A Multicentre study of 1H MRS for the Characterisation of Low Grade Brain Tumours of Childhood

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Background: Brain tumours are the commonest solid tumours in childhood, and low grade tumours constitute 40-50% of these. Low grade tumours are a diverse group, mainly gliomas, which often present diagnostic and prognostic challenges to the clinician. ^{1}H Magnetic Resonance Spectroscopy (MRS) is a non-invasive clinical method for obtaining biochemical profiles of tissue which is showing promise in aiding decision-making [1].

Methods: Single voxel MRS was performed as part of the routine clinical magnetic resonance imaging prior to treatment. Birmingham Children's Hospital (BCH), the University Hospital Nottingham (UHN), and Great Ormond Street Hospital (GOS) contributed data. MRS was performed at 1.5 T, using echo times of 20-40ms and TR 1500ms. The raw data was processed using LCModel^{TM} and the metabolite concentrations relative to water determined [2]. Differences in mean metabolite concentrations between histological diagnoses and at different brain locations were analysed. Metabolite differences between patients who progressed and those who did not were also investigated.

Patients & Results: Pre-treatment MRS was performed and data was available for 77 patients with low grade brain tumours (including DNETs). For the analysis, 9 patients were excluded due to insufficient. MRS data, and 14 were excluded on MRS quality control grounds (S/N<4 and FWHM>0.15), leaving a cohort of 54 patients (41 from BCH, 9 from QMC, 4 from GOS). Breakdown by site of tumour showed 14 cerebellar tumours, 13 suprasellar+hypothalamic+3rd ventricular, 10 cerebral and 5 brainstem+tectal plate and 12 where this information was not available. Breakdown by diagnosis showed 25 PA, 5 OPG, 5 gangliogliomas, 5 DNETs, 5 diffuse astrocytomas (+fibrillary and gemistocytic), 4 TPG, 2 pilomyxoid astrocytomas, 1 oligodendroglioma, 1 pleomorphic xanthoastrocytomas, and 1 unbiopsied low grade glioma. 10 patients progressed, 23 did not, and for 21 follow-up information was not available.

A comparison between different tumour types using ANOVA showed that PA+OPG have lower creatine (1.21 vs 3.50, p=0.035) and glutamate+glutamine (4.10 vs 7.89, p=0.012) than gangliogliomas.

ANOVA testing showed significant differences in PA+OPG at different sites. Suprasellar/hypothalamic/3rd ventricle tumours have lower creatine than cerebral tumours, mean 1.44 vs 0.16, p=0.022, and higher myo-inositol than cerebellar tumours, mean 3.51 vs 1.02, p=0.018.

When comparing patients who progressed with those who did not (excluding diffuse astrocytomas and completely resected tumours), glycerophosphocholine + phosphocholine is significantly higher in patients who did not progress, 1.28 vs 0.70, p=0.003. However, the difference can be attributed to glycerophosphocholine, as it is significantly higher in the non-progressors, 0.89 vs 0.41, p=0.024, whereas phosphocholine is not significantly different. No patients with a PA+OPG and a myo-inositol >2.9 progressed during the study period.

Discussion: MRS has shown the potential to discriminate between different low grade tumour types, and the multicentre approach taken in this study is essential to provide sufficient numbers for robust analysis of rarer tumour types. For the most common group, PA+OPG, MRS has detected differences between tumours in different areas of the brain, which concurs with the known clinical diversity of the group. MRS also shows promise as a non-invasive prognostic tool, and differences between progressors and non-progressors are starting to be apparent. However, the small number of patients means that significances are not yet established. This work provides evidence to support prior hypotheses such as myo-inositol being a biomarker of good prognosis and the prognostic importance of individual constituents of the choline peak.

Conclusion: MRS can be performed at multiple centres in children with low grade tumours as part of their routine clinical imaging and the data combined to provide robust results. MRS can discriminate low grade brain tumours on the basis of diagnosis and location and is a promising technique for predicting prognosis in low grade tumours in children.

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Glossary: PA = pilocytic astrocytoma, OPG = unbiopsied optic pathway glioma, TPG = unbiopsied tectal plate glioma, DNET = dysembryoplatic neuroepithelial tumour (biopsied + unbiopsied)

References:

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