Combined Blood:Brain Partition Coefficient and Perfusion Assessment using QUASAR

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INTRODUCTION: Perfusion is vital for the homeostasis and thereby survival of an organ and as such is a very important physiological parameter. MRI based perfusion methods include, among others, fully non-invasive arterial spin labeling (ASL) techniques. ASL is useful in the clinical evaluation of vascular diseases and it has gained great popularity within the basic neuroscience, mainly due to its potential for measuring quantitative perfusion. Also the ability of doing repetitive scans is an important asset of this technique for functional neuro-imaging. However, a few problematic factors still exist regarding the absolute quantification of cerebral blood flow (CBF). These include the estimation of the blood equilibrium magnetization M_{0b}, arrival time and shape of the bolus. While different methods have dealt with the latter two [1,2], correct estimation of M_{0b} still remains a source of error. Basically, it is needed in order to scale the acquired ΔM images from the control and label experiment, in order to obtain the flow. Unfortunately, acquiring the value is not trivial, neither within the ASL experiment itself nor in a separate scan. This is mainly due to partial volume effects with the surrounding tissue and pulsating behavior of the blood. In practice, M_{0b} is most often extracted from the sagittal sinus or by using the blood-brain partition coefficient λ, which is defined as the ratio between water content in blood and tissue ($M_{0b} = M_{0t}/\lambda$). The former suffers from partial volume problems as well as the fact that R_2* differs between the intended arterial blood and measured venous blood magnetization [1]. In single inversion time-point experiments, the signal from the control experiment is often taken as M_{0t} after correction for the T_R and expected or measured T1 of the tissue. M_{0b} is then extracted assuming the average partition coefficient for the brain $\lambda = 0.9$ [3]. However, the water density varies from region to region and in between tissues ($\lambda_{wm} = 0.82$, $\lambda_{gm} = 0.98$ [3]), thereby violating the assumption of a single partition coefficient for all tissues. Here we propose a method for estimating λ on a voxel by voxel basis, based on the multi TI data acquired using the QUASAR sequence [1].

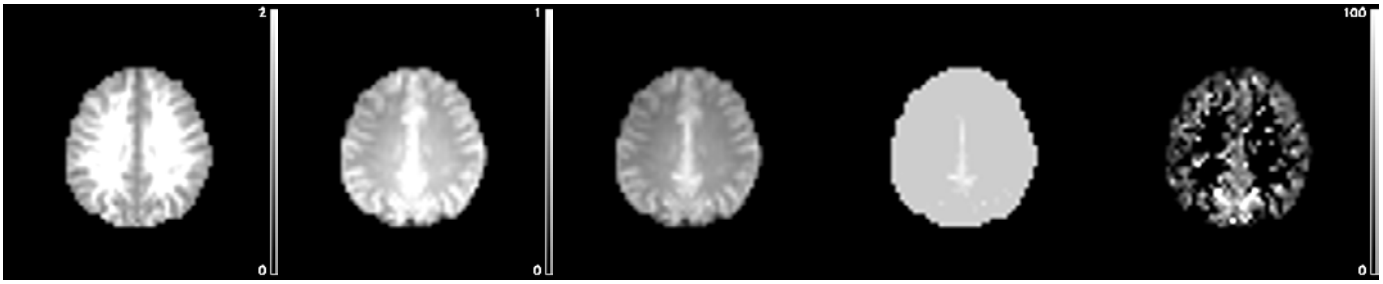
METHODS: Recalling Curie's law for magnetization, the relationship between the magnetic field, proton density, temperature and the equilibrium magnetization can be expressed as: $M_0 = \rho_0 \frac{\lambda^2 \hbar^2}{4kT} B_0$

where, ρ is the proton/water density, B_0 is the main magnetic field, γ is the gyro-magnetic ratio, h is Planck's constant, k is Boltsmann's constant and T is the absolute temperature [in K]. It can be seen that in case of constant B_0 and temperature, we have $M_{0t}/M_{0b} = \rho_{0b}/\rho_{0t}$.

The equilibrium magnetization of the tissue can be estimated from the QUASAR data, which basically uses a Look-Locker readout scheme preceded by a saturation pulse [1]. This causes a saturation recovery behavior of the tissue signal, which can be used for the estimation of M_{0t}. In practice this is done using a Levenberg-Marquardt least-squares minimization of the expression $S = M_{0t,eff} \cdot (1 - e^{-t/T1t,eff})$. True tissue M_{0t} can be obtained from fitted effective magnetization $M_{0t,eff}$ as described in [4]. Because the ratio ρ_{0b}/ρ_{0t} equals λ, it is possible to calculate λ on a voxel by voxel basis for the remaining tissue by assigning the mean white matter $\lambda = 0.82$ or mean gray = 0.98, based on previous studies using nuclear medicine methods [3]. The remaining tissue is then assigned a value according to their actual M_{0t}. Estimation of the M_{0t} and λ maps was done using IDL 6.1 (Research System, Inc.). Ten healthy volunteers were scanned at 3T Philips Achieva system using the following perfusion protocol: crushed and non-crushed perfusion scan using QUASAR: TR/TE/ΔTI/TI1= 4000/23/200/50 ms, 64x64 matrix, 4 slices, FOV=240x240, flip angle = 30°, SENSE = 2.5. Additional scans were performed in 3 volunteers at flip angles of 10 and 20° in order to validate M_{0t} estimation and the following λ correction. CBF maps were computed as explained in [1], except for the scaling factor M_{0b}.

RESULTS: The mean $M_{0t,gm}/M_{0t,wm}$ ratio from the 3 volunteers who had 3 scans at different flip angle were 1.17±0.05. The corresponding gray matter perfusion values are displayed in the table on the right. In the figure below: a), shows the R1-map from where the automatic segmentation of gray and white matter was done, b) is the calculated blood-brain partition coefficient image, c) is the corresponding M_{0t}, d) is M_{0b} and finally e) is the resulting perfusion map. The CBF values for the 10 volunteer using both the corrected M_{0b} and the traditional M_{0t}/0.9 resulted in mean GM values of: 48.4 ± 1.6 and 41.9 ± 1.4 [ml/100g/min] (mean ± s.e.m.), respectively. For WM: 23.3 ± 1.3 and 24.9 ± 1.5 Notice the change in GM/WM ratio going from 1.7 to 2.1 when correction is applied.

CBF[ml/100g/min]	10°	20°	30°
Subject 1	41.6	60.3	66.2
Subject 2	37.0	44.6	43.4
Subject 3	43.9	36.3	44.7



DISCUSSION: As expected, we obtained an homogeneous M_{0b}-map from the calculated M_{0t} maps. An extensive method for blood-brain partition coefficient mapping has been proposed earlier by Roberts et al. [5] which also included field inhomogenity correction. Alternatively, the present simplified method uses the prior information obtained for nuclear perfusion imaging methods for correction of the differences in λ across the volume and at the same time estimate M_{0b} in a consistent and user independent way. The mean $M_{0t,gm}/M_{0t,wm}$ ratio of 1.17±0.05 corresponds very well to the ratios of $\lambda_{gm}/\lambda_{wm} = 1.195$ [3]. The method is believed to improve the reproducibility of the perfusion maps. Potential issues includes the lack of field inhomogenity correction as well as the use of previous established mean values of λ. In general, the adaptation of λ to ASL experiments is suspicious when using the general kinetic model for perfusion estimation. This is mainly because it is here used as a distribution volume for our labeled blood water, which would require instantaneous exchange from the capillary bed to the extra-cellular space upon arrival, making it a measure of the distribution volume. Because the water passes the blood-brain barrier via dedicated water channels, this assumption is not fully satisfied. However, this dependence is eliminated in our recently proposed method, which uses deconvolution for the perfusion estimation [1]. Other potential issues related to the estimation of this parameter are its dependency of hematocrit [3] and the fact that λ can vary in pathological cases.

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