SBRT and Personalized Medicine in the Abdomen & Thorax

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The University of Texas MD Anderson Cancer Center

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Acknowledgments and Conflicts

- Licensing agreement with RaySearch Laboratories
- Chair, AAPM TG 132

- Martha Matuszak (UM)
- Laura Dawson (PMH)
- Mary Feng (UCSF)
- Marc Kessler (UM)
- Michael Velec (PMH)
- Molly McCulloch (UM)
- Liver and Lung SBRT teams at PMH, UM, MDACC, and around the world

Objectives

1. Discuss imaging and registration for treatment planning of abdominal & thoracic targets.
2. Discuss treatment imaging for localization and monitoring.

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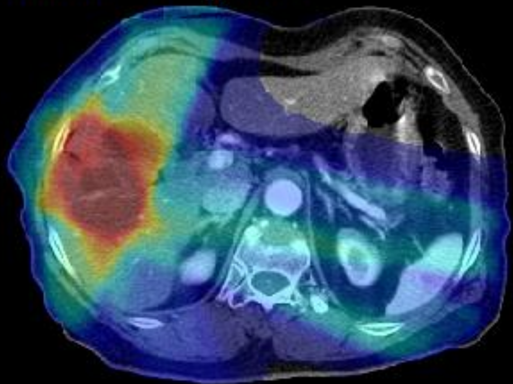

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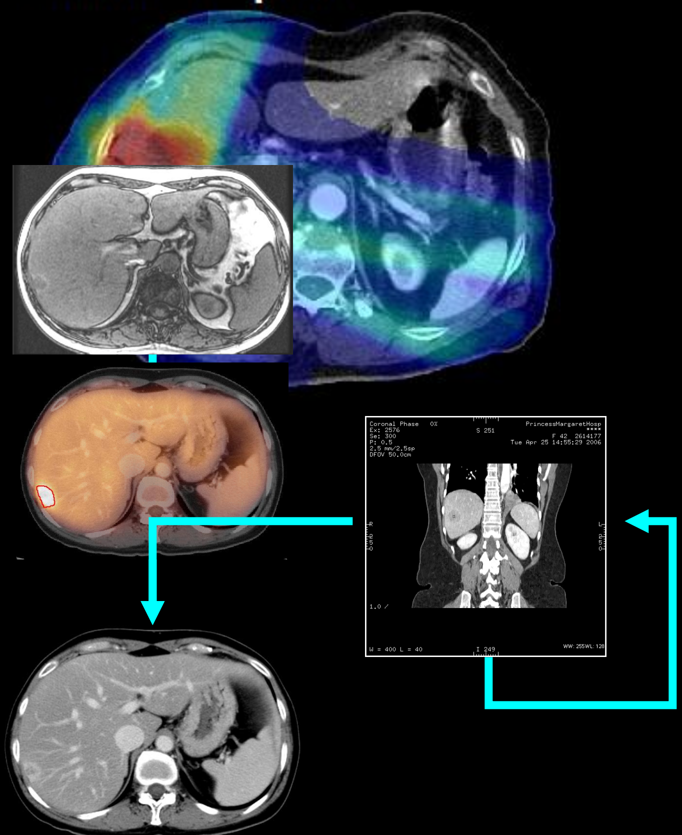

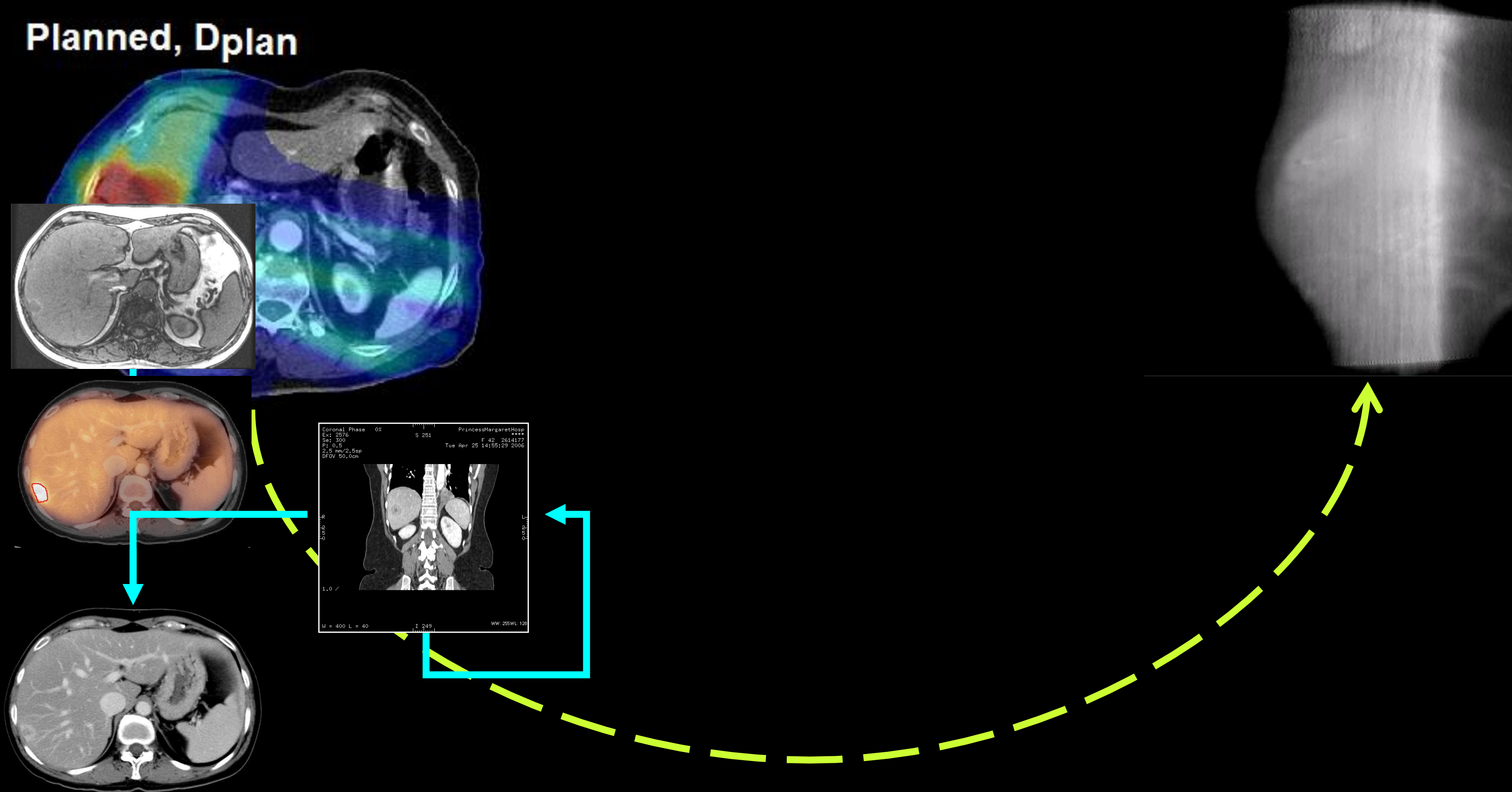
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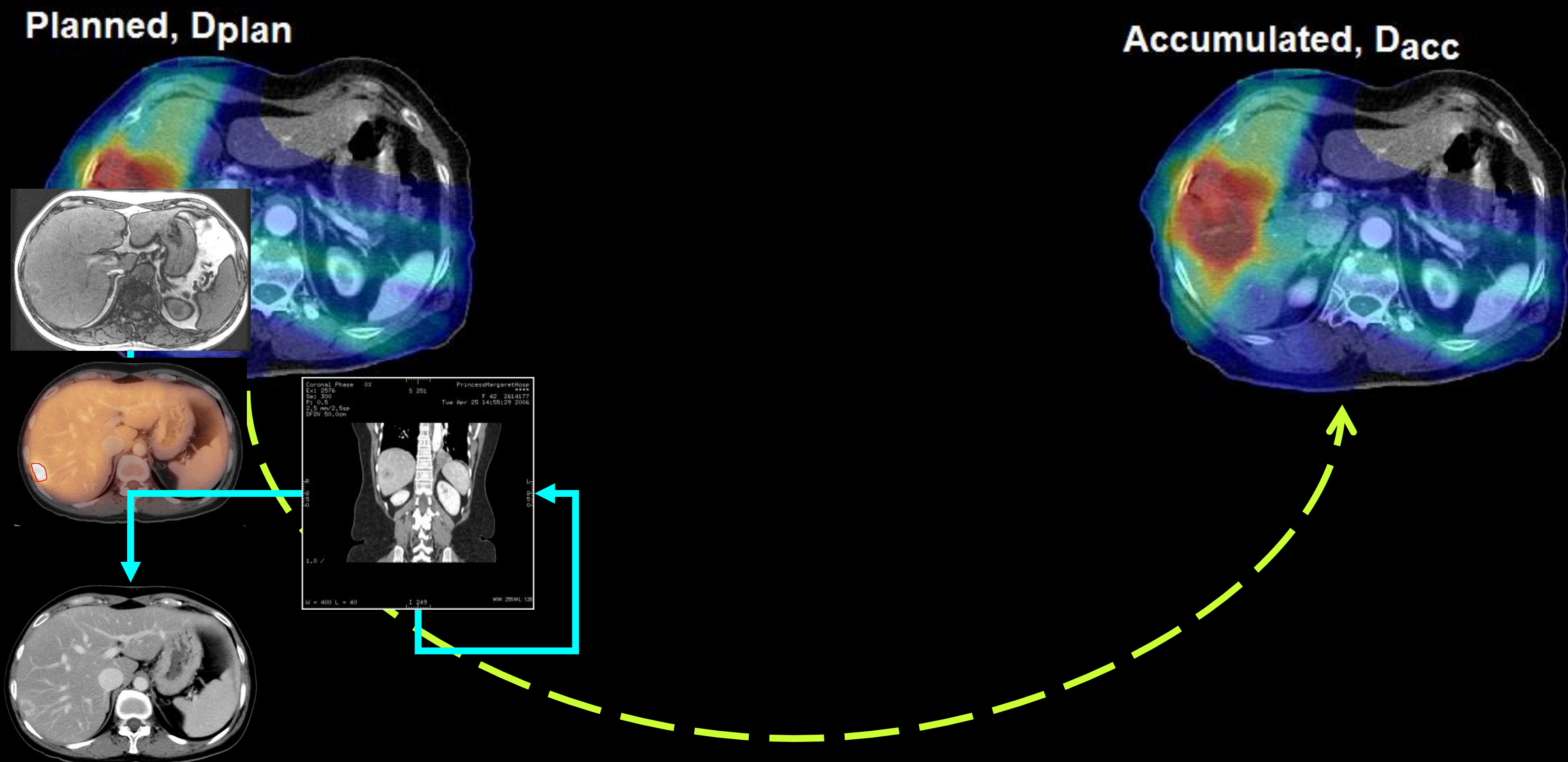
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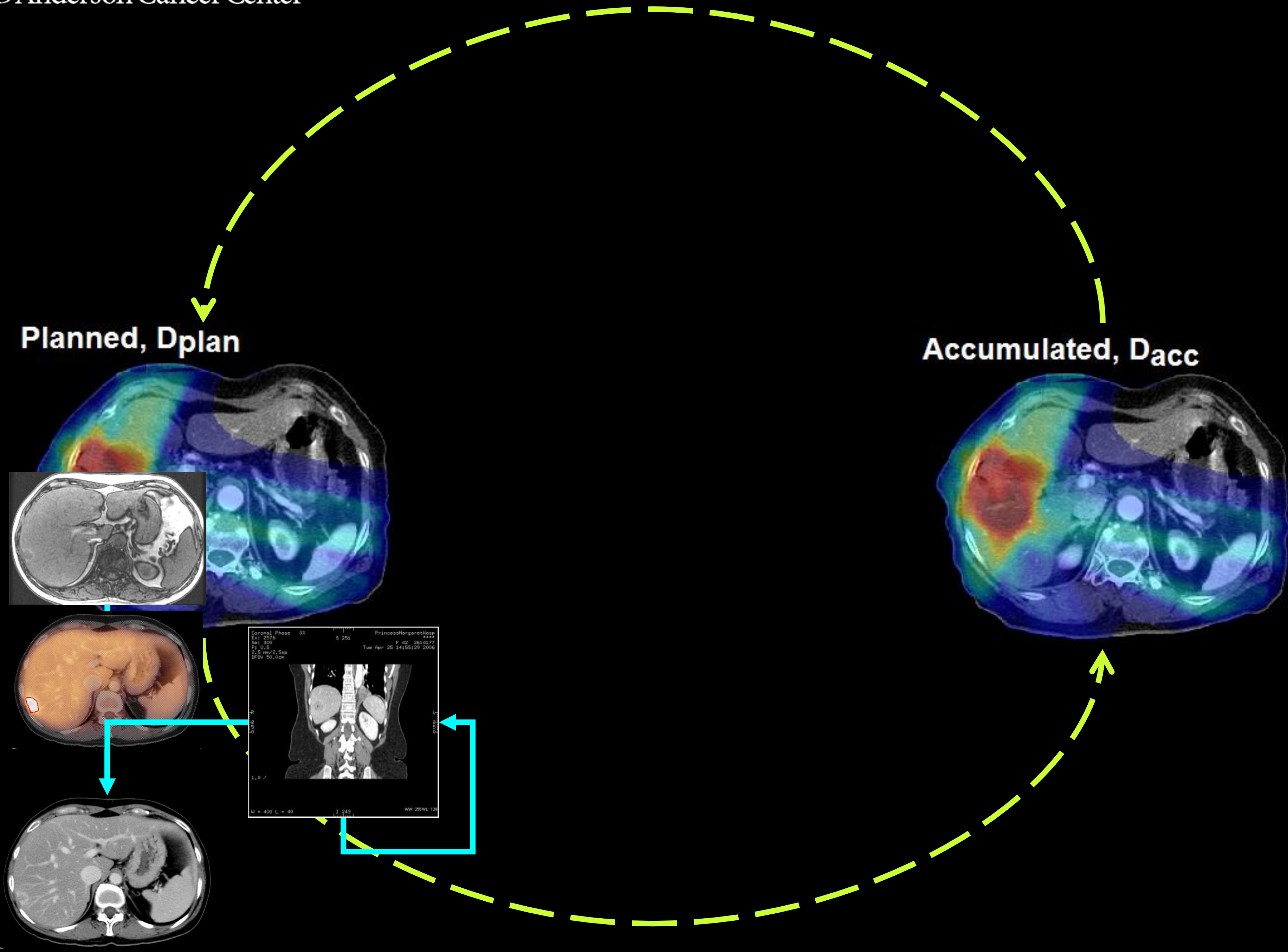
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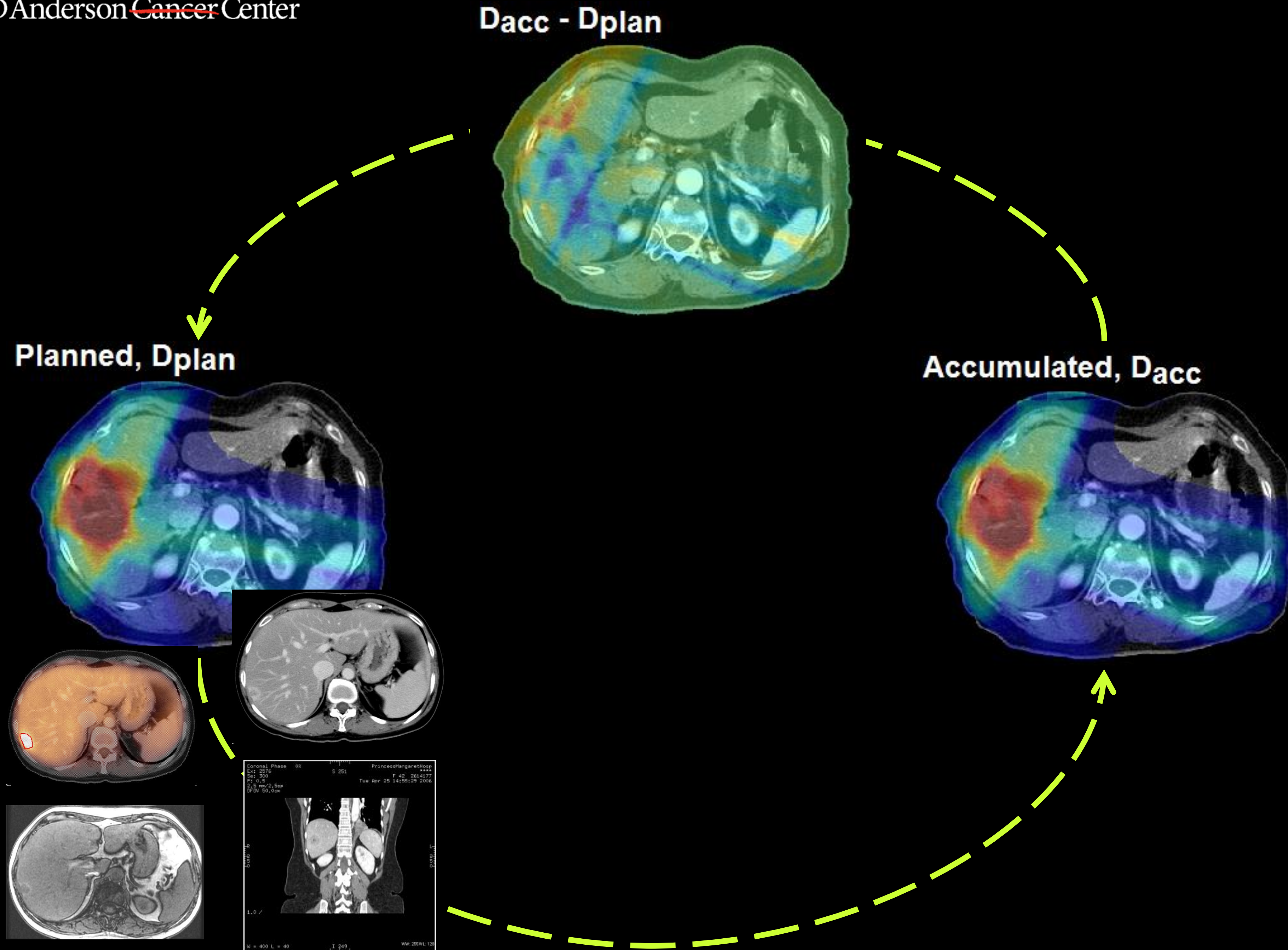

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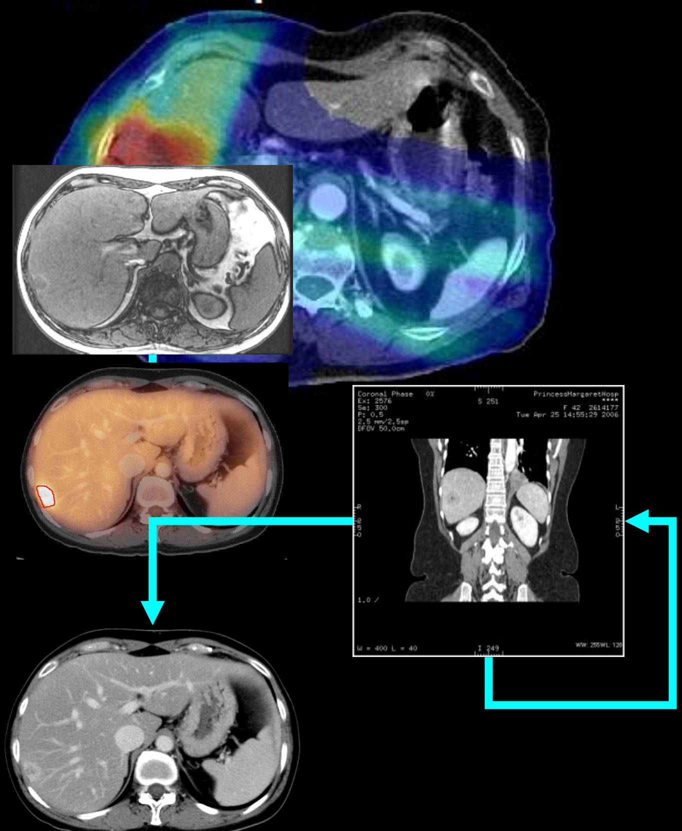

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VOLUME 28 · NUMBER 18 · JUNE 20 2010

JOURNAL OF CLINICAL ONCOLOGY 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

Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 3, pp. 780–791, 2006

0360-3016/06/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2006.05.035

CLINICAL INVESTIGATION **Liver**

PROSPECTIVE COMPARISON OF COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING FOR LIVER CANCER DELINEATION USING DEFORMABLE IMAGE REGISTRATION

JON-PAUL VORONEY, PH.D., M.D.,* KRISTY K. BROCK, PH.D.,* CYNTHIA ECCLES, M.R.T.(T)(MR), C.M.D.,* MASOOM HAIDER, M.D.,† AND LAURA A. DAWSON, M.D.*

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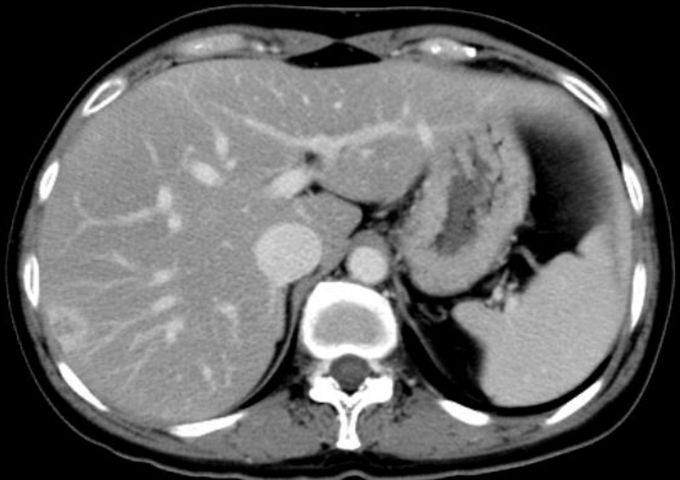
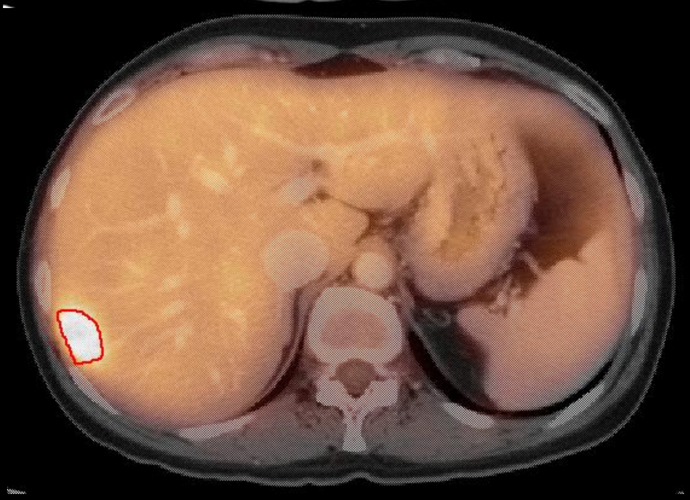
- 26 patients with liver cancer
- Tri-phasic CT and MR
- 5 patients with different number of foci
- Median of AVG distance between the CT and MRI tumor surface = 3.7 mm (2.2 –21.3 mm)

Uncertainties in RT: GTV/CTV Definition

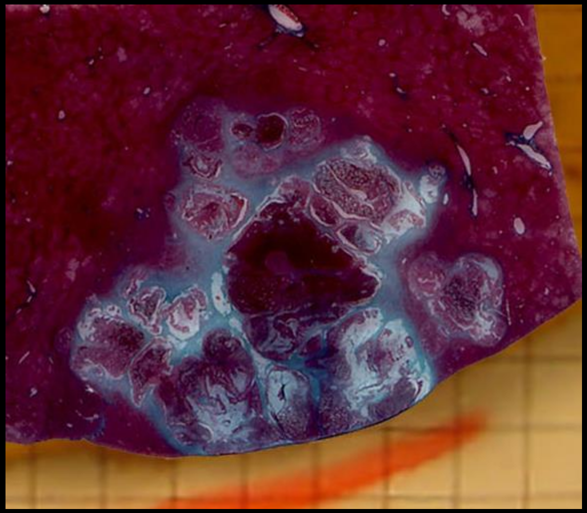
CT



MR



CT/PET



Histology

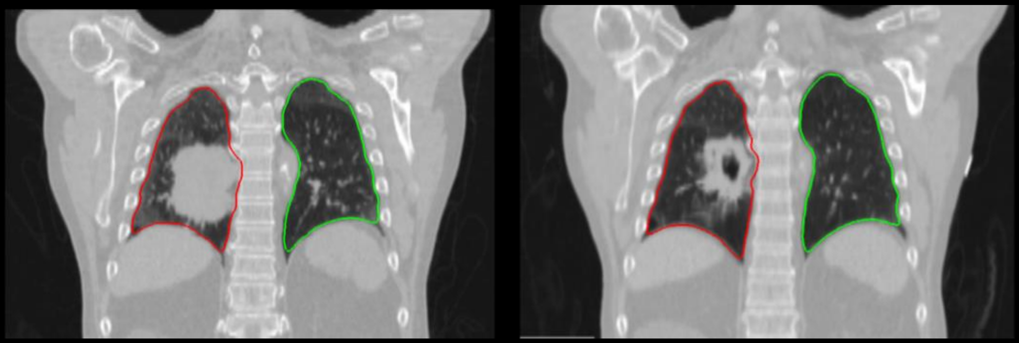
Acquire Planning Image

Acquiring Planning Image

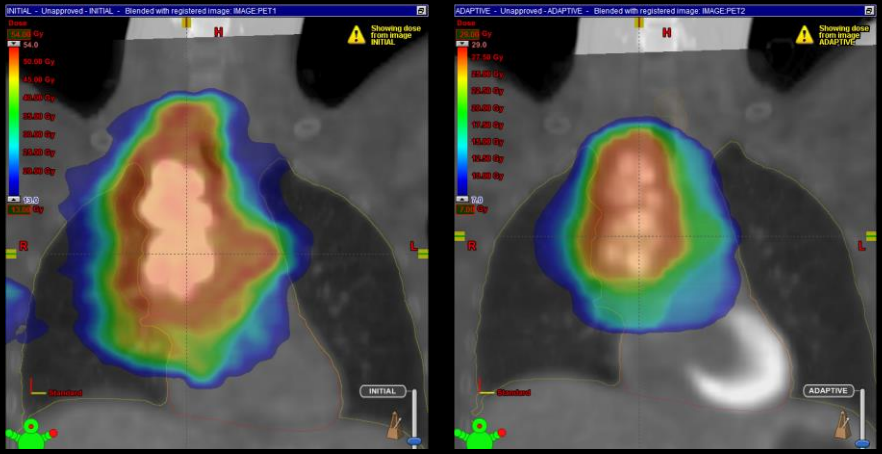
- Goal:
  - Accurately define the tumor and critical normal tissues
  - Get the “best” image possible
- Method:
  - Suspend breathing at a known phase during image acquisition
  - Acquire 4D image
- Don’t Forget:
  - Integrate the images into 1 model of the patient

Tumor Definition & Normal Tissue

- Multi-modality imaging
- Contrast Enhancement
- Optimal Imaging parameters



CT



PET

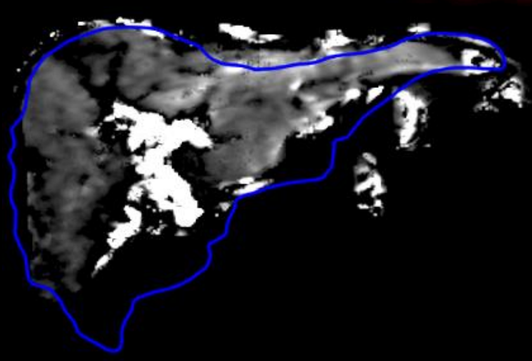
SPECT

Tumor Definition & Normal Tissue

- Multi-modality imaging
- Contrast Enhancement
- Optimal Imaging parameters

CT

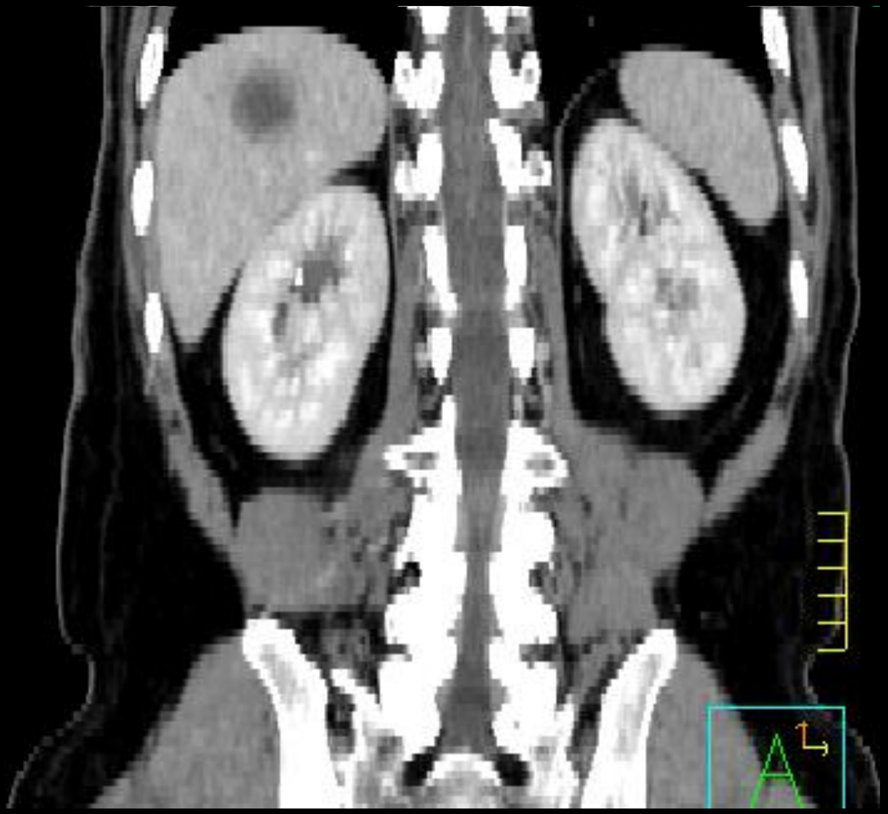
PET



MR

Liver CT: Importance of Contrast

Arterial phase contrast contrast, exhale breath hold



- Triphasic liver CT in treatment position
  - Omnipaque 300 2cc/kg to a maximum of 200cc
  - Injected 5 cc/sec
  - Arterial Delay (best for hepatoma) 30 sec
  - Venous Delay (best for metastases) 60 sec

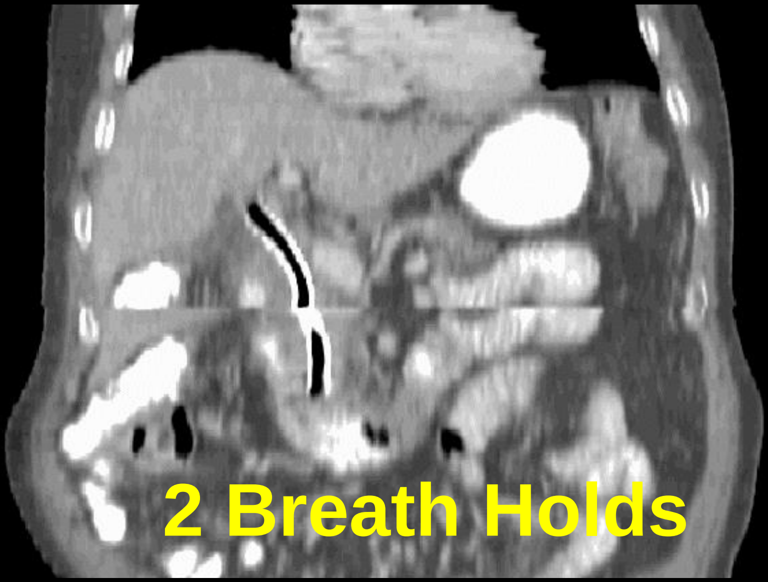
Courtesy of LA Dawson, Princess Margaret Hospital

Optimizing Imaging Time

- Obtain the entire imaging FOV in 1 Breath hold
  – Reduces repeat breath hold artifacts
  – ~15-30 s imaging time

✓ Multi-slice CT

✓ MR w/ Parallel Imaging

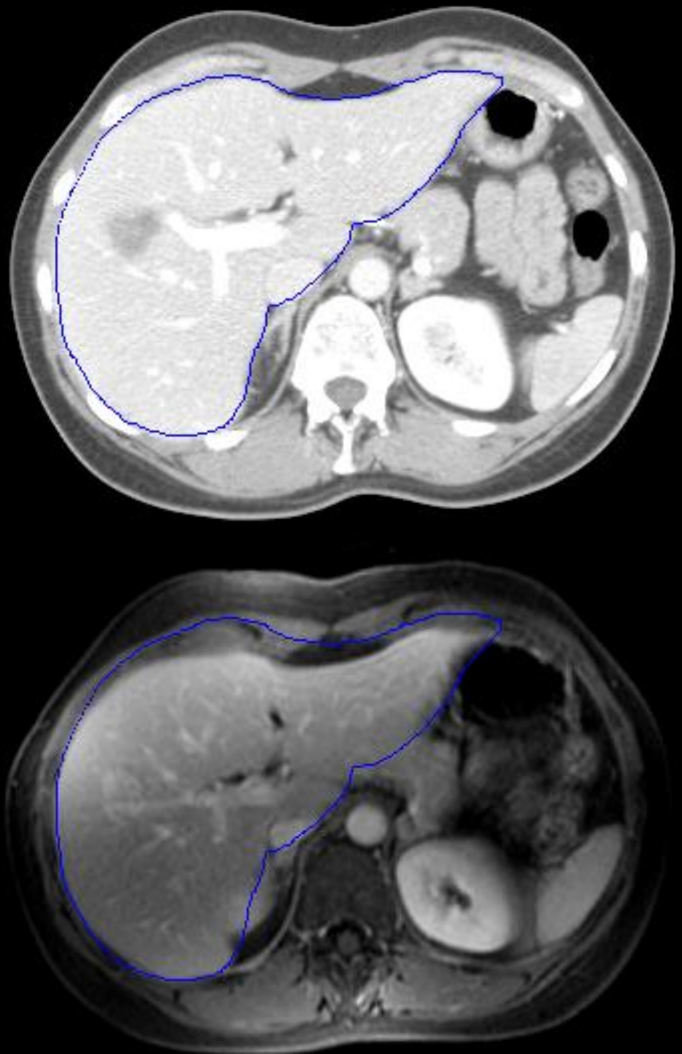


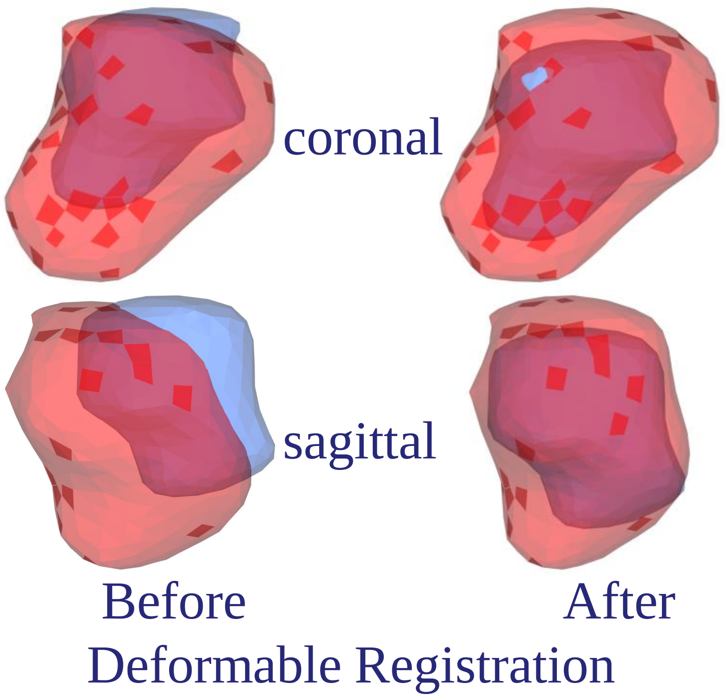
Role of Image Registration

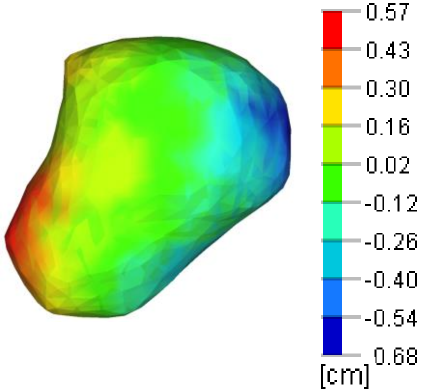
- Error in registration creates a systematic error throughout Tx
  - Error in defining the tumor
  - Error in defining critical normal tissue
- Additional uncertainty margins may come at a cost
  - Ad hoc addition of uncertainty margins may decrease prescribed dose

Image Registration: Accurate Target Definition

Prior to Deformable Registration







<u>GTV Volume</u>

CT = 13.9 cc

MR = 6.7 cc

ΔVol = 7.2 cc (52%)

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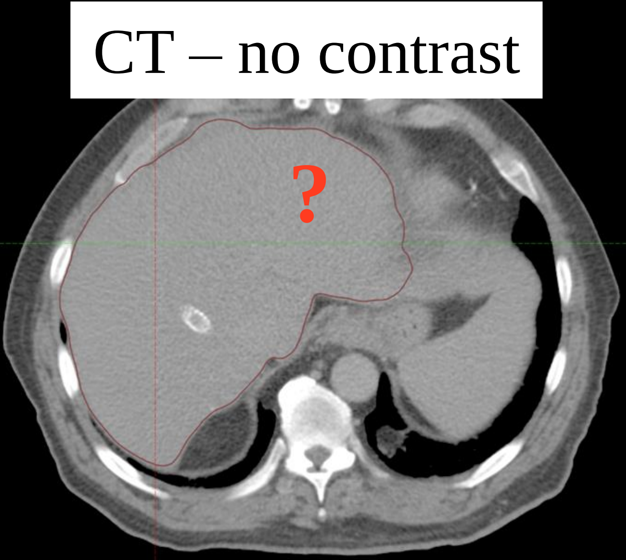
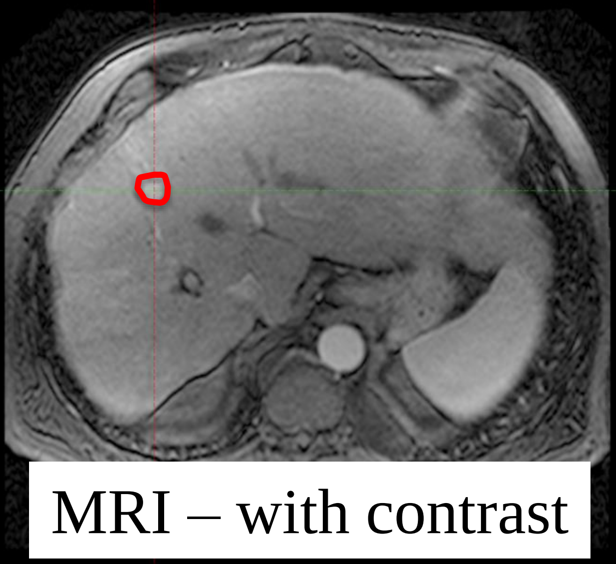
Clinical Example

DIR for Multi-Modality Planning

- Accuracy required: voxel level
- Uncertainties create a **systematic error** that propagates throughout the treatment

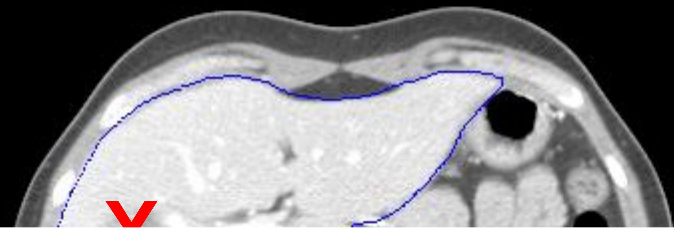


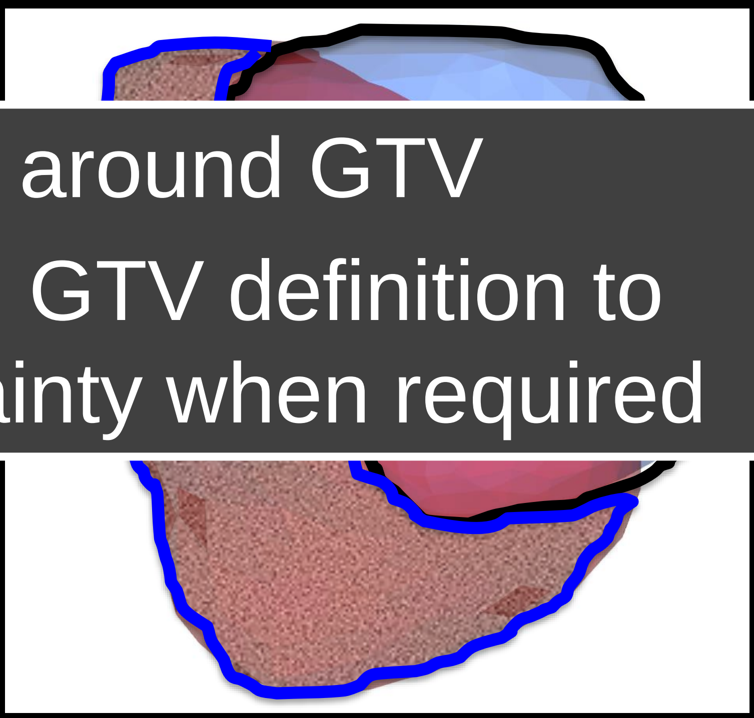


Clinical Effect

Prior to Deformable Registration

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





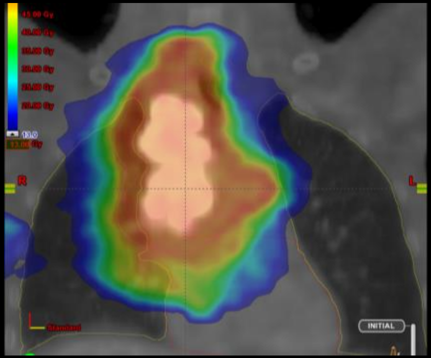
- Assess uncertainty around GTV
- Add margin around GTV definition to account for uncertainty when required

Region of CT-defined GTV that is missed

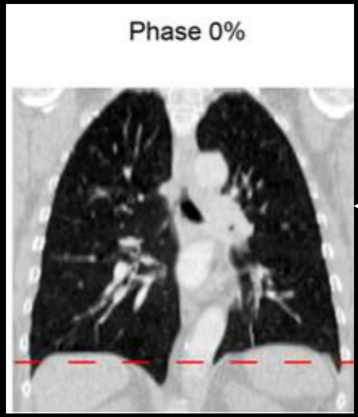
Image Registration: Free Breathing to Breath hold

Inhale

Exhale



Obtained over Multiple Breathing Cycles



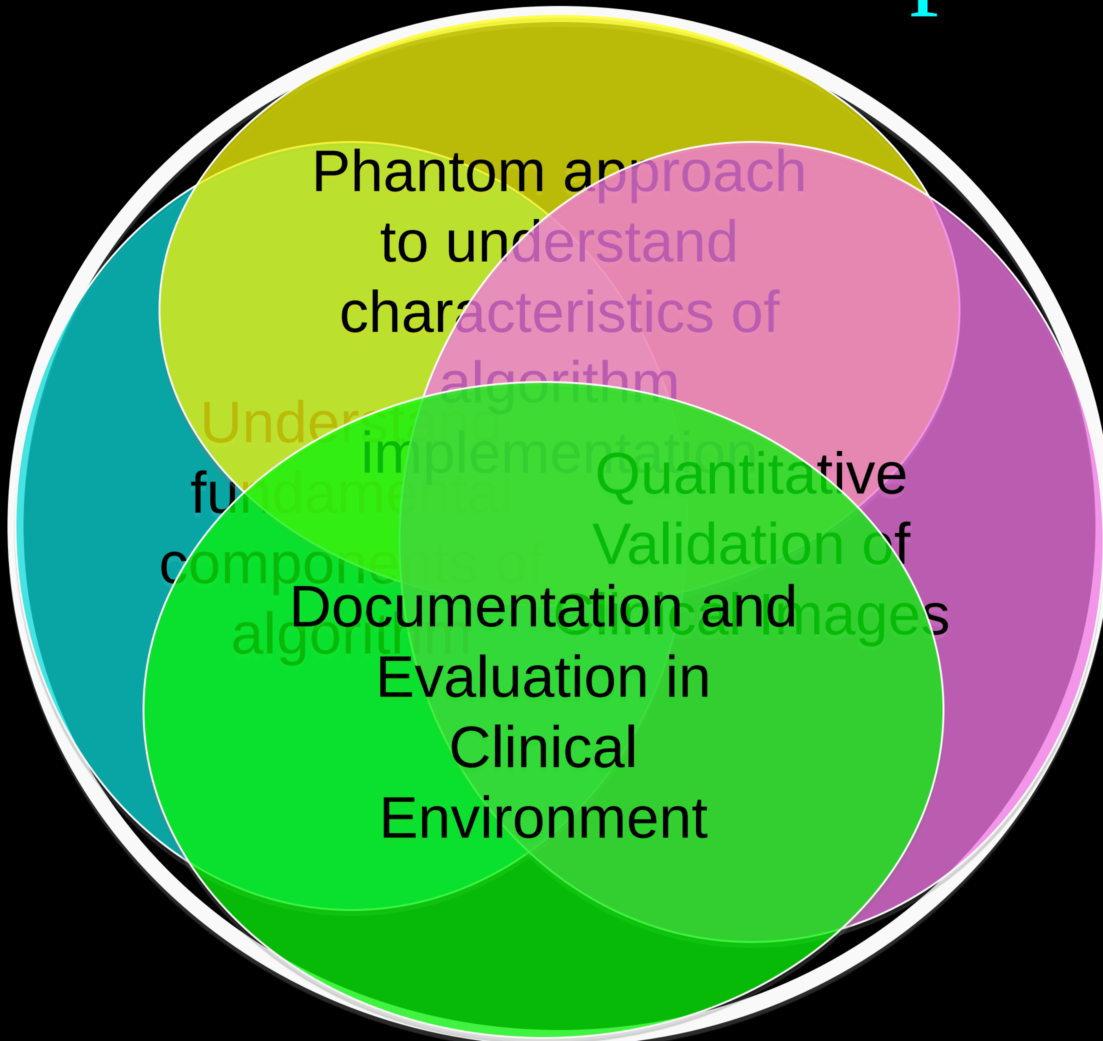
???

- DIR has an expectation of aligning corresponding pieces of anatomy between each image
- Artifacts in the image challenge the registration locally
- Deforming a single-state of anatomy to a multi-state anatomy has many challenges

Wolthaus et al, IJROBP 2008 Mar 15;70(4):1229-38

Commissioning and QA: TG 132

Understand the whole picture

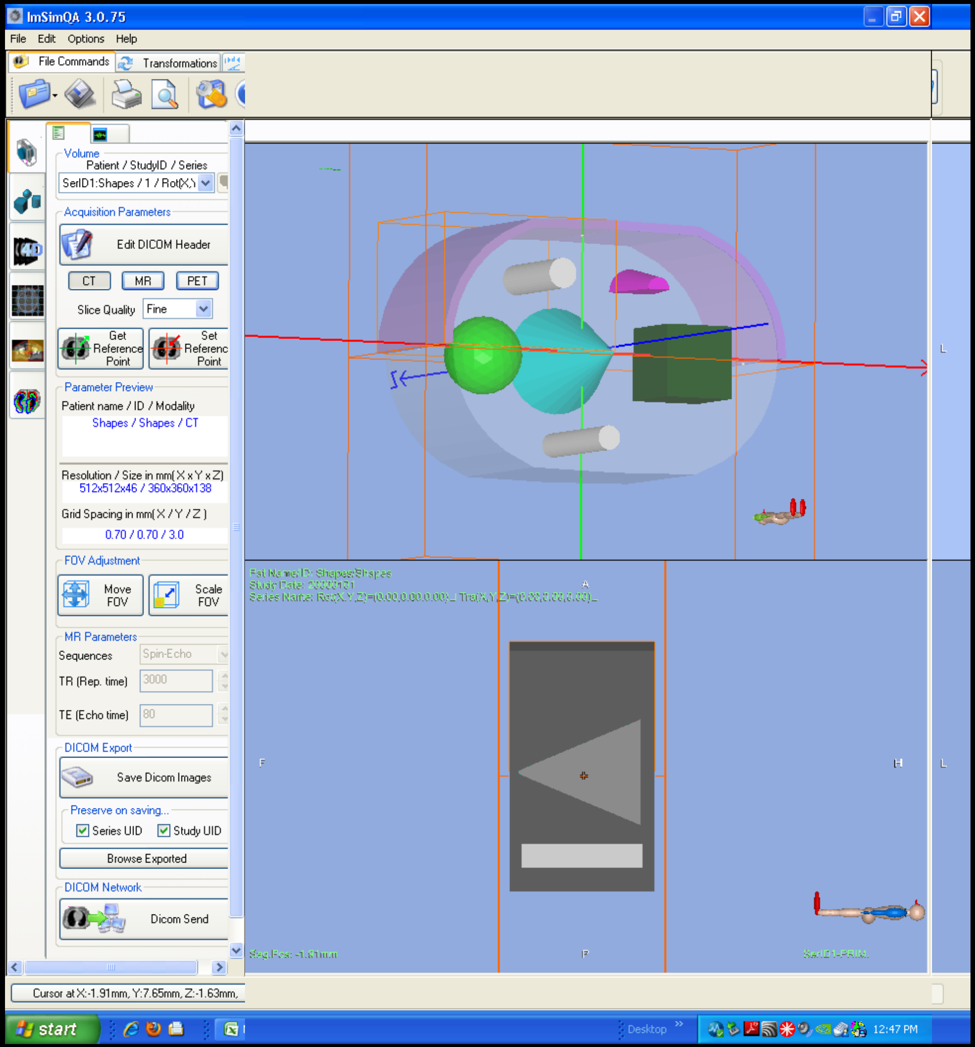


Validation Tests and Frequencies

Frequency	Quality Metric	Tolerance
Acceptance and Commissioning **Annual or Upon Upgrade**	System end-to-end tests Data Transfer using physics phantom	Accurate
	Rigid Registration Accuracy (Digital Phantoms, subset)	Baseline
	Deformable Registration Accuracy (Digital Phantoms, subset)	Baseline
	Example clinical patient case verification	Baseline

Phantom Approach: Rigid Geometric Data

- Helps us to learn the impact of the 'knobs' of the registration
- Validation of most straightforward case
- Similar to 20x20 field profile



* Phantom Data Courtesy of ImSim QA

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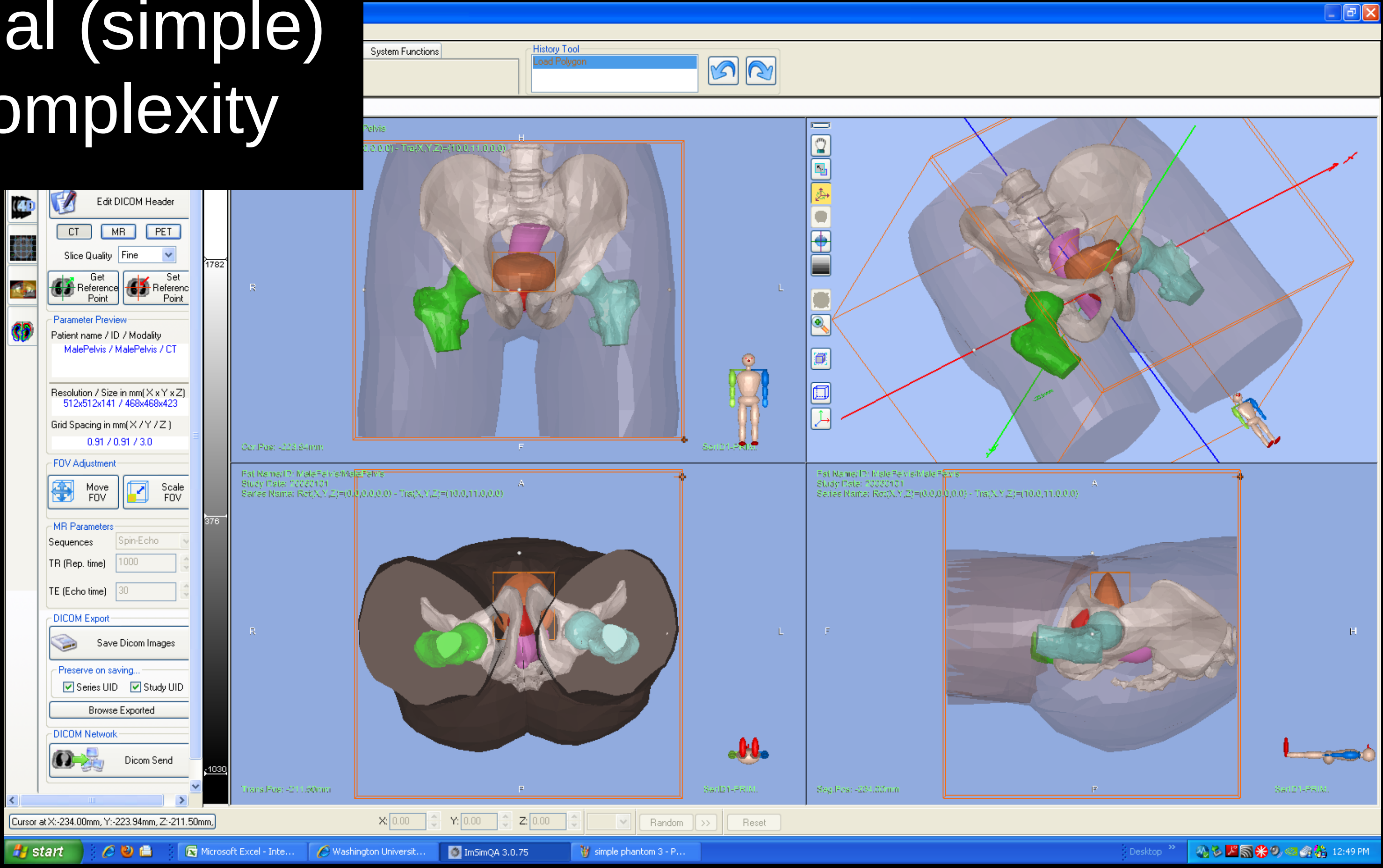
Phantom Approach: Rigid Anatomical Phantom

- Multi-Modality
- Translation Offset
- 1 additional (simple) layer of complexity



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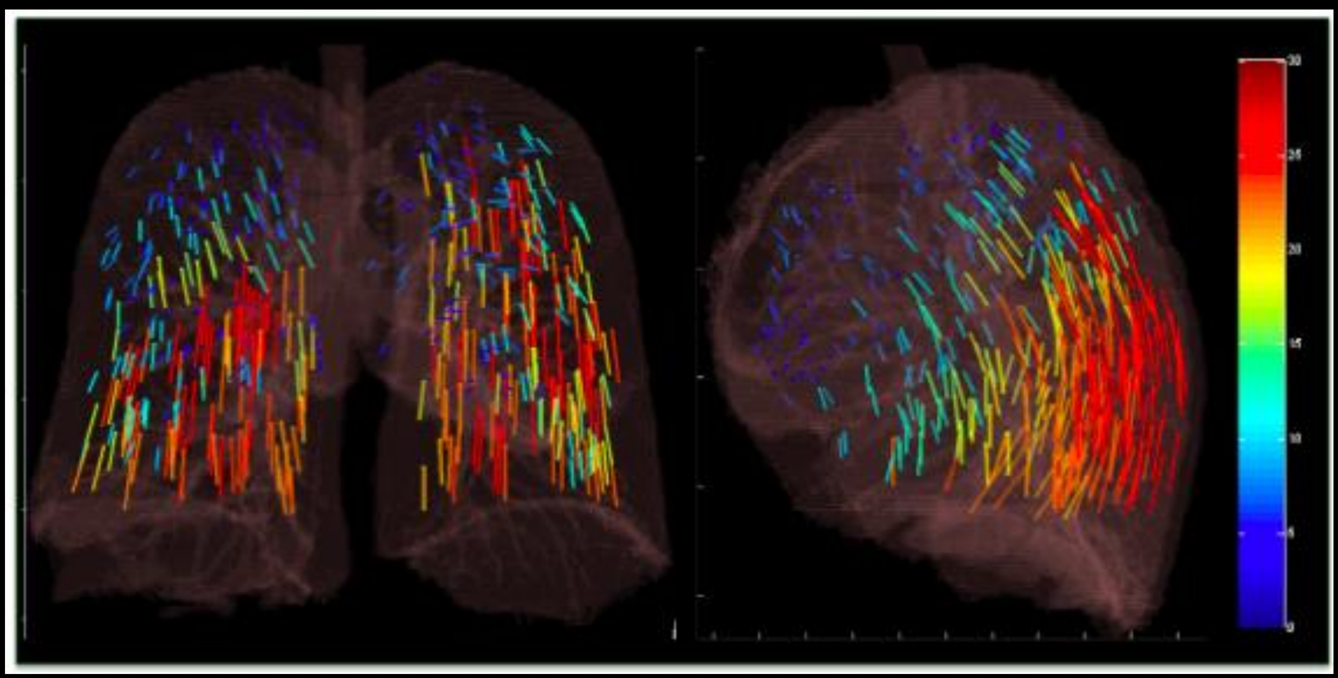
Deformable Lung

- Clinical Lung Data
- Simulated Deformed Lung



*Courtesy DIR-lab, Dr. Castillo

4DCT 8

Image Dims: 512 x 512 x 128
Voxels (mm): 0.97 x 0.97 x 2.5
Features (#): 476
Displacement (mm): 15.16 (9.11)
Repeats (#/#): 150/3
Observers (mm): 1.03 (2.19)

Lowest Error (mm): Observer Uncertainty Threshold

Clinical Images: Quantitative Validation Techniques

- Landmark Based
  - Does the registration map a landmark on Image A to the correct position on Image B?
  - Target Registration Error (TRE)
- Contour Based
  - Does the registration map the contours onto the new image correctly?
  - Dice Similarity Coefficient (DSC)
  - Mean Distance to Agreement (MDA)
- Additional Assessment
  - Jacobian, inverse consistency

Request & Report

- Clear identification of the image set(s) to be registered

Imaging and Registration

Primary Imaging:

CT **ABC:** ☐ Yes ☐ No

Secondary Imaging: ☒ MRI Date: MRI sim from perfusion protocol

Series: Images:

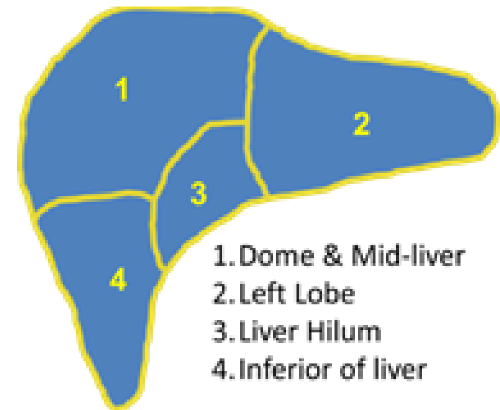
Registration Technique: ☒ Rigid ☐ Deformable

Local Region of Importance: 3 (Hepatic Duct) Comments:

Intended use of Registered Images:

☒ Tumor Definition ☐ Normal Tissue Definition

☐ Treatment Adaptation



- The intended use of the result
  - Target delineation
- Techniques to use (deformable or rigid)
- The accuracy required for the final use

Uncertainty Assessment	Phrase	Description
0	Whole scan aligned	- Anatomy within 1 mm everywhere - Useful for structure definition everywhere - Ok for stereotactic localization
1	Locally aligned	- Anatomy local to the area of interest is un-distorted and aligned within 1mm - Useful for structure definition within the local region - Ok for localization provided target is in locally aligned region
2	Useable with risk of deformation	- Aligned locally, with mild anatomical variation - Acceptable registration required deformation which risks altering anatomy - Registered image shouldn't be used solely for target definition as target may be deformed - Increased reliance on additional information is highly recommended - Registered image information should be used in complimentary manner and no image should be used by itself
3	Useable for diagnosis only	- Registration not good enough to rely on geometric integrity - Possible use to identify general location of lesion (e.g. PET hot spot)
4	Alignment not acceptable	- Unable to align anatomy to acceptable levels - Patient position variation too great between scans (e.g. surgical resection of the anatomy of interest or dramatic weight change between scans)

Respiratory Motion: Overall Strategy

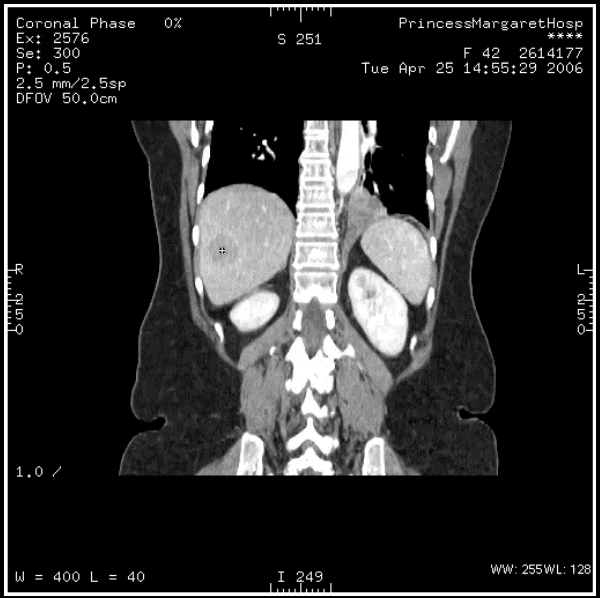
1. Remove motion for diagnostic quality planning image
2. Measure motion for evaluation of impact for therapy
3. Select appropriate motion elimination/reduction/incorporation technique
4. Design image guidance strategy

Measure Motion

Motion Measurement Techniques

- Fluoroscopy
- 4D CT
- Breath hold CT
  - Normal Inhale BH
  - Normal Exhale BH
- Breath hold MR
- Cine MR

4D CT



- External surrogate to monitor motion
- Acquire repetitive images at each anatomical location for > 1 breathing phase
- Link images with breathing phase
- Reconstruct series of images at each breathing phase
  - Inhale, exhale, series of intermediate positions

Maximum Intensity Projection – MIP

- Maximum intensity in that voxel over all phases
- Helpful for contouring ITV
- Limited to isolated tumors within the lung

Int. J. Radiation Oncology Biol. Phys., Vol. 63, No. 1, pp. 253–260, 2005

0360-3016/05/$–see front matter

Table 4. Data from 12 patients comparing MIP-based ITVs with $ITV_{10\ phases}$ and $ITV_{3\ phases}$, respectively

	A	B	C	D	E	F	G	H	I	J	K	L	Mean ± SD

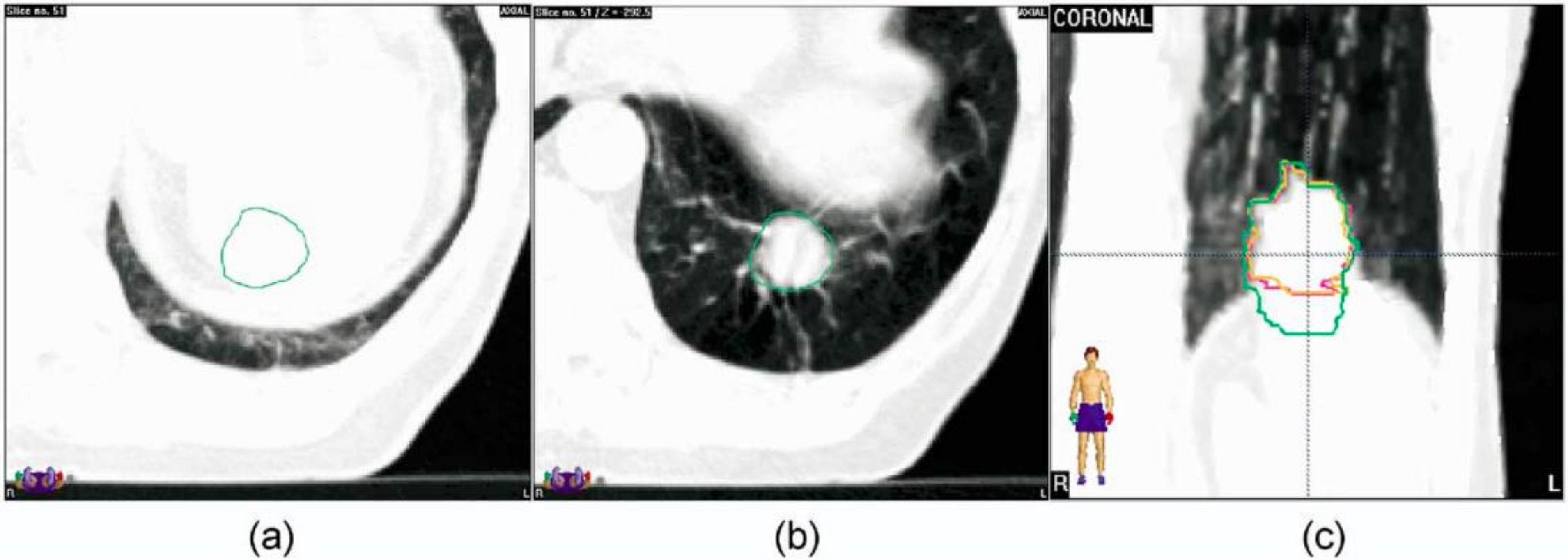
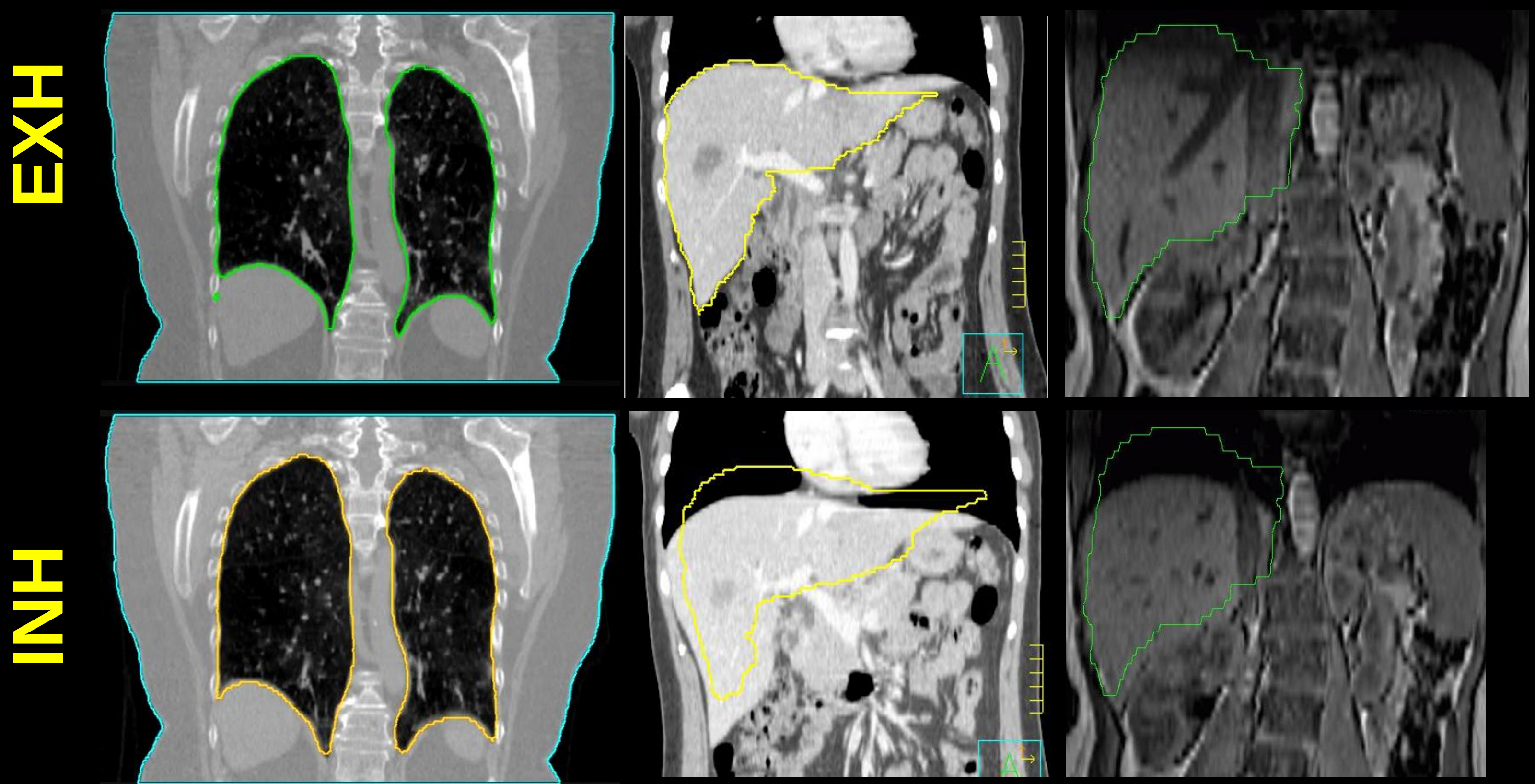


Fig. 8. (a) Example of a tumor located adjacent to the diaphragm, which was not fully visible on repeated maximum intensity projection scans as a result of the overlap with the diaphragm. (b) The extreme end-inspiratory tumor position was visible on the corresponding single-phase scan. (c) Maximum intensity projection information on this patient would underestimate the caudal extent of the internal target volume (orange and pink contours), compared with an $ITV_{10\ phases}$ (green contour).

Fig. 1. Pixel-based intensity projection protocols from four-dimensional computed tomography (CT) data sets of a mobile tumor, illustrating (a) separate phases of the four-dimensional CT, (b) maximum intensity projection, (c) minimum intensity projection, and (d) mean intensity projection.

Breath Hold Imaging

- Acquire 2 images
  - Inhale and Exhale
- Educate patient to ensure ‘normal’ exhale and inhale position



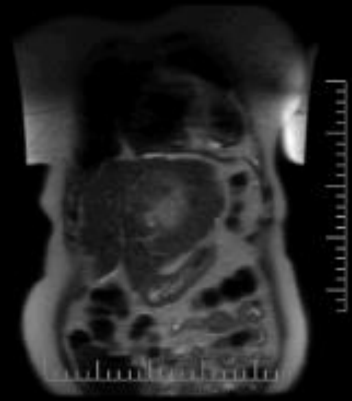
Quantifying Motion

- 2D planar
- Flexibility in optimizing imaging plane
- Soft tissue contrast
- Close to ‘real-time’

(1.5 Tesla GE)

–SSFSE ≈ 1 frame/sec. ≈ 30 sec.

–1 cm slice



Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 4, pp. 1189–1195, 2008

0360-3016/08/$–see front matter

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doi:10.1016/j.ijrobp.2007.11.026

CLINICAL INVESTIGATION **Liver**

THREE-DIMENSIONAL MOTION OF LIVER TUMORS USING CINE-MAGNETIC RESONANCE IMAGING

Anna Kirilova, B.Sc.,* Gina Lockwood, M.Math.,† Perry Choi, M.D.,‡ Neelufer Bana, B.Sc. (Hon),‡ Masoom A. Haider, M.D.,§ Kristy K. Brock, Ph.D.,* Cynthia Eccles, B.Sc.,‡ and Laura A. Dawson, M.D.‡

Departments of *Radiation Physics, †Biostatistics, ‡Radiation Oncology, and §Medical Imaging, Princess Margaret Hospital, University of Toronto, Toronto, ON, Canada

Table 3. Absolute differences between fluoroscopy and MRI craniocaudal motion

Tumor motion	n	%	>5 mm	>10 mm
Fluoroscopy less than cine-MRI	17	48.6	9 (52.9)	5 (29.4)
Fluoroscopy greater than cine-MRI	18	51.4	7 (38.9)	3 (16.7)
All	35	100	16 (45.7)	8 (22.9)

Abbreviation: MRI = magnetic resonance imaging.
Data in parentheses are percentages.

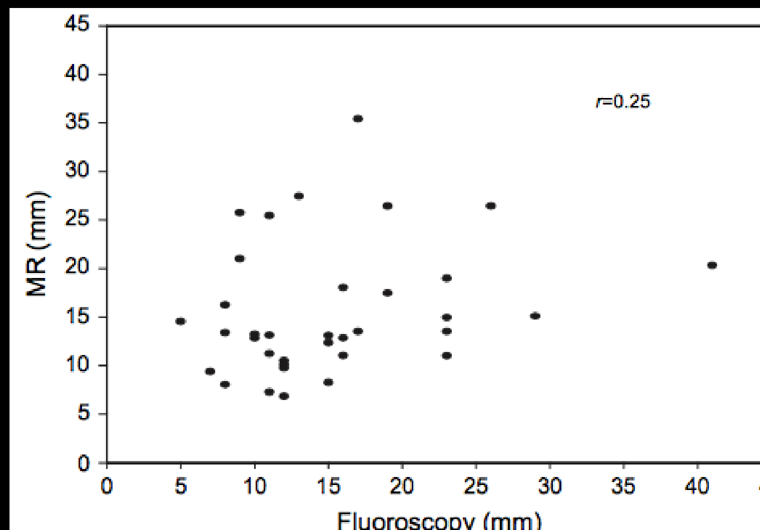

Fig. 5. Correlation between craniocaudal motion according to diaphragm motion on fluoroscopy and tumor motion on cine-magnetic resonance imaging (n = 35).

Accounting for Motion in Planning/Delivery

- Motion < 5 mm: incorporate into PTV
- Motion > 5 mm:
  - Incorporate into PTV margin
    - Asymmetric patient-specific margins
    - Statistical PTV on mean position
  - Abdominal compression
  - Breath Hold
  - Gate Tx
  - Track tumor during Tx

* Recommendations from AAPM Task Group 76

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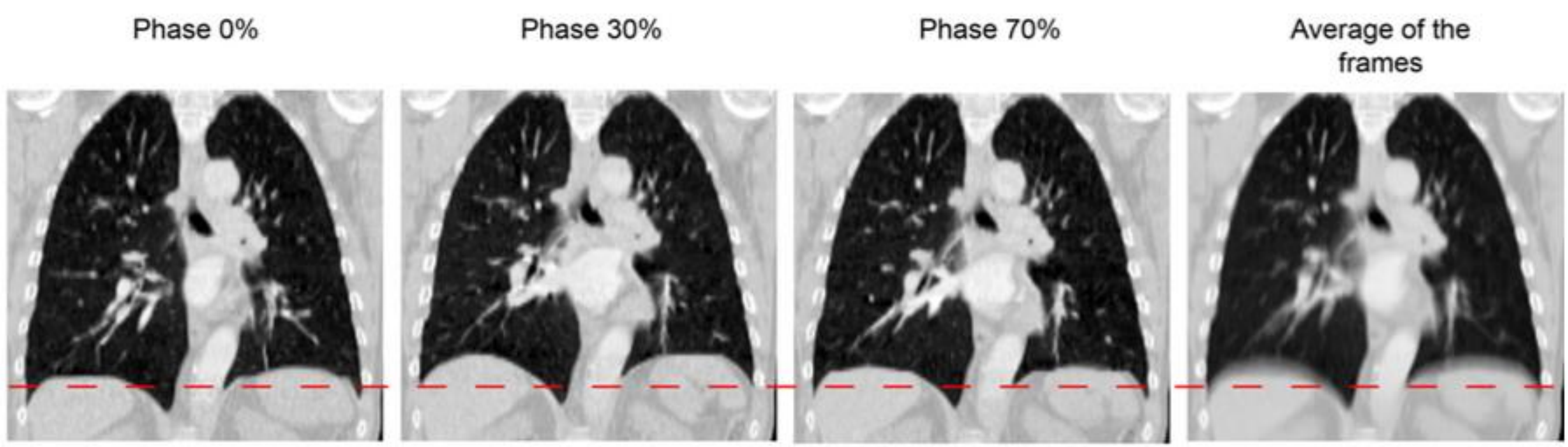
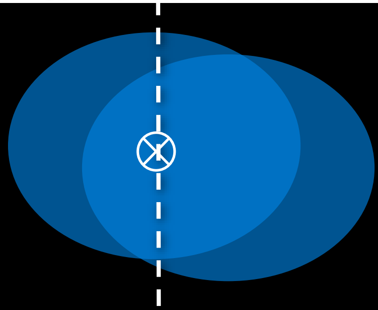
Incorporating Motion into PTV: Lung

Int J Radiat Oncol Biol Phys. 2008 Mar 15;70(4):1229-38. doi: 10.1016/j.ijrobp.2007.11.042.

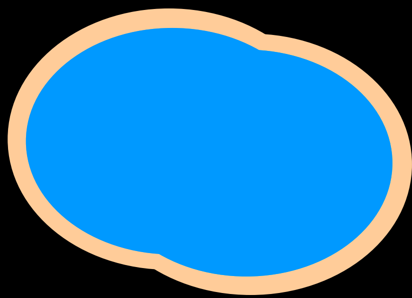
Comparison of different strategies to use four-dimensional computed tomography in treatment planning for lung cancer patients.

Wolthaus JW[1], Sonke JJ, van Herk M, Belderbos JS, Rossi MM, Lebesque JV, Damen EM.





Average Scan



Fused GTV (ITV)

PTV = Fused GTV + 5 mm Symmetric Margin

Contents lists available at ScienceDirect

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journal homepage: www.thegreenjournal.com

PET in rectal cancer

The evaluation of a deformable image registration segmentation technique for semi-automating internal target volume (ITV) production from 4DCT images of lung stereotactic body radiotherapy (SBRT) patients

Richard Speight [a,*], Jonathan Sykes [a], Rebecca Lindsay [a], Kevin Franks [b], David Thwaites [a]

[a] Department of Medical Physics and Engineering; and [b] Department of Clinical Oncology, Leeds Teaching Hospitals Trust, Leeds, UK

Results:

- <u>**18/25 ITVs had normalized DSC > 1**</u> indicating an agreement with the manually produced ITV within 1 mm uncertainty.
- **4 of the other 7 ITVs were deemed clinically acceptable**
- **3 would require a small amount of editing**.

In general, ITVs produced by DIR were smoother than those produced by manual delineation. It was estimated that using this technique would save clinicians on average 28 min/patient.

Contents lists available at ScienceDirect

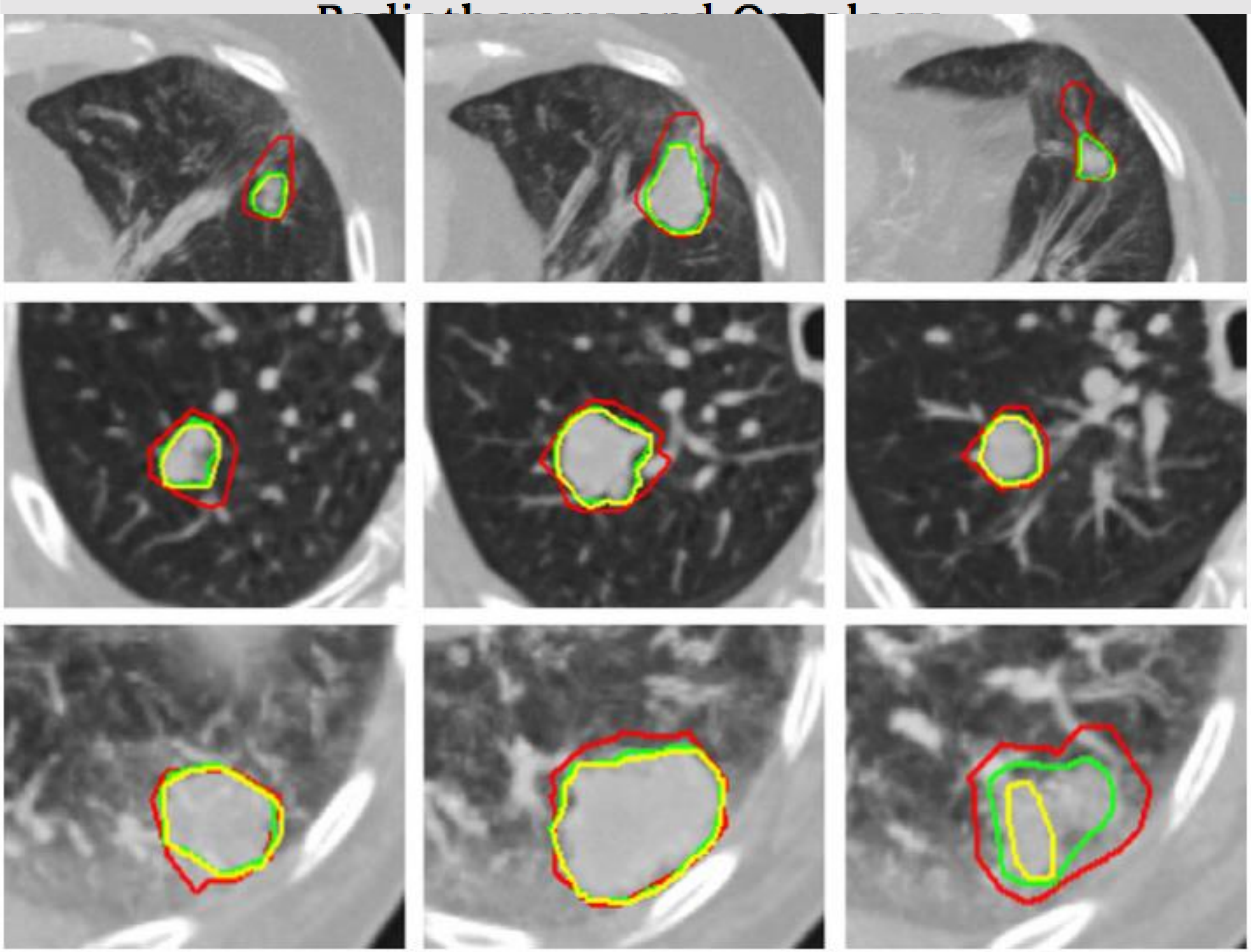
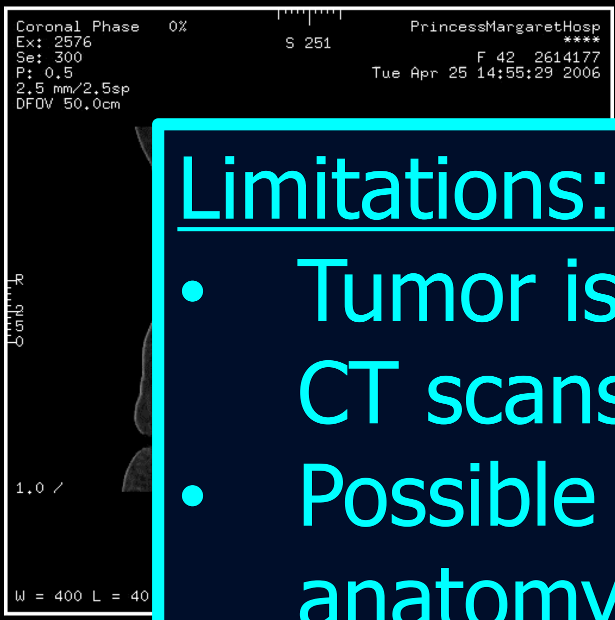


Fig. 3. Transverse MIP images showing that the ITV-CLIN volume is consistently larger than ITV-ABAS. Furthermore it appears that ITV-CLIN is overestimating the extent of tumour motion displayed on the MIP images. Images from the superior end, centre and inferior end of the ITV are shown on the left, centre and right, respectively. Images on the top, middle and bottom are from patients 7, 10 and 13, respectively. On all images the green, yellow and red contours are the ITV-ABAS-BSPLINE, ITV-ABAS-DEMONS and ITV-CLIN, respectively.

would save clinicians on average 28 min/patient.

Incorporating Motion into PTV: Liver



4DCT Datasets

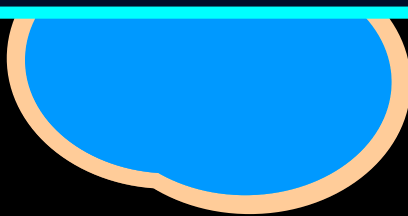
<u>Limitations:</u>

- Tumor is typically not visible on 4D CT scans
- Possible to use surrogates of the liver anatomy to measure motion
- Add motion to GTV to form ITV

x

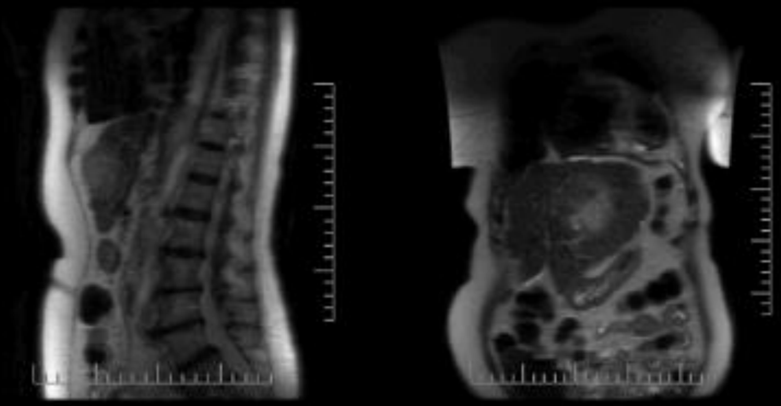
Fused GTV (ITV)

PTV = Fused GTV + 5 mm
Symmetric Margin



Incorporating Motion into PTV: Liver

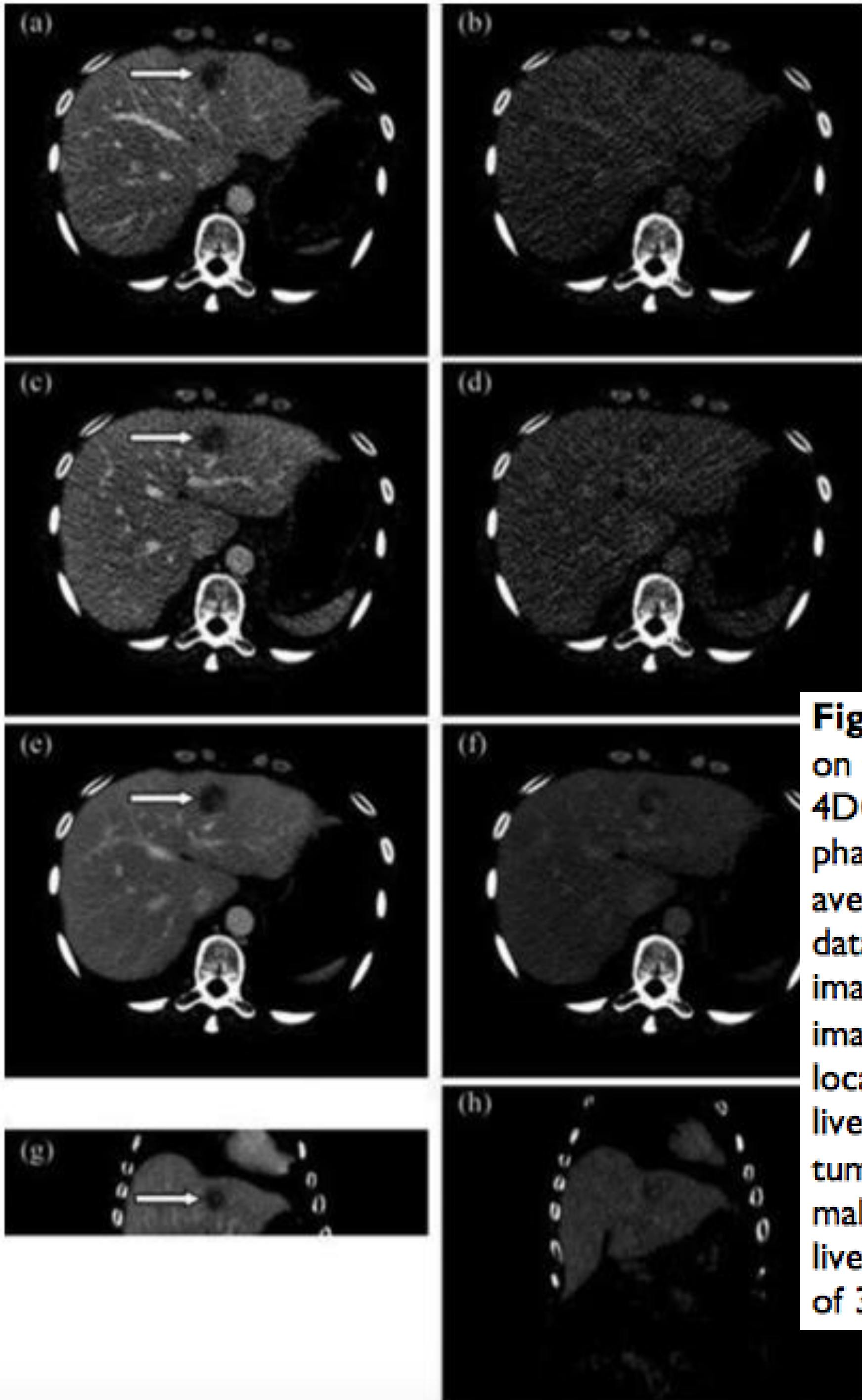
+



Breath hold image

Motion Measurements

Asymmetric Margin
for breathing



:hronized
BRT Patients

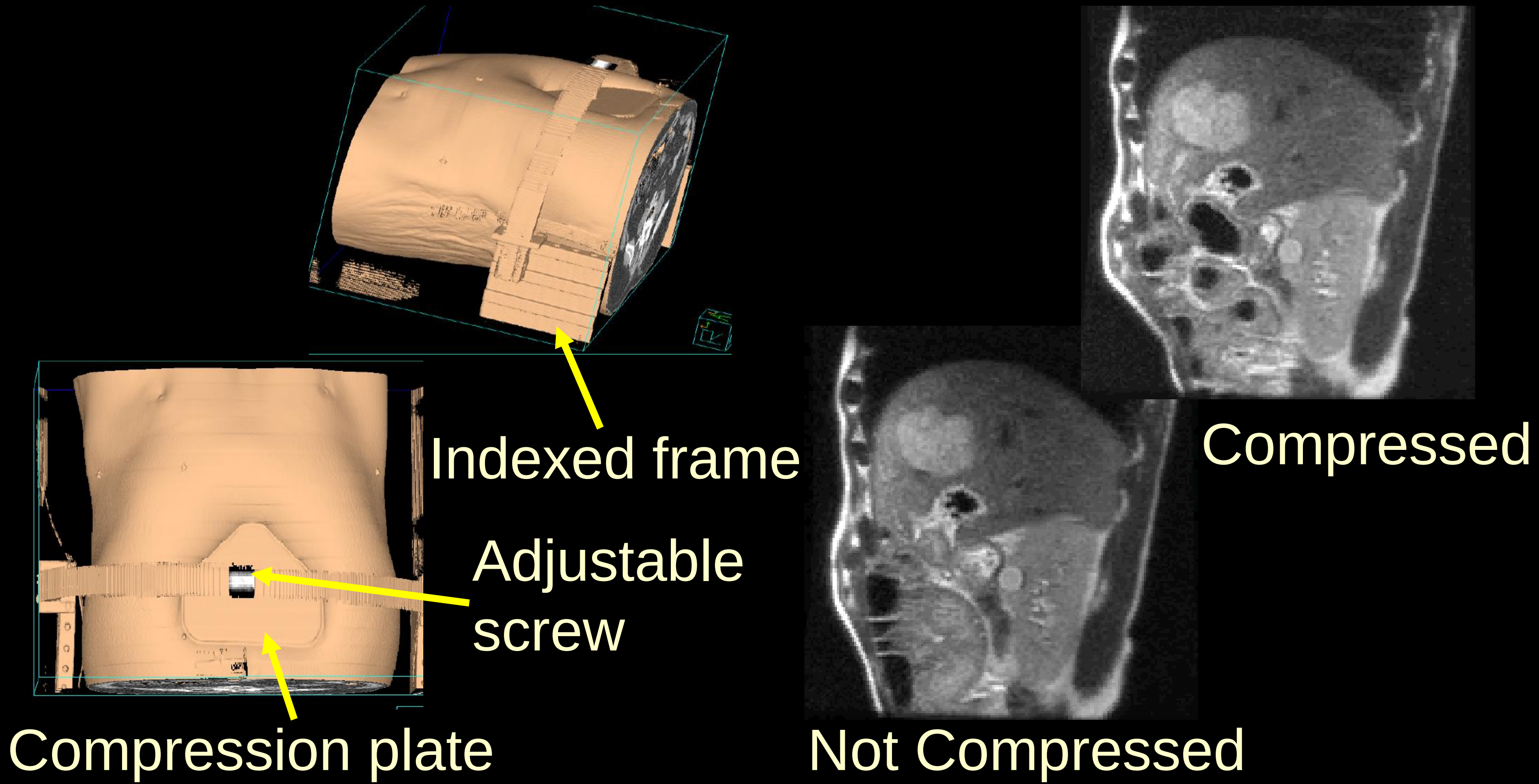
ıD[3],
ıng, MD[1,2]

Technology in Cancer Research & Treatment
2016, Vol. 15(1) 55–59

DOI: 10.1177/1533034615572341
tct.sagepub.com
SAGE

Figure 2. The images corresponding to the short and long 4DCT are on the left and right, respectively; (A) maximum inhale phase, short 4DCT; (B) maximum inhale phase, long 4DCT; (C) maximum exhale phase, short 4DCT; (D) maximum exhale phase, long 4DCT; (E) average image data set derived from short 4DCT; (F) average image data set derived from long 4DCT; (G) coronal view of the average image data set, short 4DCT; and (H) coronal view of the average image data set, long 4DCT. The arrows on the left hand side indicate location of the disease. On the long scans (B, D, F, and H), the normal liver parenchyma has a density of 78 Hounsfield units (HU) and the tumor 76 HU (difference of 2 HU), whereas with the use of an optimally timed injection on the short scans (A, C, E, and G), the normal liver parenchyma density is 100 HU and the tumor 65 HU (difference of 35 HU). 4DCT, 4-dimensional computed tomography.

Abdominal Compression



Benefits of Abdominal Compression

- 62 patients on IRB SBRT liver protocol comp/no comp cine MRI at PMH
  - 24 HCC, 33 mets, 5 cholangio
  - 33 male, 29 female
- 46 Patients evaluated under fluoro with and without compression
- 2D Fiesta T2w single shot fast spin echo (SSFSE)
  - Temporal resolution of 1-3 images/second over 30-60 seconds

Results – MRI

- In the majority of patients abdominal compression reduced tumour motion in all directions
- Maximum reductions seen in caudal-cranial directions

Motion reduction in all 3 directions	n=22 (49.0%)
Motion reduction in any 2 directions	n=17 (40.8%)
Motion increase in all 3 directions	n=5 (10.2%)

*from first 49 patients only

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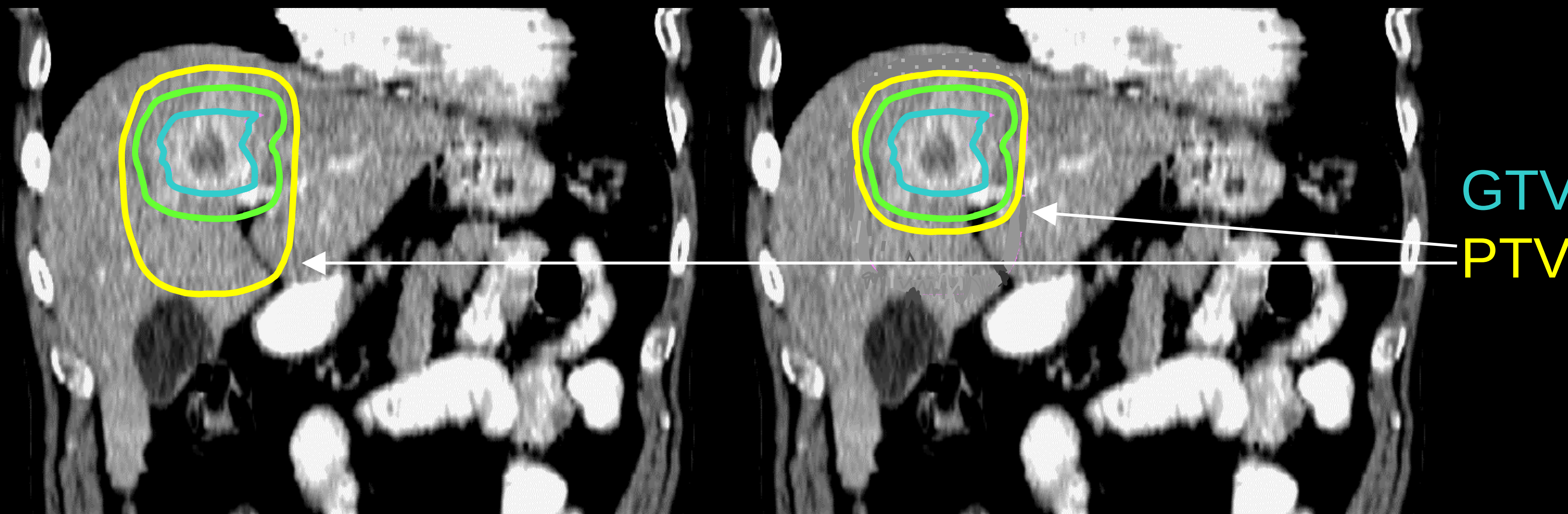
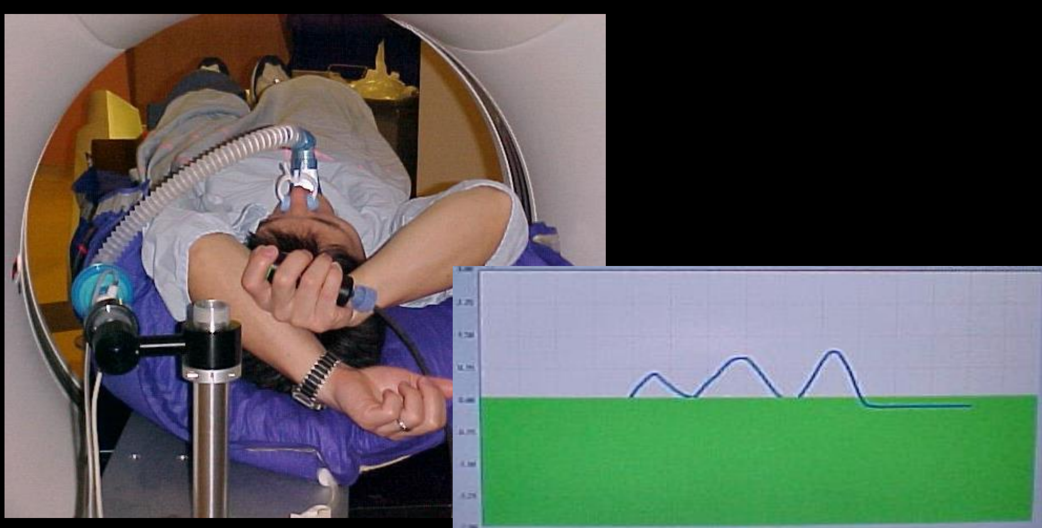
Breath Hold

Free breathing / Breath hold RT





- Importance of patient screening
- Evaluation of reproducibility
- Importance of Image Guidance

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

Dawson LA. IJROBP 2001
Eccles, C, IJROBP, 2005

So now we've planned our patient…

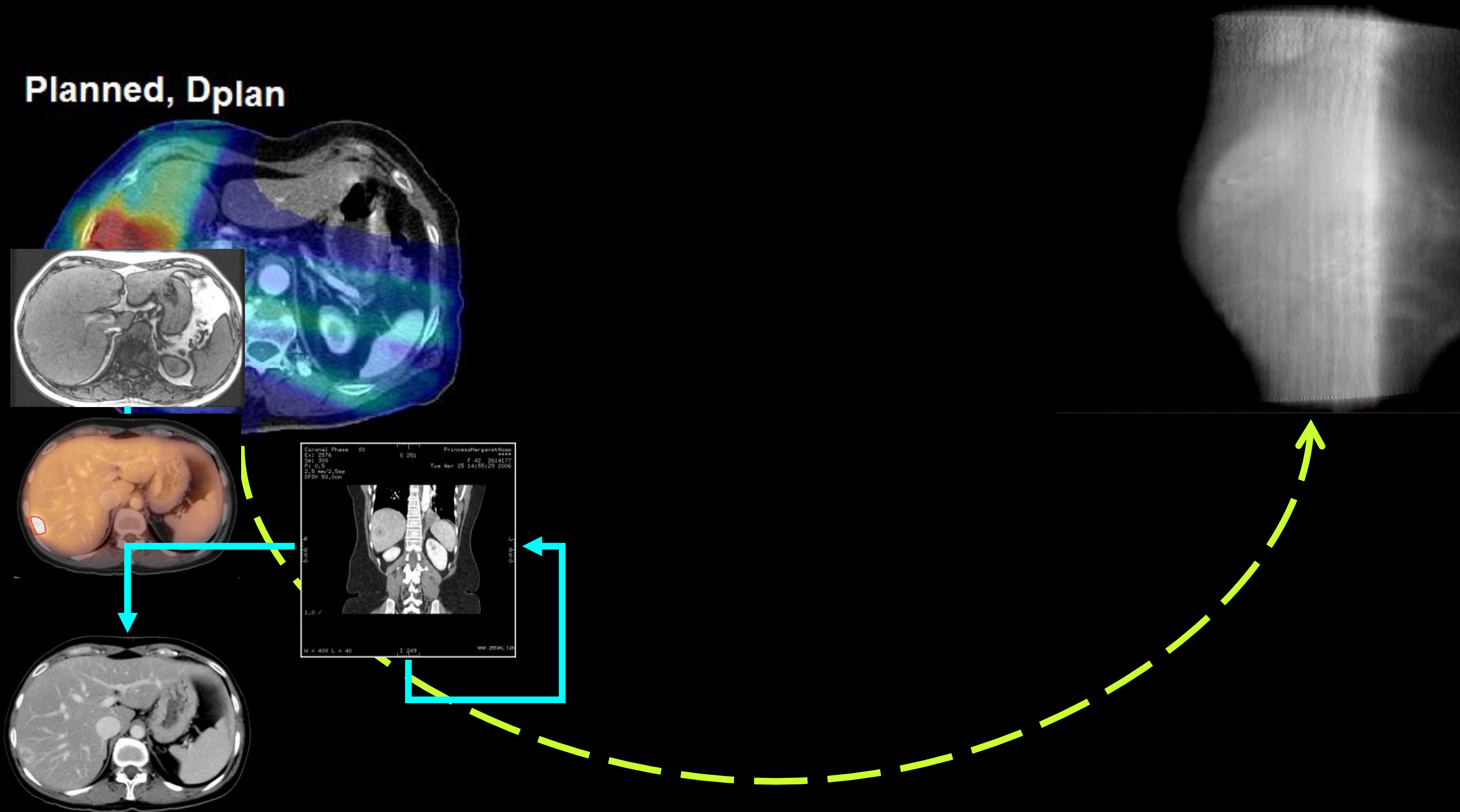

Planned, Dplan

Image Guidance Strategy

Purpose of Image Guidance

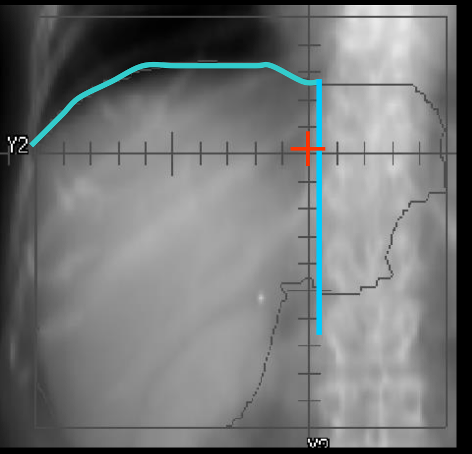
- Localize reference position of tumor and surrounding anatomy
- Verify breathing motion or stability of breath hold
- Verify correlation with tracking/gating system
- Options: 2D, 3D, and 4D

2D kV Imaging

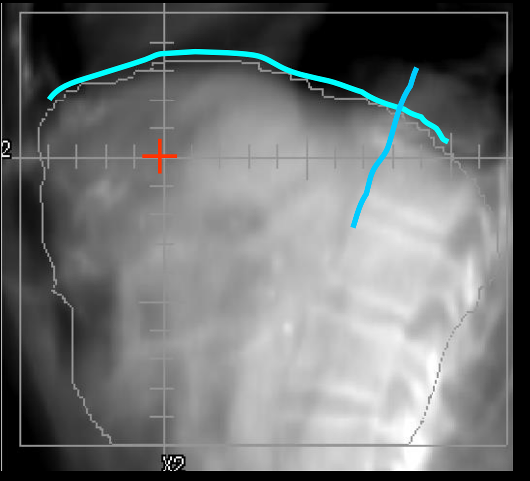
- Single image acquisition
  - At planned breathing phase for verification and alignment
- Cine image acquisition
  - Select planned breathing phase
  - Measure motion and ensure
- Alignment to DRR reference image from plan

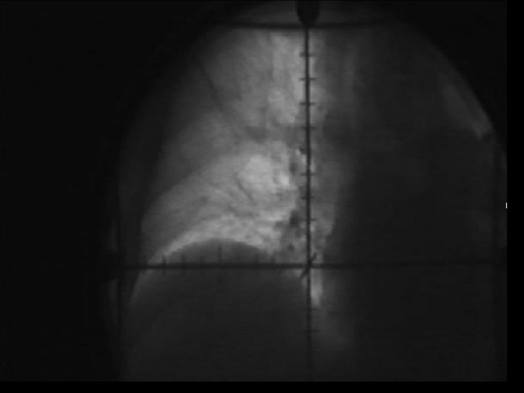
DRR

AP



Lat





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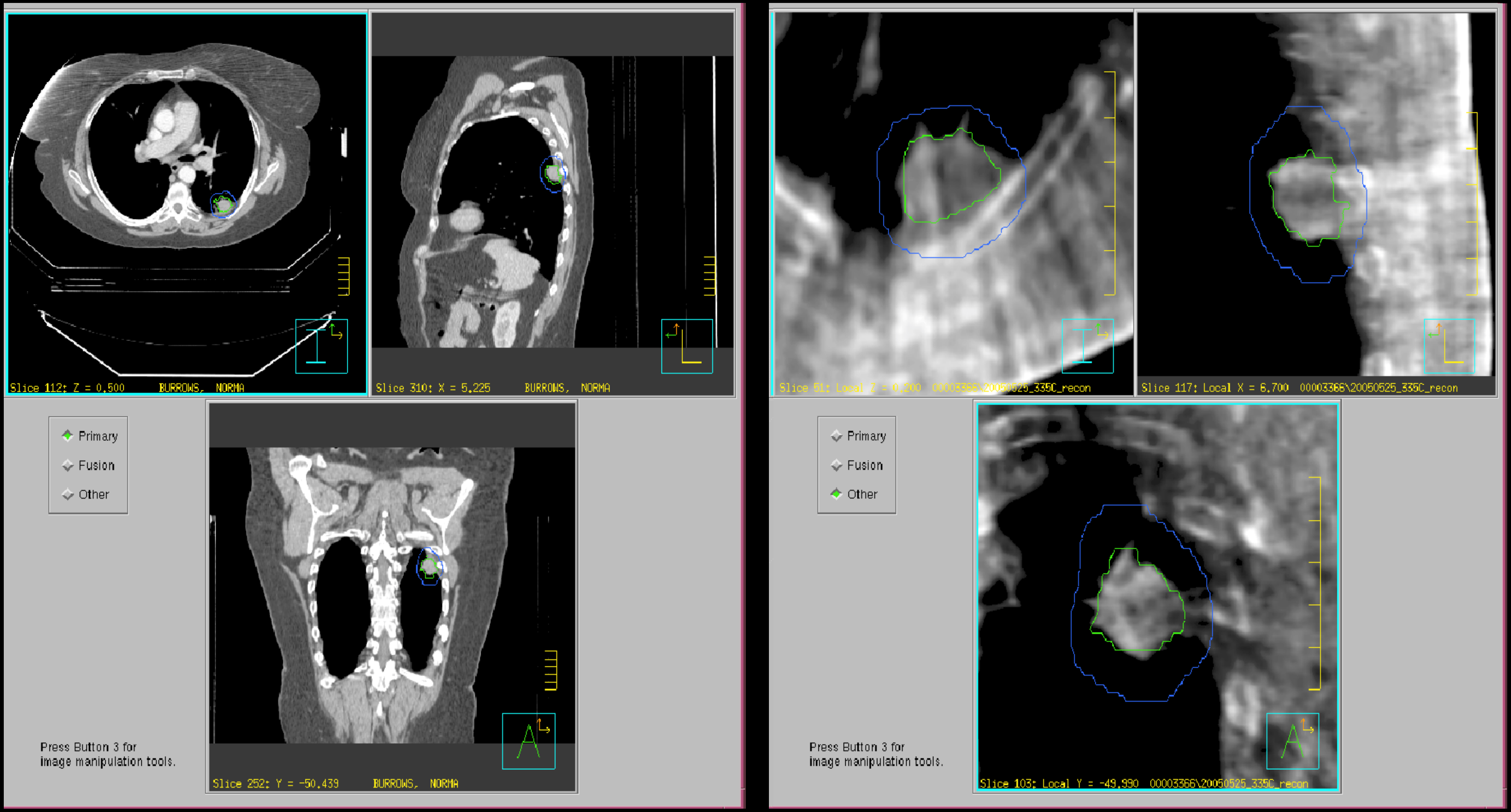
3D Image Guidance: CBCT



Focus registration on GTV, be mindful of normal tissue

A Bezjak, A Hope, Princess Margaret Hospital

Phantom and Clinical Study of Differences in Cone Beam

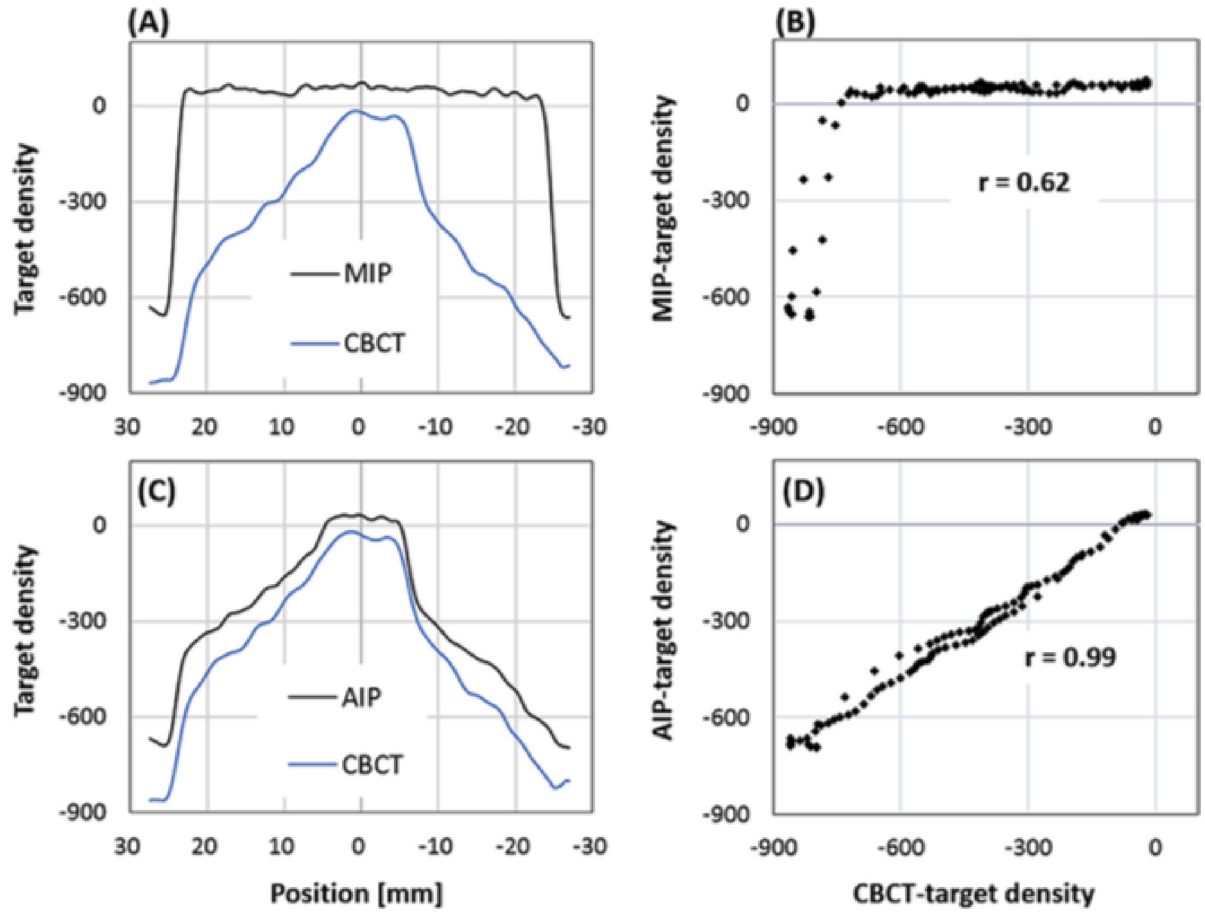


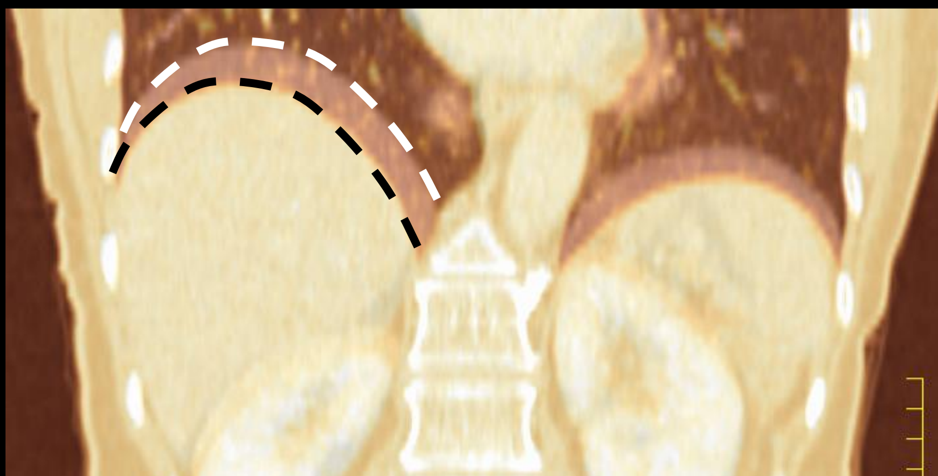
Fig. 3. Comparison of target density along the central superior–inferior line of each coronal image after registration. The target amplitude was 2 cm. (A) Profiles of the MIP and dynamic CBCT targets and (B) the density correlation. (C) Profiles of the AIP and dynamic CBCT targets and (D) the density correlation. Negative values indicate an inferior side from the center of the coronal image. AIP = average intensity projection; CBCT = cone beam computed tomography; MIP = maximum intensity projection.

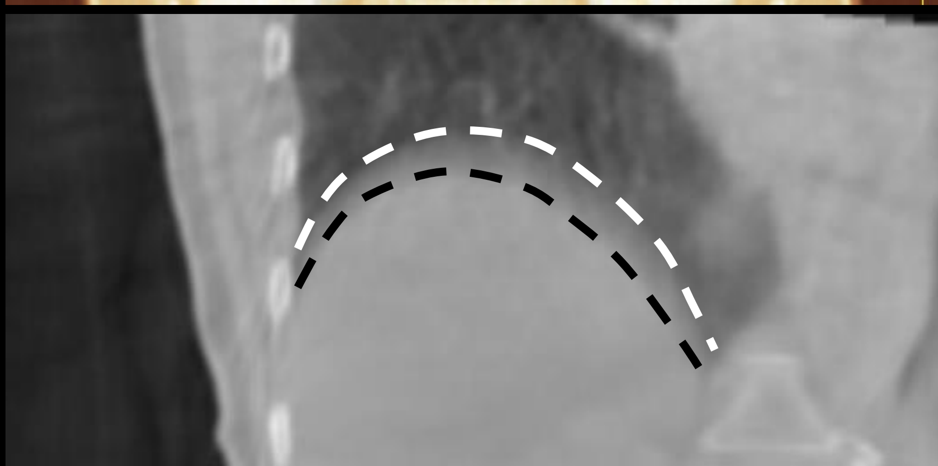
computed tomography; MIP = maximum intensity projection.

Strategies to consider breathing motion Wuerzburg

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

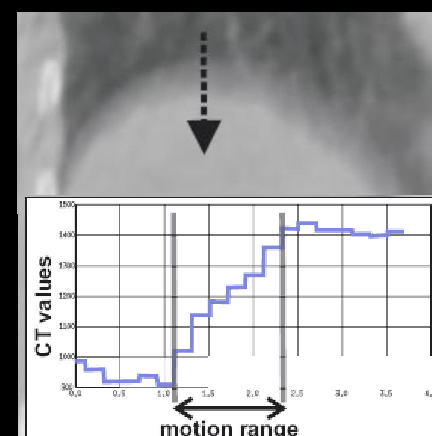
AVG CT





Free Breathing CBCT

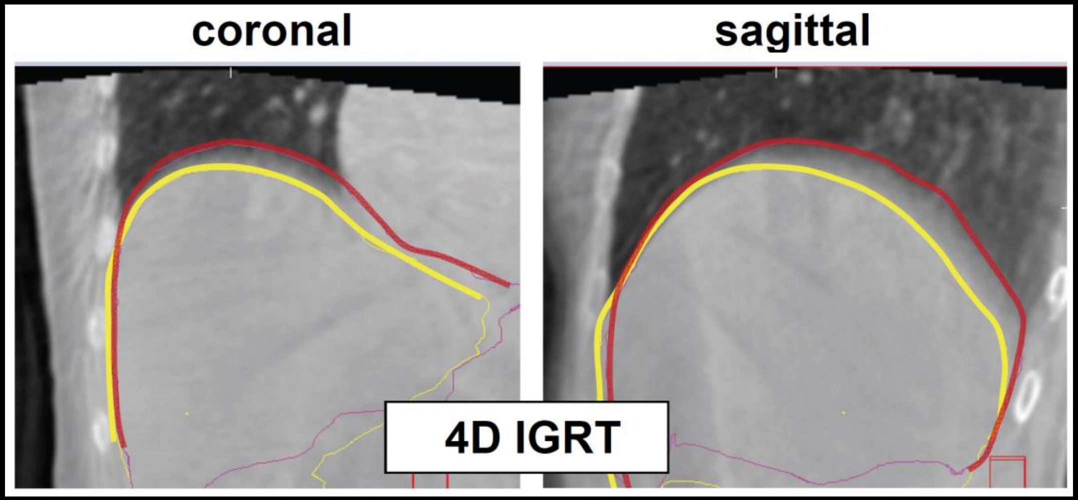
Motion amplitude



Guckenberger et al, IJROBP, 2008

Strategies to consider breathing motion Wuerzburg

Contour matching for IGRT of liver tumors



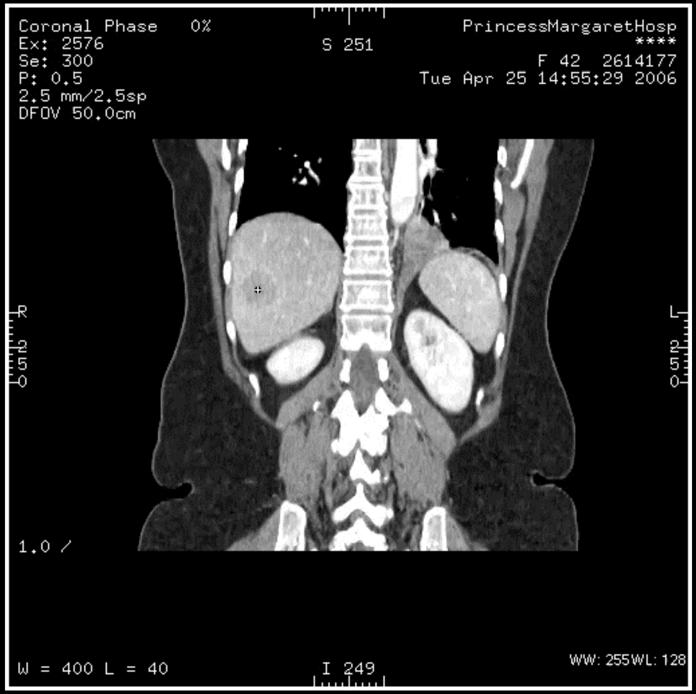
Challenges:

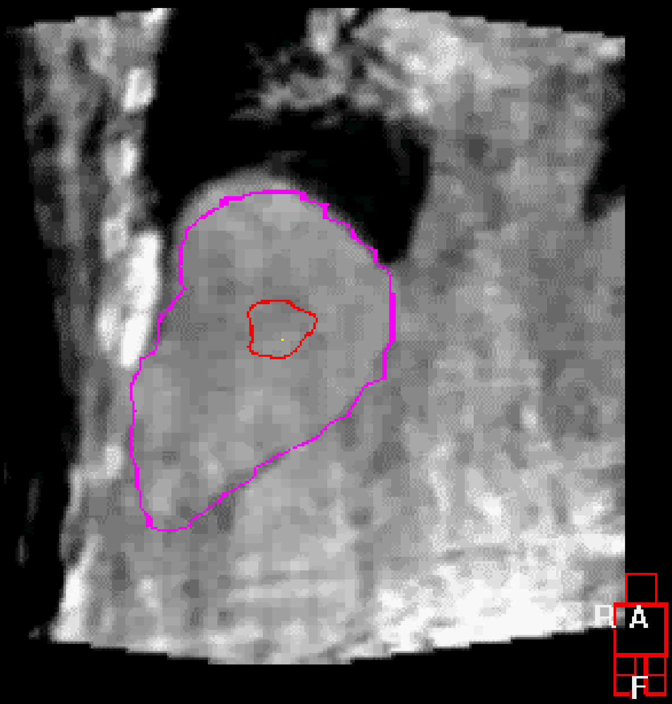
– Inhale an exhale ‘contours’ on free breathing CBCT not always clear

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

Guckenberger et al, IJROBP, 2008

Free Breathing IGRT: 4D CBCT





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

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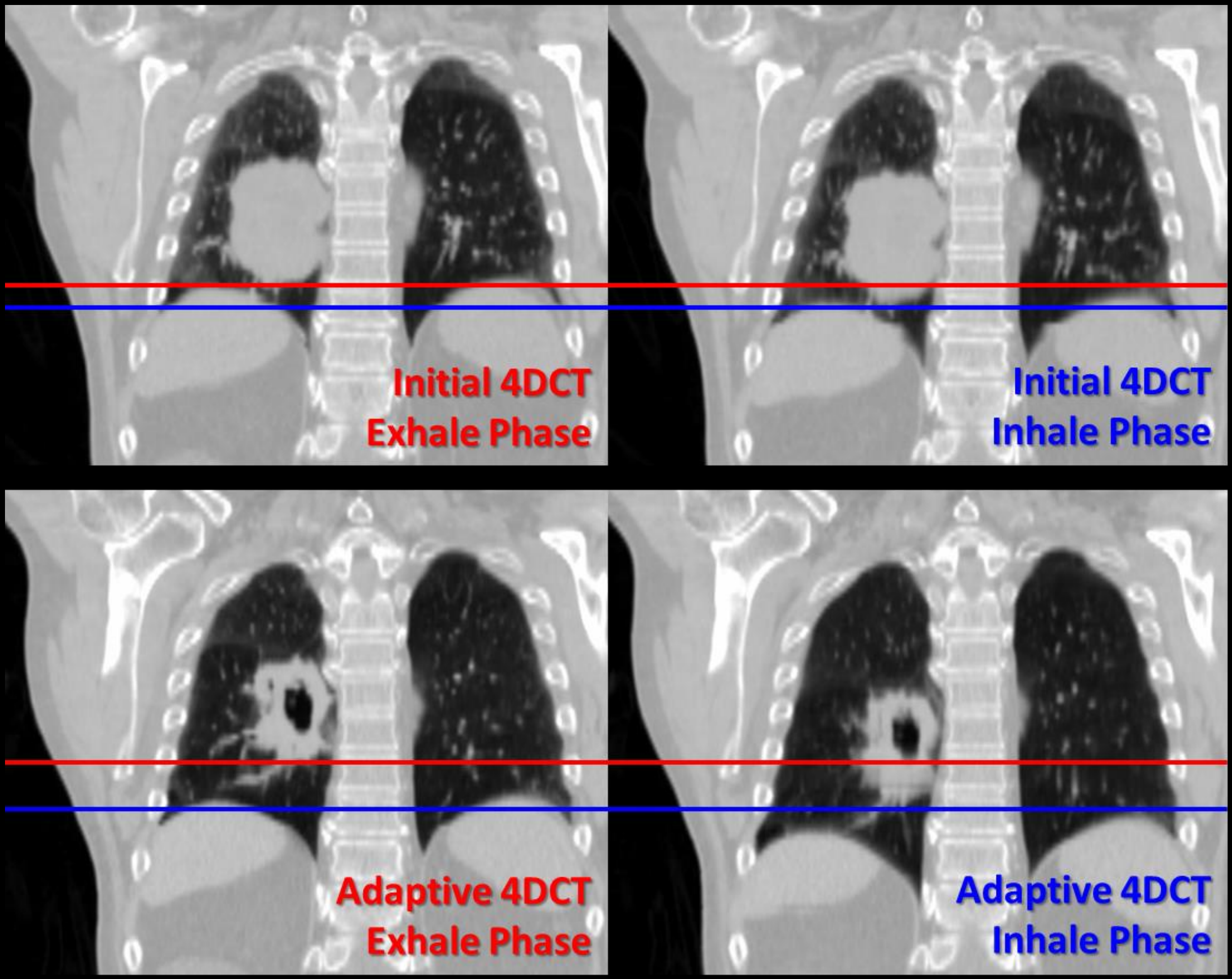
Importance of Monitoring Motion



Notable change in tumor excursion

*Courtesy of Martha Matuszak, U of Michigan

Int. J. Radiation Oncology Biol. Phys., Vol. 80, No. 3, pp. 938–946, 2011

0360-3016/$ - see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2010.08.003

PHYSICS CONTRIBUTION

INTERFRACTION LIVER SHAPE VARIABILITY AND IMPACT ON GTV POSITION DURING LIVER STEREOTACTIC RADIOTHERAPY USING ABDOMINAL COMPRESSION

CYNTHIA L. ECCLES, B.SC., LAURA A. DAWSON, M.D., JOANNE L. MOSELEY, PH.D.,
AND KRISTY K. BROCK, PH.D.

83 CBCT scans from 16 patients with 30 GTVs

Table 3. Magnitude and direction of interfraction liver shape (95th percentile) changes for all patients and resultant GTV COM displacements after rigid liver-to-liver registration described as absolute and non-absolute minimum, maximum, median, mean, and standard deviation of means in left–right (LR), anterior–posterior (AP), superior–inferior (SI), and vector directions

	LR (mm)	AP (mm)	SI (mm)	Vector (mm)	Absolute LR (mm)	Absolute AP (mm)	Absolute SI (mm)
Liver							
Mean	1.9	2.2	1.5	4.6	2.8	3.6	2.7
SD	1.9	1.5	1.1	3.1	2.2	3.6	2.7
Maximum	8.6	5.0	4.8	15.6	10.5	12.9	5.6
Minimum	0.5	−1.6	0.5	1.7	1.2	2.1	1.0
Median	1.4	2.2	1.1	4.1	2.5	2.9	2.5
Tumor							
Mean	−0.3	−0.4	−0.5	0.00	0.9	1.3	0.8
SD	0.6	2.1	0.8	0.00	1.3	1.8	0.7
Maximum	8.6	5.4	6.7	0.5	14.6	16.9	6.7
Minimum	−14.6	−16.9	−3.5	0.00	0.00	0.1	0.00
Median	−0.3	0.5	−0.6	0.00	0.6	1.0	0.8

Abbreviations: GTV = gross tumor volume; COM = center of mass; LR = left–right; AP = anterior–posterior; SI = superior–inferior.

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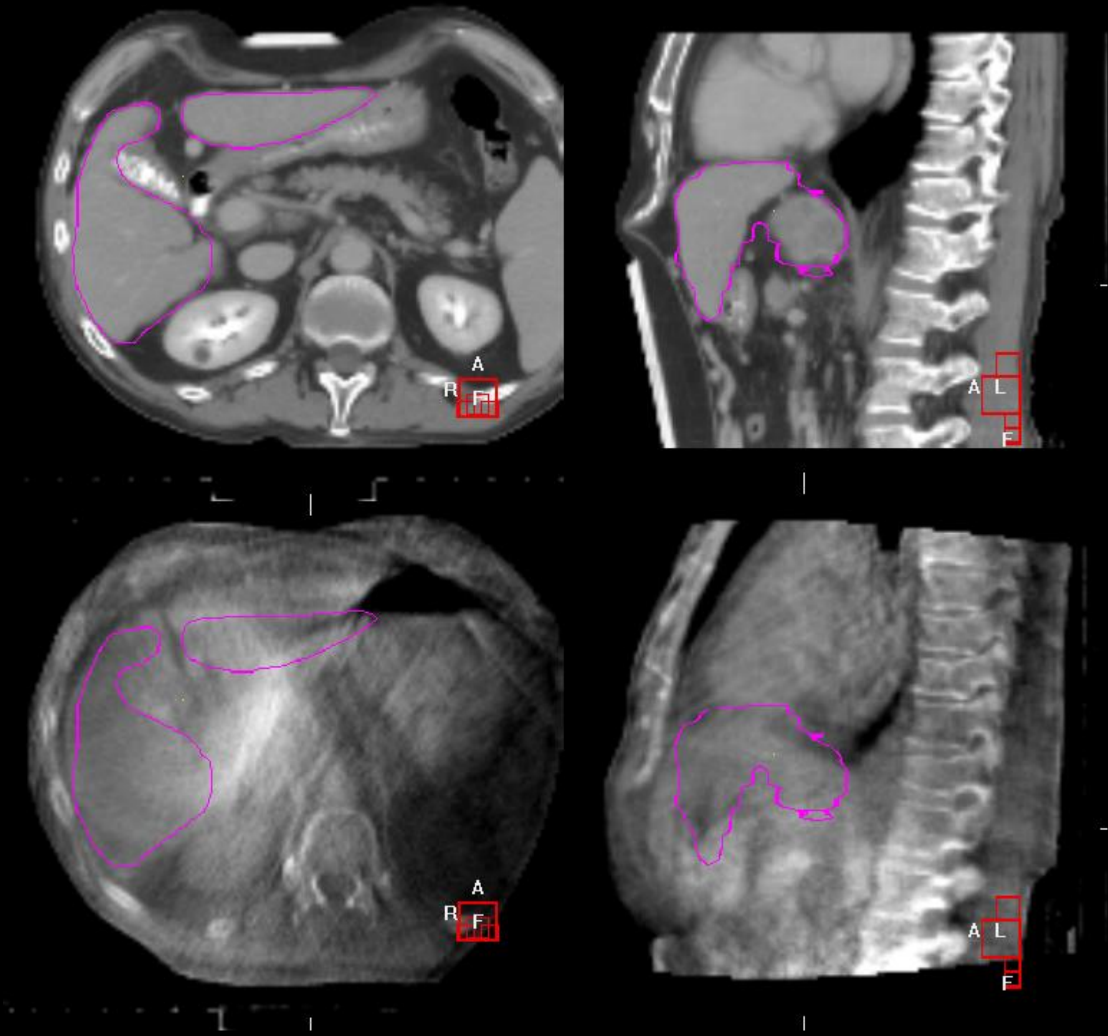
Poor placement of abdominal compression plate noted on CBCT

Planning CT

CBCT



Liver contour from planning CT

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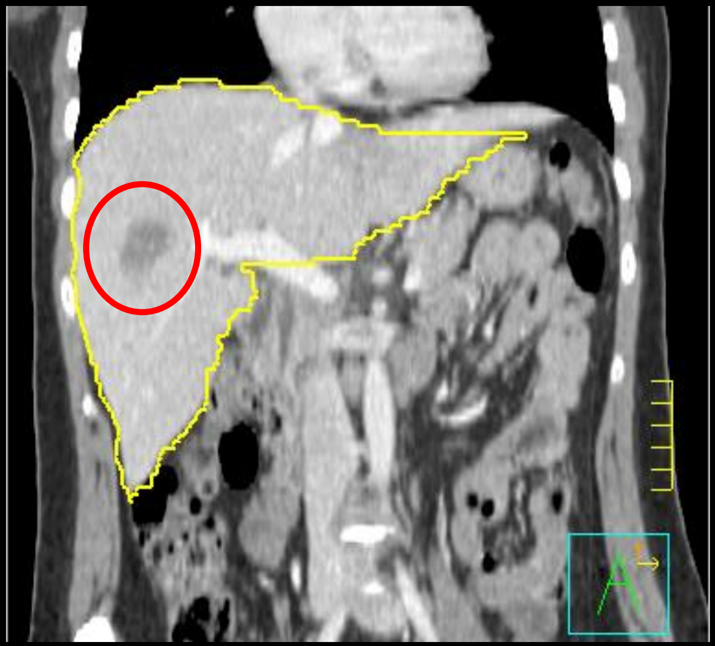
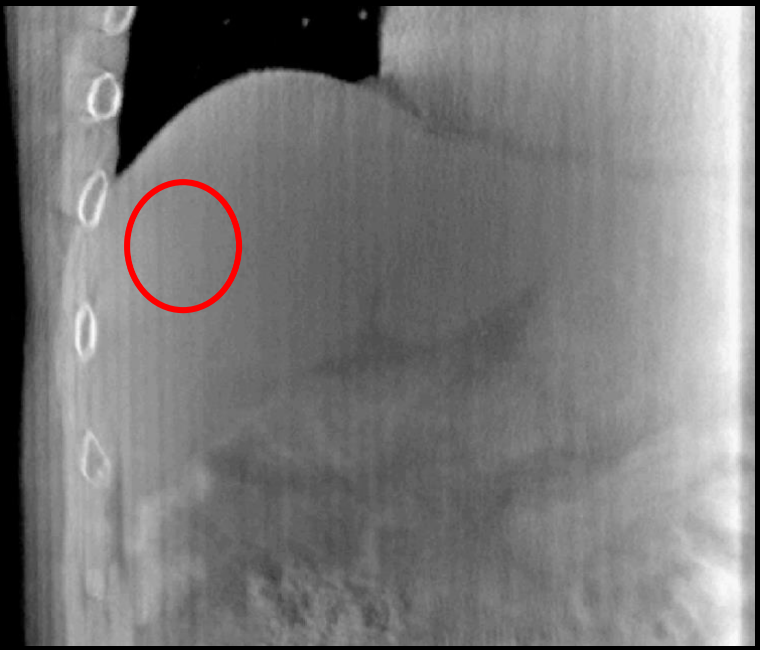
Breath Hold IGRT





- Acquire CBCT at (repeat) breath holds
- 3D alignment to reference phase
- Auto-Registration:
  - Align to GTV+margin when margin crosses an intensity gradient

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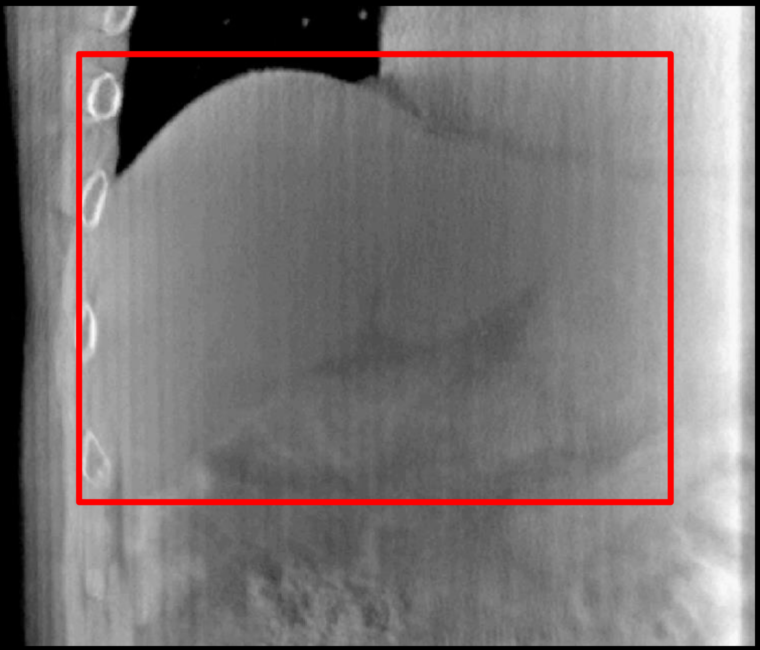
Breath Hold IGRT



- Acquire CBCT at (repeat) breath holds
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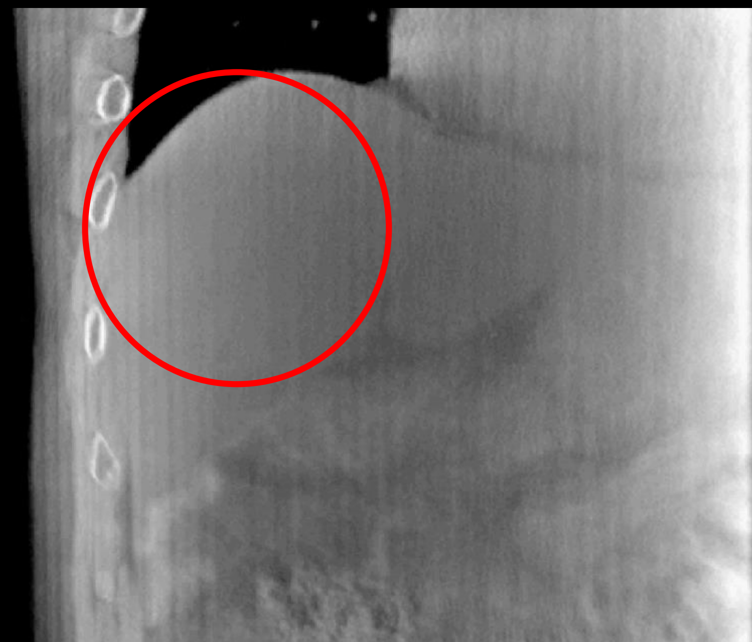
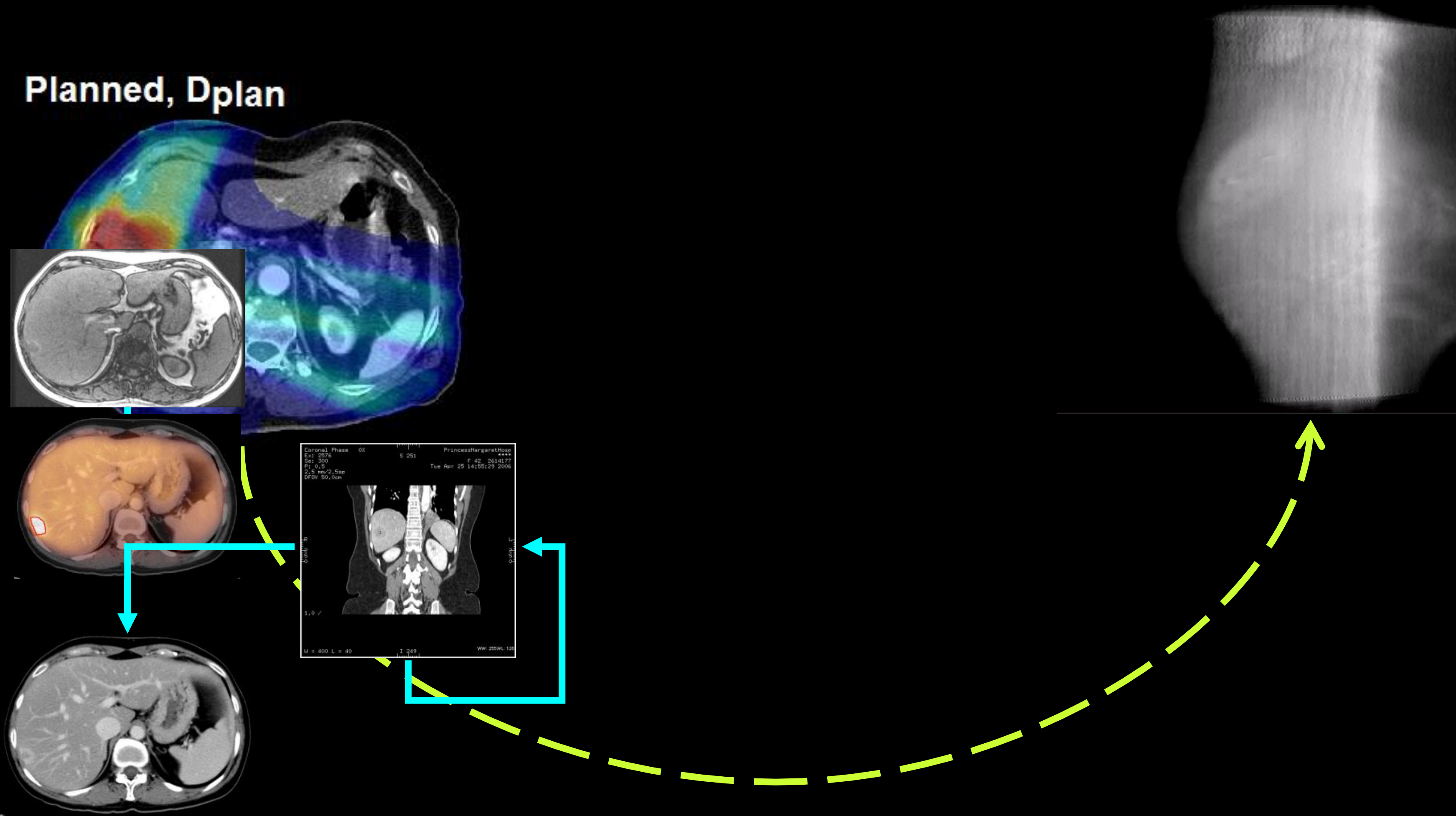
- Auto-Registration:
  - Align to GTV+margin when margin crosses an intensity gradient

Breath Hold IGRT

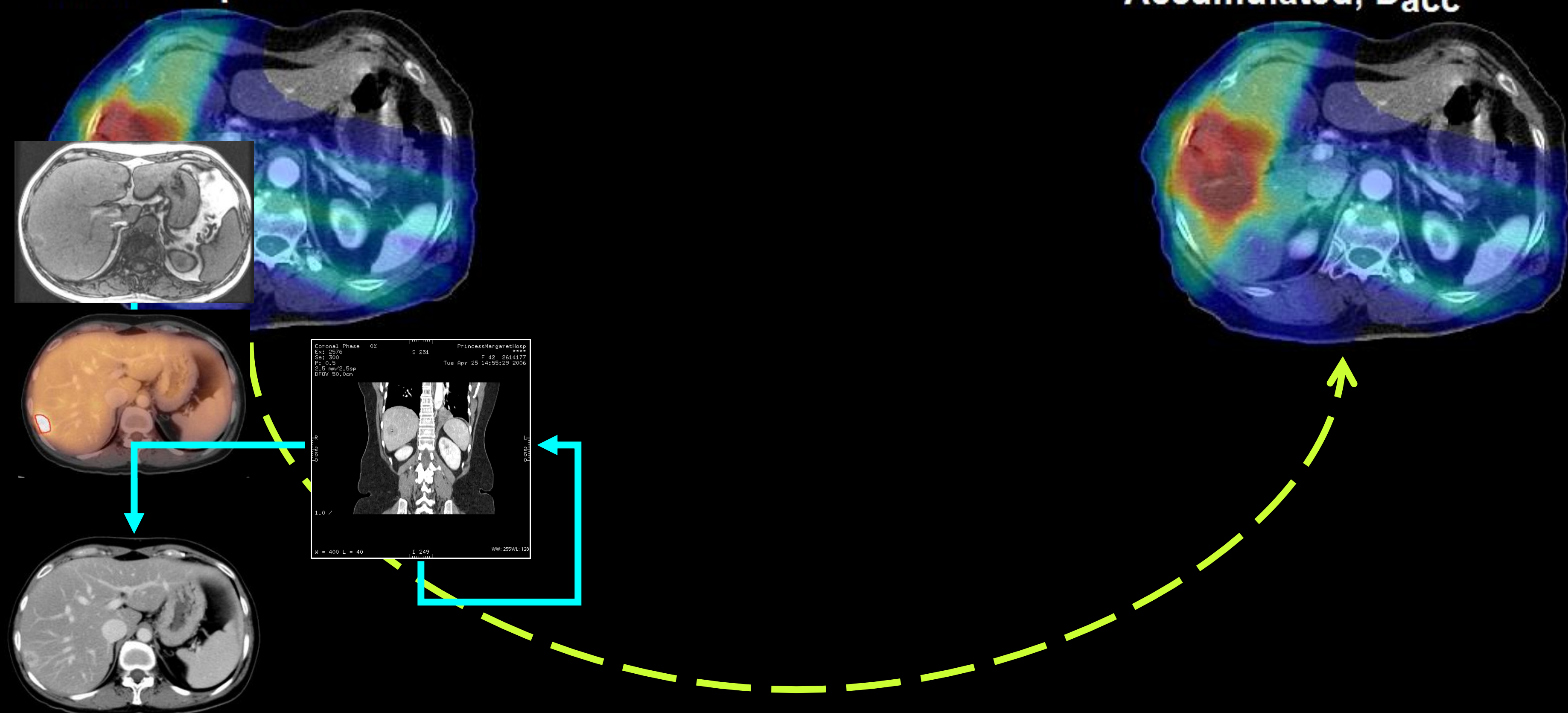


- Acquire CBCT at (repeat) breath holds
- 3D alignment to reference phase
- Auto-Registration:
  - Align to GTV+margin when margin crosses an intensity gradient


Planned, Dplan

Planned, D_{plan}

Accumulated, D_{acc}



Dose Accumulation and Adaptation

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S135–S139, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.06.093

QUANTEC: VISION PAPER

ACCURATE ACCUMULATION OF DOSE FOR IMPROVED UNDERSTANDING OF RADIATION EFFECTS IN NORMAL TISSUE

DAVID A. JAFFRAY, PH.D.,* PATRICIA E. LINDSAY, PH.D.,* KRISTY K. BROCK, PH.D.,*
JOSEPH O. DEASY, PH.D.,† AND W. A. TOMÉ, PH.D.‡

"Current efforts to maximize the therapeutic ratio require models that relate the true accumulated dose to clinical outcome. The needed accuracy can only be achieved through the development of robust methods that track the accumulation of dose within the various tissues in the body."

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Geometric Uncertainties in DIR

Impact of Dose

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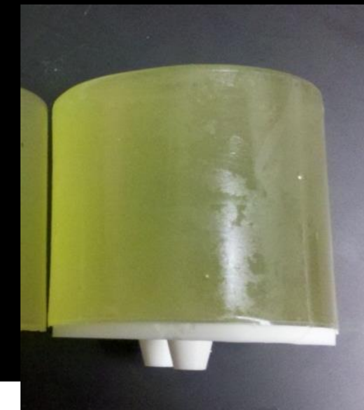
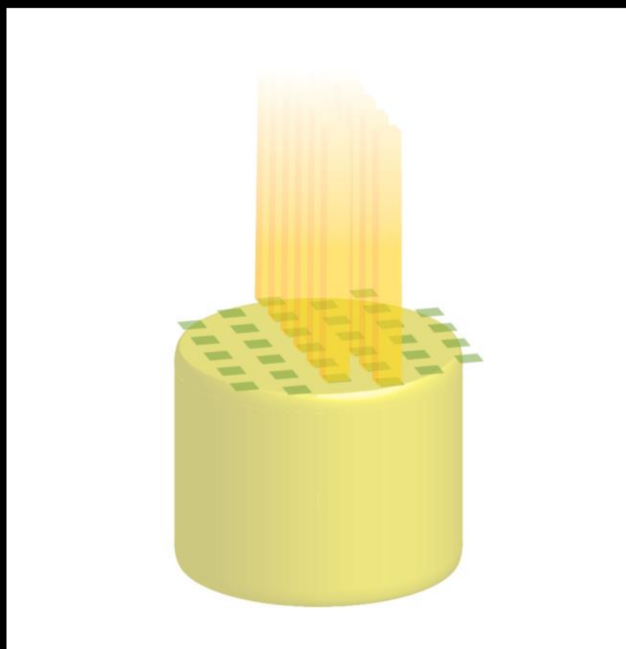
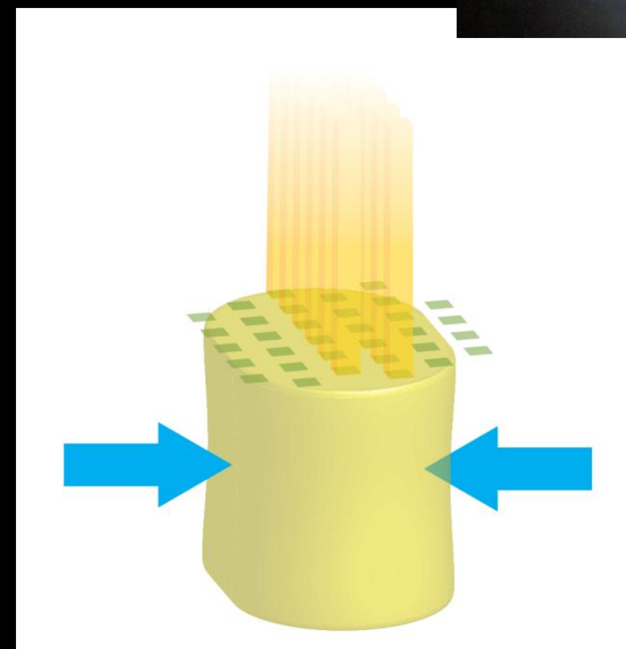
New method to validate Deformable Image Registration



Deformable 3D Presage dosimeters



Control
(No Deformation)



Deformed
(27% Lateral Compression)

DUKE UNIVERSITY
MEDICAL PHYSICS
GRADUATE PROGRAM

Slides Courtesy of Mark Oldham and Shiva Das

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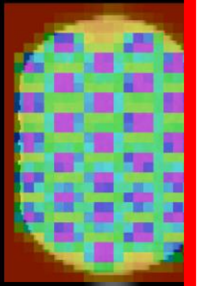
Dosimetric Accuracy of DIR for Liver

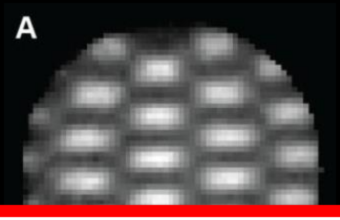
$\gamma_{3\%/3mm}$

CT of optical 3D dosimeter



Dose

Optical CT (Gold Standard)

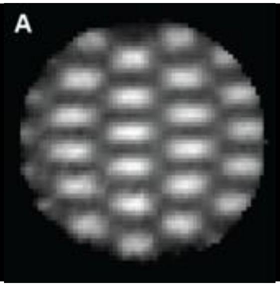


96%

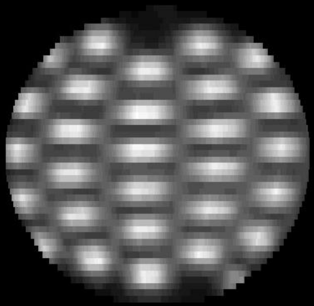
Caution must be used when accumulating dose, especially in regions of the image with homogeneous intensity.

%

Optical CT



Biomechanical DIR



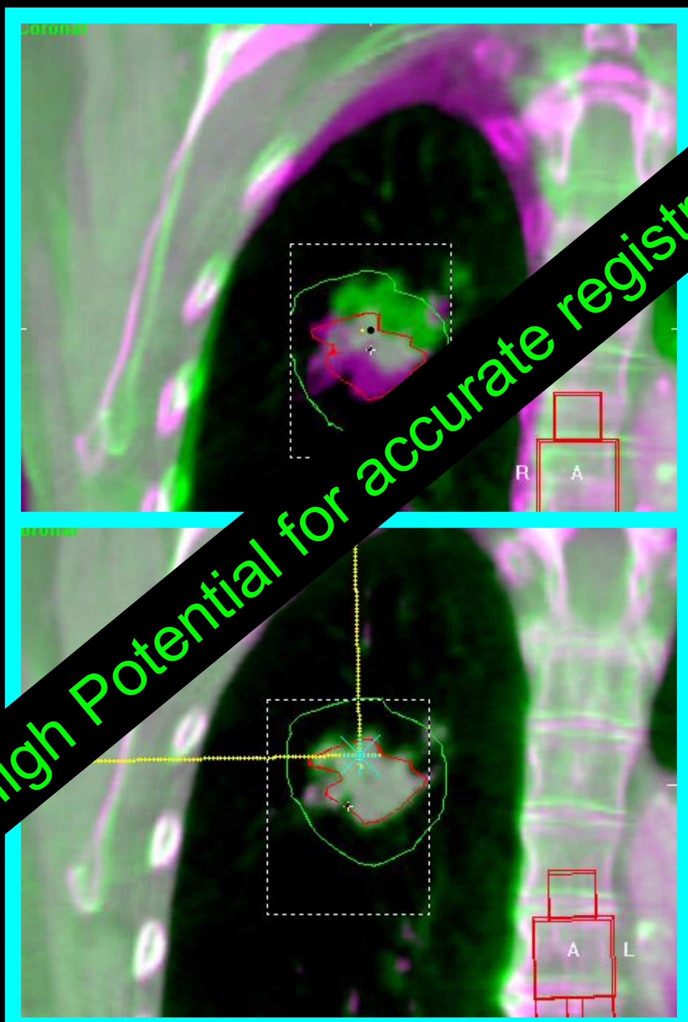
91%

*4D Dosimeter data courtesy of M Oldham

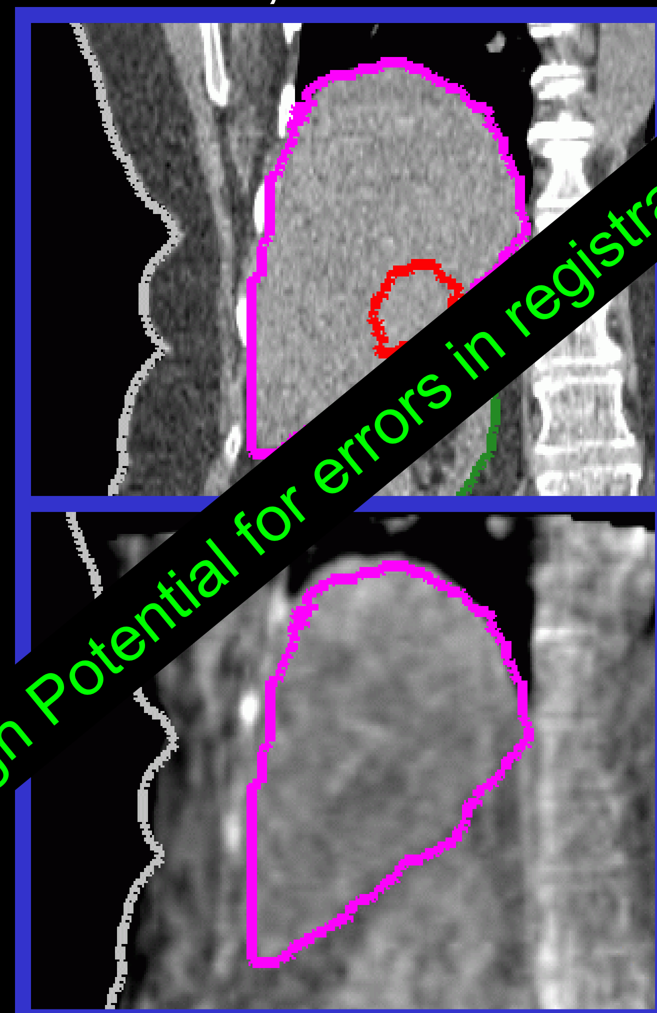
M Velec, T Juang, JL Moseley, M Oldham, KK Brock.. Pract Radiat Oncol 2015

Intensity Variation: Impact on CC/MSD

Clear intensity variation

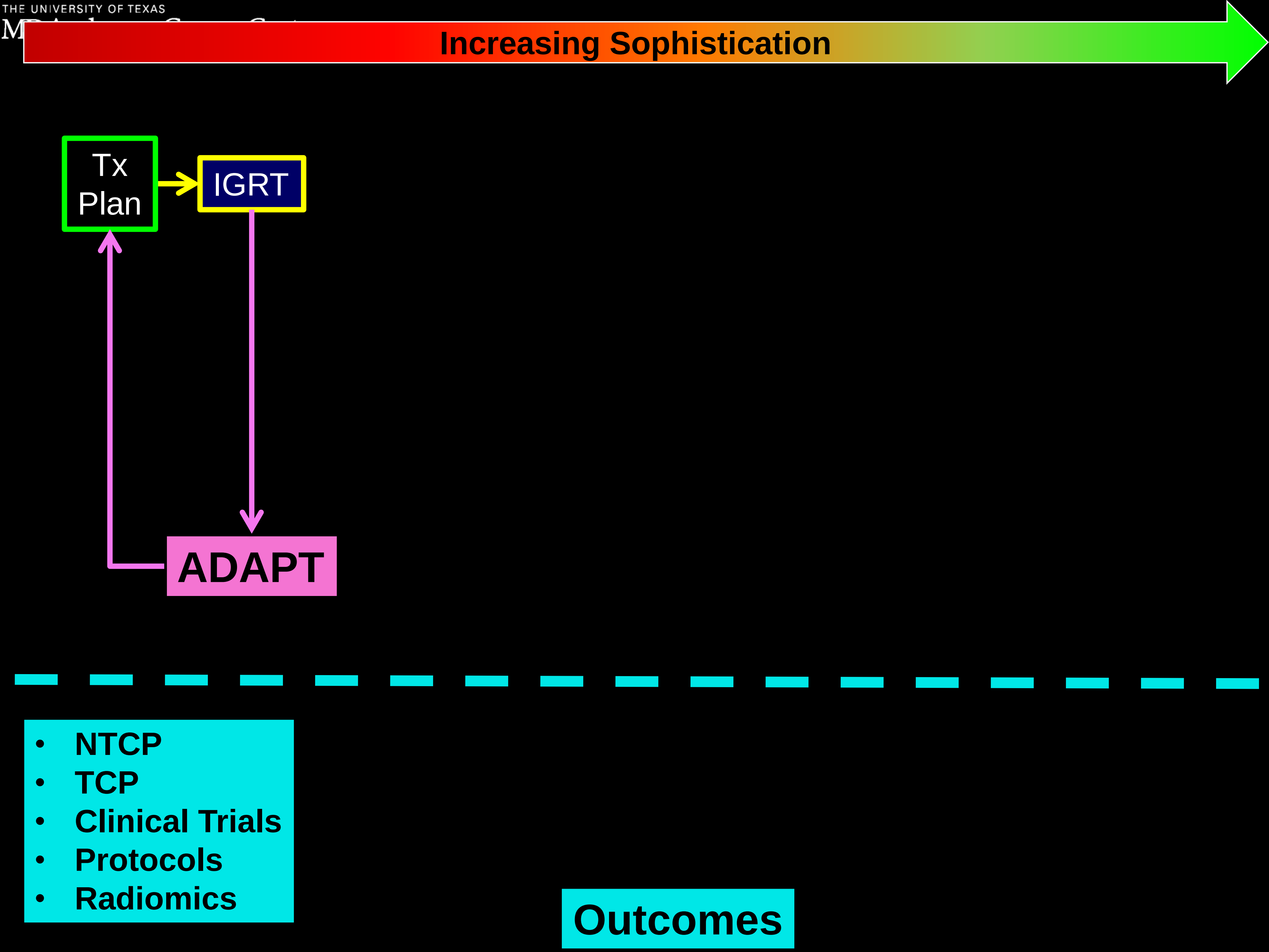


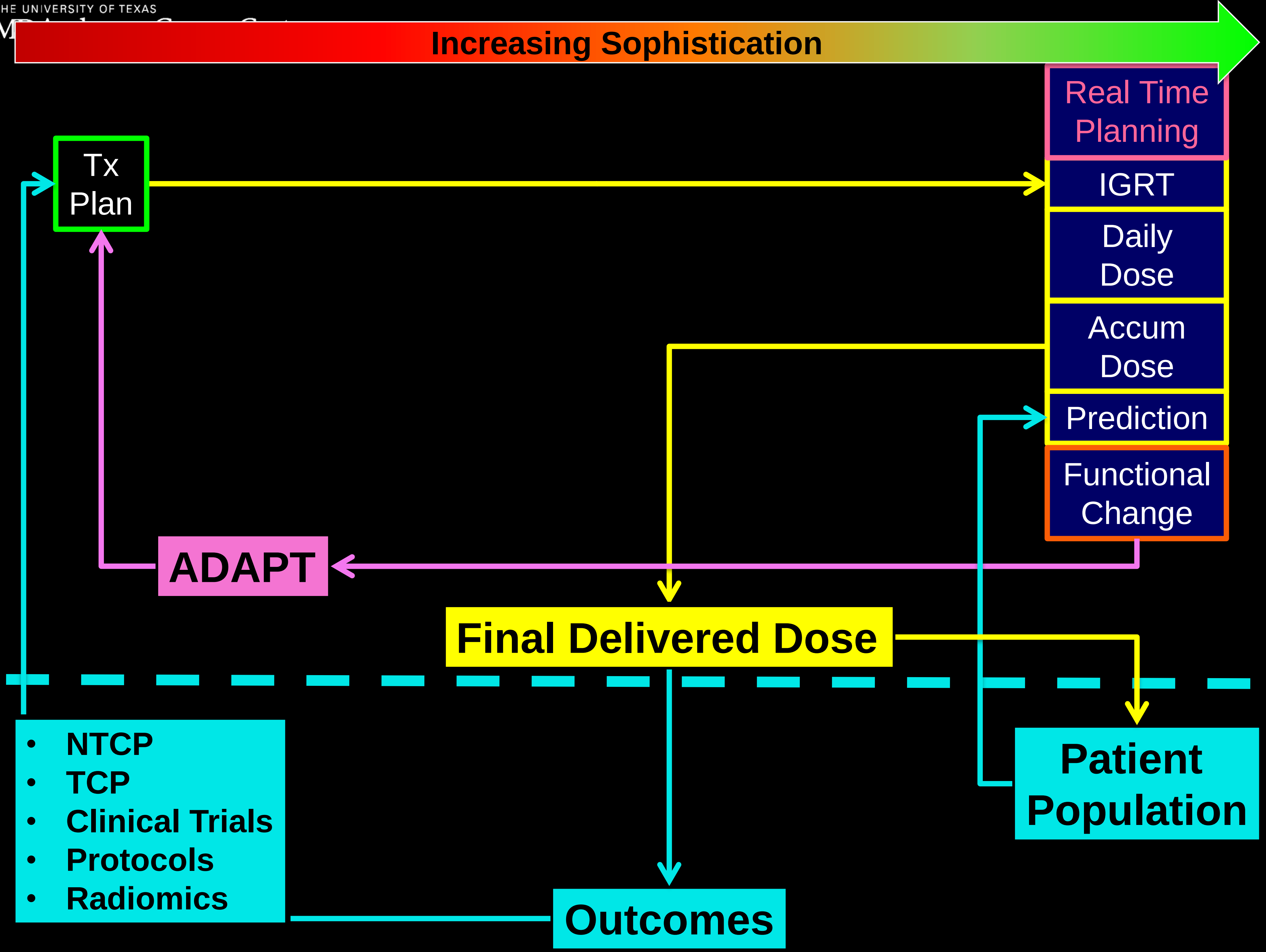
No relevant intensity variation, noise/artifact



Adaptive Radiotherapy Continuum

Increasing Sophistication


THE UNIVERSITY OF TEXAS
Increasing Sophistication
Tx
Plan
IGRT
ADAPT
• NTCP
• TCP
• Clinical Trials
• Protocols
• Radiomics
Outcomes


Increasing Sophistication
Tx Plan
Real Time Planning
IGRT
Daily Dose
Accum Dose
Prediction
Functional Change
ADAPT
Final Delivered Dose
Patient Population
NTCP
TCP
Clinical Trials
Protocols
Radiomics
Outcomes

Dosimetric Consequences of Precision

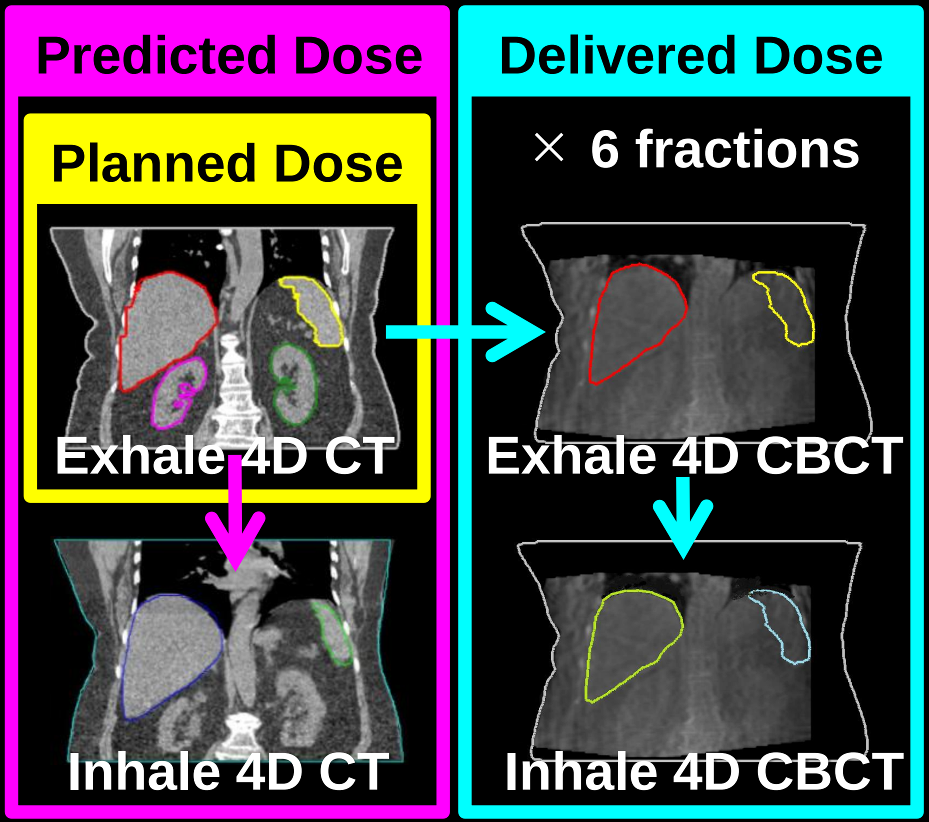
Is the Delivered Dose = Planned Dose?

- Purpose(s):
  - Calculate the delivered SBRT dose with DIR
  - Evaluate if the breathing dose from 4D CT predicts for the delivered dose better than static dose distributions

- Methods:
  - 30 previous SBRT patients with 54 GTVs
  - Planned on exhale 4D CT for 27–60 Gy in 6 fractions
  - Mean 4D CT amplitude: 9 mm
  - Treated free-breathing after rigid liver alignment on 3D CBCT (retrospective 4D-sorting)

Velec, et. al., IJROBP 2011

Delivered SBRT Doses



Planned Dose

- ✓ *Clinical standard*
- ✓ *Only solution for current treatment planning systems*

Predicted Dose

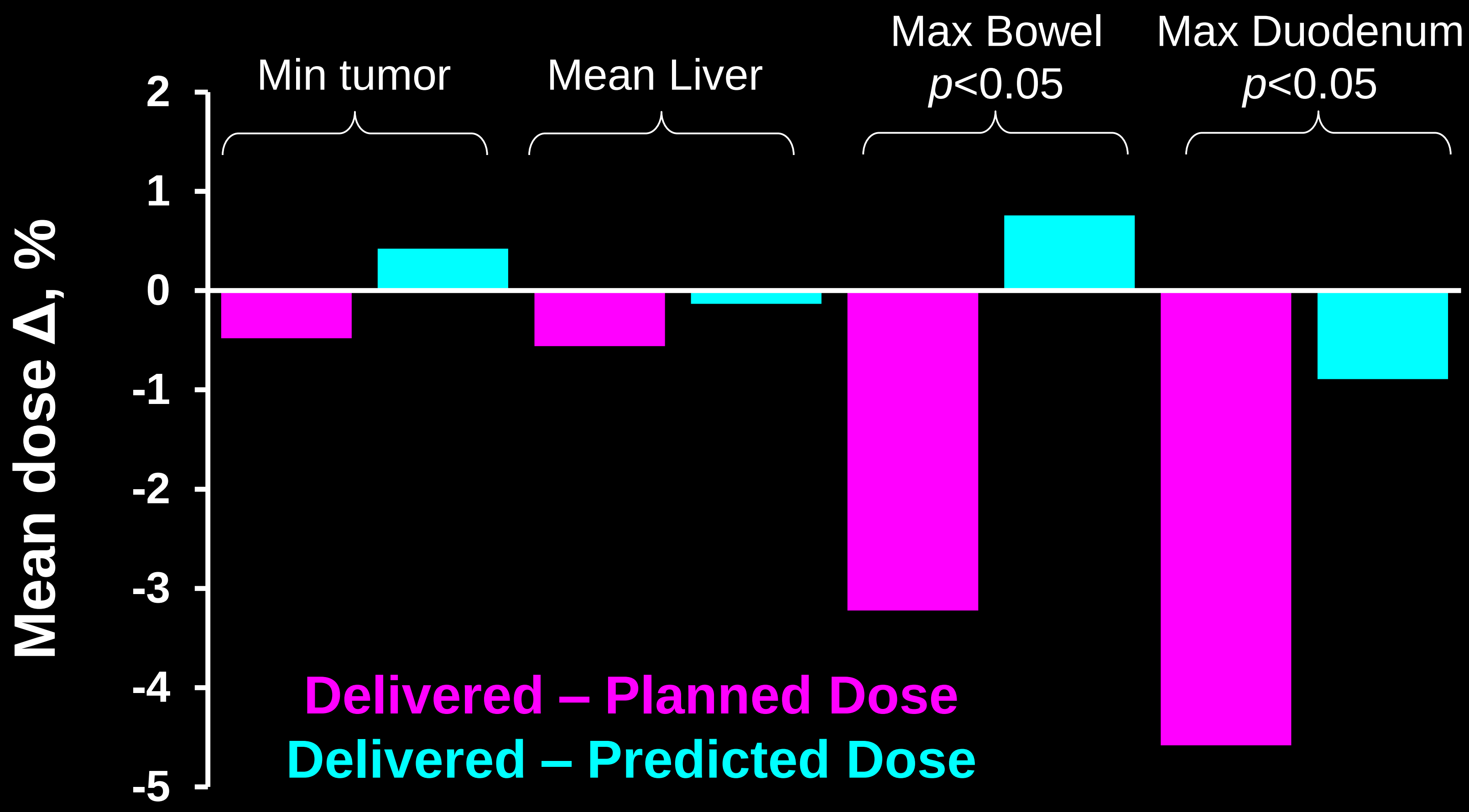
- ✓ *Incorporates effects of breathing motion*
- ✓ *'Better' dose estimate at planning*

Delivered Dose

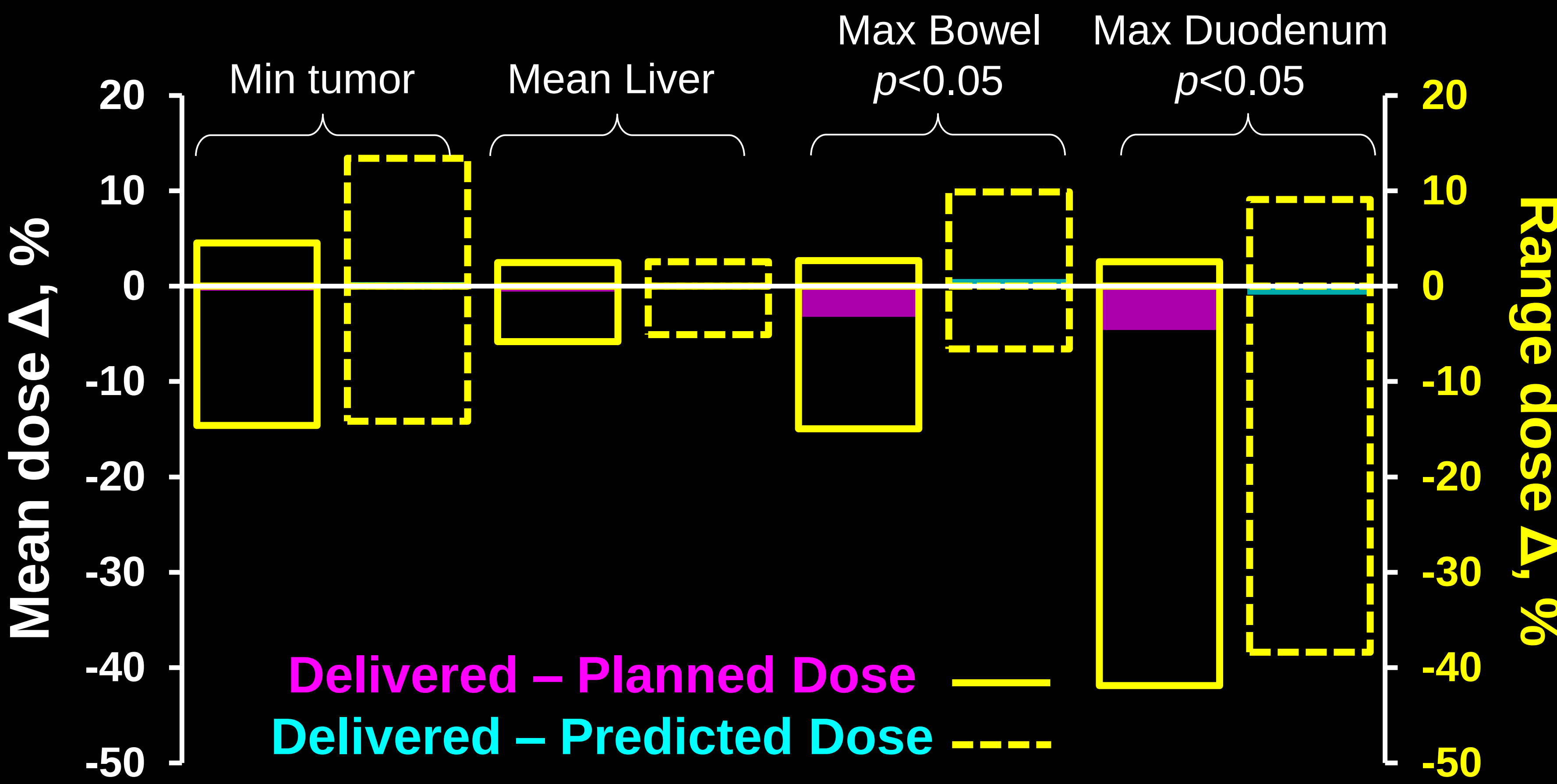
- ✓ *Incorporates most inter-fraction motion*
- ✓ *'Best' estimate of actual delivered dose*

Velec, Moseley, Craig, Dawson, Brock, IJROBP 83(4): 1132-40, 2012

Delivered SBRT Doses



Delivered SBRT Doses



Patients with a delivered dose deviation >5% to *any* tissue:

70% vs. Planned dose, 53% vs. Predicted dose

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Liver SBRT Dose Reconstruction

Clinical Relevance and Impact:

- Translates geometric uncertainties into dose deviations, potential to help interpret outcomes

Summary:

- With ITV+5 mm PTV margins, tumor doses generally not affected by the treatment uncertainties
- Normal tissues doses are often decreased from planned (effects of residual errors > deformation > breathing variations)
- Modeling breathing motion at planning better correlated with the delivered dose, but still doesn't account for all uncertainties

Velec M, et al 'Accumulated dose in liver stereotactic body radiotherapy: positioning, breathing, and deformation effects. IJROBP. 2012 Jul 15;83(4):1132-40

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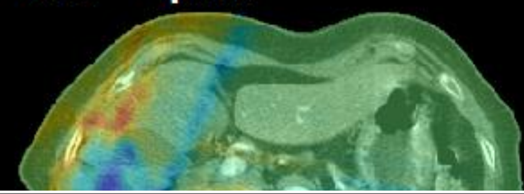
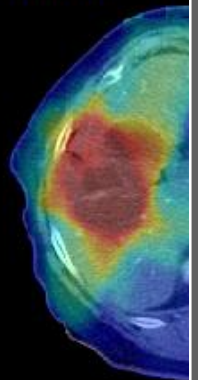
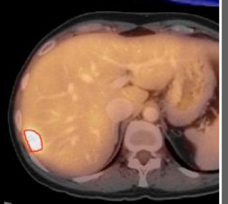
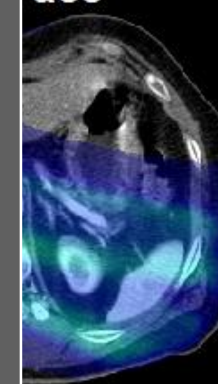


Anatomical variations lead to dosimetric discrepancies between planned and delivered dose resulting in:

1. Uncertainties in TCP calculations
2. Uncertainties in NTCP calculations
3. Uncertainties in the correlation of functional imaging with delivered therapy
4. Uncertainties in assessing the impact of novel drugs, therapy schedules, and techniques







Does Improved Accuracy in Dose Matter for Outcomes?

- 81 patients, 142 liver metastases
- accGTV calculated using DIR and daily CBCTs
- accGTV dose is a better predictor of TTLP compared to minPTV dose for liver metastases SBRT
- Univariate HR for TTLP for increases of 5 Gy in accGTV versus minPTV was 0.67 versus 0.74

Swaminath, Brock, Dawson, et al. IJROBP 2015

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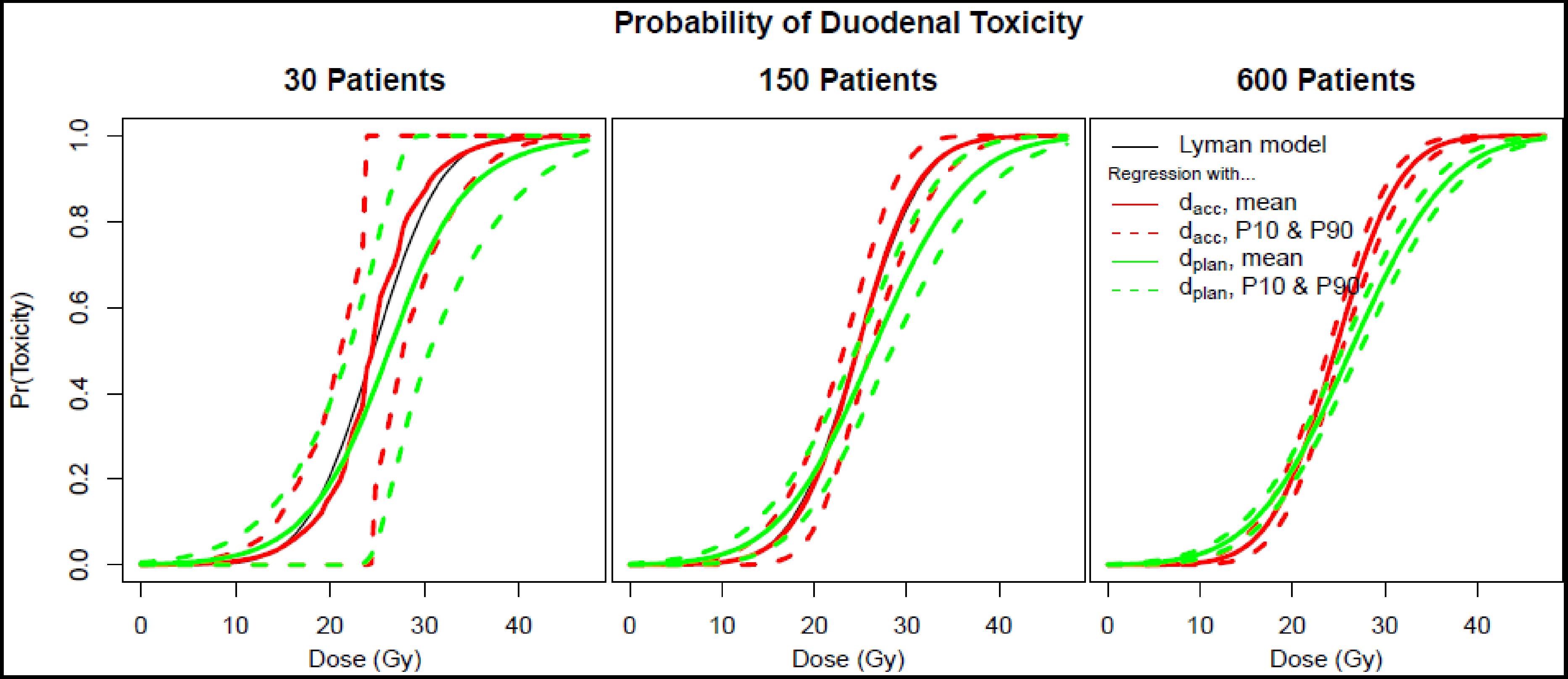
Dose Accumulated Dose Impact NTCP Models?



Molly M McCulloch, M.S., Daniel G. Meunz, M.S., Graduate Students

Summary

- Personalization of RT in the abdomen and thorax includes several aspects: imaging for planning, motion management, image guidance, and adaptation
- Careful integration of multi-modality imaging at planning is critical as it can create systematic errors
- Advanced motion managements can enable reduced dose to normal tissues
- Image guidance is critical to deliver the planned dose
- Improving the correlation between the planned and delivered dose will enable improved understanding of RT