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 dose[1], dual bolus[2], and a post-processing non-linearity correction algorithm[3]) 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).

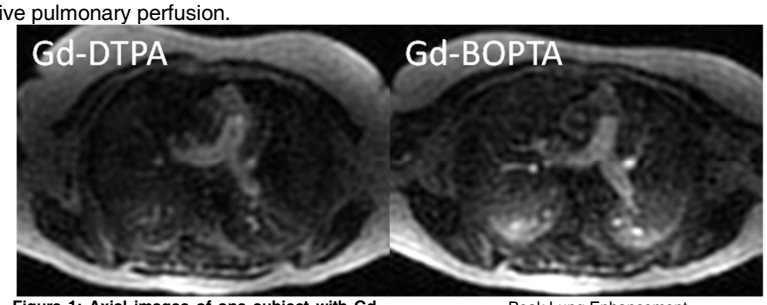

Figure 1: Axial images of one subject with Gd-DTPA (left) and Gd-BOPTA (right). Average peak lung enhancement values are tabulated for all subjects for anterior, middle, and posterior regions of both lungs.

	Peak Lung Enhancement		
	Gd-DTPA	Gd-BOPTA	*p-value*
Ant:	2.1 ± 0.5	3.0 ± 0.8	*4.5E-5*
Mid:	2.1 ± 0.8	3.2 ± 1.0	*4.4E-5*
Post:	3.5 ± 1.0	4.9 ± 1.4	*1.8E-5*

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 sampling[4] 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°, 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 Bolus[1] 2) Dual Bolus[2], and 3) Non-linear correction[3]. 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.

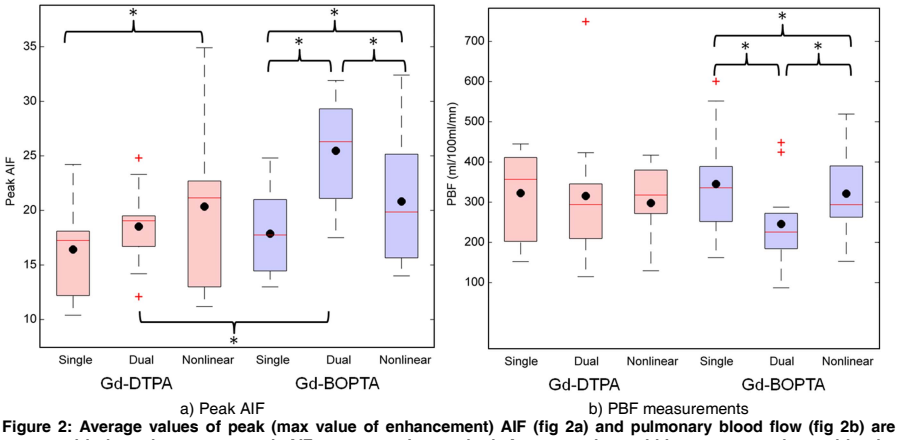

Figure 2: Average values of peak (max value of enhancement) AIF (fig 2a) and pulmonary blood flow (fig 2b) are presented in box plots across each AIF reconstruction method. Average values within groups are donated by the circles. Observed statistical differences are indicated with a bracket and one asterisk.

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 reported[5]. 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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REFERENCES: [1] Ohno Y et al, JMRI (2007) 25: 55-65 [2] Risse F et al, JMRI (2006) 24: 1284-90 [3] Neeb et al, MRM (2009) 62: 476-87 [4] Wang K et al, JMRI (2013) 38: 751-6 [5] Pintaske J et al, Invest Radiol (2006) 41: 213-21.