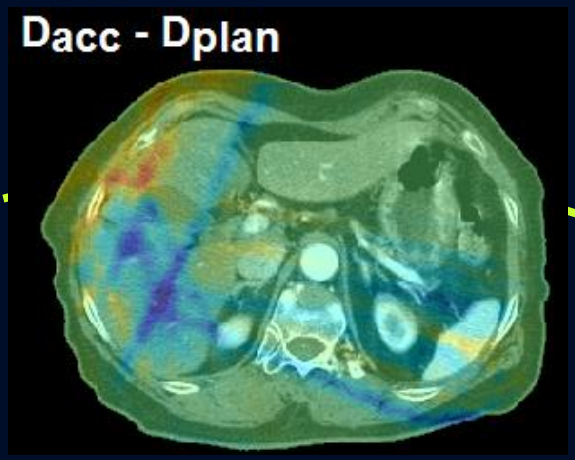
Image Guidance in the SBRT Era: Optimizing Imaging and Managing Uncertainties

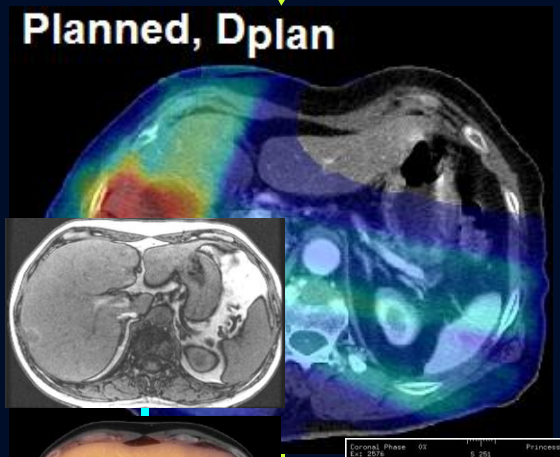
Kristy K Brock, Ph.D., DABR

Associate Professor

Department of Radiation Oncology, University of Michigan

University of Michigan
Medical School


Dacc - Dplan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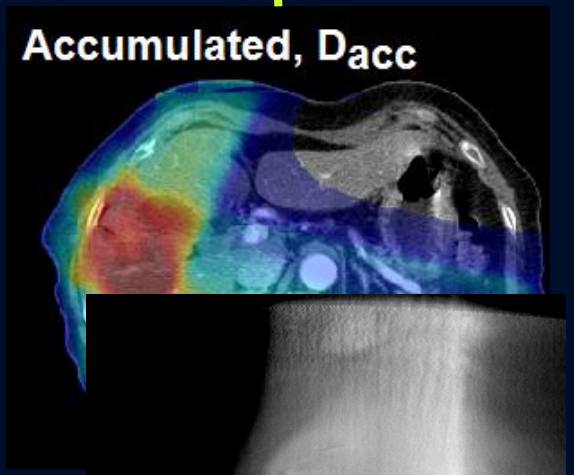
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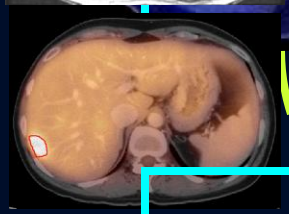

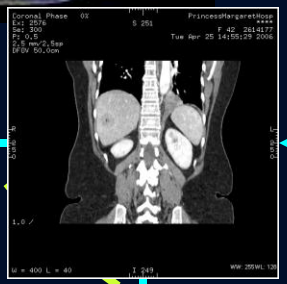

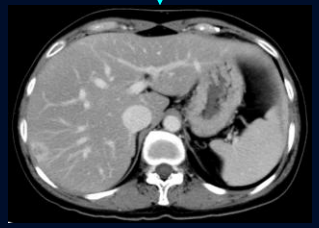

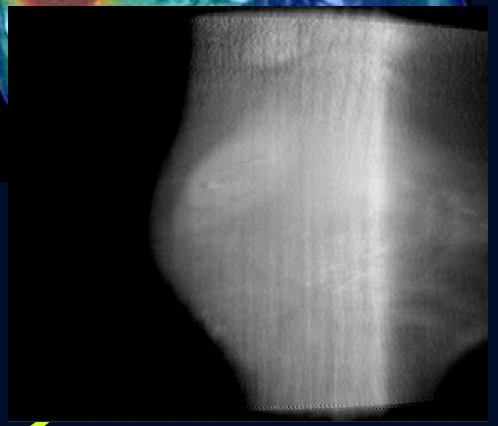

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ORIGINAL REPORT

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

Lester J. Peters, Brian O'Sullivan, Jordi Giralt, Thomas J. Fitzgerald, Andy Trotti, Jacques Bernier

What leads to deviations in plans?

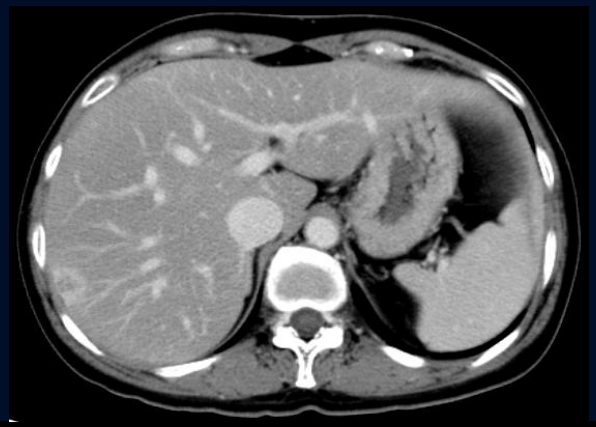
FAILURE TO ADHERE TO PROTOCOL SPECIFIED RADIATION THERAPY GUIDELINES WAS ASSOCIATED WITH DECREASED SURVIVAL IN RTOG 9704—A PHASE III TRIAL OF ADJUVANT CHEMOTHERAPY AND CHEMORADIOTHERAPY FOR PATIENTS WITH RESECTED ADENOCARCINOMA OF THE PANCREAS

ROSS A. ABRAMS, M.D.,* KATHRYN A. WINTER, M.S.,† WILLIAM F. REGINE, M.D.,‡ HOWARD SAFRAN, M.D.,§ JOHN P. HOFFMAN, M.D.,‖ ROBERT LUSTIG, M.D.,† ANDRE A. KONSKI, M.D.,¶ AL B. BENSON, M.D.,** JOHN S. MACDONALD, M.D.,†† TYVIN A. RICH, M.D.,‡‡ AND CHRISTOPHER G. WILLETT, M.D.§§

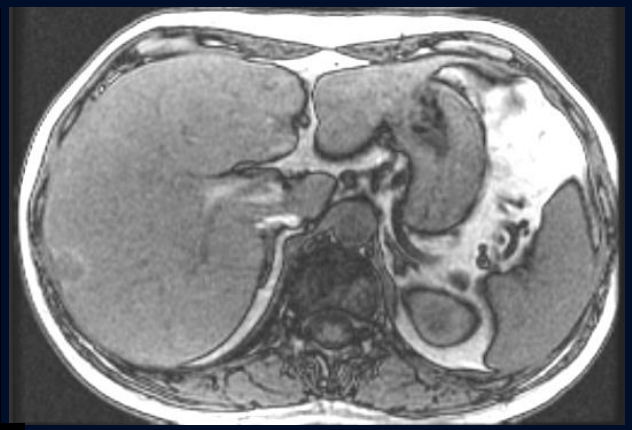
*Rush University Medical Center, Chicago, IL; †Radiation Therapy Oncology Group Statistical Center, Philadelphia, PA; ‡University of Maryland, Baltimore, MD; §Brown University, Providence, RI; ‖Fox Chase Cancer Center, Philadelphia, PA; ¶Wayne State Medical Center, Detroit, MI; **Northwestern University, Chicago, IL; ††St. Vincent's Cancer Care Center, New York, NY; ‡‡University of Virginia, Charlottesville, VA; §§Duke University, Durham, NC

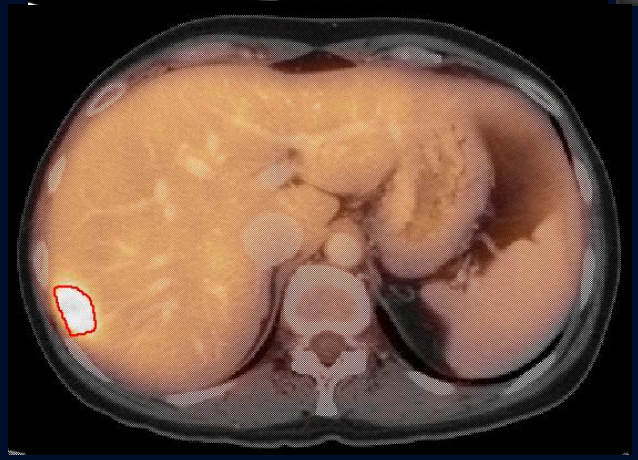
Uncertainties in RT: GTV/CTV Definition

CT

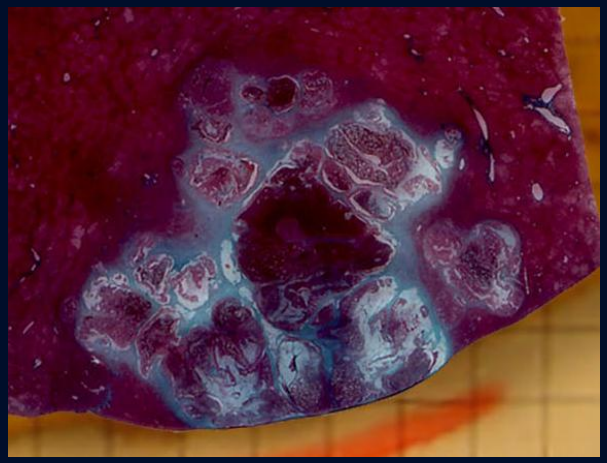


MR



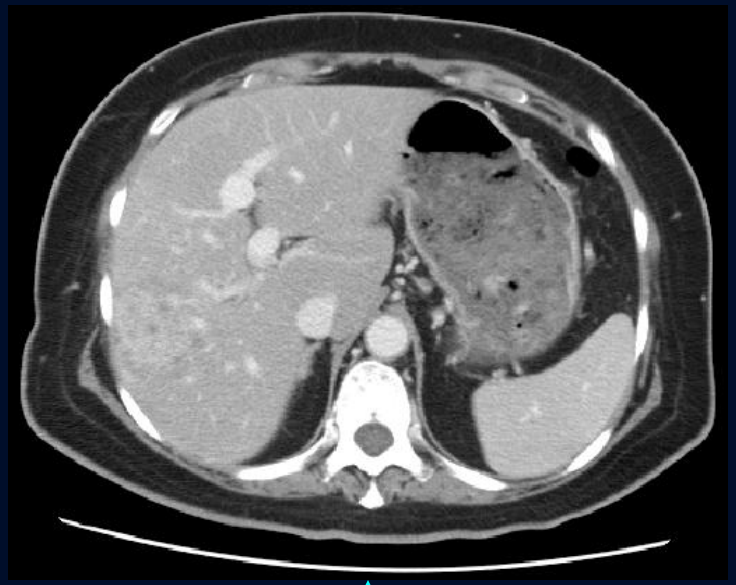


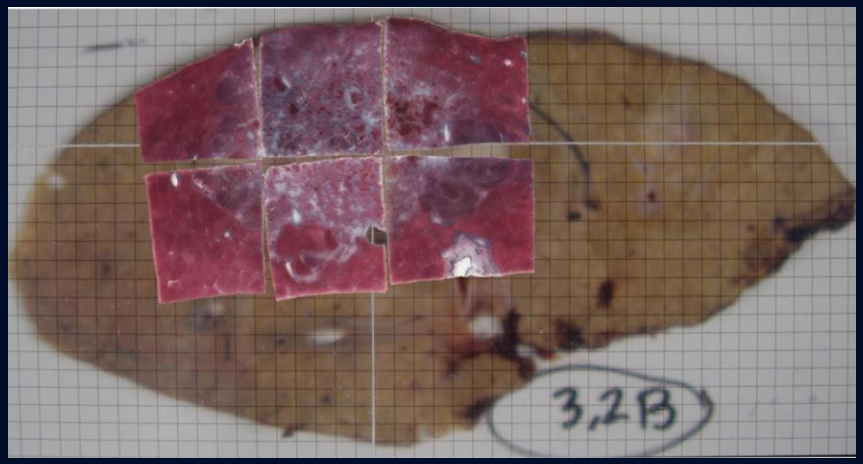
CT/PET



Histology

In Vivo Image Validation





Triphasic CT Images

Multiple Sequence MR Images

FDG-18 PET Images

Surgical Excision of Liver Lobe

Fresh Specimen MR Imaging

Specimen Fixation

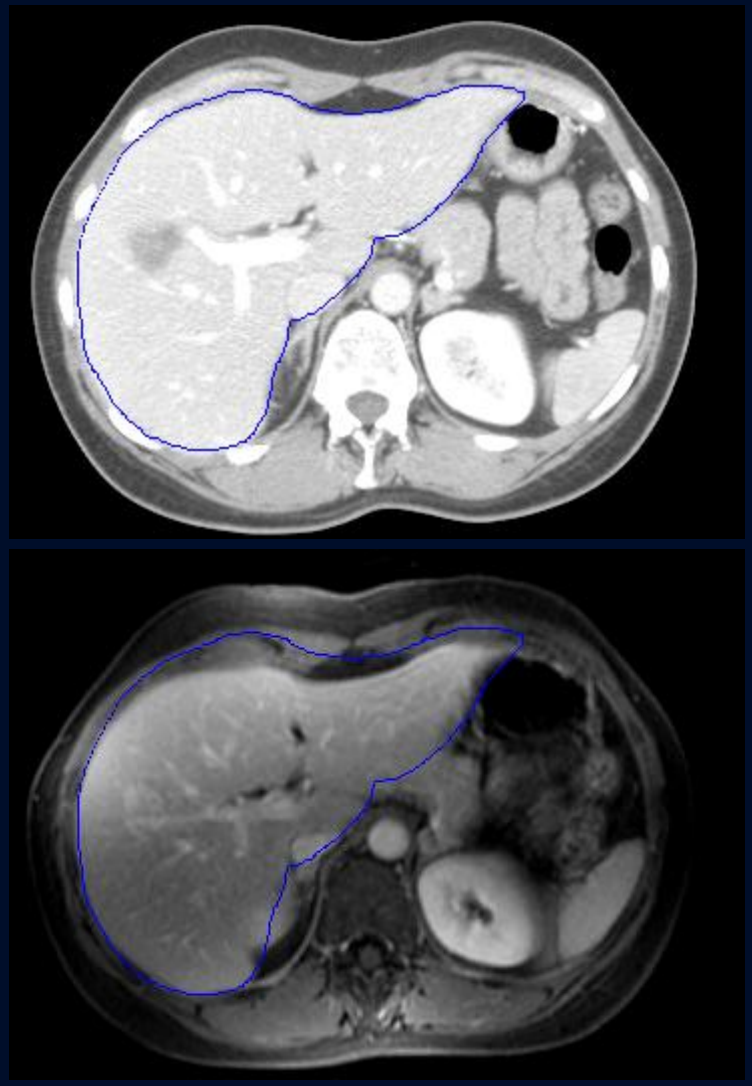
Fixed Specimen MR imaging

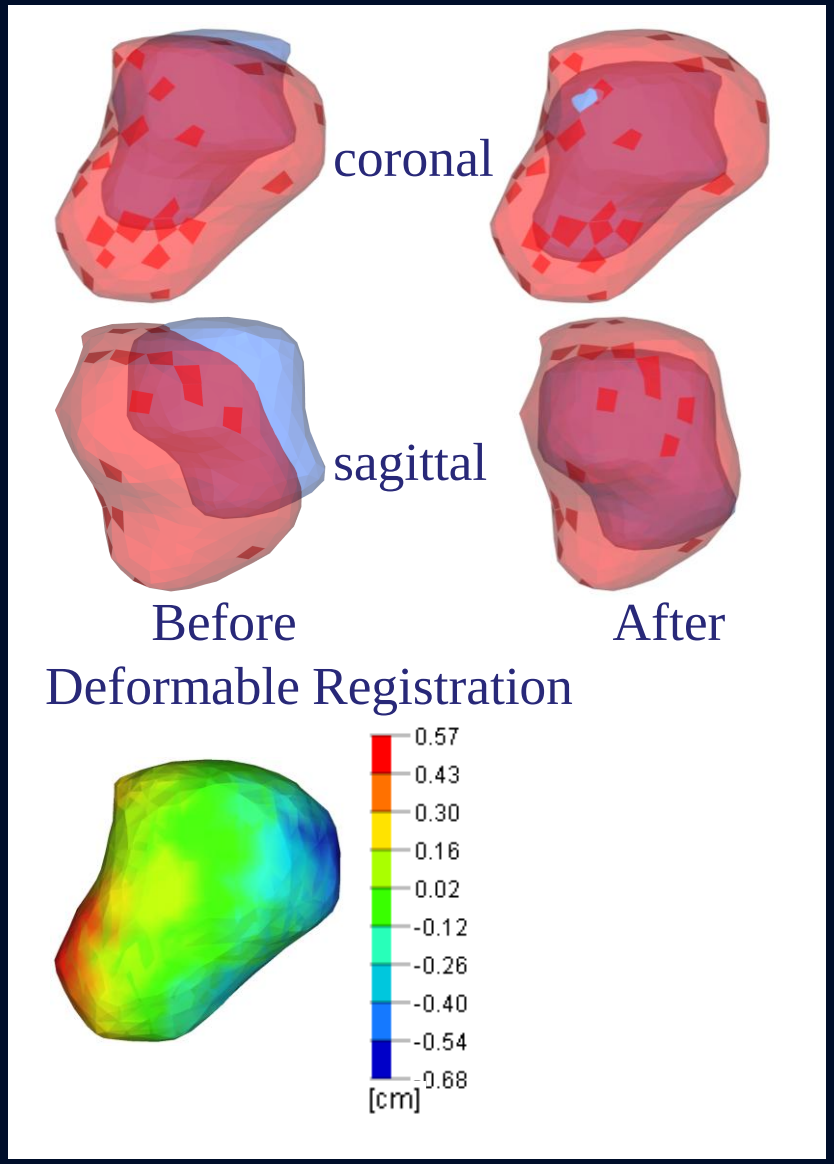
Specimen dissection

Histological Analysis of Tumor

Accurate Target Definition

Prior to Deformable Registration



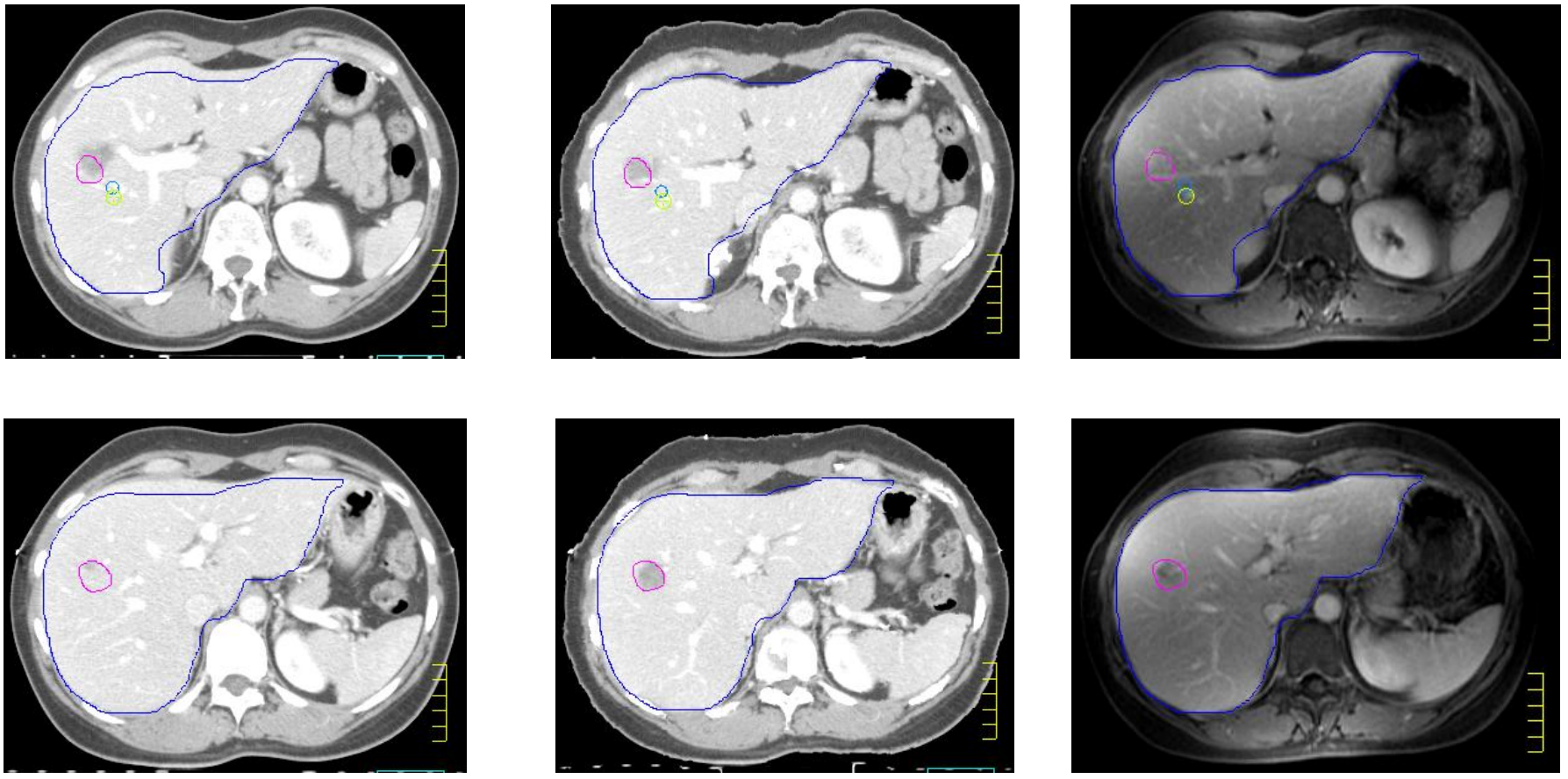


Removing Confounding Geometry

CT-exhale

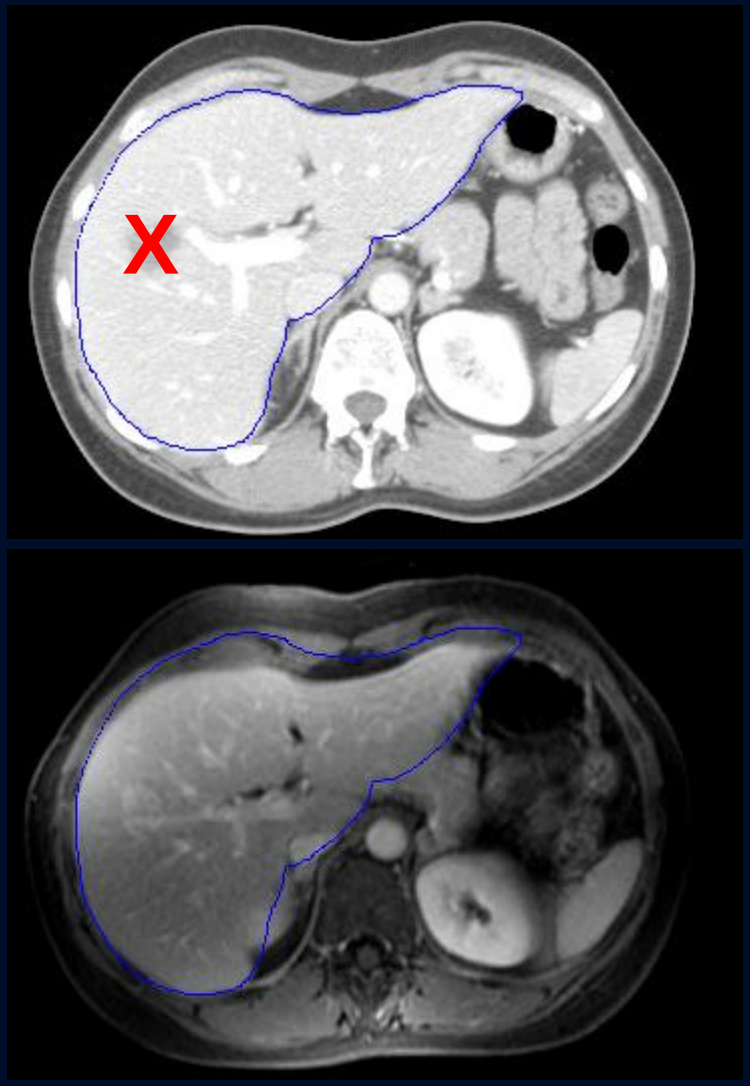
CT_{GRV}

MR-exhale

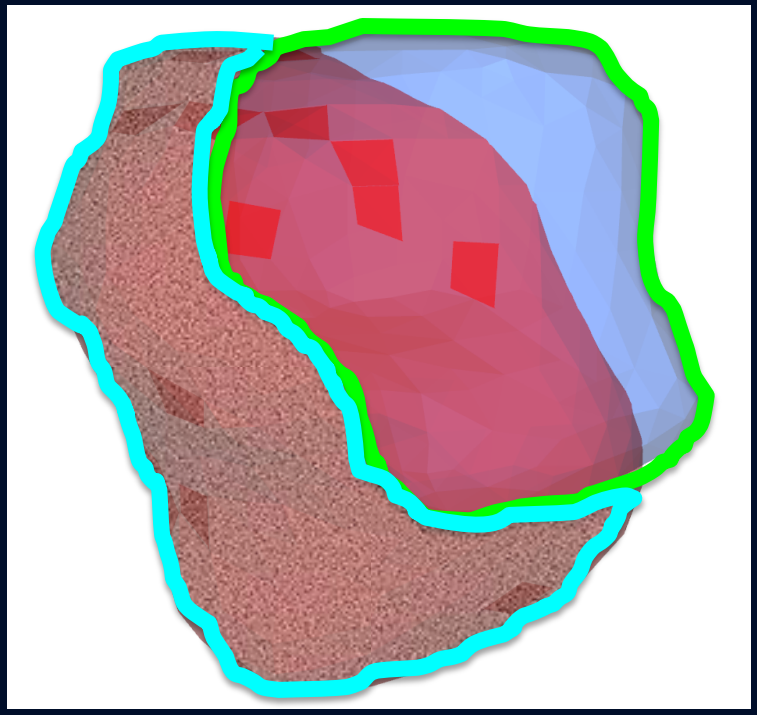


Clinical Effect

Prior to Deformable Registration



GTV (defined on MR, mapped to CT for Tx)



Region of CT-defined GTV that is missed

Target delineation variability and corresponding margins of peripheral early stage NSCLC treated with SBRT

H Peulen, J Belderbos, M Guckenberger, AHope, I Grills, M van Herk, JJ Sonke

March 2015Volume 114, Issue 3, Pages 361–366

- 16 early stage NSCLC GTV's were delineated by 11 radiation oncologists from 4 institutes.
- A median surface was computed and the delineation variation perpendicular to this surface was measured
  - Local standard deviation = SD

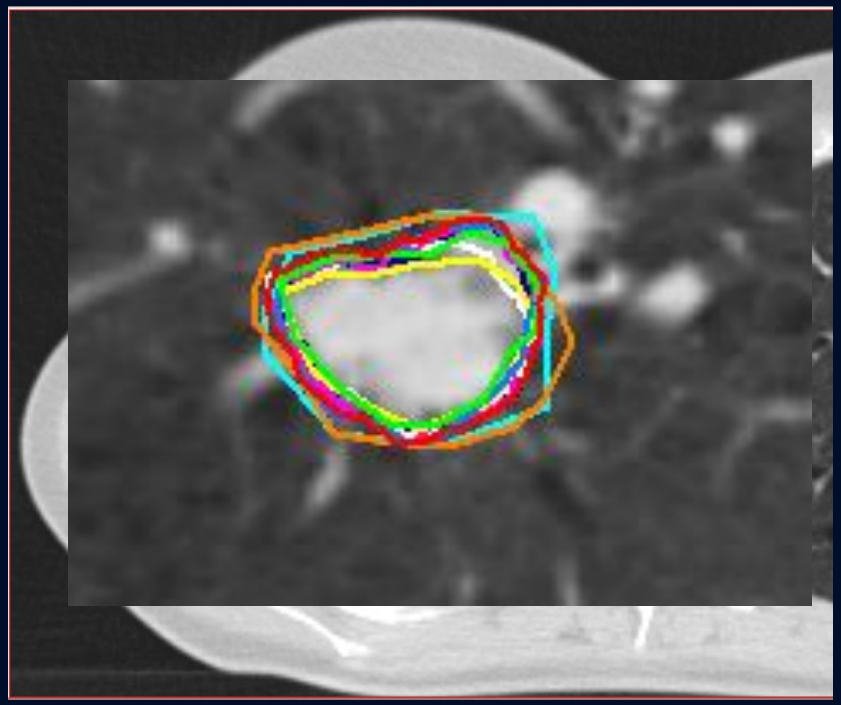
Target delineation variability and corresponding margins of peripheral early stage NSCLC treated with SBRT

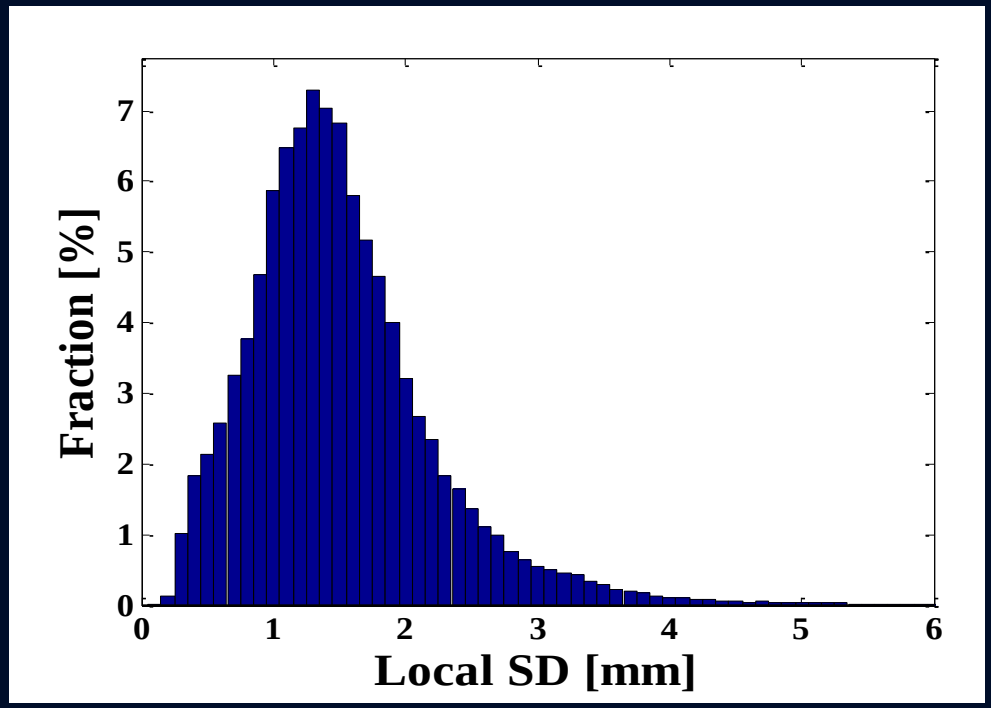
- The overall target delineation variability was quantified by the RMS of the local SD.
- The required margin was determined by expanding all delineations to encompass the median surface, where after the underlying probability distribution was modeled by a number of uncorrelated ‘pimples-and-dimples’.

Target delineation variability and corresponding margins of peripheral early stage NSCLC treated with SBRT

- The overall target delineation variability was 2.1 mm (RMS).
- Institute I–III delineated significantly smaller volumes than institute IV, yielding target delineation variabilities of 1.2 mm and 1.8 mm respectively.
- The margin required to obtain 90% coverage of the delineated contours was 3.4 mm and 5.9 mm respectively.

Target Definition Uncertainty for SBRT





16 patients

10 radiation oncologists

RMS = 2 mm (1SD)

Target delineation variability and corresponding margins of peripheral early stage NSCLC treated with SBRT

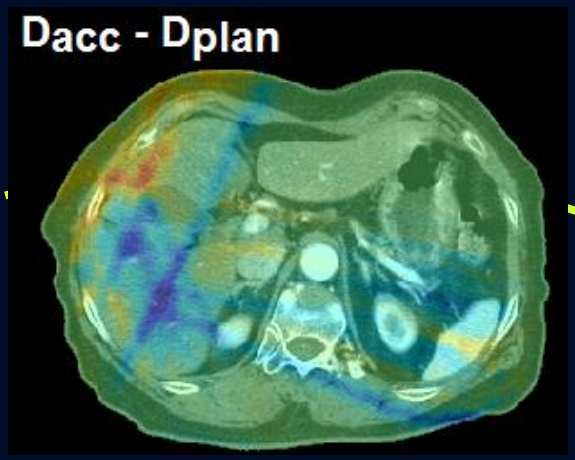
- The factor α in $M = \alpha\Sigma$ required to calculate adequate margins was 2.8–3.2, which is larger than the 2.5 found for 3D rigid target displacement.

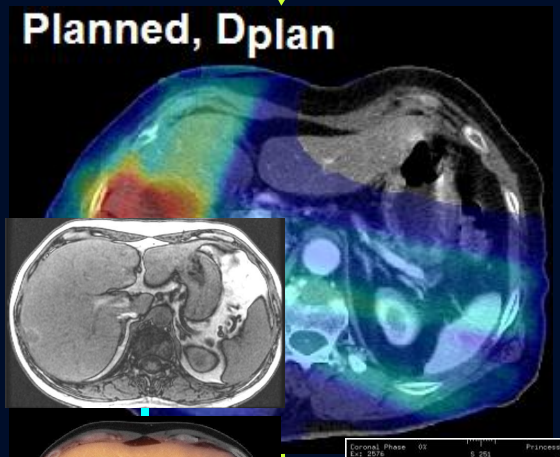
Conclusion:

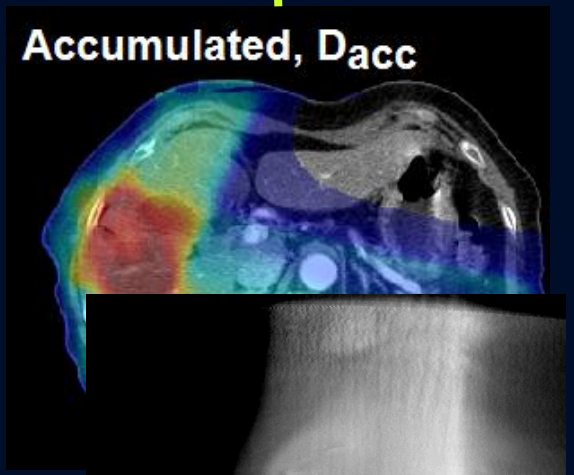
- A relatively small target delineation uncertainty of 1.2 mm–1.8 mm (1SD) was observed for early stage NSCLC.

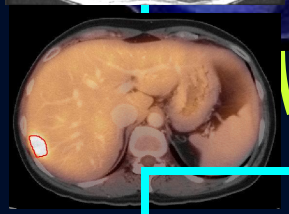
Target delineation variability and corresponding margins of peripheral early stage NSCLC treated with SBRT

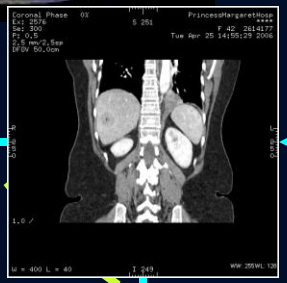
- A 3.4–5.9 mm GTV-to-PTV margin was required to account for this uncertainty alone, ignoring other sources of geometric uncertainties.

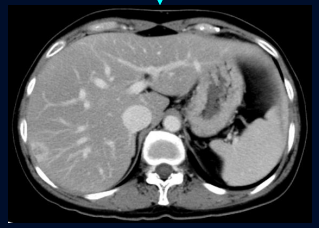

Dacc - Dplan

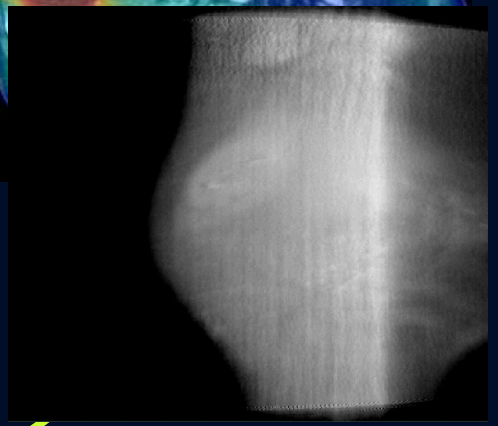

Planned, Dplan


Accumulated, Dacc









The Role of IGRT

- Patients are not consistent from day to day
  - Soft tissue moves and deforms
  - Tumor and critical normal tissue do not always track with bones and external surface
- Treating normal tissue is never beneficial
  - Reducing the volume of normal tissue treated often enables a higher dose to be delivered to the target
  - Higher doses often lead to better tumor control

In-Room Technologies: volumetric CT-based

Varian
kV planar
kV CBCT
MV planar

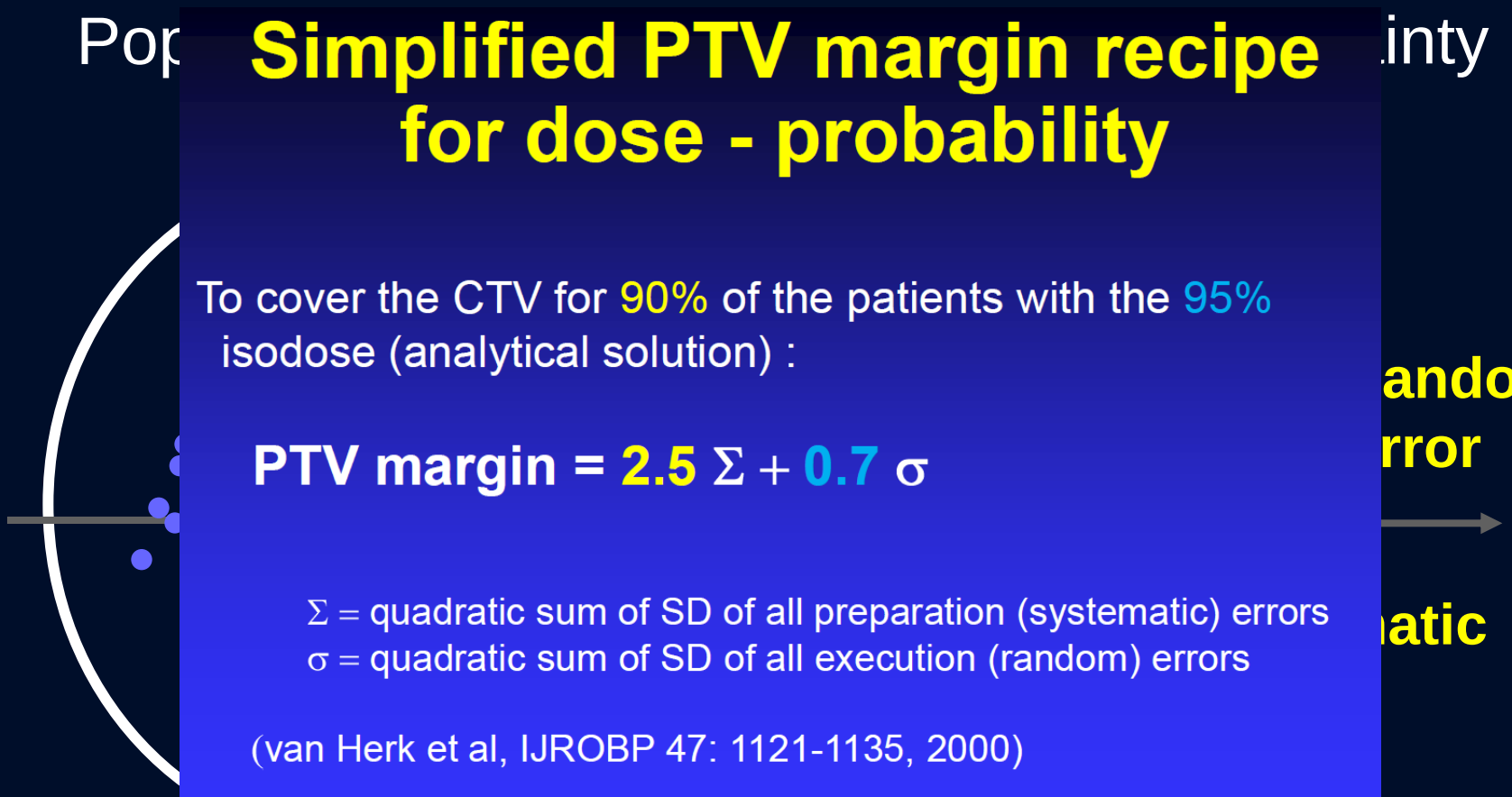
Elekta
kV planar
kV CBCT
MV planar

Siemens
MV planar
MV CBCT

Siemens
In-room CT

Accuracy
Tomotherapy
MV CT

Why In Room Imaging?



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

*Courtesy Tim Craig, Marcel van Herk

PTV Margins in SBRT

- Smaller number of fractions has an impact on the model
- “Random errors” become systematic errors in the limit of 1-5 fractions

Components of a PTV

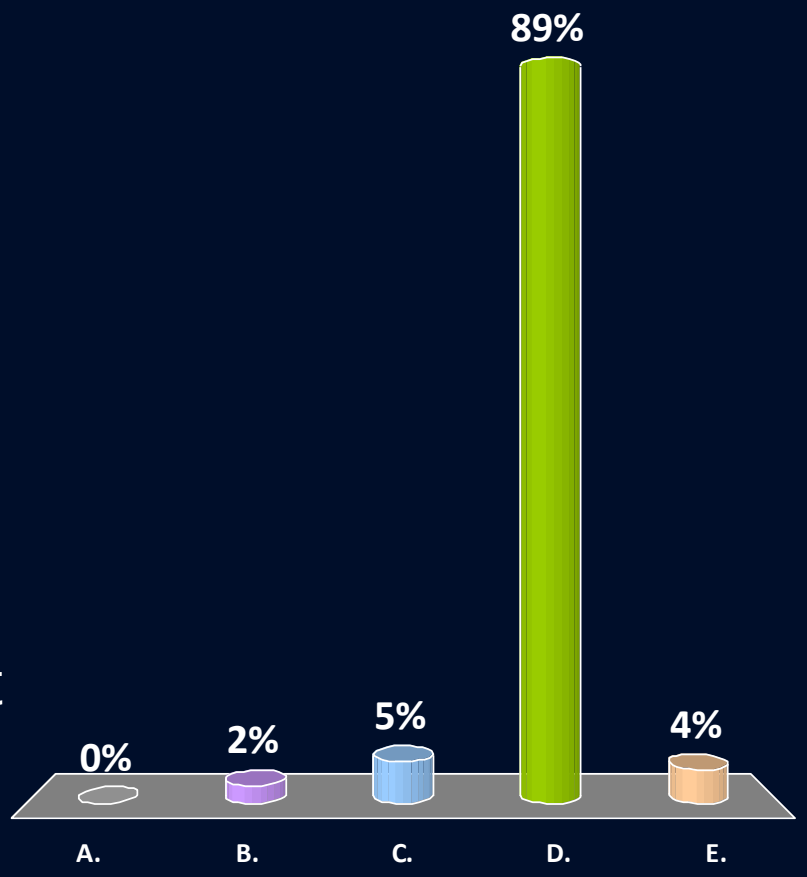
- The PTV is a geometrical concept introduced for Tx planning and evaluation.
- It is the recommended tool to shape absorbed-dose distributions to ensure that the prescribed absorbed dose will actually be delivered to all parts of the CTV with a clinically acceptable probability, despite geometrical uncertainties such as organ motion and setup variations.
- It is also used for absorbed-dose prescription and reporting.
- It surrounds the representation of the CTV with a margin such that the planned absorbed dose is delivered to the CTV.
- This margin takes into account both the internal and the setup uncertainties.
- The setup margin accounts specifically for uncertainties in patient positioning and alignment of the therapeutic beams during the treatment planning, and through all treatment sessions.

ICRU 83, 2010

SAMS Question

1. Daily image guidance allows the planning target volume to be

A. Eliminated as long as you can visualize bony anatomy on the image
B. Eliminated as long as you can visualize the tumor on the image
C. Eliminated as long as you can visualize the tumor and breathing motion is suspended
D. Reduced, but uncertainties (in processes such as image registration and corrections) but still be taken into account
E. Daily image guidance does not impact the planning target volume



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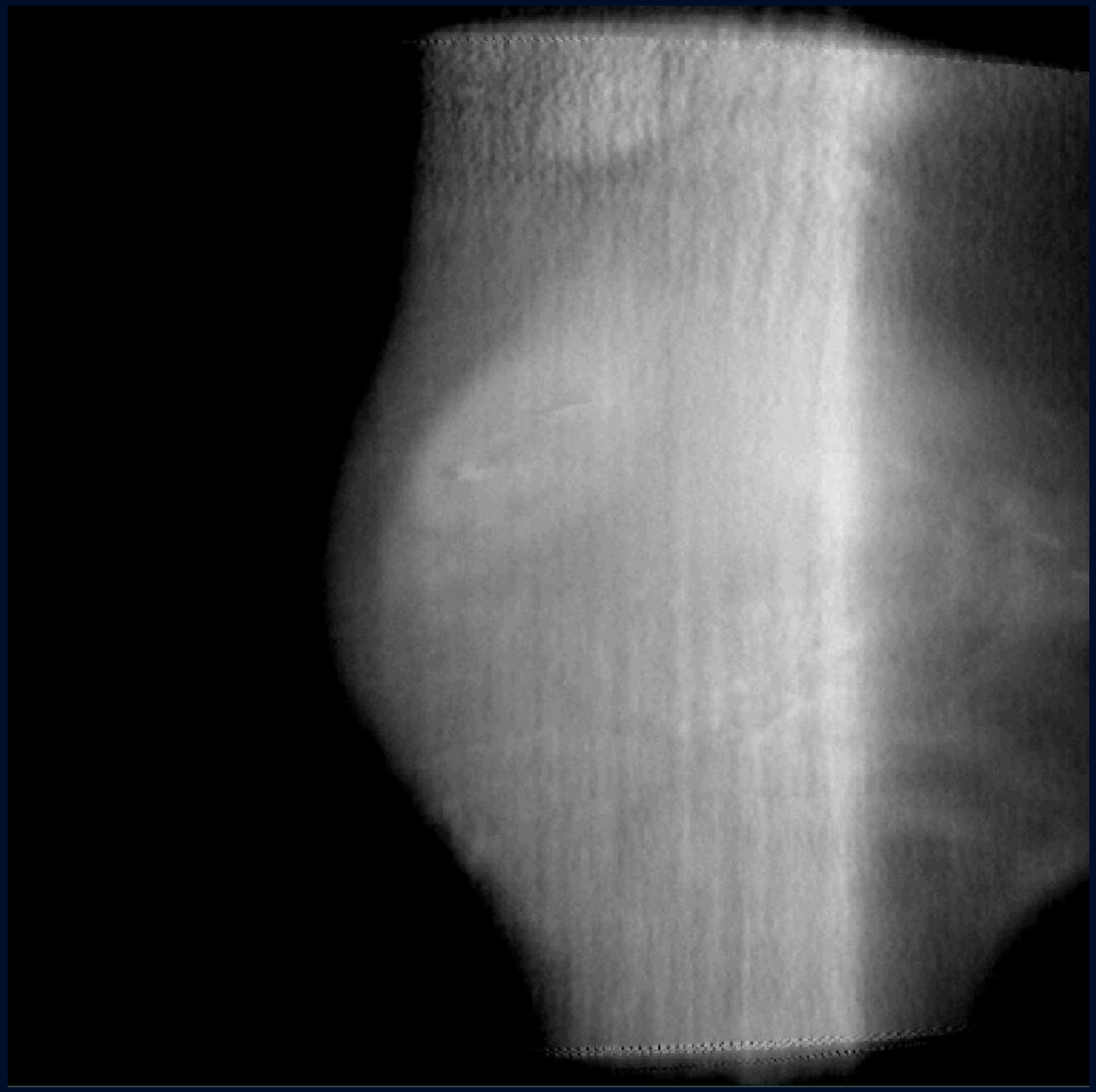
Marcel van Herk, Different Styles of Image-Guided Radiotherapy, Seminars in Radiation Oncology, 17(4), October 2007, 258-267

Image Guidance Strategy

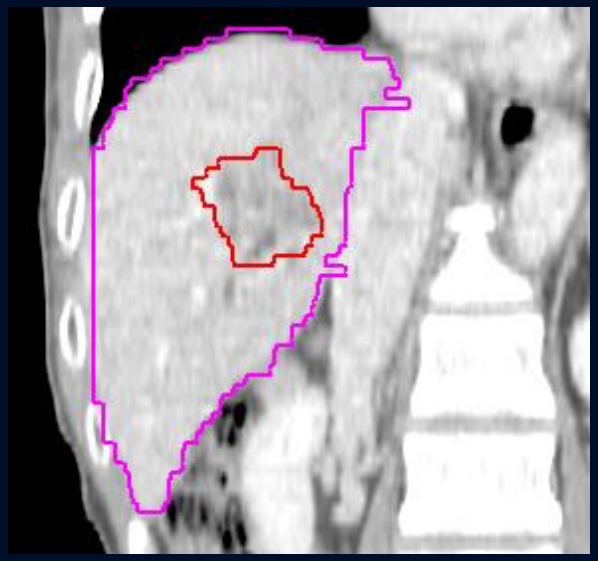
Purpose of Image Guidance

- Localize reference position of tumor and surrounding anatomy
  - Breath hold treatment
  - Free breathing treatment
- Verify breathing motion or stability of breath hold
- Verify correlation with tracking/gating system

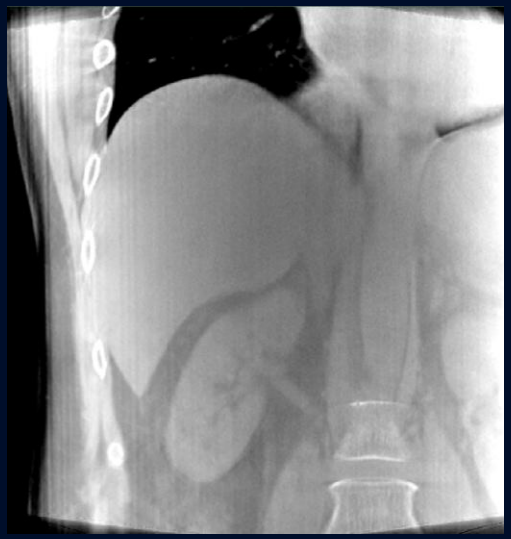
Where’s the tumor?



IGRT on an Invisible Tumor

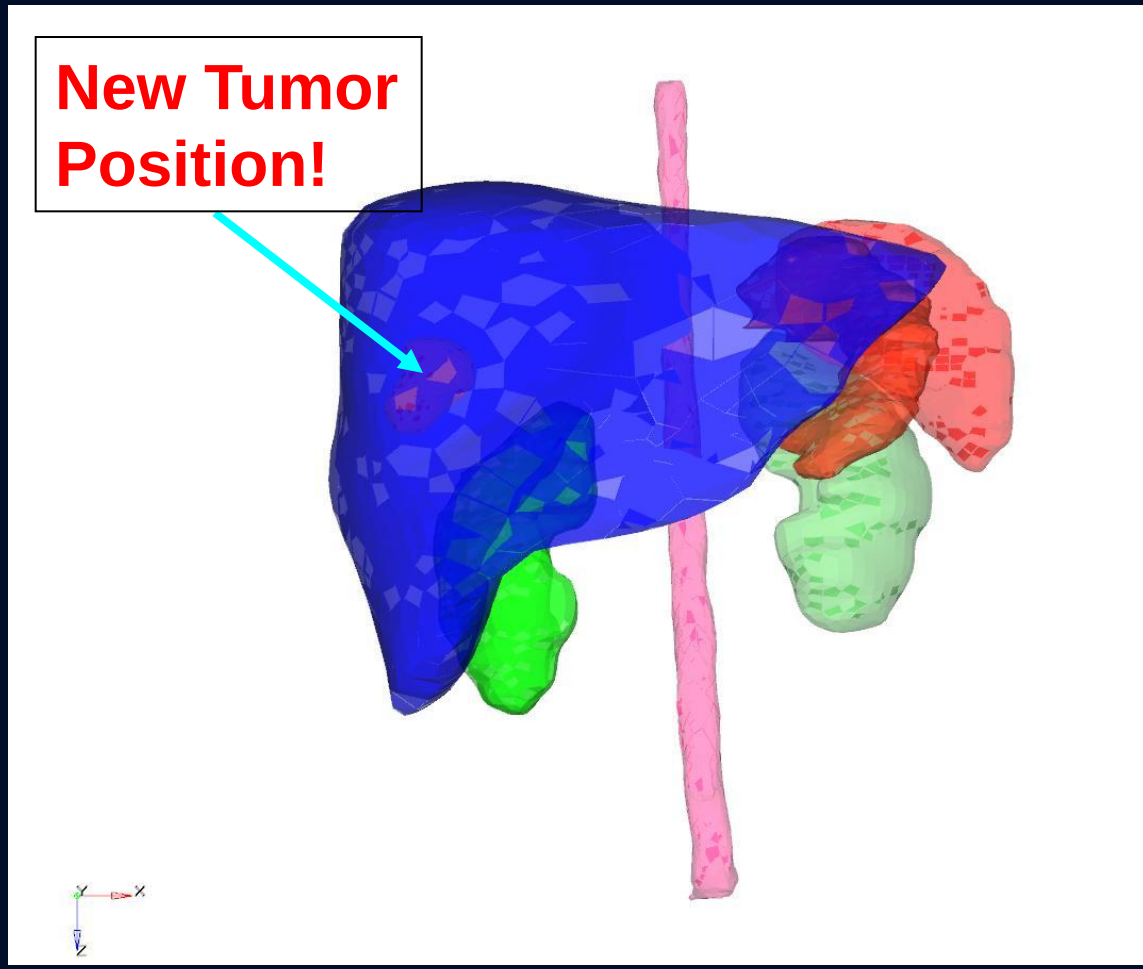


Planning CT [w contrast]



CBCT [w/o contrast]

Resolve Geometric discrepancies

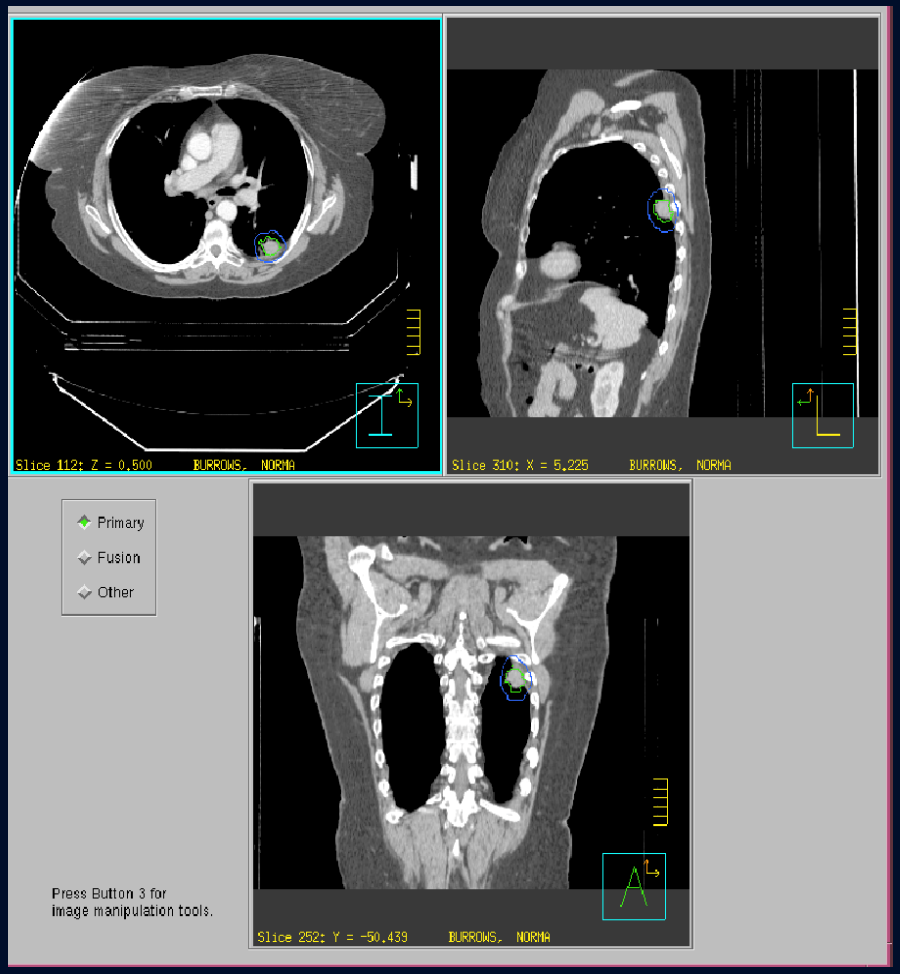


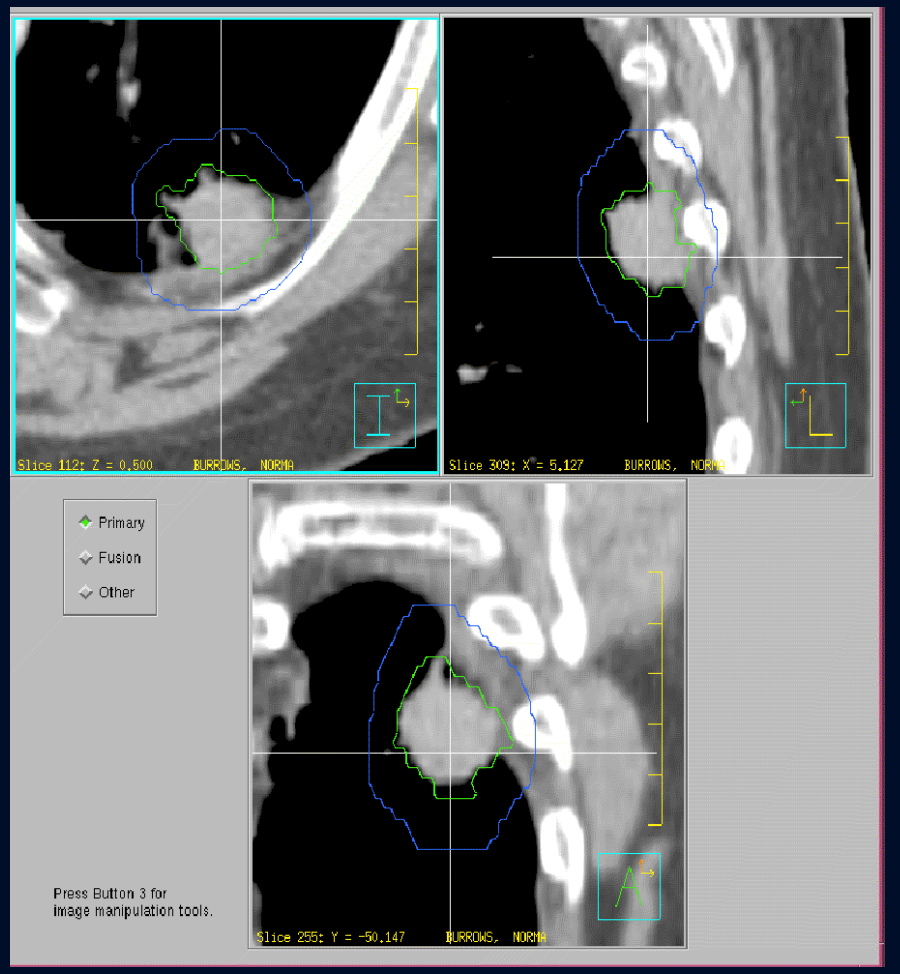
Accurate Tumor Guidance
12 Liver Patients: 6 Fx Each
Rigid Reg → Deformable Reg

Δ Tumor	dLR	dAP	dSI	abs(dLR)	abs(dAP)	abs(dSI)
AVG	-0.04	-0.01	0.01	0.08	0.10	0.10
SD	0.10	0.15	0.20	0.07	0.11	0.17
Max	0.27	0.43	0.97	**0.34**	**0.65**	**0.97**
Min	-0.34	-0.65	-0.70	0.00	0.00	0.00
Median	-0.03	0.01	0.00	0.05	0.06	0.04

- 33% (4/12) Patients had at least 1 Fx with a ΔCOM of > 3 mm in one direction
- 15% of Fx had a ΔCOM of > 3 mm in 1 dir.

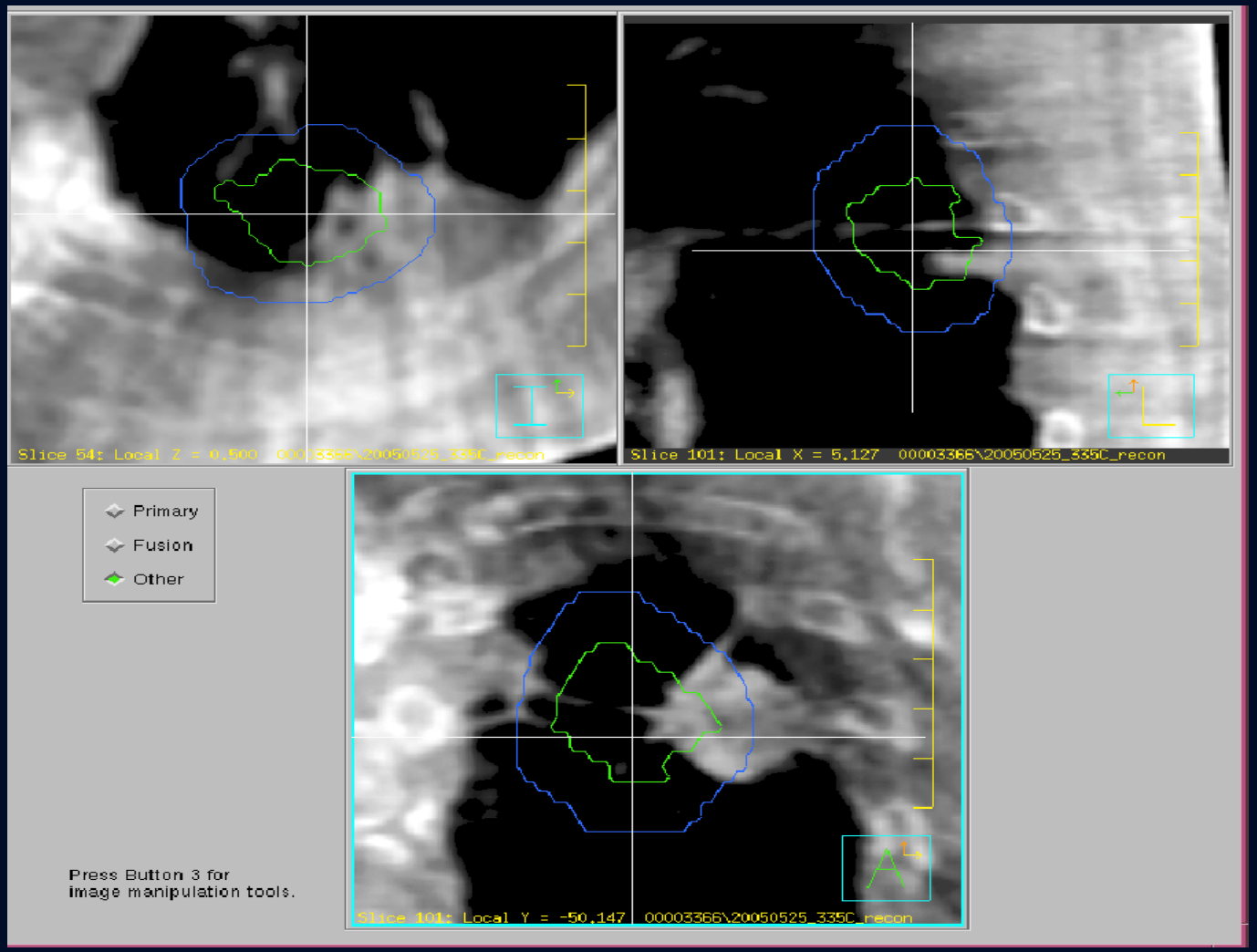
Daily Treatment Verification with Cone Beam imaging





A Bezjak, A Hope

CBCT Target Localization (1)



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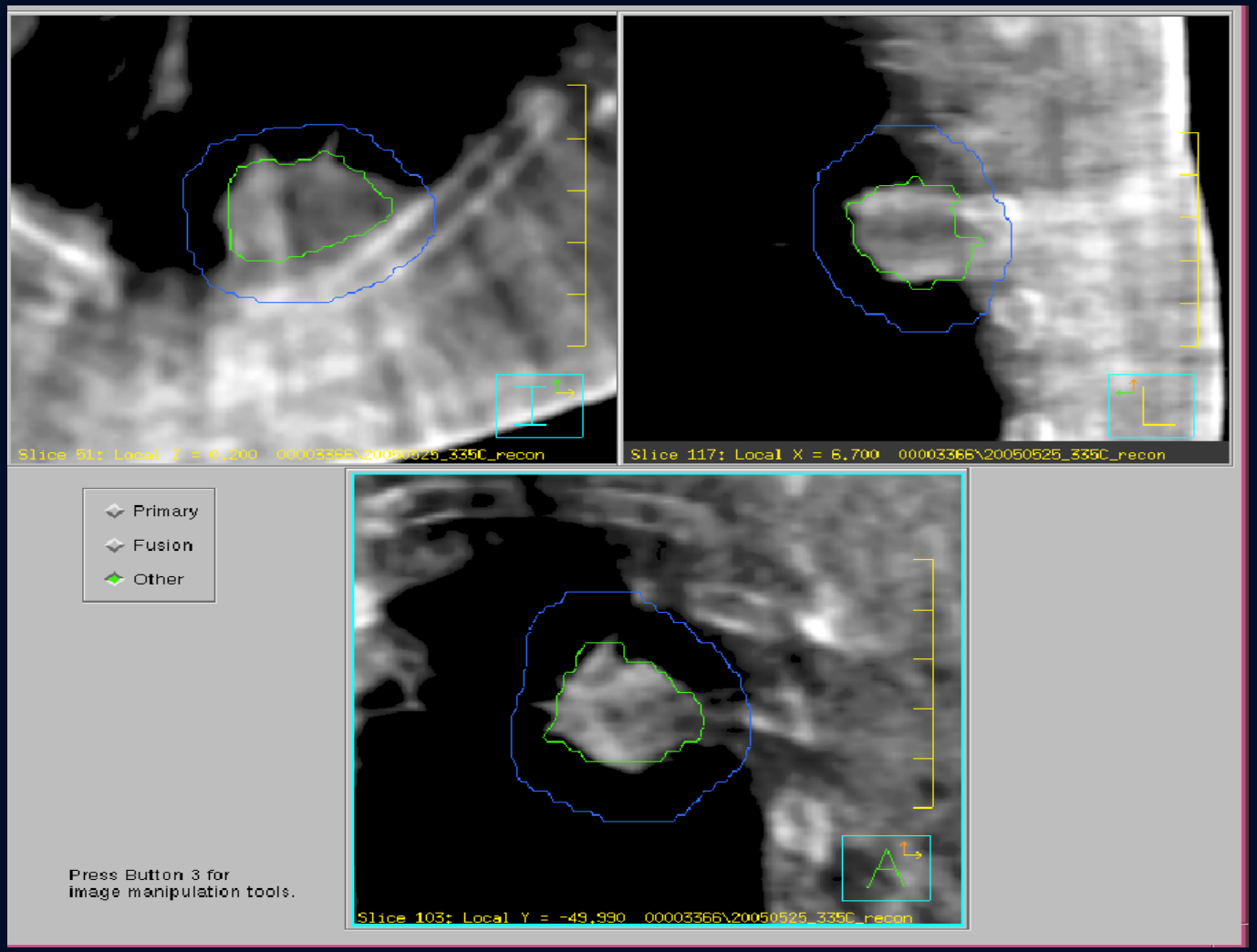
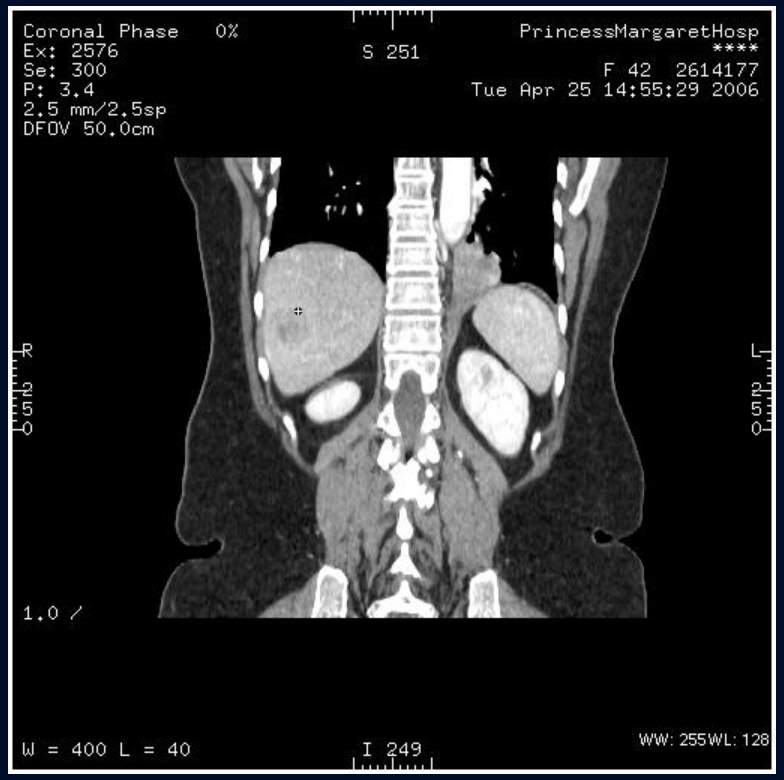
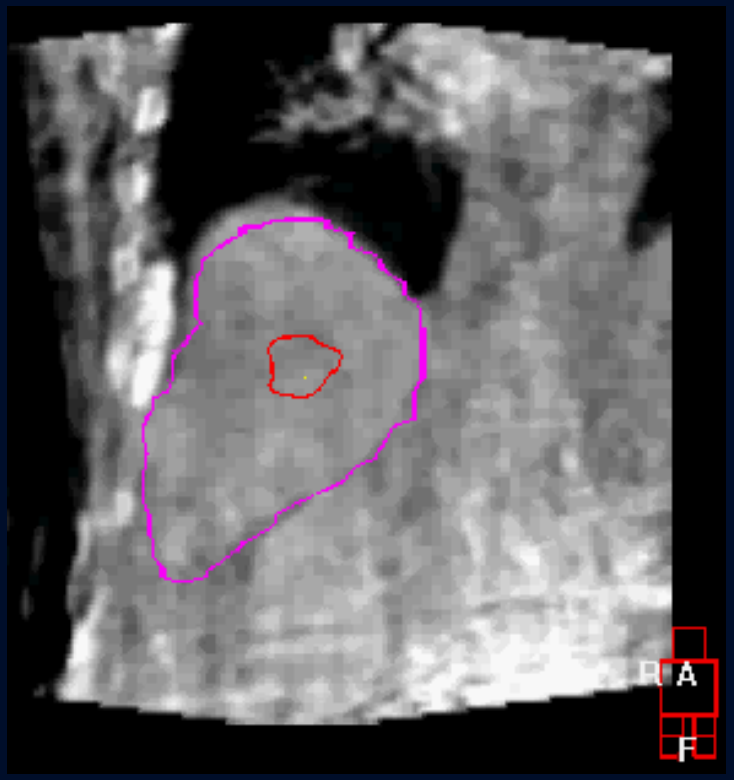


A Bezjak, A Hope

Free Breathing IGRT

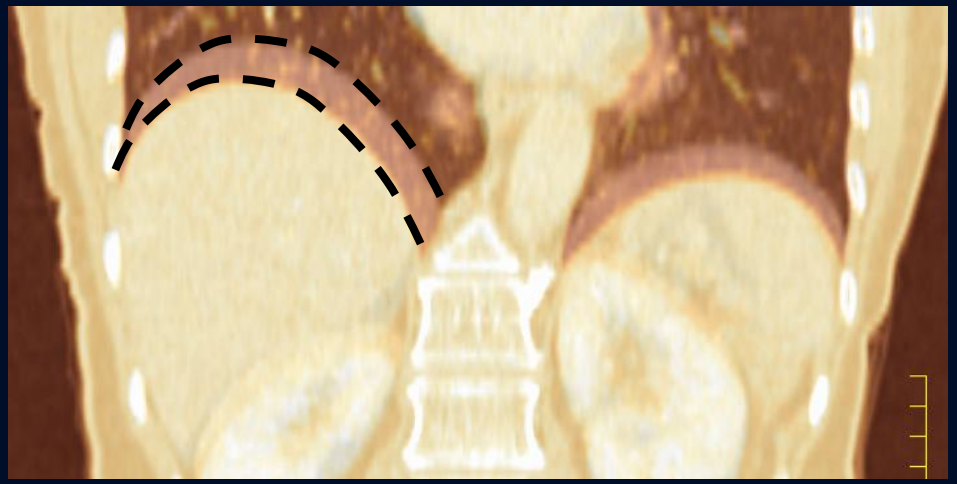


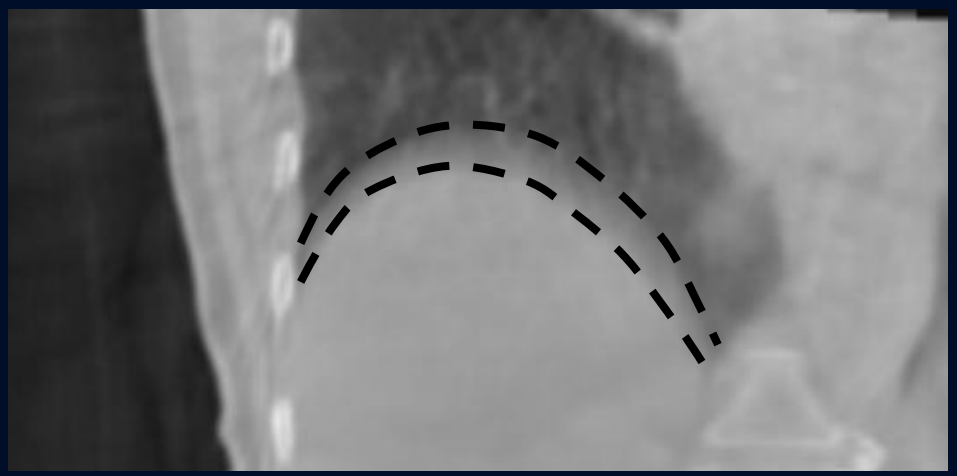


- Match tumor/critical organs at reference phase
- Ensure consistent breathing motion/coverage of PTV

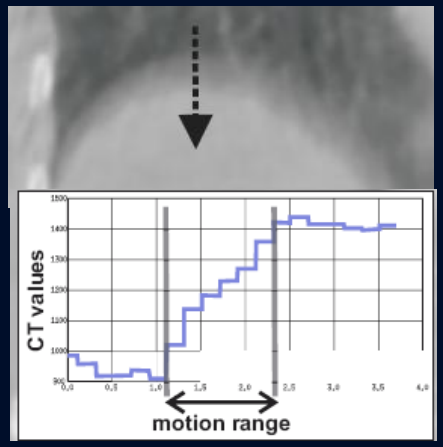
Strategies to consider breathing motion Wuerzburg

IGRT of liver tumors using 4D planning and free breathing
CBCT: Liver outline as surrogate





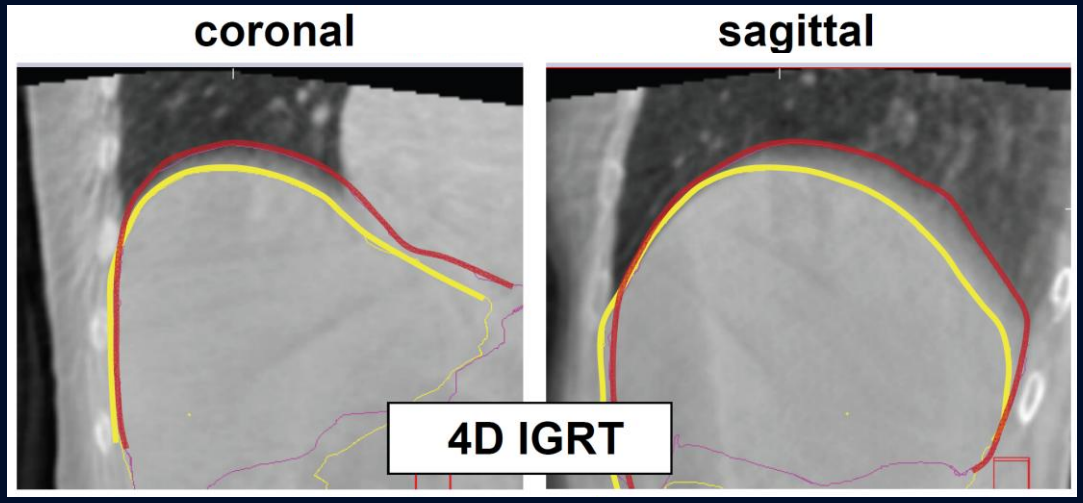
Motion amplitude



Guckenberger et al, IJROBP, 2008

Strategies to consider breathing motion Wuerzburg

Contour matching for IGRT of liver tumors



Challenges:

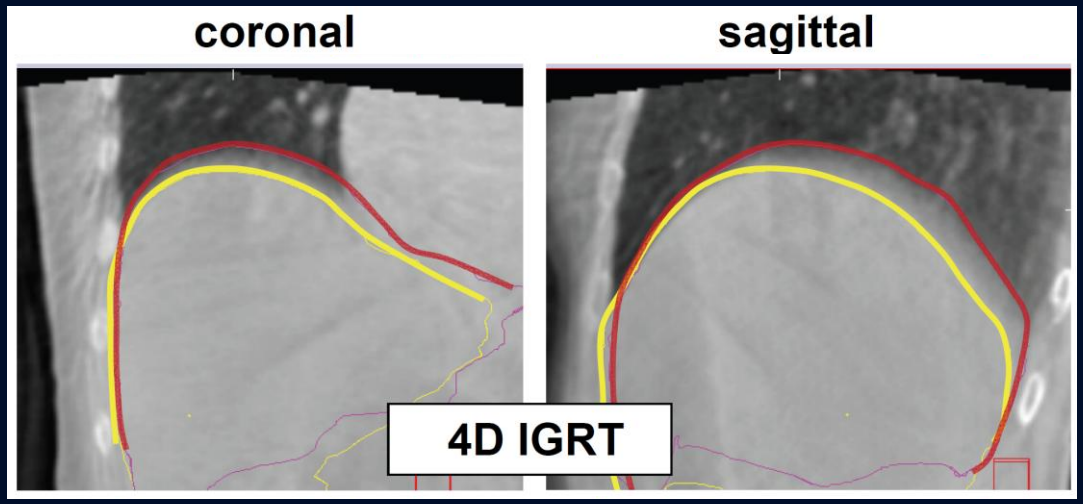
– Inhale an exhale ‘contours’ on free breathing CBCT not always clear

- Amplitude of breathing may change → then what is the best strategy for matching? → respiratory correlated CBCT and matching

Guckenberger et al, IJROBP, 2008

Stereotactic body-radiotherapy of liver tumors

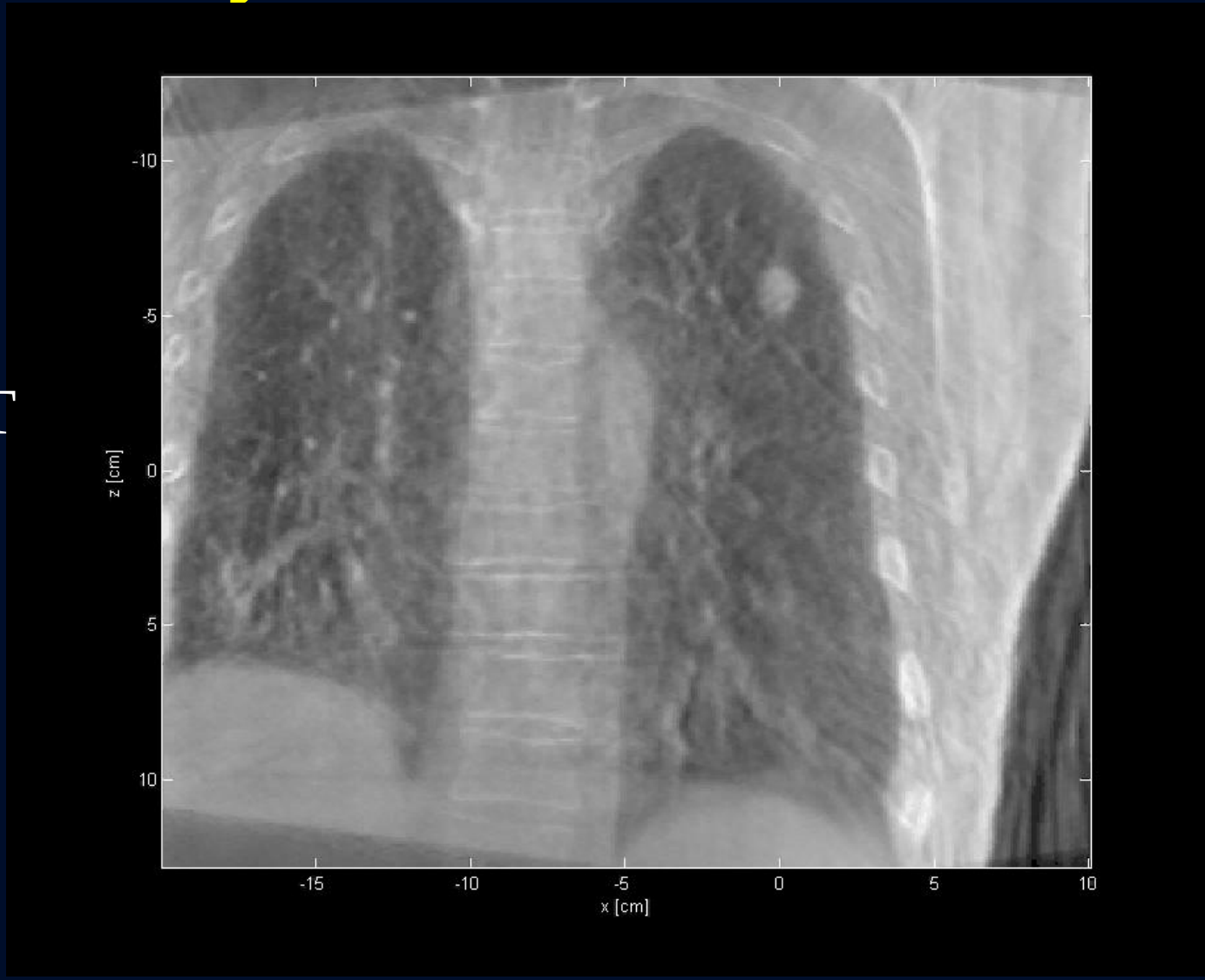
Contour matching for IGRT of liver tumors



		GME	Σ	σ	Margin		Mean	SD	Max. error
Absolute (mm)	***LR***	-1.4	3.5	2.4	10.5				
	SI	-1.8	4.3	6.4	15.2	***3D***	8.2	3.8	14.2
	AP	-0.2	4	4.3	13				
Relative (mm)	***LR***	1.2	1.6	1.6	5				
	SI	-0.5	2.6	4.2	9.5	***3D***	5.2	2.2	9
	AP	1.7	3.2	1.8	9.3				

‘4D’ Cone-beam CT from a Single Gantry Rotation

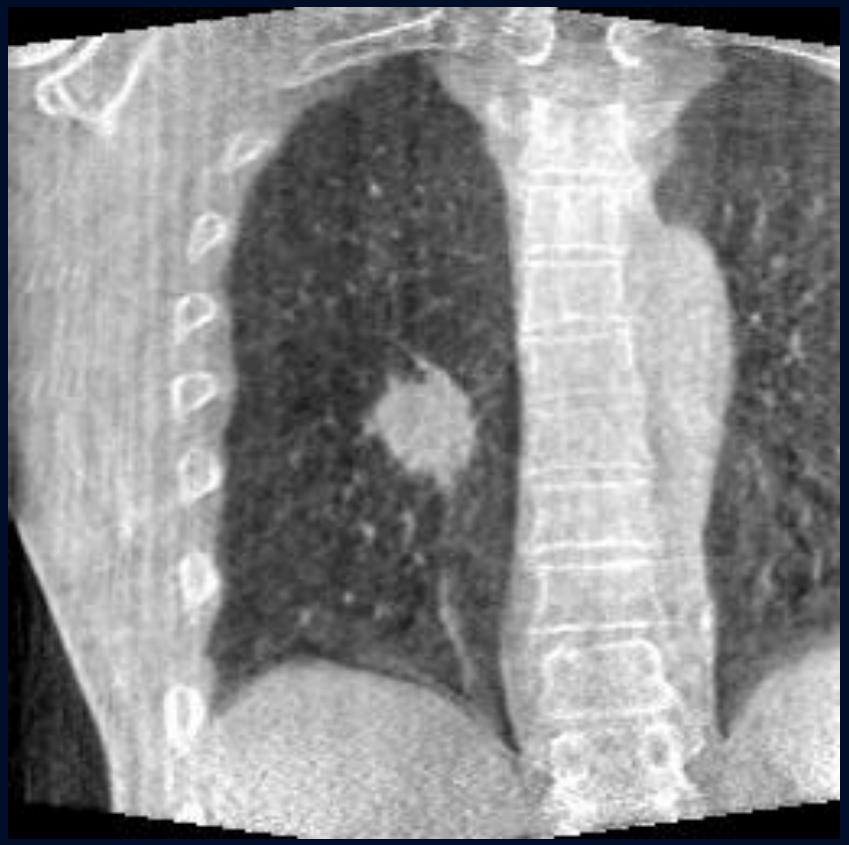
Image-based projection sorting for 4D cone-beam CT



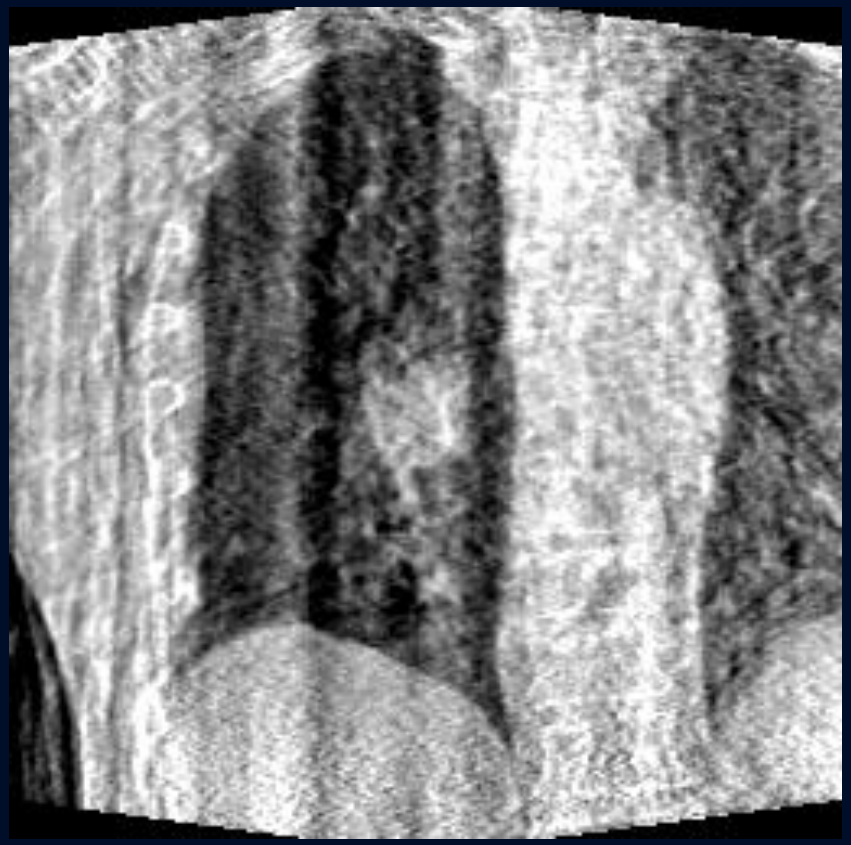
~650 projections over 360^{o}

Acquisition Time

4D CBCT



Slow acquisition (4 min)



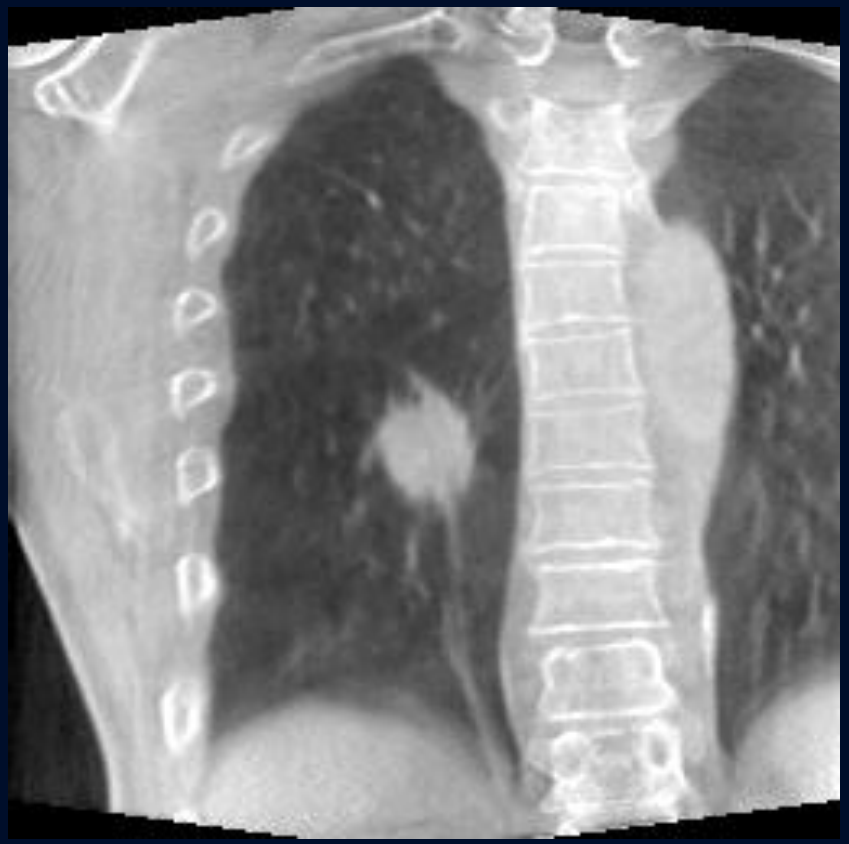
Fast acquisition (1 min)

JJ Sonke, Netherlands Cancer Institute

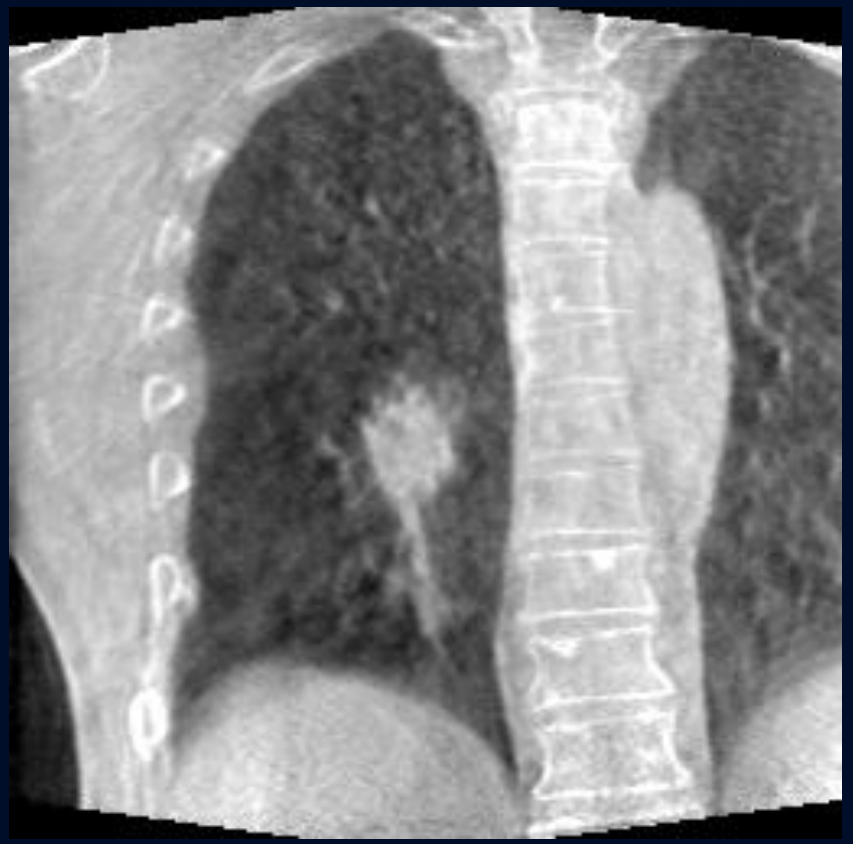
Motion compensated CBCT

Non-corrected vs. Motion-compensated

Reconstruction keeps up with image acquisition



Slow acquisition (4 min)

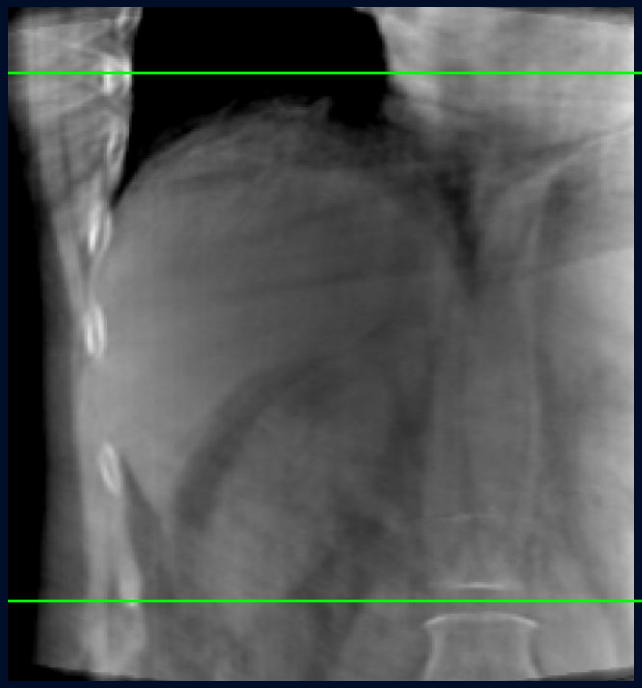


Fast acquisition (1 min)

JJ Sonke, Netherlands Cancer Institute

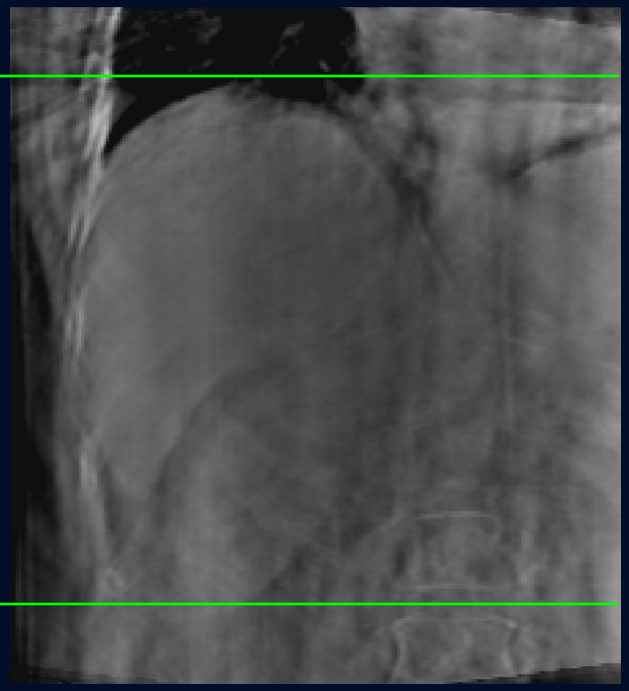
CBCT – Reconstruction Comparison

Free Breathing



325 Projections
120 kVp
2.6mAs/projection

Expiration Sorted



68 Projections
(Amplitude sorted <10%)
120 kVp
2.6mAs/projection

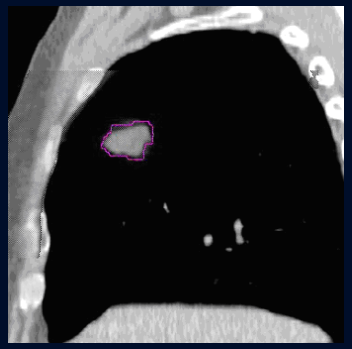
Verification of Range of Respiratory Motion at the Treatment Unit

Sample Case

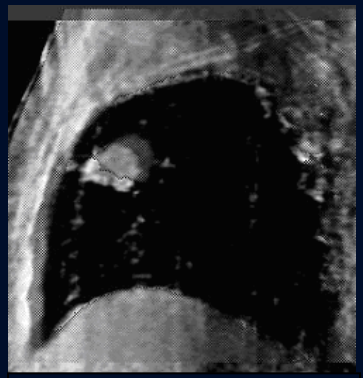
	Tumour Excursion (mm)		
	Lateral	Anterior/ Posterior	Superior/ Inferior
4DCT Planning Scan	0.7	1.0	3.1
Respiration Correlated CBCT			
Fraction 1	0.5	0.8	5.7
Fraction 2	0.3	0.8	2.9
Fraction 3	0.0	0.9	3.4

Verification of Position and Amplitude of Respiration for Margin QA

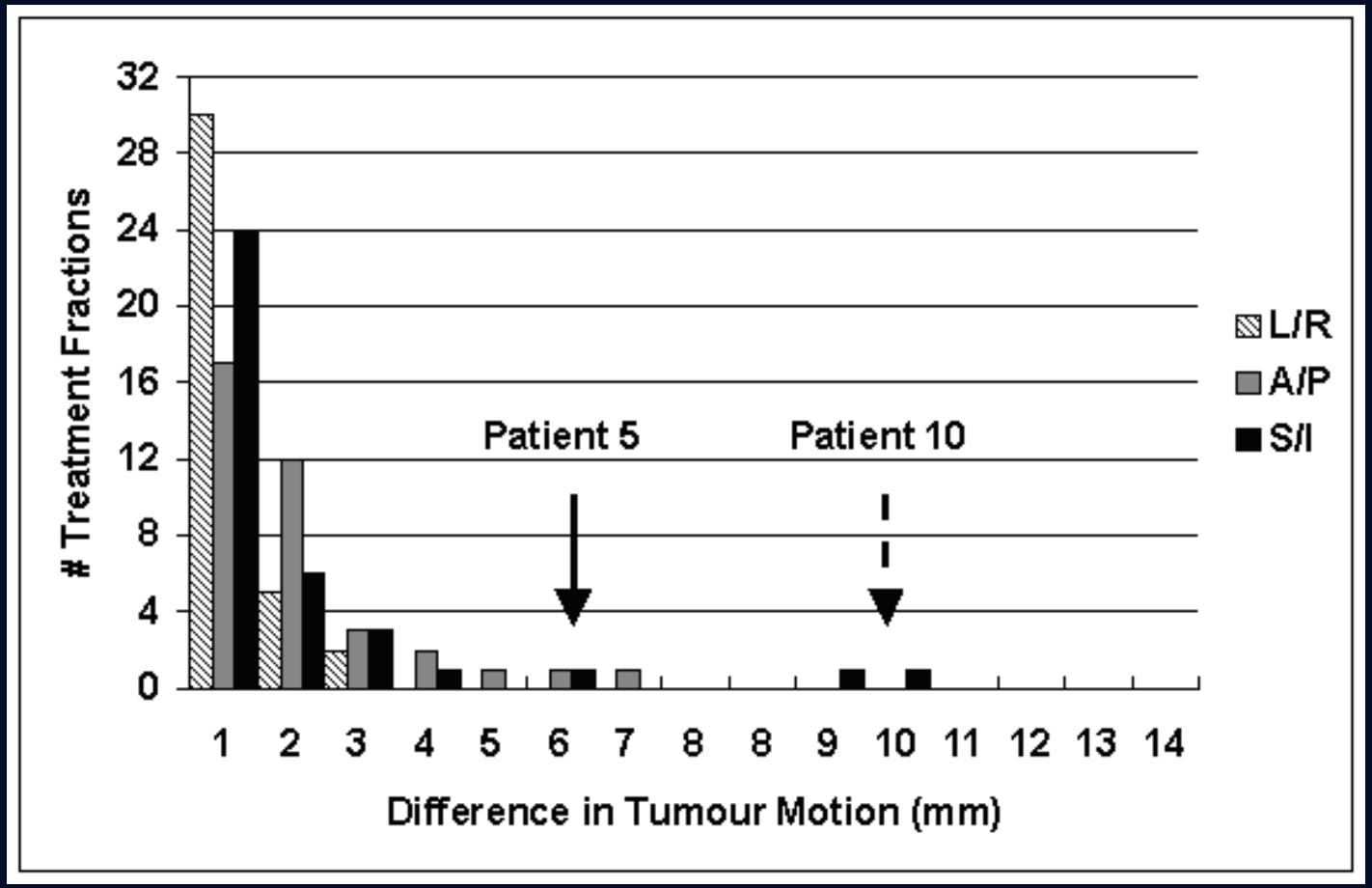
Verification of Range of Respiratory Motion at the Treatment Unit



Planning 4DCT



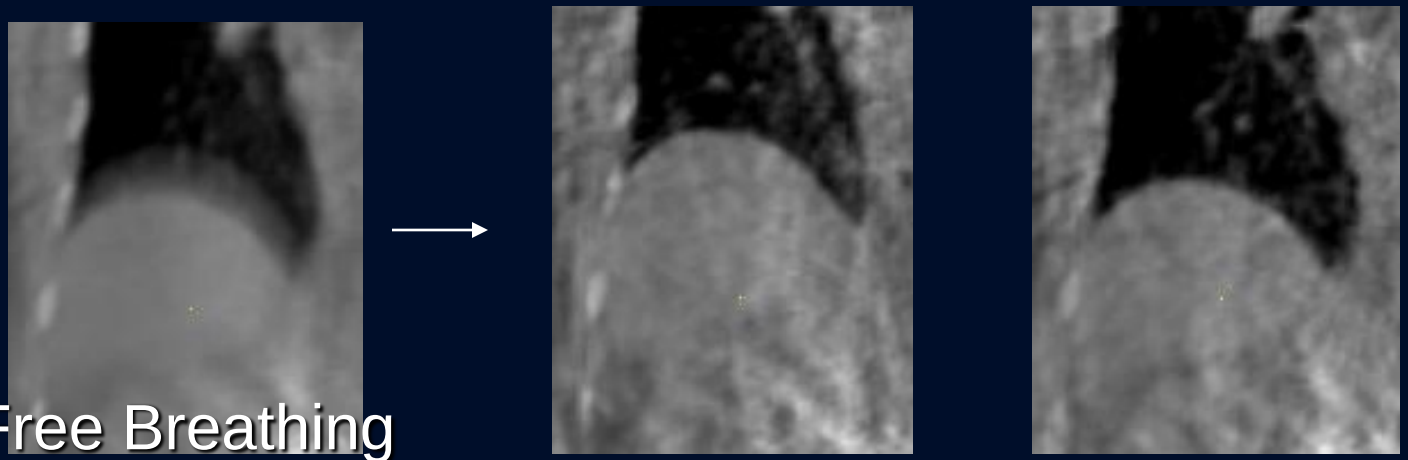
4D CBCT



The difference in tumour motion between planning and treatment for 12 patients treated using SBRT.

Purdie et al., Acta Oncologica

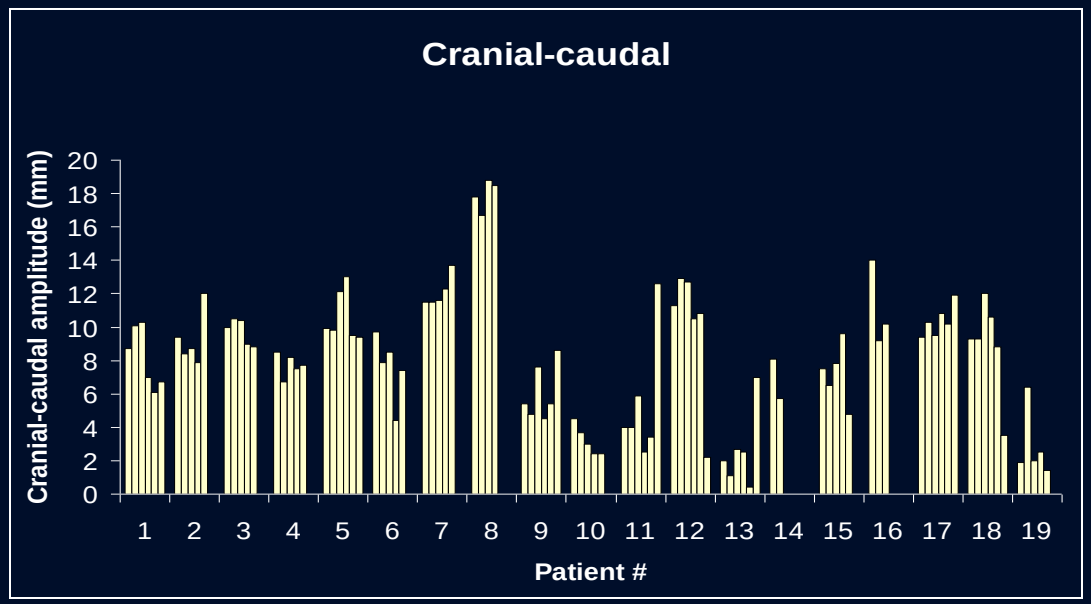
Respiratory Sorted Cone Beam CTs
– software courtesy of Sonke et al, NKI



Free Breathing CBCT

Exhale

Inhale

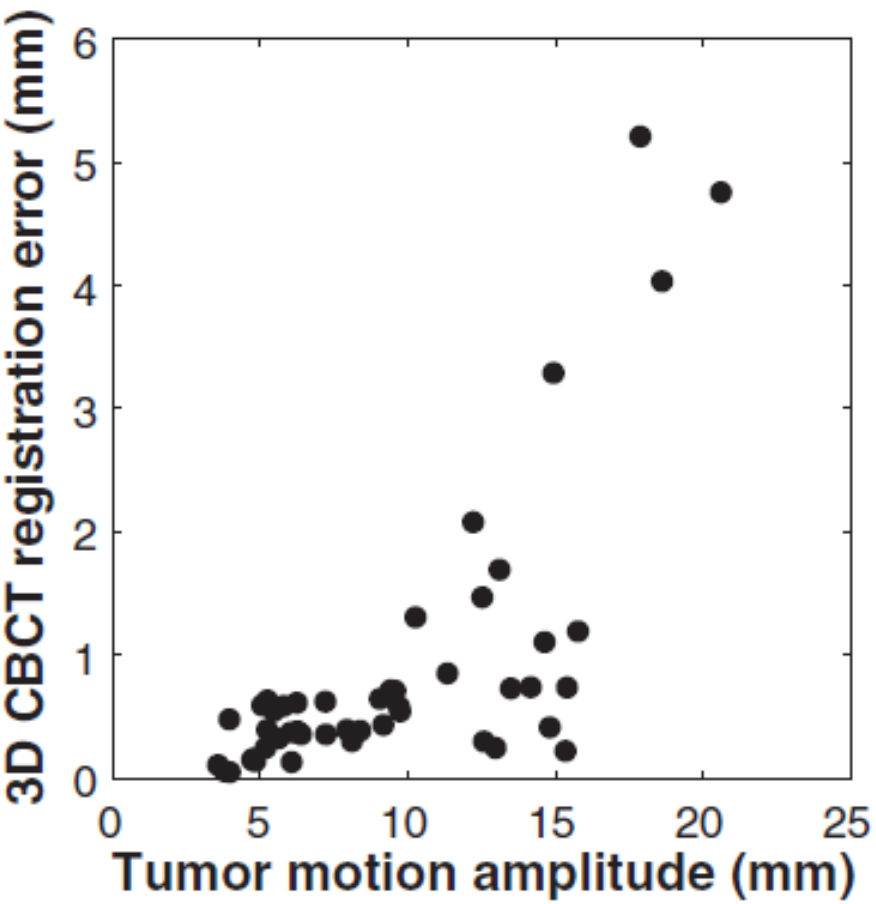


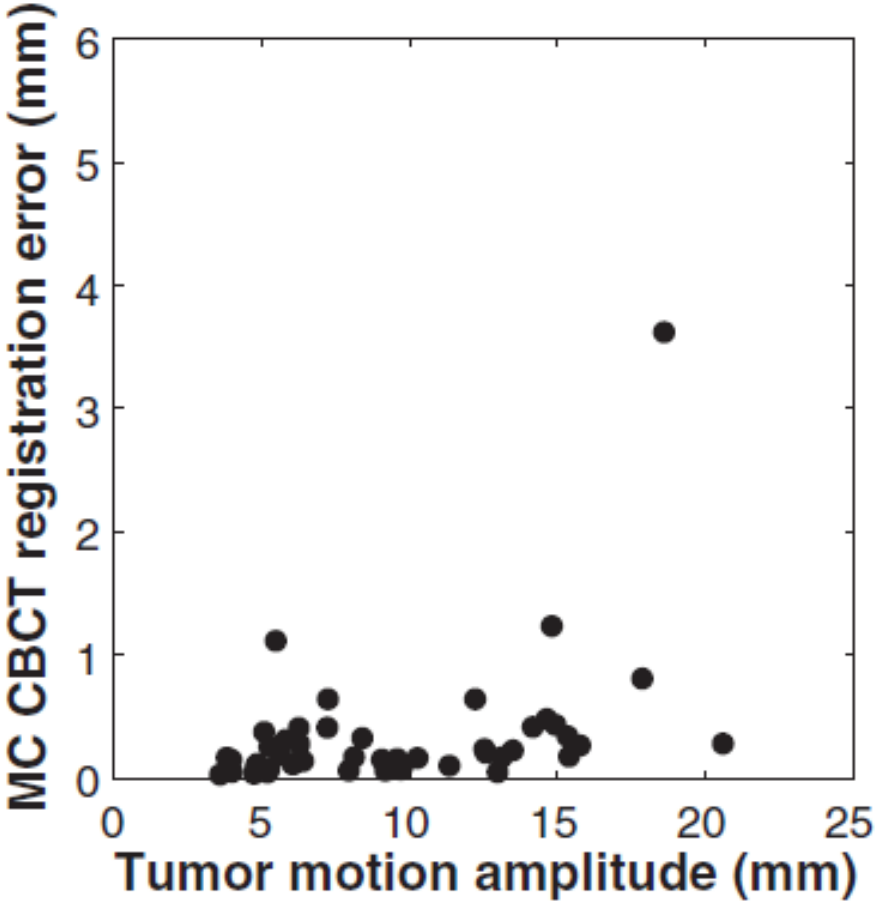
- Intra & inter fraction variability in liver motion amplitude << baseline inter-fraction shifts in liver position

- 90% of amplitude change < 4 mm

R Case, ASTRO 2007

3D Registration Error: Lung





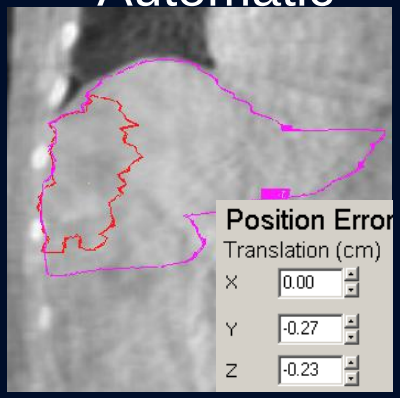
Soft Tissue IGRT

- Mean (90th percentile) differences in liver position from automated CTexh to CBCTexh registration

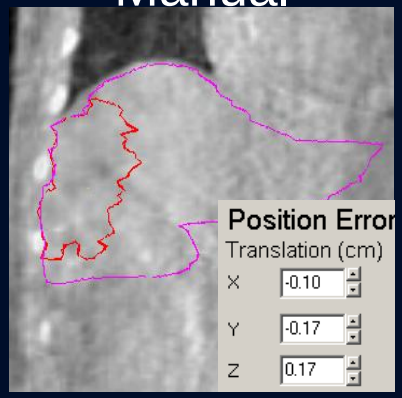
	Manual		Automated	
	CTexh-CBCTexh*	CTexh-CBCT	CTexh-CBCT**	CTave-CBCT
ML (mm)	0.5 (2.4)	1.0 (3.5)	0.3 (4.6)	1.1 (3.3)
CC (mm)	0.6 (3.0)	0.2 (2.9)	3.0 (7.6)	0.9 (5.8)
AP (mm)	1.2 (4.2)	0.8 (5.4)	1.7 (6.0)	0.4 (4.9)

CTexh-CBCTexh

Automatic

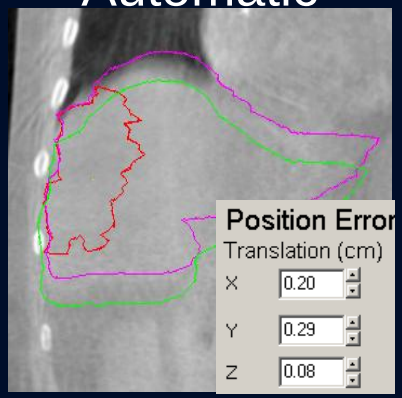


Manual

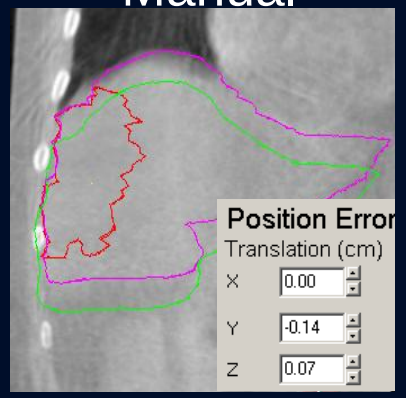


CTave-CBCT

Automatic



Manual

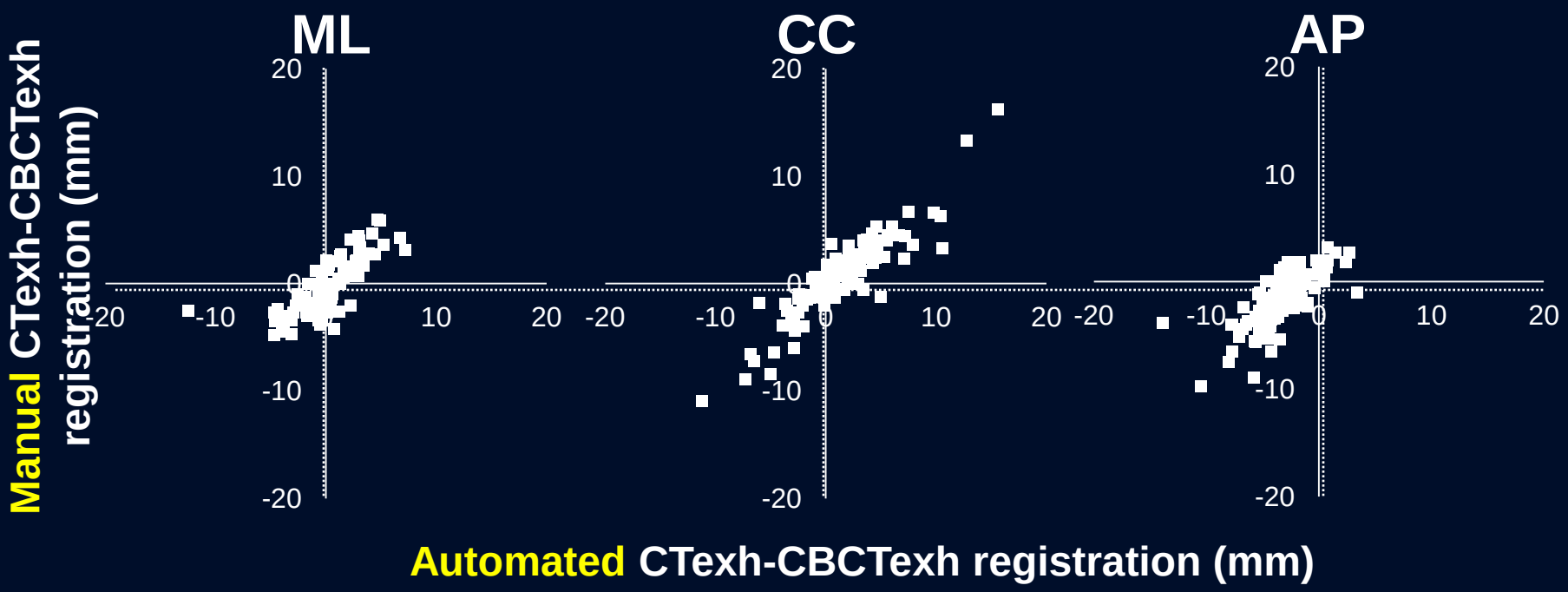


Exhale Liver GTV Inhale Liver

Rob Case, ASTRO poster discussion 2008

Manual vs Automated Liver Alignment

- Correlation automated & manual CTexh-CBCTexh registration >> free breathing CT-CBCT registration
- Automated faster and more reproducible
- Visual confirmation of registration required



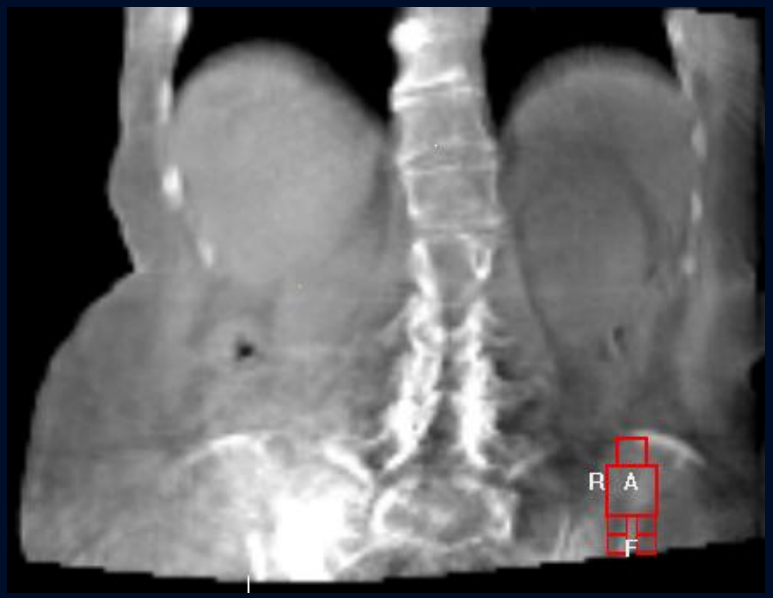
Rob Case, ASTRO poster discussion 2008

Dosimetric Implications

Motivation

- Tumor dose-response observed for liver SBRT
- Iso-NTCP dose-allocation at Princess Margaret CC
  - ↓ toxicity, no radiation-induced liver disease
  - 85% receive < maximum dose
- Internal Target Volume (ITV) results more normal tissue irradiation than dose-probability PTV*

  *Requires mean position
- Poor liver tumor contrast on 4D imaging



Free-breathing CBCT

Purpose

- To investigate the impact of PTV reduction on both the planned and delivered doses in free-breathing liver SBRT, using:
  - Mean respiratory liver position
  - Dose-probability PTV margins

Materials and Methods

- 18 previous SBRT patients with 30 GTVs
  - 8 liver metastases, 10 primary liver cancer
- 27–49.8 Gy/ 6 Fx, planned on exhale 4D CT
  - AVG 4D CT motion (mm) : 10, Range: 3 – 19
  - ITV-based PTV: 4D CT, cine-MR, fluoroscopy
- IGRT based on rigid liver alignment on free-breathing 360º 3D CBCT
- Delivered dose reconstructed with biomechanical deformable image registration (Morfeus) and retrospectively sorted 4D CBCT
  - Pinnacle^3 dose interpolated onto finite element model, and accumulated over 6 fractions

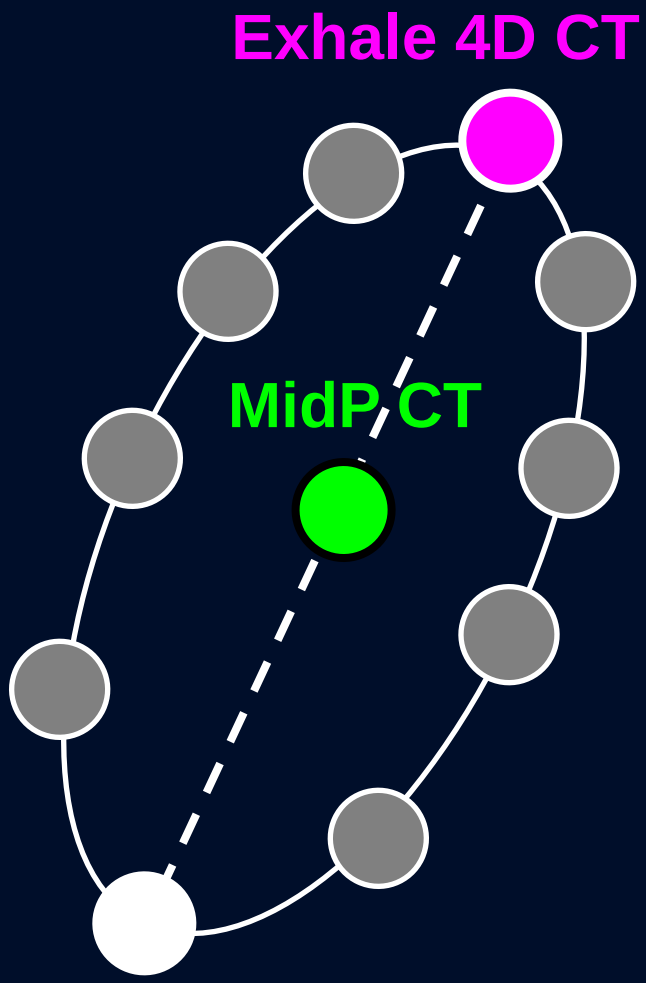
Materials and Methods

- Re-planned on the mid-position (MidP) CT
- Dose-probability PTV ensures 90% of patients receive 90% dose (Van Herk. IJROBP. 2000):

$$\text{Margin} = 2.5\Sigma + 1.28(\sigma - \sigma_{penumbra})$$

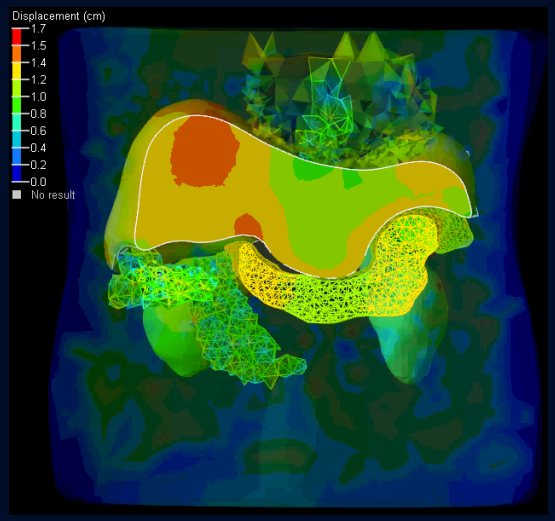
- Σ includes:
  - Inter - Fx (liver vs. GTV centre of mass)
  - Intra - Fx (pre- vs. post-treatment liver position)
  - Morfeus accuracy
- σ additionally includes:
  - 0.36 x GTV amplitude (modeled with Morfeus on 4D CT)
  - Penumbra in water
- Escalated up to 60Gy/6 Fx, iso-NTCP<10%

Methods and Materials



i. **Deform Exhale → Inhale**

E.g. 4D CT motion:
17 mm
12 mm
6 mm

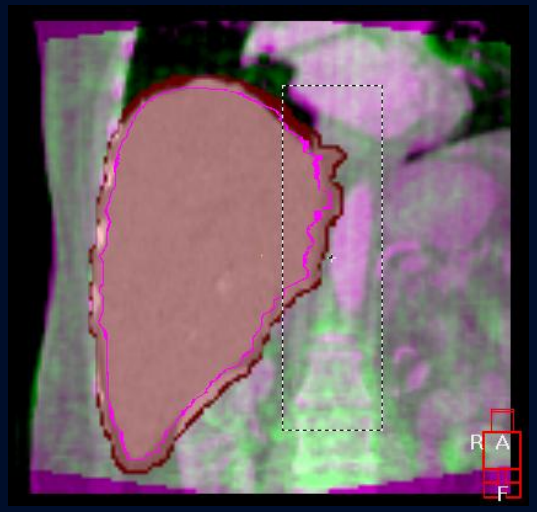


ii. **Apply 43% of deformation to Exhale CT = MidP CT**

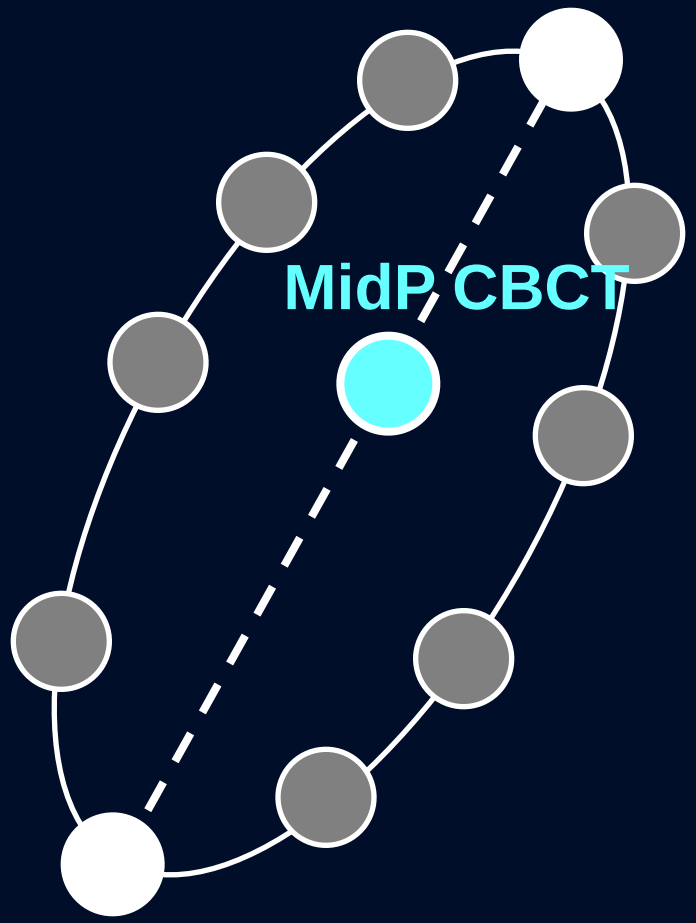
iii. **GTV error MidP CT vs. time-weighted mean, AVG (Max): 0.8±0.4 (1.5) mm**

Methods and Materials

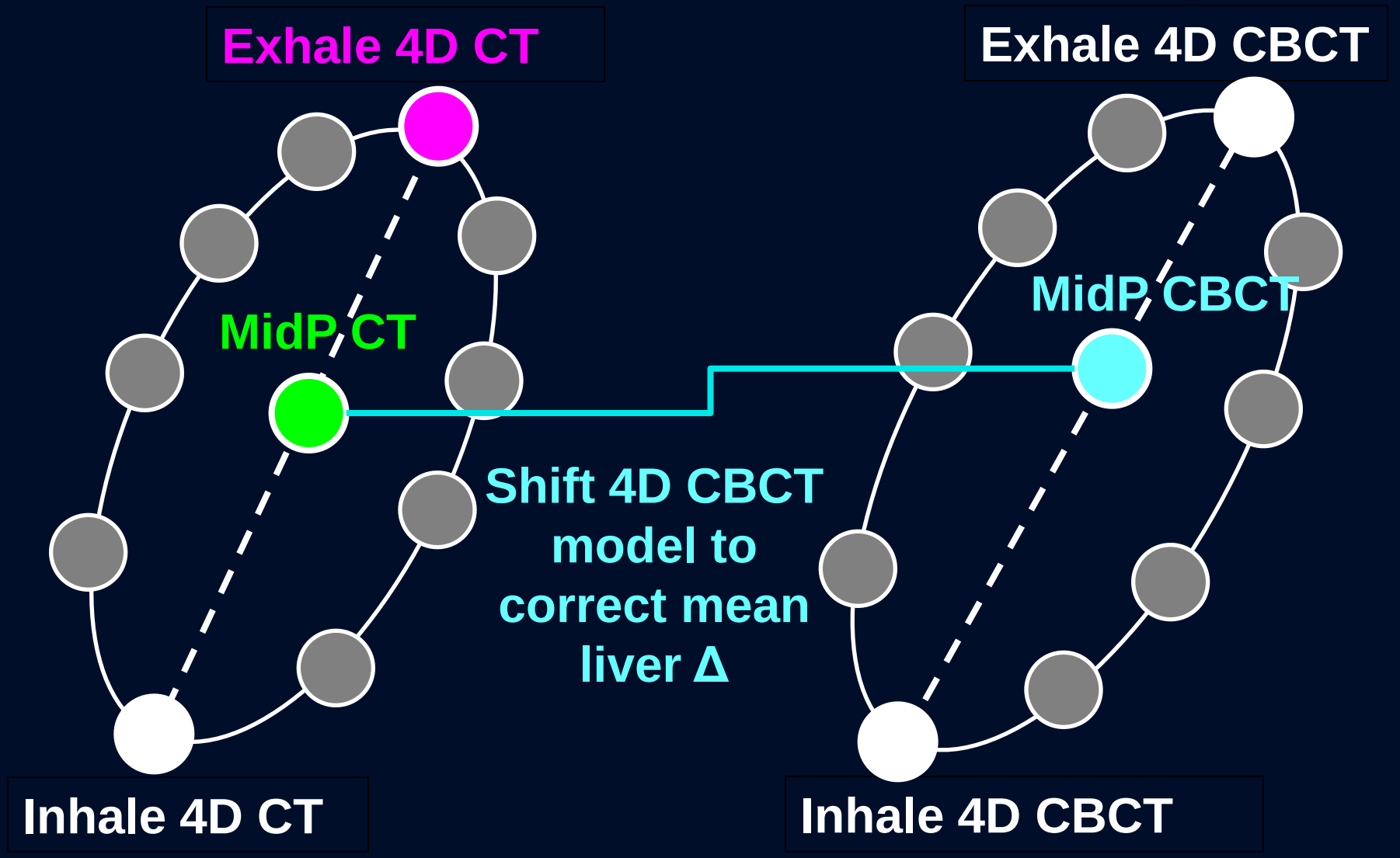
i. Deform Exhale → Inhale
ii. Determine time-weighted mean liver position across all 4D phases:



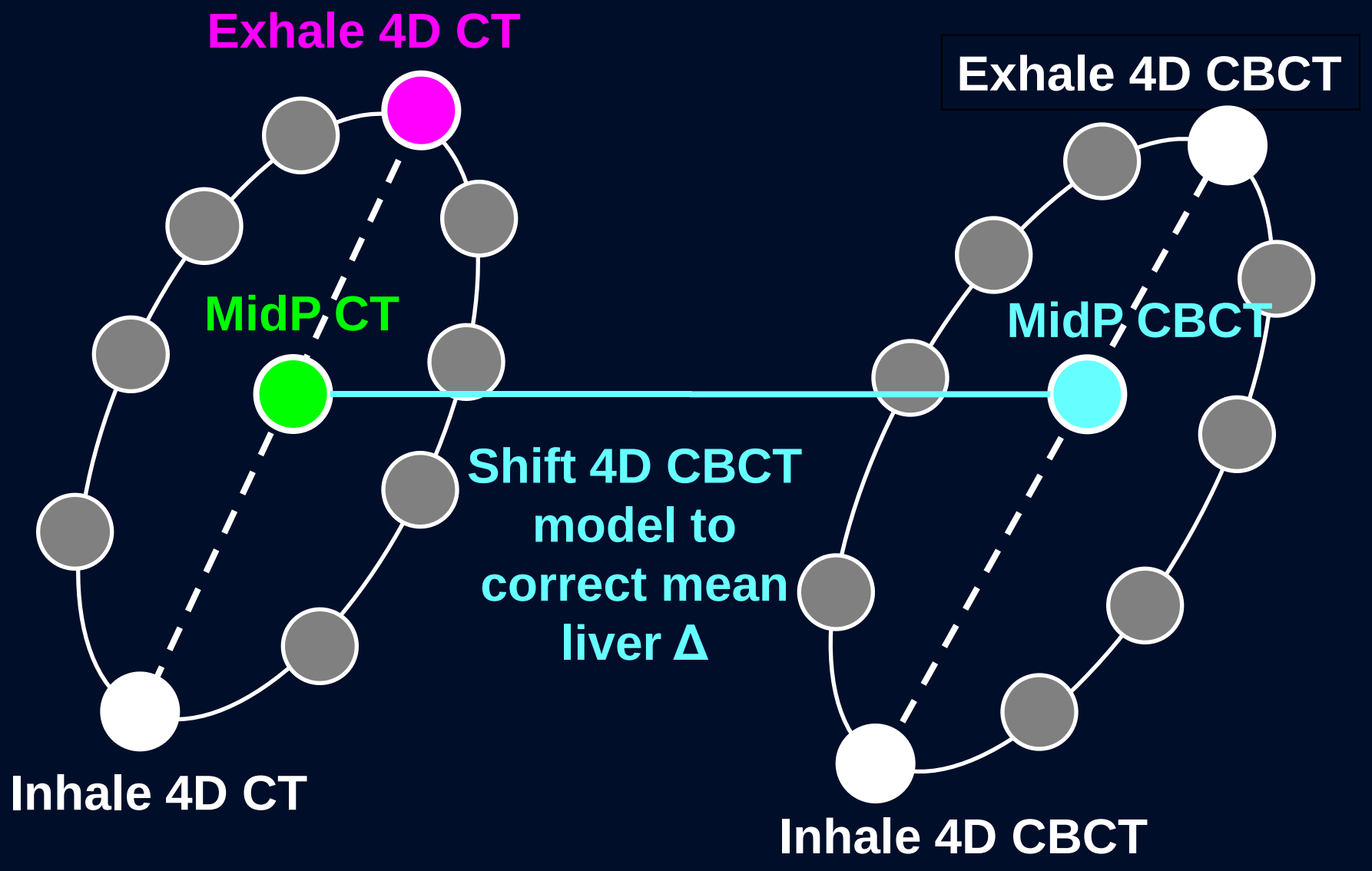
iii. Apply as % to Exhale-Inhale CBCT deformation map = MidP CBCT



Methods and Materials



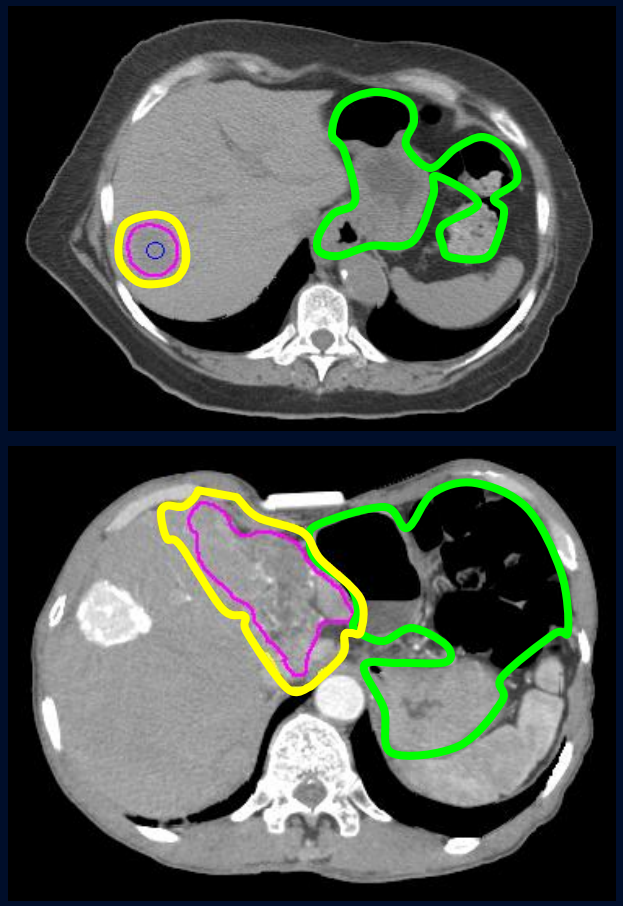
Methods and Materials



Results – Planned Dose

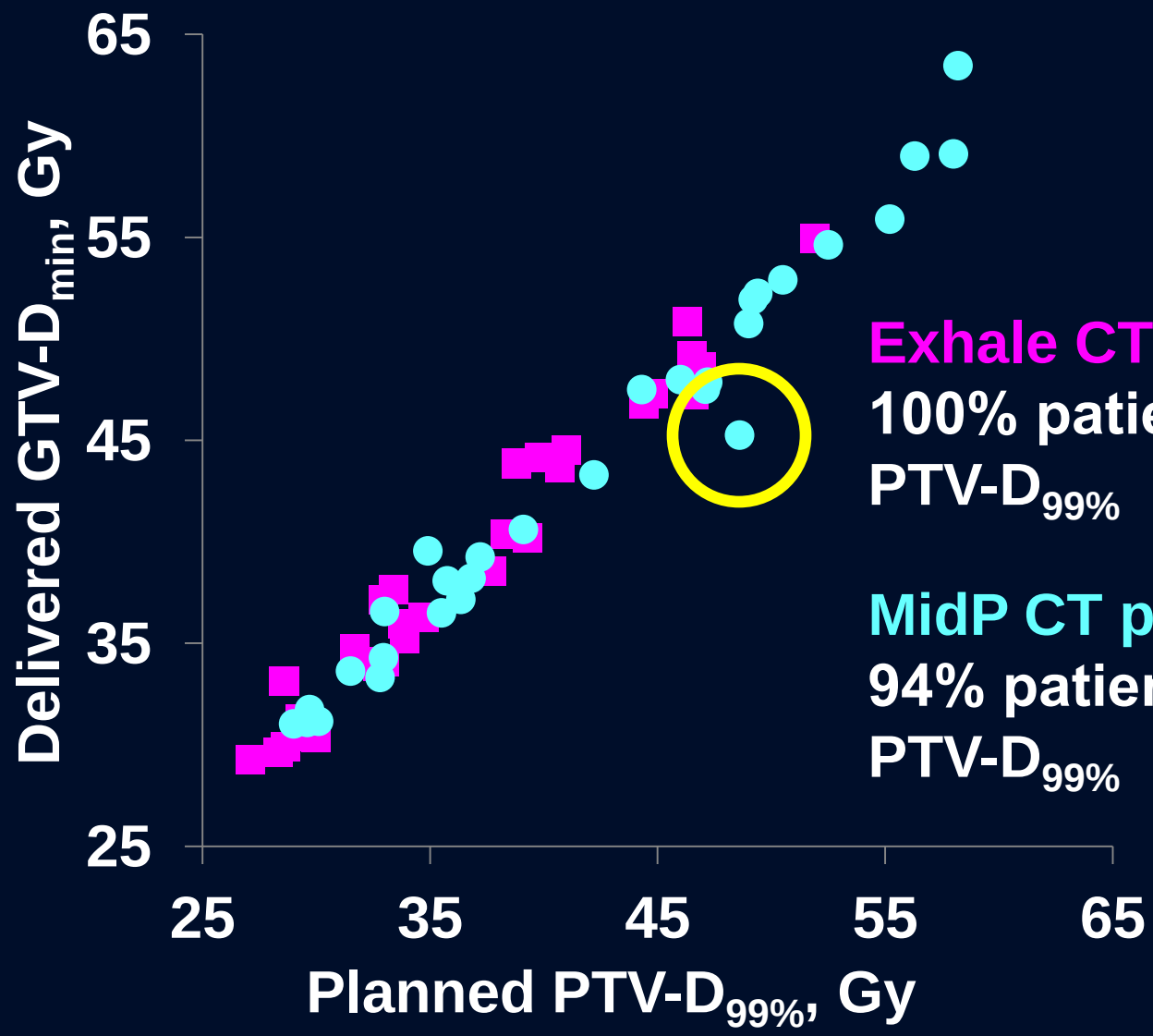
MidP CT vs. Exhale CT plans:

- Δ GTV-PTV volume, -68±49 cc (maximum↓: -216 cc)
  - -34±11% (max: 58%)
- Δ PTV-$D_{99\%}$, 4.5±3.5 Gy (maximum↑: 18.6 Gy)
  - 14±13 % (max: 65%)
  - Δ 11/30 GTVs > 5 Gy
- Normal tissue-PTV overlap:
  - AVG Δ PTV-$D_{99\%}$ no overlap vs. overlap: 1.7 vs. 6.8 Gy
  - All normal tissues met constraints



GTV, PTV, Normal tissues

Results – Delivered Dose



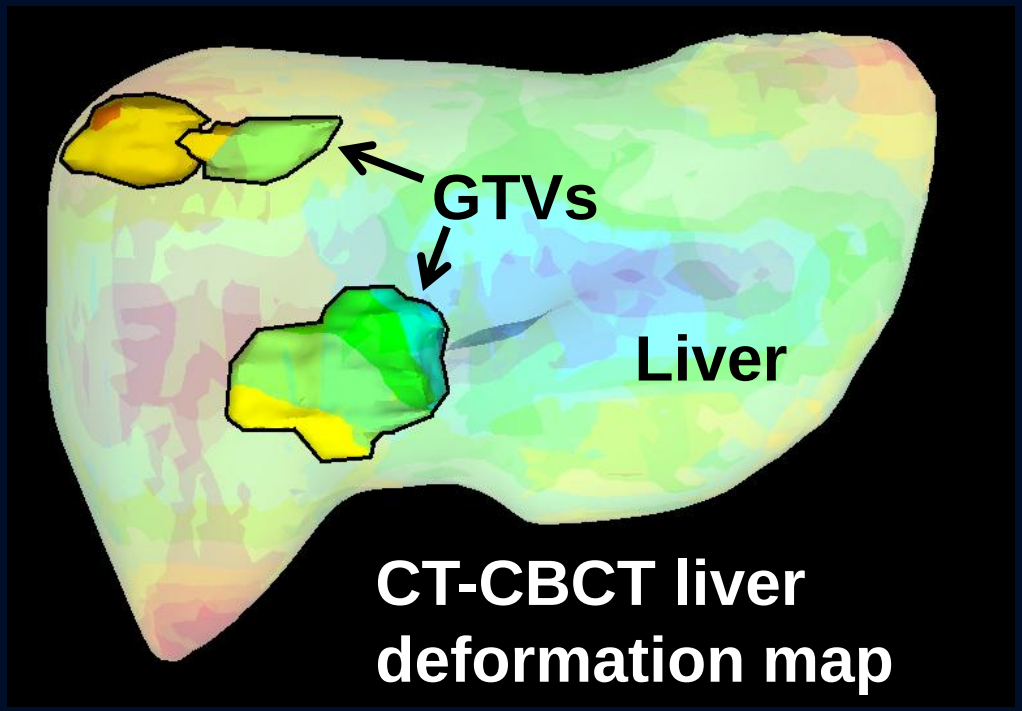
Exhale CT plan + 3D CBCT:
100% patients' GTV-D_{min} > PTV-$D_{99\%}$

MidP CT plan + 4D CBCT:
94% patients' GTV-D_{min} > PTV-$D_{99\%}$

Results – Delivered Dose

Outlier patient, with 3 GTVs:

- 8 mm more motion on 4D CBCT vs. 4D CT
- 4º liver rotation on 4D CBCT
- 3D inter-fraction error (μ) after rigid liver alignment:
  - GTV1: 5 mm
  - GTV2: 9 mm
  - GTV3: 7 mm
- **GTV2-D_{min} vs. PTV2-D_{99}: -3.3 Gy (6.8% decrease)**



Results – Delivered Dose

- Delivered Vs. Planned D_{max} for luminal G.I. tissues
  - Within 2 Gy of planning dose constraint

	Δ Delivered Vs. Planned D_{max} , AVG (Range)	**No. with delivered D_{max} > constraint (Max. magnitude)**
Exhale CT plan + 3D CBCT	**-0.9 Gy (-5.0, 1.9 Gy) -3 % (-14, 6%)**	**3 tissues (1.4 Gy, or 6%)**
MidP CT plan + 4D CBCT:	**-0.5 Gy (-2.4, 0.4 Gy) -2 % (-8, 1)**	**1 tissue (0.1 Gy, or 1%)**

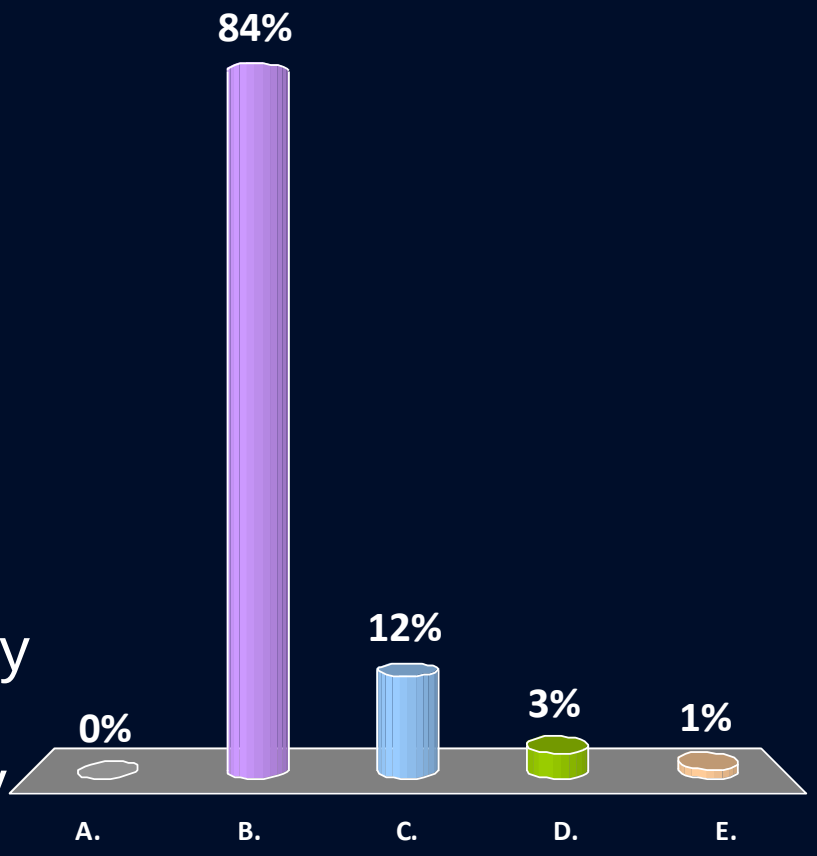
Conclusions

- Deformable dose reconstruction was used to model the delivered dose following PTV ↓
  - Role for routine QA of SBRT delivery in clinic
- Liver SBRT at the mean respiratory position, coupled with dose-probability PTV, allows for a planned dose escalation of 4.5 Gy/ 6 Fx
  - 94% (17/18) of patients received the planned dose with 4D CBCT and rigid liver registration
- Ongoing work: evaluate IGRT strategies at the mean respiratory position

SAMS Question

2. Using dose probability based planning target volume margins for liver SBRT compared to an ITV-based approach

A. Enables planning with a 0 PTV margin
B. Enables an average 38% reduction of the PTV while maintaining minimum delivered dose to the GTV
C. Should only be used if real-time monitored is employed during treatment
D. Should only be used with implanted fiducials and with daily MR guidance
E. Has been shown to dramatically increase in-field recurrence



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REFERENCE: Velec M, Moseley JL, Dawson LA, Brock KK. 'Dose escalated liver SBRT at the mean respiratory position,' Int J Radiat Oncol Biol Phys, 89(5): 1121-8, 2014.

Summary

- Uncertainties exist throughout the SBRT planning and delivery process
- Advances in imaging and image integration (e.g. DIR) help to reduce these uncertainties
- Reducing/eliminating uncertainties in image aqusition is key to the accurate delivery of SBRT dose
- Novel developments of SBRT margins can enable decreases in normal tissue while maintaining tumor dose.