Ex vivo metabolic profiles for the differential classification between Oligodendroglial and GBM tumours

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Introduction

GBM are the most aggressive brain tumour type, however low grade Oligodendroglial Tumours (OT) are more indolent, with slow growth and tend to be chemosensitive[1]. Anaplastic features in OT could be controversial in tumour grading, preventing an unambiguous prognostic factor. New support tools for a better prognostic and patient treatment for histopathological borderline or ambiguous tumours can clinically helpful. The purpose was determining whether ex vivo metabolic profiles by HR-MAS, using eTUMOR protocols[2,3], can distinguish between classes of glial tumours: low grade Oligodendroglial Tumours vs high grade GBM.

Methods

Metabolic profiles of 20 OT and 30 GBM were obtained. Spectra were acquired at 600MHz and 4ºC. CPMG sequence was used as T2 filter. In order to assess tumour tissue type and amount: cellularity, necrosis, and infiltrate normal brain, biopsies were histopathology analyzed after HR-MAS experiments. Aliphatic (0.5-4.50_ppm) and Aromatic (4.5-9.5_ppm) regions were normalized to total spectra area. Spectra were binned into 0.01 ppm buckets. 37 metabolites corresponding to 129 resonances previously assigned[4,5] were evaluated by Unsupervised analysis (PCA and Hierachical Clustering). A supervised learning approach was used to build a two class prediction model based on their histopathological class (OT_vs_GBM) and grade (II_vs_III). DLDA algorithm was evaluated and 6 different prediction model were built with 2, 5, 10, 20, 35, 40 resonances. Training error of these prediction models were determined using Leave_One_Out cross validation. The performance of classification rule was validated with 8 independent GBM_(IV), and OT_(III) not used in the feature selection process.

Results and Conclusions.

Figure 1 shows a PCA and average binned spectra for GBM and OT. Myoinositol, Creatine, Valine, Isoleucine, Choline, GABA, Alanine were among the 10 most discriminate resonances contributing to the classifier. Error rate in train set was 0.06. The application of this classification rule based on 40 resonances to an independent test set, yield an error rate of 0/4 for OT and 0/4 for GBM. Many metabolites statistically significant have been previously associated with hypoxia increasing [6].These results show that pattern recognition approach from metabolic profiles can support glial tumour classification.

References

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Acknowledgments

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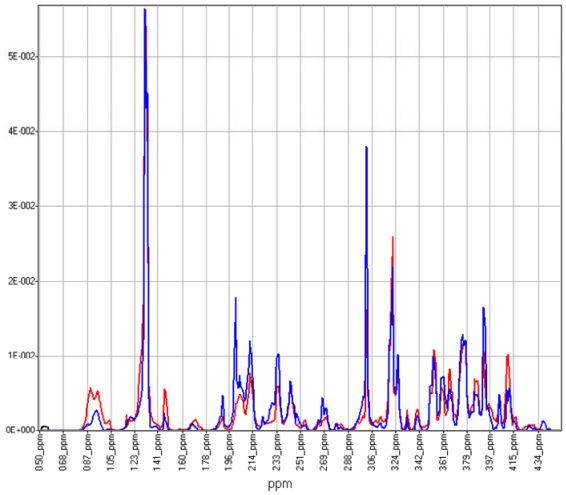

Fig.1 Average Binned spectra from GBM (red) and OT (blue).

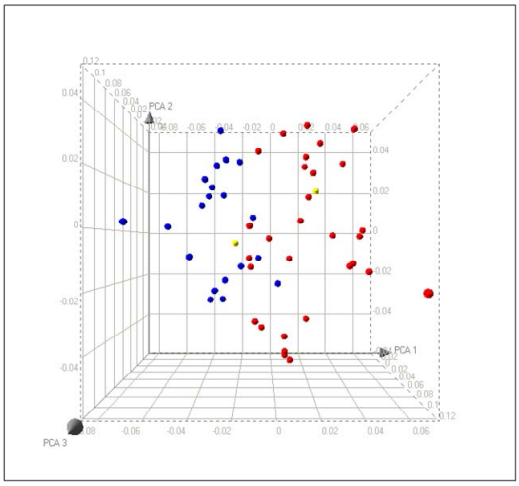

Fig.2 Scatter plot of Principal Component Analysis