Research Article

Proton MR Spectroscopy in Differenating Low Grade Glioma and Glioblastoma Multiform.

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Abstract
Purpose: To evaluate the role of proton MR spectroscopy in differentiating low grade glioma and glioblastoma multiform. **Materials and Methods:** This work included 50 patients with different brain tumors attended radiology department with their age ranged from 35 months - 80 years. **Results:** Validity measures of MRS in detecting grading of brain gliomas versus histopathological findings were sensitivity 88%, specificity 81%, PPV 80%, NPV 90% and total accuracy 85%. **Conclusion:** When paired with cMRI, MR Spectroscopy is regarded as a crucial clinical diagnostic tool that improves glioma grading accuracy.

Key words: MR, spectroscopy, glioblastoma.

Introduction
Brain tumor grade has been determined using a number of noninvasive neuroimaging techniques, such as proton magnetic resonance spectroscopy imaging (1H-MRS), diffusion-weighted MRI, and perfusion MRI [(1)]. Several studies have demonstrated that 1HMRS improves the grading of brain tumors before to surgery, while there is debate over the accuracy of noninvasive advanced neuroimaging techniques [(2)]. It has been advised to conduct more research to improve the clinical applicability of these techniques[(3)].

As a noninvasive diagnostic tool, 1H-MRS can assist predict the grade of brain tumors by providing information on the metabolic changes occurring in the tumor. A radiological measure known as choline (Cho) is thought to indicate cell turnover. Although glial neoplasms without raised Cho/Cr ratios have also been described, brain tumors typically show elevation in the ratio of Cho/Creatine (Cr)[(4)]. N-acetyl aspartate (NAA) levels drop in any condition that causes neurons to die. The metabolite Cr provides insight on how energy is metabolized.

Surprisingly, the findings of multiple research reveal that Cr levels are the same in both low- and high-grade gliomas[(5)]. Yet, earlier research has shown that lower Cr levels can be found in brain malignancies[(6)]. Moreover, within the same tumor, Cr levels may change in various areas. In the same tumor, elevated Cr may be noted in the hypometabolic regions, whereas decreased Cr may be shown in the hyper-metabolic regions[(7)]. It is unclear how crucial Cr levels are in distinguishing between low- and high-grade gliomas. It could be challenging to spot changes in metabolite ratios and it might also result in inaccuracies when estimating tumor grade if the Cr signal in the tumor area is utilized as an internal reference.

Materials and Methods
The study was carried out from January 2018 to January 2020 during a 24-month period. 50 patients with various brain tumors participated in this study and visited the radiology department. They were between the ages of 9 months and 60 years. There were 17 men and 33 women there.

All patients underwent the following procedures: an appropriate clinical history; a thorough interview to weed out patients who might be particularly vulnerable to the magnetic resonance environment; the acquisition of multiplanar (axial-sagittal, coronal) T1, T2 weighted images using the spin echo sequence for all patients; and a post contrast study

following the intravenous administration of a dose of gadolinium in all cases.

The presence of a cardiac pacemaker, ferromagnetic intracranial aneurysm clips, and certain cochlear implants are all contrain-dications to the evaluation.

A 1.5 T full body MRI machine was used for the study. The brain is examined using conventional MRI utilizing the following sequences: Axial, sagittal, and coronal T1 and T2 images. After contrast, axial and coronal T1.

In the MRS technique, a spectroscopic region of interest (ROI) is selected from the MR images. Stimulated Echo Acquisition Mode (STEAM) or Point Resolved Spectroscopy (PRESS) sequences are used to acquire the raw MRS signal with water suppression approach. employing Fourier transformation and spectrum analysis to translate the raw MRS signal into spectra.
Utilizing spectroscopic localization methods (Single and multi Voxel Method).

The sensitive volume is selected by three slice-selective 90o pulses that produce a stimulated echo from that region of interest in MRS investigation procedures that use shorter TE values.

A slice-selective 90o pulse is followed by two slice-selective refocusing pulses (180o) in the PRESS (point resolved spectroscopy) technique to produce a spin-echo from the volume of interest. In comparison to STEAM, it is more sensitive, has better voxel selection, is less motion-sensitive, and is not sensitive to multiple quantum effects. To achieve water suppression, CHESS pulses can be used before STEAM or PRESS.

Based on the purpose of the investigation, the acquisition parameter and MR pulse sequences are chosen.

The signal from most brain metabolites is lost when employing lengthy TEs, with the exception of choline (Cho), creatine (Cr), N-acetylaspartate (NAA), and lactate (Lac). On the other hand, short TEs enable the detection of numerous more metabolites (e.g. Myoinistol, glutamate, glycine and glutamine).

The location of the voxel (1-2cc) of the region of interest is defined using the post contrast MR axial T1 weighted spin echo image (ROI). Using the point resolved spectroscopy sequence (PRESS) with repetition time (TR) = 1500 and echo time (TE) = 35, localized water suppressed proton spectra were produced. A second voxel was implanted on the opposite side of the normal brain tissue (mirror image) as a control in order to acquire accurate measurements of the tumoral region.

Results

The following statistical tests were run using SPSS version 12 for data analysis and statistics: Test of Wilcoxon signed rank: When comparing measurements between two dependent groups, it was employed. When comparing measure-ments between two independent groups, the Mann-whitney test was applied. Proportion independence was examined using chi-square/Fisher exact tests. P-value at the 0.05 level was significant.

Table (1): shows the validity measures of MRS in detecting and grading of brain gliomas versus histopathological diagnosis.

Validity	Sensitivity	Specificity	PPV	NPP	Total accuracy
MRS versus histopathology findings	89%	81%	80%	90%	85%

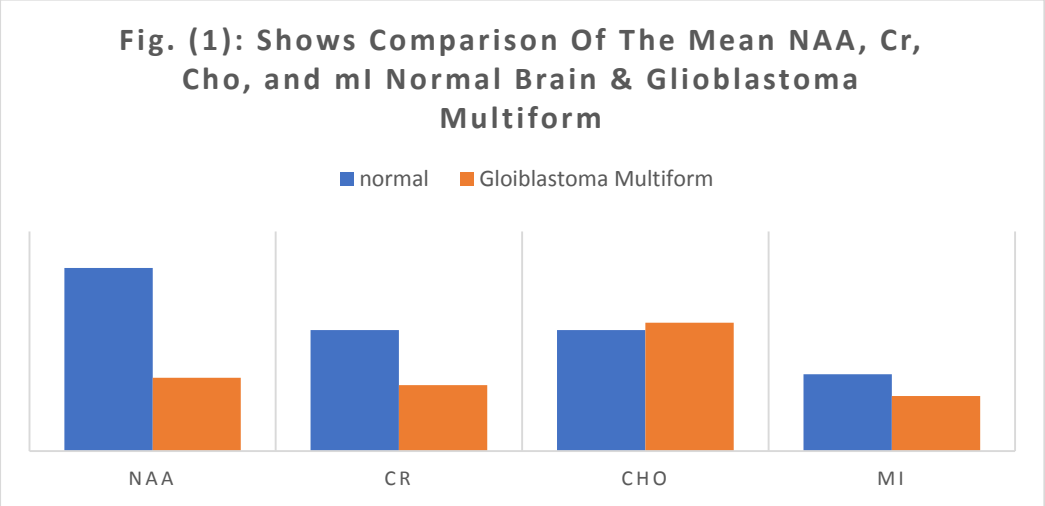

Fig. (1): Shows Comparison Of The Mean NAA, Cr, Cho, and mI Normal Brain & Glioblastoma Multiform.

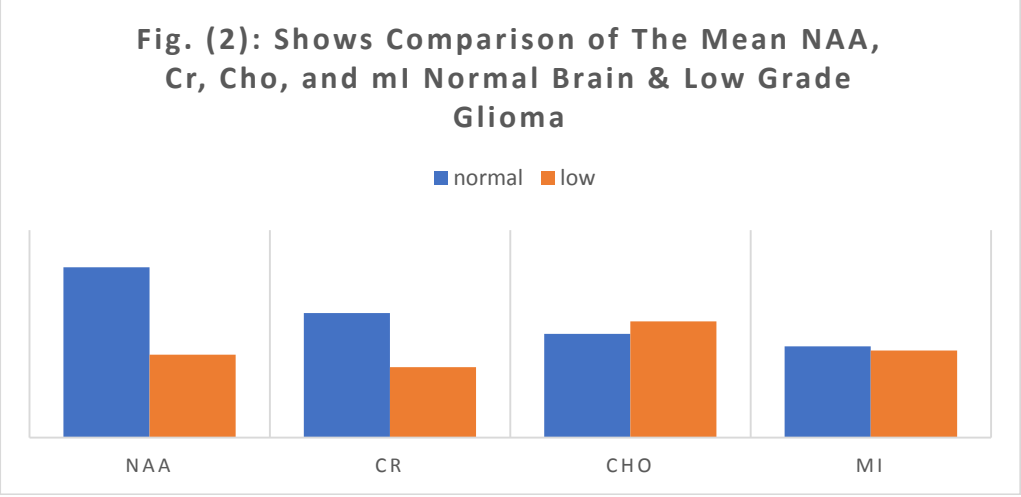

Fig. (2): Shows Comparison of The Mean NAA, Cr, Cho, and mI Normal Brain & Low Grade Glioma

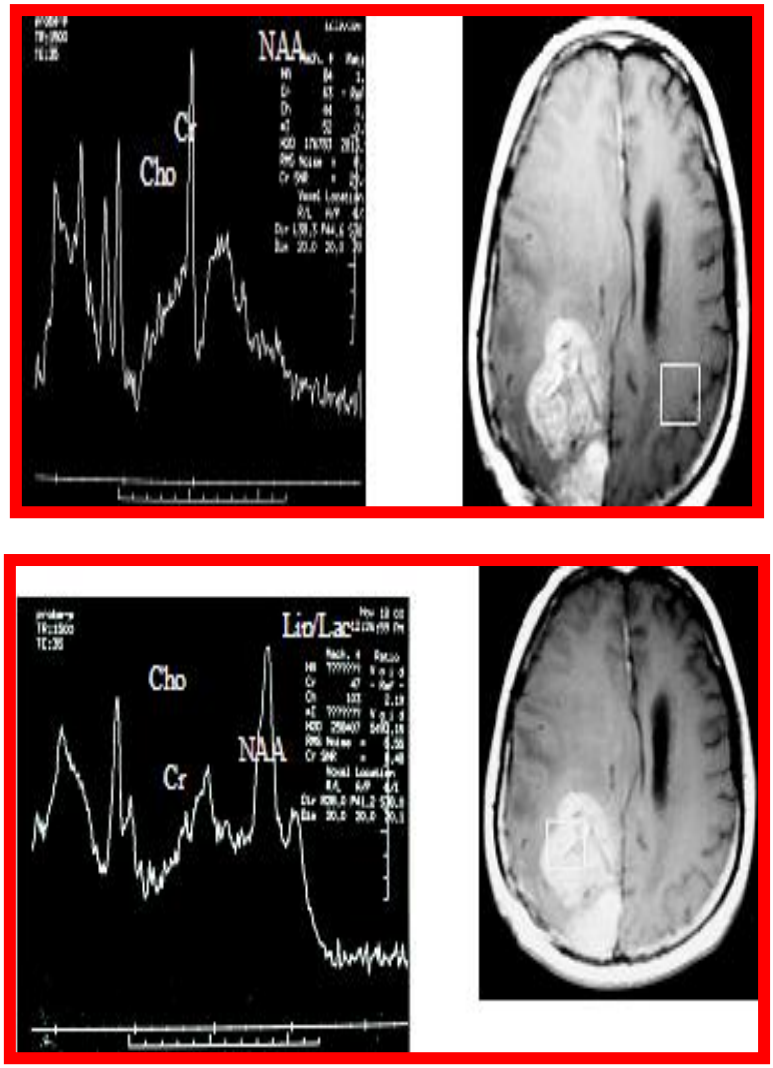

Fig. (3): (A&B) shows MRI &MRS examinations for a male patient 42 years old was right occipital lesion proved pathologically to be glioblastoma multiforme.

Discussion

MR spectroscopic imaging has been utilised in the last ten years to classify brain cancers [8]. A decrease in NAA a marker of neuronal integrity, an increase in Cho factor in increased cell membrane and myelin turnover as well as decrease in Cr a factor that supplies inorganic phosphates for the production of adenosine triphosphate involved in cellular energetics and osmotic balance, were previously observed in brain tumours [9]. The presence of the lactate and lipid peaks, which represent increased anaerobic metabolism and cellular necrosis, respectively, indicates aggressive malignancies [10].

Conventional MRI is an important method in brain tumor grading, but MRI-based tumor grading is sometimes limited and may lead to low- or high-grade is classification in some cases. In general, the 1HMRS technique cannot eliminate the need for a biopsy and histopathological confirmation; however, in some patients, operation is not possible due to impaired clinical condition and 1H-MRS provides data related to biochemical changes in the tissue and may therefore be beneficial, at least in assessing the tumor entity [11]. The advantage of using numerous spectra from many contiguous voxels in multi-voxel 1H-MRS with a 2D chemical shift imaging (CSI)

technique is that the tumour itself, the surrounding tissue, and other brain locations that could be unremarkable in traditional MRI can all be assessed. According to reports, perfusion and diffusion MRI can both be useful methods for differentiating between different grades of glial tumours, and both tools can be coupled to improve diagnostic precision [12]. Phosphocreatine and Cr are present in the Cr peak. Cr is a metabolite that plays a crucial role in the cell energy system by supplying phosphate for adenosine triphosphate (ATP) via phosphocreatine[13].

The presence of Cr in glioma tumours is debatable. No significant changes in tumour Cr between grade I and grade II gliomas were discovered in a study by Stadlbauer et al., but they did discover greater values of the Cr in grade III astrocytomas compared to other grade III gliomas, including oligodendrogliomas and oligoastrocytomas[13]. When Likavcanova et al., researched the metabolism of gliomas, they discovered that the Cr levels in both low- and high-grade gliomas were same [14]. A reason for the varying results might be the heterogenous histological and metabolic nature of gliomas [13]. In our study, the ratio of max-Cho/Crn was lower than that of max-Cho/Cr in the high-grade group (P = 0.001). This result points out that lower Cr levels might have been present in our high-grade tumor population. If Cr signal in the tumor area is regarded as the sole internal reference, the calculated ratio would not reliably reflect the amount of the metabolite tested. On the other hand, Cr is relatively constant in normal brain regions and it is considered an internal standard [15].

Stadlbauer et al., found a negative linear correlation between the total tumor NAA and the degree of tumor infiltration [13]. Grade of glioma is determined by the tumor's most malignant characteristics. The destruction of the NAA metabolite is thought to be greatest in the tumor's most malignant areas, and minimal NAA-related metabolite ratios (min-NAA/Crn and min-NAA/Cr) linked to neuron necrosis and destruction may indicate the tumor's most malignant region and consequently its grade. The min-NAA/Crn ratio seems to be a reliable metric for classifying glioma grade based on our findings. Although the decreased anabolism of tumor cells may result in a somewhat enhanced Cho signal with minimal cell membrane proliferation, we believe that NAA destruction may be important. Thus, min-NAA/Crn ratio might be more trustworthy for glioma grading than max- Cho/Crn ratio. Myo-inositol, lipid, and lactate have been shown in numerous studies to be indicators of tumor aggressiveness[16].

We found a significant relationship between lactate and tumor grade. The findings of our investigation are in good accord with those of earlier research, although we were unable to find a lipid signal-based statistically meaningful distinction between high- and low-grade cancers. This outcome was most likely a result of the impact of noise. Noise may interfere with the lipid peak, which appears as a broad peak [17]. We did not evaluate myo-inositol levels. It is known that a short TE sequence is more sensitive in detecting myo-inositol . One potential limitation of our study was the small number of patients with low-grade tumors. Our study was also limited by the fact that we calculated metabolite ratios semi quantitatively.

Conclusion

using normal side Cr as an internal reference offers a more impartial assessment for assessing brain tumors. In our study, Cr tended to be low in the region of high-grade tumors, and such a drop is crucial for classifying brain tumors. According to this theory, Cr signals from regions of the contralateral brain that appear normal can serve as an internal reference for the tumor metabolites. The ratios of min-NAA/Crn, max-Cho/Cr, and min-NAA/Cr may be helpful in classifying brain tumors. Cho/Cr ratios did not significantly rise in some malignant brain tumors, most likely because tumor cell proliferation was not very active in these tumors. This problem should be taken into account along with the possibility that evaluating all metabolite ratios could be helpful in determining the grade of a brain tumor.

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