New criterion for automatic AIF selection in DSC perfusion MRI to exclude partial volume effects

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Introduction

Partial volume effects (PVEs), which arise from the relatively low spatial resolution used in dynamic susceptibility contrast (DSC) MRI, often hamper the selection of the arterial input function (AIF, the evolution of the concentration contrast agent in a brain-feeding artery). PVEs have been shown previously to lead to shape changes in the AIF (1-3). More importantly, PVEs can lead to concentration profiles that are narrower and have a higher maximum than the true shape. This occurs when the tissue and arterial components of the signal at the peak concentration cancel out due to having opposite phases. Automatic and manual AIF selection procedures select voxels for the AIF measurement based on empirical rules (e.g. small width, high maximum and steep rise). These rules, however, do not exclude all voxels exhibiting PVEs, thus potentially leading to an erroneous measurement of the AIF. Since PVEs are inherently non-linear with respect to the concentration of contrast agent (1,2), the second passage of the contrast agent or the post-bolus equilibrium value (the 'steady state') provides additional information that can be used to identify AIF measurements affected by PVEs. In this study, we propose a method that exploits this extra information to identify AIF voxels that display minimum shape effects of partial volume (even if the partial volume itself might be present and the total scaling might vary (3)).

Theory

From tracer kinetics theory, it is known that:

$$[1] \qquad CBV = \frac{AUC_{tissue}^{1st\ passage}}{AUC_{AIF}^{1st\ passage}} = \frac{AUC_{tissue}^{2nd\ passage}}{AUC_{AIF}^{2nd\ passage}} = \frac{SS_{tissue}}{SS_{AIF}}$$

where AUC is the area-under-the-curve and SS is the steady state. This also implies that for each PVE-free voxel (irrespective whether it is an arterial or a tissue voxel):

$$[2] \qquad \frac{AUC_{tissue}^{1st\ passage}}{AUC_{tissue}^{2nd\ passage}} = \frac{AUC_{AIF}^{1st\ passage}}{AUC_{AIF}^{2nd\ passage}} = \text{constant} \qquad \text{or}$$

$$[3] \qquad \frac{AUC_{tissue}^{1st\ passage}}{SS_{tissue}} = \frac{AUC_{AIF}^{1st\ passage}}{SS_{AIF}} = \text{constant},$$

Such a relationship as Eq.[3] will not hold true when the AIF is distorted due to PVEs. Since the ratio of the first passage to the steady state will vary between subjects, this constant needs to be estimated in tissue. The constant of Eq.[3] can be estimated using voxels in tissue without any arterial signal and the ratio using Eq.[3] for the AIF can be used to distinguish AIF measurements corrupted by PVEs. We propose this as a reference-based selection criterion, which can be taken into account when designing automatic AIF algorithms or for guiding manual AIF selection.

Table 1: the mean reference ratio value and its standard deviation of the gray and white matter average of six patients

Patient	Mean GM	Standard deviation	relative stdev	Mean WM	Standard deviation	relative stdev
1	0.0236	0.0022	9.3%	0.0211	0.0038	17.8%
2	0.0208	0.0014	7.0%	0.0194	0.0019	9.8%
3	0.0262	0.0025	9.6%	0.0234	0.0016	7.0%
4	0.0363	0.0036	10.0%	0.0319	0.0018	5.5%
5	0.0261	0.0023	8.9%	0.0240	0.0018	7.6%
6	0.0349	0.0034	9.7%	0.0317	0.0023	7.4%

Methods

Both reference ratio measurements in tissue as well as AIF measurements in and near the middle cerebral artery (MCA) were investigated using simulations (implemented in MATLAB) and in vivo examples (six DSC-MRI exams of patients suffering from Systemic Lupus Erythematosus; 3T (Achieva, Philips, the Netherlands) using dual echo segmented EPI ($TE_1\backslash TE_2\backslash TR$ 11\31\600 ms), flip angle 40º, voxel size 2.3x2.3x6.2 mm^3). Equation [3] was evaluated in this study using a gamma variate fit to model the first passage and the mean value of the last ten acquired images for the steady state. Equation [2] was not investigated, because it has lower CNR and the second passage is more difficult to determine due to the overlap of the first and subsequent bolus passage. The effects of different factors, such as T_1 relaxation changes in tissue, SNR and contamination with the tissue response, on the ratio value of Eq.[3] were studied using the simulations. In vivo, a confidence interval for the ratio in Eq.[3] for gray matter and white matter was determined. In an in vivo experiment, the ratios of the AIF measurements in and near the MCA were compared to the 95% confidence interval of the ratio as determined in tissue of the same subject ($\mu \pm 2\sigma$).

Results

Simulations showed that T_1 relaxation changes in tissue seriously affect the ratio for short repetition times (used in segmented EPI) or high flip angles, which is in agreement with literature (4). Therefore, T_1 effects were corrected for in vivo data using a dual echo approach (5). The confidence intervals of the in vivo reference ratio value of gray matter and white matter were estimated. The mean ratio varies over subjects as well as the standard deviation; however, the relative standard deviation is almost constant for gray matter and has a value of approximately 10% (see Table 1) leading to a confidence interval of the mean value ± 20 %. Furthermore, the average ratio for white matter is significantly lower ($p<0.005$) than that of gray matter, possibly due to non-linearity's in the tissue contrast agent relationship (6). Figure 1 shows that AIF measurements superior to the MCA and in tissue posterior to the MCA provide correct AIF measurements, which is in agreements with previous prediction based on numerical modeling (3). However, false positives also occurred indicated with the blue dot in figure 1. This profile shows a distorted first passage and the gamma variate fit is no longer a suitable model for the AUC estimation. However, this curve also shows a wider than normal width of the ΔR_2^* profile, making detection possible with an additional criterion such as small FWHM.

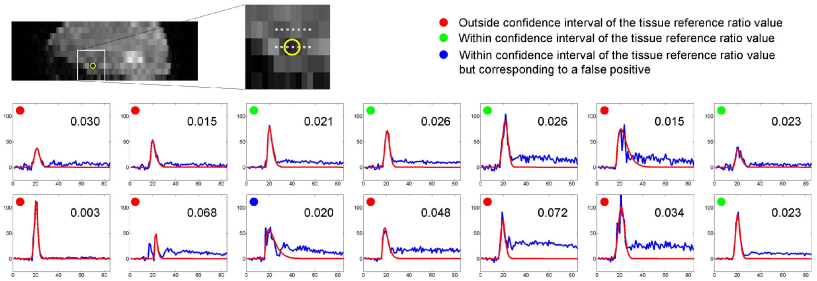

Figure 1: *AIF measurements in and around the MCA (in patient 1). The blue line is the ΔR_2^* profile and the red line is the gamma variate fit through the first passage. The steady state is estimated using the last ten acquired images. The top row of AIF profiles is in the slice superior to the MCA and the bottom row shows AIF profiles in and next to the MCA. The small colored circle indicates whether the ratio of the AIF measurement falls within the confidence interval, which is for this subject [0.019 0.028]. The yellow circle in the two sagittal images represents the location of the MCA in the patient.*

Discussion and conclusions

We propose a new criterion for AIF selection that is based on tracer kinetic theory. This criterion can aid in the exclusion of PVEs, especially those that have a high maximum value and a small width, which are normally not excluded by automatic selection criteria. The criterion should be used as an additional, rather than a sole, criterion because false positives do occur. Partial volume effects can alter the shape of the first passage making the gamma variate fit an unsuitable model; however, the erroneous profile can easily be detected using a small width criterion.

References
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