Biomechanical Modeling of Anatomical Response over the Course of Therapy

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- Daniel Polan
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- Mary Feng, MD

"How many more theses do we need on deformable image registration?"

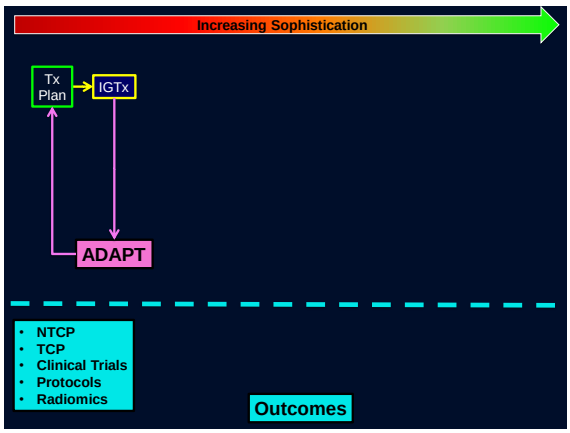
Marc Kessler
Winter Institute of Medical Physics 2016

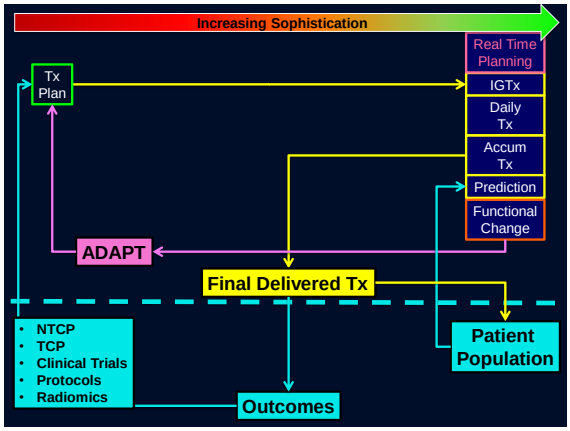
deformable image registration

Anatomical Modeling

Personalized, Evidence-Based Image Guidance Continuum

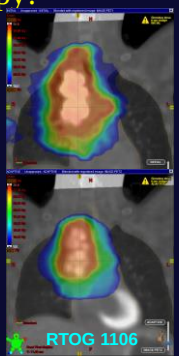
Increasing Sophistication





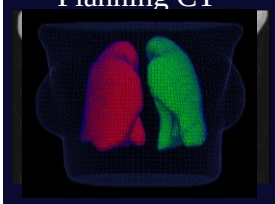
Do We Want to Deliver the original Planned Therapy?

- Anatomical response over Tx may enable an improvement in the therapeutic ratio
  - Some patients don't change
  - Some patients change a lot
- Functional imaging and biomarkers may enable personalization of treatment
- Hinges on accurate knowledge of the delivered therapy

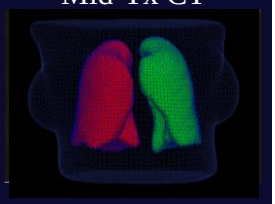


Biomechanical Modeling of Anatomical Response

Planning CT

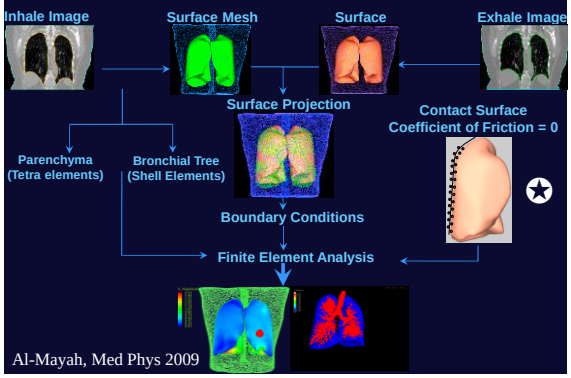


Mid-Tx CT

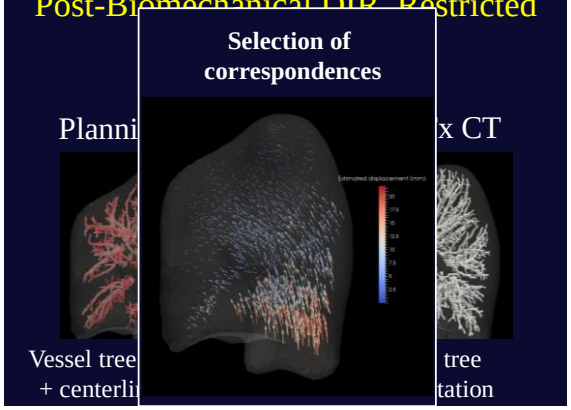


How do we model this response?

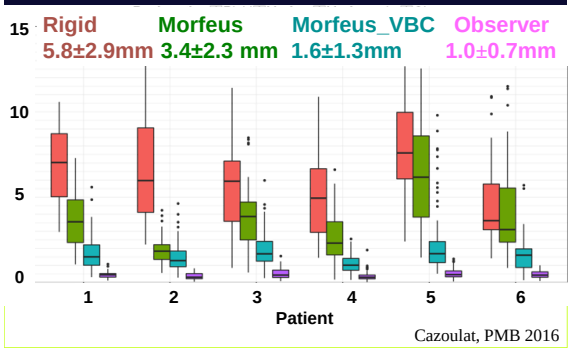
Morfeus Lung Model Development



Post-Biomechanical DIR Restricted



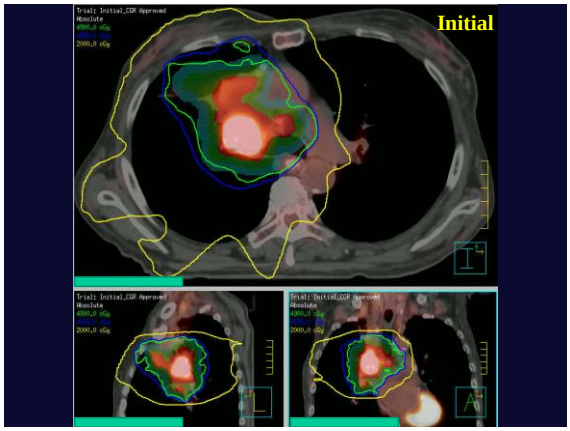
Target Registration Error [mm]

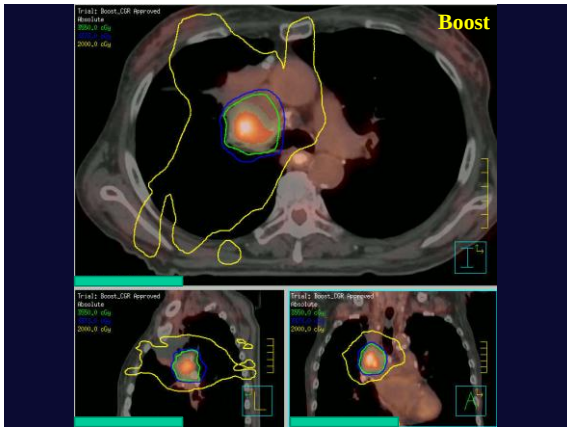


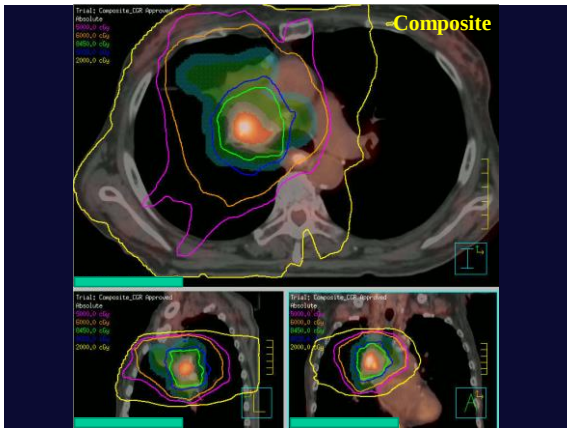
Clinical Application
Case – RTOG 1106 Adaptive

- Mid-treatment imaging **rigidly** co-registered to initial planning CT
- All contours made on secondary images propagated back to planning CT
- **All dose calculated on initial planning CT**

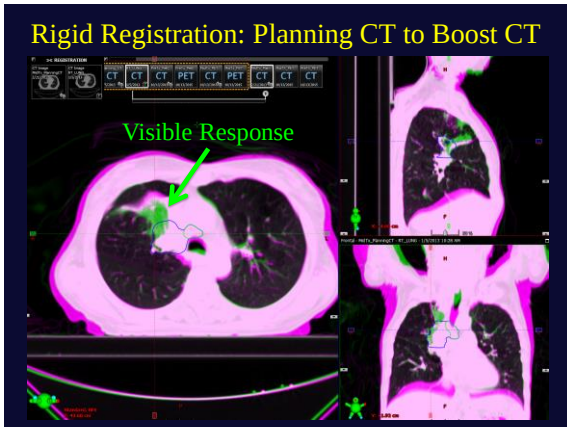
Collaboration with Cliff Robinson, Washington University, St. Louis



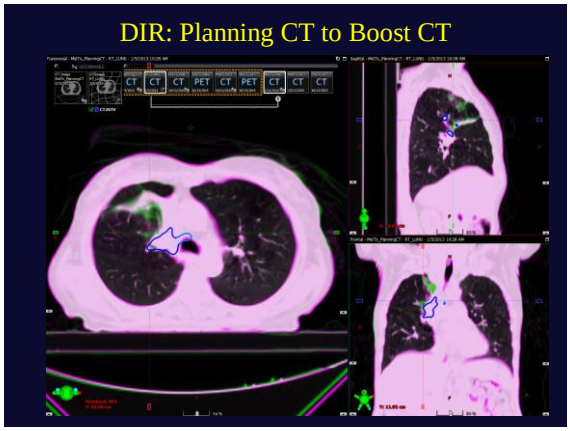




Rigid Registration: Planning CT to Boost CT

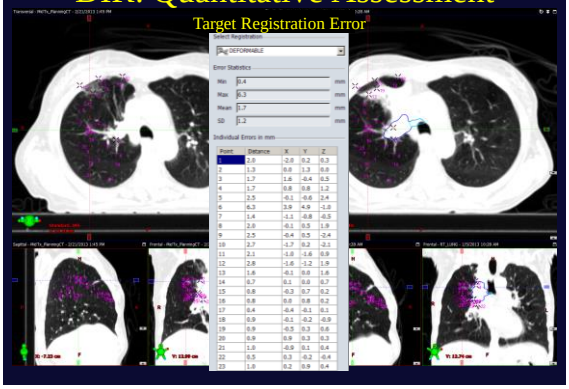


DIR: Planning CT to Boost CT

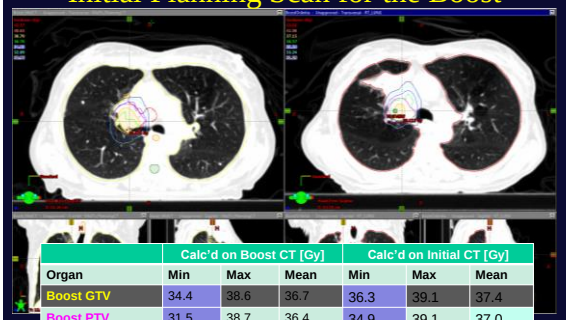


DIR: Quantitative Assessment

Target Registration Error

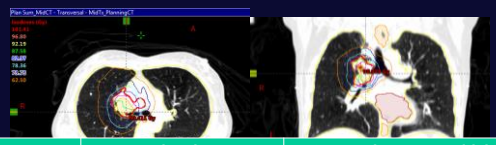


Discrepancy due to Calculating Dose on the Initial Planning Scan for the Boost



	Calc'd on Boost CT [Gy]			Calc'd on Initial CT [Gy]		
Organ	Min	Max	Mean	Min	Max	Mean
Boost GTV	34.4	38.6	36.7	36.3	39.1	37.4
Boost PTV	31.5	38.7	36.4	34.9	39.1	37.0
Lungs-GTV (Pre)	0.01	37.8	5.0	0.01	36.9	4.7

Initial Plan Mapped to Boost & Summed

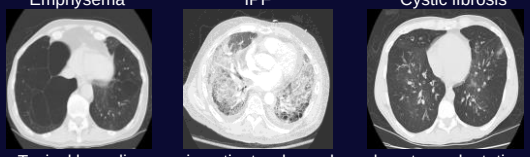


	Accumulated Dose on Boost (with DIR)			Summed Dose on Initial (no DIR)		
Organ	Min	Max	Mean	Min	Max	Mean
Esophagus	0.5	65.3	17.5	0.5	74.3	20.7
Heart	0.3	52.4	3.1	0.3	53.9	3.5
Spinal Cord	0.04	42.5	7.2	0.03	43.6	6.6
Boost GTV	85.2	91.0	88.0	86.2	91.6	88.8
Boost PTV	82.2	91.0	87.8	85.1	92.0	88.6
Pre GTV	71.4	91.0	85.3	68.9	92.0	86.0
Lungs-GTV (pre)	0.1	89.3	16.7	0.1	88.8	16.2

Response Assessment: Functional Evaluation of Chronic Lung Allograft Dysfunction

Lung transplantation is established for severe chronic lung disease

Emphysema | IPF | Cystic fibrosis



Typical lung diseases in patients who undergo lung transplantation

Chronic lung allograft dysfunction (CLAD) reduces long term survival to 50% at 5 years post surgery.

M Horie, N S Paul, U of Toronto, RSNA 2015

Background

CLAD diagnosis requires pulmonary function tests (PFT)

- Forced expiratory volume in 1 second (FEV_1)
- Total Lung Capacity (TLC)
  - TLC is not routinely measured during surveillance PFT
  - PFT + TLC is a global measurement of lung function
  - PFT are suboptimal for assessing single lung transplants

Bronchiolitis obliterans syndrome (BOS)

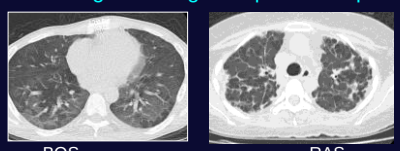
- Diagnostic criteria = FEV1<80% of baseline

Restrictive allograft syndrome (RAS)

- Diagnostic criteria = FEV1<80% of baseline + TLC<90%
- Significantly worse prognosis

Biomechanical-based Response Modeling

To distinguish RAS from BOS and No-CLAD with low dose CT images of lung transplantation patients



BOS | RAS

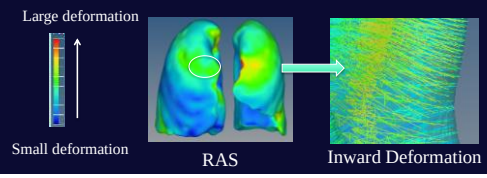
Retrospective analysis of lung transplant patients 2006-2013

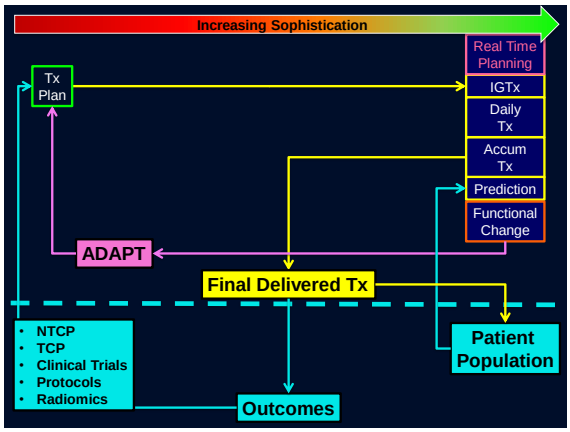
- No-CLAD (N=10), Baseline and most recent time points
- BOS (N=10), Baseline and disease onset time points
- RAS (N=10), Baseline and disease onset time points

Results

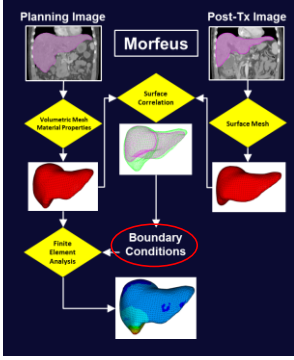
CT Lung deformation assessment in RAS
- More upper lobe deformation
- Larger inward deformation

Lung deformation:
- Lung deformation demonstrated high sensitivity and specificity (>80%) in differentiating RAS from BOS/No-CLAD ($p<0.05$)
- May replace the need for Total Lung Capacity measurements in CLAD patients
- Can be used to evaluate regional areas of disease



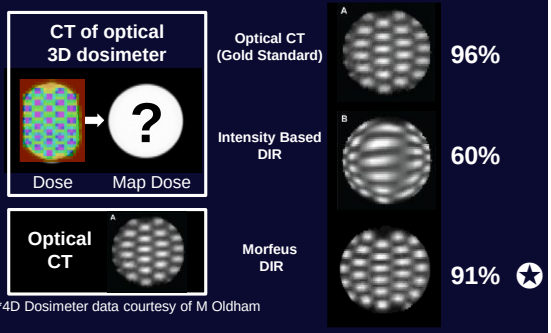


Biomechanical Modeling: Liver



Dosimetric Accuracy of Morfeus for Liver

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



*4D Dosimeter data courtesy of M Oldham

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

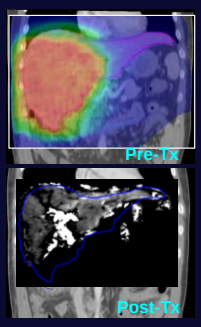
Does Improved Accuracy in Dose Matter for Outcomes?

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

Swaminath, Brock, Dawson, et al. IJROBP, 2015

Liver Response to Radiotherapy: Understanding Radiation Effects

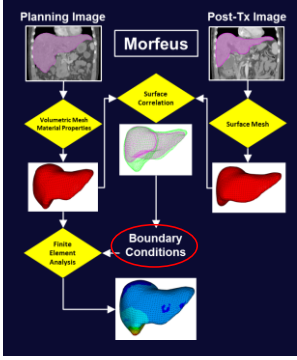
- Patients with oligometastases often have multiple courses of SBRT
  - Need: map previously delivered dose
- Advancements in functional imaging (e.g. DCE-MRI) can predict/describe function
  - Need: correlate the delivered dose
- Challenging due to the volumetric response of the tissue to radiation
  - Often variable across the tissue as a function of dose



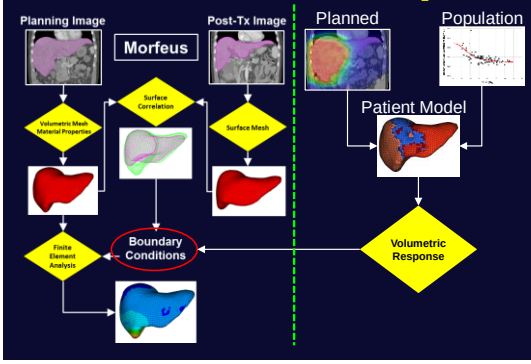
Hypothesis

- Biomechanical models can be expanded to model the volumetric response of tissue to radiation dose
  - Aid in correlating delivered dose with response
  - Assist in linking functional imaging with delivered dose
  - Map delivered dose to subsequent planning images

Addition of Volumetric Response



Addition of Volumetric Response



Causes of Volumetric Response

- Tumor shrinkage/growth (known input to model, based on images)
  - Normal hepatic tissue response (predicted from the model)

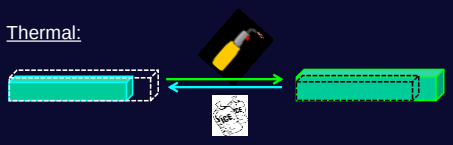
Normal Tissue Response:

Low Dose → Hypertrophy (Expansion)

High Dose → Atrophy/Fibrosis (Contraction)

Modeling Expansion/Contraction

Thermal:



$$\alpha_L = \Delta V / 3\ V_i\ \Delta T$$

Goal: Modify Existing Thermal Expansion Tools to Accurately Represent Radiological Volumetric Changes

Modeling Expansion/Contraction

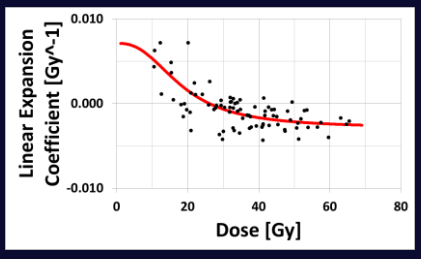
Radiological:

$$\alpha_L = \frac{V_f - V_i}{3V_i D}$$

Dose (D) replaces Temperature Change (ΔT)

Generating α_L

- 33 Liver Cancer Patients, 49-79 days post-RT
- Contoured Lobes on Pre and Post-treatment CT Scans
- Mean Dose to Each Lobe

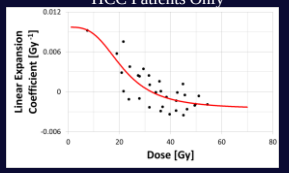


Stratified α_L Models

Hypothesized Stratifications

- Tumor Type
  - HCC (Primary)
  - Bile/CR (Secondary)
- Tumor Location
  - Right/Left Lobes
- Secondary Factors
  - Previous Liver Treatments
  - Concurrent Chemotherapy
  - Portal Vein Thrombosis

HCC Patients Only



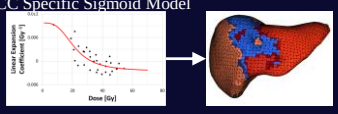
Stratification	Floor	Ceiling	D50	γ	R^2	Rho	P
All (HCC/CT/Bile)	-0.003	0.0088	17.7	0.56	0.45	-0.61	4.4 E-13
CR/Bile	-0.0029	0.0071	18.3	0.63	0.41	-0.58	5.5 E-9
HCC	-0.0026	0.0097	21.4	0.79	0.64	-0.74	1.3 E-6
Right Lobe (CR/Bile)	-0.0021	0.0053	18.5	1.09	0.53	-0.61	3.9 E-4
Left Lobe (CR/Bile)	-0.0025	0.0022	29.6	1.92	0.34	-0.57	6.2 E-6

Patient Evaluation

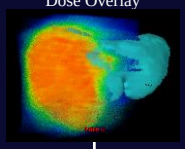
- Hepatocellular Carcinoma (HCC) Patient
  - Right Lobe Tumor
  - Portal Vein Thrombosis
- Treatment
  - 54 Gy in 27 fractions (2 Gy/fraction)
  - Needed retreatment after initial RT completion
  - Clinically significant volumetric changes
- Evaluation
  - Morfeus with dose-volume response compared to commercial treatment planning software
  - TRE and volume assessed

Patient Evaluation

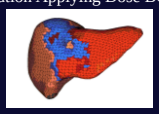
HCC Specific Sigmoid Model

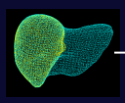


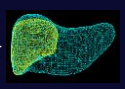
Dose Overlay



Animation Applying Dose BC

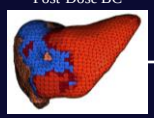






Patient Evaluation

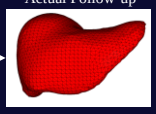
Post-Dose BC

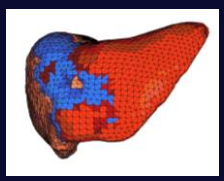


Requires Spatial Alignment

Guided Surface Projections
& Linear Elastic Material Model

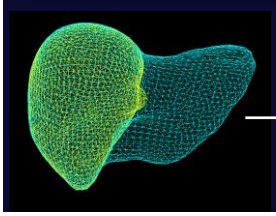
Actual Follow-up

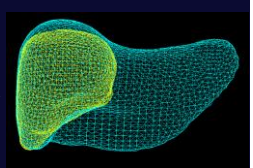




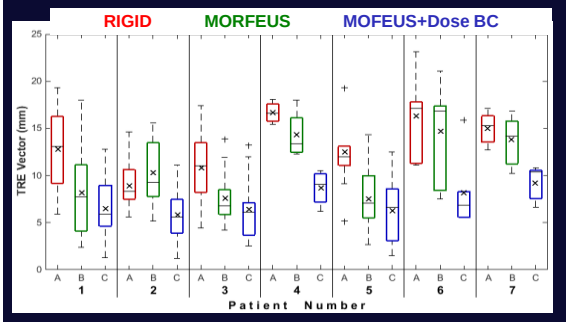
Results: Volume

Volume Change [%] (% Error)	Tumor	Normal Tissue	Total
Measured	-29	+7	-54
Commercial Tx Planning Software (Demon's Based Algorithm)	-17 (+8)	-19 (-26)	-16 (+38)
Morfeus w/Dose Response	-26 (+3)	+2 (-5)	-49 (+5)

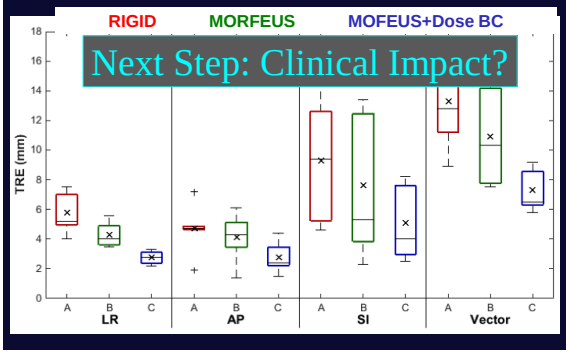




Overall Summary



Overall Summary



Summary

- Exciting time of advancement in medicine, especially in image guided therapy, response assessment and personalization.
- Moving from image registration to anatomical modeling will allow further exploration into the assessment of radiation response.
- Biomechanical modeling provides a platform that can be expanded to accommodate the dramatic changes seen in therapy response
- Whichever algorithm is used, quantitative validation is key.