Limitations of a multiplicative correction of partial volume effects on the arterial input function in bolus-tracking perfusion

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Introduction: Quantification of cerebral blood flow (CBF) using bolus-tracking MRI is critically dependent on correct determination of the arterial input function (AIF) (1,2). The AIF is the concentration of tracer which enters the brain as a function of time. It is sampled in a supplying artery, which is often subject to a partial volume effect (PVE) due to the limited spatial resolution resulting from the requirement of a short image sampling time. A commonly used correction approach entails a multiplicative scaling of a measured AIF concentration-time curve (e.g. (3-5)). Here we show using in vivo data obtained with a T_1-weighted perfusion imaging approach (6) that such a multiplicative rescaling can lead to distortion of the AIF resulting in serious errors in CBF estimates. We propose to use an easily measurable quantity denoted the tissue signal fraction (TSF) as a measure of the applicability of a multiplicative rescaling.

Theory: It is commonly assumed that a partial volume – affected AIF, $c_{PVE}(t)$, relates to the true concentration curve in the vessel $c(t)$ as $c_{PVE}(t) = K\,c(t)$. The factor K can be determined by requiring that that the time integral of $c(t)$ matches the integral of a reference concentration curve free of PVE, e.g. obtained from a posterior vein. Hence, the PVE can be corrected by a multiplicative rescaling of the measured AIF (3-5). However, can the assumption $c_{PVE}(t) = K\,c(t)$ be justified? The PVE on the AIF occurs when the measured MR signal s_{PVE} contains contributions from both blood and tissue, hence $s_{PVE}=k\,s_{blood}+(1-k)\,s_{tissue}$, where k is the blood volume fraction. If the tissue term can be neglected compared to the blood term, then $s_{PVE}=k\,s_{blood}$. If also non-linearities in the relation between MR signal and tracer concentration are ignored, then $c_{PVE}(t) = k\,c(t)$. Therefore the multiplicative rescaling approach is strictly valid only if the tissue contribution to the measured AIF signal can be neglected. To quantify the tissue contribution we define the tissue signal fraction (TSF) as $\mathrm{TSF} = \int s_{tissue,est}(t)\,dt \,/\, \int s_{PVE}(t)\,dt$. The estimated tissue signal $s_{tissue,est}$ is sampled in the vicinity of the artery used for the AIF measurement. For the T_1-weighted perfusion imaging approach used here tissue signals are lower than blood signals, hence the TSF is smaller than 1 and approach 0 when the tissue signal is small. Our hypothesis is that the multiplicative rescaling is able to successfully correct an AIF subject to PVE only if the TSF is a small number.

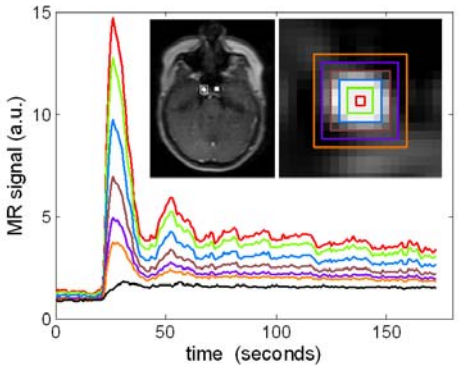

Fig. 1. AIF signals measured in the ICA. Color of curve correspond to color of ROI (insert). Black curve: estimated tissue signal.

Methods: Six patients with a primary brain tumour underwent perfusion imaging as a part of their diagnostic procedure. MRI was performed on a 3 T Philips Achieva (Philips Healthcare, The Netherlands) equipped with an eight-element receive head coil. A T_1 measurement and the bolus tracking utilized a saturation recovery gradient echo sequence. Dynamic image parameters were: saturation delay 120 ms, flip angle 30°, TR=3.9 ms, TE=1.9 ms, centric phase ordering, SENSE factor 2, matrix 96×61 (reconstructed to 256×256), FOV 230×182 mm^2, 4 slices, slice thickness 8 mm, dynamic image time 1.0 s, 180 frames. In order to obtain an AIF with minimal partial volume, the most caudal slice was placed orthogonal to a vertical segment of either the left or right ICA just below the carotid siphon based on a MR angiography. The in-plane spatial resolution was 2.4×3.0 mm^2, smaller than the typical internal carotid artery (ICA) diameter of 5-6 mm. The Gd bolus (Magnevist; 0.05 mmol/kg bodyweight) was injected after the 10th frame.
The voxel in the ICA with maximal signal during the bolus passage was first chosen for the AIF. To generate additional AIFs with increasing degree of PVE, we used larger regions of interest (ROIs), see Fig. 1. The estimated tissue contribution to the AIF was measured from the regional difference of the two largest ROIs. A reference concentration curve was measured from the voxel with maximal signal during the bolus passage in the sagittal sinus. Finally, a tissue ROI was selected in normal appearing grey matter to exemplify the CBF quantification. Tracer concentrations were calculated from the measured MR signal according to the signal equation for a saturation recovery. The AIFs were rescaled multiplicatively by the above scheme. The multiplicative correction was applied to the MR signal curves to avoid distortions from non-linearities in the relation between MR signal and tracer concentration. CBF was quantified by model-free deconvolution using Tikhonov regularization (as in (6) for all AIFs. CBF deviations ΔCBF due to PVE were calculated relative to the CBF value obtained with the AIF from a single voxel.

Results: The ICA used for AIF determination was easily identifiable when using the T_1 weighted imaging approach (Fig.1, insert). With increasing size of the AIF sampling region, and hence increasing PVE, the measured signal decreased because tissue signals are smaller than blood signals for a saturation recovery (Fig. 1). The estimated tissue signal (black curve) is smaller than all arterial input signals, but not much lower than those most affected by partial volume. Fig. 2 shows the rescaled AIFs. With increasing PVE, the AIF shape changes. The insert in Fig. 2 shows the CBF deviations obtained when employing rescaled AIFs. ΔCBF is shown as a function of the TSF calculated for each AIF. For all 6 subjects the CBF deviations increase dramatically when the TSF is larger than 0.5-0.6. For TSF < 0.4 all CBF deviations were less than 15%. Matching the peak height of the AIFs instead of the time integrals did not change the overall behaviour (data not shown).

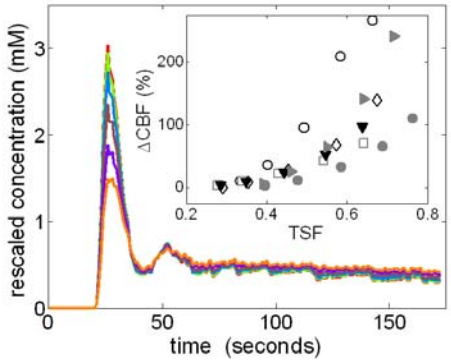

Fig. 2. Rescaled AIFs from measurements in Fig. 1, color correspond to color of ROI. Insert: CBF deviations due to PVE using rescaled AIFs for 6 subjects (different symbols), as function of the TSF.

Discussion: As demonstrated here, the multiplicative rescaling can only restore the AIF and the resulting CBF estimate below a certain level of PVE. This was expected from the arguments in the Theory section – a simple multiplication of the AIF to correct the PVE is only valid if the tissue contribution to the AIF is small. Distortions of AIF shape due to dispersion (7) and nonlinear T_2^* effects (8) in DSC perfusion have earlier been shown to lead to CBF errors. The present findings using a T_1-weighted perfusion imaging suggest that the effect of multiplicative rescaling should be evaluated for DSC perfusion as well.
The TSF is an independent measure of partial volume which is easy to obtain experimentally. The results in Fig. 2 demonstrate that for T_1-weighted perfusion imaging the TSF is a good predictor of whether a multiplicative rescaling of the AIF is capable of restoring the CBF value. Hence we suggest that the TSF is estimated before the application of a multiplicative AIF rescaling in practise.

References: (1) Calamante F, et al., Stroke 33:1146 (2002); (2) Chen JJ, et al., JMRI 22:390 (2005); (3) Ostergaard L, et al., JCBFM 18:935 (1998); (4) Ducrueux D, et al., AJNR 27:1059 (2006); (5) Knutsson L, et al., JMRI 26:913 (2007); (6) Larsson H, et al., JMRI 27:754 (2008); (7) Calamante F, et al., JMRI 22:718 (2005); (8) Calamante F, et al., MRM 58:544 (2007)