Parametric response mapping
Utility of a novel imaging biomarker in pulmonary disease
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Disclosures

• C.J. Galban has a financial interest in the underlying patented University of Michigan technology licensed to Imbio, LLC.
Scope of the problem

• COPD is a heterogeneous disorder affecting 11 million people in the US.

• Components of COPD
  - Emphysema
  - fSAD: Functional small airways disease

• Clinically manifests as any point on the fSAD - emphysema spectrum.

• Bronchiolitis obliterans
  - Important late complication of both hematopoietic stem cell and lung transplantation.
  - Manifesting as obstructive physiology on spirometry and air trapping on High resolution computed tomography (HRCT).
Challenge

• Early identification into the different phenotypes of obstructive airway disease allows early initiation of appropriate treatment.

• HRCT is a proven tool to qualitatively characterize functional small airway disease (fSAD) and emphysema.

• Subtle air trapping/fSAD can be challenging to visualize on HRCT.

• Quantitative imaging of functional small airways disease is not well established.

• **Parametric response mapping** (PRM) enables separation and quantification of underlying emphysema, fSAD, normal lung as a percentage of lung volumes.
What is Parametric response mapping (PRM)

- Quantitative imaging biomarker for the assessment of obstructive lung disease.
- It is a computed tomography (CT) voxel-wise methodology that quantifies normal parenchyma, functional small airway disease (fSAD), emphysema, and parenchymal disease as relative lung volumes.
- It is depicted as easy to follow color coded maps.
  - **Green**: Normal lung parenchyma
  - **Yellow**: Functional small airways disease (fSAD)
  - **Red**: Emphysema
Parametric response mapping - 3 key steps

- **Image acquisition**: Volumetric inspiratory and expiratory scanning.
- **Image processing**: Image co-registration from the inspiratory and expiratory acquisition on a voxel by voxel basis.
- **Voxel classification**: Enables quantitative measurement by depicting normal lung (green) functional small airways disease (yellow) emphysema/parenchymal lung disease (red) as color coded maps and percentages.
**Fig 1**

- **Green**: Normal lung parenchyma
- **Yellow**: Functional small airways disease (fSAD)
- **Red**: Emphysema
Green: Normal lung parenchyma
Yellow: Functional small airways disease (fSAD)
Red: Emphysema

Fig 2: A – Normal, B – Mild COPD, C – Upper lung emphysema, D – Diffuse small airways disease and emphysema
18 yr old with difficult to control asthma, diffuse air trapping (* *) on HRCT.
PRM of the same patient with asthma reveals functional small airways disease predominating in the mid and lower lungs, 33% functional small airways disease.

Fig 3c
58 yr old woman with end stage COPD referred for surgery (lung transplantation versus lung volume reduction surgery - LVRS), HRCT showed diffuse emphysema rendering LVRS less likely.
PRM qualified and quantified mixed disease (emphysema 20% and fSAD 46%) involving the upper and lower lungs thus rendering her unsuitable for LVRS. The fSAD was much more extensive on PRM than was appreciated on HRCT. She was listed for lung transplantation.
52 yr old woman with family history of alpha 1 antitrypsin deficiency, alpha1 antitrypsin :52 (Normal > 80), presenting with severe obstructive defect on lung function. HRCT interpreted as mild air trapping (*) suggesting functional small airways disease and mild emphysema.
PRM revealed significant diffuse functional small airways disease (50%), minimal emphysema (6%). She responded very well clinically to inhaled bronchodilators and smoking cessation therapy. PRM again reveals much more extensive fSAD than on HRCT.
59 yr old woman with severe COPD, HRCT reveals significant lower lung predominant emphysema (#).
PRM reveals diffuse fSAD (43%) with significant lower lung predominant emphysema (34%), patient was deemed unsuitable for LVRS due to the lower lung predominant disease and was listed for lung transplantation. The degree of fSAD on PRM was much more than was appreciated on HCRT.
62 yr old woman post left lung transplantation for emphysema, presenting with worsening shortness of breath. HRCT reveals normal left lung transplant and emphysematous (#)native right lung.
PRM reveals completely normal transplanted left lung with significant mixed disease in the native right lung, thus cause of worsening symptoms is not the transplanted lung but native right lung. The PRM again reveals 32% fSAD which is difficult to appreciate on HRCT.
40 yr old woman with severe COPD, in consideration for LVRS versus lung transplantation. HRCT reveals upper lobe predominant emphysema.
PRM reveals the upper lobe predominant emphysema (26%) and moderate functional small airways disease (39%). Underwent successful LVRS with improvement in lung function post surgery.
51 yr old woman, 6 yrs post allogeneic stem cell transplantation for acute lymphoblastic leukemia presenting with worsening dyspnea and lung function suggestive of an obstructive ventilatory defect. HRCT revealed moderate air trapping (*) on expiratory images suspicious forobliterative bronchiolitis due to chronic graft versus host disease (GVHD).
PRM reveals the presence of functional small airways disease (28%) as the predominant abnormality and confirming CT findings of chronic GVHD. Bronchoscopic biopsy confirmed findings and treatment was commenced for chronic GVHD.
Pearls and Pitfalls

- Needs volumetric inspiratory and volumetric expiratory datasets.
- Has to be a noncontrast acquisition.
- PRM is only as good as the underlying HRCT and cannot compensate for suboptimal expiratory acquisitions.
- The definition of normal, fSAD and emphysema is based on certain hounsfield unit cut offs which can sometimes lead to a miscalculation if the voxel attenuation value is outside the defined cutoffs.
Advantages of PRM

- No additional radiation burden for the patient.
- It is an image post processing technique.
- Easy to understand color coding for qualitative assessment
  - Normal (green)
  - Functional small airways disease (yellow)
  - Emphysema (red)
- Quantitative assessment expressed as percentages.
- Frequently more sensitive at quantification of fSAD than HRCT images alone.
Conclusion

- PRM enables early identification, quantification and treatment of fSAD which is considered a precursor of emphysema.
- PRM also enables early identification and treatment of obliterative bronchiolitis (chronic GVHD) in the context of hematopoietic stem cell (HSCT) and lung transplantation thus improving outcome.
- PRM is an unique quantitative imaging biomarker for the assessment of obstructive airways disease with tremendous potential.
Bibliography


Thank You!

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