Conclusion: Lactate Change were not identical to the region defined by DWI/PWI mismatch. Scanning with 3 mins on normoxia and 5 mins on 50%O\textsubscript{2} hyperoxia. Following an increase in the level of hyperoxia to 100%O\textsubscript{2}, a further Lactate scan was carried out.

Differentiates between anaerobic/aerobic metabolism.\textsuperscript{1}1,2 magnetic properties of deoxy- and oxyhaemoglobin in blood (paramagnetic and diamagnetic, respectively), while technique 2 uses Lactate Change Imaging, which differentiates between anaerobic/aerobic metabolism.\textsuperscript{1}2

Our aim was to demonstrate an enhancement of these techniques working concurrently in a single scanning protocol, through the addition of an oxygen-carrying perfluorocarbon (PFC) emulsion (Oxycyte®; Oxygen Biotherapeutics). Furthermore we aim to provide validation of the combined techniques by confirming on-going tissue metabolism in hypoperfused regions of the brain identified as penumbra.

Methods: Following permanent middle cerebral artery occlusion (MCAO) in rats (n=9), serial scanning (Bruker 7T Biospec) produced maps of ischaemic injury (from apparent diffusion coefficient, ADC maps) and perfusion deficit (arterial spin labelling). The combined T2* / Lactate Change penumbra imaging protocol was carried out following Oxycyte® injection (4.5ml/kg, i.v). At ~1.5hrs following MCAO an initial baseline Lactate scan was carried out on normoxia. This was followed by T2* scanning with 3 mins on normoxia and 5 mins on 50%O\textsubscript{2} hyperoxia. Following an increase in the level of hyperoxia to 100%O\textsubscript{2}, a further Lactate scan was carried out. The scanning protocol was repeated at ~2.5hrs following MCAO, followed immediately by a terminal [14C]2-deoxyglucose (2-DG) autoradiography protocol to determine glucose metabolism in the region identified as penumbra.

Results: From region of interest (ROI) analysis on T2* signal change maps it was found that in all cases and at both time points (1.5 and 2.5 hrs post MCAO), the magnitude of T2* signal change to 50%O\textsubscript{2} hyperoxia following Oxycyte® varied throughout the brain (Figure 1, Figure 2(ii)). In the ipsilateral hemisphere, the region defined as penumbra displayed a T2* signal increase significantly higher than the T2* % signal change in adjacent ischaemic core ROI identified from thresholded ADC maps (Figure 2i &2ii) and contralateral ROI. The magnitude of response to 50%O\textsubscript{2} + Oxycyte® in the penumbra ROI was similar to that previously seen with 100%O\textsubscript{2} hyperoxia alone (which has limitations for use in man due to imaging artefacts and contraindications in some patients). The addition of Oxycyte® therefore provides an improvement on the T2*OC method to detect penumbra using lower levels of inspired oxygen.

In all experiments increased lactate levels detected within the ischaemic hemisphere decreased in response to hyperoxia + Oxycyte® as indicated in the aerobic Lactate Change map (Figure 2ii). On returning to normoxia, lactate increased as indicated in the anaerobic Lactate Change map (Figure 2iv). The addition of Oxycyte® represents an improvement in the sensitivity to detect lactate change to OC, when compared to hyperoxia (100%O\textsubscript{2}) alone.\textsuperscript{2}

With both T2* and Lactate Change OC techniques, the region identified as penumbra displayed maintained glucose metabolism (25.5±2.6μmol/100g/min), comparable to values in contralateral cortex (23.2±2.5), while adjacent ischaemic core displayed low glucose use (12.4±7). Regions identified as penumbra by thresholded T2* and Lactate Change were not identical to the region defined by DWI/PWI mismatch.

Conclusion: Penumbra detection with combined dynamic T2* and Lactate Change OC imaging is improved with the addition of PFC Oxycyte®. In the clinical management of stroke it is important to accurately identify patients with potentially salvageable penumbra tissue and GOLD MR imaging has the potential to offer an improvement on current techniques by being primarily based on metabolism.


Oxycyte® was provided by Oxygen Biotherapeutics Inc. (Morrisville, NC, USA).