Evaluation of Deformable Image Registration for Improved 4D CT-Derived Ventilation for Image Guided Radiotherapy

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“Although nearly a century has passed since radiation pneumonitis and fibrosis were first described...these two side effects of pulmonary irradiation remain unable to be circumvented or effectively treated, and they continue to limit the effective treatment of lung cancer.”

From: Radiation Oncology, Rational*Techniques*Results, 8th ed, p399

- Nearly all patients receiving thoracic XRT develop some degree of lung injury, often causing loss of pulmonary function, and killing some patients.

- Consequently, the standard tolerable dose for treatment of locally advanced NSCLC is inadequate; pulmonary injury is the dose-limiting toxicity in thoracic XRT for lung cancer.
• A recent dose escalation study for NSCLC found higher radiation dose associated with improved overall survival
  – “Higher dose radiation is associated with improved outcomes in patients…treated in the range 63-103 Gy.”
  – “Future study should focus on optimizing radiation technique and maximizing radiation dose to improve outcomes…”
• If the risk of lung injury can be reduced for all patients, then a greater fraction of NSCLC patients can benefit from higher radiation doses
Background & Significance

- Currently the volume of normal lung that will receive a specified radiation dose is utilized in radiotherapy treatment planning to estimate the risk of pulmonary injury (e.g., $V_{20} < 40\%$)

- A more accurate method of risk assessment would include both the *volume* and the *functional capacity* of the portions of the lung intended for irradiation

*From: Christian JA, et al. 2005*
Developed for radiotherapy treatment planning, 4D CT images are now routinely acquired at many institutions as part of the planning process for thoracic malignancies.

4D CT images also contain CT characteristics that reflect changes in air content of the lungs due to ventilation.
Background & Significance

- Assuming the density of any pulmonary sub-volume can be expressed as a linear combination of air and water-like material, one can derive an expression for regional specific ventilation:

\[
s_{\text{Vent}} = \frac{\Delta V}{V_{\text{air}}} = 1000 \frac{(\bar{H}_{\text{inhal}} - HU_{\text{exhal}})}{HU_{\text{exhal}} (1000 + \bar{H}_{\text{inhal}})}
\]

- The incorporation of such function information into the treatment planning process for purposes of functional avoidance may prove to be a superior planning practice for the treatment of thoracic malignancies.
A 2007 study showed that CT-ventilation could be incorporated into IMRT treatment planning, resulting in improved functional dosimetry, **without compromising standard volumetric planning criteria**.

- These findings suggest that CT-derived ventilation may be well-suited for thoracic IGRT planning, providing critical additional treatment planning information at the cost of additional computations only.

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Background & Significance

Validation of the 4D-CT–derived ventilation imaging with SPECT ventilation should be performed before clinical implementation of the techniques developed in this study proceed to clinical use. Then a clinical study will be necessary to determine whether patient outcome, including reduced treatment complications, is improved through the use of functional avoidance treatment planning.

*From: Yaremko BP, et al. 2007*
Background & Significance

• The output ventilation image depends almost entirely on the DIR transformation used to determine the physical HU correspondence.

• Thus, *strategies for evaluation of DIR are crucial*, since validation of CT-derived ventilation imaging requires assessment of the DIR component as a necessary prerequisite.

*Variable DIR output leads to variable ventilation images*
HHYPOTHESIS

4D CT-derived ventilation imaging will provide an accurate assessment of pulmonary function for use in image guided thoracic radiation therapy

Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

**Rationale**

- One difficulty in determining whether clinically-relevant function information can be extracted from 4D CT is that spatial registration errors are a potential source of error that is expected to degrade the extracted information.

- Thus, we require a methodology for evaluating DIR spatial accuracy performance, in order to assess the impact of spatial registration errors on the output ventilation images.
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- **Evaluation Procedures**
  What objective metrics for DIR quality are appropriate for radiotherapy and image-guided surgery?

- **Acceptance Testing**
  What formal testing procedures should be in place, upon which to base decisions regarding acceptance for clinical implementation?

- **Quality Assurance**
  Once accepted for routine clinical use, how do we verify for any given case that the DIR quality is within accepted standards for the specific application?
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- Multiple classes of media have been utilized for evaluation of DIR
  - Rigid and deforming mechanical phantoms
  - Synthetic image pairs
- It is generally accepted that simulations and mechanical phantoms lack sufficient realism to provide credible indication of DIR performance in clinical application
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- The primary disadvantage is the lack of realism associated with, e.g., anatomical changes, involuntary motion, and image acquisition & reconstruction artifacts
- *There is not a direct association with spatial accuracy performance on clinically acquired images*
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- For clinical validation, reference data should be derived from actual patient images:
  - **Image similarity-based**
    - Correlation coefficient
    - Image fusion
    - Spatial overlap indices
  - **Physically motivated**
    - Jacobian determinant
  - **Spatial accuracy**
    - “Landmark” positions

- **Measurements of position** represent the natural units for quantifying mis-registration, since the DIR calculation is inherently to determine a spatial transformation between images

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- Difficulty arises from the fact that in clinical situations there is not a ‘known’ transformation
- One potential solution is to estimate the DIR spatial accuracy within the anatomic target by sampling the true transformation
- Assisted landmark registration of pulmonary feature points will provide an objective measure from which to compare and evaluate DIR spatial accuracy (??)
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

‘Aims’

• What process should be in place to facilitate manual registration?
• Can feature points be reliably and consistently registered on 4D CT?
• Is the quantity of identifiable features sufficient for statistical characterization and comparative evaluation among methods?

Methods

• Multiple observers will utilize a novel software package to manually determine feature correspondences b/w two component phase volumes from clinically obtained 4D CT
  – Patients treated at MDACC for thoracic malignancies: esophagus cancer, NSCLC
• 4D CT images of the entire thorax and upper abdomen obtained at 2.5 cm slice spacing; (0.97×0.97×2.5) mm³

Patient images acquired as part of an NIH-funded validation study (NIH/NCI 1R21CA128230-01), with approval by the IRB (2006-0698)
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

Preliminary Data

• A MATLAB-based interface was developed for 3D feature registration
• Feasibility study: 5 patient cases (4D CT), 3 observers, 2 DIR algorithms
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- Assessment of landmark reproducibility performed by repeat registration of 200 feature points for each case; \textit{avg. error = 0.8 mm}
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

**Preliminary Data**

- Numerical simulations were performed for each reference case to demonstrate the effect of sample size on uncertainty associated with spatial error estimation.
- Random samples of the CDF were used to simulate landmark samples ranging in size from 10 to 5,000.
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- For each sample size increment: 100,000 independent samples were obtained, and the mean of each sample calculated
- For the range of experimental sample sizes: average ± 95% CIs for sample means were determined

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**Preliminary Data**

- The simulations were compared to predicted intervals, calculated from the error statistics obtained from the validation landmark sets (*left*).
- **Comparative evaluation based on fewer than the required measurements increases the probability of misrepresenting the relative spatial accuracy performance** (*right*).
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

**Preliminary Data**

- Further preliminary work focused on the utility of a commonly-employed image similarity-based metric for performance assessment of DIR
- **Visual inspection alone provides no indication of the underlying spatial accuracy**

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A framework for evaluation of deformable image registration spatial accuracy using large landmark point sets

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• Preliminary work has demonstrated the use of manually identified pulmonary features for quantitative assessment of DIR spatial accuracy with a narrow range of uncertainty
• Reference data has been made publicly available via the Internet (http://www.dir-lab.com)
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs


### Table 1a. Available Reference Data - 4DCT

<table>
<thead>
<tr>
<th>Case ID</th>
<th>Image Dims</th>
<th>Voxel Dims (mm)</th>
<th># Landmarks</th>
<th>Avg (SD) Landmark Displacement (mm)</th>
<th># Repeated Measurements</th>
<th>Observer Error (SD) (mm)</th>
<th>Landmarked Phases</th>
</tr>
</thead>
<tbody>
<tr>
<td>c1</td>
<td>256 x 256 x 94</td>
<td>0.97 x 0.97 x 2.5</td>
<td>1280</td>
<td>4.01 (2.91)</td>
<td>200 / 3</td>
<td>0.85 (1.24)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c2</td>
<td>256 x 256 x 112</td>
<td>1.16 x 1.16 x 2.5</td>
<td>1487</td>
<td>4.55 (4.09)</td>
<td>200 / 3</td>
<td>0.70 (0.99)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c3</td>
<td>256 x 250 x 104</td>
<td>1.15 x 1.15 x 2.5</td>
<td>1561</td>
<td>8.73 (4.21)</td>
<td>200 / 3</td>
<td>0.77 (1.01)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c4</td>
<td>256 x 256 x 90</td>
<td>1.13 x 1.13 x 2.5</td>
<td>1166</td>
<td>9.42 (4.31)</td>
<td>200 / 3</td>
<td>1.13 (1.27)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c5</td>
<td>256 x 256 x 106</td>
<td>1.10 x 1.10 x 2.5</td>
<td>1268</td>
<td>7.10 (5.14)</td>
<td>200 / 3</td>
<td>0.92 (1.18)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c6</td>
<td>512 x 512 x 128</td>
<td>0.97 x 0.97 x 2.5</td>
<td>419</td>
<td>11.10 (6.58)</td>
<td>150 / 3</td>
<td>0.97 (1.38)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c7</td>
<td>512 x 512 x 136</td>
<td>0.97 x 0.97 x 2.5</td>
<td>398</td>
<td>11.59 (7.67)</td>
<td>150 / 3</td>
<td>0.81 (1.32)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c8</td>
<td>512 x 512 x 128</td>
<td>0.97 x 0.97 x 2.5</td>
<td>476</td>
<td>10.16 (5.11)</td>
<td>150 / 3</td>
<td>1.03 (2.19)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c9</td>
<td>512 x 512 x 128</td>
<td>0.97 x 0.97 x 2.5</td>
<td>342</td>
<td>7.82 (3.99)</td>
<td>150 / 3</td>
<td>0.75 (1.09)</td>
<td>[T00 : T50]</td>
</tr>
<tr>
<td>c10</td>
<td>512 x 512 x 120</td>
<td>0.97 x 0.97 x 2.5</td>
<td>435</td>
<td>7.63 (5.54)</td>
<td>150 / 3</td>
<td>0.86 (1.45)</td>
<td>[T00 : T50]</td>
</tr>
</tbody>
</table>

### Table 1b. Available Reference Data - COPDgene COMING SOON

<table>
<thead>
<tr>
<th>Case ID</th>
<th>Image Dims</th>
<th>Voxel Dims (mm)</th>
<th># Landmarks</th>
<th>Avg (SD) Landmark Displacement (mm)</th>
<th># Repeated Measurements</th>
<th>Observer Error (SD) (mm)</th>
<th>Landmarked Phases</th>
</tr>
</thead>
<tbody>
<tr>
<td>copd1</td>
<td>512 x 512 x 121</td>
<td>0.625 x 0.625 x 2.5</td>
<td>773</td>
<td>25.90 (11.57)</td>
<td>150 / 3</td>
<td>0.65 (0.73)</td>
<td>BH-CT pair</td>
</tr>
<tr>
<td>copd2</td>
<td>512 x 512 x 102</td>
<td>0.645 x 0.645 x 2.5</td>
<td>618</td>
<td>21.65 (6.58)</td>
<td>150 / 3</td>
<td>1.06 (1.51)</td>
<td>BH-CT pair</td>
</tr>
<tr>
<td>copd3</td>
<td>512 x 512 x 126</td>
<td>0.652 x 0.652 x 2.5</td>
<td>1172</td>
<td>12.29 (6.39)</td>
<td>150 / 3</td>
<td>0.58 (0.87)</td>
<td>BH-CT pair</td>
</tr>
<tr>
<td>copd4</td>
<td>512 x 512 x 128</td>
<td>0.590 x 0.590 x 2.5</td>
<td>786</td>
<td>30.00 (13.49)</td>
<td>150 / 3</td>
<td>0.71 (0.96)</td>
<td>BH-CT pair</td>
</tr>
<tr>
<td>copd5</td>
<td>512 x 512 x 131</td>
<td>0.647 x 0.647 x 2.5</td>
<td>1029</td>
<td>30.90 (14.05)</td>
<td>150 / 3</td>
<td>0.65 (0.87)</td>
<td>BH-CT pair</td>
</tr>
</tbody>
</table>

Representative cine loops (4DCT only) and surface renderings are shown below for all available reference data sets listed in Table 1 (click link to view).
Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

- **100 registered users:** representing academic, commercial, and government interests:
  - US, France, Germany, Italy, Egypt, Australia, The Netherlands, Japan, Canada, Spain, England, Thailand, Iran

- **In-house:** development and optimization of novel application-specific formulations and implementations:

**REFERENCES**


From: http://www.dir-lab.com/Templates/Results.html

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Improving Ventilation Imaging for Image Guided Radiotherapy

HYPOTHESIS

4D CT-derived ventilation imaging will provide an accurate assessment of pulmonary function for use in image guided thoracic radiation therapy.

Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs.

Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT).

Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects.

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Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

Rationale

- Pulmonary toxicity is better correlated to the volume of *functional* lung rather than total lung irradiated$^\dagger$.
- 4D CT-derived ventilation may have significant impact on treatment planning of thoracic malignancies;
  - image guidance to avoid functional lung,
  - identify hypo-functioning regions in order to remove avoidance restriction (*dysfunctional allowance*),
  - diagnostic evaluation of regional pulmonary function and injury
- *No preliminary validation studies have been performed comparing 4D CT-derived ventilation with the clinical standard SPECT ventilation*

Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

### Patient Image Data

- 25 clinically acquired treatment planning 4D CTs
- Complimentary same-day ventilation SPECT-CT
  - Submicronic $^{99m}$Tc DTPA aerosol administered to resting tidal breathing patients in seated, up-right posture
- All imaging studies performed prior to initiation of treatment

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Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

**Patient Image Data**

- SPECT acquisitions covered the entire lung in the emission image

- Co-registered CT were used for attenuation correction of the $^{99m}$Tc 140 keV photons

- CT was also used for alignment with the 4D CT-derived ventilation using the CT-to-CT fusion software in *Pinnacle* v7.6 (Philips Medical Systems, Andover, MA),
  - image reconstruction performed in MATLAB
Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

- Segmentation of lung voxels is necessary to define the spatial domain for lung function calculations, as well as to provide a reference measurement of the global volume change for self-consistency analysis
  - Performed in MATLAB using basic histogram segmentation and 3D morphological growing techniques
- Linear regression demonstrates good agreement with the image-segmentation based measure of the resting tidal volume

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Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

- Average ventilation and corresponding variance initially determined in non-overlapping octant lung regions for each case (16 ROIs per case)
  - The octants provide a natural pairing b/w techniques to account for heterogeneity over the lung
- Define the difference, $d_i = SPECT_i - CT_i$, ($i = 1, 2, \ldots, 16$), to facilitate simple paired $t$-test to compare agreement between the two techniques
Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

- A major complication arises from inherent solubility of the DTPA aerosol, which can lead to airway deposition artifacts that mask local function information, making quantitative regional comparison difficult.
Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

- One solution is to threshold the SPECT images to some fixed percentile of image intensities within the lung ROI (e.g., 90th%)
Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard \(^{99\text{m}}\text{Tc}\) DTPA aerosol SPECT ventilation (using SPECT-CT)

- Each of the \(^{99\text{m}}\text{Tc}\) DTPA aerosol SPECT ventilation images was partitioned into
  - non-overlapping regions representing fixed intervals of the percentile distribution of ventilation
- Dice similarity coefficient (DSC) determined among corresponding intervals between methods:
  \[
  DSC(V_{\text{ref}}, V_2) = \frac{2 \times |V_{\text{ref}} \cap V_2|}{|V_{\text{ref}}| + |V_2|}
  \]
- Significantly \((p < 10^{-4})\) larger DSC in the lowest functioning percentile region
Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

- For all cases, DSC < 0.7
- Hot spot artifacts in the SPECT images are not physiologically representative of the local underlying lung function
- To estimate the influence of aerosol airway deposition, the CT component of each SPECT-CT study was used to extract the main airway for overlap analysis with the registered ventilation images

SPECT/CT airway voxels have the highest probability to be found within the 90th percentile SPECT ventilation, supporting the assertion that the SPECT ventilation hotspots are primarily due to airway deposition of the DTPA aerosol.

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Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99}$mTc DTPA aerosol SPECT ventilation (using SPECT-CT)

- The set of 4D CT-based ventilation images showed good linear correlation with image segmentation-based measures of the resting tidal volume.
- The highest correlation among methods was in the lowest functioning pulmonary regions, defined as the lowest 20th percentile of lung function.
- The use of clinically acquired $^{99}$mTc DTPA aerosol SPECT ventilation as a reference for evaluation of 4D CT-ventilation is complicated by
  - the inherent qualitative nature of the nuclear medicine studies,
  - as well as the potential for image artifacts resulting from airway deposition of the DTPA aerosol.
HYPOTHESIS

4D CT-derived ventilation imaging will provide an accurate assessment of pulmonary function for use in image guided thoracic radiation therapy

Specific Aim 1: Establish a methodology for quantitative assessment and comparative evaluation of deformable image registration spatial accuracy in the lungs

Specific Aim 2: Measure the correlation between 4D CT-derived ventilation and the clinical standard $^{99m}$Tc DTPA aerosol SPECT ventilation (using SPECT-CT)

Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects
Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- Delivery of radiotherapy through hypo-perfused pulmonary regions for lung cancer treatment had been shown to result in less pulmonary injury in prospective trials
- We hypothesize that hypo-ventilated regions will correlate with hypo-perfused regions in lung cancer patients with obstructive lesions

Lung cancer in patients with borderline lung functions – zonal lung perfusion scans at presentation and lung function after high dose irradiation

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(Received 6 November 1989, revision received 14 June 1990, accepted 19 June 1990)
Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- The same patient set described in Specific Aim 2 utilized in this Aim
- Lung perfusion SPECT-CT images acquired following IV administration of $^{99m}$Tc-labeled macro-aggregated albumin (MAA)
- 2-3 day delay between V-Q scans to allow decay and clearance of ventilation radiopharmaceutical

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Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- Included images narrowed to subset of patients with radiographically demonstrated airway stenosis (narrowing that obstructs the passage of air to the lungs)
- Lesions result in hypo-perfused lung regions distal to the site of obstruction

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Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

**Study Design**

- Percentile ventilation and perfusion images were generated and imported into Pinnacle TPS, v8.1x
- Using both the raw and percentile perfusion images for guidance, manual contouring of the percentile volume was performed to include only the specific defect region distal to the known airway malignancy.
  - **For ventilation contouring**, 3 observers performed the defect segmentation; independently and without prior knowledge of the SPECT segmentations
- Normalized DSC defined as DSC of reference with reference contracted by 1mm ($NDSC_{1mm}$) or 2mm ($NDSC_{2mm}$)
  - Accounts for sensitivity of DSC when volumes are small,
  - Uncertainty in manual segmentation of the reference mask,
  - Provides reference for interpreting the measured spatial overlap in terms of a quantifiable spatial discrepancy
Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- **Data range**: [0.60 – 0.99; 0.78]_{DSC}, [0.71-1.07; 0.88]_{1mm}, [0.79-1.16; 0.99]_{2mm}
- On average, spatial overlap comparable to the threshold for agreement within 1-2 mm uncertainty (COV range: [0.10 – 26%])

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Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- Avg. V/Q volume ratio = 1.05,
  - suggests trend for relatively larger presentation of defect ROIs depicted on 4D CT ventilation

- Linear correlation between spatial overlap metric and contoured defect volume was $R^2 = 0.50$ ($p = 0.02$)
Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- Spatial overlap of segmented defect regions (red = perfusion, green = ventilation)
Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- These results point to high spatial overlap agreement between CT ventilation and SPECT pulmonary perfusion defect regions distal to obstructing lesions;
- Average spatial overlap comparable to the threshold for agreement within 1-2 mm uncertainty
  - Multi-modal image registration
  - Acquisition settings
  - Motion and/or reconstruction artifacts
Specific Aim 3: Evaluate the correlation between the pulmonary perfusion and ventilation defects

- Ventilation imaging from 4D CT is subject to degradation resulting from irregular breathing and subsequent artifacts
- Improved 4D CT acquisition and reconstruction techniques that reduce the overall frequency of 4D CT artifacts, (previously estimated to affect 90% of image acquisitions*) are needed
- Furthermore, these findings point to the need for quality control practices that ensure informed interpretation of the functional maps prior to implementation into a specific clinical application

The hypothesis of this study was that quantitative images depicting regional specific ventilation from 4D CT would provide an accurate assessment of pulmonary function for use in image guided thoracic radiation therapy.

Specific Aim 1 presents a framework and corresponding novel software infrastructure for quantitative evaluation of DIR spatial accuracy, demonstrating large landmark point sets as an effective means for objective evaluation of DIR with a narrow uncertainty range.

Specific Aim 2 investigated the correlation between the spatial distributions of ventilation derived from 4D CT and $^{99m}$TC DTPA aerosol SPECT in a population of lung and esophagus cancer patients, prior to the initiation of treatment. Findings revealed the greatest similarity in spatial distribution was within the lowest functioning percentile regions.

Specific Aim 3 investigated the correlation of regional hypo-ventilation derived from 4D CT with hypo-perfused pulmonary regions on $^{99m}$Tc MAA SPECT perfusion. Based on the findings in Aim 2, the evaluation was limited to a sub-population patients with radiographically demonstrated airway obstruction due to their gross tumor volume. Mean (and range) NDSC$_{2\text{mm}}$ between volumetric ventilation and perfusion defect regions was 0.99 (0.79-1.16), suggesting high spatial correlation between macroscopic pulmonary perfusion and ventilation defect regions in lung cancer patients with malignant airway stenosis.
The hypothesis of this study was that quantitative images depicting regional specific ventilation from 4D CT would provide an accurate assessment of pulmonary function for use in image guided thoracic radiation therapy.

Using high spatial accuracy deformable image registration to facilitate lung function quantification, we have demonstrated high spatial correlation of 4D CT ventilation with the clinical reference SPECT ventilation and perfusion imaging, within local defect regions attributable to malignant airway stenosis.

These findings limit the scope of the original hypothesis, but nonetheless demonstrate it to be true within the well-defined sub-population of lung cancer patients receiving thoracic radiotherapy.
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  - Charles Willis, PhD

- Sandra Jimenez
- Stephen Bilton

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    - Chief, Section of Interventional
    - Pulmonary Medicine UTHSCSA
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  - Milos Vicic, PhD
  - Scott Davidson, PhD
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  - Sarah Joy, MS

- Matt McCurdy, MD, PhD & Alec Block, *(almost MD)*
Dynamic Ventilation from 4DCT

http://www.dir-lab.com/rcastillo.html

Questions?