An objective method for automated classification of brain tumors using Proton MR spectroscopy

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Introduction: Preoperative classification of brain tumors such as intra-axial from extra-axial tumors, glioblastomas (GBM) from brain metastatses (MET) and astrocytomas (AS) from oligodendrogliomas (OLG) is important as these histological subtypes are treated differently[1]. Previous studies have reported the potential of ^{1}H MRS in classification of different histological subtypes with variable degree of sensitivity and specificty[2,3]. However, these ^{1}H MRS studies have employed standard spectral acquisition and analysis methods that are user-dependent and thus may involve considerable user bias in selecting the voxels and/or the metabolites of interest[4]. In order for ^{1}H MRS to become a robust clinical tool, automated pattern-recognition techniques, such as linear discrimination analysis (LDA), that can process ^{1}H MRS data and aid radiologists in categorizing the spectra according to histological subtypes are warranted. Therefore, the purpose of this study was to investigate the potential of LDA analysis of ^{1}HMRS in classification of brain tumors.

Methods: A total of 138 patients with brain tumors [astrocytoma grade II/III (AS, n=10), glioblastoma (GBM, n=66), lymphoma (LYM, n=9), meningioma (MNG, n=11), metastases (MET, n=34), oligoastrocytoma /oligodendroglioma (OLG, n=8)] that exhibited contrast enhancement on post-contrast T1-weighted images were included in this study. These patients underwent MRI and multivoxel ^{1}H MRS prior to surgery and/or chemo-radiation therapy. The solid contrast enhancing portion of the neoplasm was defined as the contrast-enhancing region (CER) while the region surrounding the enhancing part of the neoplasm, comprising of vasogenic edema and potentially containing infiltrative tumor cells, was labeled as the peri-tumoral region (PTR). The concentration ratios of NAA/Cr, tCho/Cr, glutamate+glutamine (Glx)/Cr, mI/Cr and (Lip+Lac)/Cr were computed from each voxel encompassing both CER and the PTR using a user-independent spectral fit program [Linear Combination (LC) Model]. Concentrations of metabolite with Cramer-Rao lower bounds of greater than 20% standard deviation were discarded as recommended previously[5]. LDA using Fisher's classification function coefficients was performed to differentiate different groups using SPSS 18. At each step, the variable that minimized the overall Wilk's lambda was entered for feature selection. The LDA automatically selects the first two mutually orthogonal canonical discriminant functions which maximizes the differences between the values of dependent variables. The analysis was performed to investigate the utility of LDA in identifying three groups: I) all tumor subtypes; II) GBM versus MET; III) AS versus OLG.

Results: Scatter plots demonstrating the discriminant scores for the three groups are shown in figure 1. In group I, LDA correctly categorized 117 of 138 patients resulting in 84.8% overall accuracy. All patients with OLG and 90.9% patients with GBM were correctly classified. However, moderate classification accuracies for AS (75.0%) and LYM (55.6%) were observed (Table 1).The overall accuracies of LDA in group II and III were 83.0% and 94.4% respectively. Most of the OLG (100%), MNG (81.8%) and GBM (90.9%) were separated from other tumor groups in comparison to LYM (55.6%) with other tumor subtypes (Figure 1a). While separating GBM from MET, a small overlap was seen near the GBM centroid, however, an overall 83.0% accuracy was obtained (Figure 1b). Figure 1c shows a good separation of group centroids from AS and OLG and only one OLG was miss-classified as AS in group III.

Table 1: Percentage of correctly classified tumors within each tumor group. I: Classification of all tumor subtypes; II: GBM vs MET; III: AS vs OLG.

Brain Tumors		AS	GBM	LYM	MET	MNG	OLG	Total
Correct Classification (%)	I	75.0	90.9	55.6	79.4	81.8	100	84.8
	II	—	86.4	—	76.5	—	—	83.0
	III	100	—	—	—	—	87.5	94.4

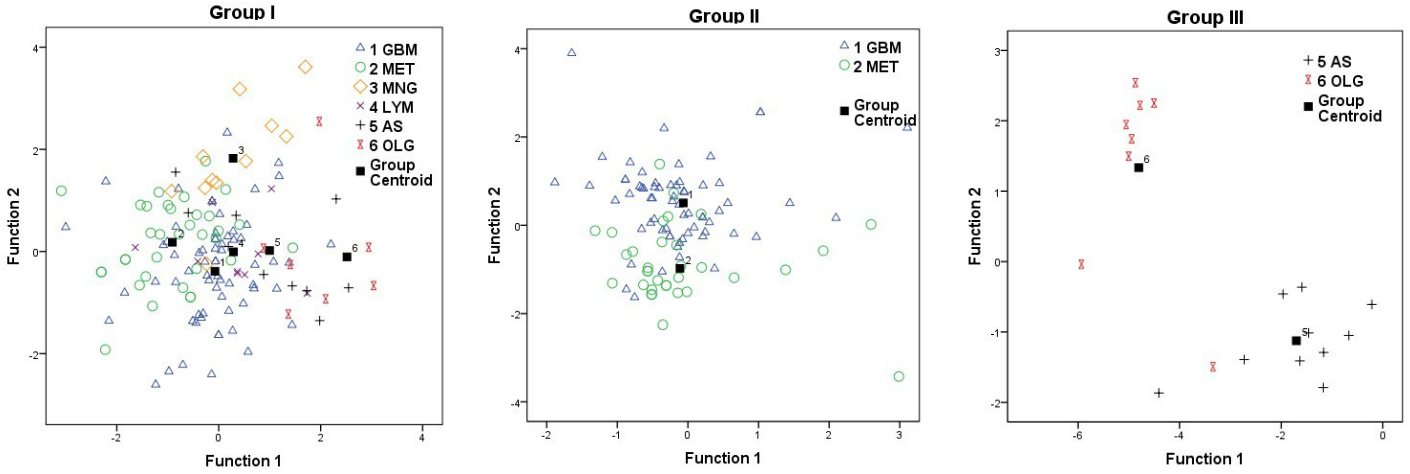

Figure 1: Scatterplots showing the values of discriminant scores for metabolites ratios of each patient together with the group centroids (indicating the average discriminant score for every subtype). The first function maximizes the differences between the values of the dependent variable. The second function is orthogonal to it (uncorrelated with it) and maximizes the differences between values of the dependent variable, controlling for the first factor.

Discussion: In this study, we demonstrate the utility of a robust, fully-automated and objective approach of ^{1}H MRS data acquisition and analysis in separating different histological subtypes of brain tumors with high diagnostic accuracy. In comparison to previous ^{1}H MRS studies, we analyzed all voxels from the CER as well as the PTR region, effectively minimizing the selection bias, which is often induced in the analysis of spectral data. Furthermore, as LC Model was used to process the spectra, user bias is further avoided. The LDA analysis used a total of seven metabolite ratios from the CER and PTR region. In a previous study a classification accuracy of 70% was observed in separating AS, GBM, MET and MNG when voxels were included only from the CER[6]. In another study, a diagnostic accuracy of 80% in discriminating between GBM and METS was obtained by using only the characteristics of lipid peaks. However, in the present study, information obtained from several metabolites was utilized and our comprehensive and objective method of ^{1}H MRS data analysis resulted in a better outcome in categorizing brain tumors.

Conclusion: A combined use of LC Model with LDA allows for a fully automated ^{1}H MRS data analysis approach with minimum operator intervention and provides high diagnostic accuracy in distinguishing different subtypes of brain tumors.

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