Quantifying Cerebral Haemodynamics beyond CBF using Control Point Interpolation Deconvolution for DSC MRI Perfusion Analysis

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Target Audience: Scientist and Clinicians with an interest in perfusion MRI

Introduction: DSC-MRI analysis is an ill-posed inverse problem that involves the deconvolution of the MR signal with an arterial input function. One aspect of quantification is the use of a deconvolution techniques to estimate the residue function [1], [2]. The residue function is an important summary of capillary haemodynamics that might provide useful clinical information regarding evolution of stroke, for example, but has been hampered by non-physiological oscillatory signals when using Singular Value Decomposition (SVD) deconvolution or its variant methods [1], [3], [4]. Control Point Interpolation (CPI) deconvolution has recently been proposed with demonstrated ability to characterise the residue function from clinical data [5]. The purpose of this study was to investigate the changes in residue function behaviour and flow heterogeneity in 8 patients with atherosclerotic disease by comparing results from SVD and CPI deconvolution methods. Also the motivation was to quantify this non-parametric residue function into physiologically interpretable and clinically useful parameters.

Material and Methods: DSC data were acquired from 8 patients (median age: 65yrs [(47-85 yrs], M:F=5:3) with atherosclerotic diseases under an Institutional Review Board approved protocol. MRI data were acquired on a Siemens 3T Trio scanner with Diffusion Weighted Imaging (DWI) and GRE-DSC: TR/TE=1.5s/30ms. 78 volumes, 128x128x22 matrix, 1.7x1.7x5mm^3 voxels. An intra-venous bolus injection of 0.1 mmol/kg Magnevist® was performed followed by a 20 ml saline flush. DSC images were analysed using the oSVD [4] and with CPI deconvolution [5]. In the CPI method, the tissue response function was estimated at a set of control points and then cubic spline interpolation was used to generate the complete smooth residue function. A Region of Interest (ROI) analysis was performed both pre and post carotid endarterectomy on the DSC data. Residue function characteristics were evaluated from ROIs based on DWI and the perfusion weighted images under three criteria: I) normal perfused regions 3x3 voxels (normal) in the contralateral hemisphere that was outside the hypoperfused and DWI infarct region [6], II) region around DWI lesion (DWI-ring) but normal DWI and III) showing positive infarct tissue within a DWI lesion (DWI+) [6]. A Maximum of four ROIs were selected from each patient in respective groups of normal, DWI-ring and DWI+ tissue. In total 32 ROIs were selected from eight patients under normal group, 26 in DWI-ring and 18 ROIs under the DWI+ group. Rigid body image registration was performed between pre- and post-surgery perfusion and DWI images using the FMRIB Linear Image Registration Tool (FLIRT) from the FSL toolbox [7] before ROI selection. ROIs were selected in the post-surgical imaging data by creating a ROI mask in pre surgery images and transforming it to later using FLIRT algorithm. Residue functions obtained from CPI deconvolution among three ROI groups were analysed for variation in shape and heterogeneity. The residue function is a monotonic decreasing function; in order to characterise it, we measure the time taken by the residue to drop to 50% and 10% of its maximum value for three ROI groups, referred to as R50 and R10 respectively. Transit time distribution ($h(t)$) in the ROI was calculated from the residue functions ($R(t)$) using, $h(t) = -dR(t)/dt$ [8]. Full-Width at Half-Maximum (FWHM) of the distribution of transit times was used as a measure of heterogeneity. Non-parametric Kolmogorov-Smirnov test was used to measure the statistical significance ($p<0.05$).

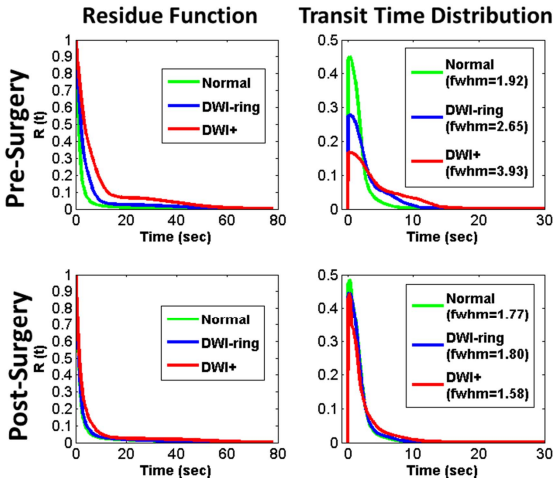

Figure 1: Mean residue function and distribution of transit times for normal, DWI-ring and DWI+ tissue pre and post-surgery. Residue function and transit time distribution both show considerable difference between tissue types which shows tendency to approach normal post-surgery.

Results: The residue function shapes estimated by CPI method were found to be smooth, whereas the SVD approach were not. Using CPI differences between normal and ischemic tissues were observed: the CPI residue function in DWI+ and DWI-ring ROIs showed a slower decay compared to normal ROIs. The residue function shapes were consistent, with high MTT in corresponding tissues. Figure 1 show the mean residue function and transit time distribution obtained with ROI analysis from pre and post-surgery perfusion imaging. Mean FWHM value of transit time distributions are shown in figure1, significant differences ($p<0.01$) were observed in FWHM values among three tissue types during pre-surgery analysis. Figure 2 shows box plots for R50 and R10 within the three ROI groups pre- and post- endarterectomy; the R50 and R10 values showed significant difference among three groups ($p<0.05$) pre-surgical intervention. Figure 3 shows the R50 and R10 map for a representative patient along with CBF, MTT, delay and DWI. R50 and R10 maps showed appreciable variation between normal, DWI-ring and DWI+ regions.

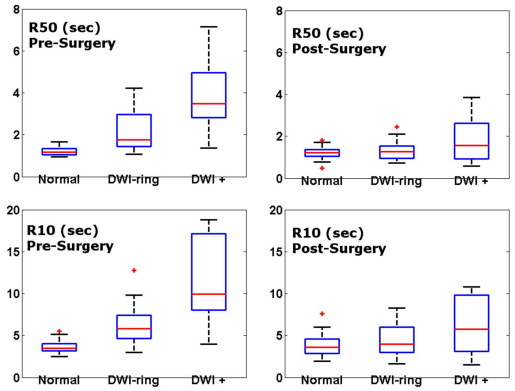

Figure 2: Box plot showing differences in R50 and R10 values of Contralateral (normal), DWI-ring ischemic and DWI+ tissue pre-surgery which becomes less obviously different post-surgical intervention, where still the infarcted tissue showed a wide distribution.

Discussion: Estimation of residue function shape may be informative in clinical situations allowing flow heterogeneity and tissue oxygen delivery to be assessed [8]. Using the CPI approach, smooth residue function shapes were obtained that might facilitate transit time heterogeneity analysis which in turn could offer more insight into cerebral haemodynamics than CBF or MTT. *In vivo* ROI analysis with CPI method for eight patients with atherosclerotic disease showed appreciable difference in shape of residue function and transit time distribution among normal, DWI-ring and DWI+ tissues. The transit time distribution appeared to have more contribution from high transit times in ischemic tissue compared to normal. R50 and R10 values were considerably higher for ischemic tissue during pre-surgery analysis which dropped significantly post-intervention. However a wide variation in values was observed in DWI+ tissue group which could be a reflection of variation within infarct tissue type. The R50 and R10 could serve as clinically useful quantitative measures for non-parametrically estimated residue function using CPI. R50 and R10 parametric maps might provide information in addition to standard perfusion and diffusion imaging. **Conclusion:** The R50 and R10 values obtained using CPI technique could provide potential useful information on capillary heterogeneity and possibly an access to study pathophysiology of stroke.

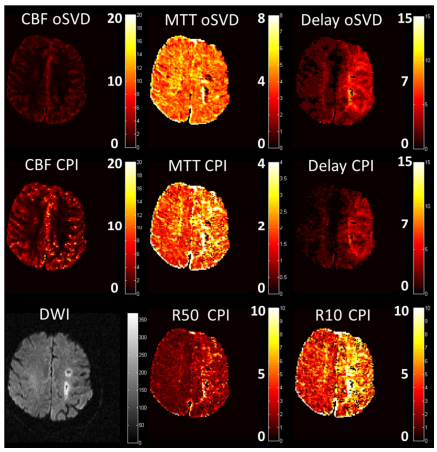

Figure 3: CBF, MTT and Delay estimates for a representative patient with oSVD and CPI methods. The DWI, R50 and R10 map of the same patient (bottom row), where R50 and R10 map clearly showed region of high R50 and R10 values in region of infarct surrounded by an area under ischemic stress in the left hemisphere compared to normal right hemisphere.

Reference:[1]F.Calamante et al; *MRM*, vol50, no6, pp1237–47, 2003. [2]K.Mouridsen et al; *NeuroImage*, vol.33, no.2, pp570–9,2006. [3]L.Østergaard et al; *MRM*, vol36, no5, pp715–25,1996. [4]O.Wu et al; *MRM*, vol50, no1, pp164–74,2003. [5]A.Mehndiratta et al;*NeuroImage*,2012.[6]K.Dani et al;*Annals of neurology*,vol70,no3,pp384–401,2011.[7] M.Jenkinson et al;*NeuroImage*,vol17,no2,pp825–841,2002.[8]L.Østergaard et al;*JCBFM,*vol19,no6,pp690–9,1999.