## Imaging COPD and Asthma - From Structure to Function

E. E. de Lange[1]
[1]University of Virginia, Charlottesville, VA, United States

Chronic Obstructive Pulmonary Disease (COPD), which includes emphysema and chronic bronchitis, and asthma are respiratory diseases of global importance that cause significant burden in terms of health care costs, lost productivity and reduced participation in family life. For both diseases the number of people affected have been rising worldwide. Of the two, COPD is the most prevalent and is projected to rank fifth in 2020 by the World Health Organization as a worldwide burden of disease. The same organization estimates that 100-150 million people suffer from asthma. Common risk factors known to contribute to both conditions include tobacco, poor nutrition, frequent lower respiratory infections during childhood and environmental air pollution. Although there may be overlap, both in terms of functional and pathologic findings, the pulmonary changes occurring within the lungs are pathologically distinct. In emphysema, which is a major cause of COPD, the airspaces distal to the terminal bronchioles are predominantly affected by breakdown of the alveolar walls and their attachments causing enlargement of the alveoli and loss of gas exchange area, whereas in asthma the alveoli are mostly spared while the small and medium bronchioles are affected by wall thickening and subsequent obstruction of airflow.

Although pulmonary function tests are important in the management of these diseases, early detection may be difficult and no information is obtained as to the regional distribution of disease. Chest radiographs play a limited role and are insensitive to early changes. With high resolution computed tomography (HRCT) detailed assessment of structural changes of the lung such as bronchial wall thickening, luminal narrowing and interstitial changes can be shown, and with use of surface rendering algorithms virtual bronchoscopic evaluation of the bronchial tree and airways can be performed. Indirect assessment of pulmonary function using CT has been done by determining quantitative changes of the lung density between inspiratory and expiratory scans. A more direct assessment of pulmonary function can be made by obtaining CT images with inhalation of stable, non-radioactive xenon gas and determining the wash-in and wash-out rates; however, this method is not widely used. More commonly used is radionucleide scintigraphy with Single Photon Emission Computed Tomography (SPECT) whereby images are obtained showing the regional distribution of inhaled gases such as $^{133}$Xenon or $^{81m}$Krypton. However, concerns regarding radiation dose may limit the utility of these methods particularly when repeated imaging is needed over time.

Conventional $^{1}$H magnetic resonance (MR) imaging of the lung is limited for assessing the pulmonary microstructure because the low proton density in the lung gives rise to a weak MR signal. Further, the many air/tissue interfaces cause considerable susceptibility effects particularly when gradient-echo sequences are used. Oxygen-enhanced spin-echo imaging has been used for studying lung ventilation, using the paramagnetic T1-shortening properties of inhaled oxygen, but to date this technique has had limited application in studying disease processes in the lung.

Hyperpolarized noble gas MR imaging following inhalation of polarized gases helium-3 ($^{3}$He) or xenon ($^{129}$Xe), which are the two non-radioactive noble gas isotopes with spin-½, is a relatively new method for evaluating lung function. Using laser-based optical-pumping methods the nuclear spins of the gas atoms are brought into alignment in a polarizer outside the MR scanner, providing polarization levels that can be $10^4$ to $10^5$ times greater than the thermal equilibrium polarization of $^{1}$H in a conventional MR scanner. Due to this high polarization, high-resolution images of the gas-filled airspaces can be obtained despite the low physical density of the gases in the lung, and the dynamics of the gas flow within the lung can be visualized. Since the magnetic moment of $^{3}$He is three times larger than that of $^{129}$Xe and the polarization levels achieved for liter quantities of $^{3}$He have traditionally been several times greater than those achieved for $^{129}$Xe, the image signal-to-noise ratio for $^{3}$He can be many times greater than that for $^{129}$Xe. Further, $^{129}$Xe causes anesthetic effects while this is not the case with $^{3}$He. For these reasons, primarily $^{3}$He gas has been used for human lung imaging, despite the fact that there is only limited availability on Earth and its costs are higher. However, significant progress is being made with achieving higher polarization levels for $^{129}$Xe, which will likely make this agent more attractive in the future.

Evaluation of hyperpolarized $^{3}$He MR imaging in patients with COPD has shown correlations with pulmonary function tests, and in asthmatics correlations have been shown between the extent of the ventilation defects and clinical severity, and with changes in spirometry that correspond to small-airway dysfunction. Hyperpolarized gas MR imaging also allows mapping of the regional oxygen tension by making use of the paramagnetic effect of oxygen on the T1 relaxation time of the hyperpolarized gas.

A focus of considerable attention is the use MR methods that are sensitive to diffusion of the $^{3}$He gas, allowing the size and connectivity of the lung airspaces to be probed. With these methods the apparent diffusion coefficient (ADC) of the $^{3}$He gas is measured from which an average distance associated with the diffusion can be determined. Studies have shown that ADC values are increased in patients with emphysema and that there are regional differences within the lung, reflecting the enlargement of the distal distal airways in the typical distribution for this condition. Increases in ADC values have also been observed during childhood reflecting the normal airspace enlargement with growth. Further, increases in ADC values have been demonstrated within the lungs of smokers who had no clinical evidence of lung disease, suggesting the high sensitivity of diffusion-weighted hyperpolarized $^{3}$He MR for detecting early emphysema.