Main Challenges in Adaptive Radiotherapy

Jan-Jakob Sonke

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Disclosure

- Research collaboration with:
  - Elekta Oncology Systems
  - Philips Radiation Oncology Systems
  - RaySearch Laboratories

- Our department licenses software to:
  - Elekta Oncology Systems
  - Precision X-Ray Inc.

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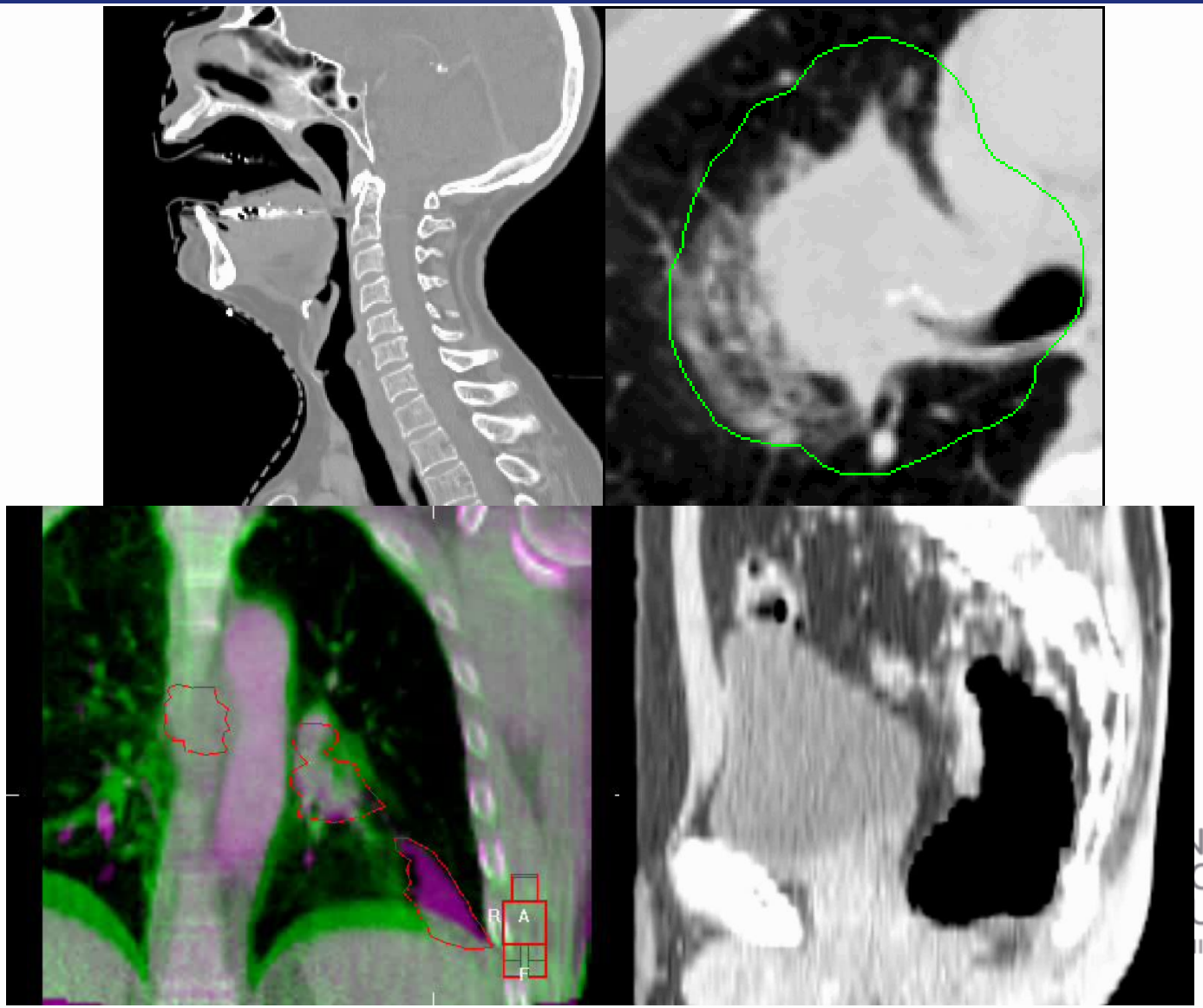
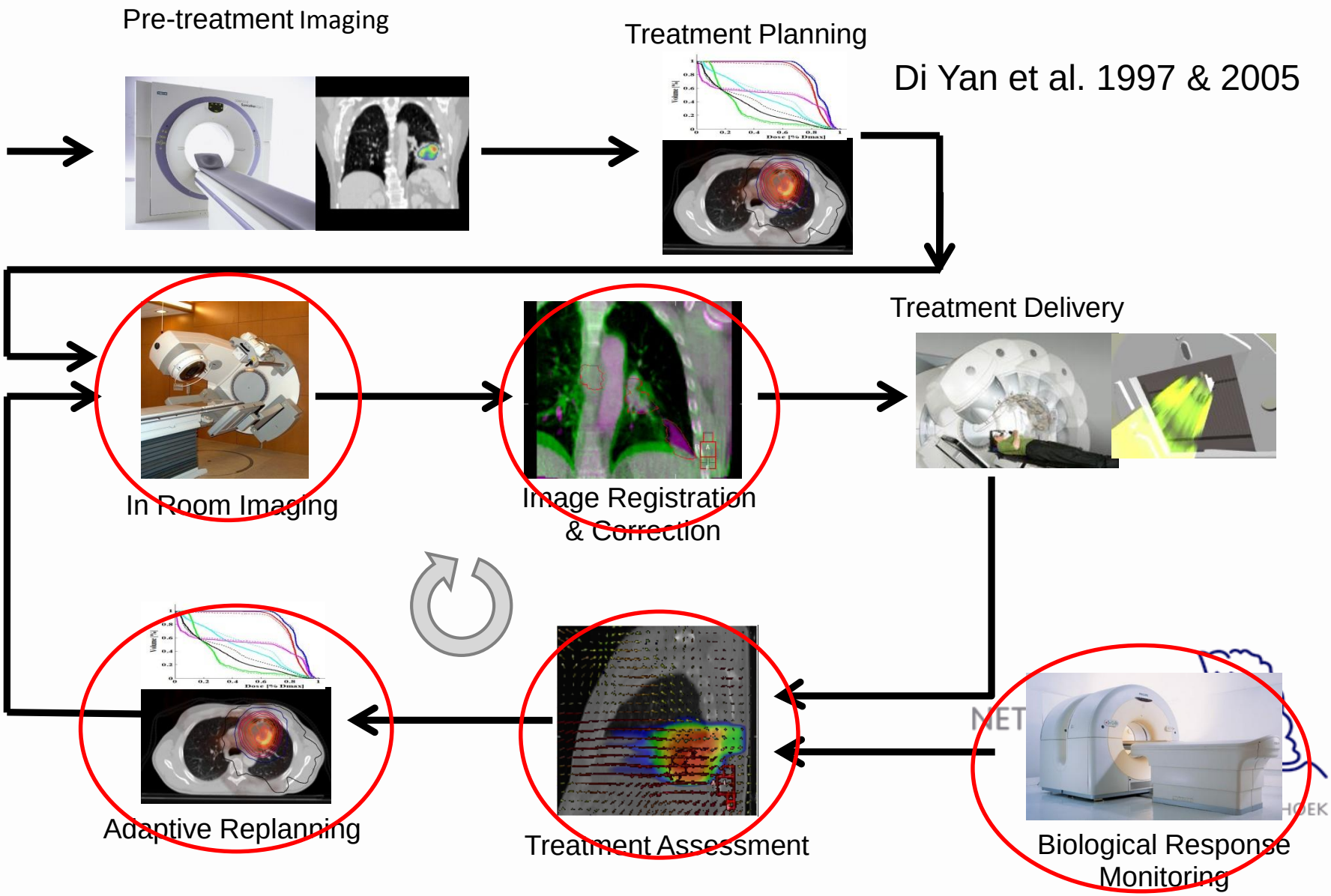
Anatomical Changes



The Adaptive Replanning Process



CBCT Image Quality

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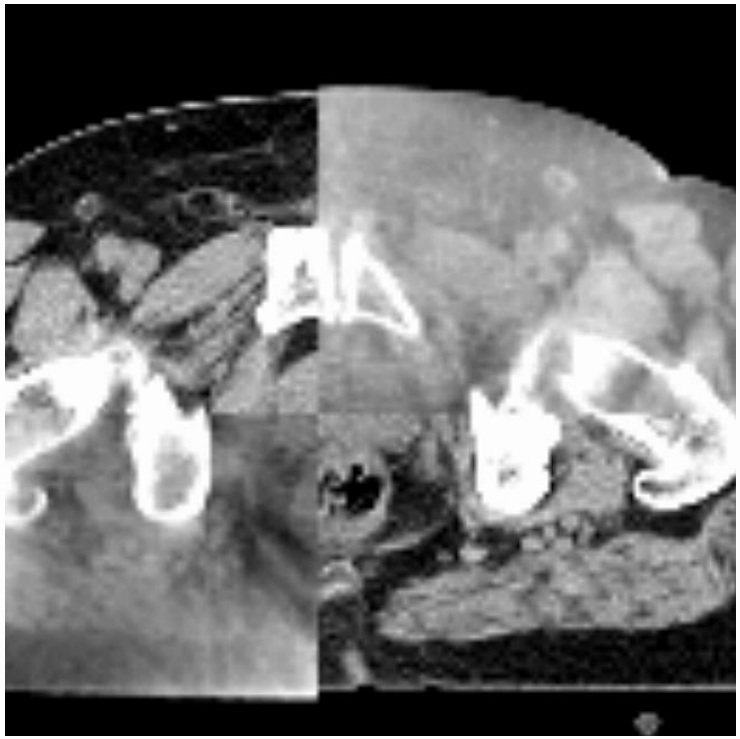
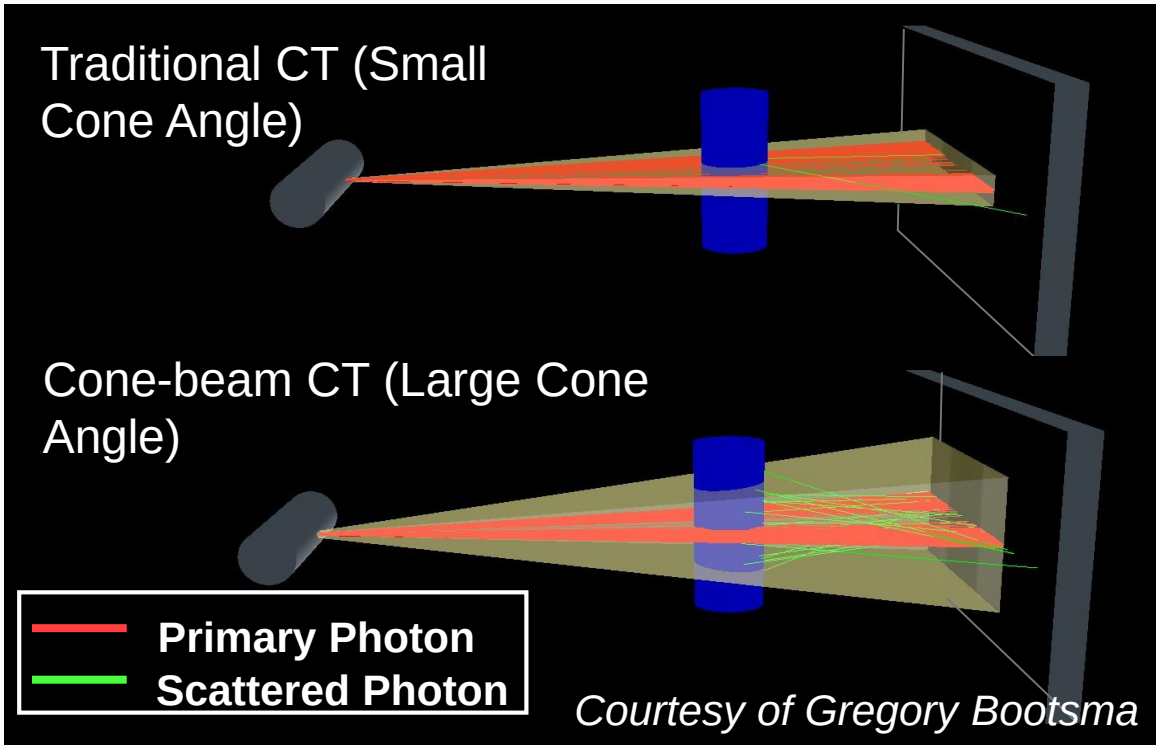
Cone Beam CT Image Quality





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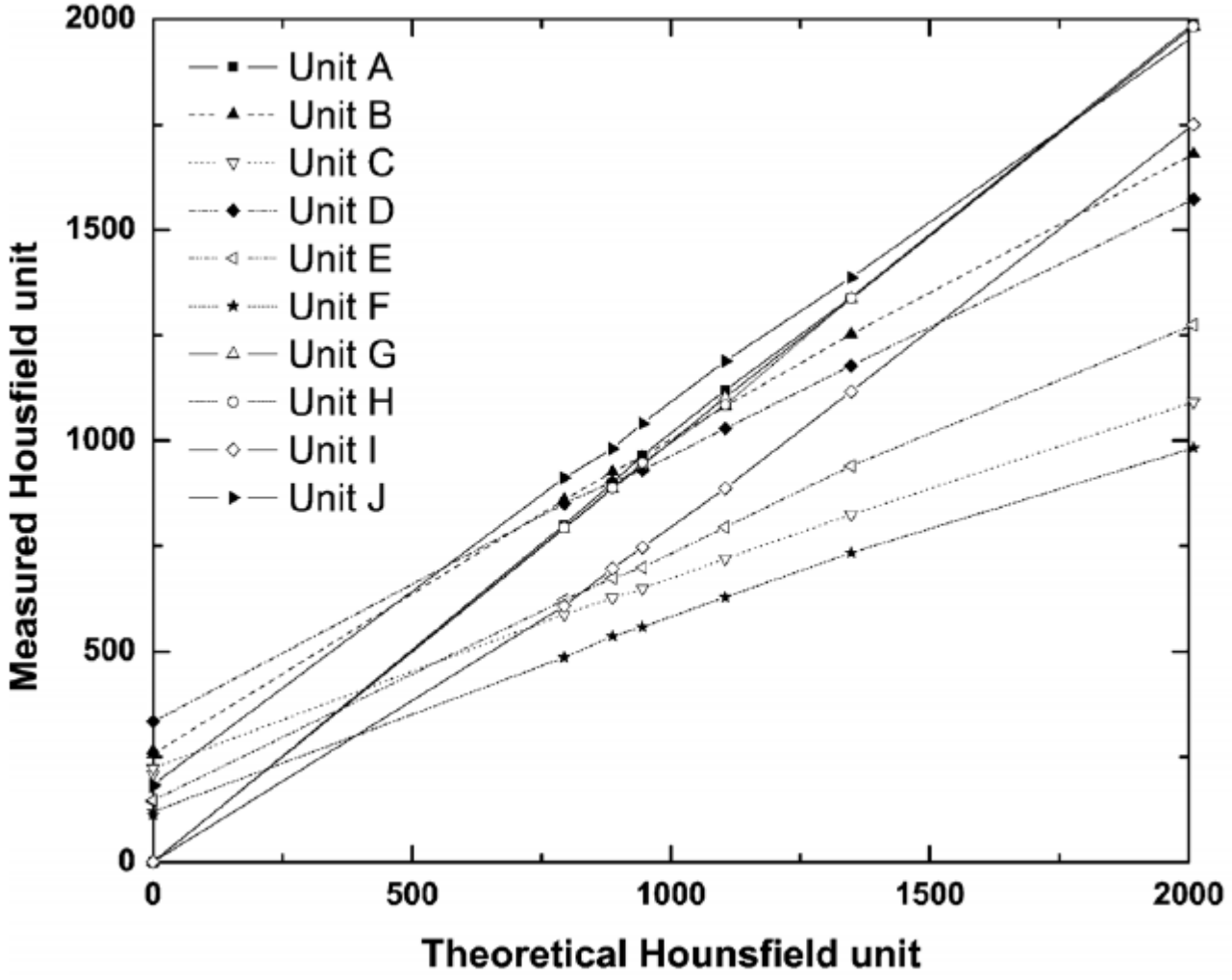
Linearity



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Modified from J.P. Bissonette et al. Med Phys 2008

Challenges

- How to improve quantitative CBCT
- How to mitigate motion artifacts
- How to improve soft tissue contrast

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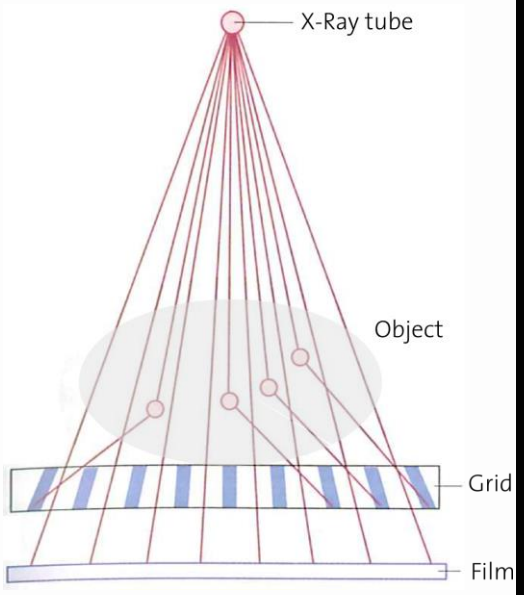
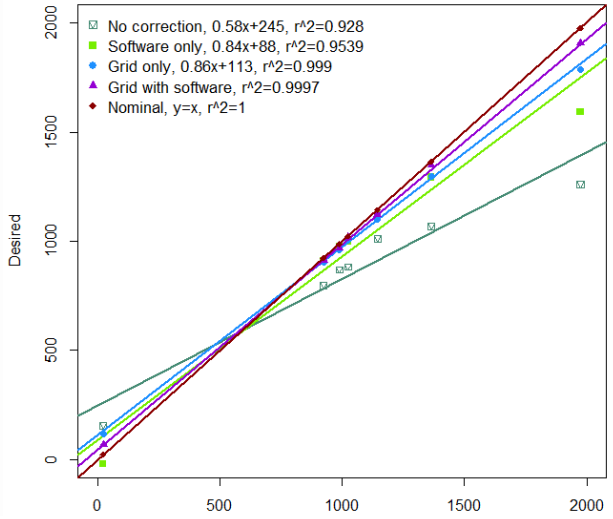
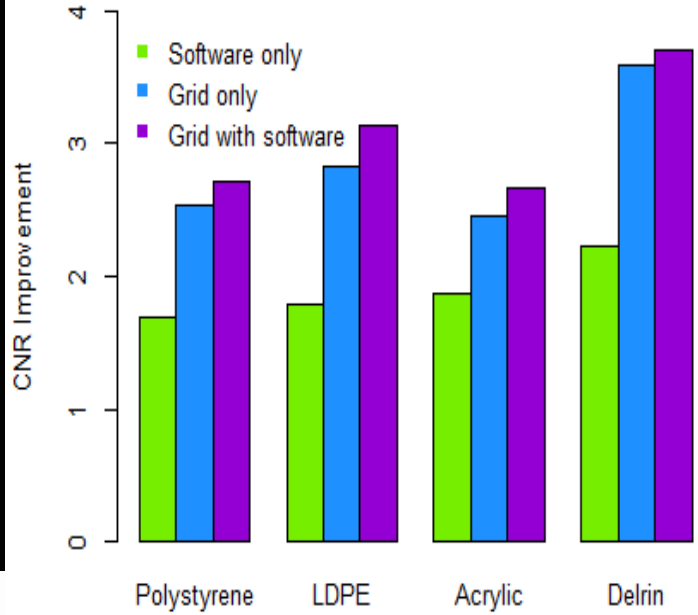
Impact of Anti-Scatter Grid



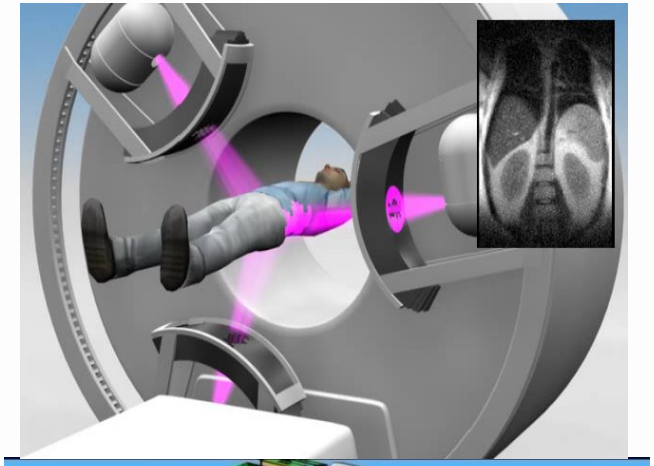


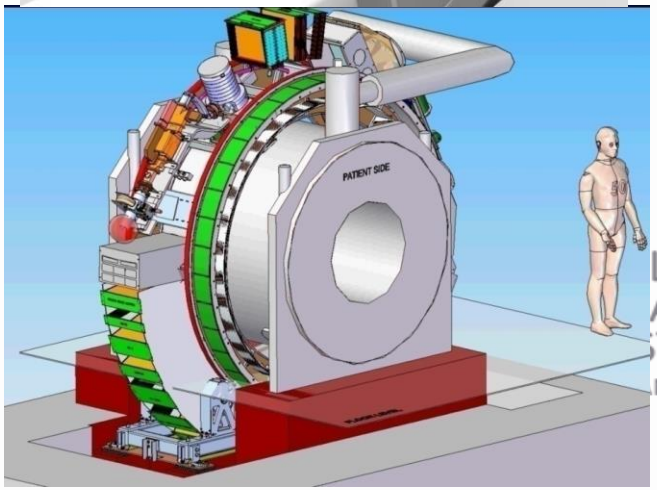


Diagnostic Quality

Diagnostic Quality CBCT

In Room MRI





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Better soft tissue contrast

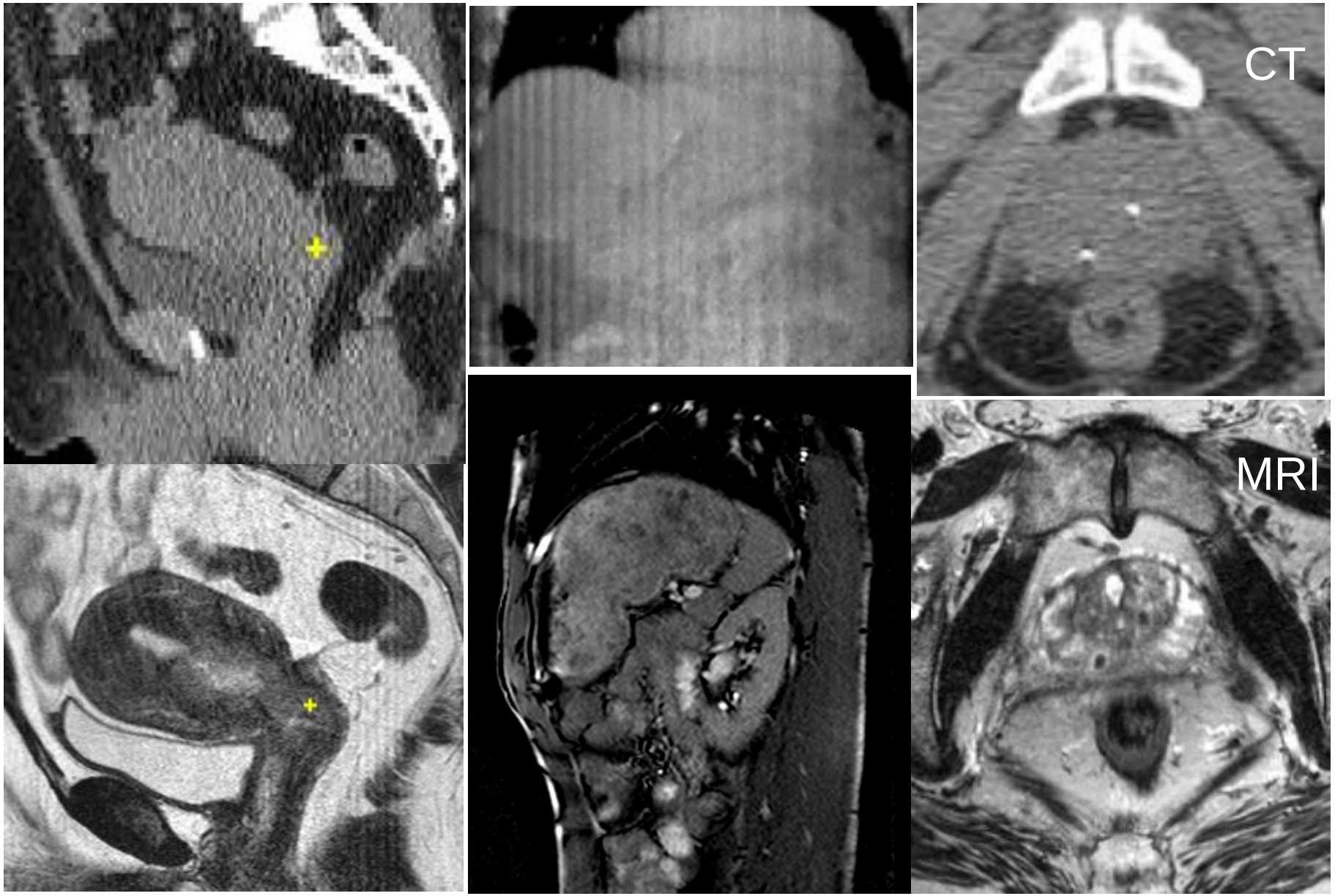

Image Registration

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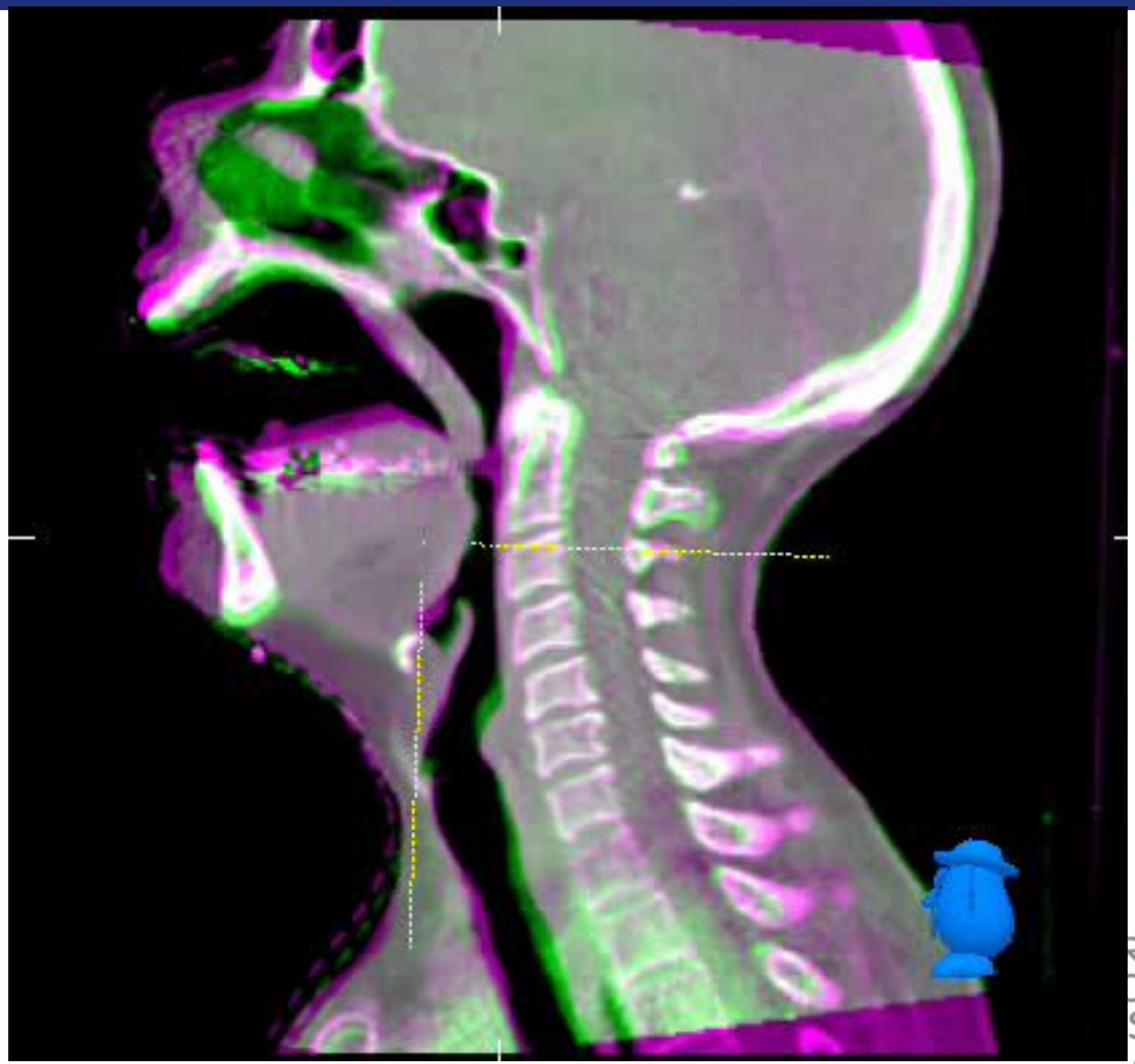
Full deformable registration



Cubic B-splines, Mutual Information

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Challenges

- How to quantify the accuracy
- How accurate is deformable registration
- How accurate should it be

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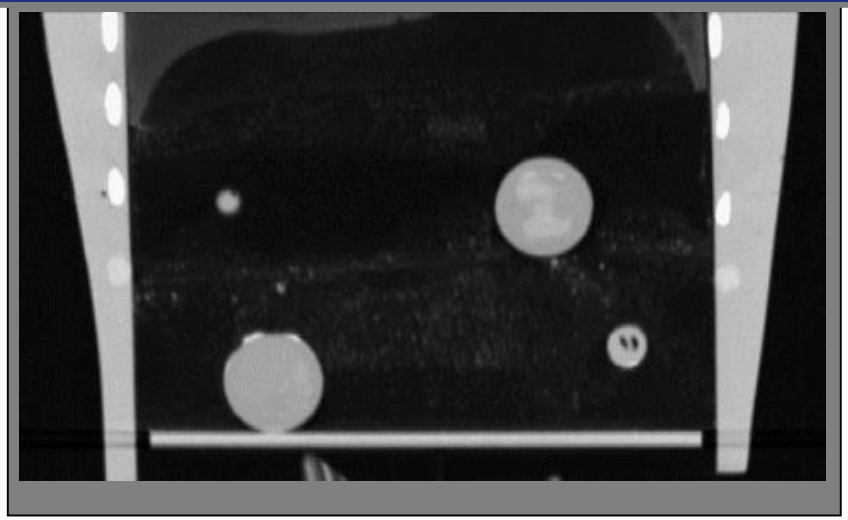
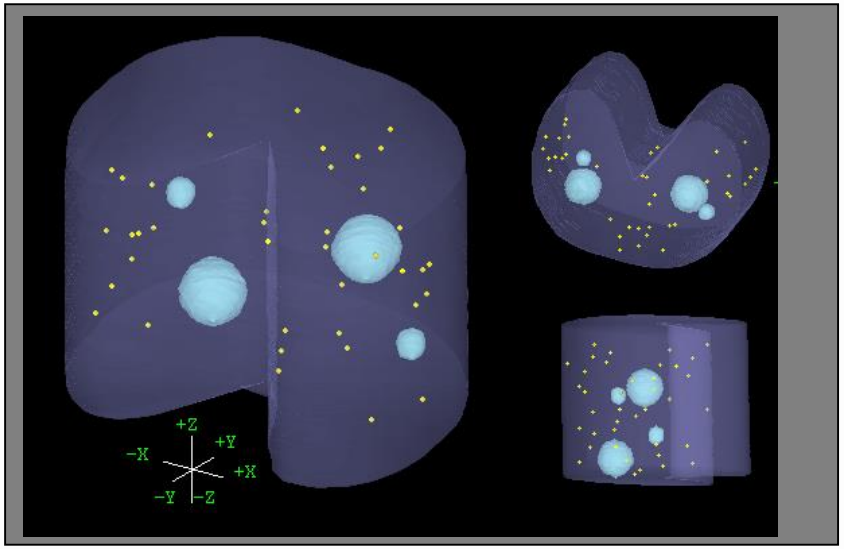
Phantoms

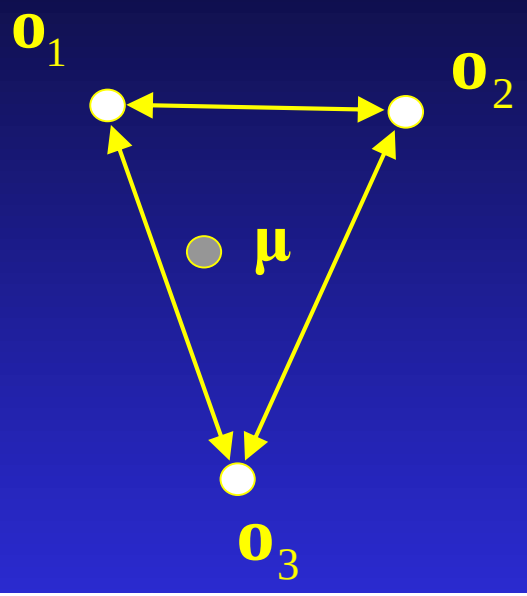




		RL[a] (cm)	AP[b] (cm)	SI[c] (cm)	3-D distance (cm)
Affine	Average	−0.01	0.00	0.05	0.38
	Stdev[d]	0.04	0.04	0.44	0.22
	Max[e]	−0.12	−0.13	0.90	0.90
B-splines	Average	−0.02	−0.01	0.05	0.18
	Stdev[d]	0.08	0.06	0.22	0.16
	Max[e]	−0.42	0.19	0.67	0.81
Thin-plate splines	Average	−0.07	−0.15	−0.14	0.37
	Stdev[d]	0.12	0.19	0.28	0.19
	Max[e]	−0.56	−0.58	−0.74	0.75

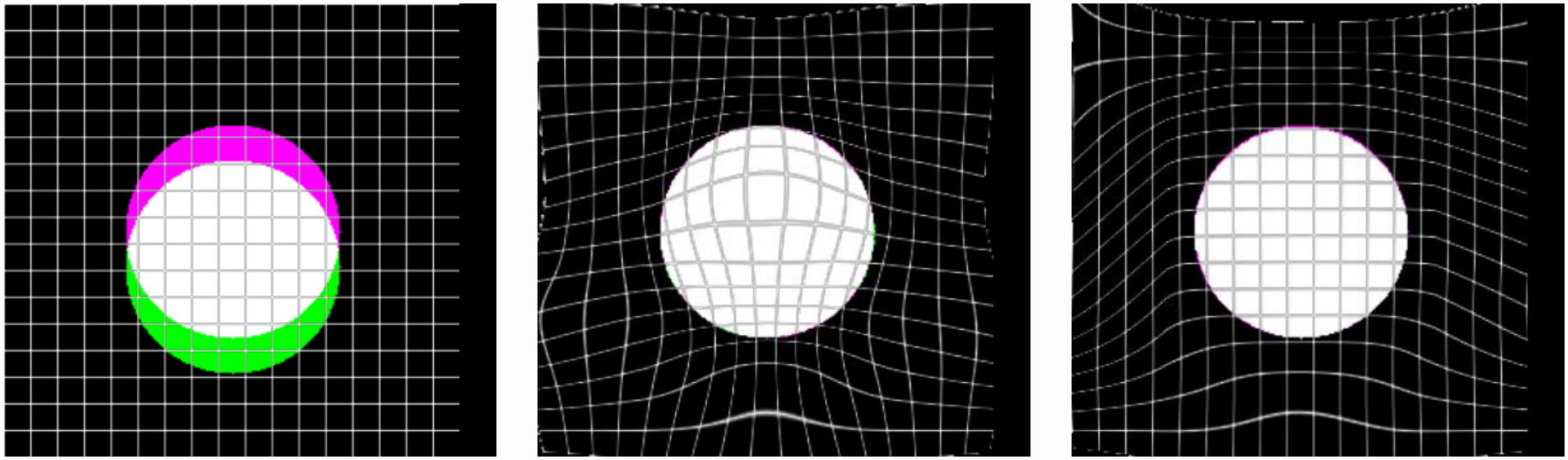
Analysis of variance

$$\sigma_1^2 = (\sigma_{2-1}^2 + \sigma_{3-1}^2 - \sigma^2{}_{3-2})/2$$
$$\sigma_2^2 = (\sigma_{3-2}^2 + \sigma_{2-1}^2 - \sigma^2{}_{3-1})/2$$
$$\sigma_3^2 = (\sigma_{3-1}^2 + \sigma_{3-2}^2 - \sigma^2{}_{2-1})/2$$



Landmarks:	Bony			Soft-tissue		
	LR	CC	AP	LR	CC	AP
Human observer	0.8	0.7	0.9	0.9	1.4	1.0
Deformable registration	1.1	1.3	0.8	1.0	1.3	1.0

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

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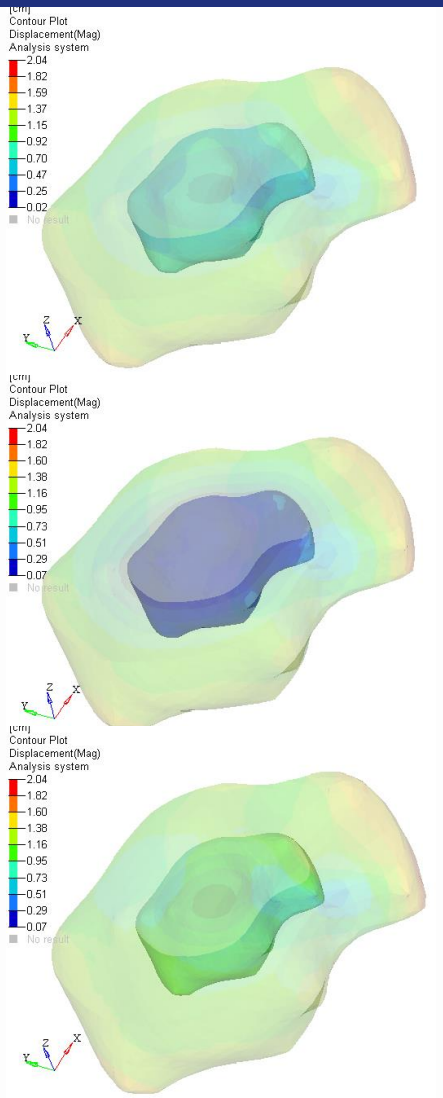
Modeling Volume Reduction



- Tumor with ‘core’
- Heterogeneous plan
- Variation in volume reduction
  - Homogeneous
  - Dissolving rim
  - Necrotic Core

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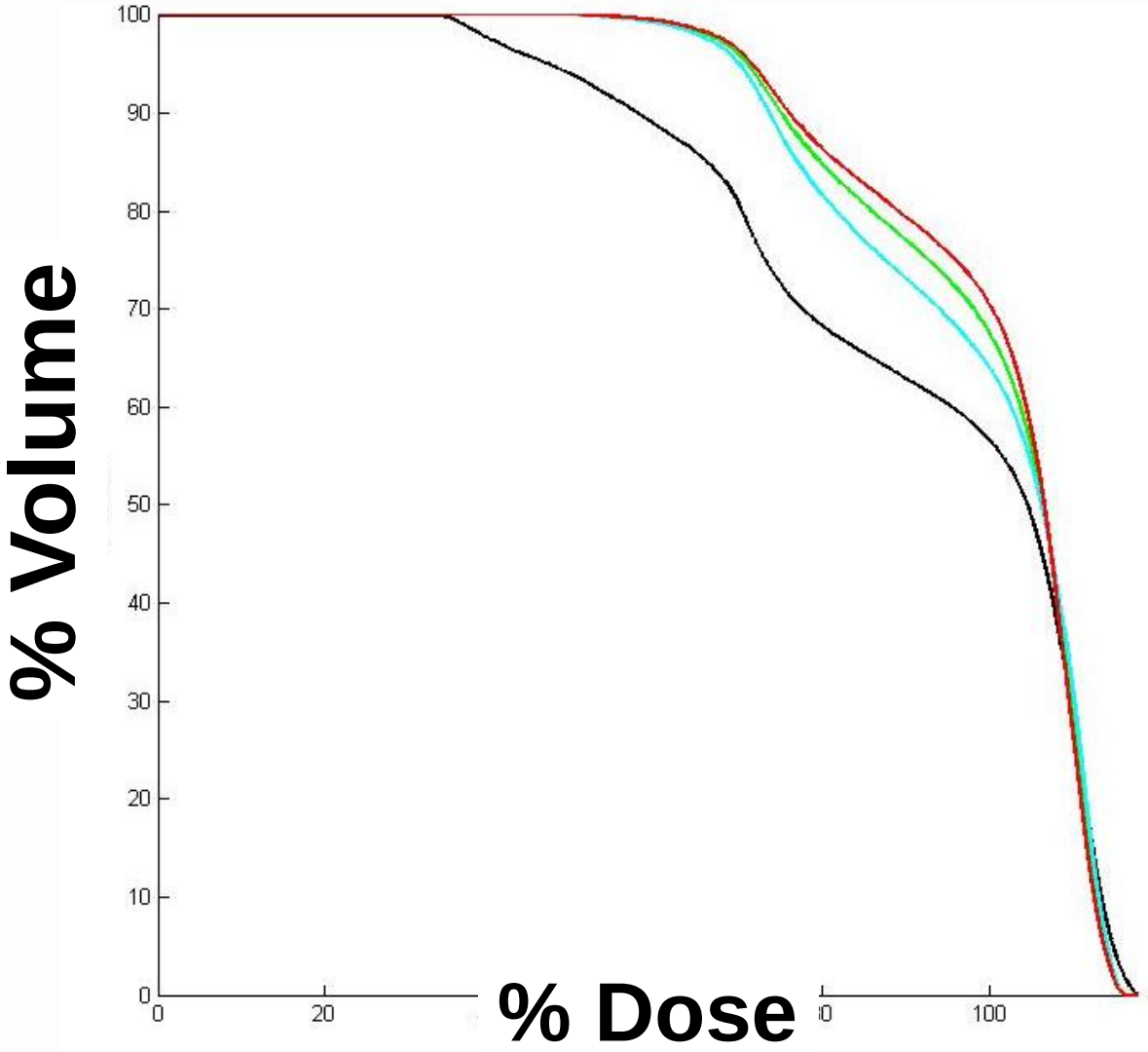
Modeling Volume Reduction Dosimetric Effect



Homogeneous

Necrotic Core

Dissolving Rim

Plan

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Dose Accumulation

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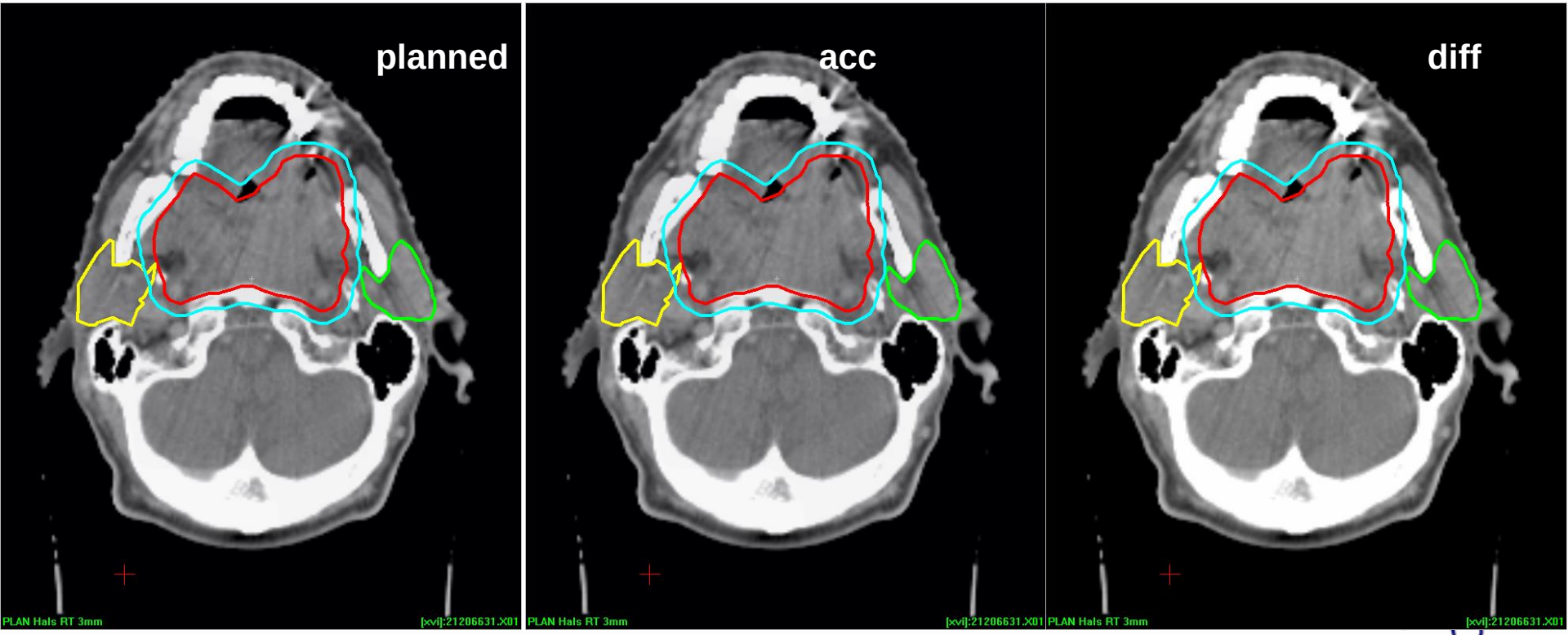
Dose accumulation



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Challenges

- How to incorporate registration and other uncertainties
- How to define threshold for intervention
- Is there indication that accumulated dose has clinical relevance

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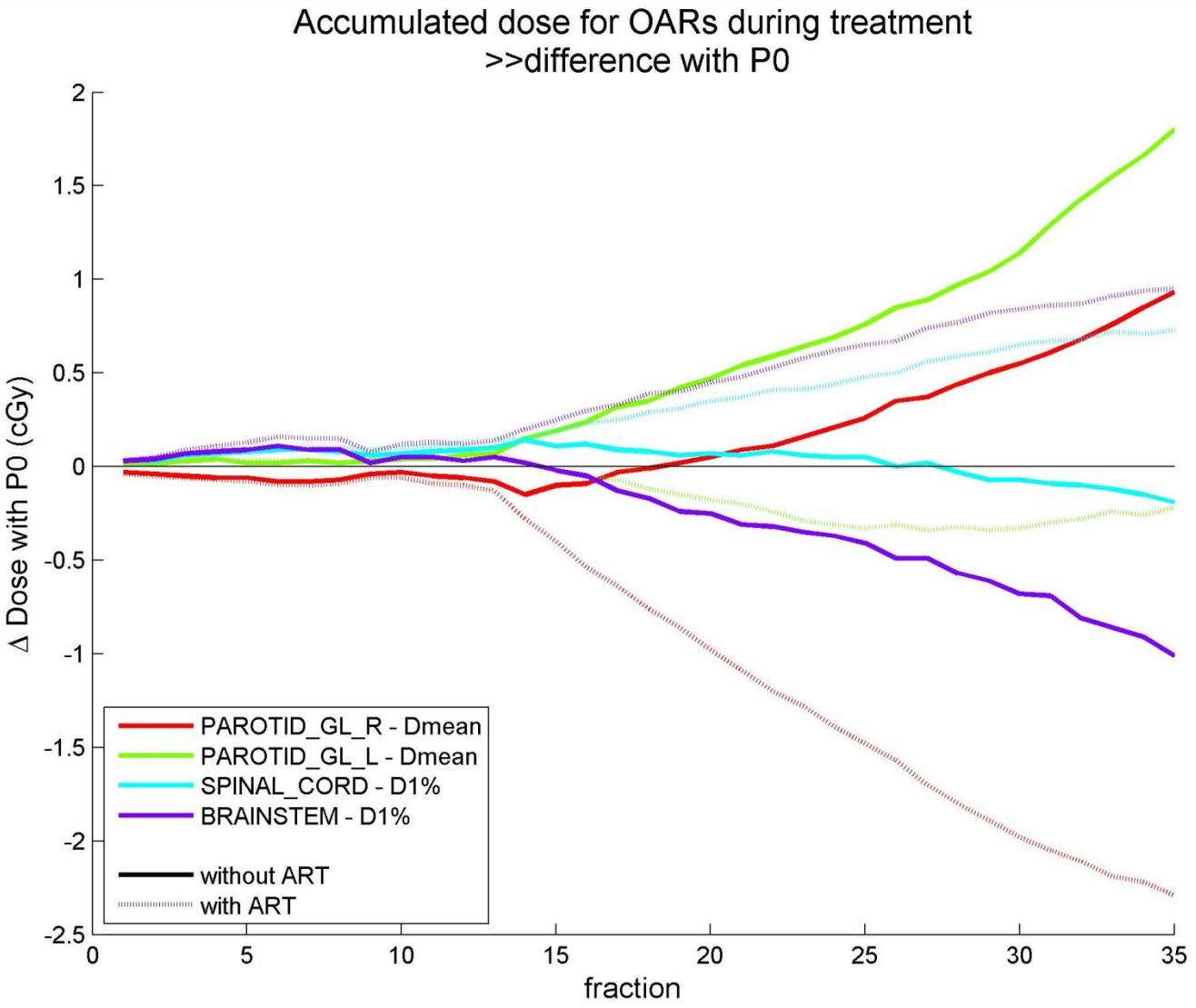
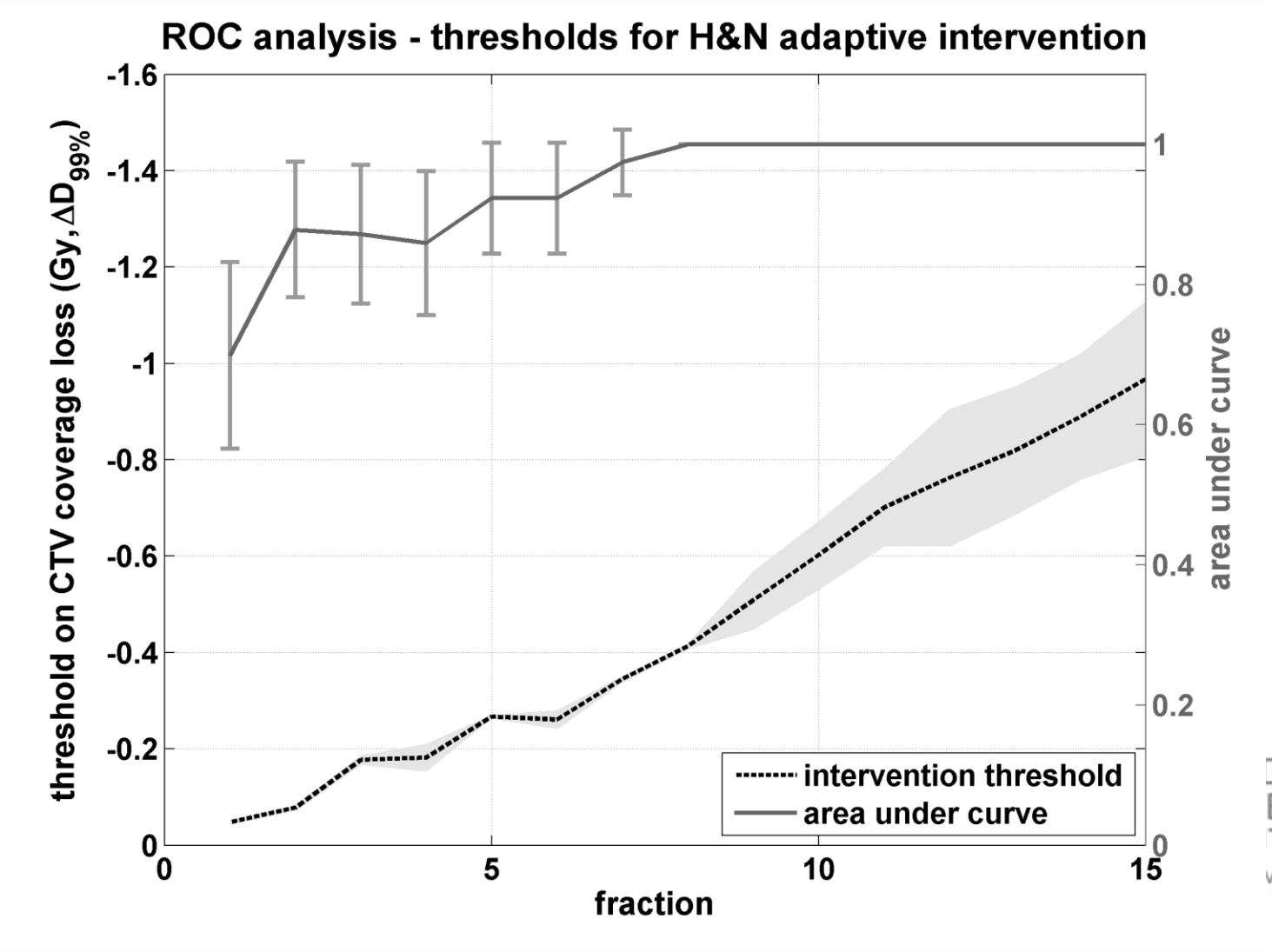
Dose accumulation during treatment



Thresholds for intervention



Improved Correlation with Outcomes

- 93 patients, 172 liver metastases
- Delivered doses to GTV calculated using dose accumulation, deformable image registration of daily CBCTs
- Greater local recurrence risk reduction with accumulated min GTV dose vs. planned min PTV dose
  - Hazard ratio: 0.45 vs 0.55 for each 10Gy increase in dose

Swaminath, Velec, Brock, Dawson,…CARO 2011

Tumor Regression

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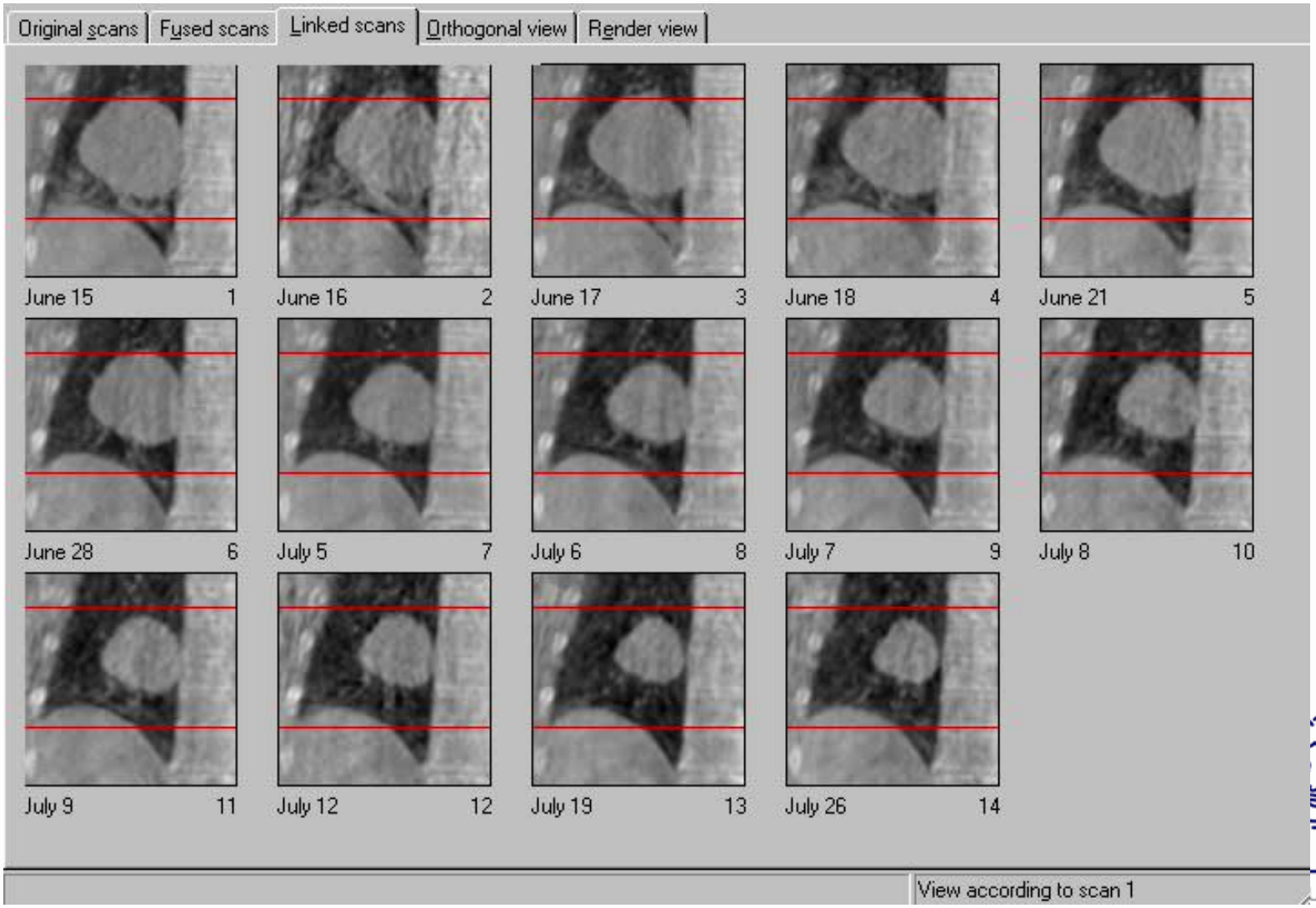
Tumor regression over the course of treatment



JWENHOEK

Challenges

- Can we safely adapt to regressing tumors
- Can we accurately register regressing tumors

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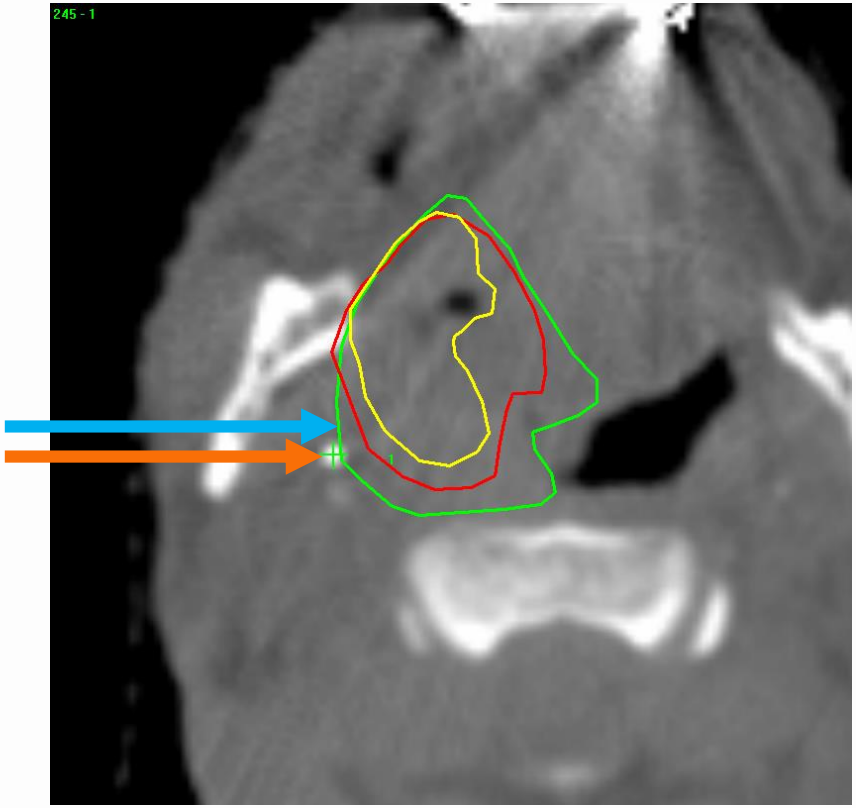
Results: Example marker displacement



GTV on MRI Pre treatment

GTV on MRI Week 3

GTV on MRI Week 6

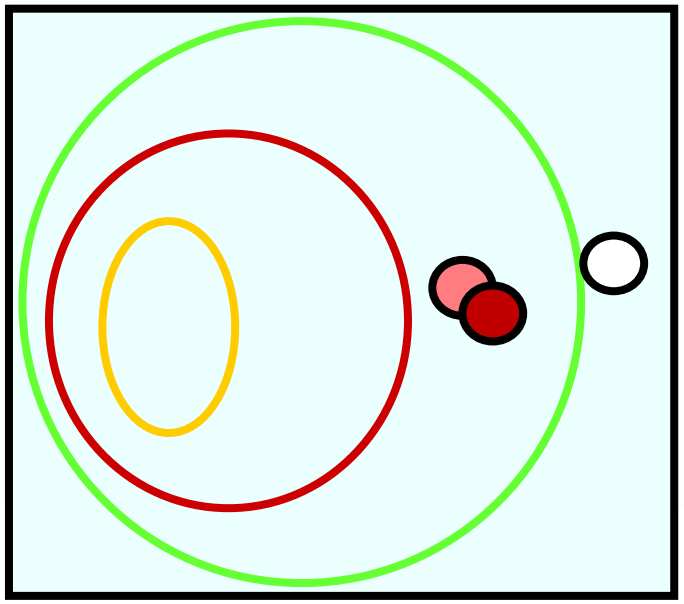
Marker position:

Fraction 1

Fraction 35

Results: Average in 6 patients

	W1→3	W1→6
Average marker displacement (cm)	0.27	0.24
Average surface displacement (cm)	0.37	0.75
% GTV reduction captured by markers	75%	31%



MRI GTV pre treatment
MRI GTV week 3
MRI GTV week 6
Average marker position w1
Average marker position w3
Average marker position w6

Tissue-to-Tissue Correspondence?

	LR	CC	AP	Vector
Landmarks in normal tissue	1.0	1.6	1.2	2.2
Fiducials Tumour regions	2.0	2.1	1.5	3.3

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Plan Adaptation

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Time needed for H&N treatment plan

1.	Import scan/delineate OARs	80 min
2.	Beam setup/objectives (scripts)	20 min
3.	Optimize	200 min
4.	Export Pinnacle/import Mosaiq	50 min
5.	Check plan	30 min
	Total	~ **7 hour**

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Challenges

- Workload of adaptive planning too high for large scale implementation
- How to automate planning
- How to reduce workload

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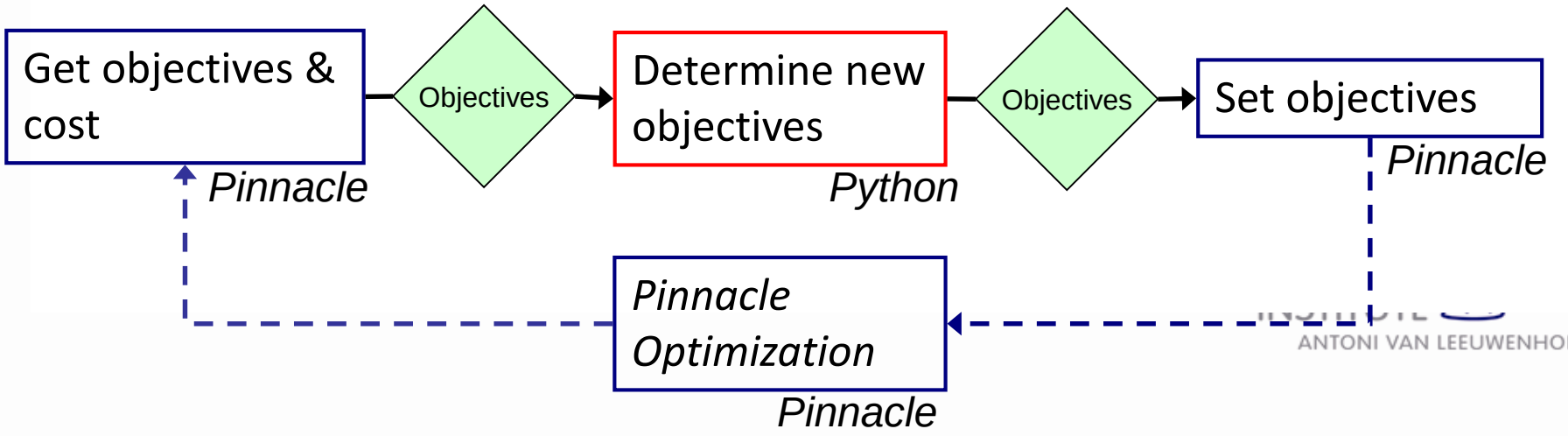
Automatic optimization

- 1st round, only objectives on: PTV's, Brainstem, Spinal cord, Ext-PTV+5
- systematically lower other objectives with 1Gy/round compared to obtained value (if penalty ≈ 0)
  Prescribe to $V_{95\%}$=99% in each round
- Repeat until all objectives create relevant cost



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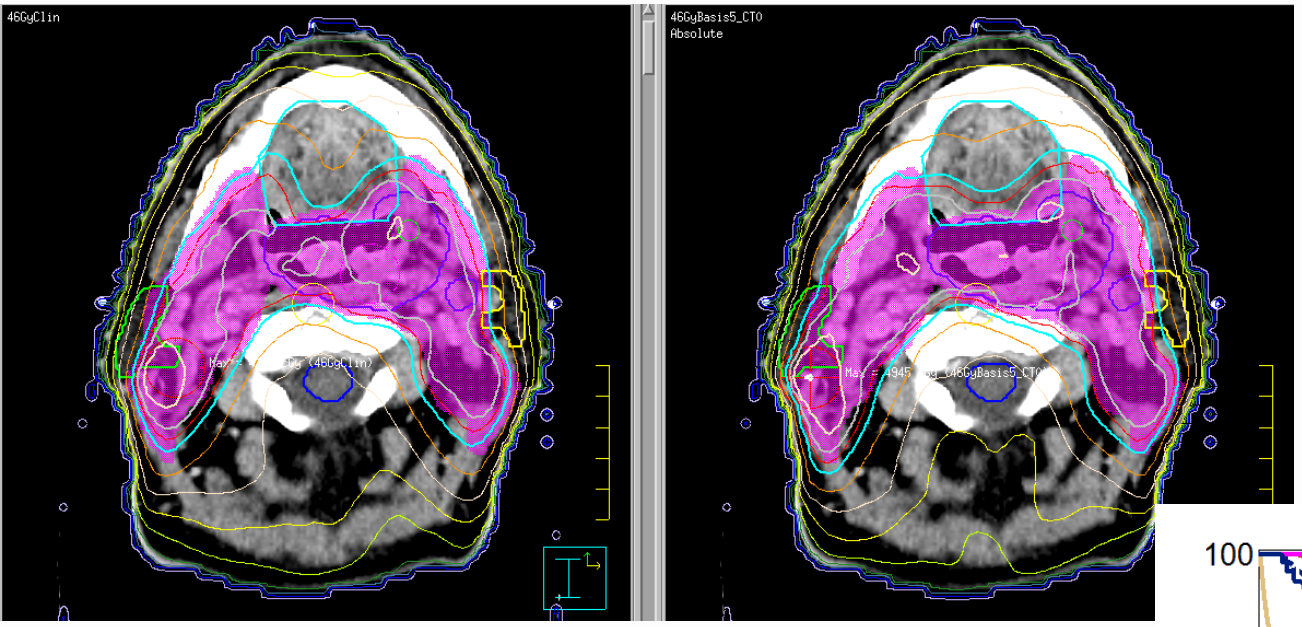
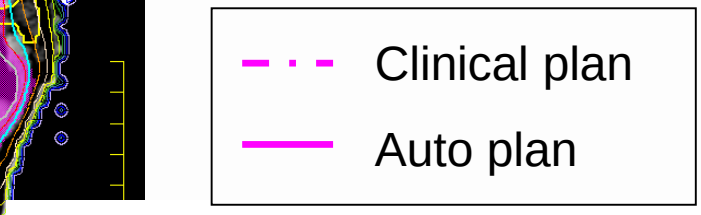
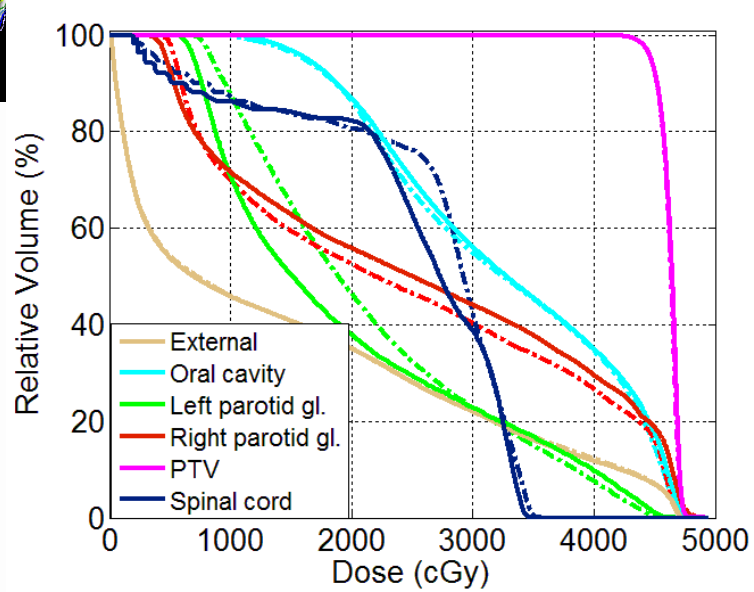
Automatic optimization: example

Clinical plan

Automatically optimized plan



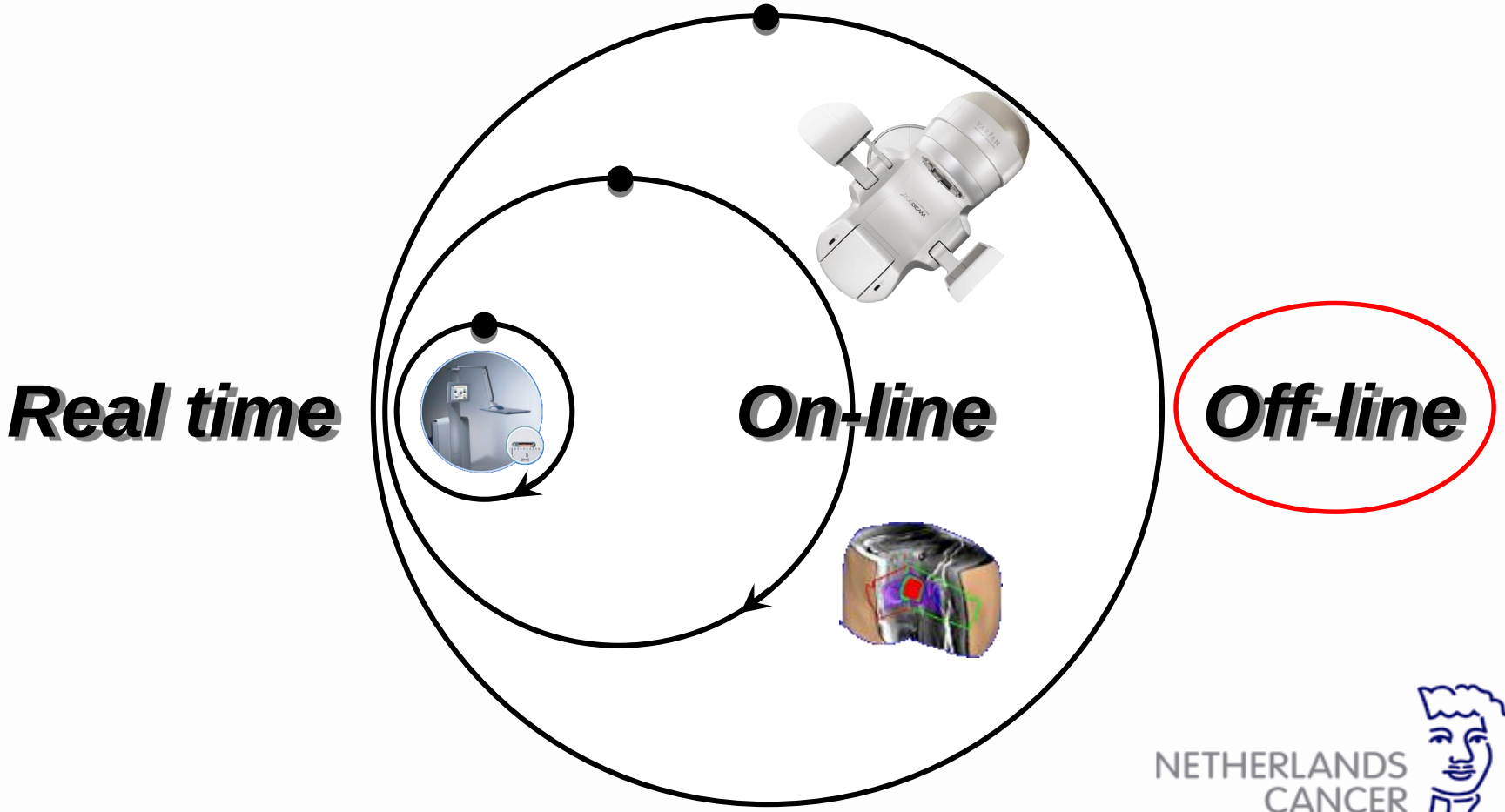




Autoplanner Prostate

- 10 clinical and automatically generated plans
- Evaluated by clinicians and dosimetrists
- Autoplan optimization: 30 minutes
- All automatic plans were clinically acceptable
- Clinicians prefered autoplan in 65%, dosimetrists 50%

Temporal Scales of Intervention



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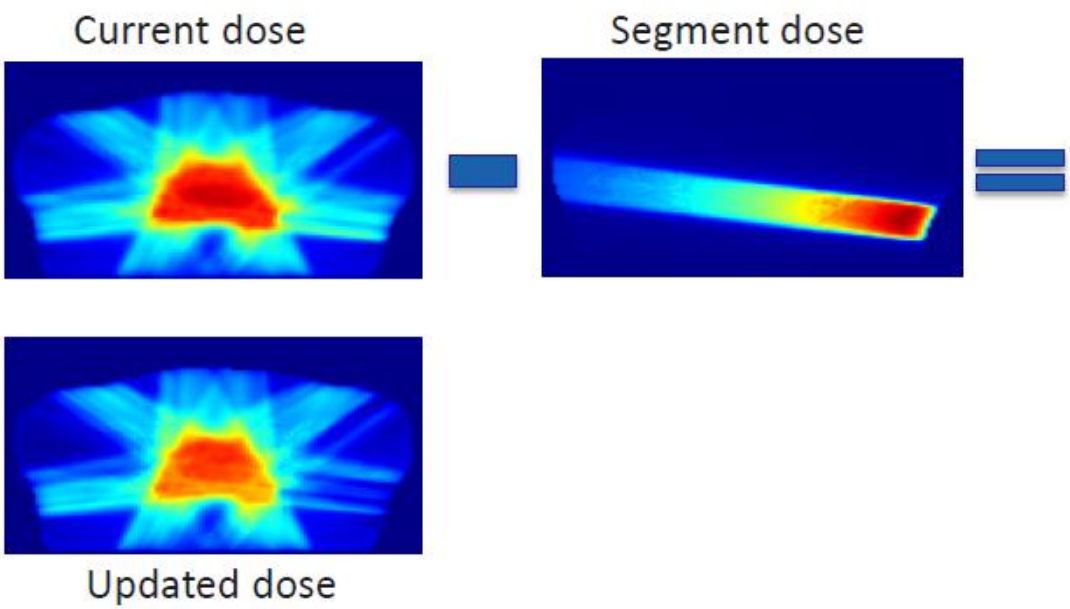
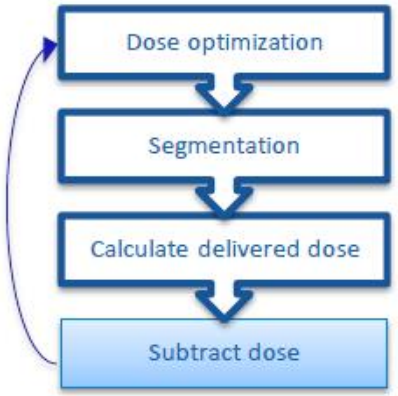
Modified from David Jaffray

Adaptive Sequencing





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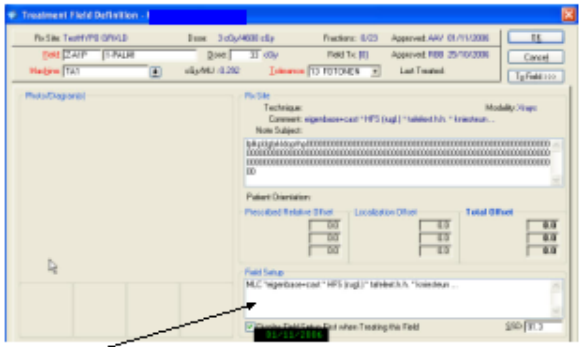
Modified from **Bas Raaijmakers**

Onder Tolerance ▼ staan de tolerantie tabellen.
ESK stuurt de bestralingsplannen door met tolerance: XRAY.
Pas dit aan indien nodig.

Tolerantie Tabellen

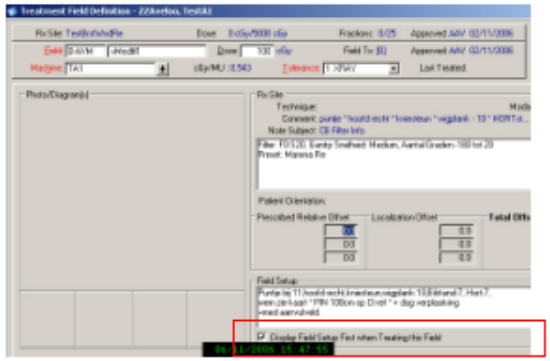
Tolerantie tabel 1 XRAY: bij instellingen met een ITA.
Tolerantie tabel 7 XRAY PIN: bij instellingen met een pin afstand.
Tolerantie tabel 2 Elektronen bij instellingen waarbij geen tolerantie gelden.
Tolerantie tabel 3 ELEKTRON7: bij instellingen waarbij de gantry hoek en de tafelrotatie vast staat.

Klik op button Field Setup. Onderstaand scherm verschijnt



Noteer de instelgegevens bij de Field Setup in hoofdletters. Gebruik hierbij de eerste 3 regels anders is de tekst niet terug te zien in de bestralingsruimte (valt van het scherm af).

Zet een vinkje onderaan bij Display Field Setup First when Treating:
Dit kan aan of uitgezet worden bij velden waar het nodig is om eerst de hulpmiddelen te bekijken voordat er wordt ingesteld/bestraald.



Als er een mal gebruikt wordt binnen het veld, vul het nummer in bij het vakje: Block.

Response Assessment

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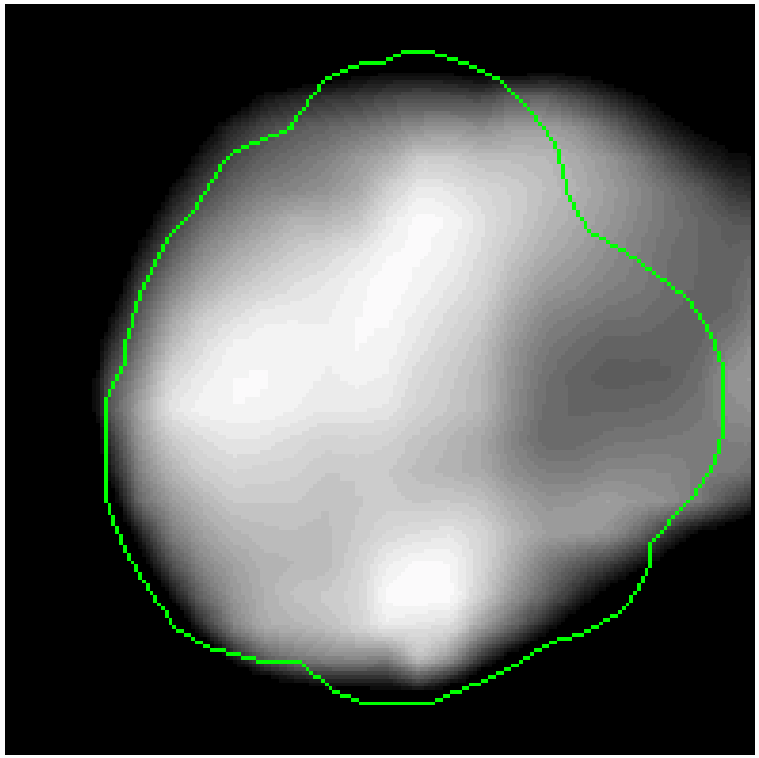
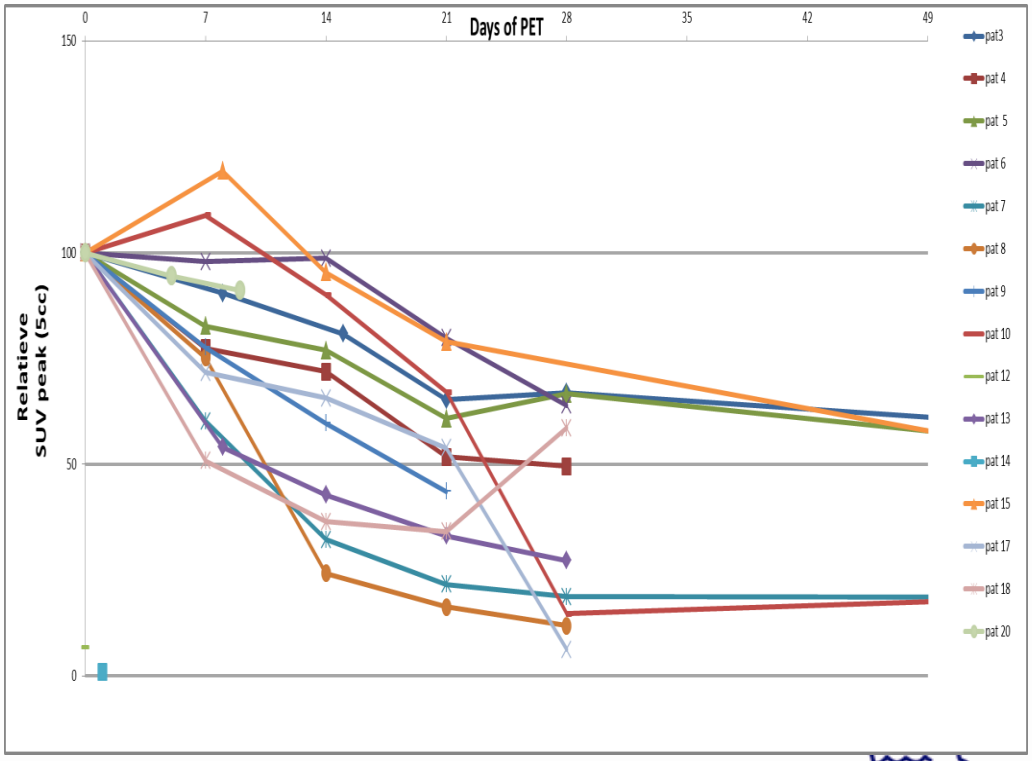
Response Monitoring in NSCLC Patients





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Challenges

- How to quantify response
- Has it prognostic value
- Has it predictive value
- How to adapt to response

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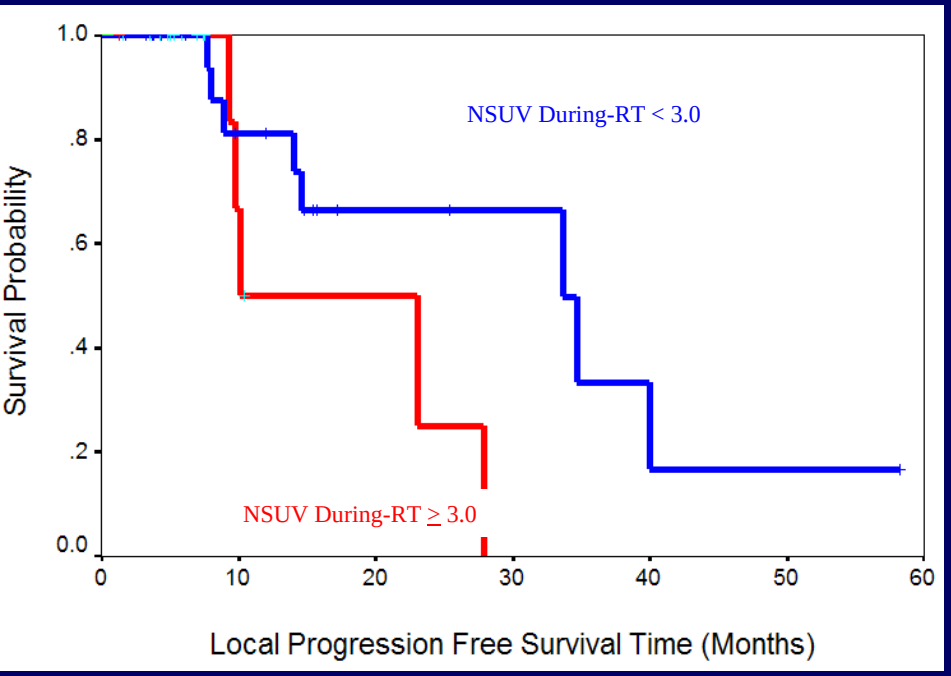
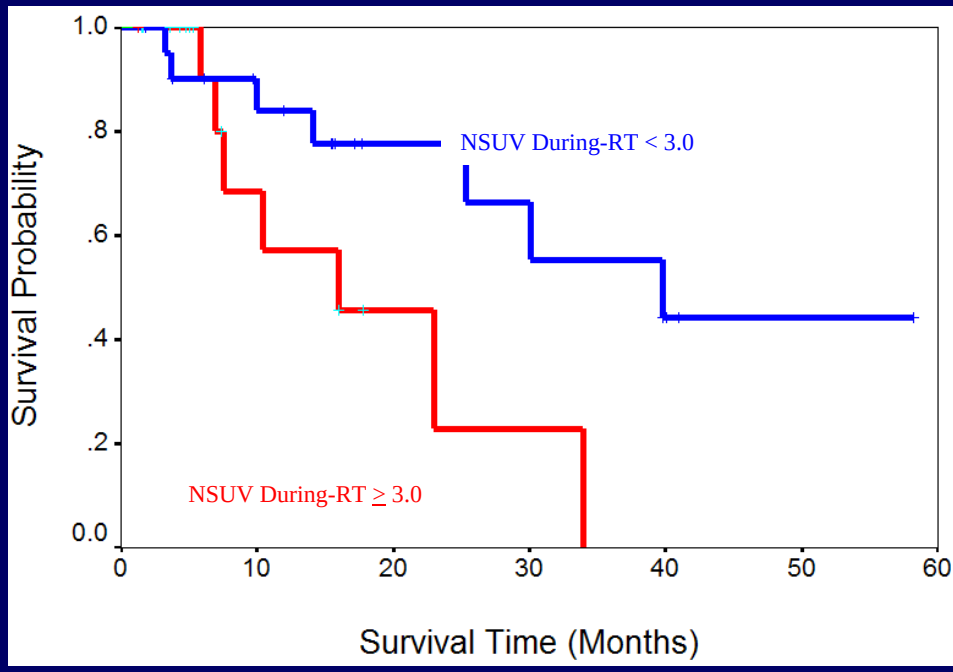
During-RT NSUV vs Survival

P=0.09



P=0.03



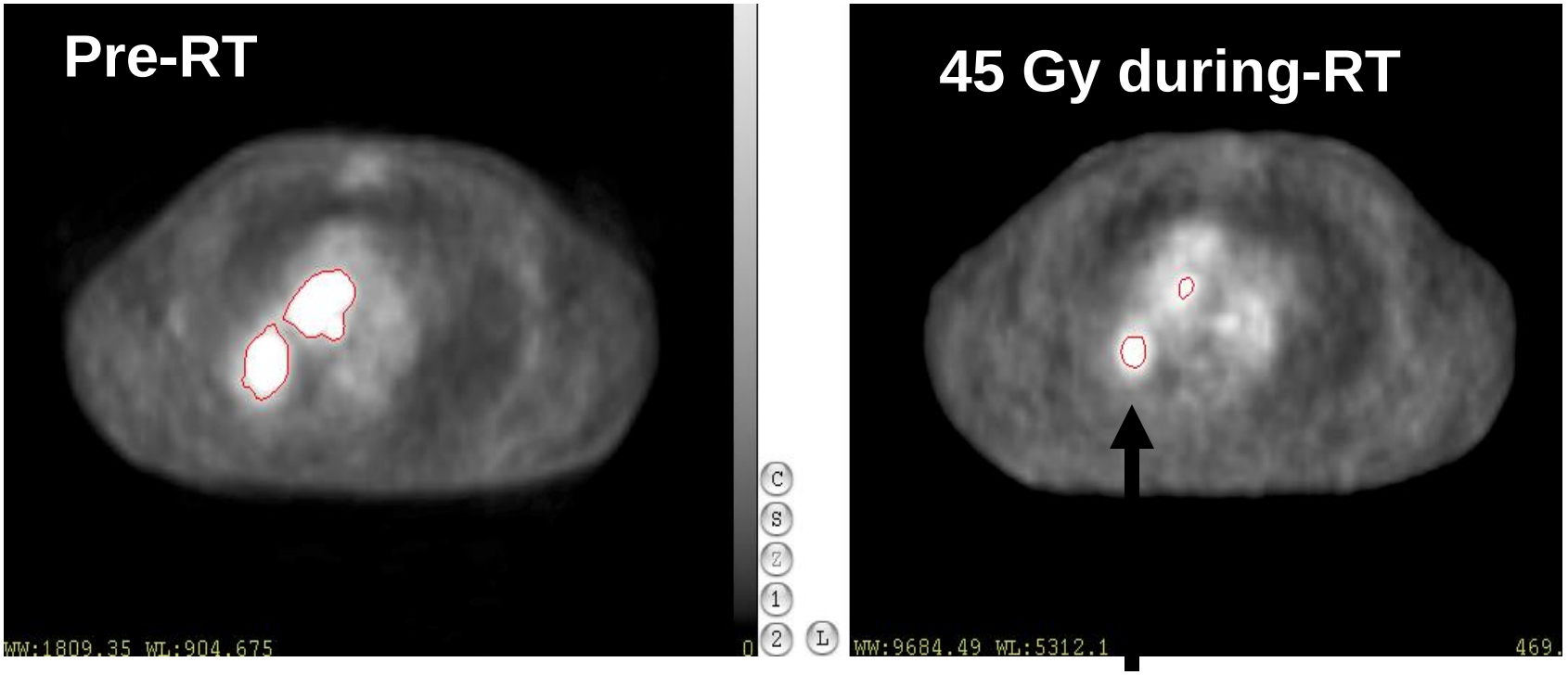
Local Progression Free Survival

Overall Survival

NSUV=SUVmax of tumor/SUVmean of aortic arch

Kong et al, ASTRO, 2009

RTOG 1106
During-RT PET to Guide Adaptive RT

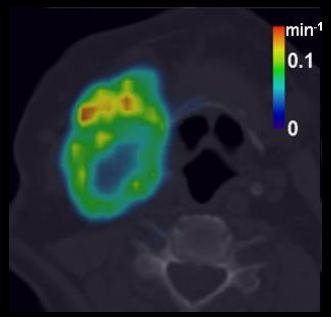


Experimental arm:

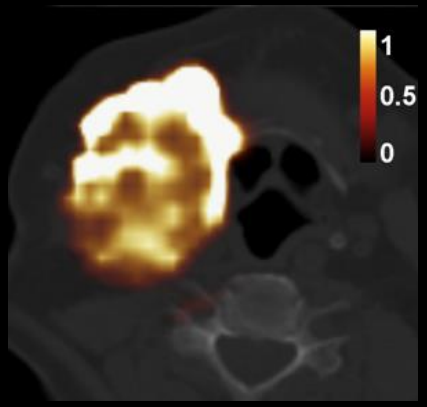
21x2.2Gy + re-PET/CT after 18 fr, replan for 9x2.2-3.8Gy up to a MLD of 20Gy, >=50Gy to original PTV

Applications – dose painting

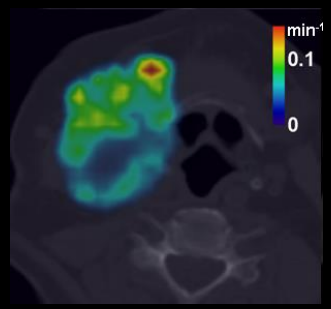
Pre-treatment



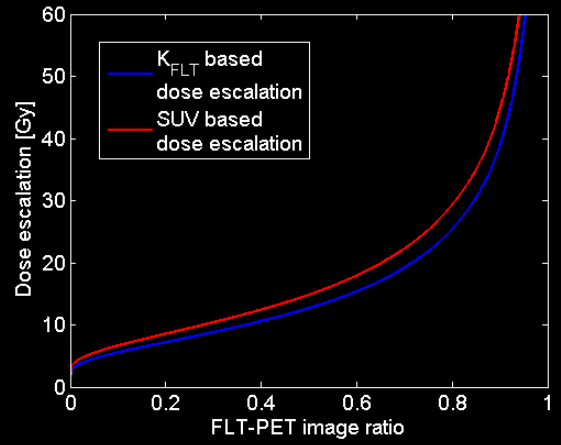
Treatment response

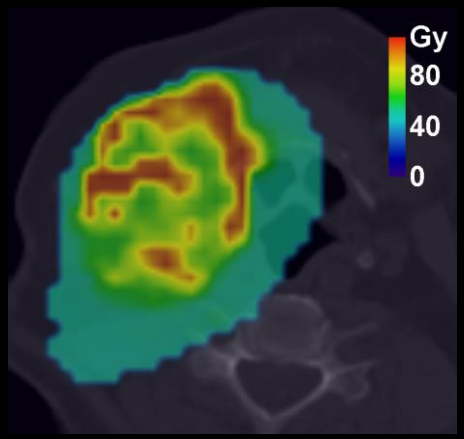


Mid-treatment



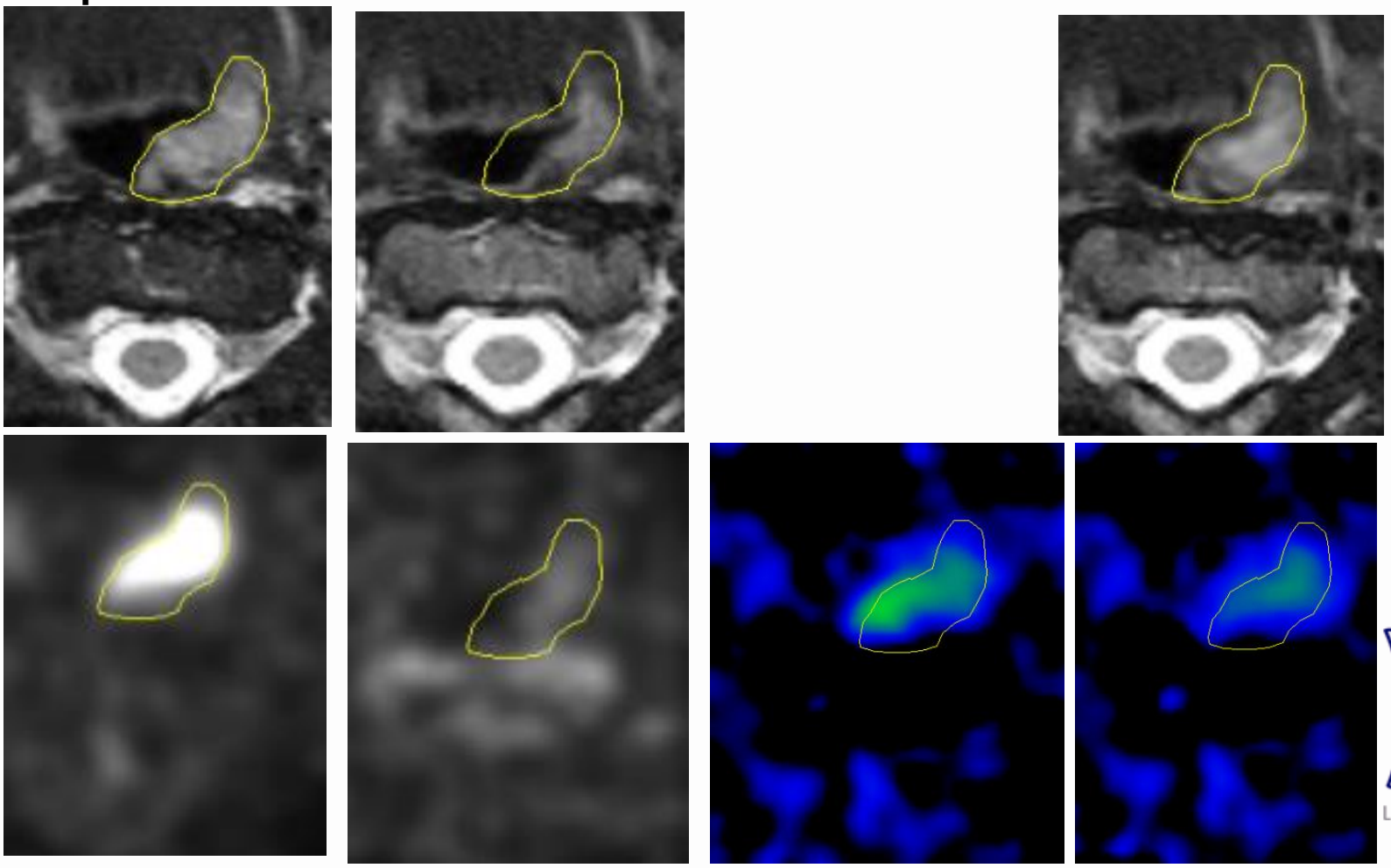
Prescription function





Tumor Regression and Response Assesment

T2 pretreatment **T2 mid-treatment** **Deformed T2 midtreatment**



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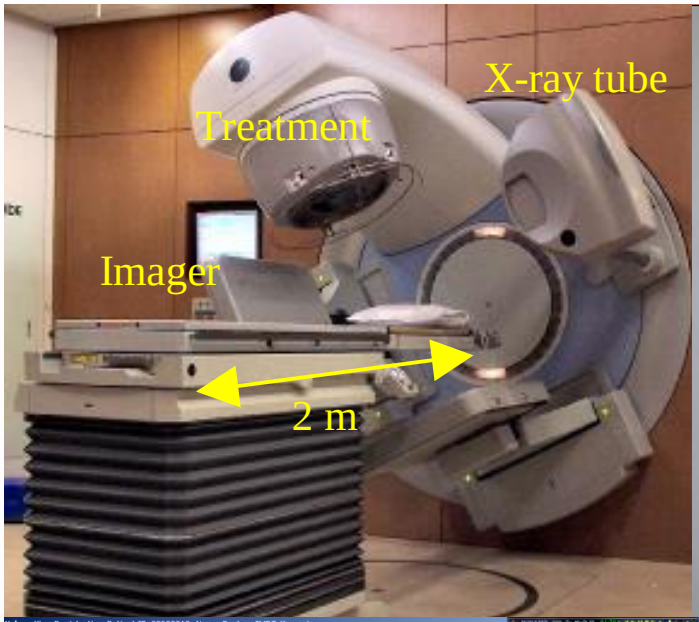
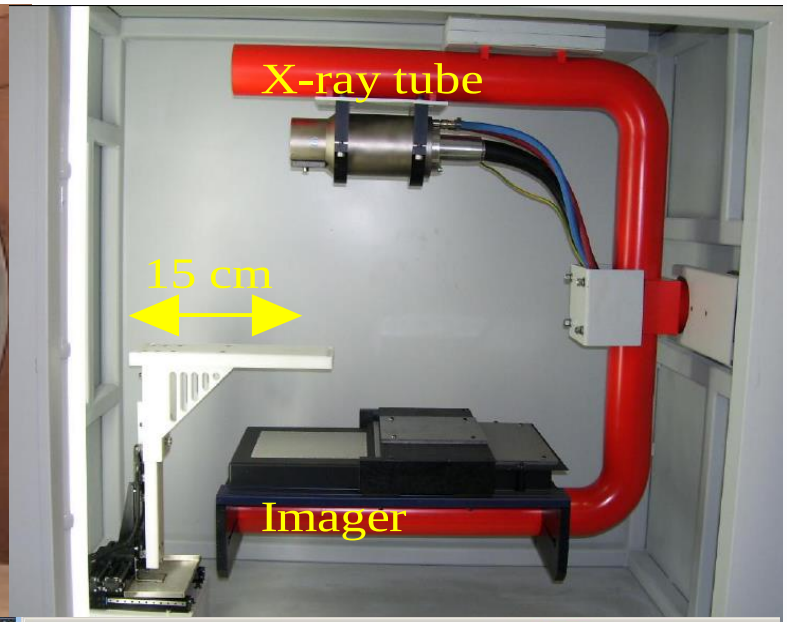
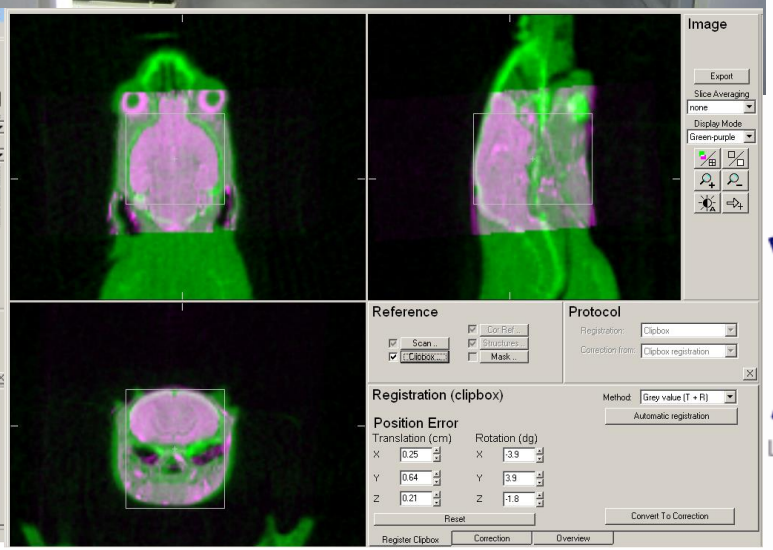
IGRT versus µIGRT







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Main Challenges

- In room image quality
- Deformable image registration accuracy
- Dose accumulation and interpretation
- Rapid plan adaptation
- Response monitoring and adaptation

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