A Multicentre Study of in vivo 1HMRS of Paediatric Brain Stem Tumours

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INTRODUCTION:

The management of tumours arising in the brain stem continues to present a major challenge to paediatric oncology. The outcome varies greatly depending on the nature of the tumour. Diffuse pontine gliomas (DPG) are the most common lesions and have a particularly poor prognosis with no improvement in the outcome for 30 years. The brain stem is a particularly difficult area to biopsy and diagnosis is often made on clinical and imaging grounds alone. Novel imaging methods offer a means of improving diagnostic accuracy and furthering our understanding of the biology of these important childhood tumours.

METHOD:

Single voxel ^{1}H Magnetic Resonance Spectroscopy (MRS) was performed on 16 children at 3 centres prior to treatment using a standardised protocol. Voxels were all cubic with a 1.5cm or 2.0cm side, the echo time was 30ms and the repetition time 1500ms. Cases were accrued for the main tumour types occurring in the brain stem. Four patients underwent biopsy, diagnosing 3 low grade and 2 high grade astrocytomas. The other tumours were diagnosed on clinical and imaging criteria alone and consisted of 3 tectal plate glioma (TPG) and 9 DPG. For analysis TPGs were combined with the low grade astrocytomas to give a group of low grade gliomas (LGG) in keeping with their presumed histopathology. Raw MRS data were processed using LCModel™ to determine metabolite concentrations, signal to noise ratio (SNR) and full-width-at-half maximum (FWHM). Cases were only included if the voxel was correctly located, the SNR was greater than 5 and the FWHM was less than 0.15ppm.

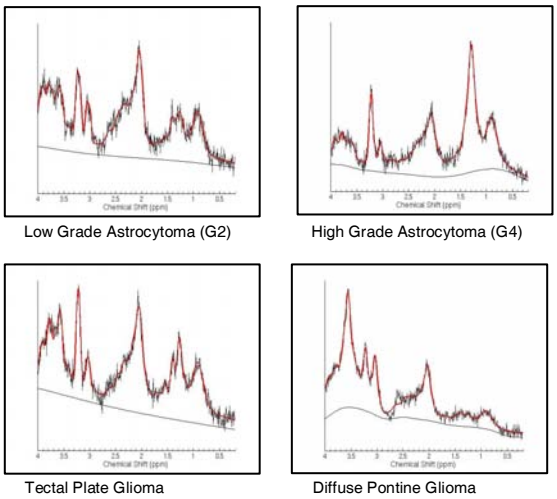

Figure 1: Examples of spectra for each of the 4 main types of brain stem tumour

RESULTS:

Example spectra for the various tumour types are shown in figure 1. The Creatine/Choline ratio was found to be significantly higher ($p<0.001$) in DPGs (2.87) than in the LGG group (1.39) and Inositol/Choline ratio was significantly higher ($p<0.001$) in the DPGs (5.57) than LGG (1.91). A scatter plot of Creatine/Choline versus Inositol/Choline is given in figure 2. This shows DPGs to be well separated from the other tumours. Low grade astrocytomas and TPGs cluster together as expected and are separated from the high grade astrocytomas which lie furthest from the DPGs. The spectra of DPGs, HGGs and LGGs possess several differentiating features in their metabolite profiles (figure 3). In particular, DPGs have high inositol, N-Acetyl Aspartate and a peak at 2.6ppm which is not assigned by LCModel™. DPG spectra show some similarities with ependymoma spectra (not presented here), including the peak at 2.6ppm and the elevated inositol level.

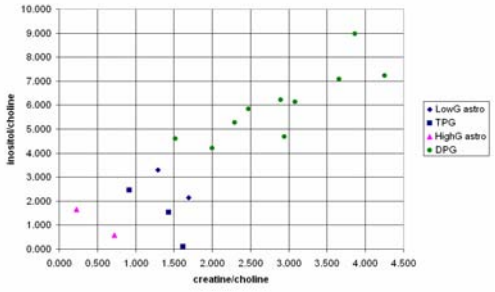

Figure 2: Scatter Plot

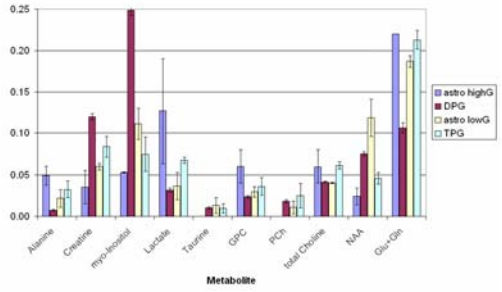

Figure 3: Metabolite Profile of average spectra of 4 main tumour types occurring in the brain stem. Error bars represent the standard error on the mean

CONCLUSIONS:

The results of this study show that MRS can be successfully collected and analysed from multiple centres to investigate rare but important tumours. The method can differentiate between the common tumour types seen in the brain stem of children. DPGs are distinct from all other astrocytomas and despite the aggressive clinical behaviour of these tumours they can be readily distinguished from high grade gliomas of the brain stem. MRS provides a non-invasive method for aiding the diagnosis of brain stem tumours and also provides an insight into the biological diversity of these important tumours.