A Preliminary Variability Study Of Hyperpolarized 3He Specific Ventilation In Human

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PURPOSE: Hyperpolarized gas MRI represents one of the few noninvasive methods for assessment of lung function in a regional manner by means of measuring the specific ventilation in human. This work presents a preliminary short- and long-term reproducibility study of the specific ventilation SV-MRI and compares the repeatability of SV to that of Pulmonary Function Test (PFT) in human subjects with and without respiratory symptoms.

METHODS: Six human subjects underwent repeated SV imaging followed by a pulmonary function test (PFT). One healthy nonsmoker (HN), one asymptomatic smoker (AS) and four COPD subjects entered the study so far and the recruitment is still in progress. The short-term studies were performed back-to-back (~10min) and follow-up studies after one year. A normoxic mixture of 3He:N2:O2 (3:1:1) based on subjects' total lung capacity was administered in a multi-breath sequence, as shown in Figure 1, and images acquired during six end-inspiratory short-breath-holds (~1s) and a longer 12-sec end-inspiratory breath-hold. HP gas mixture was administered through a passive patient-driven delivery device described earlier [2] and is shown in Figure 2, which regulated the inspired gas FiO2 at ~ 21% and the prescribed tidal volume (I:E~3:4, ~10 BPM). End-inspiratory slice-selective images were acquired covering the entire lung volume in < 2s on a 1.5-T Sonata MRI scanner (Siemens Healthcare) using an 8-channel phase array chest coil (Stark Contrast) and with parameters: Slice Thickness (ST) = 20–25 mm, planar resolution = 6.25×6.25 mm2, TR/TE = 6.7/3.2 ms, FOV = 30×40 cm2, flip angle ~ 5°, slice gap = 20% ST. This process was repeated six times to derive signal buildup in the airways, which was then used to calculate the fractional ventilation distribution according to [2]. At the end of the sequence the subjects were instructed to hold their breath for 12s during which a series of consecutive images were acquired to estimate the flip angle distribution. Accelerated imaging was performed using GRAPPA with an undersampling factor of four and 16 auto-correlating reference lines. The whole-lung SV averages and standard deviations (MSV±DSV) are then computed from a Gaussian fit to the whole-lung distribution histograms. Test-retest Pearson correlation was used to analyze the regional reproducibility. The coefficient of variance (CV) was also calculated for assessing the global variability between repeated measurements.

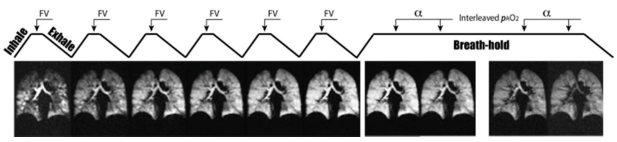

Figure 1- The multi-breath regime for specific ventilation imaging.

Figure 2- The gas delivery device.

RESULTS: Figure 3 shows the middle slice SV-maps from the repeated measurements for two representative subjects along with pixel-by-pixel test-retest correlation. Subject's demographics, repeated PFT and imaging results are presented in Table 1. The short-term studies were performed back-to-back (~10min) and follow-up studies after one year. In short-term studies, only one PFT was performed. The overall short-term repeatability was assumed to dominantly show the technical variability, since they are less affected by changes in physiology. The average global repeatability was CV=3.40±2.76% and the average regional test-retest correlations was rp=0.86±0.01. PFTs for all subjects declined in follow-up studies as listed in Table 2. SV variability is also shown in Table 2. The regional reproducibility test-retest correlations were rp=0.65±0.23. The COPD subjects with high reduction in lung function had the highest long-term SV variability. The only AS in the study showed less variability than COPD subjects both in long-term PFT and SV-MRI.

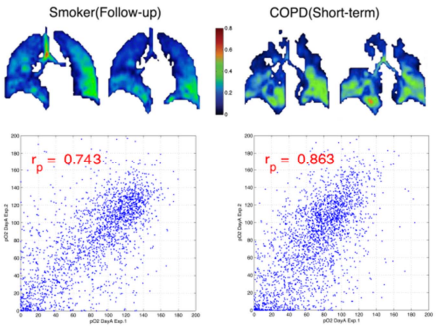

Figure 3- Two representative repeated SV maps and test-retest correlation plots for the middle coronal slices (Follow-up study for Smoker on left, and short-term regional repeatability for COPD1)

Table 1- Repeated PFT and Imaging Results and the Global and Regional Repeatability of SV

Subjects	Repeat	Smoking Hist. [Pack-yrs]	Age [yrs]	BMI [Kg/m^2]	FEV_1/FVC [%]	$\%FEV_1$ [%]	DL_{CO} [ml/min/mmHg]	TLC [L]	RV [L]	SV [0-1]	CV_{SV} [%]	r_p
Healthy*		0	28	24.3	-	-	-	-	-	0.370 ± 0.072 0.347 ± 0.076	4.54	0.878
COPD 1	Short-term†	24	52	25.3	59	85	15.93	8.1	2.68	0.367 ± 0.170 0.369 ± 0.169	0.25	0.863
COPD 2		51	67	20.4	56	85	23.23	8.3	3.36	0.526 ± 0.184 0.488 ± 0.210	5.41	0.853
Smoker 1		21 22	48 49	27.4 26.7	70 69	118 114	25.93 23.95	7.9 8.1	1.98 1.88	0.342 ± 0.147 0.308 ± 0.192	7.41	0.743
COPD 2		51 52.5	67 68	20.4 19.5	56 49	85 67	23.23 21.64	8.31 8.4	3.36 3.69	0.488 ± 0.210 0.266 ± 0.129	41.71	0.595
COPD 3	Follow-up†	20	44	34.1 32.6	49 46	58 51	14.16 12.24	6.4 5.7	2.84 2.54	0.534 ± 0.121 0.370 ± 0.12	25.66	0.792
COPD 4		36	62	31.3 33.5	61 55	63 57	23.2 18.87	6.3 5.1	3.36 1.46	0.489 ± 0.343 0.343 ± 0.190	24.96	0.351

* PFT was not performed in the healthy subject
† Short-term studies repeated in 8±4 min and follow-up studeis in 358±31 days

CONCLUSION: High global and regional repeatability of back-to-back imaging method to measure SV in Healthy and COPD subjects shows the reasonable technical variability of this measurement and indicates low physiologic changes in specific ventilation in minute's time-scale. The differences between the short- and long-term regional and global repeatability of SV for the COPD subjects demonstrate the high variability in the latter can be explained by true physiological alterations, since the minute measurements are minimally affected by physiological variability. The observed decline in the yearly results of PFT (in COPD subjects) proves the physiologic nature of the observed variability in COPD subjects. The satisfactory repeatability of imaging technique and its greater variance over time suggests that it may be more sensitive to changes over time than routine PFTs.

Table 2- Follow-up Statistic For PFT and Imaged SV

	FEV_1/FVC [% Decline]	$\%FEV_1$ [% Decline]	DL_{CO} [% Decline]	TLC [% Decline]	RV [% Decline]	SV [% Decline]
Smoker 1	-1.43	-3.39	-7.64	-2.14	5.05	-9.95
COPD2	-12.50	-21.18	-6.84	-1.56	-9.82	-45.55
COPD3	-6.12	-12.07	-13.56	10.05	10.56	-30.71
COPD4	-9.84	-9.52	-18.77	18.86	56.55	-30.00
CV*	**4.67**	**5.40**	**5.90**	**9.05**	**33.78**	**17.00**

* CV is calculated SD(Absolute Decline)/Average(Baseline)

REFERENCES: **[1]** Emami K et al., Proc 20th ISMRM 2012; [2] Emami K et al., Magn Reson Med. 2010 Jan; 63(1):137-50;