Correcting PWI-based CBF measurements for arterial input function partial volume and nonlinear contrast relaxivity: comparison with a xenon CT gold standard

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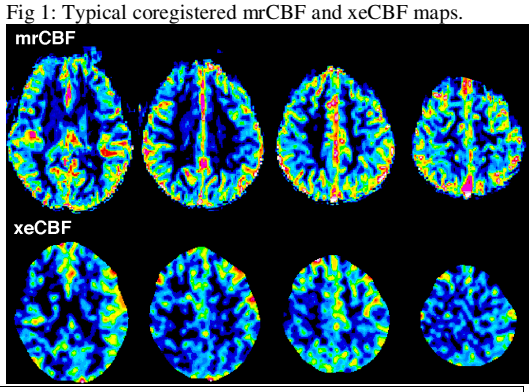
Bolus perfusion-weighted imaging (PWI) images provide reasonable relative CBF estimates and correlate well with gold standard methods such as $H_2{}^{15}O$ PET (1,2). One large problem is that the global CBF scaling factor varies between patients (3), such that absolute PWI-based CBF measurements are not reliable. Variable partial voluming (PV) of the arterial input function (AIF) is likely a major determinant of these variations (4). Since the superior sagittal sinus is larger than the typically chosen AIF arteries, the ratio of area under the curve of the AIF and the venous output function (VOF) may mitigate PV errors and improve the precision of PWI CBF. There is also evidence that the relationship between Gd concentration and $\Delta R2^*$ relaxivity is nonlinear at the concentrations found within large blood vessels (5,6). Using a gold standard xeCT CBF measurement, we examined whether PWI CBF estimates can be made more precise (i.e., less intersubject variability) by correcting for PV and bulk blood (BB) nonlinear contrast relaxivity.

Methods: 9 patients (5M, 4F, ages 19-63) with cerebrovascular disease (3 acute stroke, 4 subacute stroke, 2 TIA; of these, 5 had carotid occlusions) underwent stable xeCT (DDI, 4 10mm slices, 28% Xe gas) and MRI single-shot GE EPI based PWI (1.5 T GE, TR/TE 2000/60 ms, 12 6mm slices) within a 24-hr period. xeCBF was calculated using the Kety-Schmidt method. PWI CBF maps were calculated using circular SVD with automatic AIF and VOF detection. 4 separate post-processing corrections were applied to the PWI data: no corrections, PV correction only, BB correction only, and both PV and BB corrections. PV correction entailed multiplying the mrCBF by the ratio of the area under the VOF and AIF curves, assuming that the VOF to be 100% blood volume. BB correction was performed after estimating the contrast relaxivity in the individual AIFs, and accounting for the nonlinearity as per (5). Images were coregistered using SPM2, and 1 cc ROIs of mrCBF and xeCBF were compared (about 500 ROIs/patient). The global mean xeCBF, the global mean mrCBF using each of the 4 separate correction methods, and the CBF ratio (mrCBF/xeCBF) were determined. For each of the 4 correction methods, the mean and the patient-to-patient SD of the CBF ratios were determined. The method with the minimum variability of the CBF ratio with respect to the mean (the coefficient of variation, or COV) represents the most precise measurement. Finally, linear regression was performed between the global xeCT and each of the mrCBF correction methods in each patient.

Results: Fig 1 is an example of a coregistered MR PWI and xeCT dataset. The mrCBF maps have higher resolution and prominent large vessels, as is common for GE PWI. Mean global xeCBF was 49±16 ml/100 g/min (range 33-80 ml/100 g/min). The four different mrCBF post-processing corrections are shown in Table 1. CBF ratios were most strongly affected by the BB correction, which decreased mrCBF by an average of 4.6±0.5x. The AIF PV correction ranged from 0.49 to 0.87 (average 0.68±0.13), which led to smaller mrCBF increases of 1.5±0.3x. The highest mrCBF levels occurred without BB correction but with PV correction (170±24 ml/100 g/min), while the value closest to the xeCT CBF levels was obtained with both BB and PV corrections (37±7 ml/ 100 g/min), though this still underestimated xeCBF by 19±20% ($p>0.05$). There was no difference in the COV based on whether the BB correction was applied; however, there was a trend towards a decrease in the COV from 33% to 24-27% with PV correction. Regression between the xeCBF and the 4 mrCBF conditions demonstrated that despite having reasonable bias and precision, correlation was poor on a patient to patient basis, with R ranging from 0.23 to 0.46 (NS, $p>0.2$); when the xeCBF values are ranked in order, it becomes apparent that the bias of the mrCBF method depends on the baseline xeCBF (Fig 2).

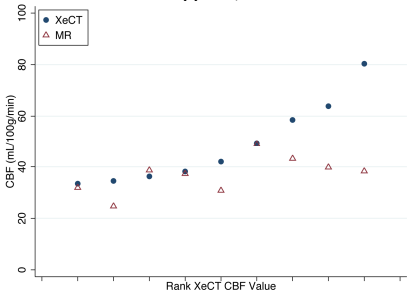
Fig 1: Typical coregistered mrCBF and xeCBF maps.



Discussion: Several previous reports focused on whether corrections for AIF PV effects lead to CBF values in the range of prior literature and whether they lead to less intersubject variability (4,7-8). However, none have examined whether these mrCBF corrections lead to less variability compared to a gold standard CBF technique. The current study examines a patient population with known cerebrovascular disease, in which intersubject CBF variability is likely to be higher than in normals. This study directly compared two potential correction algorithms with xeCBF to determine the effects on both the CBF ratio between the techniques (bias) and the coefficient of variation (precision). We believe that it is more important to improve the precision rather than the bias of the measurement, since any global scaling to bring the methods into quantitative agreement will then be patient independent.

Table 1 (mean±SD, n=9)	xeCBF	PWI MR CBF			
		PV -, BB -	PV +, BB -	PV -, BB +	PV +, BB +
Global CBF (ml/100 g/min)	49±16	116±27	170±24	25±7	37±7
CBF Ratio (mrCBF/xeCBF)	-	2.56±0.86	3.76±1.01	0.55±0.18	0.81±0.20
Coefficient of variation	-	33%	27%	33%	24%
Correlation coefficient (R)		0.23	0.28	0.37	0.46

Fig 2: Regression of xeCBF and mrCBF (PV and BB corrections applied).



For each patient, there was a significant correlation ($P<0.05$) between the two techniques, with R ranging between 0.2-0.6 (data not shown). Global xeCBF levels agreed with prior literature. mrCBF overestimated xeCBF before BB correction, and underestimated it afterwards. The PV correction (while smaller in magnitude) had a larger effect on a per person basis than the BB correction. The precision of the measurement as determined using the COV improved with PV correction, decreasing from 33% to 24-27%. No COV change was seen with the application of BB correction. Of the 4 conditions, applying both PV and BB correction yielded the least bias, but still underestimated xeCBF by 19±20%. Linear regression demonstrated that bias was dependent on baseline xeCBF; the trend is most clearly seen for the PV and BB corrected mrCBF maps (Fig 2). The physiologic basis for this is unclear, but may relate to the poorer sampling of the AIF and tissue curves under high flow conditions.

In our hands, PWI CBF maps created from single-shot EPI images underestimate xeCBF, have about 25% patient-to-patient variability, and have poor global CBF correlation with bias that is dependent on the baseline xeCBF levels. These factors limit diagnostic confidence of quantitative mrCBF measurements in individual patients. Limitations of the current study include the use of global CBF values for each technique; it is possible that there is better correlation for different tissue types (i.e., white vs gray matter) or based on CBF level (such as PWI overestimation of xeCBF in regions with large cortical vessels); examining this relationship will be a focus of future work. Further refinement in algorithms to remove PV artifact (4) and to account for BB nonlinear relaxivity, coupled with improved AIF morphology achievable with multiecho sequences (9-10) may lead to improvements in quantitative PWI CBF.

Acknowledgements: This work was supported in part by the NIH (2R01EB002711, 1R21EB006860, P41RR09784, PERFUSE), the Lucas foundation, and the Oak foundation. The authors appreciate the statistical assistance of Dr. Jarrett Rosenberg.

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