# Deformable Image Registration in Radiation Therapy


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## Acknowledgements & Conflict of Interest


- AAPM Task Group 132 Chair
- I have a licensing agreement for deformable image registration technology with RaySearch Laboratories.
- I recently held a co-development agreement with Varian Medical Systems
- Currently hold a research agreement with RaySearch Laboratories
- AAPM TG 132
- Molly McCulloch, PhD, Guillaume Cazoulat PhD, Peter Balter, PhD, Andrea Ohrt
- Clifton D. Fuller, MD, PhD – MDACC
- Morfeus Lab – past and present
- Fuller Lab


## Motivation

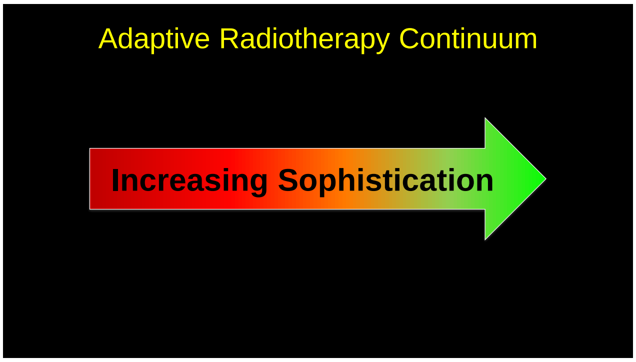
- Numerous retrospective, limited data studies showing that planned ≠ delivered dose and there is an improvement in therapeutic ratio with adaptation
  - Prospective HN trial – all patients had 1 re-plan, 33% had 2 re-plans
- Growing demand from the radiotherapy community – from large academic centers to single vault community practitioners – to have efficient, easy to use tools available
- Increasing number of RTOG/NRG trials including adaptation

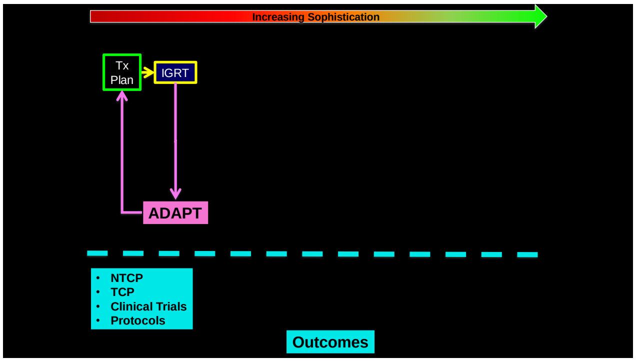
## Motivation

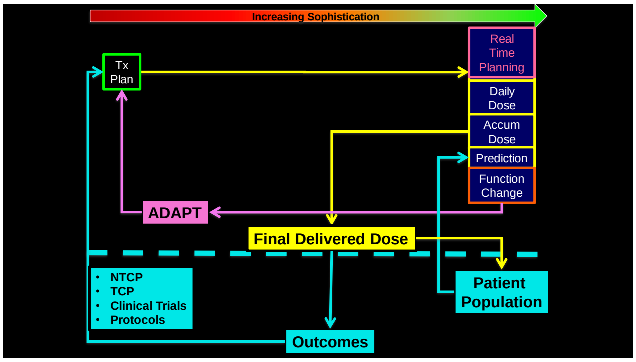
- Clinical Goal: automatically accumulate dose on <u>all patients</u>, use this data to design intelligent adaptation guidelines, and design clinical trials to reduce toxicity/improve tumor control using adaptive (anatomical and functional) tools
- Integration and automation of the tools is essential
  - Even one break in the chain or missing tool can break the whole workflow.

## Clear Display of Relevant Information


## Clear Display of Relevant Information


Adaptive Radiotherapy Continuum
Increasing Sophistication


Increasing Sophistication
Tx Plan
IGRT
ADAPT
NTCP
TCP
Clinical Trials
Protocols
Outcomes


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

# SAFETY!

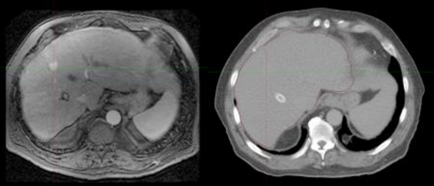
## Commissioning and QA

Recommendations from TG 132

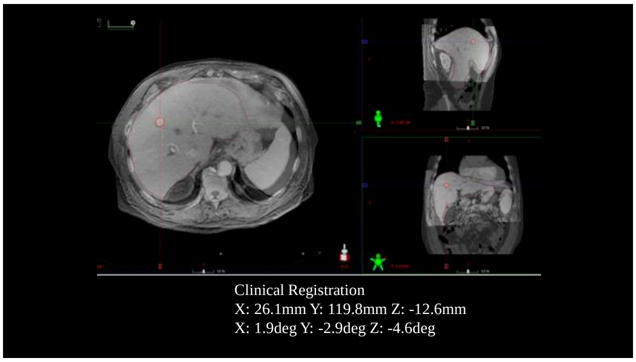
## First: A Word of Caution

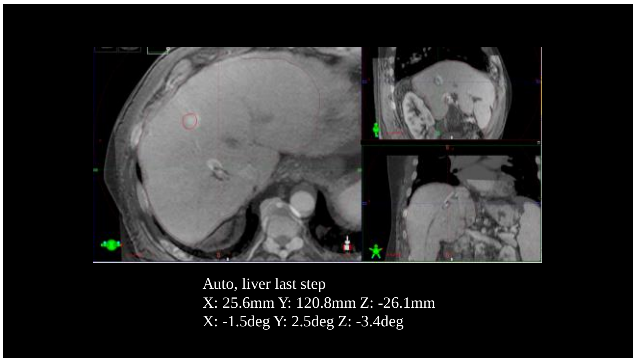
## Example: Multi-modality imaging for Planning

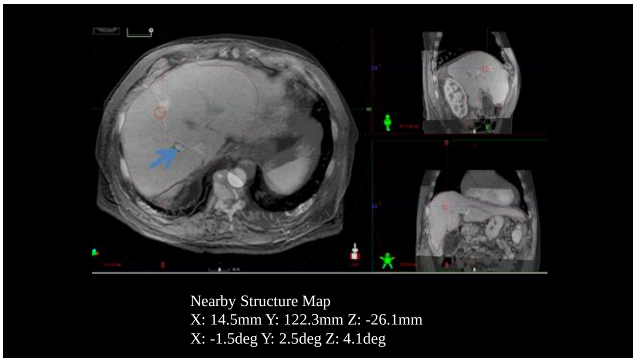
Liver: CT (No Contrast = No visible GTV)

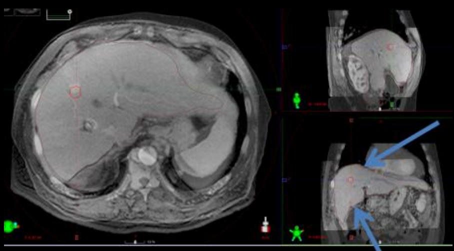


Liver: MR (Visible GTV)


Clinical Registration
X: 26.1mm Y: 119.8mm Z: -12.6mm
X: 1.9deg Y: -2.9deg Z: -4.6deg

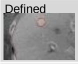

Auto, liver last step
X: 25.6mm Y: 120.8mm Z: -26.1mm
X: -1.5deg Y: 2.5deg Z: -3.4deg


Nearby Structure Map
X: 14.5mm Y: 122.3mm Z: -26.1mm
X: -1.5deg Y: 2.5deg Z: 4.1deg

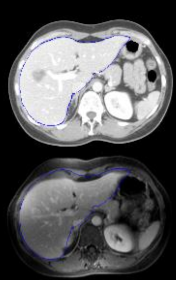


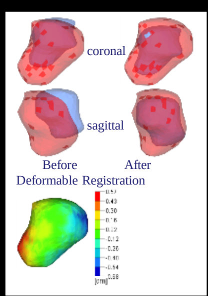
Liver Contour optimization
X: 13.0mm Y: 125.3mm Z: -19.0mm
X: 0.4deg Y: -1.3deg Z: 2.3deg

## Overall Comparison [mm, Degrees]

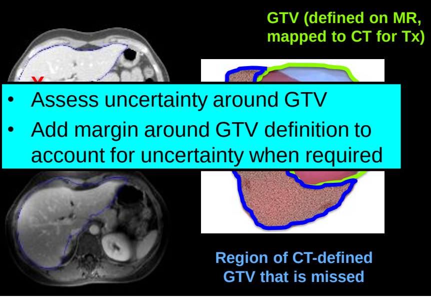
| Registration | dX | dY | dZ | $X_{ROT}$ | $Y_{ROT}$ | $Z_{ROT}$ | Overlap |
|---|---|---|---|---|---|---|---|
| Clinical | 26.1 | 119.8 | 12.6 | 1.9 | -2.9 | -4.6 | Defined  |
| Auto | 25.6 | 120.8 | -26.1 | -1.5 | 2.5 | -3.4 |  |
| Vessel | 14.5 | 122.3 | 26.1 | -1.5 | 2.5 | 4.1 |  |
| Boundary | 13.0 | 125.3 | 19.0 | 0.4 | -1.3 | 2.3 |  |

## Image Registration: Accurate Target Definition





## Clinical Effect




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

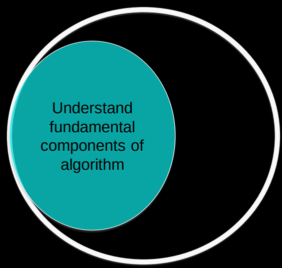
## Clinical Recommendations (1/2)

1. Understand the basic image registration techniques and methods of visualizing image fusion
2. Understand the basic components of the registration algorithm used clinically to ensure its proper use
3. Perform end-to-end tests of imaging, registration, and planning/treatment systems if image registration is performed on a stand-alone system

## Clinical Recommendations (2/2)

4. Perform comprehensive commissioning of image registration using the provided digital phantom data (or similar data) as well as clinical data from the user's institution
5. Develop a request and report system to ensure communication and documentation between all users of image registration
6. Establish a patient specific QA practice for efficient evaluation of image registration results

## Commissioning and QA
### Understand the whole picture




## How do they work?

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

## 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?

## Great Car! Right?

*Ferrari California T*

http://www.ferrari.com/en_us/

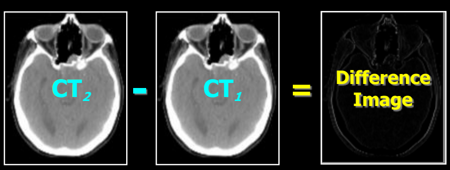
## Is it a great car for a road trip?


http://www.randalolson.com

Kessler / UM

## Sum of Squared Differences

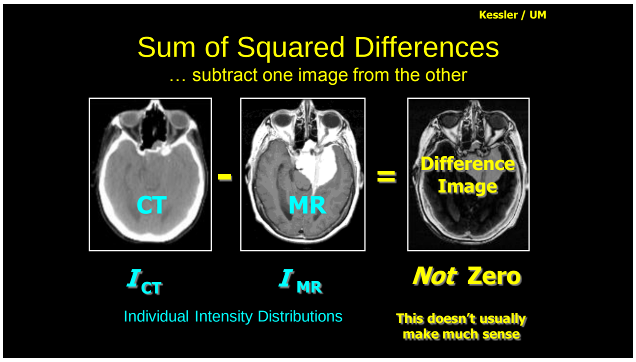
… subtract one image from the other

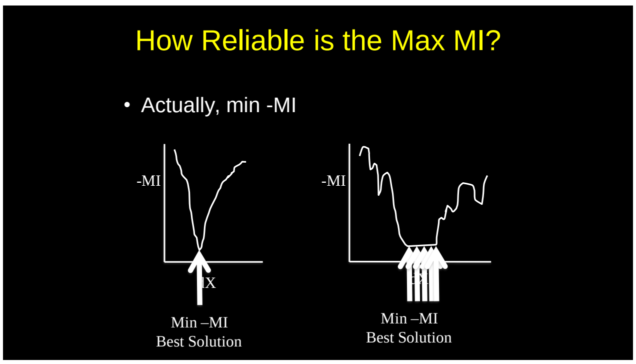


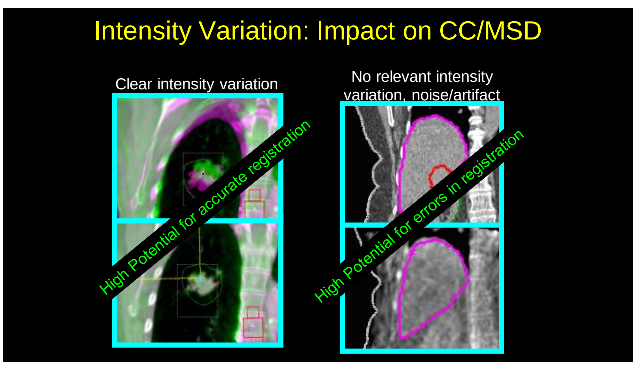

$I_{CT_2}$ $I_{CT_1}$ $\sum(I_{CT_2} - I_{CT_1})^2$

Individual Intensity Distributions

Sum of the Squares of the Differences


Kessler / UM
Sum of Squared Differences
… subtract one image from the other
CT
MR
Difference Image
$I_{CT}$
$I_{MR}$
Not Zero
Individual Intensity Distributions
This doesn't usually make much sense


How Reliable is the Max MI?
• Actually, min -MI
-MI
X
Min –MI
Best Solution
-MI
Min –MI
Best Solution

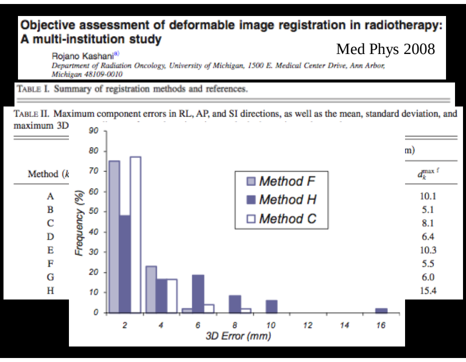

Intensity Variation: Impact on CC/MSD
Clear intensity variation
No relevant intensity variation, noise/artifact
High Potential for accurate registration
High Potential for errors in registration

## Understand the basic components of the registration algorithm used clinically to ensure its proper use

How?

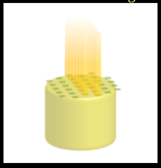
- At minimum, the vendor should disclose:
  - Simi
  - Reg
  - Trar
  - Optimization method
  - What knobs you can turn and what they do
- Read white papers

**Why do we need to know the implementation?**

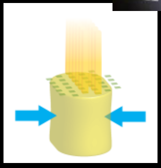



## New method to validate Deformable Image Registration

Deformable 3D Presage dosimeters

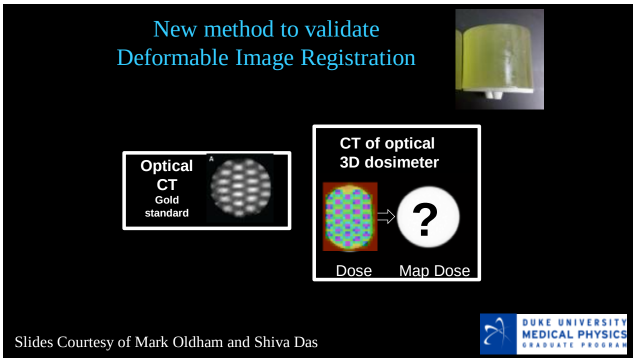


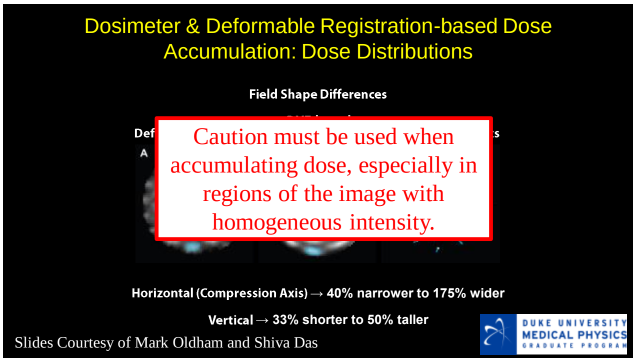
Control
(No Deformation)

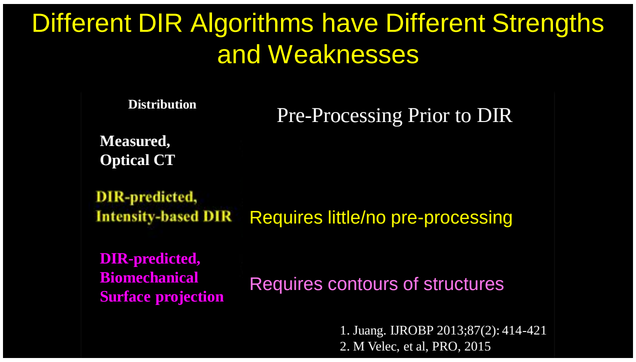


Deformed
(27% Lateral Compression)

Slides Courtesy of Mark Oldham and Shiva Das

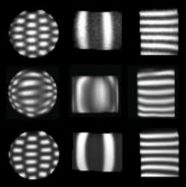

New method to validate
Deformable Image Registration
Optical
CT
Gold
standard
CT of optical
3D dosimeter
?
Dose
Map Dose
Slides Courtesy of Mark Oldham and Shiva Das
DUKE UNIVERSITY
MEDICAL PHYSICS
GRADUATE PROGRAM


Dosimeter & Deformable Registration-based Dose Accumulation: Dose Distributions
Field Shape Differences
Caution must be used when accumulating dose, especially in regions of the image with homogeneous intensity.
Horizontal (Compression Axis) → 40% narrower to 175% wider
Vertical → 33% shorter to 50% taller
Slides Courtesy of Mark Oldham and Shiva Das
DUKE UNIVERSITY
MEDICAL PHYSICS
GRADUATE PROGRAM

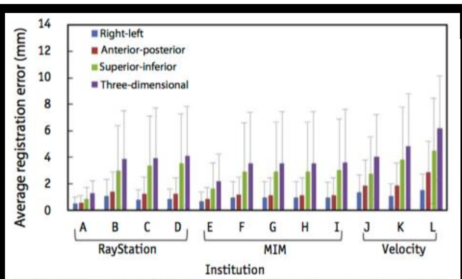

Different DIR Algorithms have Different Strengths and Weaknesses
Distribution
Pre-Processing Prior to DIR
Measured, Optical CT
DIR-predicted, Intensity-based DIR
Requires little/no pre-processing
DIR-predicted, Biomechanical Surface projection
Requires contours of structures
1. Juang. IJROBP 2013;87(2): 414-421
2. M Velec, et al, PRO, 2015

## Different DIR Algorithms have Different Strengths and Weaknesses

| Distribution | Coronal | Axial | Sagittal | 3D $\gamma_{3\%/3mm}$ |
| --- | --- | --- | --- | --- |
| Measured, Optical CT | | | | 96%[1] (control) |
| DIR-predicted, Intensity-based DIR | | | | 60%[1] |
| DIR-predicted, Biomechanical Surface projection | | | | 91%[2] |



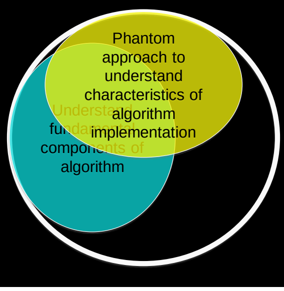
1. Juang. IJROBP 2013;87(2): 414-421
2. M Velec, et al, PRO, 2015




**Conclusions:** We evaluated the commercially available DIR software using thoracic 4D-CT images from multiple centers. Our results demonstrated that DIR accuracy differed among institutions because it was dependent on both the DIR software and procedure. Our results could be helpful for establishing prospective clinical trials

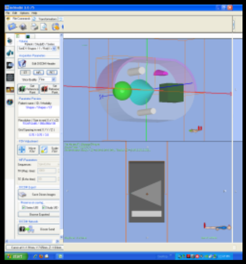
## Commissioning and QA

### Understand the whole picture



## 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



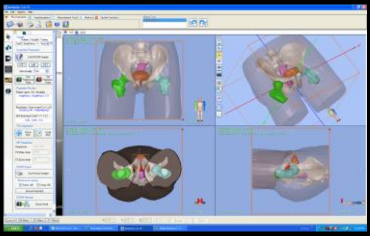
* Phantom Data Courtesy of ImSim QA

## Example Commissioning Tests

| Offset to Primary [mm] | dx | dy | dz |
|---|---|---|---|
| **Defined** | **-10** | **5** | **-15** |
| default, entire FOV | -10 | 5.1 | -12.9 |
| default, entire FOV | -9.9 | 4.5 | -13.5 |
| default, entire FOV | -10 | 4.9 | -14.1 |
| default, entire FOV | -10 | 5.2 | -13.8 |
| default, entire FOV | -8.3 | 4.4 | -13.6 |
| AVG | -9.64 | 4.82 | -13.58 |
| SD | 0.75 | 0.36 | 0.44 |
| AVG Deviation from Defined Offset | 0.36 | -0.18 | 1.42 |
| **Offset to Primary** | **dx** | **dy** | **dz** |
| **Defined** | **-10** | **5** | **-15** |
| User Defined (4th step with 1 mm resolution), entire FOV | -10 | 5 | -15 |
| User Defined (4th step with 1 mm resolution), entire FOV | -10 | 5 | -15 |
| User Defined (4th step with 1 mm resolution), entire FOV | -10 | 4.9 | -15 |
| User Defined (4th step with 1 mm resolution), entire FOV | -10 | 5 | -15 |
| User Defined (4th step with 1 mm resolution), entire FOV | -10 | 5 | -15 |
| AVG | -10 | 4.98 | -15 |
| SD | 0.00 | 0.04 | 0.00 |
| AVG Deviation from Defined Offset | 0 | -0.02 | 0 |

## Rigid Anatomical Phantom

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



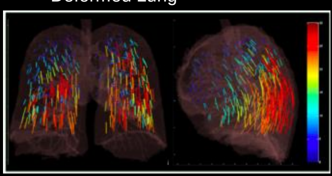
## Deformable Phantom

Commissioning Procedure:

- Run Deformable Image Registration
- Export DICOM Deformation Vector Field (DVF)
- Pseudo code provided to compare known DVF with exported DVF
- Target: 95% of voxels within 2 mm, max error less than 5 mm

## Deformable Lung

- Clinical Lung Data
- Simulated Deformed Lung



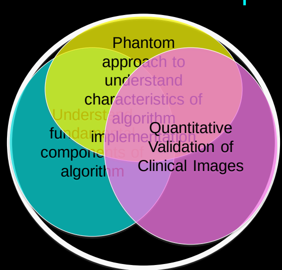
*Courtesy DIR-lab, Dr. Castillo

**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

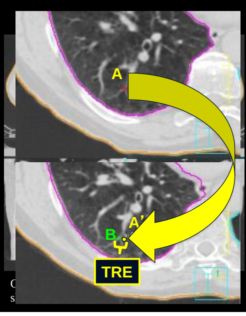
## Commissioning and QA
## Understand the whole picture



## Quantitative Validation Techniques

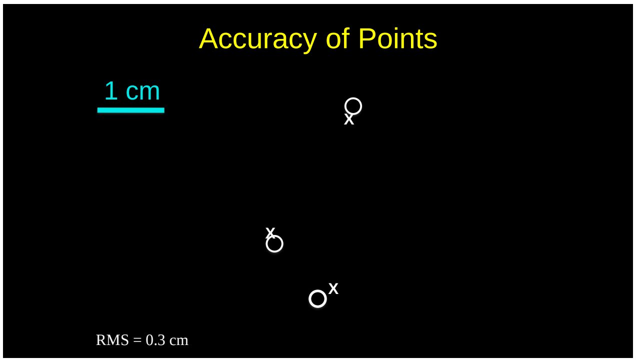
- Landmark Based
  - Does the registration map a landmark on Image A to the correct position on Image B?
  - Target Registration Error (TRE)
- Contour Based
  - Does the registration map the contours onto the new image correctly?
  - Dice Similarity Coefficient (DSC)
  - Mean Distance to Agreement (MDA)

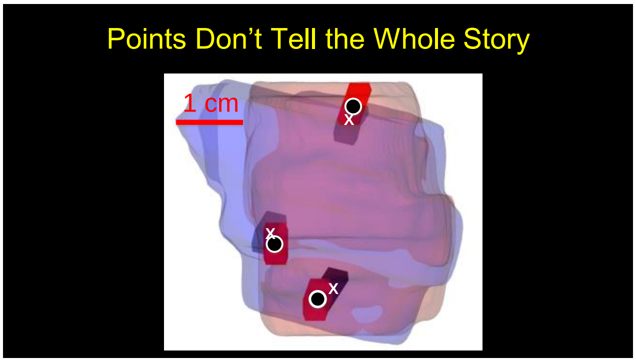
## Landmark Based (TRE)

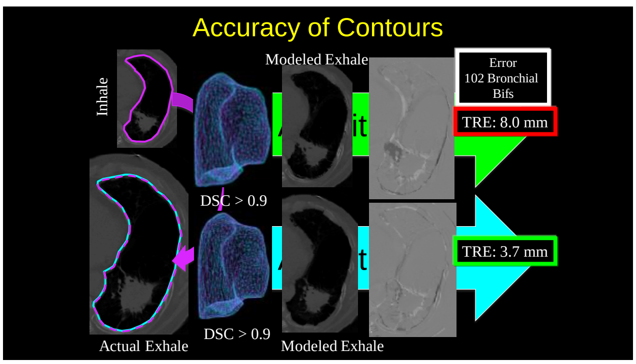



- Reproducibility of point identification is sub-voxel
  - Gross errors
  - Quantification of local accuracy within the target
  - Increasing the number increases the overall volume quantification
- Manual technique
- Can identify max errors

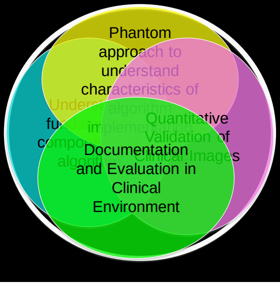
## That sounds great! Is that enough?


Accuracy of Points
1 cm
RMS = 0.3 cm


Points Don't Tell the Whole Story
1 cm

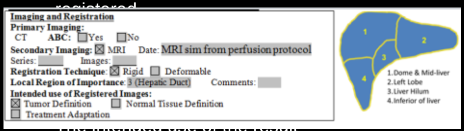

Accuracy of Contours
Inhale
Modeled Exhale
Error
102 Bronchial
Bifs
TRE: 8.0 mm
DSC > 0.9
TRE: 3.7 mm
Actual Exhale
DSC > 0.9
Modeled Exhale

## Commissioning and QA
## Understand the whole picture




## Request

- 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<br>- Useful for structure definition everywhere<br>- Ok for stereotactic localization |
| 1 | Locally aligned | - Anatomy local to the area of interest is un-distorted and aligned within 1mm<br>- Useful for structure definition within the local region<br>- Ok for localization provided target is in locally aligned region |
| 2 | Useable with risk of deformation | - Aligned locally, with mild anatomical variation<br>- Acceptable registration required deformation which risks altering anatomy<br>- Registered image shouldn't be used solely for target definition as target may be deformed<br>- Increased reliance on additional information is highly recommended<br>- 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<br>- Possible use to identify general location of lesion (e.g. PET hot spot) |
| 4 | Alignment not acceptable | - Unable to align anatomy to acceptable levels<br>- Patient position variation too great between scans (e.g. surgical resection of the anatomy of interest or dramatic weight change between scans) |

## Establish a patient specific QA practice for efficient evaluation of image registration results

Why?
- At this point we are still understanding how the the registration is performing on different types of patients

How?
- Visual Verification
- Spot checks of landmarks
- Boundary comparison

## Vendor Recommendations

1. Disclose basic components of their registration algorithm to ensure its proper use
2. Provide the ability to export the registration matrix or deformation vector field for validation
3. Provide tools to qualitatively evaluate the image registration
4. Provide the ability to identify landmarks on 2 images and calculate the TRE from the registration
5. Provide the ability to calculate the DSC and MDA between the contours defined on an image and the contours mapped to the image via image registration
6. Support the integration of a request and report system for image registration

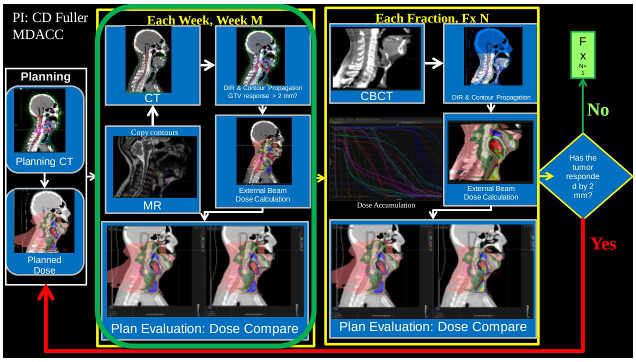
## TG-132 Product

- Guidelines for understating of clinical tools
- Digital (virtual) phantoms
- Recommendations for commissioning and clinical implementation
- Recommendations for periodic and patient specific QA/QC
- Recommendations for clinical processes

## Clinical Examples

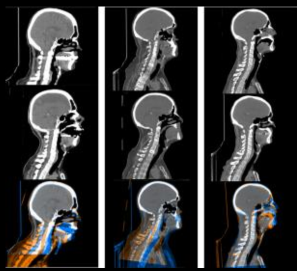
## Transitioning DIR into the Clinic

- **Commissioning the DIR system in your clinic is important**
  - It will take resources
  - Similar to the start of IMRT, extra measurements will be needed as we begin to understand the tools
  - It will have a return on investment – Improved efficiency in the process
  - Important to commission the system <u>in your clinic</u>
- Recognize the uncertainties
- Cost/benefit of Adaptive
- Design clinical workflow



## DIR Commissioning: CT to CT

- Repeat CTs
- Contours drawn on both
- DIR CT to CT
- Dice Similarity Coefficient (DSC) evaluation
  - Evaluates overlap of structures
  - Ranges from 0 (no overlap) to 1 (perfect overlap)
- Limited by manual contour reproducibility (~0.75-0.8)



## DIR Commissioning: CT to CT

9 Patients, 2 CTs, Anaconda

| Structure | Dice Similarity Coefficient (DSC) Mean | SD |
|---|---|---|
| Brainstem | 0.85 | 0.03 |
| Larynx | 0.81 | 0.03 |
| R Parotid | 0.78 | 0.04 |
| L Parotid | 0.77 | 0.06 |
| R Submandibular Gland | 0.77 | 0.06 |
| L Submandibular Gland | 0.78 | 0.04 |
| Mandible | 0.91 | 0.04 |
| Esophagus | 0.73 | 0.13 |

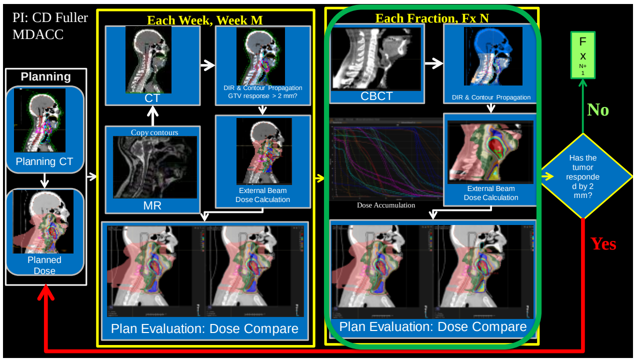
## DSC Differences in Practice

- DIR: planning CT to weekly adaptive CT
  - ANACONDA method generates a smooth DVF optimized by the quasi-Newton algorithm and guided by the correlation coefficient between the images.
- Map Contours based on registration
- Clinicians review contours and edit when needed
  - Editing is naturally driven by clinical importance
  - Dice Similarity Coefficient (DSC) has bias due to organ size and shape

## DSC Difference between DIR-propagated Contours and Final Approved Clinician Contours

| Structures | DSC: AVG | SD |
|---|---|---|
| Brain | 1.00 | 0.00 |
| BrainStem | 0.98 | 0.02 |
| Cavity_Oral | 0.99 | 0.02 |
| Cochlea | 0.94 | 0.10 |
| CTV | 0.87 | 0.10 |
| Esophagus | [illegible] | 0.12 |
| Eyes | [illegible] | 0.03 |
| Glnd_Submand | 0.96 | 0.02 |
| Larynx | 0.97 | 0.04 |
| Lenses | 0.73 | 0.31 |
| Mandible | 0.96 | 0.07 |
| NodalGTV_6996 | 0.80 | 0.15 |
| OpticChiasm | 0.90 | 0.03 |
| Optic Nerve | 0.96 | 0.03 |
| Parotids | 0.98 | 0.01 |
| Pharyngeal Constrictors | 0.96 | 0.01 |
| PrimaryGTV_6996 | 0.79 | 0.03 |
| SpinalCord | 0.98 | 0.01 |

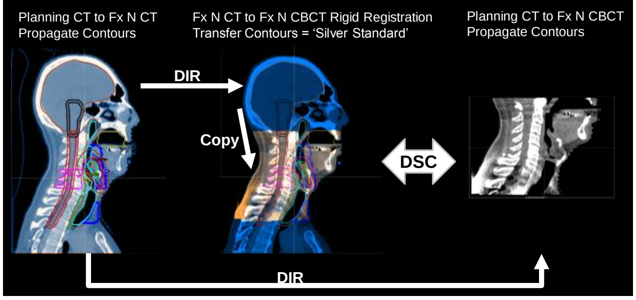
What is the dosimetric impact?



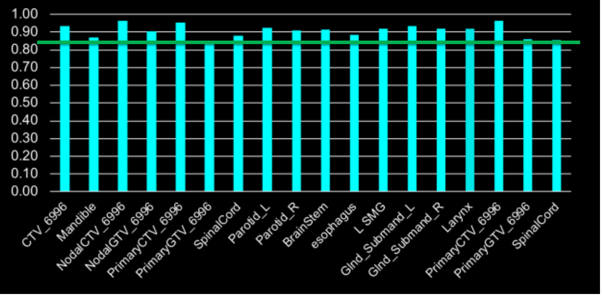

## DIR Commissioning: CT to CBCT

- Getting contours on multiple CBCTs for validation is difficult & has larger uncertainties than CT
- Alternative: indirect validation
- Logic argument:
  - CT to CT DIR has been commissioned and deemed within contour uncertainty
  - CT and CBCTs obtained on the same day with immobilization should have minimal differences after rigid registration

## DIR Commissioning: CT to CBCT




## DICE Accuracy: Relative to CT-CT DIR




## Clinical Workflow Questions

- What is the difference between dose calculated on CT vs CBCT?
- Do we need daily CBCT dose accumulation or does weekly CT (or CBCT) give us the same answer?
- If we perform an adaptive replan, how do we accumulate the dose
  - Deform daily images back to planning image or all daily images back to the initial planning image?
  - Dose A to B to C equal A to C?
- Does the predictive model hold with true dose accumulation?
- How can we extrapolate the CBCT?
- How do we distill down the data
  - I have a 125 page document of data for 1 patient!!!
- However, we don't need to have all of these answer to start!

## Summary

- DIR is a powerful tool that can help us to integrate multi-modality images, understand motion and anatomical changes, and compute an improved estimate of the delivered dose
- With power comes responsibility… we must commission the system prior to use, understand the limitations, and communicate its proper use to clinicians, dosimetrists, therapists, and others
- The presentation of information leads to decision making… we must move use the data to design intelligent adaptation strategies to improve the therapeutic ration efficiently