MicroCT analysis of paraffin embedded lung tissue: Is small airway obstruction an early feature of COPD?

Hypothsis
Small airway narrowing and obliteration precedes emphysema changes in COPD and begins in patients with mild to moderate disease

Methods and Sample Cohort

Table 4. Tissue sample collection, imaging reconstructions, and COPD severity.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal</th>
<th>GOLD 1 Mild</th>
<th>GOLD 2 Moderate</th>
<th>GOLD 3 Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>10</td>
<td>10</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>91±7.1</td>
<td>93±9.1</td>
<td>67±7.5</td>
<td>37±0.4</td>
</tr>
<tr>
<td>FVC (% of FVC)</td>
<td>0.78±0.003</td>
<td>0.65±0.006</td>
<td>0.58±0.016</td>
<td>0.30±0.006</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63±1</td>
<td>67±1</td>
<td>66±2</td>
<td>66±1</td>
</tr>
<tr>
<td>Smoking history (pack years)</td>
<td>40±12</td>
<td>43±14</td>
<td>42±13</td>
<td>42±13</td>
</tr>
</tbody>
</table>

Figure 2. Methods of tissue collection, image acquisition, and reconstruction.

Results

- Pre-operative MCT scan prior to lung resection to define large lung volumes and lung densities.
- Lung samples fixed by formaldehyde and labeled every 1-2 mm from apex to base.
- Random samples selected uniformly over lung height were embedded in paraffin and sectioned in a holder for µCT imaging.
- Sample holder placed inside the HMX 376 µCT scanner at the U-VIS Imaging Centre, Southampton, UK.
- µCT images were reconstructed using the TVIP (three-dimensional volume image projection) software.

CONCLUSIONS and CLINICAL SIGNIFICANCE
- µCT scans of FFPE lung tissue can be utilized to determine the number of terminal bronchioles and measurements of airspace enlargement (Lm) that determines emphysema.
- Our preliminary data indicates that there is a decreased number of terminal bronchioles in mild and moderate COPD lung tissue with no presence of emphysema destruction.
- On completion of this study, we hope that a further understanding of the interaction between small airways and emphysema in the early stages of COPD will be achieved.
- COPD patients are currently not treated until GOLD stage 2. Our data indicate that therapeutic interventions may need to be implemented early to change clinical outcomes.

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