Quantitative Assessment of Lung Volume Reduction Surgery Effectiveness in Improving Functional Pulmonary Performance of Emphysematous Subjects - A Small Animal Model

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INTRODUCTION: LVRS is a surgical procedure that has recently been shown to improve dyspnea, quality of life, and survival in selected patients with severe emphysema. Patient selection of has been a challenge and the exact mechanism by which LVRS improves lung function has yet to be determined. In order to help address these issues we performed a longitudinal study elucidating changes in important parameters of lung function and structure of emphysematous rats induced by LVRS.

METHODS: All experiments were conducted in accordance to an IACUC approved protocol. In order to quantify the structural and functional effectiveness of LVRS treatment on patients with severe COPD, hyperpolarized helium-3 MRI was performed on a healthy and a severely emphysematous pre– and post–LVRS. Emphysema was induced in a 450 g male Sprague-Dawley rat by a single intratracheal instillation of 25U/100g of porcine pancreatic. The healthy cohort, with similar physiological conditions was kept in same environment. Both cohorts were imaged after 10 months. One week after imaging all rats went under LVRS: they were anesthetized, intubated, and ventilated (CWE Inc, Ardmore, PA) as they underwent median sternotomies. The upper lobes of the lungs were resected and the stumps were ligated. IV catheters were placed in each hemithorax at a –2 cm-H_2O suction until extubation. 10 days after the surgery, rats were imaged for a second time. During imaging session, rats were intubated using a 14-gauge angiocatheter and induced with xylazine, ketamine anesthesia, paralyzed with pancuronium, and ventilated using an MRI compatible ventilator (GE Healthcare, Durham, NC), while vital signs where monitored. The mechanical ventilation parameters were as follows: tidal volume (TV)= 3 ml (2.5 ml post-LVRS), respiratory rate (RR)= 50 BPM, and the inspiration/expiration time ratio (I%)= 50%. Imaging was performed on a small-bore 4.7-T animal magnet (Varian Inc., Palo Alto, CA) using a 12-leg birdcage coil tuned to ^{3}He frequency of 152.95 MHz. The hyperpolarized (HP) ^{3}He was generated via the spin-exchange optical pumping method using a commercial polarizer (GE Healthcare, Durham, NC). The helium images were obtained during a breath-hold using a multi-slice gradient echo (GEMS) imaging pulse sequence with the following parameters: FOV= 5 cm x 5 cm, number of slices (NS)= 4~5, slice thickness (ST)= 4 mm, inter-slice gap= 1 mm, flip angle= 10°, matrix size= 64 x 64 pixels, TR/TE= 4/2 ms (15/2 for fractional ventilation). Flip angle map was generated using a series of images with no inter-scan time delay. Fractional ventilation (r) was measured using incremental build-up of hyperpolarized helium signal as described earlier [1] with number of HP breaths ranging from 1 to 20, with 25 normal breaths in between each step. Static compliance (c) maps were then generated by normalizing the regional ventilation maps [2] by the measured peak inspiration pressure (PIP) during the breath-hold.

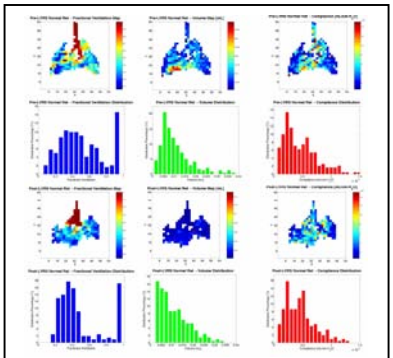

Figure 1. From left to right, regional fractional ventilation, lung volume, and compliance- for a sample normal rat. Respective histograms are shown below the corresponding images. Top two row represent pre surgery data, bottom two rows post LVRS data.

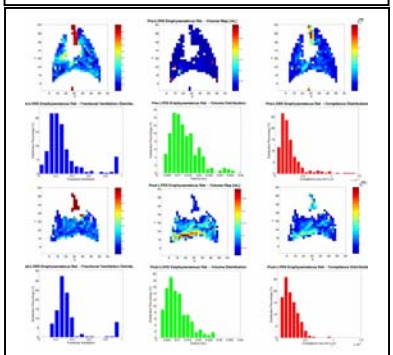

Figure 2. Functional data pre and post LVRS for a sample emphysematous rat. The order of figure is as above.

RESULTS AND DISCUSSION: Maps of fraction ventilation, compliance, and regional volume and their corresponding histograms are shown in Figures 1 and 2 for both healthy and emphysematous subjects, pre- and post-LVRS. The slices are shown containing the trachea. Similar measurements were performed at a multi-slice level to embrace the entire lung (not shown). Table below summarizes mean values of measured quantities for pre- and post-conditions. Fractional ventilation and compliance show minor variations in the normal rat before and after surgery, while the changes can be considered statistically the same. The reduction in volume is also evident in fractional volume (tidal volume) present in this slice. The regional ventilation distribution however has become narrower. The emphysematous subject on the other hand shows improvement in fractional ventilation and compliance, increase and decrease thereof respectively. These quantities can be used as measures in comparing such operations in various diseased. Narrowing of regional ventilation is also evident in the emphysematous animal and fractional volume depicts the volume reduction effect.

Type	*Weight (g)*	*r*	*c (ml/cm-H2O)*	*dv (ml)*	*PIP (cm-H2O)*
Pre-LVRS Normal	580	0.515	4.85E-04	1.16	10
Post-LVRS Normal	480	0.49	4.94E-04	1.03	10
Pre-LVRS Emphysema	550	0.286	2.69E-04	1.08	13.5
Post-LVRS Emphysema	450	0.354	2.40E-04	0.74	13

CONCLUSION: Quantitative assessment of LVRS effectiveness in improving functional pulmonary performance of COPD patients is an important tool for the surgeon to evaluate the risk and benefit of the operation as well as proper selection of patients. Preliminary results suggest that the combined pulmonary measurement of fractional ventilation and compliance at a regional level can provide a unique set of parameters to assess the lung function in COPD patients as well as for screening healthy patients. Moreover these functional and mechanical measurements show a good potential in reflecting changes induced by surgery in the operated lung performance. However performing this study on a larger group of subjects and in a longitudinal design at different time points will be necessary to indicate reproducibility and robustness of these measurements.

References: [1] Z. Z. Spector, *et.al.* Magn. Reson. Med. 53 (2005), 1341-1346. [2] K. Emami, *et al.* ISMRM 13th SM 2005.