Bronchodilatation Effect on Lung Function of Asthma Patients Measured by Static and Dynamic 3He MRI: First Results of Clinical Trial
Maxim Terekhov1, Ursula Wolf2, Klaus K Gast2, Christian Hoffmann2, Nina Bojadzic2, Sergei Karpuk3, Christian Mrozik3, Christoph Düber2, and Laura Maria Schreiber1
1Section of Medical Physics, Department of Radiology, Johannes Gutenberg University Medical Center Mainz, Mainz, Germany, 2Department of Radiology, Johannes Gutenberg University Medical Center Mainz, Mainz, Germany, 3Institute of Physics, Johannes Gutenberg University Mainz, Mainz, Germany

Motivation
Hyperpolarized 3He-MRI is known to be efficient tool to visualize and quantify Static (SV) and Dynamic Ventilation (DV) of lungs. The spatial and temporal information on regional gas distribution in lungs are available. This makes both methods particularly attractive for the diagnostics of patients with obstructive lung disease, e.g. asthma and COPD. To characterize gas distribution and delivery in the lungs a set of parameters evaluated either directly from the 3He-MR-images (SV) or calculated by analysis of the 3He signal-time profile (DV) [1] are used. However, the relevance of these parameters for the lung physiology, as well as, statistical significance of its changes under different factors influencing the respiratory function of patient is still not established firmly. Therefore, finding out how the changes these parameters correlate with clinically proved tests of lung function is a question of great importance for the diagnostic relevance of 3He-MRI results. In the present work measurements of static and dynamic lung ventilation with HP-3He-MRI were performed on bronchial asthma patients before and after bronchodilatation (BD). The particular aim was to find out if the BD-effect can be detected using parameters obtained with 3He-MRI and to correlate the variation of these parameters with the changes in the key values of the pulmonary function tests (PFT).

Materials and Method
In an open monocentric clinical trial performed after approval of the local Ethics Committee 8 (of 12) patients with confirmed bronchial asthma were examined in the first visit. 4 patients finished the study with the 2nd visit (interval 1 year). Each visit comprised two 3He-MRI as well as PFT before and after BD (250µg Salbutamol). The MRI measurements were performed on a 1.5T scanner (Avanto, Siemens, Germany) using dual-tune 3He/19F birdcage (Rapid Biomedical). The HP-3He (polarization level p=70±2%) was provided by centralized large scale polarization, delivery and recycling process approved by local Ethic Committee [2]. The 3He:N2 mixtures (200:300ml for SV and 200:800ml for DV) were administered using a Tedlar bag. The SV images were 14 coronal slices (10mm thickness) acquired using image matrix 128x81 at FOV=400mm. The DV 3He-MR-images series were coronal 2D-projections (128x64 at 400mm FOV) continuously acquired during patient inhalation of 3He:N2 mixture. This yields 3He-signal-time curve S_p(t) recorded at temporal resolution of 7 images per second. The S_p(t) was analyzed on a pixel basis using dedicated Matlab scripts. The evaluated DV parameters were: (1) rise time (RT), denoting an interval required for S_p(t) to rise from 10% to 90% of maximum value S_p,max; (2) the delivery time TD determined as (S_p(TD)=0.9&S_p,max); (3) maximal flow value FM = max(|dS_p(t)/dt|). For the SV-images the amount of ventilation defects (VD) were counted in each slice and percentage of non-ventilated lung volume (%nVV) was calculated respectively. For the statistical analysis the mean values of the parameters were used. The statistical tests were performed using Matlab Statistical toolbox and SPSS.

Results and Discussion
Figure 1 demonstrates that the SV-measurements before (Pre-) after (Post-) BD allow for detecting substantial increase of %nVV as the result of medication. The statistical analysis (Wilcoxon test) confirms the hypothesis %nVV(Pre-BD)>%nVV(Post-BD) at α=0.05 significance level. Additionally, the hypothesis for FEV1(pre-BD)>FEV1(post-BD) is confirmed both t-test and Wilcoxon test (at α=0.05). The results of DV-measurement show an increased mean 3He signal rise time and delivery time after BD. The highest significance level (unpaired t-test, α =0.01) was found for the hypothesis RT increased post-BD. The increasing of mean DT value post-BD is less significant and can be confirmed statistically (paired t-test) only at α =0.2 level. The FM values before and after BD show the largest variance among all calculated DV parameters and its changing (in both direction) post-BD cannot be statistically proved at the significance level better than α=0.4 using actual amount of measured patients data.

Conclusion
Although the trial is not yet finished, several trends can be observed. For the patient data analyzed we confirmed that both SV and DV 3He-MRI allow for detecting statistically significant differences of lung ventilation before and after bronchodilatation. For SV-images the expectable decrease of the non-ventilated volume was observed. The increase of the DV rise-up time is especially remarkable in the region of the large airways (Fig 2a) for patients with significant initial %nVV. This observation may be explained by longer and deeper inspiration (increased FIV1 and IC) caused by BD. As a consequence, gas inflow impairment is decreased which in turn reduces the absolute maximal flow peaks (FM) within a RT-period. The statistical significance of the later findings should be confirmed in course of the Clinical Study competition.

References:
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