Dependence of total-lung DVH upon respiratory phase-specific lung volume

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Outline of presentation

• Overview of lung-DVH guidelines

• Motivation for current study: DVH vs. lung volume

• Materials and methods

• Results and discussion

• Conclusions and future work
Overview of lung-DVH guidelines

• Cumulative lung DVH used to determine likelihood of respiratory complications following thoracic radiation

• In practice, specific ordinate values on the cumulative lung-DVH curve (e.g. $V_{20}$, $V_{10}$) are used to evaluate the quality of a radiotherapy treatment plan

• Lung DVH guidelines have been suggested, based on results from retrospective studies
\( V_{20}\) and respiratory complication

- M. V. Graham et al., IJROBP 45 (1999) pp. 323-329:

- Among 99 NSCLC patients in study, 20% observed with Grade 2 pneumonitis 24 months after radiation

- For patients with \( V_{20} > 40\%\): incidence = 36%

- However:
  - patients not stratified according to concurrent chemotherapy or prior lung function
  - Lung DVH evaluated without subtracting PTV from lung
V₁₀, V₂₀, and respiratory complication

- H. K. Lee et al., IJROBP 57 (2003) pp. 1317-1322:
  - 61 esophageal patients receiving concurrent chemo/RT (45 Gy median dose), followed by surgery
  - Considered total-lung DVH; CTV, PTV not expanded into lung

- 11/61 (18%) with pulmonary complications
  - For V₁₀ ≥ 40%: 35% occurrence (vs. 8% for V₁₀ < 40%)
  - For V₂₀ ≥ 20%: 32% occurrence vs. 10%
    (however, apparent increase not considered statistically significant: p=0.079)
  - Pulmonary complications not correlated with surgical procedure or site, induction vs. concurrent chemo, or smoking history
V₅, VS₅, and respiratory complication

- 110 esophageal patients considered
  - Neoadjuvant chemo/RT (41.4 to 50.4 Gy) followed by surgery
  - Includes those analyzed within H. K. Lee et al.

- 18/110 (16%) with postoperative pulmonary complications

- From univariate analyses, increased incidence seen for:
  - Increased V₅
  - Reduced VS₅ (VS₅ = absolute lung volume receiving < 5 Gy)
  - Female patients (45% vs. 19%) (likely related to smaller total lung volume, thus smaller VS₅)
**V₅, VS₅, and respiratory complication**

- Figure 2 from S.-L. Wang et al.:
  - Increasing V₅ found to correlate with increasing incidence of pulmonary complications
  - This has motivated attention to V₅ at MDACC (aim to keep it below 60%)

- Figure 4 from S.-L. Wang et al.:
  - Multivariate model: VS₅ the only significant independent predictive factor for post-op pulmonary complication
  - Ensuring adequate lung volume unexposed to radiation may effectively reduce incidence of respiratory complications

Data adapted from S.-L. Wang et al.
Respiratory-correlated lung volume and lung DVH

- Apparent lung volume appears critical in evaluating likelihood of respiratory complication
  - Especially given the correlation with $V_{S5}$
  - $V_{20}$, $V_{10}$, $V_{5}$ expected to change with lung volume as well

- However: the above lung-DVH criteria were determined from treatment plans using the apparent lung volume from CT scans acquired during free-breathing (“3D-CT”)
  - Does the resulting DVH characterize the actual total-lung dose distribution over the course of treatment?
Respiratory-correlated lung volume from 4D-CT

• Study presented by C. Stepaniak et al., AAPM 2005:
  – Use 4D-CT to correlate apparent lung volume with respiratory phase
  – Determine the phase within which the apparent CT lung volume is most consistent with the 3D-CT lung volume
    • CT data for that phase may be used to generate the treatment plan (negating the need for separate 3D-CT scan)
    • Current DVH guidelines should be applicable for that phase
  – Determine the extent to which lung volume can vary over the course of a respiratory cycle
    • Lung-volume variation may correspond to lung-DVH variation
Results from C. Stepaniak et al., AAPM 2005

- “Ave-IP”: for each voxel, determine average CT number among all respiratory-phase images, and assign that average CT number to that voxel.

- Apparent lung volume from Ave-IP (red diamonds) differs from apparent 3D-CT lung volume by 3%, at most.

- 20% phase (mid-exhalation) and 80% phase (mid-inhalation): lung volume corresponds best to apparent Ave-IP lung volume.

Individual-phase lung volume minus 3D-CT lung volume, data for two patients.
Results from C. Stepaniak et al., AAPM 2005

- 20%-phase, 80%-phase lung volumes correspond best to apparent Ave-IP lung volume
  - 20% phase: lung-volume difference 1.0±1.9%
  - 80% phase: −1.2±2.8%
- Motivated choice to use 20%-phase CT image set to develop the clinical treatment plan, for FMLH patients having undergone 4D-CT simulation
Objectives of the current study

• Evaluate variation of total-lung DVH at distinct respiratory phases

  – If beams’ paths remain entirely with lung during respiration, then may expect decrease in lung volume during exhalation ⇒ increase in DVH at low doses

  – Departures from the above: may indicate more-complex motion of lung relative to beam geometry

  – Increased density of lung during exhalation ⇒ increased attenuation of x-ray beams ⇒ reduced dose deposition interior to lung ⇒ reduced DVH at higher doses
Objectives of the current study

- Assess impact of DVH variations upon lung-DVH guidelines for routine thoracic radiotherapy, prospective gated treatments
  - Are DVH differences, from phase to phase, on the order of several percent? (for some treatment plans, criteria such as \(V_{20} < 20\%\) may be challenging to meet)
  - End-inhalation, end-exhalation gated treatment: might the “true” DVH be significantly different from the apparent DVH associated with 3D-CT lung volume?
4D-CT data acquisition

- 4D-CT hardware:
  - GE LightSpeed 4-slice CT scanner:
    - Axial scans (increment couch, acquire CT data)
    - Cine-CT mode: at each couch position, x-ray tube rotates at least 10 times around patient, acquiring axial CT image during each rotation
  - Varian Real-time Position Management (RPM) system:
    - Monitors abdominal AP displacement – correlated with respiratory phase/lung volume
GE Advantage Workstation:

- Associates “time-stamp” of each cine-CT image with RPM trace
- At each couch position, for each cine-CT image, enables association with specific respiratory phase
- Images associated with one of ten phases in respiratory cycle: 0%, 10%, 20%, … 90%
4D-CT image sets used in analysis

- Respiratory phase images used in treatment planning:
  - 0% phase
    - Peak inhalation, by definition
  - 50% phase
    - Peak exhalation, on average
    - Peak exhalation typically arises between 40% and 60% phases
  - 20% phase
    - Mid-exhalation
    - Most consistent with apparent 3D-CT lung volume
    - Routinely used to develop “clinical plan” for patient treatment

Adapted from data incorporated in C. Stepaniak et al., AAPM 2005 – 18 patients
Treatment planning processes and DVH analyses

• Contouring:
  – For each image set: patient skin surface, right lung, left lung
  – ITV/PTV not transferred, subtracted from lung

• Beam design and dose calculation:
  – Transferred the following from the “clinical” plan to the other 4D-CT phase image sets:
    • Beam orientations (gantry/collimator angles, isocenter) and energies
    • Apertures (blocks/MLCs) and wedges
    • MU per beam
  – Heterogeneity corrections turned on

• Ten clinical cases considered
  – Both lateral and medial lung targets
  – Several NSCLC cases (prescribed 63 to 66 Gy)
  – Treatments to mediastinum

• Determine cumulative DVH for total lung
  – Compute $V_{20}$, $V_{10}$, $V_5$, $VS_5$
DVH analyses: NSCLC, lateral-lung targets

- As phase changes from 0% to 50%, $V_{10}$ and $V_{20}$ tend to change by 2 to 3%
- Increase (or decrease) of DVH with respiratory phase is case-specific
DVH analyses: mediastinal targets

- Total-lung DVH may not increase or decrease monotonically with change in respiratory phase (end-inhalation to end-exhalation)
- Lung motion, in and out of treatment fields, as a function of respiratory phase, can be complex
- For one patient case presented: effect of respiratory phase upon V_{10} is substantial (~20%)
Variation in DVH: $V_{20}$ and $V_{10}$

<table>
<thead>
<tr>
<th>Patient Label</th>
<th>$V_{20}$ (%)</th>
<th>$V_{20}$</th>
<th>$V_{10}$ (%)</th>
<th>$V_{10}$</th>
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<tbody>
<tr>
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<td>phase 20</td>
<td>phase 50</td>
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<tr>
<td>Pt1 (lateral)</td>
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<td>6%</td>
<td>7%</td>
<td>1%</td>
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<tr>
<td>Pt2 (lateral)</td>
<td>41%</td>
<td>42%</td>
<td>44%</td>
<td>3%</td>
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<td>2%</td>
</tr>
<tr>
<td>Pt4 (lateral)</td>
<td>17%</td>
<td>16%</td>
<td>16%</td>
<td>1%</td>
</tr>
<tr>
<td>Pt5 (lateral)</td>
<td>17%</td>
<td>18%</td>
<td>20%</td>
<td>2%</td>
</tr>
<tr>
<td>Pt6 (medial)</td>
<td>22%</td>
<td>22%</td>
<td>22%</td>
<td>1%</td>
</tr>
<tr>
<td>Pt7 (medial)</td>
<td>19%</td>
<td>20%</td>
<td>19%</td>
<td>2%</td>
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<td>Pt8 (lateral)</td>
<td>27%</td>
<td>28%</td>
<td>29%</td>
<td>2%</td>
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<td>34%</td>
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<tr>
<td>Pt10 (lateral)</td>
<td>19%</td>
<td>19%</td>
<td>19%</td>
<td>0%</td>
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</tbody>
</table>

- Change in $V_{20}$, $V_{10}$: typically by 2%, at most by 3%
- Not always monotonic increase with decreasing lung volume
## Variation in DVH: $V_5$

<table>
<thead>
<tr>
<th>Patient Label</th>
<th>$V_5$ (%)</th>
<th>$V_5$ spread</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>phase 0</td>
<td>phase 20</td>
</tr>
<tr>
<td>Pt1 (lateral)</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td>Pt2 (lateral)</td>
<td>56%</td>
<td>57%</td>
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<tr>
<td>Pt3 (lateral)</td>
<td>42%</td>
<td>40%</td>
</tr>
<tr>
<td>Pt4 (lateral)</td>
<td>30%</td>
<td>28%</td>
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<tr>
<td>Pt5 (lateral)</td>
<td>46%</td>
<td>49%</td>
</tr>
<tr>
<td>Pt6 (medial)</td>
<td>37%</td>
<td>42%</td>
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<td>Pt7 (medial)</td>
<td>65%</td>
<td>73%</td>
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<tr>
<td>Pt8 (lateral)</td>
<td>52%</td>
<td>53%</td>
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<td>Pt9 (lateral)</td>
<td>66%</td>
<td>68%</td>
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<tr>
<td>Pt10 (lateral)</td>
<td>31%</td>
<td>30%</td>
</tr>
<tr>
<td>$\mu$ spread</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\sigma$ spread</td>
<td></td>
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</tbody>
</table>

- Typical change in $V_5$ is approximately 3%; not necessarily monotonic with respiratory phase.
- Increase in respiratory-complication likelihood: can be modest (~2%) or significant (~7%), depending on whether $V_5$ is higher or lower.

Variation in DVH: $\text{VS}_5$

<table>
<thead>
<tr>
<th>Patient Label</th>
<th>$\text{VS}_5$ (cm$^3$)</th>
<th>$\text{VS}_5$</th>
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<td>4318</td>
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<tr>
<td>Pt2 (lateral)</td>
<td>1143</td>
<td>1080</td>
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<td>Pt3 (lateral)</td>
<td>1750</td>
<td>1788</td>
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<tr>
<td>Pt4 (lateral)</td>
<td>3394</td>
<td>3408</td>
</tr>
<tr>
<td>Pt5 (lateral)</td>
<td>1650</td>
<td>1500</td>
</tr>
<tr>
<td>Pt6 (medial)</td>
<td>1832</td>
<td>1899</td>
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<tr>
<td>Pt7 (medial)</td>
<td>1087</td>
<td>808</td>
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<tr>
<td>Pt8 (lateral)</td>
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<td>2083</td>
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<tr>
<td>Pt9 (lateral)</td>
<td>792</td>
<td>701</td>
</tr>
<tr>
<td>Pt10 (lateral)</td>
<td>2635</td>
<td>2513</td>
</tr>
<tr>
<td>$\mu$ spread</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\sigma$ spread</td>
<td></td>
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</tr>
</tbody>
</table>

- Typical change in $\text{VS}_5$ is approximately 260 cm$^3$; not necessarily monotonic with respiratory phase.
- If $\text{VS}_5$ is smaller, effect of lung volume upon $\text{VS}_5$ can be significant (~5% to 7% difference in respiratory-complication likelihood).

Adapted from S.-L. Wang et al., IJROBP 64 (2006) pp. 692-699
Conclusions

• Variations in total-lung DVH with respiratory phase:
  – 2% to 3% variations can be expected
  – Low-dose DVH variations can be substantial for some patients
  – Sufficient to warrant a re-assessment of existing DVH guidelines

• Trends in DVH variations may be patient-specific

• Current DVH criteria for $V_{10}$ and $V_{20}$ (based on 20%-phase CT) might not be applicable for gated treatments (at 0%- or 50%-phase)
Areas for future study

• Investigate the more-detailed aspects of the change in lung geometry with respiratory phase
  – expansion/contraction in AP/SI/RL directions
  – local variations in lung density

• Investigate effect, legitimacy of excluding PTV from total-lung DVH calculation

• Investigate lung-DVH differences, IMRT vs. 3DCRT
  – Might IMRT yield unacceptable $V_5$, $VS_5$?

• Is there an observed reduction/increase in post-RT respiratory complication following gating or breath-hold treatments, relative to free-breathing treatments?