Stability of quantitative CBF measurements using the T1-based DCE approach

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Background:
Perfusion MRI based on use of an exogenous contrast agent can provide quantitative measures of cerebral blood flow (CBF). The limited spatial resolution during bolus-tracking often leads to a partial volume effect (PVE) on the arterial input function (AIF) [1,2] which in turn affects CBF quantitation. PVE correction of the AIF can be performed by scaling the AIF to a venous output function (VOF) free of PVE obtained e.g. in the sagittal sinus, or by calibrating CBF by the cerebral blood volume obtained with the steady state method. [3] Most previous studies have addressed this problem in dynamic susceptibility contrast (DSC) MRI and no studies have compared the effect of different correction methods. In healthy subjects, AIFs obtained from e.g. the right and left internal carotid artery (RICA and LICA) should ideally be identical and hence result in similar CBF estimates. In addition, repeated measurements using the same artery for AIF should also give similar CBF estimates. In practice however, the PVE often differs between vessels and between measurements. The aim of the study was to compare the effect of different PVE correction methods on 1) the agreement of CBF estimates, using either the RICA or LICA for the AIF measurement and 2) repeatability of CBF estimates in repeated measurements using the same vessel for AIF measurement.

Methods:
We analyzed data from 14 healthy, young subjects in whom same-day repeated DCE measurements had been performed (28 measurements in total). Dynamic T1 weighted images were acquired during administration of 0.05 mmol/kg of GdDTPA. Calculation of CBF maps was based on conversion of the MRI signal into concentration of GdDTPA in blood and tissue and subsequent deconvolution using Tikhonovs method as previously described.[4] T1 maps were used for automated segmentation into gray and white matter. Pixels with high CBV values were considered containing large vessels and segmented out.
CBF values using the different correction methods were calculated by multiplying uncorrected CBF (CBF_{TIK}) with a correction factor based on each of the four proposed correction methods: a) least square fitting of the arterial curve to the venous outflow curve by allowing time shifting of the venous curve and amplitude scaling of the arterial curve (CBF_{LSQR}), b) area under the arterial curve is increased in order to mach the area under the veine curve (CBF_{AUC}), c) estimation of CBV from the steady state arterial and tissue curve performed directly on the MR signal ($CBF_{SS\text{-}SIG}$) or d) performed after signals have been converted into concentrations ($CBF_{SS\text{-}CC}$).
For agreement mean difference is calculated as CBF_{RICA}–CBF_{LICA} and relative difference as $|CBF_{RICA} - CBF_{LICA}|/[(CBF_{RICA} + CBF_{LICA})/2]$.
For repeatability mean difference is calculated as CBF_1–CBF_2 and relative difference as $|CBF_1 - CBF_2|/[(CBF_1 + CBF_2)/2]$.
Repeatability is expressed as the difference between the first and the second measurement. CBF values are gray matter median CBF (ml/100g/min).

Results:
Agreement and repeatability of CBF values are summarized in table 1 and figure 1.
Correction based on steady state methods resulted in poorer agreement between CBF_{RICA} and CBF_{LICA} and poorer repeatability compared to least square and AUC methods, with least square yielding slightly better agreement between CBF_{RICA} and CBF_{LICA} compared to AUC. CBV correction based on concentration curves resulted in higher CBF values than the other methods. Comparing the first and the second measurement uncorrected CBF was lower in the second measurement, but there was no such bias between the two measurements using any of the correction methods

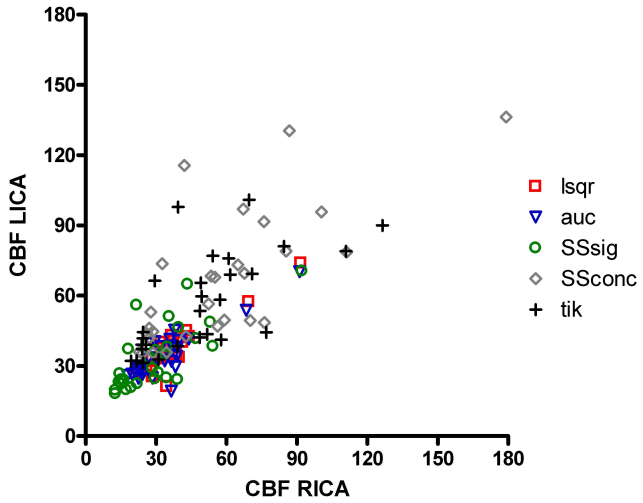

Figure 1. Agreement of CBF values using RICA or LICA for the AIF measurement

Table. 1 Influence of correction method on CBF measurements.

	Agreement (CBF_{RICA} vs CBF_{LICA})					Repeatability (CBF_1 vs CBF_2)				
	CBF_{TIK}	CBF_{LSQR}	CBF_{AUC}	$CBF_{SS\text{-}SIG}$	$CBF_{SS\text{-}CC}$	CBF_{TIK}	CBF_{LSQR}	CBF_{AUC}	$CBF_{SS\text{-}SIG}$	$CBF_{SS\text{-}CC}$
Mean ± SD	53.3±21.8	36 ±12.3	34.2±12.3	32.1±14.6	61.9±29.2	53.3±23.5	36 ±12.1	34.2±12.3	32.1±14.7	61.9±29.6
R^2	0.434	0.856	0.768	0.546	0.525	0.792	0.740	0.730	0.554	0.574
Mean diff. ± SD	-6.4±20.4	-0.2±6.3	-0.5±7.9	-3.4±11.7	-7.8±23.9	5.6±11.4*	1.7±7.8	1.5±7.9	0.6±11.6	4.8±22.5
Relative diff.% ± SD	31.6±22.3	13.2±10	18.3±12.7	29.4±21.3	31.6±22.9	16.3±11.1	14.0±11.9	15.2±11.8	17.6±14.3	19.5±15

Agreement CBF_{RICA} and CBF_{LICA} is calculated for scan 1 and 2 separately. Repeatability CBF_1 and CBF_2 is calculated for RICA and LICA separately.
p=0.01 for difference $CBF_1 - CBF_2$ (paired t-test),

Discussion
These results demonstrates that both the 1) choice of AIF for calculation of CBF and 2) the method for PVE correction of the AIF has a significant influence on calculated CBF values. Estimating the scaling factor using a least square fit of the arterial to the venous curve appeared to best compensate for the differences originating from the choice of AIF. Both for corrected and uncorrected CBF values the relative difference between CBF_{LICA} and CBF_{RICA} is smaller compared to what has previously been reported with dynamic susceptibility contrast MRI [3], still PVE causes a significant inherent error in quantitative CBF measurements using perfusion MRI.

References: [1] A.E. Hansen MRM 2009; [2] M. van Osch MRM 2003; [3] K.E. Sakaie JMRI 2005; [4] H.B.W. Larsson JMRI 2008