Comparison of AIF determination methods and gadolinium contrast agents for quantitative pulmonary perfusion
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TARGET AUDIENCE: Scientists and clinicians interested in quantitative pulmonary perfusion.

PURPOSE: The purpose is two-fold: 1) to compare pulmonary blood flow (PBF) measurements obtained using three proposed methods (low CA single dose1, dual bolus2, and a post-processing non-linearity correction algorithm3) that address the non-linear relationship between signal intensity (SI) and contrast agent (CA) concentration in the arterial input function (AIF), and 2) to evaluate lung signal and PBF using gadobenate dimeglumine (Gd-BOPTA; MultiHance) compared with gadopentetate dimeglumine (Gd-DTPA; Magnevist).

METHODS: Image Protocol - 12 healthy human subjects (7F, 5M, age: 37±13 yrs) were each scanned on two consecutive days, using Gd-BOPTA one day and Gd-DTPA on the other, in a randomized order. Scans were performed on a 1.5T scanner (SignaHDxt, GE Healthcare, WI) with a commercial 8-channel cardiac phased array coil. Dynamic perfusion MRI was performed using a 3D spoiled gradient echo pulse sequence and interleaved variable density k-space sampling4 at end-expiration. Two perfusion datasets were obtained each day: a "prebolus" acquisition using a 0.01 mmol/kg and a "bolus" acquisition using 0.025 mmol/kg with 20 mins between to allow for CA washout. The injection was performed at 3.5 mL/s and was followed by 35 mL of saline. Relevant parameters: TR/TE = 2.12/0.70 ms, flip = 30 º, acquired spatial resolution = 4(SI) x 4(AP) x 5(LR) cm 3, BW = ±125kHz, parallel acceleration 2x2, and end-expiration. Two perfusion datasets were obtained each day: a "prebolus" acquisition using a 0.01 mmol/kg and a "bolus" acquisition using 0.025 mmol/kg with 20 mins between to allow for CA washout. The injection was performed at 3.5 mL/s and was followed by 35 mL of saline. Relevant parameters: TR/TE = 2.12/0.70 ms, flip = 30 °, acquired spatial resolution = 4(SI) x 4(AP) x 5(LR) cm 3, BW = ±125kHz, parallel acceleration 2x2, and acquired temporal resolution of 1 second with 22 time frames.

Post Processing - Signal time courses were determined in 4 regions: the main pulmonary artery (AIF) and in three regions of the lung (anterior, middle, and posterior). Relative signal time courses were then calculated using $S_{rel}(t) = (S(t) - S(0))/S(0)$. The contrast concentration time course for the AIF was calculated using each of the three reconstruction methods: 1) Single Bolus1 2) Dual Bolus2, and 3) Non-linear correction3. Finally, PBF was measured by the deconvolution of lung signal time course with each proposed AIF.

Statistical Analysis - Bland Altman analysis was used to assess agreement between CA and between AIF reconstruction methods using PBF and the peak AIF as the response variables. Evidence of a significant bias was accepted if the 95% confidence interval of the bias did not contain zero in the interval. Relative peak lung enhancement was compared between CA using Student’s t-test with p-value < 0.05 for statistical significance.

RESULTS/DISCUSSION: The peak AIF was greater with Gd-BOPTA than with Gd-DTPA when using the “dual bolus” method. This may be the cause of the lower PBF observed with gadobenate dimeglumine (245 ± 103 ml/100ml/mn) compared with Gd-DTPA (315 ± 177 ml/100ml/mn). When using Gd-DTPA, the peak AIF of the “non-linear correction” was greater than the “single bolus”, suggesting that some signal saturation occurs in the “single bolus”. When using Gd-BOPTA, differences were observed between the peaks of all AIFs which also translated to a noted difference between measured PBF with all three constructed AIFs. The PBF values from all 3 reconstructions with Gd-DTPA did not differ from each other significantly. However, all 3 reconstruction methods differed from each other when using Gd-BOPTA. We suspect that the lower observed PBF with the “dual bolus” approach using Gd-BOPTA is due to the reported non-constant relationship of relaxivity to concentration that has been reported2. If relaxivity is not constant over concentrations, the dual bolus assumption of a linear time invariant system for both administered scans is violated. Lung enhancement in all planes was improved with Gd-BOPTA compared with Gd-DTPA (p < 0.05).

CONCLUSIONS: This study has three important findings with impact on calculation of quantitative pulmonary perfusion:

1) There are no significant differences in PBF measurements between any of the AIF reconstruction methods when using Gd-DTPA.
2) There are significant differences in PBF measurements between all AIF reconstruction methods when using Gd-BOPTA. Further investigation is needed to evaluate which method better correlates with true perfusion values.
3) The signal intensity within the lung tissue is greater with Gd-BOPTA than with Gd-DTPA, improving image quality and potentially the stability of the PBF calculations.

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