Benign and atypical meningioma metabolic differences by HR-MAS molecular profiling

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Purpose

Meningiomas are neoplasms that arise from the leptomeningeal covering of the brain and spinal cord, accounting for 15%–20% of all central nervous system tumors. Although the majority of these tumors are histologically benign, some meningiomas show signs of malignancy such as marked vascularity, loss of organoid structure, mitotic figures, nuclear pleomorphism, prominent nucleoli, focal necrosis, or infiltration to the adjacent brain [1]. The World Health Organization (WHO) classifies meningiomas into three histologic grades: grade I (benign), grade II (atypical), and grade III (anaplastic) in accordance with the clinical prognosis. Atypical and anaplastic meningiomas tend to recur. In this communication, we show differences in molecular profiles based on HR-MAS spectra of 15 meningioma biopsies for the distinction between benign and atypical meningiomas.

Samples and methods

HR-MAS ^{1}H NMR spectra and consequent biochemical profile determination were obtained for 15 samples of human meningioma tissue, of which 11 were benign and 4 were atypical. The amount of human meningioma tissue analysed for each subject ranged from 20 to 40 mg. The whole HR-MAS study was performed at 4 C. HR-MAS spectra were recorded in a Bruker AVANCE spectrometer at 600 MHz. Samples were spun at 5kHz. Three different types of spectral editing were obtained by recording 1D ^{1}H pre-saturation, 1D ^{1}H NOESY and 1D ^{1}H CPMG (30 ms echo time) experiments. 2D ^{1}H TOCSY and 2D ^{13}C-HSQC experiments were also recorded on selected samples for assignment purposes. 1D spectra were processed with 0.3 Hz line broadening. Central position of Alanine doublet (1.478ppm) was used for spectral referencing purposes. All samples were analyzed by post-HRMAS histopathology to assess the tissue integrity and double validate histological diagnosis.

Statistical analysis was performed using in-house MATLAB scripts and the LIBRA statistical multivariate analysis library [2]. Only two diagnosis orthogonal components were removed by orthogonal signal correction (OSC) prior to any feature reduction [3]. The orthogonal component removal was calculated in randomly chosen 50% of the cases and then applied to the remaining 50%. Robust Principal Component Analysis (RPCA) was applied to the set of spectral vectors. Principal components chosen explained at least 90% of the variance.

Results

NMR spectra showed narrow line widths and adequate signal-to-noise ratios with well resolved spin-spin multiplicities, as shown in Figure 1. Resonances were assigned by methods described elsewhere [4]. The comparison among spectra shows clear differences between benign and atypical meningiomas. The phospholipids pattern and other well known signals like Alanine and Lactate seem to have some correlation with the meningioma grade. Additionally, some signals belonging to unsaturated fatty acids seem to also discriminate the two groups of tumours. PCA analysis show major difference between benign and atypical meningioma for PC1 (see Figure 2) which major contributions are Lactate, unsaturated fatty acids and the peaks in the Choline region.
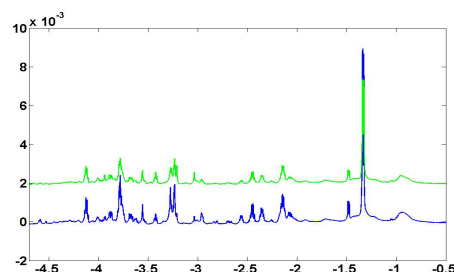

Figure 1. Comparison of the aliphatic region of 1D ^{1}H-NMR spectra for a benign (bottom, in blue) and atypical (top, in green) meningioma.
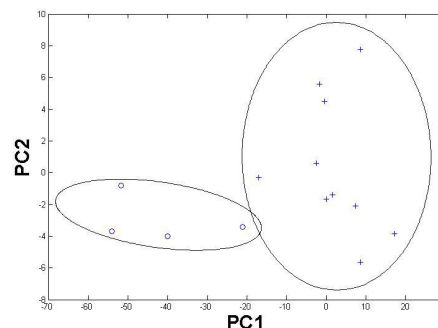

Figure 2. Diagram showing the Robust Principal Component Analysis scores plot for 4 atypical meningiomas (circles) and 11 benign meningiomas (crosses) with the correspondent tolerance ellipses.

Discussion / conclusion

HR-MAS allows to discriminate between molecular profiles of benign and atypical meningiomas. The use of orthogonal signal correction allows to remove spectral component which variations are orthogonal to the diagnosis variable (sample degradation, sample contamination, etc). Metabolic discrimination between benign and atypical meningioma according to the Principal Component Analysis, include the levels of some metabolites which can be seen by MRS 'in vivo'. These metabolites may be the basis for a non-invasive classification of benign and atypical meningioma. Addition of new cases would probably improve the outcome of the classification method.

References

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Acknowledgement