Supplementary material 3

MITOTIC INDEX IS AN INDEPENDENT PREDICTOR OF RECURRENCE-FREE SURVIVAL IN MENINGIOMA

Brain Pathology

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MINE statistics

Table S3.1: Maximal information-based nonparametric exploration (MINE) statistics. Abbreviations: MIC – maximal information coefficient, MAS – maximum asymmetry score, MEV – maximum edge value, MCN – minimum cell number.

MIC (strength)	MIC-p^2 (nonlinearity)	MAS (non-monotonicity)	MEV (functionality)	MCN (complexity)	Linear regression (p) (Pearson's correlation)
0.316	-0.092	0.100	0.311	5.087	0.639

Comment and interpretation:

Maximal information-based nonparametric exploration (MINE) statistics is used to identify and characterize relationships in datasets, including non-linear and functional relationships, that Pearson's and Spearman rank correlation coefficients cannot identify. The maximal information coefficient (MIC) is part of MINE and is utilized to measure the strength of the relationship between two variables [2-4]. In the meningioma dataset there is a modest linear relationship between mitotic index and MIB-1 index.

CART analysis

We focused on identifying trends in the dataset like the order of importance among variables (WHO grade, Simpson grade, mitotic and MIB-1 indices) possibly predictive of RFS in meningioma and the best pHH3 cutoff values for risk prediction. As a preliminary method we used the CART algorithm [1], then we confirmed our findings using the Cox proportional hazard statistical model of survival. Multiple models of CART analysis were run. The best considered models selected were all computed using 30% of the dataset as random test samples, node limits of 20/10, gini splitting rule, and equal priors. CART analysis including all variables of interest (WHO grade, mitotic index, MIB-1 index, and Simpson grade) identified the Simpson grade and the mitotic index as the most important variables in classification for meningioma recurrence with a score of 100% and 89.43% respectively (Se=73.86%, Sp=70.97%). MIB-1 had a lower importance score (37%), and the suggested cut-off was 2.45%. WHO grade did not appear in the tree model and had a low score of importance (13.28%) in the analysis. CART algorithm suggested two mitotic index values (4.5 and 2.5) of potential significance in meningioma recurrence (Se=53.41%, Sp=73.66%). Because mitotic index has to be a natural number, based on these suggested values we constructed the following mitotic index subgroups: 0 to 2 mitotic figures, 3 or 4 mitotic figures, and equal or greater than 5 mitotic figures.

References:

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