Registered ^{3}He Ventilation and ^{1}H Perfusion Dynamic Contrast Enhanced MRI in the Rodent Lung

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INTRODUCTION: The increasing use of rodent models to study human disease has spurred extraordinary interest in the development of functional imaging metrics. To study pulmonary disorders, quantitative metrics of both ventilation and perfusion are necessary. Ventilation imaging in rodents has become well established using hyperpolarized ^{3}He [1]. However, perfusion imaging in the rodents has not kept pace. In humans and large animals, perfusion may be assessed using dynamic contrast enhanced (DCE) MRI [2-5] using a single contrast bolus injection. However, the method developed in the clinic cannot be translated directly to image the rodent due to the added spatio-temporal resolution constraints. This work describes a novel use of multiple contrast agent bolus injections using an automated micro-injector, synchronized with image acquisition to achieve dynamic first-pass contrast enhancement in the rodent lung, allowing quantitative assessment of lung function.

METHODS: All animal procedures were approved by the Duke Institutional Animal Care and Use Committee, and the details of animal preparation and HP gas preparation are provided in [1]. Imaging was performed using a 2 Tesla 30-cm bore magnet (Oxford Instruments, Oxford, UK) with shielded gradients (180 mT/m, GE NMR Instruments, Fremont, CA) controlled by an EXCITE 12.0 console (G. E. Healthcare, Milwaukee, WI). A dual-frequency 7 cm diameter birdcage coil was used at 64.8 MHz to image HP ^{3}He, and at 85.5 MHz to image ^{1}H. The contrast agent gadopentetate dimeglumine (Magnevist, Berlex Inc., Wayne, NJ) was injected in the right jugular catheter placed in female Fischer 344 rats (160-190 g), using a power injector specially designed for multiple scan-synchronous injections at a flow rate of about 0.6 µl/ms, each injection being 50 ms long.

Ventilation Imaging: High-resolution static ventilation images were acquired using radial encoding k-space trajectory at end-expiration. The scan was synchronous with the ventilatory cycle with 20 radial views acquired per trigger. 1600 radial views were collected per image to reconstruct a 512^2 static ventilation image. Imaging parameters were TR = 5 ms, TE = 0.7 ms, slice thickness = 3 mm, field of view (FOV) = 50 mm, and a variable flip angle increasing from a small value to 90°. Dynamic flow non-slice selective ventilation images were acquired with a temporal resolution of 36 ms, and spatial resolution of ~190 µm (256^2), using the radial acquisition scheme, with a flip angle of 36°, TR = 6 ms, TE = 0.4 ms and an RF train of 10 killer 90° pulses, so as to capture only the fresh inflowing ^{3}He. The acquisition was triggered 36 ms prior to the start of inspiration.

Perfusion Imaging: DCE-MRI in the lungs was performed at suspended breath at end-expiration (10 sec), starting with the first detectable ECG R wave to trigger the power injector and data acquisition. A 2D radial acquisition sequence with short TE (0.7 ms) and TR (4 ms), and a flip angle of 30° was used with the FOV and slice thickness identical to that of the ^{3}He images, to maintain the registration between the ventilation and perfusion images. The data acquisition was carried out for a period of ~6 sec, that was divided into 16 sub-images, giving a temporal resolution of 400 ms to capture the dynamic first-pass curve. DCE images were reconstructed at 64^2, requiring 200 radial views per image. Considering the temporal constraints placed by the time for first-pass perfusion and the number of sub-images, the scan was carried out with controlled repeatable multiple bolus injections. Image subtraction was performed using a pre-contrast set that was collected using the same imaging strategy by turning off the power injector. Regions of interest (ROI's) were drawn in the pulmonary vein, left and right lung parenchyma, and descending aorta.

RESULTS: Fig. 1 shows dynamic ventilation images at four points (selected from a series of 12 images) in the ventilatory cycle. The images clearly show the "flow in" of ^{3}He, and its distribution in the major airways and finally in the most distal alveolar spaces. Fig. 2 shows, in another animal, static ^{3}He images overlaid with the DCE-MRI ^{1}H images, both acquired at end-expiration at 10 time points (selected from a series of 16 images) following the contrast bolus injection. Visual inspection of the images reveals matched ventilation and perfusion as would be expected in a healthy animal. Fig 3 shows the dynamic first pass for the various regions drawn within the lungs. ROIs drawn in the right and left lung show peak enhancement at around 1 sec after the contrast injection, followed by the pulmonary vein (~1.8 sec), and the descending aorta (~2 sec).

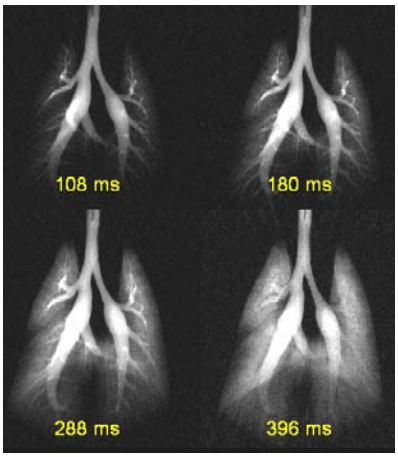

Fig. 1: Dynamic ^{3}He ventilation (gray) images in the rodent at 4 time points during inspiration.

DISCUSSION: Dynamic contrast enhanced MRI is difficult to perform in the lung due to its low proton density, and the large number of air/tissue interfaces, further complicated in the rodent due to the spatio-temporal resolution requirements. Cremillieux *et al.* [6] previously used a single manual injection of contrast to create a static perfusion image in the rat. This work now extends perfusion imaging in the rodent by providing detailed dynamic information, which is needed to study disease states where blood flow is impaired but not completely blocked. This work proposes a technique to acquire flow ventilation information using ^{3}He, and perfusion information via DCE-MRI in the rat. The combined information from the ^{3}He ventilation images and ^{1}H perfusion images is now being used to study disease models for pulmonary disorders.

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Work was performed at Duke, Center for InVivo Microscopy, an NCRR national resource (P41 RR005959), with additional support from NHLBI (R01 HL055348).

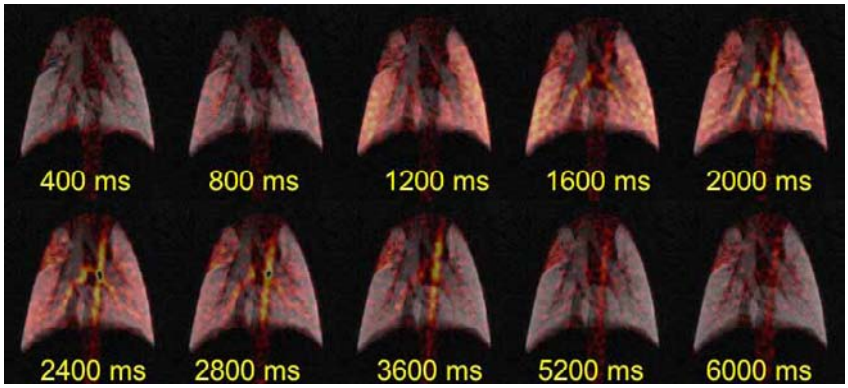

Fig. 2: Dynamic contrast enhanced MRI (color) overlaid with static ^{3}He ventilation (gray) images in the rodent, showing registered ventilation and perfusion information.

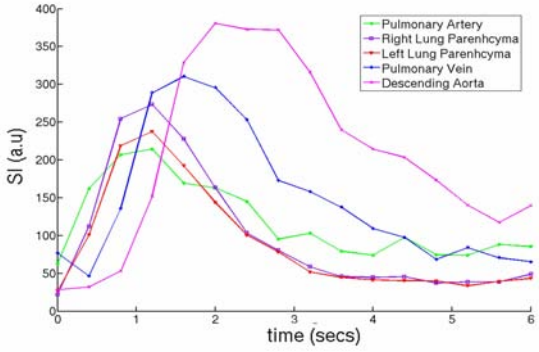

Fig. 3: Dynamic first-pass perfusion information in various regions of the lungs allowing assessment of the transit times and flow rates.