Linear Arterial Input Functions for First-pass Myocardium Blood Flow Assessment Using Calibration And Bloch Simulation

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Introduction:
Quantitative techniques, such as Fermi deconvolution analysis, are used to assess ischemic regions of the myocardium and require Arterial Input Functions (AIF) and Myocardial Response Functions (MRF). First-pass perfusion imaging, using a single bolus of Gadolinium (Gd) contrast agent, results in a linear Myocardial Response Function and a less than linear Arterial Input Function. The purpose of this study is to demonstrate a method to generate a linear AIF using a combination of imaging, calibration, and Bloch simulation.

Methods:
A cardiac gated, gradient echo sequence with EPI read out, TR=5.6, TE=1.1, ETL=4, and a non-selective saturation preparation pulse (CASH2 sequence) is used to generate first-pass perfusion images. The AIF and MRF are generated from the mean image intensity of ROIs placed in the blood pool of the left ventricle and myocardium respectively of 30 to 60 temporal phase images. The limited dynamic range of T1-weighted sequences and the decrease in T2*, due to the rising concentration of Gd contrast agent, result in a non-linear change in observed signal intensity in the blood pool. Most models used for blood flow assessment assume that signal intensity changes at a linear rate that is equal for AIF and MRF. A calibration curve is used in this study to correct the AIF so that it meets the requirement of linear signal response for a quantitative assessment of myocardial perfusion.

The calibration curve is a plot of the percent change in the observed image intensity (relative to pre-contrast signal intensity) versus the percent change in expected image intensity as shown in Figure-2. Observed image intensity curves (Figure-1) are measured from a T1 dilution phantom and Bloch simulations. The phantom consists of numerous concentrations of Gd (R1=0.33-10/Sec) in normal saline. The input variables for the Bloch simulation are T1 values starting at 10.0 mSec and going through the T1 value of blood (1250.0 mSec at 1.5Tesla) and sequence parameters such as TI, TR, TE, and flip angle. Expected image intensity curves are created by linear extrapolation from the low range of R1 values. This extended linear curve represents the percent change in the expected image intensity without the limitations from the T1-weighted sequence and T2*. An example of a corrected AIF is shown in Figure-3.

The bias of blood flow estimates was determined for a range of AIF (peak) saturation levels, using data acquired in patients (N=5), with a low-dosage bolus of contrast (0.03 mmol/Gd-DTPA). The measured AIF and myocardial tissue curves were scaled up to reproduce the setting of higher contrast dosages, and the measured calibration curves were used for AIF saturation. Figure-4 shows the percent bias toward overestimating myocardial blood flow, at rest, over a range of AIF peak saturation levels. Error bars represent SD from repeating the simulations, using data from N=5 patient studies.

Results:
There was no evidence, from paired t-test, of a significant difference between simulated and measured observed calibration curves. Further analysis by the Bland-Altman method gave the following 95% confidence limits for agreement of individual measurements: 3.2% for TI 98-148 ms; 8.5% for TI=88 ms; 10.5% for TI=78 ms. In all likelihood the smaller confidence intervals for longer TIs reflect a parallel increase on signal-to-noise for increasing TI. The example in Figure-3 shows peak AIF saturation occurring at 900% change from the baseline, which means a 10.5% confidence limit corresponds to an error of about 1%. The bias of blood flow estimates, due to signal saturation, increased in proportion to the peak AIF saturation as shown in Figure-4. The peak AIF saturation increased as the contrast dosage increased and, to a lesser degree, with increases in flip angle and TI. For contrast doses of 0.025 and 0.05 mmole/kg the peak concentrations in the LV corresponds to R1 values of approximately 9 and 16 Sec^{-1} respectively [3]. This produces peak AIF saturation of approximately 7 and 25 percent, which corresponds to approximately 7 and 30 percent bias toward overestimating myocardial blood flow at rest.

Conclusions:
Our study shows that Bloch simulations can be used in place of actual measurements to determine calibration curves on the fly. This calibration method opens up a wide choice of imaging parameters for perfusion studies, with different levels of linearity and signal-to-noise, than if the pulse sequence and contrast dosage must be primarily optimized for linearity. Simulations, based on AIF and tissue curves measured in patients with low Gd dosages, demonstrate that the AIF peak saturation provides a reasonably good predictor of the resulting overestimate of blood flow. Other parameters such as area-under-the-curve changed to a much lesser degree.

Figure-1

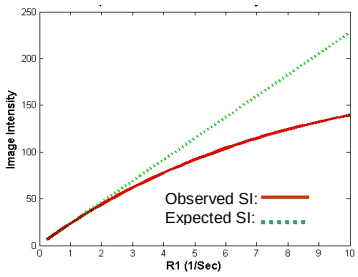

Figure-2

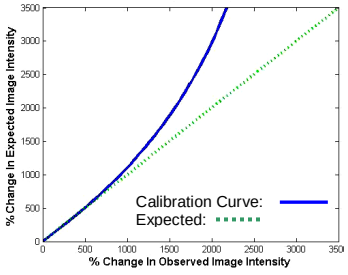

Figure-3

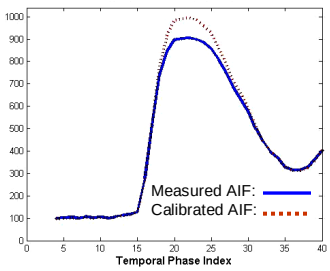

Figure-4

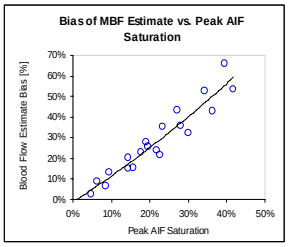

Figure-1: The plot of the observed signal intensity (derived from Bloch simulation) shows a non-linear change in signal intensity as R1 (or concentration of Gd) increases. The expected (ideal linear change) is depicted by the dashed line. For the low values of R1 the change is linear. **Figure-2:** The calibration curve shows the percent change in AIF saturation relative to the expected (ideal linear change) value. **Figure-3:** Shows an example of an AIF with approximately 10% peak saturation that has been corrected with the calibration data. The bias toward overestimating the blood flow is about 12% in this example. Note that the vertical axis is given in percent change in signal intensity relative to the baseline, which has a value of 100 %. **Figure-4:** This plot shows the relationship between peak AIF saturation and bias toward overestimating blood flow in perfusion imaging.

References:
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[2] Jerosch-Herold M, et al, "Magnetic Resonance Quantification of the Myocardial Perfusion Reserve with a Fermi Function Model for Constrained Deconvolution"; Med. Phys 25(1), January 1998, pp 73-84.
[3] McKenzie C A, et al, Improved Contrast Agent Bolus Tracking Using T1 FARM, Magnetic Resonance in Medicine 41:429–435 (1999)