Biomechanical Modeling of Anatomical Response over the Course of Therapy

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Lung:
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• Cliff Robinson, MD (Washington University, St. Louis)
• M Horie, N S Paul (University of Toronto)

Liver:
• Daniel Polan
• Molly McCulloch
• 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

- NTCP
- TCP
- Clinical Trials
- Protocols
- Radiomics

Outcomes
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

- Parenchyma (Tetra elements)
- Bronchial Tree (Shell Elements)
- Boundary Conditions
- Finite Element Analysis
- Contact Surface
- Coefficient of Friction = 0

Al-Mayah, Med Phys 2009

Post-Biomechanical DIP_ Restricted

- Selection of correspondences
- Planning CT
- Vessel tree segmentation
- Vesselness image + centerline extraction

Vessel tree segmentation

Target Registration Error [mm]

- Rigid: 5.8±2.9mm
- Morfeus: 3.4±2.3mm
- Morfeus_VBC: 1.6±1.3mm
- Observer: 1.0±0.7mm

Cazoulat, PMB 2016
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
Composite Rigid Registration: Planning CT to Boost CT

Visible Response

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

<table>
<thead>
<tr>
<th>Organ</th>
<th>Calc'd on Boost CT (Gy)</th>
<th>Calc'd on Initial CT (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boost GTV</td>
<td>34.4 38.6 36.7</td>
<td>36.3 39.1 37.4</td>
</tr>
<tr>
<td>Boost PTV</td>
<td>31.5 38.7 36.4</td>
<td>34.9 39.1 37.0</td>
</tr>
<tr>
<td>Lungs-GTV (Pre)</td>
<td>0.01 37.8 5.0</td>
<td>0.01 36.9 4.7</td>
</tr>
</tbody>
</table>

Initial Plan Mapped to Boost & Summed

<table>
<thead>
<tr>
<th>Organ</th>
<th>Accumulated Dose on Boost (with DIR)</th>
<th>Summed Dose on Initial (no DIR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosophagus</td>
<td>0.5 55.3 17.5 0.5 74.3 20.7</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>0.3 52.4 3.1 0.3 53.9 3.5</td>
<td></td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>0.04 43.5 7.2 0.03 43.6 6.6</td>
<td></td>
</tr>
<tr>
<td>Boost GTV</td>
<td>85.2 91.0 88.0 86.2 91.6 88.8</td>
<td></td>
</tr>
<tr>
<td>Boost PTV</td>
<td>82.2 91.0 87.8 85.1 92.0 88.6</td>
<td></td>
</tr>
<tr>
<td>Pre GTV</td>
<td>71.4 91.0 85.3 68.9 92.0 86.0</td>
<td></td>
</tr>
<tr>
<td>Lungs-GTV (pre)</td>
<td>0.1 89.3 16.7 0.1 88.8 16.2</td>
<td></td>
</tr>
</tbody>
</table>
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 (FEV₁)
  • 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

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Biomechanical Modeling: Liver

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Increasing Sophistication

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Real Time Planning
- IGTV
- Daily Tx
- Accum Tx

Prediction
- Functional Change

Outcomes
- NTCP
- TCP
- Clinical Trials
- Protocols
- Radiomics

Patient Population

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ADAPT

Final Delivered Tx

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Real Time Planning

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Dosimetric Accuracy of Morfeus for Liver

CT of optical 3D dosimeter

Optical CT (Gold Standard)

Intensity Based DIR

Morfeus DIR

\[ V_{3\%/3mm} \]

96%

60%

91%

*4D Dosimeter data courtesy of M Oldham


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**

Planning Image | Post-Tx Image
---|---
**Morfeus**

**Boundary Conditions**

**Population**

**Patient Model**

**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:

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

\[ \alpha_L = \frac{\Delta V}{3 V_i} \Delta T \]

Radiological:

\[ \alpha_L = \frac{V_f - V_i}{3V_i D} \]

Dose (D) replaces Temperature Change (\(\Delta T\))
Generating $\alpha_L$:
- 33 Liver Cancer Patients, 49-79 days post-RT
- Contoured Lobes on Pre and Post-treatment CT Scans
- Mean Dose to Each Lobe

Stratified $\alpha_L$ Models:
Hypothetically stratified:
- Tumor Type
  - HCC (Primary)
  - Bile/CR (Secondary)
- Tumor Location
  - Right/Left Lobes
- Secondary Factors
  - Previous Liver Treatments
  - Concurrent Chemotherapy
  - Portal Vein Thrombosis

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
  - Morpheus with dose-volume response compared to commercial treatment planning software
  - TFE 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

Patient Evaluation

Results: Volume

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

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Overall Summary

Next Step: Clinical Impact?

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.