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[abstract only]**

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Physiological noise reduction for multi-inversion time ASL

Kevin Murphy¹, Anja Hayen², Mari Herigstad², and Kyle T.S. Pattinson²

¹CUBRIC, School of Psychology, Cardiff University, Cardiff, Wales, United Kingdom, ²Nuffield Dept Clinical Neurosciences & FMRIB Centre, University of Oxford, United Kingdom

Target Audience Researchers using multi-TI ASL imaging

Purpose Due to the inherently low signal-to-noise ratio (SNR) of arterial spin labelling (ASL) methods, minimisation of noise sources is important for accurate cerebral blood flow (CBF) quantification. One source of noise arises from physiological processes such as respiration and cardiac cycles which introduce fluctuating confounds into the MR time series. Methods have been developed to remove such noise in standard BOLD fMRI imaging such as RETROICOR [1]. Restom and colleagues extended this method to ASL time series [2], demonstrating that the optimal approach to applying this technique is to remove physiological noise from tag and control time series separately before combining them to quantify CBF. The purpose of this study is to extend this finding to determine the optimal approach to removing physiological noise from multiple inversion time (multi-TI) ASL data.

Methods Twenty participants were scanned on two occasions at 3T using a multi-TI pseudo continuous ASL (PCASL) sequence (scan parameters: TIs = 1.65, 1.9, 2.15, 2.4, 2.65, 2.9s; TI cycles = 6; tag duration = 1.4s; TR = 4s; TE = 13ms; num slices = 24; matrix = 64x64; slice thickness = 5mm; num volumes = 72). During one session (REMI), the participants received an intravenous target-controlled infusion of remifentanyl for 45 minutes. During the other session (SAL), saline was infused. Respiration and cardiac traces were recorded throughout the scanning with the expectation that physiological traces would differ between the two sessions. Slice-wise RETROICOR physiological noise regressors were calculated using the first and second harmonics of the phase of the respiratory and cardiac cycles at the time of acquisition along with an interaction term. Three versions of RETROICOR were performed: *No-Sep* – time points were not separated before regressing the noise from the signals; *TC-Sep* – the time series were separated into tag and controls before regressing the noise from each individually and then recombining into a single time series (the Restom approach [2]); *TI-Sep* – the time series were separated into tag/controls and by TI to yield 12 time series before noise regression. CBF time series were calculated after motion correction by subtracting successive tag/control pairs, yielding 36 volumes (6 TIs x 6 TI cycles). Gray matter masks were calculated from a structural image, and the average subtraction time series was calculated for each ASL run (SAL and REMI) for each participant. To assess noise removal efficacy, intra-class correlation coefficients (ICCs) were calculated across TI time points. A general kinetic model [3] was fit the 36 point time series. Fits were compared across correction types.

Results Figure 1 demonstrates the effect of noise correction using the different correction schemes for the SAL and REMI data. The across-subject average time series shows that the *No-Sep* and *TC-Sep* methods introduce a large amount of variance into the data. Separating the time series by tag/control and TI (*TI-Sep* method) before removing the physiological noise does not introduce this confound. If physiological noise is removed properly, the repeatability of each TI value across the 6 TI cycles should improve, i.e. ICC values should increase. Figure 2 compares the ICC values with no correction (*NoCorr*) to the *TI-Sep* method for each subject. The mean ICCs for the *NoCorr* method are 0.71 ± 0.19 and 0.83 ± 0.18 and for the *TI-Sep* method are 0.65 ± 0.31 and 0.82 ± 0.18 for SAL and REMI respectively. Figure 2 demonstrates that with the *TI-Sep* method, the ICCs improve for some subjects but not others and therefore no consistent differences to the *NoCorr* method are observed. Figure 3 shows the R^2 fits of the kinetic model to the 36 time point data for each of the 4 methods for each subject. As expected, the fits are poor to the *No-Sep* and *TC-Sep* data. The fits are broadly similar for *NoCorr* and *TI-Sep* for both the SAL and REMI runs with means of approximately 0.75 and no significant difference observed between the methods.

Discussion This study demonstrates that correction of physiological noise in multi-TI ASL data can introduce serious confounds if not performed correctly. Both the naive approach of not separating the data at all (*No-Sep*) and the Restom approach [2] of separating the tags from the controls (*TC-Sep*) introduce far more noise than they remove (Fig 1) resulting in very poor kinetic model fits (Fig 3). This is probably due to the non-linear increase in signal with TI leading to errors in the GLM fit. Separating both TIs and tags/controls alleviates this problem allowing for good repeatability of signal across TIs (Fig 2) and improved fits of the kinetic curve model (Fig 3). However, there is no significant or consistent improvement on any measure with the *TI-Sep* method over the uncorrected data. This is probably due to nature of multi-TI ASL in which data is essential averaged over TI cycles and thus inherently removes noise. However, if multi-TI data are to be used in dynamic fashion rather than through averaging, correction of physiological noise may be beneficial and should be performed with the *TI-Sep* method.

References [1] Glover (2000), MRM:44,162; [2] Restom (2006), NeuroImage:31,1104; [3] Buxton (1998), MRM:40,383

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