Classification of human brain tumors with quantitative short echo ^{1}H MRS

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Introduction ^{1}H MRS metabolic profiles can provide information on tumor type and grade. Long echo-time (TE=136ms) data are generally used *in vivo* (1) but provide limited information compared to that available from high resolution spectra of tumor extracts (2). Short echo-time data (TE=30ms) have an increased SNR and give potentially more metabolic information. The aim of this study was to obtain quantitative data to compare absolute metabolite concentrations between tumor types and assess whether short echo-time data provide better discrimination between tumor classes than long echo-time data.

Methods Thirty-five STEAM (TE 30ms, TR 2020ms) and metabolite nulled (TI 700ms) spectra were acquired from 31 patients with brain tumors subsequently graded post surgery. A) 4 meningiomas (*mm*); B) 5 astrocytoma grade II (*ast II*); C) 5 astrocytoma III (*ast III*); D) 13 glioblastomas (*gbm*); E) 4 metastases (*met*). The VARPRO time domain technique with tumor water as a reference was used for metabolite quantitation.

Results Absolute metabolite concentrations provide discrimination between certain tumor types. [NAA] < 5mM indicated abnormal tissue compared to normal parietal white matter (NPWM) and [mI] > 2mM distinguished all astrocytomas from *gbm/mets* and *mm* with (P<0.0001). [Cho] discriminates *ast* from *gbm/mets* (P<0.005) and Cr discriminates *ast* from *gbm/mets* and *mm* (P<0.0001). For 15/17 high grades the total lipid was > 2 a.u. Ala was only quantifiable in 3/5 *mm* so the ala concentration alone was not sufficient to discriminate all *mm* from other tumors. However, observing that high Cho and Ala, but low Cr occur in *mm*, high mI and Cr in *ast* suggests a linear combination of metabolite concentrations as "discriminating vectors". DV1=Cho+Ala-Cr, DV2=mI+Cr. On a 3D data plot, planes at DV1=2, DV2=3 and lipid=2 discriminated 5/5 *mm*, 12/13 *ast* and 15/17 high grades. 1 *ast* was misclassified as high grade and 2 high grades were unclassified. *Gbm* and *mets* were not distinguishable, but for a [Cr]/[Cho] > 1.4, (*ast II* = 2.4±1.3, *ast III* = 1.2±0.5, *gbm* = 0.9±0.7), all *ast II* were distinguished from *ast III*, but 2 *ast III* were misclassified as *II*. NAA was observed in 7 *ast* and Lac in 15 spectra of various tumor classes, but was not useful for discrimination between tumor types. A Pearson correlation analysis using all spectral points between pairs of tumors (1) indicated discriminatory spectral regions with correlation coefficients ≥ 0.7 for regions corresponding to: mI, Cr, Glx/MM and Ala for *mm* v. *ast*; Cho, Glx/MM, lipids for *mm* v. *gbm*; mI, Cho, Cr and lipids for *ast* v. *gbm*.

Discussion Distinct patterns in the average short echo-time spectra (Fig 1) enabled surprisingly good discrimination to be made between four tumor groups on the basis of metabolite concentrations. mI, a major metabolite in glial cells was strongly

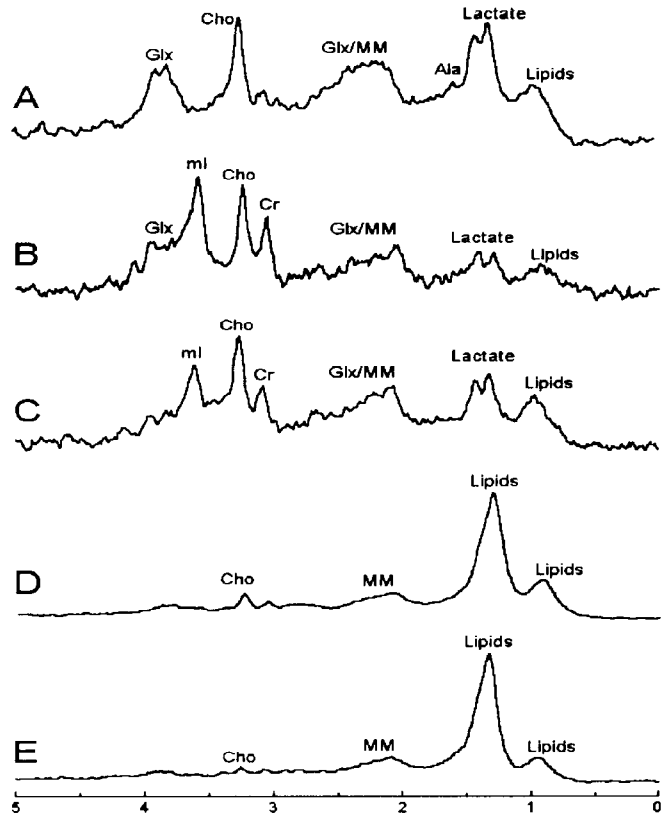

Figure 1 Average spectra for each tumor type

associated with low grade astrocytomas. mI is not observed in long echo time data, for which discrimination of some *ast* v. *gbm* can be problematic (1). The association of increased [Cho] with cell proliferation and higher grades is confounded by dilution effects due to micronecrosis, but the [Cr]/[Cho] ratio is not effected by dilution and decreased with grade. Metabolite nulling enabled Ala and Lac to be quantified in the presence of lipids, but only [Ala] was an aid to classification. Correlation analysis of the spectra indicate Glx, prominent at short echo time in *mm* and *ast II* at 3.8 ppm and 2-2.5 ppm, to be a possible classifier. This initial study suggests short echo time data may provide very good tumor classification. A more sophisticated pattern recognition analysis is underway.

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References

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Table 1 Metabolite concentrations, mean (mM) ± sd

	mI	Cho	Cr	NAA	Ala	Lac	Lipids (au)	DV1	DV2
Meningioma	<0.2[#]	2.5±1.2	0.5±0.8	nq	1.8±0.9	4.3 ±3.4	0.6±1.4	4.6±0.2	0.3±0.8
Astro II & III	6.8±2.6	2±0.7	3.3±1.0	1.5±1.8	<1[#]	1.9±3	0.7±1.4	-1.2±1.1	10±2.3
Gbm & Met	<0.4[#]	1.1±0.8	0.9±1.4	0.2±0.7	<0.8[#]	1.4±0.4	23±26	0.1±1.1	1.1±1.6
Normal PWM	5.1 ±0.9	1.8±0.2	6.2±0.4	11.3±1.6	nq	nq	nq	-4.4	11.3

No visible peaks to quantify so maximum concentrations estimated on the spectrum SNR