The value of MRS detectable lipids as prognostic markers in paediatric brain tumours

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Introduction

Brain tumours are an important cause of childhood morbidity and mortality and new approaches to brain tumour assessment and therapy are a priority for cancer research. Biomarkers which are predictive of patient survival can be used to individualise the treatment, discovery and evaluation of such biomarkers is a key component of many research strategies. Non-invasive biomarkers have many advantages clinically and in-vivo 1H MRS in particular has shown promise by detecting a number of biomolecules that are markers of tumour aggressiveness. Small studies have indicated that total choline and lipids are biomarkers of both grade[1] and prognosis[2] in childhood brain tumours but their evaluation as markers of survival requires studies with larger numbers of patients followed up for many years. Furthermore, studies which have not used short echo time 1H MRS may have underestimated the importance of mobile lipids since these are attenuated significantly at longer echo times. In this study we report the largest cohort of childhood brain tumours studied at diagnosis by short echo time 1H MRS with follow-up to period of up to 5 years.

Method

MRS data was collected from a cohort of 152 patients each presenting with a suspected brain tumour at Birmingham Children's Hospital. All tumour types were included and no patients were lost to follow-up. Patients were scanned prior to treatment and follow-up times were defined as starting on the date of the first scan (median follow-up time of 18 months). Single Voxel Spectroscopy was performed using a PRESS sequence with an echo time of 30ms collected on GE and Siemens scanners at a field strength of 1.5T. Each spectrum was analysed using the LCModel[3] fitting algorithm and molecular concentrations were calculated relative to a corresponding un-suppressed water reference spectrum. Spectra with outer-volume lipid contamination due to poor voxel positioning, a SNR value of less than 4 or a metabolite FWHM value of more than 10 were removed from the study leaving 121 cases. Lipid, macromolecule and metabolite quantities were imported into the R statistical package. Kaplan-Meier analysis was performed on patients with high and low values of each measured quantity and a log-rank test was used to investigate whether patient survival was significantly related to these levels. Cut-off values were determined by maximising the significance of the log-rank test.

Results and Discussion

Both of the lipid quantities in figures 1 and 2 show a lower survival rate for tumours with higher levels of lipids at the end of follow-up. Lipid signals at 1.3ppm give better separation between the two groups ($p<0.05$) when compared to the lipid signal at 0.9. This may be due to interference with other broad signals such as proteins resulting in a reduced accuracy. Figures 1 and 2 also show that in the first 400 days of follow-up the survival curves are similar for tumours with both high and low levels of lipids. This may indicate that lipids have a greater prognostic power for identifying long term rather than short term survivors. There was also a trend towards lower choline ($p=0.074$) and taurine ($p=0.073$) in survivors.

Conclusion

Tumour lipid levels measured by short-echo time single voxel MRS are predictive of long term outcome in children with brain tumours offering a potential non-invasive biomarker to aid current diagnostic methods.

Acknowledgements

References

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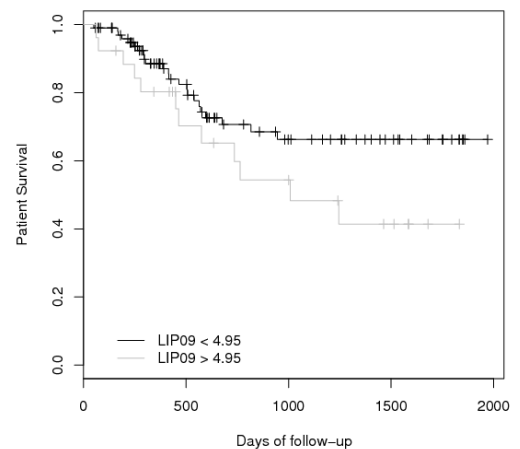
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Figure 1 Kaplan-Meier curves for Lip0.9, p=0.089.

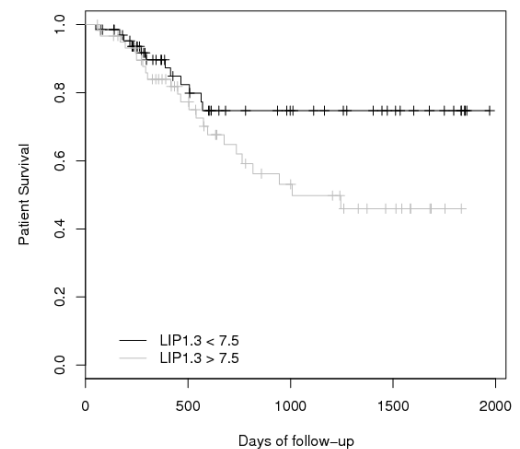Figure 2 Kaplan-Meier curves for Lip1.3, p=0.049.