Characterizing CT-Derived Mass Change of Non-Tumor Pathology During Lung Radiotherapy

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Conflicts of Interest

The authors have no conflicts of interest.
Longitudinal Tissue Changes in Lung

Tumor Regression
Atelectasis Resolution

Significant regression within few weeks of starting treatment

- Response to radiation and chemotherapy

End of treatment, tumor shrinks by:

- Up to 80% 
- Average of 44.3%
- 0.6% - 2.4% per day

1 Siker et al. 2006  2 Fox et al. 2009  3 Sonke et al. 2010  4 Woodford et al 2007
Longitudinal Tissue Changes in Lung

Tumor Regression
Atelectasis Resolution

- Centrally-located tumor restricts airflow to lobe
- Lobe collapses to uniform, high-intensity region
- In response to treatment, tumor regresses
- Airflow restores, re-aerating lobe
Longitudinal Tissue Changes in Lung

Tumor Regression
Pleural Effusion
Atelectasis Resolution

Lobar Atelectasis:

- Collapse may be partial or full
- Expansion may be complete, partial, or no change

Focus of Study
Deformable Image Registration (DIR) Failure

Correspondence problem arises
- Matching voxels have very different intensity or do not exist

Standard Algorithm (SSD)
- Pulls high-intensity structures to fill atelectatic region
Deformable Image Registration (DIR) Failure

Poor DIR prohibits accurate plan adaptation and safe dose escalation

Characterization of Large Geometric Changes

• Assess appropriateness of DIR algorithm components (similarity metrics)
• Develop an improved DIR algorithm for such cases
Characterization of Atelectasis

Must understand:
- Mass Preservation
- Location / Appearance
- Collapse type (full lobe or partial lobe)
- Resolution type (complete, partial, none)

Full Lobe Collapse Complete Resolution
Partial Lobe Collapse Partial Resolution
Characterization of Atelectasis

Hypotheses:
• Density changes in proportion to degree of resolution
  ▪ No change < Partial resolution < Full resolution
• Mass is preserved as atelectasis resolves
  ▪ $\text{Mass}_{\text{collapsed}} = \text{Mass}_{\text{expanded}}$
All have NSCLC

12% have complete resolution (n = 2)

65% have partial resolution (n = 12)

Average of 6.5 weeks between baseline and follow-up scan

<table>
<thead>
<tr>
<th>Subject</th>
<th>Location</th>
<th>Resolution</th>
<th>Weeks Between Scans</th>
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<tbody>
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<td>1</td>
<td>RLL, RML</td>
<td>No Change</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>LLL</td>
<td>Partial</td>
<td>3</td>
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<td>3</td>
<td>LUL</td>
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<td>Complete</td>
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<tr>
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<td>RLL</td>
<td>No Change</td>
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<td>17</td>
<td>RML</td>
<td>Partial</td>
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</tbody>
</table>
Lobe Delineations

Physician delineated:
- All lung lobes
- Tumor
- Atelectasis

Difficult to determine accurate tissue correspondence
- Especially with partial response
- Whole lobes investigated instead

Atelectatic Lobe
Re-aerated Lobe
Contour Pre-processing

Converted to binary masks
- 1 on and within contour
- 0 outside contour

Tumor excluded from masks
- Mass known to change

3D erosion by 2 voxels
- Removes extra-pleural tissue included in delineation
Image Pre-processing

Images are linearly calibrated\(^5\)
- Blood in descending aorta
  - + 50 HU
- Air outside body
  - -1000 HU
- Eliminates variability in scanner performance

Value of 1000 added to each voxel
- Converts to relative physical density

**Air:** -1000 HU \(\rightarrow\) \(~0\) mg/cc (relative)

**Blood:** 50 HU \(\rightarrow\) \(~1050\) mg/cc (relative)

\(^5\)Staring et al. 2014
Mass Calculation

Goal of study:
- Investigate relative density / mass
  - Not absolute

Using pre-processed image:
Relative Density x Voxel Volume = Relative Mass

Mass change from planning to mid-treatment calculated
- Done for each lobe of each patient
- Healthy lobes used as control
Slight decrease in density found for healthy lobes

- Pathology-free Ipsilateral (n = 27): mean = -5.2%
- Contralateral (n = 39): mean = -7.2%

No significant difference between groups

- $p = 0.519$ (Wilcoxon signed-rank test)
No mass change found for healthy lobes
- Pathology-free Ipsilateral (n = 27): mean = 0.5%
- Contralateral (n = 39): mean = -2.0%

No significant difference between groups
- $p = 0.727$ (Wilcoxon signed-rank test)
Results – NTP Lobes (Density)

Density decreases in proportion to resolution vs. healthy lobes

- -63.5% for full resolution (n = 3) \( p = 3.75 \times 10^{-3} \)
- -38.2% for partial resolution (n = 10) \( p = 2.82 \times 10^{-5} \)
- -8.6% for no change (n = 5) \( p = 0.849 \) (insignificant)
Decrease in mass for lobes with pathology
- -20.0% for all resolution types combined
  - -23.3% for full resolution (n = 3)
  - -22.8% for partial resolution (n = 10)
  - -12.3% for no change (n = 5)

Significant difference in pathology vs. healthy lobes
p = 0.010
Conclusions

• Control lobes (healthy ipsilateral & contralateral)
  ▪ No mass change occurs (as hypothesized)
  ▪ Slight decrease in density

• NTP lobes experience density decrease in proportion to degree of resolution
  ▪ Full resolution > partial resolution
  ▪ No change lobes no different than healthy

• NTP lobes lose mass as re-aeration occurs
  ▪ Thought to be due presence of additional matter during collapsed state (unexpected)
    ➢ Edema & infiltrate
Conclusions

Observed density changes

- Straight-forward intensity matching (e.g. SSD, Demons) not appropriate

Observed mass changes

- Mass preserving algorithm (e.g. SSTVD) cannot be used for atelectasis

DIR algorithm for large geometric changes in lung must properly account for observed mass and density changes
Thank You!