

# Deformable Image Registration in Radiation Oncology

Sarah Geneser, Ph.D.

Medical Physicist

Department of Therapeutic Radiation Oncology

Yale University and Yale-New Haven Hospital



Yale University



# Overview

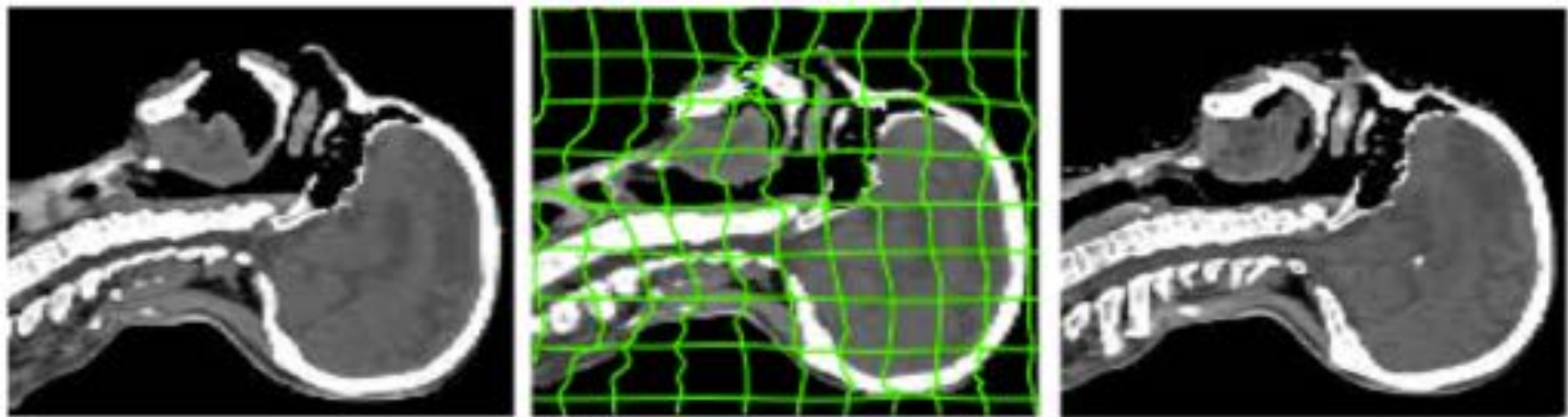
- When is deformable image registration (DIR) useful?
- Deformable image registration basics
- Commercial DIR options
- DIR advantages/challenges  
(i.e. where things go right/wrong)



What is DIR?

# Deformable Image Registration

- Deformable registration warps moving image (M) via deformation field (DF) to align (M) to the target image (T).
- DF defines the motion of each image voxel from M to T.
- This produces a registered image (R).



moving (M)

registered (R)

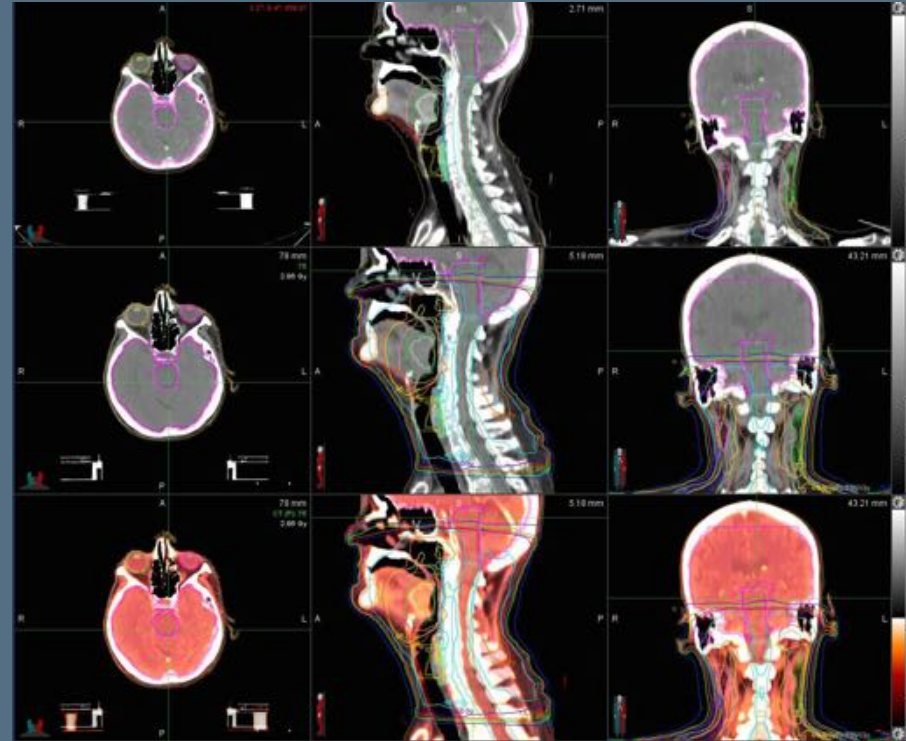
target (T)

deformation field (DF)



When is DIR Useful?

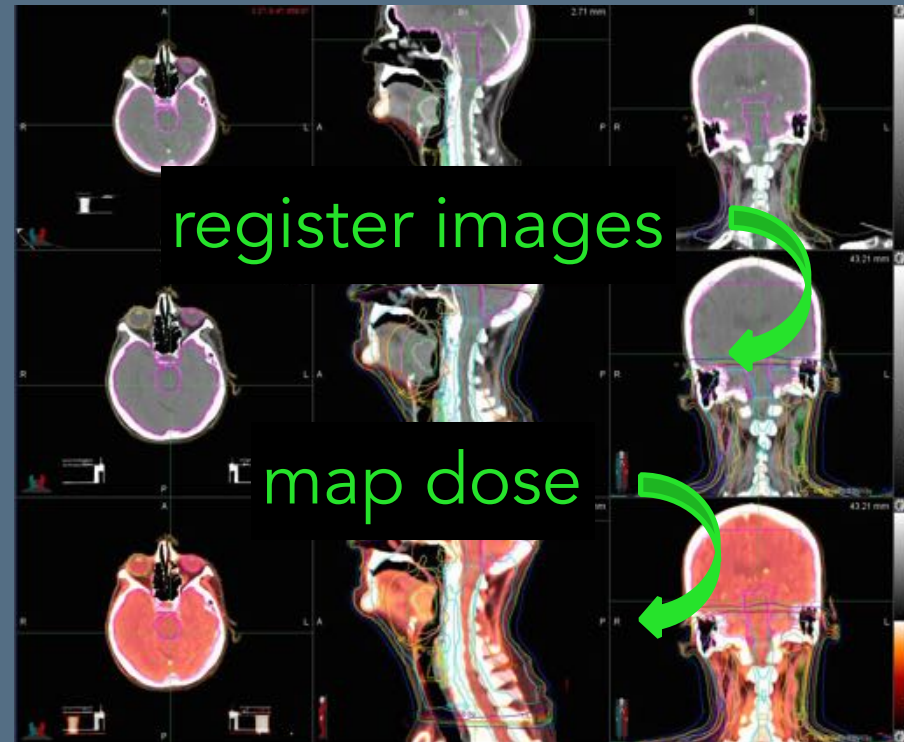
# Dose Fusions



# Dose Fusions



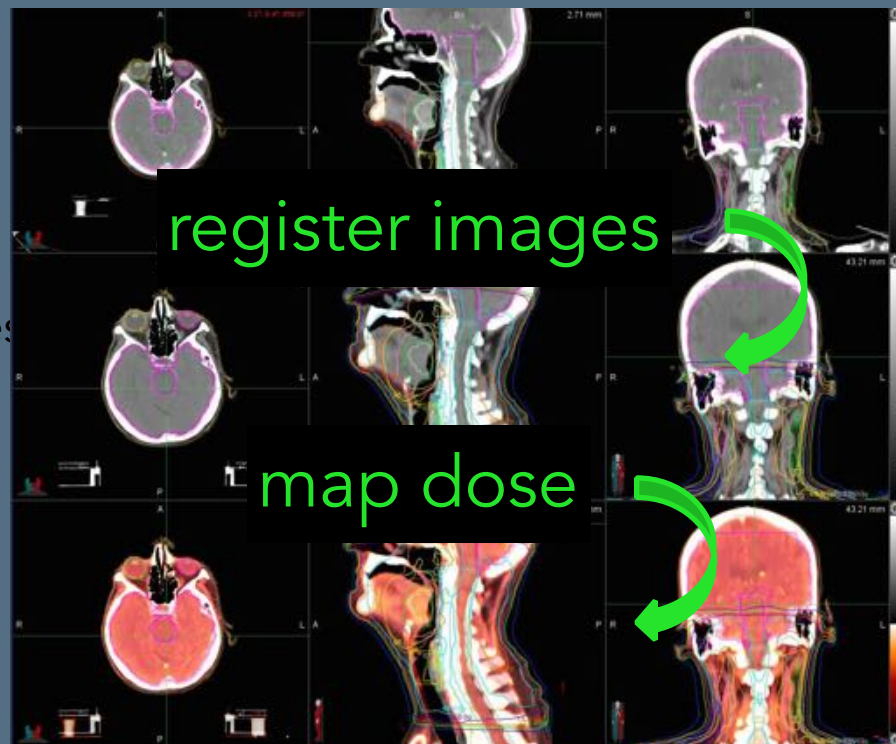
# Dose Fusions





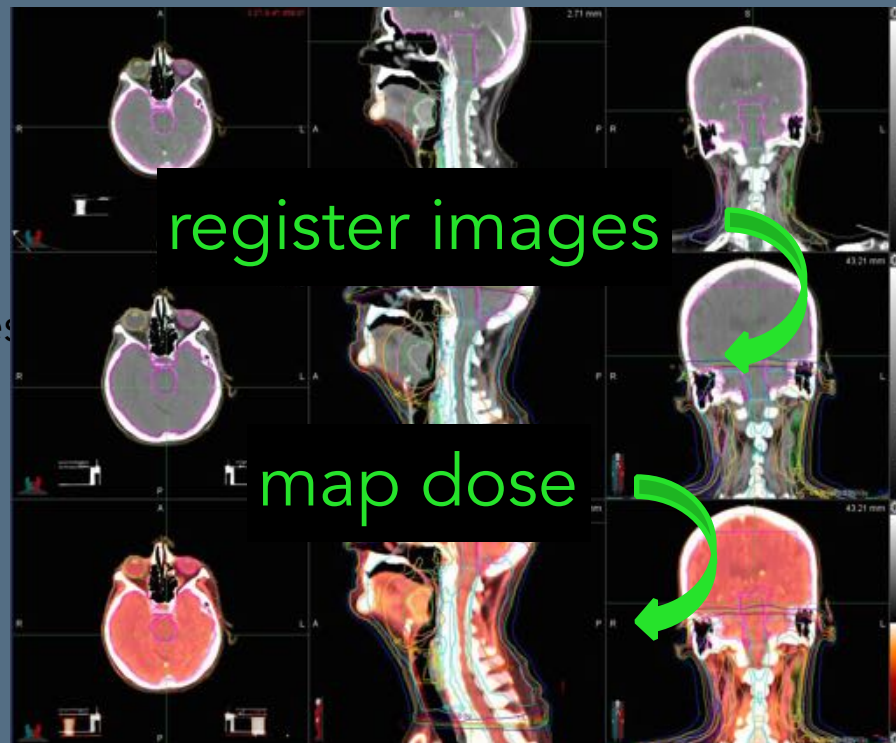
# Dose Fusions

- Re-treatment
- Re-planning
- Respiratory motion
- Adaptive RT
- Treatments planned on differing modalities with different clinical setup  
(e.g. prostate IMRT with HDR boost)



# Dose Fusions

- Re-treatment
- Re-planning
- Respiratory motion
- Adaptive RT
- Treatments planned on differing modalities with different clinical setup  
(e.g. prostate IMRT with HDR boost)



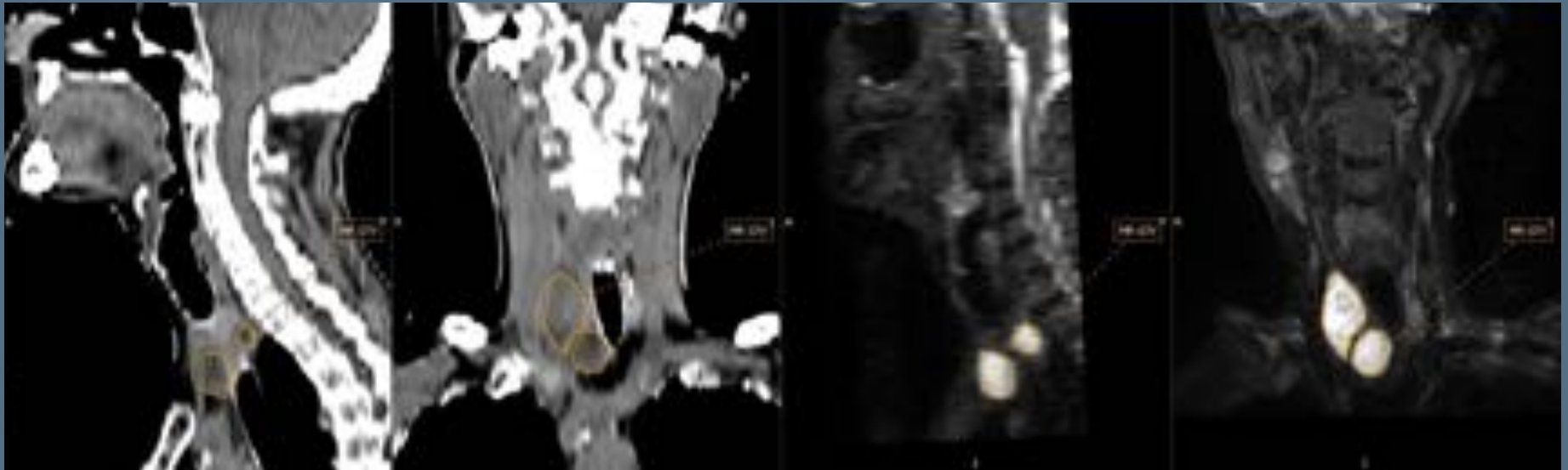
***Comparing/summing doses calculated on different image volumes.***

# Contour Guidance

- Fuse multiple modalities to aid physician with target contours.

planning CT

diagnostic MRI



(Images courtesy of Mirada Medical)

# Contour Guidance

- Fuse multiple modalities to aid physician with target contours.

planning CT

diagnostic MRI



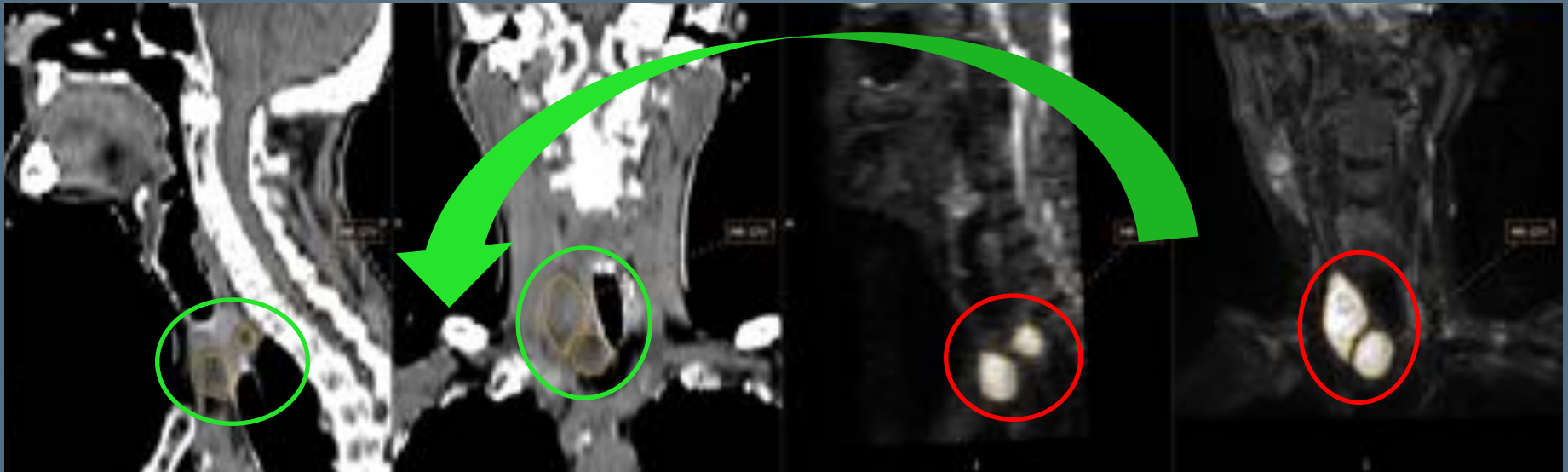
(Images courtesy of Mirada Medical)

# Contour Guidance

- Fuse multiple modalities to aid physician with target contours.

planning CT

diagnostic MRI



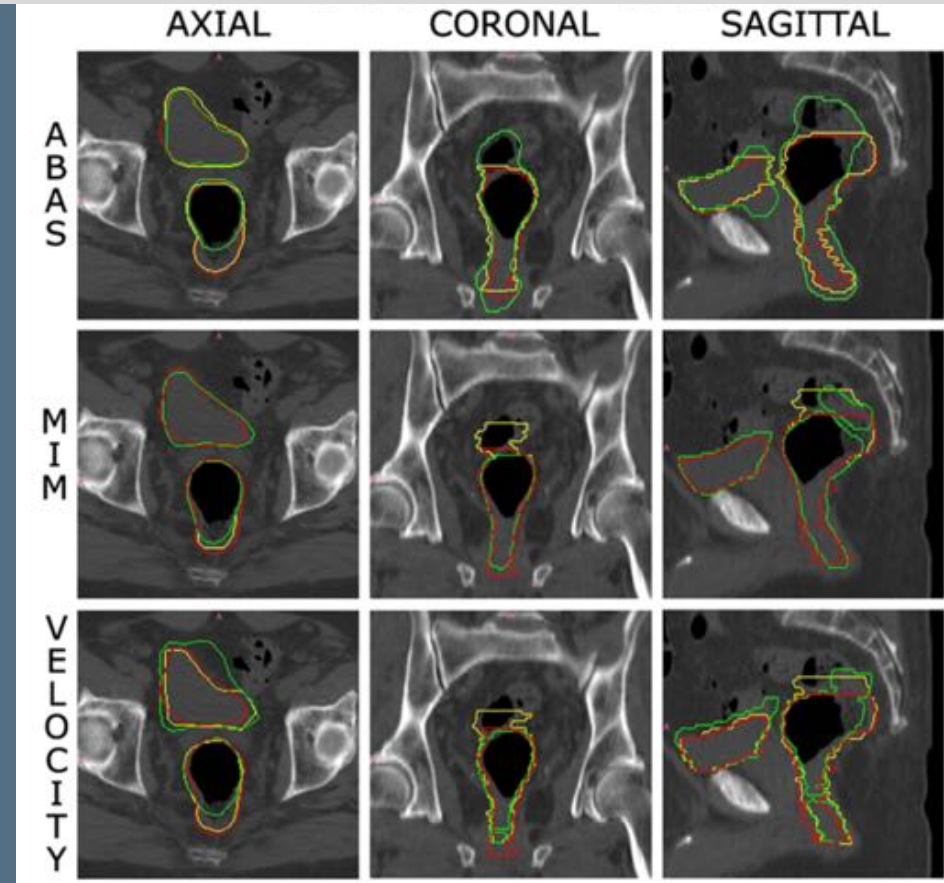
(Images courtesy of Mirada Medical)

# Atlas-Based Contouring

- Contours are generated from patient-atlas
- Can improve contouring efficiency
- Requires building atlas
- Often requires contour corrections (“cleanup”)

# Atlas-Based Contouring

- Contours are generated from patient-atlas
- Can improve contouring efficiency
- Requires building atlas
- Often requires contour corrections (“cleanup”)

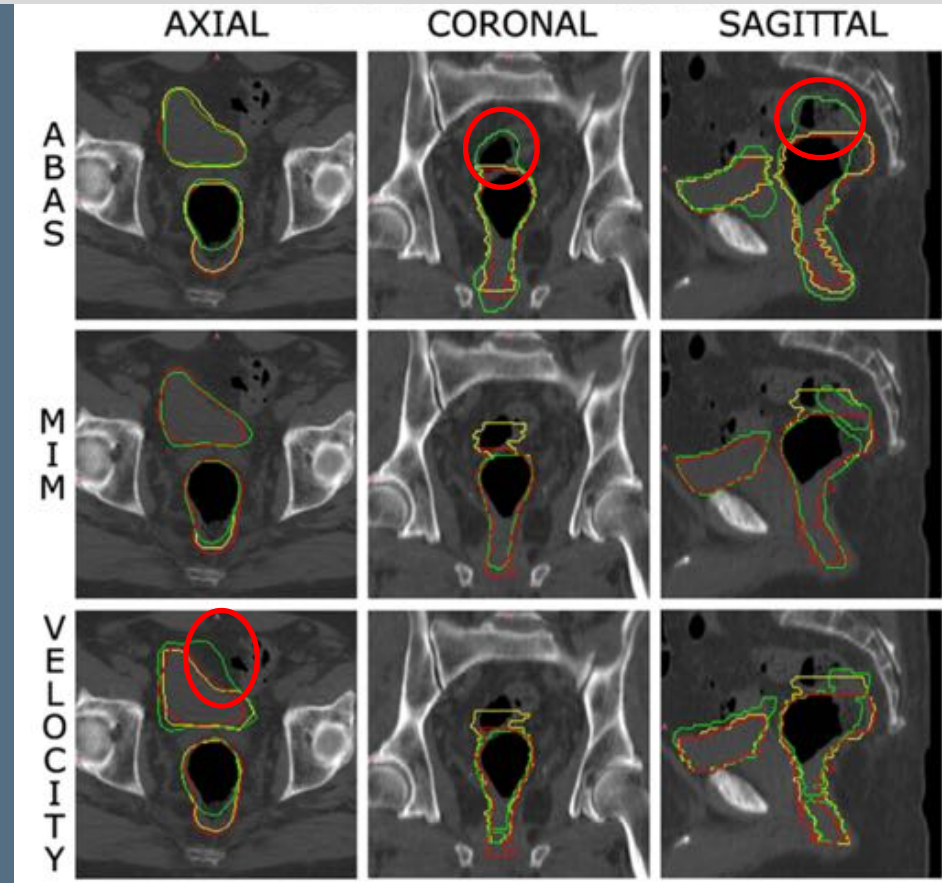


\*Atlas-Based Auto-segmentation of H&N CT • *MICCAI* • Xiao Han *et al.* • 2008

\*Evaluation of Commercial Solutions for Auto-seg • *RO* • La Macchia *et al.* • 2012

# Atlas-Based Contouring

- Contours are generated from patient-atlas
- Can improve contouring efficiency
- Requires building atlas
- Often requires contour corrections (“cleanup”)



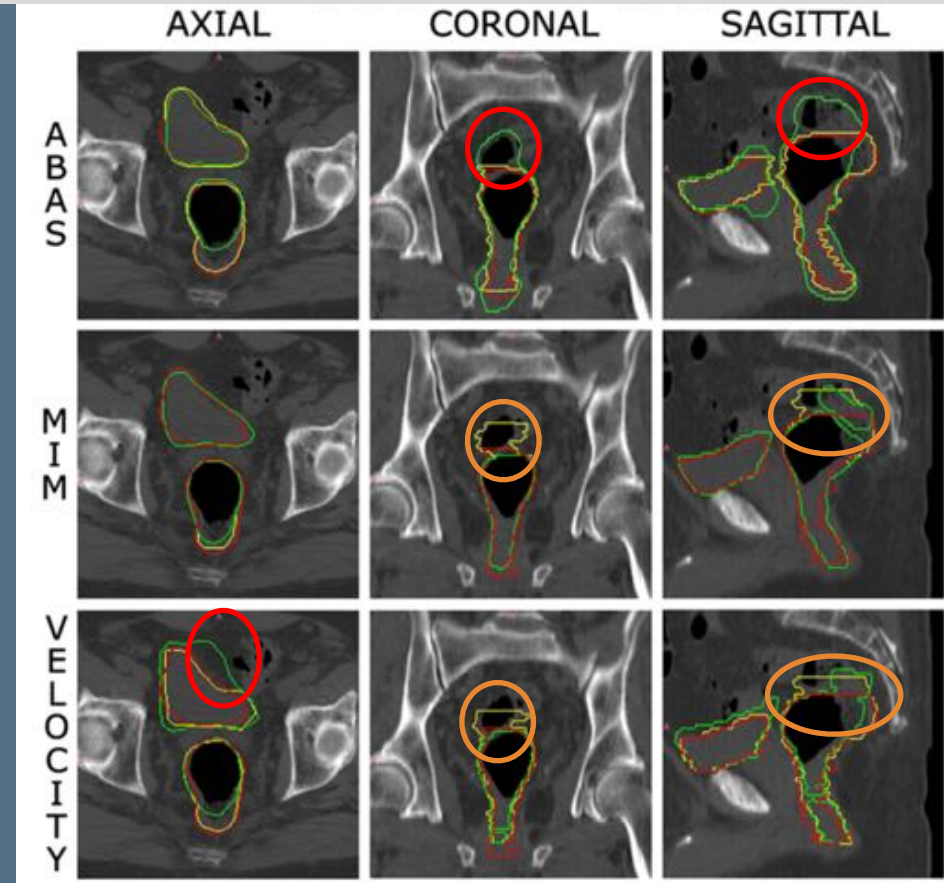
\*Atlas-Based Auto-segmentation of H&N CT • *MICCAI* • Xiao Han *et al.* • 2008

\*Evaluation of Commercial Solutions for Auto-seg • *RO* • La Macchia *et al.* • 2012



# Atlas-Based Contouring

- Contours are generated from patient-atlas
- Can improve contouring efficiency
- Requires building atlas
- Often requires contour corrections (“cleanup”)

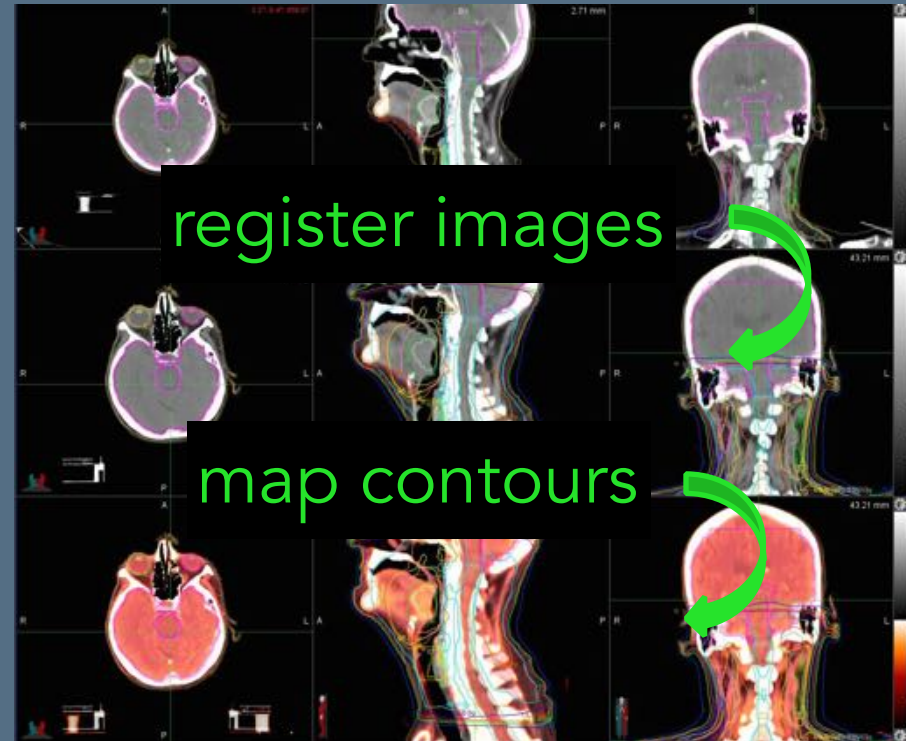


\*Atlas-Based Auto-segmentation of H&N CT • *MICCAI* • Xiao Han *et al.* • 2008

\*Evaluation of Commercial Solutions for Auto-seg • *RO* • La Macchia *et al.* • 2012

# Contour Propagation

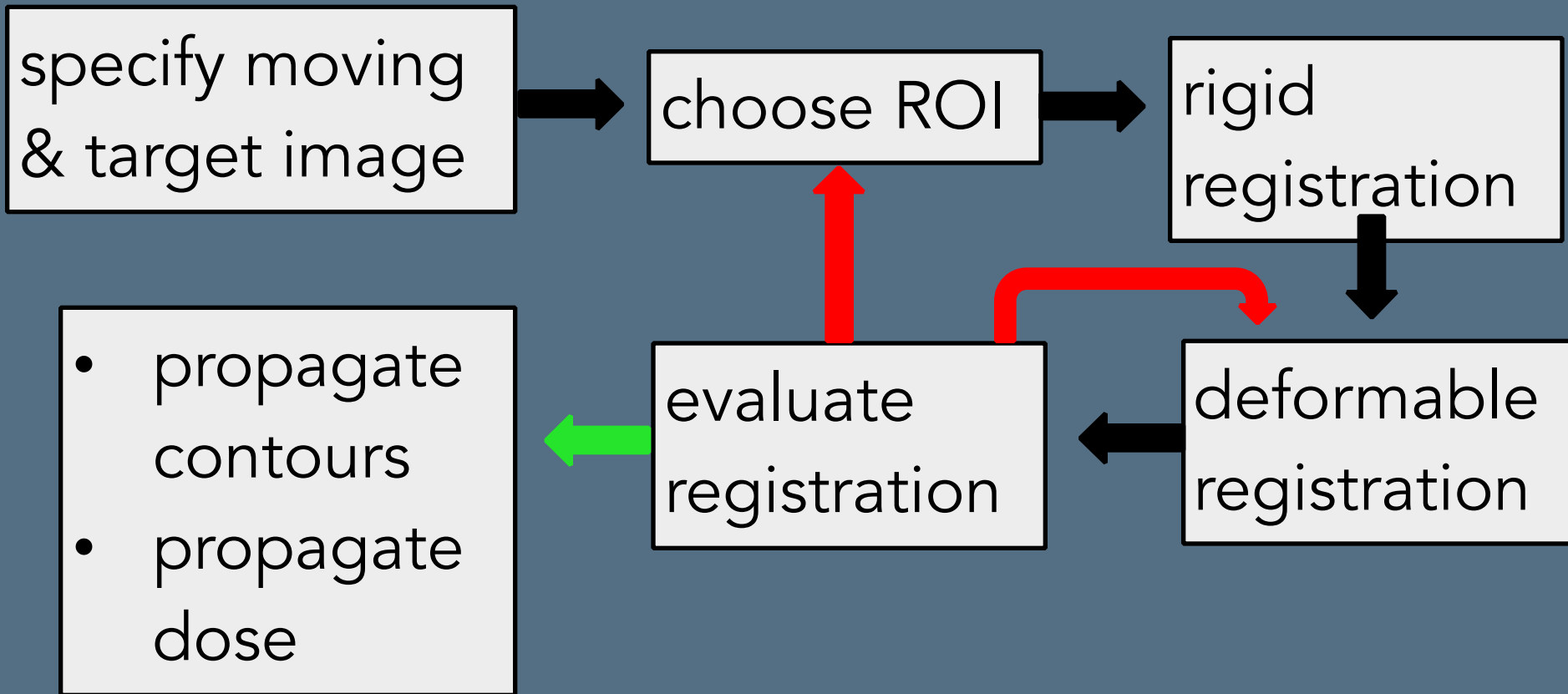
- Re-treatment
- Re-planning  
(planning on new CT)
- Adaptive RT



***Relatively straightforward. Can speed workflow.***

➤ Deformable Image Registration  
Basics

# General DIR Workflow



# Forward Problem

To register images, a transformation is required that maps voxels of one image onto another image's coordinate system.

1. Translations & Rotations (rigid)
2. Parameterized Basis Functions
3. Fluid/Elastic
4. Tissue Mechanics

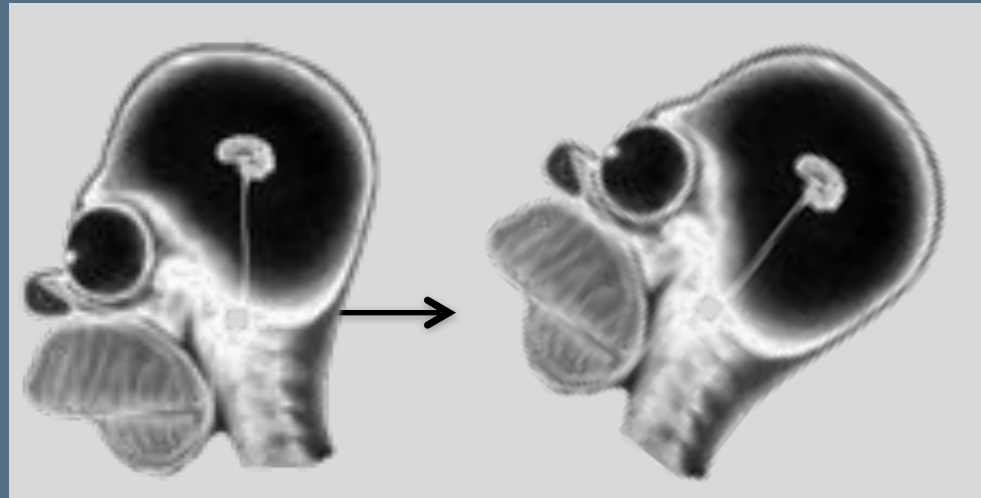
# Rigid Transformations (Global)

Rigid transformations in 2D:

$$T(\vec{x}) = \begin{bmatrix} \cos(\theta) & -\sin(\theta) \\ \sin(\theta) & \cos(\theta) \end{bmatrix} \vec{x} + \begin{bmatrix} t_x \\ t_y \end{bmatrix}$$

Rigid transformations in 3D:

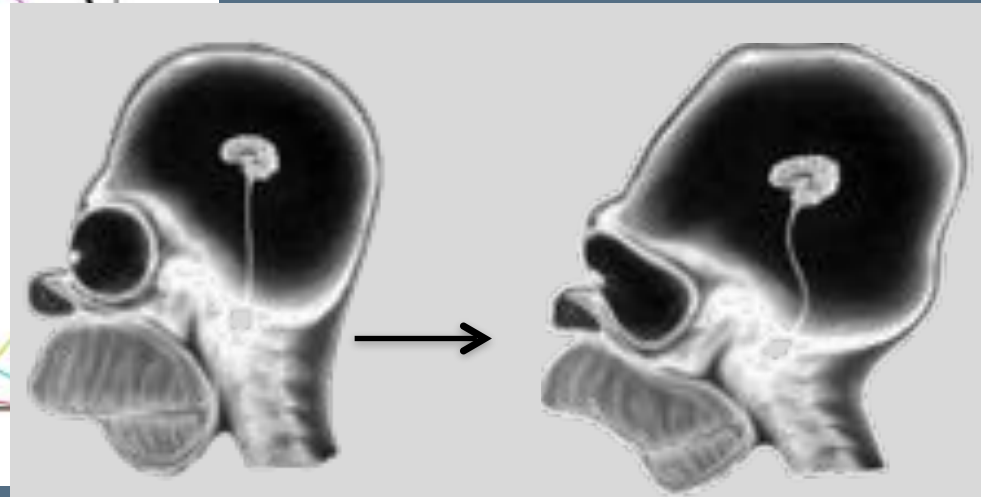
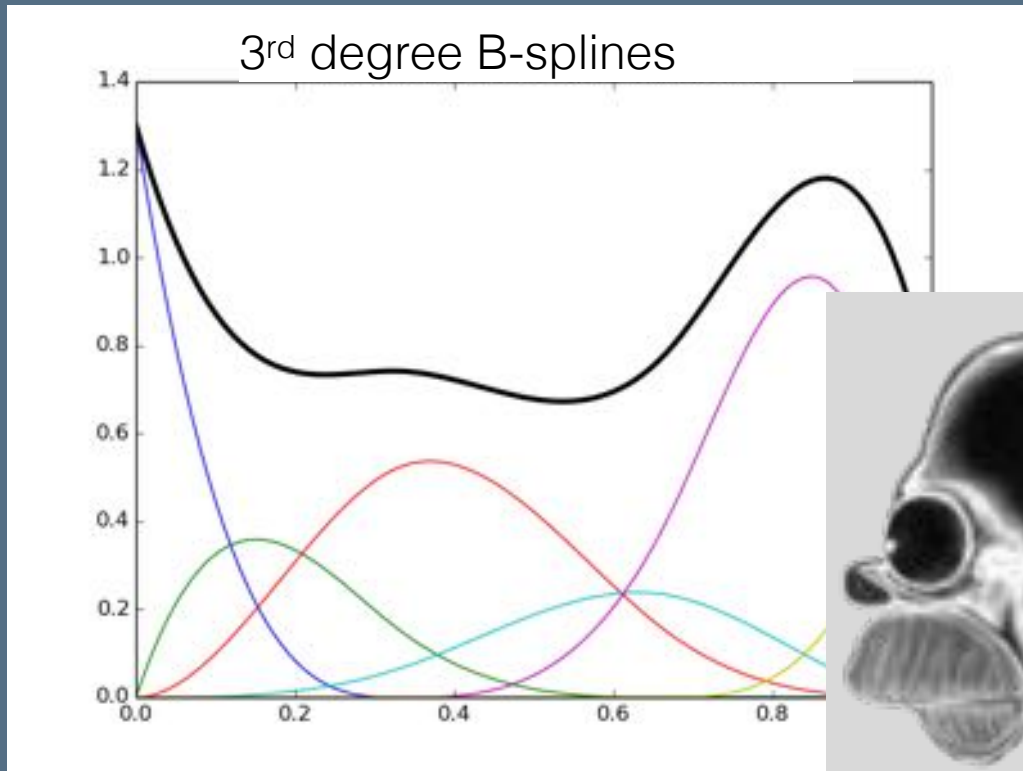
$$T(\vec{x}) = R_x R_y R_z \vec{x} + T$$



\* Augmented Reality in Surgery • *ARISER*  
*Summer School* • Casciari *et al.* • 2005

# Parameterized (Local or Global)

e.g. B-Splines: piecewise polynomials that form a set of basis functions.



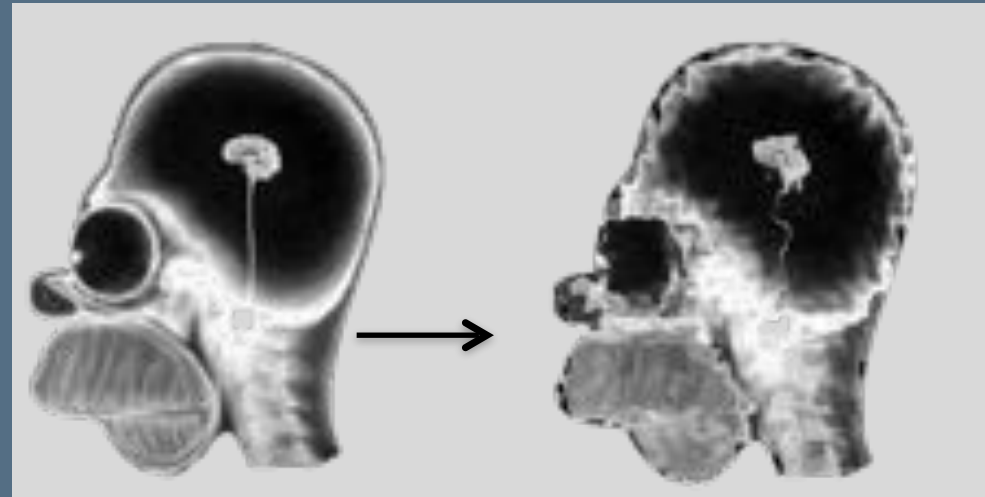
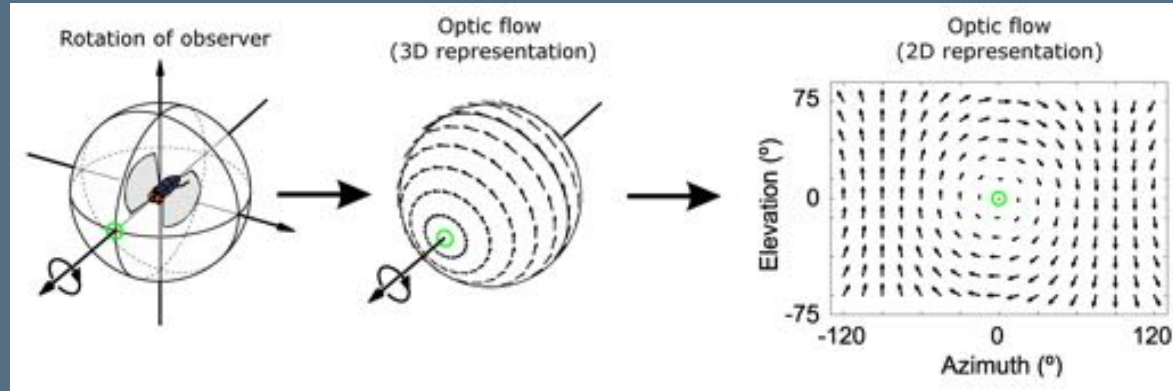
\* Augmented Reality in Surgery • *ARISER Summer School* • Casciari *et al.* • 2005

# Fluid/Elastic (Local)

Borrowed from fluid and optical mechanics.

e.g.:

- Optical Flow (Fast Demons)
- Karhunan Loeve
- Horn & Schunk



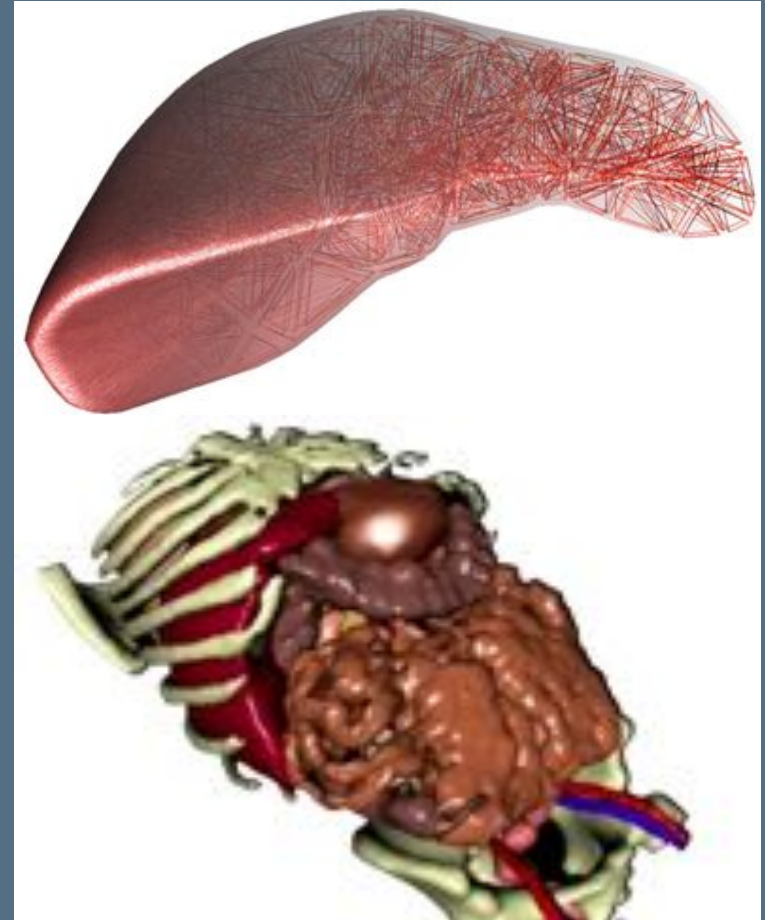
\* Augmented Reality in Surgery • *ARISER Summer School* • Casciari *et al.* • 2005



# Biomechanical Models (Local)

Models including tissue mechanics (a set of PDEs)  
– discretized and solved using, e.g.:

- Finite Boundary Elements
- Finite Element Methods



Deformable models for surgery • Bro-Neilson *et al.* • *Comp. Graphics Forum* • 1996

Feasibility of a novel DIR technique • Brock *et al.* • *IJROBP* • 2006

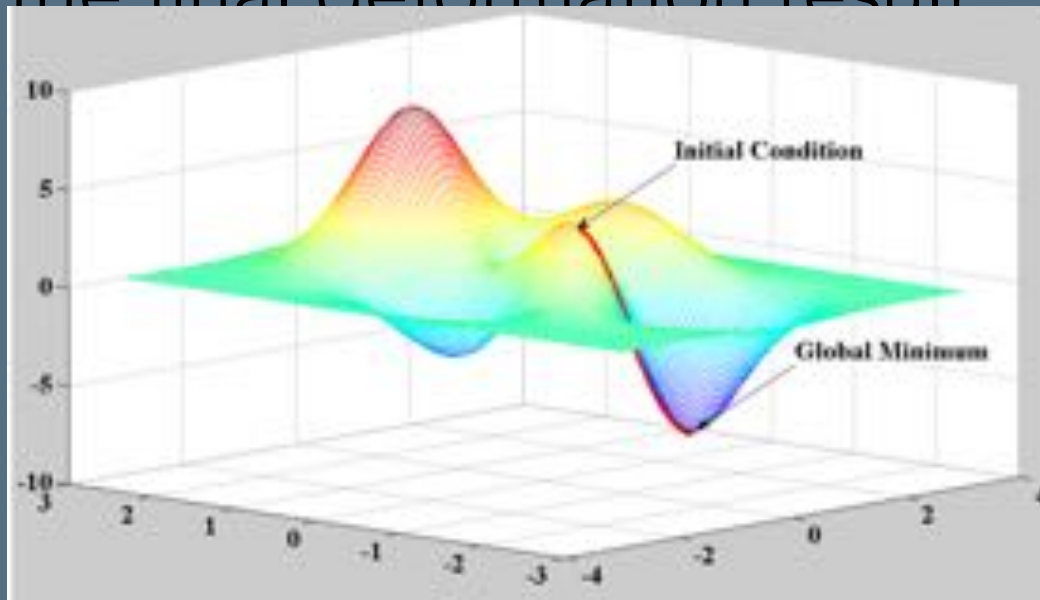
# Inverse Problem

Once appropriate candidate transformations chosen, define cost function/error metric to identify "best" transformation.

Cost function =  
image similarity  
+  
regularization

# Choice of Optimization

While the optimizer impacts solution speed, as long as the optimizer does not stagnate in local minima, the cost function has a much greater effect on the final deformation result



Tyler Bischel: [bleedingedgemachine.blogspot.com/](http://bleedingedgemachine.blogspot.com/)

# Image Similarity

- Landmark-based: Distance between landmarks
- Segmentation-based: DICE-similarity between contours
- Intensity-based: Sum of squared differences between voxel HU values

$$\sum_{i=1}^N (\textit{Registered}_i - \textit{Target}_i)^2$$

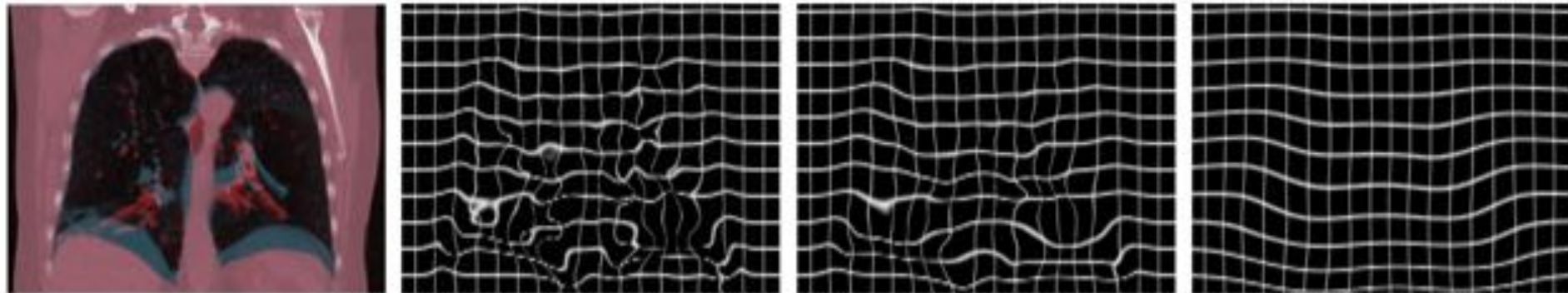
- Correlation-based: Mutual Information

# Regularization

Constrains “bendiness” of the deformation field.

Many options exist (e.g. penalize thin plate bending energy, local Jacobian values, linear elastic energy, differences in b-spline parameters for adjacent voxels, etc.)

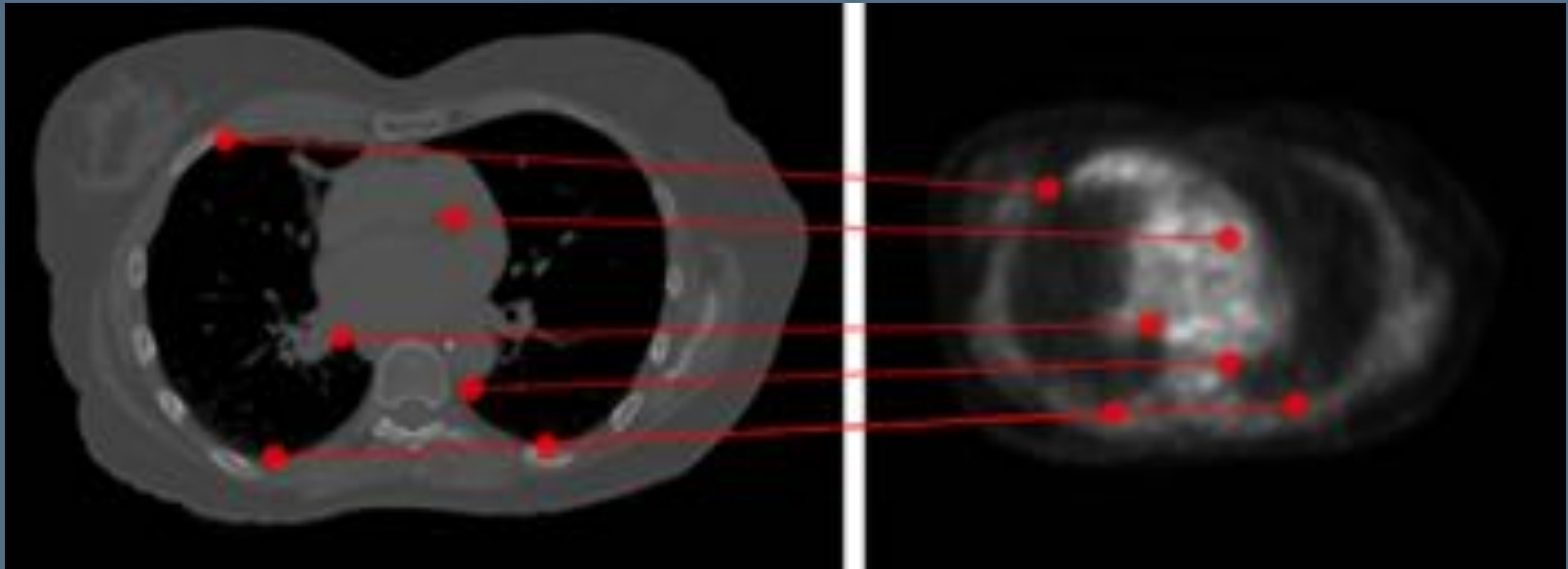
increasing regularization 



\*Analytic Regularization Uniform Cubic B-splines • MICCAI • Shackelford *et al.* • 2012

# Landmark Registration

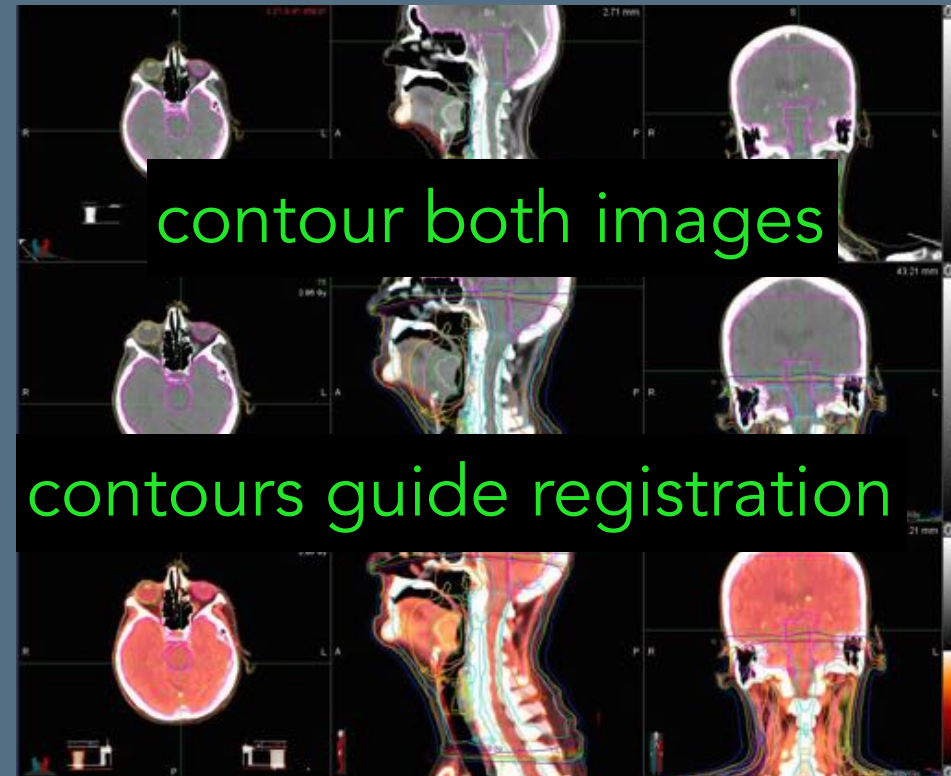
- Time-consuming (numerous landmarks)
- Provides only sparse data for driving the registration



\* <http://www.ariser.info/training/imgproc.php>

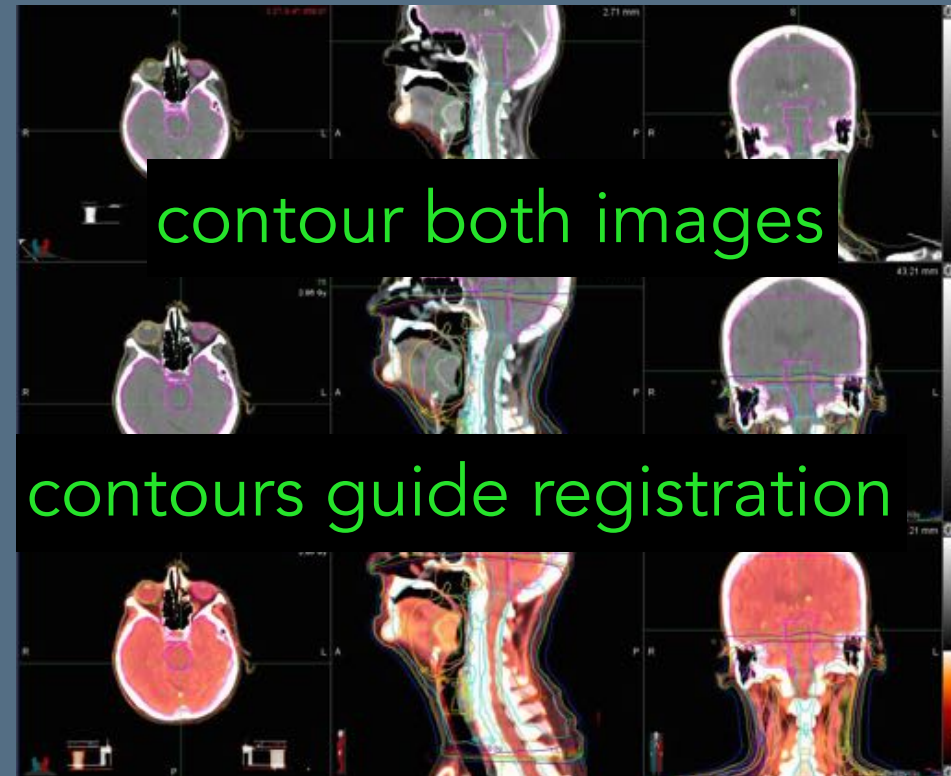
# Segmentation-Based

- Also termed contour guided DIR
- Differences between registered and target contours are included in the cost metric
- Requires contouring both image volumes



# Segmentation-Based

- Also termed contour guided DIR
- Differences between registered and target contours are included in the cost metric
- Requires contouring both image volumes



*Does not provide additional information  
internal to contours!*



# Voxel-Based Registration

- Sum of square differences of image intensity values (per voxel)
- When fusing images of differing modalities, (CT, MRI, PET, MVCT, etc.) mutual information metric is used.



# Commercial DIR Options

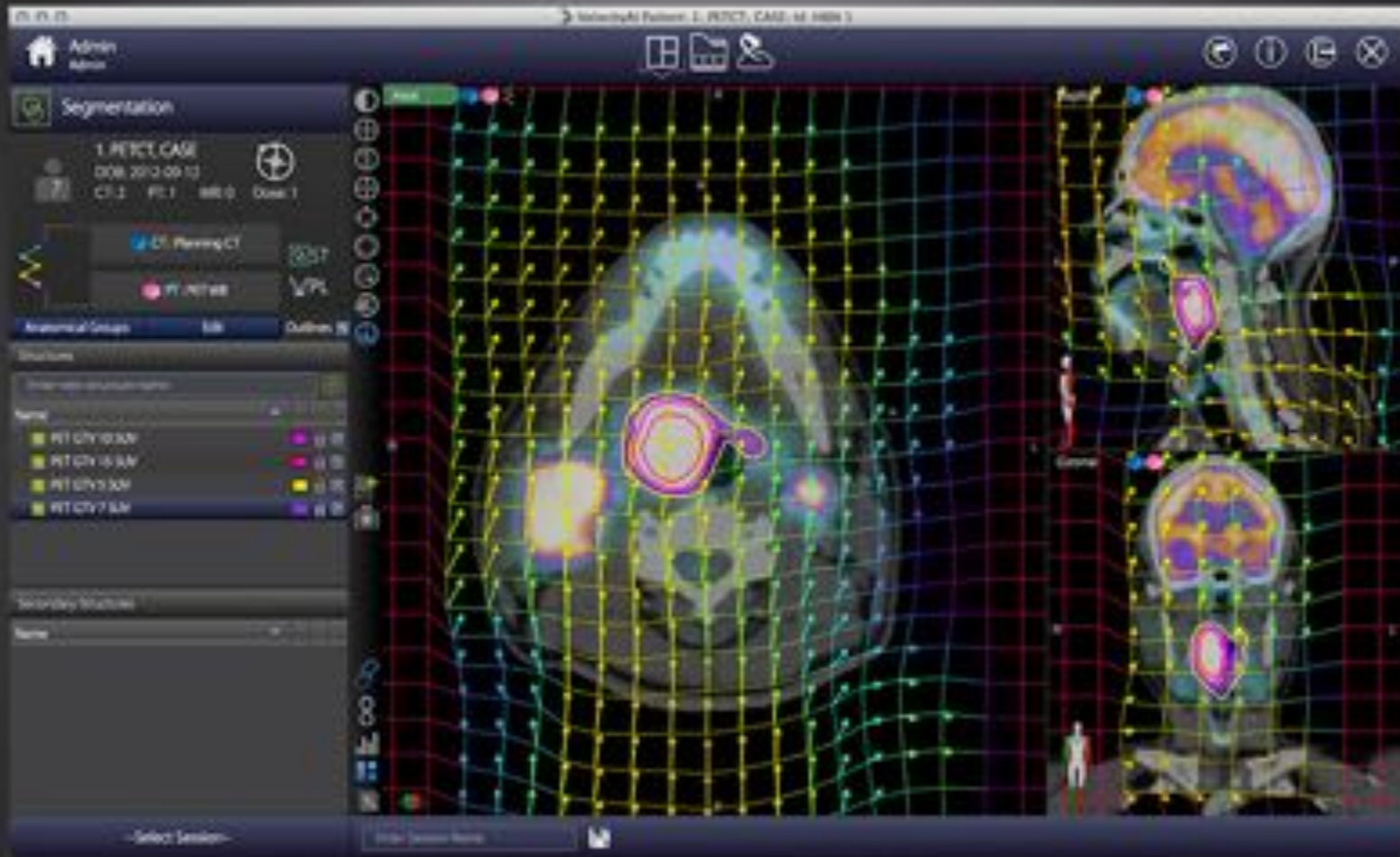
# MIMVista



# MIMVista

- Deformation: Demons optical flow
- Image Similarity: [unimodal – least squares of voxel differences] & [multimodal – mutual information (MI)]
- Regularization: proprietary – prevents tears & folds in deformation field. Additional regularization performed after optimal deformation identified.
- Optimization: Modified gradient descent
- Reg Reveal and Reg Refine provide interactive means of assessing and altering deformation fields

# Velocity

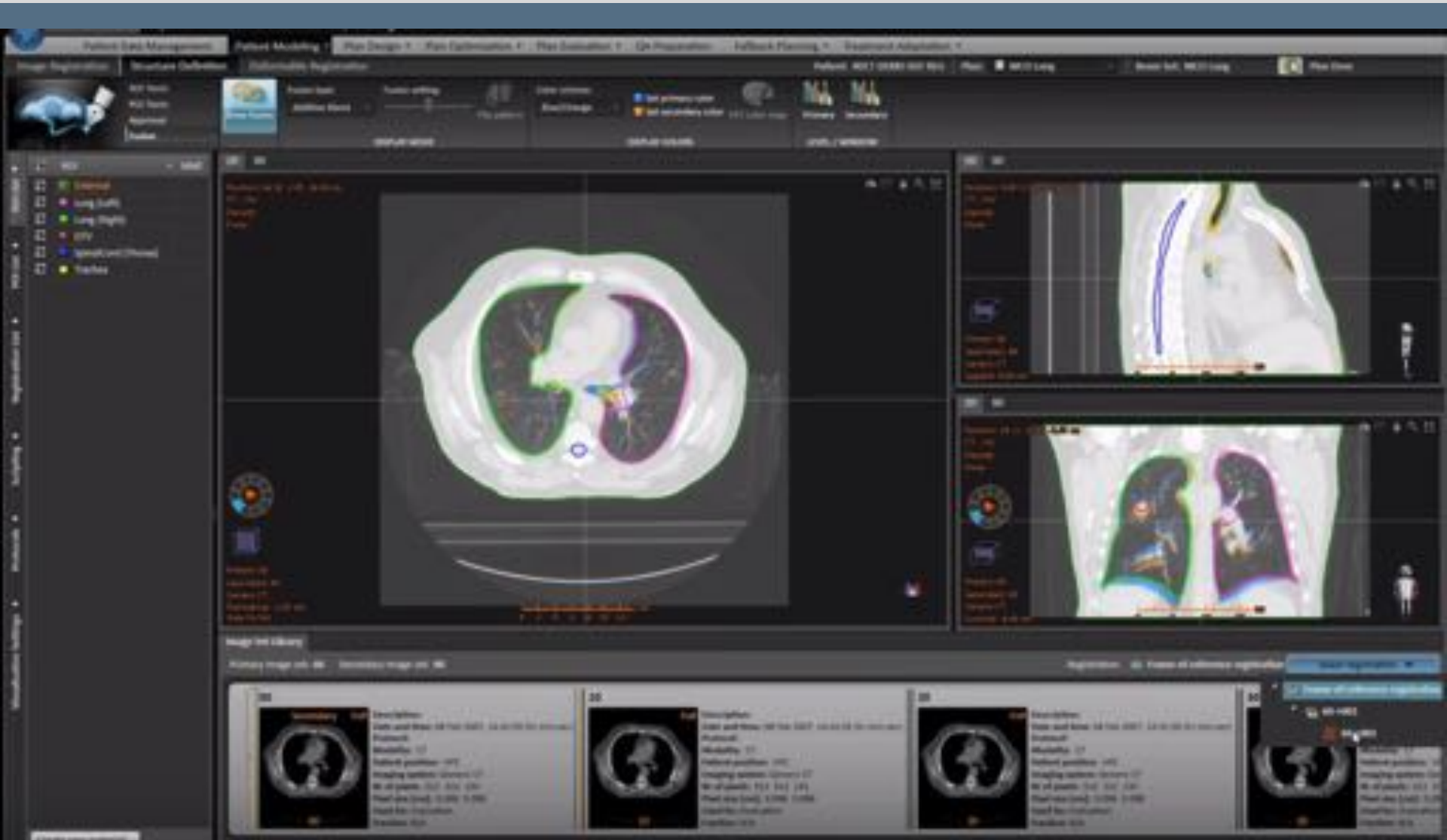


(Images courtesy of Velocity)

# Velocity

- Deformation: B-splines
- Image Similarity:
  - unimodal = least squares voxel differences
  - multimodal = mutual information
- Regularization: no post-optimization regularization
- Optimizer: gradient descent
  
- Allows voxel-wise query of deformation fields
- Built-in QA tools (Version 3.2)

# Raystation

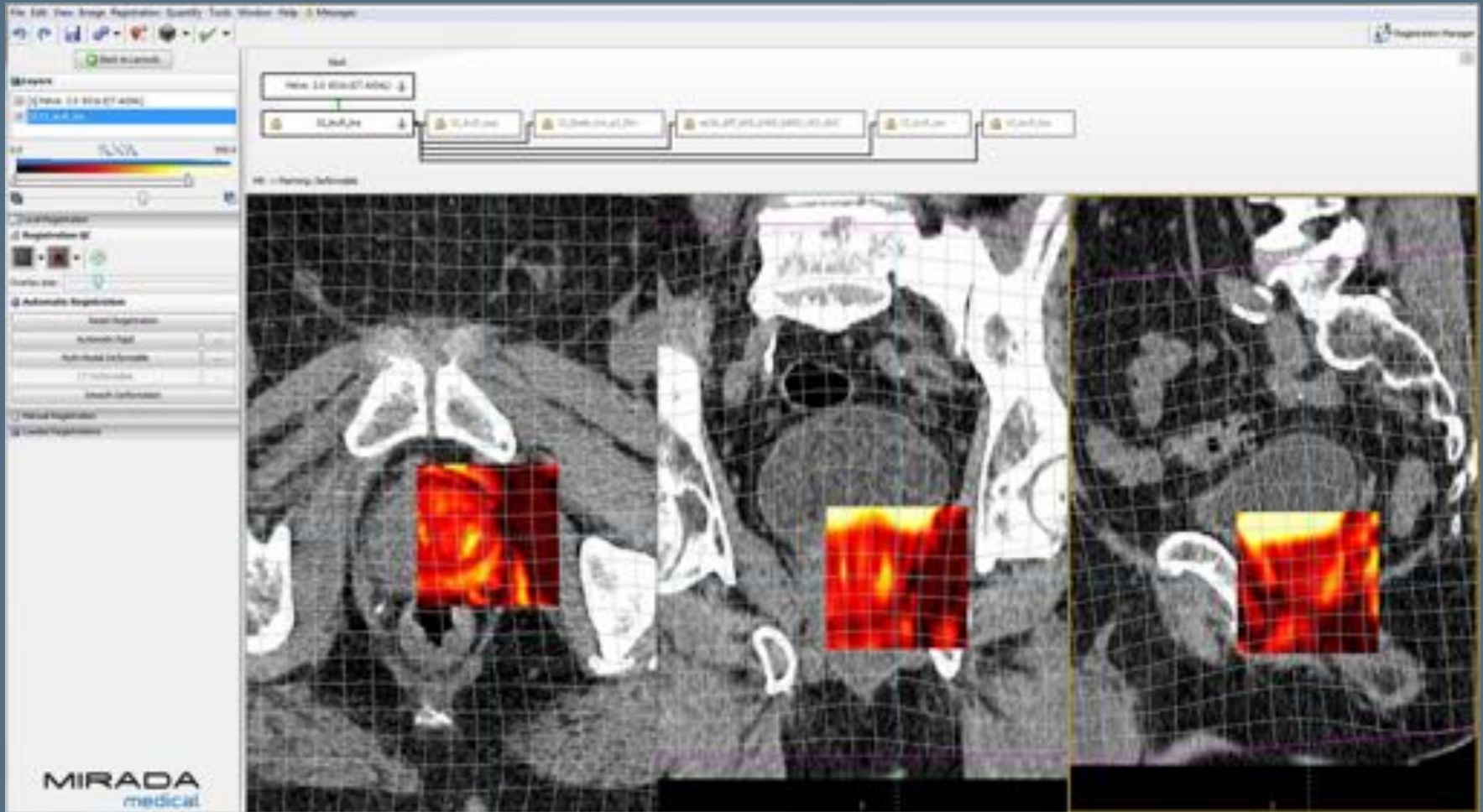


# Raystation

- Deformation: BEM-based tissue mechanics model
- Image Similarity:
  - unimodal = least squares voxel differences
  - multimodal = mutual information
- Regularization: grid-based term (maintain smooth and invertible deformations) + shape based term (maintains reasonable contours when present)



# Mirada RTx

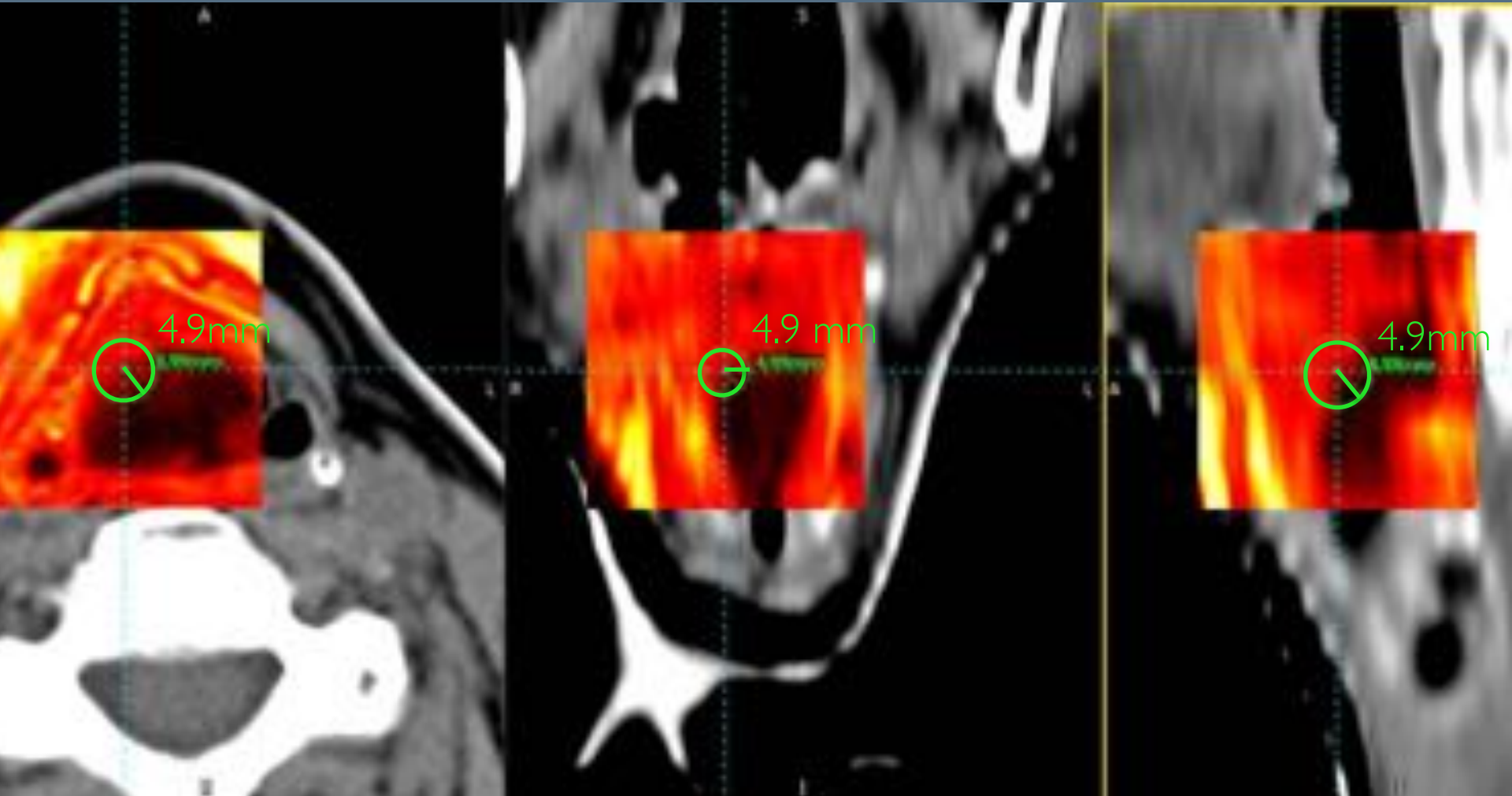


(Image courtesy of Mirada Medical)

# Mirada RTx

- Deformation:
  - unimodal = Lucas Kanade optical flow
  - multimodal = radial basis functions
- Image similarity:
  - unimodal = least squares voxel differences
  - multimodal = mutual information
- Regularization: penalization of diffusion PDEs
  
- Deformations can be signed and locked
- Can quantitatively query the deformation on a per-voxel basis

# Mirada RTx



(Images courtesy of Mirada Medical)

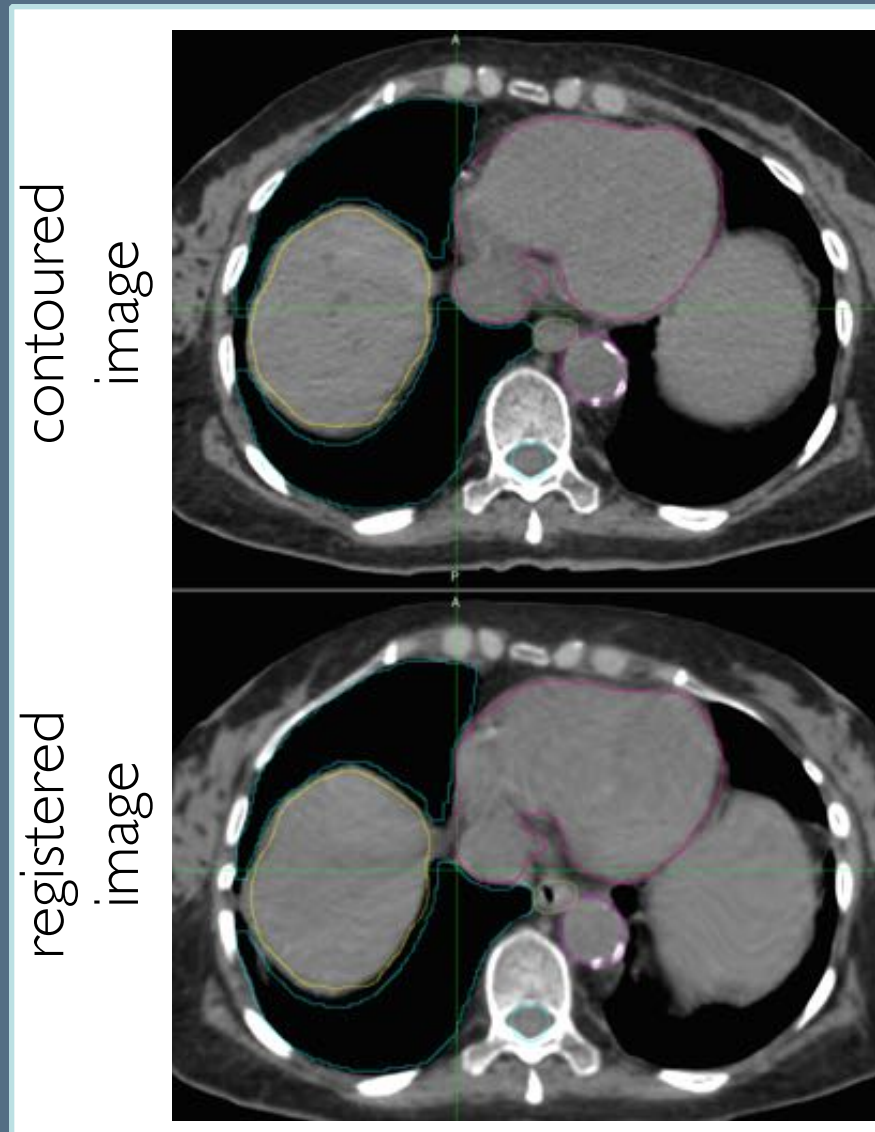
➤ DIR Advantages/Challenges

# Contour Propagation

Contours transferred from previous to new imaging.

Because image similarity guides registration particularly at high contrast areas (edges), contour propagation is reasonably reliable.

*MD second check of contours – sufficient for patient-specific QA.*

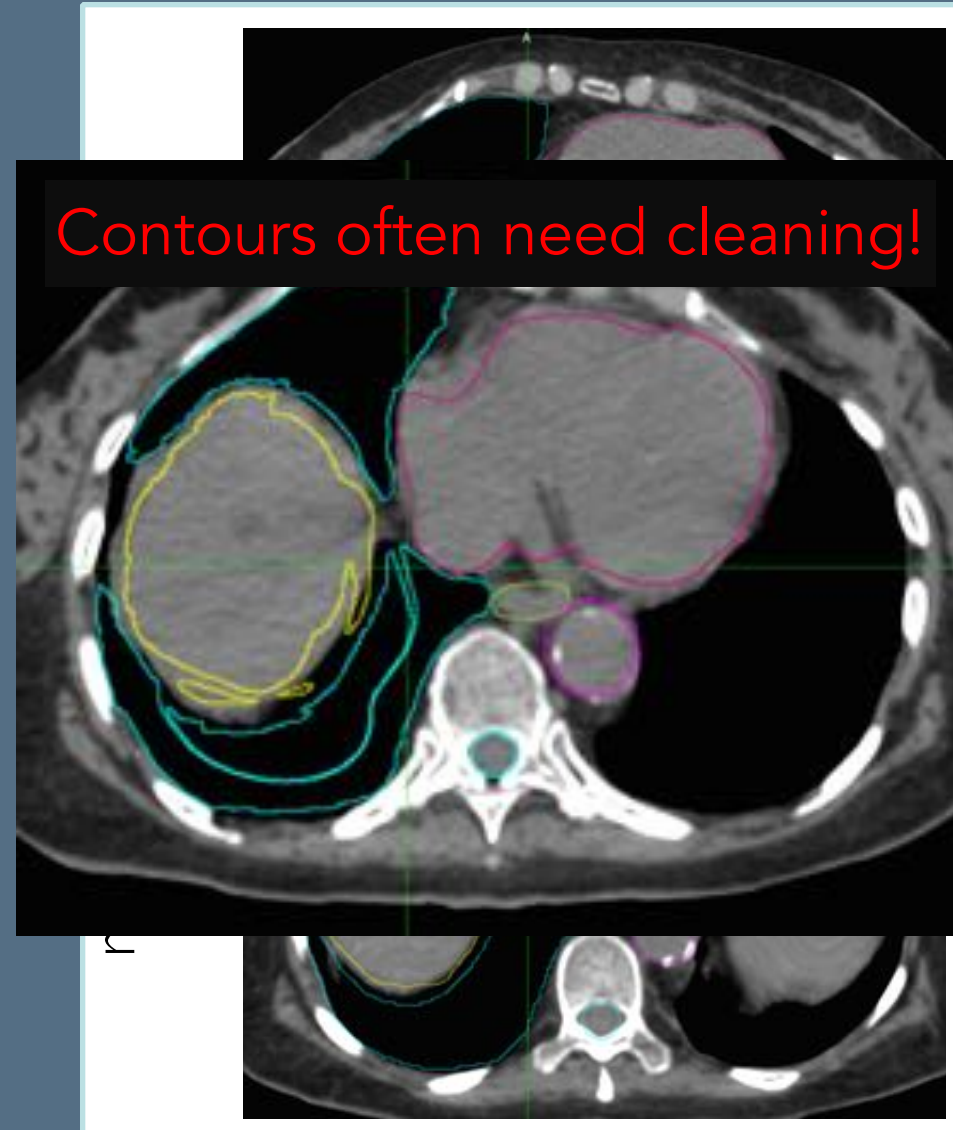


# Contour Propagation

Contours transferred from previous to new imaging.

Because image similarity guides registration particularly at high contrast areas (edges), contour propagation is reasonably reliable.

*MD second check of contours – sufficient for patient-specific QA.*



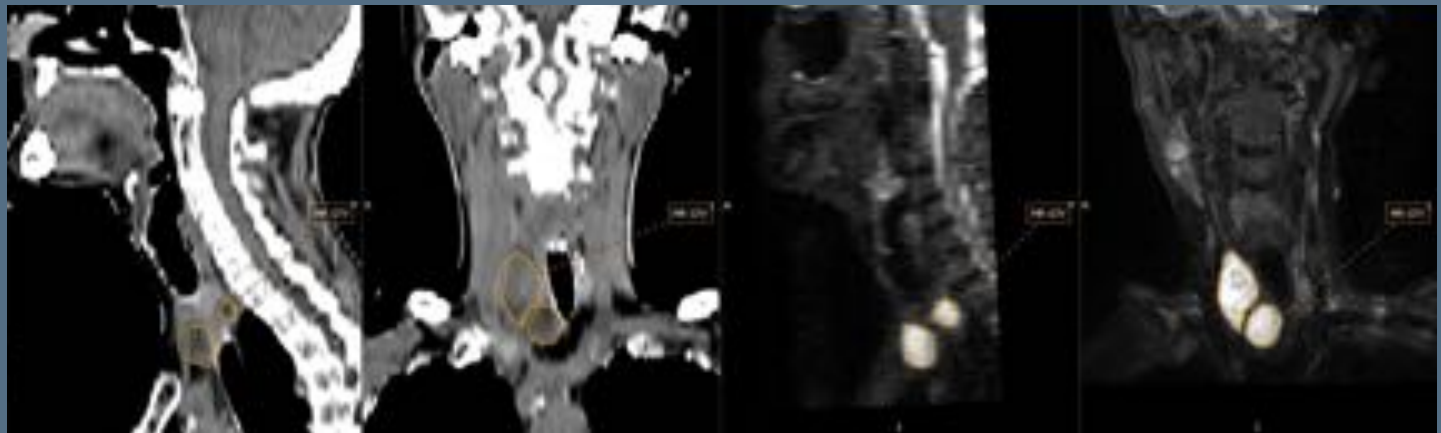
# Contour Guidance

More reliable than dose warping, because only need accurate deformations near contours of interest.

However, registering different modalities is challenging!

- Mutual information is not as reliable as image similarity metric
- Different patient positions, slice thickness, and resolutions further challenge the registration algorithms

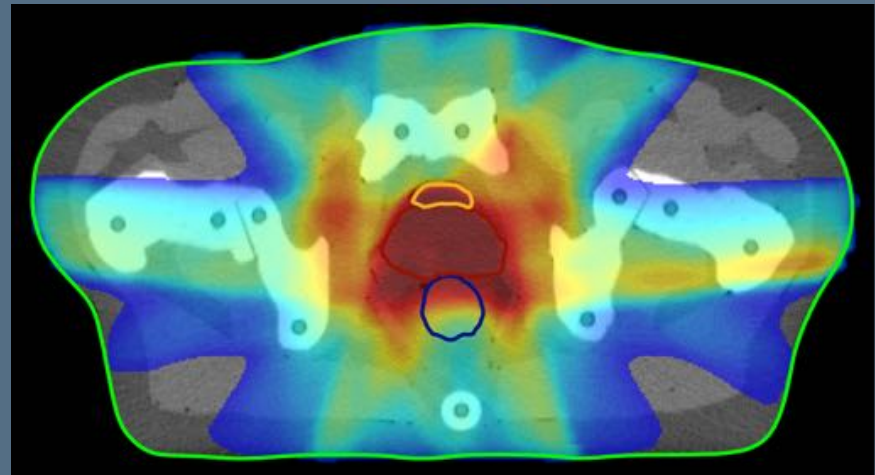
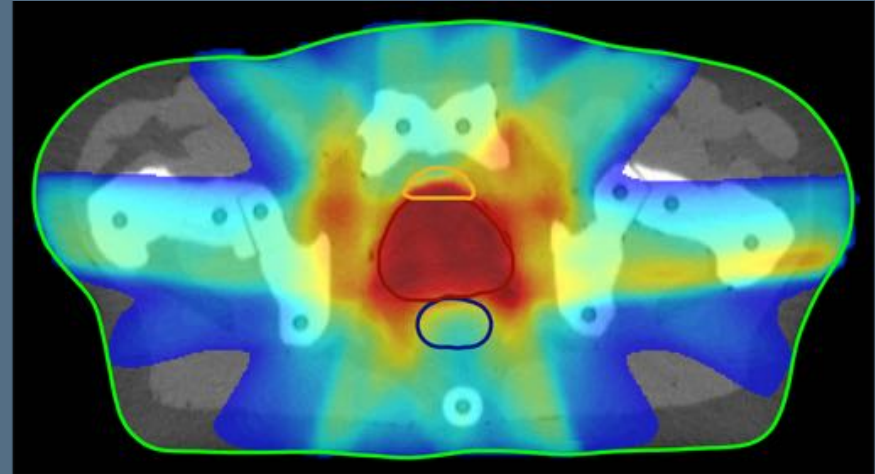
*Patient specific QA challenging, because no ground truth available.*



# Dose Registration/Summation

More difficult than contour guidance, because deformations must be accurate across entire treated volume.

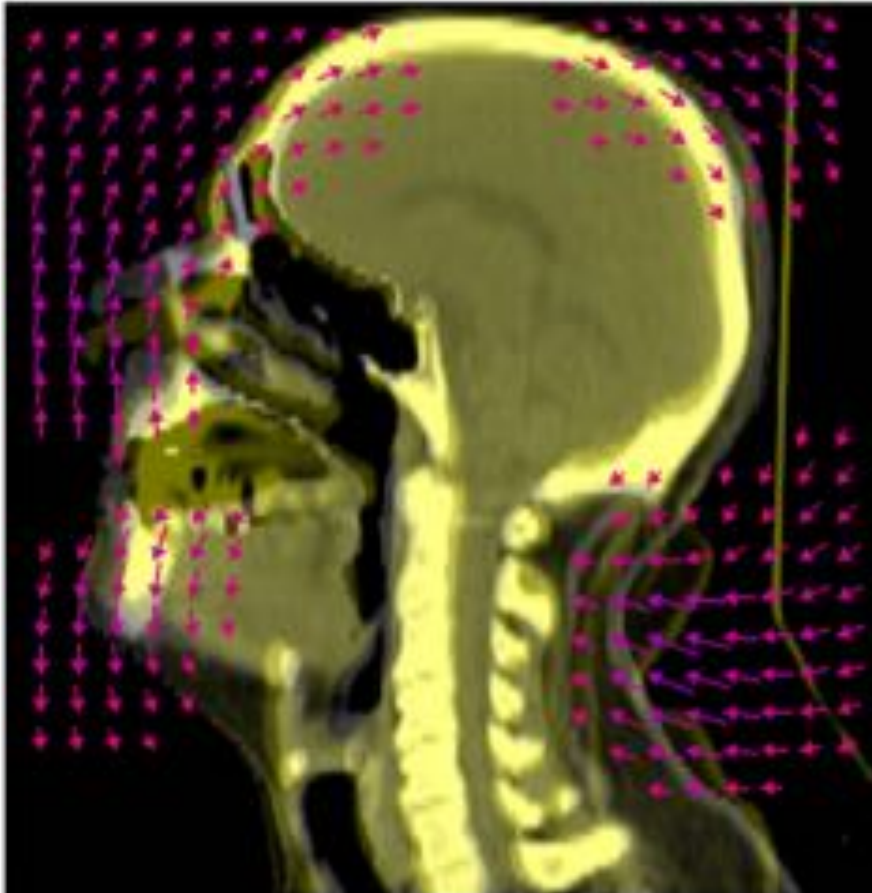
*Patient specific QA challenging, because no way to determine true deformations.*



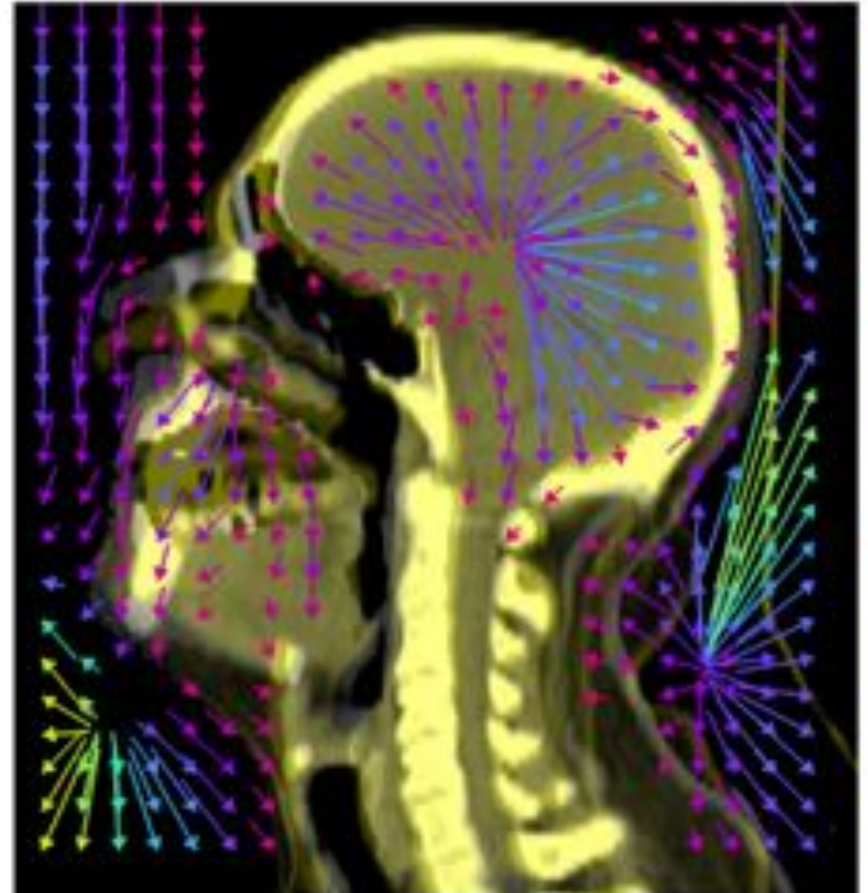


# Transformation Type Matters!

Bspline Transform

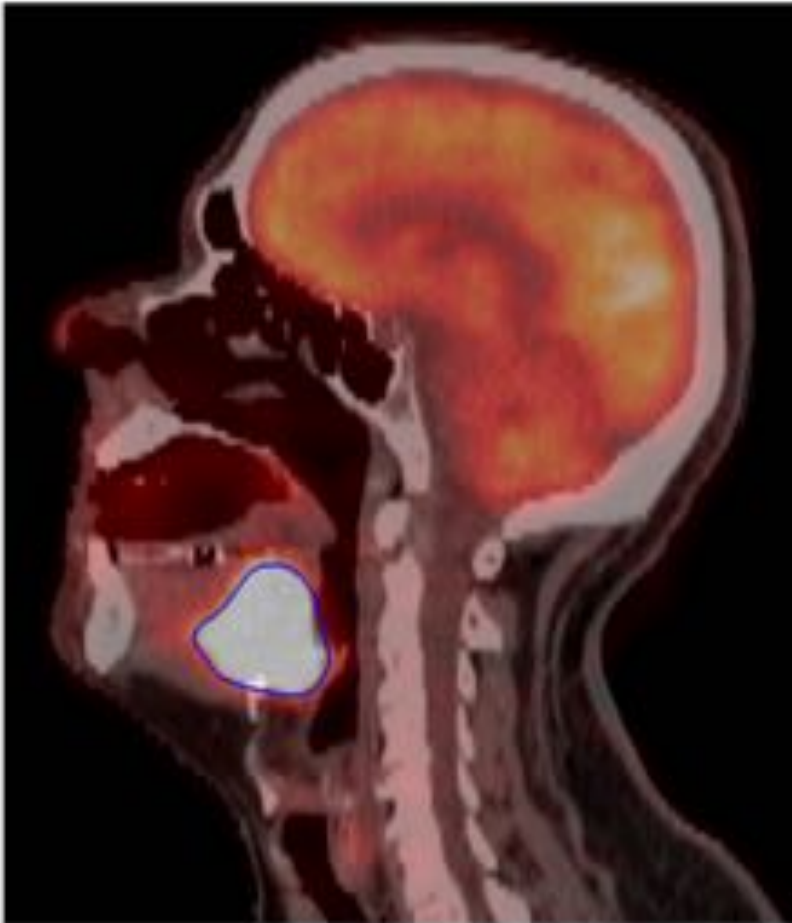


Demons Transform

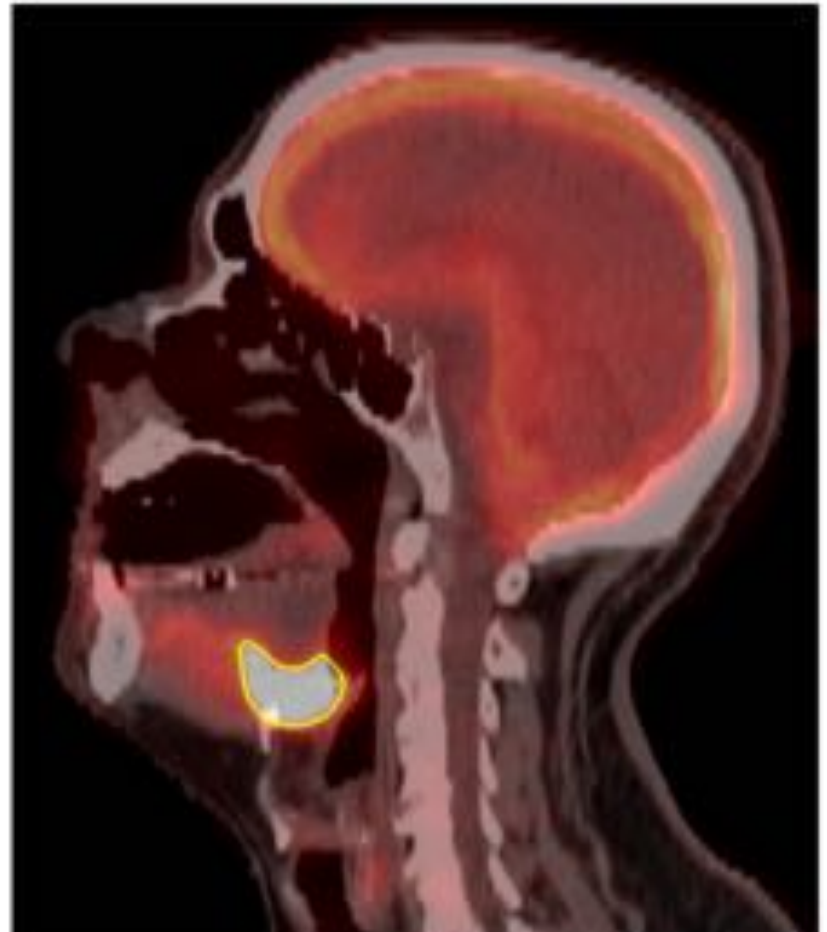


# Transformation Type Matters!

Bspline Transform



Demons Transform



# Deformable or Rigid?

Accuracy depends on registration method:

- Rigid registration is more accurate than deformable registration

rigid: ~1-2 mm uncertainty\*

deformable: ~5-7 mm uncertainty\*\*

\*Benchmark Test of Cranial CT/MR Registration • *IJROBP* • Kenneth *et al.* • 2010

\*\*Need for application-based adaptation of DIR • *Med. Phys.* • Kirby *et al.* • 2013

\*\*Performance of DIR in low contrast regions • *Med. Phys.* • Supple *et al.* • 2013

# Regions of Low Contrast

Image similarity not always sufficient to guide deformations.

Registrations accuracy is better in areas of high HU contrast (e.g. borders of organs), poor in areas of homogeneous intensity (e.g. liver)

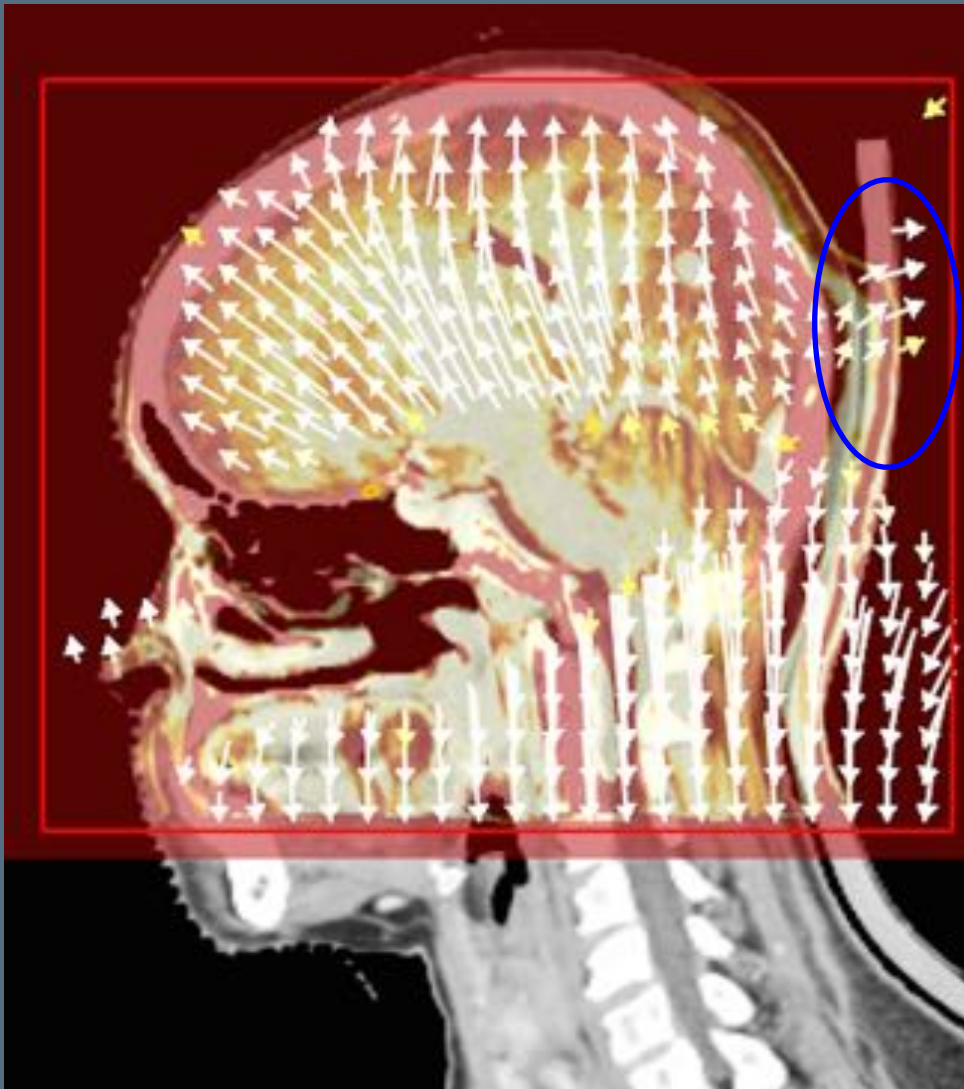
# Regions of Low Contrast

Image similarity not always sufficient to guide deformations.

Registrations accuracy is better in areas of high HU contrast (e.g. borders of organs), poor in areas of homogeneous intensity (e.g. liver)

underconstrained/underdetermined problem:  
insufficient information to accurately  
drive the deformation

# Setup Differences



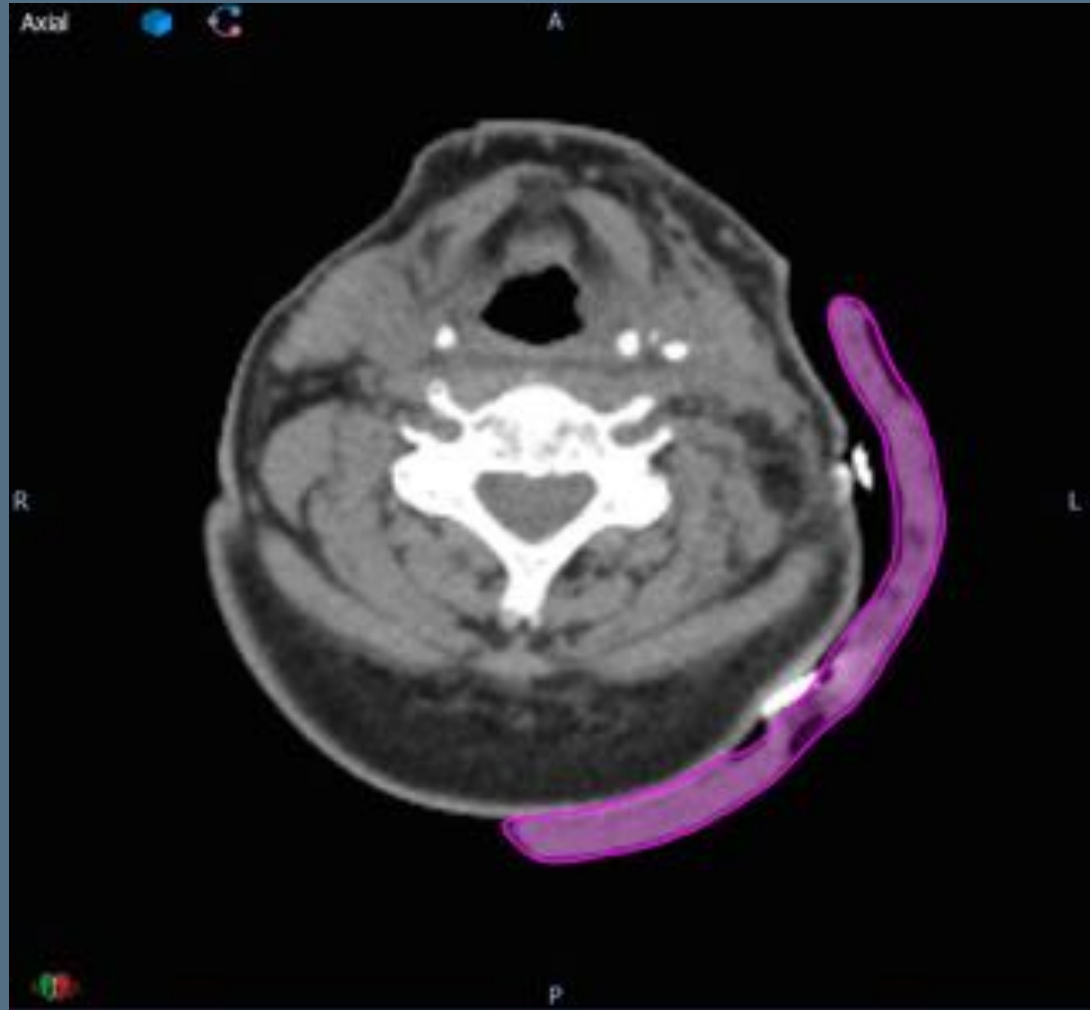
Registration methods cannot differentiate between patient tissue and setup materials, (e.g. pads, bolus, etc.)

Registration may push patient tissue to match setup materials.

# Setup Differences

How to address?

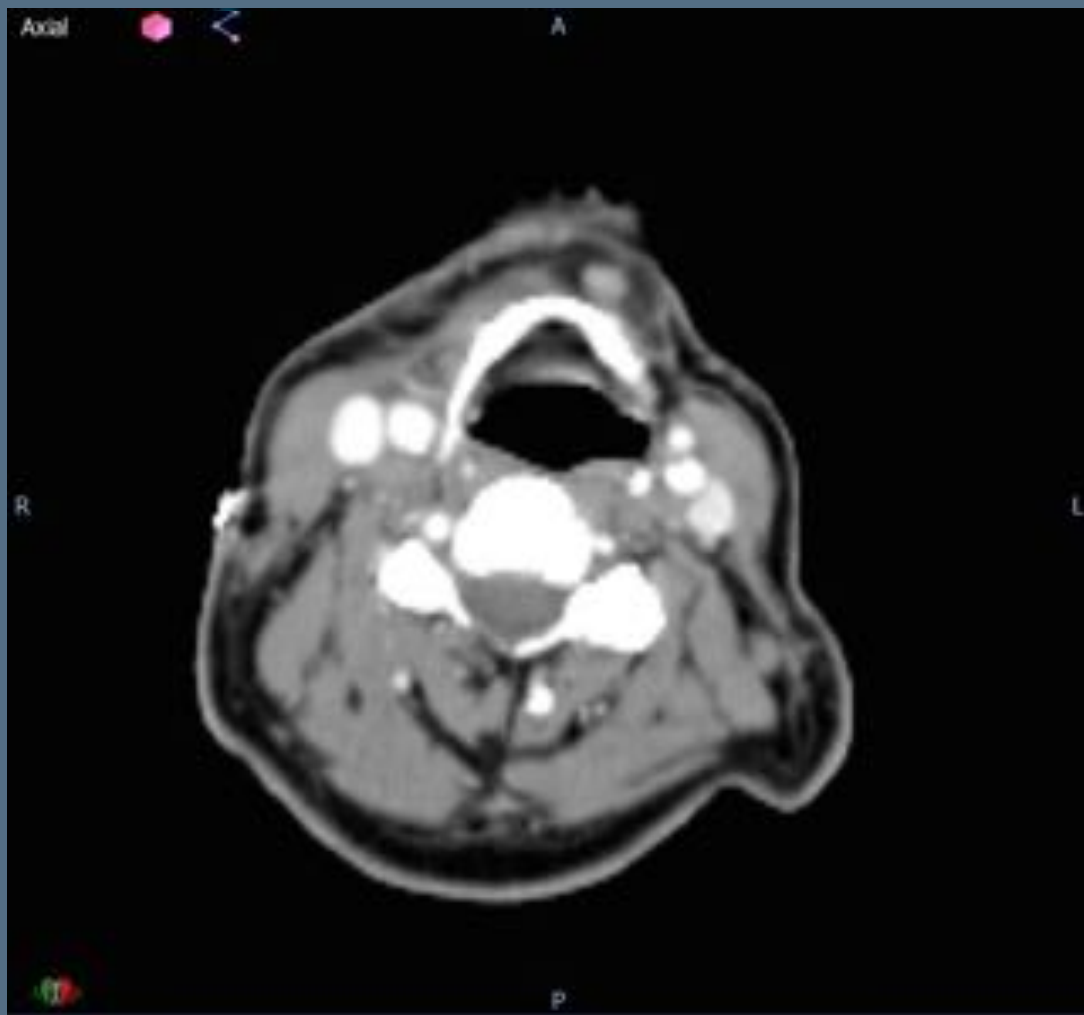
1. Exclude additional materials from registration ROI
2. Mask out additional material (similar to tissue override in treatment planning).



# Setup Differences

How to address?

1. Exclude additional materials from registration ROI
2. Mask out additional material (similar to tissue override in treatment planning).

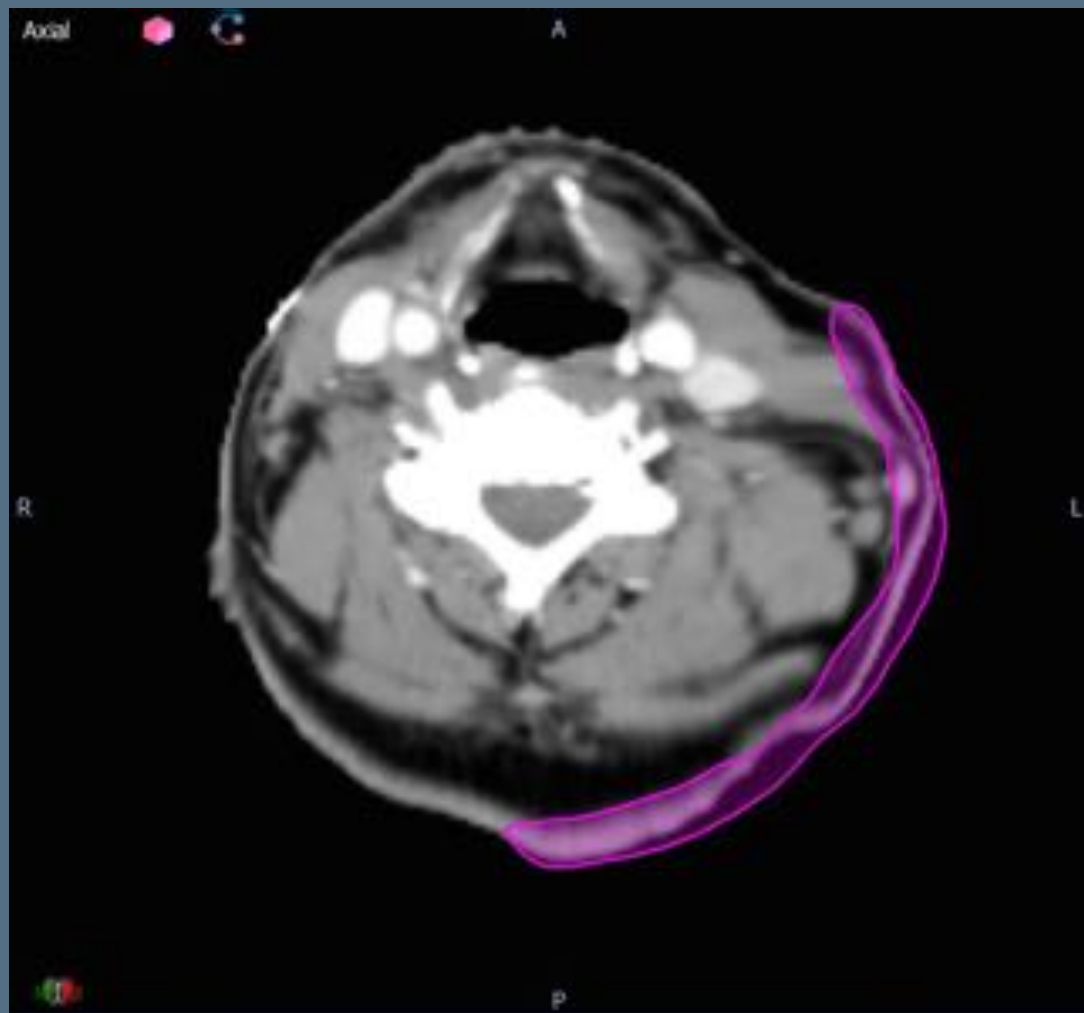




# Setup Differences

How to address?

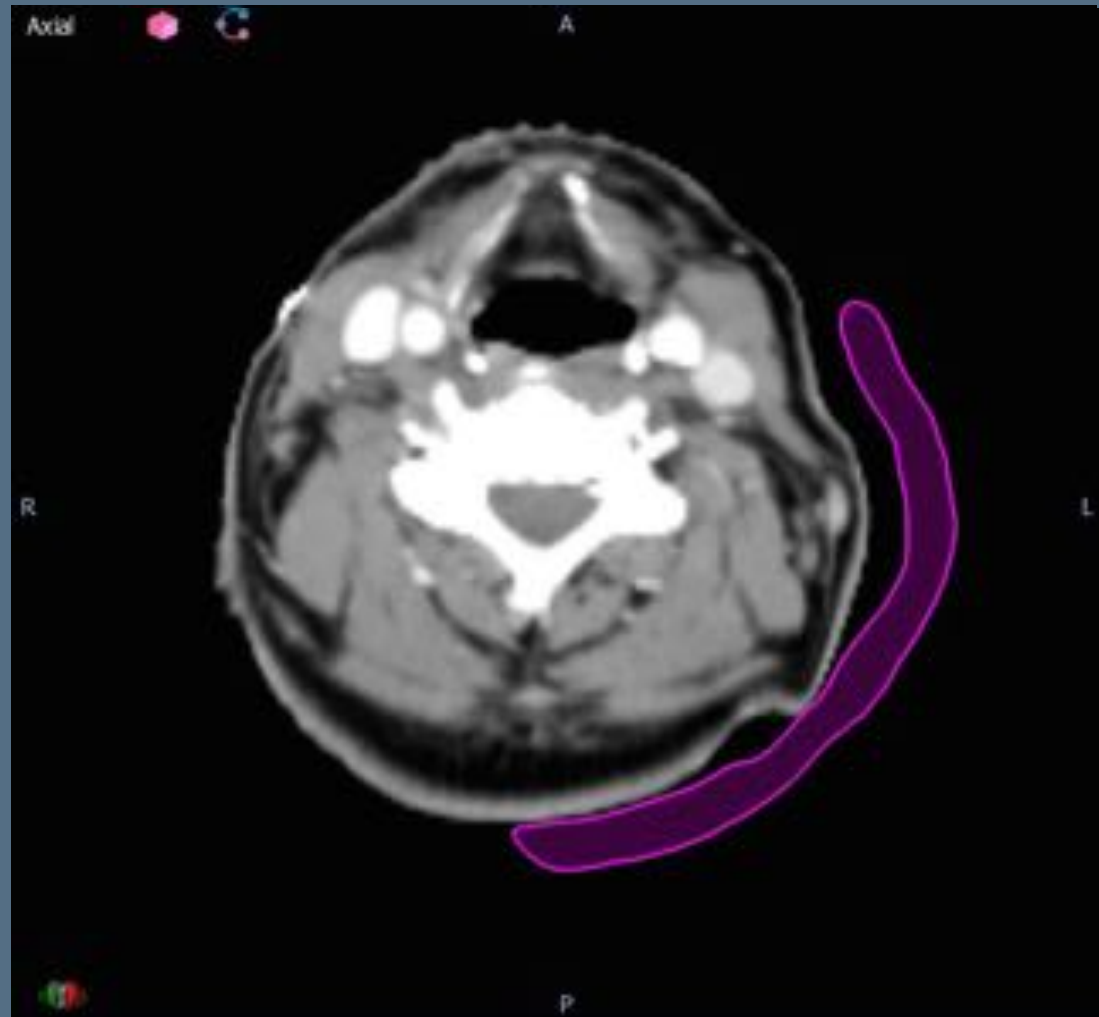
1. Exclude additional materials from registration ROI
2. Mask out additional material (similar to tissue override in treatment planning).



# Setup Differences

How to address?

1. Exclude additional materials from registration ROI
2. Mask out additional material (similar to tissue override in treatment planning).



# Biological Changes

- (1) Tumor growth/shrinkage/surgical removal
- (2) Radiation induced pulmonary fibrosis
- (3) Weight changes

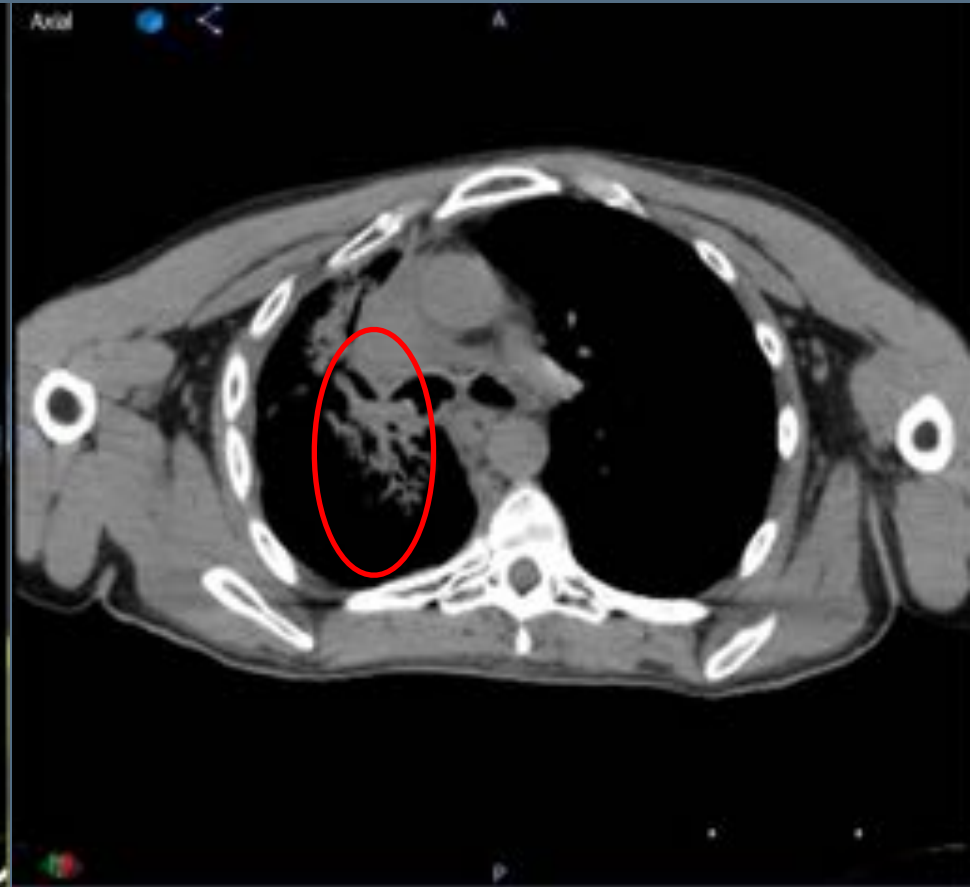
## Considerations:

- (1) How to produce good registrations?
  - introduction/removal of tissue presents substantial challenge to registration methods.
- (2) How to compute radiation physics?
  - Simply warping dose same as the images is insufficient.

# Example: Pulmonary Fibrosis

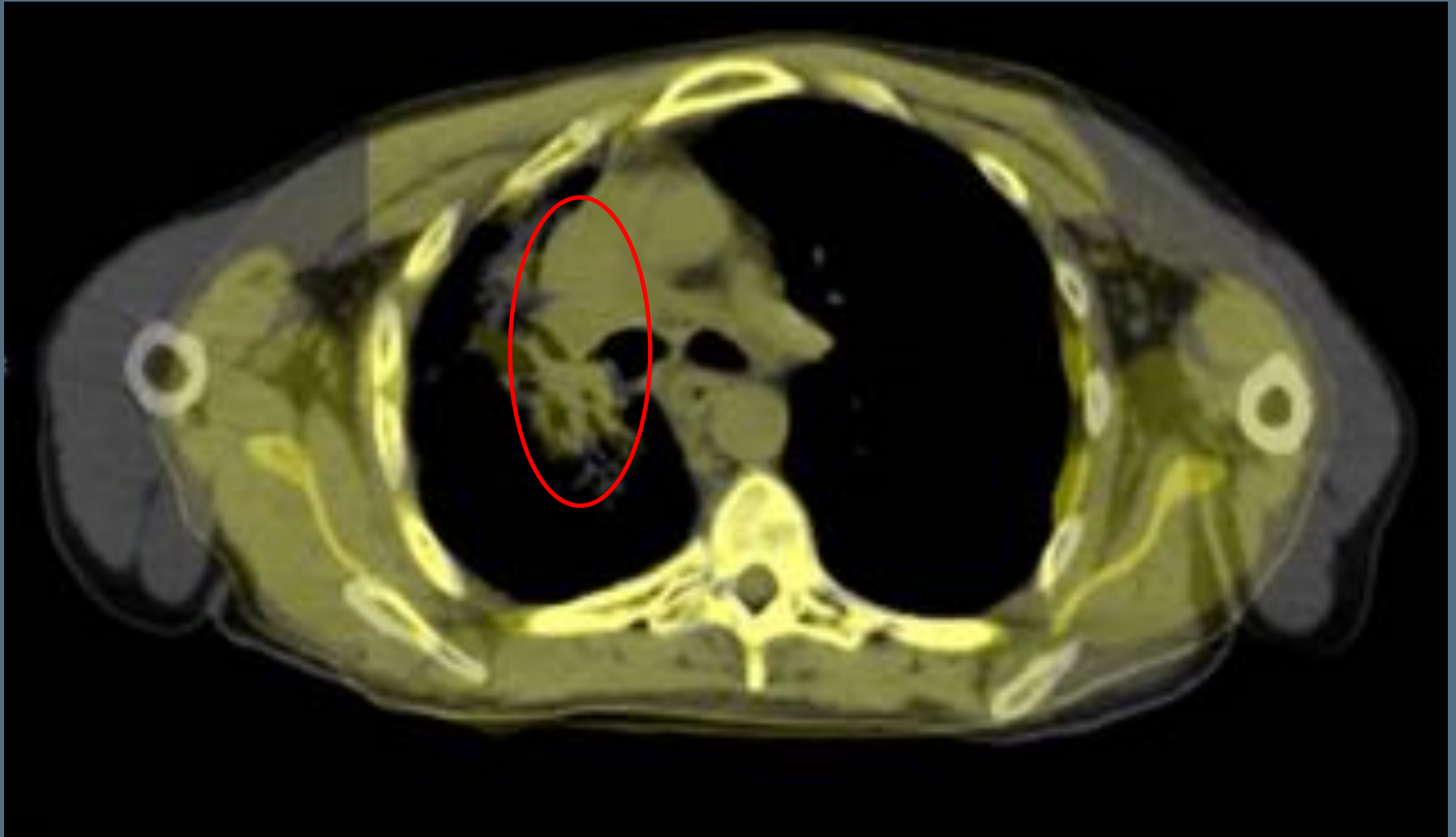
before treatment

following treatment



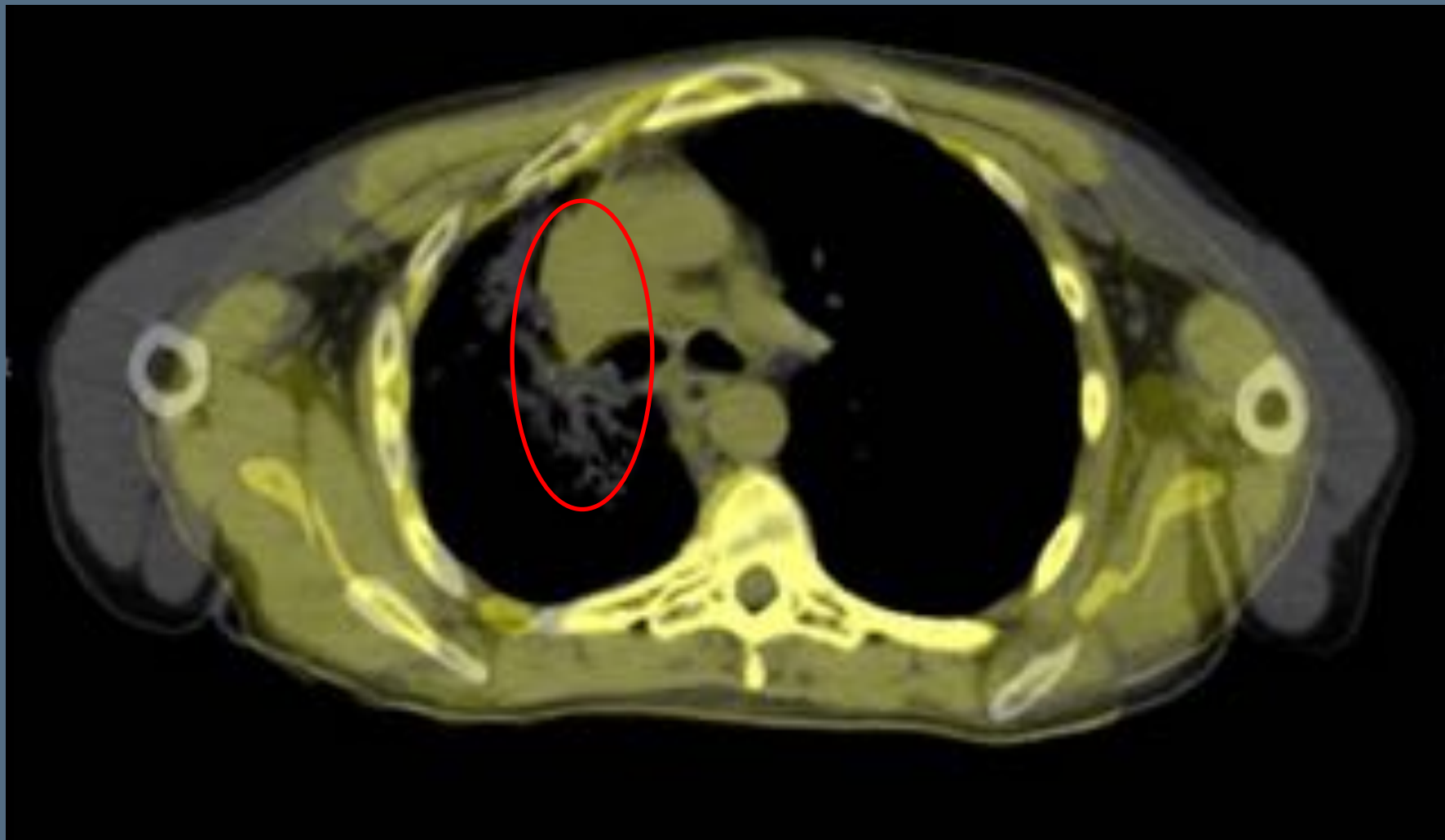
(Images courtesy of Velocity)

# Example: Pulmonary Fibrosis



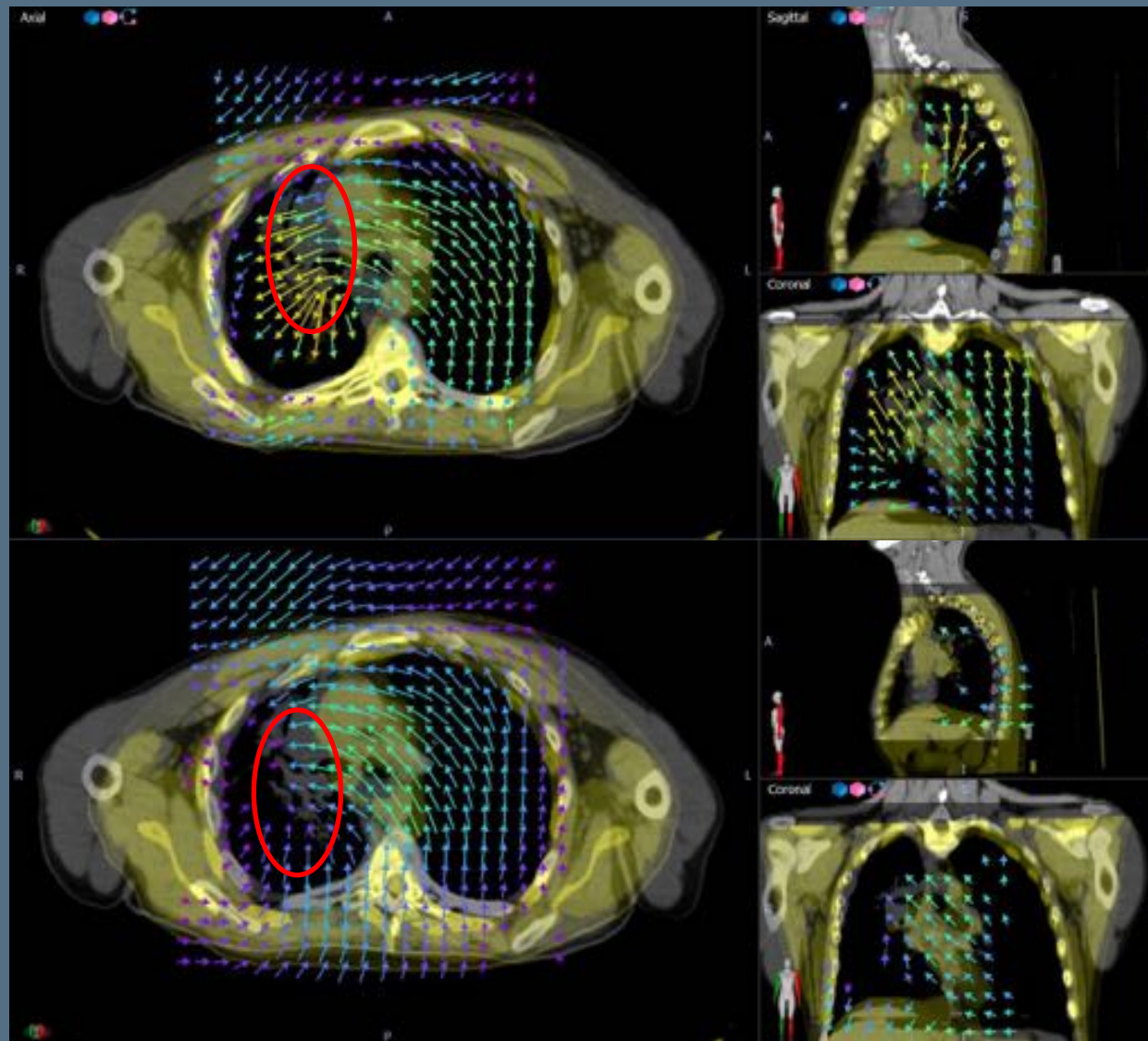
(Image courtesy of Velocity)

# Example: Pulmonary Fibrosis



(Image courtesy of Velocity)

# Example: Pulmonary Fibrosis





# SAMs Questions



Which of the following situations is of LEAST concern for producing inaccurate/unreliable dose deformations?

- (a) rigid registration for brain
- (b) deformable registration for liver
- (c) deformable registration for head and neck
- (d) deformable registration for lung
- (e) deformable registration for prostate

Which of the following situations is of LEAST concern for producing inaccurate/unreliable dose deformations?

- (a) rigid registration for brain
- (b) deformable registration for liver
- (c) deformable registration for head and neck
- (d) deformable registration for lung
- (e) deformable registration for prostate

Which of the following situations is of LEAST concern for producing inaccurate/unreliable dose deformations?

Answer: (a) rigid registration for brain.

Rigid registration for small regions of bony anatomy remain higher accuracy than deformable registrations (in general). DIR should not be used when rigid registrations will suffice.

Refs: Crum et al. “Non-rigid Image Registration: Theory and Practice”, *British Inst. Radiol.*, 77:S2, p. S140-S153, 2004.

Kirby, et al. “The need for application-based adaptation of deformable image registration”, *Medical Physics*, 40:1, p. 1-9, 2013.

Hoffmann et al. “Accuracy quantification of a deformable image registration tool applied in a clinical setting”, *JACMP*, 15:1, p. 237-245, 2014.

Which of the following situations is of LEAST concern for producing inaccurate/unreliable dose deformations?

Answer: (a) rigid registration for brain.

Rigid registration for small regions of bony anatomy remain higher accuracy than deformable registrations (in general). DIR should not be used when rigid registrations will suffice.

Refs: Crum et al. “Non-rigid Image Registration: Theory and Practice”, *British Inst. Radiol.*, 77:S2, p. S140-S153, 2004.

Kirby, et al. “The need for application-based adaptation of deformable image registration”, *Medical Physics*, 40:1, p. 1-9, 2013.

Hoffmann et al. “Accuracy quantification of a deformable image registration tool applied in a clinical setting”, *JACMP*, 15:1, p. 237-245, 2014.

True or False, contours fused onto a newly acquired CT are sufficiently reliable that they need not be evaluated?

- (a) True
- (b) False

True or False, contours fused onto a newly acquired CT are sufficiently reliable that they need not be evaluated?

- (a) True
- (b) False

True or False, contours fused onto a newly acquired CT are sufficiently reliable that they need not be evaluated?

Answer: (b) False.

Though the reliability of contour fusion can be higher than dose fusion, propagated contours should always be double-checked by the attending.

Refs: Lardue et al. "Assessment of Contour Fusion Methods for Auto-Contouring of the Male Pelvis", IJROBP, 87:S2, p. 374, 2013.

Li et al. "Propagation of Pancreas Target Contours on Respiratory Correlated CT Images Using Deformable Image Registration", Med. Phys., 41, p. 209, 2014.

True or False, contours fused onto a newly acquired CT are sufficiently reliable that they need not be evaluated?

Answer: (b) False.

Though the reliability of contour fusion can be higher than dose fusion, propagated contours should always be double-checked by the attending.

Refs: Lardue et al. "Assessment of Contour Fusion Methods for Auto-Contouring of the Male Pelvis", IJROBP, 87:S2, p. 374, 2013.

Li et al. "Propagation of Pancreas Target Contours on Respiratory Correlated CT Images Using Deformable Image Registration", Med. Phys., 41, p. 209, 2014.



Which statement is MOST correct?

- (a) Visual comparison of the deformed and target images is sufficient to ensure deformation accuracy.
- (b) Registering with larger regions of interest boxes generally produces more accurate deformations.
- (c) Image transformations are always defined globally.
- (d) DIR can produce inaccurate deformations in areas of low HU contrast.

Which statement is MOST correct?

- (a) Visual comparison of the deformed and target images is sufficient to ensure deformation accuracy.
- (b) Registering with larger regions of interest boxes generally produces more accurate deformations.
- (c) Image transformations are always defined globally.
- (d) DIR can produce inaccurate deformations in areas of low HU contrast.

Which statement is MOST correct?

Answer: (d) DIR can produce inaccurate deformations in areas of low HU contrast.

DIR in areas of low HU contrast like liver can produce inaccurate deformations because the lack of image information cannot accurately drive the inverse solver.

Refs: Zhong et al., “A finite element method to correct deformable image registration errors in low-contrast regions”, Phys Med. Biol., 57:1, p. 2012.

Which statement is MOST correct?

Answer: (d) DIR can produce inaccurate deformations in areas of low HU contrast.

DIR in areas of low HU contrast like liver can produce inaccurate deformations because the lack of image information cannot accurately drive the inverse solver.

Refs: Zhong et al., “A finite element method to correct deformable image registration errors in low-contrast regions”, Phys Med. Biol., 57:1, p. 2012.

# Acknowledgements:

Deborah Hodefi, M.Sc., DABR, MCCPM  
(Yale-New Haven Hospital)

Sharon Callaway, Anthony Waller, & Michael Crocker (Varian  
Medical Systems:Velocity)

Doug Phillip & Timor Kadir (Mirada Medical)

Kyle Ostergren (MIMVista)

Neil Kirby, Ph.D., DABR (UCSF)

Jean Pouliot, Ph.D. (UCSF)

# Additional Resources

# Practical Workflow Tips

- Use appropriate deformation direction (i.e. choice of moving and target image).
- Initial rigid registration can substantially impact deformable registration.
- Be careful of ROI box size choice.
- Keep organized and name fusions appropriately!



# Image Similarity vs. Regularization

The two terms are weighted, and the relative balance substantially effects the registration outcome.

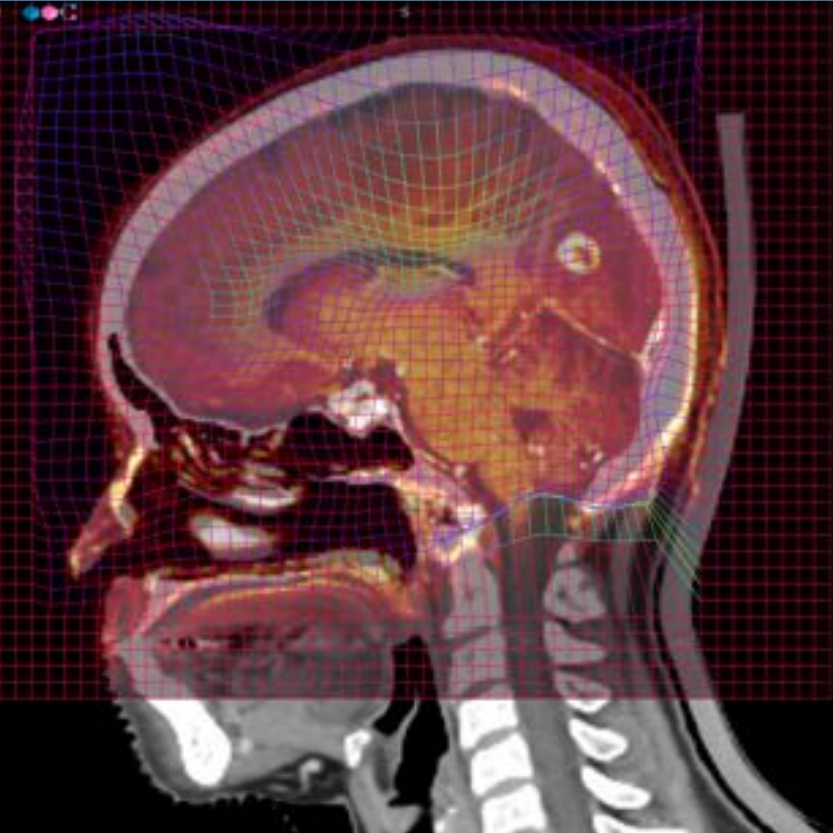
Too much regularization – the transformation motion is too constrained, which can prevent decent registrations.

Too much image similarity – registration may warp voxels in very non-physical ways to match the images on the order of noise.



# Rigid vs. Deformable

deformable

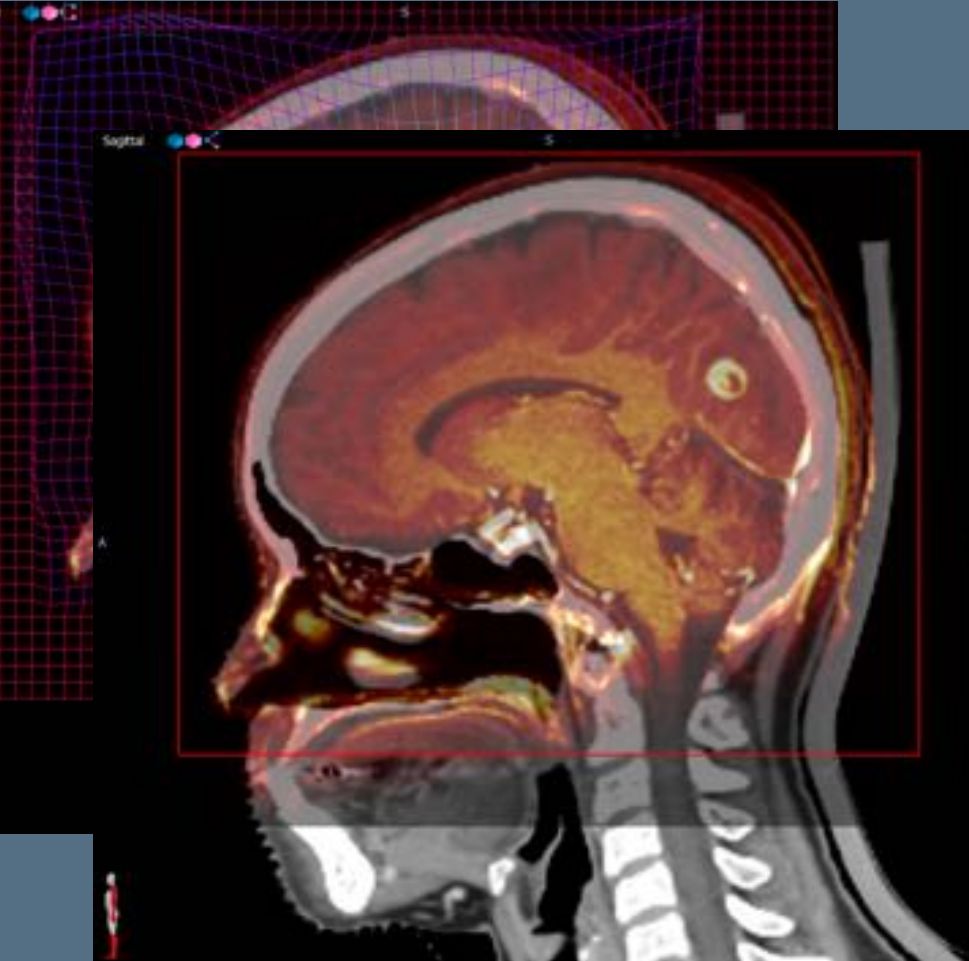


In some cases, rigid is preferable to deformable.

Here, the rigid registration is sufficient, and likely more accurate than deformable.

# Rigid vs. Deformable

deformable



rigid

In some cases, rigid is preferable to deformable.

Here, the rigid registration is sufficient, and likely more accurate than deformable.



# Evaluating Registrations: Tools for Visual Assessment

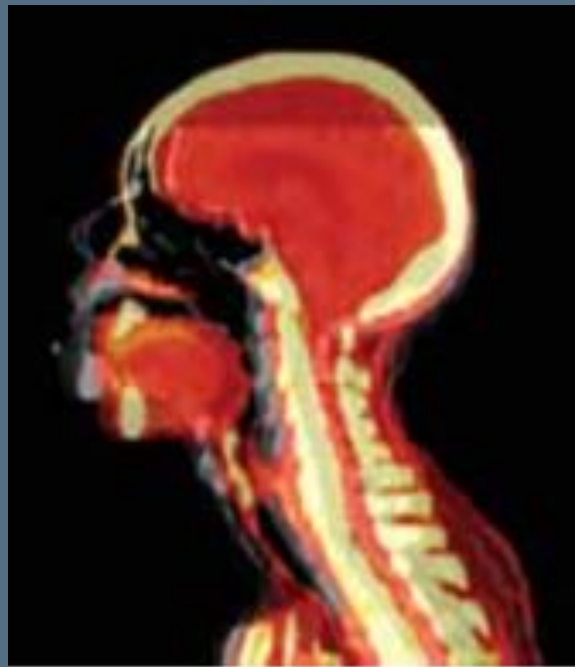
# Registration Evaluation

Important to assess registration quality of each registration performed and identify and discard unacceptable registrations

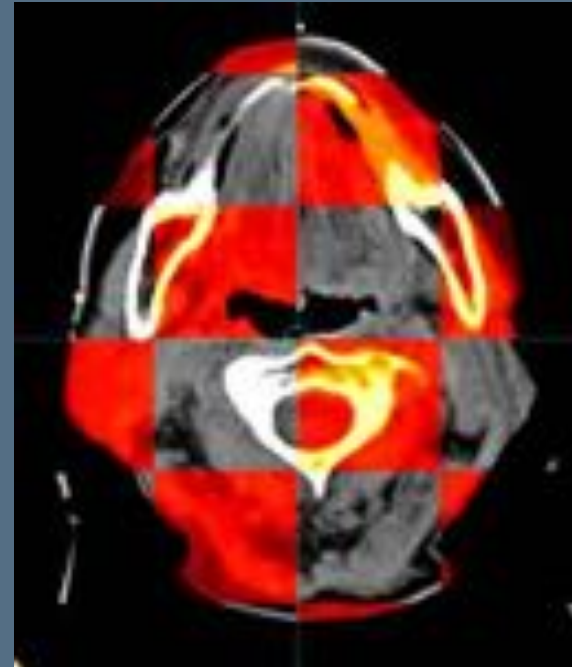
- (1) Visual comparison of deformed and target images  
(insufficient to detect all possible registration mishaps)
- (2) Visual inspection of deformation field  
(potentially catch additional registration errors)

# First Step: Deformed Image

(Can catch many registration errors)

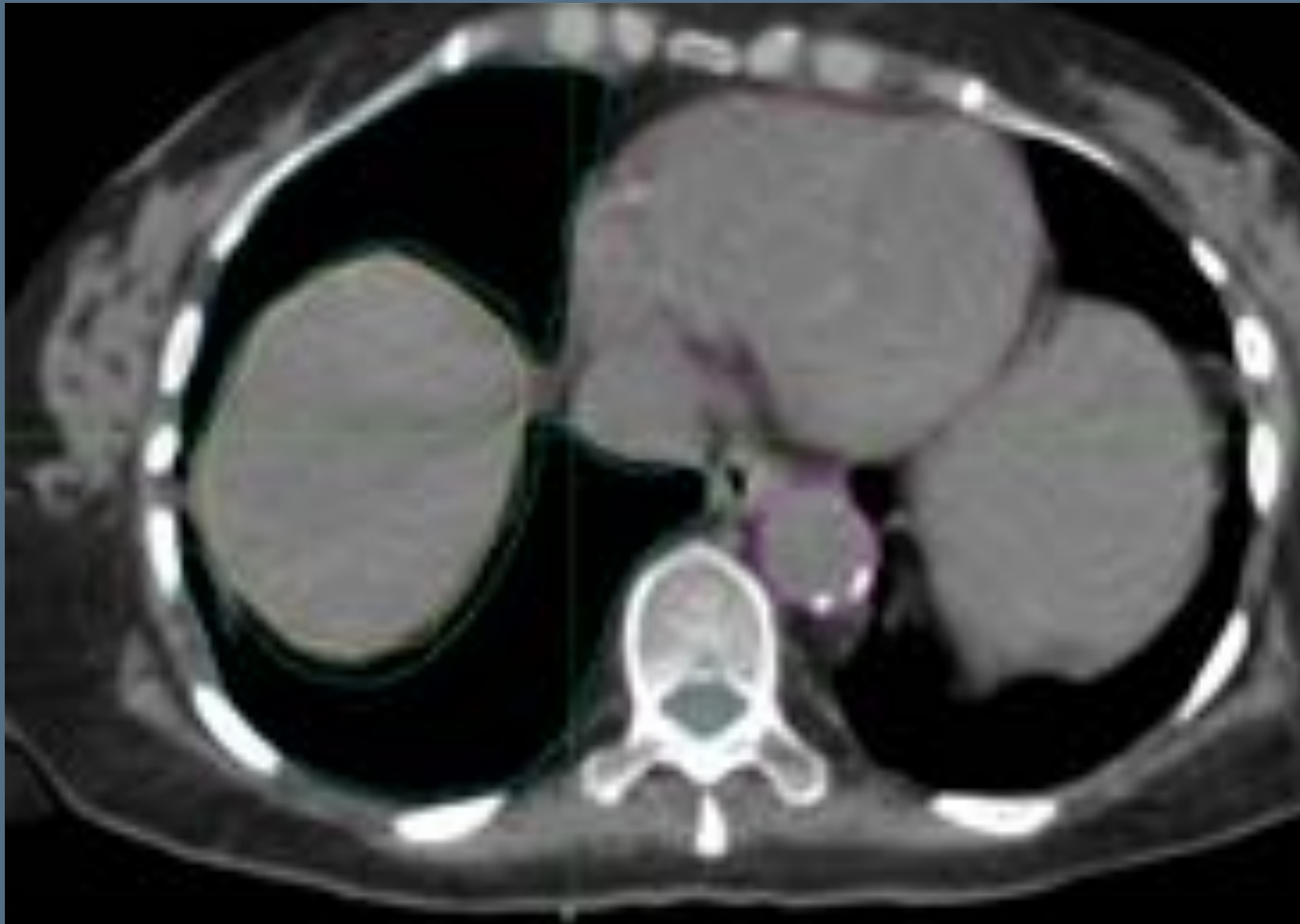


blend

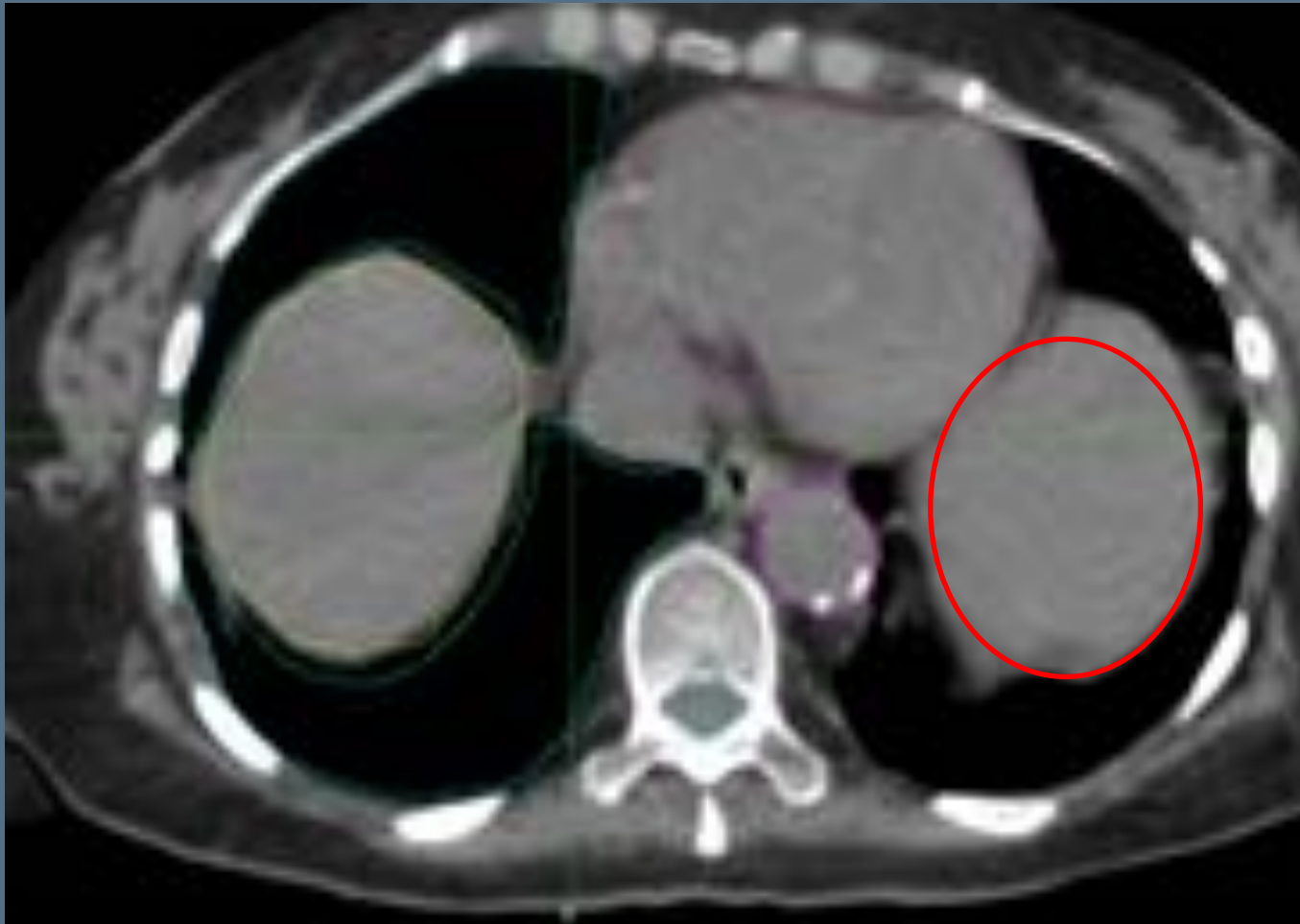


checker board

# Visual Comparison: Example



# Visual Comparison: Example



# Visual Comparison: Example



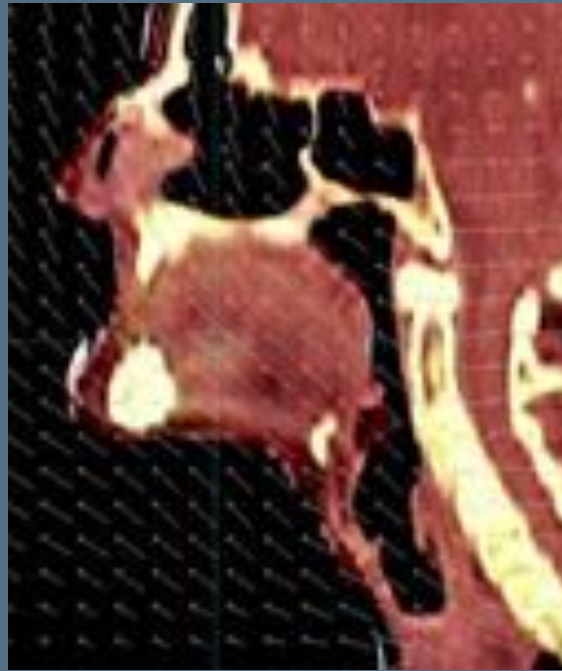


# Second Step: Deformation Field

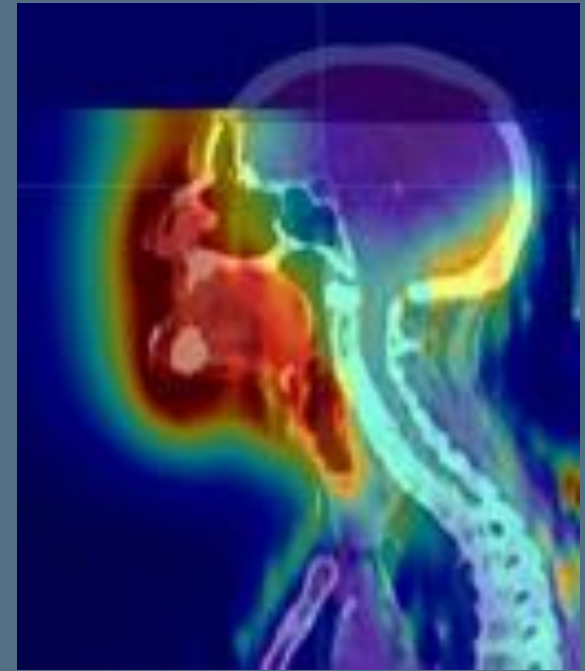
(Can catch more registration errors)



warped grid



vector field



heat maps

(Images courtesy of Mirada Medical)

# DIR White Papers

Some companies white papers are more informative than others. Below is a list of URLs for the major commercial options.

- **Raystation:** [http://www.raysearchlabs.com/Global/Publications/White%20papers/White%20paper%202%20-%20Deformable%20\(web\).pdf](http://www.raysearchlabs.com/Global/Publications/White%20papers/White%20paper%202%20-%20Deformable%20(web).pdf)
- **MIMVista:** Call 216-455-0600 to request white paper.
- **Mirada:** <http://www.mirada-medical.com/solutions/deformable-image-registration> - (white paper is located at bottom of page)