Cerebral blood flow quantification from QUASAR ASL by Stable Spline

Marco Castellaro, Amit Mehdiratta, Denis Peruzzo, Gianluigi Pillonetto, Esben T. Petersen, Xavier Golay, Michael A. Chappell, and Alessandra Bertoldo
Department of Information Engineering, University of Padova, Padova, PD, Italy, 2Institute of Biomedical Engineering, University of Oxford, Oxford, United Kingdom, 3Departments of Radiology and Radiotherapy, University Medical Center Utrecht, Utrecht, Netherlands, 4UCL Institute of Neurology, London, United Kingdom

Target audience: Scientists and clinicians with interest in perfusion MRI.

Purpose: QUASAR ASL permits the extraction of both Arterial Input Function and Tissue signal from data in order to estimate cerebral blood flow (CBF) using deconvolution techniques [1]. The transit delay from the chosen AIF to the tissue will cause the AIF to decay according to the blood T1 enhanced by the look-locker readout used. This drop in ASL signal requires correction by scaling the estimated CBF after deconvolution [1]. Hence accurate estimation of delay is vital during the analysis process. The motivation of our study was to investigate the accuracy in delay and CBF estimation as illustrated in [1] and assess the performance of stable spline (SS) method [2], a non-parametric deconvolution approach based on kernel methods already used in DSC [3].

Methods: The ASL signal was simulated according to the kinetic model from Buxton [4] under several conditions, including different levels of perfusion (90, 50, 20 ml/100gr/min), noise (SNR=100, 20, 10, 5), delays (0-0.6s) with no dispersion and in presence of dispersion. A gamma dispersion kernel (s=exp(2); p=0.1) was used to describe the AIF kinetics [5]. Monte Carlo simulations with 100 realizations were performed for each combination. Clinical data: A subset of the QUASAR reproducibility data set presented in [6] was used, comprising seven subjects each scanned four times, giving a total of 28 datasets. Analysis: conventional QUASAR ASL analysis was performed using edge detection for delay estimation followed by oSVD deconvolution as in [7]. SS is an alternative deconvolution method that was formulated to estimate the residue function \(R(t)\) in a Bayesian context, solving a Tikhonov like optimization problem. \(R(t)\) was described by two components, a stochastic and a deterministic part. The stochastic component includes a prior knowledge on \(R(t)\), describing it as a zero-mean Gaussian random process with a Wiener process as auto-covariance (smoothness) and an opportune transformation in the time domain to achieve the BIBO-stability of the system [2]. The deterministic part was modelled as an exponential function. SS analysis for QUASAR ASL consists of a 3 step procedure. Firstly, we run SS obtaining a first approximation for \(R(t)\). Re-convolving the estimated \(R(t)\) with the AIF produced a new denoised version of the original signal. Secondly, in order to take into account the delay between the AIF and tissue signal, we estimated the delay by computing the cross-correlation between the denoised signal and the AIF, both having been smoothed using the first approximation of the wavelet transform of the signals (Haar, 3 levels). Then we translated the AIF using the estimated delay and re-computed the \(R(t)\) with the SS deconvolution. The root mean square error (RMSE) of the peak of \(R(t)\) (RMSEp) was computed between the true simulated value and SS and oSVD estimates in order to evaluate the bias on CBF. To assess the best approximation of the AIF a gamma influence and in cyan the T1 decay. For simulated GM tissue, SNR 10, delay 0s (top) delay 0.6s (bottom). SS (Blue) oSVD (Red) Confidential interval and median value. With correction for delay (right) and without (left).

**Fig. 1** The red curve shows the total error in CBF quantification as function of error in delay estimate. In blue the influence of the Look-Locker readout and in cyan the T1 decay.

**Fig. 2** Estimation of \(R(t)\) for simulated GM tissue, SNR 10, delay 0s (top) delay 0.6s (bottom). SS (Blue) oSVD (Red) Confidential interval and median value. With correction for delay (right) and without (left).

**Table 1** Performance index of results in simulated data. RMSE: between true peak level, delay and curve and estimated one with both oSVD and SS, computed with both SS and oSVD for each subject. SS CBF values (61±1.1 ml/100g/min) showed a significant increase (p<0.05) compared to oSVD (51±1.0 ml/100g/min). Delay estimation showed a lower trend for SS compared to edge detection but not statistically significant.

**Fig. 3** Subject #4 - CBF maps obtained with oSVD (left), Stable Spline (middle) and the relative ratio between the two methods (SS-oSVD)/oSVD (right).

**Results** Fig. 1 illustrates the error in delay propagated to CBF estimation. Simulations: Table 1 summarizes the success percentages. Errors in the estimation of delay led to bias in CBF quantification of 75-82% with edge detection and 31-42% with SS (25-75th percentile of difference percentages distribution) Fig. 2 shows the deconvolved \(R(t)\) (median [5th-95th percentile]) showing a wide variation after delay correction for oSVD.

**Clinical data:** Fig. 3 shows GM CBF maps from a representative subject. CBF mean ± SD in GM was considered better and percentage was calculated as a measure of success.

**Conclusion** Delay estimation between AIF and tissue is a significant issue for the precise assessment of CBF from QUASAR ASL data. It may be particularly problematic in the presence of dispersion, where the mixed effects of dispersion and delay might be more evident. Here we show that SS can give reliable estimates of delay and a reliable approximation of the true \(R(t)\) in most of the simulated cases. This was confirmed also in presence of dispersion, which remains be investigated further within the SS method. Its application in clinical environment is promising in light of its physiological results and low computational cost (30 min for each subject).

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