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Medical application of spin-polarized noble gases: Emphysema index based on polarized He-3 and Xe-129 diffusion in the lung

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Over the past few decades, spin-polarized noble gases He-3 and Xe-129 have been used extensively as imaging media for magnetic resonance imaging (MRI) in medical research to characterize abnormalities in the lungs such as chronic obstructive pulmonary disease (COPD), which is the 4th leading cause of death worldwide. In particular, diffusion-weighted magnetic resonance imaging (DW-MRI) of spin-polarized Xe-129 has shown potential to serve as a clinical diagnostic tool for such diseases. DW-MRI of inhaled polarized He-3 and Xe-129 generates maps of apparent diffusion coefficient (ADC) throughout the lung; these maps represent mean squared displacement of individual gas molecules diffusing within the alveolar microstructure. Since displacement of the polarized gas inside the lungs is severely limited by the alveolar walls and microstructure of the lung tissue, elevated ADC indicates enlargement of alveolar volumes. ADC maps provide sensitivity to a finer length scale than computed tomography (CT) and 1H (conventional) MRI and can be used to study emphysema, which is a disease that causes destruction of alveolar walls leaving enlarged airspaces and effectively compromising microstructure of the lungs. CT provides a direct measure of lung tissue density and is considered the gold standard for image-based characterization of emphysema, despite its ionizing radiation exposure to the patient. In particular, emphysema index (EI) using CT, defined by the fraction of image pixels with attenuation coefficient less than an established threshold corresponding to no discernible tissue density, provides a quantitative measure of emphysema burden over the whole lung.

Inspired by EI based on CT, here we propose EI based on polarized He-3 and Xe-129 ADC values and compare its performance with CT-based EI. Healthy volunteers as well COPD patients (with varying stages of COPD determined by pulmonary function tests) were given CT along with He-3 and Xe-129 DW-MRI scans. We define EI based on polarized He-3 and Xe-129 ADC values: fraction of the volume elements (voxels) with ADC values greater than a threshold we determined based on 95th percentile of the distribution for all the voxels in our healthy volunteers. While low CT values correspond to low tissue density, elevated ADC values correspond to enlarged airspaces where the gas can more freely diffuse. The threshold based on healthy voxels' ADC values essentially separates out emphysematous regions that have higher ADC values than 95% of ADC values corresponding to voxels in healthy volunteers. Comparison of EI based on polarized He-3 and Xe-129 ADC and EI based on CT reveals that in our subjects, ADC-based emphysema index is significantly more sensitive to emphysema detection (particularly separating healthy from early stages of emphysema) than CT-based EI. We found significantly more elevated ADC values in COPD subjects, corresponding to emphysema, than depressed CT values associated with emphysematous regions. Another key finding of this study is that both He-3 and Xe-129 are found to be equally more sensitive to emphysema than CT. Similarity in performance of He-3 and Xe-129 is critical because going forward, in clinical applications of spin-polarized gas as a diagnostic tool, Xe-129 is the only viable option because it is a naturally abundant noble gas.

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