WHICH IS BEST FOR CLASSIFYING BRAIN TUMOURS FROM 1H SPECTRA: EXPERT INTERPRETATION, METABOLITE RATIOS, CLASSIFIERS OR THE INTERPRET DECISION-SUPPORT SYSTEM?

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Introduction: Analysis of MR spectra can be performed using various systems: visual identification of peaks and comparison with published results, calculation of peak height ratios and application of thresholds, automated classifier systems based on multivariate techniques and decision-support systems (DSS).

Purpose: To test which method works best when for predicting the type of tumor in a patient with an abnormal brain mass.

Methods: ***Patient selection***: Data from 40 consecutive adult patients were prospectively acquired during a 15-month period at one institution. ***Data acquisition***: Single voxel (SV) point-resolved ^{1}H MR spectroscopy (MRS) was performed after the conventional MR imaging examination, using the standard receiver head coil in all cases, with an ACS-NT or an Intera-Master at 1.5 T. Acquisition parameters for the SV exam were PRESS, TE= 30 ms and 136 ms, TR= 2000 ms, Number of acquisitions= 128-192 for metabolites and 16 for water, SW= 1000 Hz, VOI size= (1.5-2.0 cm)^3. MRS evaluation (MRS-E) was conducted before the histopathology results were known. ***Data processing***: Formal criteria for the MRS evaluation were used. MR spectra were evaluated using a pre-defined protocol that included: a) Structured description of the short (STE) and long TE (LTE) spectra by a panel of spectroscopists; b) Analysis of the STE spectrum with the INTERPRET DSS 1.0 ([1], [2]); c) Calculation of a mIno/Gly ratio ([3]) where, "mIno/Gly = (3.55 ppm height at STE/3.03 ppm height at STE)/(3.55 ppm height at LTE/3.03 ppm height at LTE)"; d) Classifiers at short and at long TE for astrocytoma WHO grade II vs. astrocytoma WHO grade III vs. glioblastomas and metastases vs. low-grade meningiomas ([4]). The following diagnoses were rated through a 5-point confidence scale (0: definitely not; 4: definitely yes): Meningioma WHO grade I, astrocytoma WHO grade II, astrocytoma WHO grade III, glioblastoma, metastasis, abscess, lymphoma, primitive neuroectodermal tumor (PNET), oligodendroglioma WHO grade II, oligodendroglioma WHO grade III and two additional free diagnoses, if considered necessary. The four systems used were analyzed independently with ROC curves (SPSS 14) and their areas under the curve (AUC) were calculated. Classes were analyzed through dichotomization. Tumor classes were also merged into superclasses (for example: "glial"); $p \leq 0.05$ was considered as significantly different.

Results: The INTERPRET DSS gave the best results (Table 1). Expert spectroscopic judgment was the second-best system, although not all 40 cases were rated. It was better than chance when the panel was asked if the tumor was aggressive, in meningiomas of WHO grade I, low grade meningiomas, glial and pooled glial II-III tumors, allowing calculation of ROC curves for 5 tumors and all the superclasses. It performed better than chance in meningioma WHO grade I, glioblastoma and astrocytoma WHO grade III and in all superclasses except "tumor". With the mIno/gly index for grading glial tumors, only two of the 4 possible ROC curves could be calculated (glioblastoma and astrocytoma WHO grade III) as there was only one astrocytoma of WHO grade II in the set. The calculated AUCs were equivalent to chance. The classifiers based on integrated areas allowed calculation of 5 ROC curves (astrocytoma WHO grade III, glioblastomas, metastases, glioblastomas and metastases together, and low-grade meningiomas). Only for low-grade meningiomas, astrocytomas WHO grade III and glioblastomas did the AUC differ from chance, being AUC (CI) =0.97 (0.92-1.02), AUC (CI) =0.85 (0.70-1.00) AUC (CI) =0.78 (0.59-0.95), respectively.

Results from INTERPRET Decision-Support System for all tumor types, based on a classifier for low-grade meningiomas, low-grade glial tumors and aggressive (glioblastomas and metastases)

classes and superclasses	n	AUC (CI)	P decision-support system vs. CD
MENINGIOMA I	6	0.99 (0.97-1.02)	<0.001
MENINGIOMA II	2	0.72 (0.28-1.17)	0.30
METASTASIS	5	0.75 (0.50-099)	0.08
GLIOBLASTOMA	7	0.77 (0.60-0.95)	0.03
ASTROCYTOMA III	9	0.87 (0.72-1.02)	<0.001
LOW-GRADE MENINGIOMAS	8	0.98 (0.93-1.02)	<0.001
GLIOBLASTOMAS AND METASTASES	12	0.89 (0.77-1.00)	<0.001
WHO GRADE IV	14	0.85 (0.73-0.97)	<0.001
GLIAL III	12	0.87 (0.74-1.00)	<0.001
GLIAL II-III	13	0.91 (0.79-1.04)	<0.001
GLIAL III-IV	24	0.87 (0.73-1.00)	<0.001
OLIGODENDROGLIOMAS AND OLIGOASTROCYTOMAS	3	0.88 (0.76-1.00)	0.03
GLIAL	20	0.88 (0.77-1.00)	<0.001
AGGRESSIVE(GRADES III-IV)	26	0.78 (0.59-0.96)	0.01

***Table 1**: Numerical results of the INTERPRET DSS for the classes and superclasses analyzed. CI: confidence interval, n: number of cases, P: p value. CD: chance diagonal.*

Conclusion: The best system for evaluating the 1H-MR spectrum of an unknown brain mass in a clinical environment is a DSS, as classifiers or ratio-based systems are limited to a predefined set of pathologies. The DSS tested performs better than expert evaluation, as its embedded classifier incorporates quantitative measurements (2) whereas expert interpretation - even when performed following a protocol – can only be qualitative.

References:

1. INTERPRET-SV prototype v1.0 http://azizu.uab.es/INTERPRET/
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