QUANTIFICATION OF FETAL BRAIN LACTATE WITH MR SPECTROSCOPY

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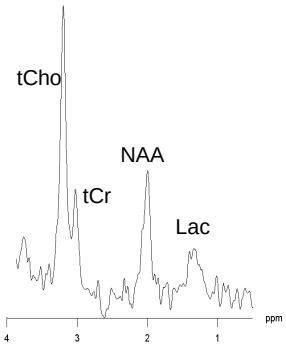
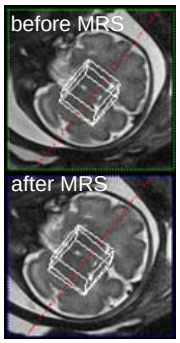
Introduction.
Magnetic resonance spectroscopy (MRS) has been used to measure cerebral lactate levels in a range of human populations, from elderly stroke patients to pre-term neonates. Although MRS has demonstrated elevated lactate in the sheep fetal brain during hypoxic injury [1] there is little evidence of its application to the measurement of fetal cerebal lactate in humans. The aim of this study was to assess the feasibility of lactate detection and quantification using MRS on a clinical 1.5 T MR system in a group of patients at high risk of fetal hypoxia.

Methods.
Six women with singleton pregnancies were recruited to the study through the fetal medicine department. Inclusion criteria were intra-uterine growth restriction (IUGR) and/or absent or reversed end-diastolic flow (EDF) in the umbilical artery, together with a cephalic presentation to minimise the potential of fetal head motion. MRS data were acquired on a Siemens 1.5 T Avanto system using spine and body matrix coils. An asymmetric PRESS sequence with an echo time (TE) of 288 ms was used to provide an in-phase lactate peak with minimal signal reduction from the spatial interference effect [2]. This long TE also produced a flatter baseline and helped to reduce the significance of any contamination from maternal lipid, observed in previous work [3, 4]. Other sequence parameters were: TR = 2000 ms, 256 signal averages. The MRS voxel (25×25×25 mm) was positioned in the centre of the fetal brain, as visualized on single shot T_2-weighted MR images. Further MRS data were acquired from the same voxel position without water suppression to provide an internal reference for quantification purposes, and again with a short TE of 30 ms to permit a measurement of water transverse relaxation and to check for lipid contamination. MRI was repeated after MRS to check for fetal movement. No sedation was used. Spectra were processed with the AMARES algorithm [5] within jMRUI [6]. Metabolites were T_2-corrected with literature values measured in neonates at similar postconceptional ages [7] and referenced to the unsuppressed water signal. The water concentration reference was adjusted for gestational age [8]. Apgar scores, which have previously been shown to correlate with MRS findings in perinatal asphyxia [9], were recorded at birth. In one subject, spectra were acquired at both TE = 288 ms and 144 ms (128 signal averages) to enable a comparison of lactate detection at these different echo times and assess the impact of the spatial interference effect. A similar comparison of the lactate signal at these TEs was made using a test object containing 5 mM lactate.

Results.
A successful MRS acquisition was obtained in four patients, demonstrating a small peak around 1.3 ppm, consistent with the presence of lactate, although in one case (subject 3) this was shown by the short TE MRS data to be confounded by the presence of significant lipid contamination. This contamination was consistent with an observed shift in fetal position between the MRI images acquired before and after MRS. The two unsuccessful cases were due to claustrophobia and a technical failure. An example MR spectra is shown (subject 1) with lactate (Lac), total choline (tCho), total creatine (tCr) and N-acetyl aspartate (NAA) peaks labeled accordingly, and the voxel position displayed on the pre and post MR images. The table below lists clinical details with gestational ages (GAs) and measured metabolite concentrations for each subject. Standard deviations are obtained from the peak fitting in jMRUI. For the one case where MR spectra were acquired at both TE = 288 ms and 144 ms, the fitted lactate peak integrals (± standard deviation) were 10.5 ± 1.3 and 4.8 ± 1.7 arbitrary units respectively, demonstrating the reduced lactate signal from the spatial interference effect at the shorter TE. Similar results were found using the test object, with a 40% increase in the integral of the lactate doublet for TE = 288 ms compared to TE = 144 ms.





Subject	Clinical history	GA at MR scan [weeks + days]	Metabolite concentrations (± standard dev) [mmol/kg]				GA at birth [weeks + days]	Apgar scores at 1 and 5 minutes
			Lactate	NAA	tCho	tCr		
1	Absent EDF	31 + 6	2.9 (0.3)	5.0 (0.3)	6.6 (0.2)	9.3 (0.7)	40	9, 10
2	severe IUGR + absent EDF	32	3.5 (0.4)	5.0 (0.3)	4.4 (0.2)	9.0 (0.9)	32	3, 8
3	IUGR and absent EDF	29 + 5	Not quantified. Significant lipid contamination observed from short TE MR spectra. Movement between pre and post MRI				33 + 2	9, 9
4	IUGR	37 + 4	2.7 (0.6)	12.5 (0.9)	4.4 (0.3)	12.0 (1.7)	38	9,10

Discussion.
To the authors' knowledge this is the first MRS study to quantify lactate in the human fetal brain. The concentrations of lactate measured here are comparable to levels observed in MRS studies of normal preterm neonates [10], despite the high risk suggested by conventional clinical assessment in these patients. This was consistent with the high Apgar scores in all cases. Concentrations of NAA, total choline and total creatine measured in this work are comparable with literature values for normal fetal brain at these gestational ages [4]. In summary, this work demonstrates that acquisition of MRS data with sufficient quality for the quantitative assessment of lactate in the fetal brain is achievable at 1.5 T in this group of patients. Further investigations may provide a valuable direct and non-invasive assessment of fetal hypoxia.

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References.
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