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"Brain Lesions: Clinical Applications of Magnetic Resonance Spectroscopy"

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This study explores the overlooked potential value of certain forms of magnetic resonance spectroscopy (MRS) when diagnosing brain lesions. Images from a group of follow-up patients with brain lesions suggest the procedure's diagnostic importance in differentiating between neoplastic and non-neoplastic lesions. This research has been conducted for three years at the medical imaging department in the Royal Care International Hospital (RCIH), Khartoum, Sudan. The sample included a total of 50 patients with intracranial tumours, which have been grouped into the following categories: group (A), 30 patients, 13 male and 17 female, who underwent magnetic resonance imaging (MRI), proton MRS, and stereotactic biopsy; group (B), 20 patients, 13 male and 7 female, who underwent a follow-up course of MRS to compare the improvement and status of patient's pre- and post-treatment. Patients' age ranged from (4-74years), mean ± SD 44 ± 18 years. This study revealed that in group (A), (30%) of brain lesions occurred in the parietal lobe, malignancy was common in MRS findings (56.7%), and increased Cho/Cr (choline-creatine) peaks with NAA (N-acetyl aspartate) remained unchanged since prior imaging sessions while also presenting as a common chemical spectral analysis. In group (B), glioma and inflammatory process were the highest percentage (30%), while (5%) presented no active tumoral cells, and increased Cho with reduction of NAA and Cr accompanied by increase lactate was a common to chemical spectral analysis of the cases. For post-treatment (follow-up) cases, signs of improvement presented as reduction in size and oedema. The distribution of this improvement include {3} of {6} glioma cases, {3} of {6} inflammatory process cases, {2} of {5} malignancy cases, {1} of {1} abscess case, {1} of {1} no active tumoral cells case, and {1} of {1} arterial ischemic insult which showed further complication (increase in size).The study proves that MRS together with MRI and histopathology is a reliable method for determining whether a brain lesion is or is not a tumour, within acceptable statistical values.

Keywords: Brain lesions, Clinical Applications, MRS, Cho/Cr, Cho/NAA ratio.

INTRODUCTION

Diagnosing primary and secondary brain tumours and other focal intracranial lesions with imaging procedures alone is still a challenging problem in Sudan. Accurate diagnosis is essential for optimum clinical management in patients with intracranial tumours (Howe and Opstad 2003). When accessible, most tumours are surgically resected. However, a balance must be achieved between removing as much tumour tissue as possible while maintaining vital brain functions, and radiotherapy is often required to treat any

remaining cancerous tissue (Stadlbauer et al. 2006).

Conventional MRI provides highly detailed anatomic information and has become a mainstay in the diagnosis of suspicious brain lesions (Sartor 1999). Several advances, most notably the development of contrast-enhanced MRI, have greatly improved the diagnostic accuracy of these procedures. Despite this progress, the accurate characterization of brain lesions with MRI alone remains problematic in many cases (Nelson 2003). Proton MRS (1H-MRS) is an appealing, non-invasive adjunct to MRI that can provide additional information on the metabolic composition of a given affected area. By comparing the relative concentration of certain metabolites, clinicians can judge factors such as neuronal viability, presence of neurotoxins, membrane turnover within the volume of interest, and, thereby, the likely underlying pathology (Barker 2005). The collection of 1H-MRS data requires that the MRI time is extended for an additional 15 to 30 minutes while further acquisition sequences are performed. In August 2002, the American College of Radiology requested that the Center for Medicare and Medicaid Services (CMS) reconsider the 1994 non-coverage decision for 1H-MRS. In September 2004, based largely on 2 technology assessments (New England Medical Center EPC 2003, Technology Evaluation Center 2003), it was determined that MRS could differentiate benign from malignant tumours, but was not useful in the process of tumour grading (Majos et al. 2004).

The aim of this study is to demonstrate the overlooked value of MRS for characterizing brain lesions by exhibiting its capacity to differentiate neoplastic, non-neoplastic and other intracerebral lesions.

MATERIALS AND METHODS

To determine the usefulness of MRS in the diagnosis of brain lesions, we performed a retrospective study in which patients with brain lesions from both sexes and all ages were collected. To investigate recurrence or response to treatment, other patients included those with previous surgery of known tumour pathology and a normal control group. The duration of the study was extended to three years. This study was carried out in the Department of Diagnostic Radiology, Royal Care International Hospital (RCIH), Sudan. It was a cross-sectional comparative study. Data was collected with help of a Performa, including name and gender of the patients, lesion sites, clinical findings pertaining to the MRI and the MRS scans, operative findings and histopathological findings. Patients and histopathology diagnosis were based according to the World Health Organization (WHO) classification. All patients included in the studies diagnosed with a primary or secondary brain tumour and/or other brain lesions were advised to receive MRS.

This was a descriptive, quantitative and observational cross-sectional study of 50 patients, divided through two subgroups:

(Group A): Included 30 patients with intracranial tumours who underwent MRI, proton MRS, and stereotactic biopsy. The MRS findings were evaluated for the distribution pattern of pathologic spectra (NAA/Cho ratio > 1) across the lesion and neighbouring tissue, for signal ratios in different tumour types, and for their potential to improve preoperative diagnostic accuracy.

Group (B): Included 20 patients who underwent a follow-up course of MRS to compare the improvement and status of patient's pre- and post-treatment.

Equipment used: (Toshiba Excelart Vantage 1.5T)

The Toshiba Excelart Vantage 1.5T MRI machine is an ultra-short, ultra-wide-bore system with adjustable lighting and ventilation features. As the Toshiba Excelart Vantage 1.5T MRI system delivers high-resolution images with faster imaging times than standard MRI, patients also received a standard MRI to make accurate diagnostic comparisons possible.

The MRS sequencing studies were performed using standard imaging head coil. Routine brain MRI was performed in 3 orthogonal planes, including at least T1, T2, and FLAIR weighted images. T1-weighted images, after intravenous gadolinium-based contrast material administration, were obtained in at least 2 planes. All spectroscopy images were performed using single voxel technique. Initially, post-contrast imaging was done to localize the lesion, and then voxel was placed in the volume of interest.

An appoint-resolved spectroscopy (RESS) technique was applied for lesion localization after water suppression, and the studies were obtained with parameters including TE and TR. In general, the methodology was used in this research work to evaluate and assess the health risks from brain lesions.

Health risk analysis for the development of standards pertaining to these procedures might

permit MRS to function as a less invasive diagnostic approach that may thereby reduce the necessity for the invasive imaging methods described in cases1-4.

Data synthesis and statistical analysis

The findings in both MRI and MRS were analysed by experienced radiologists who were unaware of the pathological results. These data were correlated with the pathologic findings of lesions acquired by surgery or biopsy. Statistical analysis of the different spectra was done. The result of pathologic tissue diagnosis was the reference standard. Due to the different diagnostic purpose in multiple studies, different positive sets were defined. Continuous data were presented as mean ± standard deviation (SD) and compared using the t test. Categorical data were expressed as percent frequencies, and differences between proportions were compared using the chi square test. Statistical correlation between continuous variables was tested using the Pearson's product-moment coefficient of correlation (r). All analyses were performed using SPSS version16. Statistical software (SPSS Inc., Chicago, Illinois). Regarding the groups, the average of the values for each metabolite with their standard deviations based on their relation (reason) with the was calculated and the results were gathered into tables from which we obtained the respective graphs for each group.

RESULTS AND DISCUSSON

Regarding the spectroscopy findings, all the patients had a previous conventional MRI image which was not conclusive.

The sample size in this study was 50 patients who attended radiology department in RCIH and investigated by MRS for evaluation of intracerebral lesions. The participants were divided into two sub groups A and Ba.

MRS is a technique that basically generates a non-invasive analysis of the tissue metabolism, indicating the relative concentrations of their metabolites and the interactions produced between them. Consequently, the morphological information produced by MRI is combined with the biochemical information produced by the MRS, while the biopsy technique is till the 'gold standard 'to determine the definitive diagnosis of a brain lesion. However, the MRS would help in certain cases to avoid unnecessary biopsies (in non-neoplastic processes or non-accessible tumours), and in other cases, it would help to lead the biopsy to the area of greatest anaplasia. The aim of this study is to describe the value of MR spectroscopy for characterizing brain lesions. The second aim is to show the capability of differentiating neoplastic and non-neo plastic and other intra cerebral lesions.

This study was done at the Department of Diagnostic Radiology, Royal Care International Hospital, - Khartoum, Sudan. Group (A) Included 30 patients 13 Male and 17 Female, with intracranial tumours underwent MR imaging, proton MR spectroscopy, and stereotactic biopsy. MR spectroscopic findings were assessed for the distribution pattern of pathologic spectra (NAA/Cho ratio > 1) across the lesion and neighbouring tissue, for signal ratios in different tumour types, and for their potential to improve preoperative diagnostic accuracy. Regional involvement of brain lesion is parietal lobe (30%) Fig (1), malignancy is the common MRS findings of the cases (56.7%), which Meningioma is (10%), Unremarkable (13.3%), Glioma (10%), High Grade Glioma (3.3%), Abscess (3.3%), and Astrocytoma (3.3%). Increase Cho/Cr peaks with NAA remains unchanged was a common chemical spectral analysis of the cases. Fig (2)

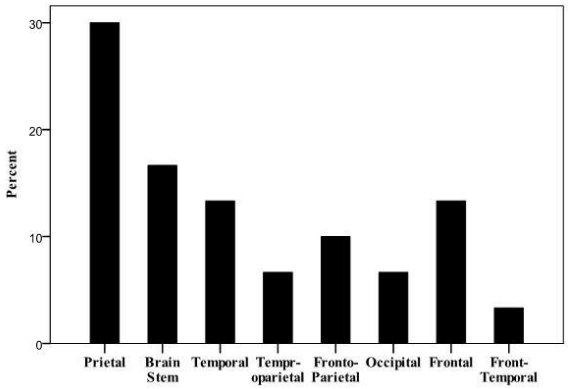

Figure 1: Area involvement of brain lesion

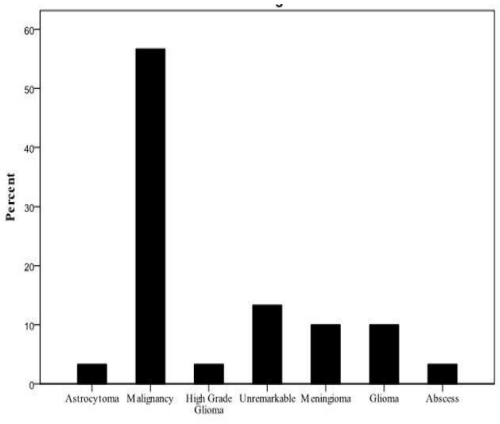

Figure 2: MRS findings- Group (A)

Table 1: Spectral Analysis * MRS Findings Cross tabulation

Spectral Analysis		MRS Findings							Total
		Astrocytoma	Malignancy	High Grade Glioma	Unremarkable	Meningioma	Glioma	Abscess	
	High Cho/Cr, High Cho/NAA	1	4	0	0	0	3	0	8
	Increase Cho/Cr peaks with NAA remains unchanged	0	12	0	0	0	0	0	12
	Increase Cho with reduction of NAA and Cr with increase Lactate	0	0	1	0	0	0	0	1
	Normal Curves	0	0	0	4	0	0	0	4
	Raised Cho, Low Cr and NAA	0	0	0	0	2	0	0	2
	Significant elevation of both Lipid and Lactate peaks ,moderately reduced NAA peak	0	1	0	0	1	0	0	2
	No Evidence of Neoplastic Process	0	0	0	0	0	0	1	1
Total		1	17	1	4	3	3	1	30

Table 2: Values corresponding to the Correlation to the different metabolites

Metabolites		Frequency	Percent	Valid Percent	Cumulative Percent
	High Cho/Cr, High Cho/NAA Ratio	5	25.0	25.0	25.0
	Increase Cho with reduction of NAA and Cr with increase Lactate	6	30.0	30.0	55.0
	Normal Curves	1	5.0	5.0	60.0
	Fixed elevation of Cho/Cr ratio ,reduced NAA peak ,elevated Lipid and Lactate peaks	1	5.0	5.0	65.0
	Preserved NAA, No significant reversal of the Cho/ Cr ratio, breakdown of lactate and lipid peaks	1	5.0	5.0	70.0
	Non-significant Cho/ Cr ratio peak (1.6) (significant 2) and normal NAA peak	1	5.0	5.0	75.0
	Moderate increase in the Cho/ Cr ratio, significant increase in the lipid and lactate peaks. Slightly reduced NAA peak	1	5.0	5.0	80.0
	Decrease NAA, decrease in Cr, increase in Cho with reversed Cho/ Cr ratio and high lipid lactate peak	1	5.0	5.0	85.0
	High lactate level reduce NAA, Cho/Cr = 1.4	1	5.0	5.0	90.0
	Mild increase in Cho/ Cr ratio, low NAA	1	5.0	5.0	95.0
	Increased lactate with no evidence of increased Cho	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

Table 3: MRS Findings * Post Treatment Cross tabulation

MRS findings	Post Treatment			
	Improved (reduction in size and edema)	**Not Improved (static)**	**Complicated (increase in size)**	**Total**
Glioma	3	3	0	6
Inflammatory Process	3	2	1	6
Malignancy	2	3	0	5
Arterial ischemic insult	0	0	1	1
Abscess	1	0	0	1
No active tumoral cells	1	0	0	1
Total	10	8	2	20

Group (B)included 20 patients 13 Male and 7female their age ranged from (4-74years) mean age± SD 44.27± 18.311, with follow up by MRS and comparing the improvement and status of patients pre and post treatment. In (Table 3)

MRS Findings the Glioma and inflammatory process were the highest percentage (30%) for each, which Malignancy (25%), Arterial ischemic insult (5%), Abscess (5%), and no active tumoral cells (5%). Fig (3) Increase Cho with reduction of NAA and Cr with increase Lactate was a common chemical spectral analysis of the cases. (Table 2)

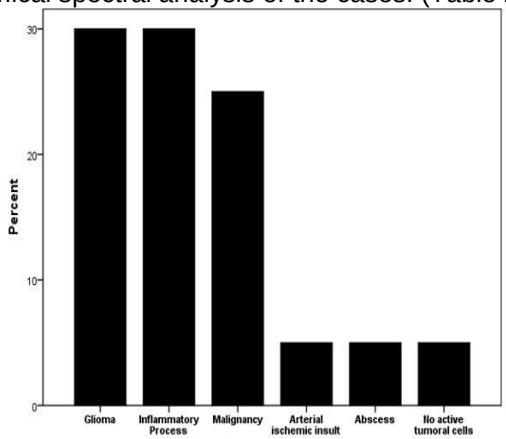

Figure 3: MRS Findings- Group (B)

Franklyn H et al. studied the benefits of 1H MR spectroscopy of brain tumours and masses (Howe and Opstad 2003), Sergio Luiz Ramen et al. studied the benefits of proton resonance spectroscopy and its clinical applications in patients with brain lesions (Ramin et al. 2003), Moller-Hartmen W et al. started a study to evaluate the clinical utility of 1H-MRS added to MRI for the differentiation of intracranial neoplastic and non- neoplastic mass lesions (Möller-Hartmann et al. 2002), and Majós C et al. started a study to help in, differentiating between tumours and pseudotumoral lesions (Majós et al. 2008). For MRS Findings of post treatment cases (follow up) was improved in (reduction in size and edema), {3} of {6} Glioma cases, {3} of {6} inflammatory process cases, {2} of {5} Malignancy cases, {1} of {1} Abscess case, {1} of {1} no active tumoral cells case, and {1} of {1} Arterial ischemic insult was complicated (increase in size). A tumours subtype in this study was in accordance with the previously published data. In the present study magnetic resonance spectroscopy MRS was used for diagnosis of brain lesions, in Sudan. MRS studies were performed using 1.5 Tesla whole body MR systems using standard imaging head coil. All MR Spectroscopies were done by single voxel technique. Initially, post contrast conventional MRI was collected to localize the lesion and then voxel was placed in the volume of interest. A point-resolved spectroscopy (PRESS) technique was applied for localization after water suppression. The studies were achieved with parameters including TE and TR of 135 and 1500, respectively.

Then, all MR images were interpreted by consultant radiologists having experience in MRI field. Reporting was performed on console as well as hard copies. The spectra were investigated for the signal intensity of NAA, choline, and creatine and for the presence of lipid and lactate peak. The Cho/Cr and Cho/NAA ratio are manually calculated. In addition, Lesions were also evaluated on conventional MR sequences before making the final MRS diagnosis. All mass lesions studied indicated abnormal MR Spectra as compared to normal parenchyma.

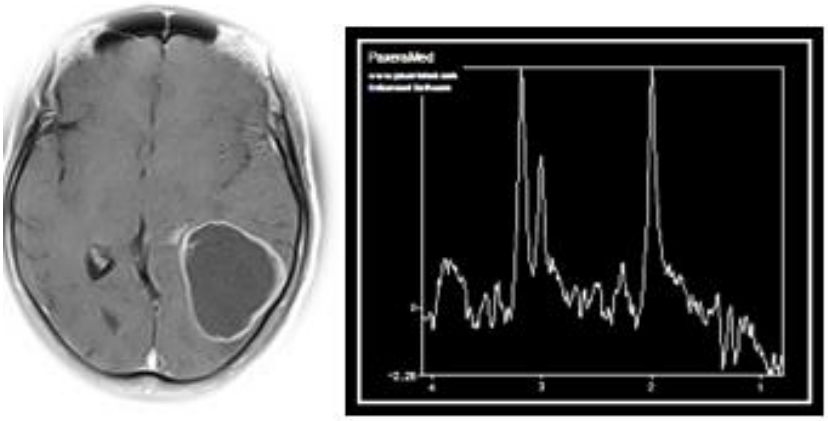

Figure 4: Case 1. 54 years old, Female, high Cho/Cr and Cho/NAA peak, Necrotic area with high lipid / lactate peak. Overall features suggestive of neoplastic Cyst-Astrocytoma.

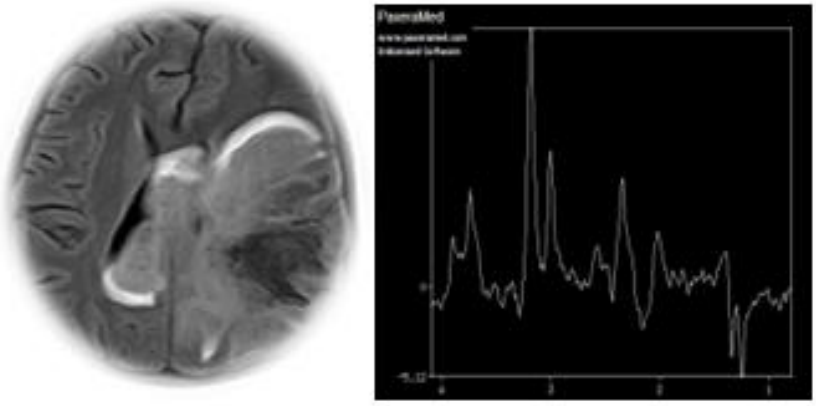

Figure 5: Case 2. 13 Years old/ Female, significant increase in choline with reduction of NAA and Cr associated with increase lactate. Features are suggestive of high grade glioma.

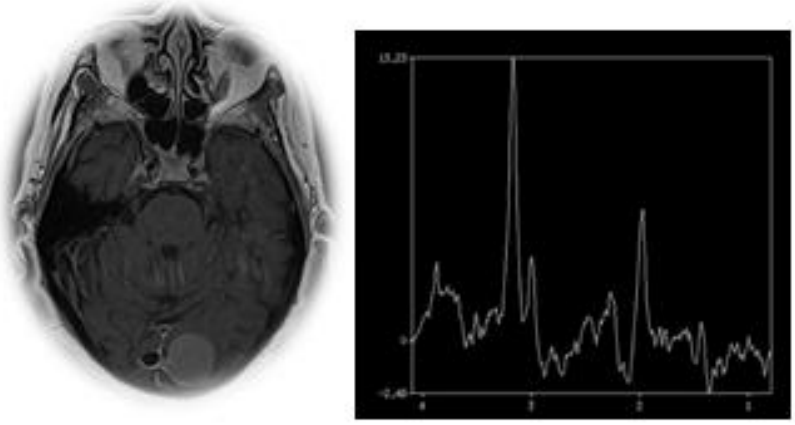

Figure 6: Case 3. 52 years old, Female, enhancing of left extra occipital lesion. Fixed elevation of the creatine peak rather than choline. Slightly reduced NAA. No impressive changes in lactate or lipid peaks, Overall features favor Meningioma rather than malignant process.

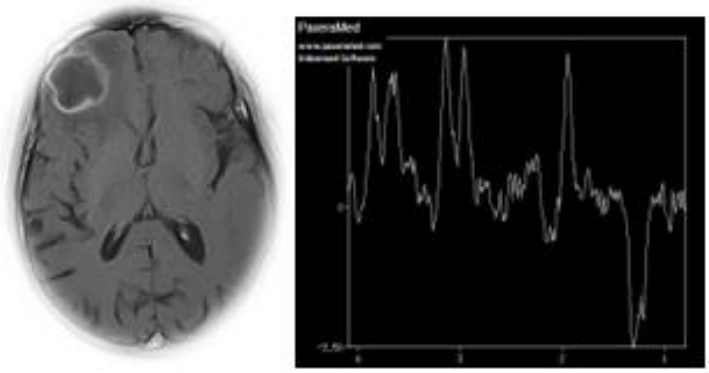

Figure 7: Case 4. 67 years /Female, no evidence of increase in the choline and creatine peaks, NAA is preserved. The lactate is showing a peak. The appearance is in favor of abscess rather than metastasis.

When the pattern of MRS metabolites consisted of abnormally increased pattern of MRS and metabolites consisted of abnormally increased choline and decreased N-acetyl aspartate (NAA) resonances, histological findings of the biopsy were positive for brain lesion. (Table 1). Our results are consistent with those of previous reports of Gill SS et al. Neff B et al. and Lin A et al. (Neff et al. 2003). Three cases of glioma were included in this study, grading of glioma can be obtained on the basis of Cho/Cr and the presence of lipid/lactate peak; both grades of glioma showed High Cho/Cr ratio, but in high grade glioma the presence of lactate peak was noted. found that the increase in Cho/Cr ratios in high grade glioma that were higher than those found in low grade glioma was significantly correlated with the expression of proliferating cell nuclear antigen that was determined immune histological, which reflect the potential of proliferation of gliomas and hence their prognosis (Raschke et al. 2011).

In this part of the study, there is total agreement between MRS, and histopathological results in all the 3 cases of Meningioma included in the study. The study showed that the specific MR spectroscopic finding for Meningioma reported was the absence or very small peak of neuronal markers NAA and Cr, and markedly elevated Cho. These results were similar to many previous studies in Single-voxel proton (Bulakbasi et al. 2007). One study suggested a statistically significant dependence of Cho levels on the malignancy of gliomas. MRS have been applied for the evaluation and grading of brain tumours. Previously studied MRS findings in brain tumours included a decrease in NAA, a marker of neuronal integrity, and a decrease in Cr, which provides inorganic phosphates for adenosine triphosphate production involved in cellular energetics and osmotic balance. However, a Cho is increased which involved in increased cell membrane and myelin turnover. The ratio of the Cho level of tumours to that of the contralateral hemisphere was significantly higher in high-grade gliomas than in low grade gliomas. Also some literature reports have shown increased Cho/Cr and Cho/NAA ratios in the tumour region compared to the normal parenchyma and this increase has been related to a decrease in NAA due to neuronal loss and increase in Cho due to cell membrane destruction (Bizzi 2009). The present study finding are in consistence with Kinoshita et al.. which reported that MRS technique could showing the changes in metabolites concentrations by indicate the types of tumours and the degree of malignancy. It is consistent with that reported by previous study. For example, high grade tumours had lower NAA and Cr concentrations and higher Cho concentrations than low-grade tumours (Kinoshita et al. 2000). Tien et al. concluded that NAA is lowered in all grades of gliomas, with the high-grade gliomas having the lowest levels of NAA. In present study, the Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios showed lower values in both non-neoplastic and low-grade neoplastic lesions compared to high-grade neoplastic lesions agree with previous studies (Inoue et al. 2005, Alshammari et al. 2021). In Poptani et al. study compared high grade and low-grade neoplastic lesions and found that high-grade neoplastic lesions showed higher values of Cho/NAA and Cho/Cr ratios than did low-grade lesions. In this study all neoplastic lesions showed increased Cho and decreased NAA and this was more prominent in high-grade neoplasm. The limitation of this study was

including the retrospective design of study, the small number of patients and the variety of intracranial lesions. The MRS together with the MRI proved to be a reliable method to determine whether a brain lesion is a tumour or not, with acceptable statistical values.

CONCLUSION

MRS can be used as an additional tool prior to biopsy which is highly specific and sensitive. This modality should be considered as an adjunct to conventional imaging rather than replacement for histopathological evaluation. MRS added to conventional MRI helps in tissue characterization of intracranial mass lesions, leading to improvement in diagnosis and management of focal brain diseases.

This study showed that the presence of elevated choline and decreased NAA is correlated with tumour histopathological findings. MR spectroscopy can improve diagnostic accuracy in the differentiation of circumscribed brain lesions from histological infiltrating processes, which is often difficult or impossible by conventional morphologic methods. Such a differentiation is of potential clinical importance, since in circumscribed lesions, surgery might be curative whereas infiltrative lesions, especially in eloquent areas, are generally better handled by other treatment methods, such as irradiation or chemotherapy. On the other hand, while MRS might not help in differentiating the various infiltrative lesions, it may provide valuable support to MR imaging in detecting and selecting an appropriate target point for stereotactic biopsy in these cases.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

QTA designed the experiments and also wrote the manuscript. MS, EY, and EE performed the data collection. MG performed the data analysis. BA designed experiments and reviewed the manuscript. All authors read and approved the final version.

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