Diagnostic value of brain functional imaging in the assessment of intraaxial tumors

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Introduction

MRI provides a differential diagnosis of brain tumors to establish an optimal therapeutic strategy. Brain tumors can be classified according to histological type or grade. According to the World Health Organization (WHO), cerebral neoplasms can be divided into four pathologic degrees (I to IV) although in a clinical setting the main concern is to separate low (I and II) from high (III or IV) degrees as only high-grade lesions require adjuvant chemotherapy o radiation therapy after resection.

MRI with gadolinium-based contrast agents is the most established tool for the clinical evaluation of cerebral tumors. Assessment of these studies relies on the presence or absence of several images features with neuropathologic basis (1). However, several authors state that this approach is sometimes unreliable, reporting sensitivities ranging from 55.1 to 88.3 % for gliomas (2). Functional MR techniques, such as Perfusion Weighted Imaging (PWI), Diffusion-Weighted Imaging (DWI) or Magnetic Resonance Spectroscopy (MRS) are claimed to increase diagnostic accuracy.

PWI provides parameters related to microvasculature characteristics. Cerebral blood volume (CBV) is increased in tumors. In DWI, the Apparent Diffusion Coefficient (ADC) is known to be lower in high-grade tumors. MRS features related to high-degree tumors include elevation of the ratio Choline (Cho) / Creatine (Cr), reduction of the N-Acetyl-Aspartate (NAA) / Cr ratio or the presence of abnormal metabolic peaks (lactate or lipids).

The usefulness of the functional techniques as compared to conventional MRI in grading tumors has been evaluated in different studies with diverse results (2-6). The objective of our work is to assess the additional diagnostic accuracy achieved when combining conventional imaging with perfusion, diffusion and MRS data in a real clinical environment. To this end, we compared the accuracy of two automatic classifiers: one that only uses the image-derived variables and another one based on the functional information.

Material and methods

The study included 134 patients with intraaxial brain tumors recruited over 4 years in the Radiology Department of our institution with no prior selection. Tumor grade was determined by histologic assessment. The sample included 25 low-grade and 109 high-grade tumors (10 oligodendrogliomas, 73 gliomas, 34 metastasis, 1 hemangiogliomas, 3 DNET, 5 TNEP, 6 lymphomas, 1 neurocytoma, 1 gliomatosis).

Variables used for image-based diagnosis were necrosis, gadolinium enhancement, neovascularization, haemorrhage, calcifications and edema. These variables were binary coded (present / not present). Functional MR studies performed were perfusion, diffusion and spectroscopy. The quantitative variables obtained from these studies were the cerebral blood volume (CBV) measured in the tumoral tissue and normalized by CBV in healthy contralateral white matter, the apparent diffusion coefficient (ADC) also normalized to contralateral healthy tissue, and the Choline/Creatine and n-Acetylaspartate/Creatine ratios.

The complete set of variables could only be reliably obtained in 63 cases, due to clinical circumstances, such as the presence of haemorrhage. Because of this fact we decided to perform the analyses on two different datasets: one including all the cases, in which only the imaging variables were used, and another one in which the data retrieved using the functional studies were used. For the first dataset, 113 cases were used for training and 21 for testing. For the second dataset, 48 cases were used for training and 15 for testing. Two different classifiers were computed for each dataset using SPSS v13. The first one was a forward stepwise linear Fisher discriminant analysis, with F-to-enter and F-to-remove values of 3.84 and 2.71, using Wilk's lambda to perform the calculations. The second was a forward stepwise binary logistic regression, with p-to-enter and p-to-remove values of 0.05 and 0.1, for a confidence interval of 95%.

Results

For the image-based dataset, only necrosis and enhancement were included as independent significant predictors in the statistical model. For functional studies, CBV and ADC were selected as independent significant predictors. The Fisher classification functions were $Low = 0.361 * necrosis + 4.732 * enhancement - 2.474$ and $High = 2.949 * necrosis + 11.343 * enhancement - 6.928$ for the imaging variables and $Low = 13 * ADC + 0.204 * CBV - 11.672$ and $High = 9.96 * ADC + 0.509 * CBV - 7.503$ for the functional variables. The binary logistic regression models were $p(high\ grade) = \frac{1}{1 + e^{-(-1.522 + 2.588 * enhancement + 1.79 * necrosis)}}$ for the image-based variables and $p(high\ grade) = \frac{1}{1 + e^{-(-1.855 + 0.982 * CBV)}}$ for the variables obtained from the functional studies.

The linear discriminant correctly graded 95,23% of the tumors in the first test dataset (imaging data) and 86,67% of the tumors in the second test dataset (data only from functional studies). The binary logistic regression graded correctly 95,23% of the tumors in the first dataset and 93,33% of the tumors in the second dataset. Functional data showed no additional predictive value when combined with image-based data.

Discussion and Conclusion

According to our results, data provided by functional studies do not seem to significantly improve diagnostic accuracy, in contradiction with several previous reports. We hypothesize that the use of functional studies may not provide a very clear advantage in a real clinical environment where no previous patient selection is performed and when modern contrast agents are used, at least for the detection of high-grade tumors. Of course, functional techniques may still prove more useful for the differential diagnosis of some diagnostic subgroups, although this was not addressed in our study. It is also possible that a finer assessment of the qualitative (7) and quantitative data could provide different results. Presently, we are increasing the sample size and incorporating some additional quantification tools to further verify our findings.

References

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