

ORIGINAL RESEARCH

CAN MAGNETIC RESONANCE SPECTROSCOPY ADEQUATELY DIFFERENTIATE NEOPLASTIC FROM NON-NEOPLASTIC AND LOW-GRADE FROM HIGH-GRADE LESIONS IN BRAIN MASSES?

Ozan Karatağ¹, Gülden Yenice Karatağ², Ender Uysal³, S.Meltem Can⁴, Mehmet Ertürk³, Muzaffer Başak³

¹Çanakkale Onsekiz Mart Üniversitesi, Tıp Fakültesi, Radyodiagnostik, Çanakkale, Türkiye

²Çanakkale Devlet Hastanesi, Radyodiagnostik, Çanakkale, Türkiye ³Şişli Etfal Eğitim ve Araştırma Hastanesi, Radyodiagnostik, İstanbul, Türkiye ⁴Şişli Etfal Eğitim ve Araştırma Hastanesi, Nöroşirurji, İstanbul, Türkiye

ABSTRACT

Objective: The aim of this study was to evaluate the usefulness of Magnetic Resonance Spectroscopy in the differential diagnosis of brain lesions.

Materials and Methods: Forty-six patients with cerebral lesions were examined by Magnetic Resonance Spectroscopy. Choline, creatine, N-acetyl aspartate and lipid-lactate peaks were evaluated. Forty of the 46 patients underwent stereotactic biopsy or surgery. Histopathological results were compared with the Magnetic Resonance Spectroscopy results.

Results: The Choline / N- acetyl aspartate ratio had the highest sensitivity (87.2%) in neoplastic versus non-neoplastic differentiation and the specificities of the Choline / Creatine, Choline / N-acetyl aspartate and Choline+Creatine / N-acetyl aspartate ratios were found to be 100%. Choline / Creatine ratios showed the highest sensitivity (95.7%) in low-grade versus high-grade differentiation and specificities of Choline / N-acetyl aspartate, Choline+Creatine / N- acetyl aspartate ratios and lipid-lactate levels were found to be 100%. Consequently, a value of Choline / Creatine > 2.2 and an accompanying lipid-lactate peak differentiated neoplasms as low-grade versus high-grade with a sensitivity of 100% (82.2-100%) and a specificity of 100% (71.7-100%).

Conclusion: The presence of elevated Choline and decreased N-acetyl aspartate levels are effective in the differentiation of neoplastic versus non-neoplastic lesions with high sensitivity and specificity. A proposed ratio of Choline / Creatine > 2.2 and an accompanying lipid-lactate peak provide valuable information in differentiating low-grade from high-grade lesions.

Keywords: Brain neoplasms, Magnetic resonance imaging, Magnetic resonance spectroscopy, Stereotactic biopsy

İletişim Bilgileri:

Ozan Karatağ, M.D.

Çanakkale Onsekiz Mart Üniversitesi, Tıp Fakültesi, Radyodiagnostik,

Çanakkale, Türkiye

e-mail: okaratag17@gmail.com

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BEYİN KİTLELERİNDE NEOPLASTİK / NEOPLASTİK OLMAYAN VE YÜKSEK EVRE / DÜŞÜK EVRE AYRIMINDA MR SPEKTROSKOPİNİN YERİ

ÖZET

Amaç: Bu çalışmanın amacı serebral lezyonların ayırıcı tanısında Manyetik Rezonans Spektroskopinin etkinliğini araştırmaktır.

Yöntem: Serebral lezyonu olan 46 olgu Manyetik Rezonans Spektroskopi ile incelendi. Kolin, kreatin, N-asetil aspartat ve lipid-laktat pikleri değerlendirildi. Kırk altı olgunun 40'ına stereotaktik biopsi ya da operasyon uygulandı. Histopatolojik sonuçlar ile Manyetik Rezonans Spektroskopi sonuçları karşılaştırıldı.

Bulgular: Lezyonların neoplastik/neoplastik olmayan ayrımında Kolin/N-asetil aspartat en yüksek duyarlılığa sahipti (%87.2) ve Kolin/Kreatin, Kolin/N-asetil aspartat, Kolin+Kreatin/N-asetil aspartat oranlarının özgüllük değerleri %100 olarak hesaplandı. Düşük/yüksek evre ayrımında Kolin/Kreatin en yüksek duyarlılığa sahipti (%95.7) ve Kolin/N-asetil aspartat, Kolin+Kreatin/N-asetil aspartat, lipid-laktat oranlarının özgüllüğü %100 olarak hesaplandı. Sonuç olarak Kolin/Kreatin oranının 2.2'den yüksek olması ve eşlik eden lipid-laktat pikinin neoplastik lezyonların düşük/yüksek evre ayrımında %100 (%82.2-100) duyarlılık ve %100 (%71.7-100) özgüllüğe sahip olduğu görüldü.

Sonuç: Yüksek Kolin ve düşük N-asetil aspartat piklerinin lezyonların neoplastik/neoplastik olmayan ayrımında etkili olduğu görüldü. Neoplastik lezyonların yüksek/düşük evre ayrımında ise 2.2'den yüksek Kolin/Kreatin oranı ve eşlik eden lipid-laktat pikinin değerli bilgiler verdiği sonucuna varıldı.

Anahtar Kelimeler: Beyin neoplazmları, Manyetik rezonans görüntüleme, Manyetik rezonans spektroskopi, Stereotaktik biyopsi

INTRODUCTION

Magnetic resonance imaging (MRI) is considered to be the gold standard for preoperative diagnosis, local staging and posttherapeutic monitoring for brain tumors¹⁻³. In many instances, reliable differentiation of neoplastic from non-neoplastic brain masses, or of high-grade from low-grade tumors, is difficult with conventional MRI^{2,4}. Non-invasive and accurate differentiation between neoplastic and non-neoplastic brain lesions is important in determining the correct treatment and, in some cases, may avoid the necessity of performing a biopsy². Several types of non-neoplastic brain lesions (abscess, vasculitis, etc.) can be misdiagnosed as brain tumors. As a result, some patients with benign lesions may undergo unnecessary brain biopsies². Stereotactic biopsies are often used for histopathological diagnosis and tumor grading. This invasive technique has a morbidity of up to 3.6%, a hemorrhage rate of up to 8%, and a mortality of up to 1.7%, as assessed over a large number of studies^{3,5-9}.

The classification and grading of gliomas with conventional MRI is sometimes unreliable, with the sensitivity for glioma

grading, ranging from 55.1% to 83.3%¹⁰. Conventional MRI provides evidence of contrast material enhancement which is often associated with a higher tumor grade. However, any pathological process associated with disruption of the blood-brain barrier can result in enhancement on MRI². Thus, there is a need for additional imaging modalities, such as proton magnetic resonance spectroscopy (MRS) which may aid in improving the diagnosis of unknown brain lesions^{2,11}. MRS imaging is a non-invasive tool for investigating the spatial distribution of metabolic changes in brain lesions³. It is becoming an accurate non-invasive complement to MRI for initial diagnosis of brain masses, since it provides useful chemical information about metabolites for characterizing brain tumors¹². Also MRS is useful in the differential diagnosis of brain tumors and the characterization of metabolic changes associated with tumor progression, degree of malignancy, and response to treatment⁴.

The aim of this study was to provide objective data on the clinical utility of MRS in differential diagnosis of brain lesions and also

to provide some quantitative guidelines for distinguishing neoplastic from non-neoplastic lesions and low-grade from high-grade neoplasms.

MATERIAL AND METHOD

Forty-six patients (28 male, 18 female; age range 6 - 75 years) who were found to have cerebral mass lesions by computed tomography (CT) and conventional MRI and from whom high quality MRS imaging data were obtained, were retrospectively assessed and included in this study. The interpreters were blinded to the final diagnosis, to clinical information regarding presentation and to the laboratory tests and the demographics. Some cases, for which we could not obtain a good quality diagnostic spectrum due to the patient's non-cooperation, with masses close to the calvarium or paranasal sinuses were excluded from the study. Forty of the 46 cases underwent stereotactic biopsy or surgery. All specimens were histologically examined by a neuropathologist and graded according to the World Health Organization (WHO) classification. Histopathological results were compared with MRS results.

MRI and MRS imaging were performed by a 1.5T clinical whole-body imager (Signa; software 5.4.2 GE Medical Systems, Milwaukee, WI) equipped with the standard head coil. Routine brain MRI was performed in 3 orthogonal planes, including at least T1, T2, and fluid-attenuated inversion recovery (FLAIR) weighted images. T1-weighted images after intravenous gadolinium-based contrast material administration (0.1 mmol/kg) were obtained in at least 2 planes. In all cases, single-voxel or two dimensional (2D) multivoxel MRS was performed regarding the numerical and volumetric features of the lesions after administration of gadolinium. Some published results show that gadolinium has a negligible effect on metabolite ratios and peak areas¹³⁻¹⁵. Spectroscopic information was obtained from mainly contrast-enhanced areas of lesions by using a double-SE point-resolved spectroscopy (PRESS) sequence with one-pulse water signal suppression and with

1500/144 ms repetition time/echo time (TR/TE). The volume of interest (VOI) was selected as the lesion identified on MRI, and compared with the contralateral hemisphere having a normal MRI appearance. The VOI was positioned to exclude lipids of the skull and subcutaneous fat. Appropriate automatic shimming and water suppression were achieved by automated software developed by the manufacturer. Spectroscopic data from cubic volumes of $1 \times 1 \times 1 - 2 \times 2 \times 2 \text{ cm}^3$ were obtained depending on the size of the lesion.

We fitted the signals of choline (Cho), creatine (Cr), N-acetyl aspartate (NAA), and lactate-lipid (LL) to a Gaussian line shape using a simplex routine. The peak area ratios of Cho/Cr, Cho/NAA, Cho+Cr/NAA and NAA/Cr were calculated from the peak areas of the respective signals. To ensure quality control and acceptable quality of spectroscopic data, normal values for Cho/Cr, Cho/NAA and NAA/Cr were obtained in normal-appearing parenchyma in the contralateral hemisphere. The metabolite peaks were assigned as follows: Cho, 3.22 ppm; Cr, 3.02 ppm; NAA, 2.02 ppm; mobile lipids, 0.5–1.5 ppm. Lactate was identified at 1.33 ppm by its characteristic doublet and inverted at TE of 144 ms.

On the basis of radiological evaluation, we made a preliminary differentiation of the lesions into neoplastic or non-neoplastic and then subcategorized the neoplastic group into low- or high-grade tumors. The association between the spectroscopic metabolite ratios and histopathological results were assessed by a Receiver Operating Characteristic (ROC) curve analysis. The area under the curve (AUC) was used to calculate the optimal cut-off values for differentiating low- grade versus high-grade neoplasms and neoplastic versus non-neoplastic lesions. This statistical technique allows determination of specificity and sensitivity as a function of a threshold value for identification of neoplastic lesions and high grade tumors.

RESULTS

Forty-six high-quality MRI and MRS examinations with 40 histological diagnoses were available for the evaluation. Forty-one of the 46 patients were found to have intracranial mass lesions. The variety of these lesions are shown in Table I. Forty of these 41 cases underwent stereotactic biopsy or surgery and were diagnosed histopathologically. One case with a tectal glioma had no biopsy or surgery and was followed-up clinically and radiologically. The remaining 5 cases were diagnosed with vasculitis based on a clinical and radiological follow-up.

In all of the cases, except for 2 abscess cases, Cho/Cr, Cho/NAA, Cho+Cr/NAA and NAA/Cr ratios obtained from the pathological and contralateral normal parenchyma showed statistically significant difference. In abscess cases no NAA was recorded. Therefore, Cho/NAA, Cho+Cr/NAA and NAA/Cr ratios could not be calculated. The metabolite peak ratio intervals of the lesions are given in Table II.

The statistical results of ROC curve analysis:

The Cho/Cr, Cho/NAA, NAA/Cr and Cho+Cr/NAA ratios revealed valuable results for the differentiation of neoplastic versus non-neoplastic lesions (Table III). Because the LL peak was not detected in any of the low-grade neoplastic lesions and was only detected in two of the non-neoplastic lesions (abscess cases), it was not used for the neoplastic versus non-neoplastic differentiation.

The Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios revealed valuable results in the differentiation of low-grade versus high-grade neoplastic lesions. The AUC value for

NAA/Cr was found to be very low so that the sensitivity and specificity could not be calculated. The NAA/Cr ratio was not useful in differentiation of low-grade versus high-grade neoplastic lesions (Table IV).

The LL peak was evaluated as positive or negative in all cases and because we could not obtain a numerical value, the ROC curve analysis could not be applied and only the sensitivity and specificity were calculated. In the differentiation of low-grade versus high-grade neoplastic lesions, the sensitivity and specificity of LL were calculated as 69.6% and 100% respectively (Table III).

According to the statistical results of our study Cho/NAA has the highest sensitivity (87.2%) for the differentiation of neoplastic versus non-neoplastic lesions. The specificities of the Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios were 100% for the neoplastic versus non-neoplastic differentiation. Cho/Cr showed the highest sensitivity (95.7%) for the differentiation of low-grade versus high-grade neoplastic lesions; but in one of the cases this finding was discordant with the statistical results. The specificities of the Cho/NAA, Cho+Cr/NAA ratios and LL values were 100% in the differentiation of low-grade versus high-grade neoplastic lesions. The case with the discordant Cho/Cr ratio showed an LL peak. Thus, the Cho/Cr ratio and the LL peak together have a sensitivity of 100% for the differentiation of low-grade versus high-grade neoplastic lesions. Consequently, Cho/Cr > 2.2 and an accompanying LL peak differentiates neoplastic lesions as low-grade versus high-grade with a sensitivity of 100% (82.2-100) and a specificity of 100% (71.7-100).

Table I. Distribution of patients according to histopathological results

	Diagnosis	Number of patients
Non-neoplastic	Vasculitic process	5
	Abscess	2
Neoplastic	High-grade astrocytoma	15
	Low-grade astrocytoma	4
	Gliomatosis cerebri	3
	Metastasis	3
	High-grade oligodendroglioma	2
	Low-grade oligodendroglioma	2
	Medulloblastoma	2
	Malignant B-cell lymphoma	2
	Tectal glioma	1
	Ependymoma	1
	Central neurocytoma	1
	DNET	1
	Ganglioglioma	1
	Gliosarcoma	1

Table II. The metabolite peak ratio intervals of the brain lesions.

	Cho/Cr	Cho/NAA	NAA/Cr	Cho+Cr/NAA
Benign	0.67-1.98	0.44-1.83	0.88-1.51	1.11-2.81
Low-grade	0.69-2.91	0.49-3.2	0.45-1.41	1.2-5.08
High-grade	1.03-9.4	1.06-9.76	0.31-1.64	2.09-12.89

Table III ROC curve analysis results for metabolite ratios in neoplastic versus non-neoplastic differentiation of intracranial lesions

	AUC	cut-off	sensitivity(%)	specificity(%)
Cho/Cr	0.883* (0.754-0.958)	>1.98	71.8 (55.1-85.0)	100 (58.9-100)
Cho/NAA	0.96* (0.856-0.994)	>1.83	87.2 (72.6-95.7)	100 (58.9-100)
NAA/Cr	0.67 (0.516-0.802)	≤1.23	84.6 (69.5-94.1)	57.1 (18.8-89.6)
Cho+Cr/NAA	0.952* (0.845-0.992)	>2.81	84.6 (69.5-94.1)	100 (58.9-100)

Table IV. ROC curve analysis results for metabolite ratios in low-grade versus high-grade differentiation of neoplastic intracranial lesions

	AUC	Cut-off	sensitivity(%)	specificity(%)
Cho/Cr	0.931* (0.842-1.0)	>2.2	95.7 (76.0-99.8)	84.6 (53.7-97.3)
Cho/NAA	0.923* (0.832-1.0)	>3.23	82.6 (60.5-94.3)	100 (71.7-100)
NAA/Cr	0.395 (0.198-0.591)	**	**	**
Cho+Cr/NAA	0.89* (0.783-0.996)	>5.16	73.9 (51.3-88.9)	100 (71.7-100)
LL	***	***	69.6 (47-85.9)	100 (71.7-100)

* AUC is the area under curve. Values greater than 0.85 are assumed to be significant in statistical tests.

** Could not be calculated because of very low values of "AUC", cut-off, sensitivity and specificity.

*** ROC curve analysis could not be applied because of lack of a numerical value; only sensitivity and specificity were calculated.

Note: The values written in parenthesis are 95% confidence intervals for both AUC values and sensitivity/specificities; this means that if the experiment is repeated endless times the results will be between these intervals 95% of the time.

DISCUSSION

Single-voxel and multivoxel proton MRS have been used for the assessment and grading of brain tumors¹⁶. Previously reported MRS findings in brain tumors included a decrease in NAA, a marker of neuronal integrity, an increase in Cho involved in

increased cell membrane and myelin turnover; and a decrease in Cr, which provides inorganic phosphates for adenosine triphosphate production involved in cellular energetics and osmotic balance^{4,17-21}. The presence of the LL peak was usually consistent with aggressive tumors, reflecting

increased anaerobic metabolism and cellular necrosis^{4,17,18,20,21}. The diagnostic accuracy of MRS in differentiating neoplastic from non-neoplastic lesions was found to be 0.96 and 0.83^{4,22}.

The majority of the previous reports failed to find spectroscopic parameters that characterize the tumor type or malignancy^{21,23-26}. Using the single-voxel method, Kugel et al. found a clear difference in spectra between gliomas and meningiomas. However, these researchers concluded that the malignancy of gliomas could not be estimated^{26,27}. One study suggested a statistically significant dependence of Cho levels on the malignancy of gliomas^{26,28}. The ratio of the Cho level of tumors 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 tumor 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 destruction²⁸. In contrast to this, Kinoshita et al. reported that MRS can indicate the types of tumors and the degree of malignancy by showing the changes in metabolite concentrations. For example, high-grade tumors had lower NAA and Cr concentrations and higher Cho concentrations than did low-grade tumors^{26,29}. Tien et al. found NAA to be decreased in all grades of gliomas, with the high-grade gliomas having the lowest levels of NAA. They also reported that high-grade gliomas tend to have an LL peak³⁰.

In our study, the Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios showed higher values in high-grade neoplastic lesions than in non-neoplastic and low-grade neoplastic lesions. We detected increased Cho levels in all neoplastic lesions. These results were consistent with the literature^{4,31,32}. We did not detect any LL peak in the benign lesions except for the abscess cases in which the

presence of an LL peak was due to nonfunctioning normal oxidative respiration and increased anaerobic glycolysis^{4,33} and it was represented as a loss of normal brain parenchyma and necrosis on MRI^{4,21}.

In one study, Poptani et al. 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. These authors also reported that the LL peak is an indicator of a higher grade malignancy. As a consequence they explained that MRS helps the tissue characterization of lesions; the combination of Cho/Cr and Cho/NAA ratios with LL peak positivity is reliable in grading of neoplastic lesions³⁴. In our study all neoplastic lesions showed increased Cho and decreased NAA and this was more prominent in high-grade neoplasms. While we did not detect any LL peak in 13 low-grade neoplasms, 19 of 26 high-grade neoplasms showed an LL peak (Figs. 1, 2).

Some reports state that increased Cho levels with an LL peak indicate high-grade malignancy^{23,26,35}. Martin et al., found that the Cho/NAA ratio shows the most significant difference between high-grade and low-grade tumors³⁶. In our study, we found that an increased Cho/Cr (>2.2) ratio associated with an LL peak together have a sensitivity and specificity of 100% in the differentiation of high-grade versus low-grade neoplastic lesions.

Two of our cases diagnosed with B-cell lymphoma showed increased Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios while one showed a lipid peak consistent with the literature findings³⁷.

In 3 metastasis cases, we found high Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios with LL peaks. The metabolite ratios obtained from the peripheral T2 hyperintense areas of these lesions were all within normal limits in accord with the literature findings³⁸ (Fig. 3).

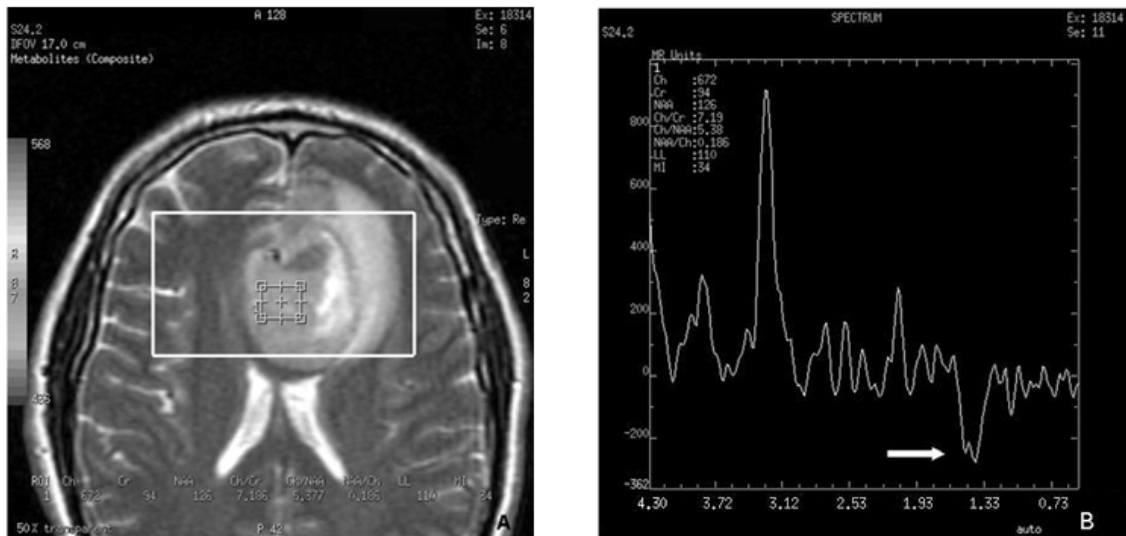


Figure 1: Thirty-five year old male; glioblastoma multiforme. A. T2-weighted axial image shows a hyperintense mass lesion and surrounding edema area. B. Multivoxel MRS obtained with TE 144 ms shows a prominent Cho peak; Cr is not well-assessed and there is significant decrease in the NAA peak. There is also a lactate peak (arrow).

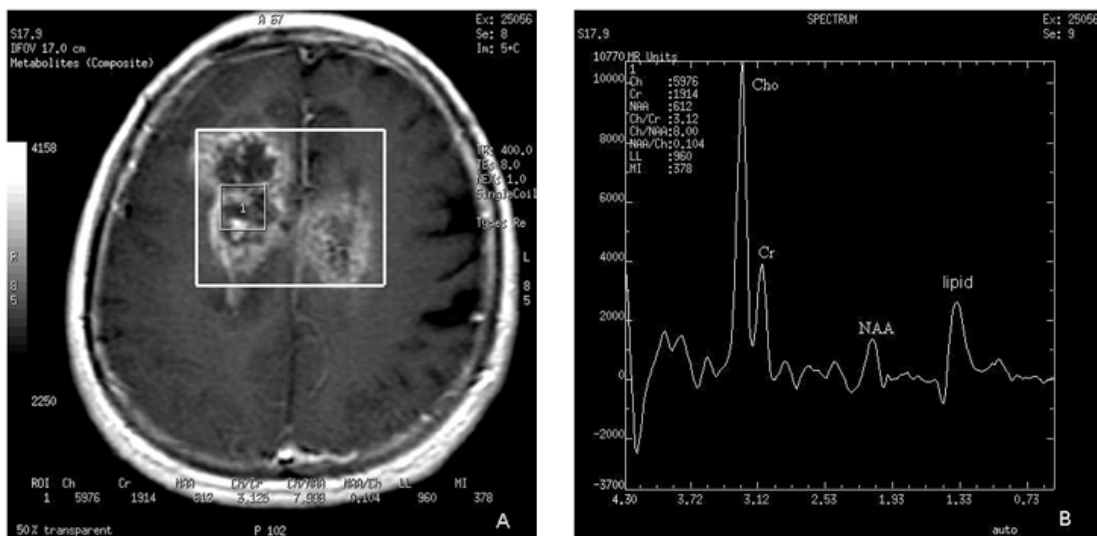


Figure 2: Forty-nine year old female; glioblastoma multiforme. A. Contrast enhanced T1 weighted axial image shows a mass lesion passing across the midline which was enhanced heterogeneously due to central necrotic areas. B. Multivoxel MRS shows increase in Cho, decrease in Cr and NAA as well as a lipid peak.

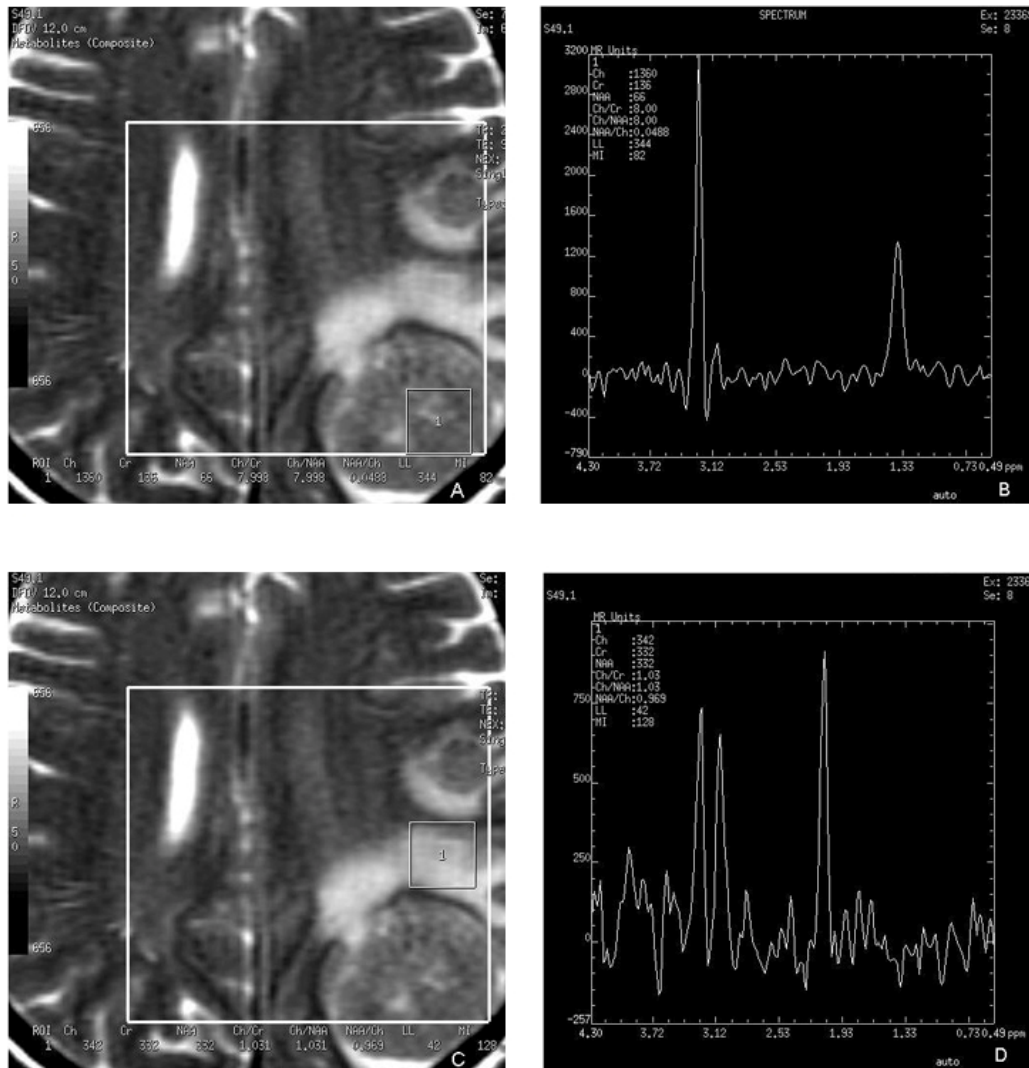


Figure 3: Fifty-three year old female; metastases from lung cancer. A. T2 weighted axial image shows two mildly hyperintense lesions and surrounding edema. B. Multivoxel MRS obtained from the bigger lesion shows an increased Cho peak and a lipid peak. C-D. MRS obtained from the peripheral edema area of the lesion shows that metabolite values are nearly within normal limits.

Several studies have reported increased Cho/Cr and Cho/NAA ratios in gliomatosis cerebri³⁹⁻⁴¹. Also Bendszus et al., have stated that Cho/Cr and Cho/NAA ratios are mildly elevated in low-grade gliomatosis cerebri while elevation is much more prominent in higher grades³⁹. There were 3 gliomatosis cerebri cases in our study with increased Cho/Cr, Cho/NAA and Cho+Cr/NAA ratios. In two of them with low-grade gliomatosis cerebri (WHO grade II) the elevation of

Cho/Cr and Cho/NAA ratios was mild relative to the third case with high-grade gliomatosis cerebri (WHO grade IV). The measurements of Cho/Cr and Cho/NAA ratios in 2 low-grade lesions were 1.35 ; 2.92 and 1.22 ; 2.73 respectively. In the high-grade one these values were 5.15 ; 4.79 respectively and an LL peak was present.

In brain abscesses, MRS shows an elevation of acetate, succinate, and some amino acids, as well as lactate and lipid, which appear

significantly different from the spectra of cystic or necrotic brain tumors. Detection of resonance peaks from acetate, succinate, and such amino acids as valine and leucine has not been reported in MRS of brain tumors. Therefore, if there are resonance peaks at around 0.9 to 1.5 ppm on MRS, an additional spectrum obtained at an echo time of 135 or 144 ms would be necessary to discriminate lactate or amino acid signals from a lipid signal. With an echo time of 135-144 ms, phase inversion occurs as a result of J-coupling in lactate and amino acids, but not in lipid, which may be helpful, along with the presence or absence of acetate or succinate, in differentiating a brain abscess from a tumor⁴². In our abscess cases the spectrum showed a high lactate peak as well as amino acid peaks at about 0.9 ppm consistent with the literature findings.

In our study, in one central neurocytoma case MRS showed high Cho/Cr and Cho/NAA as well as another peak at about 3.55 ppm representing inositol or glycine. This was consistent with a previous report⁴³.

In our study, the dysembryoplastic neuroepithelial tumor (DNET) case was easily discriminated from other benign tumors because it showed normal spectra, and this finding was consistent with that of a previous report^{4,44}.

MRS data of our tectal glioma case showed a Cho/Cr ratio of 1.87 and a Cho/NAA ratio of 2.66. According to Law et al.'s study¹⁰ these findings were compatible with a low-grade glioma. When the threshold values of Cho/NAA ratio are considered in the same study¹⁰ our findings were in accord with the values for high-grade gliomas. Control conventional MRI following radiotherapy did not show any significant difference, whereas MRS showed decreased Cho/Cr and Cho/NAA ratios obtained from the same tumor region. Following radiotherapy; the values were 1.36 and 1.46 respectively. This decrease was evaluated as an indicator of regression.

In the literature there are few reports about MRS findings for vasculitis. In one study

Sener RN found no abnormal MRS findings in neuro-Behcet's disease⁴⁵. Baysal et al., stated that patients with neuro-Behcet's disease had significantly higher NAA/Cr and Cho/Cr ratios for the basal ganglia and an elevated Cho/Cr ratio in the periventricular white matter. In their study MRS enabled a clear discrimination of patients from controls and also revealed spectral differences between non-neuro-Behcet's disease and neuro-Behcet's disease in the basal ganglia. They concluded that MRS can be used to assess brain involvement in Behcet's Disease even if structural changes are absent⁴⁶. In another study Appenzeller et al. reported that systemic lupus erythematosus (SLE) patients had an increased Cho/Cr ratio compared with a control group. In addition, there was an increase in the Cho/Cr ratio when patients' baseline and follow-up MRS examinations were considered. They concluded that increased Cho/Cr in normal appearing white matter may be indicative of the future appearance of hyperintense T2-weighted MRI lesions in SLE patients⁴⁷. In our study, five cases were evaluated as vasculitis based on clinical and radiological findings and one of them was Neuro-Behcet's disease. These 5 cases were found to have T2-weighted hyperintense MRI lesions without any mass effect. MRS showed no abnormality (Fig. 4). These MRS findings were not consistent with the limited literature reports available.

The retrospective design of this study was the first limitation to be considered. Another limitation was the small number of cases and the variety of intracranial lesions. We think that this was the main reason why our study came to a conclusion with very high sensitivity and specificity values of different metabolite ratios. Further prospective studies with larger groups of patients including a larger variety of non-neoplastic lesions in the control group and better statistical data obtained from similar types of lesions are desirable to support or contradict our results and to determine the accuracy of MRS in differential diagnosis and grading of intracranial space occupying lesions.

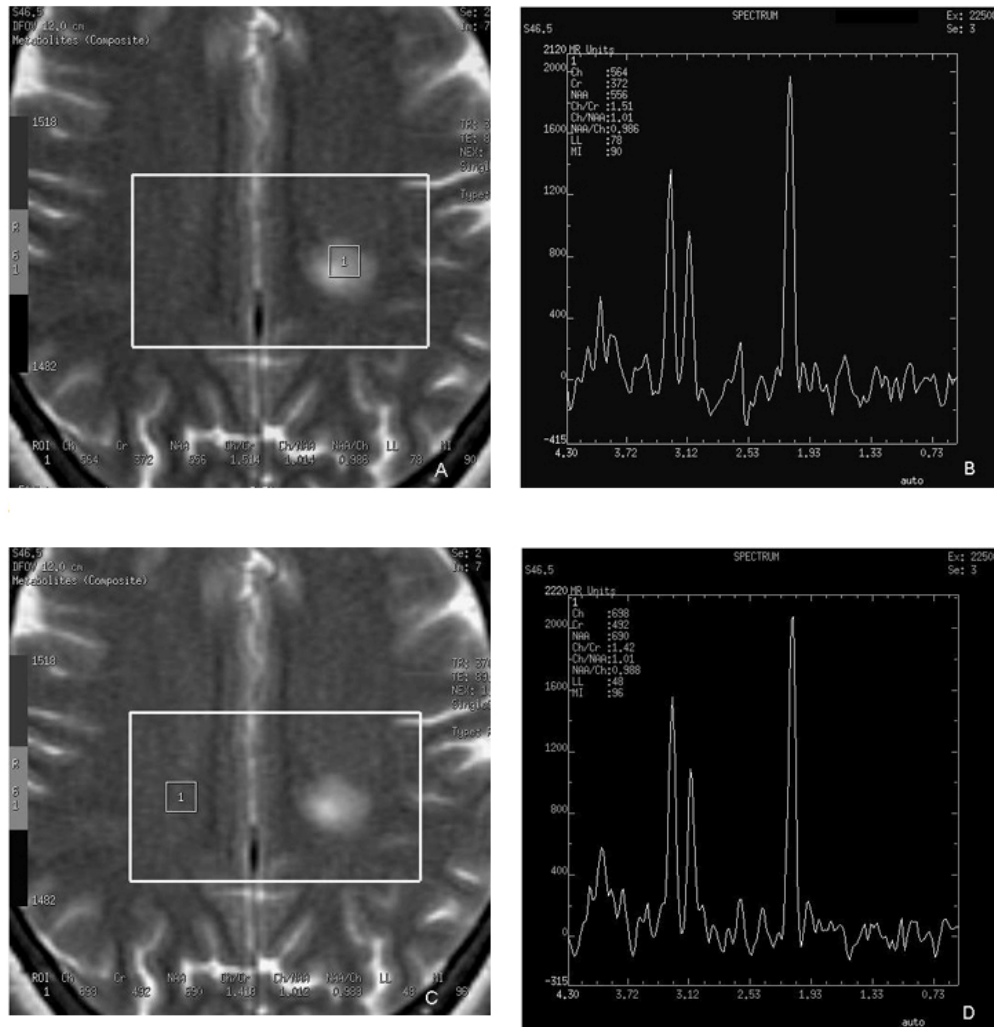


Figure 4: Twenty-nine year old female; vasculitic process. A-B. Multivoxel MRS obtained from the lesion area on the left hemisphere and, C-D. Spectra obtained from contralateral normal parenchyma both show normal metabolite values.

This study has shown that tissues appearing similar on conventional MRI may have different spectral characteristics. We concluded that the presence of elevated Cho and decreased NAA is effective in differentiation of neoplastic versus non-neoplastic lesions with high sensitivity and specificity. Also we showed that the accompanying LL peak provides useful information in non-invasive grading of neoplastic lesions preoperatively or before biopsy. We have suggested a resonance intensity ratio (Cho/Cr ratio > 2.2 and the

accompanying LL peak positivity) can be used to differentiate low-grade from high-grade neoplastic lesions. This data differentiates neoplastic lesions as low-grade versus high-grade with a sensitivity of 100% (82.2-100%) and specificity of 100% (71.7-100%) and can be used in daily clinical practice to improve accuracy and the neuroradiologists' confidence in differential diagnosis and grading of cerebral lesions.

Stereotactic biopsy and even resection may reflect sampling errors of the tumor that can be removed. Histology is not always

reflective of the actual tumor grade and therefore MRS can be helpful.

As a result we believe that MRS plays a critical role in pre-operative or pre-interventional differential diagnosis of cerebral mass lesions by distinguishing neoplastic from non-neoplastic lesions, by grading neoplastic lesions and by improving the accuracy and confidence level of neuroradiologists in their diagnoses. It is also an effective method complementing conventional MRI in following response to therapy.

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