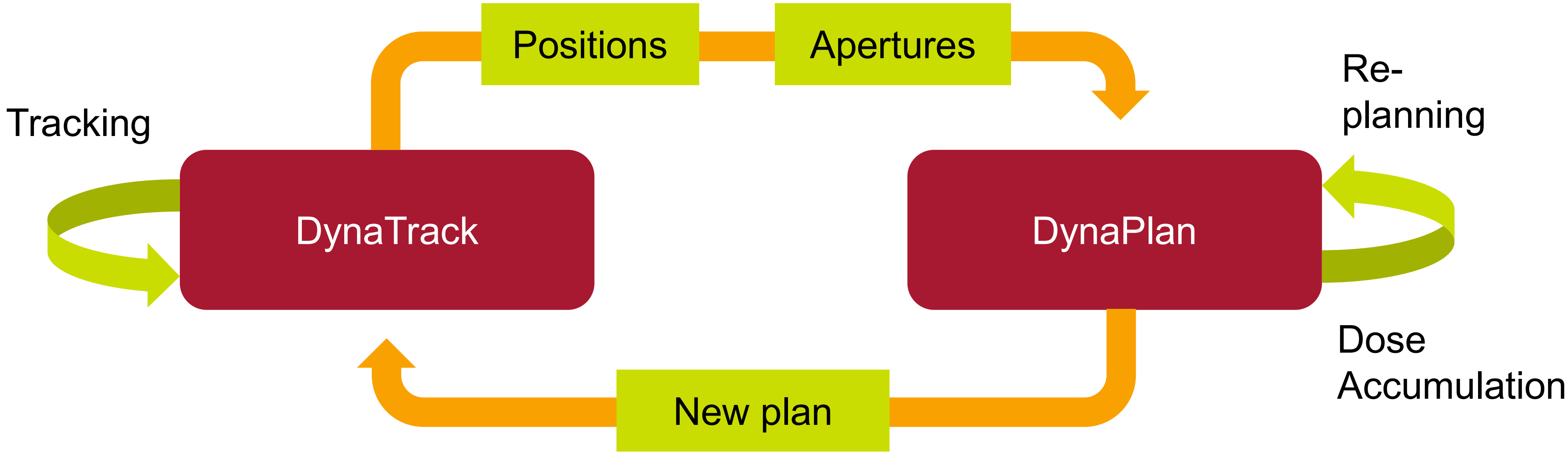
Dose reconstruction scenarios:

1. Static delivery (no motion, no tracking)
2. Conventional delivery (motion, no tracking)
3. Adaptive delivery (motion, tracking)

Experimental set-up: Maple



Dose reconstruction & re-planning



- QA/safety aspect
- Differential target-OAR motion

DynaTrack + DynaPlan

Clinical Expectations for MR guided radiation therapy: Current Processes

Parag Parikh, BSE, MD

Associate Professor of Radiation Oncology & Biomedical Engineering

Washington University School of Medicine

St. Louis, Missouri, USA

Disclosures

Research Funding

- Philips Medical
- Varian Medical Systems
- Viewray Inc

Ownership

- Holaira, Inc

Consulting

- Oraya, Inc.
- Holaira, Inc
- Newlink Genetics
- Ethicon
- Medtronic
- Litigation

Objectives

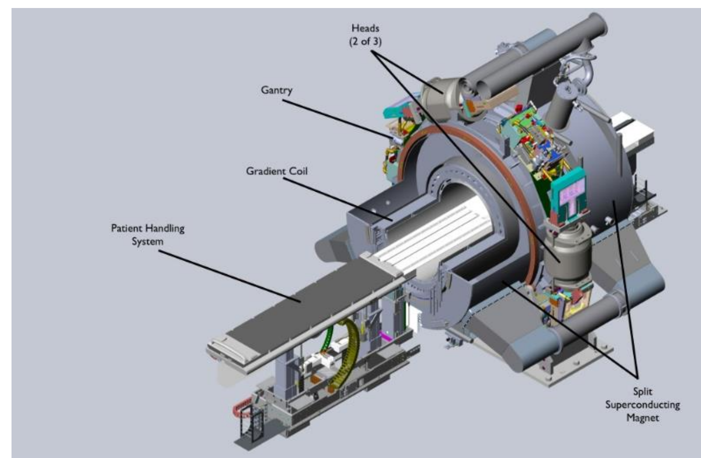
To understand that there are institutions already performing MRgRT with custom integrated MR-RT systems

To list anatomic sites that may better be visualized with MR as compared with CBCT

To be able to give examples of current organ sites treated with MRgRT

First clinical implementation of MRgRT

- 0.35T MRI integrated with 3 Co-60 heads
  - ~550 cGy/min @ iso
- 3 fully divergent MLCs (minimized penumbra)
- Large imaging FOV (50 cm) and Tx volume (27cmx27cm)
- 4 frames / second saggital cine imaging during
- Integrated planning system
  – Monte Carlo dose calculation



MRgRT timeline

1/2014 -First patient treatment

9/2014 -First online adaptive treatment
(Conventional fractionation)

1/2015 - First online adaptive SBRT

2/2015 - First online adaptive SBRT
with MRTC (gating)

Today 6 clinical sites

Washington University, St. Louis, Missouri, USA

UCLA, Los Angeles, California, USA

University of Wisconsin, Madison, Wisconsin, USA

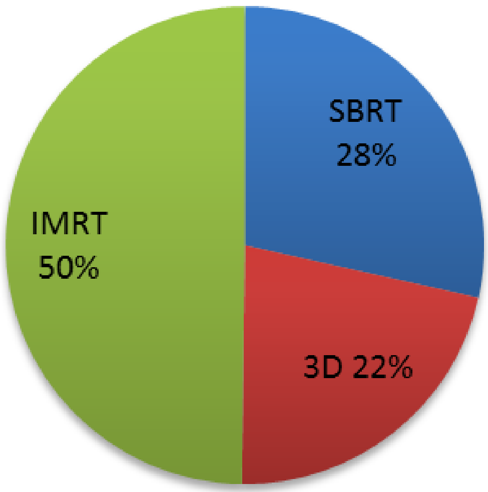
University of Miami, Miami, Florida, USA

Seoul National University Hospital, Seoul, South Korea

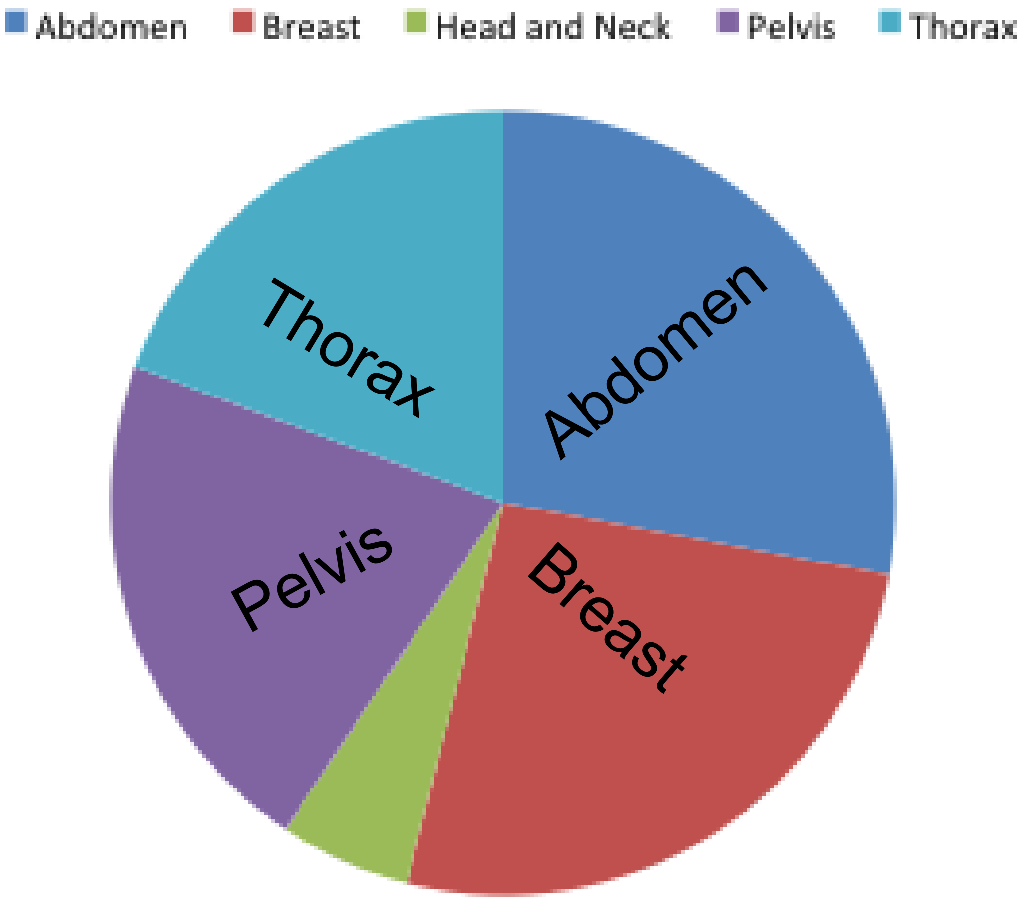
VUMC, Amsterdam, Netherlands

>500 total patients treated!

WashU MRgRT Treatment Case Makeup



Treatment Type (%)



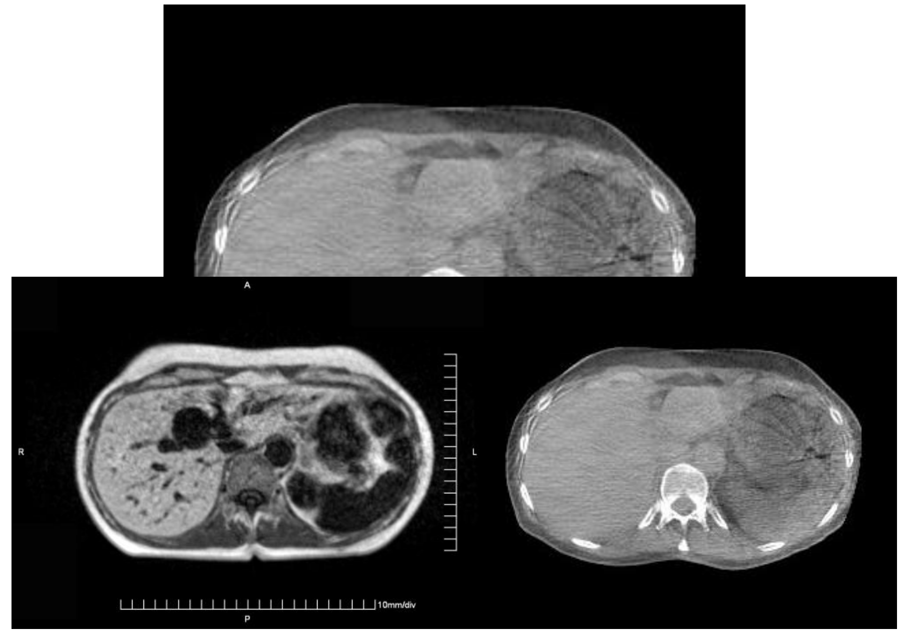
September, 2016

MRI imaging is better than CBCT

Onboard CT images used for routine treatment localization were collected

- MVCT or kVCT
- In-plane resolution: ~1-1.5mm
- Slice thickness: 2.5 - 4.0 mm

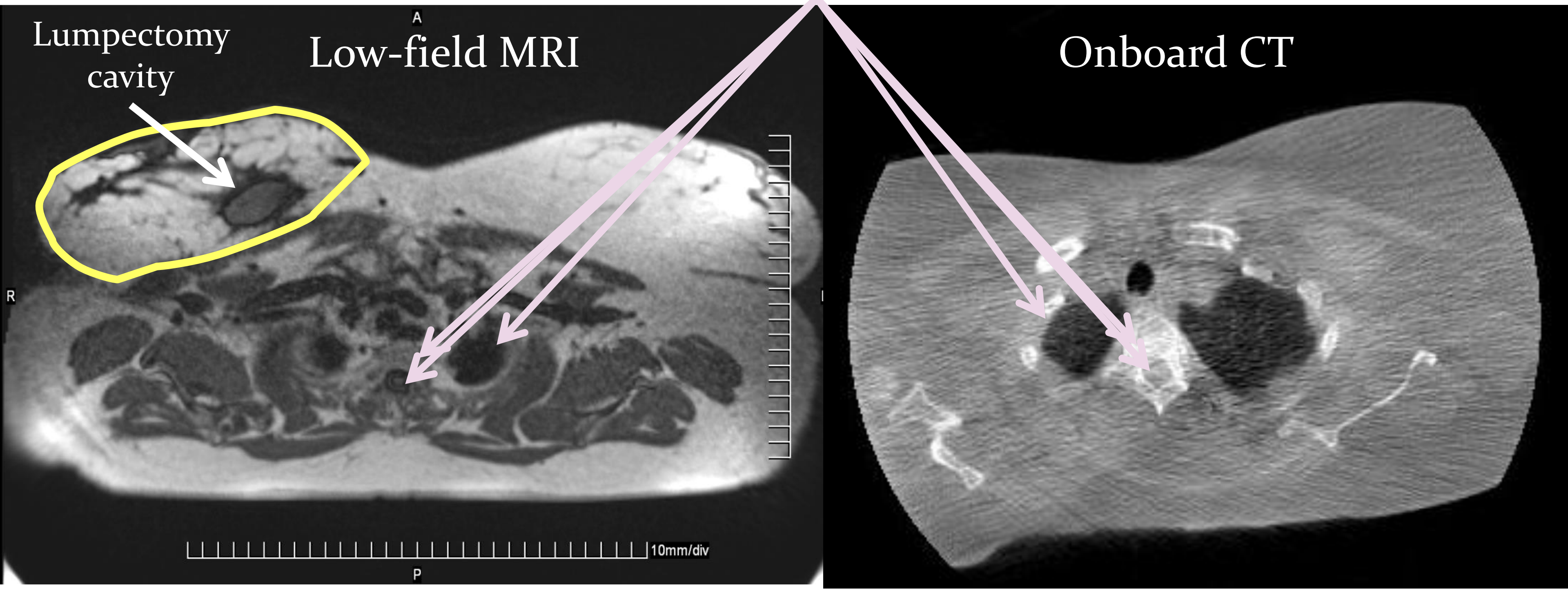
3 radiation oncologists evaluated the low-field MRI & onboard CT images side-by-side



Breast Cancer Patient

Spinal Cord

Bone



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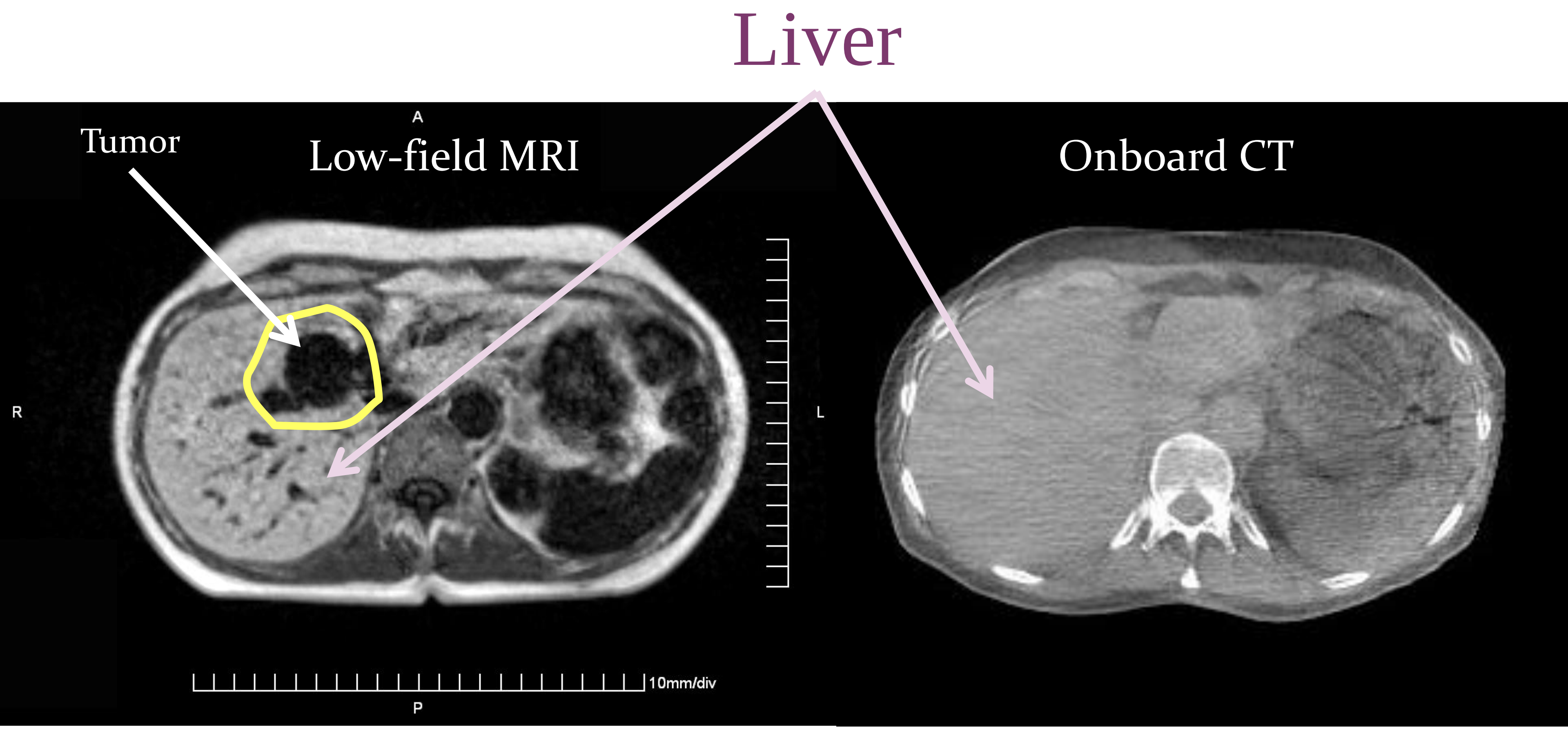
Liver Metastasis Patient



Then, do a bunch of physics stuff

Mazur TR et al, SIFT-based dense pixel tracking on 0.35 T cine-MR images acquired during image-guided radiation therapy with application to gating optimization. Med Phys. 2016 Jan;43(1):279.

Hu Y et al , Characterization of the onboard imaging unit for the first clinical magnetic resonance image guided radiation therapy system. Med Phys. 2015 Oct;42(10):5828-37.

Wooten HO et al, Quality of Intensity Modulated Radiation Therapy Treatment Plans Using a ^{60}Co Magnetic Resonance Image Guidance Radiation Therapy System. Int J Radiat Oncol Biol Phys. 2015 Jul 15;92(4):771-8.

Wooten HD et al, Benchmark IMRT evaluation of a Co-60 MRI-guided radiation therapy system. Radiother Oncol. 2015 Mar;114(3):402-5.

Li HH et al, Patient-specific quality assurance for the delivery of (60)Co intensity modulated radiation therapy subject to a 0.35-T lateral magnetic field. Int J Radiat Oncol Biol Phys. 2015 Jan 1;91(1):65-72

Mutic S et al, The ViewRay system: magnetic resonance-guided and controlled radiotherapy. Semin Radiat Oncol. 2014 Jul;24(3):196-9.

Simulation: CT- and MR- for all patients

Localization: Daily high resolution MR

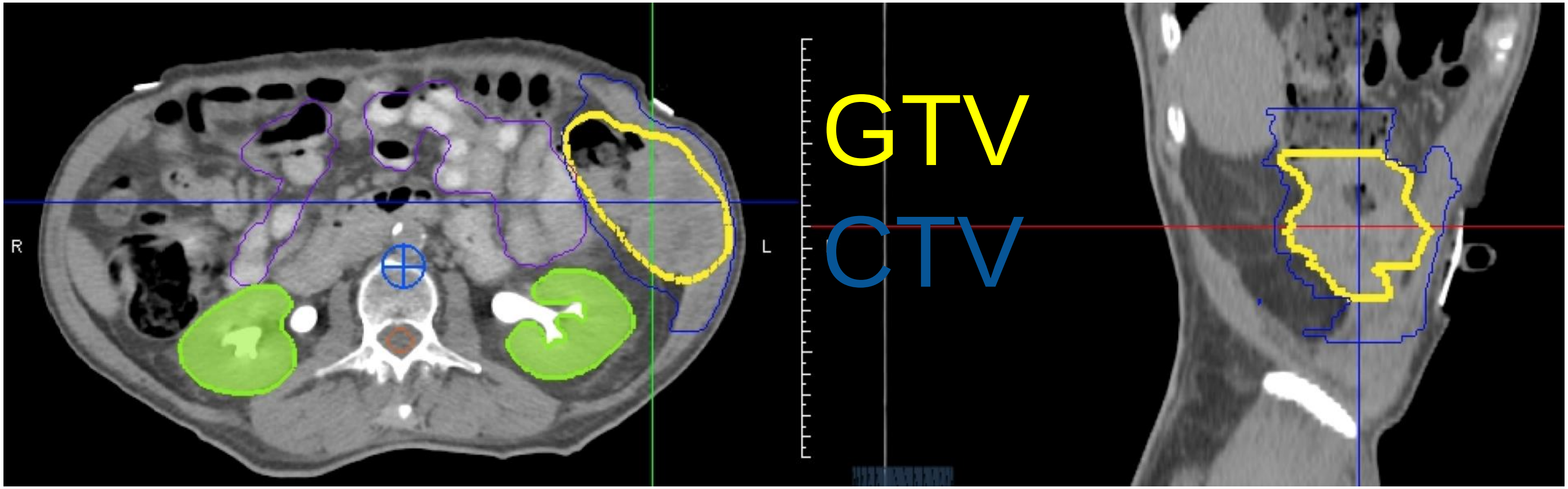
- Deformable registration applied to transfer contours & electron density from initial sim onto daily MR

Case 1:
Locally advanced colon cancer

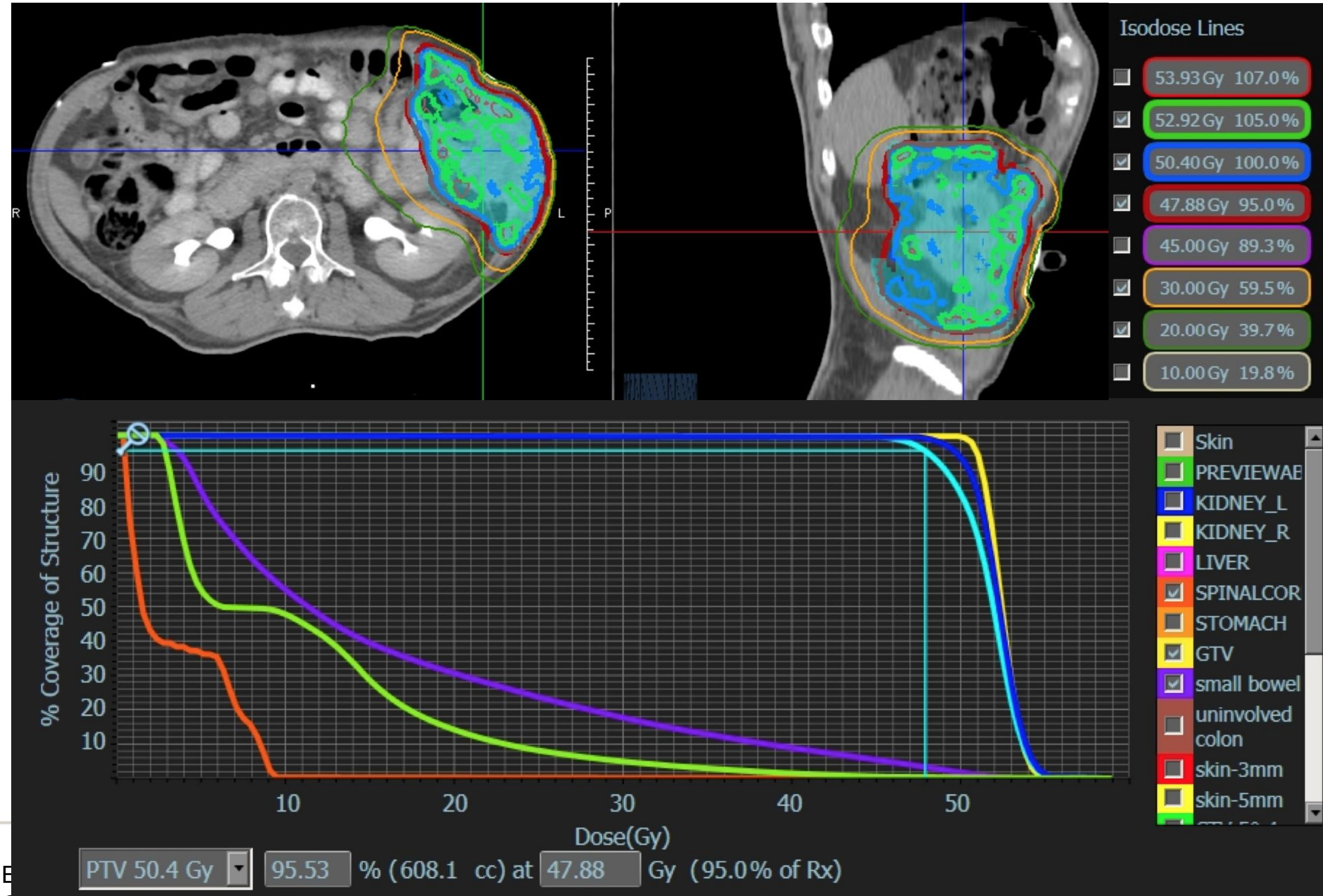
MRG-RT: Initial Experience

64 yo M with T4N0M0 colon cancer (abd wall invasion), s/p FOLFOX x 4 cycle with stable disease referred for pre-op RT

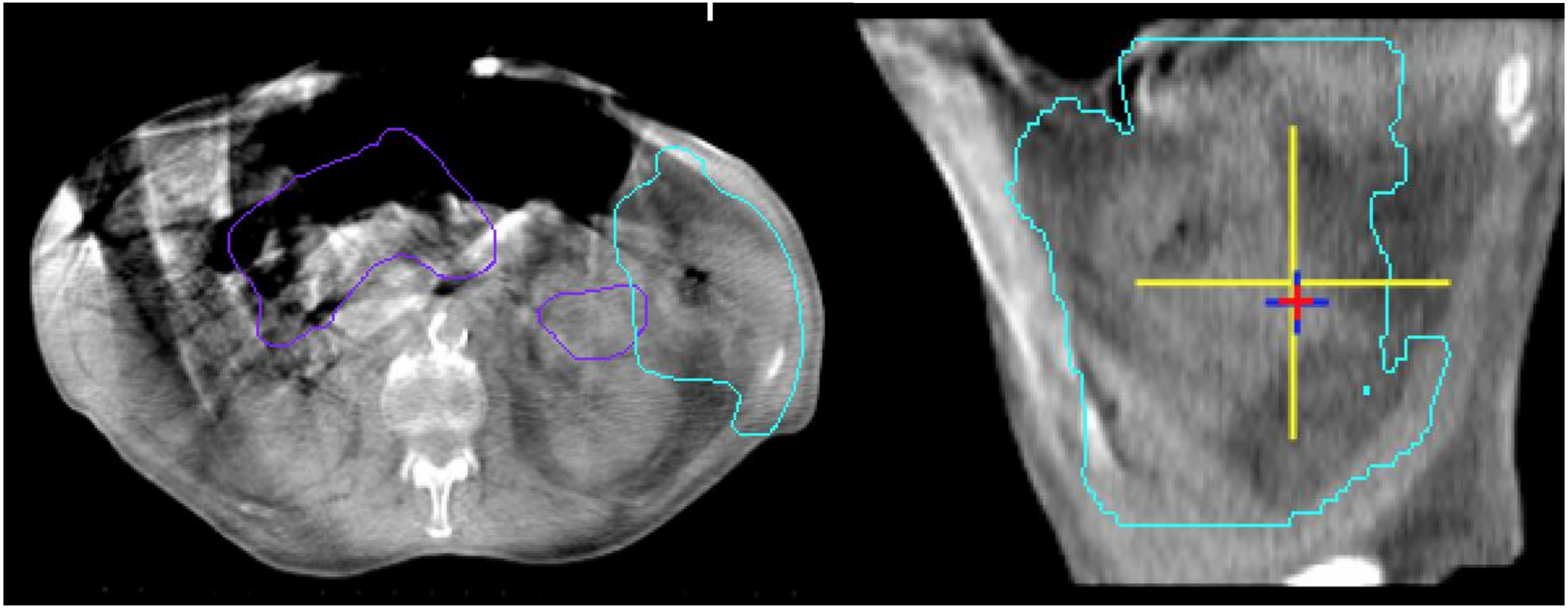
Plan: 50.4 Gy /28 fx with concurrent C.I. 5-FU



MRG-RT: Initial Experience

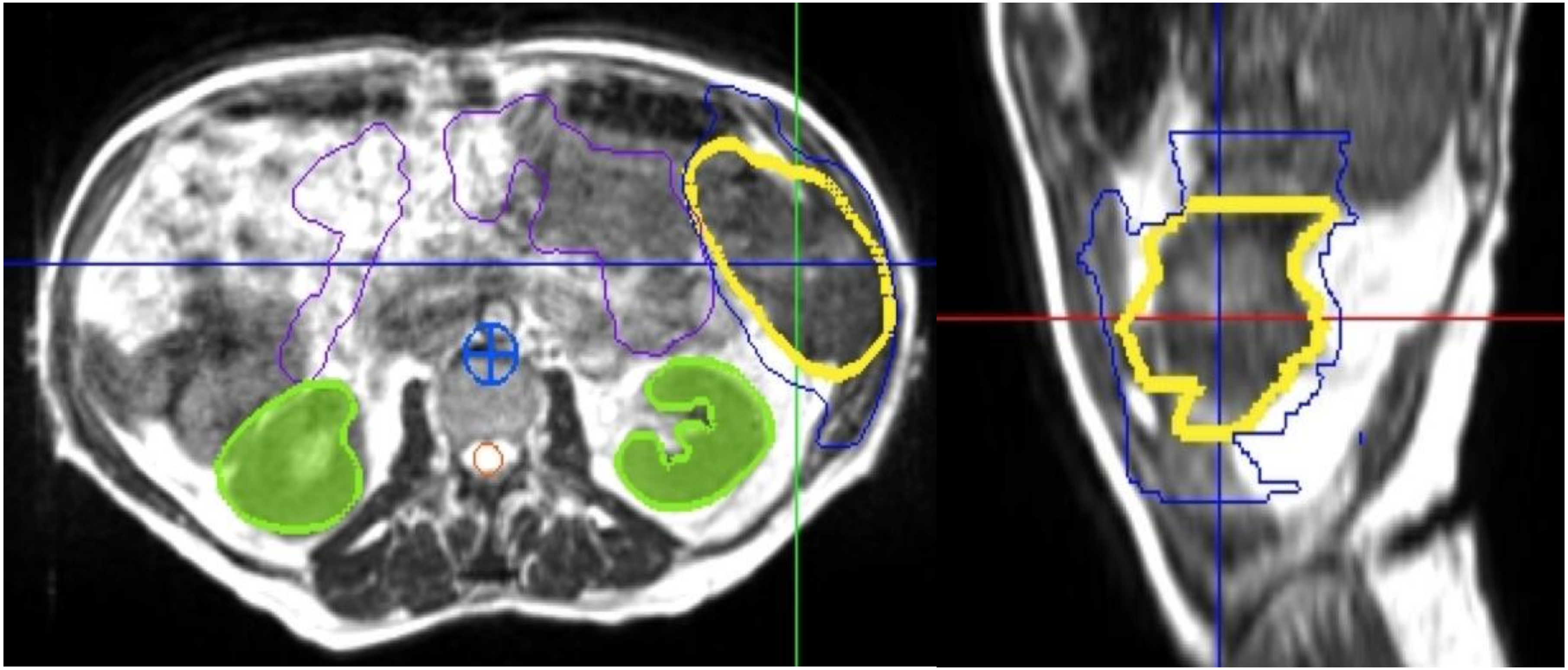


MRG-RT: Initial Experience



- CBCT localization based on tumor/abd wall anatomy

MRG-RT: Initial Experience



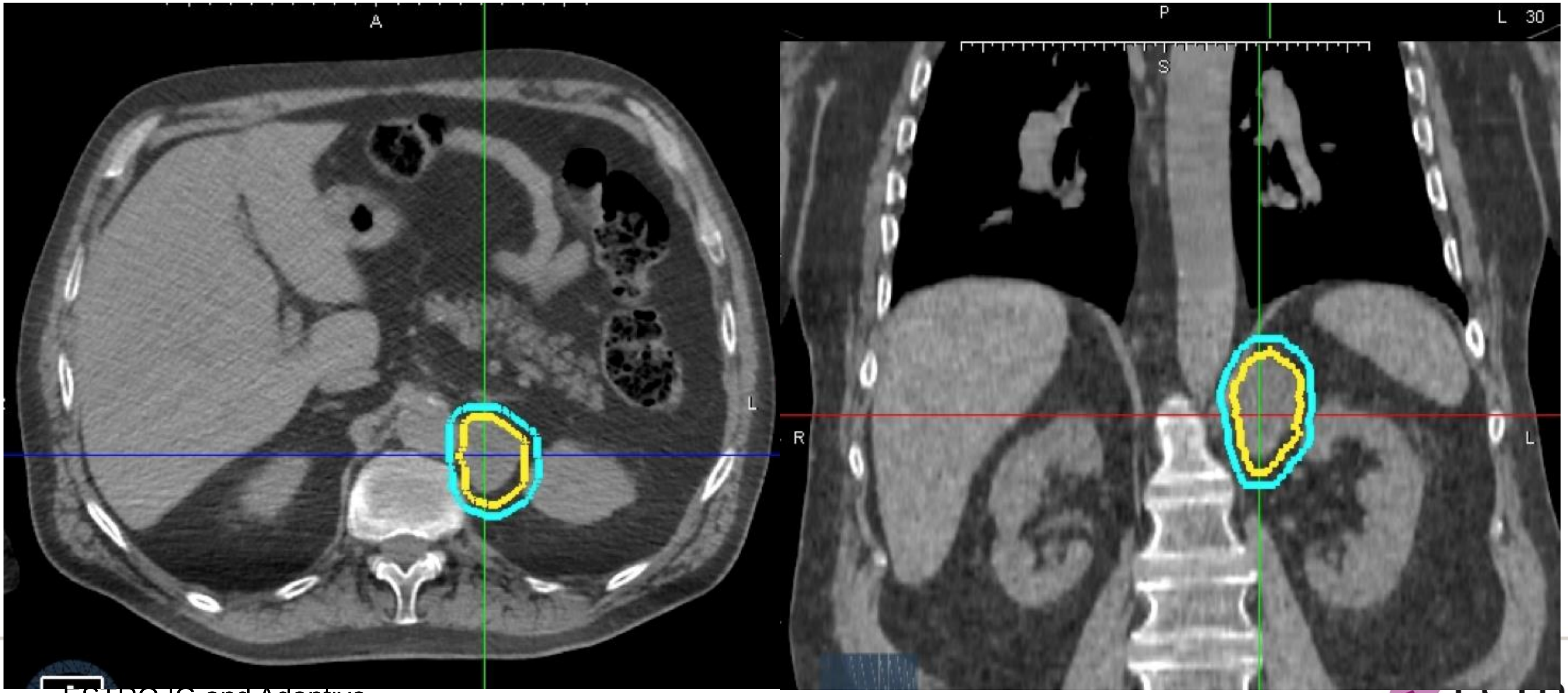
- MR localization based on tumor anatomy

Case 2:
Abdominal SBRT

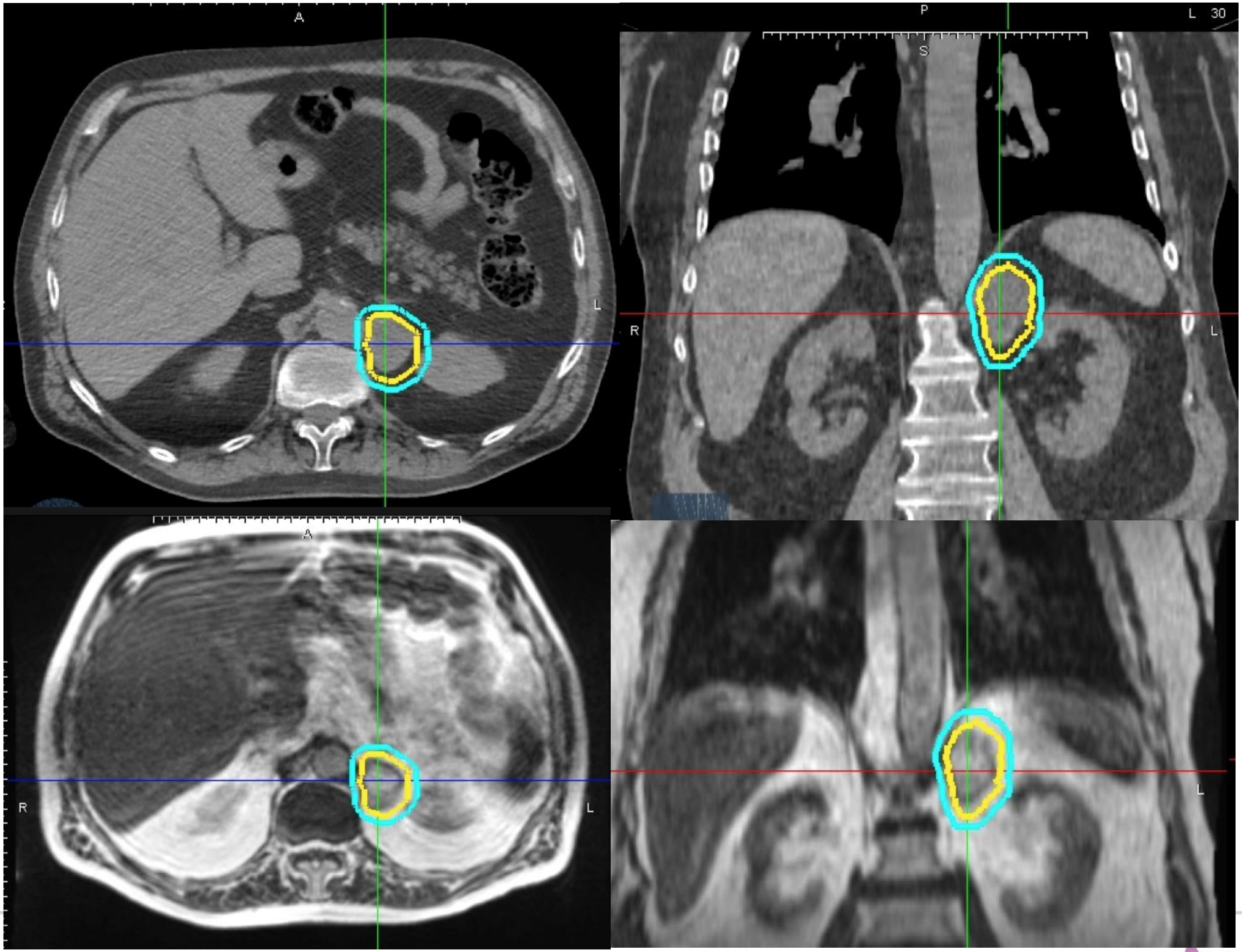
MRG-RT: Initial Experience

71 yo medically inoperable M with pheochromocytoma

Plan: SBRT (50 Gy/5 fx)



MRG-RT: Initial Experience



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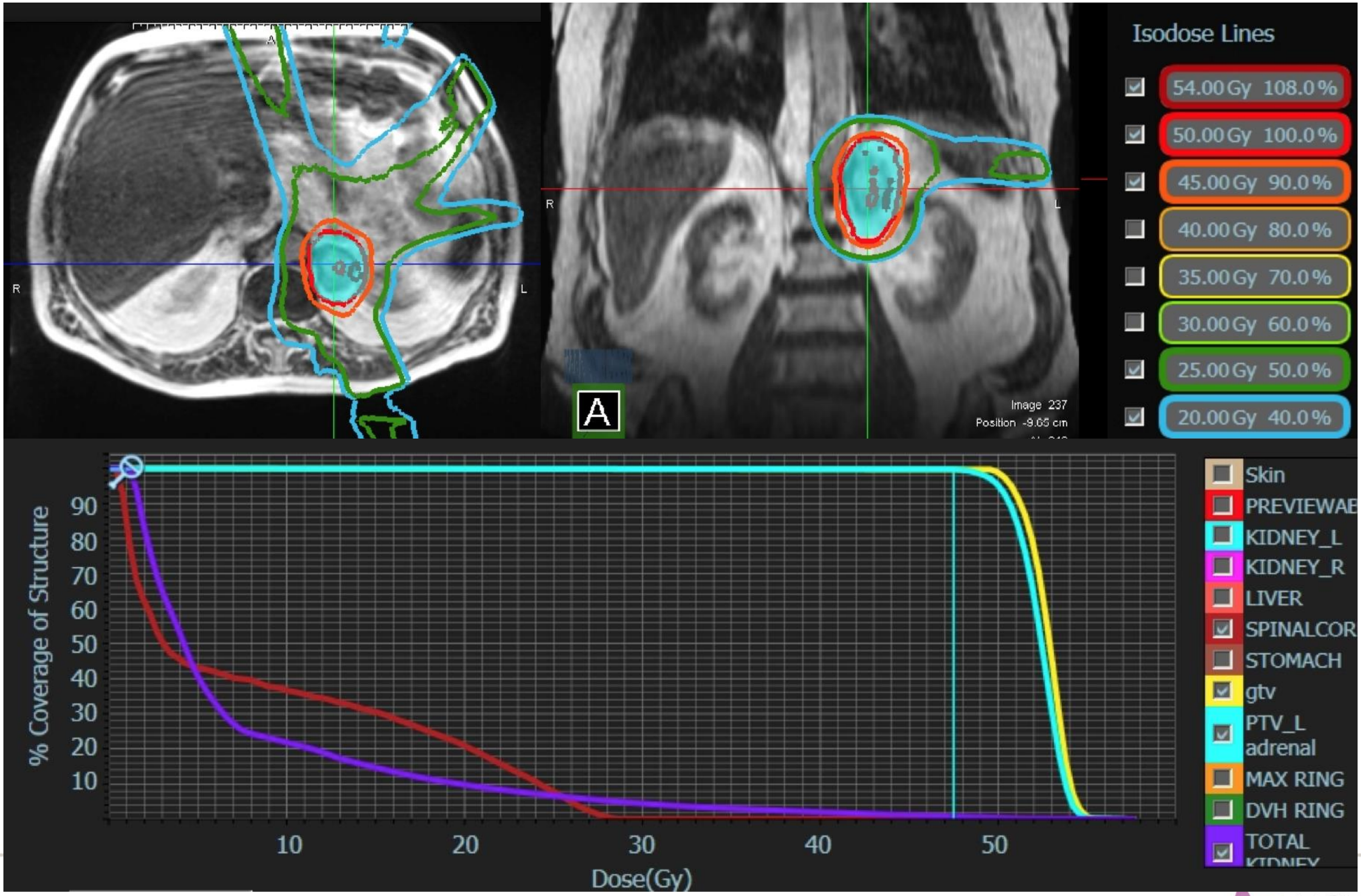
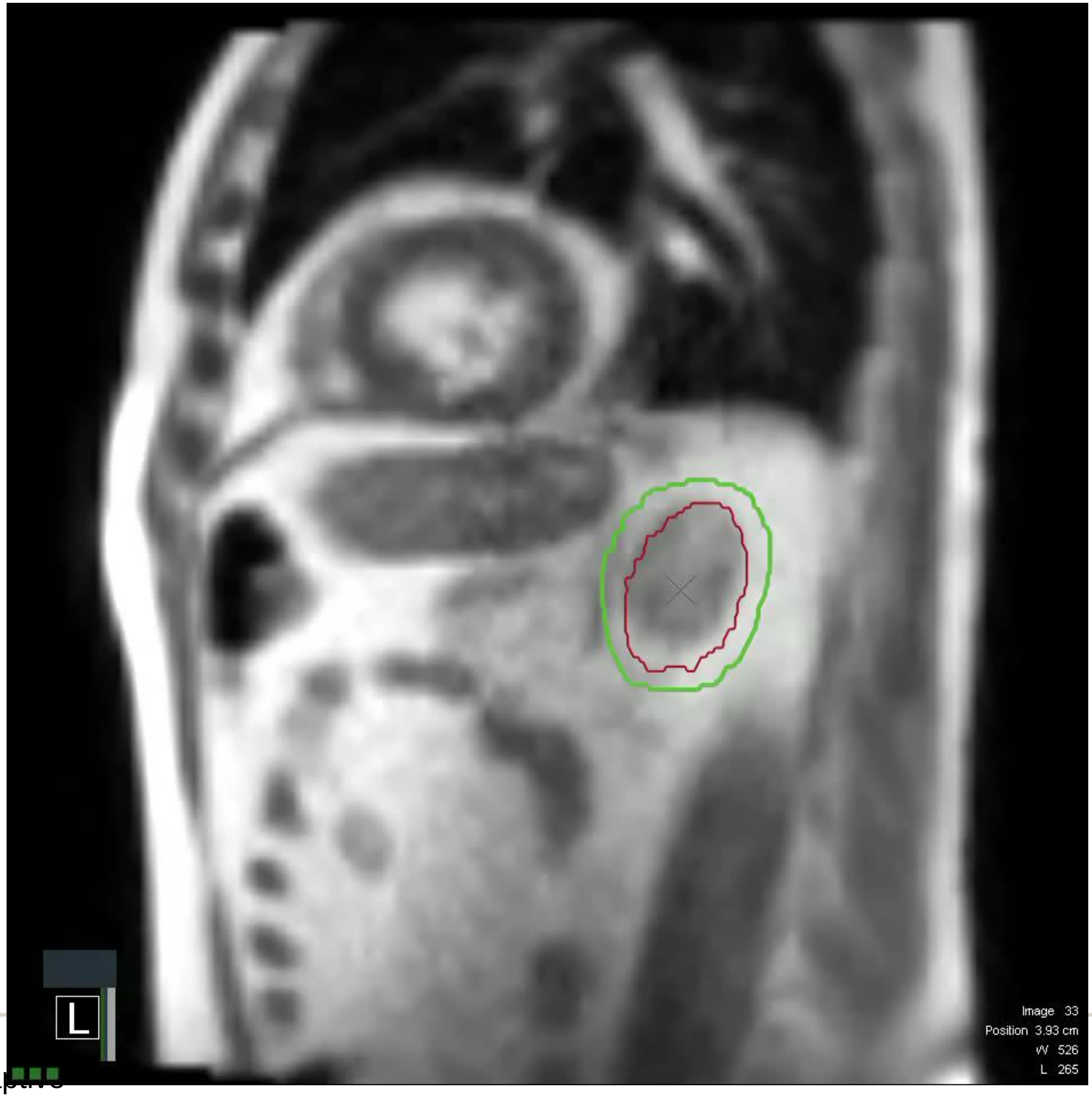
MRG-RT: Initial Experience



MRG-RT: Initial Experience



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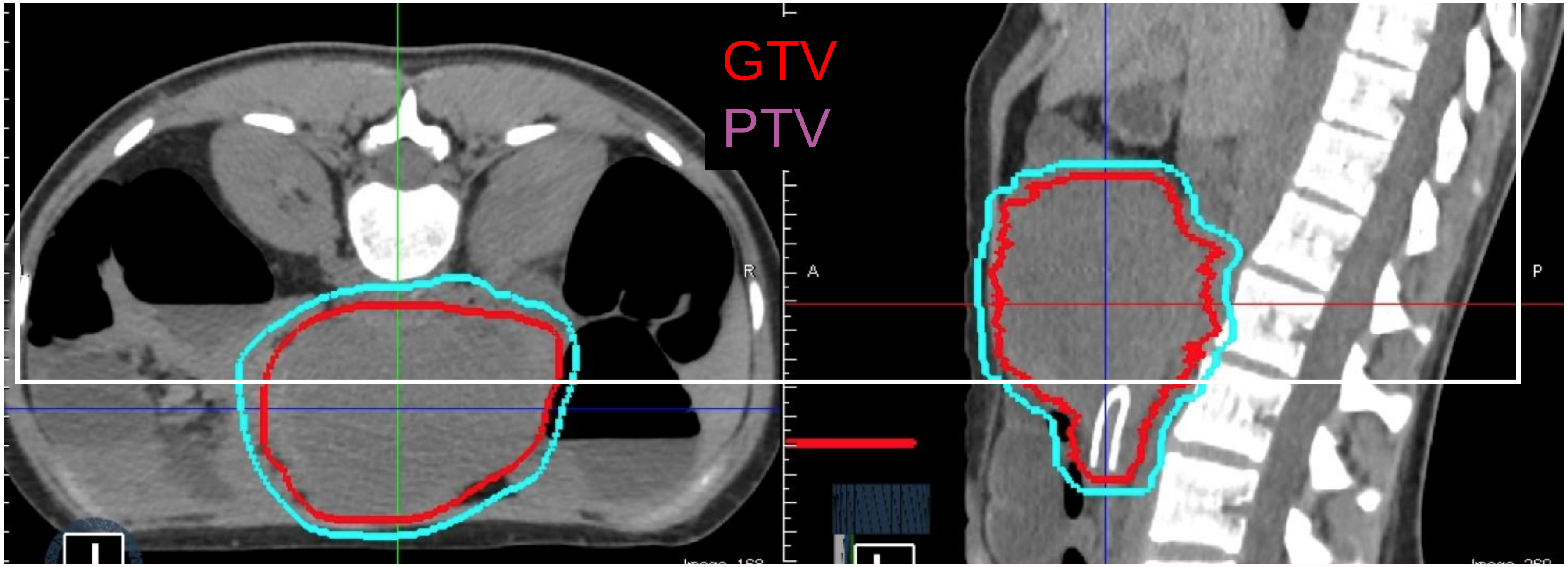
Case 3:
Unresectable Desmoid

MRG-RT: Initial Experience

29 yo F with Gardner's sx and progression of unresectable abdominal desmoid tumor following tamoxifen, imatinib, sorafenib.

Plan: Definitive RT (54 Gy / 30 fx)



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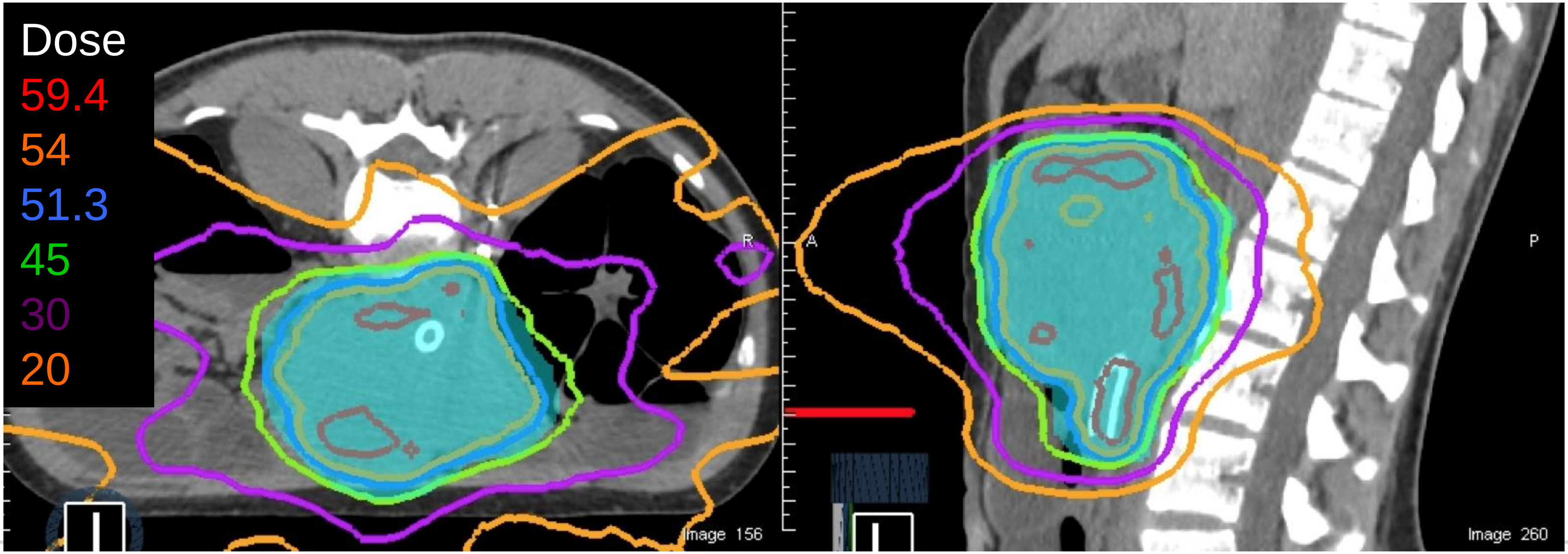
MRG-RT: Initial Experience

29 yo F with Gardner's sx and progression of unresectable abdominal desmoid tumor following tamoxifen, imatinib, sorafenib.

Plan: Definitive RT (54 Gy / 30 fx)



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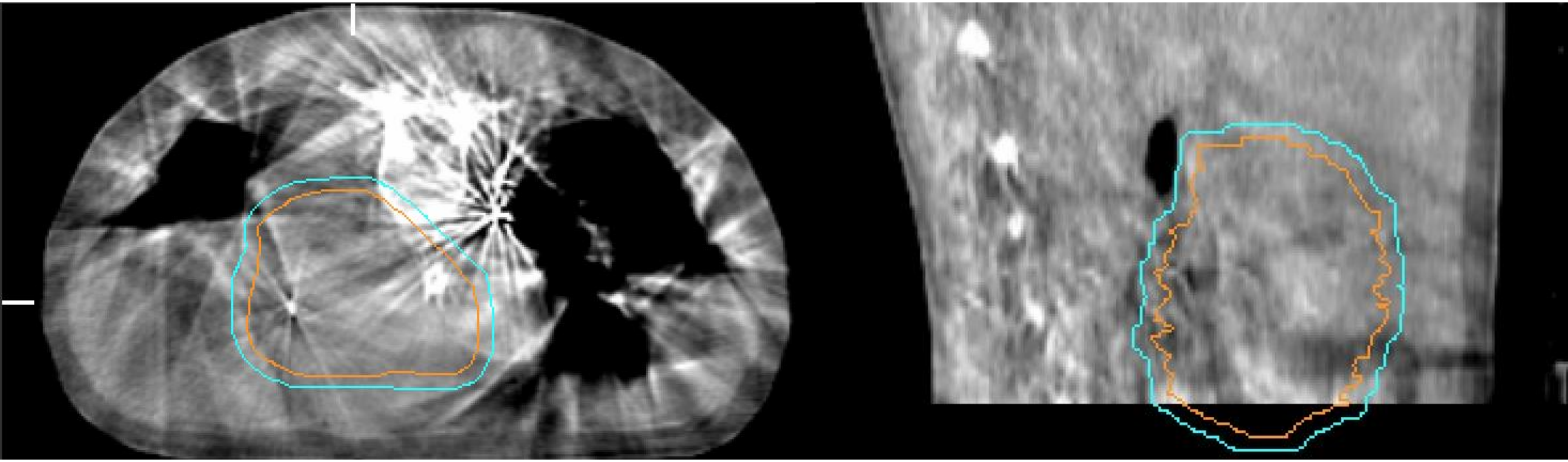
MRG-RT: Initial Experience

29 yo F with Gardner's sx and progression of unresectable abdominal desmoid tumor following tamoxifen, imatinib, sorafenib.

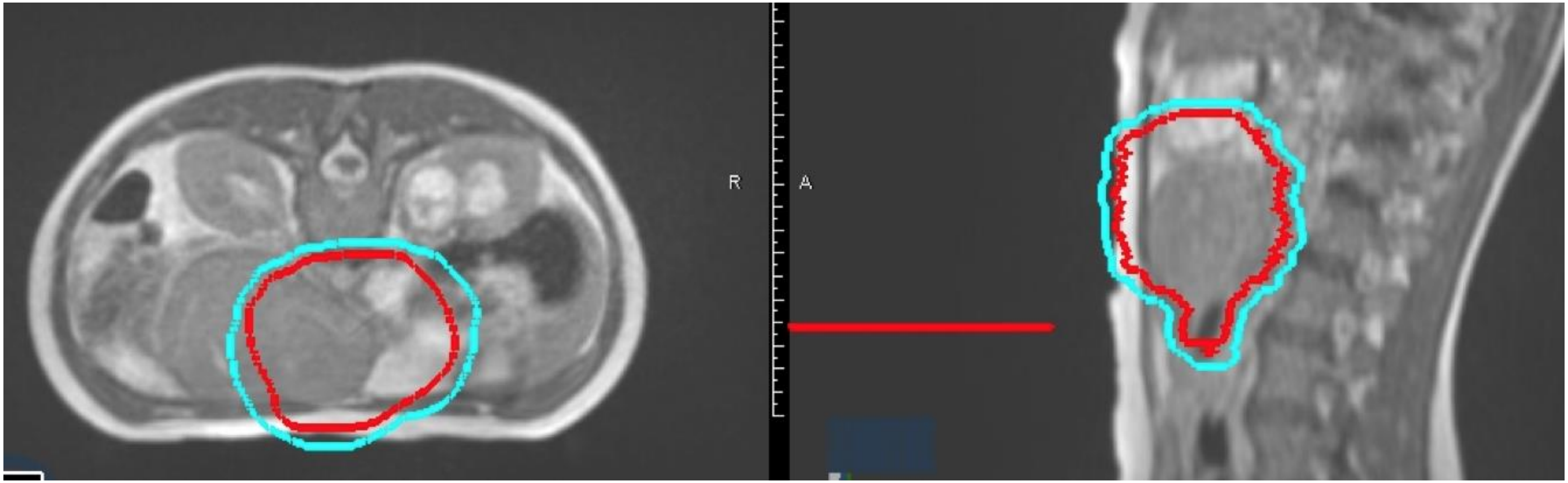
CBCT



MRG-RT: Initial Experience

29 yo F with Gardner's sx and progression of unresectable abdominal desmoid tumor following tamoxifen, imatinib, sorafenib.

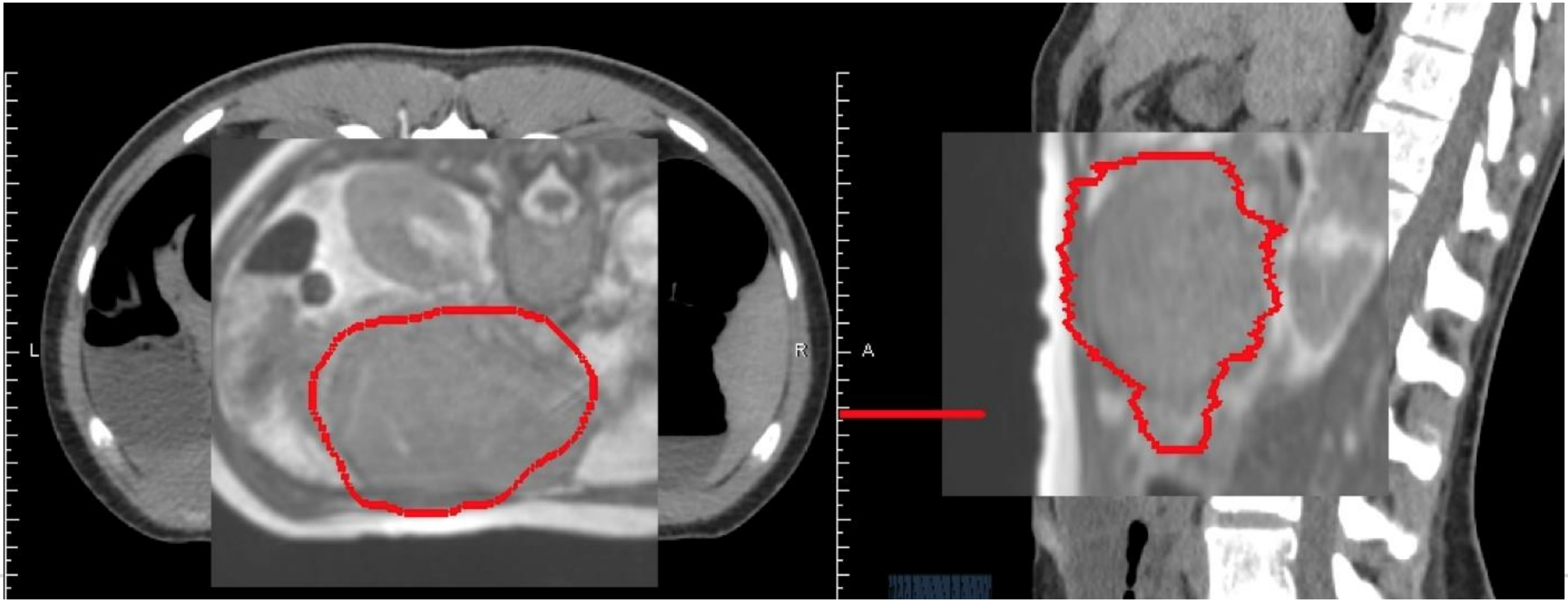
MR Localization



MRG-RT: Initial Experience

29 yo F with Gardner's sx and progression of unresectable abdominal desmoid tumor following tamoxifen, imatinib, sorafenib.

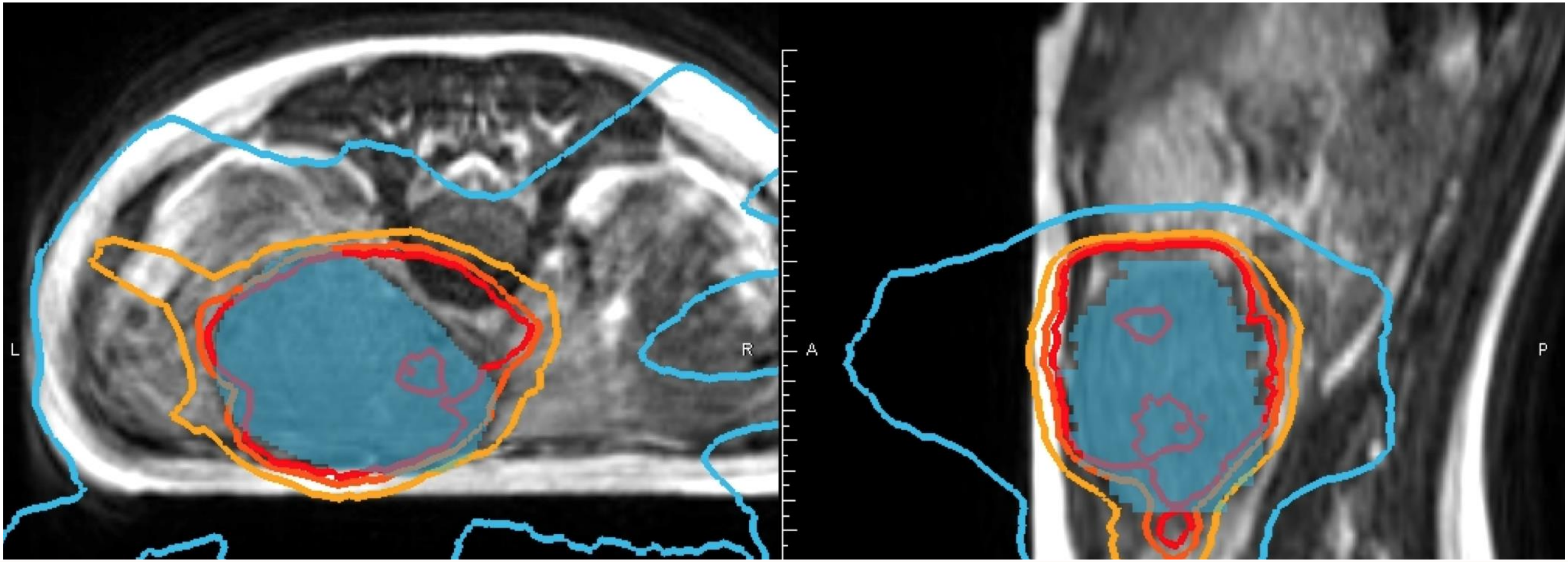
MR Localization



MRG-RT: Initial Experience

29 yo F with Gardner's sx and progression of unresectable abdominal desmoid tumor following tamoxifen, imatinib, sorafenib.

Dose calculation with shift



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Case 4:
Accelerated partial breast radiation

MRG-RT: Moderate Experience - Breast

CTV, PTV margins for APBI:

Brachytherapy (Mammosite, SAVI):

Preferred Cavity + 1 cm = CTV = PTV

EBRT:

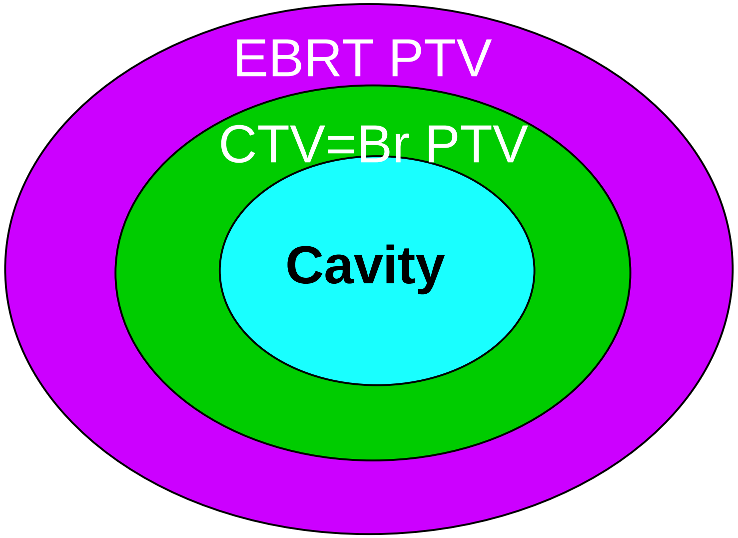
Alternative Cavity + 1-1.5 cm = CTV.

CTV + 1 cm = PTV

PTV = Cavity + 2-2.5 cm

Larger PTV margins needed due to:

- Setup uncertainty
- Intra-fraction motion



We sought to evaluate MR-IGRT for delivery of APBI given easy localization of cavity on MRI (setup) and ability to monitor intra-fraction motion.

Courtesy of Maria Thomas, MD, PhD

MRG-RT: Moderate Experience - Breast

Patient characteristics: Women with Stage 0-1 breast cancer, status post lumpectomy, appropriate candidates for APBI, who were not eligible for brachytherapy. Enrolled on institutional registry. (N = 30 patients)

Treatment: MR-IGRT APBI, 38.5 Gy/10 fx BID

Treatment planning:

CT and MRI simulation (Supine, arms up, AC, Lucite brackets)

PTV = CTV = Cavity + 1 cm

Cavity localization on volumetric MRI prior to each fraction

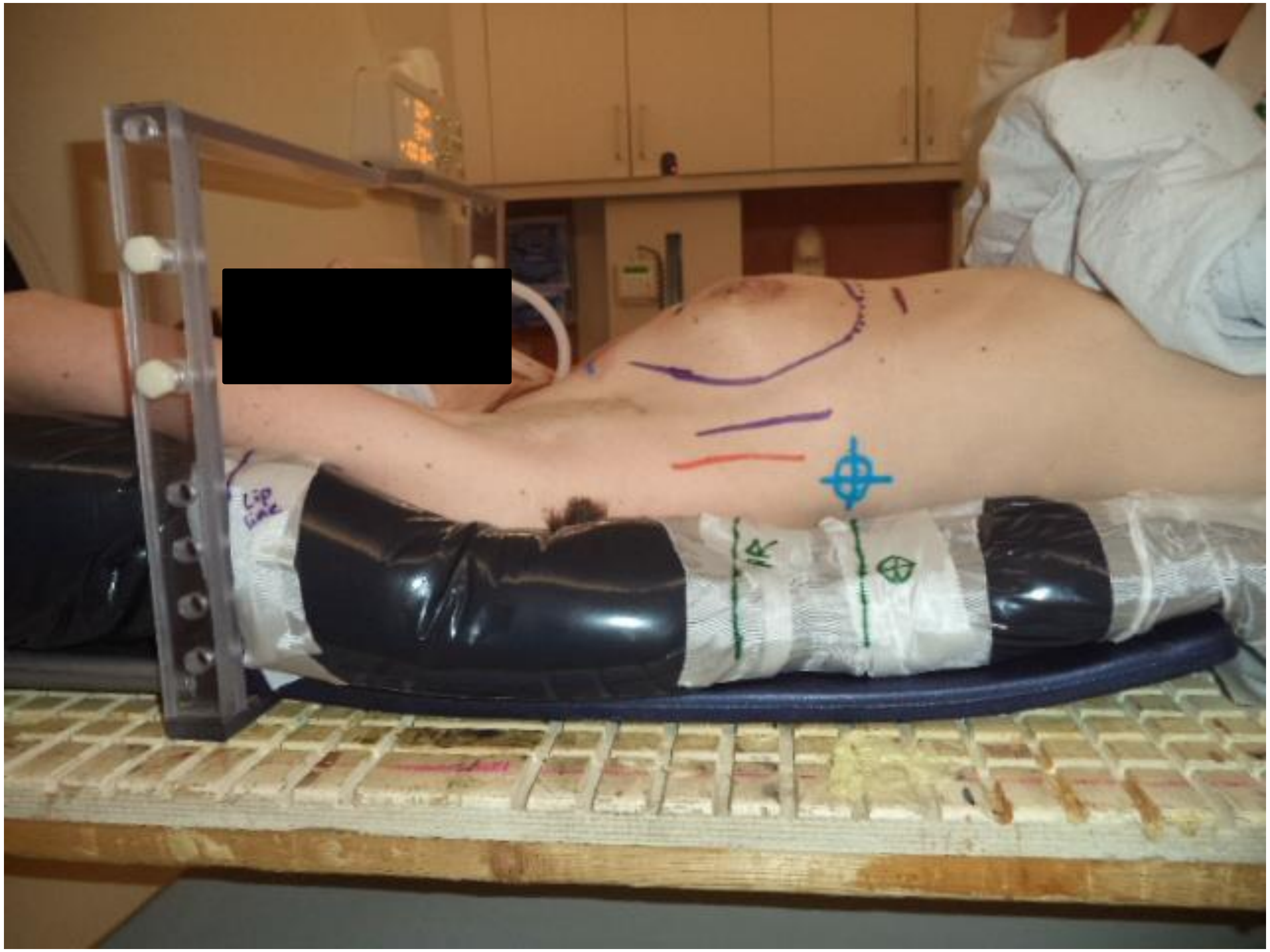
Continuous cine acquisition during delivery of each fraction

Patient time in room per fraction: mean 36 minutes

Courtesy of Maria Thomas, MD, PhD

MRG-RT: Moderate Experience - Breast

MRG-RT: Moderate Experience - Breast



MRG-RT: Moderate Experience - Breast

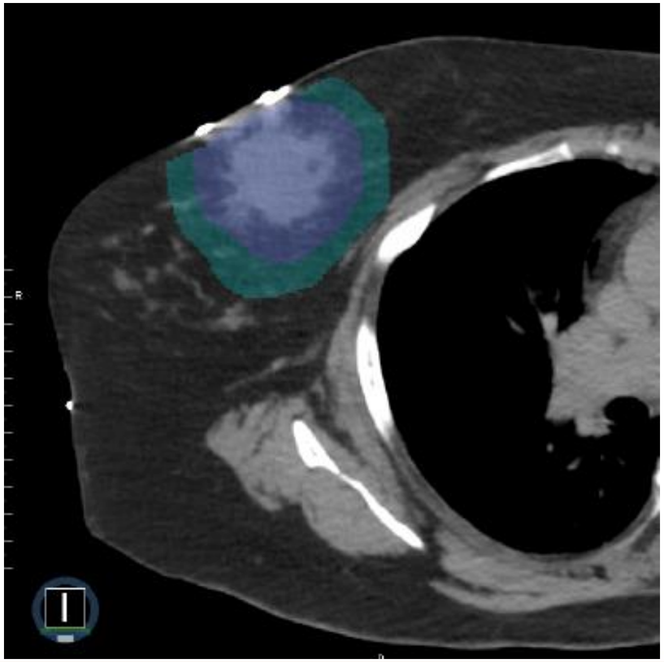
MRG-RT: Moderate Experience - Breast

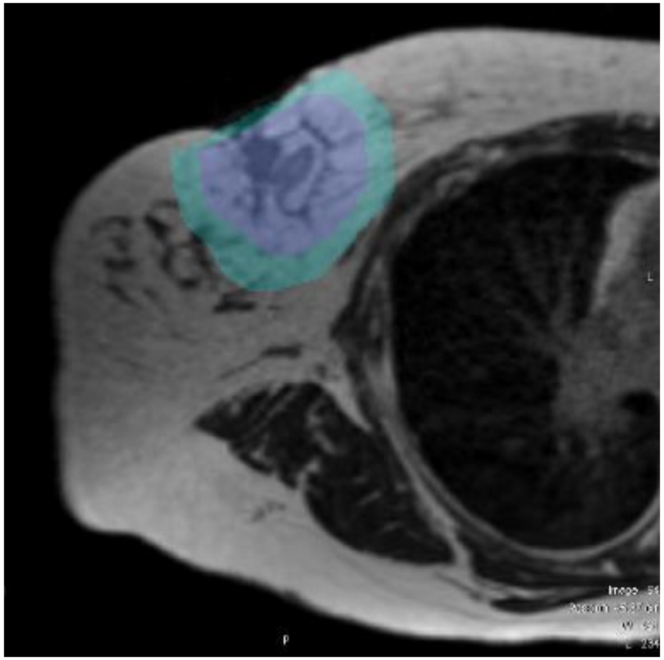
Comparison of PTV volumes:

<u>3D-CRT</u>: Mean PTV = 177 cc *Cyan colorwash*

<u>MR-IGRT</u>: Mean PTV = 85 cc *Dark blue colorwash*

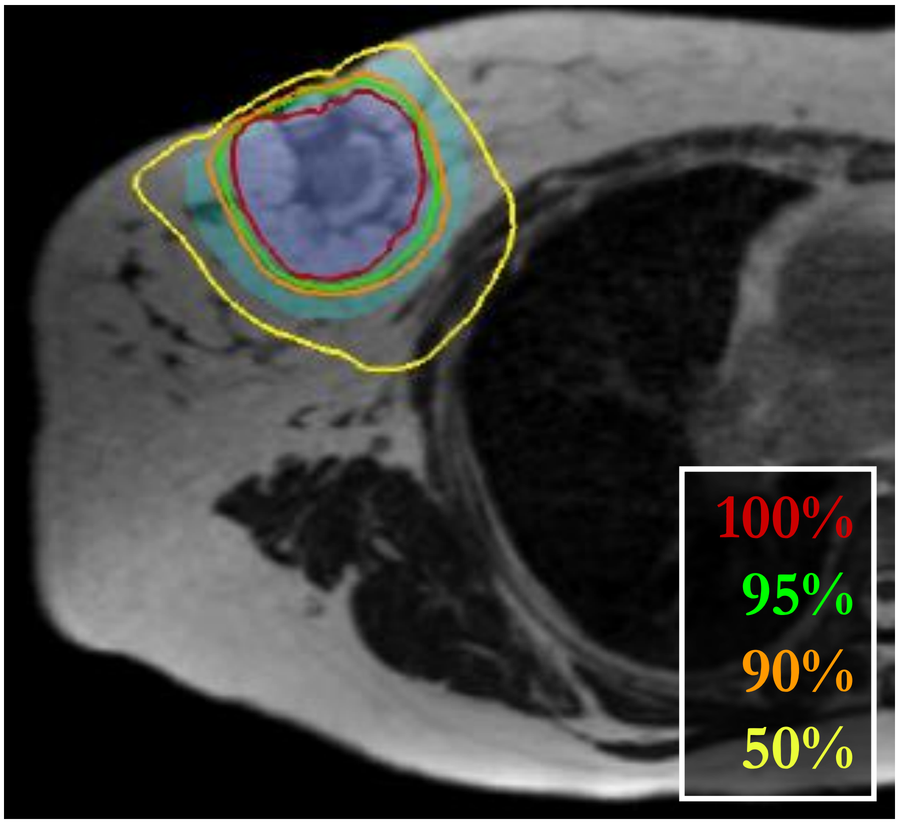
*52% reduction in volume with MR-IGRT





Courtesy of Maria Thomas, MD, PhD

MRG-RT: Moderate Experience - Breast



	MR-IGRT	3D-CRT
PTV:		
Volume	85 cc	177 cc
V(95%)	99.5%	99.5%
Ipsilateral Breast:		
V(20%)	51.7%	64.8%
V(50%)	31.3%	52.7%
V(75%)	17.6%	34.6%
V(90%)	12.6%	27.4%
V(100%)	11.7%	21.6%

Courtesy of Maria Thomas, MD, PhD

MRG-RT: Moderate Experience - Breast

Courtesy of Maria Thomas, MD, PhD

MRG-RT: Moderate Experience - Breast

Courtesy of Maria Thomas, MD, PhD

MRG-RT: Moderate Experience - Breast

Acute toxicity:

Well tolerated.

Minimal acute skin toxicity: Grade 0 - 1.

Ongoing evaluations:

<u>Median follow up</u>: < 1 year.

<u>Outcomes</u>: No recurrences to date.

<u>Late toxicity</u>: Grade 0-1 skin and subcutaneous tissue.

<u>Cosmetic result</u>: 100% Excellent/Good cosmesis scores to date.

MRG-RT: Online adaptive therapy in abdomen

Experiences in abdominopelvic tumors

Parag Parikh, BSE, MD

Associate Professor of Radiation Oncology & Biomedical Engineering

Washington University School of Medicine

St. Louis, Missouri, USA

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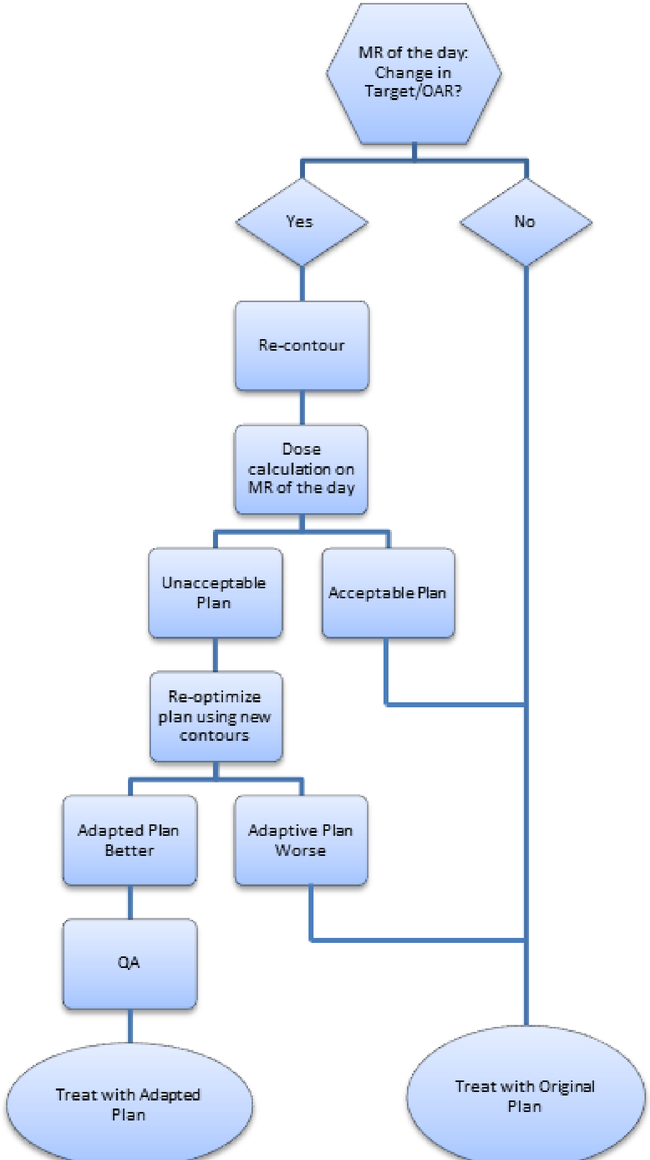
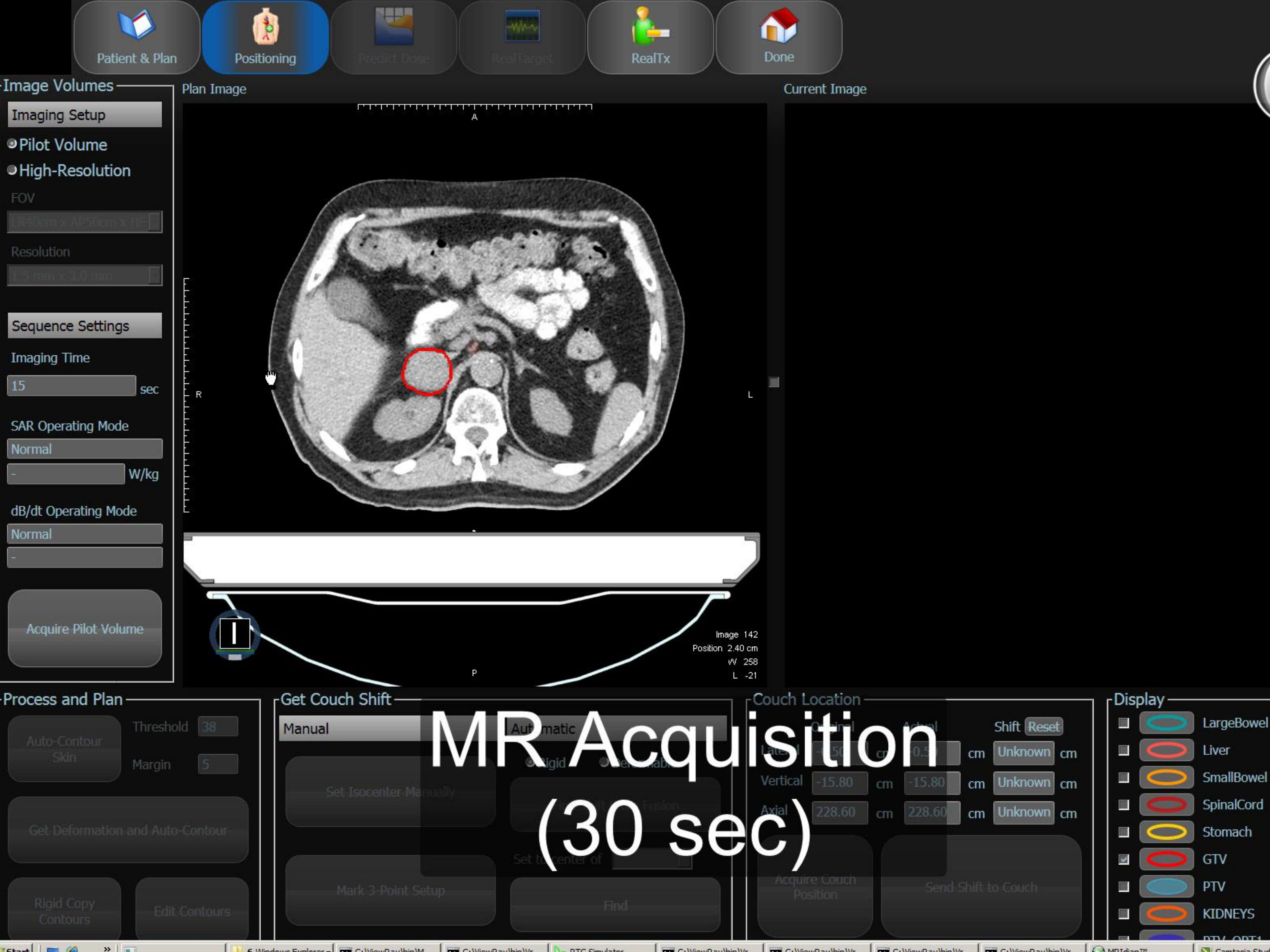
Objectives

To understand the online, daily organs at risk approach of adaptive radiation therapy of the pancreas with hypofractionation and abdominal oligometastases SBRT techniques

About 50 patients (both on and off trial) have had at least 1 fraction of online adaptive radiation therapy



Online Magnetic Resonance Image Guided Adaptive Radiation Therapy: First Clinical Applications, Acharya, et al. IJROBP Vol. 94, No. 2, pp. 394e403


MR Acquisition
(30 sec)
Patient & Plan
Positioning
RealTx
Done
Image Volumes
Imaging Setup
Pilot Volume
High-Resolution
FOV
Resolution
Sequence Settings
Imaging Time
15
sec
SAR Operating Mode
Normal
W/kg
dB/dt Operating Mode
Normal
Acquire Pilot Volume
Plan Image
Current Image
A
R
L
P
Image 142
Position 2.40 cm
W 258
L -21
Process and Plan
Auto-Contour Skin
Threshold 38
Margin 5
Get Deformation and Auto-Contour
Rigid Copy Contours
Edit Contours
Get Couch Shift
Manual
Set Isocenter Manually
Mark 3-Point Setup
Find
Couch Location
Shift Reset
Vertical -15.80 cm -15.80 cm Unknown cm
Axial 228.60 cm 228.60 cm Unknown cm
Unknown
Acquire Couch Position
Send Shift to Couch
Display
LargeBowel
Liver
SmallBowel
SpinalCord
Stomach
GTV
PTV
KIDNEYS

Adaptive Workflow

Simulation / Planning

- MR compatible immobilization
- CT + MR

Localization

- Daily high resolution MR
- Deformable registration
  - Contours
  - Electron density

Dose prediction

- Manual edits to OARs / targets if necessary
- Eval initial plan on daily anatomy

Adapt ???

- If anatomy and plan stable, tx w/initial plan
- If anatomy or dose different, adapt

QA Needs

Noel et al, Med Phys 2014

Reviewed each step in online adaptive process

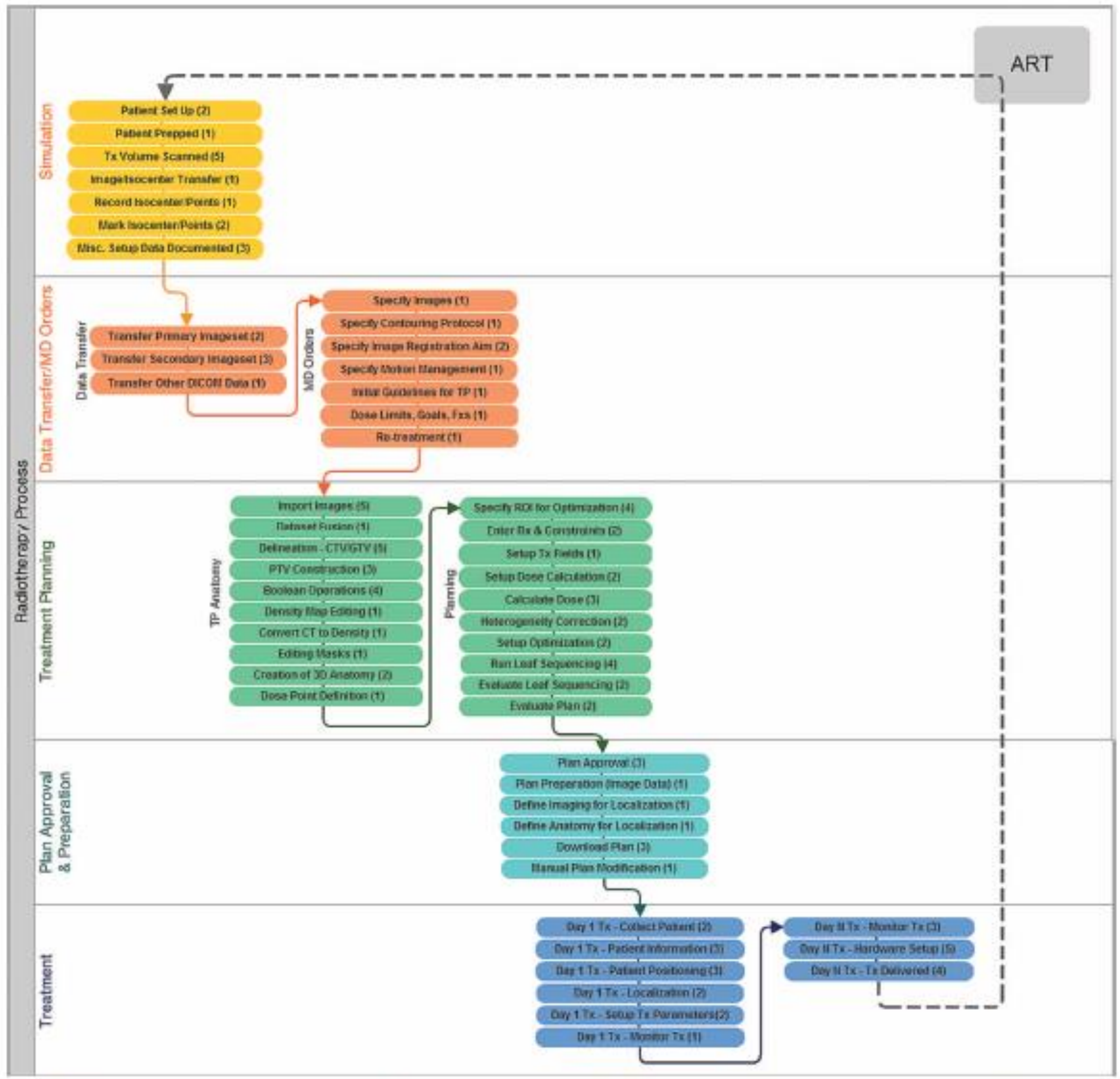
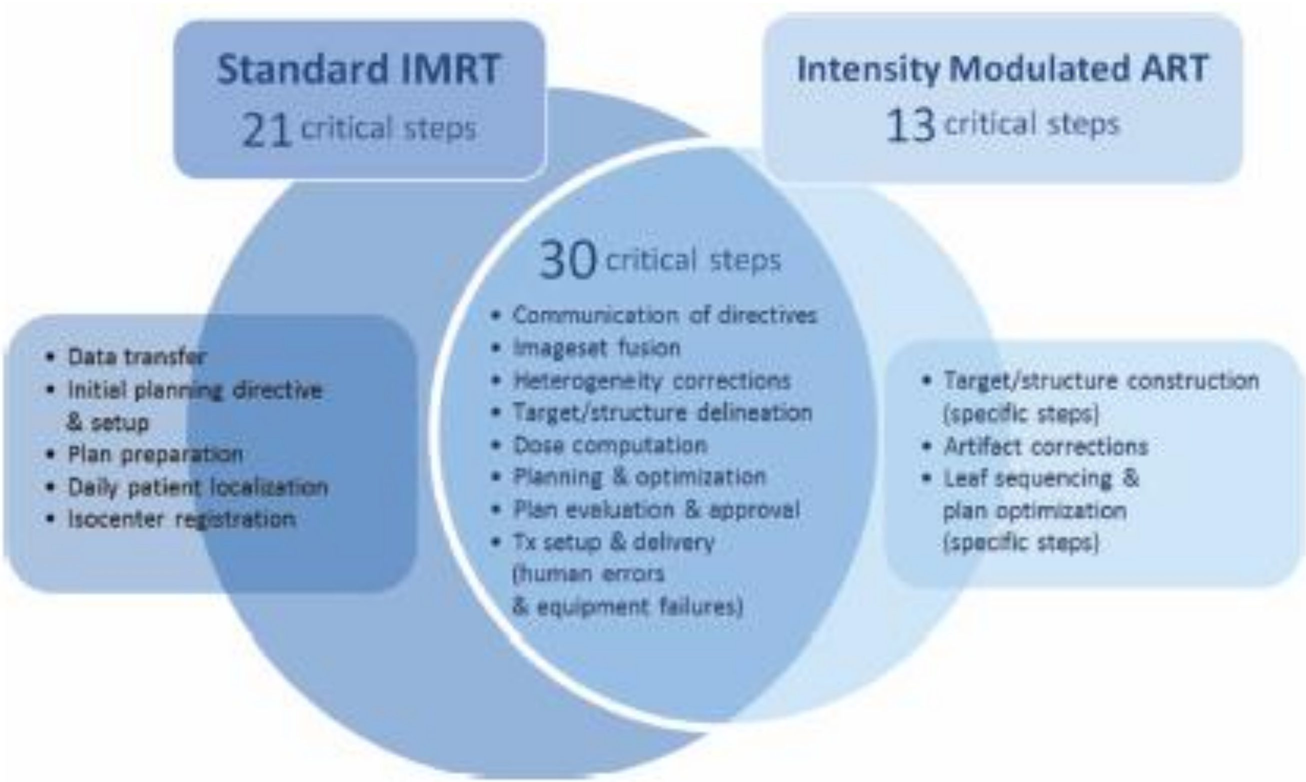


Fig. 1. Flow diagram of major intensity-modulated ART processes and subprocesses. The number of failure modes per subprocess is included in parenthesis.

FMEA analysis of QA



Found unique points of failure in ART, but some issues in standard IMRT not found. Created processes to review contours and perform virtual QA

Need definitions

Most important aspect!

- MR guided radiation therapy is still just radiation therapy
- Same dose / volumes / fractionation = same outcomes
- Physicians will need to identify
  - Clinical sites with insufficient control, toxicity
  - Changes in dose / volume / fractionation with MR guidance

Adaptive radiotherapy checklist

Goal?

- Treatment intensification
- Treatment accuracy
- Toxicity reduction

Frequency?

- Daily
- Weekly
- At pre-determined image evaluation during tx

Imaging surrogate?

- MR anatomy/function/motion

Adaptive radiotherapy checklist

Goal?

- Treatment intensification
- Treatment accuracy
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- Weekly
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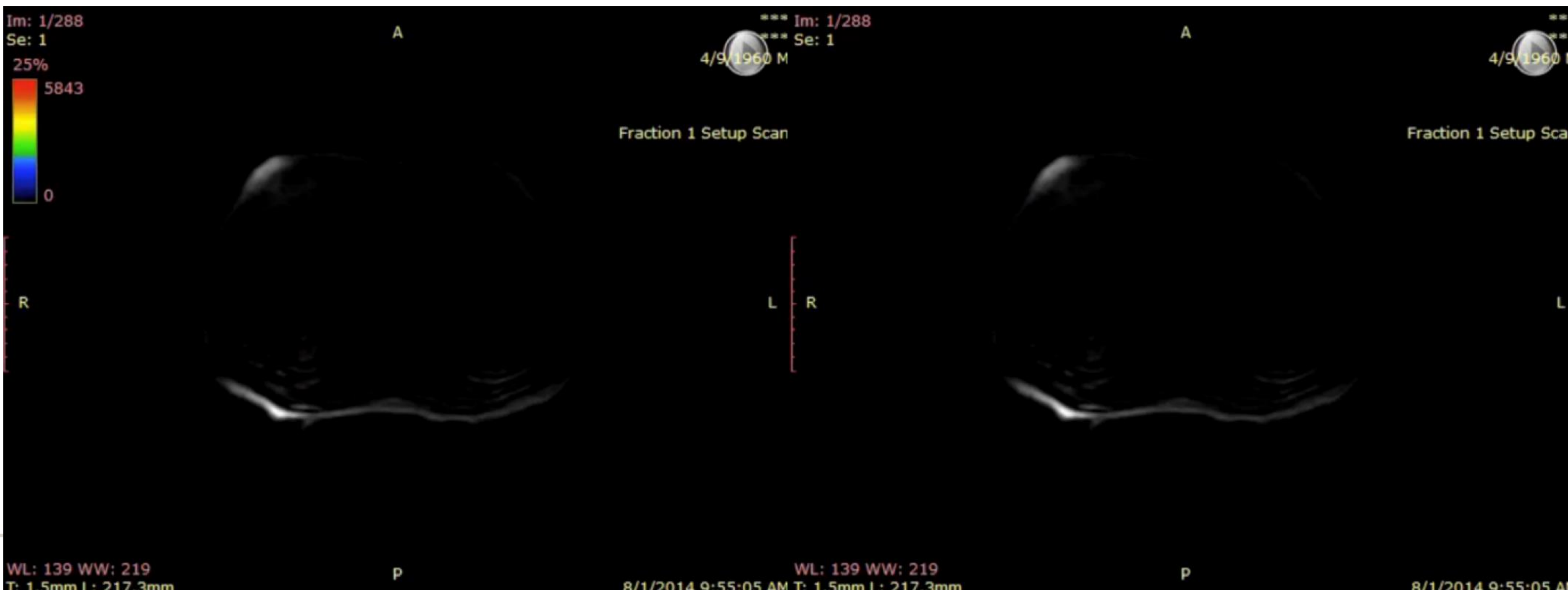
- MR anatomy/function/motion

Initial Adaptive – Tumor based

- T4N2M0 obstructing sigmoid adenocarcinoma
- MRI: Bladder invasion, focal abutment of pelvic sidewall
- Plan: Neoadjuvant CRT (50 Gy tumor, 45 Gy nodes / 25 fx)



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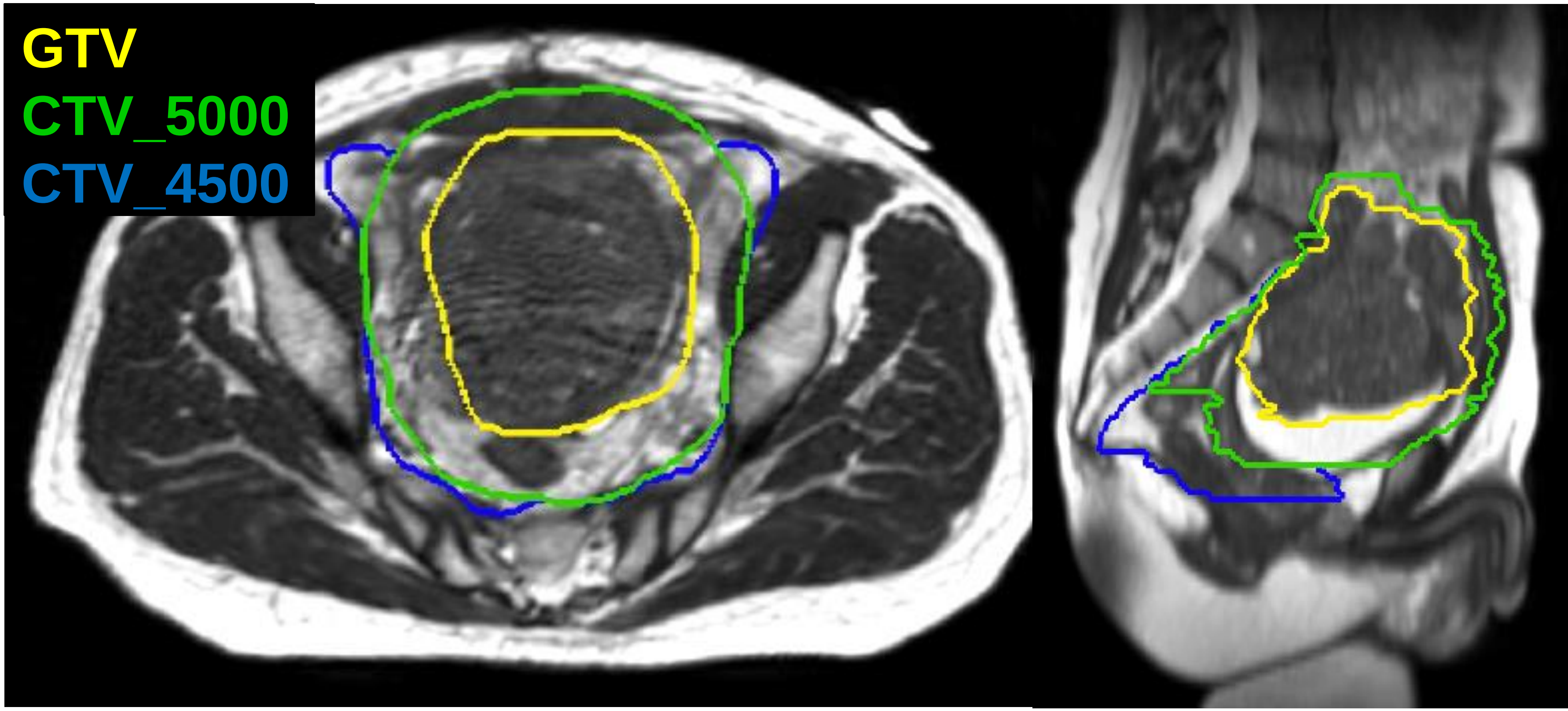
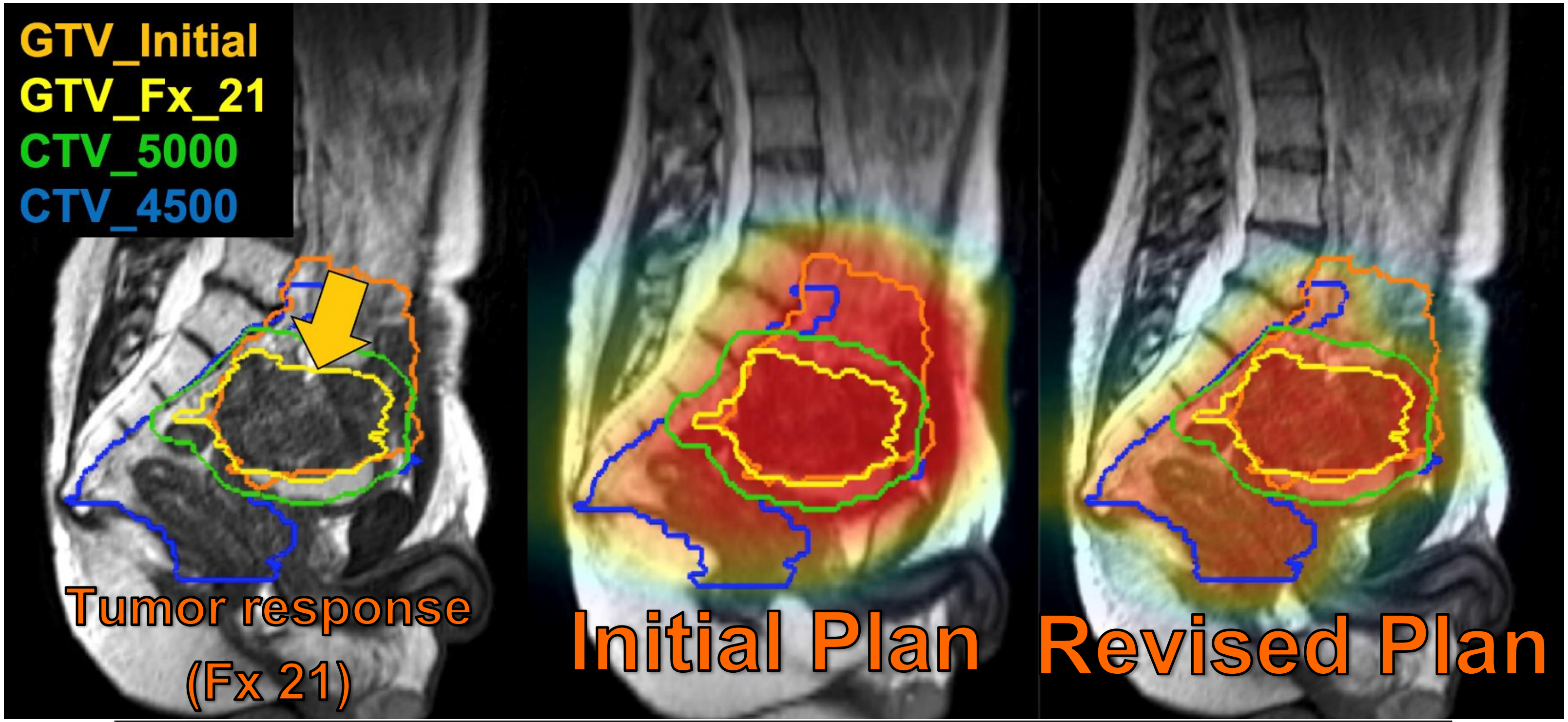
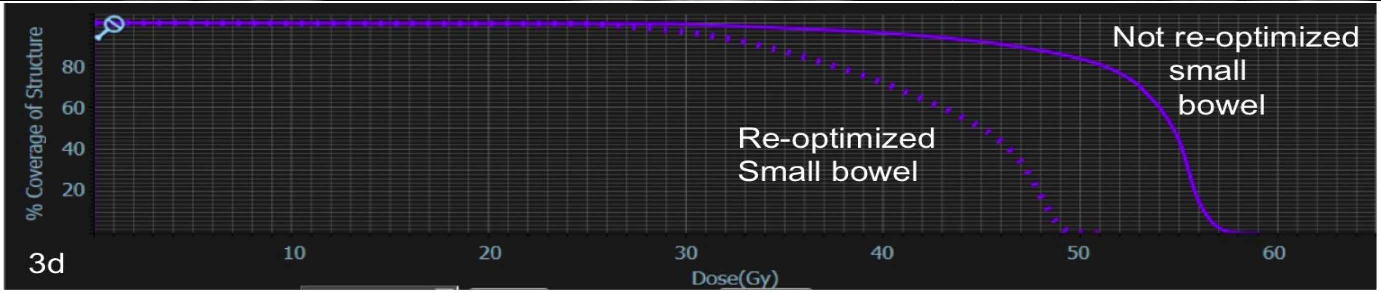
Initial Adaptive – Tumor based



Initial Adaptive – Tumor based





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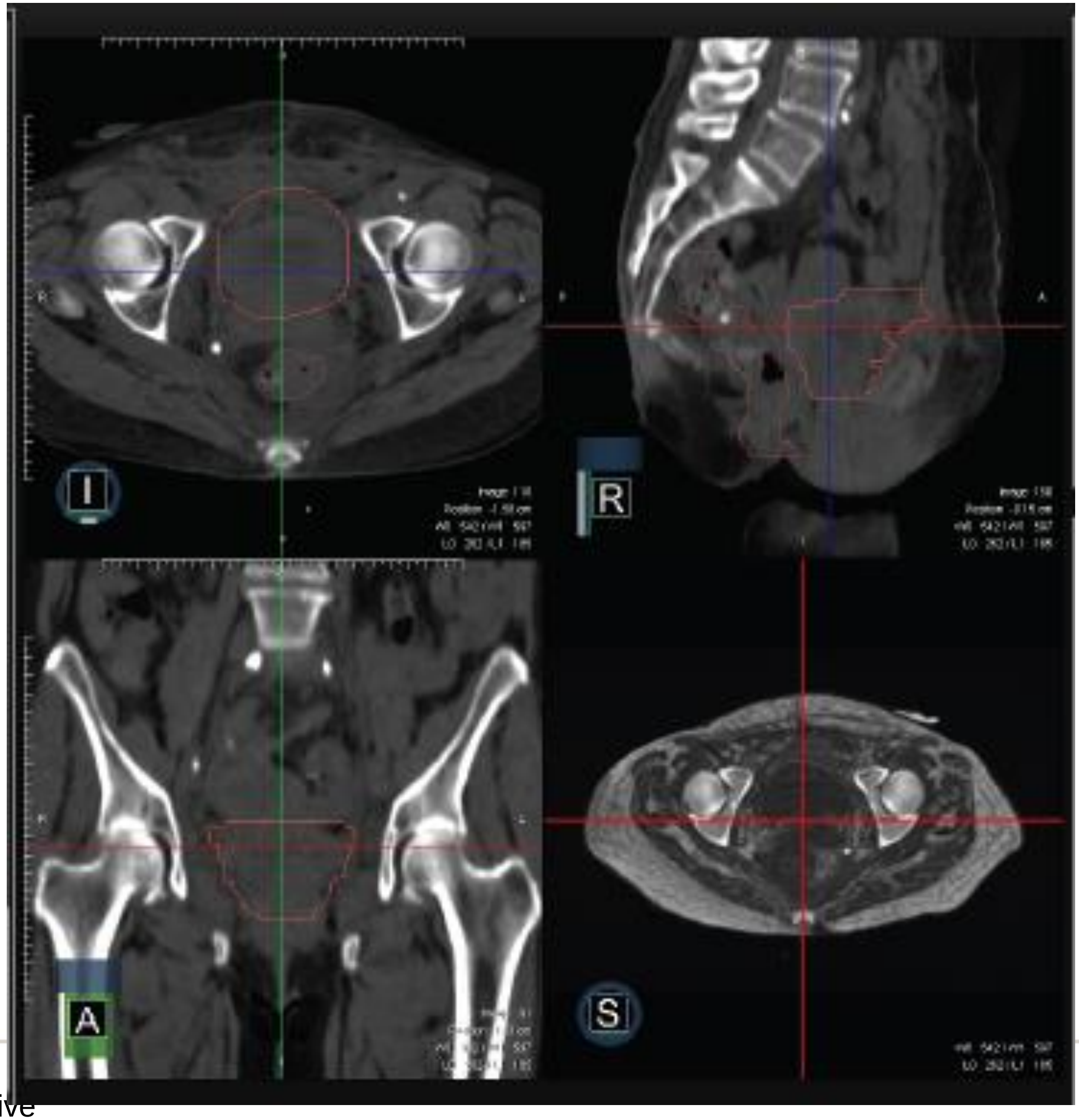
Initial Adaptive – Tumor based

70 year old with locally advanced bladder cancer, not an operative candidate

RT to bladder and pelvic lymph nodes, 39.6 / 1.8 Gy fractions on conventional linac

RT boost to bladder 25.2 Gy / 1.8 Gy fractions using Viewray

Initial Adaptive – Tumor based



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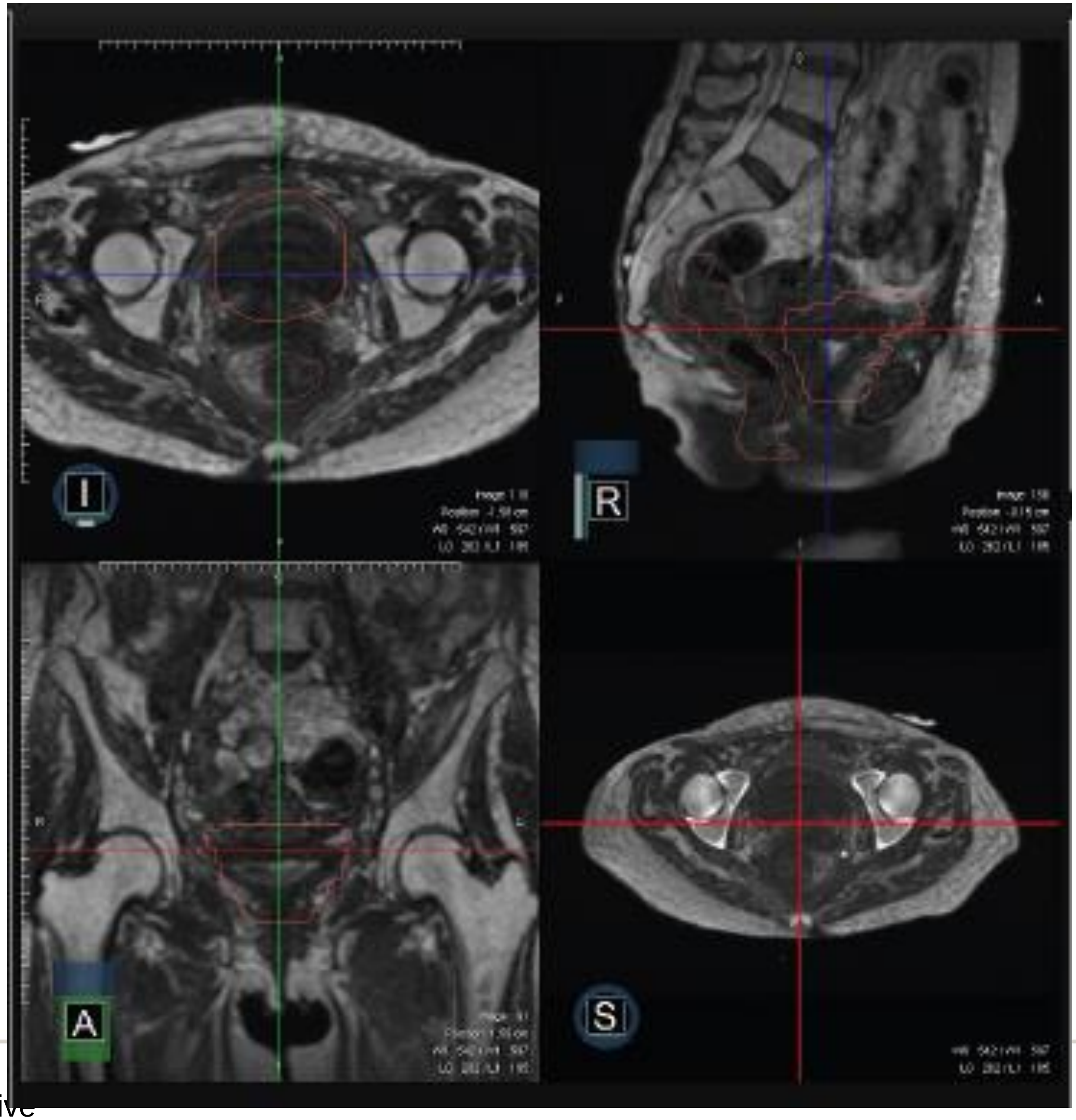
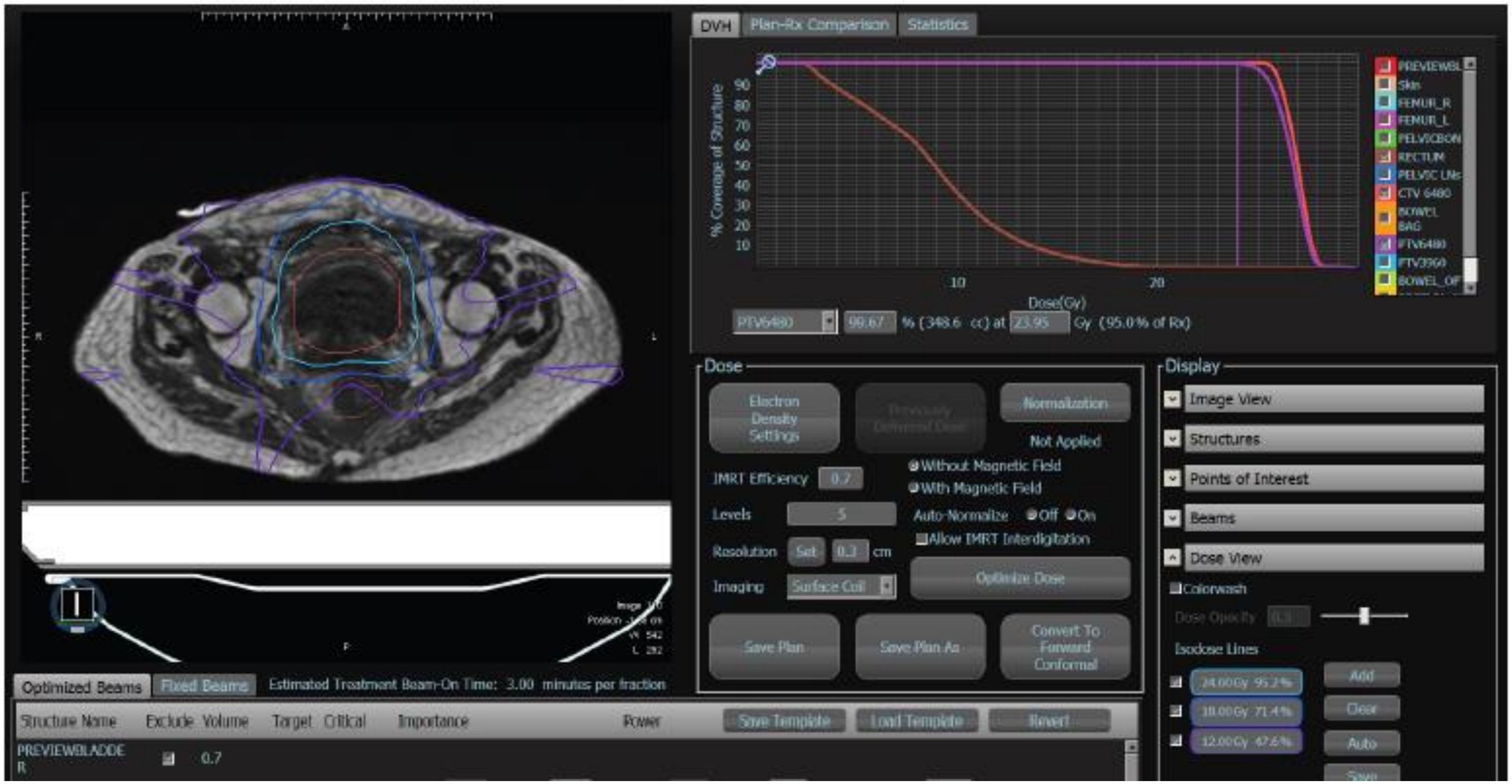
Initial Adaptive – Tumor based

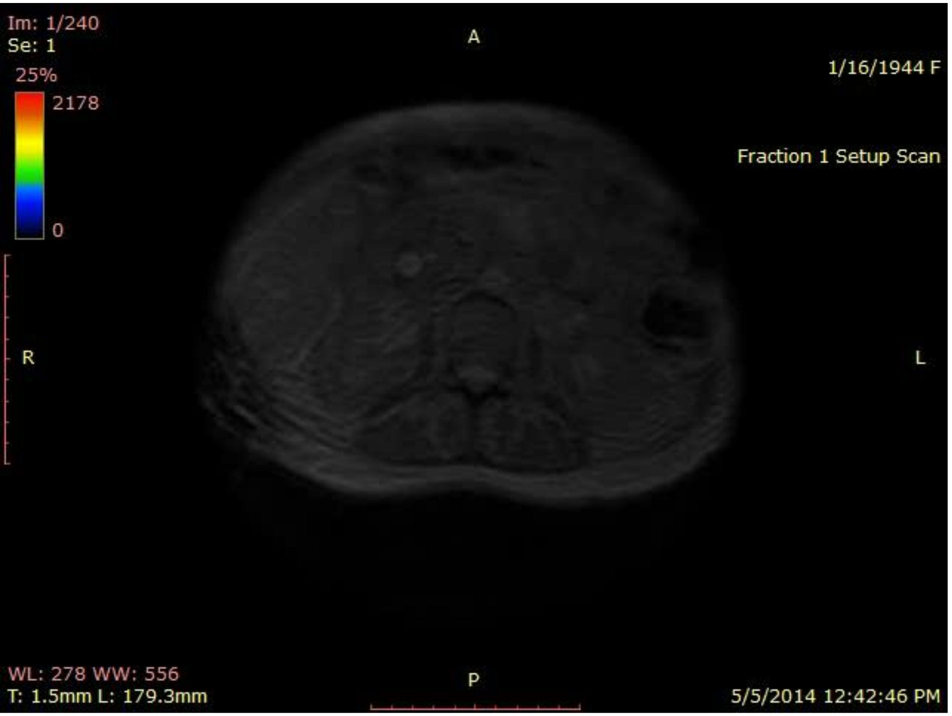


Initial Adaptive – Tumor based



ESTRO IG and Adaptive
Course Parikh 25.10.2016

Original Bladder Plan



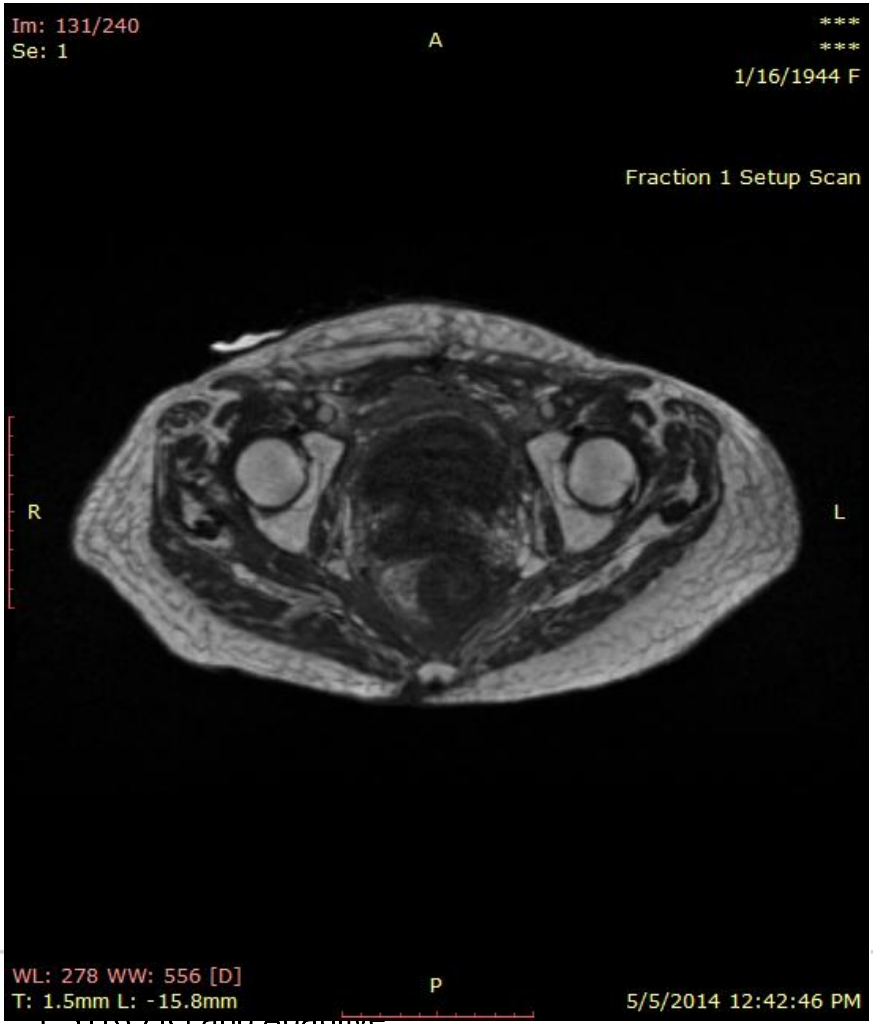
Initial Adaptive – Tumor based

Patient has intercurrent illness and loss of nutritional status

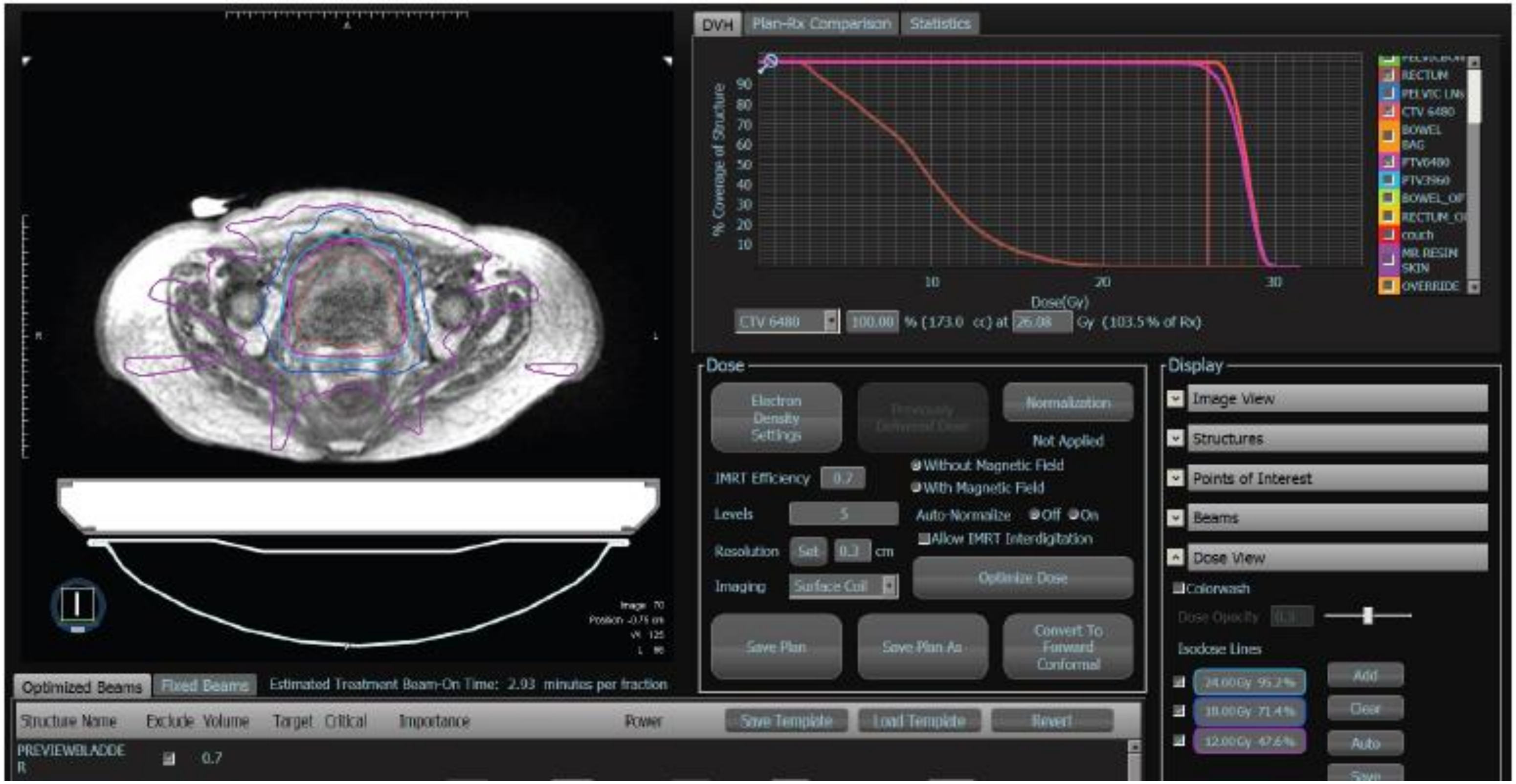
Develops anasarca, takes treatment break

Needs replanning due to tumor change and external contour change

Bladder 1st and 13th fraction



Initial Adaptive – Tumor based



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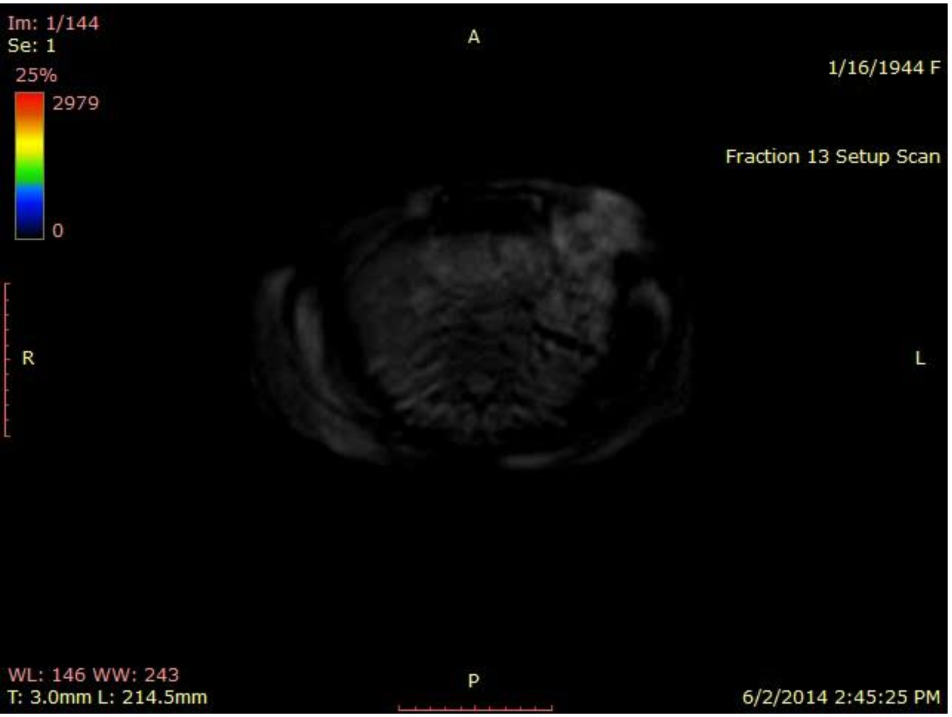
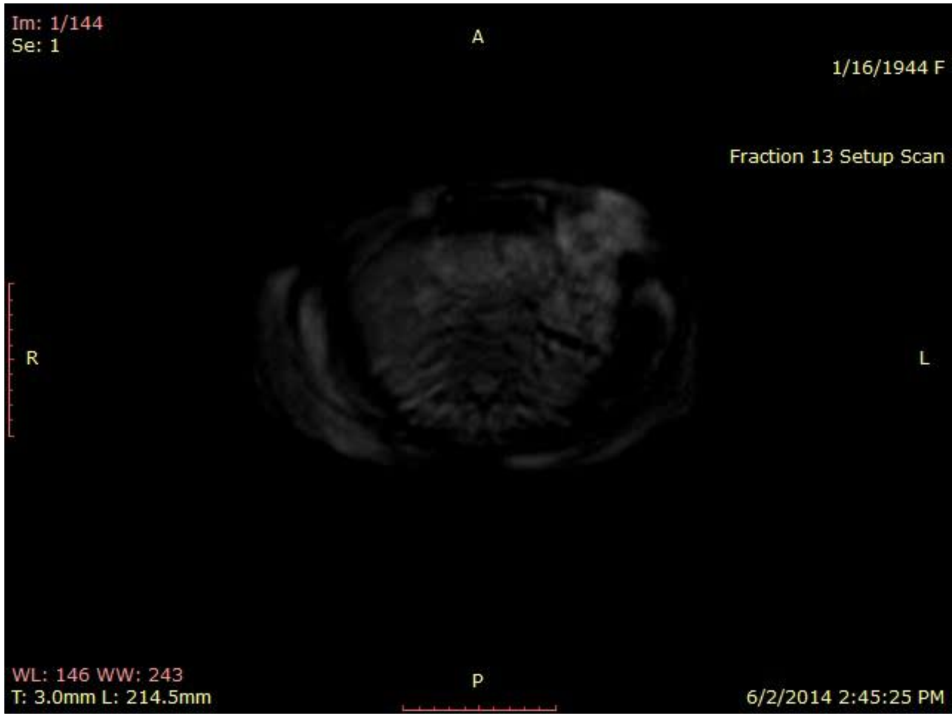
Replanned Bladder





Initial Adaptive – Tumor based

Abdomen adaptive radiotherapy checklist

Goal?

- Treatment intensification
- Treatment accuracy
- Toxicity reduction

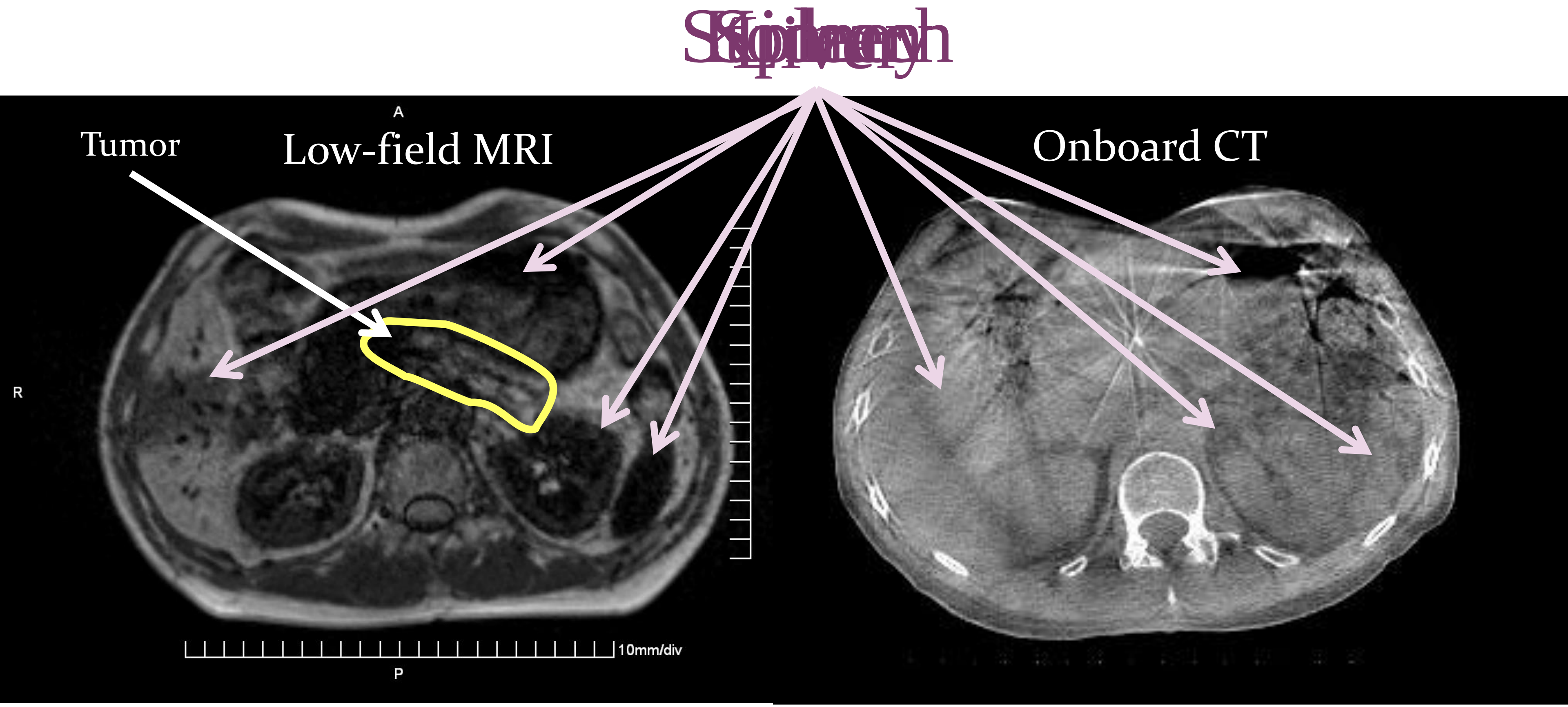
Frequency?

- Daily
- Weekly
- At pre-determined image evaluation during tx

Imaging surrogate?

- MR anatomy/function/motion

Pancreatic Cancer OARs better seen on MR than CBCT



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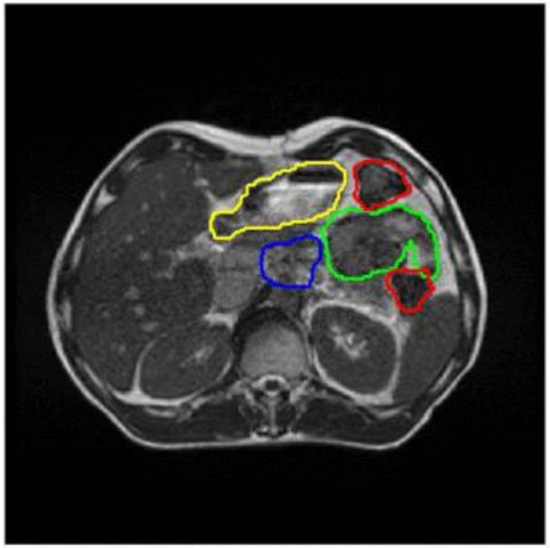
Pancreatic Cancer OARs move day by day

- 5 patients with daily MR
- 18-25 images per patient
- A motivated medical student recontoured each one and assessed margin to encompass 95% of voxels



	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Average
Stomach	1.8	0.9	1.5	1.8	1.5	1.5
Duodenum	0.6	0.9	0.9	0.9	0.9	0.8
Small int	1.8	0.9	1.5	1.8	2.7	1.7
Colon	1.2	3.6	2.7	1.2	0	1.7

cm

Online Adaptive SBRT Phase I Study

Co-PIs: Henke, Olsen, Parikh, Kashani

(NCI 02264886)

20 patients with unresectable primary or oligometastatic disease of the liver (n = 10) & non-liver (n=10) abdomen planned for SBRT

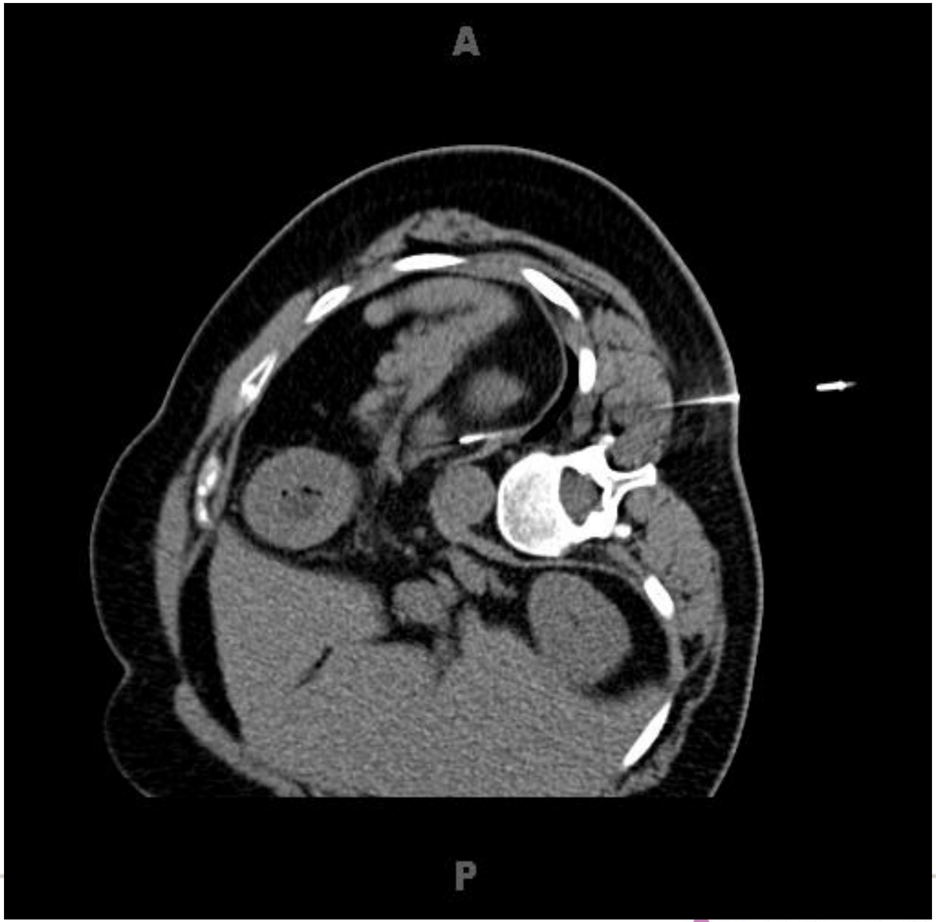
Prescription: 50Gy/5fx with online, adaptive MR-IGRT approach

Isotoxicity approach, with dose escalation (or de-escalation) based on hard OAR constraints

Phase I Trial Example Case

Solitary NSCLC Adrenal Metastasis

- 51yo woman, 1 year disease-free period
- Biopsy-proven, solitary 1.8cm adrenal ADC metastasis
- KPS 100%
- Preferred non-surgical option



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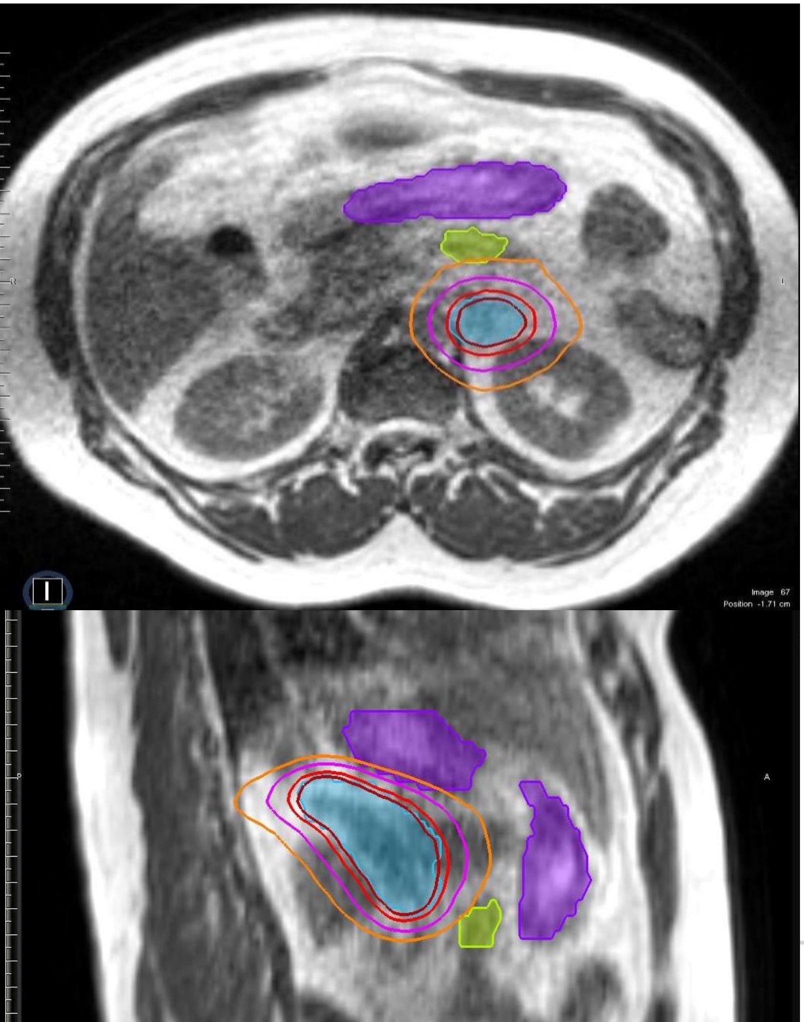
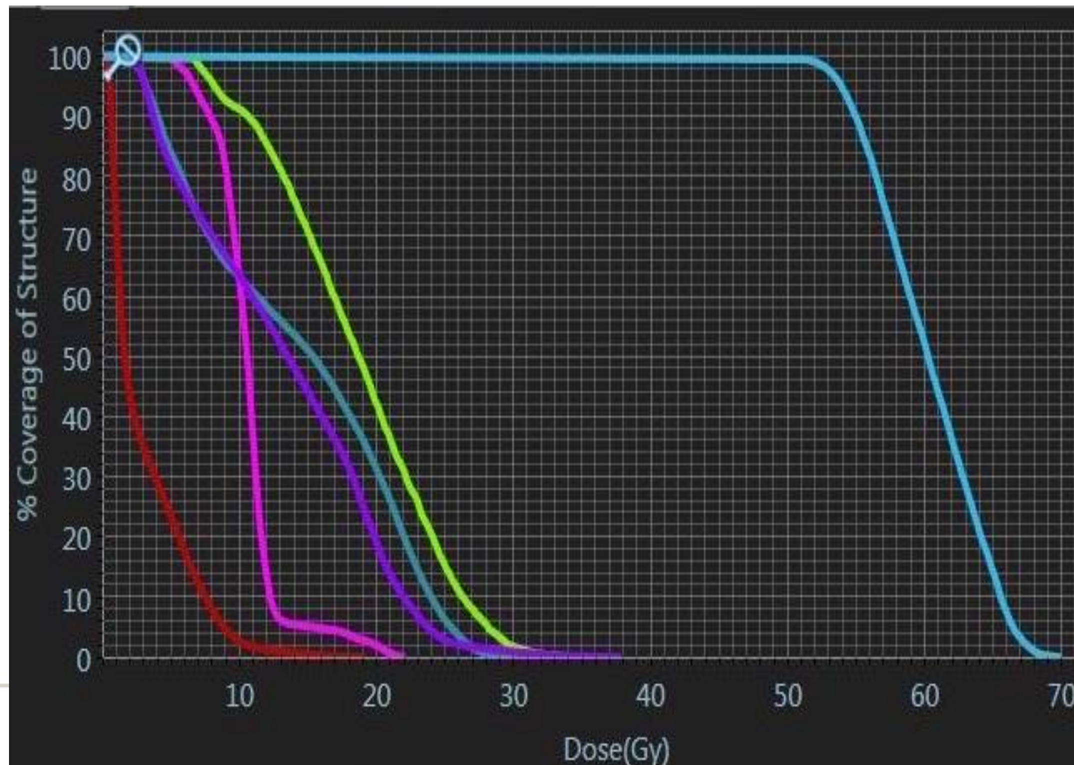
Phase I Trial Example Case

Solitary NSCLC Adrenal Metastasis

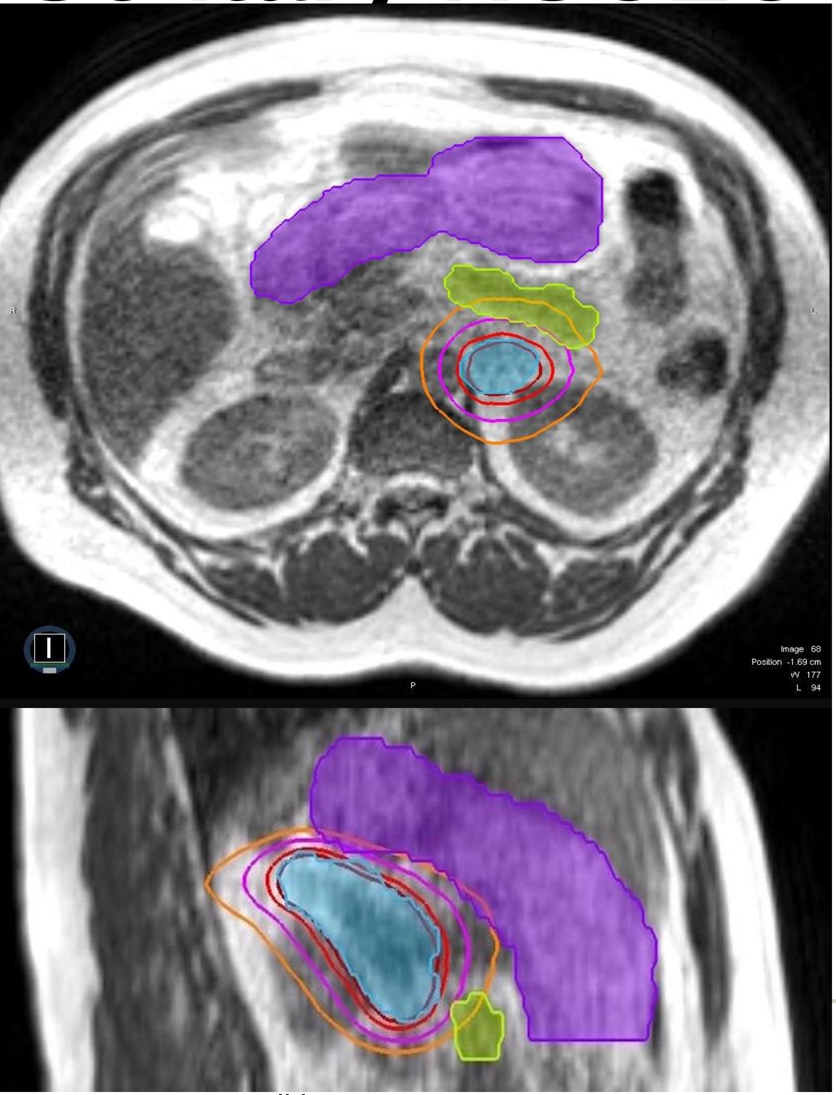


Day 1- All OAR constraints met, including small bowel & stomach



Phase I Trial Example Case

Solitary NSCLC Adrenal Metastasis

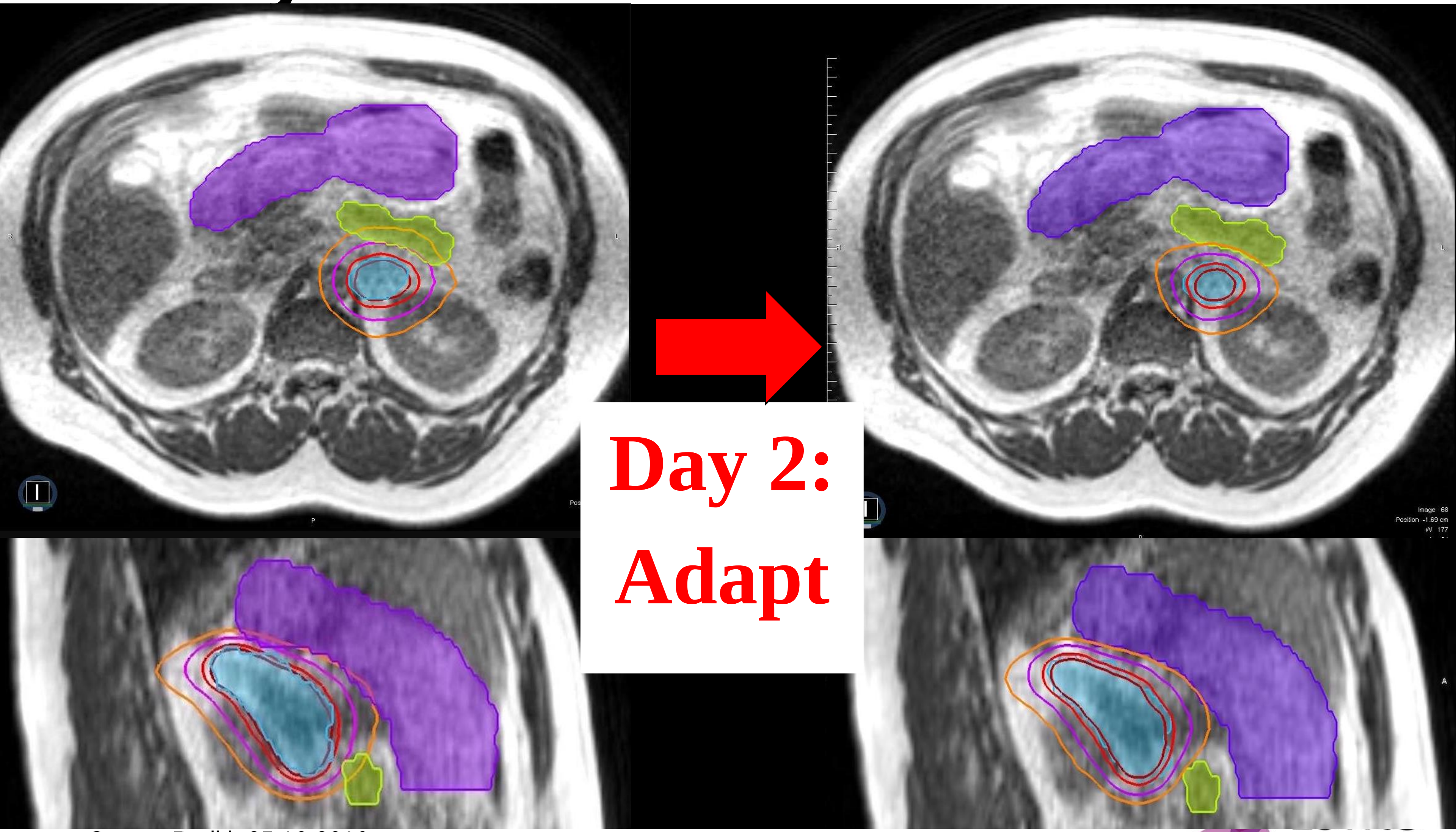


Day 2- Application of day 1 plan violates small bowel & stomach OAR constraints

Absolute
(% Isodose)
55 Gy (110%)
50 Gy (100%)
40 Gy (80%)
30 Gy (60%)

Phase I Trial Example Case

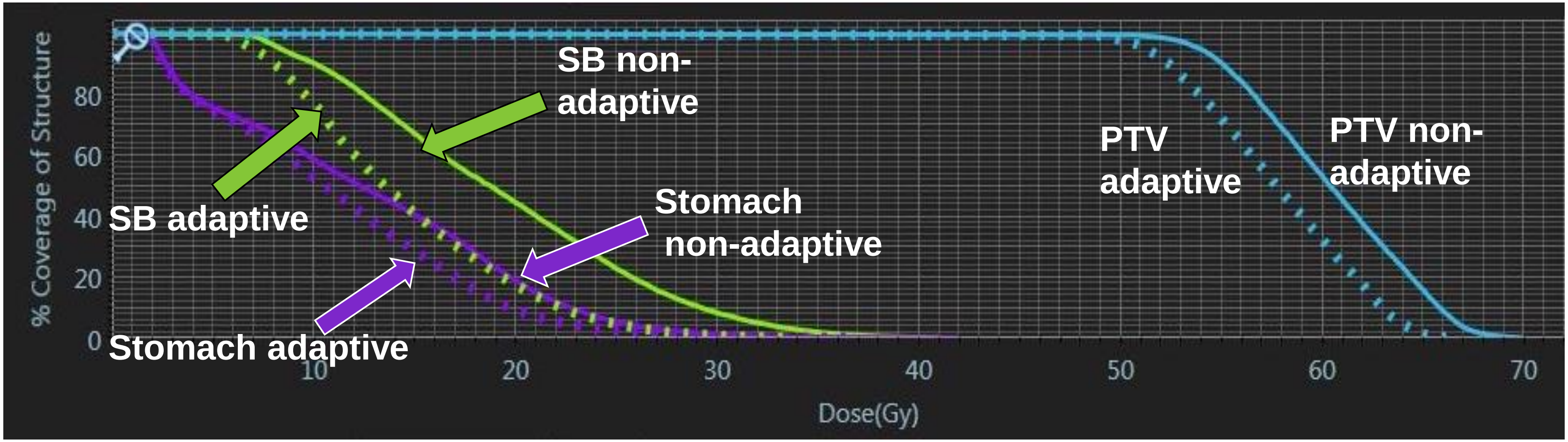
Solitary NSCLC Adrenal Metastasis



Day 2: Adapt

Phase I Trial Example Case

Solitary NSCLC Adrenal Metastasis



Adaptive plan reduces small bowel and stomach dose

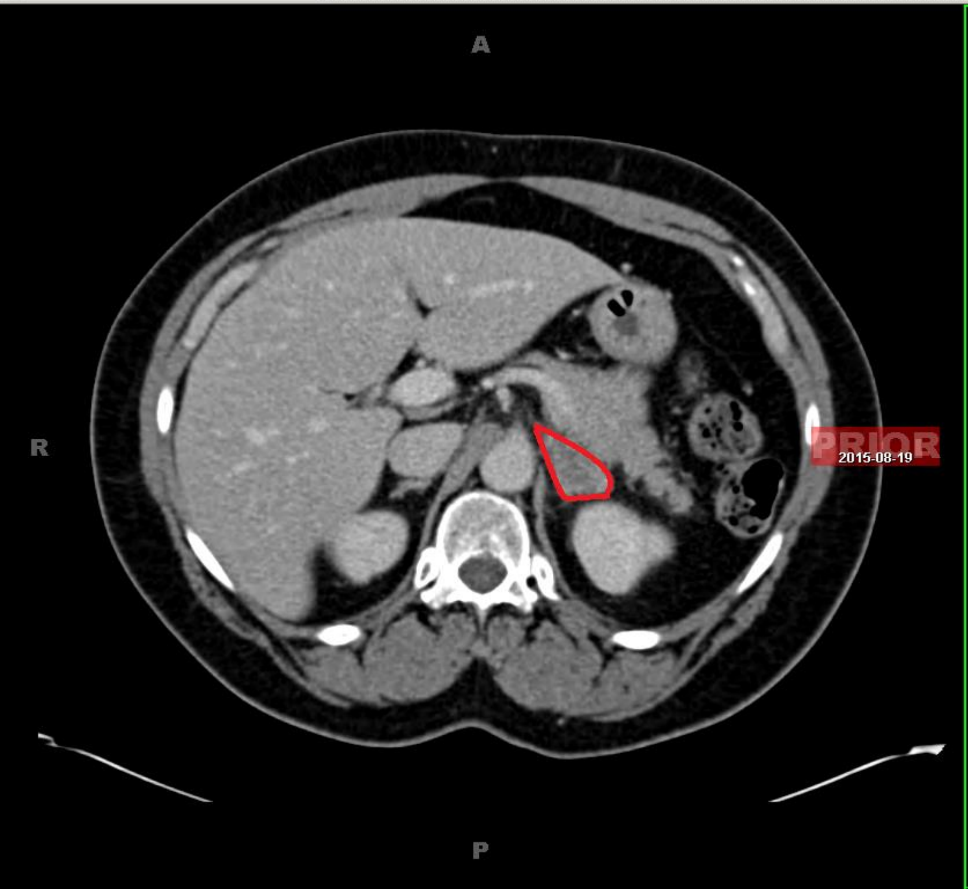
PTV coverage minimally sacrificed

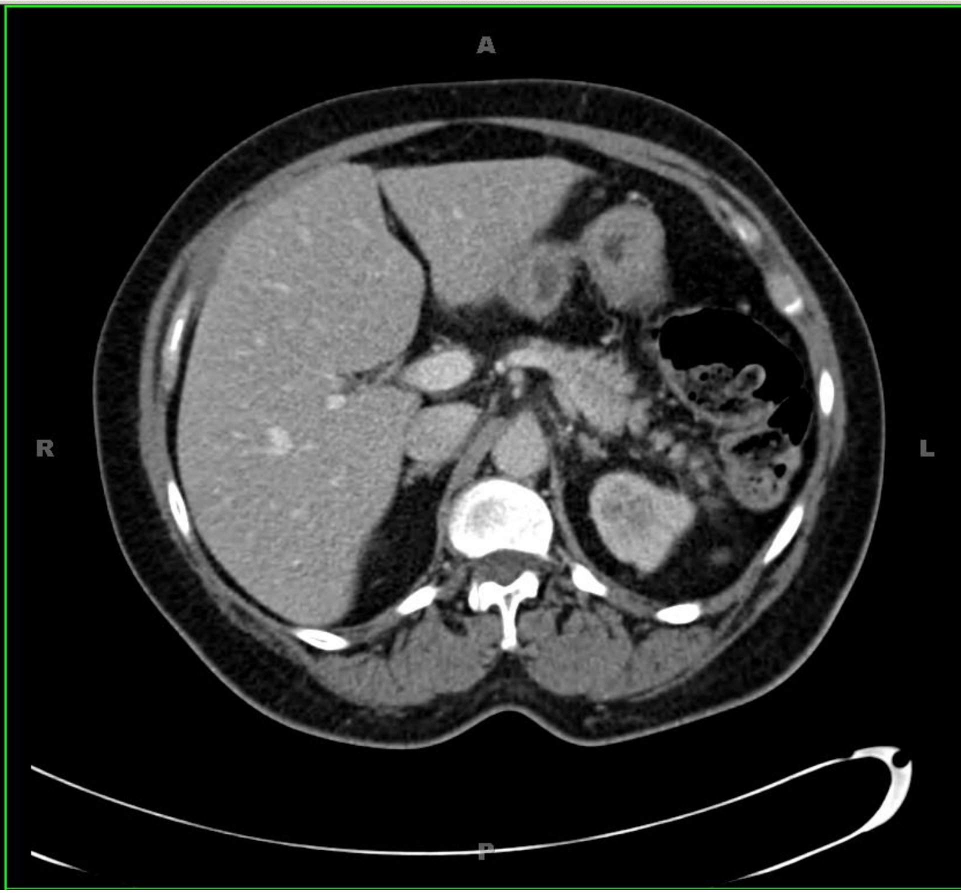
PTV coverage remains at goal 50Gy

School

Phase I Trial Example Case

Solitary NSCLC Adrenal Metastasis





Patient with zero reported acute or late toxicity

Radiographic CR at 3 and 6 months

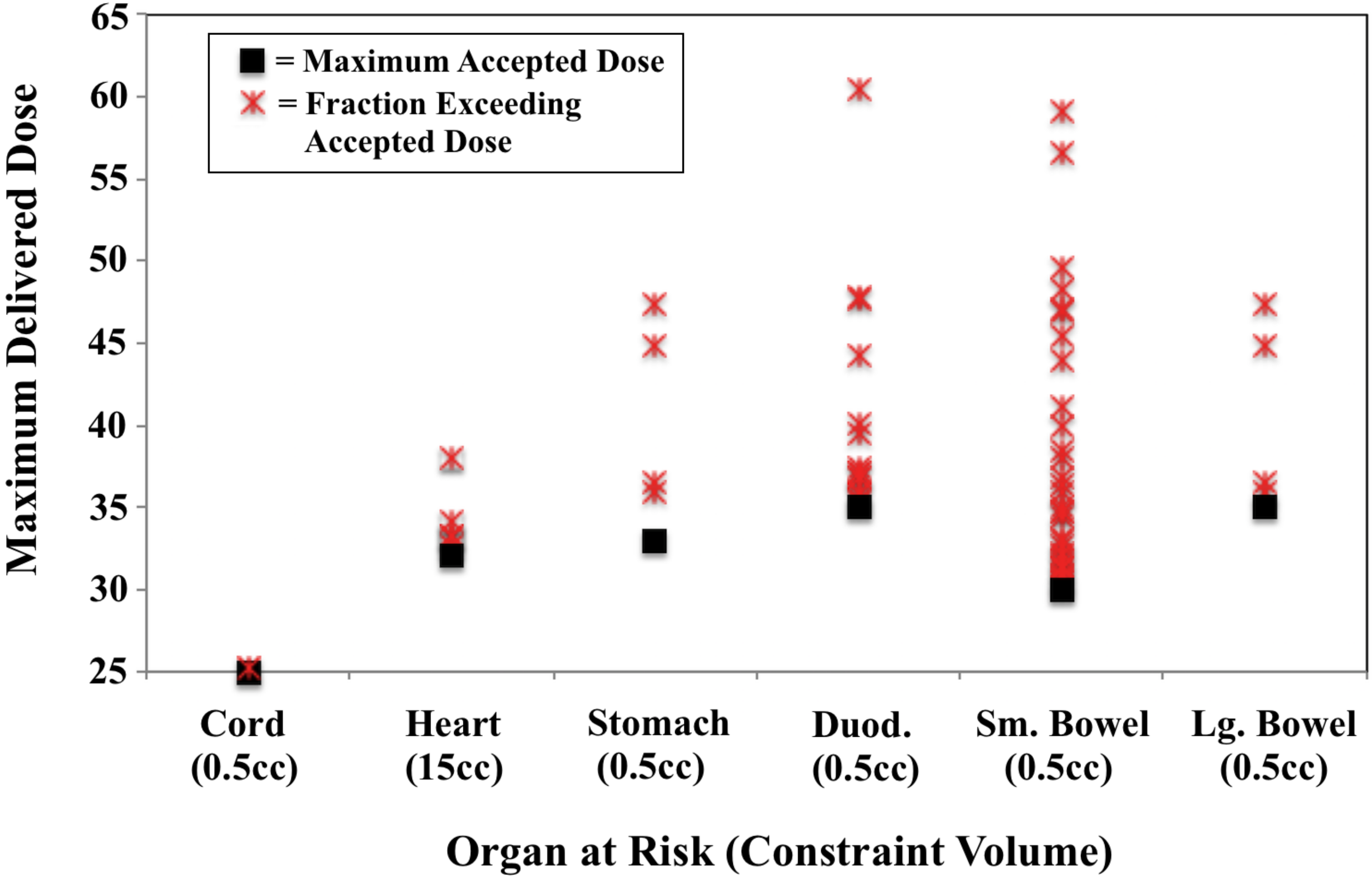
Phase I Results—Timing

- Median on table time: 79 minutes
- Median segmentation time: 9 min
- Median re-planning time: 10 min
- Median QA time: 5 min

Phase I Results—Plan Adaptation

- 83% (79/95) fx adapted—all patients had ≥1
- Plans adapted for 64% of liver & 98% of non-liver abdomen fx
- Initial plans would have violated OAR constraints in 70/95 fx
- 100% of OAR violations resolved with adaptive planning

Phase I Results—OAR Sparing



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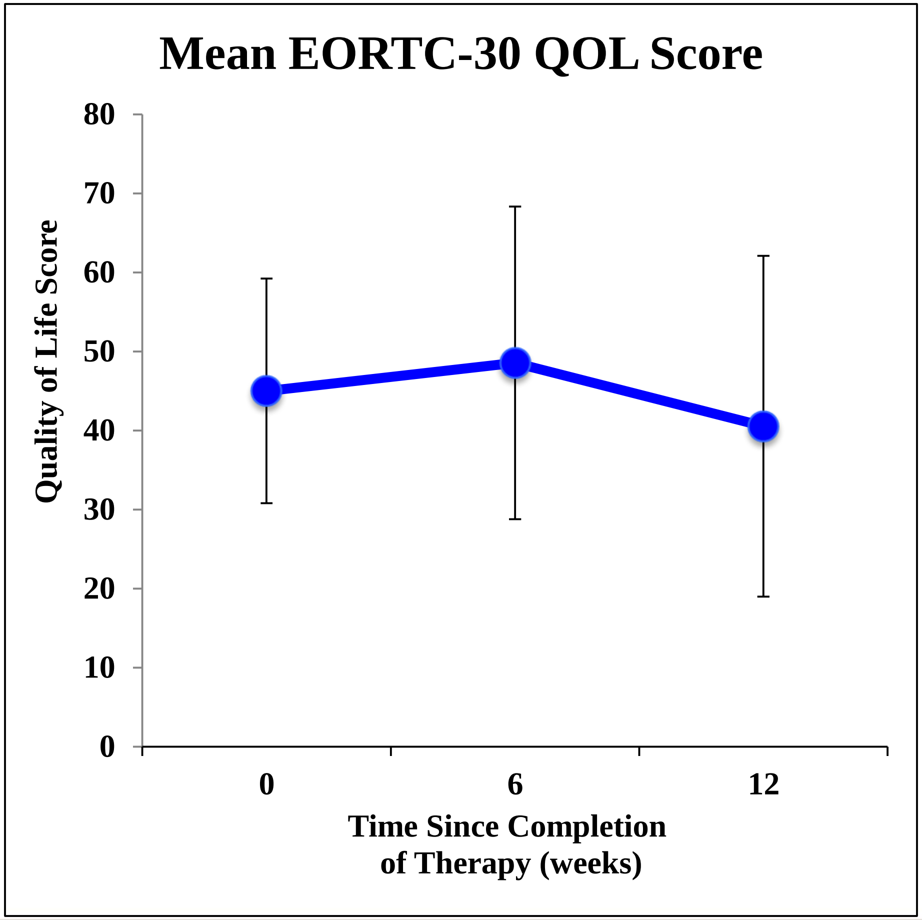
Phase I Results—Clinical Outcomes

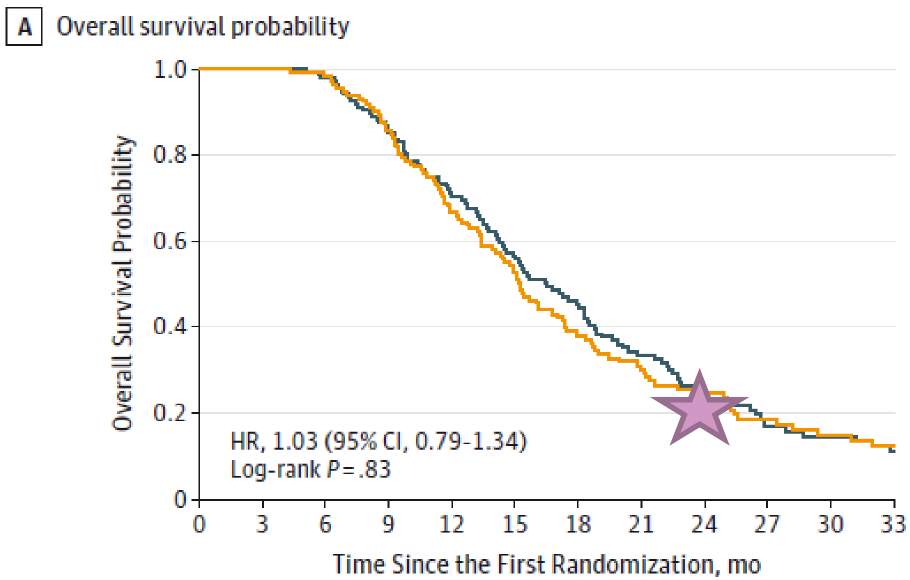
No Grade 3 toxicity at median 11.8 mo f/u

Expected 20-30% using aggressive dose regimen

No change in patient-reported EORTC-qlq 30 QOL scores (*P* = 0.29) at 0, 6, and 12wks.



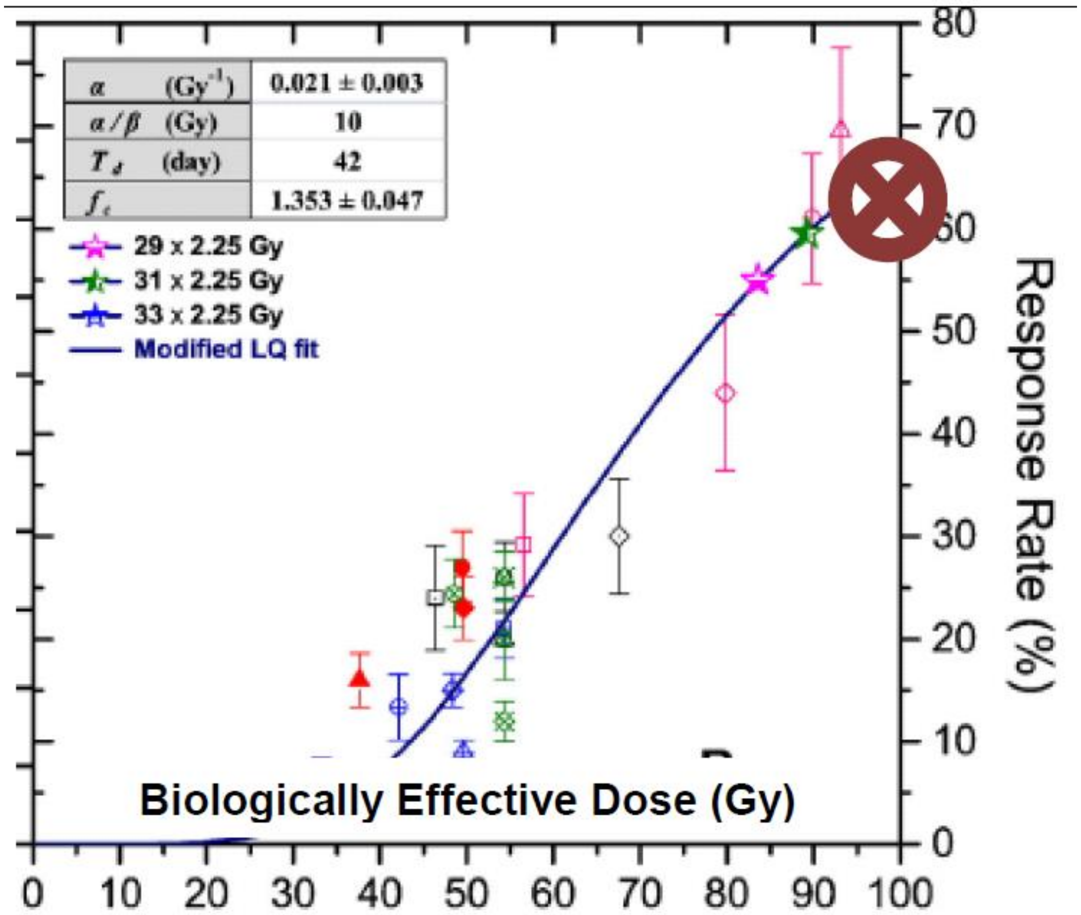
Locally Advanced Pancreatic Cancer is Bad



Chemotherapy												
No. at risk	136	136	133	117	94	70	55	39	24	14	12	8
No. of events	0	0	4	20	40	60	73	87	99	104	106	109
Chemoradiotherapy												
No. at risk	133	133	131	113	87	66	45	34	26	18	12	9
No. of events	0	0	3	20	45	63	80	89	96	101	105	106

"If cancer is the emperor of all maladies, then pancreatic adenocarcinoma is the ruthless dictator of all cancers" – Deborah Schrag

Could dose escalation help?



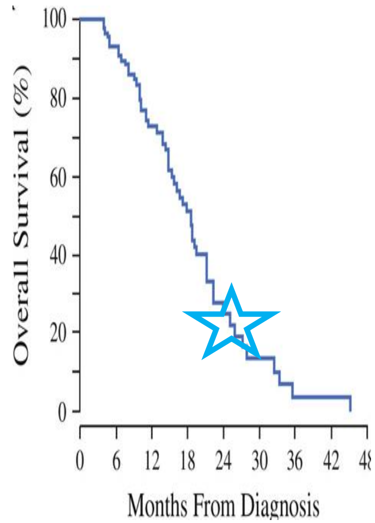
Dose escalation may improve SURVIVAL in Pancreatic Cancer

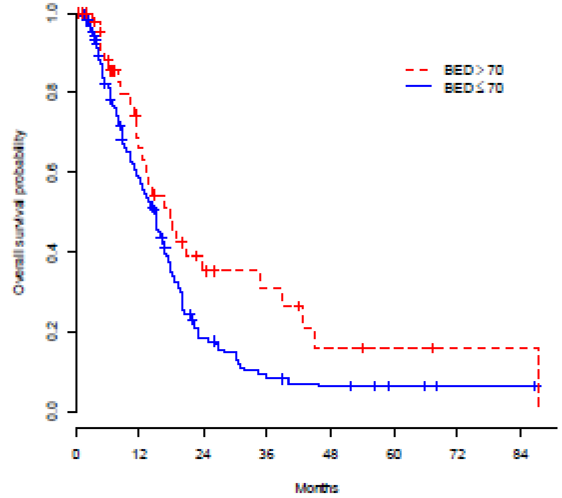
- Retrospective report from MD Anderson
- Tumors at least 1 cm from a GI structure (25% of patients) were considered for hypofractionated dose escalation
- Patients who received radiotherapy with BED > 70 Gy had an improved overall survival of 36% versus 19% at 2 years, and 31% versus 9% at 3 years

Table 1 Dose fractionation schedules, biologically effective dose, and dose-volume constraints

Dose and no. of fractions	Biologically effective dose (Gy)	No. of patients	Average stomach V50 (cm^3) or maximum point dose if V50 = 0 cm^3	Average duodenum V50 (cm^3) or maximum point dose if V50 = 0 cm^3
63 Gy in 28 fx	77.2	14	25.5	22.8
70 Gy in 28 fx	87.5	11	25	27.6
67.5 Gy in 15 fx	97.9	7	0; 44.8 Gy	0; 44.9 Gy
60 Gy in 10 fx	96.0	1	0; 41.3 Gy	0; 43 Gy
50 Gy in 5 fx	100.0	1	0; 26.3 Gy	0; 36.1
51.3-70.4 Gy in 13-39 fx	70.4-84.3	13	33.9	15.2

Abbreviations: fx = fractions; V50 = volume of organ receiving >50 Gy.
α/β = 10 for calculation of biologically effective dose.





OARs movement = toxicty – even if you have protons!

- 19 liver cancer patients
- 26% needed replanning after weekly slow CT
- 2 still developed grade 3 toxicity!

RESULTS

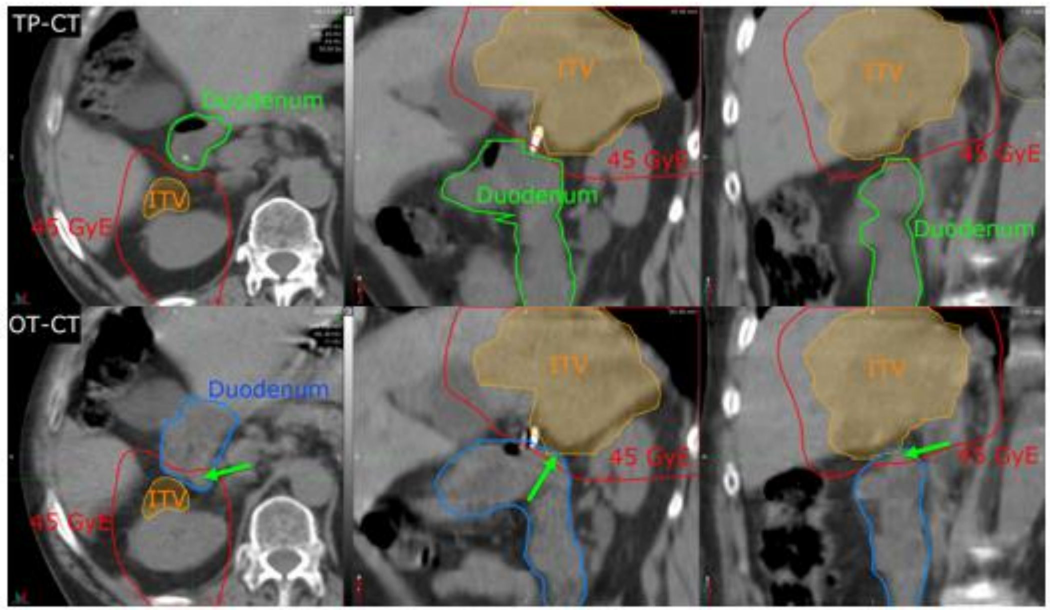


Figure 2. 66 y/o WM with central IHCC s/p TACE and gem/cis treated with PBT to 58.0 GyE in 15 fx. Abdominal compression was used with fiducial marker alignment. OT-CT after fx 10 showed duodenum exceeding dose tolerance (V45 = 2 cc), resulting in re-planning.

Apistharanax, ASTRO, 2016

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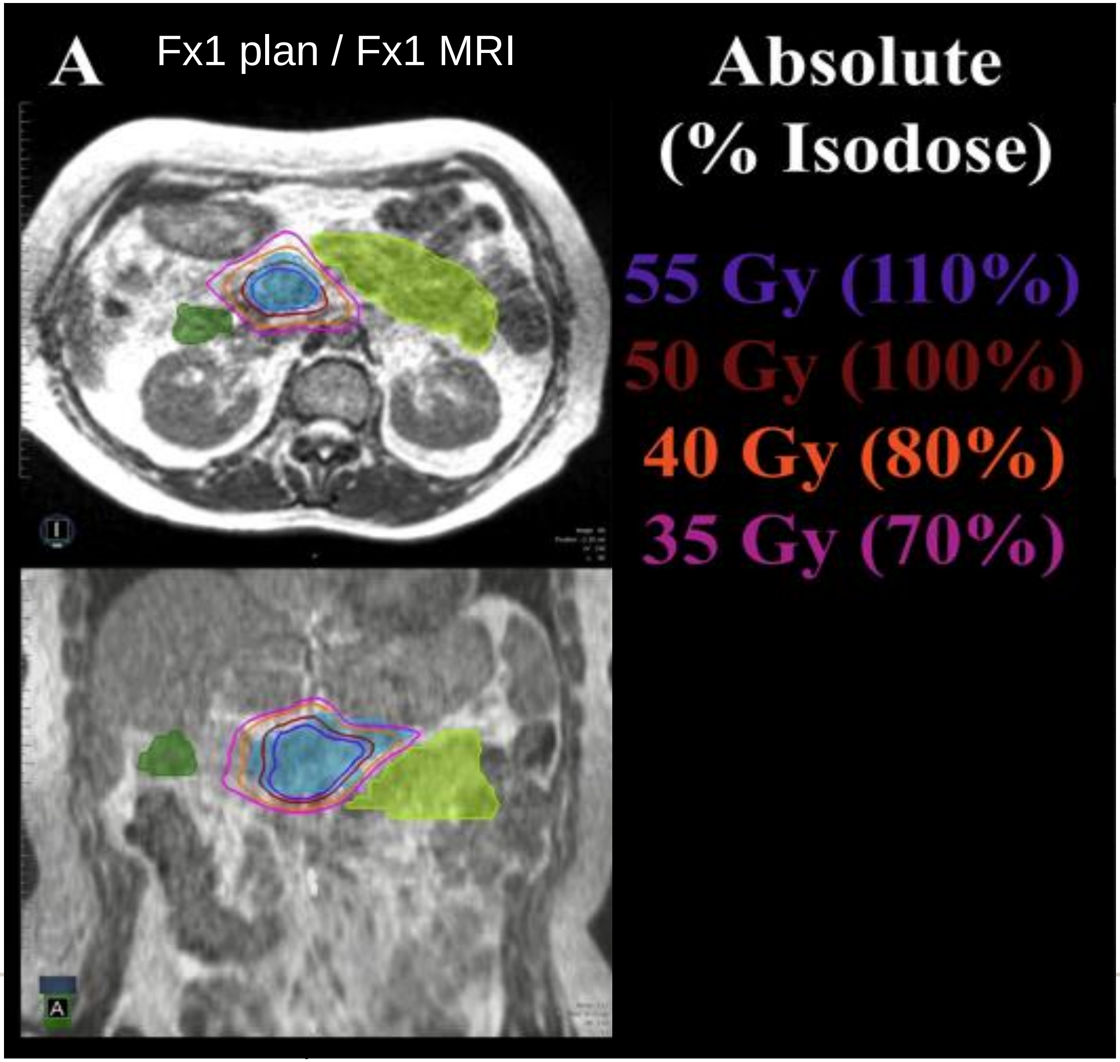
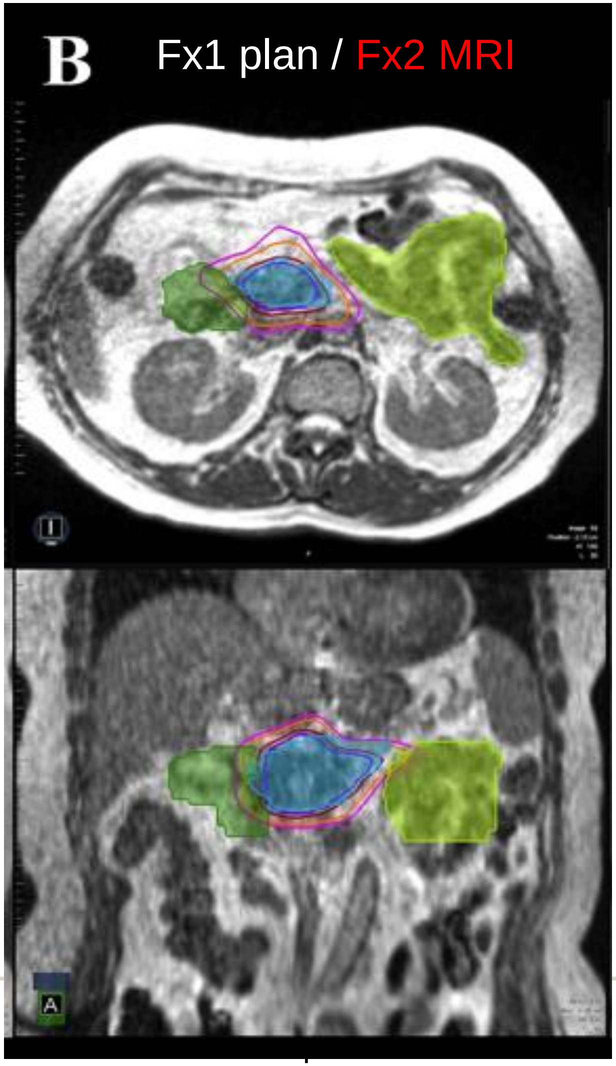
Patient Population

Pt ID	Oncologic History	Dose (Gy)/ Fx	Concurrent chemo	OARs for re-contouring	Additional OARs in replanning optimizer	Motion Management	Re-planning constraints
1	57 y/o with LAPC with continued encasement of celiac artery after gemcitabine/nab-paclitaxel and FOLFIRINOX. Planned for resection.	50.7/15	gemcitabine	Stomach Small Bowel Duodenum	Large Bowel Spinal Cord Kidneys	Expiratory gating with 3 mm boundary. 5 mm PTV.	Stomach - Re-plan if 0.5 cc > 40 Gy Small bowel - Re-plan if 0.5 cc > 40 Gy Duodenum - Re-plan if 0.5 cc > 40 Gy PTV - Re-plan if > 83% receives > 48.17 Gy Dmax - Re-plan if > 70 Gy
2	71 y/o with BRPC with SMV abutment after gemcitabine/nab-paclitaxel	60/15	gemcitabine /nab-paclitaxel	Stomach Small Bowel Duodenum	Large Bowel Spinal Cord Kidneys	Expiratory gating with 3 mm boundary. Pt with poor breath hold.	Stomach - Re-plan if 0.75 cc > 40 Gy Small bowel - Re-plan if 0.75 cc > 40 Gy Duodenum - Re-plan if 0.75 cc > 40 Gy GTV - Re-plan if > 70% receives > 57 Gy Dmax – no hot spot near GI tract
3	63 y/o with LAPC with SMA encasement after gemcitabine/nab-paclitaxel and FOLFIRINOX	60/15	capecitabine	Stomach Small Bowel Duodenum	Large Bowel Spinal Cord Kidneys	Expiratory gating with 3 mm boundary. 6 mm PTV.	Stomach - Re-plan if 0.75 cc > 40 Gy Small bowel - Re-plan if 0.75 cc > 40 Gy Duodenum - Re-plan if 0.75 cc > 40 Gy CTV - Re-plan if > 95% receives > 40 Gy Dmax – Re-plan if > 72 Gy
4	59 y/o with metastatic pancreatic cancer with response of hepatic metastasis to FOLFIRINOX and FOLFIRI and progression of primary tumor	60/15	gemcitabine	Stomach Small Bowel Duodenum	Large Bowel Spinal Cord Kidneys	Expiratory gating with 3 mm boundary. 6 mm PTV.	Stomach - Re-plan if 0.75 cc > 40 Gy Small bowel - Re-plan if 0.75 cc > 40 Gy Duodenum - Re-plan if 0.75 cc > 40 Gy GTV - Re-plan if > 95% receives > 40 Gy Dmax – no hot spot near GI tract

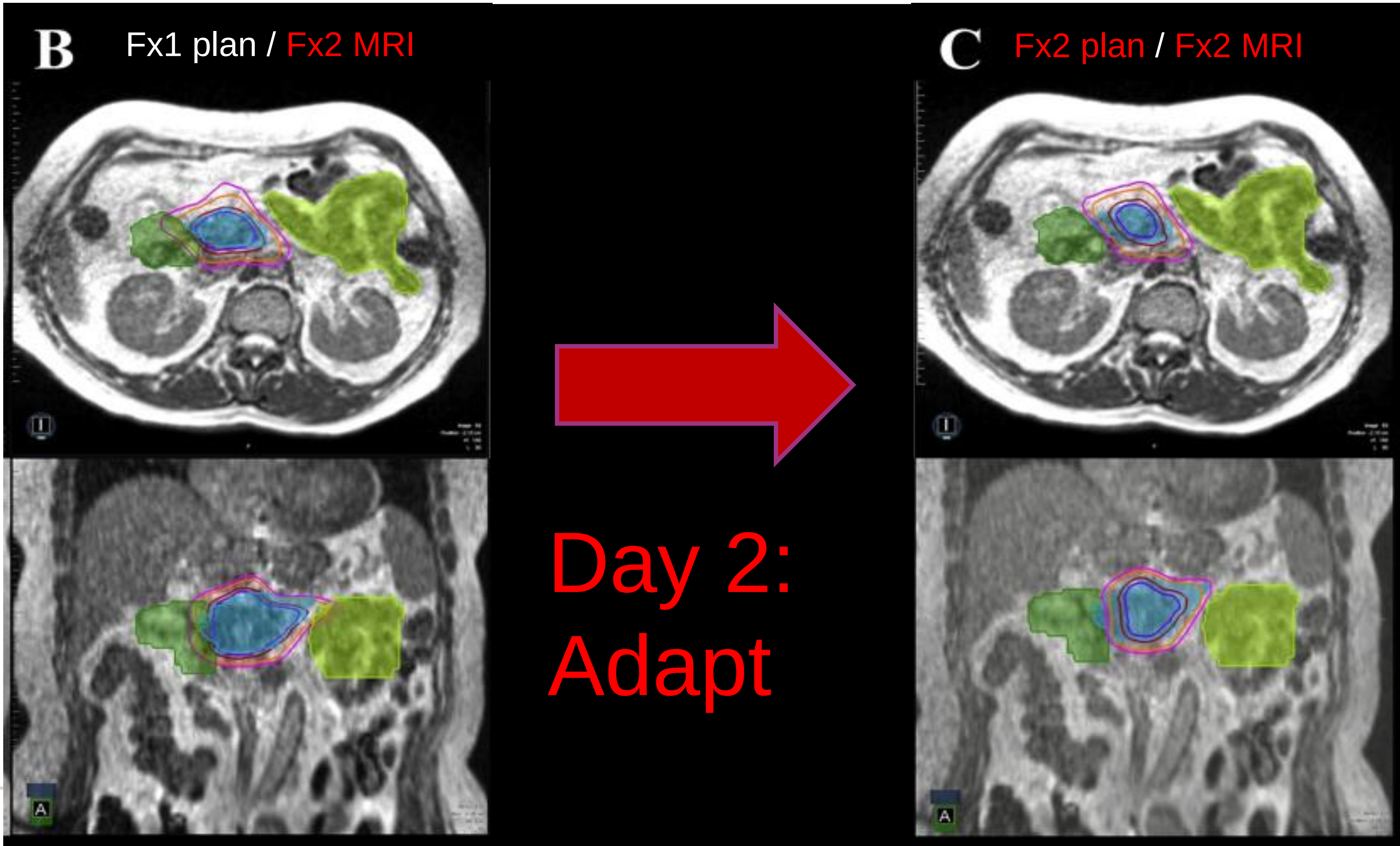
After chemo

Before chemo


A
Fx1 plan / Fx1 MRI
Absolute
(% Isodose)
55 Gy (110%)
50 Gy (100%)
40 Gy (80%)
35 Gy (70%)



Day 2 – Application of fraction 1 plan violates duodenal and small bowel OAR constraints


B
Fx1 plan / Fx2 MRI
C
Fx2 plan / Fx2 MRI
Day 2:
Adapt

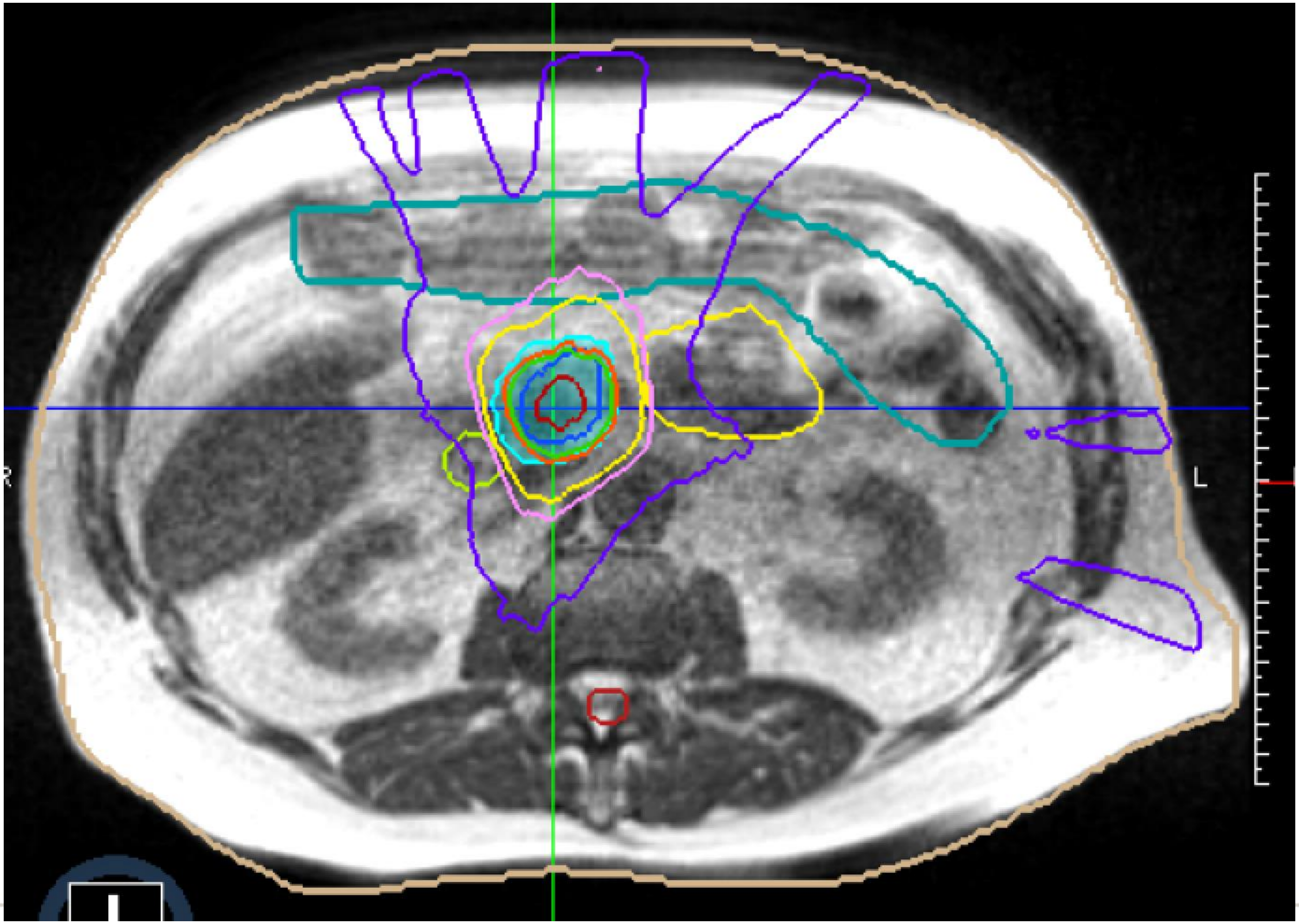
Not as easy patient

71 year old with borderline operable pancreatic cancer and significant comorbidities

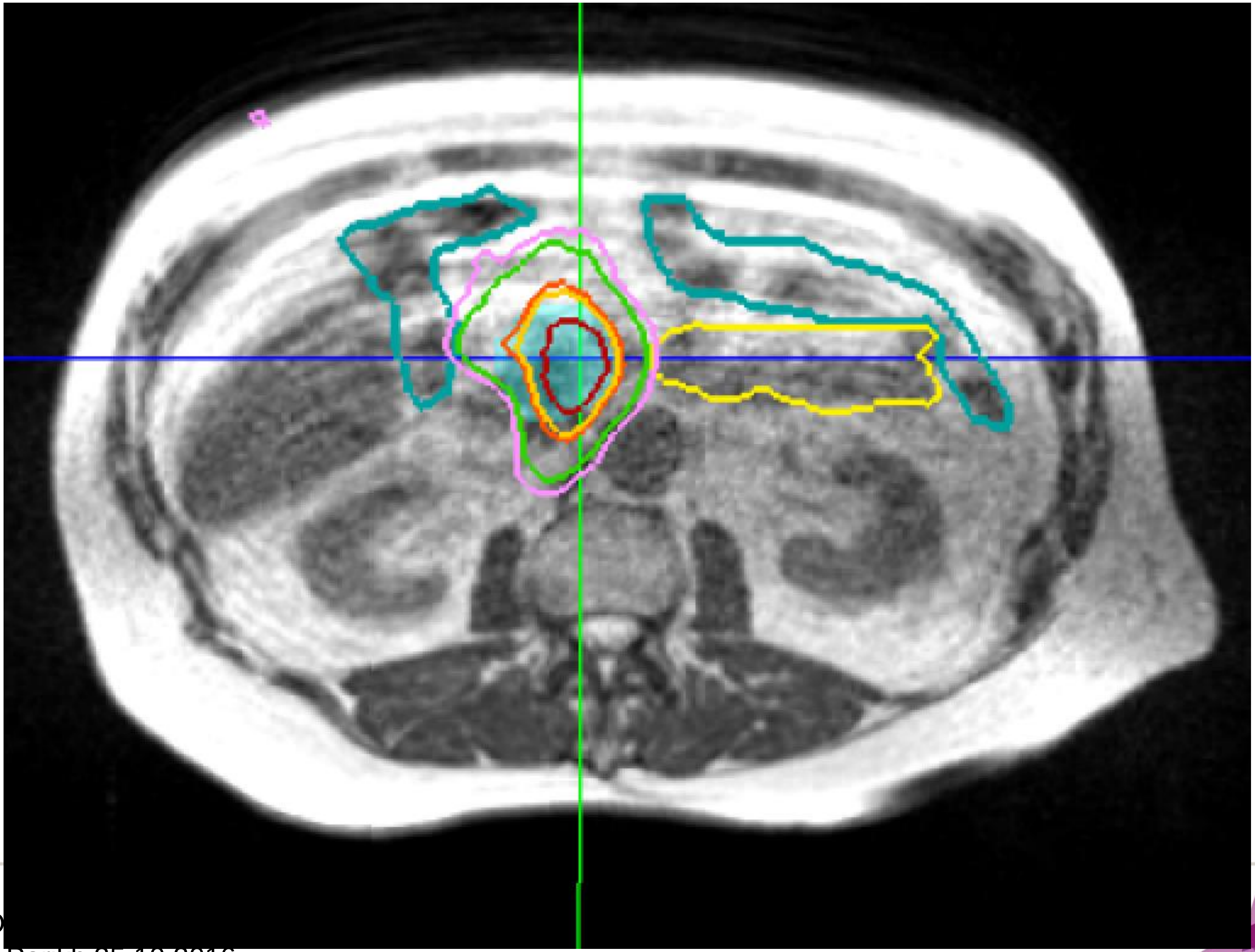
Treated on a protocol with concurrent full dose gemcitabine and abraxane and radiation

Dose of 60 Gy / 15 fractions with daily adaptation

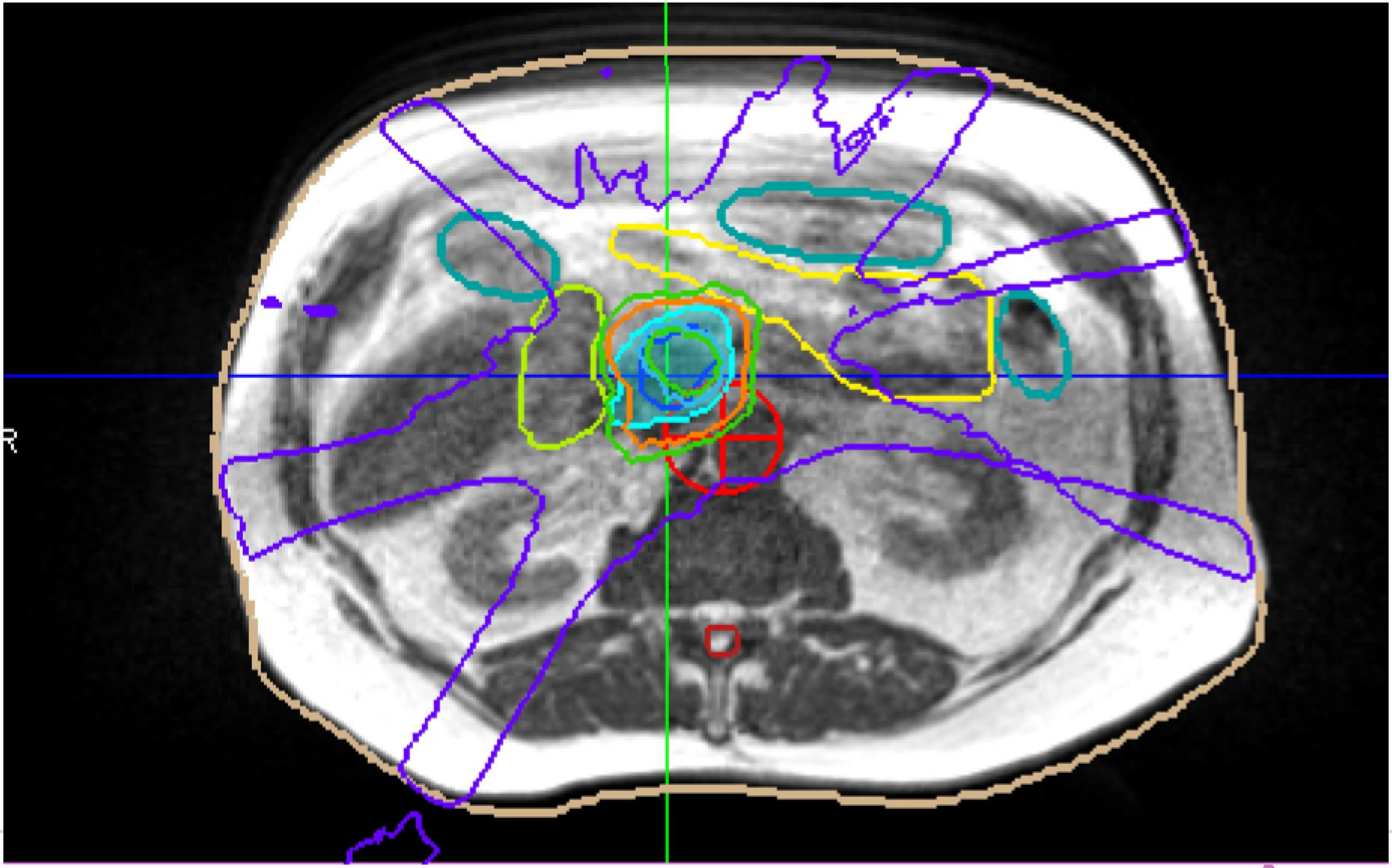
One fraction



Another fraction



Yet another



Older Patient's Tolerance

Date	Time Pt entered Room	Pt Setup/Image Acquisition	Wait for MD	Time of Localization (send shift to couch)	Time of Physician Contouring	Time of Replanning	Start time of QA check	Scan set up	QA check end	Start Tx time	End of Tx time	Comments
4-18 2016	1543	1552	1555 1602	1601	1602	1617	1641	1644	1645	1654	1720	ROI 15 ADAPTED
4-19-16	1302	1311 *1319	1315 *1323 *1327	—	—	—	—	—	—	—	—	*had to rescan *No Tx Today
4/20/16	9:54	10:01	10:02 10:03(R) 10:19(A)	10:23	10:24	10:38	10:51	10:57	10:57	11:09	1136	
4-21-16	1226	1233	1235 1237	1238	1238	12:59	13:16	—	—	—	—	*Pt in too much pain No treatment
4-22-16	1465	15:01	15:06 15:09(R) 15:35(A)	15:06	15:09	1537	1545	1550	1550	1559	1621	
4-25-16	1608	16:16	16:17(A)	16:20	1623	1637	1645	16:50	16:50	16:53	17:09	ADAPTED to Fx-4-Adapted-Abdomen 4-25-16

Note: Replanning includes Boolean Structure, Dose evaluation, optimization, normalizing plan and saving and exporting plan

Older Patient's tolerance (2)

Date	Time Pt entered Room	Pt Setup/Image Acquisition	Wait for MD	Time of Localization (send shift to couch)	Time of Physician Contouring	Time of Replanning	Start time of QA check	Scan set up	QA check end	Start Tx time	End of Tx time	Comments
4/26/16	1410	1417 took 3 scans	—	1430	1430	1438	1446	1446 1529	1448	1458 *1532	*1526 1546	* Rescan Adapted ROI 17%
4/27/16	9:54	10:00 *10:06	10:07 10:11	10:10	10:11	10:20	10:30	10:34	10:37	10:42	1102	* MR ERROR Adapted ROI 10%
4/28/16	831	837	839 844	842	847	859	907	910	911	916	933	Adapted ROI → 10%
4/29/16	1150	1156	1159 1207	1207	1208	1219	1228	1231	1231	1236	1258	Adapted ROI → 10%
5/2/16	1357	1408	1413 1415	1412	1415	1426	1438	1441	1441	1449	1511	Adapted
5/3/16	13:07	1314	1320 1343	1321	Physic Contour 1321 Doc 1342	1343	—	—	—	1353	1412	Did not adapt

Note: Replanning includes Boolean Structure, Dose evaluation, optimization, normalizing plan and saving and exporting plan

Overall Tolerance

2/5 patients needed pain medication, anxiolytics or both to tolerate MRgRT

No acute GI toxicity!

Fatigue was present

Would normally expect ~22% rate of grade 3 acute GI toxicity with a dose of 55 Gy in 25 fractions! (Badiyan, AJCO, 2016)

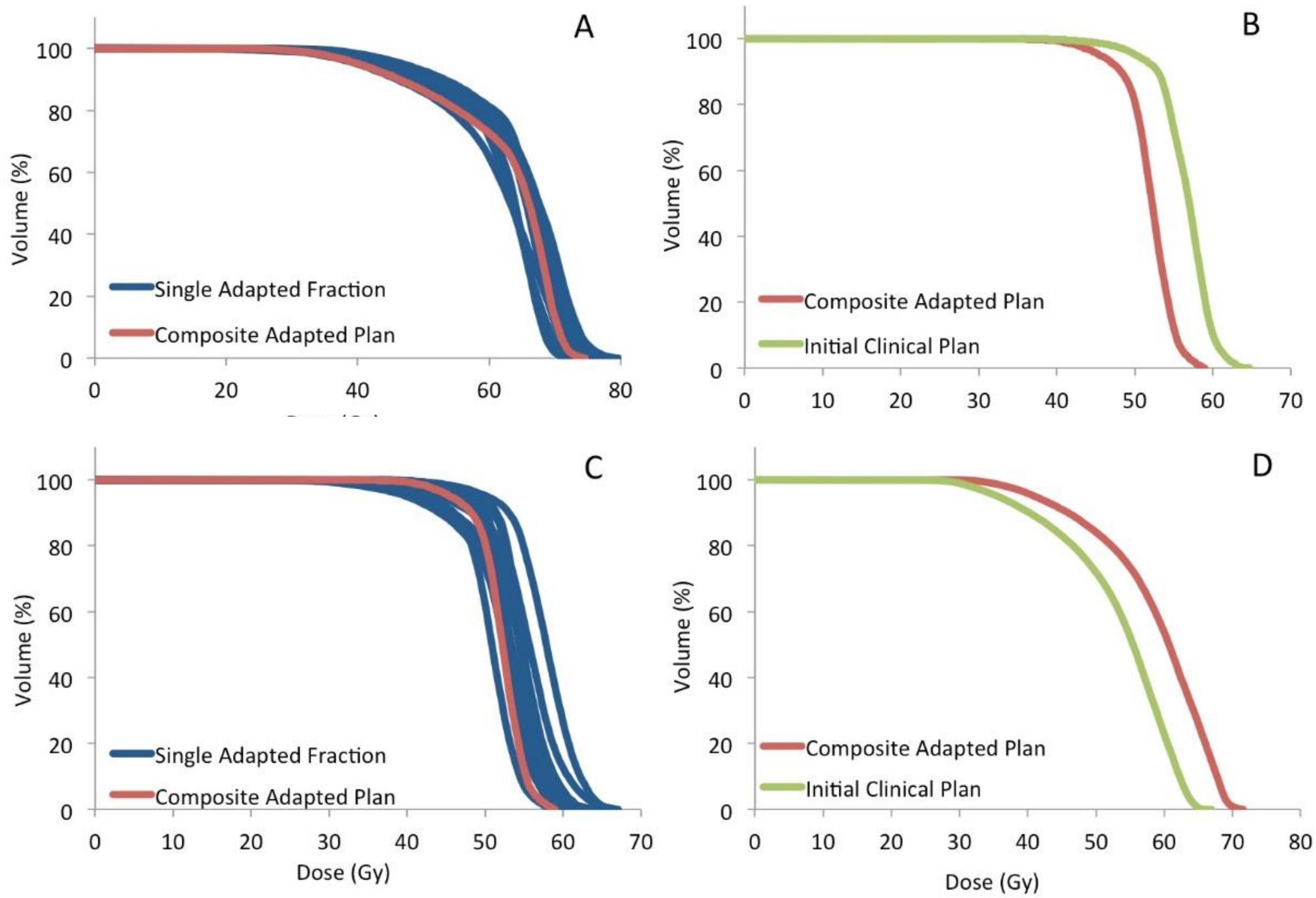
Plan adaptations

Pt ID	Adapted Fractions	Reason for Adaptation
1	13	Stomach – 9 Small bowel – 1 Stomach and small bowel – 2 Stomach and duodenum - 1
2	14	Target coverage – 2 Duodenum – 3 Large bowel – 3 Duodenum and small bowel – 3 Stomach and duodenum – 1 Small bowel – 1 Large bowel, small bowel, stomach - 1
3	10	Target coverage – 2 Duodenum – 6 Small bowel and duodenum – 1 Small bowel – 1
4	14	Target coverage – 2 Stomach – 2 Duodenum – 7 Small bowel and duodenum – 1 Small bowel – 1

Patients had plan adaptation for most of their fractions

Varied reasons, mostly for OAR constraints

Cumulative Target Dose



Early Clinical Response

Patient 1: No CT response, Ca 19-9 remained low, surgery with microscopic disease only

Patient 2: No MR response, PET response, Ca 19-9 decrease

Patient 3: No MR response, No PET response, Ca 19-9 decrease

Patients 4 and 5 pending evaluation

Challenges

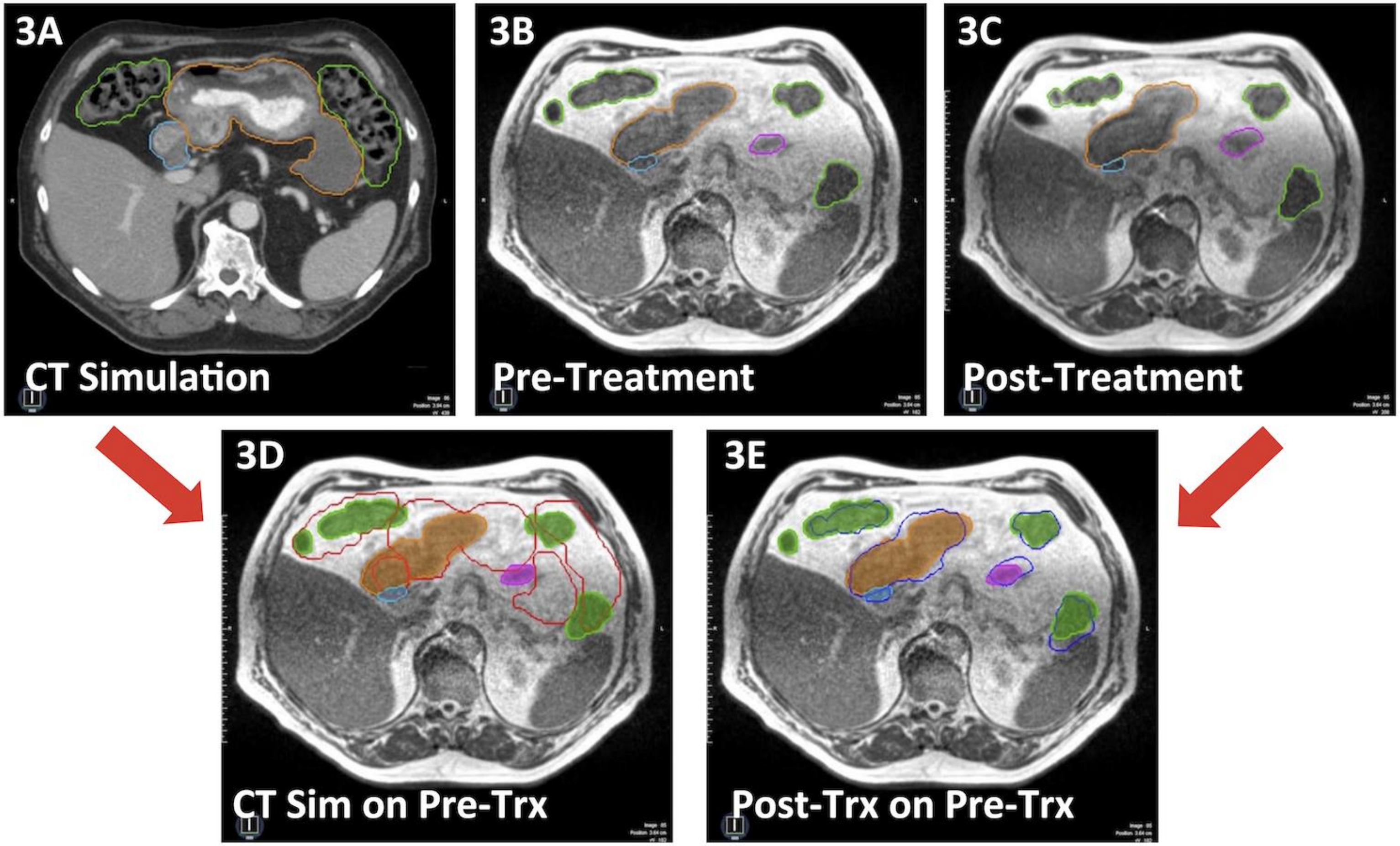
Assessing Intrafraction Motion during Plan Adaptation

Patients received 2 sets of images on a delivery day due to machine errors or patient intolerance

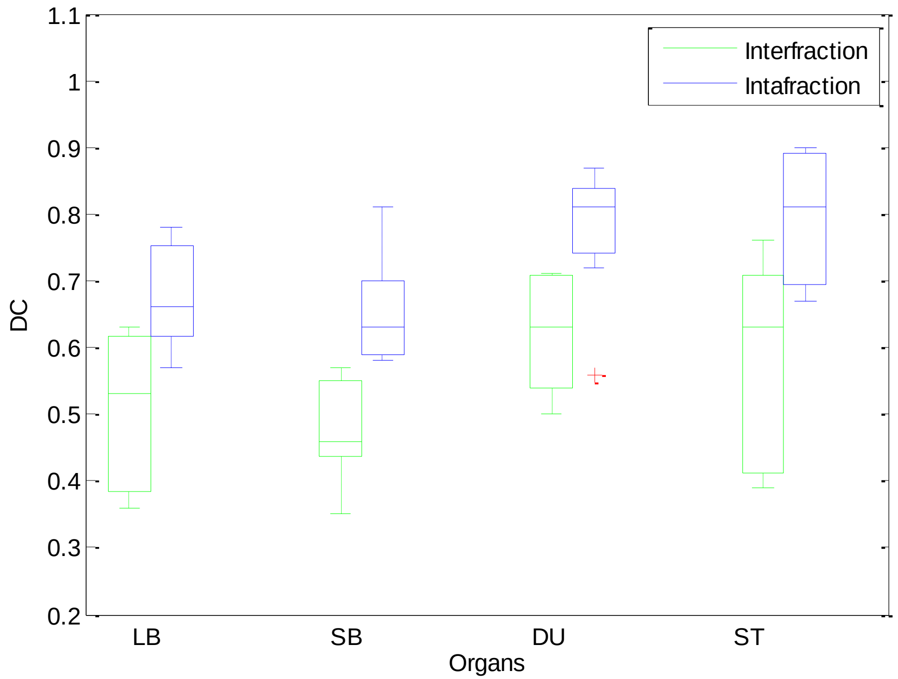
Images compared with simulation images taken at the beginning of therapy

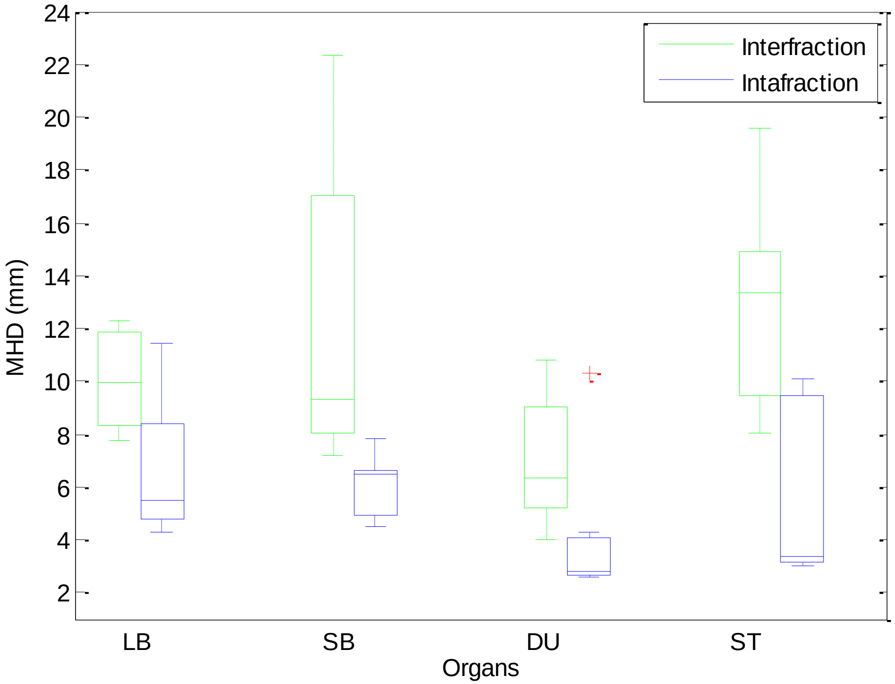
The viscous GI structures – stomach, duodenum, small intestine and large intestine were contoured on each image

Patient example (intrafx motion)



Early image analysis





Meaningful dose constraints

Current dose constraints based on non-adaptive plans (ie 45 Gy maximum dose to GI structures in hypofractionated regimen; 33 Gy to proximal GI structures in SBRT regimen)

These are not necessarily applicable to a ‘plan of the day’ regimen

There are residual errors in the ‘plan of the day’ regimen

We will need to increase these tolerances to make a ‘real’ dose constraint

Therapist change in requirements

Therapists already had to learn MR based localization and safety

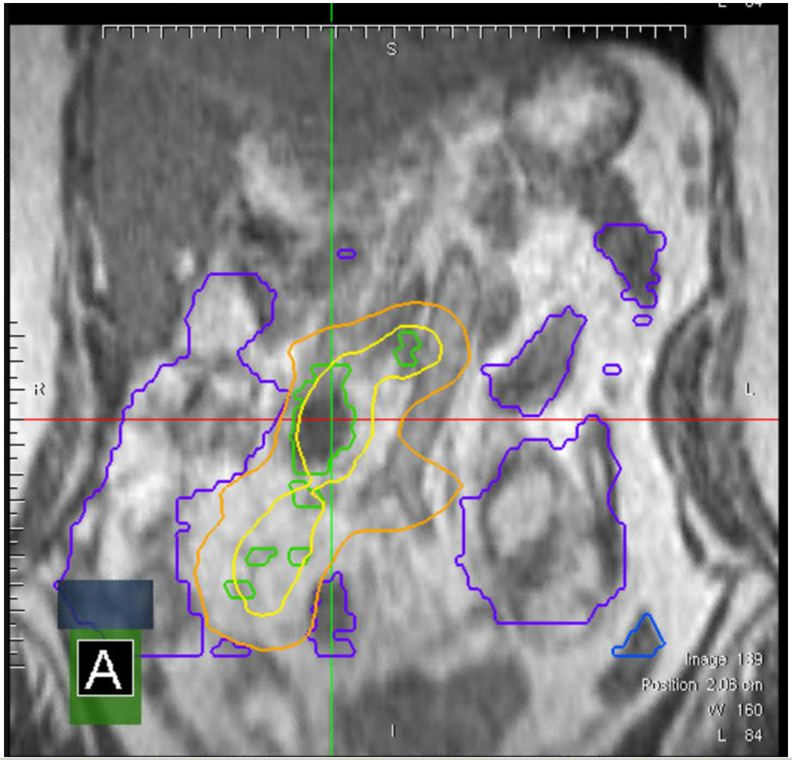
Now learning MR based segmentation for normal tissue structures

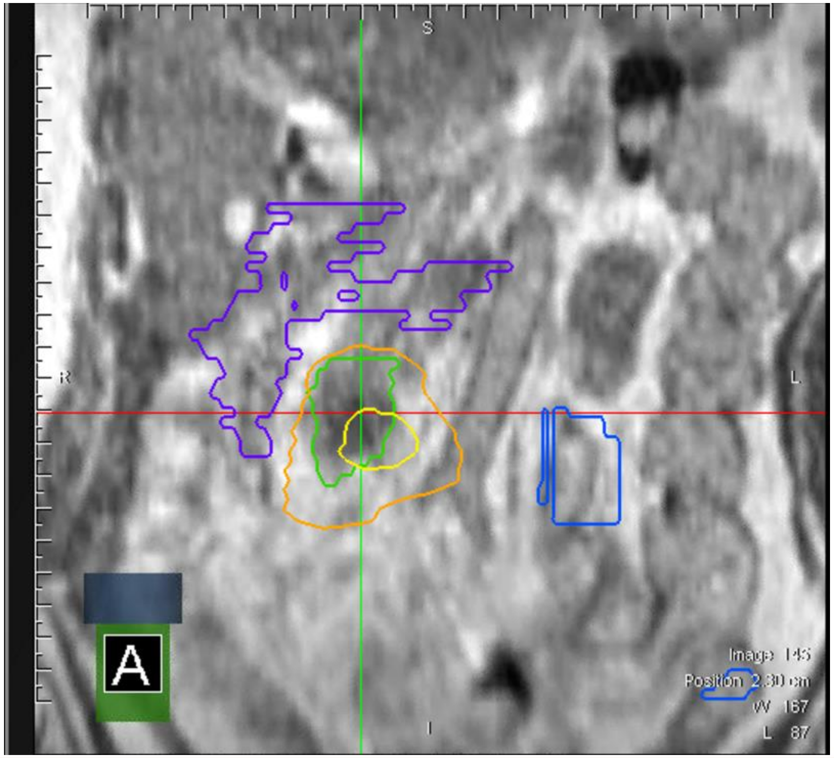
Not common skills in US based radiation therapists!

Physician contouring on demand – not good at it

Changing targets

2 MD can mean 2 gold standard segmentation





Next Steps – 2 protocols

Abdominal oligometastases

LAPC or BRPC

MRgRT 50 Gy / 5 fractions

MRgRT 67.5 Gy / 15 fractions with cape or gem

Localize and Treat

Adapt and Treat

Power both for control, assess for a 20% change in grade 3 GI-toxicity at 6 months, look for 2 year survival of >= 30%.

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- Vivian Rodriguez, PhD
- Sasa Mutic, PhD
- Jeff Michalski, MD

- Jeff Bradley, MD
- Jeff Olsen, MD
- Cliff Robinson, MD
- Ben Fischer-Valluck, MD
- Sahaja Acharya, MD

www.siteman.wustl.edu

Additional Publications

Henke et al, Simulated Online Adaptive Magnetic Resonance-Guided Stereotactic Body Radiation Therapy for the Treatment of Oligometastatic Disease of the Abdomen and Central Thorax: Characterization of Potential Advantages. Int J Radiat Oncol Biol Phys. 2016 Aug 31

Mazur TR et al, SIFT-based dense pixel tracking on 0.35 T cine-MR images acquired during image-guided radiation therapy with application to gating optimization. Med Phys. 2016 Jan;43(1):279.

Acharya S et al, Online Magnetic Resonance Image Guided Adaptive Radiation Therapy: First Clinical Applications. Int J Radiat Oncol Biol Phys. 2016 Feb 1;94(2):394-403.

Noel CE et al, Comparison of onboard low-field magnetic resonance imaging versus onboard computed tomography for anatomy visualization in radiotherapy. Acta Oncol. 2015;54(9):1474-82.

Noel CE et al, Process-based quality management for clinical implementation of adaptive radiotherapy. Med Phys. 2014 Aug;41(8):081717.

Advanced imaging and the 4th dimension

Jan-Jakob Sonke

NKI-AVL

Het Nederlands Kanker Instituut
Antoni van Leeuwenhoek Ziekenhuis

ESTRO IGRT 2015

The time component of imaging

- Inter-fraction changes – from treatment planning to treatment delivery and between treatment fractions
- Irregular intra-fraction changes such as bowel movements and external positioning
- Regular intra-fraction changes such as respiration (and bladder filling)

Weeks

Days

Hours

Minutes

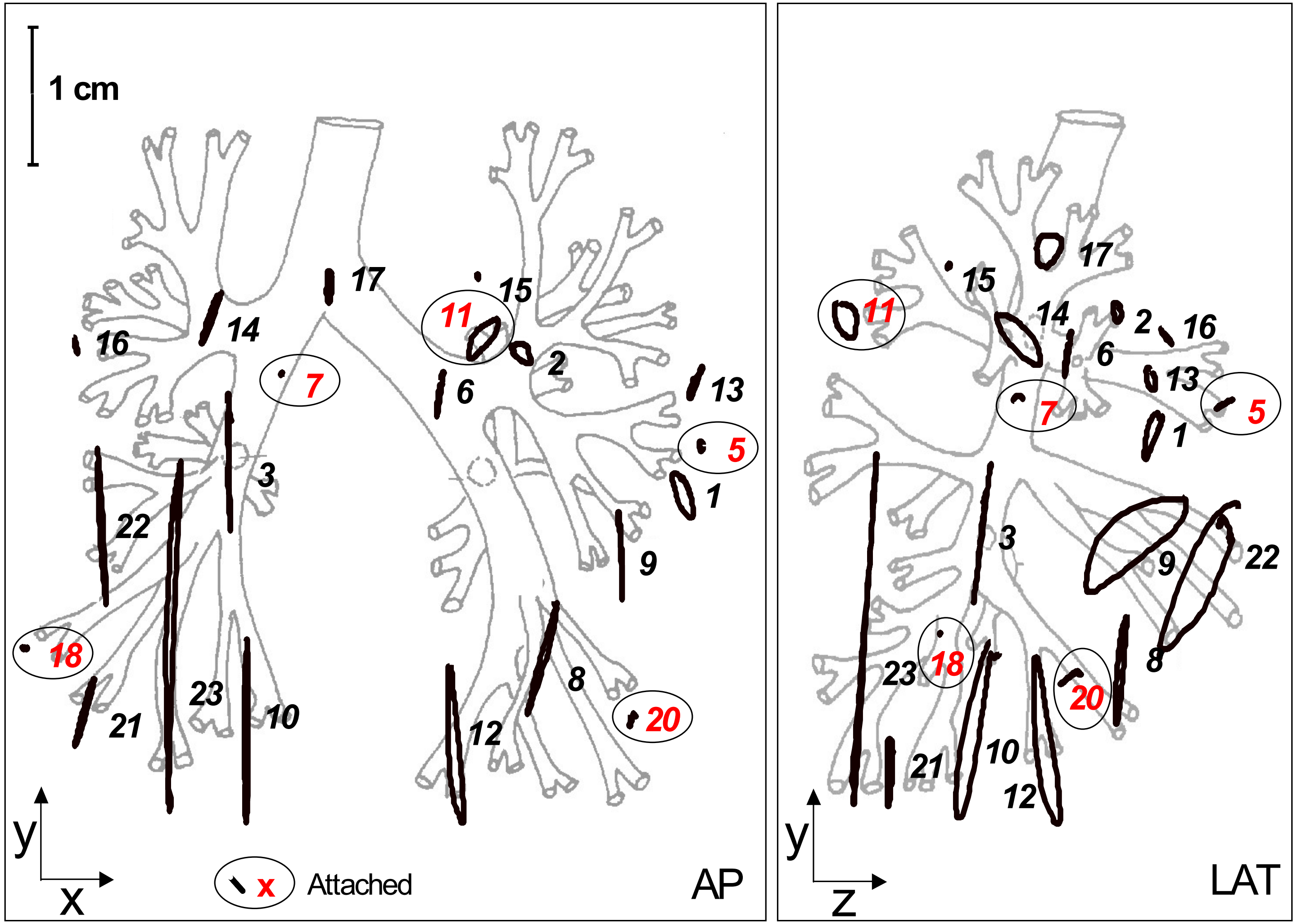
Seconds

The time component of imaging

- Regular intra-fraction changes such as respiration

Seconds

Respiration motion (not to scale)



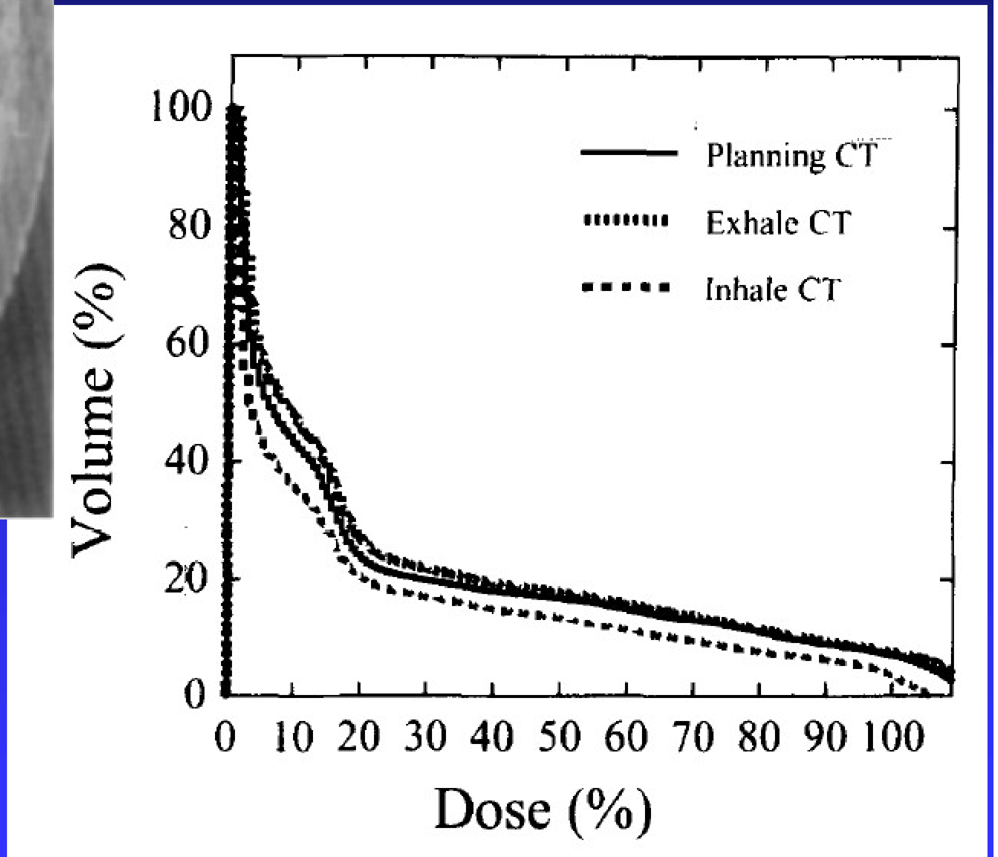
From Seppenwoolde et al., IJROBP 2002 53:822-834

Agenda

- Effects of the time component on images
- 4D CT scanning
- 4D in treatment planning
- 4D PET scanning
- 4D MRI

4D CT

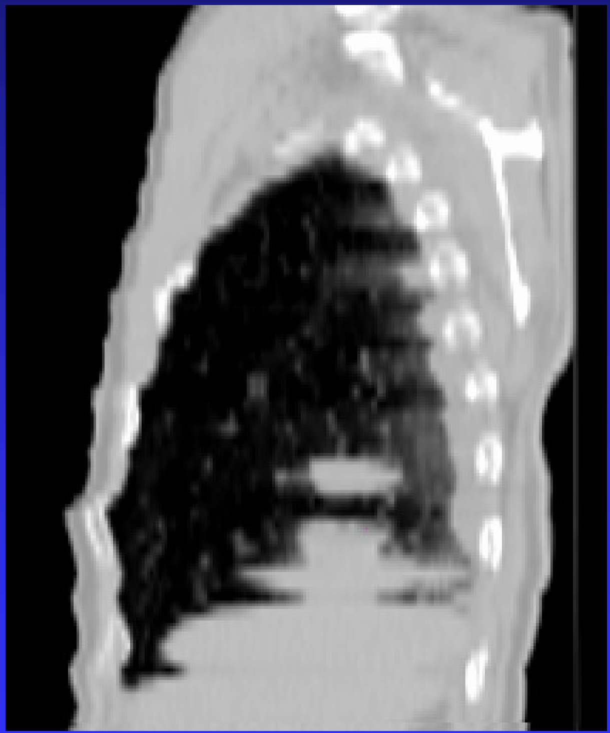
Effect of motion on CT and Dose



Balter et al. IJROBP 1996

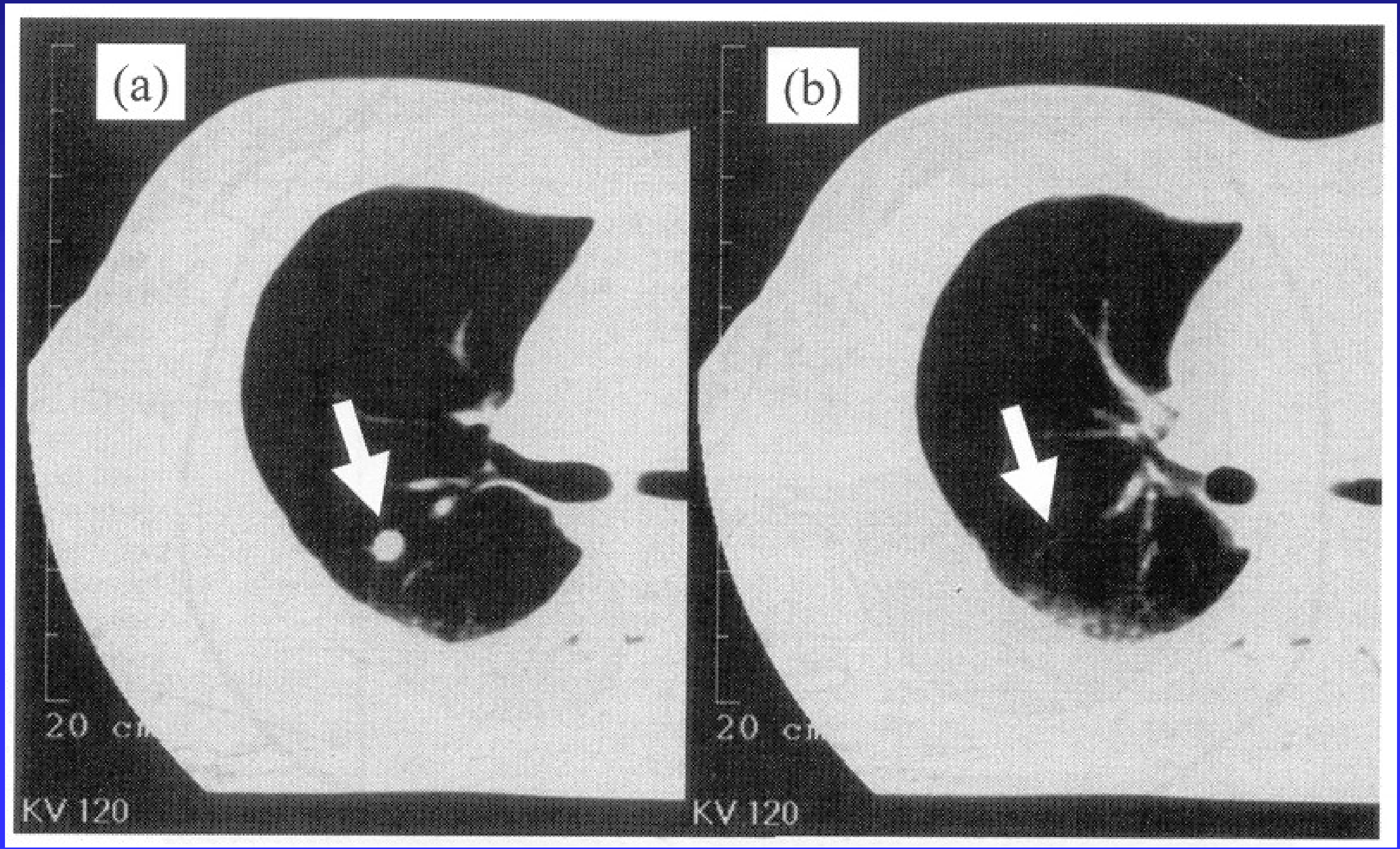
CT - effects of respiration

- Partial viewing and blurring



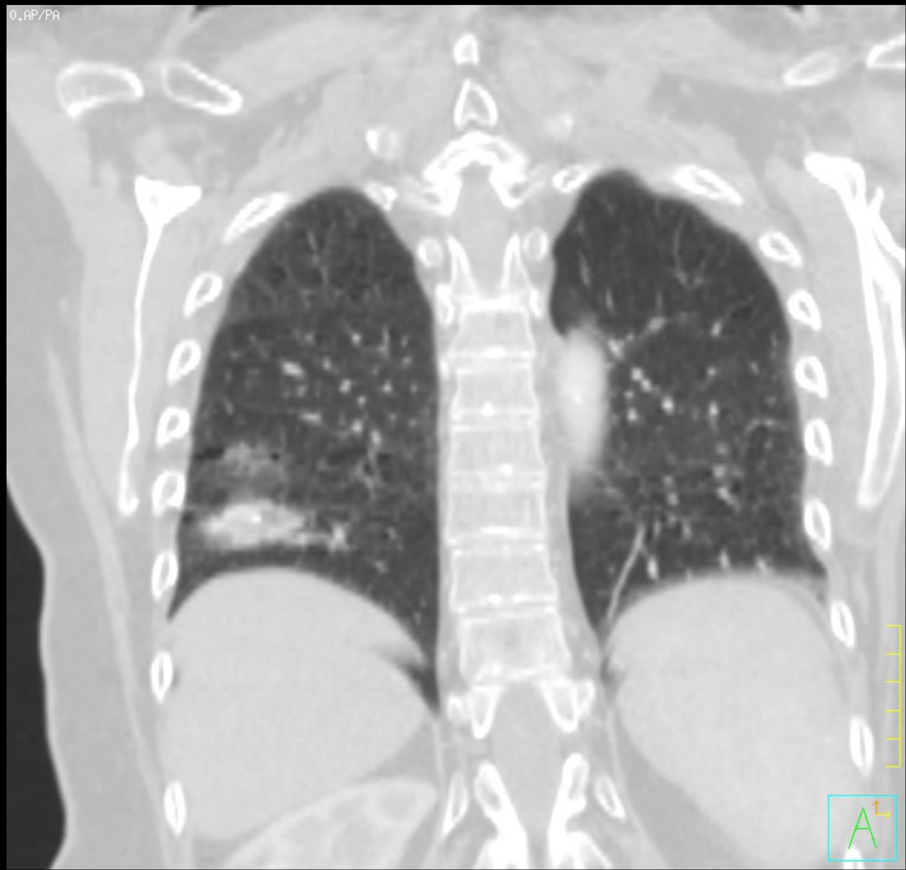
CT - effects of respiration

- Volume effects and disappearing structures

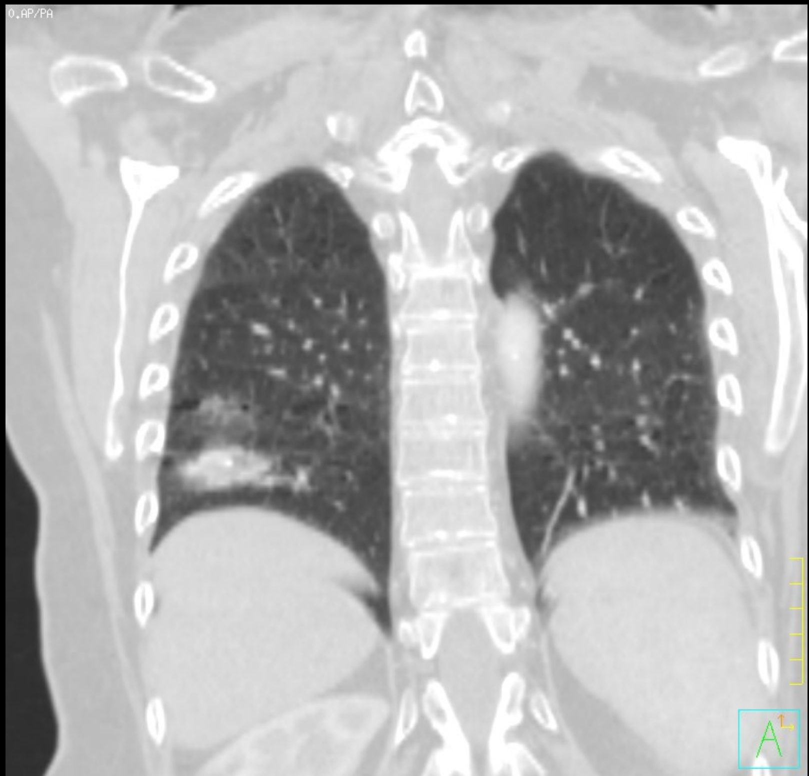


Shimizu *et.al.*, IJROBP 2000

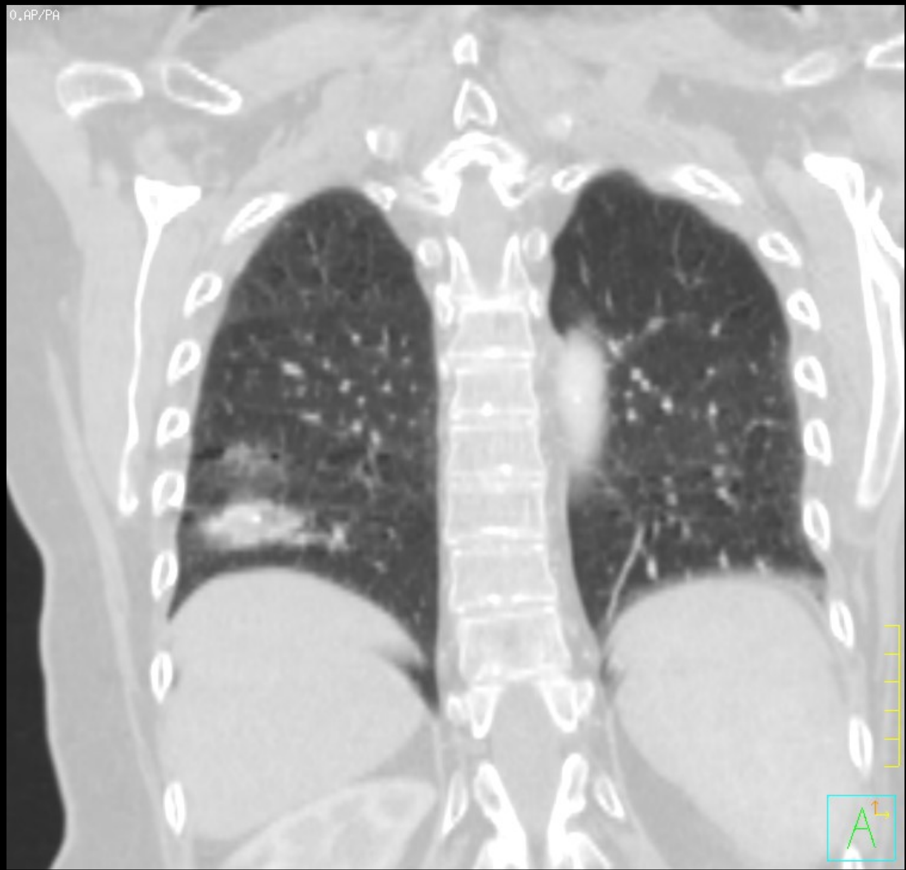
Contour the tumor



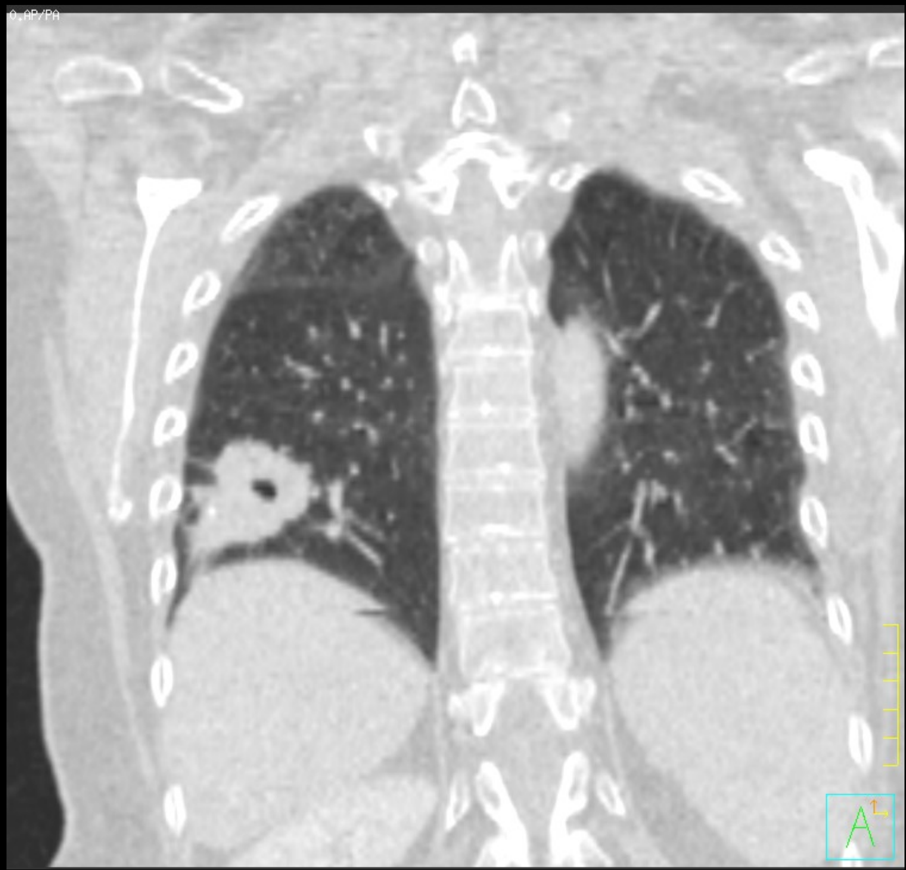
Reasonable?



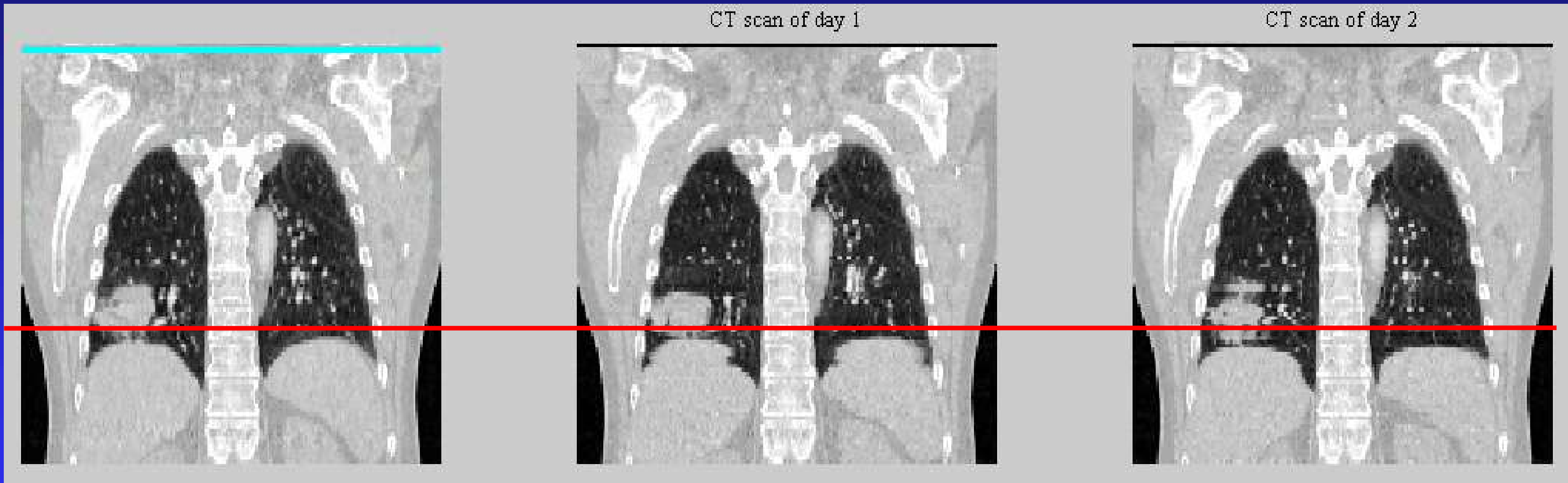
Helical



Exhale



The CT imaging problem



CT and time management

Approaches to CT time management

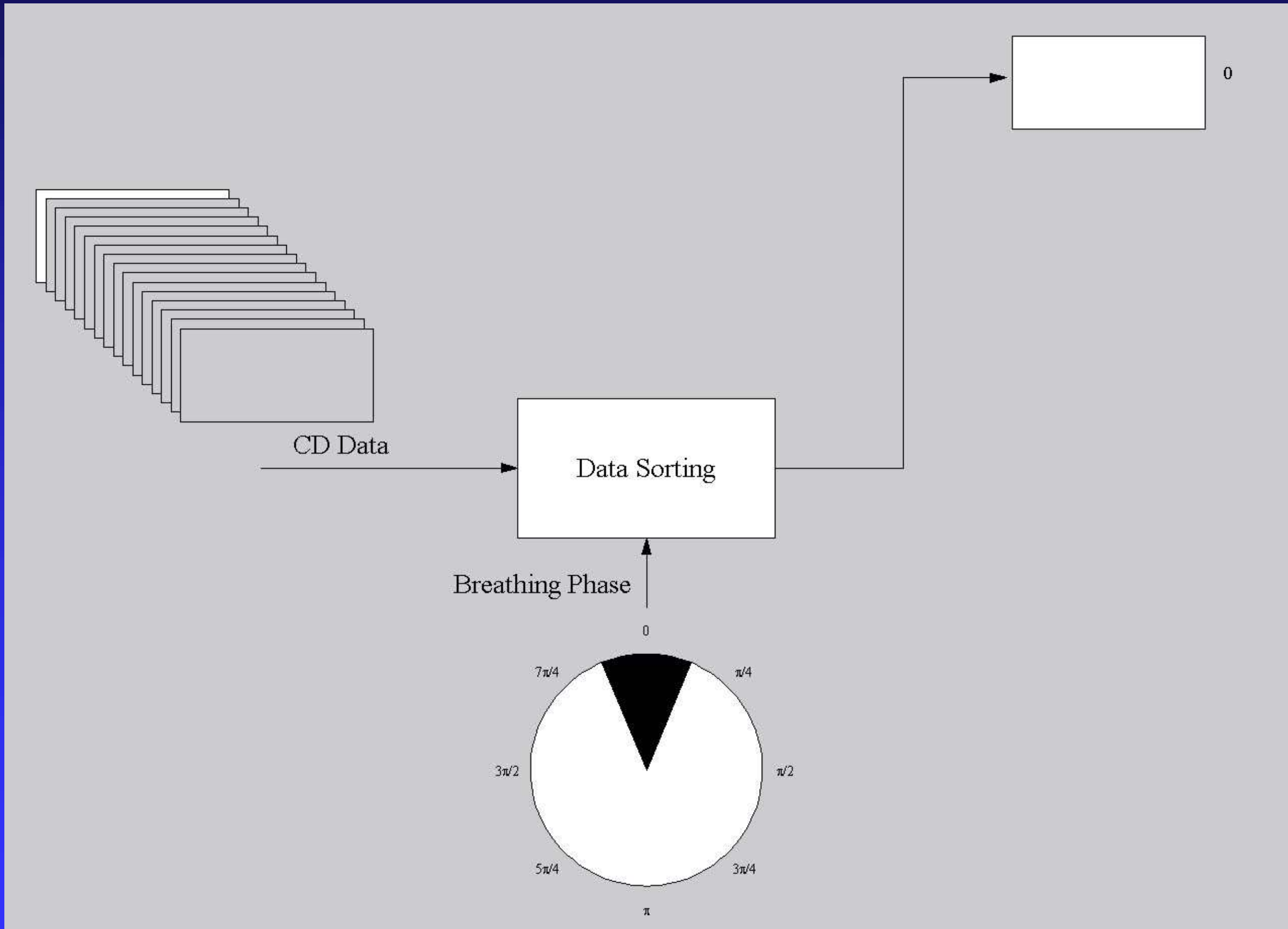
- Slow scanning
- Repeated fast scanning
- Gating/breath-hold (prospective respiratory correlation)
- Retrospective respiratory correlation (4D)

Brief history of 4D CT

Development	Year	First author	Institution
Single slice helical	2003	Ford, Vedam	MSKCC, VCU
Multi-slice cine (commercial)	2003	Pan	GE/MGH/MSKCC
Cone beam (benchtop)	2003	Taguchi	Toshiba
Multi-slice cine	2003	Low	Wash U
Multislice helical	2004	Keall	VCU, MDACC
Multislice cine PET/CT	2004	Nehmeh	MSKCC
Cone beam (clinical)	2005	Sonke	NKI
Applications outside Rad Onc	…	Guerrero, Low, Keall	MDACC, Wash U, Stanford

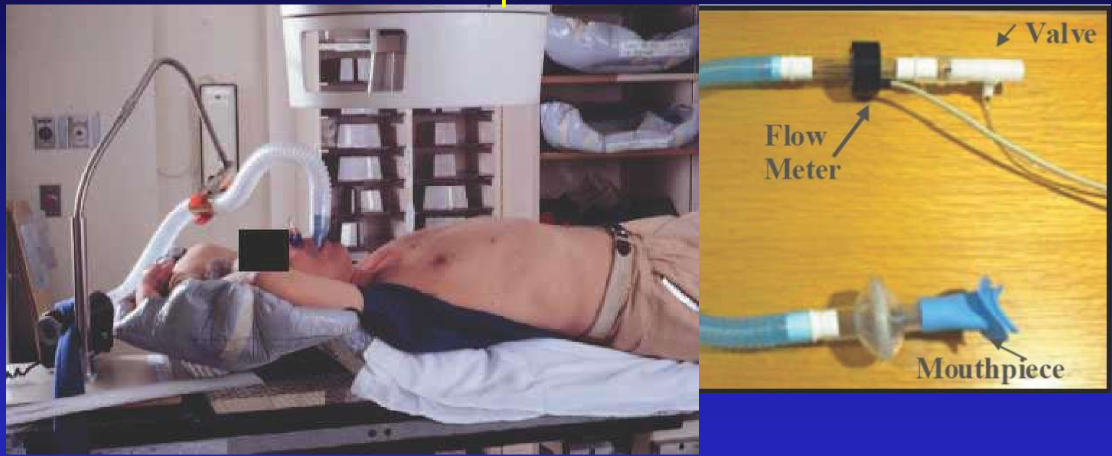
* Courtesy of Paul Keall

Retrospective Sorting



Recording respiration

MSKCC & Beaumont Hospital



Spiro meter

Siemens Medical

Anzai belt, Siemens

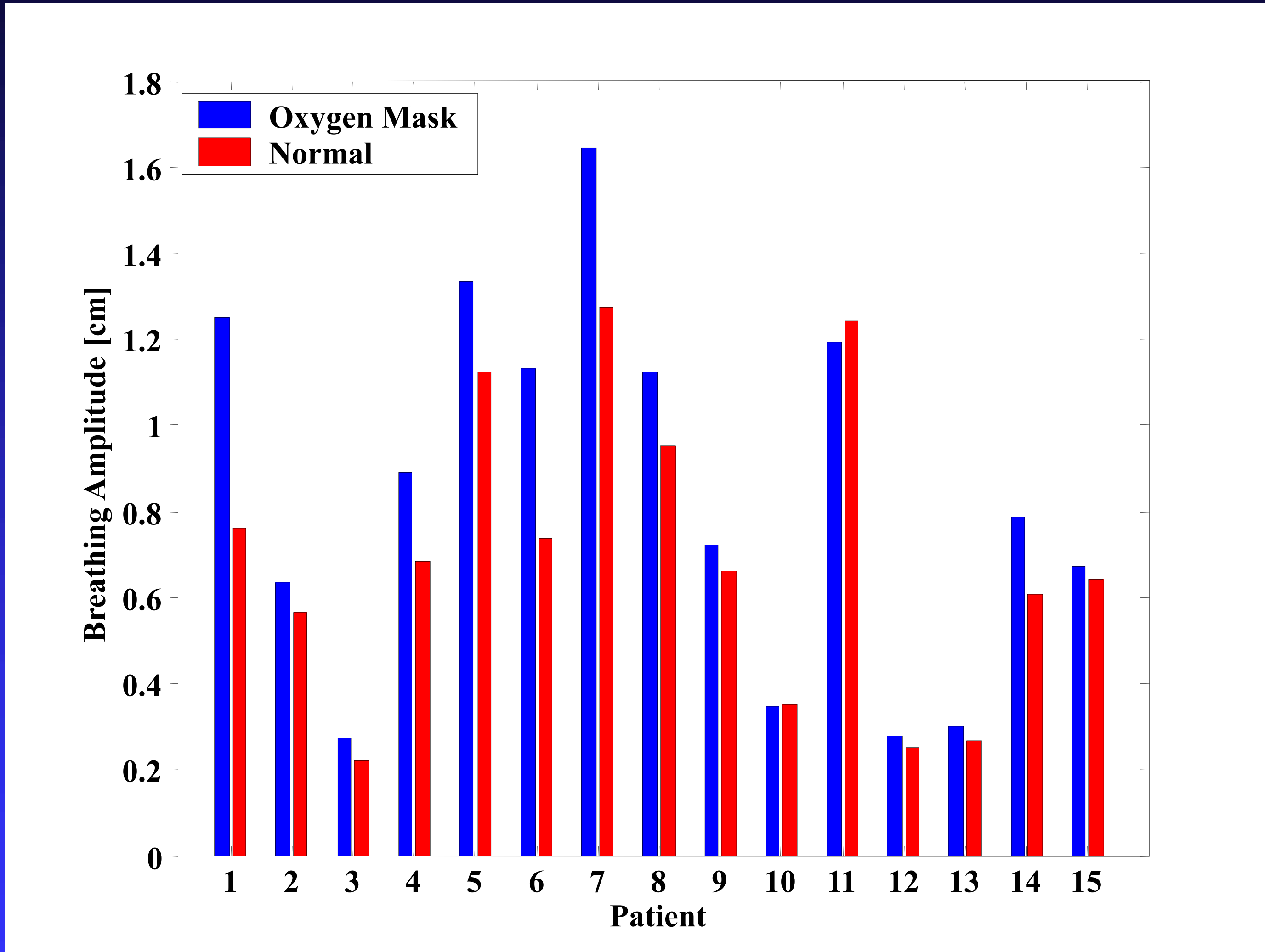
Varian RPM system

Stine Korreman

Catherina Hospital Eindhoven

Stretch belt, Philips

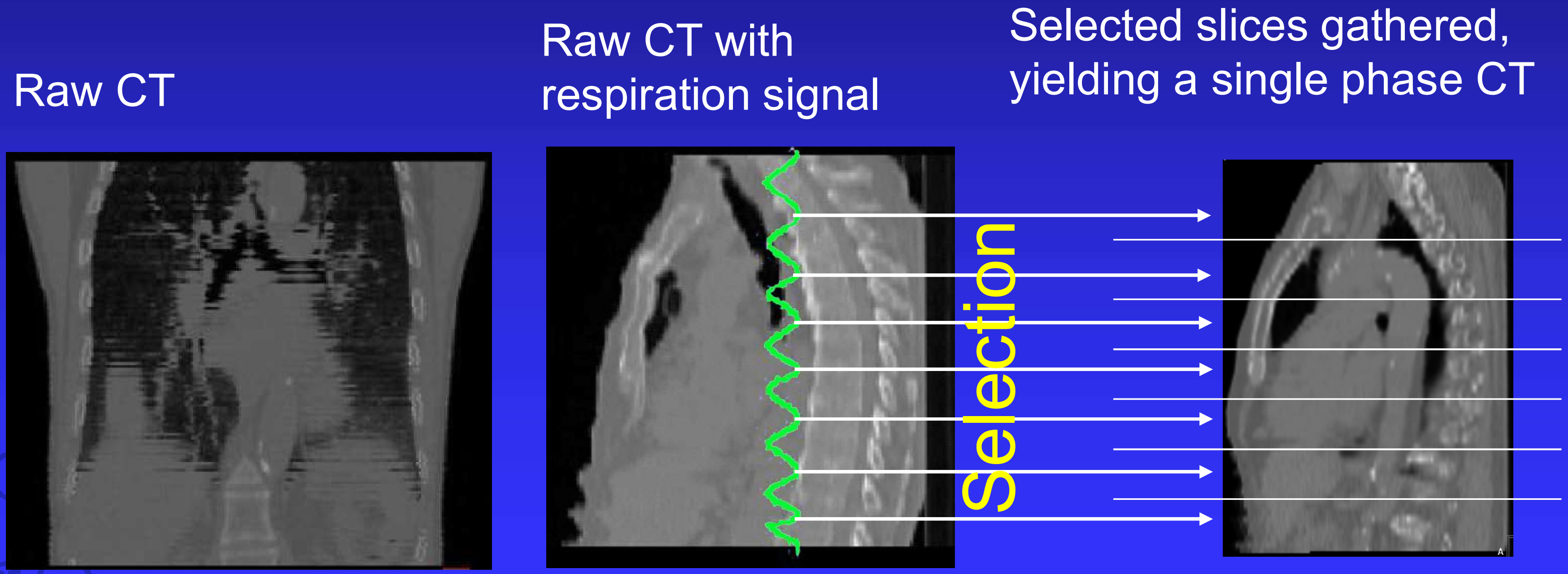
Change in breathing amplitude



M = 21%, SD = 19%, p = 0.00076

Sort slices

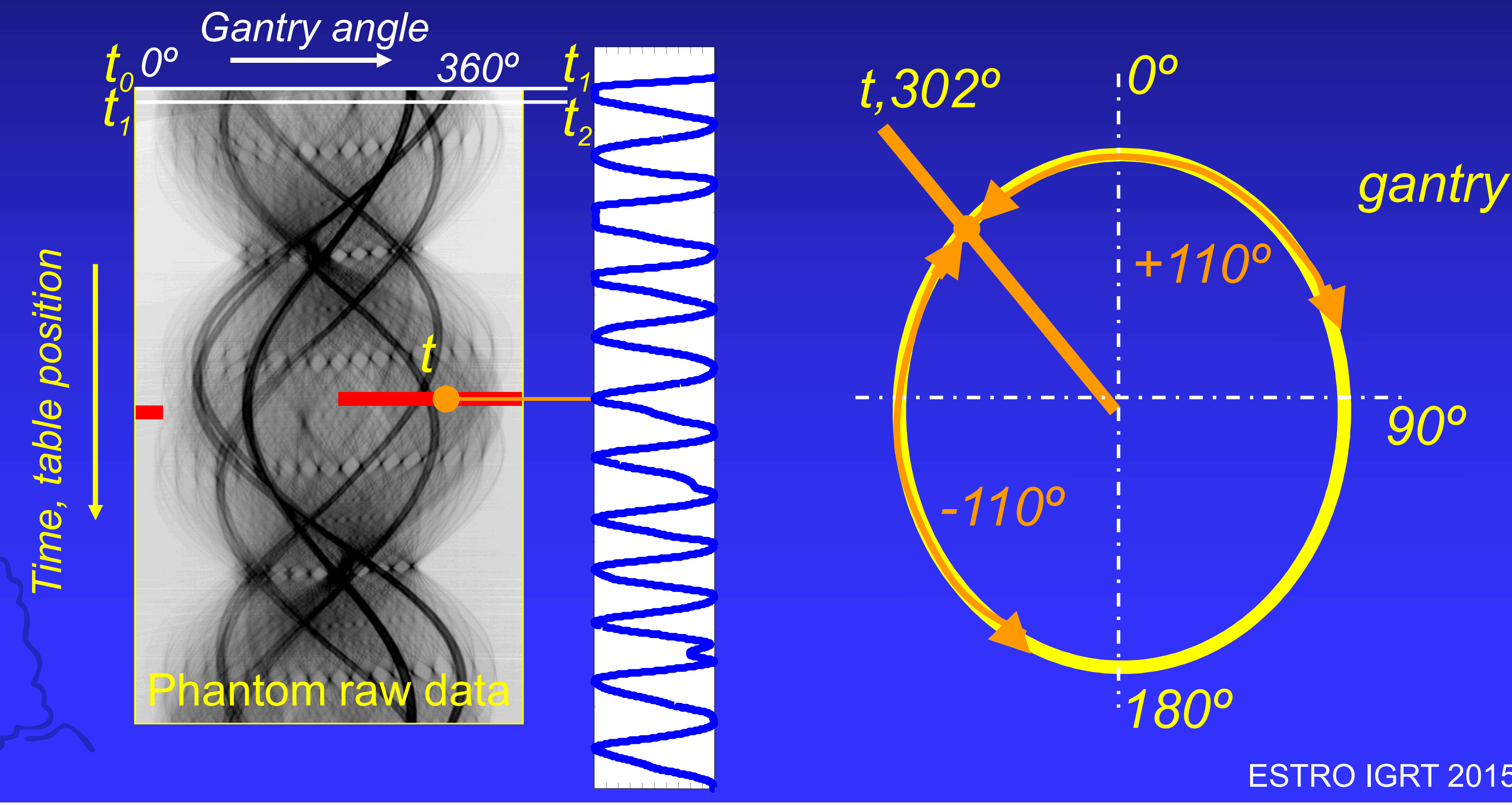
(1) Reconstructing many slices (2) Sorting CT slices



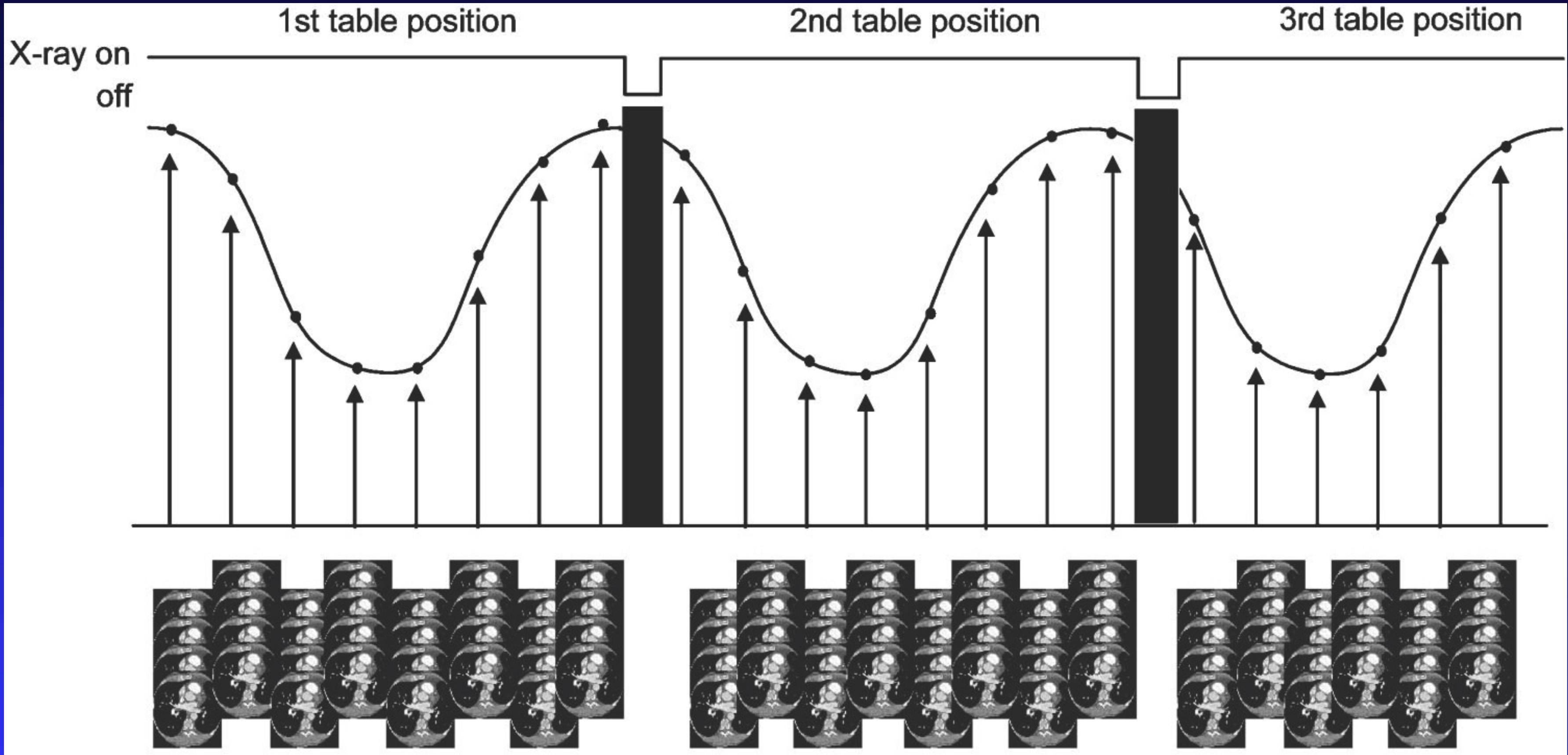
Sort sinogram

Selection by respiratory phase of raw CT sinogram data

→ (1) Sorting raw CT data. (2) Reconstructing slices



Acquisition – Ciné mode

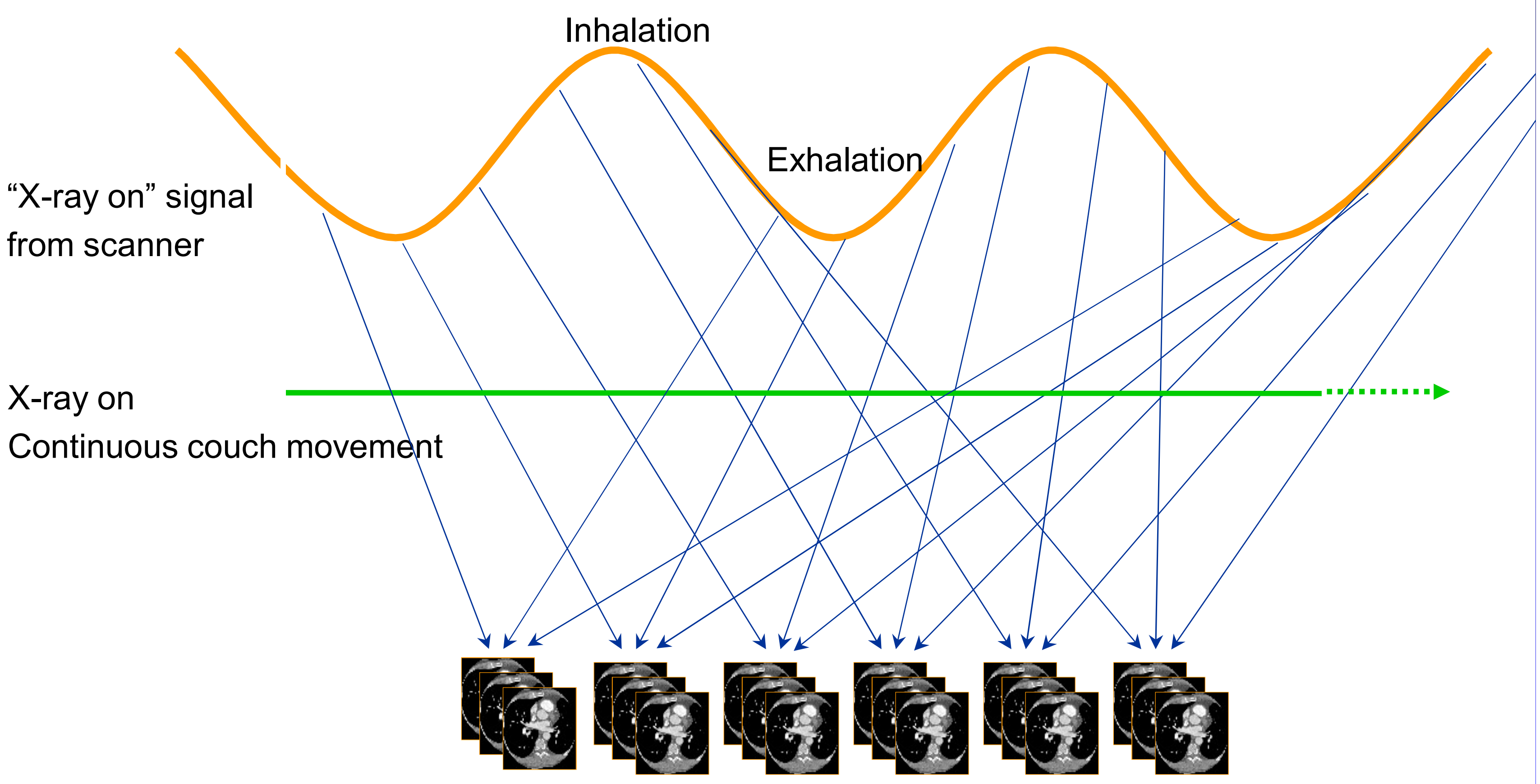


Each step: continuous acquisition of slices for time interval (average CL + 1 Slice time)

* Tinsu Pan, Med.Phys. 31 (2), 2004
GE LightSpeed MS CT

Helical 4D CT

Stine Korreman / Rigshospitalet



4D CT Example

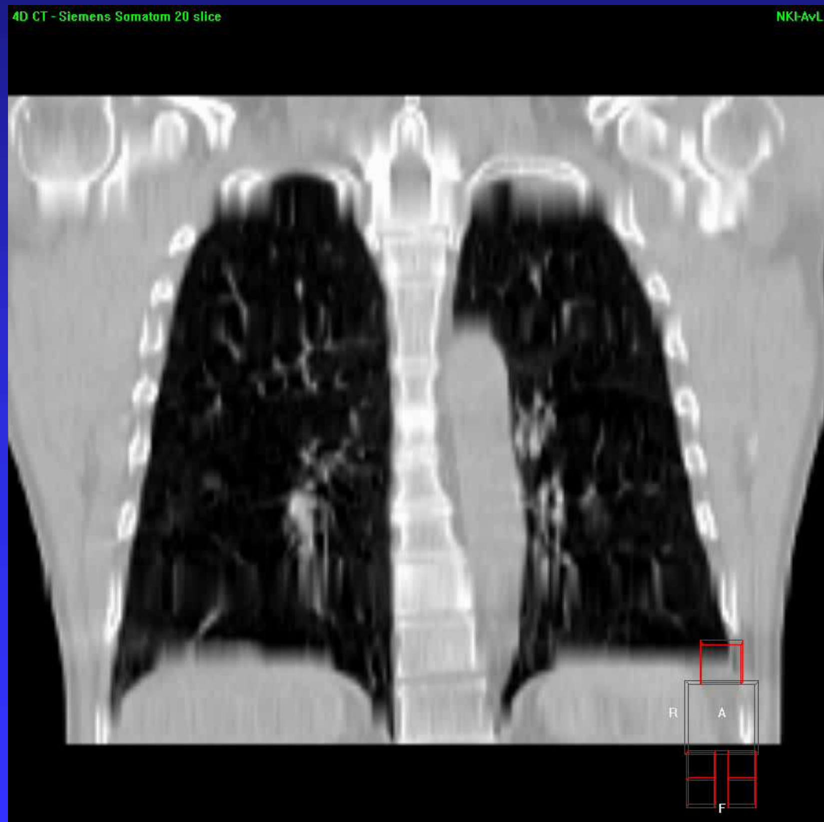
Multi slice Siemens Sensation (Sinogram sorting)

4DCT Non Idealities

Scan speed vs. respiration cycle

Fast breathing + Slow scanner = blurring

Slow breathing + Fast scanner = gaps



$$CL_{Tube-rotation} = pitch \times CL_{Respiration}$$

4DCT

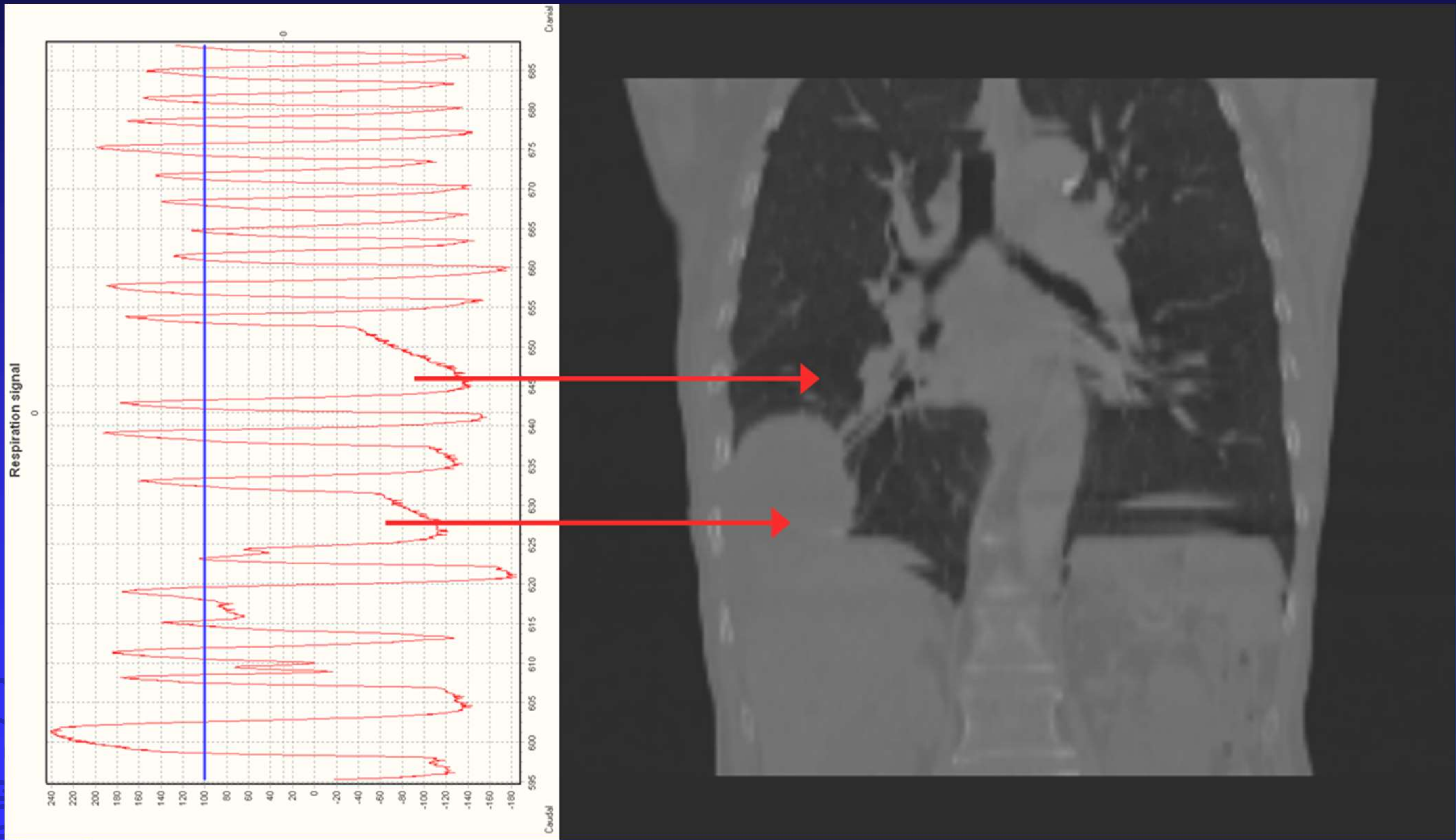
At the NKI-AvL:

- Siemens Sensation Open CT scanner
- Thermo-couple device
- Phase binning in sinogram space

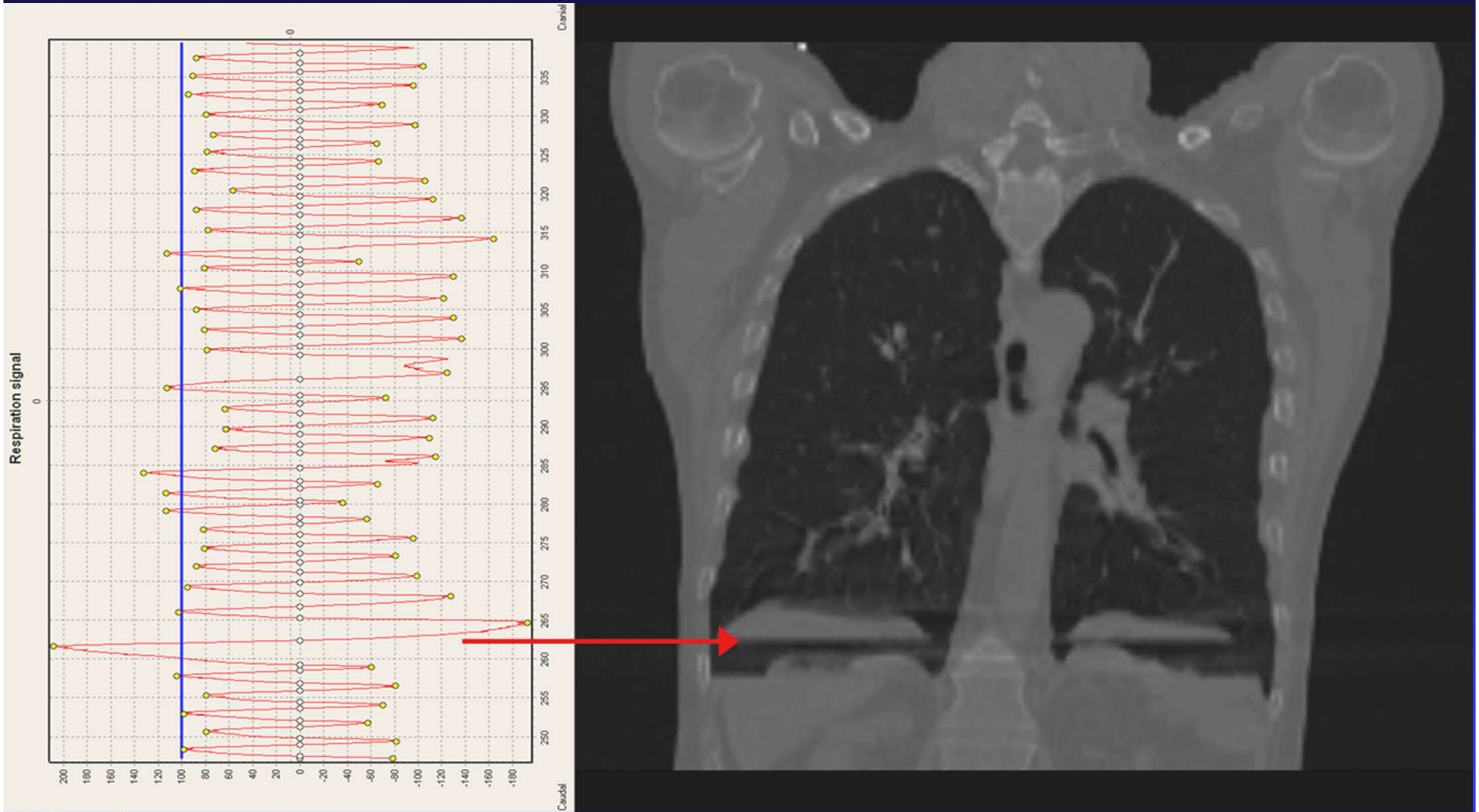
Acquisition protocols:

- Fast: 0.5 s rotation time, pitch 0.10, 5.0 s
- Middle: 1.0 s rotation time, pitch 0.15, 6.7 s
- Slow: 1.0 s rotation time, pitch 0.10, 10 s

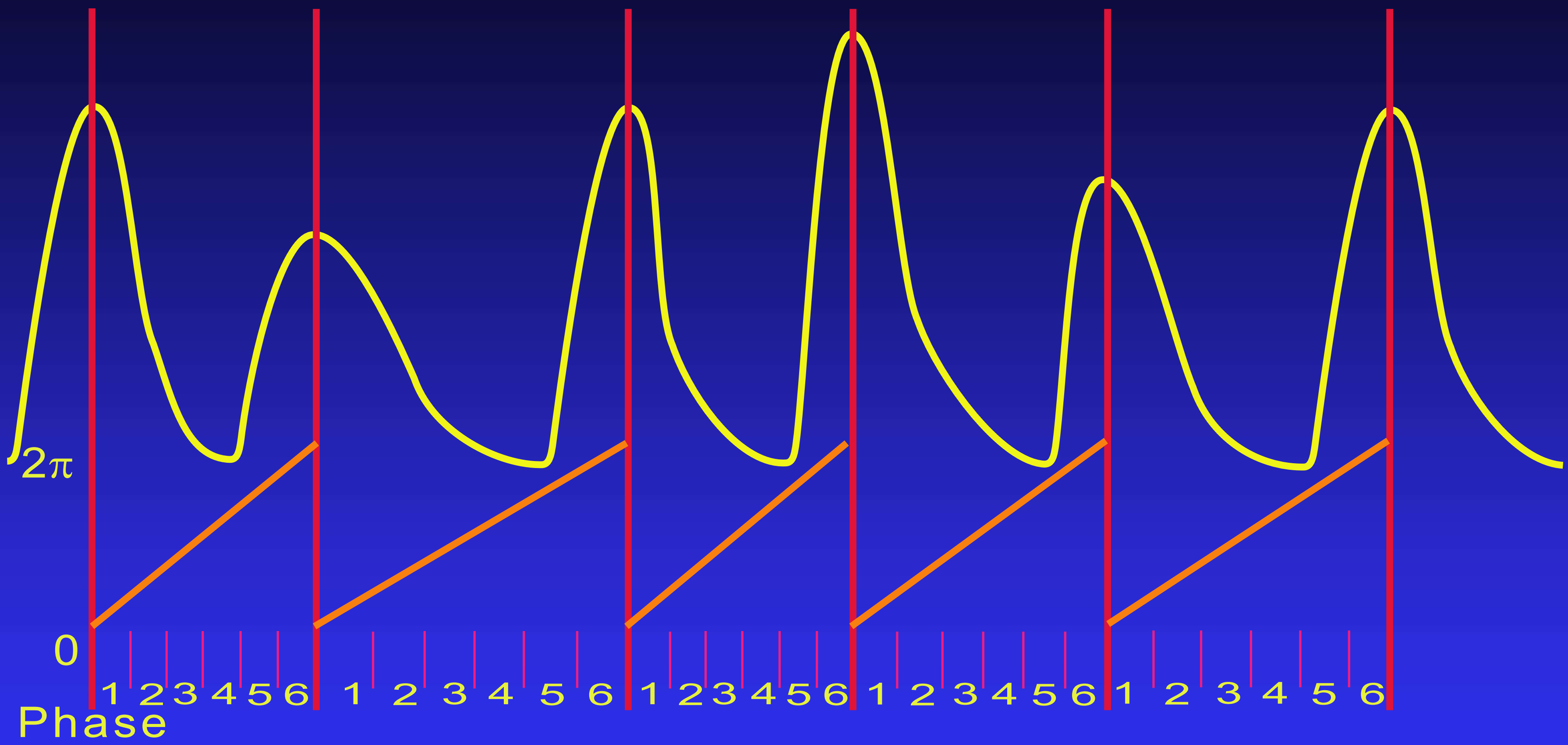
CT Artefacts



CT Artefacts

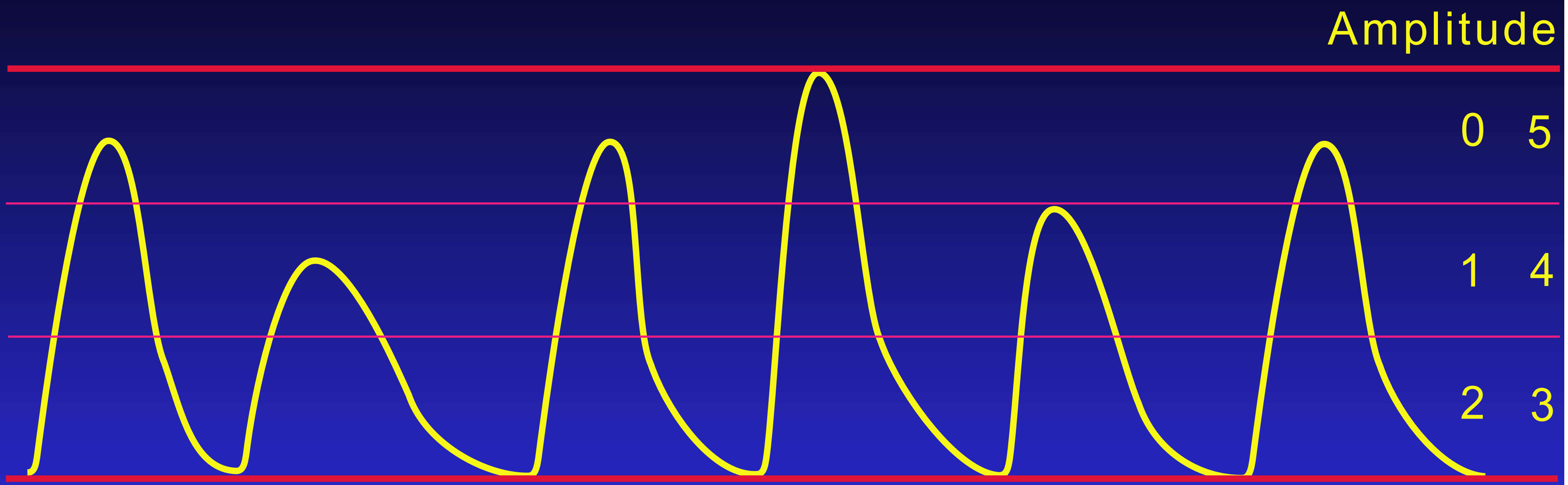


Phase vs. Amplitude sorting



- Data is linearly divided over the respiratory cycle
- More frames in exhale than inhale
- If amplitude is irregular → slices do not concatenate (blurring/distortions)

Phase vs. Amplitude sorting



- Data is sorted to the amplitude
- Same number of frames in exhale and inhale
- Gaps if no data is available
- Maximum inhale is less reproducible

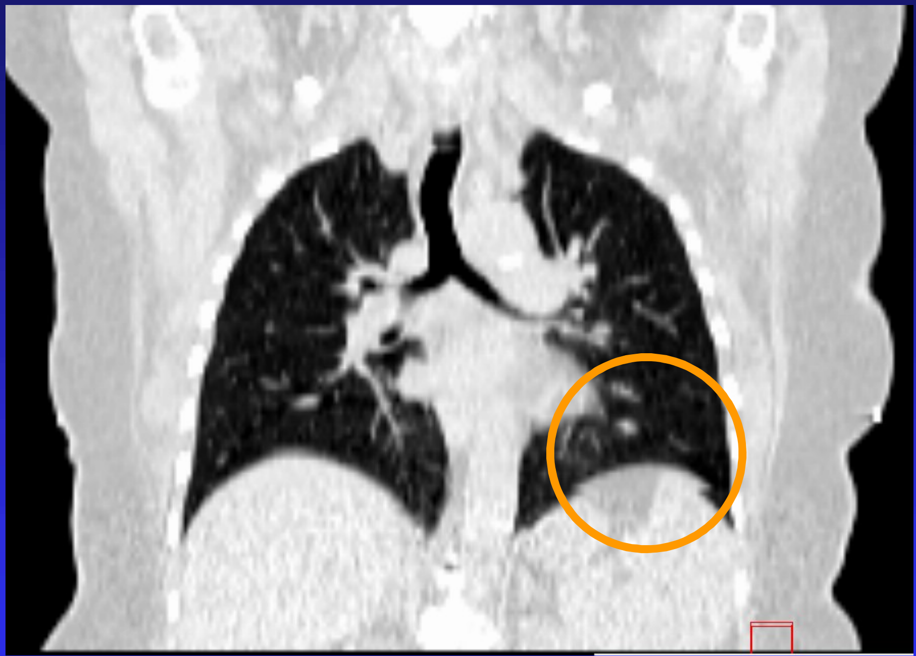
Examples – Phase vs Amplitude

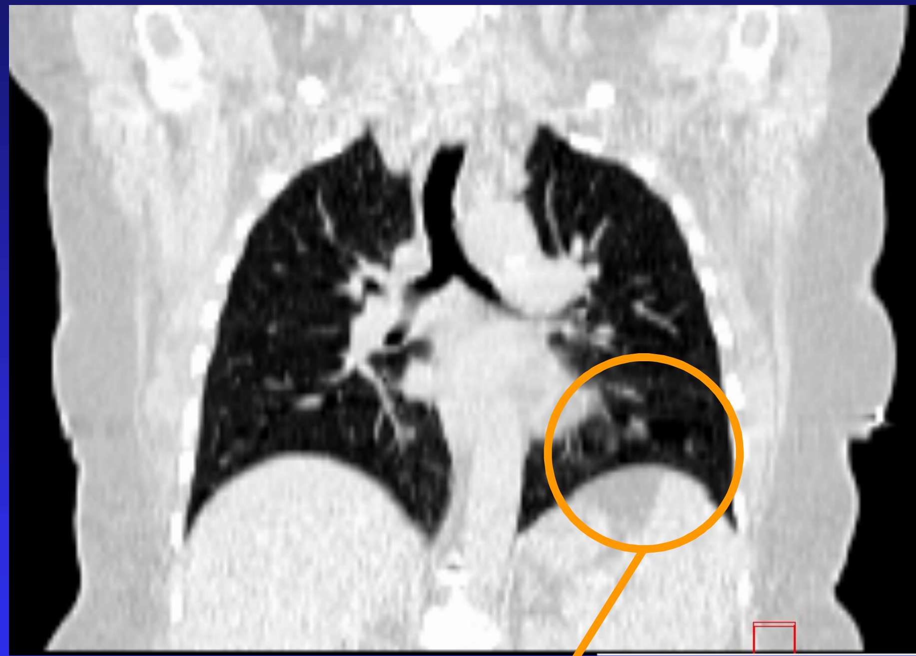
Phase wise

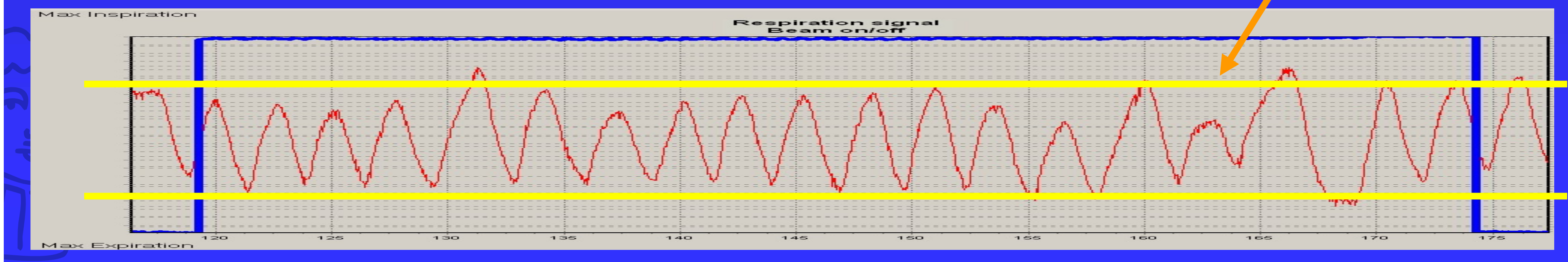
Amplitude wise

Examples – Phase vs Amplitude

Phase wise | Amplitude wise







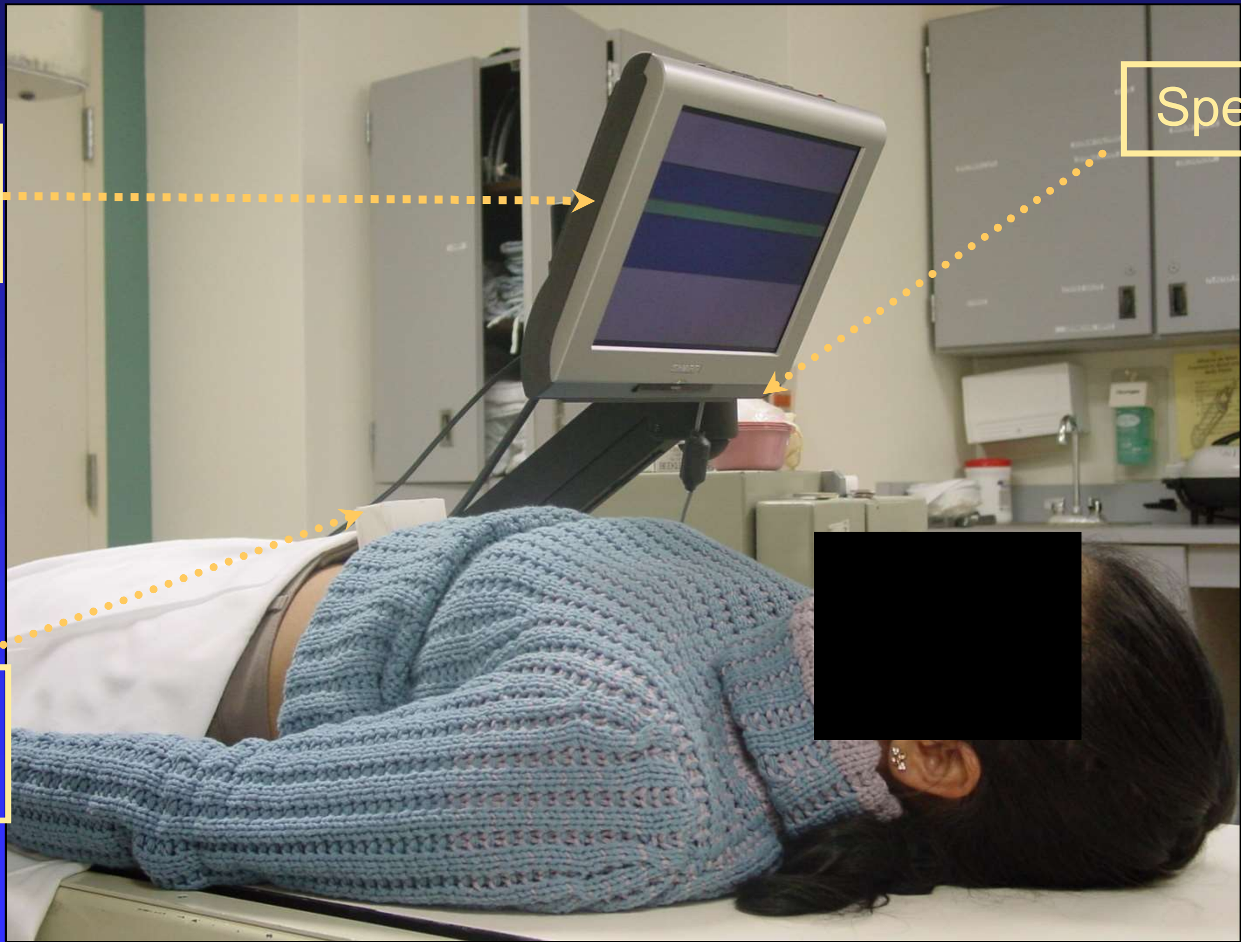
Current developments in 4D CT

- Audio-Visual feed-back to reduce motion
- Adaptive control
- Motion Compensation

Paul Keall

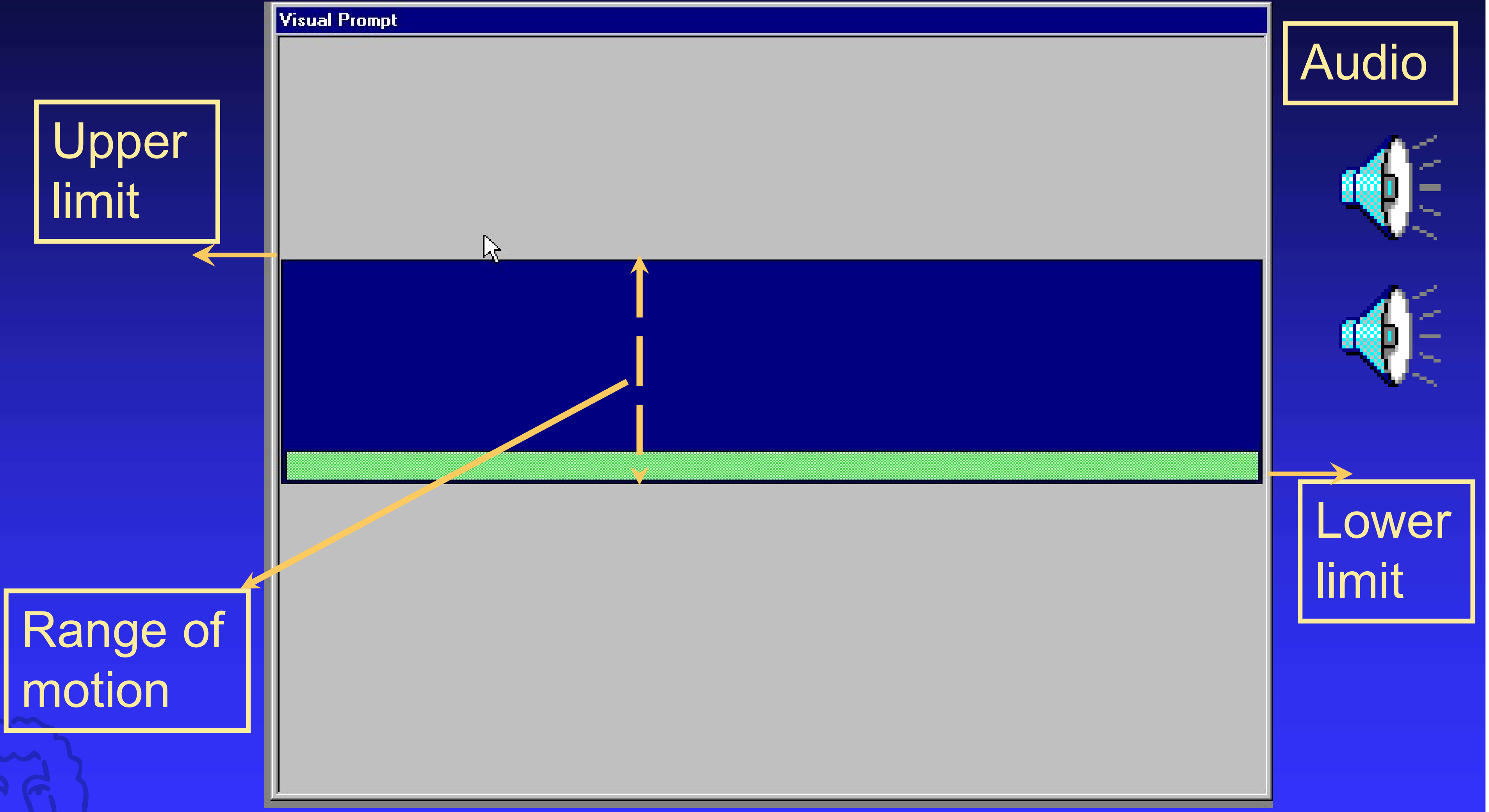
Audio-Visual Feed-back

Improve regularity of input signal



Paul Keall

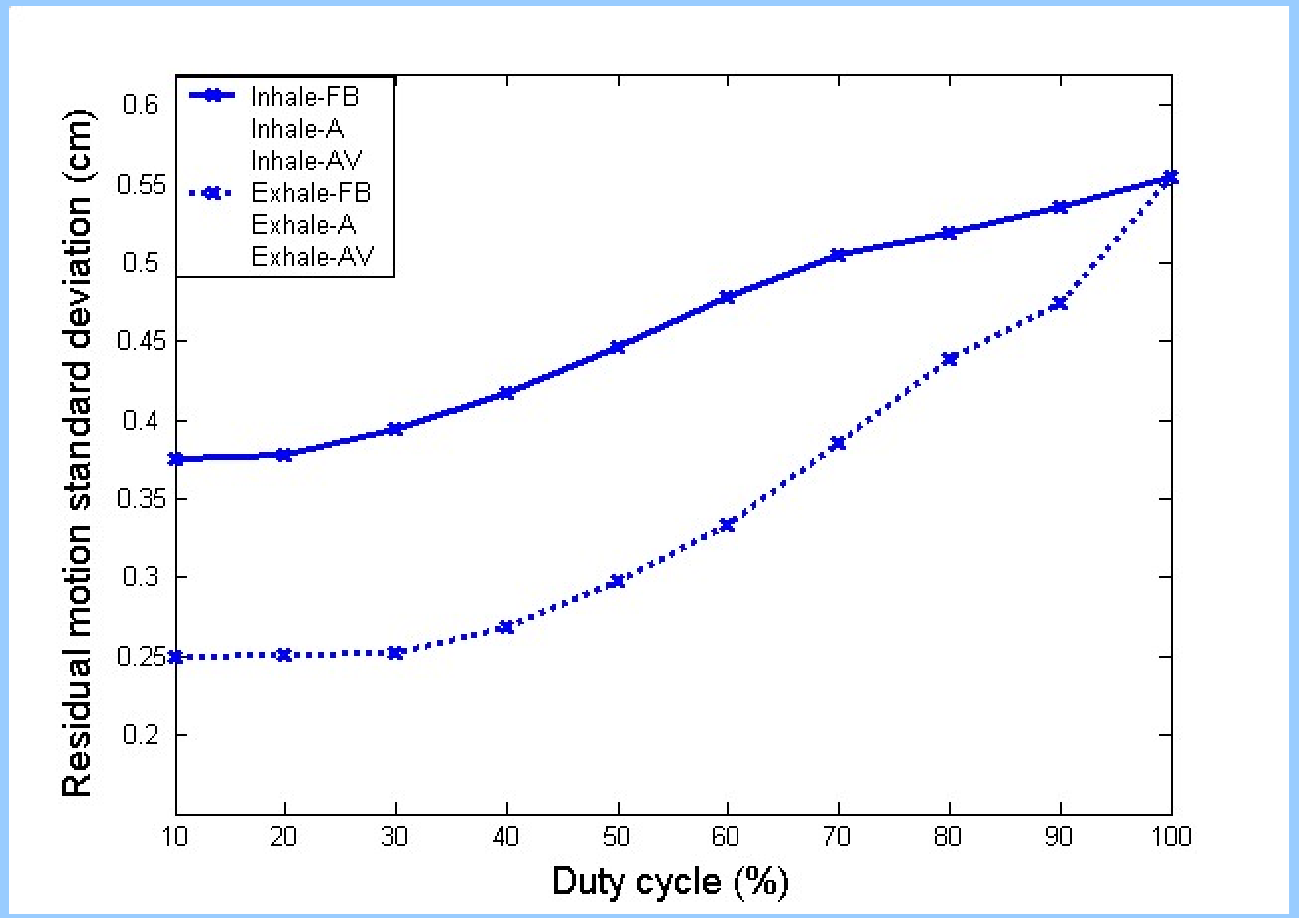
Audio-Visual Feed-back



Audio-Visual Feed-back

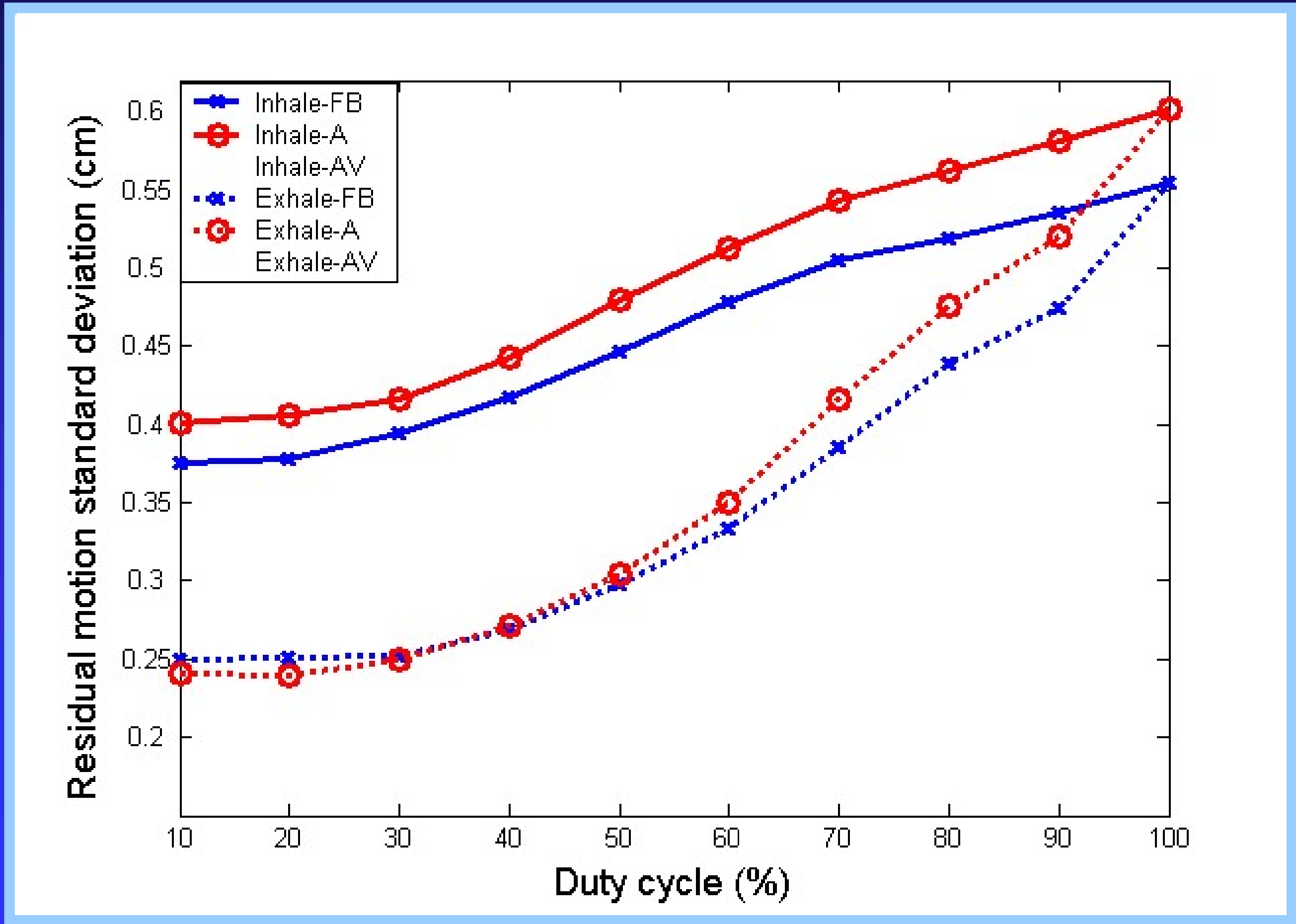
Paul Keall

Free breathing



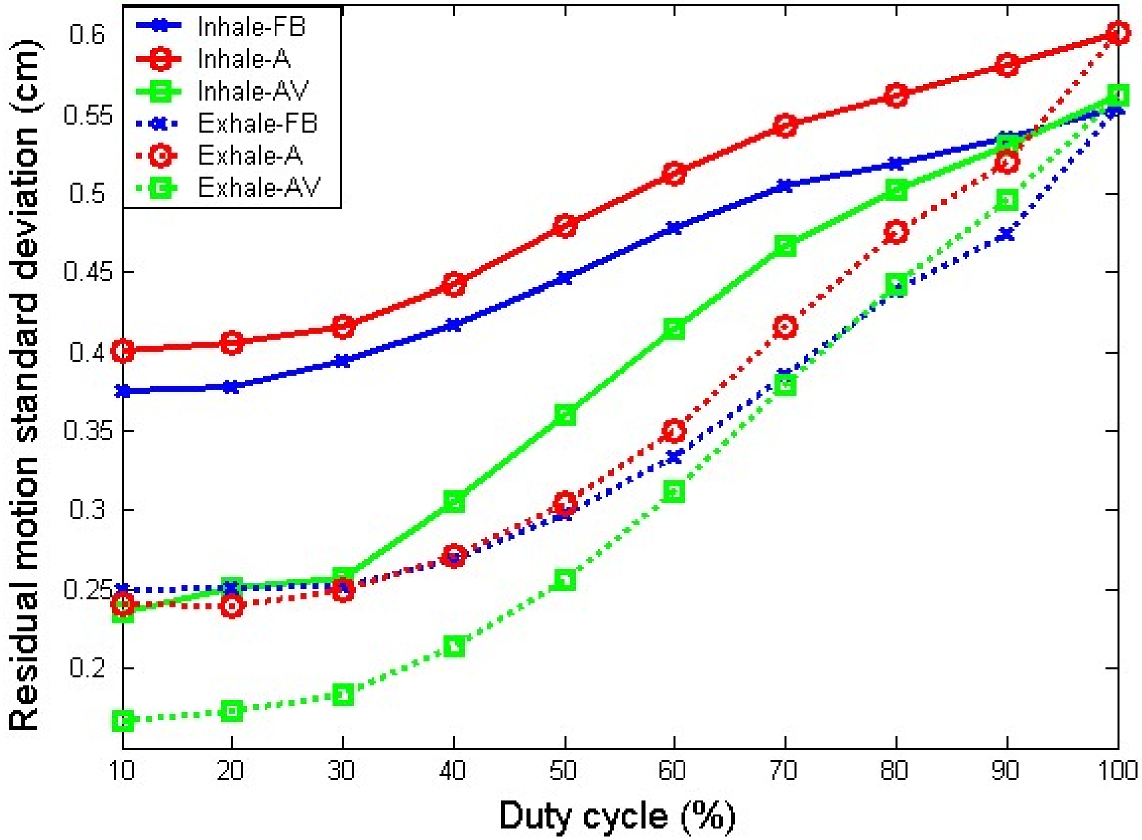
Audio-Visual Feed-back

Audio instruction



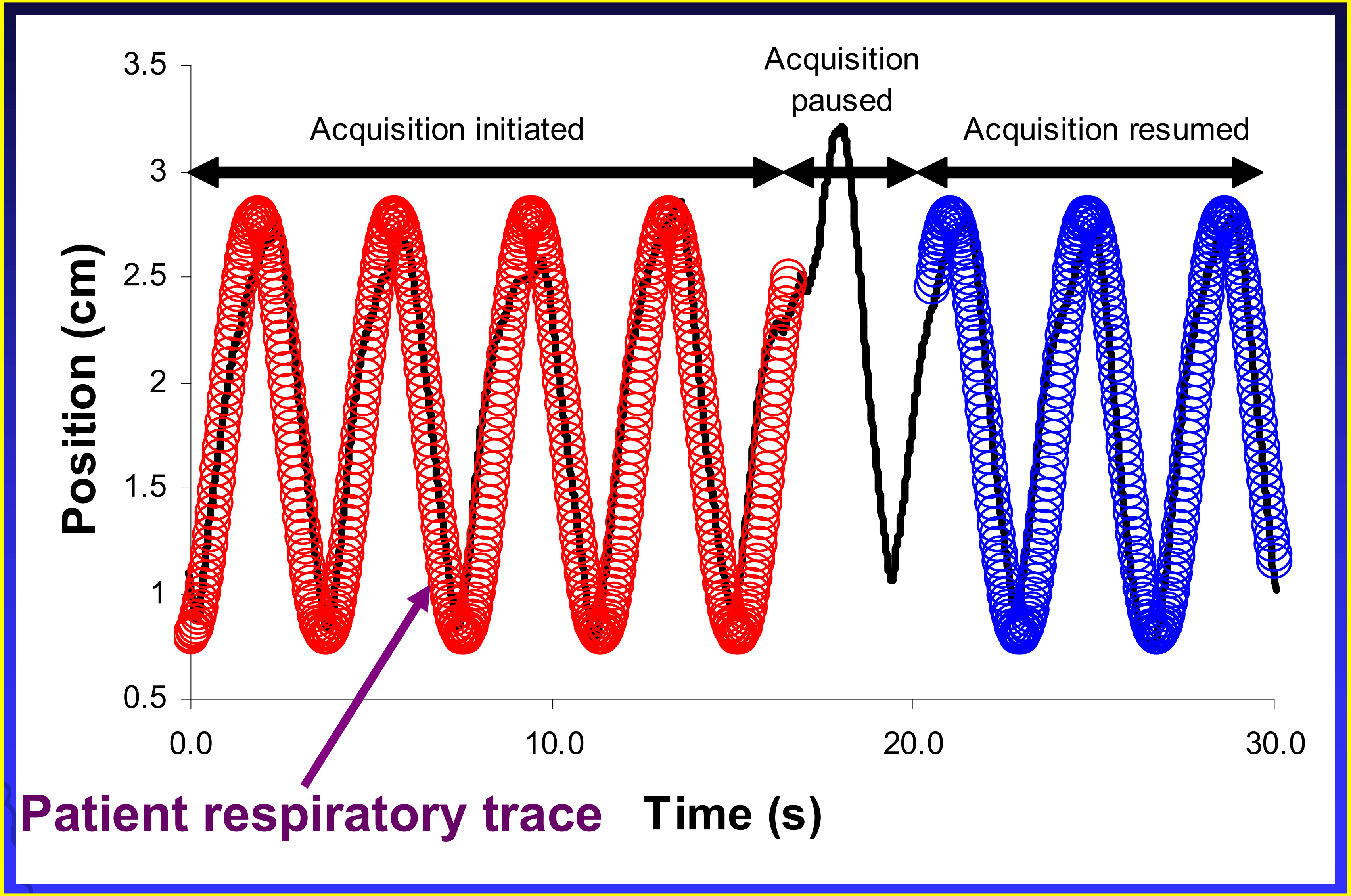
Audio-Visual Feed-back

Audio-visual biofeedback



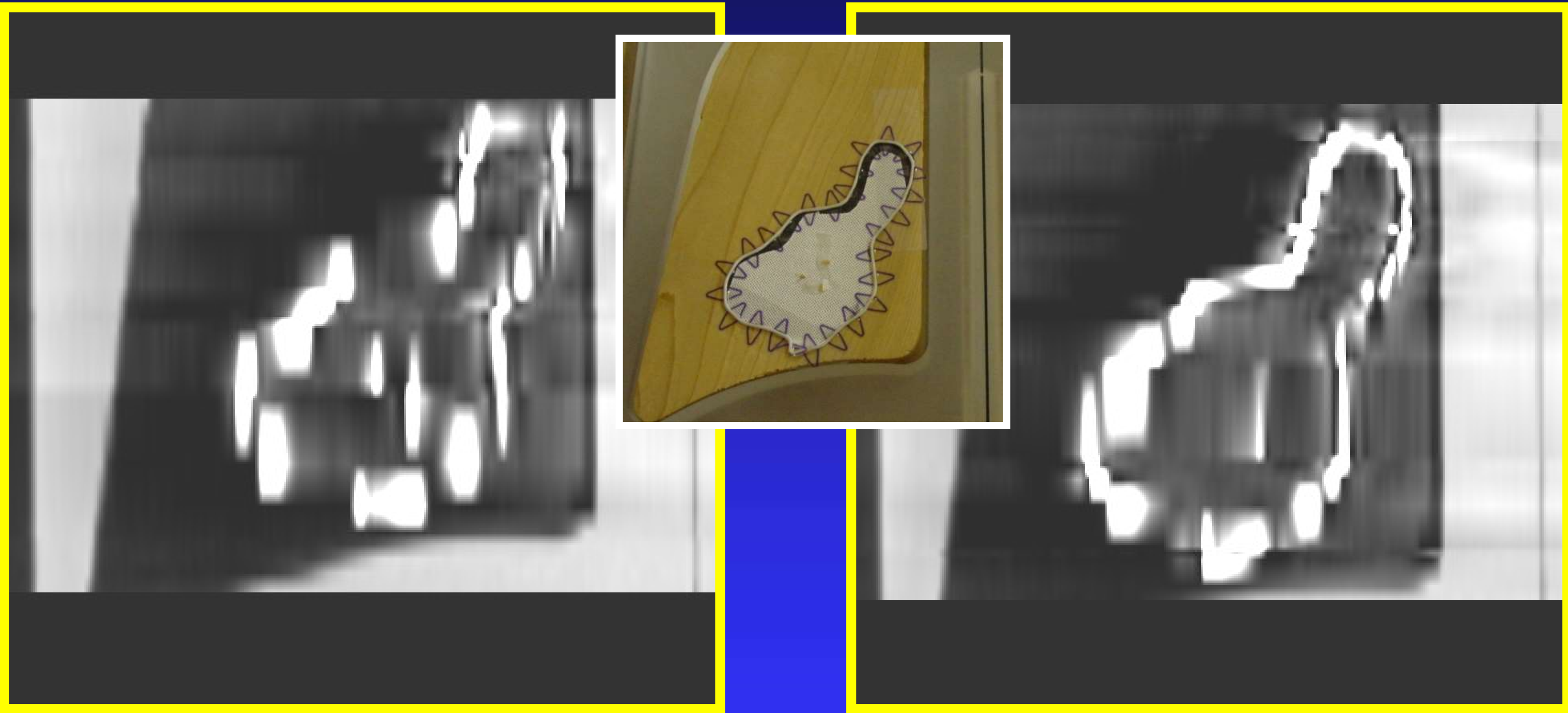
Adaptive control

Paul Keall



Adaptive control

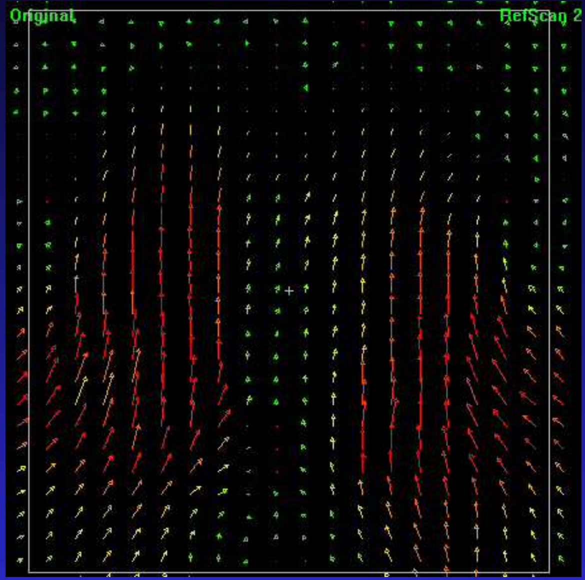
Paul Keall



Conventional 4D CT

Adaptive 4D CT

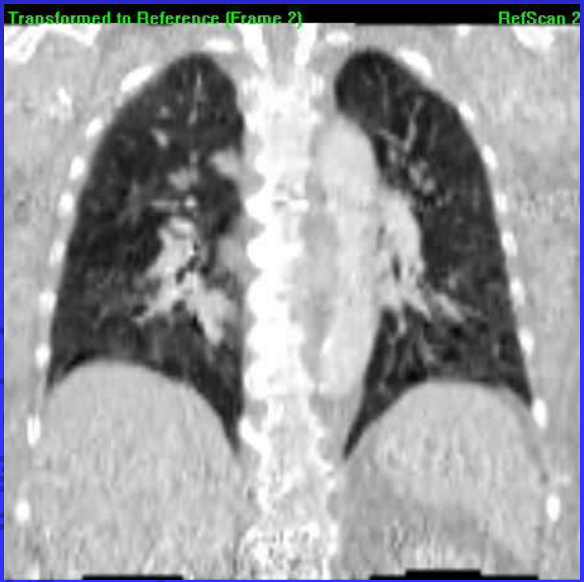
Image Enhancement



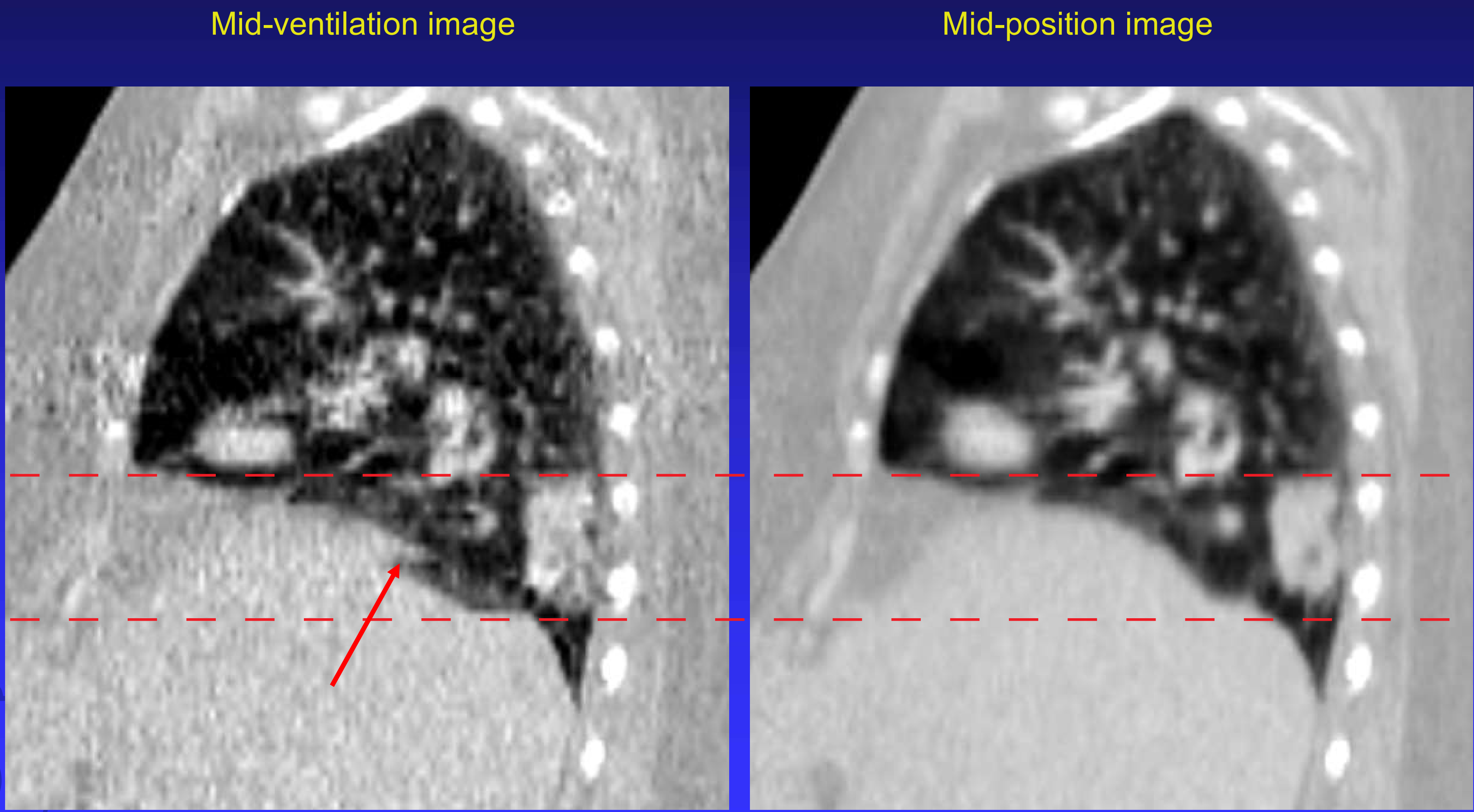
4DCT → Full 3D DVF

4DCT + Full 3D DVF → Motion corrected 4DCT @ mean pos.

Motion corrected 4DCT @ mean pos. → Average frames → Mid-position CT



Mid-position CT: deform all anatomy to its mean position and average over all frames



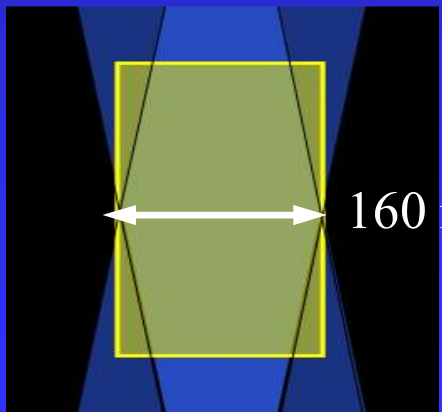
Reduces noise and artifacts

Wolthaus et al, Med Phys 2009

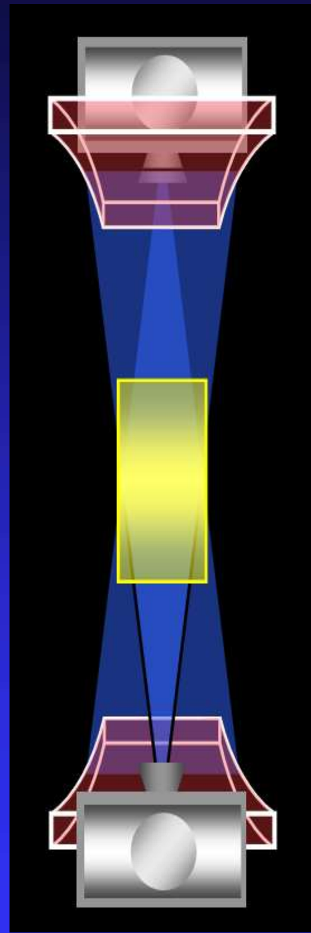
Courtesy of Catherine Coolens, PMH

Background – Dynamic Volume

320-slice CT



- Solid state detector
- 512 x 512 x 320
- 0.5 mm resolution
- 0.35 sec rotation
- Cone Angle 15.2°

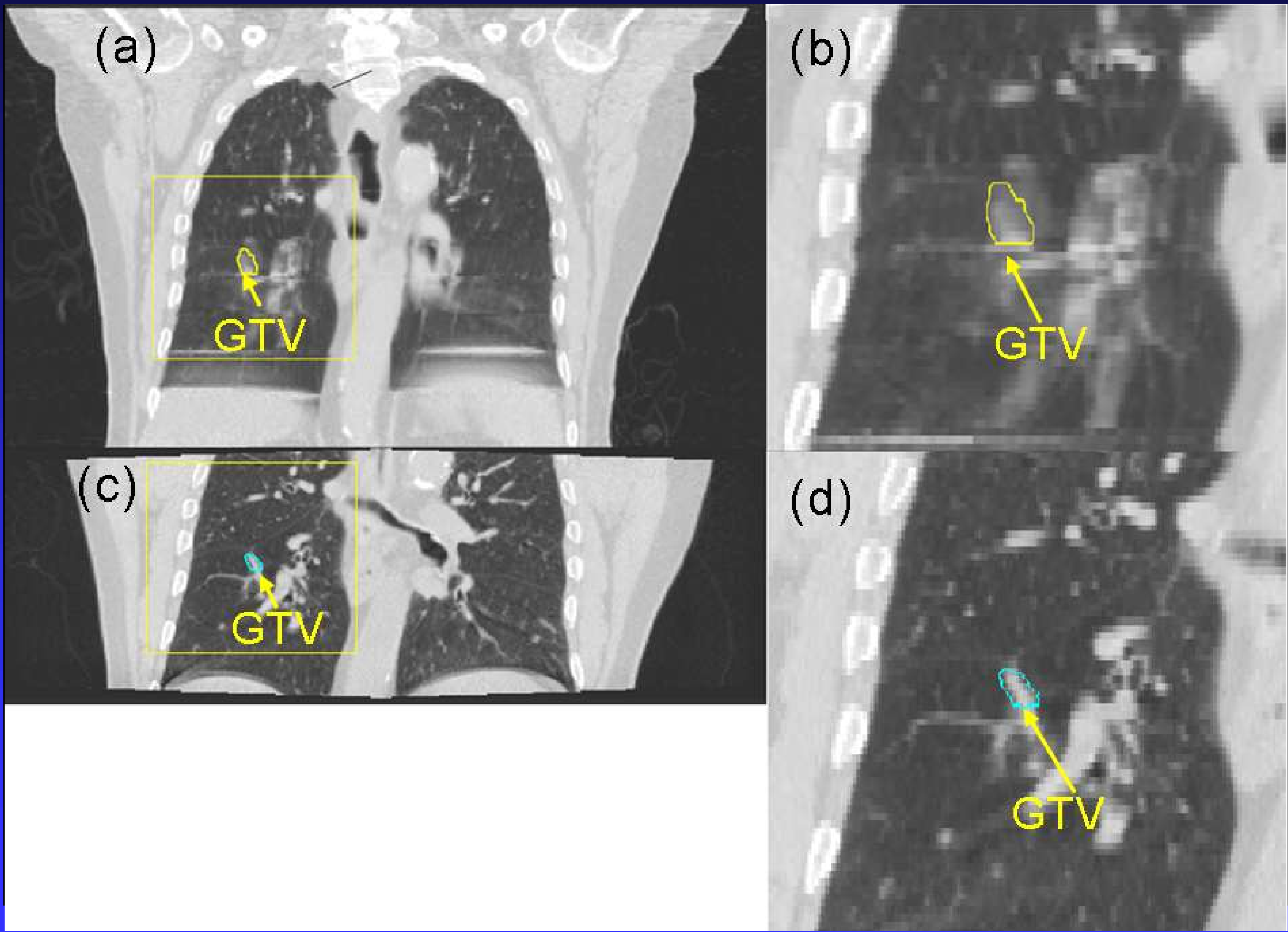


Coolens *et al*. (2009), Implementation and Characterisation of a 320-slice CT scanner for radiotherapy simulation, Med. Phys., vol. 36 (11), pp. 5120-5127.

Respiratory Correlated 4DCT   Volumetric 4DCT

Courtesy of Catherine Coolens, PMH

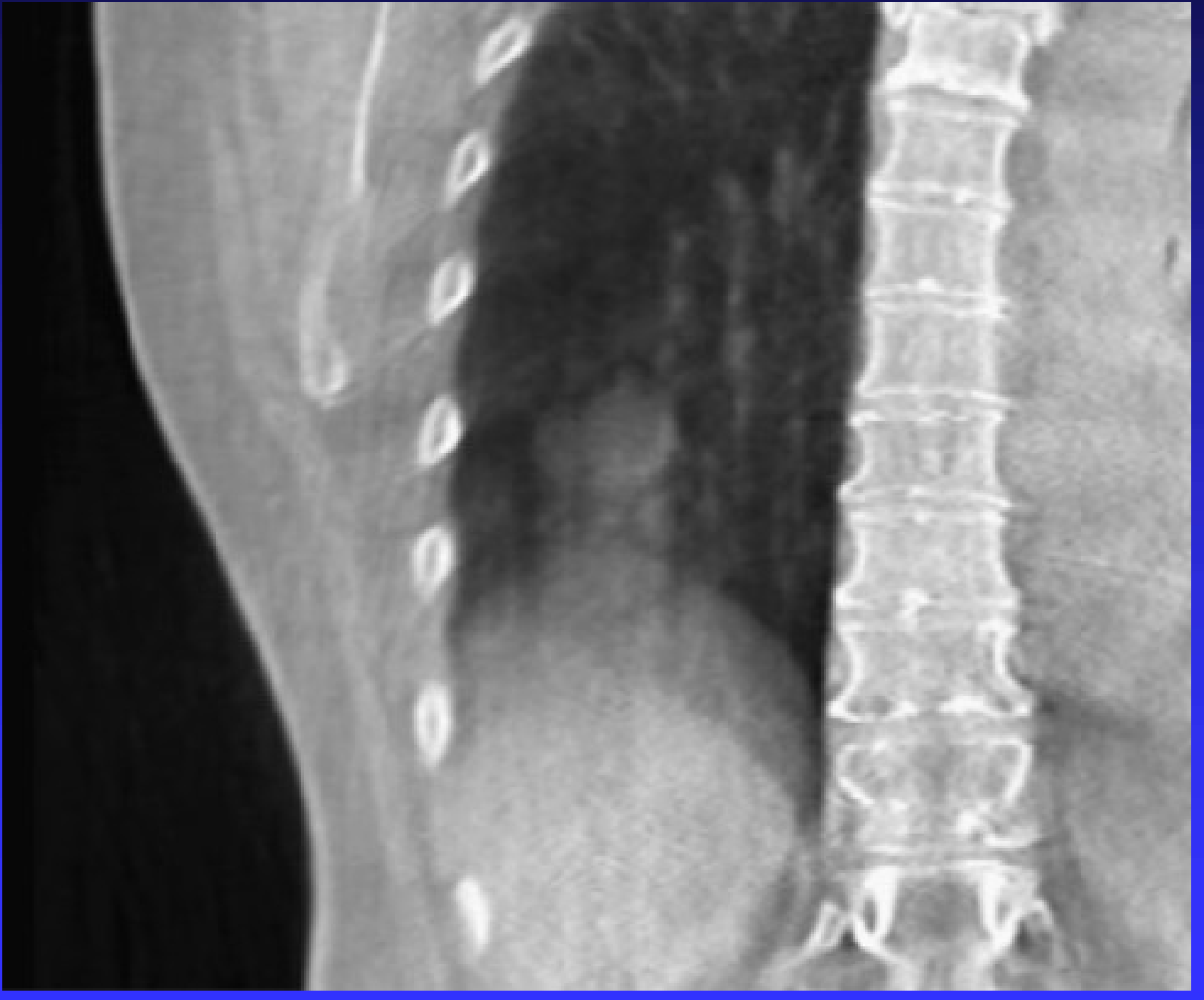
Results – Image Quality



4D Cone Beam CT

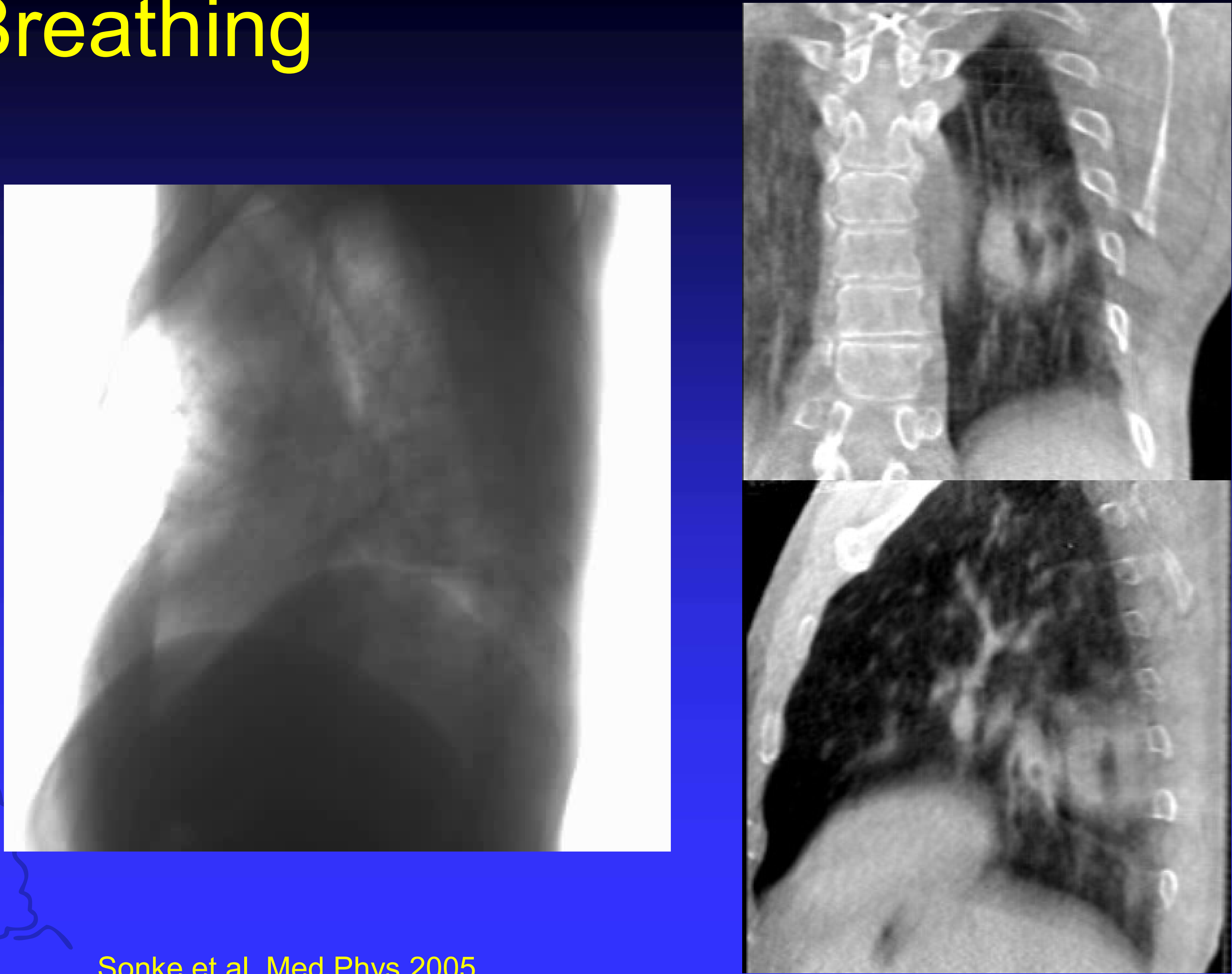
Cone Beam CT - effects of respiration

- Blurring and disappearing structures



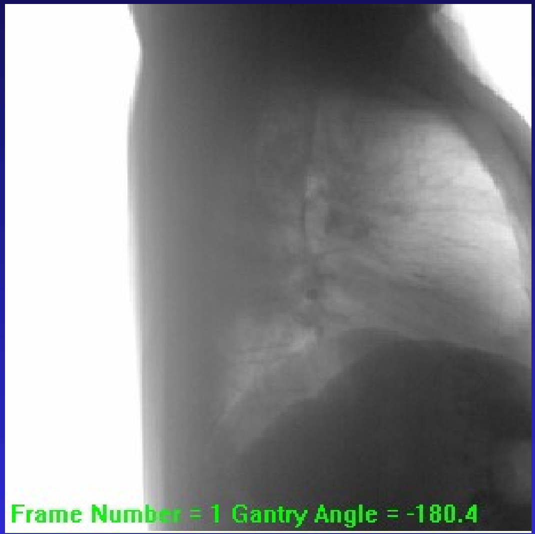
Sonke *et.al.*, IJROBP 2008

Breathing

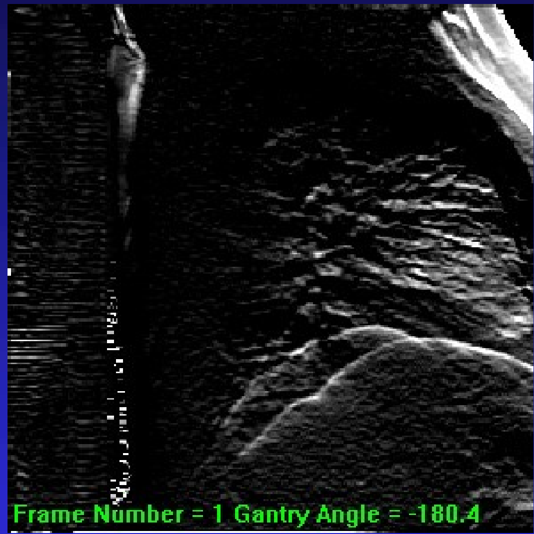


Sonke et al, Med Phys 2005

Respiratory Signal Extraction

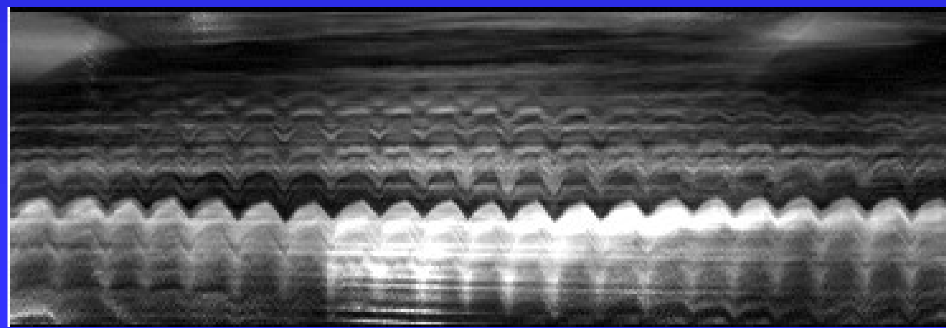


Vertical derivative filter



Horizontal projection

Temporal concatenation

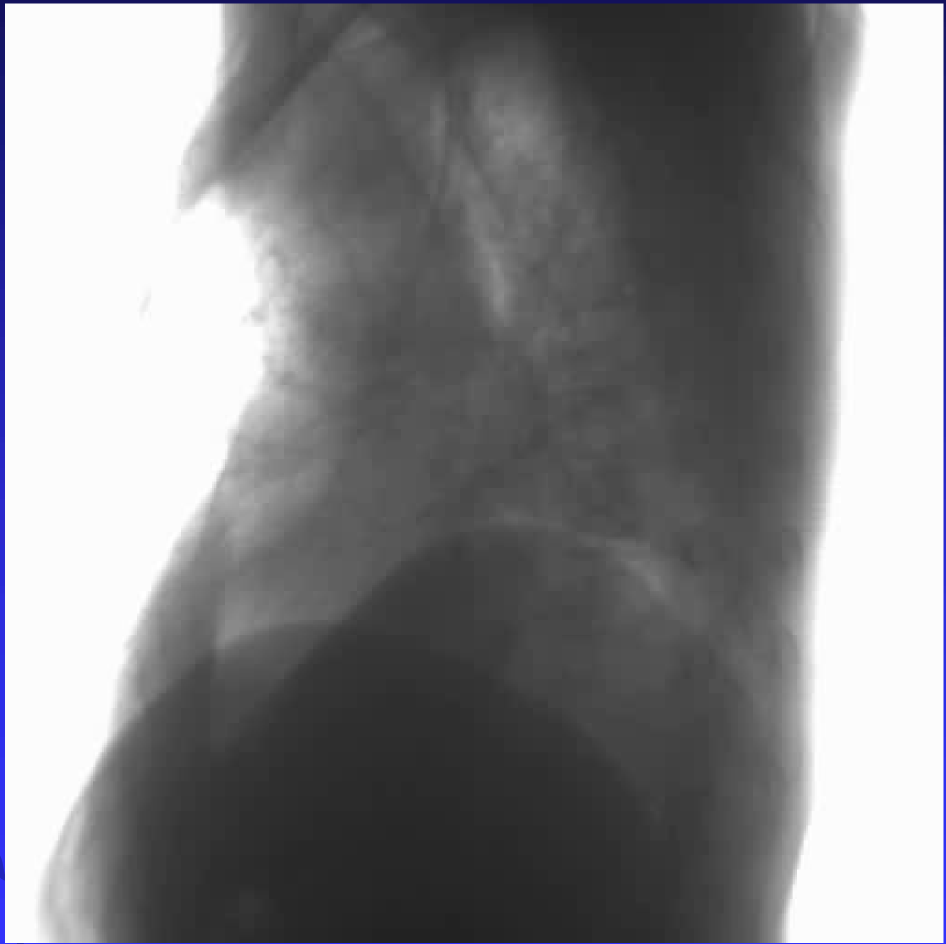


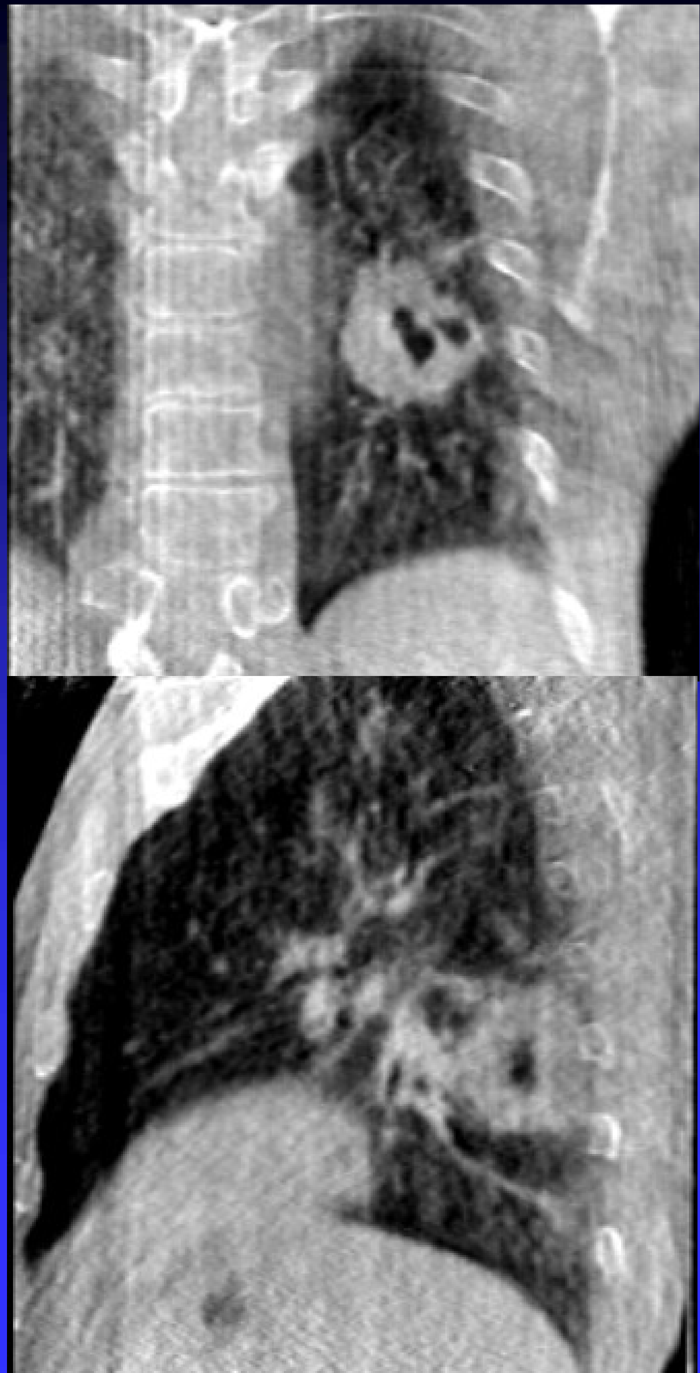
Amsterdam shroud (2D image)

Zijp et al., ICCR. 2004

van Herk et al., ICCR. 2007

RCCBCT

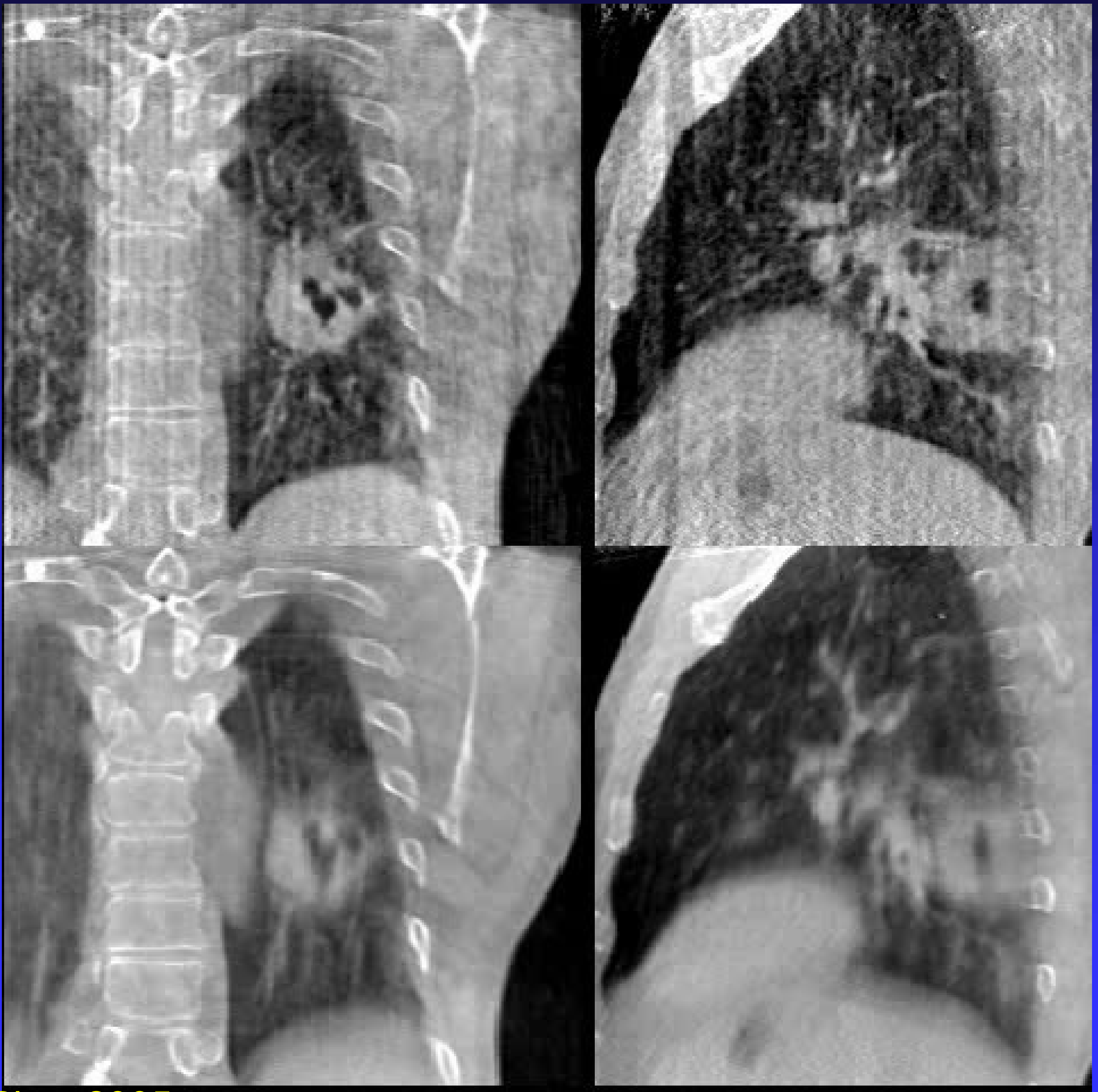




Sonke et al, Med Phys 2005

3D versus 4D CBCT

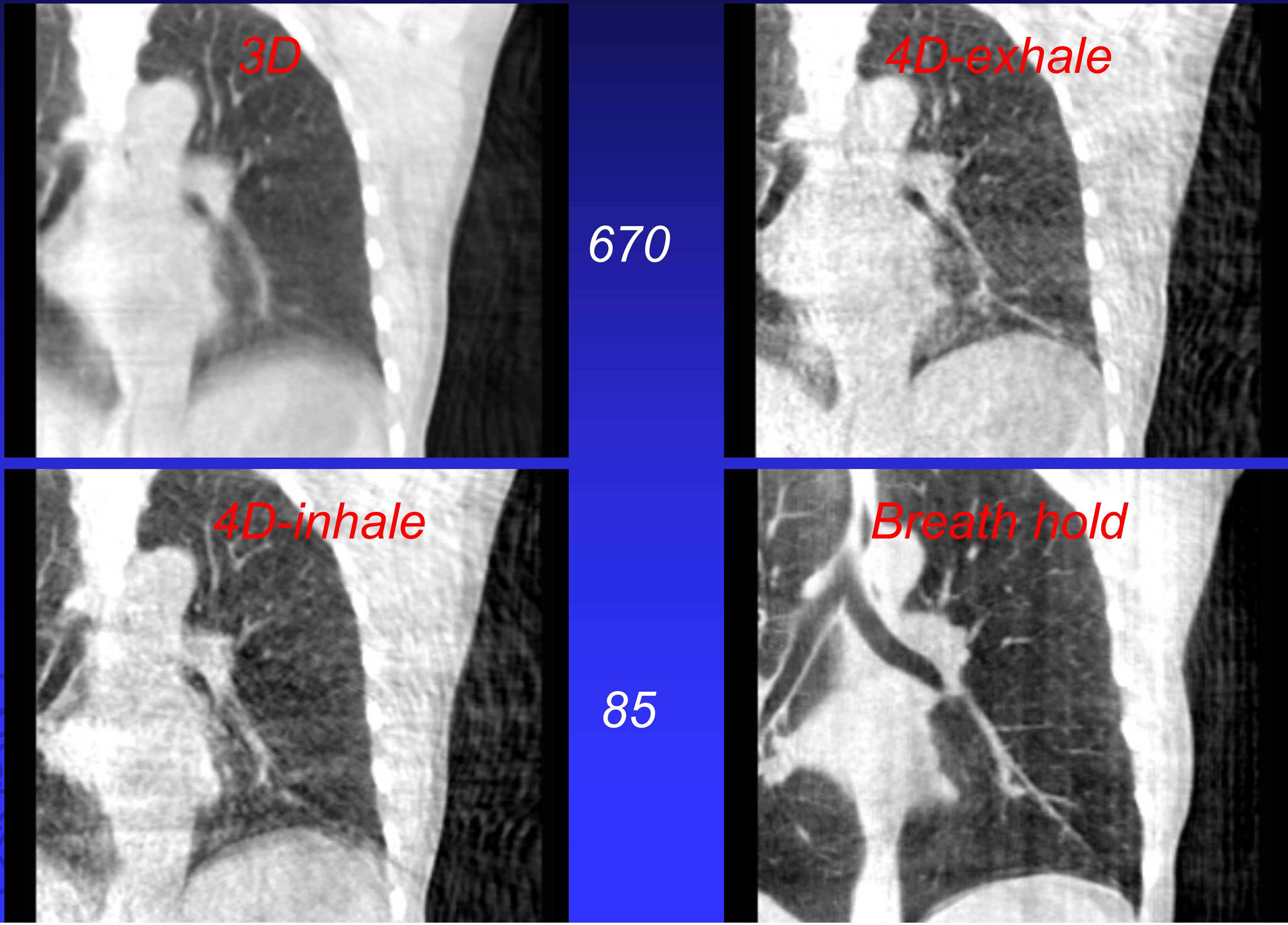
- 4D Data set
- 8 x 84 projections



- 3D Data set
- 670 projections
- Same dose for 3D and 4D

Sonke et al, Med Phys 2005

Cone beam CT Image Quality



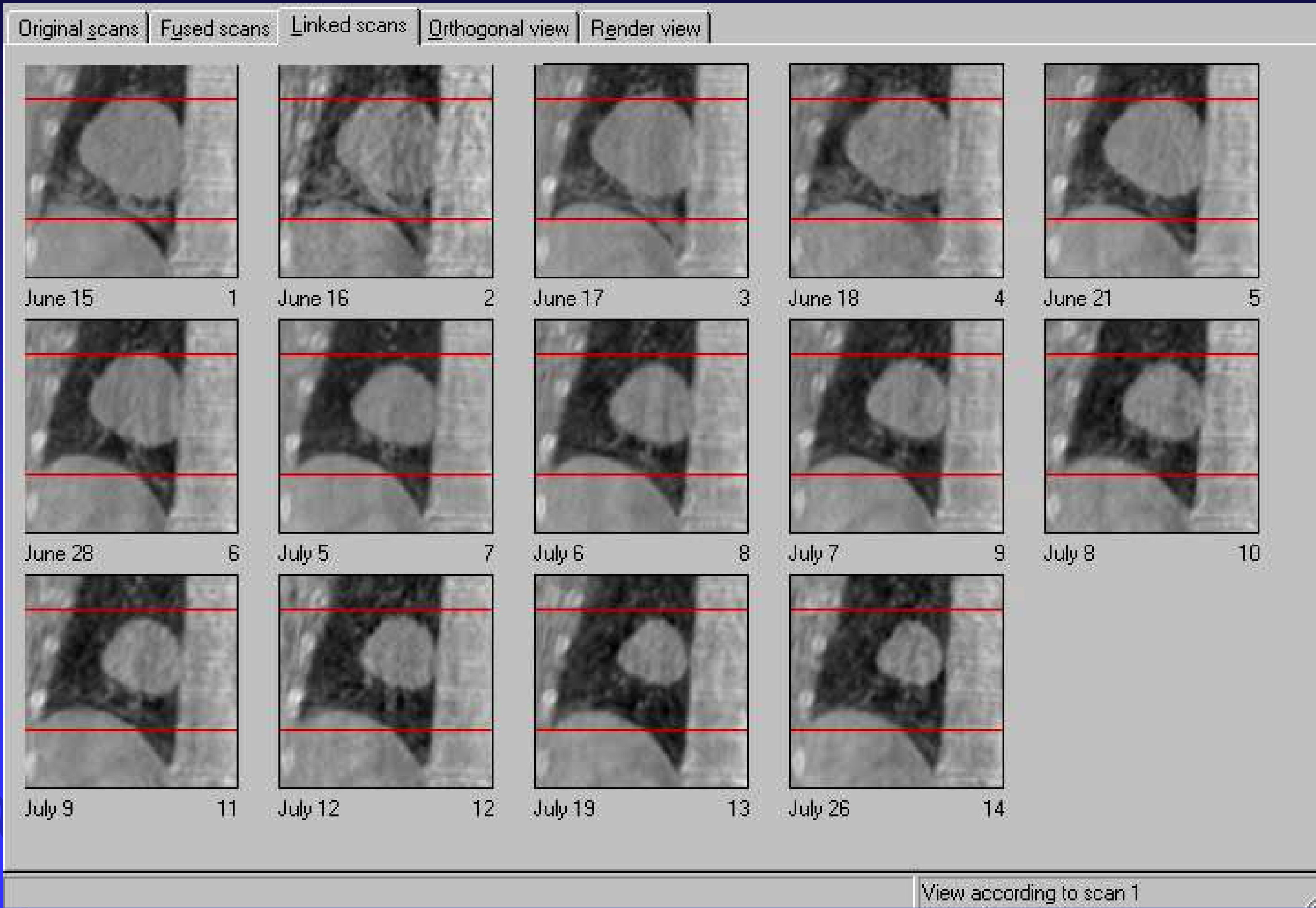
670

85

85

95

Repeat 4D cone beam CT



Shows respiration, tumor shrinkage and baseline position variation

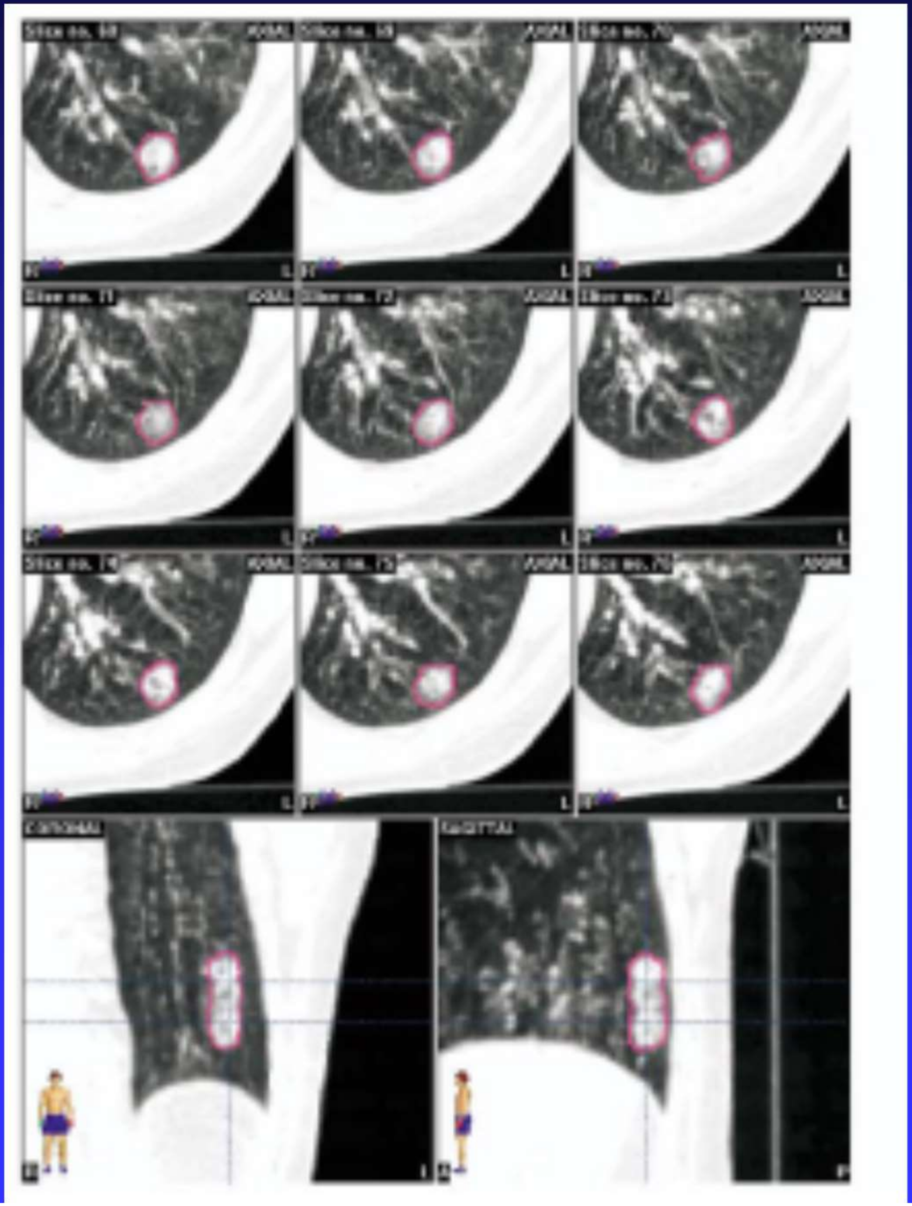
4D in Treatment Planning

Contouring in 4DCT

- Maximum intensity projection
- Average intensity projection

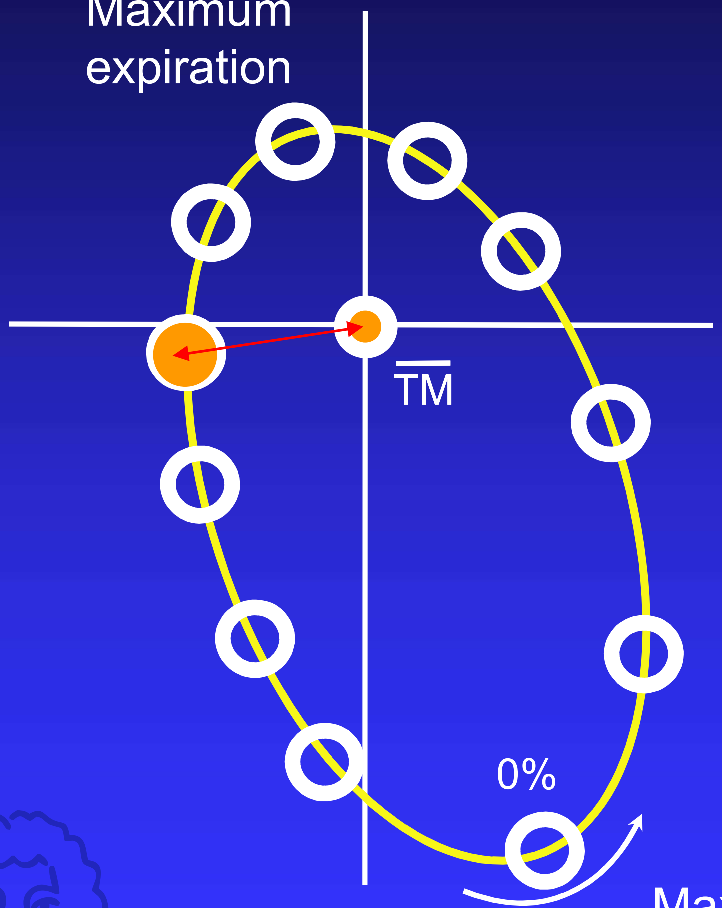
Can be used for in-room matching

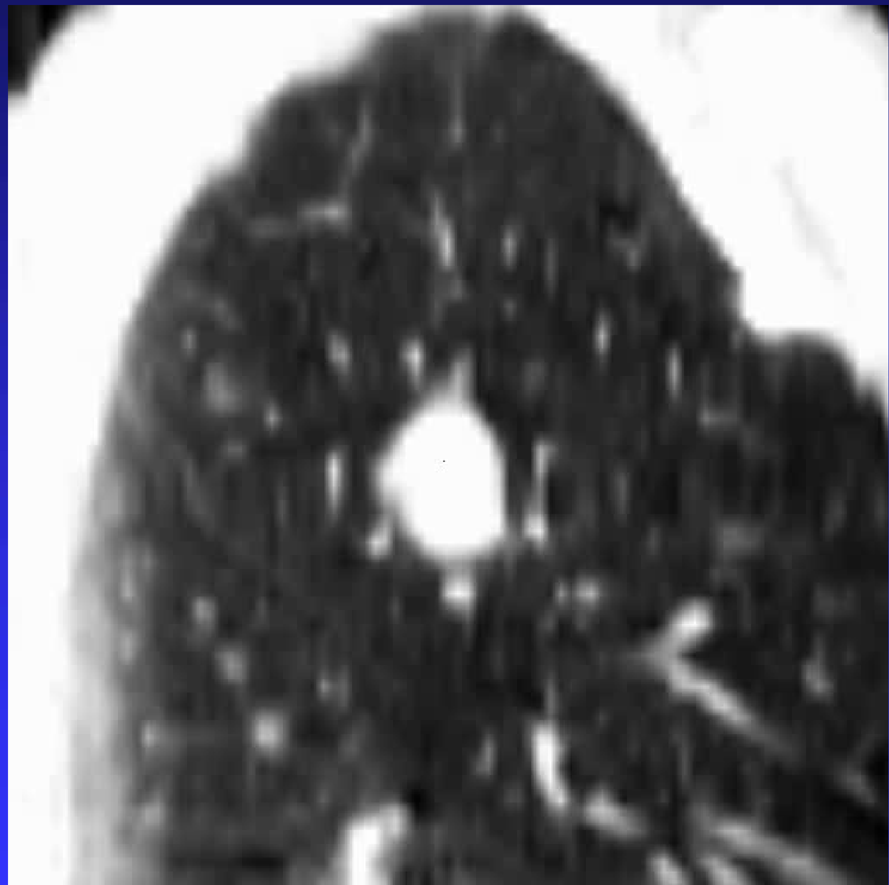
Underberg et al, IJROBP, 2005



Mid-ventilation

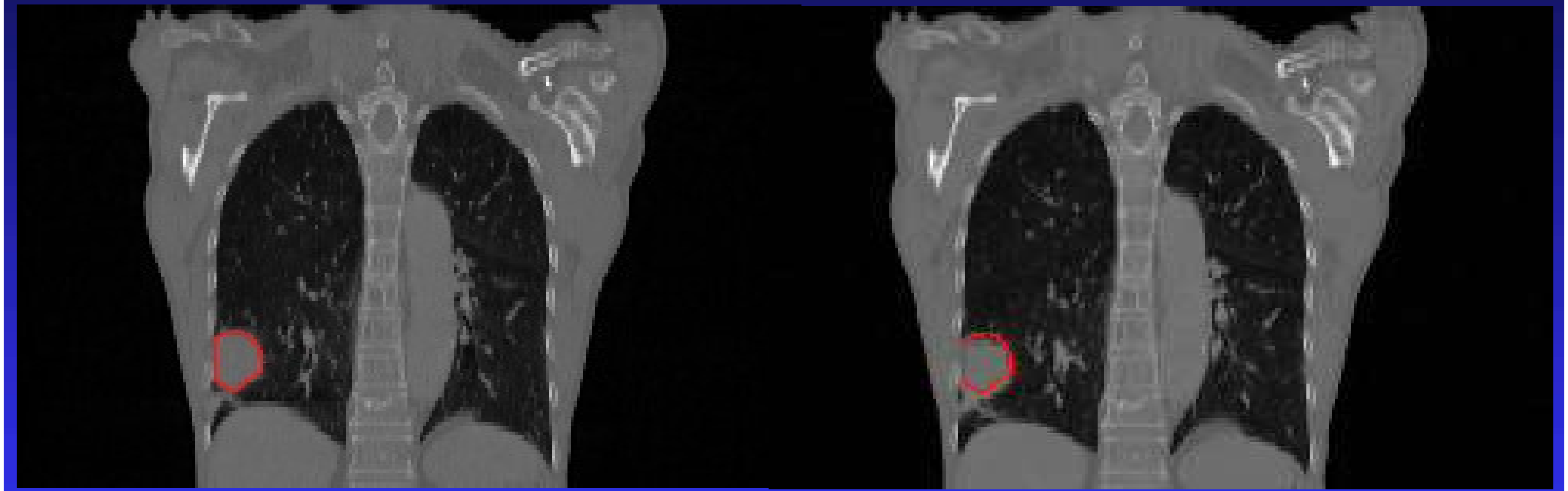
Selection of a single appropriate CT scan





Wolthaus et al, IJROBP 2006; Nijkamp et al ICCR 2007

Mid-ventilation is very simple (used clinically on hundreds of patients)



Mid-ventilation CT

4D CT

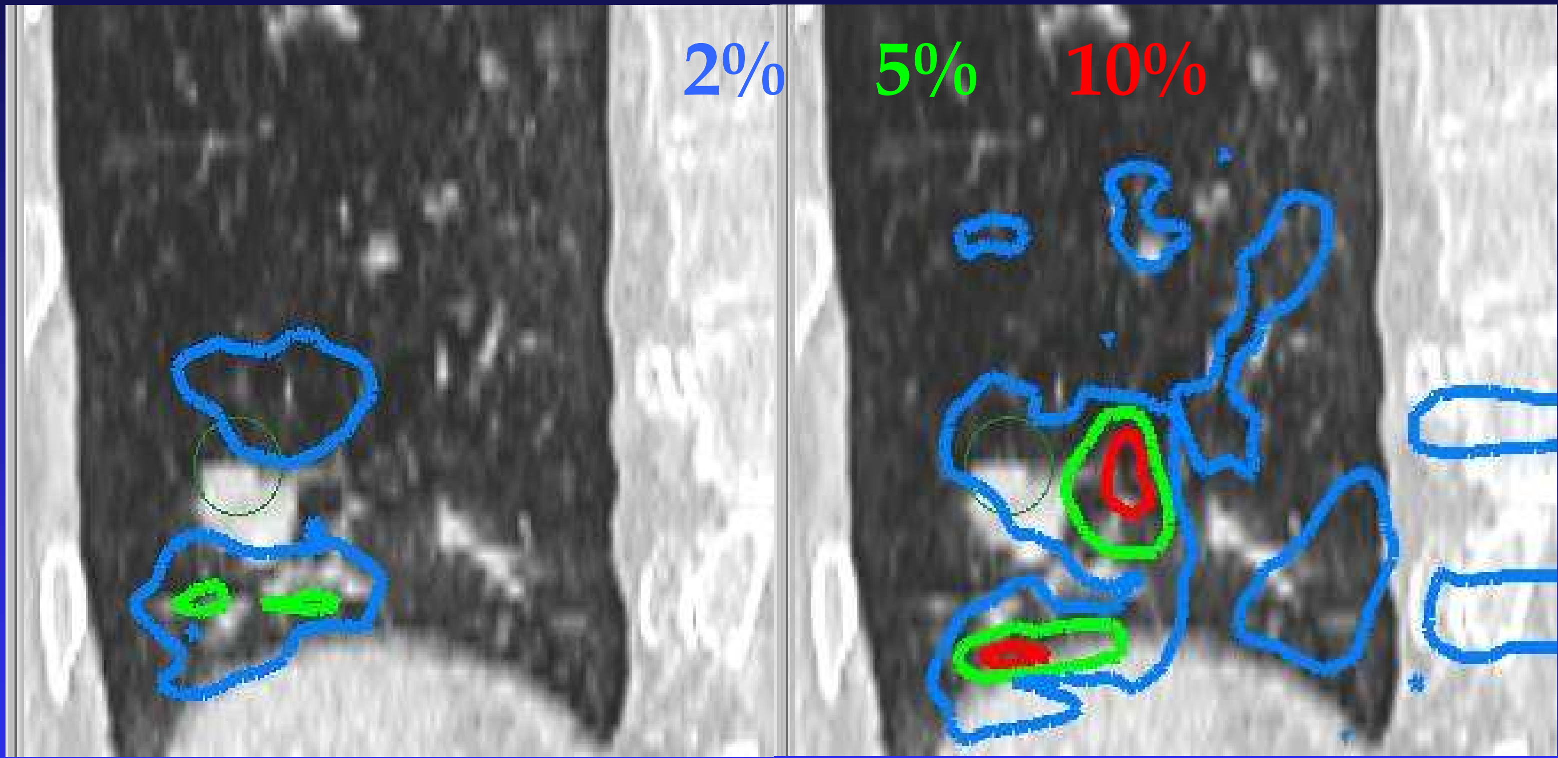
Eliminates systematic error due to imaging (except hysteresis)
Geometrically and dosimetric very close to full 4D plan!

Wolthaus et al, IJROBP 2006; Nijkamp et al ICCR 2007

Dose Distribution

•Spatial dose distribution varies as a function of time if patient global matter distribution changes significantly

Dose discrepancy *due to changing anatomy*
Patient with a large tumor motion (3 cm)

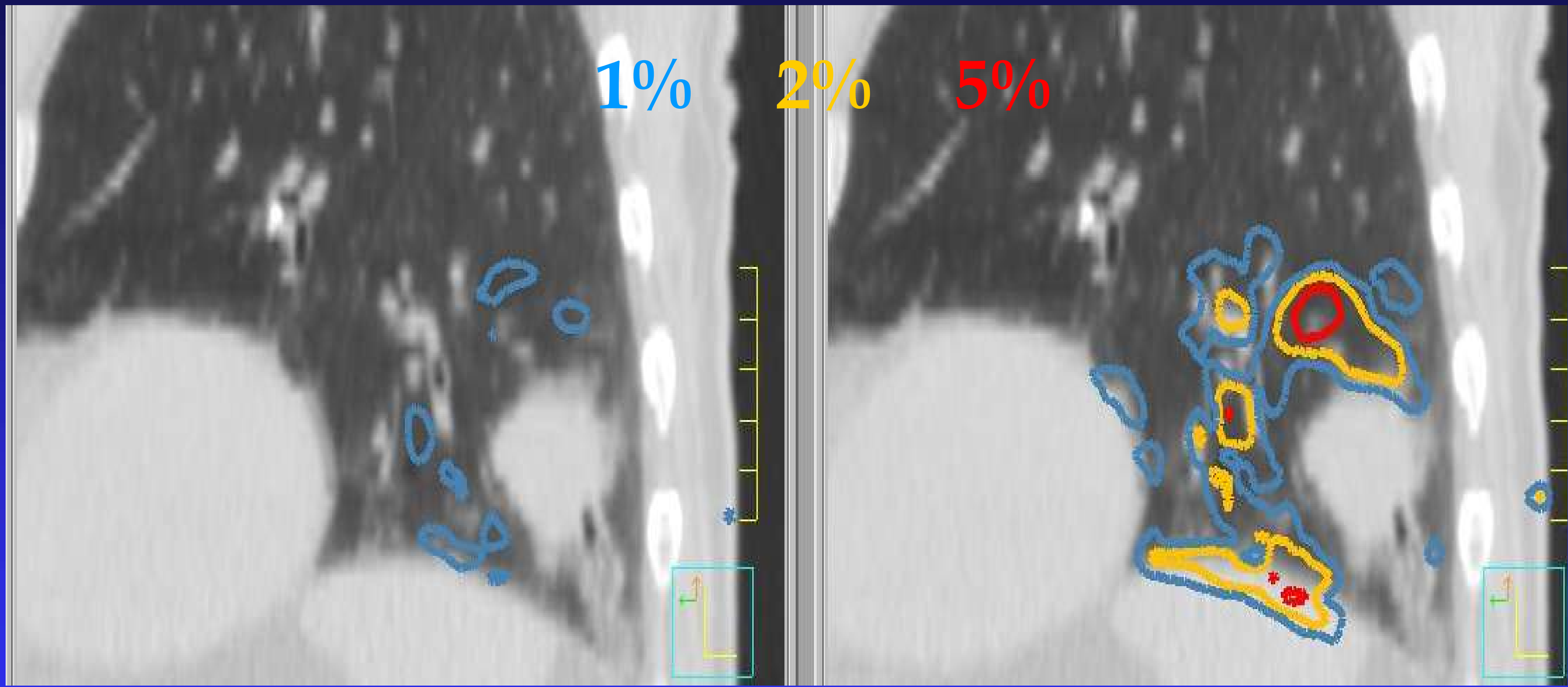


Max Dose Discrepancy	Tumor % in 1cc	Lung % 1cc
Mean CT	1.3%	6.0%
Single CT	3.1%	10%

Beaumont
William Beaumont Hospital

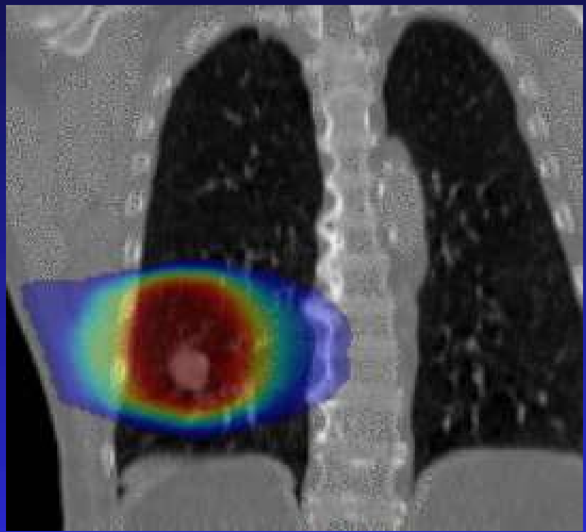
Dose discrepancy due to changing anatomy

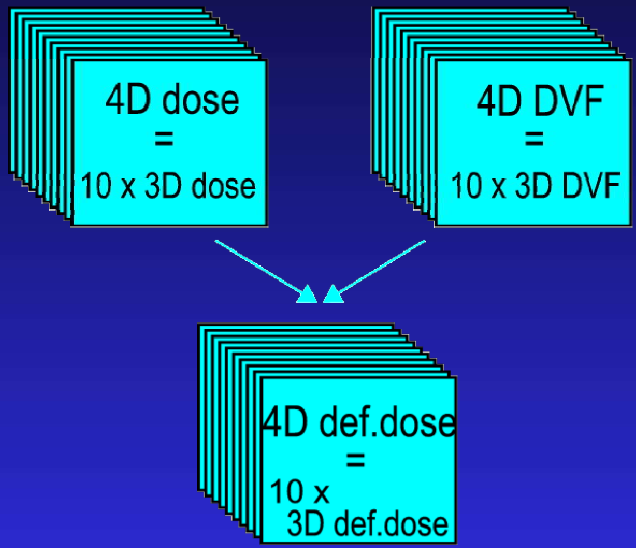
Patient with a small tumor motion (1.5 cm)

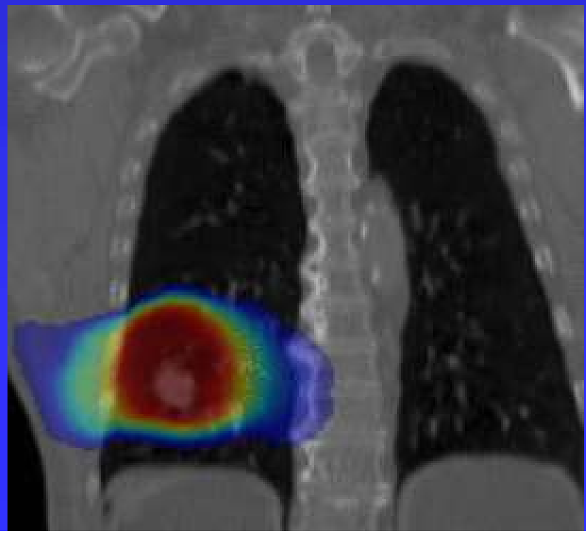


Max Dose Discrepancy	Tumor % in 1cc	Lung % 1cc
Mean CT	0.3%	1.3%
Single CT	1.5%	5%

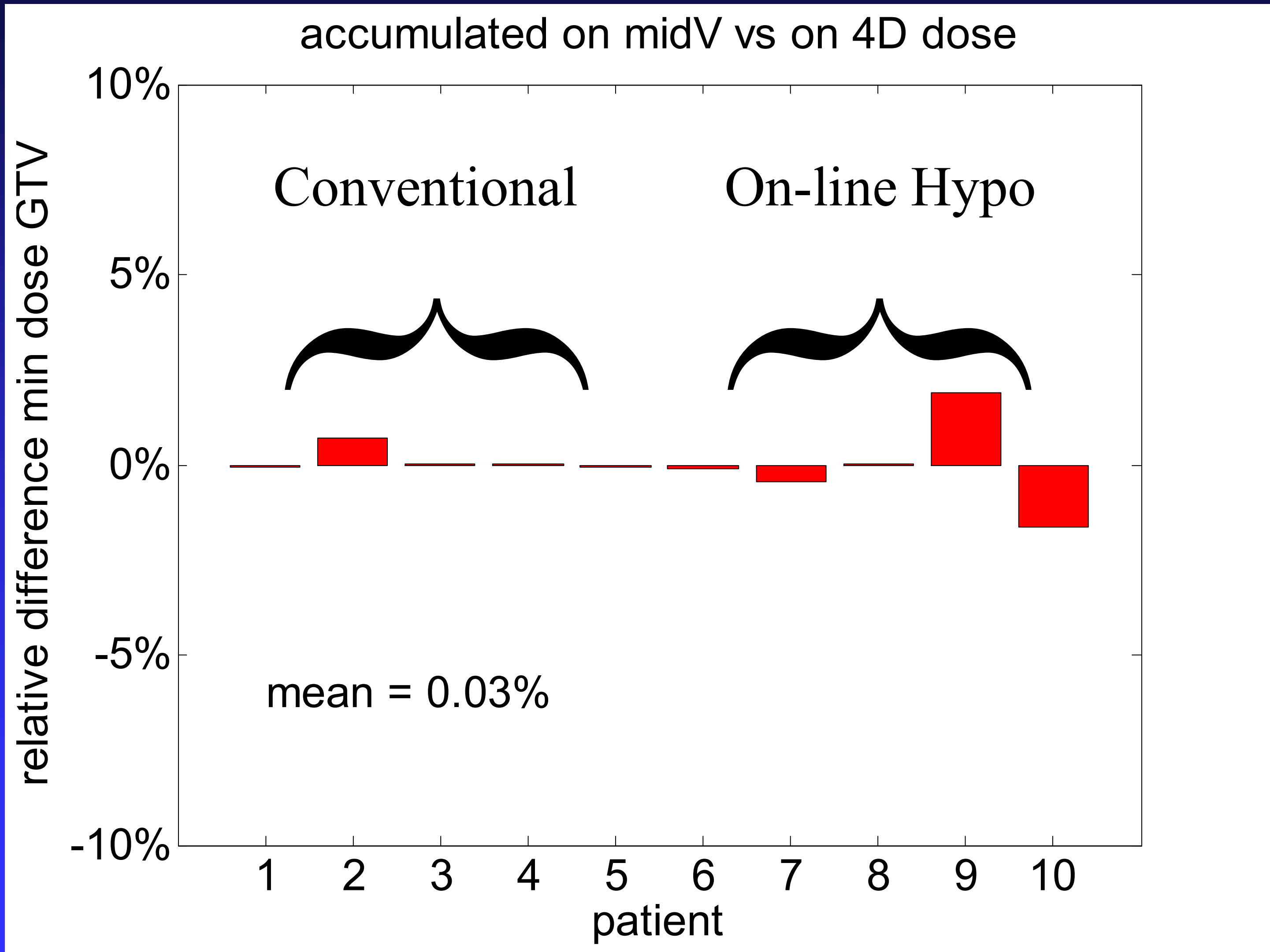
Deformed Dose





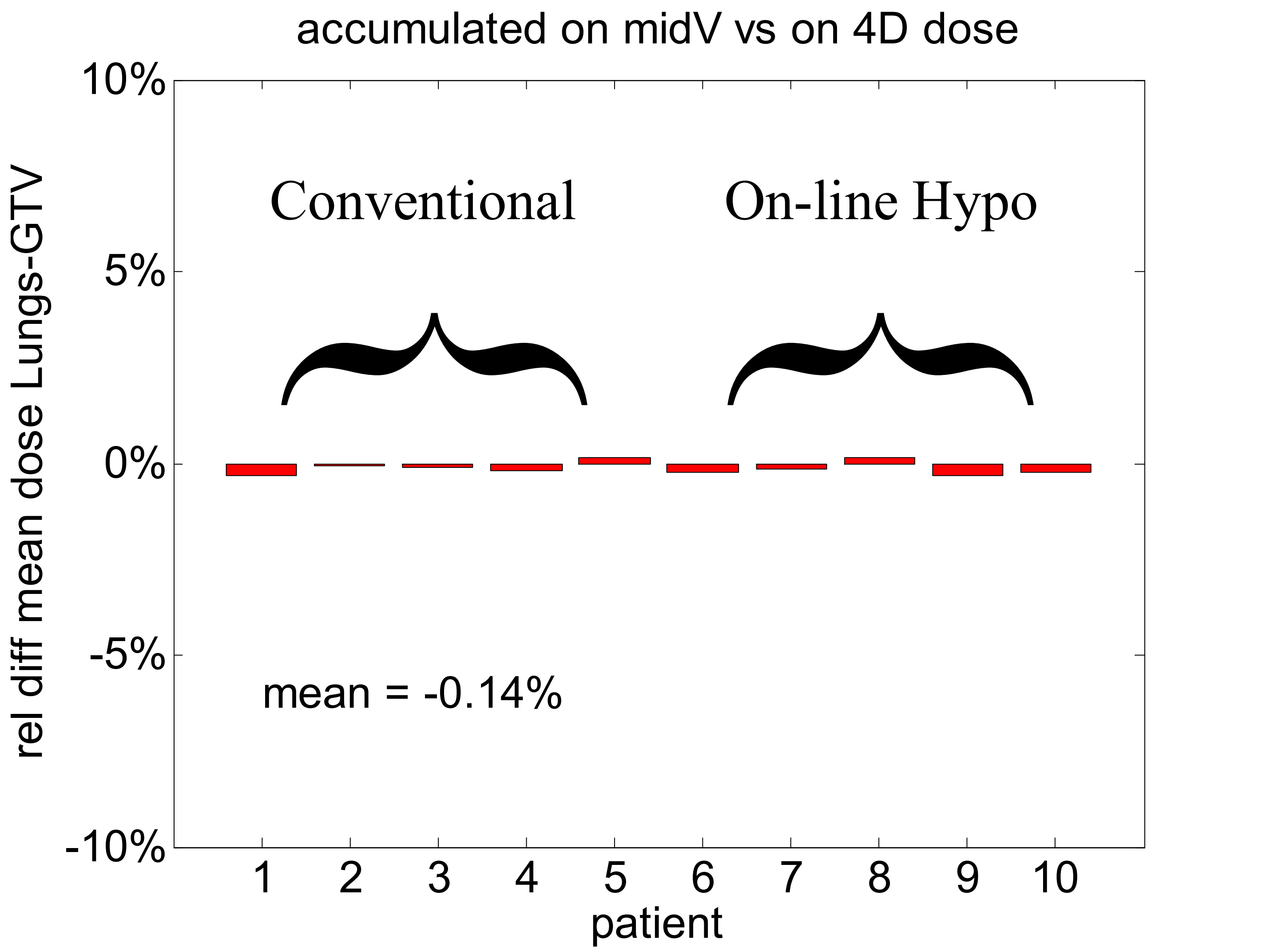


Tumor minimum dose



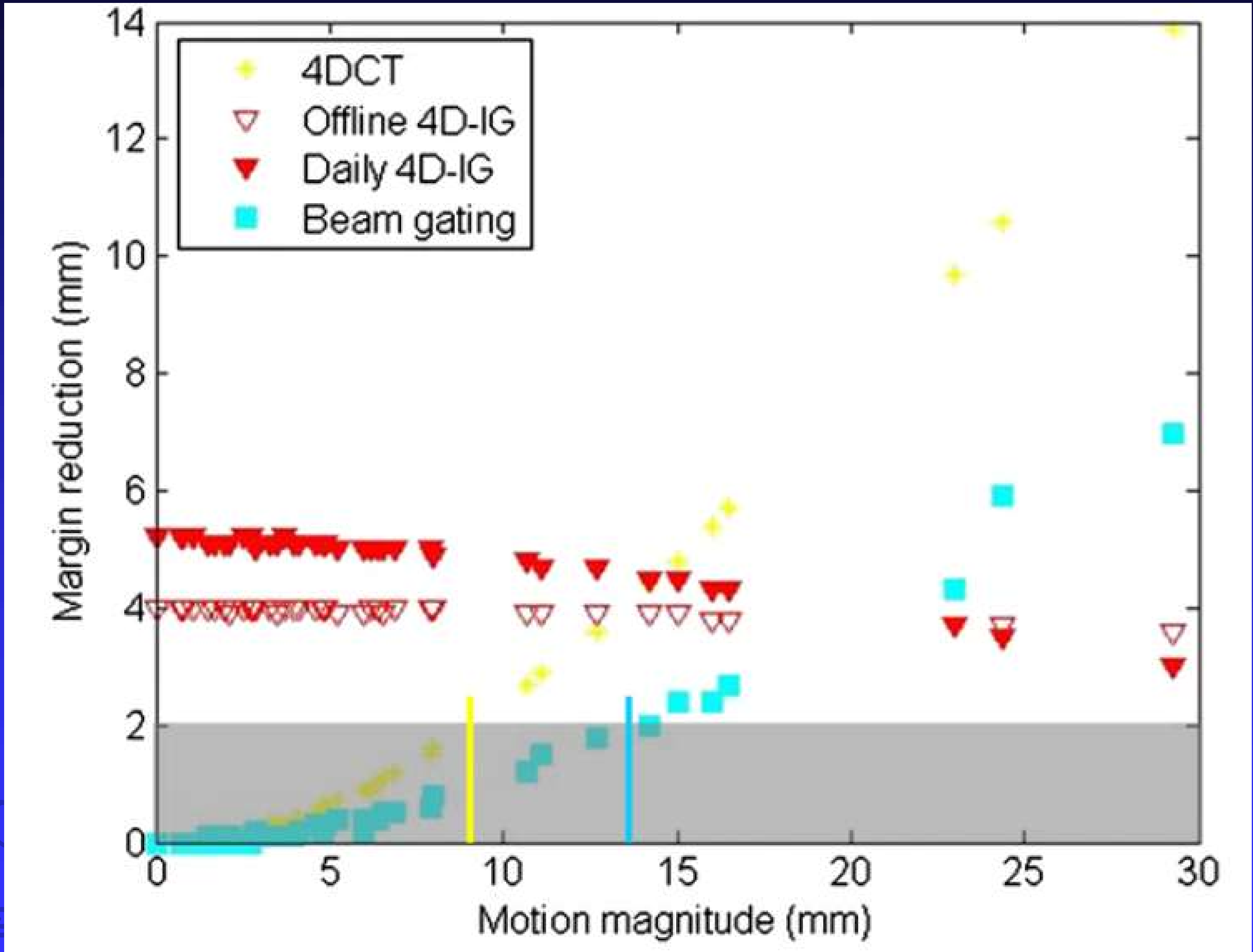
Mexner et al. IJROBP 2008

Lung mean dose



Mexner et al. IJROBP 2008

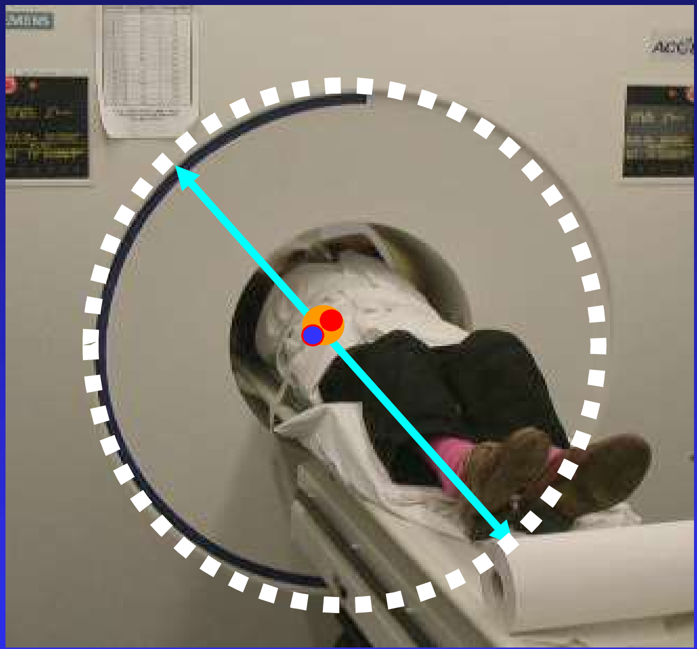
Conventional Fractionated RT

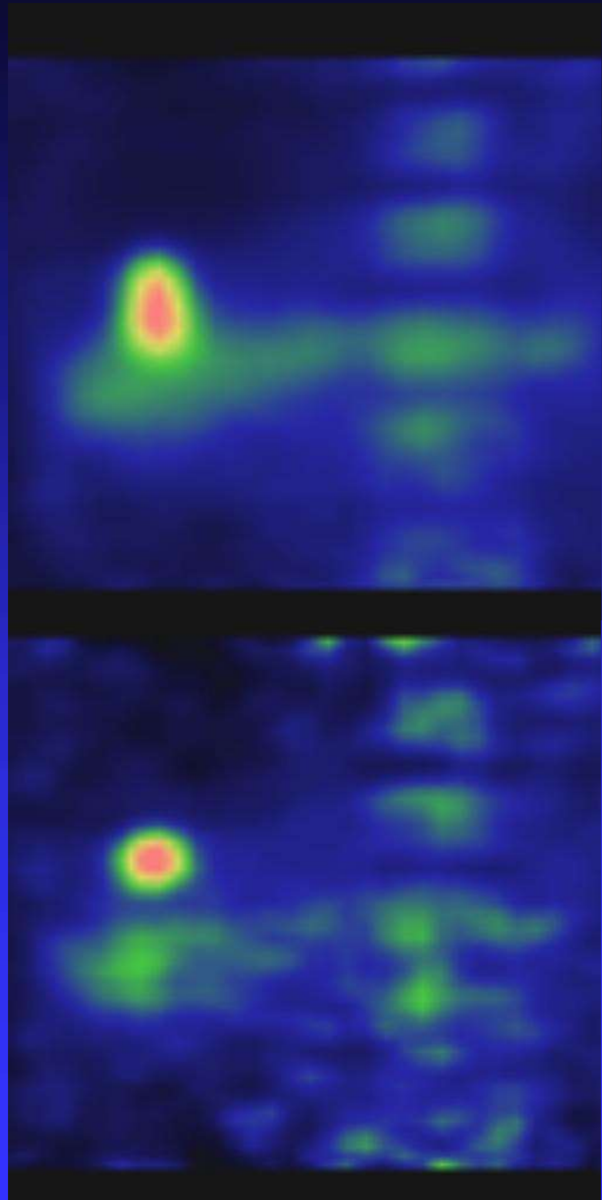


Korreman et al. IJROBP, 2010

4D PET

Motion Artifacts in PET

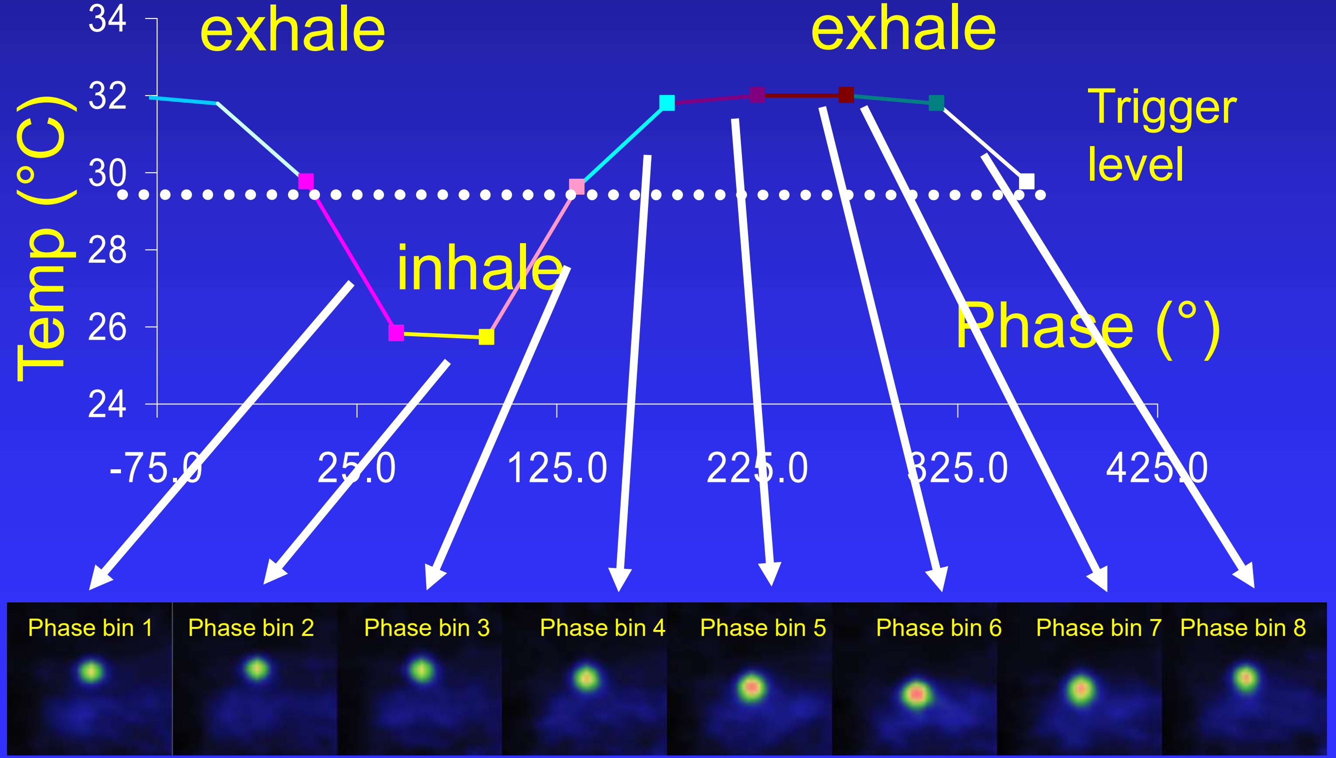




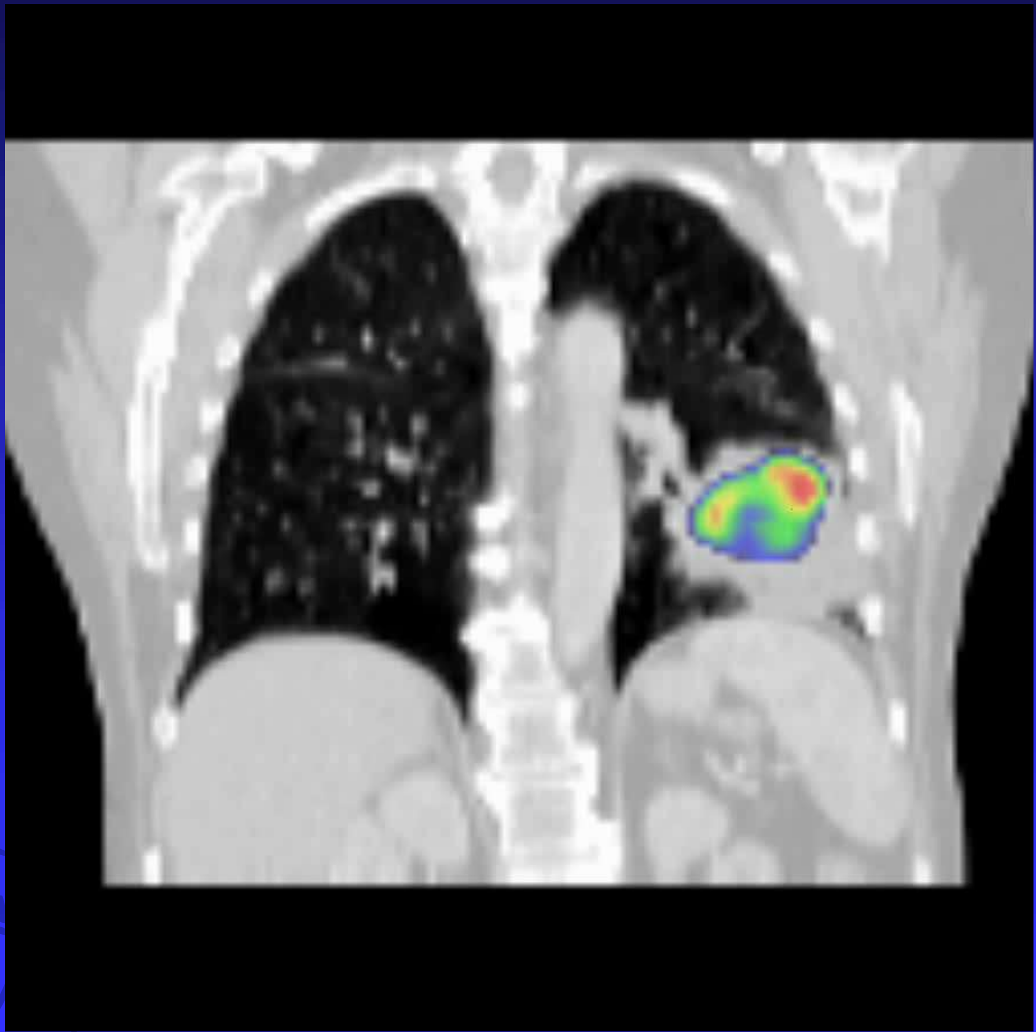
Tumor is enlarged due to blurring

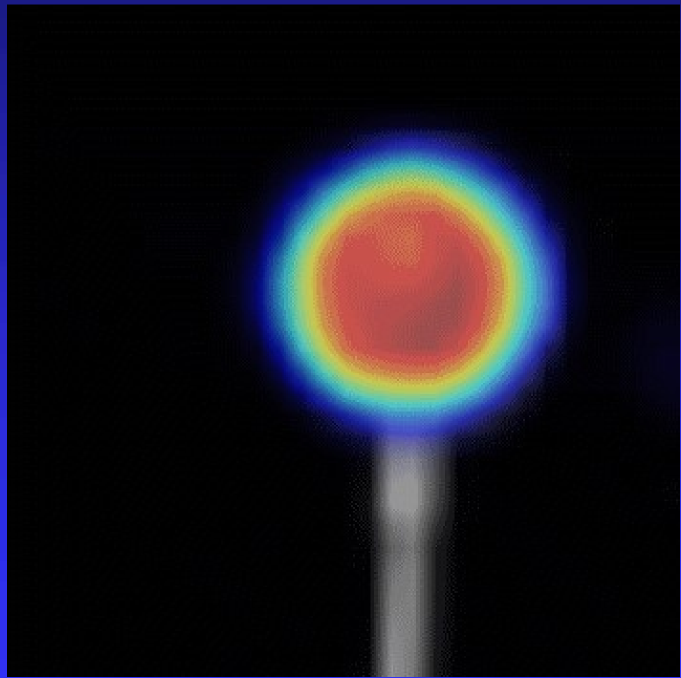
Respiration Correlated PET

- Continuous emission → division based on respiration phase
- Prospective gating:Respiratory trace triggers onset of binning for each breathing cycle
- Retrospective: Respiratory trace is used to bin counts from listmode



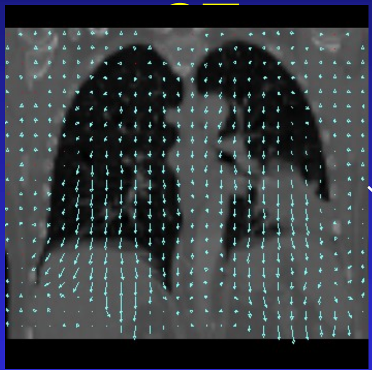
PET motion imaging





CT based Mid-Position PET

Motion detection in 4D



Deformation of 4D PET to CT MidP

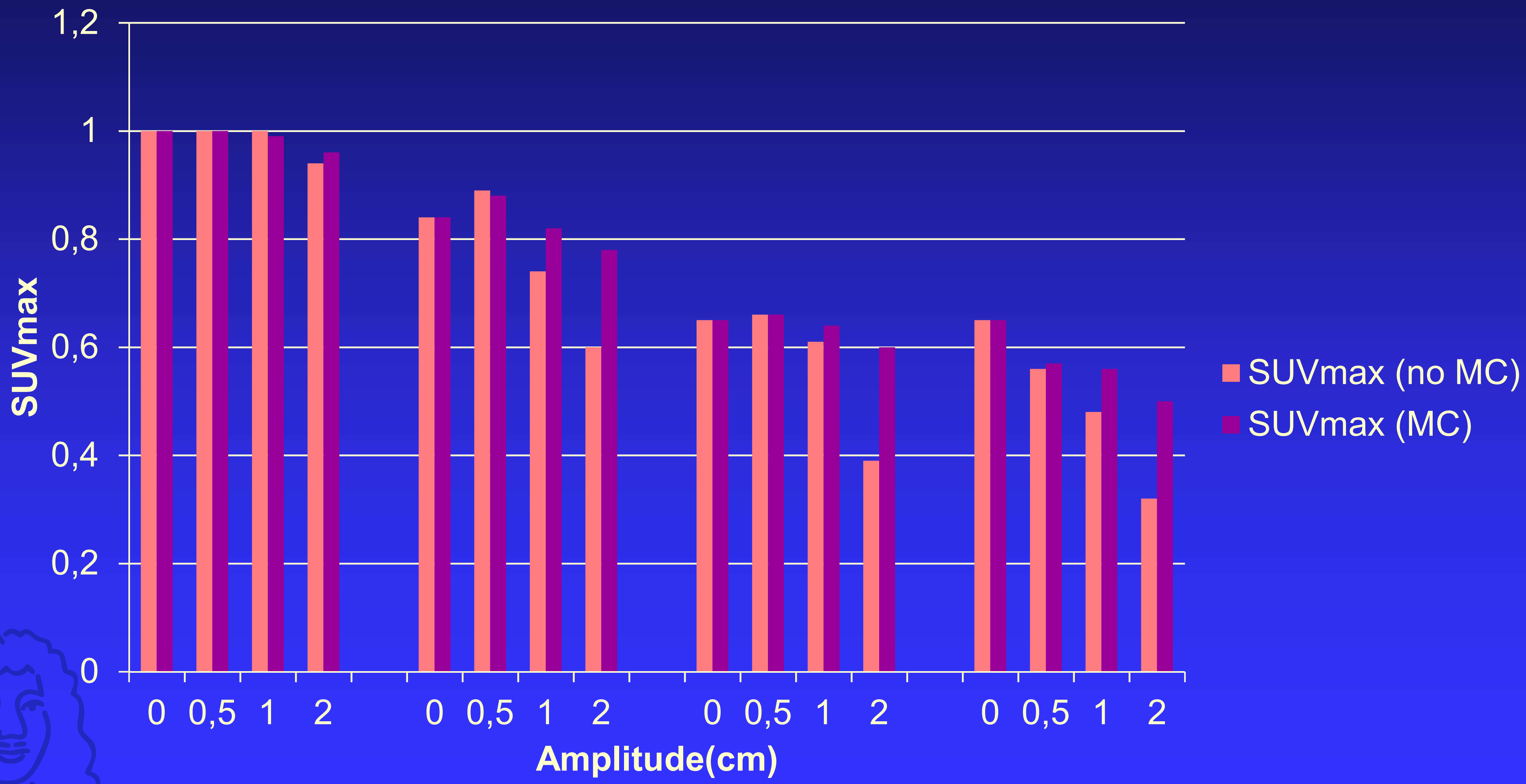
Average of Respiration Phases

Wolthaus et al,
Medical Physics, 2008 (35)

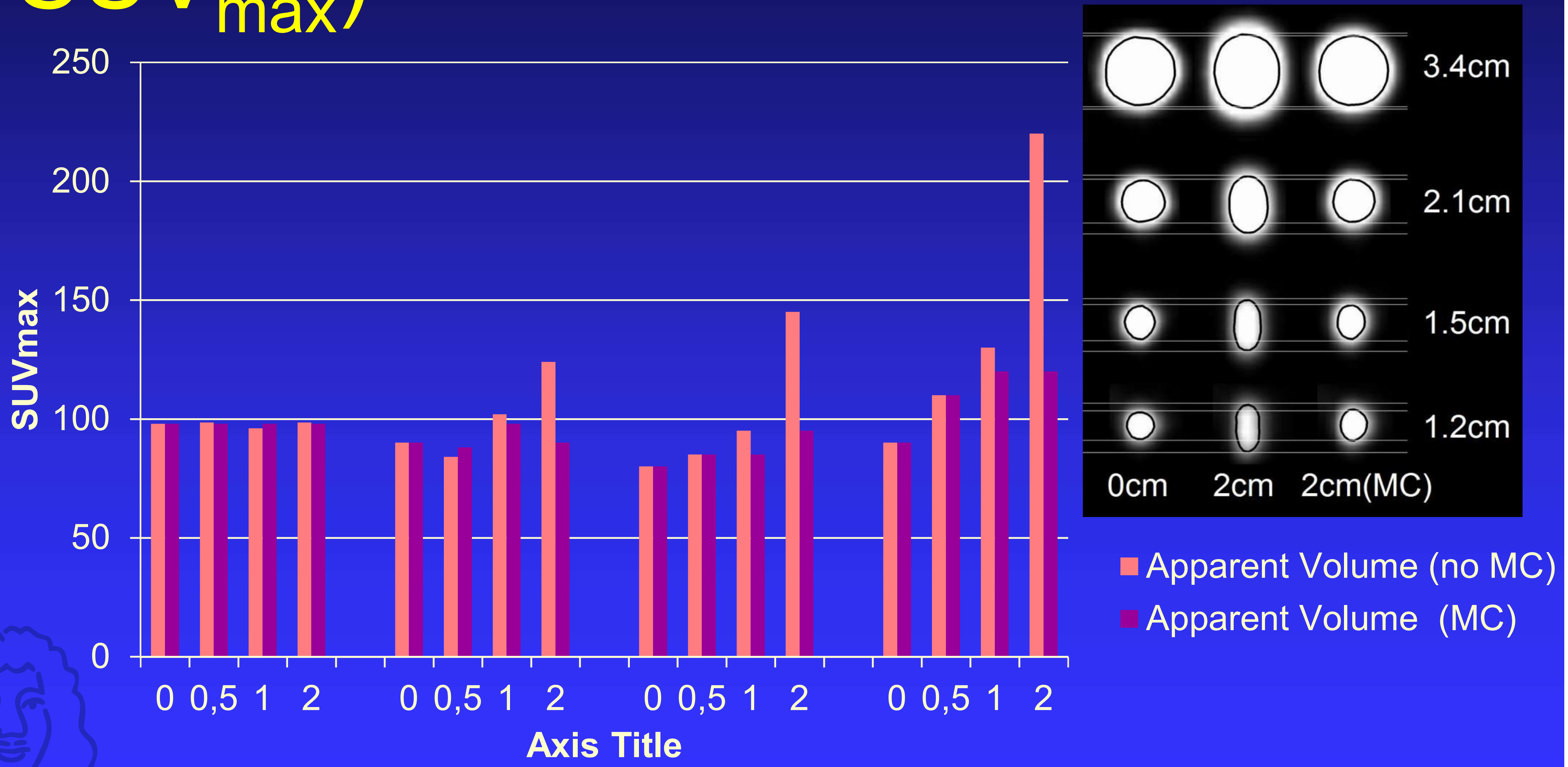
Phantom Experiments

- Philips Gemini TF PET/CT
- Sinusoidal respiration phantom
- 4 radioactive spheres (diameters: 1.2cm, 1.5cm, 2.1cm, 3.4cm)
- 4 different amplitudes:
  (static, 0.5cm, 1cm, 2cm)

Maximum SUV in spheres



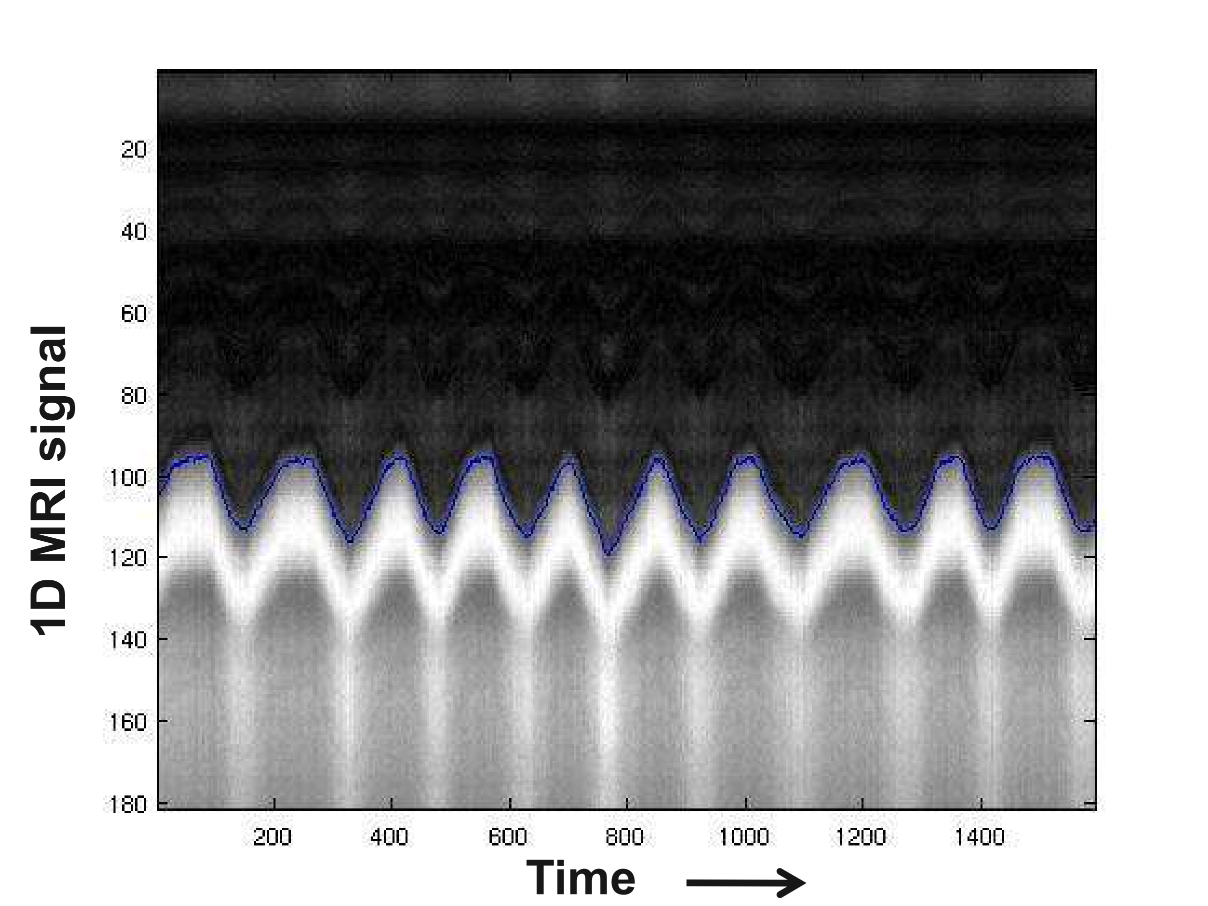
Apparent volume in spheres (based on threshold of 40% of SUV_{max})



4D MRI

1D MRI, Navigator echos (NE)
15 ms per acquisition

University Medical Center Utrecht

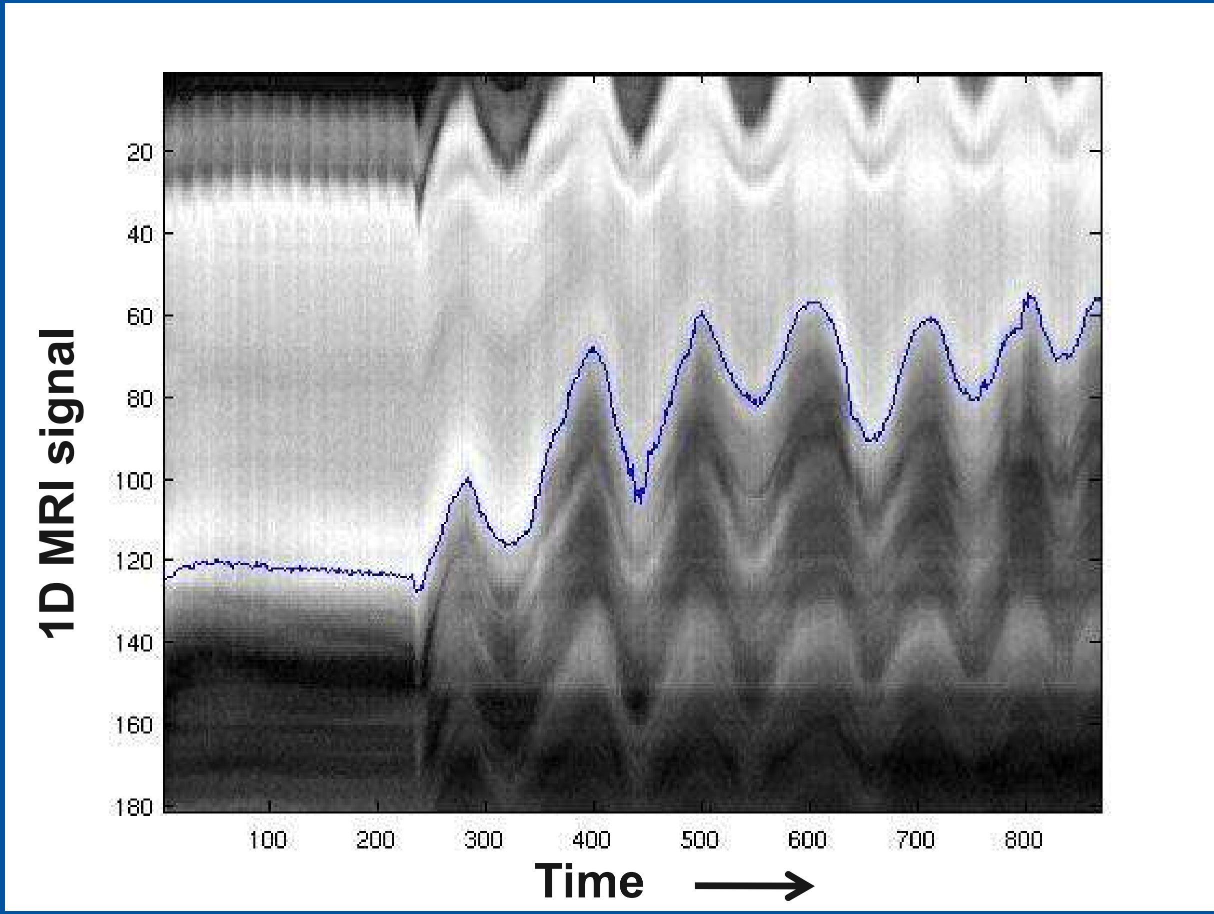


- In diagnostics used to track/gate respiration
- Imaging stack is moved according to NE signal
- Diaphragm monitored
- Can be positioned anywhere in any orientation

Monitoring breathing at superior side of liver

1D MRI navigators, monitoring breath hold stability and on-set of breathing

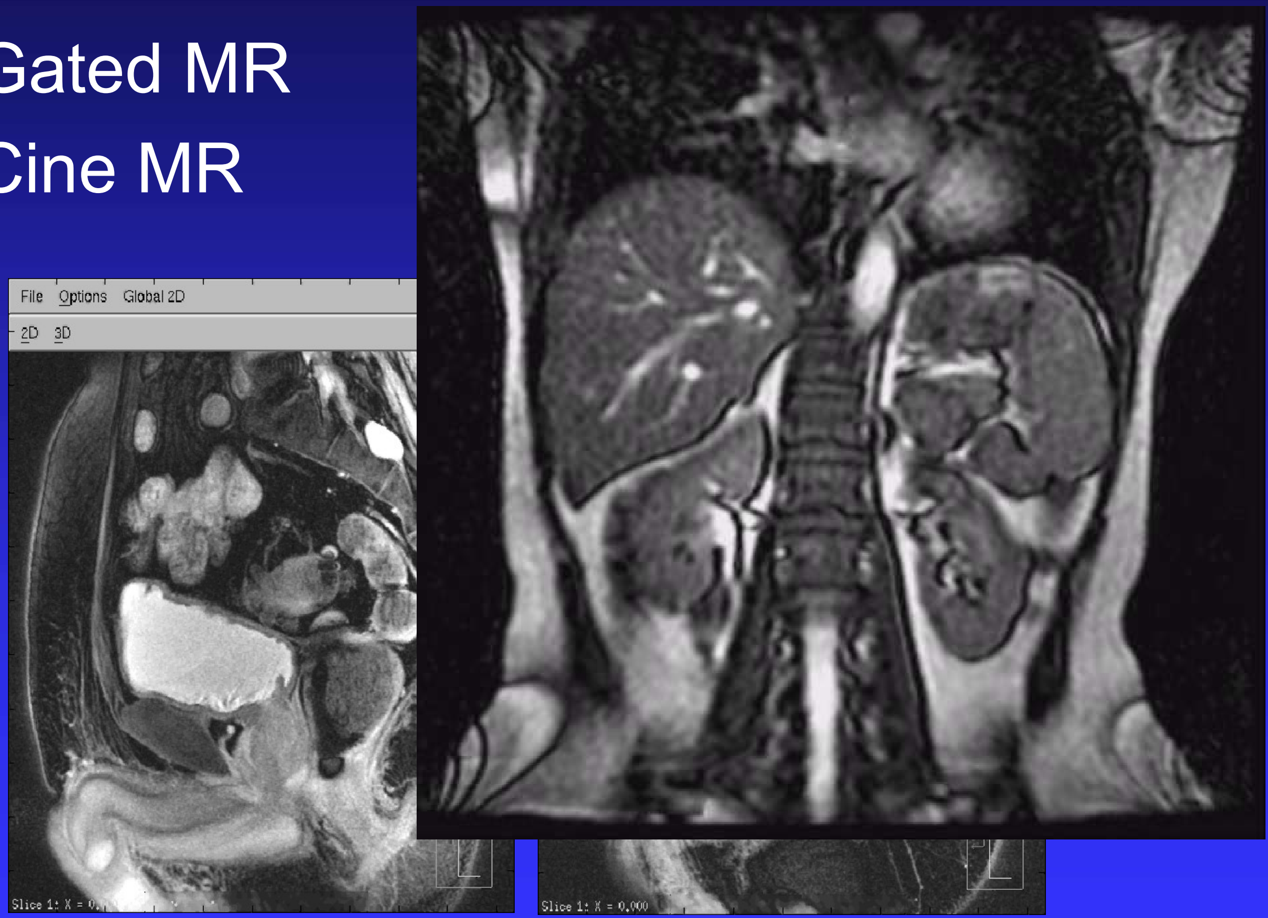
University Medical Center
Utrecht



Monitoring breath hold at inferior side of liver

MRI and time management

- Gated MR
- Cine MR



- Mostly used for motion assessment

Summary

- Motion during imaging causes artifacts and distortions
- Effective ‘shutter time’ of the equipment determines type of artifacts
- Time resolved imaging through retrospective sorting reduces artifacts
- Irregular breathing remains a challenge

Thanks to

- Stine Korreman
- Christoph Schneider
- Vanessa Mexner
- Jochem Wolthaus
- Mathijs Kruis
- Marcel van Herk
- Di Yan
- Paul Keall
- Jochem Wolthaus
- Bas Raaymakers

Rigshospitalet
Department of Oncology,
Section of Radiotherapy

Faculty of Health and Medical Sciences
University of Copenhagen

Technology: 4D-IGRT

Marianne Aznar

What is 4D?

- Usually respiration (not time)
  - ➢ Regular, predictable
- By extension: any intra-fraction motion

How much does it matter?

- Uncertainties from planning:
  - ➢ Catching the tumour in a ”un-representative position”
  - ➢ Under /over-estimating the tumour volume

- Uncertainties from delivery:
  - ➢ Mis-registration on a given day (wrong alignment between beam and average tumour position)
  - ➢ Interplay effect
  - ➢ Anatomical changes

ESTRO School

Three approaches to motion management

- Removing motion
  - breath hold,
  - abdominal compression

- Assessing motion (”passive” strategies)
  - Adapt the treatment strategy **<u>prior</u>** to delivery

- Following motion (”active” strategies)
  - Adapt the treatment strategy **<u>during</u>** delivery

SUPPRESSING/MINIMIZING THE DISPLACEMENT

Abdominal compression

Elekta Stereotactic Body Frame®

Can reduce the motion in CC direction

May introduce interfraction variations in tumour position (Mampuya Med Phys 2013)

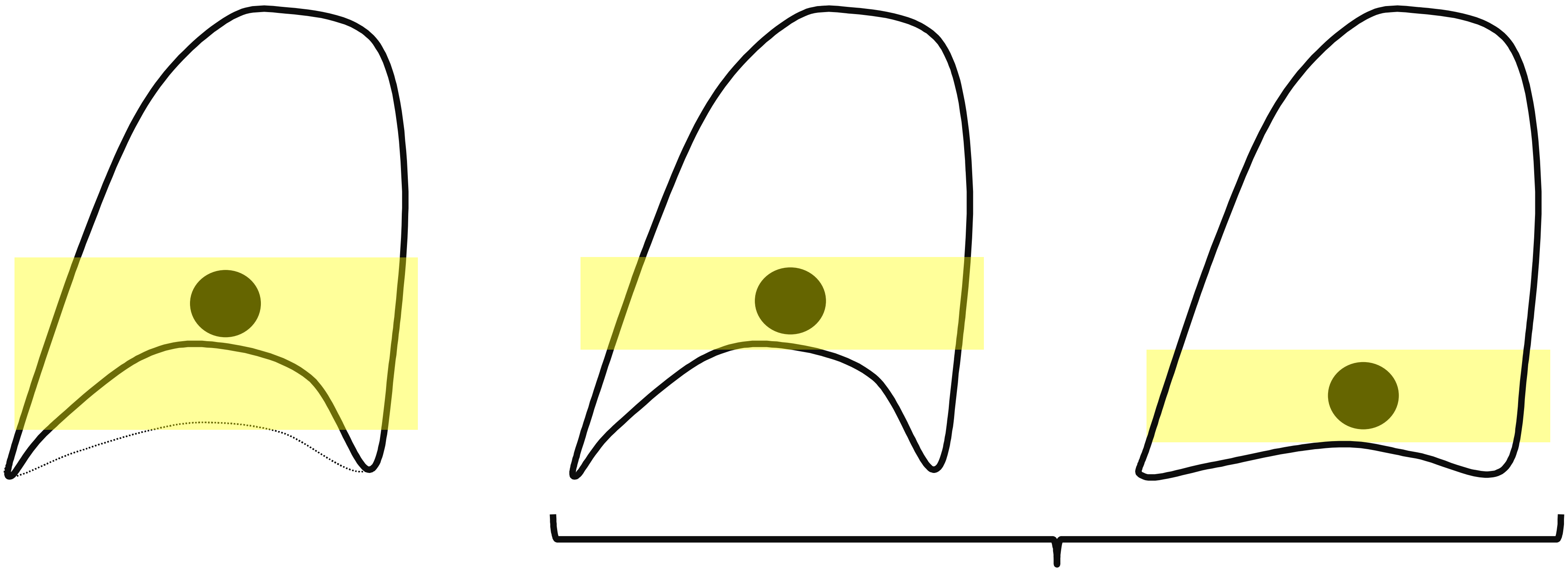
IGRT is still necessary (AAPM TG 101)

Gating / breath hold radiotherapy

Free-breathing

Gating in Exhalation

Breath-hold in Deep Inhalation



In Inspiration Breath-hold:

Lung is inflated and smaller lung volumes are irradiated

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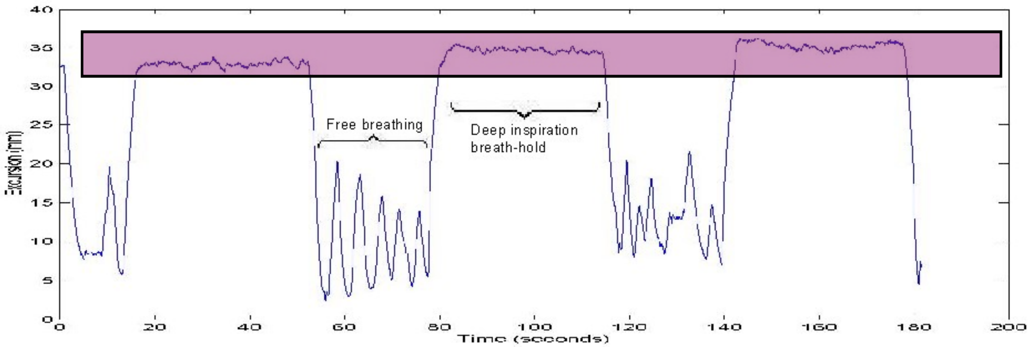
Deep inspiration gating / breath hold

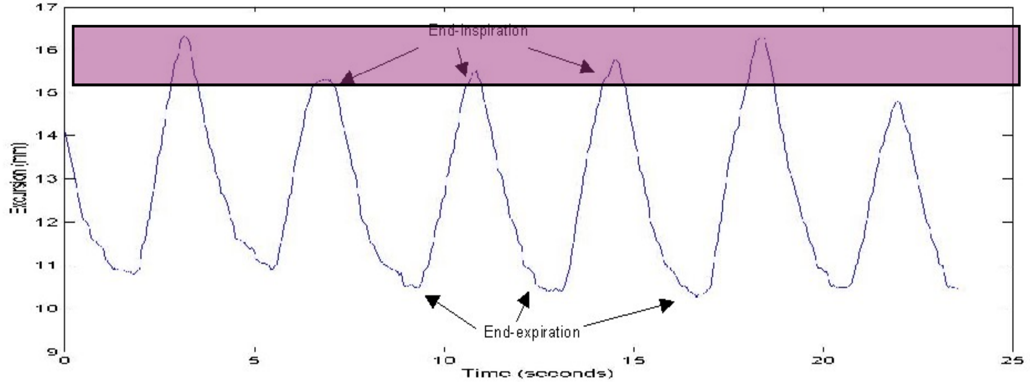
Breath hold (ca 20 sec)



Advantages:

- "natural" breath hold
- Separation between target and OAR
- Same dosimetric benefits

"hyperventilation"



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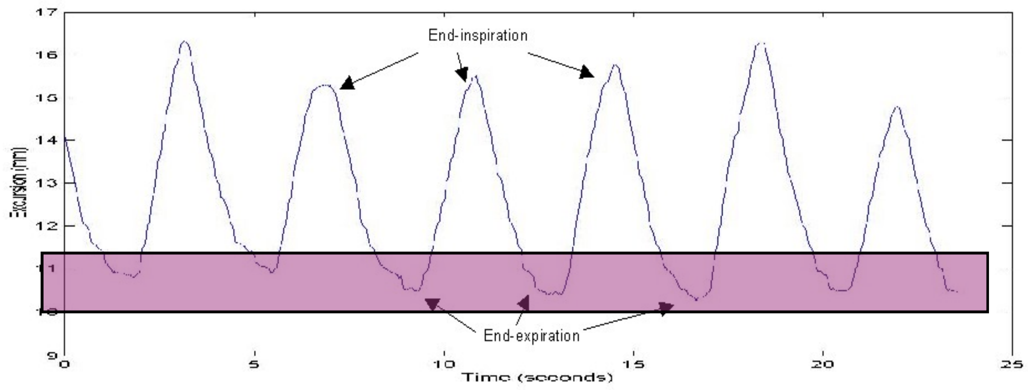
Expiration gating / breath hold

Advantages:

- Most "stable" position in the breathing cycle
- Duty cycle possibly longer than at end inspiration



Most commonly used systems (non-exhaustive)

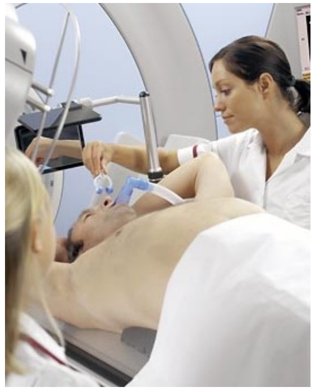
Based on an external signal (e.g. marker, surface)

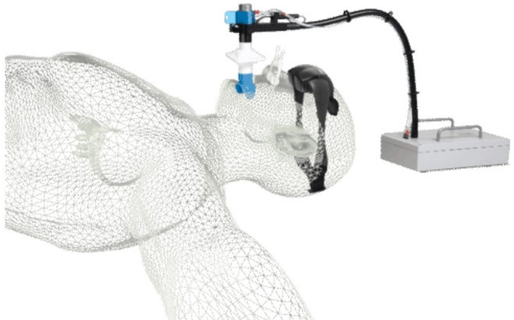
RPM/Gating

VisionRT

Based on expiratory volume

ABC





SpiroDynR'x

The simpler, the better?

Radiotherapy and Oncology 108 (2013) 242–247

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Phase III randomised trial

The UK HeartSpare Study: Randomised evaluation of voluntary deep-inspiratory breath-hold in women undergoing breast radiotherapy

Frederick R. Bartlett [a,*], Ruth M. Colgan [b], Karen Carr [a], Ellen M. Donovan [b], Helen A. McNair [a], Imogen Locke [a], Philip M. Evans [b,c], Joanne S. Haviland [d], John R. Yarnold [a,e], Anna M. Kirby [a]

[a] Department of Academic Radiotherapy, Royal Marsden NHS Foundation Trust; [b] Joint Department of Physics, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton; [c] Centre for Vision, Speech and Signal Processing, Faculty of Engineering and Physical Sciences, University of Surrey, Guildford; [d] Clinical Trials and Statistics Unit (ICR-CTSU); and [e] Division of Radiotherapy and Imaging, Institute of Cancer Research, Sutton, UK

Voluntary breath hold preferred over “forced”

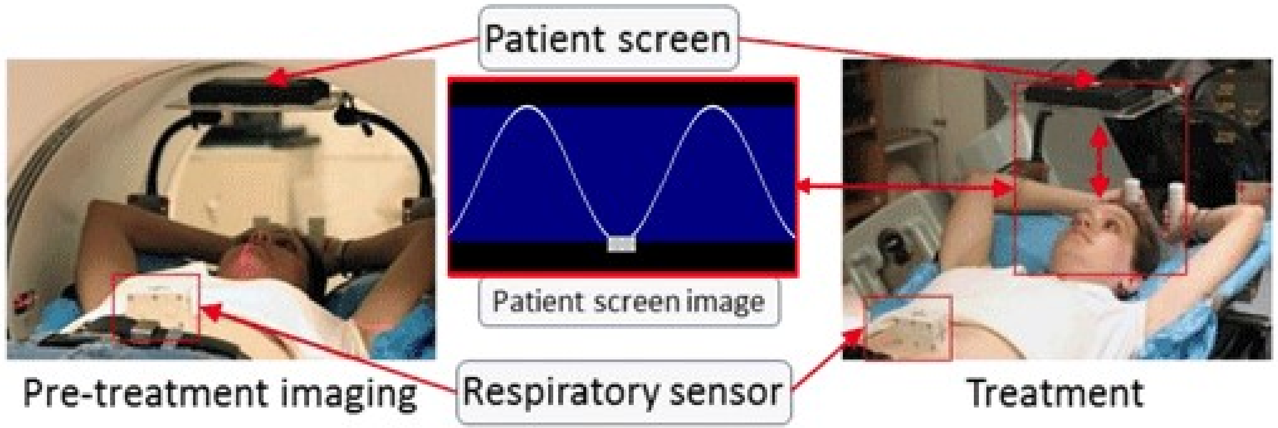
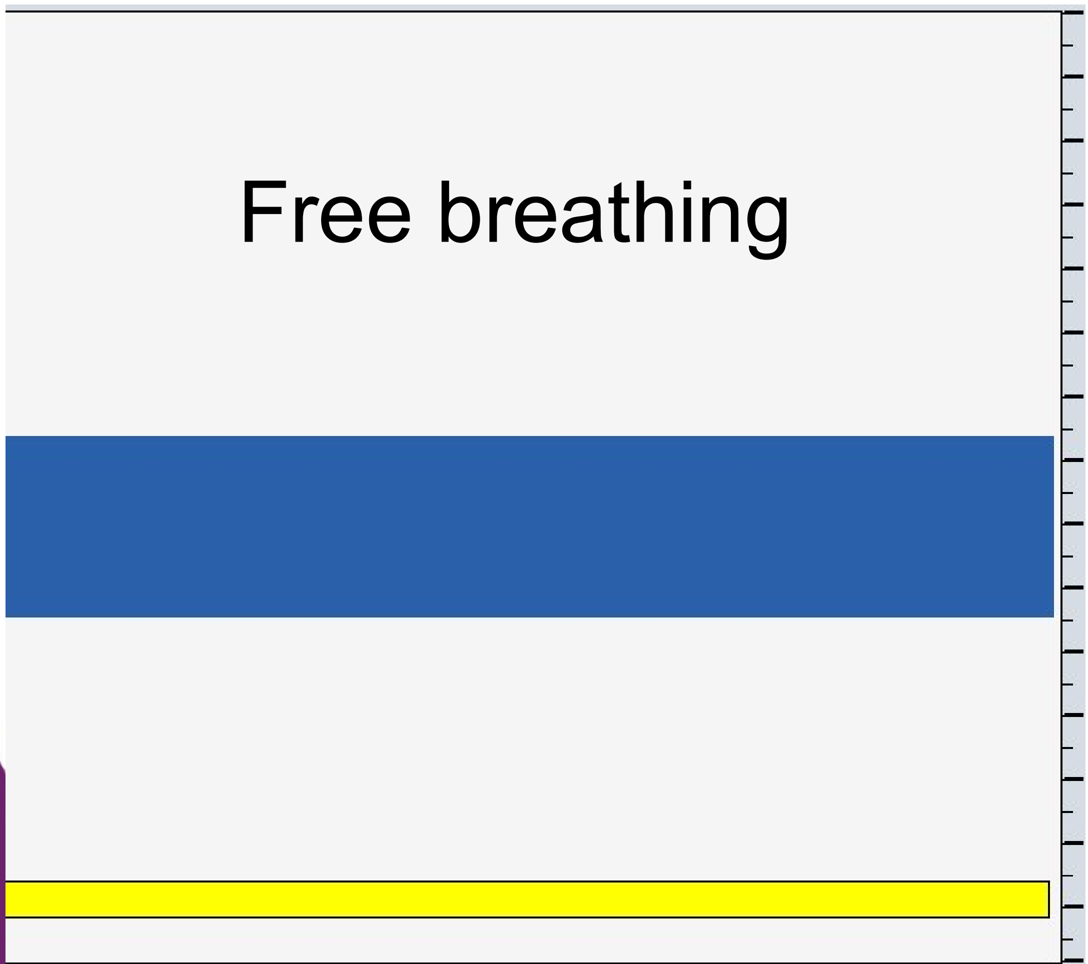


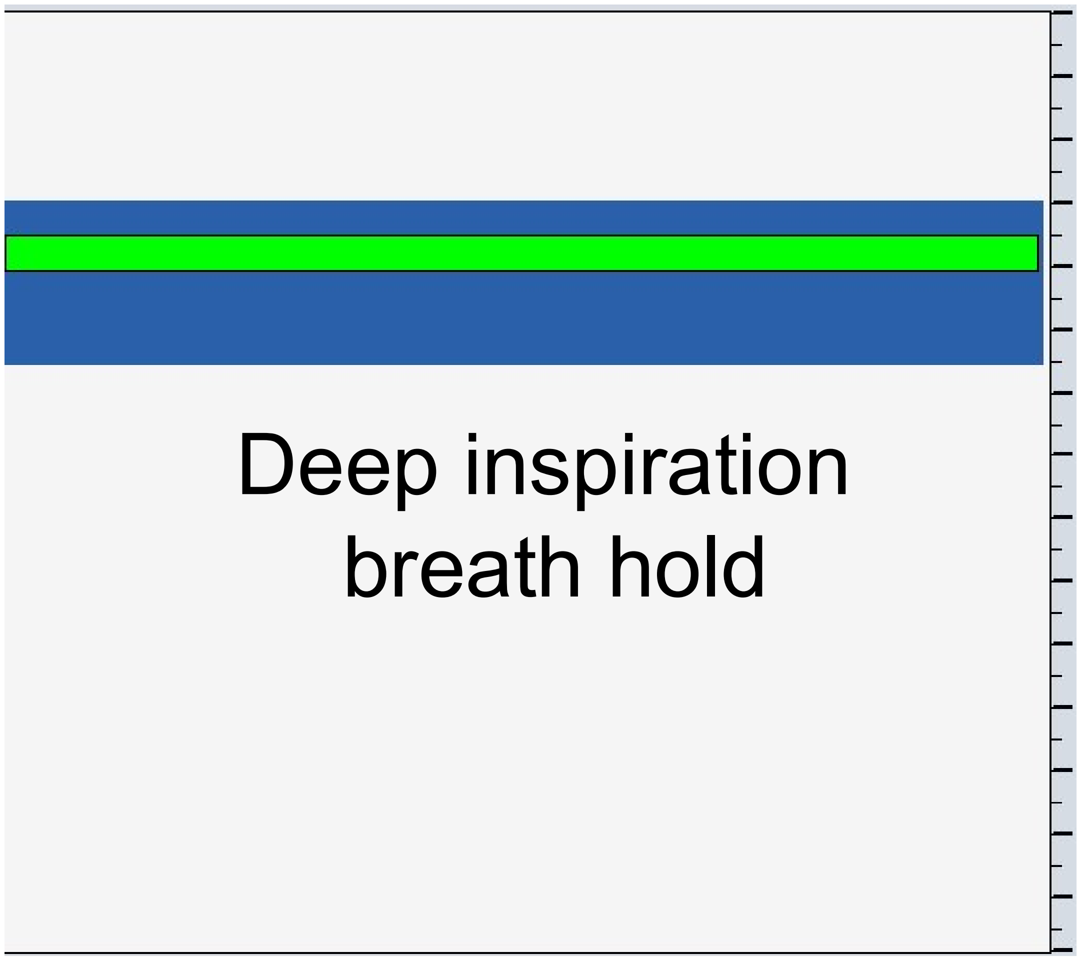
Figure 1. AV biofeedback system. Display screen and marker block on the abdomen shown. The visual display (centre) as seen by the subject (sans arrows) of the AV biofeedback system shows the guiding wave (white curve) and a marker position (marker block) in real time. The AV biofeedback system is compatible for both imaging (left) and treatment (right) environments.

Paul Keall
Sydney

Audio/visual Coaching:

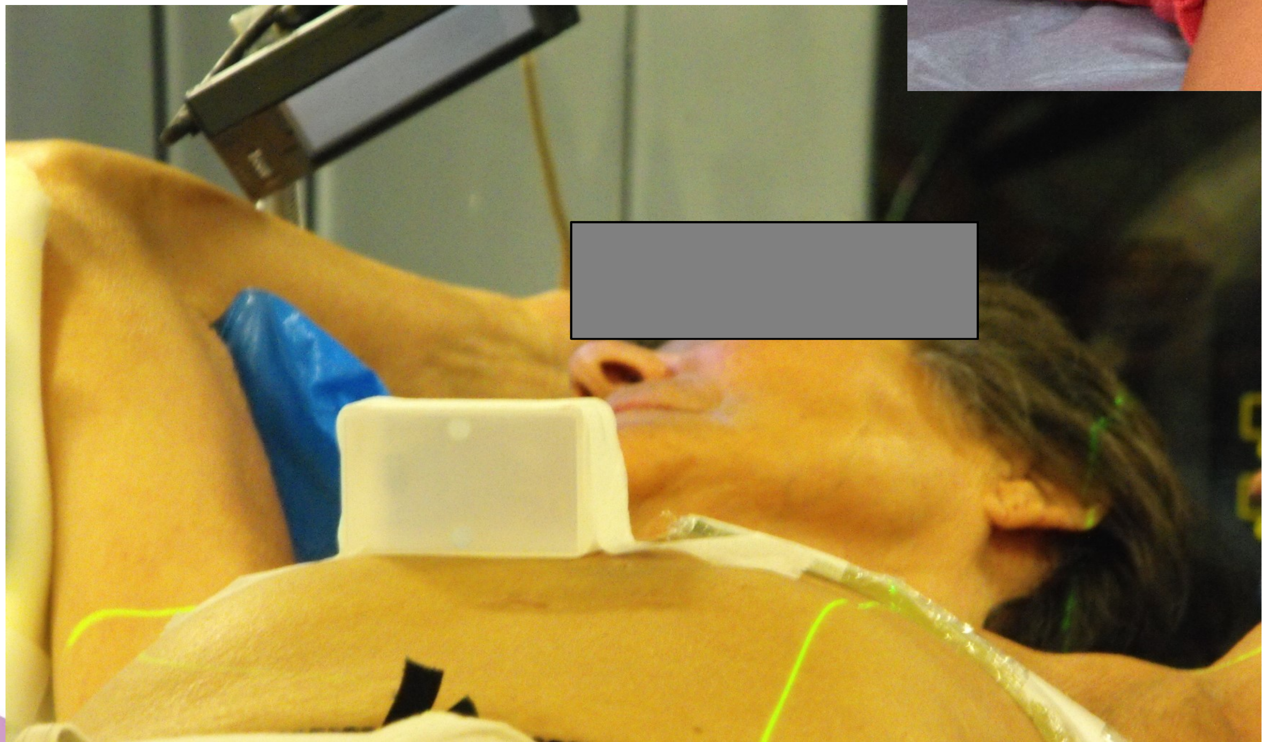
- Can improve performance / reproducibility
- Risk of having the patient “over-perform”
- Visual may be faster/more convenient





Visual guidance:

- Scanner
- linac



Methods

All images in DIBH throughout the treatment course

Example: Hodgkin Lymphoma

Staging PET/CT → Chemotherapy (4-8 cycles) → Planning CT or PET/CT → Verification images at the linac

2-3 months

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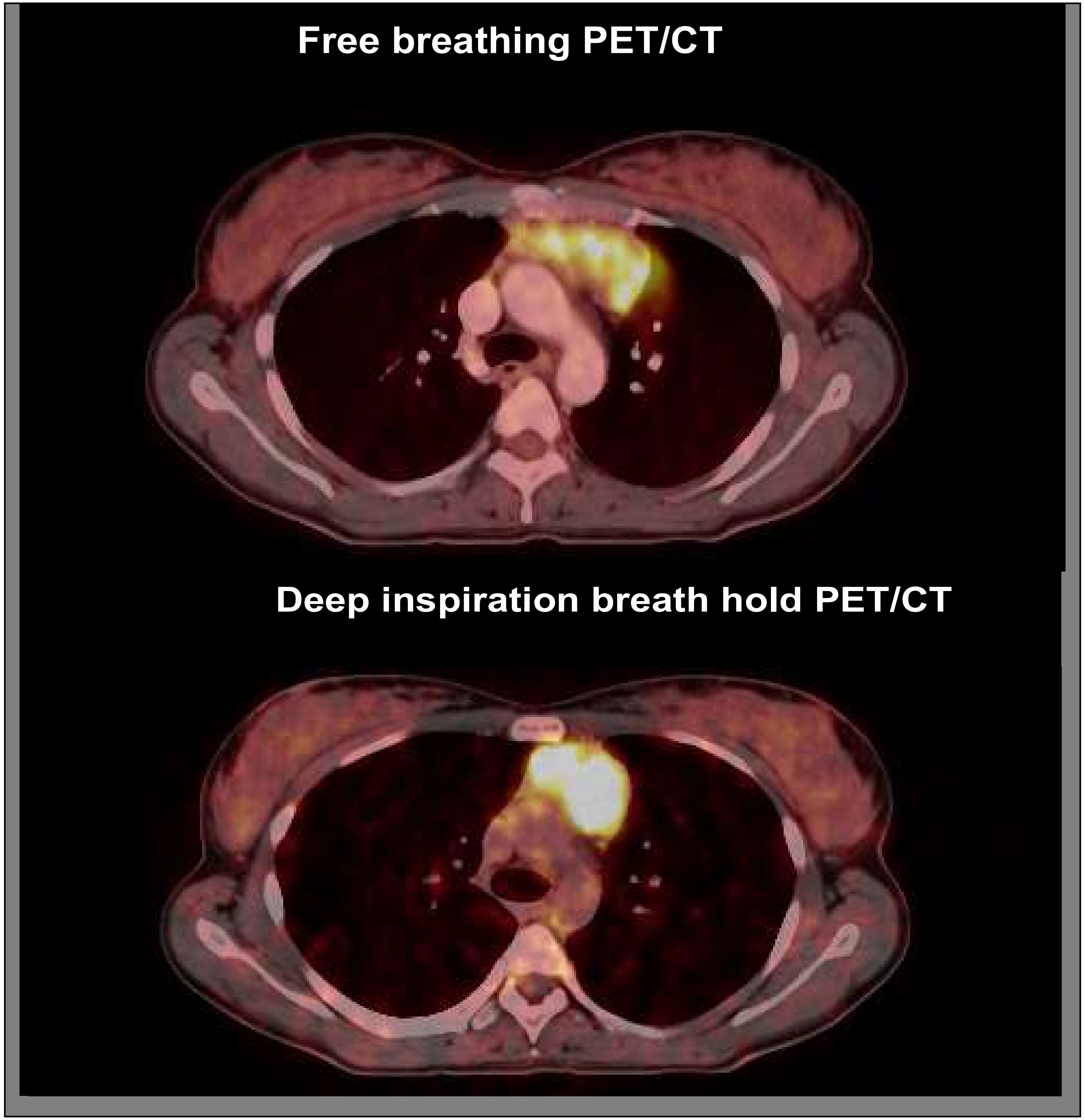
Results: reduced respiration artifacts



How much can these methods facilitate margin reduction?

1. breath hold

Dawson et al, IJROBP 2001

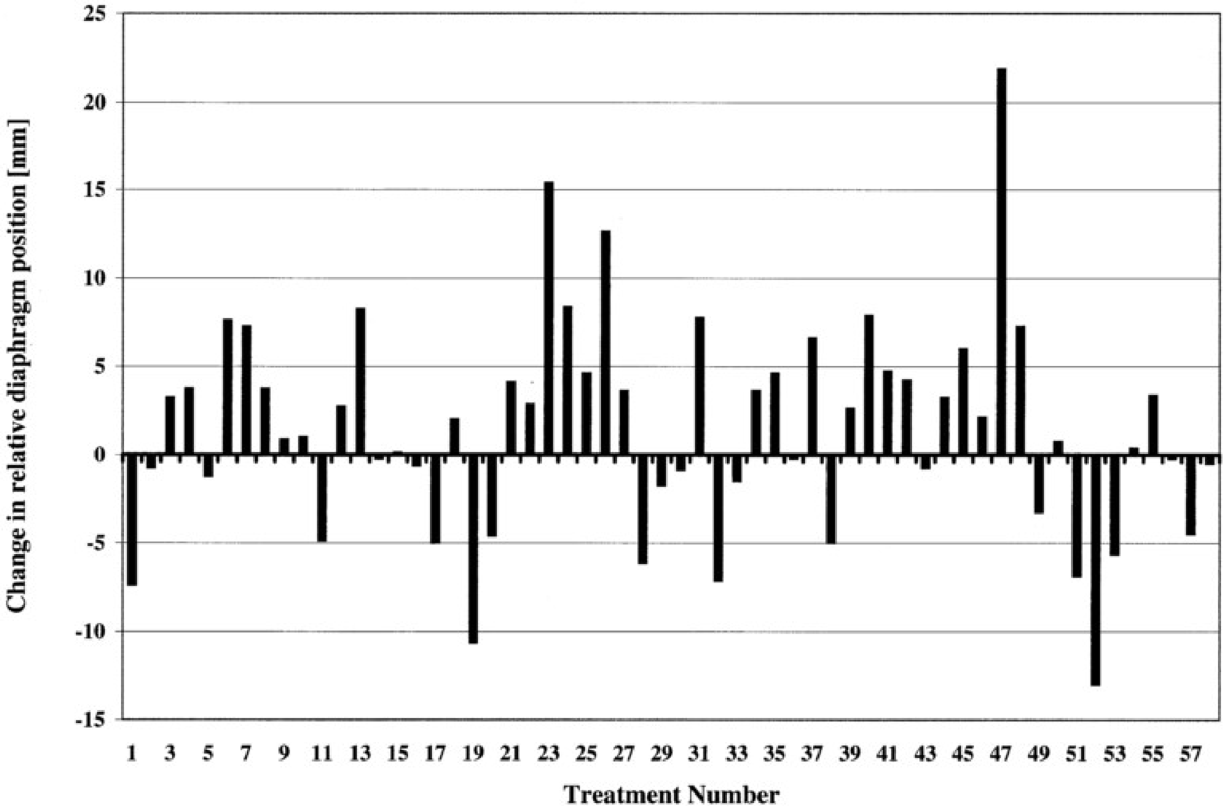


Fig. 6. An example of the interfraction variability of diaphragm-skeleton position for 1 patient (Patient 8) ove radiation course. Number of sequential treatments is displayed on *x* axis.

- Variation in position between the diaphragm and bony structures for the same inhale volume
- Up to 2 cm interfraction variation

Cheung et al, IJROBP 2003, 10 patients

field for a given breath hold. As such, we do not advocate reducing the daily PTV margin with the use of ABC breath hold for the treatment of peripheral lung tumors.

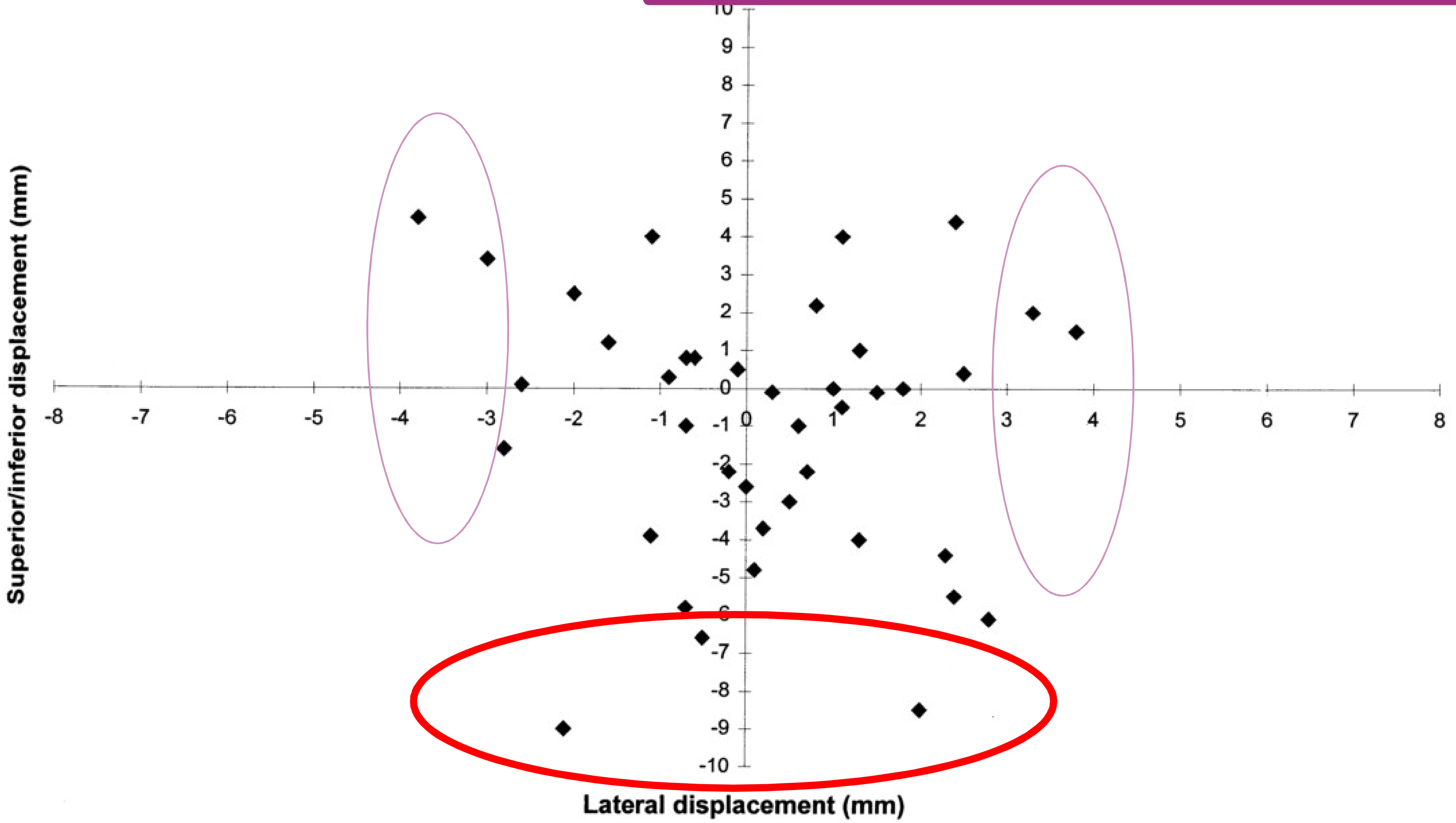


Fig. 1. Inter–breath hold displacements of daily GTV positions with ABC inspiration breath hold for all patients in the superior-inferior vs. lateral directions.

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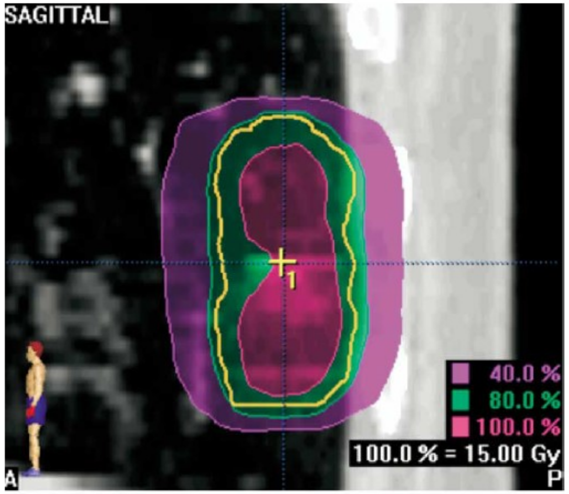
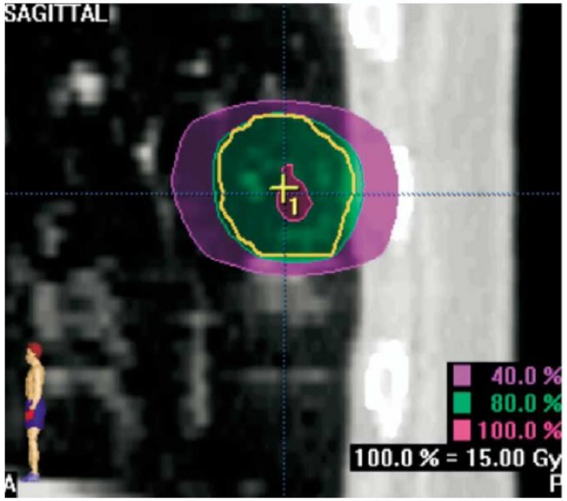
How much can these methods facilitate margin reduction?

2. gating

Gating and margin reduction

BENEFIT OF RESPIRATION-GATED STEREOTACTIC RADIOTHERAPY FOR STAGE I LUNG CANCER: AN ANALYSIS OF 4DCT DATASETS





Reduction of motion amplitude
from 8.5mm to 1.4mm

Reduction of PTV volume by 45%

Duty cycle 30 %

Underberg IJROBP 2005

But.. This is a planning study !!!

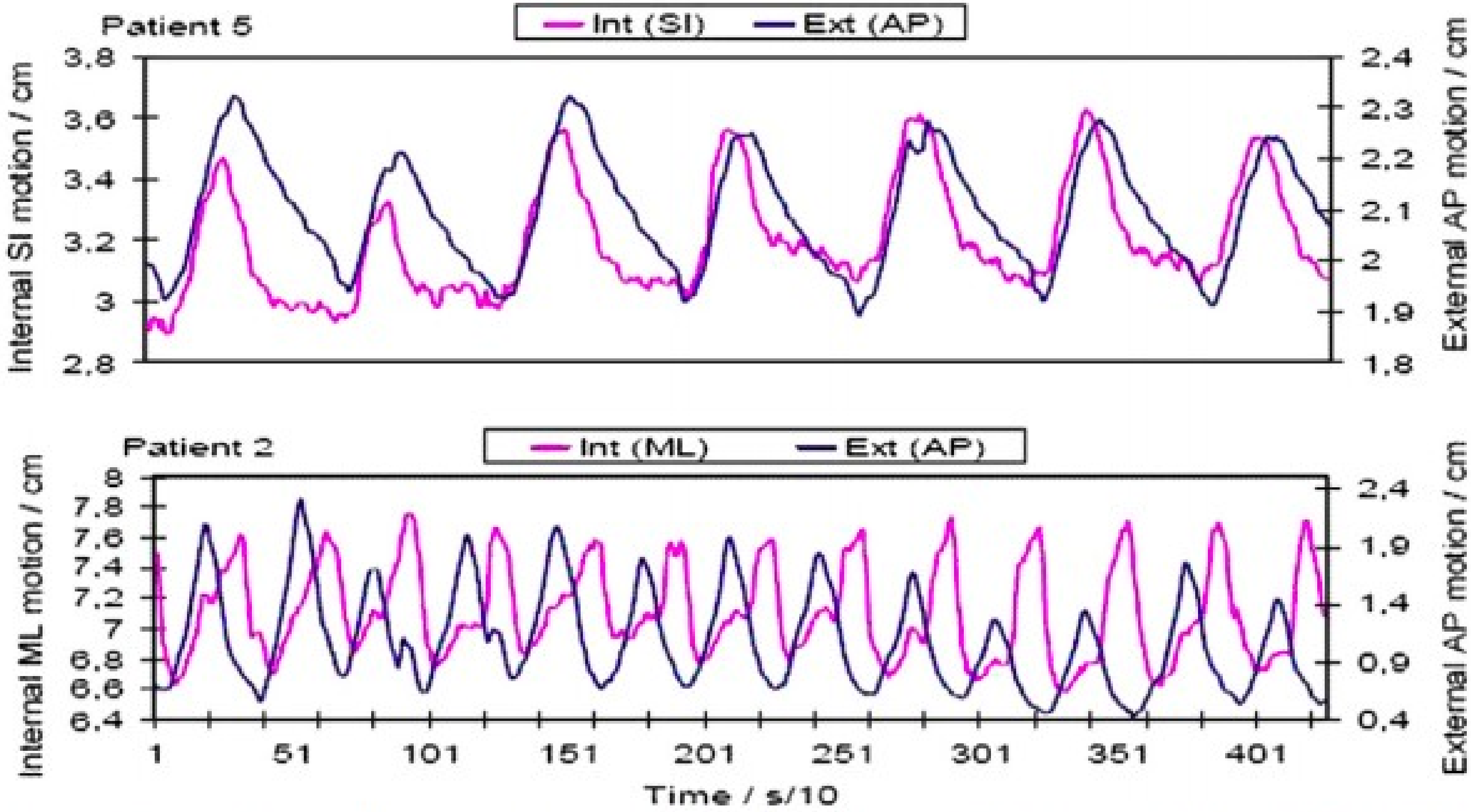


Fig. 2. Three examples of synchronously measured external optical marker and internal gold marker positions for three different patie
the Stanford protocol. The magenta curves are the internal marker positions and the blue curves are the external marker positions.

reminder

- Gating can not reduce margins without image verification of the tumour position

Korreman et al RO 2008

Can there be a good surrogate for the position of a lung/liver tumour?

- No surrogate is so good that you can avoid IGRT

- Solution 1: use large margins (approx equal to free breathing)

  - Starkschall et al IJROBP 2011: ***treatment using methods designed to mitigate the effects of respiratory motion (breath hold or gating) with setup based on landmarks other than the actual tumour position requires margin of 0.7 to 0.8 cm***

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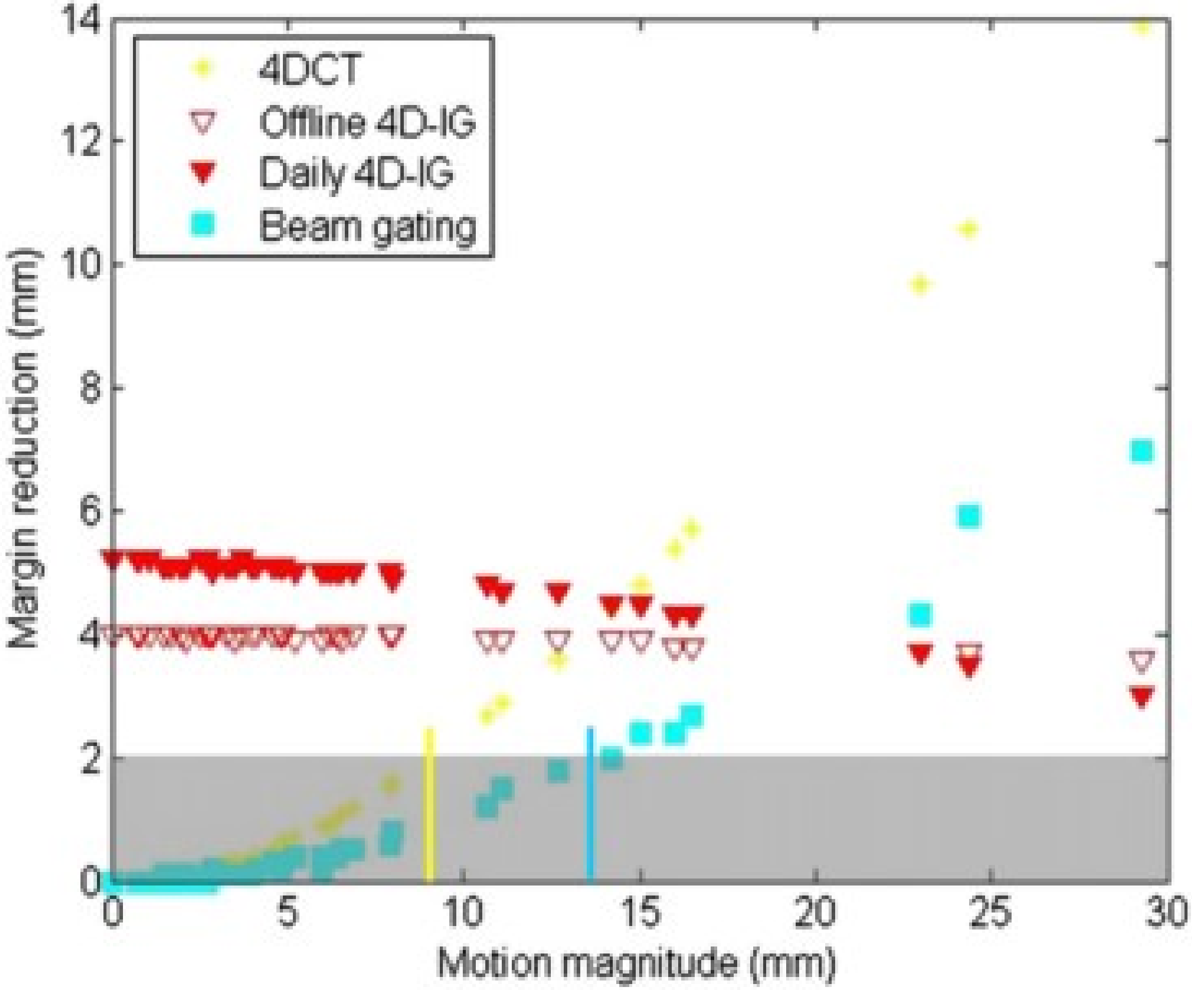
Can there be a good external surrogate for the position of a lung/liver tumour?

- No surrogate is good enough
- Solution 1: use large margins (approx equal to free breathing)
- Solution 2: image the tumour position daily with respiration-correlated (4D) IGRT
  - 4D-CBCT for gated treatment
  - Breath hold CBCT
  - 2D + markers in the tumour



Soft-tissue (or marker based) IGRT is the most efficient

(includes fluroscopy, 3D or 4D CBCT)

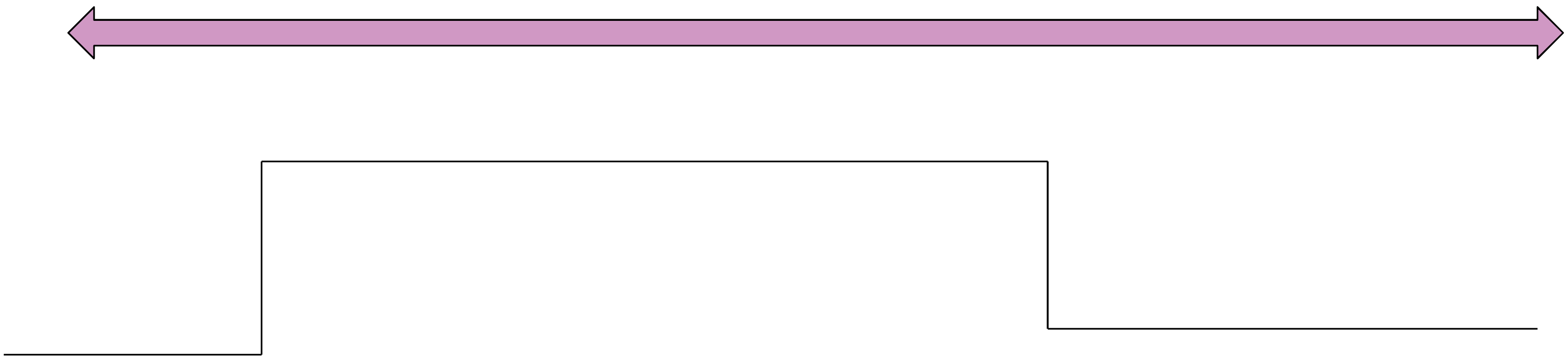
Korreman et al IJROBP2012

How much can these strategies reduce margins?

Gated/breath hold IGRT

Planar : markers or tumour shadow (if lucky)

CBCT acquisition



Single breath hold CBCT

Zongh Radiat Oncol 2014

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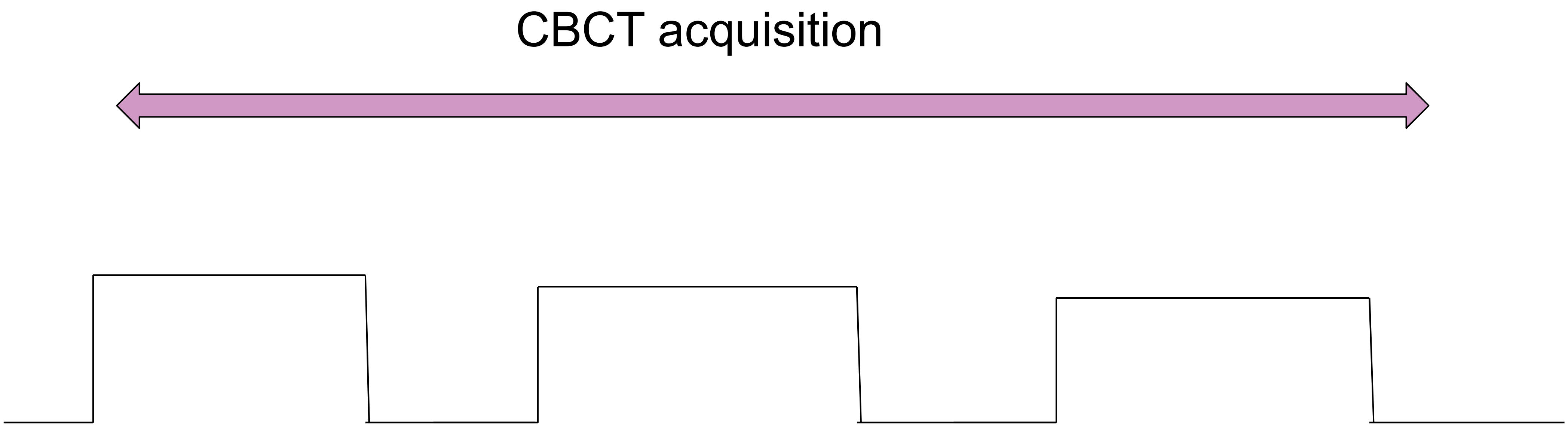
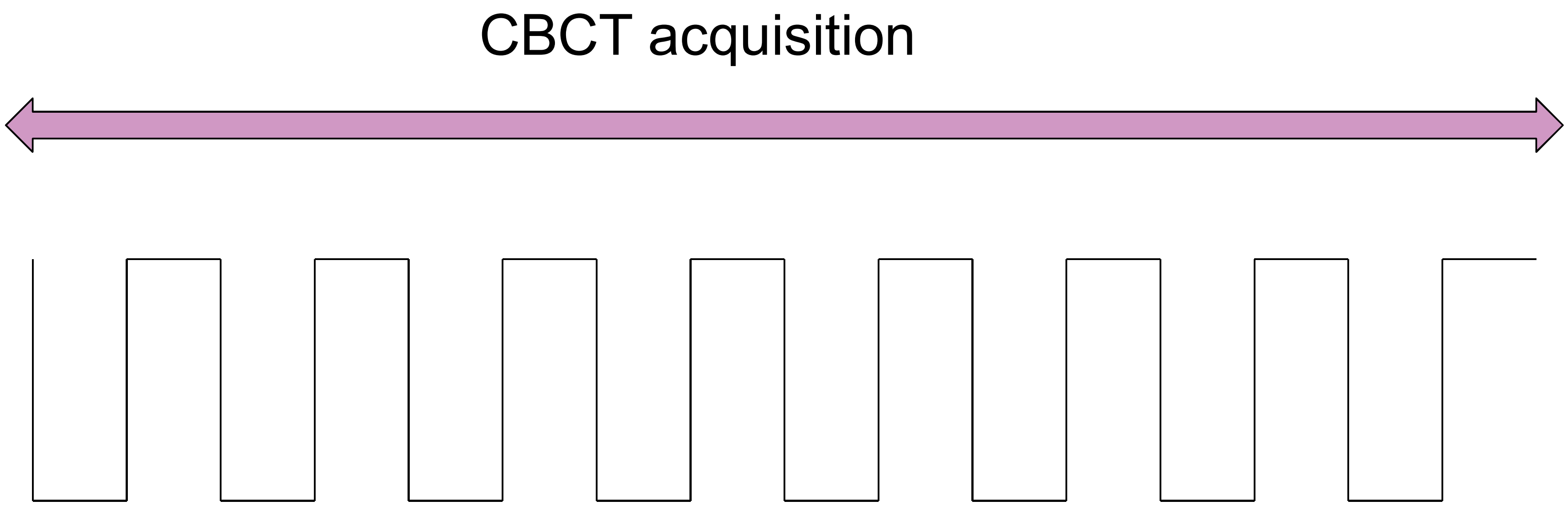
Gated/breath hold IGRT



“multiple breath-hold” CBCT

Boda Heggemann et al RO 2011

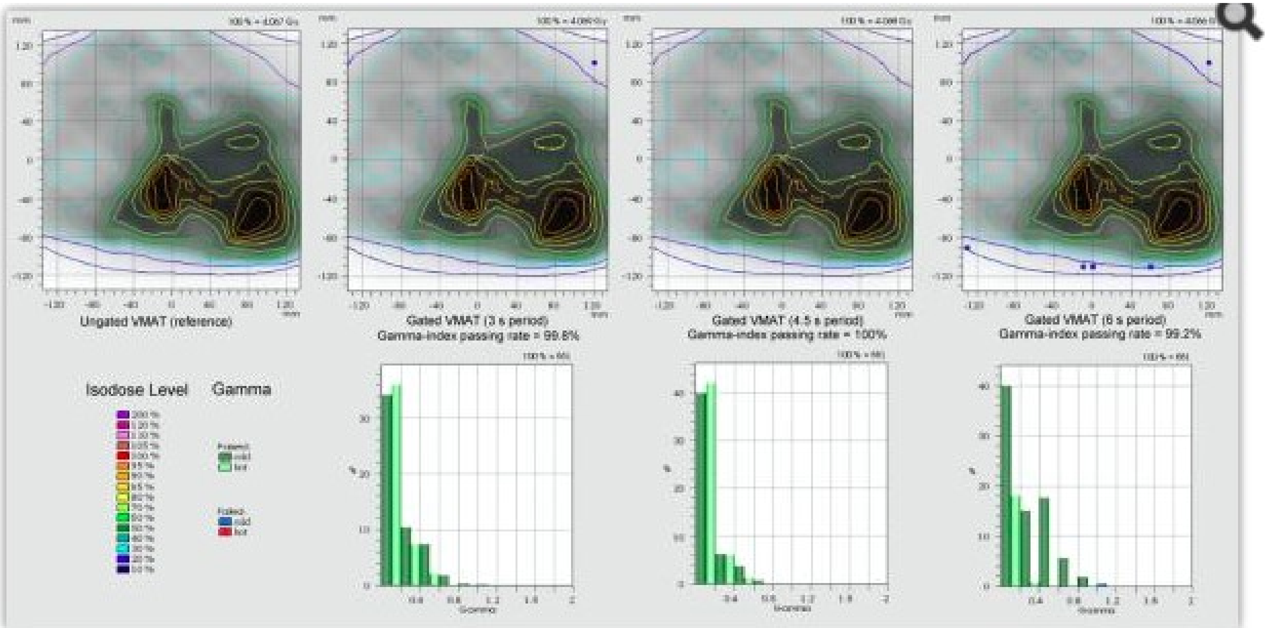
Gated/breath hold IGRT



Kincaid et al RO 2013 "gated CBCT"
Cooper et al Med Phys 2013

Not in clinical practice

QA of treatment delivery for gated/breath hold



Gamma-index analyses in the #1 lung patient case with the ungated PTW-Seven29 measurement as reference for the Seven29 measurements of gated VMAT deliveries under the three simulated respiratory periods, i.e., 3, 4.5 and 6 s.

Qian et al PMB 2011

Check the mechanical uncertainties associated with frequent gantry/MLC interrruptions

Take home message
Gating/breath hold delivery

- All external surrogates are suboptimal

- <u>No *a priori* margin reduction from breath hold or gating</u>

- Respiration-correlated IGRT is necessary to limit interfraction uncertainties

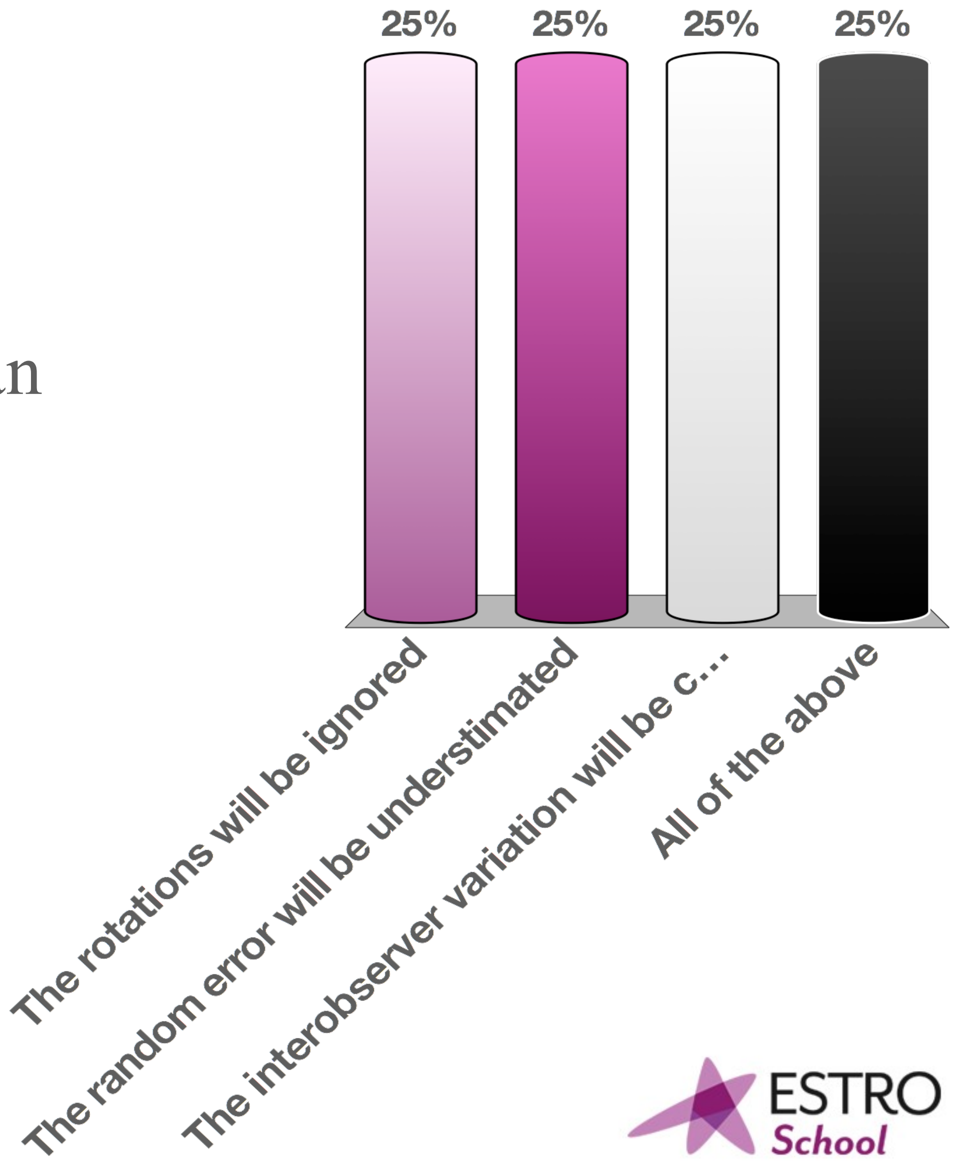
Do you use breath hold / gating strategies?

A. No

B. We're implementing them and we pinky-swear that we won't reduce our margins without solid data that we can safely do so.

C. We're using them and have investigated which margins we could safely use.

D. We've reduced our margins and as Frankie said we did our way



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ASSESSING THE DISPLACEMENT OF THE TUMOUR

After the 4D CT acquisition…

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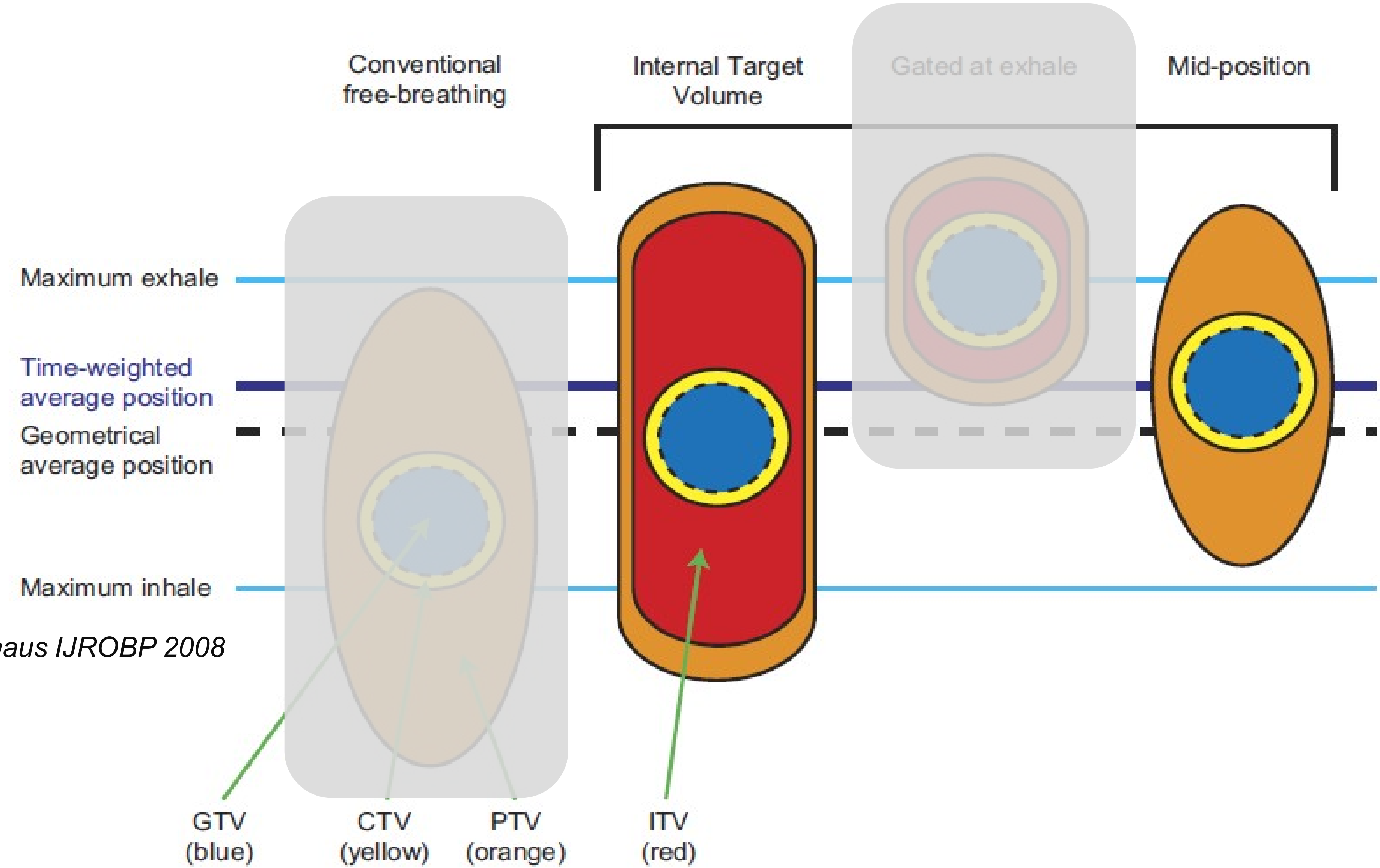
2 main strategies



Wolthaus IJROBP 2008

ITV	**MidVentilation**
• Straightforward (?)	• Counterintuitive (?)
• Physician time (contouring)	• Physicist time (choice of phase + margin calculation)
• Coverage is ensured	• Smaller lung volume irradiated
• Larger volumes of lung irradiated if large motion	
• Needs an elaborate 4D viewer?	• Requires special software?

Do not delay the introduction/routine use of 4D-CT because of this issue!

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Commercial/pragmatic solution for the midventilation

- Scripting within the TPS
- Third part software (home made)
- Several companies are working on a solution

Method	Geometric error [mm]
1: Semi-automatic method	1.4 ± 0.7
2: Visual method	1.4 ± 0.7
3: Reference method	1.1 ± 0.8

Table 3: Mean geometric error ± SD for the evaluated methods and the reference method [mm].

Nygaard DE et al, Acta Oncol 2013

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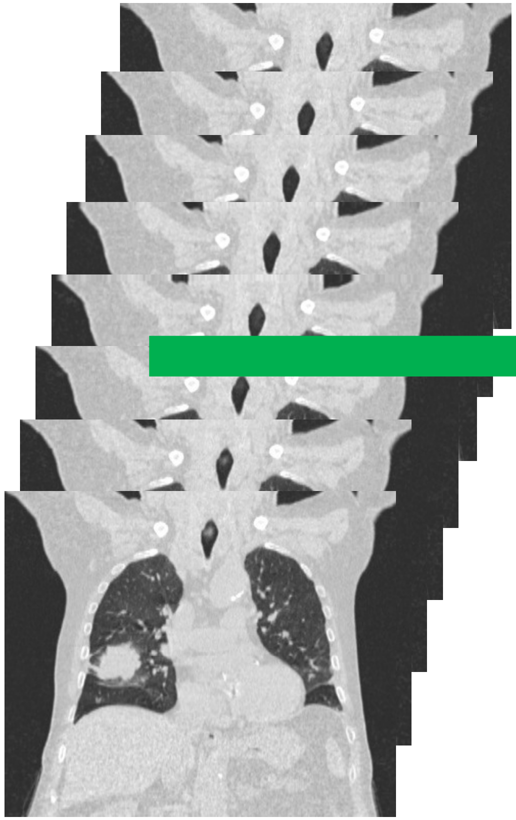
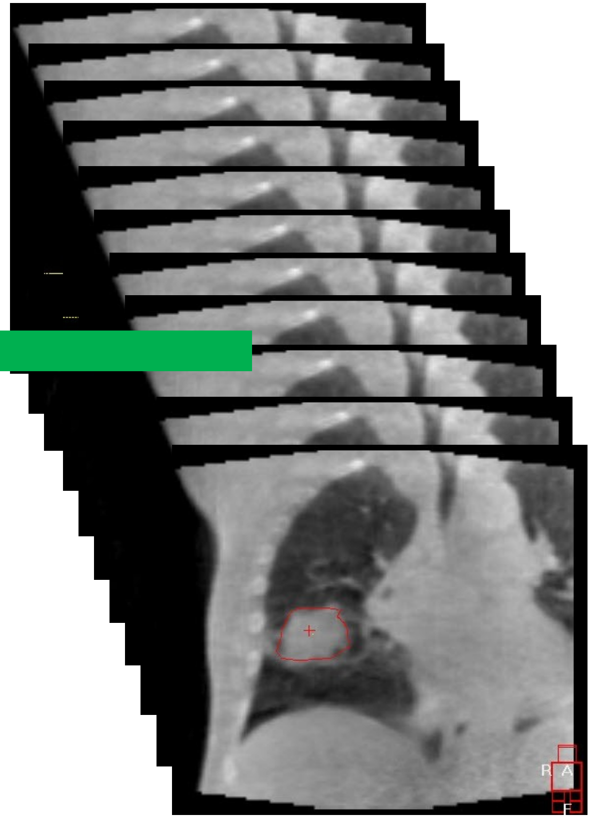
In-room image guidance

Treatment planning:
Reference Image

Treatment delivery:
Verification Image



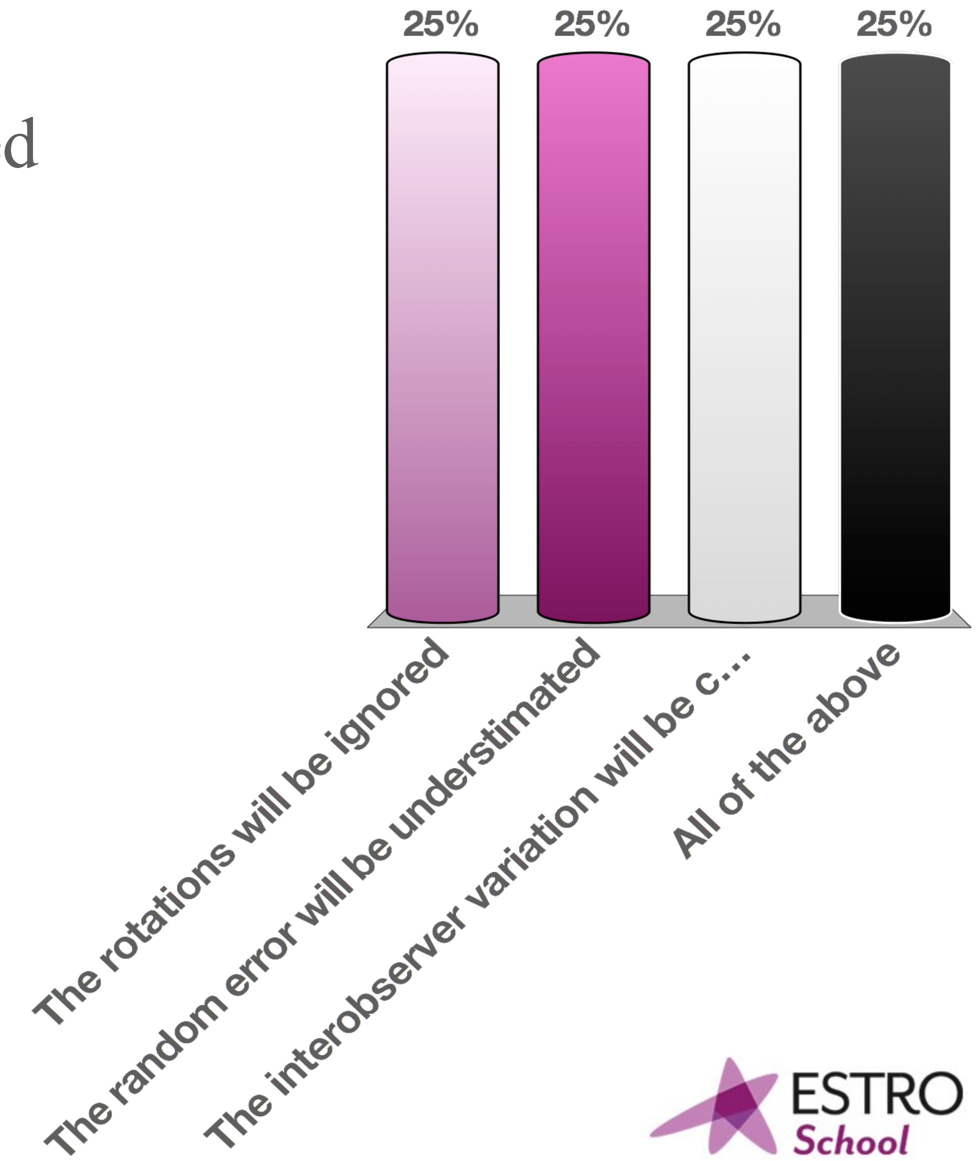
4D
IGRT



Delivery in free breathing and image verification : 3D CBCT will be blurry

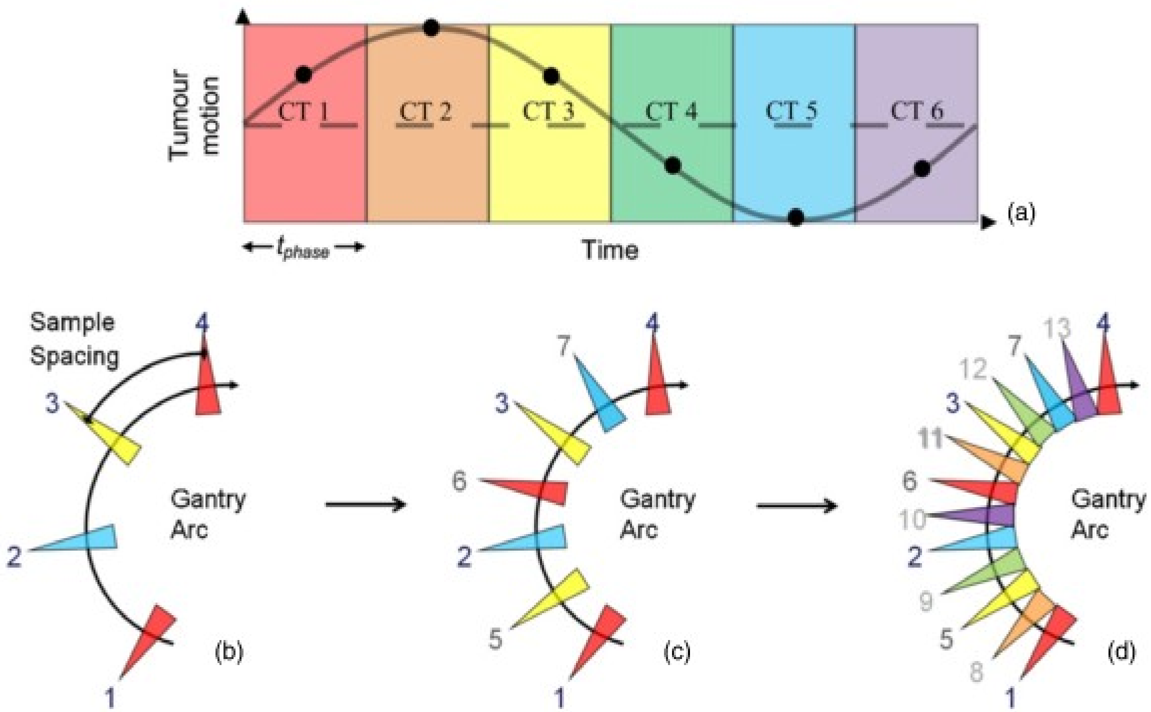
What is most likely to occur when manually registering a contour to a ”blurry” structure?

A. The rotations will be ignored
B. The random error will be understated
C. The interobserver variation will be considerable
D. All of the above



Integrating 4D CT information directly into treatment planning

- Could make treatment faster (Ong et al 2010, 2012,Holt et al 2011, Brock et al 2012).
- Dosimetric results like gated VMAT, but with a time efficiency like 3D VMAT.

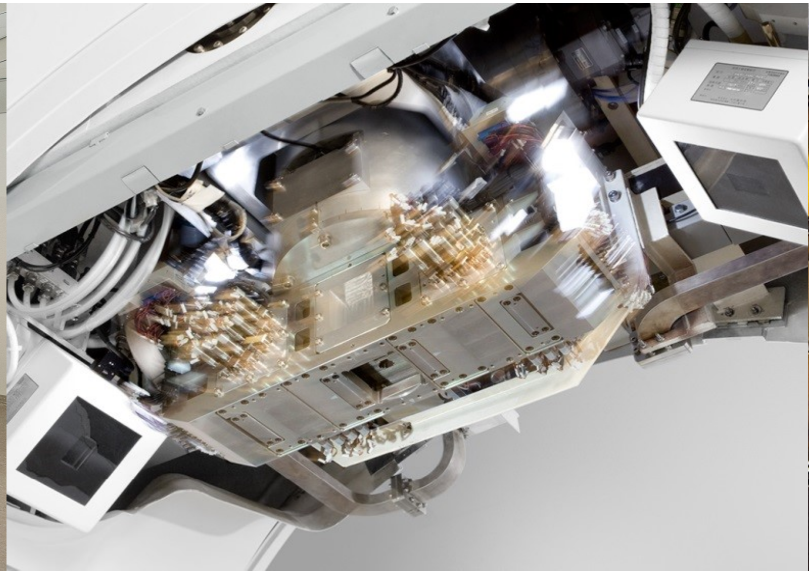


Chin at al PMB 2013

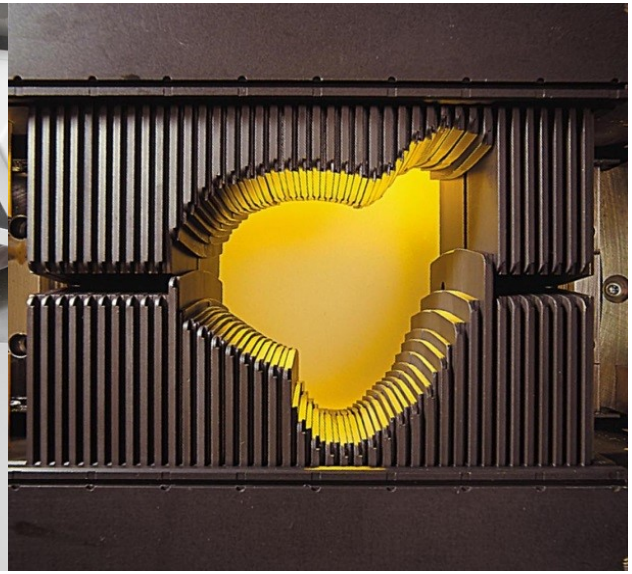
QA of treatment delivery for free-breathing treatment

- How do you measure the dose actually received by the tumour?
- How do you control the consistency of the patient’s breathing pattern inter/intra-fraction ?
- Should one use respiration monitoring systems during treatment?

Robot arm and linear accelerator



Gimballed linear accelerator



Breathing MLCs

FOLLOWING MOTION

Courtesy of Dirk Verellen,
free university Brussels
Mischa Hoogeman,
Erasmus, Rotterdam

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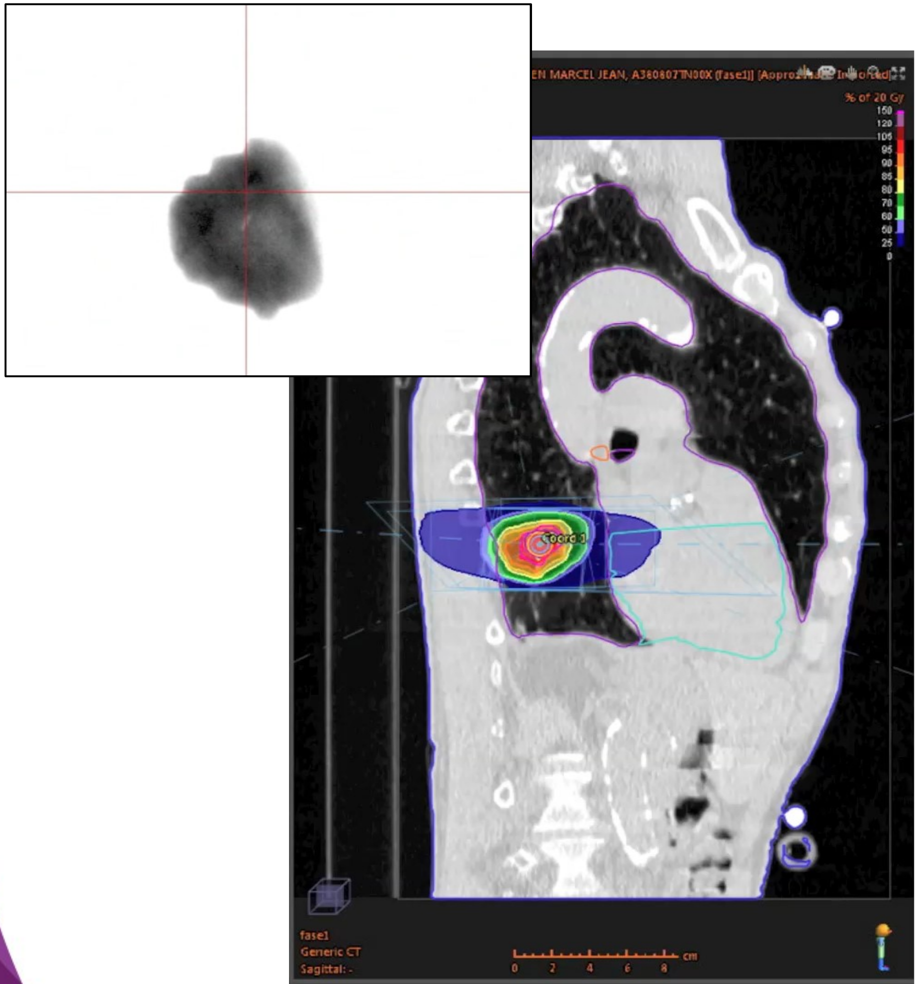
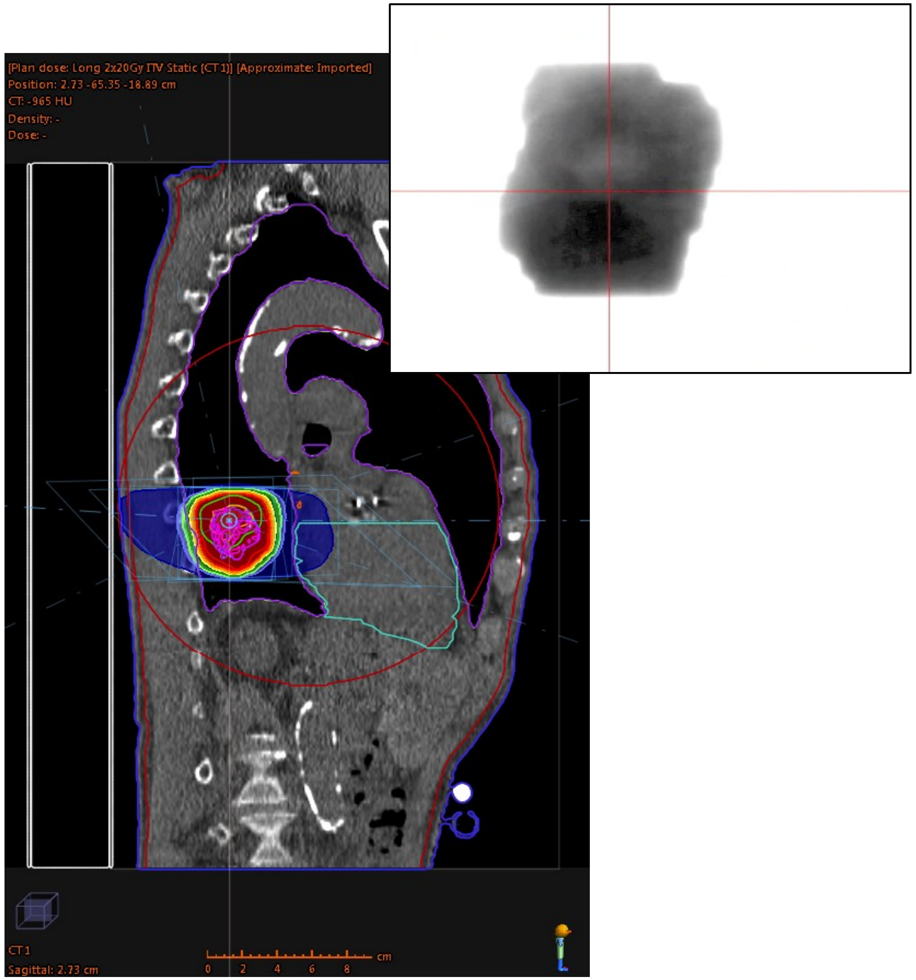
Tracking: "sticky" dose





D. Verellen

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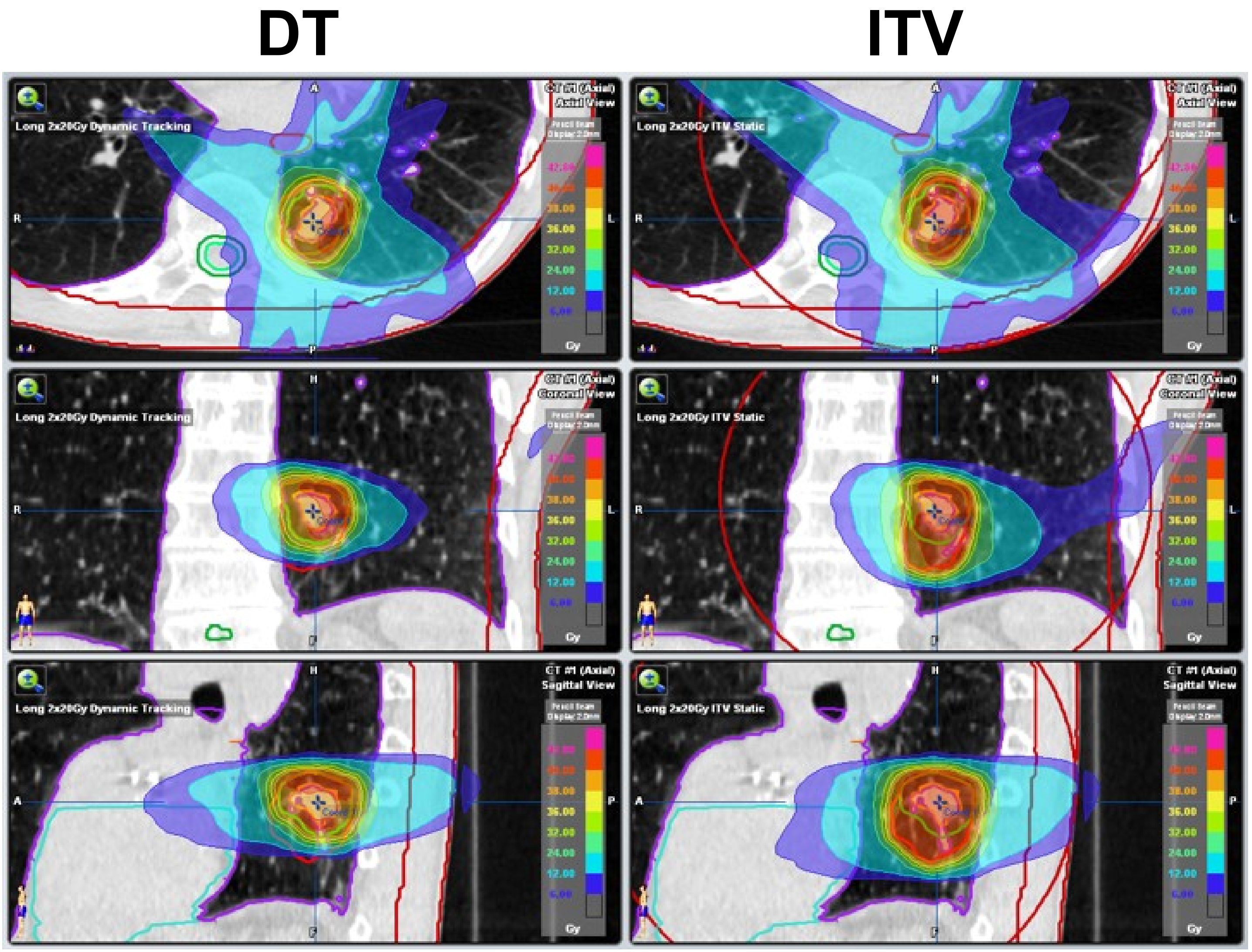
PTV volume reduction

	Site	PTV volume reduction [%]
Patient 1	lung	**-39,50**
Patient 2	lung	-37,59
Patient 3	liver	-16,21
Patient 4	liver	-46,00
Patient 5	liver	-37,75
Patient 6	lung	-52,72
Patient 7	lung	-44,37
Patient 8	lung	-29,47
Average		**-38,0**



Dynamic tracking patients @ UZ Brussel (2012-2013)

D. Verellen

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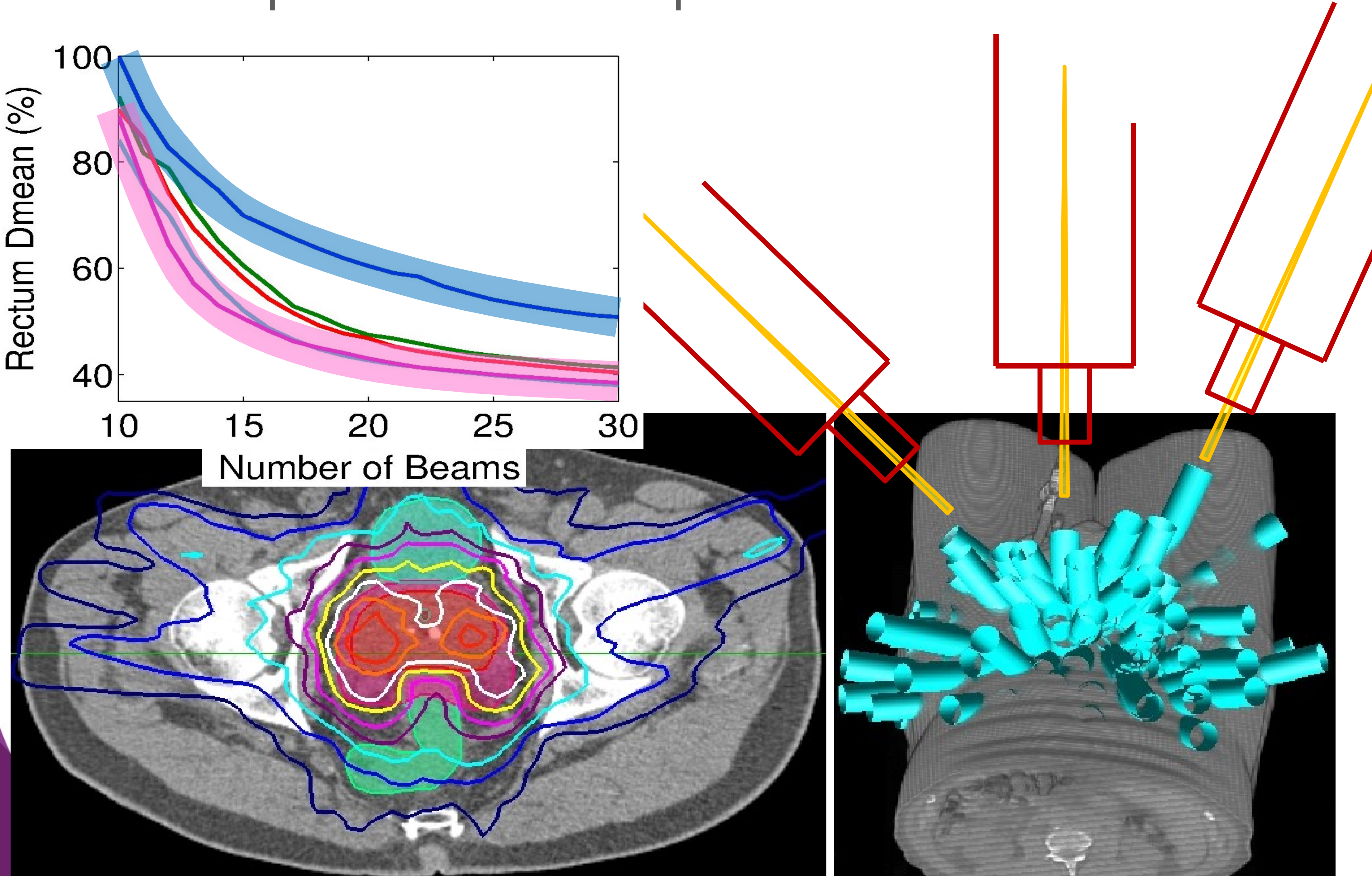
Cyberknife

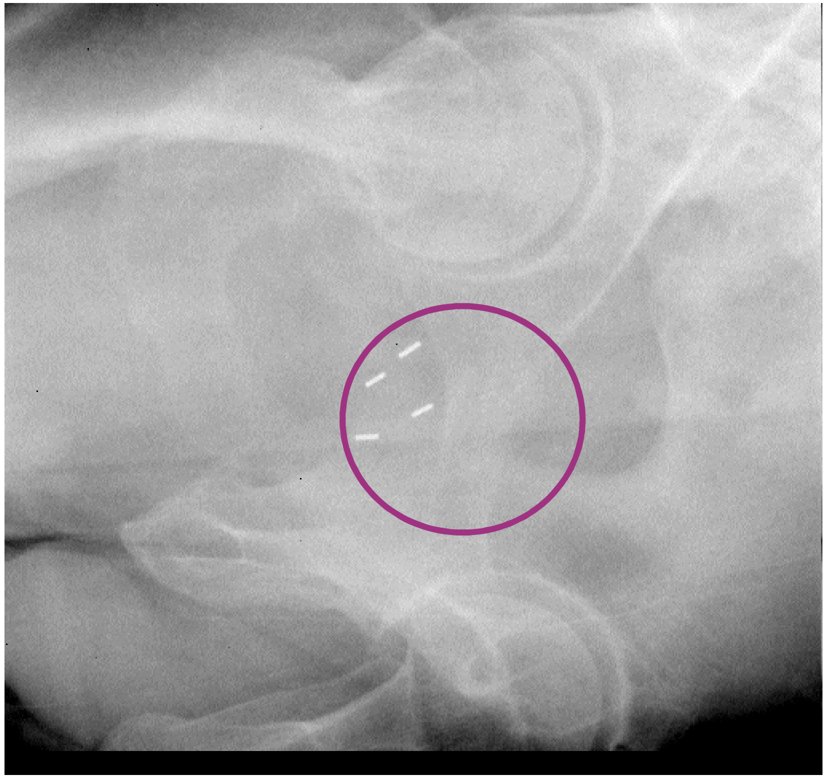
X-ray Sources
Synchrony
Camera
Linear
Accelerator
Robotic
Arm
Robotic
Treatment Couch
Image Detectors

Coplanar vs non-coplanar beams



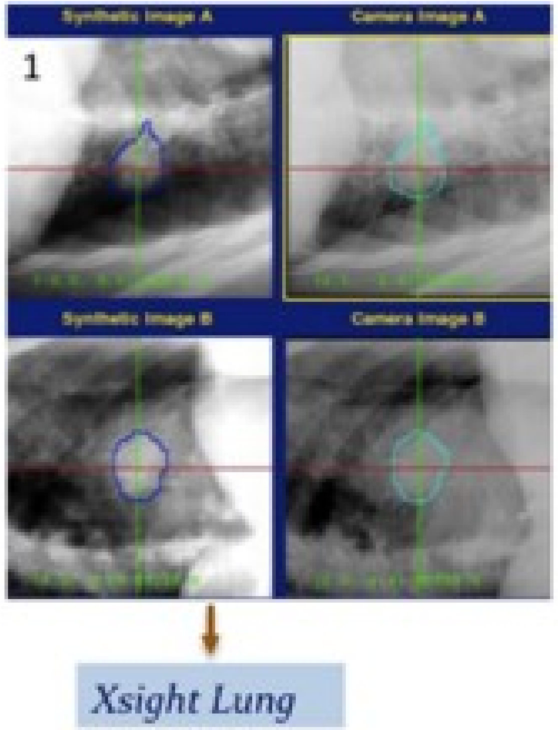
What can you track ?

- Markers



Bone: spine, skull,…

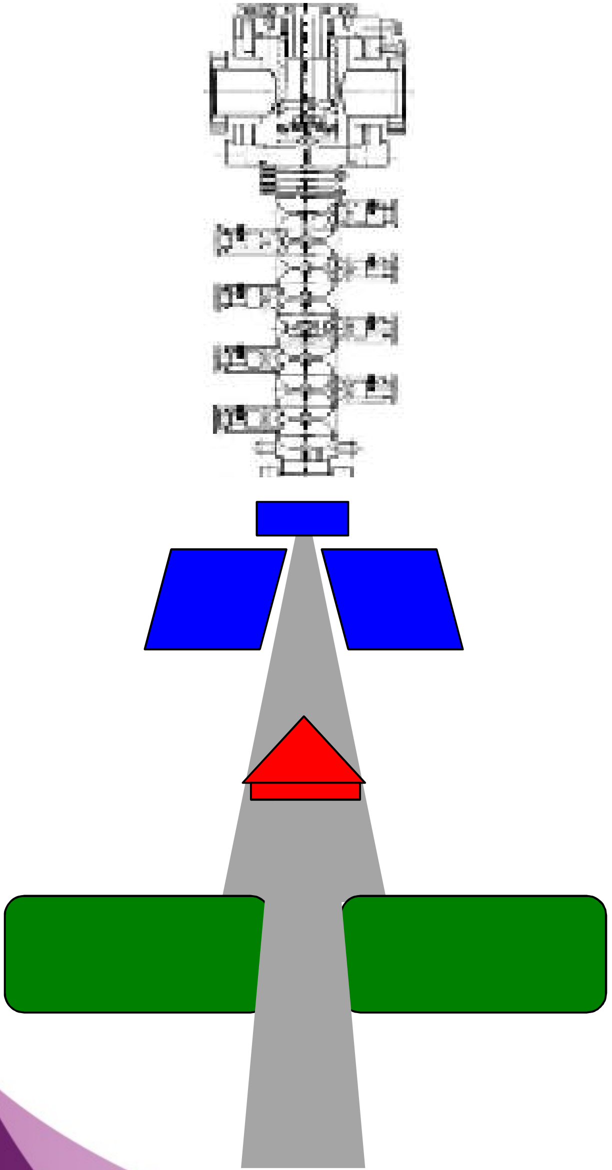
Soft tissue: 60% of tumour are visible



Bahig IJROBP 2013

Vero

Medical linac "reduced" beam line



Electron Gun

Accelerator

Target

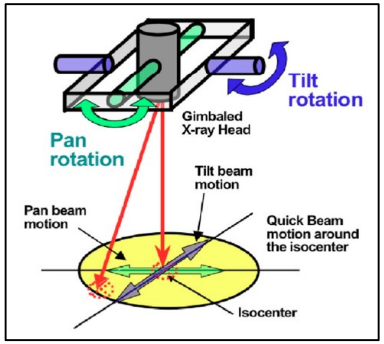
Primary collimator

Flattening filter

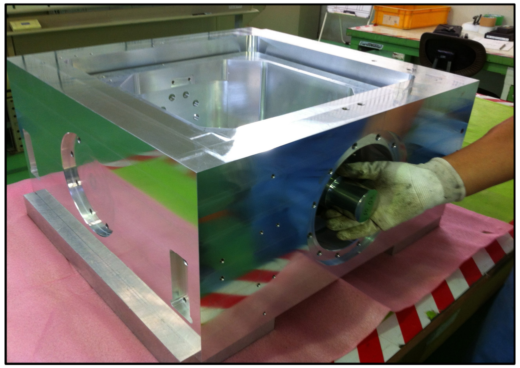
MLC

VERO

Still very heavy (700kg)



Astronaut training:
"the gimbals chair"



-Rotation of the linac/MLC assembly around the "Center of mass"

-Only 2 DOF dynamic (Pan/Tilt rotation)

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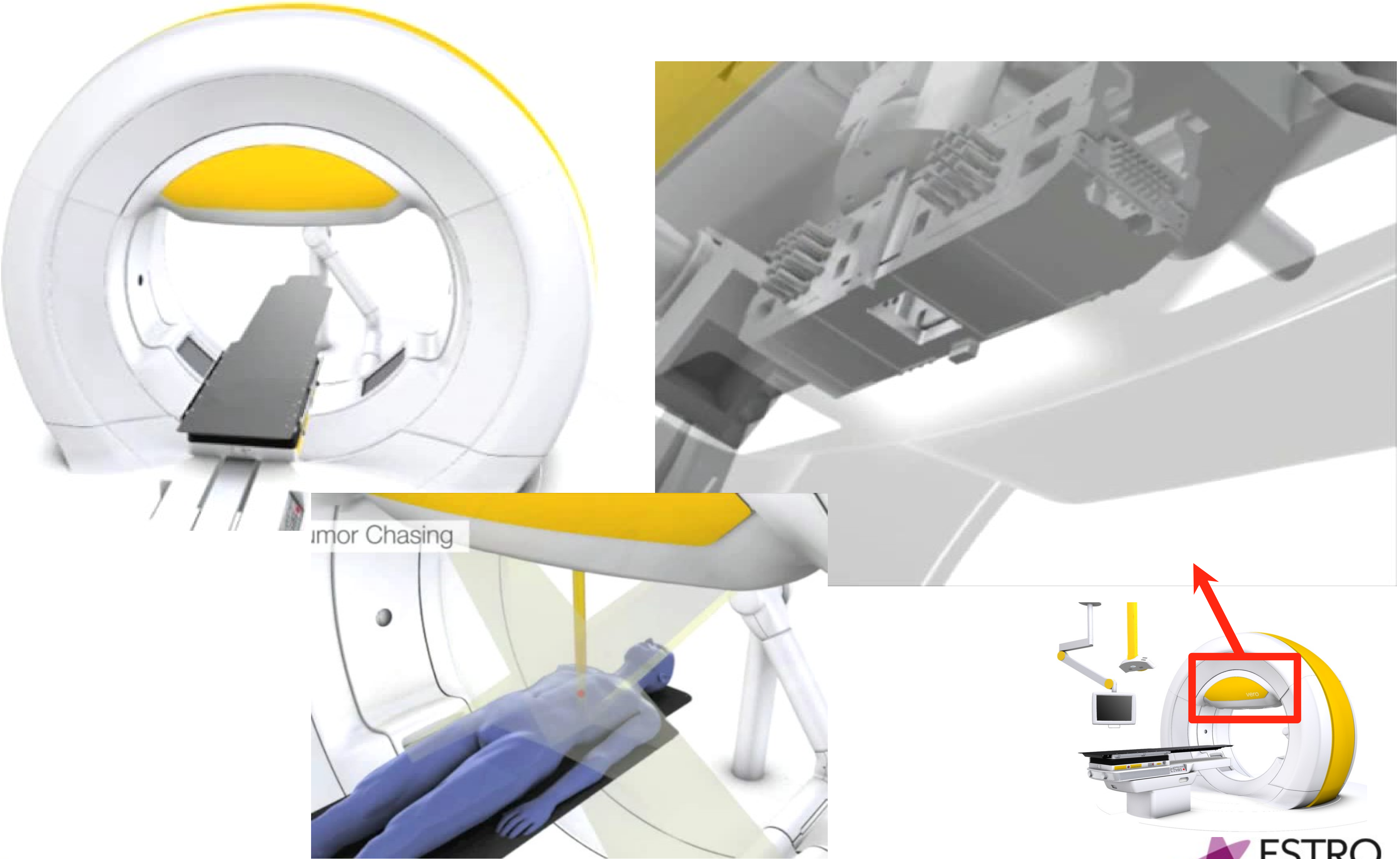
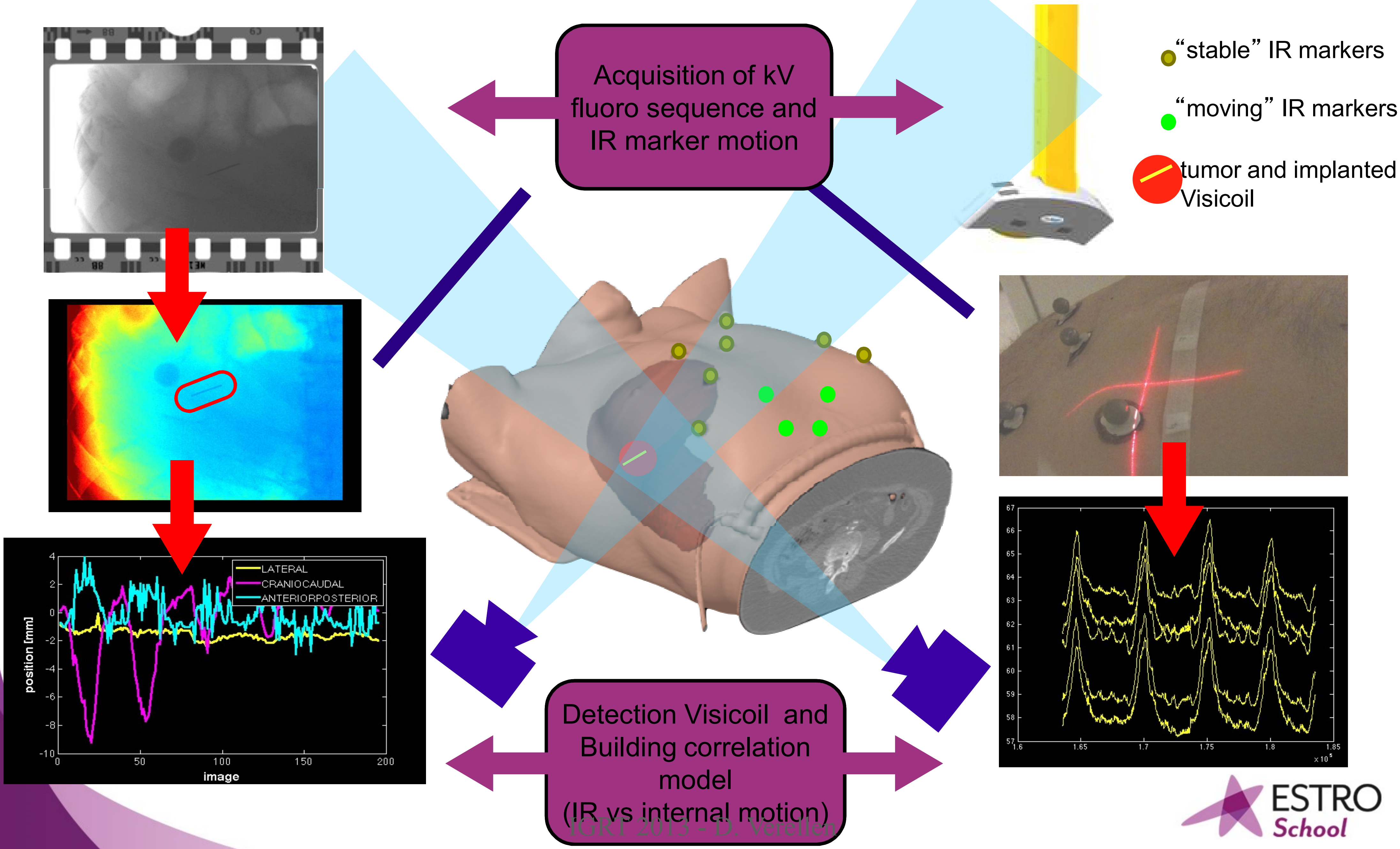
Tumor tracking: VERO



Courtesy of D. Verellen

Tracking: Correlation models



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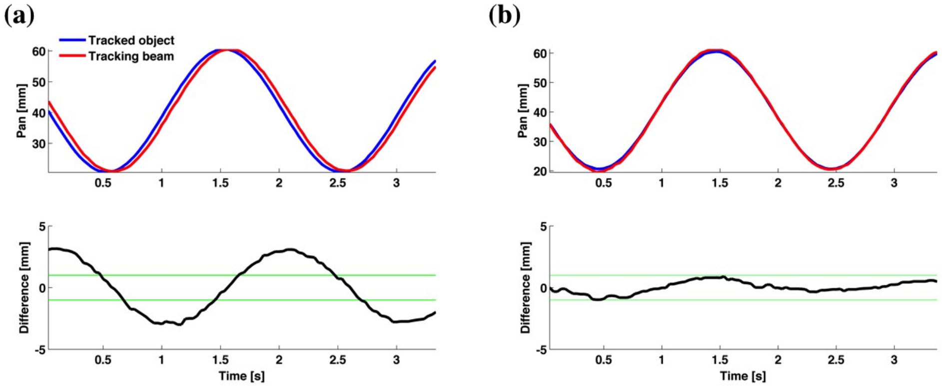
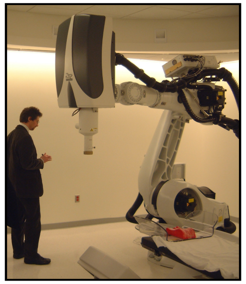
Tracking: system latency

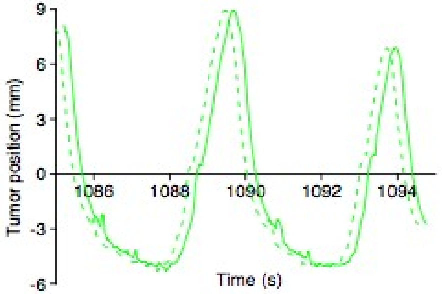
- VERO: system latency = 50ms
  - ➢ Depuydt *et al.*



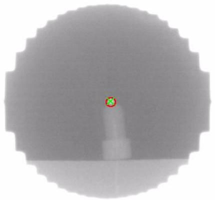
- Cyber Knife: System latency = 115 ms
  - ➢ Hoogeman *et al.*

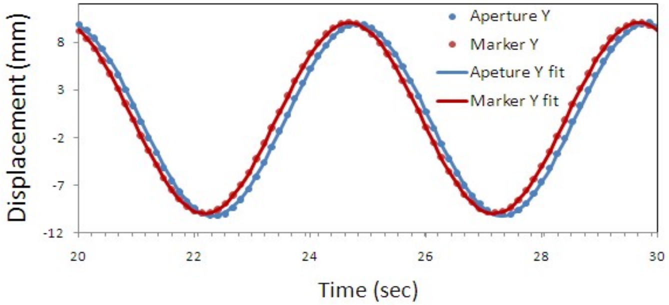


- Data processing
- Communication to robotic controller
- Inertia of robotic manipulator and linear accelerator



- MLC tracking, "breathing leaves": system latency = 140 ms
  - ➢ Poulsen *et al.*





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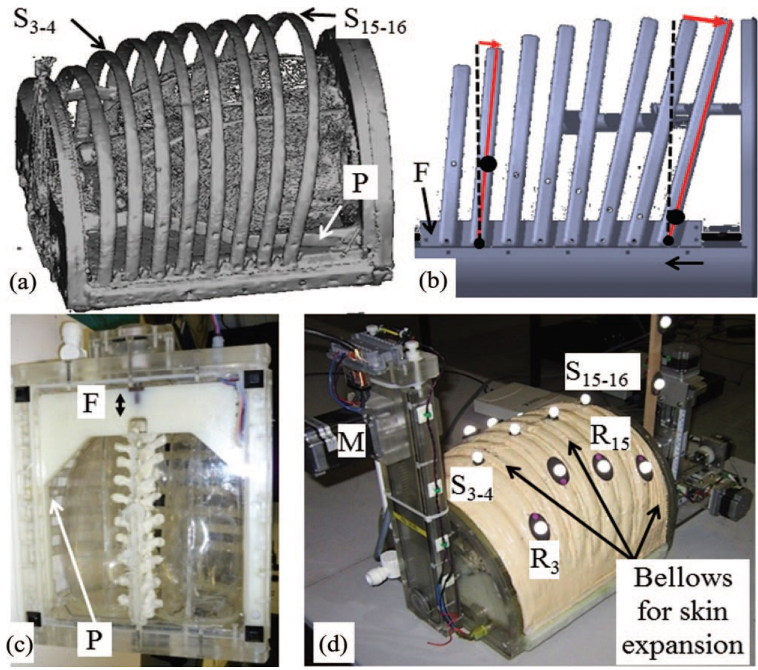
CIRS

QUASAR



QA of treatment delivery for tracking

Olivier MP 2014

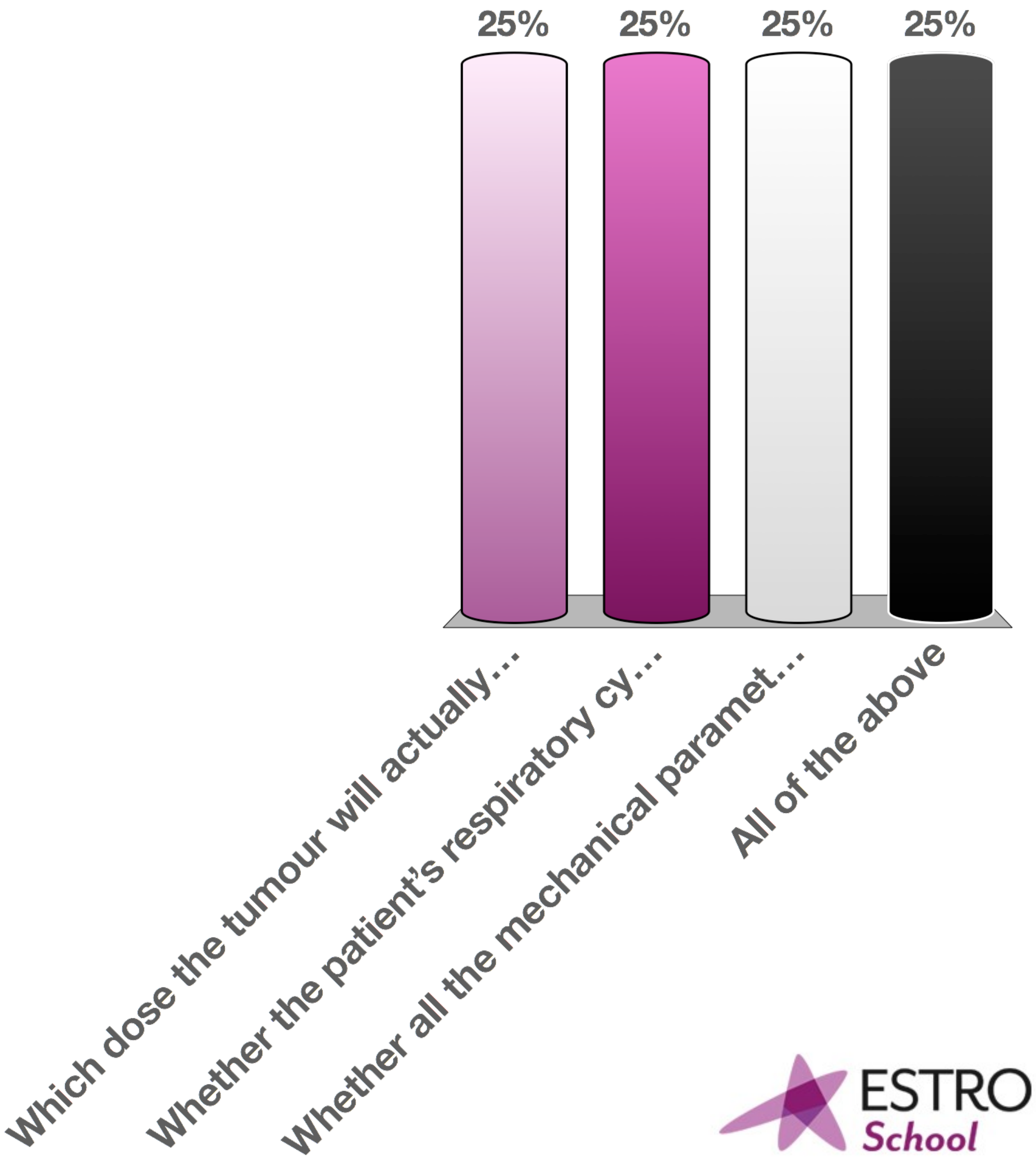
By using the patient's breathing trace (from an external surrogate) and a 4D phantom, are you checking…?

A. Which dose the tumour will actually receive over the whole treatment course

B. Whether the patient's breathing is similar to what you expected from your 4DCT

C. Whether all the technical parameters (alignment of the imaging system, etc…) are within constraints

D. All of the above



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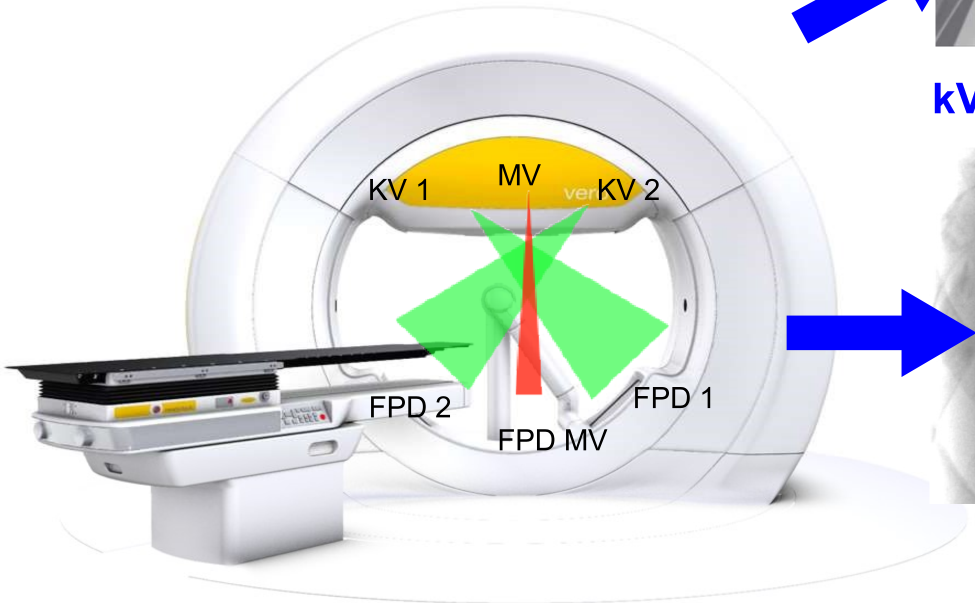
QA of treatment delivery for tracking

- “Real” 4D is not tested
- This is NOT individual patient QA
  - Irregular breathing?
  - Loss of surrogate/tumour relationship?

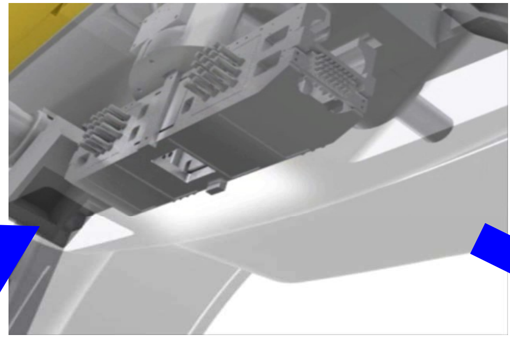
- You are still pretty much only checking the machine

- This will NOT give you any info on how the patient actually breathed during treatment
  - Unless you have thorough imaging
  - Log files of the beam/tumour position

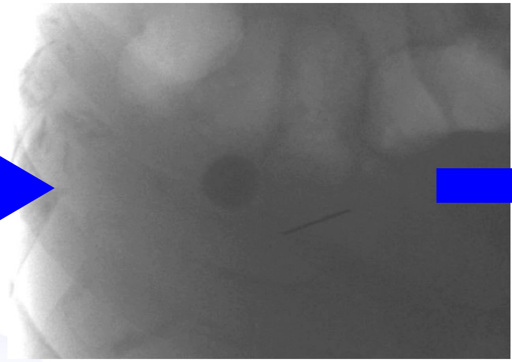
Tumour Tracking Verification



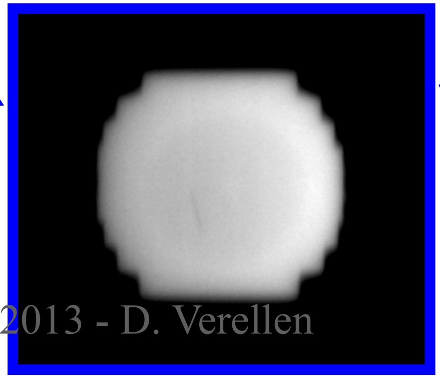
Gimbals position logging



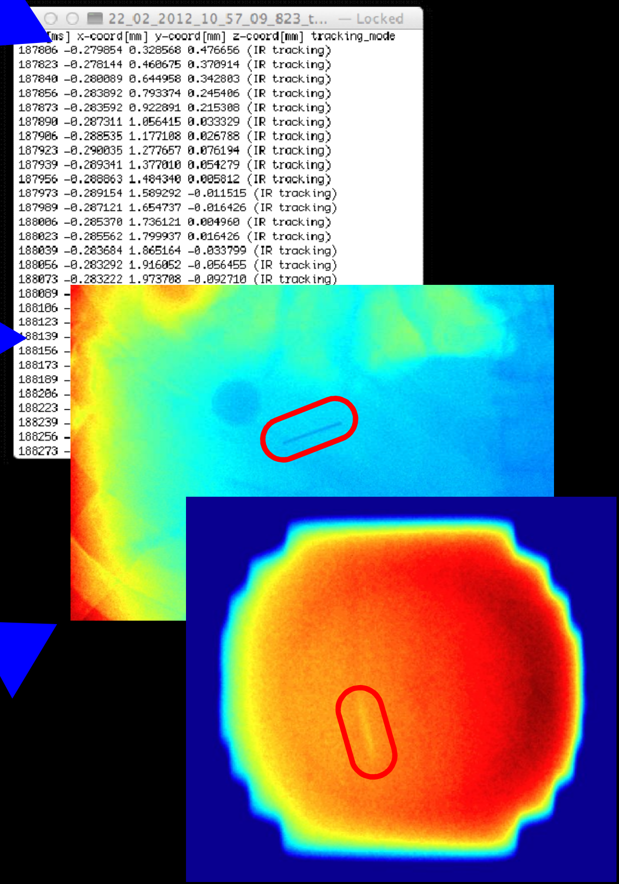
kV Monitoring Imaging



EPID MV Imaging

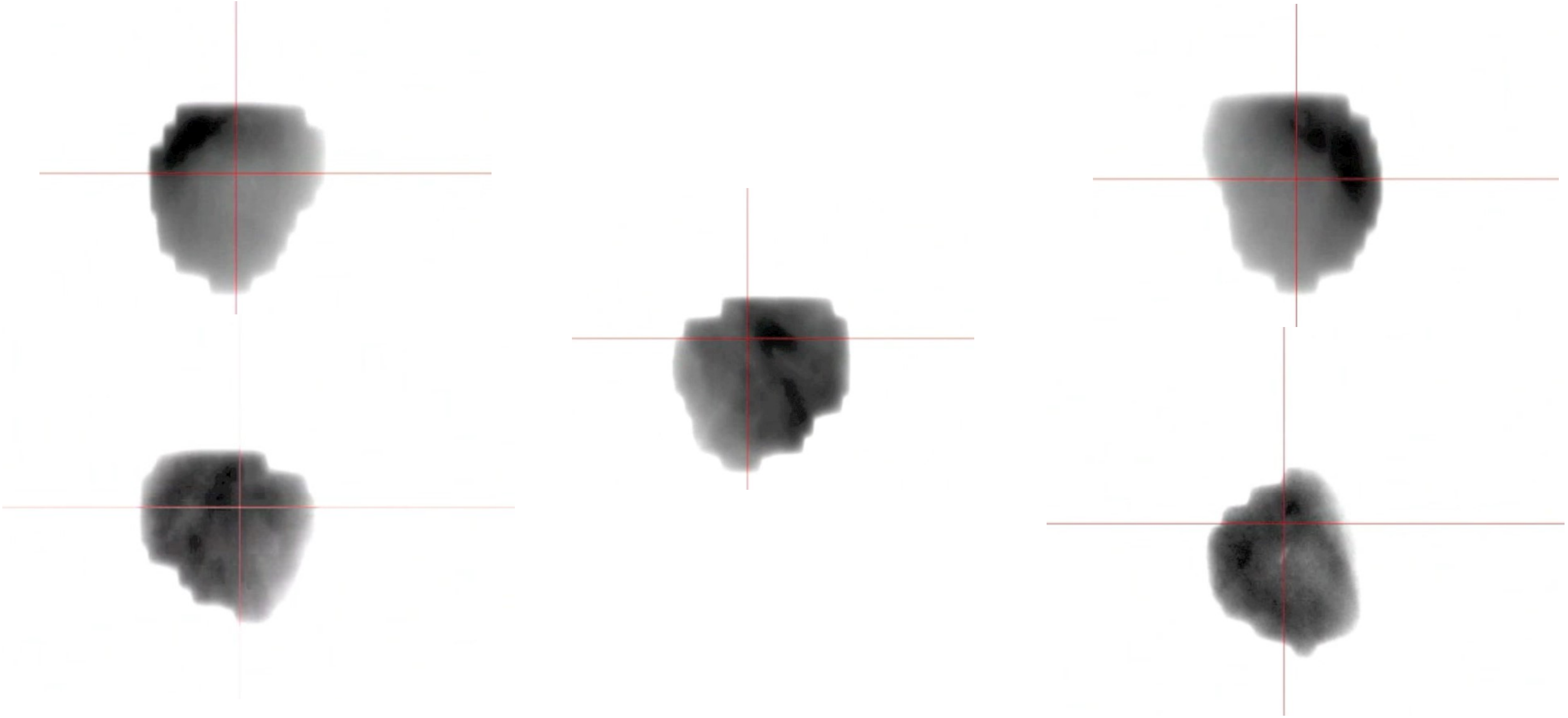


Per fraction QA through combination of different information sources



Tumour Tracking Verification

Visibility in some frames of tumour and of implanted fiducial marker



EPID: "*The proof of the pudding ...*"

- More on MLC tracking: Keall, results from first experience. Consider taking out a couple of CK/Vero slide.

Caveat: you can only track one target at a time

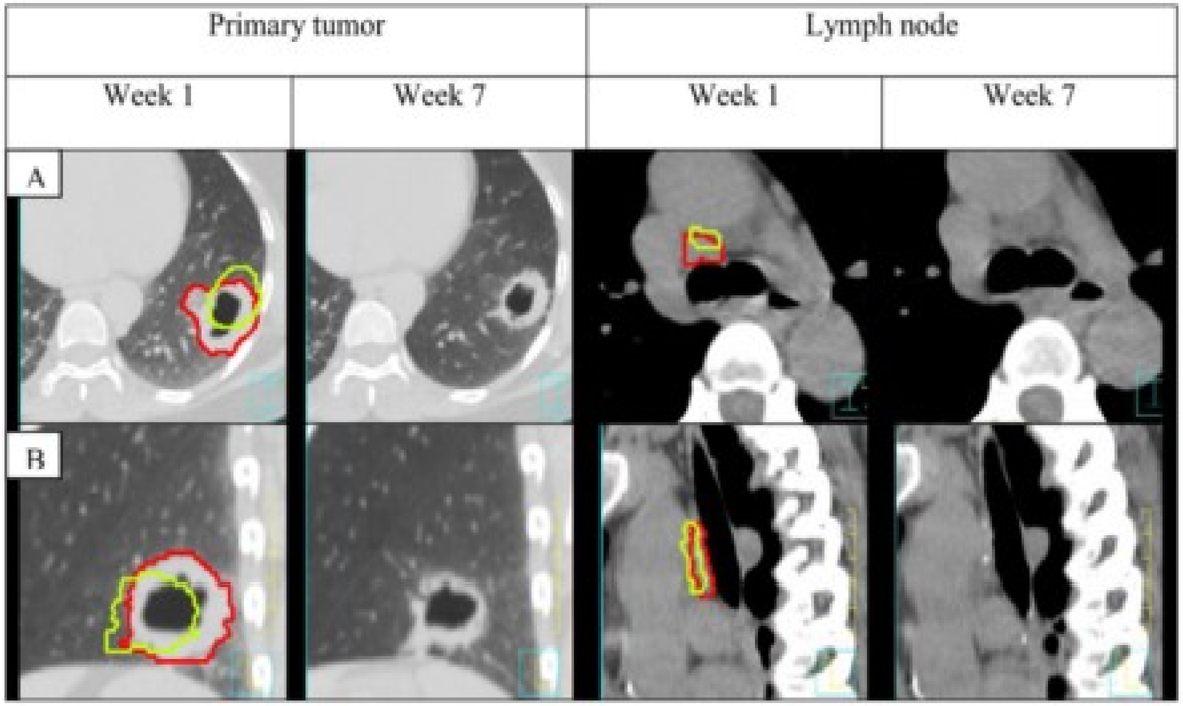


Figure 1.
Example of primary tumor and lymph node shrinkage and change in position between week 1 and 7 in patient 17. Week 1 contours are shown in red, week 7 in green. Week 7 contours are superimposed on week 1 images for better comparison.

So what if you have a peripheral and a mediastinal target ?

Weiss IJROBP 2012

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Conclusions

- Breath and gating should not be considering "margin reducing" strategies for most patients (though they may have other considerable advantages!!)

  - ➢ Don't blindly trust your surrogates

- Smörgåsbord of technologies available, ranging from the simple to the highly elaborate

- Some room for improvement in terms of QA solution (during /after treatment)

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THANK YOU FOR YOUR ATTENTION

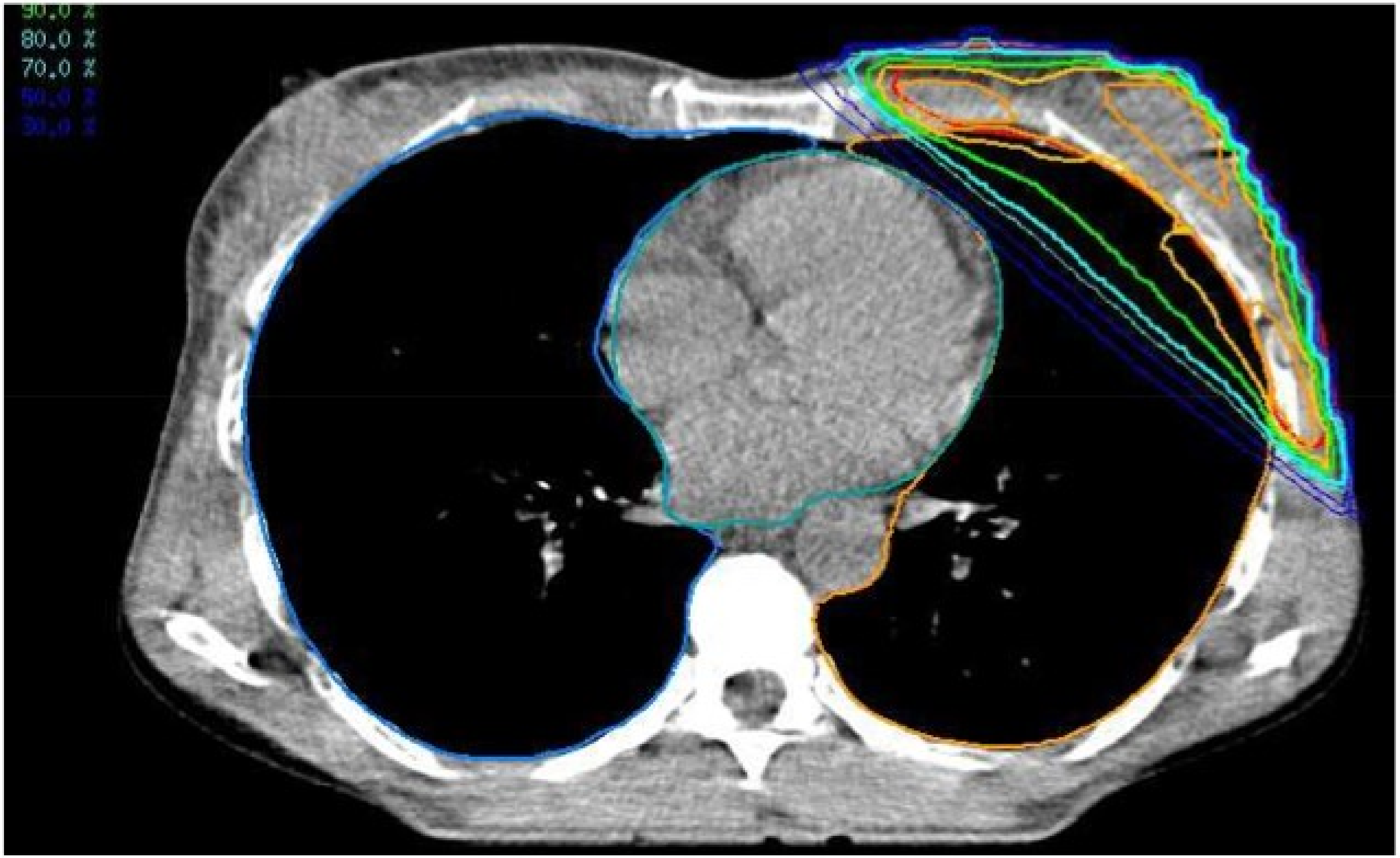
Image guided radiotherapy in breast and lung

Marianne Aznar

Andrew Hope

Thanks to Matthias Guckenberger!

Breast Cancer



Radiotherapy in breast cancer

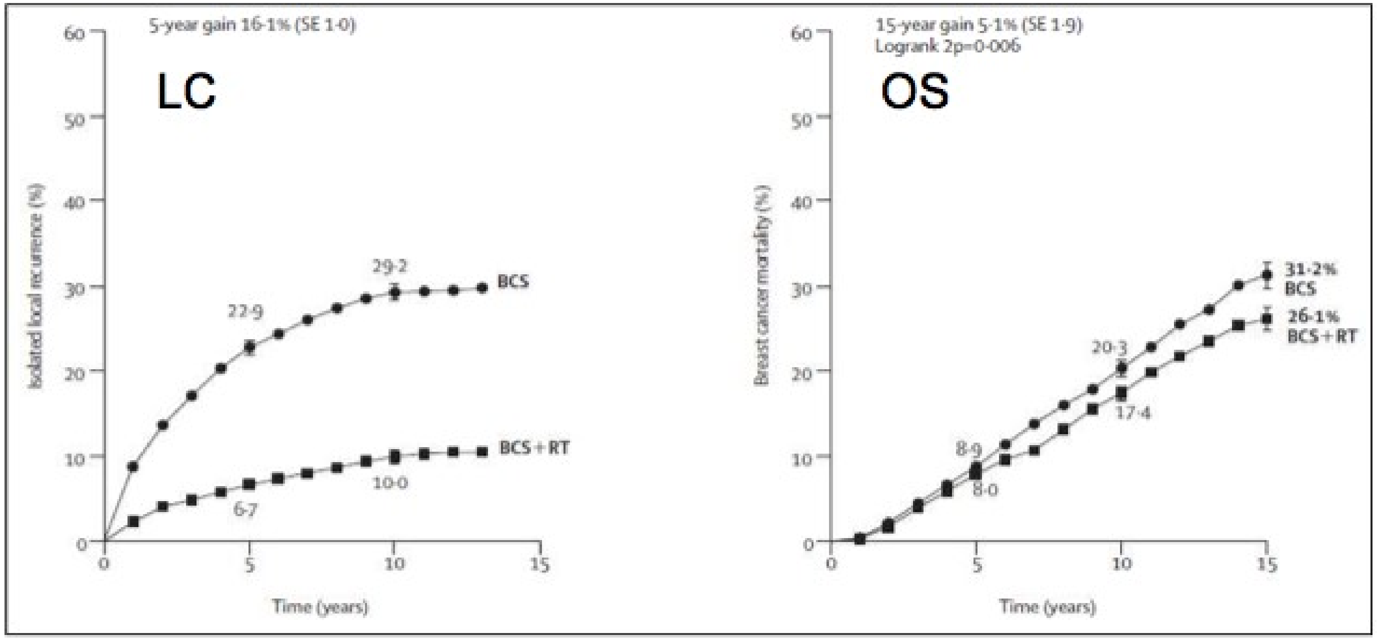
Irradiation increases overall survival after breast conserving surgery and mastectomy

EBCTCG Lancet 2005

Excellent or good cosmesis achieved in 80% of the patients

Taylor 1995 IJROBP

Breast conserving surgery
pN0



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Radiotherapy in breast cancer

Long term toxicity in EBCTCG 2005

Long term toxicity	HR	P-value
Contralateral breast cancer	1.18	0.002
Other cancer	1.20	0.001
Death due to heart disease	1.25	0.00003

Late effects are a function of radiotherapy technique

Radiotherapy in breast cancer: Heart Toxicity

- Latency of 15-20 years
- Myocardial scintigraphy can detect perfusion changes as early as 6 mo

- Target structures:
  - Myocardium (e.g. left ventricle)
  - Vessels (e.g. left anterior descending coronary artery)

- Toxicity
  - Myocardial infarction
  - Angina
  - CHF
  - Valvular disorders
  - Electrical conductivity alterations

- Dose threshold??

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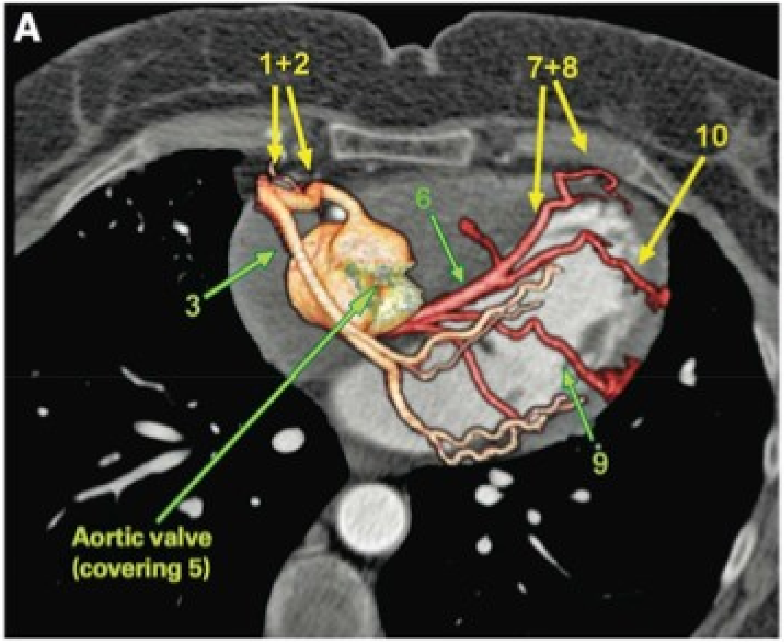
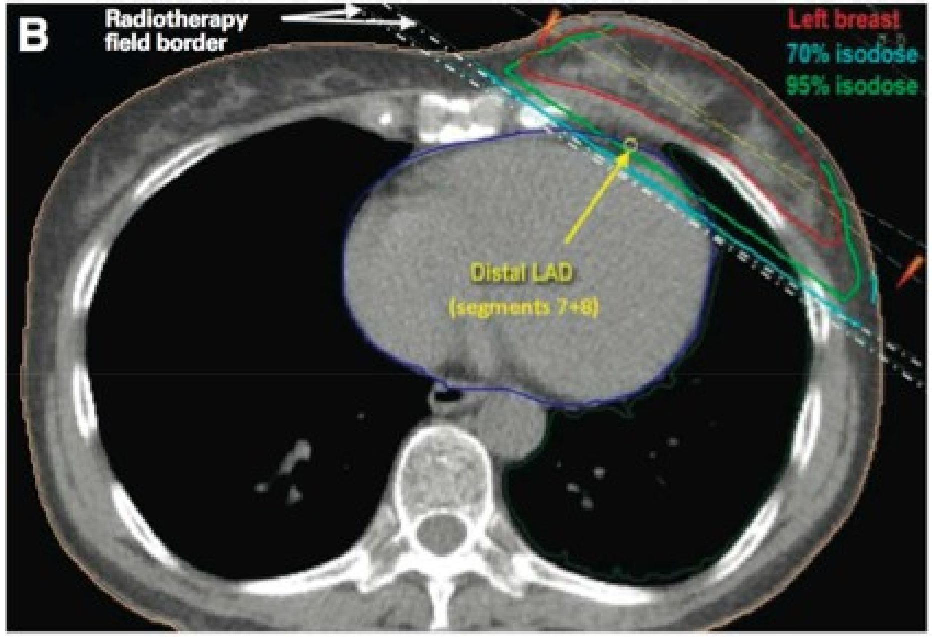
Radiotherapy in breast cancer: Heart Toxicity





left **a**nterior **d**escending artery

Nillson JCO 2012

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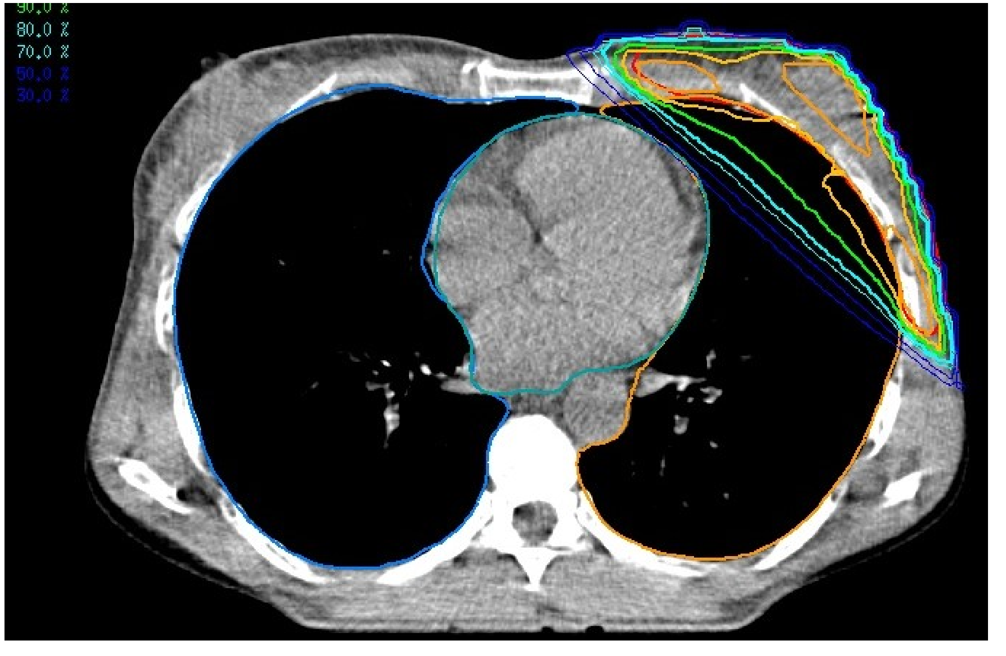
Image guidance

- Which modality?
- How often?
- whole breast vs partial/boost
- Image guidance for respiratory gating /inspiration breath hold



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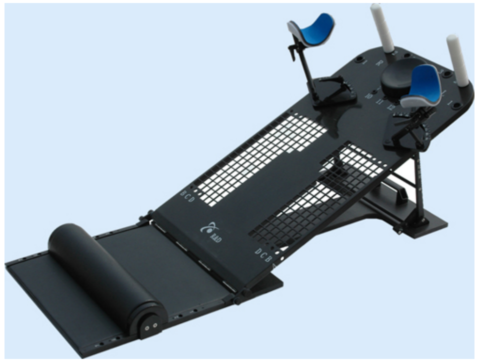
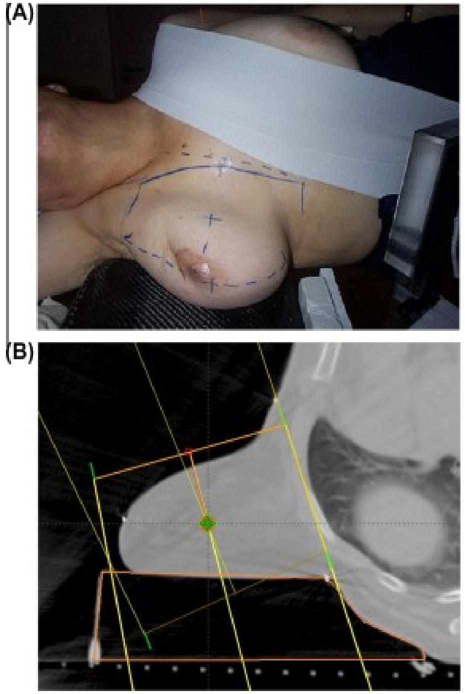
Imaging: Immobilisation techniques



Kirova et al RO 2014

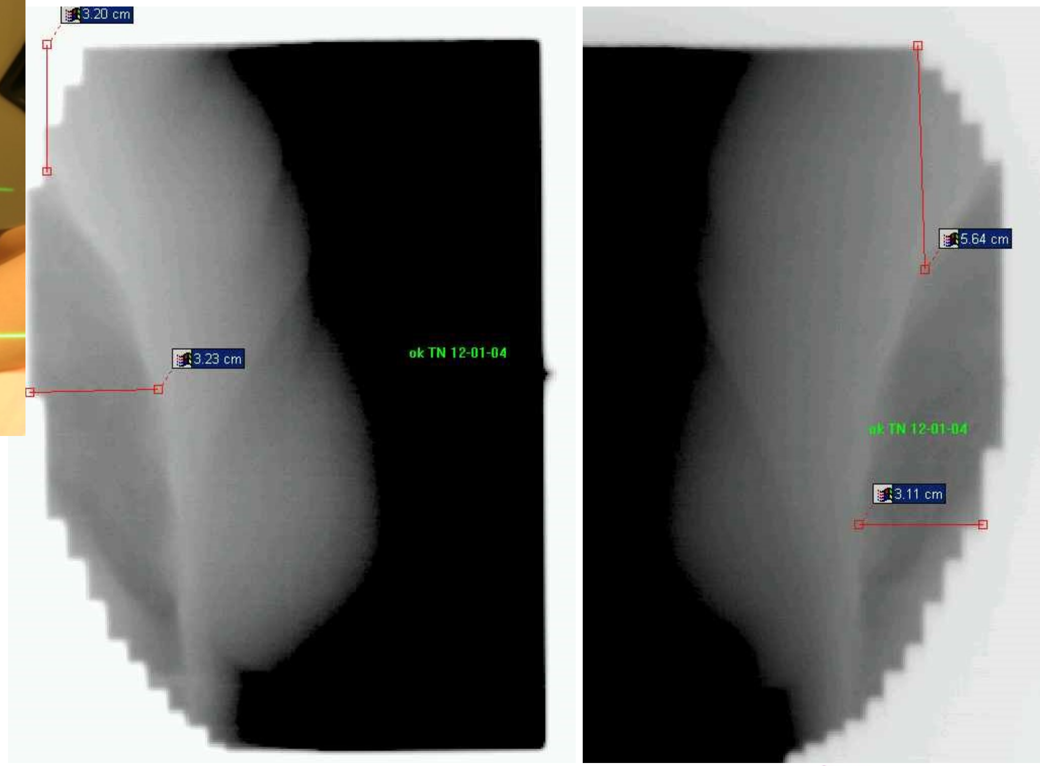


Lymberis et al IJROBP 2012

WHOLE BREAST (+/- LN)

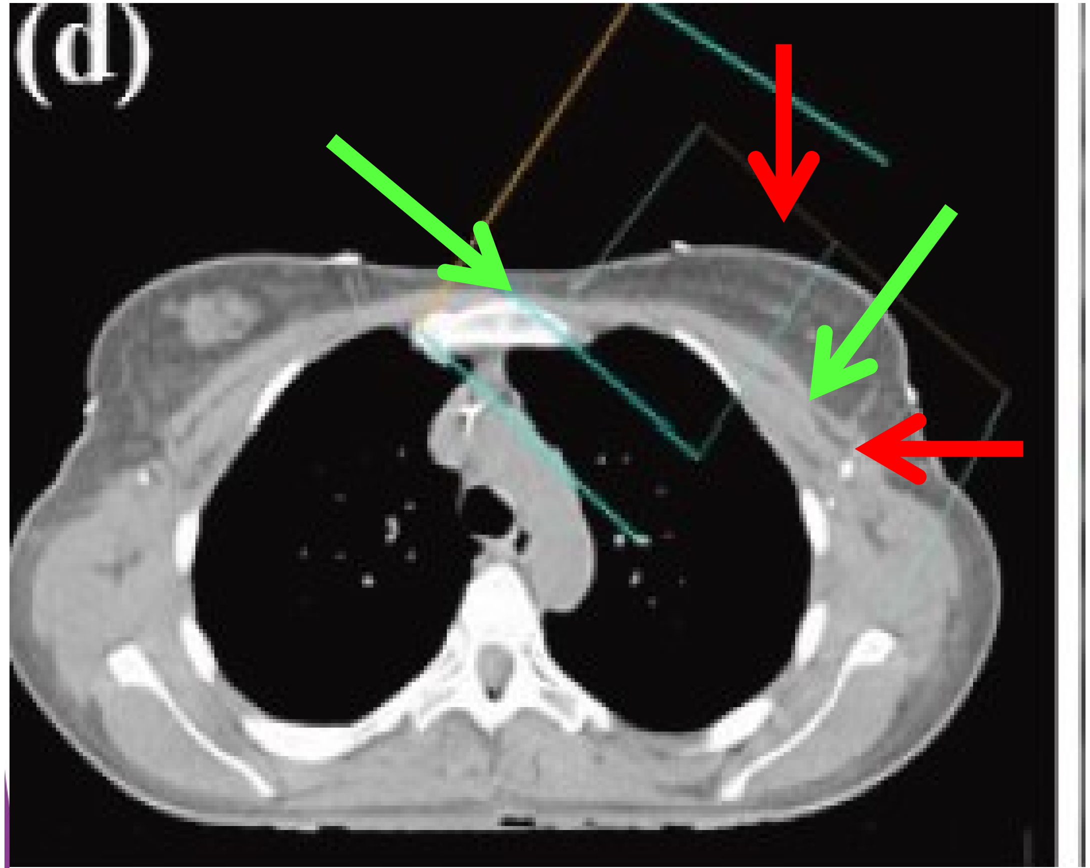
Image guidance

Field light / Beam's-eye-view (portal) images, MV



- Check the CLD
- long or vert ?
- Only one "direction"

Image-guidance for whole breast (+/- nodes)



Alternative 2D imaging strategy
•AP-lat
•tangential
+orthogonal
•kV-MV
•kV-kV

Petillion et al JACMP 2015 :
Tangential kV-kV (green) superior to AP-lat kV-MV (red)

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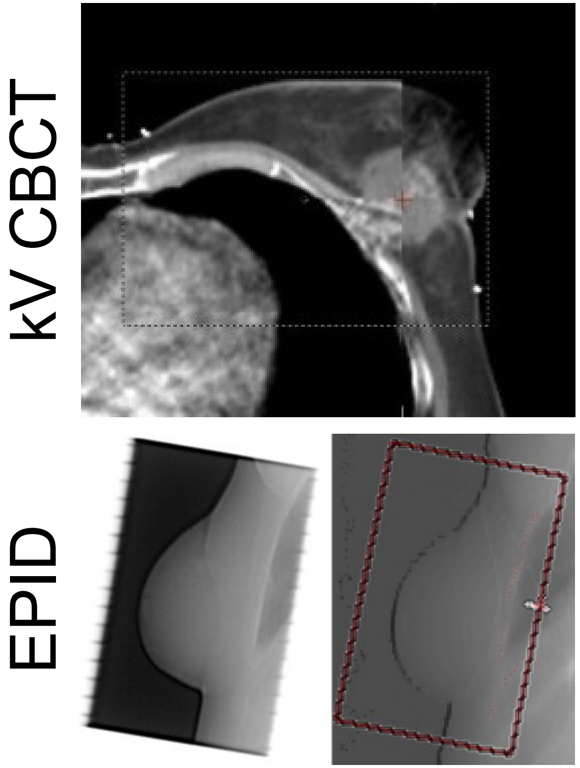
Image-guidance for whole breast (+/- nodes)



Topolnjak IJROBP 2010

- EPID field images (i.e. not orthgonal) underestimate bony set-up errors by 20% to 50%
- Difference probably insignificant for tangential whole breast irradiation
- Loco-regional treatment or more advanced techniques (SIB? IMRT?) could benefit from a more accurate set up.

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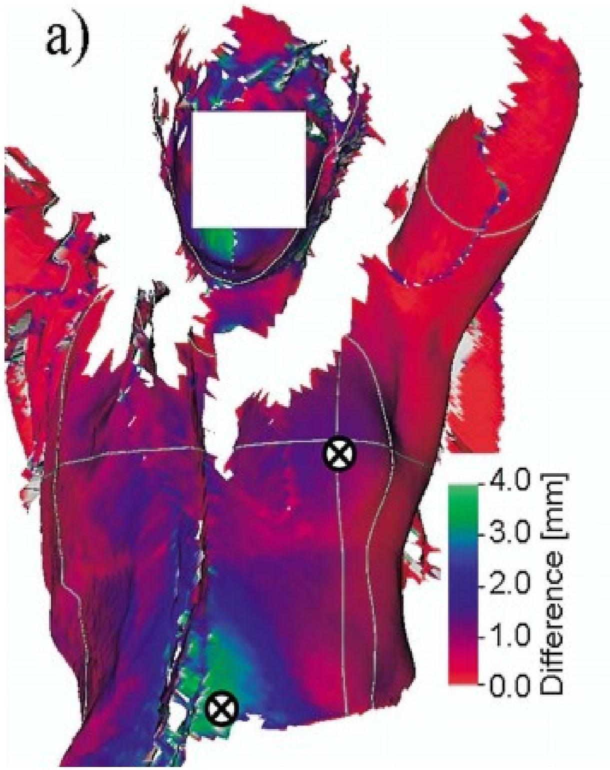
Image-guidance for whole breast (+/- nodes)

- Target with "high deformability"
- Number of cameras ???

Bert et al (2 cameras)



- Difficult to distinguish between set-up error and anatomical changes (or breathing)

- Combination with x-ray IGRT still recommended (Betgen RO 2013)

How much accuracy do we actually gain ??

Comparing no images at all to one image on first day: no reduction of the systematic uncertainty

1SD	systematic [mm] lat	Ing	vrt
1st fraction tolerance of 5 mm	3.7	3.3	3.4
no imaging no tolerance	3.7	3.3	3.5
with eNAL 3 mm tolerance	1.5	1.6	1.6
with eNAL 2mm	1.1	1.0	1.0

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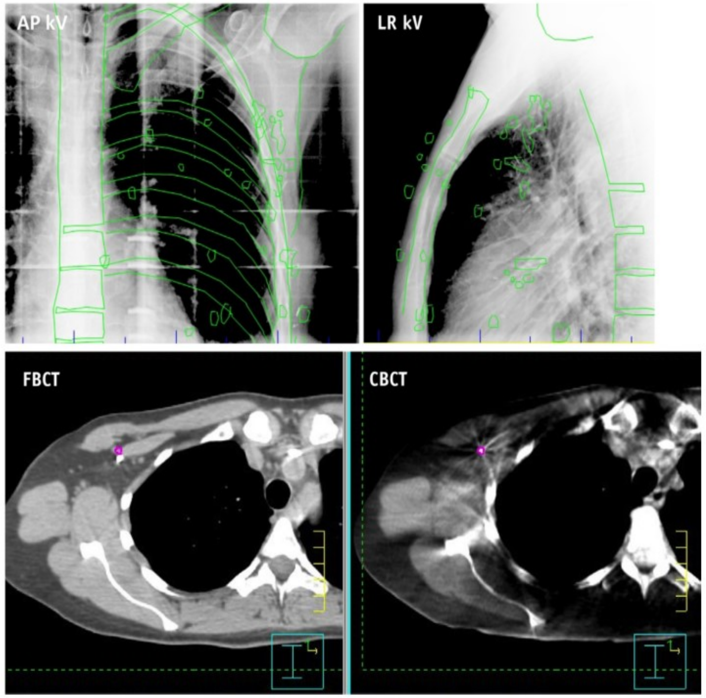
Image-guidance for whole breast (+/- nodes)

- Highly conformal /complex techniques



Feng et al IJROBP 2014

Even with daily kV, the remaining set up error justifies a considerable margin (8mm SI)

(compared to CBCT, registered on clips)

Take home message:
IGRT for whole breast (+/- nodes)

•Imaging only in the beam direction will underestimate the set up error

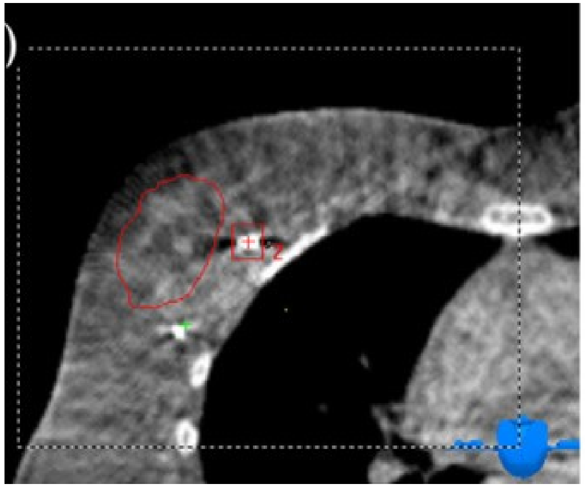
•No clear benefit of CBCT in terms of accuracy for “robust” techniques (3D tangents)

- but other considerations: workflow? SIB? IMRT?

•Surface image has interesting potential and properties (no dose) but shouldn’t be the only modality for set-up (rotations, DIBH…)

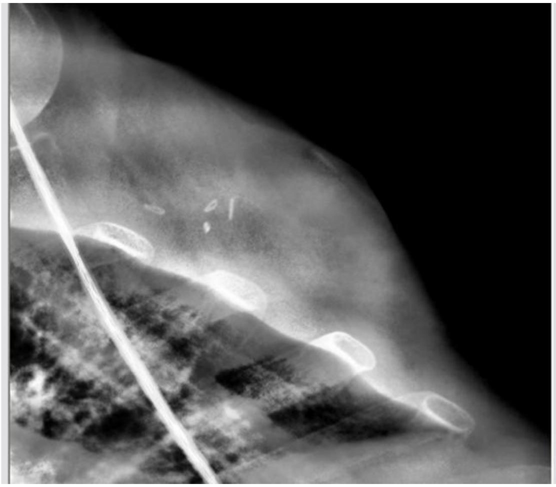
PARTIAL BREAST / BOOST

Image-guidance in partial breast irradiation: implanted markers

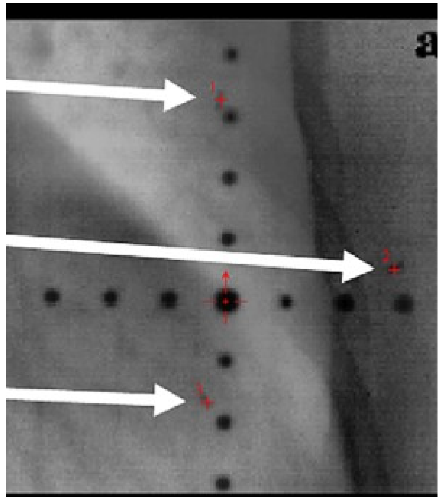


CBCT: match on soft tissue/clips

Topolnjak 2011



2D kV images: match on clips



MV images: match on clips

Leonard 2010

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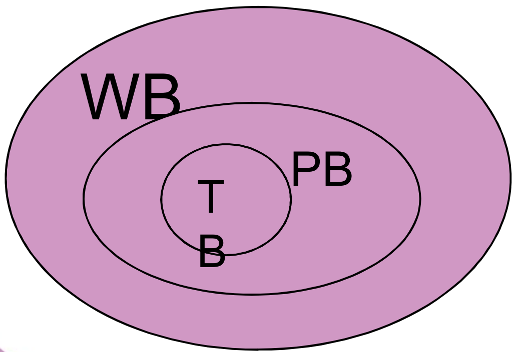
Partial breast /integrated boost

A multicentre observational study evaluating image-guided radiotherapy for more accurate partial-breast intensity-modulated radiotherapy: comparison with standard imaging technique

Emma J Harris,[1†] Mukesh Mukesh,[2†] Rajesh Jena,[2] Angela Baker,[3] Harry Bartelink,[4] Corrinne Brooks,[1] June Dean,[2] Ellen M Donovan,[1] Sandra Collette,[5] Sally Eagle,[6] John D Fenwick,[7] Peter H Graham,[8] Jo S Haviland,[9] Anna M Kirby,[10] Helen Mayles,[3] Robert A Mitchell,[1] Rosalind Perry,[11] Philip Poortmans,[12] Andrew Poynter,[13] Glyn Shentall,[14] Jenny Titley,[9] Alistair Thompson,[15] John R Yarnold,[10] Charlotte E Coles[2‡] and Philip M Evans[1,16*‡] on behalf of the IMPORT Trials Management Group

[1]Joint Department of Physics at The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK
[2]Oncology Centre, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
[3]Department of Radiotherapy and Physics, The Clatterbridge Cancer Centre NHS Foundation Trust, Wirral, UK
[4]Department of Radiation Oncology, The Netherlands Cancer Institute, Amsterdam, the Netherlands
[5]Statistics Department, EORTC Headquarters, Brussels, Belgium
[6]Department of Radiotherapy, Royal Marsden Hospital NHS Foundation Trust, London, UK
[7]Department of Oncology, University of Oxford, Oxford, UK
[8]Cancer Care Centre, St George Hospital, Kogarah, Sydney, NSW, Australia
[9]ICR-CTSU, Institute of Cancer Research, London, UK
[10]Breast Unit, Royal Marsden NHS Foundation Trust, London, UK
[11]Radiotherapy Department, Ipswich Hospitals NHS Trust, Ipswich, UK
[12]Department of Radiation Oncology, Dr Bernard Verbeeten Instituut, Tilburg, the Netherlands
[13]Radiotherapy Department, Peterborough City Hospital, Peterborough, UK
[14]Rosemere Cancer Centre, Lancashire Teaching Hospitals NHS Trust, Preston, UK
[15]School of Medicine, University of Dundee, Dundee, UK
[16]Centre for Vision, Speech and Signal Processing, Faculty of Engineering and Physical Sciences, University of Surrey, Guildford, UK



Comparing bone registration to clips-based reg

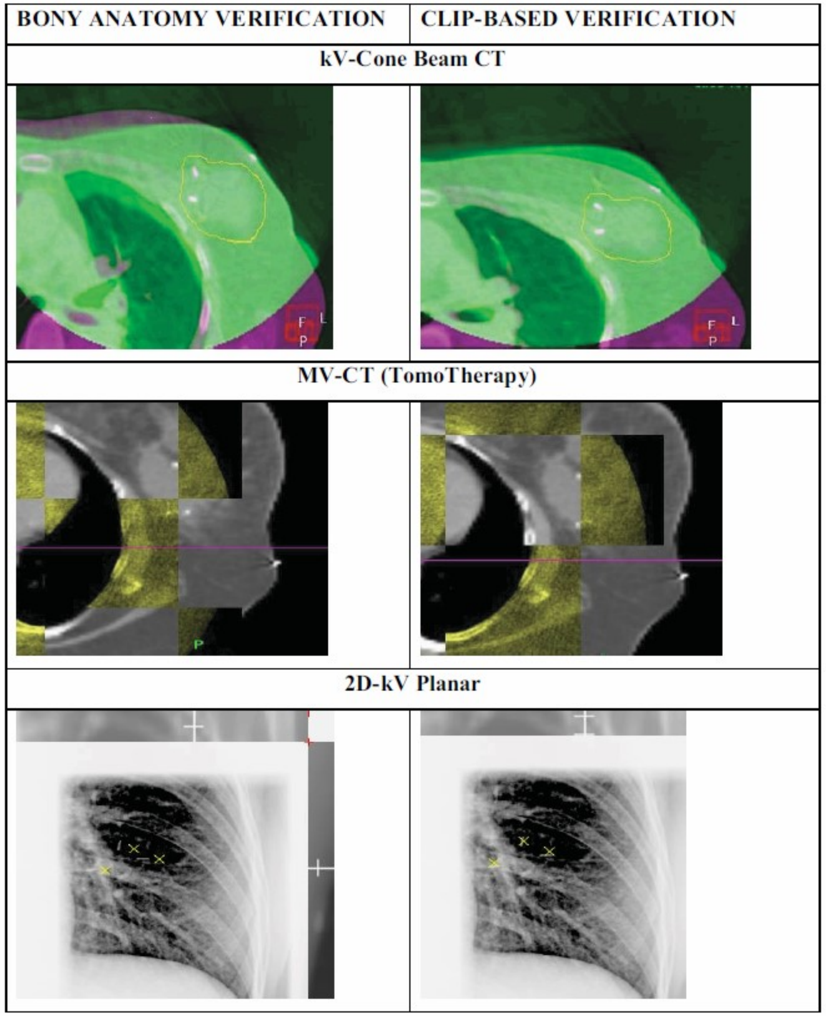


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TABLE 8 Delta errors (difference between bony anatomy and clips, S_{DIFF}) in the LR, SI and AP directions and the magnitude of their 3D vector. Time required for image matching with both techniques has also been summarised

	Delta error (S_{DIFF}), mean absolute delta [cm (range)]				Time, median [seconds (range)]	
Centre	LR	SI	AP	3D vector	T_{BA}	T_{clips}
All	0.20 (0–1.7)	0.26 (0–3.2)	0.21 (0–2.0)	0.32 (0–10.2)	73 (8–240)	66 (8–178)
A (kV-CBCT)	0.19 (0–0.7)	0.24 (0–3.2)	0.22 (0–1.7)	0.28 (0–10.2)	26 (8–51)	92 (11–177)
B (MV-CT)	0.14 (0–0.7)	0.12 (0–1.2)	0.18 (0–1.3)	0.17 (0–2.0)	102 (70–230)	110 (25–178)
C (2D-kVPI)	0.23 (0–1.7)	0.29 (0–2.4)	0.20 (0–2.0)	0.38 (0–6.29)	22 (20–76)	16 (8–52)
D (2D-kVPI)	0.21 (0–1.3)	0.32 (0–1.3)	0.21 (0–1.0)	0.35 (0–2.2)	79 (60–154)	28 (20–85)
E (2D-kVPI)	0.20 (0–1.5)	0.31 (0–1.4)	0.23 (0–1.0)	0.36 (0–3.3)	110 (28–240)	34 (16–120)

Difference between bone reg and clips reg: 2-3 mm

Reduction in PTV (tumourbed) from 8 to 5 mm with clips-based IGRT, daily or with eNAL

Modest dosimetric impact

TABLE 8 Delta errors (difference between bony anatomy and clips, S_{DIFF}) in the LR, SI and AP directions and the magnitude of their 3D vector. Time required for image matching with both techniques has also been summarised

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Time varies per institution, even when using the same technique
2D kV scores both as fastest and slowest !
Inter and intra- observer error < 1.4mm for all modalities

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Take home message: Image-guidance for partial breast irradiation

Clips <u>can</u> be representative for
•the location of the tumor bed
•the location of the whole breast

Penninkhof Radiother Oncol 2009

Registering on clips is time-efficient and can allow for margin reduction of the tumour bed PTV

- ➢ Daily or eNAL

kV-CBCT, MV-CBCT, 2D kV are equivalent in terms of accuracy if registering on clips

- ➢ 2D MV as well, if clips are visible

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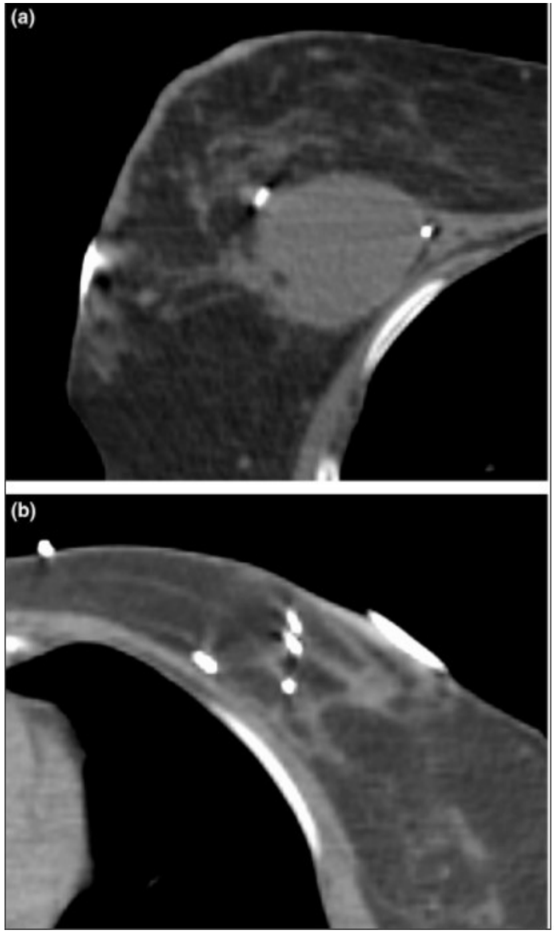
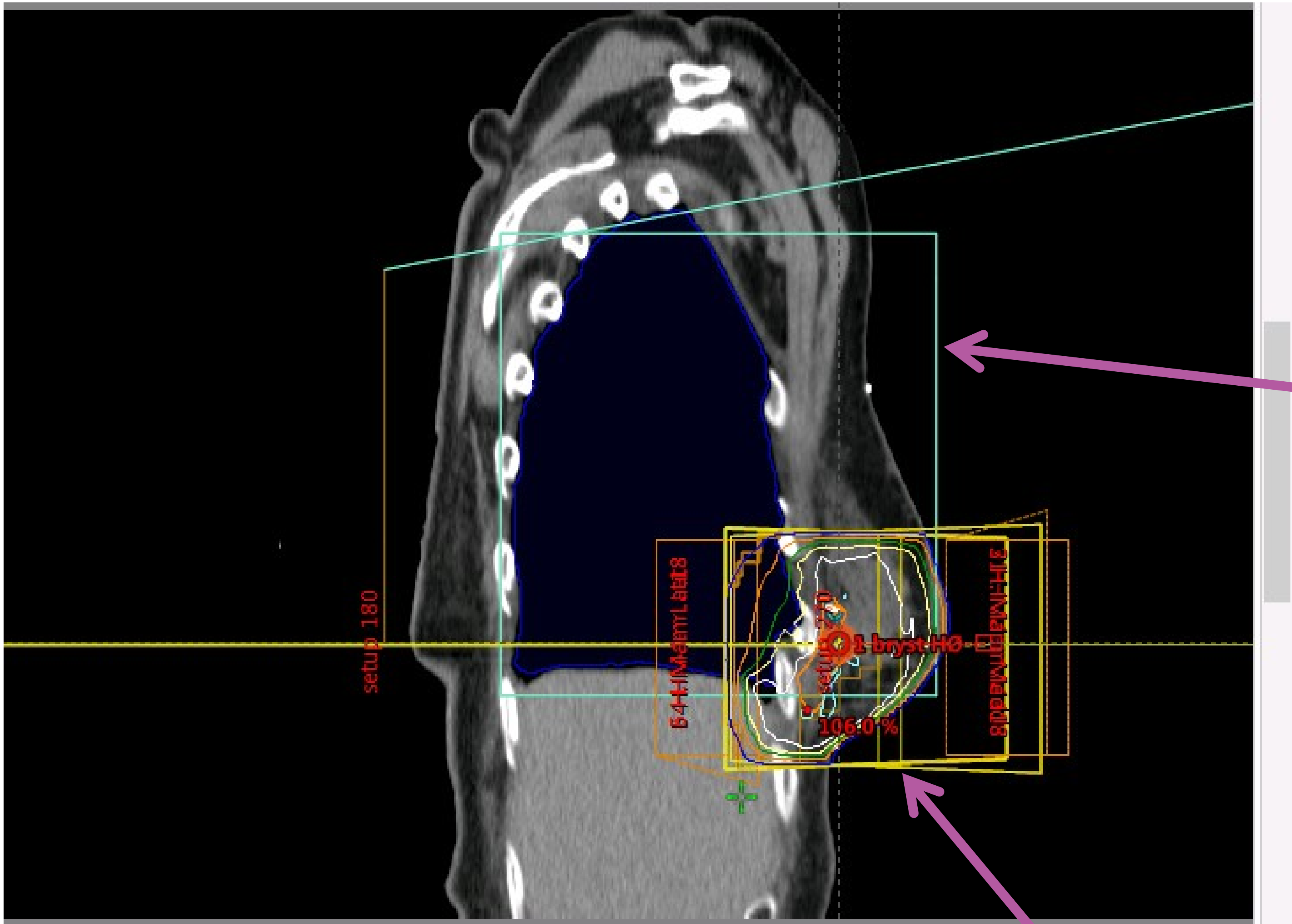
Note of caution using clips for registration

- seroma



Lewis et al J Med Rad Sci 2015



Setup fields

Treatment fields

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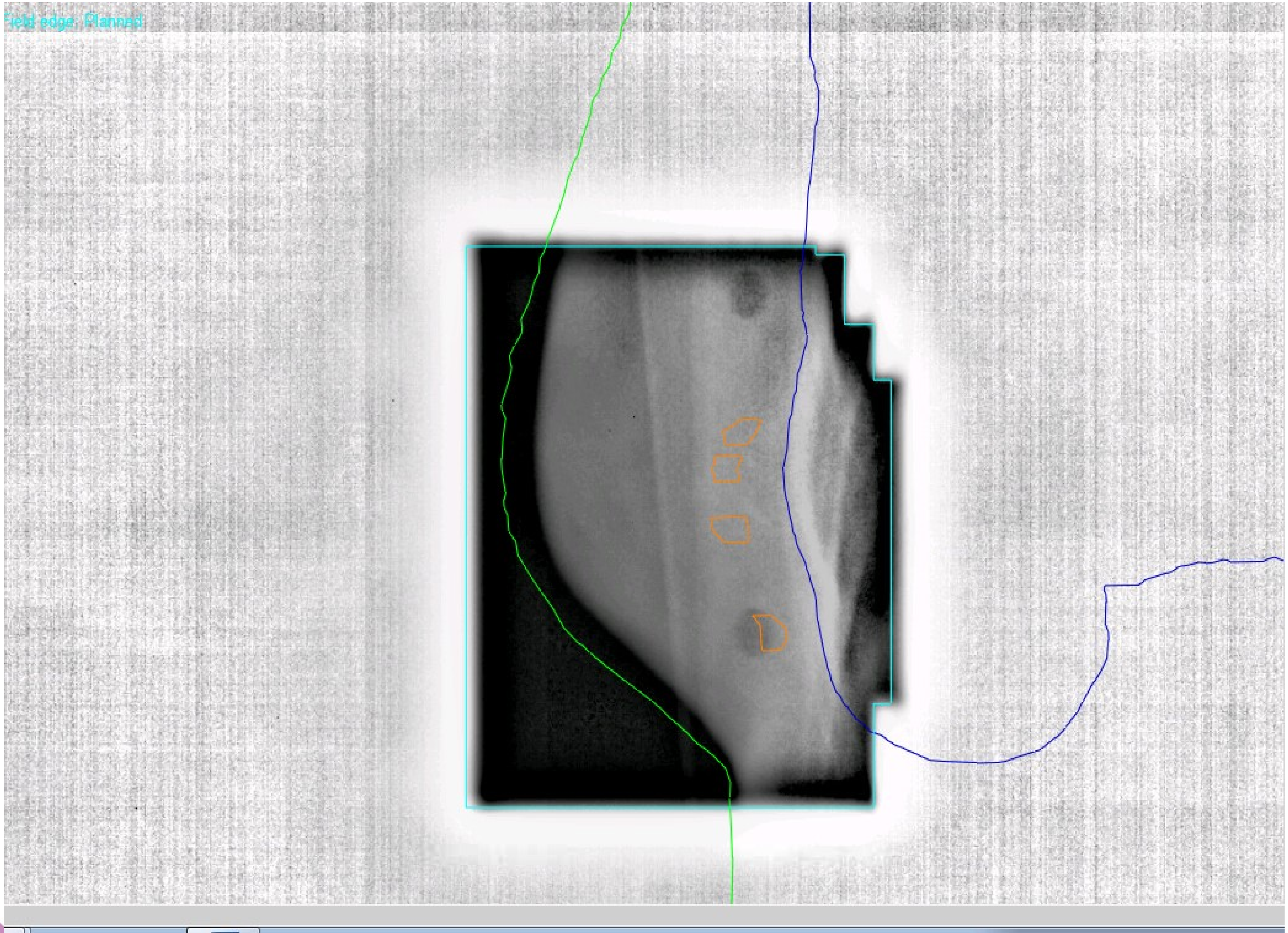
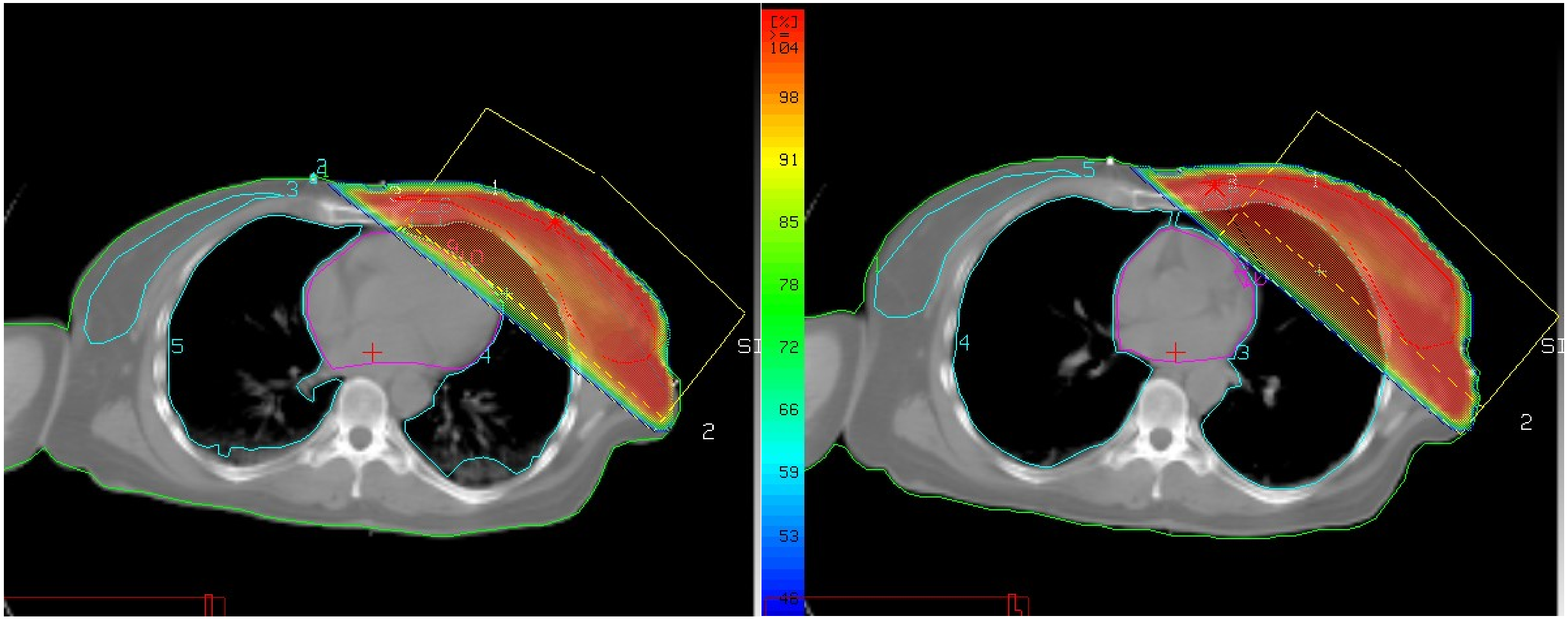

Field edge: Planned

GATING /BREATH HOLD

Techniques for reduction of cardiac toxicity

FB DIBH



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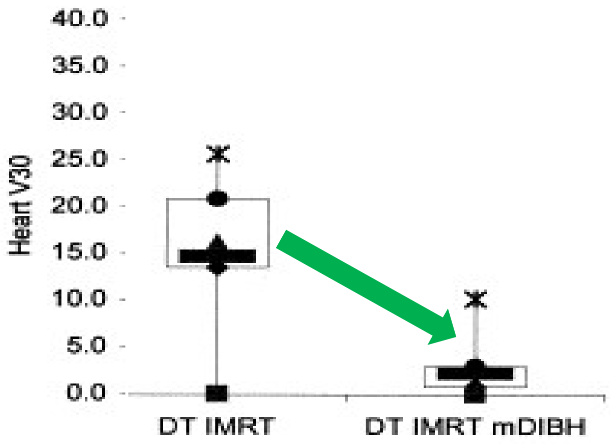
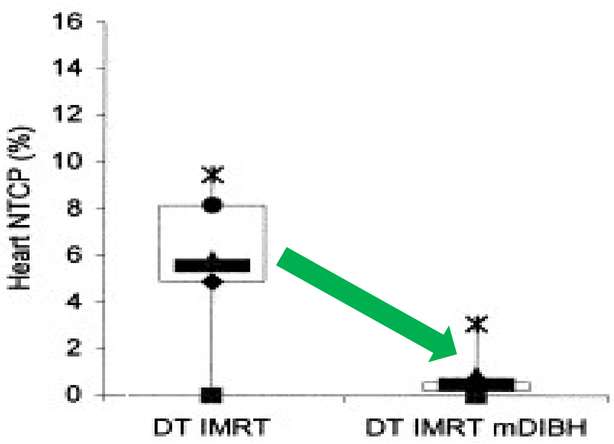
Techniques for reduction of cardiac toxicity



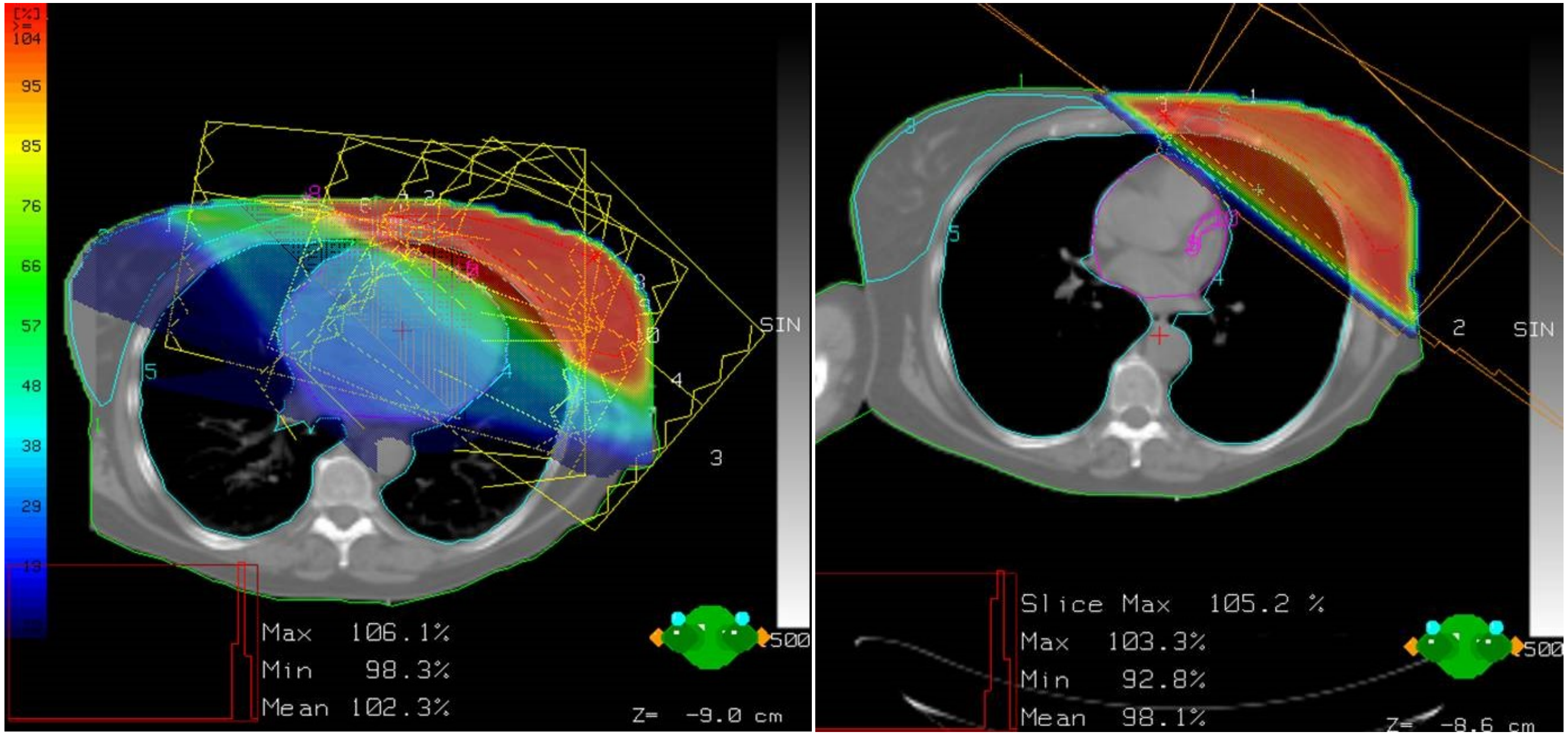
Remouchamps IJROBP 2003

Significant reduction of heart dose and heart NTCP in left sides breast cancer



Remouchamps IJROBP 2003

Techniques for reduction of cardiac toxicity
IMRT or inspiration gating?



Patients with unfavorable thoracic anatomy:

➢Improved sparing of the heart with IMRT at cost of increased dose to the normal tissue (e.g. contralateral breast)

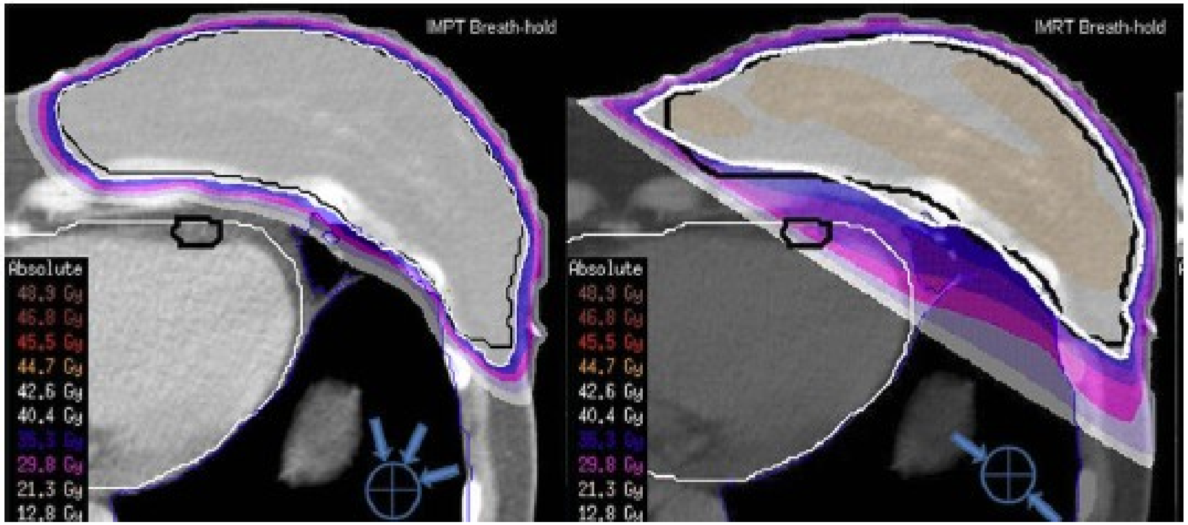
➢Sparing of the heart can be more efficient with 3D_DIBH than with IMRT_FB.

Don’t get too fancy… at least until we have better evidence !

- ASTRO “choose wisely”
- (1) consider hypofractionation (>50 y, early stage)

- (5) don't routinely use ***(multi-field)*** IMRT to deliver whole-breast radiation therapy as part of breast conservation therapy.

IMPT IMRT



Mast BCRT 2014

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Image guidance for deep inspiration: DIBH/gating monitoring

- Voluntary breath is hold is as efficient and more comfortable

Bartlett 2013

- The ”no equipment” solution:
  - short hyperventilation follwed by breath hold
  - Monitoring is visual (draw the light field on the patient, observed through control room monitors)
  - Video article: ***Bartlett et al J Vis Exp 2014***

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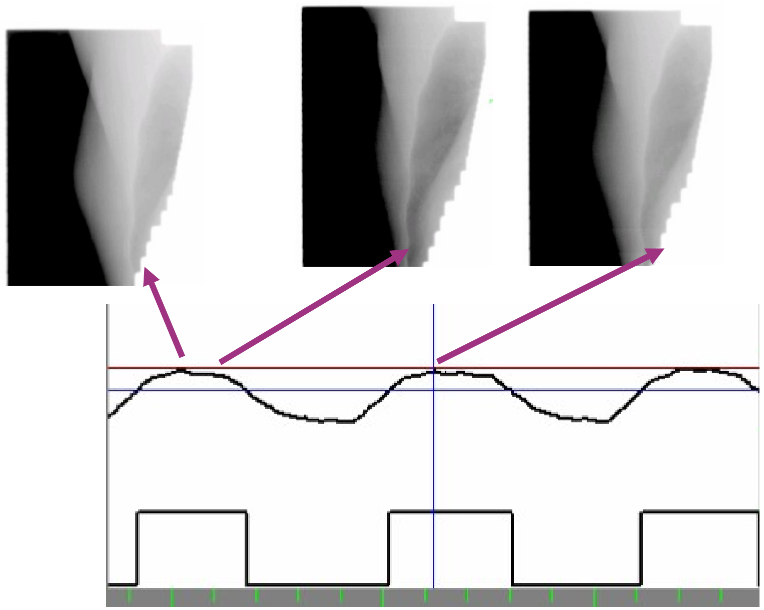
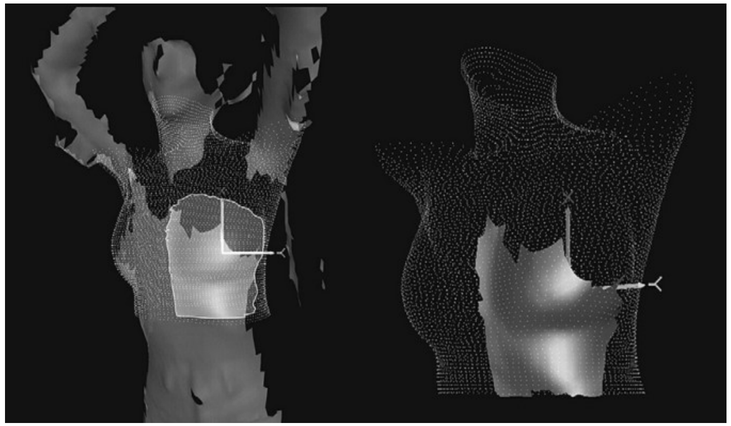
Image guidance for deep inspiration: DIBH/gating monitoring

- Patient set up as for conventional treatment (i.e. planar or CBCT)



Residual motion can be verified by cine EPID



Align RT: potential for breath hold monitoring
Maintain use of CBCT for set-up
Alderliesten et al IJROBP 2012

Take home message: image-guidance for DIBH/gating monitoring

- Deep inspiration techniques are easy to implement and effective in reducing heart and lung dose
- They are vey well tolerated
- Many technical solutions are available and they are all valid
  - ➢ choose what fits your workflow/resources best
- X-ray based imaging is still recommended in addition to ensure proper set-up

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Take home message: image-guidance for breast cancer

- MV can be acceptable is you have a good surrogate (e.g. visible clips, not only ribs)
- The less robust your treatment technique, the more advanced the IGRT
- An offline strategy (NAL, eNAL, SAL, etc…) will go a long way towards reducing uncertainties
- Deep inspiration: just do it !

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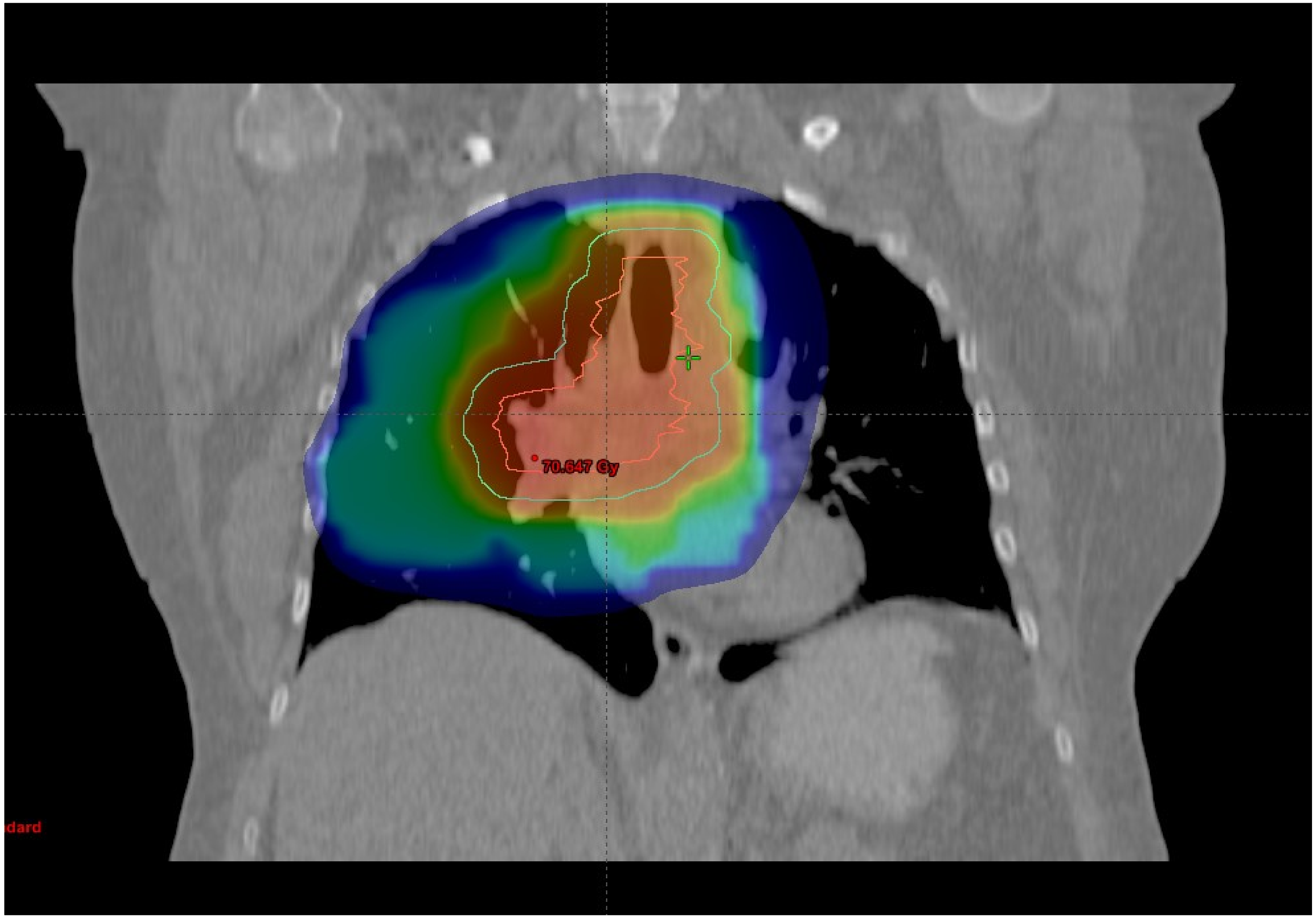
Lung Cancer



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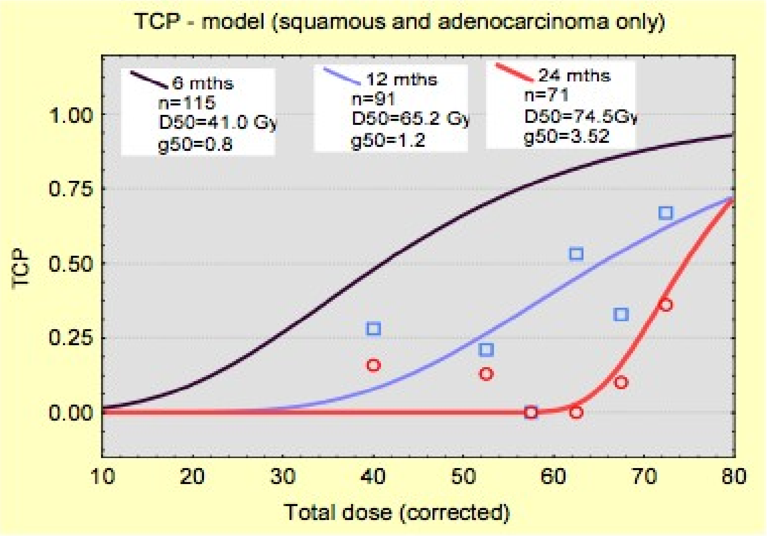
Dose escalation in lung NSCLC

High rates of local tumor recurrence with conventional irradiation doses (60-66Gy) and conventional RT techniques

- Early stage: >50% with RT only
- Advanced stage: >70% with RCHT

Sibley Cancer 1998

Le Chevalier J Natl Cancer Inst 1991



- ➢ Escalation of the irradiation dose increases local control and has the potential to increase overall survival

Willner IJROBP 2002
Kong IJROBP 2005

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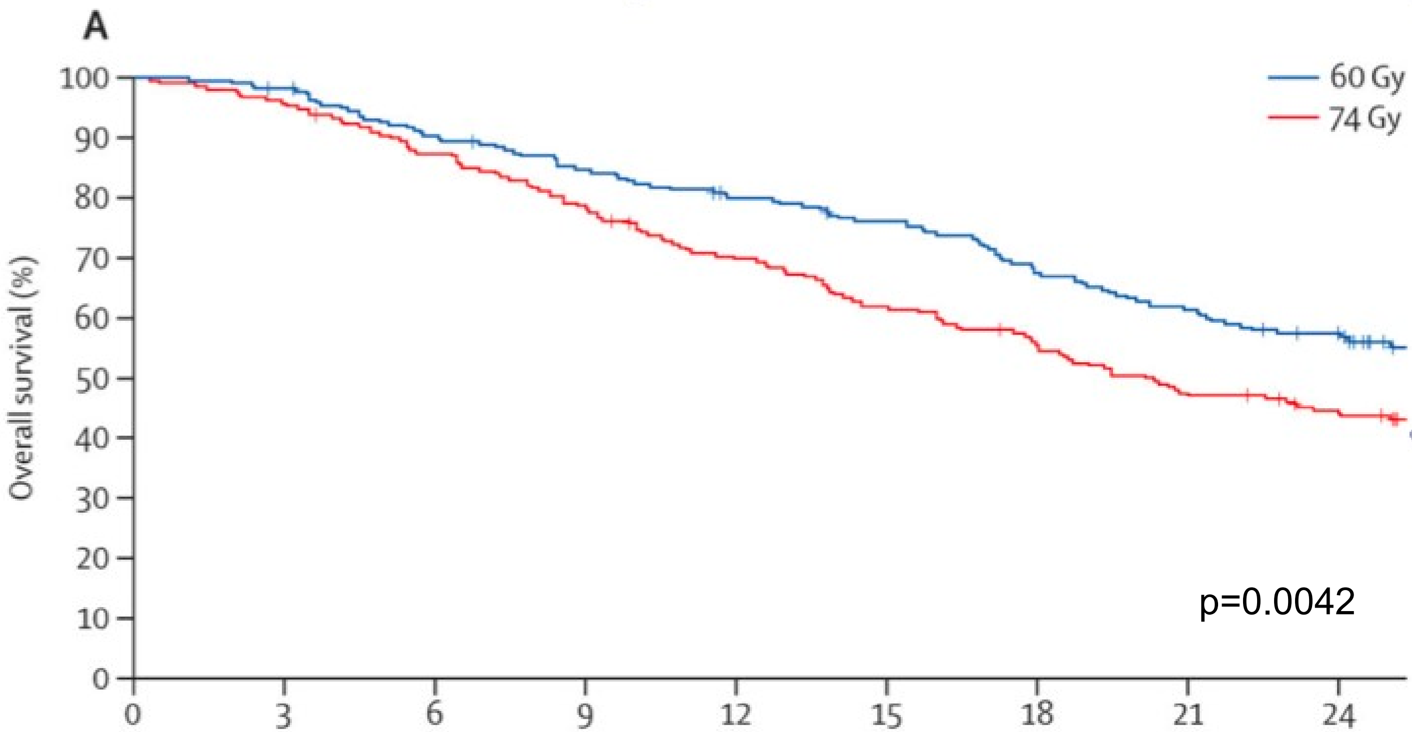
Is more dose better?

- RTOG 0617
  - Randomized controlled trial
  - Inoperable Stage III NSCLC
  - Concurrent radiation + chemotherapy
  - 2x2 randomization

60Gy	74Gy
RT + chemotherapy	RT + chemotherapy + cetuximab

Bradley et al., *Lancet Oncology* 2015

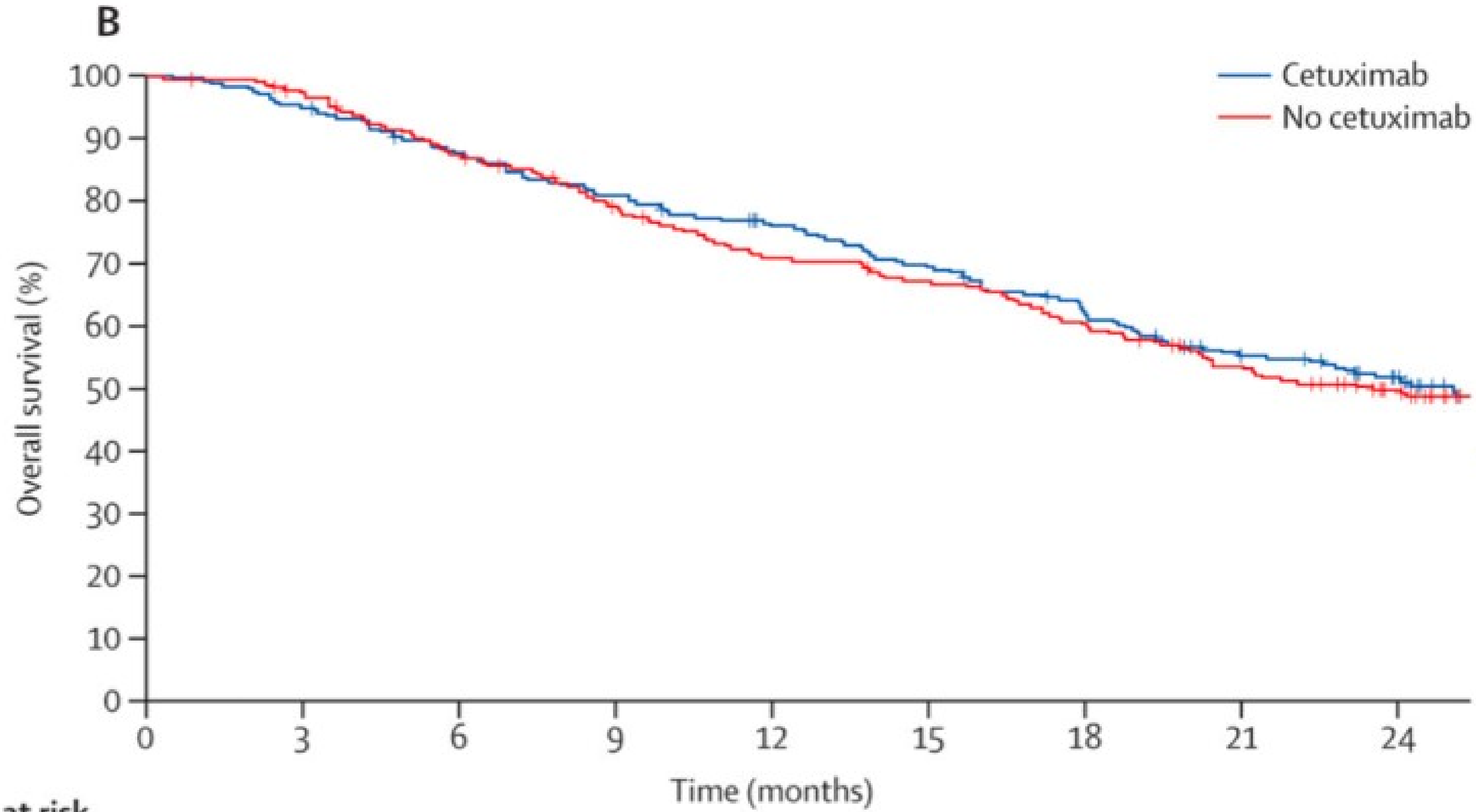
RTOG 0617 – Overall survival (+/- Dose escalation)



Number at risk									
60 Gy	217	212	194	181	169	160	142	129	116
74 Gy	207	198	180	162	142	126	112	95	87

Bradley et al., *Lancet Oncology* 2015

RTOG 0617 – Overall survival (+/- Cetuximab)



Number at risk

Cetuximab	237	225	206	190	175	160	141	121	103
No cetuximab	228	219	196	174	155	146	131	113	96

Bradley et al., *Lancet Oncology* 2015

RTOG 0617 – Overall survival modeling

Overall survival

Multivariate Cox Model Backwards Selection

Covariate	Comparison	HR (95% CI)	p-value
Radiation dose	60 Gy v 74 Gy	1.55 (1.07, 2.23)	0.020
Histology	Non-squam v Squam	1.37 (0.94, 1.98)	0.097
GTV (ITV if GTV unavailable)	Continuous	1.002 (1.000, 1.003)	0.034
Heart V5	Continuous	1.010 (1.004, 1.017)	0.002

Bradley et al., *Lancet Oncology* 2015

RTOG 0617 – Outcomes

Toxicity and mortality

September 2011	Standard Dose: 60 Gy (n=192) Grade			High Dose: 74 Gy (n=183) Grade		
	3	4	5	3	4	5
Worst non-hematologic	79 (41.1%)	14 (7.3%)	4 (2.1%)	85 (46.4%)	17 (9.3%)	8 (4.4%)
Worst overall	84 (43.8%)	45 (23.4%)	4 (2.1%)	78 (42.6%)	52 (28.4%)	8 (4.4%)
Grade 5 Events	(n=4)			(n=8)		
As scored by institution No significant difference	2 Pulmonary 1 Thrombosis 1 Death NOS			2 Pulmonary 1 Thrombosis 1 Upper GI Hemorrhage 1 Pulmonary Hemorrhage 1 Pneumonia NOS 1 Esophageal 1 Death NOS		

Bradley et al., *Lancet Oncology* 2015

RTOG 0617 – Dose escalation

Local failure rate at 18 months post-treatment:

60 Gy	74 Gy
25.1%	34.4%

Does this make sense?

Reasons?

Bradley et al., *Lancet Oncology* 2015

RTOG 0617 – Dose escalation

Local failure rate at 18 months post-treatment:

60 Gy	74 Gy
25.1%	34.4%

Does this make sense?

Reasons?

Minimum margin was smaller in the high-dose group (mean 4·5 mm [2·9] in the standard-dose group *vs 3·9 mm [3·0] in the high-dose group; p=0·0047)*

Bradley et al., *Lancet Oncology* 2015

RTOG 0617

ARE THE RESULTS OF RTOG 0617 MYSTERIOUS?

JAMES D. COX, M.D.

Division of Radiation Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX

74Gy compared to 60Gy is **neither safe nor effective** for the patient population and using the technology of RTOG 0617

Bradley et al., *Lancet Oncology* 2015

Interpretation of RTOG 0617

Technology	Study protocol
FDG-PET	encouraged, not mandatory
4D-CT	highly, encouraged not mandatory
IMRT	optional

74Gy feasible in the study patient population with the technology above?

- Violation OAR constraints?
- Smaller than necessary target safety margins?
- Experience in the centers?
- Necessary to „boost“ all macroscopic tumor?

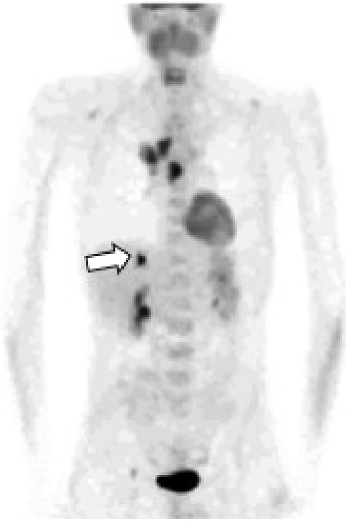
Outline

1. Staging & patient selection
2. Tumor characterization
3. Normal tissue characterization
4. Target volume definition
5. Treatment delivery
6. Response assessment

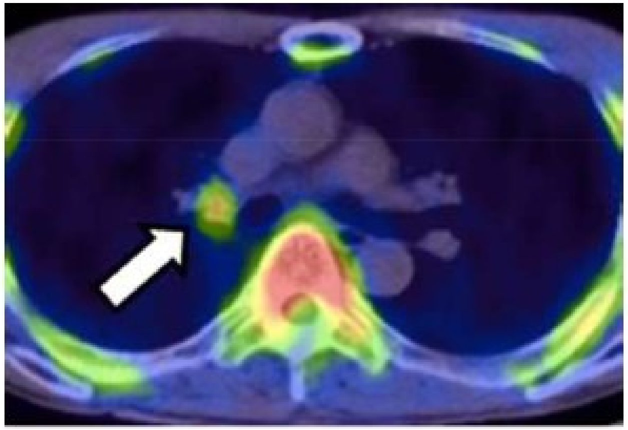
Staging and patient selection – FDG-PET

Staging of

Distant metastases

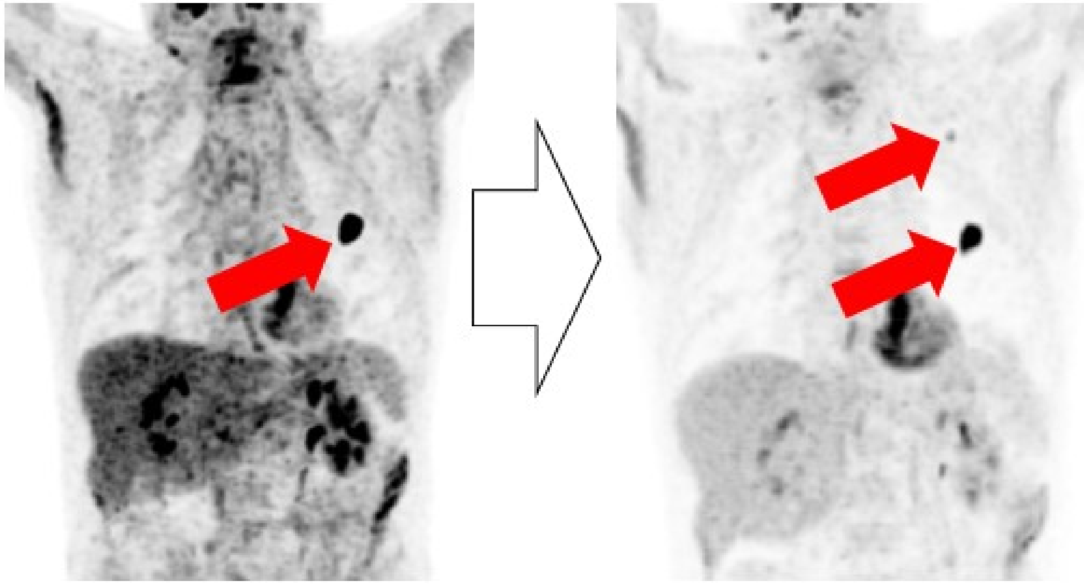


Nodal metastases



FDG-PET provides important information to select patients for high precision radiotherapy

Staging and Patient Selection: Disease Progression



6 weeks

Median 23 days (max 176)

Progression to stage IV:

3 / 21 patients

Mac Manus Radiat Oncol 2013

Repeat Staging!
What time interval?

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Staging and Patient Selection: FDG-PET

Results of a prospective study: locally advanced NSCLC

CT staging	PET-CT staging	Outcome
76 patients	50 radical RT possible	OS 78% @ 1a
	26 radical RT **not** possible	OS 16% @ 1a

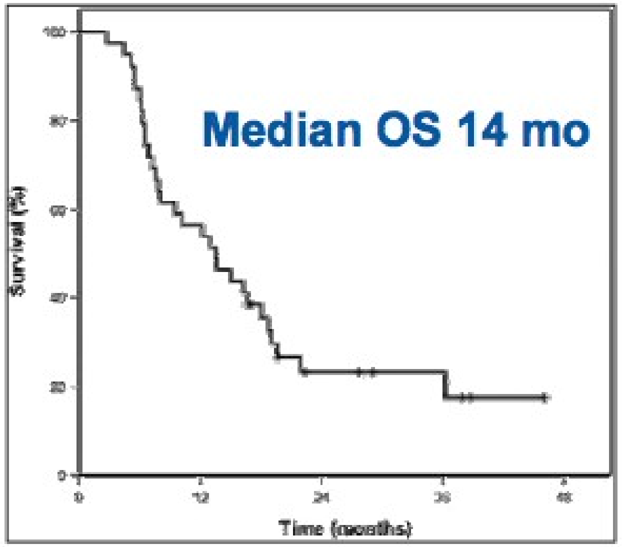
Mac Manus Radiat Oncol 2013

FDG-PET detected metastases in 12/76 patients
Treatment intent changed from curative to palliative

Staging and Patient Selection: Advanced disease

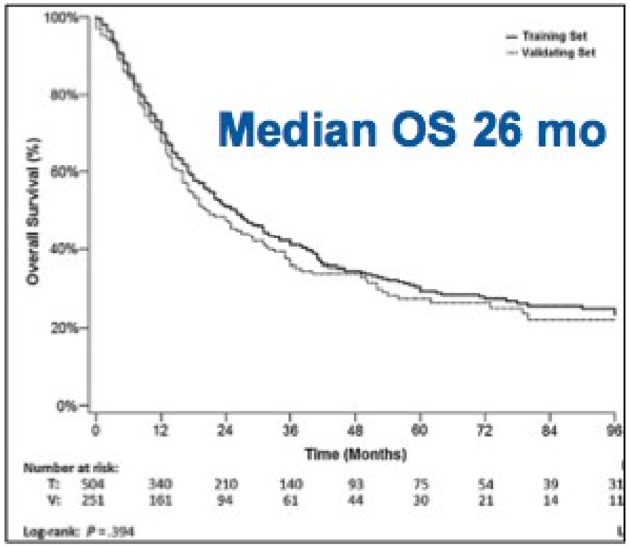
Radical treatment DESPITE stage IV disease

Prospective phase II trial: n=39



De Ruysscher JTO 2012

Multicenter analysis: n=757

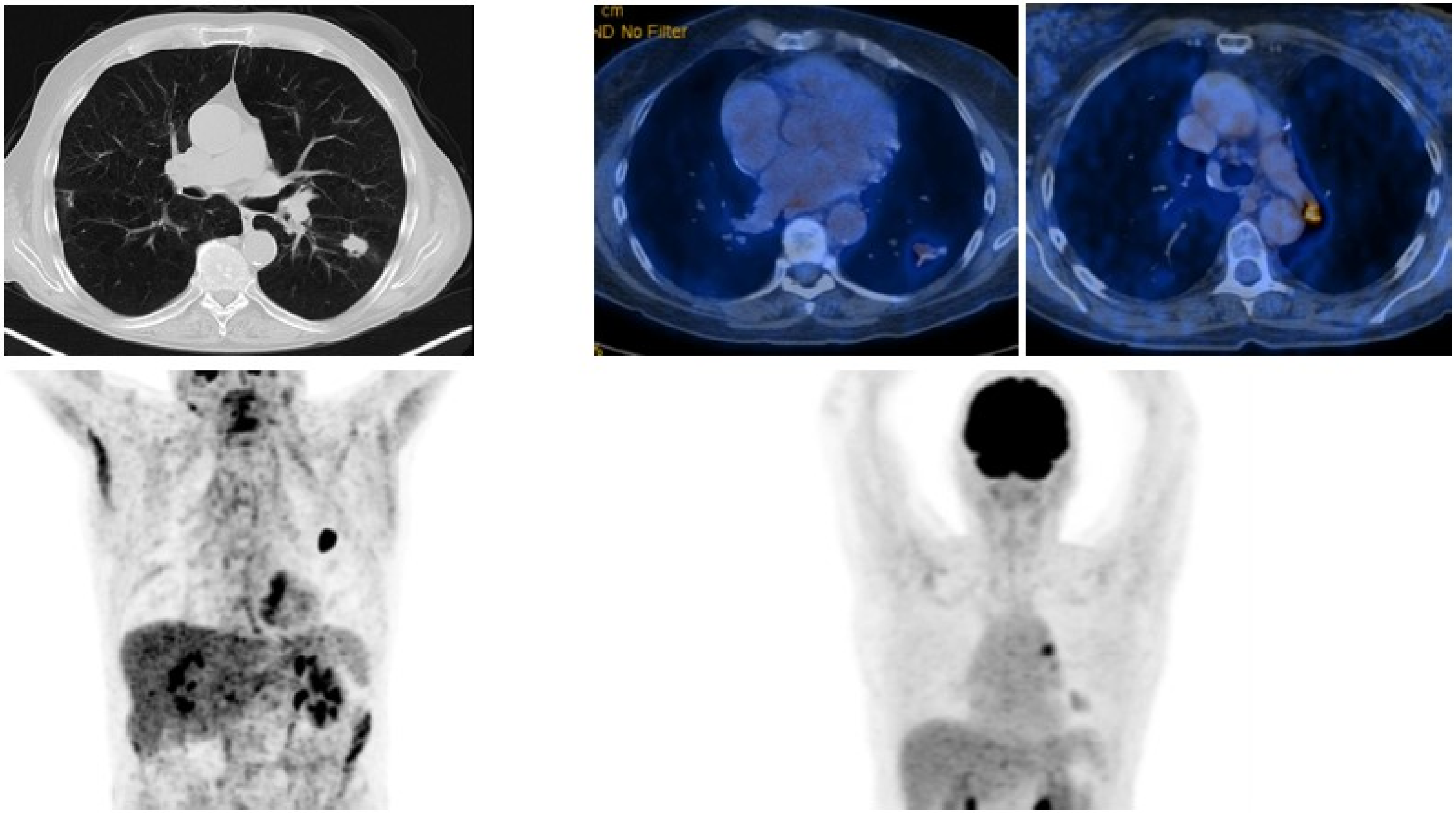


Palma Clinical Lung Cancer 2014

Overall survival similar to Stage III NSCLC

Careful patient selection

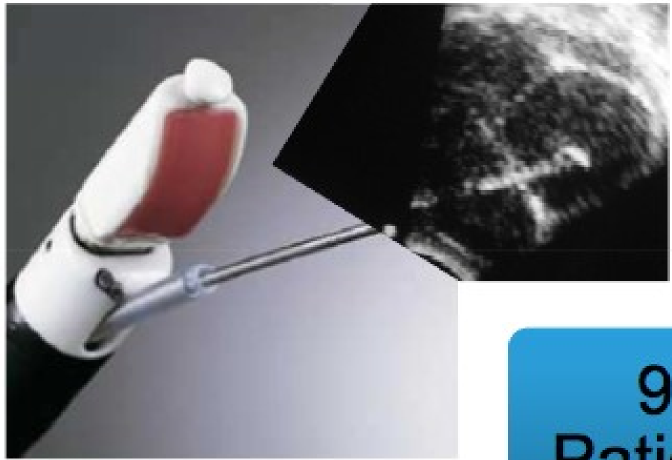
Nodal Staging in Stage I NSCLC



Nodal failure after local treatment with SBRT
Rates similar to surgical series (~10%)

Nodal Staging in Stage I NSCLC: EBUS

EBUS for staging of CT and FDG-PET N0 disease



- Systematic imaging of mediastinum and hilar regions (stations 2, 4, 7, 10, 11)
- Puncture of all visualized nodes with a size of 5 - 10mm

97 Patients → 156 LN biopsied → N+ 8 / 97 patients

Herth CHEST 2008

EBUS requires experienced providers, more common now
Pathologic "confirmation" of ultrasound imaging

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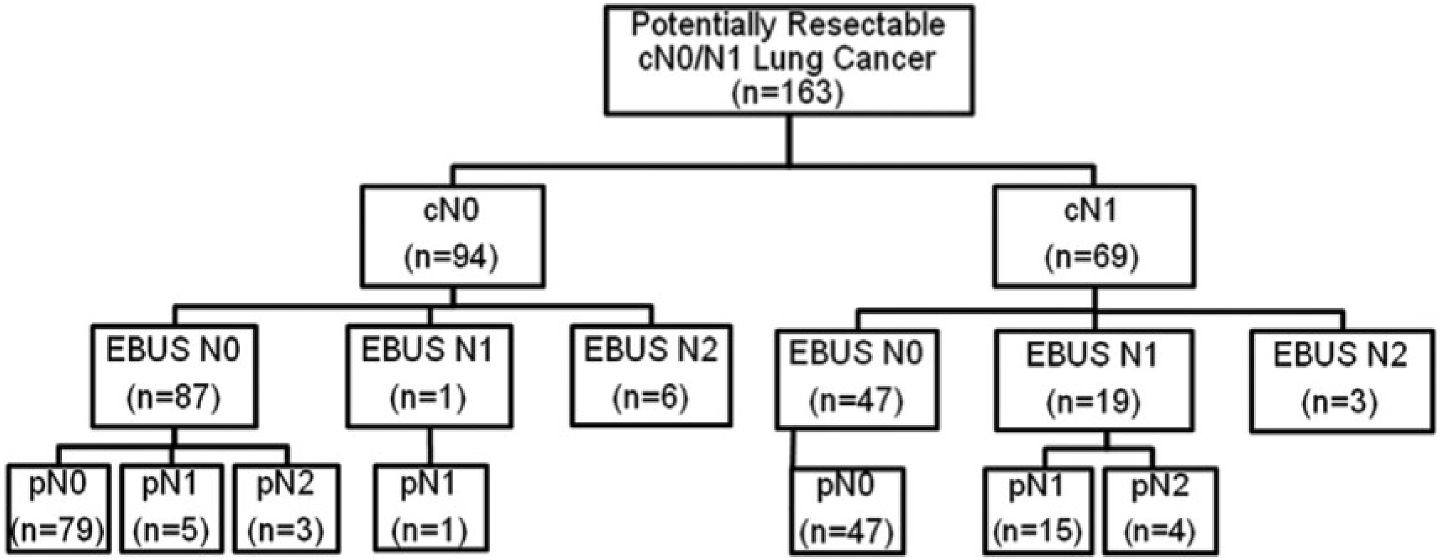
Nodal Staging in Stage I NSCLC: EBUS

CT/PET negative patients planned for lobectomy



Differentiating N0 from N1
Sensitivity: 76%, Specificity: 100%
Accuracy: 96%, NPV: 96%

Yasufuku et al., *Ann Thorac Surg, 2013*

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Elective nodal irradiation in N+ disease

Study	# of patients	Isolated regional failure
Graham 1995	179	8%
Kong 2005	106	6%
Rosenzweig 2001	171	6.4%
Senan 2002	50	0
De Ruysscher 2005	44	2%
Belderbos 2006	67	3%
Rosenzweig 2007	524	6.1%

Randomized trial of ENI (60-64Gy) and IF (68-74Gy) N=200

Patients in the IF arm had significantly
- Increased local control and no increased regional failure
- Decreased rates of pneumonitis
- A trend to improved OS

Yuan American Journal of Clinical Oncology 2007

Elective nodal irradiation in N+ disease

Practical considerations of selective nodal / involved field RT

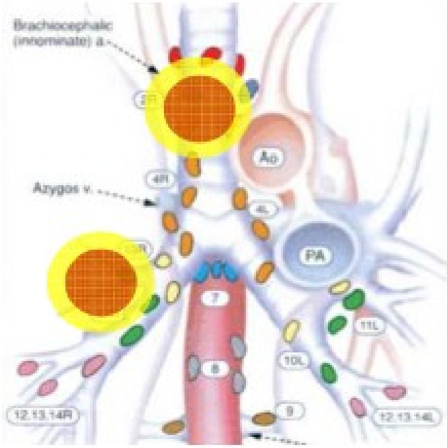
Study	CT criteria	FDG-PET
Graham 1995	≥ 1cm	-
Kong 2005	≥ 1cm	-
Rosenzweig 2001	≥ 1.5cm	-
Senan 2002	-	-
De Ruysscher 2005	1cm	„increased uptake“
Belderbos 2006	-	„increased uptake“
Rosenzweig 2007	≥ 1.5cm	„increased uptake“

➢ **No standard how to define an involved lymph node**

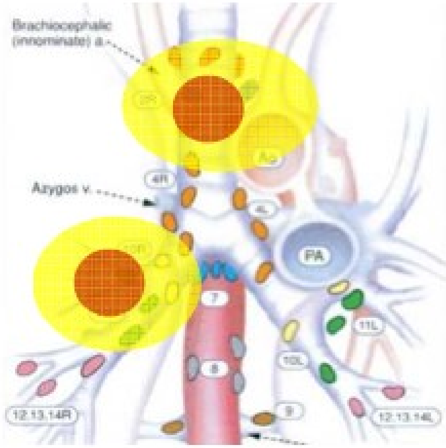
Nodal staging/treatment

Practical considerations of selective nodal / involved field RT

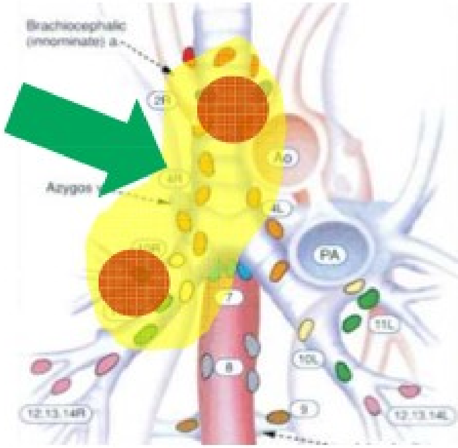
Involved node



Involved station



Involved station +



➢ **No standard how to define an involved lymph node**

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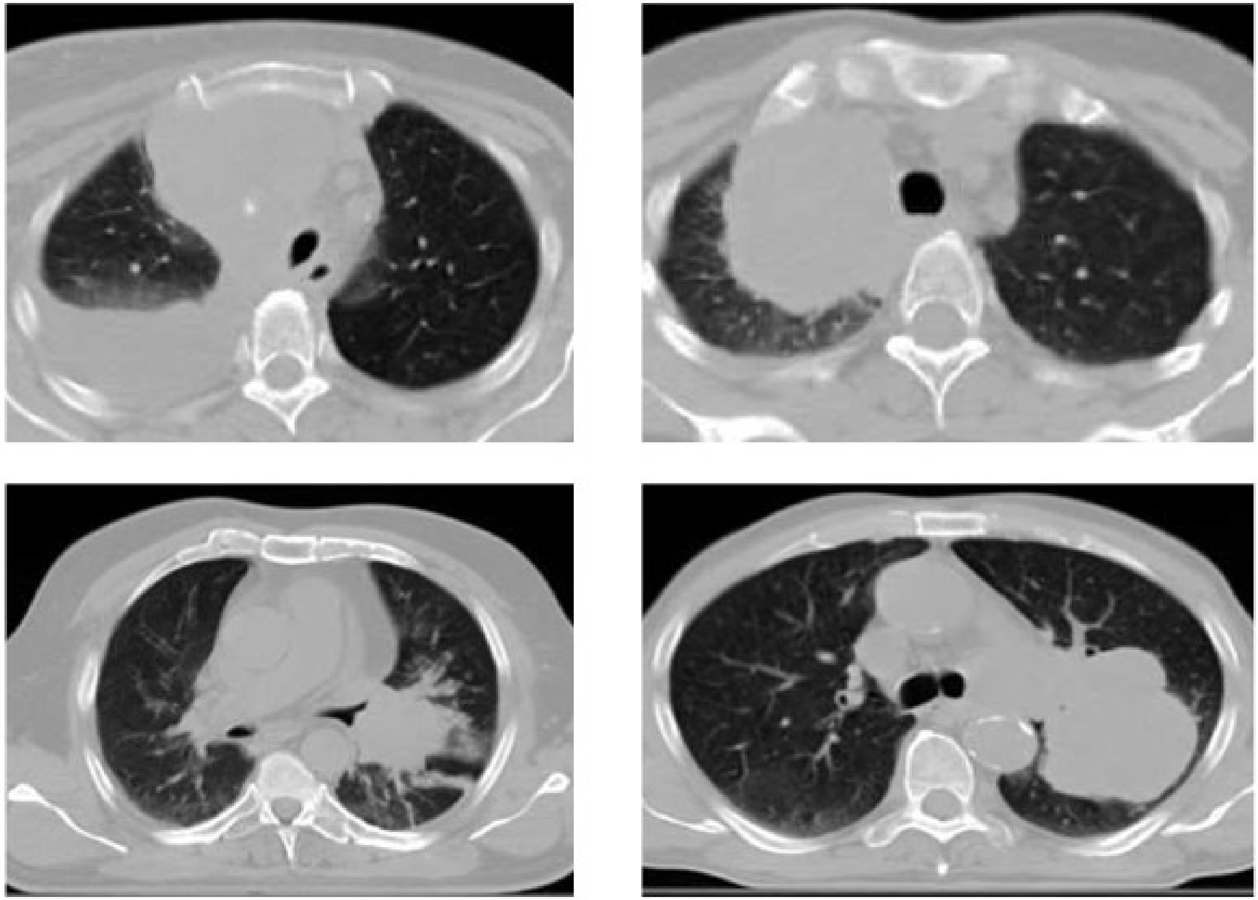
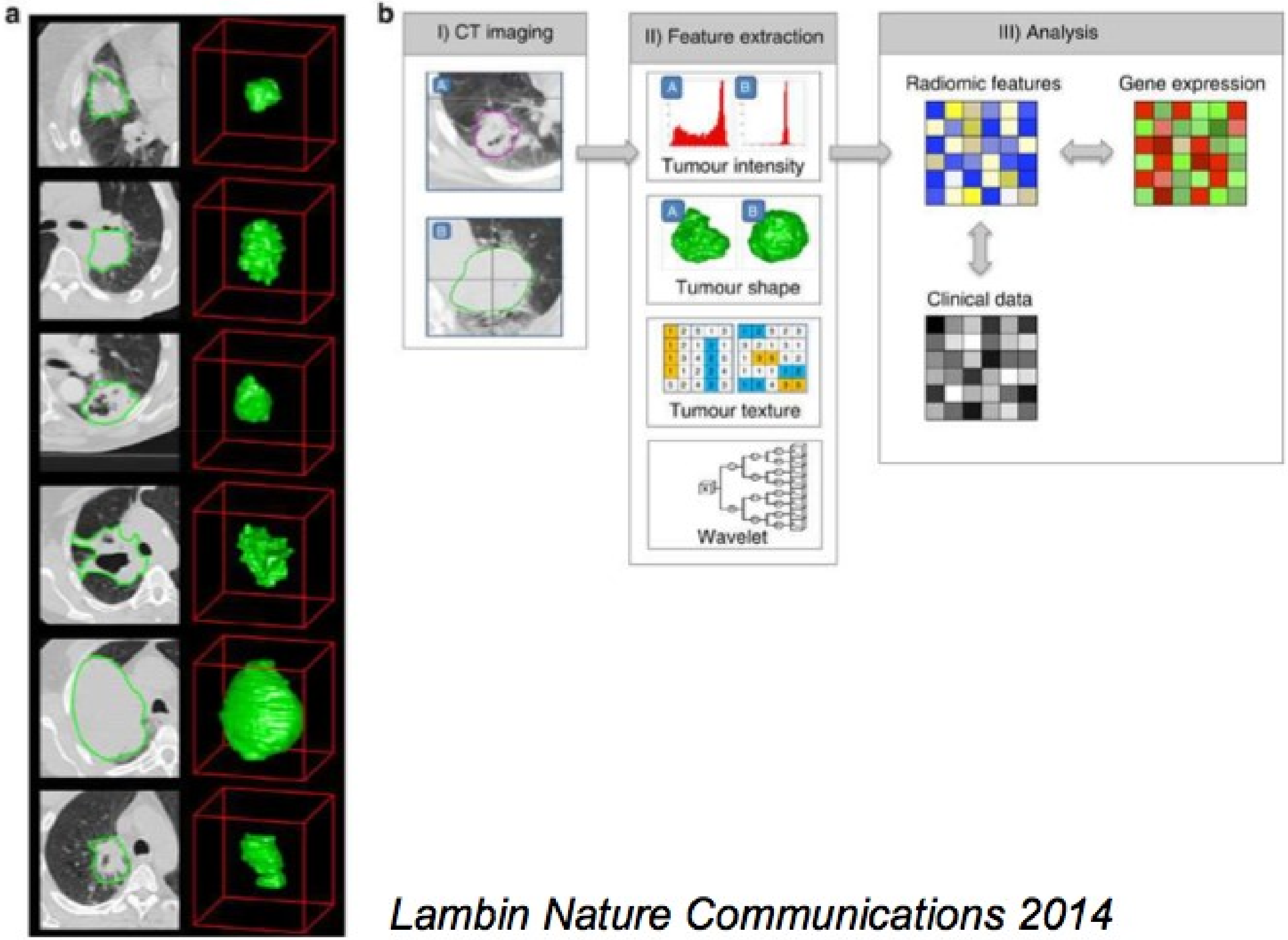
Tumor characterization: Radiomics



Different lung tumors look different!

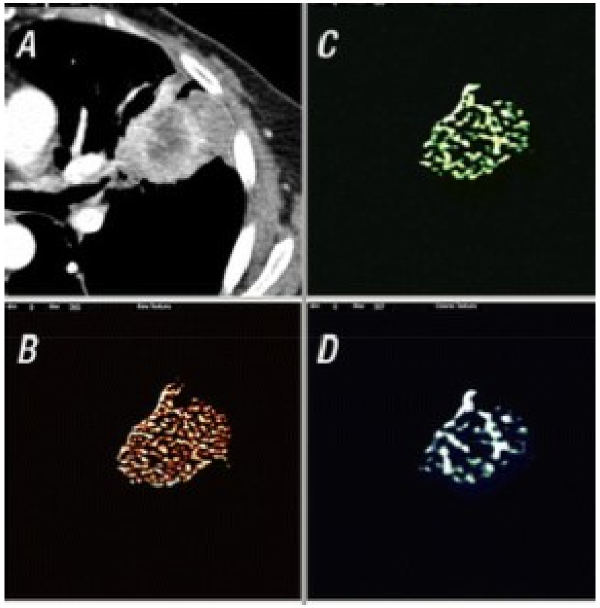
Tumor characterization: Radiomics



Lambin Nature Communications 2014

Tumor characterization: Radiomics

CT texture analysis



Ganeshan Radiology 2013

CT textures correlated with …

… histopathological tumor characterization:

- Tumor staining with pimonidazole
- Glut-1 expression

Ganeshan Radiology 2013

- Microscopic disease extension

Salguero Radiother Oncol 2013

➢ Loco-regional recurrence after SBRT

Salguero Radiother Oncol 2013
Mattonen Med Phys 2014

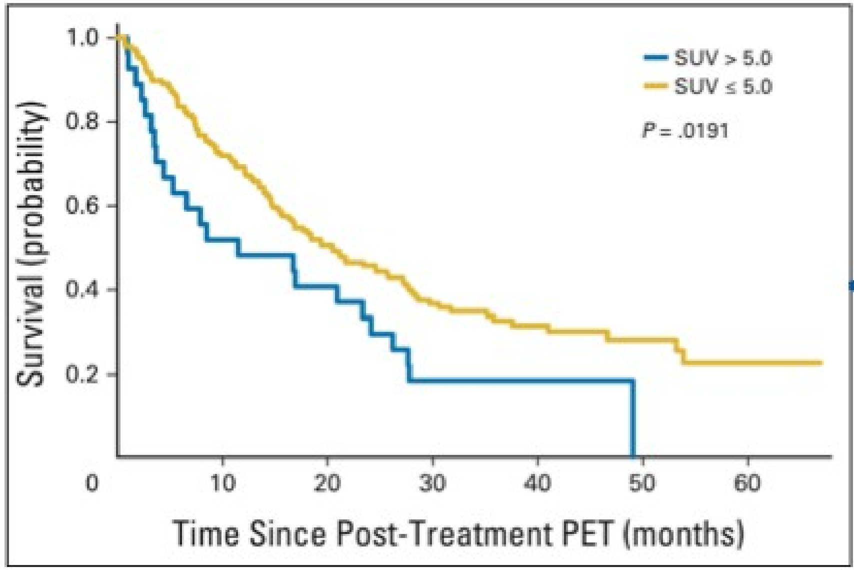
➢ Overall survival after RCHT

Fried IJROBP 2014

Most reports use 'standard' CT
Standardization and validation required

Tumor characterization: FDG-PET

Post-treatment FDG-PET



Machtay JCO 2013

Pre-treatment FDG-PET

Aerts Radiother Oncol 2009
Shusharina IJROBP 2014

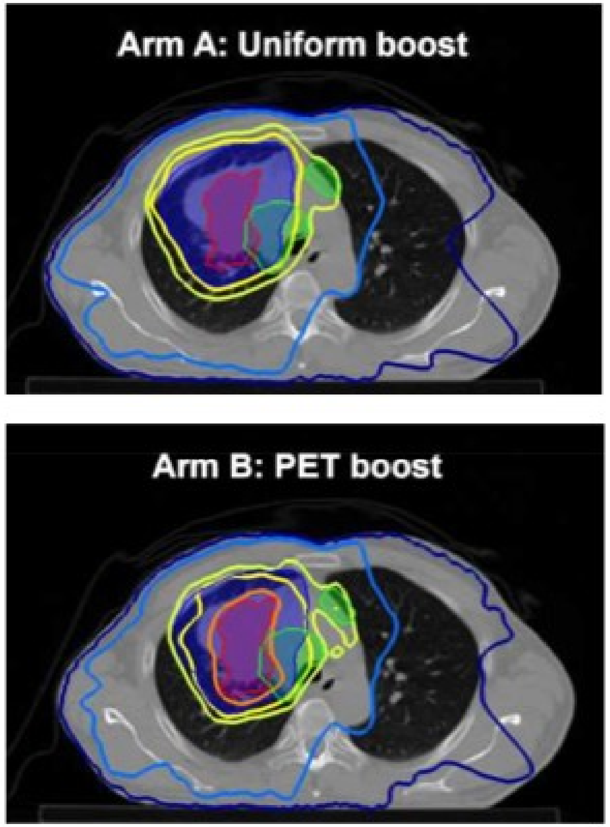
Mid-treatment FDG-PET

Kong JCO 2007

Residual FDG-PET activity associated with worse LC/OS

FDG-PET at early time-points (during treatment?) may be associated with outcomes

Tumor characterization: FDG-PET



Van Elmpt Radiother Oncol 2012

Pre-treatment FDG-PET

Homogeneous boost	PET-Boost
79Gy	87Gy

Van Elmpt Radiother Oncol 2012

Mid-treatment FDG-PET

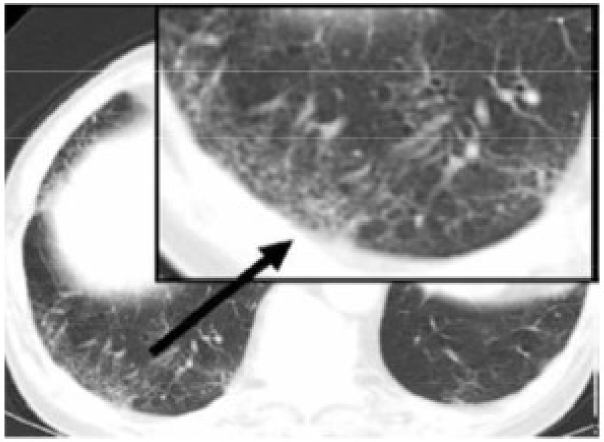
CT volume decrease	PET volume decrease
- 26%	- 44%

Feng IJROBP 2009

Boost limited to areas of high FDG-PET activity
Multiple on-going prospective studies

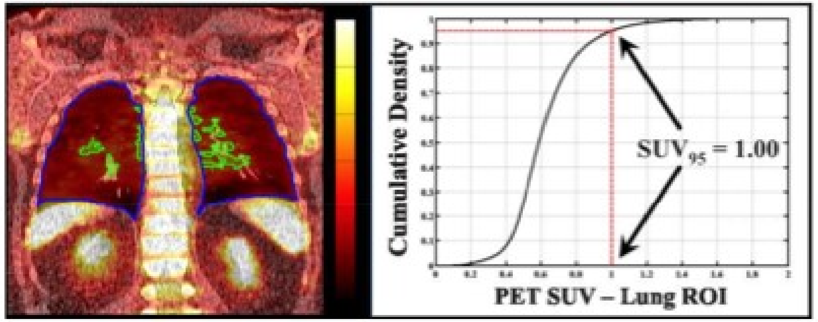
Normal Tissue Characterization

Interstitial pulmonary fibrosis



Increased risk (26% vs 3%) of RP
Sanuki J. Radiat. Res. 2012

Pulmonary FDG uptake



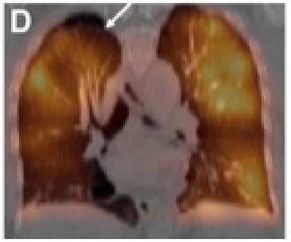
Increased risk in high FDG uptake lung volumes, especially when exposed to RT
Petet IJROBP 2012, Castillo Radiat Oncol 2014

Normal Tissue Characterization

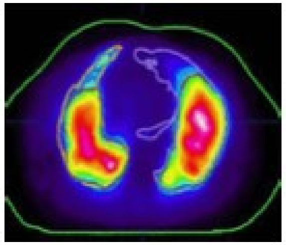
Regional lung function

Perfusion

SPECT

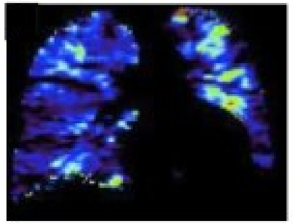


PET



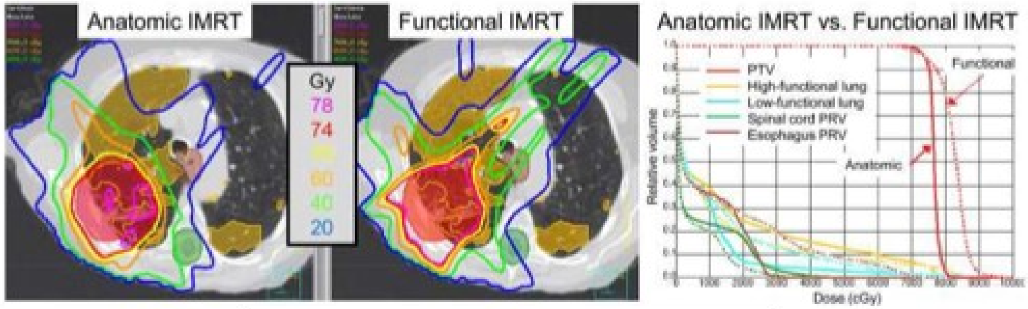
Ventilation

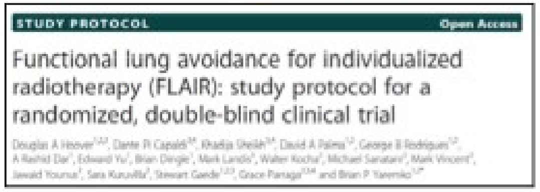
4D-CT



^{3}He MRI

Adaptive planning





STUDY PROTOCOL — Open Access

Functional lung avoidance for individualized radiotherapy (FLAIR): study protocol for a randomized, double-blind clinical trial

- Dose re-distribution from functional to non-functional lung tissue

McGuire IJROBP 2006; Shioyama IJROBO 2007; Yamamoto IJROBP 2010

Hard to implement as ‘bad’ lung tissue isn’t always in the same location day to day.

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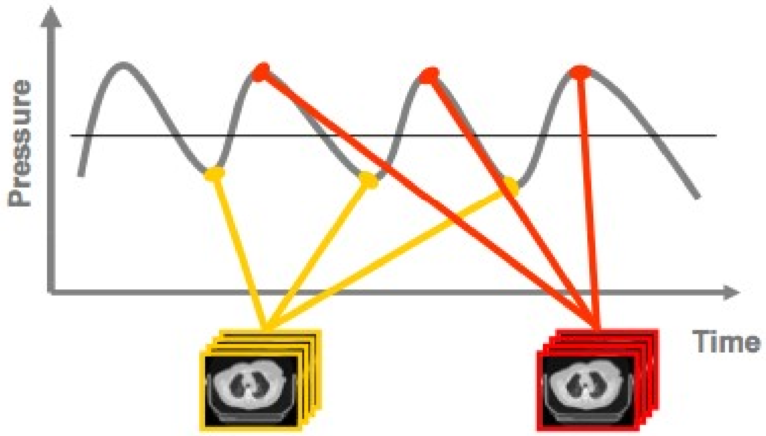
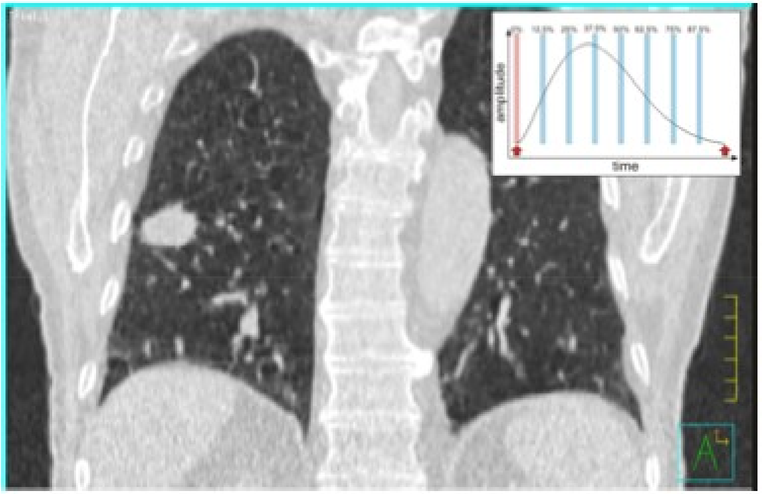
Target Volume Delineation – 4DCT

Respiration correlated 4D-CT





Patient specific motion analysis
Selection of appropriate motion management strategy

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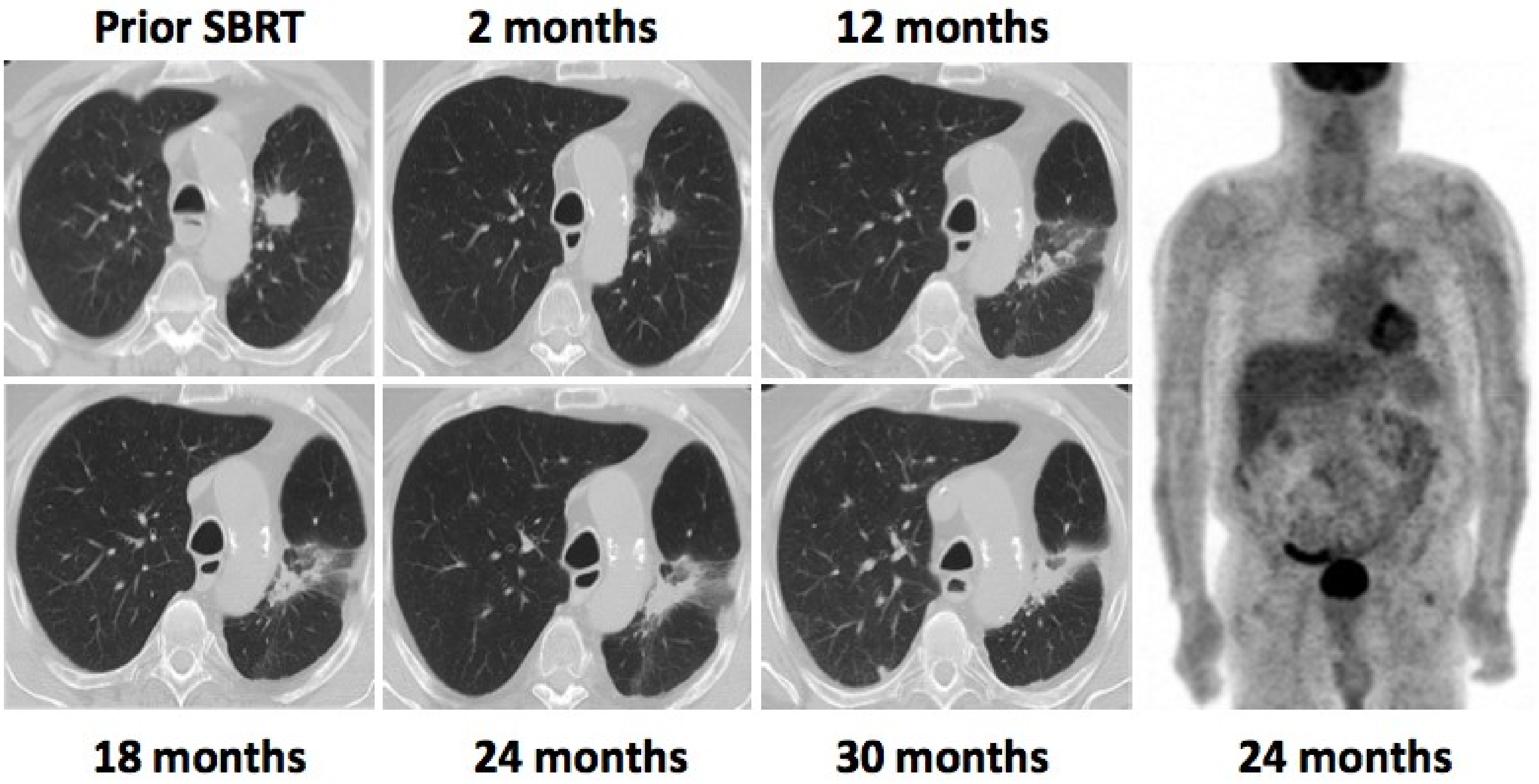
Follow-up imaging and response assessment



Normal tissue reaction vs. local failure?

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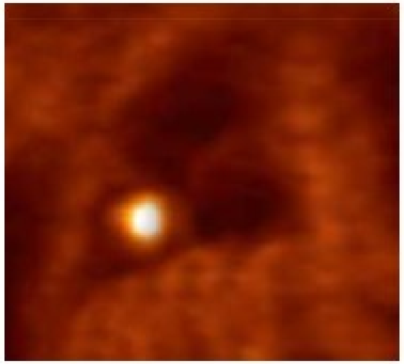
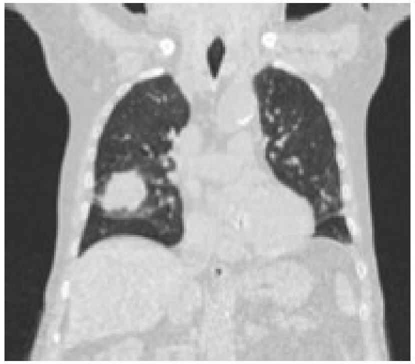
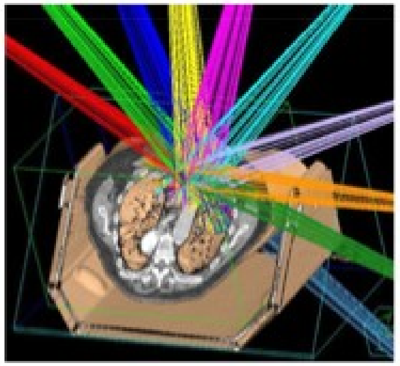
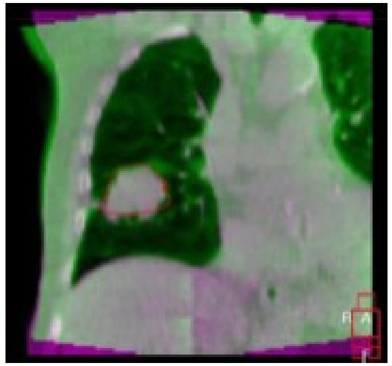
Stereotactic Body radiation therapy (SBRT)

Combination of different high precision radiotherapy techniques

Staging LK Status	4D target volume definition	Highly conformal treatment planning	Image guided radiotherapy

Safe dose escalation to maximize local control

SBRT for early stage NSCLC

SBRT compared to conventionally fractionated RT

CF-RT

Study	Year	Local control
Hayakawa	1999	76%
Jeremic	1997	37%
Kaskowitz	1993	50%
Krol	1996	32%
Morita	1997	56%
Nguyen-Tan	1998	59%
Sandler	1990	57%
Sibley	1998	78%
Slotman	1996	94%

60%

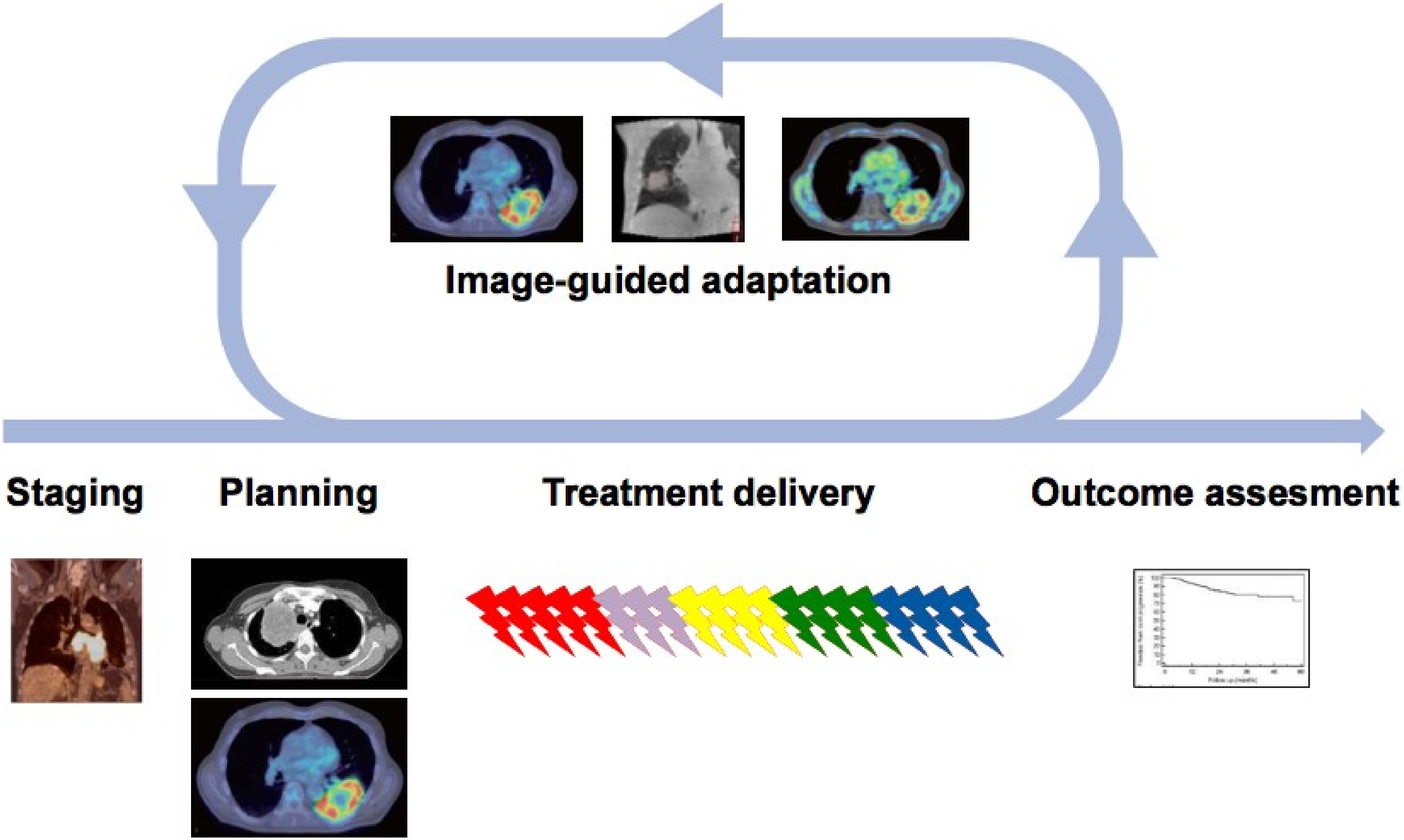
SBRT

Study	Year	Local control
Nagata	2005	98%
Baumann	2009	92%
Fakiris	2009	88%
Ricardi	2010	88%
Bral	2010	84%
Timmerman	2010	98%

90%

SBRT: Higher LC and higher OS

Imaging in the RT process for NSCLC



In-room image guidance: seeing the tumour

At Rigshospitalet

For all locally-advanced NSCLC patients

3D PET/CT with IV contrast

4D CT + short breath hold CT

- Contrast if central tumour

Visual review of the 4D CT (by a dosimetrist):

- if < 5mm peak-to-peak motion, plan on the PET/CT, where contouring is most reliable
- if > 5 mm peak-to-peak motion : MidVentilation

Occasional use of the ITV approach (e.g. if too many artifacts)

In-room image guidance

Modalities

- Field light
- EPID
- kV verification imaging
- In-room CT/CBCT

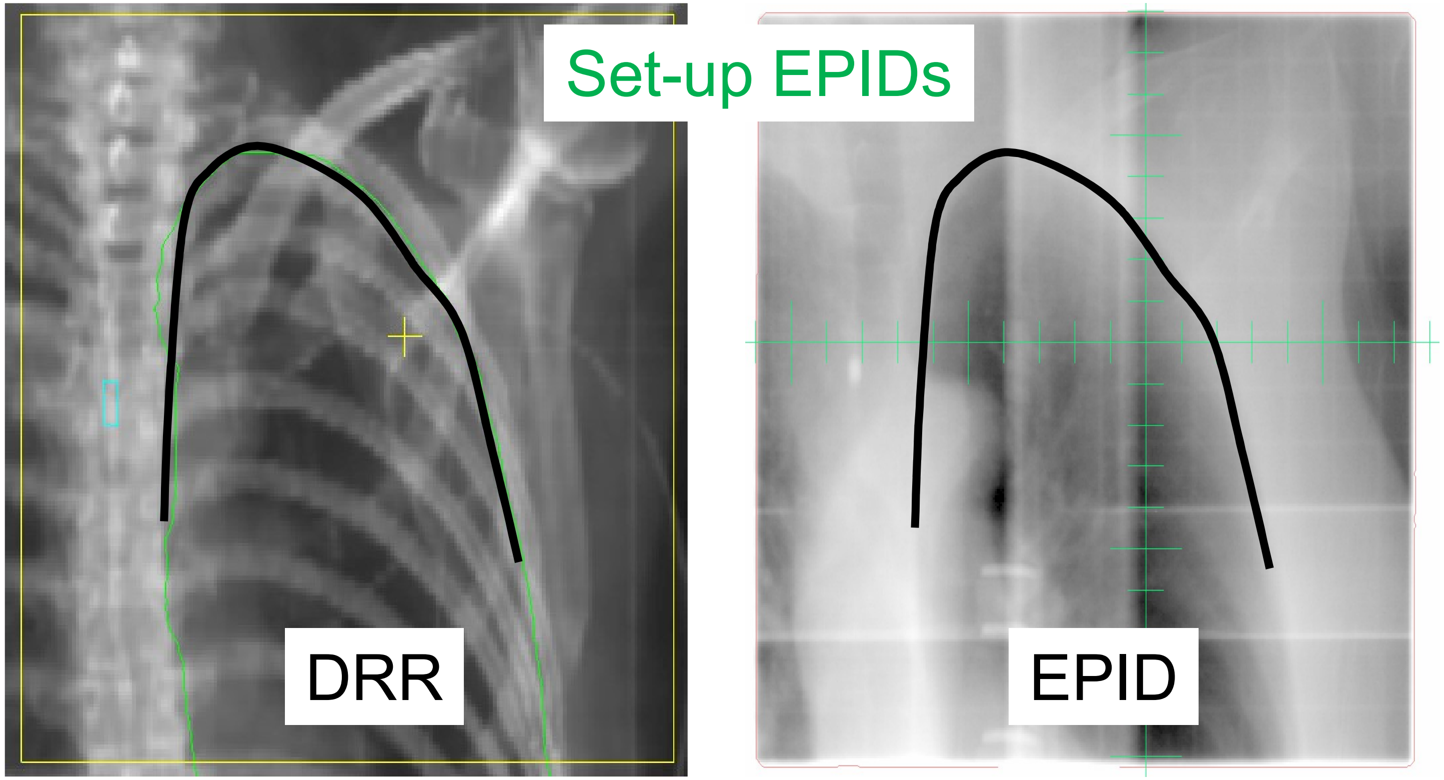
Goals

- **Inter-fraction imaging**
  - Reproducibility of patient positioning
  - Reproducibility of organ / target positioning
  - Adaptive planning
- **Intra-fraction imaging**
  - Catching intra-fraction baseline shifts

1. Field light / surface markers/surface matching

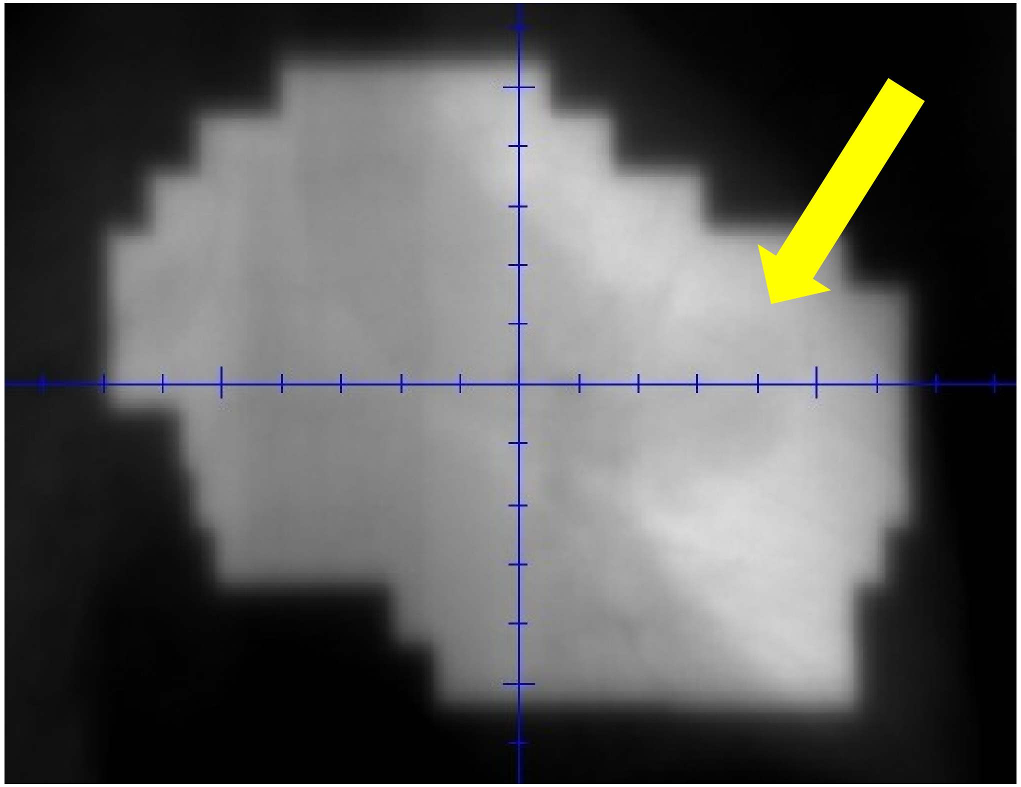
Verification that correct patient on the couch
Set-up verification of external target volumes (skin cancer…)

2. Electronic portal images (set up)



Pros: Large images with suitable anatomical landmark structures
Cons: Landmark structure might not be representative for target

2. Electronic portal images (field or cine mode)

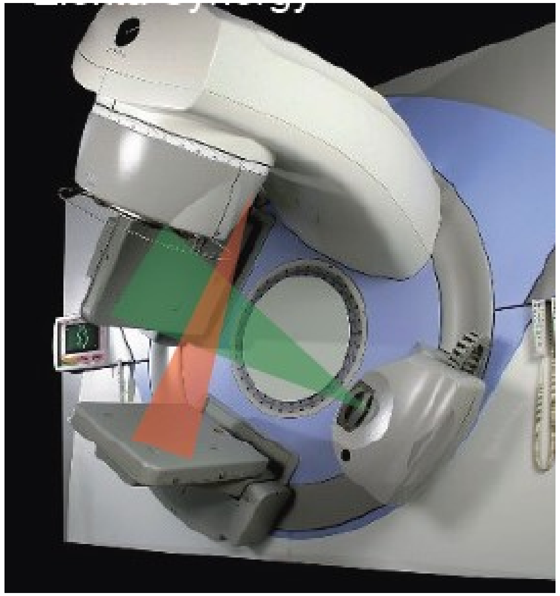


- ”on flight” images
- NB: mostly if 3D- CRT planning

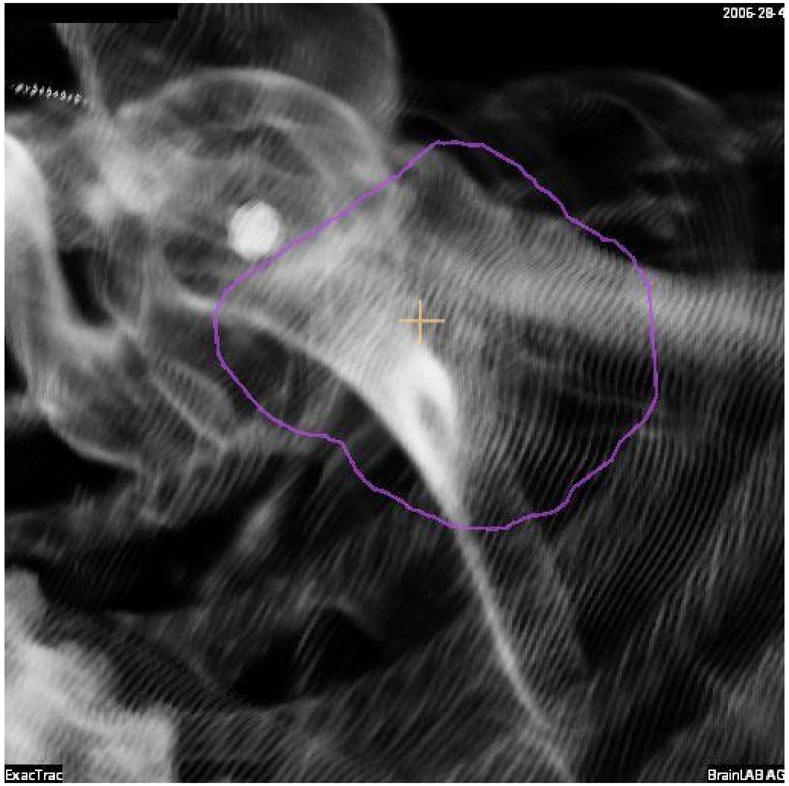
Pros:	No additional patient dose;
	Pulmonary tumor sometimes visible itself
Cons:	Difficult to interpret when only limited landmark structures in field

In-room image guidance

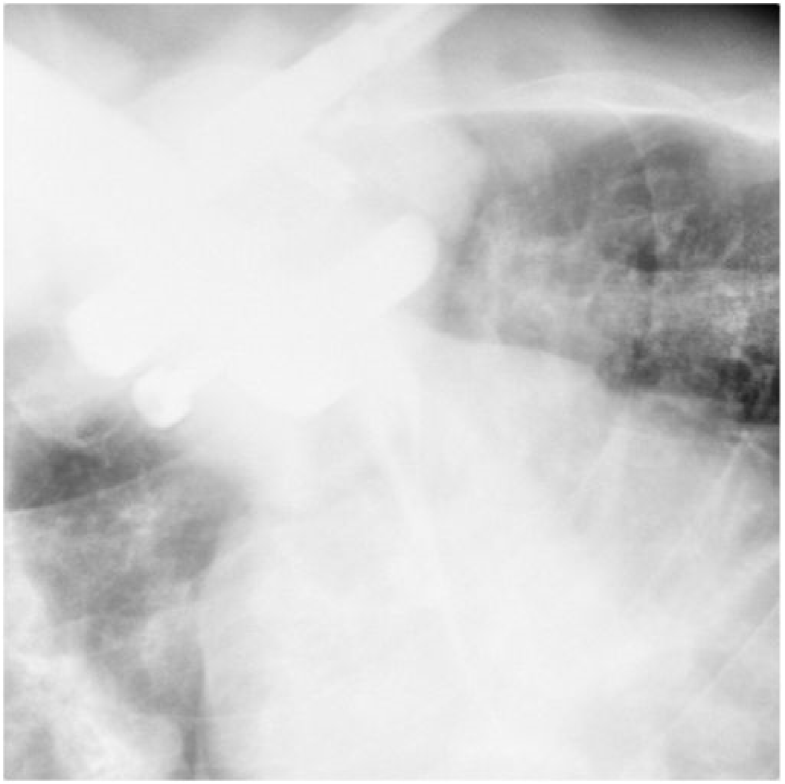
3. kV planar images



3. kV planar images



DRR image



kV image: better constrast than EPID… but still poor!

In-room image guidance

3. kV planar images

Markers required: poor soft-tissue contrast

•Surrogate, not the target itself

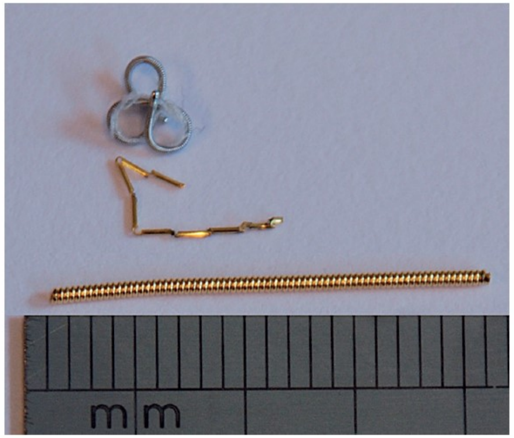
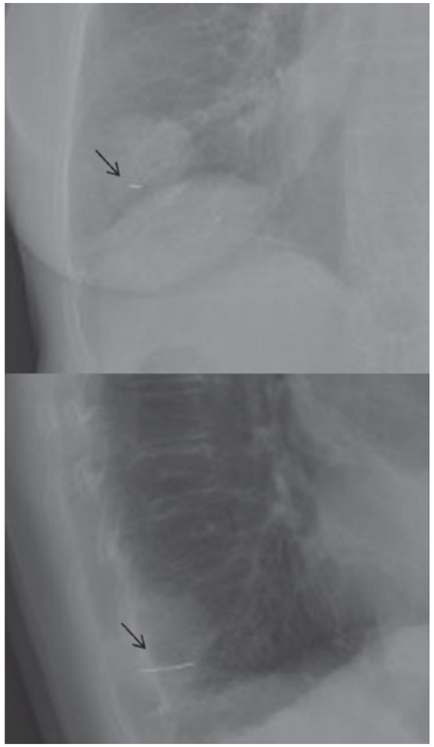


Figure 1. Photo showing the complex helical platinum marker (top), the Gold Anchor™ marker (middle) and the Visicoil™ gold marker (bottom).

4 out of 15 patients developped pneumothorax (transthoracic implantation)



Persson et al Acta Oncol 2012

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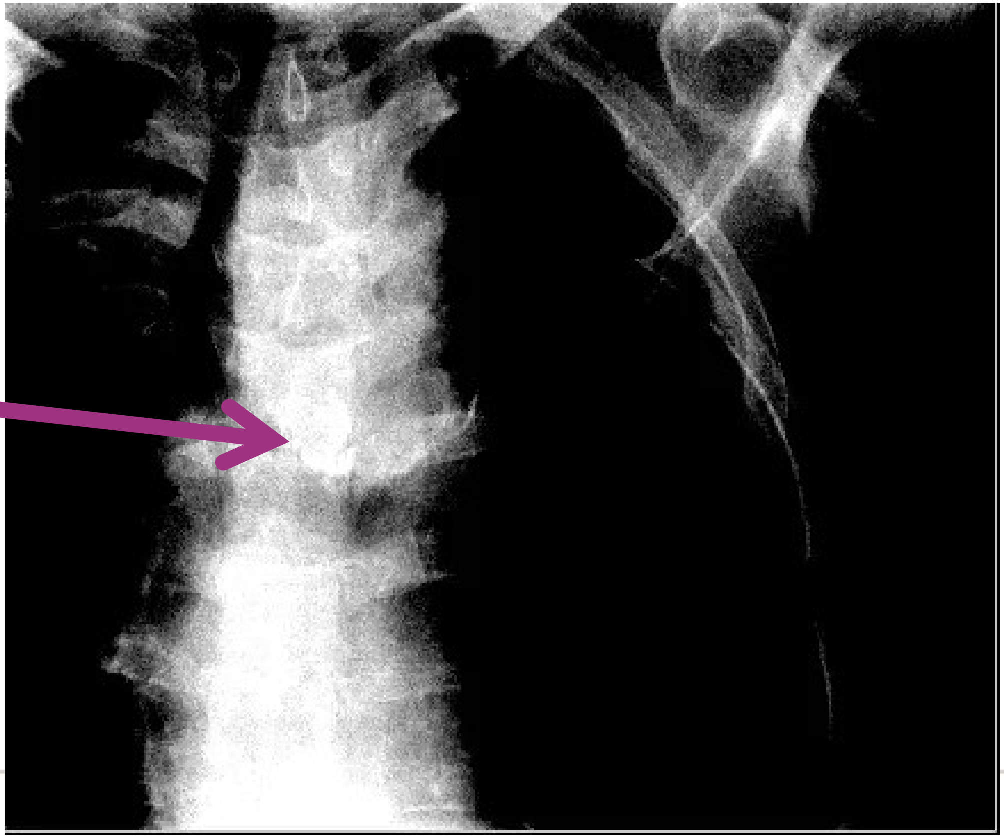
3. kV planar images

Markers required: poor soft-tissue contrast

•Surrogate, not the target itself



19 patients

broncoscopic Bioxmark^{TM}

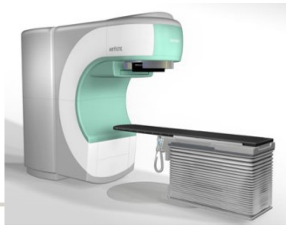
Can be implented in lymph nodes

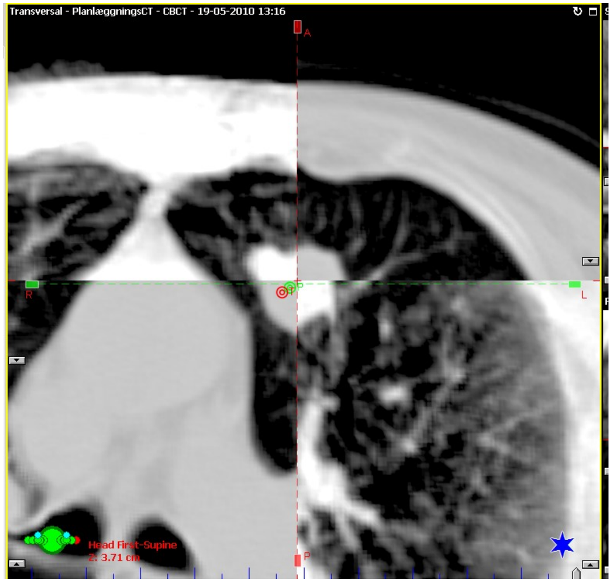
4. Volume imaging

In-room CT

beam

MV CT

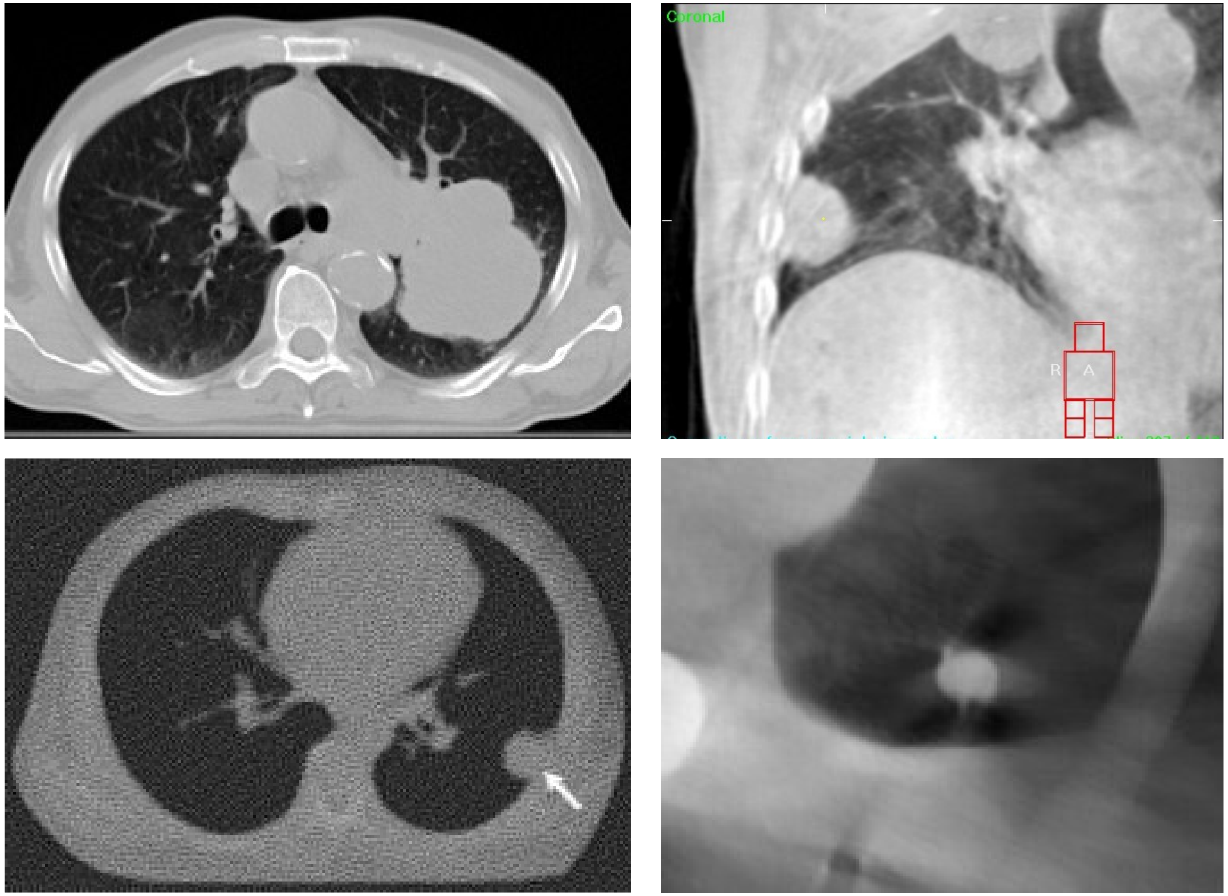




4. Volume imaging

Helical

kV CBCT



MV CT

kV/MV CBCT

- Intra-pulmonary targets clearly visible in all imaging modalities
- IQ for mediastinum suitable only in kV helical CT

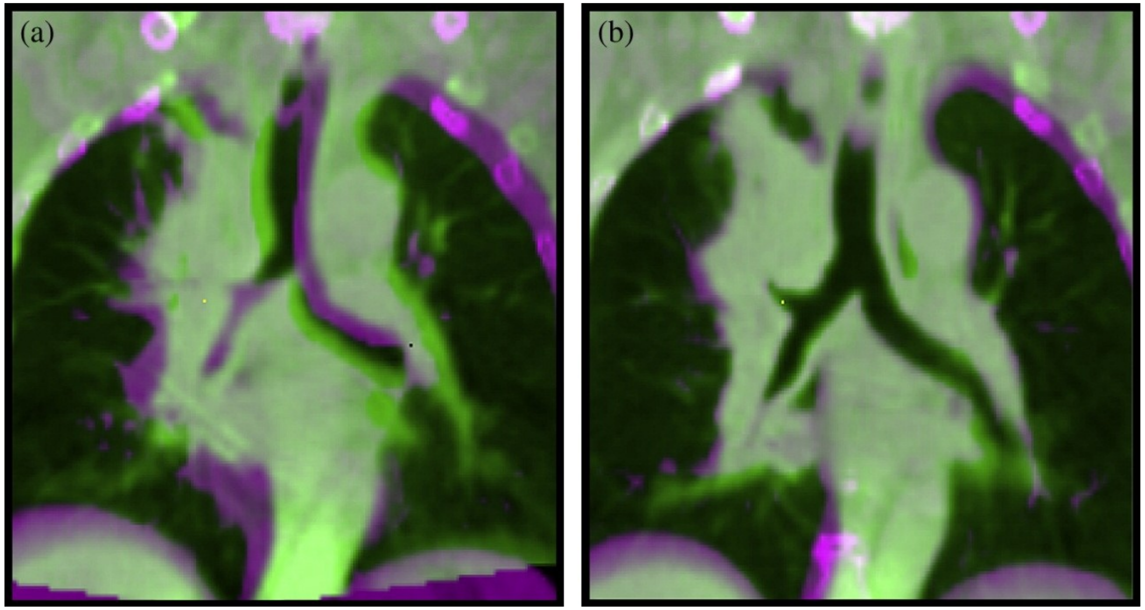
A side note: setting up according to landmarks

Spine vs Carina

Higgins et al (IJROBP 2009): feasible, better inter-observer agreement with match on the carina

Lavoie et al (IJROBP 2012): especially node coverage is improved

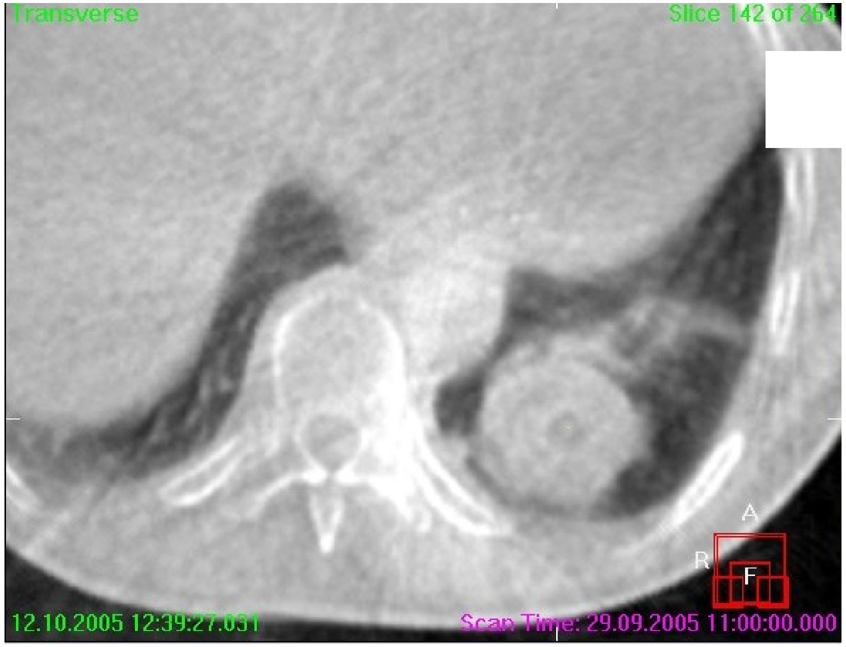
Schaake et al (IJROBP 2014): reduced LN margins if match on carina instead of bones



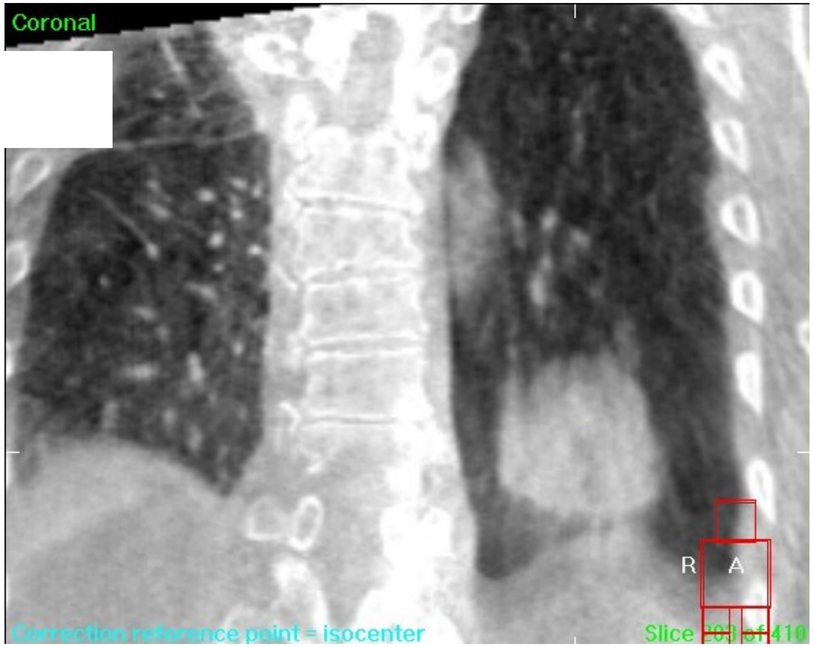
Spine match Carina match

In-room image guidance

4. Volume imaging



Lower lobe tumor
with large motion amplitude



Blurred target because of
long image acquisition time

Integration of 4th dimension into IGRT

Planning

Treatment

Manual contour registration

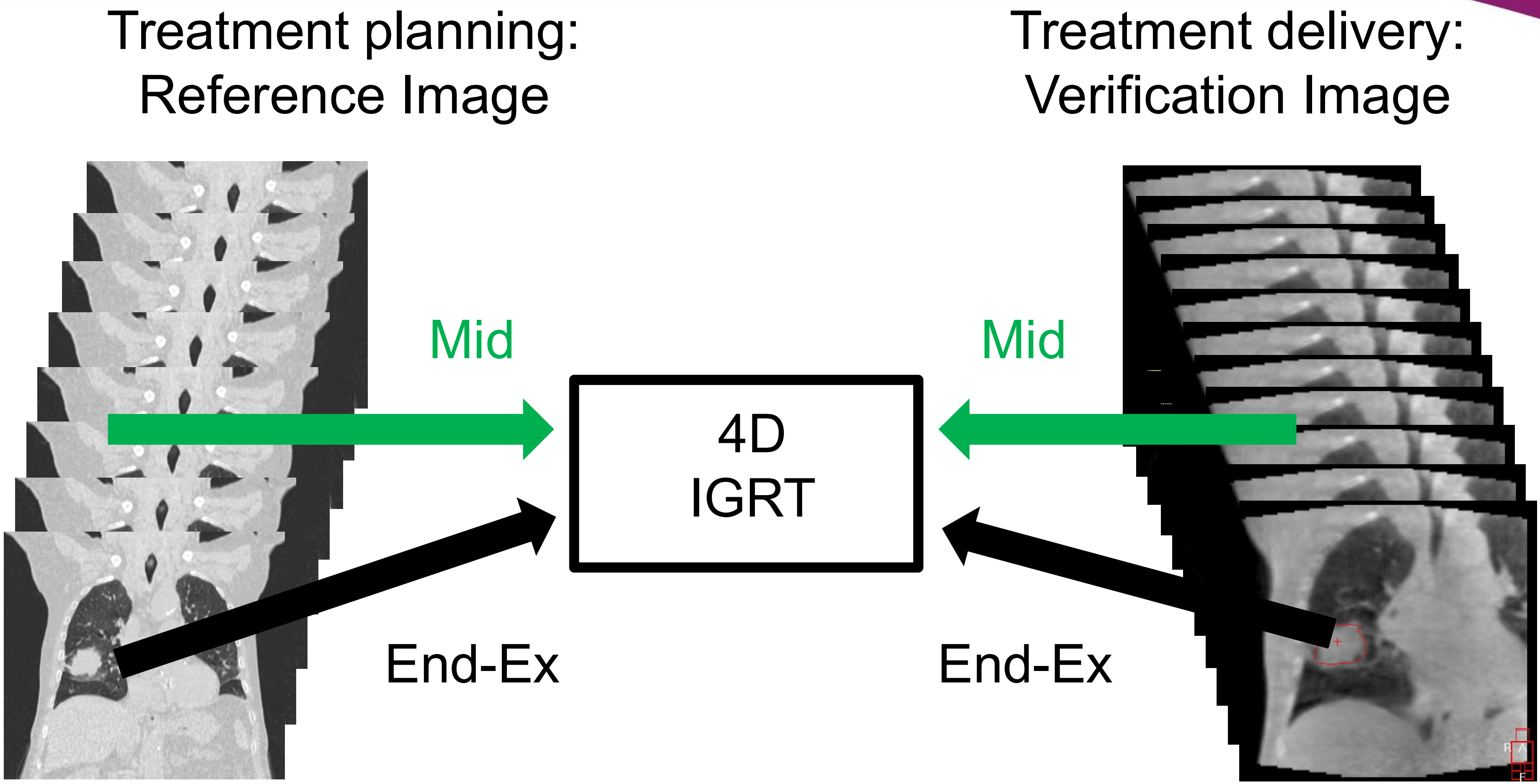
Respiration correlated CT

„Conventional“ slow CBCT

Guckenberger Acta Ocol 2006

NB: what you see is a pseudo ITV/midventilation

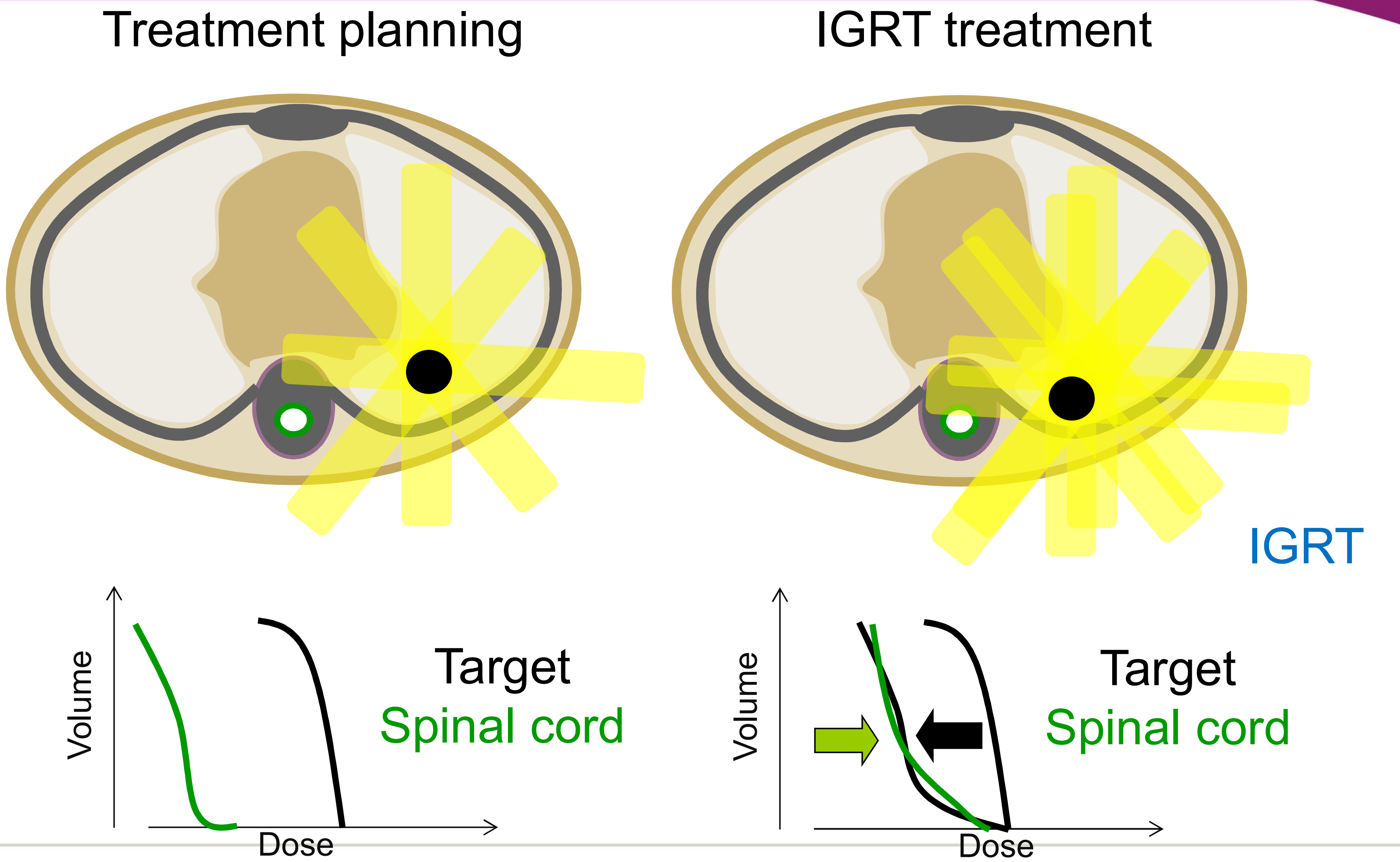
In-room image guidance



Possibility of matching a specific phase

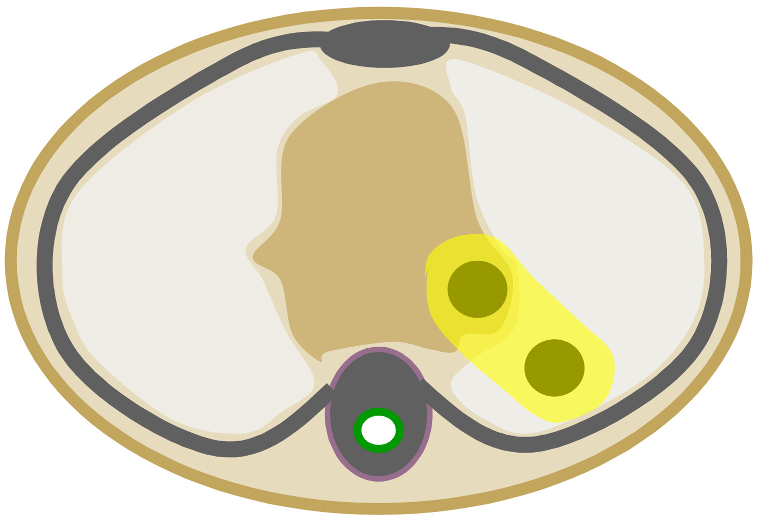
Interobserver variability reduced (Sweeney at al RO 2012)

Registration challenges (1)

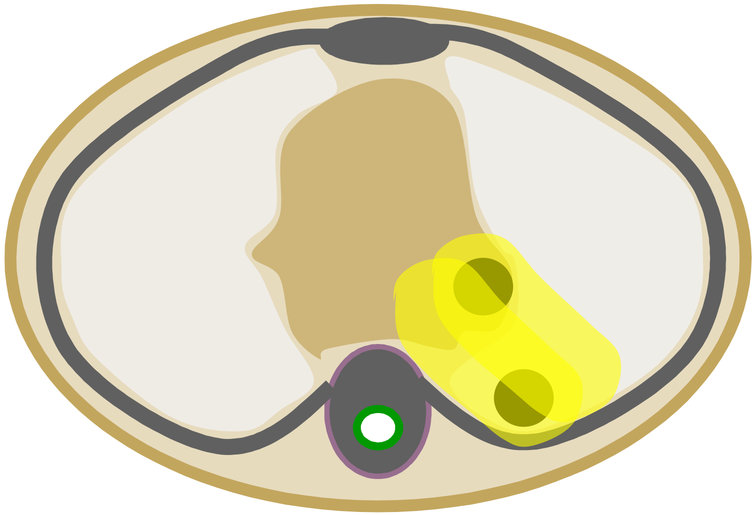


Matching challenges (2)

Treatment planning



IGRT treatment



Shift of the primary relative to the nodal target

- Volume imaging is required for visualization of the these effects
- Shifting the patient does not solve the problem

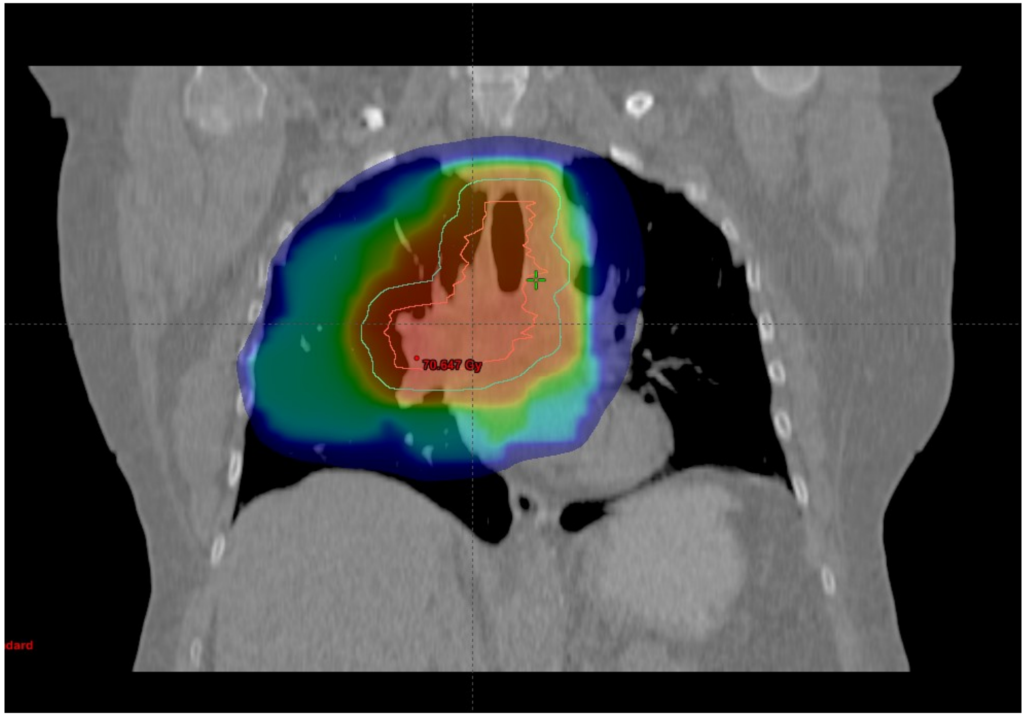
How to deal with these non-rigid changes of target volumes and organs at risk?

1. Volume image required to visualization
2. Quantification would require deformable image registration
   -> available but only offline
3. Online dosimetric evaluation would be required for a decision making process
   -> not available, yet
4. Compensation strategies:
   - Perform an average IGRT shift
   - Adapted PTV margins
   - Re-planning

Pre-treatment image guidance

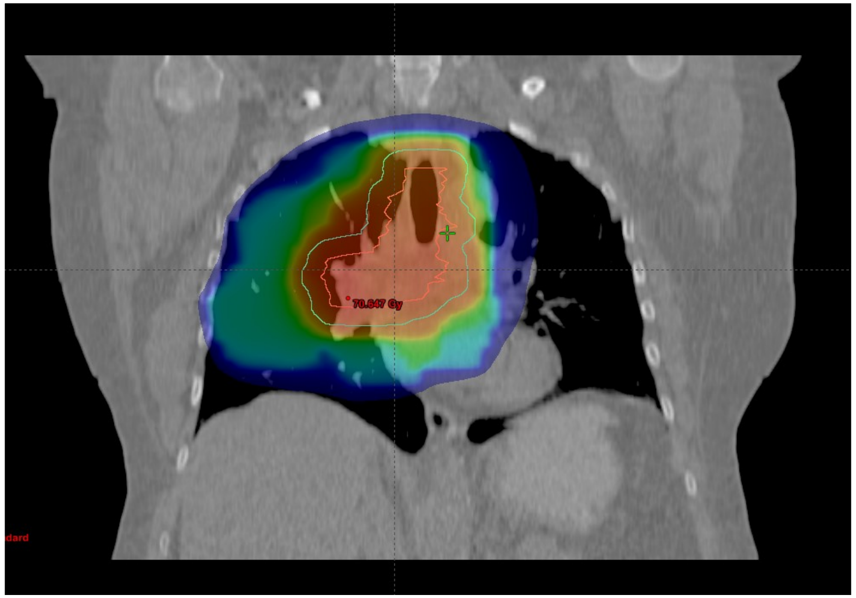
Gating /breath hold

Challenge 2: how to deal with large tumours?

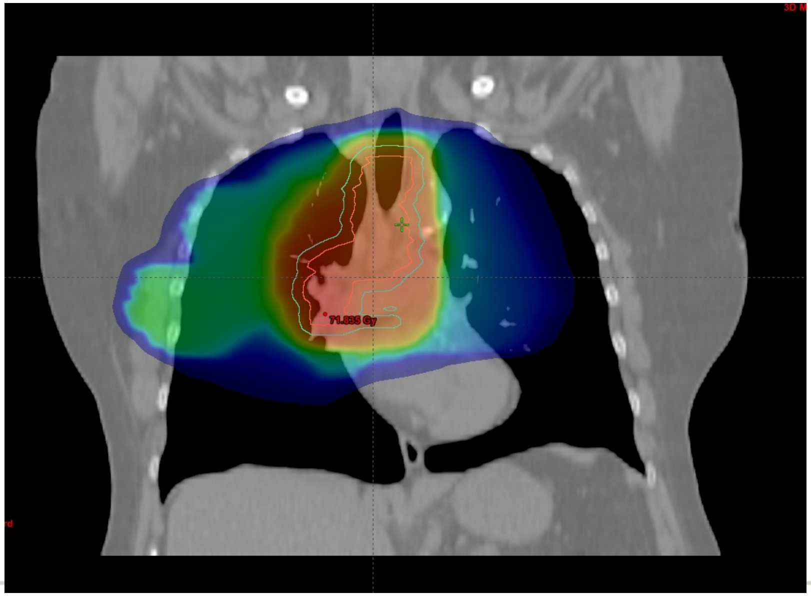


- 70-year old patient with poor pulmonary function
- Tumour motion < 5mm
- MLD unacceptable if a curative dose (66Gy) is delivered
- Gating won't help (neither will tracking!)

Deep inspiration breath hold: not a motion-limiting strategy !!

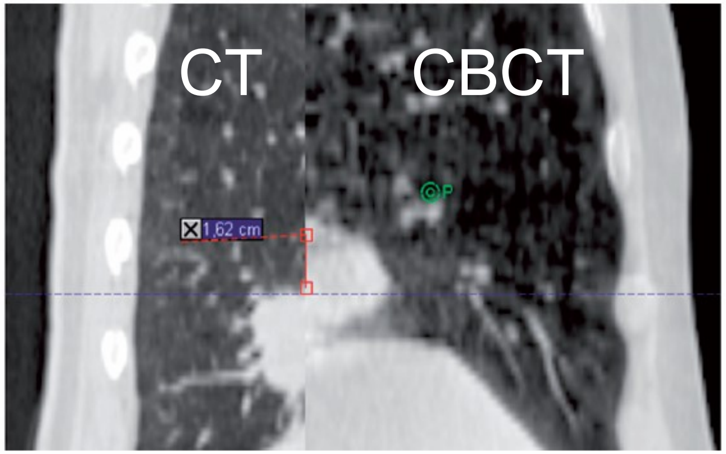


Free breathing
(MLD 23.6Gy)



Deep inspiration
(MLD 19.7 Gy)

Some caveats of breath hold (1)



Josipovic et al Acta Oncol 2014

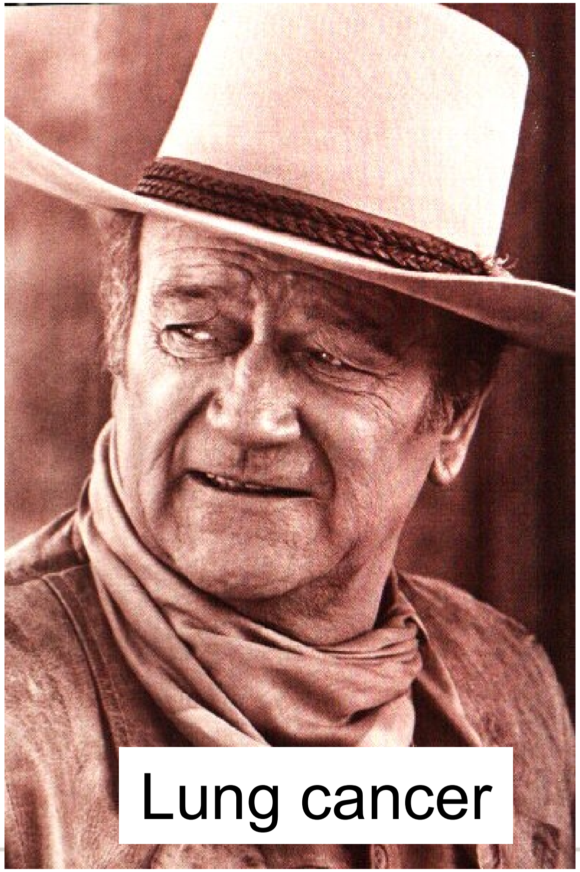
2nd patient treated in DIBH

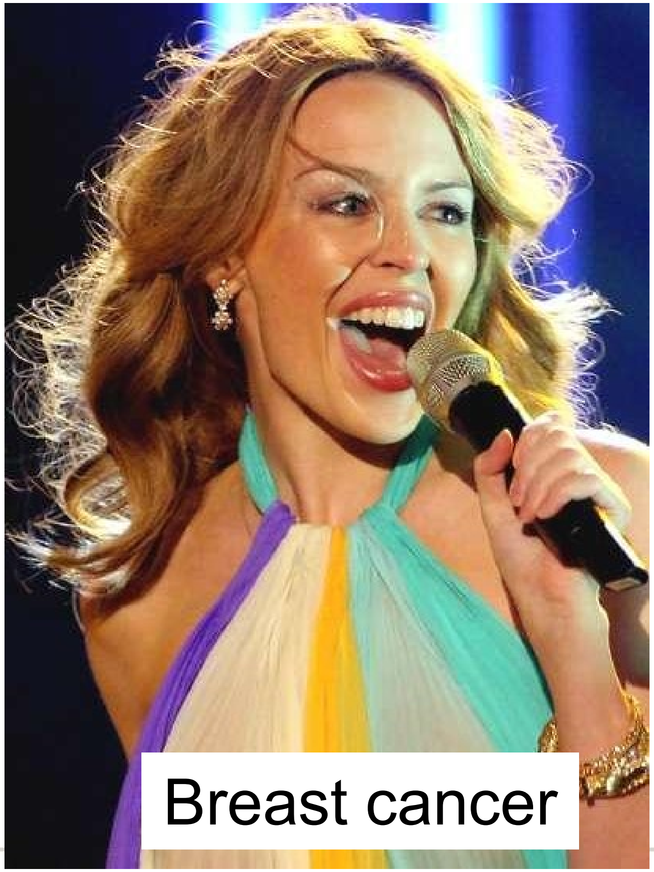
•peripheral target + mediastinal lymph nodes

•10th fraction: match on mediastinum, 1.6 cm shift CC direction for peripheral tumour

Don't (blindly) trust external surrogates: markers, spirometry, surface based etc…

Compliance ? Pulmonary function ?





Compliance

All NSCLC patients perform a voluntary DIBH after 4DCT

Pilot study (17 patients)

Treated in free breathing

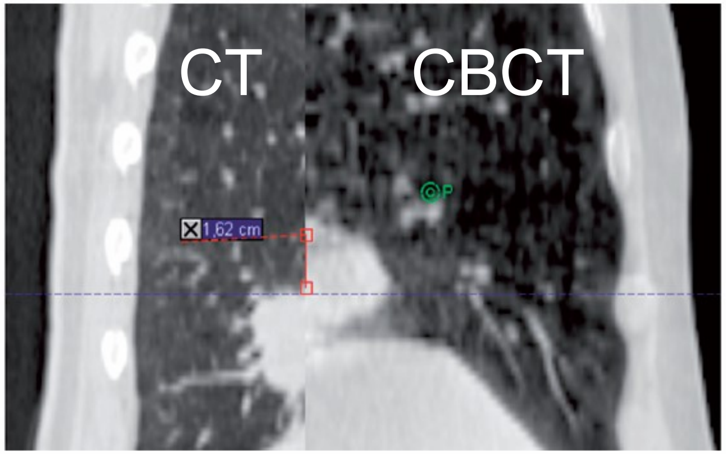
- 3 time points: DIBH CT and CBCT

15 could perform DIBH until the end of their treatment course

- 1 develop radiation pneumonitis
- 1 wished to drop out of the study
- All others had “reproducible” breath holds

Data submitted to Acta Oncol
Persson et al

Some caveats of breath hold (1)



Josipovic et al Acta Oncol 2014

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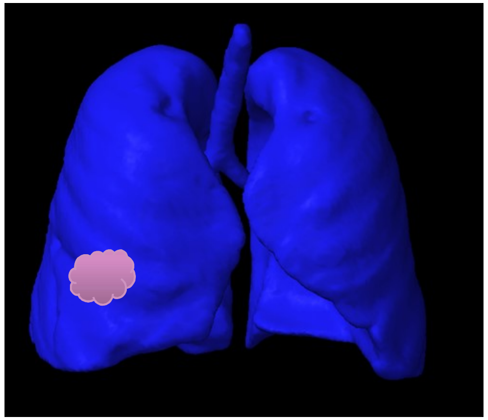
INHALE
(phase 2 trial, target 80 patients)



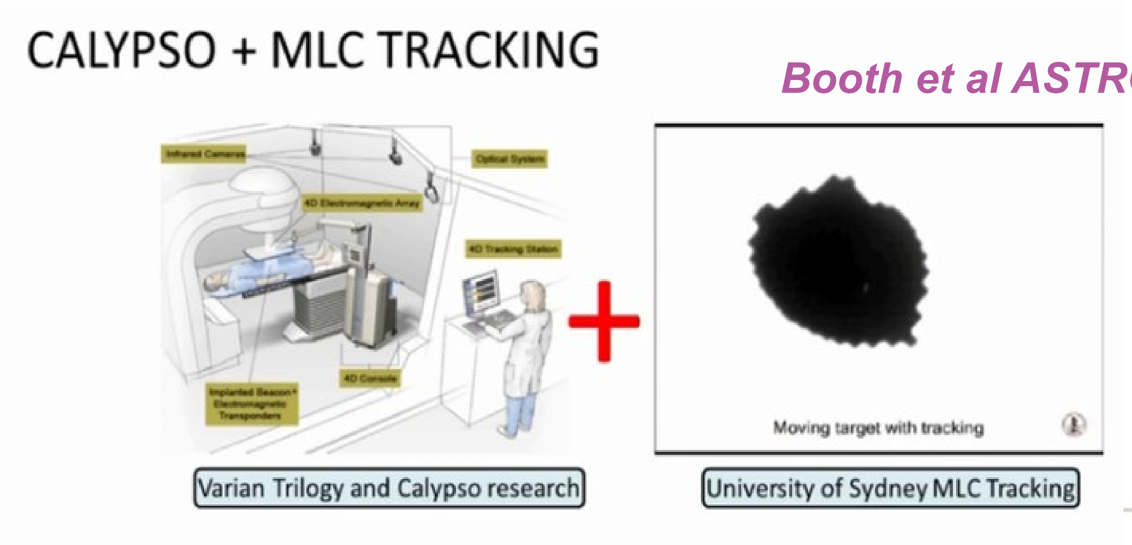
Registration on tumour
Verify OAR/bone

Registration on carina
Larger margins on peripheral tumour

LR

Josipovic et al R&O 2016

Tracking



Booth et al ASTRO 2014

Take-home messages for treatment verification in current clinical practice

- The most important is to see the tumour
  - ➢ in a representative position
- 2D imaging modalities (markers)
- 3D imaging modalities
  - \+ Volume imaging
  - \- No real-time imaging

- 4D imaging modalities
  - \+ fewer breathing motion artifacts
  - \- Actual benefit?

No single solution will be appropriate for every patient

ESTRO School

Keep breathing ☺

Quiet free breathing

Breath hold

ESTRO School

WWW.ESTRO.ORG/SCHOOL

Universitätsklinikum Würzburg

Rigshospitalet

Image guided radiotherapy in the thoracic region:

Lung cancer

Matthias Guckenberger, MD
Marianne Aznar, PhD

ESTRO School

Universitätsklinikum Würzburg

Rigshospitalet

In-room image guidance: seeing the tumour

ESTRO School

In-room image guidance

Modalities

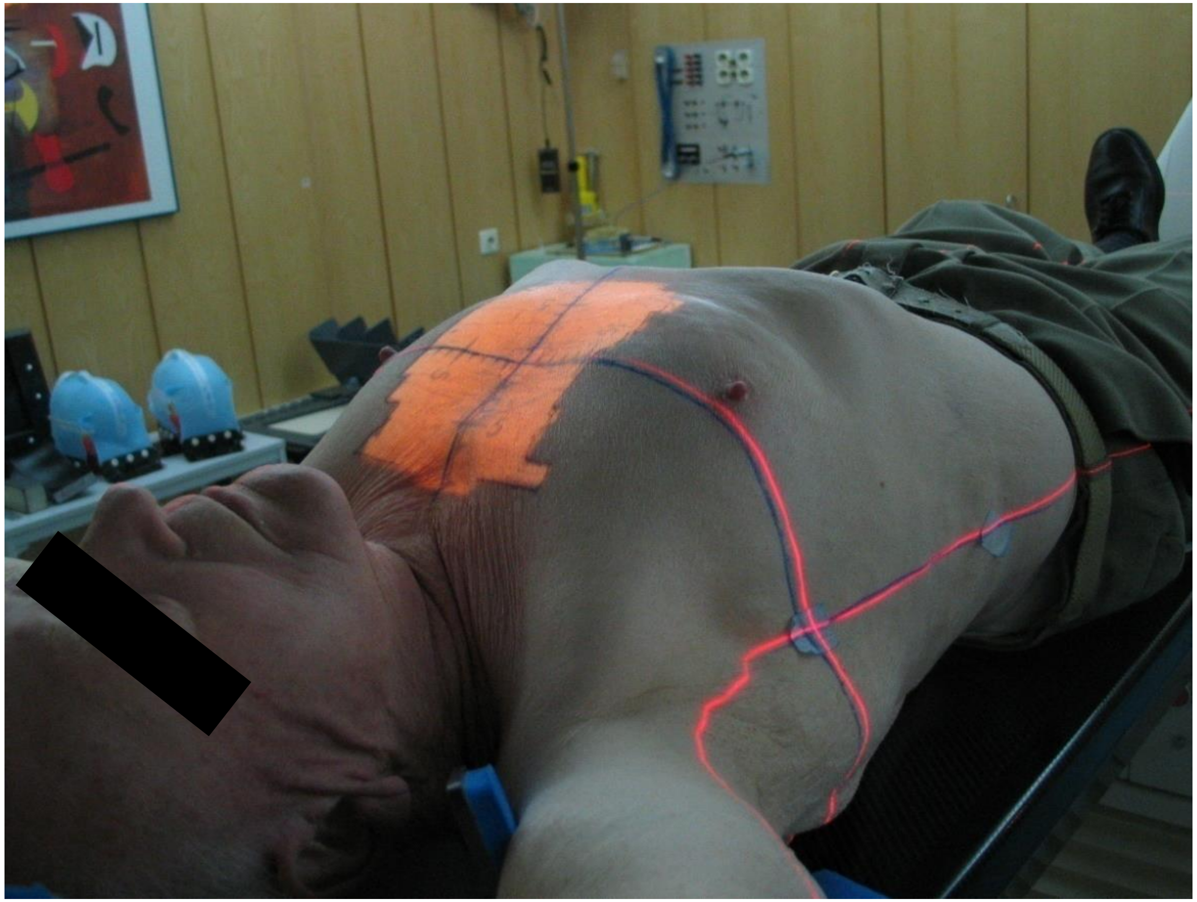
- **Field light**
- **EPID**
- **kV verification imaging**
- **In-room CT/CBCT**

Goals

- **Inter-fraction imaging**
  - Reproducibility of patient positioning
  - Reproducibility of organ / target positioning
  - Adaptive planning
- **Intra-fraction imaging**
  - Catching intra-fraction baseline shifts

In-room image guidance

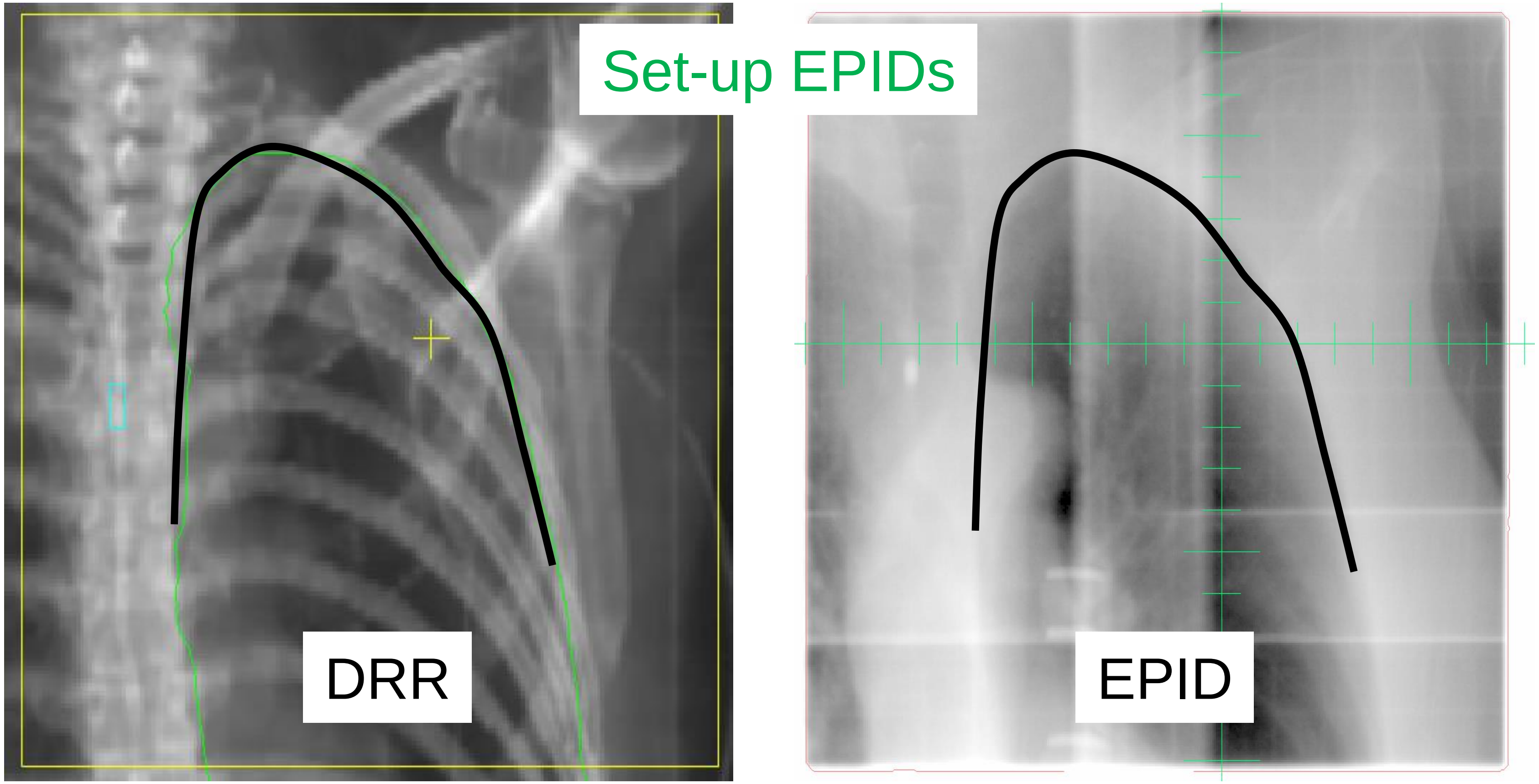
1. Field light / surface markers



Verification that correct patient on the couch
Set-up verification of external target volumes (skin cancer…)

In-room image guidance

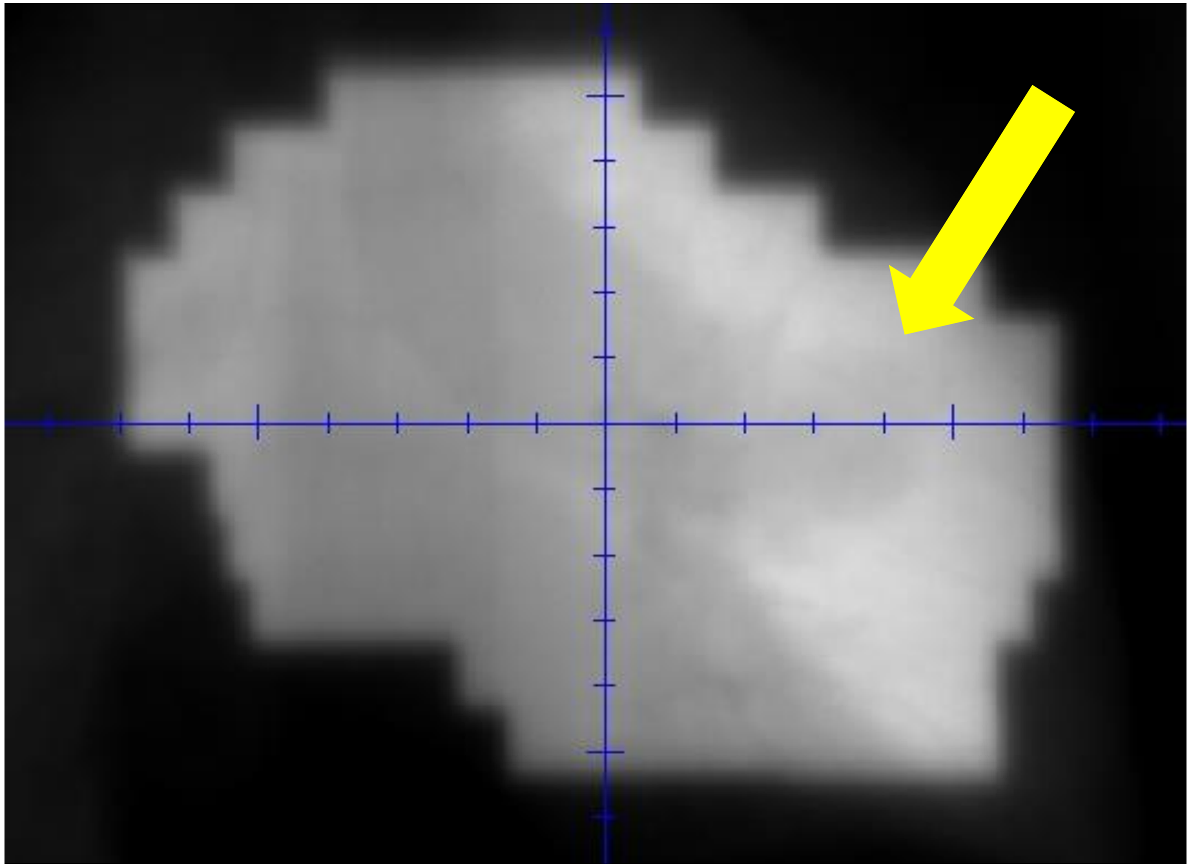
2. Electronic portal images (set up)



Pros: Large images with suitable anatomical landmark structures
Cons: Extra dose to the patient
Landmark structure might not be representative for target

In-room image guidance

2. Electronic portal images (field or cine mode)

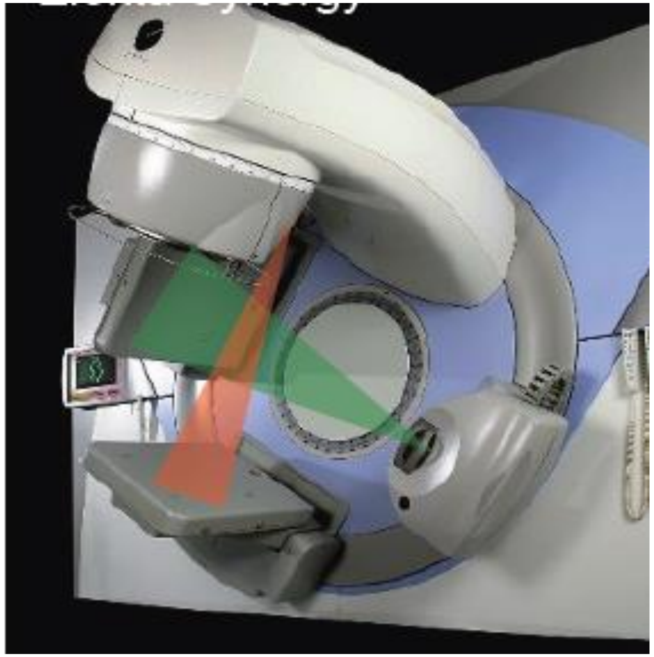


•"on flight" images
• NB: only if 3D- CRT planning

Pros: No additional patient dose;
Pulmonary tumor sometimes visible itself
Cons: Difficult to interpret when only limited landmark structures in field

In-room image guidance

3. kV planar images



In-room image guidance

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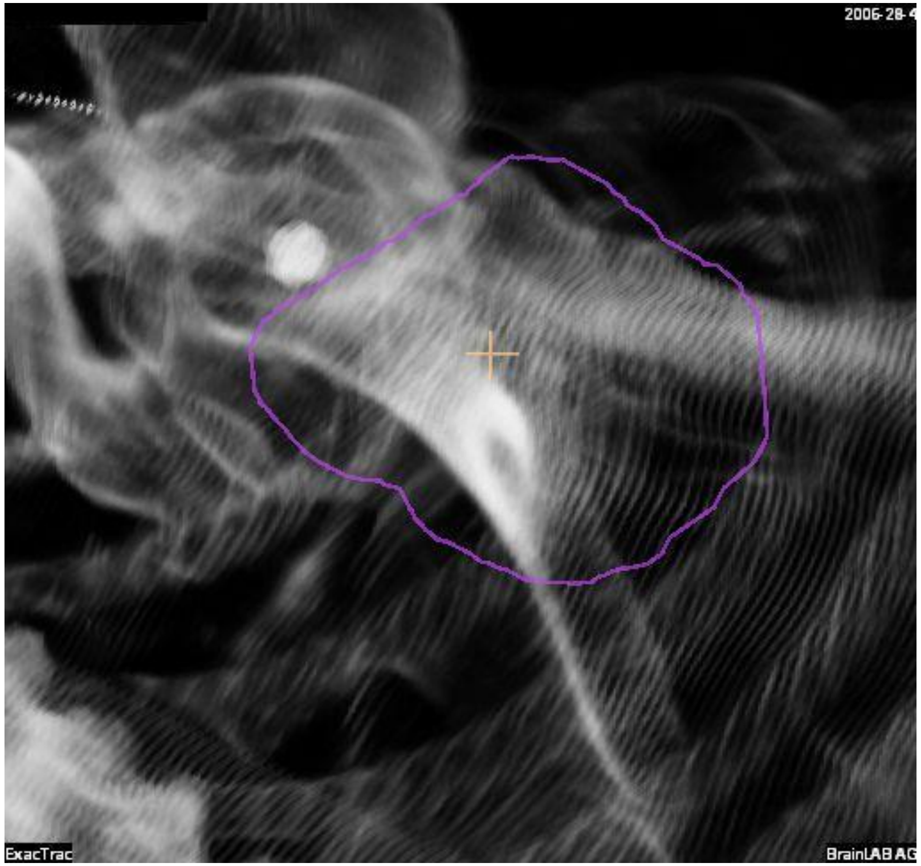
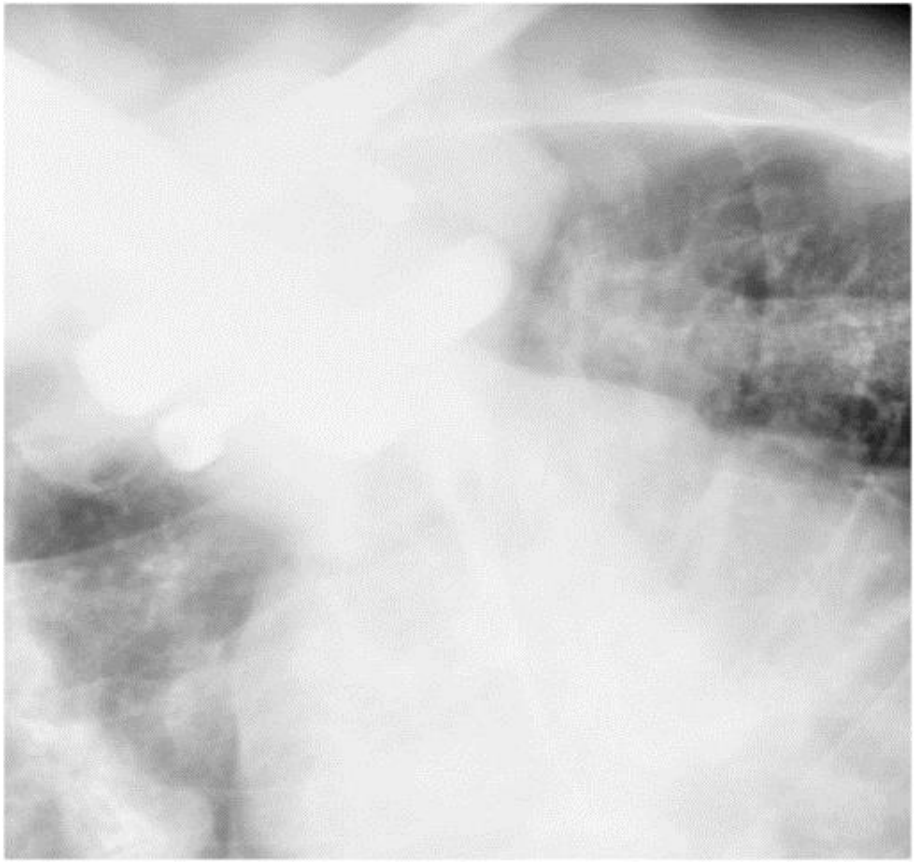


DRR image



kV image: better constrast than EPID… but still poor!

In-room image guidance

3. kV planar images

Markers required: poor soft-tissue contrast

•Surrogate, not the target itself

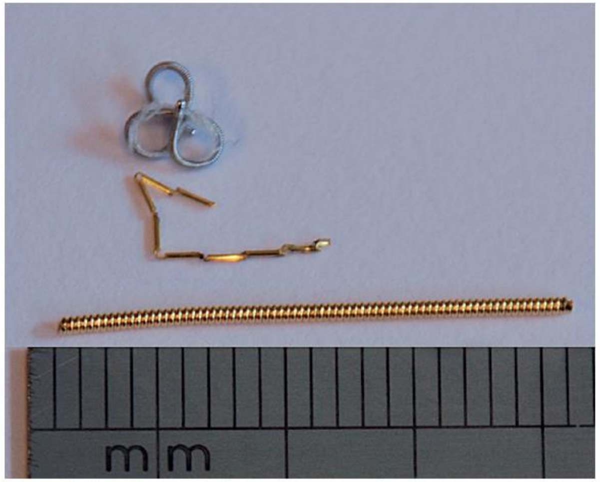
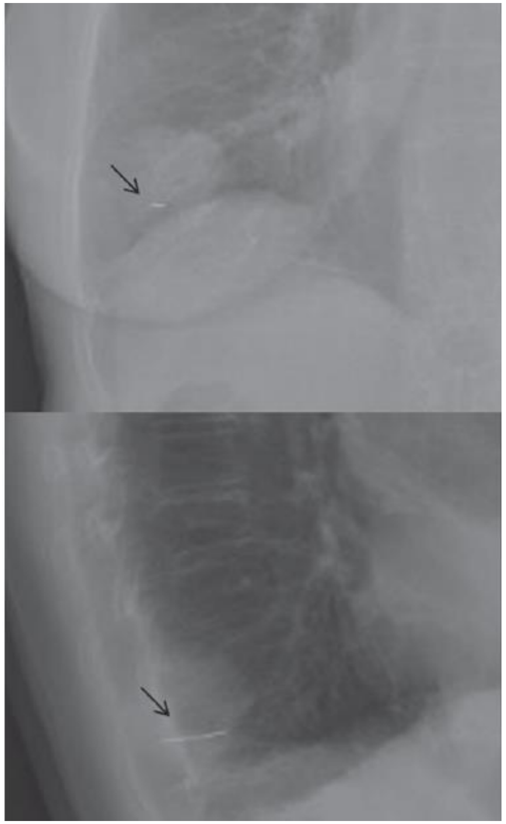


Figure 1. Photo showing the complex helical platinum marker (top), the Gold Anchor™ marker (middle) and the Visicoil™ gold marker (bottom).

4 out of 15 patients developped pneumothorax (transthoracic implantation)



Persson et al Acta Oncol 2012

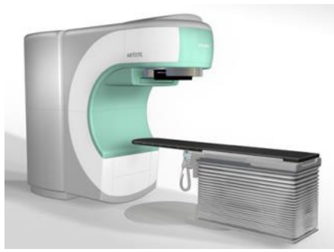
In-room image guidance

4. Volume imaging

In-room CT

Cone-beam CT

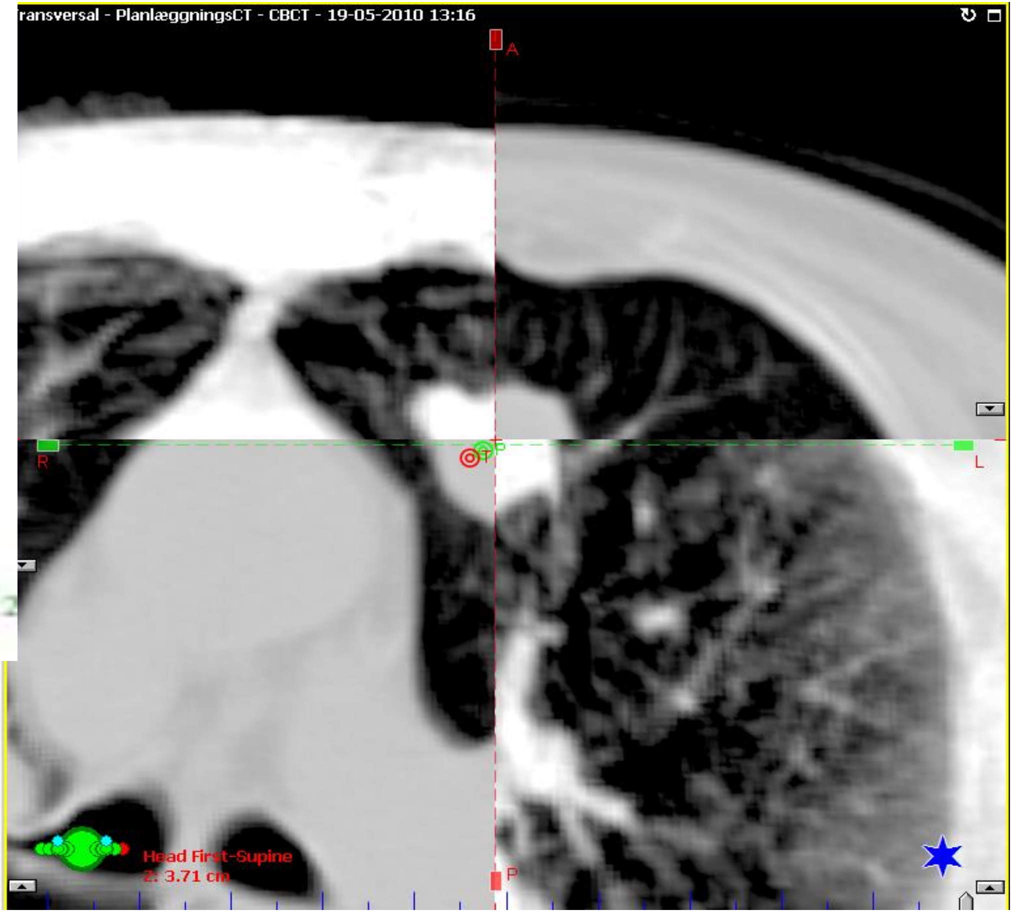
MV CT



In-room image guidance

4. Volume imaging

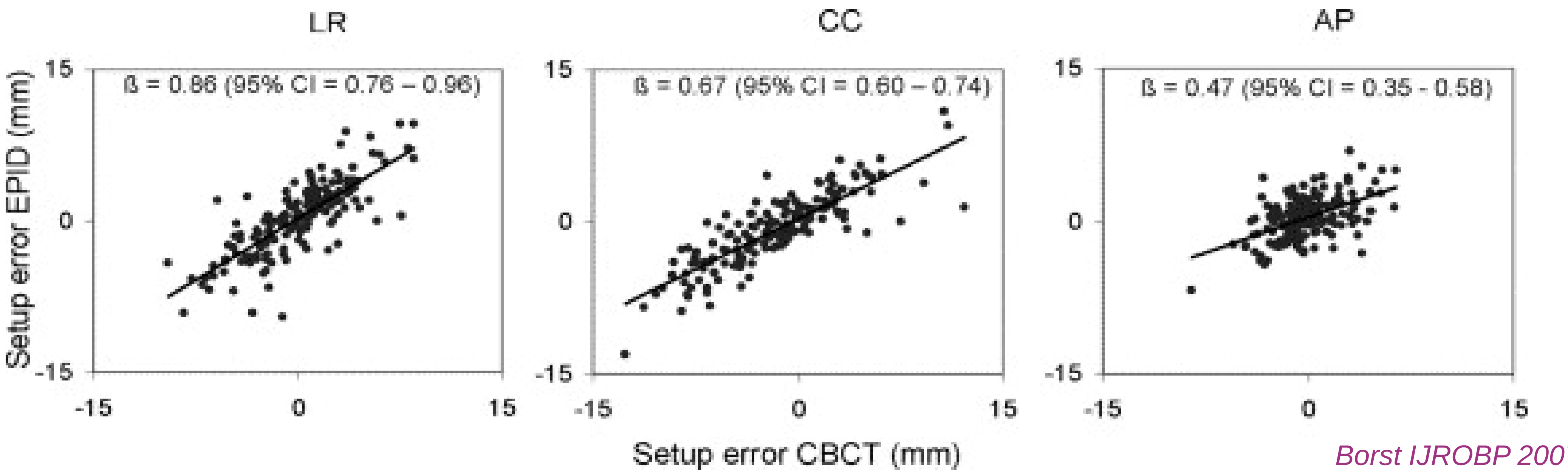
At last… better visibility of the target!



In-room image guidance

4. Volume imaging

Comparison of EPID and CBCT for patient set-up



Borst IJROBP 2007

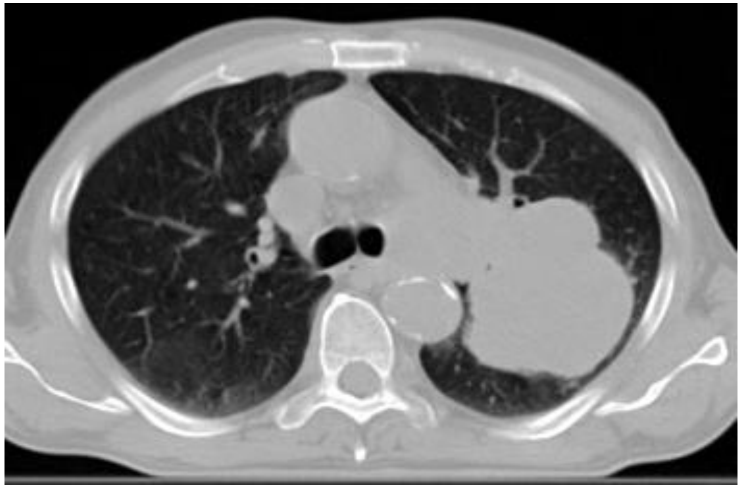
LR: Good correlation CC & AP: EPID underestimated set-up error

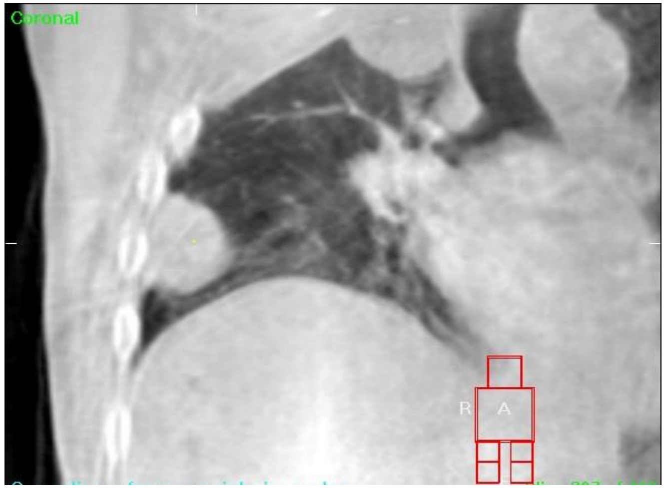
Improved accuracy of patient set-up with CBCT volume imaging compared to bony set-up with EPID

In-room image guidance

4. Volume imaging

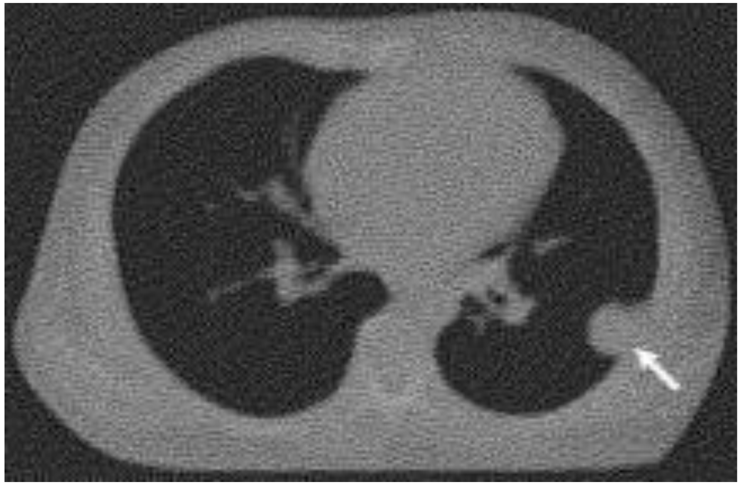
Helical

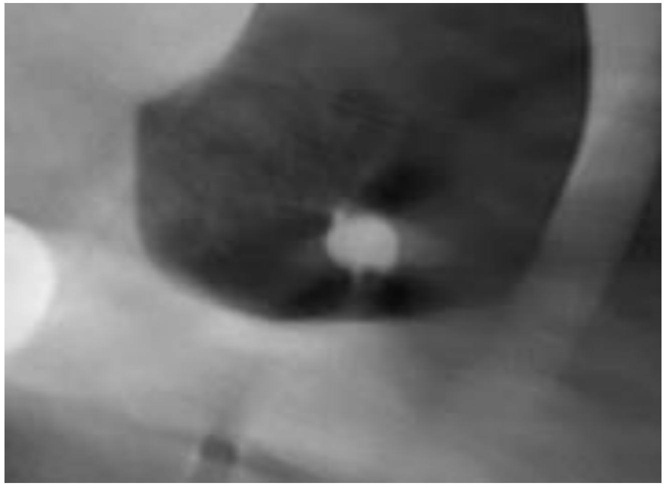




kV CBCT

MV CT





kV/MV CBCT

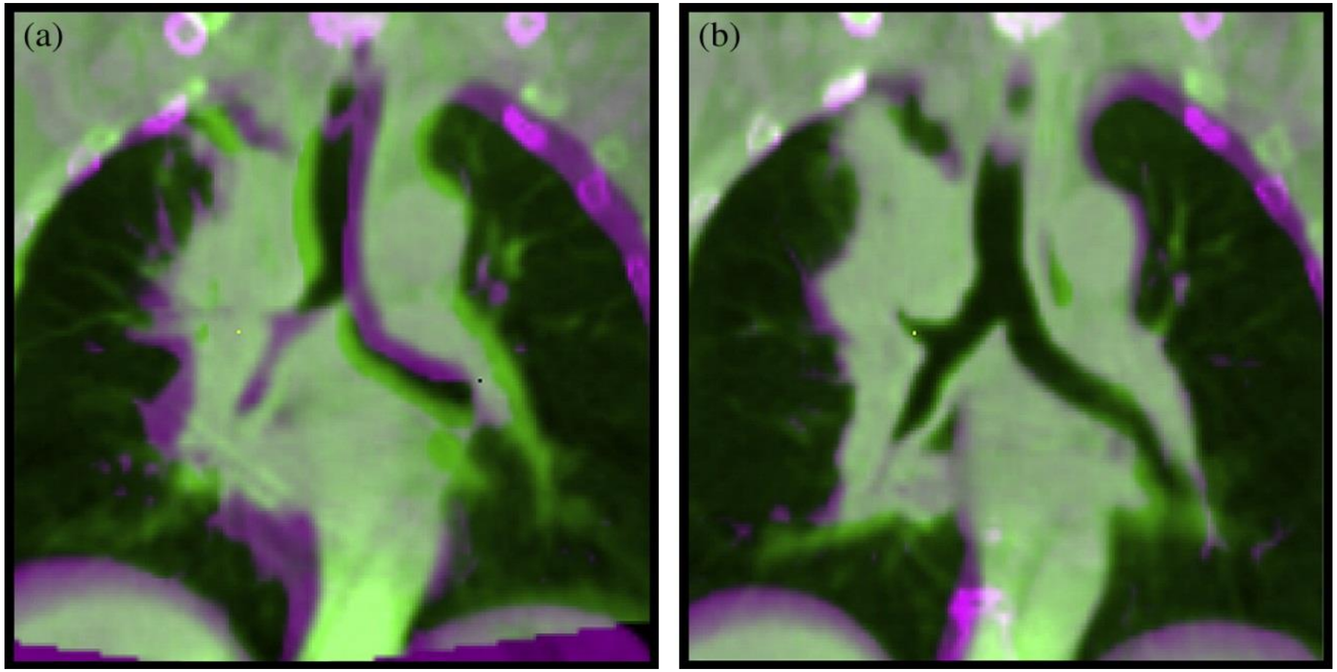
- Intra-pulmonary targets clearly visible in all imaging modalities
- IQ for mediastinum suitable only in kV helical CT

A side note: setting up according to landmarks

Spine vs Carina

- Higgins et al (IJROBP 2009): feasible, better inter-observer agreement with match on the carina
- Lavoie et al (IJROBP 2012): especially node coverage is improved

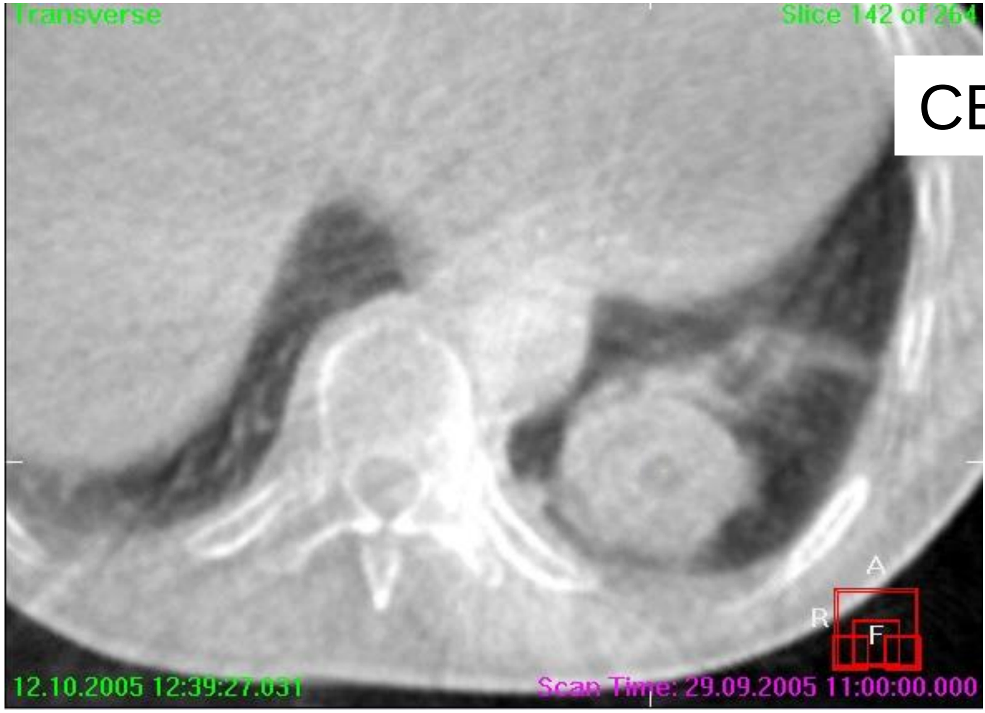
- *Dosimetric impact?*
- *Dependent on tumour location (nodes+ central disease)?*



Spine match   Carina match

In-room image guidance

4. Volume imaging



CBCT

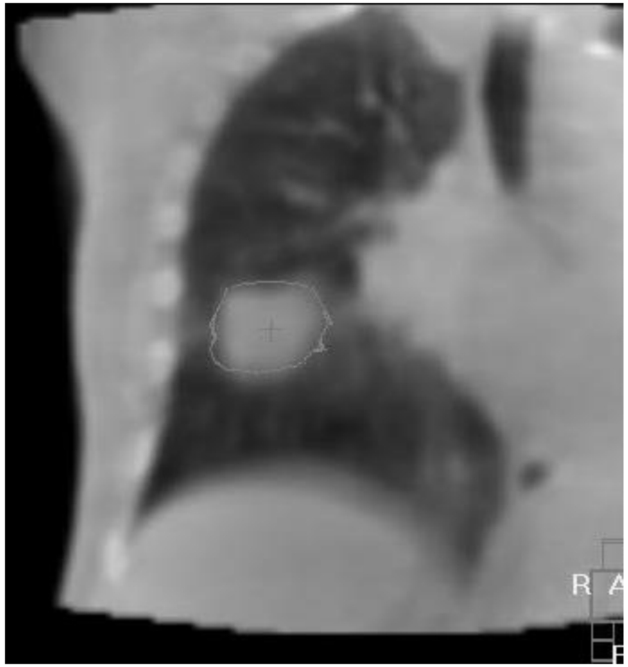
Lower lobe tumor
with large motion amplitude

Blurred target because of
long image acquisition time

Integration of 4th dimension into IGRT

Planning

Treatment



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Guckenberger Acta Ocol 2006

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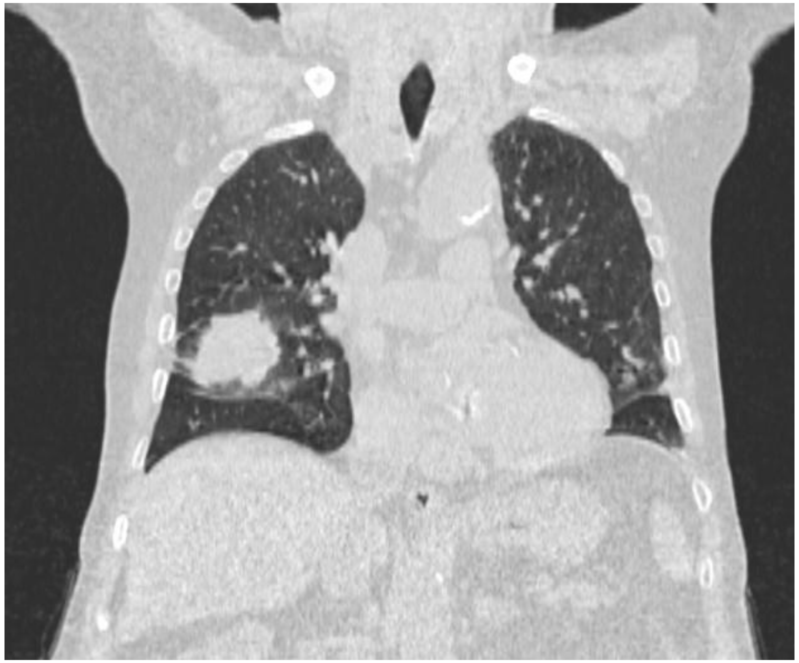
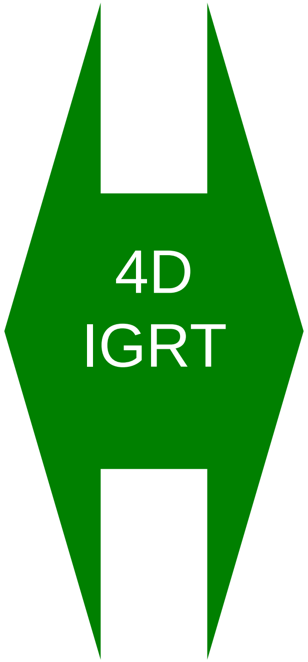




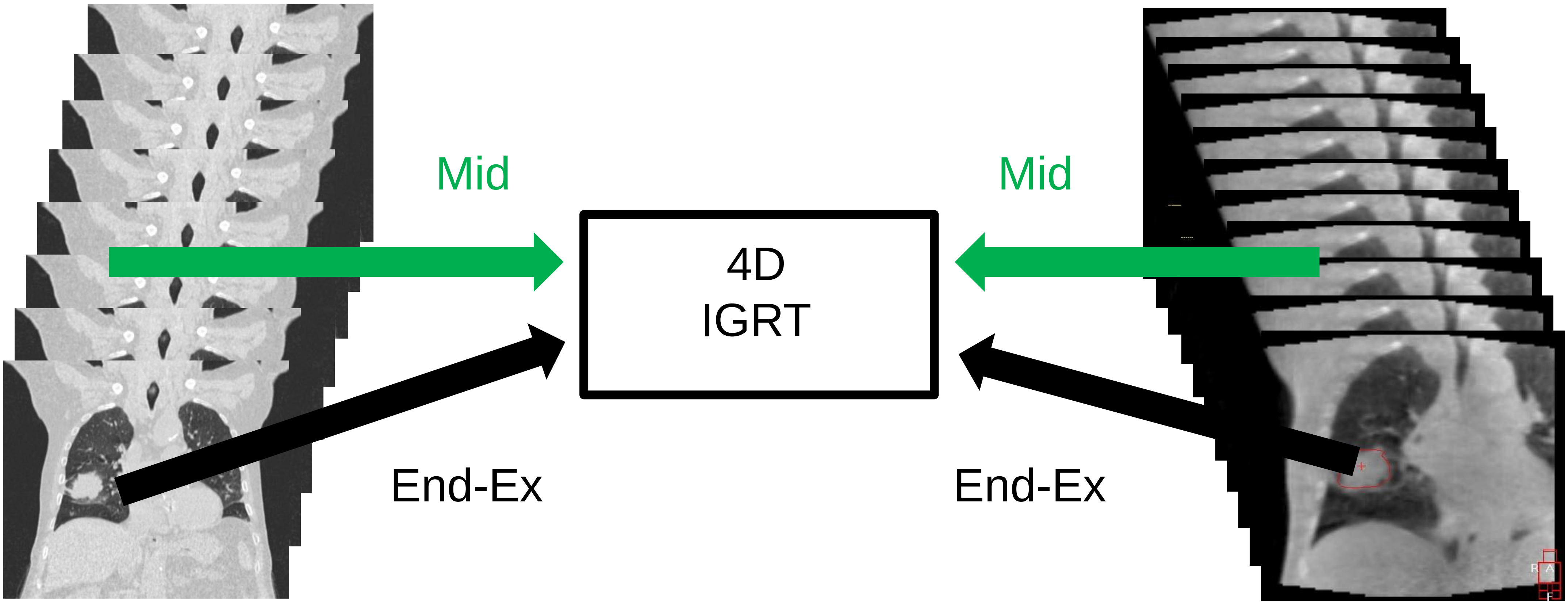
Respiration correlated CT

Respiration correlated CBCT

In-room image guidance

Treatment planning:
Reference Image

Treatment delivery:
Verification Image



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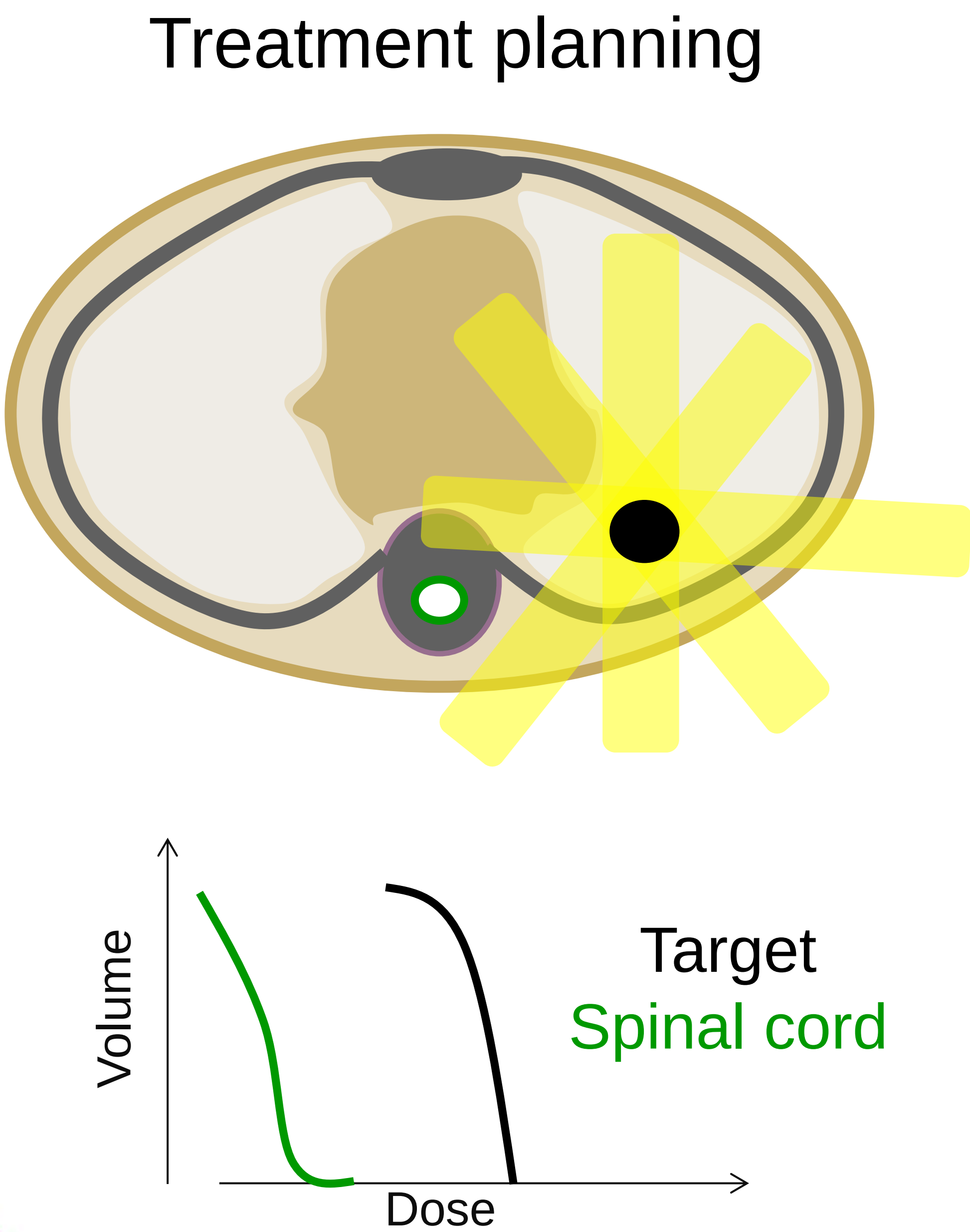
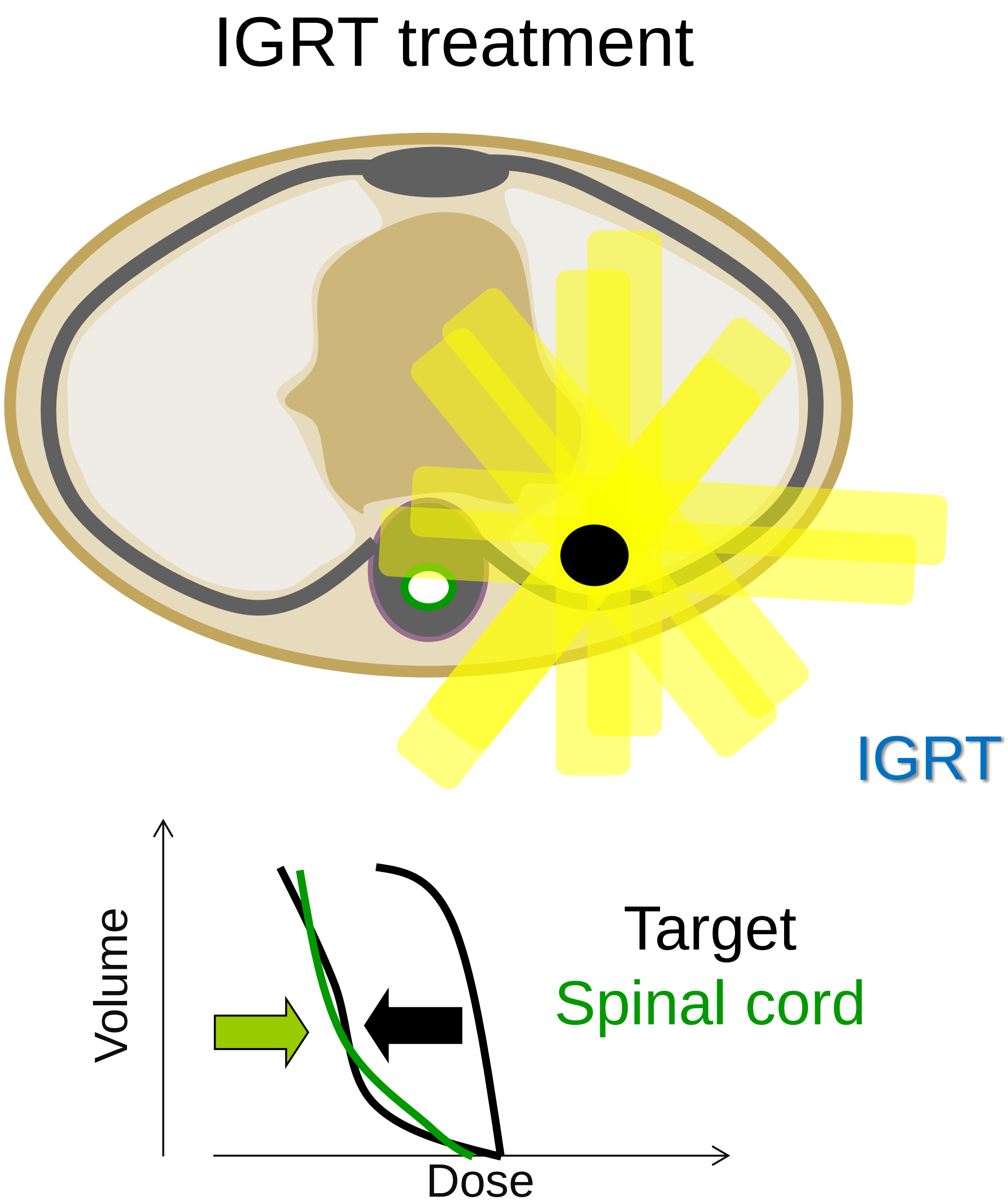
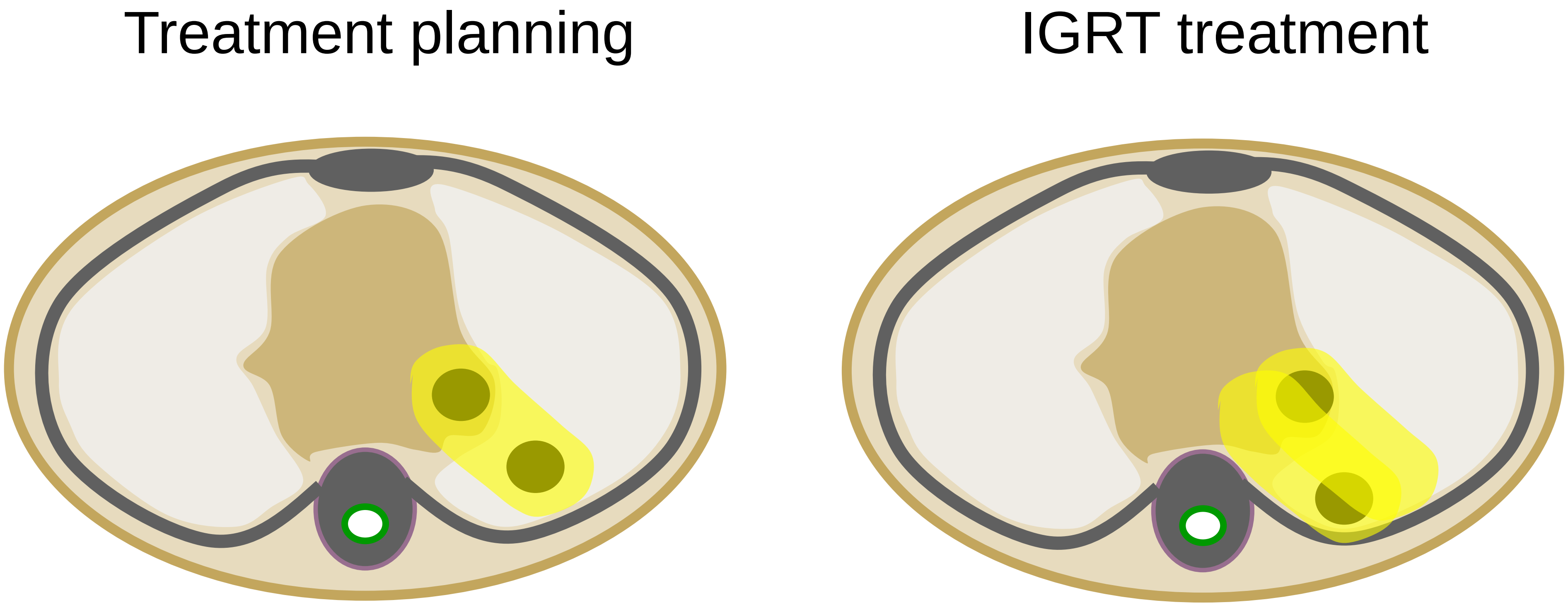




Matching challenges (2)



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adaptive

Universitätsklinikum Würzburg

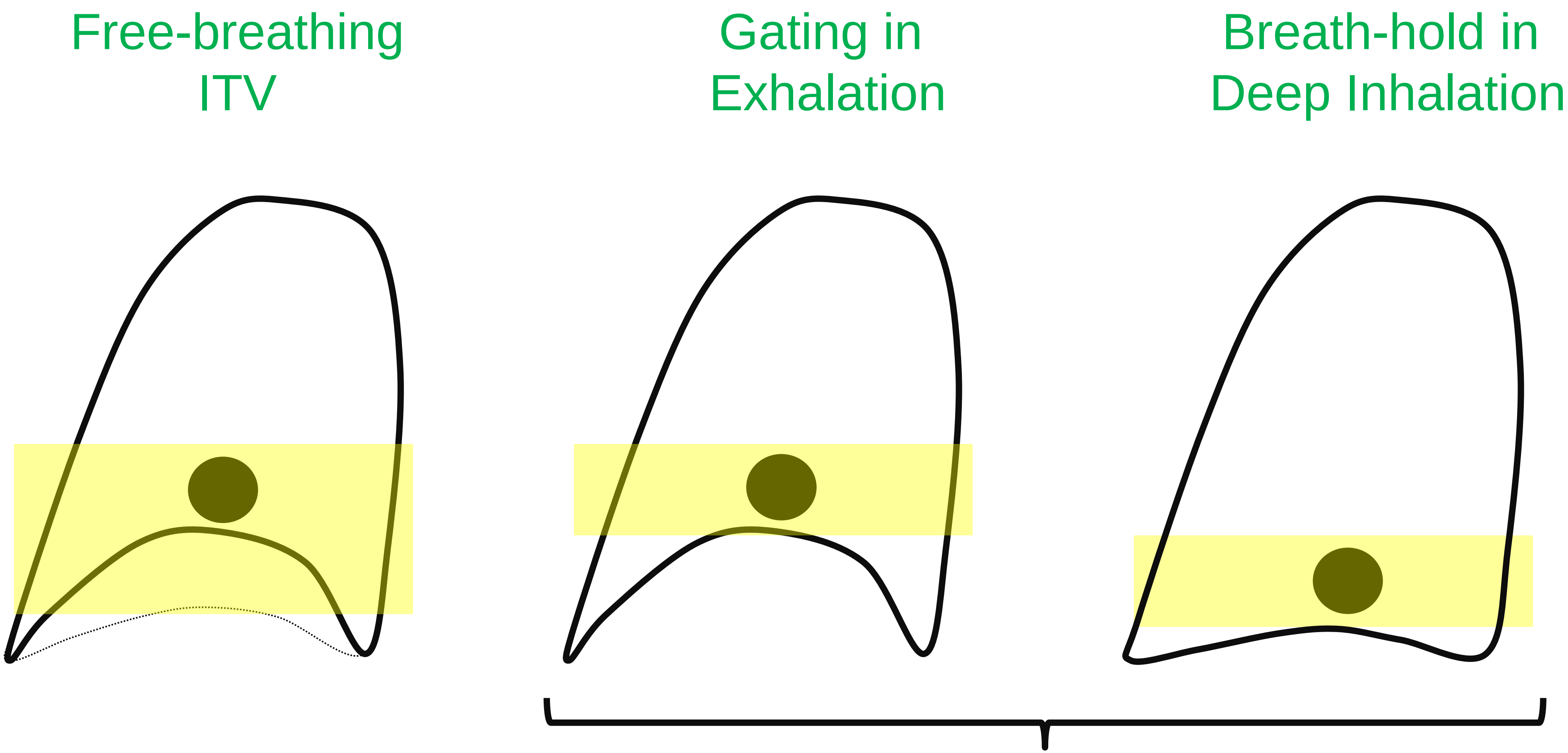
Rigshospitalet

Pre-treatment image guidance

Gating /breath hold

ESTRO School

Gating / breath hold radiotherapy

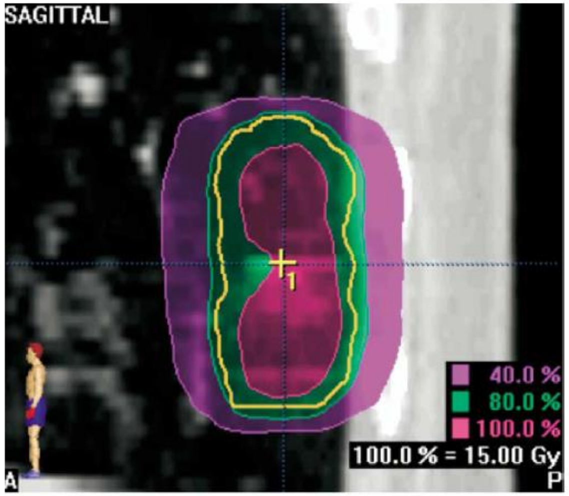


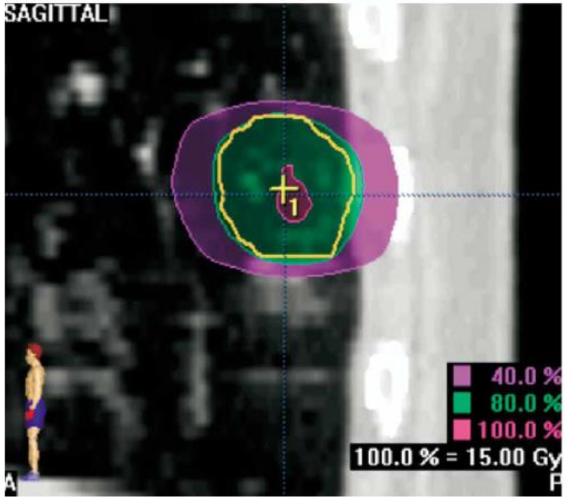
In Inspiration Breath-hold:

Lung is inflated and smaller lung volumes are irradiated

Gating and margin reduction

BENEFIT OF RESPIRATION-GATED STEREOTACTIC RADIOTHERAPY FOR STAGE I LUNG CANCER: AN ANALYSIS OF 4DCT DATASETS





Reduction of motion amplitude from 8.5mm to 1.4mm

Reduction of PTV volume by 45%

Duty cycle 30 %

Underberg IJROBP 2005

Gating and duty cycle

Challenge 1: how to keep a sustainable duty cycle forhighly mobile tumors?

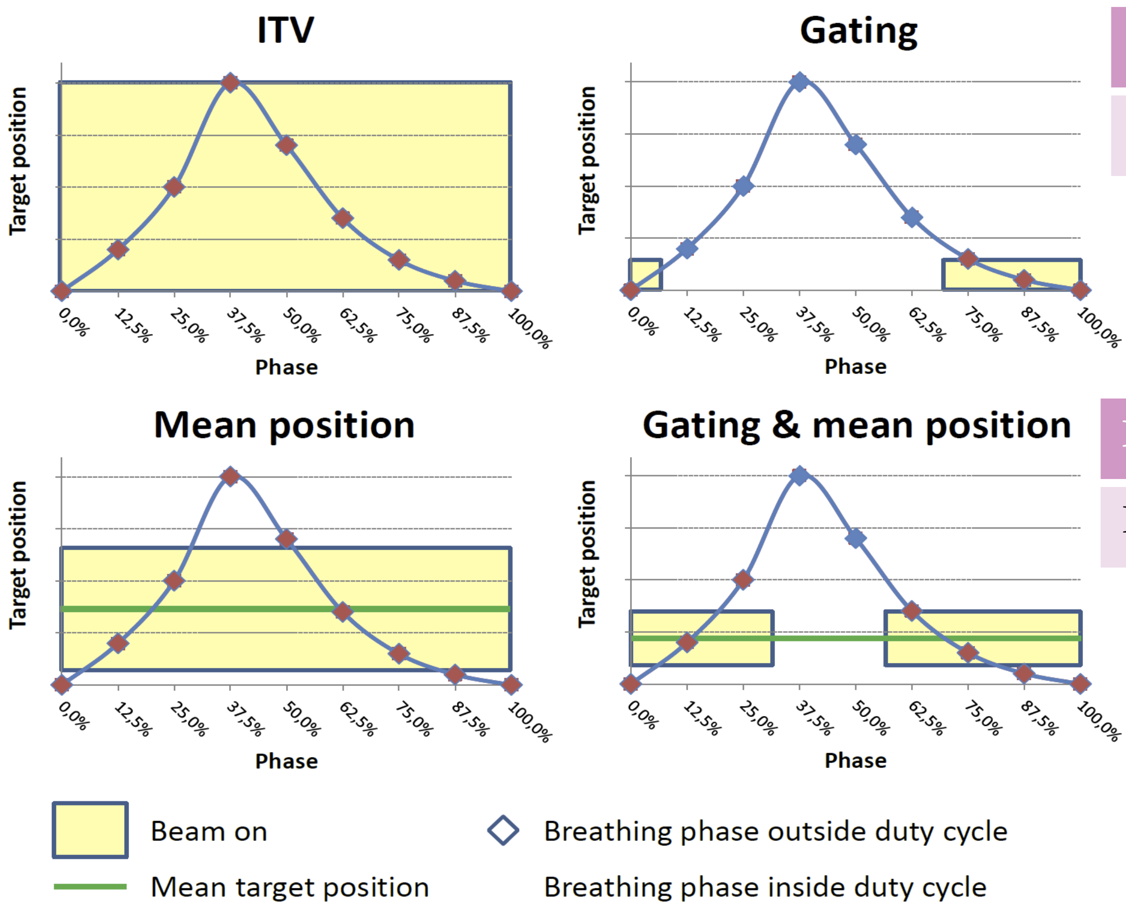
Case example: SBRT for a 2cm NSCLC, 20mm motion

Margin	10mm
Duty cycle	100%

Margin	0mm
Duty cycle	37.5%

Margin	6mm
Duty cycle	100%

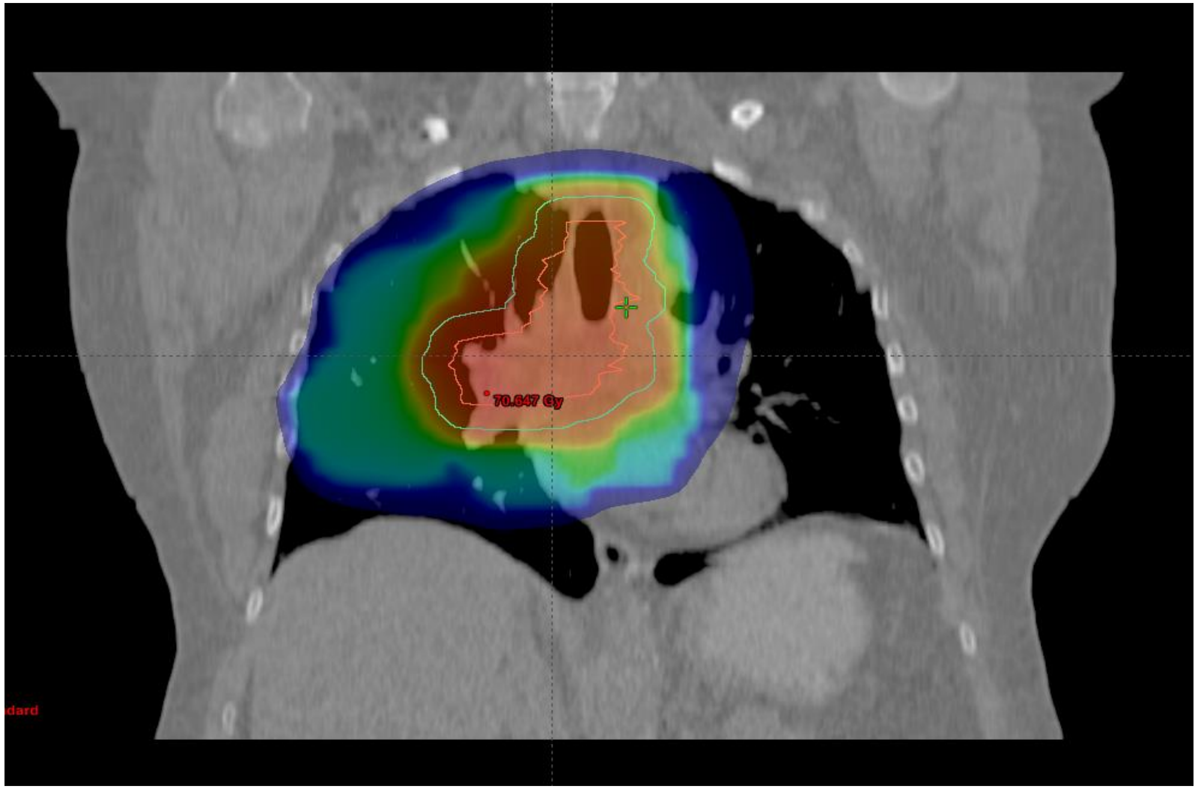
Margin	2mm
Duty cycle	75%



Guckenberger 2011

Breath hold radiotherapy

Challenge 2: how to deal with large tumours?



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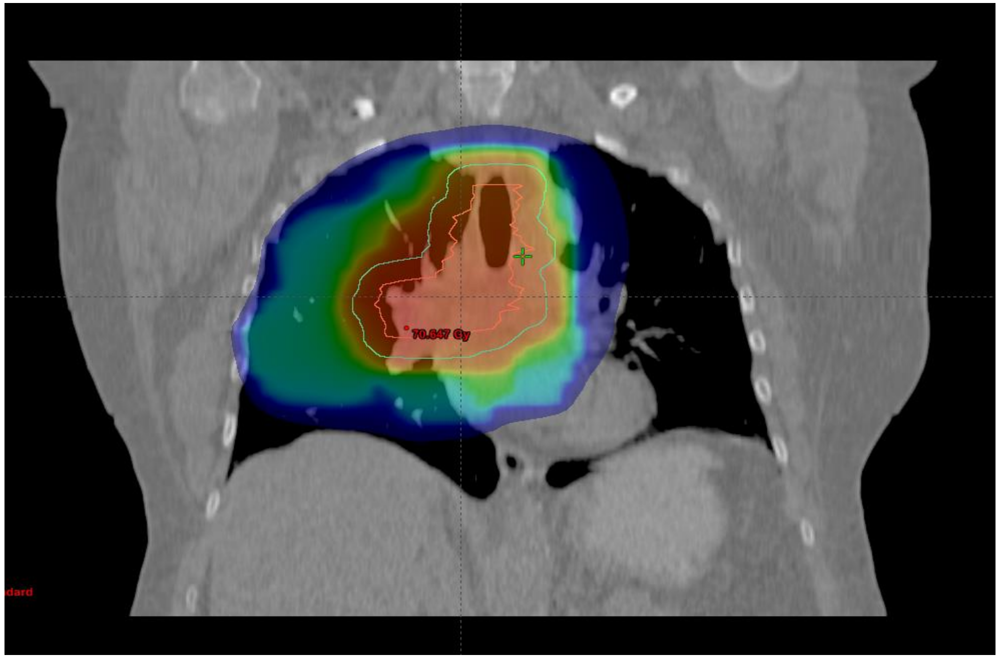

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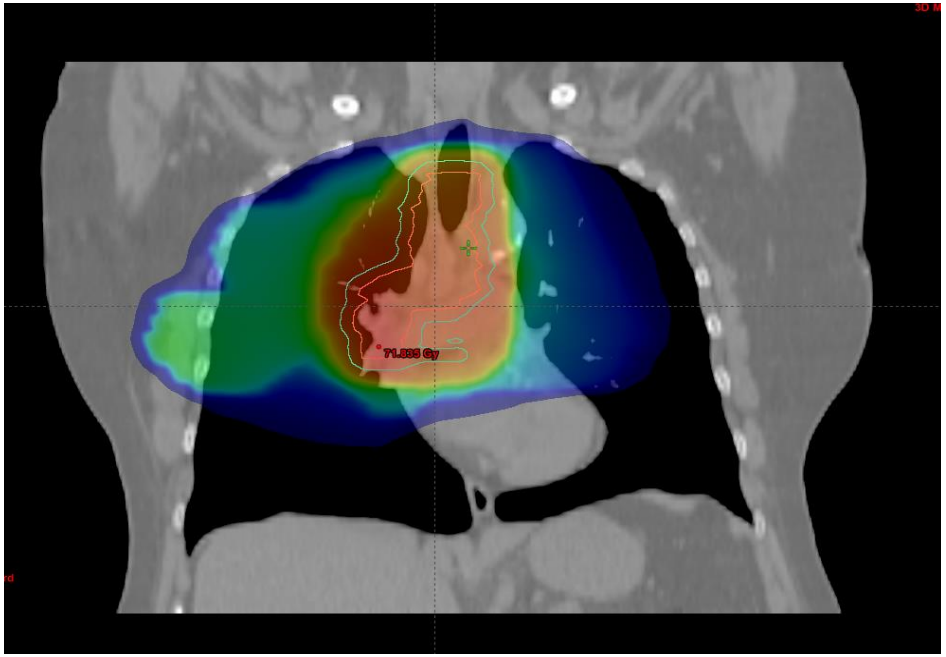
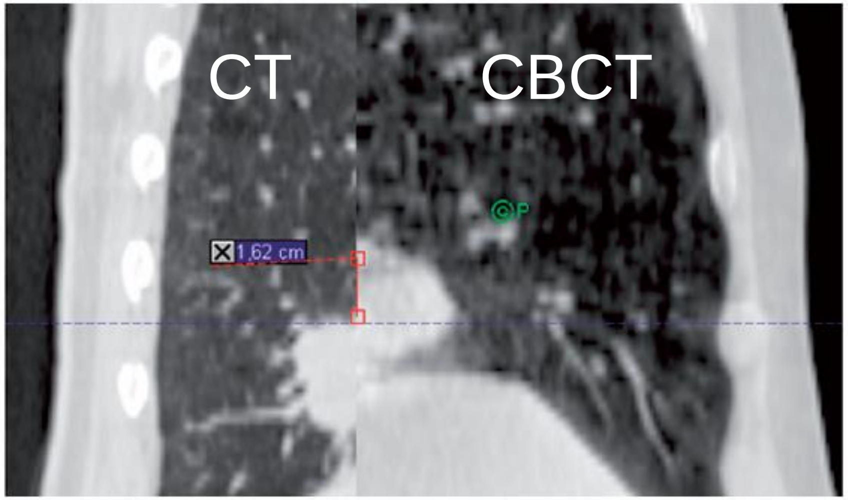


Deep inspiration
(MLD 19.7 Gy)

Dosimetric benefit

One illustration



Josipovic et al Acta Oncol 2014

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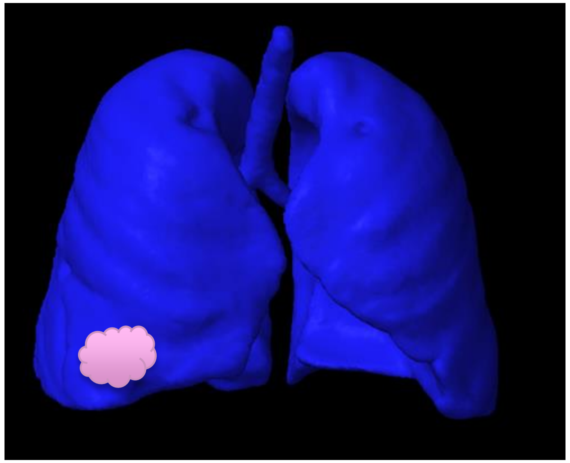
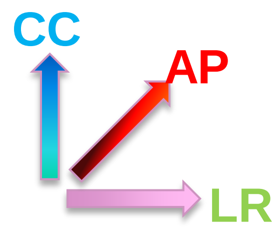
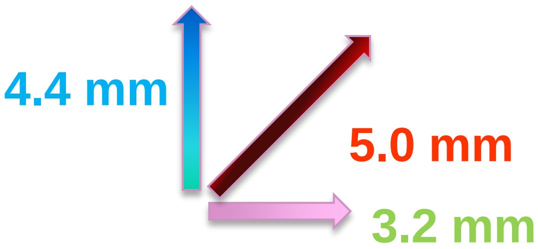
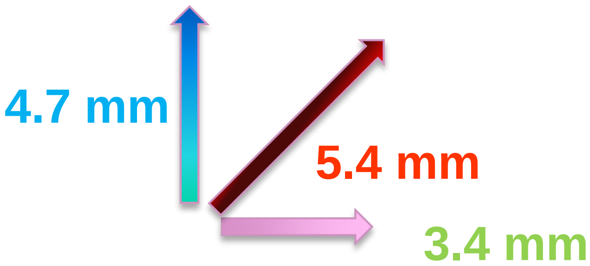
Margins – simple target

Daily IGRT - tumour match

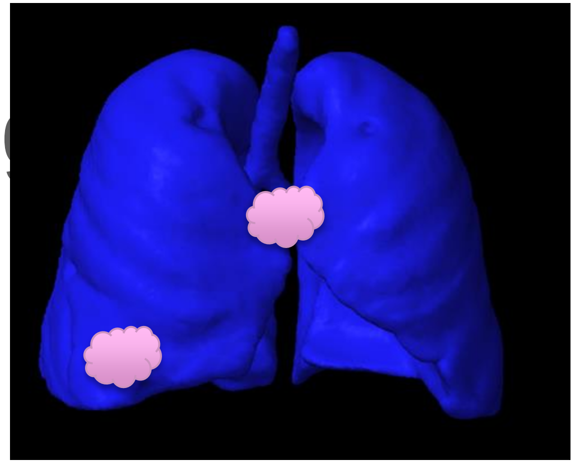








Margins – complex tar



peripheral tumour match

carina match

10.4 mm

6.3 mm

10.4 mm

margin
for
mediastinum

3,7 mm*

4,1 mm*

2,8 mm*

CC

AP

LR

4.4 mm

5.0 mm

3.2 mm

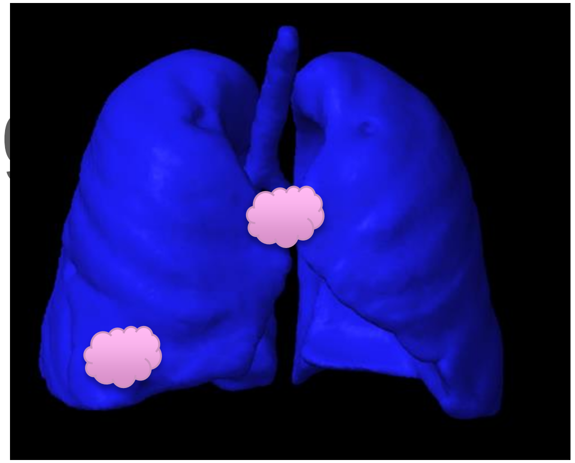
margin
for
peripheral
tumor

9.9 mm

6.7 mm

9.9 mm

Margins – complex tar



peripheral tumour match

carina match

10.4 mm

6.3 mm

10.4 mm

margin
for
mediastinum

5,4 mm*

6,1 mm*

5,1 mm*

CC

AP

LR

4.4 mm

5.0 mm

3.2 mm

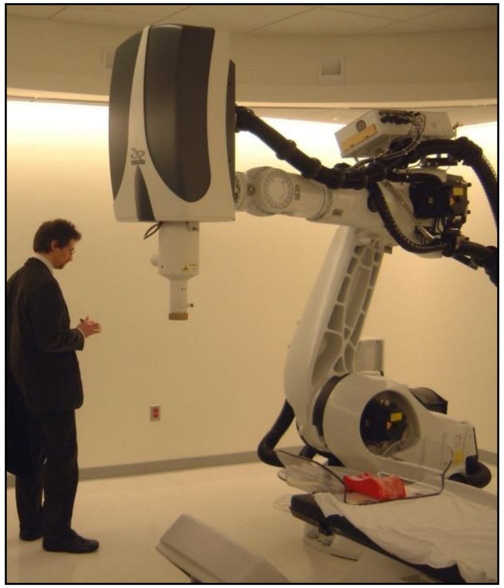
margin
for
peripheral
tumor

9.9 mm

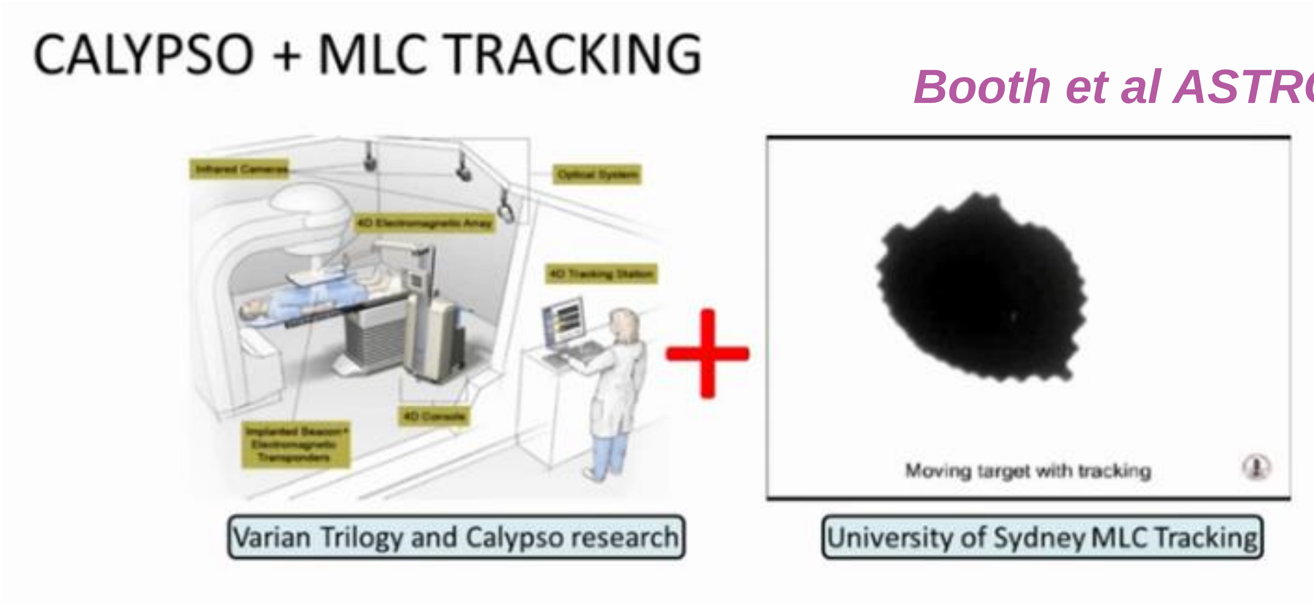
6.7 mm

9.9 mm

Tracking



Booth et al ASTRO 2014



Take-home messages for treatment verification in current clinical practice

- Inter-fractional base-line shifts of pulmonary tumors are well established
- 2D imaging modalities
  - \+ Real-time imaging
  - \- Implanted markers, No volume information
- 3D imaging modalities
  - \+ Volume imaging
  - \- No real-time imaging
- 4D imaging modalities
  - \+ fewer breathing motion artifacts
  - \- Actual benefit?

Motion compensation techniques

Take-home messages for treatment delivery in current clinical practice

- No universal solution
  - Gating: increased treatment time, image-verification at treatment not straightforward (gated CBCT?).
  - Breath hold requires compliance (breath hold CBCT?).
  - Tracking challenging and hardly available

Tracking / Gating only for large (>10-15mm) motion

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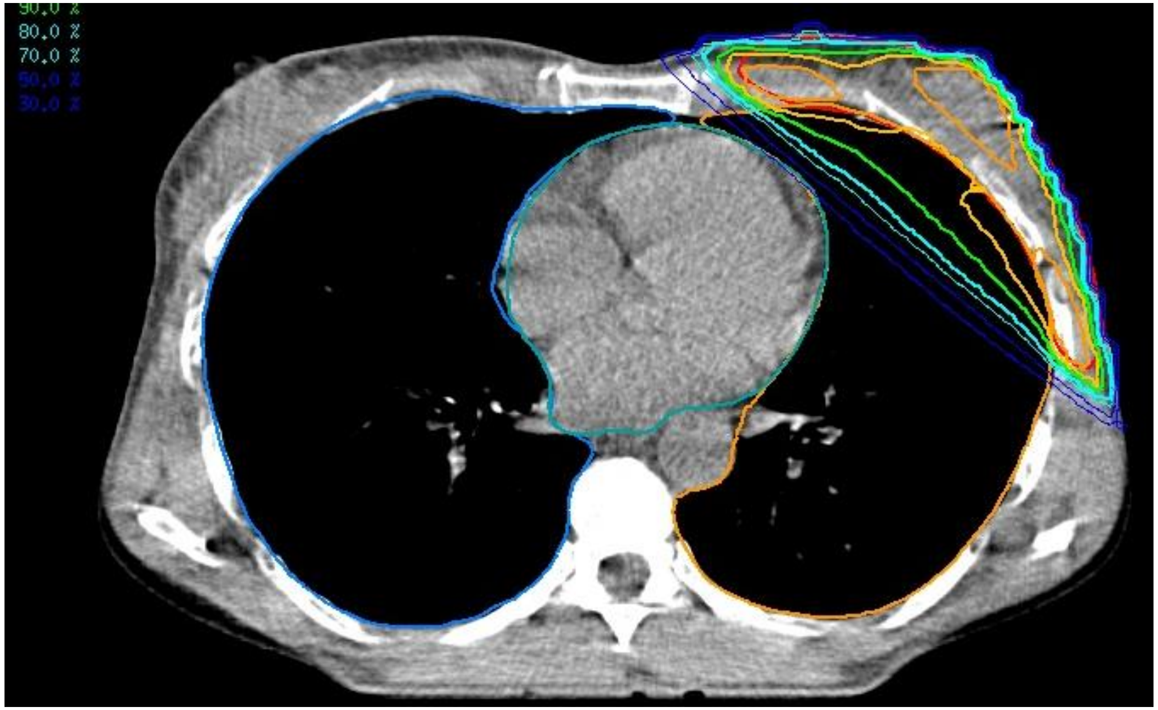
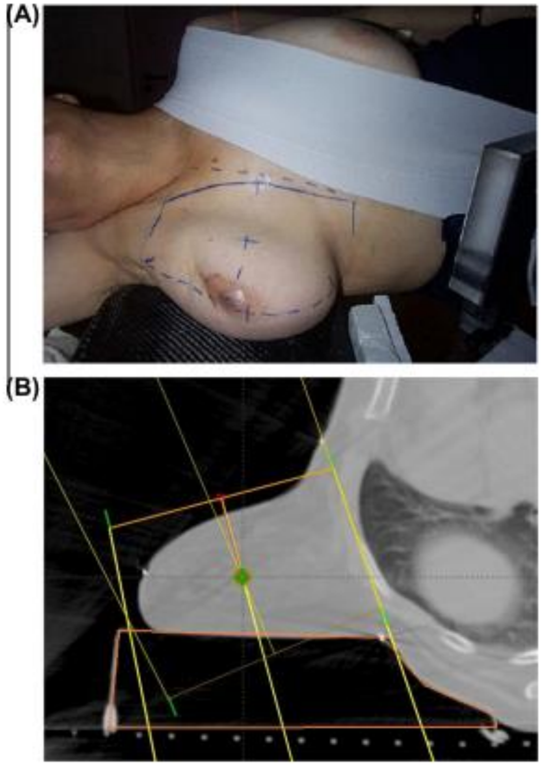
Image guidance

- Which modality?
- How often?
- whole breast vs partial/boost
- Image guidance for respiratory gating /inspiration breath hold



Imaging: Immobilisation techniques

Kirova et al RO 2014



Lymberis et al IJROBP 2012

WHOLE BREAST (+/- LN)

Universitätsklinikum Würzburg

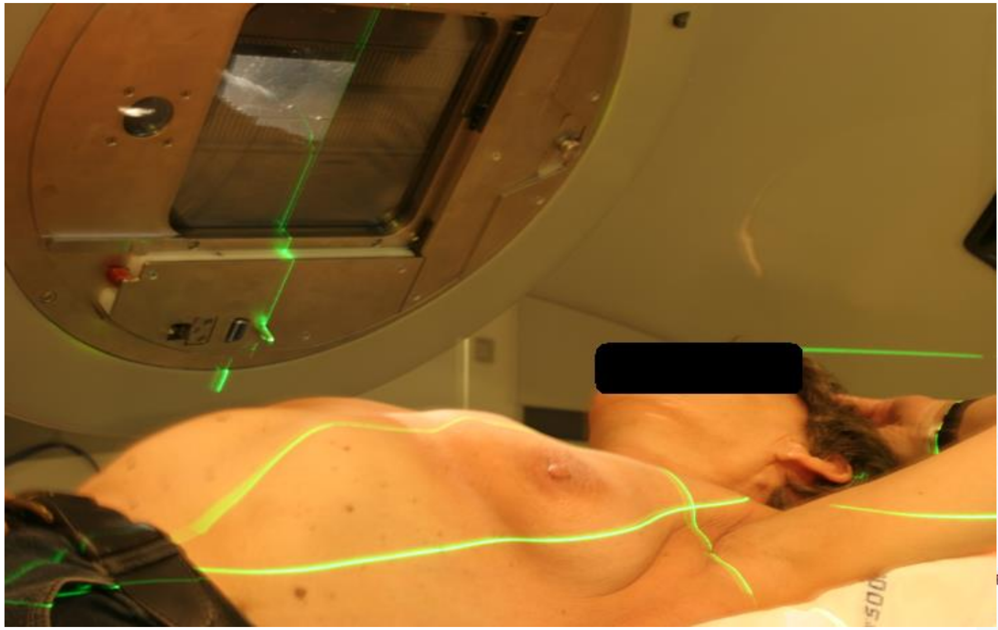
REGION H Rigshospitalet

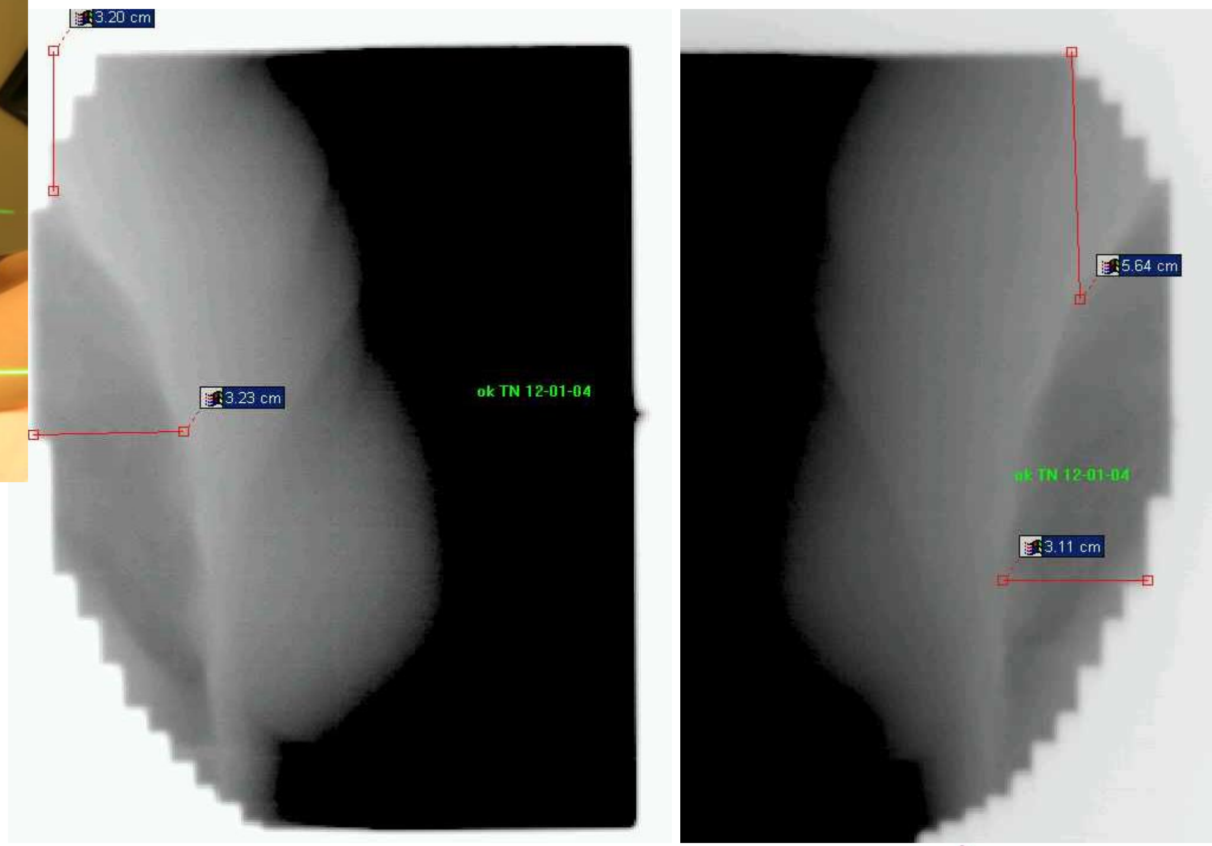
UK

ESTRO School

Image guidance

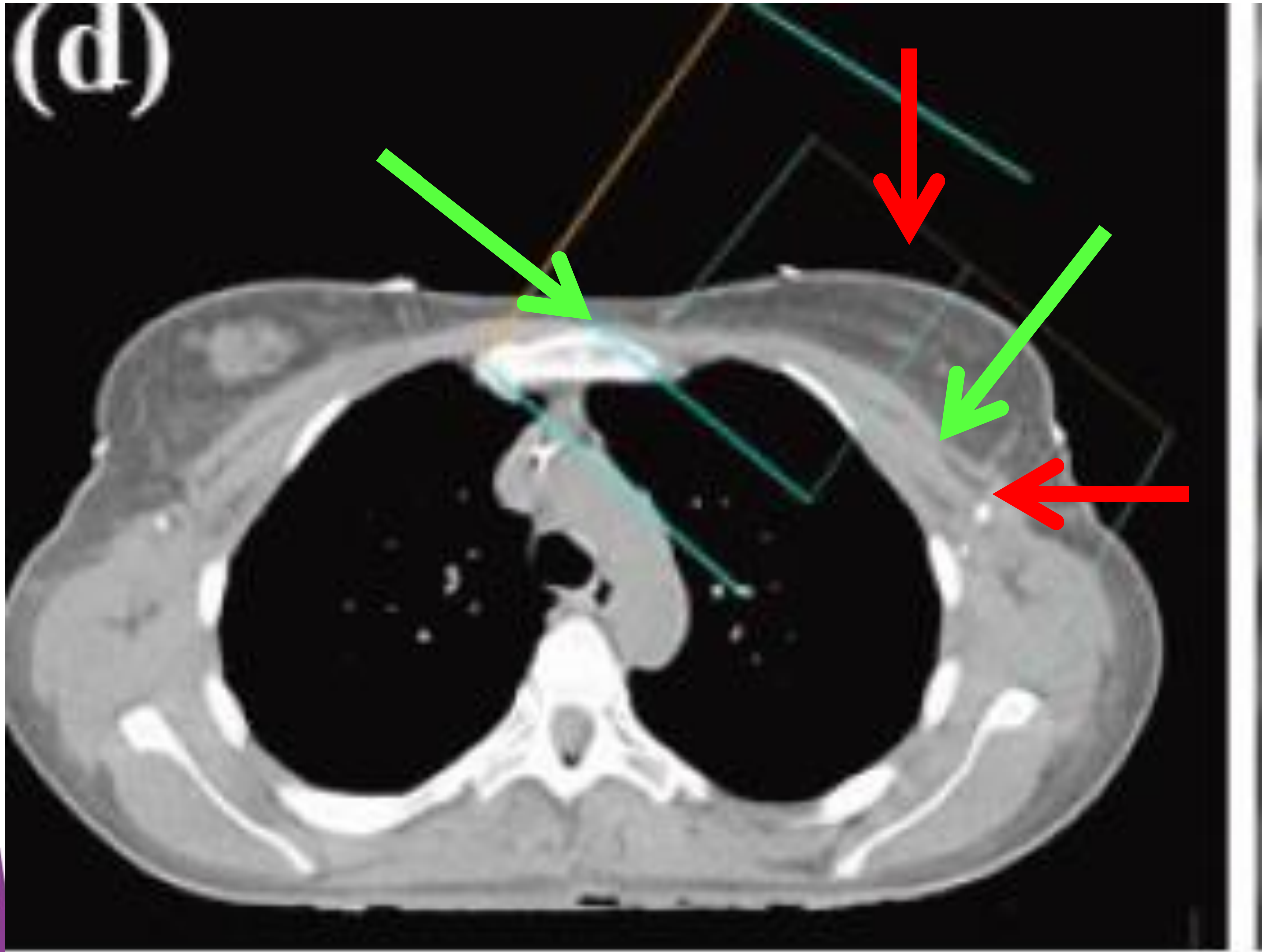
Field light / Beam's-eye-view (portal) images, MV





- Check the CLD
- long or vert ?
- Only one "direction"

Image-guidance for whole breast (+/- nodes)



Alternative 2D imaging strategy

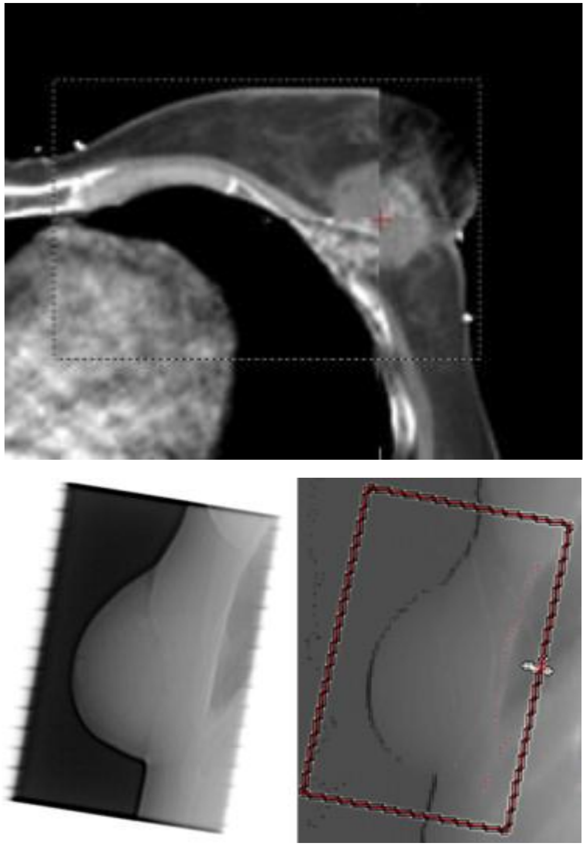
- AP-lat
- tangential +orthogonal
- kV-MV
- kV-kV

Petillion et al JACMP 2015 :
Tangential kV-kV (green) superior to AP-lat kV-MV (red)

Image-guidance for whole breast (+/- nodes)

kV CBCT

EPID



Topolnjak IJROBP 2010

- EPID field images (i.e. not orthgonal) underestimate bony set-up errors by 20% to 50%

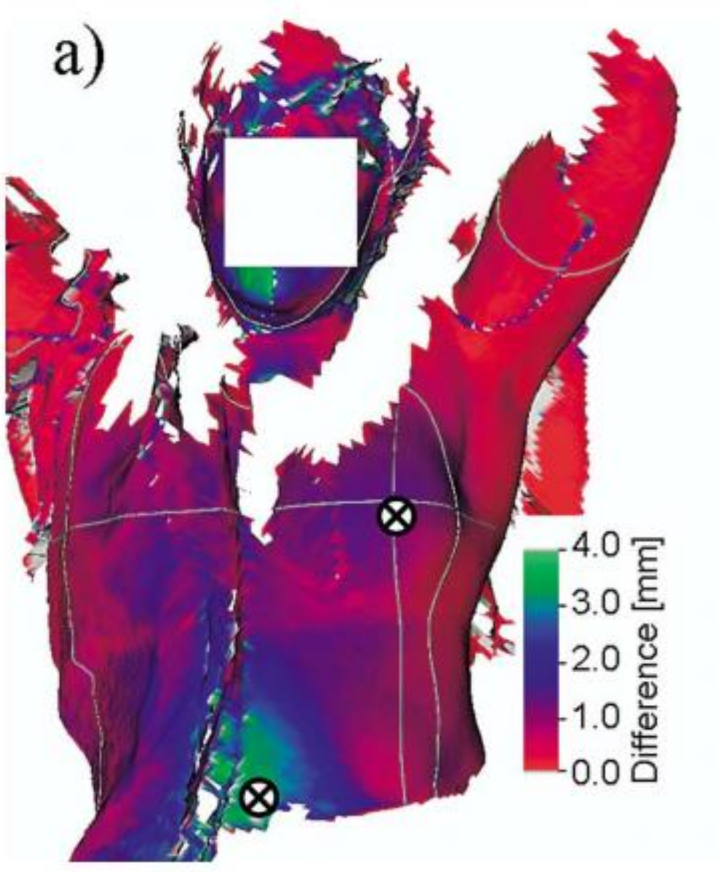
- Difference probably insignificant for tangential whole breast irradiation

- Loco-regional treatment or more advanced techniques (SIB? IMRT?) could benefit from a more accurate set up.

Image-guidance for whole breast (+/- nodes)

- Target with “high deformability”
- Number of cameras ???

Bert et al (2 cameras)



- Difficult to distinguish between set-up error and anatomical changes (or breathing)

- Combination with x-ray IGRT still recommended (Betgen RO 2013)

How much accuracy do we actually gain ??

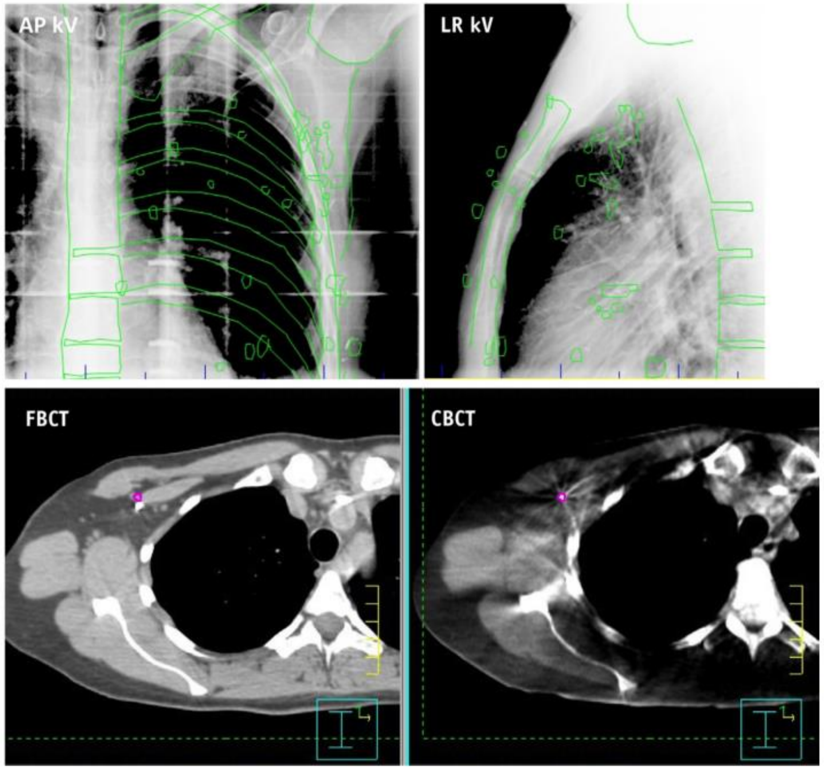
Comparing no images at all to one image on first day: no reduction of the systematic uncertainty

1SD	systematic [mm] lat	lng	vrt
1st fraction tolerance of 5 mm	3.7	3.3	3.4
no imaging no tolerance	3.7	3.3	3.5
with eNAL 3 mm tolerance	1.5	1.6	1.6
with eNAL 2mm	1.1	1.0	1.0

Unpublished data, courtesy of M Josipovic

Image-guidance for whole breast (+/- nodes)

- Highly conformal /complex techniques



Even with daily kV, the remaining set up error justifies a considerable margin (8mm SI)

(compared to CBCT, registered on clips)

Feng et al IJROBP 2014

Take home message:
IGRT for whole breast (+/- nodes)

•Imaging only in the beam direction will underestimate the set up error

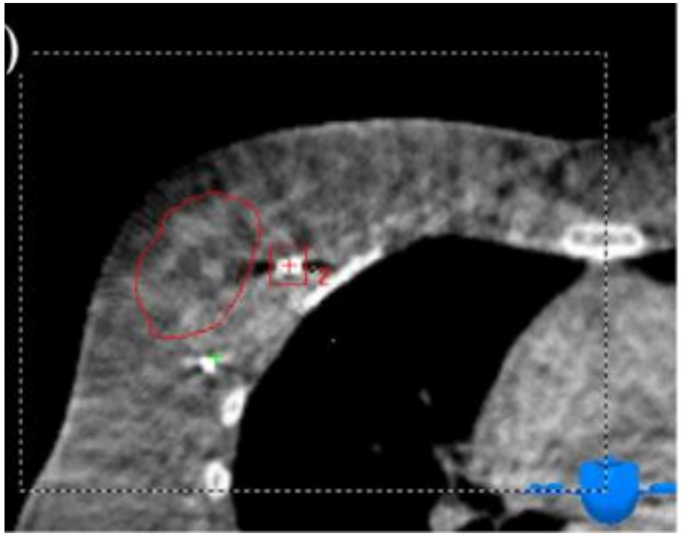
•No clear benefit of CBCT in terms of accuracy for “robust” techniques (3D tangents)

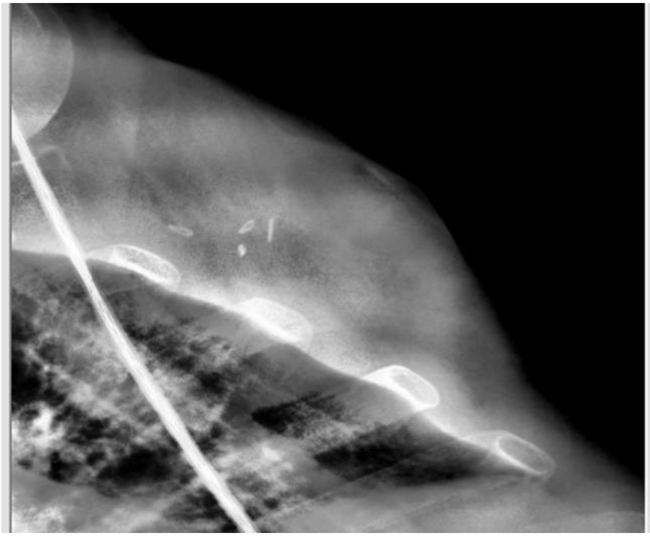
➢but other considerations: workflow? SIB? IMRT?

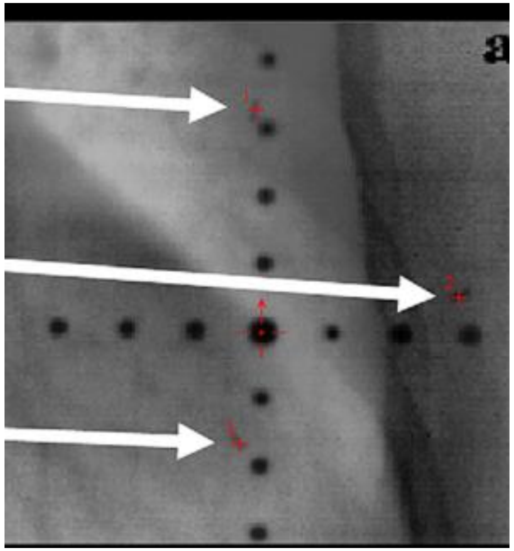
•Surface image has interesting potential and properties (no dose) but shouldn’t be the only modality for set-up (rotations, DIBH…)

PARTIAL BREAST / BOOST

Image-guidance in partial breast irradiation: implanted markers







CBCT: match on soft tissue/clips

Topolnjak 2011

2D kV images: match on clips

MV images: match on clips

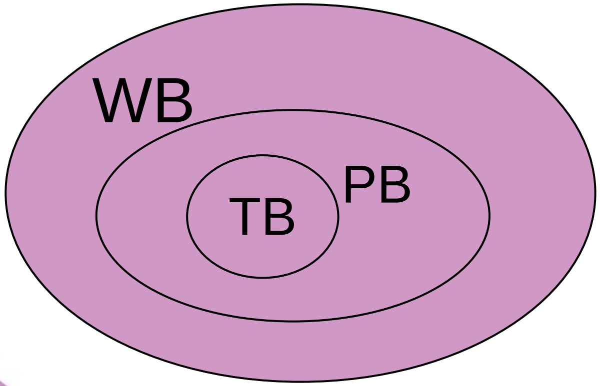
Leonard 2010

Partial breast /integrated boost

A multicentre observational study evaluating image-guided radiotherapy for more accurate partial-breast intensity-modulated radiotherapy: comparison with standard imaging technique

Emma J Harris,[1†] Mukesh Mukesh,[2†] Rajesh Jena,[2] Angela Baker,[3] Harry Bartelink,[4] Corrinne Brooks,[1] June Dean,[2] Ellen M Donovan,[1] Sandra Collette,[5] Sally Eagle,[6] John D Fenwick,[7] Peter H Graham,[8] Jo S Haviland,[9] Anna M Kirby,[10] Helen Mayles,[3] Robert A Mitchell,[1] Rosalind Perry,[11] Philip Poortmans,[12] Andrew Poynter,[13] Glyn Shentall,[14] Jenny Titley,[9] Alistair Thompson,[15] John R Yarnold,[10] Charlotte E Coles[2‡] and Philip M Evans[1,16*‡] on behalf of the IMPORT Trials Management Group

[1]Joint Department of Physics at The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK
[2]Oncology Centre, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
[3]Department of Radiotherapy and Physics, The Clatterbridge Cancer Centre NHS Foundation Trust, Wirral, UK
[4]Department of Radiation Oncology, The Netherlands Cancer Institute, Amsterdam, the Netherlands
[5]Statistics Department, EORTC Headquarters, Brussels, Belgium
[6]Department of Radiotherapy, Royal Marsden Hospital NHS Foundation Trust, London, UK
[7]Department of Oncology, University of Oxford, Oxford, UK
[8]Cancer Care Centre, St George Hospital, Kogarah, Sydney, NSW, Australia
[9]ICR-CTSU, Institute of Cancer Research, London, UK
[10]Breast Unit, Royal Marsden NHS Foundation Trust, London, UK
[11]Radiotherapy Department, Ipswich Hospitals NHS Trust, Ipswich, UK
[12]Department of Radiation Oncology, Dr Bernard Verbeeten Instituut, Tilburg, the Netherlands
[13]Radiotherapy Department, Peterborough City Hospital, Peterborough, UK
[14]Rosemere Cancer Centre, Lancashire Teaching Hospitals NHS Trust, Preston, UK
[15]School of Medicine, University of Dundee, Dundee, UK
[16]Centre for Vision, Speech and Signal Processing, Faculty of Engineering and Physical Sciences, University of Surrey, Guildford, UK



Comparing bone registration to clips-based reg

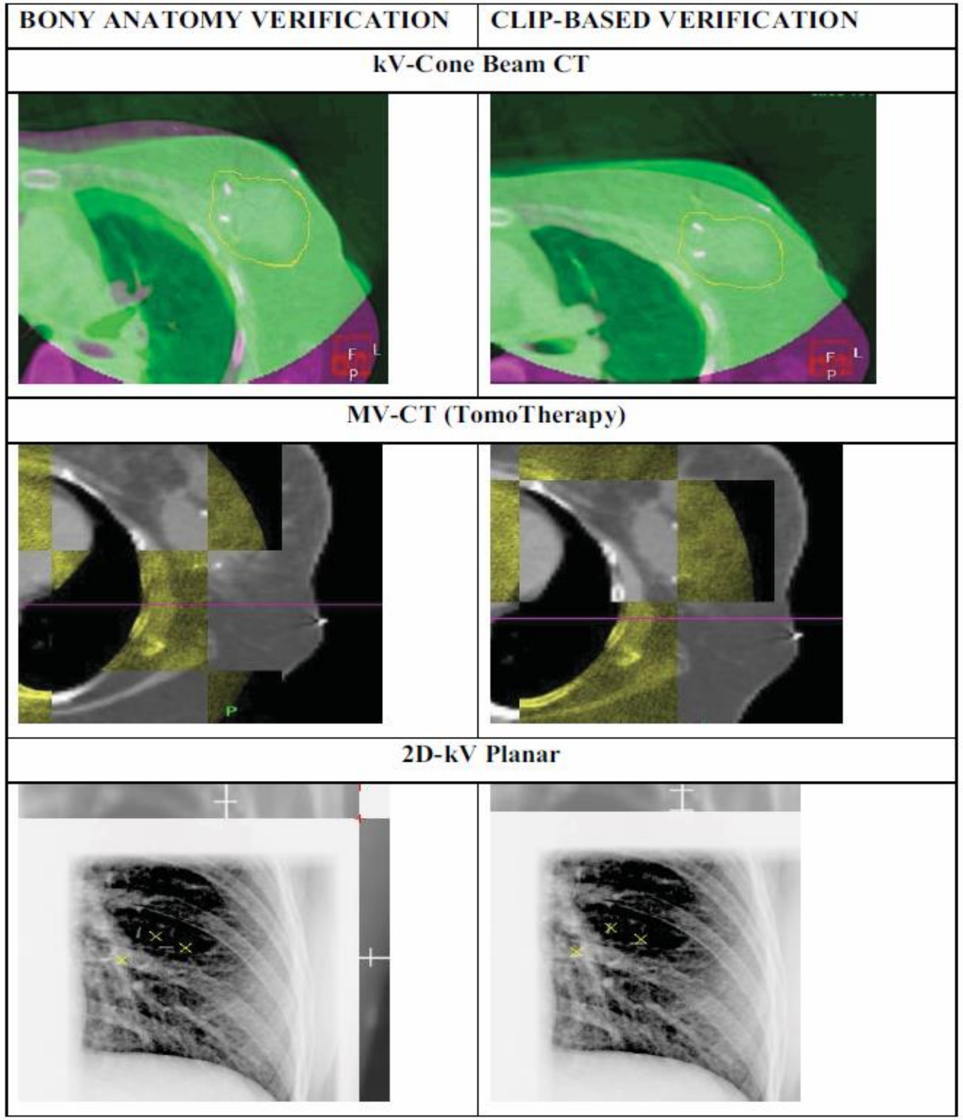


TABLE 8 Delta errors (difference between bony anatomy and clips, S_{DIFF}) in the LR, SI and AP directions and the magnitude of their 3D vector. Time required for image matching with both techniques has also been summarised

	Delta error (S_{DIFF}), mean absolute delta [cm (range)]				Time, median [seconds (range)]	
Centre	LR	SI	AP	3D vector	T_{BA}	T_{clips}
All	0.20 (0–1.7)	0.26 (0–3.2)	0.21 (0–2.0)	0.32 (0–10.2)	73 (8–240)	66 (8–178)
A (kV-CBCT)	0.19 (0–0.7)	0.24 (0–3.2)	0.22 (0–1.7)	0.28 (0–10.2)	26 (8–51)	92 (11–177)
B (MV-CT)	0.14 (0–0.7)	0.12 (0–1.2)	0.18 (0–1.3)	0.17 (0–2.0)	102 (70–230)	110 (25–178)
C (2D-kVPI)	0.23 (0–1.7)	0.29 (0–2.4)	0.20 (0–2.0)	0.38 (0–6.29)	22 (20–76)	16 (8–52)
D (2D-kVPI)	0.21 (0–1.3)	0.32 (0–1.3)	0.21 (0–1.0)	0.35 (0–2.2)	79 (60–154)	28 (20–85)
E (2D-kVPI)	0.20 (0–1.5)	0.31 (0–1.4)	0.23 (0–1.0)	0.36 (0–3.3)	110 (28–240)	34 (16–120)

Difference between bone reg and clips reg: 2-3 mm

Reduction in PTV (tumourbed) from 8 to 5 mm with clips-based IGRT, daily or with eNAL

Modest dosimetric impact

TABLE 8 Delta errors (difference between bony anatomy and clips, S_{DIFF}) in the LR, SI and AP directions and the magnitude of their 3D vector. Time required for image matching with both techniques has also been summarised

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Time varies per institution, even when using the same technique
2D kV scores both as fastest and slowest !
Inter and intra- observer error < 1.4mm for all modalities

Take home message:
Image-guidance for partial breast irradiation

Clips can be representative for
- the location of the tumor bed
- the location of the whole breast

Penninkhof Radiother Oncol 2009

Registering on clips is time-efficient and can allow for margin reduction of the tumour bed PTV

➢ Daily or eNAL

kV-CBCT, MV-CBCT, 2D kV are equivalent in terms of accuracy if registering on clips

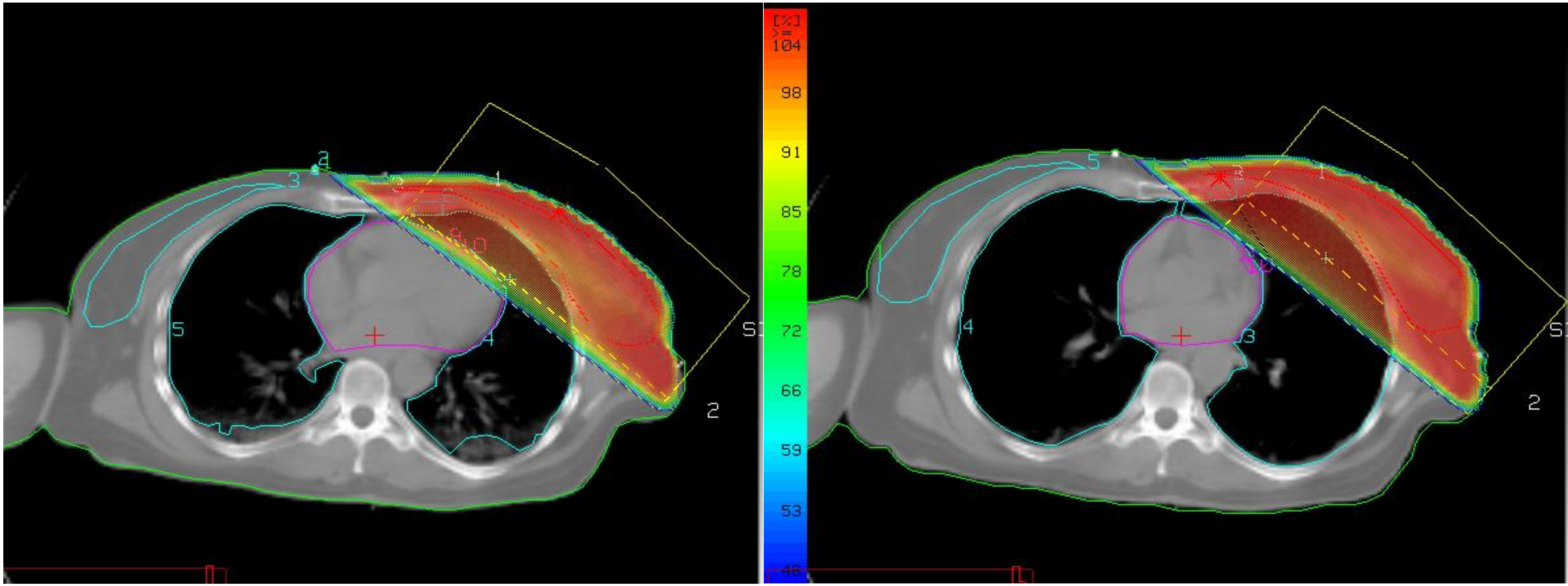
➢ 2D MV as well, if clips are visible

GATING /BREATH HOLD

Techniques for reduction of cardiac toxicity

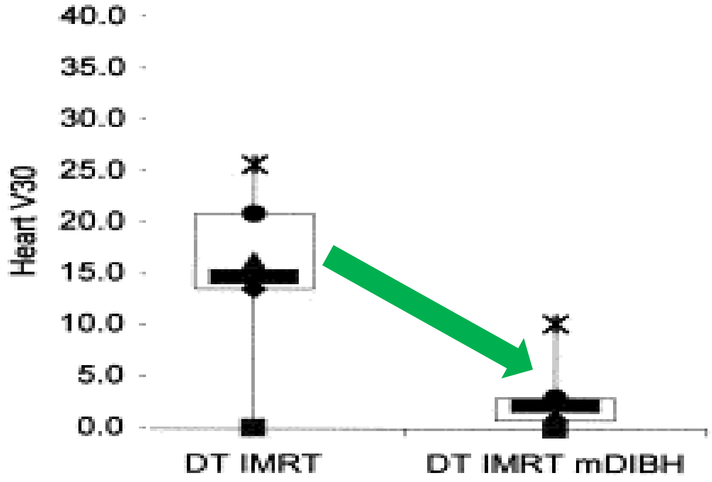
FB

DIBH



Techniques for reduction of cardiac toxicity

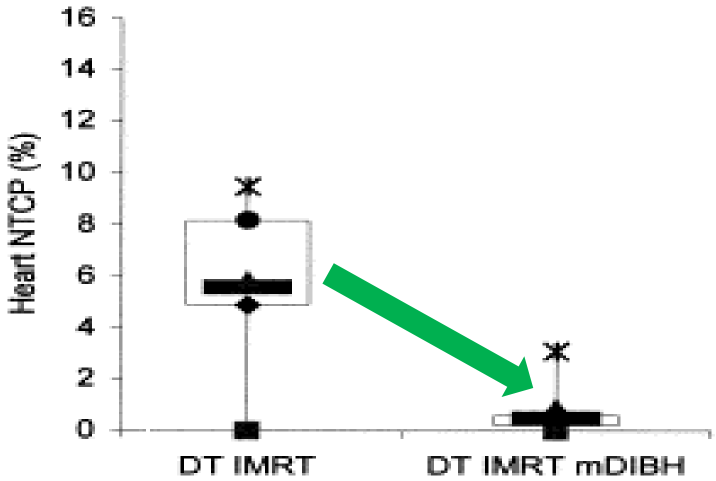
Heart V30



Remouchamps IJROBP 2003

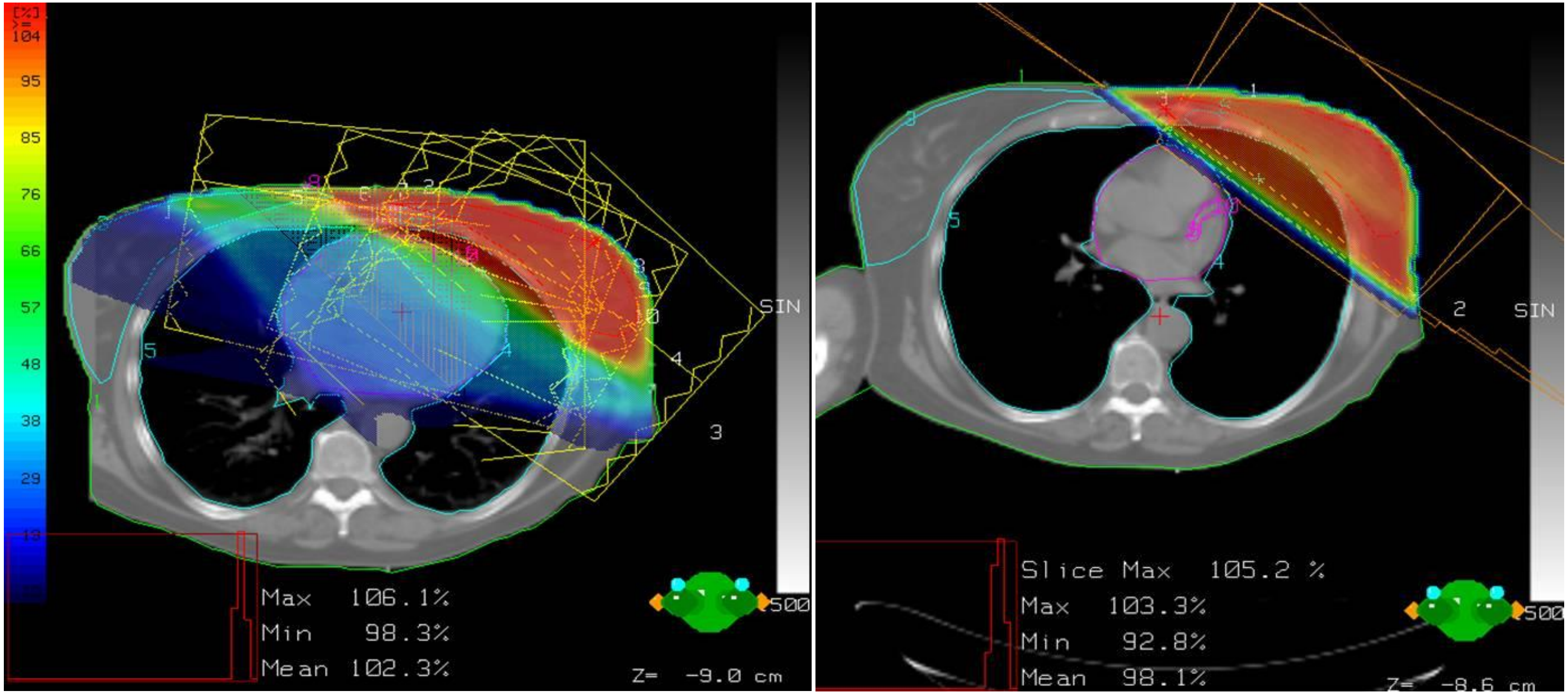
Significant reduction of heart dose and heart NTCP in left sides breast cancer

Heart NTCP



Remouchamps IJROBP 2003

Techniques for reduction of cardiac toxicity
IMRT or inspiration gating?



Patients with unfavorable thoracic anatomy:

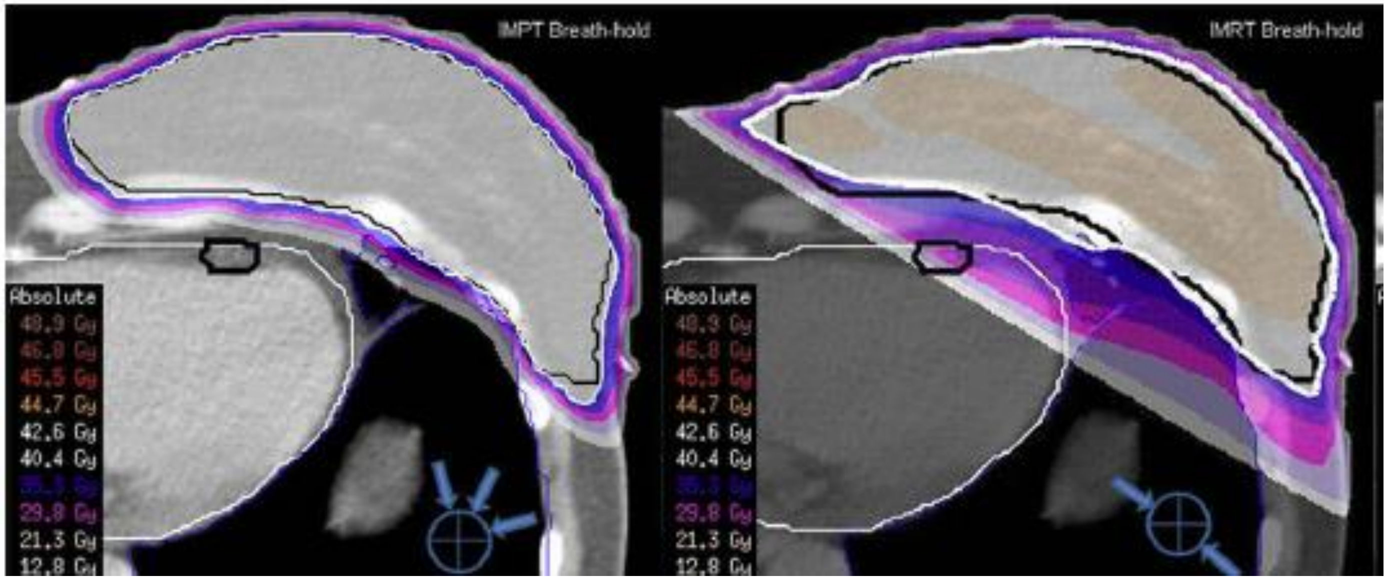
- Improved sparing of the heart with IMRT at cost of increased dose to the normal tissue (e.g. contralateral breast)
- Sparing of the heart can be more efficient with 3D_DIBH than with IMRT_FB.

Don’t get too fancy… at least until we have better evidence !

- ASTRO “choose wisely”
- (1) consider hypofractionation (>50 y, early stage)

- (5) don't routinely use ***(multi-field)*** IMRT to deliver whole-breast radiation therapy as part of breast conservation therapy.

IMPT IMRT



Mast BCRT 2014

Image guidance for deep inspiration: DIBH/gating monitoring

- Voluntary breath is hold is as efficient and more comfortable

Bartlett 2013

- The ”no equipment” solution:
  - short hyperventilation follwed by breath hold
  - Monitoring is visual (draw the light field on the patient, observed through control room monitors)
  - Video article: ***Bartlett et al J Vis Exp 2014***

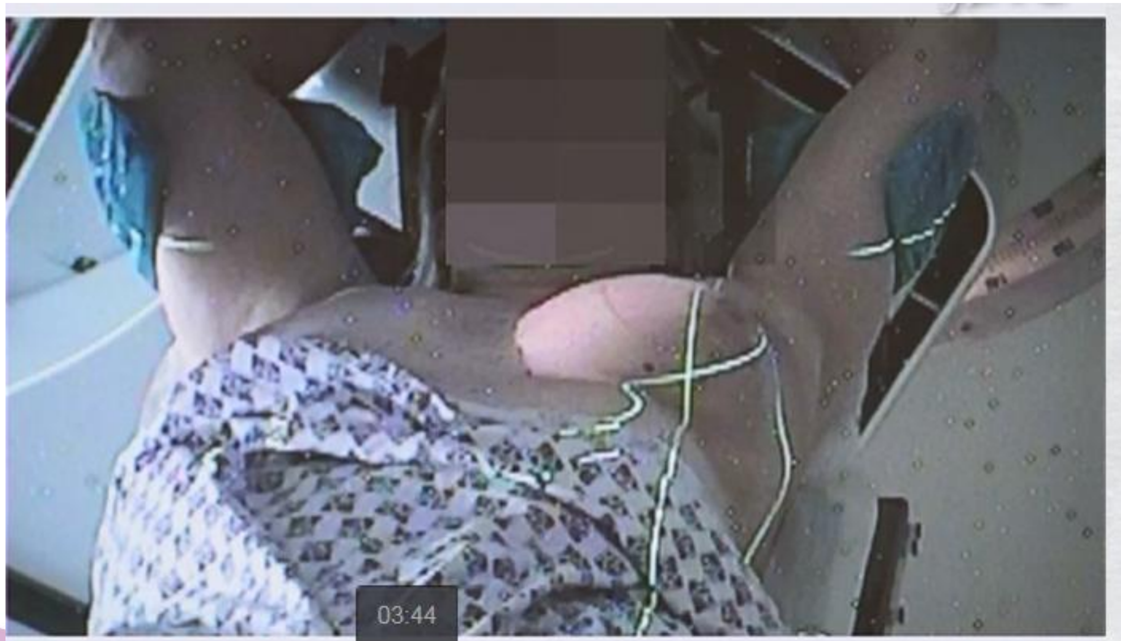


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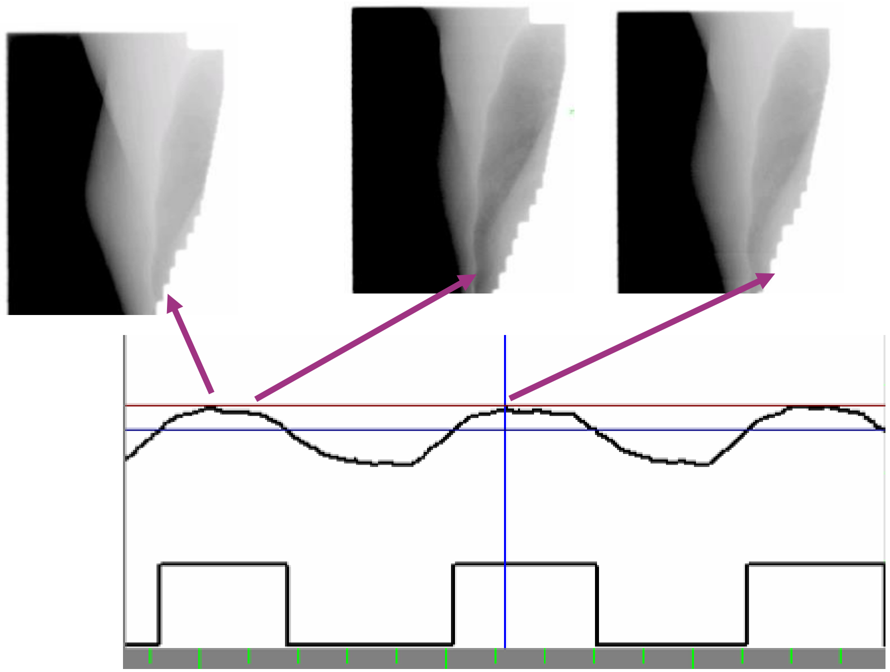
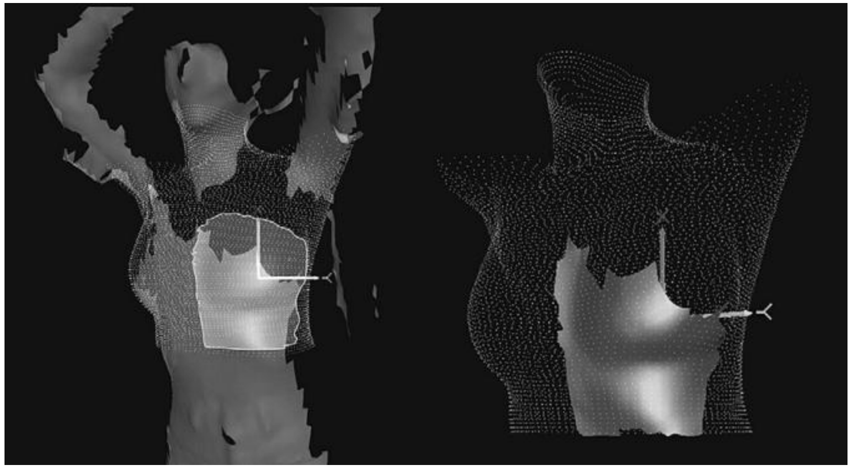
Image guidance for deep inspiration: DIBH/gating monitoring

- Patient set up as for conventional treatment (i.e. planar or CBCT)



Residual motion can be verified by cine EPID



Align RT: potential for breath hold monitoring
Maintain use of CBCT for set-up

Alderliesten et al IJROBP 2012

Take home message: image-guidance for DIBH/gating monitoring

- Deep inspiration techniques are easy to implement and effective in reducing heart and lung dose

- They are vey well tolerated

- Many technical solutions are available and they are all valid
  - ➢ choose what fits your workflow/resources best

- X-ray based imaging is still recommended in addition to ensure proper set-up

Take home message: image-guidance for breast cancer

- MV is acceptable is you have a good surrogate (e.g. visible clips, not ribs)
- The less robust your treatment technique, the more advanced the IGRT
- An offline strategy (NAL, eNAL, SAL, etc...) will go a long way towards reducing uncertainties
- Deep inspiration: just do it !

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Alternative 2D imaging strategy

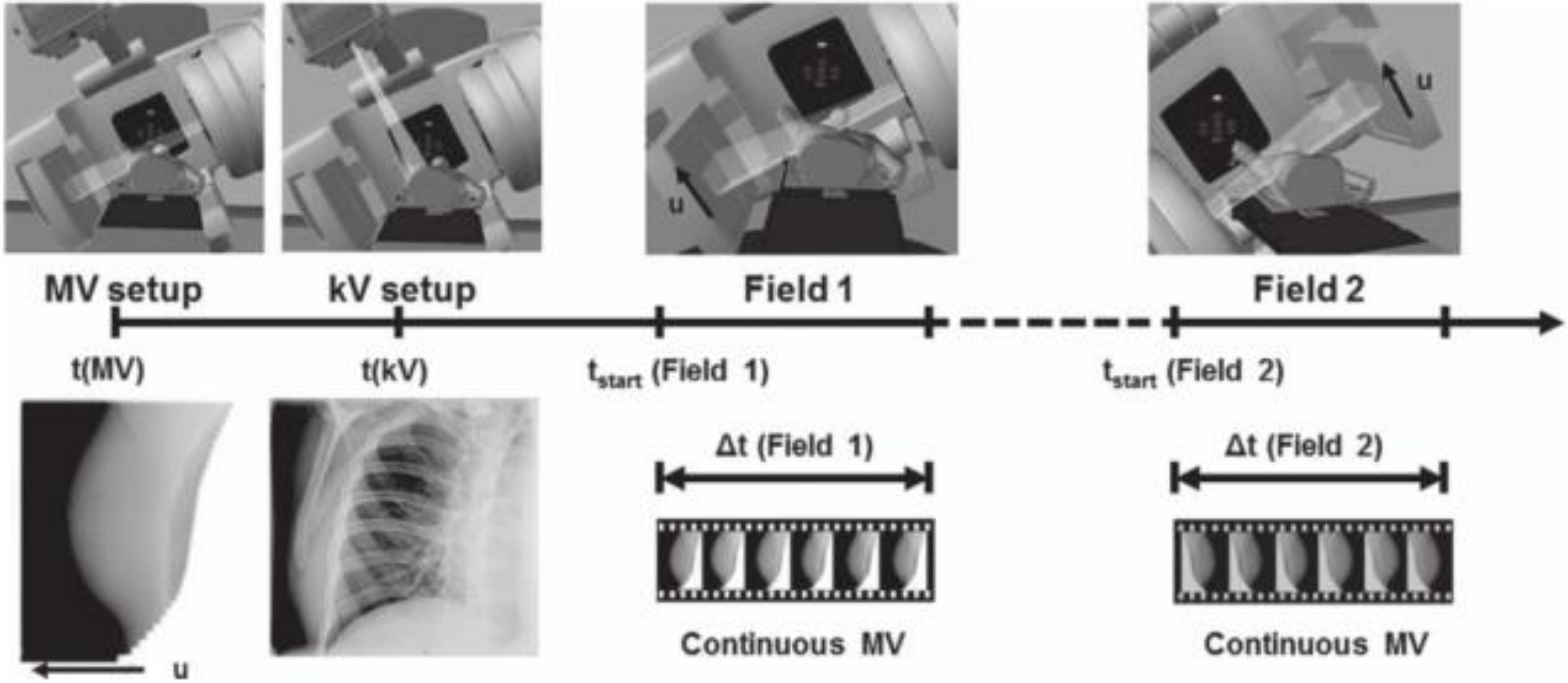

Figure 1. Daily setup procedure and imaging for a right-sided breast cancer patient. The MV and kV setup images were acquired at the same gantry angle (~60°).

Thomsen, Acta Oncol 2014

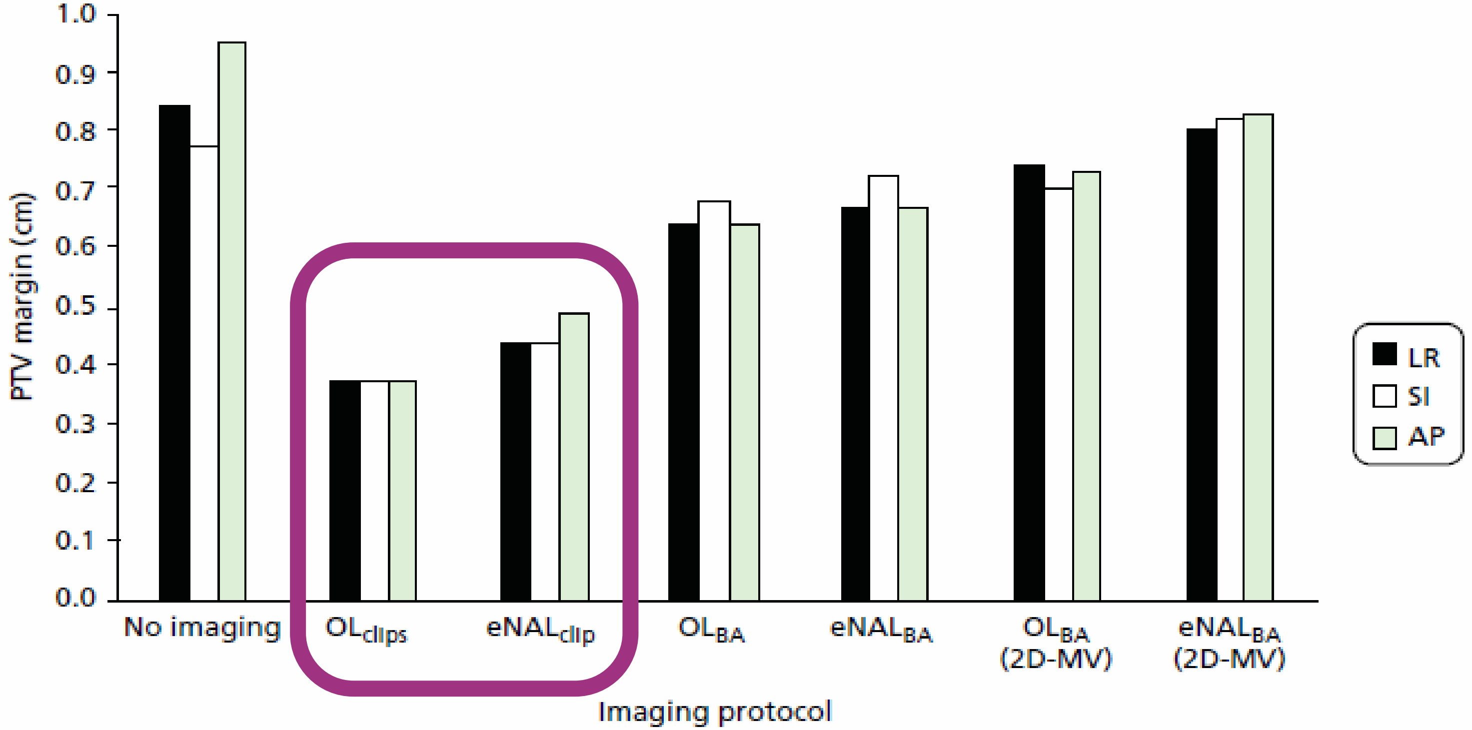

FIGURE 11 Tumour bed PTV margins required for the different imaging verification protocols considered in this study. Margins are given for the LR, SI and AP directions.

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Image Registration Issues for Breast

Madrid 2016

Helen McNair
Rms.nhs, London

Rianne de Jong
Academic Medical Centre, Amsterdam

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CBCT Registration

- Bony anatomy registration (ribs)
- Surface registration
- Marker registration

  - Definition of the region of interest (clipbox)
  - Choice of algorithm

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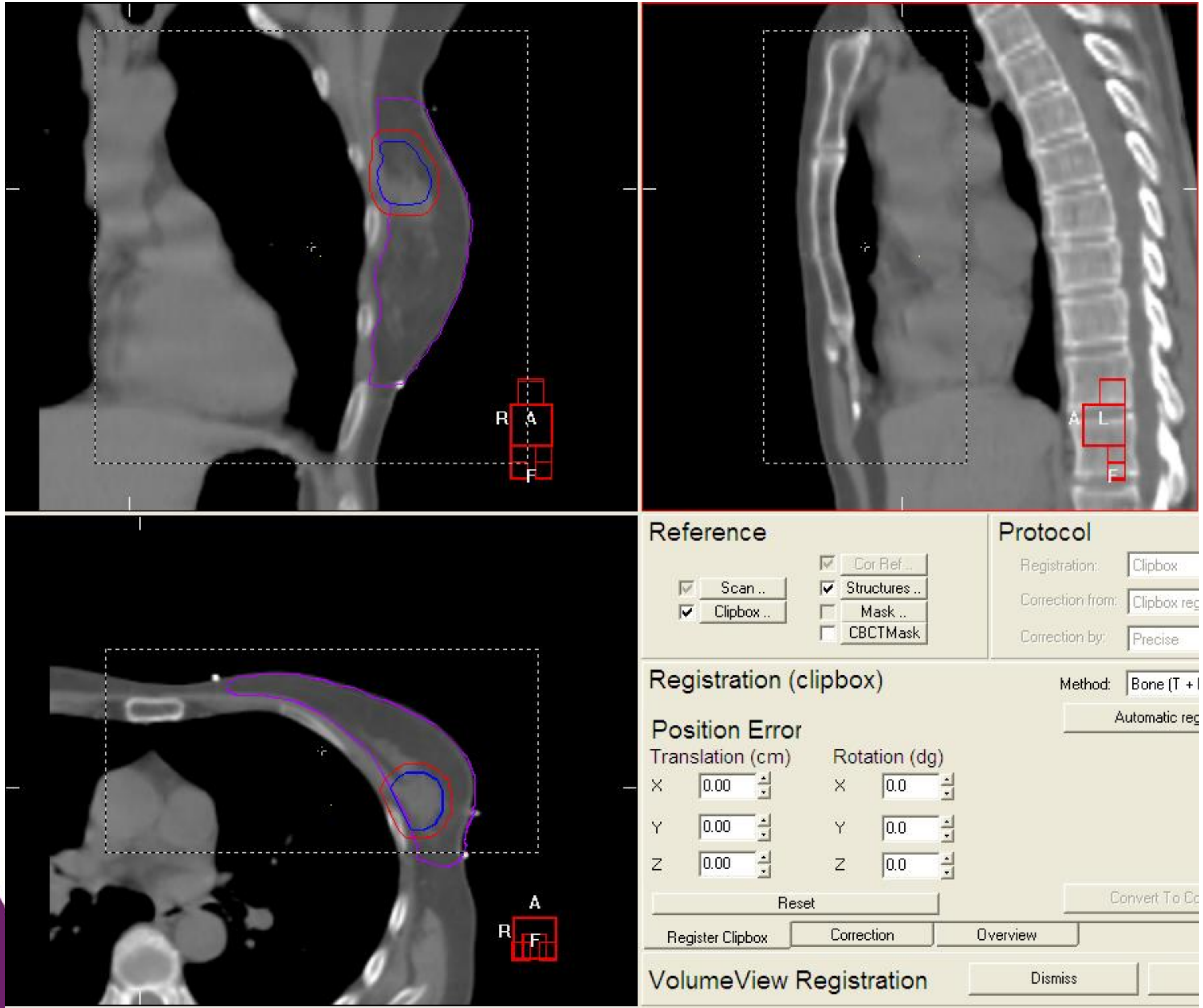
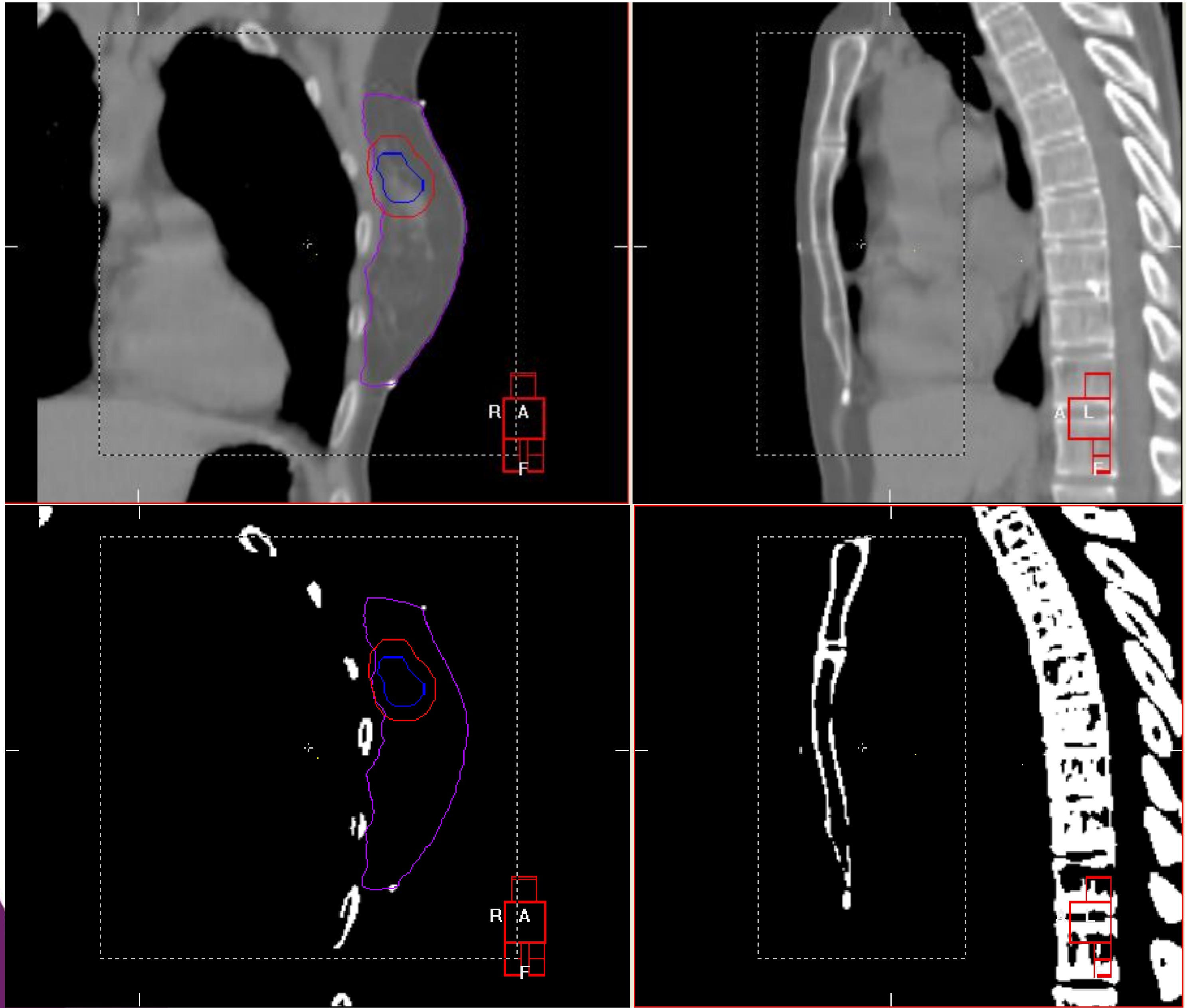
Registration on ribs



Bony anatomy that is a good surrogate: ribs

What are you registering with this ROI?

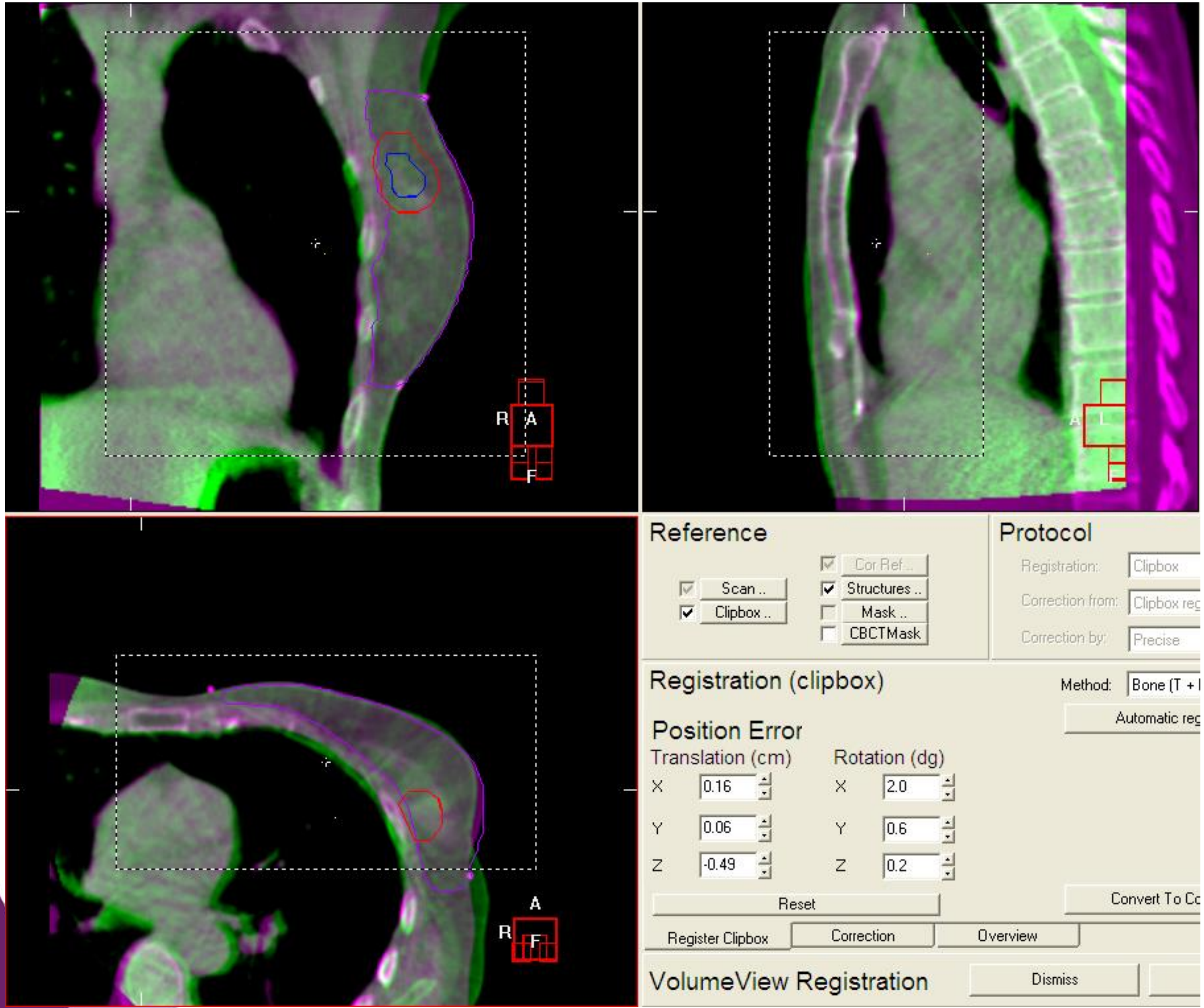
Registration on ribs



Chamfer registration

Segmentation of range of HU
- bones -

Registration on ribs



CT ref

CBCT

Bony anatomy that is a good surrogate: ribs

What are you registering with this ROI?

Bone algorithm (chamfer match)

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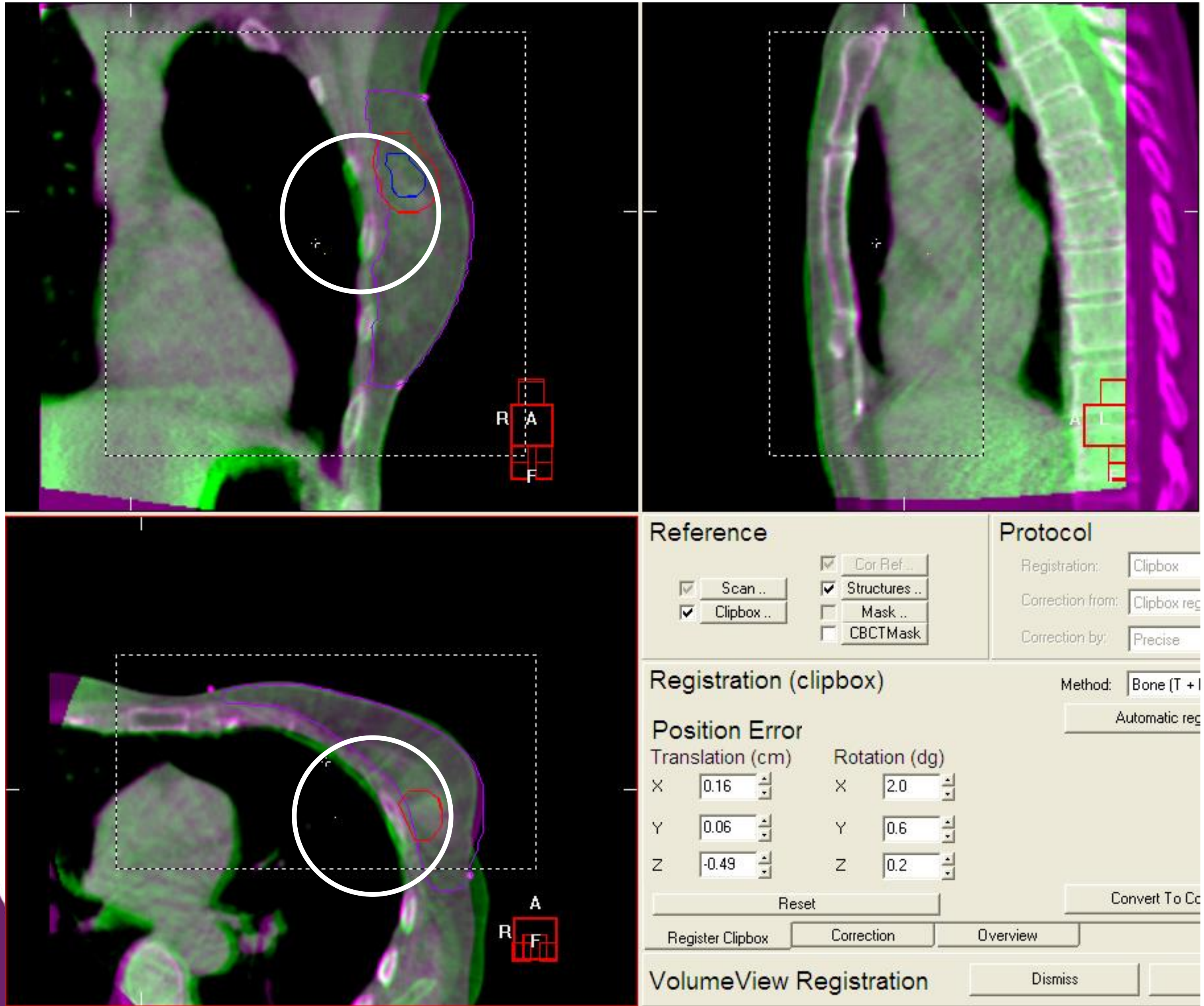
Breathing artefact ref CT

Registration on ribs



CT ref

CBCT

Bony anatomy that is a good surrogate: ribs

What are you registering with this ROI?

Bone algorithm (chamfer match)

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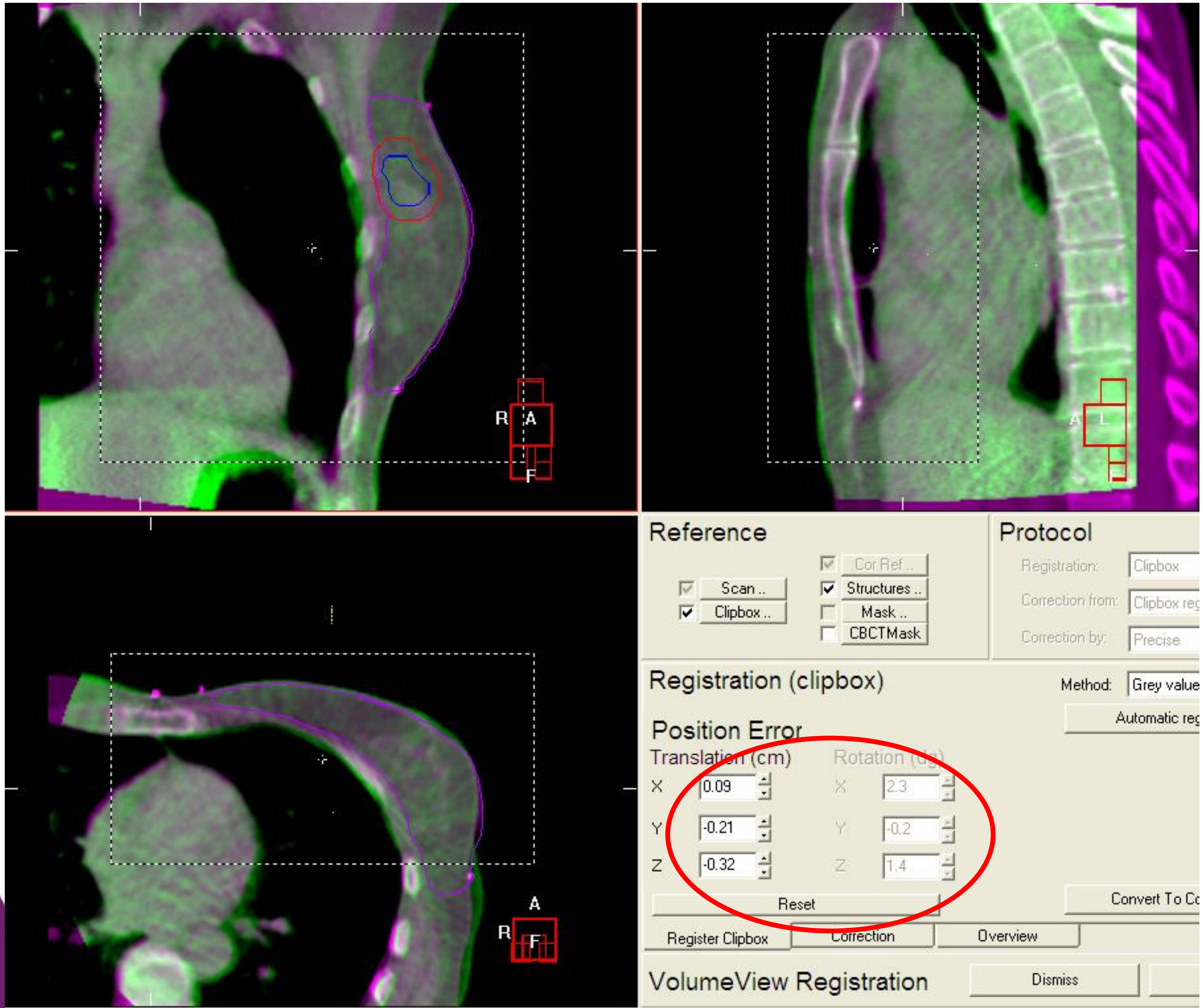
Registration on ~~ribs~~ surface!



CT ref

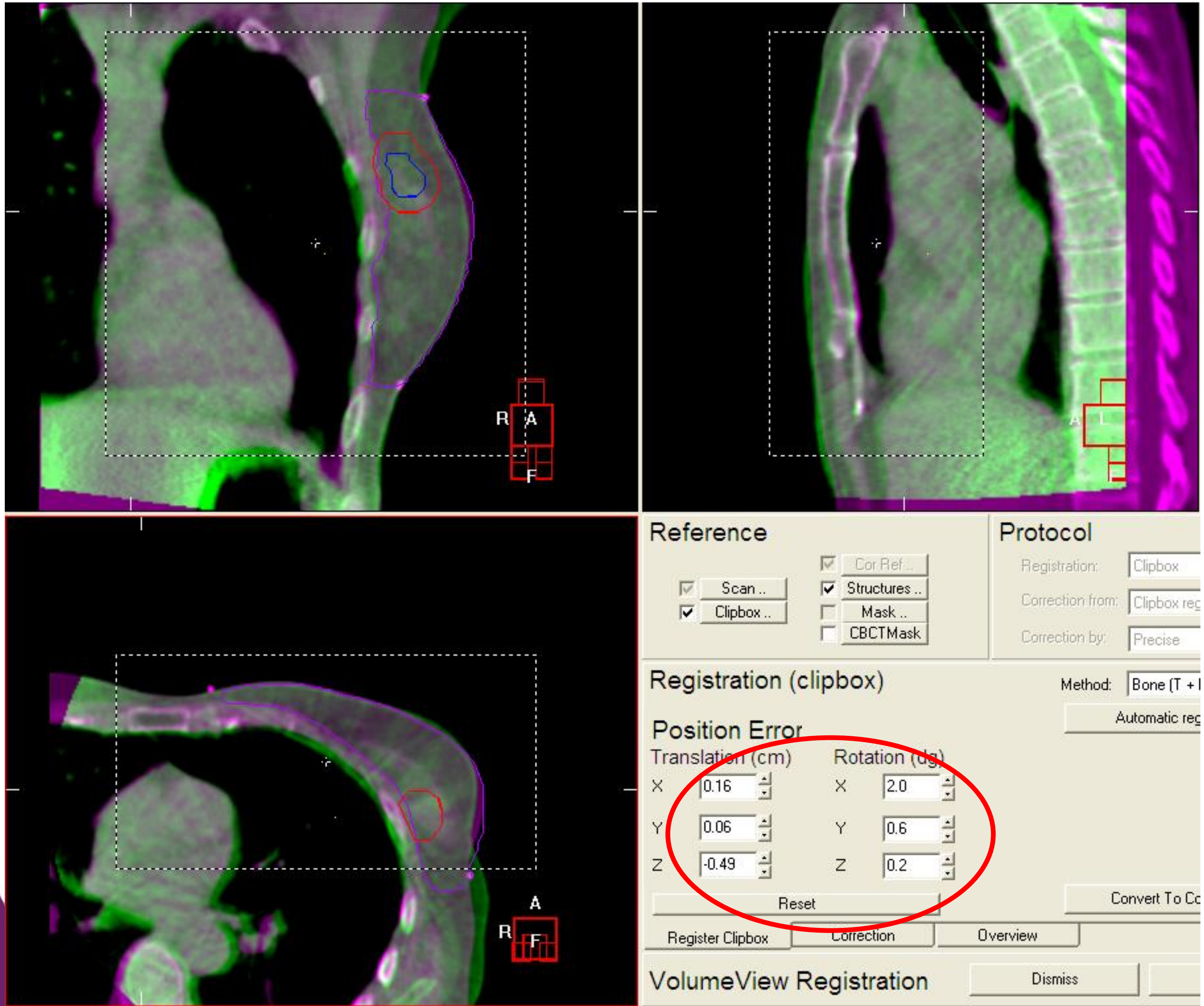
CBCT

Bony anatomy that is a good surrogate: ribs

What are you registering with this ROI?

Grey value algorithm

Registration on ~~ribs~~ surface!



CT ref

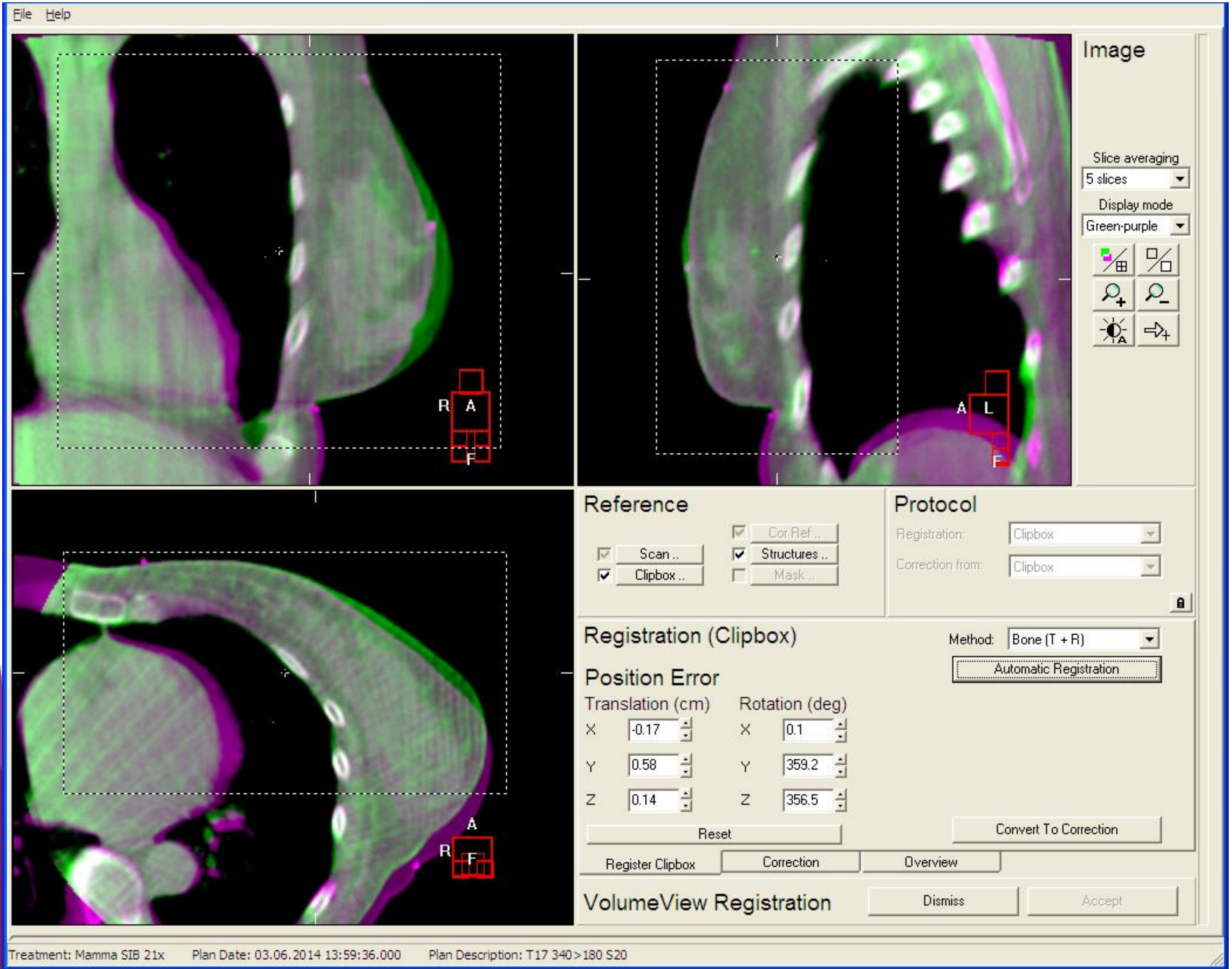
CBCT

Bony anatomy that is a good surrogate: ribs

What are you registering with this ROI?

Bone algorithm (chamfer match)

Registration on …

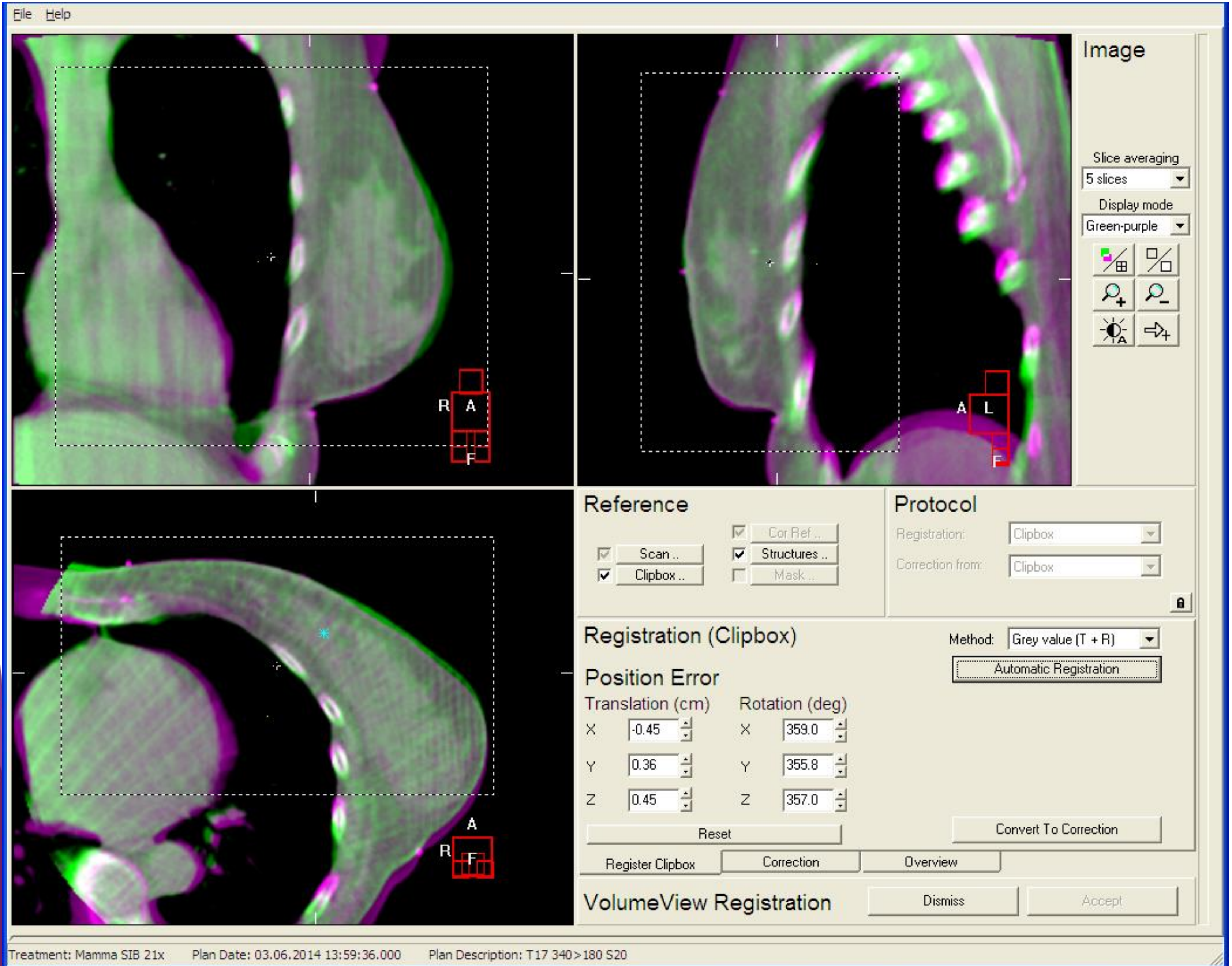


CT ref
CBCT

Ribs using:

Clipbox
&
Bone algorithm
(chamfer match)

Registration on …



CT ref

CBCT

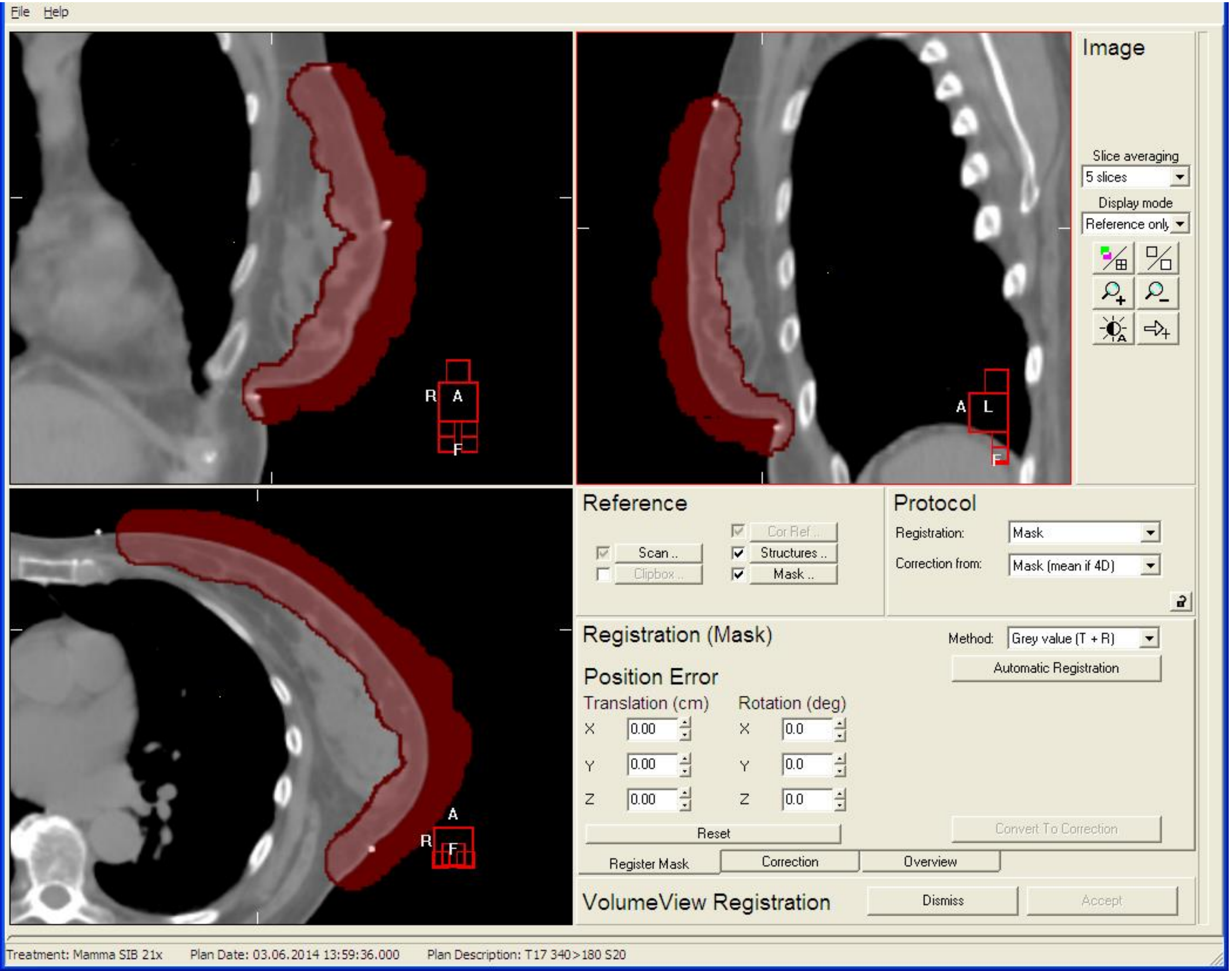
Surface using:

Clipbox

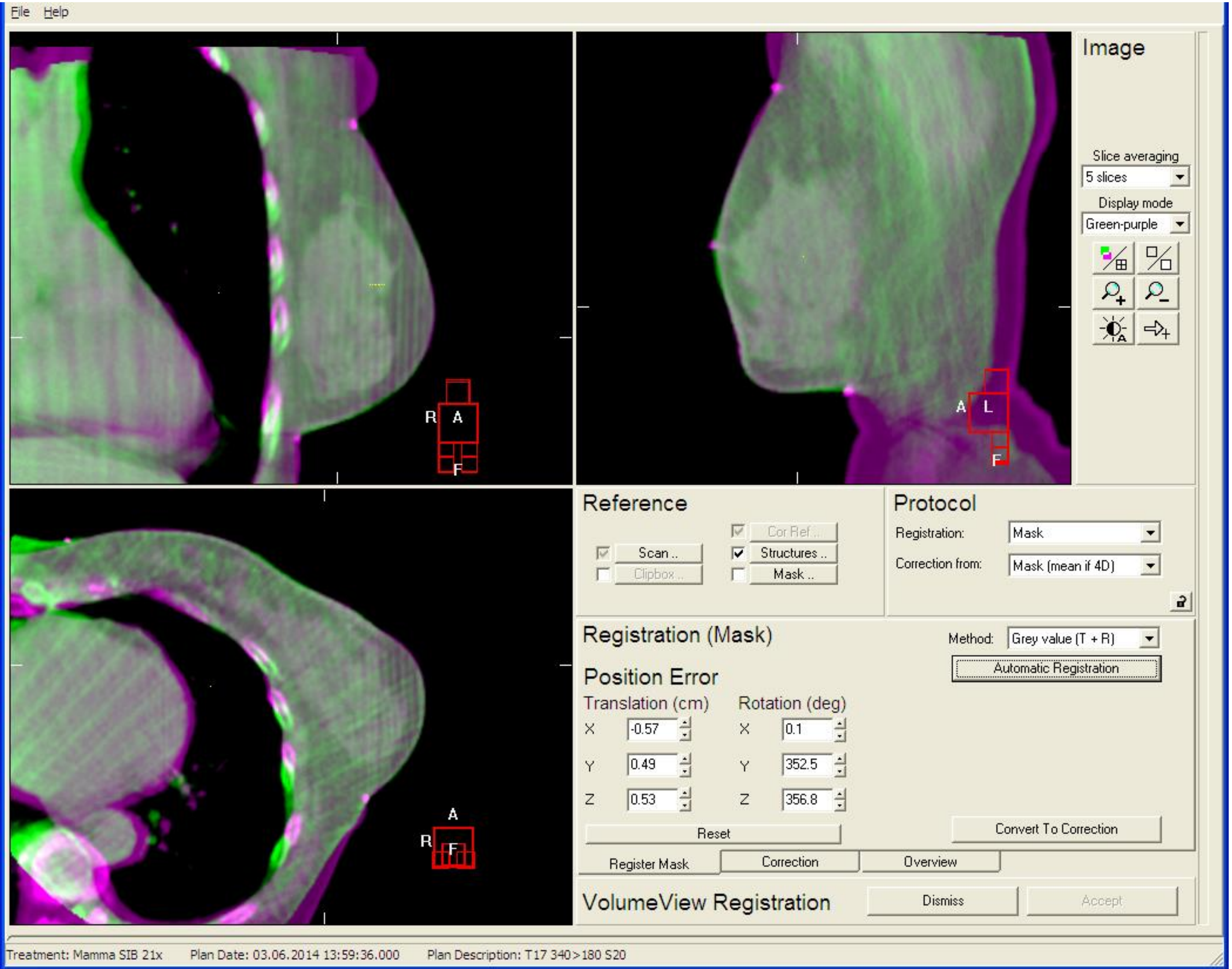
&

Grey Value algorithm

Registration on …



Registration on …



CT ref

CBCT

Surface using:

SROI

&

Grey Value algorithm

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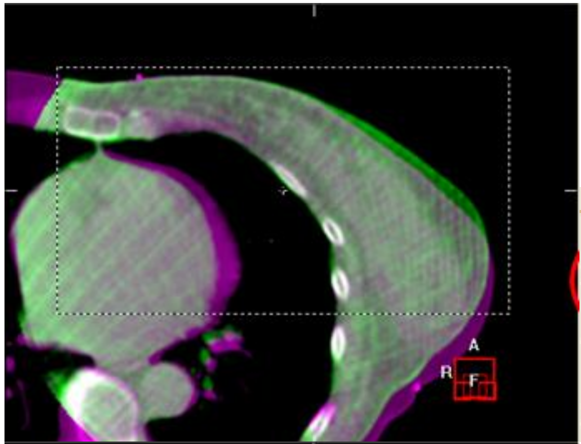
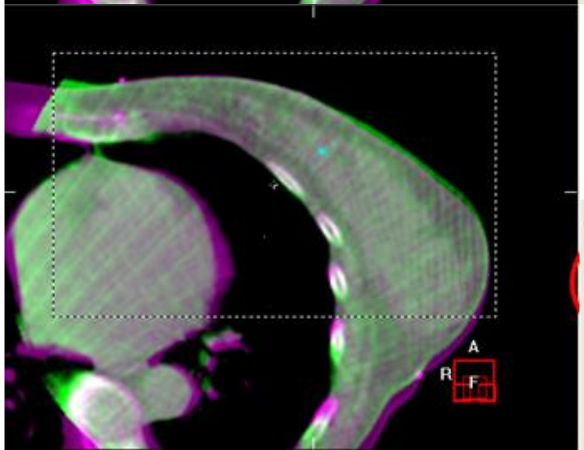
CT ref
CBCT

Registration on …



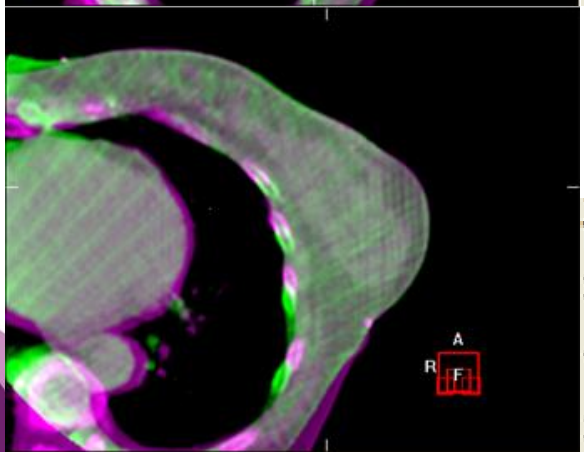
Translation (cm)		Rotation (deg)	
X	-0.17	X	0.1
Y	0.58	Y	359.2
Z	0.14	Z	356.5

Ribs using clipbox and bone



Translation (cm)		Rotation (deg)	
X	-0.45	X	359.0
Y	0.36	Y	355.8
Z	0.45	Z	357.0

Surface using clipbox and grey value



Translation (cm)		Rotation (deg)	
X	-0.57	X	0.1
Y	0.49	Y	352.5
Z	0.53	Z	356.8

Surface using shaped ROI and grey value

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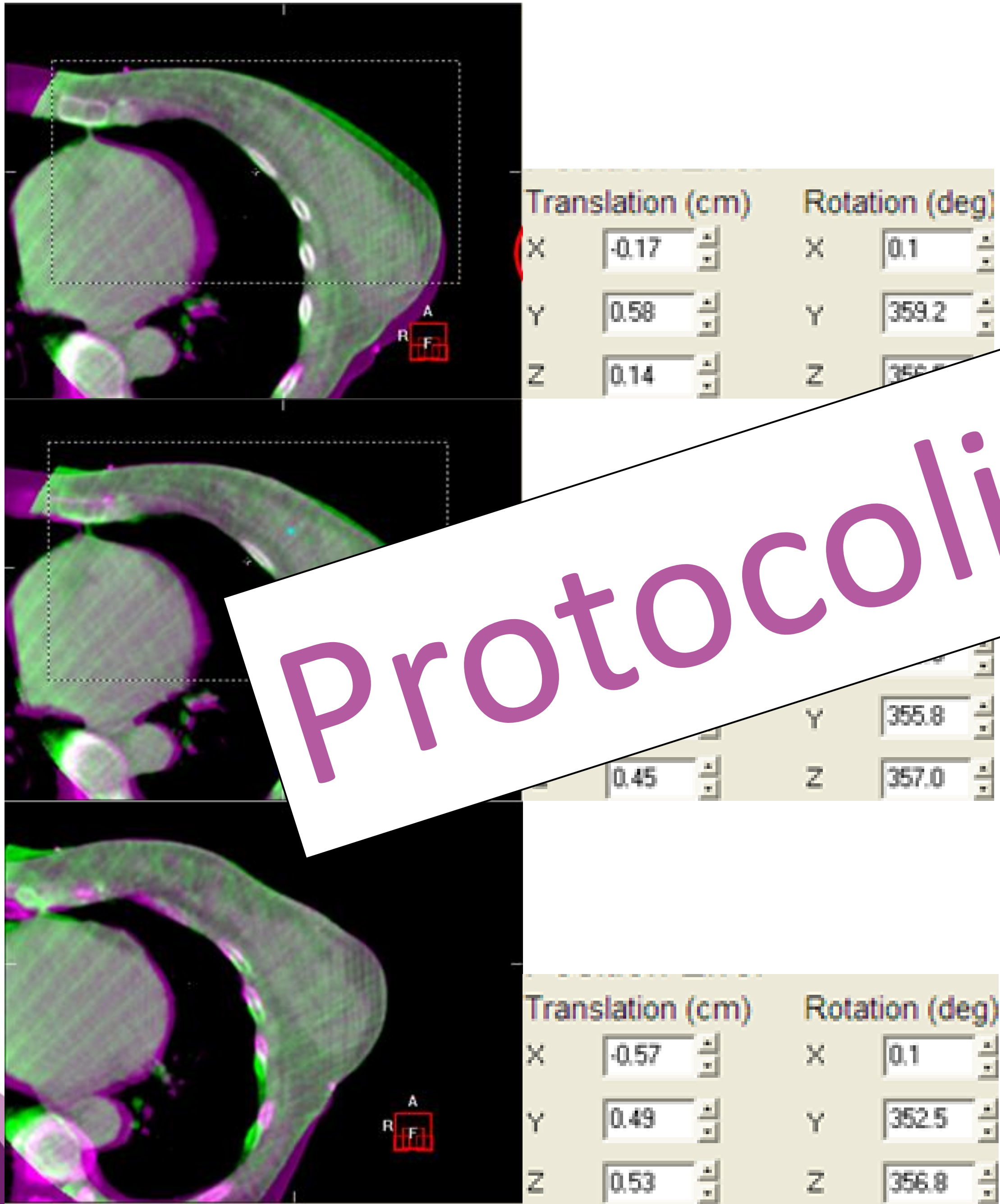
CT ref
CBCT

Registration on …



Ribs using clipbox and bone

Protocolize!!

Surface using clipbox and grey value

Surface using shaped ROI and grey value

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Breast

MATCH PARAMETERS		SCAN PARAMETERS	
Structures	TV_IMRT	**Preset selection**	Breast left/right
Correction ref point	TV_IMRT	**Gantry rotation**	Breast right: -180° → 25° Breast left: 330° → 180°
Registration	Clipbox	**Gantry speed**	0.5 rpm
Method	Bone (T + R)	**Detector position**	S
Restriction Rotation	5°	**Filter**	F1
Restriction Translation	[illegible]	**Collimation**	S20

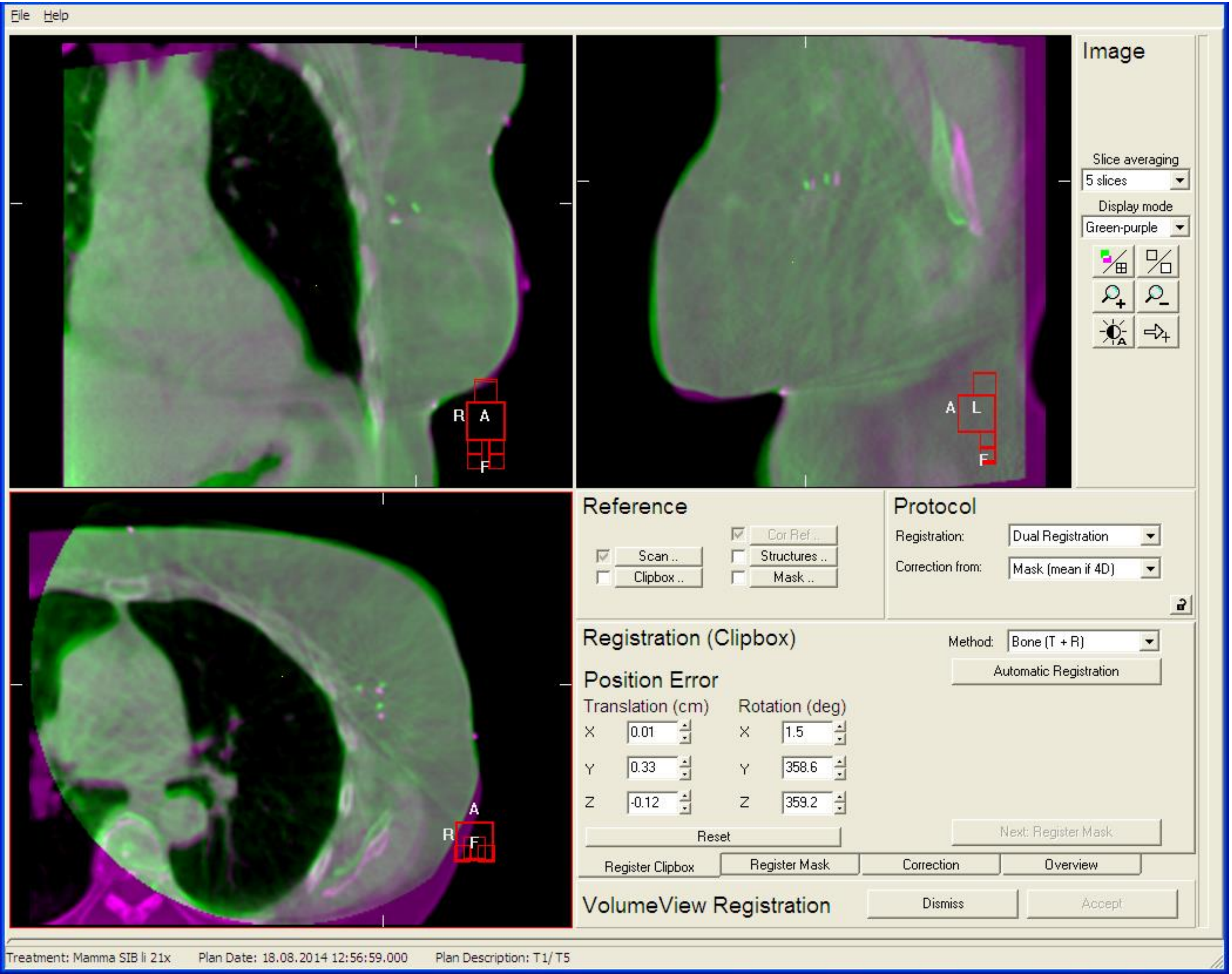
Example clipbox:

For setting the clipbox:

- Include as much breast tissue as possible in the clipbox and also include part of the sternum.
- Do not include (any) vertebrae.

<u>Breast including integrated boost</u>: the correction ref point is placed in de PTV of the boost area. If the boost area is placed asymmetrically within the breast tissue, consider placing the correction reference point on the edge of the boost area more towards the centre of the breast PTV. This can be done by placing a marker in this position and putting the correction reference point on the marker.

Marker registration with shaped ROI



CT ref

CBCT

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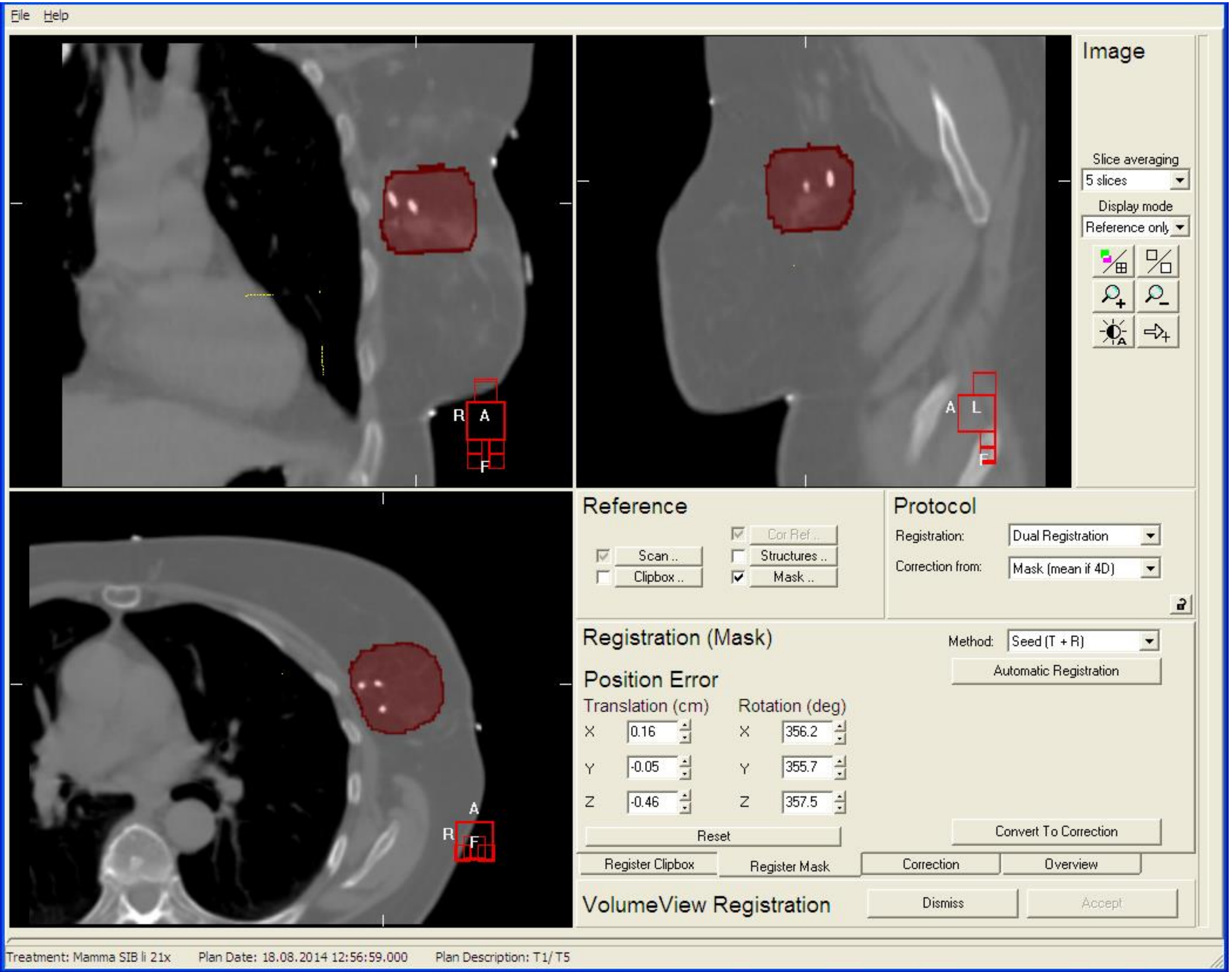
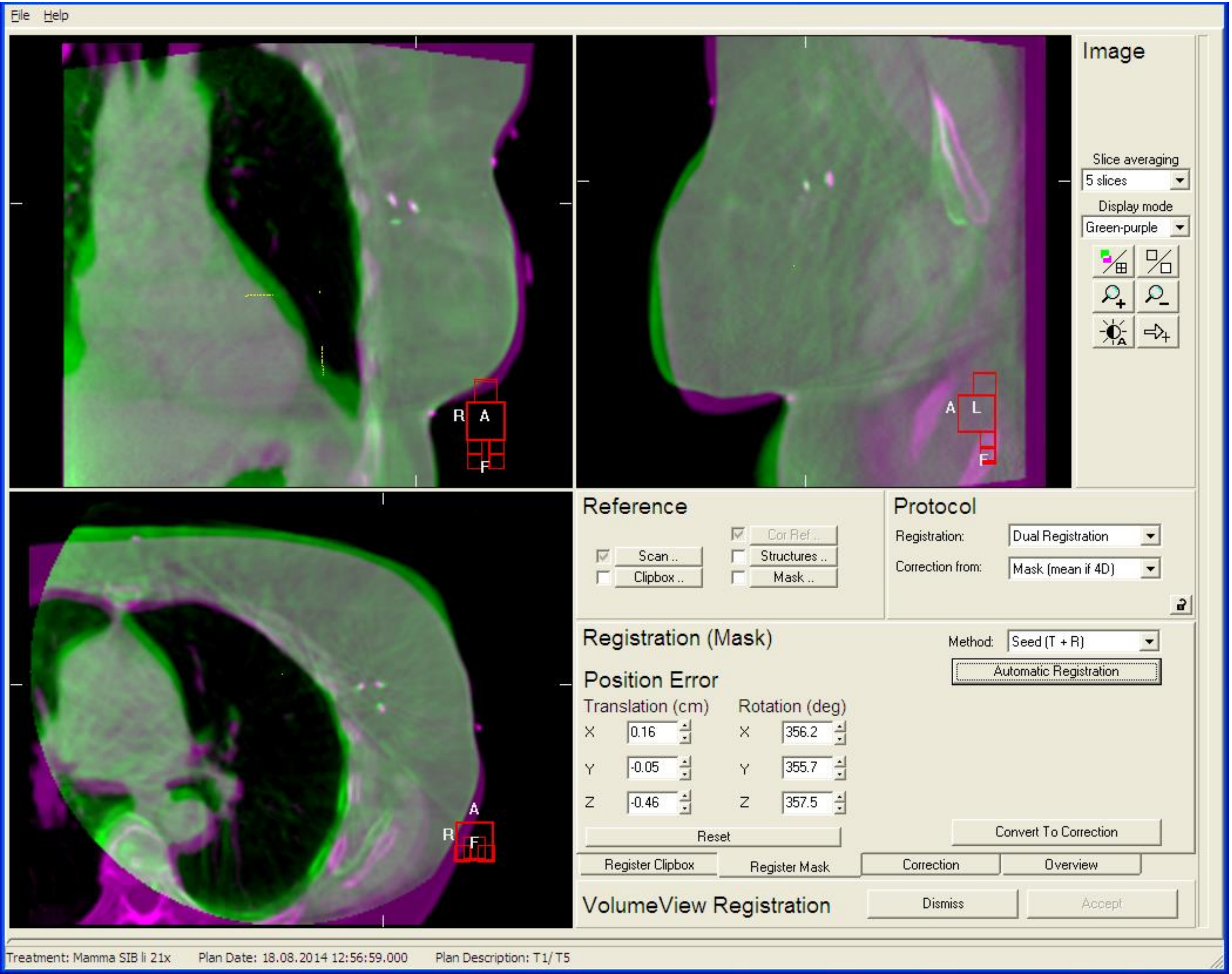
Marker registration with shaped ROI



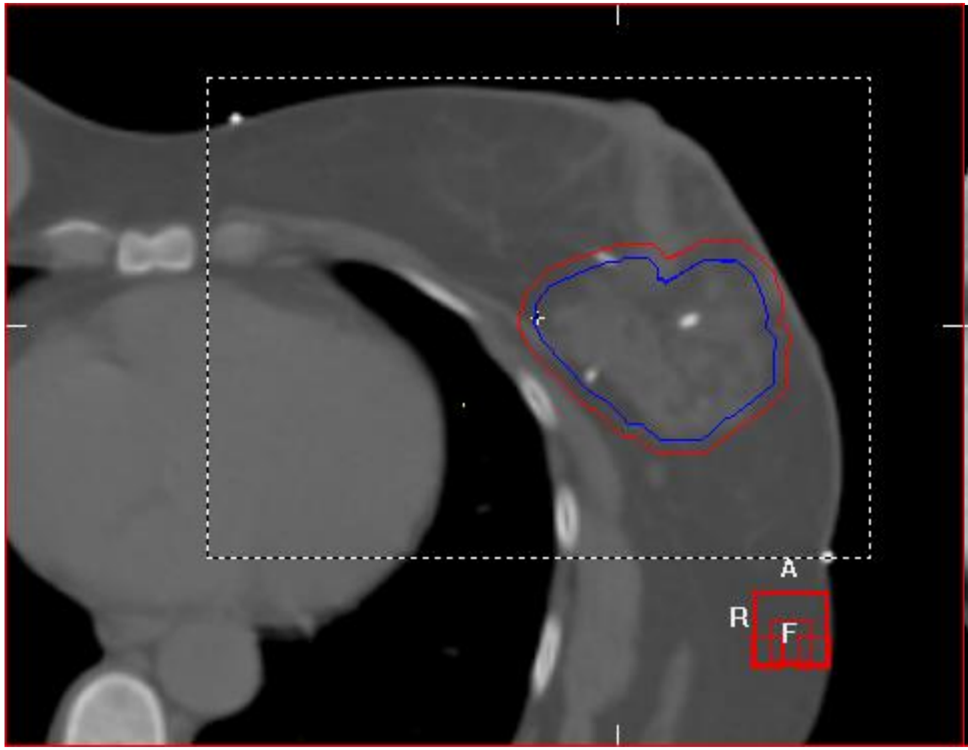
Marker registration with shaped ROI

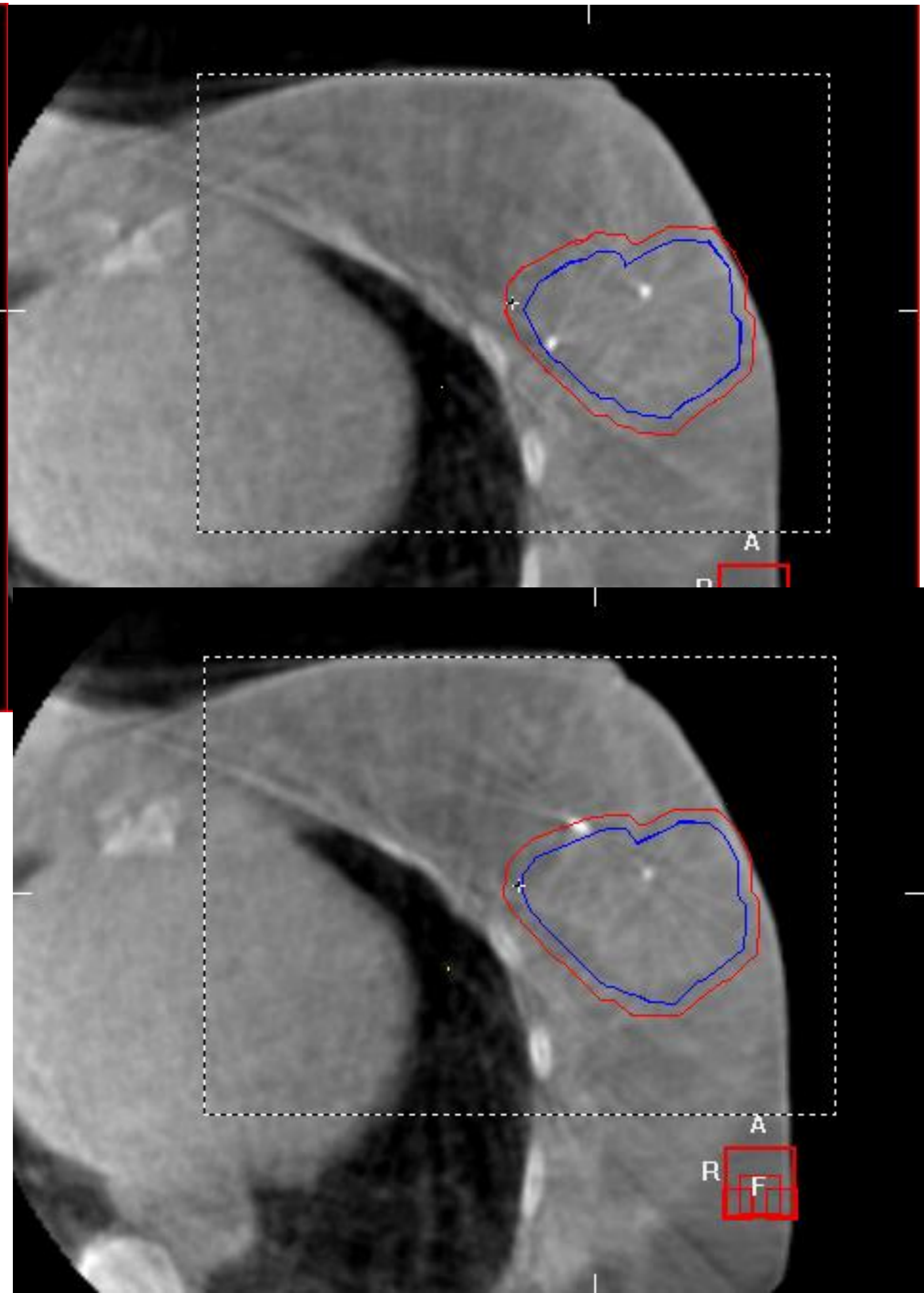


CT ref

CBCT

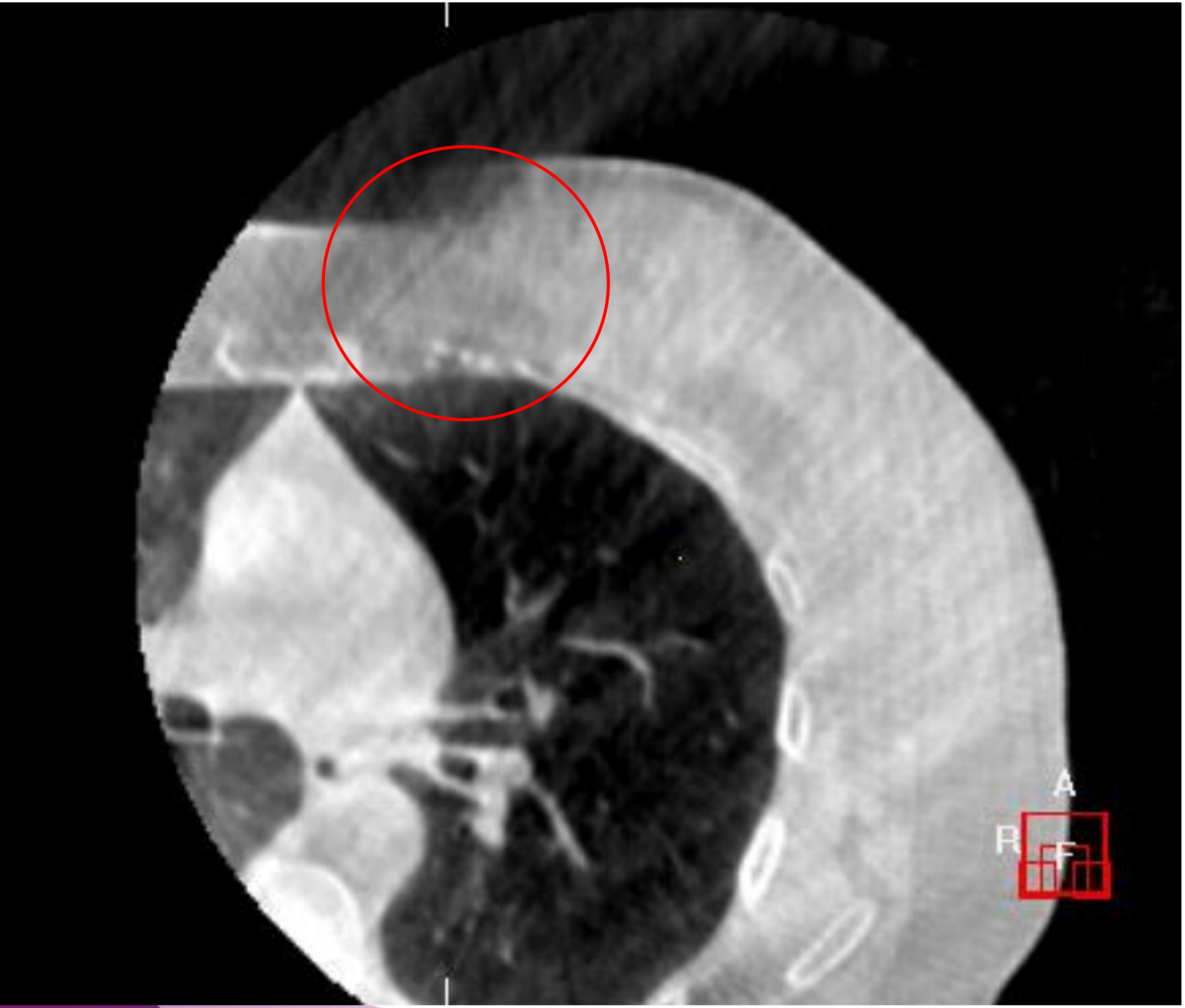
Marker check @AMC





After registration on the ribs

Breathing artefact CBCT



Shallow breathing during acquisition CBCT, except for a few deep sighs.

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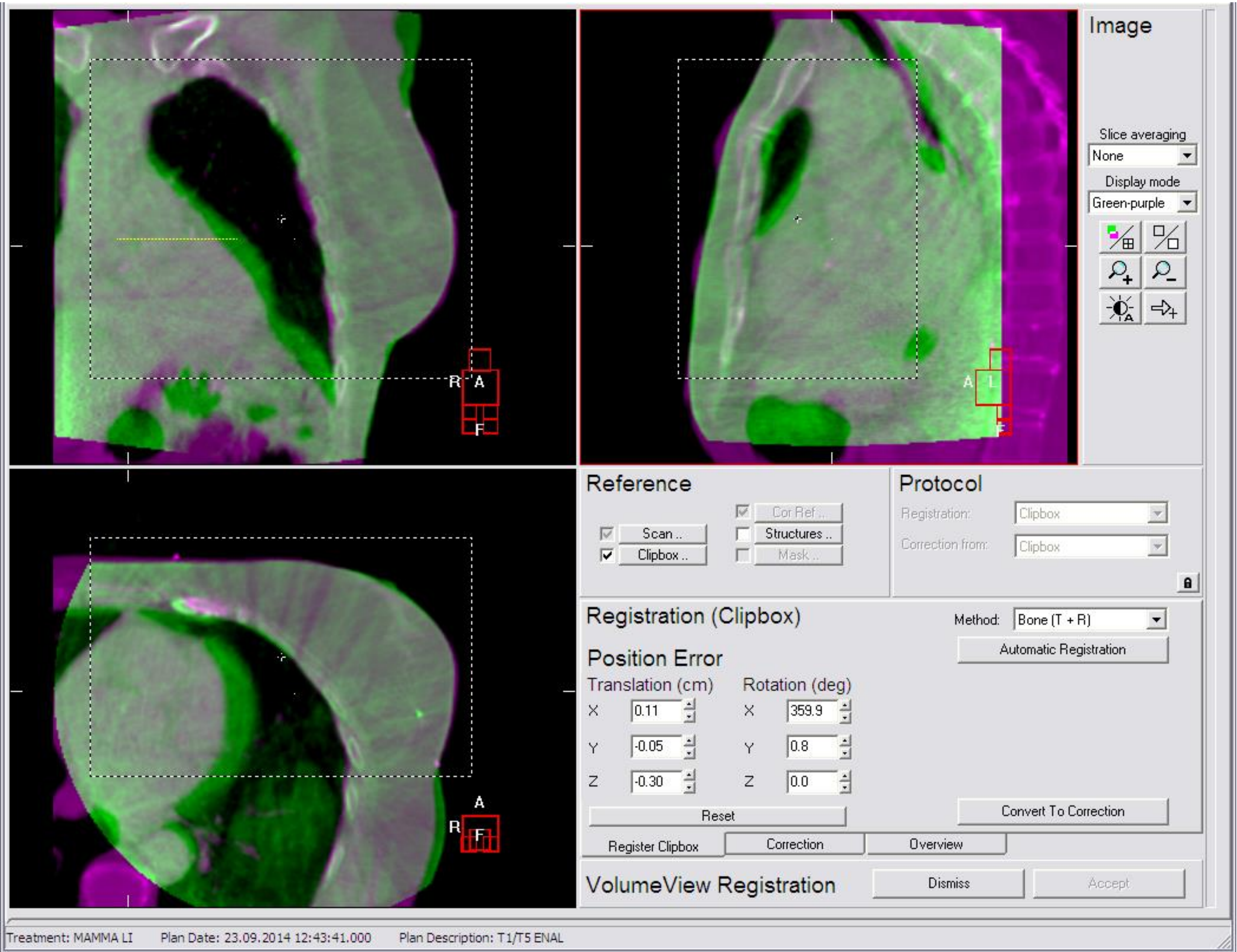
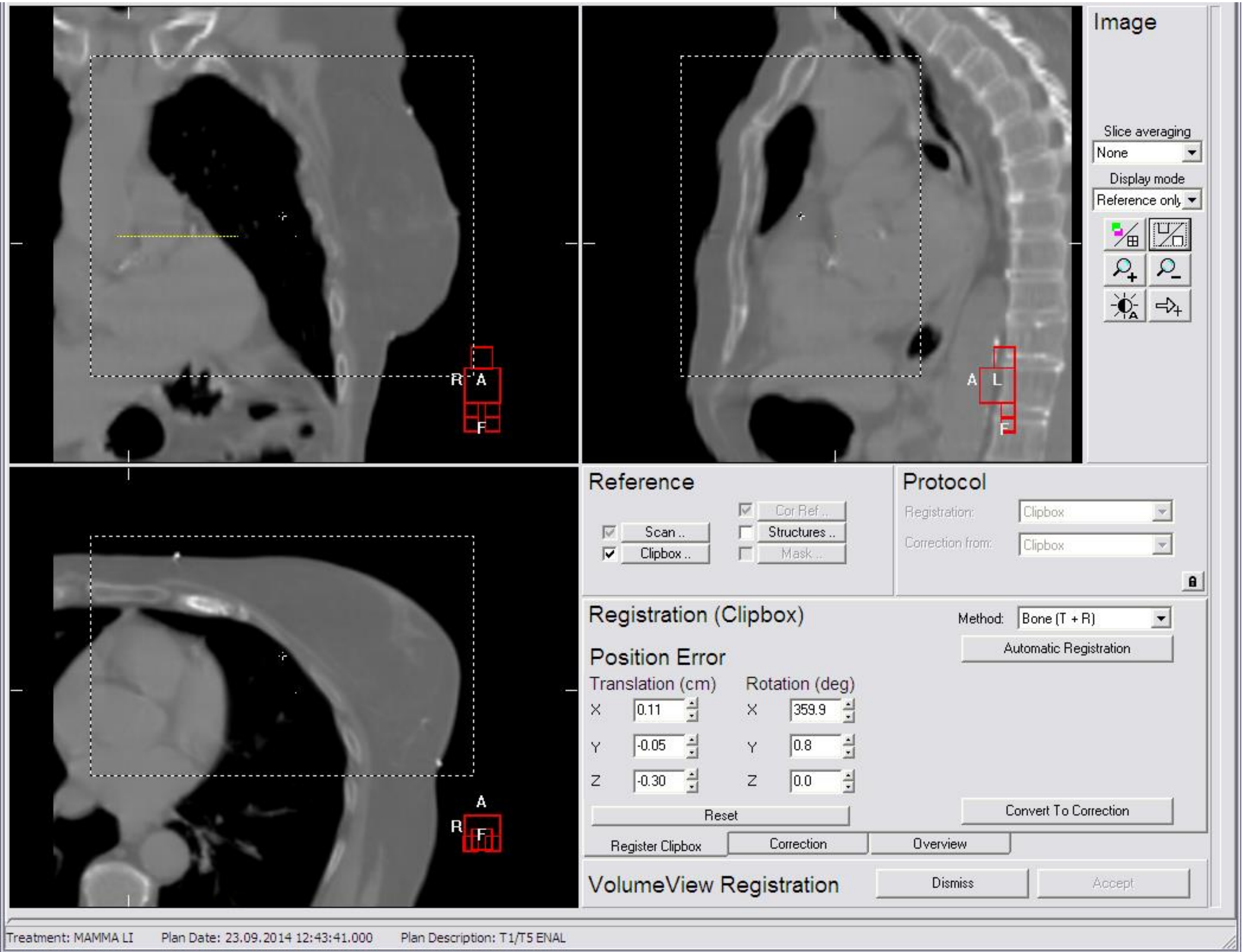
Breathing artefact CT ref



Breathing artefact CT ref

Breathing artefact CT ref



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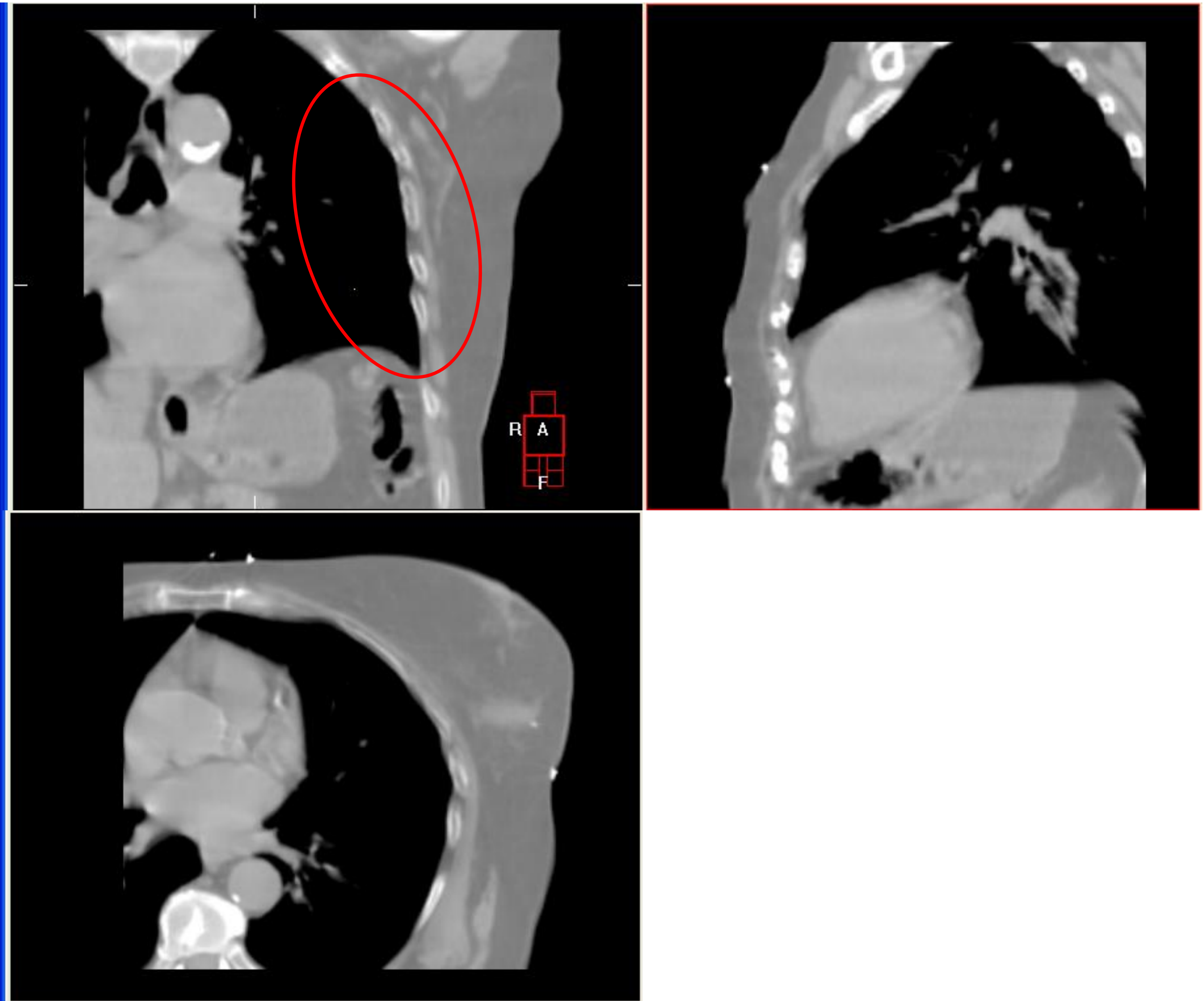
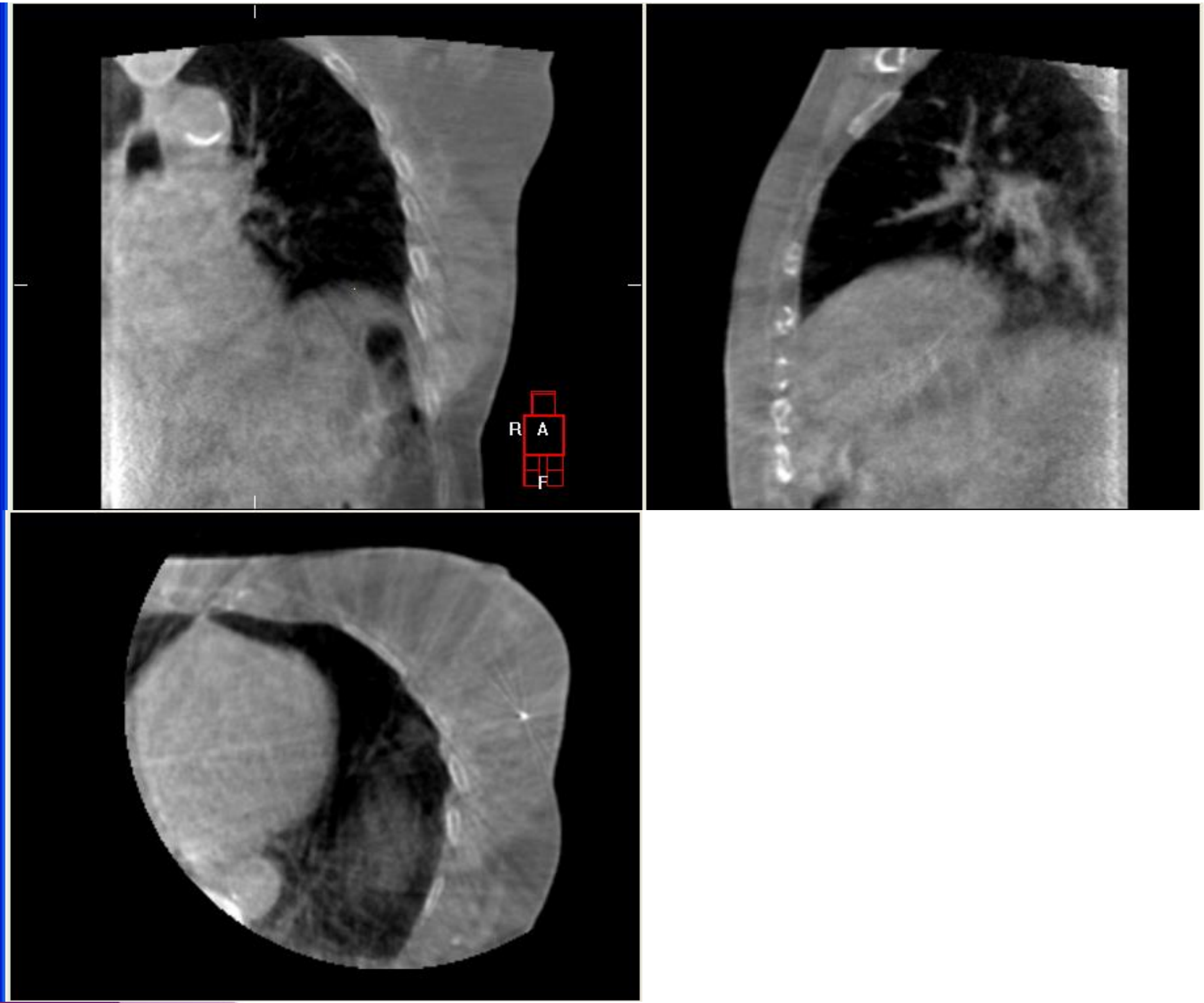
Anatomy changes



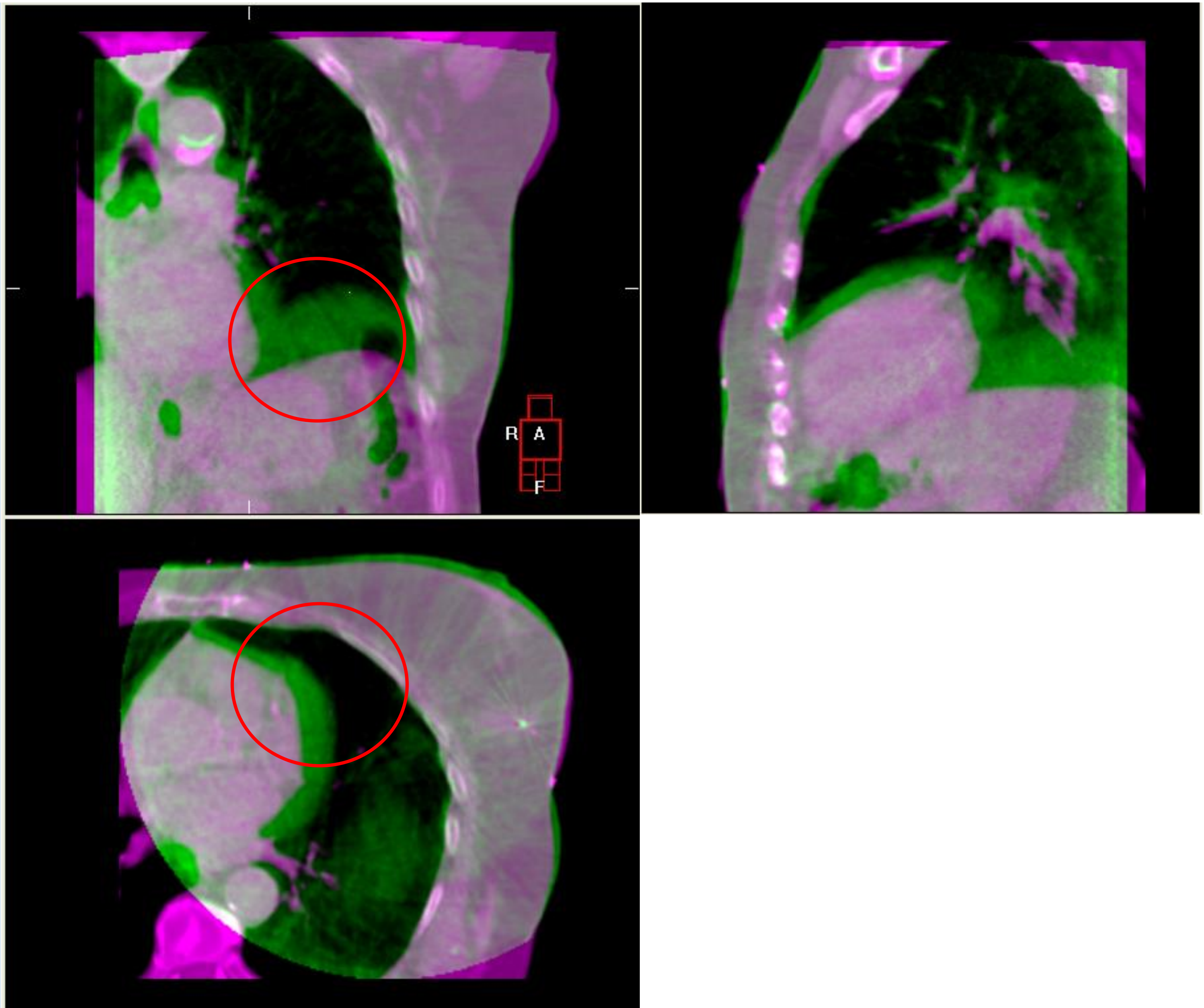
Free breathing CT ref scan …

Anatomy changes



CBCT scan

Anatomy changes



CT ref

CBCT

Registration on ribs

Average breathing position changed
- baseline shift –

Heart moves into treatment fields: BreathHold?

Traffic Light System

"decision support system to guide the RTT in prioritizing anatomy changes"

Level green, no action needed.

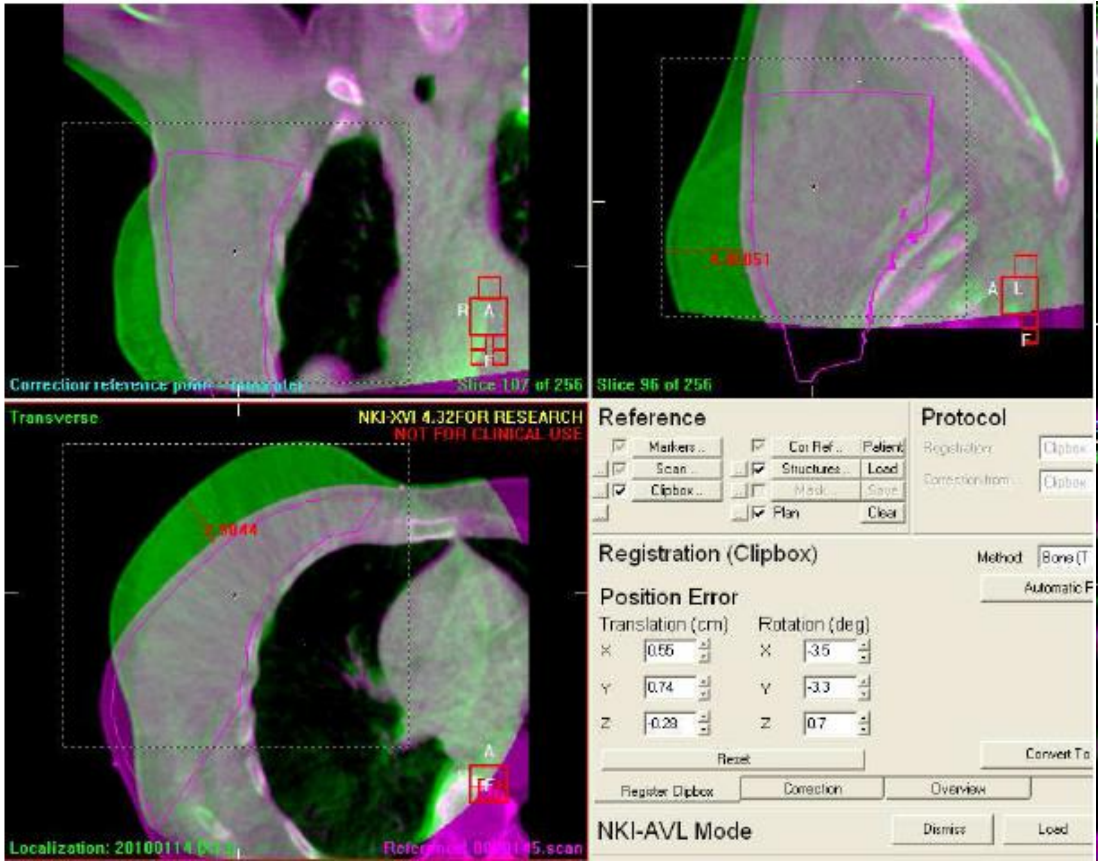
Level yellow, the radiation oncologist is notified by email, but no response is required to continue treatment.

Level orange, the treating radiation oncologist (or back-up colleague) is informed by email and a response is required before the next fraction.

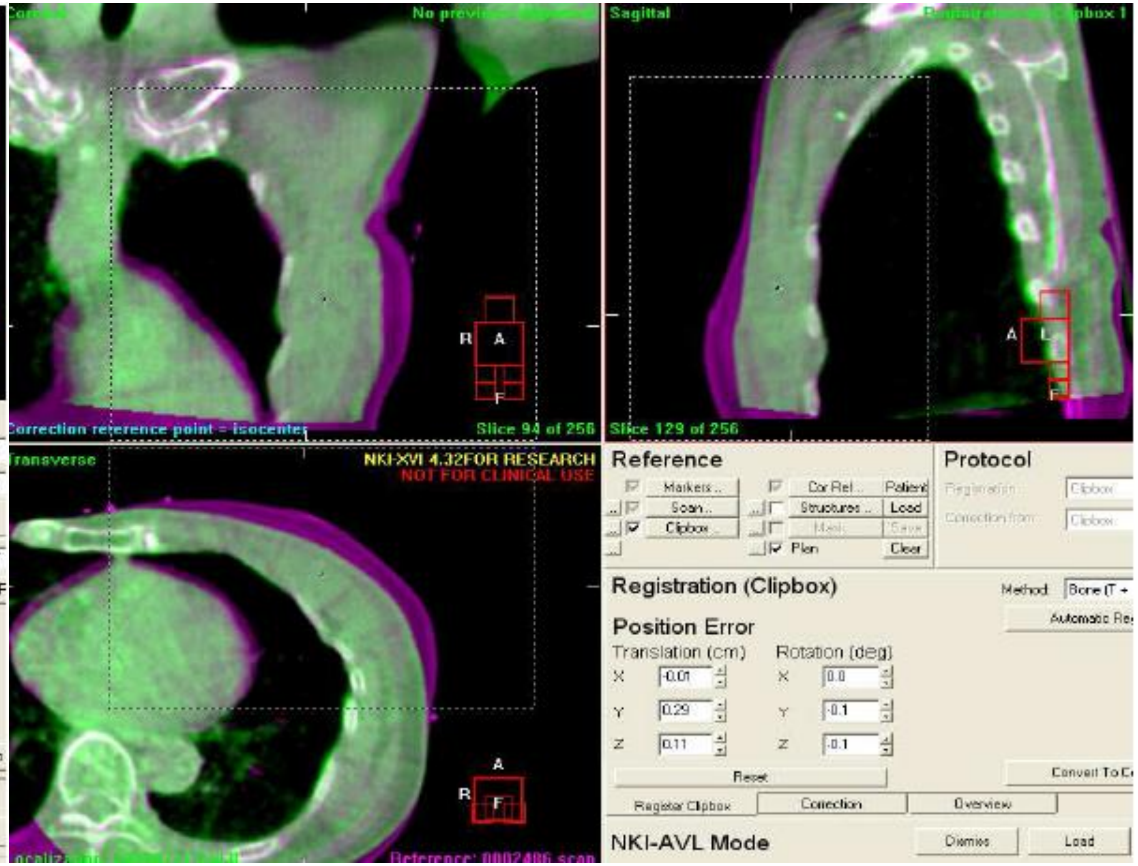
Level red changes, the radiation oncologist must be consulted immediately before the treatment fraction is allowed to be delivered.

http://www.avl.nl/media/291805/xvi_engelse_protocols_16_7_2014.pdf

Traffic Light System



Shift/increase contour



decrease contour

Contour change is < 2 cm.

Contour change is ≥ 2cm.

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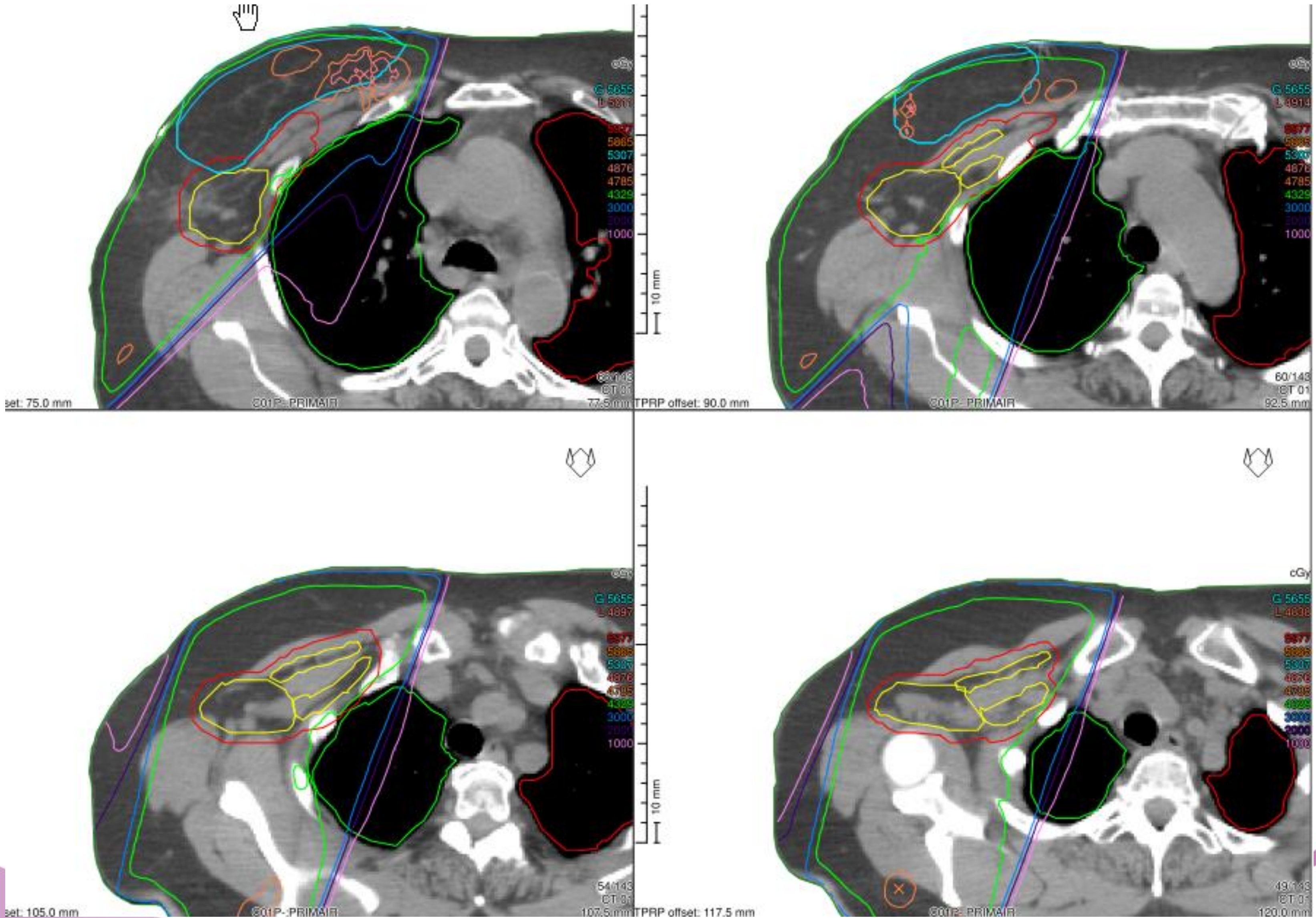
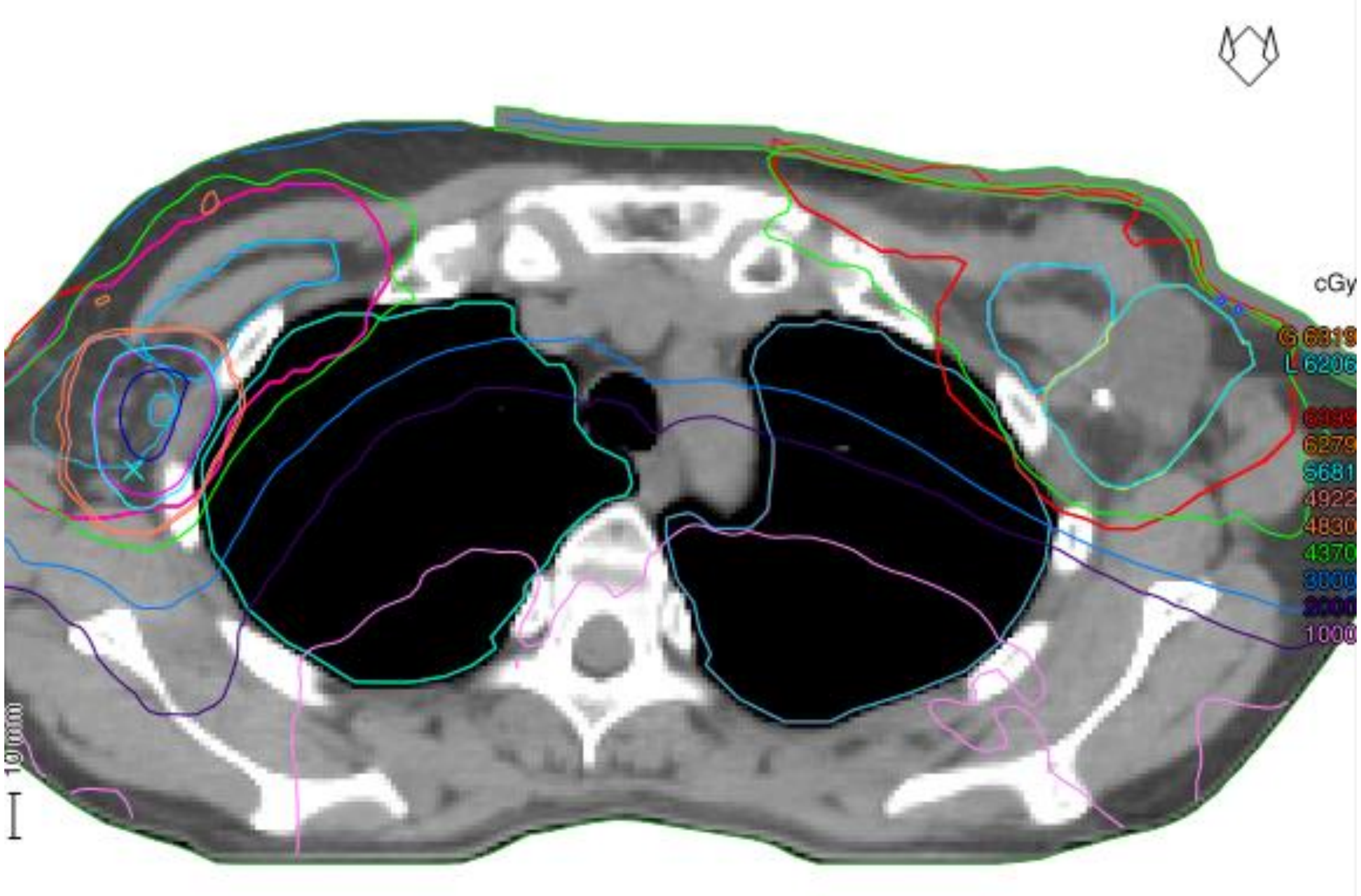
Conformal to IMRT/VMAT:
Reducing dose to humerus head/shoulder





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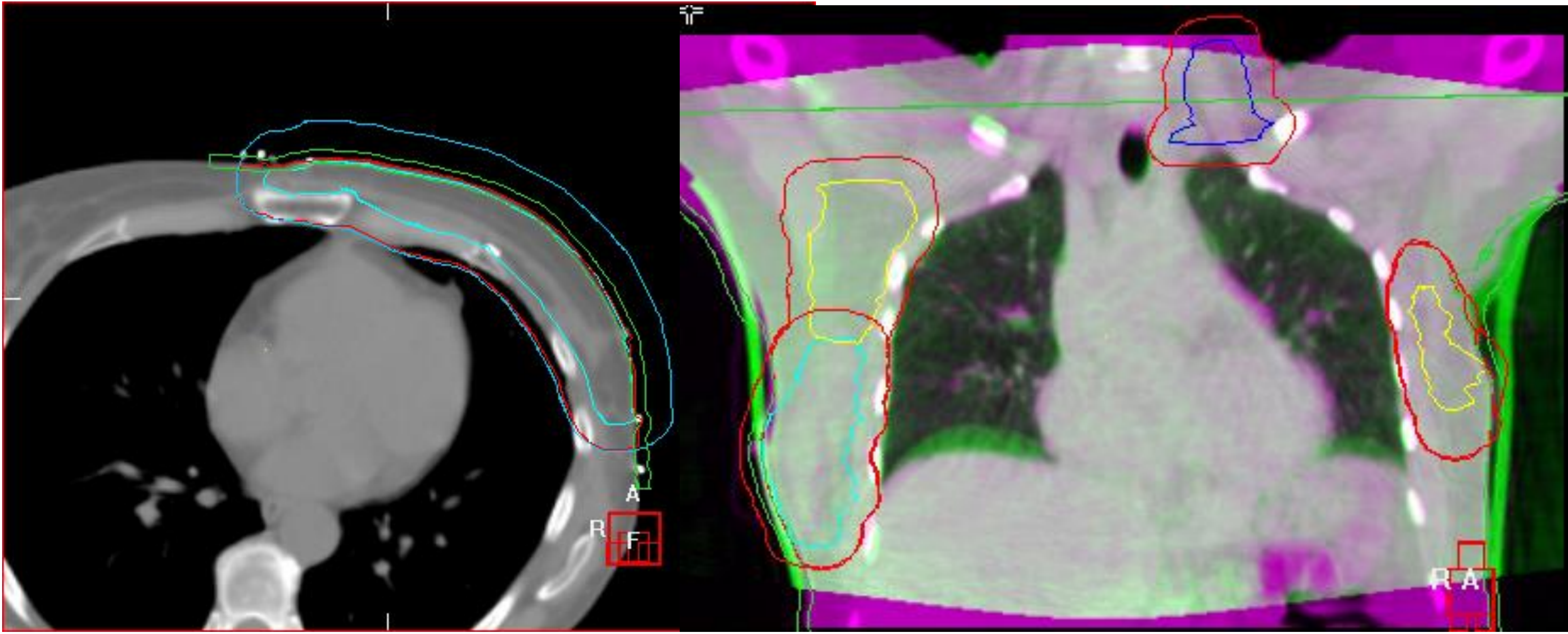
Design of breast boards:

Margin calculation level 1-4

Residual error (mm) nodes after registration of thoracic wall

		LR (X)	CC (Y)	AP (Z)
Level 1		7.5	10.7	14.8
Level 2		8.0	7.7	7.8
Level 3		6.7	6.1	6.5
Level 4		6.1	7.1	6.3



- New structure for anatomical change: PTV + 10mm into air (blue)
- CTV inside PTV
- Position of the arm: blocking treatment

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Discussion

Let the software work for you! Majority can be registered automatically!

Think margins when moving from conformal to IMRT/VMAT

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Image Registration Issues for Mediastinum and Lung

Madrid 2016

Helen McNair
Rms.nhs, London

Rianne de Jong
Academic Medical Centre, Amsterdam

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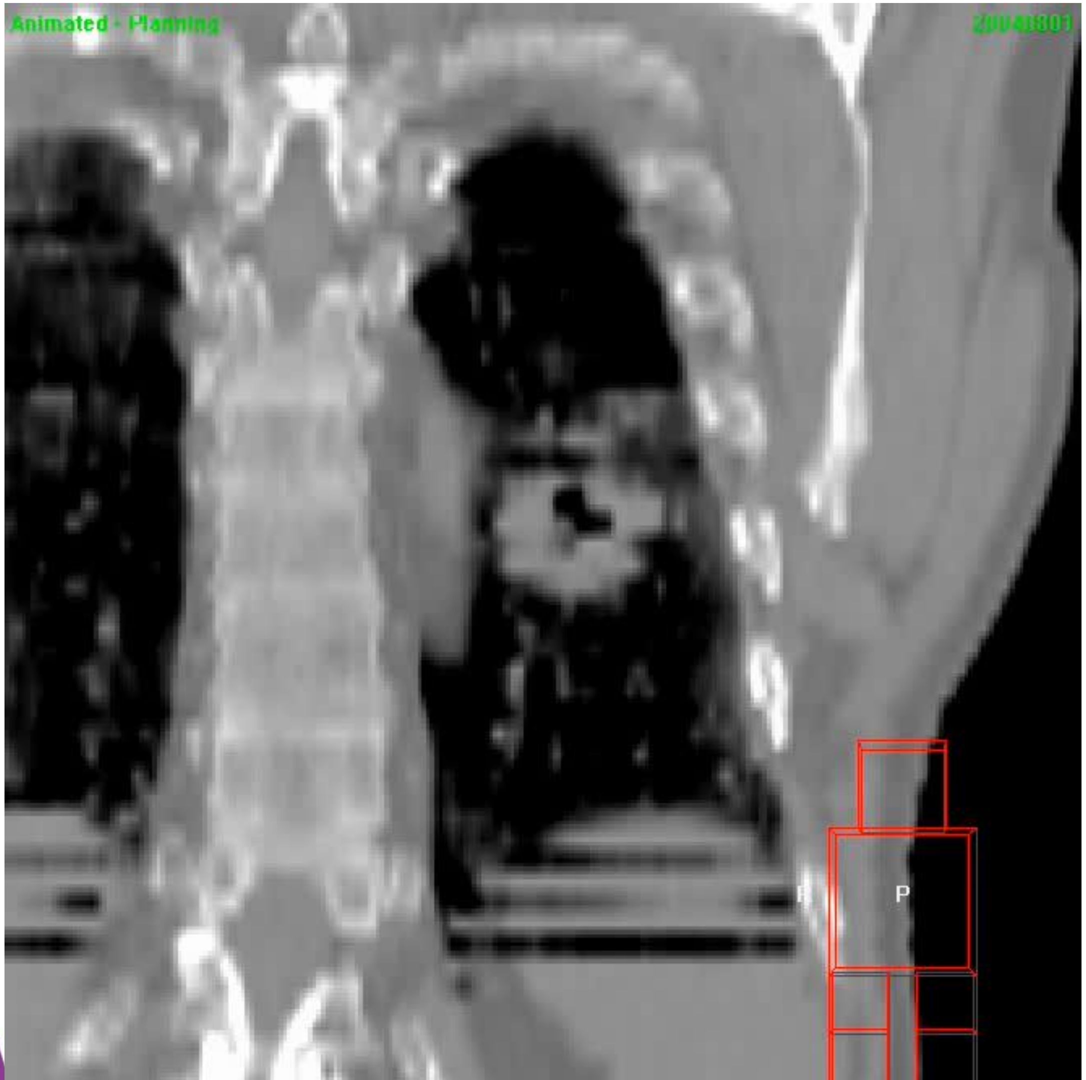
Bony anatomy registration: vertebrae



Marcel van Herk

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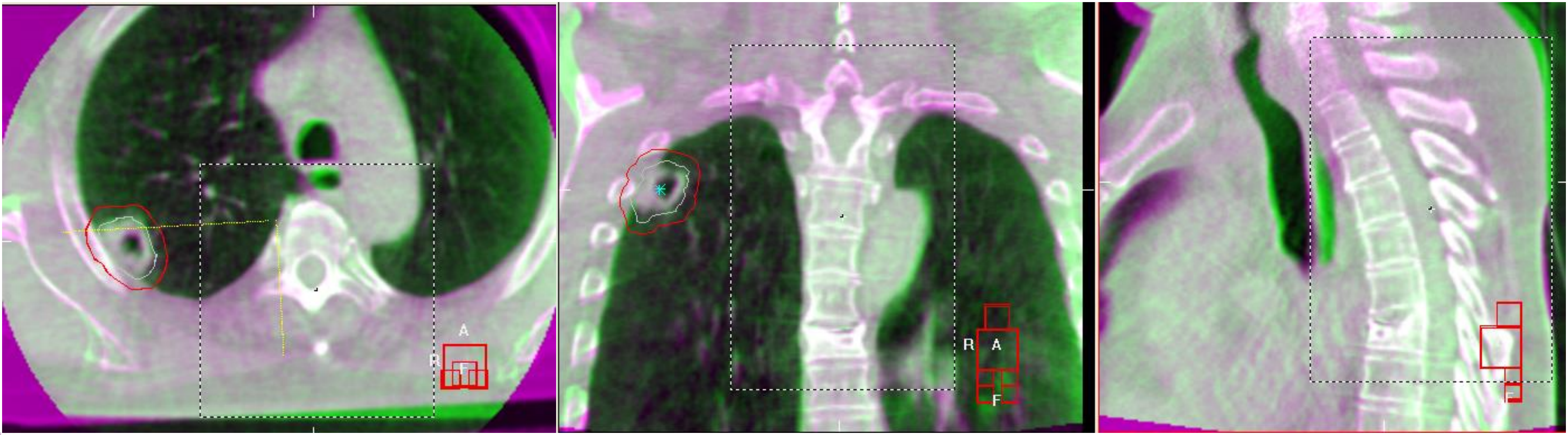
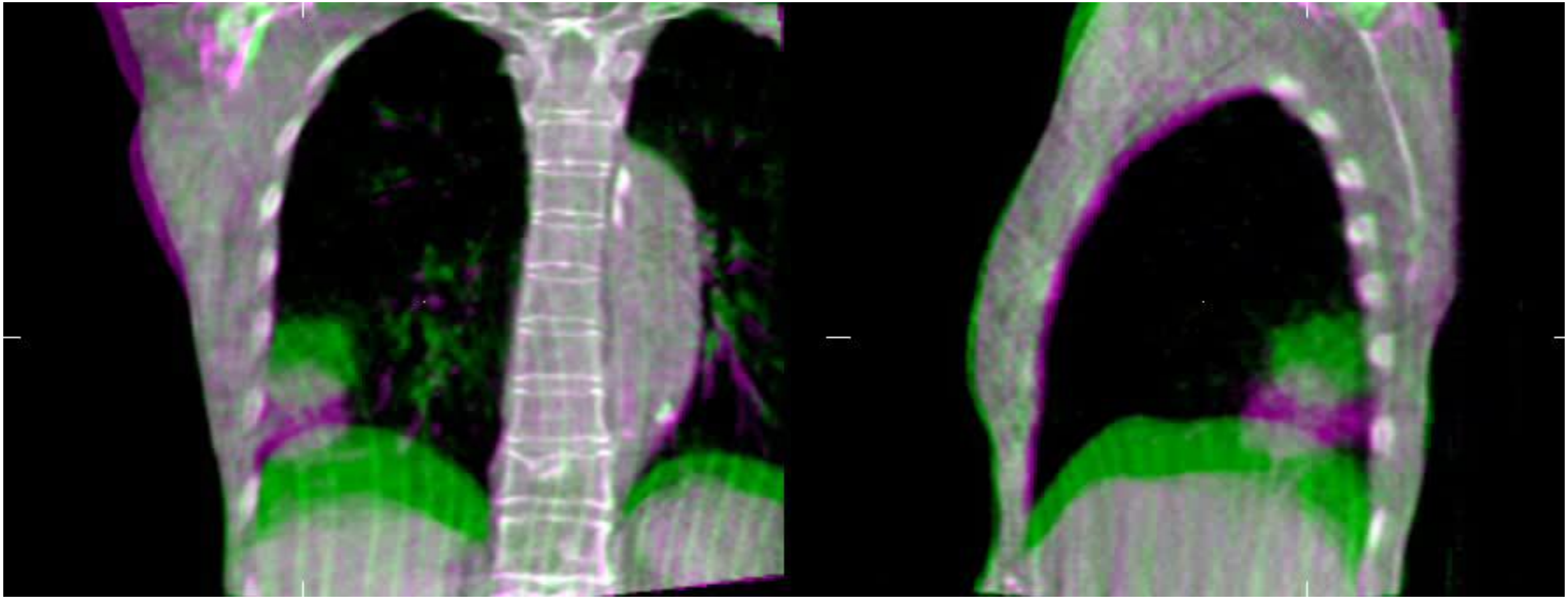
Bony anatomy registration: vertebrae



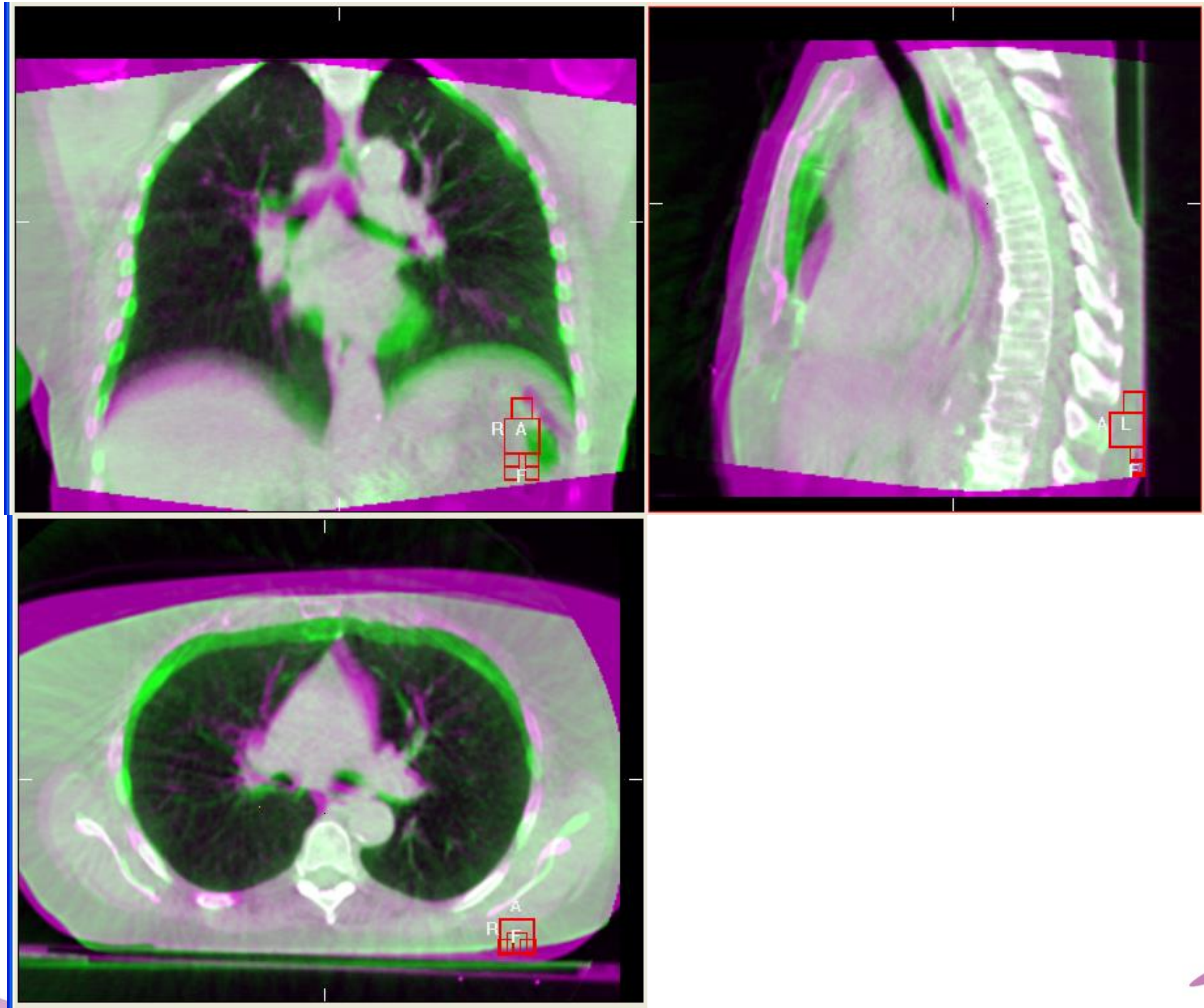
Bony anatomy registration: vertebrae



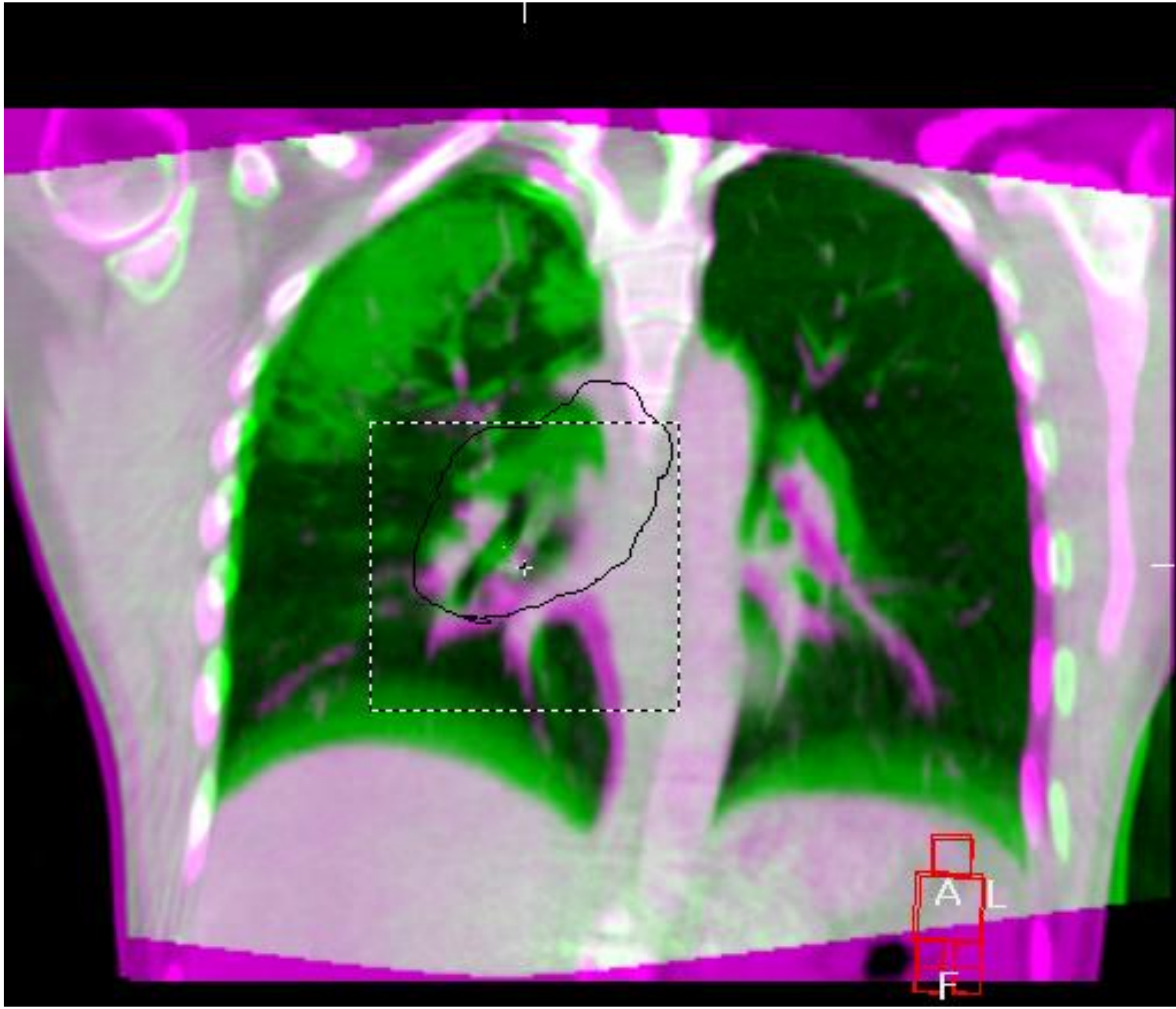
Base line shift

Jan-Jakob Sonke

Anatomy changes



Anatomy changes



Managing Lung and Mediastinum

Protocols for registration

- Tumours and mediastinum (lymph nodes)
- Solitary tumours

Management system for RTTs for anatomy changes:

- Target coverage
- Dosimetry

Registration protocols

Lung tumour with lymph nodes &

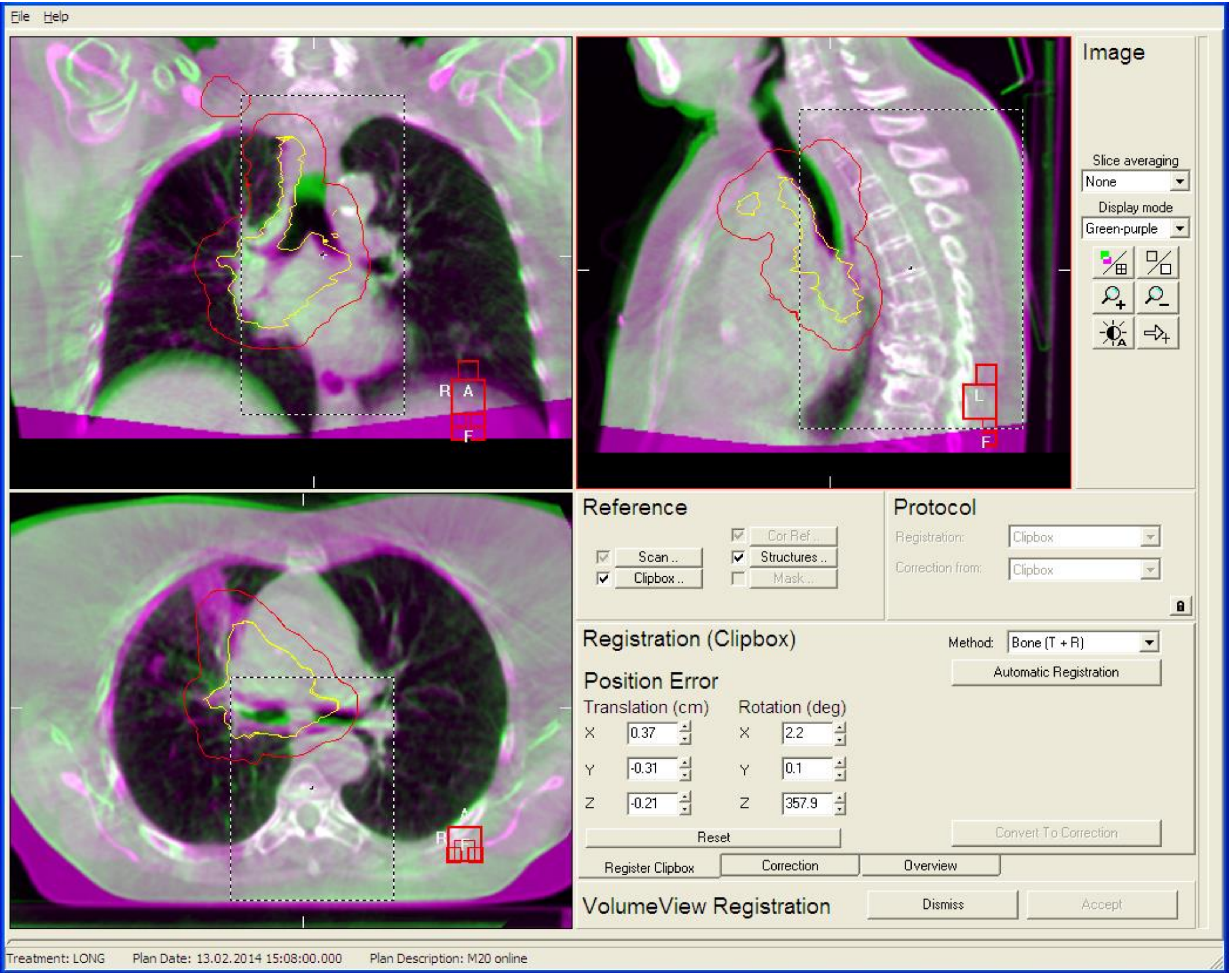
Mediastinum tumours:

- Bony anatomy registration (vertebrae)
- Carina registration
- Critical dose line check

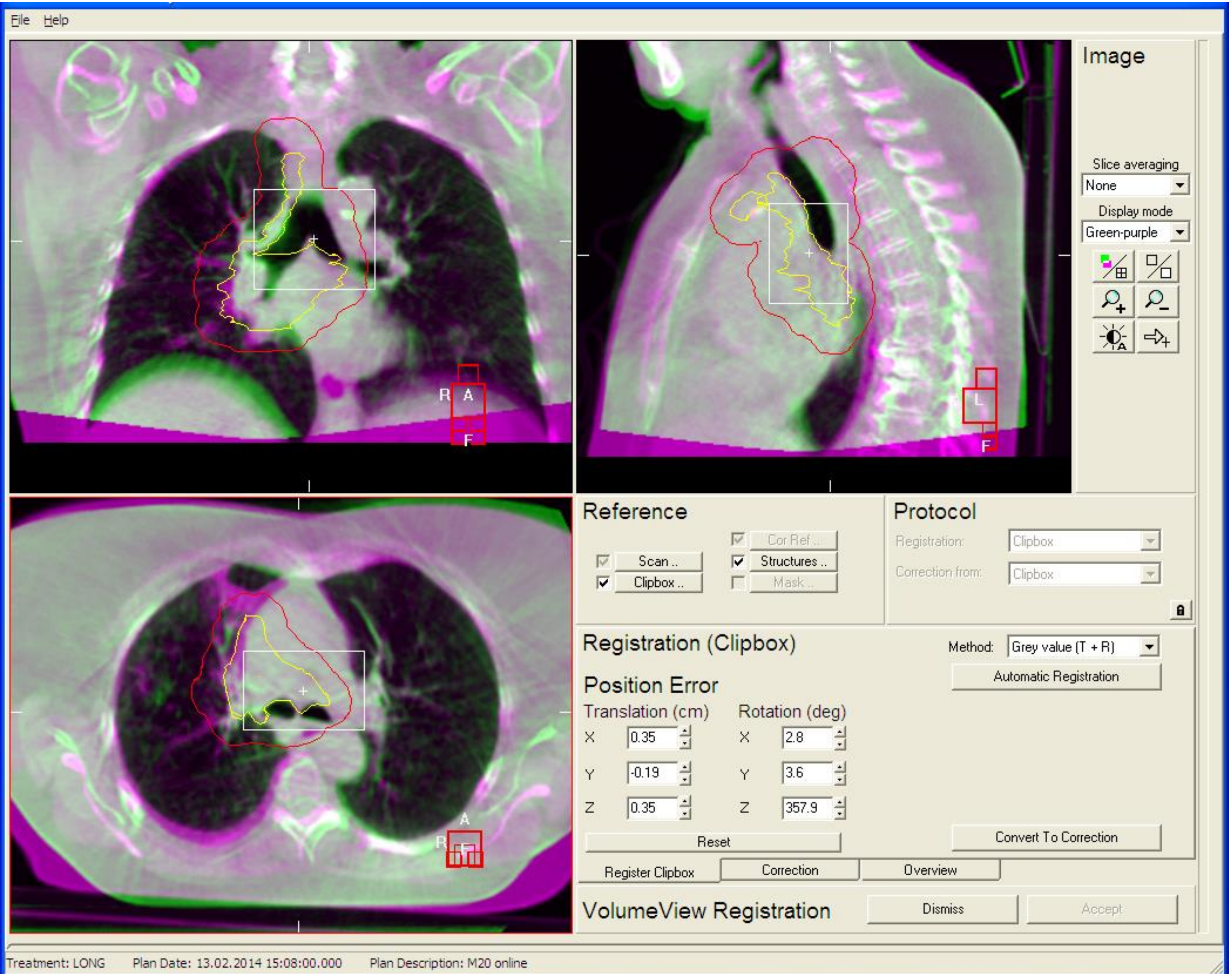
Solitary tumours:

- Tumour registration in two steps (dual registration) using Critical Structure Avoidance Strategy
  - Stereotactic treatment

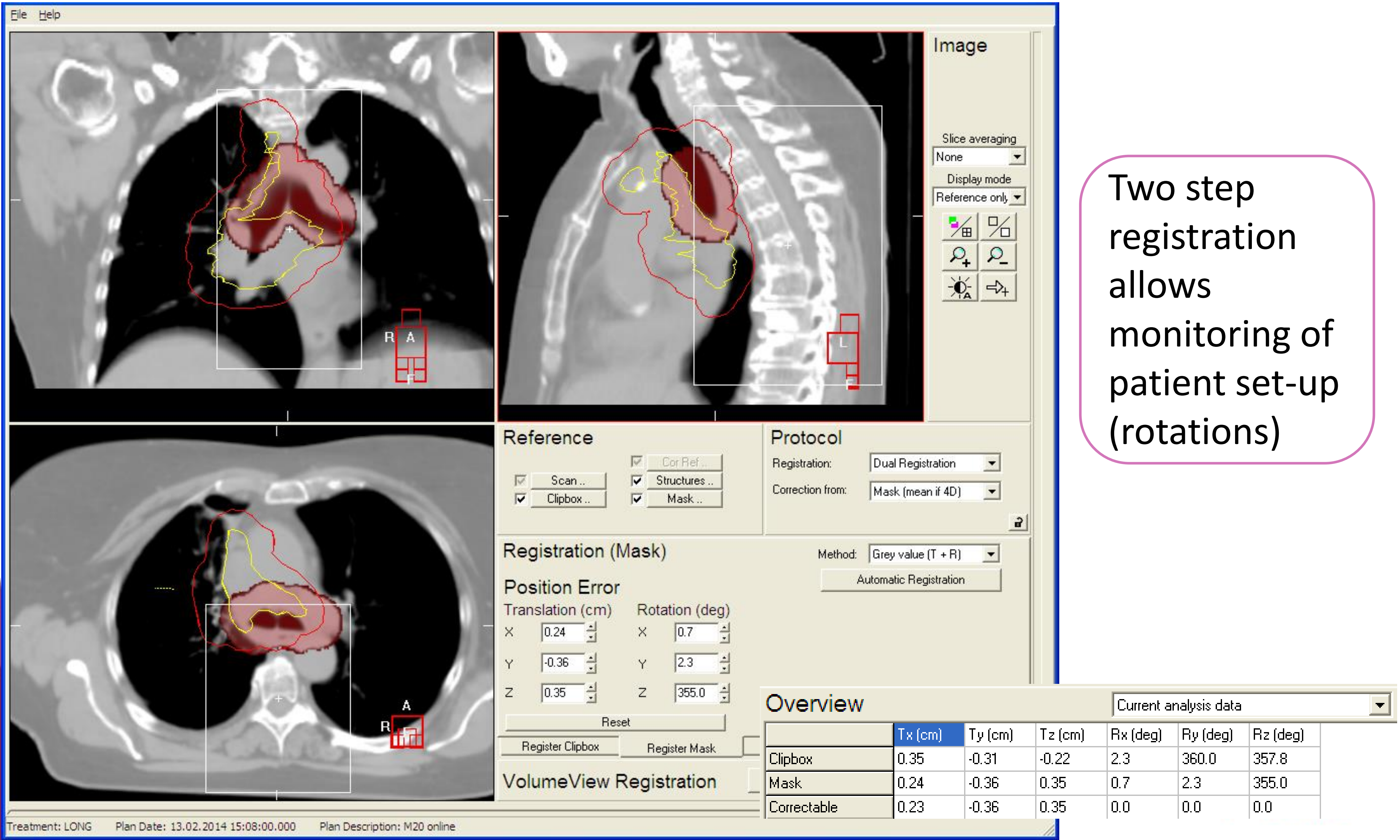
Bony anatomy registration



Carina registration with ROI (clipbox)

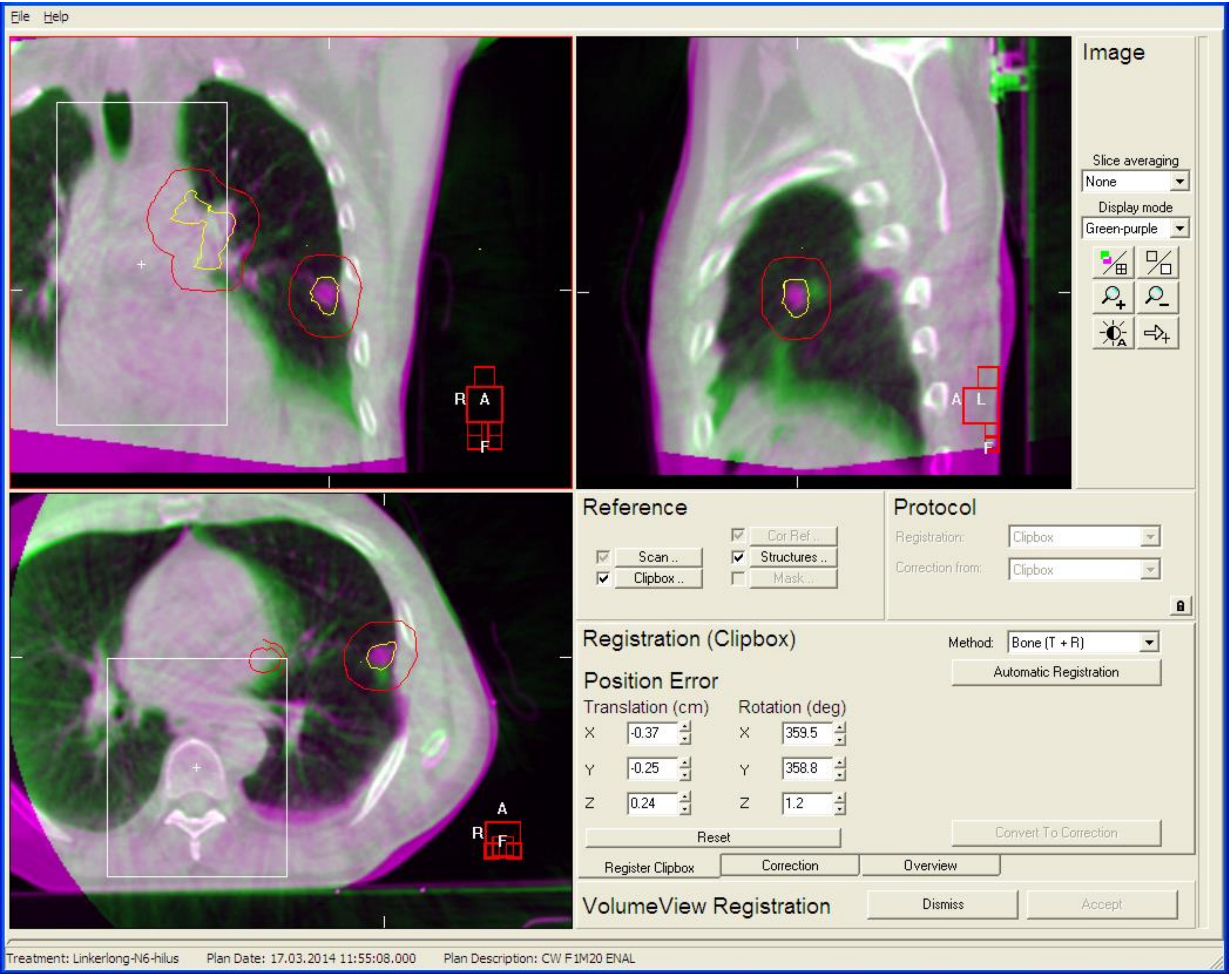


Carina registration with SROI (mask)



Two step registration allows monitoring of patient set-up (rotations)

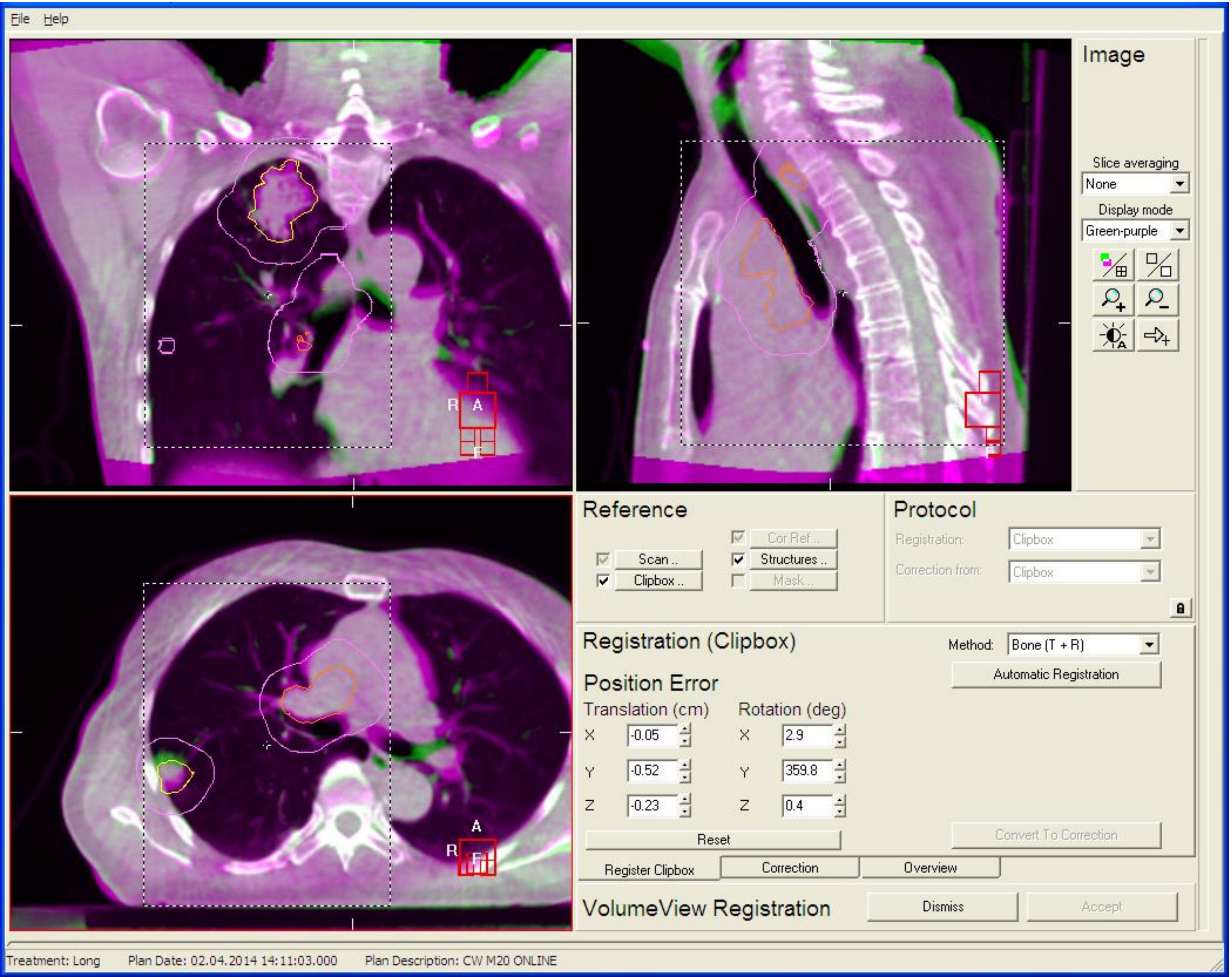
Bony anatomy registration



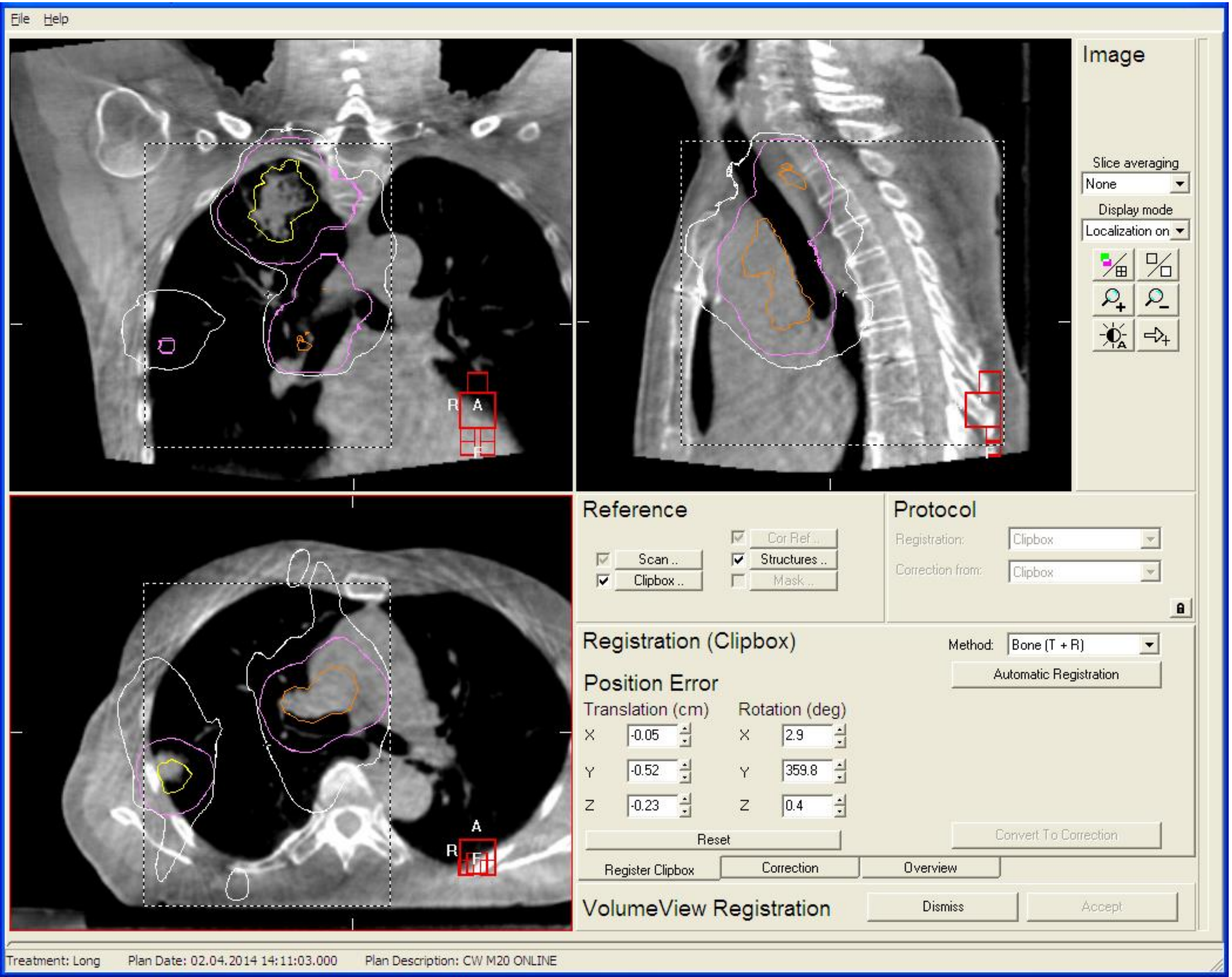
Target volume inside PTV?

! Margin is not just for interfraction anatomy changes …

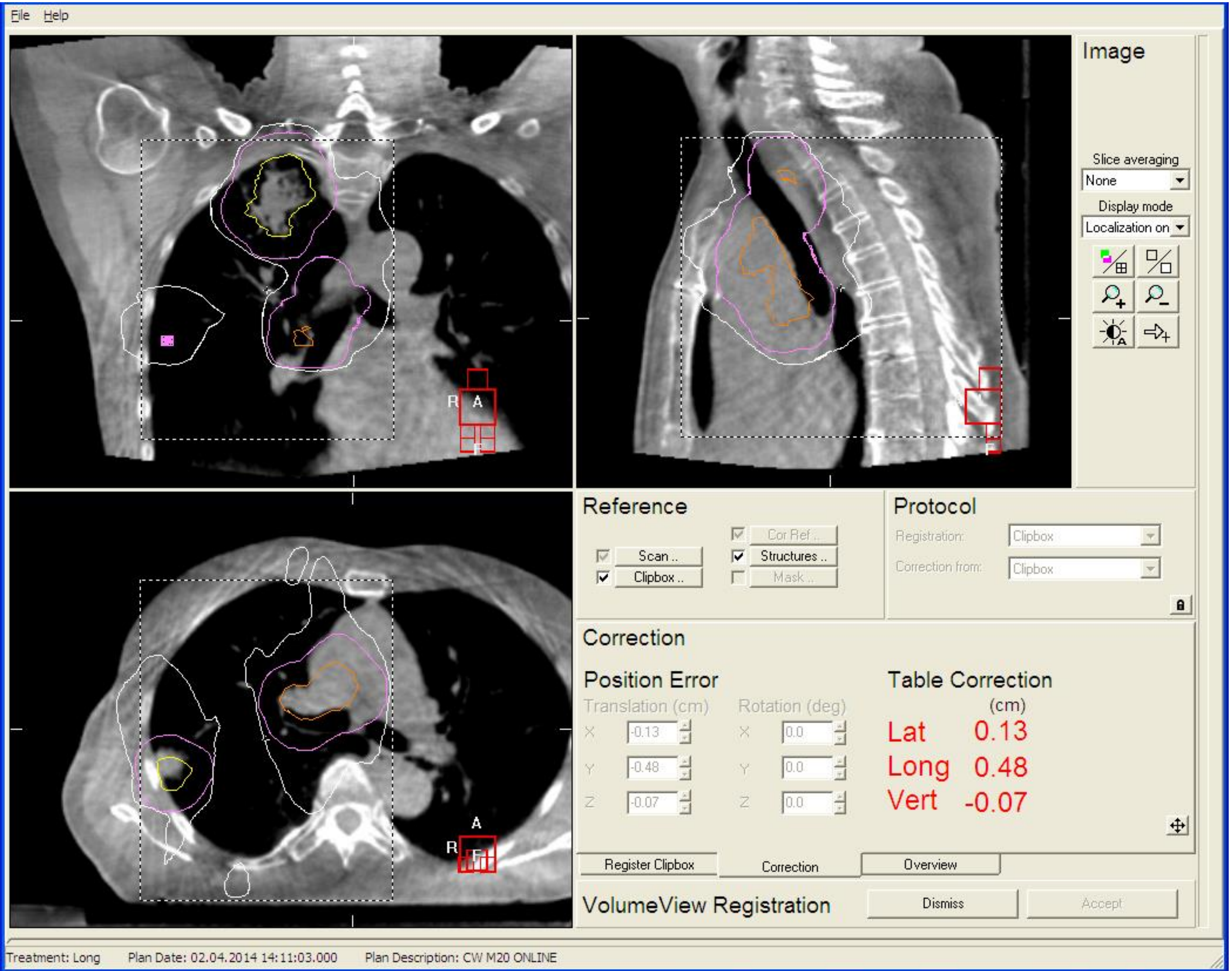
Critical dose line check



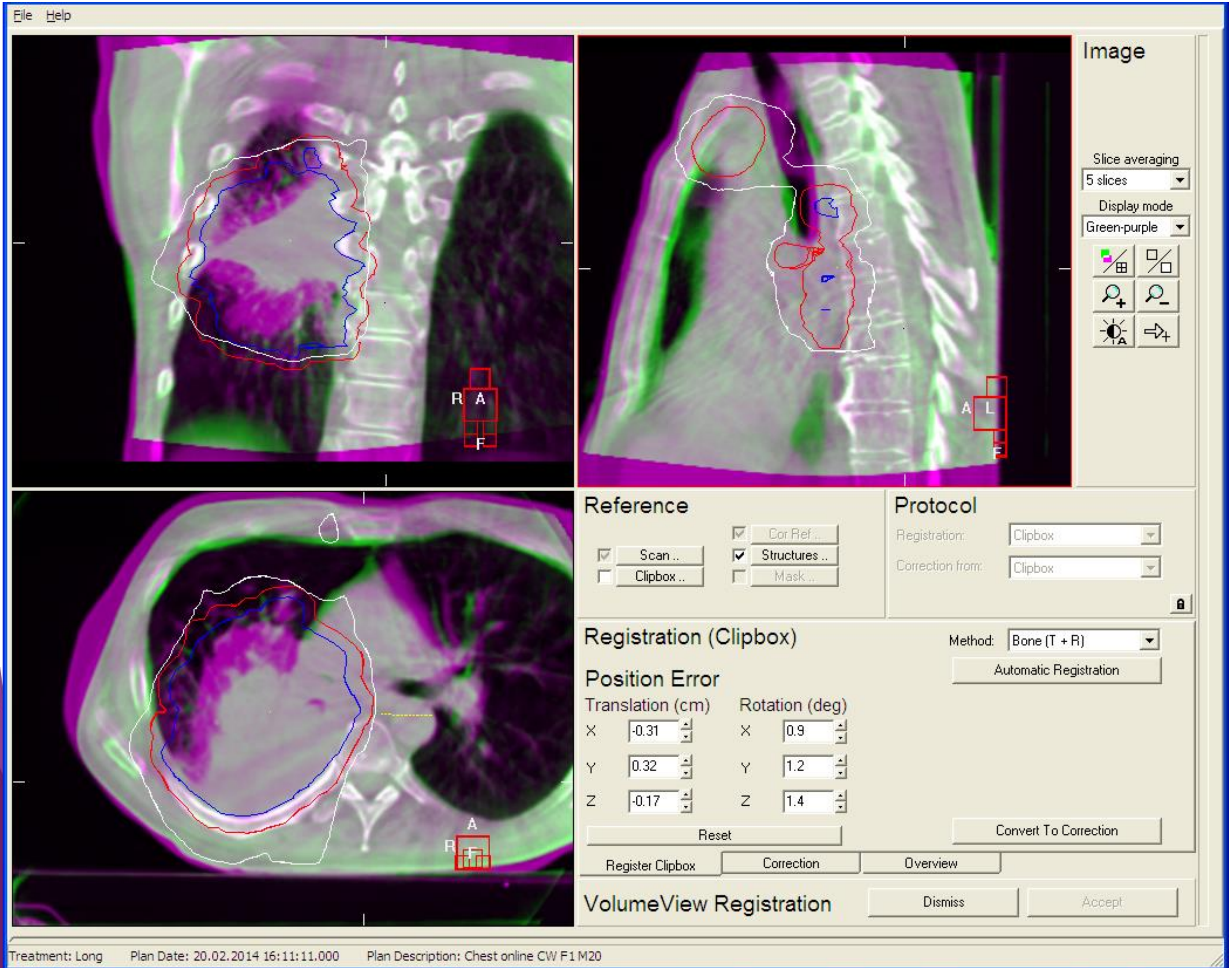
Critical dose line check



Critical dose line check



Critical dose line check



Need a dosimetry check as well!

Registration protocols

Lung tumour with lymph nodes &

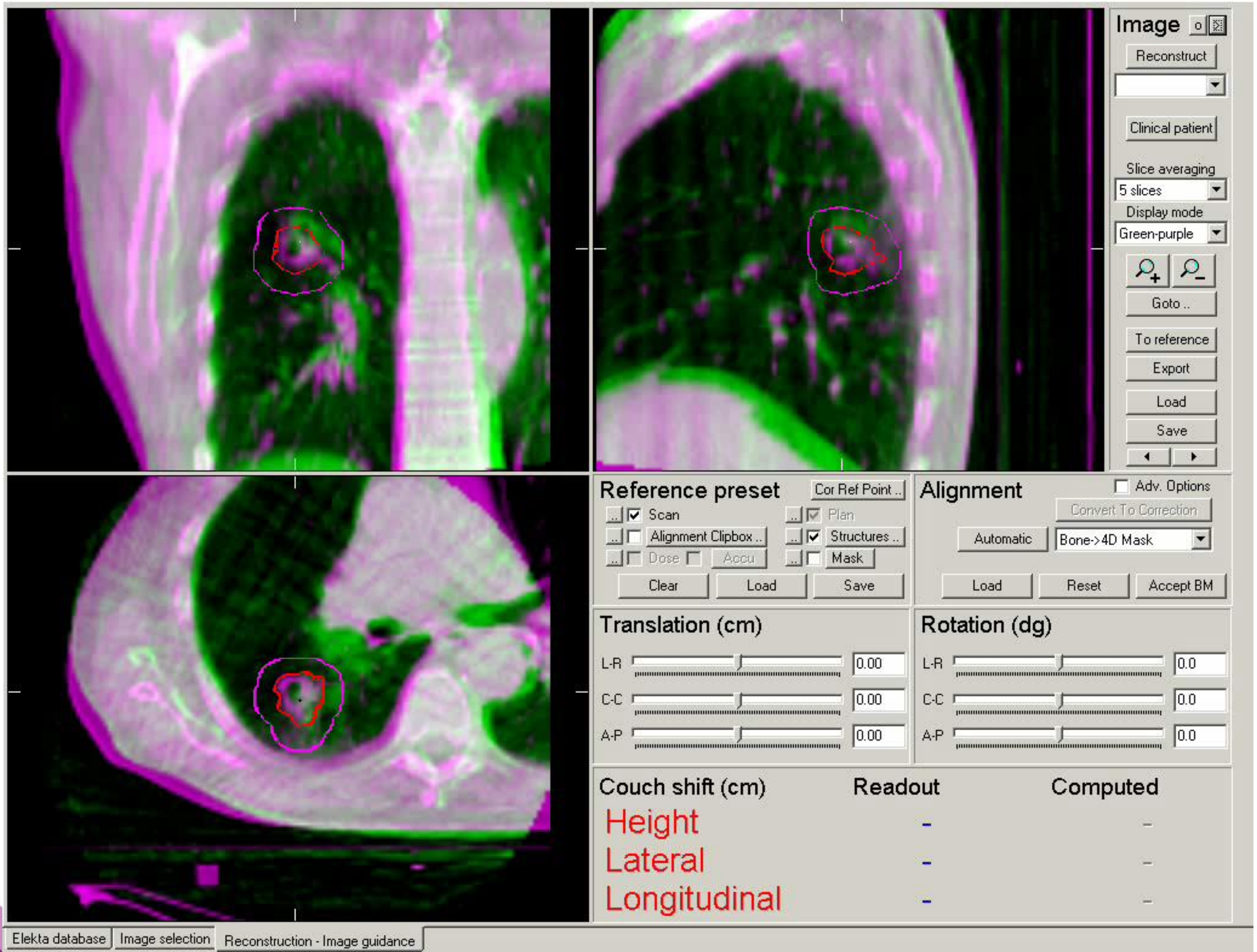
Mediastinum tumours:

- Bony anatomy registration (vertebrae)
- Carina registration
- Critical dose line check

Solitary tumours:

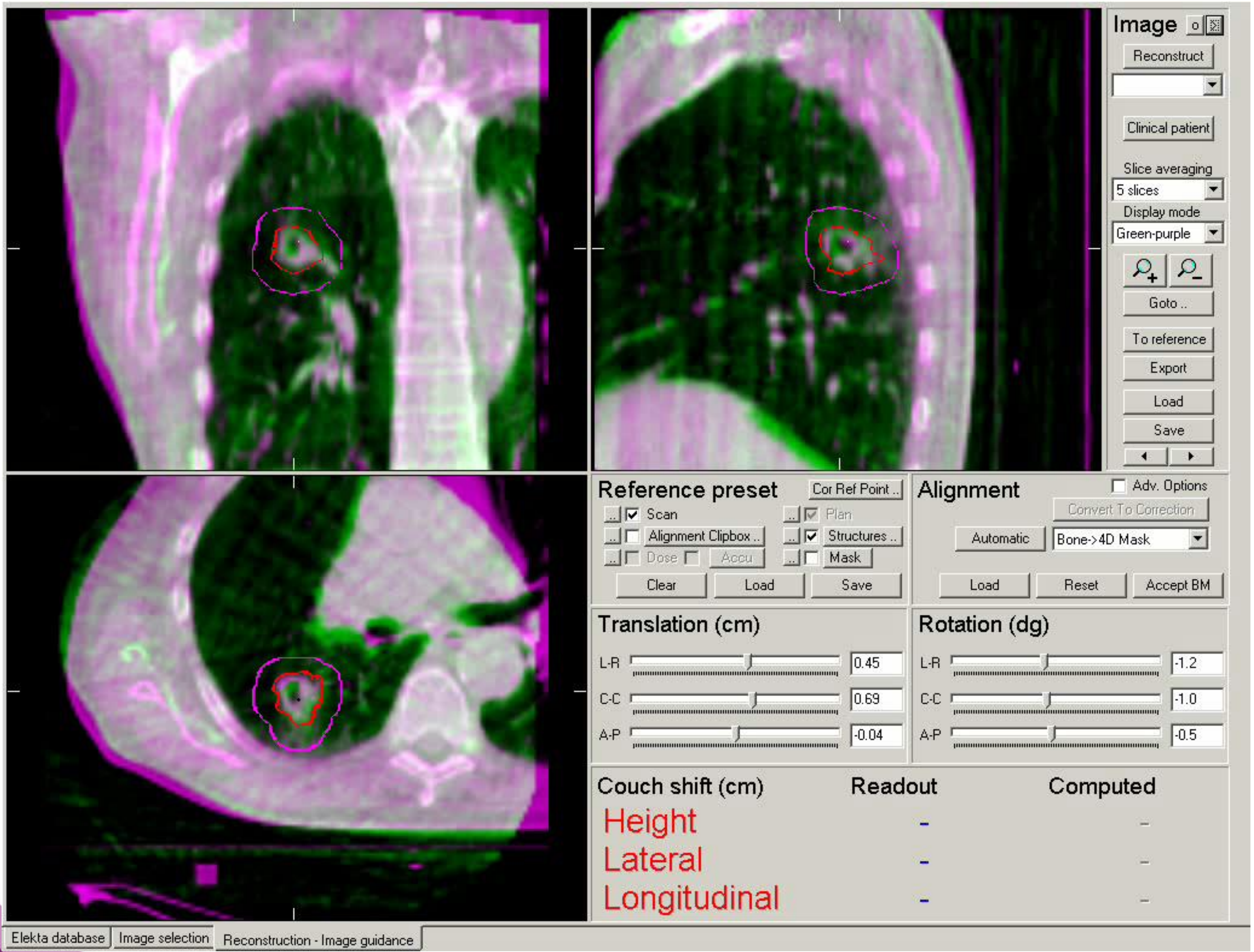
- Tumour registration in two steps (dual registration) using Critical Structure Avoidance Strategy
  - Stereotactic treatment

Stereotactic - Dual registration



first scan - unregistered

Stereotactic - Dual registration



matched on bone

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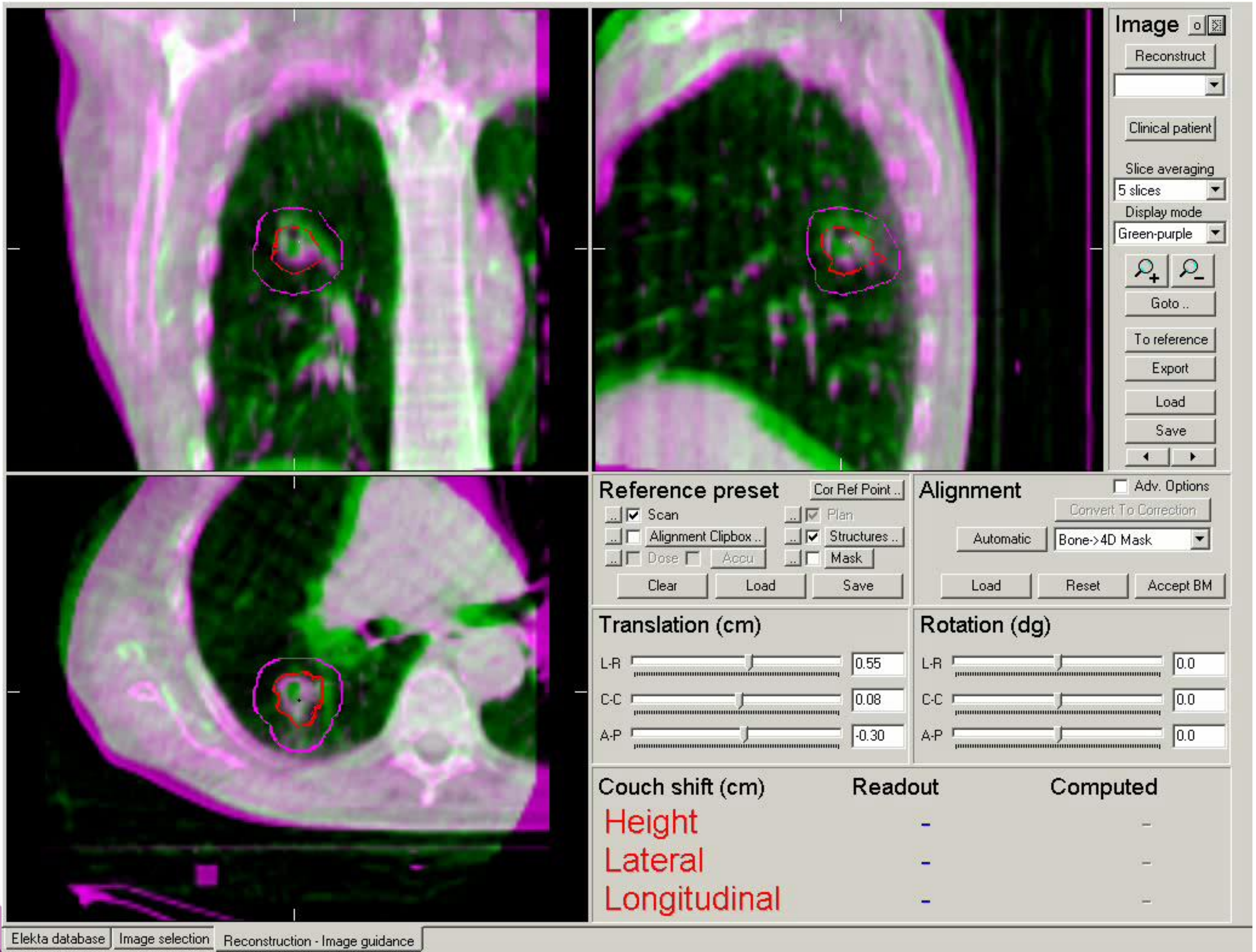
Stereotactic - Dual registration



matched on tumor (T_only)

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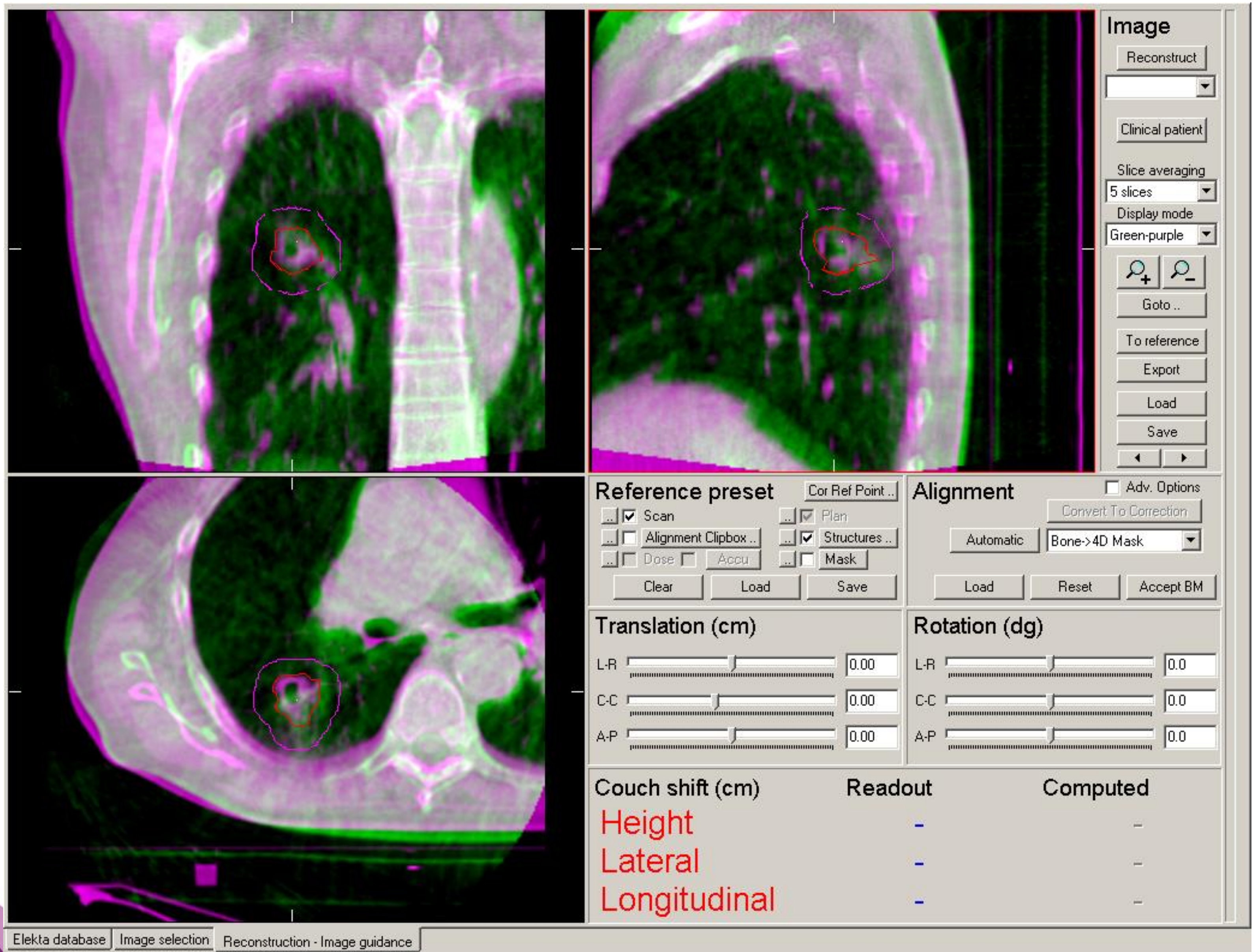
Stereotactic - Dual registration



prior to treatment

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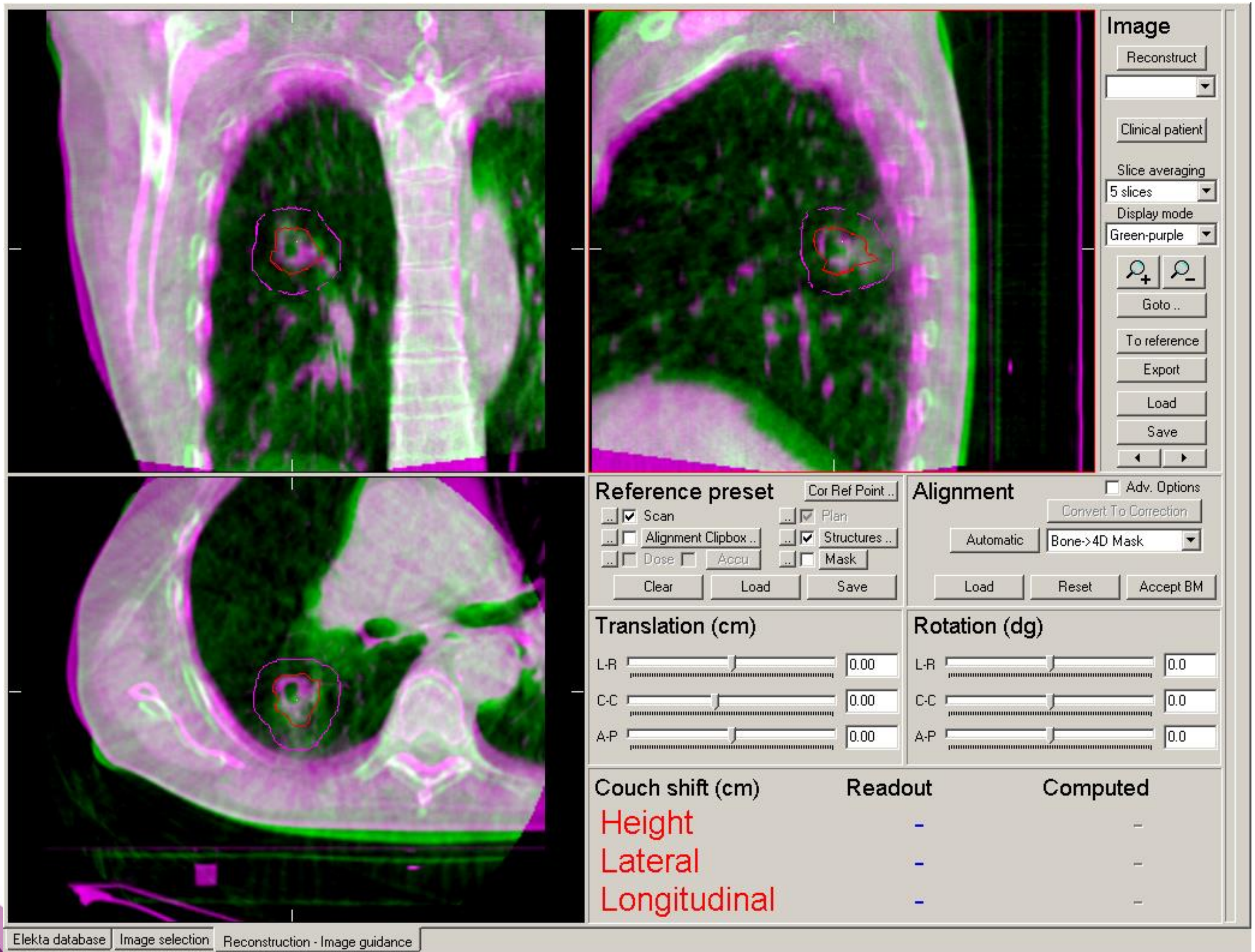
Stereotactic - Dual registration



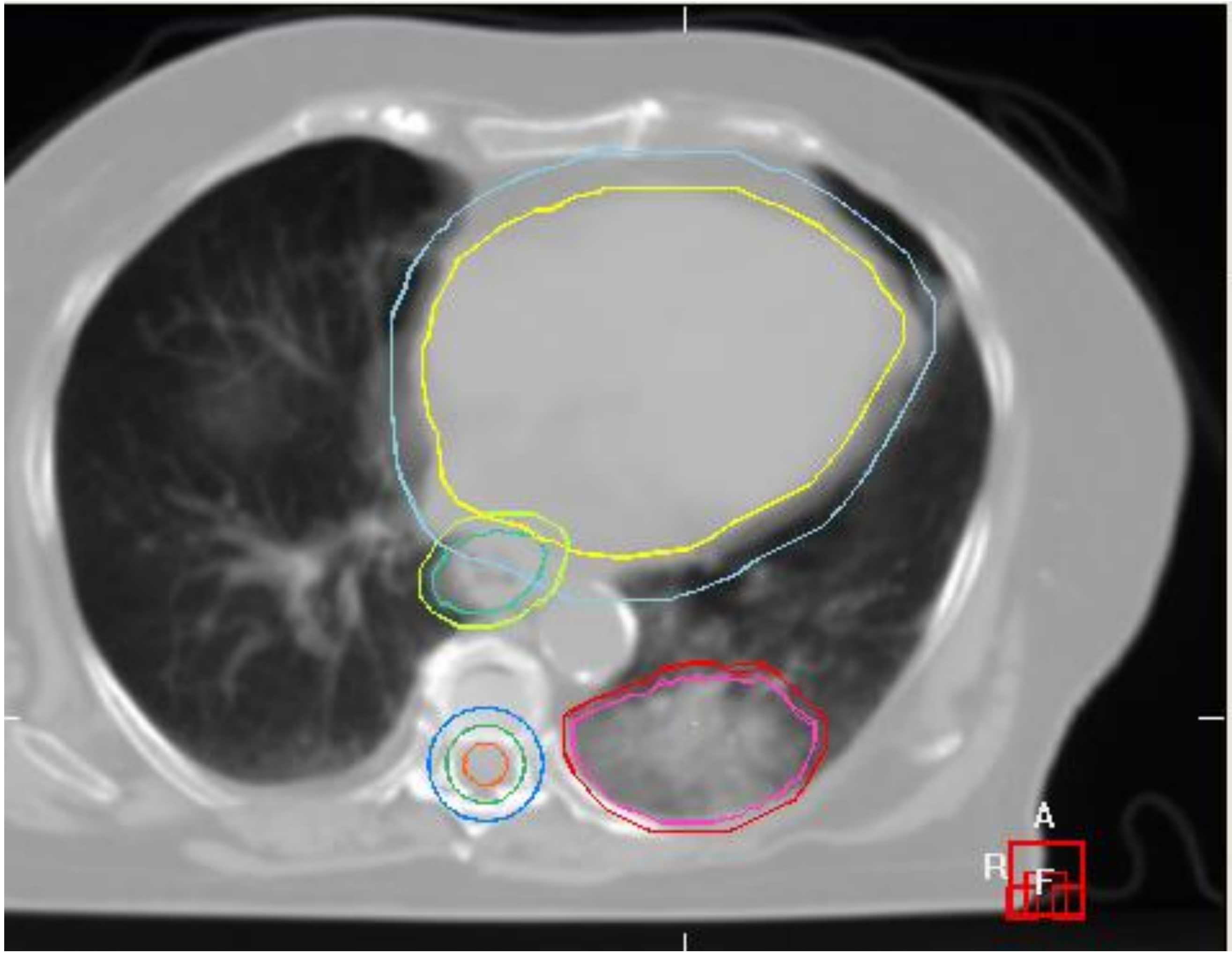
after treatment - intra fraction motion check

Stereotactic - Dual registration

VMAT introduction:
Where to choose isocenter? → Collision with patient/table

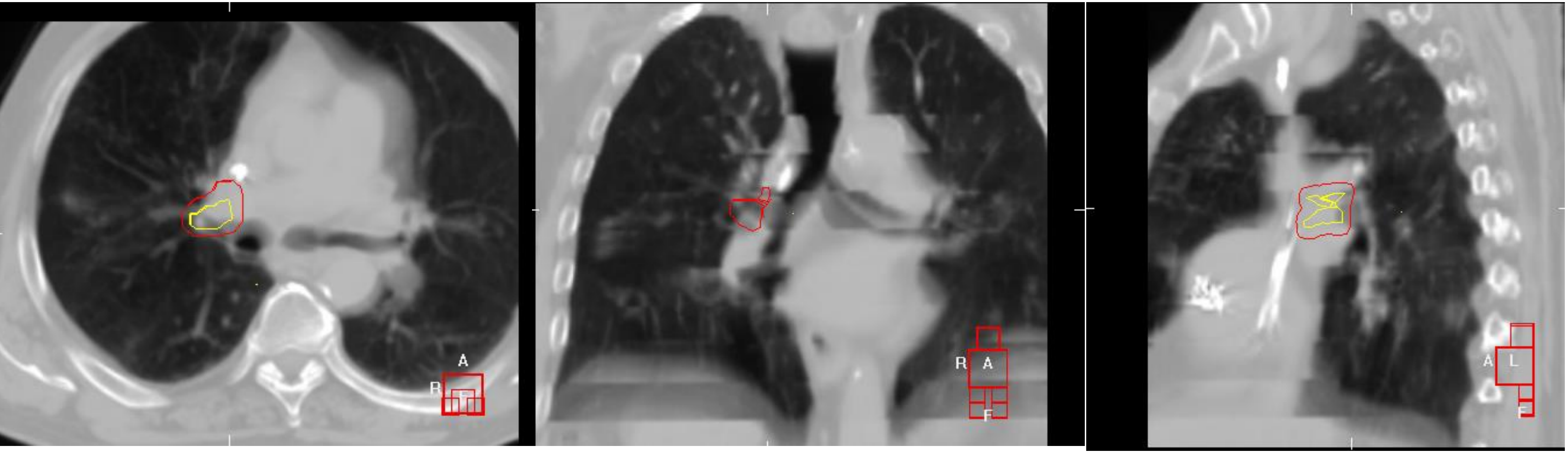
Critical structure avoidance works when isocenter is in the tumor and tumor match is in Translations_only

Challenges



More indications:
centrally located tumors
8x 7.5 Gy
3 OAR, 1 clipbox

Challenges



Sub-optimal Average CT scan

Protocolize!

Lung

MATCH PARAMETERS		SCAN PARAMETERS	
Structures	GTV and PTV	**Preset selection**	Lung left/right
Correction ref point	PTV	**Gantry rotation**	Lung right: -180° → 25° Lung left: 330° → 180°
Registration	Clipbox	**Gantry speed**	ampl. ≥ 0.8 cm:0.125 rpm* ampl.< 0.8 cm: 0.5 rpm*
Method	Bone (T + R)	**Detector position**	S
Restriction Rotation	5°	**Filter**	F1
Restriction Translation	10 mm	**Collimation**	S20

Example clipbox:

Example clipbox *:

- Put the clipbox around the vertebrae.
- If the tumor is located ventrally then include the sternum in the clipbox (*),
- If the tumor is located laterally then include the ribs.
- Do not include (too much) of the scapula and/or the humerus head.

Traffic Light System

"decision support system to guide the RTT in prioritizing anatomy changes"

Level green, no action needed.

Level yellow, the radiation oncologist is notified by email, but no response is required to continue treatment.

Level orange, the treating radiation oncologist (or back-up colleague) is informed by email and a response is required before the next fraction.

Level red changes, the radiation oncologist must be consulted immediately before the treatment fraction is allowed to be delivered.

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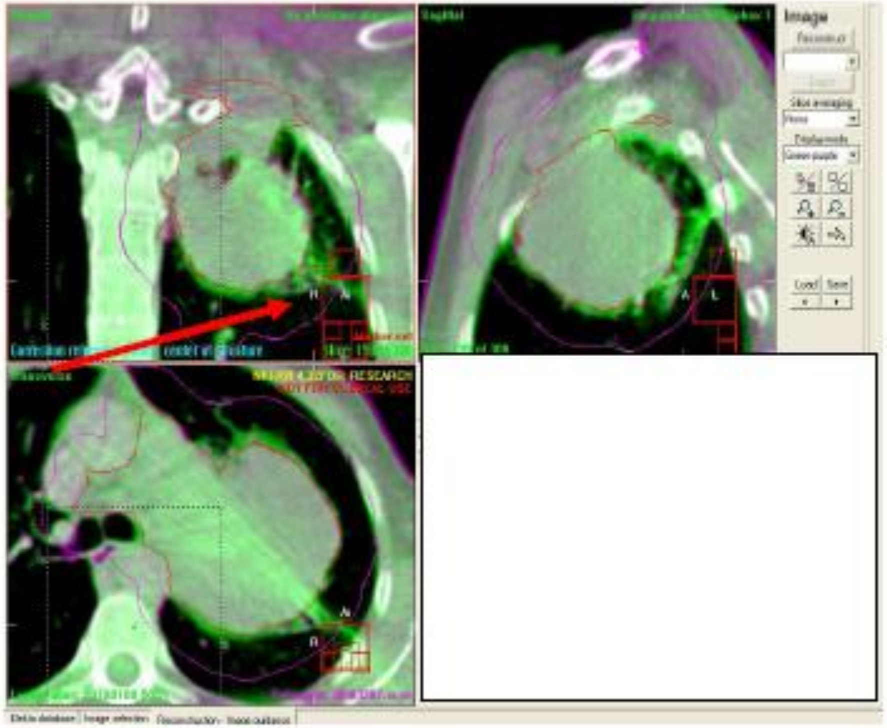
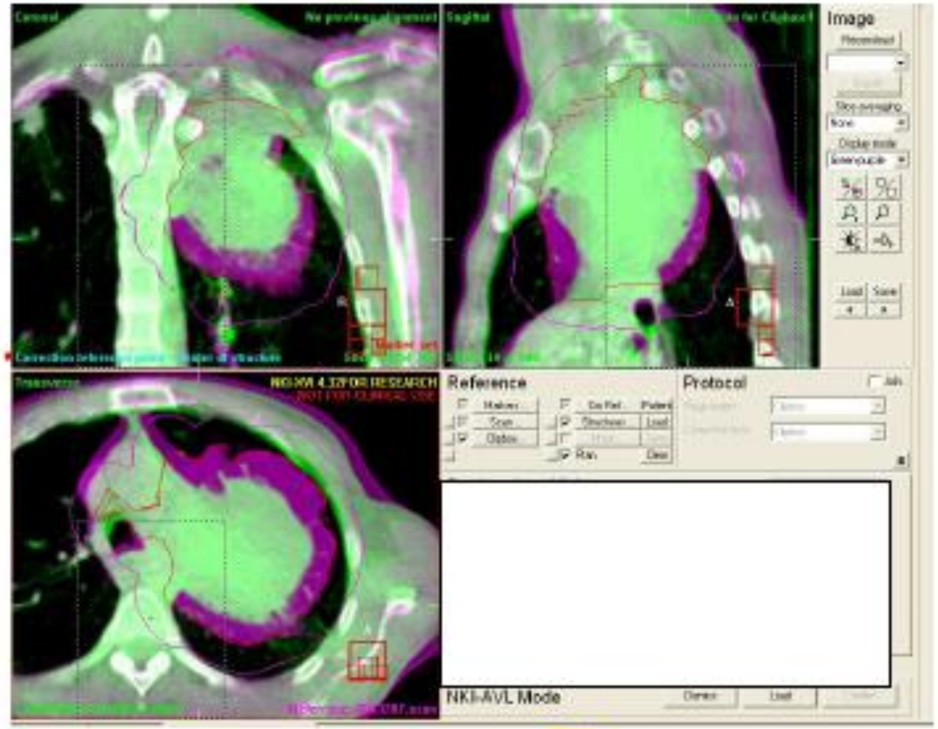
http://www.avl.nl/media/291805/xvi_engelse_protocols_16_7_2014.pdf

Traffic Light System – progression/regression

Lung



Tumour progression.



Tumour regression.

Progression within the PTV	
Progression only just inside PTV:	
Progression, outside PTV:	

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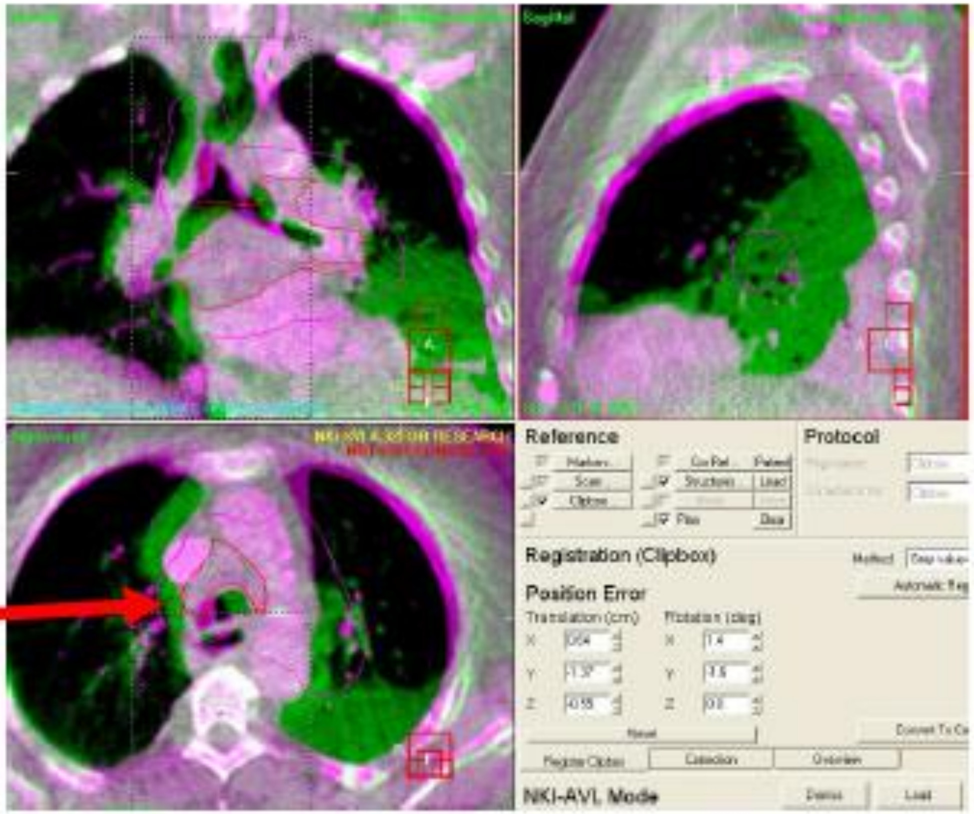
Traffic Light System – Anatomy Change



Increase of atelectasis (green),;this causes a shift of the mediastinum (red arrow).

The lymph nodes can shift outside the PTV.

Tumourshift

Tumour shift within the PTV:

Tumour shift outside the PTV

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IGRT strategies in clinical practice : bladder/rectum/gynaecological cancers

Gilles Créhange, MD, PhD

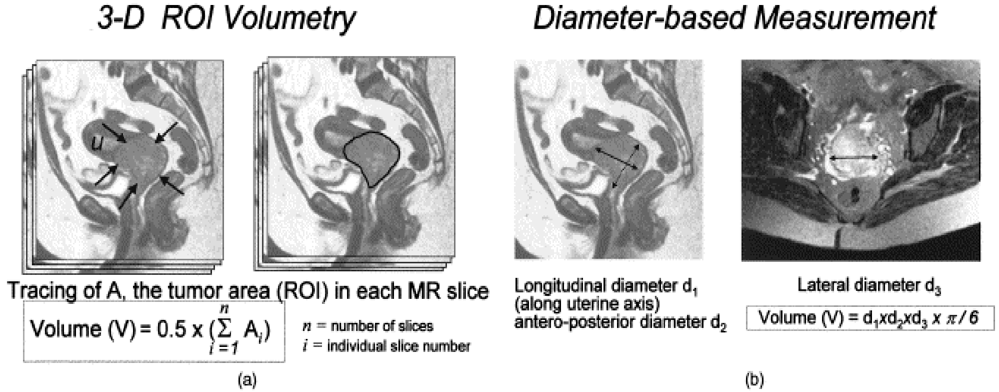
1- Department of Radiation oncology, Centre Georges François Leclerc, Dijon, France

2- Medical Imaging Group, Laboratory of Electronics, Computer Science and Imaging, (Le2I), CNRS 6306, University of Burgundy

IGRT in Cervix cancer

GTV Definition : Primary tumor

	US		CT		MRI	
	sensitivity	specificity	sensitivity	specificity	sensitivity	specificity
Vagina	100%	75%	29-87%	68-100%	33-100%	50-97%
Parametrium	78-89%	88-89%	28-100%	73-92%	20-100%	76-97%
Pelvic Wall	/	/	50%	95%	67-100%	76-96%
Rectum	95%	97%	92%	87%	67-100%	73-100%
Bladder	100	85%	40-65%	87-100%	67-100%	69-96%



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GTV Definition : Positive nodes

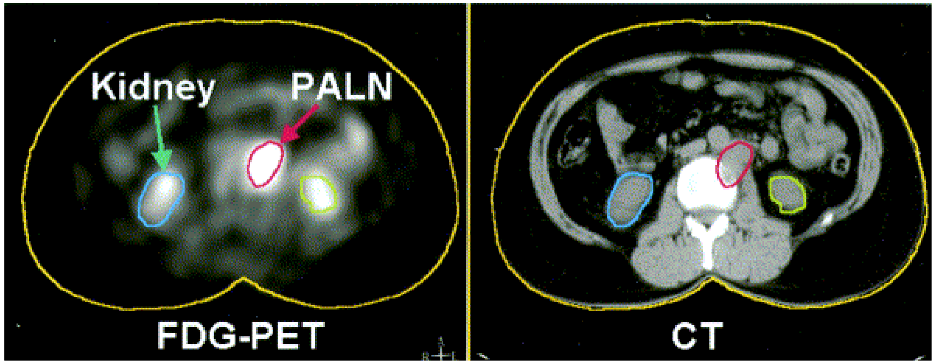
Lymphangiogram		CT Positive node ≥ 1 cm		MRI Positive node ≥ 1 cm	
sensitivity	specificity	sensitivity	specificity	sensitivity	specificity
29-78%	62-98%	24-80%	78-93%	24-75%	88-100%

NEEDS FOR IMPROVEMENT

- **Node sampling by laparoscopy in non bulky Stage I and II**
- **Enhanced contrast dynamic MRI, specific contrast agents for detection of occult metastasis**
- **PET-CT**

GTV Definition : Positive nodes

Stage	Number of patients	Cervix Positive		Pelvic Lymph Node Positive		Para-Aortic Lymph Node Positive		Supraclavicular Lymph Node Positive
		PET	CT	PET	CT	PET	CT	PET
Ia	2	1	0	1	0	0	0	0
Ib1	8	8	5	4	0	0	0	0
Ib2	18	18	15	14	3	4	1	1
IIb	39	39	28	22	7	5	2	2
III	29	29	25	22	8	9	2	4
IVa	1	1	1	0	0	0	0	0
IVb	4	4	3	4	2	3	2	1
Total	101	100	77	67	20	21	7	8



FDG-PET detects abnormal lymph node regions more often than does the CT and
the findings on pet are better predictor of survival than those of CT in patients with Carcinoma of the cervix

Grigsby et al JCO 2001

Consensus guidelines for delineation of CTV in endometrial or cervix cancer

- **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

Small W, IJROBP Nov 2007

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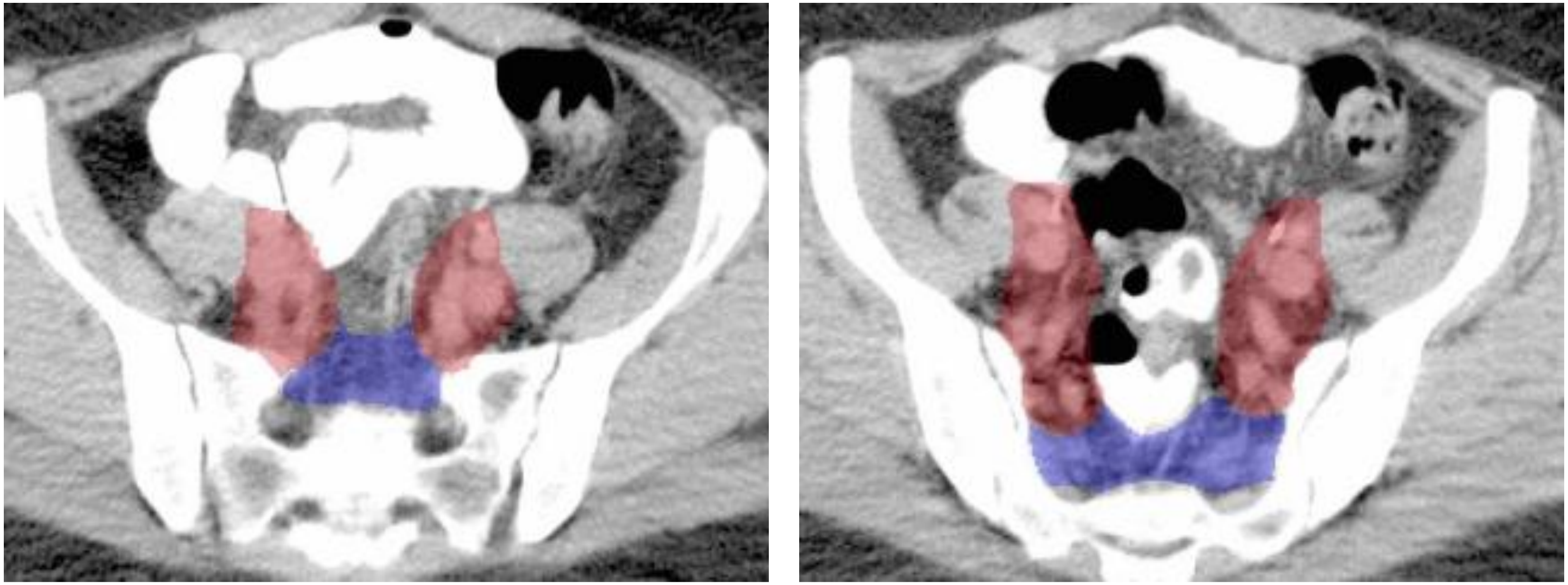
Consensus guidelines for delineation of CTV in endometrial or cervix cancer



- **Presacral lymph nodes** : Lymph node region anterior to S1and S2 region
- *If patient has cervical cancer or endometrial cancer with cervical stromal invasion.*

Small W, IJROBP Nov 2007

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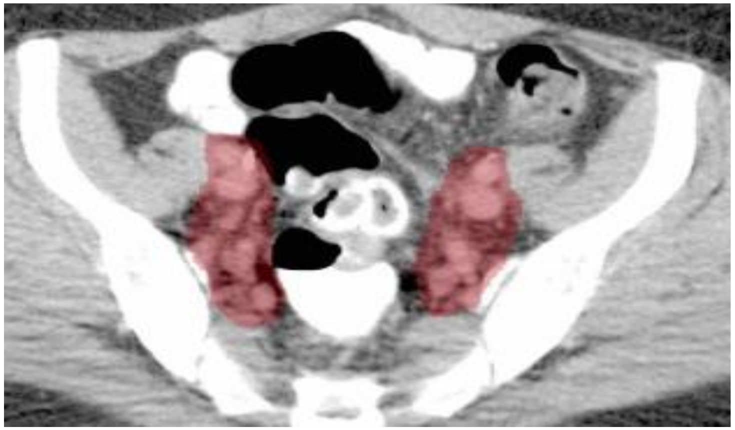
Consensus guidelines for delineation of CTV in endometrial or cervix cancer



- **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

Small W, IJROBP Nov 2007

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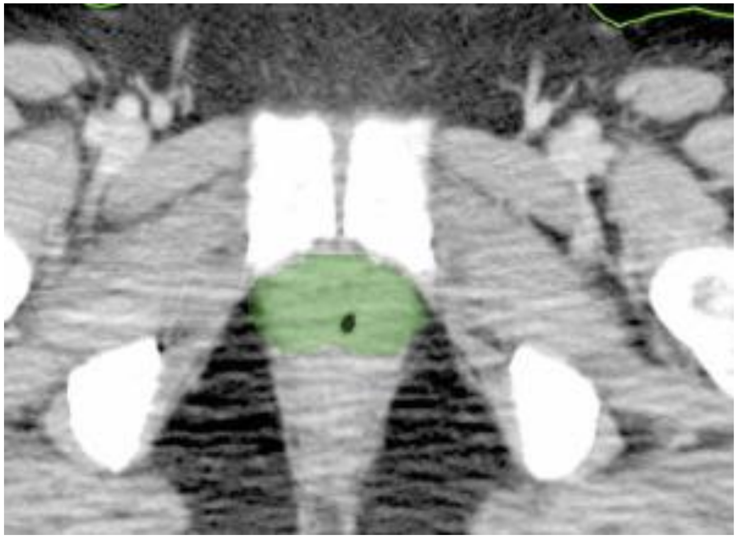
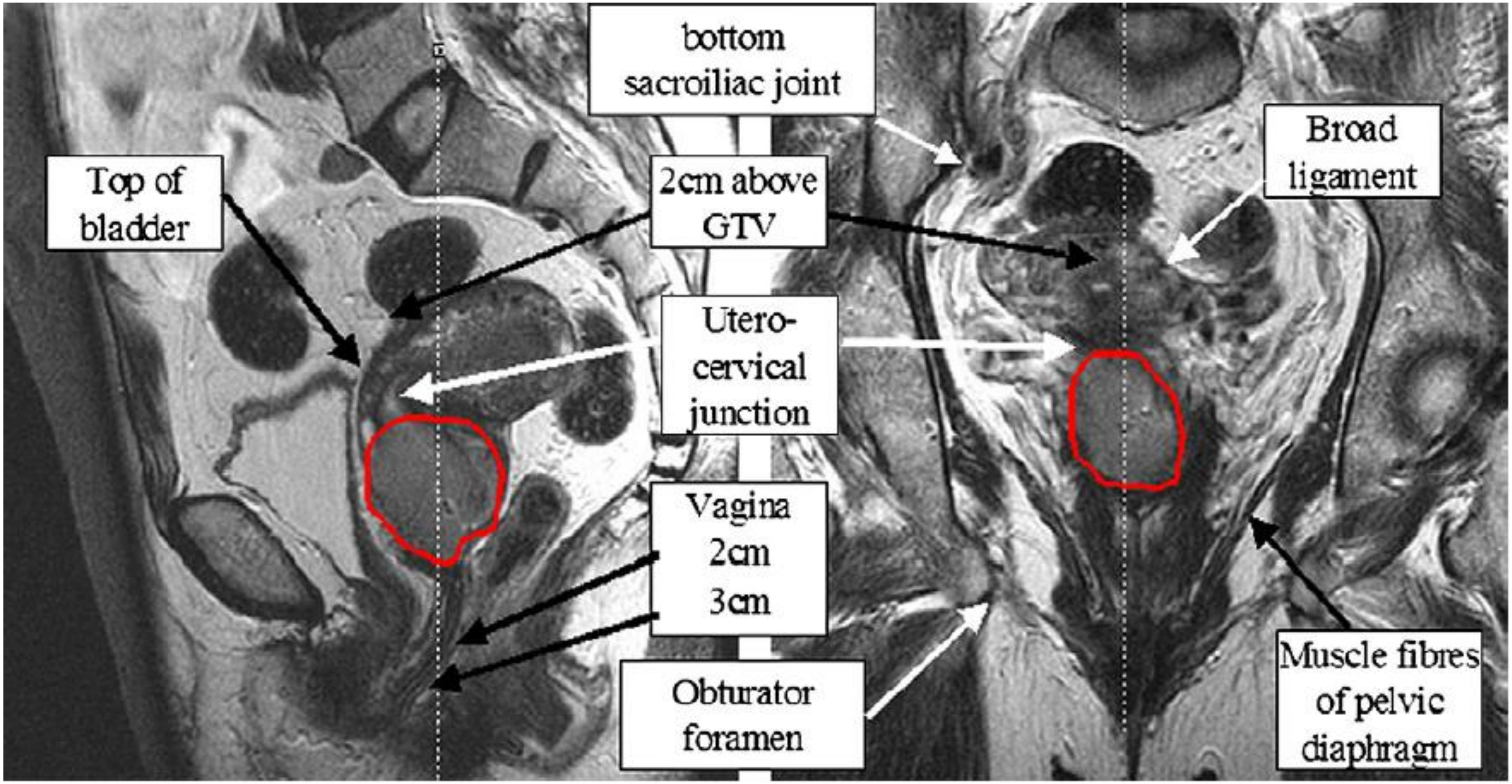
Consensus guidelines for delineation of CTV in endometrial or cervix cancer



- **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

Small W, IJROBP Nov 2007

Consensus guidelines for delineation of CTV in IMRT



Lim K et al. IJROBP 2011

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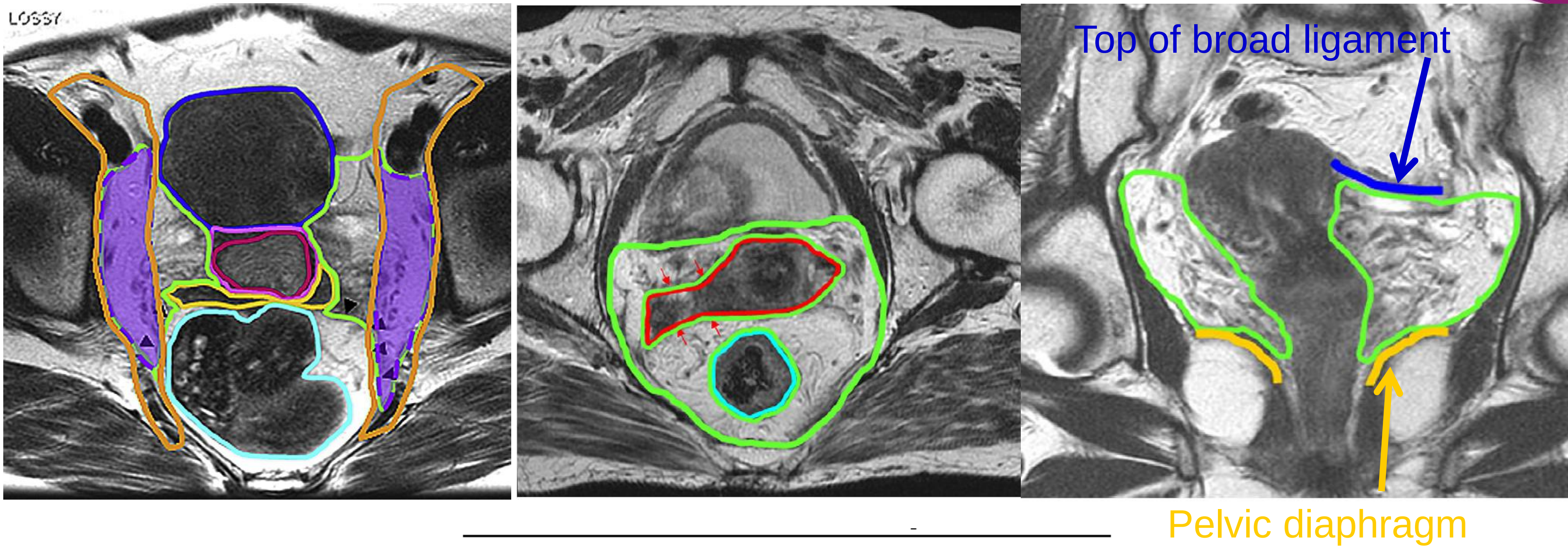
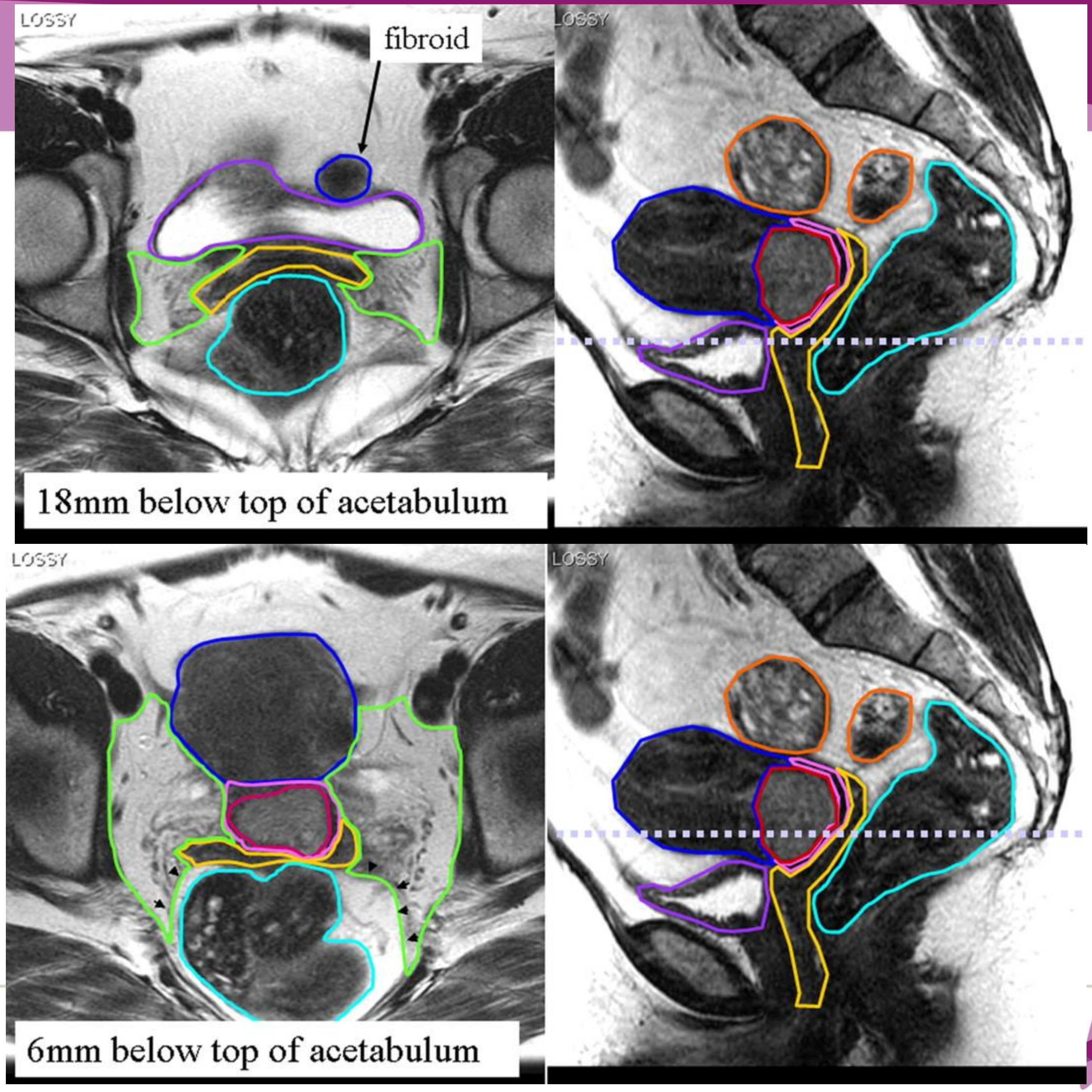
Radiological definition of the Parametrium



Location	Anatomic structures
Anteriorly	Posterior wall of bladder or posterior border of external iliac vessel
Posteriorly	Uterosacral ligaments and mesorectal fascia
Laterally	Medial edge of internal obturator muscle/ ischial ramus bilaterally
Superiorly	Top of fallopian tube/ broad ligament. Depending on degree of uterus flexion, this may also form the anterior boundary of parametrial tissue.
Inferiorly	Urogenital diaphragm

Lim K et al. IJROBP 2011



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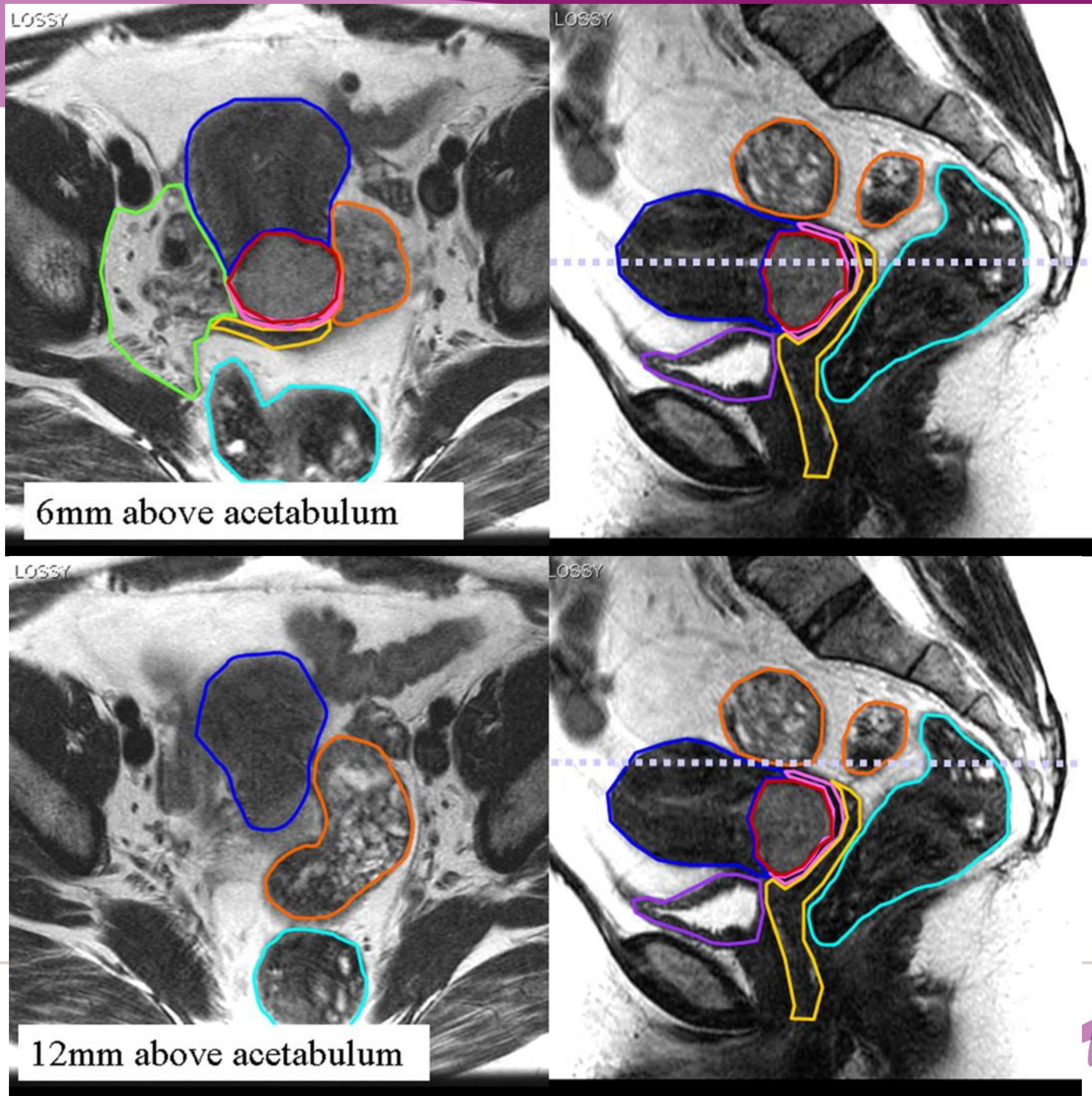

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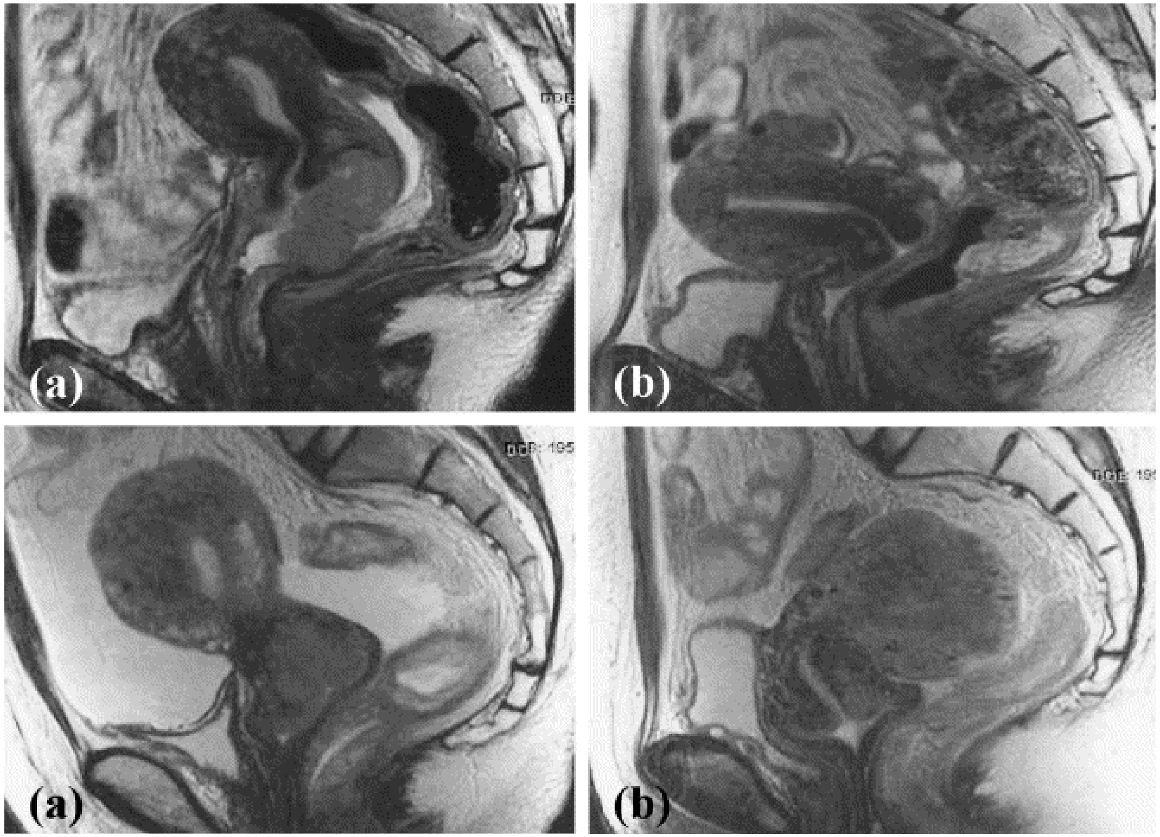
Consensus guidelines for delineation: Cervix

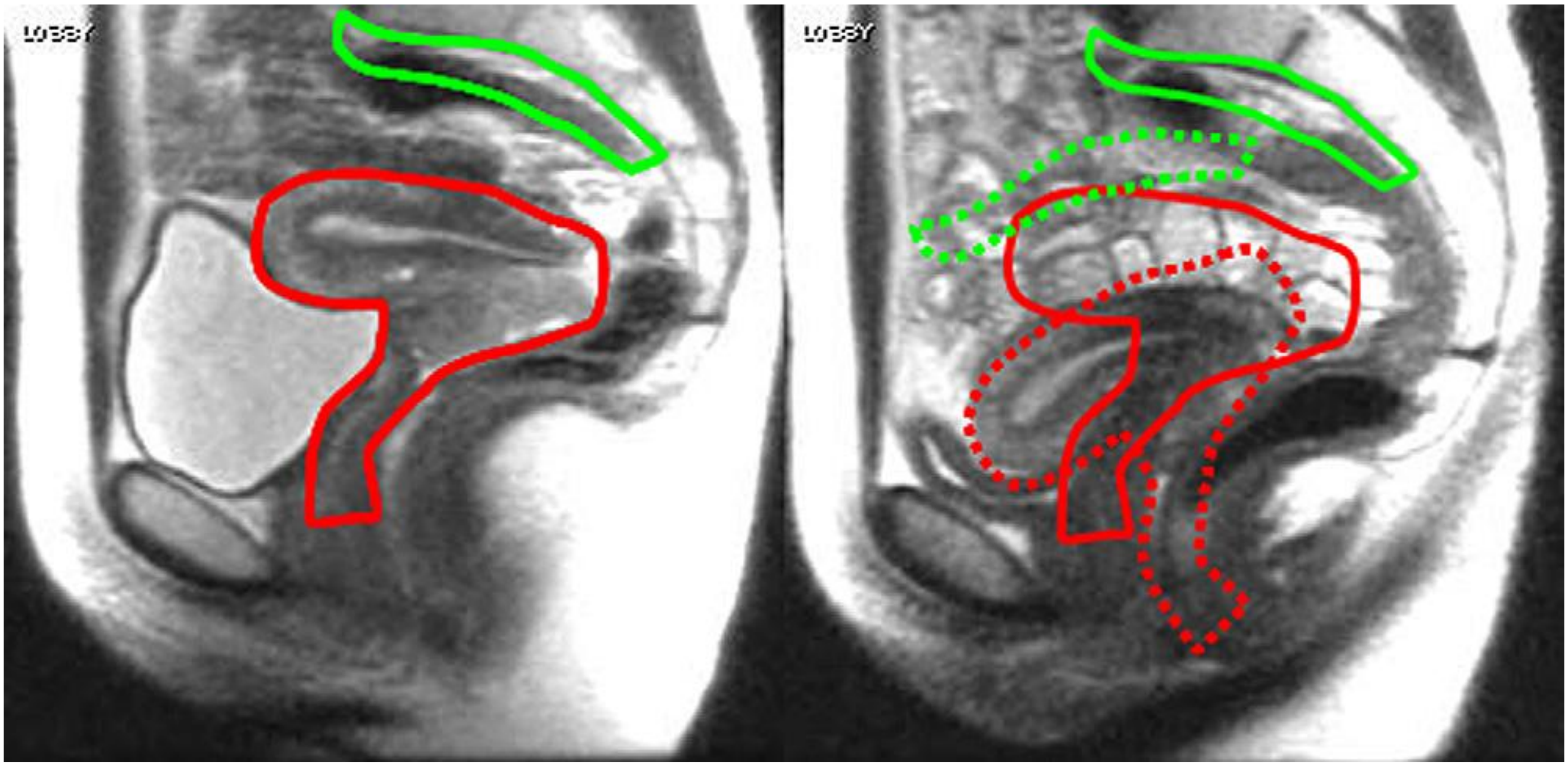
Table 2. CTV components

GTV	Entire GTV; intermediate/high signal seen on T_2-weighted MR images
Cervix	Entire cervix; if not already included within GTV contour
Uterus	Entire uterus
Parametrium	Entire parametrium, including ovaries; include entire mesorectum if uterosacral ligament involved
Vagina	Minimal or no vaginal extension: upper half of the vagina
	Upper vaginal involvement: upper two-thirds of the vagina
	Extensive vaginal involvement: entire vagina

PTV definition
ORGAN MOTION



- **According to tumour size and regression**
  - **Mean displacement**
  - **- 8 mm in small Tumour**
  - **- 18 mm in large Tumour**
- **According to age**
  - **Mean angulation of cervical canal**
  - **- 17.5° < 60 years**
  - **- 9.5° > 60 years**



1 week after

PTV margins and image guidance

- PTV margin published recommendations : **0.6-4.0cm**
- Large margin still recommended :

- because of unpredictable organ motion
- Substantial tumor regression

- **Up to 1.5-2cm if (good quality) soft tissue daily image guidance**
- **0.7cm for nodal CTV**

- Larger margins if bone matching alone

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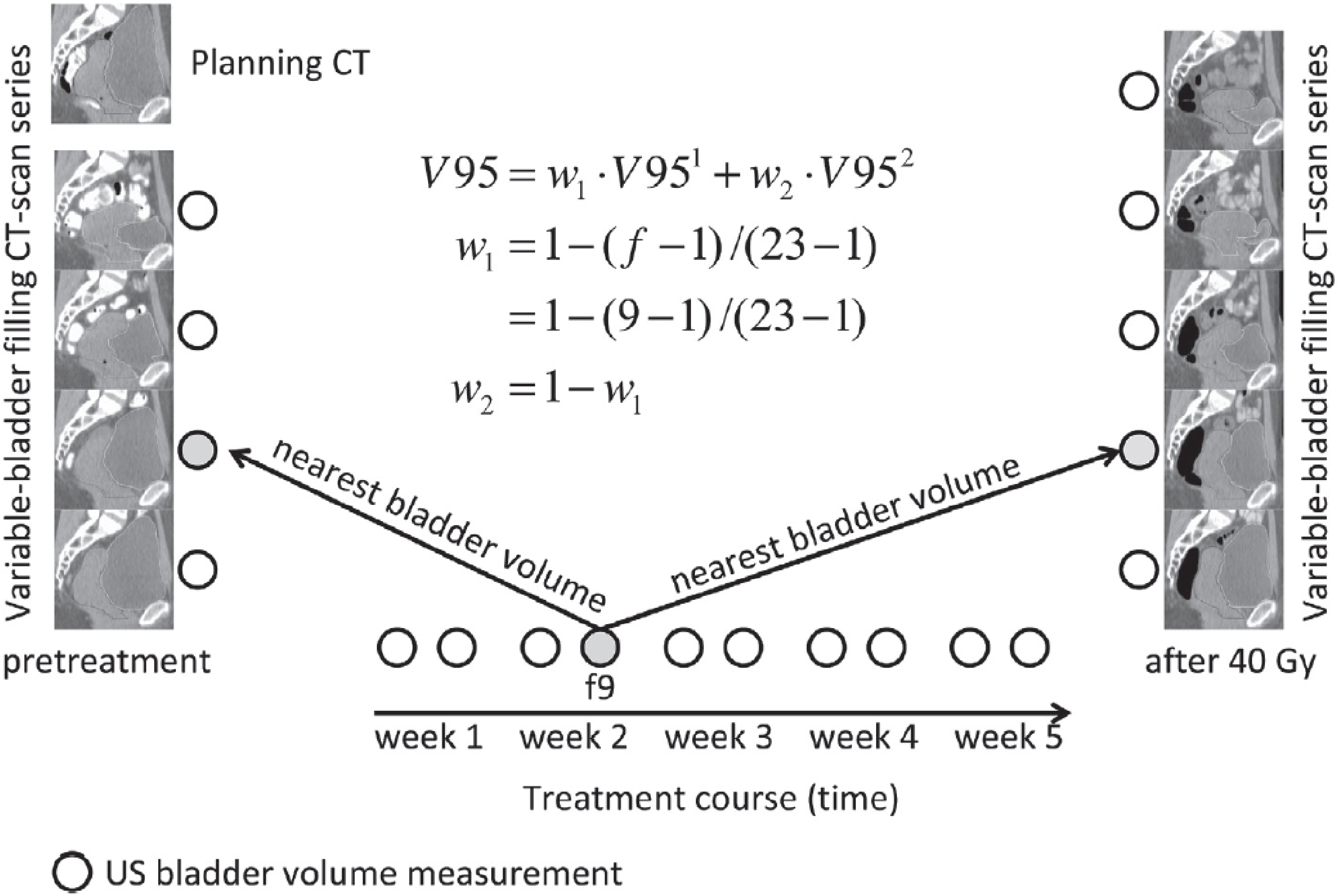
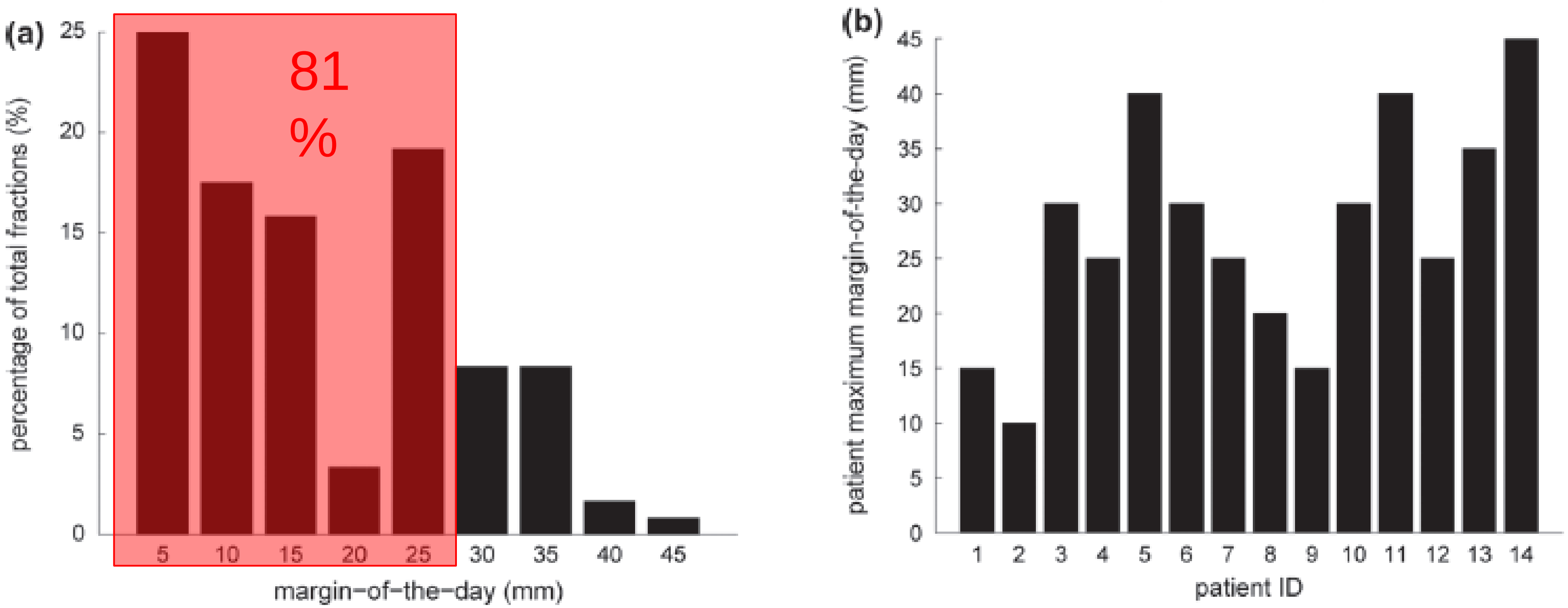
Margin of the day on line adaptive strategy and cervival cancer



Ahmad R et al. Acta Oncol 2013

Margin of the day on-line adaptive strategy and cervival cancer



Ahmad R et al. Acta Oncol 2013

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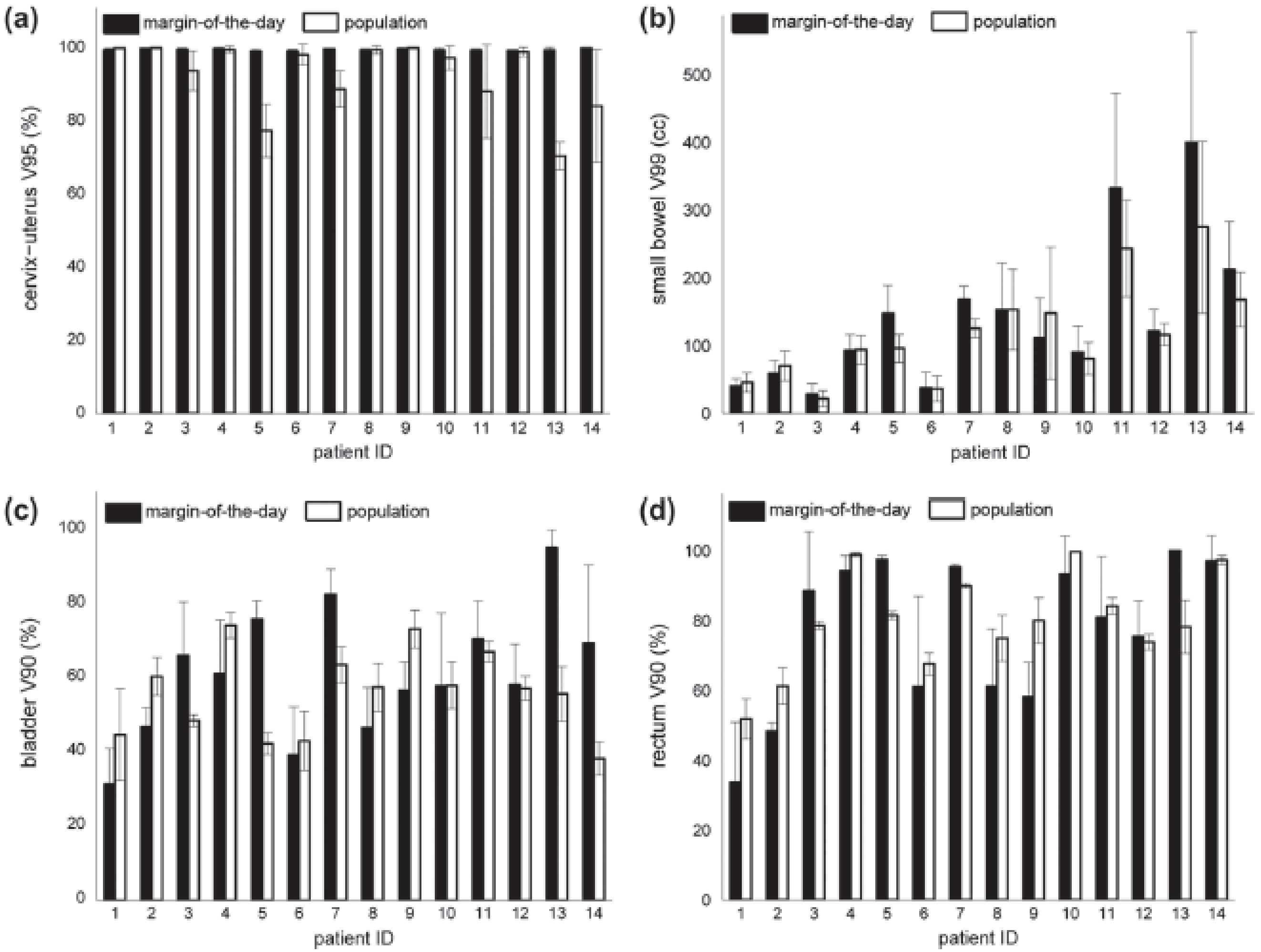
Margin of the day on line adaptive strategy and cervival cancer



Ahmad R et al. Acta Oncol 2013

Cervix cancer =
on-line adaptive vs population-based margin

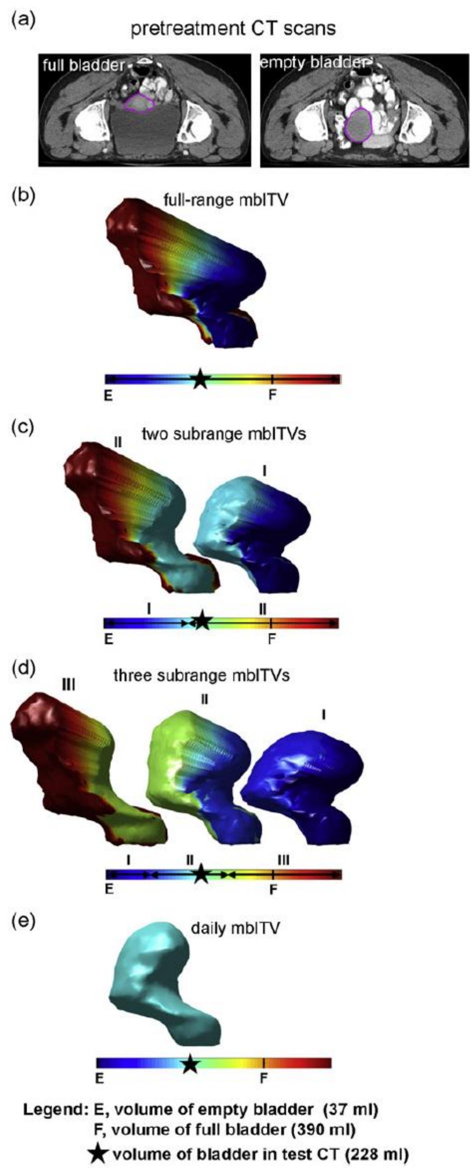
- Bladder-based ITV

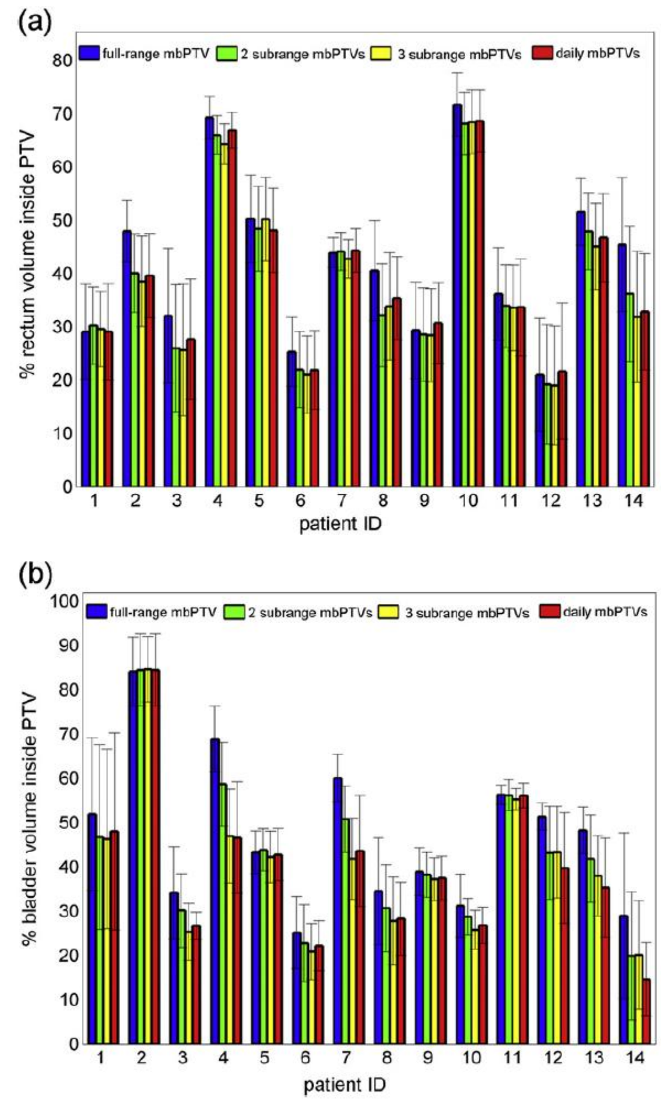
  (Margin 38mm)

  vs

- Adaptive strategy (library of plans based on 10 pretreatment CT + after 40Gy with varying bladder filling)

  (Margin 7-10mm)



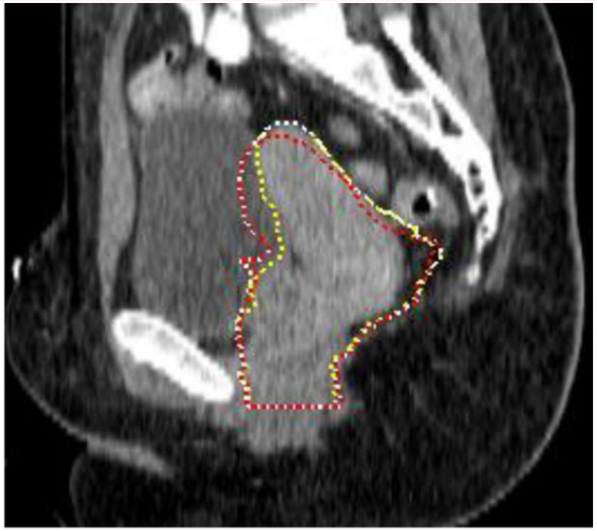


- **volume reduction**
- **PTV : 48%**
- **Bladder 5to 45%**
- **Rectum 26% to 74%**

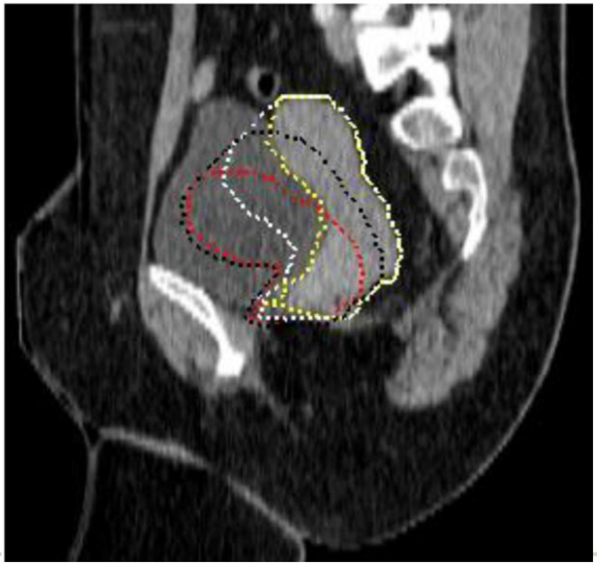
Bondar M et al., IJROBP 2012

On-line adaptive plan-of-the-Day

- N=64
- 2 planning CT (full and empty bladder)
- Plan library with model predicted ITV
- PTV = ITV + nodal CTV + 1cm



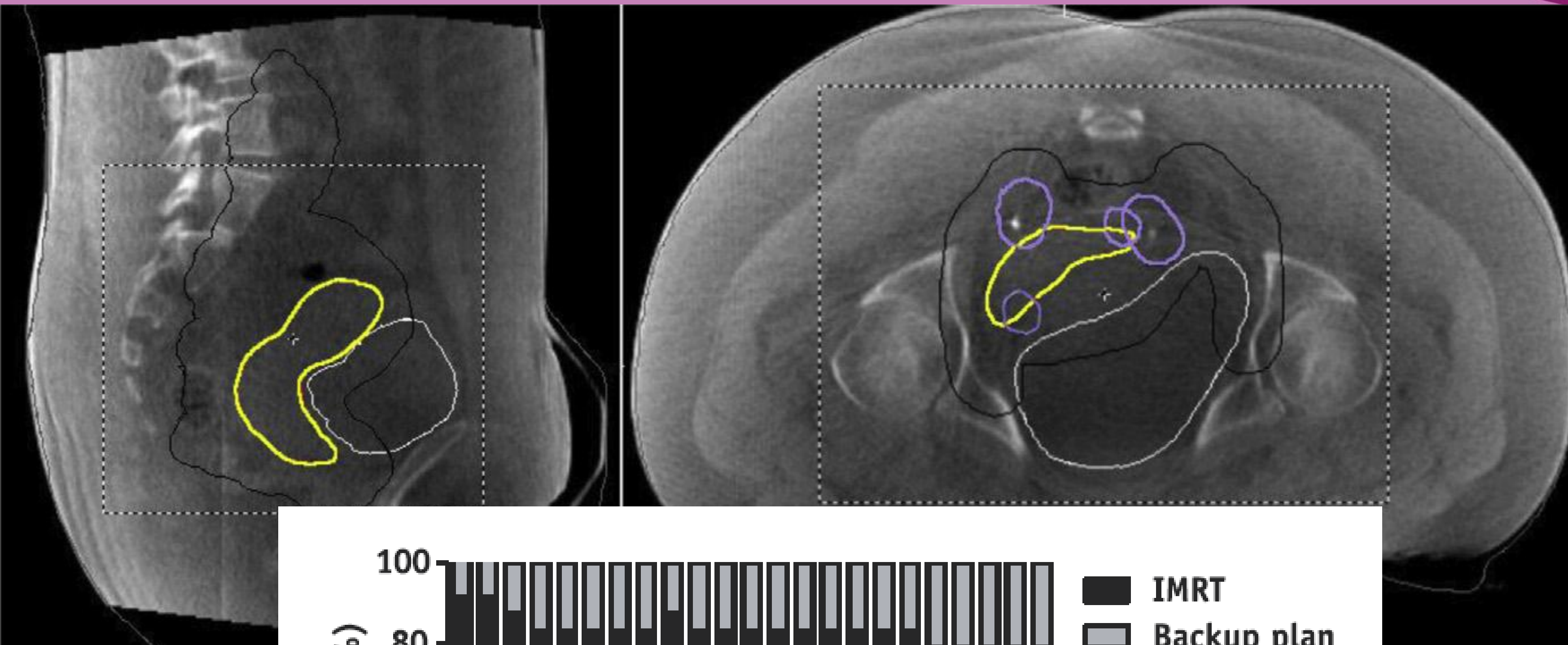
Small motion

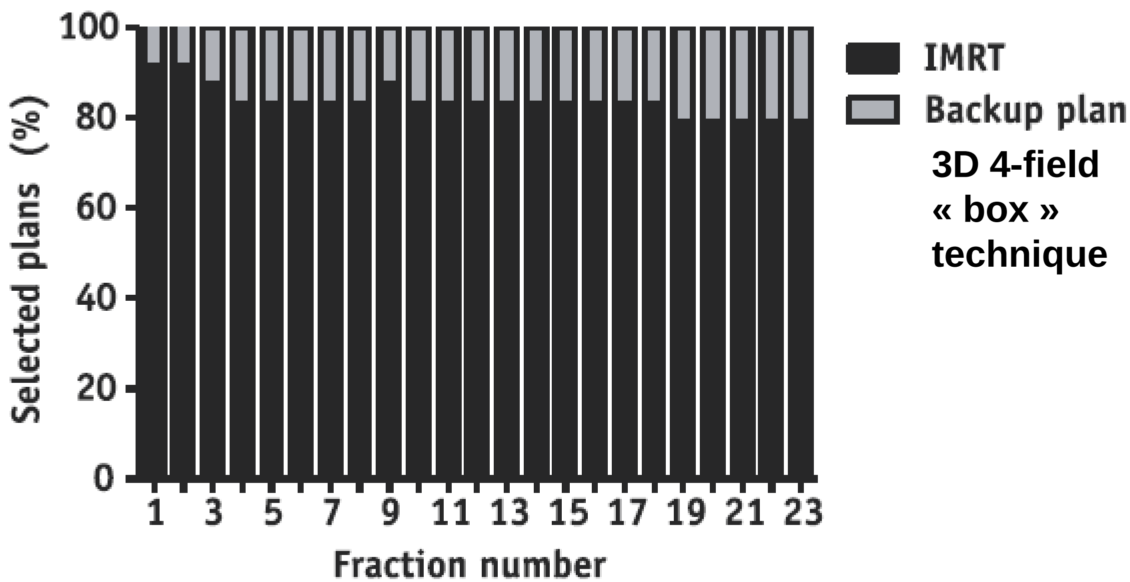


Large motion

Heijkoop S et al., IJROBP 2014

Half full to full bladder PTV





3D 4-field « box » technique

Heijkoop S et al., IJROBP 2014

IGRT in rectal cancer

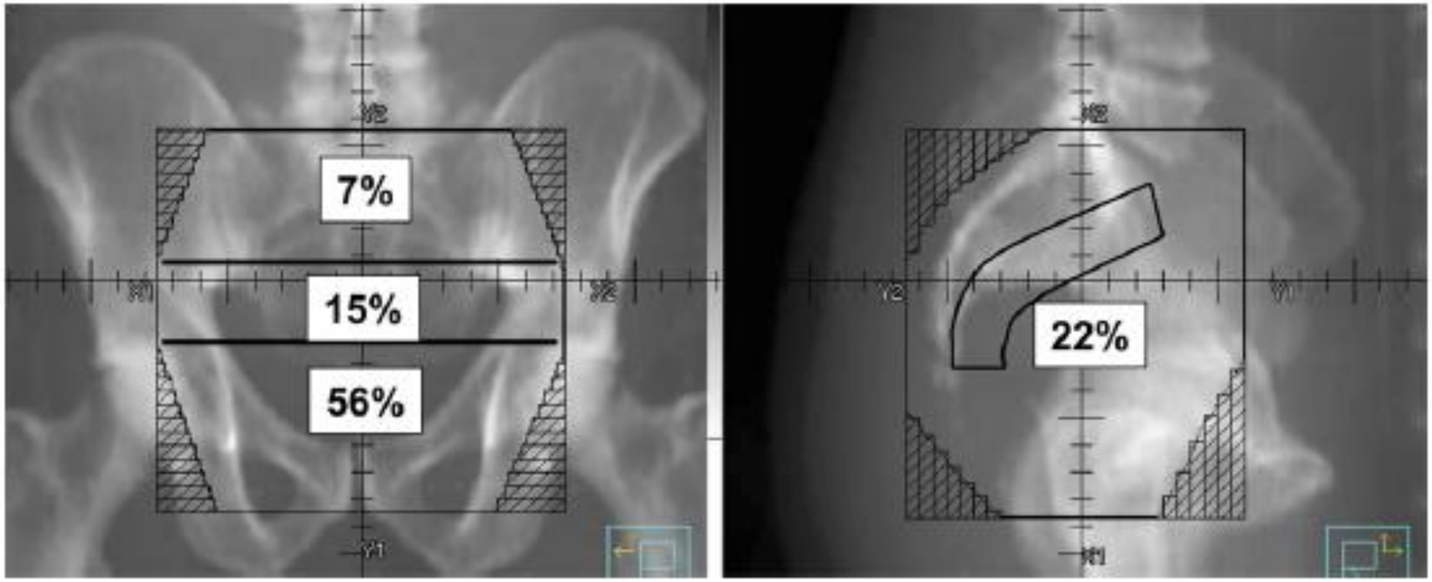
XRT-CT
CAO/ARO/AIO-94

TME SURGERY

5-y outcome	Post-op (n=394)	Pre-op (n=405)	p
Survival %	74	76	0.80
LF %	13	6	0.006
acute toxicity	40 (Diarrhea)	27	0.001
chronic toxicity	24 (Anastomotic stricture)	14	0.01

Rodel C et al., NEJM 2004

Patterns of loco-regional recurrences



1. Distribution of in-field recurrences. The numbers denote the percentage of in-field recurrences at each region.

Table 2. Patterns of locoregional recurrence

Region	No. of recurrences (%)
In-field	28 (65)
Marginal	7 (16)
Out-of-field	8 (19)

Tse-Kuan Yu IJROBP 2008

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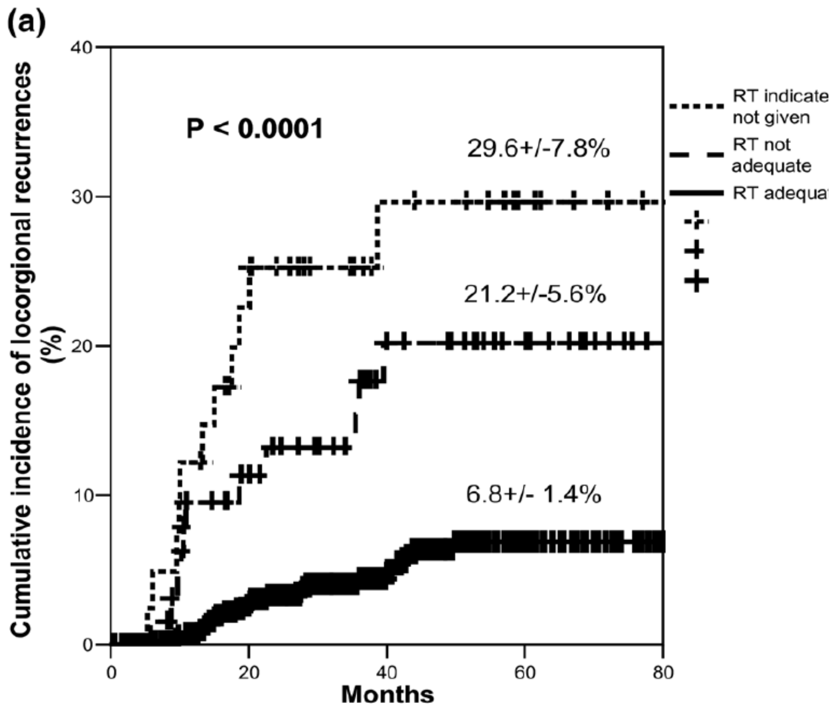
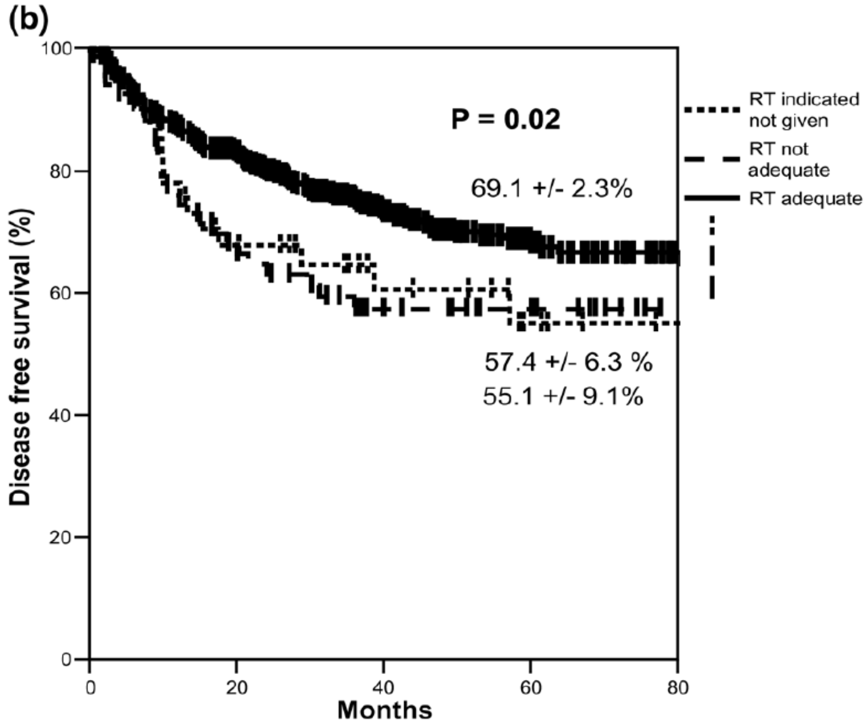
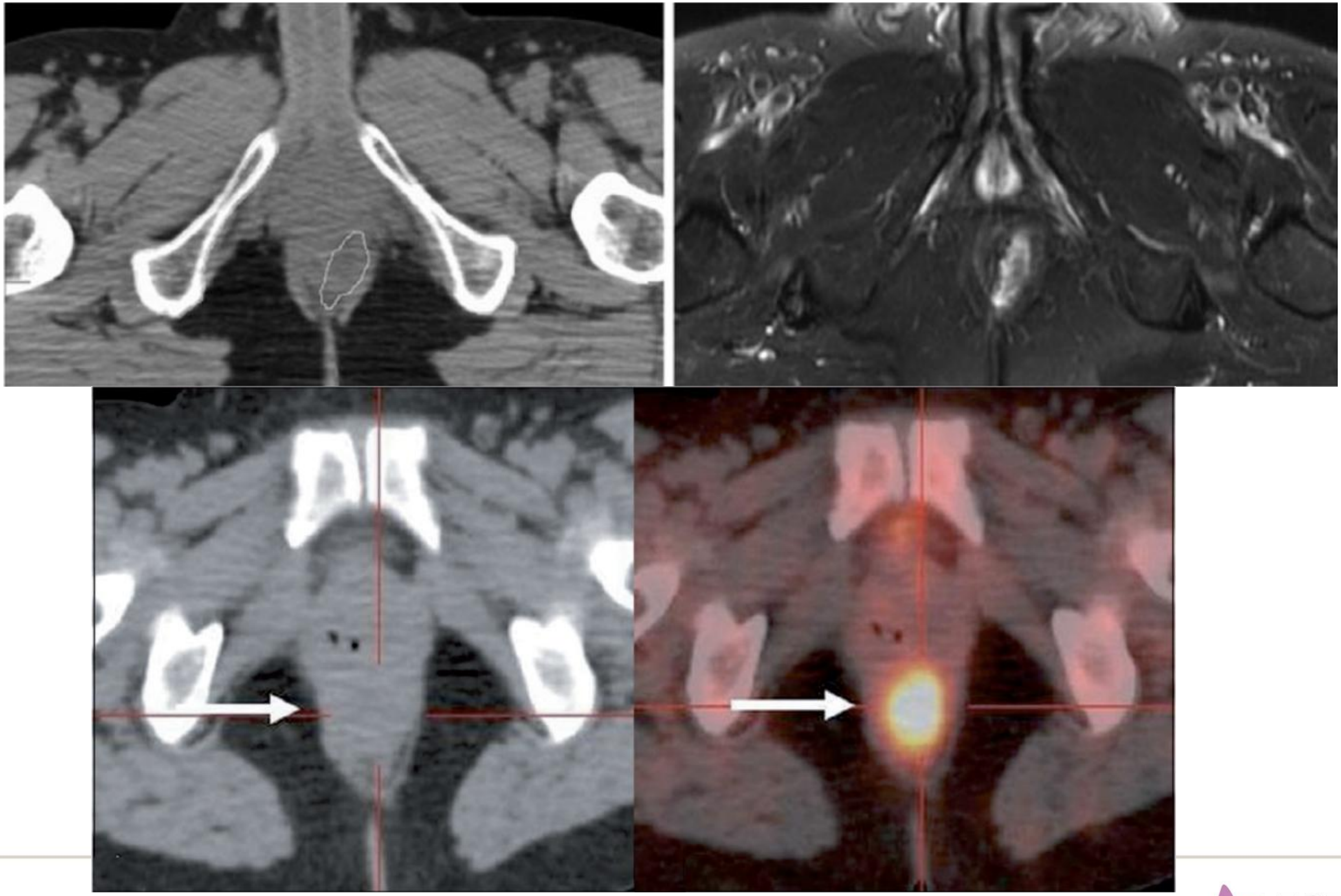
CAO-AIO-ARO 94 Quality Assurance of RT (QART)



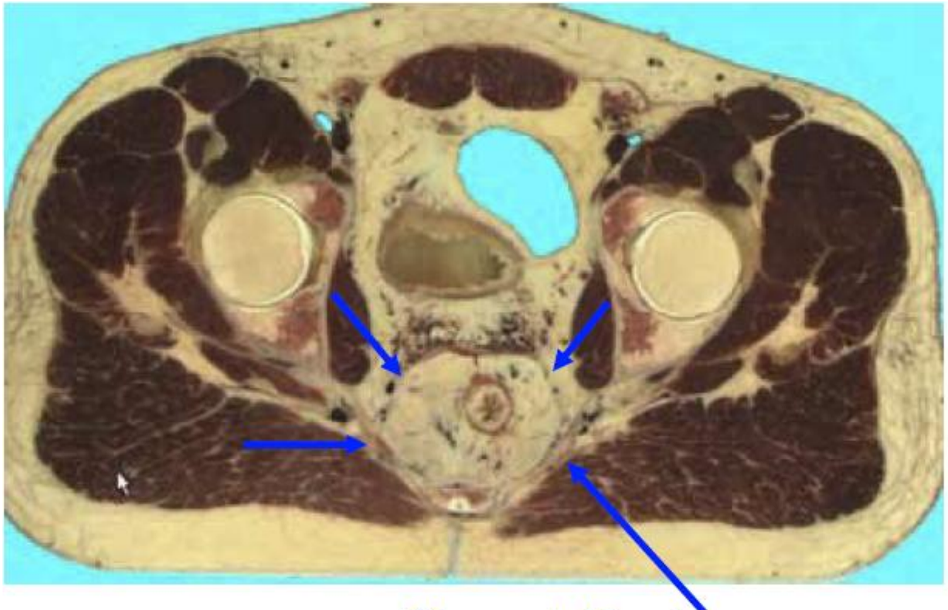


Fietkau R, IJROBP 2007

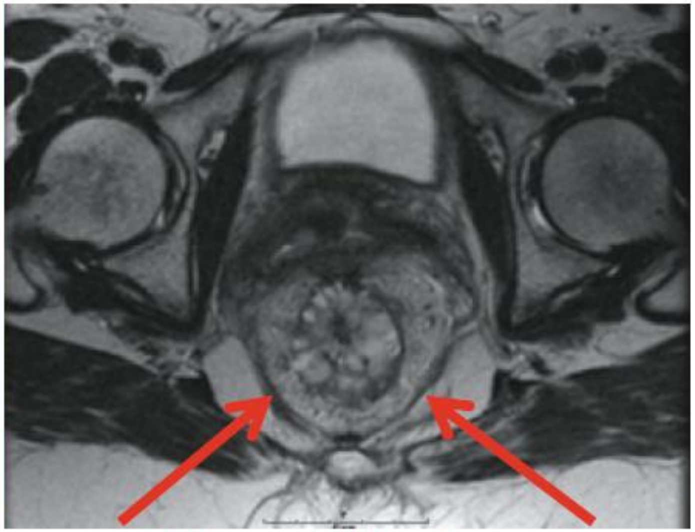
MRI or PET helps better defining GTV



ANATOMICAL CONSIDERATIONS



Mesorectal Fascia



Mesorectal Fascia

- Axial T2-w MR images
- Circumferential involvement of the mesorectal fascia+++

Rectal constrast

- AP displacement

Brierley JD, IJROBP 2011

Guidelines : CTV → PTV

- Planning CT : 50ml air
- Inter and intrafraction mvts = negligeable

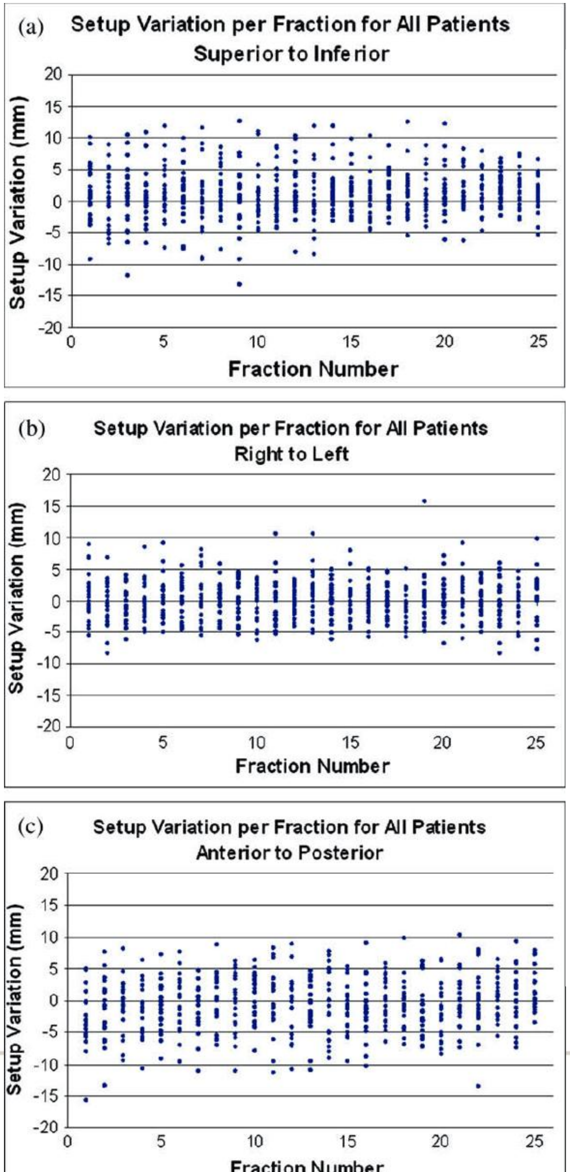
  (Tinger et al., IJROBP 1996)

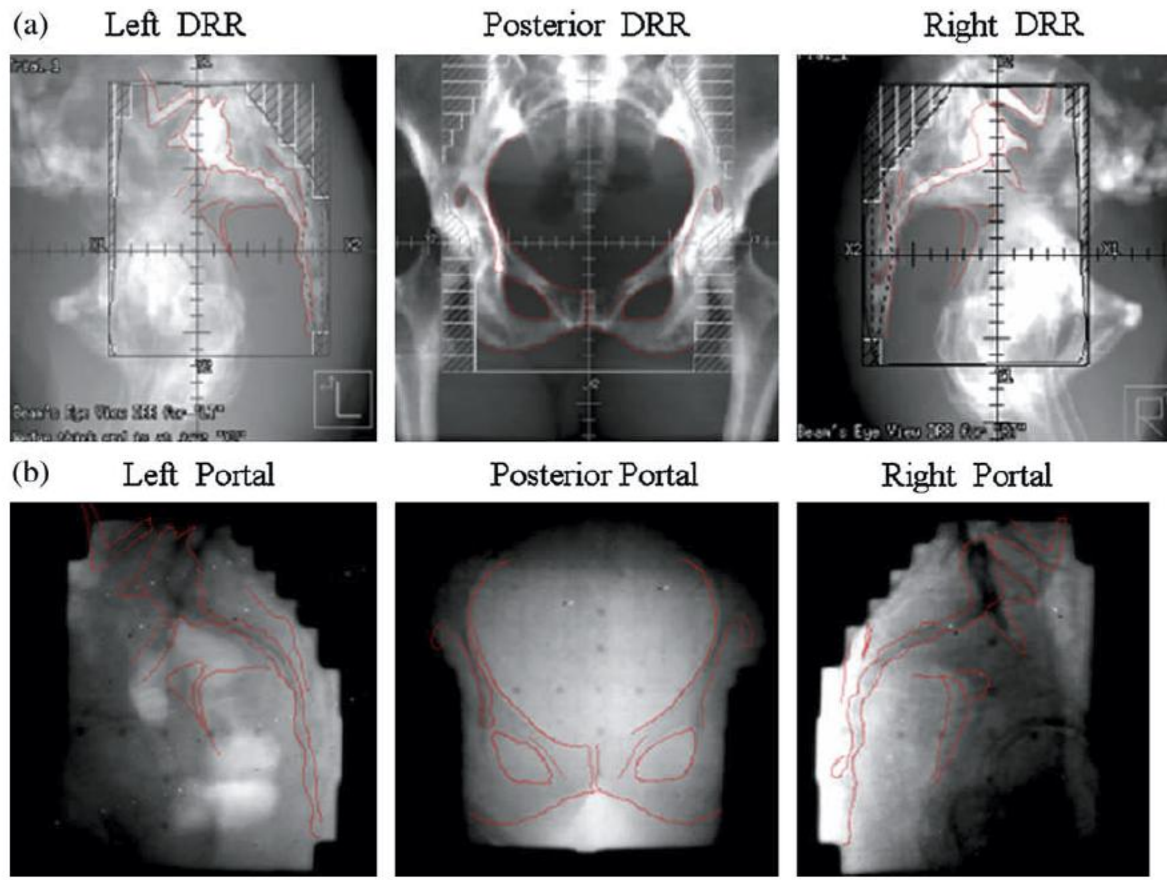
- Physiological mvts of the rectum ~ 1cm

  (Nuyttens et al., IJROBP 2002)

- Set-up margin ~ 1cm

Myerson et al., Sem Rad Oncol, 2003





Robertson J, IJROBP 2009

Target Volumes

- **GTV : Tumor + involved nodes**
- From DRE, EUS, MRI, CT and/or ^{18}FDG-PET

- **CTV : ENI +/- ischiorectal fossa (low rectum)**
- Whole mesorectum
- Standard : perirectal nodes, internal iliac, superior rectal artery
- T4 anterior (+ external iliac nodes)
- T4 anal canal (+ external iliac and inguinal nodes)

Myerson RJ, Kachnic LA, IJROBP, 2009.

Guidelines
Gasthuisberg University Hospital

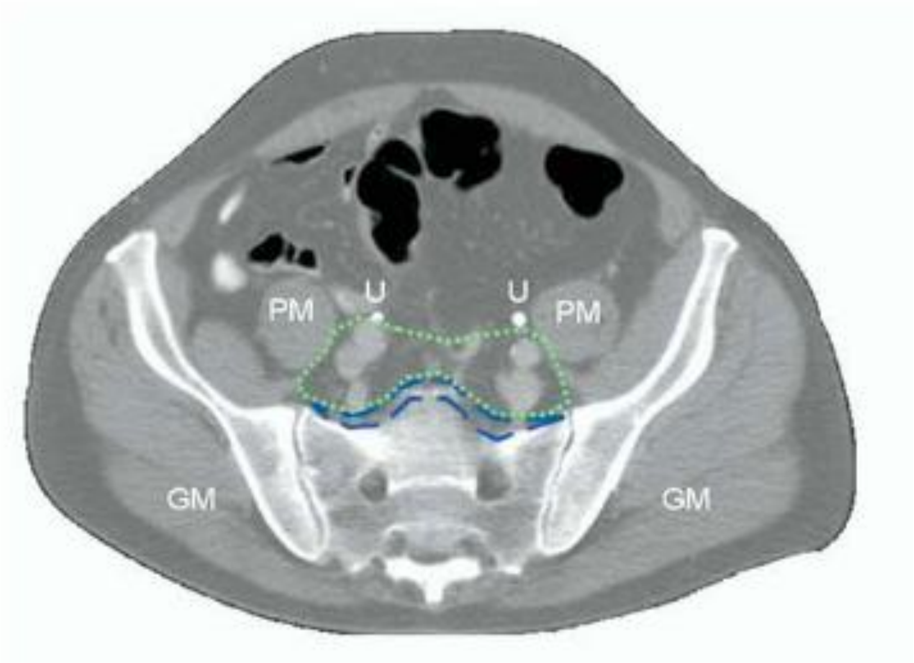
- 17 articles : Sites of relapses
- - anastomosis 10-21%
- - LN+ :

Table 4. Lymph node involvement per lymph node region

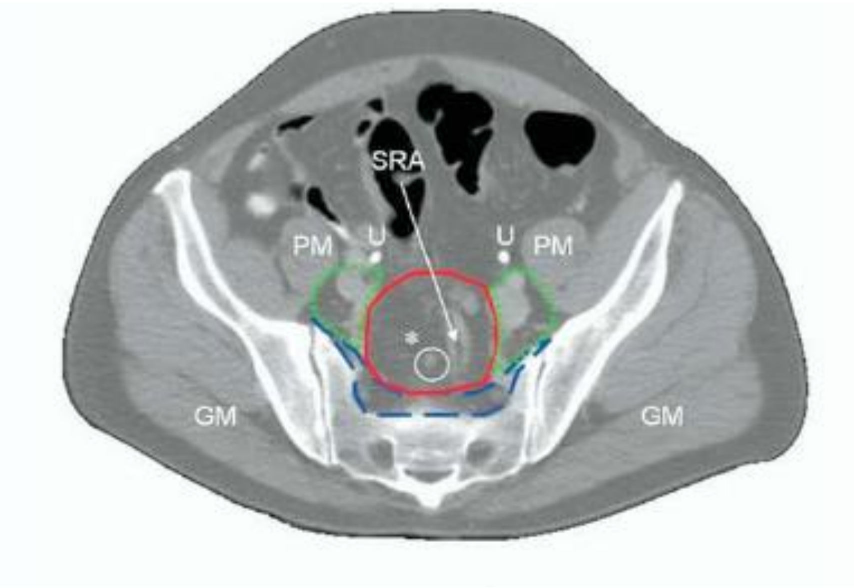
LNR	Patient group	References	No. at risk (*n*)	No. N+ (*n*)	No. N+ in specified LNR (*n*)	Risk for N+ in specified LNR (%)	Involvement of LNR in N+ pts (%)
MLN	All	27, 30, 31, 36	1347	706	615	46	87
ULN	All	27, 30, 31, 35, 36	2092	1033	578	28	56
LLN	All	27, 30, 31†, 32, 35, 36*	2187	1043	285	13	27
	T1-2	27, 28*, 29, 30, 35, 38*	595		28	5	
	T3	27–30, 35, 37*, 38	1004		142	14	
	T4	27–30, 35, 37, 38	742		112	15	
	HS/MiS	27, 30, 31, 35, 36, 38	924		42	5	
	LS	27, 28, 29–32‡, 35–38	2071		276	13	
ELN	All	36	605	285	25	4	9
	HS/MiS/AR	36	232		8	3	
	LS/APR	28, 36	443		22	5	
ILN	All	27, 36	994	505	8	1	2
	HS/MiS	27, 36	380		0	0	
	LS	27, 29‡, 36	832		10	1	

Abbreviations: APR = abdominoperineal resection; AR = anterior resection; ELN = external iliac lymph nodes; HS = high-seated = tumor located above the peritoneal reflection (PR); ILN = inguinal lymph nodes; Involvement of LNR in N+ patients = ratio of No. N+ in specified LNR over No. N+; LLN = lateral lymph nodes; LNR = lymph node region; LS = low-seated; MiS = middle seated = defined as located 1 cm above or 1 cm below the PR in [36] and as located between S2 and PR in [38]; MLN = mesorectal lymph nodes; No. N+ = number of patients with positive lymph nodes (in any LNR, unless specified); No. at risk = number of patients at risk for lymph node involvement; Pts = patients; Risk for N+ in specified LNR = ratio of No. N+ in specified LNR over No. at risk; ULN = upward lymph nodes.

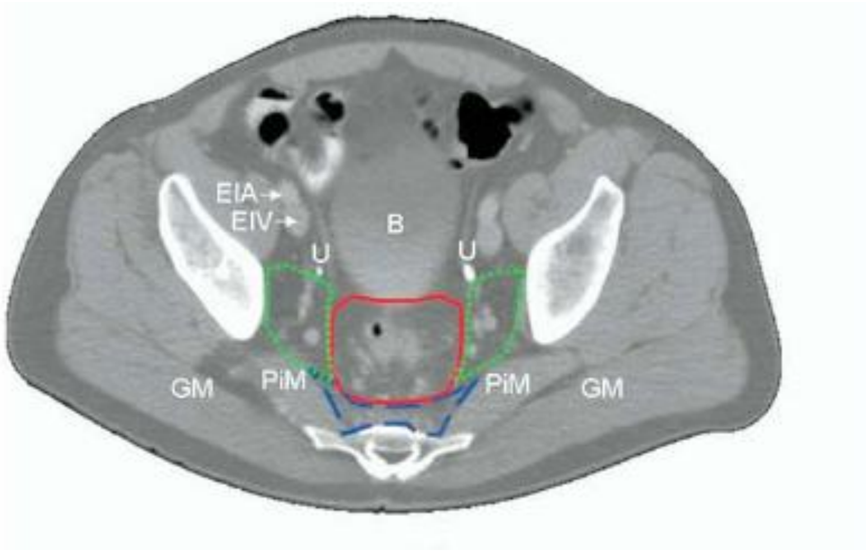
CTV-N



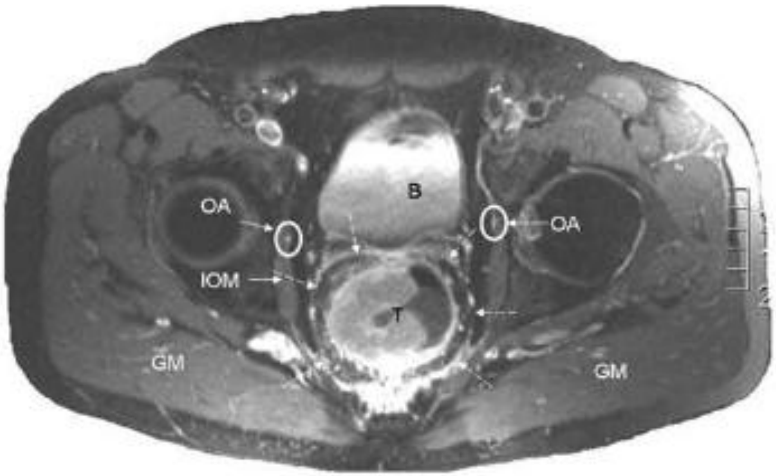
CTV-N

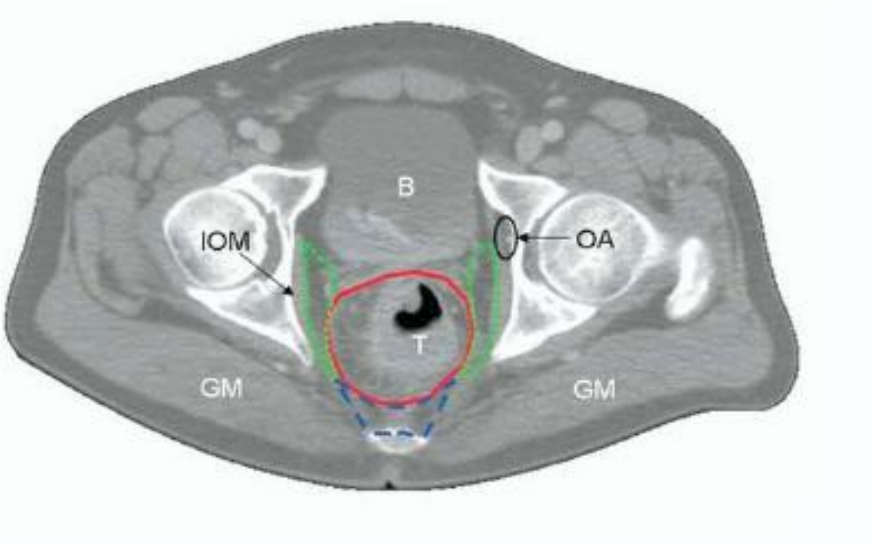


CTV-N

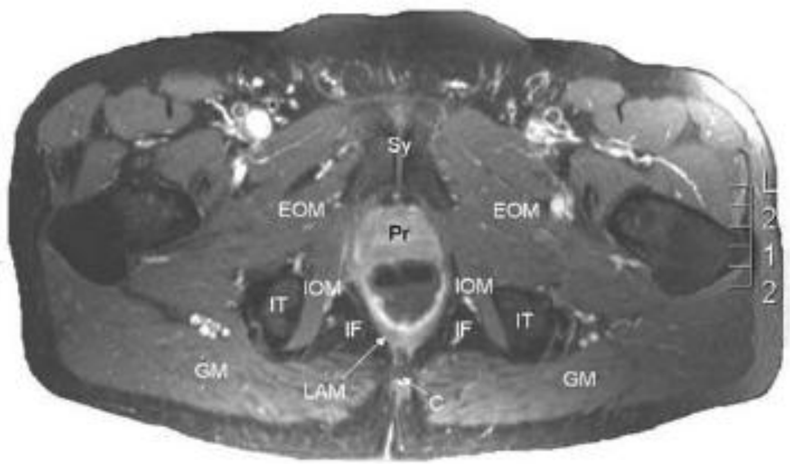


CTV-N





CTV-N



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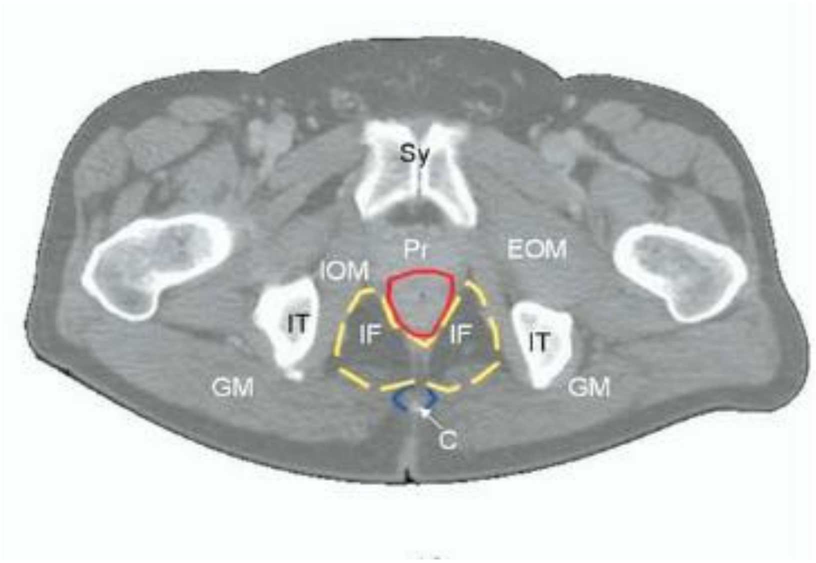

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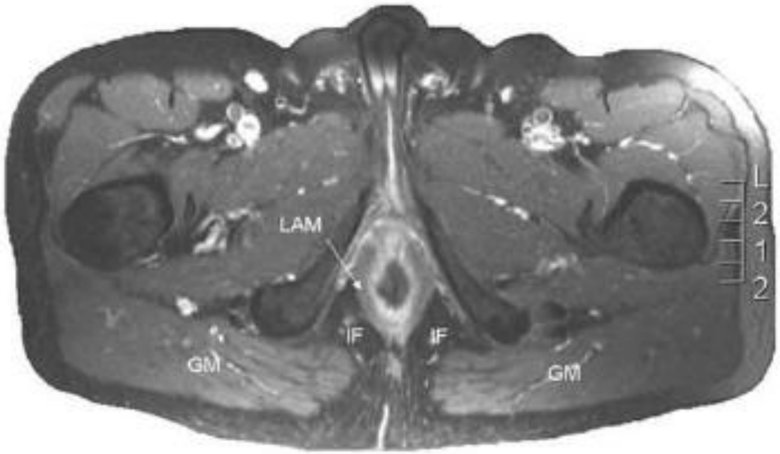
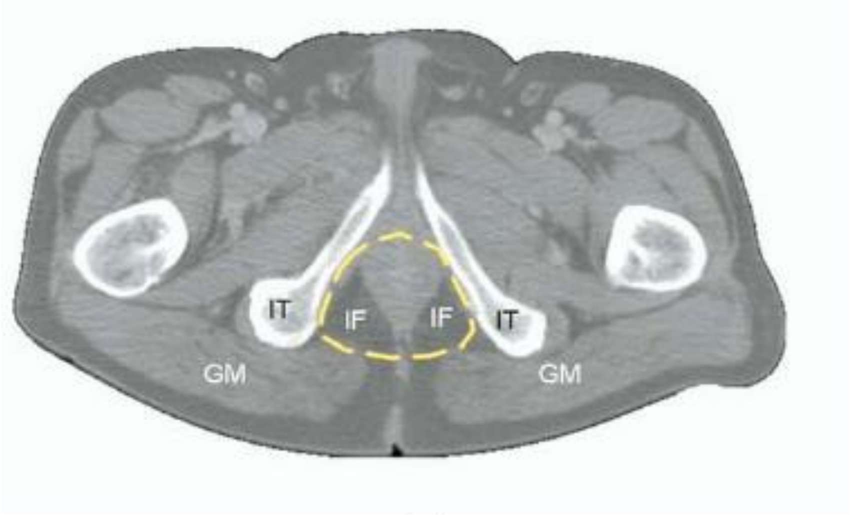
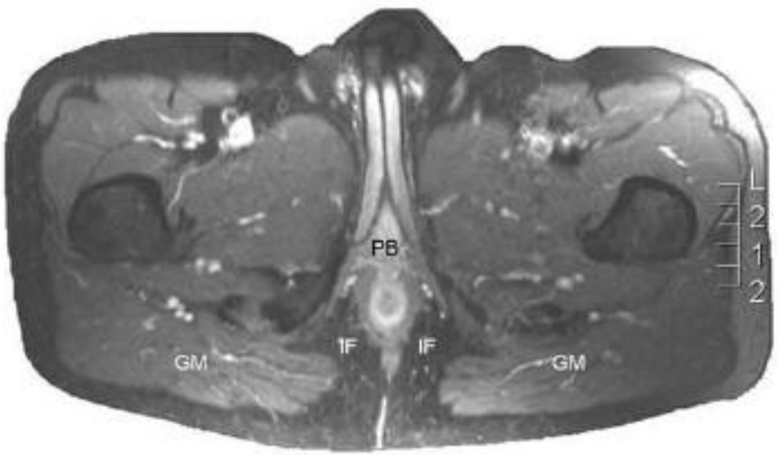
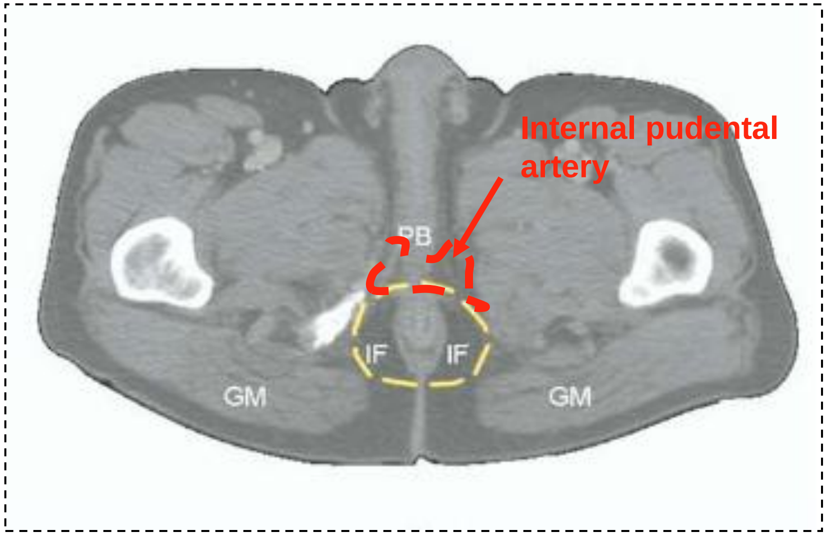
CTV-N



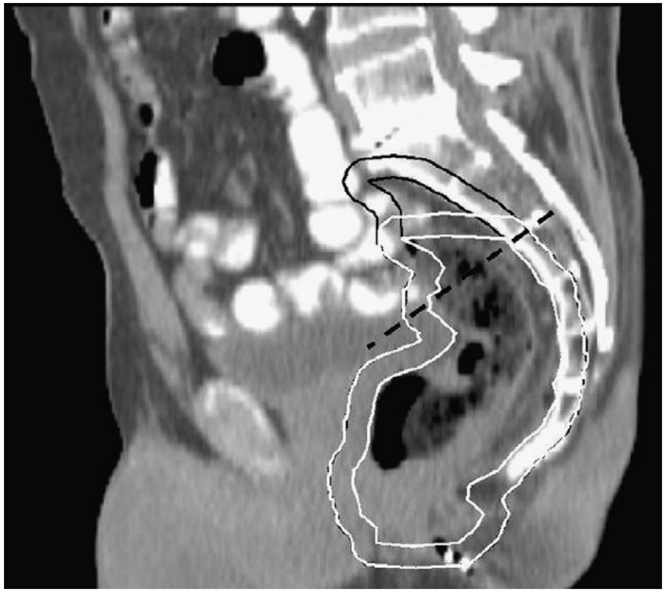


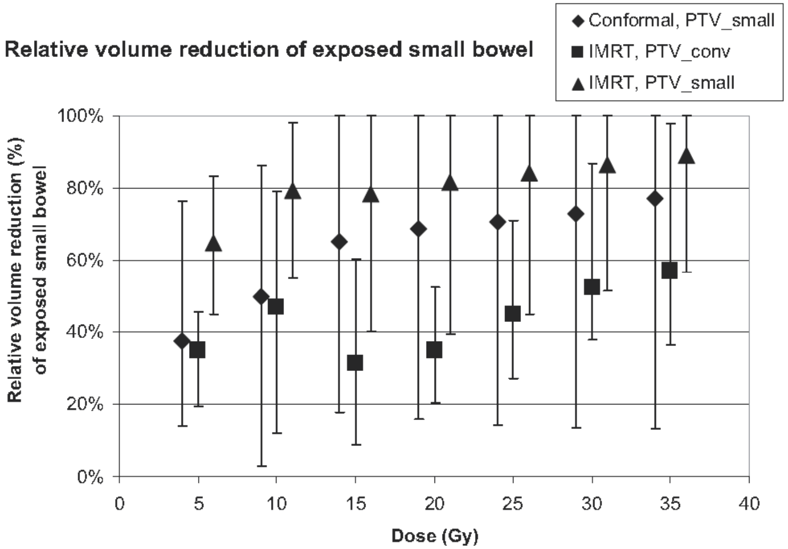
CTV-N





CTV : Upper limit S2/S3 if CRM-

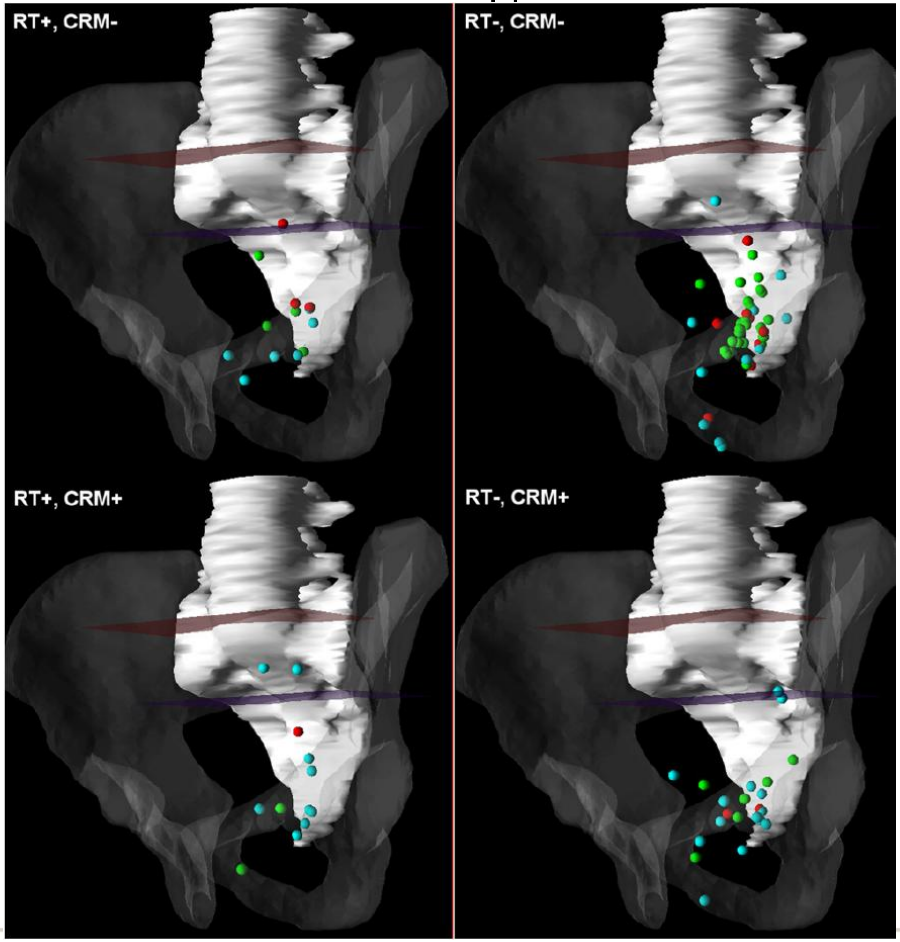




Lower third rectum

Mid rectum

Upper third rectum

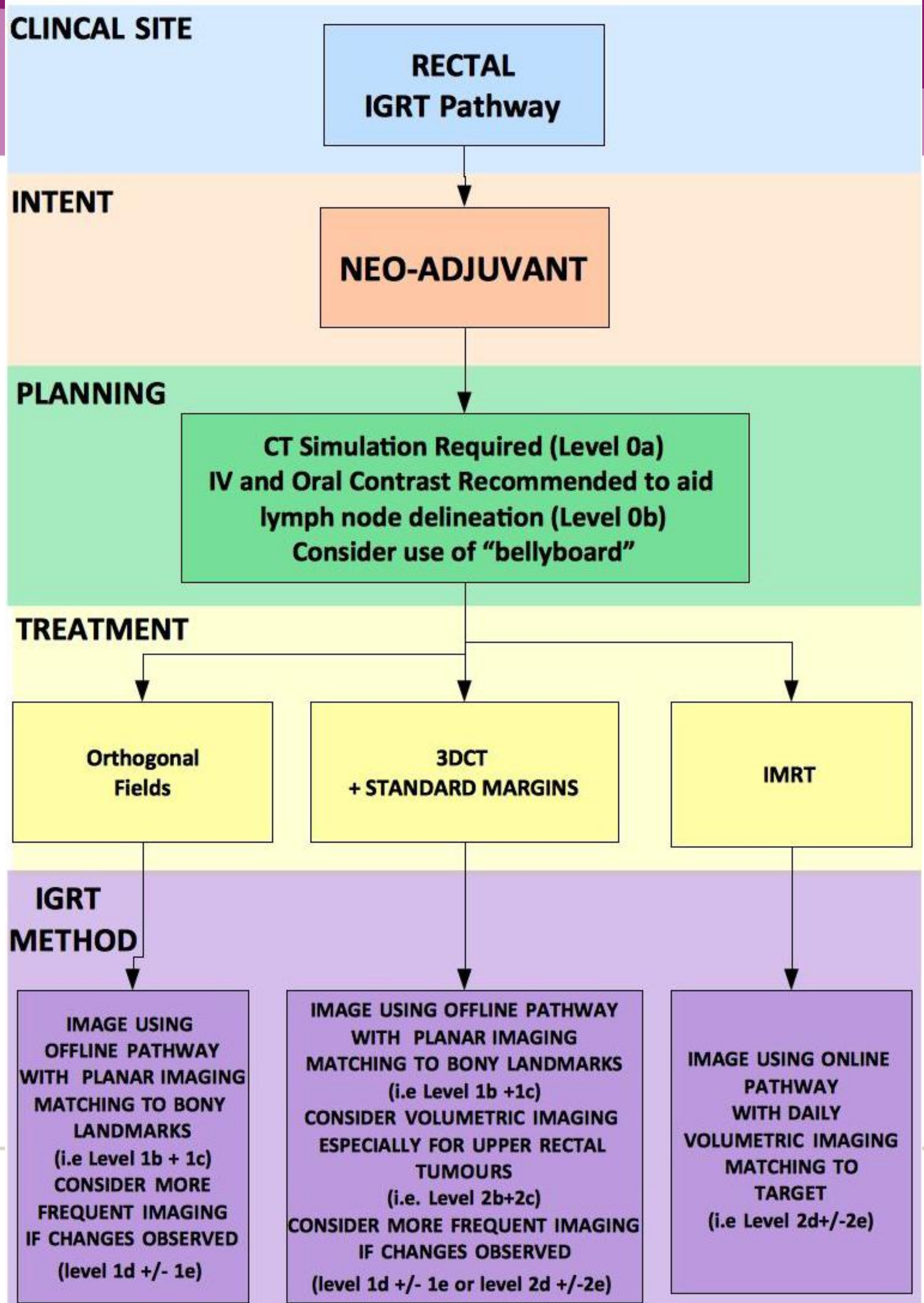


Nijkamp J et al., IJROBP 2011

IMRT and rectal cancer

- Dosimetric benefit+++
- 2DRT vs. 3DCRT, vs 3-field sIMRT vs IMRT
- Better PTV coverage and better sparing of bowels

Urbano M, IJROBP, 2006
Callister M, Proc ASTRO, 2006
Guerrero Urbano MT, IJROBP 2006
Arbea L, Radiat Oncol, 2010
Tho LM, IJROBP. 2006


CLINCAL SITE
RECTAL
IGRT Pathway
INTENT
NEO-ADJUVANT
PLANNING
CT Simulation Required (Level 0a)
IV and Oral Contrast Recommended to aid lymph node delineation (Level 0b)
Consider use of "bellyboard"
TREATMENT
Orthogonal Fields
3DCT + STANDARD MARGINS
IMRT
IGRT METHOD
IMAGE USING OFFLINE PATHWAY WITH PLANAR IMAGING MATCHING TO BONY LANDMARKS (i.e Level 1b + 1c) CONSIDER MORE FREQUENT IMAGING IF CHANGES OBSERVED (level 1d +/- 1e)
IMAGE USING OFFLINE PATHWAY WITH PLANAR IMAGING MATCHING TO BONY LANDMARKS (i.e Level 1b +1c) CONSIDER VOLUMETRIC IMAGING ESPECIALLY FOR UPPER RECTAL TUMOURS (i.e. Level 2b+2c) CONSIDER MORE FREQUENT IMAGING IF CHANGES OBSERVED (level 1d +/- 1e or level 2d +/-2e)
IMAGE USING ONLINE PATHWAY WITH DAILY VOLUMETRIC IMAGING MATCHING TO TARGET (i.e Level 2d+/-2e)

Overutilization of IMRT/IGRT in treatment of rectal cancer: Cost implications of deviation from evidence-based practices.

- 98% of deviations involved use of IMRT and/or IGRT

- Justification for IMRT/IGRT use included :
- **treatment volumes comparable to anal cancer**
- **inadequate bowel displacement by routine techniques**
- **obesity.**

- Cost for a course of 3D CRT + weekly port films was $6,591 vs. **$32,292 for IMRT + daily IGRT**

Curry AH et al., 2014 ASCO Quality Care Symposium, Abstr 34

Room for IGRT in rectal cancer?

- **Pros=**

-Large prostate movements correlated w/ the rectum in prostate ca+++
- IMRT useful (tighter gradient)
- Might become mandatory in a 'Wait and see' scenario (with a boost to the tumor)

- **Cons=**

- Low total dose 45/50Gy over 5w
- Large CTV w/ENI
- Local failure rates <10% after surgery

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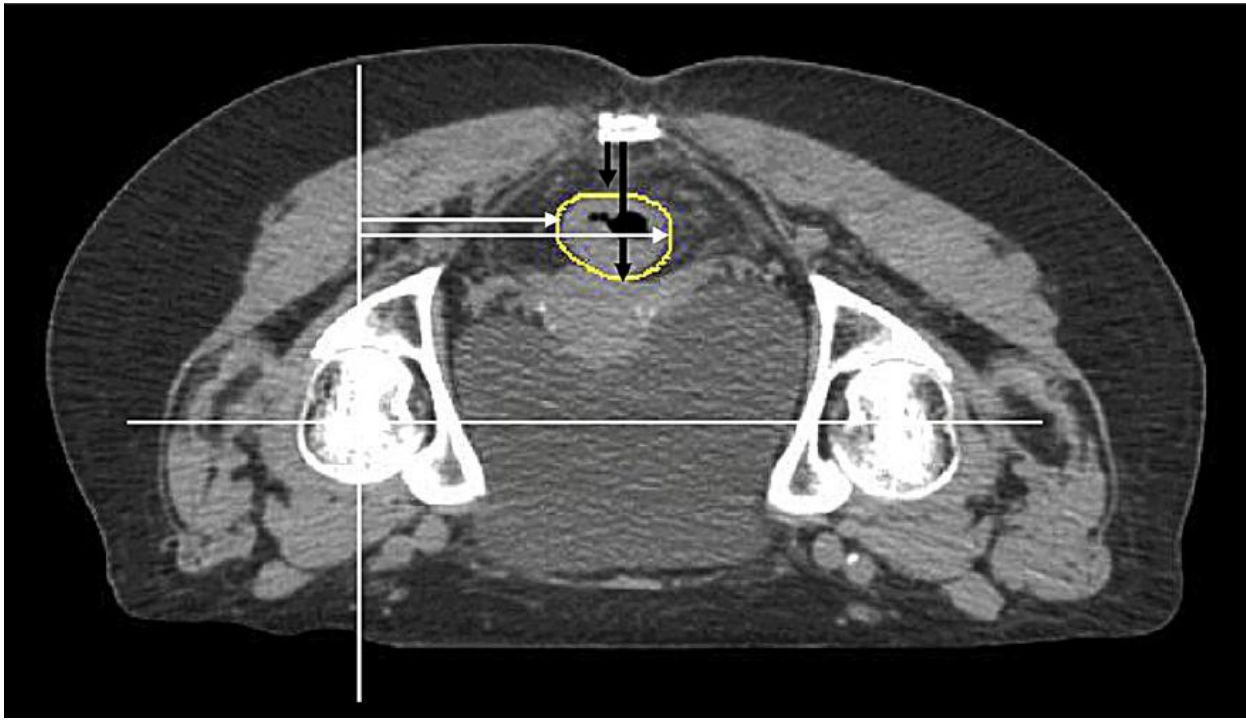
Reference	Topic	Pts	CT/pt	Comments	Rectal vol Variations	Mvts
Tinger	Prostate	8	5-7	WeeklyCT + daily PID	Mean (cc) 30±5-127±36 76±34	
Stroom	Prostate ca	15	4	CT W2,4,6 w/ laxation	Mean (cc) Supine: 123 Prone 166	
Nuyttens	Rectal ca	10	5-6	Weekly CT Potop Clip motion		**1.5cm caudal**
Muren	Bladder ca	20	7-8	Weekly CT+ daily PID	Mean cc 62±25-72±29	**30mm anterior and left wall**
Hoogeman	Prostate ca	19	8-13	CT D1, 2, 3, 7, 11 then W Empty rectum	Mean cc 74±17	**8mm ant side**
Fokdal	Bladder ca	15	5	3CT w/ rectum filling 2CT w/o rectum filling	Mean (cc) 51(26-20)-185(70-307)	
Stasi	Prostate ca	10	11-14	Empty rectum	Mean (cc) 53±11.5	**9.1mm ant wall, rectum superior half**
Lotz	Bladder ca	21	8-11	Daily CT 1st W Then W	Mean (cc) 51±8.4-243±5.3	

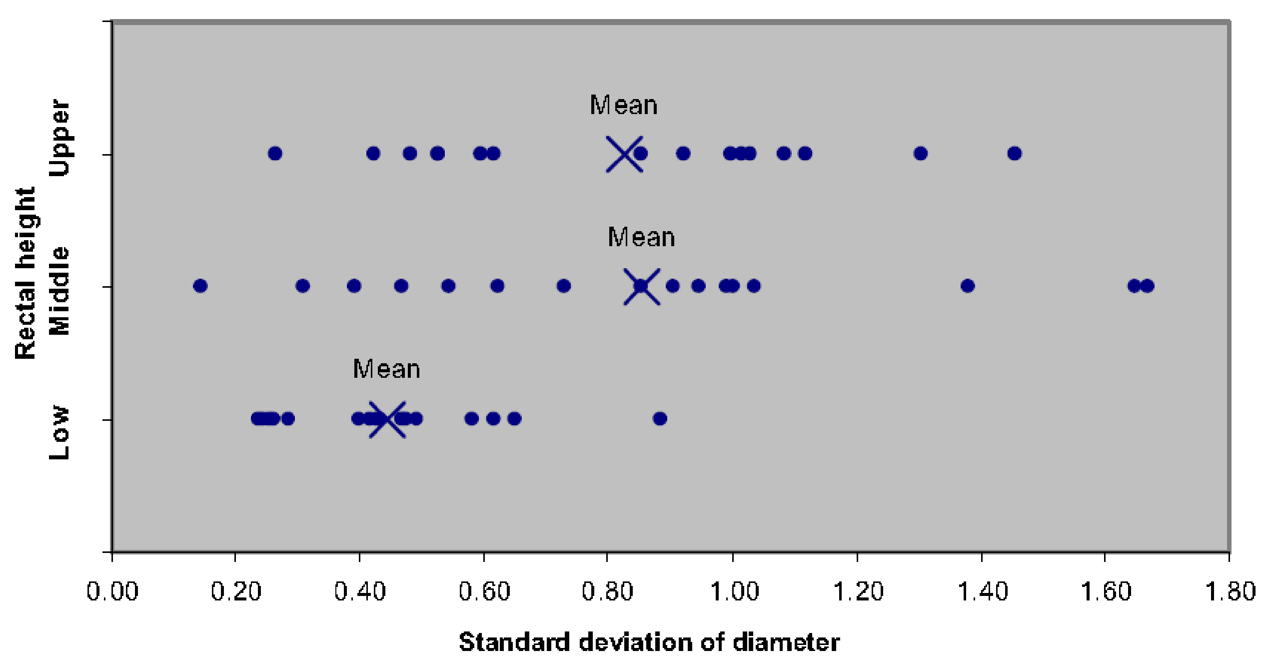
Rectal motion on CBCT

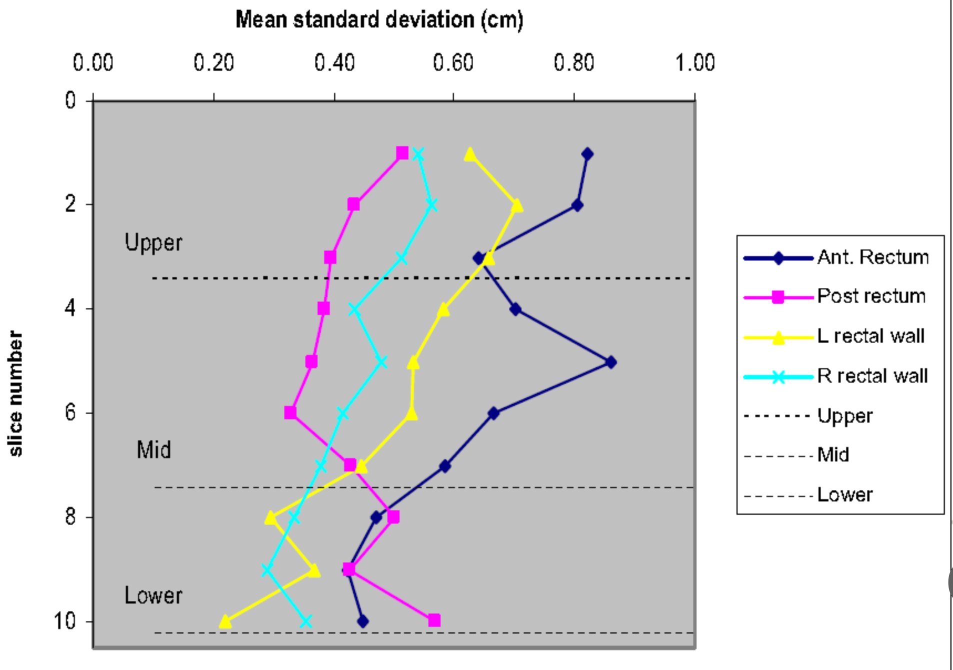
- 16 pts
- Rectum and bladder outlined first 3 days then weekly
- 123 CBCT



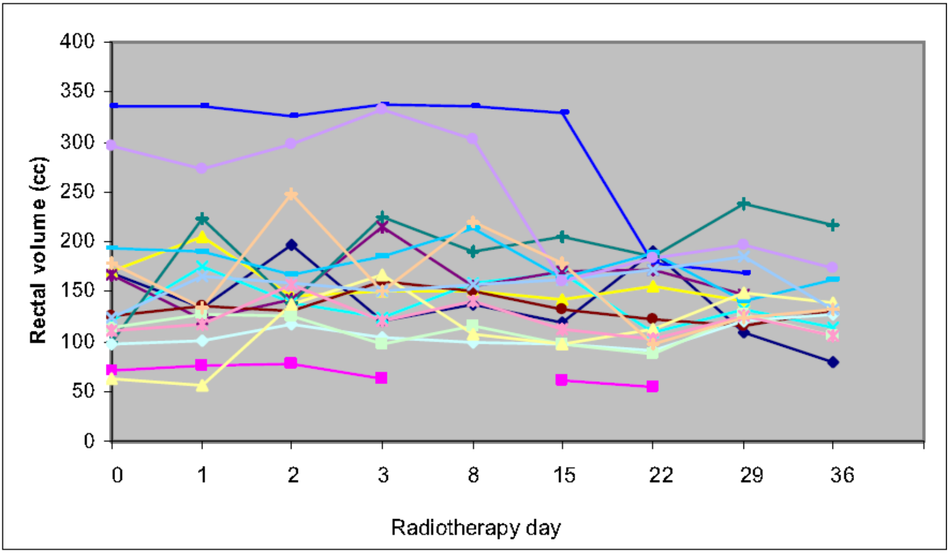
Chong I, IJROBP 2011

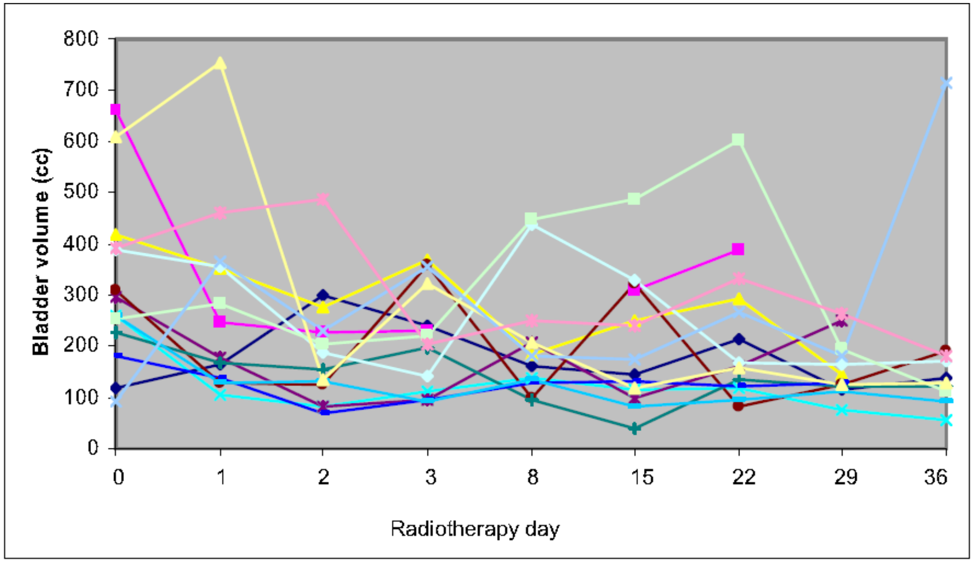
Rectal motion





Chong I, IJROBP 2011



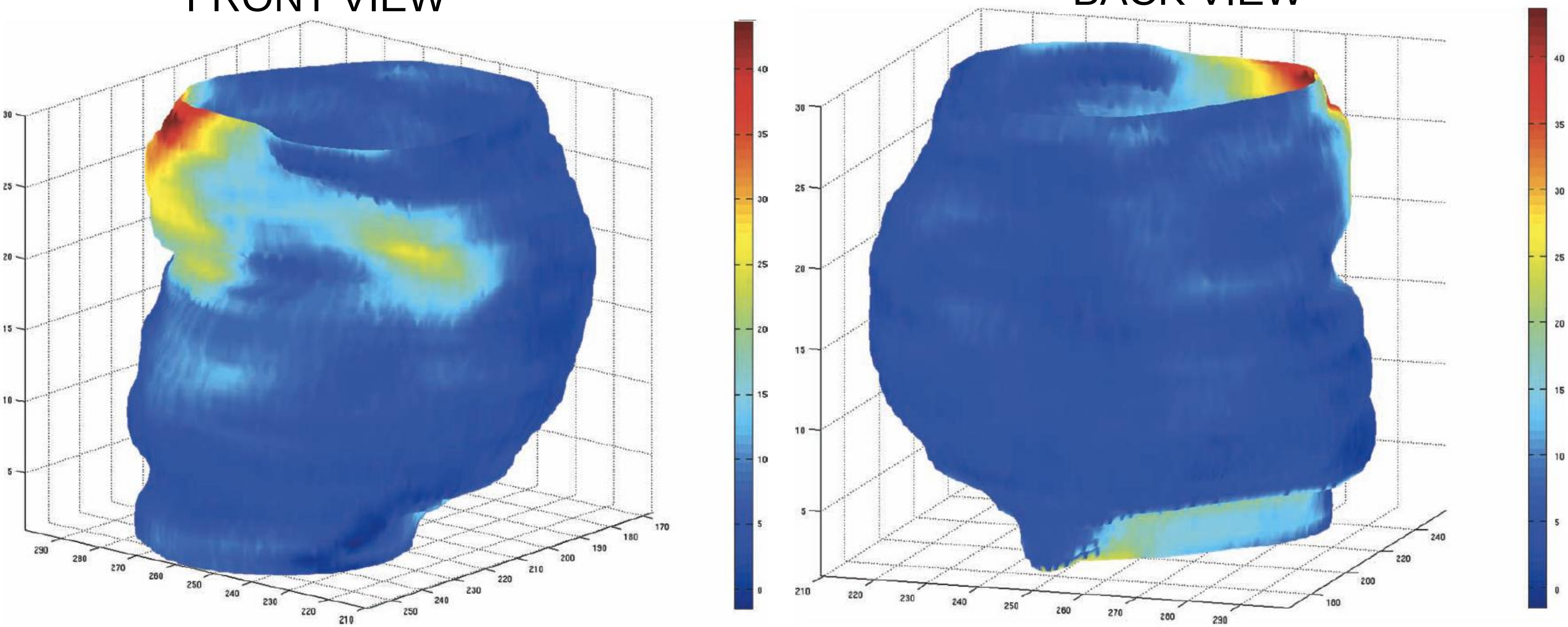


- No relation between rectal and bladder volumes

Chong I, IJROBP 2011

Movements of the mesorectum : Leuven preliminary report (n= 20)

FRONT VIEW BACK VIEW

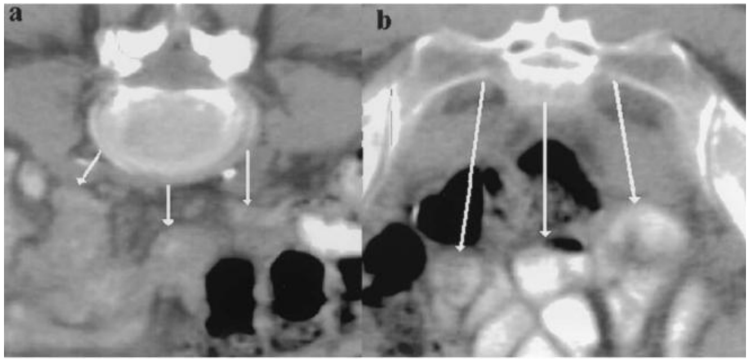


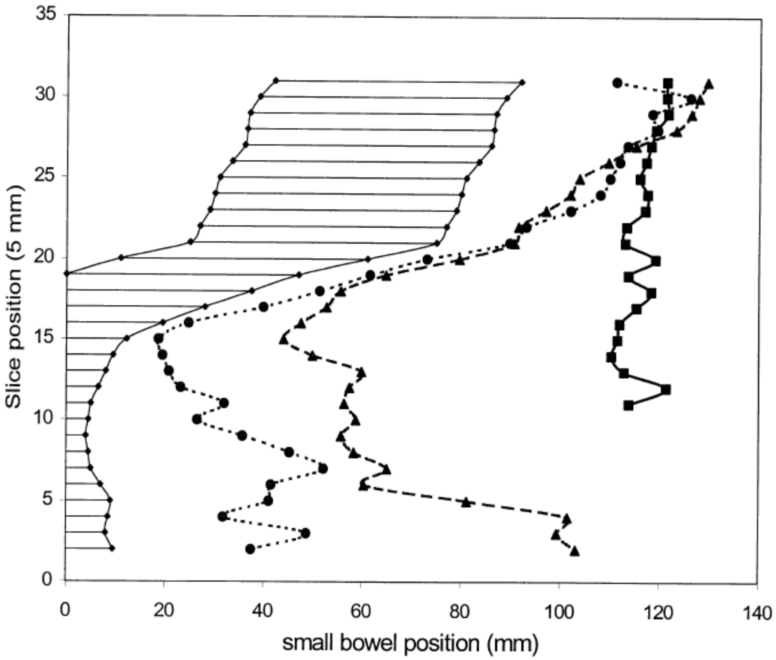
- Decrease of the mesorectum over RT course
- No correlation between bladder and mesorectal volumes
- Correlation between rectal air volume and mesorectal volume

Ippolito E et al. Acta Oncol 2008

Small bowel : preop vs postop

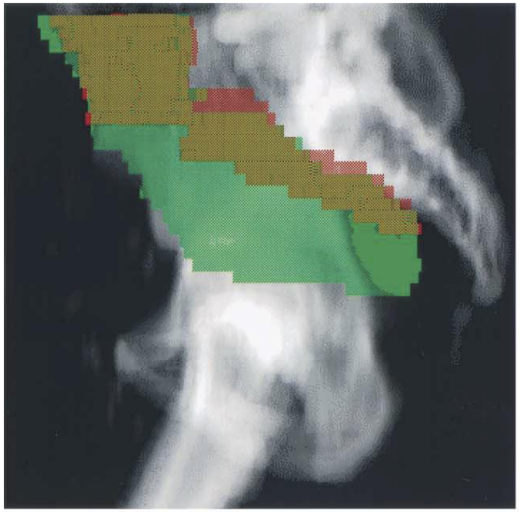
- N= 30 pts (10 preop, 10 LAR, 10 APR)
- Weekly CT during RT course (65 scans)



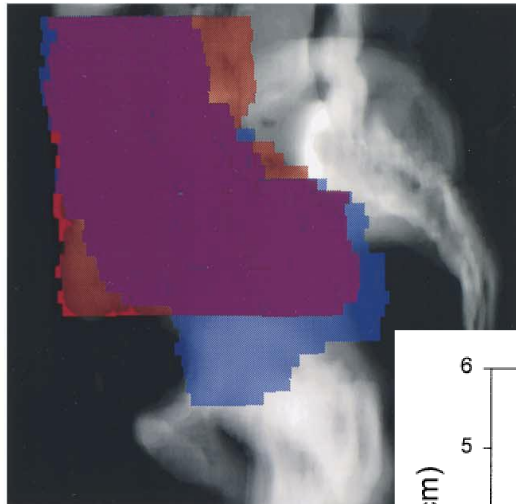


Nuyttens J. et AL, IJROBP 2001

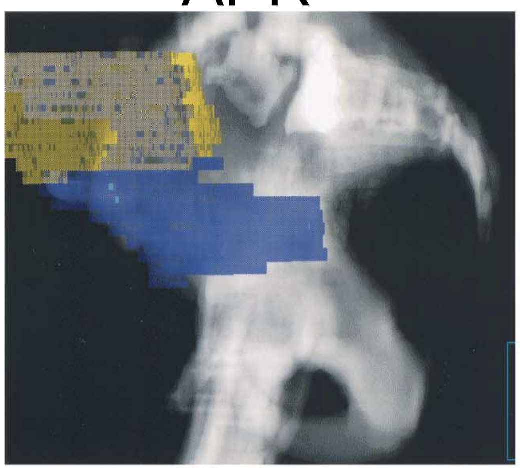
Maximum and mimum position of small bowel



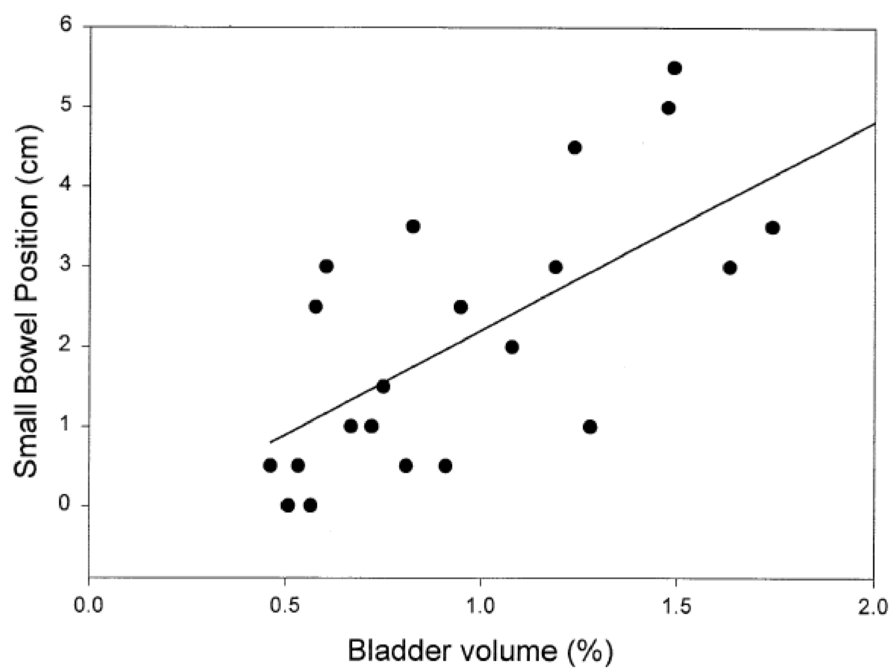
(a) APR



(b) LAR



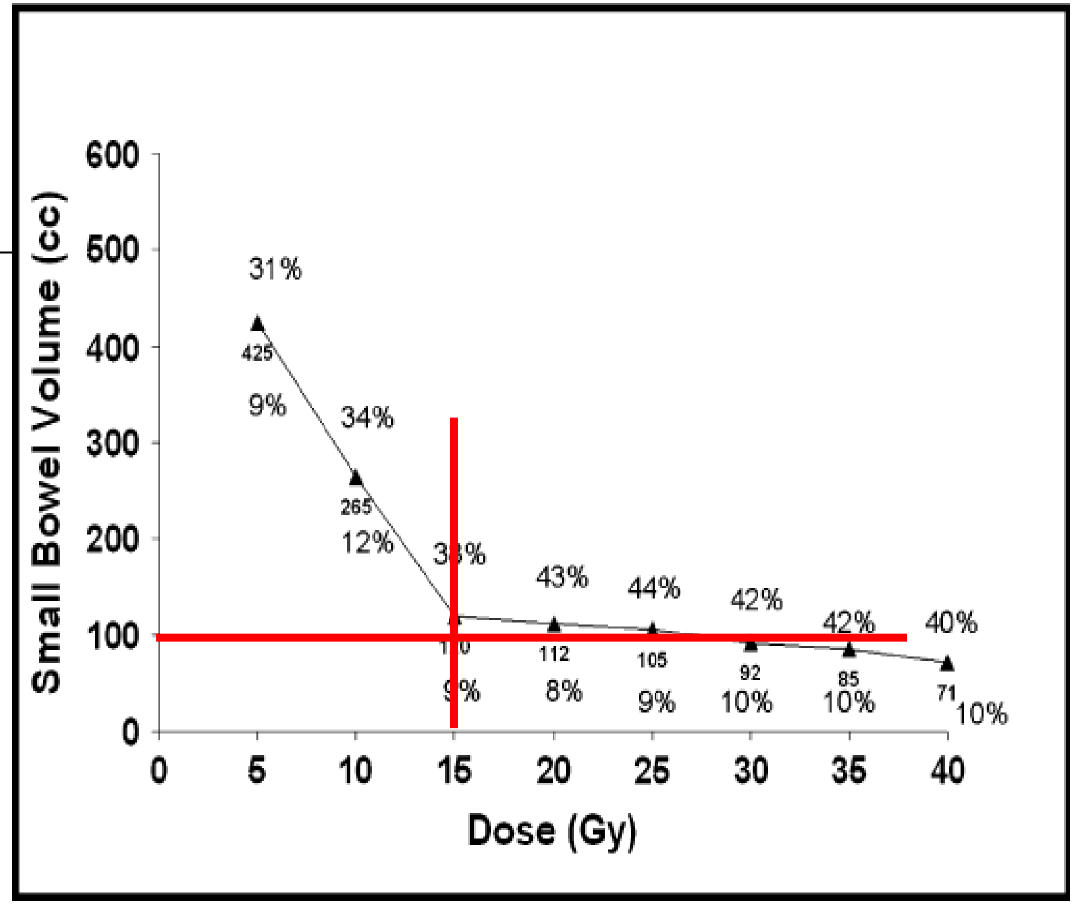
(c) PREOP



Nuyttens JJ, IJROBP 2001

Threshold doses for G3 diarrhea
Pre/Postop CRT, Rectal cancer, n= 96

Dose (Gy)	Volume (cc)	Incidence of Grade 3 toxicity
5	500	45%
10	300	53%
15	150	50%
20	145	53%
25	140	59%
30	135	59%
35	130	59%
40	125	59%



Robertson, IJROBP 2008

Prone vs Supine

- N= 19 pts
- Planning CT w/ full bladder in prone and supine positions
- Dose prescription: 45 Gy / 25 fr
- DVH for small bowel: V5Gy +5 +5+….V45Gy
- V5 and V10 : small bowel volume >> in supine position ($p<0.001$)
- V20….V45 : No differences

Drzymala et al., BJR 2009

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International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

Clinical Investigation: Gastrointestinal Cancer

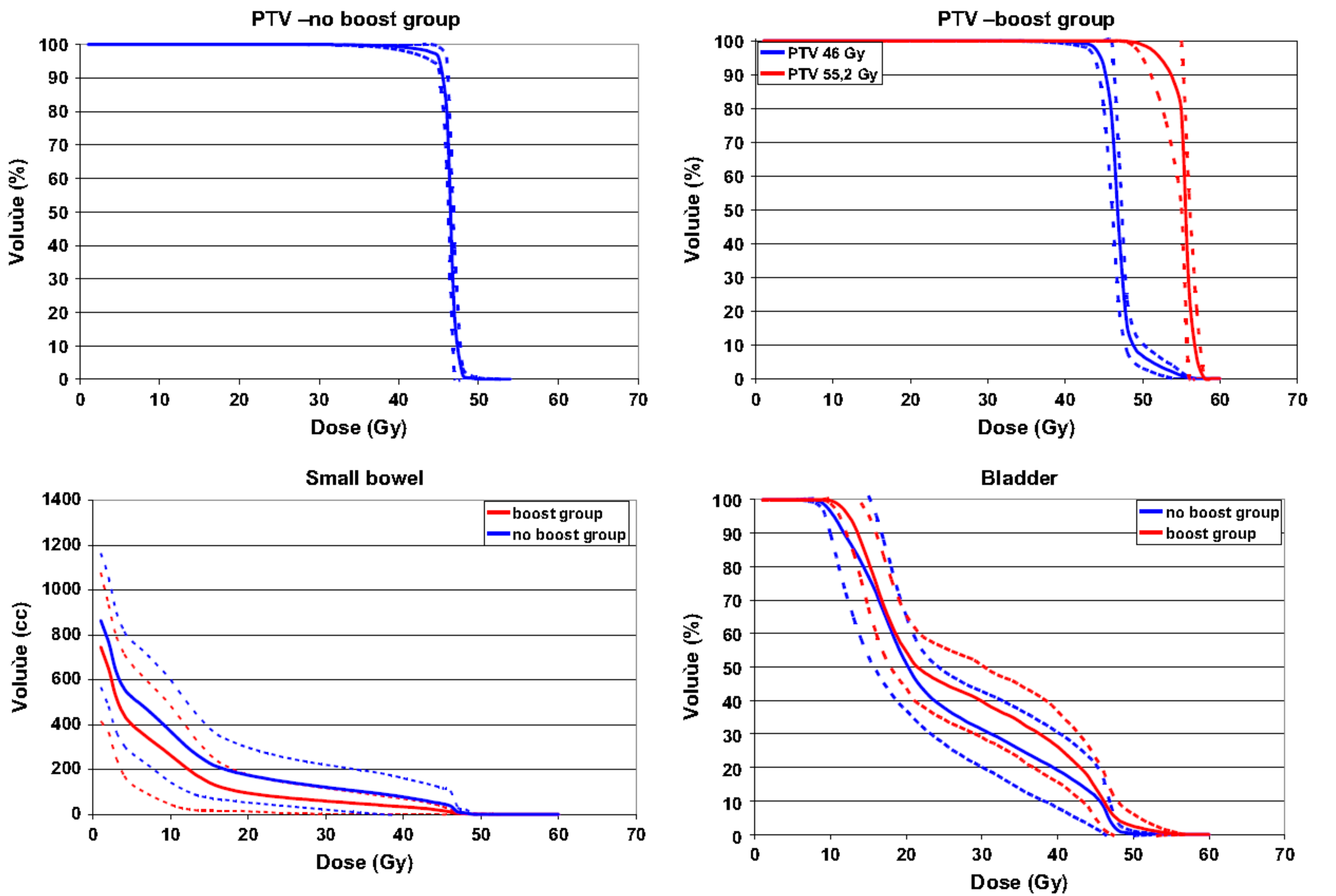
Phase II Study of Preoperative Helical Tomotherapy With a Simultaneous Integrated Boost for Rectal Cancer

Benedikt Engels, M.D.,* Koen Tournel, M.Sc.,* Hendrik Everaert, M.D., Ph.D.,† Anne Hoorens, M.D., Ph.D.,‡ Alexandra Sermeus, M.D.,§ Nicolas Christian, M.D., Ph.D.,* Guy Storme, M.D., Ph.D.,* Dirk Verellen, Ph.D.,* and Mark De Ridder, M.D., Ph.D.*

- Phase IIR (n=108)
- XRT **w/o** CT
- IG-IMRT (HT Hi Art II)

Pelvic CTV = 46Gy@2Gy/fx

Pelvic CTV = 46Gy@2Gy/fx + GTV Boost 55.2Gy (SIB)



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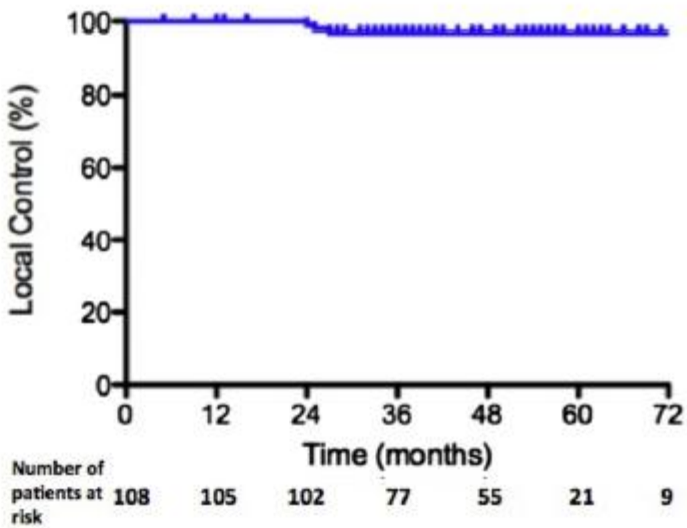
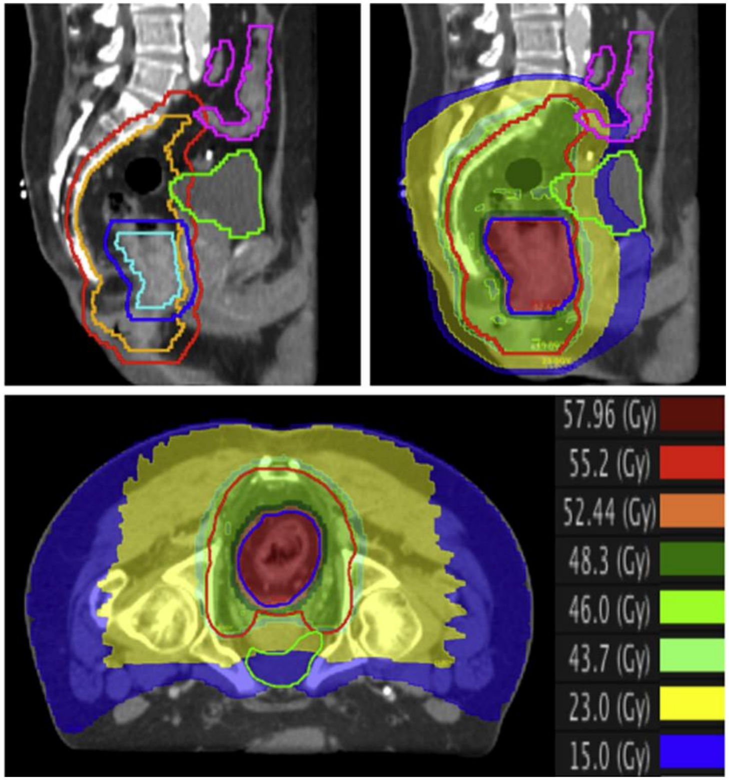
IG-IMRT Dose escalation w/o CT

Late toxicity.

Toxicity		Grade				
		1	2	3	4	5
Gastrointestinal	Diarrhea/enteritis	38	9	2	0	1
	Ileus	4	1	2	1	0
	Incontinence	24	10	0	1	0
	Stricture	16	7	2	0	0
	Fistula	0	0	1	0	1
Urinary	Frequency	45	6	0	0	0
	Cystitis	4	1	0	0	0
	Incontinence	21	8	0	2	0
	Retention	5	3	1	0	0
	Ureteral stricture	0	2	0	1	0
Sexual	Vaginal dryness	5	4	0	0	0
	Dyspareunia	1	5	1	0	0
	Erectile dysfunction	1	10	24	0	0



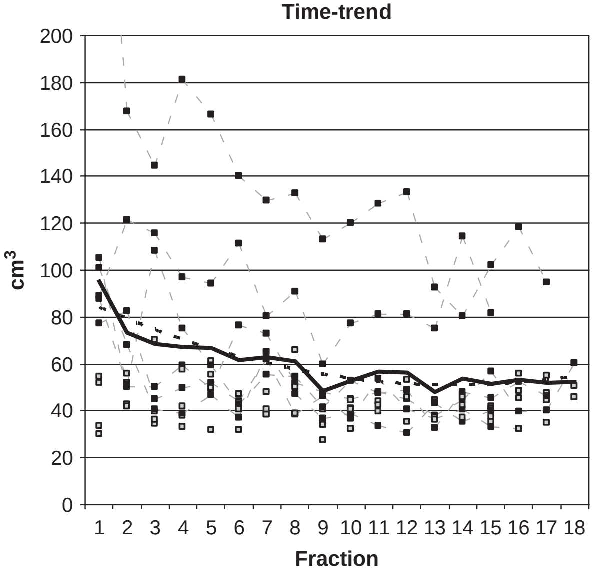


pCR = 8% (15-20% w/ conco CT)

No soft tissue guidance

Engels B et al. , IJROBP 2012

Boost : What margin?



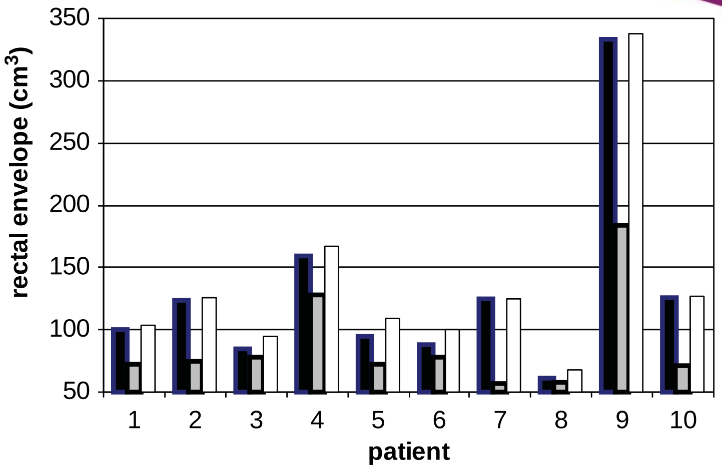
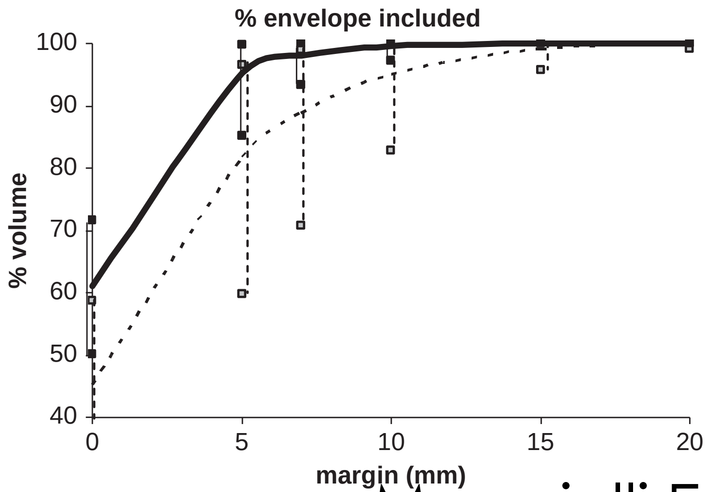


Figure 2. The volumes of the rectal envelope of the first half (dark), second half (grey) and total treatment (white) are plotted for each patient.



12mm = 95% of the rectum covered

5mm sufficient in the second half

Maggiulli E et al. Acta Oncol 2012

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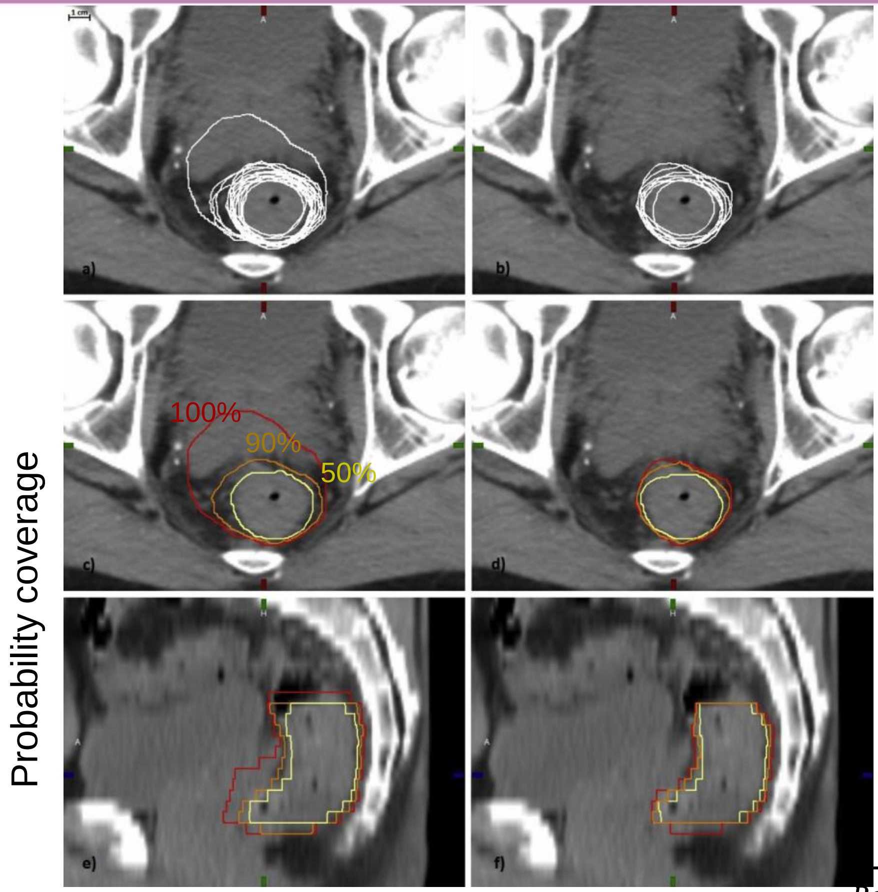
Adaptive RT : Boost margin



Whole RT course

Second half

Reference contour	UP-ANT	UP-POST	UP-R	UP-L	LOW-ANT	LOW-POST	LOW-R	LOW-L
M(90,90) (mm)								
1st fraction	9.0	3.0	3.0	4.5	4.9	1.9	4.5	3.3
9th fraction	5.8	2.3	3.4	3.5	6.5	3.3	3.4	4.7

Raso R et al., Physica Medica 2015

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Adaptive RT

- CT scan daily week 1 and weekly thereafter

	Start of treatment (PTV_clin)					
	Anterior (cm)	Posterior (cm)	Left (cm)	Right (cm)	Cranial (cm)	Caudal (cm)
LN_L	1.5	0.7	0.7	1.0	1.0	1.0
LN_R	1.5	0.7	1.0	0.7	1.0	1.0
Presacral	1.5	0.7	0.7	0.7	1.0	1.0
MesoRect upper half	2.4	0.7	0.7	0.7	1.0	1.0
MesoRect lower half	1.5	0.7	0.7	0.7	1.0	1.0
Sphincter	1.0	1.4	1.0	1.0	1.0	1.0
Plan adaptation after the 4th treatment fraction (PTV_ART_clin)						
LN_L	1.0	0.7	0.5	0.7	0.7	0.7
LN_R	1.0	0.7	0.7	0.5	0.7	0.7
Presacral	1.3	0.7	0.5	0.5	0.7	0.7
MesoRect upper half	1.7	0.7	0.5	0.5	0.7	0.7
MesoRect lower half	1.0	0.7	0.5	0.5	0.7	0.7
Sphincter	0.7	1.0	0.7	0.7	0.7	0.7

	PTV (1SD)	PTV_ART (1SD)	Statistical difference
Bladder Dmean (Gy)	26.3 (2.4)	23.6 (3.1)	$p < 0.0001$
Bowel area V15 (cc)	372 (199)	358 (199)	$p = 0.0077$
Bowel area V45 (cc)	92 (70)	73 (59)	$p < 0.0001$
Bowel area V50 (cc)	44 (36)	27 (24)	$p < 0.0001$
	PTV_clin (1SD)	PTV_clin_ART (1SD)	Statistical difference
Bladder Dmean (Gy)	27.4 (3.7)	24.9 (2.4)	$p < 0.0001$
Bowel area V15 (cc)	436 (206)	402 (200)	$p < 0.0001$
Bowel area V45 (cc)	111 (76)	81 (60)	$p < 0.0001$
Bowel area V50 (cc)	49 (39)	29 (25)	$p < 0.0001$

Nijkamp J et al., IJROBP 2012

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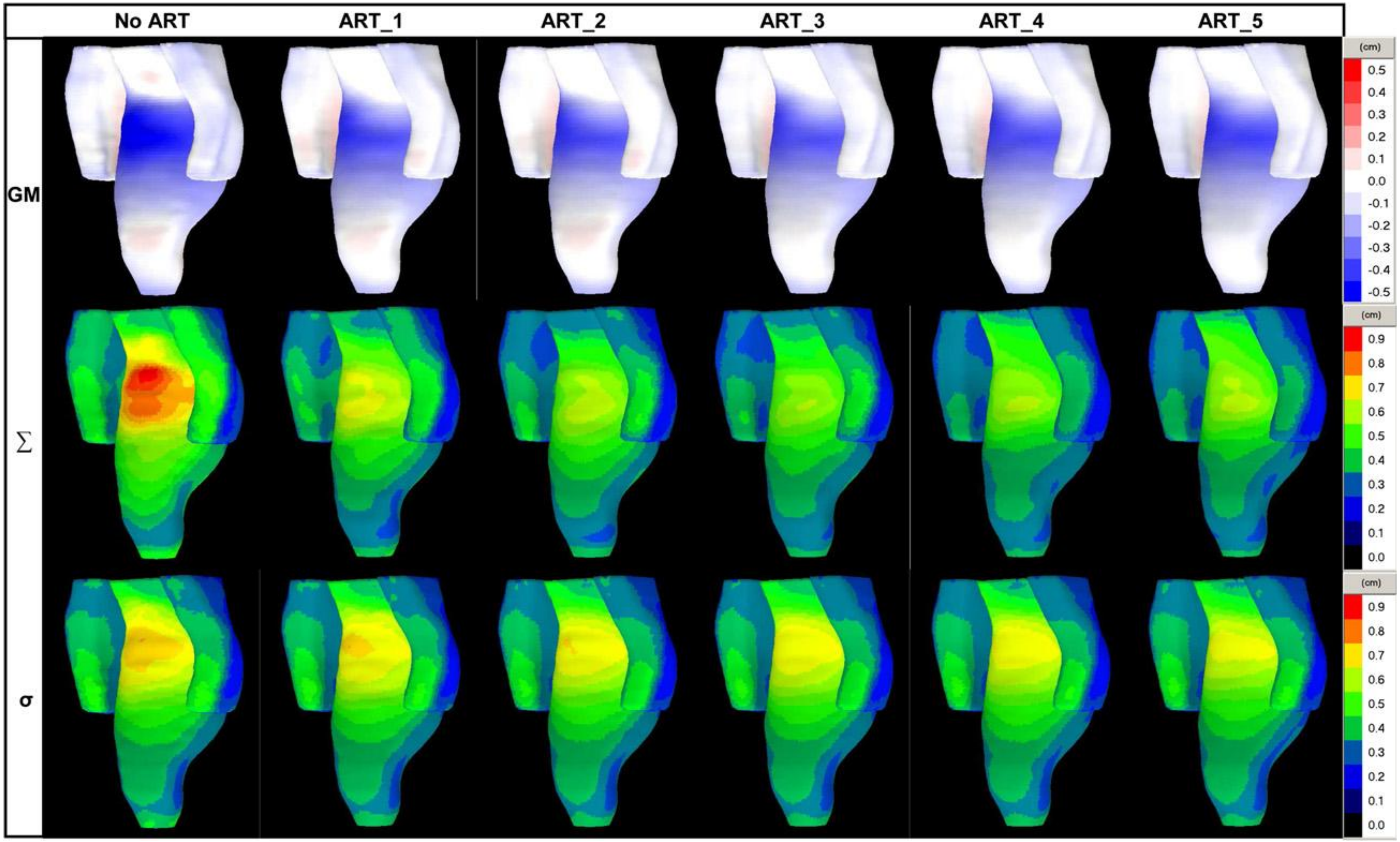


Nijkamp J et al., IJROBP 2012

Good candidates for rectal IGRT?

- Preop: T4/CRM+
- T involving upper rectum (AP displacements>>)
- N+ > S2-S3
- Boost on GTV limited to the tumor (+5-10Gy)

- Postoperative setting: motion of the anastomosis
- Pelvic relapses and reirradiation

IGRT in Bladder cancer:

TURBT

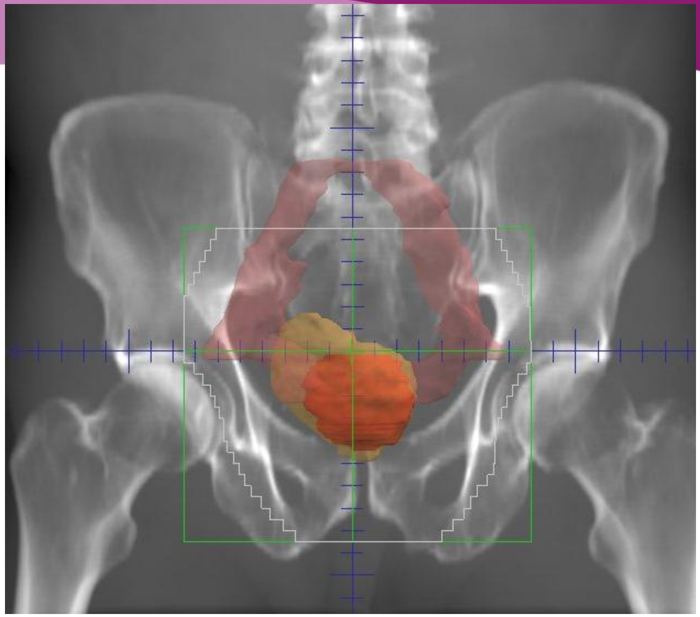
↓

XRT (40-45 Gy)
+
Concomitant Chemotherapy

↓

Cystoscopic response evaluation

CR	*Non-CR*
Consolidation Chemo-radiation (64Gy)	**Radical Cystectomy**



Long-term MGH Experience 1986-2006

CR rate	**72%**
Overall Survival	
5 yrs	52%
10 yrs	35%
15 yrs	22%
Disease Specific Survival	
5 yrs	64%
10 yrs	59%
15 yrs	57%
% undergoing Cystectomy*	**29%**
Immediate (non-CR)	17%
Salvage	12%

*No patient required cystectomy due to treatment-related toxicity

Efstathiou et al Eur Urol 2011

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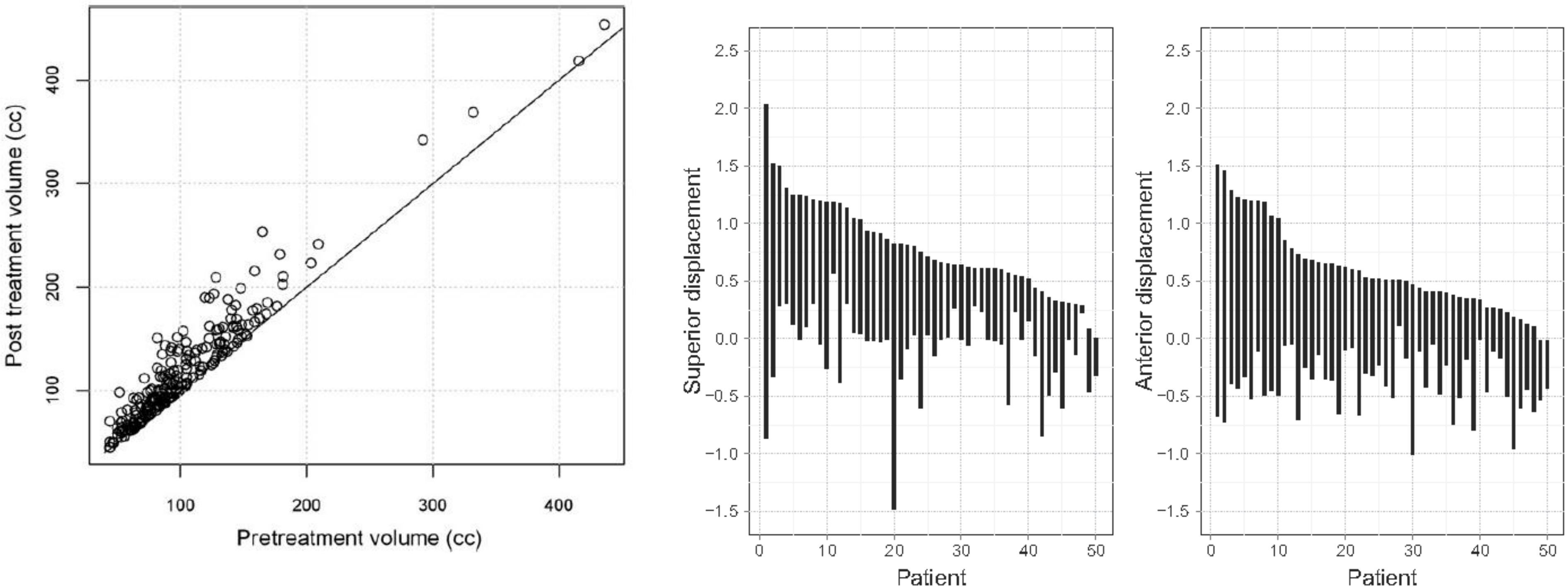
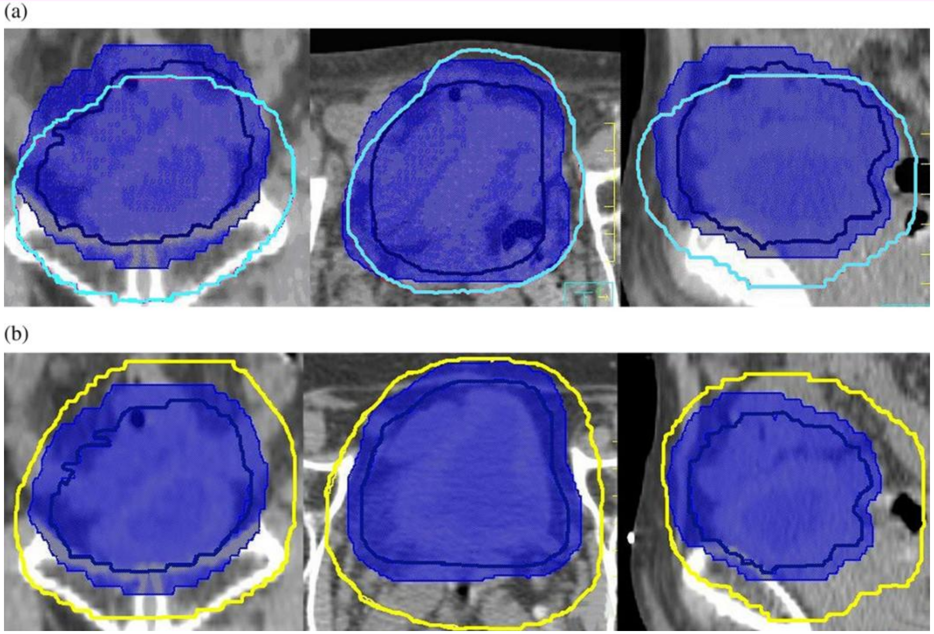
Intrafraction mvts



- Weekly pre vs post-ttt CBCT
- No change in volumes but Ant and Superior shifts
- Large margins (≥1.5cm) are required w/o IGRT/IGART

Foroudi F et al., IJROBP 2013

A-POLO (Royal Marsden NHS)



- PTV 0' after voiding
- PTV15'
- PTV30'

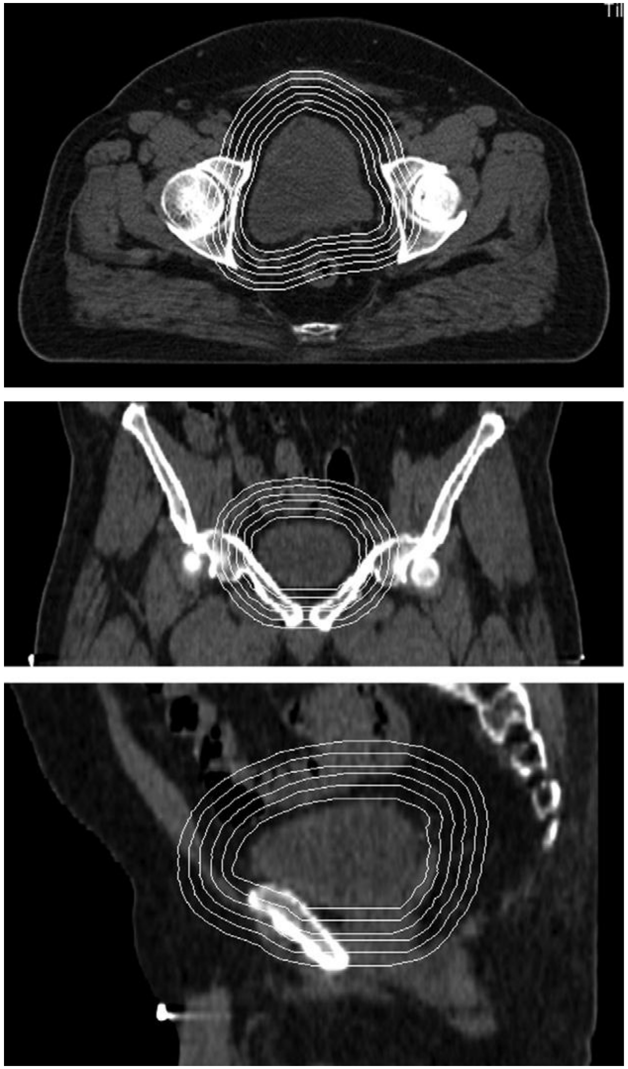
- PTV margin = 1.5cm

Max mvts during RT course =
cranially (maximum 2.5 cm)
anteriorly (maximum 1.75 cm)

Risk of geographic miss in 50% of the patients
Correct TV coverage with IGART : 73% of the patients

Lalondrelle S et al., IJROBP 2011

Plan of the day: Workflow



Suitable patient selected for the protocol

Planning CT done with full/empty bladder

Contouring: 6 isotropic PTVs generated (0.5-3.0 cm at 0.5cm step size)

6 separate plans generated and approved on the HT planning system

Patient Treatment begins

Daily pre-treatment MVCT done for setup

MVCT registration with planning KVCT

Automatic Bone match (Errors noted) → Additional Soft-tissue match (Errors noted)

Final shifts implemented

'PTV of the day' chosen and patient treated

Daily post-treatment MVCT acquired in the treated position

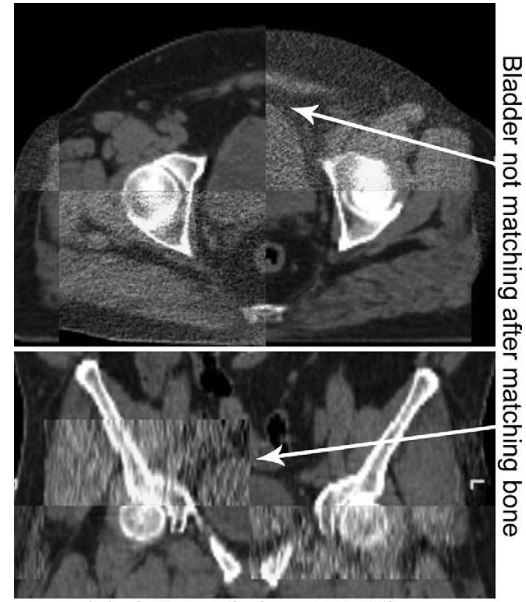
Data processing begins

Post-treatment images transferred to Planned Adaptive module of HT

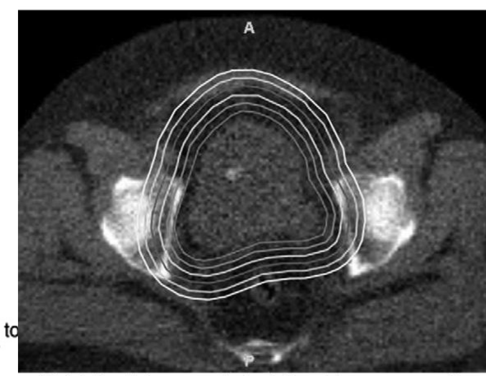
For each fraction, smallest PTV margin covering bladder wall in each direction noted in relation to

Automatic bone match | Soft-tissue match

Anisotropic PTV margins generated for defined resource based scenarios



(a) Automatic bone match



(b) Bladder match: Bladder moved to fit into 5mm PTV

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What PTV margin?

% geographical miss of the bladder wall	Sup	Inf	Ant	Post	L Lat	R Lat
Treated w/ full bladder	**16.1**	**0**	**12.1**	**0.5**	**4.5**	**8.0**
Treated w/ empty bladder	**11.5**	**0**	**7.3**	**3.1**	**4.2**	**4.2**
All patients	**13.8**	**0**	**10.3**	**1.3**	**4.4**	**6.9**

Frequencies of PTVs selected as 'plan of the day'	5 mm	10 mm	15 mm	20 mm	25-30mm	Total
Treated w/ full bladder	42.0%	46.6%	11.0%	0.5%	0.0%	100%
Treated w/ empty bladder	20.8%	69.8%	8.3%	1.0%	0.0%	100%
All patients	35.6%	53.7%	10.2%	0.6%	0.0%	100%

Murthy V et al., Radiother Oncol 2014

TROG study (10.01-BOLART) « Plan of the day »

- Planning CT after voiding
- 10 first fractions CBCT
- 2 other plans :
- A small plan (2 smallest CTV)
- A large plan (all the CTV)
- PTV reduction from 1.5cm to 7mm
- (PTV reduction = 45%)

Variable	Category	Count	% (95%CI)
Conventional plan used <3 times after the 9th fx?	Yes No	41 8	84 (70-93) 16 (7-30)
Adaptive plan created on time for the 10th fx	Yes No	49 0	100 (93-100) 0 (0-7)
CTV within PTV	Yes No	40 9	82 (68-91) 18 (9-32)
Treatment feasible?	Yes No	34 15	69 (55-82) 31 (18-45)

Foroudi F et al., Radiother Oncol 2014

Which margin for which strategy?

Measure	Method	Plan	Pt1	Pt2	Pt3	Pt4	Pt5	Pt6	Pt7	Pt8	Pt9	Pt10
D100	Skin	5 mm	32	17	26	27	32	24	11	30	23	12
		10 mm	32	3	16	9	27	3	3	20	18	1
		15 mm	31	3	2	3	12	1	1	0	0	0
		20 mm	27	0	1	1	0	0	1	0	0	0
	Bone	5 mm	32	10	31	30	32	23	10	29	22	9
		10 mm	32	3	20	13	31	3	3	11	10	0
		15 mm	32	0	2	5	21	2	1	1	1	1
		20 mm	30	0	1	1	5	0	1	0	1	0
	Soft tissue	5 mm	32	9	6	20	31	6	5	25	10	2
		10 mm	32	0	1	0	19	0	1	6	2	0
		15 mm	25	0	0	0	7	0	1	0	0	0
		20 mm	5	0	0	0	0	0	0	0	0	0
D95	Skin	5 mm	32	3	4	3	19	1	1	13	3	0
		10 mm	28	1	1	1	3	0	1	0	0	0
		15 mm	23	0	1	1	0	0	1	0	0	0
		20 mm	14	0	1	1	0	0	0	0	0	0
	Bone	5 mm	32	3	8	8	22	0	1	5	1	0
		10 mm	29	1	2	1	4	0	1	1	0	0
		15 mm	24	0	1	1	0	0	0	0	0	0
		20 mm	12	0	1	1	0	0	0	0	0	0
	Soft tissue	5 mm	31	1	0	0	13	0	1	3	0	0
		10 mm	8	0	0	0	0	0	1	0	0	0
		15 mm	0	0	0	0	0	0	0	0	0	0
		20 mm	0	0	0	0	0	0	0	0	0	0

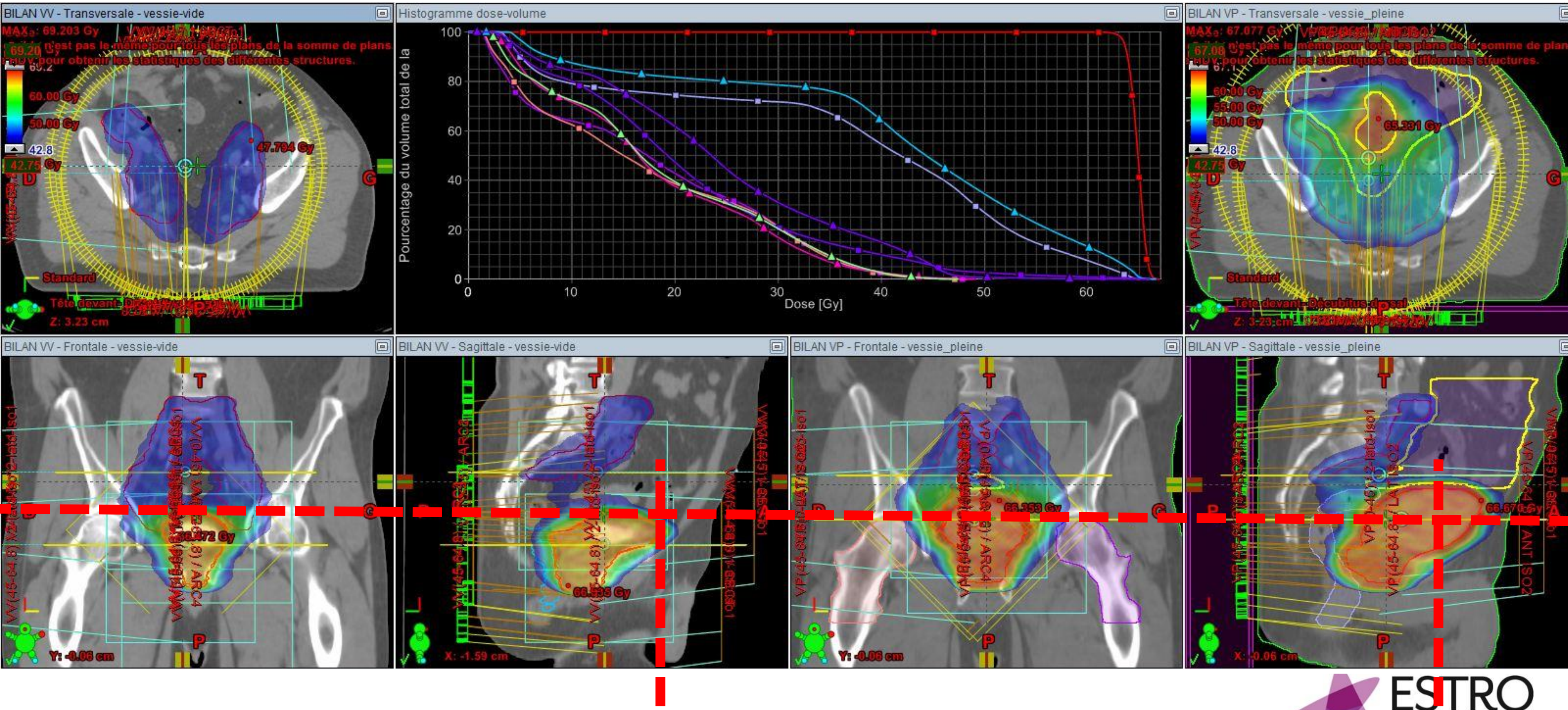
- 15 mm PTV margin if bone-based guidance
- 10 mm margin if daily on-line adaptive RT

Foroudi F et al., Clin Oncol 2014

CGFL, Dijon : IGART strategy

3 CT / 3 dosimetric plans

- Full bladder
- Empty bladder
- Half full bladder



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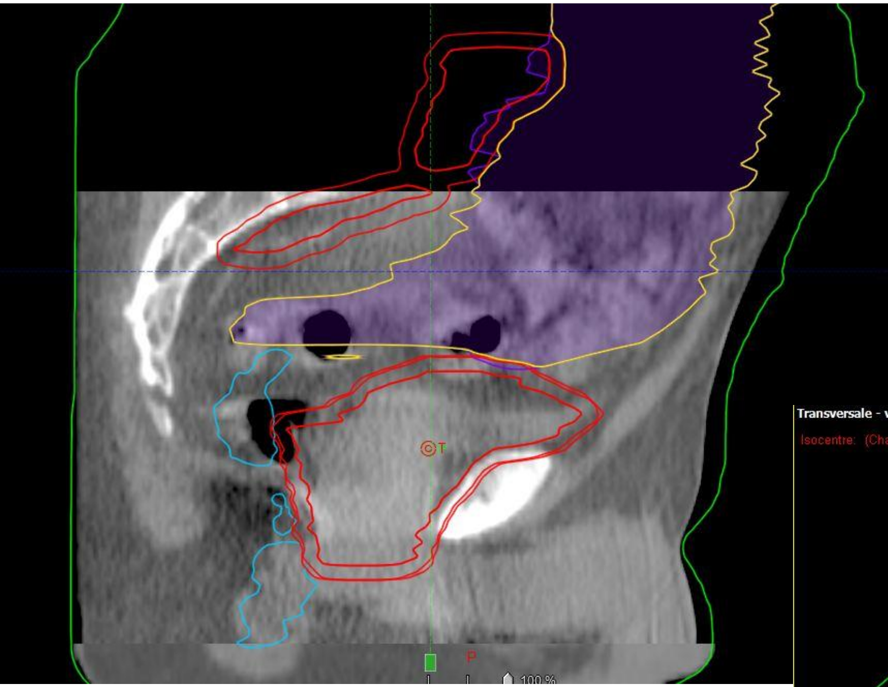
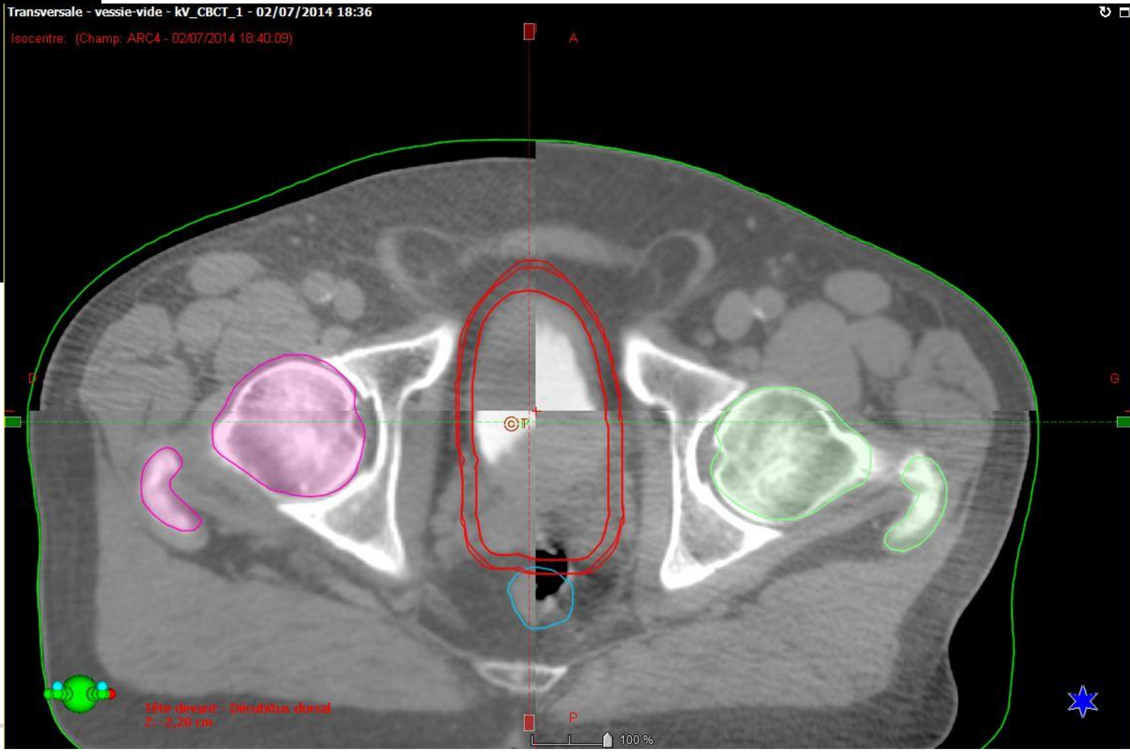
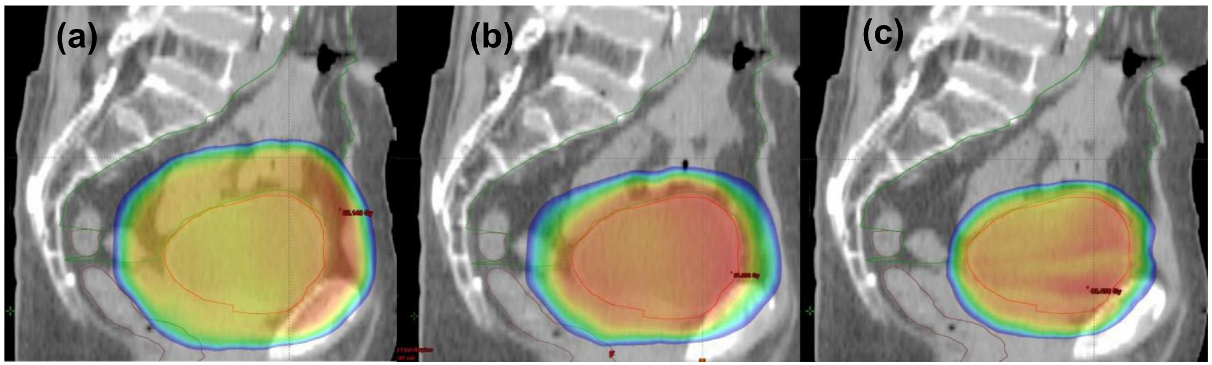
kV CBCT for selecting the plan of the day

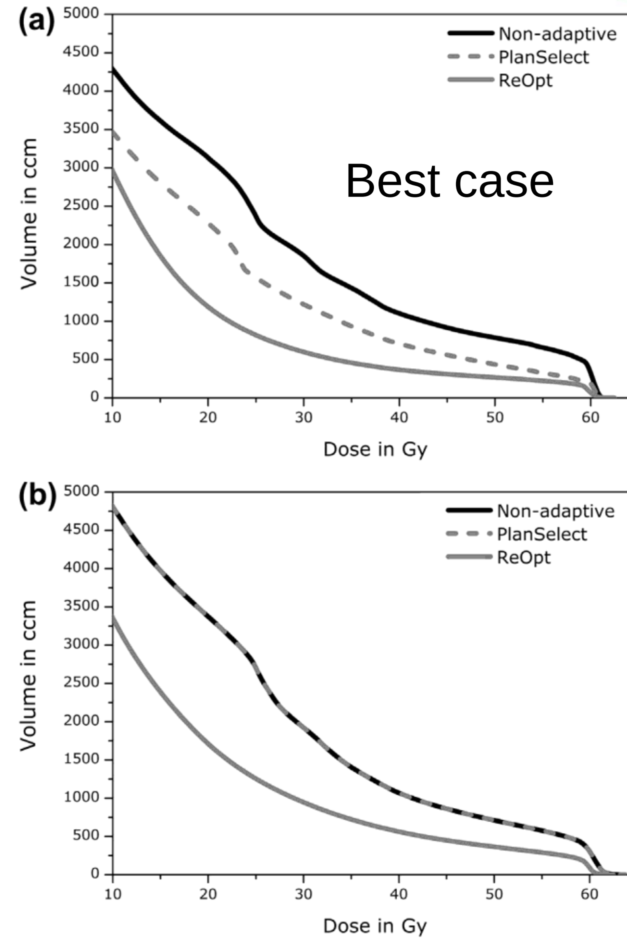




Plan of the day or Replan?



No adaptation | Plan of the day | Replan



Worst case : the large plan fits all the fractions!!!

Vestergaard A et al., Radiother Oncol 2013

CONCLUSIONS

RECTAL CANCER

•Little room in routine as <10% LF

•IGRT might be useful for upper 1/3 or nodes >S2-S3

•GTV dose escalation

•No robust literature – very preliminary experiences

BLADDER CANCER

- 30% LF (salvage cystectomy)
- Ideal model for IGART
- Or partial bladder RT
- Plan-of-the day

CERVICAL CANCER

- Young patients
- IMRT still controversial
- Large PTV margins required
- Margin-of-the day

Library of plans

Helen McNair

Royal Marsden NHS Foundation Trust and Institute of Cancer Research

Rianne de Jong

Academic Medical Centre, Amsterdam

The ROYAL MARSDEN
NHS Foundation Trust

ICR The Institute of Cancer Research

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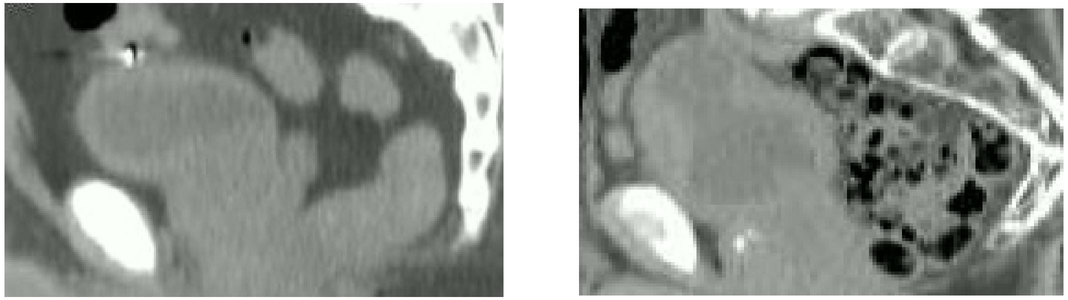
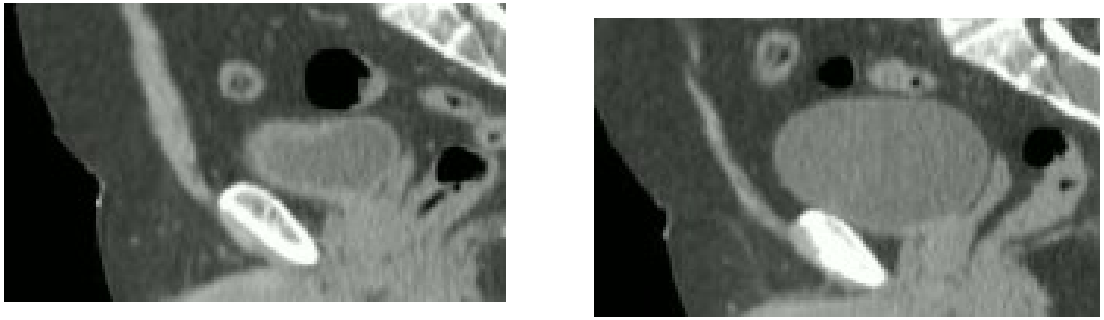
Tumour sites

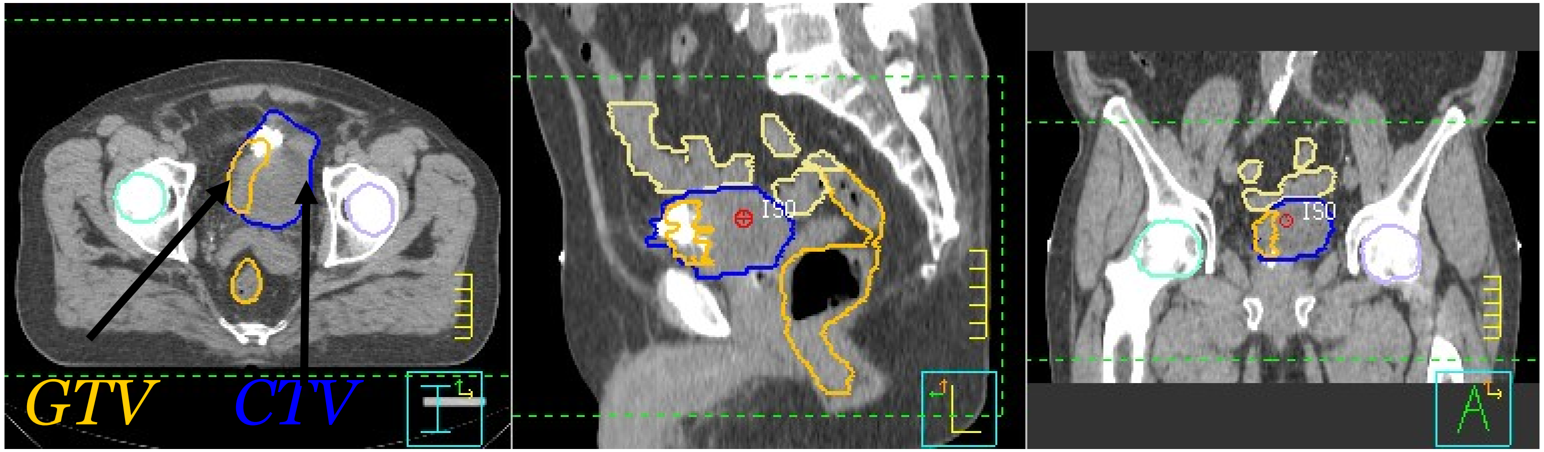


Rectal changes



Bladder changes

Plan of the day



No significant difference outlining on CT compared to CBCT

Faroudi Med Imaging Radiat Oncol 2009

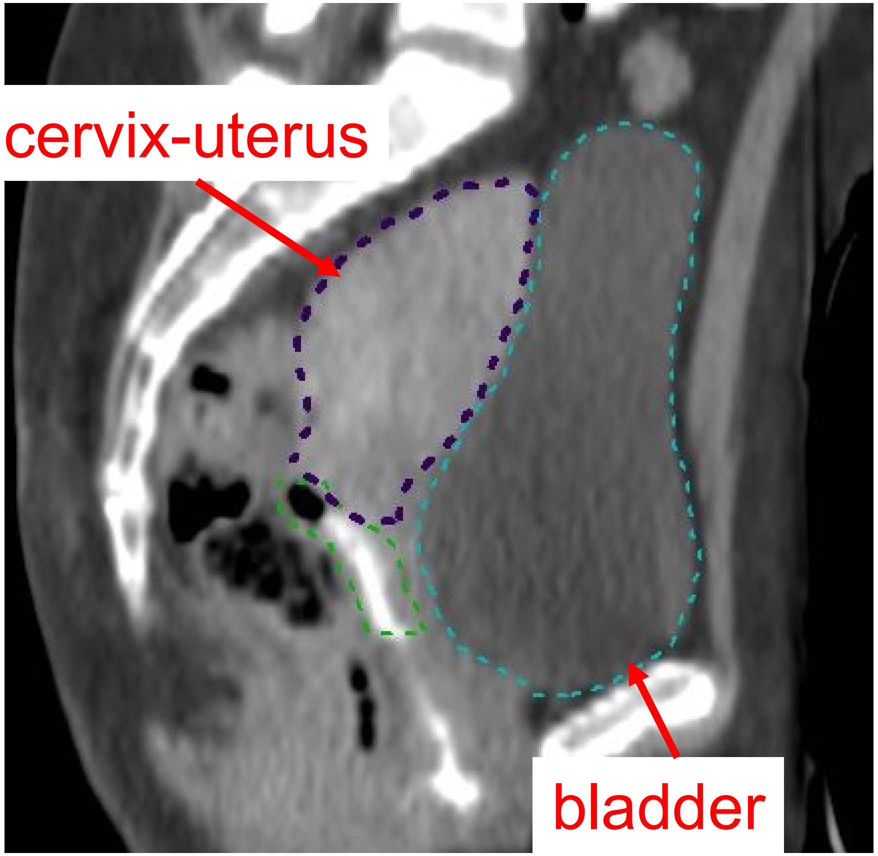
Nishioka et al Radiat Oncol 2013

Lütgendorf-Caucig J Eur Society for Therapeutic Rad Oncol 2011

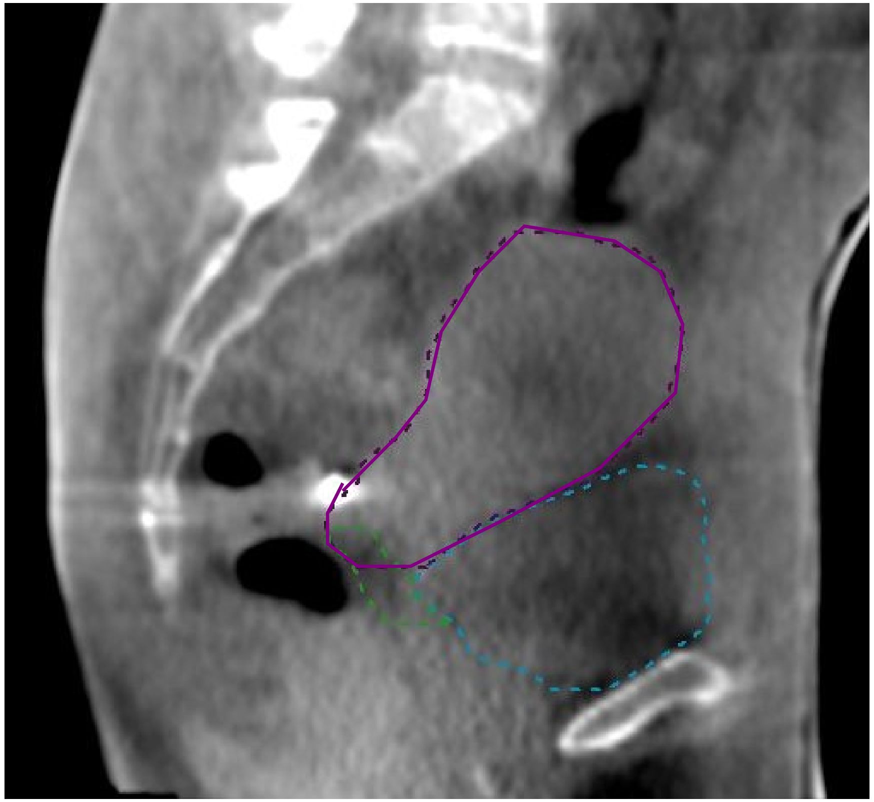
Weis Int J Radiat Oncol Biol Phys 2010

Tumour sites

Planning CT



Conebeam CT



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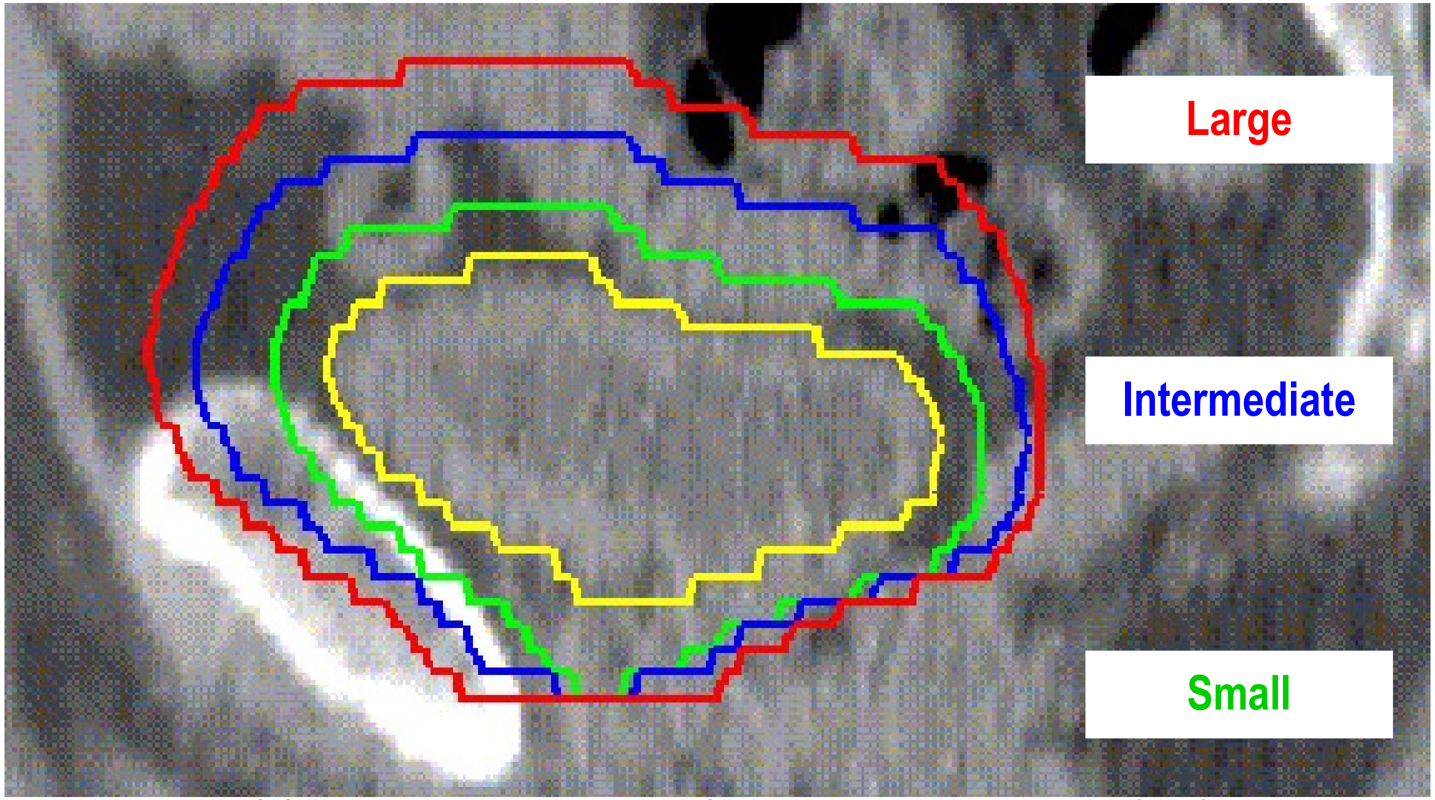
Adaptive-predictive organ localisation



51% of fractions in 10 out of 15 patients required adaptive

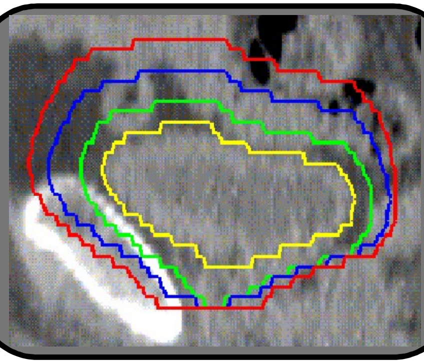
73% fractions delivered correctly using adaptive

Remaining 27% improved coverage

Lalondrelle , IJROBP, 2011

Treatment planning

Planning
CT0 and CT30
post-void



Individualised
library of plans

Planning Target Volume margins

CTV → PTV (cm)	Small PTV	Intermediate PTV	Large PTV Based on CT30	Large PTV Based on CT0
Anterior	**0.5**	**1.5**	**1.5**	**2.0**
Posterior	**0.5**	**1.0**	**1.0**	**1.2**
Lateral	**0.5**	**0.5**	**0.5**	**0.75**
Superior	**0.5**	**1.5**	**1.5**	**2.5**
Inferior	**0.5**	**0.5**	**0.5**	**0.75**

Courtesy of Fiona McDonald

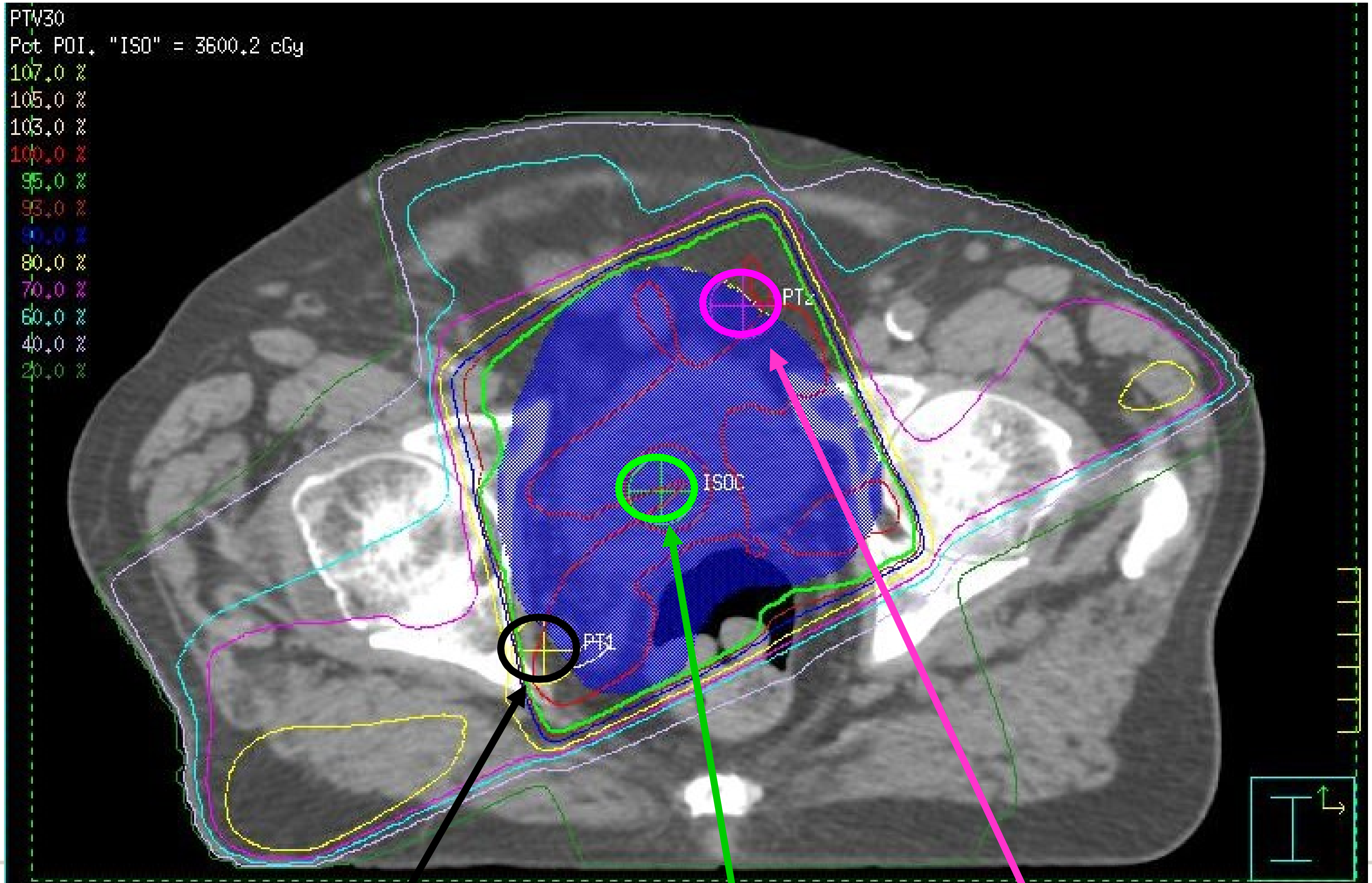
Plan of the day

PTV small

PTV medium

PTV large

Treatment delivery-plan of day



Point 1 Isocentre Point 2

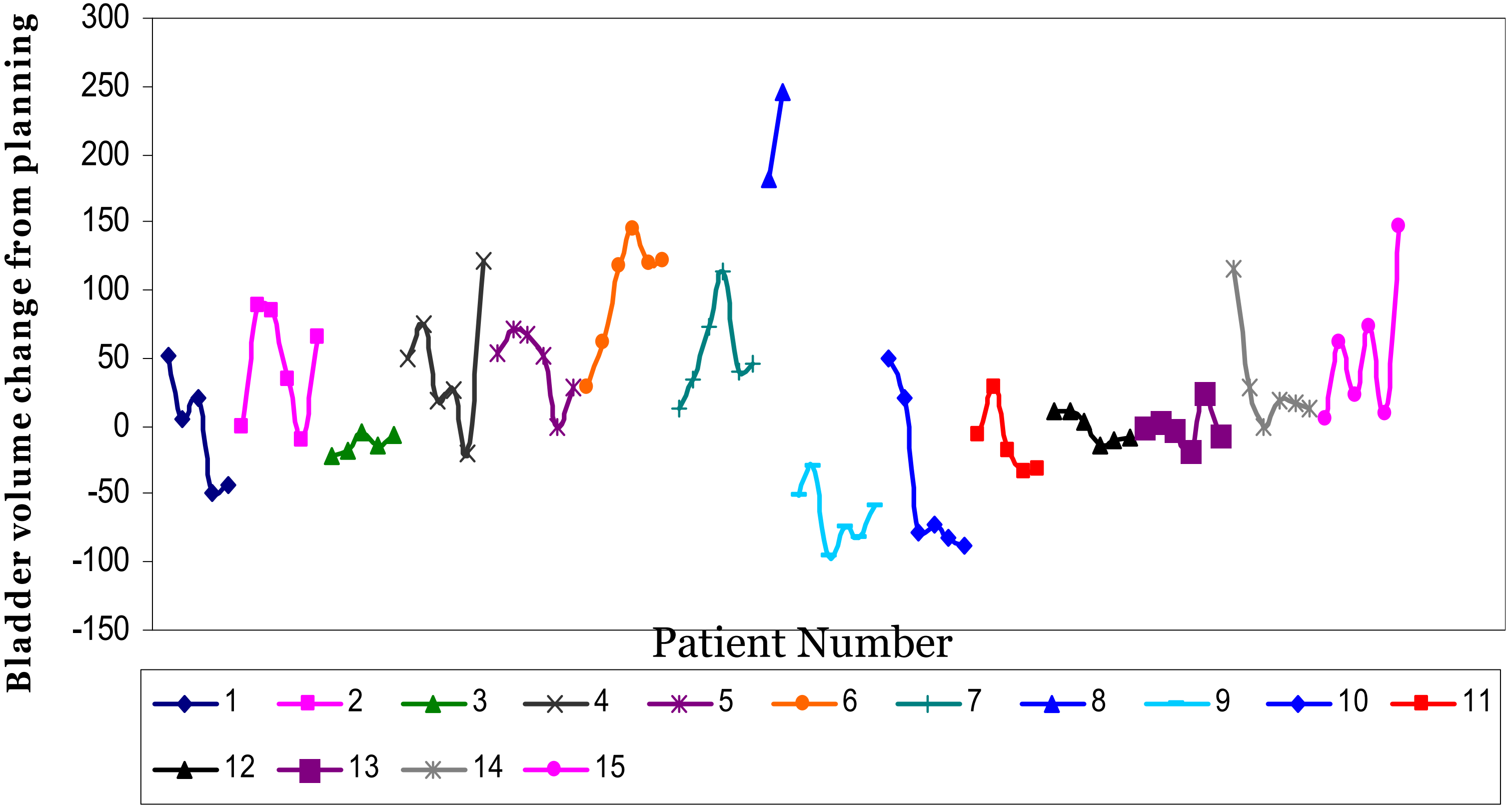
Registration issues

Representative reference image

Empty bladder

Full bladder

Interfraction volume variation



No predictive factors

Lalondrelle , IJROBP, 2011

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Registration issues

Consistent PTV selection between observers

No PTV is suitable- too large

No PTV is suitable – too small

Registration issues

Consistent PTV selection between observers

No PTV is suitable- too large

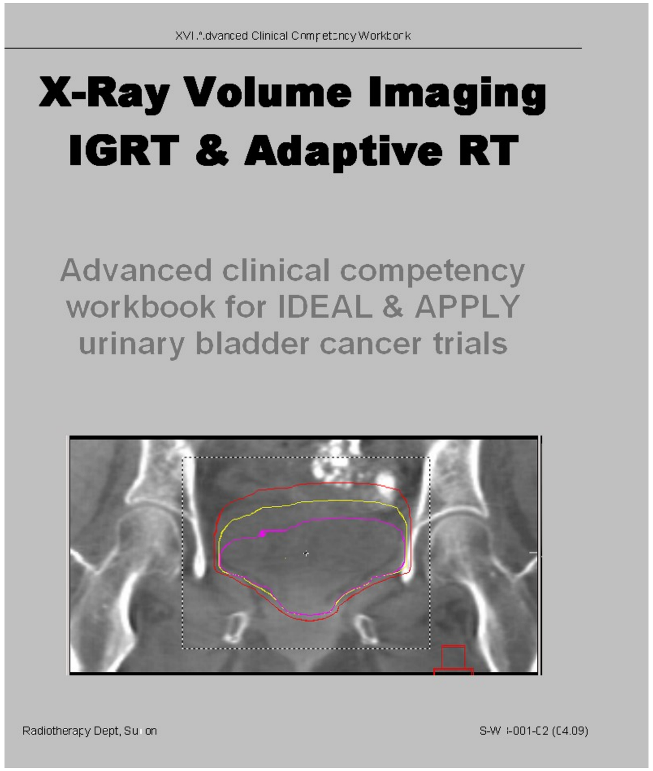
No PTV is suitable – too small

Training

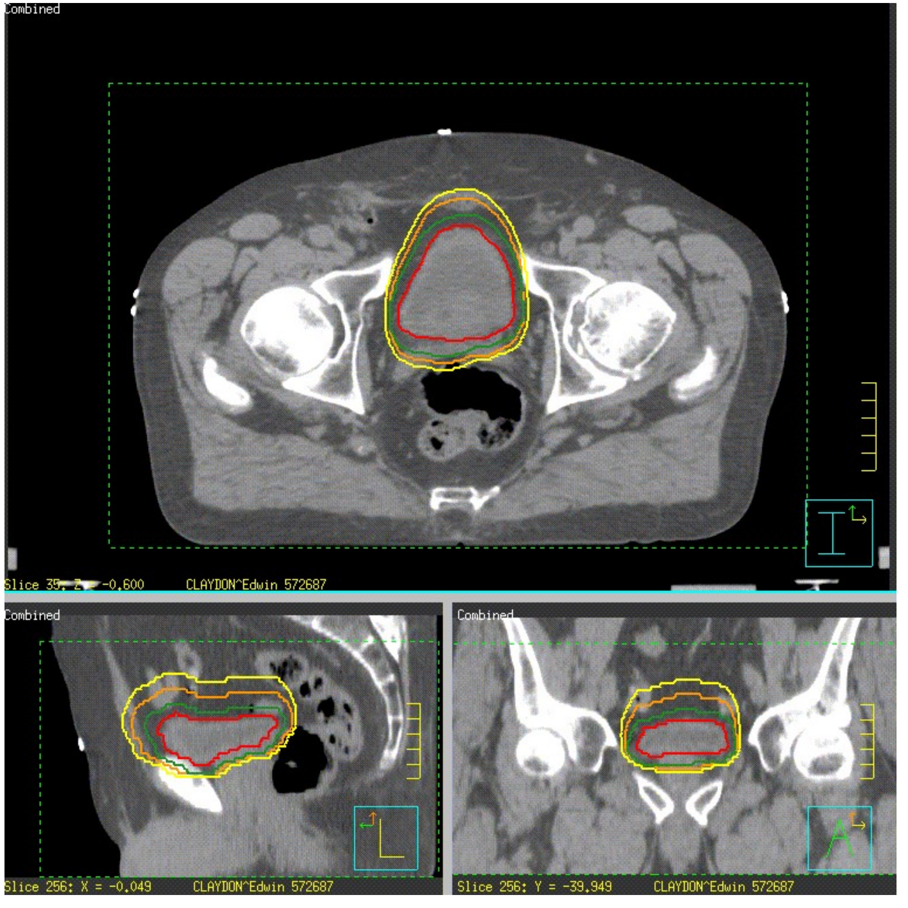
Anatomy teaching provided by University & clinicians

Normal/abnormal pelvic pathology

Complete competency workbook



Training-Bladder



12 radiographers

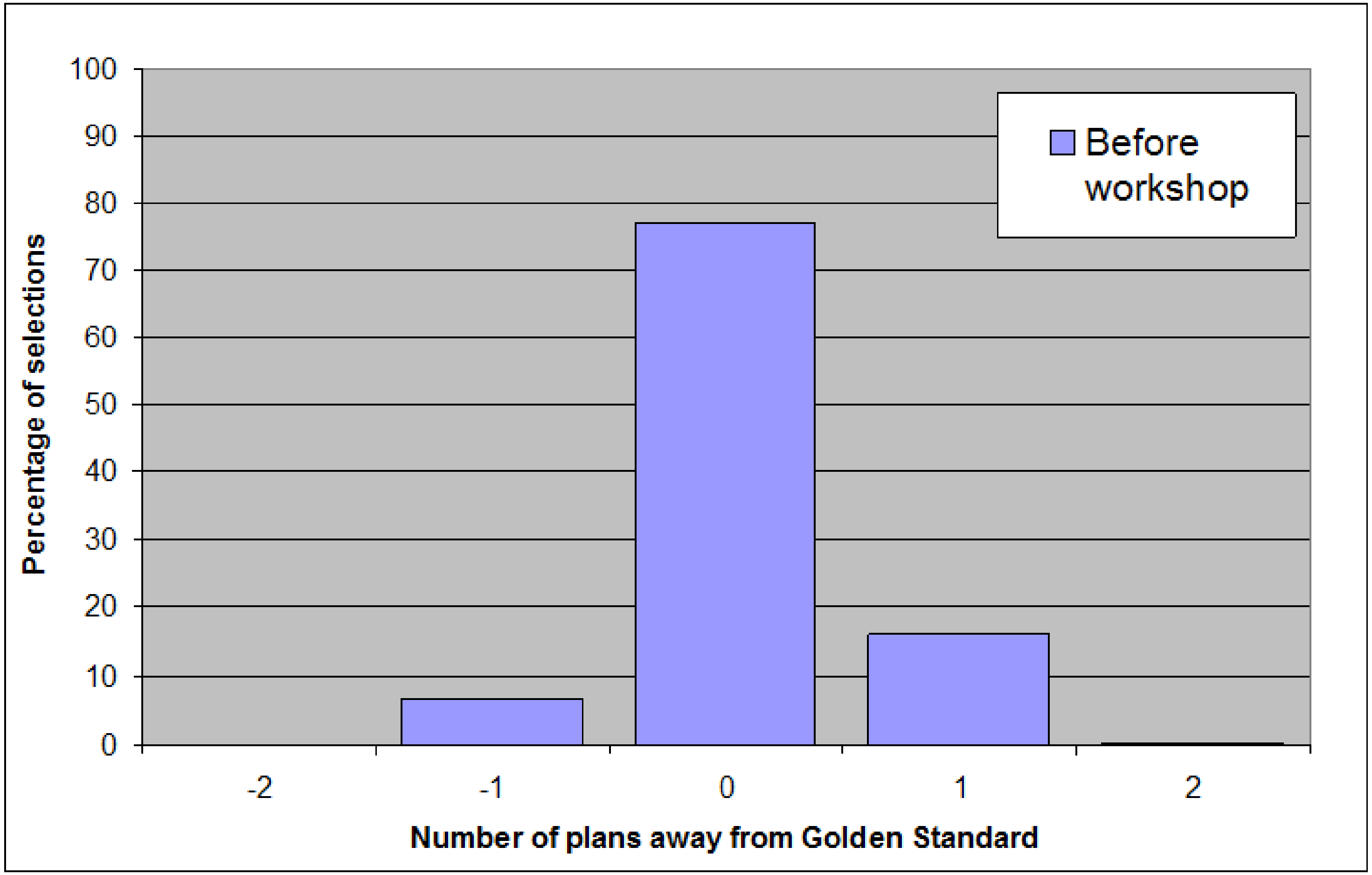
2 clinicians

Mean concordance 76%

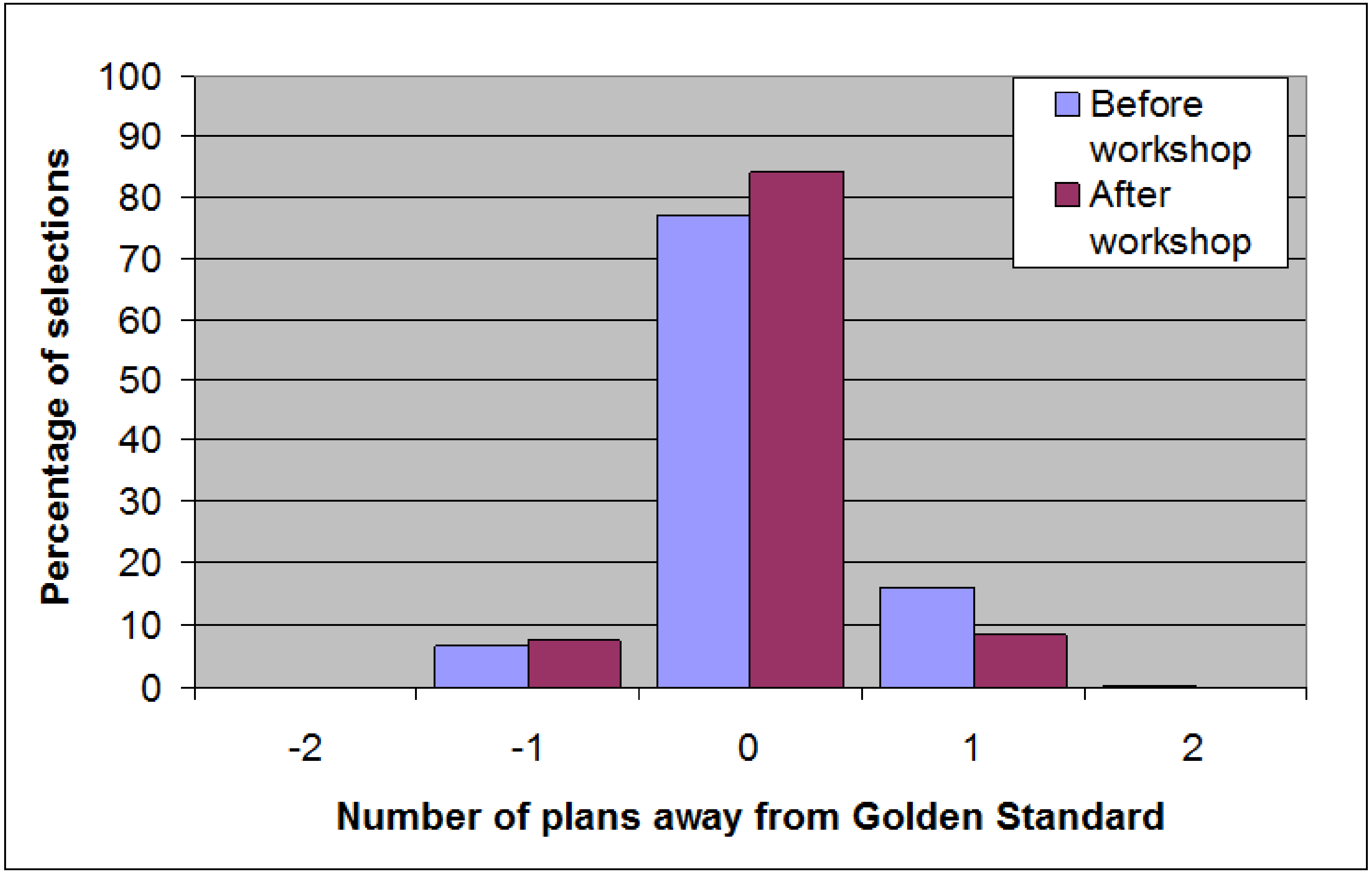
Matching/ set up: 2 min 28s

Plan selection: 1 min 24s

Training- cervix



Training-cervix



Volume selection

On-line by 2 trained observers

CBCT → Set-up correction → Volume selection → Treatment 6Gy → CBCT

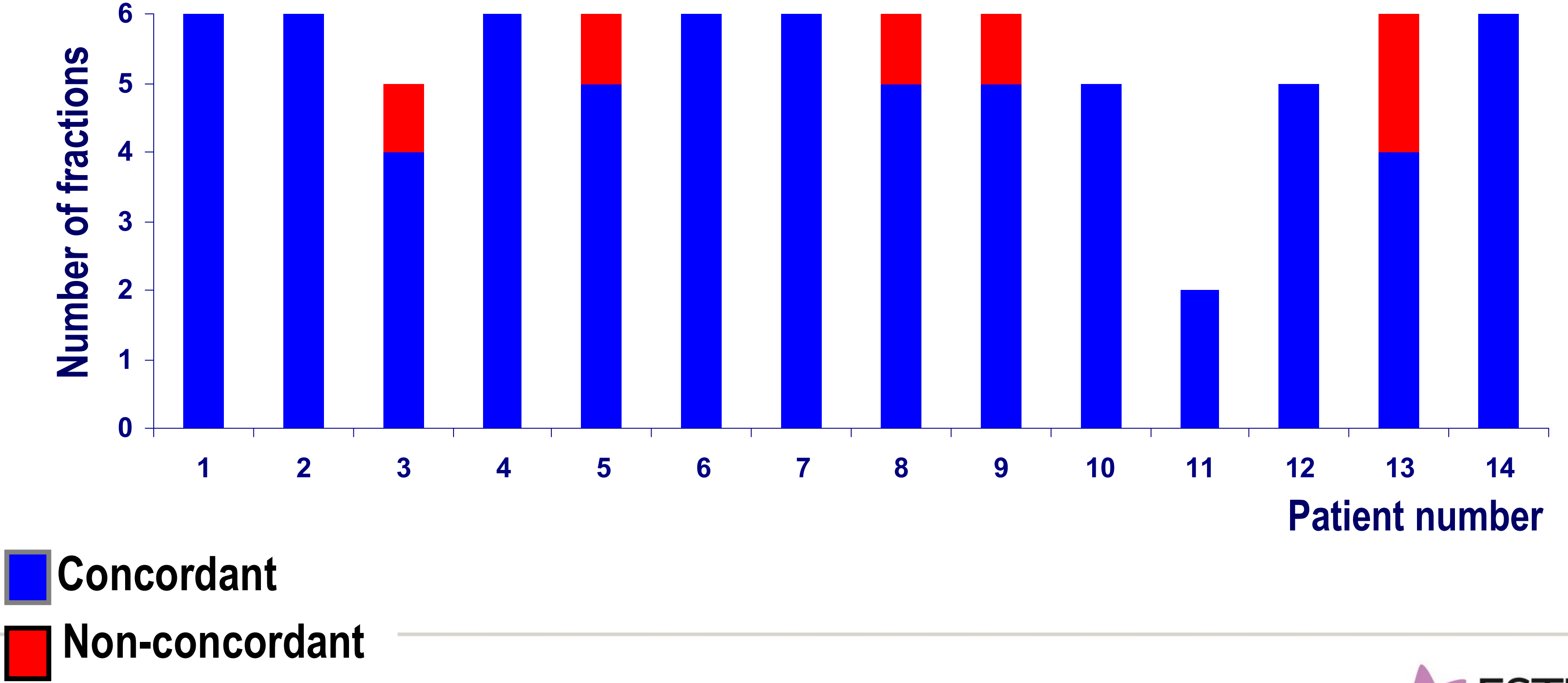
Off-line by independent blinded observer

CBCT → Bony match → Volume selection

Courtesy of Fiona McDonald

Volume selection

Concordance rate 92% **(71/77#)**



Courtesy of Fiona McDonald

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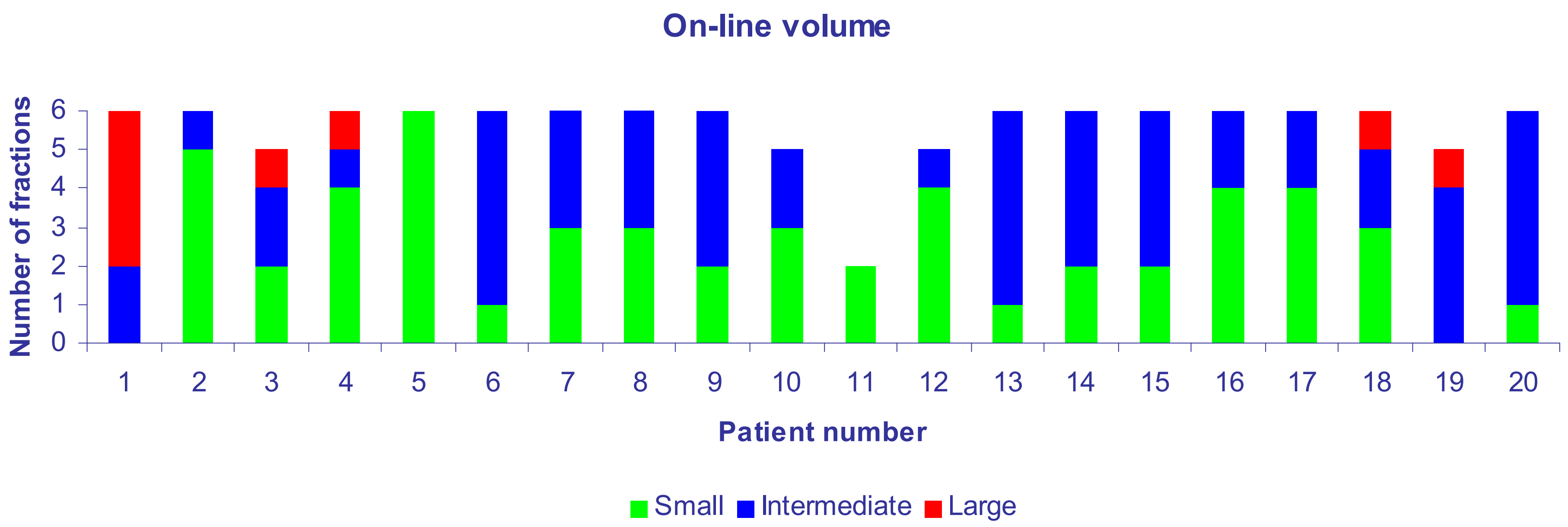
On-line volume



139 RT fractions assessed

•68 (49%) small, 63 (45%) medium and 8 (6%) large selected

•3 (12%) same plan throughout the course

•Manual isocentre shift in 15 fractions (10%)

•1 fraction CTV considered too large for the large plan

National Trial HYBRID

62 patients with **pT2-T4a N0 M0** bladder carcinoma unsuitable for standard daily radiotherapy

↓

Due to receive six 6Gy fractions of radiotherapy delivered weekly (total dose: 36Gy over 6 weeks)

↓

RANDOMISE

1:1

Group 1:	Group 2:
STANDARD PLANNING (CONTROL)	ADAPTIVE PLANNING (EXPERIMENTAL)

↓

Follow up

- Weekly on treatment
- 4 weeks after last treatment
- **3 months after last treatment**
- 6, 12 and 24 months

Endpoints

HYBRID

Primary endpoint

•Acute non-genitourinary grade 3 or greater toxicity (up to 3 months following treatment completion)

Secondary endpoints

•Local disease control rate at 3 months
•Control rate of presenting symptoms
•Patient reported outcomes
•Late toxicity
•Time to local disease progression
•Overall survival
•Proportion of fractions benefiting from adaptive planning
•Appropriate identification and correction of fractions requiring adaptive planning

Planning CT

Patient preparation

Advise no drinking 30min prior to scanning

Void immediately before planning CT

Encourage rectal emptying

Local rectal preparation protocols permissible (micro enemas etc.)

Patient positioning

CT scanning

Slice thickness $\leq$3mm

Scan at least 4cm above bladder dome and 2cm below ischial tuberosities

RTTQA IGRT Credentialing programme

Evidence of in-house IGRT training programme (bladder)

HYBRID specific training programme

IGRT independent review cases: this acts as competency assessment

Verification of electronic data transfer: CBCT and registration objects

IGRT site visit: during first patient's treatment. Review process/decision making

RTT QA for plan selection

Remote access to Elekta/Varian databases

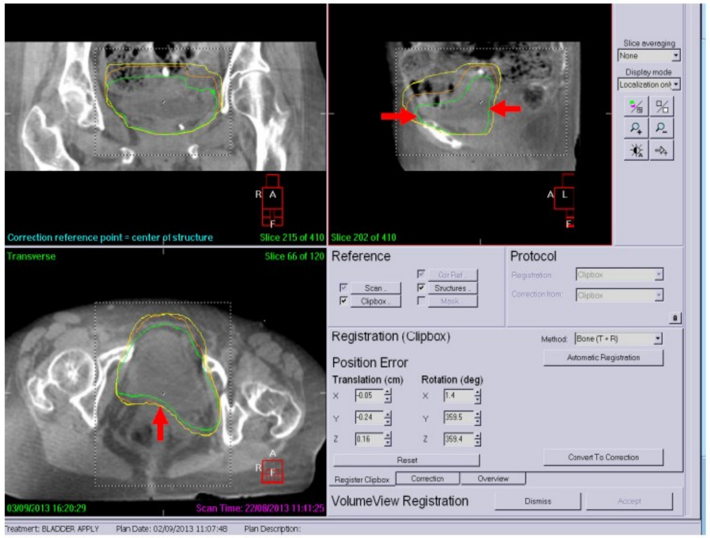
5 patients, 6 CBCT each

Patient 1: step by step process of how plan selected

Patient 2-3: practice with answers provided

Patient 4-5:test cases

Figure 1: Axial, sagittal and coronal view of PTVsmall (green), PTVmedium (orange) and PTV large (yellow) with arrows highlighting where the bladder is close to the boundary of PTVsmall.



- Remove PTV small as it does not incorporate the bladder volume and a margin of 3mm in the anterior-posterior dimension (Figure2).

51 Staff assessed, 9 centres

Maintenance of competency

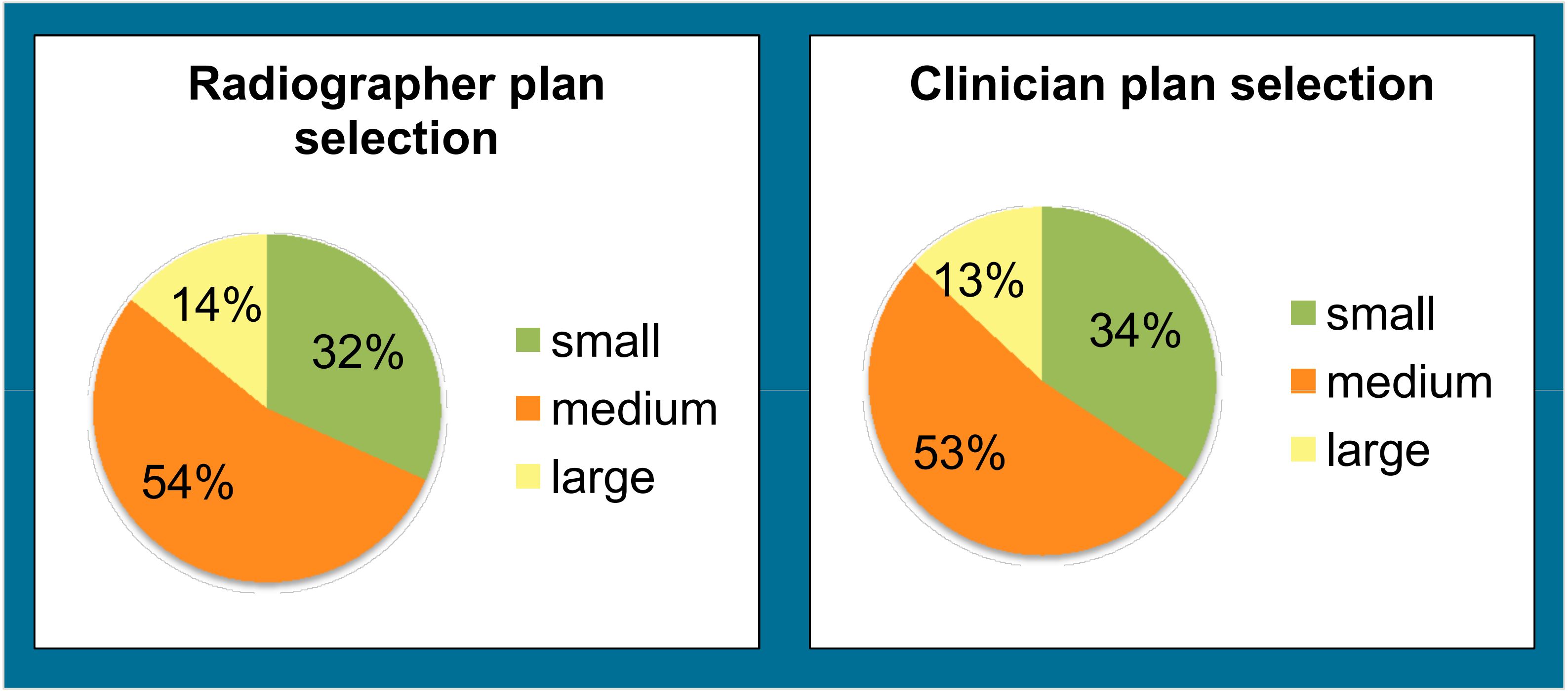
Advanced competency assessment record of practise in adaptive bladder radiotherapy for bladder cancer

A maximum of 2 scans per patient, should be recorded as part of the competency assessment.

Date	Relevant Experience	Outcome / Reflection
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	

Maintenance of competency

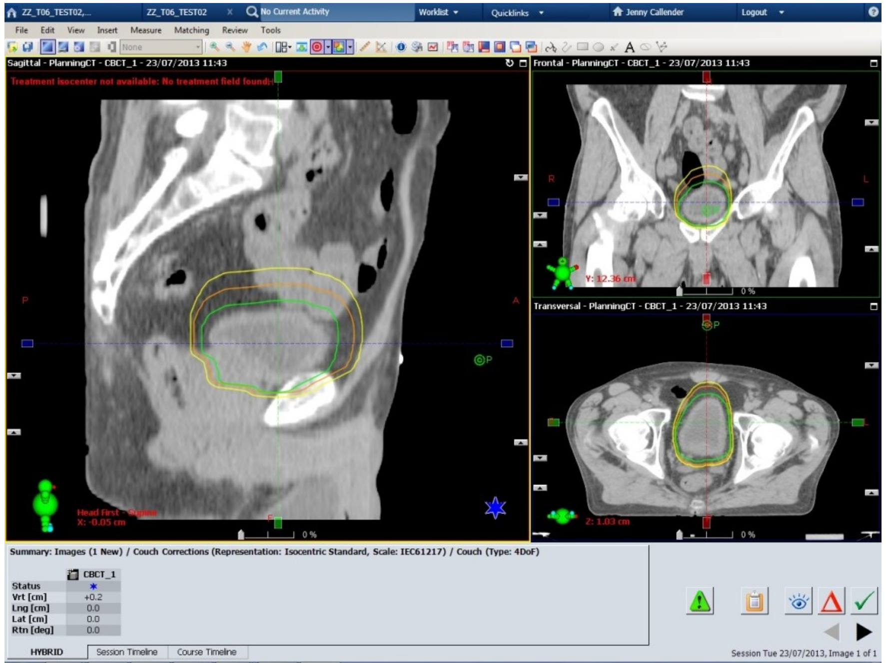
16 radiographers trained
Audit 3 years after

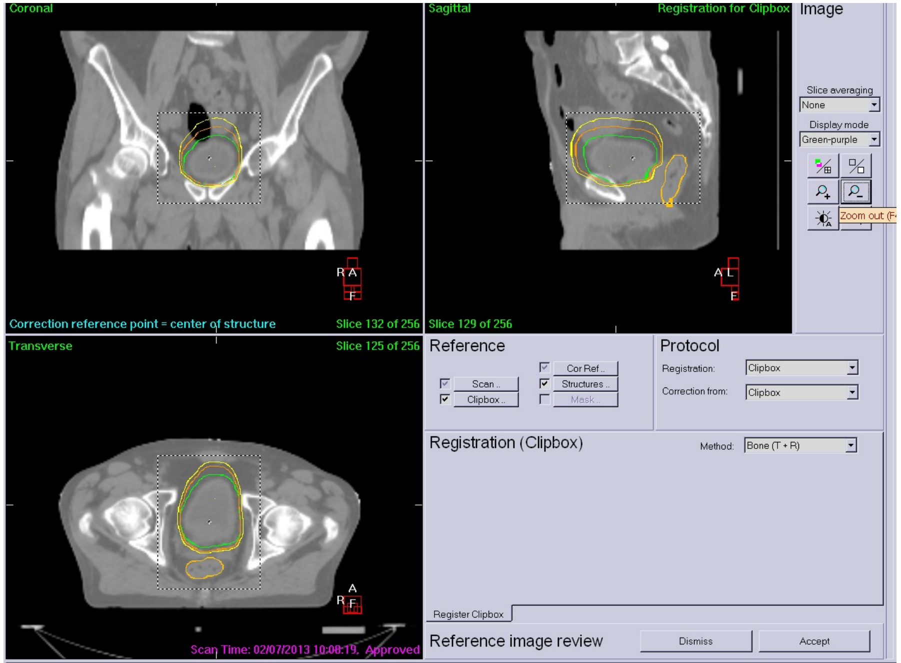


125 CBCTs (63 pre; 62 post radiotherapy) were evaluated
Concordance of plan selection was 92% (58/63)

Registration-guidelines

Assess reference image





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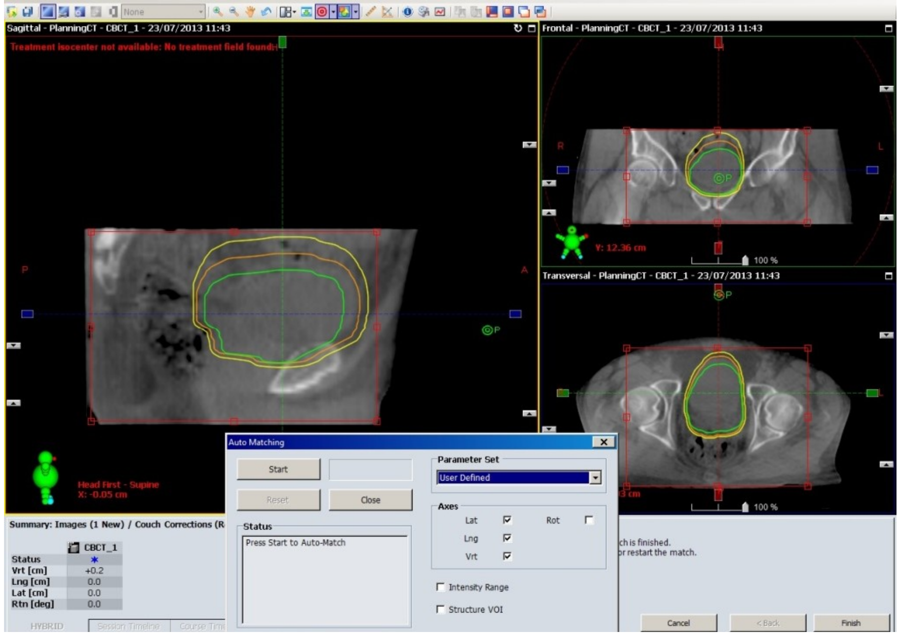
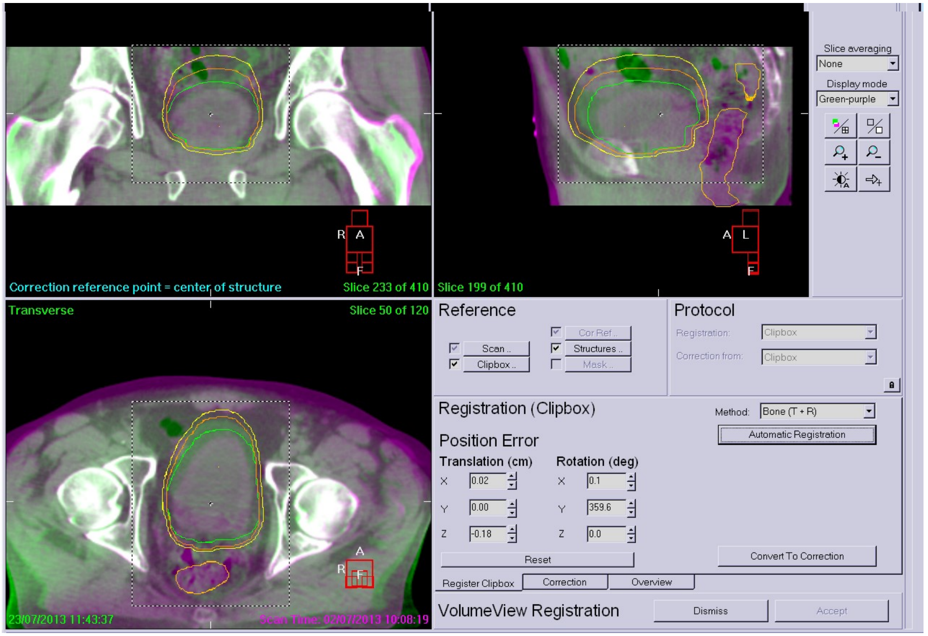
Registration-standard process

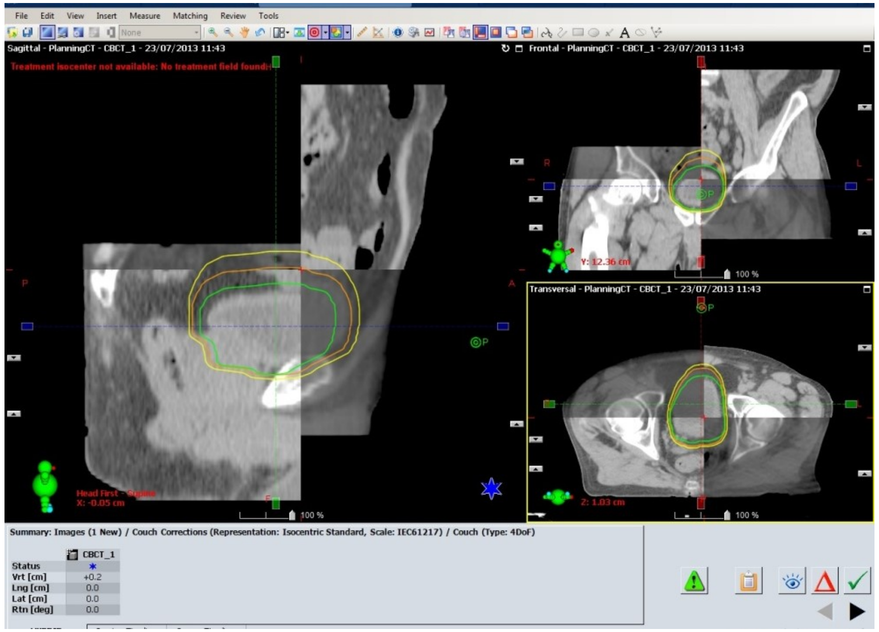
Contrast and Bone registration

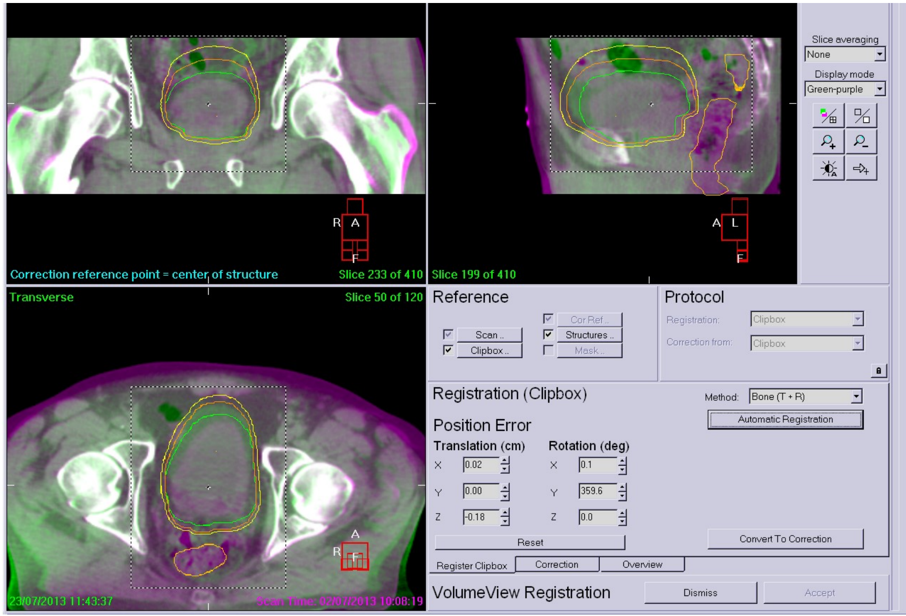




Registration-guidelines

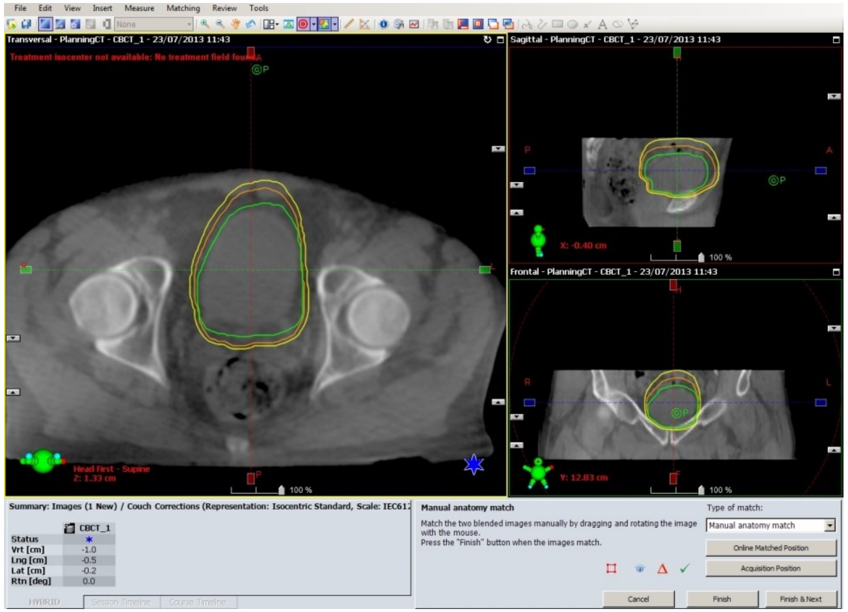
Check match

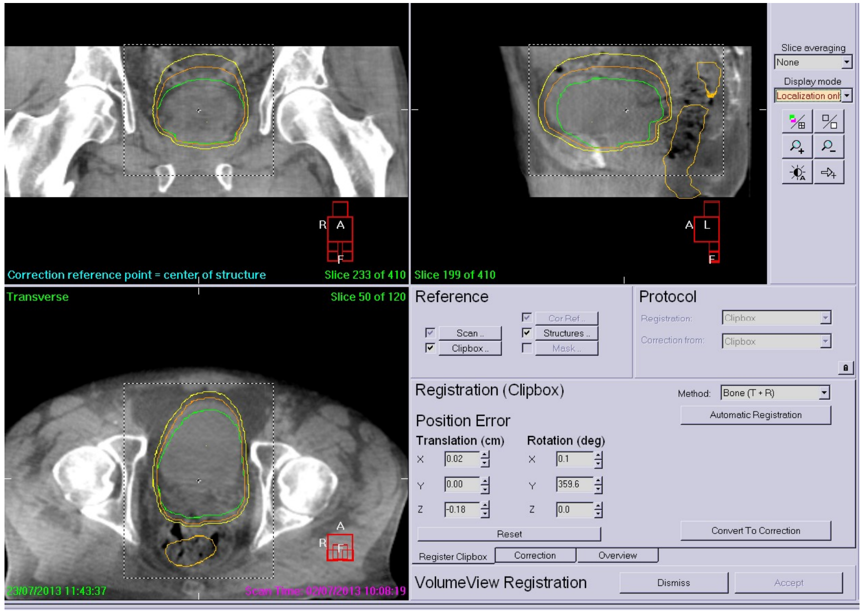




Registration-guidelines

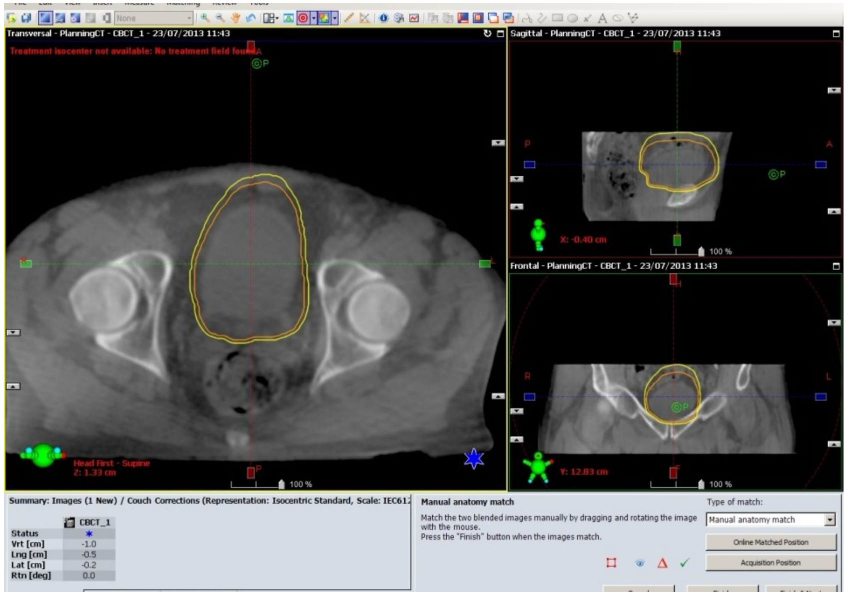
Quick gross assessment

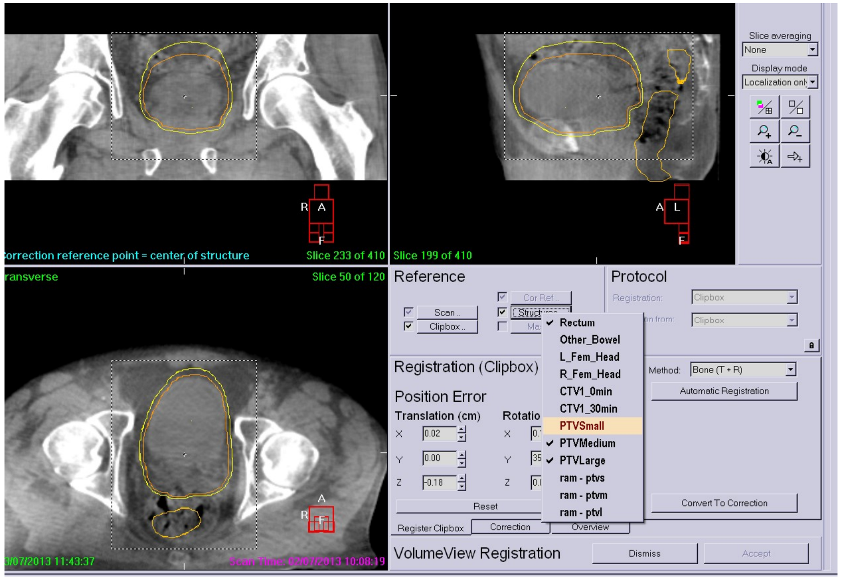




Registration-guidelines

Assess next plans

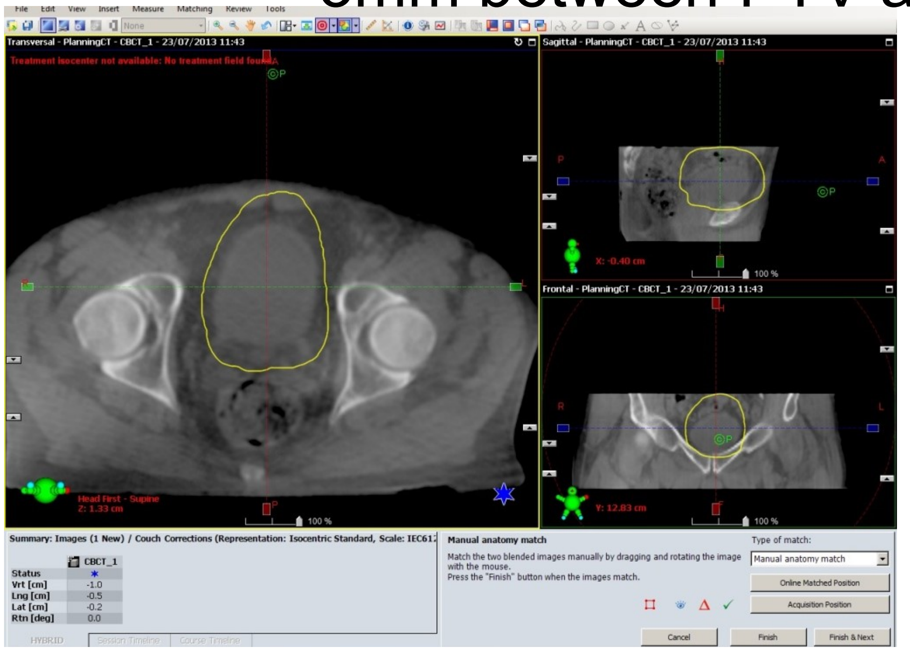


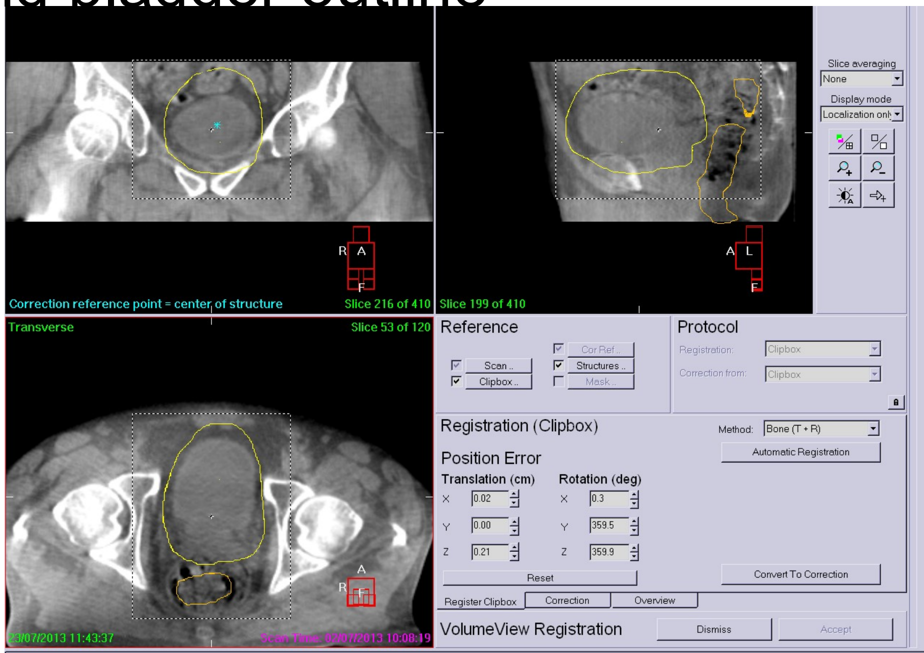


Registration-guidelines

Manual adjustment

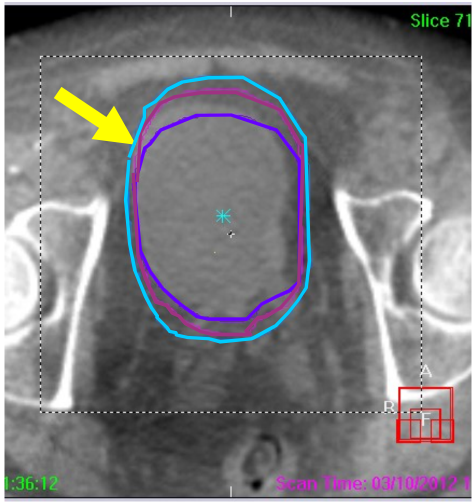
3mm between PTV and bladder outline

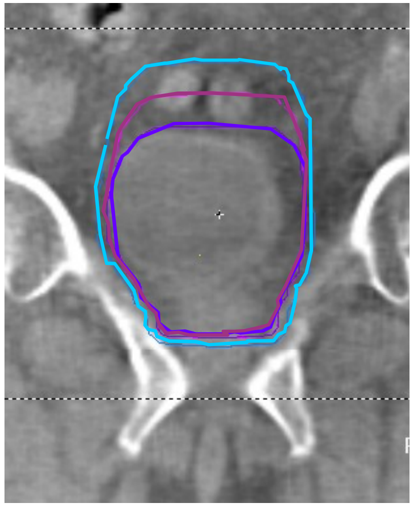


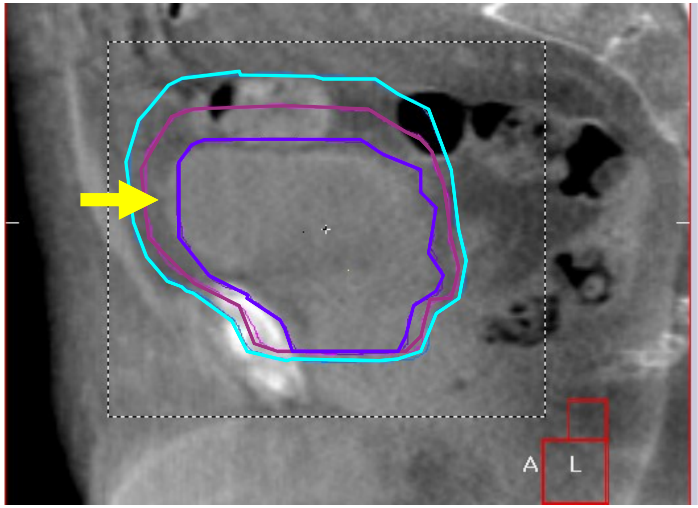


Case 1

Gross assessment



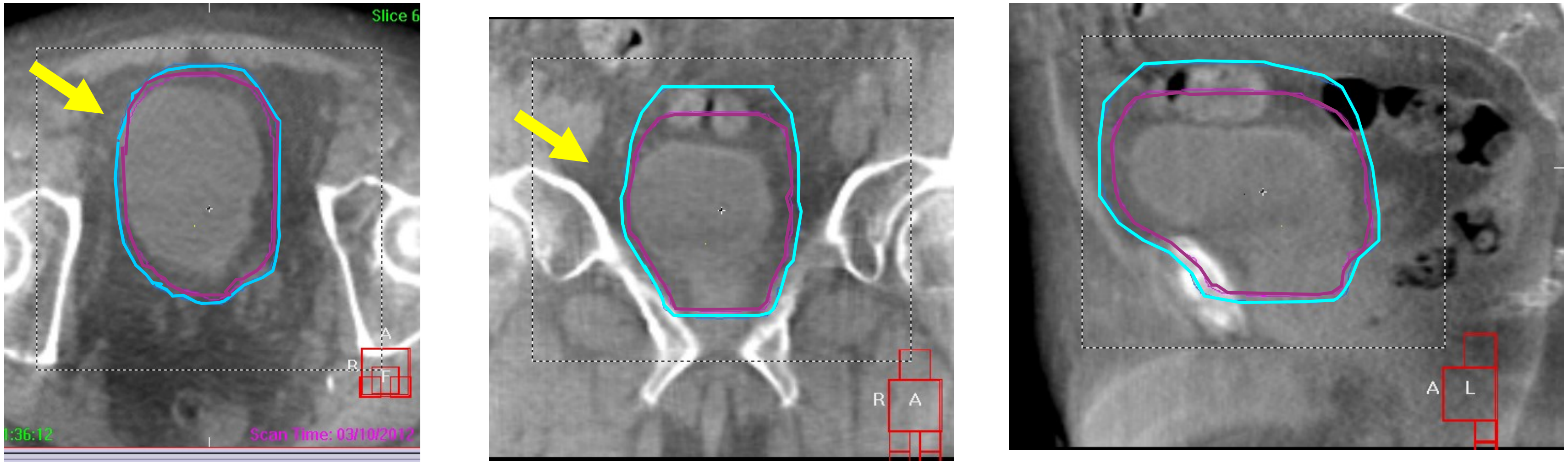




Small too small

Case 1

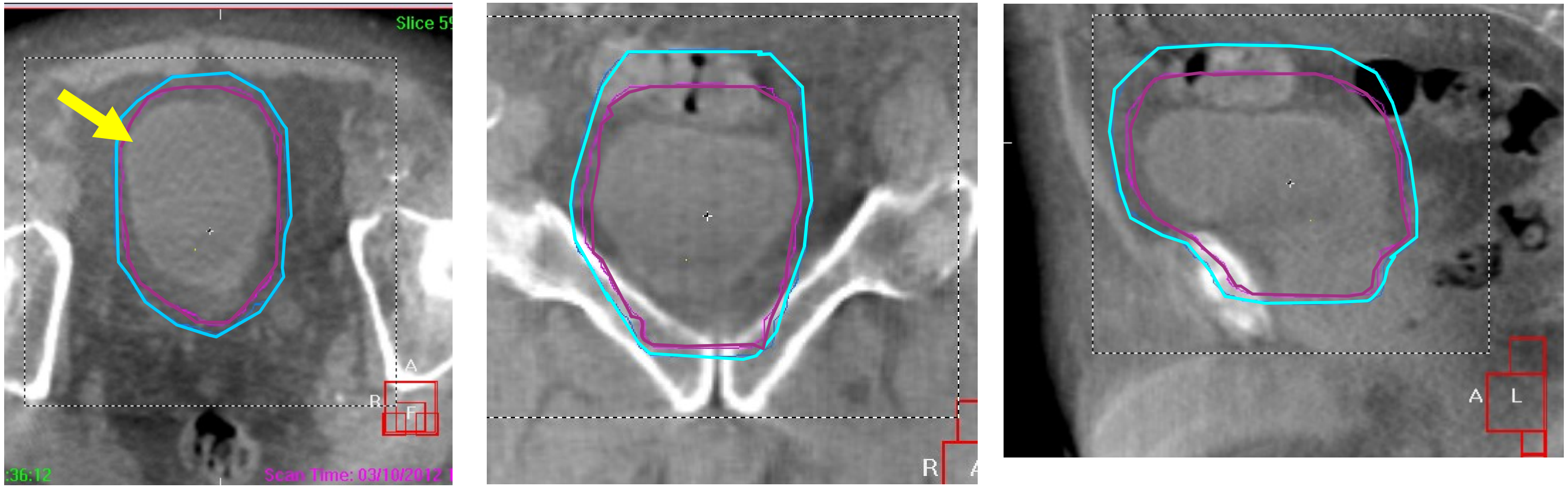
View all images/slices



Needs right left shift

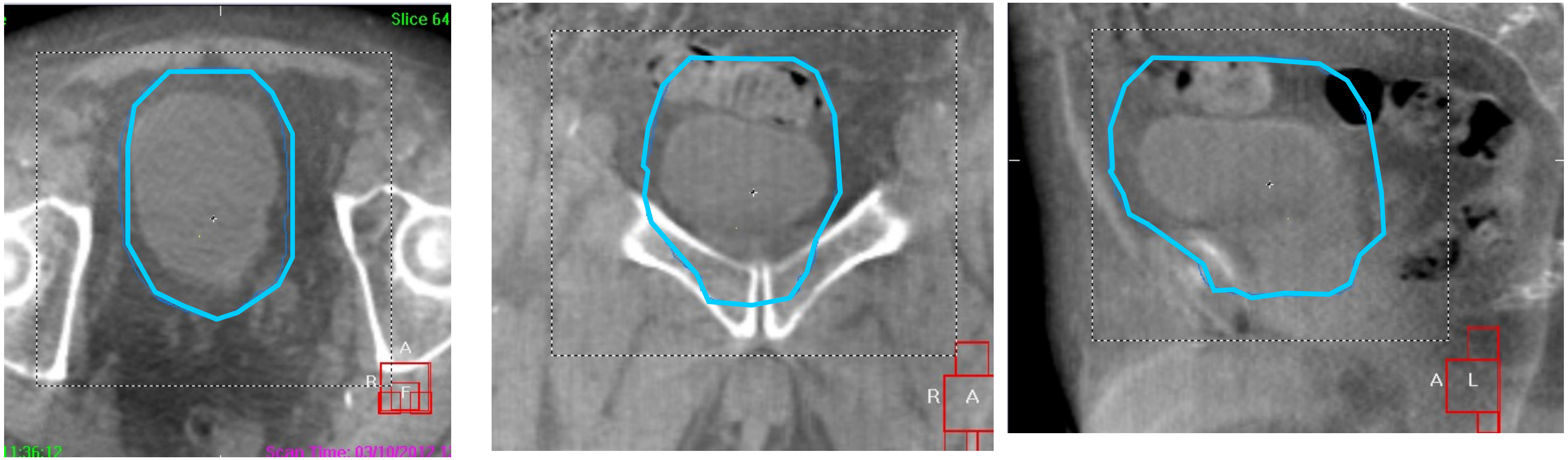
Case 1

Shift Right-left



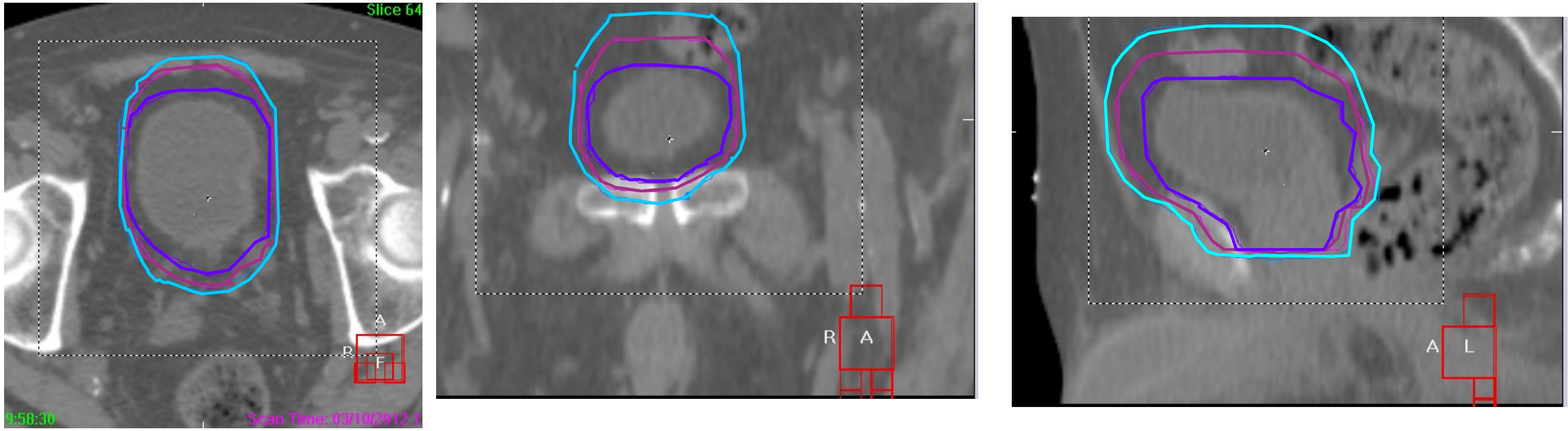
Medium still too tight

Case 1

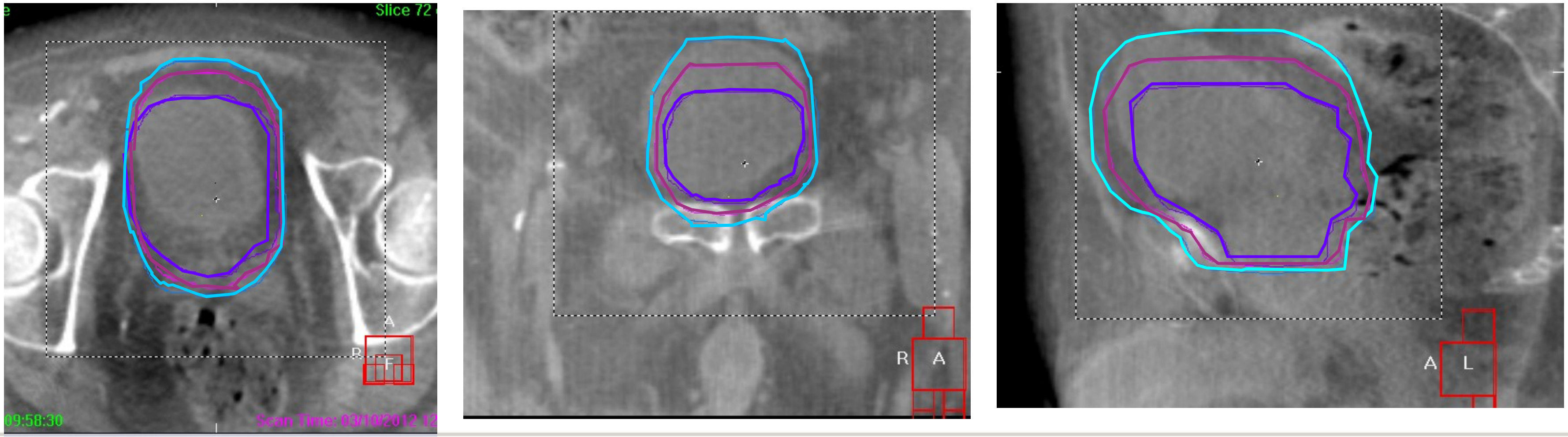


Select large

Case 2



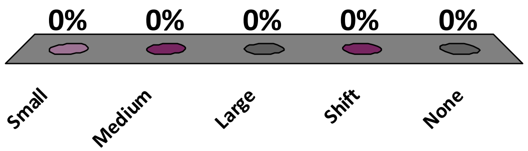
Reference image



Treatment image

Which choice is best?

A. Small
B. Medium
C. Large
D. Shift
E. None



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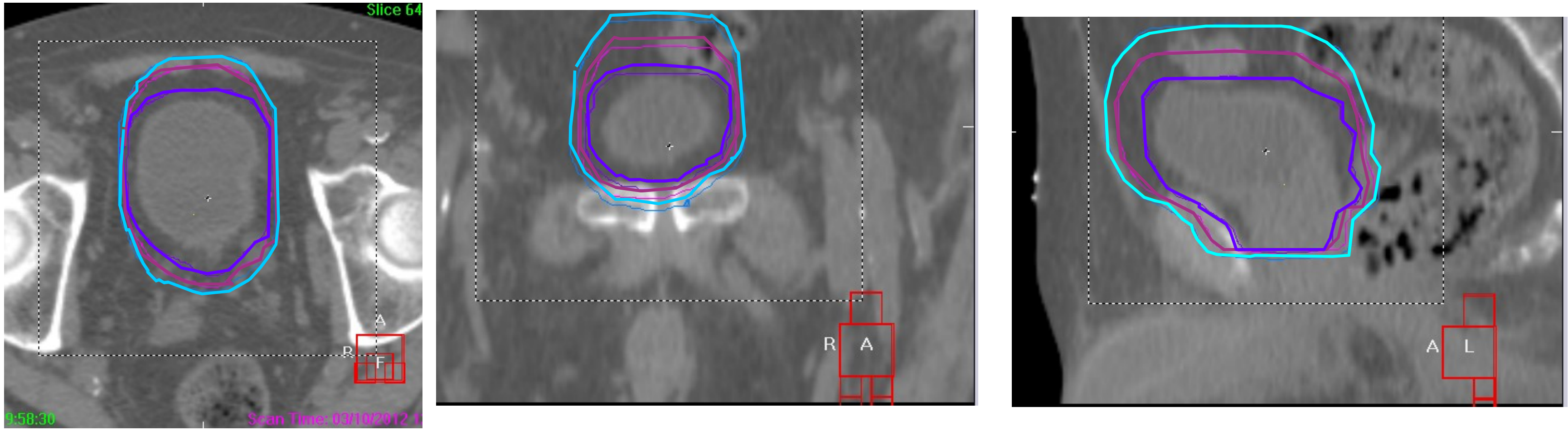
Registration issues

Consistent PTV selection between observers

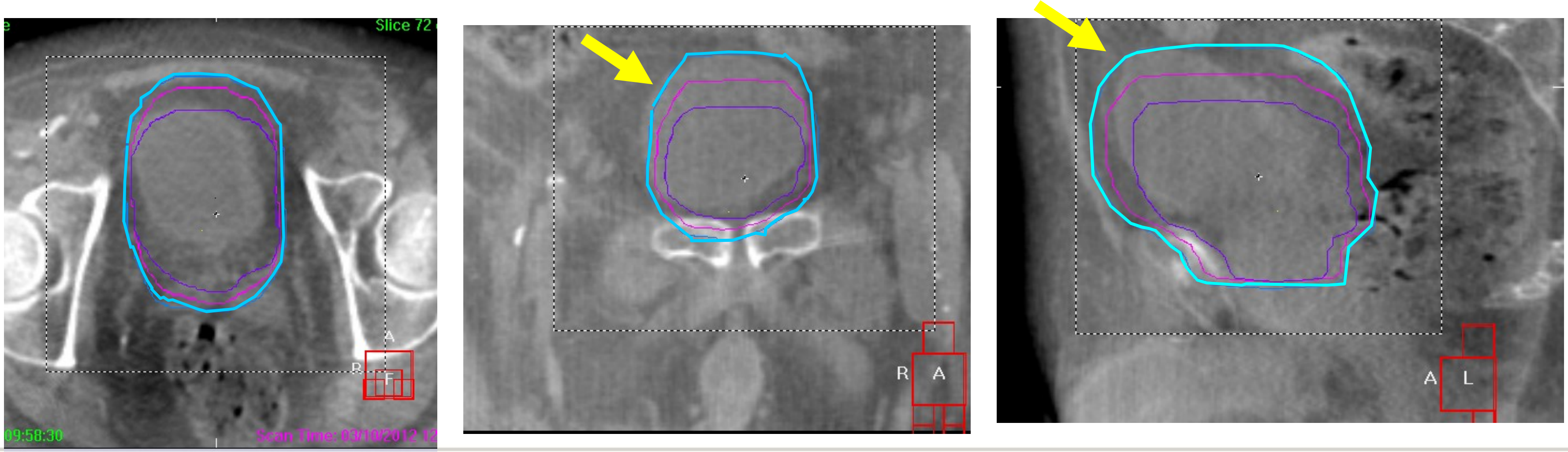
No PTV is suitable- too large

No PTV is suitable – too small

Case 2 Too large- empty bladder



Reference image



Treatment image

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Significant shape change

Bladder too big

No plan provides appropriate coverage

Shape change due to bladder overfilled

Shape change due to rectal filling (flatus/faeces)

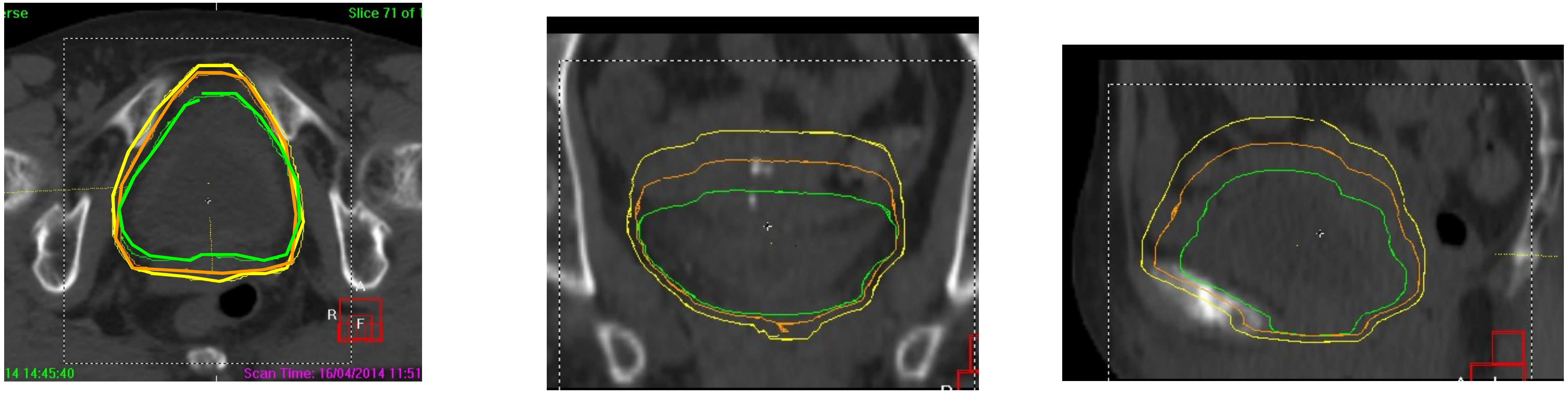
Remove patient from couch, void bladder, repeat drinking protocol but review

i) volume of fluid drank and or

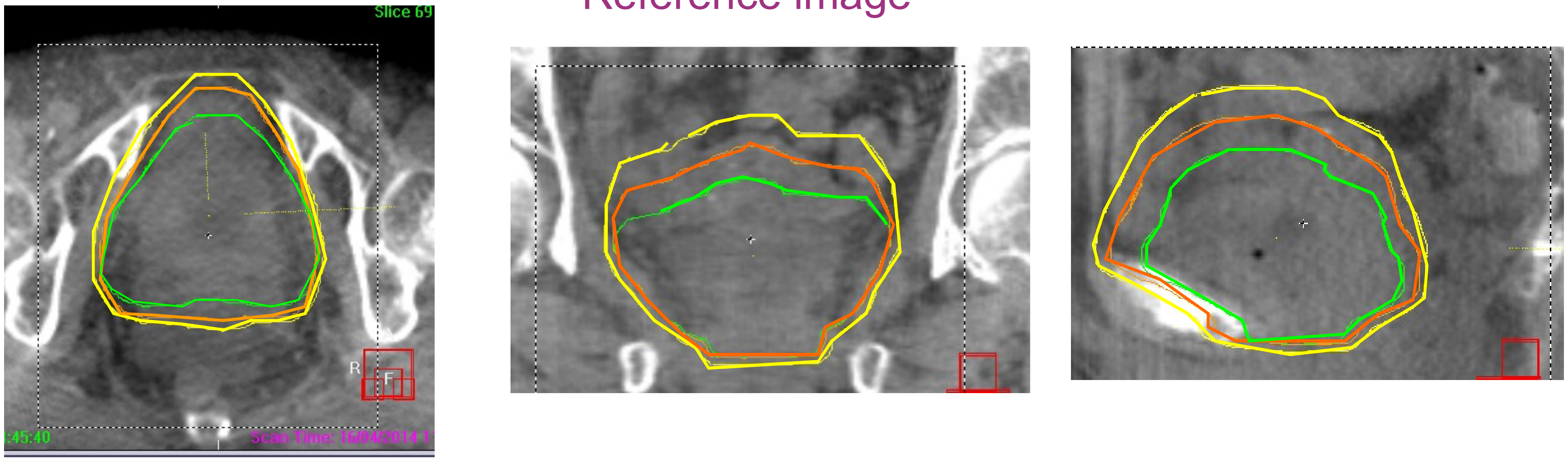
ii) reducing time to image acquisition (<30mins),

iii) ensure appropriate clinical assessment is made and that patient is not developing toxicity necessitating intervention and preventing from appropriate voiding

Case 3



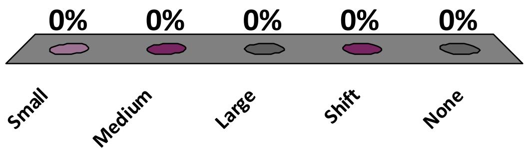
Reference image



Treatment image

Which choice is best?

A. Small
B. Medium
C. Large
D. Shift
E. None



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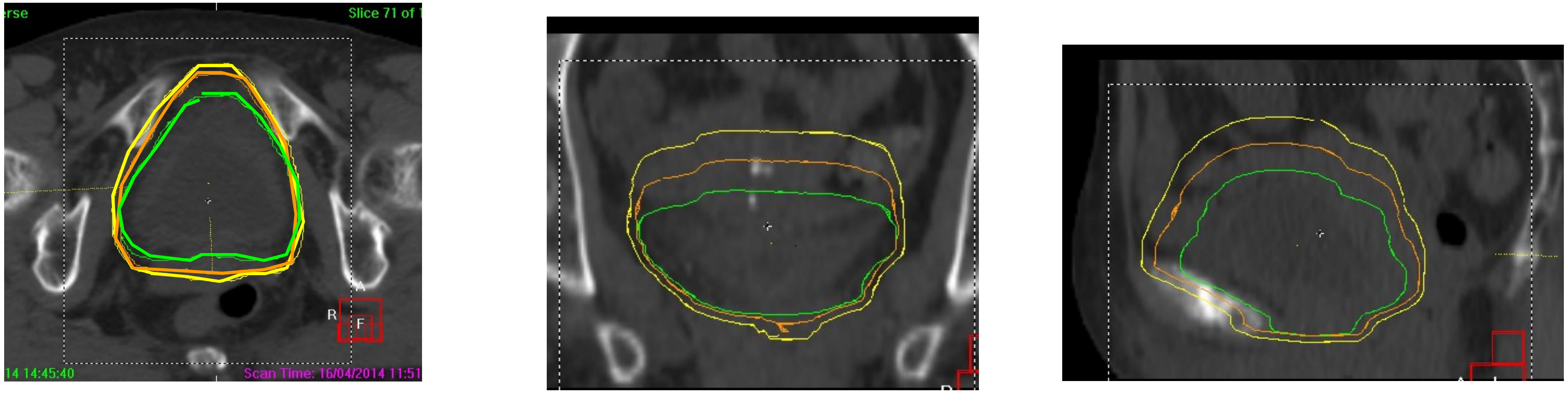
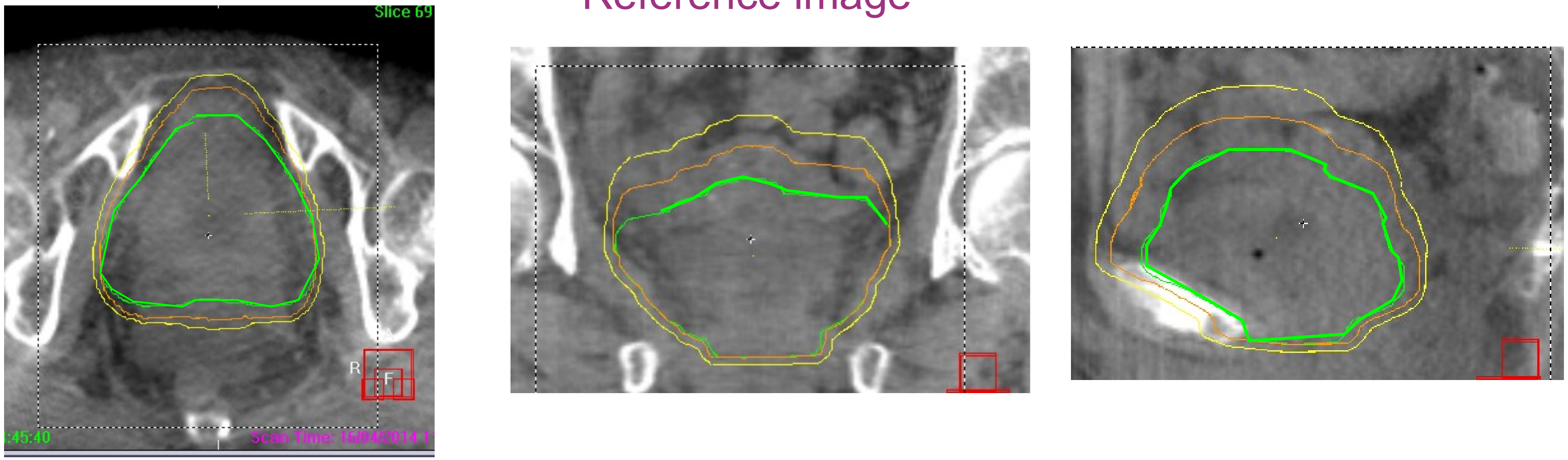
Case 3-Small



Reference image



Treatment image

Registration issues

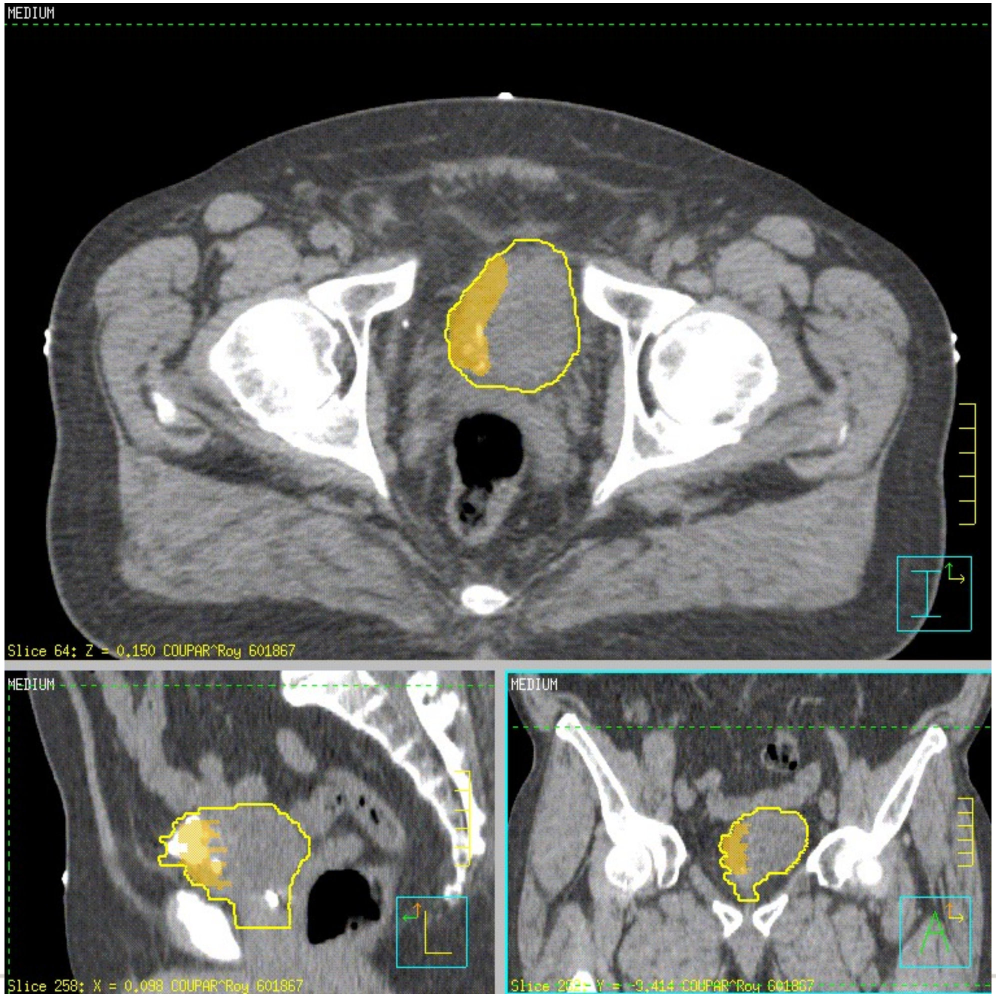
Consistent PTV selection between observers

No PTV is suitable- too large

Small

Replan of systematically smaller ?

Plan of the day – Full bladder



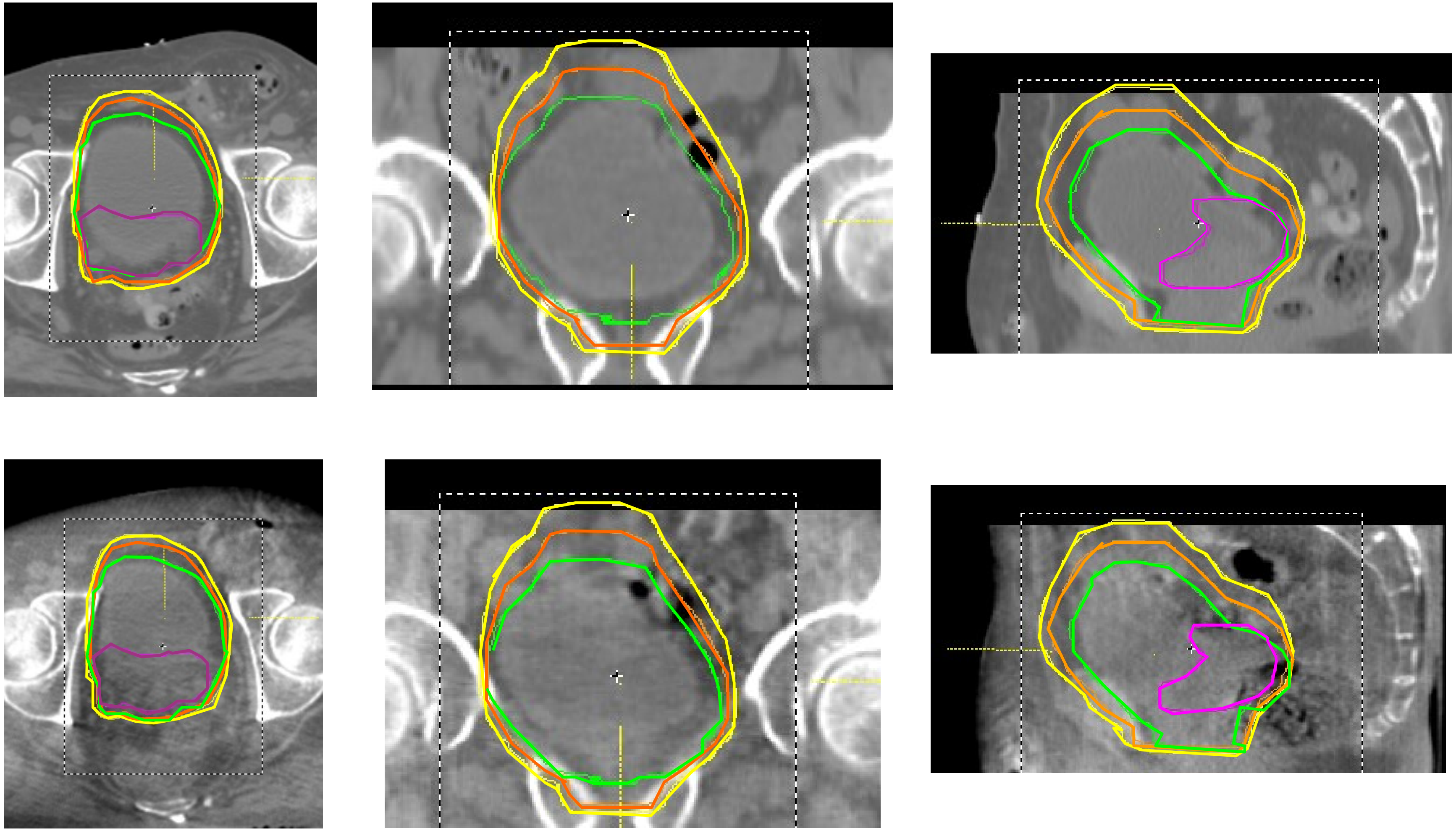
Partially' full bladder

30 and 60 min scans after emptying + 350mls of fluid

Concomitant boost

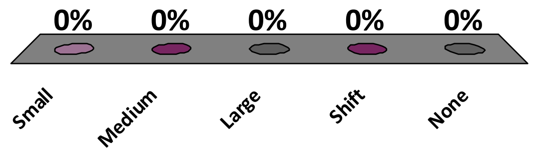
Plan of the day – Full bladder

Which outline is not good?



Gross assessment – which outline is NOT good

A. Small
B. Medium
C. Large
D. Shift
E. None



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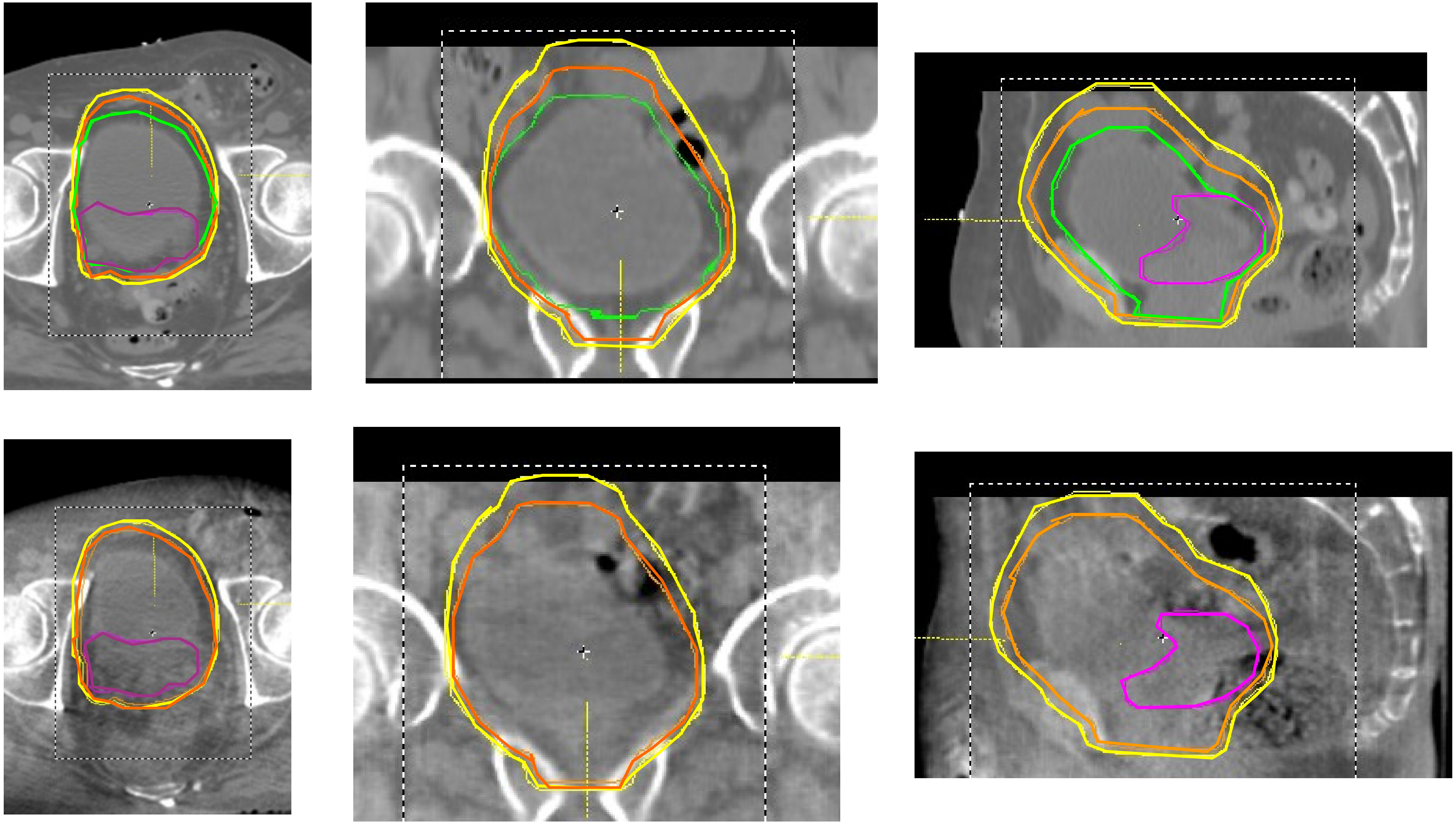
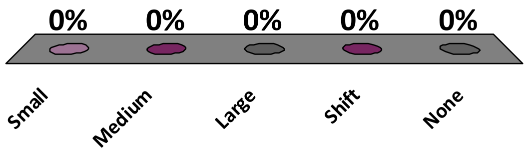
Plan of the day – Reject small



Which choice is best?

A. Small
B. Medium
C. Large
D. Shift
E. None



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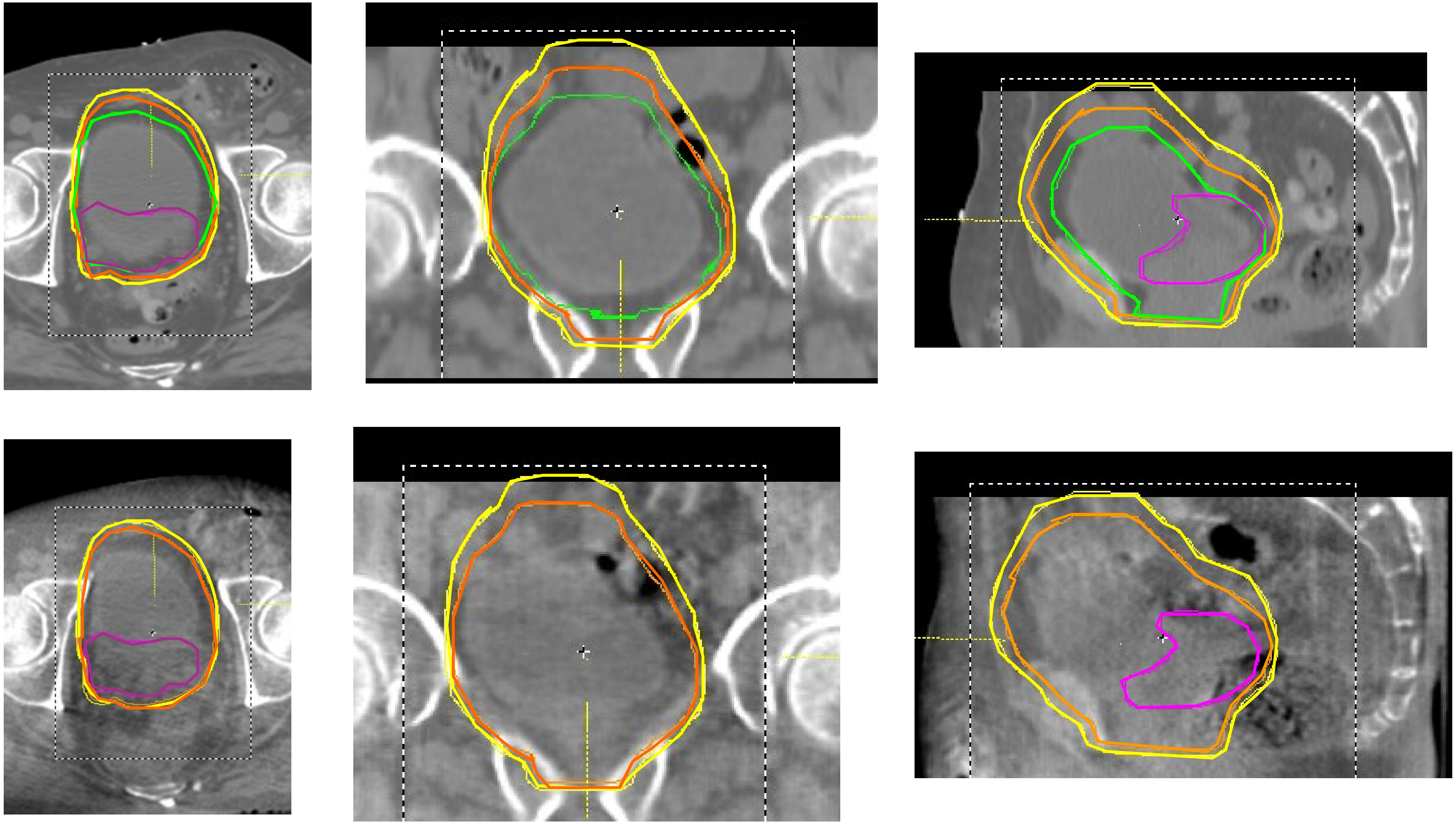
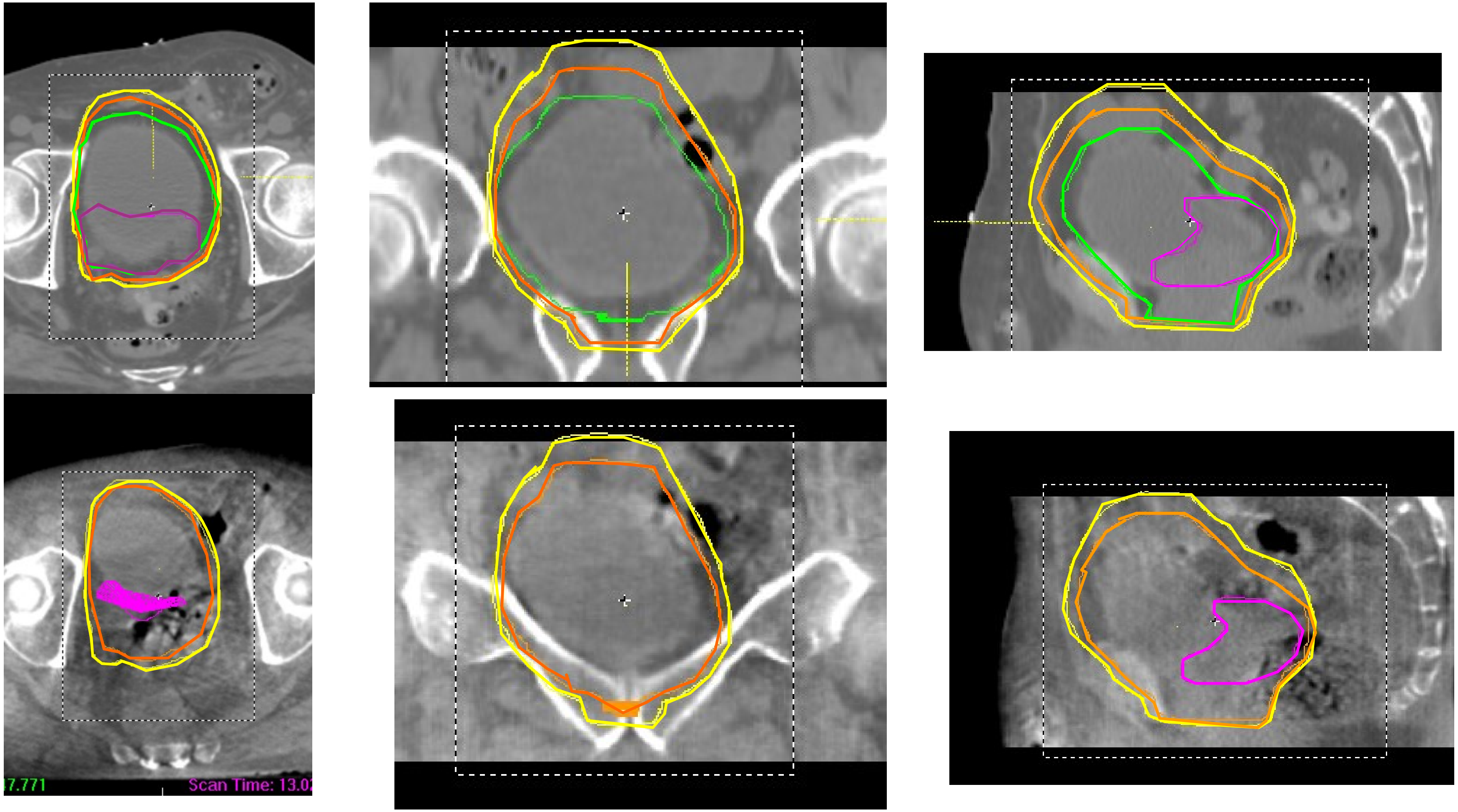
Plan of the day – Shift



Plan of the day – check



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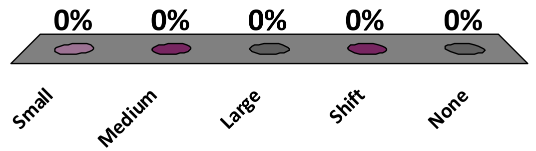
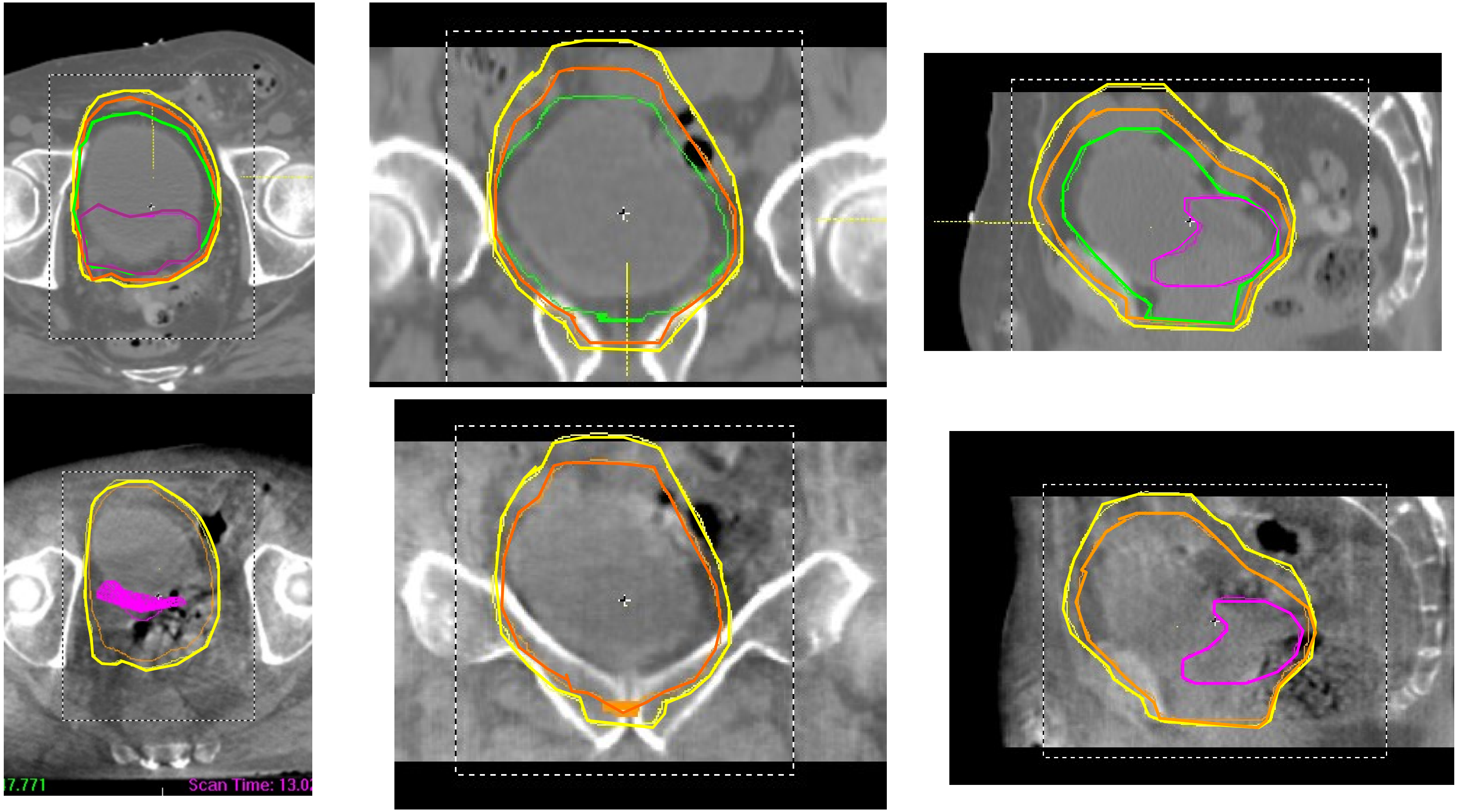
Which choice is best?

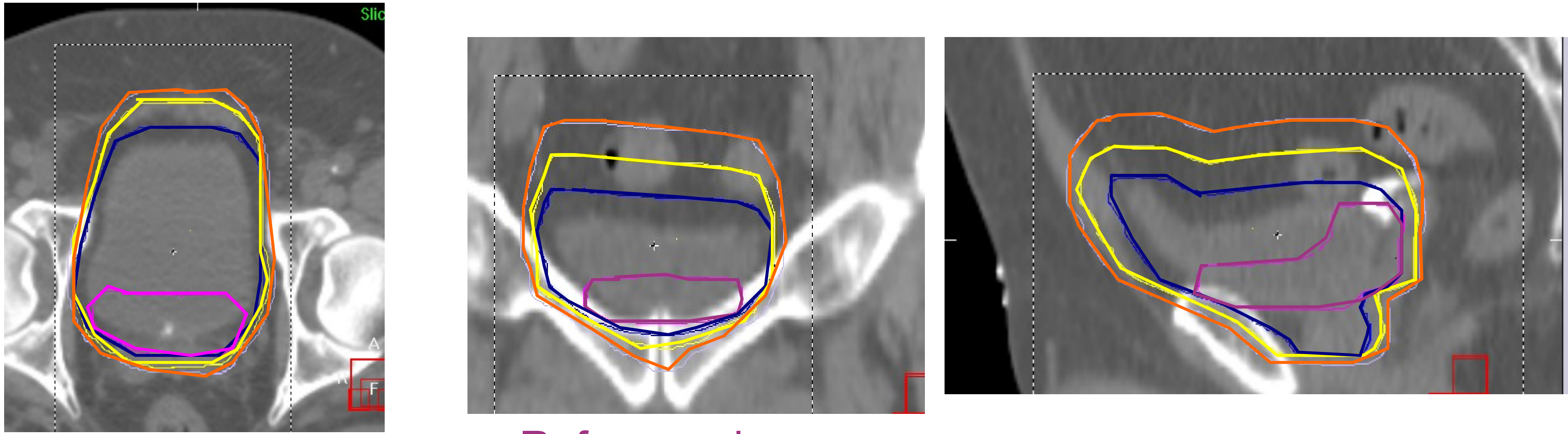
A. Small
B. Medium
C. Large
D. Shift
E. None



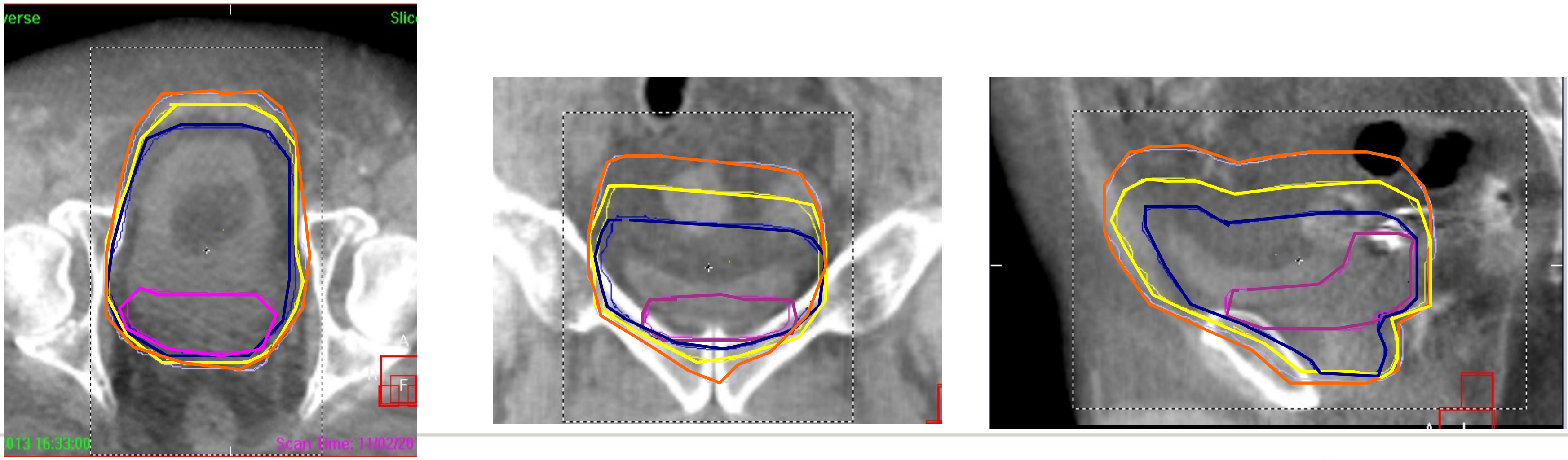
Plan of the day – check



Case 5



Reference image



Treatment image

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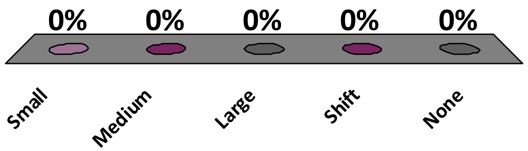
Which choice is best?

A. Small
B. Medium
C. Large
D. Shift
E. None



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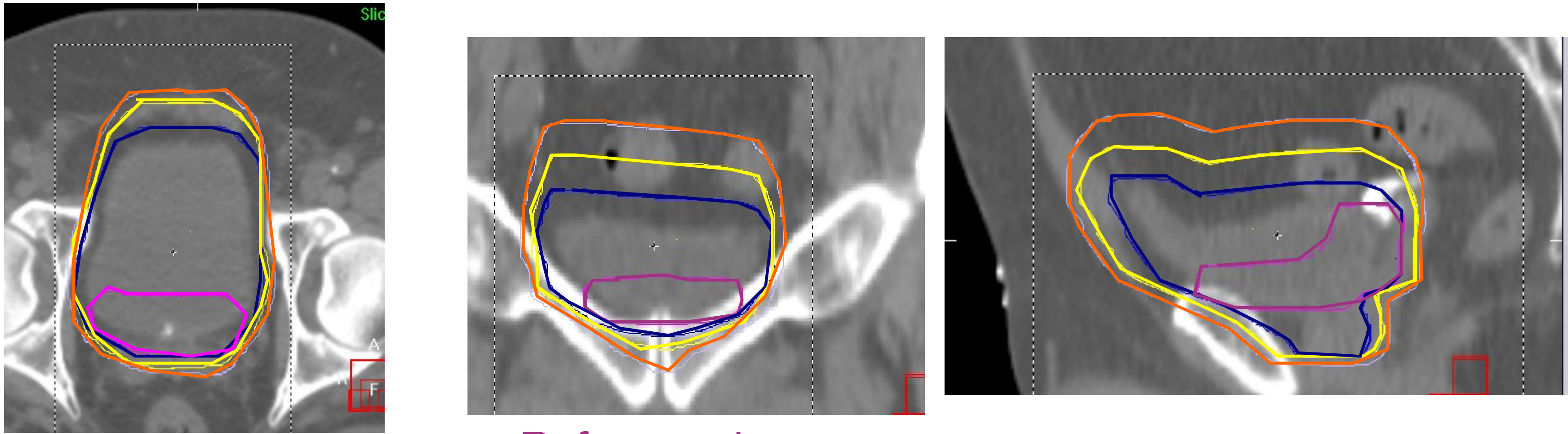
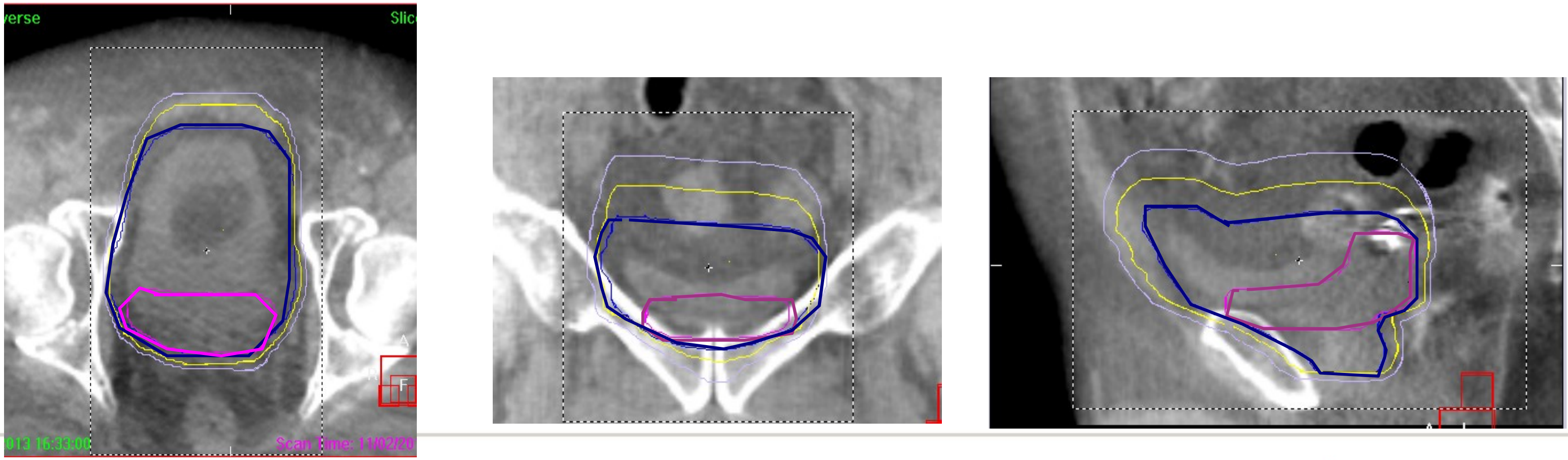
Case 5



Reference image



Treatment image

Significant shape change

Bladder too small

↓

Small plan provides appropriate coverage of bladder but normal tissue sparing from high dose region compromised

↓

Appropriate to consider treatment with small plan

↓

Requires clinical review prior to next fraction.
Assessment :-
i) general hydration status
ii) development of urinary toxicity requiring intervention (preventing from appropriate holding)
iii) increasing time to image acquisition>30mins and, or
iv) increasing volume of fluids in drinking protocol

Registration issues

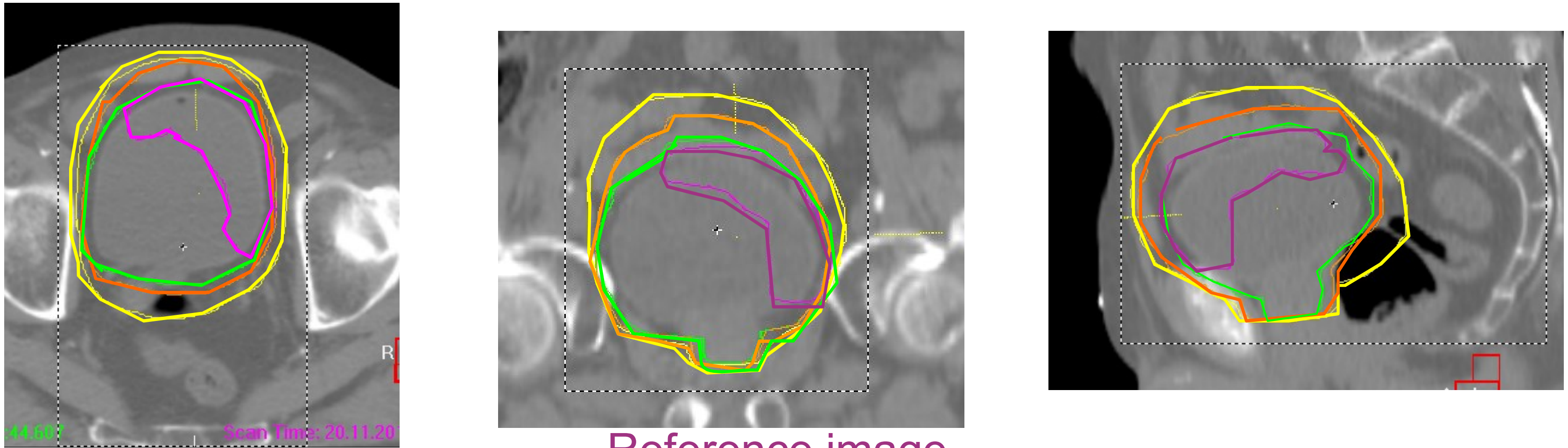
Consistent PTV selection between observers

No PTV is suitable- too large

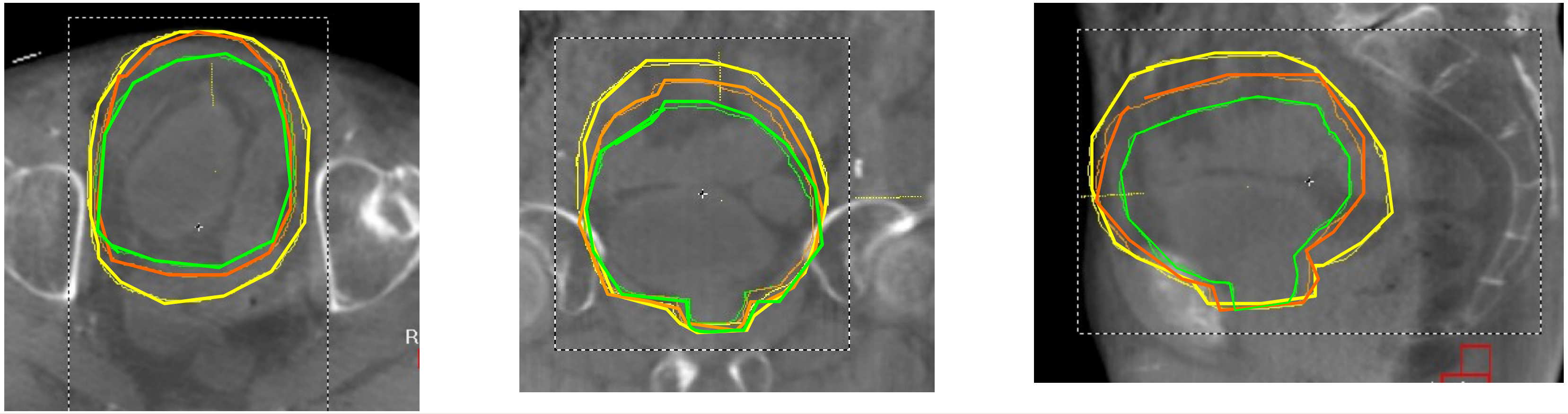
No PTV is suitable – too small

Replan of systematically smaller ??

Case 6



Reference image



Treatment image

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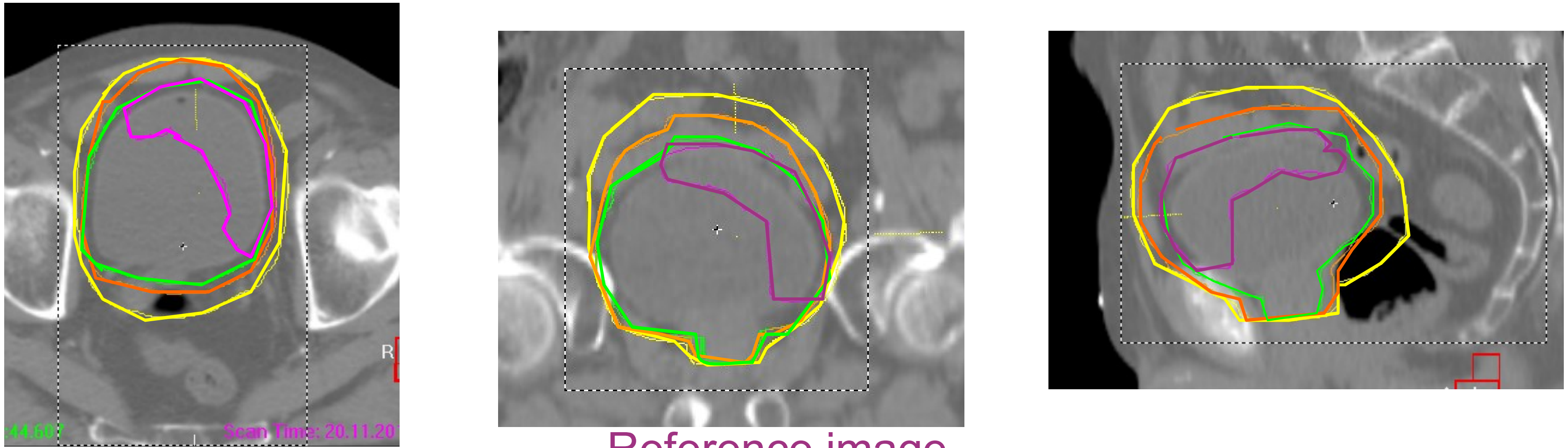
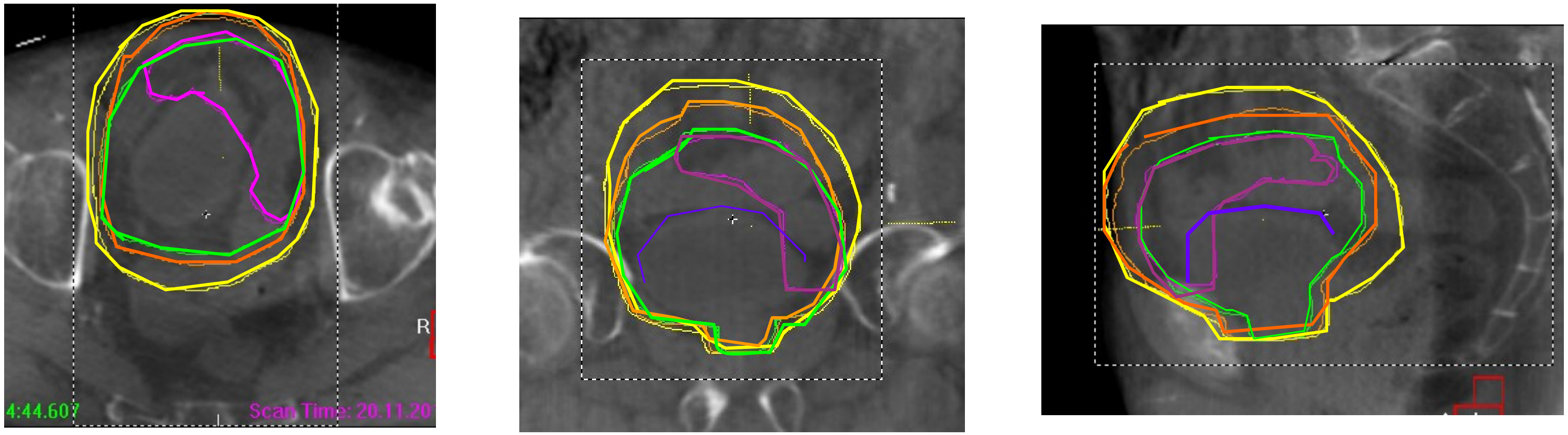
Case 6



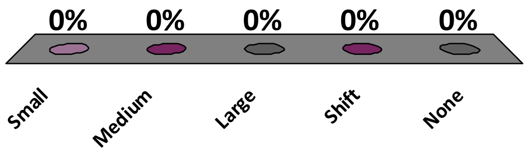
Reference image



Treatment image

Which choice is best?

A. Small
B. Medium
C. Large
D. Shift
E. None



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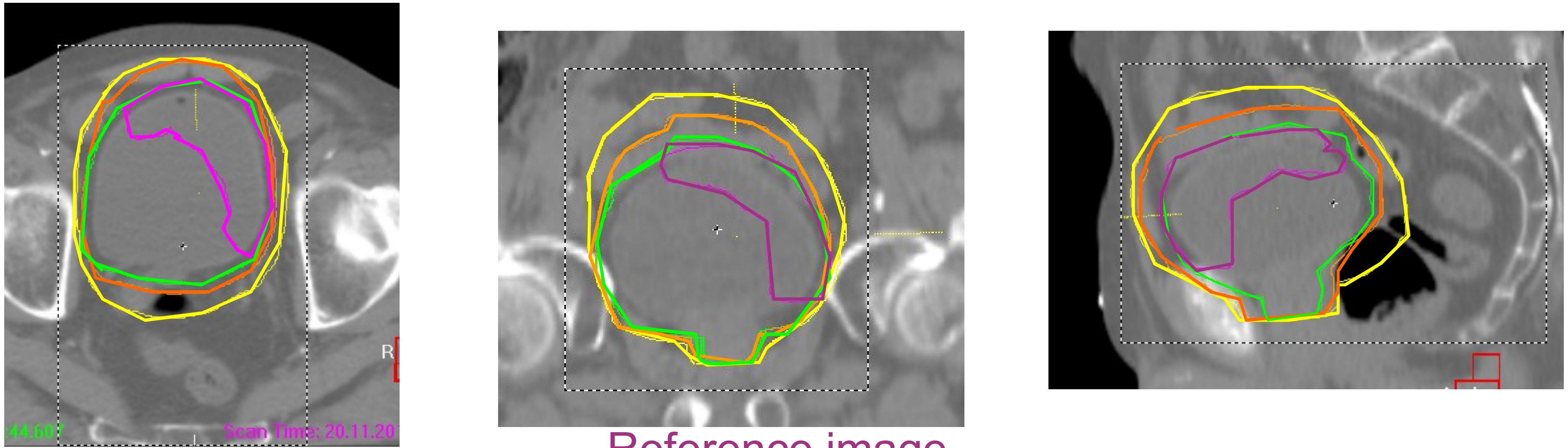
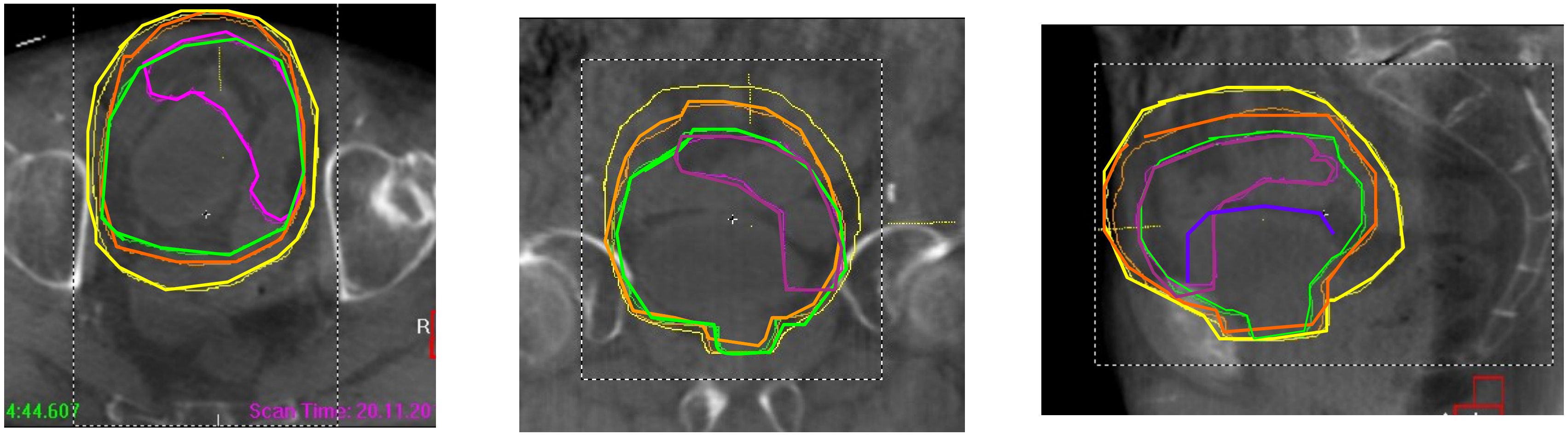
Case 6-bowel boost!



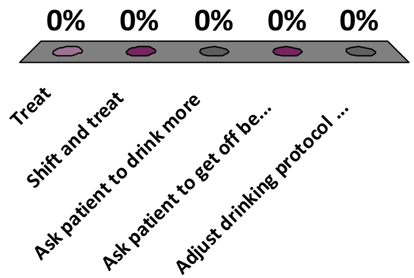
Reference image



Treatment image

Action

A. Treat
B. Shift and treat
C. Ask patient to drink more
D. Ask patient to get off bed and drink more
E. Adjust drinking protocol for tomorrow



Significant shape change

Bladder too small

↓

Small plan provides appropriate coverage of bladder but normal tissue sparing from high dose region compromised

↓

Appropriate to consider treatment with small plan

↓

Requires clinical review prior to next fraction.
Assessment :-
i) general hydration status
ii) development of urinary toxicity requiring intervention (preventing from appropriate holding)
iii) increasing time to image acquisition>30mins and, or
iv) increasing volume of fluids in drinking protocol

Significant shape change

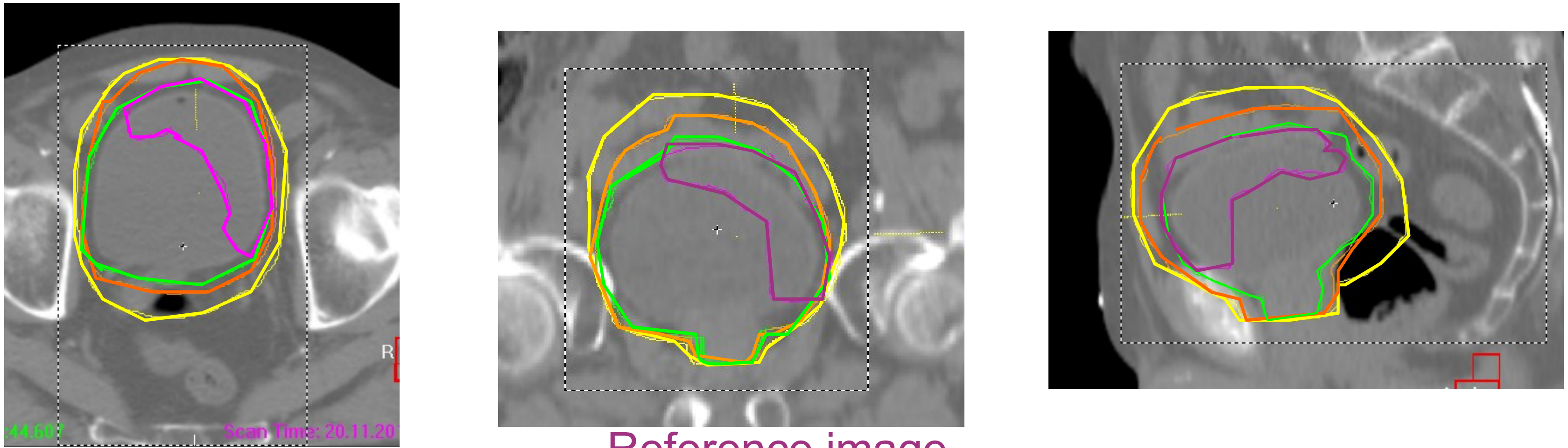
Bladder too small

Small plan provides appropriate coverage of bladder but normal tissue sparing from high dose region compromised

Appropriate to consider treatment with small plan

Requires clinical review prior to next fraction.
Assessment :-
i) general hydration status
ii) development of urinary toxicity requiring intervention (preventing from appropriate holding)
iii) increasing time to image acquisition>30mins and, or
iv) increasing volume of fluids in drinking protocol

Case 6 – extra drinking-40mins + more water



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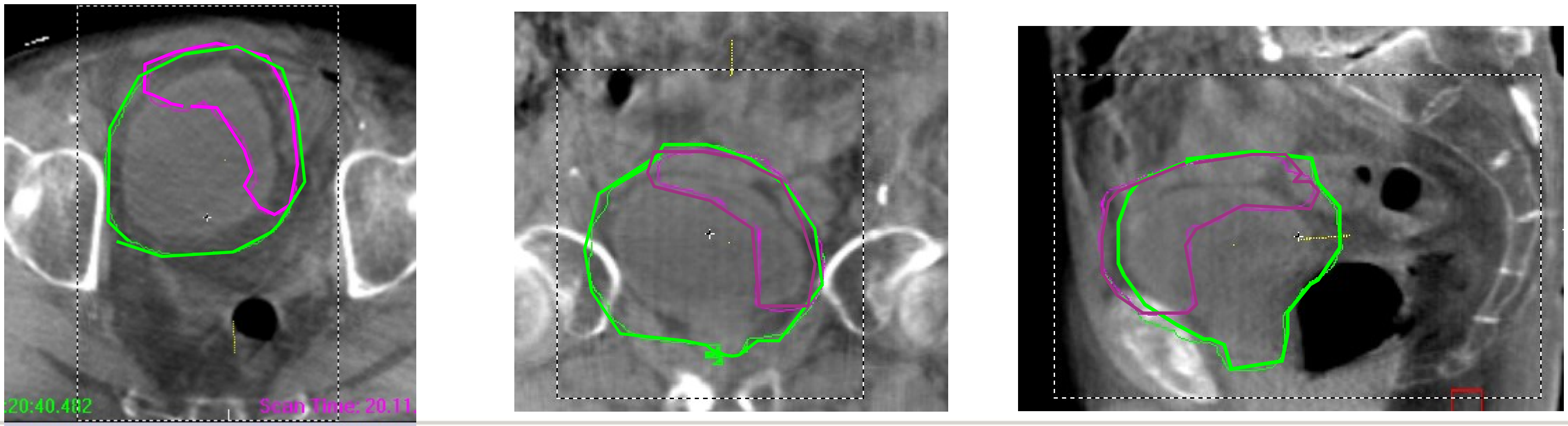
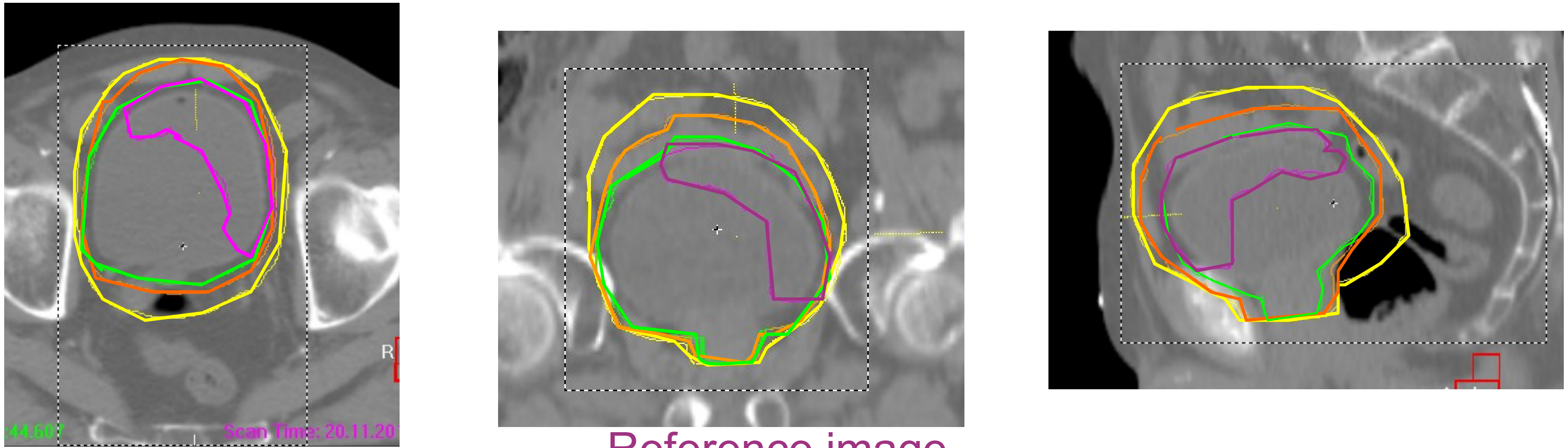


Treatment image

Case 6 (Day 2)- bony match



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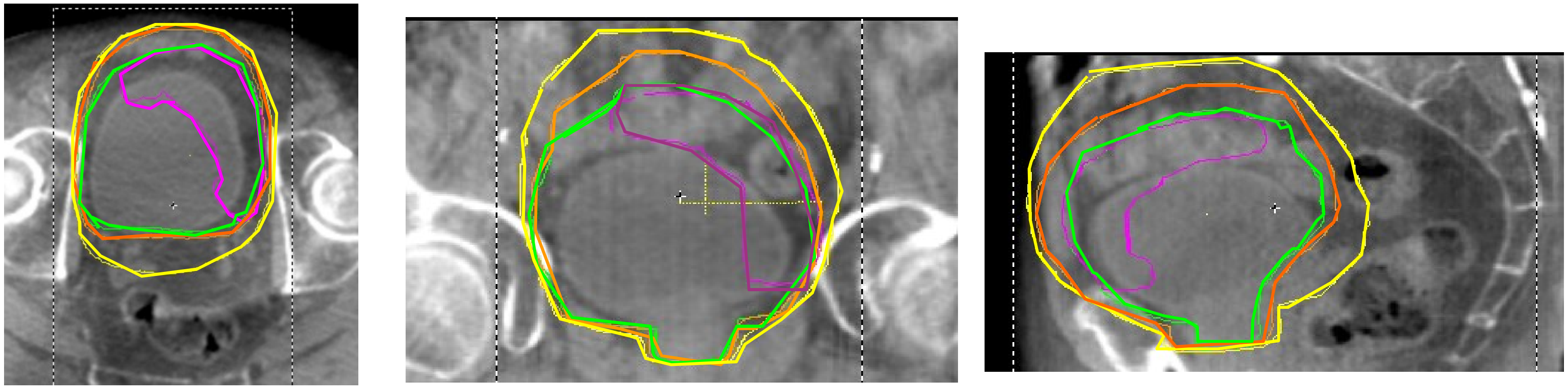
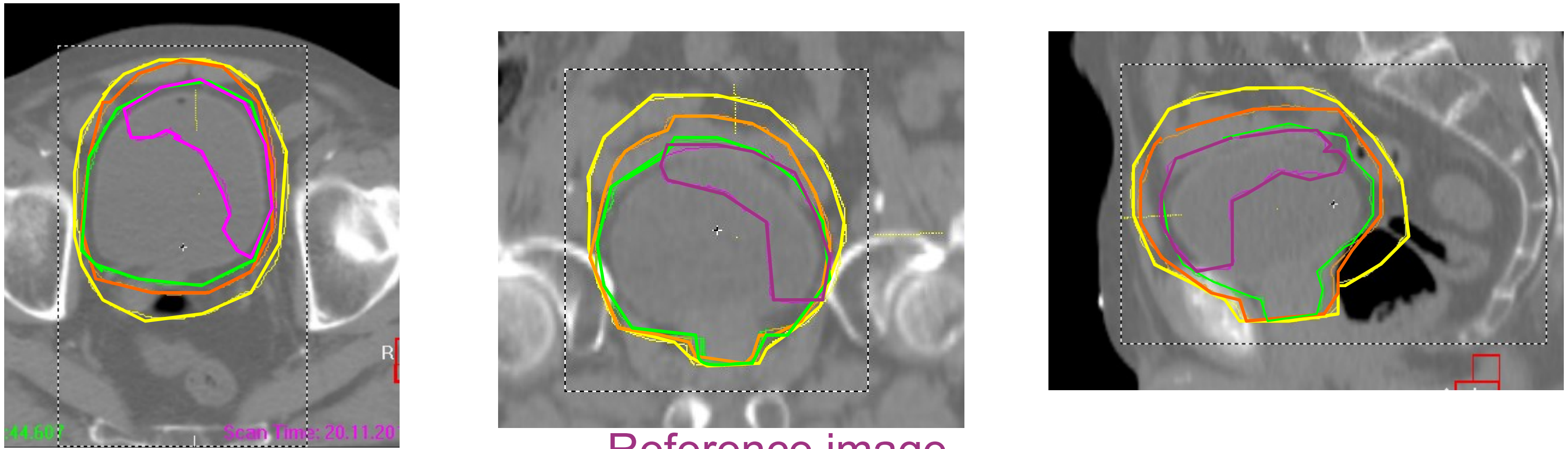


Treatment image

Case 6 - soft tissue adjustment



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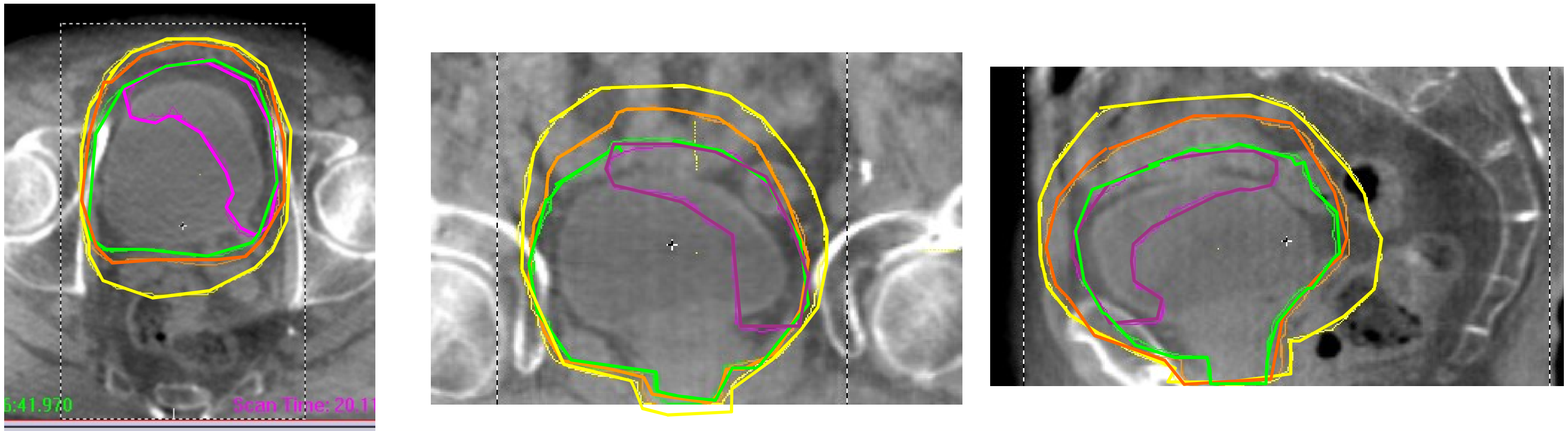
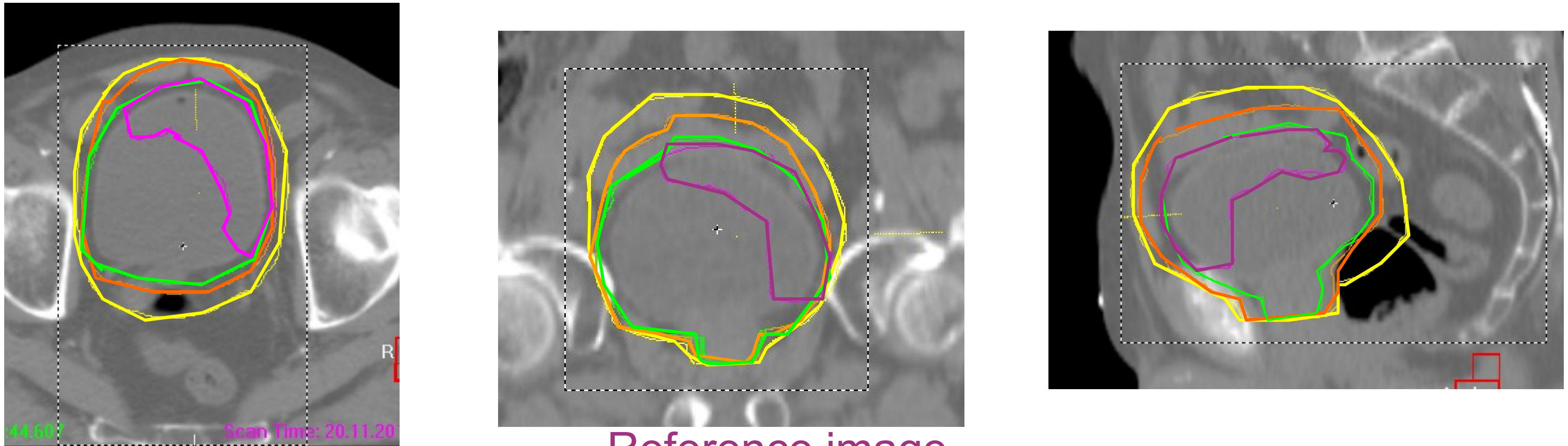


Treatment image

Check coverage



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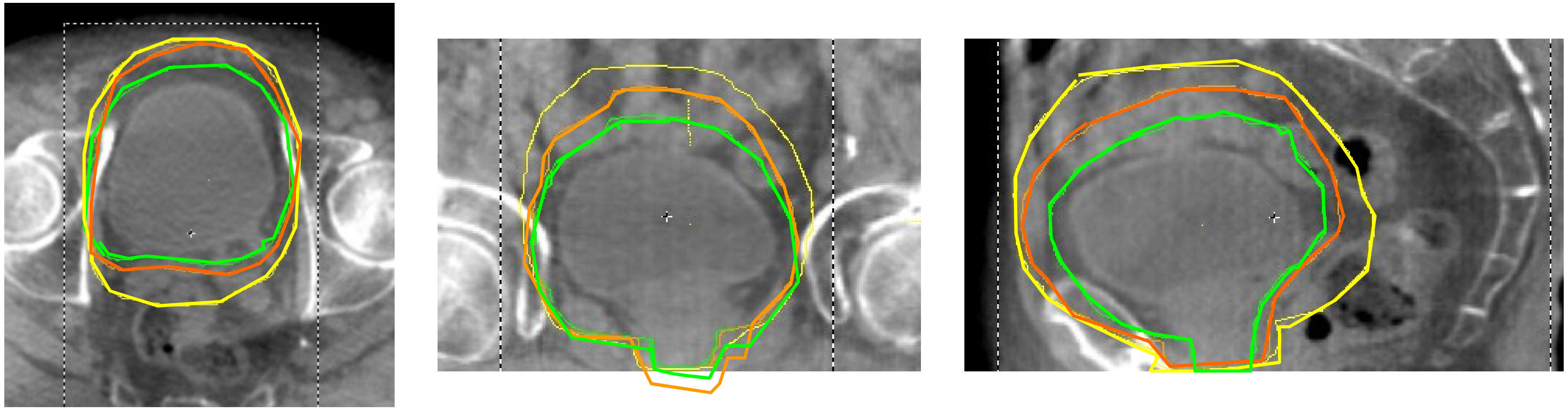

Treatment image

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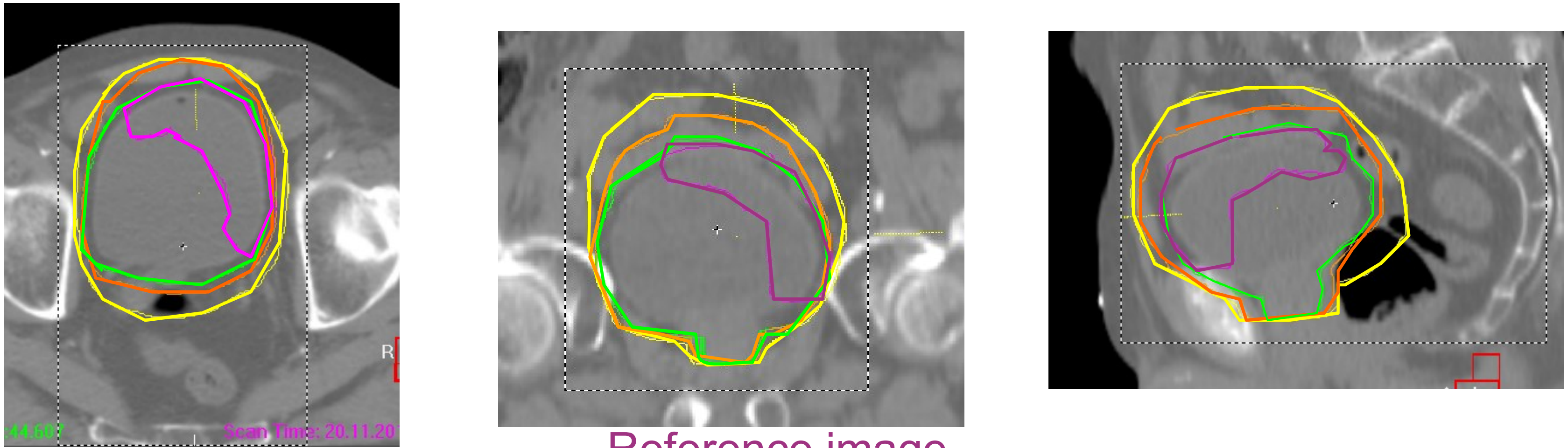
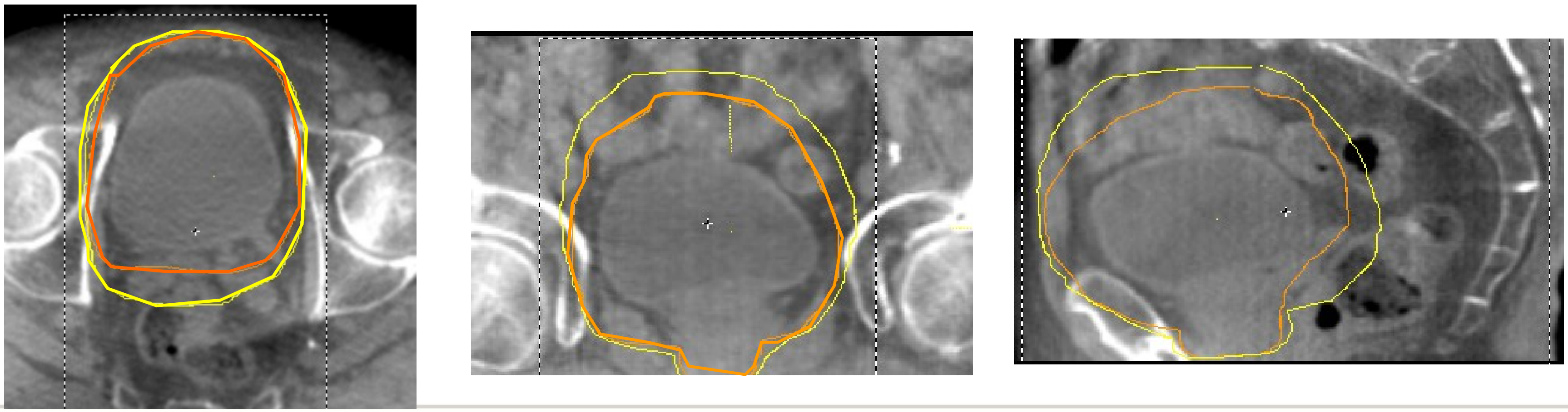
Check coverage

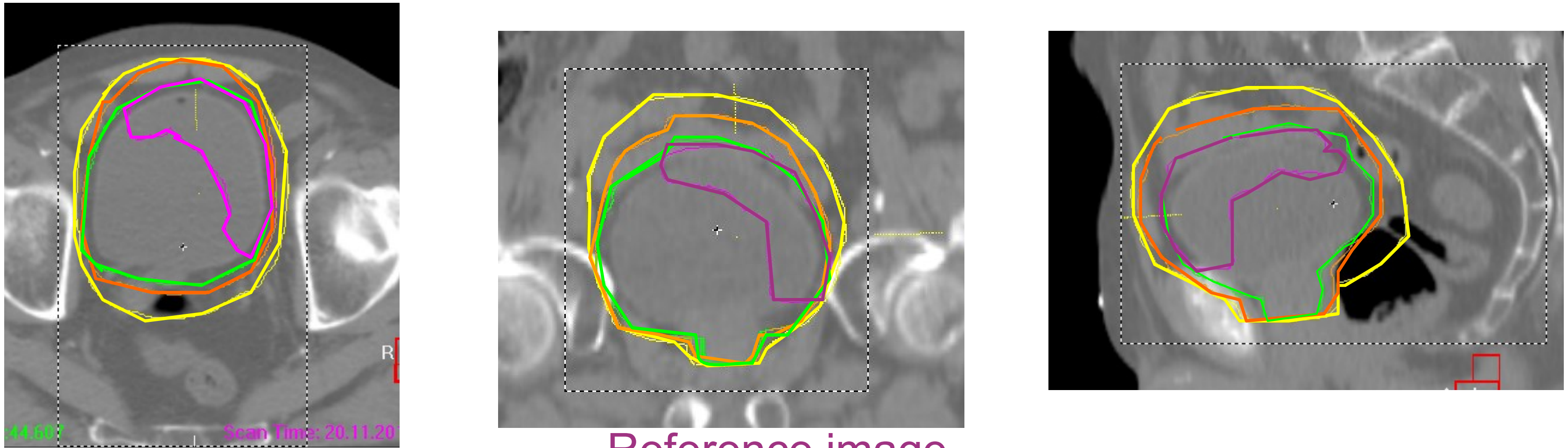


Reference image



Treatment image

Check boost



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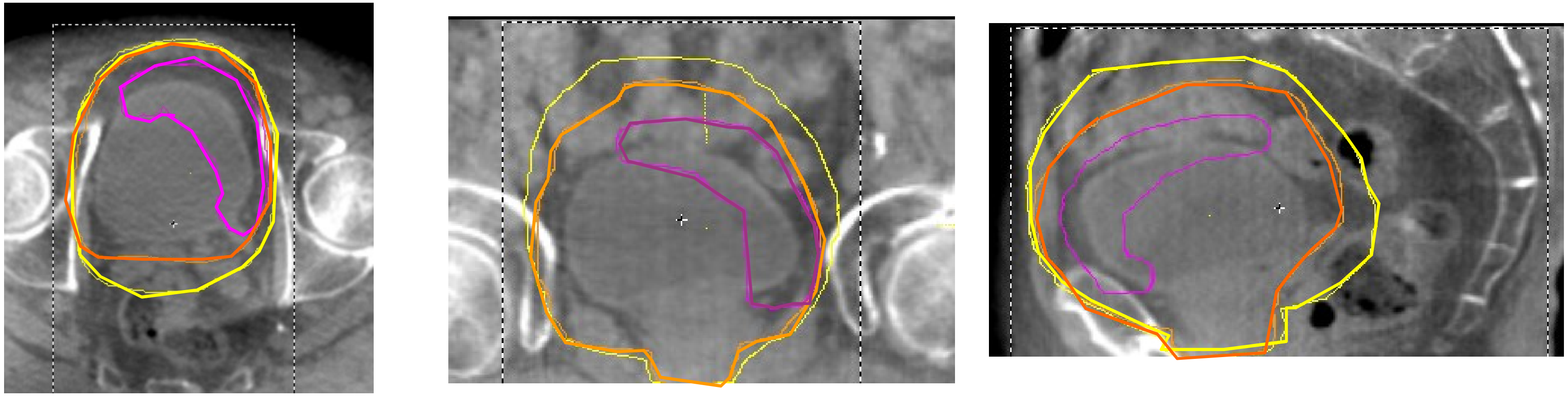
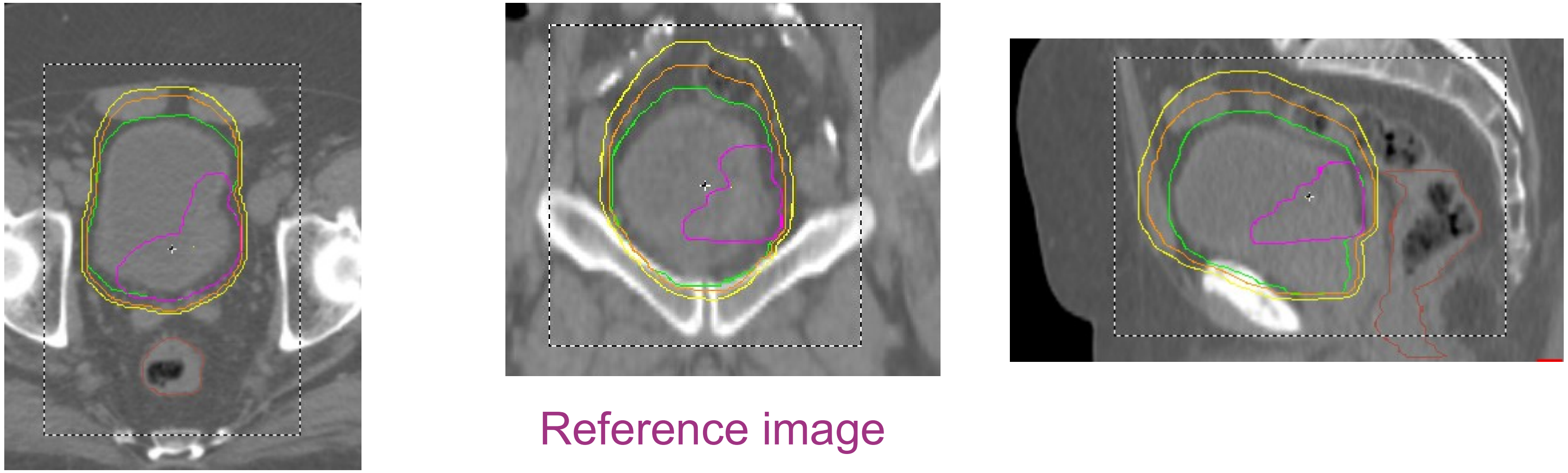


Treatment image

Case 7 - gas



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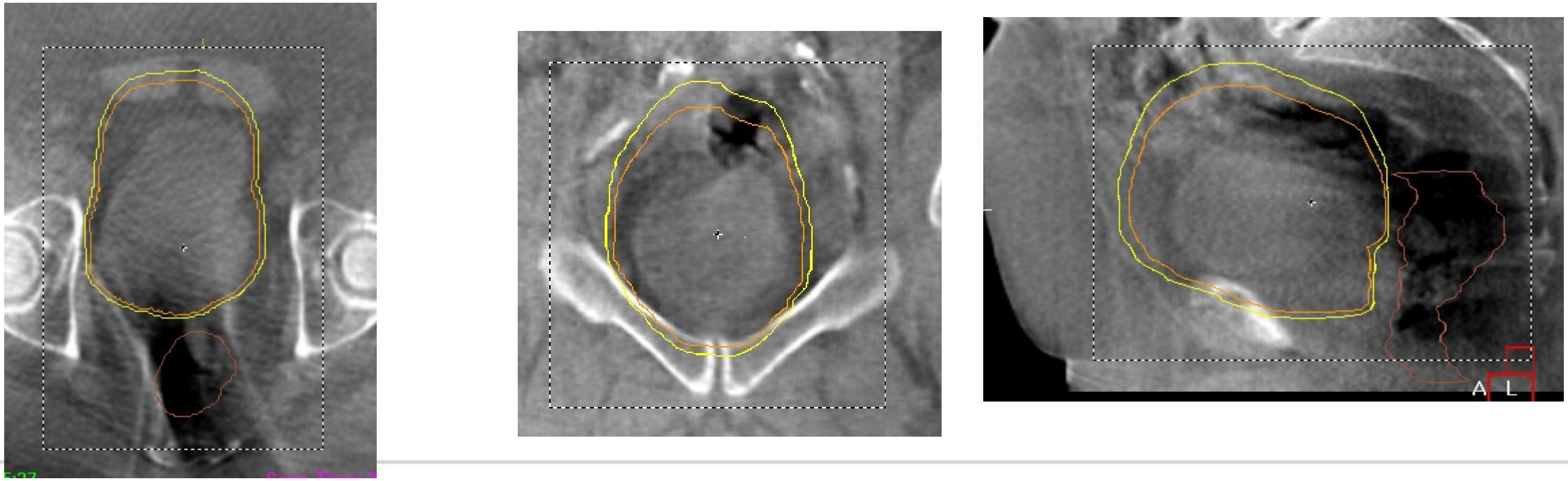


Treatment image

Significant shape change

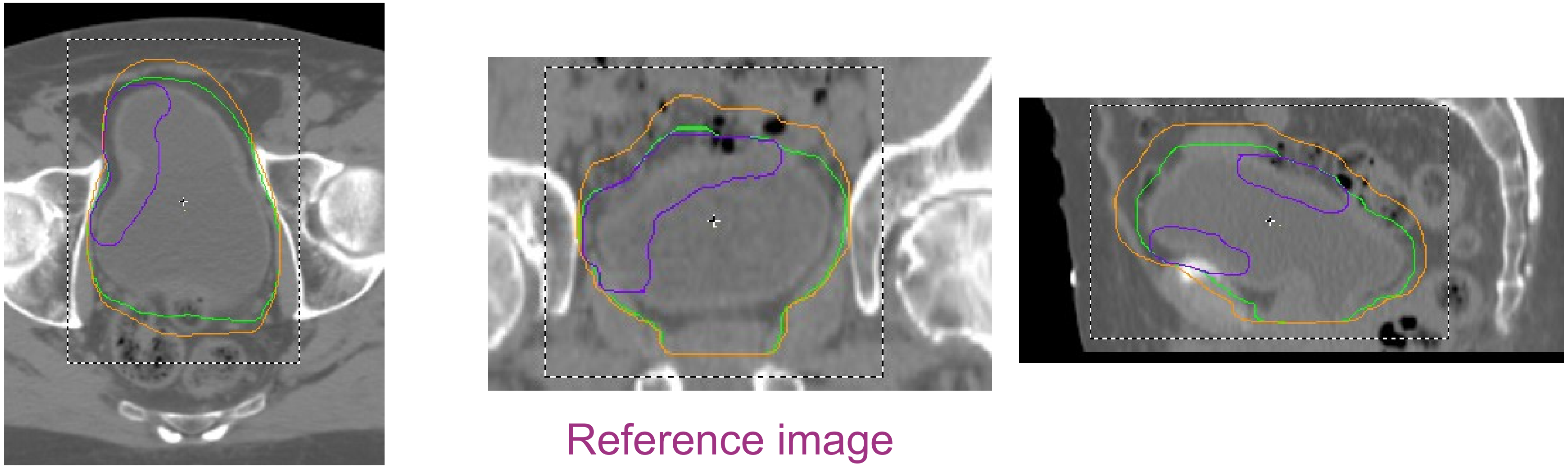
Bladder too big

No plan provides appropriate coverage

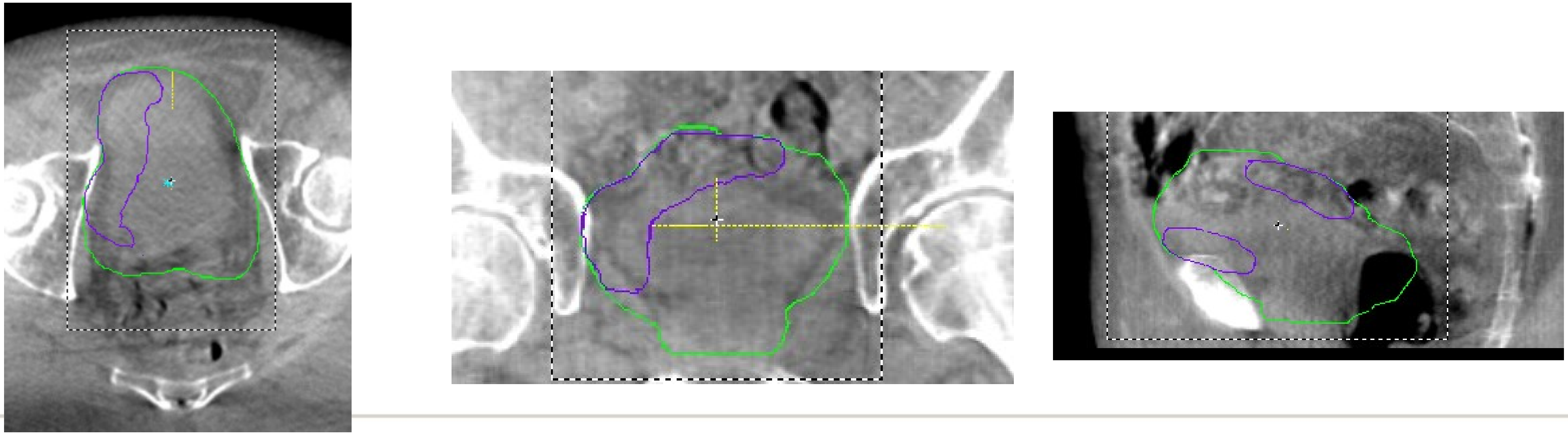
Shape change due to rectal filling (flatus/faeces)

Remove patient from couch, empty bowel (and bladder), repeat drinking protocol but consider clinical review prior to next fraction to determine whether laxative or suppositories indicated

Case 8 - unusual

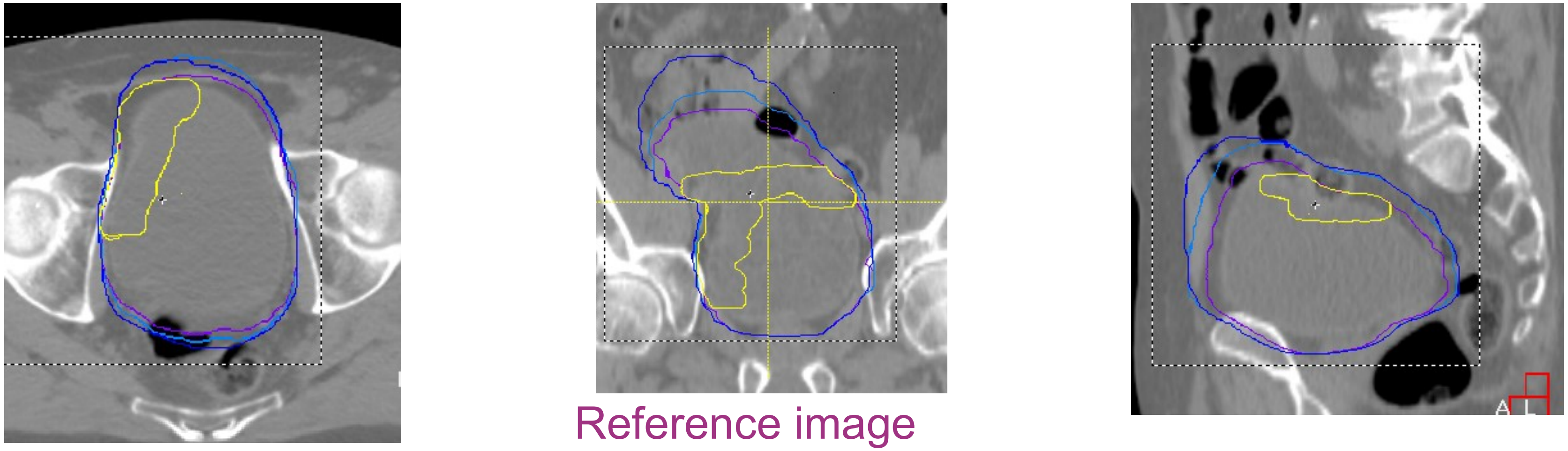


Reference image

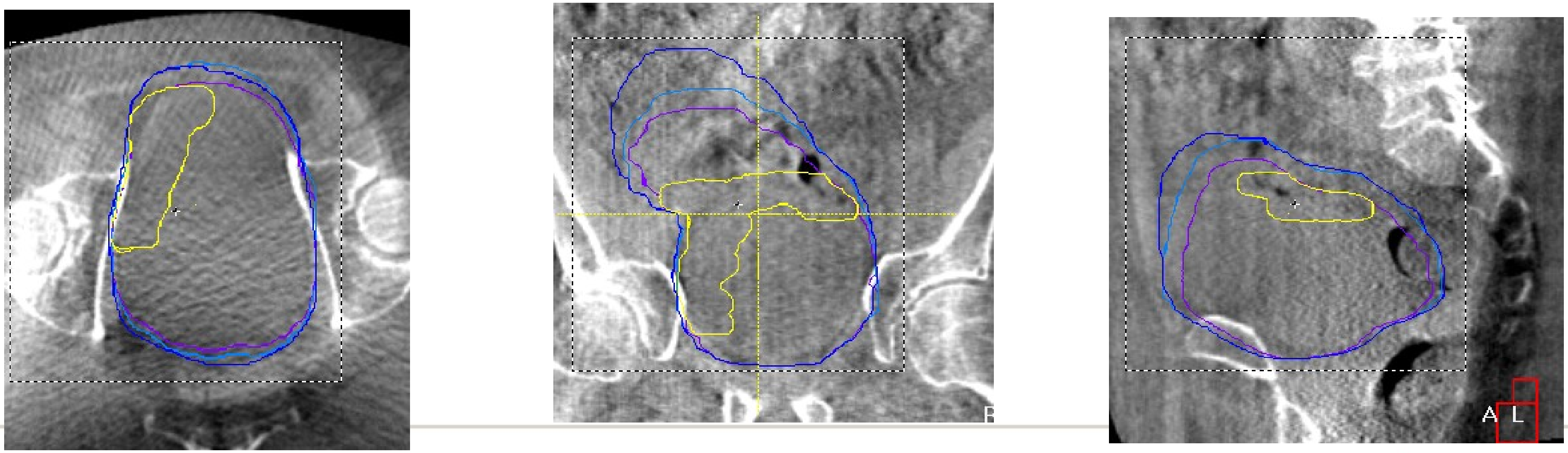


Treatment image

Case 8- unusual

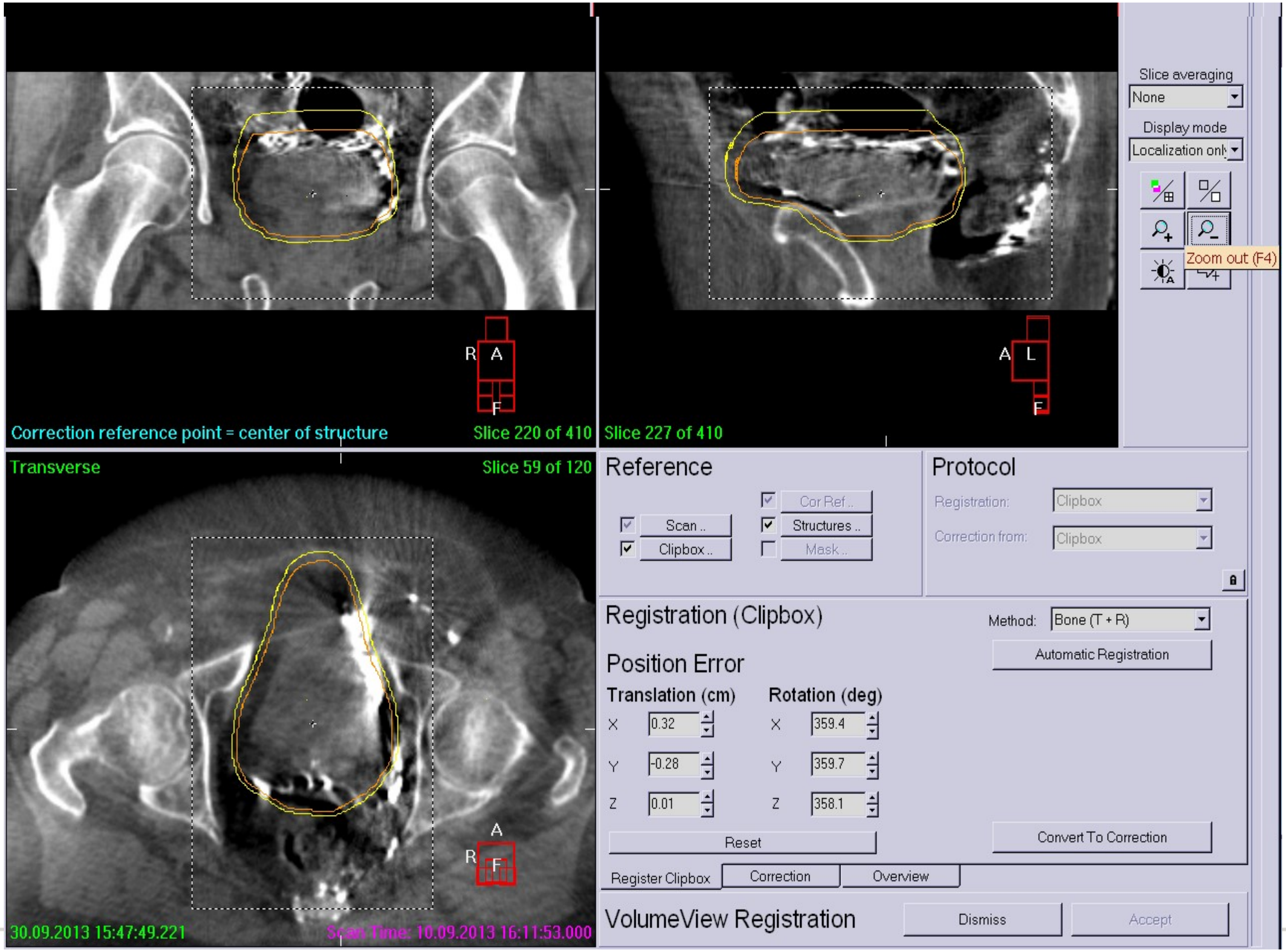


Reference image



Treatment image

Case 9- boost and contrast?



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HYBRID and RAIDER- assessment

HYBRID

RAIDER

244 individuals (HYBRID=73, RAIDER=171)

24 recruiting centres.

86% of individuals achieved the score required for the QA approval on their first attempt

More Registration issues

Tolerance for movement   for example >1cm

Re plan if systematically smaller

Bladder and nodes

Training for selection

Guidelines for selection

Acknowledgements

Robert Huddart

Shaista Hafeez

Susan Lalondrelle

Fiona McDonald

Helen Taylor

RTTQA team

QA of deformable image registration and contour propagation

Marcel van Herk

on behalf of the imaging group

Institute of Cancer Sciences,
University of Manchester / The Christie

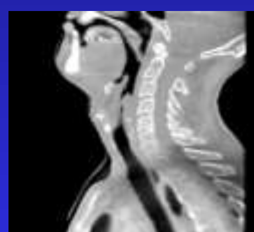
With slides from:

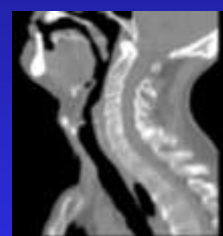
Netherlands Cancer Institute

Academic Medical Center

Terminology

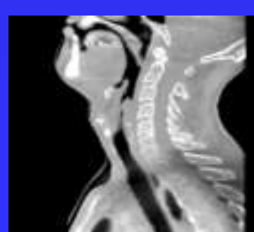
- Image registration:
  - The process of finding the transformation that aligns two images

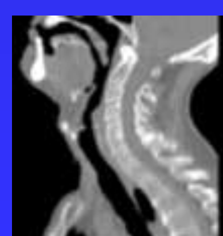




1	0	0	Tx
0	1	0	Ty
0	0	1	Tz
0	0	0	1

- Image fusion:
  - Displaying a combination of aligned images





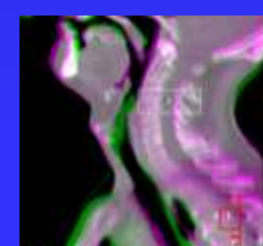


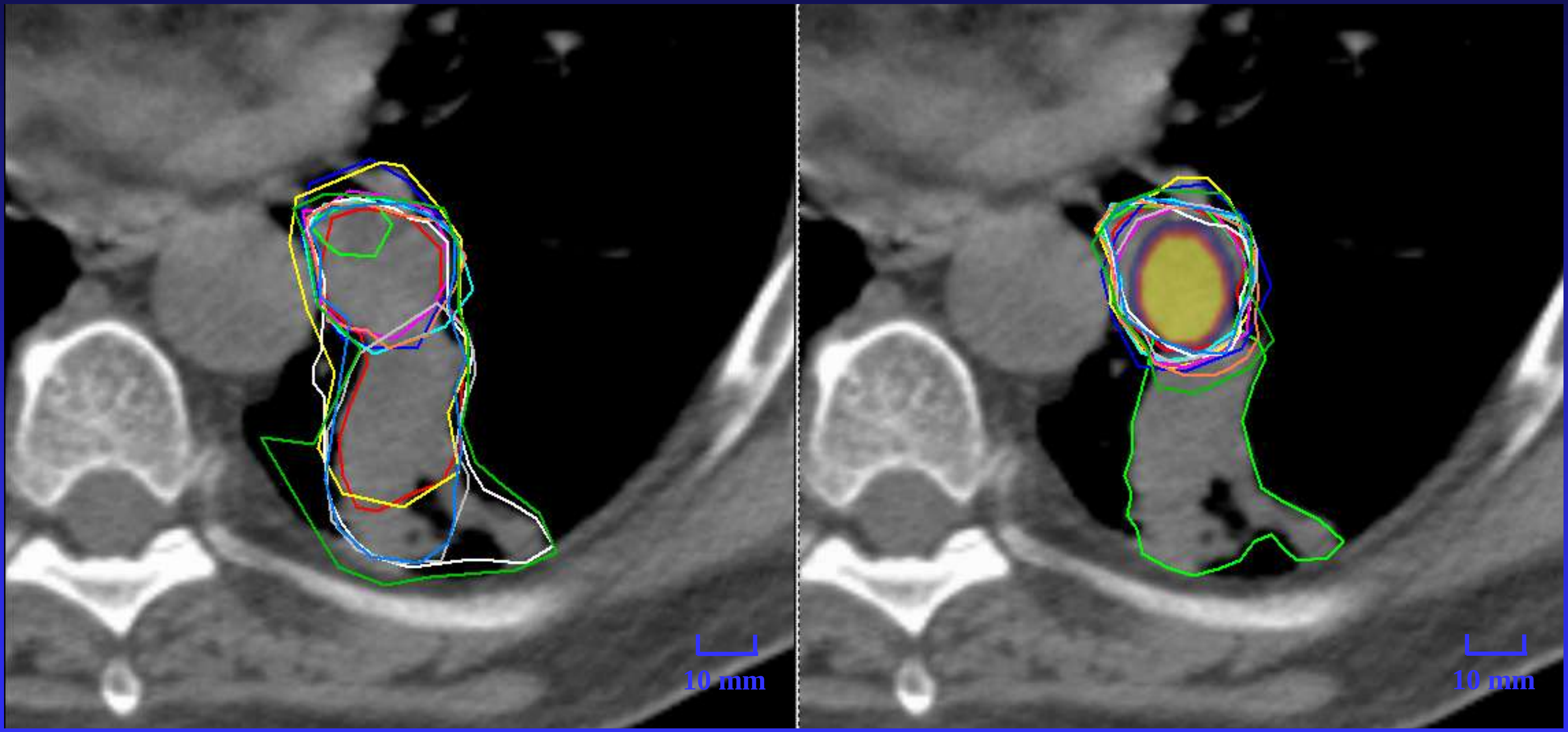
Image registration

- Find translation….deformation to align two 2D..4D data sets (2 .. 1000000 degrees of freedom)
- Allows combination of scans on a point by point basis
- Applications:
  - Complementary data
  - Motion tracking and compensation (imaging)
  - Image guidance
  - Adaptive radiotherapy
  - Response monitoring
  - Dose accumulation
  - Data mining

easy

difficult

Delineation: CT versus CT + PET reduce observer variations

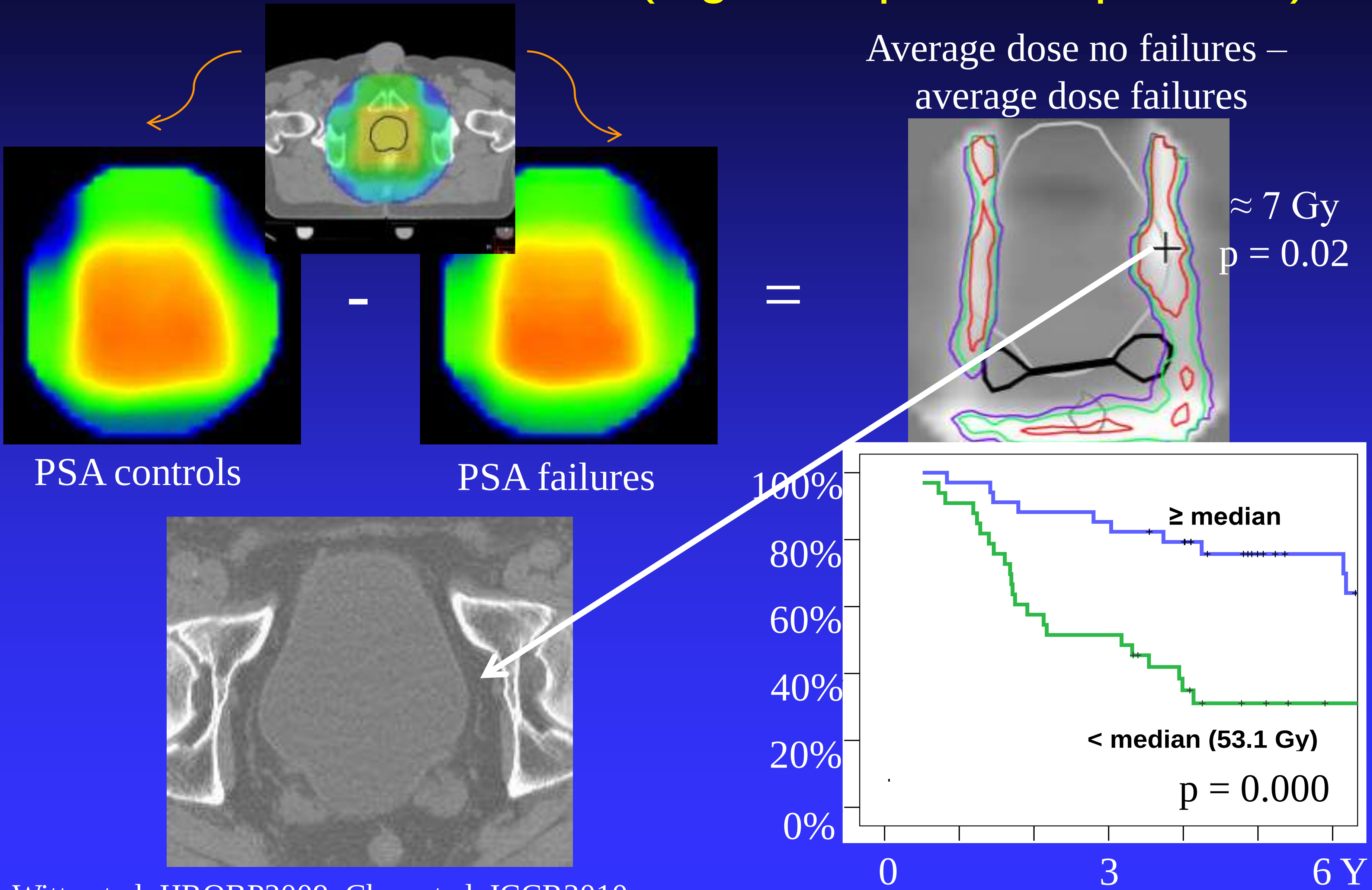


CT

CT + PET

11 observers from 5 institutions delineated
22 patients (stage I to IIIB)

Estimate pattern of spread from response to incidental dose in clinical trial data (high risk prostate patients)



Witte et al, IJROBP2009; Chen et al, ICCR2010

Types of transformation

Rigid:

- Translation → for round objects (single seed)
- Translation + Rotation

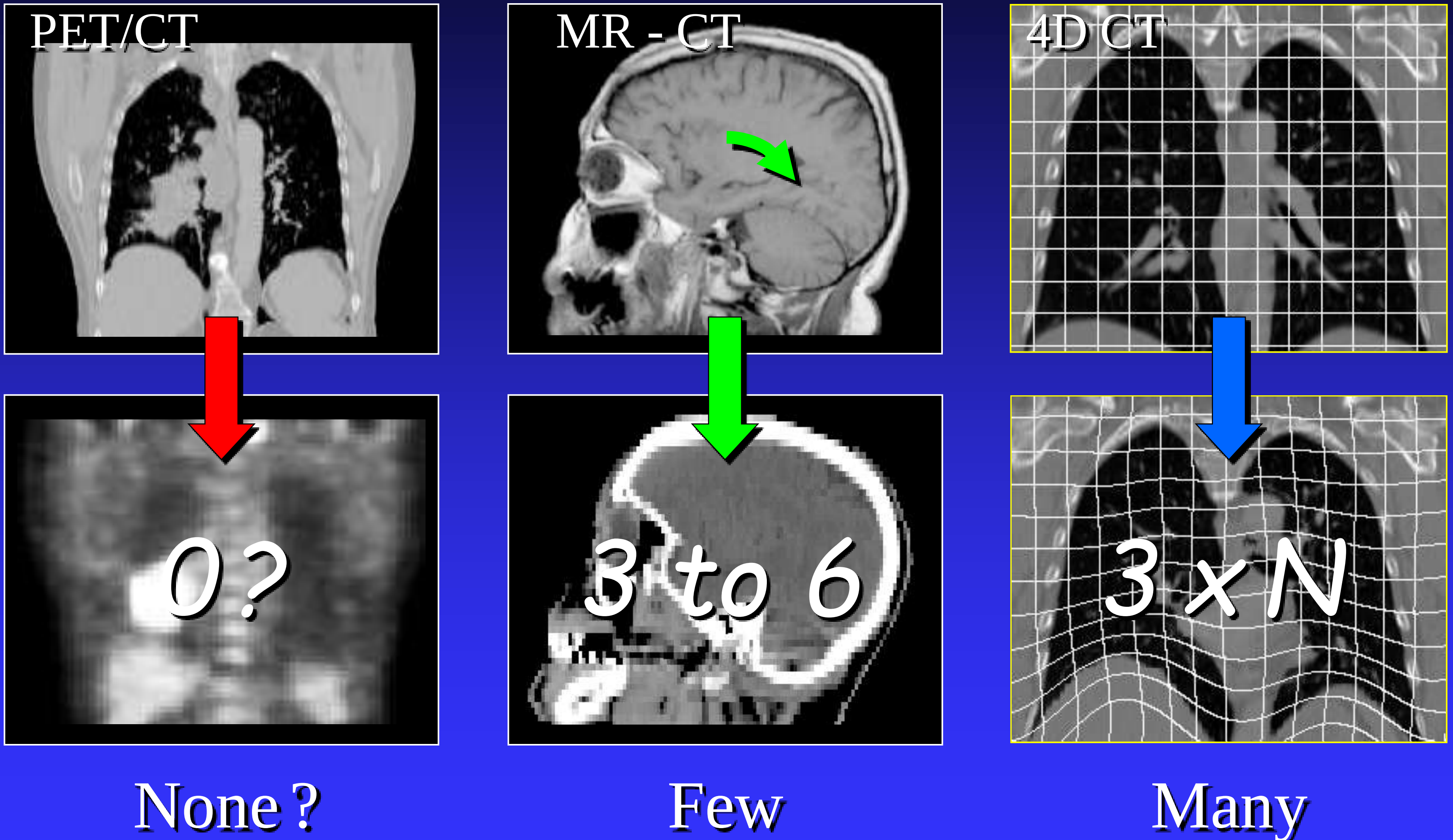
Deformable:

- Deformation based on control points

Rigid registration for deformed patients only works well if you limit the region of interest

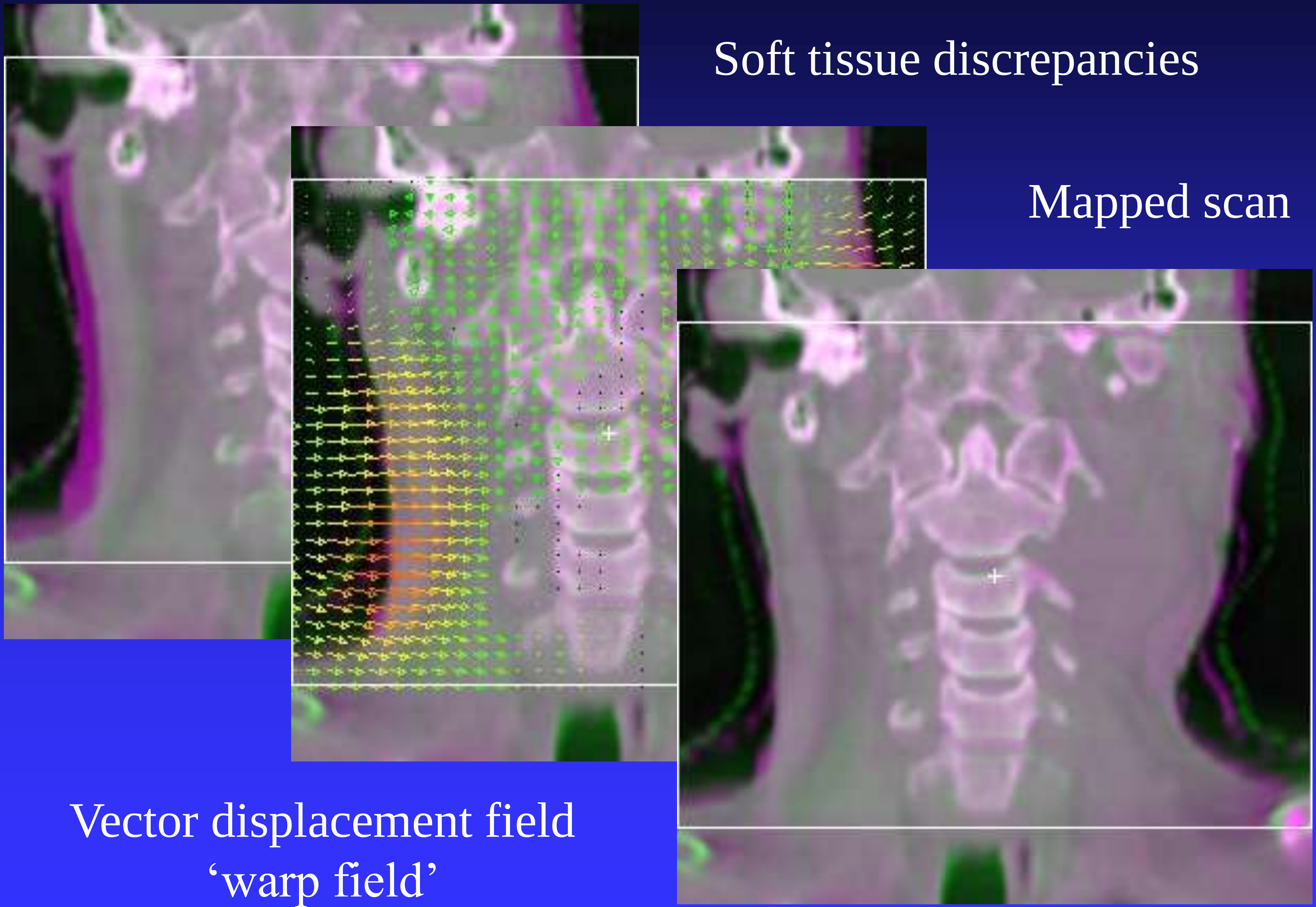
Marc Kessler / UM

Degrees of Freedom



By enforcing smoothness the optimization becomes tractable

Deformation vector fields



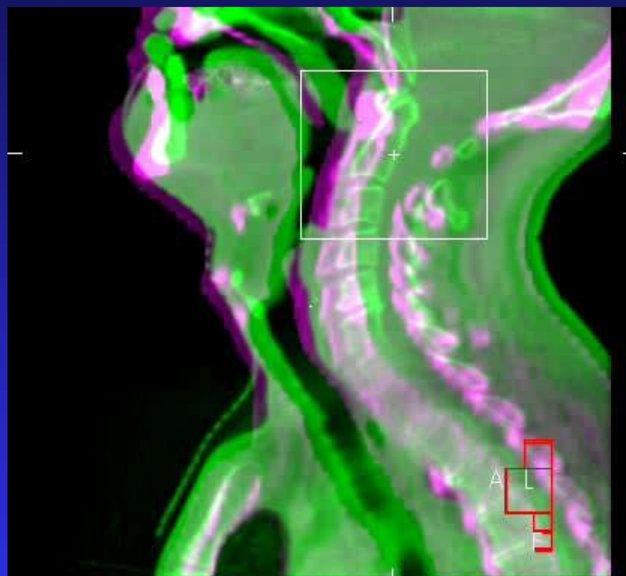
Soft tissue discrepancies

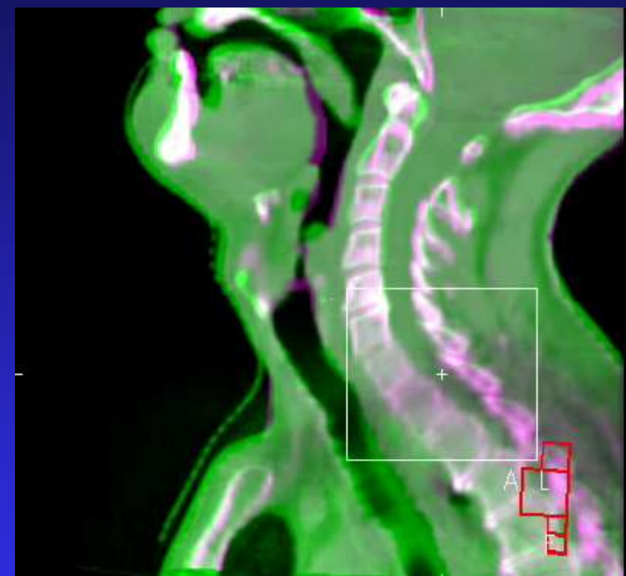
Mapped scan

Vector displacement field
'warp field'

Rigid registration is still the standard.
Which region of interest ?

reference localization reference localization





Tumor in top of neck

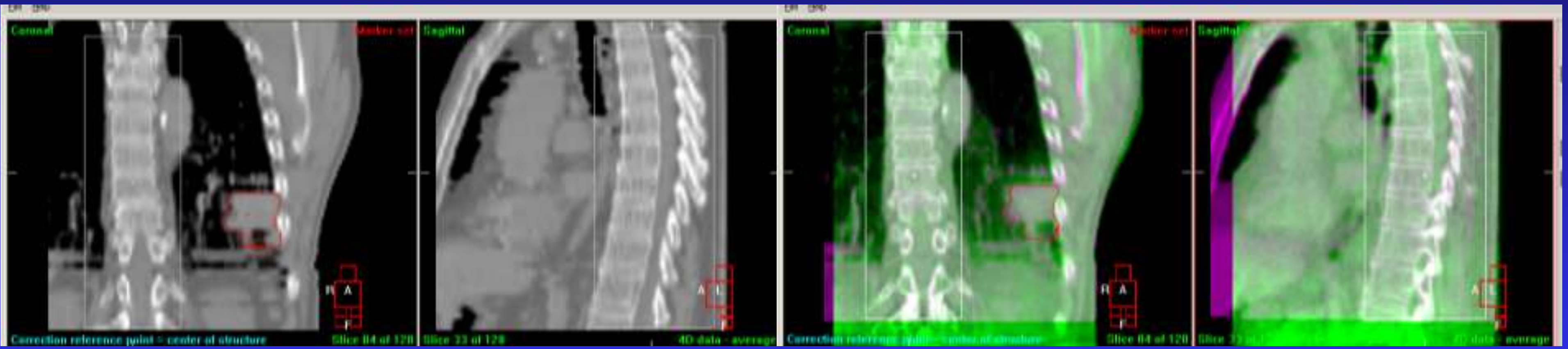
Required table shift:
(-3.2, -1.5, -0.6) mm

Tumor in lower part of neck

Required table shift:
(+1.5, -3.2, -6.1) mm

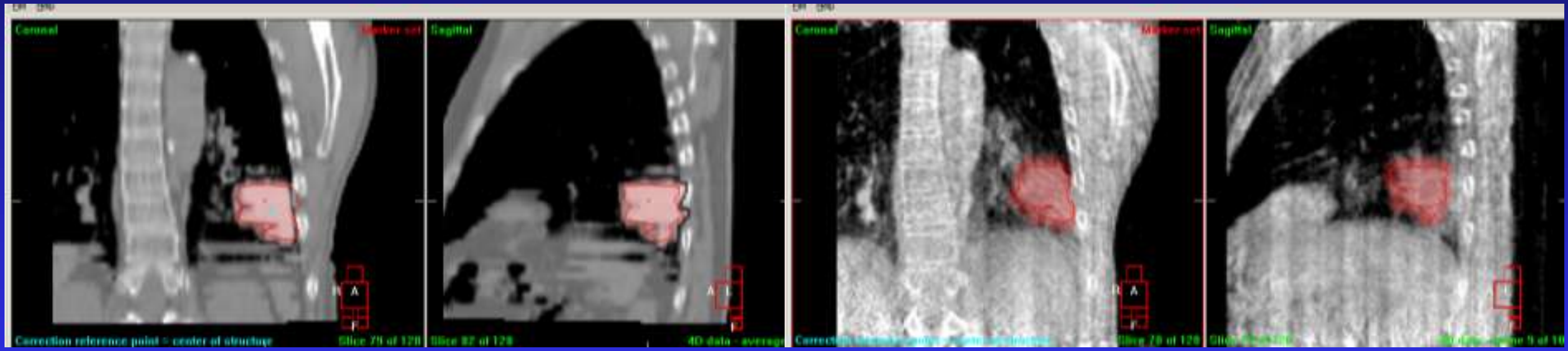
Sub-mm accuracy can be achieved for bony anatomy

2. Region of interest: rectangular



Easily defined: well suited for ‘easy’ registration (e.g., bone)
Pitfall: contrast may look like bone and cause problems

2. Region of interest: shaped



Define by expanding delineation: well suited for local registration (e.g., tumor)
Need tools for editing.
Pitffall: tumor region of interest contains a rib with different movement

Wolthaus et al 2005, Smitsmans et al 2004/2005

5. Similarity measures (cost function)

Based on segmentation: distance/area

Used for contour or bone matching

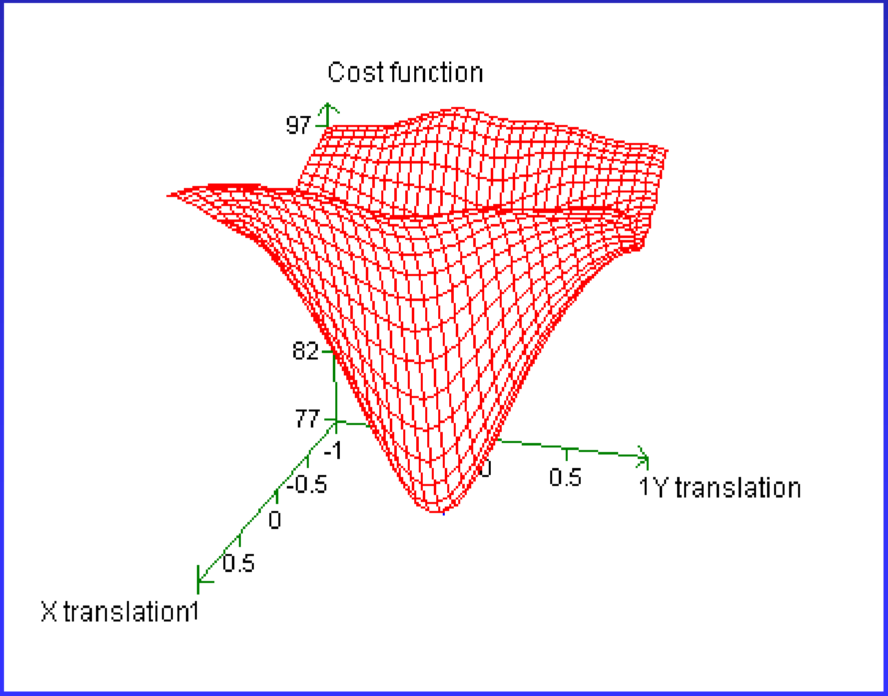
Based on pixel gray values:

Mean absolute difference

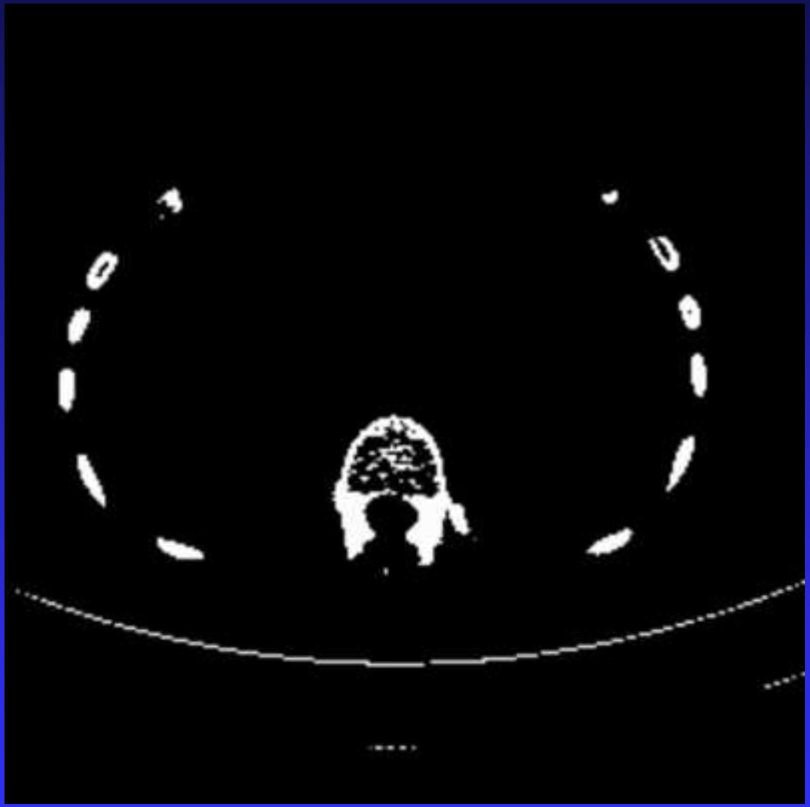
Correlation

Mutual information

Pitfall: noise causes local minima

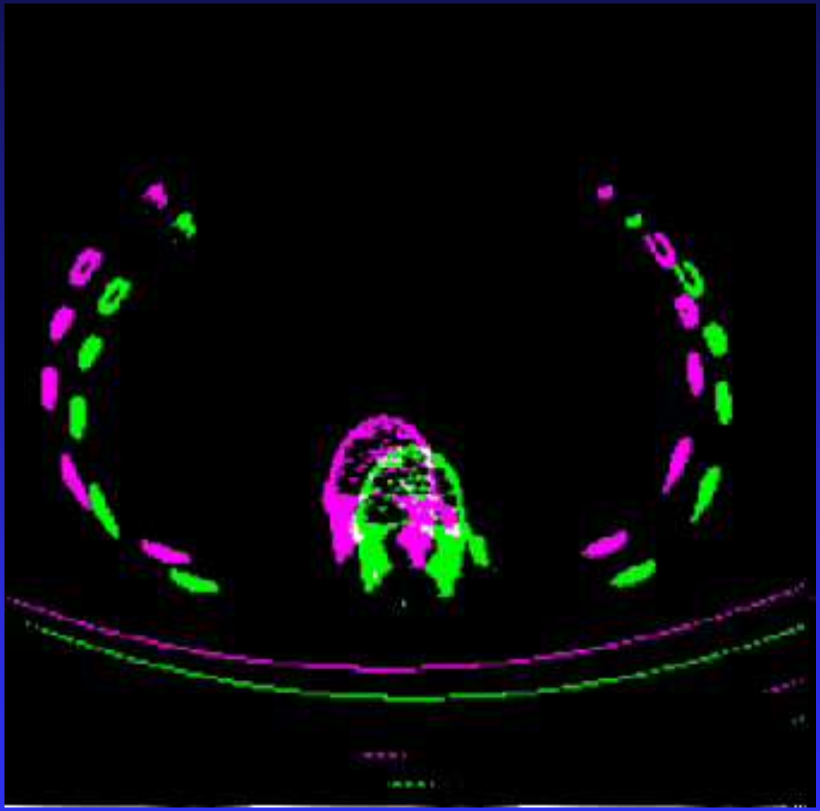


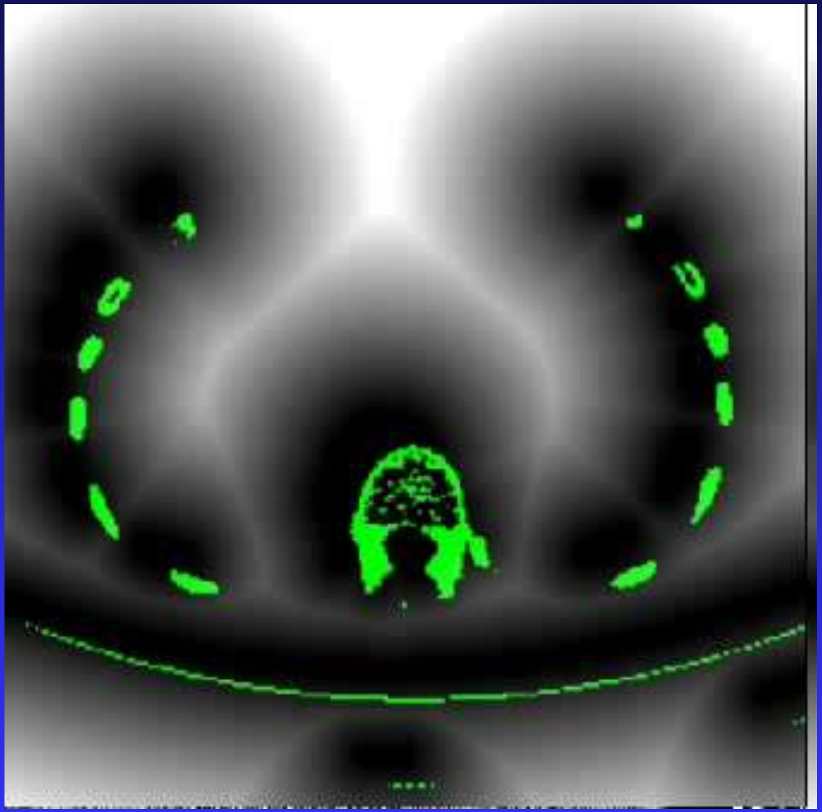
Chamfer matching (bone algorithm) segmentation



Segment all voxels above a certain intensity

Chamfer matching
minimize (mean absolute) distance



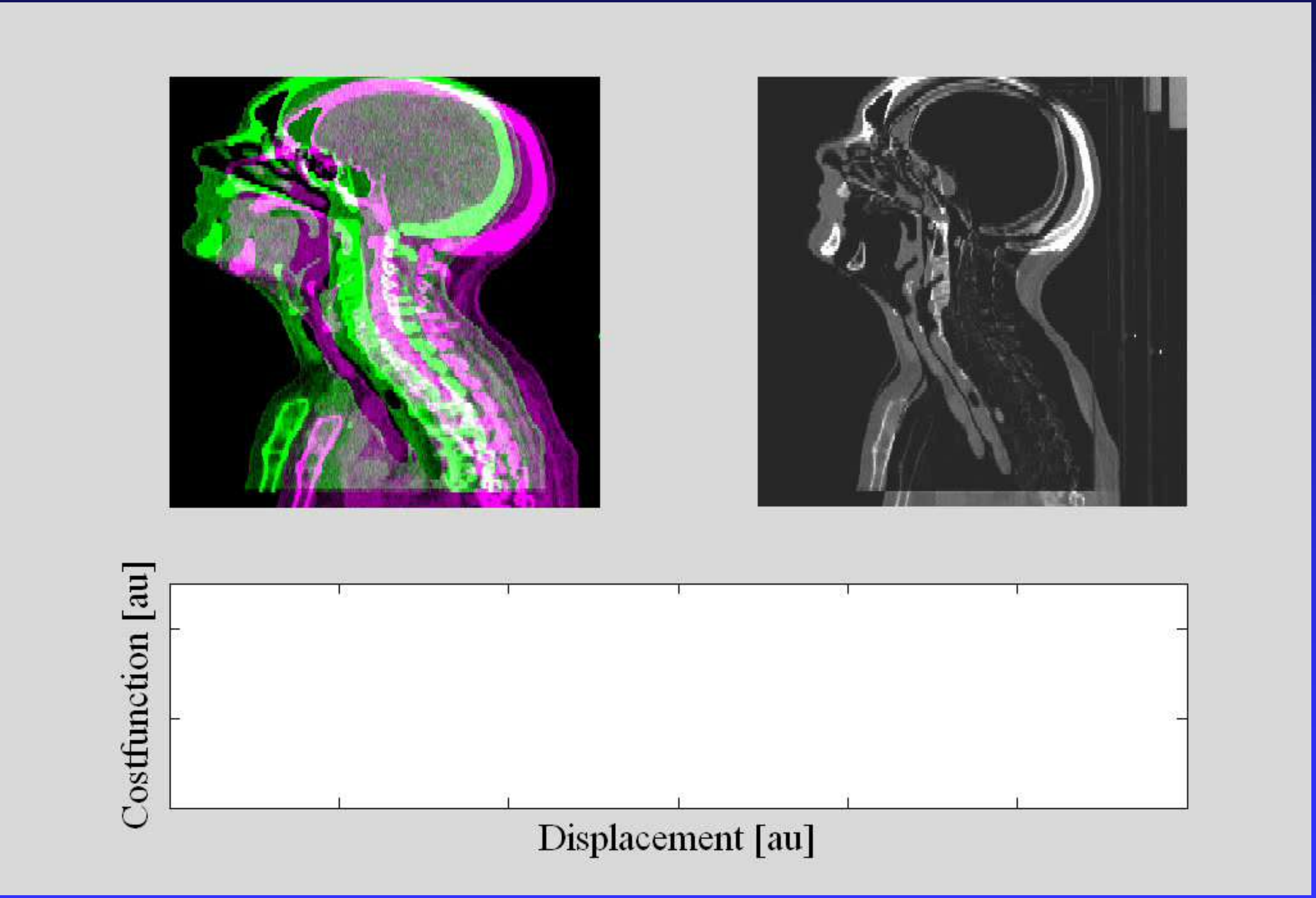


Very fast (1 s): well suited for bony anatomy alignment

Minimize the sum of all distances for the floating images in the corresponding distance transform

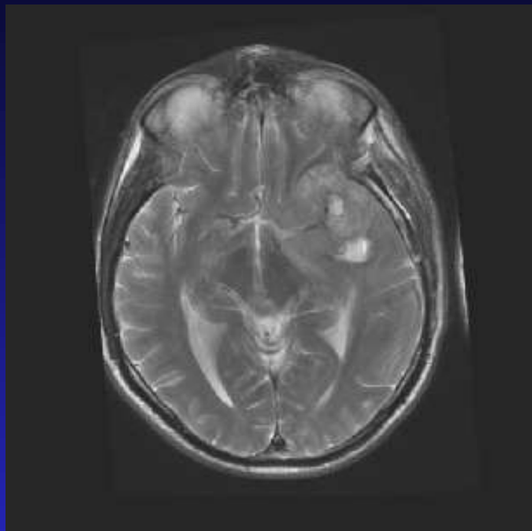
Grey Value / Intensity matching

Uses all pixel values in ROI: e.g., sum of squared differences

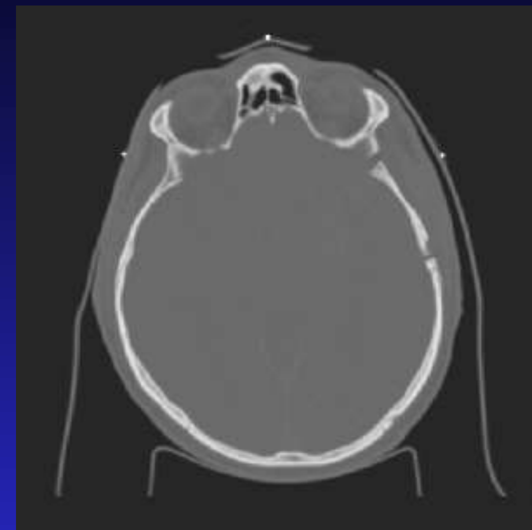


Somewhat slower to process all voxels: depends on the size of the ROI

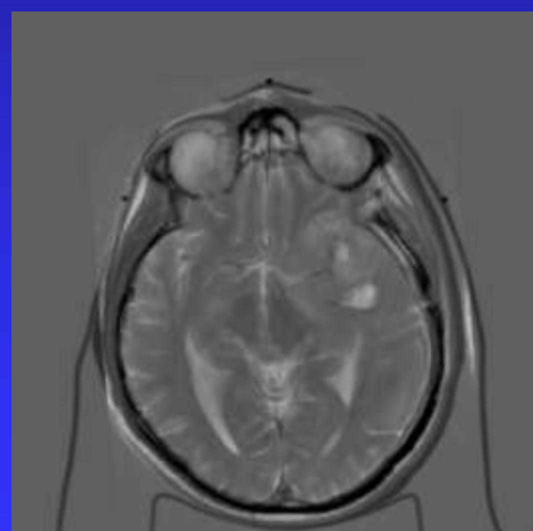
Root Mean Square Difference



$H(I_{MRI})$



$H(I_{CT})$



$H(I_{MRI-CT})$

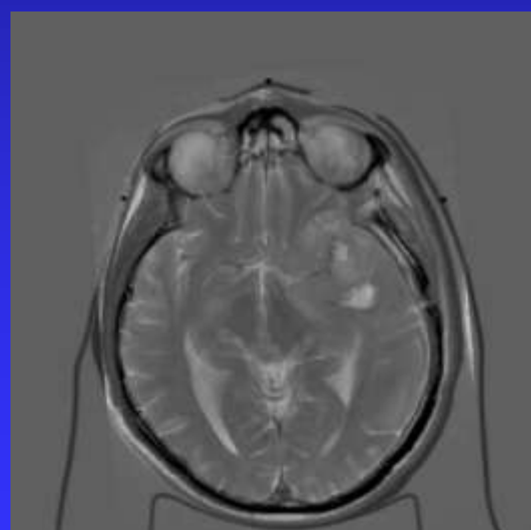
Mutual Information

$$MI(I_1,I_2) = \sum p(I_1,I_2)\log_2\left[\frac{p(I_1,I_2)}{p(I_1)P(I_2)}\right]$$

$$H(I_{MRI\text{-}CT}) = H(I_{MRI}) + H(I_{CT}) - MI(I_{MRI},I_{CT})$$

The Mutual Information of 2 images is the information that is common to both images

The Mutual Information of 2 images is maximized when the are registered

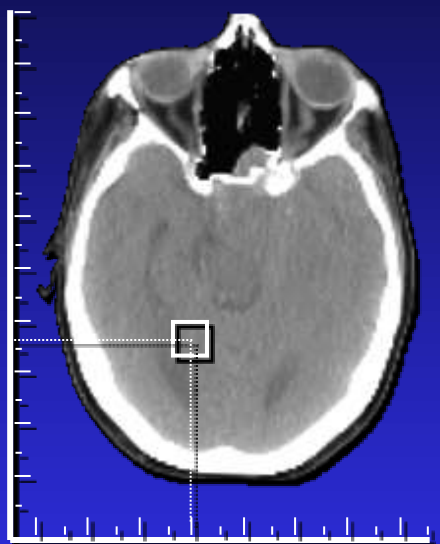


$H(I_{MRI\text{-}CT})$

Marc Kessler / UM

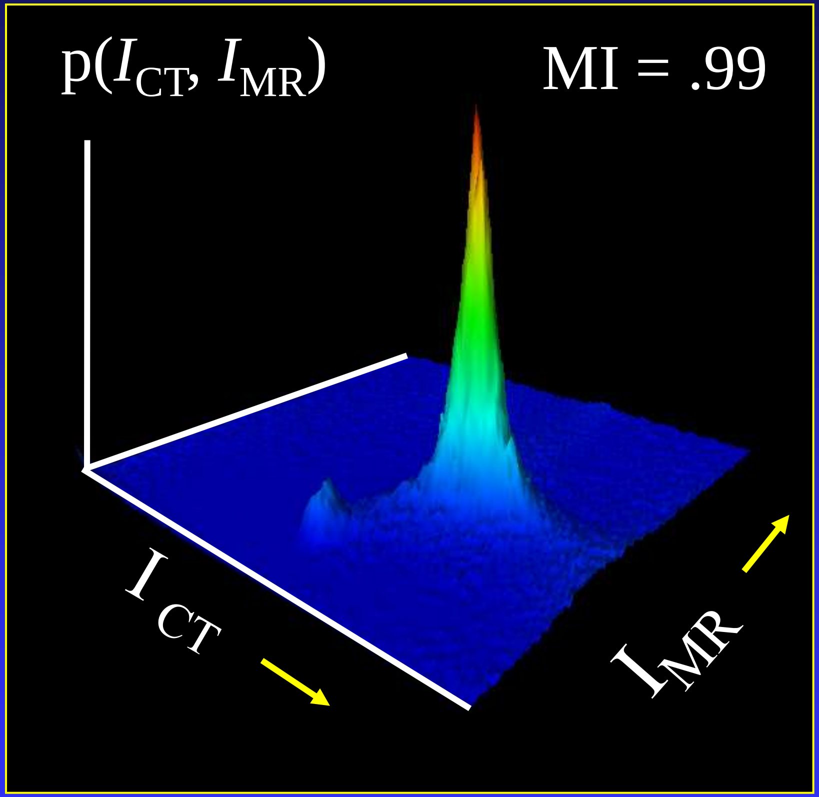
Mutual Information

Aligned!



reformatted
CT

original MR

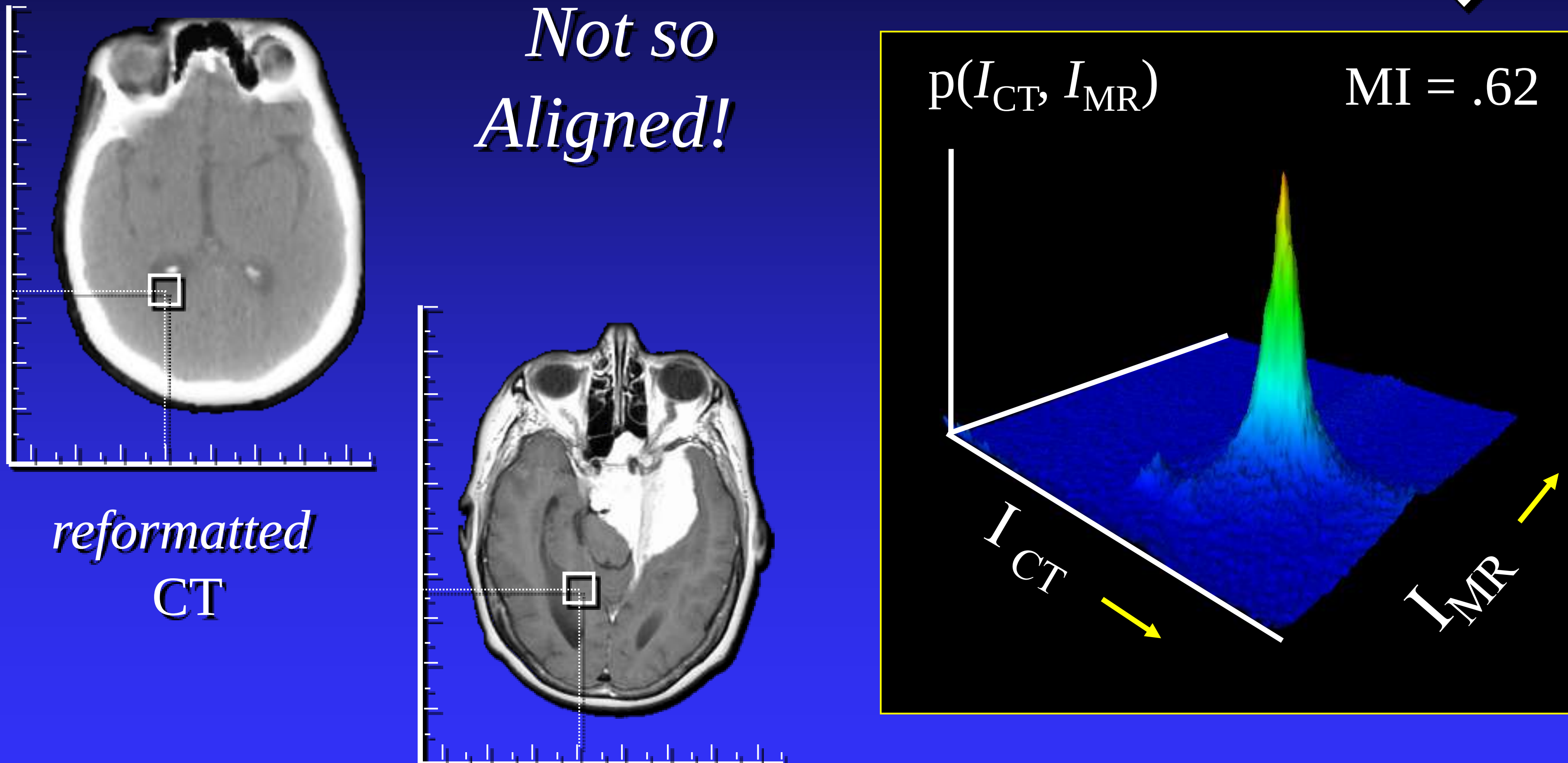


2D joint intensity histogram

Marc Kessler / UM

Mutual Information

Not so Aligned!



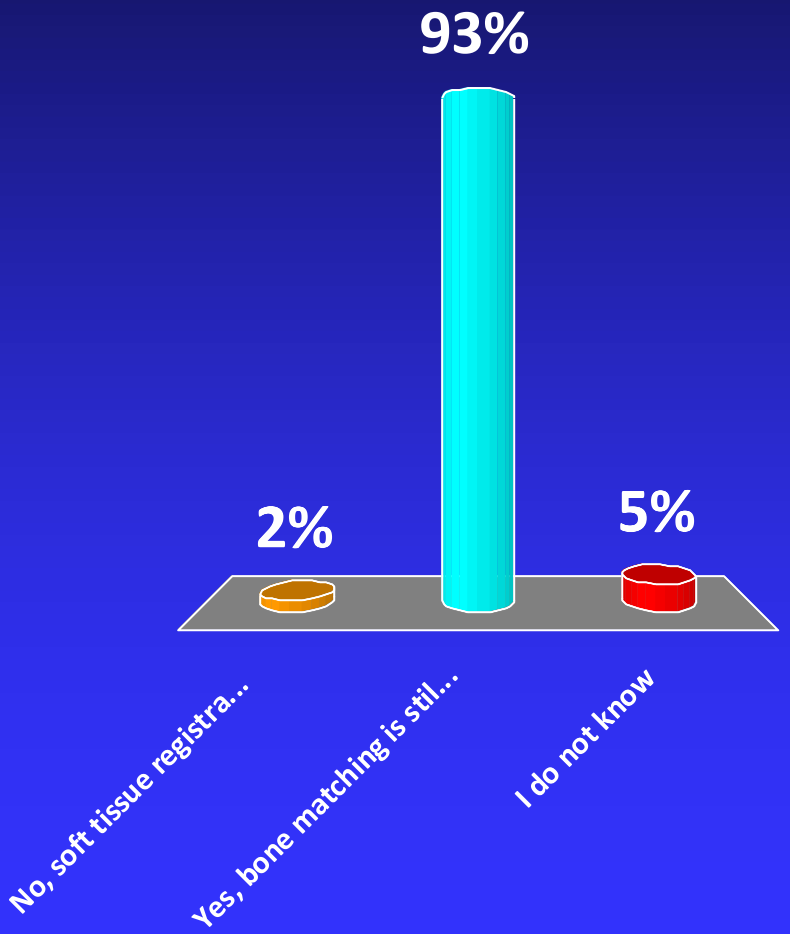
reformatted CT

original MR

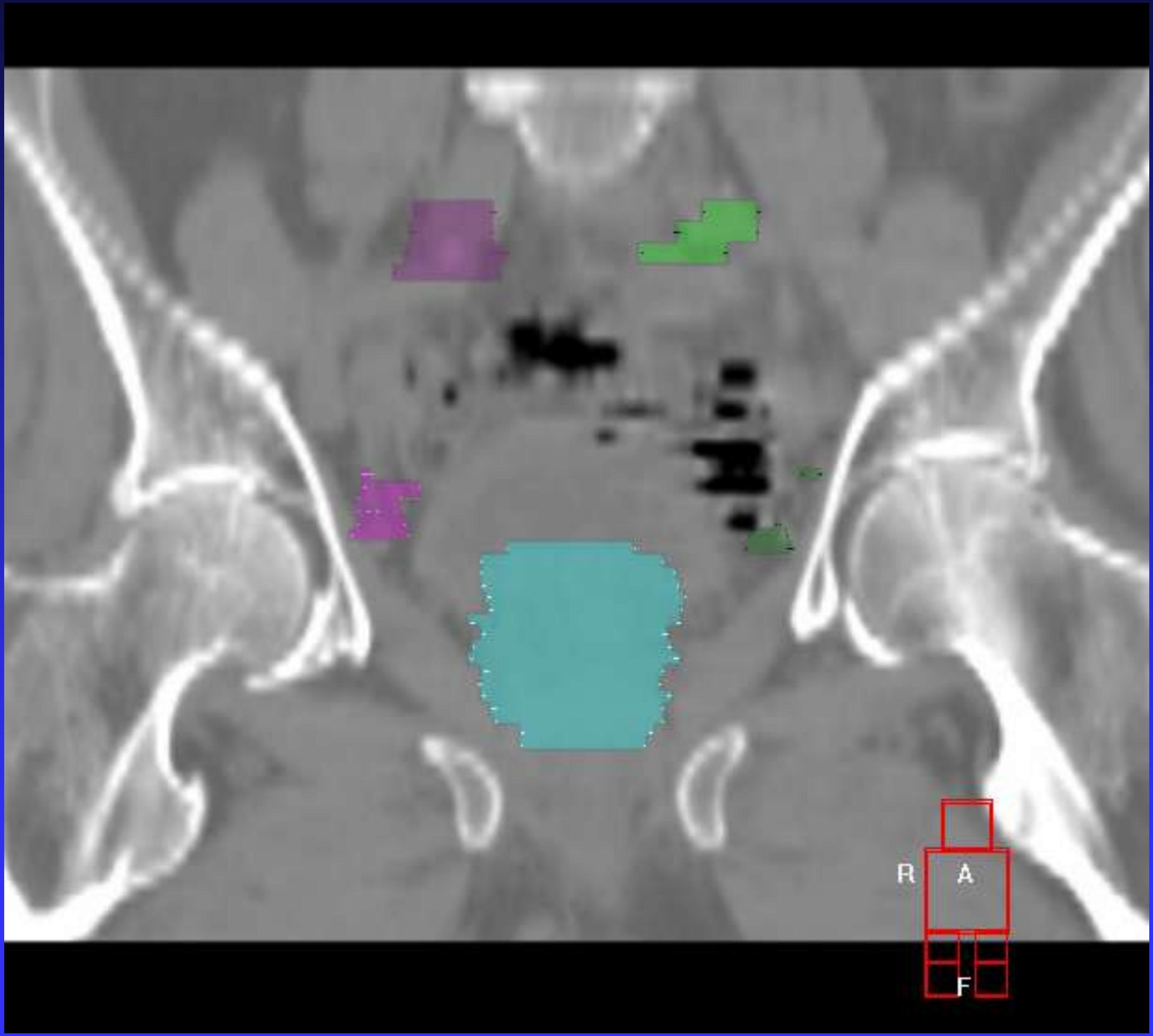
2D joint intensity histogram

Computers are so fast that soft tissue registration is no longer slower – is there still and application for bone matching?

A. No, soft tissue registration more relevant
B. Yes, bone matching is still important
C. I do not know

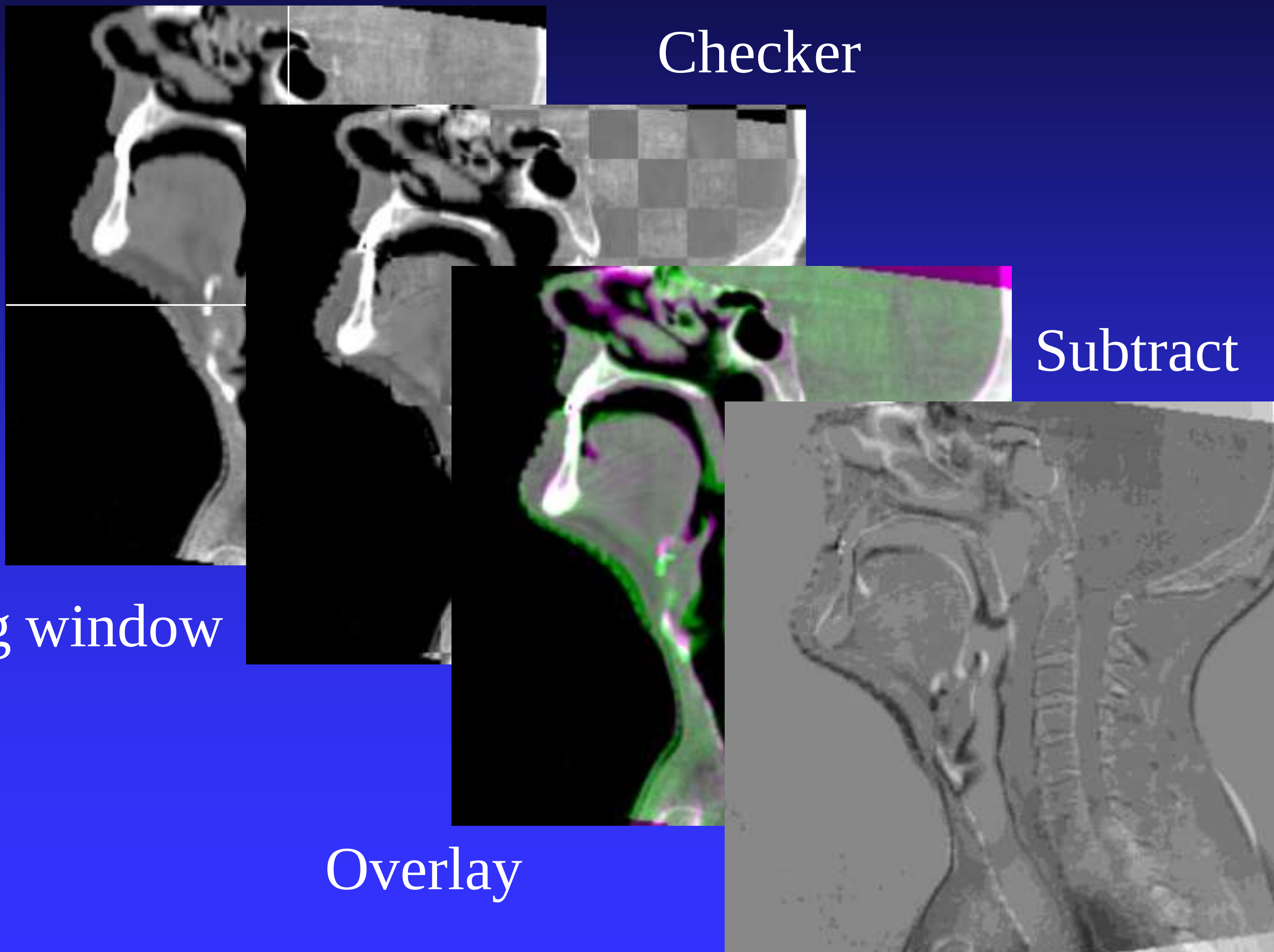


Bone is a valid surrogate for LN



Registration is poorly defined when there are large deformations

Visual verification



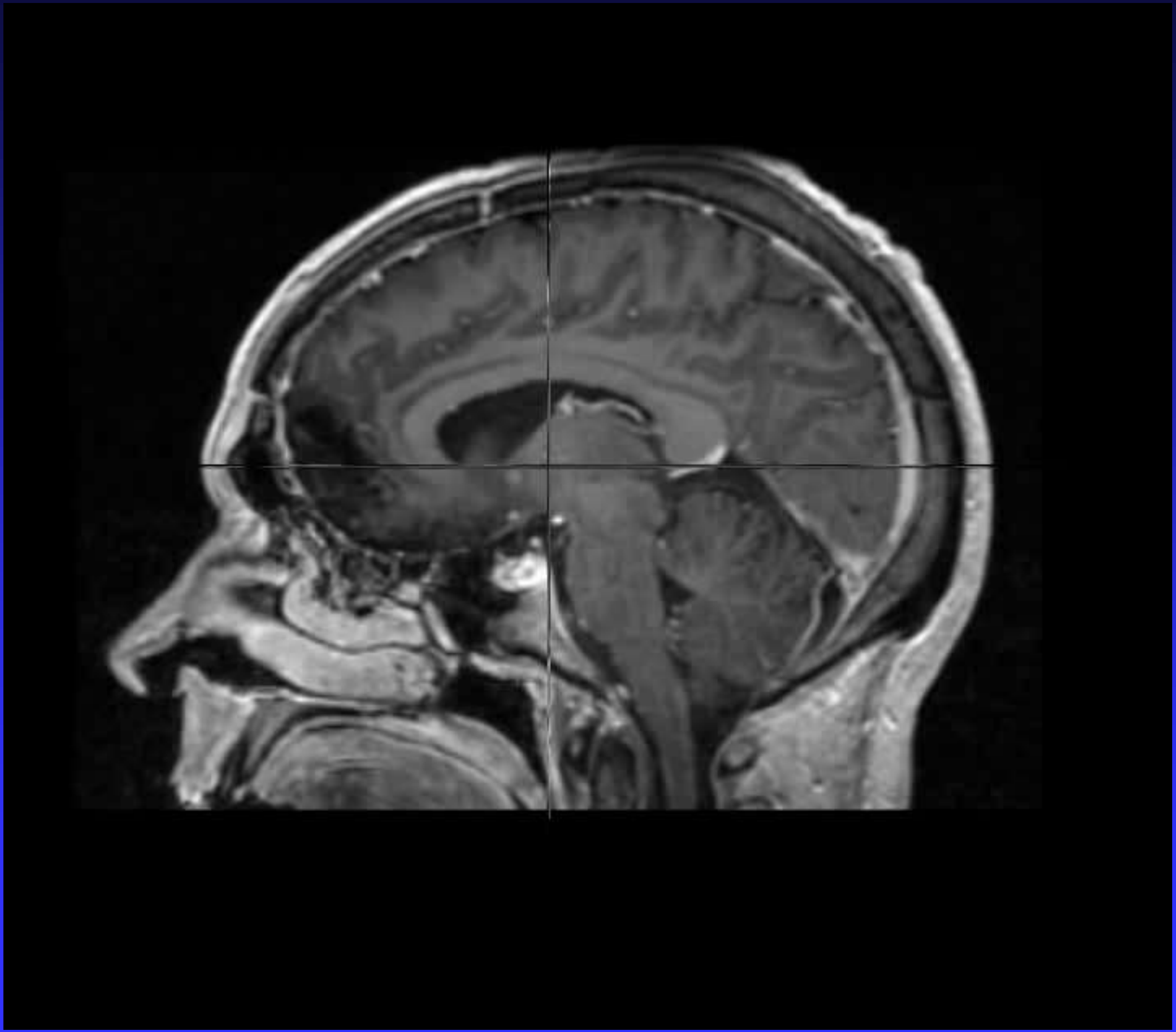
Checker

Subtract

sliding window

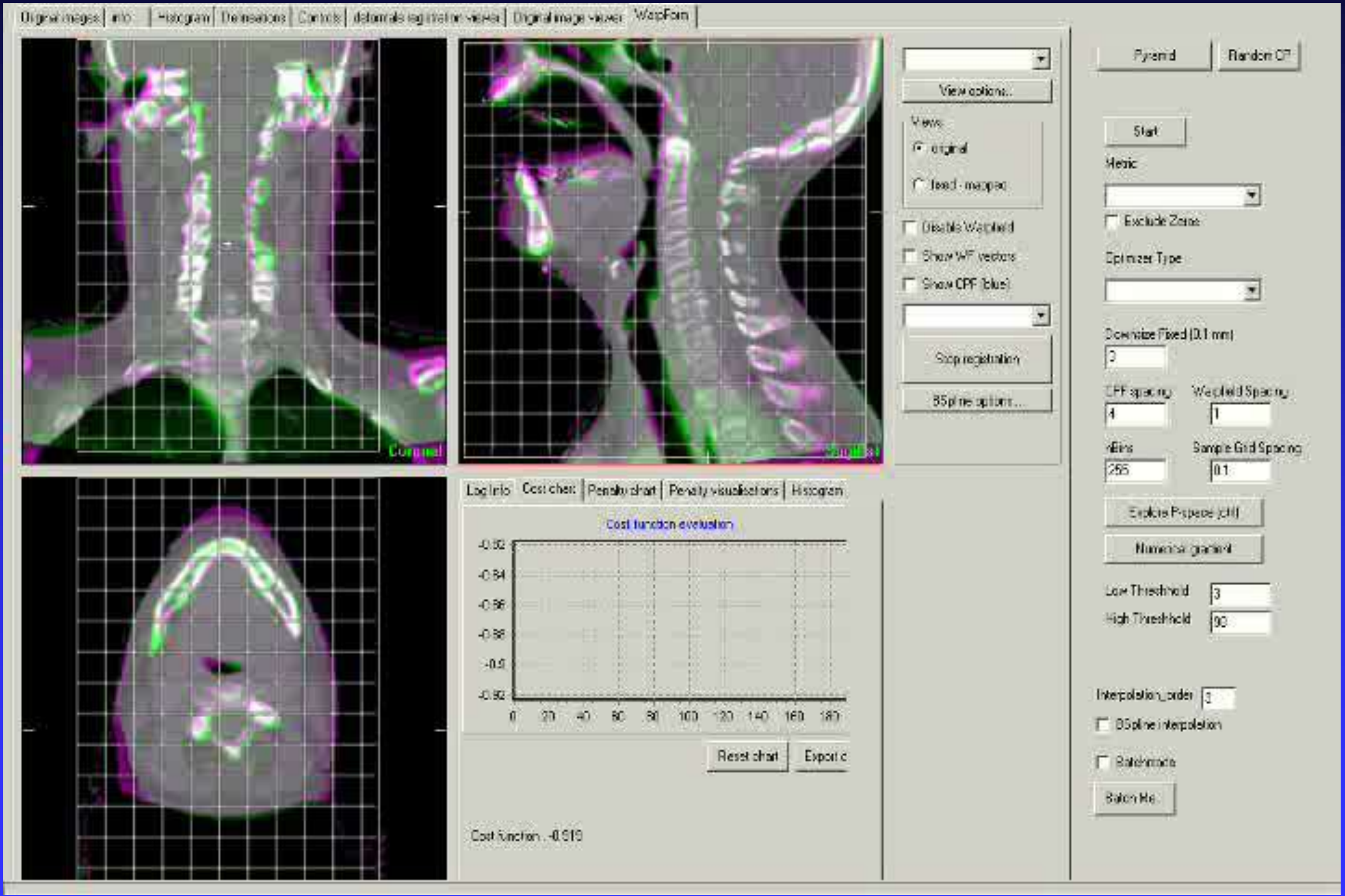
Overlay

The power of 4D animation



Simon van Kranen/ NKI

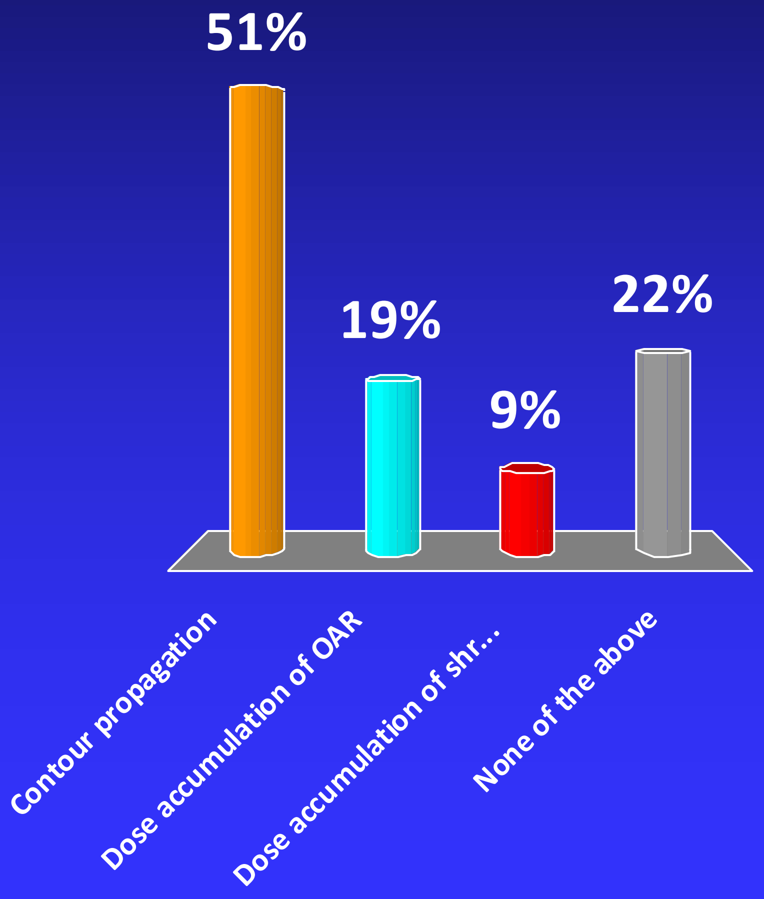
Deformable Registration Movie



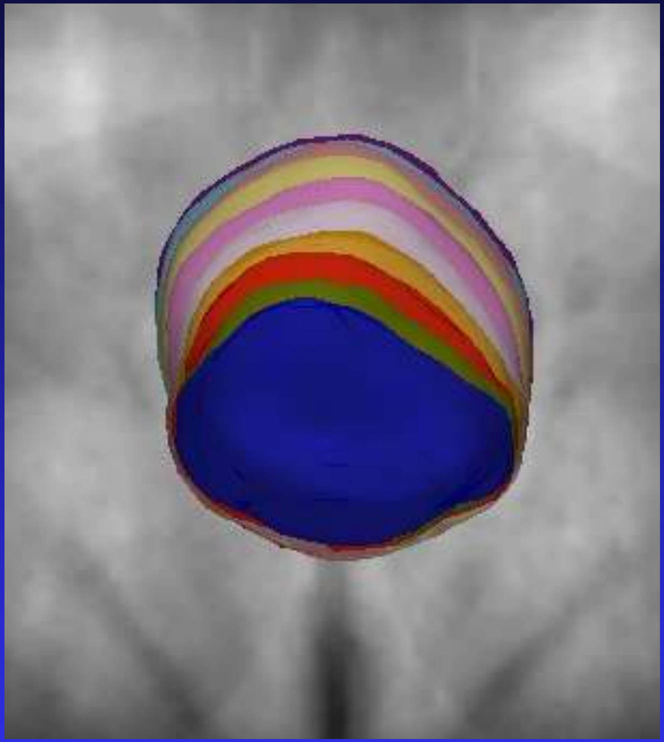
Deformable image registration is considered a cornerstone of 4D and adaptive RT

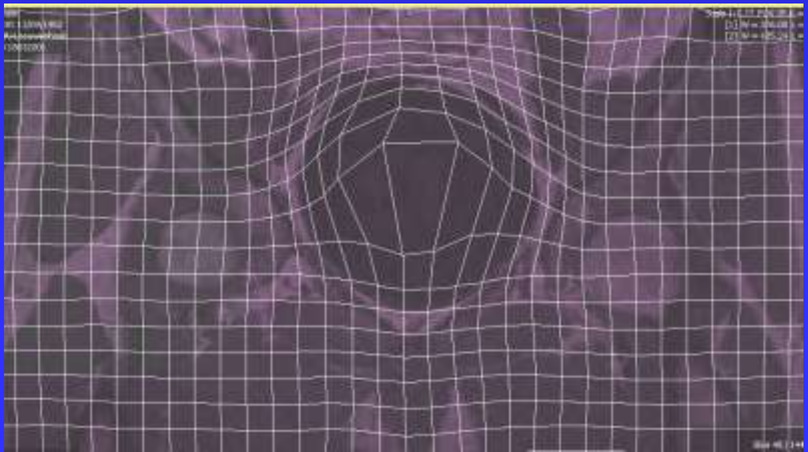
What applications of deformable registration are safe in a clinical setting?...

A. Contour propagation
B. Dose accumulation of OAR
C. Dose accumulation of shrinking tumors
D. None of the above



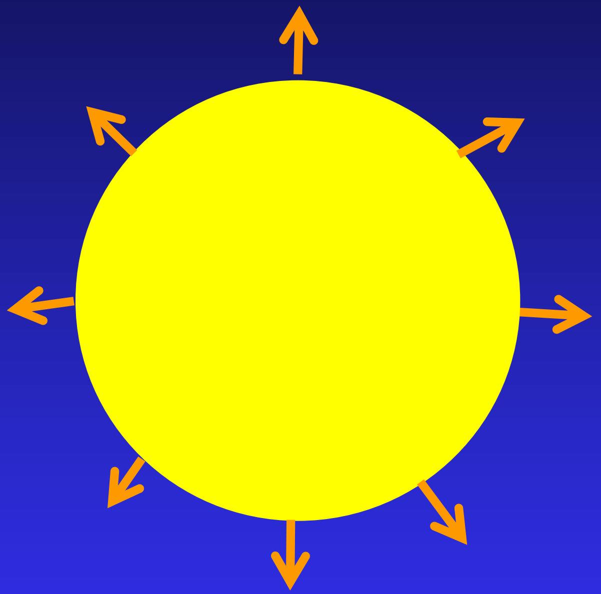
Easy deformable registration of the bladder?

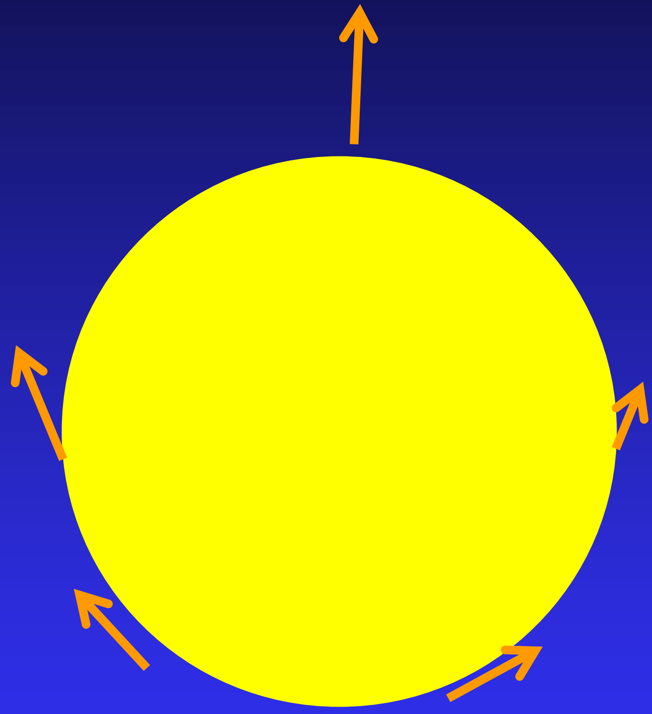


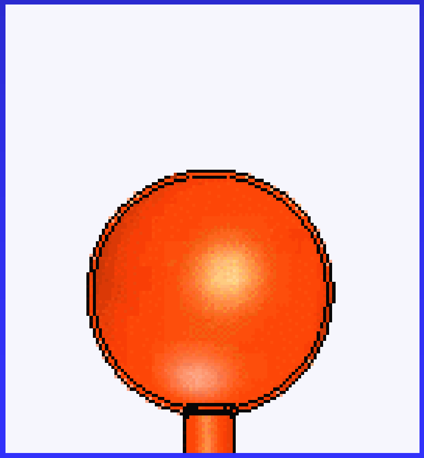


Very high contrast but does software 'understand' the anatomy ?

The bladder is a balloon in a box with stuff – it expands isotropic constrained by the organs around it







You get the contours right, but not the tissue cells → danger for dose accumulation

Landmark validation of contour-based bladder registration

Control over structure-specific flexibility improves anatomical accuracy for point-based deformable registration in bladder cancer radiotherapy

S. Wognum, L. Bondar, A. G. Zolnay, X. Chai, M. C. C. M. Hulshof, M. S. Hoogeman, and A. Bel

Citation: Medical Physics **40**, 021702 (2013); doi: 10.1118/1.4773040

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View Tal

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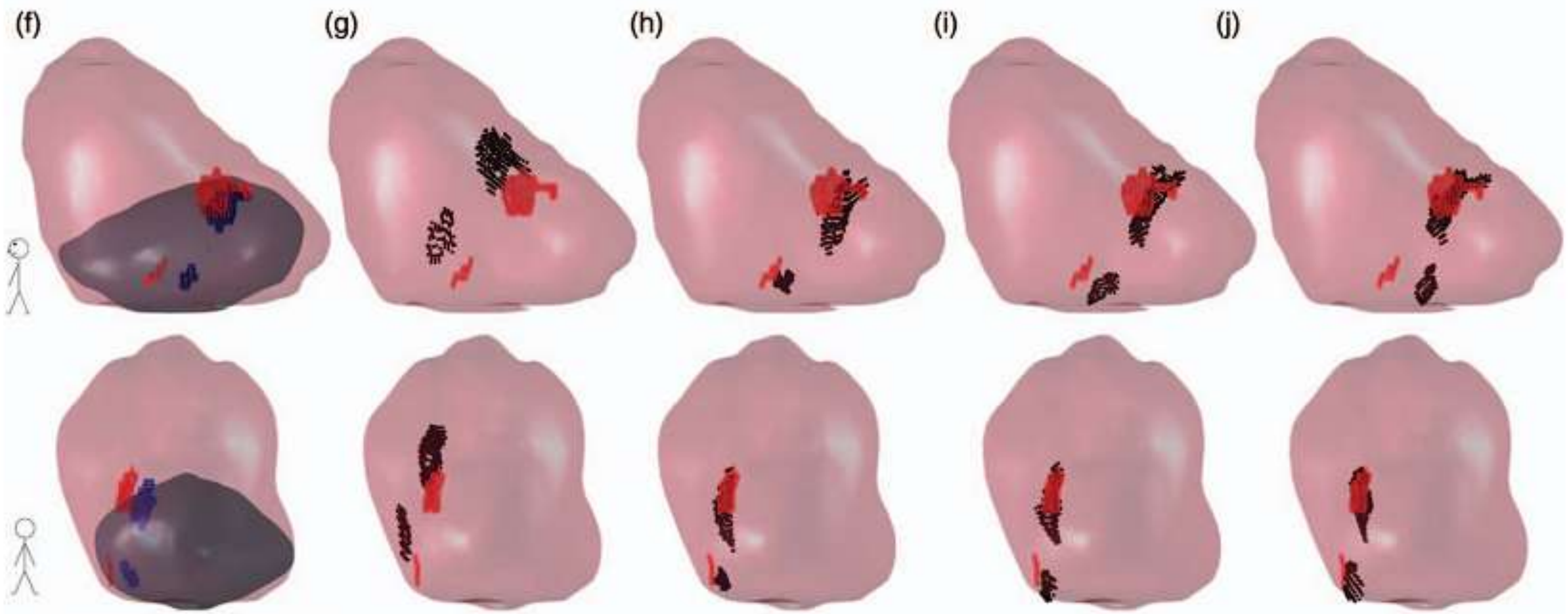
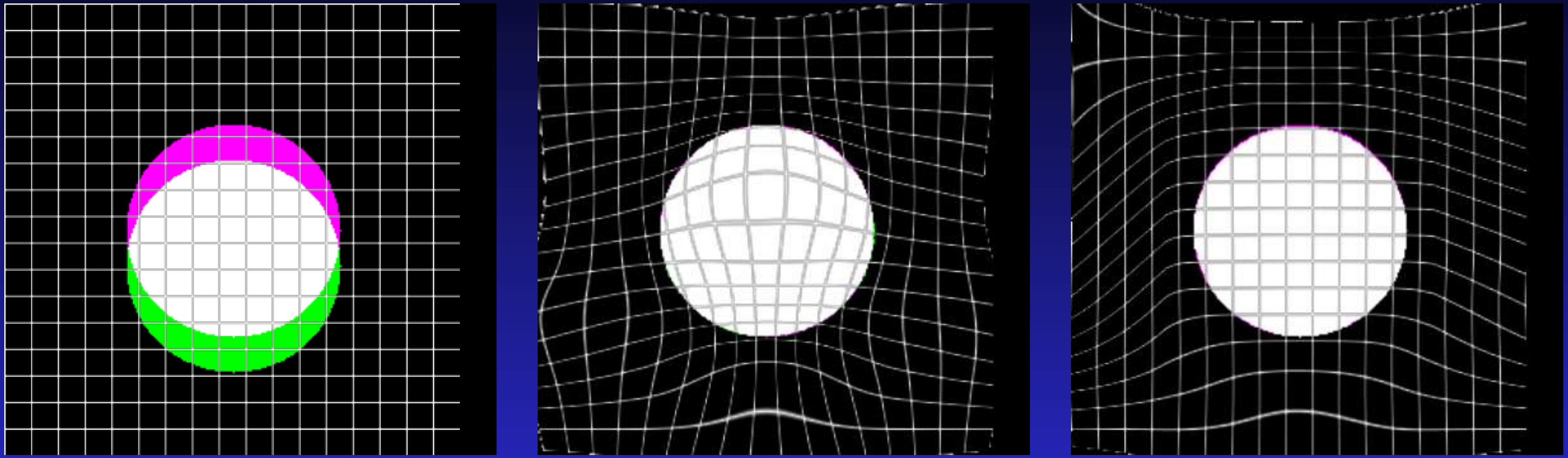


RDE lipiodol (mm)

1	5.9	6.4	3.6	3.1	2.2
2	11.8	8.9	4.0	8.6	14.1

Deformable registration classes

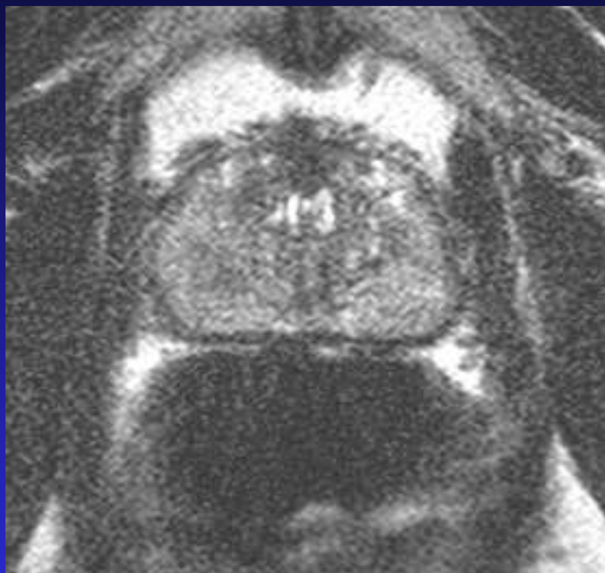


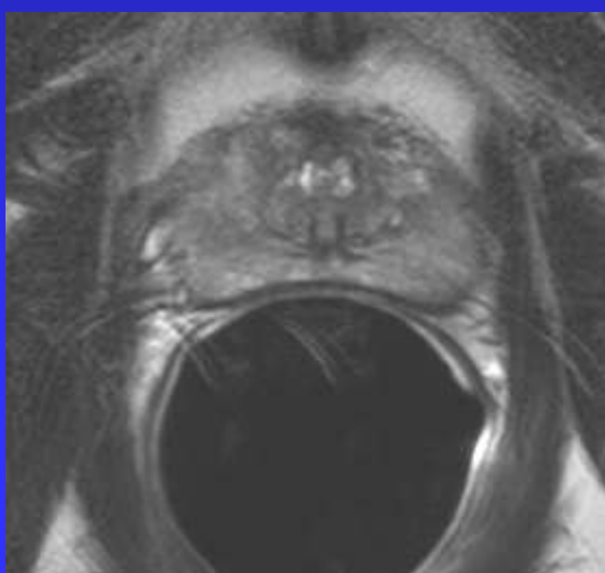
Different DVF provide same visual registration result

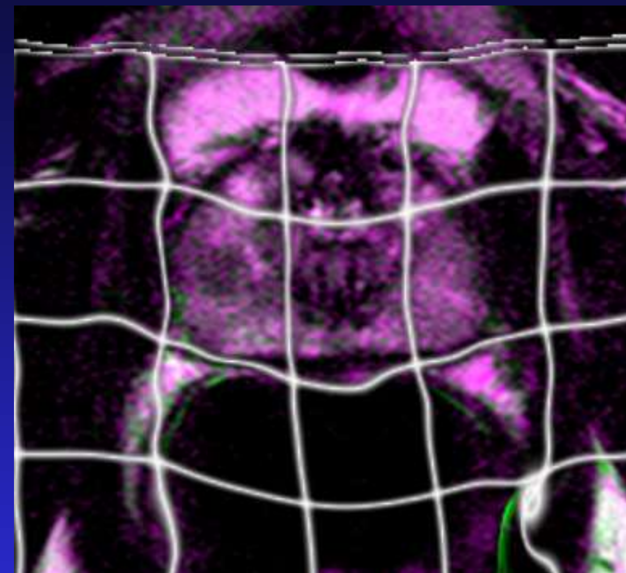
- Descriptive: it must look good
  - e.g. contour propagation
- Quantitative: it must be an anatomically correct, also inside homogeneous organ
  - e.g. dose accumulation

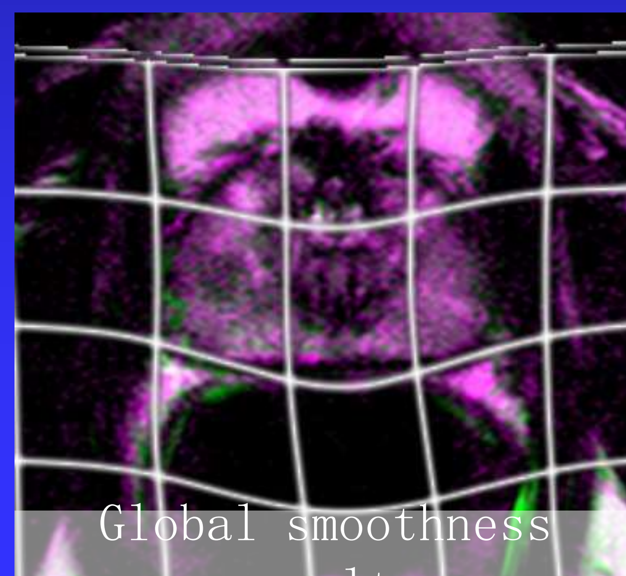
You can morph anything to anything but do you add information?

Prostate MRI w/wo Endo Rectal Coil





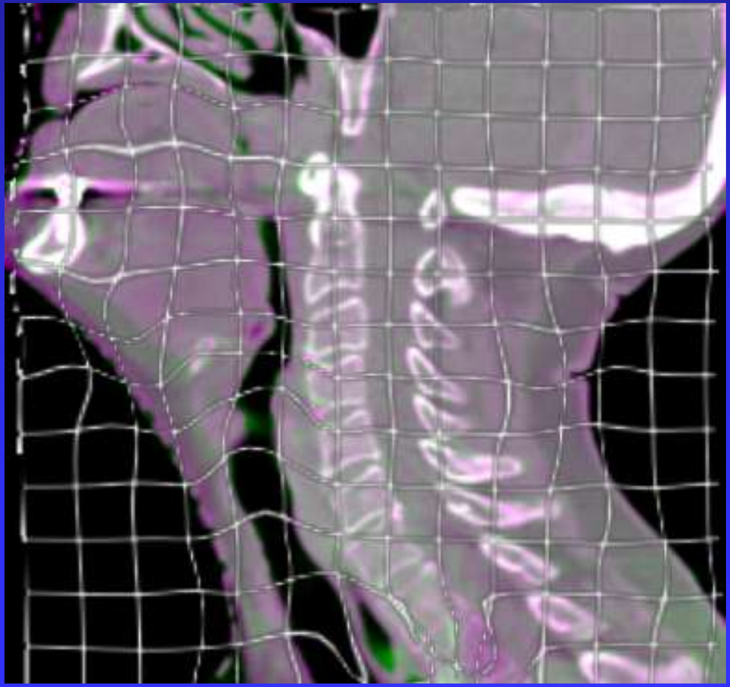




CBCT – Planning CT Registration

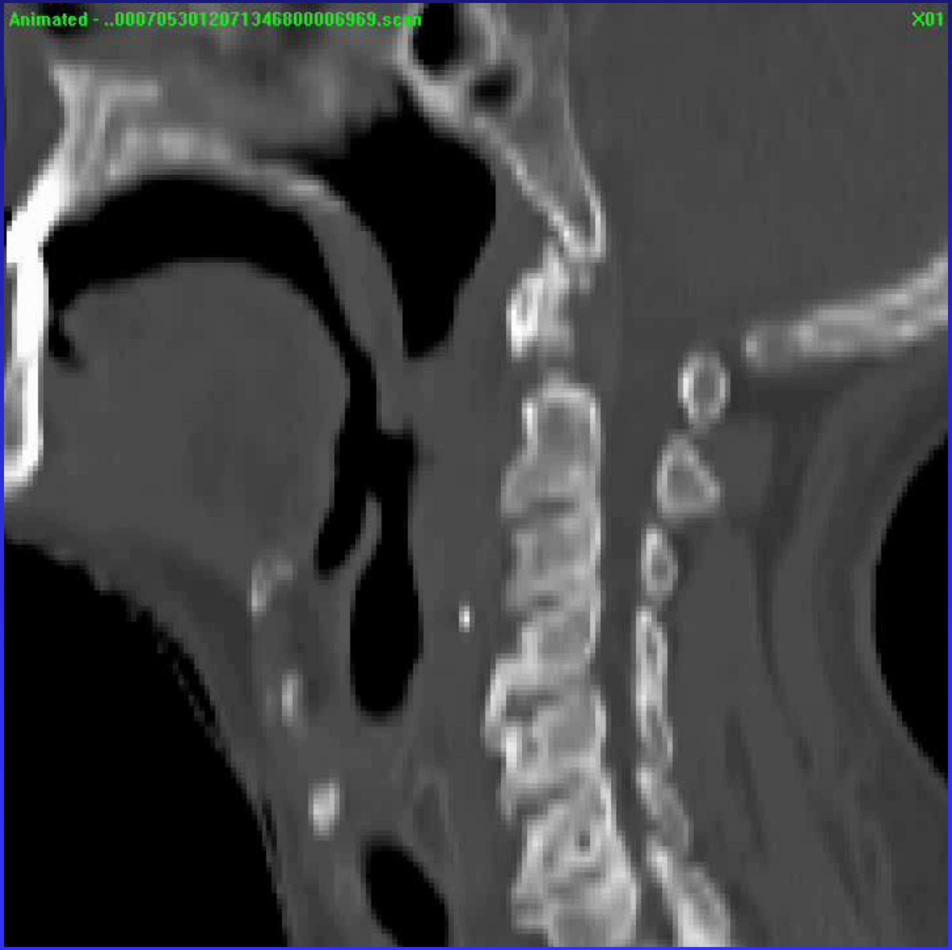
Planning CT

CBCT



Constrained Deformable B-Spline
Registration

Can you see all anatomical changes ?



Deformable registration will not pick up motion parallel to interfaces

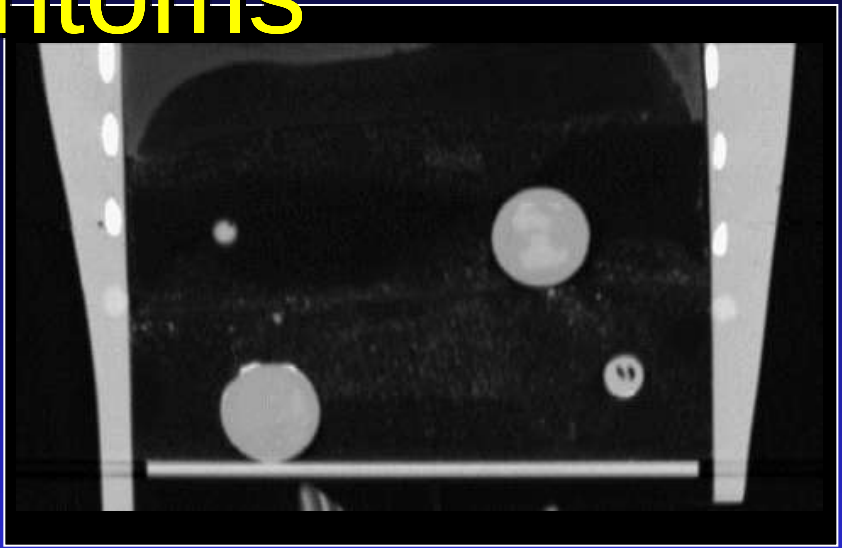
O Hamming, NKI

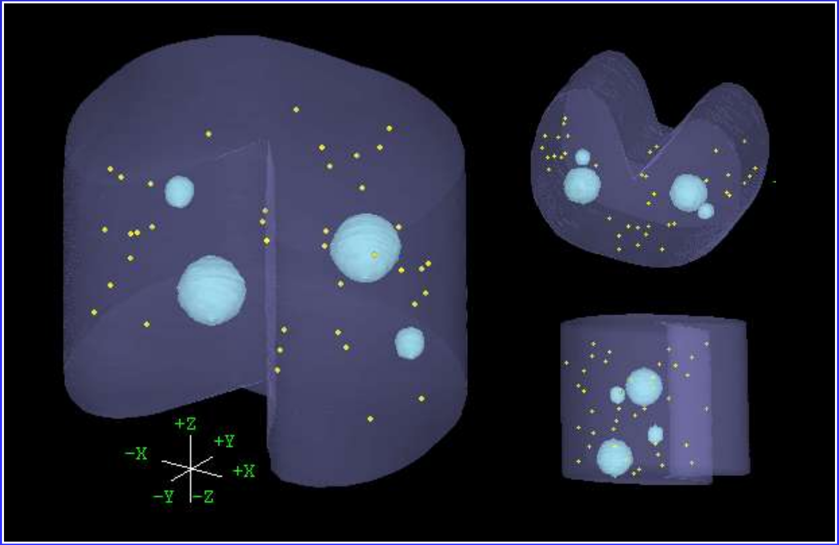
Validation

QA methods

- The algorithm works technically
  - Use phantom or simulated data
- The program works in general
  - Best: use patients with implanted markers (data scarce)
  - Second: compare with human observers
- The program works for this patient
  - Visual verification
  - Consistency, plausibility

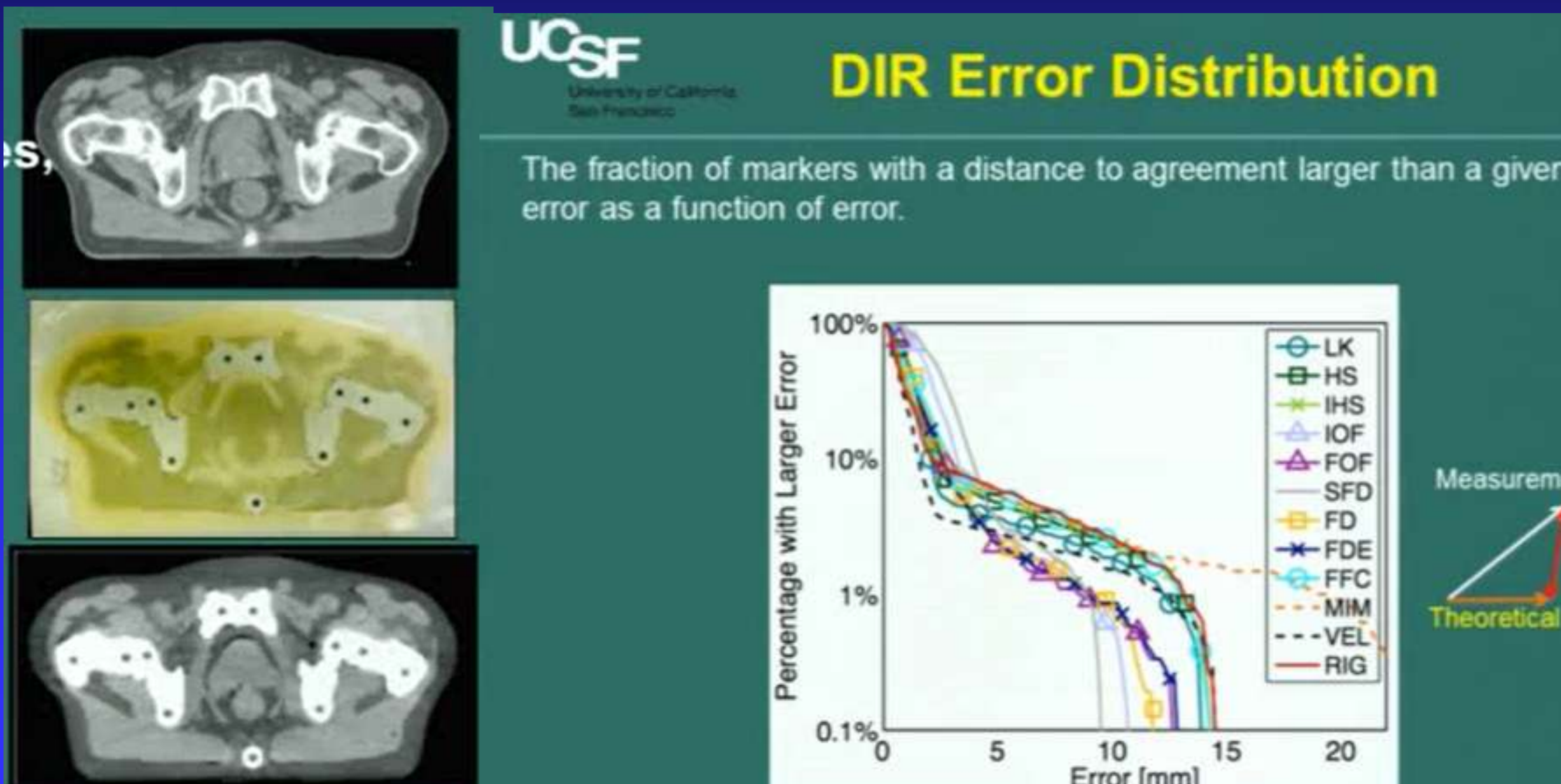
4D Phantoms





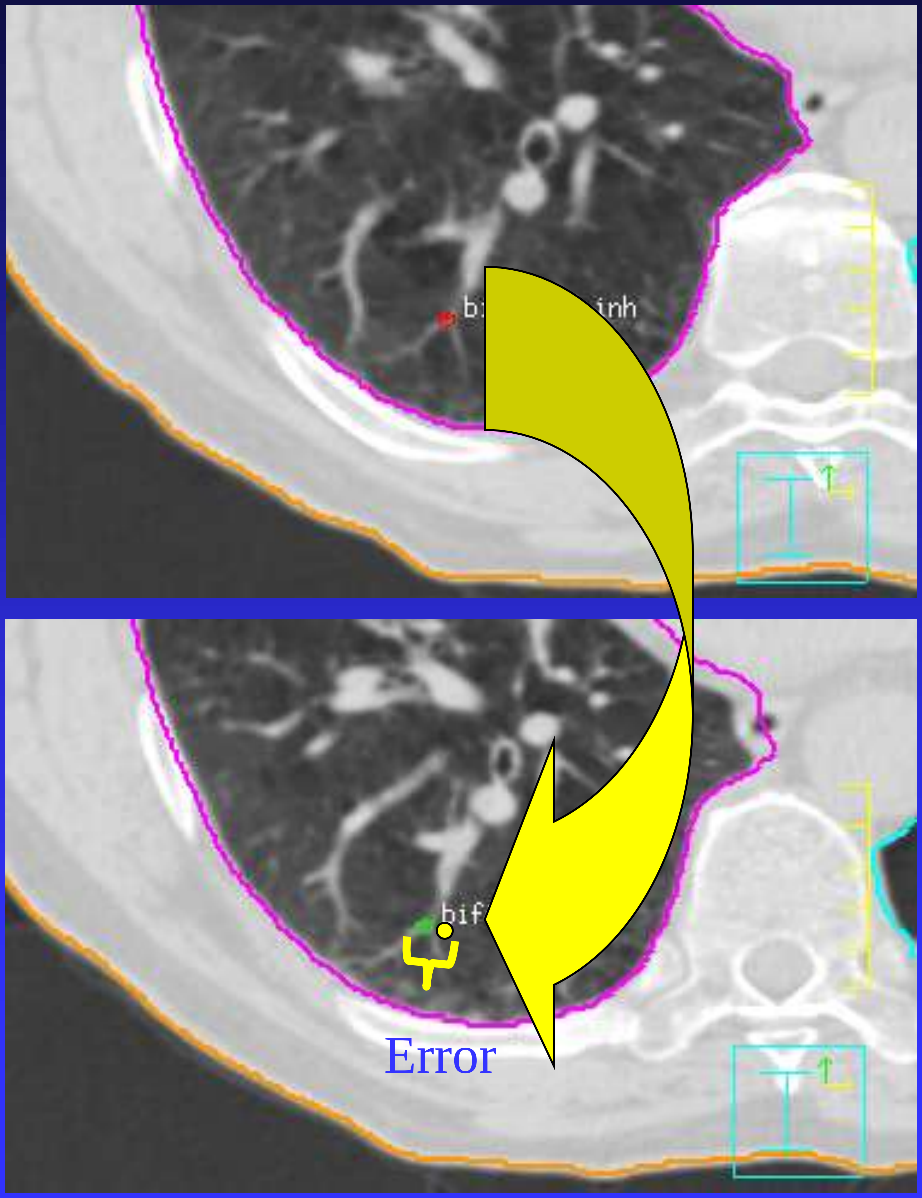
		RL[a] (cm)	AP[b] (cm)	SI[c] (cm)	3-D distance (cm)
Affine	Average	–0.01	0.00	0.05	0.38
	Stdev[d]	0.04	0.04	0.44	0.22
	Max[e]	–0.12	–0.13	0.90	0.90
B-splines	Average	–0.02	–0.01	0.05	0.18
	Stdev[d]	0.08	0.06	0.22	0.16
	Max[e]	–0.42	0.19	0.67	0.81
Thin-plate splines	Average	–0.07	–0.15	–0.14	0.37
	Stdev[d]	0.12	0.19	0.28	0.19
	Max[e]	–0.56	–0.58	–0.74	0.75

Registration of anatomically realistic phantom in pelvis

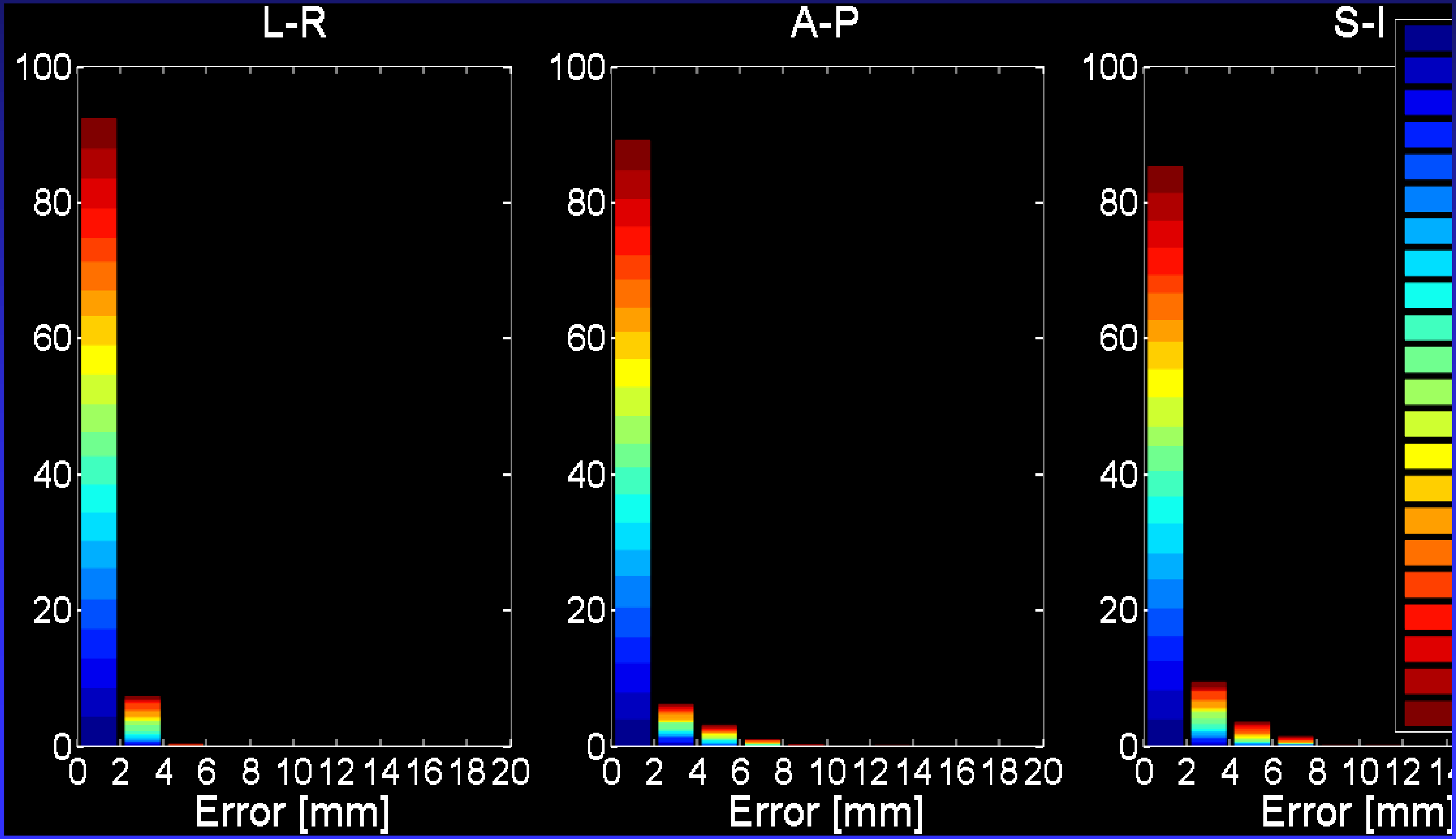


J Pouliot, UCSF

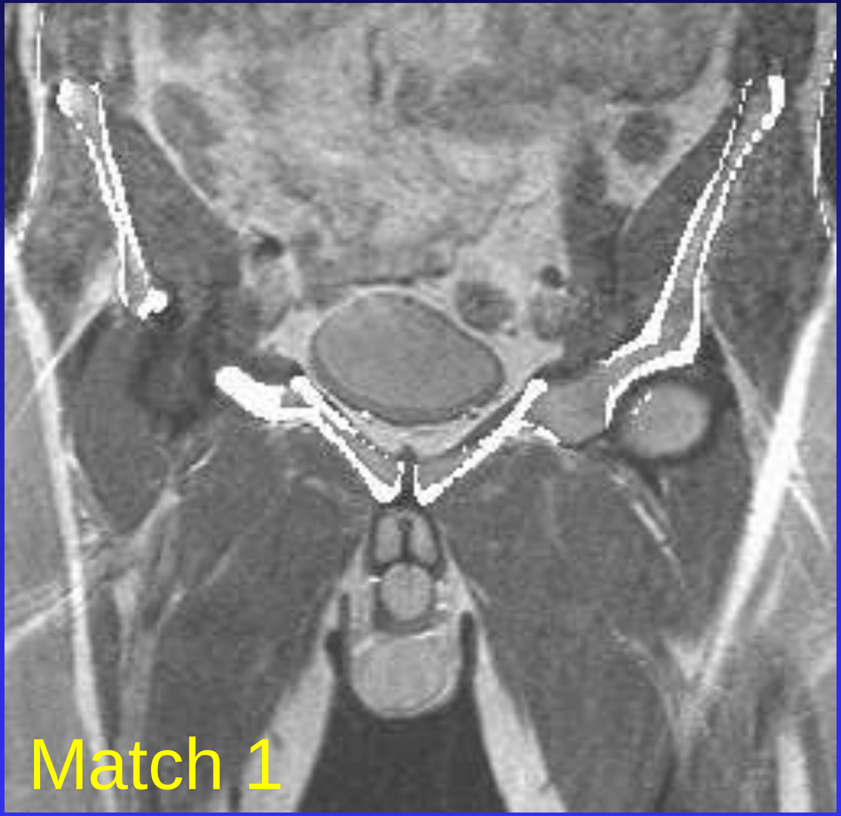
Natural Fiducials

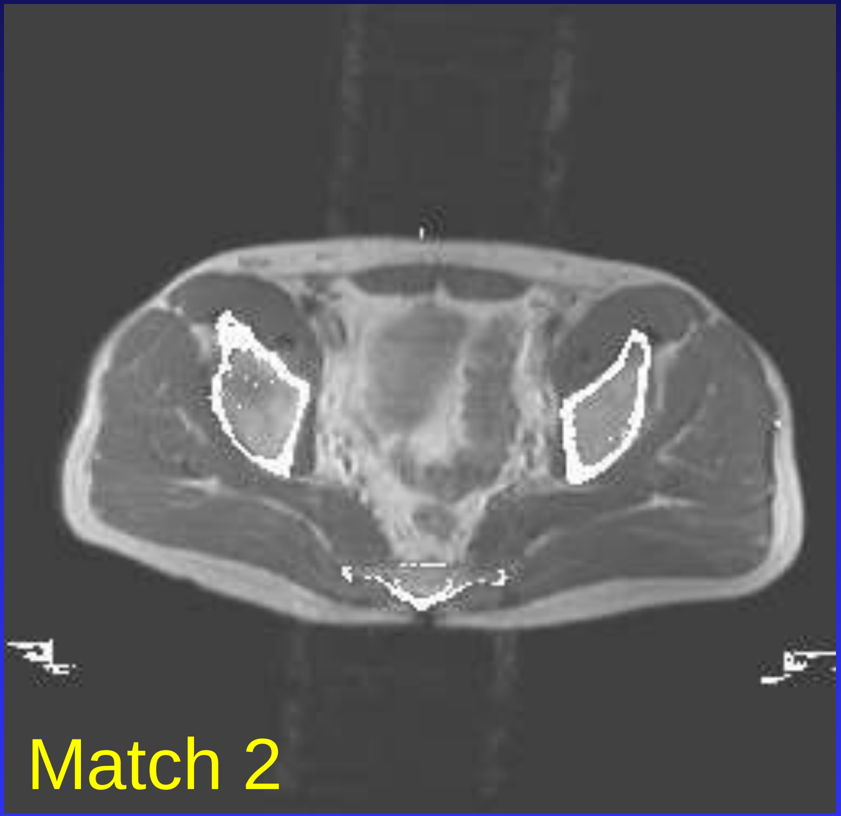


Results: Lung 4D CT (22)
% Bifurcation Points



Consistency check as QA tool



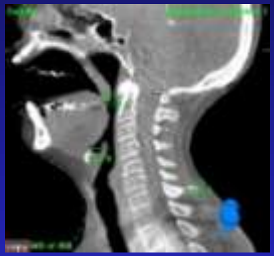


Deviation	Δ x (L-R)	Δ y (A-P)	Δ z (C-C)	Δ rx (L-R)	Δ ry (A-P)	Δ rz (C-C)
between match 1 and 2	-0.5 mm	2.0 mm	-1.6 mm	-0.9 dg	-0.8 dg	-0.7 dg

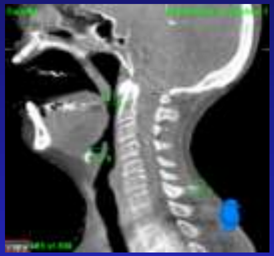
Van Herk et al, 1998

Analysis of variance

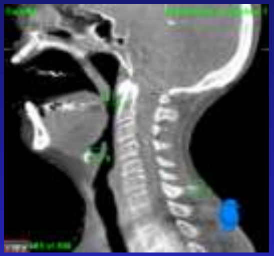
$\mathbf{O}_1$



$\mathbf{O}_2$



$\mathbf{O}_3$



Analysis of variance

Accuracy of the observers $\mathbf{O}_1$, $\mathbf{O}_2$, $\mathbf{O}_3$

$\mathbf{O}_1$: First human observer

$\mathbf{O}_2$: Second human observer

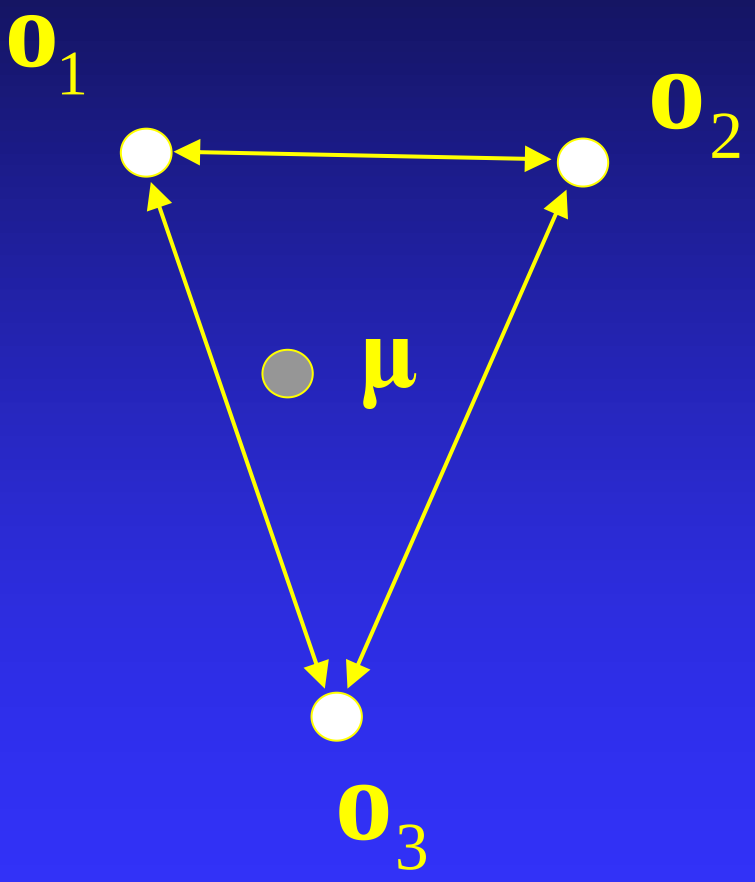
$\mathbf{O}_3$: Registration method

Analysis of variance

$$\boldsymbol{\sigma}_1^2 = (\boldsymbol{\sigma}_{2-1}^2 + \boldsymbol{\sigma}_{3-1}^2 - \boldsymbol{\sigma}^2{}_{3-2})/2$$

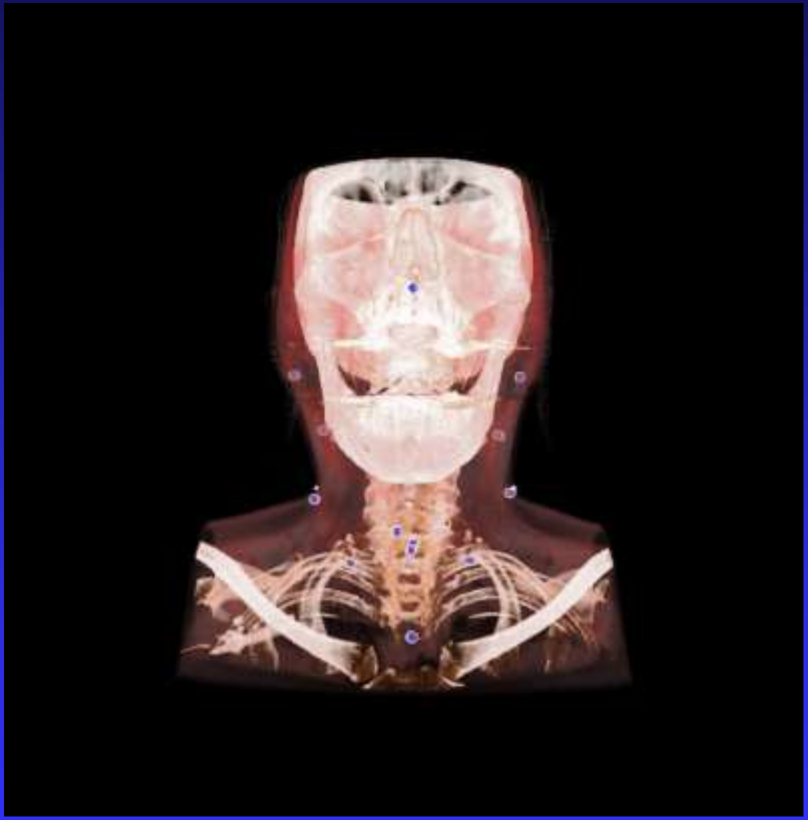
$$\boldsymbol{\sigma}_2^2 = (\boldsymbol{\sigma}_{3-2}^2 + \boldsymbol{\sigma}_{2-1}^2 - \boldsymbol{\sigma}^2{}_{3-1})/2$$

$$\boldsymbol{\sigma}_3^2 = (\boldsymbol{\sigma}_{3-1}^2 + \boldsymbol{\sigma}_{3-2}^2 - \boldsymbol{\sigma}^2{}_{2-1})/2$$



Analysis of variance

- Landmark validation
- 7 patients, 7 - 8 fractions
- 23 landmarks per CBCT, two human observers
- B-spline deformable registration for landmark propagation
- Use of ANOVA method to correct for observer variation

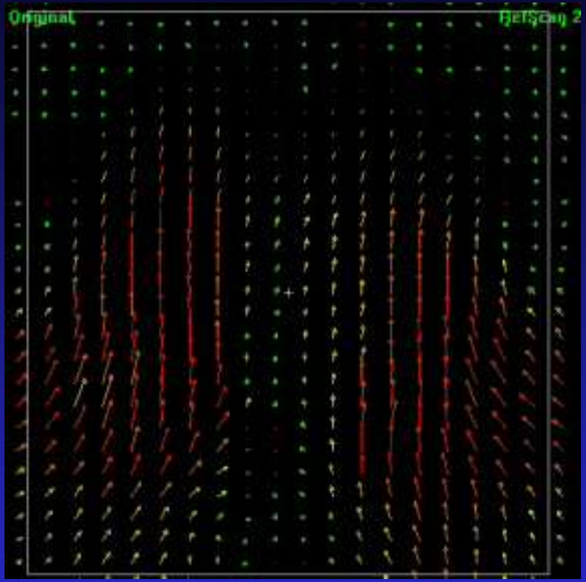


Results

Method	Accuracy (1SD mm)		
	SD_{LR}	SD_{CC}	SD_{AP}
Rigid registration	**1.8**	**2.0**	**1.7**
B-spline *No penalties*	**1.4**	**1.5**	**1.1**
B-spline + *penalties*	**0.9**	**1.0**	**0.9**

Applications

Image Enhancement

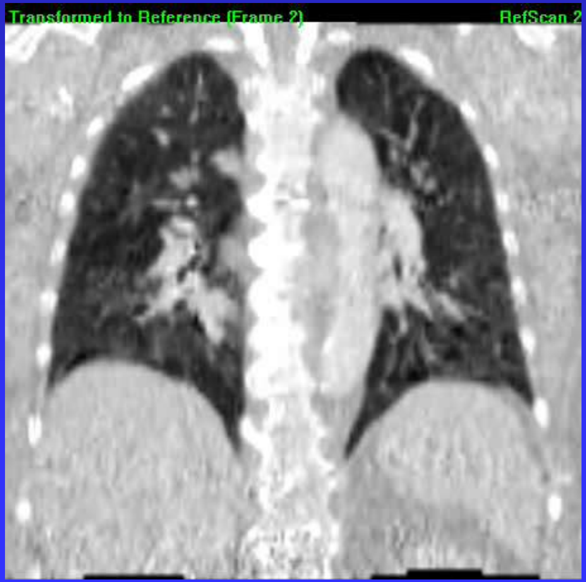


4DCT → Full 3D DVF

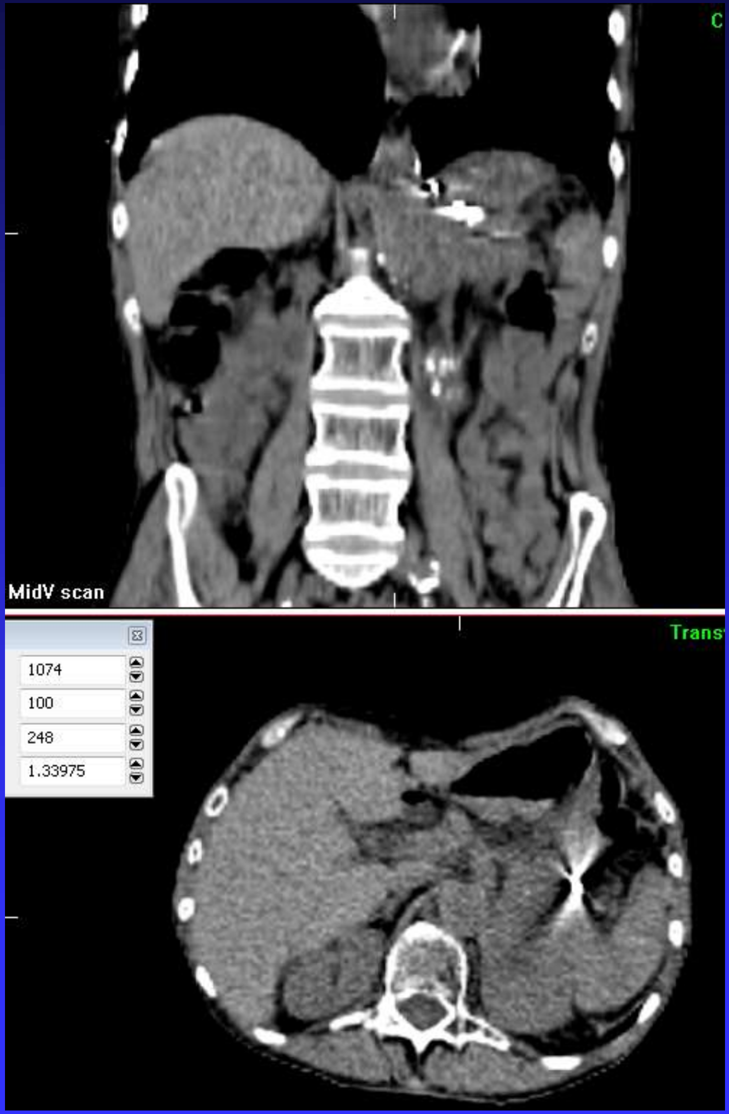
4DCT + Full 3D DVF → Motion corrected 4DCT @ mean pos.

Motion corrected 4DCT @ mean pos. → Mid-position CT

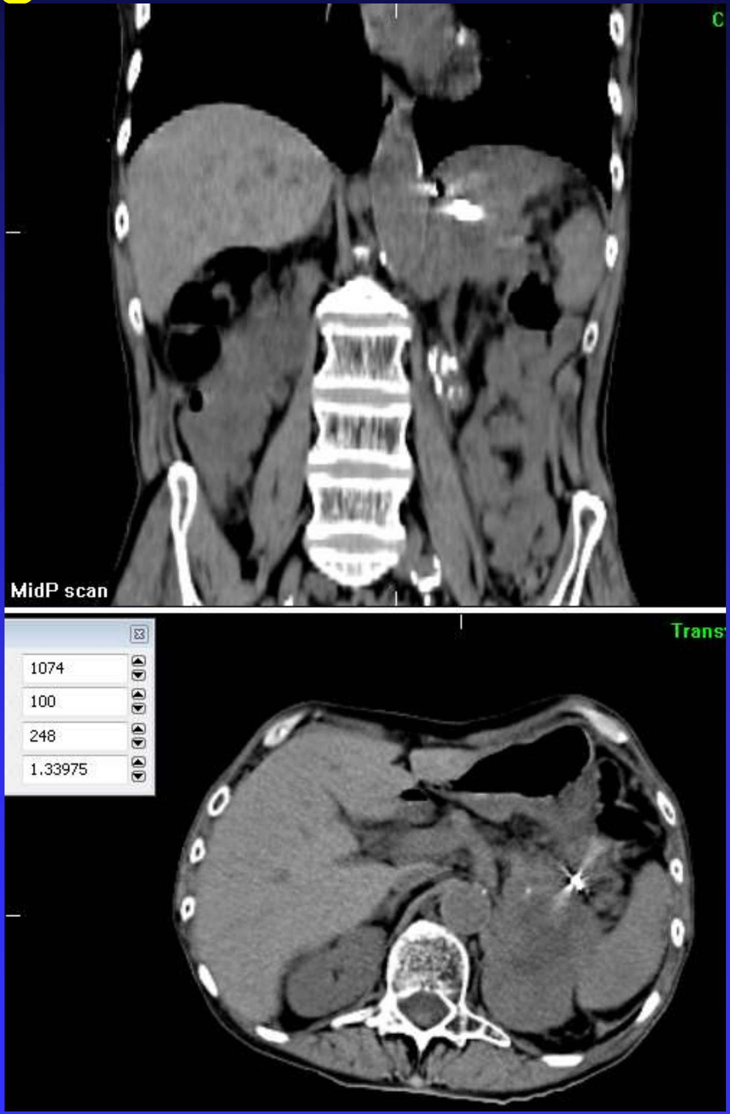
Average frames



Mid-ventilation method versus mid-position reconstruction (motion compensated 4DCT) using deformable registration

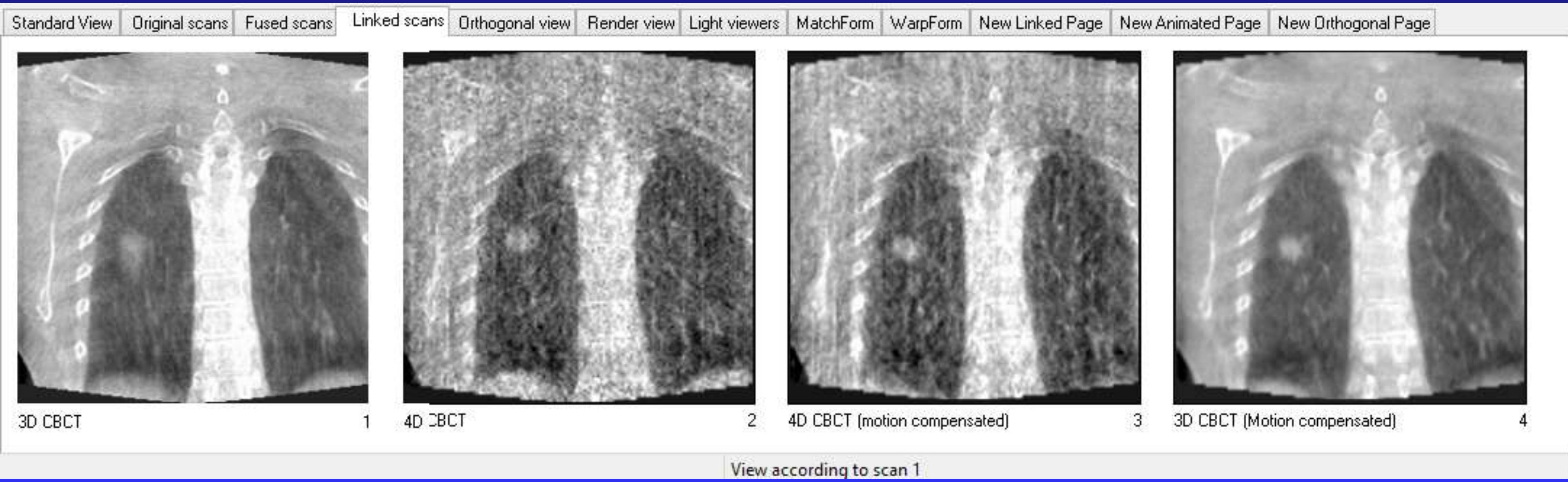


Mid-ventilation (one bin)

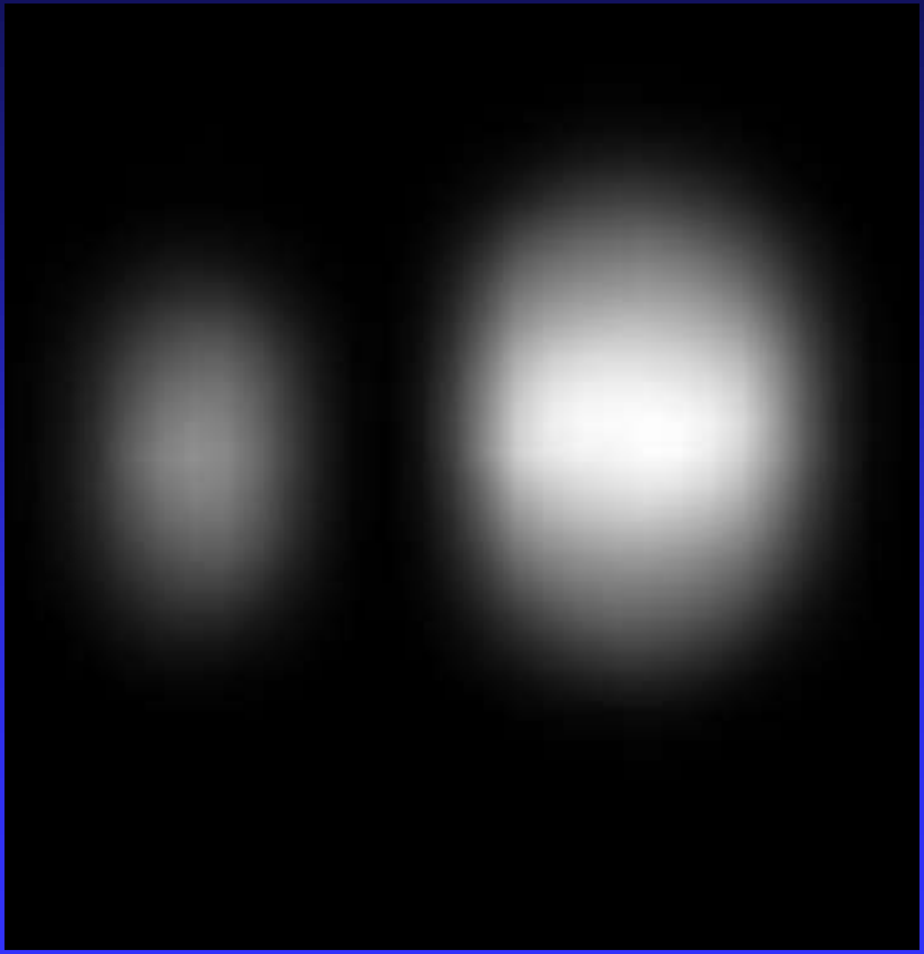


Median of all bins deformed pixel by pixel to mid-position

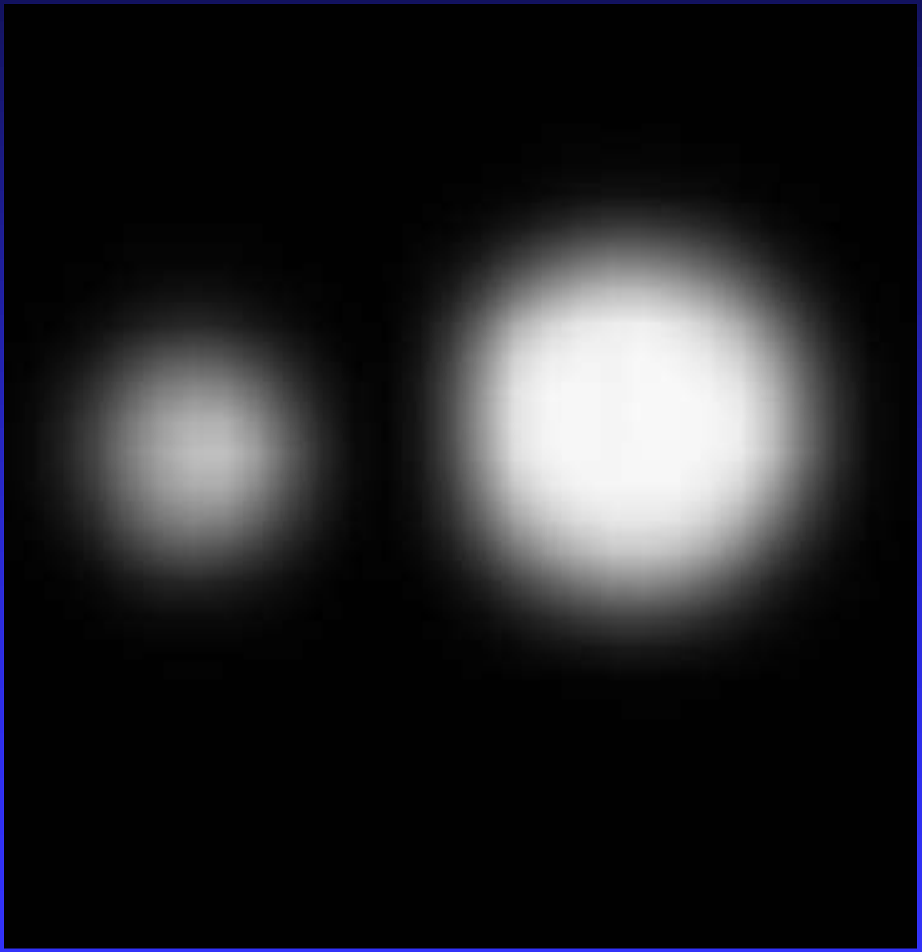
Motion compensated CBCT



PET-CT motion compensation



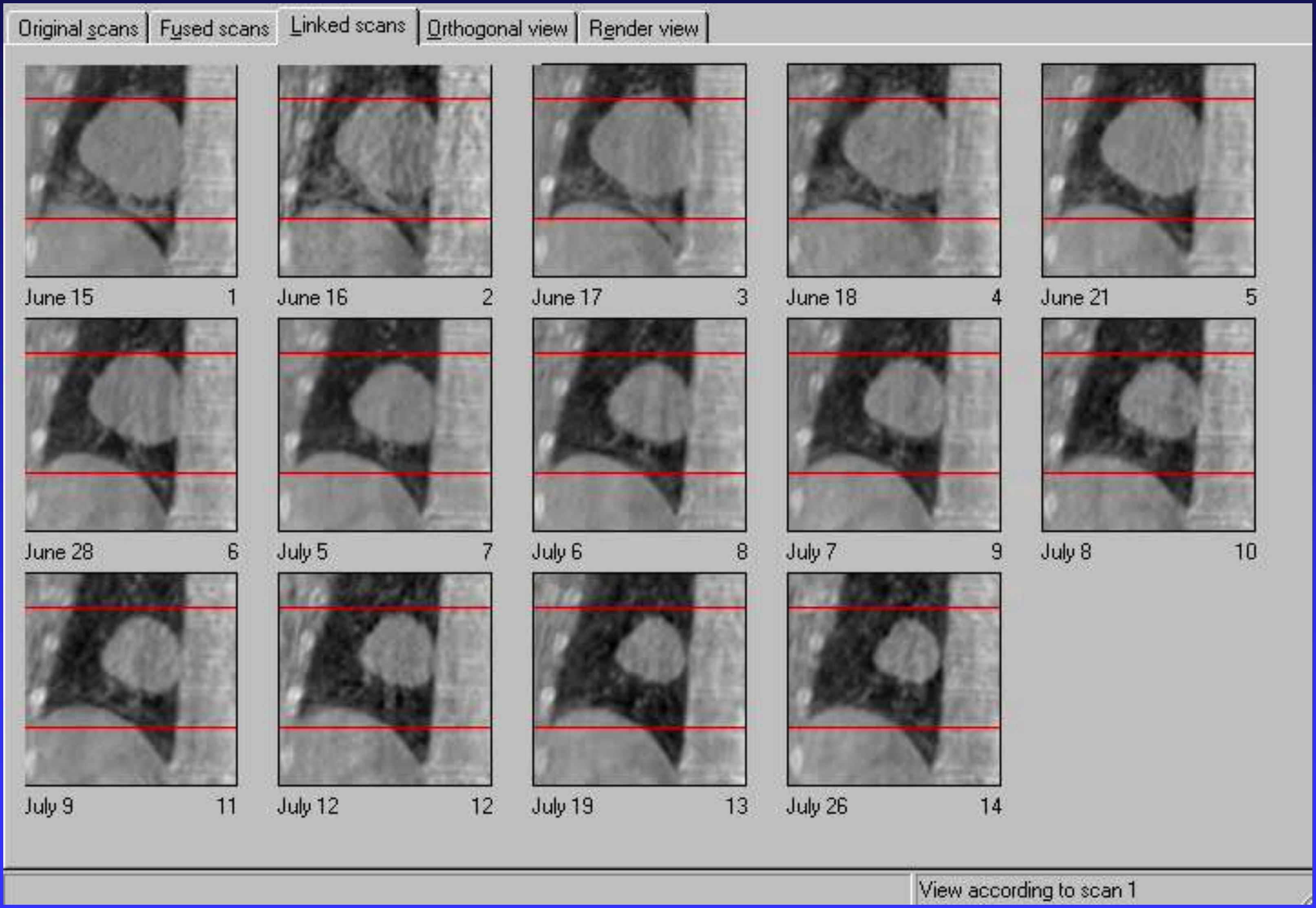
2.5 cm motion



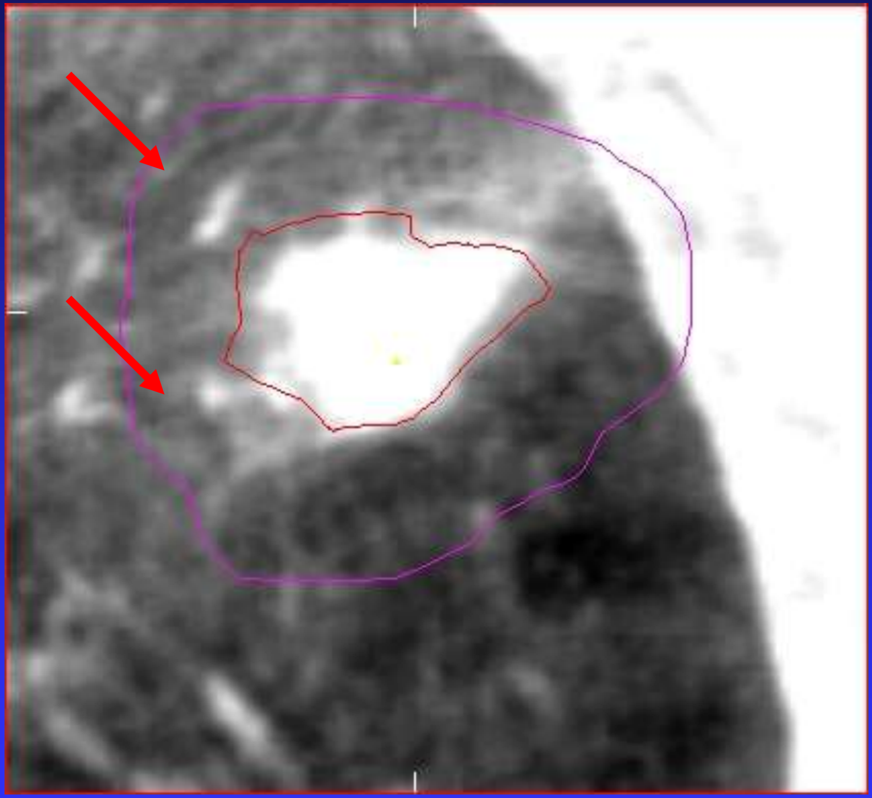
Compensated

Lung DIR easy ?

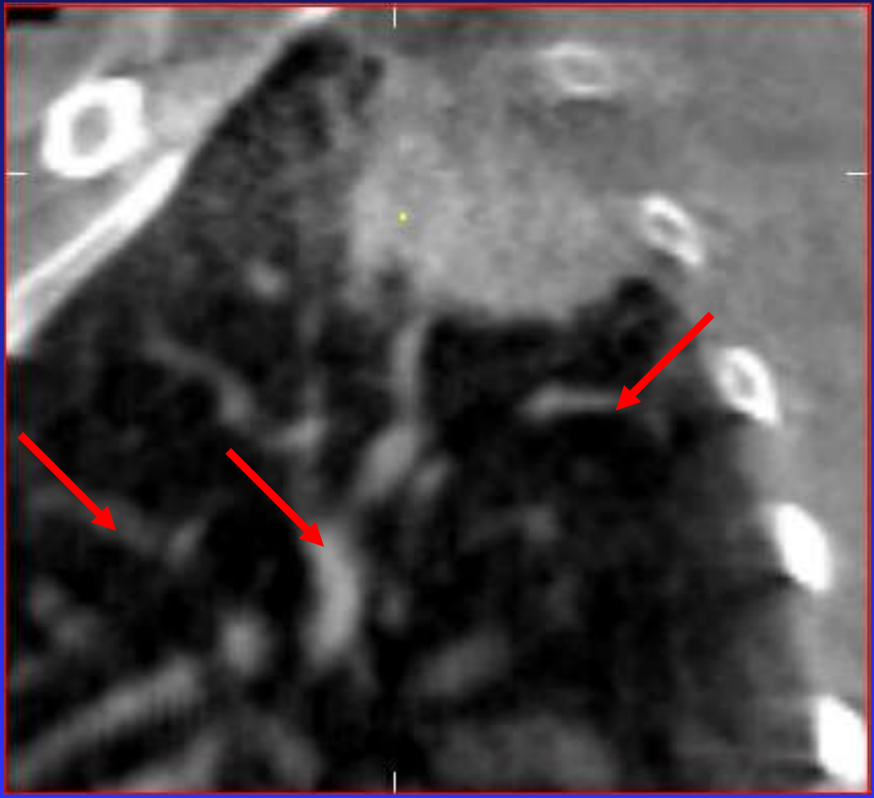
Repetitive 4D CT: treatment response



Modes of Tumor Regression

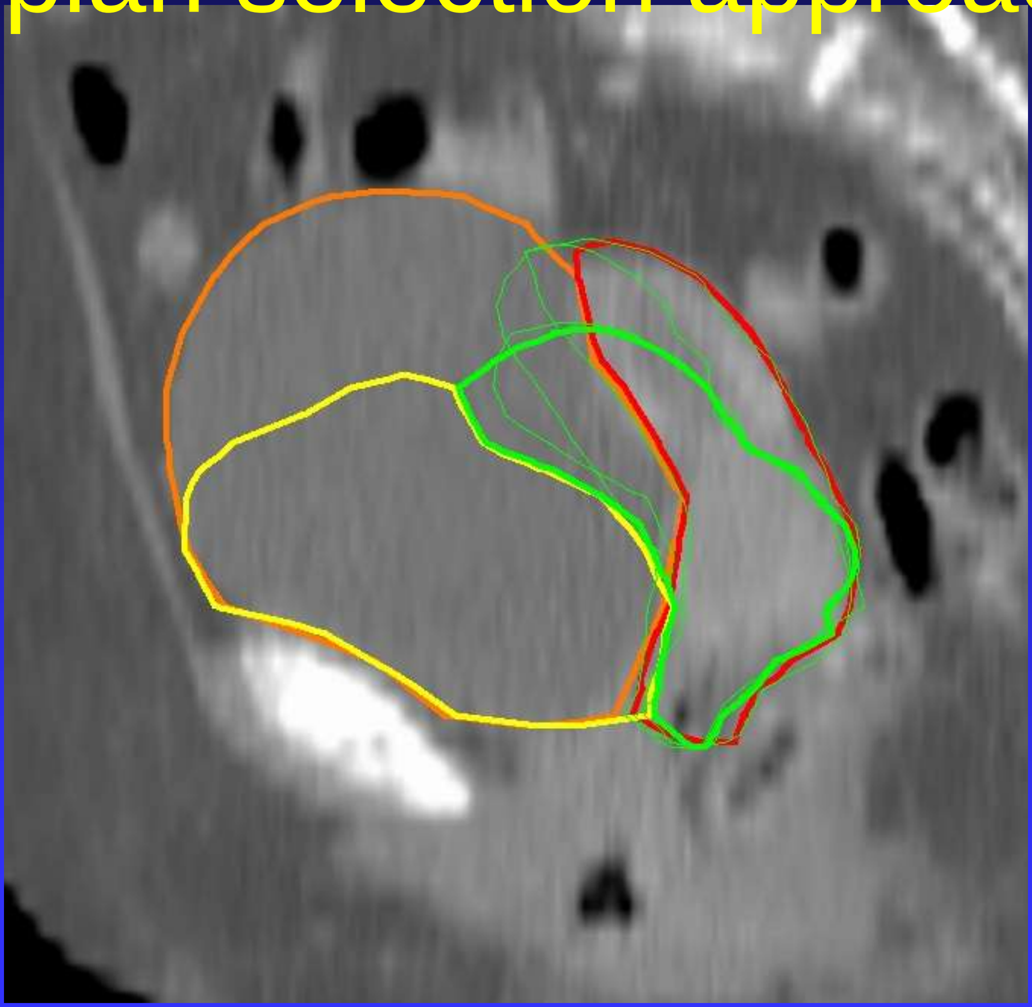


'elastic'

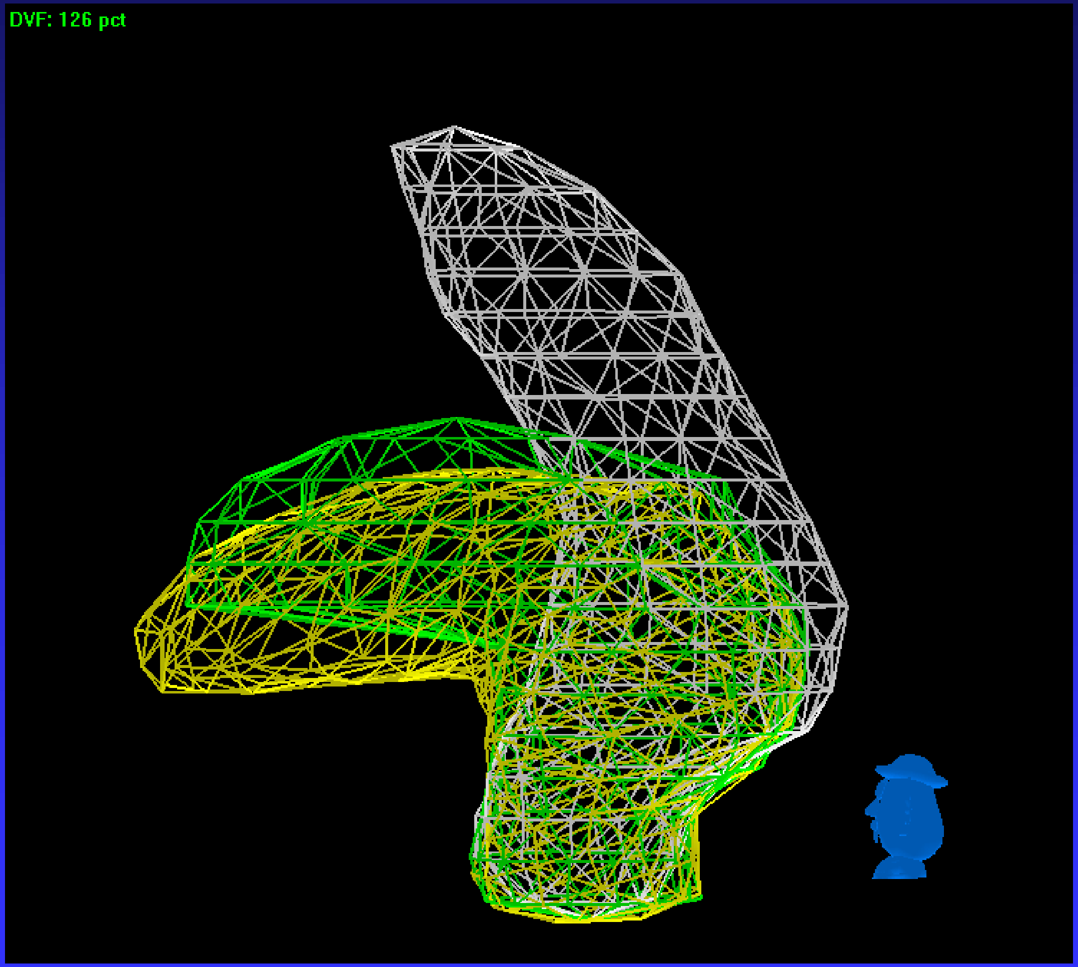


'erosion'

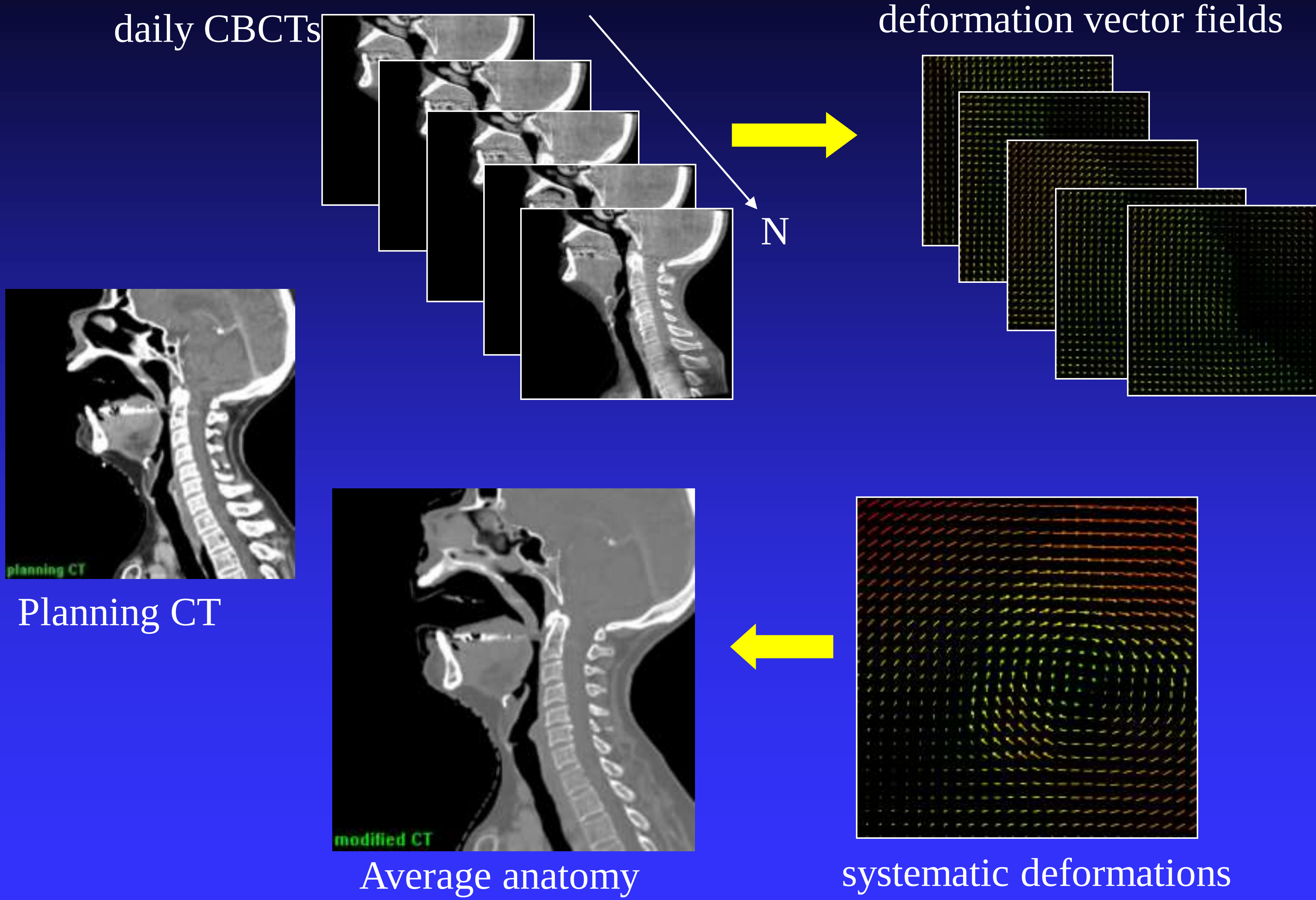
Generate intermediate contours for plan selection approaches



Interpolation of cervix motion



Adaptive replanning on average anatomy



Kranen et al, IJROBP 2013

Summary

- Deformable image registration plays an important role in target definition, advanced treatment planning and image guidance
- Validation of registration accuracy is essential for each clinical problem
- Visual verification remains essential as automatic algorithms are never perfect
- Work towards faster and more robust deformable images registration continues
- In our clinic, rigid registration is still a cornerstone, e.g. for tumor contour propagation

Summary 2

- Image registration does not know about biology and biomechanics
  - Sliding tissue
  - Tumor growth and regression
  - Weight loss
- This is OK to make pretty pictures and propagate HU and OAR contours
- This is not OK for dose accumulation
- The best deformable registration between image A and B: copy A B
- In strongly believe DIR is not a solved problem!

Thank you for your attention!

The Netherlands Cancer Institute

Antoni van Leeuwenhoek Huis

IGRT for stereotactic RT using cone beam CT

Marcel van Herk, Peter Remeijer, Anja Betgen,
Danny Minkema, Luc Dewit, Jan-Jakob Sonke, and Coen Rasch

Introduction

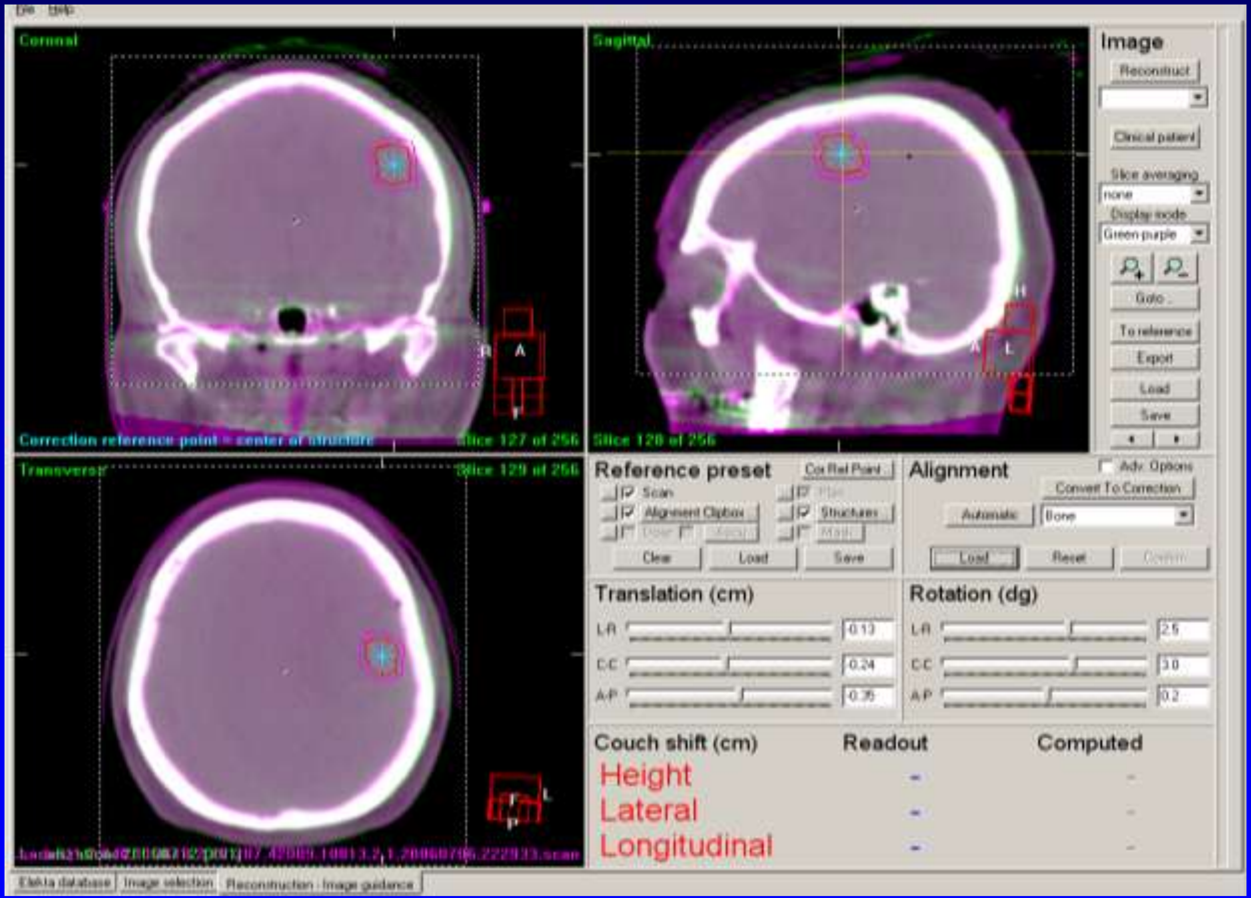
- High precision stereotactic treatments of the brain often involves the use of invasive frames
- Short term stability of mask fixation may be sufficient
- Accurate registration to reference data will be necessary

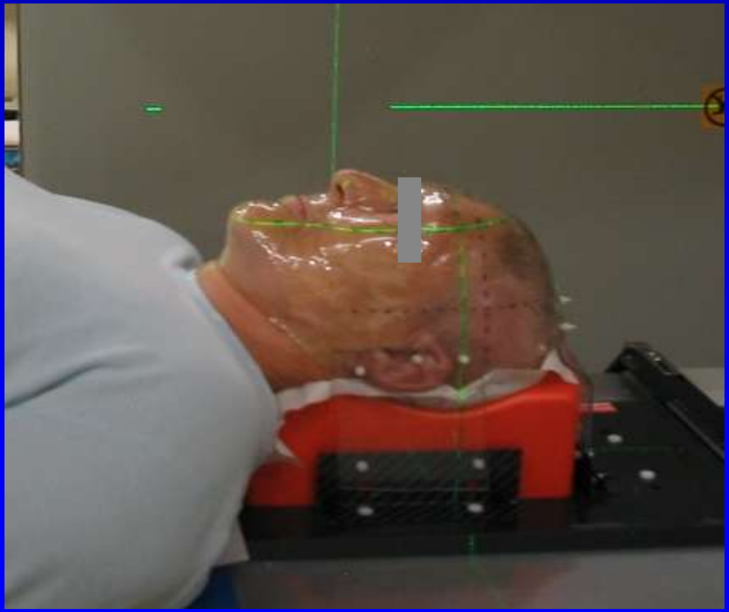
Aim:

Determine precision of online setup corrections for brain patients using cone-beam CT

With IGRT, this is no longer needed to precisely irradiate a brain tumor

We can use this instead: focus on patient stability, but let computer position the patient with better than one mm precision



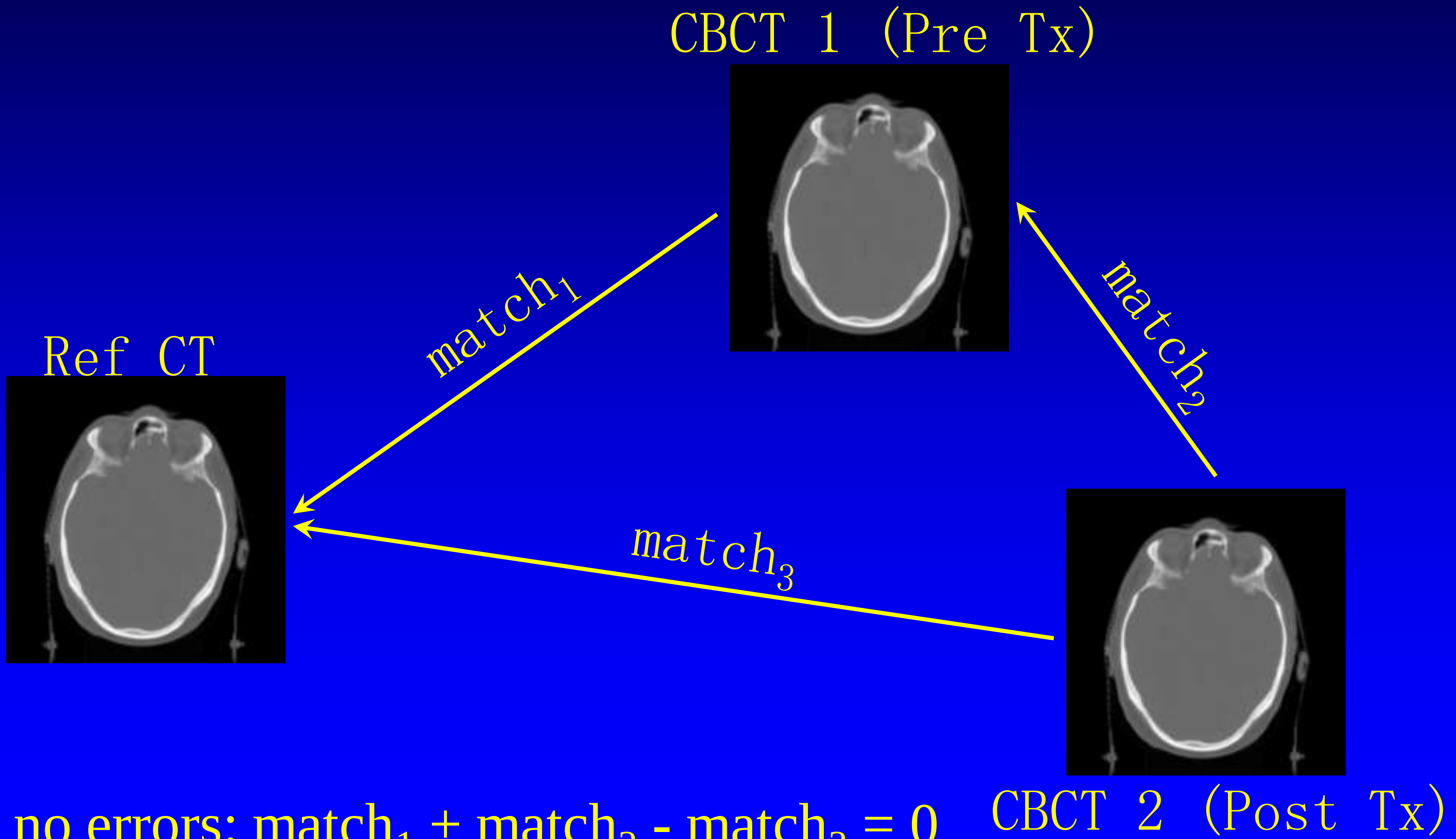


- Accuracy registration: 0.1 mm SD
- Accuracy table: 0.2 mm SD {x, y, z}
- Intra-fraction motion: 0.3 mm SD

v Beek et al, R&O 2011

Demo brainstem IGRT

Registration accuracy – Full circle method

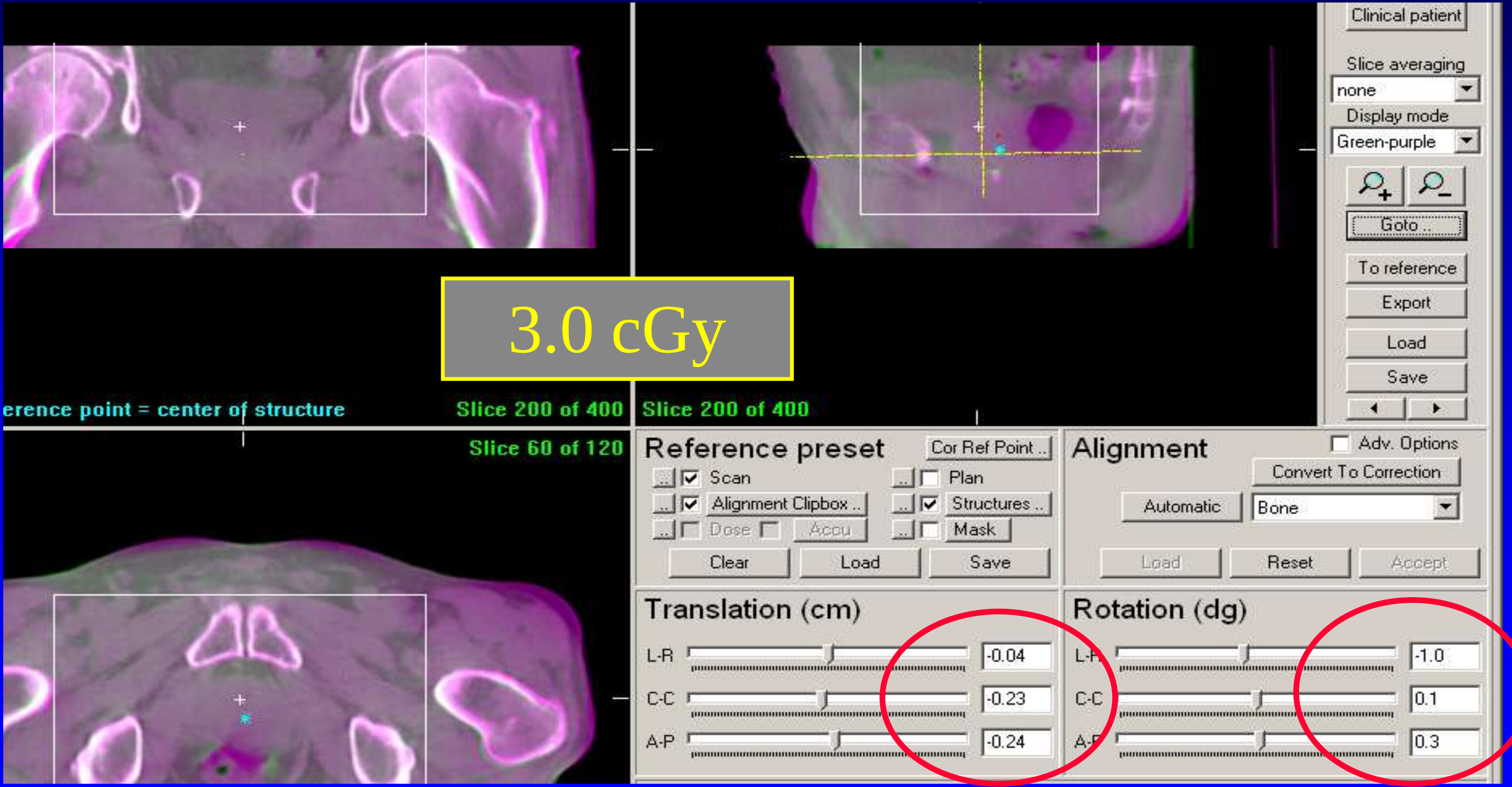


If no errors: $\text{match}_1 + \text{match}_2 - \text{match}_3 = 0$

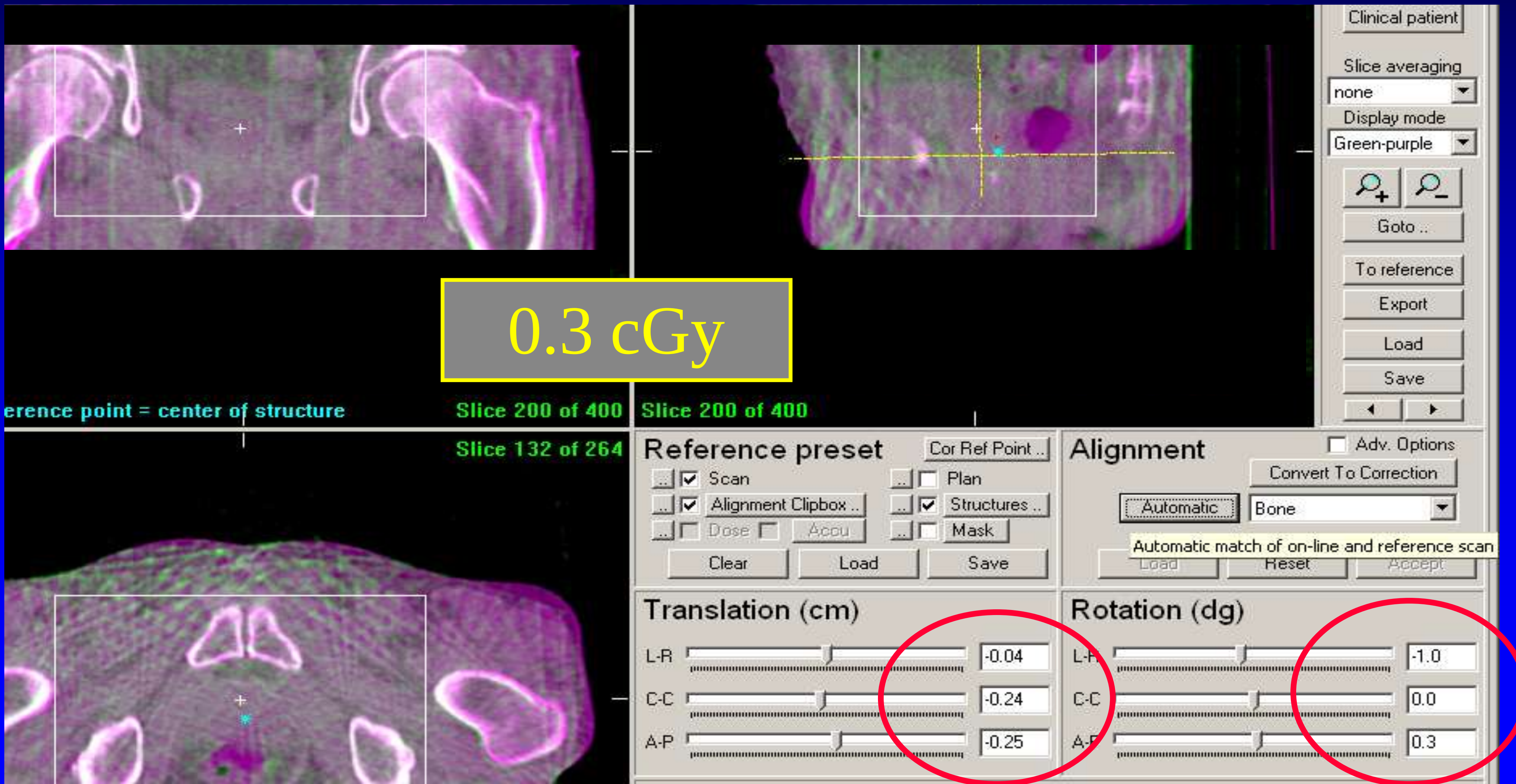
Results – Registration accuracy: bone matching for skull

Left-right (mm)		Cranial-caudal (mm)		Ant-post (mm)	
Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
0.0	0.2	-0.2	0.2	-0.1	0.3

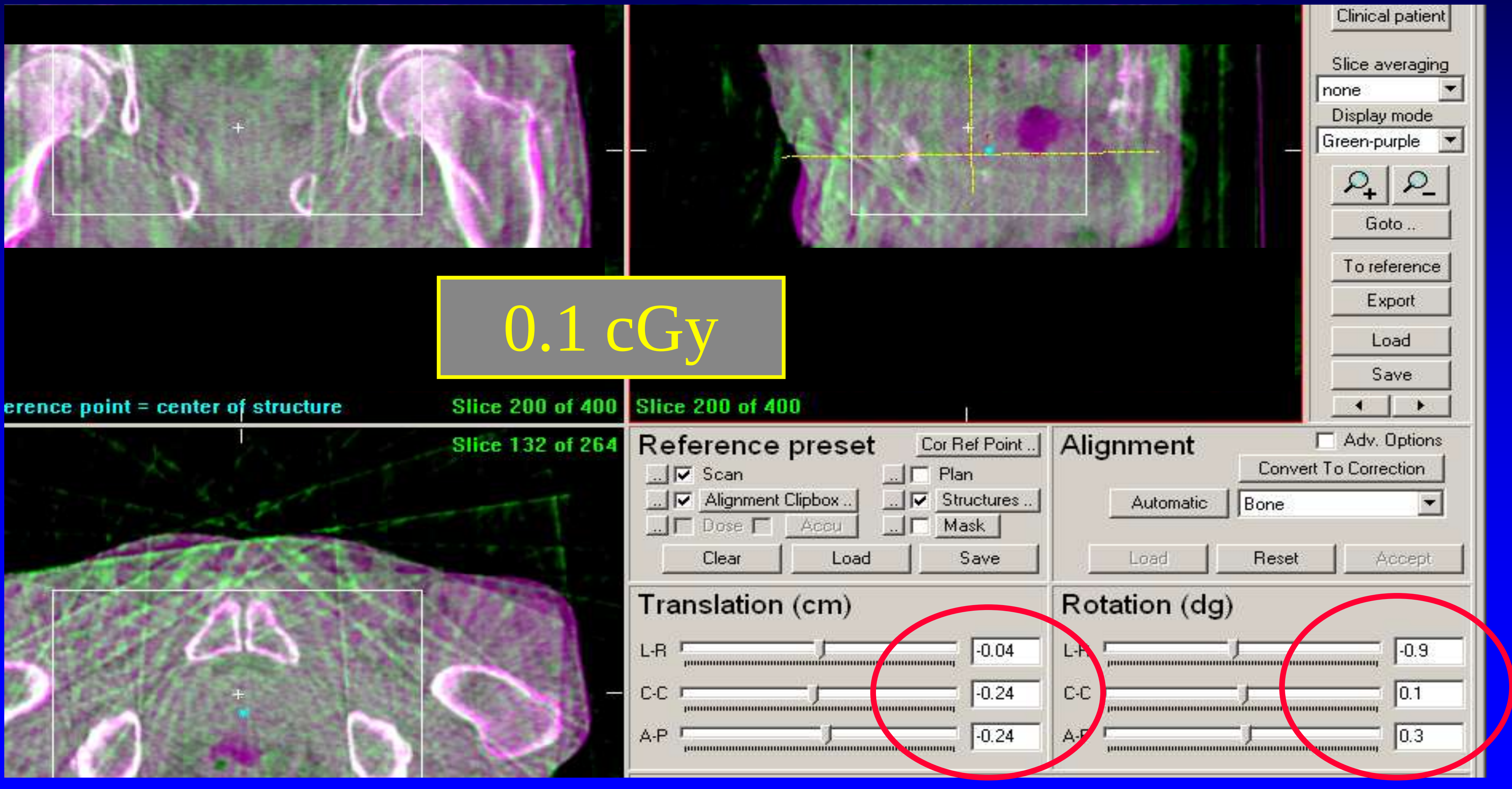
Dose required to localize bone with CBCT



Dose required to localize bone with CBCT



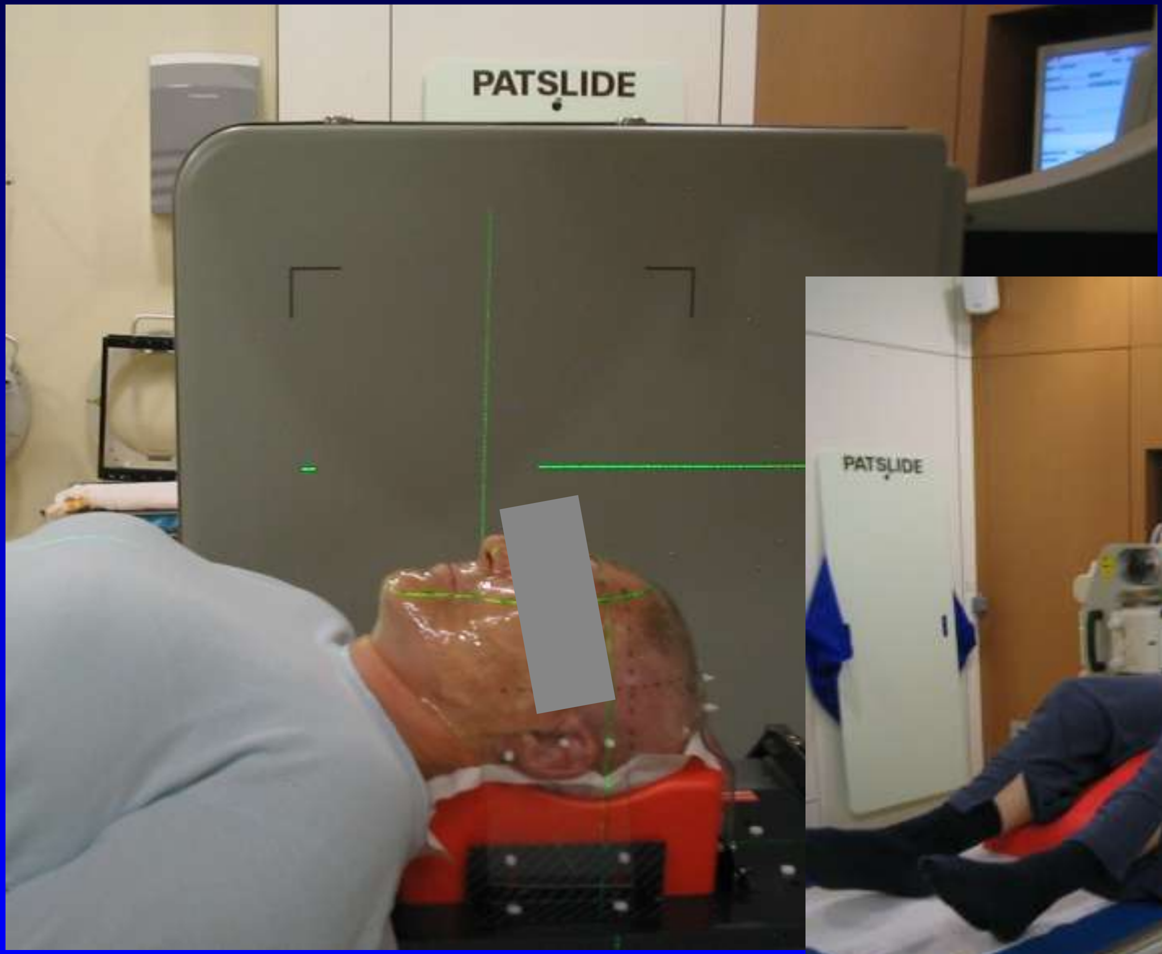
Dose required to localize bone with CBCT



Patient study: setup accuracy

- 10 patients
  - Posicast mask fixation
  - Single fraction boost of 15-20 Gy
  - Minimum field size 3 cm
  - Regular MLC (5 mm leaves)

Methods - Patient set-up



Procedure

Scan

↓

Match and convert to correction

↓

Correct all errors

↓

Pre-treatment scan (to check patient position)

↓

Treat & Scan

↓

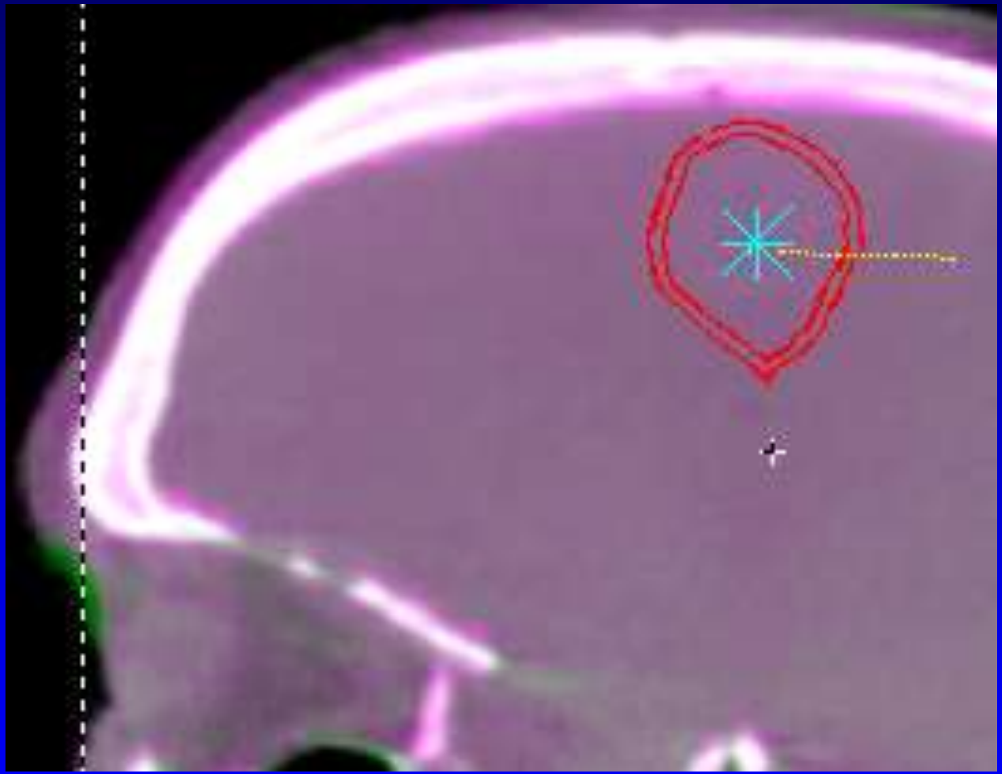
(Post-treatment scan to check patient position)

- Use of 1 minute scans, 1 cGy dose per scan

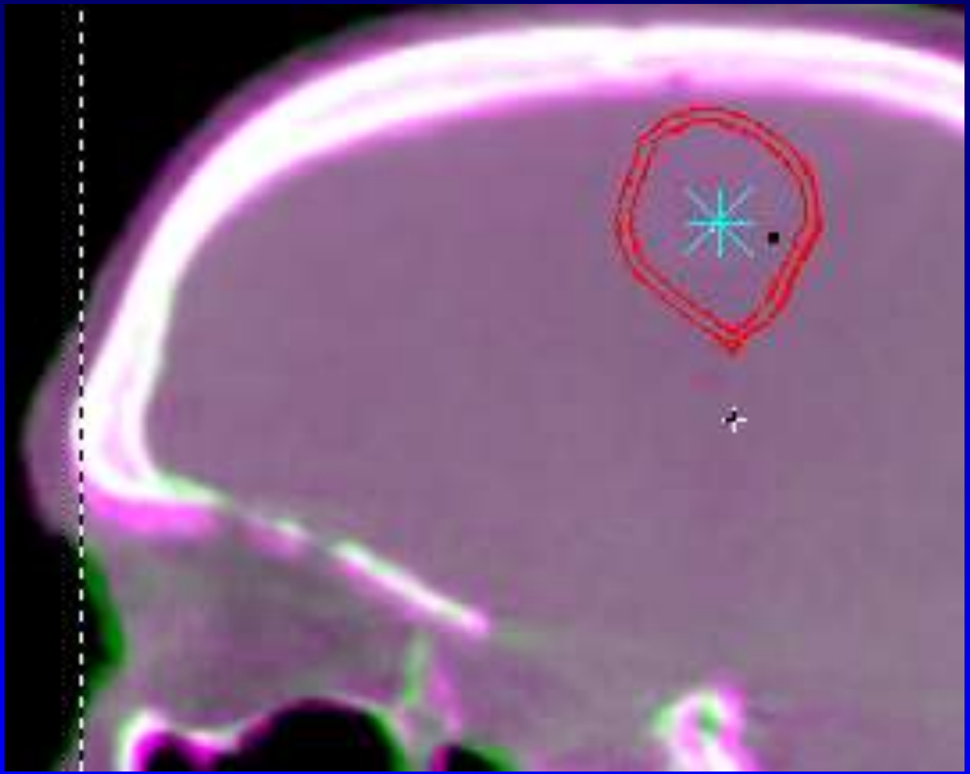
Online Correction Protocol at NKI (brain metastasis 1 x 18 Gy)

• scan patient with CBCT	1 min
• image analysis + visual verification	2 minutes
• correct errors	0.5 min
• rescan for verification	1 min
• treat & image during treatment (2 arcs)	2-5 min
• rescan after treatment	1 min
	+4.5 min

Registration procedure – Rotational errors

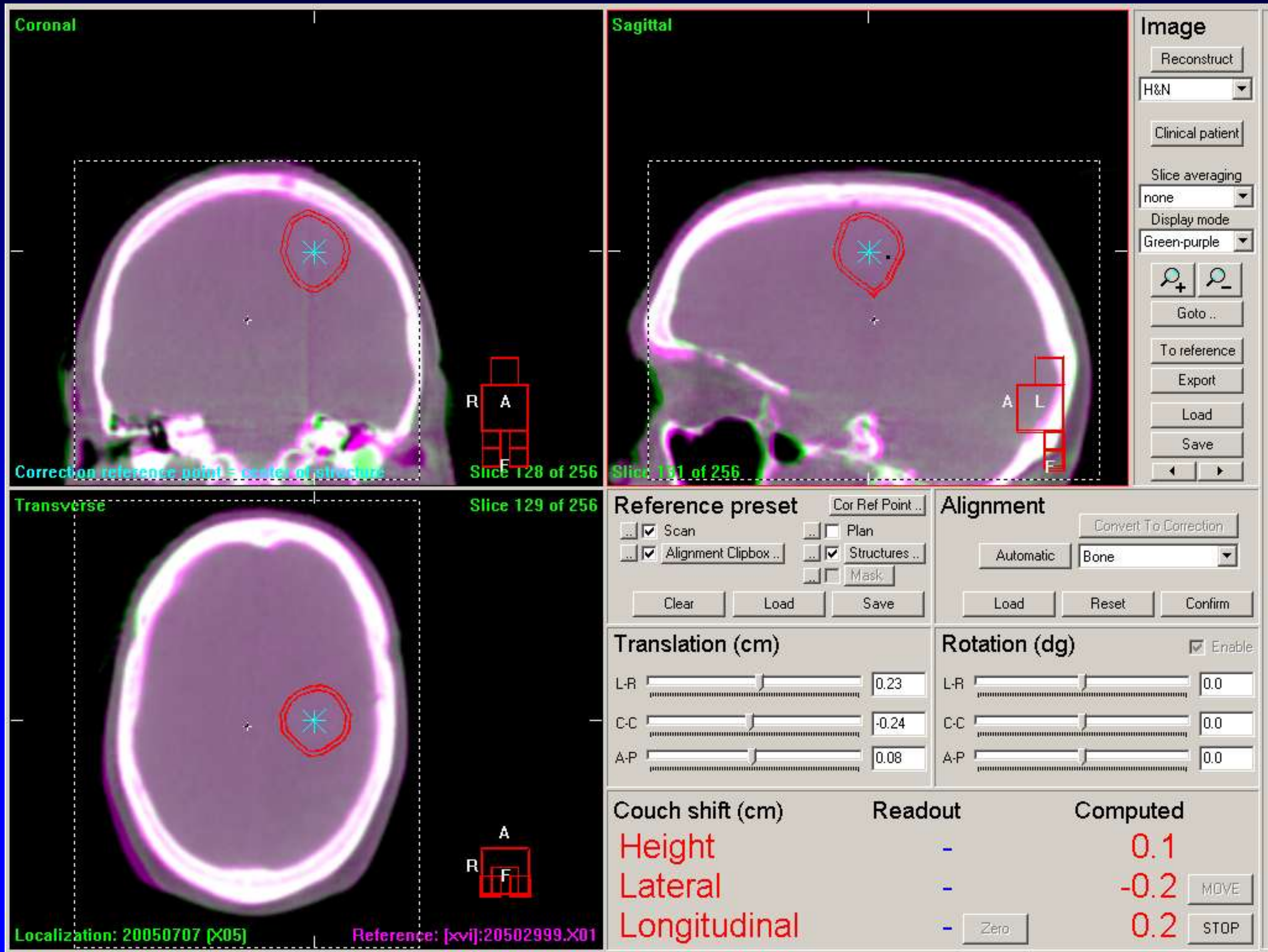


Match including rotations

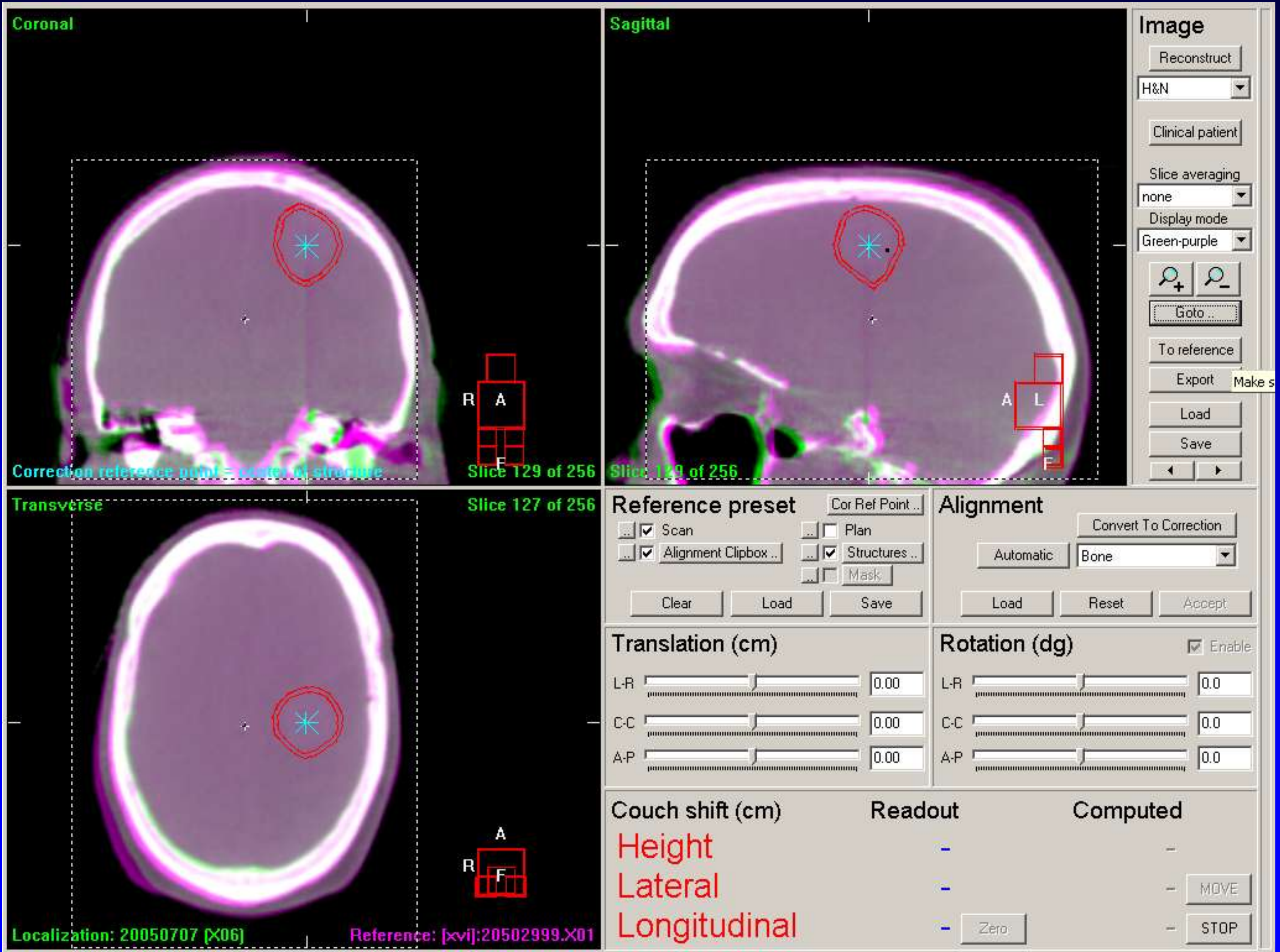


Match without rotations

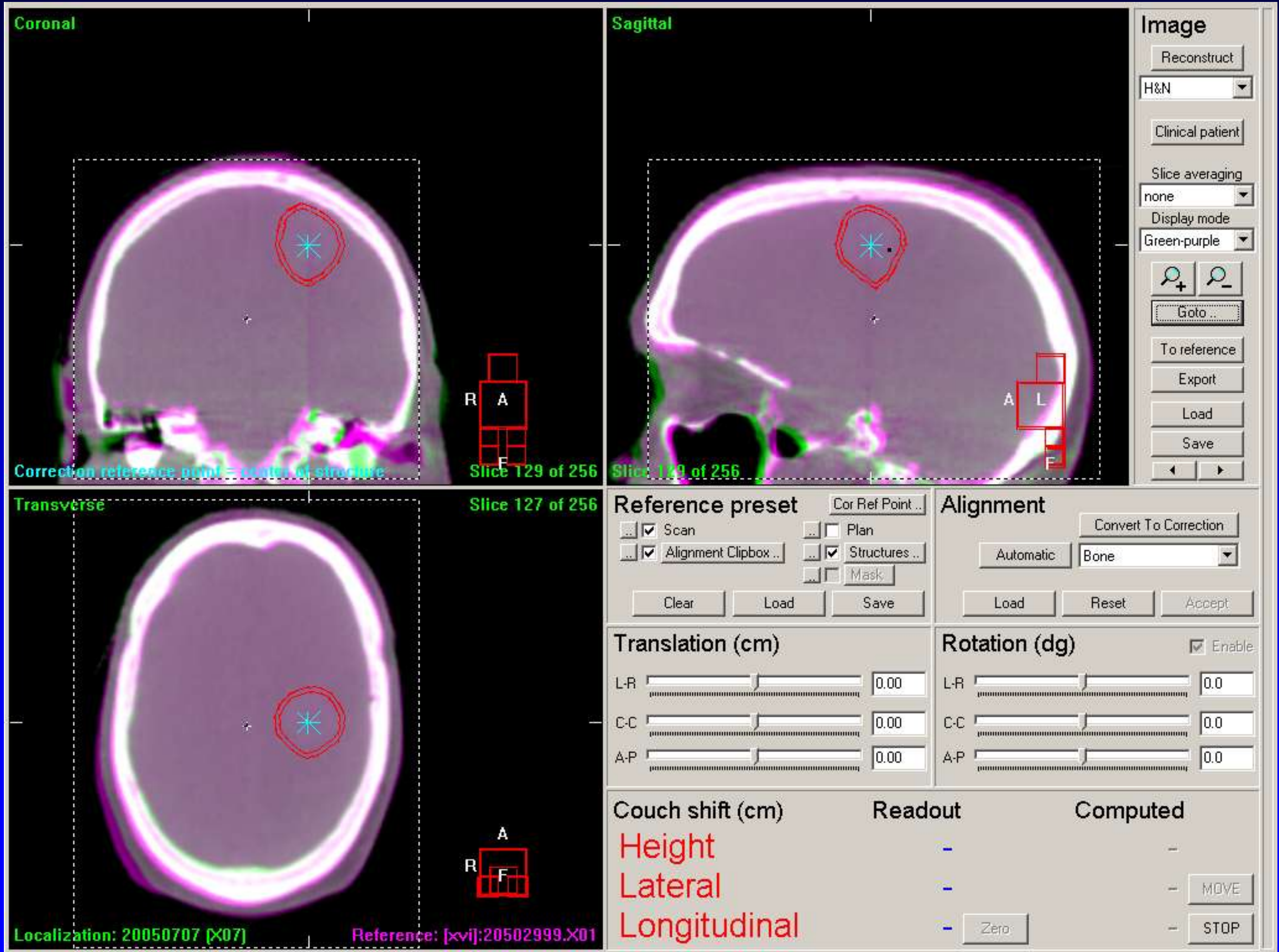
Match procedure – First scan, CTC



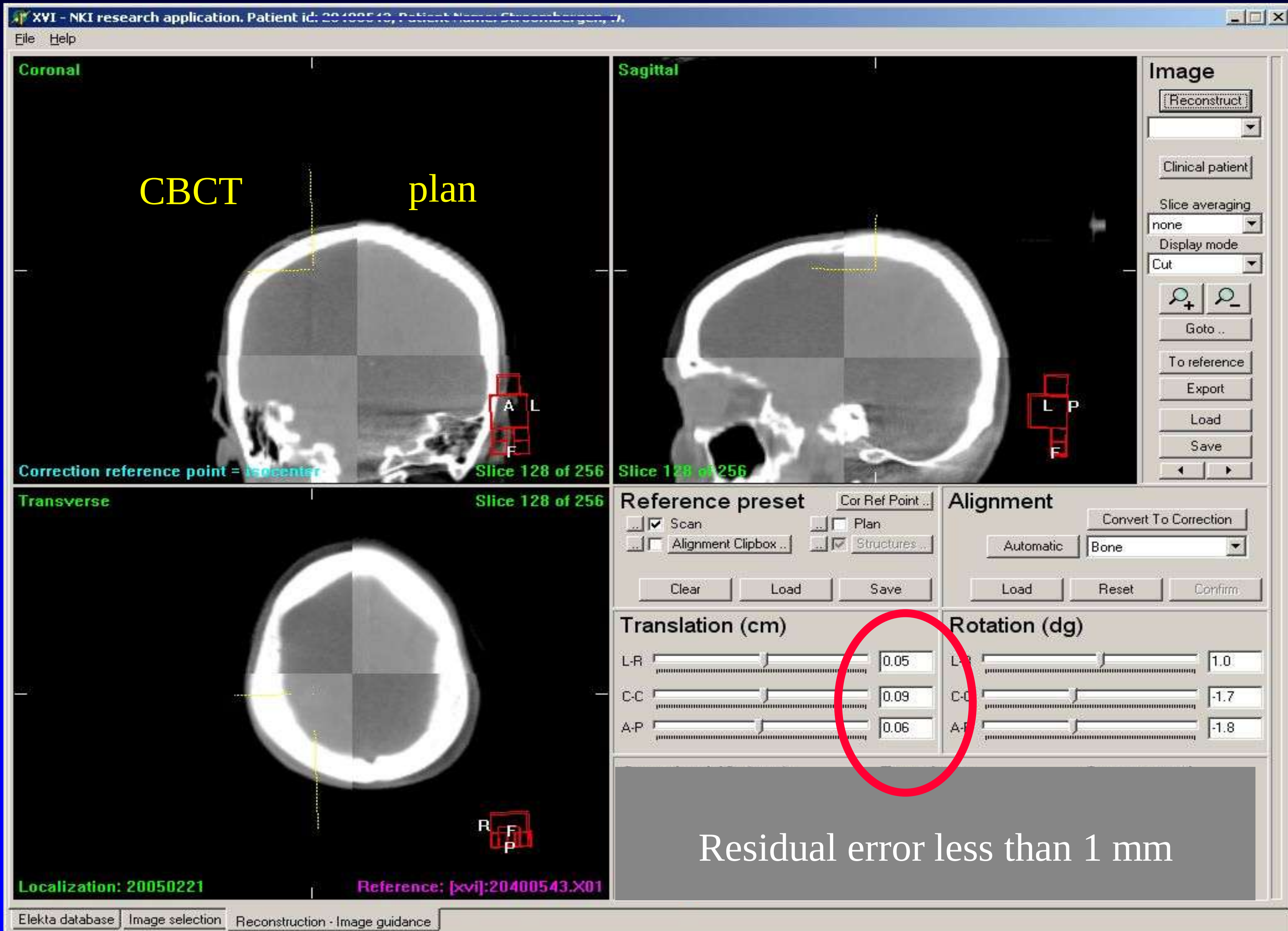
Match procedure – Pre-treatment scan



Match procedure – Post-treatment scan

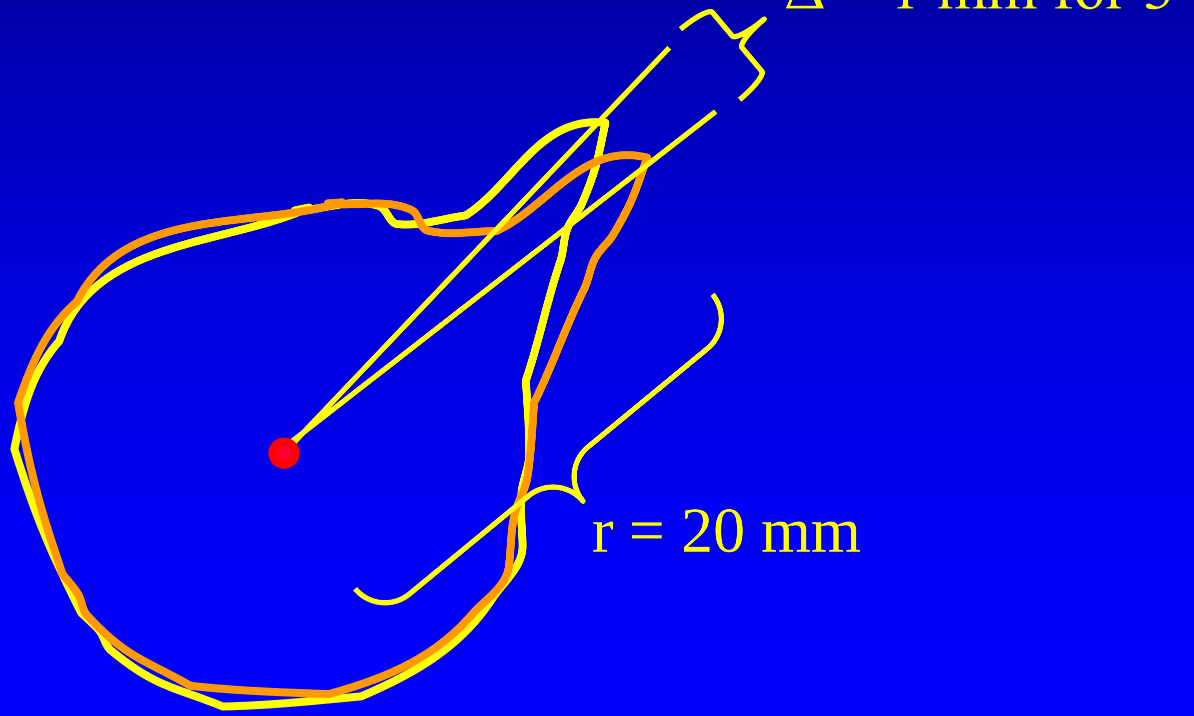


Post Treatment (and after couch shift)



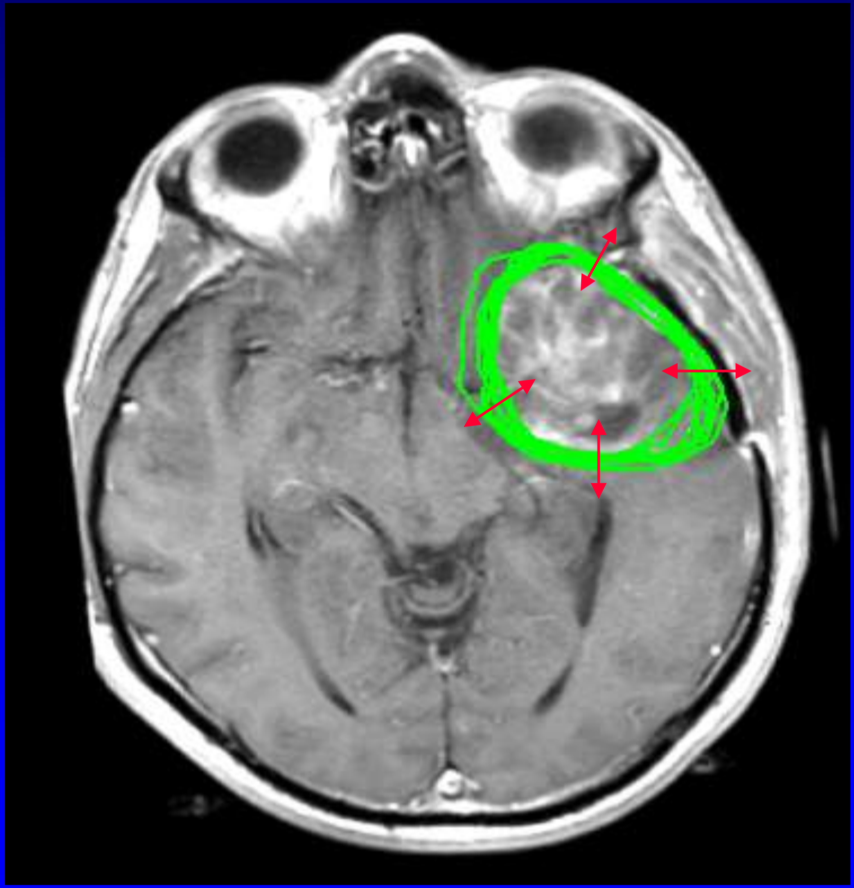
Rotations

- Largest rotation found: 3 degrees (SD 1 degree)
- Errors will be smaller than 1 mm



Glioma delineation variation (Beijing 2008)

	SD (mm)	SD (mm) outliers removed	Margin (mm)
Homework	3.6	2.3	5.8
Groups	1.3	1.3	3.2
Validation	2.6	2.3	5.8



- Delineation uncertainty is a systematic error that should be incorporated in the margin
- Consistency is imperative to gather clinical evidence

Why is SD between observers important?

- Assume each group is equally skilled
- Let one group prepare plan
- Evaluate DVH of delineation other group given dose distribution of this plan
- Since one group is not more correct than another, this DVH should show adequate coverage
  - → Need to add SD between groups in CTV-PTV margin

CNS: single fraction IGRT for brain metastasis

all in cm	**systematic errors**	squared	**random errors**	squared	
delineation	**0.13**	0.0169		0	
organ motion	**0**	0		0	
setup error	**0.03**	0.0009		0	
CBCT accuracy	**0.02**	0.0004		0	
intrafraction motion			**0.02**	0.0004	
total error	**0.13**	0.02	**0.02**	0.0004	
	times 2.5		**times 0.7**		
error margin	**0.34**		**0.01**		
total error margin		**0.35**			

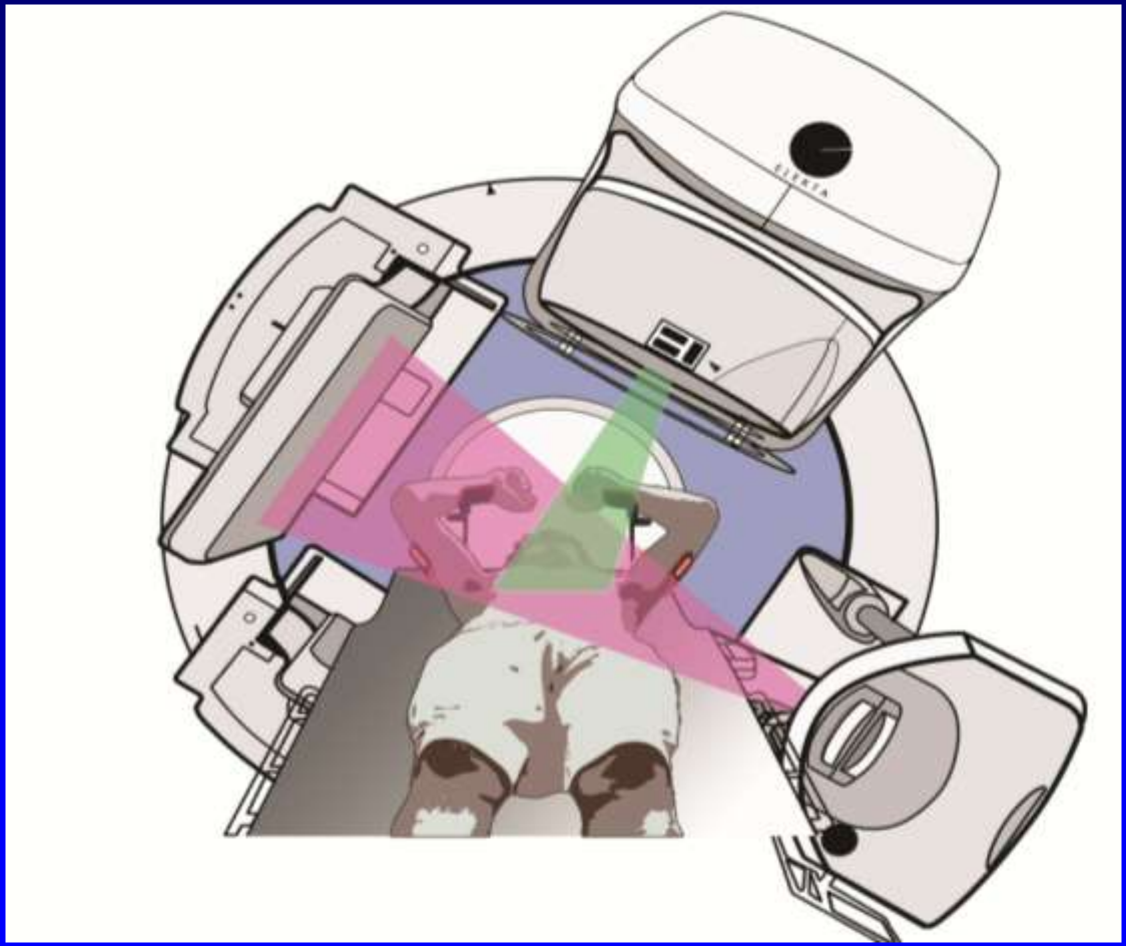
•Tightest margin achievable in EBRT ever due to very clear outline on MRI

Conclusions

- Intra-fraction movement in a mask is about 0.2 - 0.3 mm, registration accuracy comparable
- With automatic couch shift, the accuracy of IGRT is extremely high
- Rotational errors have a negligible effect for CTV coverage in most cases
- Cone-beam CT guidance of stereotactic treatments achieves comparable results to methods based on invasive frames
- Post treatment scan important to validate workflow

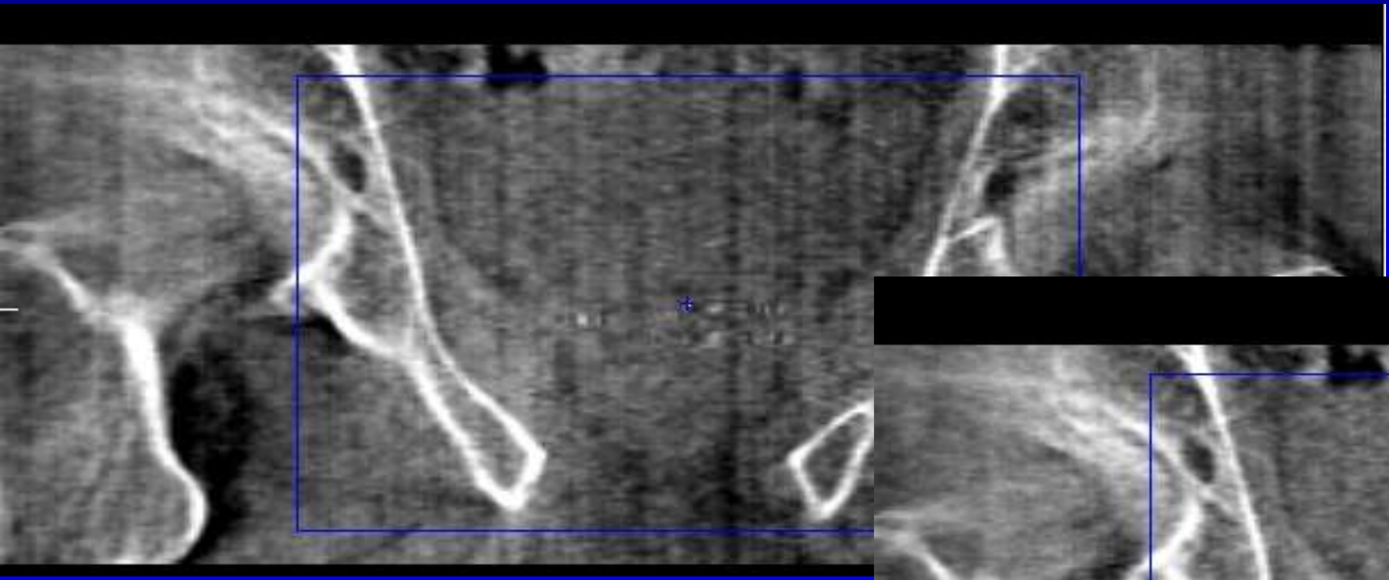
Intra-fraction monitoring

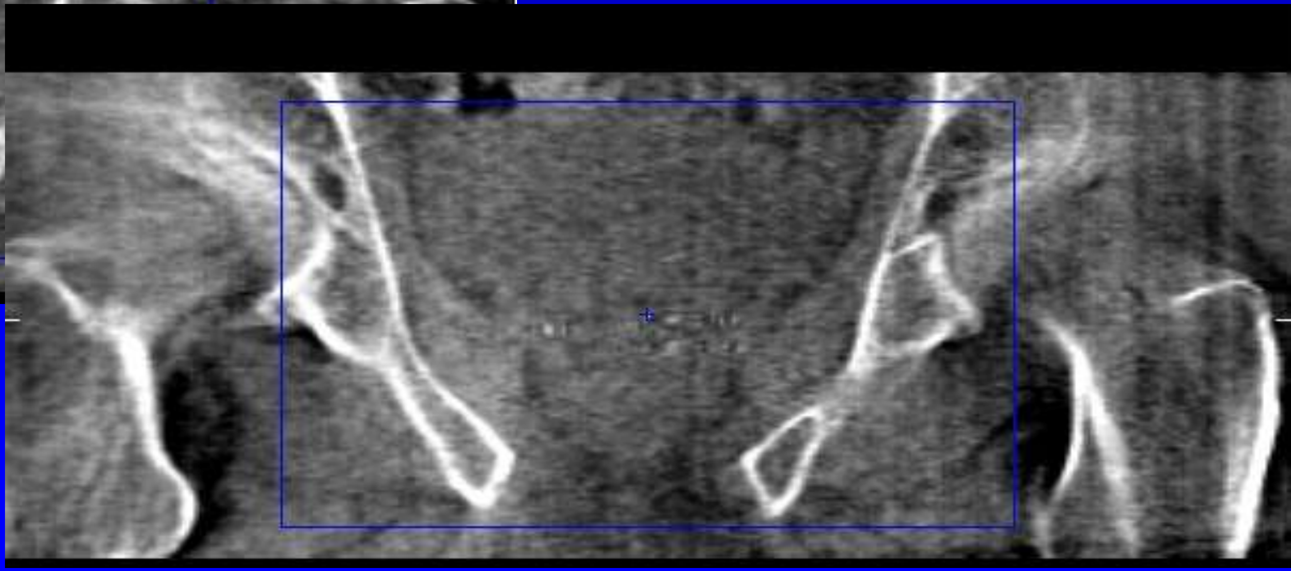
Simultaneous kV imaging with VMAT delivery



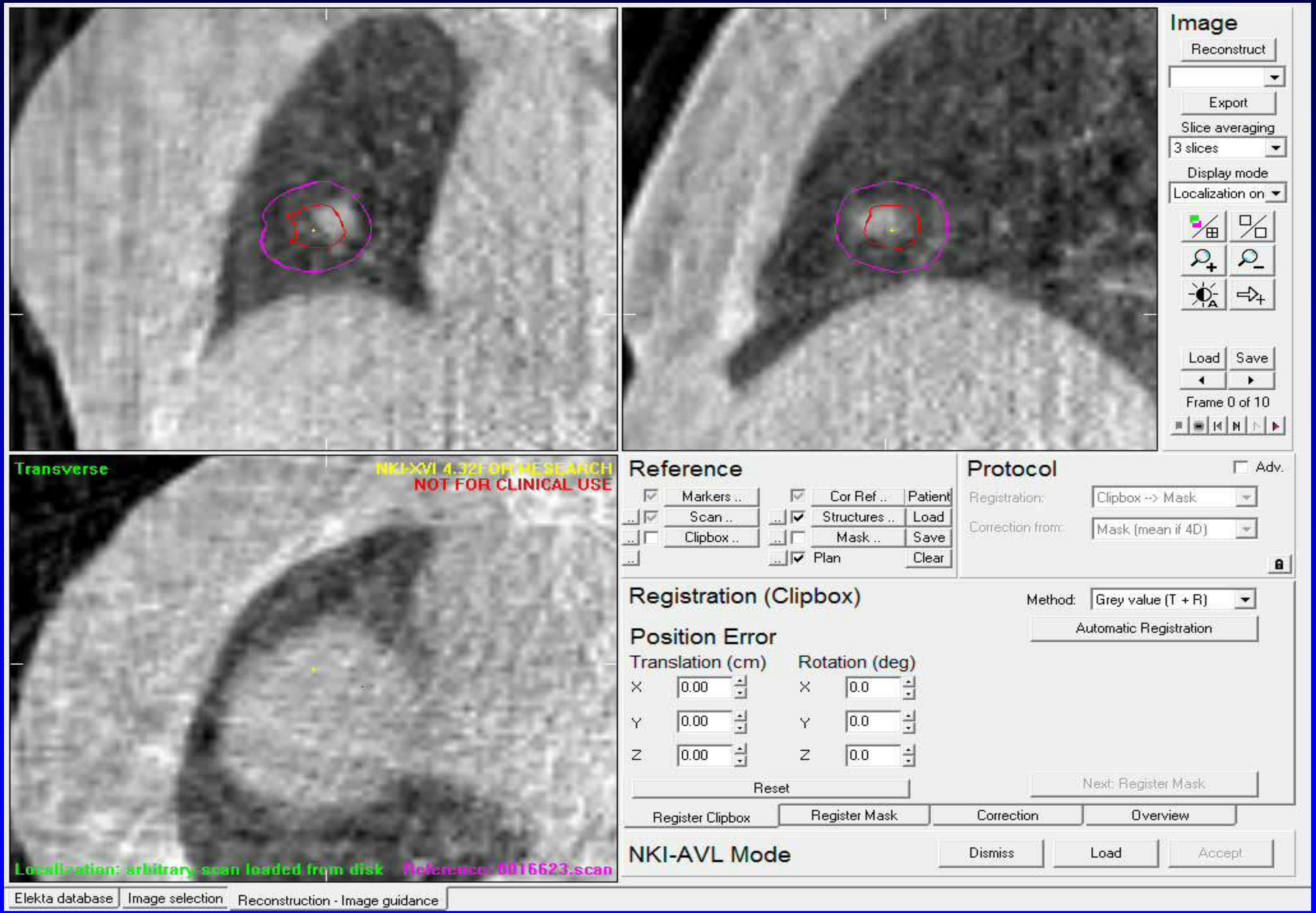
- •Pulse line artifact
- •Scattered MV dose
- •1-3 minutes per arc
- •300-1000 projection images per arc (1-1.5 cGy kV dose)

Pulse line artifact supression





Validation scan during first VMAT arc



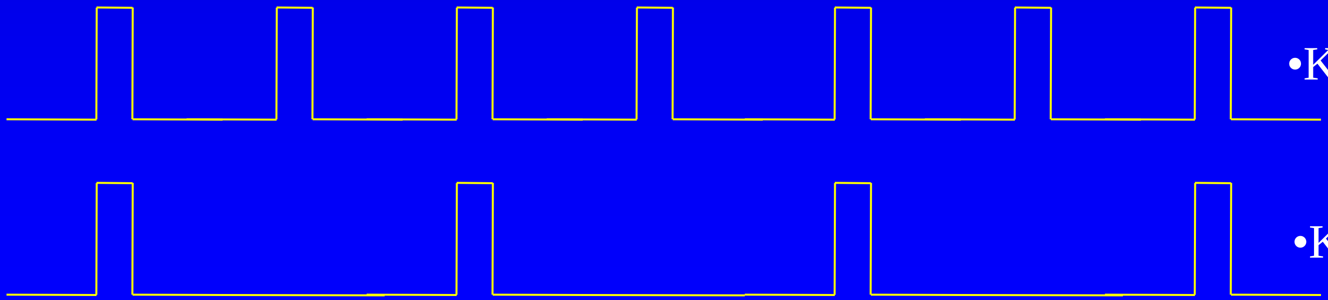
•Image quality deteriorated somewhat by scatter

•This amount of intra-fraction baseline shift (4 mm) is rare

Alternating image acquisition for scatter correction

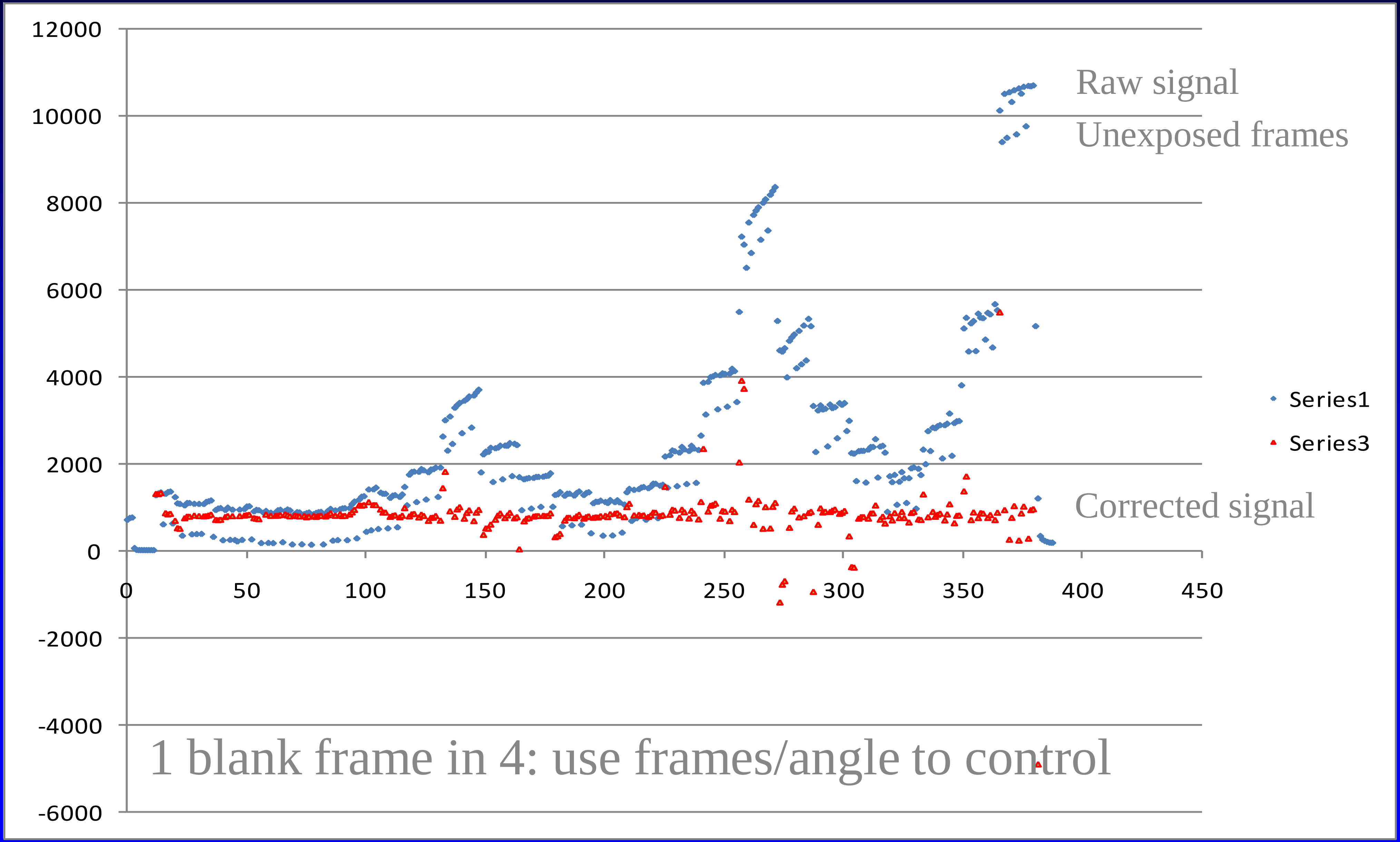
- Elekta DCB board
- Arduino microcontroller
- KV generator

- USB control

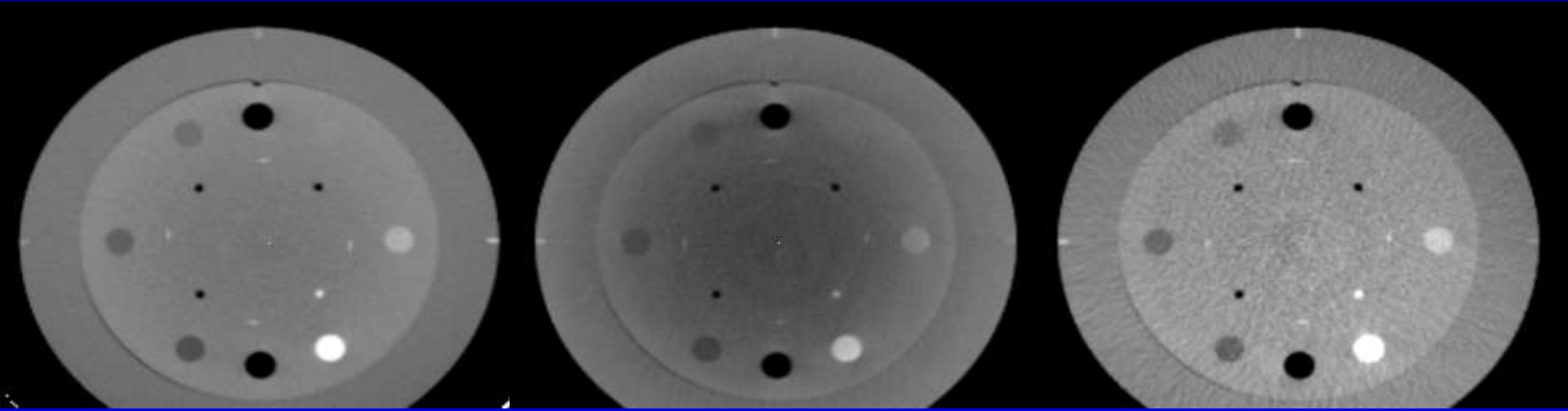


- KV control in
- KV control out

How much scatter from MV beam?



MV scatter correction
CAT Phantom



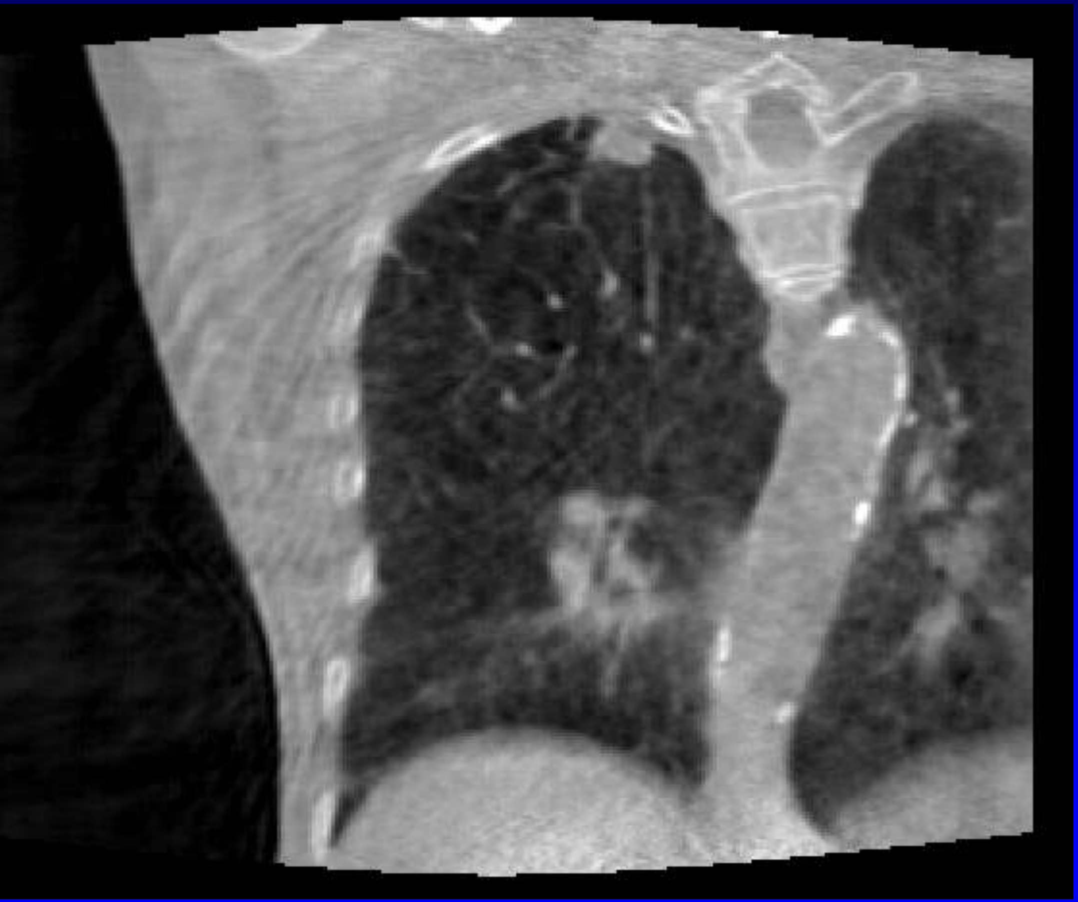
•Regular CBCT

•CBCT during VMAT

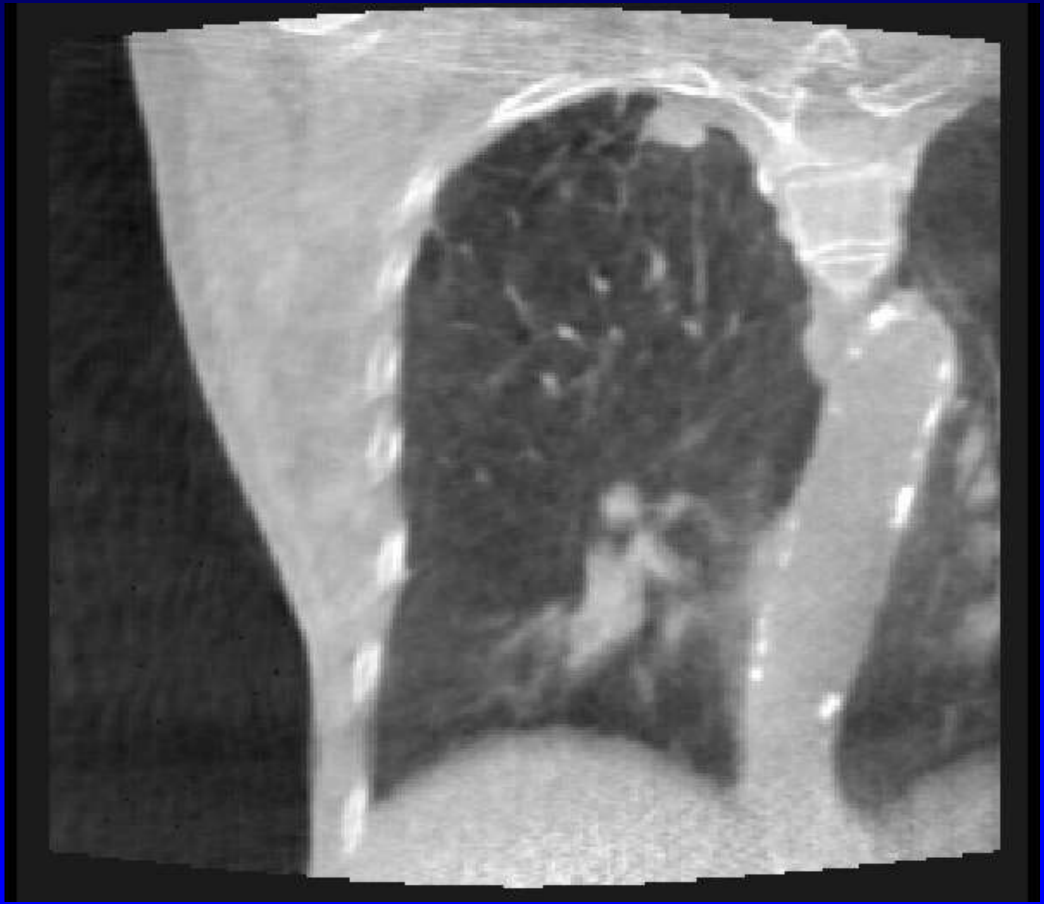
•Corrected CBCT

•MV scatter onto kV panel estimated from kV-off frames corrected for ghosting

First patient result

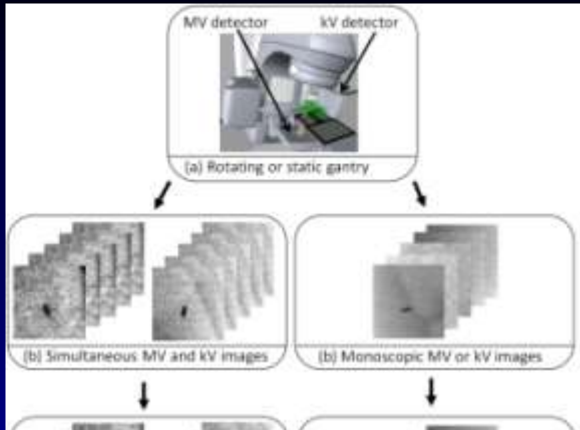


•Regular CBCT



•During VMAT: corrected/uncorrected

Alternatively: use markers

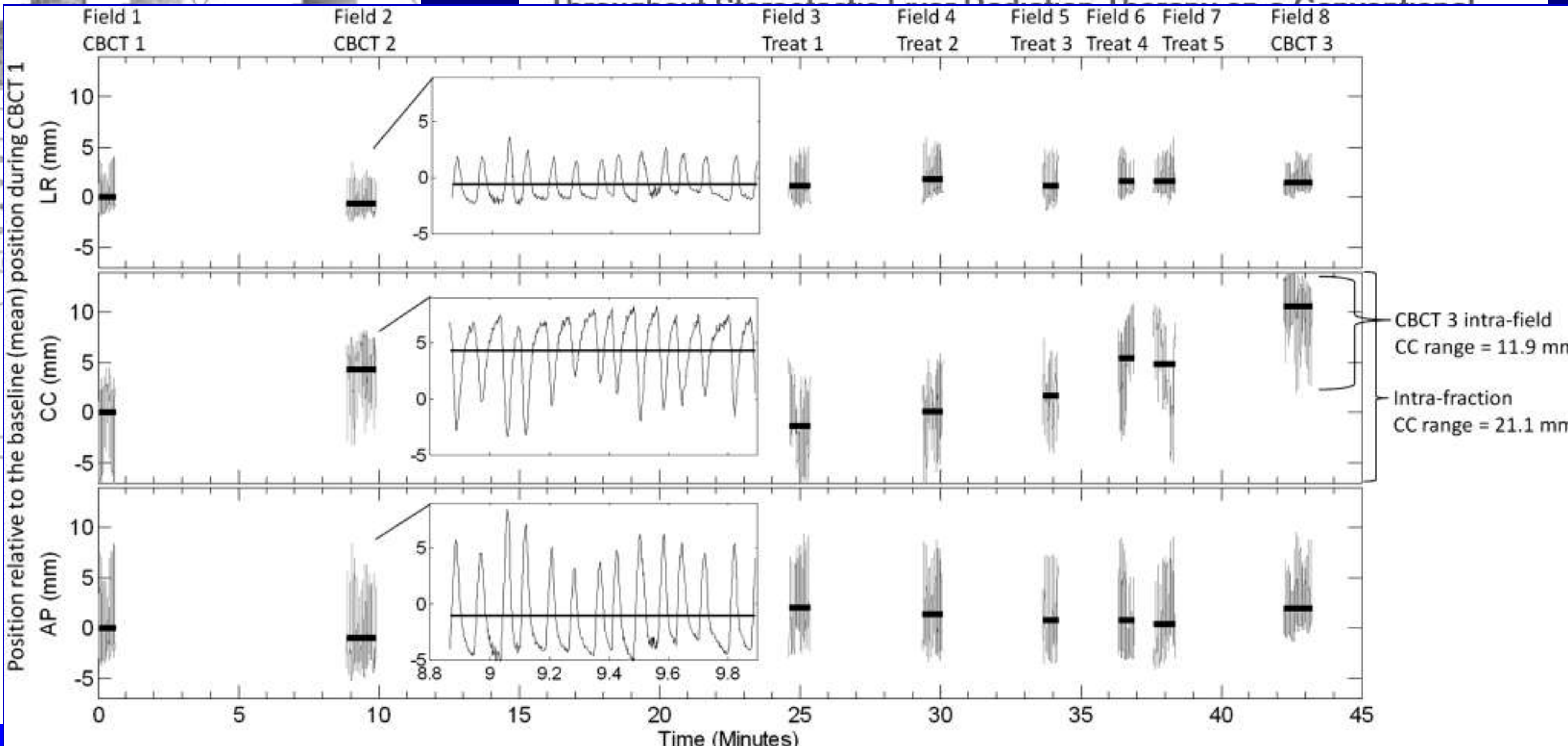


International Journal of Radiation Oncology*Biology*Physics

Volume 86, Issue 1, 1 May 2013, Pages 190–197

Physics Contribution

Three-dimensional, Time-Resolved, Intrafraction Motion Monitoring



Conclusions

- In stereotactic radiosurgery, patient stability is very important

- Methods to validate your radiotherapy procedure are:
  - CBCT after end of treatment
  - CBCT during VMAT delivery
  - Fluoroscopy during delivery

- Stability seems adequate unless treatment time too long

IGRT for Head and Neck

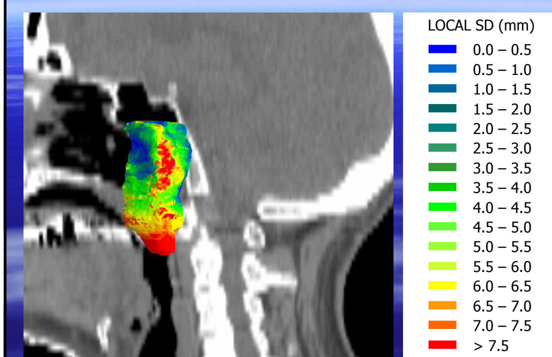
Coen Rasch

Head and Neck

Delineation of GTV in H&N

- 10 patients with NPC (cT2b – cT4, Nx)
- 10 Observers from 6 institutes in NL, D and US
- Phase I
  - Delineation of GTV on CT
  - Diagnostic MRI copy available
- Phase II, after > 1 year
  - Improved delineation protocol
  - Delineation on co-registered CT/MRI

3-D median surface with local SD



Overall observer variation (SD)

Anatomical regions	Phase 1		Phase 2	
	SD CT (mm)	*Agreement (%)*	SD CT/MRI (mm)	Agreement (%)
All regions	**4.4**	**36**	**3.3**	**64**
Anterior – Air	3.4	62	2.7	79
Dorsal – Bone	3.6	49	2.7	84
Contra lateral	4.2	16	3.5	66
Pterygoid M.	4.3	35	3.1	61
Parapharyngeal	4.4	31	3.3	59
Soft Palate	4.7	37	3.0	67
Sphenoid	5.0	28	4.2	48
Caudal side	7.7	5	3.3	56

Delineation effect on dose in conformal and IMRT plans

- Paranasal sinus cancer, nine patients
- Two observers
  - Elective CTV (described in anatomical terms)
    - Mean ratio 0.9
  - Boost CTV (the tumor plus margin)
    - Mean ratio 2.6
- Two treatment planners
  - IMRT
  - 3D conformal

•Rasch et al IJROBP 2002

Delineation effect on dose

Observer and technique effect on the irradiated volume
Mean Planning Target Volume: 36.3 cm3

	Observer 1	Observer 2	Mean
IMRT	135 cm3	115 cm3	125 cm3
3D Conformal	241 cm3	195 cm3	218 cm3
Mean	188 cm3	155 cm3	

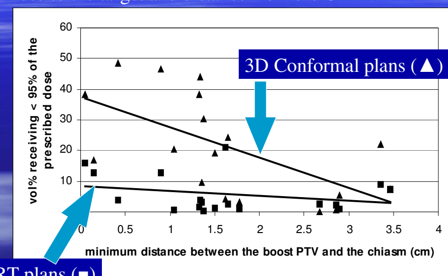
Mean observer effect: 33 cm3
Mean technique effect: 93 cm3

•Rasch et al IJROBP 2002

am

Delineation effect on dose

Dose to the target and distance from the OAR



•Rasch et al IJROBP 2002

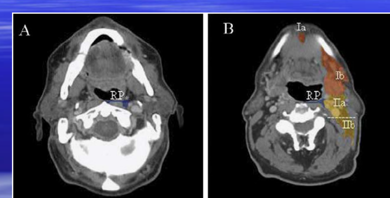
am

Observer variation in the neck

- 18 observers
  - MCA, AvL, VUMC, ARTI, RISO, MST, MCH, UMCG, RIF, MAASTRO, UMCN, DDHK, UMCU, Leuven, Middelheim,
- 1 patient
- Delineation according to guidelines as published by Gregoire et al
  - R&O 2003

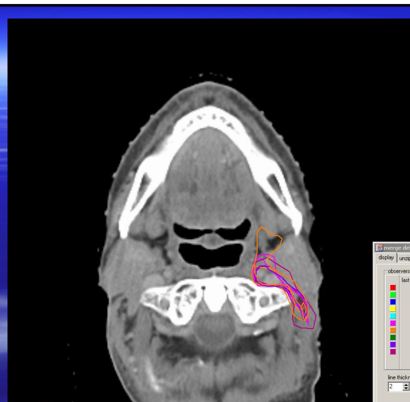
am

Prevertebral Level 1-2



Gregoire et al 2003 R&O

am



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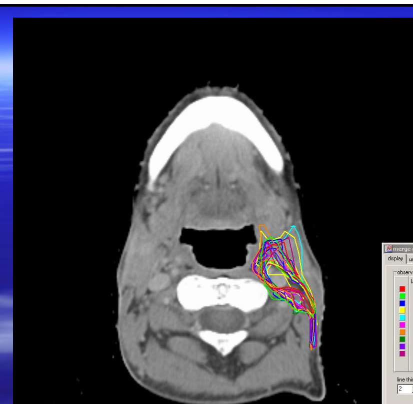

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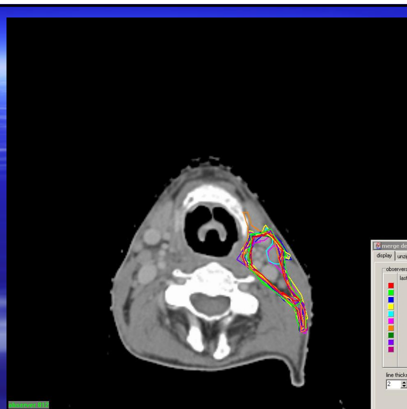


Overall observer variation (SD)

Anatomical regions	Lymph nodes SD CT (mm)	GTV CT SD CT (mm)	GTV CT MRI SD CT (mm)
All regions	**3.6**	**4.4**	**3.3**
Anterior	4.4	3.4	2.7
Dorsal	3.7	3.6	2.7
Caudal	4.6	7.7	3.5
Cranial	3.8		
L-R	3.0		
Parotid	4.0		
Vertebrae	2.2		
Vessels	2.3		

Overall observer variation (SD)

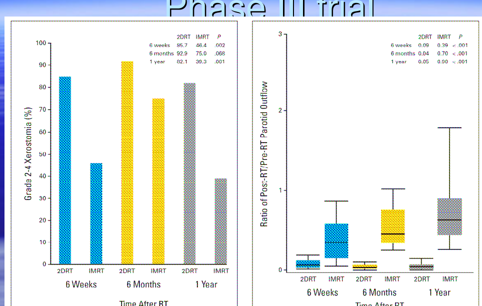
Anatomical regions	Lymph nodes SD CT (mm)
All regions	**3.6**
Level 1	3.1
Level 2	2.5
Level 3	2.1
Level 4	3.0
Level 5	6.1
Level 6	3.1
Prevertebral	3.1
Level 234	2.4

Phase III trial

- 60 patients early nasopharynx cancer
  - T1-2, N0-1, M0
- 66, 60, 54 Gy 33 fractions, 6.6 week
  - + brachytherapy boost if applicable
- 2DCRT versus IMRT
- Mean parotid dose 61-32 Gy

•Kam et al JCO 2007

Phase III trial



•Kam et al JCO 2007

Is toxicity decreased ?

- Various reports with retrospective comparisons on salivary gland sparing including randomized trials
- No Phase III trial on safety performed yet

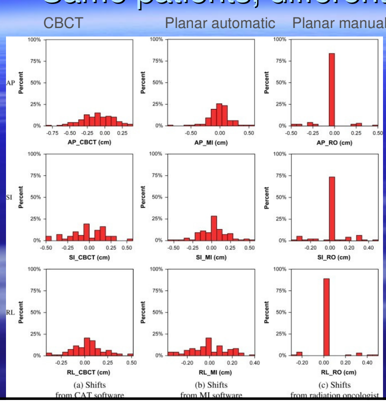
2D vs 3D setup

- Varian users use more frequently 2D planar setup correction as opposed to Elekta users
- Why?
  - Speed
  - Ease of use
  - Tradition?
- Does it make a difference?

2D vs 3D setup correction

- Li et al 2008
  - 21 pts, 98 images
  - 3 methods of registration:
    - CBCT, automated match
    - (LR and AP) Planar, automated match
    - (LR and AP) Planar, manual match

Same patients, different shifts



C/Planar imaging underestimates the setup error

Li et al 2008

2D vs 3D setup

- 10 pts, 65 images
- Comparing:
  - CBCT
  - 2D Planar
  - (Digital Tomosynthesis)

ON-BOARD PATIENT POSITIONING FOR HEAD-AND-NECK IMRT: COMPARING DIGITAL TOMOSYNTHESIS TO KILOVOLTAGE RADIOGRAPHY AND CONE-BEAM COMPUTED TOMOGRAPHY

Q. Jackie Wu, Ph.D., Devon J. Godfrey, Ph.D., Zhiheng Wang, Ph.D., Junan Zhang, Ph.D., Sumin Zhou, Ph.D., Sua Yoo, Ph.D., David M. Brizel, M.D., and Fang-Fang Yin, Ph.D.

65pts 10 fractions registration on CBCT en 2D planar imaging

Table 2. Positioning difference between 2D radiography and CBCT

Variable	Vertical (cm)	Longitudinal (cm)	Lateral (cm)	Vector (cm)
Mean	0.11	0.10	0.17	0.28
SD	0.10	0.12	0.16	0.15
P	0.14	0.45	0.0002	0.0001

Wu et al 2007

2D vs 3D setup

- 33 patients, 100 paired CBCT-planar images
- Varian OBI

Method comparison of automated matching software-assisted cone-beam CT and stereoscopic kilovoltage x-ray positional verification image-guided radiation therapy for head and neck cancer: a prospective analysis

2009

Clifton D Fuller[1,2,3,7], Todd J Scarbrough[3,4], Jan-Jakob Sonke[5], Coen R N Rasch[5], Mehee Choi[3], Joe Y Ting[4], Samuel J Wang[3], Niko Papanikolaou[1,2] and David I Rosenthal[6]

2D vs 3D setup

- Phantom test: identical
- Detected error in CBCT larger in all directions
- CBCT measurements better reproducable

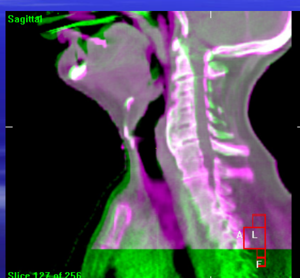
Fuller et al. 2009

2D vs 3D setup correction

- Planar imaging underestimates the setup error, especially if you do it manually
- Deformation might contribute to this (Li et al)

How flexible is the neck ?

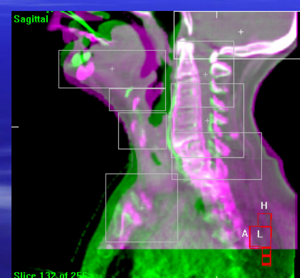
- Purple: reference CT scan
- Green: daily localization Cone Beam CT scan



- Need for choices in alignment!

How flexible is the neck ?

- PTV conflicts with OAR
- You cannot align all at the same time: Compromise!



How flexible is the neck ?

- 31 patients
- 8 CBCT scans per patient:
  249 scans evaluated
- 9 ROIs per patient
- Retrospectively:
  Larynx assumed as PTV
  Vertebrae assumed as OAR

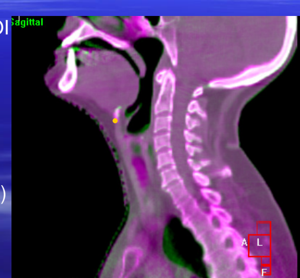
How flexible is the neck ?

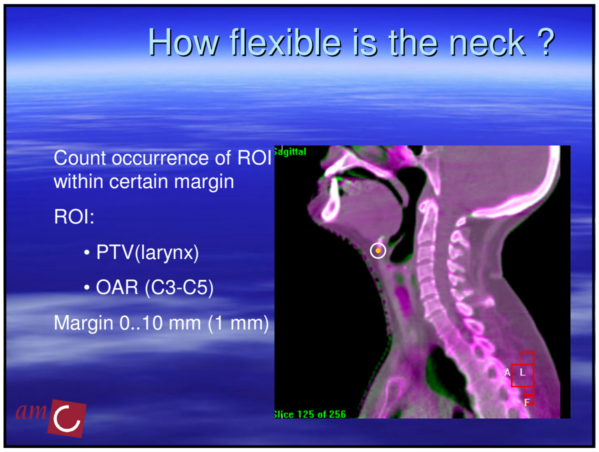
Count occurrence of ROI within certain margin

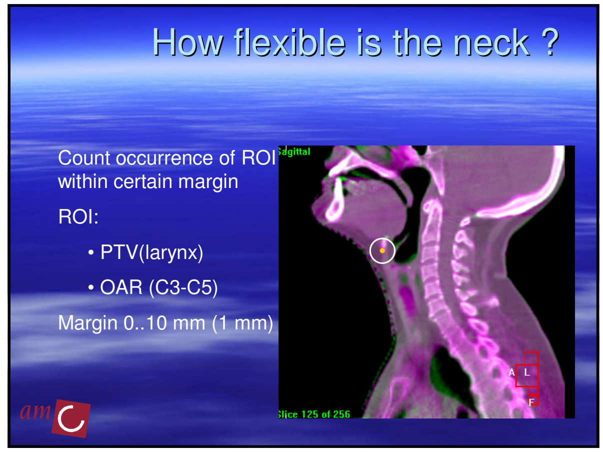
ROI:

- PTV(larynx)
- OAR (C3-C5)

Margin 0..10 mm (1 mm)




How flexible is the neck ?
Count occurrence of ROI within certain margin
ROI:
• PTV(larynx)
• OAR (C3-C5)
Margin 0..10 mm (1 mm)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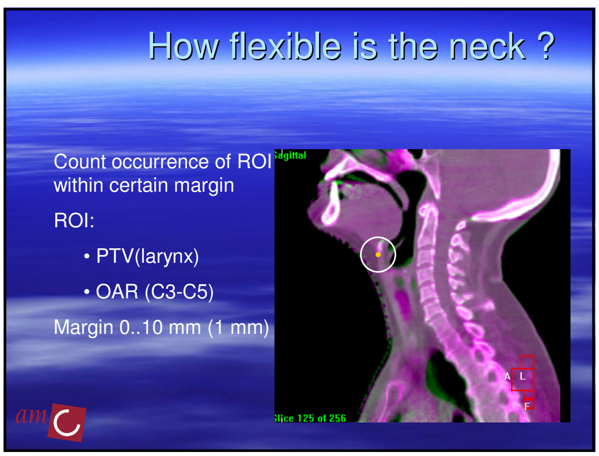
Margin 0..10 mm (1 mm)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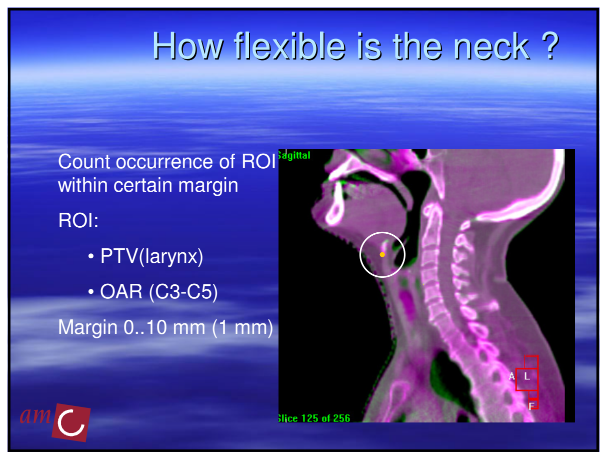
Margin 0..10 mm (1 mm)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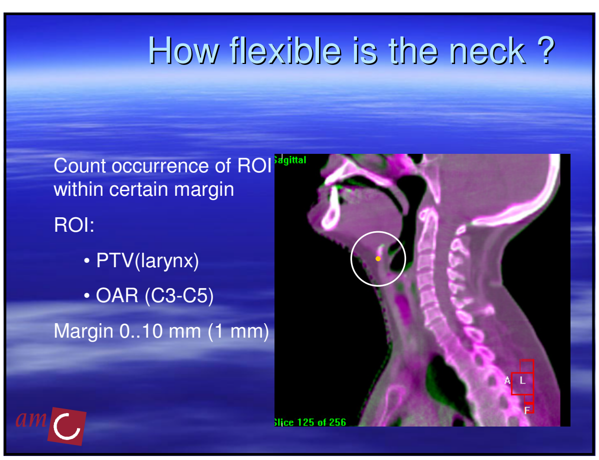
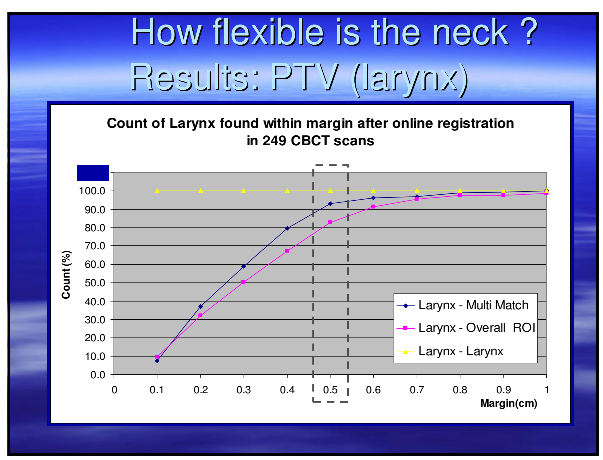
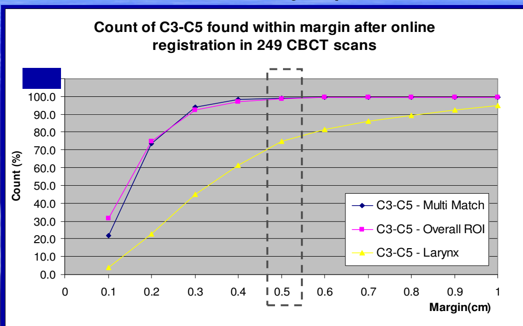
Margin 0..10 mm (1 mm)


How flexible is the neck ?
Count occurrence of ROI within certain margin
ROI:
• PTV(larynx)
• OAR (C3-C5)
Margin 0..10 mm (1 mm)


How flexible is the neck ?
Results: PTV (larynx)
Count of Larynx found within margin after online registration
in 249 CBCT scans
Count (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Margin(cm)
Larynx - Multi Match
Larynx - Overall ROI
Larynx - Larynx

How flexible is the neck ?

Results: OAR/lymphnode



Conclusions

- IMRT/IGRT for Head and Neck results in:
  - Better target coverage
  - Lower toxicity
  - Higher dependence on target volume delineation
  - Patient is more flexible than one margin
  - 2D detects less than 3D

Special thanks to:

- Marcel van Herk
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- Jochem Wolthaus
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- Lambert Zijp
- Joop Duppen
- Simon van Kranen
- Angelo Mencarelli
- Joos Lebesque
- And many Others….

Adaptive RT

Coen Rasch

- No disclaimers

A reminder:

- GTV
  - Imaging, Clinical investigation
- CTV
  - Statistics, Experience
- PTV / ITV
  - Possible positions of the CTV
- Treated Volume / irradiated Volume
  - Collateral damage

• IGRT
• ART
• IMRT

What is adaptive RT

- Adaptive radiotherapy (ART) is an approach to correct for variations in geometry of tumor and bystander anatomy with repeated (imaging-based (?)) modification of treatment delivery

- Schwartz et al Curr Oncol Rep 2012

How does adaptive RT translate

- (4D) adaptive RT is RT with time weighted adaptation
  - I.e.
    - Measuring and correcting for day to day variation
    - Adaptation of RT based upon (anatomical, functional, biological) changes during RT either expected (weight loss, shrinkage) or unexpected like atelectasis
    - Basics: it is per patient, not per group

Ask yourself:

- Do I want adaptation for:
- 1) Day to day, random changes
  - Bladder, cervix
- 2) Expected changes
  - Head and Neck
- 3) Random occurring systematic changes?
  - (base line shift, suddenly changed anatomy in e.g. Lung)

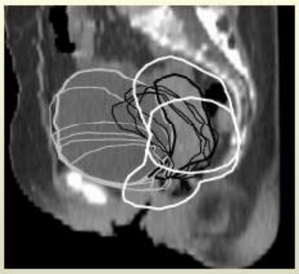
1: Day to day, random changes

- Cervix
- Bladder

Cervix cancer, classical approach

- Uterus motion: large and depending on bladder filling
- Cervix motion: smaller and depending on rectal filling
- Margin proposals:
  - Taylor: 15, 15 and 7 mm
  - Chan et al:
    - (90% of the fractions within the PTV)
      - 40 mm at fundus (top of uterus)
      - 15 mm at cervix
    - 90% for <u>intrafraction</u> (30 minutes) only:
      - 10 and 5 mm

Example of target outside PTV
"mover"

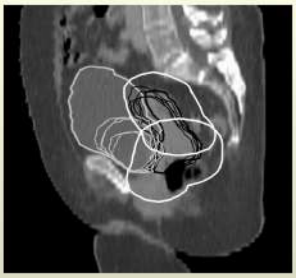


<u>CT and CBCT week 1-5</u>

Grey: Bladder
Black: CTV combined
White: - PTVuterus (CT)
- PTVcervix (CT)

Courtesy Peter de Ruyter and Monique Bloemers

Example of target inside PTV
"non-mover"

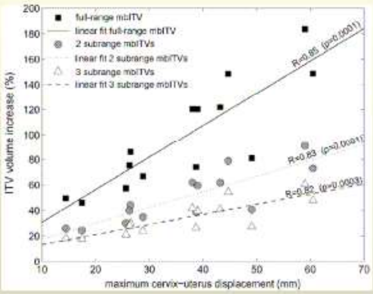


<u>CT and CBCT week 1-5</u>

Grey: Bladder
Black: CTV combined
White: - PTVuterus (CT)
- PTVcervix (CT)

Courtesy Peter de Ruyter and Monique Bloemers

Cervix plan of the day made easy



1 PTV

2 PTV's

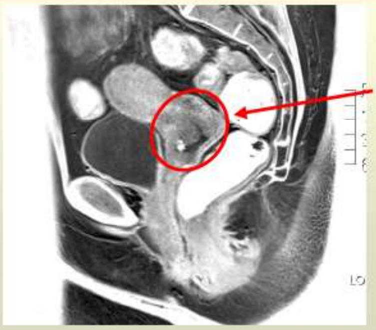
3 PTV's

•Bondar et al IJROBP 2011

Cervix: back to the basics:
The Target

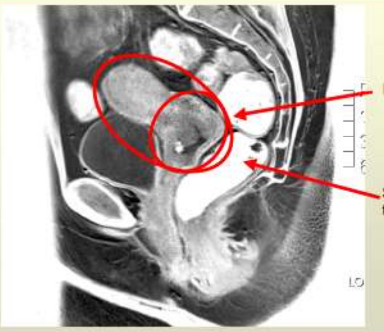
Cervix Target

Cervix Target



Here it is

Cervix Target



Here it is

Should this be the target?

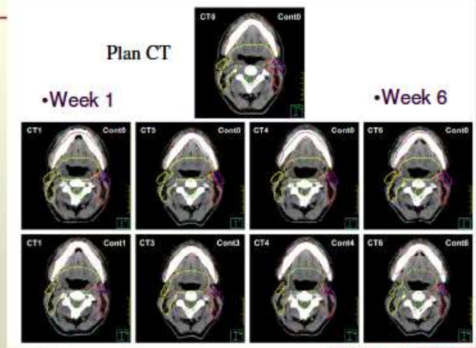
2: Art for expected changes

- Head and neck cancer

Adaptive RT for head and neck tumors

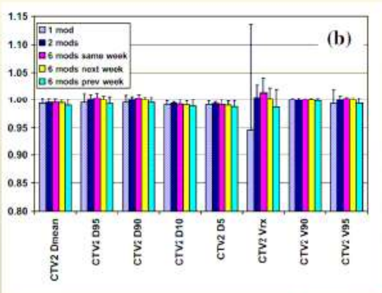
- Should we redesign our treatment plan along the way?
  - Adaptive RadioTherapy (ART) for expected changes

Changes over treatment time



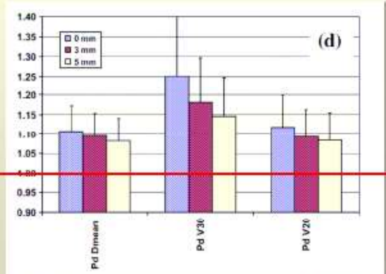
Wu et al 2009 IJROBP

Target dose with replanning remains good



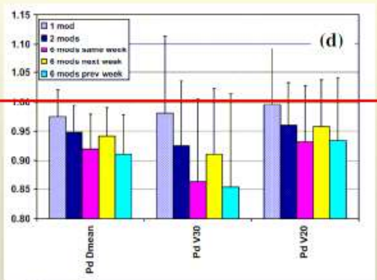
Wu et al 2009 IJROBP

Relative dose to the Parotid without replanning is around 10% higher



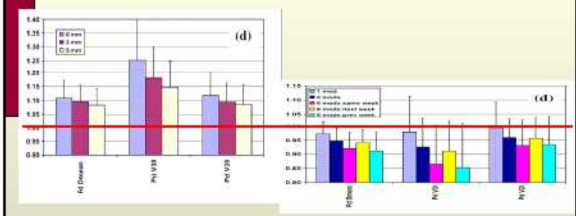
Wu et al 2009 IJROBP

Parotid dose and replanning improves with around 5%



Wu et al 2009 IJROBP

Largest gain with replanning y/n



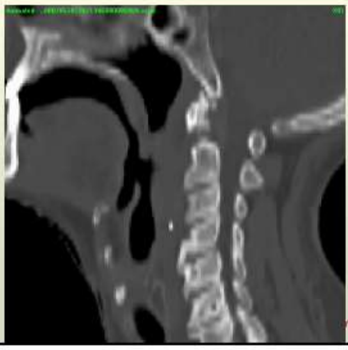
Wu et al 2009 IJROBP

Warning….

- Supposedly a large portion of the observed effect is because of shrinking of the target!

Patient change over time

Patient change over time



Warning….

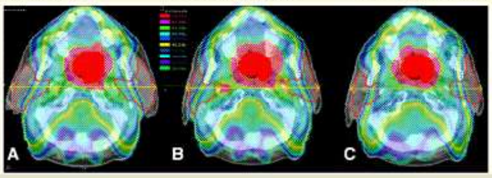
- Supposedly a large portion of the observed effect is because of shrinking of the target
- What if you do not decrease the size of your target?

Adaptive RT in Head and Neck

- 15 patients with advanced HN cancer
- 70 Gy 7 weeks
- Weekly repeat CT
- Results:
  - 4 Gy more mean dose to the parotid without adaptation
  - 5 Gy less mean dose to the parotid gland with weekly replanning compared to no adaptation

Castelli 2015

Planning | No adaptation | With adaptation

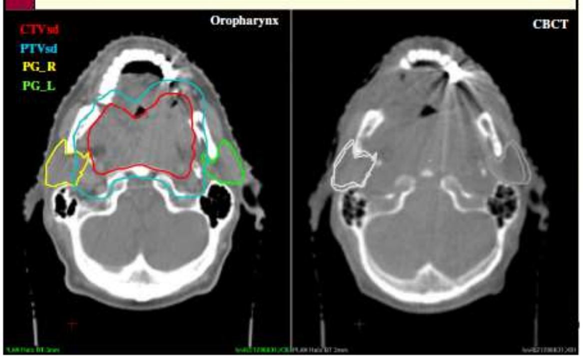


Castelli 2015

Clinical trial on dose redistribution with adaptation

- Advanced head and neck cancer
- 70 (ICRU)vs 84 Gy focussed on FDG with 66 Gy at the edge of the tumor
- Two adaptations in 6 weeks
- Ongoing trial

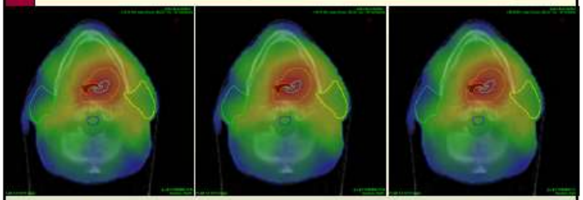
Contour Propagation



Dose accumulation during treatment

Initial plan | Without ART | With ART

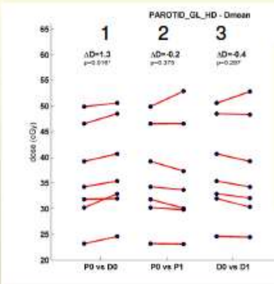
Dose accumulation during treatment



Initial plan | Without ART | With ART

Impact of Adaptation ARTFORCE Trial

7 patients: Mean Dose difference – parotid gland



1. planned vs delivered dose, no adaptation
2. planned vs adapted planned dose
3. non adapted delivered vs adapted delivered dose

ART for head and neck

- Careful when adapting for tumor shrinkage
- You can overcome the deleterious effect of parotid gland shrinkage on parotid dose
- One adaptation dose most of the tric
- You do not need deformable registration:
  - if the individual plans are safe the summation is also safe

3: Art for (Un) expected changes

- Lung cancer, tumor regression (?), atelectasis (either appearing or dissolving)
- Cervix, void of hematocolpos (Uterus with blood)

Adaptive RT for lung cancer

- What ig you would want to adapt to the shrinking tumor?
  - Is it predictable?
  - Is replanning advisable?

Tumor reduction during RT

	No. Patients	Modality	Regression Rate (%/d)	Observations
Erridge 2003 Edinburgh–NKI/AvL	25	EPID	−0.9	Microscopic extensions mentioned
Kupelian 2005 M.D. Anderson	10	In room MV-CT	−1.2	Increased dose to PTV and lungs
Siker 2006 Wisconsin	25	MVCT	−2.4	Mixed group, radical, palliative and stereotactic RT
Bosmans 2008 Maastro	23	FDG-PET/CT	−0.39	Lymph node regression only
McDermott 2006 NKI/AvL	1	EPID	−1.5	Increased dose to PTV and lungs
Underberg 2006 VUMC	40	4D-CT and conventional CT	−1.4	Volume. increase 1st and 2nd wk
Britton 2007 M.D. Anderson	8	In room KV-CT	−1.3	Volume increase 1st and 2nd wk
Woodford 2007 Ontario	17	In room MV-CT	−0.79	
Fox 2009 Johns Hopkins	22	MVCT	−1.2	Regression greater (−1.4%) in first 3 wk
Feng 2009 Michigan	14	Mid-RT FDG-PET/CT	−1.4	Planning study
Van Zwienen 2008 NKI/AvL	114	In room kV-CBCT	−0.6	Frequent anatomical changes occurred

C/ 1vol%/day

Sonke et al 2010

Radiotherapy am

Tumor reduction during RT

- Zwienen et al 2008
  - 114 patients
  - 1 pt with progression
  - 40% noticable regression
  - 8% >25% regression in third week
  - When present at beginning:
    - Atelectasis changed in 29% (23% smaller, 6% larger)

Radiotherapy am

ART for (un-)expected changes

- Lung cancer and atelectasis
  - Rianne demonstrates the traffic light warning system (i.e. guidelines on what to do with an image finding at the treatment machine)

Radiotherapy am

ART for un-expected changes

- Kwint et al. 2014
  - In 128 patients (72%), 210 anatomical changes were observed with a maximum level of red (12%), orange (36%) and yellow (24%).
  - Types of observed changes were,
    - tumor regression (35%)
    - tumor baseline shift (27%)
    - changes in atelectasis (19%)
    - tumor progression (10%)
    - pleural effusion (6%)
    - and infiltrative changes (3%)
  - Plan adaptation in case of safety issues (under or overdosage)

Radiotherapy am

ART for un-expected changes

- So, it is used for safety or quality control not for improved dose distribution perse

Radiotherapy am

ART for lung: mid-treatment adaptation

Adaptive radiotherapy in lung cancer: dosimetric benefits and clinical outcome

T KATARIA, MD, DNB, D GUPTA, MD, S S BISHT, MD, N KARTHIKEYAN, MSc, S GOYAL, MD, DNB, L PUSHPAN, DNB, A ABHISHEK, MD, HB GOVARDHAN, MD, DNB, V KUMAR, MD, K SHARMA, MD, DNB, S JAIN, MD, T BASU, MD and A SRIVASTAVA, MD, DNB

15 patients stage III lung cancer
Replanning after 44 of 66 Gy with new target delineation
Clinical trial

Radiotherapy am

ART for lung: mid-treatment adaptation

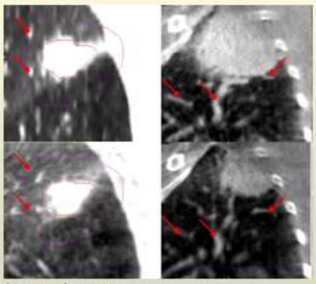
Delineated structure	Pre-treatment median (range)	Mid-treatment median (range)	Median reduction (%) (range)	p-value
GTV primary (cm^3)	313 (45.0–429.0)	135 (30.0–495.0)	34.80 (12.8–73.0)	0.02
GTV nodal (cm^3)	13 (8.4–141.0)	8 (4.0–30.0)	49.00 (0.0–53.0)	0.14
PTV (cm^3)	773 (169.0–1826.0)	565 (130.0–1272.0)	34.75 (32.0–76.0)	0.06

GTV, gross tumour volume; PTV, planning target volume.

ART for lung: mid-treatment adaptation

Dose parameters	Pre-treatment mean ± SD (range)	Mid-treatment mean ± SD (range)	Mean reduction (%)	p-value
Ipsilateral lung without PTV				
V20 (cm^3)	238.51 ± 169.25 (98–471)	114.00 ± 118.63 (40–317)	52.15	0.01
V5 (cm^3)	518.65 ± 165.30 (285–912)	399.49 ± 155.13 (239–612)	21.76	0.05
Mean (cGy)	784.39 ± 302.05 (392–1182)	596.69 ± 237.33 (345–983)	23.93	0.00
Contralateral lung				
V20 (cm^3)	23.09 ± 12.58 (11–39)	1.24 ± 3.00 (1–9)	62.83	0.15
V5 (cm^3)	351.00 ± 222.65 (112–803)	297.22 ± 200.67 (126–640)	15.68	0.34
Mean (cGy)	402.49 ± 107.06 (193–697)	284.00 ± 131.79 (78–380)	29.43	0.01
Heart				
V20 (cm^3)	36.06 ± 29.16 (1–85)	2.12 ± 0.23 (1–4)	61.47	0.12
V10 (cm^3)	97.57 ± 63.56 (0–184)	42.31 ± 32.99 (3–97)	56.62	0.08
V5 (cm^3)	169.38 ± 07.94 (0–278)	115.00 ± 56.46 (3–294)	31.42	0.04
Mean (cGy)	531.33 ± 447.03 (31–1477)	344.38 ± 241.26 (12–736)	35.21	0.02
Oesophagus				
Mean (cGy)	1022.00 ± 251.00 (616–1241)	709.00 ± 370.00 (464–1138)	19.03	0.77
Spine				
D2 (cGy)	1148.87 ± 848.03 (321–1701)	706.10 ± 131.78 (153–1311)	37.34	0.00
D_{max} (cGy)	1213.02 ± 884.84 (356–3969)	771.09 ± 174.69 (259–1817)	36.53	0.06

Shrinkage Dissolvement



Note: Arrows point at vessels

Sonke et al 2010

ART for lung: mid-treatment adaptation

Adaptive radiotherapy in lung ... simetric benefits and clinical outcome

T KATARIA, MD, DNB, D GUPTA, MD, S S B... EYAN, MSc, S GOYAL, MD, DNB, L PUSHPAN, DNB, A ABHISHEK, MD, HB GOVARDHAN, M... K SHARMA, MD, DNB, S JAIN, MD, T BASU, MD and A SRIVASTAVA, MD, DNB

15 patie... ll lung cancer
Repl... er 44 of 66 Gy
O... al

DON't DO THIS OUTSIDE a CLINICAL TRIAL

Do you need deformable registration if you want to do adaptive radiotherapy?

- **No**: if all individual plans are safe AND with adequate coverage, the summation will be safe and appropriate for the target as well
- **Yes**: if you want to know the actual dose to the OAR's

Conclusion

- Is there clinical evidence for the usefullness of adaptive RT?
  - Yes and no
  - Yes:
    - Less irradiation reduces toxicity in earlier efforts in shrinking the irradiated volume (plan of the day, expected changes)
    - Adaptation is a QA instrument (plan of the day, unexpected changes)
  - No:
    - No randomized trials performed, therefore no information on safety available
    - Replanning on tumor regression is not advised unless obvious borders
    - Results are theoretical only yet


Special thanks to:
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Josien de Bois
Lambert Zijp
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Simon van Kranen
Joos Lebesque
Caro Koning
Peter de Boer
Maarten Hulshof
Monique Bloemers
Michiel van den Brekel
Fons Balm
Ludy Smeele
Dept. RT AMC en AvL
And many Others………
Radiotherapy

Safety and procedures

Helen McNair, DCR(T), PhD

Research lead Radiographer

Royal Marsden NHS Foundation Trust and Institute of Cancer Research

The ROYAL MARSDEN
NHS Foundation Trust

ICR The Institute of Cancer Research

ESTRO School

November 2014

Understanding errors - What type of errors occur

active failures: 'unsafe acts'	Committed by those working at the sharp end of a system Usually short-lived and often unpredictable
latent conditions:	Can develop over time and lie dormant before combining with other factors or active failures to breach a system's safety defences. Long-lived and, unlike many active failures, can be identified and removed before they cause an adverse event

Understanding errors - What type of errors occur

Active failure	Error	
Slips	Lack of attention Skilled	
Lapses	Memory failure- Omitting planned action Skilled	
Mistakes	Conscious control Skilled	
Violations	Deliberate deviation Skilled	

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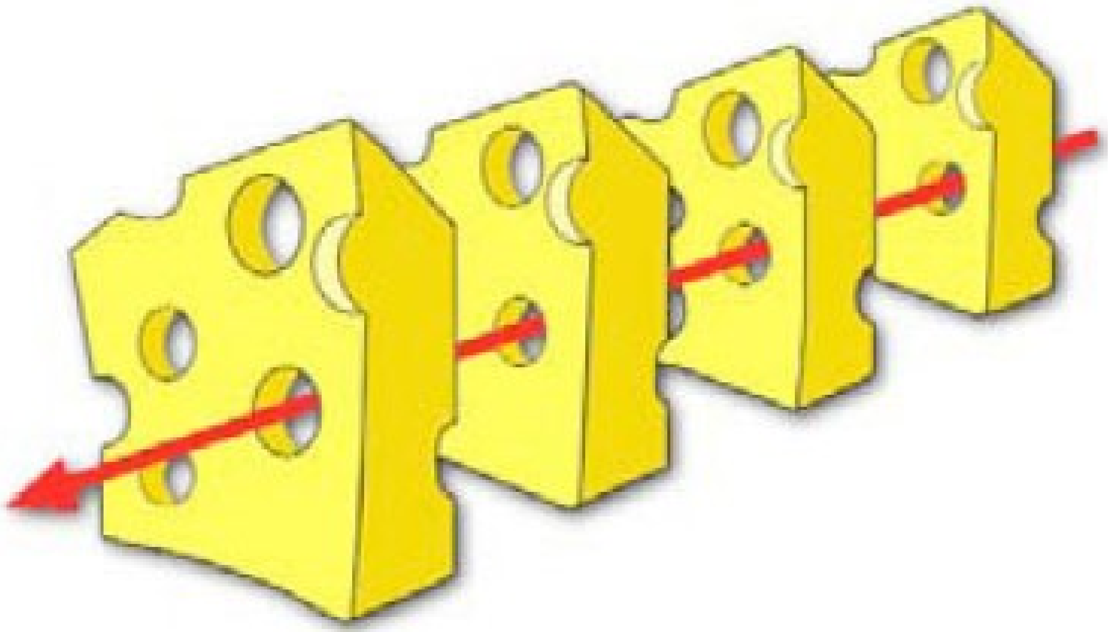
Understanding errors - What type of errors occur

Latent conditions	Error	Example
time pressures targets, understaffing, inadequate equipment, inexperienced staff	**Lead to error and violation**	Incorrect registration and action
unworkable procedures design problems	**Create weaknesses in the defences**	Ad hoc pathway

Understanding errors - What type of errors occur

Systematic	Random
Incorrect protocol input into management system	Incorrect image acquisition selected on one day

Understand radiotherapy pathway



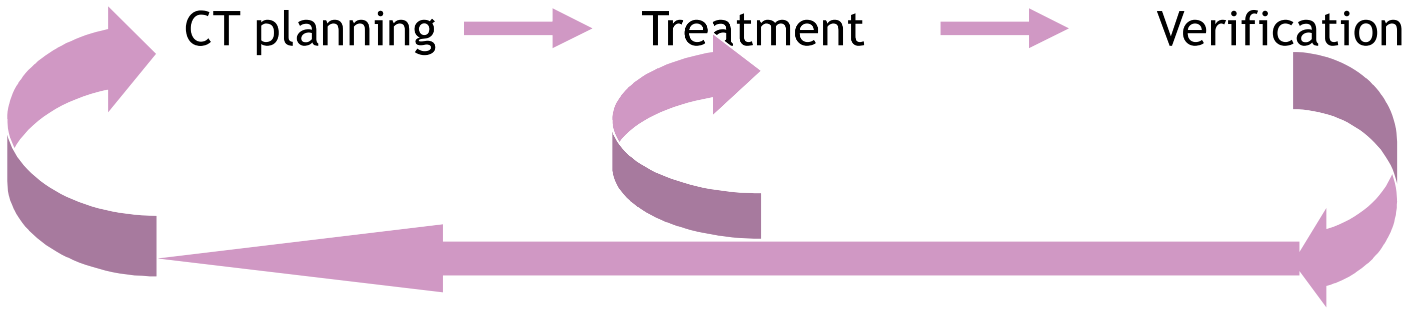
Reasons 'swiss cheese' model

Safety considerations for IGRT: Executive summary

"The safe application of IGRT technology is not limited to the operation of the technology at the treatment unit "

Practical Radiation Oncology
Volume 3, 2013, Pages 167–170

CT planning → Treatment → Verification



Assessment

↓

CT scanning

↓

Verification

Assessment

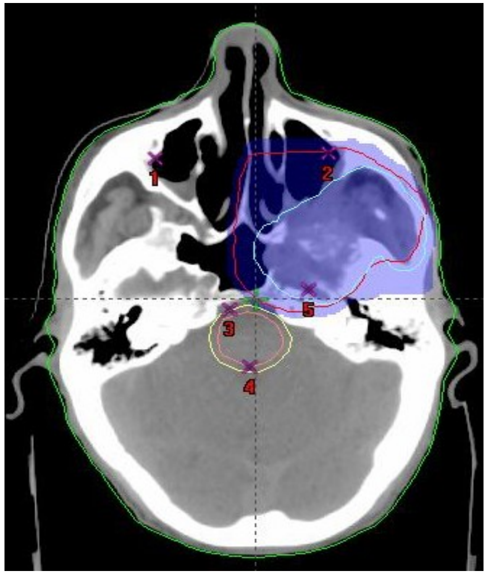
↓

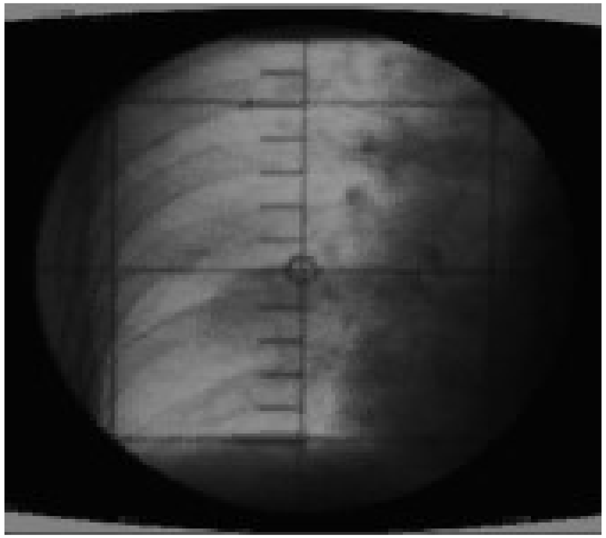
CT scanning

↓

Verification

Assessment: Understanding patient tumour and motion

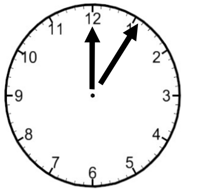


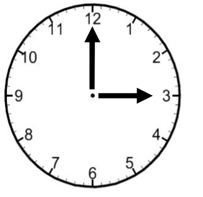


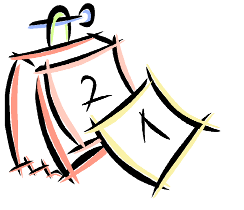
Magnitude of movement

Motion

Breathing motion	Patient motion	Organ motion
Cardiac motion	Peristalsis	Organ motion
Patient motion	Weight loss	Organ changes





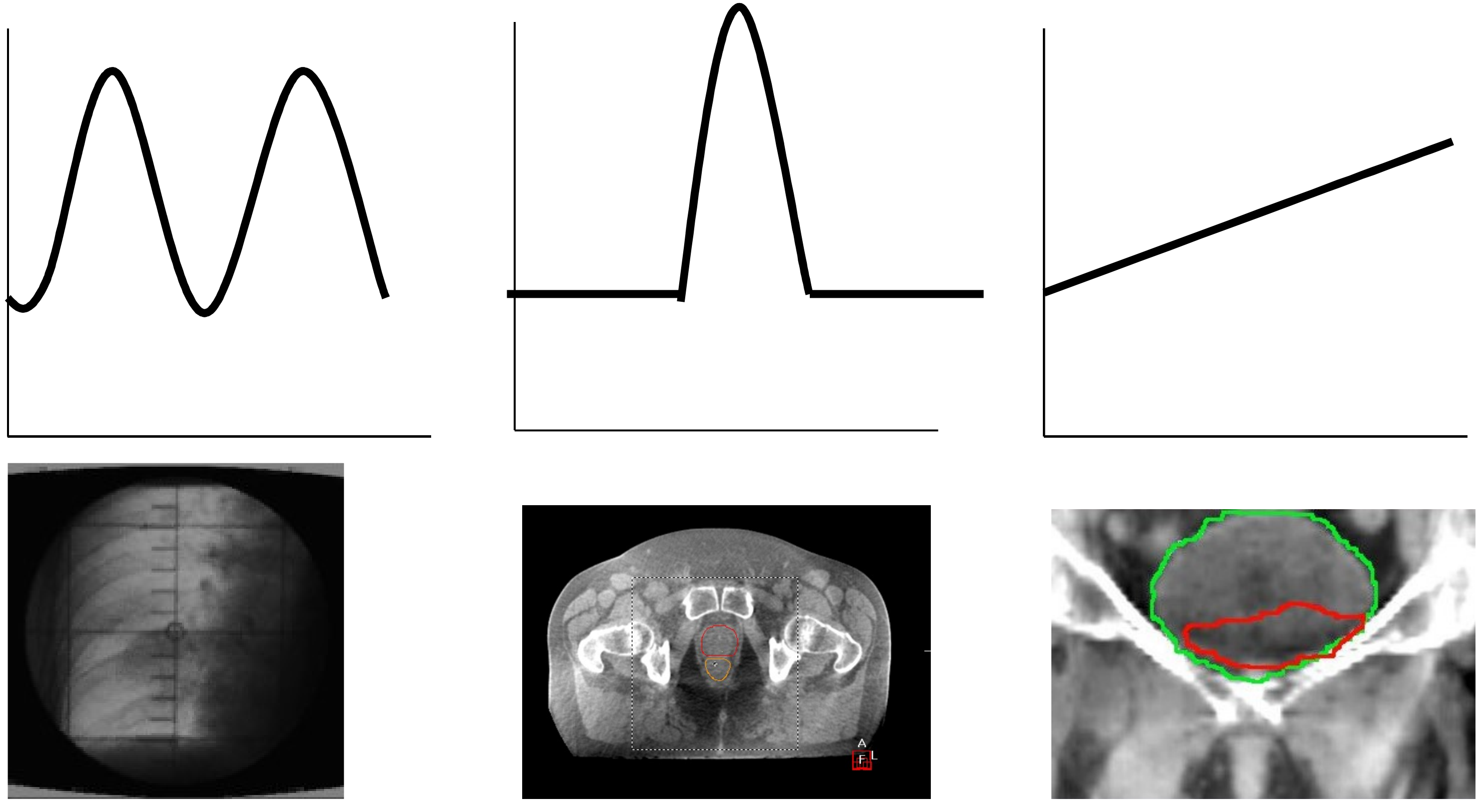


Frequency of movement

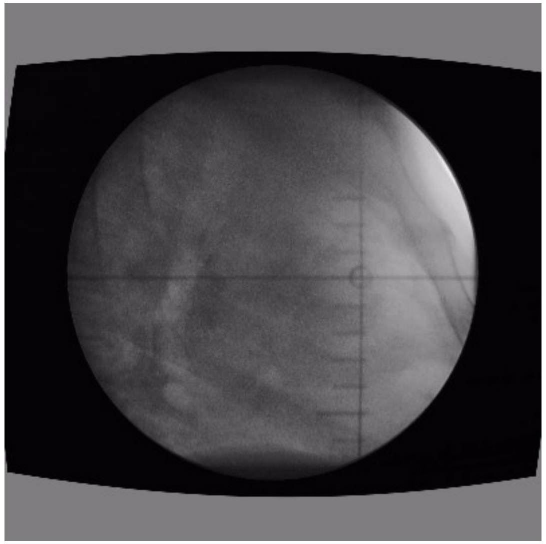
Motion

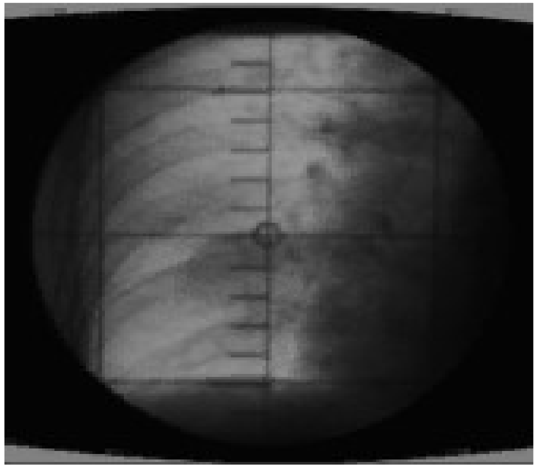
Breathing motion	Patient motion	Organ motion
Cardiac motion	Peristalsis	Organ motion
Patient motion	Weight loss	Organ changes

Assessment



Assessment





Risk

Incorrect pathway booked

delay for treatment
Ineffective use of resources

Patient cannot tolerate procedure

delay for treatment
Ineffective use of resources

Incorrect planning or margins

irradiation of normal tissue
miss the target

Incorrect planning or margins

	No markers	Implanted markers
No of patients	213	25
Margins (mm)	6 mm right left (RL) 10 mm anterior posterior (AP) and cranial–caudal (CC)	3 mm LR and 5 mm AP and CC.
5-year freedom from biochemical failure	91%	58%

Engels IJROBP 2009

Clinician

RTT

Physicist

→

Assessment

↓

CT scanning

↓

Verification

Assessment

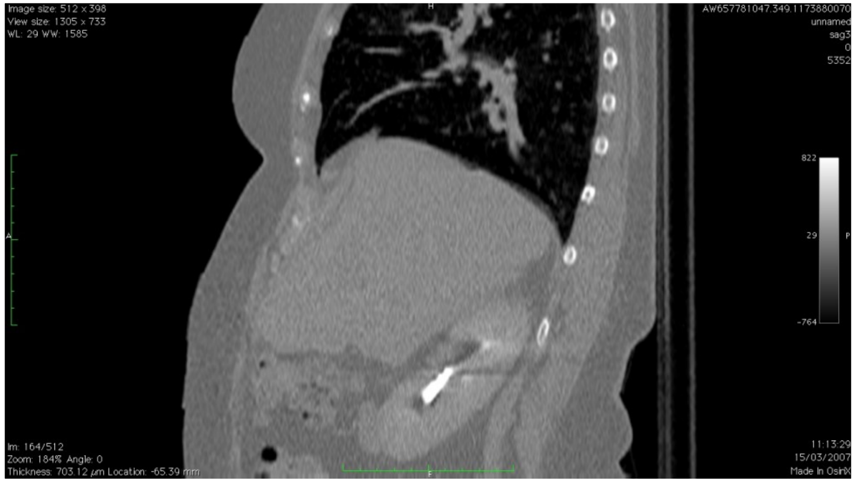
↓

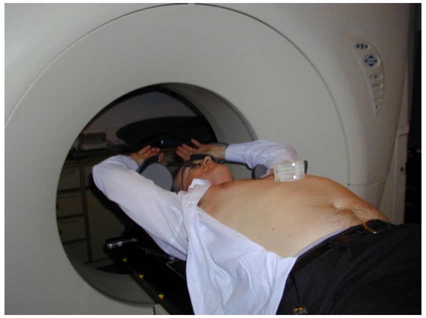
CT scanning

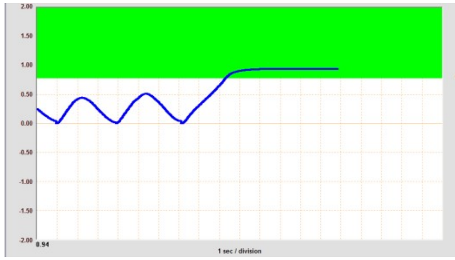
↓

Verification

CT planning

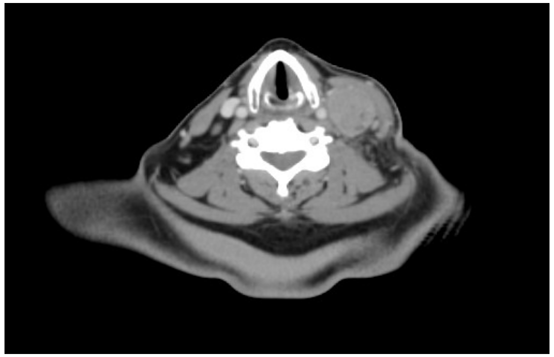


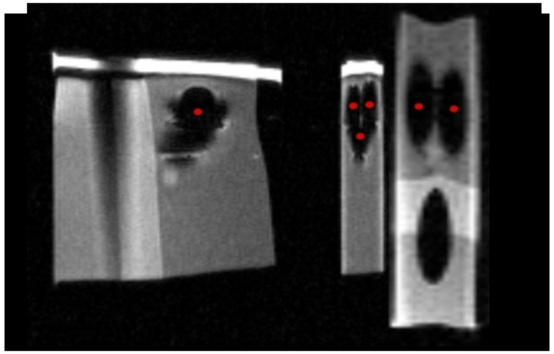




Courtesy of M Hawkins

Image Quality



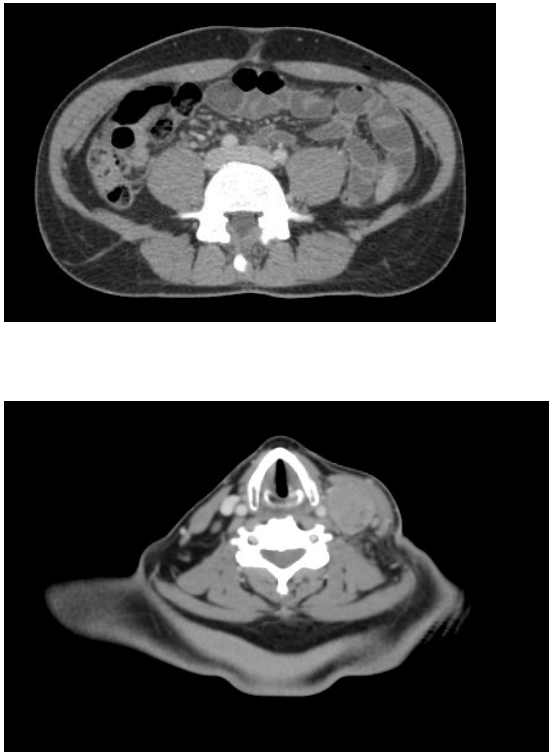


Contrast

Markers

Courtesy of C Ockwell

Image Quality



Contrast

Slice thickness

Risk

Oct 2007

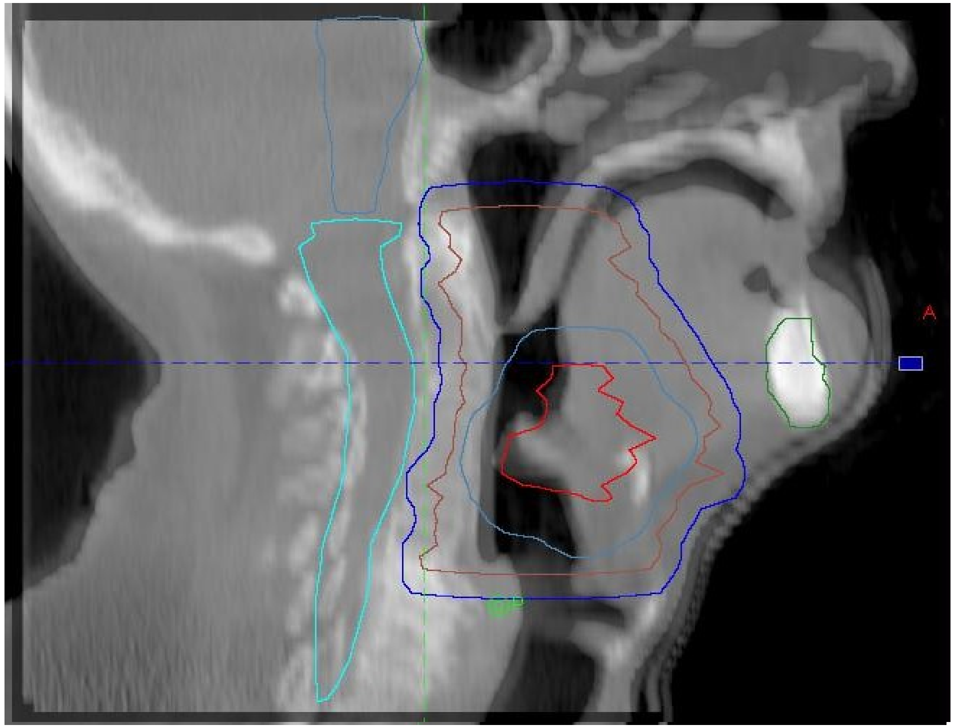
Standard practice is to position the patient "head first"

The patient was positioned "head first", but "feet first" scan technique was chosen on the unit

The KCC in Detroit

written protocols

Risk

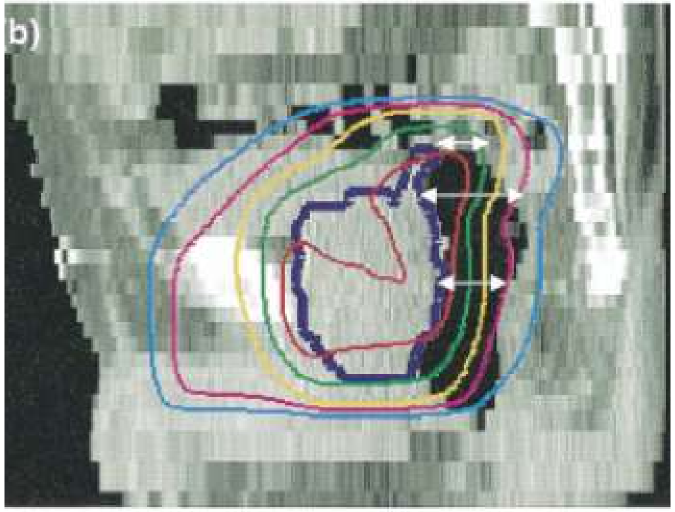


Reference image not reproducible

Courtesy of A Baker

Risk

Rectal distension at CT = poor outcome

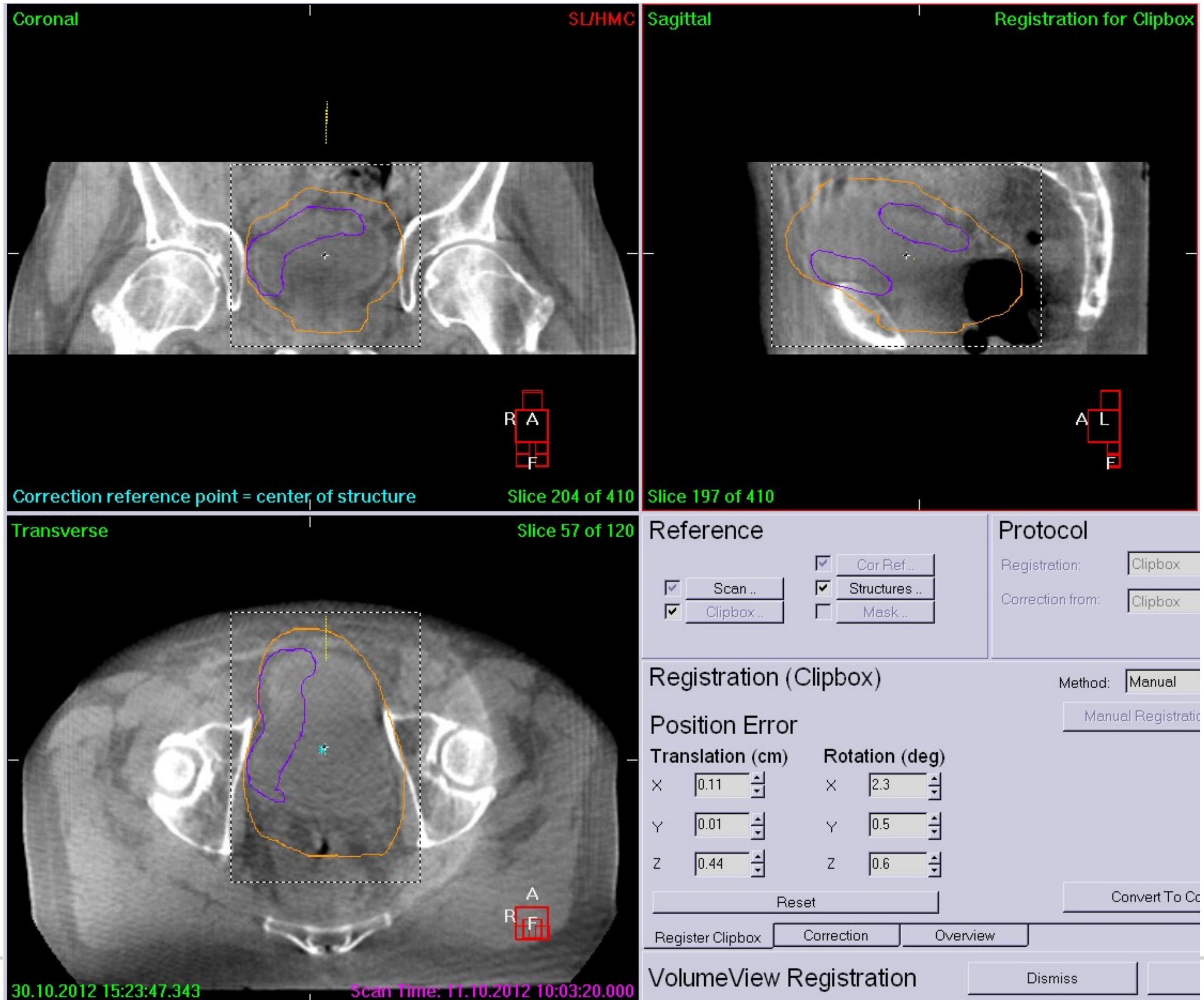


	p value
(1) CSA >11.2cm²	0.0009
(2) CSA ≥ 8cm² + (2) Diarrhoea ≥ 25% RT time	0.02

Reference image not reproducible

(1) De Crevoisier IJROBP 2005
(2) Heemsbergen IJROBP 2007

Risk



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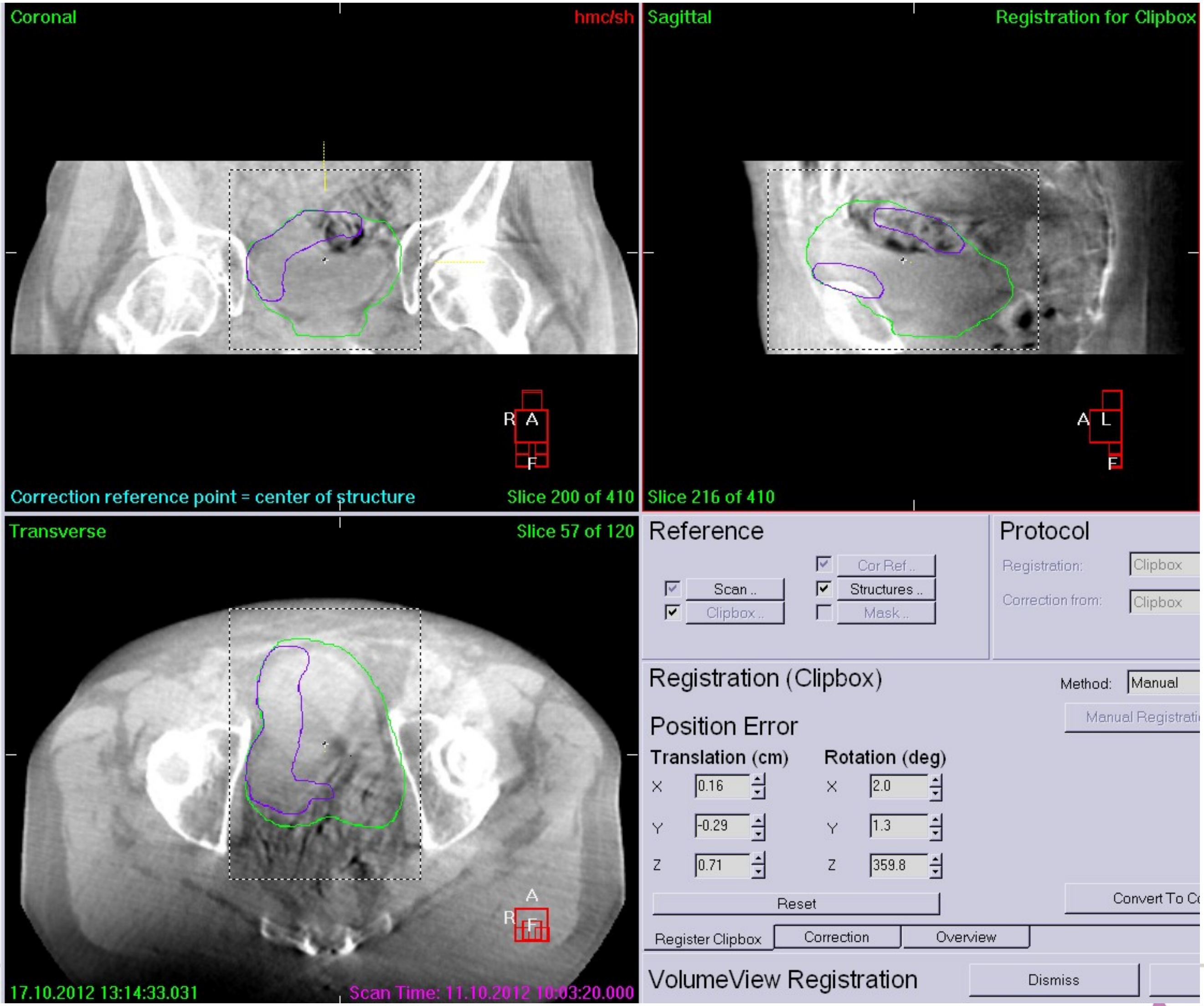
Risk



Coronal
hmc/sh
R A
F
Correction reference point = center of structure
Slice 200 of 410
Sagittal
Registration for Clipbox
A L
F
Slice 216 of 410
Transverse
Slice 57 of 120
A
R F
17.10.2012 13:14:33.031
Scan Time: 11.10.2012 10:03:20.000
Reference
Scan ..
Clipbox ..
Cor Ref ..
Structures ..
Mask ..
Protocol
Registration:
Clipbox
Correction from:
Clipbox
Registration (Clipbox)
Method:
Manual
Position Error
Translation (cm)
Rotation (deg)
X 0.16
Y -0.29
Z 0.71
X 2.0
Y 1.3
Z 359.8
Reset
Register Clipbox
Correction
Overview
VolumeView Registration
Dismiss

Helical TomoTherapy

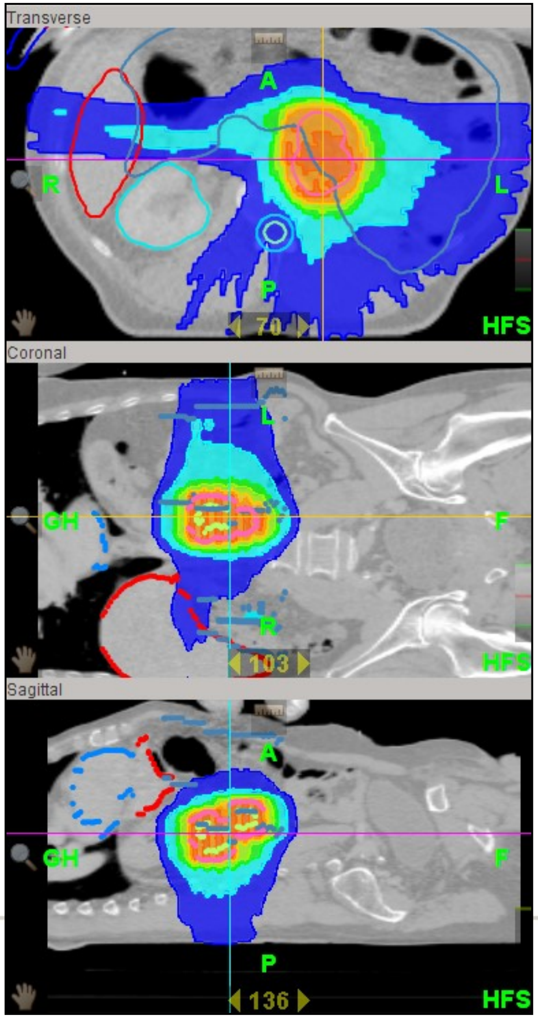
Near-incidents related to IGRT @ UZB

"Pure" image-guided

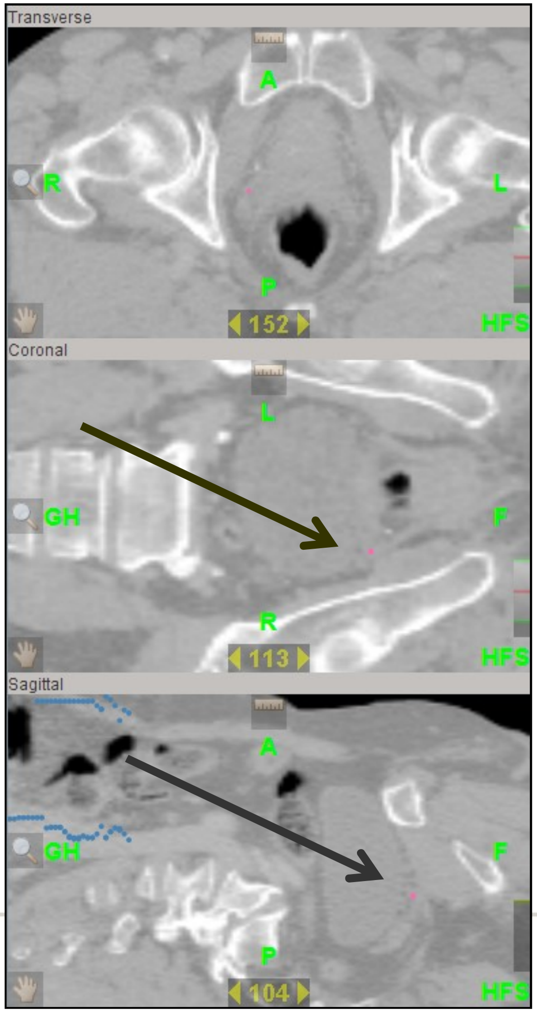
- No visual control of beam alignment
- Patient slides into the boar for treatment, once properly positioned.
- TomoTherapy treats all voxels that are designed "target"

Helical TomoTherapy

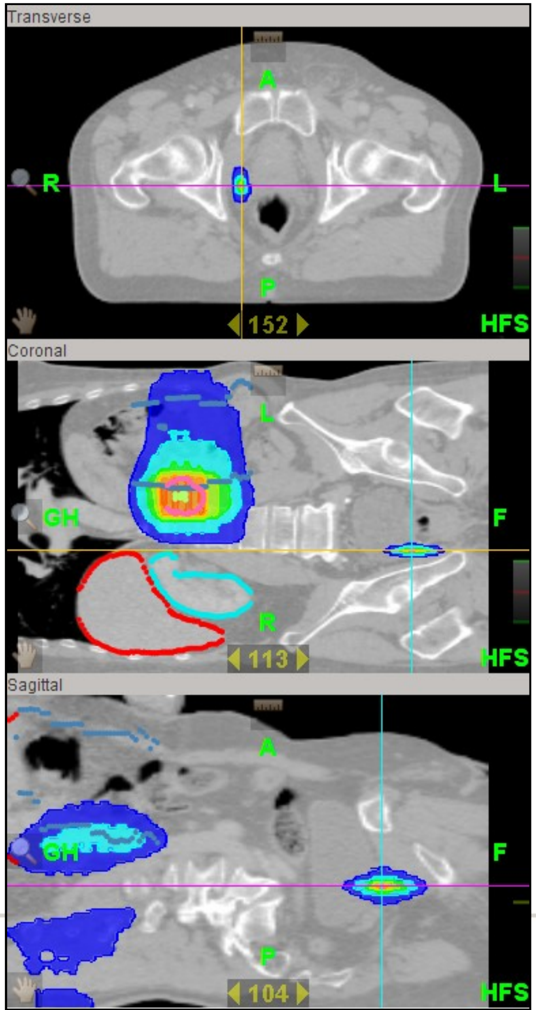
Intended treatment



"Little" delineation problem



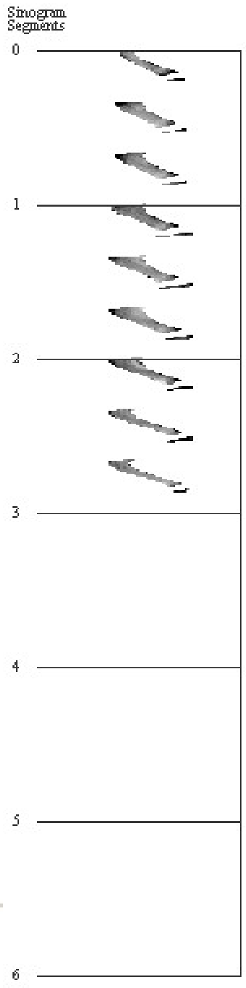
"serious" consequences

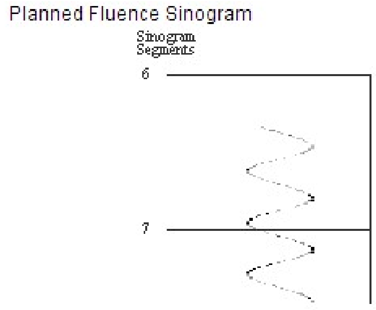


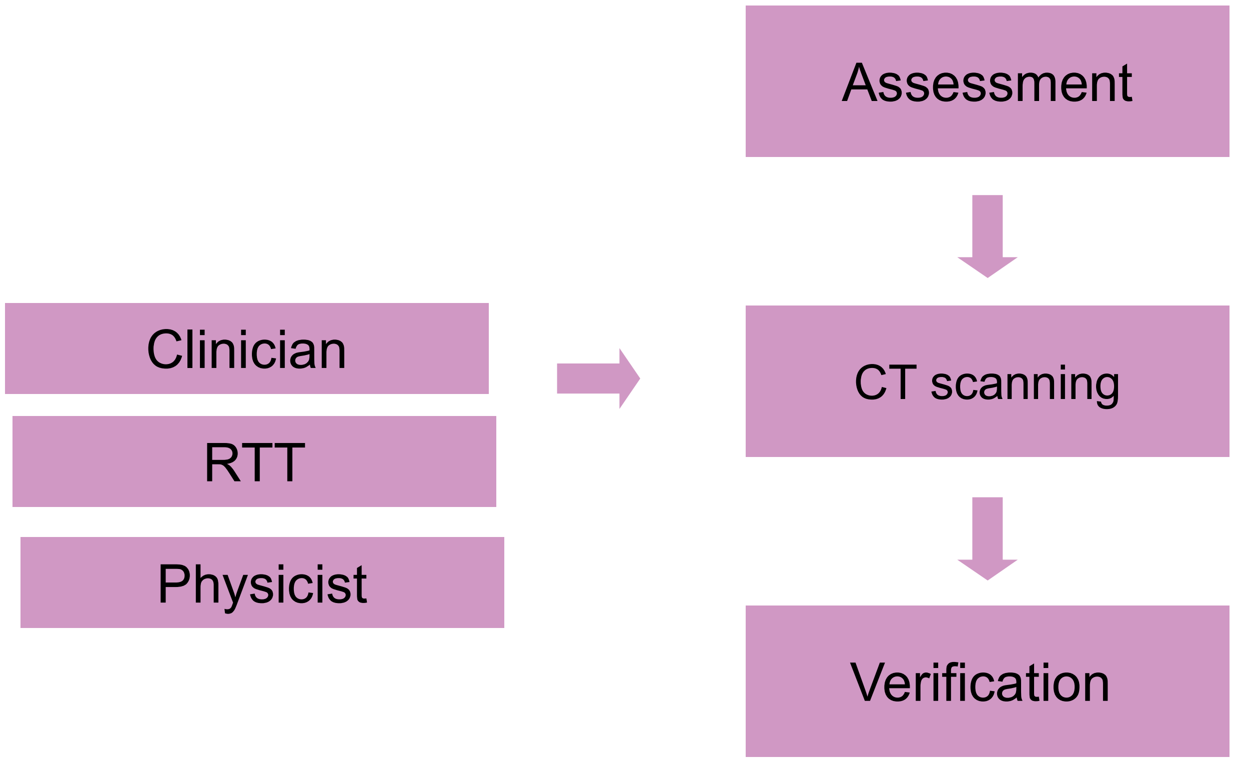
School

Helical TomoTherapy

Sinogram, reveals problem






Assessment
CT scanning
Verification
Clinician
RTT
Physicist

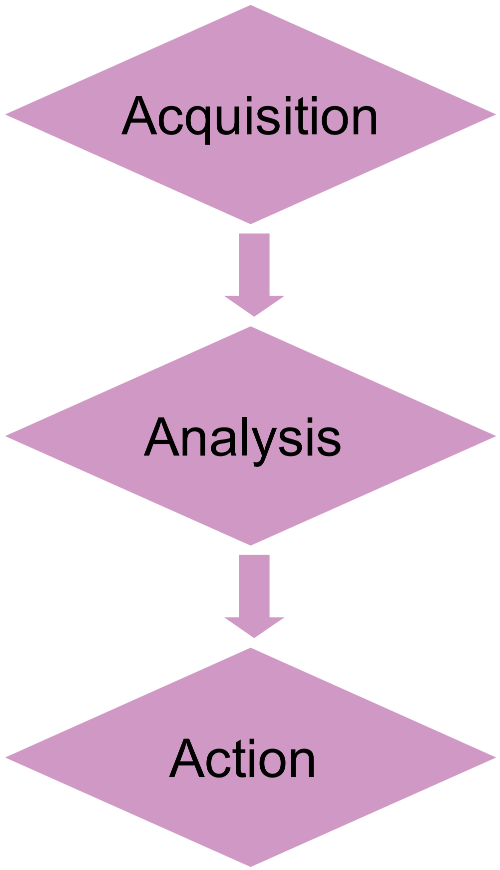
Assessment

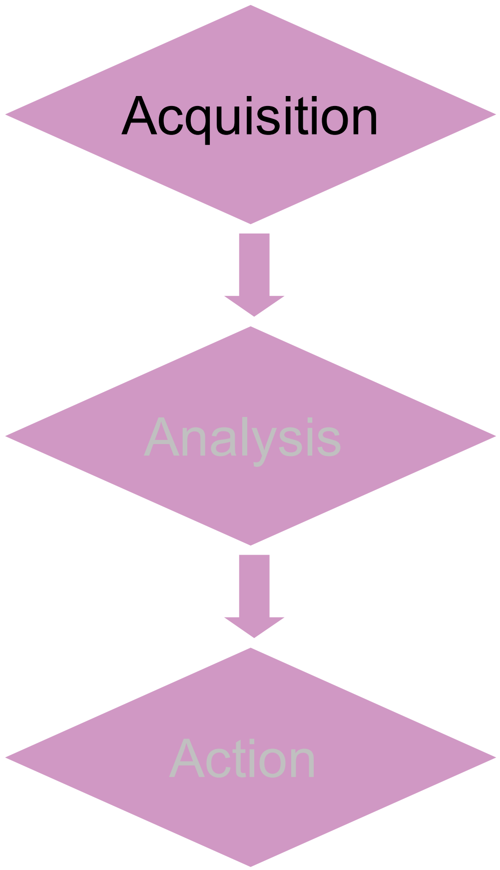
↓

CT scanning

↓

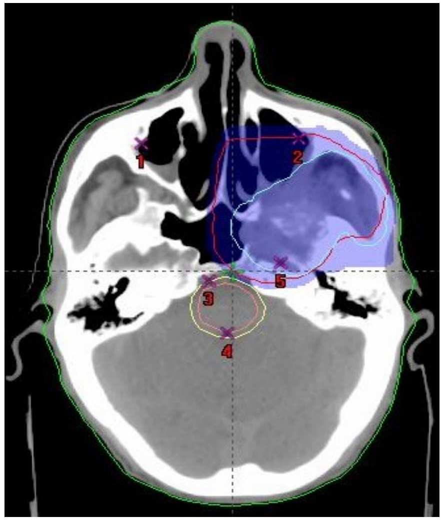
Verification

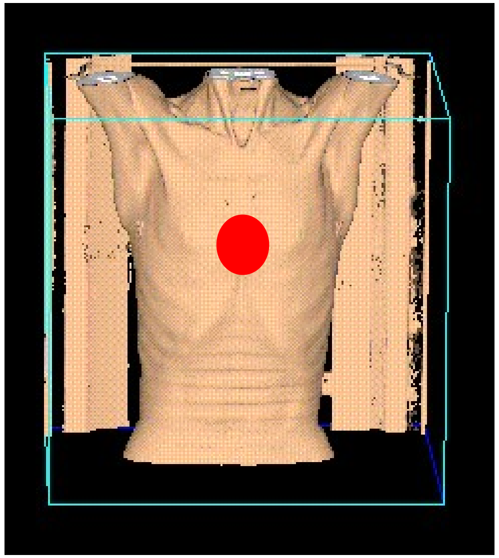

Acquisition
Analysis
Action

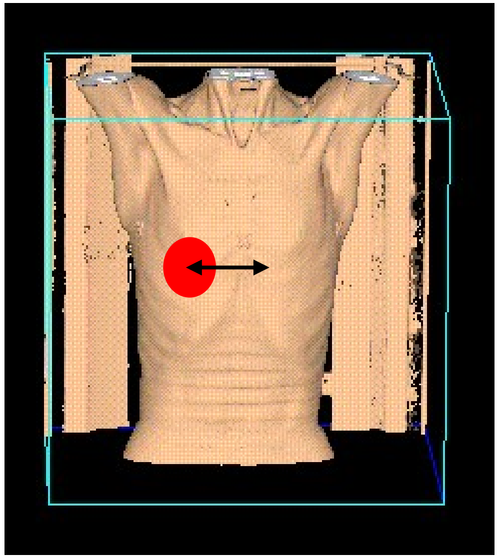

Acquisition
Analysis
Action

Acquisition

Factors affecting protocol choice







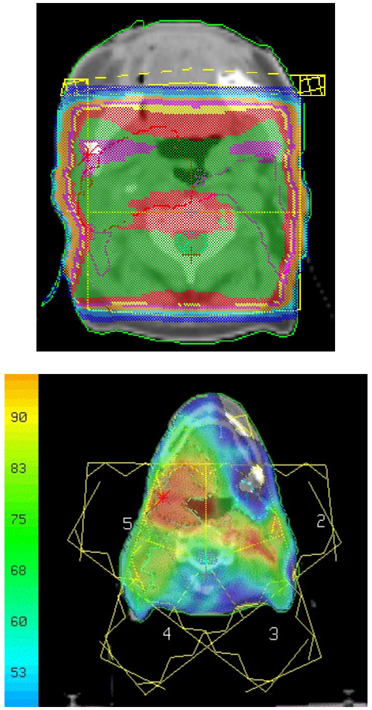
Tumour site

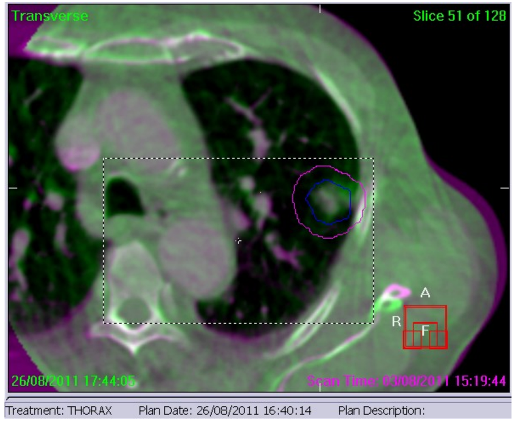
Tumour location

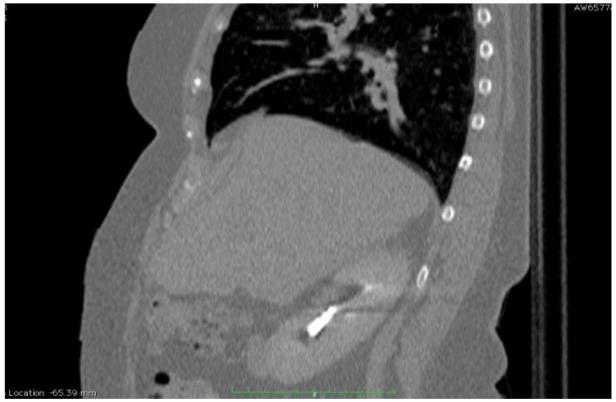
Tumour location

Acquisition

Factors affecting protocol choice







Technique | Technique | Technique

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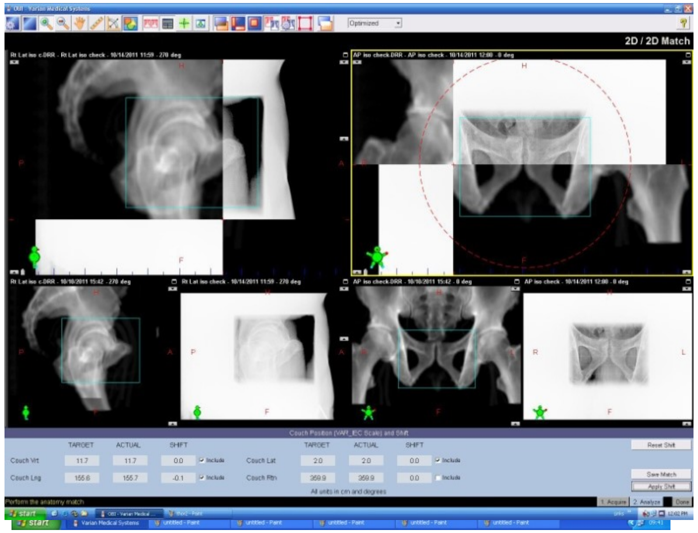
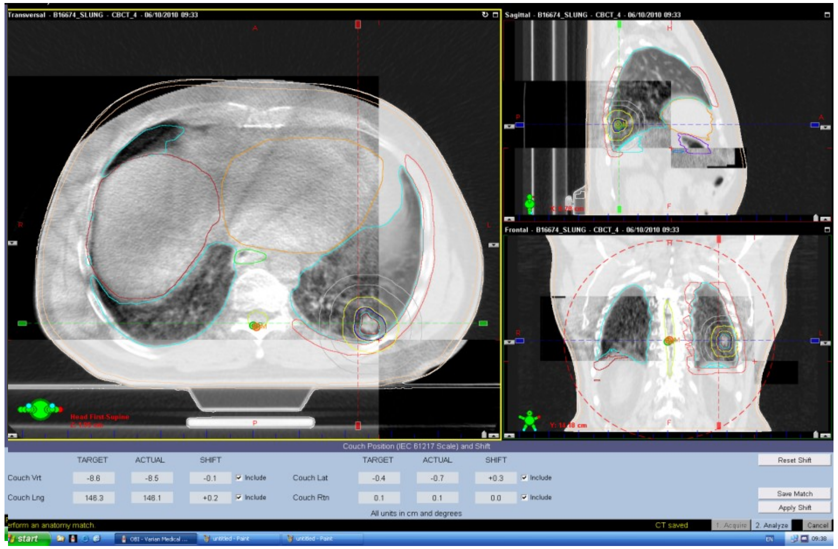
Acquisition

Preparation – choice of modality





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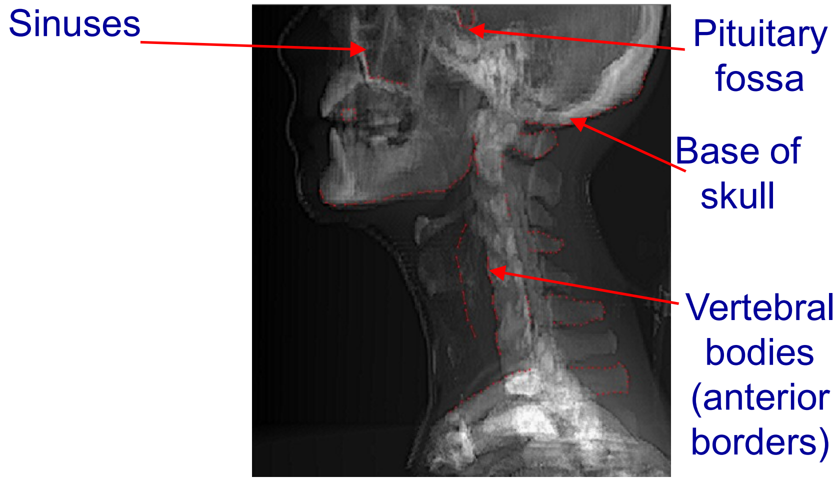
Anatomy for template

Preparation – Protocols

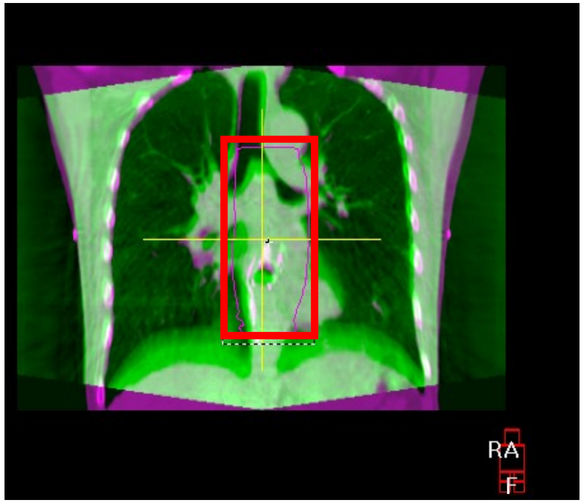
Stable anatomy



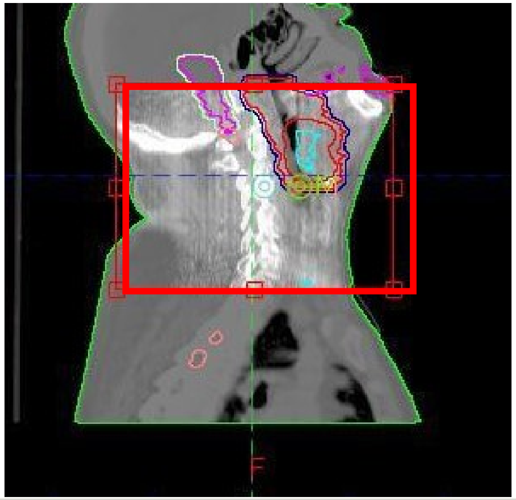
http://www.rcr.ac.uk/docs/oncology/pdf/BFCO(08)5_On_target.pdf

Acquisition

Preparation – Protocols



Region/Volume of Interest

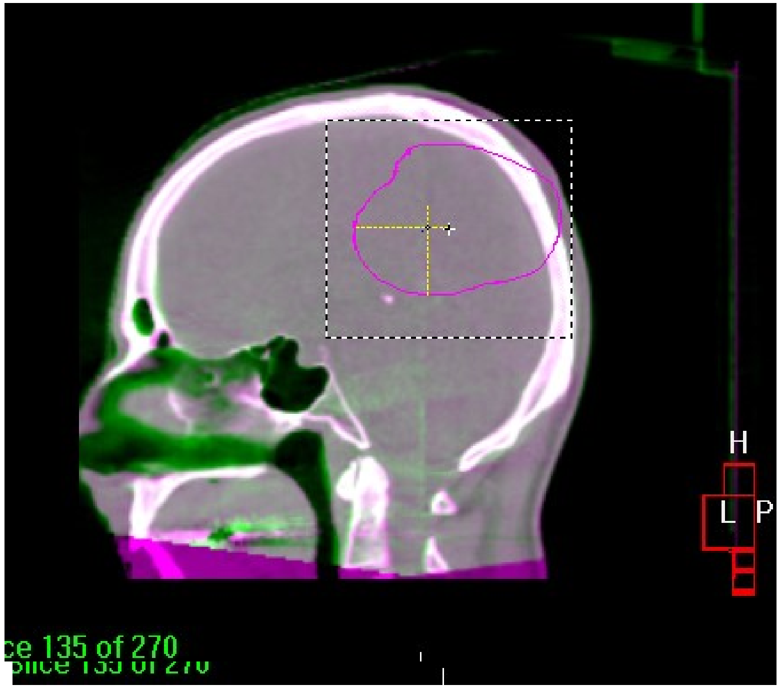


Acquisition

Image Registration

Preparation – Protocols

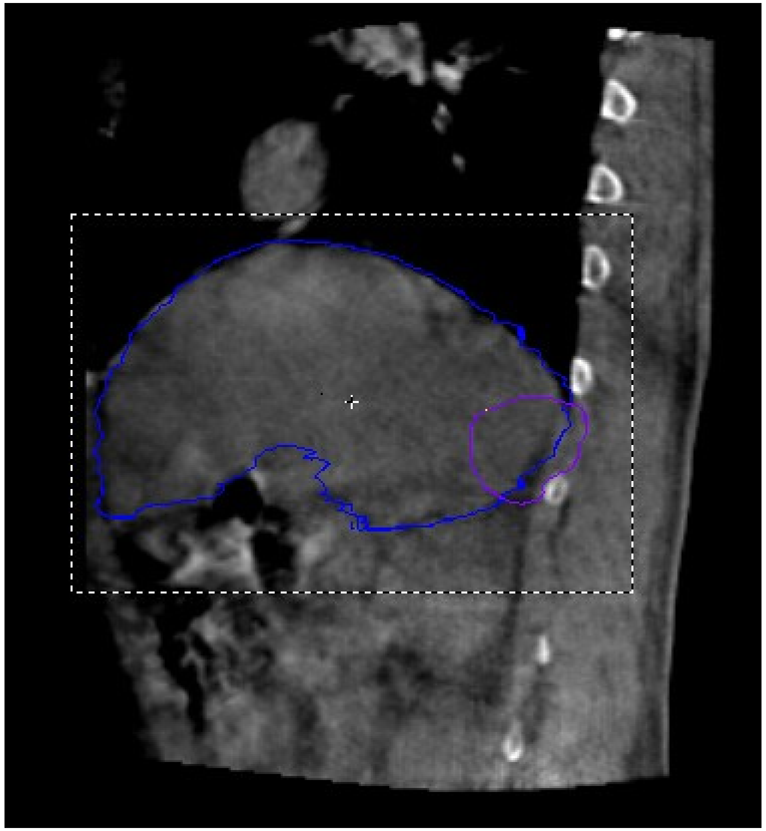
Region/Volume of Interest



Acquisition

Preparation

Length/Field of View



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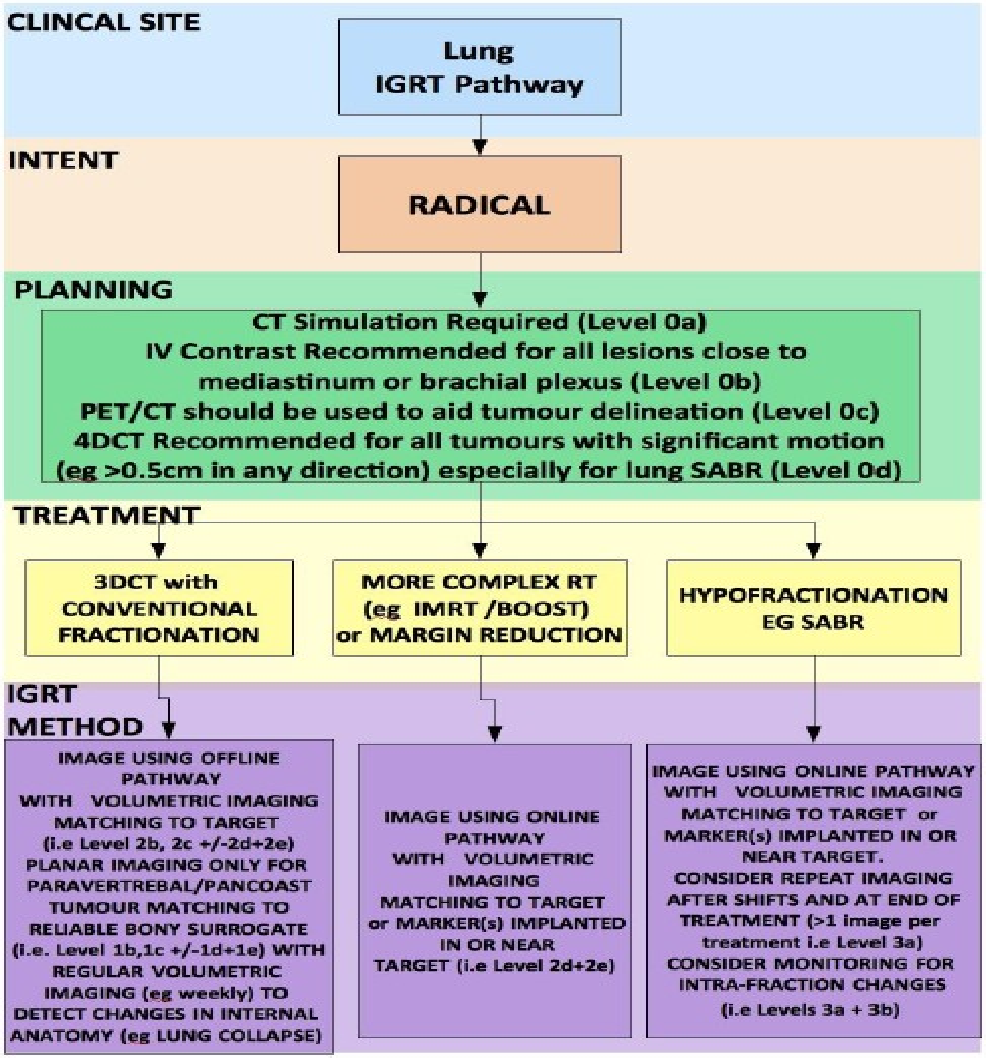


National Radiotherapy Implementation Group Report
Image Guided Radiotherapy (IGRT).
Guidance for implementation and use.
August 2012 UK

Risk

Incorrect protocol

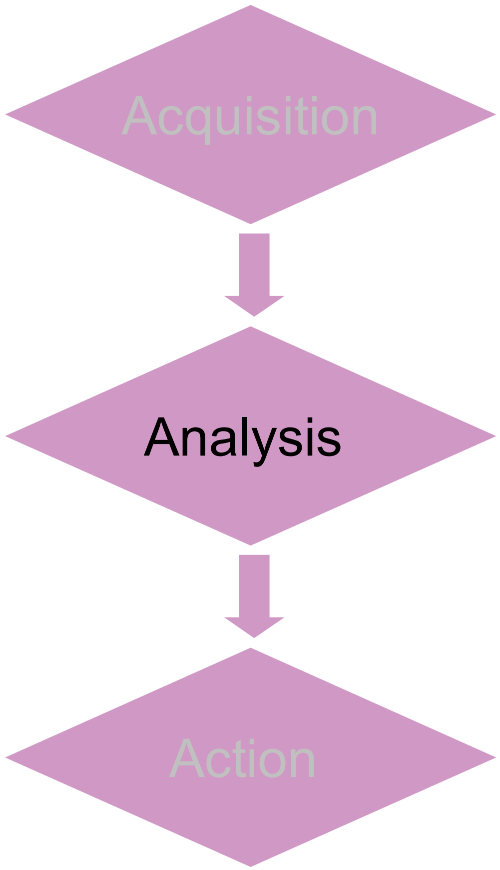
- Repeat imaging
- Increase dose
- Increase time

Incorrect imaging modality

- Repeat imaging
- Increase dose
- Increase time

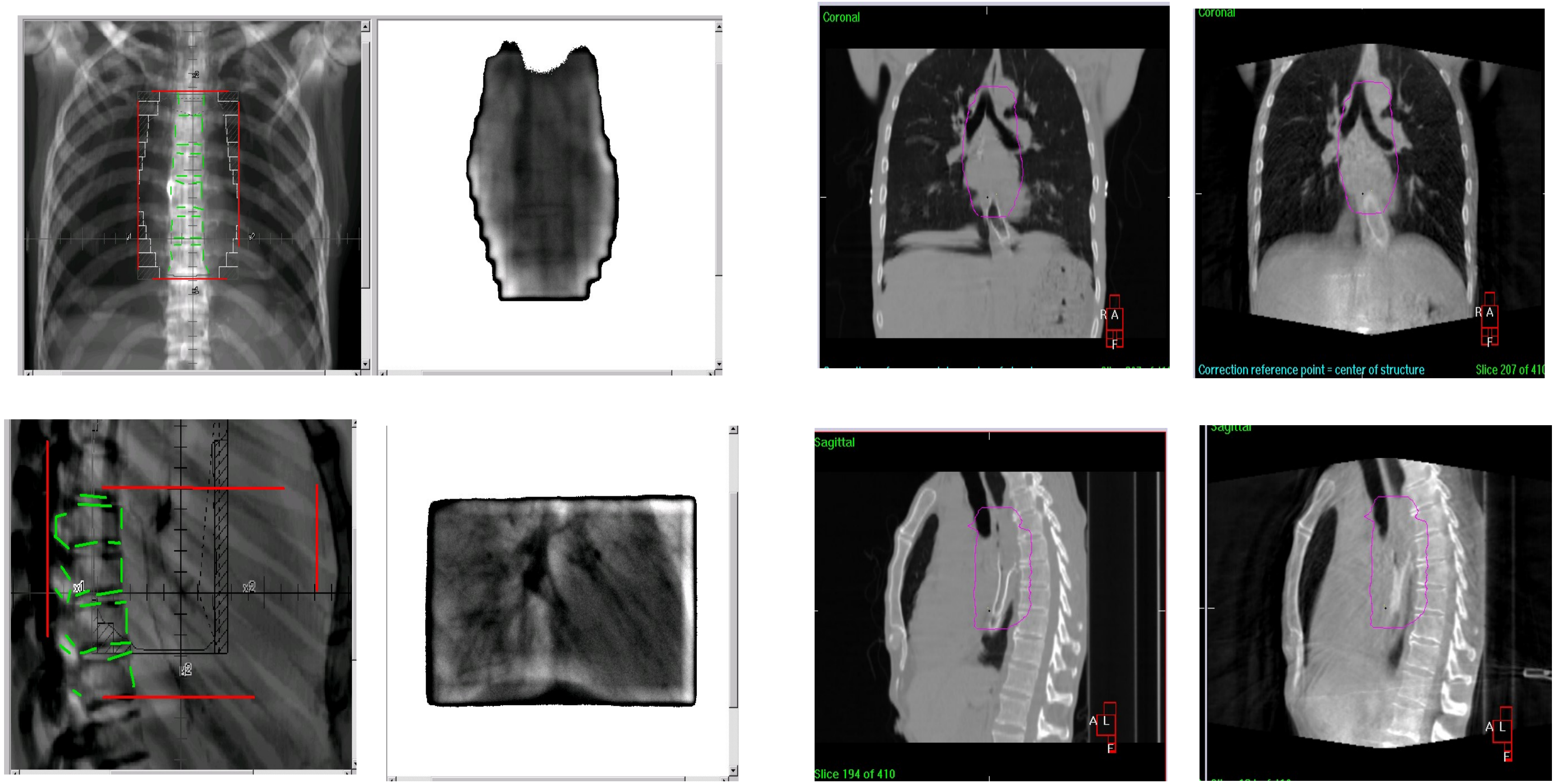
Collision

- Patient safety


Acquisition
Analysis
Action

Analysis

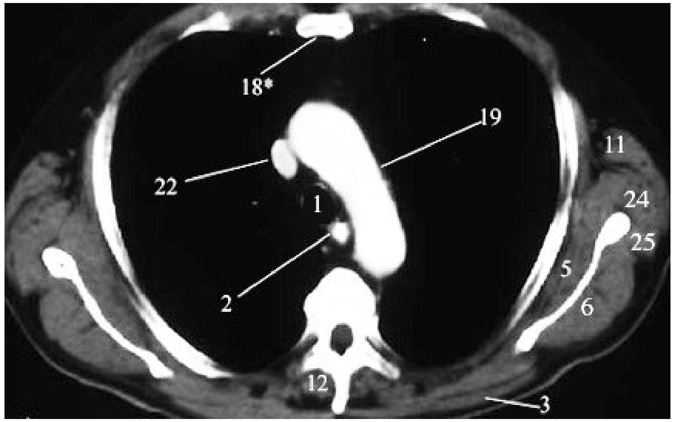
CT anatomy

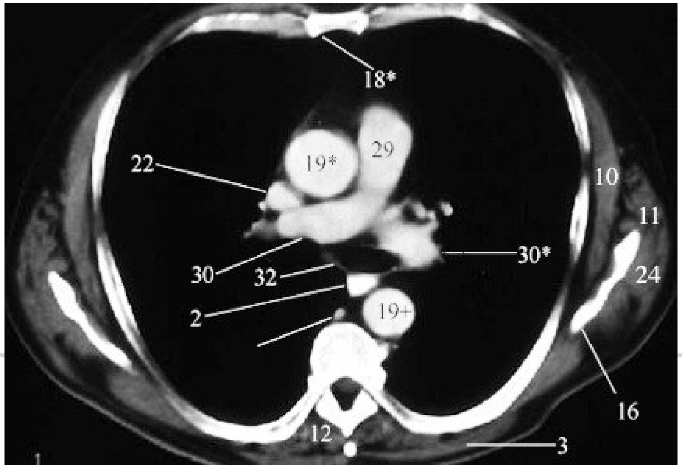


DRR MV EPI Planning CT CBCT

Analysis

CT anatomy

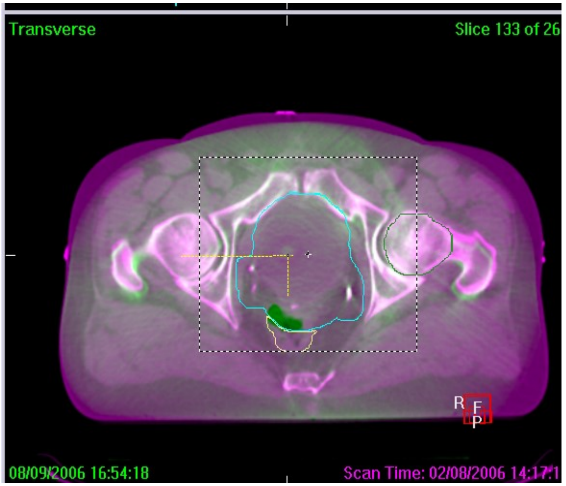


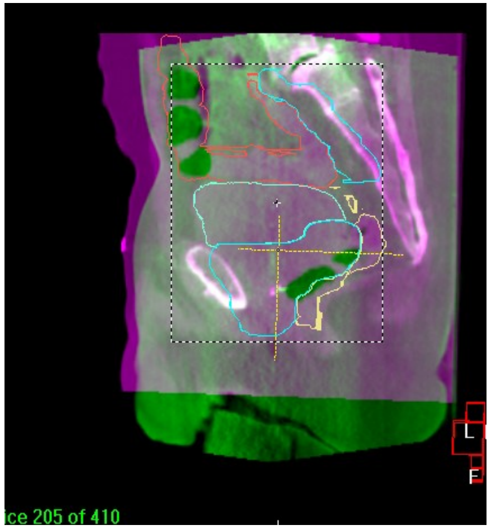


1 Trachea
2 Oesophagus
3 Trapezius Muscle
5 Subscapularis
6 Infraspinatus
10 Serratus Anterior
11 Latissimus Dorsi
12 Erector spinae
16 Scapula
18* Body of sternum
19* Ascending aorta
19+ Descending aorta
22 SVC
24 Teres major muscle
25 Teres minor
30 RT Pulmonary Artery
30* LT Pulmonary Artery
32 Carina

Analysis

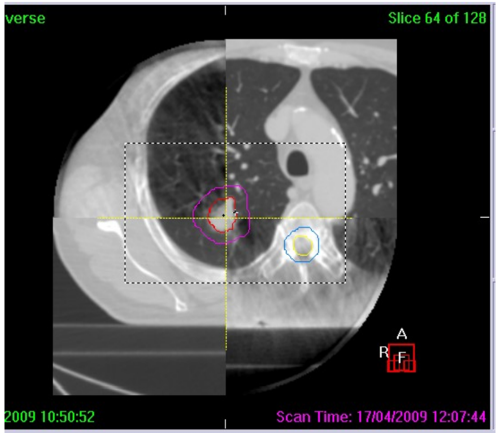
Gross error

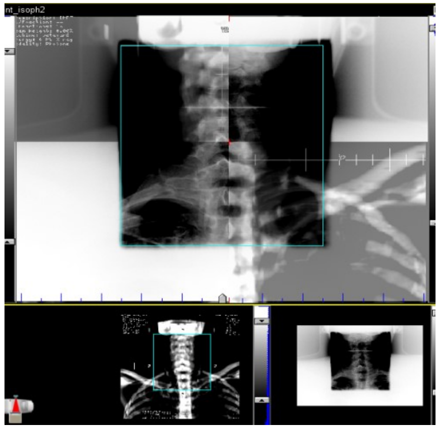


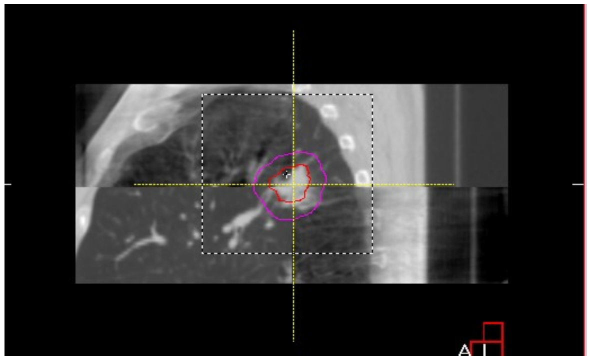


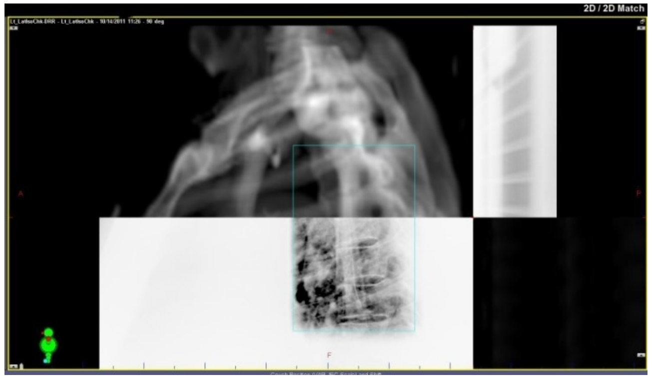
Analysis

Cut plane









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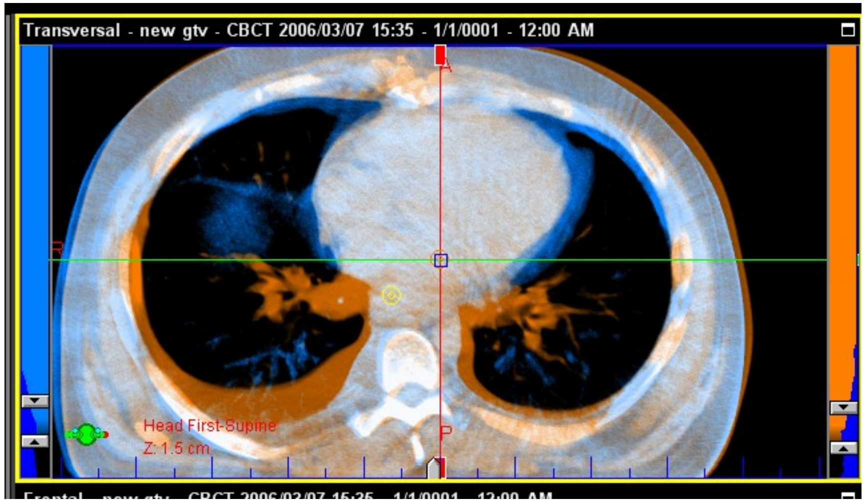
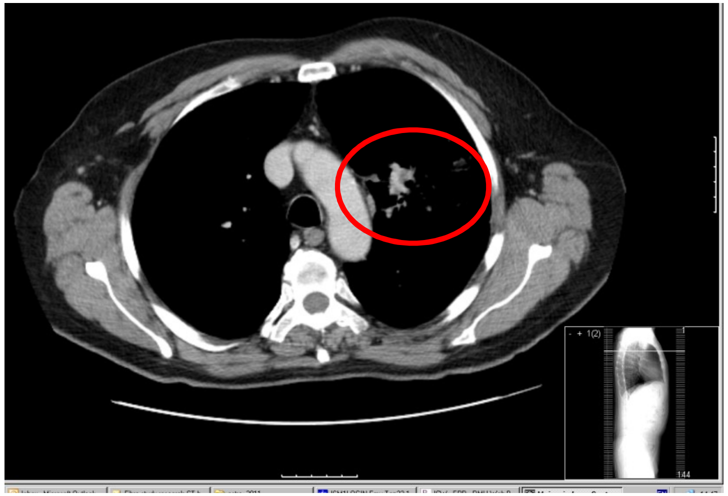
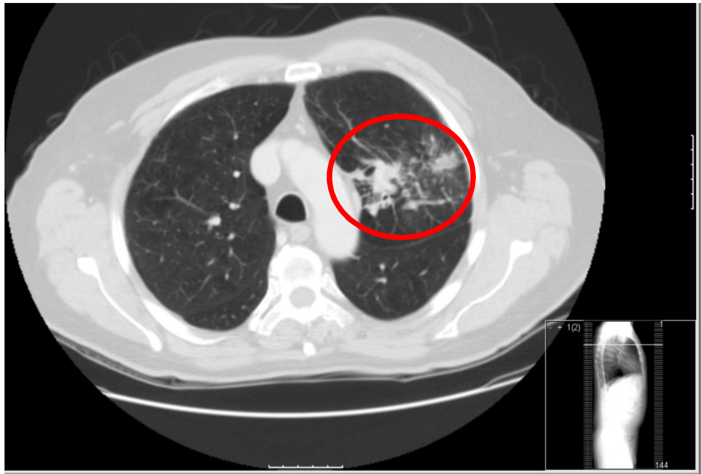
Analysis

Window levels

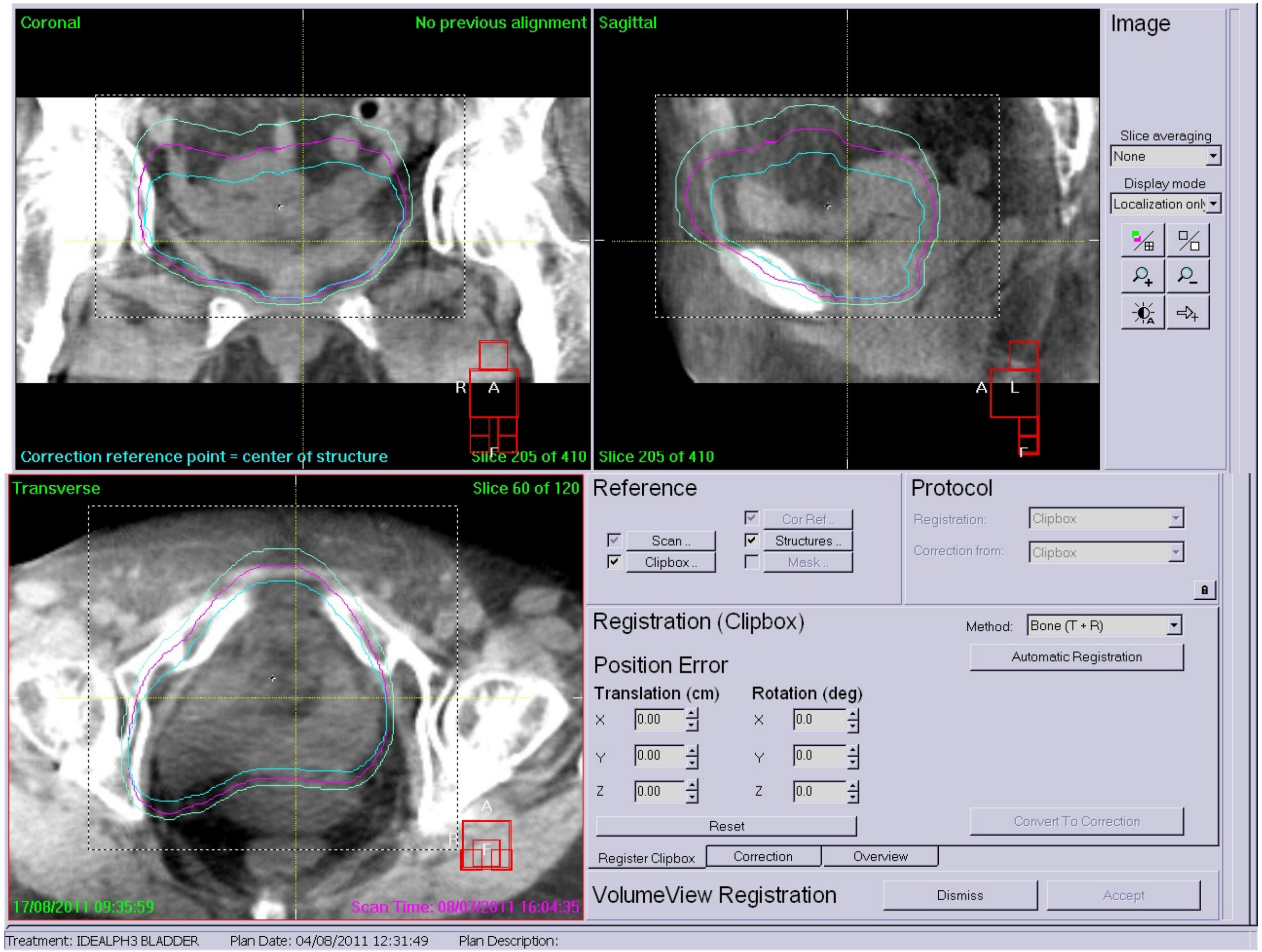






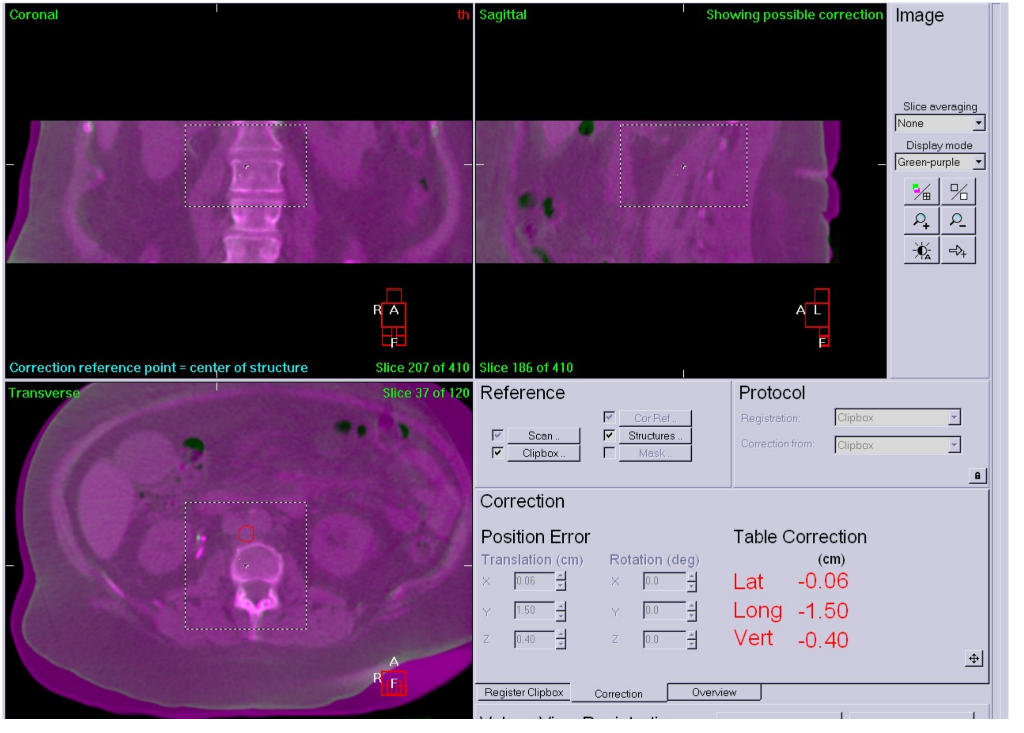
Analysis

3 views



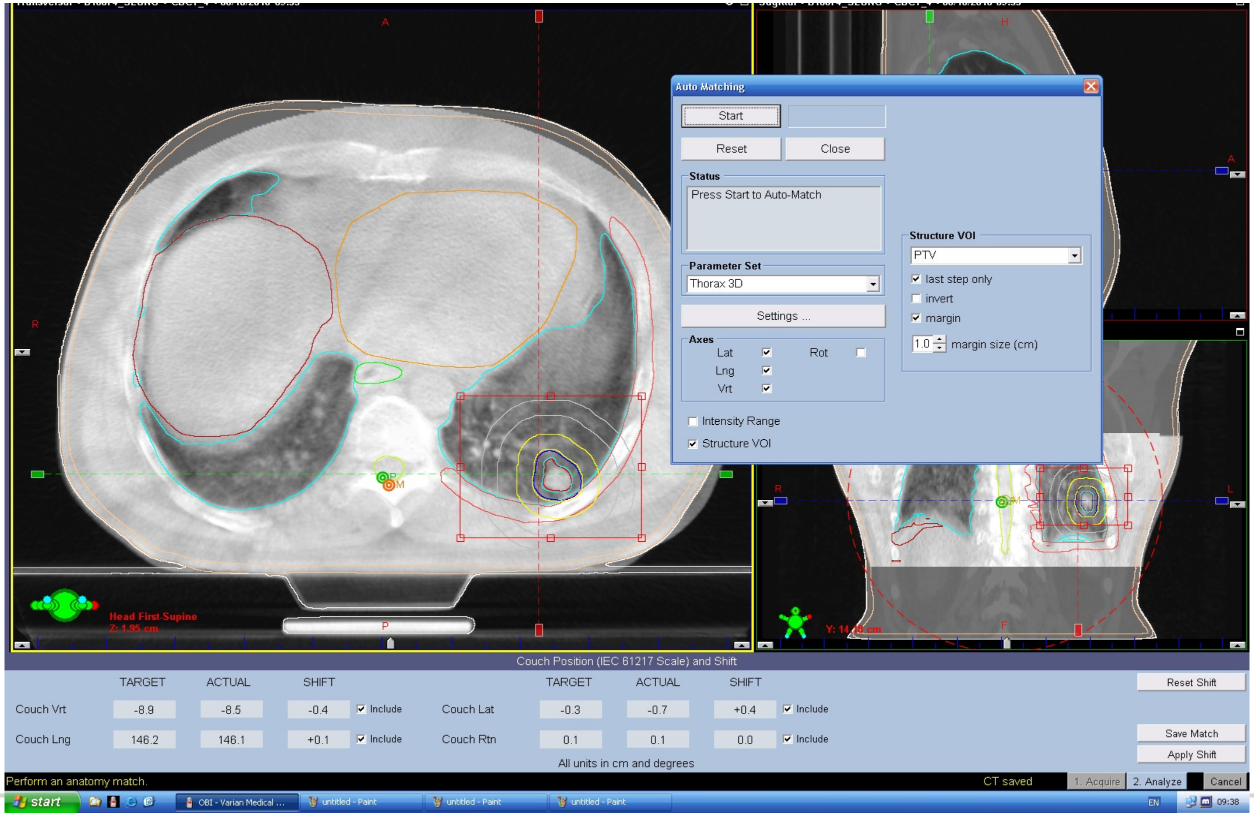
Analysis

Registration-rotation



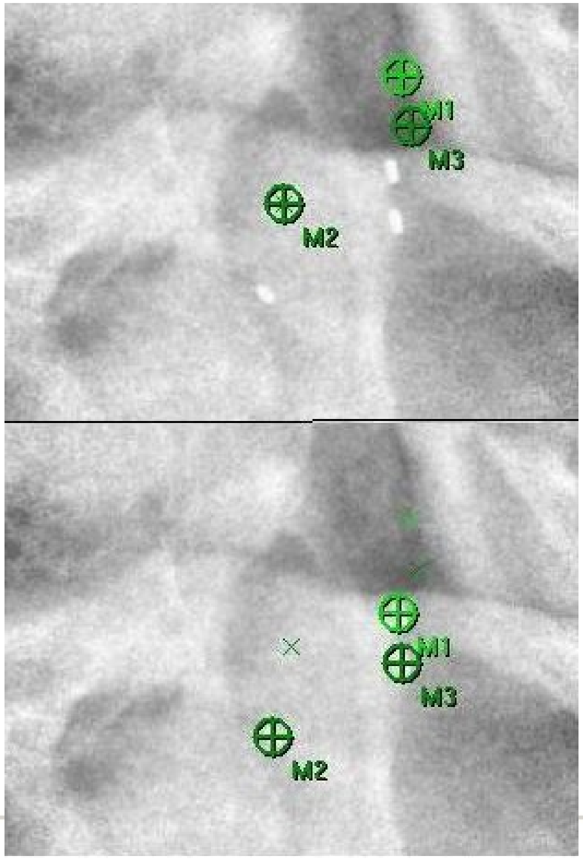
Analysis

Registration-rotation



Analysis

Registration-rotation



Correction requirement
in 6D

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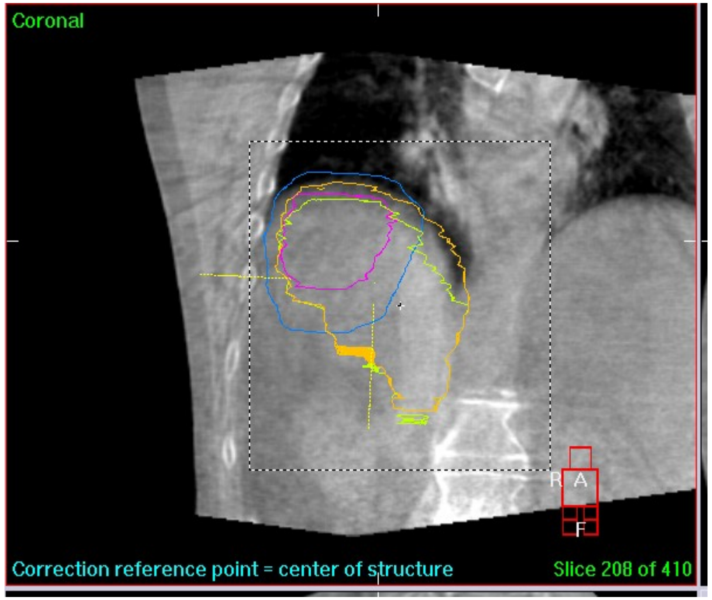
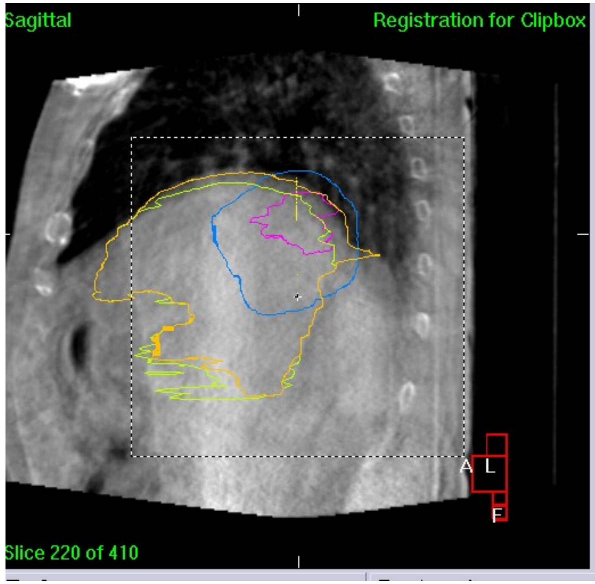
Analysis

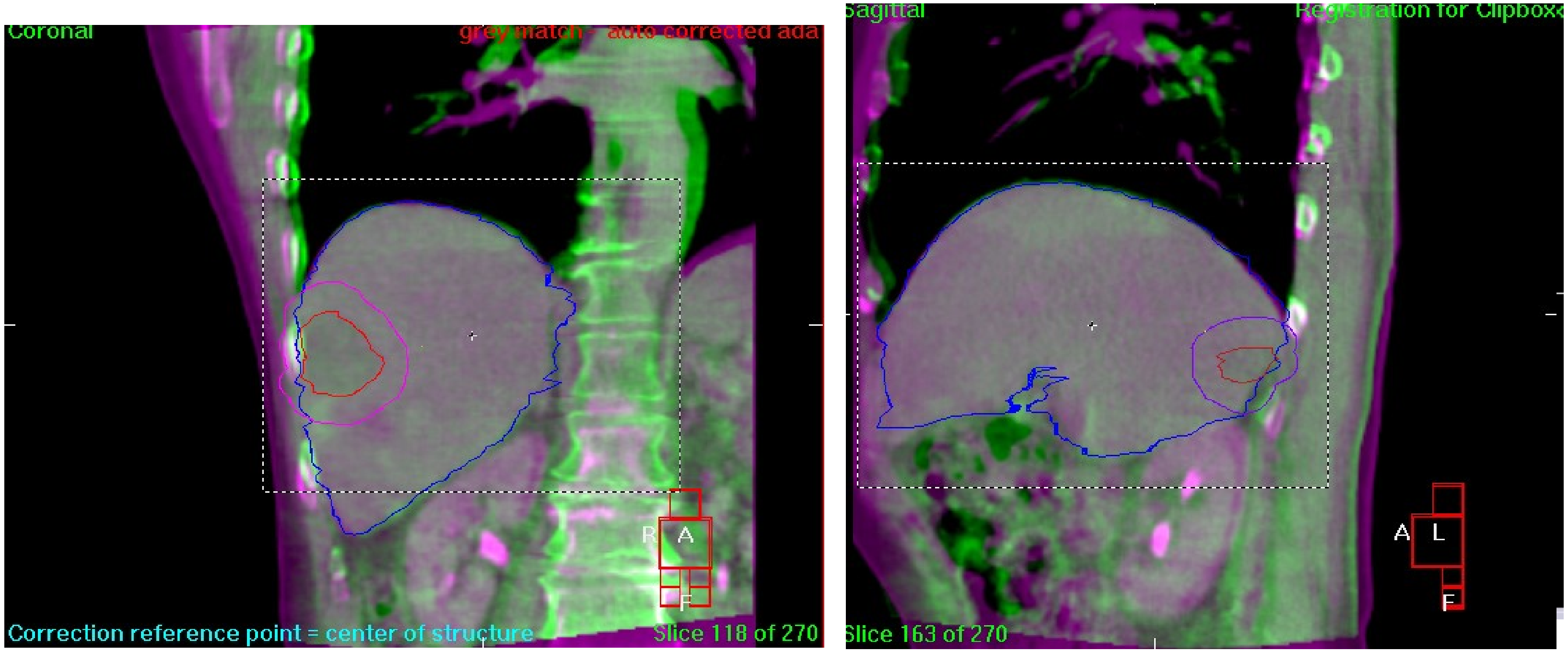




Free Breathing

Courtesy of M Hawkins

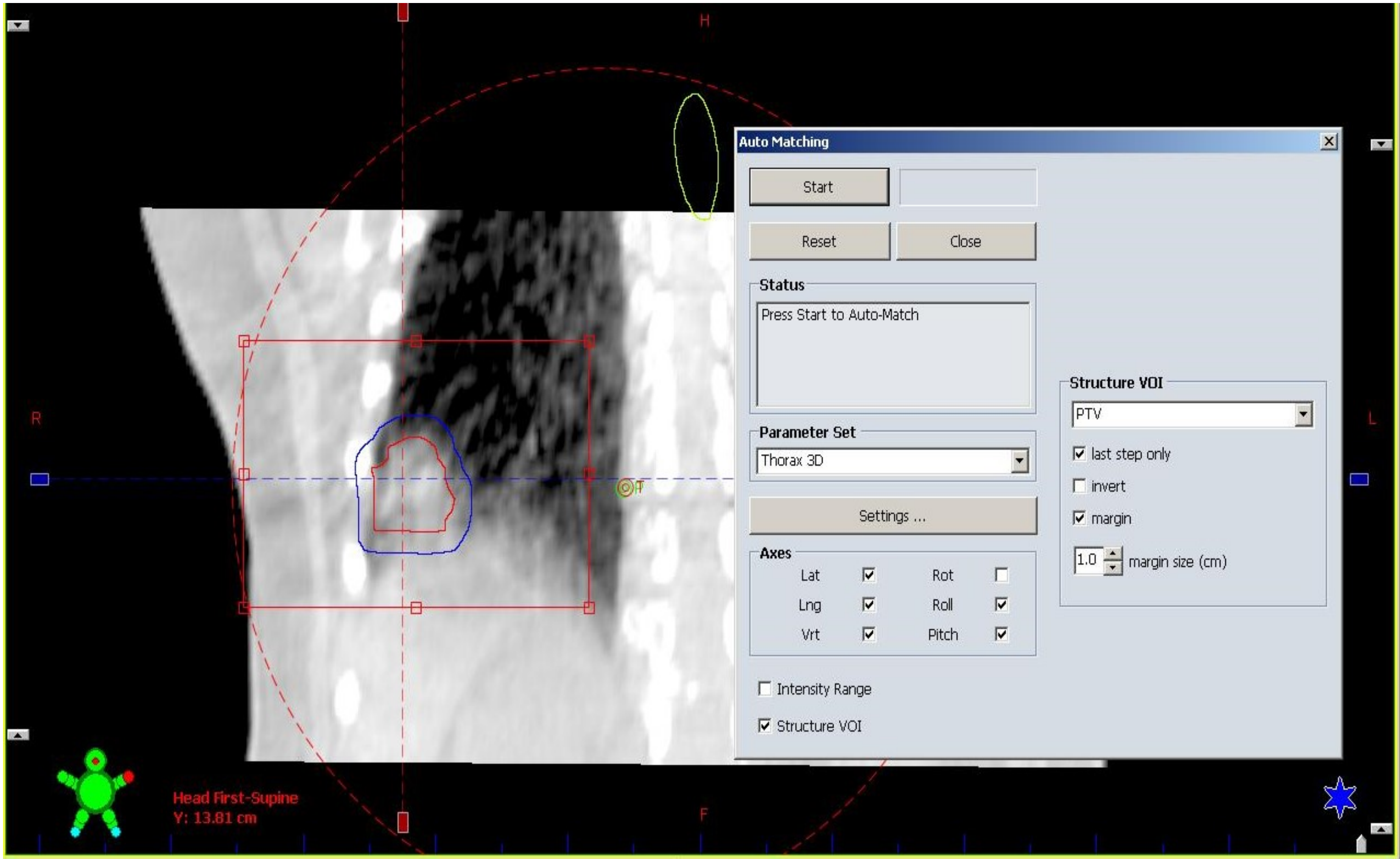
Analysis



Breath hold

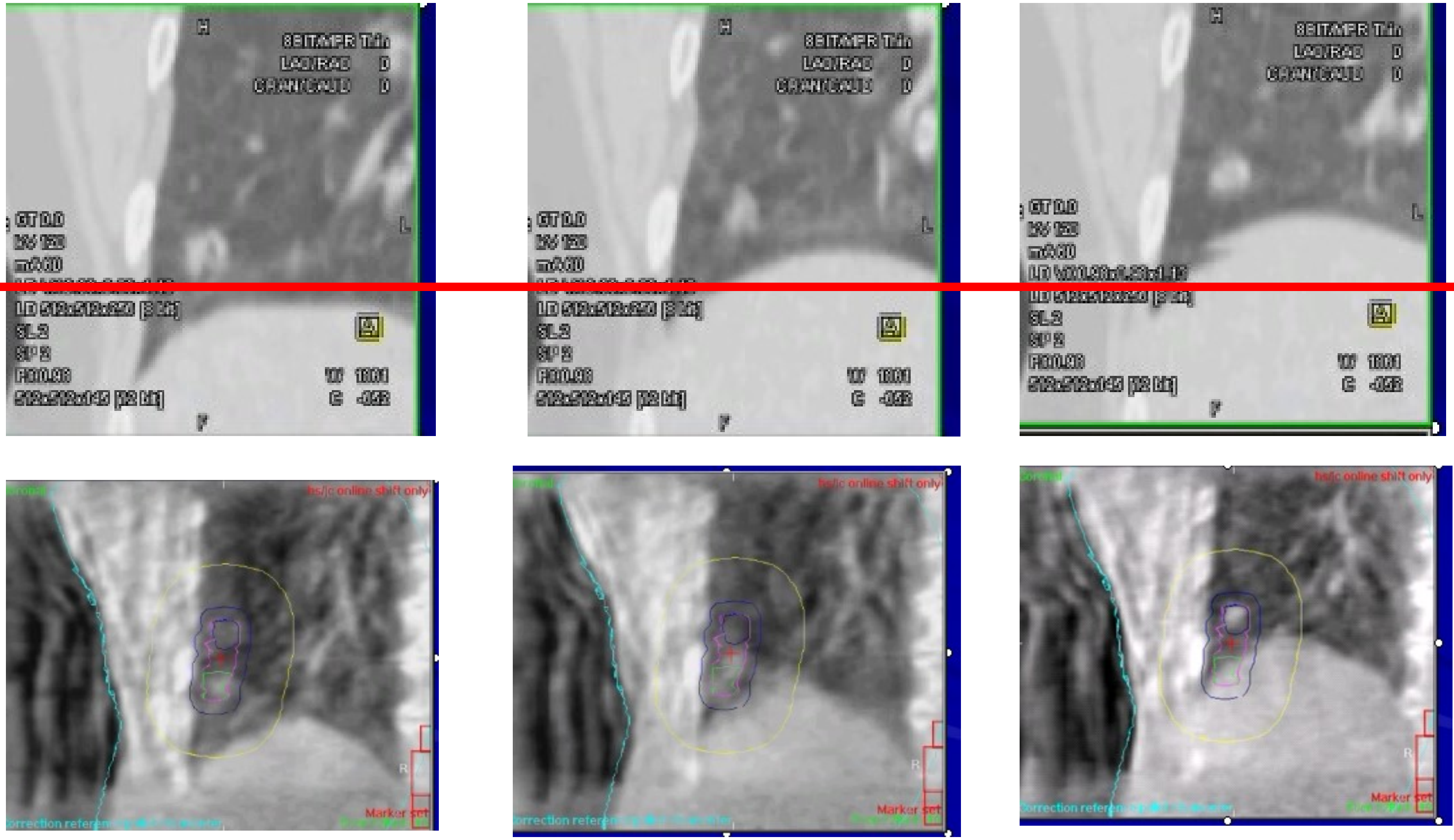
Courtesy of M Hawkins

Analysis



Courtesy of A Baker

Analysis



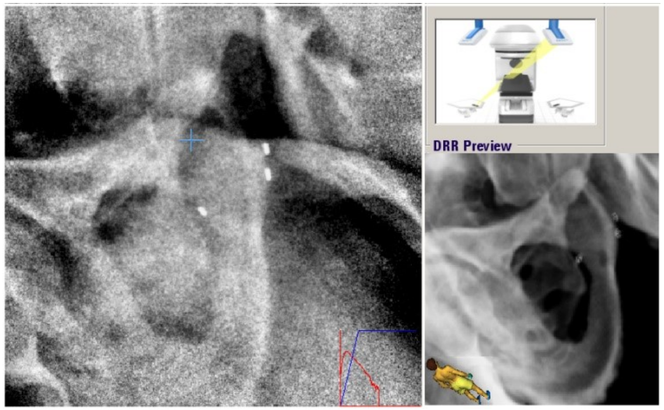
4DCT

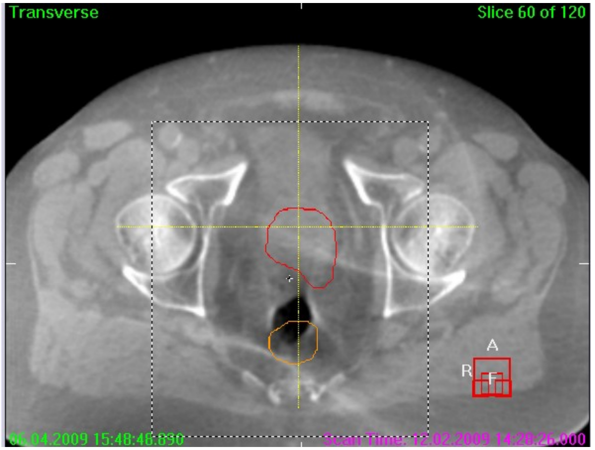
4D
Cone Beam
CT

Coronal View

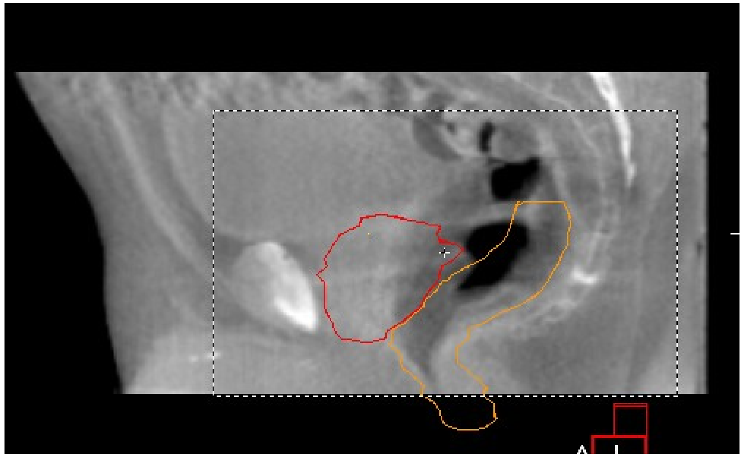
Courtesy of J Lilley, Leeds

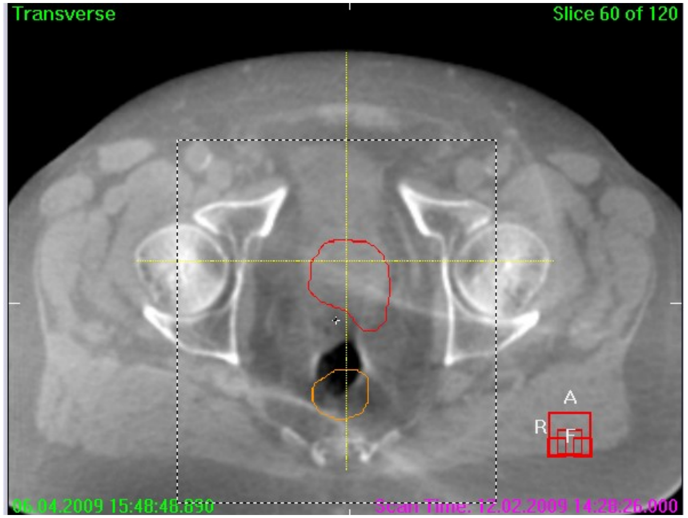
Analysis





Analysis

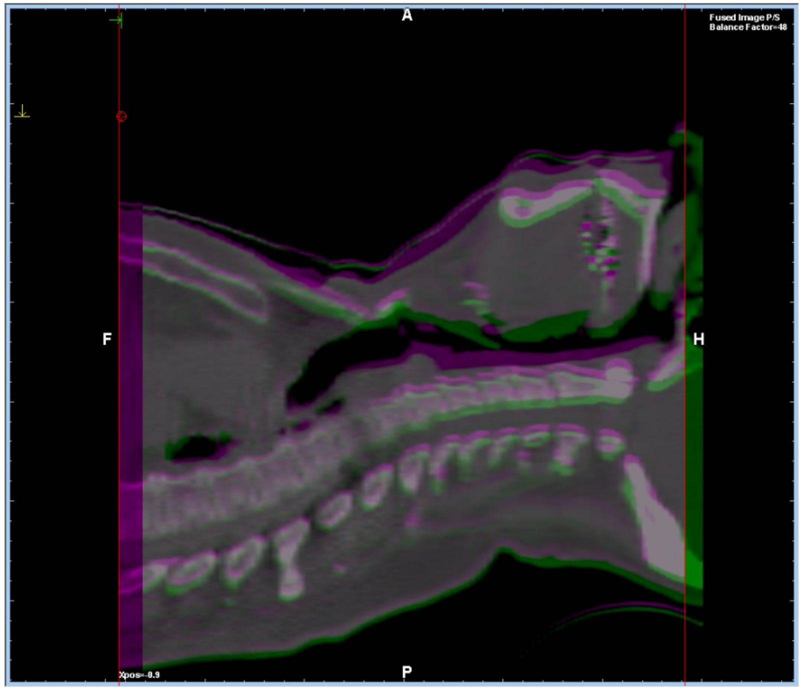




Decision

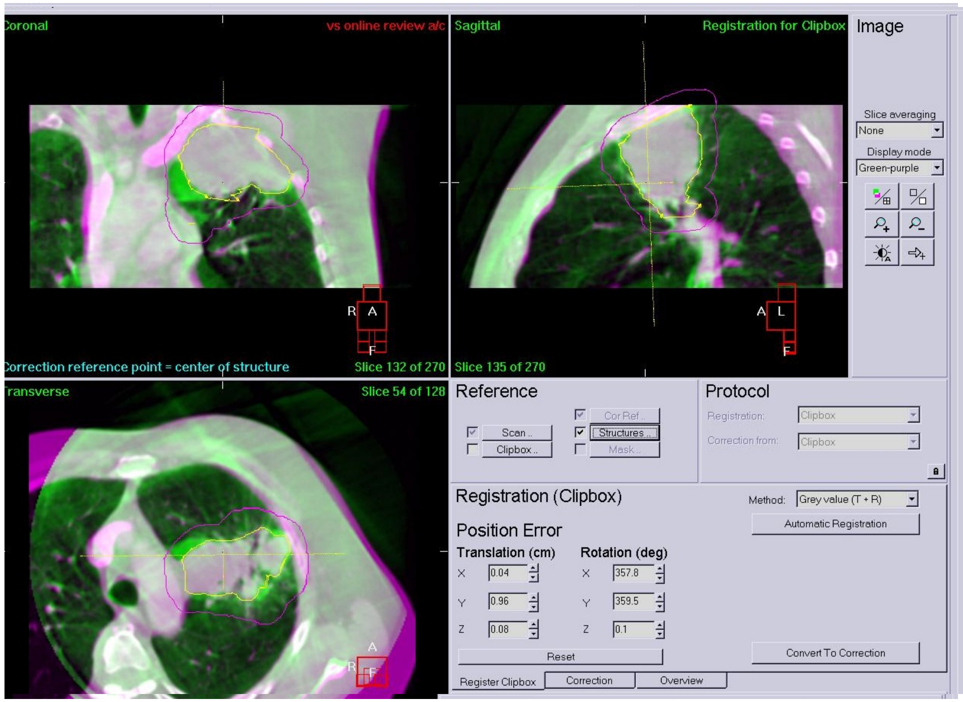
Analysis

Patient motion



Analysis

Detecting changes anomalies



Risk

Misinterpretation of structures

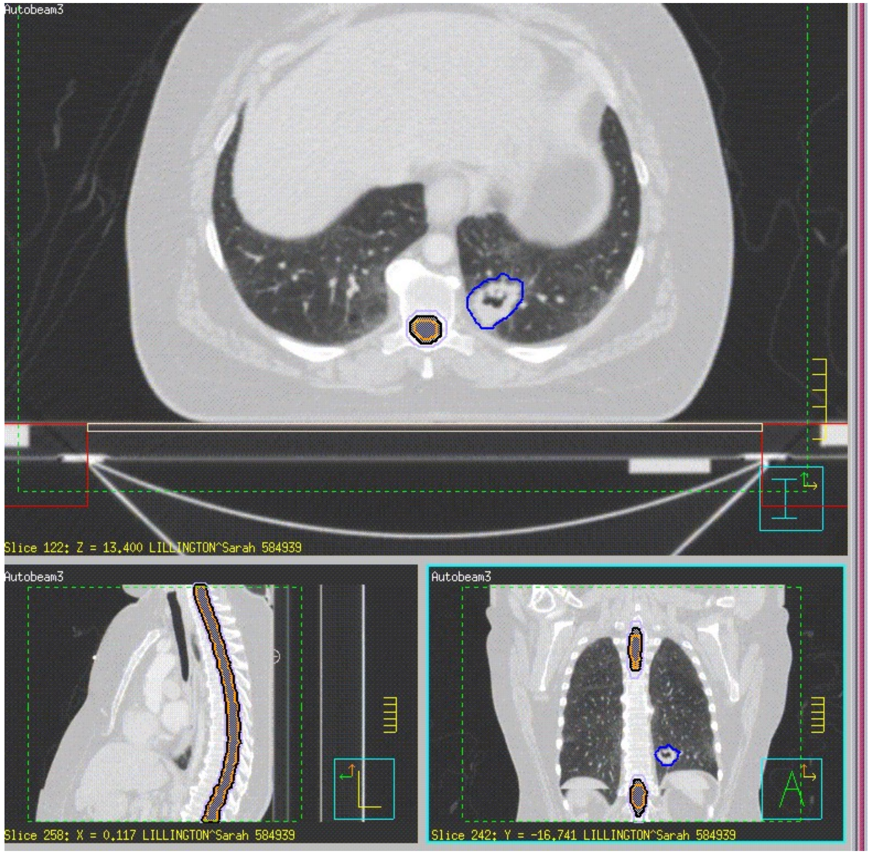
incorrect adjustment

Incorrect visualisation

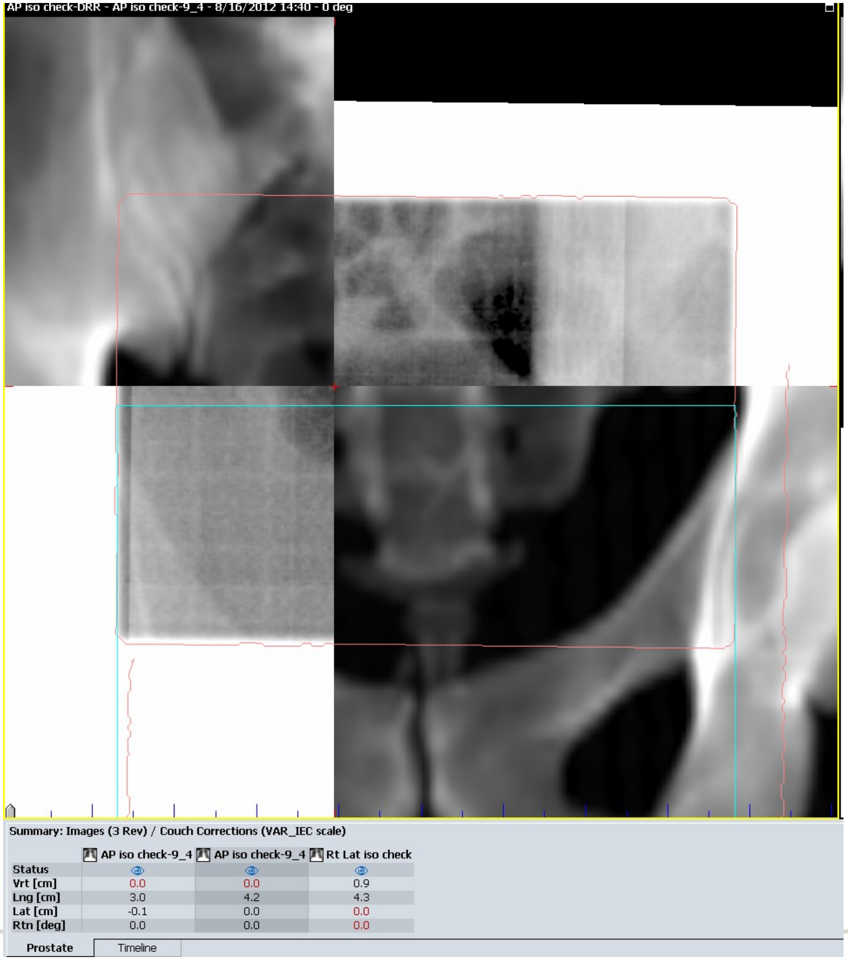
incorrect adjustment

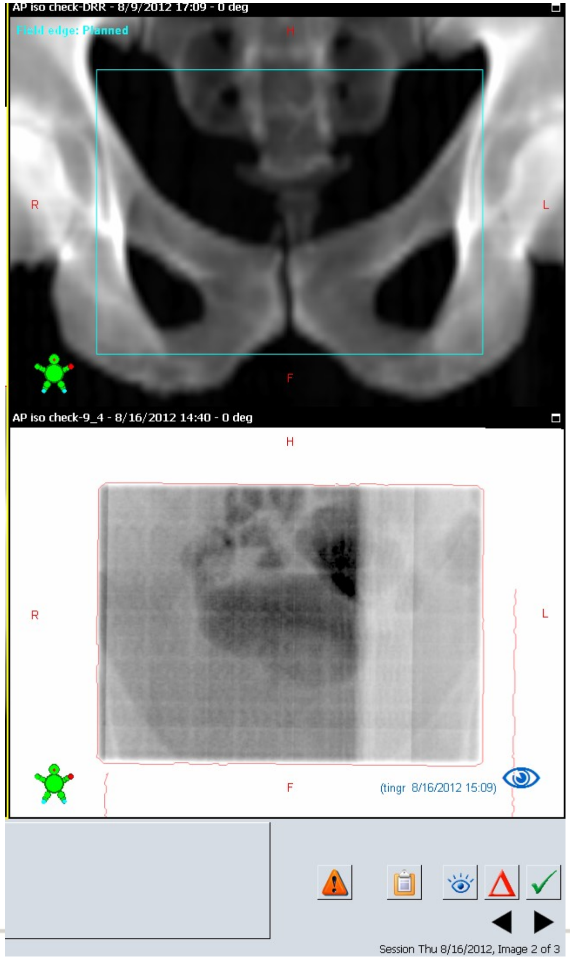
Inadequate knowledge

incorrect decision



Risk - Misinterpretation of structures





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There are known knowns

there are things we know we know.

There are known unknowns

there are some things we do not know.

But there are also unknown unknowns

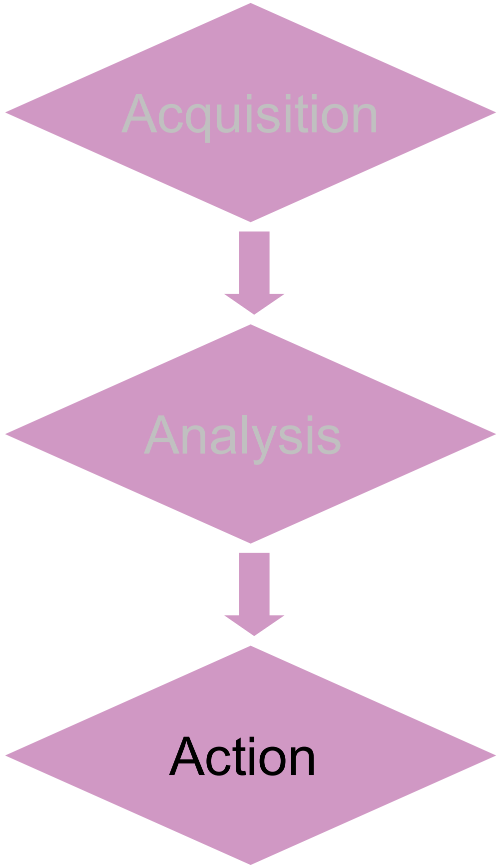
there are things we do not know we don't know.

Level of observability

Level of risk

Known Unknowns	Unknown Knowns
Known Unknowns	Unknown Unknowns

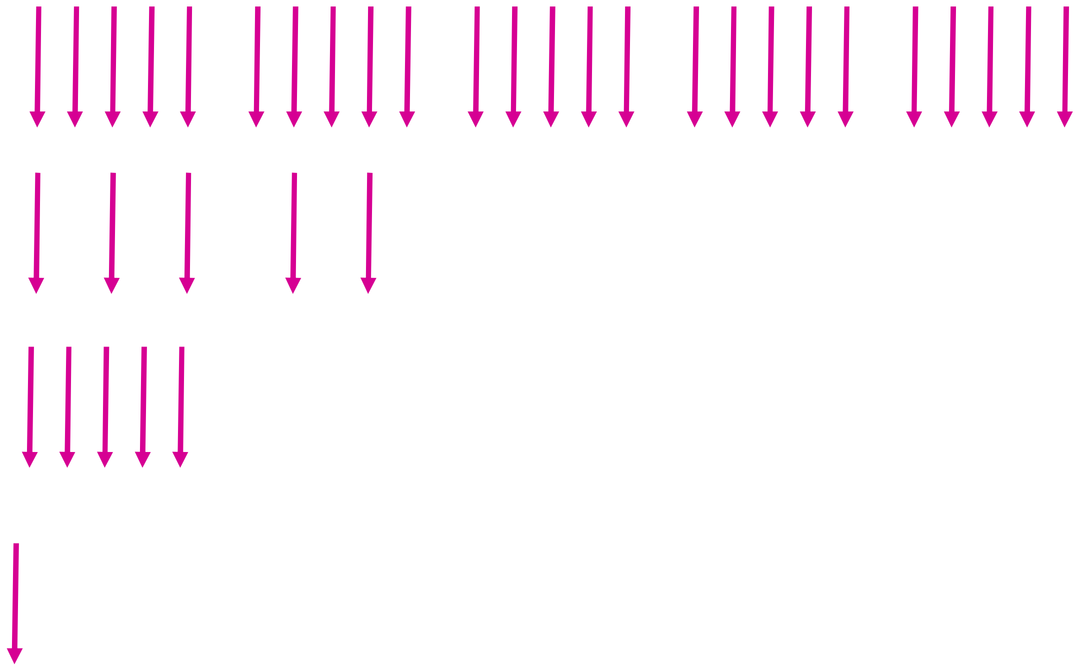
Rumsfield matrix


Acquisition
Analysis
Action

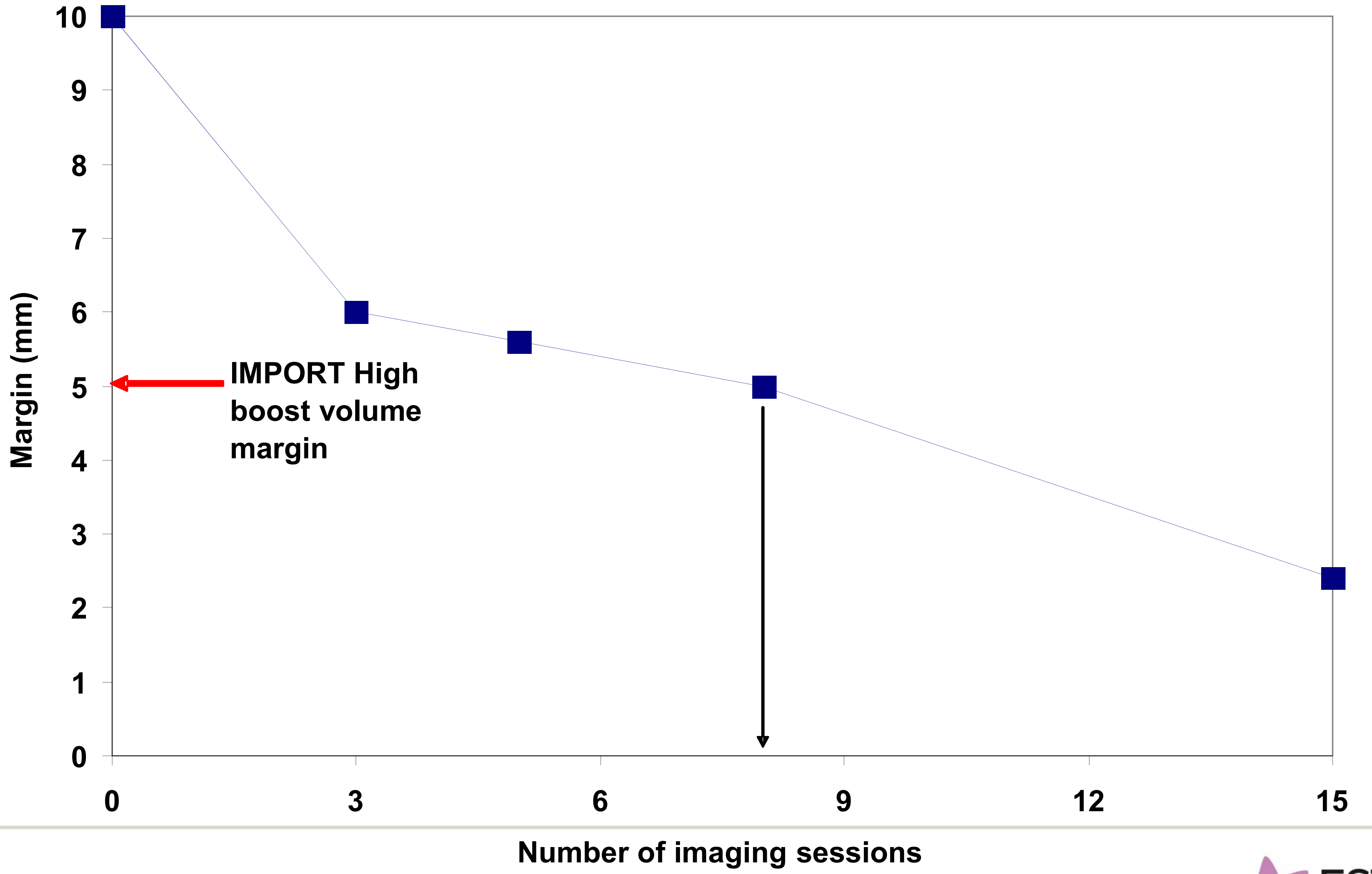
Off line/On line

On line	Off line
Immediate	Time for review
Random and Systematic	Systematic
Audit?	Audit?

Fractionation



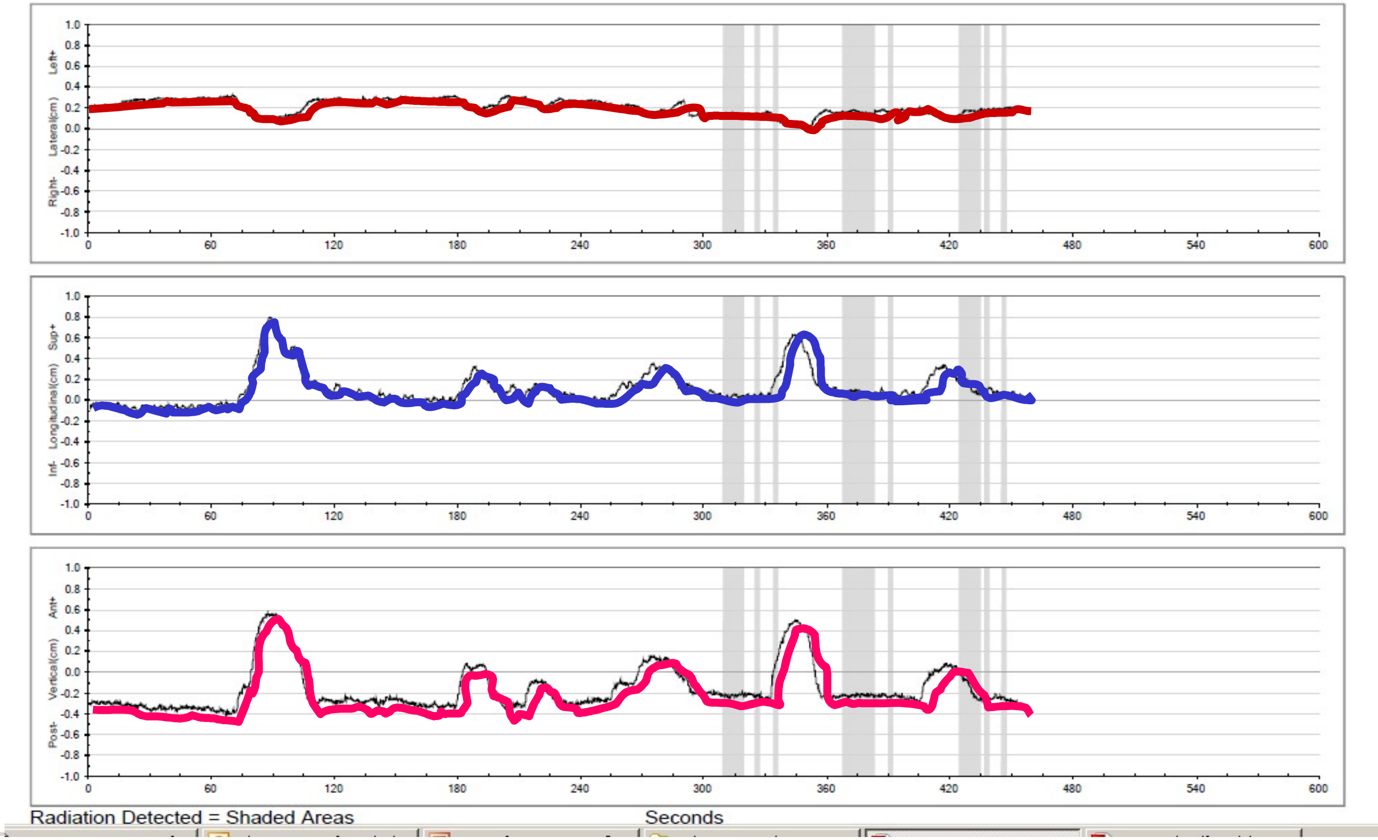
Effect of number of imaging sessions on margin for breast



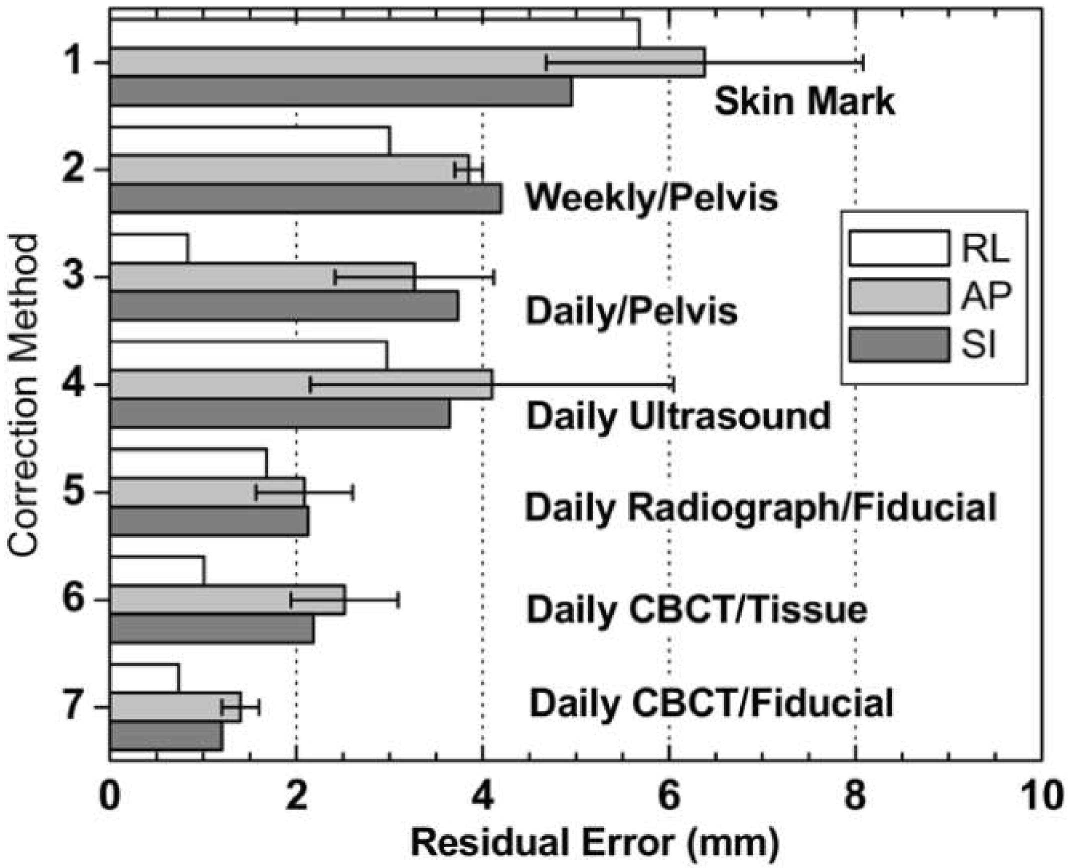
Courtesy of Ellen Donovan

Risk – underestimate intrafraction motion

Intra fraction motion – prostate



Risk – underestimate residual errors



Mageras Sem Rad Onc 2007

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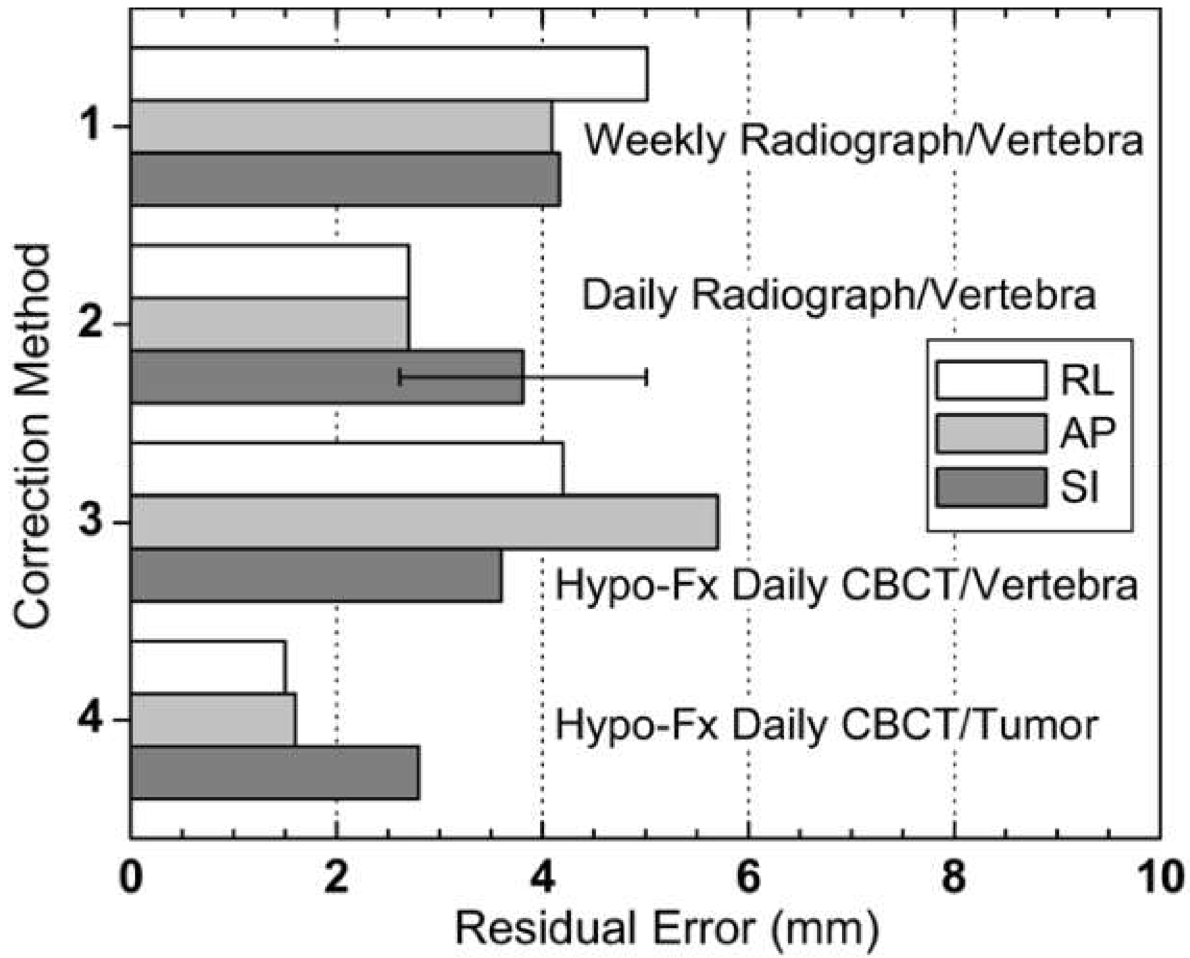
Risk – underestimate residual errors



Mageras Sem Rad Onc 2007

Risk

Incorrect protocol/frequency of imaging

Increase dose to patient

Geographic miss target

Incorrect decision

incorrect move or incorrect 'NOT' move

Not confident decision making

increase time for patient on bed - motion

Unawareness of lack of knowledge

incorrect move or incorrect 'NOT' move

incorrect treatment delivery

2012, 2014 and 2016 reported error trends.

	Number of reports	Percentage of IGRT errors
2012	65	2.0
2014	302	3.5
2016	825	6.9

Radiotherapy Errors and Near Misses Data Report (December 2013 to November 2015)
Public Health England , UK

Process code	Activity code	Example
13i	Use of on-set imaging	Imaging according to protocol
13z	On-set imaging: production process	Inappropriate exposure used Image not captured CBCT filter left in for kV image
13aa	On-set imaging: approval process	Image review not done Image review inaccurate Image matched to inappropriate reference image
13bb	On-set imaging: recording process	Recording of image review not undertaken Actions following image review not undertaken

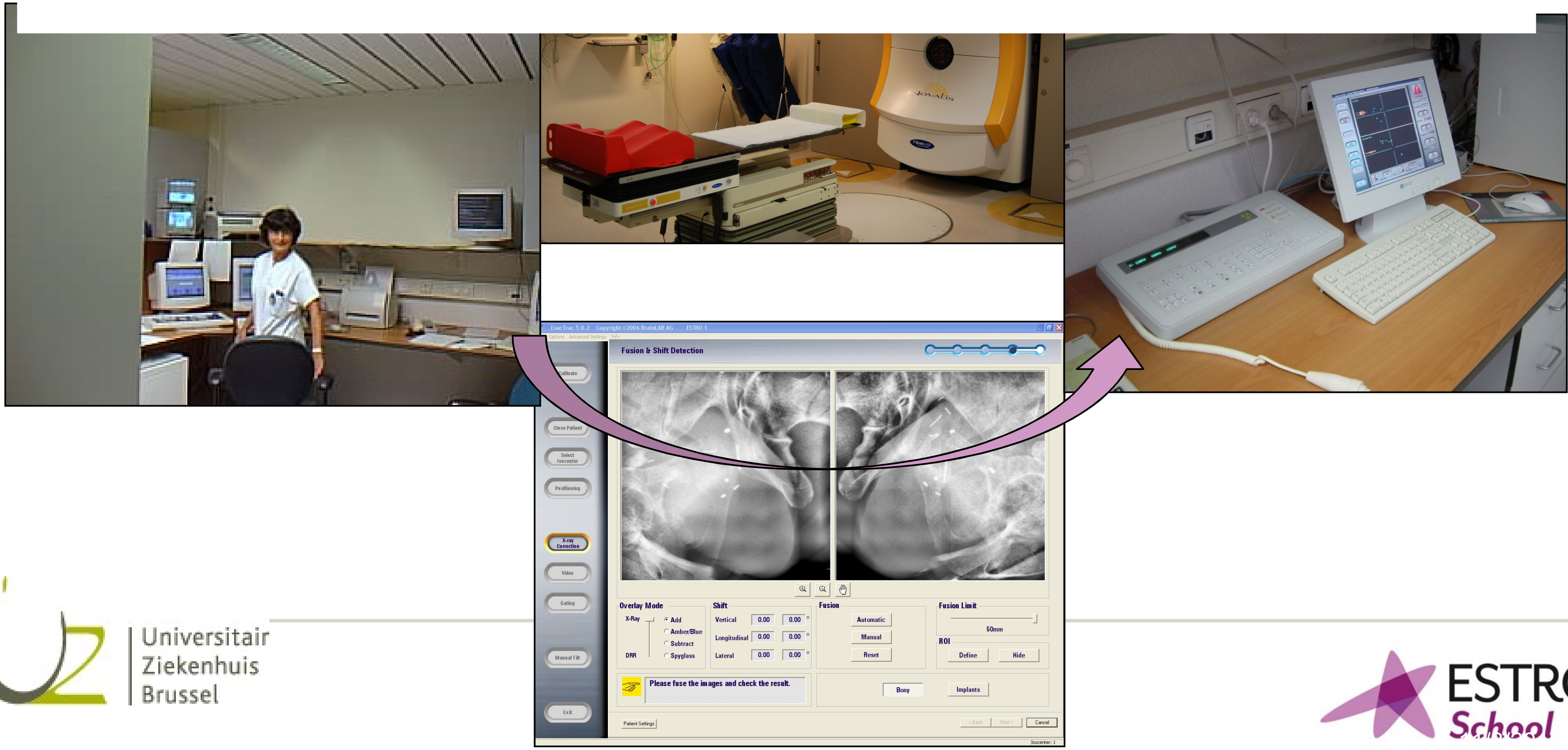
Courtesy Helen Best PHE

Novalis ExacTrac

Near-incidents related to IGRT @ UZB

IGRT data base ≠ R&V data base

Treatment parameters need to be transferred twice



Universitair Ziekenhuis Brussel

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Novalis ExacTrac

Patient plan was prepared for morning staff

Treatment parameters transferred to both data bases (Varis and ExacTrac: labeled "ready for approval") for QA purposes

CTV was rejected and adjusted at morning staff

This resulted in a change of isocentre co-ordinates

Final plan was transferred to Varis R&V (labeled "approved by staff dd/mm/yy) … but not to ExacTrac

RTT discovered discrepancy in isocentre co-ordinates while dubble checking print out of treatment chart.

Risk-assessment

IGRT Process	Description of risk	What factors may cause this risk to occur	Existing control measures for each potential hazard	Risk Level (1 low -5 high)
Acquisition	Gantry collision with patient	Off set isocentre	Safety check for gantry clearance before each acquisition	3
	Treated with Incorrect isocentre	Isocentre has to be moved for CBCT	Record and verify system	3
Analysis process	Anatomy changes missed	Lack of training/awareness	Training	4
	Potential for geographical miss if on line matching	Lack of training	Training Clinician to be present if staff not trained to advanced level	4
	Incorrect target surrogate i.e. seed outlined	Poor image quality on reference images	Seeds marked on TPS by planner then marked with cross on DRR by treatment staff.	1
	Seed position inconsistent	Marker migration	Training regarding risk of migration and effect of rotations	2
Action	Potential for geographic miss	Lack of understanding of protocols	Training regarding protocol action levels	2
	Potential for geographic miss	Individual patient anatomy anomalies	Training with specific case examples	2

Training

Assessment

CT scanning

Verification

Training

Key trainer – may need more than 1!

Site specific?

Training

Key trainer – may need more than 1!

Site specific

Competency assessment

Self assessment (Image review issues)

Record of image analysis registrations

Specific learning objectives

Portfolio

Evidence of observation registration and action

Questions asked to verify learning

Training

	Clinical Competency	*Comp*	*Expert*	*Comments*
1	Ability to acquire images, match and record isocentre displacement			
2	Online correction of displacement using remote table movement			
3	Pelvic 3D CT anatomy ♀♂			
4	Plan selection online having reviewed coverage of bladder by 3 different PTVs			
5	Use of Mosaiq to safely deliver appropriate treatment on plan selected			
6	Accurate documentation of XVI preRT, plan selected and post RT XVI			
7	Underpinning knowledge of bladder cancer, rationale for treatment and aims of current trials.			

Maintaining Competency

Advanced competency assessment record of practise in adaptive bladder radiotherapy for bladder cancer

A maximum of 2 scans per patient, should be recorded as part of the competency assessment.

Date	Relevant Experience	Outcome / Reflection
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	
	Patient ID: PTV selected: Agreement with comparative match*: Y / N	

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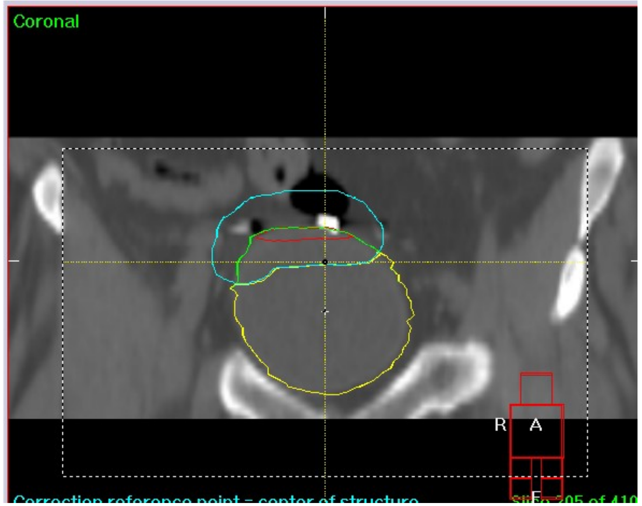
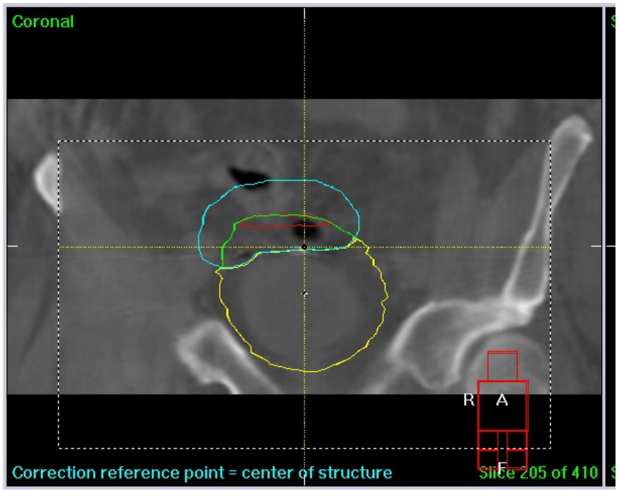
Risk – inadequate training





Chasing target - can lead to overdose of normal tissues

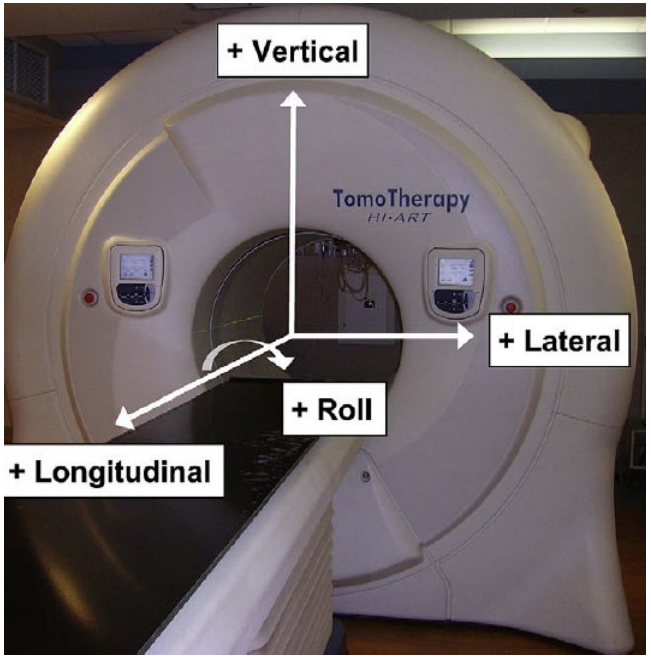
Risk – inadequate training

Recommended Activities	Comments	Refs.
1. Assure RTT curriculum includes IGRT theory and practice.	Technology awareness is not sufficient. RTTs also need to understand concepts of margin design, residual uncertainty, and inter-observer variability to knowledgeably apply IGRT.	None
2. Assure DP curriculum includes IGRT theory and practice, dose reconstruction, normal tissue delineation, and understanding of ART concepts.	Understanding concepts of margin design, residual uncertainty, and inter-observer variability are relevant to DP's practice. Future adaptive processes will be coordinated by this profession and this requires curriculum expansion.	None
3. Assure MP residency training in imaging (eg, CT, MR, US), IGRT theory, and process management.	Imaging technologies need to be understood if they are to be properly applied. In addition, the MP has a leadership role in margin design and the link to planning. Curriculum extensions are needed.	None
4. Assure RO residency curricula explicitly include IGRT theory and practice.	PTV/PRV margin approval requires a sound understanding of IGRT concepts. Target delineation is another critical area for dedicated training. Physicians in practice need to access CME opportunities.	None
5. Facilitate cross-profession engagement between RTTs, DPs, MPs, and ROs for decision-making and delegation issues.	Clarity in decision-making role is critical for safe IGRT. Educational programs that reinforce this engagement are desirable.	11
6. Facilitate the generation of a lexicon for IGRT practice.	ICRU has provided powerful tools for dose prescription and the airline industry has demonstrated the value of consistent language to communicate in complex situations. Furthermore, the development of ART will challenge our current lexicon.	34,42,43,45
7. Include testing on IGRT in the board certification process for all professions.	Including margin design, correction strategies, and quality assurance practices.	39

Abbreviations: IGRT (Image Guided Radiation Therapy); RTT (Radiation Therapist); DP (Medical Dosimetrist and Other Qualified Planner); ART (Adaptive Radiation Therapy); MP (Medical Physicist); CT (Computed Tomography); MR (Magnetic Resonance); US (Ultrasound); RO (Radiation Oncologist); PTV (Planning Target Volume); PRV (Planning Organ at Risk Volume); CME (Continuing Medical Education); ICRU (International Commission on Radiation Units).

Risk- belief in 'new' technology

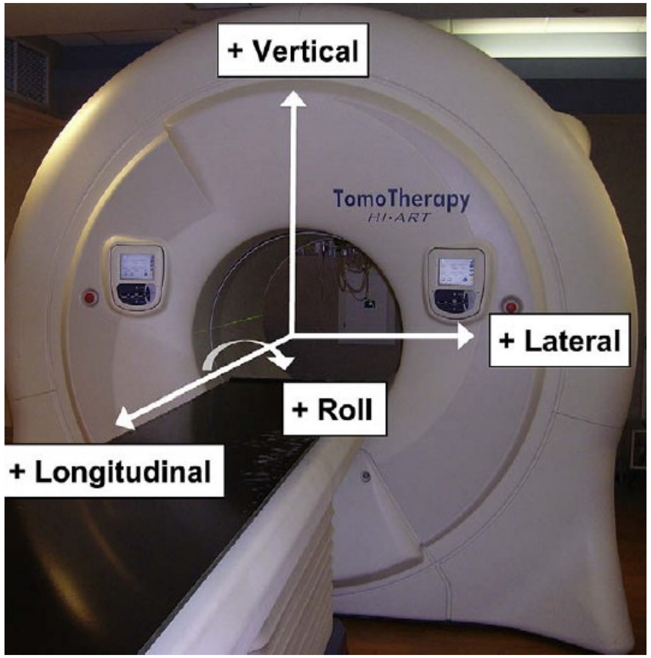
Prostate
Mean error
AP 4.7mm (p<0.001)
SI 2.3 mm



Schubert 2009

Risk- belief in 'new' technology

Head and Neck
Mean error
AP 3.0mm (-2.3 to 5.8mm)
SI -2.8mm (-5.6mm to 0.8mm



Recommended activities for assuring quality in IGRT practice within a clinical program

Safety considerations for IGRT: Executive summary
Practical Radiation Oncology
Volume 3, 2013,

Houghton 2009

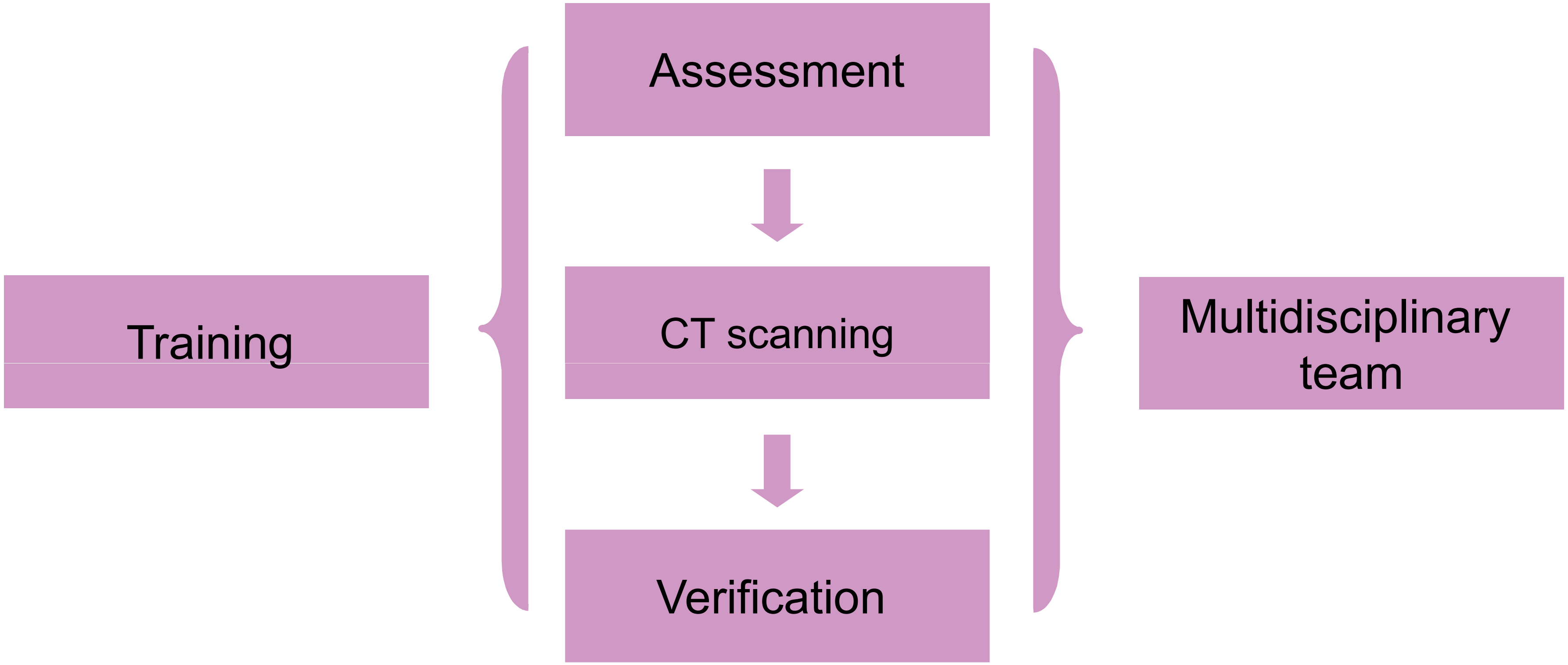
Risk-assessment

Table 2: Recommendations to establish a foundation for safe and effective IGRT practices

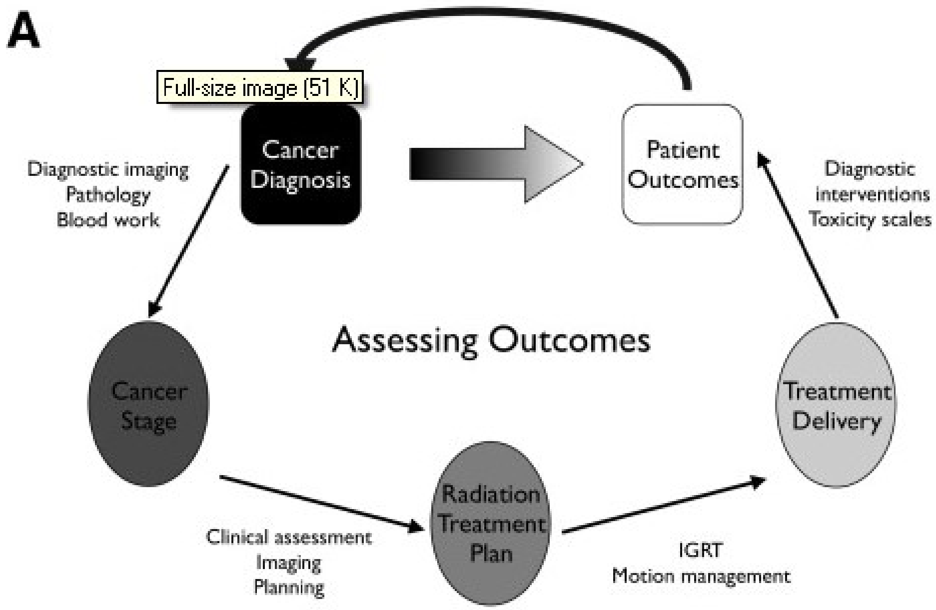
Recommendation	Comments	Refs.
1. Establish a multi-professional team responsible for IGRT activities.	MP, DP, RTT, and RO membership; responsible for leading IGRT initiatives. Collectively, this team has deep expertise on IGRT. The program should make educational investments in this team.	37
2. Establish and monitor a program of daily, monthly, and annual QA for all new or existing IGRT sub-systems.	Led by MPs with participation by RTTs. Reporting and results should be transparent to other professions and administrators. See AAPM Task Group reports for test frequency.	12,13
3. Provide device- and process-specific training for all staff operating IGRT systems or responsible for IGRT delivery.	Applications training needs to be augmented by internal process-specific training with competency testing for all professions and supported by the IGRT team (see Recommendation 1, above).	13
4. Perform end-to-end testing for all new IGRT procedures (from simulation to dose delivery) and document performance prior to clinical release.	The combination of various sub-systems is typically not certified by vendors and needs to be tested before use. Tests should be specific to the process and include staff that will be performing the procedure in the clinical setting.	13

Safety considerations for IGRT: Executive summary
Practical Radiation Oncology
Volume 3, 2013,

ESTRO School


Assessment
CT scanning
Verification
Training
Multidisciplinary team

IGRT in context



'the whole chain of interventions in the RT process should be prospectively assessed. This is particularly important because other steps in the RT process (eg, contouring or valid measurements of toxicity) are at least as important as high geometric precision'

Bujold, Sem Radiat Oncol (22), 2012, 50–61

Reports

Imaging for Treatment Verification Work Group Task Group #179

Quality assurance for image-guided radiation therapy utilizing CT-based technologies: A report of the AAPM TG-179. Medical Physics, Vol 39, Issue 4

http://www.rcr.ac.uk/docs/oncology/pdf/BFCO(08)5_On_target.pdf

National Radiotherapy Implementation Group Report

Image Guided Radiotherapy (IGRT). Guidance for implementation and use. August 2012 UK

The European Society of Therapeutic Radiology and Oncology-European Institute of Radiotherapy (ESTRO-EIR) report on 3D CT-based in-room image guidance systems: a practical and technical review and guide.

Korreman S, Rasch C, McNair H, Verellen D, Oelfke U, Maingon P, Mijnheer B, Khoo V. Radiother Oncol. 2010 Feb;94(2):129-44.

Safety considerations for IGRT:Executive summary

Practical Radiation Oncology. 2013:3(3):167-170

Acknowledgements

Academic Urology Unit

Academic Lung unit

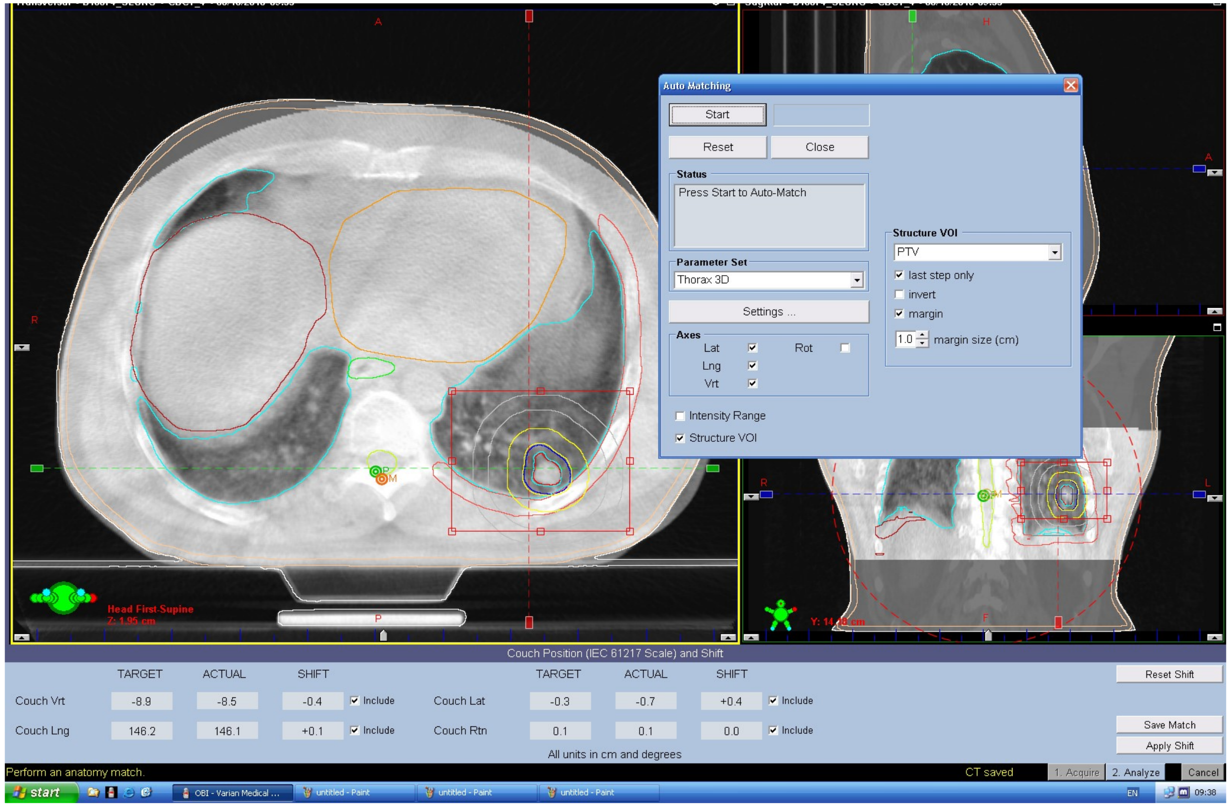
Academic Breast Unit

Joint department of Physics

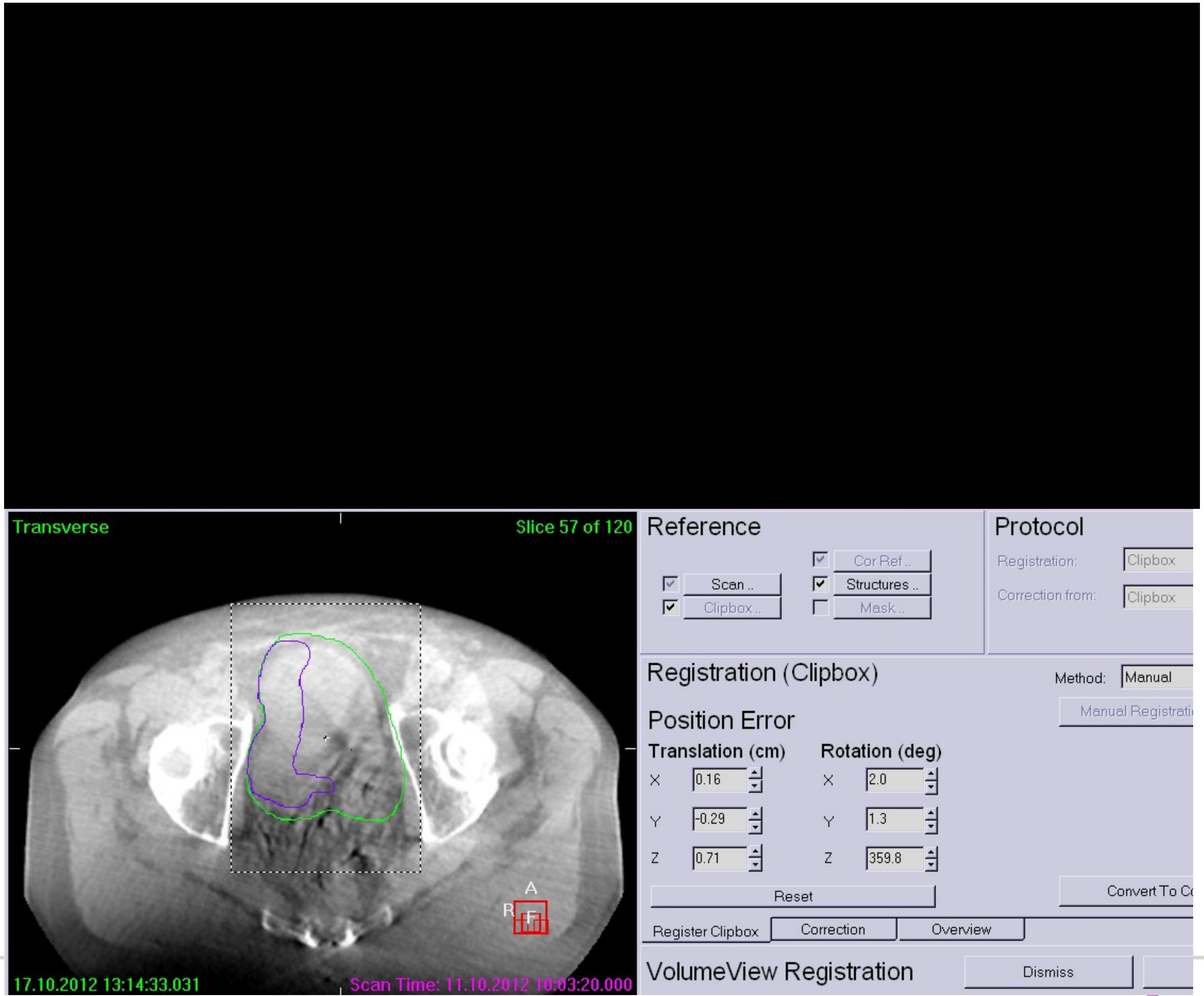
Radiotherapy department

Action

Hypofractionated lung- on line



Risk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Slice 57 of 120
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Reference
Scan ..
Clipbox ..
Cor Ref ..
Structures ..
Mask ..
Protocol
Registration:
Clipbox
Correction from:
Clipbox
Registration (Clipbox)
Method:
Manual
Position Error
Translation (cm)
Rotation (deg)
X 0.16
Y -0.29
Z 0.71
X 2.0
Y 1.3
Z 359.8
Reset
Register Clipbox
Correction
Overview
VolumeView Registration
Dismiss

Frameless IGRT and stereotactic radiotherapy

Andrew Hope, MD

Disclosures

Research support provided:

Elekta

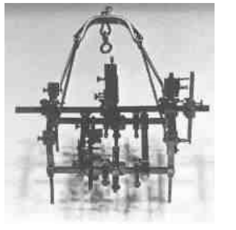
Philips

Thanks to Dr. M. Guckenberger

Stereotactic techniques are old

1908: Robert Henry Clarke and Victory Horsley

Stereotactic technique based on the reproducibility of the relationships between landmarks on the skull (external auditory canals, midline) and anatomical structures within the brain



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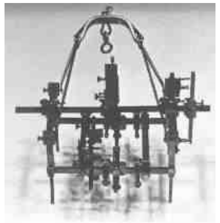

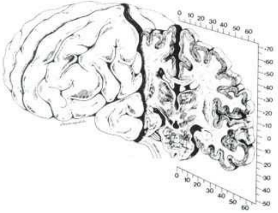

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Problem: unsure relationship between bony landmarks and cerebral structures

- Targeting of subcortical structures only e.g. gasserian ganglion with foramen ovale as landmark
- Imaging e.g. ventriculography -> stereotactic atlas

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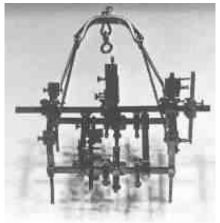

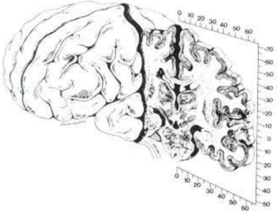

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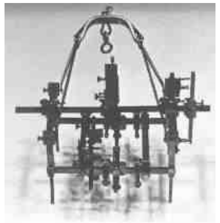
Lars Leksell

1950s: Experiments with stereotactic proton therapy

1967: Gamma-knife radiosurgery using Co-60 for treatment of functional disorders

Stereotactic techniques are old



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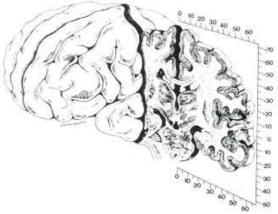

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Since 1980s: CT localization and linac based stereotactic radiotherapy

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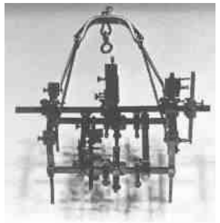
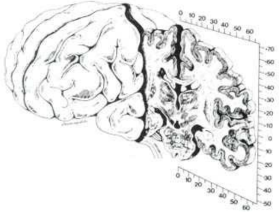
Stereotactic techniques are old





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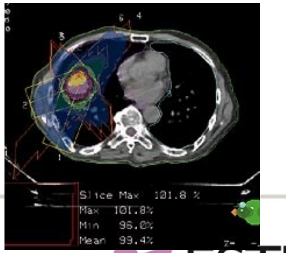

Since 1980s: CT localization and linac based stereotactic radiotherapy

Since 1994: (Lax & Blomgren): Stereotactic body radiotherapy

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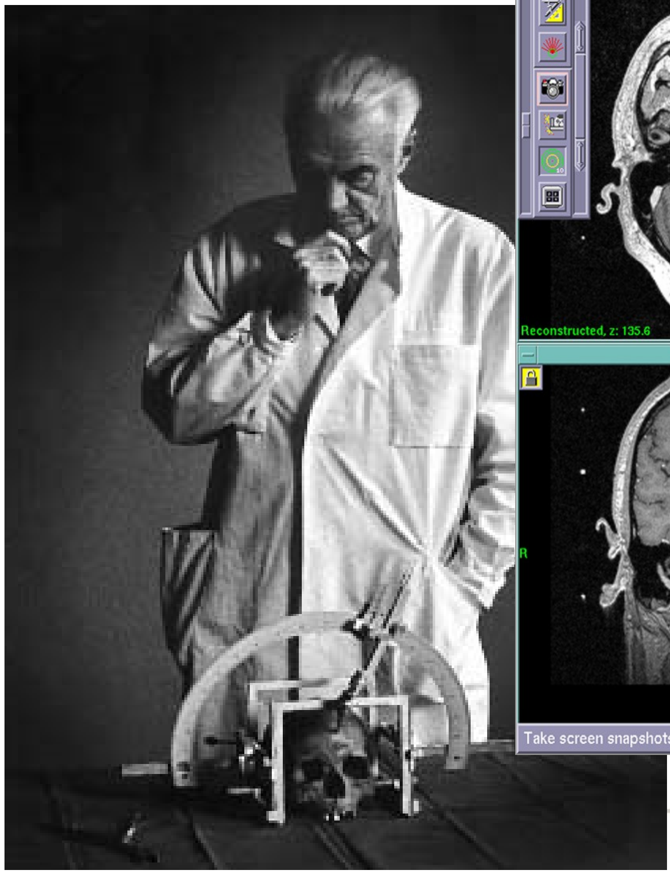
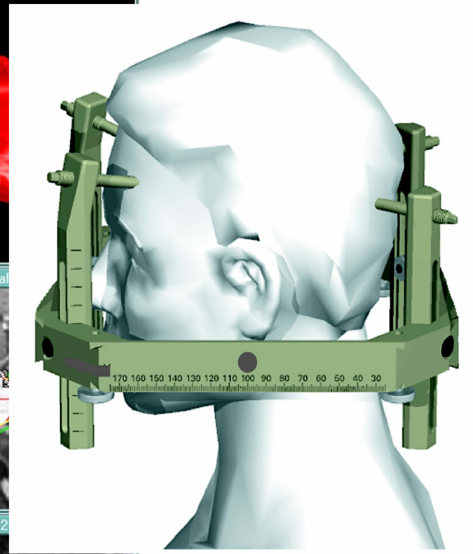
Intra-cranial stereotactic radiation

- :





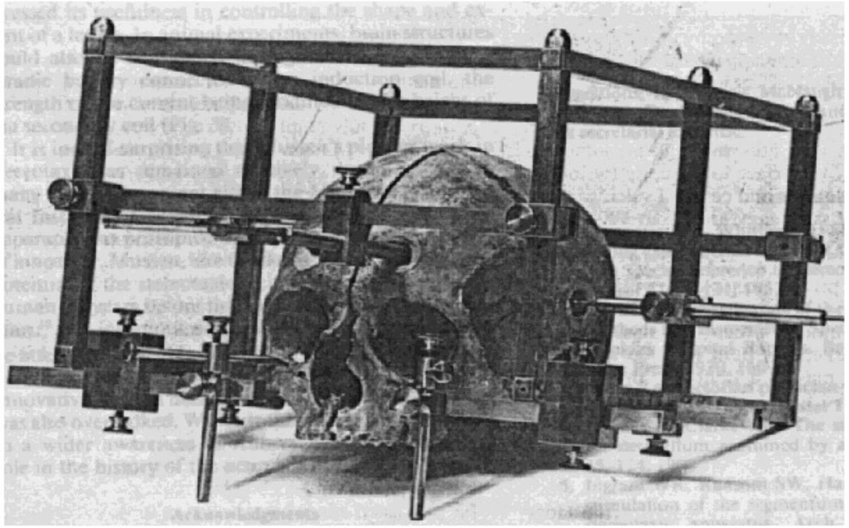
What is the ‘stereotactic’ frame?

Stereos (gr.): rigid, fixed

Taxis (gr.): ordering

Rigid relationship between an external system of coordinates and the internal anatomy of the brain (and the targets)

Invasive fixation of the stereotactic frame to the bony skull ensured sub-millimeter accuracy of surgery / radiotherapy



Nomenclature

Frame vs. Frameless

Invasive vs. Non-invasive

Nomenclature

Frame vs. Frameless

Are external coordinate systems used?

Invasive vs. Non-invasive

Nomenclature

Frame vs. Frameless

Are external coordinate systems used?

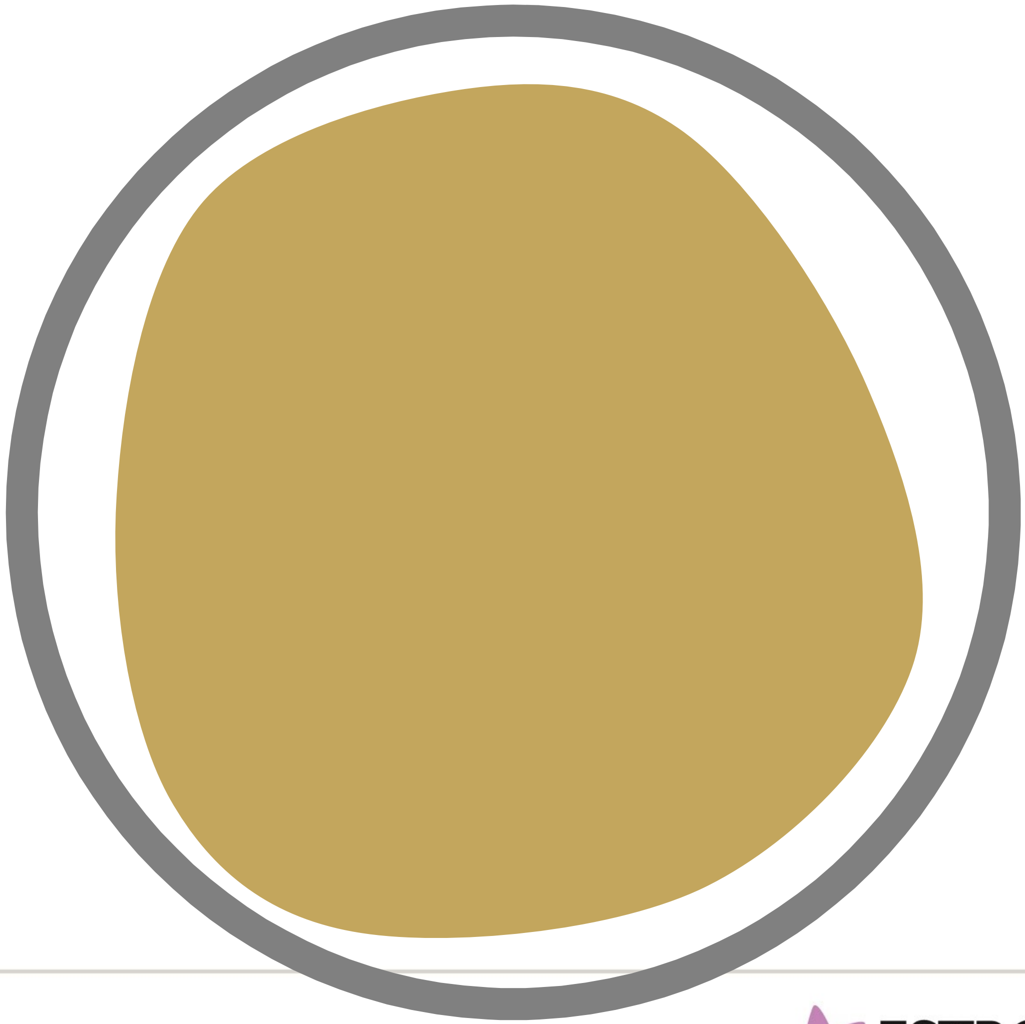
Invasive vs. Non-invasive

Is the patient fixed directly to the stereotactic system (screws, pins)?

Stereotactic: Invasive frame

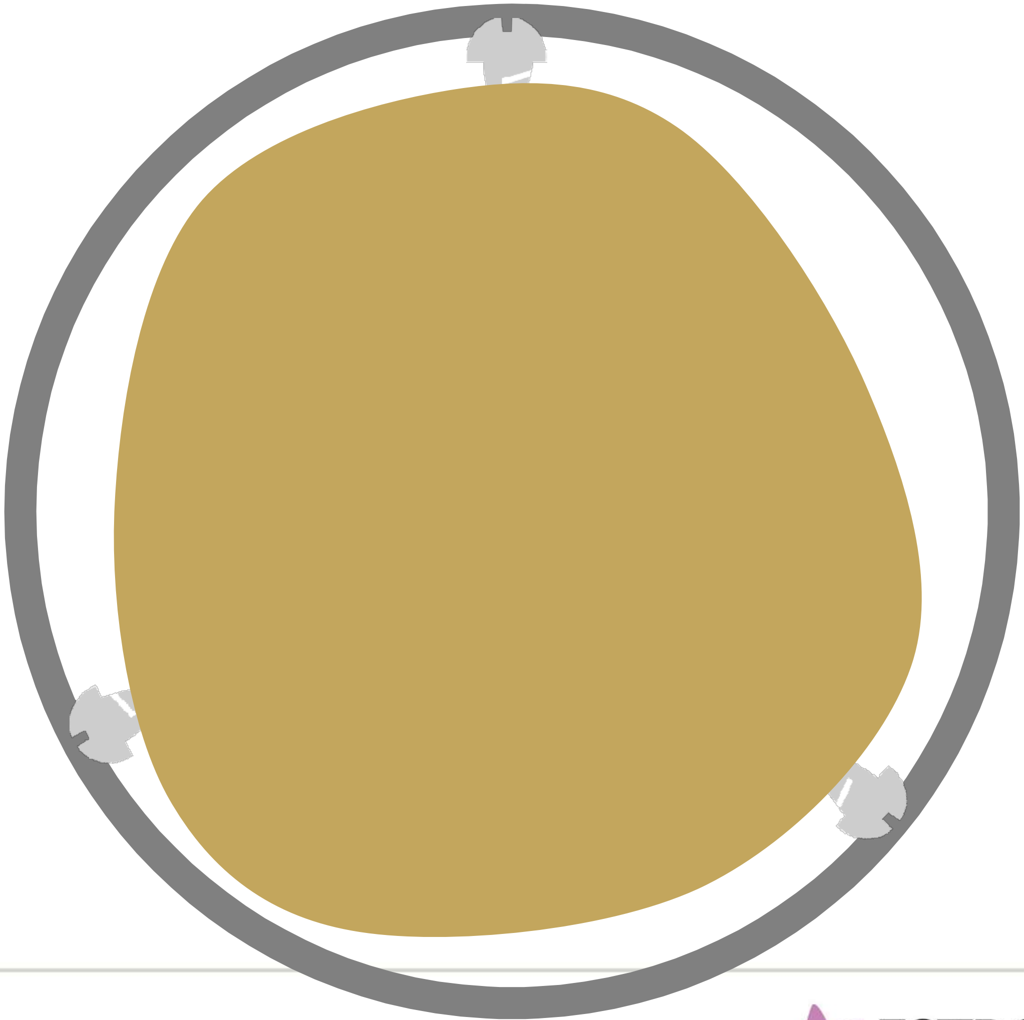
Stereotactic: Invasive frame

1. Invasive ring



Stereotactic: Invasive frame

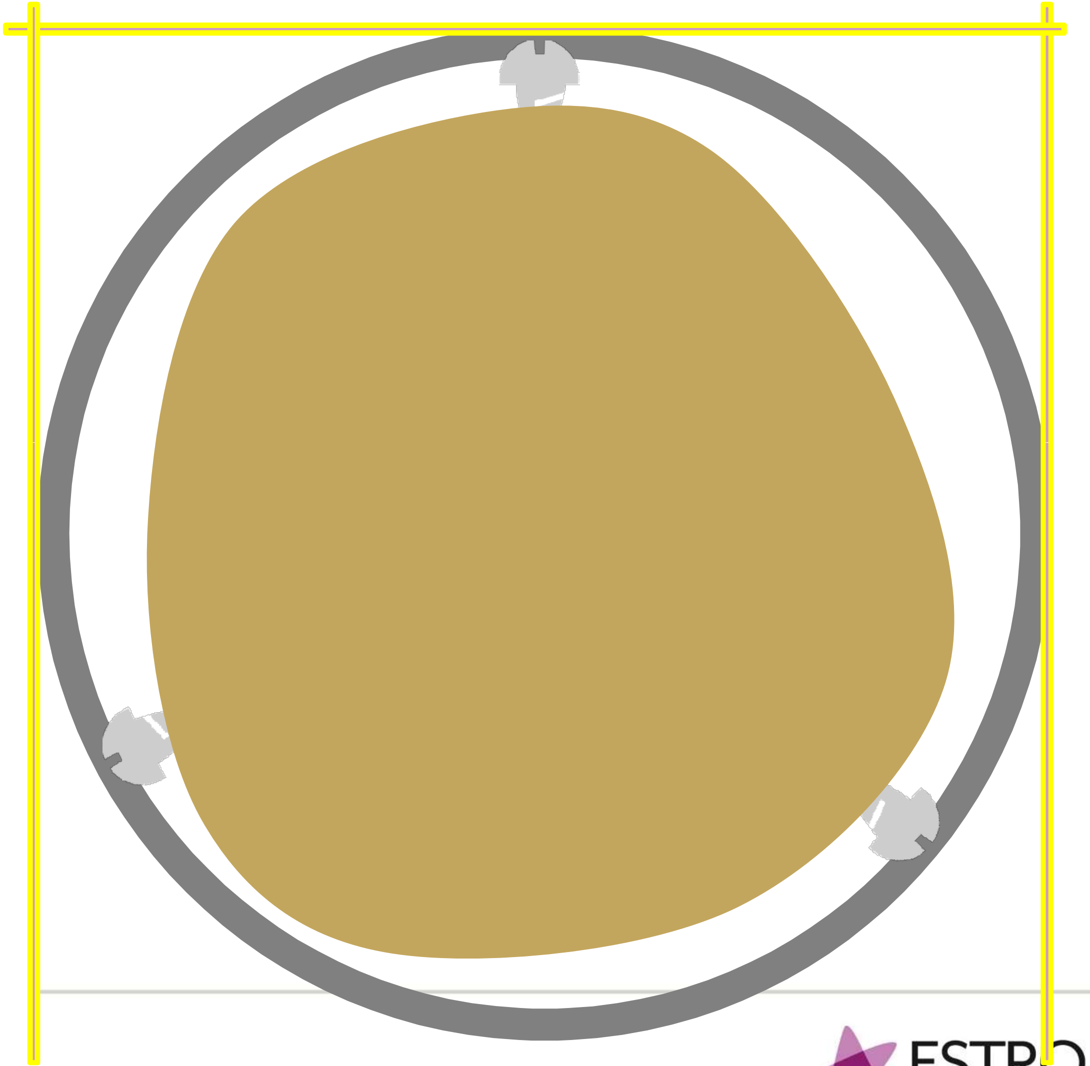
1. Invasive ring



Stereotactic: Invasive frame

1. Invasive ring

2. Localization system



Stereotactic: Invasive frame

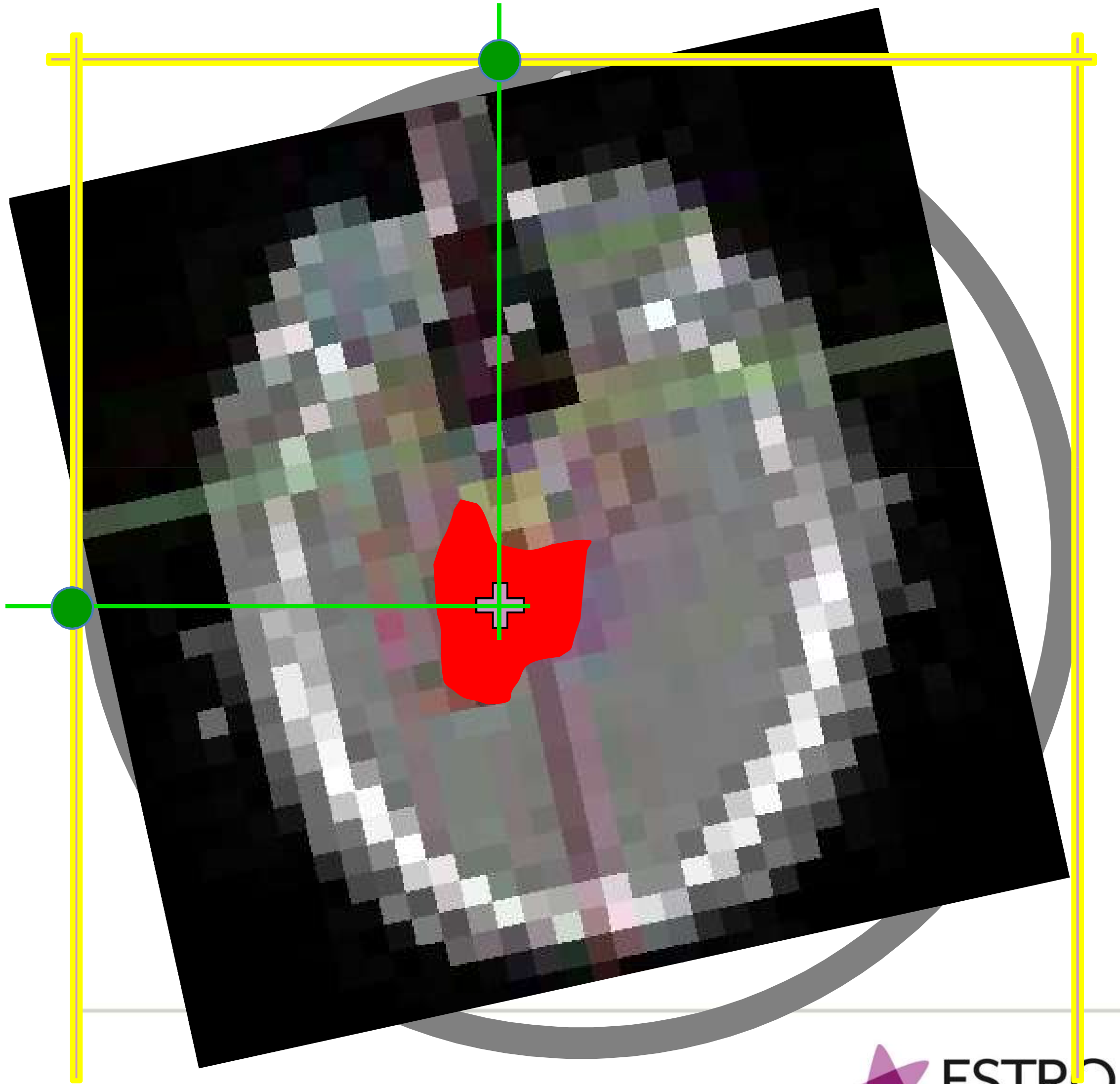
1. Invasive ring
2. Localization system
3. Imaging

Stereotactic: Invasive frame

1. Invasive ring
2. Localization system
3. Imaging
4. Target definition

Stereotactic: Invasive frame

1. Invasive ring
2. Localization system
3. Imaging
4. Target definition
5. Stereotactic isocenter position



Stereotactic: Invasive frame

1. Invasive ring
2. Localization system
3. Imaging
4. Target definition
5. Stereotactic isocenter position
6. Stereotactic positioning

Stereotactic: Invasive frame

1. Invasive ring
2. Localization system
3. Imaging
4. Target definition
5. Stereotactic isocenter position
6. Stereotactic positioning
7. Treatment

Intracranial stereotactic radiotherapy

<u>Stereotactic radiosurgery (SRS)</u>

- Single fraction treatment
- AVM, vestibular schwannoma, brain metastases, …
- Usually invasive frame-based techniques

<u>Multiple fraction stereotactic radiotherapy</u>

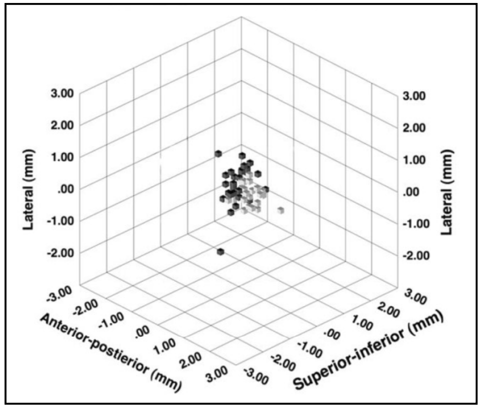
- Theoretical benefit of fractionation, if organs-at-risk with low α/β value are close to the target
- For large target volumes
- Usually practiced non-invasively (masks, bite-blocks,….)
  - patient comfort
  - risk of infection

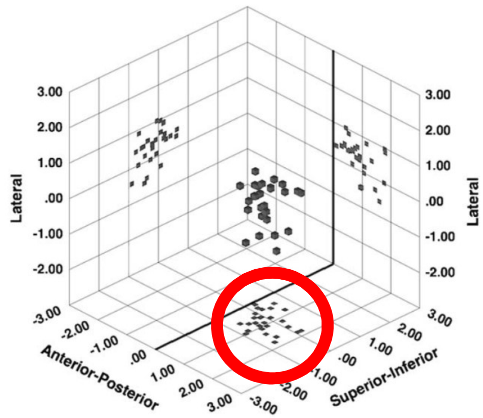
Accuracy differs between invasive and non-invasive stereotactic systems!

Invasive frame-based stereotactic radiosurgery

Novalis system:

- Phantom positioning:
  - frame-based vs. image-guided
- Patient set-up:
  - frame-based vs. image-guided





Lamba et al., IJROBP 2009

Invasive frame-based stereotactic radiosurgery

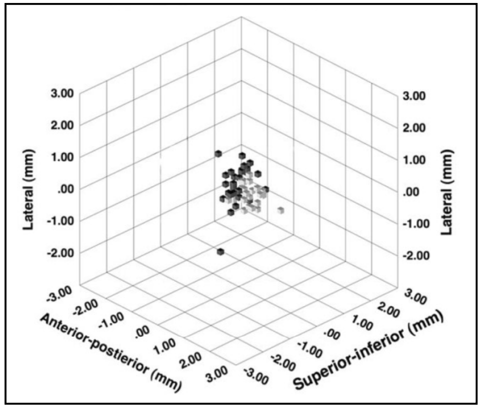
Novalis system:

Phantom positioning:

frame-based vs. image-guided

Patient set-up:

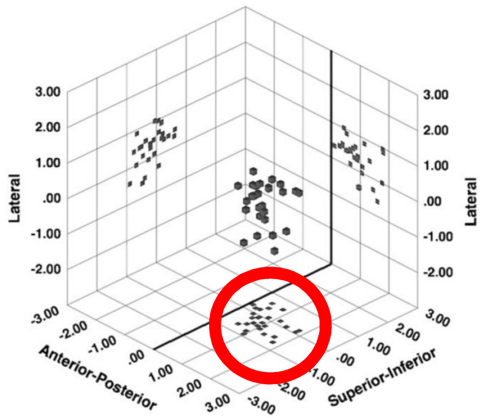
frame-based vs. image-guided



Why the difference?

Flex in the ring fixation system when attached to the couch

Torque due to placement of the localizer device on the ring



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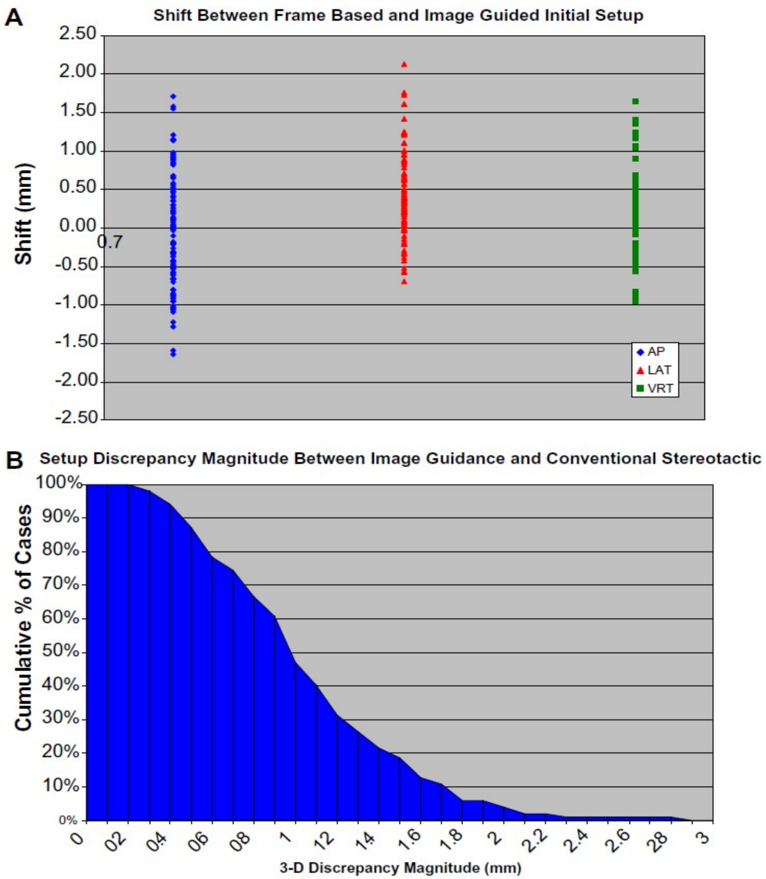
Lamba et al., IJROBP 2009

Accuracy of frame based SRS

102 Patients treated with frame-based SRS

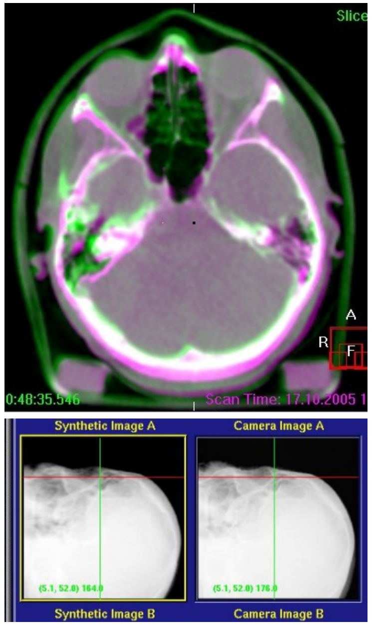
Passive verification of frame-based set-up with IGRT (CBCT)

Detected one patient with a 4.3mm frame “slip”



Ramakrishna et al., Radiotherapy and Oncology 20120

Moving from frame to frameless



Frameless stereotactic radiotherapy:

Replace the stereotactic external coordinate system with imaging-based patient positioning

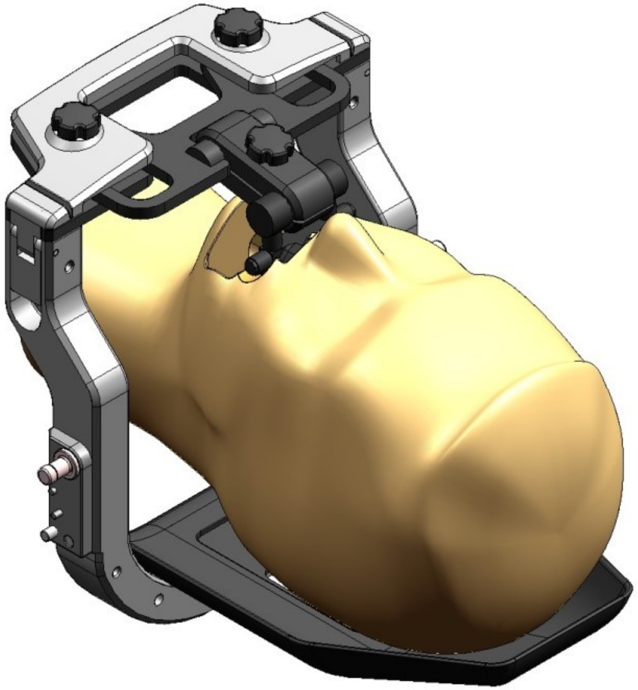
Requirements for frame-less image-guided radiosurgery

Accuracy to detect set-up errors

Accuracy to correct set-up errors

Ability to immobilize the patient in treatment position

Non-invasive Immobilization



Immobilization margin with Extend frame at Princess Margaret Hospital

1mm R-L and A-P
1.5 mm S-I

C. Chung, personal communication 2012

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Fractionated non-invasive SRS

Study	SRT positioning system	Imaging modality	Positioning error
2D-2D image registration for verification of set-up			
Rosenthal 1995	Dental fixation	Orthogonal radiographs	**2.3mm ± 1.6mm**
Sweeney 2001	Vogele Bale Hohner head holder	Portal imaging	**1.9mm ± 1.2mm**
Kumar 2005	Gill-Thomas-Cosman	Portal imaging	**1.8mm ± 0.8mm**
Georg 2006	Brain Lab Mask	Portal imaging	**1.3mm ± 0.9mm**
3D-3D image registration for verification of set-up			
Baumert 2005	Stereotactic mask	CT	**3.7mm ± 0.8mm**
Boda-Heggemann 2006	Scotch cast mask	Cone-beam CT	**3.1mm ± 1.5mm**
Guckenberger 2007	Scotch cast mask	Cone-beam CT	**3.0mm ± 1.7mm**
Masi 2008	Thermoplastic mask & Bite block Bite-block	Cone-beam CT Cone-beam CT	**2.9mm ± 1.3mm** **3.2mm ± 1.5mm**

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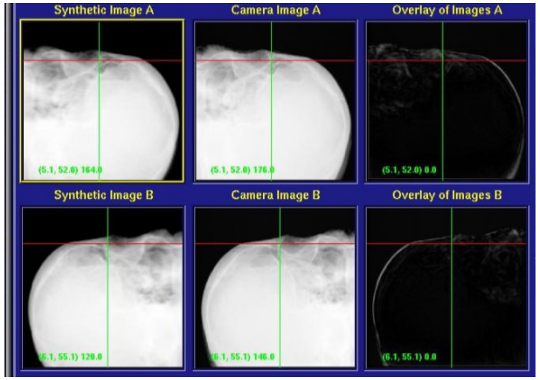
Frameless stereotactic RT: Bony landmarks?

2D



3D

Direct imaging of target

?

?

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Reliability of bony anatomy

If visualization of the target is not possible, one has to use the bony skull as a surrogate for the actual intra-cranial target in IGRT

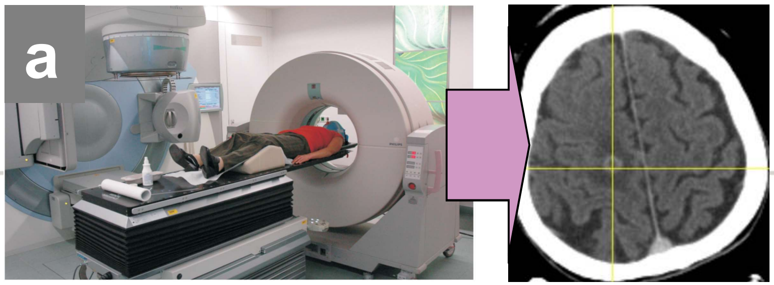
However, internal “motion” of intra-cerebral tumor could be caused by:

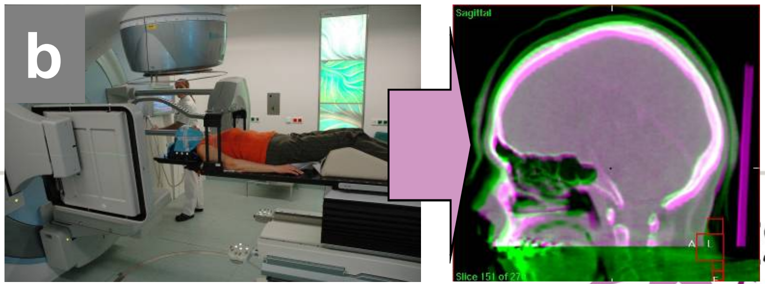
- Tumor progression
- Tumor shrinkage
- Changes of peritumoral edema

Set-up prior to treatment was verified based on the

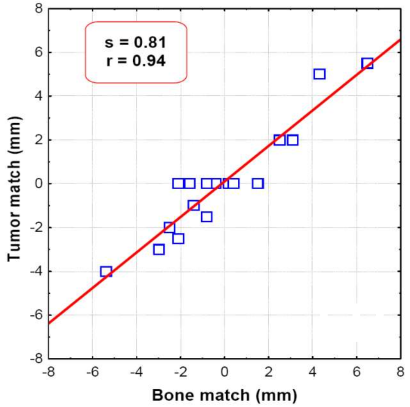
a) position of the metastasis (soft tissue match): imaging using an in-room CT scanner after application of iv contrast

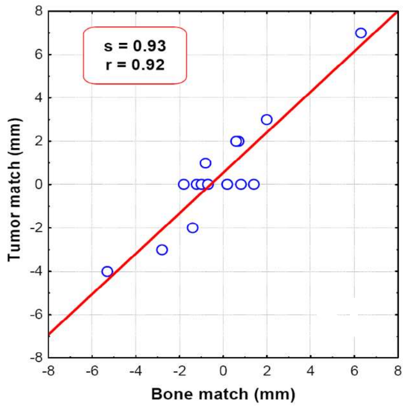
b) position of the bony anatomy (bone match): imaging using cone-beam CT

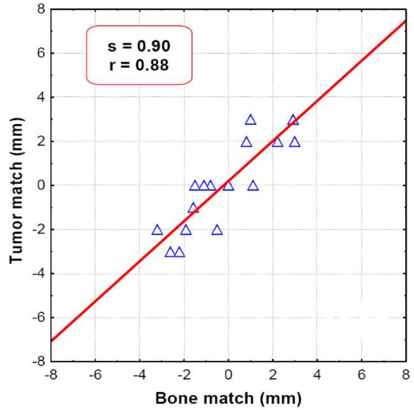




Reliability of bony anatomy







Correlation between soft-tissue registration and bone match

Differences between bone and tumor match (mm)

	LR	SI	AP	3D
Mean ± SD	-0.6 ± 1.0	0.0 ± 1.1	-0.2 ± 1.0	**1.7 ± 0.7**
Maximum	1.8	2.3	2	**2.8**

Stable tumor position relative to the skull for one week interval between planning and treatment

No influence of pre-treatment steroids (>48h prior)

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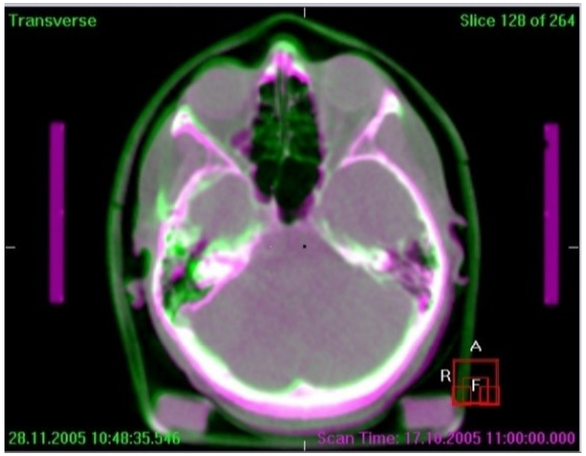
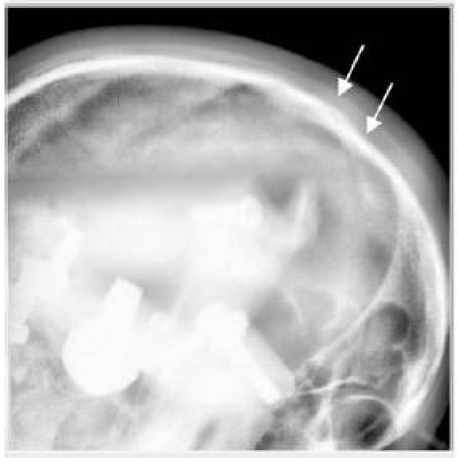
Accuracy of imaging

Accuracy of IGRT to detect set-up errors






Cone-beam CT: Elekta Synergy S system

Meyer et IJROBP 2008

3D error always <0.5mm, "never observed a fusion error"

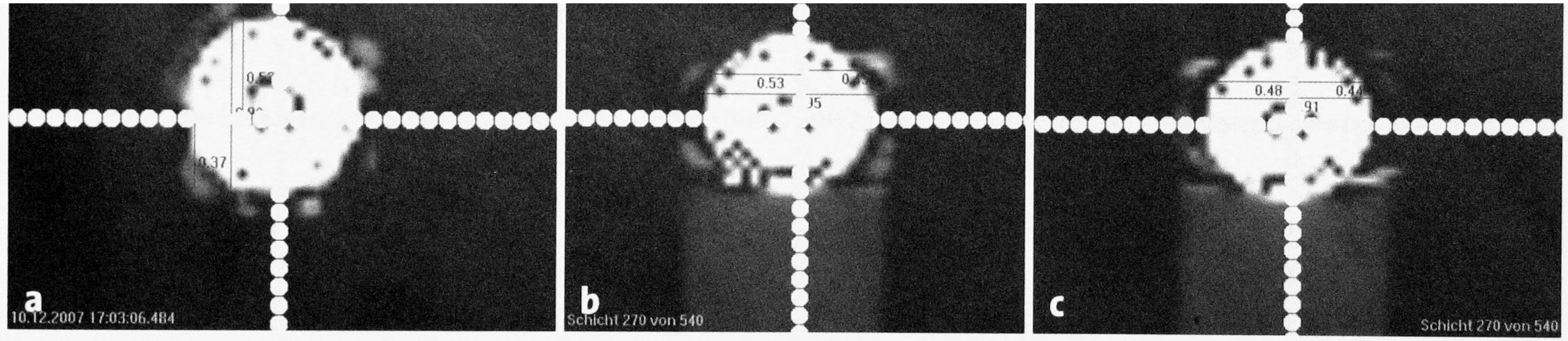
Orthogonal X-rays: Novalis Exactrak system

Ramakrishna Radiother Oncol 2010

Fusion errors in 3 / 102 patients: difference between DRR and X-ray

Alignment of imaging and treatment isocenter

Precise alignment of imaging and treatment isocenter is crucial in image-guided SRS



Ball bearing phantom:

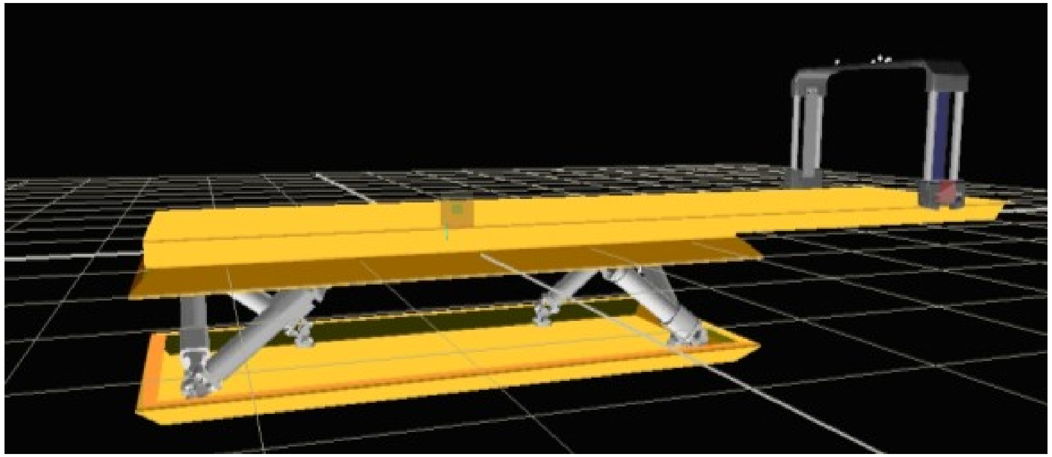
1. Phantom is positioned in the MV-treatment isocenter
2. Distance or phantom to imaging isocenter is measured

Accuracies of < 1mm are usually specified

- ➢ Alignment stable over time (Wiehle et al. 2009)
- ➢ Verification prior to each single fraction radiosurgery

Accuracy of correction

Accuracy of HexaPOD & XVI to correct set-up errors

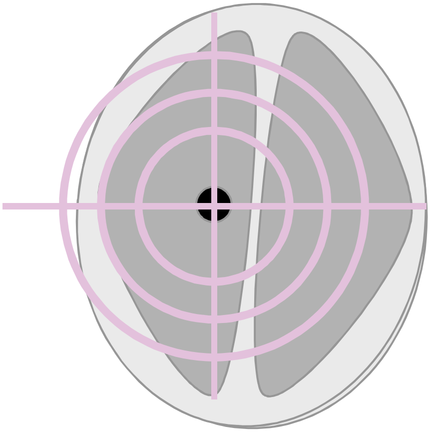


Residual errors after XVI and HexaPOD correction:
< 0.3mm <0.3°

Meyer et al. IJROBP 2008

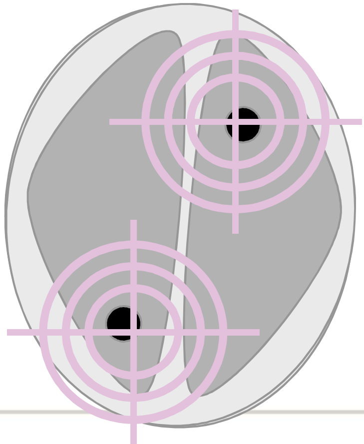
IGRT work-flow with CBCT imaging and robotic correction of set-up errors achieved sub-millimeter accuracy in phantom studies

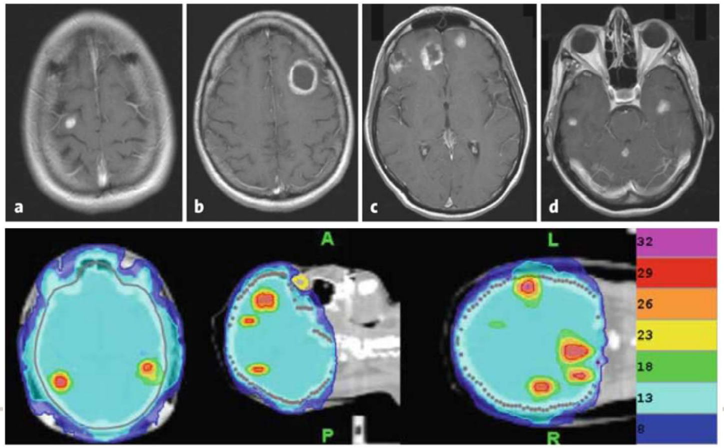
Correction of rotational errors



Rotations are probably not of highest priority for:

1. Single lesions
2. Small, spherical targets
3. Beams not immediately next to OARs





Sterzing et al. 2009

Simultanous SRS / Boost to multiple lesions

Intra-fractional stability

Intra-fractional uncertainties in frame-less IGRT

Study	Immobilization system	Imaging modality	Intrafractional error 3D vector
Boda-Heggemann 2006	Thermoplastic masks Scotch cast mask	Cone-beam CT	**1.8mm ± 0.7mm** **1.3mm ± 1.4mm**
Masi 2008	Thermoplastic mask & Bite block Bite-block	Cone-beam CT	**< 1mm** **< 1mm**
Lamda 2009	BrainLab mask	Orthogonal x-rays	**0.5mm ± 0.3mm**
Ramakrishna 2010	BrainLab mask	Orthogonal x-rays	**0.7mm ± 0.5mm**
Guckenberger	Scotch cast mask Thermoplastic masks	Cone-beam CT	**0.8mm ± 0.4mm** **0.8mm ± 0.5mm**

Intra-fractional uncertainties of ~ 1mm need to be considered in non-invasive frame-less IGRT

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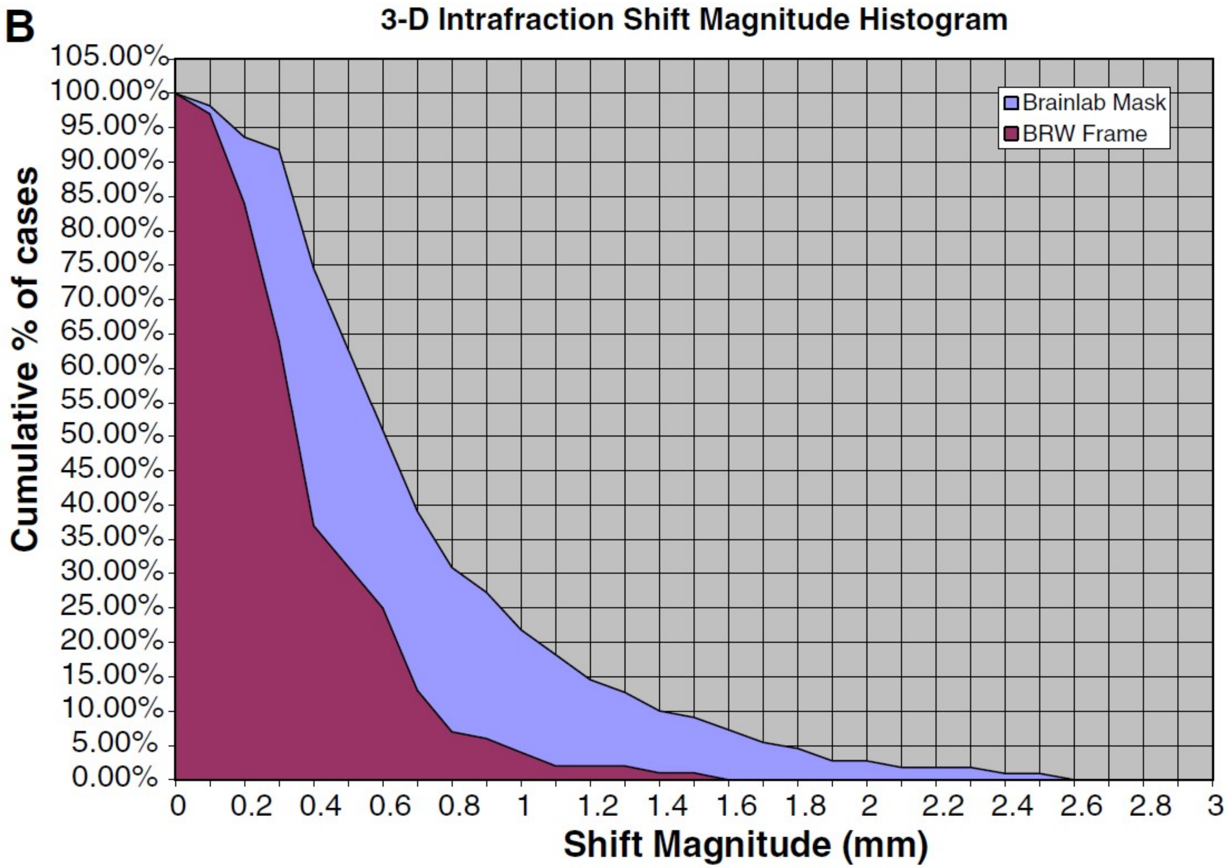
Intra-fractional stability

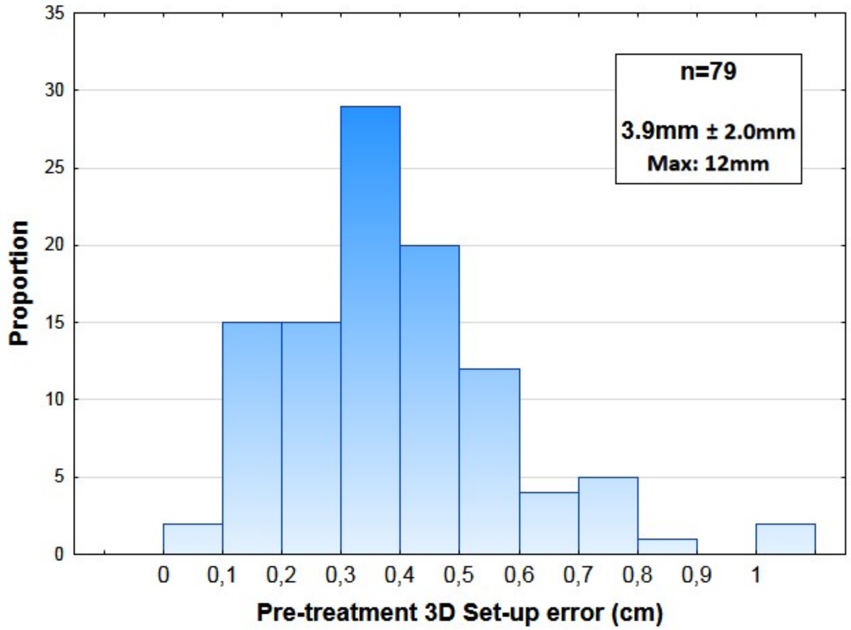


Frame based vs. frameless intrafraction motion

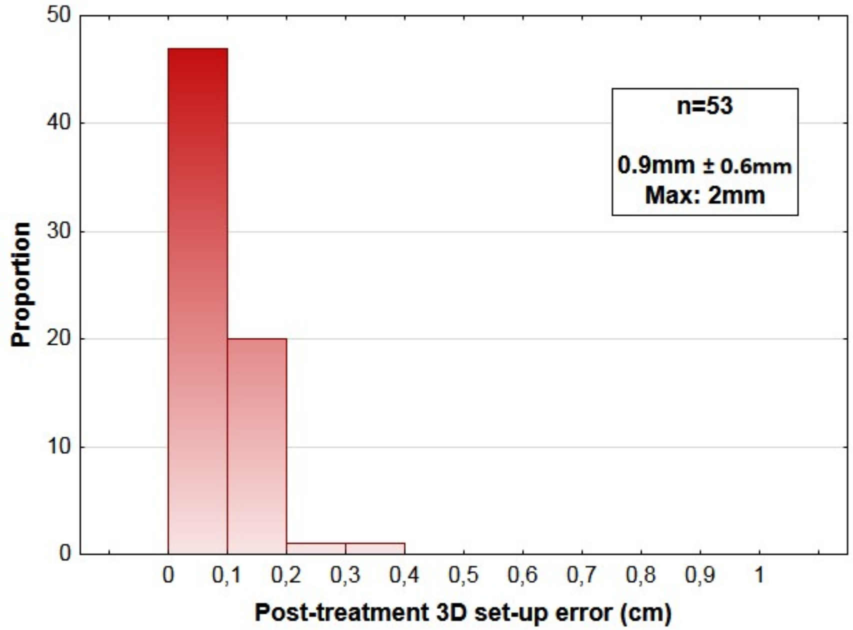
Ramakrishna Radiother Oncol 2010

Pre- and post treatment accuracy of frame-less SRS

Pre-treatment 3D errors

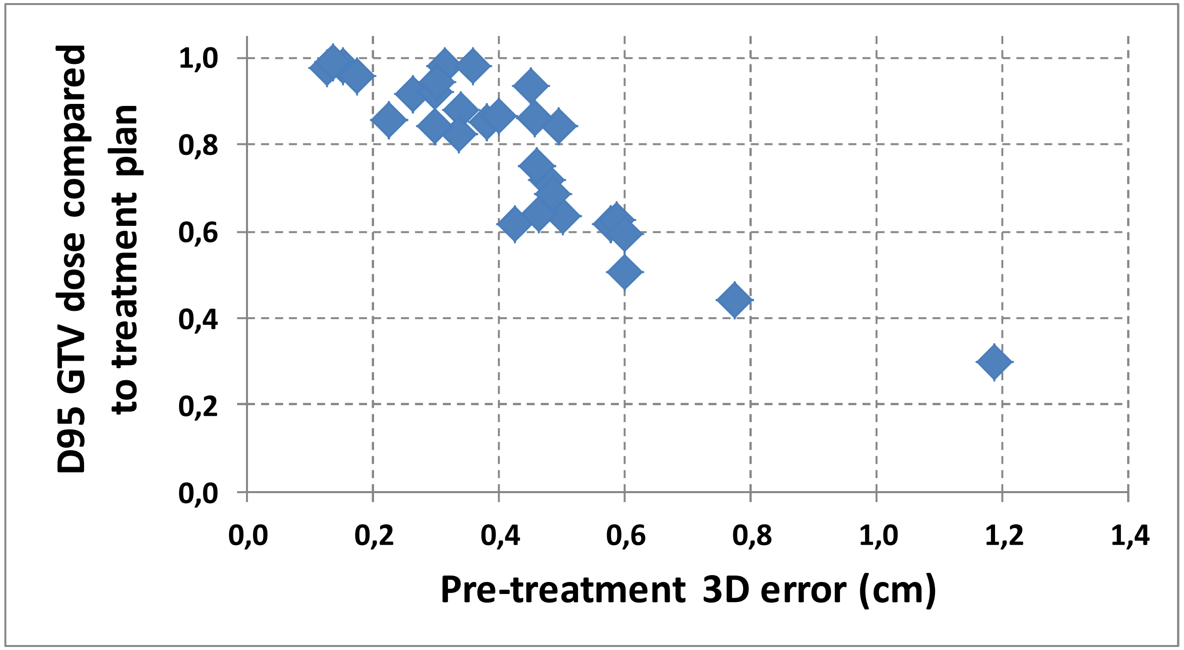


Post-treatment 3D errors



Excellent geometric accuracy with frame-less SRS

Dosimetric consequences of errors in frame-less SRS



D95 of GTV	Planned	Pre T & R	Pre R	Post T & R
Av ± StDev	100% ± 0	**78 ± 18%**	99 ± 2%	100 ± 4%

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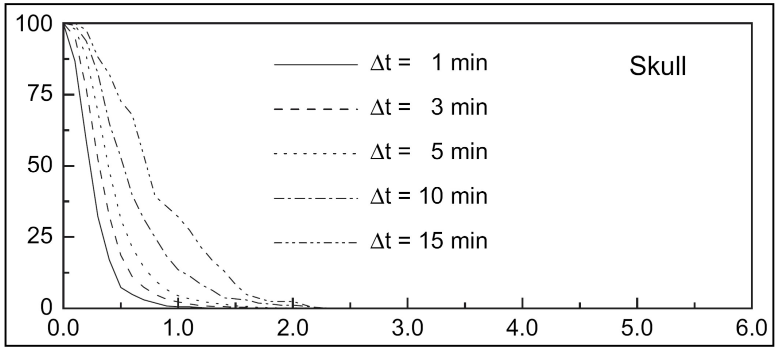
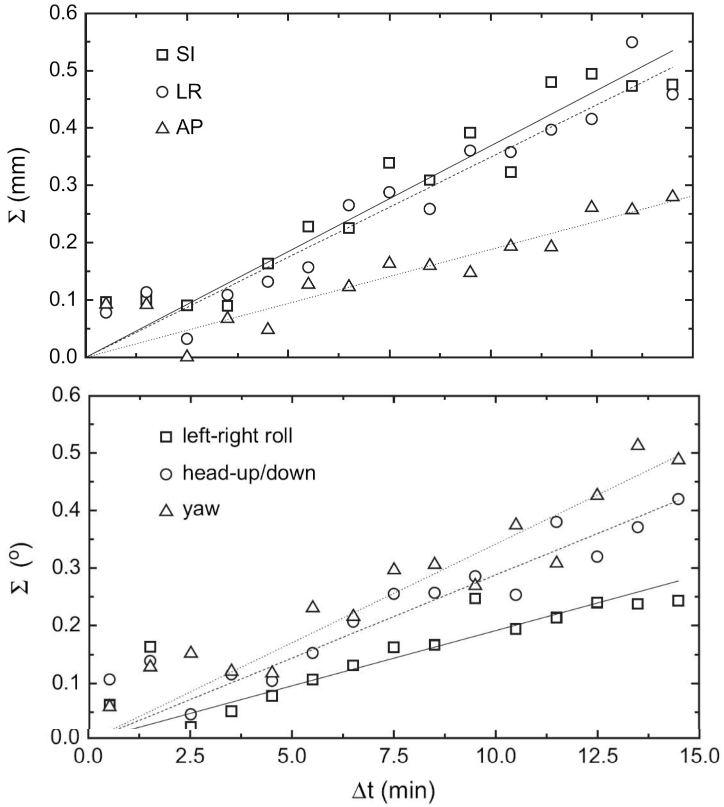
Movement during treatment?





Time dependence of intra-fractional patient motion:

Immobilization in conventional thermoplastic head masks

Keep total treatment time as short as possible !!!

Frame-based vs. Frameless stereotactic RT

Comparison of accuracy

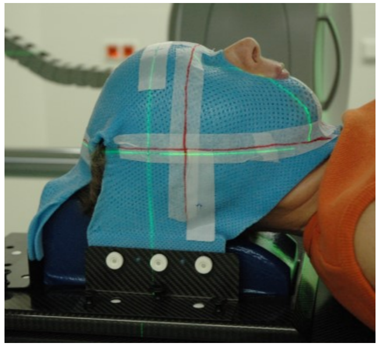
	Framebased FSRT	Framebased SRS	Frameless IGRT
Positioning error (3D)	3 – 3,5 mm	0,5 – 1,5 mm	< 1 mm
Intrafractional error (3D)	1 – 1,5 mm	< 1 mm	1 -1,5 mm
	Baumert 2005 *Boda-Heggemann 2006* *Guckenberger 2007*	*Maciunas 1994* *Lamba 2* *Ramakrishna 2010*	*Murphy 2003* *Boda-Heggemann 2006* *Guckenberger 2007* *Lamba 2009* *Ramakrishna 2010*

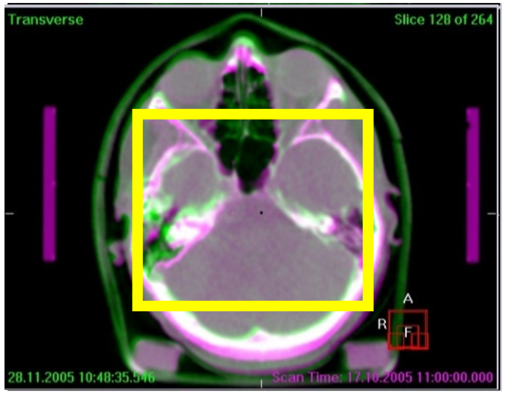
- Framebased FSRT: Precision is overestimated !
- Framebased SRS: Submillimeter precision ?
- Frameless IGRT: High precision with efficient work-flow

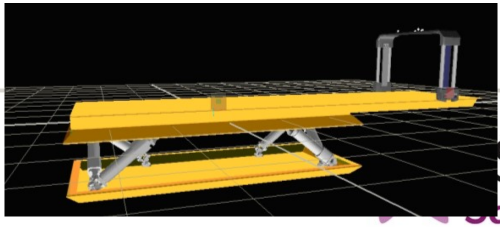
Intra-cranial stereotactic radiotherapy

Work-flow of frame-less cranial SRT using CBCT imaging and robotic online correction of set-up errors

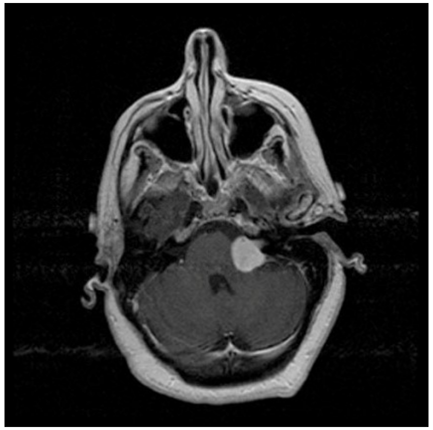
1. Double layer thermoplastic mask
2. Patient positioning based on drawings on the mask
3. Cone-beam CT imaging
4. Definition of region of interest for image registration
5. Registration planning CT vs verification CBCT
6. Automatic correction of errors in 6 DOF
7. Verification CBCT in SF treatment
8. Start of treatment

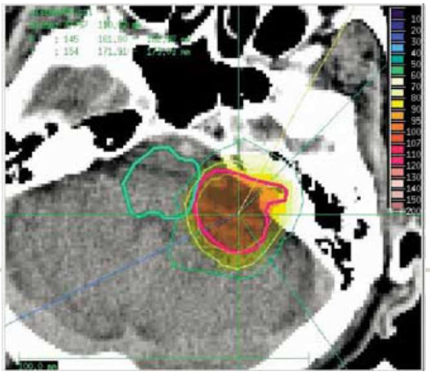






Intra-cranial stereotactic radiotherapy





Traditional frame-based SRS:

0mm margins

Minimum dose 13Gy

➢EXCELLENT local control & low Tox.

➢Delivered dose probably lower

Image-guided SRS:

Uncertainties similar to frame-based SRS

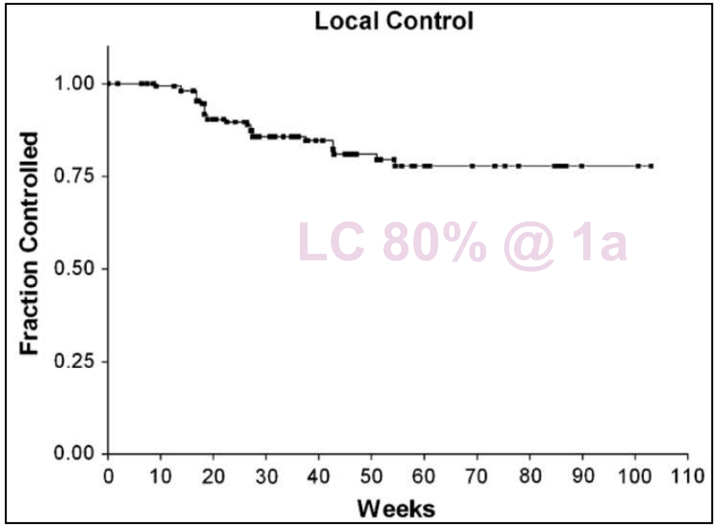
➢Should we add margins?

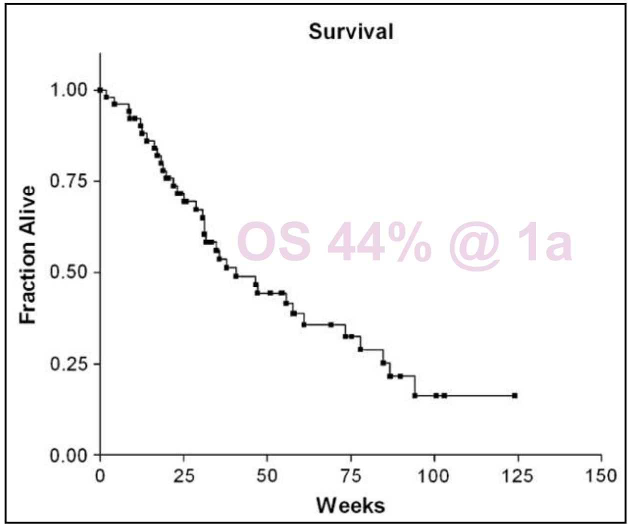
➢Should we prescribe lower doses if margins are used?

Clinical outcome after frameless stereotactic radiosurgery

Breneman IJROBP 2009

- 2005 – 2006
- 53 patients with 158 metastases
- Frame-less radiosurgery with median dose 18Gy
- BrainLab Novalis system





➢ **Very similar to invasive frame-based SRS results**

Conclusions: Intra-cranial

Why adopt non-invasive, frame-less IGRT for stereotactic techniques?

Frame-less fractionated cranial SRT

Improved accuracy

Efficient work-flow

Frame-less single fraction cranial SRS

Patient comfort, no risk of bleeding or infection

More time for multi-modality, complex treatment planning

No difference in accuracy ?

- Consistent work-flow with optimization of all steps of radiotherapy planning and delivery, strict QA and definition of standardized protocols to achieve maximum accuracy of treatment

SBRT has been used since 1990s.

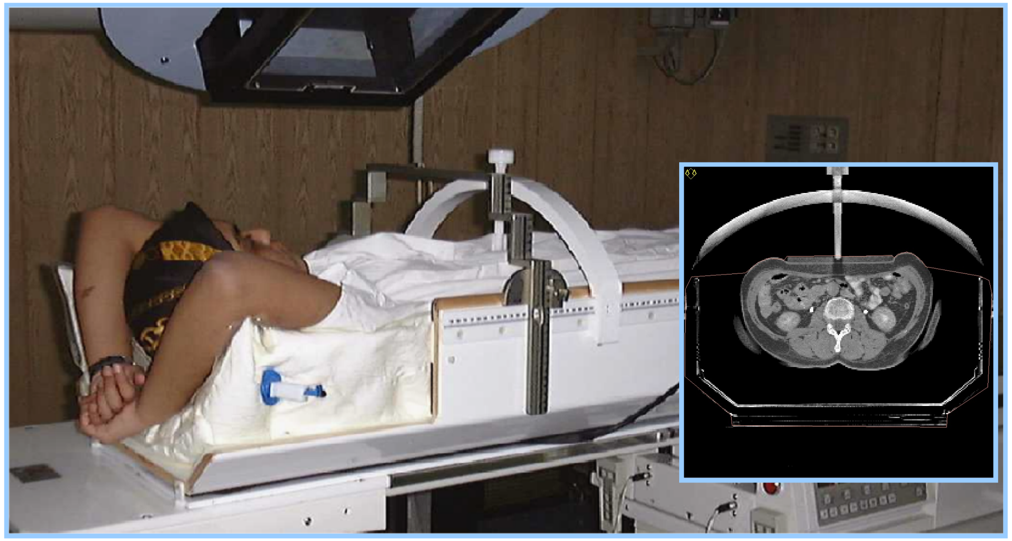
Six main "requirements" (as of 2005):

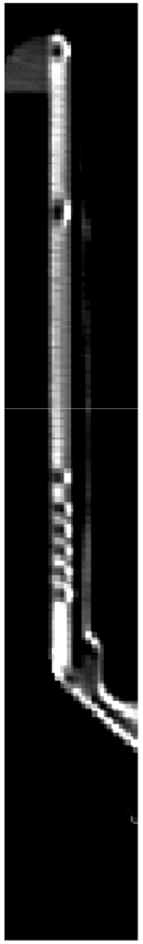
- Secure immobilization
- Accurate repositioning of the patient from planning to treatment
- Accounting for internal motion (breathing)
- Highly conformal dose distributions
- **Registration to stereotactic frame (?)**
- Few fractions, high doses

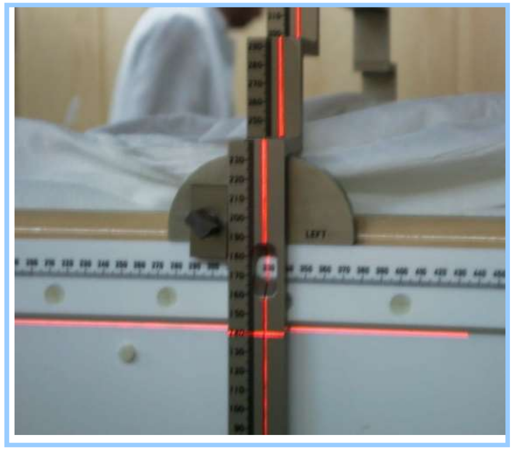
Stereotactic Bodyframe

Characteristics:

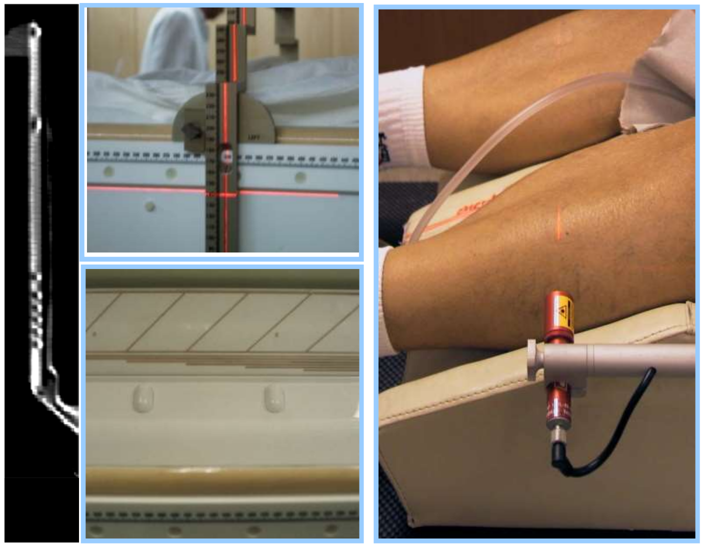
1. System of external stereotactic coordinates
2. Individualized vacuum cushion
3. Abdominal compression for reduction of breathing motion

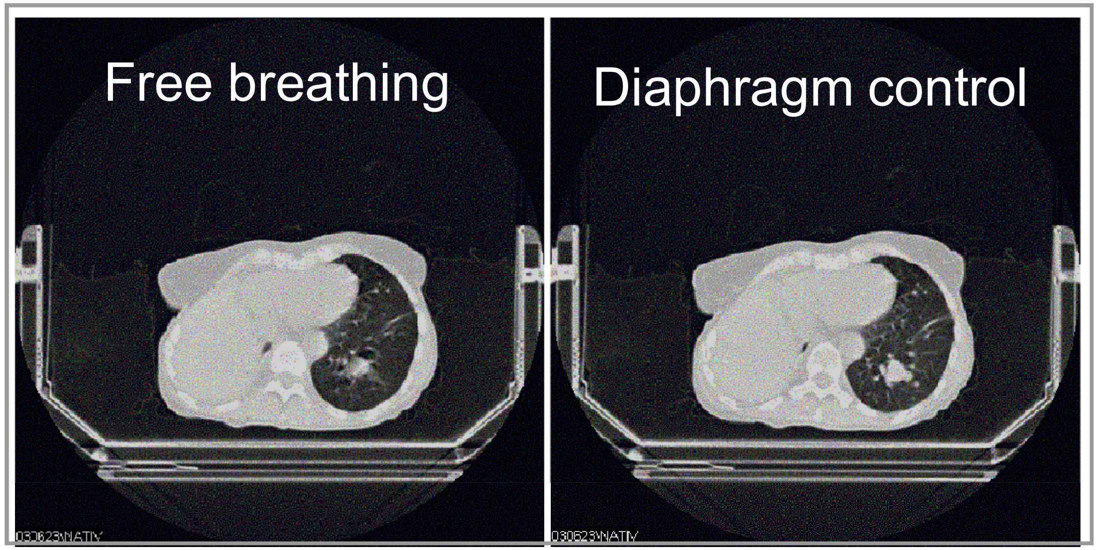






Pulmonary SBRT



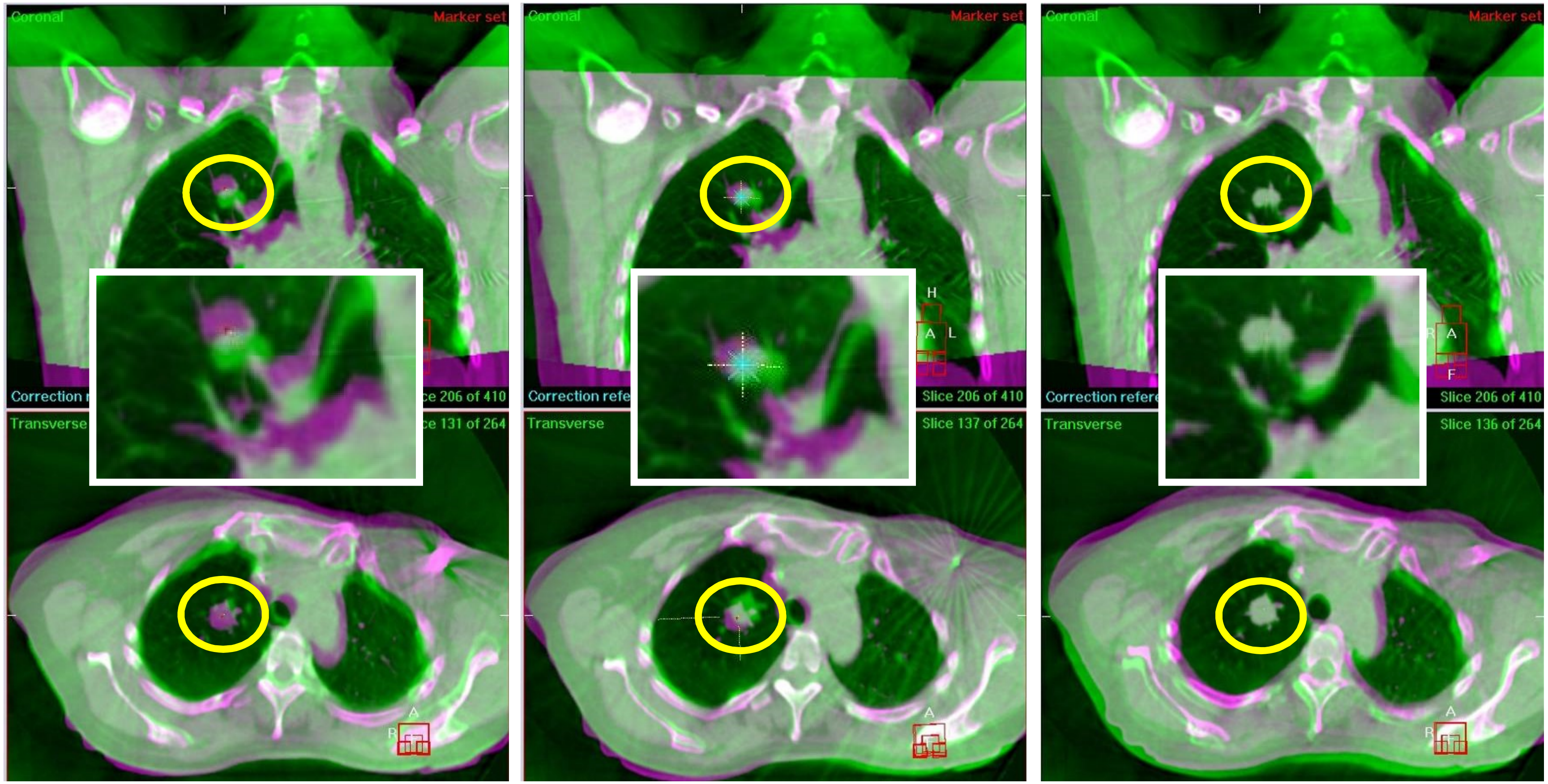


Basic assumptions of the stereotactic technique in the body region using the Stereotactic Bodyframe:

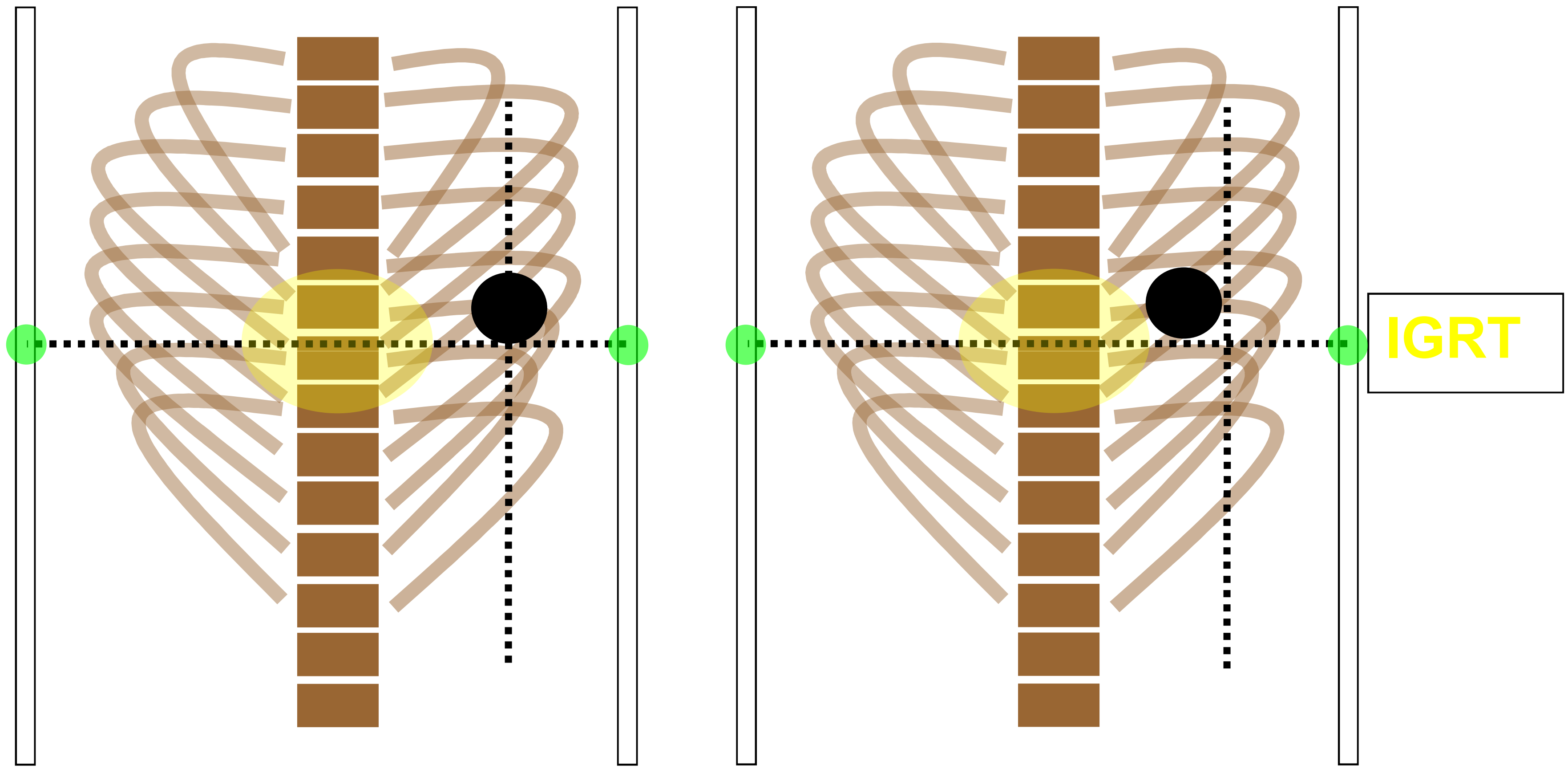
- Reproducible positioning of the frame
- Reproducible positioning of the patient within the frame
- Reproducible positioning of the target within the patient

Pulmonary SBRT

Patient positioning **Bone set-up** **Tumor set-up**



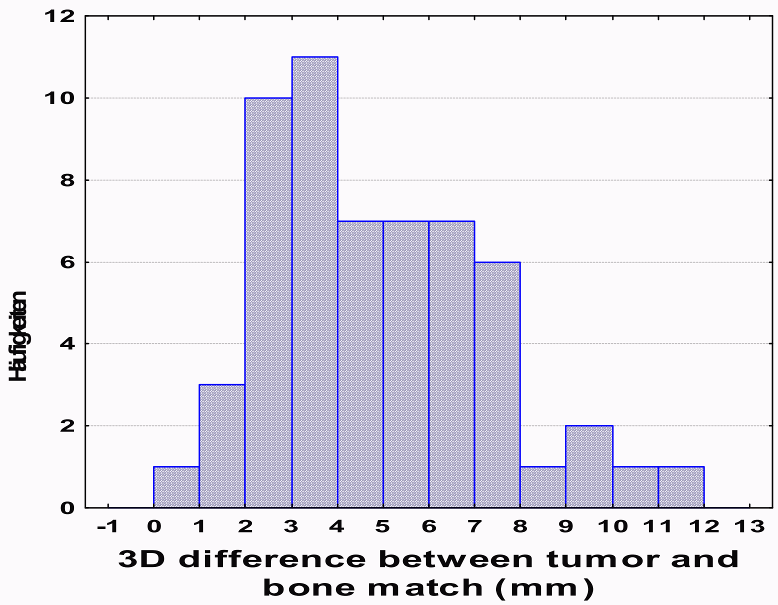
Internal target position variability – base line shift



Planning: **Treatment:**

Pulmonary SBRT

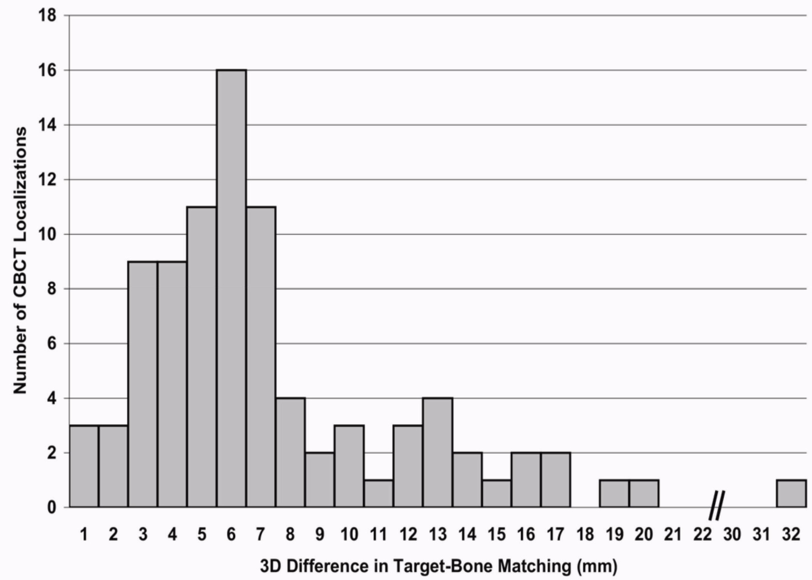
Magnitude of internal tumor position variability / base-line shifts in pulmonary SBRT



Mean: 5.3mm

90th percentile: 8mm

Guckenberger et al. 2006



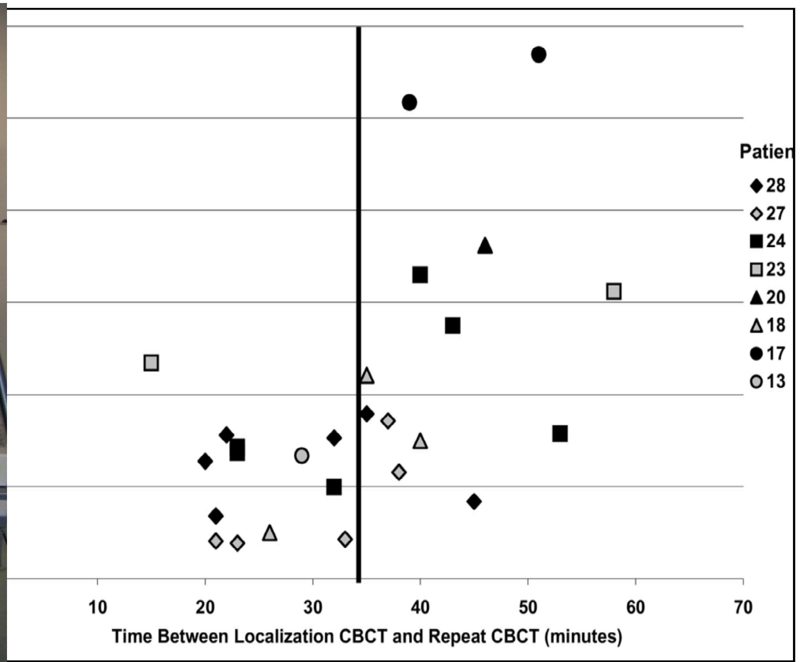
Mean: 6.8mm

90th percentile: 13.9mm

Purdie et al., 2007

Pulmonary SBRT

Intra-fractional changes of the tumor position



2.8mm ± 1.6mm

Patient immobilization with vacuum cushion and double vacuum technique

Guckenberger Radiat Oncol 2006

Pulmonary SBRT

	Immobilization	LR (mm)	SI (mm)	AP (mm)
Σ	Yes	1.3	1.1	1.3
	No	1.2	1.2	1.8
σ	Yes	1.4	1.4	1.6
	No	1.3	1.5	1.8

Guckenberger 2007
Sonke 2009

Intra-fractional changes of the tumor position seen in CB-CT images after treatment

Assuming gross motion in 1% of the fractions:

➤Limited relevance in conventionally fractionation (blurring)

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Conclusions: SBRT

Why adopt frame-less IGRT stereotactic techniques for SBRT?

Frames in SBRT (without IGRT) are prone to geometric miss

IGRT (with or without immobilization) allows accurate, safe, reproducible setup

- Consistent work-flow with optimization of all steps of radiotherapy planning and delivery, strict QA and definition of standardized protocols to achieve maximum accuracy of treatment

Questions?

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WWW.ESTRO.ORG/SCHOOL

Patient Preparation and Positioning

Rianne de Jong *RTT*,
Academic Medical Centre, Amsterdam
Madrid 2016

m.a.j.dejong@amc.uva.nl

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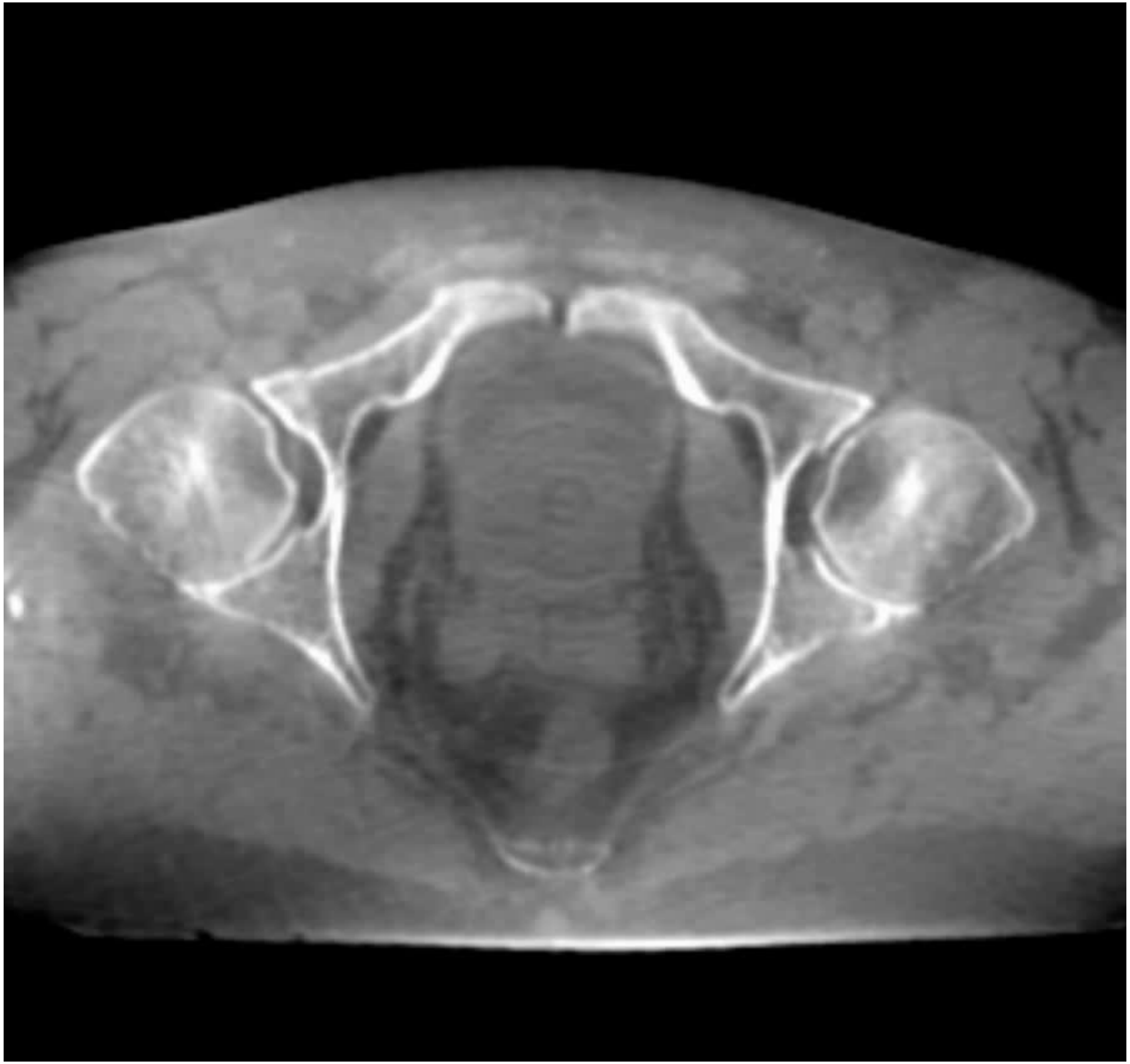

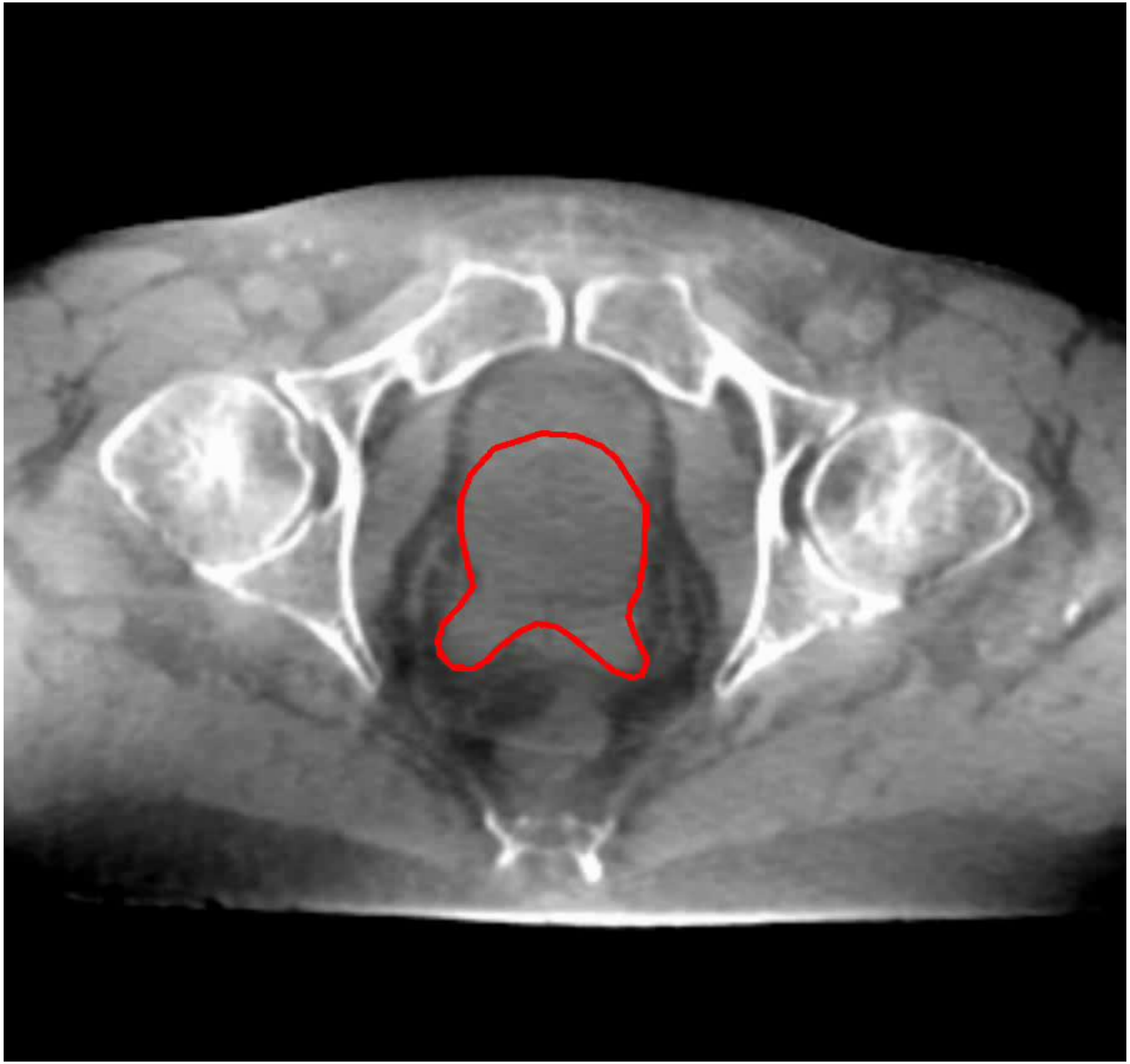

Introduction

In-room imaging enables the visualization of the target just prior to treatment.

On-line image guidance minimizes target position variability.

Is there still a need for patient immobilisation and preparation?

Aim of Patient preparation and positioning

- Minimize the difference in patient position
  - between simulation and treatment sessions
  - during the treatment session
- Maximize the distance between target volume and organs at risk

1. Patient compliance
2. Immobilization and fixation

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Aim of Patient preparation and positioning

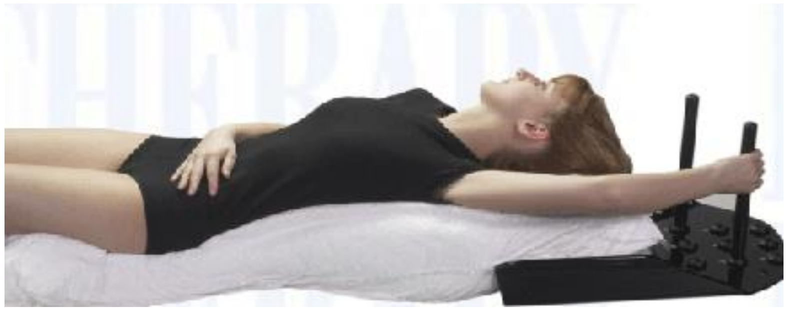
→ Patient compliance

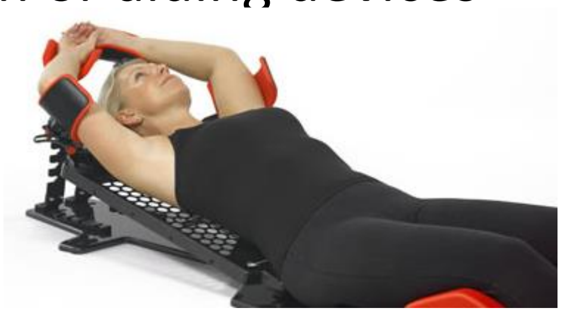
- Information and education
  - Using photo books, DVD's, folders etc.
  - Tour through department
- Psychological support to minimize fears
- Medication
  - Pain control

Aim of Patient preparation and positioning

→ Immobilization

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





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Patient Preparation

- Prostate patients
- Rectum patients

Prostate patients

Off-line correction on bony anatomy with SAL protocol

- Portal imaging
  - Kilo voltage CBCT

Soft tissue registration on prostate?

Prostate patients

Prostate patients

Projection images

CBCT

Prostate patients

Reconstructed

CBCT

Prostate patients

To improve image quality:

Dietician

- Mild regimen of laxatives
- Diet

Fixed treatment times

Prostate patients

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

- Improved image quality for registration and delineation
- Reduced intra fraction motion

For all prostate patients

Courtesy Josien de Bois

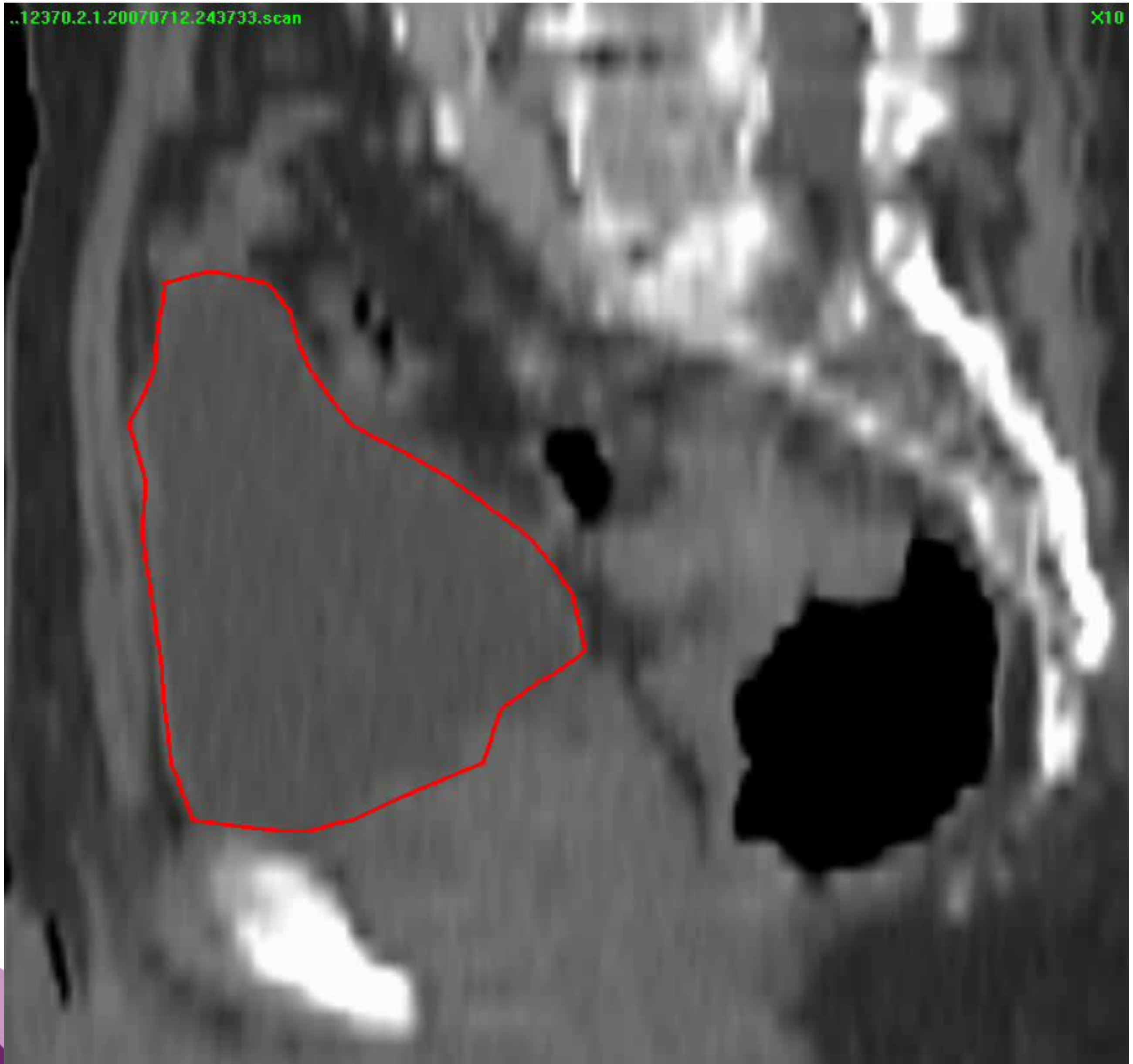
Prostate patients

Lips et al. Ijrobp 2011
739 patients without diet, 205 patients with diet
Diet instructions on leaflet
No reduction of **intrafraction** movement

McNair et al. 2011
22 patients using questionaires
Rectal filling consistency not improved
Diet + fixed treatment times, **no laxatives**

McNair and van Vulpen 2013

Rectum patients

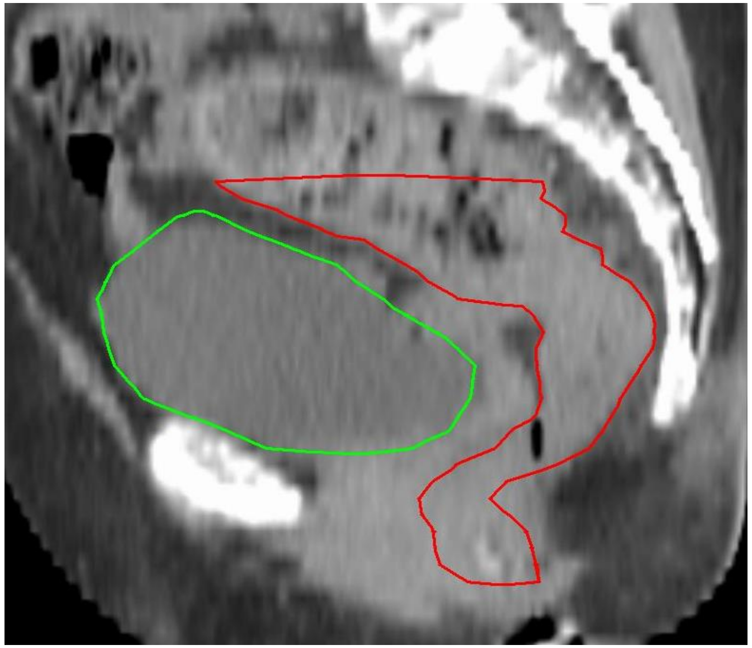


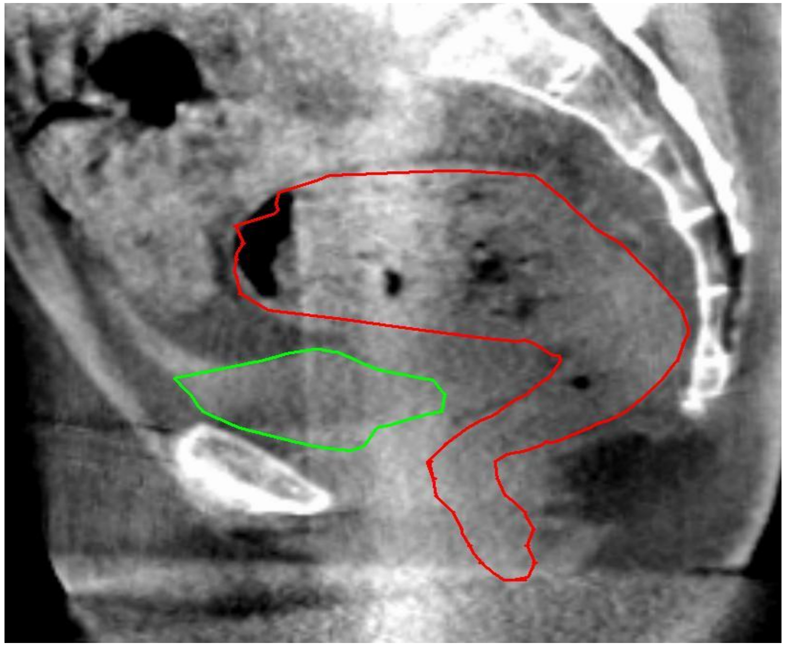
Series of repeated CT scans

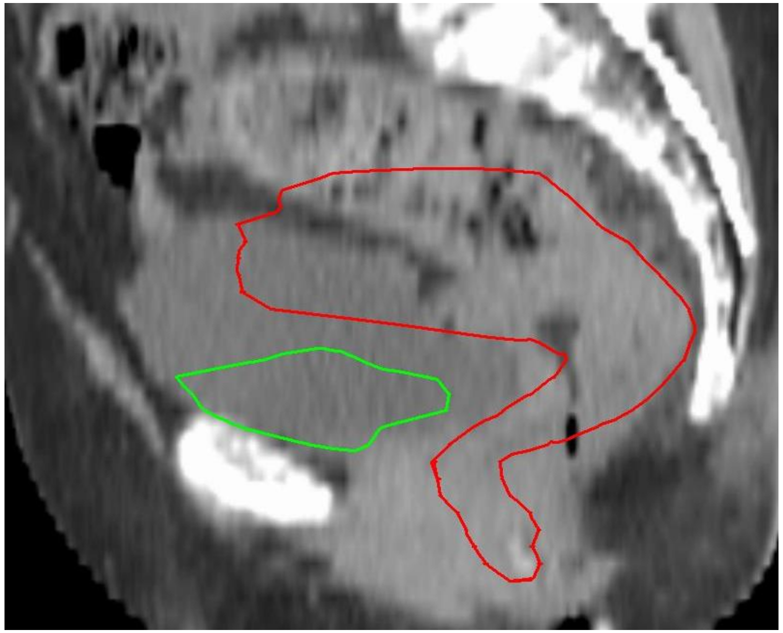
Bladder filling over different fractions

With drinking protocol

Rectum patients

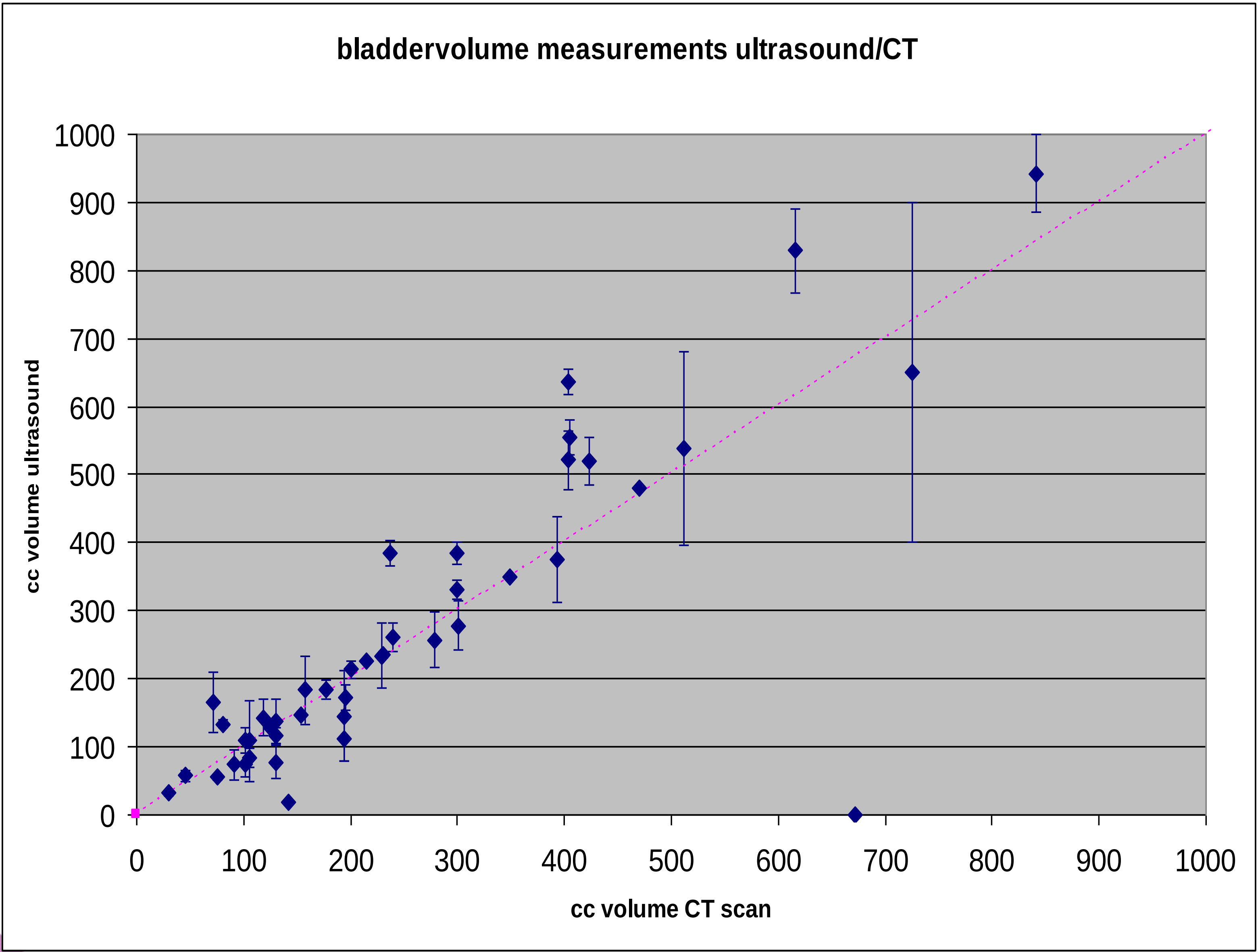






Influence of bladder filling on CTV of rectum

Rectum patients



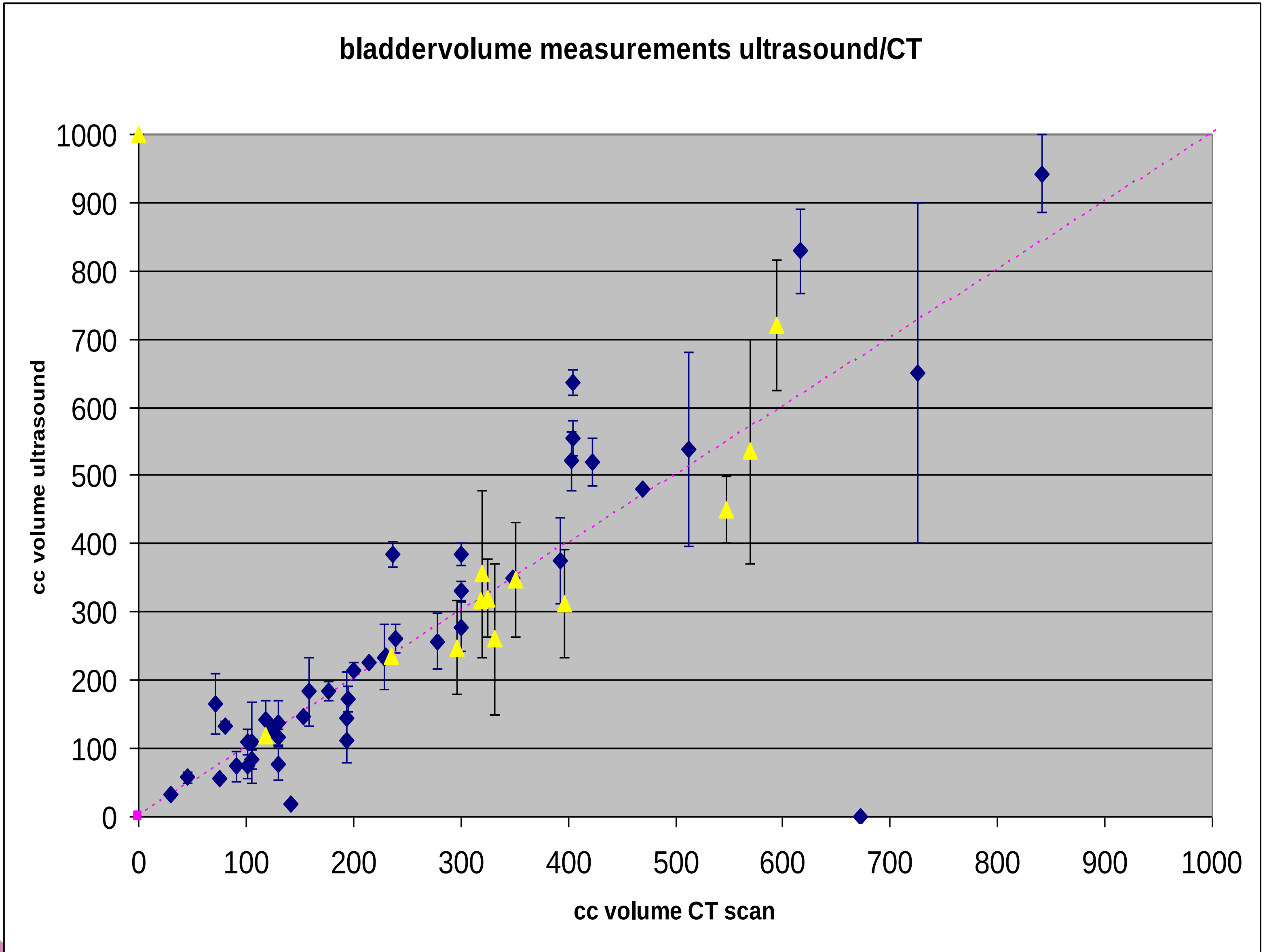
Drinking protocol:

30 min prior to treatment

+

250 cc water

Rectum patients



Drinking protocol:

60 min prior to treatment

+

350 cc water

+

total 2 liter water during day

Contents

Introduction

Aim of patient preparation and positioning

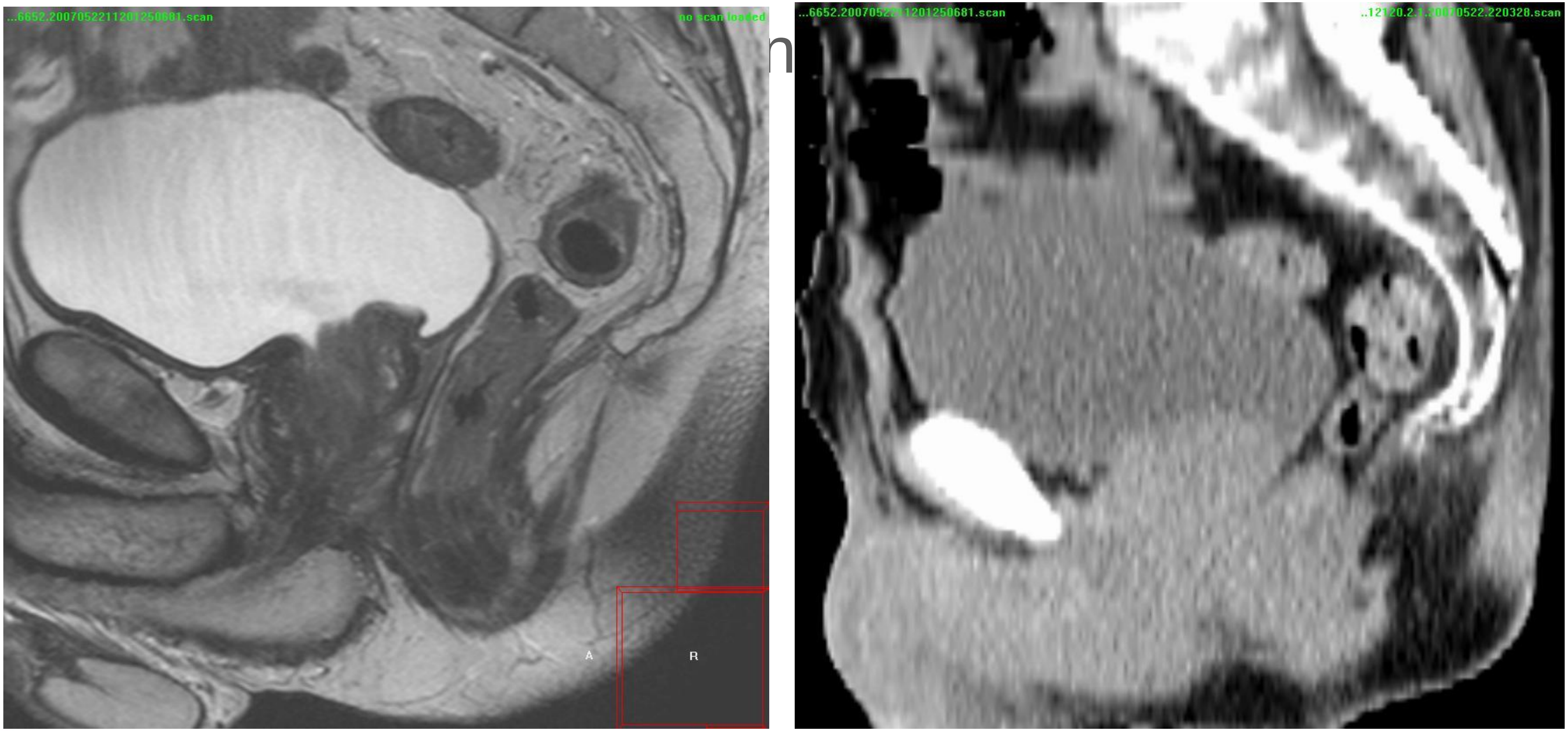
Patient Preparation

Patient Positioning

- **Prostate patients**
- **Rectum patients**
- **Pelvic patients**
- **Lung patients**

Managing breathing motion

Discussion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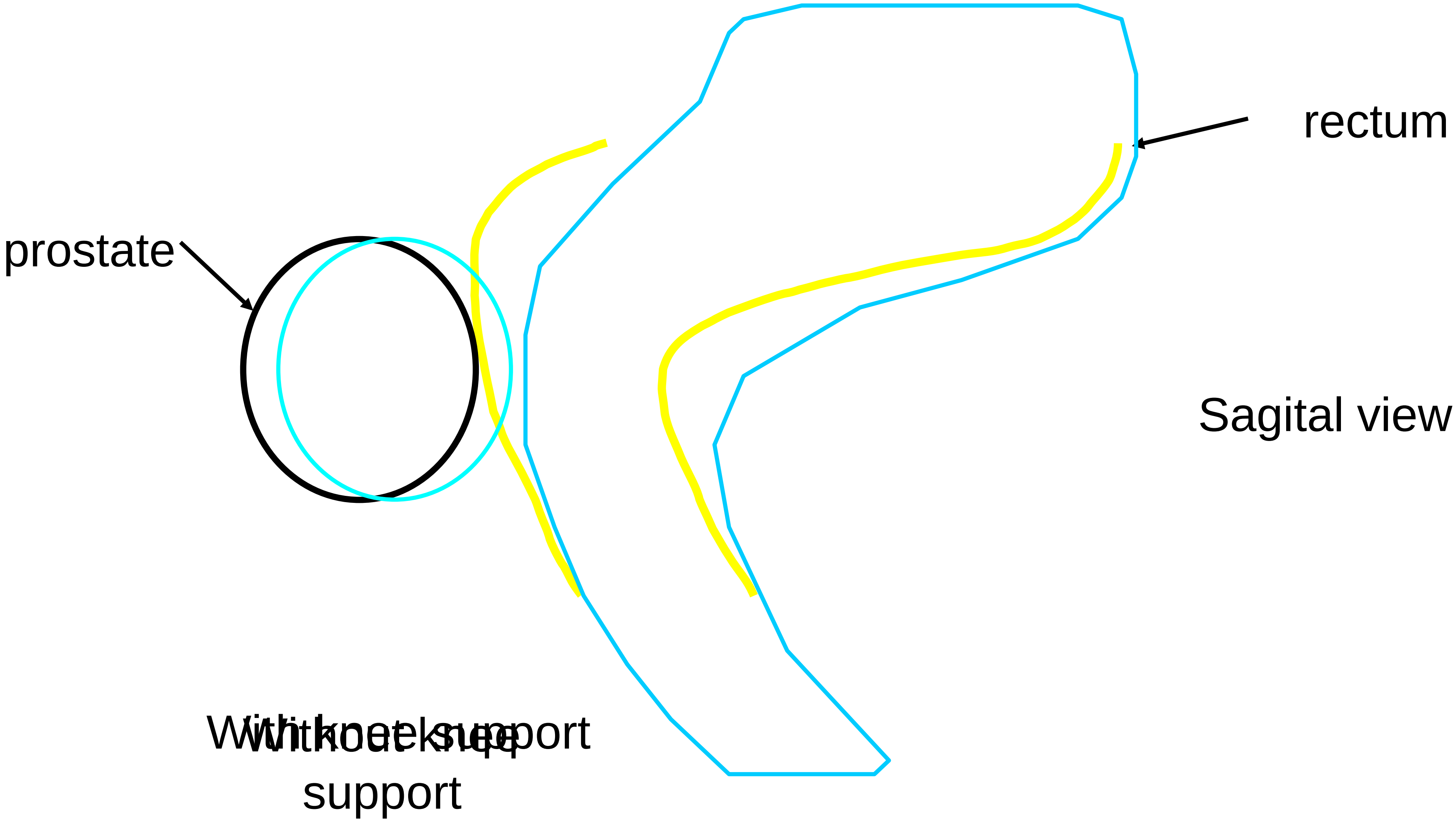
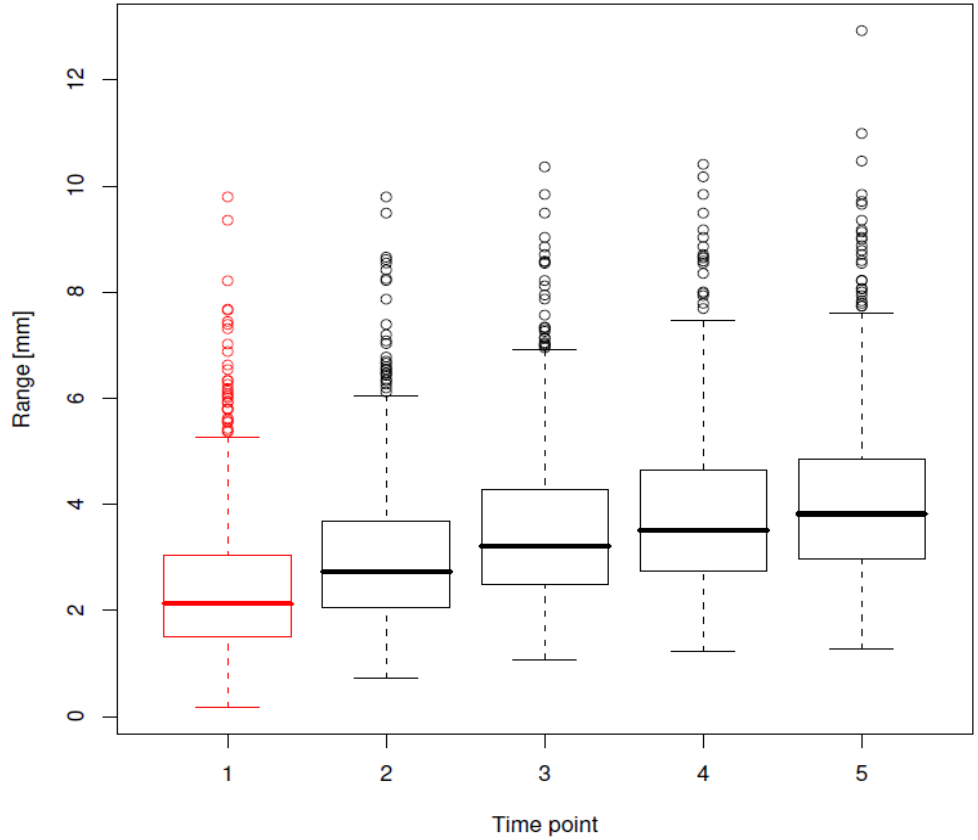
...6652.20070522112012506681.scan
..12120.2.1.20070522.220328.scan


rectum
prostate
Sagital view
With knee support
Without knee support

Prostate patients

- Already at the first time point (after online verification) the median range is 2 mm



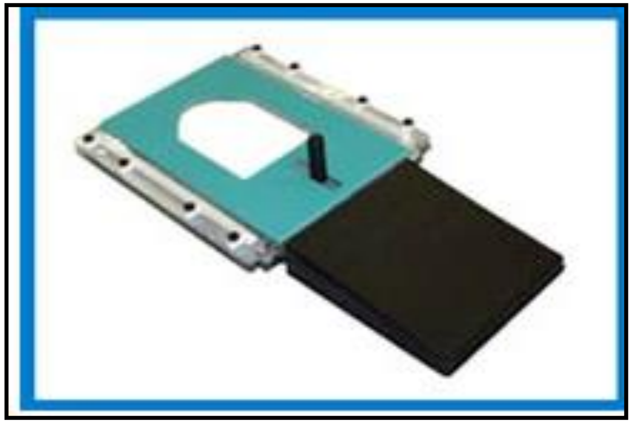
Coutesy Alexis Kotte, Utrecht MC

Rectum patients

Prone position

- Belly board
- Intra fraction stability prone/supine

Rectum patients

Belly board

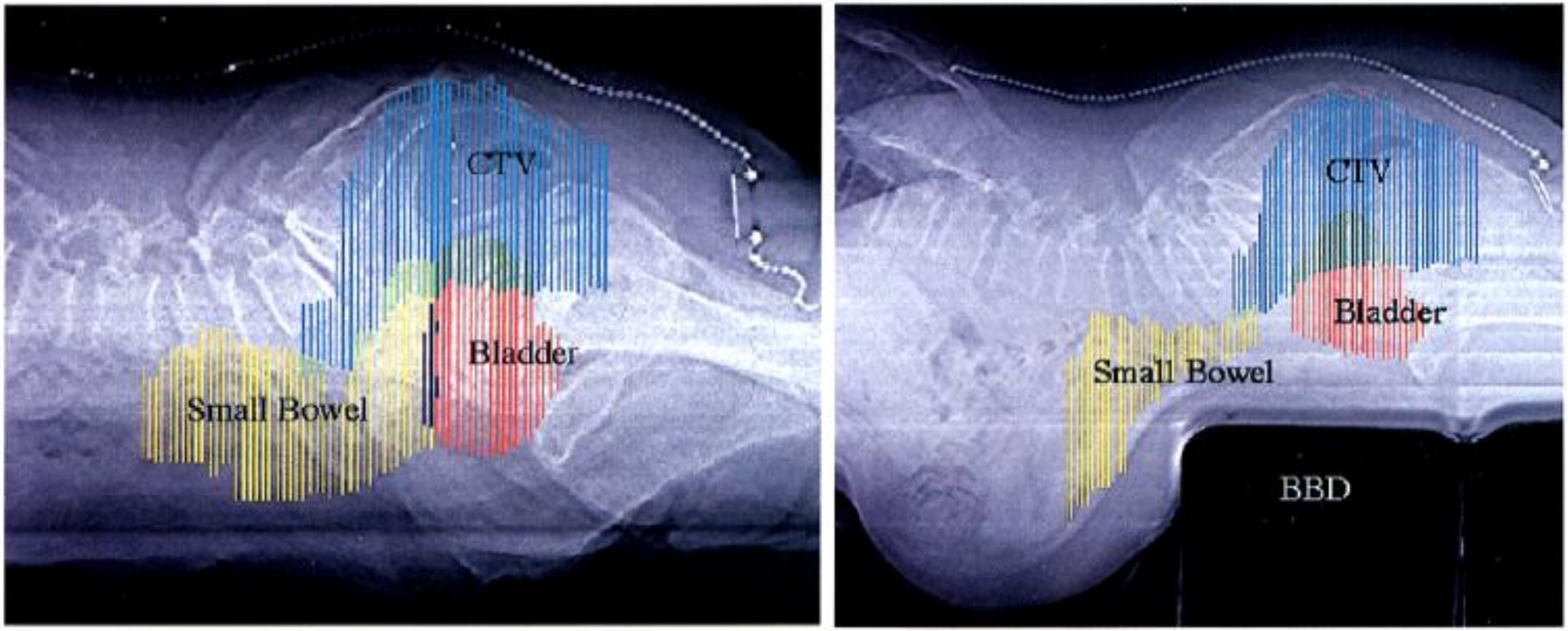



Fig. 2. Pilot localization, lateral view is shown (a) for simulation without BBD and (b) with BBD. The clinical target volume (CTV), small bowel, and bladder are shown. Note a dramatic shift in small bowel in the cephalic direction with the BBD.

Das *et al,* 1997

Rectum patients

On-line bony anatomy registration 5x5 Gy

Introduction of IMRT

RTT in the clinic: impression prone not as stable as supine

- Kilo voltage CBCT
- Prone versus supine

Prone position

Supine position

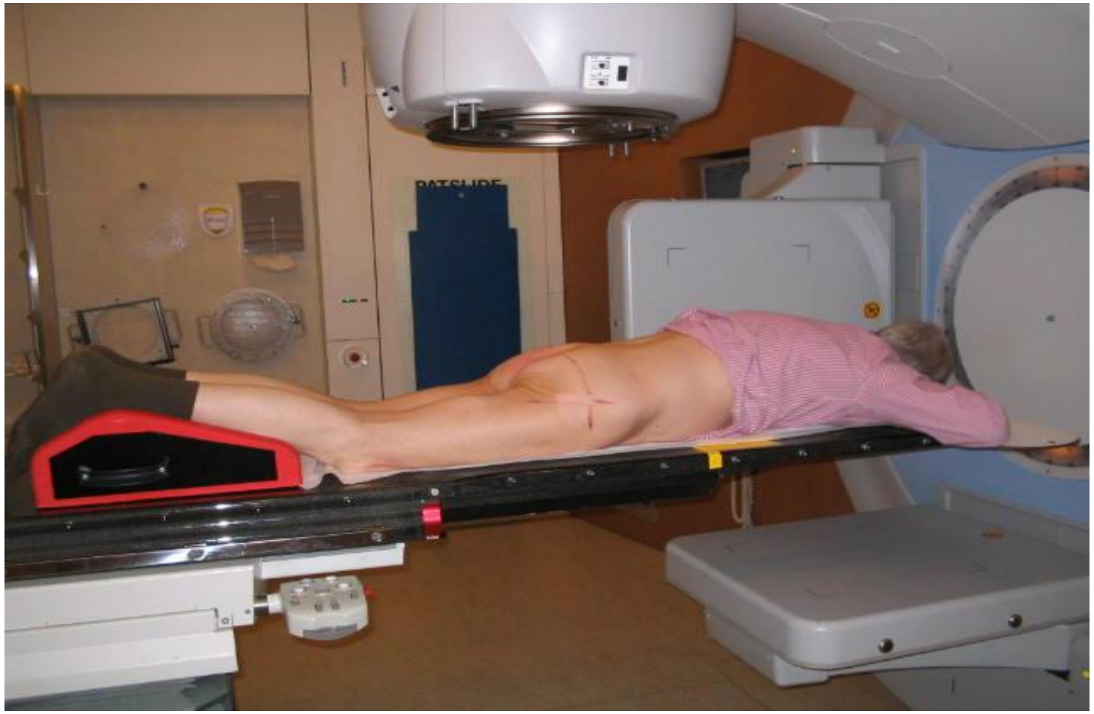
Image quality of CBCT

Rectum patients

- Arms over chest
- Knee support
- Pillow under head

- No interventions

Rectum patients



- Hands under forehead
- No turning of the head
- Ankle support

- Tape over back side of patient: 60%
- Repositioning on lasers between fields: 5%
- Additional support (like pillow): 5%
- No intervention: 40%

Rectum patients

prone	Translations (mm)			Rotations (dg)		
	L-R	C-C	A-P	L-R	C-C	A-P
Mean	-0.3	0.4	-0.8	1.3	0.6	-0.1
Σ	**2.1**	**0.8**	**1.3**	**1.2**	**1.0**	**0.5**
σ	2.5	1.1	1.0	0.7	0.8	0.4
Supine	Translations (mm)			Rotations (dg)		
	L-R	C-C	A-P	L-R	C-C	A-P
Mean	0.1	-0.4	-0.5	-0.5	0.2	0.0
Σ	**0.5**	**0.4**	**0.5**	**0.7**	**0.3**	**0.3**
σ	0.9	0.6	0.6	0.8	0.4	0.3

P<0.05

Rectum patients

prone	Translations (mm)			Rotations (dg)		
	L-R	C-C	A-P	L-R	C-C	A-P
Mean	-0.3	0.4	-0.8	1.3	0.6	-0.1
Σ	2.1	0.8	1.3	1.2	1.0	0.5
σ	**2.5**	**1.1**	**1.0**	0.7	**0.8**	0.4
Supine	Translations (mm)			Rotations (dg)		
	L-R	C-C	A-P	L-R	C-C	A-P
Mean	0.1	-0.4	-0.5	-0.5	0.2	0.0
Σ	0.5	0.4	0.5	0.7	0.3	0.3
σ	**0.9**	**0.6**	**0.6**	0.8	**0.4**	0.3

P<0.05

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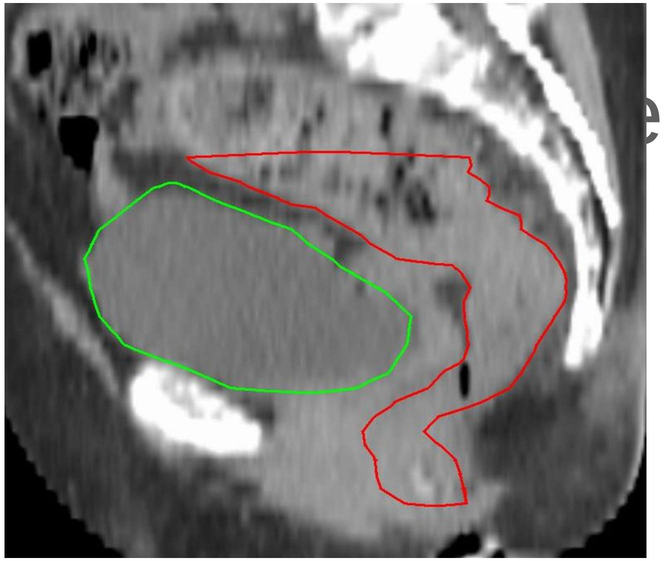
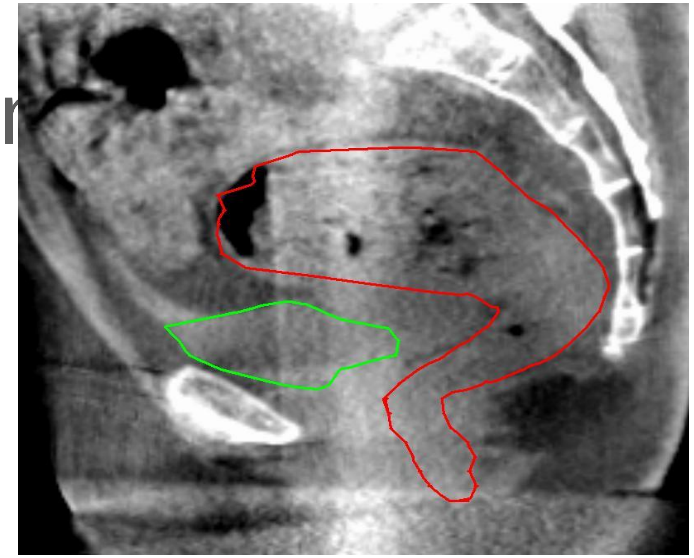
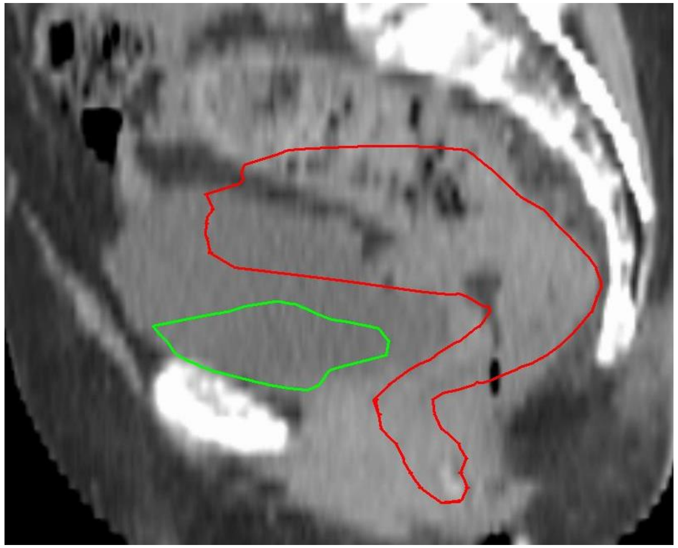
Rectum patients

Intra fraction motion in prone is around a factor of 2 or more larger than supine

(with this immobilisation)

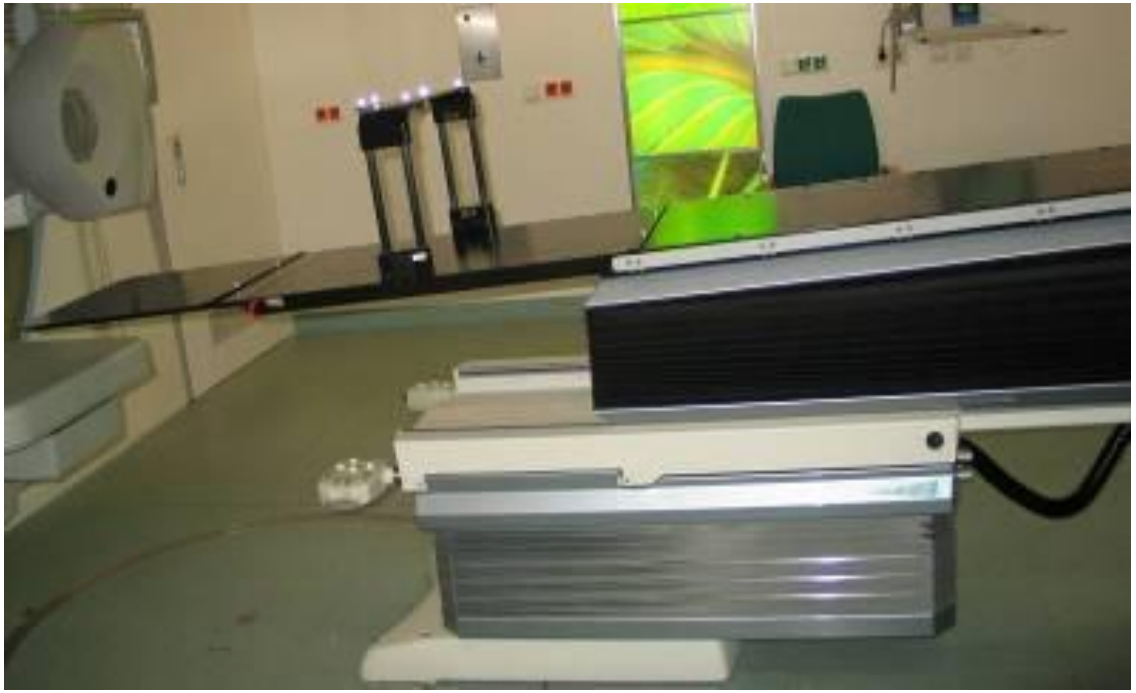






Influence of bladder filling on CTV of rectum

Pelvic patients and hexapod



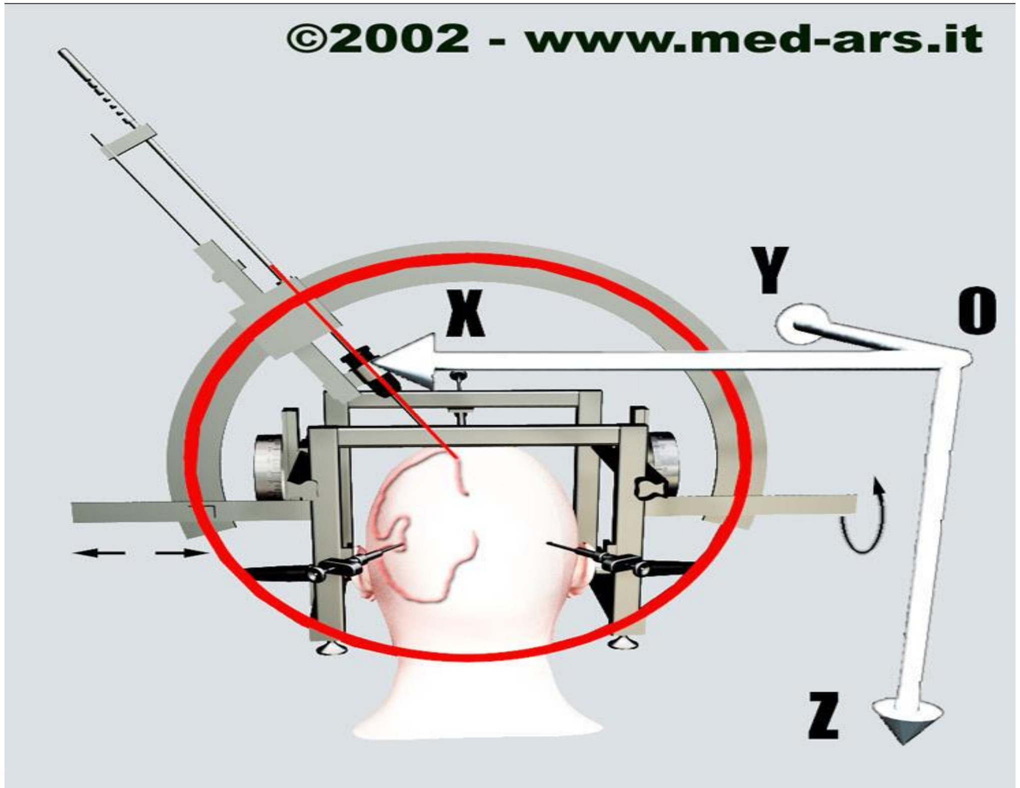
<u>Without proper fixation:</u>

Correction of 3º rotational error

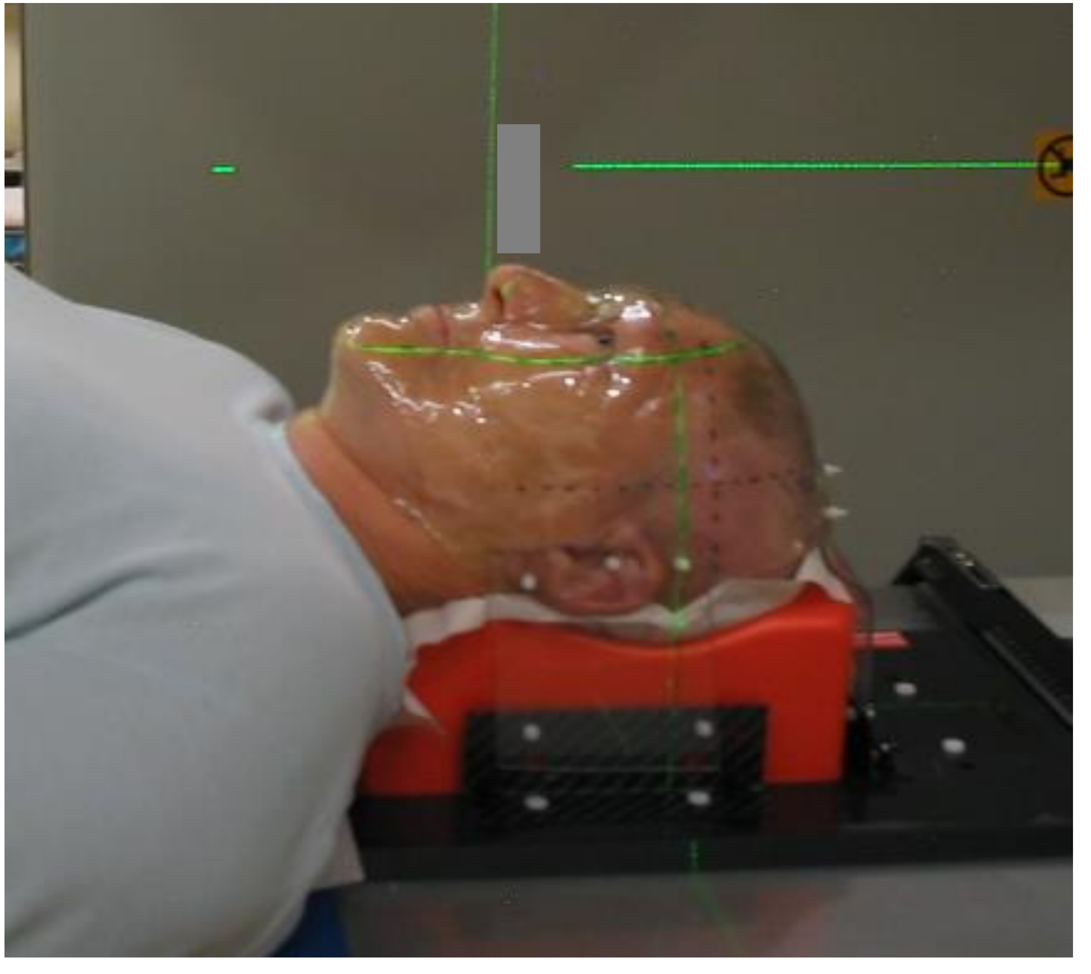
→ displacement of ~ 2mm

Courtesy Matthias Guckenberger, Wuerzburg

Head and Neck stereotactic treatment



Head and Neck stereotactic treatment

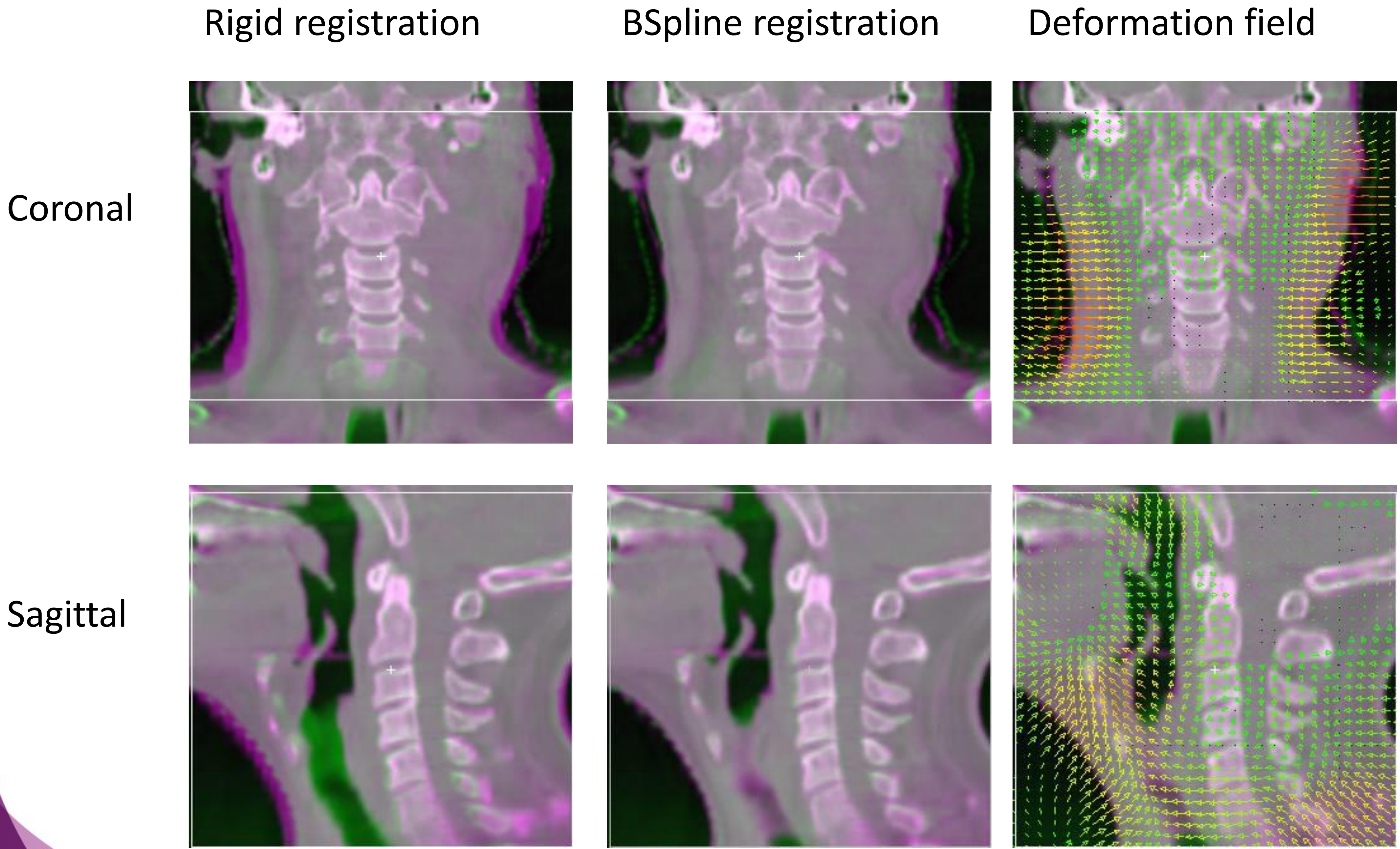


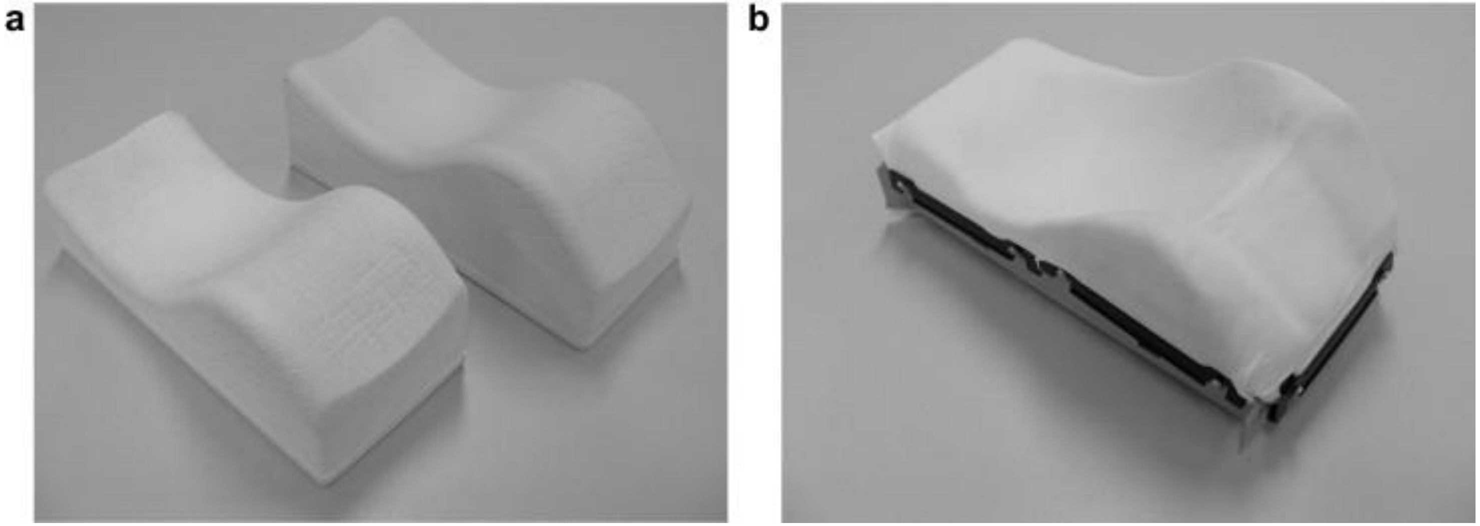
Head and Neck stereotactic treatment

	Left-right (mm)		Cranial-caudal (mm)		Ant-post (mm)	
	Mean	SD	Mean	SD	Mean	SD
Before corr.	-0.8	1.5	-0.1	2.3	-0.5	2.0
After corr.	-0.1	0.7	0.1	1.0	-0.1	0.9
Intra frac.	-0.1	0.3	0.1	0.3	-0.1	0.2

Peter Remeijer, NKI

Deformable registration to asses anatomy changes

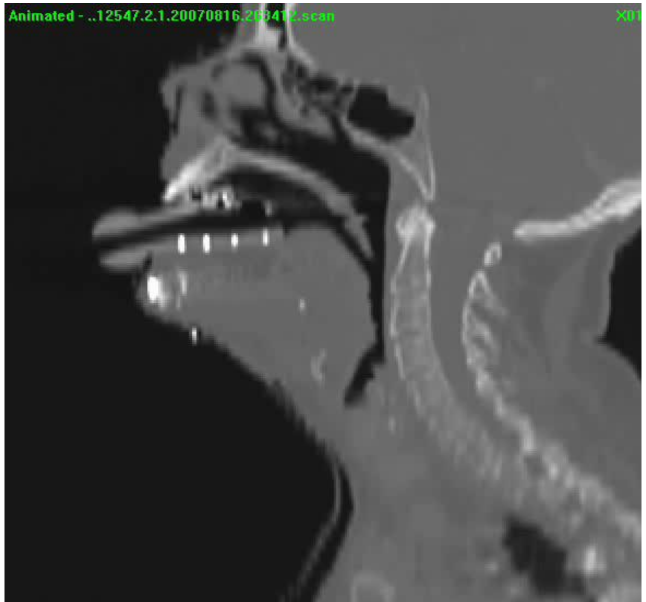


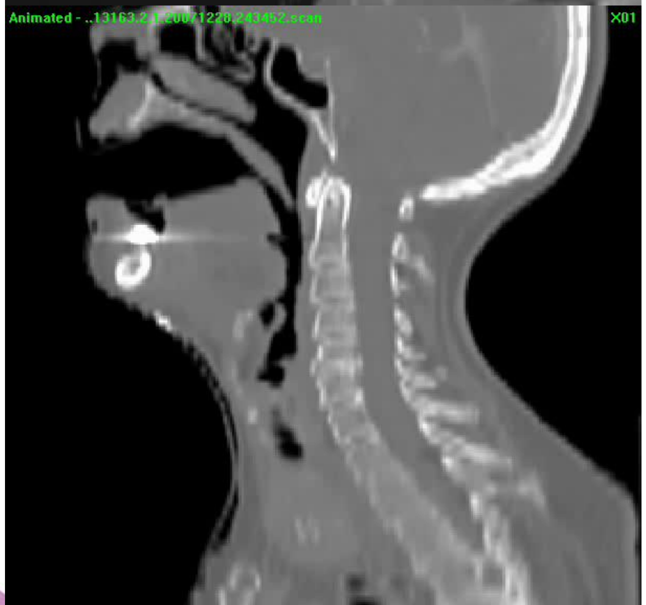


Reduction of systematic error for inter and intra fraction motion.
Reduction of deformations.

Houweling et al. 2010

Head and Neck





Hypofractionated lung treatment

On-line lung tumor match with CBCT: 3 x 18 Gy (old protocol without arc therapy and inline scanning)

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

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Hypofractionated lung treatment

100x real speed

Hypofractionated lung treatment

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
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	σ	1.2	1.4	1.7

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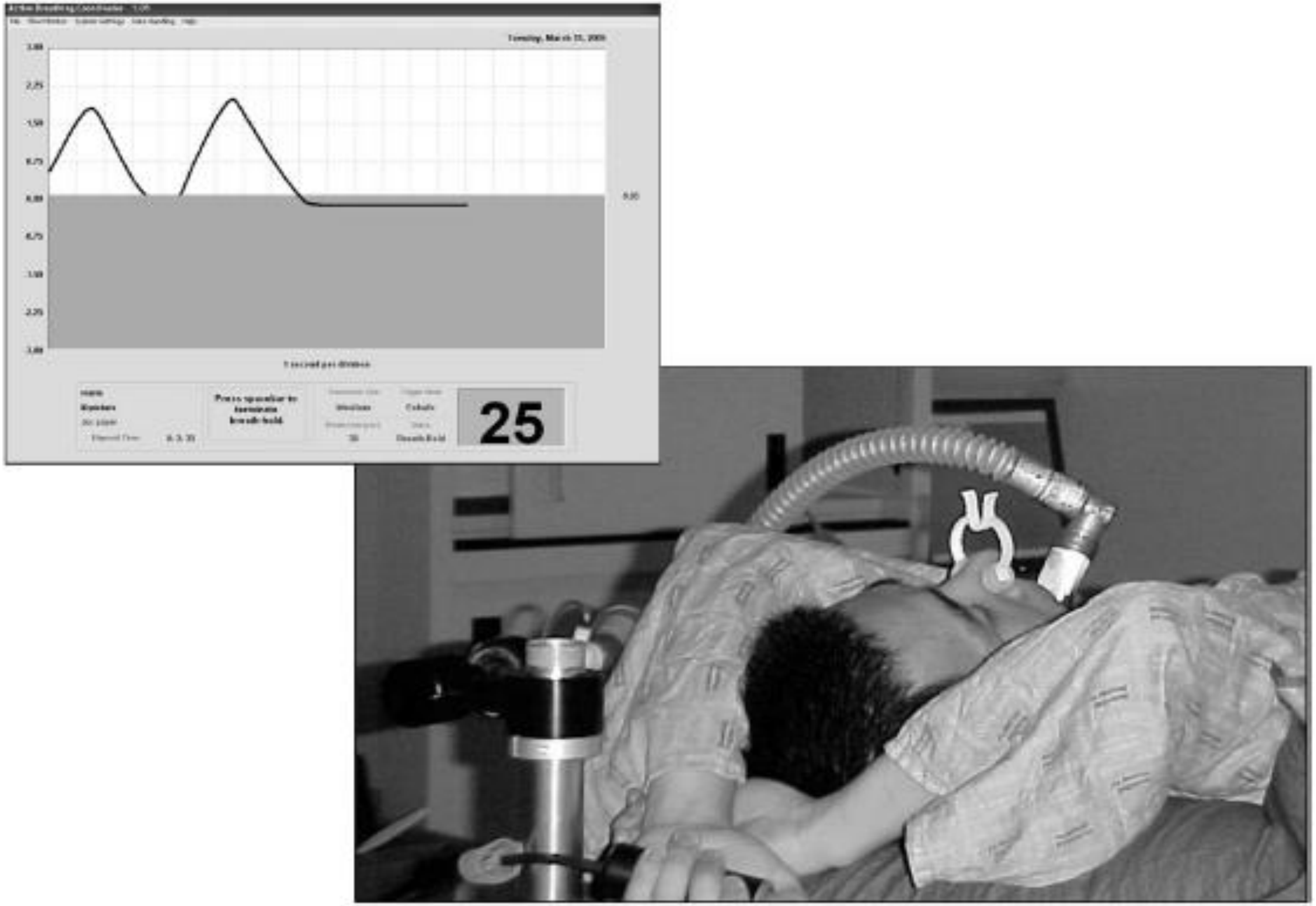
Managing breathing motion

Breath hold techniques

Respiratory monitoring system

Coaching



Courtesy to Laura Dawson

CC Reproducibility of ABC Breath Hold

	No. Images	Inter-fract. Reprod. (σ)	Intra-fract. Reprod. (σ)
Michigan	262	4.4 mm	2.5 mm
Toronto	257	3.4 mm	1.5 mm

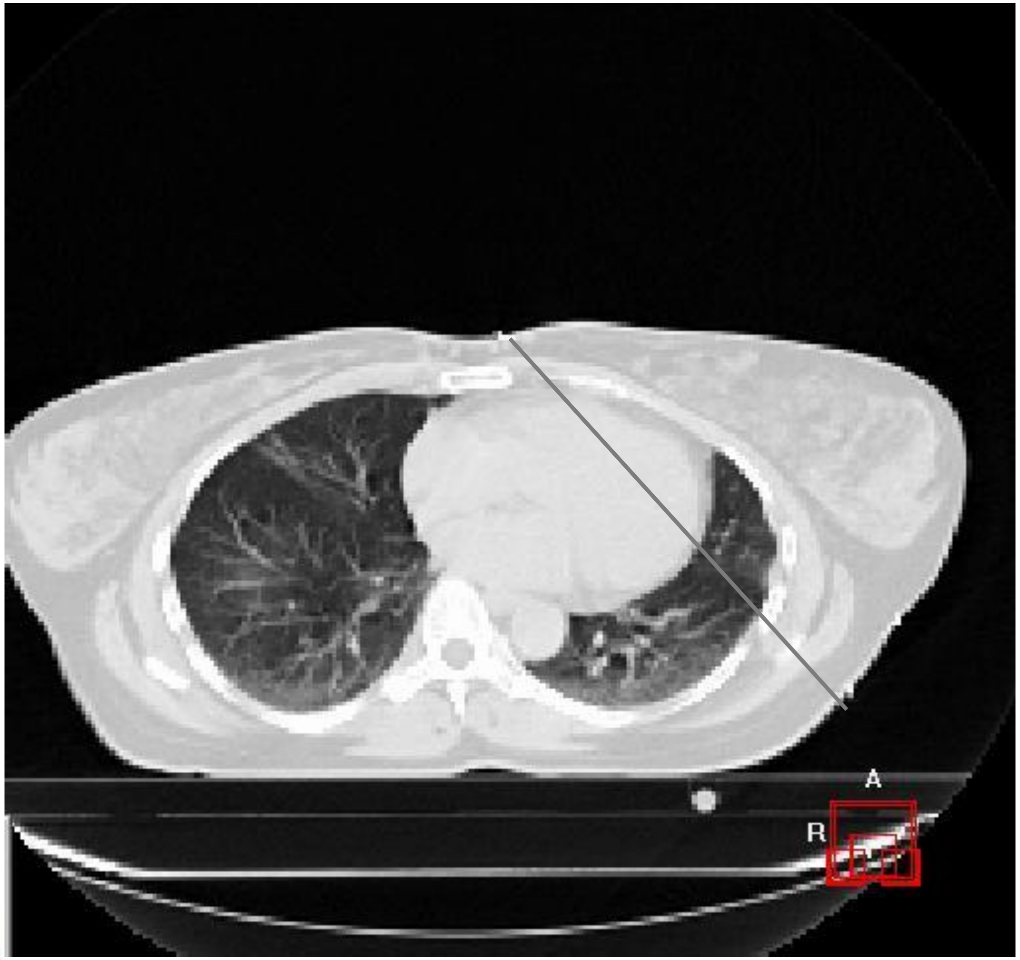
IGRT required for maximal PTV reduction

Courtesy to Laura Dawson

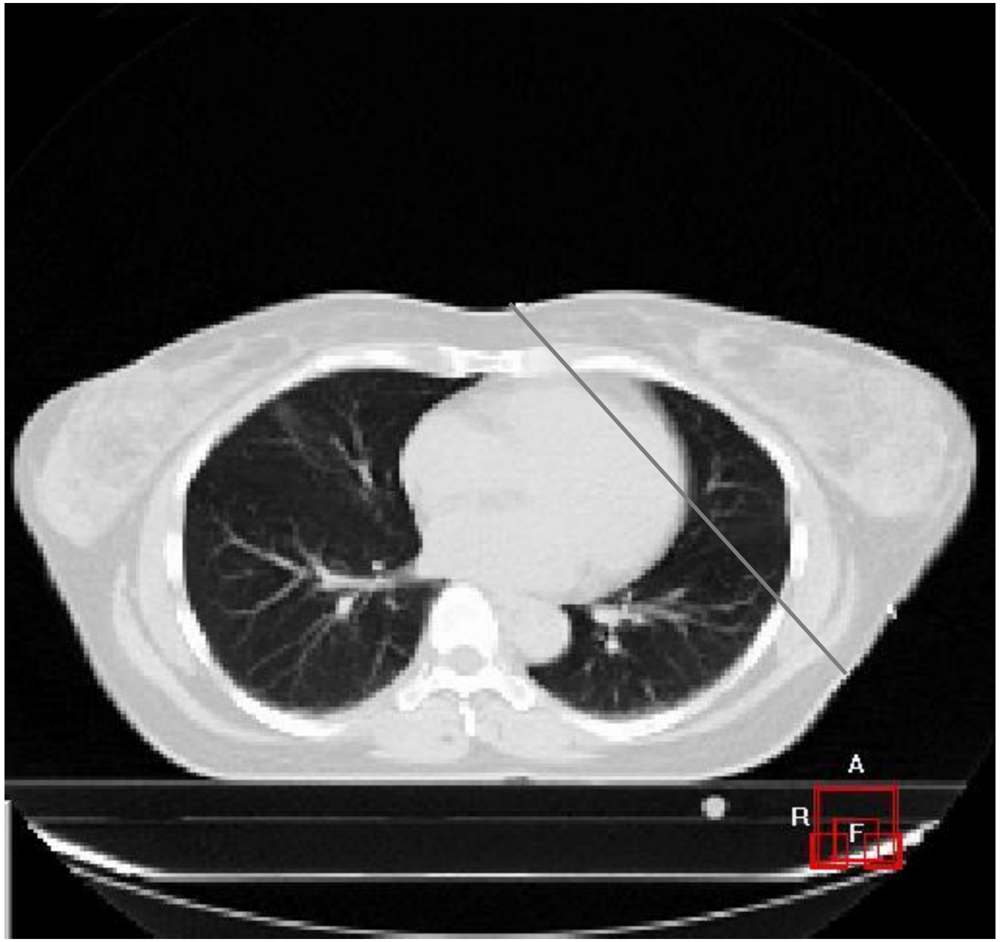
Dawson LA. IJROBP 2001
Eccles, C, IJROBP, 2005

Breath hold

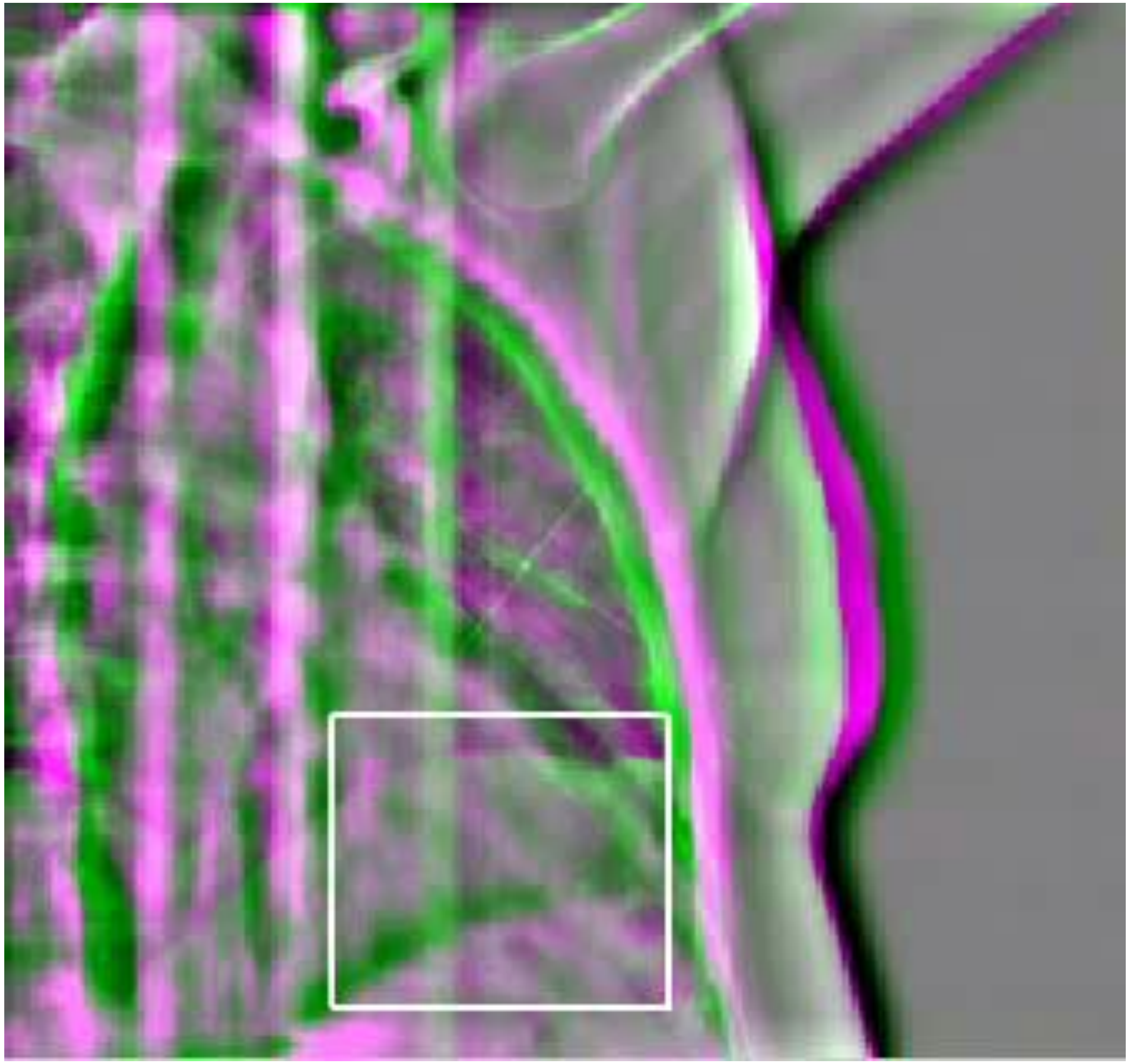
Normal inspiration



Deep inspiration



Jan-Jakob Sonke



Set-up error voluntary breath-hold

	Translations		
	LR (cm)	CC (cm)	AP (cm)
M	0.20	0.18	0.10
Σ	0.26	0.28	0.45
σ	0.25	0.28	0.38

Set-up error voluntary breath-hold

	Chest Wall			Diaphragm
	LR (cm)	CC (cm)	AP (cm)	CC (cm)
M	0.20	0.18	0.10	0.08
Σ	0.26	0.28	0.45	0.88
σ	0.25	0.28	0.38	0.58

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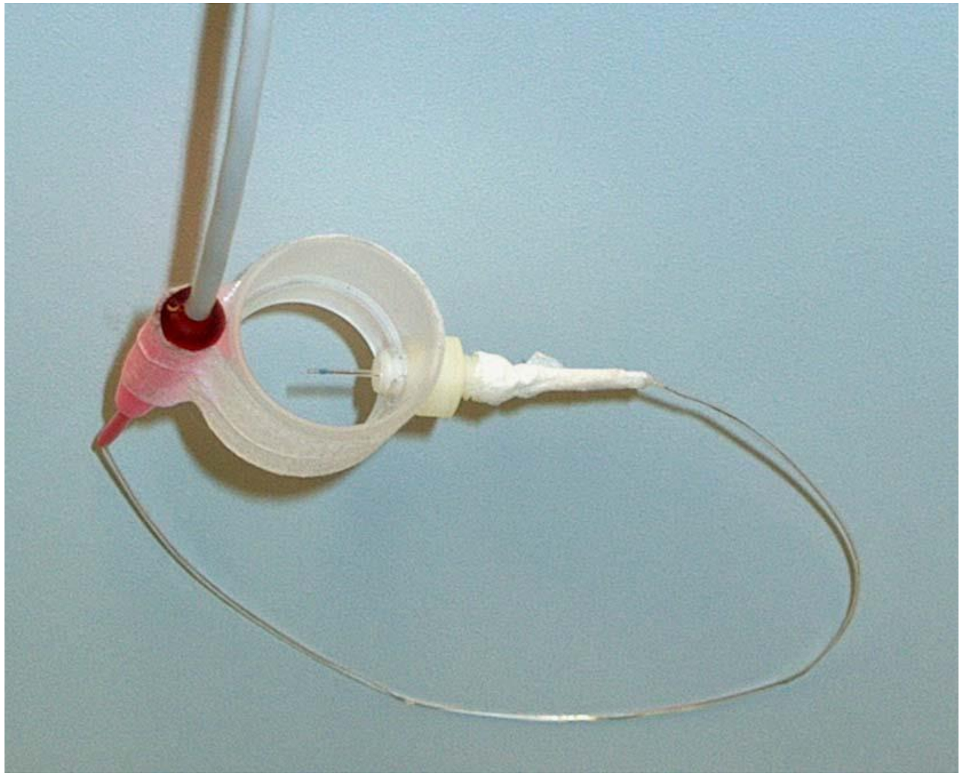
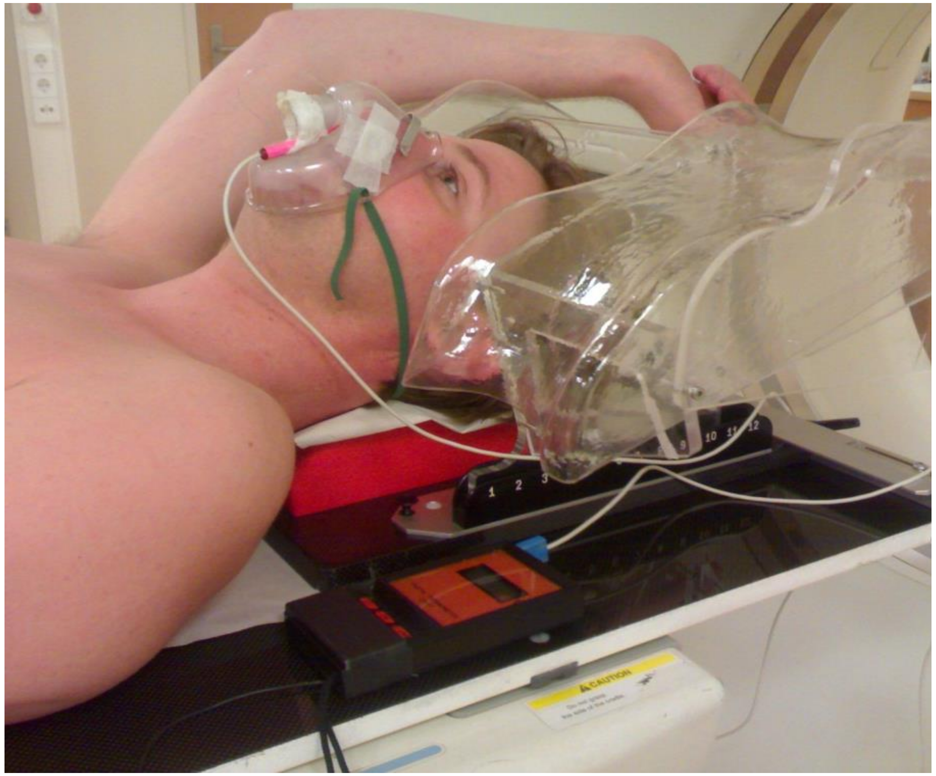
Respiratory monitoring system





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

Respiratory monitoring system

With oxygen mask

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

Without oxygen mask

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

No significant difference in tumor mean position

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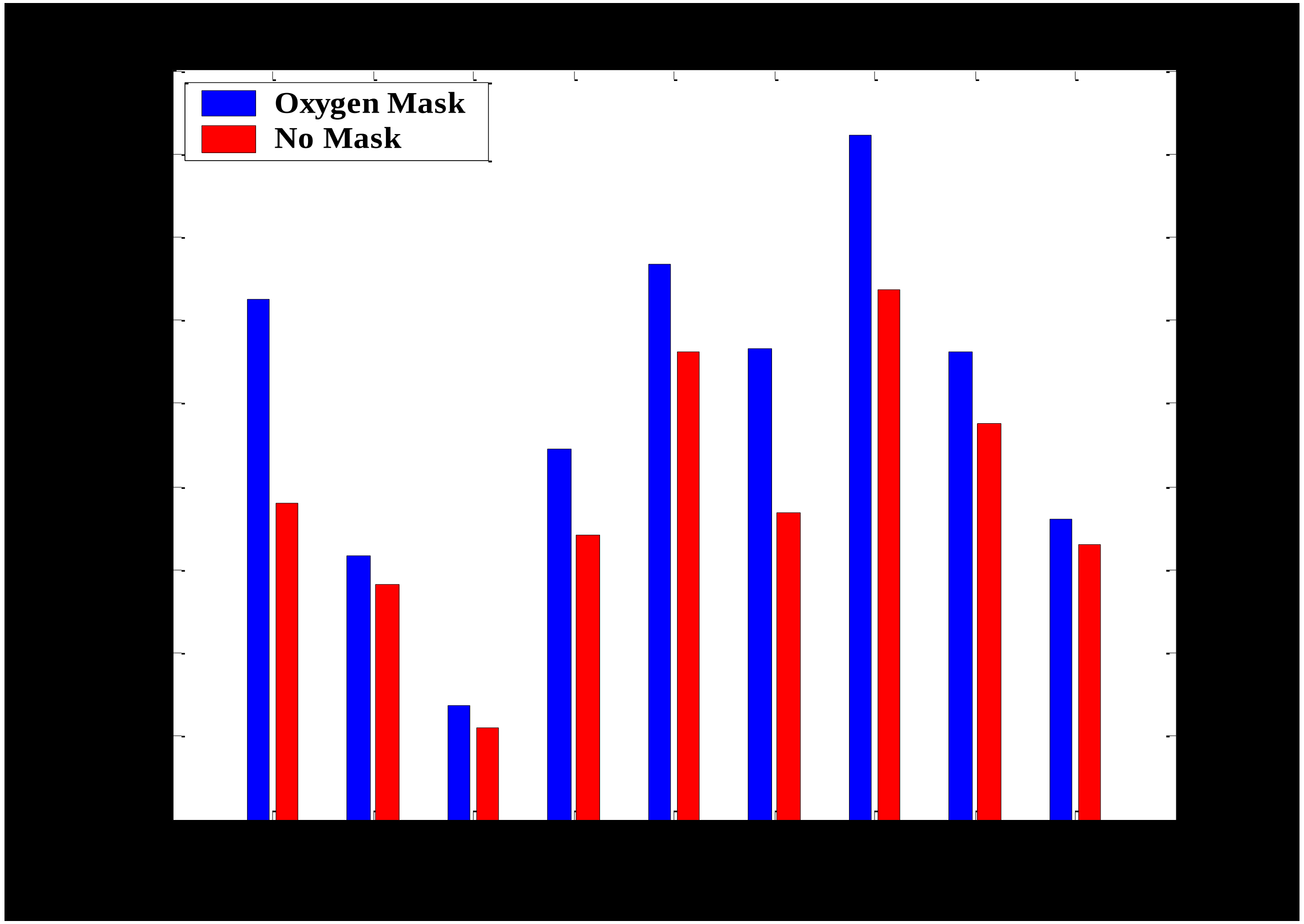
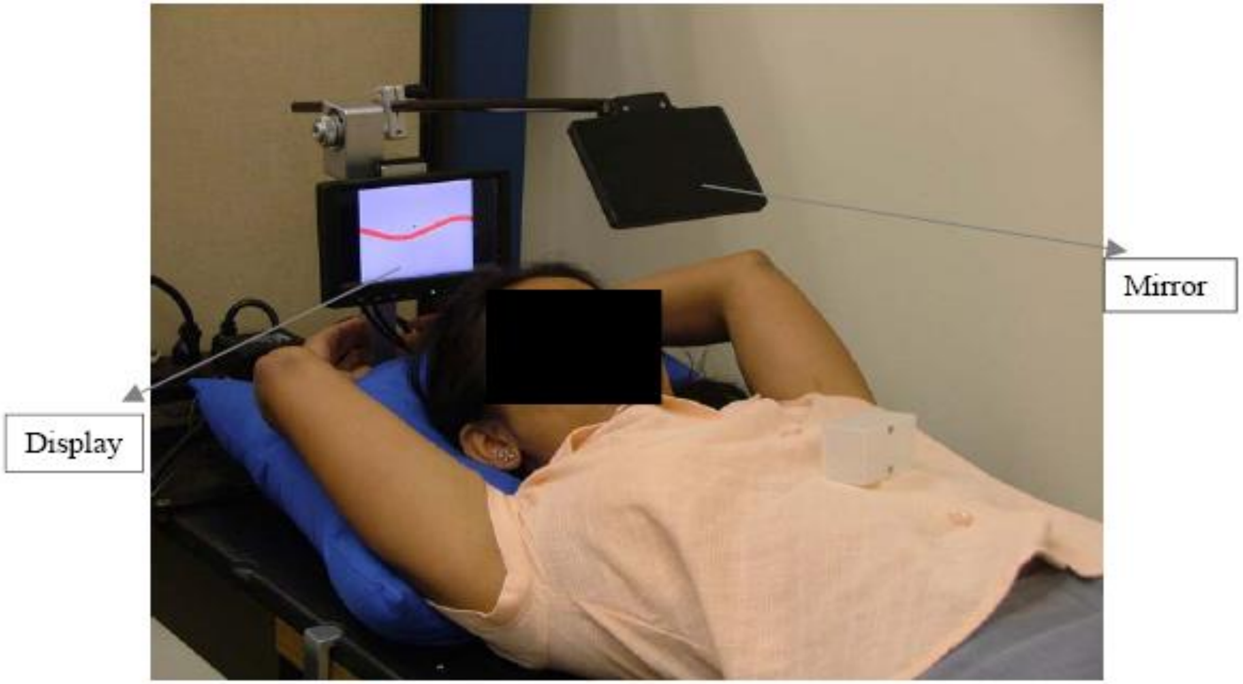
Respiratory monitoring system

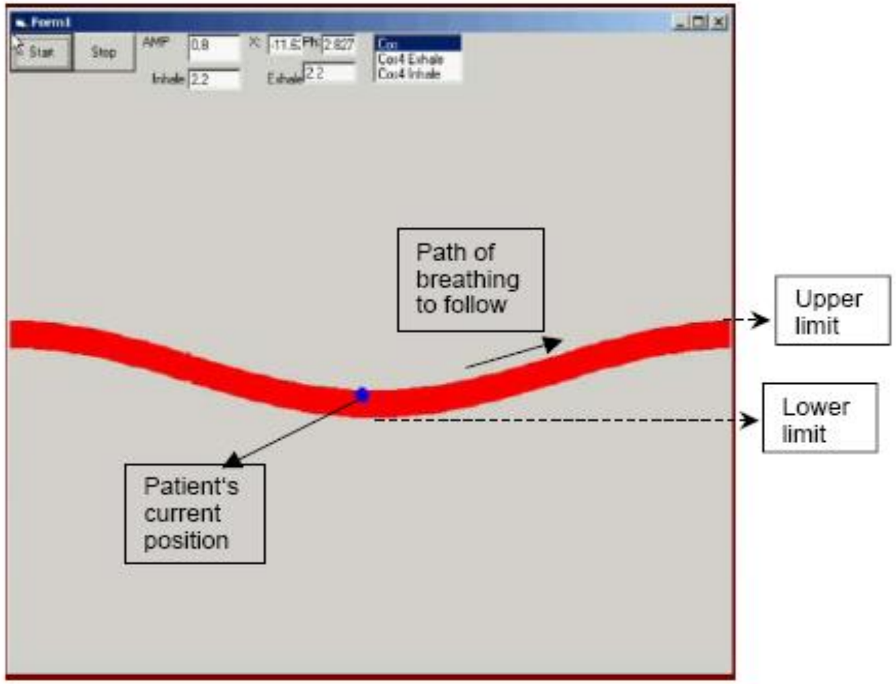


M = 29%, SD = 19%, p = 0.0017

Relative change in breathing amplitude

Coaching


Display
Mirror


Start
Stop
AMP
Inhale
Exhale
Path of breathing to follow
Upper limit
Lower limit
Patient's current position

Coaching

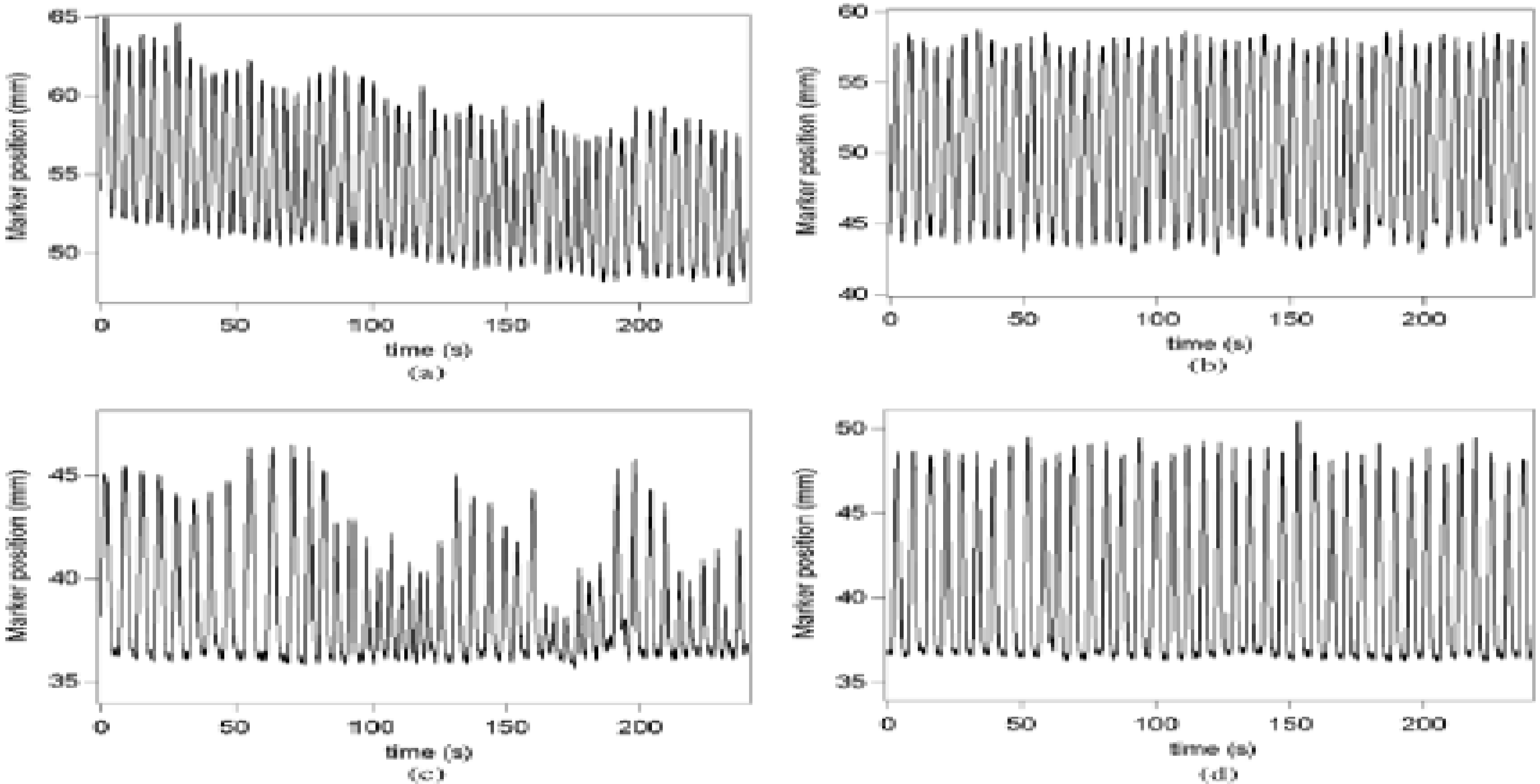


Figure 2. Example of time dependence of breathing trace acquired during free breathing (a) and (c) and audio–visual coaching (b) and (d). Data sets (a) and (b) belong to one volunteer while (c) and (d) belong to another. The free breathing data exhibit baseline shifts (a) and irregular breathing (c). Those problems were eliminated with breath coaching (b, d).

Neicu *et al. 2006*

Conclusie

IGRT does **not** make patient positioning and preparation obsolete

- **Intra-fraction motion**
- Rotational and deformation errors
- Off-line protocols
- Moving the organs at risk away from target volume

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Conclusie

IGRT does **not** make patient positioning and preparation obsolete

- Intra-fraction motion
- Rotational and deformation errors
- Off-line protocols
- **Moving the organs at risk away from target volume**

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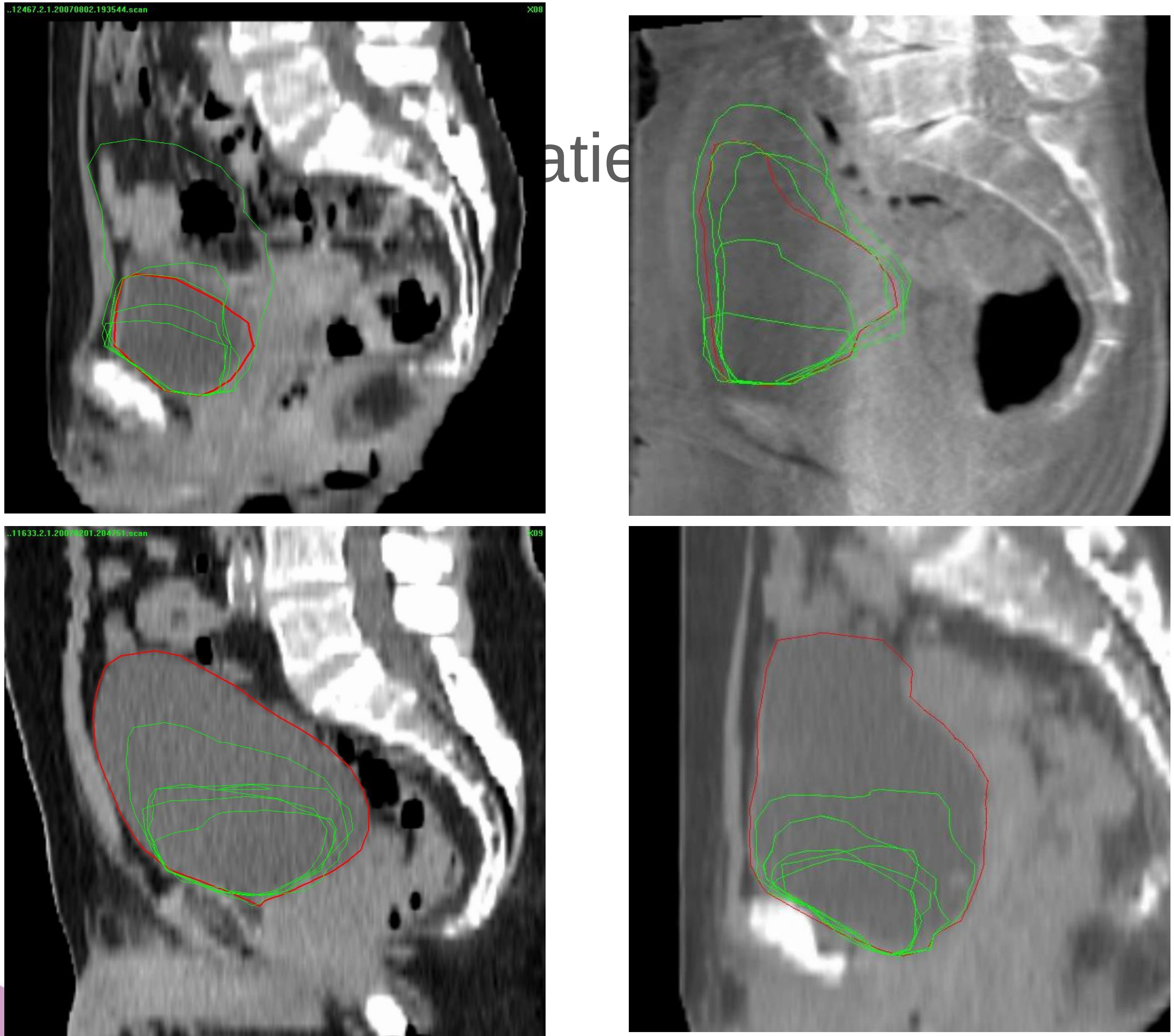
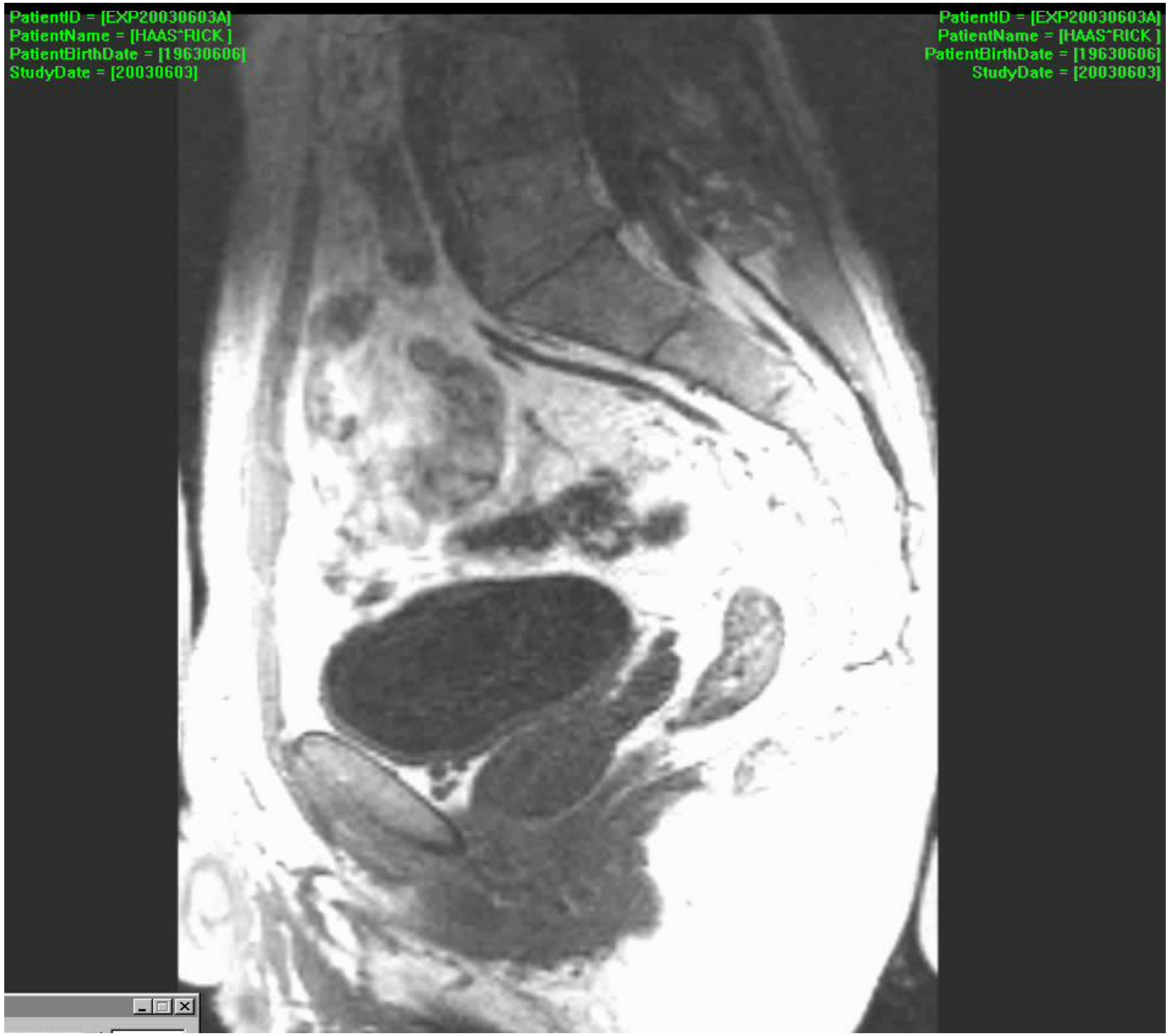
Conclusie

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

‘Recommendations for organ depending optimized fixation systems’ atie





Bony anatomy match

Bladder filling in 1 hour

MRI scans

Bladder filling in 1 hour

Healthy volunteer

Image Guided Proton Therapy

Jan-Jakob Sonke

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Acknowledgements

- Martijn Engelsman
- Tony Lomax
- Hanne Kooij
- Coen Rasch

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Proton Therapy

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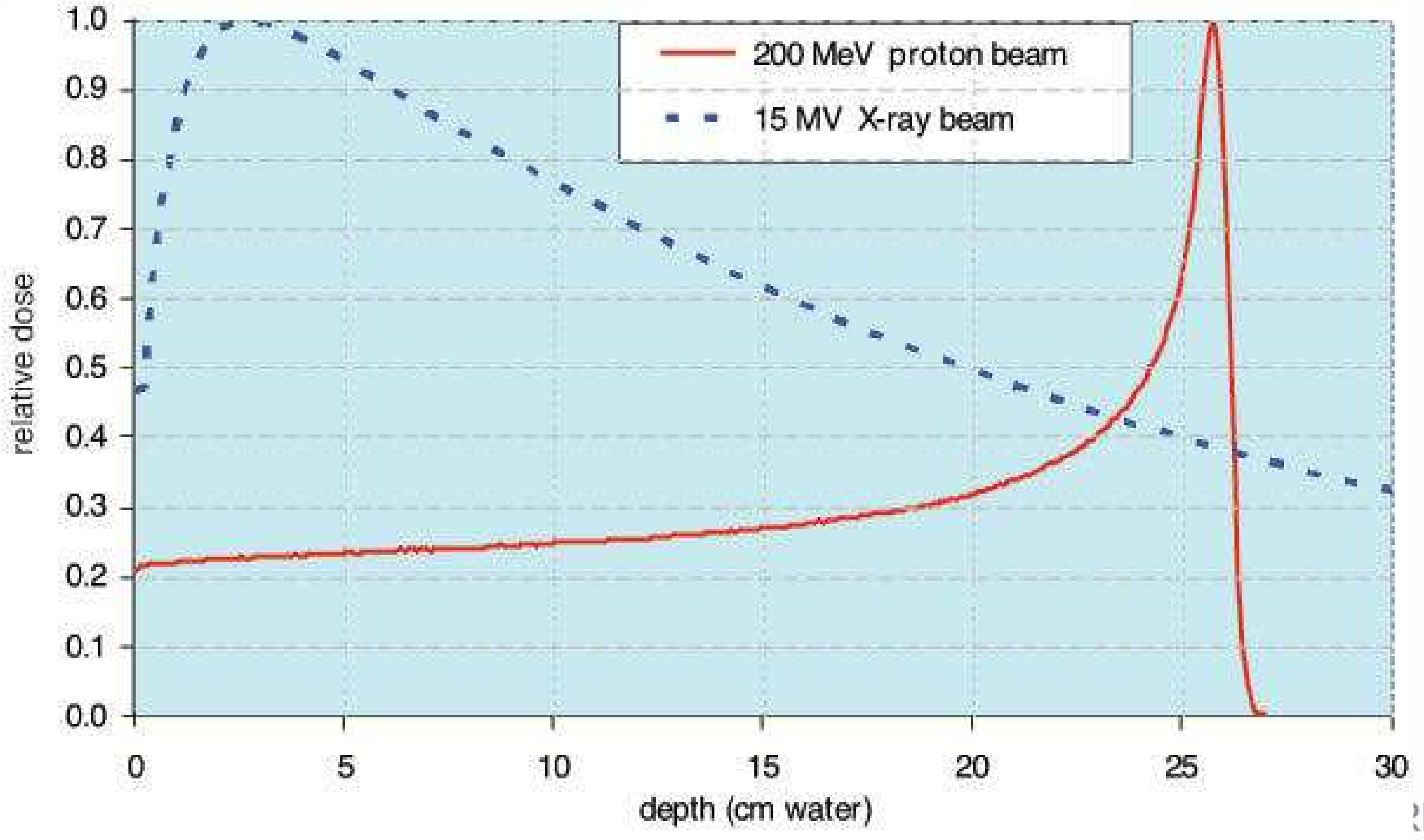
Protons versus photons
Favorable beam properties: Bragg peak



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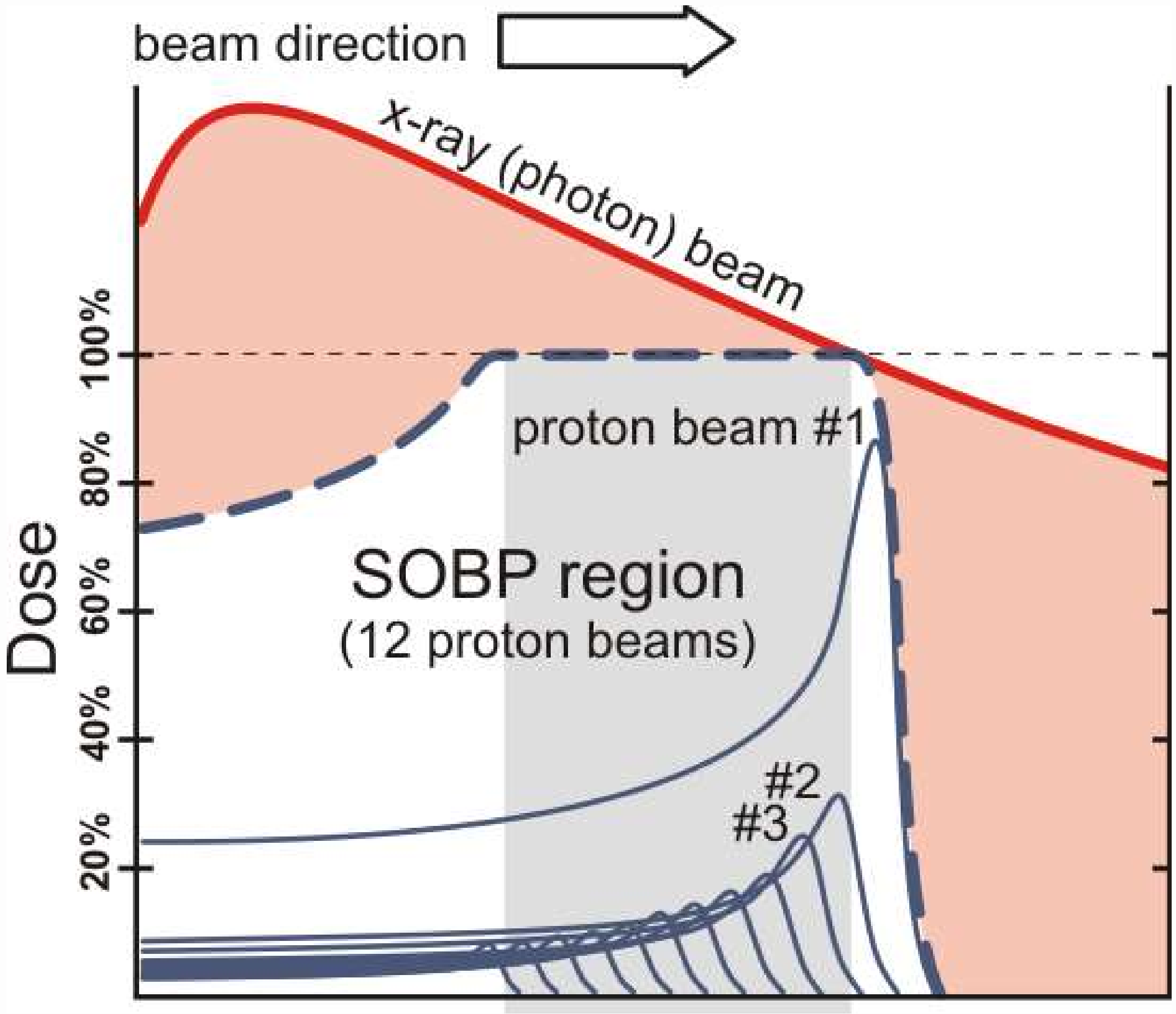
medicalphysicsweb.org

Protons versus photons
Favorable beam properties: Bragg peak



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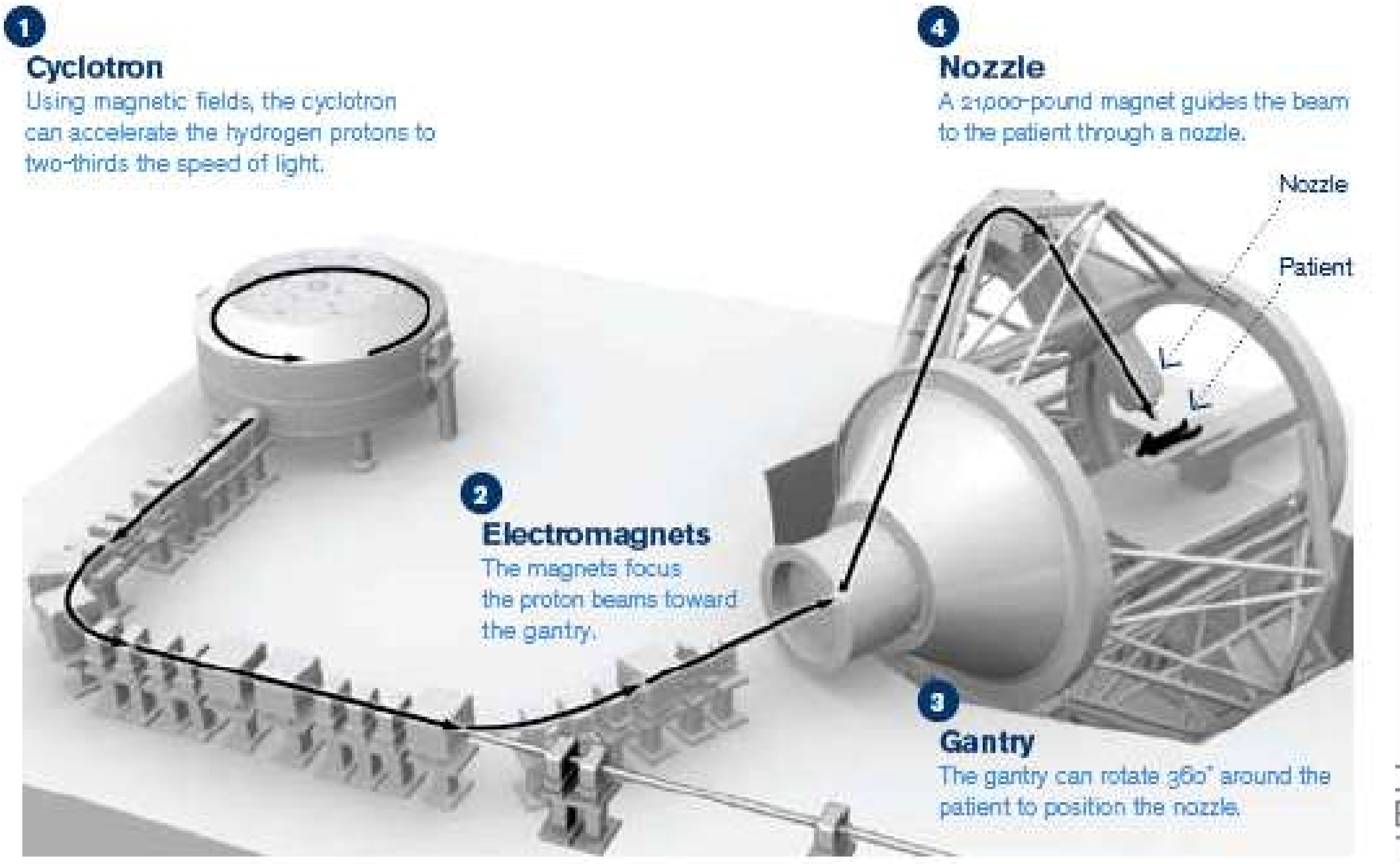
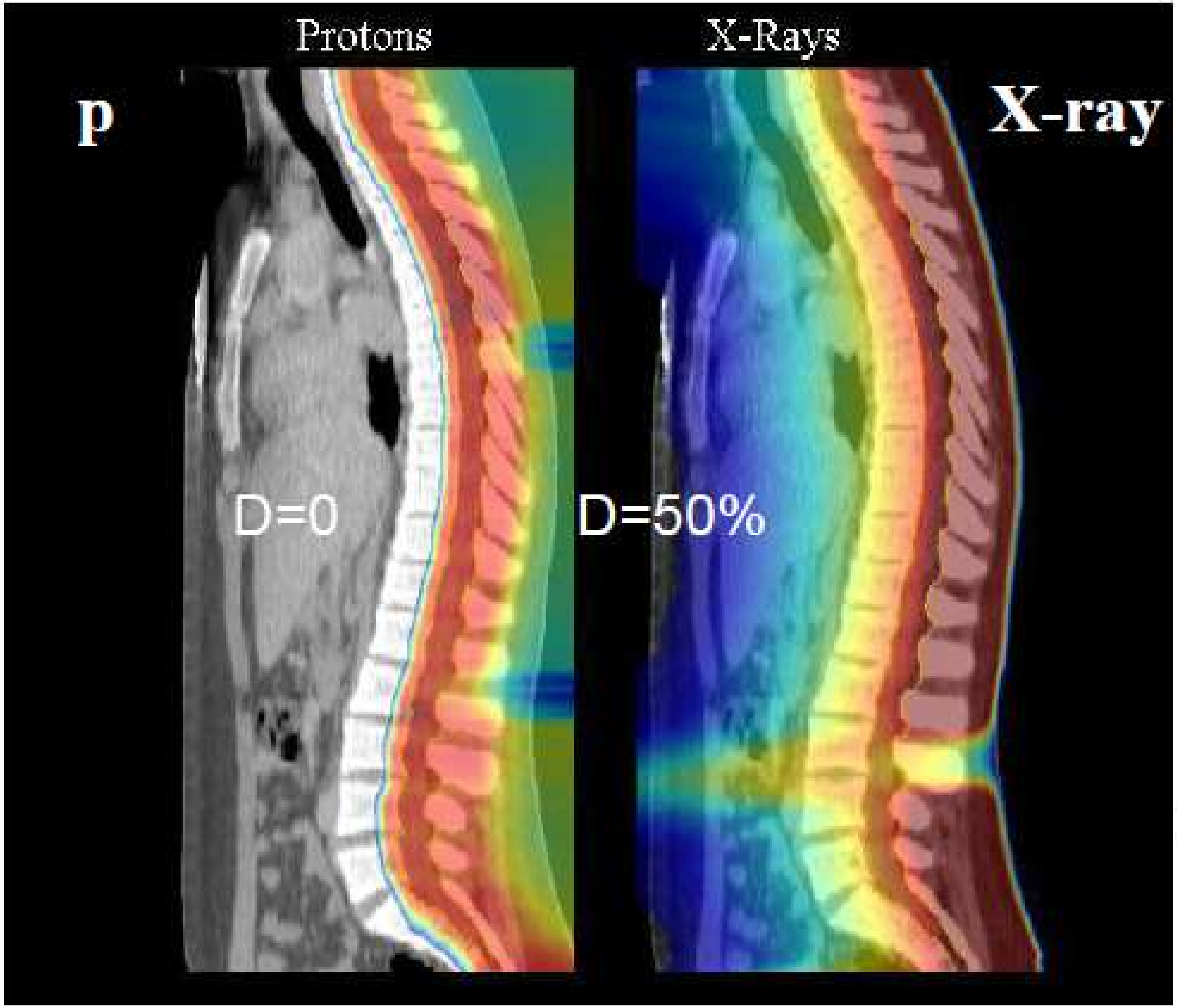
en.wikipedia.org/wiki/Proton_therapy

Large Facilities



symmetrymagazine.org

Craniospinal irradiation



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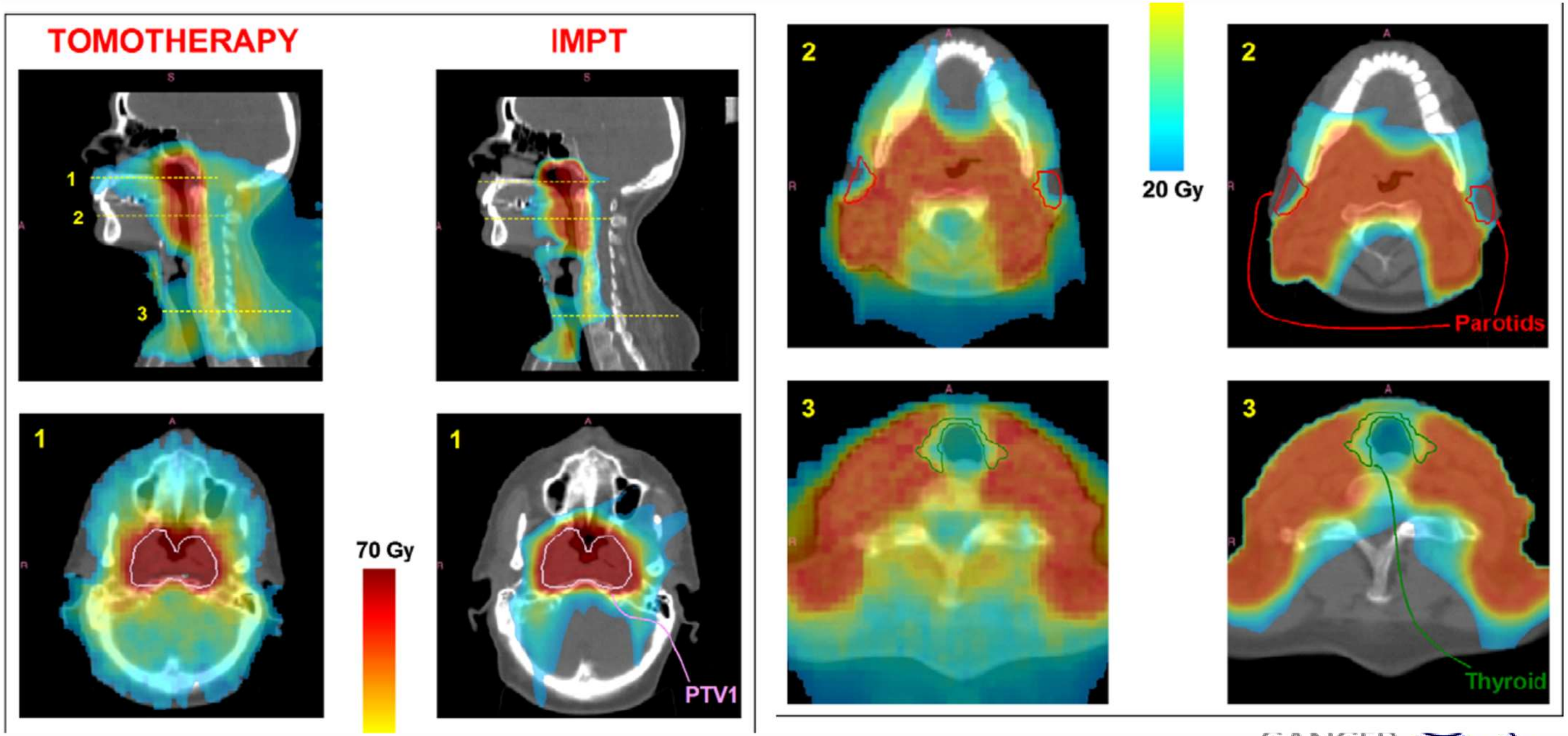
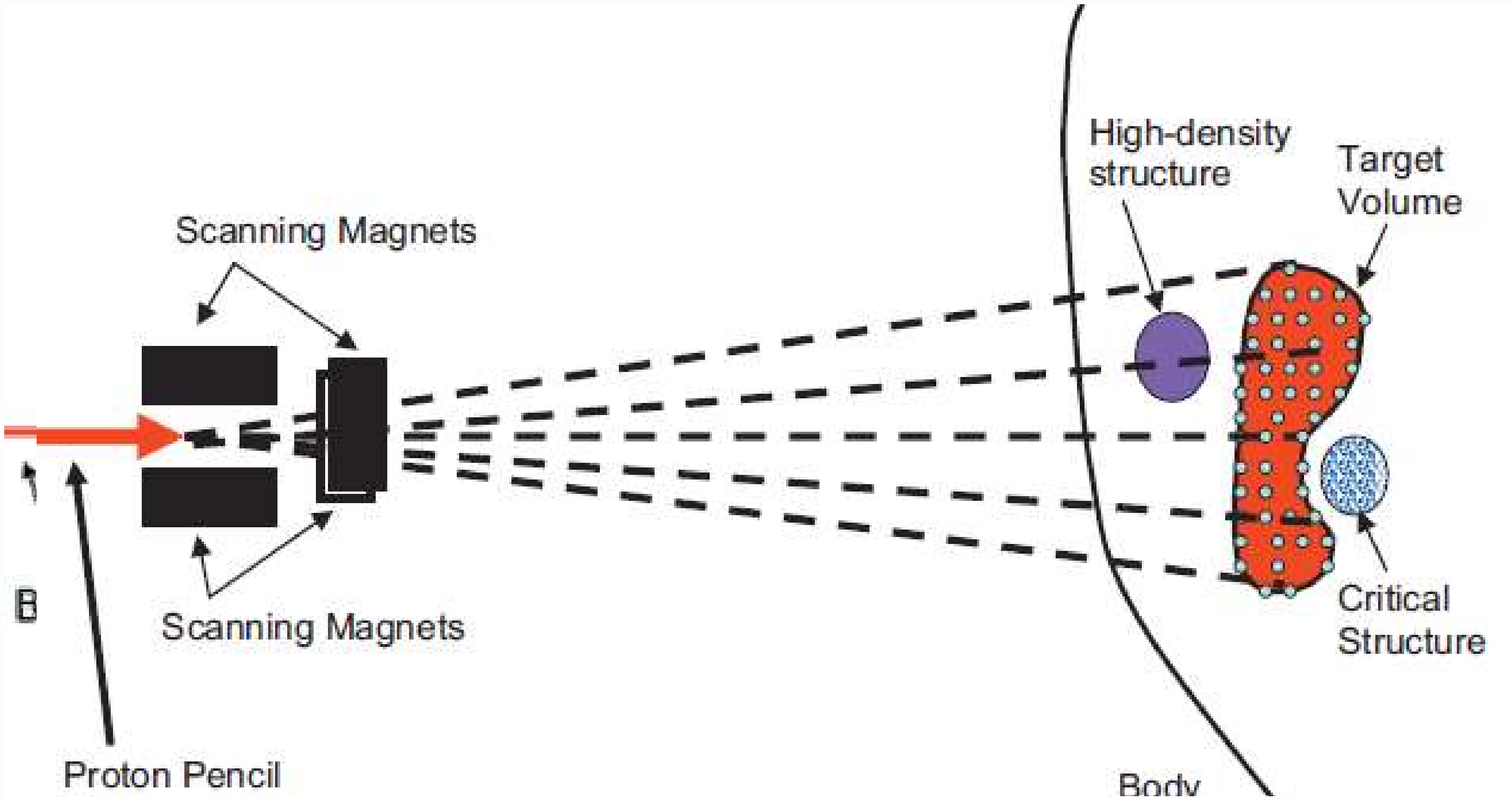
Tomo vs Proton nasopharynx



Widesott et al. 2009

Proton Delivery Systems

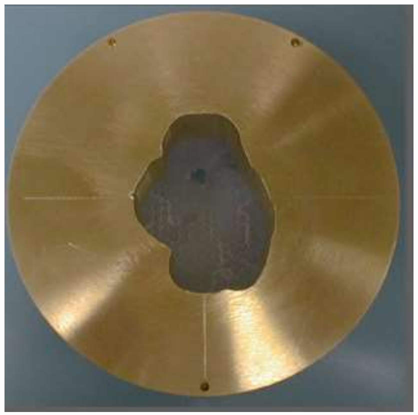


Pencil Beam Scanning

Double scattering versus Scanning

Double Scattering

- Distal conformality
- Easier to QA
- No intensity modulation
- Difficult for dose painting
- Time consuming



Scanning

- Distal + proximal conformality
- More difficult QA
- Intensity Modulation
- Dose painting
- Faster to deliver \ higher doserate
- Easier to adapt

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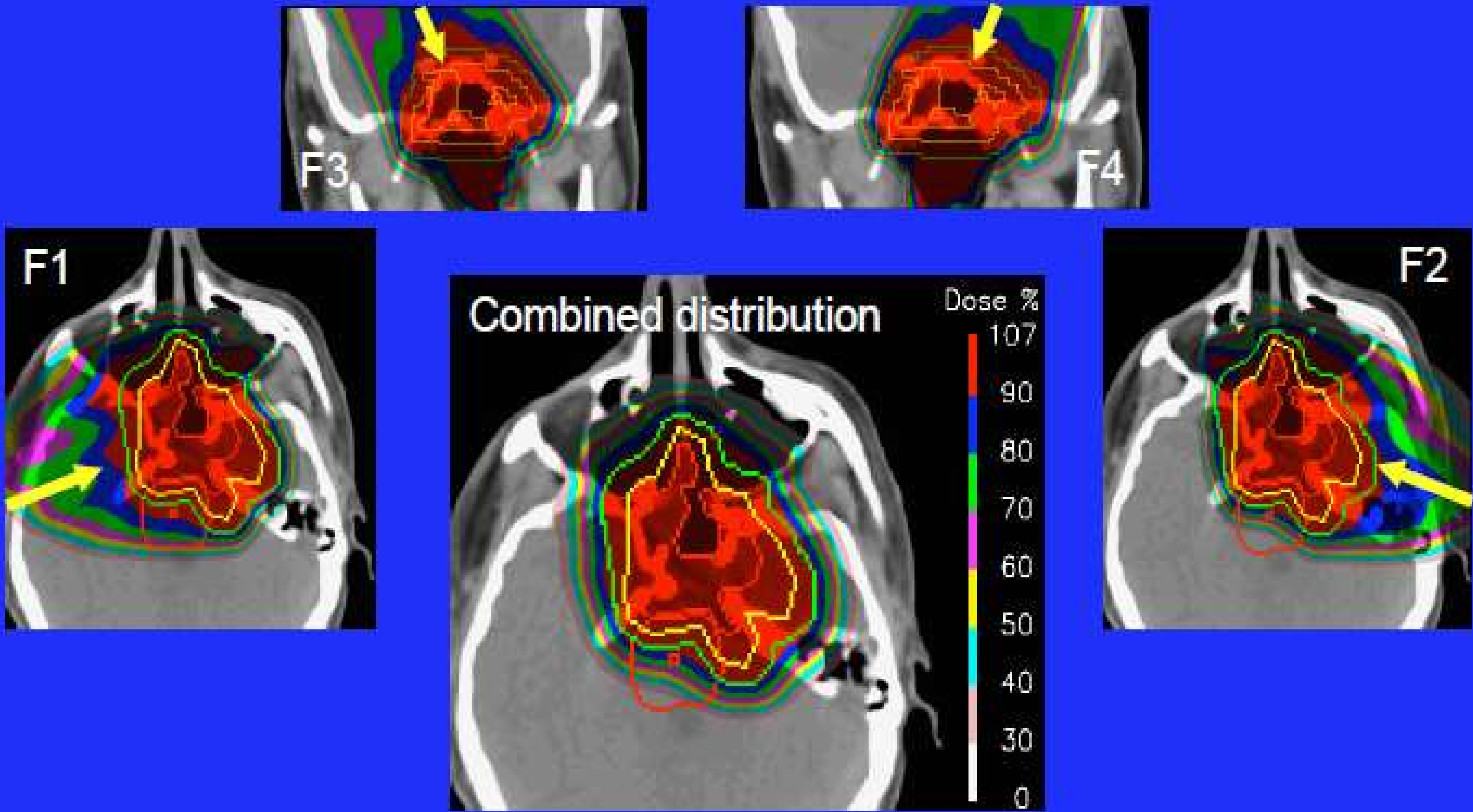
Single Field, Uniform Dose (SFUD)

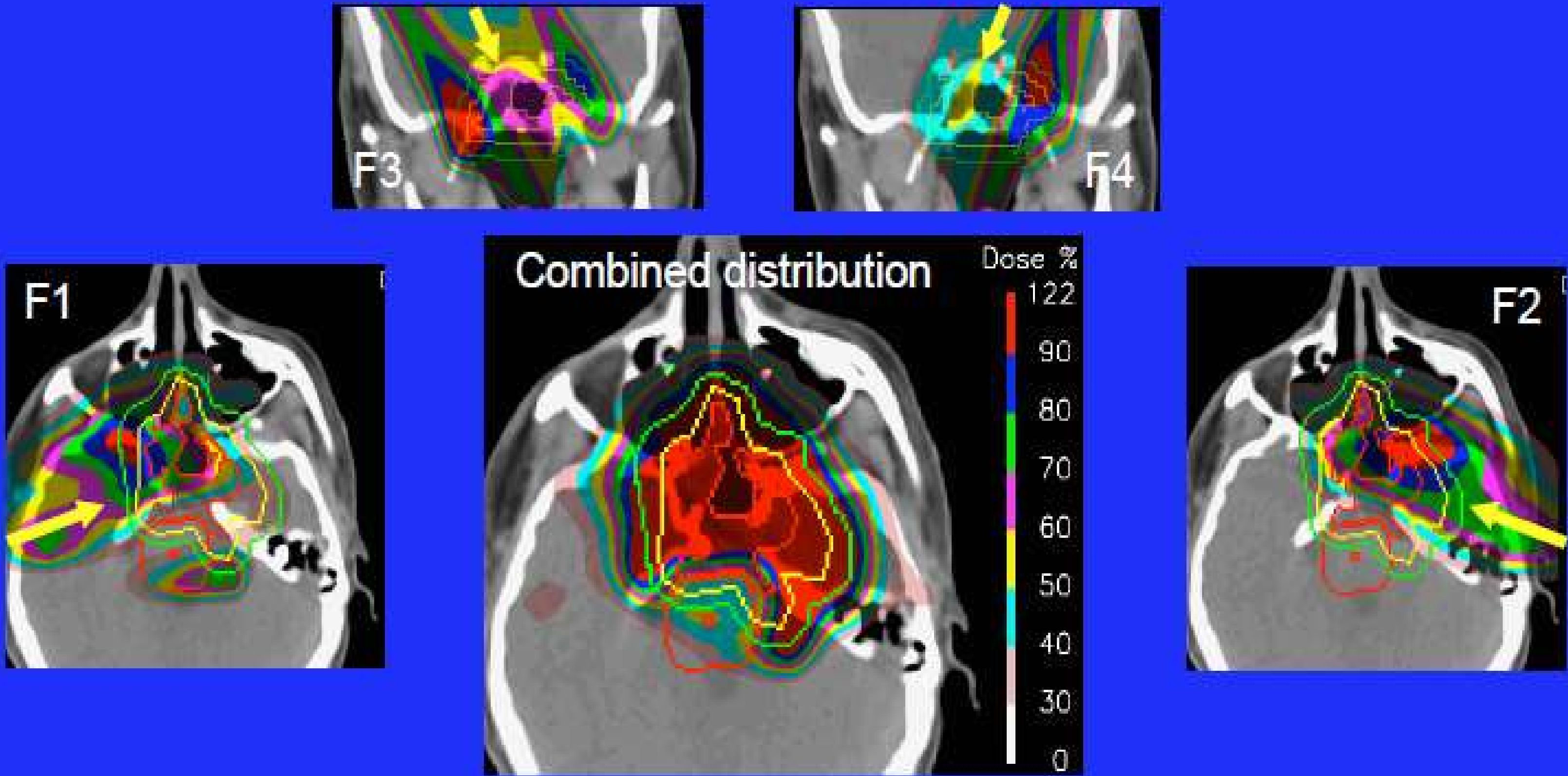
PAUL SCHERRER INSTITUT

A SFUD plan consists of the addition of one or more individually optimised fields.



Note, each individual field is homogenous across the target volume

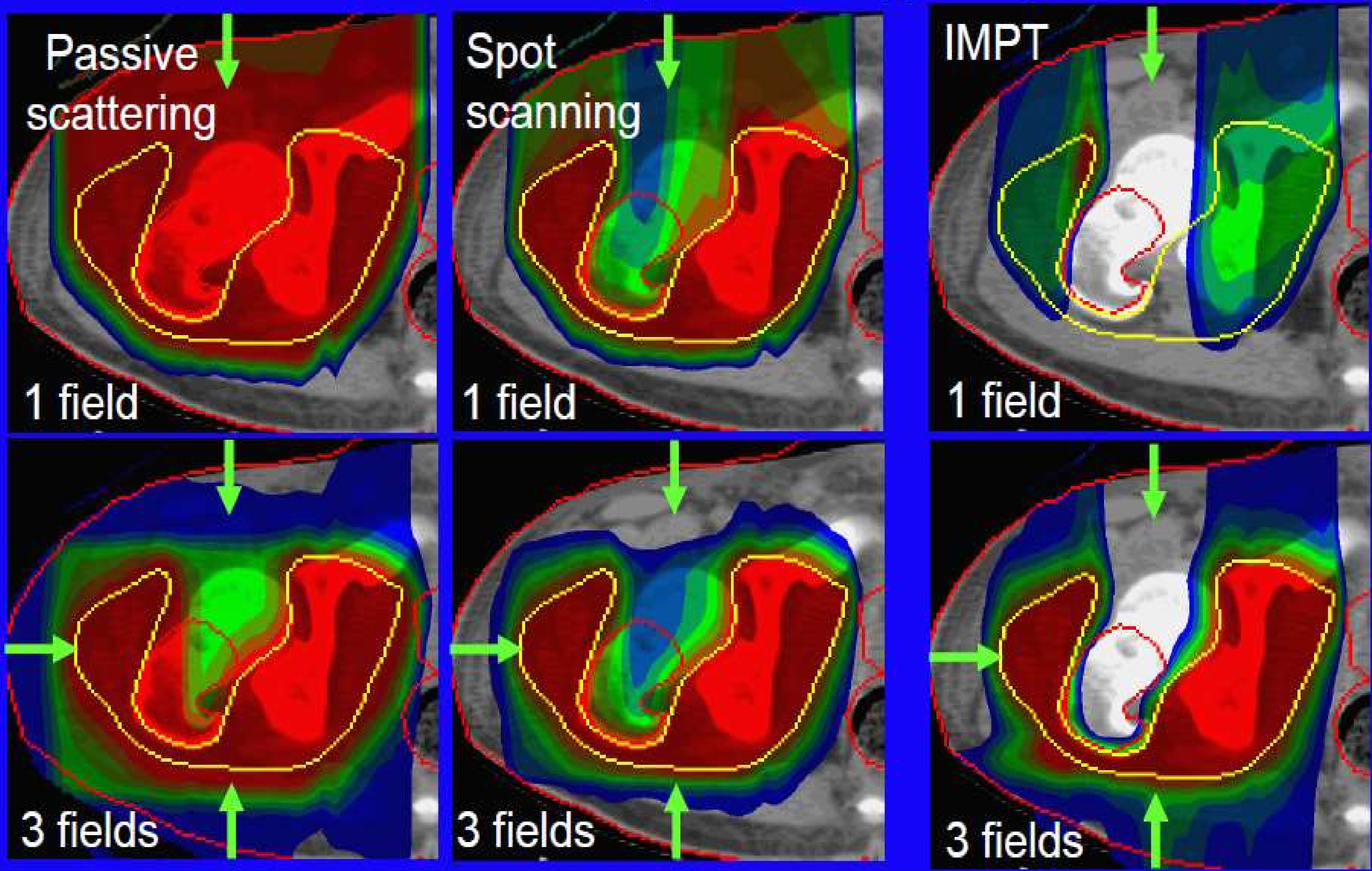
The simultaneous optimisation of all Bragg peaks from all incident beams. E.g..



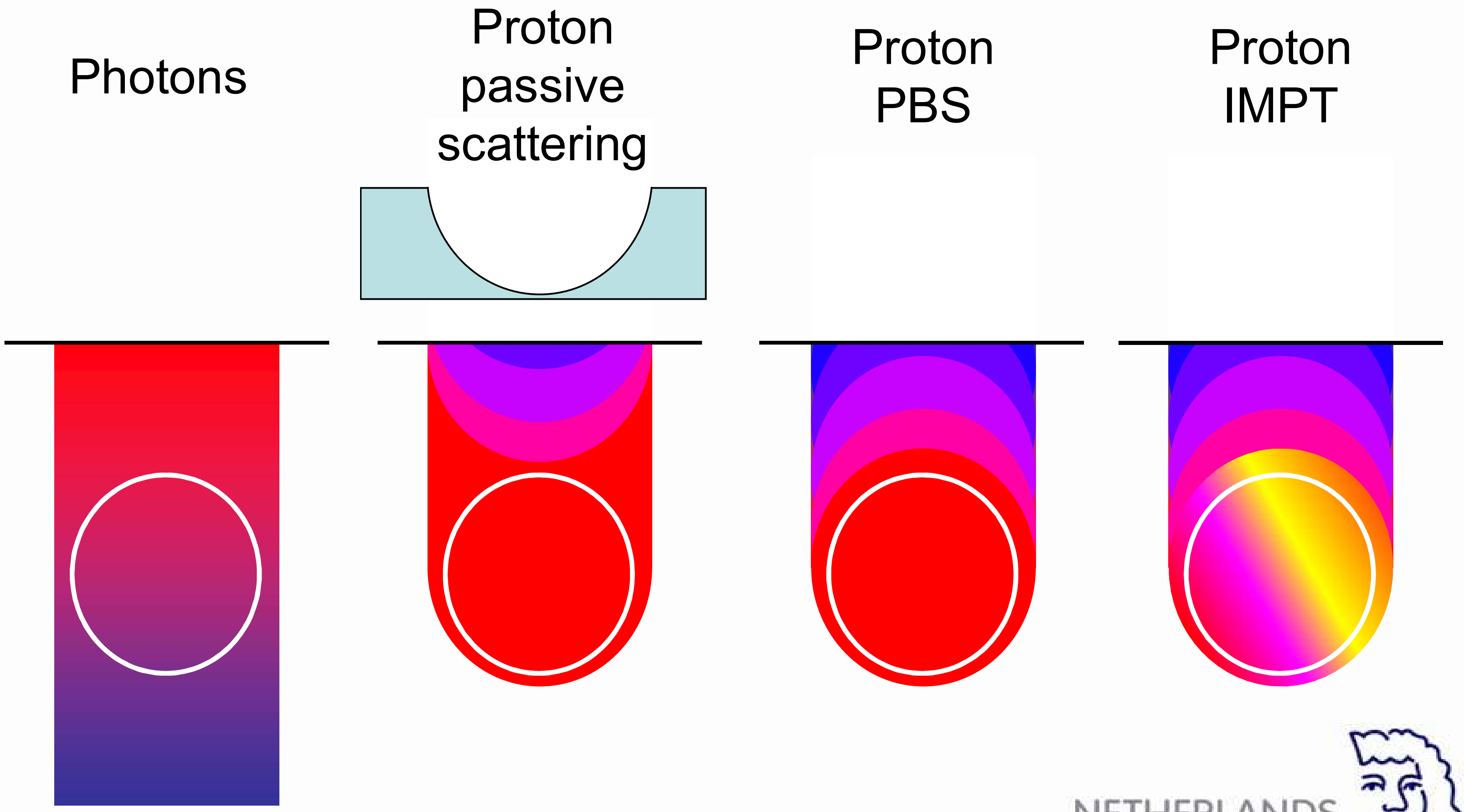
Lomax 1999, PMB 44: 185-205

Intensity Modulated Proton Therapy (IMPT)

The three 'orders' of proton therapy compared



Dosimetric Advantage



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Courtesy of Martijn Engelsman

Proton Penumbra

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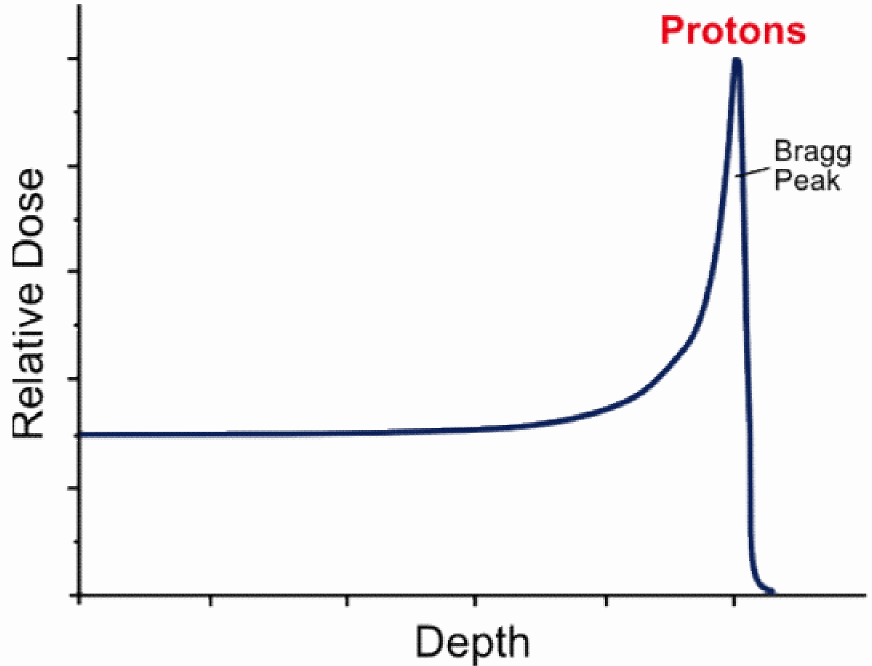
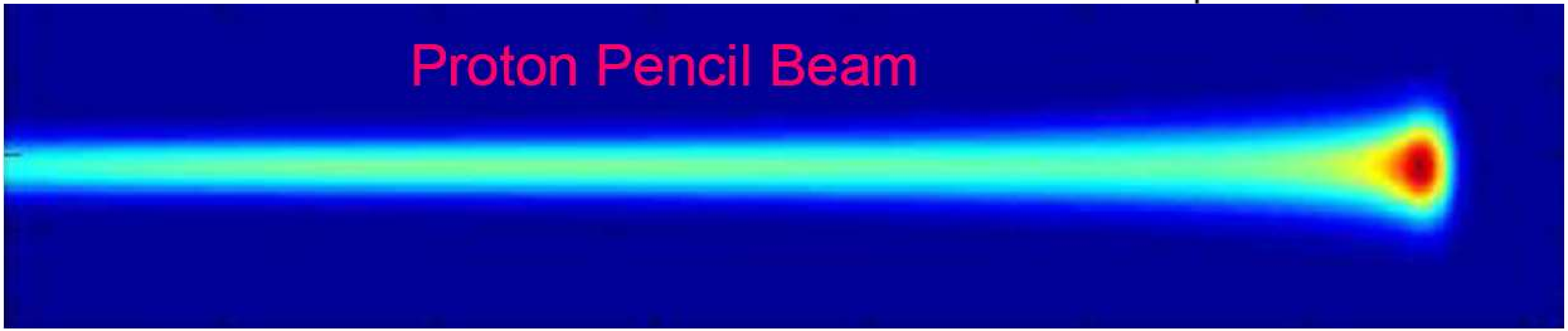
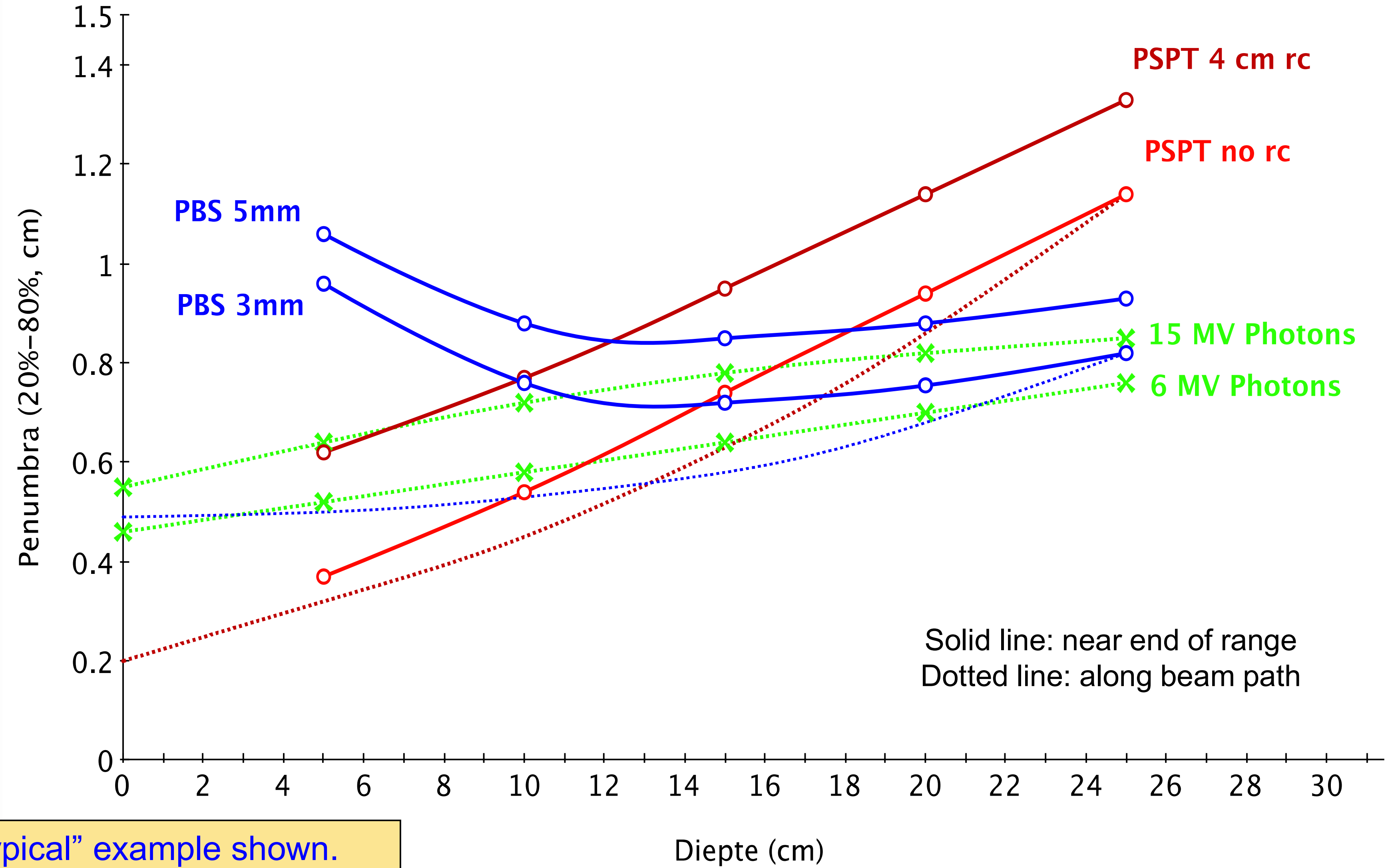
Lateral Penumbra





Paganetti, Physics of Particles, PTCOG 52

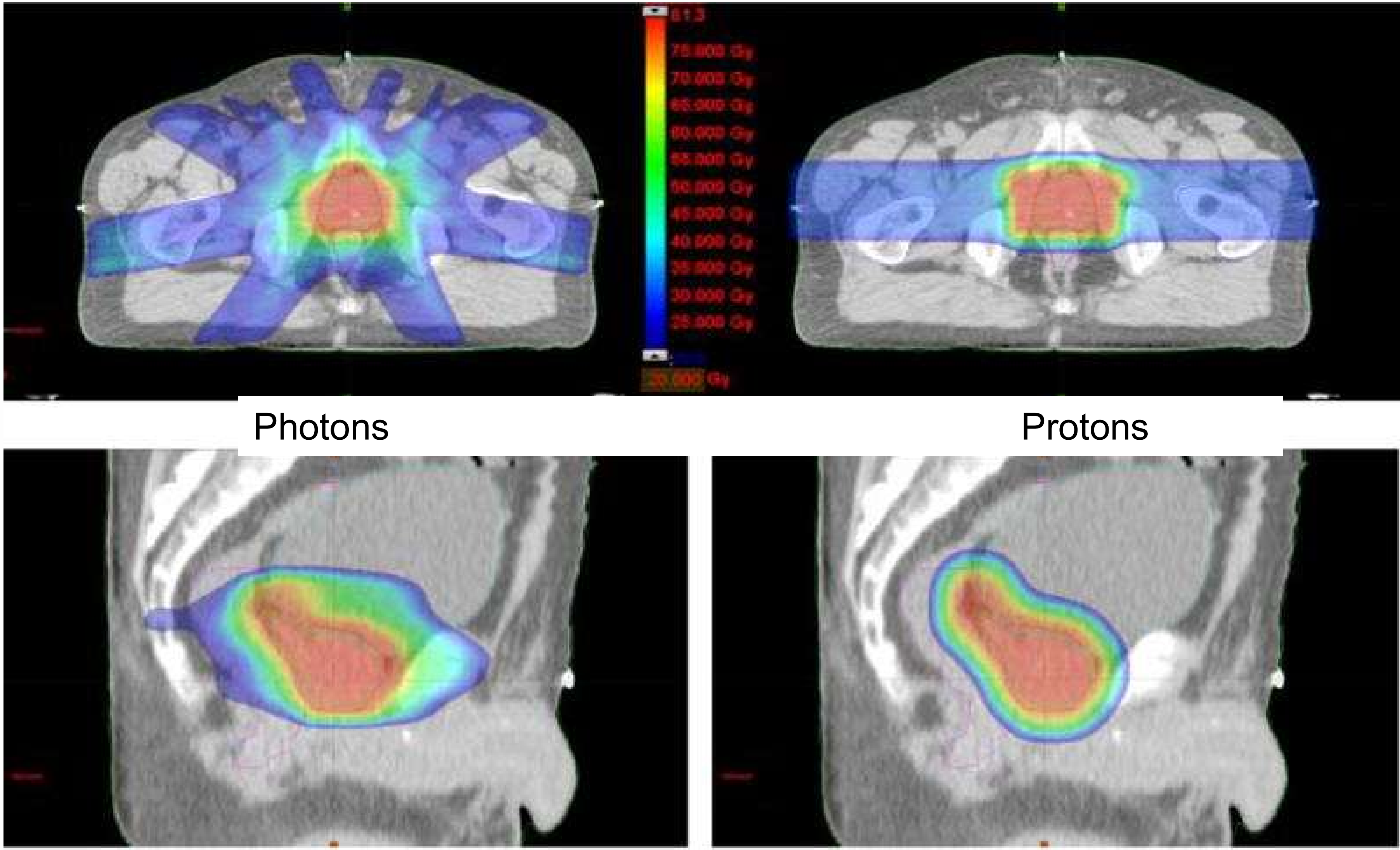
Lateral dose fall-off



"Typical" example shown. Penumbra depends heavily on beam-line layout/optics.

Courtesy of Martijn Engelsman

IMRT vs Proton, prostate



Zhang et al., IJROBP, 2007

Proton Benefit

- Proton penumbra not steeper than photons
  - Dose distribution in high dose region not superior than photons
  - OAR near target with max dose constraint not spared
- Advantage manifested in intermediate and low dose levels
- Model based advantage most likely in OAR with considerable volume effects:

  +Lung, Liver, Parotids

  - Spinal Cord, Rectum, Brainstem

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Range Uncertainties

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Protons Stop

Protons Stop … somewhere

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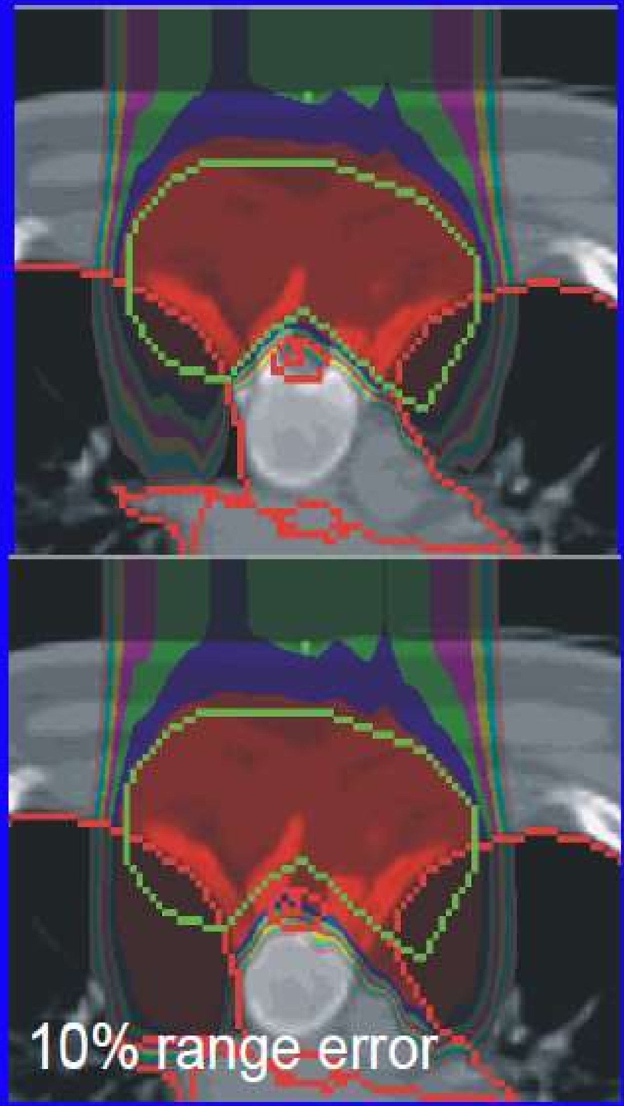
Dealing with uncertainties – range uncertainties.

The advantage of protons is that they stop.

The disadvantage of protons is that we don't always know where…

Range uncertainty will generally be systematic!



Sources of Range Uncertainty

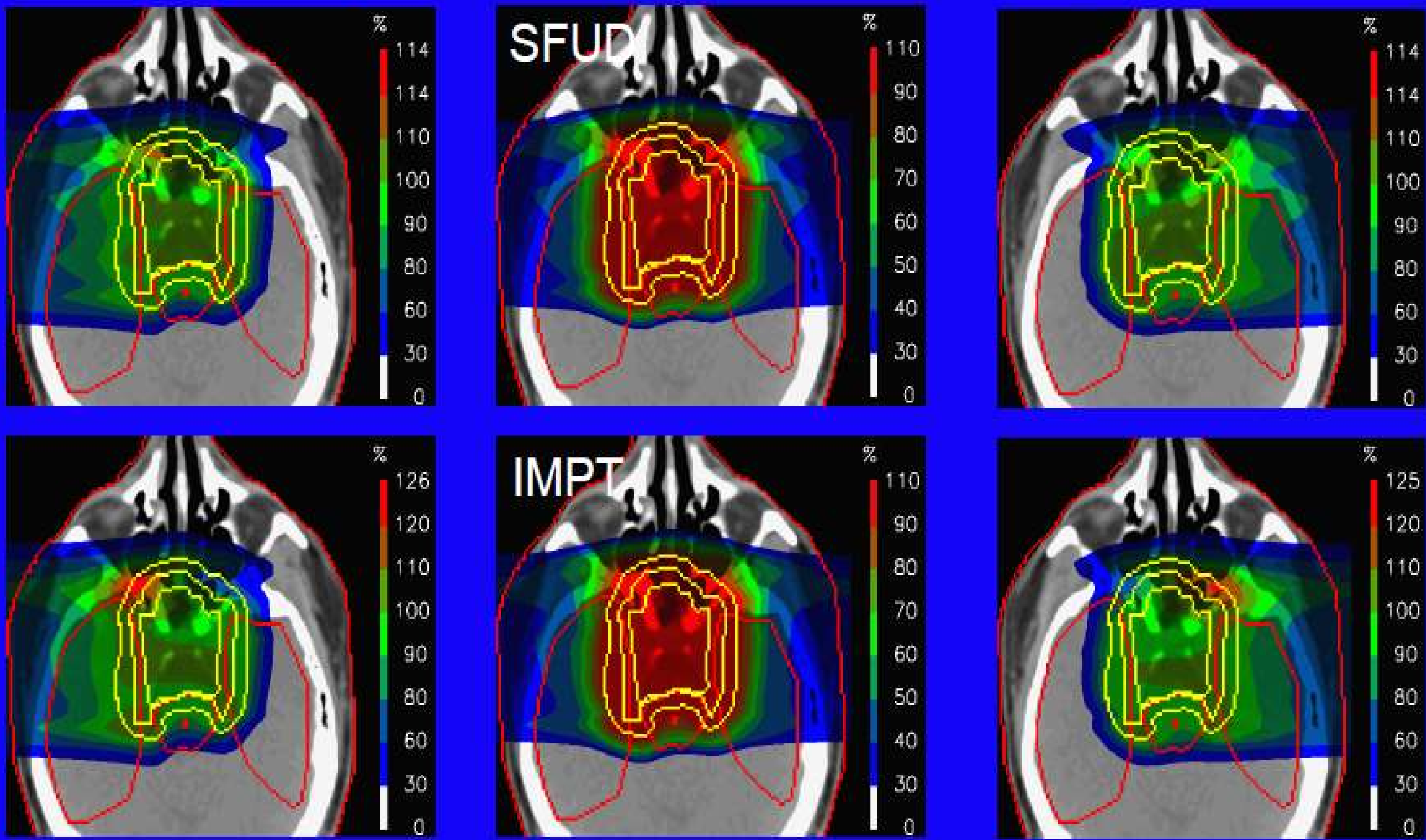
Table 1. Estimated proton range uncertainties and their sources and the potential of Monte Carlo for reducing the uncertainty. Paganetti and Goitein (2000), Robertson *et al* (1975) and Wouters *et al* (1996). The estimations are average numbers based on 1.5 standard deviations. Extreme cases, such as lung treatments, might show bigger uncertainties.

Source of range uncertainty in the patient	Range uncertainty without Monte Carlo	Range uncertainty with Monte Carlo
Independent of dose calculation		
Measurement uncertainty in water for commissioning	± 0.3 mm	± 0.3 mm
Compensator design	± 0.2 mm	± 0.2 mm
Beam reproducibility	± 0.2 mm	± 0.2 mm
Patient setup	± 0.7 mm	± 0.7 mm
Dose calculation		
Biology (always positive) ^	$+\sim 0.8\%$	$+\sim 0.8\%$
CT imaging and calibration	$\pm 0.5\%$[a]	$\pm 0.5\%$[a]
CT conversion to tissue (excluding I-values)	$\pm 0.5\%$[b]	$\pm 0.2\%$[g]
CT grid size	$\pm 0.3\%$[c]	$\pm 0.3\%$[c]
Mean excitation energy (I-values) in tissues	$\pm 1.5\%$[d]	$\pm 1.5\%$[d]
Range degradation; complex inhomogeneities	-0.7%[e]	$\pm 0.1\%$
Range degradation; local lateral inhomogeneities *	$\pm 2.5\%$[f]	$\pm 0.1\%$
Total (excluding *, ^)	$2.7\% + 1.2$ mm	$2.4\% + 1.2$ mm
Total (excluding ^)	$4.6\% + 1.2$ mm	$2.4\% + 1.2$ mm

Paganetti, PMB, 2012

Dealing with uncertainties – range uncertainties.

Range uncertainty for SFUD and IMPT plans

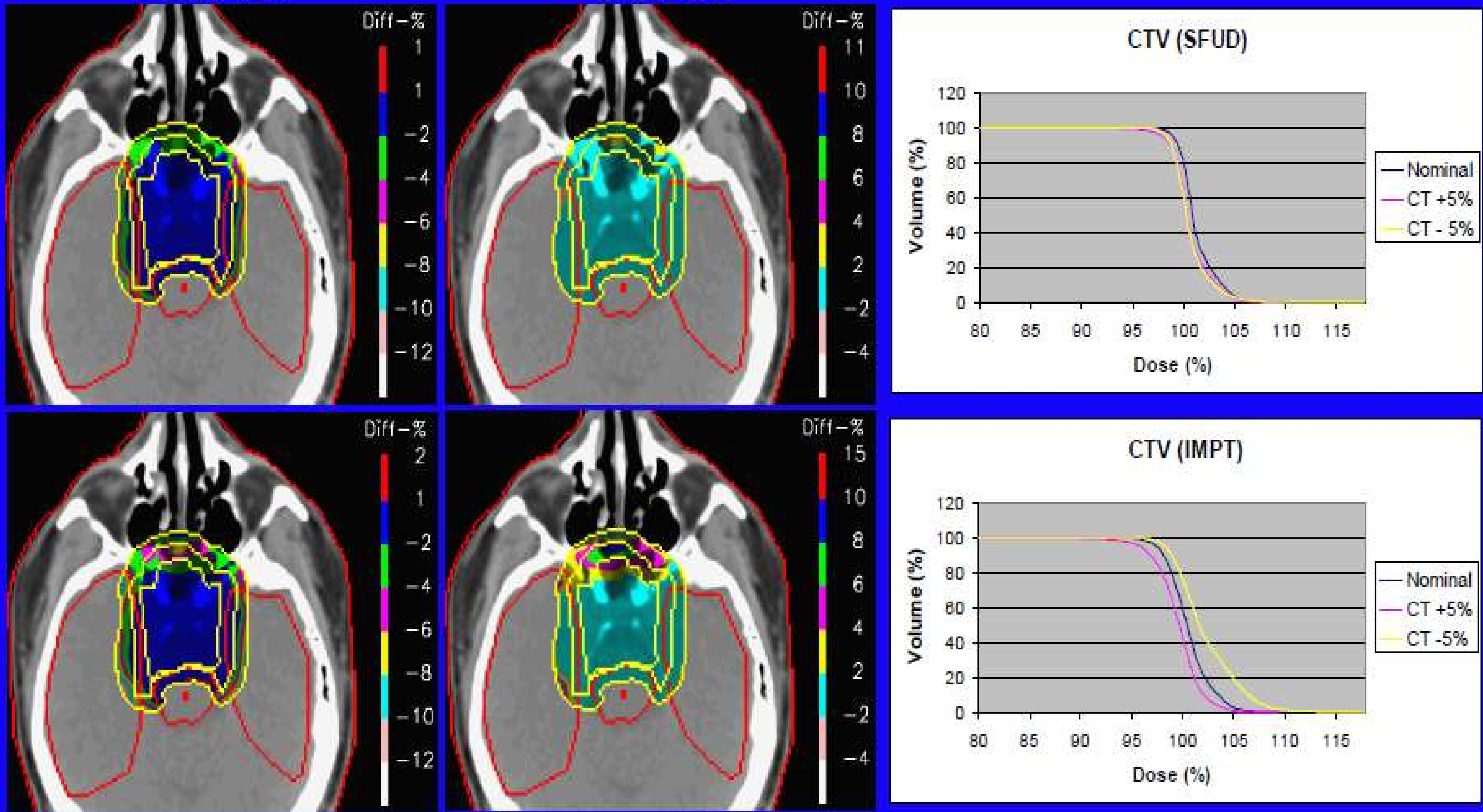


Lomax AJ (2007) in 'Proton and charged particle Radiotherapy', Lippincott, Williams and Wilkins

Dealing with uncertainties – range uncertainties.

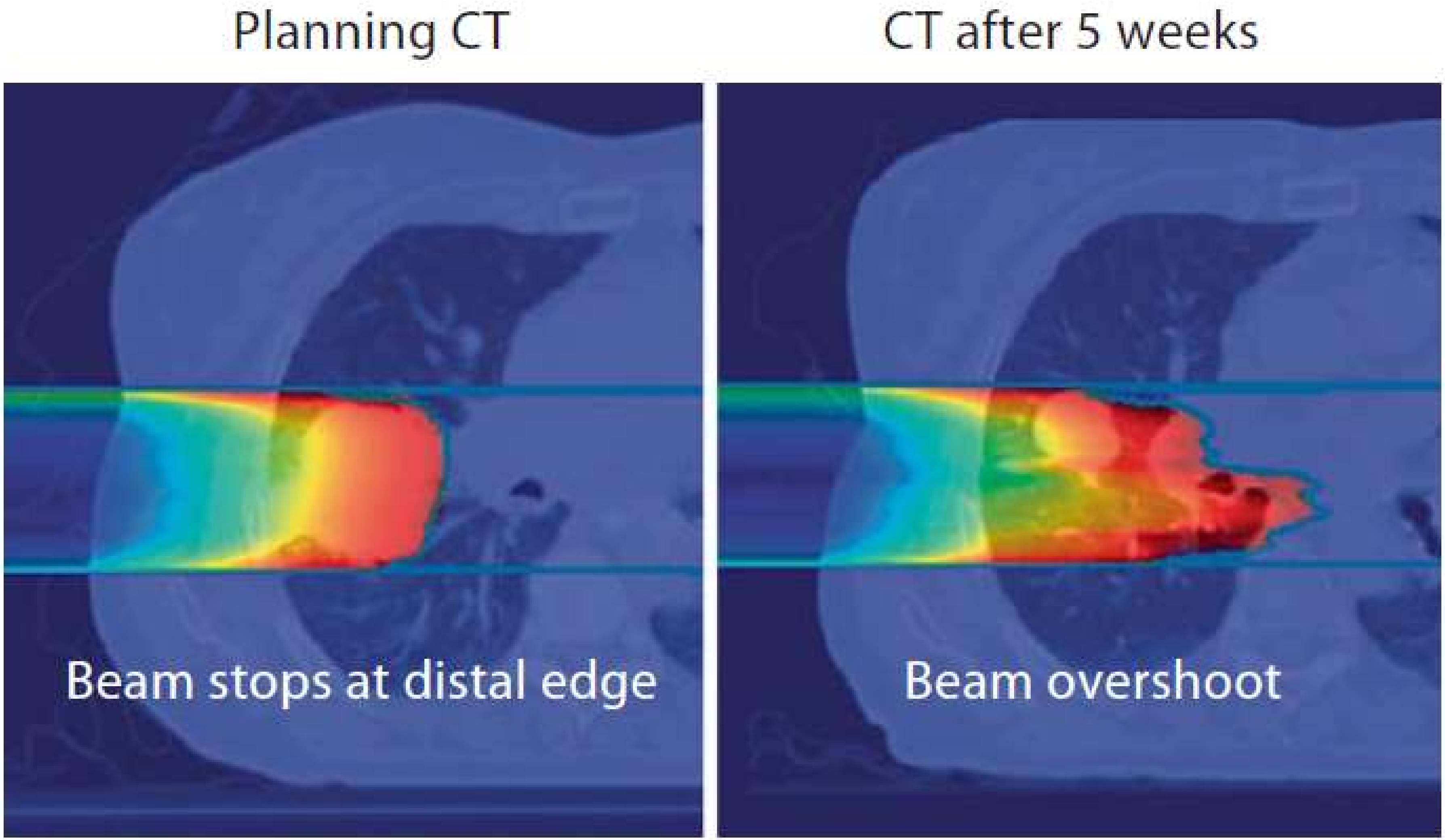
Range uncertainty for SFUD and IMPT plans

+5% CT　　　　-5% CT



Lomax AJ (2007) in 'Proton and charged particle Radiotherapy', Lippincott, Williams and Wilkins

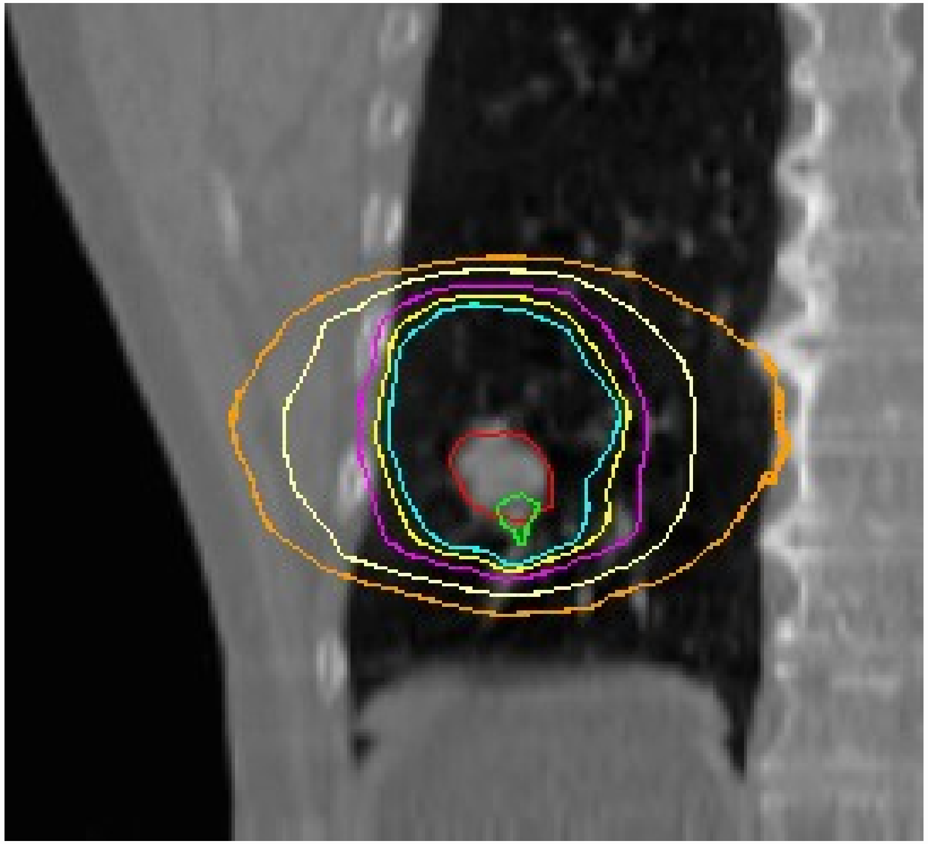
Anatomical Changes



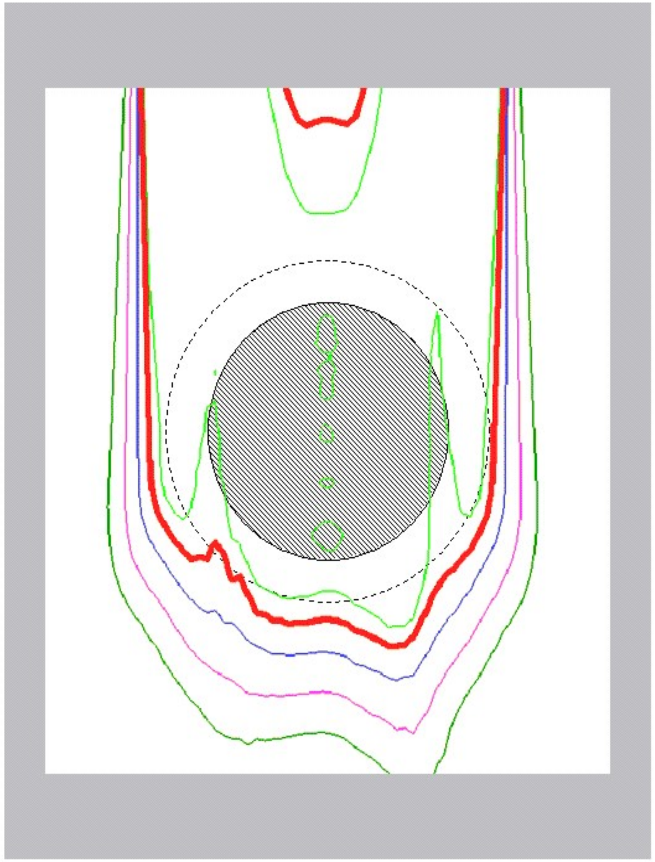
Mohan et al. Front Radiat Ther Oncol, 2011

Respiratory Motion

Photons



Protons



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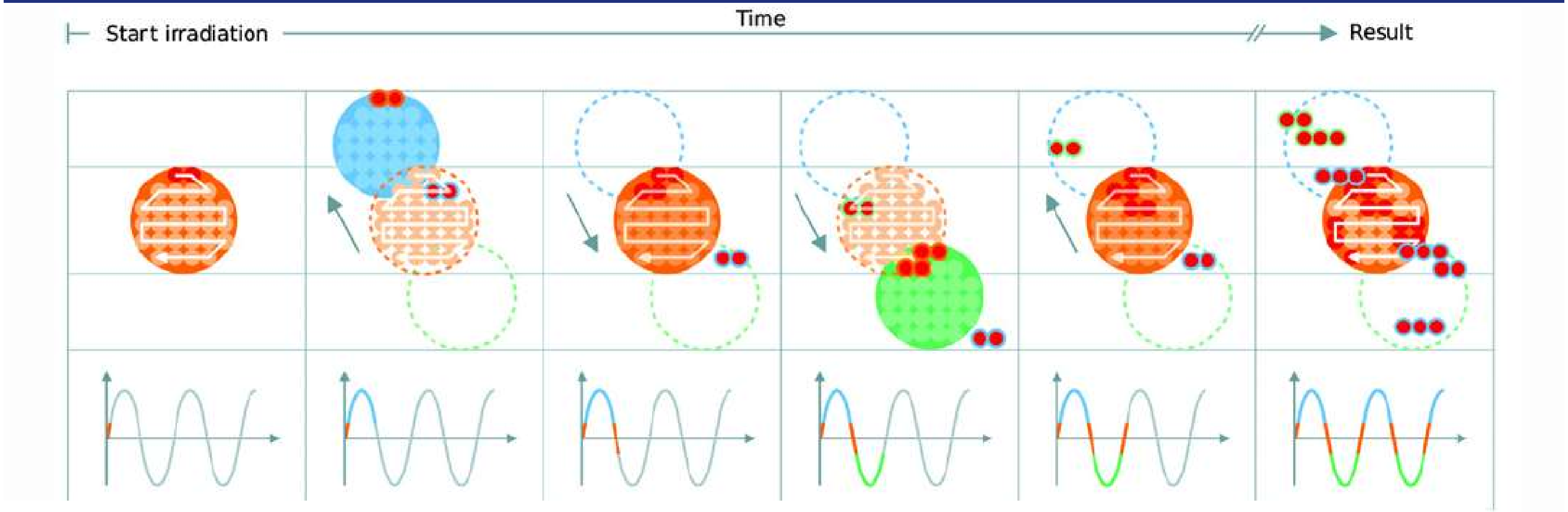
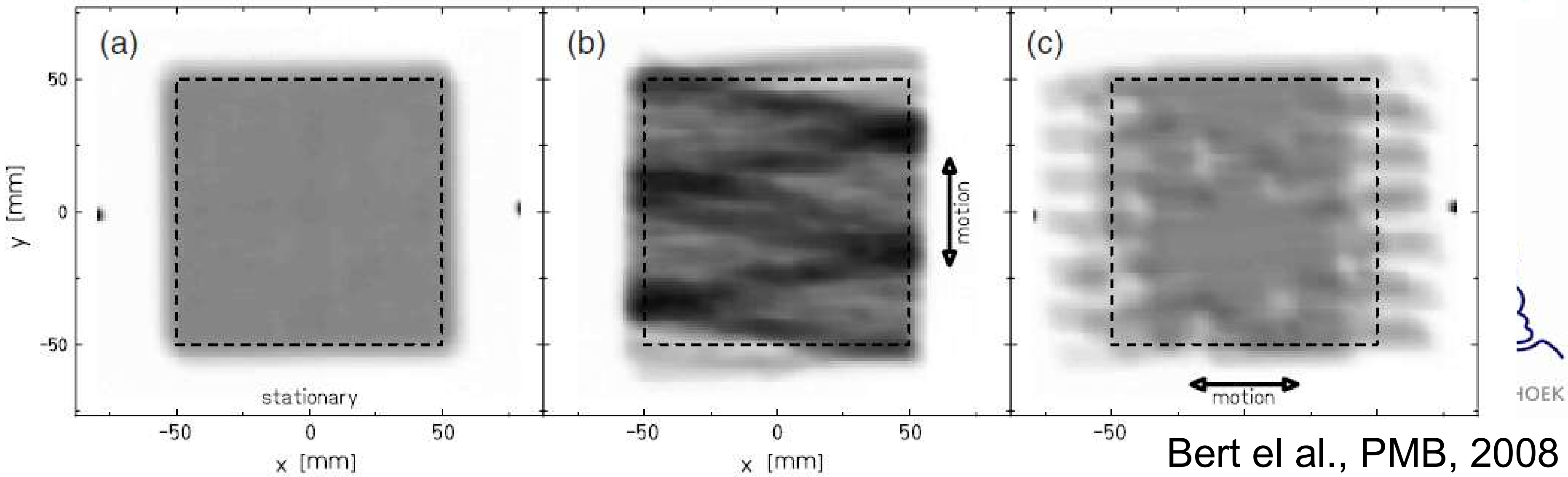
Courtesy of Martijn Engelsman

Interplay Effect

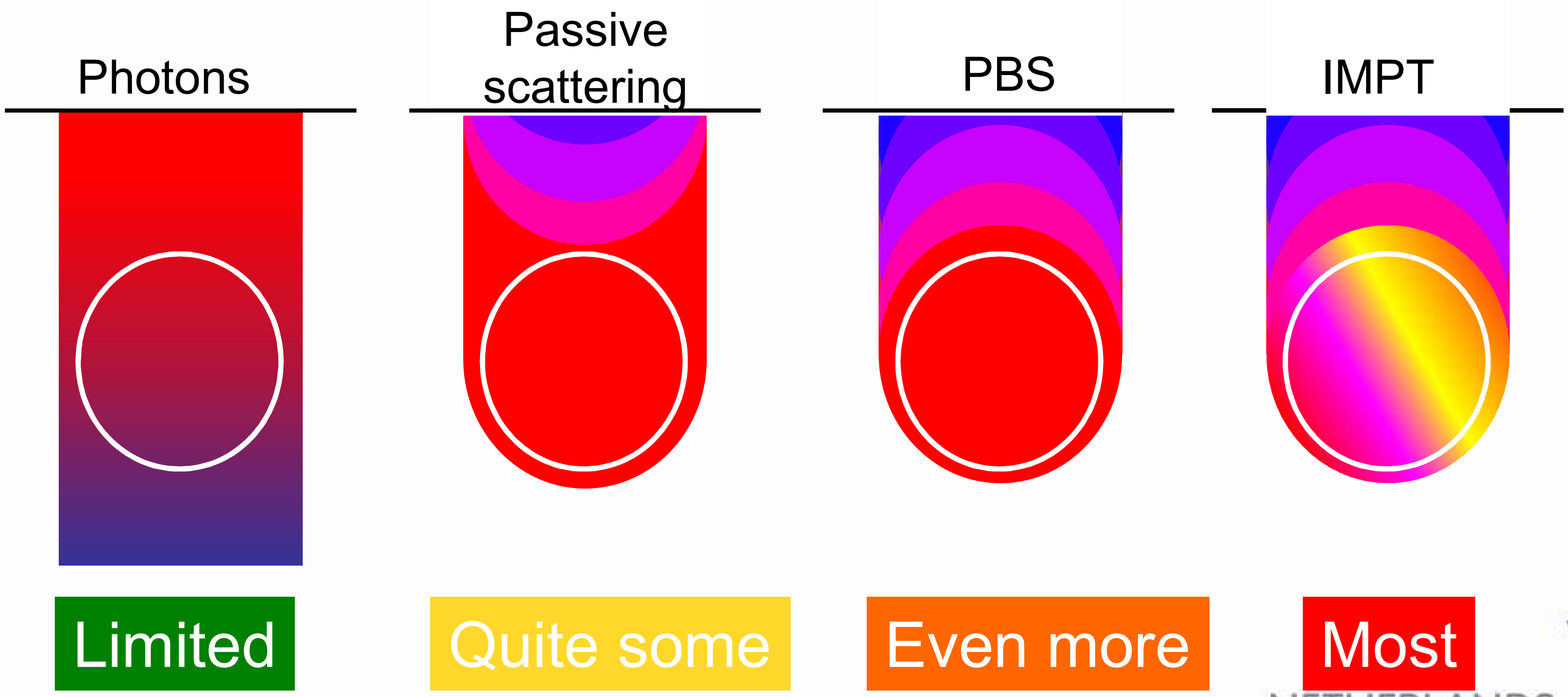




Bert el al., PMB, 2008

Sensitivity

To anatomical (density) changes, setup errors, interplay effect, etc.



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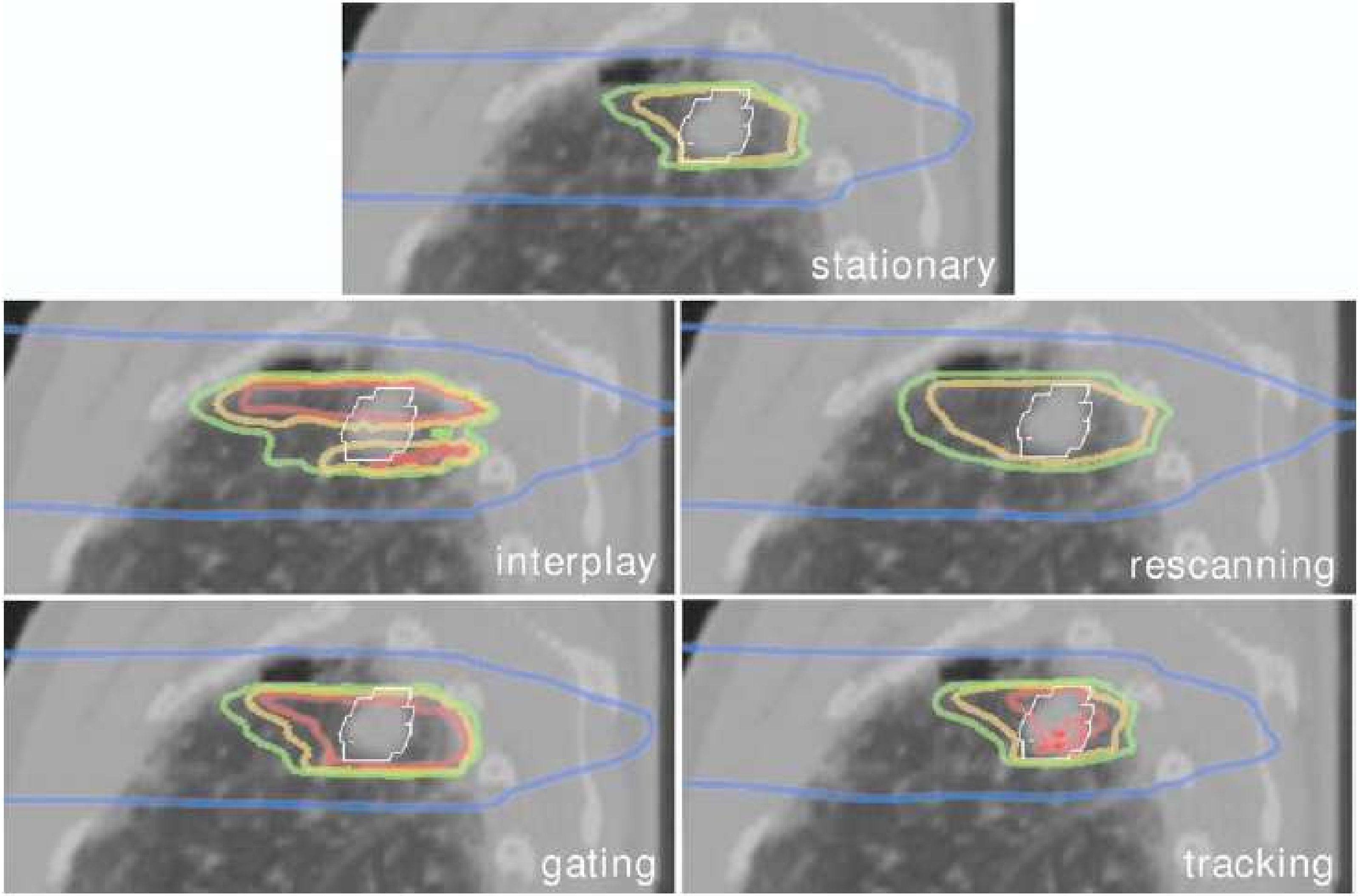
Courtesy of Martijn Engelsman

Motion Management



NHOEK

Rietzel et al, Med Phys, 2010

Margins

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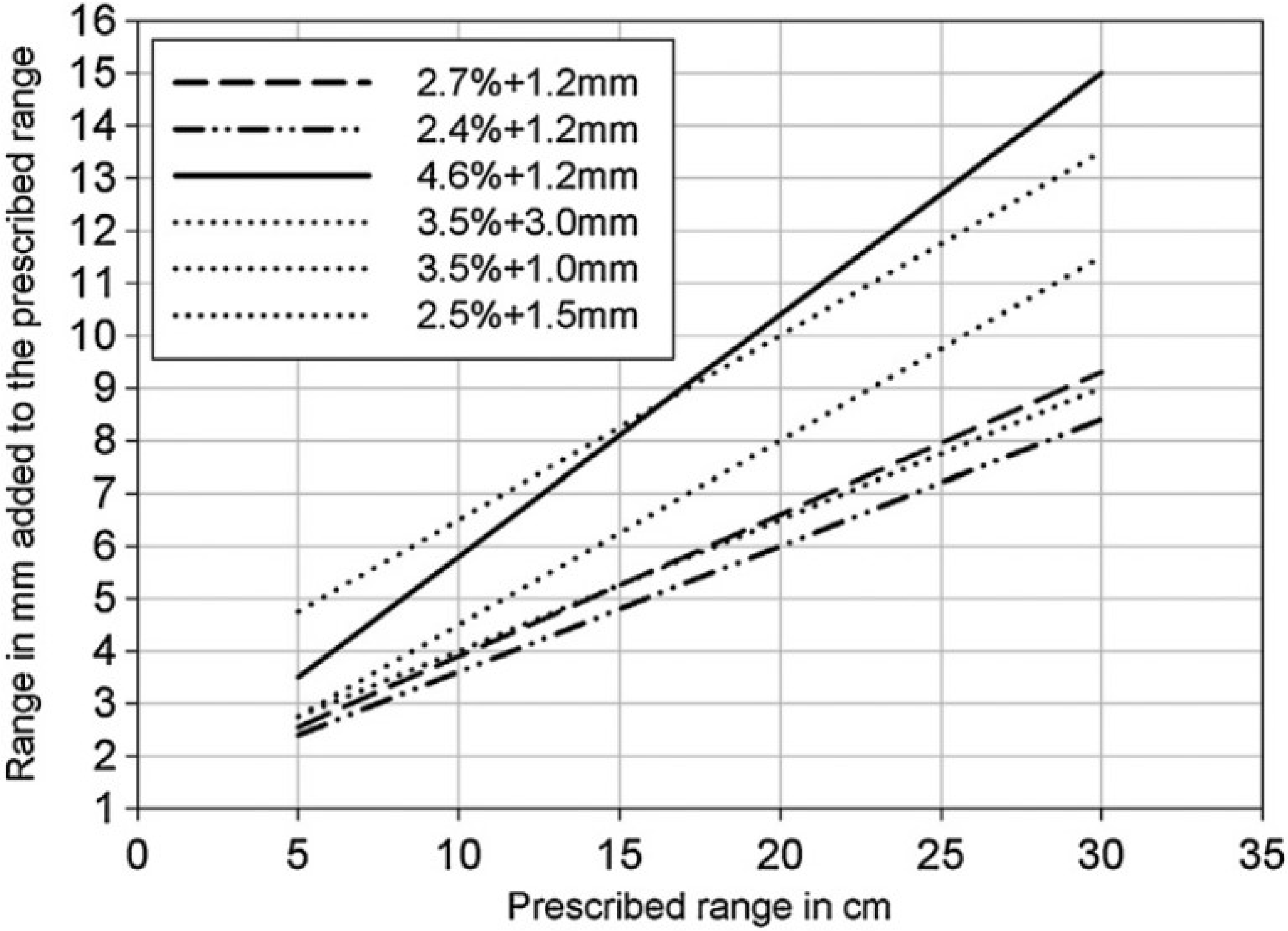
Margin for range uncertainties



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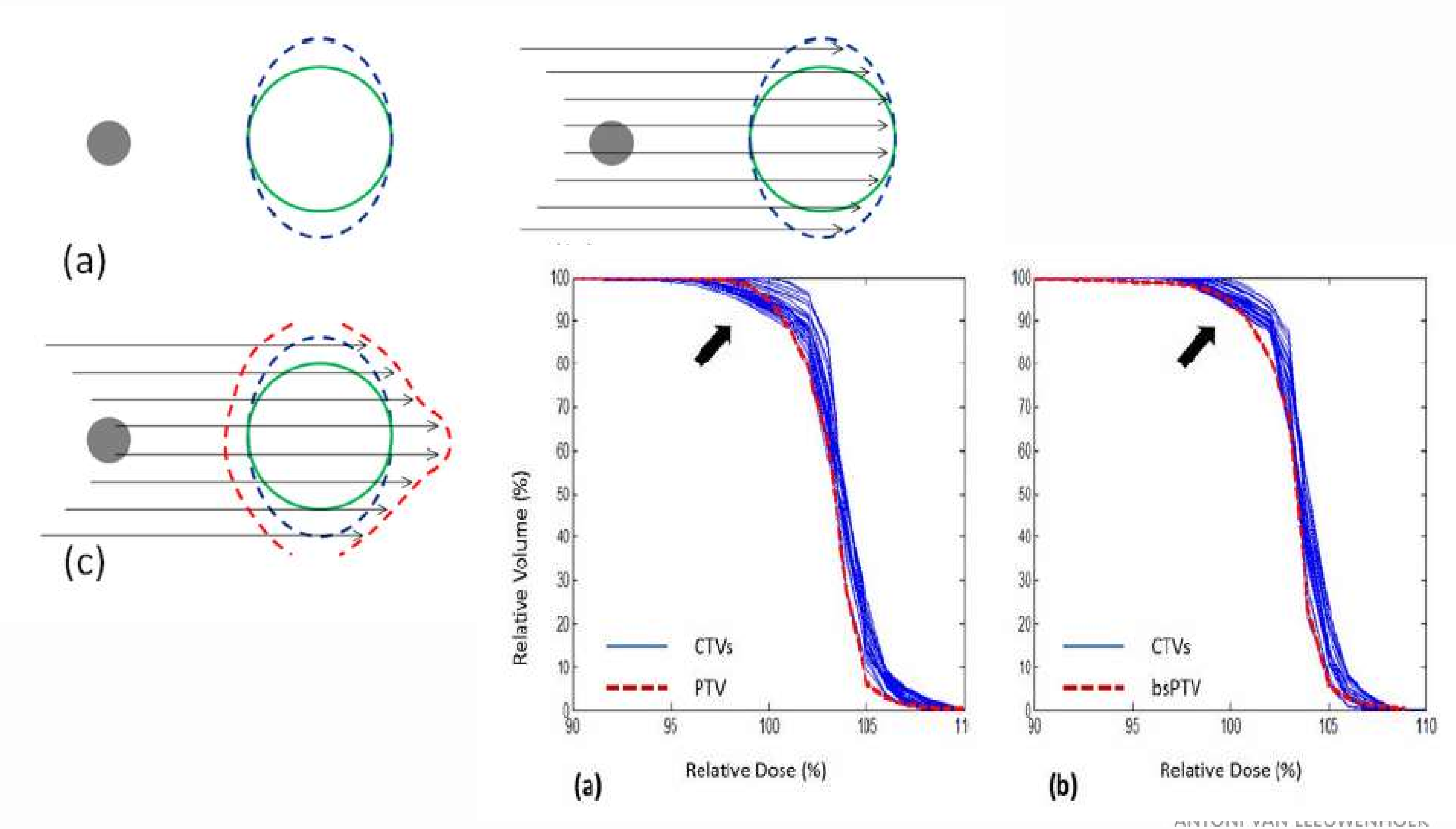
Paganetti, PMB, 2012

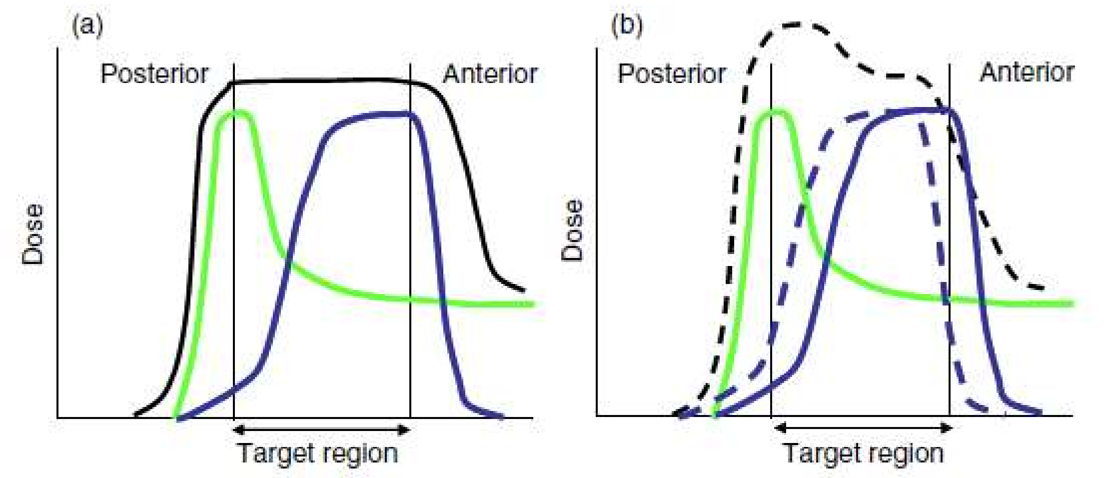
Beam Specific PTV



Parks et al., IJROBP, 2012

Robustness in head and neck
0.5 cm shift

Original | 0.5 cm error



Patient treated with a posterior an lateral field, positioning error in appa direction affects only lateral field

Lomax PMB 2008

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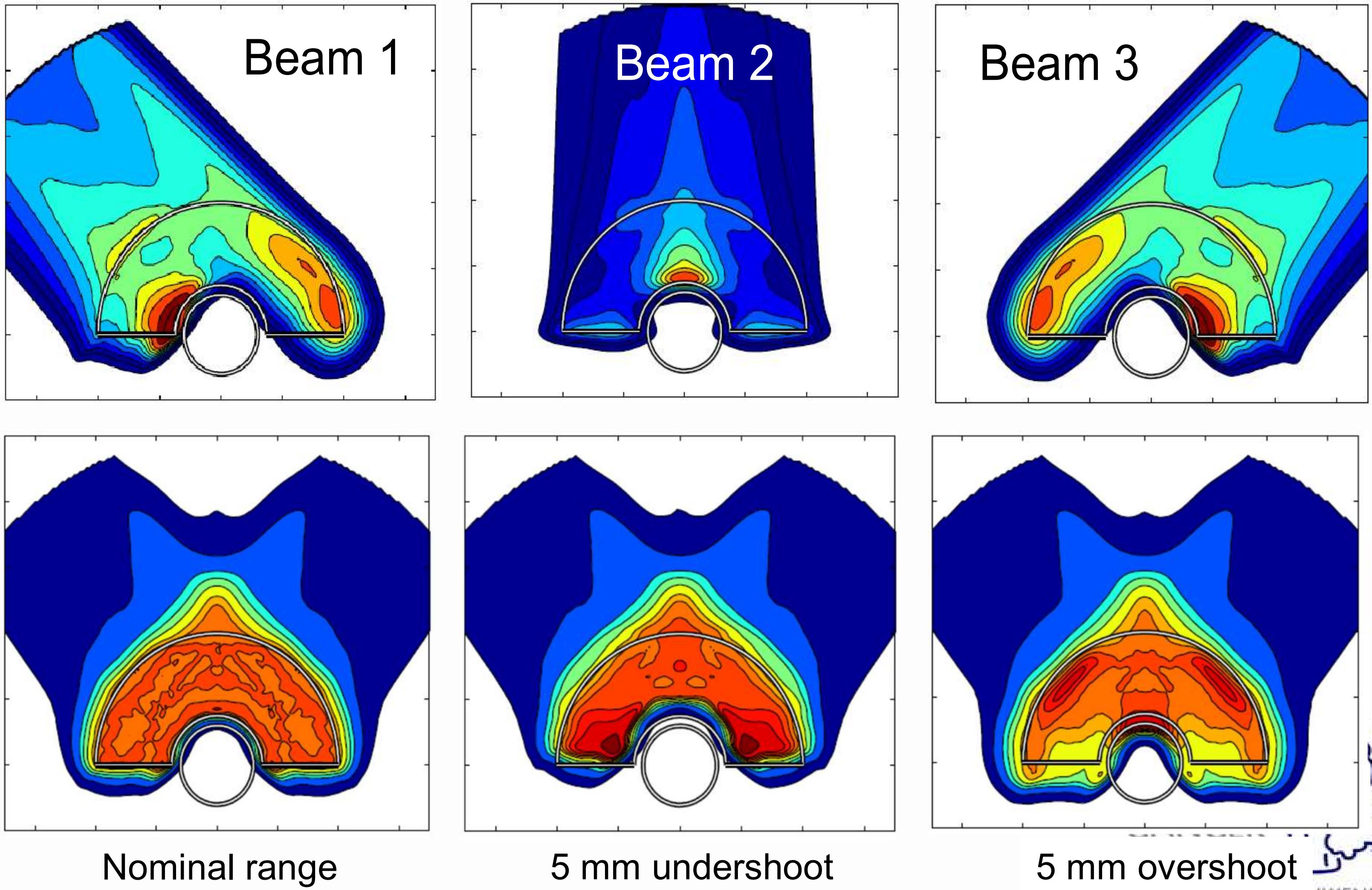
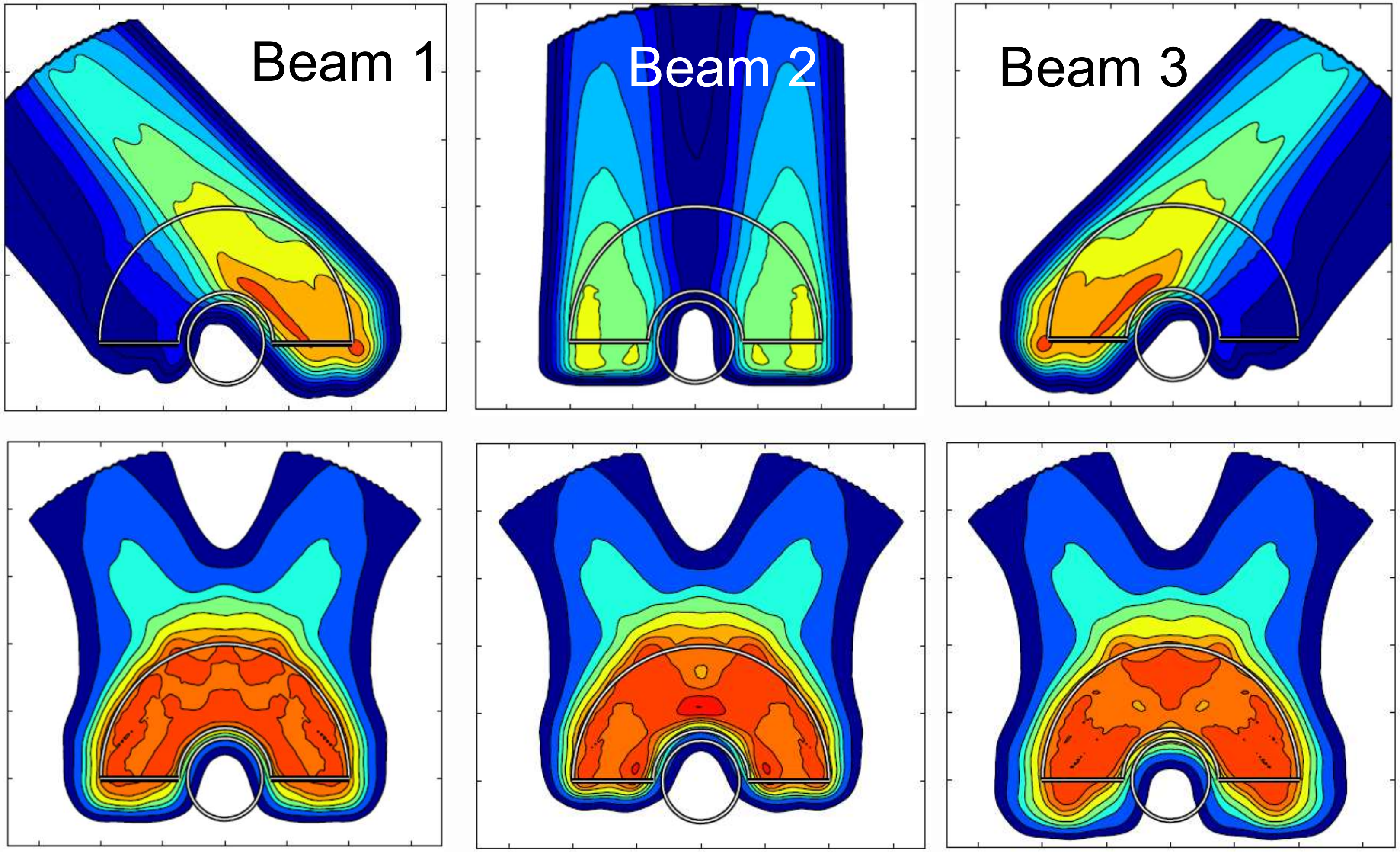
Standard optimization



Unkelbach et al. Med Phys. 2009;36(1):149-63.

Robust optimization



Nominal range | 5 mm undershoot | 5 mm overshoot

Unkelbach et al. Med Phys. 2009;36(1):149-63.

Image Guidance

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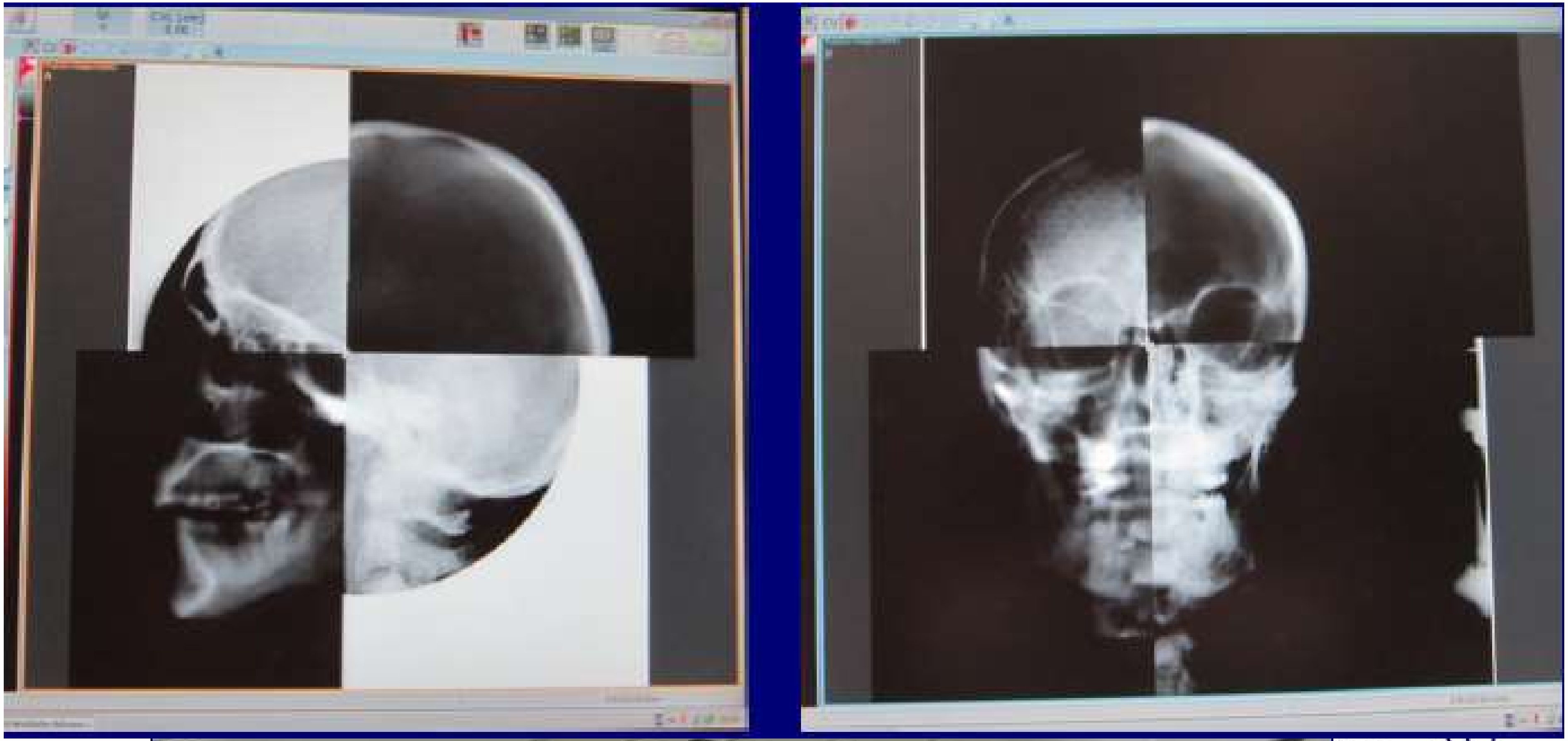
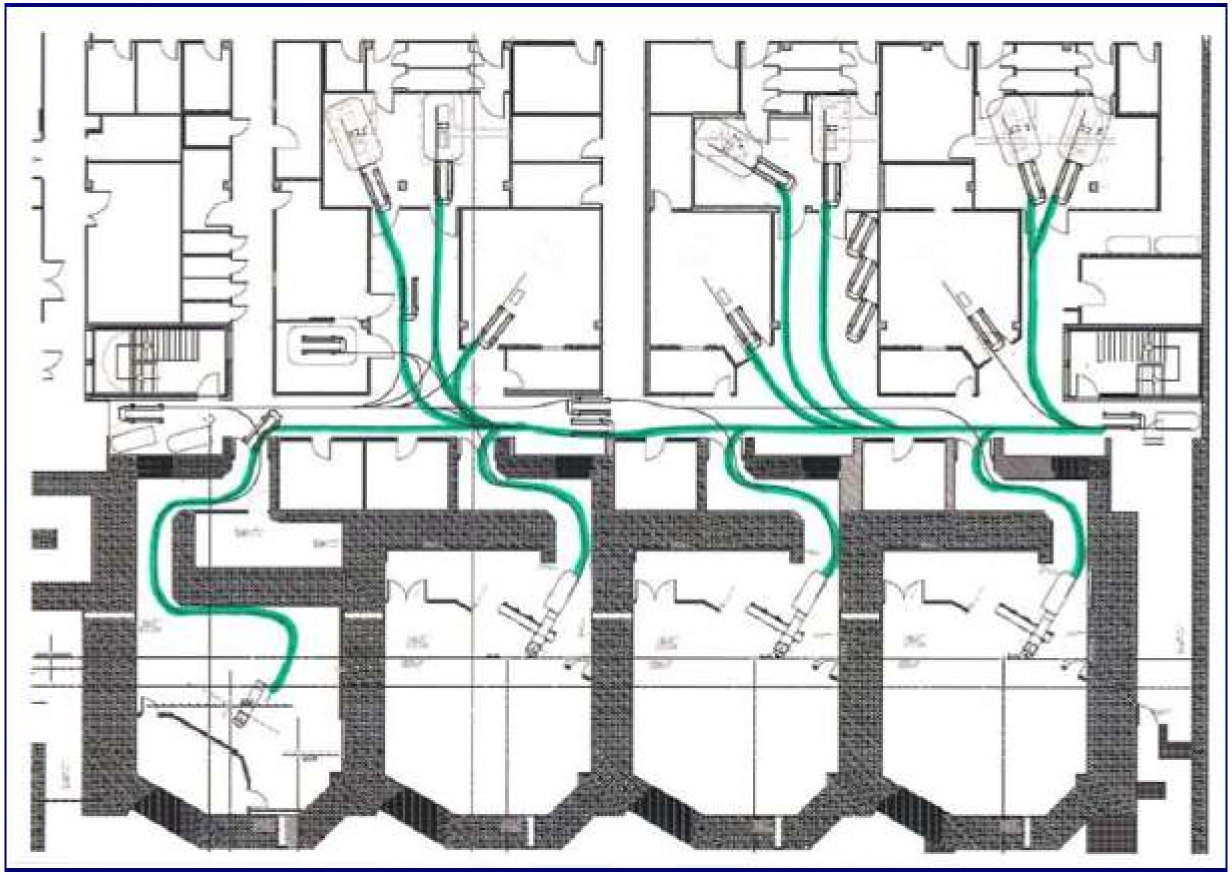
State of the art in room imaging



2D/3D Registration

Courtesy of Lamberti, WPE

Near room imaging



Oncolog Trolley System

Courtesy of Lamberti, WPE

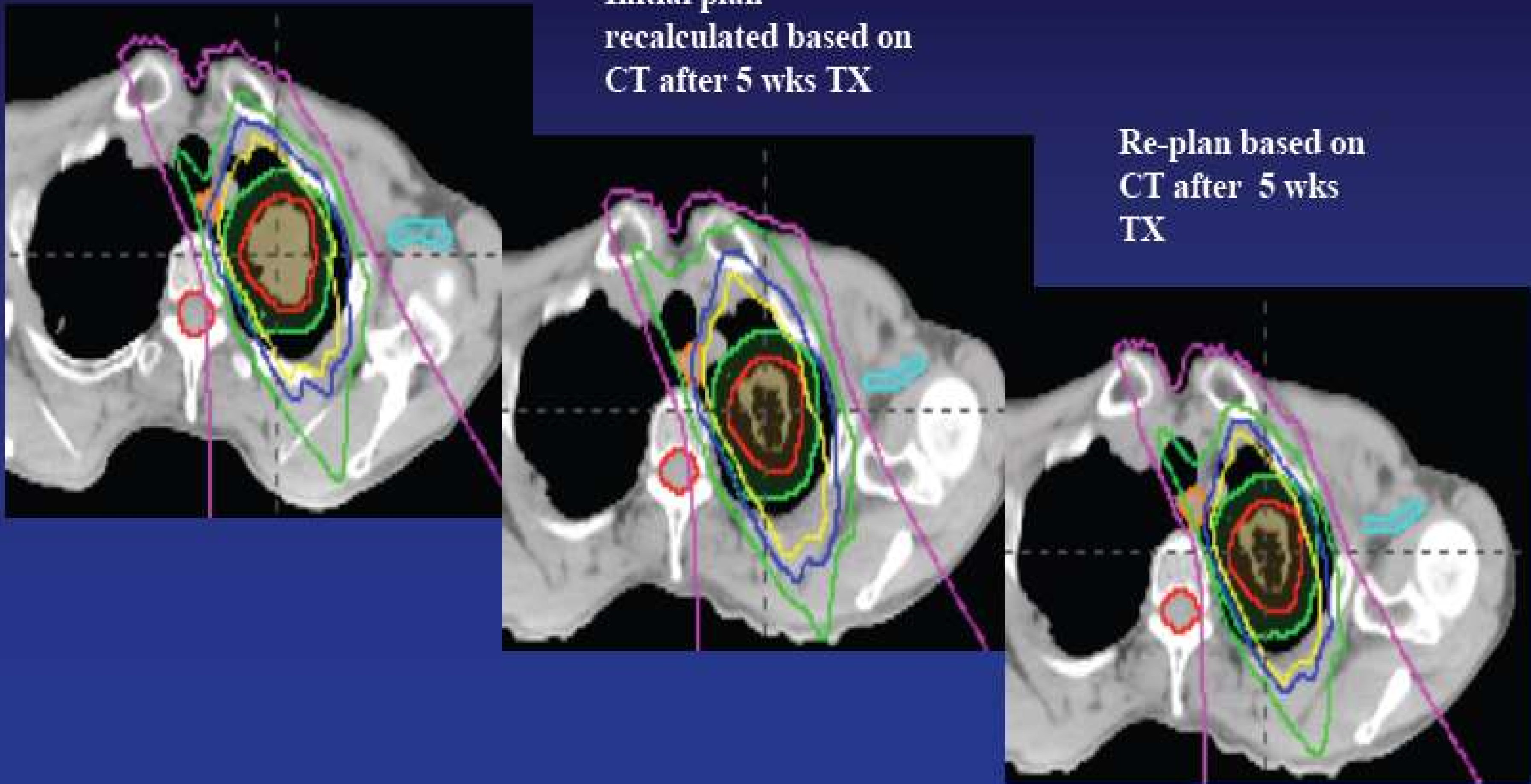
Adapted proton therapy

87.5 CGE in T2N0M0 NSCLC

Initial plan

Initial plan recalculated based on CT after 5 wks TX

Re-plan based on CT after 5 wks TX



Courtesy of Joe Y Chang, MD Anderson

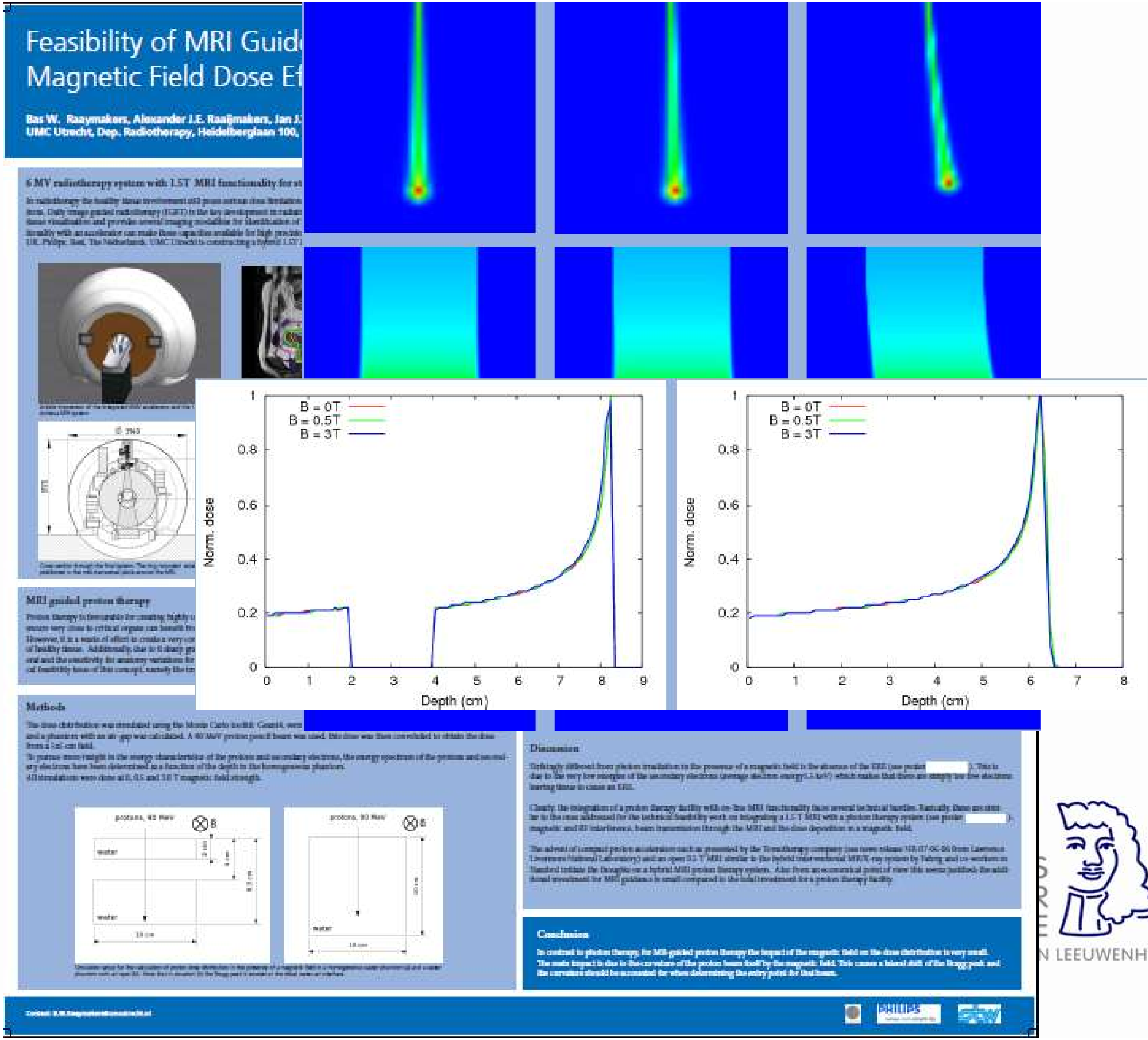
‘Future’ - In Room Imaging

MedPhoton

IHOEK

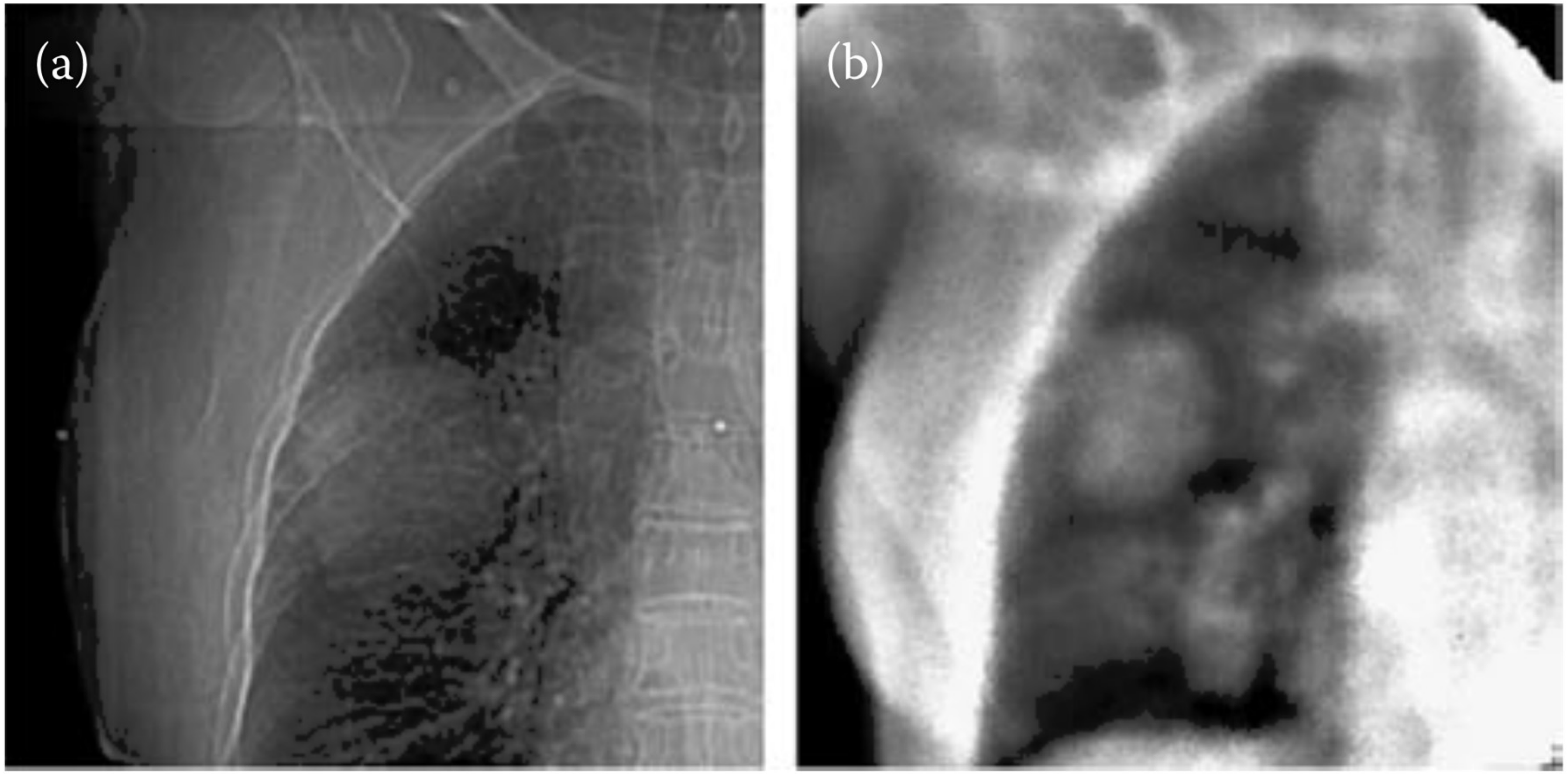
Integra

in room CT


Feasibility of MRI Guid
Magnetic Field Dose Ef
6 MV radiotherapy system with 1.5T MRI functionality for st
MRI guided proton therapy
Methods
protons, 90 MeV
B
water
Discussion
Conclusion
PHILIPS
B = 0T
B = 0.5T
B = 3T
Norm. dose
Depth (cm)
0
0.2
0.4
0.6
0.8
1
1
2
3
4
5
6
7
8
9
N LEEUWENHOEK

Proton radiography

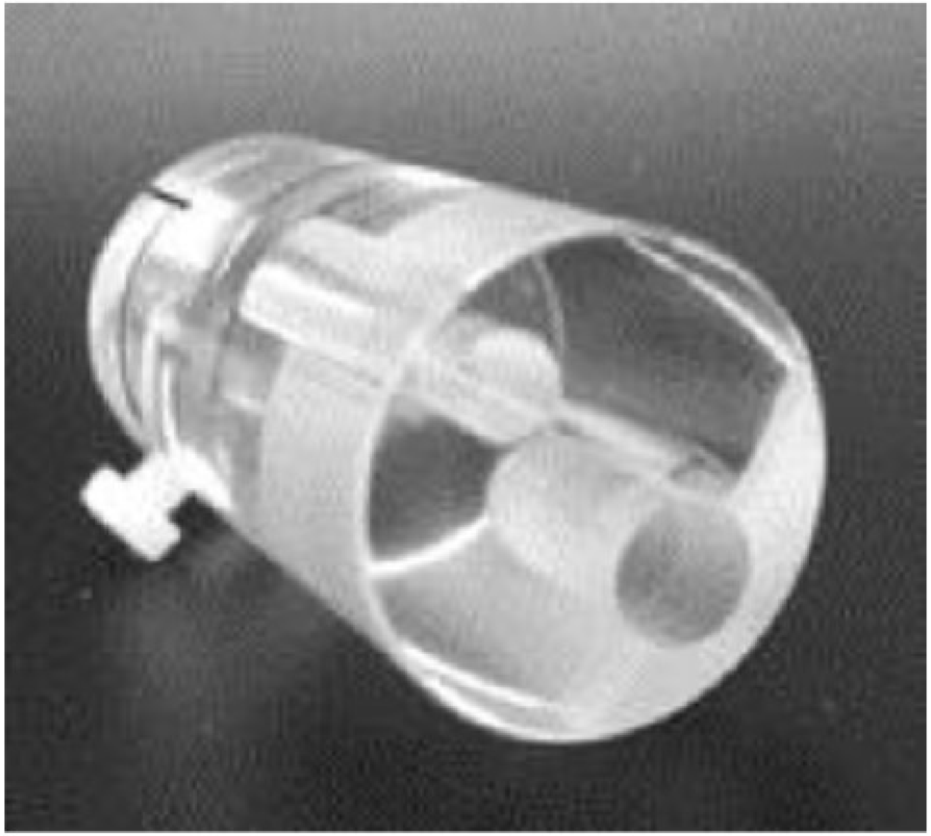
X-ray | 490 MeV proton radiograph

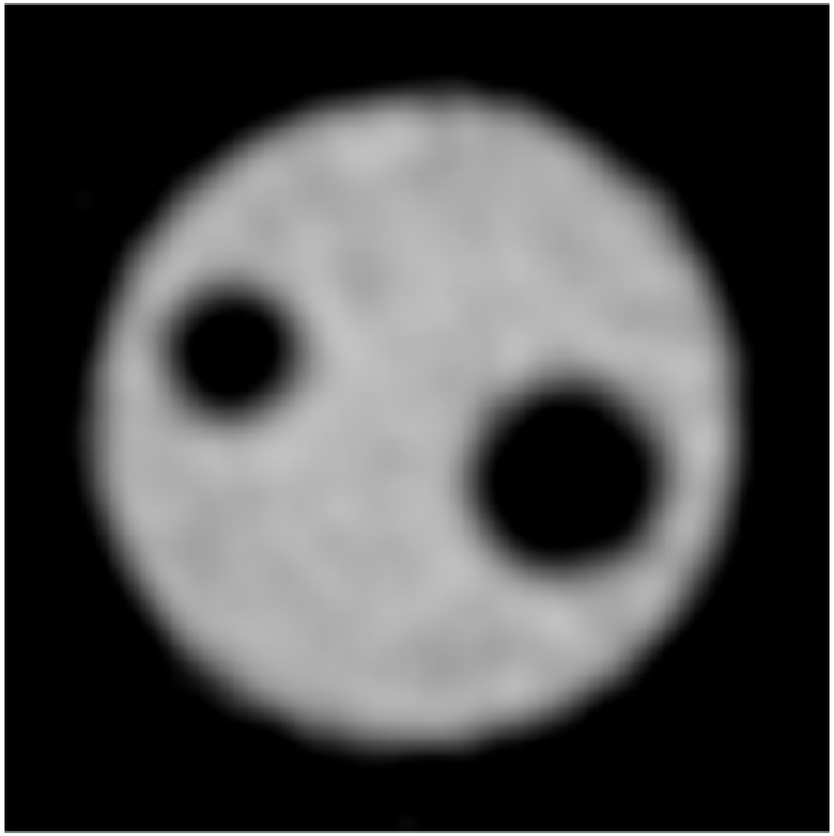


Depauw *et al.* Phys Med Biol 56, p.2407

medical delta | Erasmus MC Universitair Medisch Centrum Rotterdam | LUMC Leids Universitair Medisch Centrum | TU Delft

Proton CT





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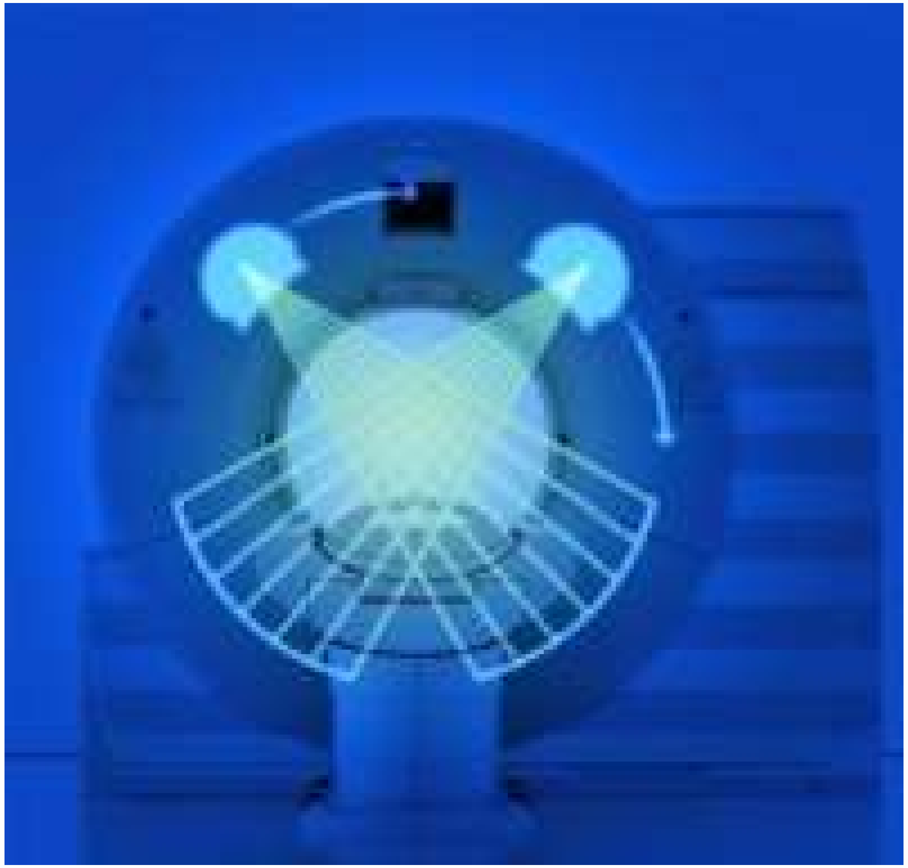
Current Alternatives



Dual Energy CT

MV CT

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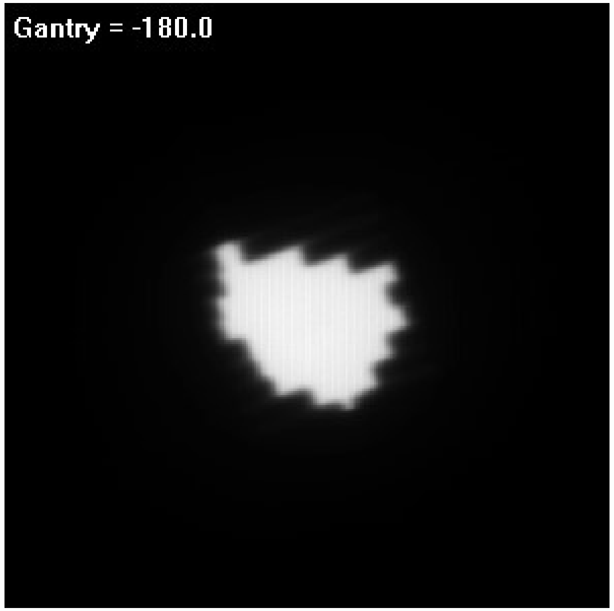
3D EPID Dose reconstruction prostate VMAT plan



EPID movie

Dose per frame

Accumulated dose

axial slice through isocentre

- Energy: 10 MV
- 243 frames
- delivery time: 96 s

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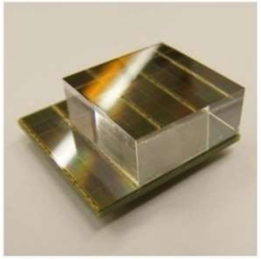
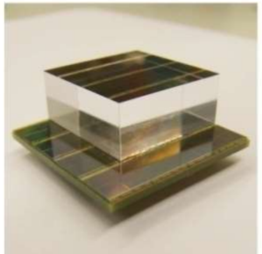
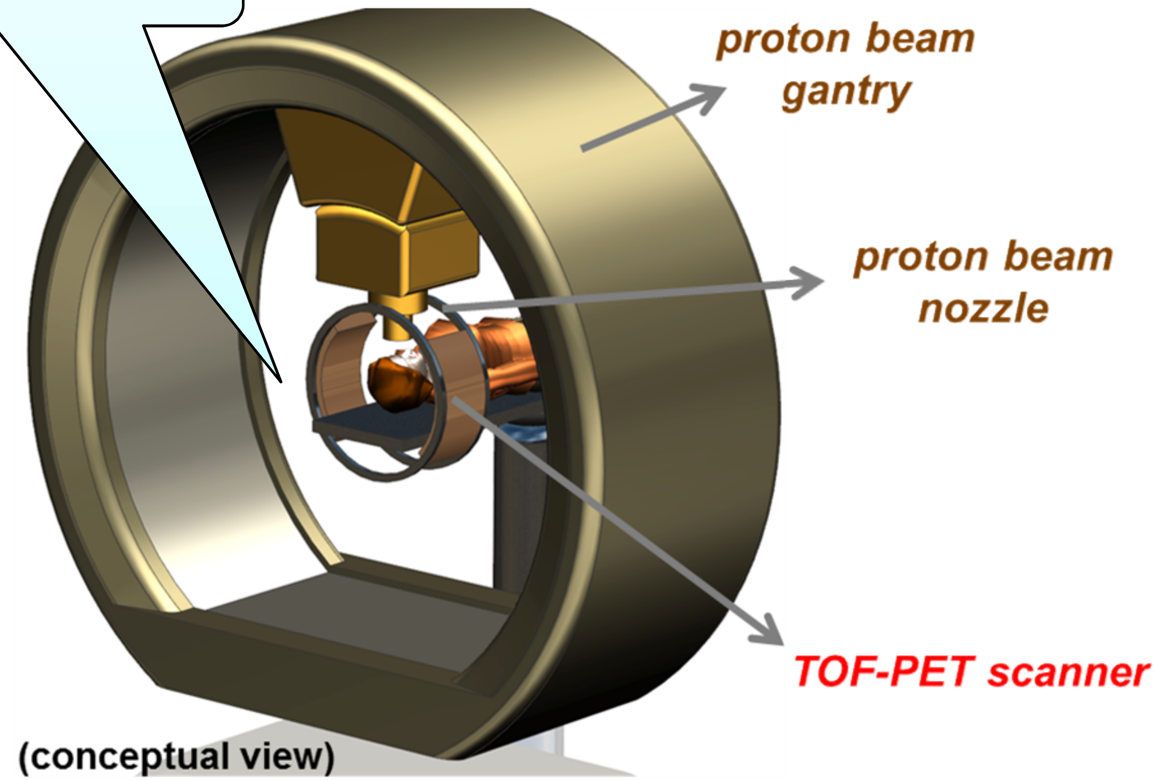
Example: in-situ dose imaging

Incentive
Use revolutionary detection technology, under development for PET-MRI by TU Delft and Philips, to realize clinically useful in-situ dose imaging device





www.sublima-pet-mr.eu



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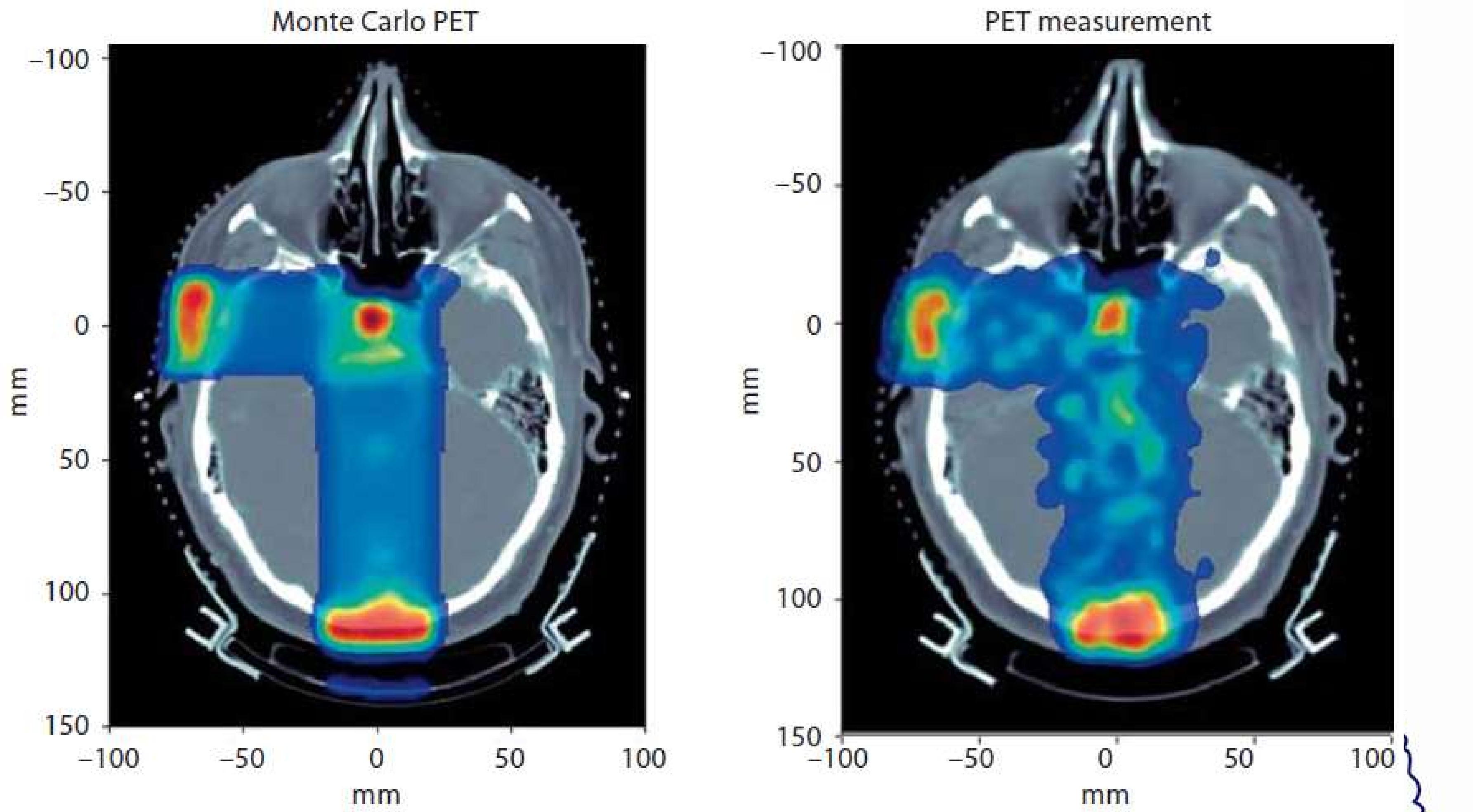
Range Verification: PET



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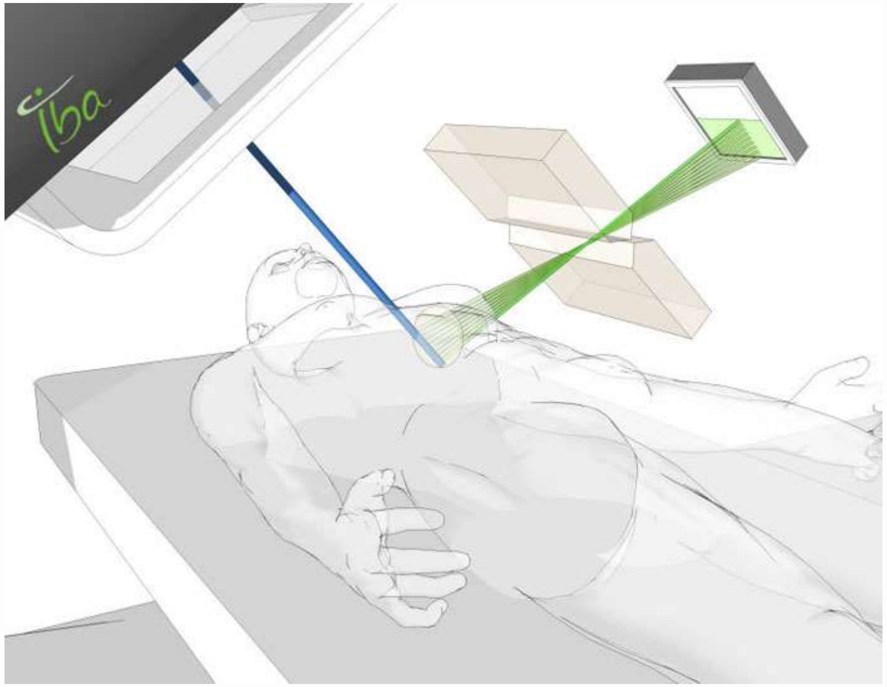
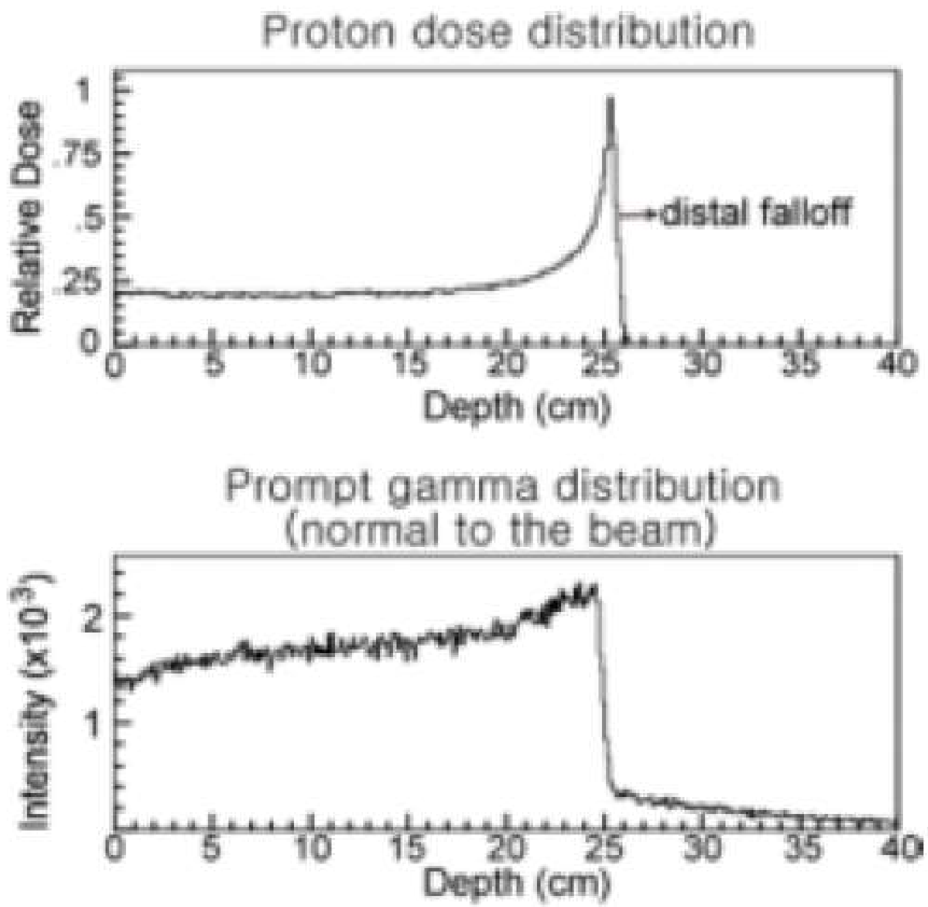
Courtesy of Martijn Engelsman

Range Verification: Prompt Gamma





B. Kang, J. Kim, IEEE Nucl. Sci. 2009

Thought experiment

	PROTONS	PHOTONS
Intensity modulation	Yes	Yes
3D/4D on-line alignment	No	Integrated
In-vivo dosimetry	No	Yes
Dose distribution sensitivity	High	Non-existent
Integral dose	Very low	Somewhat higher
Price per patient	€25,000	Cheaper: 2x to 3x

Conclusions

- Protons stop, providing great potential for organ at risk sparing
- Range uncertainties require larger ‘margins’ for target/OAR and/or more advanced correction strategy
- IGRT is currently underdeveloped for proton therapy

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