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ORIGINAL ARTICLE

Role of magnetic resonance spectroscopy in grading of primary brain tumors

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Abstract *Objective:* To assess the usefulness of MR spectroscopy (MRS) in grading of primary brain tumors.
Methods: MRS was performed in 22 patients with primary brain tumors. Metabolite ratios of Choline (Cho)/N-acetylaspartate (NAA), Cho/Creatine (Cr), Cho + Cr/NAA as well as lipids and lactate (LL)/Cr were calculated at short and intermediate echo times (TEs). Additionally, myo-inositol (mI)/Cr was calculated at short TE. Tumors were subdivided into low grades and high grade on the basis of histopathology. Receiver operating characteristic analysis of metabolite ratios was performed to find cutoff values between high and low grade tumors. The resulting sensitivity, specificity and accuracy were calculated.
Results: At intermediate TE, Cho/NAA, Cho + Cr/NAA and Cho/Cr were significantly higher in high grade tumors than in low grade tumor. At short TE, Cho/Cr and LL/Cr ratios were significantly higher in high grade tumors than in low grade tumor. The diagnostic accuracy of metabolite ratios at intermediate TE was 86% whereas at short TE, the diagnostic accuracy was 75%. Combination of both TEs revealed a diagnostic accuracy of 88%.
Conclusion: Cho/NAA, Cho + Cr/NAA and Cho/Cr are reliable in determining the tumor grade. LL/Cr is highly related to high grade tumors. Combination of both short and intermediate TEs provides better accuracy, in grading of brain neoplasm, compared to that when using each TE separately.

1. Introduction

Brain tumors are major health problem that increases annually. Of all primary brain tumors, gliomas are the most common. Tumor grading is important for the determination of appropriate treatment strategies (1).

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Despite the excellent soft tissue contrast provided by MRI, the sensitivity and specificity with which this modality defines tumor type and grade are limited (2) MR spectroscopic imaging (MRS) provides metabolic information regarding the tissue under study, complementing the anatomic information obtained with conventional MRI (3). Thus, MRS has been proposed as an alternative modality for grading of brain tumors (4). For a reliable MRS procedure, spectroscopic localization methods and data acquisition should be properly adjusted (5).

Multivoxel MRS (MRSI) provides high spatial coverage and may be more useful than single-voxel techniques for obtaining a metabolic map of a large size of tumors. Yet, single-voxel MRS (SVS) also has been reported to be useful for assessment of glioma grade (6). Another important parameter that can largely influence the spectrum is the echo time (TE). At short TE, it is possible to detect more metabolites. However, there are several disadvantages such as the distortion of the spectra baseline under the effects of eddy current, water contamination and the overlapped lipids and lactate peaks, resulting in higher shimming demands. On the contrary, intermediate TE MRS may be chosen to detect the metabolites of longer relaxation times with little or no contamination of residual water, lipids, or fat tissue and thus without baseline distortions (5). Few studies have been devoted to the contribution of both short and intermediate TE MRS for tumor grading (5–8). Therefore, *the purpose of this study* was to evaluate the usefulness of short and intermediate TEs MRS in differentiation of high from low grade tumors.

1.1. Patients and methods

22 patients (13 males, 9 females; age range, 2–72 years) have been examined using 1.5 Tesla MRI scanner (Magnetom Avanto, Siemens, Erlangen, Germany).

MRI protocol: All the cases were examined in supine position with standard circularly polarized head coil using the following sequences.

Axial and Sagittal T1WI (550/8.7 ms) TR/TE spin echo. Coronal T2WI (5000/96 ms) TR/TE spin echo. Axial FALIR (9000/92/ms) TR/TE spin echo. 5 mm section thickness, 230 × 230 Field of view (FOV) and 256 × 256 matrix size. After intravenous administration of Gadolinium- DTPA, contrast enhanced T1WI in axial, sagittal and coronal planes was obtained.

MRS protocol: Two localization methods have been performed, each has a different TE. Data were acquired using Point RESolved Spectroscopy (PRESS) pulse sequence and spectroscopic localization has been performed on post contrast T1WI with automatic shimming. Measurement parameters used in 2D-MRSI were TR/TE: 1500/135 ms, (FOV): 120 × 120 mm, section thickness: 10 mm and total scan time was 7 min. The Region of interest (ROI) was carefully placed to avoid strong interference from subcutaneous fat and lipids of the skull, and outer volume suppression (OVS) slabs outside the ROI was used to further reduce the potential for artifact. Measurement parameters used in SVS scans were 1500/35 ms (TR/TE) and voxel size was about 1.5 cm^3. The total Scan time was 3.14 min.

1.2. Analysis of the spectroscopic data

The main metabolites identified by MRS are (NAA) at 2.02 ppm, (Cr) at 3.0 ppm, (Cho) at 3.2 ppm and (mI) at 3.6 ppm. Concerning lipids and lactate we qualitatively defined and estimated their sum (LL) between 0.9 and 1.3 ppm.

The following metabolite ratio was calculated using the standard commercial software: Cho/NAA, Cho + Cr/NAA, Cho/Cr, LL/Cr and NAA/Cr in addition to MI/Cr in the second technique when the short TE has been used. In case of 2D-MRSI, only voxels presenting the highest Cho/NAA, Cho + Cr/NAA, Cho/Cr, LL/Cr and the lowest NAA/Cr in the solid part of the tumor were considered. A spectrum was excluded for analysis if integration of any peak could not be accomplished using the automated analysis software.

1.3. Histopathology classification

Histopathological diagnosis obtained either by biopsy or by surgical resection and the specimens were graded according WHO criteria into four grades. Then they were classified into low and high grades considering the tumors of grade I and II as low-grade tumors, while tumors of grade III and IV as high-grade tumors.

1.4. Statistical analysis

Data analysis was performed using the SPSS statistical software package. Nonparametric Mann–Whitney *U* tests were used to evaluate the significance in the metabolites and metabolic ratio differences between high and low grade tumors in both groups. *P* values less than 0.05 were considered statistically significant. In order to identify the optimal cut-off values of the most discriminative metabolic ratios, receiver-operating characteristic (ROC) curve analysis was performed. The efficacies of the significant parameters were assessed in terms of sensitivity, specificity, positive and the accuracy. The logistic regression analysis was then performed to determine the combination of the most discriminative parameters.

2. Results

Examples of low grade and high grade gliomas are given in Figs. 1 and 2 respectively.

On the basis of histological diagnosis, the tumors were subdivided, in our results, into high-grade tumors (13 cases = 59%) and low-grade (9 cases = 41%) tumors. Glioblastoma multiform was the commonest among the pathological diagnosis, and represented about third of the tumors (30%).

2.1. Comparison of different metabolite ratios between high-grade and low-grade tumors at both short and intermediate TE

The metabolite ratios of cerebral tumors at both TEs according to the tumor grade are given in Table 1. At intermediate TE, lesions in the high-grade group had significantly higher Cho/NAA, Cho + Cr/NAA and Cho/Cr ratios than those in