Quantitative Assessment of Lung Volume Reduction Surgery Effect in a Small Animal Model Using Hyperpolarized Gas MRI

J. B. Shrager[1], K. Emami[2], J. Zhu[1], M. C. Fischer[2], V. Vahdat[2], M. Ishii[3], S. Kadlecek[2], R. R. Rizi[2]

[1]Department of Surgery, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [3]Department of Otolaryngology, Johns Hopkins University, Baltimore, MD, United States

Introduction: Lung Volume Reduction Surgery (LVRS) is a surgical procedure that has recently been proven to improve dyspnea, quality of life, and survival in selected patients with severe emphysema. ^{3}He MRI has been proposed as a means of elucidating the physiological basis of these improvements and ultimately aiding in selection of LVRS candidates. We chose to evaluate regional fractional ventilation (r) as a quantitative index, which we have previously shown to be reduced in emphysematous rats.

Method: Experiments were conducted in accordance to an IACUC approved protocol. Emphysema was induced in four 3-month old (~400±25g) male Sprague-Dawley rats by a single intratracheal instillation of 25u/100g of porcine pancreatic elastase. LVRS was then performed on two of these rats 3 months following emphysema induction. The animals were anesthetized and intubated with a 14-gauge, nonocclusive IV catheter. While ventilated with a rodent ventilator (CWE Inc, Ardmore, PA), the rats underwent median sternotomies. The upper lobe on the right and approximately the upper one third of the left lung were resected, and the stumps were ligated. IV catheters were placed into each hemithorax and left at -2 cm-H2O suction until extubation. One of these animals was selected for imaging 4 weeks after LVRS. The animal's pulmonary parameters (tidal volume (TV), respiratory rate (RR) and inspiration time ratio (I%) were measured on an unrestrained plethysmographic measurement system (Buxco Electronics, Wilmington, NC) on the same day of imaging. These parameters were then used to normalize the mechanical ventilation parameters. The rat being imaged was intubated with a 14-gauge angiocatheter and maintained on IP xylazine and ketamine anesthesia, paralyzed with pancuronium, and ventilated using an MRI compatible small animal ventilator (Amersham Health, Durham, NC). Imaging was performed on a small-bore 4.7 T animal magnet (Varian Medical Systems, Palo Alto, CA) using a 12-leg birdcage coil tuned to 3He frequency of 152.95 MHz. The hyperpolarized 3He was generated via the spin-exchange optical pumping method with the use of a commercial polarizer (Amersham Health, Durham, NC). Fractional ventilation was determined using the method introduced by Deninger, et al [1]. The helium images were obtained using the following imaging parameters: FOV= 5 cm x 5 cm, slice thickness (ST)= 4 mm, flip angle= 10 degrees, matrix size= 128 x 128 pixels, TR= 6.6 ms and TE= 3.3 ms. The presence and extent of emphysema in all rats was confirmed pathologically. The results obtained were compared to normal rats and non-operated emphysematous rats.

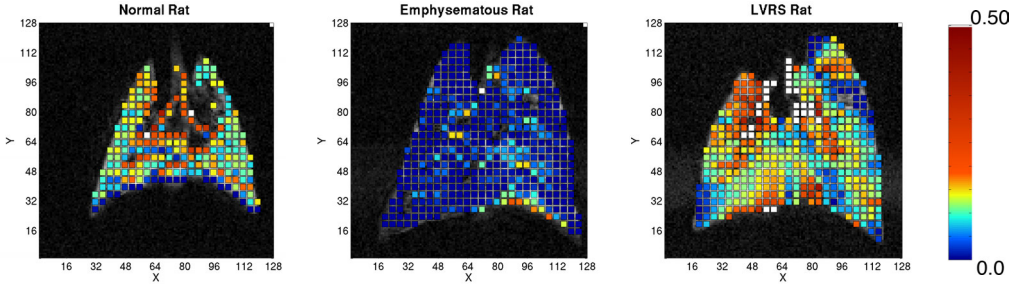

Figure 1. Regional ventilation distribution Mmap in **A.** Normal Rat, **B.** Emphysematous Rat and **C.** LVRS Rat. Values above 0.5 are shown in white.

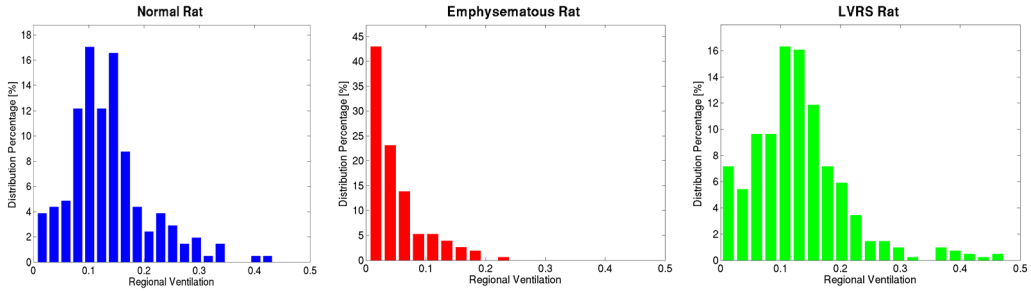

Figure 2. Regional Ventilation Frequency Distribution Curves in **A.** Normal Rat (Blue), **B.** Emphysematous Rat (Red) and **C.** LVRS Rat (Green).

Results and Discussion: Typical regional ventilation maps superimposed on the MR images for a normal, emphysematous, and LVRS-treated rat are shown in Fig 1. The corresponding frequency distributions of this quantity for the three subjects are shown in Fig 2. The analysis is limited to ventilation (r) values of less than 0.5 to validate comparison among various slices and subjects [2]. It is evident that the emphysematous lung (Fig 1.B) exhibits a much lower regional ventilation distribution throughout the lung than the normal lung (Fig 1.A). Also note the relative larger size of the emphysematous lungs compared to that of the normal lung. The LVRS lung (Fig 1.C) distribution of regional ventilation is much more similar to the normal lung. The histograms in Fig 2 reveal the resemblance between the normal and LVRS lungs. The mean ventilation value in emphysematous lung is markedly less than that of the other subjects in the group.

Conclusion: Although additional animals will need to be imaged after LVRS to confirm this finding, this preliminary data suggests that LVRS restores more normal fractional ventilation within the lung in this rat model of emphysema and LVRS.

Acknowledgments: This work was supported by NIH grants RO1-HL64741, RO1-HL77241-01, and P41-RR02305.

[1] Deninger, A.J., et al., *Quantitative measurement of regional lung ventilation using ^{3}He MRI.* Magnetic Resonance in Medicine, 2002. **48**(2): p. 223-232.
[2] Spector, Z.Z., et al., *A small animal model of regional alveolar ventilation using HP ^{3}He MRI.* Academic Radiology, In press.