Quantitative Analysis of pulmonary inflammation after endobronchial allergen challenge using T1-mapping MRI

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Target audience: Radiologists and pneumologists with interest in imaging of allergic pulmonary reactions as well as physicists dedicated to develop clinical applications for pulmonary magnetic resonance imaging.

Purpose: Endobronchial allergen challenge is an established method for the evaluation of new anti-allergic drugs. Today the standard readout parameter is the concentration of eosinophilic cells in the bronchoalveolar lavage fluid, requiring repeated bronchoscopies that are a substantial burden for the volunteers. Therefore the purpose of this study was to establish and evaluate a non-invasive method for monitoring pulmonary inflammatory reaction using oxygen enhanced T1-mapping MRI.

Methods: 9 volunteers with allergic asthma and 4 healthy volunteers participated in this study. The protocol followed established procedures [1] for endobronchial allergen challenge: First MRI scan at baseline (0h) followed by the first bronchoalveolar lavage and the endobronchial allergen challenge in segments 4/5 in the left and right lung with different allergen concentrations. 6h hours after the challenge the second MRI scan was performed. 24h after challenge the last MRI scan and afterwards the second bronchoscopy and alveolar lavage were completed. For MRI scans an Inversion Recovery SnapShot fast low-angle shot (FLASH) sequence (T_E: 0.8ms, T_R: 3.0ms, FA: 8°, 32 inv. times [100ms-6000ms], matrix size: 128x64, FOV: 50cm x 50cm, slice thickness 15mm, gap 7.5mm) on a 1.5T MRI with an 8 channel torso phased array coil was used [2] . Images for one slice were acquired in single breath hold. The volunteers were instructed to breath normally and stop breathing at the end of a normal inspiration. 3-5 Slices covering the challenged lung segments were acquired. Images were obtained while breathing room air and while breathing 100% oxygen. Registration of the magnitude images obtained under 100% oxygen onto the room air images was performed with a non-rigid registration algorithm and T1 maps were calculated with a self-developed MATLAB script: Segmentation of both lungs separately, visually excluding the great vessels and calculation of T1 mean under room air, T1 mean under 100% oxygen as well as the oxygen transfer function (OTF) [3] with MATLAB. As a threshold for detection of inflamed tissue we defined the mean T1 value at the baseline scan + 2SD. The volume of lung tissue over this threshold was calculated on all three MRI scans. In this volume and in corresponding areas in the healthy volunteers oxygen transfer function was calculated. Concentration of eosinophils in bronchoalveolar lavage fluid served as reference. Statistical analysis was performed using non-parametric Kruskall-Wallis and Wilcoxon test as well as Spearman correlation. Results are given as median and 25% - 75% quartile.

Results: Volume over threshold differed significantly between all three time points for the asthmatic volunteers (p=0.04). After a baseline volume of 11ml [9;19] an increase to 109 ml [51;164] (p<0,0001) and an incomplete decrease to 46ml [22;104] (compared to baseline p=0.0001) could be observed. For the healthy volunteers volume changed from 12ml [3;18] to 62ml [9;153] (p=0.02) and back to 15ml [3;24] (compared to baseline p=0.38).

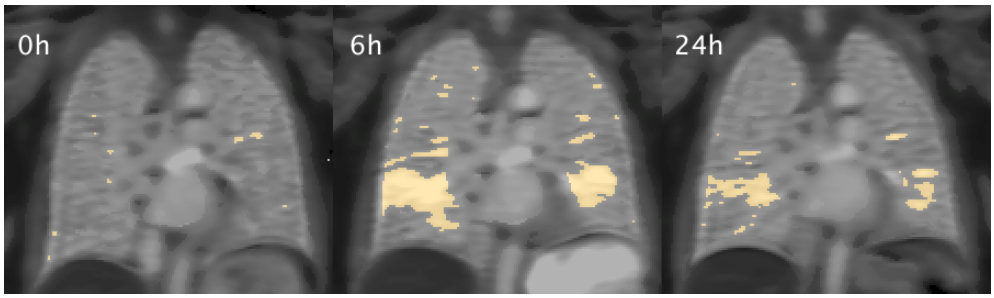

Figure 1: T1-mapping of a volunteer with allergic asthma before (0h), 6h and 24h after endobronchial allergen challenge in segments 4/5 in both lungs. Marked are values over a threshold, serving for detection of inflamed tissue.

Equally the OTF in the inflamed areas differed significantly for allergic volunteers (p=0.04), while there was no difference for the control group (p=0.27). For the allergic group there was a decrease in the OTF from $9.8x10^{-4}$ s^{-1} $\%O2^{-1}$ to $6.4x10^{-4}$ s^{-1} $\%O2^{-1}$ at 6h (p=0.02) and again an increase to $8.0x10^{-4}$ s^{-1} $\%O2^{-1}$ at 24h. In the total study group there was a significant correlation between the concentration of eosinophilic cells in the bronchoalveolar lavage fluid and the volume over threshold at 24h (r=0,68; p=0.0001) as well as with the OTF at 6h (r=-0.66; p=0.0002).

Discussion: The data suggest that the evaluated MRI-derived parameters OTF and Volume over threshold can monitor noninvasively local allergen response in the lung tissue of volunteers with asthma and healthy controls. Asthmatic subjects show stronger decrease in OTF 6h after bronchoalveolar challenge and also a prolonged increase in T1 values in the challenged regions compared to healthy volunteers. Furthermore these values show a correlation with the established marker for airway inflammation after endobronchial challenge, the concentration of eosinophilic cells. Therefore these MRI-based non-invasive measurements may serve as a replacement for repeated bronchoscopies in future trials.

References:

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