Identifying constituent tumor tissue subclasses in HR-MAS spectra using advanced blind source separation techniques

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Introduction

Glial tumors have proved to be very heterogeneous. This heterogeneity is reflected both in the grade of malignancy and in the tumor tissue type. Histopathological studies reported that along with high cellular tumor cells there may be necrotic regions as well as contributions from normal brain tissue at the border of the affected area. Metabolic information coming from ex vivo HR-MAS (high-resolution magic angle spinning spectroscopy) technique can preserve tissue histopathological features. Still, till now, accurate grading of glial tumors has not been completely achieved by HR-MAS due to the tumor tissue heterogeneity. In this study we address this problem by analyzing the mixture of different tumor tissue types within HR-MAS spectra and by separating between the different sources that contribute to the profile of each spectrum. Techniques for blind source separation are applied, resulting in characteristic profiles for each tissue subtype, and providing the contribution (abundance) of each tumor tissue type within each case.

Methods and data

Brain tumor biopsies were carried out on 27 patients with glioblastoma (GBM), following the eTumour project protocols [1]. The tissue specimens extracted from the tumor region were analyzed using HR-MAS, followed by standard histological examination. Based on the histology the samples are highly variable in their composition, as different content of necrotic, high cellular or border tumor tissue was reported. The spectra were preprocessed [2] and peak integration was used for extracting the concentration of the following metabolites considered as feature vectors in this study: lipids (Lip1-0.9ppm, Lip2-1.3ppm, Lip3-2.82ppm), NAA, Cr and tCho group (Cho-3.19ppm, PCho-3.20ppm, GPCho-3.23ppm), see Figure 1. Non-negative matrix factorization (NMF) [3] and independent component analysis (ICA) [4] are then separately used to extract the constituent feature vector profiles for necrotic, high cellular and border tumor tissue and their abundance distributions within all samples. Thus each feature vector is represented as a linear combination of profiles corresponding to constituent tissue types.

Results

The accuracy of the obtained tumor tissue profiles and of the estimated abundances is validated based on the previous studies [5] and on the histopathology results. Both methods, NMF and ICA, perform well and the resulting feature profiles are very similar to the metabolite profiles of pure tissue samples, see Figure 2. For 23 out of 27 cases, the highest abundance coefficient was reported for the same tissue type identified in high concentration in the histopathological exam.

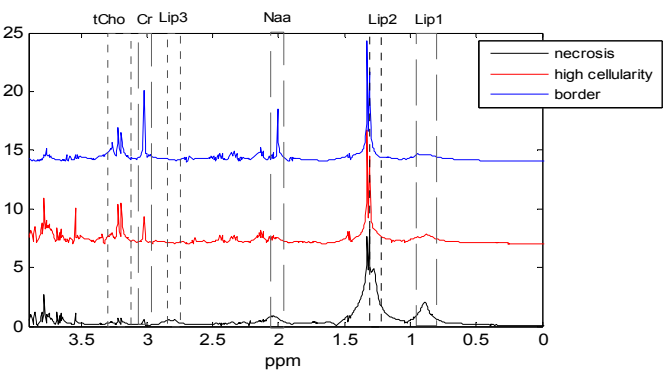

Figure 1 HR-MAS data coming from different tissues within GBM tumor region. Clear differences in the profile of the considered metabolites can be visualized.

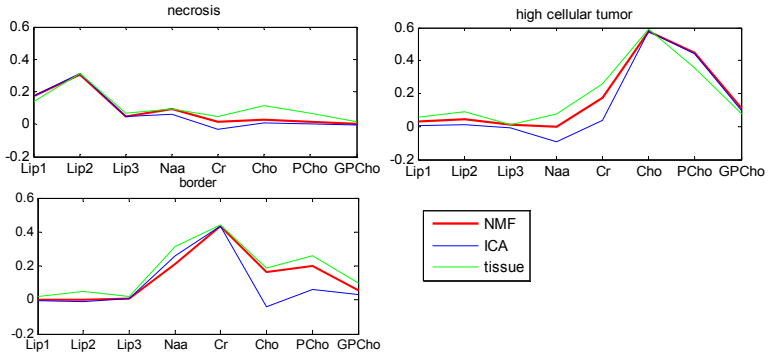

Figure 2 Constituent tumor tissue subclass profiles identified with ICA and NMF. The profile of the constituent subclass is compared with the profile of a pure tissue sample, according to histology.

Conclusions

Using advanced source separation techniques we can correctly decompose the observed HR-MAS data into constituent tumor tissue subclasses and further quantify the abundance of each considered tissue. Both methods, NMF and ICA, can provide relevant additional information for a better interpretation and classification of in vivo and ex vivo NMR spectroscopy techniques and therefore increase their contribution to brain tumor classification.

References

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