CLASSIFICATION ON EX-VIVO MRS SIGNALS OF GLIOMA SAMPLES

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Introduction:

Gliomas are the most common brain tumors in adults. A well-known difficulty is to know whether a surgical resection was extensive enough or whether tumor tissue was left after the intervention [1]. A first differentiation of the tissue between tumor center and margin/healthy is hence indispensable. Ex-vivo high resolution MR-Spectroscopy (HR-MRS) has proven to show metabolic characterizations of human brain tissue biopsates. In this work, we supplement the analysis of glioma biopsates by applying automated pattern recognition techniques on ex-vivo HR-MRS signals. The biopsates were taken from healthy reference, tumor margin, and tumor center tissue. Supervised and unsupervised data reduction techniques combined with different classification methods are used to improve and accelerate the classification of the biopsates. An extensive study allows for a qualitative and quantitative comparison of the results. Further objectives in this work are the finding of chemical substances in a sample tissue being deterministic in brain tumor diagnosis and to determine the malignancy of the samples with respect to the marker metabolites found before.

Material / Methods:

A total of 47 biopsates was taken from 28 glioma patients including 4 from healthy, 14 from tumor margin and 29 from tumor center tissue. A retrospective exact mapping of the extraction area was carried out by tracked biopsies, so that the sample's position could be found again in conventional or functional MR images. By using a dual-phase extraction technique with chloroform, methanol and bidistilled water (1:1:1), lipophilic as well as hydrophilic compounds were extracted simultaneously. The MR spectra were acquired on a Bruker Avance DRX-600 spectrometer at 300K using a 5mm H, C, N inverse probe with actively shielded gradient coils (16k points, spectral width 6.6 kHz (hydrophil) respectively 5.2 kHz (lipophil)). In this study, only the hydrophilic compounds are analyzed.
For feature reduction, several subsampling methods were used: a correlation-based feature selection (CFS) with different evaluators as well as subsampling with varying frequencies, region averaging and different statistical approaches, particularly Independent Component Analysis (ICA) [2]. The spectra were classified with different commonly used classifiers, e.g. Random Forest, Decision Tree, 1R, SVM, and Bayesian Net, combined with cross-validation to evaluate the models [3].

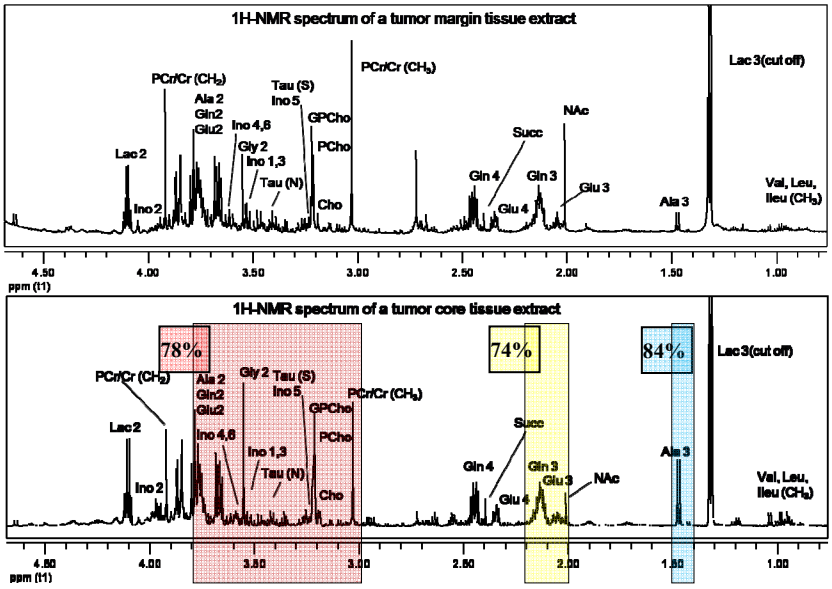

Fig.2: Hydrophilic spectra of glioma tissue (0.8 – 4.6 ppm). *Top:* tumor margin; *Bottom:* tumor core (Ala=Alanin, Cr=creatine, GPCho=glycerophosphocholine, Gln=glutamine, Glu=glutamate, Gly=glycine, Ile=isoleucine, Ino= Inositol, Lac=lactate, Leu=leucine, NAc=N-acetyl, PCho=phosphocholine, PCr=phosphocreatine, Succ=succinate, Tau=taurine, Val=valine)

Results:

To reveal hidden factors underlying the MRS signals and to differentiate between core vs. margin/healthy tissue, we applied an ICA. A data alignment algorithm (COW) is used to obtain the same general characteristics from each spectrum in a preprocessing step. This removed 8 spectra with apparent disparities. The remaining substances were explored with a peak picking algorithm (up to 10 peaks). The resulting 39x10-mixing matrix, obtained from the center tissue spectra, showed apparent differences in the first two columns, belonging to Lactate3 (cf. Fig. 1). The fifth column (peak) was related to Cr(CH3)/GABA4. Further peaks could not be assigned yet.

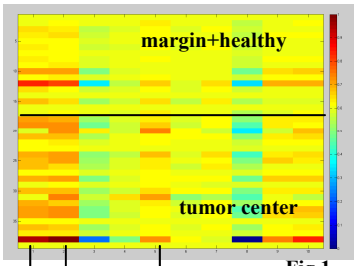

Fig.1

To compare these findings, 26 chemical substances (25 to 250 data points) were separately classified with the above mentioned methods and the following best results: → The percentage refers to all instances being classified. To define a reference result, we performed a classification on the whole dataset using a common Random Forest method, providing 75% correctly classified instances. An additional approach in this work was to combine substance groups. Here, merging the spectral parts from Lactate3 and Cr(CH3)/GABA4 resulted in 79% correctly classified instances. With a CFS, the dataset was reduced to 13 data points (originally about 16k), ranging from 1.4 to 8.5ppm. The data points can be split up into separate ppm-classes: [1.4-1.5] with #3 (blue color in Fig.2), 1.86 with #1, [2.0;2.2] with #2 (yellow), [3.0;3.8] with #5 (red), 4.0 with #1 and 8.5 with #1. The best classification results on each of the colored intervals can be seen in Fig.2. A comparison of these results with a visual signal inspection (Fig.2) shows a correspondence to a low signal intensity of Ala3 (1.48ppm) and a high PCr (3.03ppm) in the tumor margin, for instance. Other results are more difficult to interpret.

Glycine2 (1R classifier)	**83%**
Lactate3 (Random Forest)	**73%**
Alanine3 (1R classifier)	**73%**
Cr(CH3)/GABA4 (Decision Tree)	**73%**

Conclusion / Discussion:

We have successfully classified healthy and margin vs. tumor center tissue in MRS biopsates spectra of glioma patients. However the ratio of spectra vs. number of data points is still too low. The results of the ICA analysis are comparable to those achieved with further classification methods. Fast feature reduction methods provide additional information about interesting spectral parts, although some of which still lack interpretation. Furthermore, it is surprising that metabolites of interest which are important at in-vivo MRS (like Cho, Glu, Gln and Ino) do not play an important role in our investigations. In future work, we want to extend the classifications by analyzing also MR spectra of the lipophilic compounds of the biopsates and to correlate the obtained information with pre-operative conventional anatomic and functional MR images. This will give valuable hints about the additional benefit of MRS measurements, regarding the validation of in-vivo MRS data with pattern recognition algorithms.

References:

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