SAMPLING STRATEGY FOR PERFUSION QUANTIFICATION USING PASL-MRI

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ABSTRACT

Arterial spin labeling (ASL) techniques have been developed over the past decade for mapping blood perfusion using MRI. However, their unique potential for the absolute quantification of perfusion, in a completely non-invasive manner and with greater spatial and temporal resolution than alternative methods, has not yet been fully realized. The main limitations of ASL techniques are their intrinsically low SNR and the complexity of the underlying kinetics. In this study, we investigated different sampling strategies for perfusion quantification based on multi-time point pulsed ASL acquisitions. We found that, for the same number of acquisitions, sampling the kinetics curve over a larger number of different time points yields more stable results than averaging over a limited number of time points.

Index Terms— arterial spin labeling, magnetic resonance imaging, perfusion, kinetic modeling, quantification

1. INTRODUCTION

Perfusion describes the distribution of nutrients to the tissues by blood flow through the capillary bed and is defined as volume of blood per unit time and per unit volume of tissue. Arterial spin labeling (ASL) magnetic resonance imaging (MRI) techniques offer a noninvasive way of generating perfusion images that are potentially quantitative [1]. They consist on magnetically labeling the water molecules in the arterial blood and then measuring the magnetization of the tissues after a certain time interval. Labeling is usually achieved by inversion of the magnetization and the delay between labeling and acquisition is then referred to as the inversion time (TI). One of the possible labeling strategies consists on applying a short 180° radio-frequency (RF) pulse to a thick slab of tissue upstream from the region of interest, thereby inverting the magnetization of the water protons flowing towards the tissues. Following transit in the arterial blood and exchange into the tissues, the labeled water molecules will contribute a fraction of the measured magnetization that is related to the perfusion rate at which they were delivered to that region. A difference will therefore be observed between labeled and non-labeled images, which can be used to obtain information about local perfusion.

Models based on tracer kinetics theory have been developed to describe the magnetization change between a control and a labeled image (ΔM) as a function of various physiological parameters, including perfusion (f), the arterial transit time (δt), the time width of the label (τ) and the exchange time between blood and tissue (τ_{ex}) (Figure 1) [2]. In principle, the magnetization collected at a single TI point is sufficient to obtain a perfusion estimate, provided that the values of the other model parameters are available or can be assumed. Otherwise, it is possible to estimate perfusion, as well as other unknown parameters, if magnetization difference images are measured at multiple TI points, by fitting a model of the PASL signal to the data.

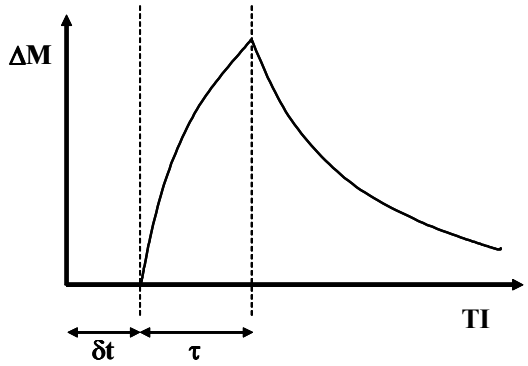

Figure 1: Magnetisation difference ΔM as a function of the inversion time TI, predicted by the standard model of PASL (in Equation 1), illustrating the arterial transit time δt, as the delay of water molecules between arterial labelling and exchange into tissue, and the tag width τ, as the duration of the arrival of labelled water molecules at the tissue.

Modifications to the basic techniques have been introduced to minimise sensitivity of the magnetisation difference measured in a single-TI experiment to τ and δt [3]. These are based on delimitation of the time width of the label (i.e., fixing τ to an imposed value) and by adopting a delayed acquisition (to account for an unknown δt), respectively. The reduced sensitivity to δt may, however, be compromised whenever transit times that are longer than the image acquisition delay are present (~1 second). This situation may be observed due to slower flow in disease or

simply as a consequence of very long transit delays for certain regions of the brain. In order to accommodate such potentially prolonged transit delays, the inversion time would have to be increased to values that would compromise the signal-to-noise ratio (SNR) of the magnetisation difference images. Moreover, uncertainties in the time width of the bolus are also present, due to imperfections in the pulse inversion profile and associated labelling efficiency. Taken together, these factors lead to a realistic distribution of both transit times and tag time widths, which must be taken into account for the accurate quantification of perfusion over the whole range of brain regions and possible physiological conditions [4]. A multiple-TI experiment is then necessary to measure δt and τ, as well as perfusion, by fitting of the appropriate kinetic model.

Because of the small blood volume fraction in the brain (~4%) and the loss of the magnetization label with time as a result of longitudinal relaxation, the signal-to-noise ratio (SNR) of PASL data is intrinsically very small, with the maximum of the observed magnetization differences being on the order of only ~1% for the conditions commonly studied (brain gray matter in humans at 3 Tesla). For this reason, substantial signal averaging is usually performed in order to achieve sufficient SNR, which is reflected in proportionally increased acquisition times. This limitation is especially critical when multiple TI points should be sampled in order to perform quantitative parameter estimation. In this case, a trade-off exists between the number of TI points sampled and the number of averages collected at each point.

In this study, we aimed to investigate the performance of model fitting for estimation of various kinetic parameters using different sampling strategies in PASL experiments, in terms of the number of time points and the number of averages.

2. METHODS

5.1. Kinetic model definition

In the general kinetic model commonly used for PASL quantification [2], the magnetisation difference of labelled blood water is treated as a bolus of tracer that is delivered to each imaging voxel by arterial flow at a rate equal to the local perfusion (f), while decaying away by longitudinal relaxation and washout by venous outflow. By using the principles of tracer kinetic theory, if the standard assumptions are made of delivery by uniform plug flow and complete and immediate exchange of labelled water between blood and tissue, then the model equations for the magnetisation difference ΔM, normalised to a reference tissue equilibrium magnetisation M_{0t}, as a function of the inversion time TI, are given by:

$$\frac{\Delta M(TI)}{M_{0t}} = \frac{2\alpha f}{\lambda} \begin{cases} 0 & 0 \le TI < \delta t \\ e^{-R_{1t}^{app} TI} e^{-D_1 \delta t} \dfrac{1 - e^{-D_1 (TI - \delta t)}}{D_1} & \delta t \le TI < \delta t + \tau \\ e^{-R_{1t}^{app} TI} e^{-D_1 \delta t} \dfrac{1 - e^{-D_1 \tau}}{D_1} & \delta t + \tau \le TI \end{cases}$$

with:

$$D_1 = R_{1a} - R_{1t}^{app}$$

$$R_{1t}^{app} = \frac{1}{T_{1t}} + \frac{f}{\lambda}$$

$$R_{1a} = \frac{1}{T_{1a}}$$

where α is the labelling efficiency, defined as the fraction of inversion of the arterial magnetisation at the time of tagging (α=1 for complete inversion and α=0.5 for complete saturation); λ is the water partition coefficient between tissue and blood; and T_{1a} and T_{1t} are the longitudinal relaxation time constants of arterial blood and tissue, respectively.

5.2. Monte Carlo simulations

The kinetic model described by the equations above was used to simulate the normalized magnetization difference data, $\Delta M/M_{0t}$, obtained from PASL experiments with different sampling strategies. Each strategy covered a total period of 4 seconds with a certain number of uniformly distributed TI points. The number of averages collected at each TI point was determined so that the total number of acquisitions was the same for all strategies. We first considered a typical, reduced number of TI points (5) with substantial averaging (60) and then investigated the possibility of increasing the number of TI points, by decreasing the number of averages so that the number of pairs of labeled and non-labeled images (300), and therefore the same total acquisition duration, remained the same:

- 5 TI points, 60 averages
- 10 TI points, 30 averages
- 50 TI points, 6 averages
- 300 TI points, 1 average (no averaging)

The parameters used in the model simulations correspond to typical gray matter values of the human brain at 3 Tesla: f = 0.01 s^{-1} (60ml/100ml/min), δt =0.7 s, τ = 1.0 s, α = 0.9, λ = 0.9, T_{1a} = 1.5 s and T_{1t} = 1.3 s.

Four different noise levels were considered, in order to investigate the noise performance of the parameter estimation for each type of sampling strategy. Gaussian

noise was considered and added to the simulated data at each time point, with 0 mean and a standard deviation equal to a percentage of the maximum measured signal difference: 10, 20, 50 and 100 %. Gaussian, rather than Rician, distributed noise is valid in this case, since the difference data are assumed to originate from tag and control images that themselves have high SNR, and hence Gaussian distributed noise.

Model parameters were estimated by performing a least squares fit of the non-linear kinetic model functions using Matlab. Two sets of parameters were considered for estimation by model fitting:

- 2 parameters, f and δt (assuming a known τ);
- 3 parameters, f, δt and τ.

Monte Carlo simulations were performed by generating a set of 1000 curves at each noise level and then fitting the kinetic model by performing either a 2-parameter or 3-parameter estimateof *f* and δt (and τ for the 3-parameter fit). The means of the distributions of *f* and δt (and τ) estimates were determined for each noise level.

3. RESULTS

An example of the curves of the normalized magnetization difference as a function of the inversion time, obtained by simulation of the standard kinetic model, are shown in Figure 2, for the 4 sampling strategies investigated, at a noise level of 20% of the maximum measured signal. Note that the SNR observed at each TI point increases with the square root of the number of averages, therefore yielding an apparently lower noise for the sampling strategies with fewer TI points (but more averaging).

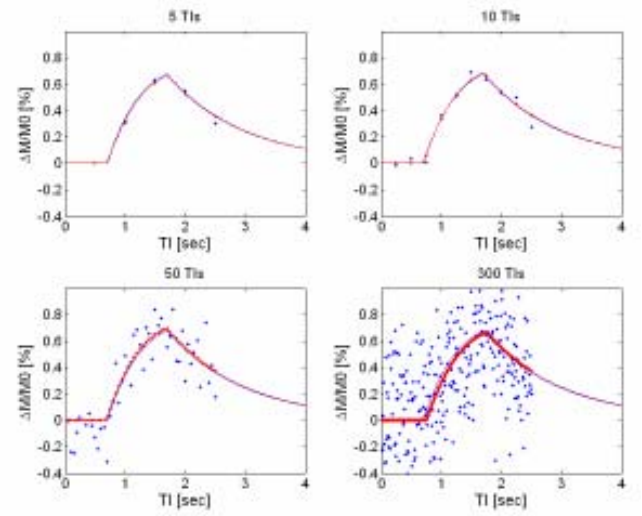

Figure 2: Simulated magnetization difference curves as a function of the inversion time, for the 4 sampling strategies investigated and 20% noise level: simulated data (blue) and fitted curves, obtained by a 2-parameter estimation (red).

The mean estimation errors for each parameter, noise level and sampling strategy, averaged over all simulated datasets, are shown in Figures 3 and 4, for 2-parameter and 3-parameter model fitting, respectively. For a 2-parameter fit, the estimation errors are not significantly different between the various sampling strategies investigated (Figure 3). However, when a 3-parameter fit is performed for the estimation of τ, then the common 5-TI point experiment becomes highly unstable and yields a much larger perfusion estimation error than the other sampling strategies employing more TI points and fewer averages (Figure 4).

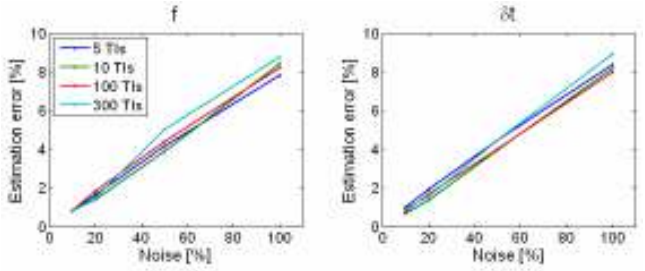

Figure 3: Mean estimation errors for f and δt, obtained by performing a 2-parameter fit, for each sampling strategy, as a function of noise level.

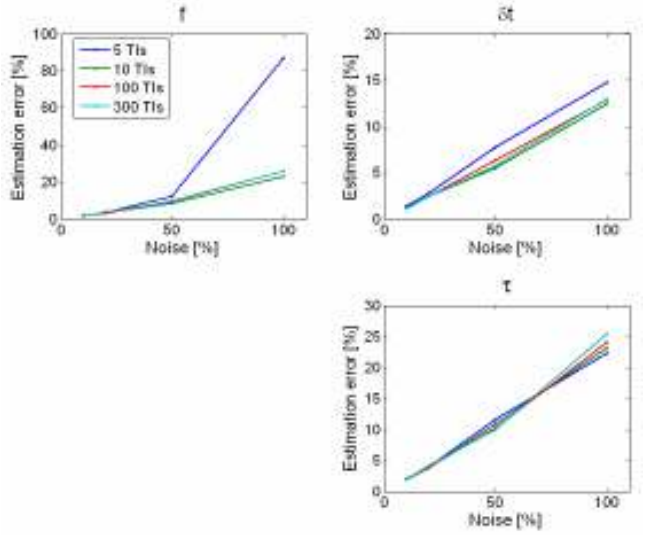

Figure 4: Mean estimation errors for f, δt and τ, obtained by performing a 3-parameter fit, for each sampling strategy, as a function of noise level.

4. DISCUSSION

In this study, we have investigated the performance of parameter estimation through kinetic model fitting, at different noise levels, for a number of sampling strategies in multiple time point PASL-MRI experiments. In particular, we assessed the effects of trading off the number of time points sampled along the kinetic curve with the number of

averages performed at each sampling point, when performing a 2-parameter or a 3-parameter estimation.

By performing Monte Carlo simulations of a standard kinetic model of the PASL magnetization difference at four different noise levels, we have found that the errors in parameter estimation increase as a function of noise for all sampling strategies. When only 2 parameters are estimated, no significant differences are observed between the various sampling strategies. However, we have shown that, at high noise levels, sampling a reduced number of TI points with substantial averaging produces much greater perfusion estimation errors than sampling larger numbers of TI points with reduced averaging. In fact, the sampling strategy that yielded the most robust parameter estimation results, as a function of noise, was the one that employed no averaging at all, trading it off for the largest possible number of time points over the kinetic curve, performed better

Further investigations are necessary in order to take into account the physiological variations of the kinetic parameters during measurement, which will probably deepen the differences between the various sampling strategies. Moreover, our results point towards the need to employ objective criteria in the choice of the time points to be sampled in a PASL experiment, if accurate measurement and quantification of perfusion is sought. Finally, not only the number of time points but also their exact positions along the kinetic curve, should be taken into account when designing the optimal sampling strategy for multiple-TI PASL acquisitions.

4. REFERENCES

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