

# Quantifying cerebral haemodynamics and maximum potential oxygen delivery in patients with chronic ischemia using DSC perfusion MRI

Amit Mehndiratta<sup>1</sup>, Chang Sub Park<sup>1</sup>, David E Crane<sup>2</sup>, Bradley J MacIntosh<sup>2</sup>, Stephen J Payne<sup>1</sup>, and Michael A Chappell<sup>1</sup>

<sup>1</sup>Institute of Biomedical Engineering, University of Oxford, Oxford, Oxfordshire, United Kingdom, <sup>2</sup>Medical Biophysics, Sunnybrook Research Institute, University of Toronto, Toronto, ON, Canada

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

**Introduction:** Accurate analysis of dynamic susceptibility contrast (DSC)-MRI depends on the precise estimation of the tissue residue function, which is a measure of the underlying capillary haemodynamics. It has been suggested that variations in capillary haemodynamics could affect local tissue oxygen delivery and hence tissue metabolic state [1–3]. From direct microscopy studies in animals [4,5] and recently theoretically using a mathematical model of haemodynamics [2] it has been speculated that capillary haemodynamics might undergo profound changes when faced with ischemic conditions. An experimental investigation of such effects in carotid stenotic-occlusive disease has been performed in this study, whereby a non-parametric [6] estimation of the tissue residue functions from DSC-MRI was used to examine capillary haemodynamics. These were examined in a cohort of patients both at baseline and after carotid endarterectomy (CEA).

**Material and Methods:** DSC data were acquired both pre- and post-CEA from 17 patients (age: 69.7±10.4 years; M:F=12:5) with carotid atherosclerotic disease 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<sup>3</sup> 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 control point interpolation (CPI) method [6] that estimates the tissue residue function ( $R(t)$ ) from a set of control points and then cubic spline interpolation is used to generate a smooth residue function. The transit time distribution ( $h(t)$ ) was calculated from the residue functions using,  $h(t) = -dR(t)/dt$  [2]. The Standard Deviation (capillary transit time heterogeneity (CTTH)) [2] of the transit time distribution was used for evaluation of haemodynamics. Maximum available tissue oxygen extraction fraction ( $OEF^{\max}$ ) and corresponding cerebral metabolic rate of oxygen ( $CMRO_2^{\max}$ ) were calculated using a haemodynamic model which is broadly similar to the model recently developed by Ostergaard et al. [2]. The key difference being that in [2] a gamma distribution was used to model  $h(t)$ , however in our implementation no prior assumption on the form of  $h(t)$  is required: the non-parametric  $h(t)$  estimated from the data being used directly. Five of the 17 patients had regions of restricted diffusion on DWI and thus the following Region of Interest (ROI) analysis was performed: ROIs were selected for each patient in three respective regions of normal, DWI-ring and DWI+ tissue (normal: ROI in contralateral hemisphere; DWI-ring: hypoperfused region around DWI lesion; DWI+: infarcted tissue within DWI lesion). In total 20 ROIs were selected in each of the tissue groups. A student paired t-test was used to test for statistical significance ( $p<0.05$ ) between pre and post-CEA as well among the three tissue types for estimated mean transit time (MTT) and CTTH.

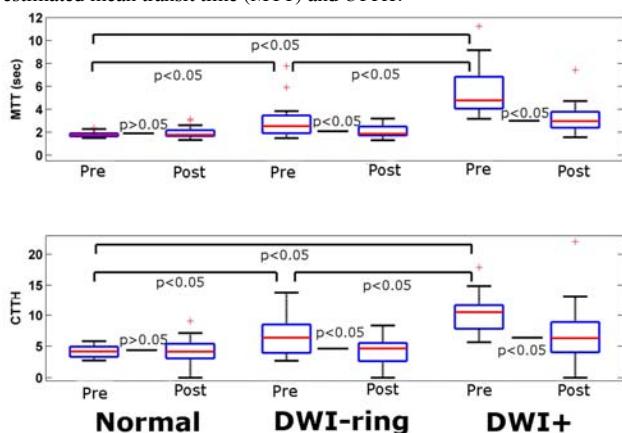


Figure 2: Box and whisker plot showing distributions of MTT (top) and CTTH (bottom) for the three tissue types in pre- and post-surgery perfusion analysis and comparisons for statistical significance.

**Discussion:** Estimation of residue function shape and haemodynamics may be useful in clinical situations since it might permit the assessment of maximum available tissue oxygen and corresponding maximum tissue metabolic rate of oxygen consumption, thereby building from the work described in [2]. Results from a group of carotid stenosis patients are shown in our study using the CPI method for perfusion MRI; where non-parametrically estimated transit time distribution has shown that heterogeneity increased in ischaemic tissue (increase in MTT was found to be associated with a proportionate increase in CTTH). Using our new haemodynamic model, the transit time heterogeneity information was further used to measure maximum available tissue oxygenation and metabolic activity.  $OEF^{\max}$  was found to increase in regions of ischemia (increased MTT) where  $CMRO_2^{\max}$  was found to be maintained; whereas in areas of infarction (DWI+) the  $OEF^{\max}$  compensation appeared inadequate leading to reduction in  $CMRO_2^{\max}$ , which is consistent with literature [2].

**Conclusion:** Analysis of DSC data using the CPI method revealed an increase in capillary heterogeneity which could be linked via a mathematical model of haemodynamics to increases in the maximum achievable  $OEF$  ( $OEF^{\max}$ ) in tissue with ischemia. This provides some support to the theory that haemodynamic mechanisms are at work in ischemic tissue to attempt to maintain oxygen delivery inspite of lowered perfusion. **Reference:** 1. Zheng et al., *NeuroImage* 2002, 16, 617–637. 2. Ostergaard et al., *JCBFM* 2013, 33, 635–48. 3. Christen et al., *AJNR* 2013, 34, 1113–23. 4. Hudetz et al., *The American journal of physiology* 1995, 268, H2202–10. 5. Tomita et al., *JCBFM* 2002, 22, 663–9. 6. Mehndiratta et al., *NeuroImage* 2013, 64, 560–570.

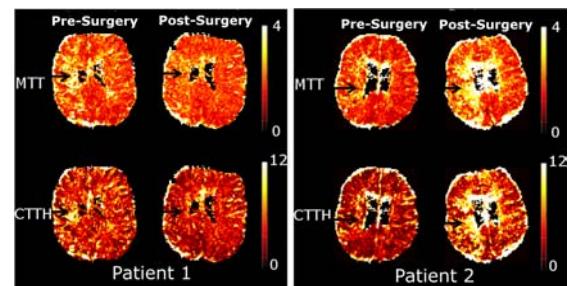


Figure 1: Axial brain slice from two representative patients with atherosclerotic disease showing MTT and CTTH both pre- and post-CEA. Patient1) Increase and Patient2) Decrease in perfusion after CEA. Patient1 (right 40%, left 90%, CEA: left), Patient2 (right 40%, left 80%, CEA: left)

**Results:** From visual inspection six patients showed an increase in cerebral perfusion after CEA, five patients showed a decrease and six showed no change. Figure 1 (patient 1) shows an example of a patient with an increase in tissue perfusion after CEA. Pre-surgery maps show high values of MTT in the right MCA territory which appeared to decrease to normal (same as contralateral hemisphere values) post-surgery. The CTTH value was higher in the right MCA region compared to the contralateral left side before surgery; the CTTH in the right side reduced to values similar to those on the contralateral side after surgery. Figure 1 (patient 2), from a patient that showed a decrease in tissue perfusion after CEA: The right MCA territory showed an increase in MTT and CTTH after CEA. Figure 2 shows the variation in MTT and CTTH pre- and post-surgery in the three ROIs, with corresponding statistics reported. No changes were observed in normal tissue, whereas a significant decrease in both MTT and CTTH after surgery in DWI-ring and DWI+ tissue were seen. Both MTT and CTTH also showed significant differences between tissue types in the pre-surgery analysis. Figure 3 shows a representative patient where high MTT was observed in the left hemisphere, and with an associated elevated  $OEF^{\max}$  but unaffected  $CMRO_2^{\max}$  map; except in a small region within the white matter where  $CMRO_2^{\max}$  was lower than normal (marked with arrowhead, corresponding to DWI+ region).

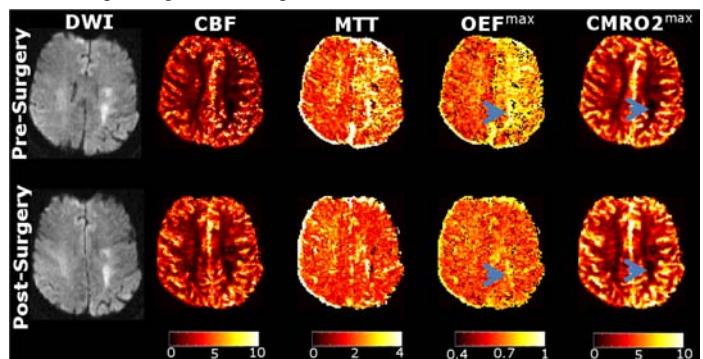


Figure 3: DWI, CBF, MTT,  $OEF^{\max}$  and  $CMRO_2^{\max}$  analysis from a representative patient.

haemodynamics to increases in the maximum achievable  $OEF$  ( $OEF^{\max}$ ) in tissue with ischemia. This provides some support to the theory that haemodynamic mechanisms are at work in ischemic tissue to attempt to maintain oxygen delivery inspite of lowered perfusion.