Oscillometry, the missing piece
in lung transplant rejection

Transplanted lungs are at risk of rejection after transplant. Frequent surveillance, and early diagnosis are essential for clinical outcomes. Rejection is diagnosed primarily using spirometry and bronchial biopsy, but there is a need for additional, more sensitive, and less-invasive tests.

Oscillometry (OS) is a technology that measures lung mechanics during tidal breathing and has been shown recently to be a useful adjunct method to detect and monitor acute and chronic lung transplant rejection as well as other airway diseases[1].

Key measurements using OS:

Key Measurement	Description
R5	Resistance to airflow of the whole lung.
R5-19	Resistance heterogeneity of the airways. *Increased R5-19 signals potential small airway dysfunction.*
X5	Elastance of the respiratory system. *Decreased X5 implies increased tissue elastance.*
AX	Increased AX correlates with airspace de-recruitment, ventilation defects, and increased lung stiffness.

Acute cellular rejection (ACR)

ACR begins in the small airways (i.e. the 'silent zone'[2]). Currently, bronchial biopsy is the gold standard to diagnose ACR in addition to monitoring with spirometry at a patient's home or at pulmonary function labs.

Challenges present with conventional diagnostic methods:

Spirometry	Spirometry lacks sensitivity to detect biopsy-proven episodes of ACR3[2]. • Up to 75% of all the small airways must change before being detected by forced expiratory volume (FEV_1)[4] • Spirometry has 60% sensitivity for detecting clinically significant grade 2 ACR (10% drop in FEV_1) or higher[5] • Up to 25% of patients are asymptomatic and would only be diagnosed if surveillance bronchoscopy is performed[6,7]
Bronchial Biopsy	• Transbronchial biopsy is limited by the sampling of a small region of the lung and usually contains only a few small airways • Bronchoscopy and transbronchial biopsies have associated risks, procedure-related morbidity, and costs • Routine surveillance bronchosocopy with transbronchial biopsies is not universally adopted by lung transplant centers

Find the missing piece for ACR

OS has been shown to assess lung function including the small airways. It has the potential to detect subtle physiological changes associated with rejection in transplant patients, prior to symptomatic presentation or spirometry findings.

In a recent publication by Cho et al.[3], it was shown that OS results can assist:

Early diagnosis - Abnormal OS parameters are detected 2 weeks prior to scheduled transbronchial biopsy. This is as early as 4 weeks post-transplant for patients with grade 2 ACR.

Surveillance - OS detects significant airway obstruction in double lung transplant patients with grade 2 ACR, while FEV_1 measurements were stable or improved for patients post-transplantation.

Treatment evaluation - OS measurements return to normal as early as 1 week after treatment starts, suggesting treatment efficacy can be monitored using OS.

> *"The data of Cho and colleagues support... the utility of OS as an essential adjunct to spirometry in [ACR] patients, particularly in centers that do not perform routine surveillance bronchoscopy with transbronchial biopsy."*[2]
>
> *-Usmani et al. 2020*

Chronic lung allograft dysfunction (CLAD)

Chronic rejection, or CLAD, develops in 50–70% of patients within 5 years and is the primary cause of death in recipients[8]. CLAD is diagnosed by a 20% decline in FEV_1 when compared to the average of the two of the best post-transplant measurements taken at least 3 weeks apart[7].

Find the missing piece for CLAD

Patient Surveillance - Intra-subject variance of OS parameters (R5-19, X5, AX), but not FEV_1, was strongly and independently associated with an increased risk of CLAD in double lung transplant recipients measured a year post transplant[8].

Diagnosis - In patients with high and low bronchial biopsy A-scores with similar FEV_1, intra-subject variance showed significant difference between the two groups, suggesting OS may be helpful in detecting CLAD in patients prior to the drop of FEV_1.

Additional research is ongoing to uncover the potential of OS to discern the various CLAD phenotypes including bronchiolitis obliterans syndrome (BOS), restrictive allograft syndrome (RAS), and mixed phenotypes[9].

> *"OS could be combined with other non-invasive biomarkers, such as computer aided quantitative analysis of chest imaging, or molecular signature of mucosal biopsies to provide a cumulative risk with improved sensitivity and predicative value than individual metrics alone"*
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> *-Vasileva et al. 2023*

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Looking for additional information on oscillometry?
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