Effects of Contrast Agent Accumulation on Background Correction of Phase-Based Arterial Input Functions

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Introduction
The quality of pharmacokinetic parameters derived from Dynamic Contrast-Enhanced MRI (DCE-MRI) and perfusion estimates from Dynamic Susceptibility Contrast MRI (DSC-MRI) depends strongly on the accuracy of the measured Arterial Input Function (AIF). Traditionally, the AIF is calculated from magnitude signal intensity but this is complicated by issues such as signal saturation, non-linear contrast agent (CA) concentration dependence in blood and in-flow effects. A promising alternative to the standard intensity based methods is to use the phase shift induced by the CA [1]. The phase shift is linear with CA concentration and phase measurements are also beneficial in terms of SNR [2]. The phase is sensitive to motion and $B_0$ drift, and a background phase is thus normally subtracted from the AIF phase. However, the background region may also contain CA which can lead to erroneous phase AIFs after background subtraction, typically an unrealistically low CA concentration in the AIF tail. The purpose of this study was to investigate the importance of CA in the background and to develop a background correction method that is less sensitive to CA accumulated in the background.

Method
Six patients were investigated and a total of 18 exams were performed (1.5 T Siemens Espree). The AIF was obtained from a prebolus injection (1/3 of the total dose of 0.1 mmol/kg body weight, Magnevist, Bayer Schering Pharma) using a 2D spoiled gradient echo (SPGR) sequence with TR/TE = 9.2/5.58-5.91 ms, FA = 15°, matrix = 128 × 96-104 × 1 and bandwidth per pixel = 190-200 Hz. The temporal resolution of the sequence was 0.57 s and 450 images were acquired. The imaging slice was placed approximately 5 mm below the nose and through the lower part of the cerebellum. AIFs were extracted from the right and left internal carotid arteries using a pair-wise subtraction and summation method [1] and automatic tracking of vessel movement [3]. Background ROIs were placed in non-cerebral tissue as annuluses around the AIF ROIs. In addition to the AIF registration, standard DCE-MRI images were acquired, using 3D SPGR sequences, during and after the main injection of CA. To assess the accumulation of CA in the background the background ROI was divided into eight parts based on the magnitude signal intensity. It was assumed that the partition with the smallest phase ($Φ_{\text{min}}$) corresponded to voxels with none or small CA content and that the difference between the partition with the largest phase ($Φ_{\text{max}}$) and $Φ_{\text{min}}$ was proportional to the CA content in the background. The proportionality constant $k$ was found from a least squares solution of

$$Φ - Φ_{\text{min}} = k (Φ_{\text{max}} - Φ_{\text{min}})$$

where $Φ$ is the phase of the entire background except the 20% most hyperintense pixels which were excluded to remove large vessels from the background region. The AIFs, i.e. the average of right and left ICA, corrected for CA in the background were, in combination with tissue concentration data obtained by the standard DCE-MRI experiment, used for estimation of blood plasma volume $v_p$ in gray matter. Both the peak and tail data were used and the results were compared using Chen’s modified t-test for paired samples and skewed distributions.

Results
Fig. 1a shows an example of AIF phase data before and after correction for the CA in the background. In Fig. 2b, the average correction for CA in the background is displayed together with the average AIF from all exams. From Fig. 2b it is clear that correction for the CA accumulation in the background is significant especially for the tail of the AIF. The plasma volumes estimated from the peak and tail parts of the AIFs were 2.74 ± 0.98 % and 6.19 ± 2.9 %, respectively. The paired test showed that $v_p$ based on the AIF tail was significantly larger ($p < 0.0001$) than $v_p$ based on peak data. The difference indicates that the simple model presented above for estimation and correction of CA in the background was helpful but most likely insufficient.

Conclusions
This study shows that CA accumulated in the region used for background correction of phase AIF data can present a significant problem, especially for DCE-MRI where the tail of the AIF is of particular importance. The problem can be reduced using the method presented in this study, but, the present results also indicate that further in-vivo research is needed to obtain accurate phase-based AIFs over an extended time.

References