Variability In qCBF Obtained From Deconvolution-based Perfusion-Weighted MR Techniques

D. J. Niven[1], J. C. Kosior[1,2], P. J. Dickhoff[3], I. Dzialowski[4,5], S. Subramaniam[4,5], A. M. Demchuk[4,5], R. Frayne[1,6]

[1]Seaman Family MR Centre, Foothills Medical Centre, Calgary Health Region, Calgary, Alberta, Canada, [2]Electrical and Computer Engineering, University of Calgary, Calgary, Alberta, Canada, [3]Diagnostic Imaging, Rockyview General Hospital, Calgary Health Region, Calgary, Alberta, Canada, [4]Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada, [5]Calgary Stroke Program, Foothills Medical Centre, Calgary Health Region, Calgary, Alberta, Canada, [6]Radiology, University of Calgary, Calgary, Alberta, Canada

Introduction

Cerebral blood flow (CBF) maps generated from a perfusion-weighted MR imaging sequence require deconvolution of a tissue signal-versus-time curve by the selected arterial input function (AIF). The AIF is typically obtained by placing a cursor in a major cerebral artery and selecting input voxels that have an early rise in contrast concentration, a small bolus width, and a large signal change.[1] Quantitative CBF (qCBF) values are then determined by deconvolution of the tissue by the arterial signals. Identification of AIF is one issue complicating qCBF. To decrease partial volume effects, the AIF should be measured in a large artery, but to minimize bolus dispersion effects, the AIF should also be measured close to the tissue-of-interest.[2] Thijs *et al.* demonstrated that there is a large variation in perfusion-weighted imaging (PWI) lesion volume with different AIF locations and that AIF-selection variation results in different qCBF values.[3] CBF measurements also require identification of a region of normal white matter (NWM) to a value of 22 ml/min/100 g.[4] Currently, most perfusion maps are generated from operator-selected AIF; likewise, qCBF estimates rely on user-determined NWM regions, leading to potentially high variability. In this study we sought to evaluate the inter- and intra-observer variability due to AIF and NWM region selection on qCBF.

Methods

This study was a retrospective cohort study in which DWI and PWI images were acquired on a 3T MR scanner (General Electric Healthcare; Waukesha, WI). Twelve (12) patients with acute ischemic stroke (AIS) were imaged. Inclusion criteria for this study were (a) a non-lacunar acute ischemic stroke (AIS) involving the middle cerebral artery (MCA) and (b) the presence of a DWI lesion at initial and follow-up (7 day to 30 day) imaging. qCBF maps were produced on a workstation (Apple Computer; Cupertino, CA) using PerfTool.[5] Unscaled qCBF values were cross-calibrated by setting a region in NWM to 22 ml/min/100 g. Other tissues, including normal gray matter (NGM), infarcted tissue core (IN), and tissue contralateral to the infarcted tissue (CL), were scaled accordingly. To determine the inter- and intra-reviewer variability in CBF measurements, as well as the relative contributions from AIF and ROI selection on overall variability, the assessment of PWI image quantification was conducted in four stages. At each stage the reviewers were permitted to choose regions for CBF quantification. For comparison, qCBF values using regions selected by consensus prior to image review were also calculated. Outliers (qCBF > mean + 2 standard deviations in NGM) were removed prior to employing a generalized linear model to determine the effects of the factors on CBF values. Factors input into the model included AIF selection (manual vs semi-automated), ROI selection (user vs pre-determined), reviewer (reviewer 1 vs 2), embolic AIS origin, and trial number. To determine intra- and inter-rater variability we performed regression analyses on combined intra- and same-trial inter-reviewer variability data respectively.[6] For all analyses, a two-sided α-level of 0.05 was considered significant.

Table 1. Results of a full-factorial multivariate analysis-of-variance performed to determine the effects of various factors on qCBF. CBF values are provided as mean ± standard deviation.

	NGM		IN		CL	
	CBF	p	CBF	p	CBF	p
Pooled Data	50.8 ± 20.2		31.4 ± 18.2		44.3 ± 18.5	
ROI Selection		<0.001[a]		0.850[a]		0.020[a]
User	36.8 ± 15.0	<0.001	31.1 ± 20.4	0.830	39.8 ± 18.3	0.006
Pre-determined	61.4 ± 17.0		31.7 ± 16.6		47.8 ± 18.0	
AIF Selection		0.840[a]		0.750[a]		0.630[a]
Manual	51.1 ± 19.7	0.862	30.8 ± 16.4	0.646	43.9 ± 18.7	0.779
Semi-automated	50.6 ± 20.9		32.1 ± 19.9		44.7 ± 18.4	
Embolic AIS		<0.001[a]		0.001[a]		<0.001[a]
No	55.8 ± 19.4	<0.001	27.2 ± 16.5	<0.001	50.3 ± 18.1	<0.001
Yes	44.3 ± 19.6		37.1 ± 19.0		36.5 ± 16.1	
Observer		0.490[a]		0.010[a]		0.280[a]
Reviewer 1	50.9 ± 19.9	0.930	34.7 ± 19.6	0.031	45.6 ± 18.5	0.310
Reviewer 2	50.7 ± 20.6		28.7 ± 16.7		43.0 ± 18.5	

[a]*A measure of the significance of the effect of each factor on variability in qCBF for each tissue region. All other p-values are a result of post-hoc t-tests.*

Results

The average age of our population was 73.0 ± 7.3 years old with 6 males and 6 females. There were equal numbers of left and right MCA infarcts with 5 of 12 infarcts having an embolic etiology. Of the 192 measurements, 25 (13.0%) exceeded the outlier threshold and were excluded. The impact of each factor on the individual tissue regions are given in Table 1. ROI selection ($p < 0.0001$) and embolic etiology ($p < 0.0001$) were found to significantly impact the overall variability in the pooled qCBF. ROI selection was a significant contributor toward variability in NGM, and CL CBF values, whereas embolic AIS etiology was significant for all tissue regions. Observer was only significant for IN CBF. However, a sub-analysis suggested that the Observer factor was correlated with excluded outlying data. Interestingly, AIF selection did not contribute significantly to overall and tissue-specific variability ($p > 0.05$). The results of simple regression analyses performed on combined intra- and same-trial inter-reviewer data respectively suggested poor intra- and inter-observer variability. More specifically, the R^2 for the intra-observer analysis in NGM, IL, and CL were 0.241, 0.214, and 0.230, respectively. For the inter-rater analysis, the R^2 were 0.232, 0.276, and 0.009 for NGM, IL, and CL, respectively.

Conclusions

There was significant variation in qCBF obtained from deconvolution-based perfusion-weighted MR techniques. ROI selection, embolic AIS etiology, and to a lesser extent the observer (IN only) had the greatest impact on qCBF variation. Interestingly, AIF selection, *i.e.*, manual versus semi-automated, did not contribute significantly to overall or tissue-specific qCBF variability. The low values of R^2 obtained from the regression analysis suggested that there is significant inter- and intra-rater variation in qCBF for each tissue region; likely a result of ROI selection and embolic AIS origin. These results suggest that the level of discordance in qCBF resultant of operator and AIS etiology is such that these values should not yet be incorporated into clinical decision making.

References

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