

Using Hyperpolarized ^3He MRI to Evaluate Therapeutics in Cystic Fibrosis Patients

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Introduction:

Cystic fibrosis (CF) is a genetic disease impairing chloride permeability in exocrine epithelial cells in the lungs, sweat glands, and digestive system in affected individuals. The impaired chloride transport results in thick, viscous mucus, which causes congestion in the lungs and results in frequent lung infections. Over time, the congestion and infection lead to structural lung damage and progressive loss of pulmonary function. A number of treatment options have been developed for CF, including medicines that dilate airways, medicines that make mucous less viscous, and antibiotics that treat resulting infections. Assessment of the efficacy of therapeutics has been limited, however, by limitations in existing tests of lung function. In this study, we tested the efficacy of using hyperpolarized noble gas MRI to assess the effectiveness of intravenous antibiotics in combination with hypertonic saline as a therapy for improving pulmonary function in patients with CF.

Materials and Methods:

The HIPAA-compliant research protocol in this study was approved by the local Institutional Review Board. Informed consent was obtained from all recruited subjects. Data were obtained from three patients with cystic fibrosis undergoing a two-week, in-patient treatment. The treatment consisted of daily administration of intravenous tobramycin and a beta-lactam antibiotic, inhalation of 4 ml of 7% hypertonic saline bid, inhalation of 2.5 mg of recombinant human DNase (rhDNase) daily, and chest physiotherapy t.i.d. HP ^3He static ventilation MRI scans were performed on a Philips 3.0T Achieva MRI using a flexible wrap-around ^3He RF coil (Clinical MR Solutions) with a Fast Gradient Echo pulse sequence acquiring coronal multi-slice images with interleaved data acquisition and the following parameters: 46 cm FOV, 128x64 matrix, 15 mm slice thickness, TR/TE 120ms/1.5ms. For each scan, 1 liter of an approximately 33% HP ^3He - 67% N_2 mixture was administered for the subject to inhale. The ventilation volume of each slice was calculated using a semiautomatic segmentation algorithm comprised of the following five steps: (1) statistical noise subtraction, (2) segmentation refinement, (3) automated trachea removal, (4) smoothing and artifact removal, and (5) voxel summation. Ventilation volumes for each slice were summed to determine the ventilation volume for the entire lung. FEV₁ and FVC were measured daily during the treatment regimen.

Results and Discussion:

Figure 1 shows the center hyperpolarized ^3He slices before (top row) and after (bottom row) treatment in a male 17-year old subject that received 11 days of treatment. There was clear improvement in ventilation following combined intravenous antibiotics and hypertonic saline treatment, most notably in the upper lung lobes. The calculated ventilation volume of each slice shows an increase in the ventilation after treatment, predominantly in the center and posterior slices. The summated ventilation volume for the whole lung in this subject increased 25% following treatment. FEV₁ in this subject increased from 44% of predicted before treatment to 69% after treatment, and FVC increased from 80% of predicted to 108% following treatment. There was a clear correspondence between the improvements in ventilation volume as measured by hyperpolarized ^3He MRI, and FEV₁ and FVC in this subject. No improvement in either ^3He ventilation or spirometry was observed in a 19-year old subject. A third subject, 40 years in age, displayed improvement in spirometry following treatment, but no improvement in ^3He ventilation.

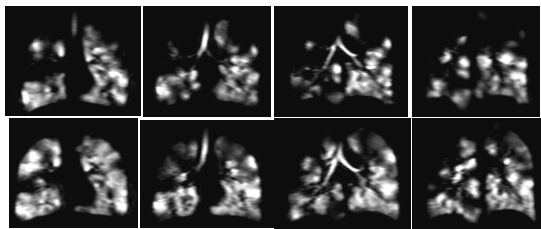


Figure 1. Center hyperpolarized ^3He slices before (top row) and after (bottom row) treatment.

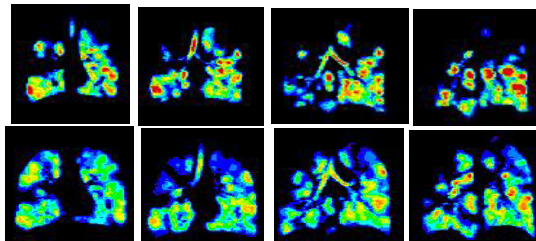


Figure 2. Color-coded ventilation map of center hyperpolarized ^3He slices before (top row) and after (bottom row) treatment.

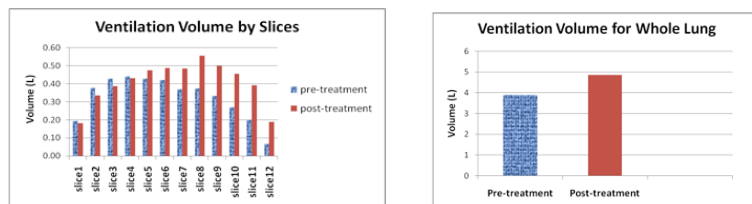


Figure 3. Plot of ventilation volumes for each slice (left chart) and ventilation volumes for the whole lung (right chart), before and after treatment.

Conclusion:

Hyperpolarized ^3He MRI is a useful tool for evaluating treatment in patients with cystic fibrosis. Ventilation volumes can be calculated from the ^3He images in a semi-automated fashion. In a 17-year old patient, we observed increases in ^3He ventilation volume following administration of intravenous antibiotics, hypertonic saline, and rhDNase, and these increases in ^3He ventilation volume corresponded with FEV₁ and FVC. This was a preliminary study; a more extensive study, involving a much larger sample size of subjects and testing several specific hypotheses, is under development.