Optimization of Arterial Input Function Selection for Cerebral Perfusion Imaging with Quantitative Blood Volume Correction

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Introduction: Dynamic susceptibility contrast-enhanced (DSC) magnetic resonance (MR) imaging is increasingly practiced in clinical settings to evaluate cerebral perfusion because it can produce parametric maps that contain important physiological and hemodynamic information of the brain tissue. Commonly used parametric maps include the cerebral blood volume (CBV), the cerebral blood flow (CBF) and mean transit time (MTT). In order to calculate these, MR signal in the brain is measured as a function of time after a bolus of MR contrast is administered. The contrast concentration curve in a carefully selected arterial voxel ($C_a(t)$) is used as the arterial input function (AIF). CBV is calculated as $CBV = \int C_t(t)dt / \int C_a(t)dt$ and the AIF is deconvolved from the tissue curve ($C_t(t)$) to obtain the tissue residue function ($R(t)$) and blood flow: $CBF \cdot R(t) = C_t(t) \otimes^{-1} C_a(t)$ [1]. The selection of the AIF in a previous work is primarily based on its early arrival time and signal change [2]. Since the AIF is very likely to suffer from partial volume effects to various degrees or MR signal saturation, it is difficult to obtain absolute quantitative CBV and CBF maps. The ability to measure perfusion quantitatively would greatly facilitate patient diagnosis, and enable comparisons among patients or repeated scans for the same patient. More accurate CBV measurement can be achieved with techniques such as the T1 bookend method [3] or the infusion method [4], which can correct the CBV measured with the bolus data. In such a combined measurement, the selection of AIF can be optimized to more accurately capture contrast dynamics rather that contrast volume.

Theory: An ideal AIF voxel should be completely composed of arterial blood. Therefore, several desirable characteristics of the AIF contrast concentration-time curve include: early arrival time, large signal change and fast passage. The blood fraction in the brain tissue, however, is typically only a few percent in volume. In order to produce sufficient signal in the tissue, the MR contrast can easily saturate MR signals in a voxel that contains mostly blood, leading to underestimated area under the curve (AUC) for the AIF and overestimated CBV calculation. Another factor that affects perfusion calculation is the partial volume effects, primarily due to the large slice thickness needed for sufficient brain coverage. In our simplified model for the mixed voxel, a fraction (β) of the total voxel volume is occupied by arterial blood and the MR signal of the tissue in the remaining volume is ignored. The apparent AIF ($C_a'(t)$) becomes $C_a'(t)=\beta*C_a(t)$, and therefore the CBV is scaled: $CBV' = \int C_t(t)dt / \int C_a'(t)dt = CBV/\beta$. The deconvolution is then $C_t(t) \otimes^{-1} C_a'(t) = CBF \cdot R(t)/\beta$. Since the peak of $R(t)$ is normalized to unity, the calculated $CBF'=CBF/\beta$ is scaled by $1/\beta$. Nonetheless, MTT calculated by the central volume theorem $MTT'=CBV'/CBF'$ is not affected by β. Hence, a voxel of mixed arterial blood and tissue may better reflect the temporal information of the true AIF than a saturated voxel with a larger fraction of arterial blood.

Methods: The selection process has been refined into an automated selection process followed by a user-supervised process. In tailoring our AIF selection for bolus data with CBV correction, voxels are examined and filtered with specific criteria designed to optimize depiction of temporal dynamics. The automated process begins with a conventional removal of voxels with low pre-contrast MR signals. Then the time series of MR signals for the remaining voxels are normalized to their pre-contrast background signal and rectified; voxels in the top 10% AUC are kept. Next, the arrival time and an oscillatory index (based on the 2nd order differential) are calculated to select arterial voxels not corrupted by physiologic noise. Voxels with top 10% early arrival times and top 90% non-oscillatory voxels are kept. The signals of the remaining candidates are converted to contrast concentration curves, which are fitted with the gamma-variate function. Voxels with large fitting errors are removed, and the fitted curve used to calculate the AUC and full width at half maximum (FWHM) of the candidate AIF curves. Finally, a predetermined number of AIF candidates are chosen based on a simultaneous maximization of the AUC and minimization of the FWHM, until the desired number of candidates has been obtained. The locations and concentration-time curves of all AIF candidates are then shown to the operator who then chooses from the remaining AIF candidates based on location and quality of the fitted curves.

Our human subjects underwent a series of scans, including two T_1 weighted Look-Locker EPI scans before and after an intravenous injection (1.0 mmol/kg at 3 mL/s) of Gadodiamide (Omniscan, GE Healthcare, Princeton NJ) . The change between pre-contrast and steady-state T_1 values were used to quantify the CBV of a slice in the volume of interest [3]. During the contrast bolus passage, a T_2* weighted EPI sequence was used to obtain DSC MR signals. The algorithm was compared to a published method for automated AIF selection designed for relative CBF and CBV from bolus data (hereafter, the "standard" algorithm) alone using criteria that emphasize AUC and early arrival time only [2].

Results and Discussion: Typical AIF candidates (red in the MCA and blue in the circle of Willis) resulting from the automatic AIF selection algorithm are shown in Fig. 1. The AIF in green was selected by the standard algorithm. Although the green curve has a larger AUC, indicating less partial volume averaging, it has a longer transit time (FWHM=6.94 s) and is not modeled well by a gamma-variate function. With an independent assessment of CBV, the AUC is no longer a central selection criterion. Moreover, an AIF with artificially long transit time may lead to underestimated MTT and overestimated CBF in the tissue. Therefore, we chose the AIF candidate with the shortest transit time (#1, FWHM=5.19 s) for perfusion calculation. The resulting corrected CBF map is shown in Fig. 2. The CBF map was corrected with the T1 bookend technique, which produced reasonable results: 48±19 and 28±8 ml/100g/min for GM and WM.

Conclusions: When a bolus perfusion measurement in conjunction with a quantitative CBV correction technique, the AUC criterion for AIF selection may be relaxed and the transit time characteristics may be emphasized for more accurate CBF map calculation.

References: **1.** Ostergaard et al, MRM 1996; 36:726-736. **2.** Carroll et al, Radiology 2003; 227:593-600. **3.** Shin et al MRM 56:138-145. **4**.Newman et al, MRM 50:844-855.

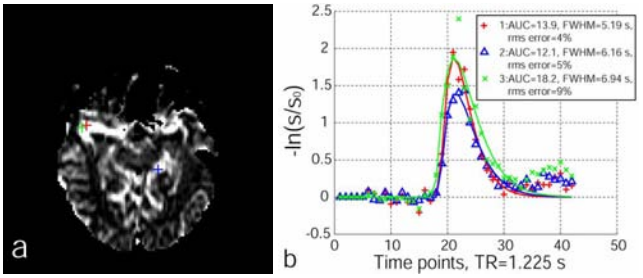

Fig. 1 AIF candidates: (a) locations, and (b) contrast concentration curves at these locations.

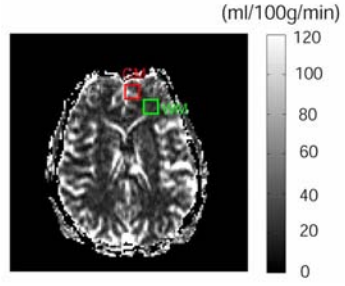

Fig. 2 CBF maps corrected with independent T1 measurement of CBV.