Cerebral blood flow quantification from QUASAR ASL by Stable Spline

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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 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].

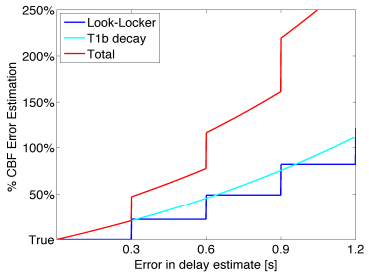

Fig. 1 The red curve shows the total error in CBF quantification as function of error in delay estimate. In blue the influence of the Look-Locker readout influence and in cyan the T1 decay.

Methods **Simulations:** 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 true *R(t)*, the RMSE of the curve (RMSEc) and the RMSE of the area under the curve (RMSEa) were calculated. The RMSE of the delay (RMSEd) obtained with standard edge detection implemented as in [1] and with the proposed method were computed. The impact of delay estimation on CBF quantification was determined computing the percentage differences between unbiased CBF (obtained by using the true simulated delay) and CBF using the delay estimated with SS and oSVD respectively. The method scoring the lowest RMSE was considered better and percentage was calculated as a measure of success.

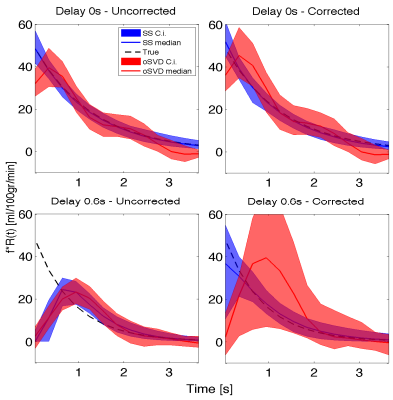

Fig. 2 Estimation of *R(t)* for simulated GM tissue, SNR 10, delay 0s (top) delay 0.6s (bottom). SS (Blue) oSVD (Red) Confidential interval and median value. With correction for delay (right) and without (left)

Success %	oSVD	SS
RMSEp	26%	74%
RMSEc	5%	95%
RMSEa	4%	96%
RMSEd	12%	88%

Tab.1 Performance index of results in simulated data. RMSE between true peak level, delay and curve and estimated one with both oSVD and SS

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^{th}-75^{th} percentile of difference percentages distribution) Fig. 2 shows the deconvolved *R(t)* (median [5^{th}-95^{th} 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 computed with both SS and oSVD for each subject. SS CBF values (61±11 ml/100g/min) showed a significant increase ($p<0.05$) compared to oSVD (51±10 ml/100g/min). Delay estimation showed a lower trend for SS compared to edge detection but not statistically significant.

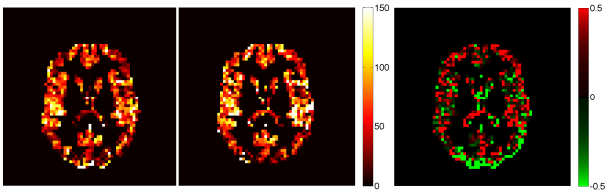

Fig. 3 Subject #4 - CBF maps obtained with oSVD (left), Stable Spline (middle) and the relative ratio between the two methods (SS-oSVD)/oSVD) (right).

Discussion Here we present an alternative to the conventional method for estimation of the CBF and the delay from QUASAR data. *R(t)* approximation from SS was closer to the true simulated value in almost all of the cases. SS showed more accurate delay estimates compared to edge detection in the large majority of the simulated data. For both methods presence of dispersion led to a systematic overestimation of the delay. However, SS delay estimates were less biased even in presence of dispersion (90% of the cases). SS provided physiologically realistic *R(t)* that oSVD could not provide when applied to real data. GM CBF values were significantly higher than oSVD ones within physiological range.

Conclusion Delay estimation between AIF and tissue is a significant issue for the precise assessment of CBF from QUASAR data. It may be particularly problematic in the presence of pathologies, 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).

References [1] E. T. Petersen et al., MRM 55, 219–32 (2006) [2] G. Pillonetto et al., Automatica, 46, 81–93 (2010) [3] M. Castellaro et al., ISMRM 19th Scientific Meeting & Exhibition, Montreal, CANADA, 3923, (2011). [4] R. B. Buxton et al., MRM, 40, 383–96, (1998). [5] M.A. Chappell et al., MRM, Epub (Apr 2012). [6] E. T. Petersen et al., NeuroImage, 49, 104–13, (2010). [7] M.A. Chappell et al., MRM, Epub (Jun 2012).

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