Pulmonary perfusion imaging in the rodent lung using Dynamic Contrast Enhanced MRI

N. N. Mistry[1,2], J. Pollaro[2], J. Song[2,3], and G. A. Johnson[2]

[1]Dept. of Biomedical Engg., Duke University, Durham, NC, United States, [2]Center for In Vivo Microscopy, Duke University Medical Center, Durham, NC, United States, [3]Dept. of Electrical and Computer Engg., Duke University, Durham, NC, United States

INTRODUCTION: Perfusion imaging in humans and large animals [1-3] can be assessed using dynamic contrast enhanced (DCE) magnetic resonance imaging with a single contrast bolus injection. But, the method developed for the clinic cannot be translated directly to image the rodent due to the combined requirements of both higher spatial and temporal resolution. The 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 rat lung, was described earlier [4]. In this work, improvements are made in the spatial and temporal resolution by combining the multiple injection acquisition method with Interleaved Radial Imaging and "Sliding window-keyhole" reconstruction technique, called IRIS for brevity. The results demonstrate a simultaneous increase in spatial and temporal resolution over the previous method, with limited loss in signal-to-noise-ratio.

METHODS: All animal procedures were approved by the Duke Institutional Animal Care and Use Committee. Experiments (N=6 rats) were carried out by placing catheters (3 French) in the right jugular vein of female Fischer 344 rats (Charles River Lab, MA) weighing 192-224g. All physiologic signals were continuously collected (Coulbourn Instruments, Allentown, PA) and displayed on a computer using LabVIEW software (National Instruments, Austin, TX). These signals were also used to control the triggering of the imaging sequence and the micro-injector designed to deliver 20 µl of Gd-DTPA contrast agent in 50 ms in a repeatable manner. **Interleaved Radial Imaging and "Sliding window-keyhole (IRIS):** Imaging was carried out on a 2 T magnet at 62.5 kHz bandwidth, with a flip angle of 40°, TE/TR = 0.7/4 ms, FOV = 50 mm, and a slice thickness of 3 mm. Fig. 1 shows the acquisition view ordering over multiple time-points (Tp1-Tp4) and multiple injections (Inj1-Inj3). The acquisition for a single injection (Inj1) was performed in an interleaved pattern. The interleaved pattern was created by adding a small angle ($\Delta\phi$) to the start angle of the earlier time-point given by $\Delta\phi = 360^{\circ}/views$, where *views* is the total number of *k*-space lines acquired during the complete acquisition. The acquisition for the next injection started with an angular offset $\Delta\theta = \Delta\phi$. ($\#Tp$) where, $\#Tp$ is the total number of time-points into which the total acquisition was divided. This ensured that when the *k*-space lines acquired over the multiple injections were combined, as shown in last row of Fig. 1, *k*-space for each time-point was uniformly sampled. Each view acquired throughout the acquisition was unique to ensure that the combined *k*-space from all the views resulted in a high SNR time-averaged reference *k*-space. Image reconstruction for the interleaved data was carried out as shown in Fig. 2. The central core of the reference *k*-space was updated at time-interval Tp1-Tp4 from the undersampled *k*-spaces shown in the last of row of Fig. 1. The later half of the earlier time-point and the earlier half of the next time-point were combined to create the intermediate time-points Tp1.5, Tp 2.5, and Tp 3.5. Finally, reconstruction was carried out onto a 256^2 grid using a standard regridding algorithm. Sampling density compensation was performed to compensate for the non-uniformity of the *k*-space data collected by IRIS.

RESULTS: The IRIS sampling pattern used 4 injections each of 20 µl Gd-DTPA contrast agent. 1600 radial samples were acquired during each injection leading to 6400 radial views for the complete dataset. The 6400 views were binned into 16 equal time-points resulting in a temporal resolution of 400 ms at acquisition, and a spatial undersampling factor of 2. Reconstruction for IRIS using the sliding window approach was performed at 16 + 15 (intermediate) time-points at a temporal resolution of 200 ms. Fig. 3 shows 6 different time-points from a series of 31 images at a spatial resolution of 195 µm. Fig. 4 shows the DCE curves created by manually placing ROIs in the pulmonary artery, and right and left lung that show peak enhancement at approximately 1 second after the contrast injection, followed by enhancement in the pulmonary vein (~1.8 sec), and the descending aorta (~2 sec).

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. This work extends the previously demonstrated perfusion imaging in the rodent by providing detailed dynamic information at a higher spatial resolution of ~200 µm and a higher temporal resolution of ~200 ms. Quantitative pulmonary measurement in 6 rats show that the values for mean transit time lie within the range of values reported for isolated rat lungs [5]. IRIS is in principle very similar to the technique discussed in [6]. However, the combination of multiple contrast injection and a different view-ordering scheme combined with the reconstruction makes pulmonary perfusion imaging at high spatial and high temporal resolution feasible in the rat.

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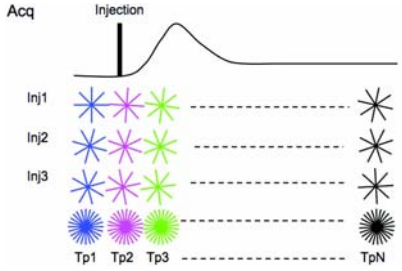

Fig. 1: Data are acquired over multiple injections (Inj). Each set of radial lines is rotated by a small increment ($\Delta\phi$) with respect to the trajectories of the previous time interval. Each radial line acquired throughout the acquisition is unique.

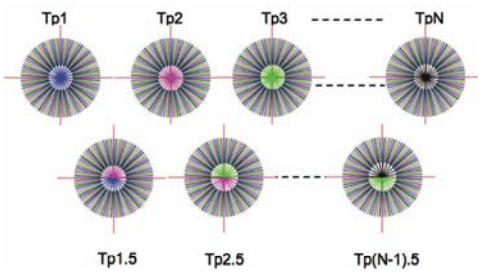

Fig. 2: The "sliding window-keyhole" reconstruction updates the core of the time-compressed *k*-space. The 1st row shows the core with a single color, while the 2nd row shows the core with colors from the two closest time-points.

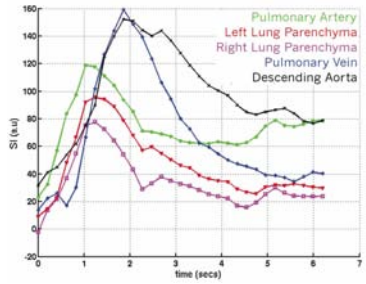

Fig. 4: Dynamic first-pass curves created by selecting ROIs over parts of the cardio-pulmonary circuit show subtle variations in different regions such as the pulmonary artery, the parenchyma, the pulmonary veins and the descending aorta.

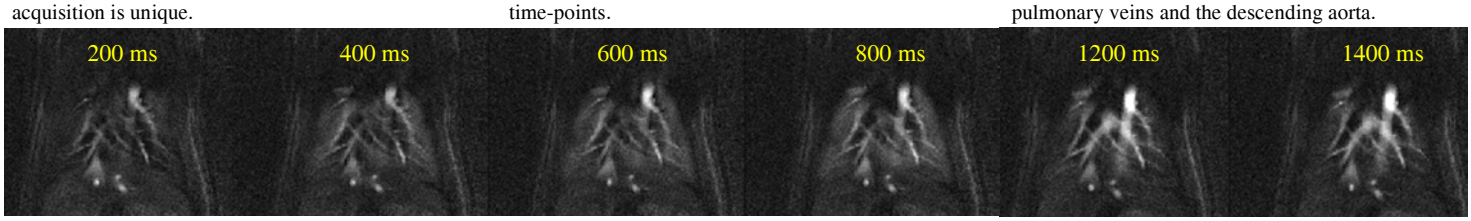

Fig. 3: Post-contrast injection scan in a rat lung, reconstructed at a spatial resolution of ~195 µm and a temporal resolution of 200 ms using four 20 µl injections of Gd-DTPA. Only 6 images from a series of 31 are shown in the panel.