Title: Measuring Small Airway (Versus Large Airway) Inflammation and Hyper-responsiveness using MRI in Severe Asthmatics

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Structured Abstract:

Introduction: Pulmonary functional magnetic resonance imaging (MRI) identifies the exact location of functional abnormalities within the asthmatic lung. MRI ventilation defects have been shown to be spatially-related to large [1] and small [2] airway obstruction. Such ventilation defects may serve as important targets for novel asthma therapies, but the relative contribution of large versus small airway abnormalities to ventilation heterogeneity has never been determined. Thus, our objective was to develop image processing methods to differentiate the contributions of large and small airways to ventilation abnormalities in severe asthmatics. This is important because abnormalities in the small versus large airways will necessitate the clinical use of different therapies.

Methods: Airway trees were segmented from thoracic computed tomography (CT) images up to the 7th-8th generation using PW2.0 (VIDA, USA). Segmented airways were considered large or central airways and those that could not be segmented due to image spatial resolution constraints (diameter<2mm) were assumed to be small or peripheral airways. 3D airway tree volumes were non-rigidly co-registered to MRI static ventilation using the modality-independent neighbourhood descriptor (MIND) method [3] in MATLAB R2015a (Mathworks, USA) and used to stratify the functional image space by proximity to the large or small airways. Using this method, we evaluated five asthmatics as a proof-of-concept demonstration, who underwent hyperpolarized 3He MRI and CT. MRI was acquired using a 3.0T MR750 system (GE Healthcare, USA) as previously described [4], and CT was acquired within ten minutes after MRI using a 64-slice Lightspeed VCT system (GEHC) volume-matched to MRI. MR images were segmented to generate whole-lung and respective large and small airway volume ventilation defect percent (VDP), which is the ventilation defect volume normalized to the thoracic cavity volume [5].

Results: For subjects with ventilation defects (whole-lung VDP≥3%, n=4), small-airways VDP was significantly larger than large airway VDP. For the single asthmatic without ventilation defects, small and large airway VDP were not significantly different.

Discussion: In this proof-of-concept demonstration, we classified 3He MRI ventilation based on the spatial relationship to large or small airways using individual patient airway trees, and quantified VDP based on these spatial relationships. Importantly, this approach is patient-specific and based on individual airway trees. The relative and independent contributions to ventilation heterogeneity from the large and small airways are important to determine for individualized treatment decisions and to evaluate efficacy of new treatments.

References: [1] Svenningsen et al. Thorax 2014. [2] Fain et al. Acad Radiol 2008. [3] Heinrich MP et al. MedIA 2012. [4] Parraga et al. Invest Radiol 2007. [5] Kirby et al. Acad Radiol 2012.