The Effects of Background Micro-circulation in the AIF Measured from DSC MRI of the Brain

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Introduction: Dynamic susceptibility-contrast (DSC) MR imaging can provide measures of various hemodynamic properties [1], most notably cerebral blood flow (CBF), cerebral blood volume, and mean transit time (MTT). At the basis for these measurements is obtaining an accurate arterial input function (AIF). Most studies use a relative arterial input function that contains only the shape information of the AIF. In the rest of this abstract, AIF only refers to the shape of the arterial input function.

A well accepted starting point for obtaining the AIF is to measure the change in R2* (1/T2*) in the region of a major artery. Using sampling points in the near vicinity of the middle cerebral artery (MCA) is common in clinical studies. Because of susceptibility phenomena, the areas that best reflect the true arterial input function are actually found in the near vicinity of the vessel [2-4], where large signal intensity change can be detected in certain isolated pixels. We note that the signal intensity in the region used for sampling the AIF is affected not only by the tracer in the artery, but also by tissue perfusion (microcirculation) at the sampling location. The purpose of this study is to demonstrate how the effect of background perfusion can be corrected and to investigate the changes in the measured AIF parameters and MTT value with this correction.

Rationale: The AIF is measured through the R2* change, $\Delta R2^*$, in the vicinity of MCA. We assume that the $\Delta R2^*$ can be divided into two parts. First, as a tracer passes through an artery, the magnetic susceptibility of the blood in the vessel increases and the pixels in the vicinity of the vessel, where the AIF is sampled, experience a magnetic field gradient that is linearly proportional to the tracer concentration. Secondly, the perfusion of the tracer in the sampling region also causes an R2* change. Therefore, the observed R2* change at the point of AIF sampling can be written as: $\Delta R2^*_{near} = \Delta R2^*_{AIF} + \Delta R2^*_{background}$. The AIF is linearly proportional to the first term on the right hand side only. We assume the second term on the right hand side can be obtained from another brain tissue location, $\Delta R2^*_{away} \approx \Delta R2^*_{background}$, where the influence from a major vessel is negligible but that is also as close as possible to the sampling points to avoid changes in tracer arrival time. Therefore the R2* change due to arterial input of the tracer is simply:

$$\Delta R2^*_{AIF} \approx \Delta R2^*_{near} - \Delta R2^*_{away} \qquad (1)$$

Methods: Using a 1.5 T Gyroscan Intera scanner, T2*-weighted EPI perfusion imaging was performed on 13 children (7 F, 6 M; age range = 5 - 20 yrs, median = 15 yrs) with clinically diagnosed brain tumors. The patients were already planned to receive a contrast agent (Magnevist, Berlex Laboratories, Wayne, New Jersey) as part of the standard clinical imaging protocol. This investigation was performed under a protocol approved by the Institutional Review Board. In all cases, the locations of the tumors were sufficiently far from the MCA to avoid any effect on our measurements.

The MRI parameters were: TE = 47 ms, flip angle = 40º, TR = 1.5 s, fov = 230 x 230 mm and sampling matrix size = 128 x 128. Ten transverse slices with a thickness of 6 mm were obtained. The recommended dosage of Magnevist injection is 0.1 mmol/kg. Depending on the situation (e.g., expected vascularity of the lesion), a double-dose (≈ 0.2 mmol/kg) was sometimes used. A power injector was used for all cases with injection rates 2-3 cc/s. Contrast injection was initiated at about 8 sec into the scan. Between 15-20 cc of saline was injected immediately after the contrast agent.

We used the region around the MCA in the transverse slice containing the base of the Sylvian fissure (Figure 1) for determining $\Delta R2^*_{near}$ and $\Delta R2^*_{away}$. We generally obtained 4-5 $\Delta R2^*$ time curves near the MCA and included pixels from both hemispheres. However, the difference, if any, between the AIF curves in the two hemispheres were found to be small, which is what would be expected considering that the sampled points were sufficiently far from any lesions. A region of gray matter (GM) not immediately surrounding the MCA was used to sample $\Delta R2^*_{away}$. After $\Delta R2^*_{near}$ and $\Delta R2^*_{away}$ were determined, $\Delta R2^*_{AIF}$ was calculated from Eq. (1). An IDL (Research Systems Inc., Boulder, Colorado) curve fitting routine was used to fit a gamma variate function to the tracer signal as a function of time for all regions of interest to obtain the time of arrival, time-to-peak (TTP), and the width (FWHM) of the $\Delta R2^*_{near}$ and $\Delta R2^*_{AIF}$ time curves. The average value and standard deviation of these parameters were calculated. The MTT of normal appearing white matter in frontal lobe (or occipital lobe when frontal lobe data were not available) and gray matter in putamen were estimated using the AIFs with and without the background correction, using a model independent approach [5,6]. The analysis was done using internally developed software. The tissue region of interest was traced out manually. The dynamic data, both AIF and the bolus in the tissue, were interpolated to a time resolution of 0.75 sec. The tracer residual function $R(\tau)$ was obtained by a SVD procedure. The vascular transport function $h(\tau)$ was calculated from $R(\tau)$, and MTT was calculated from the first moment of $h(\tau)$.

Results: The pixels showing the most prominent changes on the EPI amplitude images were generally not in the artery but instead nearby. The size of $\Delta R2^*_{near}$ was typically 3 to 4 times that of $\Delta R2^*_{away}$. Correcting the effect of the background microcirculation had a significant impact on the time dependence of $\Delta R2^*$ (Table 1 and Figure 2). A significant narrowing of the $\Delta R2^*$ curve was detected in most cases (Table 1). Furthermore, the center position of the arterial input bolus moved to a slightly earlier time. Longer MTT values were obtained using the AIF with correction (Table 2).

Discussion and Conclusions: The correction procedure introduced significant changes in the results of MTT quantification. The correction is more important for gray matter regions where blood flow is faster and the bolus is shorter.

Table 1. Parameters characterizing AIF (mean ± s.d.).

Without correction		With correction	
TTP (s)	FWHM (s)	TTP (s)	FWHM (s)
4.7 ± 0.9	7.3 ± 2.0	4.3 ± 0.8*	6.4 ± 1.7*

* $p < 0.001$, paired two-tailed t-test

Table 2. MTT (sec) in white matter and putamen (mean ± s.d.).

AIF without correction		AIF with correction	
White matter	Putamen	White matter	Putamen
4.1± 0.8	2.6 ± 0.7	4.8 ± 1.0*	3.3 ± 1.0**

* $p = 0.02$, ** $p = 0.0001$, paired two-tailed t-test

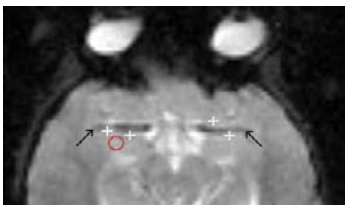

Fig.1. Locations of sampling for AIF (white crosses) and background perfusion (red circle).

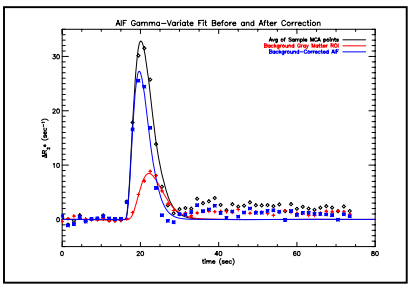

Fig.2. Time courses for uncorrected (black) and corrected (blue) AIF and the background perfusion (red).

References: 1. Rosen BR, et al. MRM 1991; 22:293-299. 2. Ostergaard L, et al. MRM 1996; 36:726-736. 3. Rausch M, et al. MRI 2000; 18:1235-1243. 4. Duhamel G, et al. ISMRM 11th meeting, 2003, p 2199. 5. Ostergaard L, et al. MRM 1996; 36:715-725. 6. Liu HL, et al. MRM 1999; 42:167-172.