Measuring the Progression of Emphysema in a Canine Model with ^{3}He Diffusion MRI

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Introduction

Hyperpolarized ^{3}He MRI is becoming known as a new investigative tool in the measurement of emphysema in lungs. Short length (ADC, or D_{msec}) and long length (D_{sec}) diffusion measurements by hyperpolarized ^{3}He gas MRI have been shown to increase in emphysematous lungs [1-4], and there is a correlation to histological and other radiological measures of disease [5,6]. To date, we know of no study which evaluates the changes in ^{3}He MRI diffusivities with the progression of emphysematous lung disease. This study sets out to assess the changes in the ^{3}He MRI diffusivity with the progressive development and increasing severity of emphysema in a canine model of panacinar emphysema. A comparison of the ^{3}He MRI diffusivity to histological measures of disease will further validate the measurements.

Materials and Methods

Three mongrel dogs (mean mass 22 kg) were utilized for the study. These three dogs were given unilateral panacinar-like emphysema in the right lung only using a lavage technique [7]. In brief, the entire right lung was lavaged with porcine pancreatic elastase using a double-lumen endotracheal tube while the dog was under general anesthesia. The process was repeated approximately monthly for a total of three treatments. Two of the dogs were imaged before the first and approximately four weeks after each lavage. Due to scheduling and equipment problems, the third dog was imaged only after the third lavage. We note that since the left lung was untreated, it served as a control during each imaging session. To show emphysematous progression, the average ADC in the right lung and in regions of highest diffusivity (> 40 pixels) after each lavage are presented in the Table.

350-mL doses of hyperpolarized ^{3}He gas (35-50% polarization) were prepared using a home-built apparatus and a commercial polarizer (G.E.). Each was mixed with 200-400 mL of N_2 for imaging at full inspiration. A Helmholtz pair operating at 63.63 MHz (^{1}H) and 48.47 MHz (^{3}He) was used with a Siemens Vision 1.5 T whole-body imager for obtaining 25 transverse, diffusion-weighted, 10-mm images (b = 1.38 s/cm^2) using FLASH (5 x 5 mm).

After sacrifice, the lungs were frozen at constant volume in cold N_2 vapor, sliced into transverse sections, and sampled with a cork-borer for histological measurements of emphysema, with 15-30 samples per lung. Later the samples were fixed in cold alcohol, warmed, and processed into paraffin. The ratio of surface area to volume (SA/V) was measured in a 10-μm slice of each section using a variation of the multipurpose test system proposed by Weibel [8].

Results and Discussion

MR Measurements indicate a progressive increase of the ^{3}He ADC in the lavaged lungs, compared to control (left lungs). In addition, selected regions of interest show marked progression after each lavage in both dogs that were monitored at multiple timepoints (see Table). ADC increased by an average of 90% in the three right lungs after three lavages. Stereological measurements of the ratio of surface area to volume clearly indicate the emphysema (see Figure) after sacrifice. Notably, histological slides (which sample only a small portion of the 2-cm section) hint that ^{3}He ADC may be sensitive to small, emphysematous lesions (1 to 5 mm) that are notoriously difficult to quantify by CT (see microscope images in Figure).

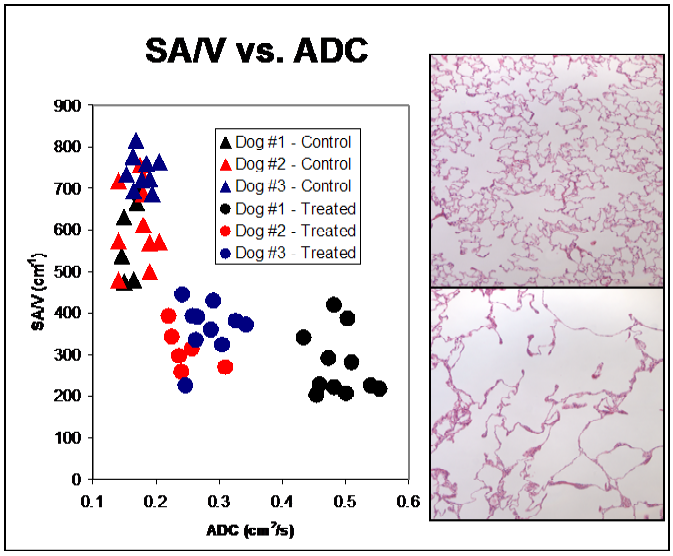

Figure: Graph comparing histologically-derived SA/V (ratio of surface area to volume) to ^{3}He ADC; data points are slice-averages for both measurements. These stereological measurements indicate tissue destruction and validate the diffusivity as a measure of emphysema in this model; both SA/V and ^{3}He ADC clearly separate healthy from emphysematous lung. Images at right (healthy and emphysematous at top and bottom,respectively) are captured under a microscope at 10x magnification and demonstrate small, emphysematous lesions on the order of 1-2 mm. The slides are estimated to be 3-4 mm on a side.

Table	ADC	ADC	ADC	SA/V	SA/V
Dog #1	control	treated	R.O.I.	control	treated
no lavage	0.178	0.177	0.181		
lavage 1	0.164	0.281	0.292		
lavage 2	0.158	0.388	0.369		
lavage 3	0.167	0.455	0.642	580	272
Dog #2					
lavage 3	0.159	0.294	0.625	631	300
Dog #3					
no lavage	0.189	0.190	0.191		
lavage 1	0.179	0.235	0.298		
lavage 2	0.183	0.239	0.388		
lavage 3	0.193	0.258	0.430	735	374

R.O.I. = most affected region of right lung (> 40 voxels)

Table: ^{3}He ADC after each lavage and ratio of surface area to volume after sacrifice in control (left) and emphysematous (right) lungs. ROI's were chosen by visual inspection at histology and MR.

Conclusions

^{3}He MRI can be used to monitor the progression of emphysema; histological examination validates the measurements. This small study helps demonstrate the validity of ^{3}He diffusion MRI as a tool for longitudinal studies that can be used to monitor the effects of possible new therapeutic agents on the cessation of emphysematous progression.

Acknowledgments

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References

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