Functional Lung Avoidance with CT-Ventilation

Yevgeniy (Jenia) Vinogradskiy, PhD

University of Colorado Cancer Center
Functional Lung Avoidance with CT-Ventilation
Functional Lung Avoidance with CT-Ventilation
Functional Lung Avoidance with CT-Ventilation
Functional Radiotherapy For Lung Cancer

4DCT-Ventilation

- 4DCT acquired for simulation (reduced time, cost, dose)
- Anatomical + Functional information
- Good spatial resolution

4DCT

4DCT-Ventilation
Calculating Ventilation Images

Calculating ventilation maps

4DCT – 10 phases
Calculating Ventilation Images

Link lung voxel elements from inhale to exhale using deformable registration

\[
\frac{V_{in} - V_{ex}}{V_{ex}} = 1000 \frac{HU_{in}^{voi} - HU_{ex}}{HU_{ex}(1000 + HU_{in}^{voi})}
\]

(Castillo et al., 2010)
Calculating Ventilation Images
Functional Imaging to Functional Radiotherapy: Validation

Castillo et al - SPECT

Kipritidis et al – PET 68Ga

Vinogradskiy et al - VQ scans
Functional radiotherapy example with CT Ventilation

Standard Plan No Avoidance

Ventilation Functional Avoidance

Functional Avoidance

Ventilation Defect

GTV

40.0 GY
35.0 GY
30.0 GY
25.0 GY
Predicting pneumonitis: dose + function > dose

• 96 NSCLC patients
• Radiation pneumonitis toxicity information using CTCAE grading
• Calculated dose metrics
  • Mean lung dose
  • V20 Gy = Volume of lung receiving 20 Gy or higher
• Calculated dose + function metrics
  • Functionally weighted mean lung dose
  • FV20 Gy = Amount of functioning lung getting 20 Gy or higher
Functional planning

MLD = 22.9 Gy
No pneumonitis

MLD = 23.2 Gy
Grade 3 pneumonitis

Dose  Ventilation

Dose  Ventilation

MLD = 23.2 Gy
Grade 3 pneumonitis
4DCT-ventilation conformal avoidance – Will it work?

Ability of dose and dose + function metrics to predict for grade 3+ radiation pneumonitis: area under the curve (AUC) and logistic regression (Vinogradskiy et al 2013, Faught et al 2017)

<table>
<thead>
<tr>
<th></th>
<th>MLD</th>
<th>fMLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.55</td>
<td>0.66</td>
</tr>
<tr>
<td>V20</td>
<td>0.57</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Dose+function >> Dose alone
CT Ventilation Functional Radiotherapy Clinical Trial

- 67 lung cancer patients at University of Colorado + William Beaumont (NCT02528942)
- Use 4DCT to calculate ventilation imaging
- Use 4DCT-ventilation to design functional radiation plans
- Reduce functional dose metrics using favorable arc geometry + optimization
- Single-arm, early phase trial looking at feasibility, safety, toxicity rates to be compared to current standard of care techniques
Inclusion/Exclusion Criteria

- Trial inclusion/exclusion criteria
  - No SBRT, No palliative RT
  - Definitive Rx dose ≥ 45Gy
  - Planned concurrent chemotherapy regimen
  - Image heterogeneity criteria
Trial Design

- Phase II study, compare functional avoidance against historical control
- Primary endpoint: grade ≥ 2 Radiation Pneumonitis
- Hypothesis: Rate of grade ≥ 2 Radiation Pneumonitis can be reduced to 12% with functional radiotherapy compared to 25% rate of grade ≥ 2 Radiation Pneumonitis with historical control
- Simon’s Two-Stage design
- 67 patient total enrollment, futility analysis at 17 patients
Outcome assessments

- Assess lung function in a variety of ways
  - CTCAE Toxicity (Pulmonary toxicity, pneumonitis, esophagitis)
  - PFTs
  - QOL Questionnaires
  - Imaging: CT, 4DCT-Ventilation, PET, VQ
Implementation: Treatment planning

Structure-based treatment planning

Functional Image

Functional Image + Structure

Functional Planning Structure
Implementation: Treatment planning

- Start with standard (non-functional) plan, proceed to functional plan using favorable arc geometry + optimization techniques
- Planning priorities 1) Target coverage 2) OAR constraints 3) Reducing dose to functional lung
Implementation: Adaptive planning

- Image guidance per institutional protocol (CBCT daily, 4D CBCT @ Beaumont)
- Adaptive planning per attending discretion
- If an adaptive plan is needed, a 4DCT is done and a functional adaptive plan is made
Multi (2) – Institution Trial Credentialing

- Identical versions of CT Ventilation code installed at both institutions
- Site Initiation Visits performed at both institutions
- CT ventilation physicist (+ backup) identified and trained at both institutions
- 3 sample CT ventilation cases run at both institutions, evaluated for reproducibility
Feasibility: Trial Enrollment

- 95 patients consented in ~2.5 years
- 62 evaluable patients
- Trial met futility criteria, progressed with accrual
- 8 (8.4%) ineligible per imaging criteria
Patient plan example

Functional Plan

Non-Functional Plan
Functional V20 Trial Dosimetry

Mean Improvement in Functional V20: 3.2% [0.1% to 7.9%]

- 65% ≥3% Improvement in Functional V20
- 35% <3% Improvement in Functional V20
Conformal Avoidance: Future/On-going work

SBRT Conformal Avoidance


Proton Conformal Avoidance

IMPT

M Dougherty

Photon VMAT

Improved calculation robustness

Conformal avoidance + PET dose escalation (RTOG 1106)

SR Bowen, J Zeng, University of Washington
Thank you