QUANTITATIVE FUNCTIONAL RESPIRATORY IMAGING MAY PREDICT THE MECHANISM OF FEV1 DECLINE AFTER LUNG TRANSPLANTATION

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Introduction
• Within five years of lung transplantation surgery (LTx), up to 50% of patients die following chronic rejection after onset of bronchiolitis obliterans syndrome (BOS).
• Early detection of BOS may increase the probability of successful treatment with novel therapeutic agents.

Functional Respiratory Imaging

Aim of the study
• Show that Functional Respiratory Imaging (FRI) can assess post LTx changes in lung structure and function that can identify BOS early on, discriminating it from respiratory infection by identifying the lung zones driving the FEV1.

Study population

<table>
<thead>
<tr>
<th>Study subjects</th>
<th>Total subjects</th>
<th>71 (41 BOS / 30 non-BOS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>26 Male / 18 Female</td>
<td></td>
</tr>
<tr>
<td>Transplant Type</td>
<td>14 right / 17 left / 40 bilateral</td>
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<tr>
<td>BOS onset</td>
<td>19 early-onset (15 ± 9 months after LTx)</td>
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<tr>
<td></td>
<td>13 late-onset (56 ± 26 months after LTx)</td>
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<tr>
<td></td>
<td>9 unknown</td>
<td></td>
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<tr>
<td>Pre-transplant diagnosis</td>
<td>26 IPF / 23 COPD / 7 CF / 5 A1AD / 4 sarcoidosis / 6 other</td>
<td></td>
</tr>
<tr>
<td>Number of Scans / Patient</td>
<td>3 ± 3 paired functional residual capacity (FRC) and total lung capacity (TLC) CT scans, ranging from 2 to 8</td>
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<tr>
<td>Follow-up CT scans</td>
<td>4.1 ± 3.3 years after transplant, ranging from 15 days to 13 years</td>
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Table 1: The study population

Methods
• CT scans of LTx recipients were analyzed retrospectively (Table 1).
• The PFTs performed closest to each scan were examined to evaluate if the patient met the criteria for BOS 0-p.
• The BOS cohort experienced a reduction in FEV1 >10% compared to baseline (BOS 0-p).
• Multivariate regression modeling was performed to determine the most relevant image metrics to predict FEV1, decline in both BOS and non-BOS cohorts.

Results and discussion
• The FEV1 decline in the BOS cohort correlated with an increase in lung volume (p = 0.027) and central airway volume at FRC (p = 0.013, see Figure 3). These parameters did not change in non-BOS patients with changes in FEV1.
• In contrast, the non-BOS cohort experienced a decrease in central airway volume at TLC with declining FEV1 (p = 0.039).
• An example of the difference between a BOS and non-BOS patient is shown in Figure 2.

Figure 2: Case study

FRI visualization of the changes in:
• lobar volume at FRC
• airway volumes at FRC
• airway volumes at TLC

of two patients (one BOS and one non-BOS), 4 years and 2 years after the initial evaluation, respectively. During this period the BOS patient had a reduction of 11.85% in FEV1, and the non-BOS patient had a reduction of 2.80% in FEV1. The regions experiencing a volume reduction appear in blue, while the regions in yellow/red represent an increased volume in comparison with the baseline scan. Regions in green represent almost no change.

From a pathophysiological point of view, BOS is a small airways condition which, in CT images, is often reflected in hyperinflation and bronchodilation at the expiratory level. Respiratory infections, on the other hand, affect the central airways leading to a more stable image at expiration but bronchoconstriction in the central airways observed at inspiration.

Conclusion
FRI could distinguish the onset of BOS from reversible causes of FEV1 decline, such as pulmonary infection, in patients that underwent LTx and presented with FEV1 decline. The results illustrate the potential of FRI derived quantitative imaging biomarkers to assist in early diagnosis of BOS and in the elucidation of the mechanism accounting for FEV1 decline.

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Figure 1. Correlation between the central airway volume at FRC and FEV1 in the BOS and non-BOS cohort

Reference

CLINICAL IMAGING