Uncertainties in Deformable Image Registration

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VELUT ARBOR ÆVO

STTARR

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Princess Margaret Hospital

University Health Network

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Objectives

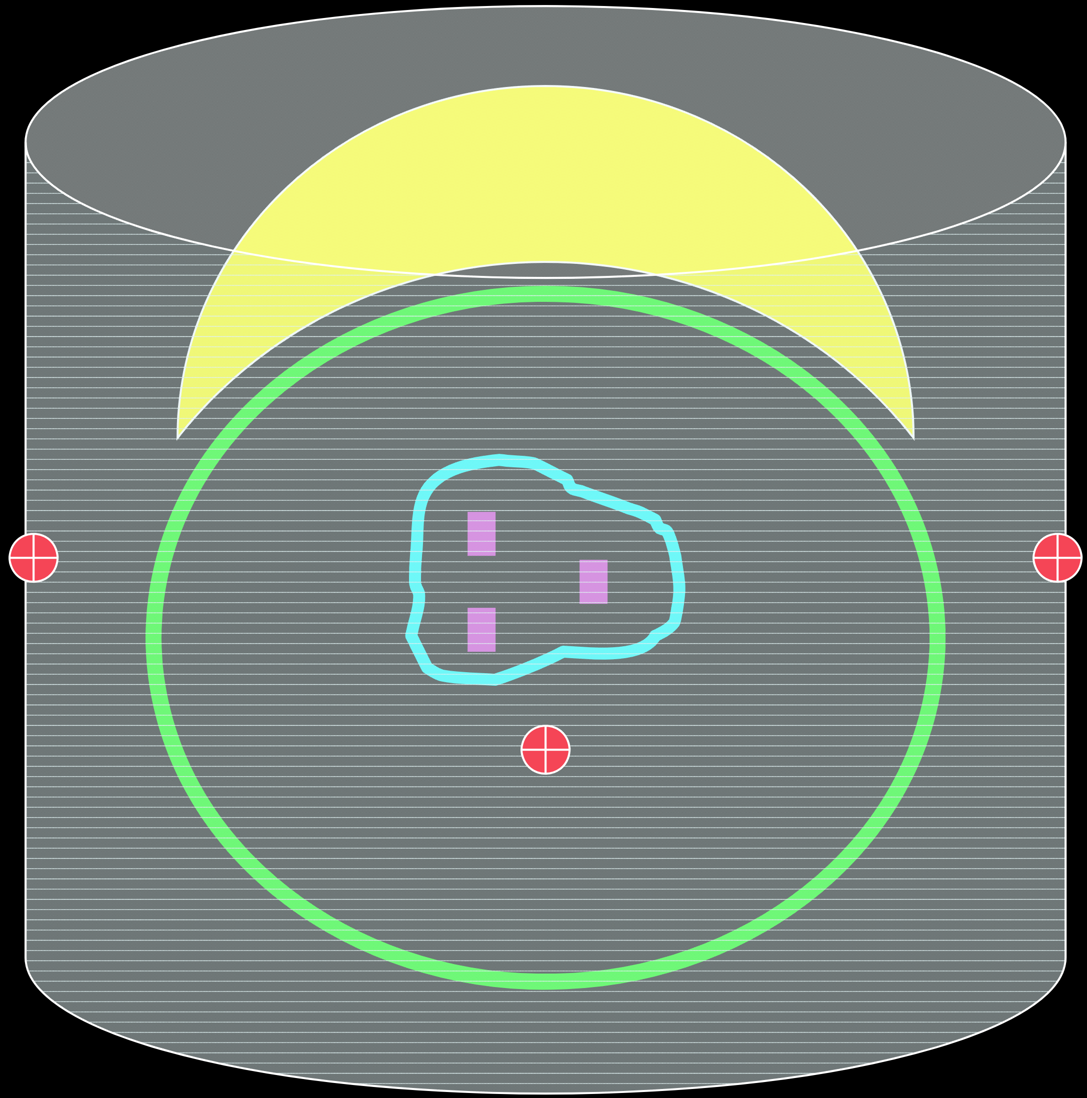
- Uncertainties in not using Deformable Registration
- Techniques for Deformable Registration
  - Similarity metrics (‘Are they the same yet?’)
  - Regularization (‘If it’s not rigid, how is it moving?’)
- Validation & QA
  - How certain are they and do they need to be?
- Uncertainties in Clinical Implementation

Role of Image Registration in RT

- Treatment Planning
  - Motion Assessment (e.g. 4D CT)
  - Multi-modality Images (e.g. MR-CT-PET)
  - Predictive Dose Accumulation (e.g. delivered dose)
- Treatment Delivery
  - Image guidance (e.g. CBCT-MVCT)
  - Motion Assessment (e.g. 4D CBCT)
  - Deformable Dose Accumulation
- Treatment Assessment/Response
  - Assessing tumor/normal tissue response (e.g. serial imaging)
  - Adaptive radiotherapy

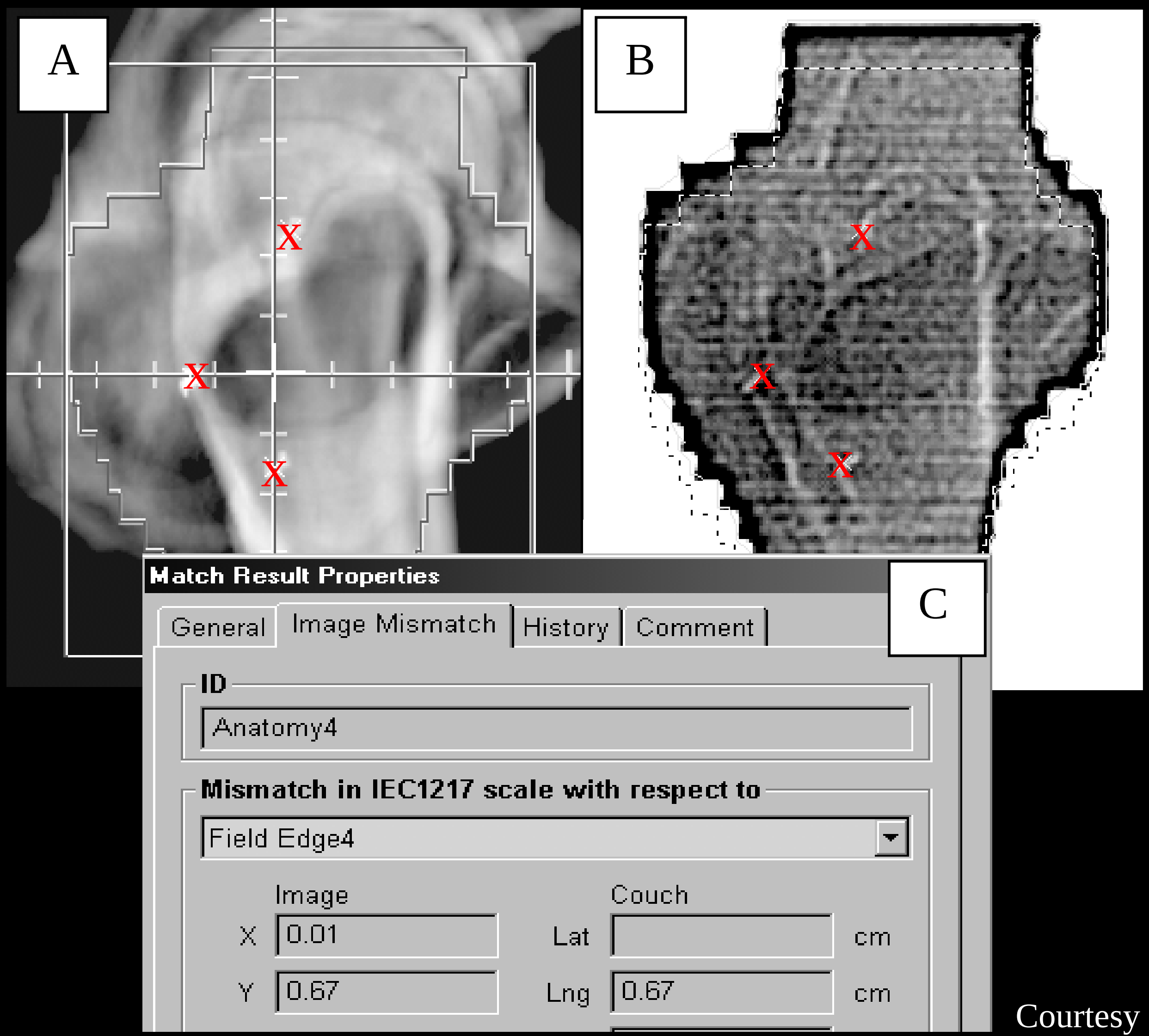
Quick Review: Uncertainties in <u>NOT</u> using Deformable Registration

Anatomical Surrogates



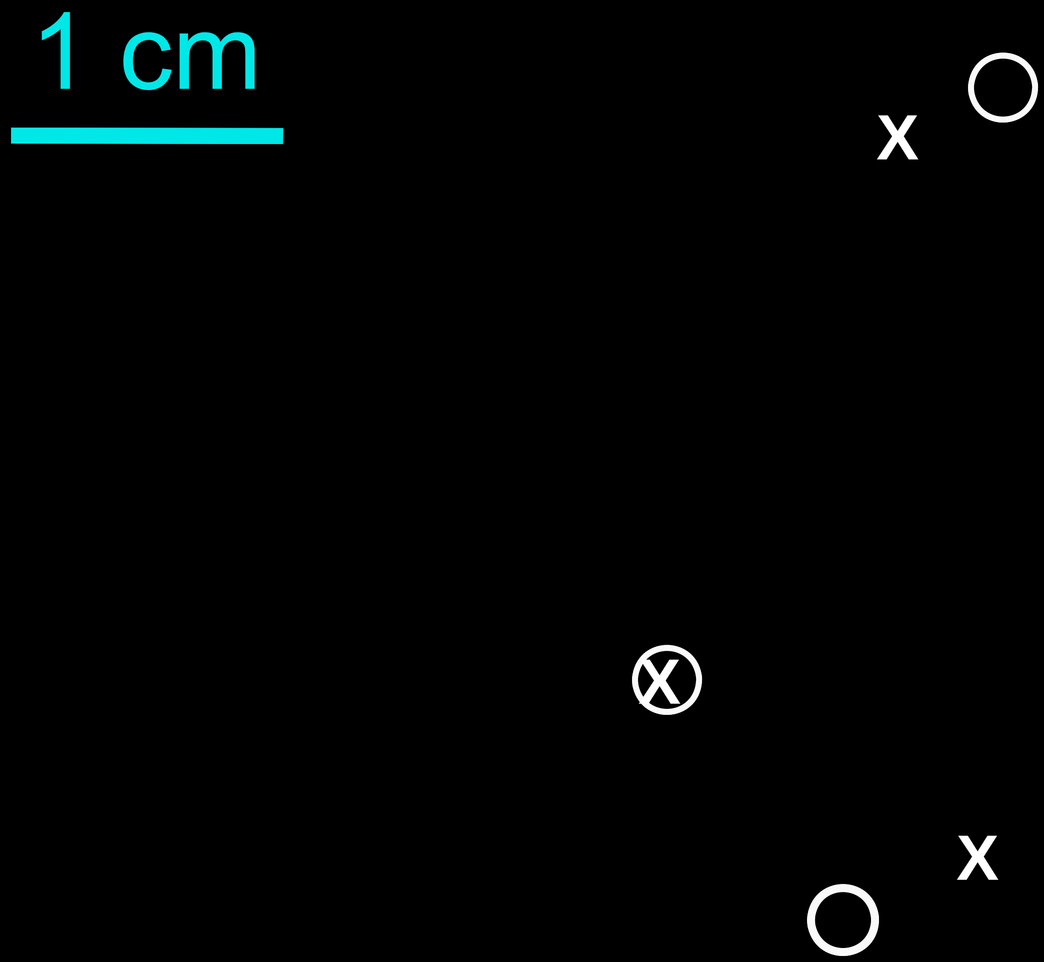
Tumor
Markers in Tumor
Tumor bearing Organ
Neighboring Organ
External Body
External Markers

Registration using Surrogates



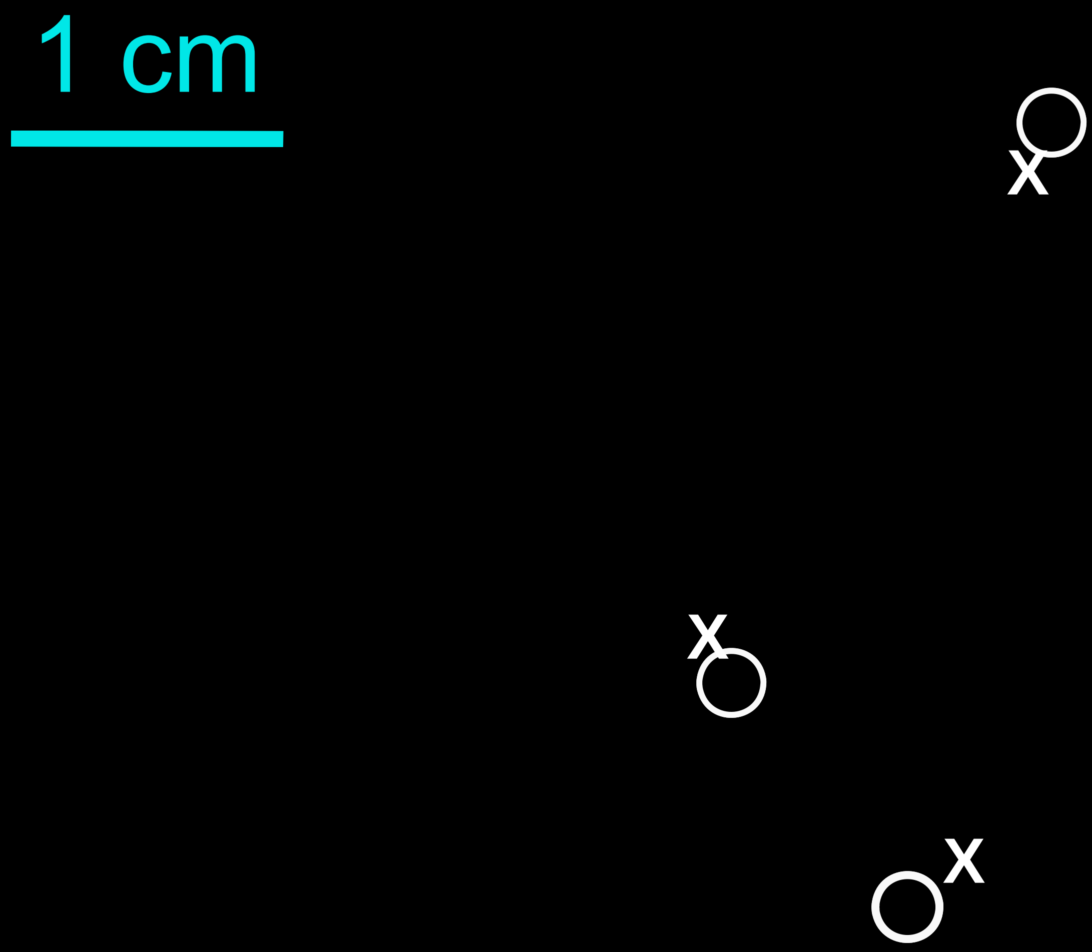
Courtesy of Peter Chung, M.D.

Rigid Registration (Translation)



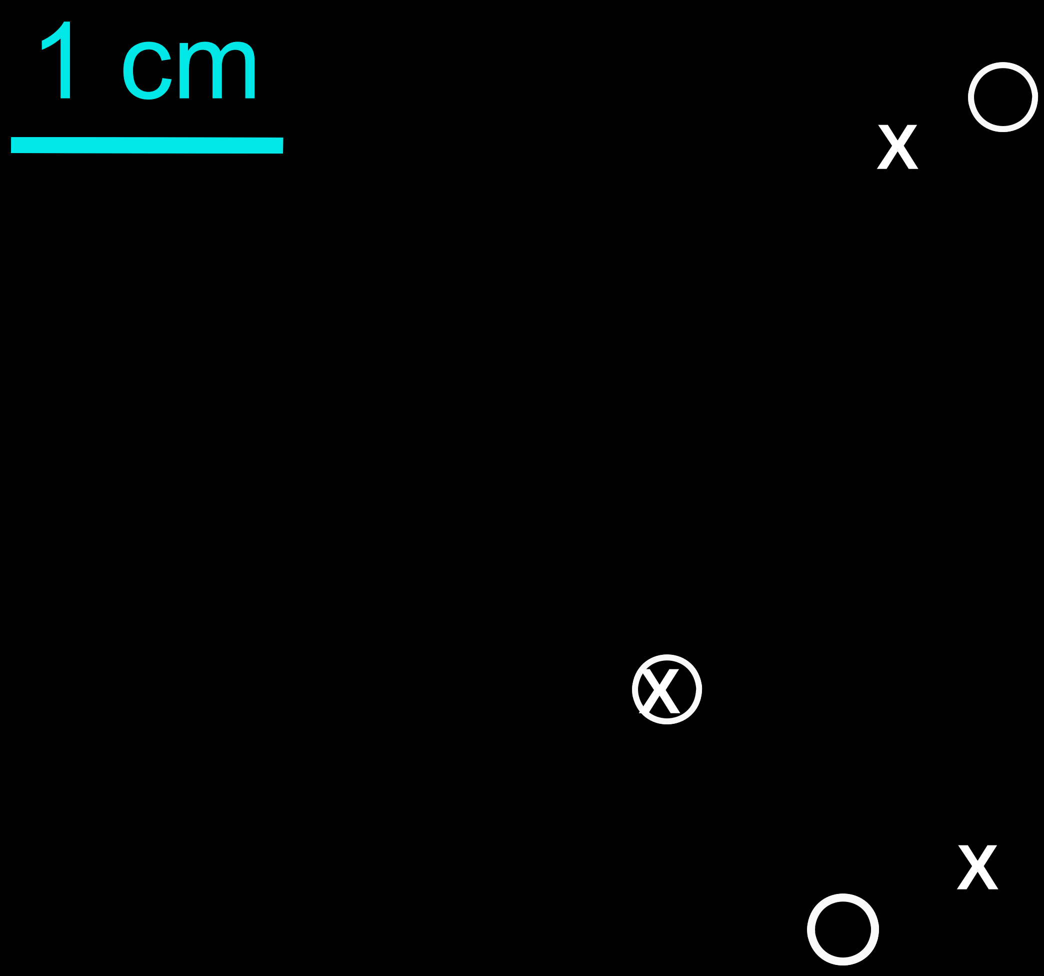
RMS = 1.5 mm

Rigid Registration (with Rotation)



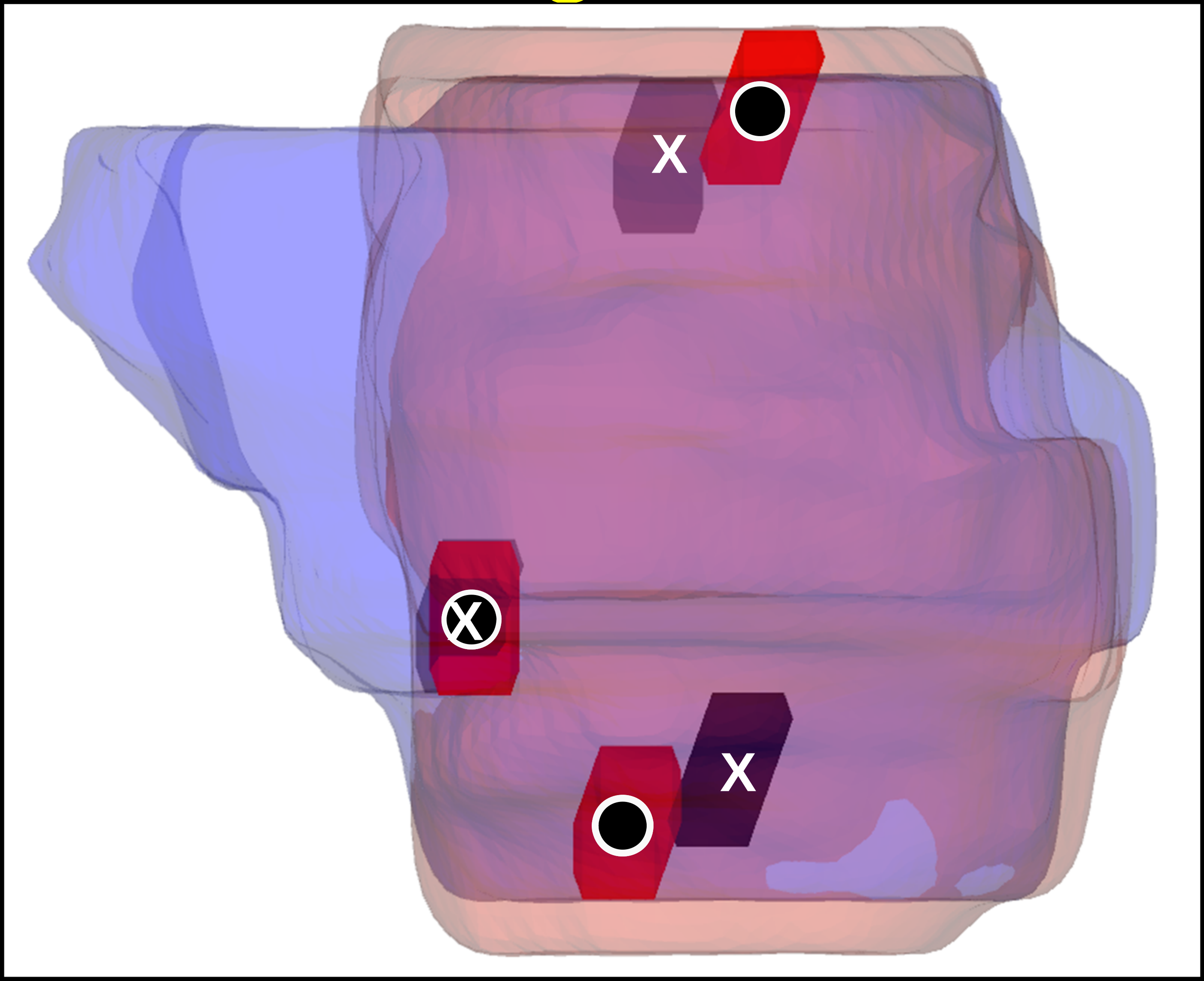
RMS = 0.3 mm

Rigid Registration (Translation)

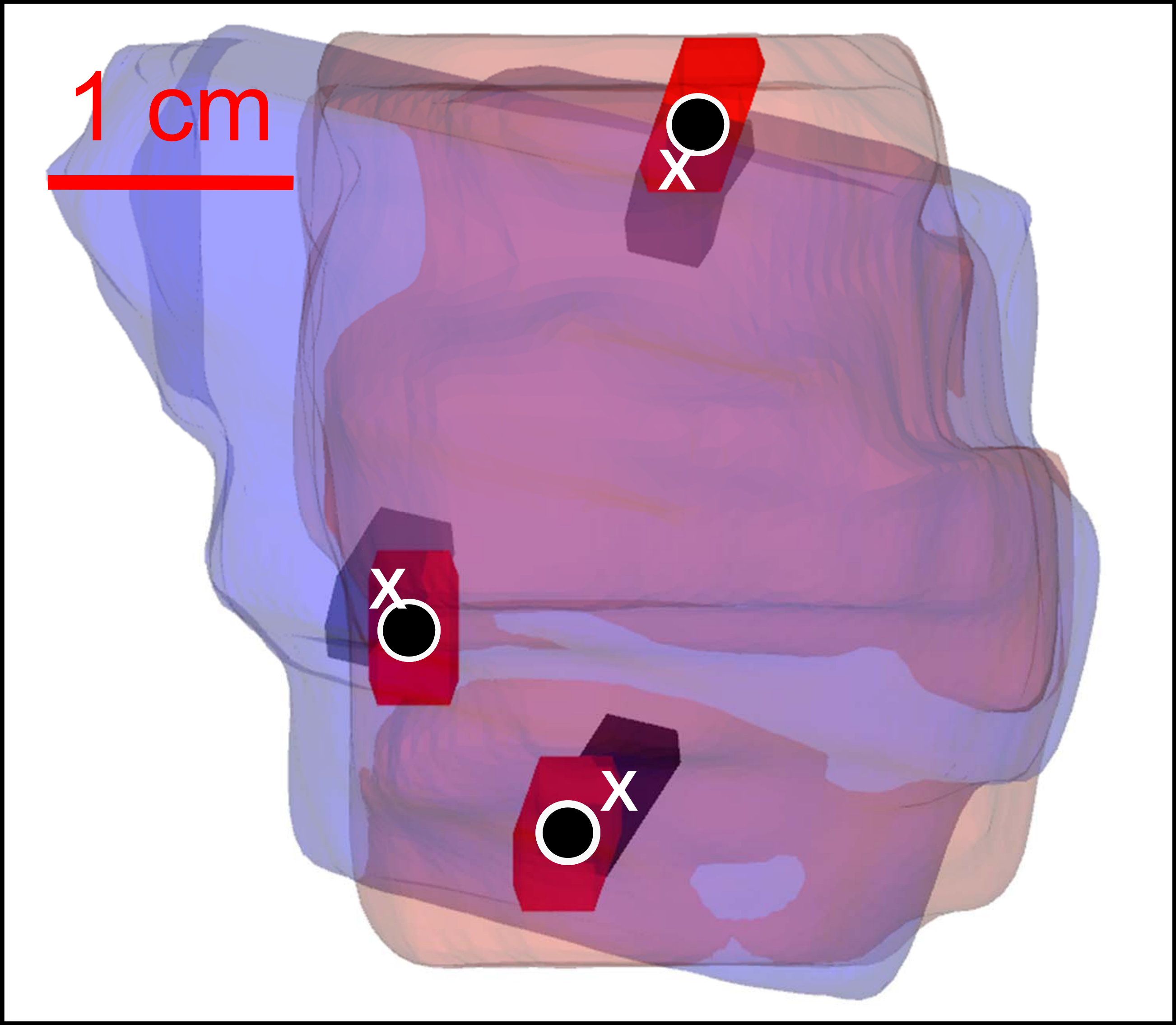


RMS = 1.5 mm

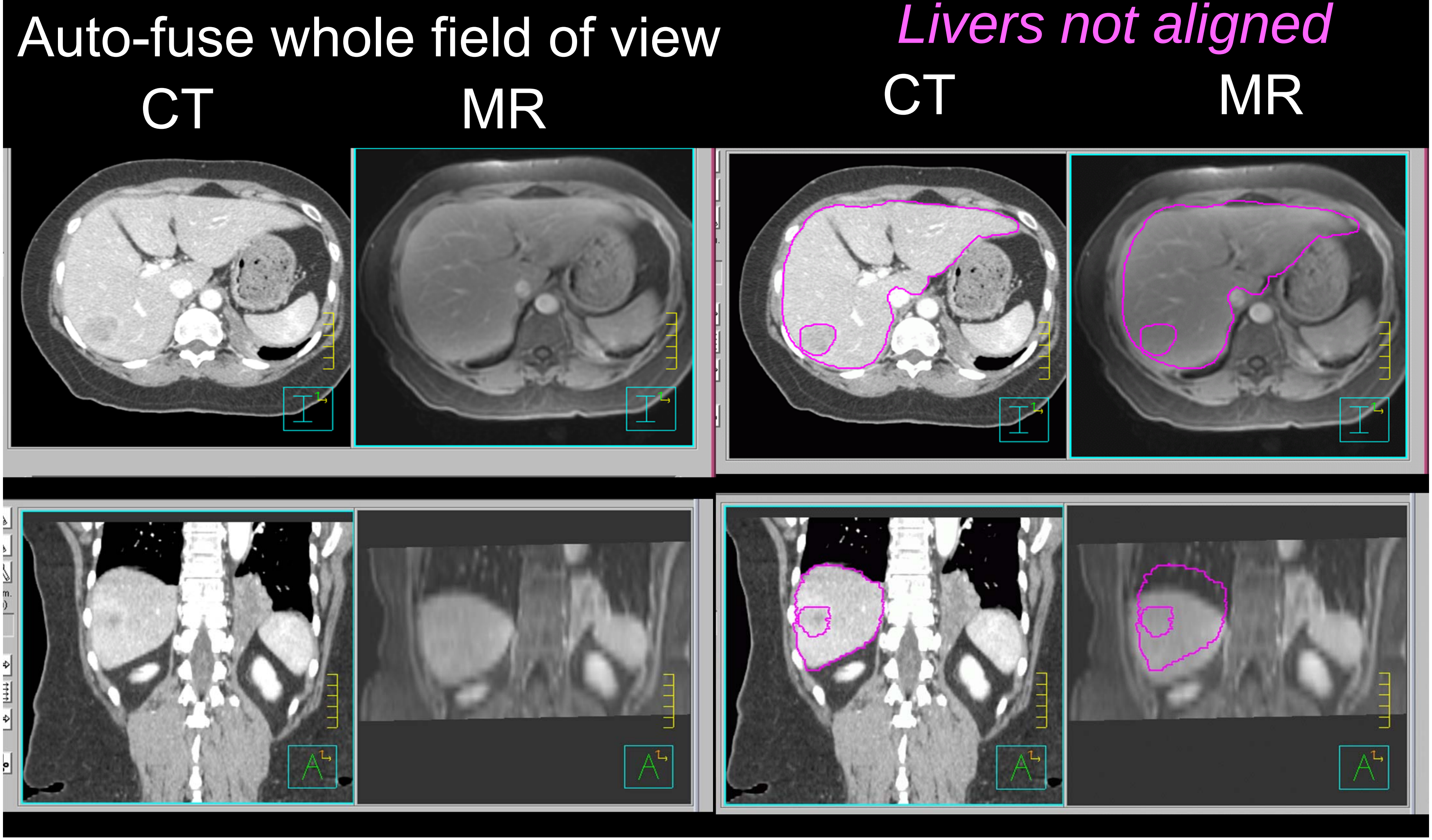
Uncertainty in Surrogate-based Registration



Uncertainty in Surrogate-based Registration



Using Rigid Registration in the Presence of Deformation



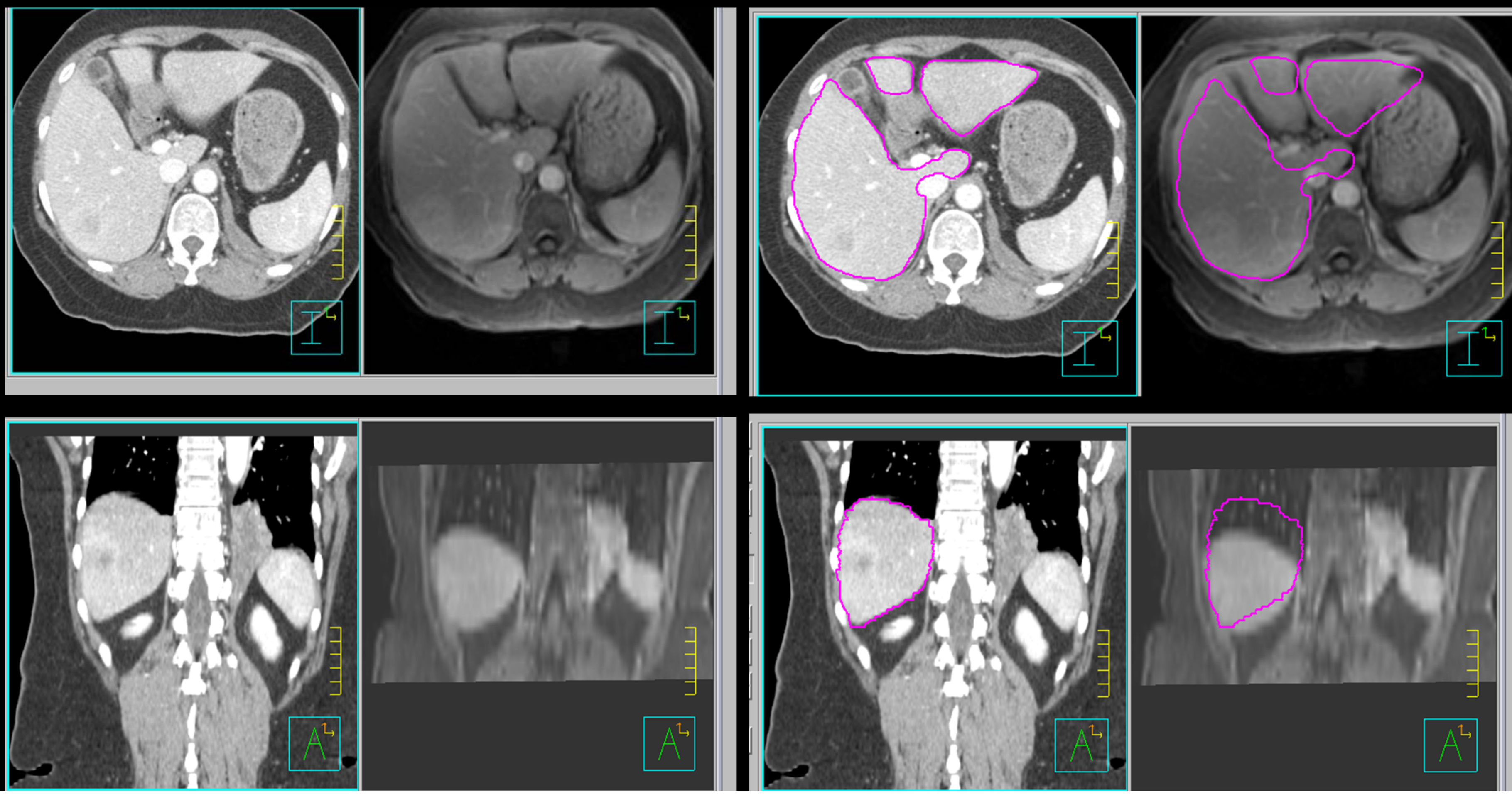
Example: CT-MR for liver cancer

Vertebral body match

CT MR

Livers not aligned

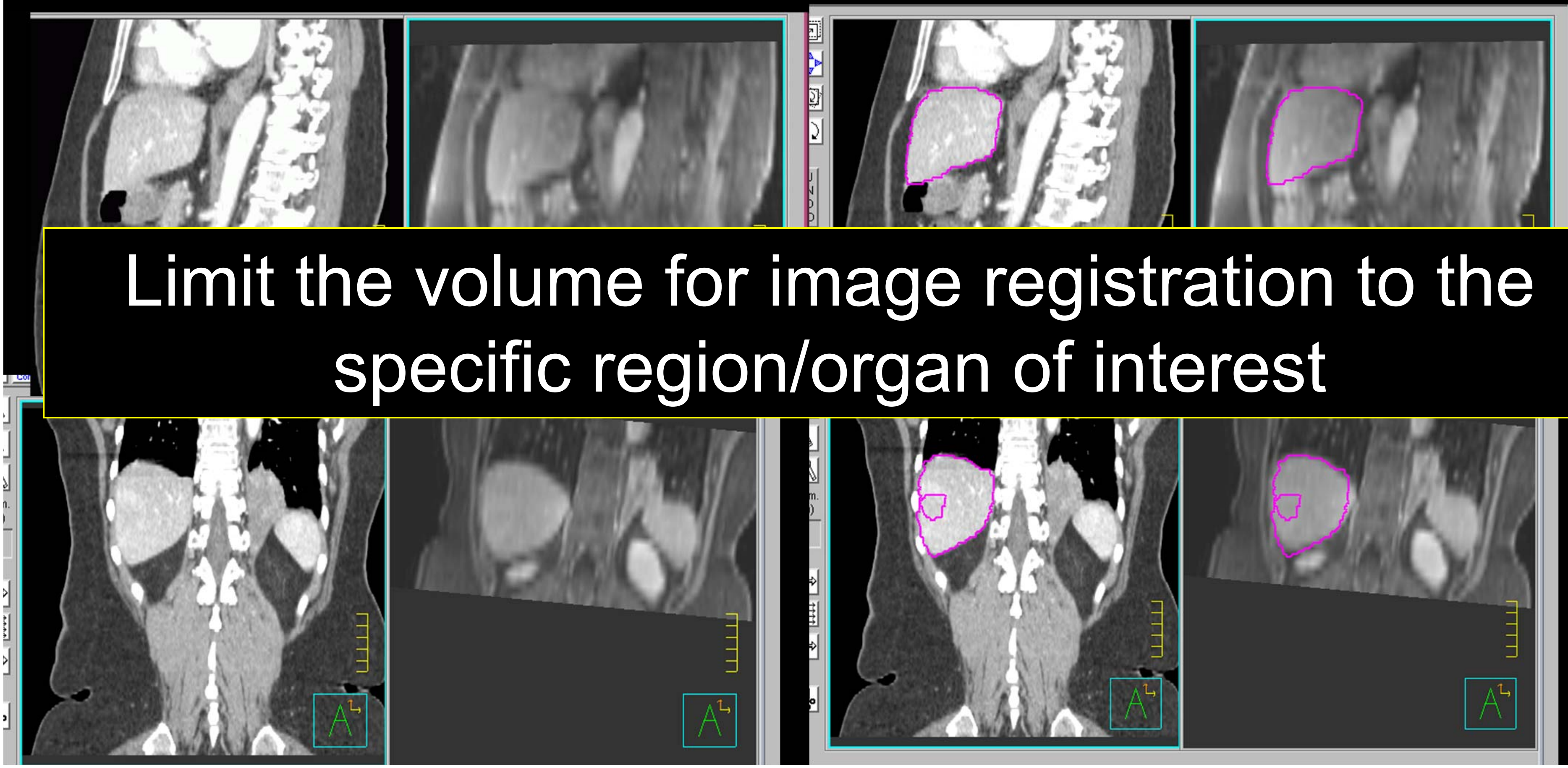
CT MR



Example: CT-MR for liver cancer

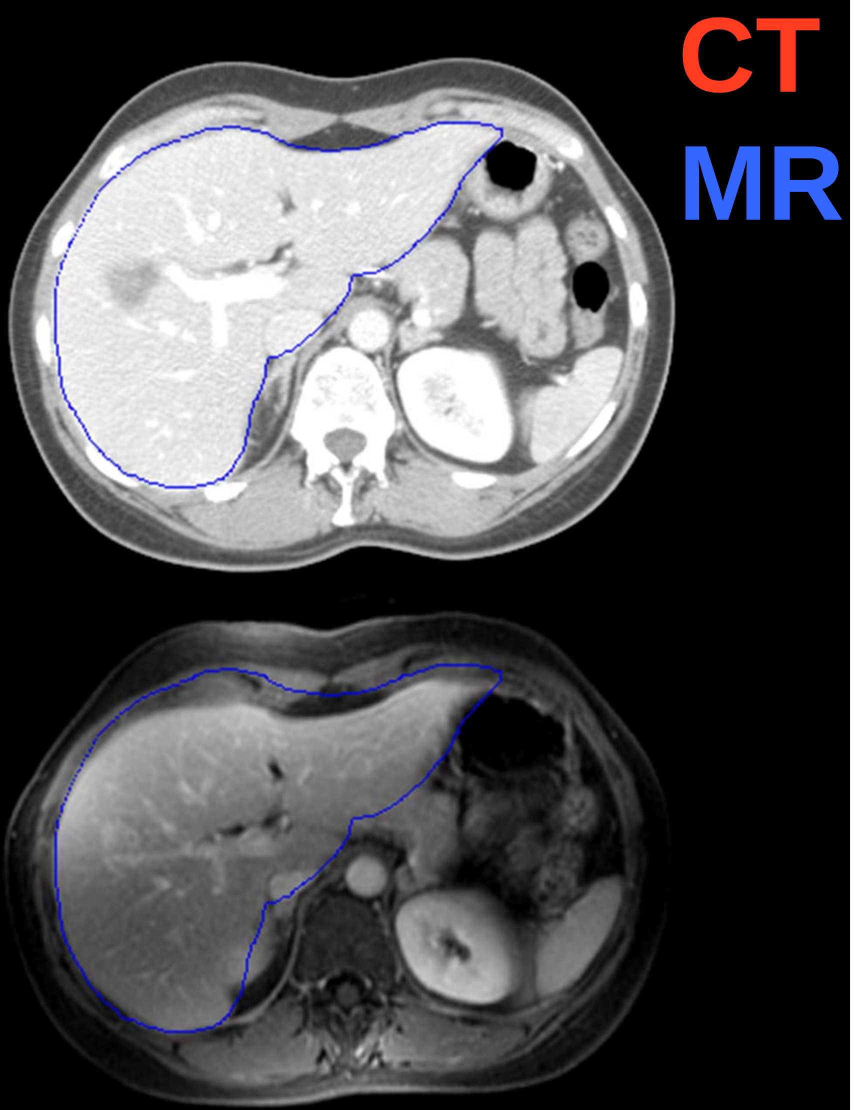
Liver match | *Livers aligned*

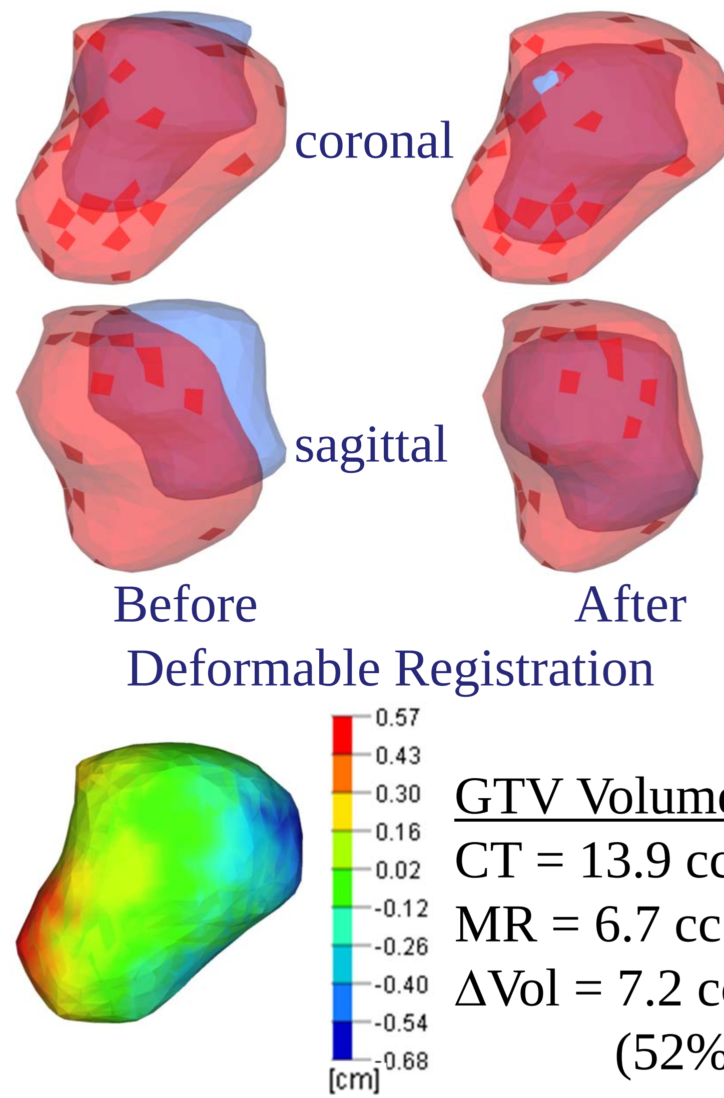
CT | MR | CT | MR



Limit the volume for image registration to the specific region/organ of interest

Accurate Target Definition





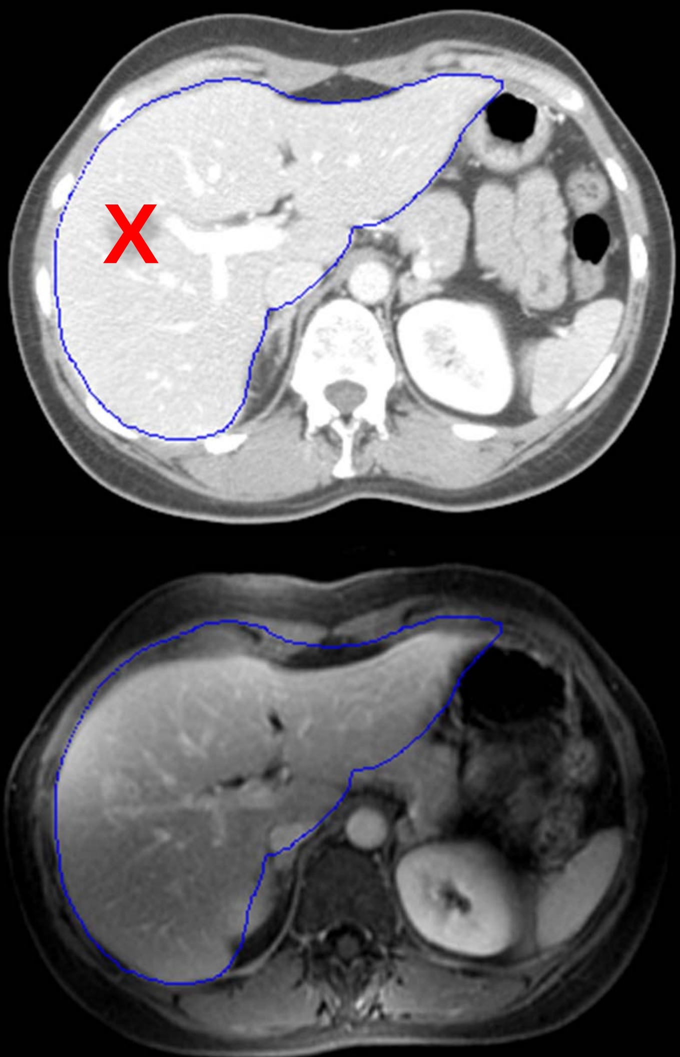
GTV Volume

CT = 13.9 cc

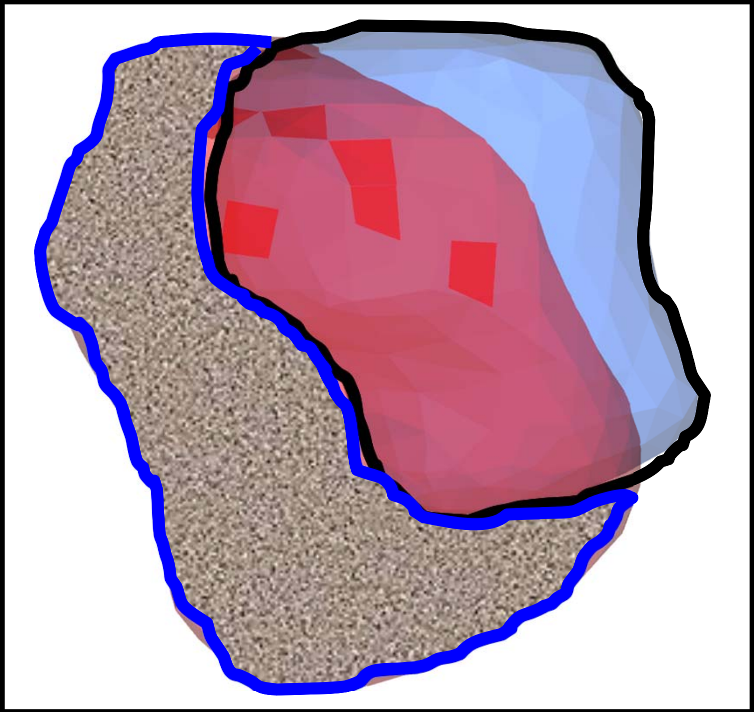
MR = 6.7 cc

ΔVol = 7.2 cc (52%)

Clinical Effect



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



Region of CT-defined GTV that is missed

Accurate Target Definition

- 26 patient with liver cancer
- Tumor concordance improved from 65% to 73% with deformable registration
- Results in a 16% reduction in GTV volume
  - 80 cc for 500 cc tumor
  - 160 cc for 1000 cc tumor

Accurate Tumor Guidance
12 Liver Patients: 6 Fx Each
Rigid Reg $\rightarrow$ Deformable Reg

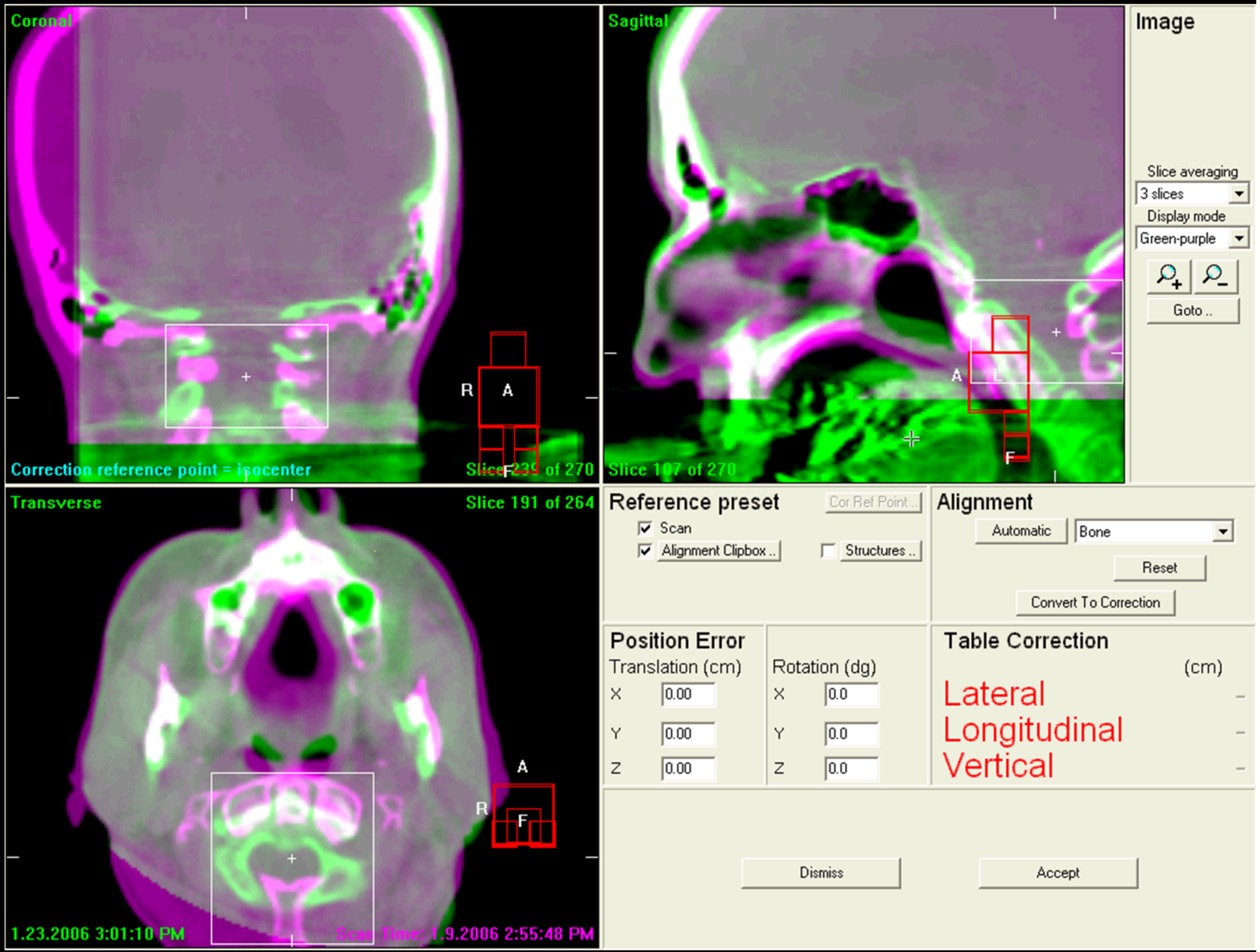
Δ Tumor	**dLR**	**dAP**	**dSI**	**abs(dLR)**	**abs(dAP)**	**abs(dSI)**
AVG	-0.04	-0.01	0.01	0.08	0.10	0.10
SD	0.10	0.15	0.20	0.07	0.11	0.17
Max	0.27	0.43	0.97	**0.34**	**0.65**	**0.97**
Min	-0.34	-0.65	-0.70	0.00	0.00	0.00
Median	-0.03	0.01	0.00	0.05	0.06	0.04

- 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.

Limitation of Locally Rigid Registration

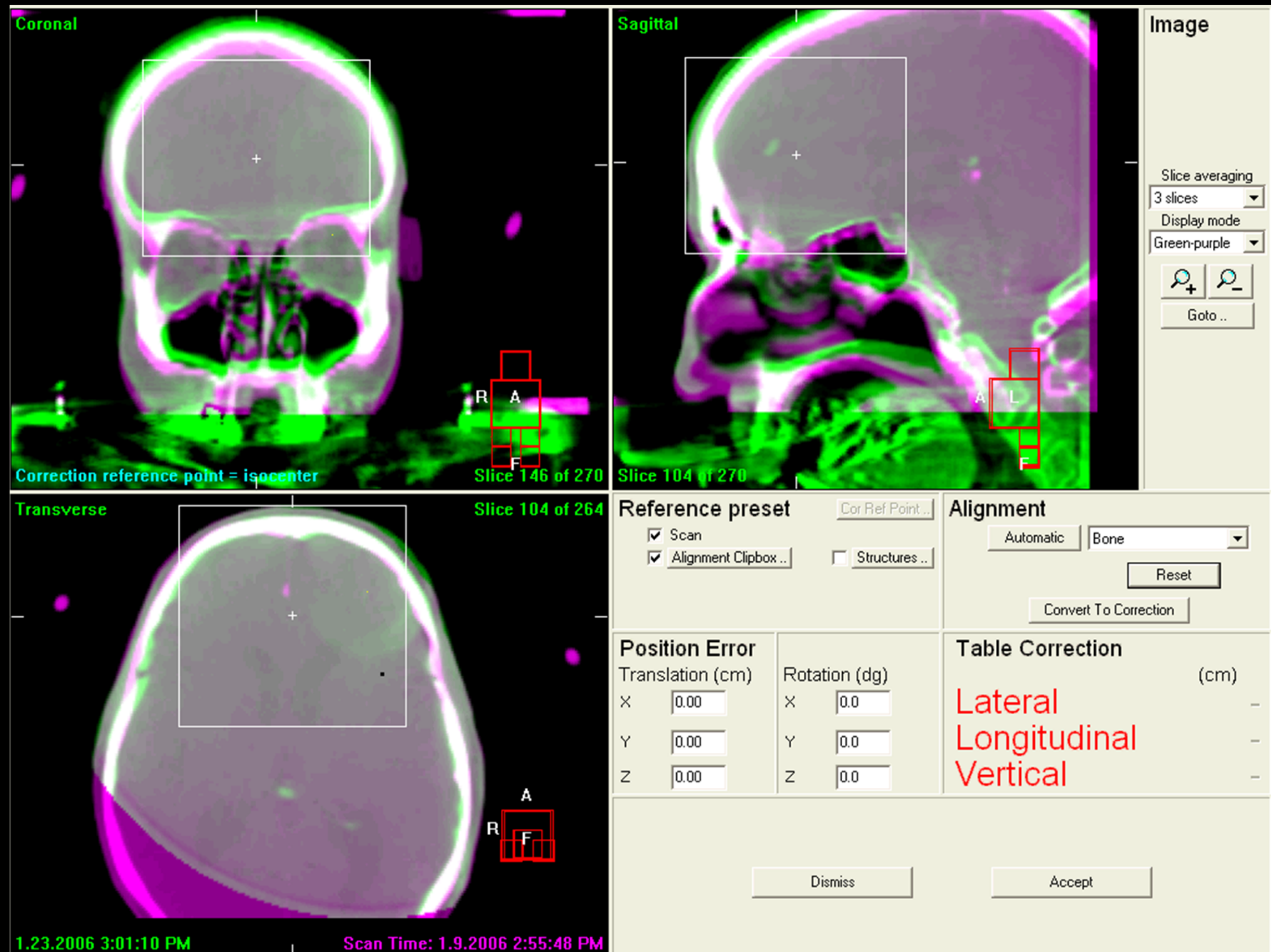
Intensity-based registration focused in the clip box

Neck:
- 3.6, 5.3, 5.7 mm



Limitation of Locally Rigid Registration

Intensity-based registration focused in the clip box



Neck:

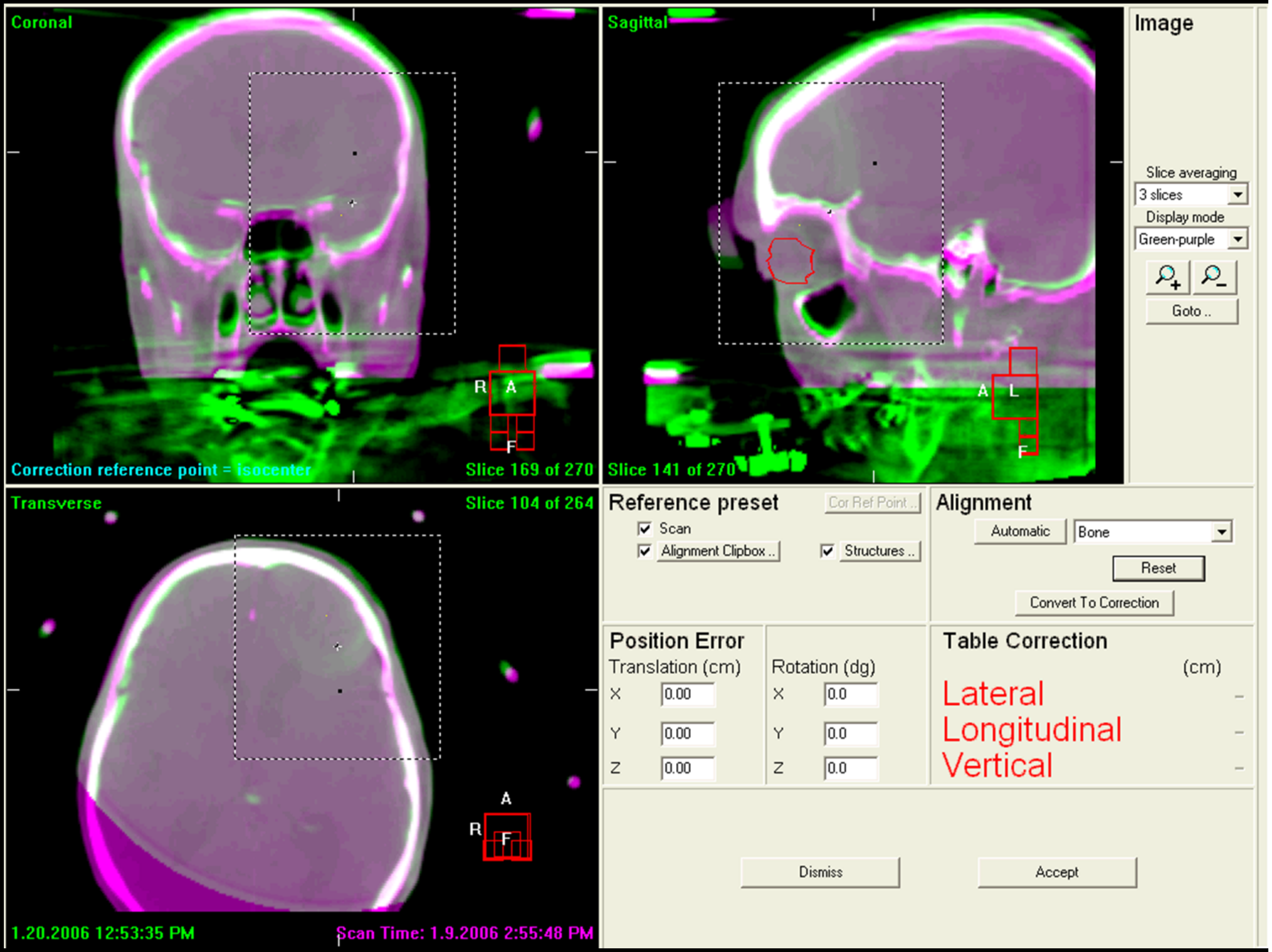
- 3.6, 5.3, 5.7 mm

Parietal/Sinus

- 1.7, 3.6, 1.1 mm

Limitation of Locally Rigid Registration

Intensity-based registration focused in the clip box



Neck:
- 3.6, 5.3, 5.7 mm

Parietal/Sinus
- 1.7, 3.6, 1.1 mm

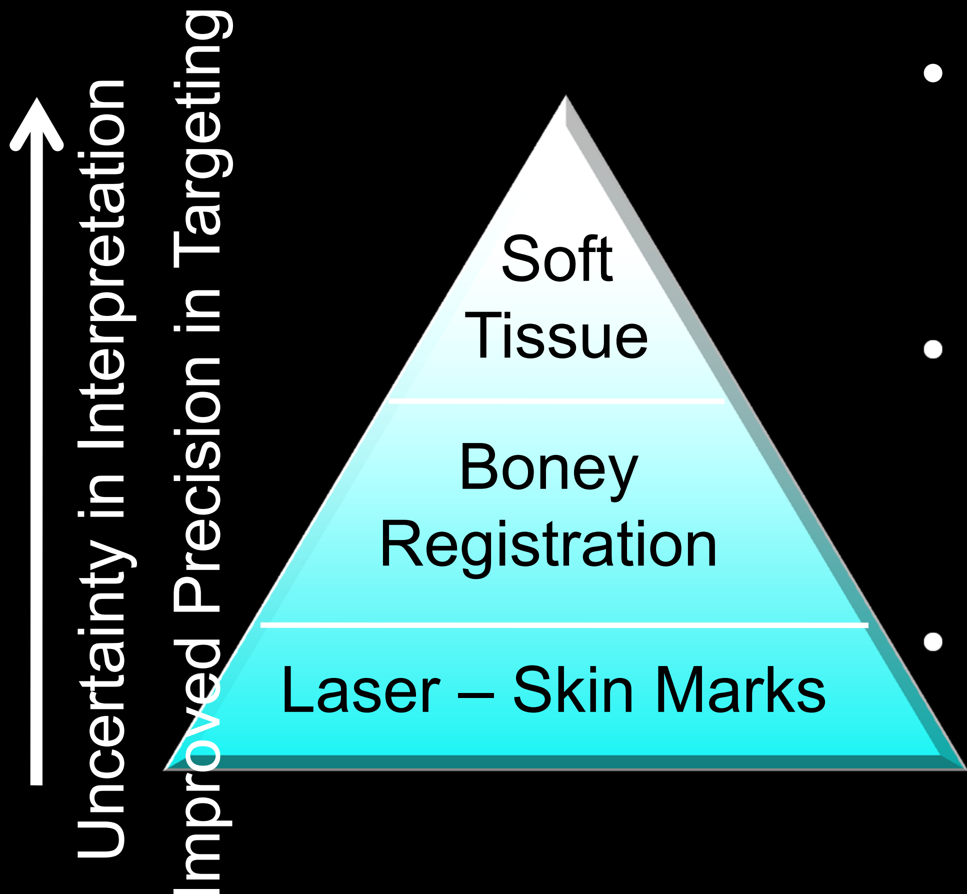
Target:
- 1.1, 3.0, 0.7 mm


I'm not seeing a button for this…

Practical Solutions for Deformable Tissue with Rigid Registration

- Planning:
  - Use limited field of view
  - * Limited confidence outside of FOV
  - * Be careful not to use rotation to incorrectly account for deformation
- Delivery
  - Use limited field of view – multiple times!
  - Send isodose lines as contours with IGRT
  - Need to specify the IGRT protocol and implement PTV margins accordingly
- Document!
  - What the protocol is
  - What was used

Limiting the Uncertainty of Soft Tissue Registration



- 1st – Align to lasers
  - Get the patient in the room
- 2nd – align to the bones
  - Evaluate registration
  - Constrains shifts
- 3rd – Align to soft tissue
  - Refine the registration under the constraint of the boney registration

Summary (1/5)

- Limitations when using rigid registration for a soft tissue structure
- Surrogates have strengths and limitations
- Uncertainties need to feed into margins

Techniques

Deformable Registration Algorithms
How do they work?

- Match something
  - Intensity, gradients, boundaries, features
- Constrain by a function
  - Geometric, physical, biomechanical

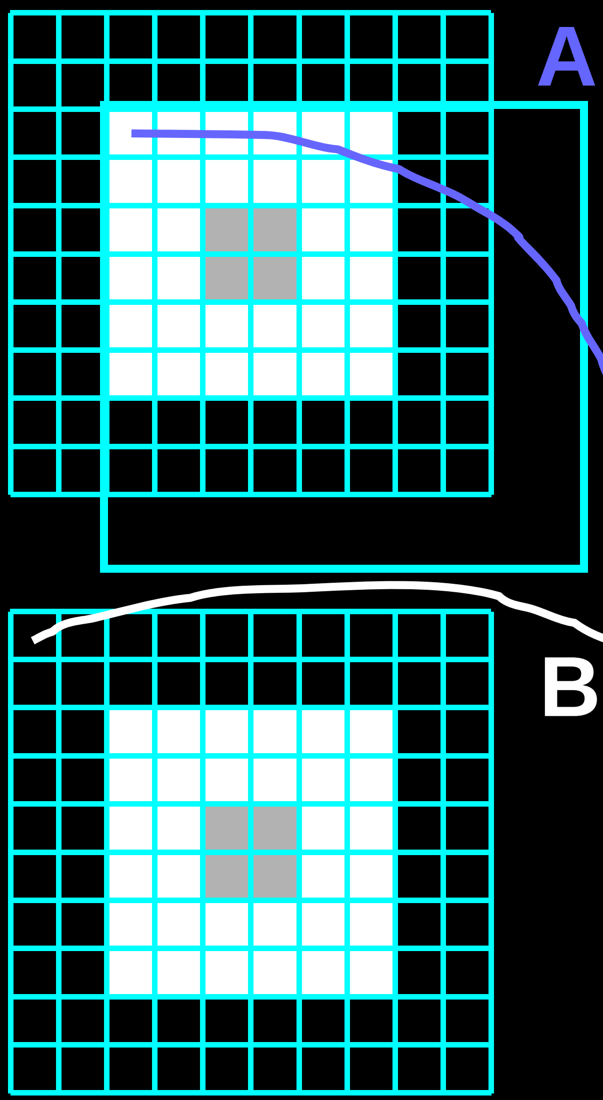
Deformable Registration Algorithms How do they work?

- Match something
  - Intensity, gradients, boundaries, features
  - What happens when the intensity correspondence varies?
  - What happens when the gradient isn’t there?
  - What happens when the boundaries aren’t well defined?
  - What happens with the features aren’t visible?
- Constrain by a function
  - Geometric, physical, biomechanical
  - Can you rely on this model when the match above is missing?

How is Registration Performed?

Metric	Regularization	Optimization
Your Eye	Translation	Brain-power
Least Squares (Points)	Translation + Rotation	Simplex
Chamfer Matching (surface matching)	Affine (Translation + Rotation + scaling + shearing)	Gradient descent
Contour matching		etc…
Mean Square Difference	Spline (B-spline, Thin plate spline)	
Correlation Coefficient	Physical (optical/fluid flow, elastic body)	
Mutual Information	Biomechanical	

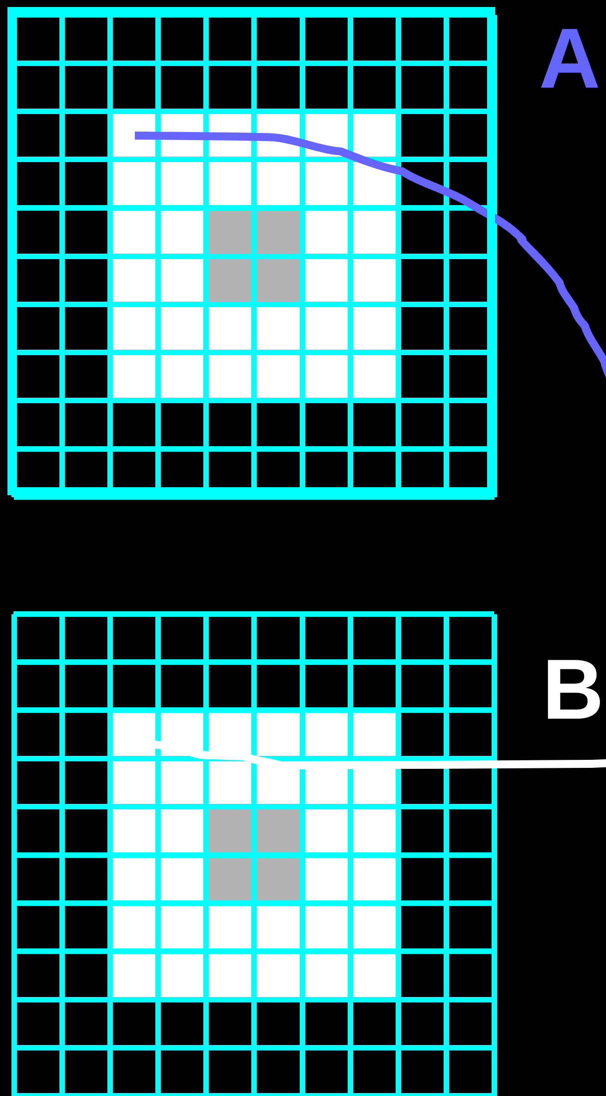
Sum of Squared Differences



- Evaluate the voxel value in each image, A and B
- SSD = $\Sigma[A(i)-B(i)]^2$

$A(i) = 0$, $B(i) = 10$ $\Big\}$ $[0-10]^2 = 100$

Sum of Squared Differences



- Evaluate the voxel value in each image, A and B
- SSD = $\Sigma[A(i)-B(i)]^2$

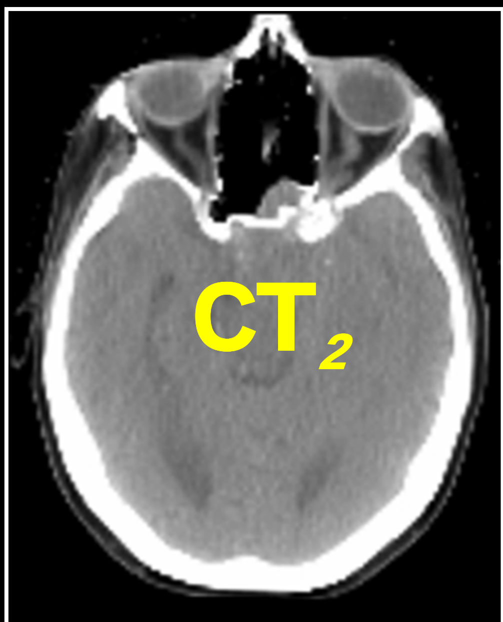
$$\left.\begin{array}{l} A(i) = 0 \\ B(i) = 0 \end{array}\right\} [0-0]^2 = 0$$

- Minimize SSD!
- Must have the exact same intensities on each image
- Noise in the image introduces uncertainties

Kessler / UM

Sum of Squared Differences

... subtract one image from the other



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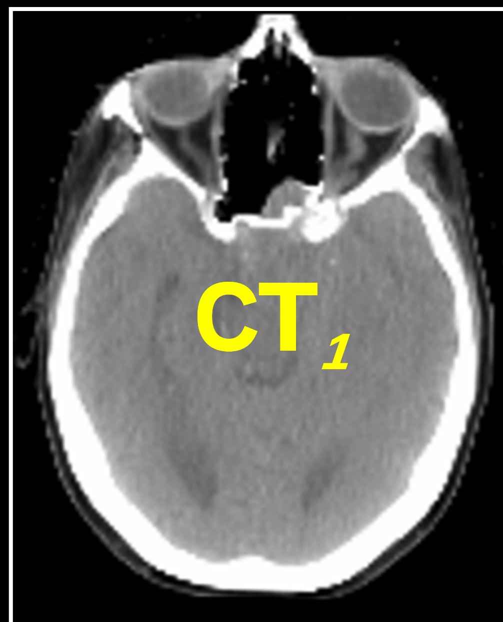

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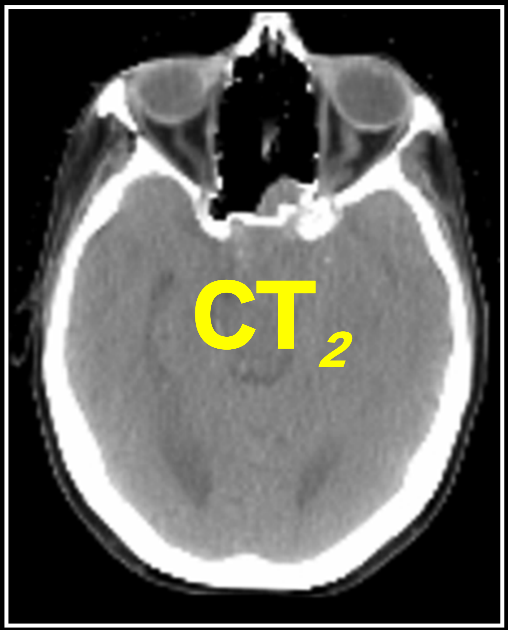
I_{CT_2} $\quad$ I_{CT_1} $\quad$ $\sum (I_{CT_2} - I_{CT_1})^2$

Individual Intensity Distributions

Sum of the Squares of the Differences

Sum of Squared Differences

... subtract one image from the other



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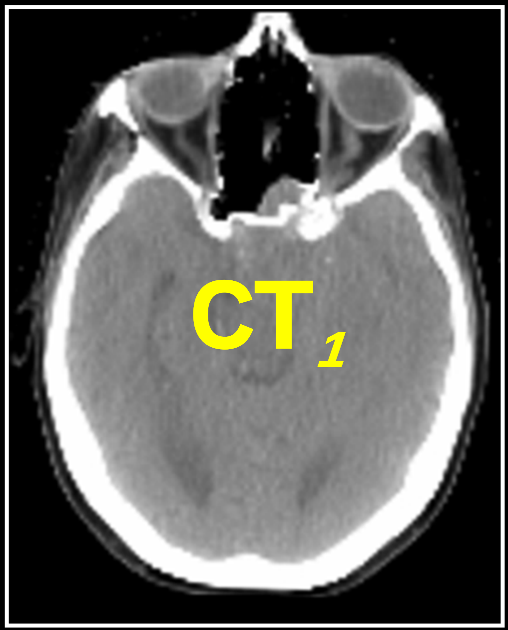

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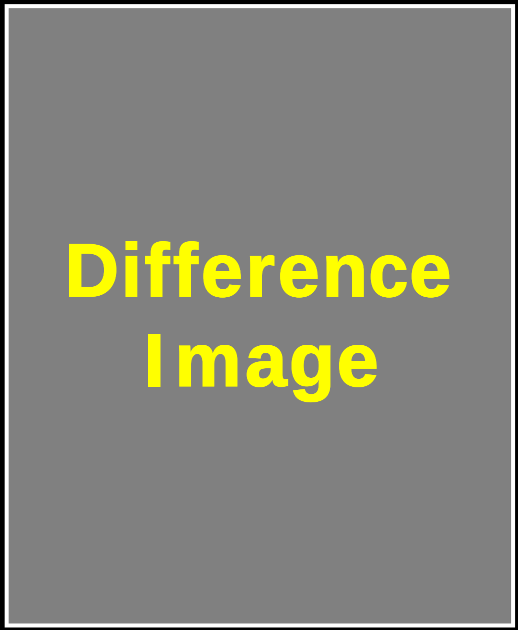


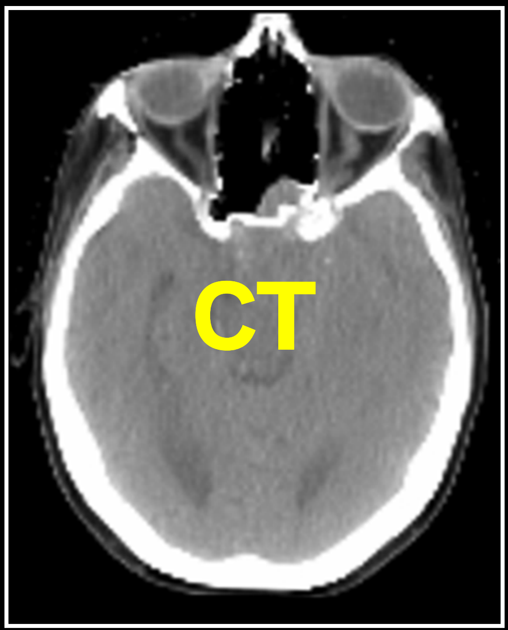
I_{CT_2} $\quad$ I_{CT_1} $\quad$ **Zero**

Individual Intensity Distributions $\quad$ **Registered**

Kessler / UM

Sum of Squared Differences

... subtract one image from the other



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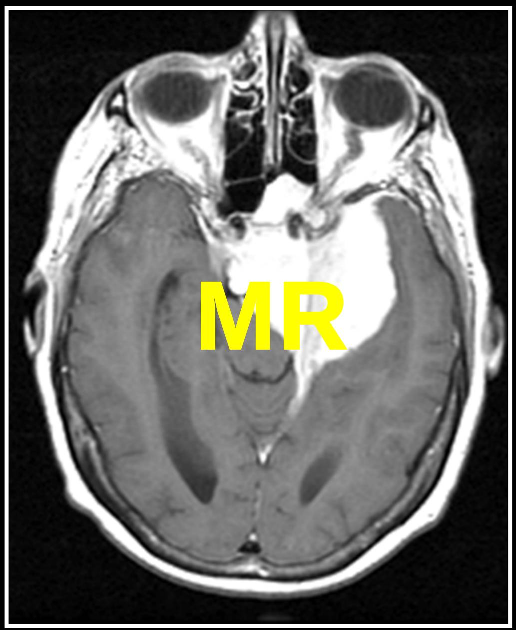

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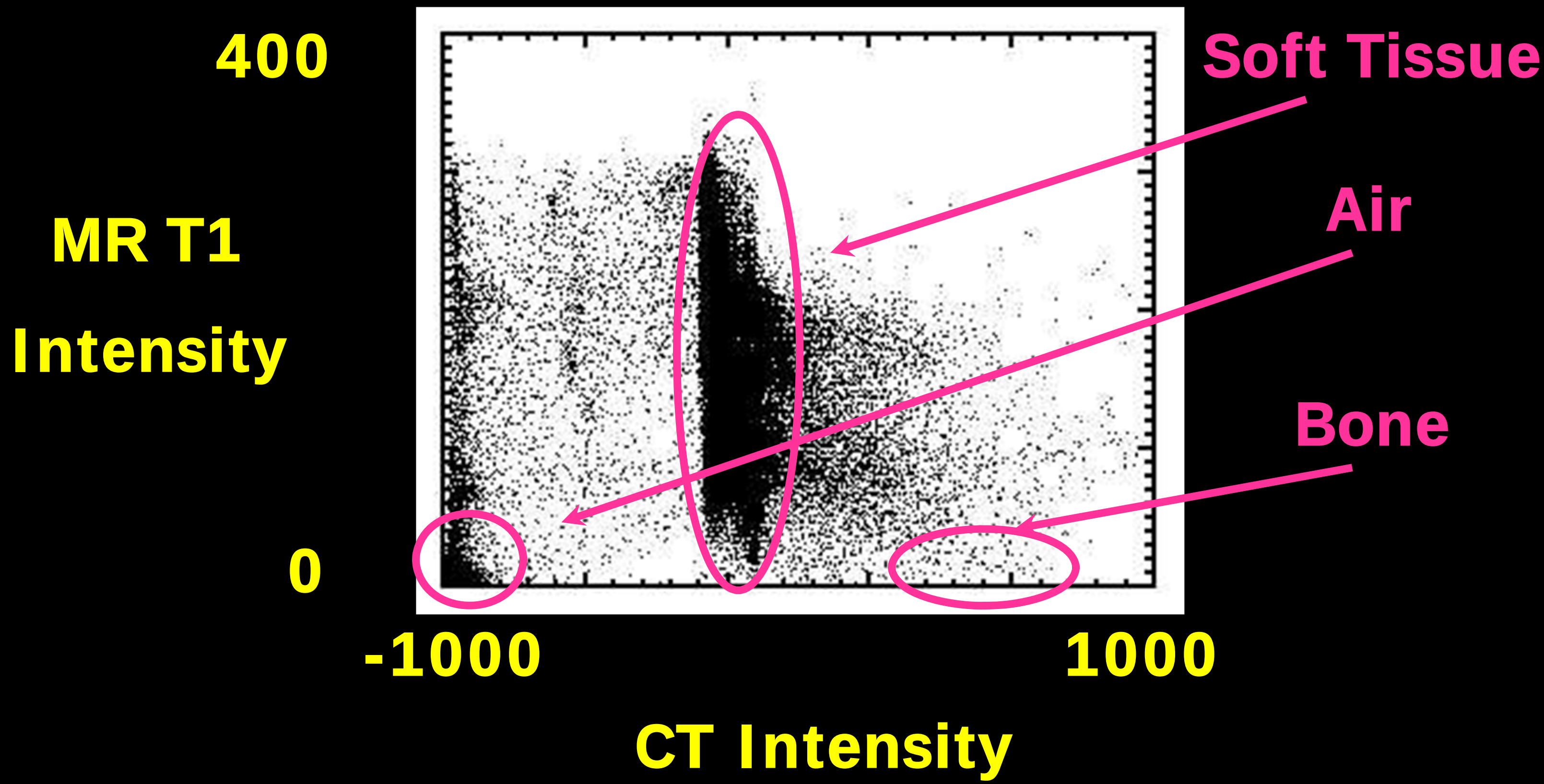
I_{CT} I_{MR} ***Not* Zero**

Individual Intensity Distributions

This doesn't usually make much sense

Inter-Modality Correspondence



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ARTIFICIAL INTELLIGENCE LABORATORY

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Paul A. Viola CHAPTER 4. MATCHING AND ALIGNMENT

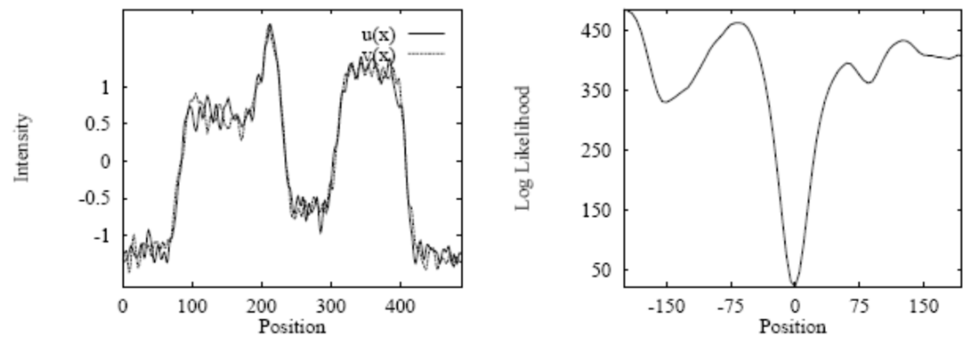


Figure 4.6: On the left is a plot of image and model that are identical except for noise. On the right is a plot of the logarithm of weighted neighbor likelihood versus translation.

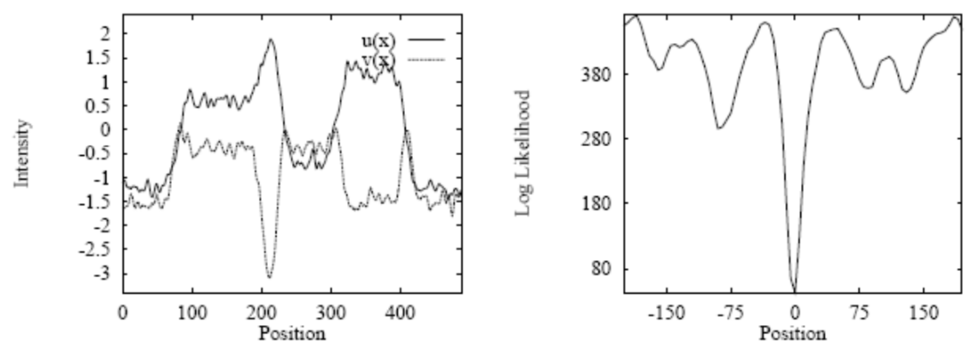
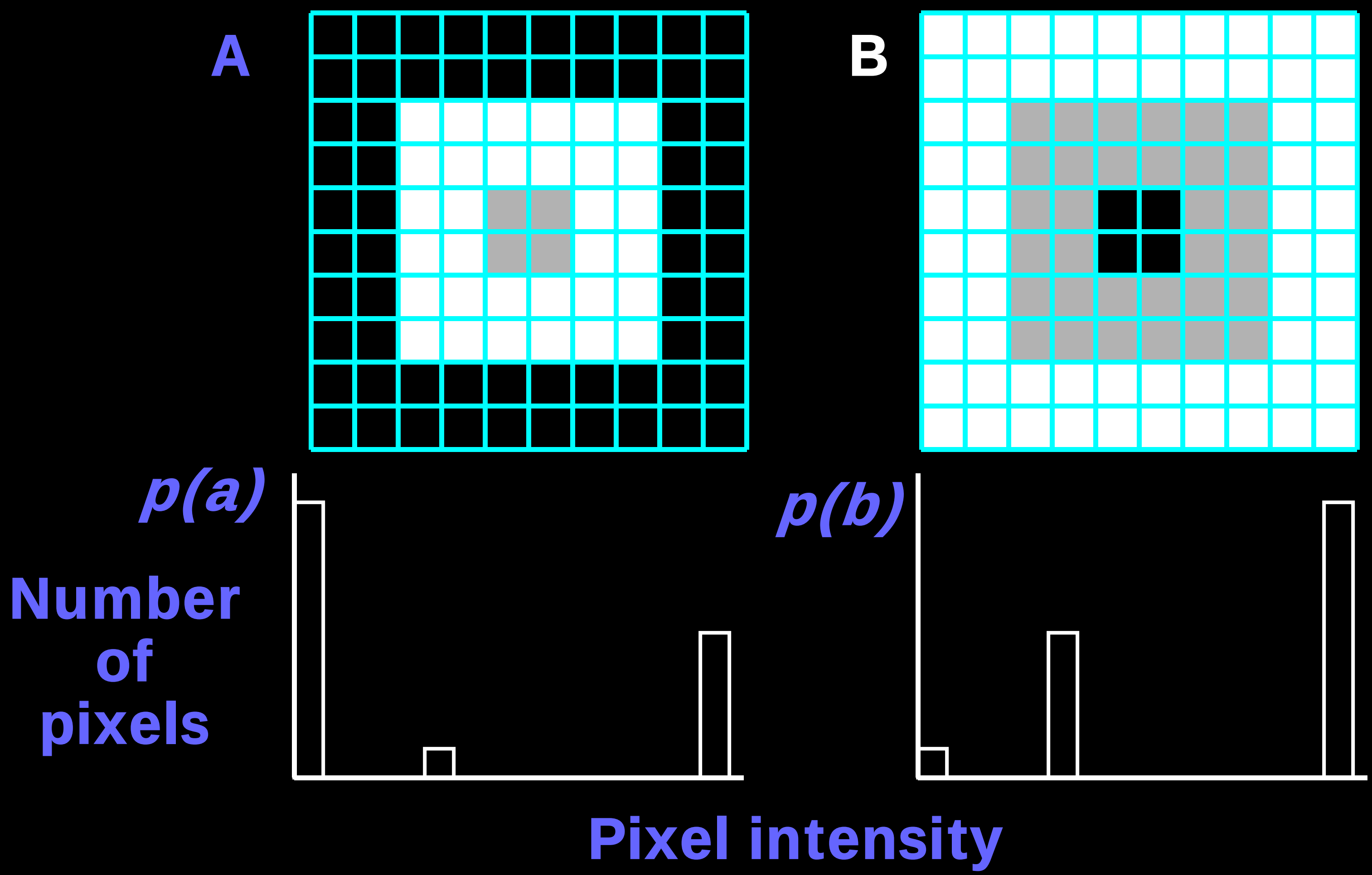


Figure 4.7: On the left is a plot of image and model that are related non-linearly. On the right is a plot of the logarithm of weighted neighbor likelihood versus translation.

1-D Histogram

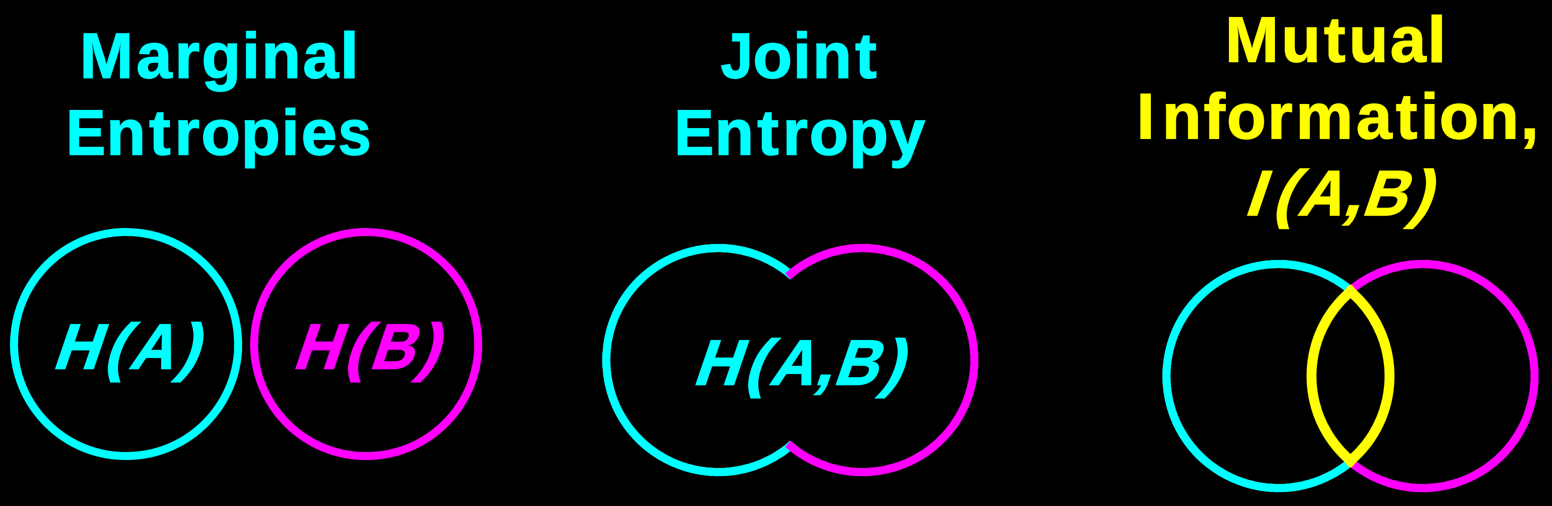


*Adapted from S. Breen

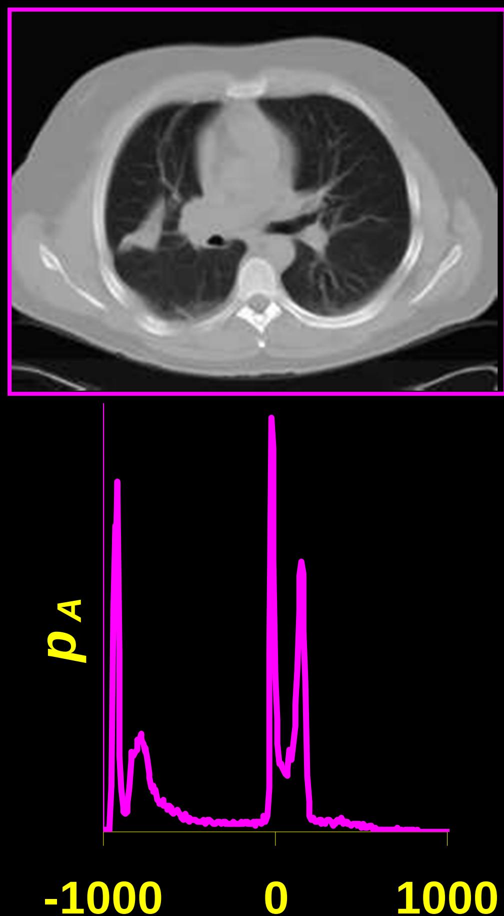
Mutual Information

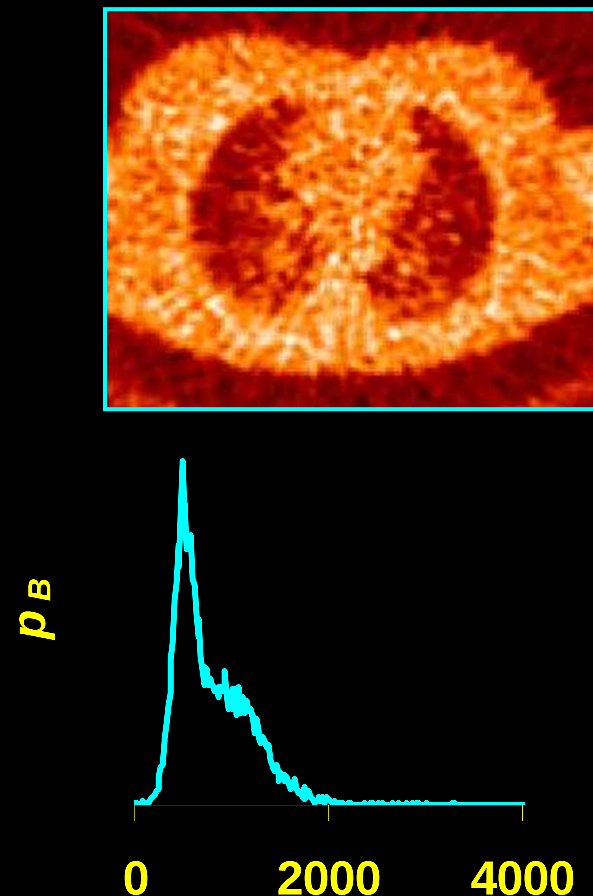
- Maximise the mutual information

$$I(A,B) = H(A) + H(B) - H(A,B)$$

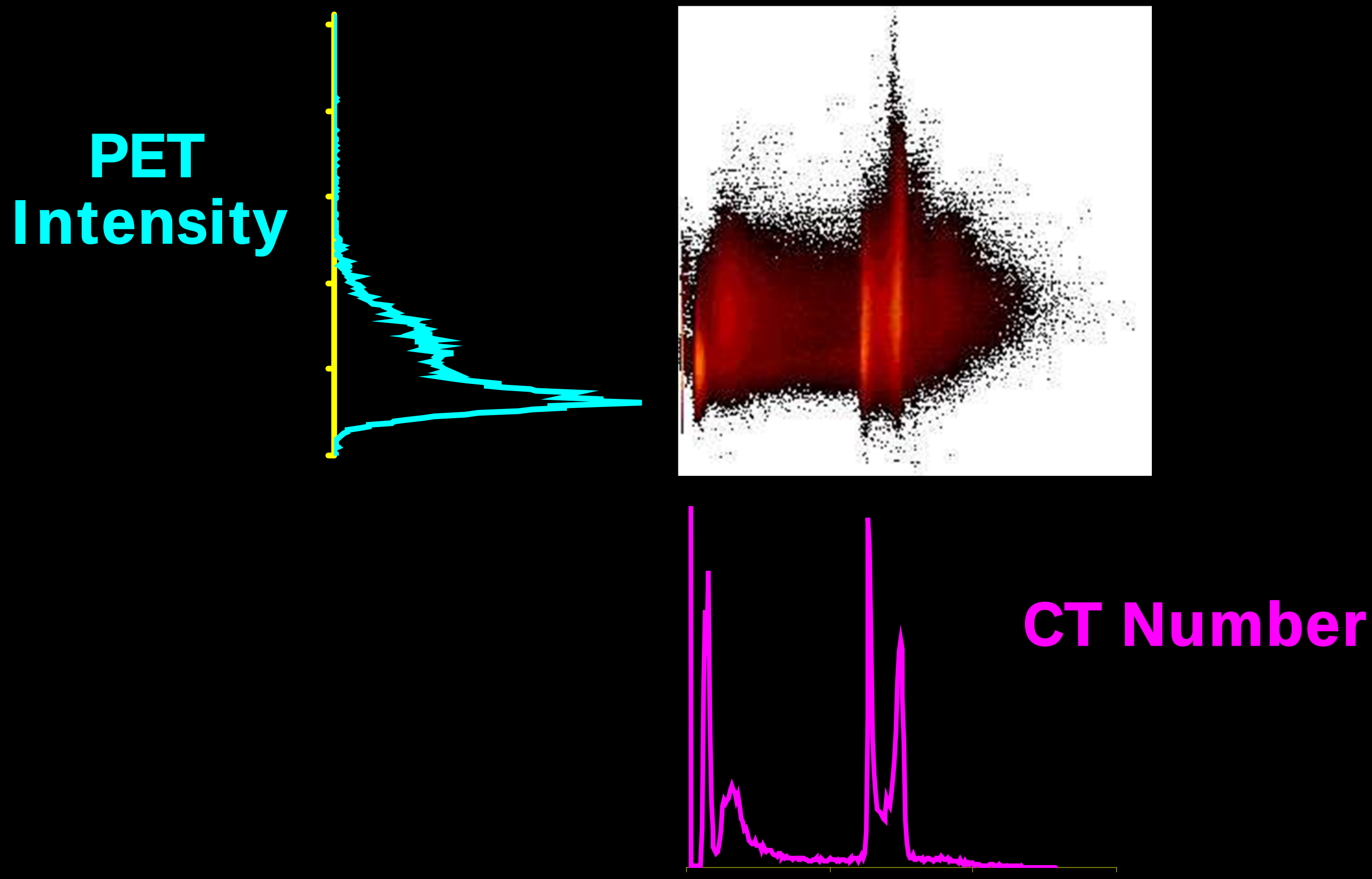


Entropy





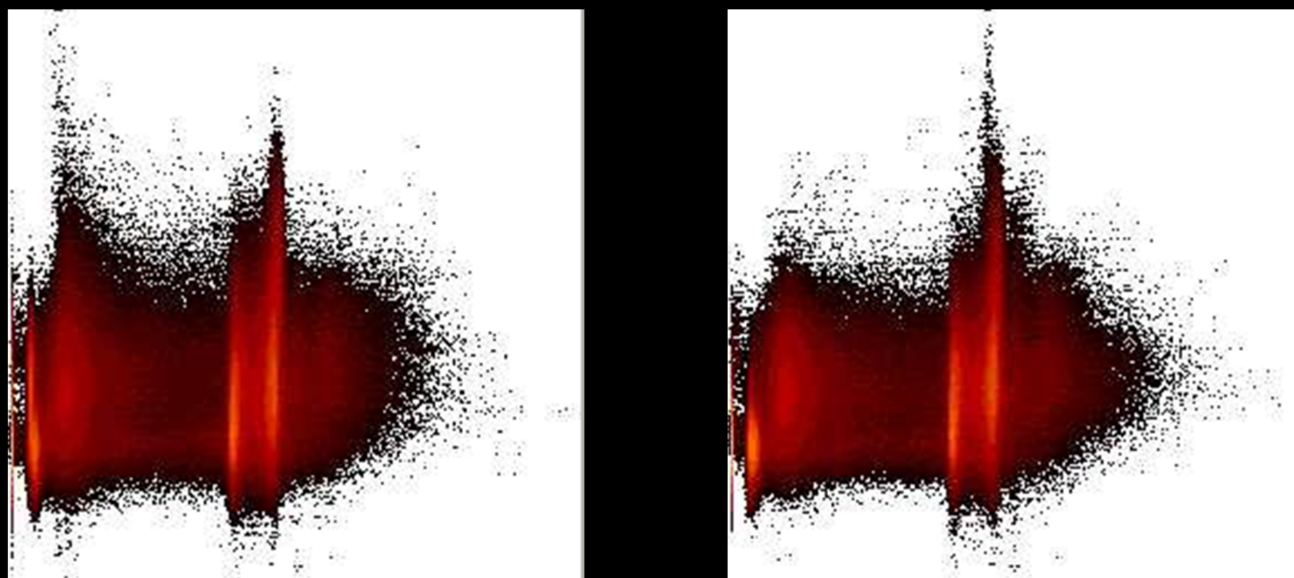
Joint Entropy



Mutual Information

2° Axial Rotation
$\Delta x = 6$
$\Delta y = -8$

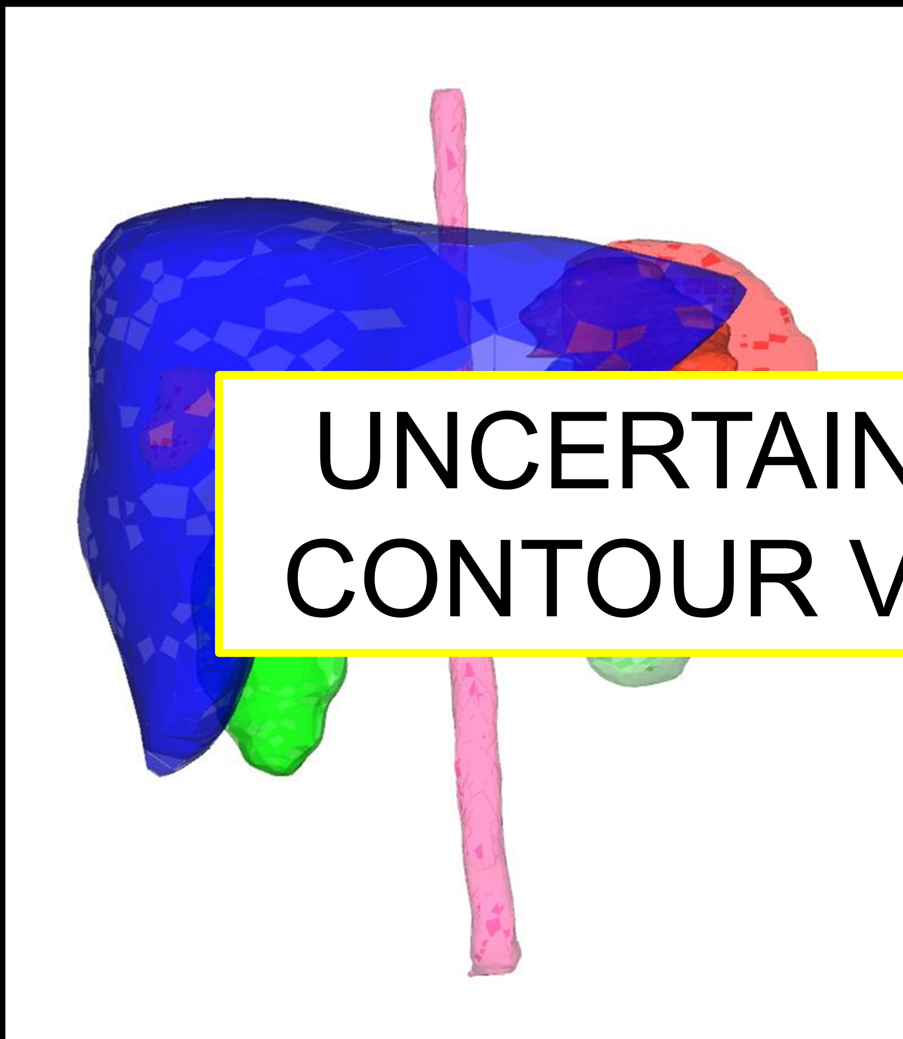
Registered

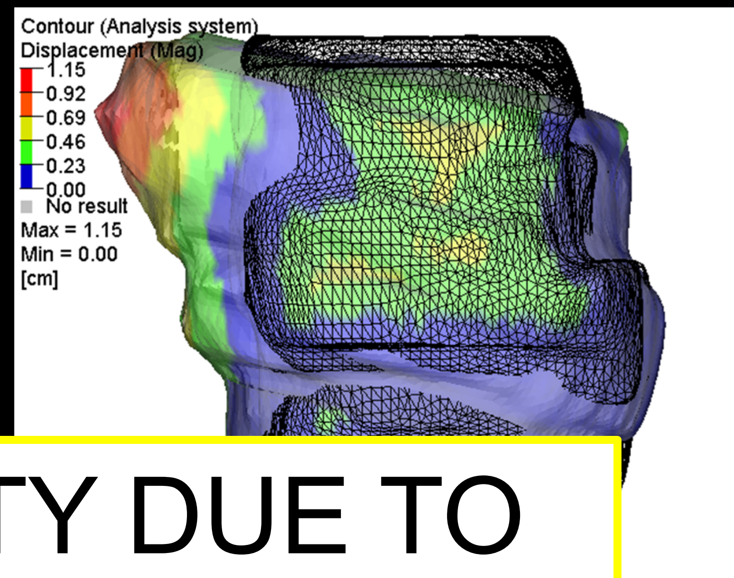


PET Intensity

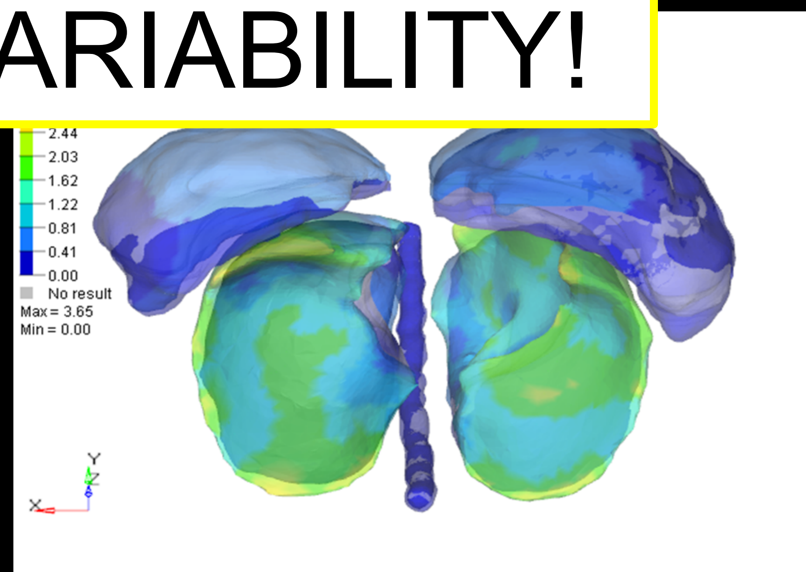
CT Number

Contour Matching

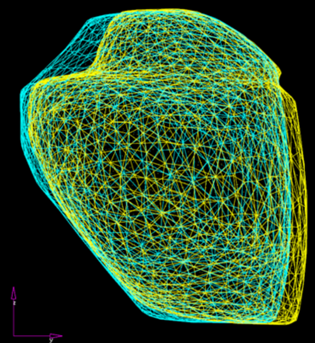




UNCERTAINTY DUE TO CONTOUR VARIABILITY!



Uncertainty in Contour Residual Error [cm]



	LR	AP	SI
B to A	0.03 (0.06)	-0.04 (0.12)	-0.02 (0.12)
B to A2	0.01 (0.07)	-0.08 (0.12)	0.04 (0.12)
Difference	-0.01 (0.01)	-0.04 (0.01)	0.06 (0.00)
P-Value	0.22	0.18	0.053

- 21 prostate patients, MR image, intra-observer uncertainty
- 95% of the prostate surface for 95% of patients: 3.4 mm

Brock, Med Phys, 2008

Summary (2/5)

- Several candidates for similarity metrics
- Intensity-based metrics
  - More information in the image = more information for registration
  - Noise in the image acquisition = uncertainty in the registration
- Contour based metrics
  - Inter/Intra observer variation = uncertainty

How is Registration Performed?

Metric	**Regularization**	**Optimization**
Your Eye	Translation	Brain-power
Least Squares (Points)	Translation + Rotation	Simplex
Chamfer Matching (surface matching)	Affine (Translation + Rotation + scaling + shearing)	Gradient descent
Contour matching		etc…
Mean Square Difference	Spline (B-spline, Thin plate spline)	
Correlation Coefficient	Physical (optical/fluid flow, elastic body)	
Mutual Information	Biomechanical	

Picture Tutorial

Image blending
Functional mapping
Image fusion

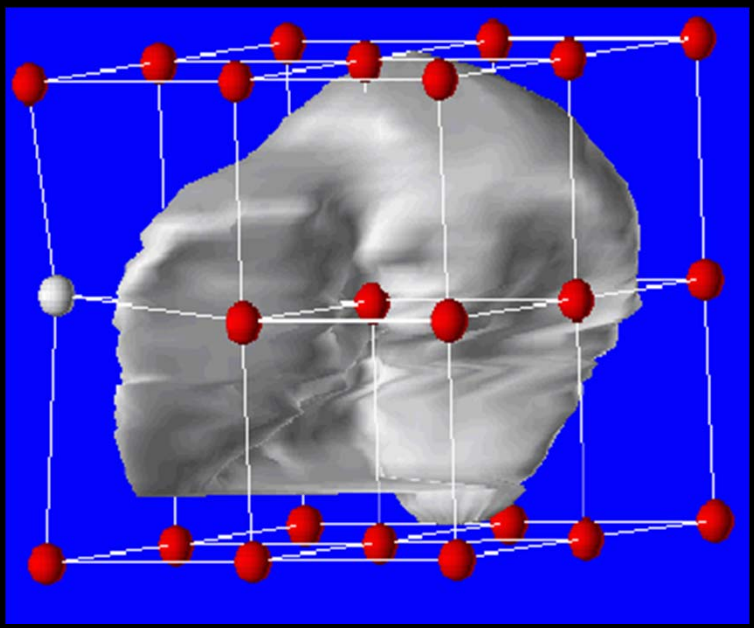
Deformable image registrati
(transformation matrix)

Courtesy of Lei Dong

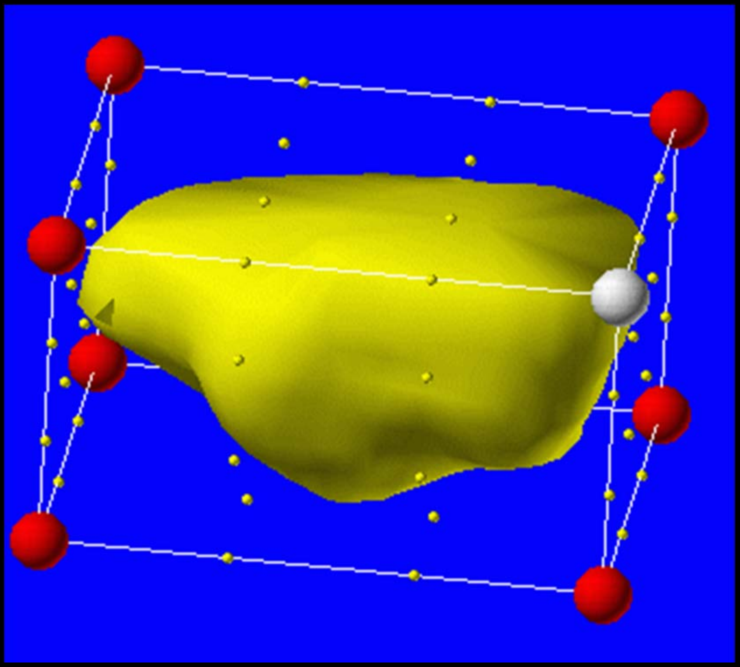
Kessler / UM

Thin-Plate Splines

Liver



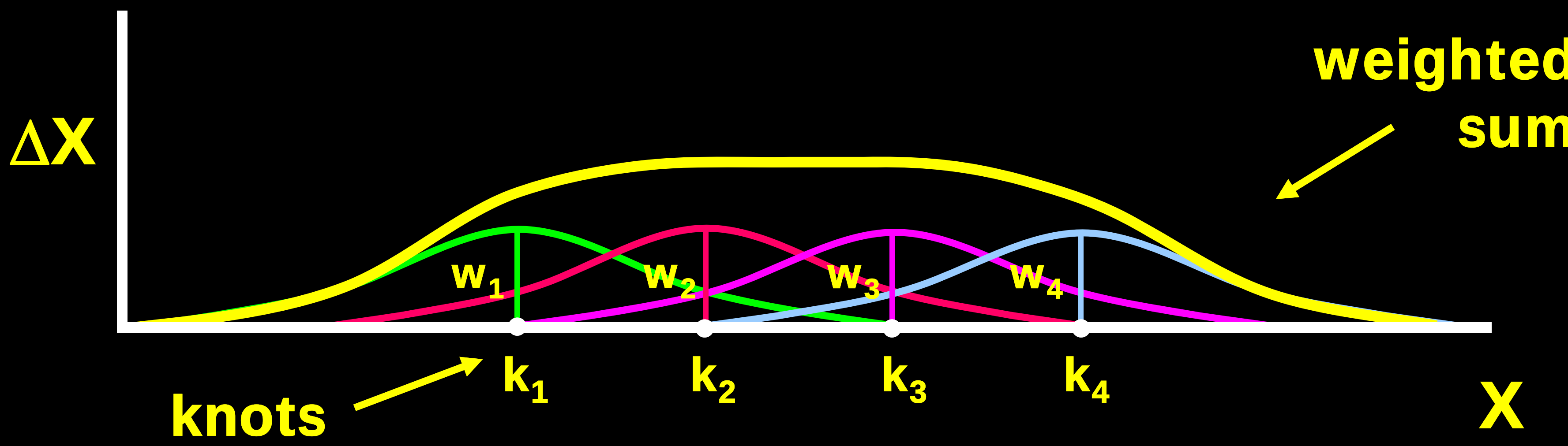
Bladder



$$T(P) = \underbrace{a_0 + a_x x + a_y y + a_z z}_{\textit{affine}} + \underbrace{\sum_{i=1}^{n} w_i U(P - P_i)}_{\textit{warping}}$$

B-Splines

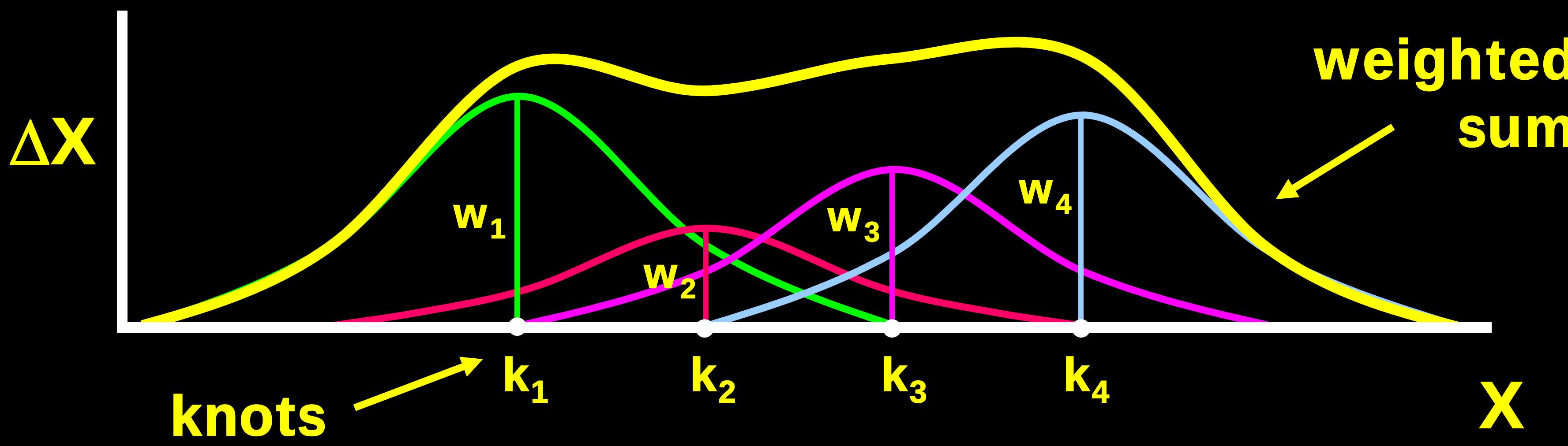
Transformation is built up using a set of weighted basis splines



$$X' = X + \Delta X = X + \sum w_i \cdot \beta(X - k_i)$$

B-Splines

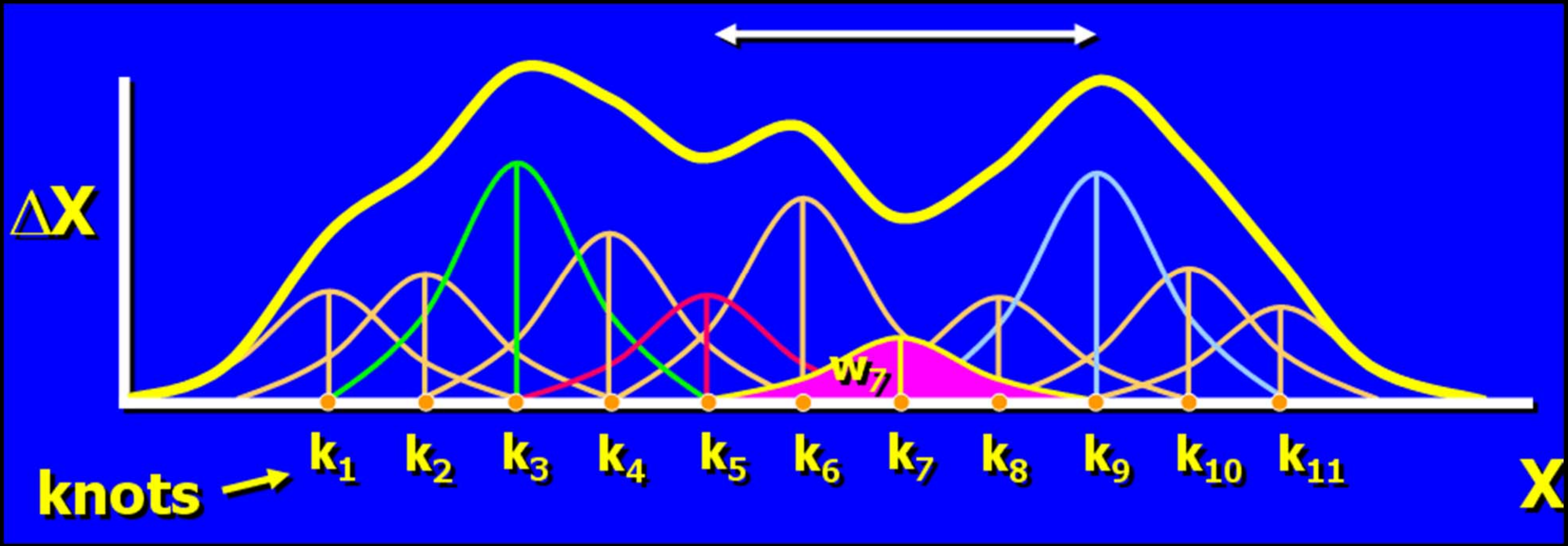
Transformation is built up using a set of weighted basis splines



$$X' = X + \Delta X = X + \sum w_i \cdot \beta(X-k_i)$$

B-Splines

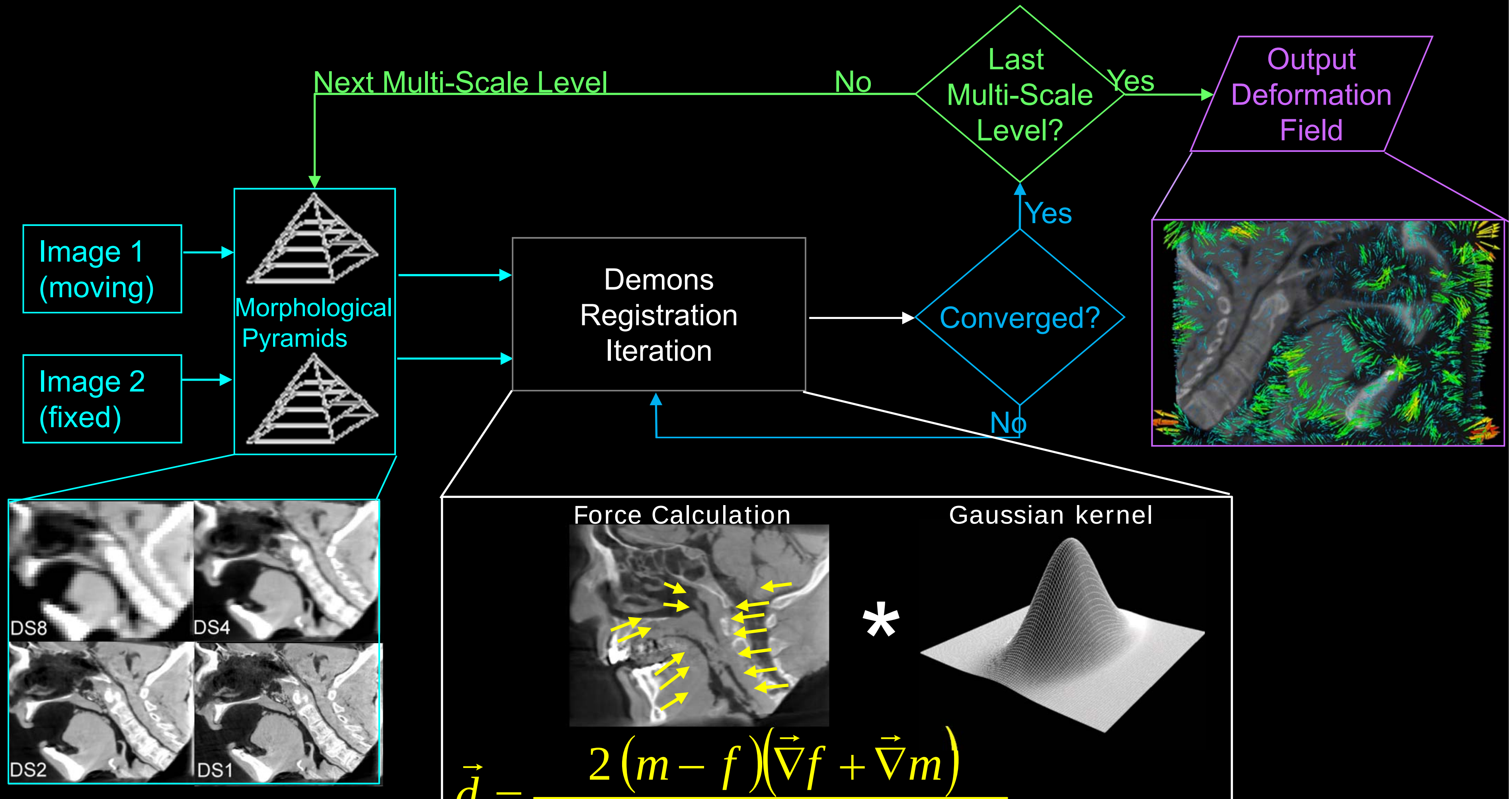
Basis function has finite range



$$X' = X + \Delta X = X + \sum w_i \cdot \beta(X - k_i)$$

This seems a lot like intensity modulation!

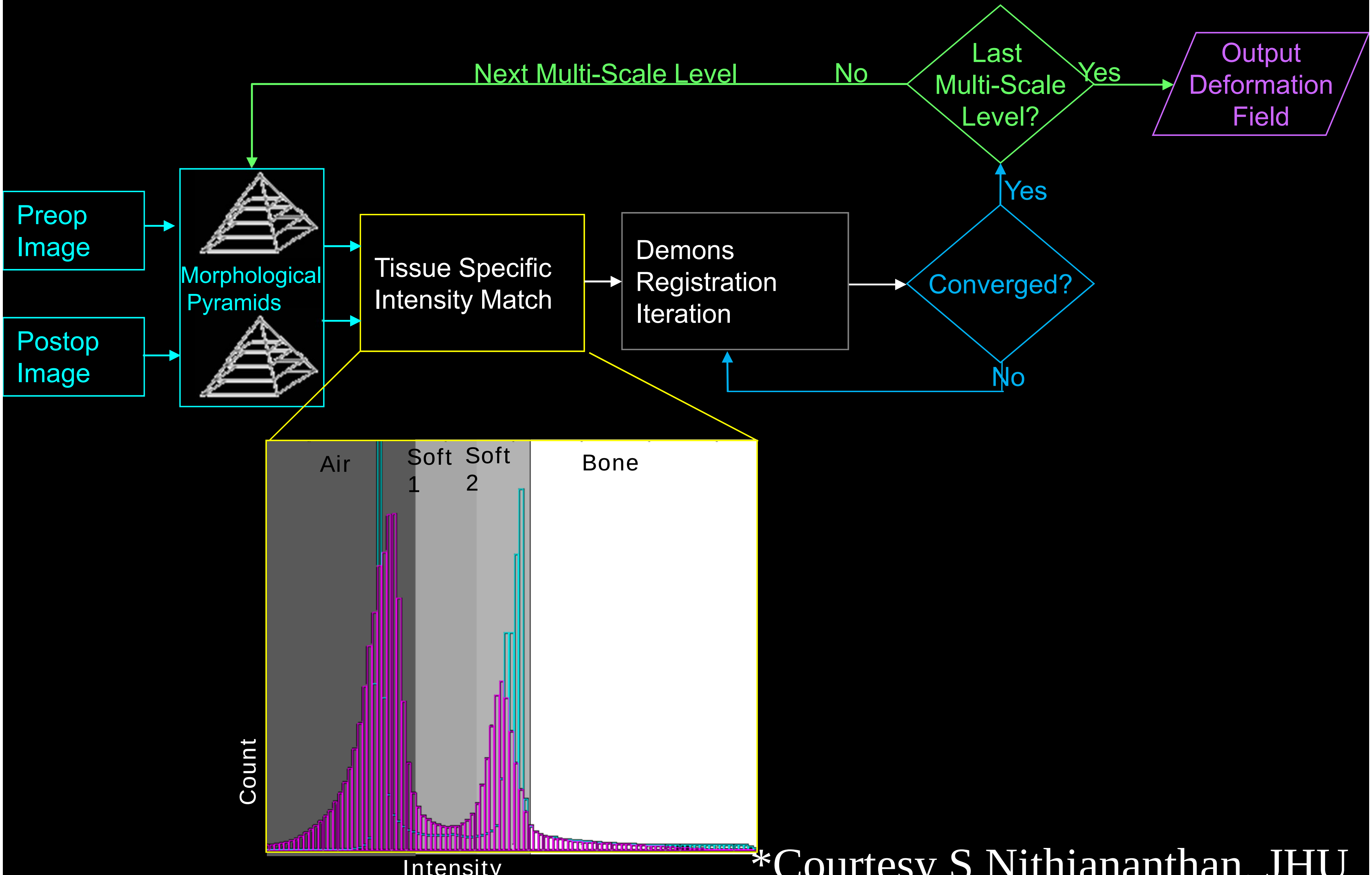
Multi-Scale Demons Registration



$$\vec{d} = \frac{2\,(m-f)\left(\vec{\nabla} f + \vec{\nabla} m\right)}{k\,(m-f)^2 + \left|\vec{\nabla} f + \vec{\nabla} m\right|^2}$$

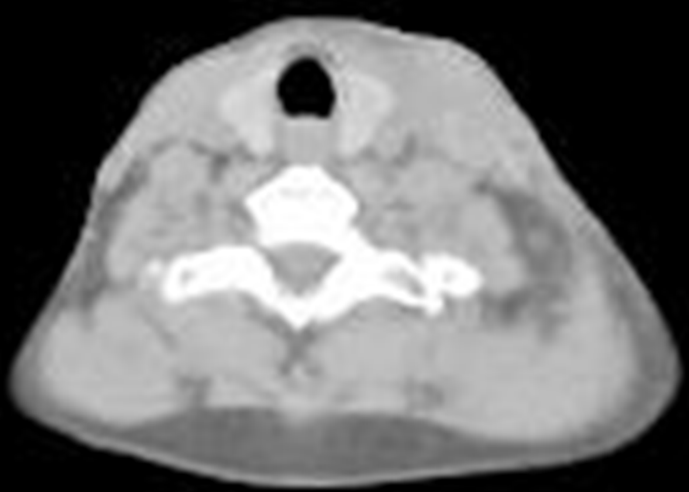
*Courtesy S Nithiananthan, JHU

Iterative Intensity Match

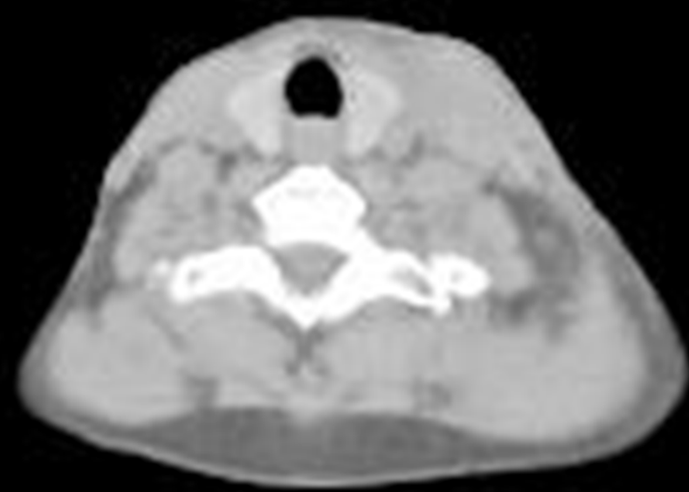


*Courtesy S Nithiananthan, JHU

Faster Convergence With Symmetric Force

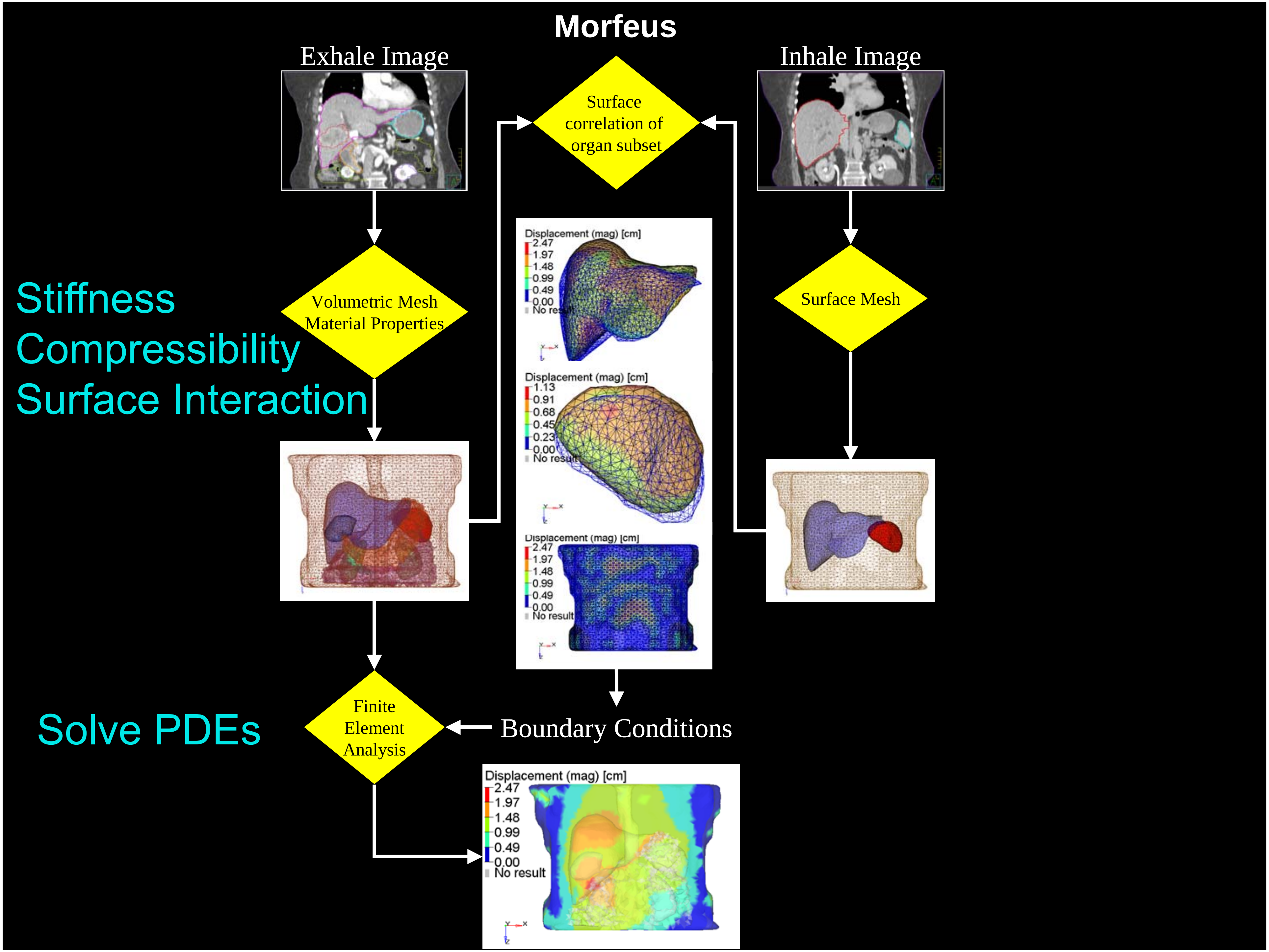


Original demons



Efficient demons

L. Dong, MD Anderson


Morfeus
Exhale Image
Inhale Image
Surface correlation of organ subset
Volumetric Mesh Material Properties
Surface Mesh
Stiffness
Compressibility
Surface Interaction
Displacement (mag) [cm]
2.47
1.97
1.48
0.99
0.49
0.00
Displacement (mag) [cm]
1.13
0.91
0.68
0.45
0.23
0.00
No result
Displacement (mag) [cm]
2.47
1.97
1.48
0.99
0.49
0.00
No result
Solve PDEs
Finite Element Analysis
Boundary Conditions
Displacement (mag) [cm]
2.47
1.97
1.48
0.99
0.49
0.00
No result

Summary (3/5)

- Many regularization techniques
- Most are geometric approximations to a physical problem
  - Used to avoid ‘chaos’ in the voxel alignment
  - Play a larger role when contrast is limited in the images
- Biomechanical Methods
  - Uncertainty in the biomechanical properties

Validation and QA

Deformation in RT

Shrinking

Breathing

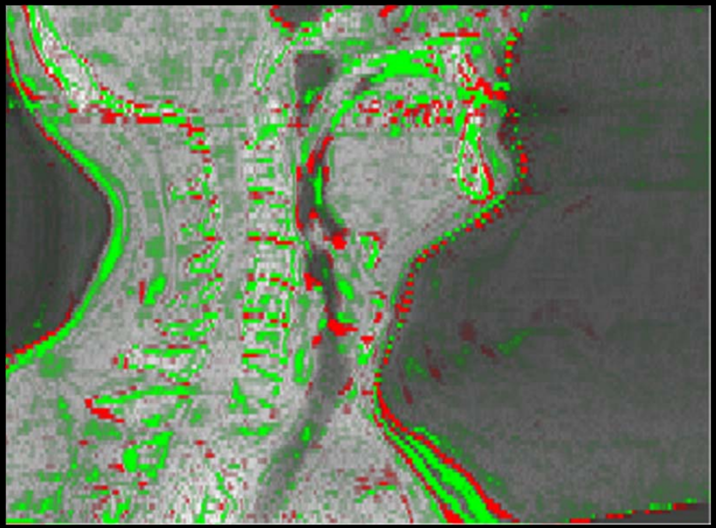
Filling

How do we make sure we are improving treatment and not introducing more error?

Validation for Deformable Registration

- Goal: Identification of boundary, internal structures, volume change, dose accumulation…
- Issues: What are the boundaries? How are the internal structures/volume changing? What is the 'true' accumulated dose?
- Potential Solutions: Indistinguishable boundaries from observer, visual validation, phantoms, matching of naturally occurring and implanted fiducials, mathematical criteria, similarity index, deformable dosimetry…

Validation Techniques



$$DSI = \frac{2\cdot |A \cap B|}{|A| + |B|}$$

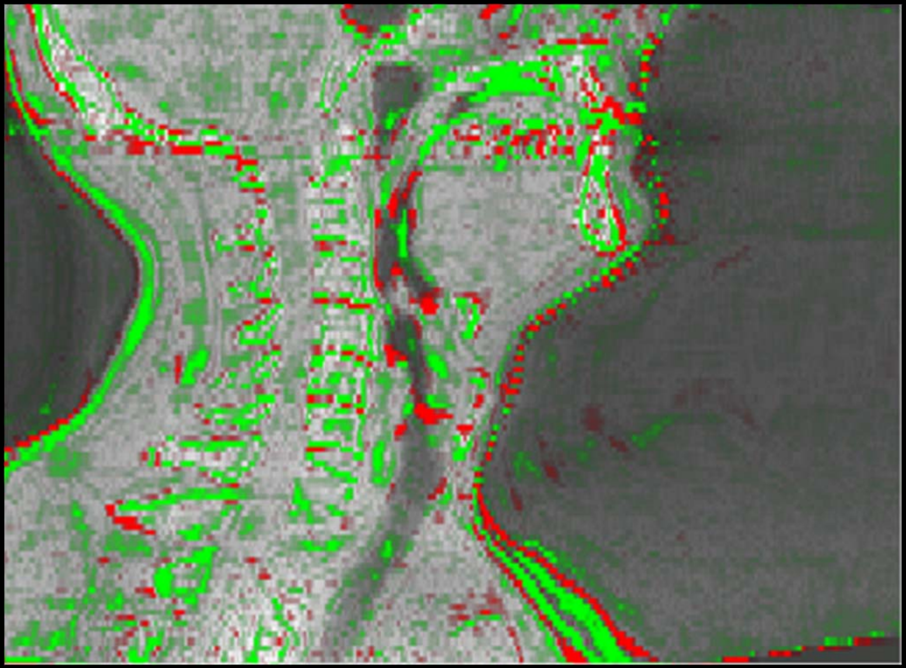
$$NCC(A,B) = \frac{\sum (A-\overline{A})(B-\overline{B})}{\sqrt{\sum (A-\overline{A})^2}\sqrt{\sum (B-\overline{B})^2}}$$

- Matching Boundaries
- Visual Comparison
- Volume Overlap
  - DICE, etc
- Intensity Correlation
  - Difference Fusions
  - CC, MI, etc
- Landmark Based
  - TRE, avg error, etc

Indistinguishable Boundaries from Observer

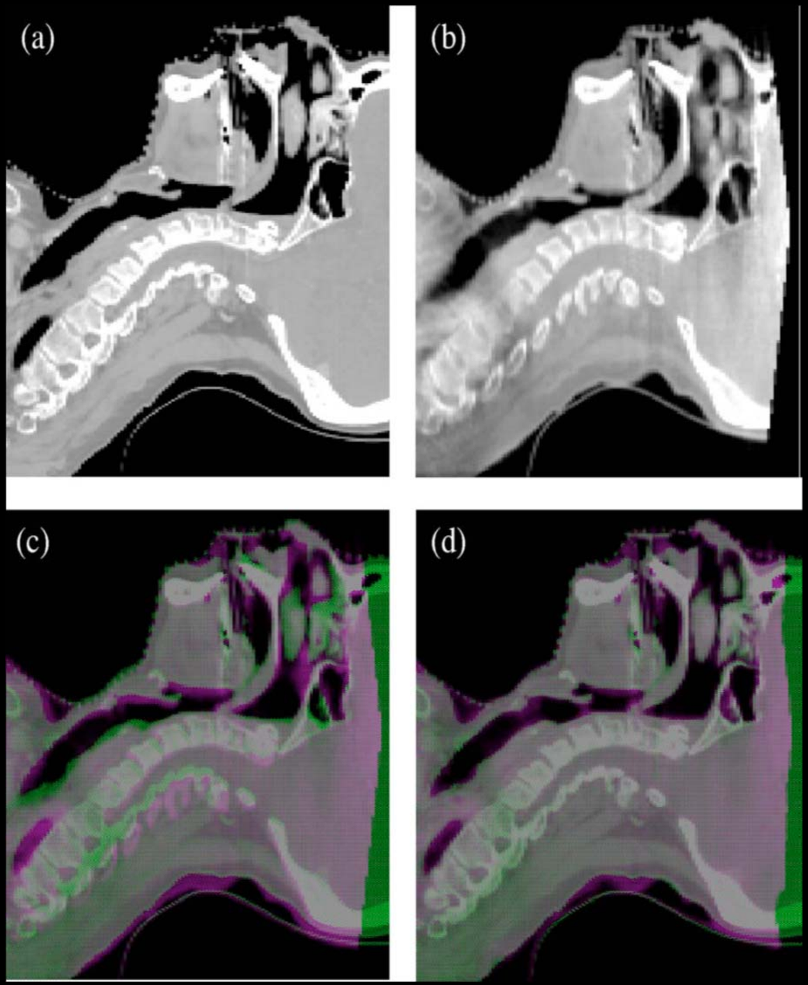
- Series of experts contour a series of structures on a series of patients
  - Hope they are somewhat consistent!
- Perform deformable registration to map structures
- Compare auto-segmentation to observers
  - DCE similarity metric, statistical tests to prove if indistinguishable, etc
- Says nothing about the internal volume of the anatomy!

Visual Verification

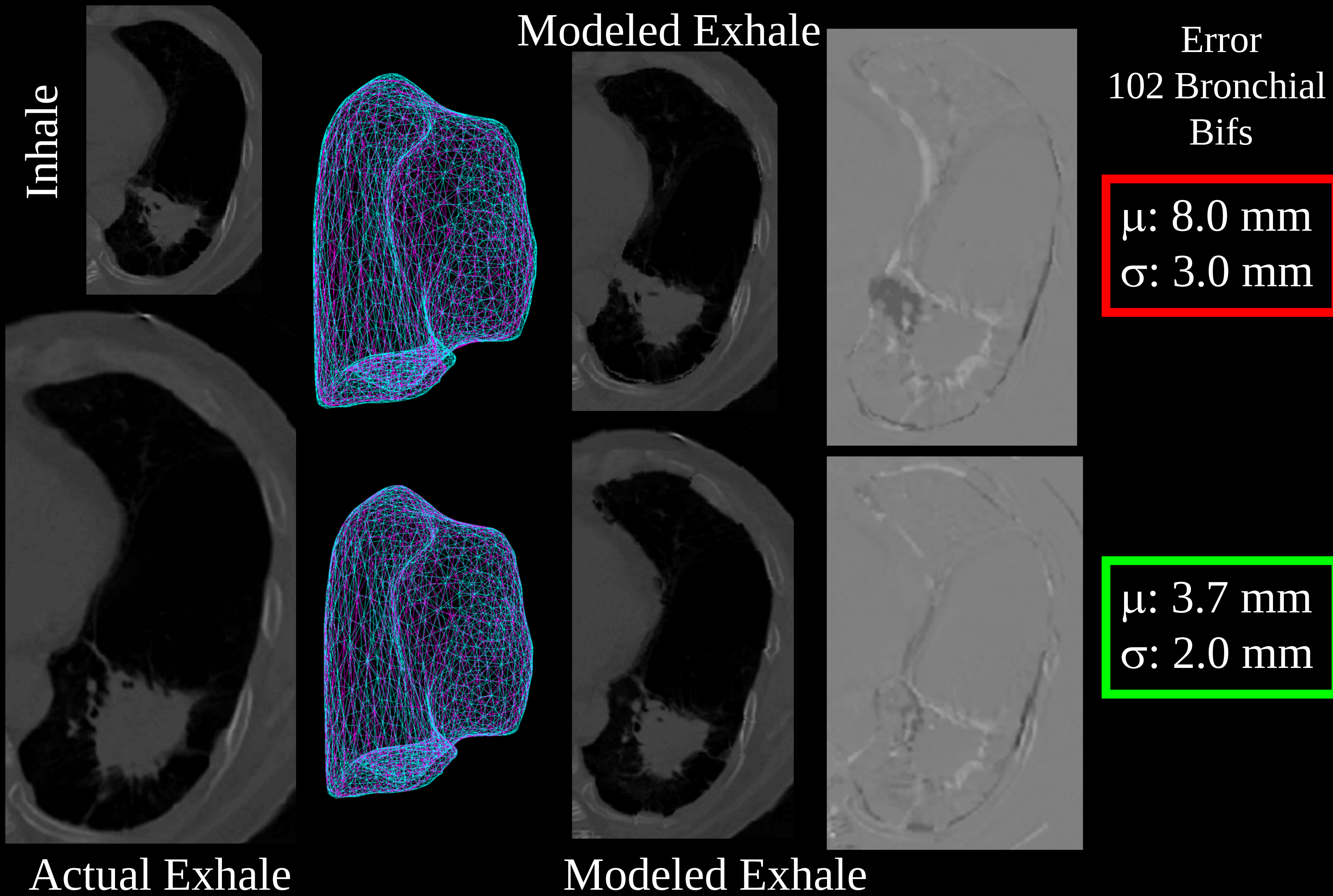


S. Nithiananthanet. al. , Med Phys 2010

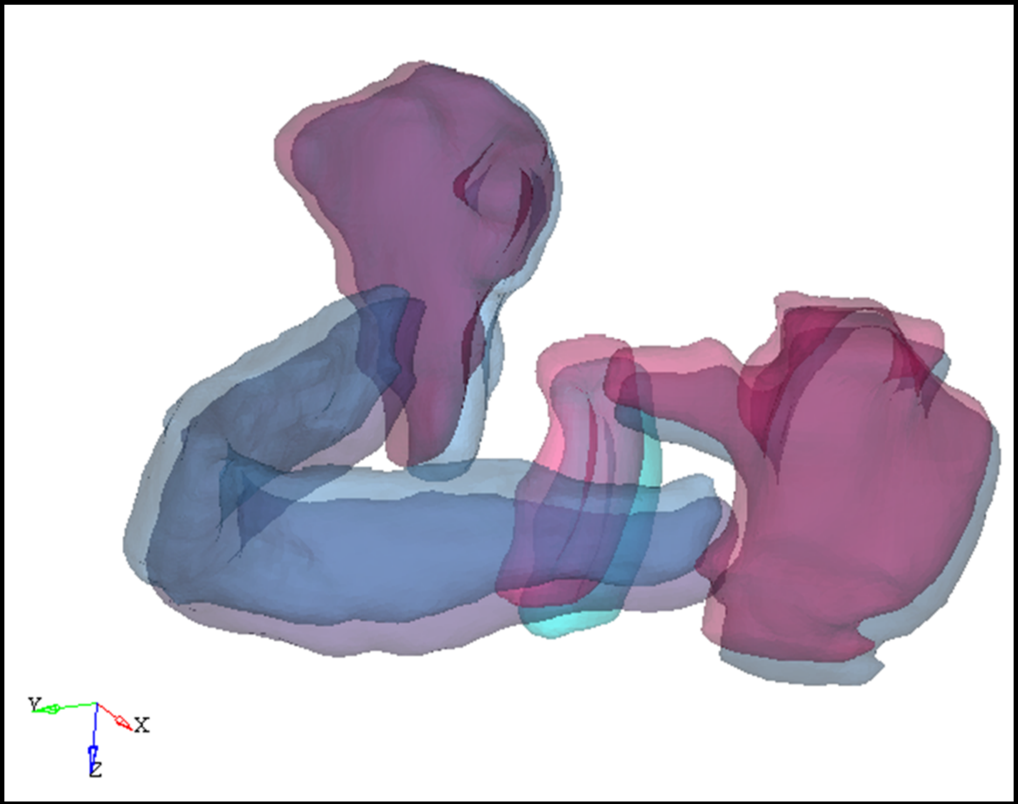
M Söhn et. al. , Med Phys 35(3) 2008



Is Contour Matching Enough?

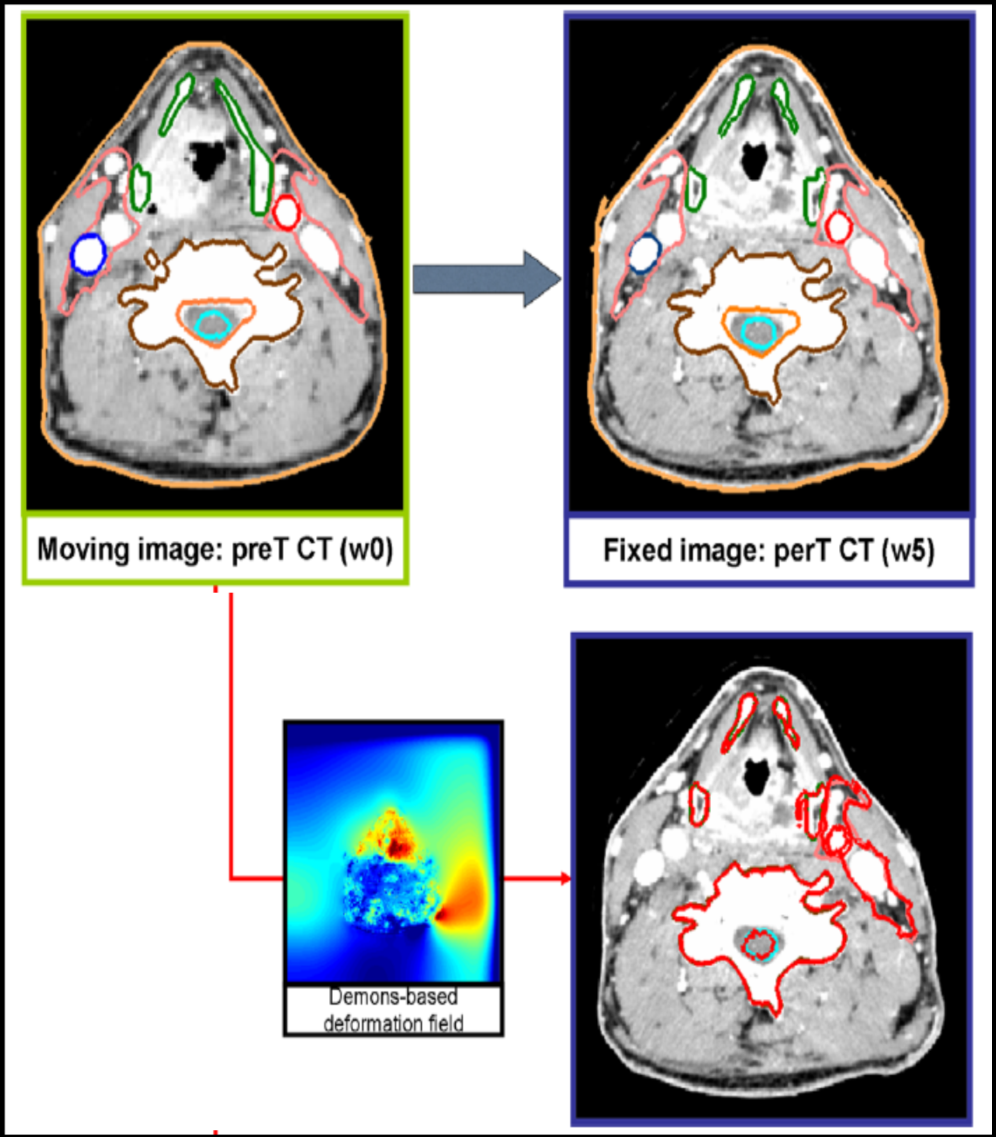


Biomechanical Models



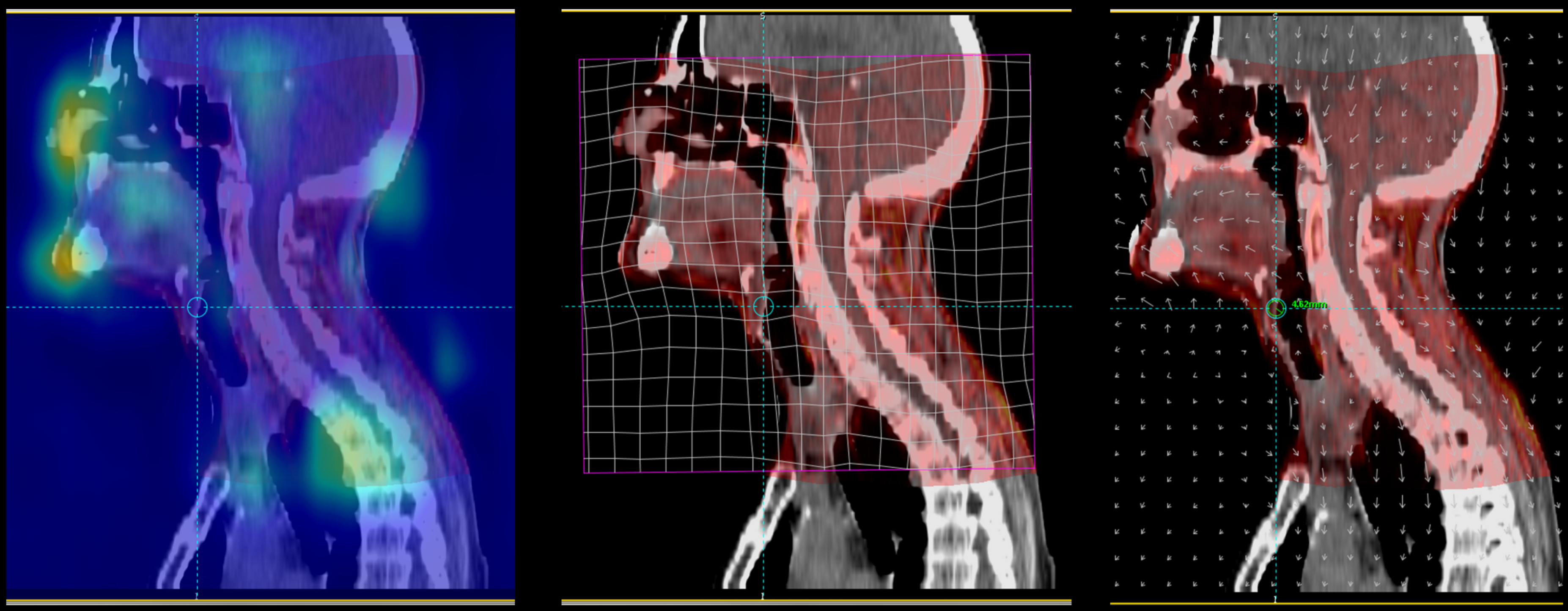
- Surface-based Accuracy
- Initial (Rigid Reg at Tx)
- 5.4±0.3 (GTV) mm
  4.1±0.4 (LPG) mm
  3.1±0.7 (RPG) mm
- 0.7±0.2 (GTV) mm
  0.7±0.2 (LPG) mm
  1.7±0.4 (RPG) mm

Demons Implementation



- P Castadot, et. al, Rad Onc 89, 2008
- 5 Patients
- Repeat CT images
- Edge-preserving denoising filter followed by level-set
- DSI median 0.85
- CC median 0.97

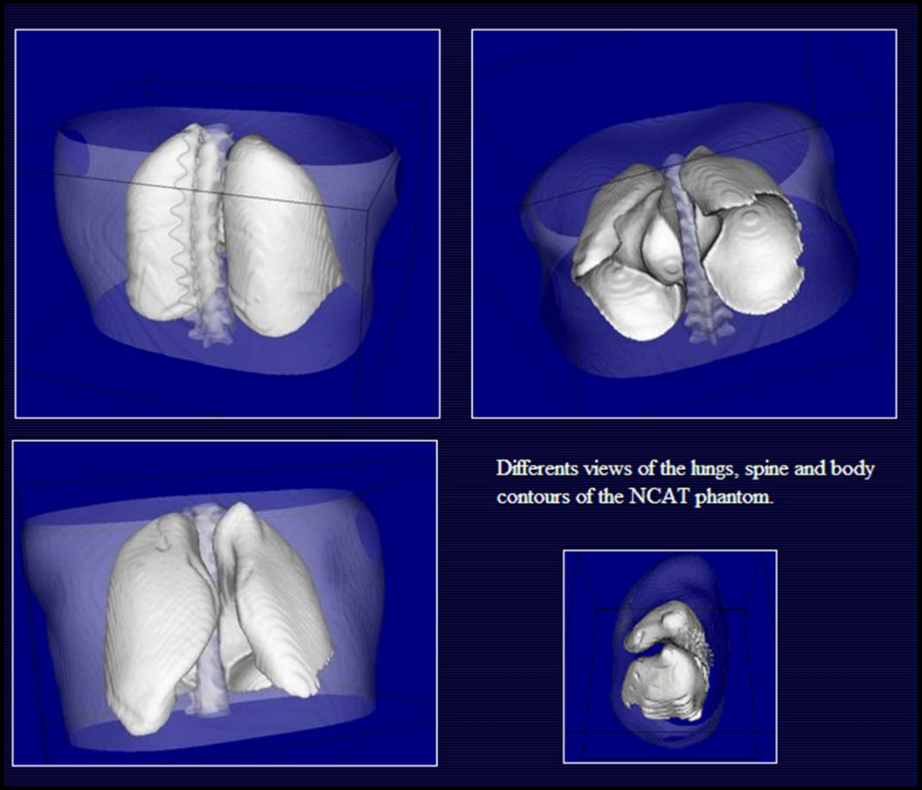
Additional Visual Information



MIRADA medical

Make every image count

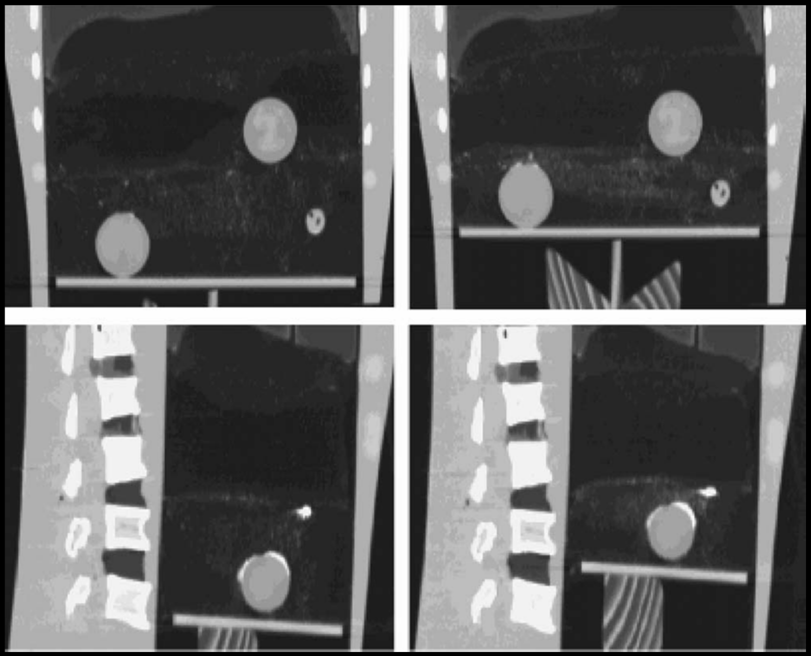
Digital or Physical Phantoms



B-spline deformation from the Visible Human data

- NCAT Phantom (Segars)
- U of Mich lung phantom
- McGill lung phantom
- Can know the true motion of all points
- Doesn't include anatomical noise and variation, likely not as complex as true anatomical motion
- Does give a 'best case' scenario for similarity/geometric defm reg algorithms

Digital or Physical Phantoms



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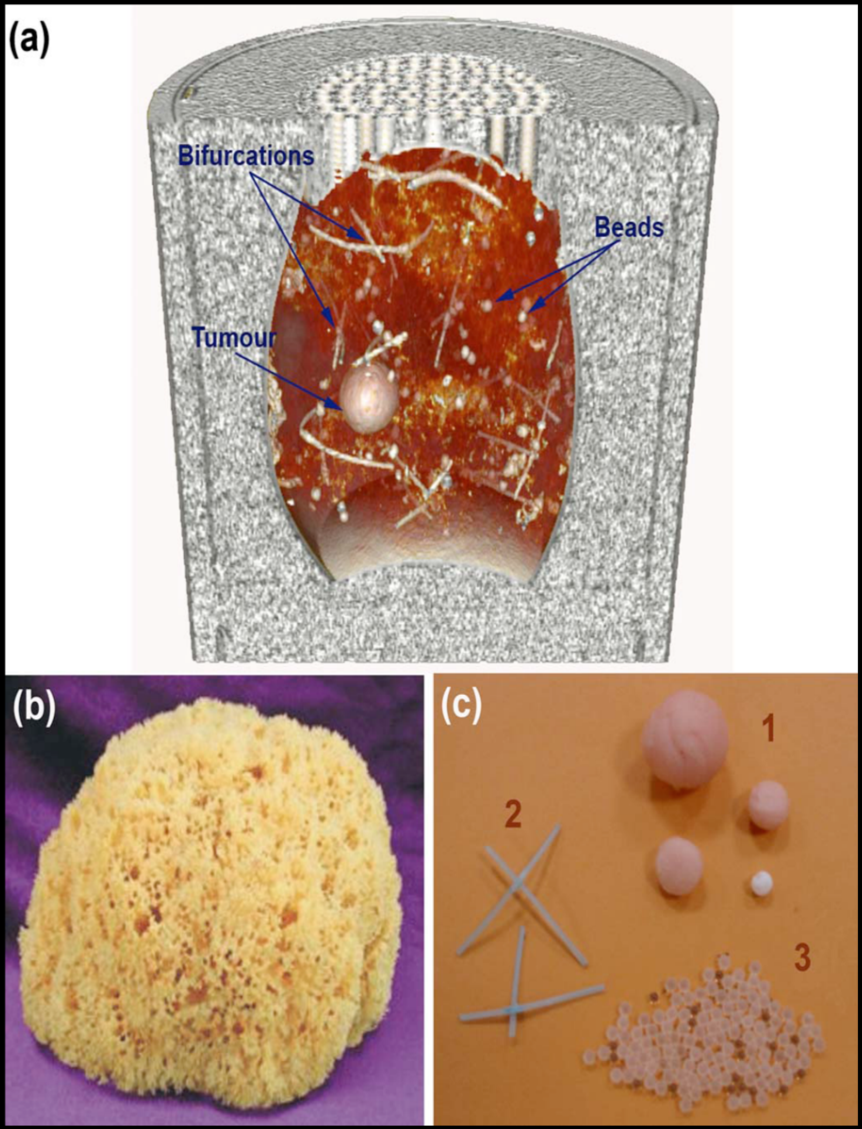
R. Kashani, Med Phys, 2008

Digital or Physical Phantoms



M. Serban, Med Phys, 2008

- NCAT Phantom
- U of Mich lung phantom
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- Does give a ‘best case’ scenario for similarity/geometric defm reg algorithms

Demons Implementation

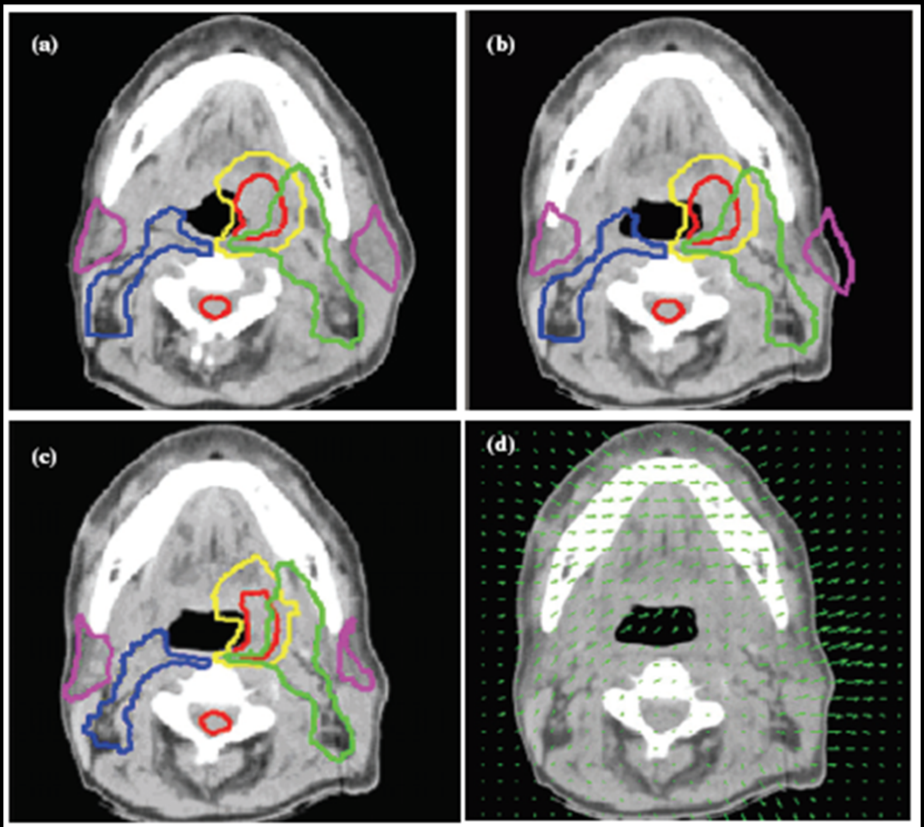
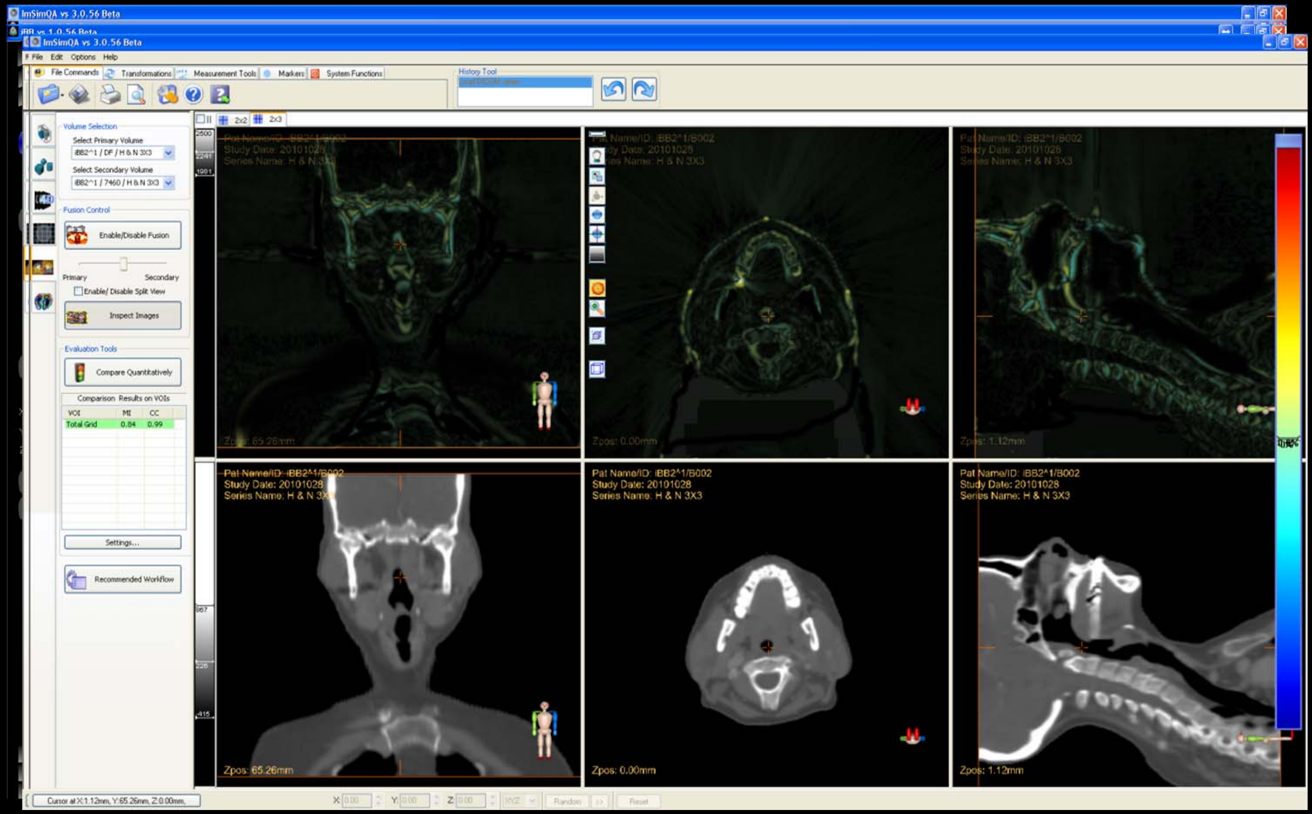


Figure 9. Autocontouring on head-and-neck images. (a) One slice of the planning CT with physician-drawn contour overlaid. (b) Corresponding slice on daily CT with planning contours directly overlaid. (c) Daily CT with deformed planning contours obtained by deformable registration algorithm. (d) Daily CT with displacement overlaid (scaled).

- Wang, et al, PMB 2005
- Difference in images (ext) and gradient of image (int) act as forces
- Addition of active force (gradient of moving image)
- Accuracy: 96% voxels < 2 mm for mathematical phantom

DIR QA in *5 Steps*

Step 5. Compare original and deformed images Quantitatively and Qualitatively – Result After DIR



ImSimQA.com

Objective assessment of deformable image registration in radiotherapy: A multi-institution study

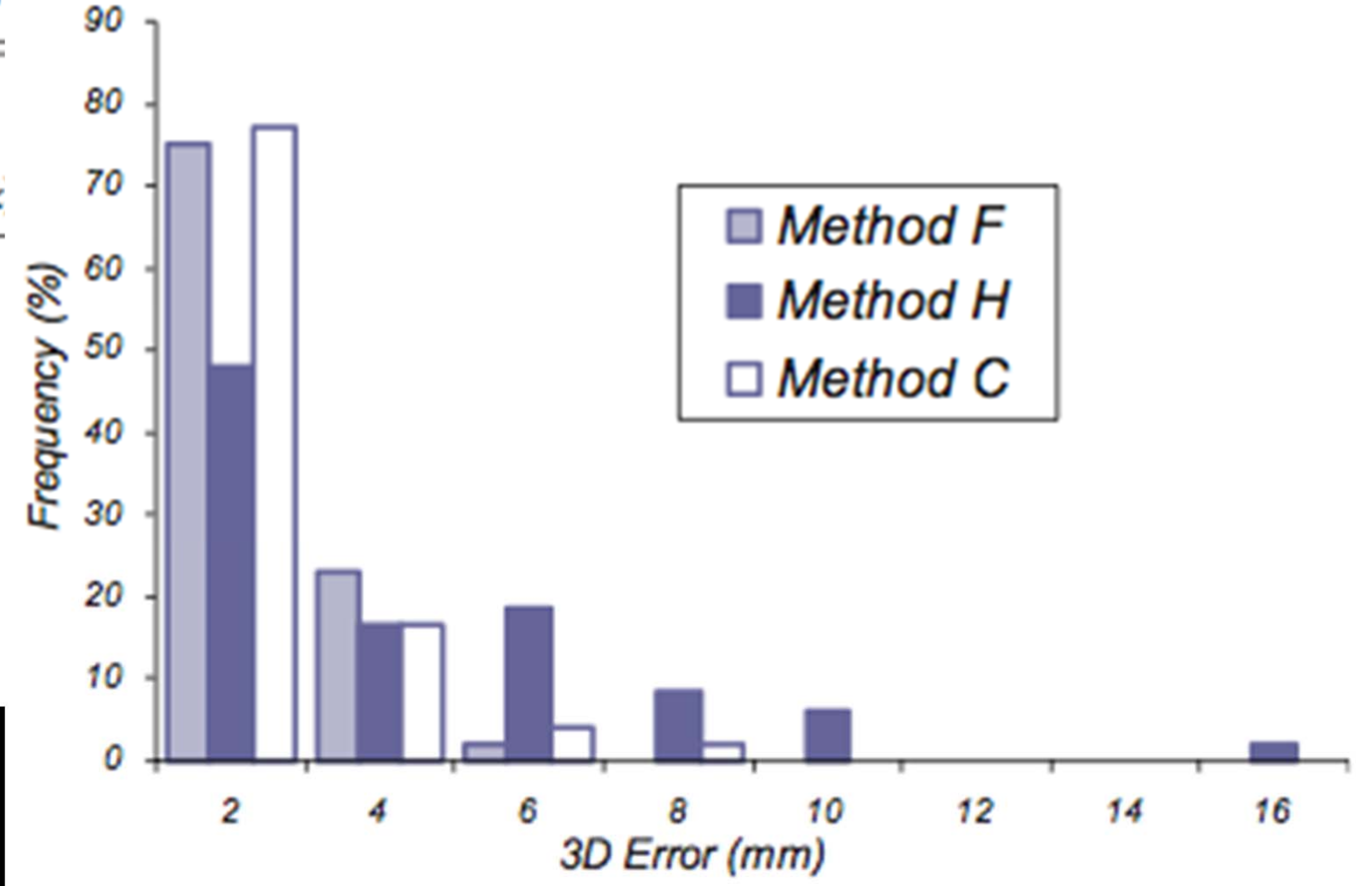
Rojano Kashani[a)]
Department of Radiation Oncology, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, Michigan 48109-0010

et. al. Med Phys 2008

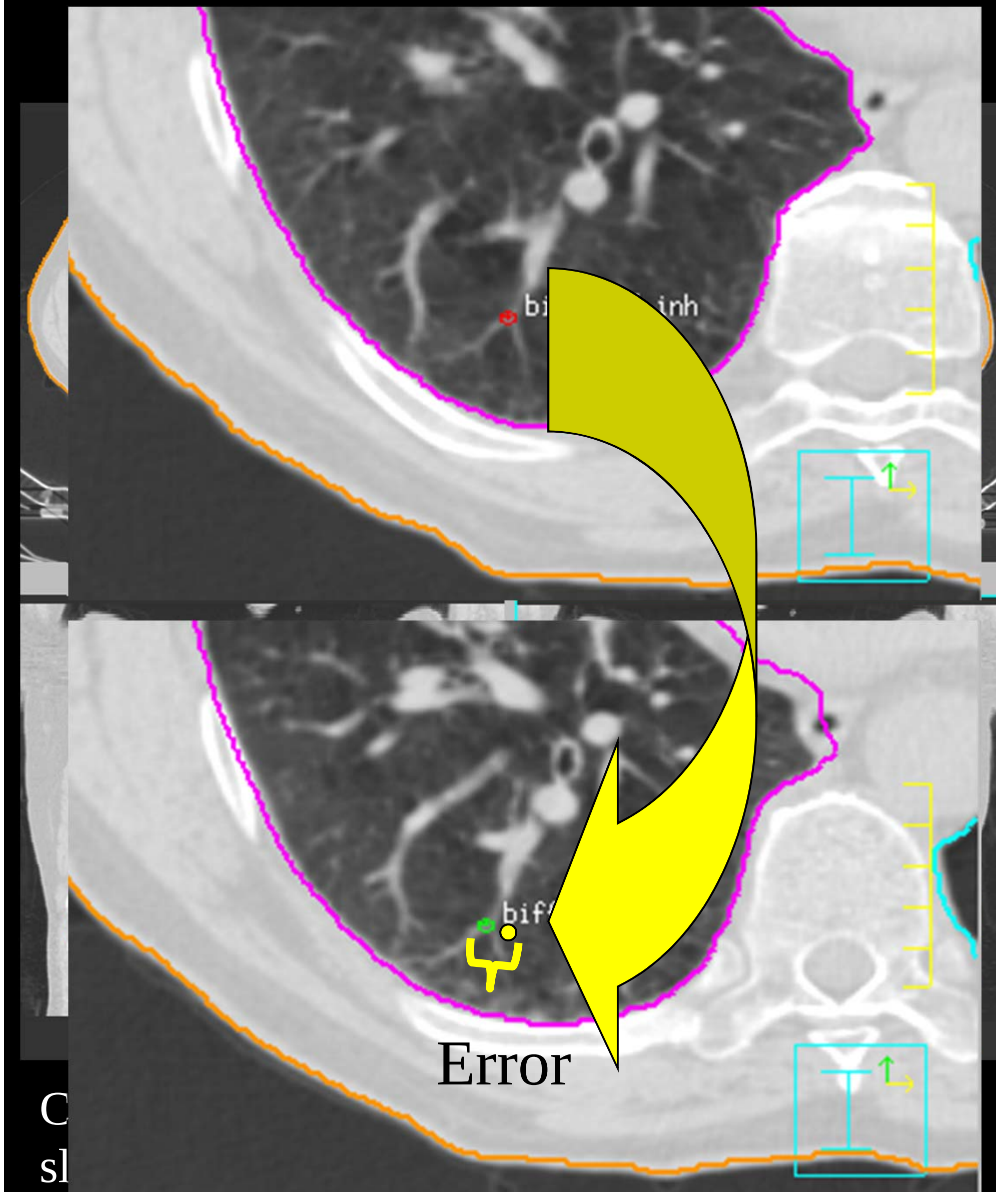
TABLE I. Summary of registration methods and references.

TABLE II. Maximum component errors in RL, AP, and SI directions, as well as the mean, standard deviation, and maximum 3D

Method (k	$d_k^{max\ f}$
A	10.1
B	5.1
C	8.1
D	6.4
E	10.3
F	5.5
G	6.0
H	15.4

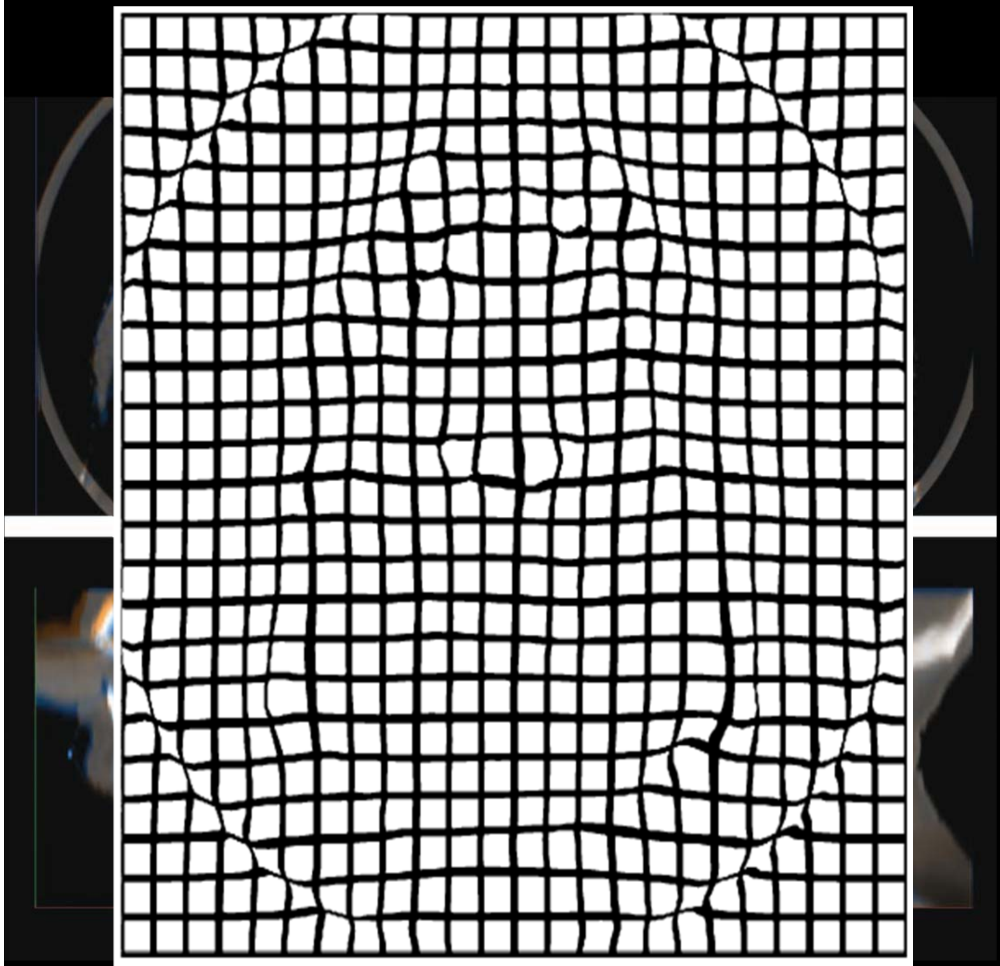


Natural/Implanted Fiducials



- Reproducibility of point identification is sub-voxel
  - Gross errors
  - Quantification of local accuracy within the target
  - Increasing the number increases the overall volume quantification
- Manual technique
- Can identify max errors

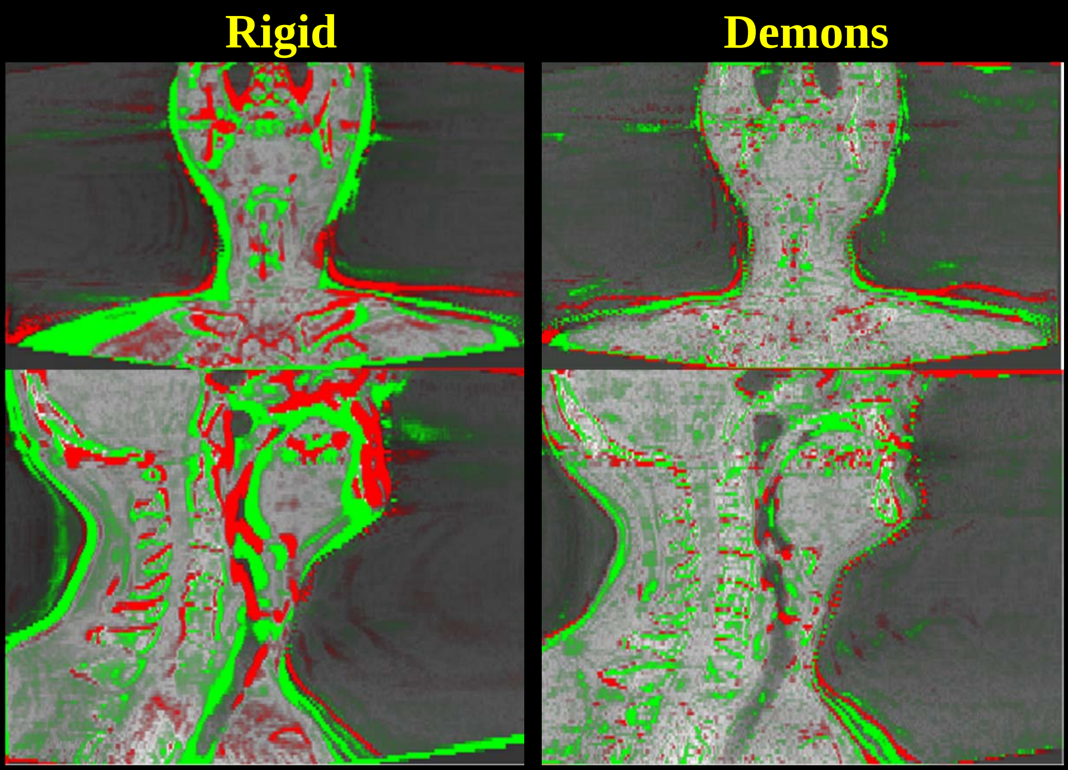
Additional Visual Information



- K Noe, et.al., Acta Onc 47(7) 2008
- Planning CT + 6 CBCTs
- 6 boney anatomy points
- Errors reduced from 2.2 ± 0.6 mm (rigid) to 1.8 ± 0.6 mm
- Time: 64 s

Red/blue visualization of the difference between the rigid registration (left) and the deformable registration (right) of CBCT image 3 to CBCT image 1

Demons Implementation



Voxel size: 1x1x2 mm^3

S. Nithiananthan, et. al.

10 H&N Radiotherapy Patients

- CBCT images acquired on Fx 1 and Fx "N" (weeks apart)

Eight Target Points

Left & right temporal bone
Left & right coronoid process
Cervical vertebra inferior aspect
Left & right auditory canal
Soft tissue point in oropharynx

Accuracy: 0.8-1.6 mm (TRE)
Time: ~ 50 s

Deformable Registration Accuracy Consortium

38 Initial Contacts; 27 Signed-up; 23 Submitted

- Aarhus – Noe, Tanderup
- Beaumont – Yan, Chi
- CMS – Han
- Lyon – Sarrut, Boldea
- McGill – Heath
- MDACC – Dong
- MGH – Sharpe
- MSKCC – Mageras, Hu
- NKI – Sonke
- Philips – Kaus, Vik
- PMH – Brock, Nguyen
- Stanford – Xing, Xie
- TMX – Dufort, Stundzia
- U FL – Xia, Samant
- KUL – Van den Heuvel
- U MD – Shekhar, Plishker
- U MD – Shekhar, Wu
- UCL (UK) – Hawkes, Crum
- UCL (UK) – Hawkes, McClelland
- UCL (BE) – Lee, Parraga
- UNC – Foskey, Chaney
- Varian – Nord
- WUSTL – El Naqa, Yang

Europe (7) - North America (12) – Industry (4)

Study Goals

- Provide a common dataset to multi-institutions
- Determine preliminary accuracy results for multiple algorithms and multiple implementations
- Report quantitative accuracy in a common format
  - Identified naturally occurring fiducials
  - Vector magnitude of error (mean and SD)

Algorithms

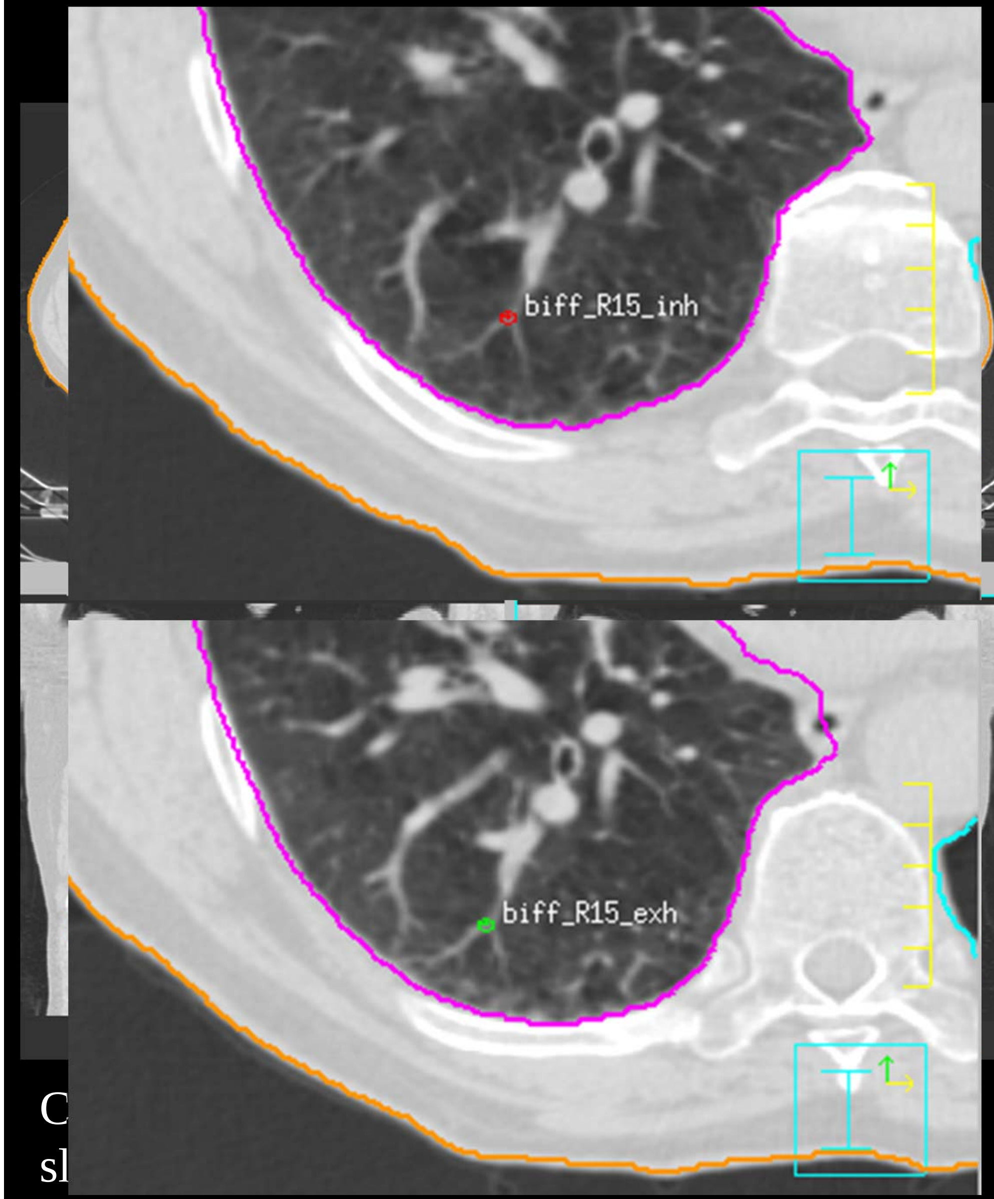
SIMILARITY METRIC

- MSE/MSD/SSD: 14
- CC: 3
- MI: 2
- Contour matching: 2
- Points: 1
- N/A: 1

INTERPOLANT

- B-Spline: 5
- Demons/Optical Flow: 5
- Free Form: 4
  - Constrained by E min, linear elastic, and smoothing
- Thin-Plate Spline: 3
- Viscous/Fluid Flow: 3
- Finite element analysis (linear elastic): 1
- Juggler Algorithm: 1
- Quadrature constraint motion Est: 1

MIDRAS Data: Lung



C
sl

- 4D CT – Lung
  - 0% and 50%
- Deform INH to EXH
- Contours:
  - External (INH & EXH)
  - Lung (INH & EXH)
  - Tumor (INH only)
- 'Gold Standard'
  - 17 bifurcation R lung
  - 17 bifurcations L lung
  - 2 calcifications Heart
  - 2 calcifications Aorta

Brock, Deformable Registration Accuracy Consortium, IJROBP 2009

Data: Lung Motion [mm]

Right Lung:

LR: $\mu = -0.5$ $\sigma = 1.0$

- Range: -2.0 – 1.0

AP: $\mu = 1.6$ $\sigma = 1.2$

- Range: 0 – 4.9

SI: $\mu = 2.1$ $\sigma = 4.0$

- **Range: 0 – 15.0**

Heart:

LR: -3.9, -3.9

AP: 2.9, 0

SI: 5.0, 5.0

Left Lung:

LR: $\mu = -1.1$ $\sigma = 1.6$

- Range: -2.9 – 1.0

AP: $\mu = -1.0$ $\sigma = 2.1$

- Range: -2.9 – 4.9

SI: $\mu = 4.1$ $\sigma = 4.8$

- **Range: 0 – 15.0**

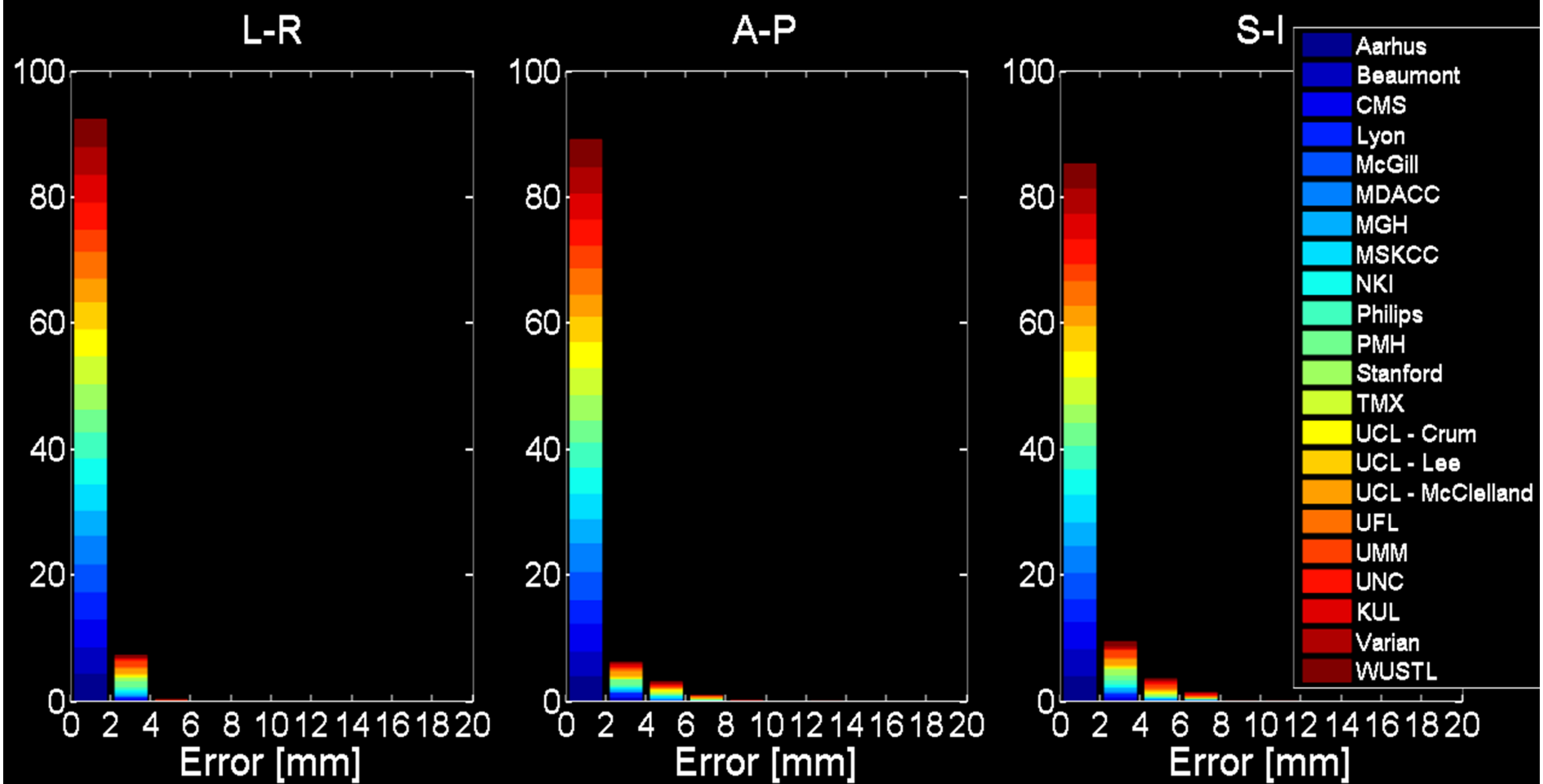
Aorta:

LR: -1.0, -5.9

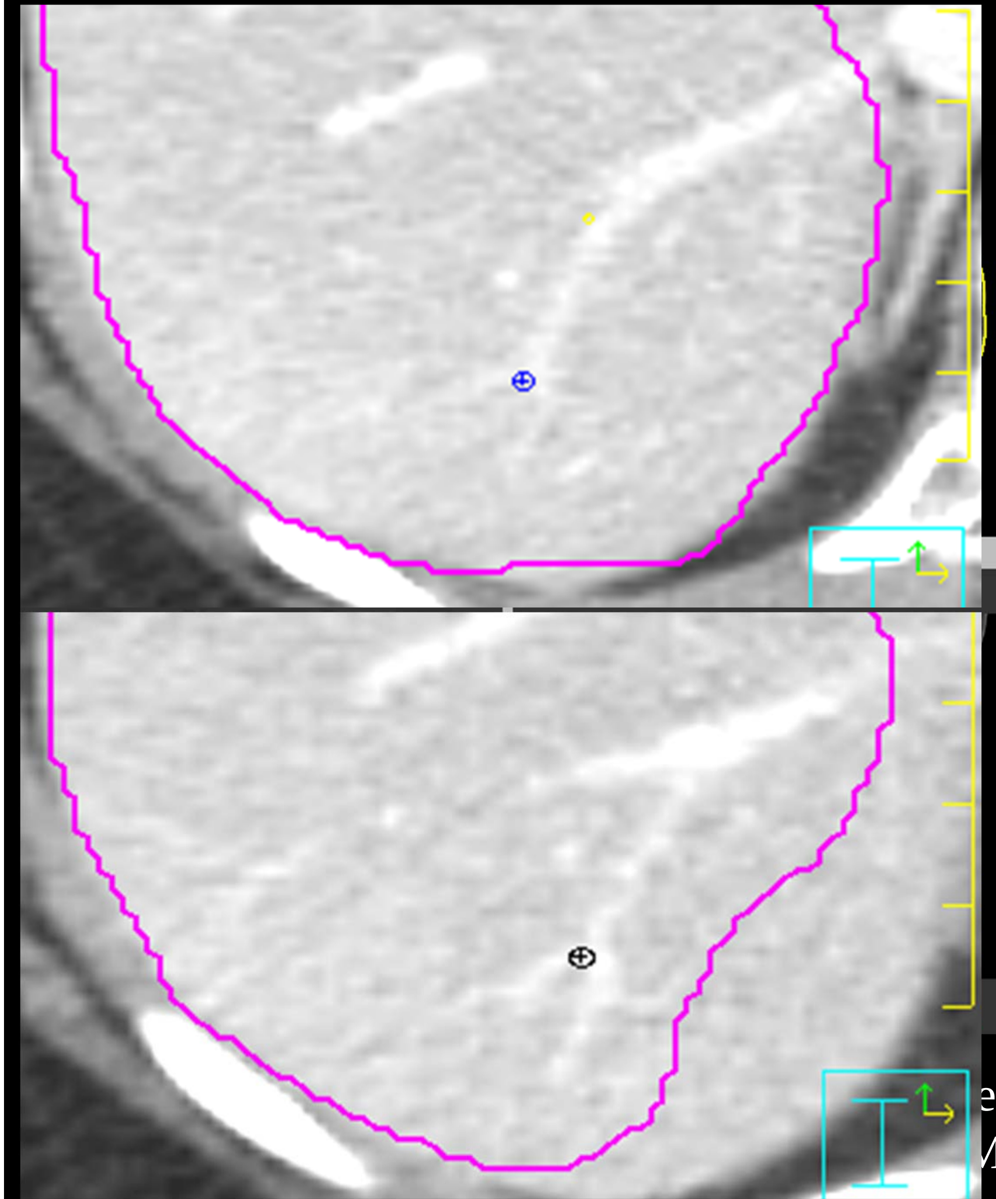
AP: -1.0, 0

SI: 0, 2.5

MIDRAS Results: Lung 4D CT (22)
% Bifurcation Points



Data: Liver



- 4D CT – Liver
  - 0% and 50%
  - With IV contrast
- Deform EXH to INH
- Contours
  - External
  - Liver
  - Tumor (EXH only)
  - Kidneys
- 'Gold Standard' – 4D CT
  - 25 bifurcations in the liver
  - 5 bifurcations in the L kidney
  - 6 bifurcations in the R kidney

Data: Liver Motion [mm]

<u>Liver</u>

LR: $\mu = -0.7$ $\sigma = 1.4$

- Range: -3.9 – 2.0

AP: $\mu = -4.1$ $\sigma = 2.2$

- Range: -8.8 – 2.9

SI: $\mu = -11.9$ $\sigma = 1.9$

- **Range: -7.5 – -15.0**

<u>Kidneys</u>

LR: $\mu = -0.8$ $\sigma = 1.4$

- Range: -2.9 – 1.0

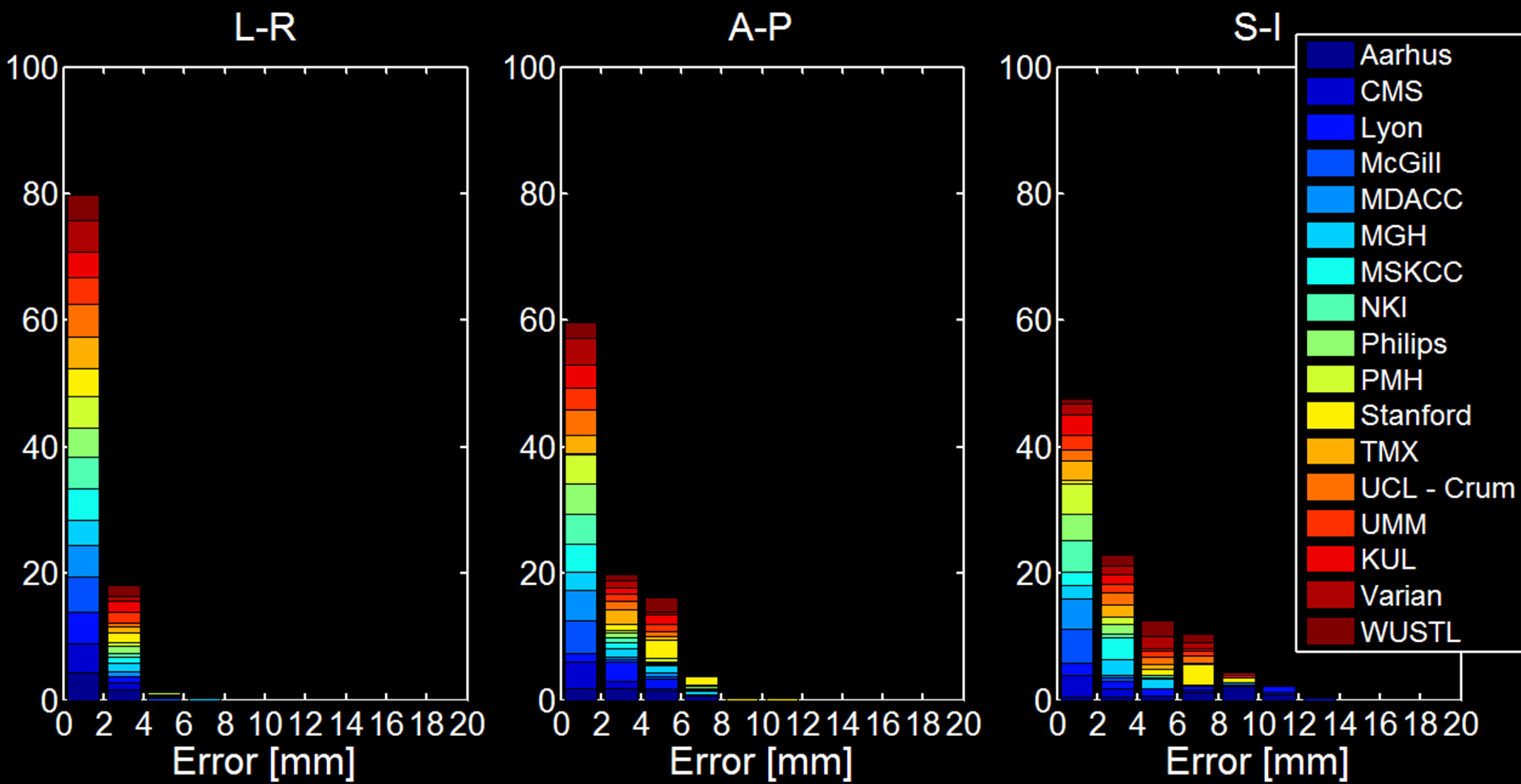
AP: $\mu = -3.2$ $\sigma = 2.9$

- Range: -6.8 – 1.0

SI: $\mu = -7.3$ $\sigma = 3.8$

- **Range: -2.5 – -12.5**

Results: Liver 4D CT (17)
% Bifurcation Points



MIDRAS Results

- Lung:
  - max error > 5 mm SI, N = 14
  - max error > 10 mm, N = 2
  - NO max error > 5mm, N = 3
- Liver:
  - max error > 5 mm SI, N = 12
  - max error > 10 mm, N = 4
  - NO max error > 7 mm, N = 7
- Implementation matters
  - 3 Demons algorithms (Liver): μ = 2.3, 3.3, 4.8 mm
  - 3 Thin Plate Spline (Liver): μ = 2.1, 2.9, 7.8 mm
  - 4 B-Spline (Lung): μ = 1.6, 2.0, 2.5, 3.0 mm
- Time: 100s – 100,000s!

Mathematical and Similarity Metrics

- Jacobian: identifies volume change and inversion
  - Inversion = physical violation
  - Volume change – what is right?
- Similarity Metric (SSD, MI, NCC)
  - Must be independent of technique
  - Only MI for multi-modality

Understand Uncertainties Present

- 30% uncertainty in biomechanical model $\rightarrow$ up to 4.5 mm uncertainty in volume organ deformation
  - Chi, et. al., Med Phys 2006
- SD 0.8 mm contour uncertainty (prostate MR) has no detectable change in geometric accuracy for contour-guided deformation
  - Brock, et. al., Med Phys 2008
- Sensitivity of results: Vary the vector field and evaluate the change in similarity metric
  - Hub, et. al., IEEE TMI 2009
- Does mapping B to A = A to B?

Summary (4/5)

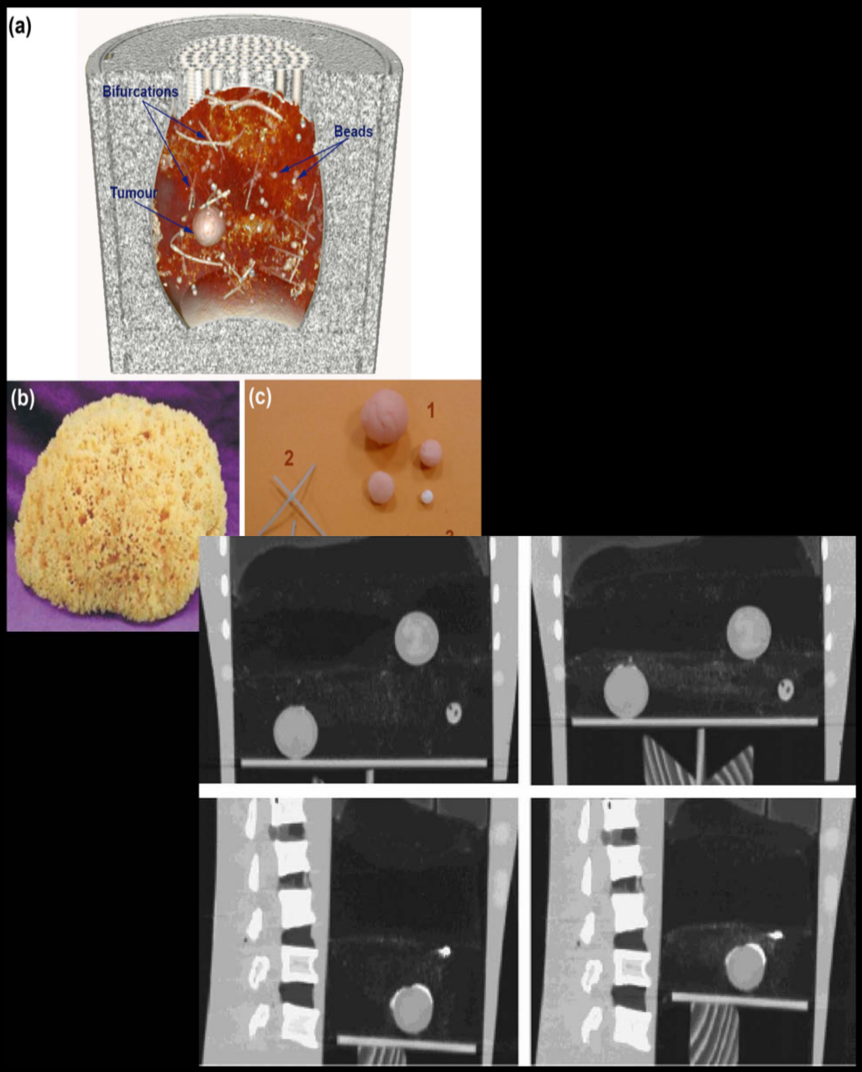
- Validation is critical!
- Quantitative validation is necessary when implementing a new algorithm
  - TG 132
- Qualitative validation will have to be sufficient for clinical use
  - Must remember the limitations of the algorithm!

Uncertainties in the use of Deformable Registration

Clinical Application: Accuracy of Dose Accumulation

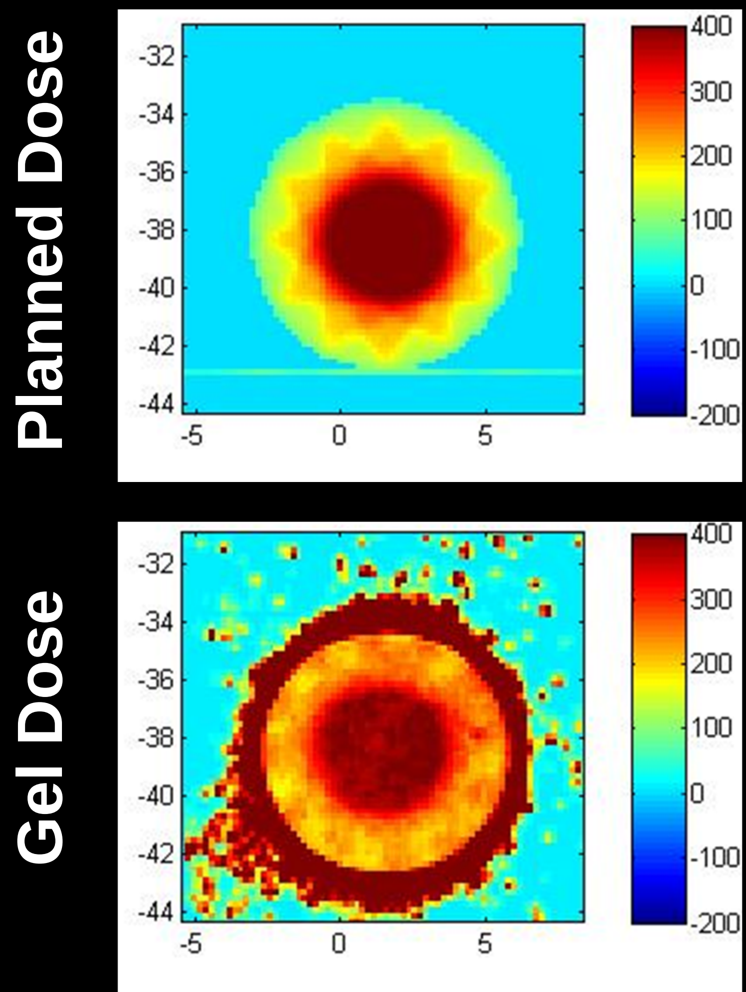
- How do we QA dose accumulation?
- What is the 'gold' standard?
  - Ion chambers/TLDs/Film can't deform
  - Put them in a deforming phantom?
- How accurate does it need to be?
  - Every voxel exactly right?
  - Isodose line comparison (2%/2mm)?

Deformable Phantom with Point Dosimeters



- Excellent accuracy of dosimeters
- Limited to local (and rigid) dose validation

Use of Deformable Gel Dosimeter

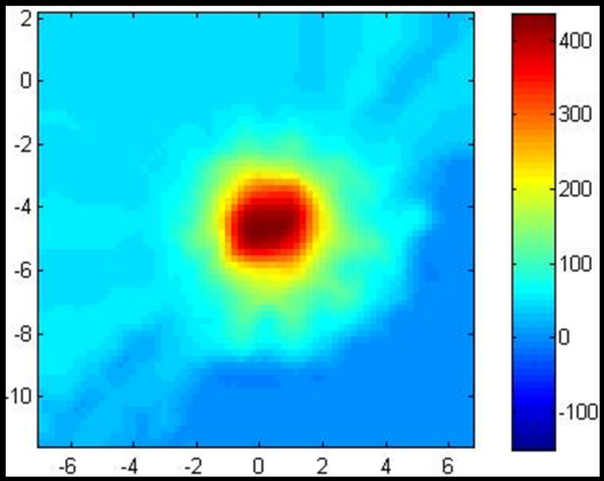


- Polymer based gel
- MR read out
- Mean difference (4 Gy max):
  - ~ 1% ± 5%
- 95% of isodose surfaces are within 1.5 mm

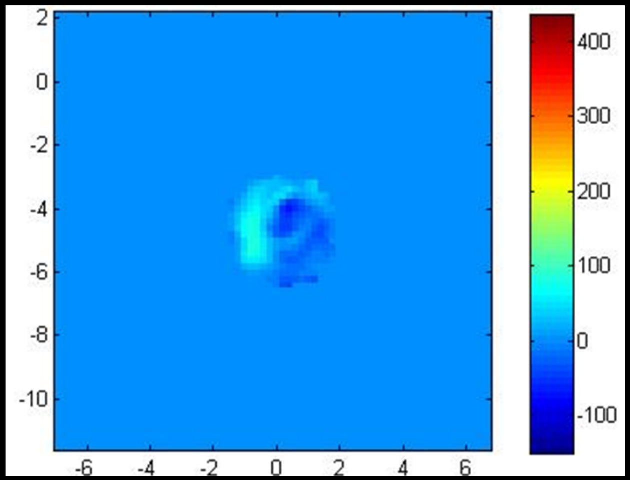
Niu, Med Phys, submitted

Use of Deformable Gel Dosimeter

Accumulated Dose



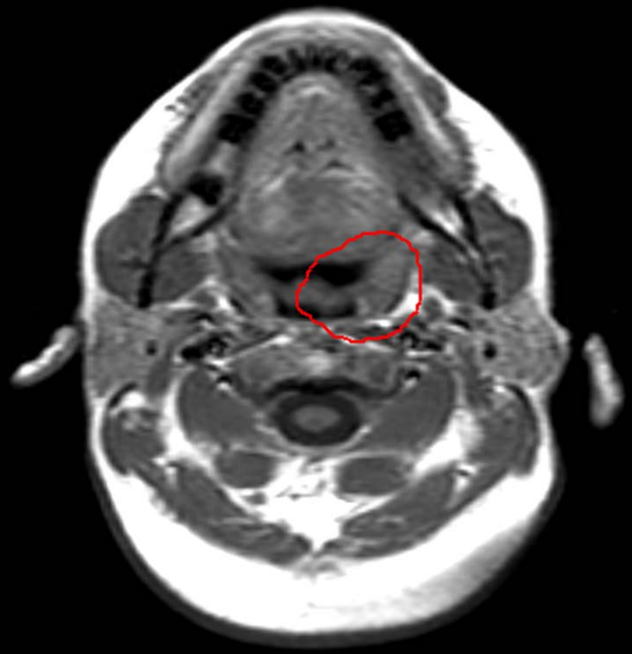
Gel Dose



- Deform gel cyclically by 1 cm
- Deliver 4 Gy in 8 beam plan
- Defm Acc: < 2 mm
- Gel readout in MR
- Calibration using control gel
- Difference:
  - Mean: 1% ± 13%
- 95% Isodose within 2.5 mm
- 92% of voxels within SD of reference

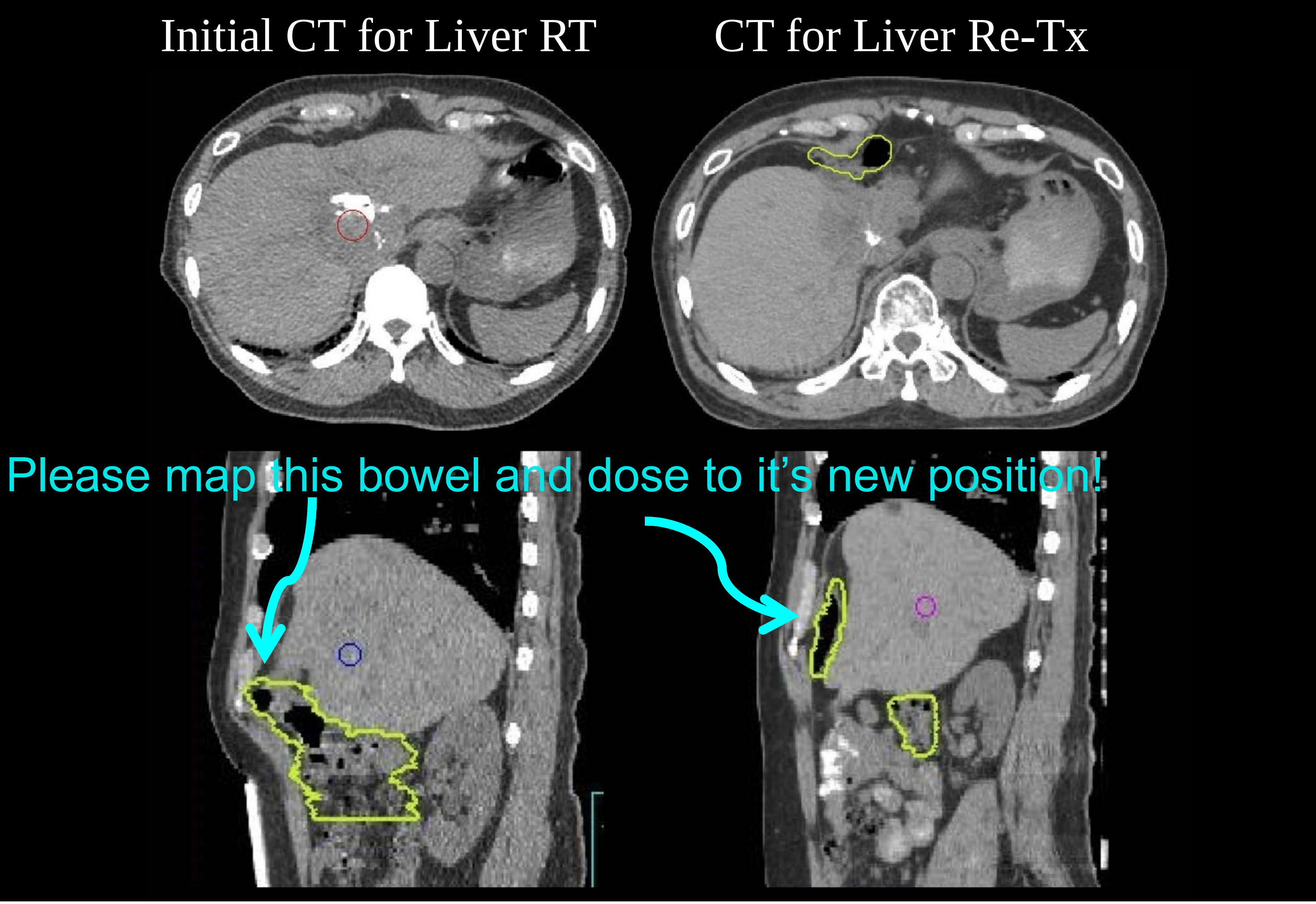
Pushing the Limits!
Deformable Registration for Adaptive and Re-Treatment

Response Happens!

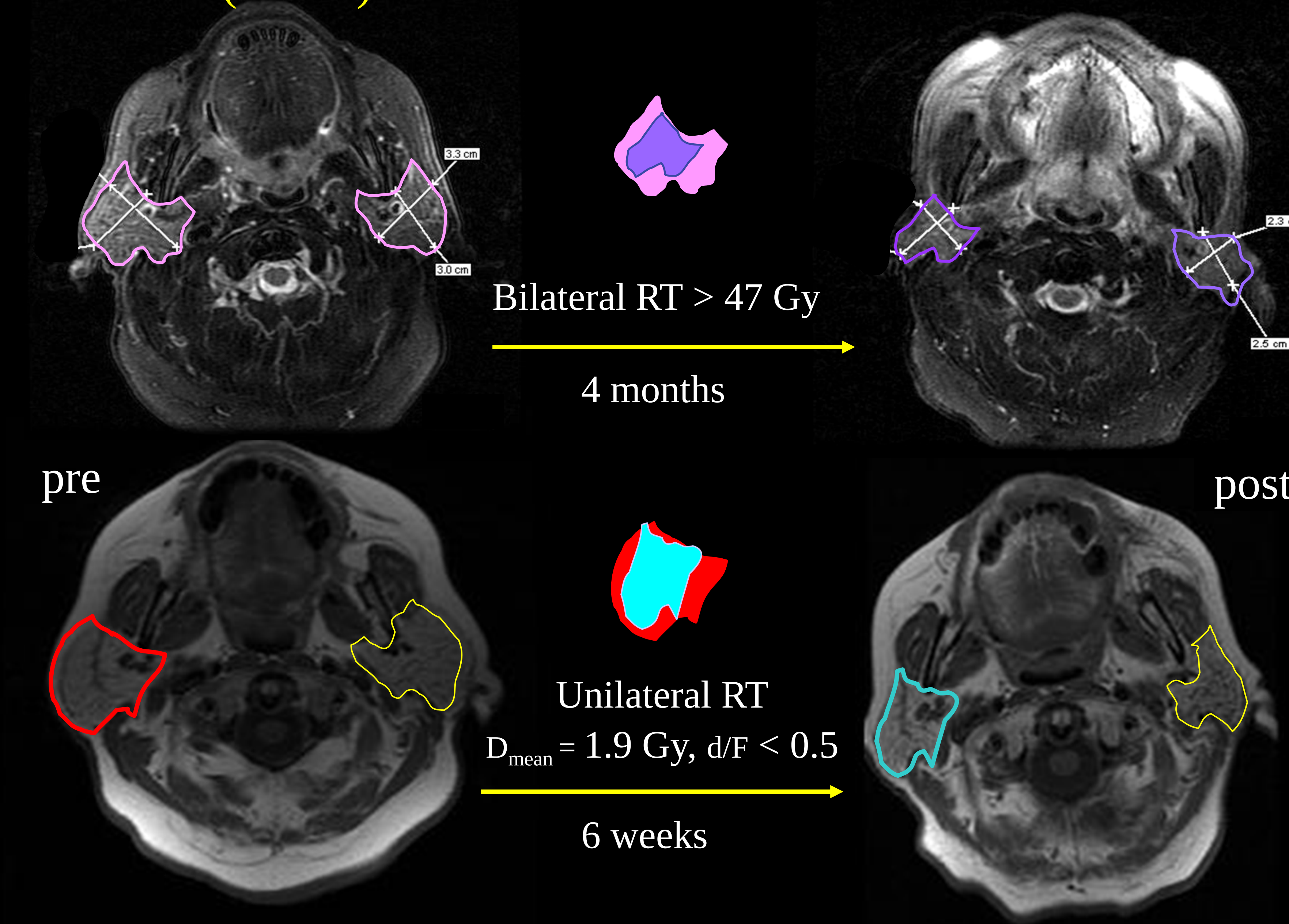


- We are replanning now, without deformable registration
- Safely integrate new tools
  - DIR for contour propagation
    - Don't like the results? Edit the contours!
  - Dose Accumulation
    - Don't manually edit the DVF!
- Use EXTREME caution if you are using deformable dose accumulation to push the re-Tx limits!

Deformable Registration for Re-Tx



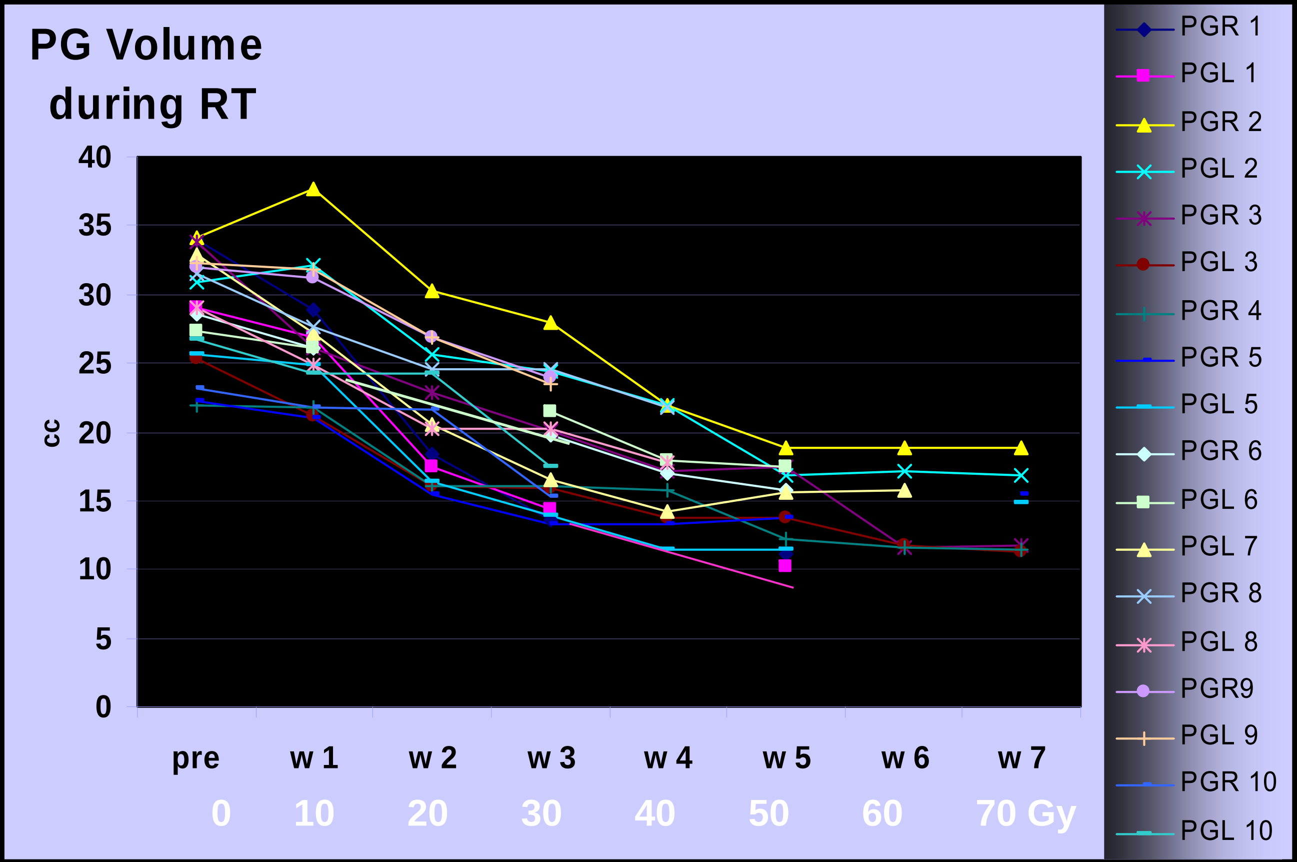
Retrospective Study of Volumetric Changes in Major Salivary Glands (MSGs) with curative RT in H & N Cancer Patients



Prospective Monitoring of Changes in Parotid Gland (PG) Size vs Dose Accumulated

10 patients: weekly MRIs during RT

29 cc



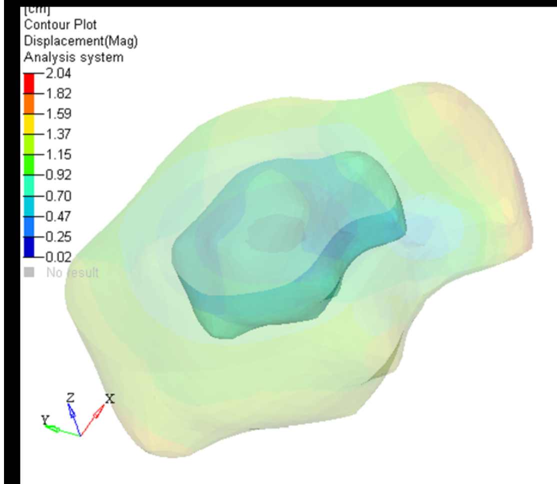
14.8 cc

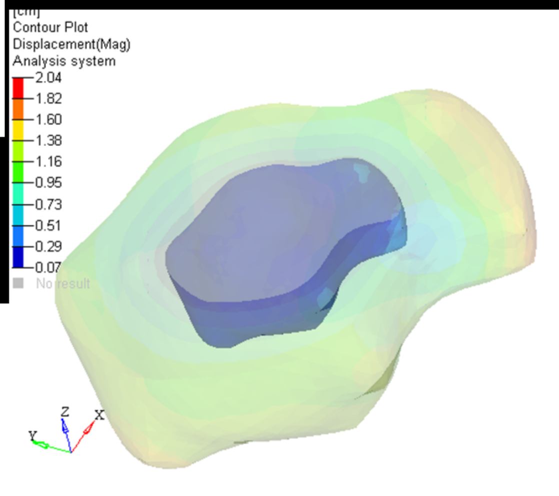
Average Reduction: 48 %

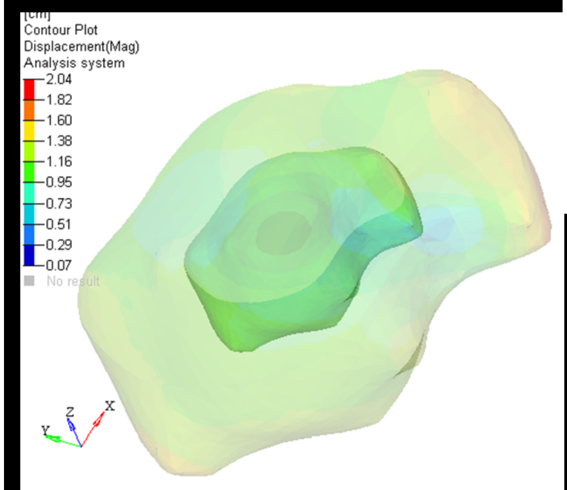
Shrinking Volume

- How do we model the reduction?
- Does it have dosimetric consequences?
- What volume to we use for the DVH?

Modeling Volume Reduction

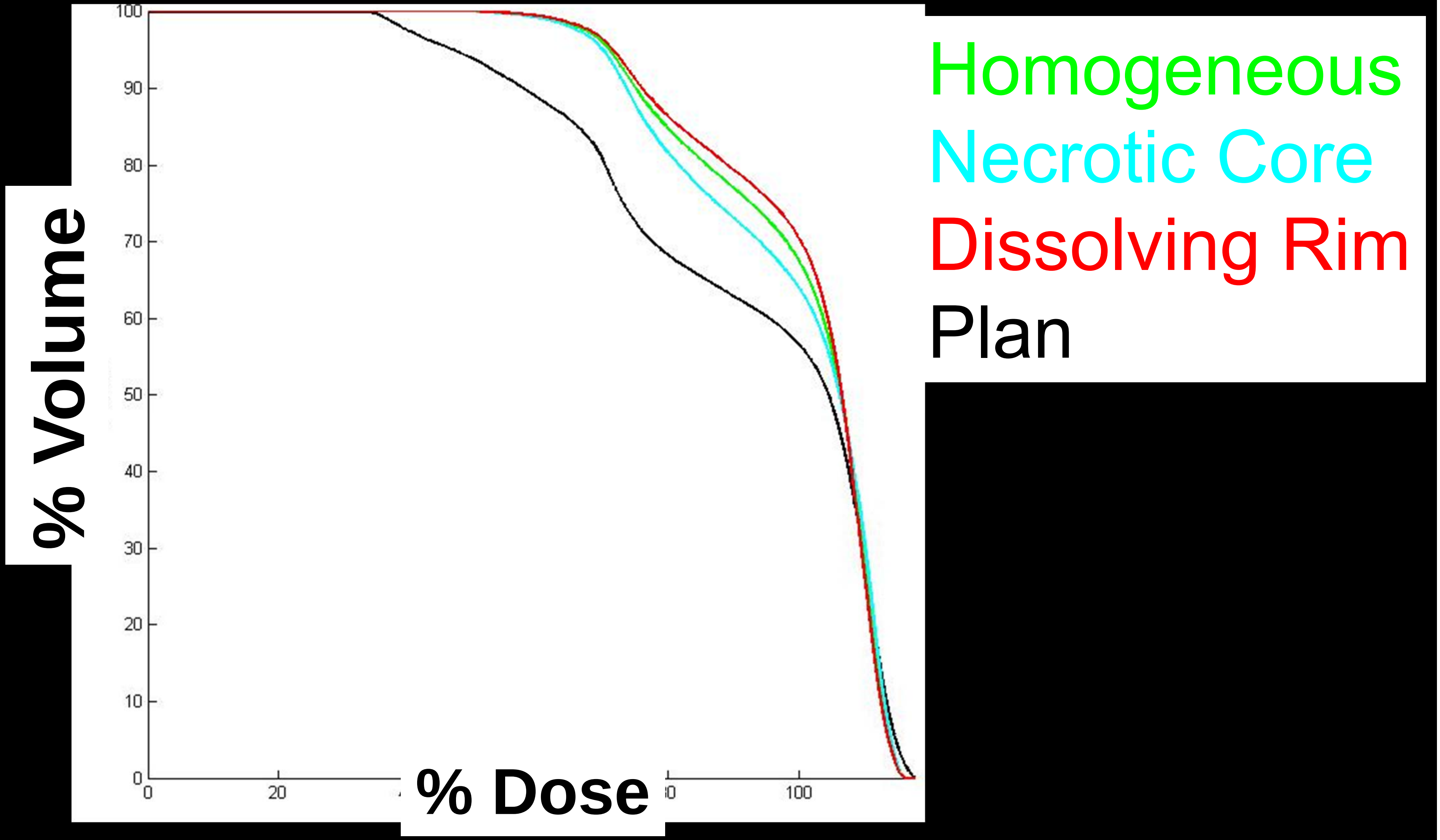






- Tumor with ‘core’
- Heterogeneous plan
- Variation in volume reduction
  - Homogeneous
  - Dissolving rim
  - Necrotic Core

Modeling Volume Reduction Dosimetric Effect



Implementation

Implementation Issues

- How to transfer the clinical reference frame?
  - 30 Gy max dose really *wasn't* 30 Gy?
- How to do patient specific QA?
  - Quantitative? Qualitative? Nothing?

Uncertainties in Deformable Dose Accumulation

- Deformable registration
  - Geometric Accuracy
- Dose calculations
  - Original, high quality CT (discussed)
  - Recalculate dose on CBCT, MVCT, MR, new CT?
- Dose output of machine
  - (Discussed)

How do we generate a new dose grid?

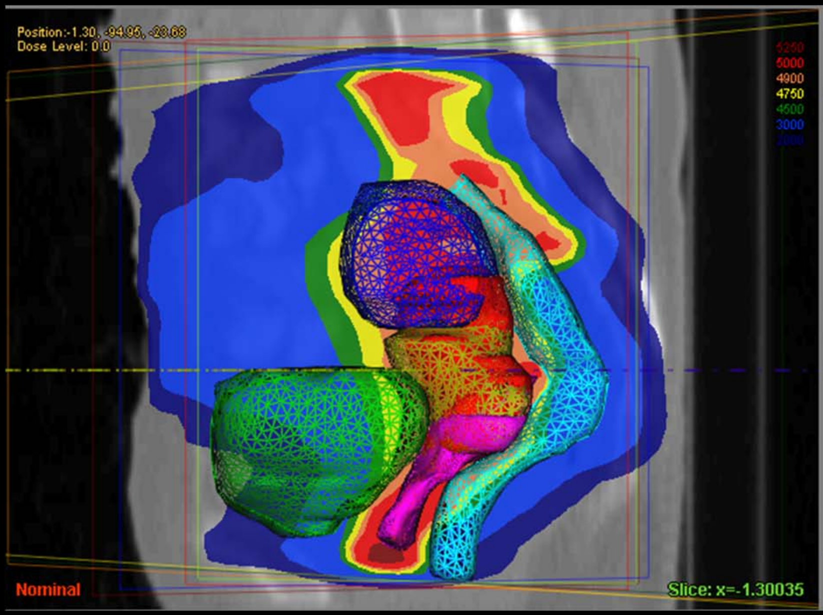
- Do we need to?
  - Can we just use the original dose grid?
  - Probably ok if the patient mass/organ/tumor volume isn't changing
- Can we use an MR/CBCT/MVCT?
- Should we deform the planning CT to the new image and re-calculate the dose on this image?

Katja will tell us tomorrow!!!

What you plan is NOT what you get!

Baseline Organ Geometry

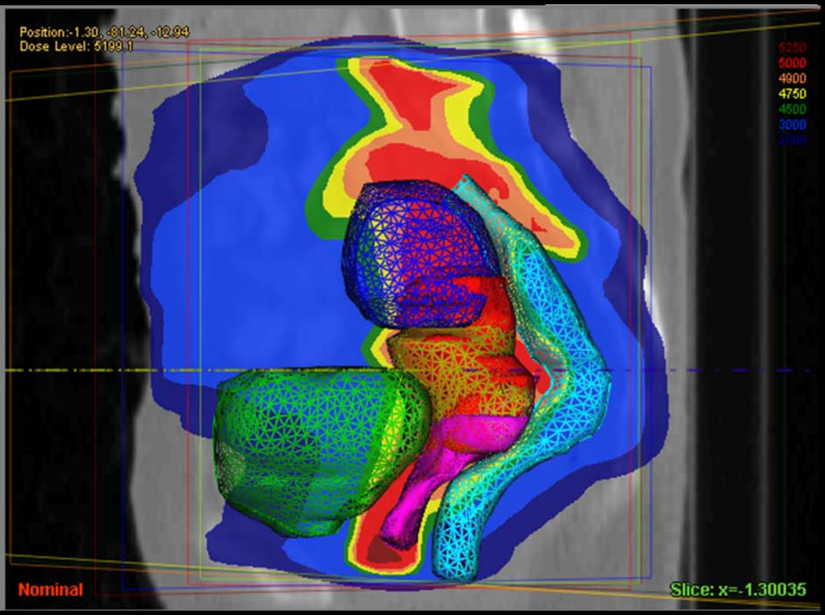
"Planned" dose distribution



Planned Dose

Baseline Organ Geometry

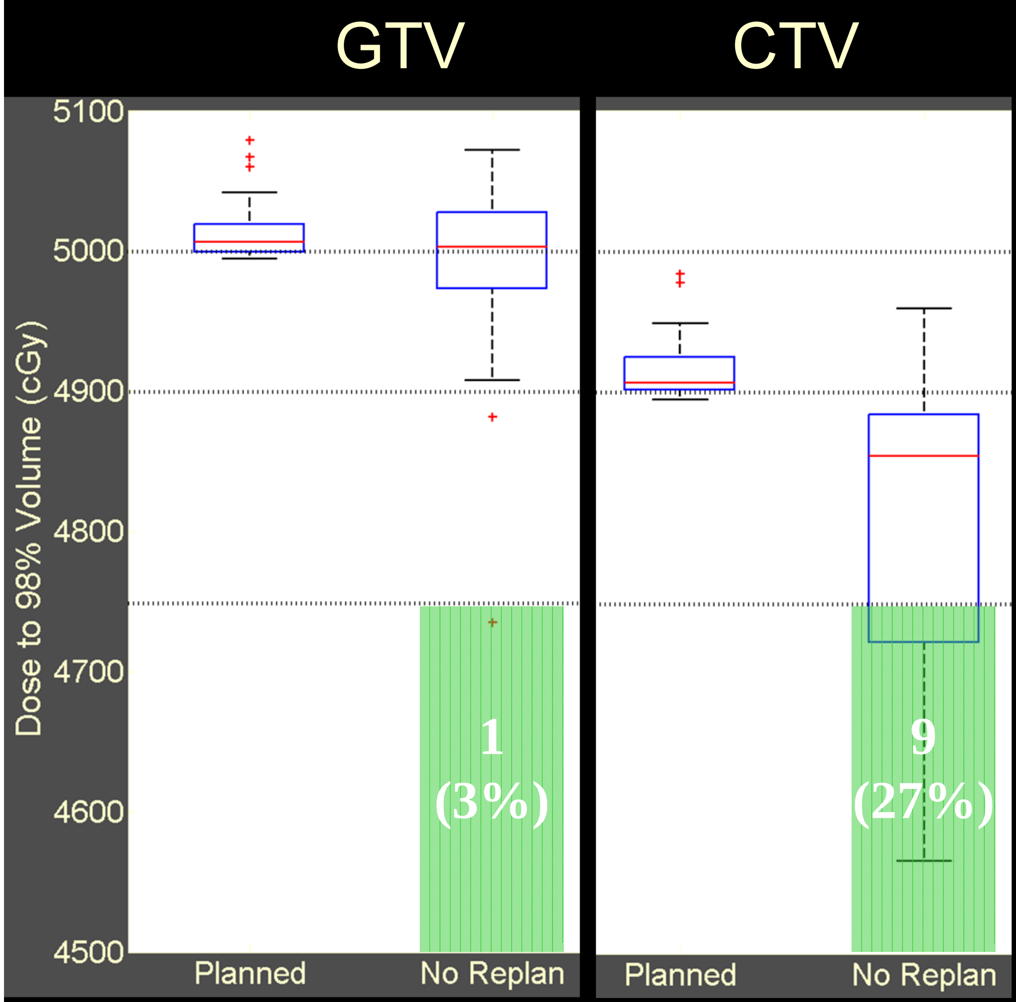
Updated dose distribution

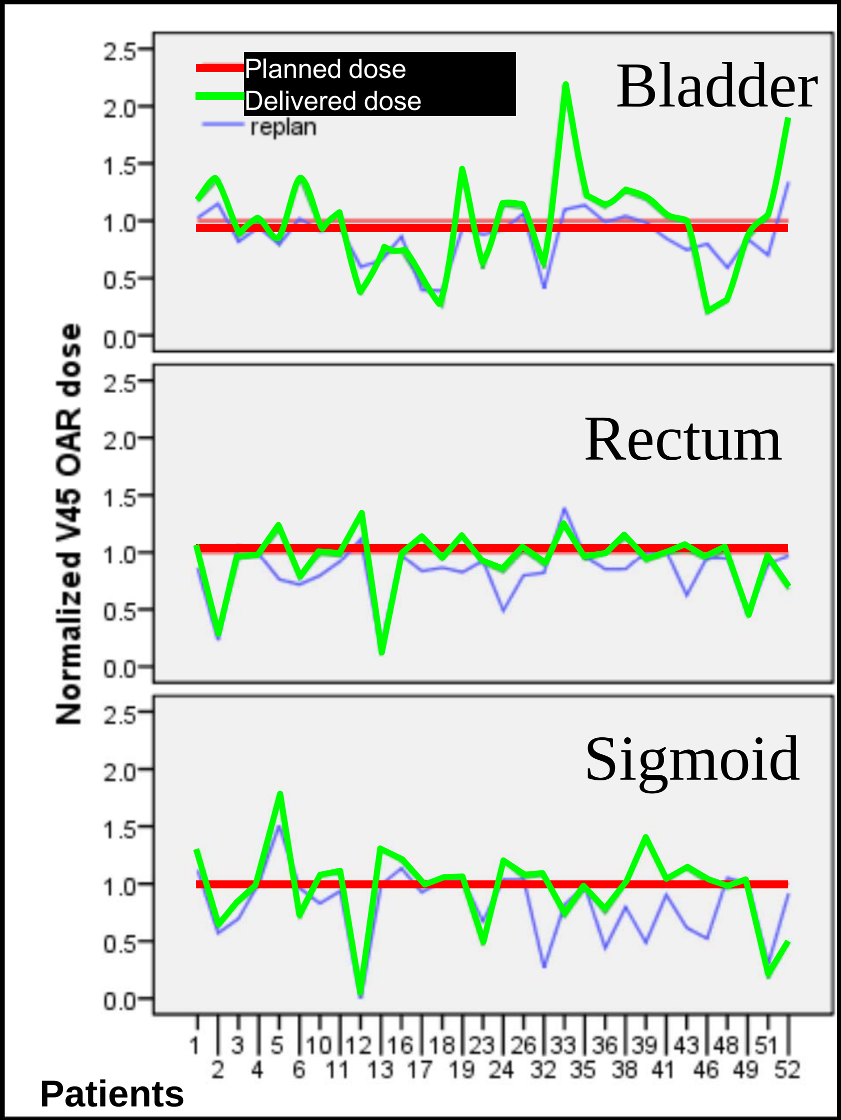


Delivered Dose

Lim, et. al., IJROBP 2009

What you plan is NOT what you get!

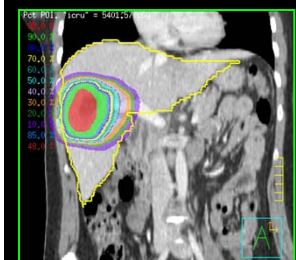




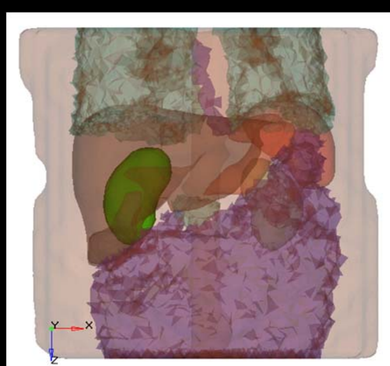
Lim, et. al., IJROBP 2009

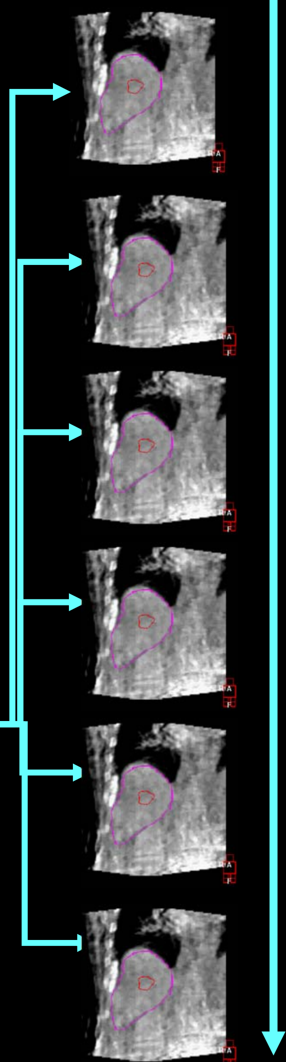
What you plan is NOT what you get!

Delivered Dose



EXH



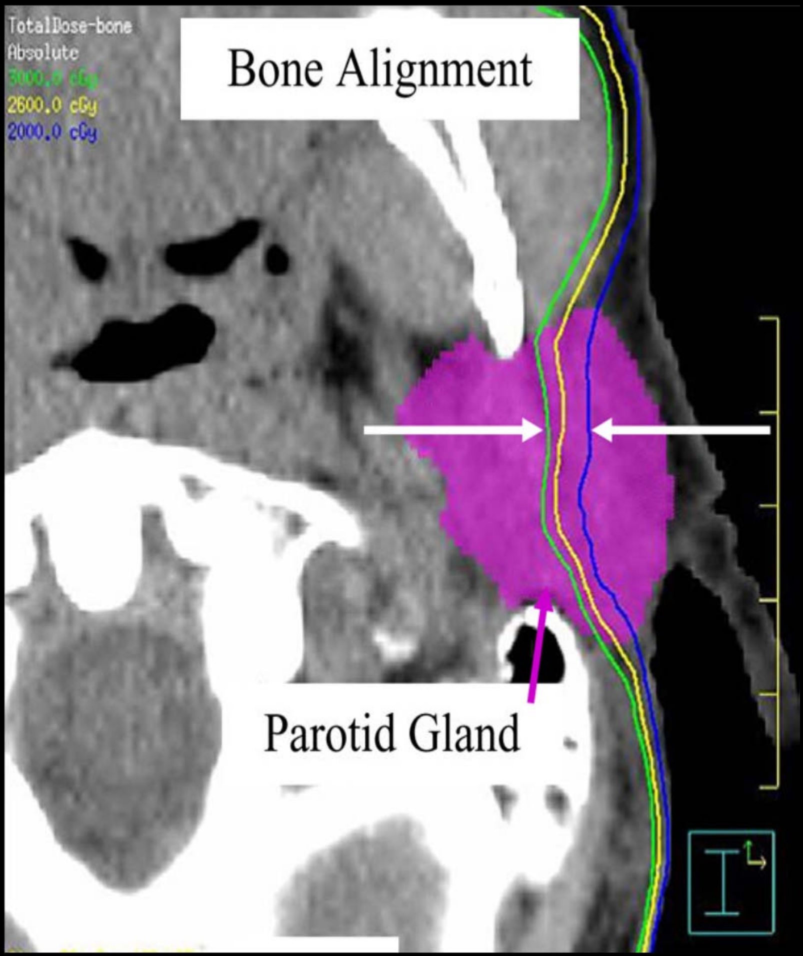


Tx

Δ Dose (Gy)	30 SBRT Pts |AVG Δ|, (|MAX Δ|) Accumulated – Static
D_{MIN} GTV	0.6 (2.2)
D_{MAX} Stomach	1.1 (5.0)
D_{MAX} Bowel	1.6 (4.8)
D_{MAX} Duodenum	1.2 (7.4)
D_{MAX} Esophagus	0.5 (1.8)

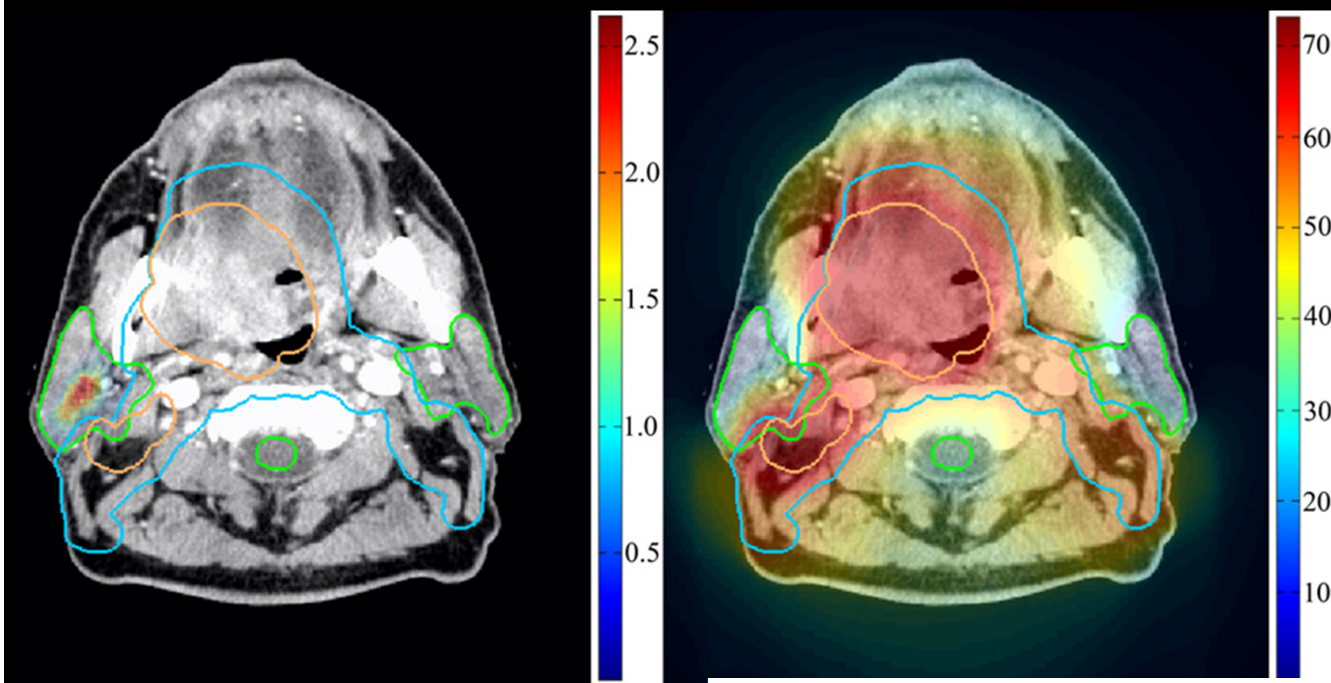
Velec, IJROBP, submitted

What you plan is NOT what you get!



- O'Daniel et. al. IJROBP 2007
  - 11 patients, 2 CTs/week
  - Increase in parotid dose: median 1 Gy
- Lee et. al., IJROBP 2008
  - 10 patients, daily MVCT
  - Mean 15% change
  - 3 Pts > 10% increase
- Wu et. al., IJROBP 2009
  - 11 patients, weekly CTs
  - 10% increase in parotid dose

Do we need to include Radiobiology in Dose Accumulation?



If using current radiotherapy practices and clinical recommendations based on dose surrogates computed globally on OARs and TVs, one does not need to take radiobiological effects into account while accumulating total dose as these lead to very small differences compared to a simple accumulation technique consisting of a linear sum of the dose fractions.

However, care must be taken if other adaptive strategies, based on local rather than global information, are used.

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Head and neck radiotherapy

Evaluation of the radiobiological impact of anatomic modifications during radiation therapy for head and neck cancer: Can we simply summate the dose?

Jonathan Orban de Xivry [a,*,1], Pierre Castadot [b,1], Guillaume Janssens [a], John Aldo Lee [b], Xavier Geets [b], Vincent Grégoire [b], Benoît Macq [a]

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Words of Caution

- Visual validation should only be used as a qualitative, spot check test <u>after</u> you have quantitatively validated the algorithm on your data
- Understand how the algorithm behaves when limited information/uncertainties are presented
- Matching the organ boundary does not guarantee accurate modeling of internal volume
- Manually adjusting auto-segmentation is fine, manually adjusting deformable registration is <u>not</u>

Questions for your DIR

- What is the algorithm?
  - Similarity metric, regularization
  - What are it's appropriate uses?
  - What are the limitations?
- How does it fit into my clinic's workflow?
  - End to end test
- How can I perform quantitative validation/commissioning
  - For the sites/images you plan to use
  - TG 132 will help provide data

Summary (5/5)

- Many different deformable registration options
- Validation is a must prior to clinical integration
- Visual validation is not enough! (initial validation)
- Boundary matching is enough ONLY for auto-segmentation
- Phantoms are useful for benchmarking, but likely do not include the complexities of true clinical imaging
- Implanted and naturally occurring fiducials give us a ‘spot check’
- Mathematical/Similarity metrics are easy automated checks

Summary (5/5)

- Validation using dosimetric techniques can give us a clinical perspective for IGRT/Dose Accumulation studies
- It's integration into the clinic can help us to ensure quality Tx
  - Deformable dose accumulation
- Must use with caution
  - Pushing the limits on re-Tx
  - Adaptive RT