Automating brain tumour classification using high resolution magic angle spinning data

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INTRODUCTION – Biopsy extraction is a routine procedure in the clinical practice. High resolution magic angle spinning (HR-MAS) NMR spectroscopy on brain biopsies might contribute to improve brain tumour diagnosis. Compared to *in vivo* NMR, HR-MAS spectra are characterized by narrow line widths and large signal-to-noise ratios allowing the identification of an important number of metabolites. In this study, we propose a fully automated procedure (preprocessing, quantitation, classification) for classifying brain tumour biopsies by HR-MAS spectra and we study the necessity of using nonlinear classifiers. Classification accuracy is assessed using a stratified random sampling scheme.

METHOD - Brain tumor biopsies were obtained from 112 patients and stored at -80°C until use. The biopsies were gathered in 5 brain tumor classes: 27 glioblastoma (GBM), 6 Glioma grade III (GIII), 19 Glioma grade II (GII), 11 metastasis (MET) and 49 meningioma (MEN). HR-MAS data were acquired at 11.7 T and 14.1 T (500 and 600 MHz for ^{1}H) using BRUKER Analytik GmbH spectrometers. The 1D "presat" spectra were aligned with respect to Alanine doublet at 1.47 ppm, truncated to suppress the offset (first point removed), normalized (divided by the norm of the frequency domain signal between 0.25 and 4.2 ppm), and corrected for the baseline (by subtracting the product of the signal and an apodization function). Peak integration was used as feature selection method, where the integrals were calculated in the frequency intervals [1.30 1.34], [1.45 1.49], [1.84 1.94], [1.99 2.025], [2.09 2.17], [2.39 2.50], [3.01 3.03], [3.19 3.205], [3.205 3.23], [3.235 3.245],[3.255 3.275], [3.33 3.36], [3.39 3.435], [3.50 3.58], [3.58 3.70], [3.71 3.82], [3.91 3.945], [4.03 4.075], [4.08 4.14] ppm. The obtained data (integrals) are 100 times randomly split in a stratified way in a set for training and validation (*i.e.*, 2/3 of the data) and one for testing (*i.e.*, 1/3 of the data). Two types of binary classifiers were studied: linear discriminant analysis (LDA) and least-squares support vector machines (LS-SVM) using radial basis functions (RBF) as kernels [1]. Classification accuracy is given for each pair of class and each procedure.

RESULTS and DISCUSSION - The automated classification results are reported in Table 1 for the different pairs of brain tumours. Using LS-SVM as classification method (top row) provides better results than using the linear method LDA (bottom row). The t-test comparisons show significant differences (with a 5% significance level) in all cases except for the brain tumor pairs GBM vs GII, GBM vs MEN and GIII vs MEN. Strongly significant differences (0.1% significance level) are especially observed for brain tumor pairs that are difficult to classify such as GBM vs GIII, GBM vs MET, GII vs GIII or GIII vs MET. As in *in vivo* NMR, the largest classification problem lies in separating GBM from MET. To facilitate the automation of the procedure, the cut-off values of the latent variables have been fixed. This might result in pessimistic accuracy estimates, especially if the brain tumor groups are not well balanced (equal number of samples in each group). The relatively weak separation between GBM and MEN may be due to the limited use of lipids in this procedure (largely reduced by the 'baseline correction' step).

GBM vs GII	GBM vs GIII	GBM vs MEN	GBM vs MET	GII vs GIII	GII vs MEN	GII vs MET	GIII vs MEN	GIII vs MET	MEN vs MET
77.0 +/- 8.8%	79.3 +/- 5.6% ***	80.3 +/- 7.0%	68.0 +/- 4.8% ***	74.4 +/- 5.1% ***	90.3 +/- 5.6% *	80.0 +/- 12.1% ***	92.6 +/- 4.0%	81.0 +/- 12.8% ***	80.4 +/- 4.8% **
75.0 +/- 9.2%	62.5 +/- 14.9%	80.2 +/- 8.3%	51.6 +/- 11.2%	66.0 +/- 19%	88.5 +/- 6.2%	58.6 +/- 16.8%	91.4 +/- 5.9%	70.3 +/- 18.4%	77.8 +/- 7.6%

Table 1: Percentage of correctly automated classified data (mean +/- standard deviation) for each possible brain tumour pair. Top row: results with LS-SVM. Bottom row: results with LDA. The 5%, 1% and 0.1% significance levels are represented by *, ** and ***, respectively.

CONCLUSIONS – A fully automated procedure has been proposed to classify HR-MAS spectra. The nonlinear classification method LS-SVM should be preferred to the linear method LDA.

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