## Assessment of pulmonary perfusion reserve with adenosine using quantitative MRI lung perfusion

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Background: Lung perfusion, assessed quantitatively by dynamic MRI, is reduced in patients with primary pulmonary hypertension and in patients with chronic obstructive pulmonary disease. However, little is known whether quantitative lung perfusion can be used to evaluate pulmonary vascular reserve. In this study we sought to investigate the lung perfusion response to adenosine challenge using lung perfusion quantitation by MRI in volunteers.

Methods: Twenty six volunteers were prospectively recruited. All underwent MRI in a 1.5T scanner. Dynamic images were acquired in 3 parallel coronal views with equal distance representing anterior, mid and posterior lung fields using breath-holding ECG gated saturation recovery steady state free precession sequence during gadolinium DTPA infusion (0.01 mmol/kg) at a rate of 6 ml/sec. A voxel spatial resolution of  $4\times2.6\times15$  mm³ was achieved using the specifications as follows: inversion time 90 ms, field of view 500 mm, TE 0.92 ms, image acquisition window 160 ms per slice, flip angle  $50^{\circ}$  and an acceleration factor of 2. Following rest imaging stress lung perfusion images were acquired during adenosine infusion ( $140\mu g/kg/min$ ) using the same imaging protocol. A total of 312 lung sections were quantitatively analyzed using a custom model-independent deconvolution program in left and right anterior, mid and posterior lung fields. Global lung perfusion was determined as the average of all 6 sections. Through plane phase contrast imaging of the main pulmonary artery was performed to assess cardiac output at rest and during stress. A questionnaire with detailed medical history was obtained. All subjects underwent pulmonary function test (PFT) prior to MRI. Paired-t test was performed comparing rest and stress indices.

Results: Average age was 51±18 years, ranging from 20 to 83 years, and 20 (77%) were male. The prevalence of past smoking was 31% and current smoking 19%. Mean actual FEV1/FVC was 77±12%. The average heart rate increased from baseline 63 bpm to 80 bpm during adenosine infusion (p<0.001) while cardiac output increased from 4.9 L/min to 7.9 L/min (p<0.001). The average lung perfusion at rest was 86±27 ml/100ml/min which increased to 165±76 ml/100ml/min during adenosine infusion (p=0.005). Perfusion augmentation was consistent in all lung fields from 49 ml/100ml/min to 112 ml/100ml/min in anterior lung (p=0.065), from 86 ml/100ml/min to 158 ml/100ml/min in mid lung (p=0.001), and from 124 ml/100ml/min to 224 ml/100ml/min in posterior lung (p=0.002) comparing rest and stress perfusion, respectively. The gravitational perfusion gradient from anterior to posterior lung fields was present at rest and during stress while the perfusion favored more towards posterior lung field during stress with linear regression slope 0.556 compared to slope 0.378 at rest (p=0.001). Based on PFT the cohort was divided into 3 groups: normal (actual FEV1/FVC>76%), borderline (actual FEV1/FVC 71%-75%) and impaired (actual FEV1/FVC≤70%). There was a graded decrease of rest lung perfusion in 3 groups, 95±23 ml/100ml/min, 80±27 ml/100ml/min and 59±24 ml/100ml/min for normal, borderline and impaired PFT group (p=0.011), respectively. While a perfusion augmentation was achieved in all 3 groups with absolute perfusion of 188±75 ml/100ml/min, 151±60 ml/100ml/min and 94±61 ml/100ml/min (p=0.027) during adenosine infusion, respectively, there was a trend with the highest perfusion reserve ratio in normal (2.1) followed by borderline group (1.9) and with the least in PFT impaired group (1.5).

Conclusion: With adenosine challenge the absolute lung perfusion was increased by about 2 folds on average. Perfusion augmentation was achieved in all lung fields. Reduced lung perfusion was associated with impaired PFT at rest and during stress. Our findings suggest that quantitative assessment of pulmonary perfusion reserve is feasible using lung perfusion quantitation by MRI.