Automated classification of ^{1}H MRS brain tumour spectra: a linear discriminant analysis comparison of LCModel quantification versus complete spectra

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Introduction

In this study we investigated the use of pattern recognition techniques, using leave-one-out linear discriminant analysis (LDA) of single voxel ^{1}H MRS, to distinguish metastases from glioblastomas; so far unachieved by current pattern recognition studies. A comparison is made of i) LCModel[1] quantification versus the whole spectra, ii) the effects of combining PRESS and STEAM data versus STEAM data alone; and iii) the effects of using principal component analysis (PCA) versus manually chosen metabolite concentrations from the LCModel[1] quantification.

Methods

^{1}H spectra were obtained using the automated PROBE acquisition with PRESS or STEAM (TE=30ms, TR=2000ms, 2048dp) on a 1.5T Signa Horizon, (GE, Milwaukee). Pathologies were radiologically verified and consisted of: 8 astrocytoma grade II (AS2 - 7 STEAM, 1 PRESS), 26 meningiomas (MNG - 15 STEAM, 11 PRESS), 22 glioblastomas (GBM - 14 STEAM, 8 PRESS) and 25 metastases (MET - 10 STEAM, 15 PRESS). Biochemicals [Alanine, Creatine (Cr), Glucose, Glutamate + Glutamine, Glutathione (GSH), myo-Inositol (Ins), Lactate, NAA, scyllo-Inositol, Taurine, total Cholines and lipid/macromolecule areas δ1.3, δ0.9 and δ2] were quantified using LCModel[1], optimised to include the lipid and macromolecule signals observed in high-grade tumors.. The Mann Whitney U-test was used for statistical comparison of the individual LCModel[1] quantified metabolite concentrations between tumour groups, and LDA of LCModel[1] concentration estimations was compared with LDA of whole spectra. The number of quantified metabolites used for LDA were reduced either by: i) selecting particular biochemicals according to the Mann Whitney comparisons (in this study Cr, Ins, GSH and δ1.3 showed the biggest differences between groups); or ii) using PCA. The spectra were linebroadened by 0.8Hz and a study carried out on i) real and ii) magnitude spectra using PCA and LDA. 0.8Hz linebroadening and magnitude spectra had previously been used in pattern recognition studies for the INTERPRET[2] project (EU collaboration to develop a decision support system for classifying brain tumours by ^{1}H MRS). LDA studies were carried out on each dataset to classify i) AS2, MNG and HG (high-grades comprising GBM + MET), ii) AS2, MNG, GBM and MET; and iii) AS2, GBM and MET. An initial statistical analysis of PRESS and STEAM spectra from the same voxel (Wilcoxon signed-ranks test) revealed differences in the metabolite concentration estimations by LCModel, but the heterogeneity of tumors causes greater variance within tumor groups. LDA was carried out on STEAM data alone and with PRESS and STEAM combined to assess how combining the data affects classification.

Results

All LDA studies to classify AS2, MNG and HG, all gave similar results to those found with the INTERPRET[2] study protocol (92% correctly classified). Analyses with HG separated into GBM and MET (AS2, MNG, GBM and MET) resulted in poor separation (59 - 74%) for all LDA carried out after a PCA. In contrast, using LCModel[1] concentrations of the 4 manually selected metabolites achieved a maximum 80% classification using STEAM data alone. A final LDA was carried out primarily to separate GBM from MET (AS2, GBM and MET) and results obtained followed a similar pattern to the previous LDA (AS2, MNG, GBM and MET). LDA of complete spectra and of the PCA of all concentrations gave poor classification (54 - 72% correct). Using 4 manually selected LCModel[1] concentrations on PRESS + STEAM only provided 75% classification whereas the STEAM data showed 87% correctly classified. The plot (Fig. 1) shows the LDA separating AS2, GBM and MET using STEAM data and the 4 manually selected LCModel[1] concentrations, with the arrows marking the misclassified cases; Table 1 shows the misclassification details. STEAM δ1.3 quantitation showed statistical differences between all the tumor groups shown here with $P < 0.02$ (Table 2) whereas, the PRESS δ1.3 results showed no difference between GBM and MET ($P = 0.728$).

Fig. 1

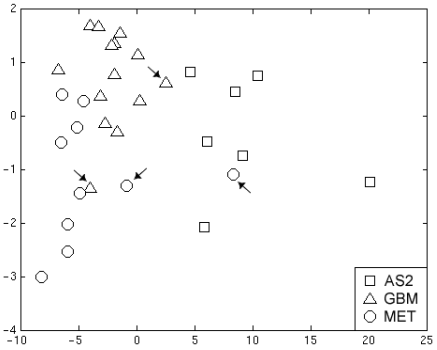

Table 1

	AS2	GBM	MET
AS2	7	0	0
GBM	1	12	1
MET	1	1	8

Table 2

	AS2	MNG	GBM	MET
AS2	*	0.005	<0.001	<0.001
MNG	*	*	<0.001	<0.001
GBM	*	*	*	0.016
MET	*	*	*	*

Discussion

The principal components (PCs) chosen by the PCA, and the spectral peaks and concentrations used are very similar and strongly feature Cr, Ins, GSH and δ1.3 as used in the manual selection of concentrations. This is also true of the INTERPRET[2] study. However, our results suggest a benefit of using concentrations rather than spectral data alone. The INTERPRET[2] pattern recognition study is able to achieve 92% classification of AS2, MNG and HG, using combined PRESS and STEAM spectra and leave-one-out LDA, comparable to the results shown here. However, all INTERPRET[2] studies have been unable to classify GBM and MET spectra, but our LDA on STEAM data alone, using only 4 concentrations from LCModel[1] analysis, has achieved good results (Fig. 1, Table 1). Comparing the δ1.3 standard deviations (SD) in PRESS and STEAM GBM and MET data, the PRESS dataset has much larger SD although the means are similar. This was also true when directly comparing PRESS and STEAM data acquired from the same voxels. The reasons for this difference are, as yet, unknown. Preliminary work comparing PRESS and STEAM has revealed that there are differences in the macromolecular baseline of normal subjects and differences in the measured effective T_2 relaxation times in lipid phantoms. These differences may be due to modulation effects caused by spin-spin couplings within the broad, overlapping lipid (Lip) and macromolecule (MM) signals. Our current method of estimating the concentrations of Lip and MM components does not take coupling effects into account, quantifying each component individually by a simple calculation of area under the curve. This, together with differences found in the δ1.3 effective T_2 relaxation times between the HG tumor groups[3], may be contributing towards the statistical differences between PRESS and STEAM in the high-grade tumor LCModel analyses.

In conclusion, we have demonstrated that using LCModel[1] analysis concentrations provides a similar degree of separation when compared with pattern recognition on ^{1}H brain tumor spectra but unlike spectral pattern recognition, concentrations determined from STEAM spectra provides very good separation (87%) of GBM from MET.

References

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