A Model-Free Quantitative Arterial Spin Labeling Approach for Perfusion MRI

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INTRODUCTION: Brain perfusion is a very important physiological parameter providing information on whether it is still viable or ischemic. Conventional techniques for perfusion measurements use exogenous contrast agents or radioactive tracers, and may be restricted in patients with particular conditions, such as kidney failure or in pediatric populations. Arterial spin labeling (ASL) techniques are non-invasive and thus desirable in these populations as well as in repetitive perfusion follow-ups of patients or perfusion studies in healthy individuals. The quantitative cerebral blood flow (CBF) estimation from these data is traditionally calculated using a single compartment kinetic model. However, the validity of the assumptions behind such a general model is questionable, especially in pathological cases. Therefore a model-free ASL approach based on deconvolution techniques is proposed in this work for simultaneous CBF and arterial blood volume (aBV) measurements.

THEORY: Perfusion imaging encompasses both physiological mass transport and exchange mechanisms, which are considered as linear stationary systems. For the case of ASL-based perfusion imaging, a general kinetic model was formulated by Buxton at al. (1):

$$\Delta M(t) = 2 \cdot M_{a,0} \cdot f \cdot \int_0^t c(\tau) \cdot r(t-\tau) \cdot m(t-\tau) d\tau \qquad [1]$$

where $M_{0,a}$ is the equilibrium magnetization for arterial blood, f is the flow, $c(t)$ is the delivery function, $r(t-\tau)$ is the residue function describing the clearance of spin from the tissue and $m(t-\tau)$ describes the longitudinal magnetization relaxation. Traditionally, the magnetization difference ΔM(t) between label and control acquisition can be solved analytically, assuming single compartment behavior and plug flow. ΔM is then acquired at one or more time points and subsequently fitted to the model. Alternatively, if we measure the arterial input function, $AIF(t) = 2 \cdot M_{a,0} \cdot c(t)$ then a deconvolution of the measured perfusion-weighted signal time curve ΔM(t) by this AIF provides the residue function multiplied by the relaxation function and the perfusion rate: $f \cdot r(t-\tau) \cdot m(t-\tau)$, which maximum equals f.

METHODS: Local AIFs can be estimated by the subtraction of two perfusion-weighted images, acquired respectively with and without crusher gradients aimed at suppressing intravascular labeled signal. Furthermore, by knowing the duration of the bolus of tagged arterial blood, aBV can be estimated on a voxel-by-voxel basis. The locally estimated aBV is then used for scaling the AIF and absolute CBF is obtained by subsequently using singular value decomposition (SVD) for the deconvolution of the tissue perfusion curve (acquired with crusher gradients) by the AIF, (2,3). In order to know the exact temporal length of the bolus, we developed a new MRI pulse sequence, named **qua**ntitative **S**TAR labeling of **a**rterial **r**egions (QUASAR), that combines a **pul**sed **S**TAR labeling of **a**rterial **r**egions (PULSAR) labeling technique (4) with a Look-Locker strategy for sampling at multiple time-points (5) and a repetitive Q2-TIPS like bolus saturation scheme for clear definition of the arterial blood bolus (6). For validation of the method, six healthy volunteer were scanned, all giving written informed consent before participation. The experiments were approved by the local ethics committee. Average CBF values were calculated in four slices using the new deconvolution method as well as fitted to the standard model (1), modified for the Look-Locker readout (5). Scan parameters: 4 slices; thickness = 7 mm; gap = 2 mm; matrix = 64 × 64; FOV = 240 mm; α = 30°; T_R / T_E = 4000 / 23; ΔTI = 200 ms; number of time points = 18; SENSE factor = 3; labeling slab = 150 mm; inversion gap = 30 mm; crusher encoding velocity V_{enc} = [∞, 3 cm/s]; 80 averages; total scan time = 10min 40s. In addition to these perfusion scans, experiments were designed to optimize the value of the crusher gradients and the bolus duration. Also, validation of the assumption that arterial blood is completely renewed in between successive excitations of the Look-locker readout were performed, together with those concerning the eventual saturation effects experienced by the traversing blood moving from lower to upper slices.

RESULTS and DISCUSSION: The CBF and aBV values are summarized in Table 1 for total, gray (GM) and white matter (WM) respectively. CBF_1 is obtained using the deconvolution method and CBF_2 is gathered by fitting the data acquired with crusher gradients to the standard kinetic model. Values are mean/(mean ± s.e.m). Figure 1 shows from left to right: a deconvolved CBF-map; a fitted CBF-map, both in [ml/min/100g]; an aBV-map in [%]; and the fitted $R_{1app,eff}$ –map (5) of a representative volunteer in [s^{-1}]. Figure 2 shows from left to right: a single voxel AIF; the corresponding GM tissue curve; a neighboring WM tissue curve; and the calculated GM residue function, which in this particular case corresponds to a perfusion of 75ml/100g/min. Generally, our method provided CBF values 50% lower than those obtained using the general kinetic model. However, both values fall within the range of published literature (7). There could be several reasons for this discrepancy. The deconvolution method is known to underestimate the true flow (3), which a Monte-Carlo analyses confirmed (results not shown). On the other hand, perfusion values obtained by the standard kinetic model are based on assumptions that might be violated in reality, which would result in overestimated perfusion values. The validation studies showed that arterial blood was renewed in between excitations and negligible saturation effect was experienced by the traversing blood.

CONCLUSION: In the present work, a robust model-free method for absolute quantification of cerebral blood flow has been developed based on an SVD-deconvolution technique. It was evaluated on 6 healthy volunteers and the measured perfusion was in good agreement with the literature. A new pulse sequence has also been implemented, allowing independent measurement of the AIF on a voxel-by-voxel basis. This new approach provided lower CBF values than those obtained using the standard kinetic model. However, based on Monte-Carlo simulations, this approach appeared more robust than a 3-parameter fit based on the general kinetic model.

Figure 1

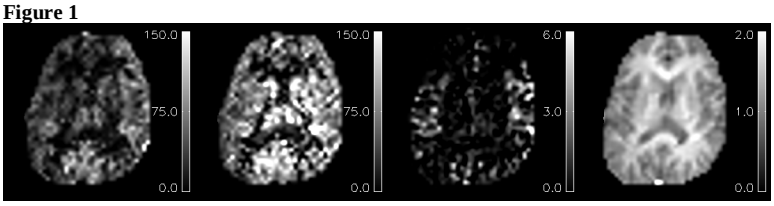

Figure 2

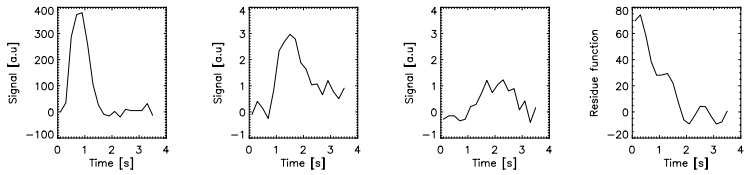

Table 1

	CBF_1 [ml/100ml/min]			CBF_2 [ml/100ml/min]			aBV [%]		
Subject	Total	GM	WM	Total	GM	WM	Total	GM	WM
1	55	70	40	86	97	75	0.8	1.3	0.2
2	66	77	51	92	98	85	0.6	1.2	0.1
3	32	38	27	52	53	51	0.7	1.2	0.1
4	39	51	25	62	69	38	0.5	0.9	0.0
5	37	43	28	56	58	53	0.6	0.8	0.2
6	45	56	29	64	74	51	0.9	1.5	0.2
Total	46±5	56±6	33±4	69±7	75±8	59±7	0.7± 0.0	1.2± 0.1	0.1± 0.0

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