For a variety of lung pathologies, it is crucial to assess lung function in order to quantify the severity of the disease, assess treatments, and predict clinical outcome. Obstructive lung diseases such as chronic obstructive pulmonary disease (COPD) and asthma affect millions of people worldwide. The improvement of therapies for COPD such as lung volume reduction surgery and anti-inflammatory drugs for asthma highlight the continued need for regional assessment of the extent and severity of disease. However, the techniques used to assess regional lung function are limited:

- Regional ventilation can be assessed noninvasively with isotopic techniques using radioactive gases such as Xe-133 or Kr-81, but the temporal resolution of these techniques is of several seconds and do not allow real-time investigation of gas dynamics within the lungs. Moreover, the subject is exposed to ionizing radiation during the examination which may not be suitable for iterative follow-up, especially in young population.

- Traditional pulmonary function tests, such as spirometry evaluate the lung as a whole and this technique is relatively insensitive of early disease particularly during peripheral airways abnormalities. In some cases, bronchoconstrictive drugs such as metacholin can be added to PFT to assess bronchic hyper-responsivness. However, this test is incapable of identifying the magnitude and distribution of disease on a regional basis. For example, in unilaterally lung-transplanted patients, PFT results may be influenced by both evolution of disease in the native lung and chronic rejection in the graft.

3He ventilation MRI is a promising new tool for investigating lung physiology and diseases. It is a straightforward procedure that consists of inhalation of 3He with image acquisition during gas inhalation or breath-hold period. Static ventilation imaging allows the visualization of airspaces during a single apnea. In paediatric patients with cystic fibrosis, airflow obstruction leads to a reduced level of 3He in the distal lung regions, allowing for sensitive detection of ventilation abnormalities. Several studies have revealed that 3He-MRI demonstrates a significant correlation with FEV and CT abnormalities in cystic fibrosis (1-4). 3He-MRI is a suitable method for pulmonary imaging after lung transplantation (5). The amount of ventilation defects in lung transplant recipients correlated well with observed declines in pulmonary function in patients with known or suspected allograft rejection and with the clinical grade of bronchiolitis obliterans syndrome. Gast et al (5) in a series of 9 patients, demonstrates that all cases of chronic graft rejection as diagnosed by follow-up pulmonary function testing were also detected by an increase of non-ventilated lung parenchyma at 3He-MRI. Although, 3He-MRI predicted chronic allograft rejection prior to its detection by spirometry in two of these cases.

This approach is able to detect ventilation defects with a very high sensitivity, but does not provide any dynamic information. Other imaging strategies that rely on the use of fast imaging sequences during a single gas inspiration or expiration can provide functional information. Typically, a temporal resolution of a few hundreds of milliseconds is required in order to monitor the ventilation process during gas inspiration and expiration. Several fast imaging sequences have been applied to 3He ventilation imaging, including echo-planar imaging (EPI), rapid acquisition with relaxation enhancement (RARE), fast low-angle shot (FLASH), and spiral acquisition. Spiral sequences have been combined successfully with
sliding-window methods, and have been demonstrated to yield high-temporal resolution images. These dynamic images yield mainly qualitative information but they also offer the possibility of quantitative distribution analysis by generating signal time curves in defined lung areas.

Signal intensity of 3He is influenced by several factors during a breathing cycle. First, there is the initial rise of intensity when the hyperpolarized gas is flowing into the lungs at inspiration. Second, the pulse sequence itself is attenuating the signal by destroying longitudinal magnetization. The use of a large flip angle facilitates measurement of regional function in the major airways, while a small flip angle enable measurements in the peripheral airspace (6). A small flip angle makes possible to image the gas distribution in the lungs during the whole respiratory cycle. Third, there is the paramagnetic effect caused by molecular oxygen, which shortens the T1 of hyperpolarized 3He.

The NMR signal increases during 3He inhalation and then decreases during the breath-hold period as a consequence of the RF depolarization effects.

Diagram showing the evolution of the raw NMR signal inside the lung:

![](Diagram1.png)

The raw NMR signal can be corrected for these depolarizing effects (T1 relaxation effects in the lung can be neglected considering the short duration of the inhalation process) (7).

Using small flip angle it can be hypothesised that the shape of the MR SI curve of a pixel is strongly linked to the gas volume in the this pixel and lung functional parameters (during
inspiration or expiration) can be extracted and quantified from this high resolution image series:
- gas arrival time
- gas flow rate
- maximum gas volume

If total volume of injected gas is known, the number of spins measured at the plateau value can be easily calibrated and its value assigned to the total volume of gas injected. However, the total gas volume injected inside the lungs needs to be corrected from the dead space volume.

In rats, quantitative regional gas dynamic information demonstrated significant between the baseline and constricted states following metacholine injection (8,9).

Studies of dynamic inhalation and expiration in human subjects have demonstrated qualitative gas trapping in asthma and cystic fibrosis. From a starting position of functional residual capacity the subject performed a deep inspiration maneuver (inhaling the contents of the bag) and a slow expiratory maneuver (removing the bag from the mouth and exhaling into free space)

Semi-quantitative approaches using the regional slope of gas uptake normalizes to the uptake in trachea (in order to normalize for subject-dependent factors such as the inspiratory effort or the mode of gas delivery) have also been applied to CF (2). Since all gas will pass via the trachea, it is possible to use the tracheal signal intensity as an “input function” to normalize for input flow effects.

Although because ventilation is associated with motion, especially in the lower regions of the lung and in the cranio-caudal axis, this may have a severe impact on the quantitative evaluation of lung function (10). Recently, Grid tagging has been used in 3He-MRI to quantify the motion and deformation of lung tissue (11). This technique may lend new insights into the regional biomechanics of the healthy and diseased lungs.

DW MRI can be used to measure the physical diffusion coefficient of 3He within the lung airspaces. In regions such as the trachea, the gas is mostly unrestricted, but in the lung parenchyma, the gas is restricted by the walls of the alveoli and terminal bronchioles (12). Although, the monoexponential decay model is straightforward and provides regional information, it is now widely recognized that the signal decay due to diffusion in the lungs is multiexponential. In patients the apparent diffusion coefficient (ADC) is a sensitive measure for the airspace size. ADC values have been shown to increase from the anterior to posterior regions of the lungs due to expected gravity dependent changes in alveolar volume (13). Several studies (12,14) have shown that ADC values are increased in emphysema, likely reflecting the decreased restriction of the gas due to disruption of the lung parenchyma.

Regional ADC maps in COPD patient’s demonstrated increased severity of emphysema in the apical vs. the basal lung regions compared to a more diffuse increase ADC in α1 antitrypsin-deficient patients (14). The ADC measures have been shown to be highly reproducible and to be potentially more sensitive than HRCT of early detection of emphysema in asymptomatic smokers and aging never-smokers (15).

According to the nature of the method, dynamic and diffusion imaging are procedures that are sensitive only to regions of the lung, which are ventilated. The technique will therefore have limited use in diseases that cause permanent obstruction, such as the late stages of CF or COPD. In childrens with CF, the relatively lesser extent of fibrotic change means that the
lungs are generally more homogeneously ventilated and a systematic analysis of dynamic ventilation and/or diffusion may be more useful.

References:


