

Combined use of arterial spin labeling and MRS to determine the severity of injury in neonates with hypoxic-ischaemic encephalopathy

Magdalena Sokolska^{1,2}, Maia Proisy³, Cristina Uria-Avellanal³, Alan Bainbridge², Ernest Cady², David Thomas¹, Nicola Robertson³, and Xavier Golay¹
¹UCL Institute of Neurology, London, London, United Kingdom, ²UCH Medical Physics and Bioengineering, London, London, United Kingdom, ³UCL Institute for Women's Health, London, United Kingdom

TARGET AUDIENCE – Neonatologists and researchers involved in neonatal imaging

PURPOSE. Cerebral blood flow (CBF) reflects cerebral metabolic demand, and can be altered in neonates with brain injury. Proton MR spectroscopy (MRS), in particular thalamic Lac/NAA peak ratio, has been shown to be the best predictor of clinical outcome so far¹. Adding estimation of CBF to MR spectroscopy (MRS) has the potential to both increase understanding of the injury cause and progression and to help develop and assess new neuroprotective treatments. CBF can be quantified non-invasively using Arterial Spin Labeling (ASL). The aim of this study was to investigate neurophysiological changes in babies with suspected hypoxic ischaemic brain injury using MRS and ASL.

METHODS. The study was approved by the local ethics committee. Seven neonates (one pre-term) with suspicion of acute brain injury were enrolled in the study. The infants were appropriately prepared for the MRI examination, placed in an MR compatible incubator and monitored throughout the scan (3T Philips Achieva). All infants were sedated either with an oral dose of chloral (5) or intravenous morphine in the case of ventilated babies (2). Additionally to standard structural imaging, 6 neonates underwent MRS and 5 the full ASL protocol.

An MRS voxel was positioned in the left thalamus. Water-suppressed spectra were acquired using PRESS (64 averages, TR/TE = 2288/288ms, voxel size 15x15x15mm (~7 min)). The spectra were manually corrected for phase and frequency shifts and fitted using the AMARES algorithm as implemented in the jMRUI software package. The following peak-area ratios were calculated: N-acetylaspartate to lactate (NAA/Lac), NAA to creatine (NAA/Cr) and choline to Cr (Cho/Cr). Pseudo-continuous ASL² (pCASL) was chosen for CBF measurement due to its intrinsic highest signal-to-noise ratio. The labeling plane was positioned based on ToF angiography images to ensure that it was perpendicular to the feeding arteries. The labeling duration was 1.7s with a post-labeling delay of 1.5-1.7s. For readout, GE-EPI was used with FOV 240x240, acq matrix 64x64 and TR/TE 4000/20ms. An M0 image was also acquired (5 neonates), with the same acquisition parameters as the pCASL readout.

Motion Correction was performed by rigid registration (based on normalized mutual information) of all time series images to a subject template created from every other control image using DTITK³. Images with significant motion (> 3mm translation or >2degrees rotation) were automatically identified and discarded before pairwise subtraction. An additional check for miss-registration was performed before final averaging. Although this reduced the number of repetitions in the CBF maps, thereby decreasing its SNR, the quality of the resulting maps were significantly improved on average.

Quantification. The single compartment Buxton model was used for CBF quantification using FSL^{4,5}. Blood T1 (T1b) was calculated for each baby based on measured hematocrit values according to equation $1/T1b = 0.5 \cdot Htc + 37^6$. Labeling efficiency was estimated to be 0.75 for the range of velocities found in neonates by numerical simulations of Bloch Equations.

Condition	tNaa/Cr	tCho/Cr	Lac/tNaa	WB_CBF	TH_CBF
Mild HIE	1.83	2.17	0.15	24.2	42.7
Seizures	1.77	2.08	0.14	33.9	73.0
Severe HIE	0.82	0.94	1.94	48.0	67.1
Moderate HIE	1.53	1.95	0.18	21.3	38.9
Mild HIE	1.56	1.59	0.12	18.6	19.1
Seizures	1.64	1.75	0.12	29.4	46.7
Cyst	-	-	-	33.2	48.7

Table1. MRS peak to area ratio from thalamus and CBF (ml/100g/min)) results

RESULTS. Peak Area ratios and CBF values for the whole brain and thalamus are presented in Table 1. Mean CBF in the whole brain and thalamus was 30 (STD 9) and 48 (STD 17) ml/100g/min respectively, which is in broad agreement with the literature⁷. In mild/moderate HIE babies, WB-CBF and TH-CBF were lowest: 21.2 and 33.6 ml/100g/min respectively (Figure 1A). In a very severe case of HIE, both WB-CBF and TH-CBF were elevated, along with an increased Lac/NAA ratio indicating severe brain injury (Figure 1 B). In a baby suffering from seizures, elevated focal CBF in the thalamus was observed with normal Lac/NAA (Figure 1 C).

DISCUSSION & CONCLUSION. This study investigates the use of two potentially complementary MR biomarkers of perinatal brain injury: MRS and ASL. 1H MRS provides a measurement of the current cerebral neuronal metabolic status, whereas CBF assesses nutrient delivery to the brain. Mismatch between these two measurements may allow discrimination of irreversibly damaged tissue and tissue at risk of injury, and therefore provide crucial prognostic information in HIE babies.

In this study, a constant labeling efficiency was assumed for all babies. However, it is possible that carotid artery flow may vary between babies, particularly those that are severely ill, and this will affect CBF quantification unless accounted for. Phase contrast MRA can be used to assess this, but this is not always feasible given the time constraints and priorities of clinical scans. The importance of this factor will be investigated in future studies.

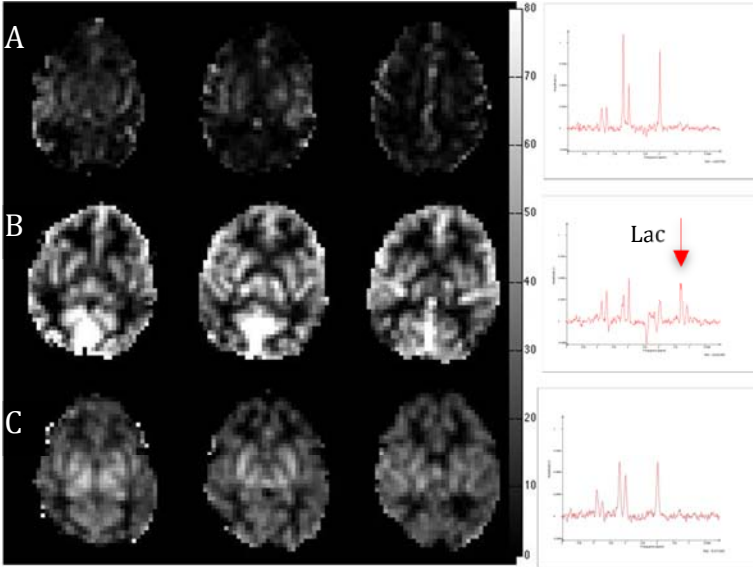


Figure1. CBF maps of neonates with A – mild HIE, B – severe HIE, C - neonatal seizures. Corresponding raw spectra on the right

REFERENCES
1.Thayyil S et al. 2010 *Pediatr Res* 125(2):382-95 2. Dai et al. *MRM* 60:1488–1497 (2008) 3.<http://dti-tk.sourceforge.net> 4. <http://fsl.fmrib.ox.ac.uk/fsl> 5.Chappell et al. *IEEE Transactions on Signal Processing* 57(1):223-236, 2009 6.Varela et al. *NMR Biomed.* 2011; 24: 80–88 7.Wintermark et al. *AJNR Am J Neuroradiol* 32:2023–29