Functional Respiratory Imaging (FRI) and machine learning to predict organ rejection shortly after lung transplantation

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FRI: A NOVEL BIOMARKER

FUNCTIONAL RESPIRATORY IMAGING

- Functional Respiratory Imaging (FRI)
  - High Resolution CT Thorax (HRCT)
  - Flow simulations (Computational Fluid Dynamics, CFD)

- Regional information
  - Lung structure (HRCT measurements)
  - Lung function (flow simulation)

- Reduction
  - Study sample size
  - Study time
FRI: A NOVEL BIOMARKER

Functional Respiratory Imaging (FRI) has been applied to:

- Asthma
- COPD
- ACOS
- IPF
- PH
- BPD
- SLEEP APNEA
- BOS
- SINUSITIS
FUNCTIONAL RESPIRATORY IMAGING (FRI)
Lung Structures and Zones

Functional Respiratory Imaging Endpoints

Ventilation

- $iVlobe = \text{image-based volume of the lobe in liters}$
- $iVlobe \text{ predicted} = \text{image-based volume of the lobe in %predicted}$
- $iVaw = \text{image-based airway volume}$
- $siVaw = \text{specific image-based airway volume}$
- $iSaw = \text{image-based airway surface area}$
- $iRaw = \text{image-based airway resistance}$

Perfusion and Tissue

Aerosol Deposition
Organ rejection, FRI and Artificial Intelligence
Study Design

- **Study**

41 patients
- 15 BOS developers
- 26 non-BOS developers
- All patients were considered non-BOS patients at baseline (first visit after transplantation) based on conventional clinical measures

205 parameters
- 8 clinical parameters (based on FEV₁ and FVC)
- 197 FRI parameters
PROCESS FOR BOS IDENTIFICATION

Collection of clinical and FRI parameters for all patients

Student t-tests for individual baseline parameters

Artificial Intelligence

BOS PHENOTYPE
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STUDENT T-TEST ON BASELINE DATA

SINGLE PARAMETER PREDICTIONS

• **21 FRI parameters** at FRC are predictors for early stage BOS detection

• **2 FRI parameters** at TLC are predictors for early stage BOS detection

• **No clinical parameters** were able to predict eventual BOS development

• \( p < 0.05 \)
CONCLUSION

Eventual BOS developers have:

- significantly smaller lobe volumes at baseline,
- significantly smaller airway volumes at baseline,
- significantly smaller airway surfaces at baseline,
- significantly higher airway resistances at baseline

Onset of BOS?
Underexpansion of transplanted lung

BOS progression?
Increases in lobe and airway volumes, by a destruction of bronchioli caused by bronchiolitis obliterans
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BOS PHENOTYPE
ARTIFICIAL INTELLIGENCE

MACHINE LEARNING: SUPPORT VECTOR MACHINES

- Machine learning uses retrospective data
  - Significant baseline parameter $X_1$

- BOS development

- non-BOS development

$X_1$
MACHINE LEARNING: SUPPORT VECTOR MACHINES

- Machine learning uses retrospective data
  - Significant baseline parameter $X_2$

- BOS development
- non-BOS development
MACHINE LEARNING: SUPPORT VECTOR MACHINES

- Machine learning uses retrospective data
- Machine learning tries to find the set of significant parameters that separates the classes best

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- Machine learning tries to look for hyperplanes that classify data points into categories with the maximum margin
MACHINE LEARNING: SUPPORT VECTOR MACHINES

• Machine learning uses retrospective data
• Machine learning tries to find the set of significant parameters that separates the classes best
• Machine learning tries to look for hyperplanes that classify data points into categories with the maximum margin
• Once a model is constructed, new patients can be validated and a prediction can be made
MACHINE LEARNING: SUPPORT VECTOR MACHINES

- Validate Model?
  - Exclude one sample (test)
  - Make model with other samples (training)
  - Predict excluded sample
  - Repeat for all samples
  - Accuracy = % correctly predicted samples
  - = Leave One Out Cross Validation
MACHINE LEARNING - RESULTS

3 features (optimized for accuracy)

- **85,0% accuracy**
- **73,3% sensitivity**
- **92,3% specificity**

**BEST PREDICTOR WITH 3 FEATURES**

- **FRC**
- **iRaw of RUL**
- **Central iSaw**
- **TLC**
- **iVlobe of RML**
STUDY LIMITATIONS

- Limited patient sample size
- Single center study
- Retrospective study
- Inclusion of unilateral and bilateral transplants

➢ More studies will be performed to expand database for more robust predictions
STUDY CONCLUSIONS

Functional Respiratory Imaging in BOS

- BOS → heterogeneity in lung structure and function.
- Phenotype patients accurately → disease progression
- Study results:
  - 23 baseline FRI predictors
  - No baseline clinical predictors
  - Accuracy of 85.0% through Support Vector Machines.

- Functional Respiratory Imaging + AI
  - Novel biomarkers
  - Quantification of regional lung structure and function
  - Determine BOS developers in an early stage
ARTIFICIAL INTELLIGENCE, THE FUTURE OF MEDICINE?

FRI

PHENOTYPING

PERSONALIZED HEALTHCARE

PRECISION MEDICINE