

脳腫瘍の治療計画の新しい評価法-MRSによる悪性度の診断(基礎と臨床研究)-

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脳腫瘍の治療計画の新しい評価法
-MRS による悪性度の診断（基礎と臨床研究）-

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脳腫瘍の悪性度は摘出標本の病理検査によってはじめて可能であるが、最近の研究により、磁気共鳴スペルトロスコピー(MRS)による生化学的分析により、頭蓋内病巣の腫瘍性-非腫瘍性の鑑別、腫瘍の悪性度の診断が可能となった。増殖性病巣においては、細胞の分裂周期が早まるとともに細胞膜の生合成が盛んとなる。プロトン MRS で観察可能な trimethyl amine group は、細胞の増殖により増加すると報告されて以来(nature)、臨床において腫瘍性病変の診断に応用できないかが検討されてきた。プロトン MRS で検出する trimethyl amine の信号は、細胞膜に存在するコリンの濃度には影響されない。細胞膜の生合成の過程で必要な重合前で細胞質に存在する trimethyl amine の濃度が MRS の信号に関与する。具体的には、生体内で trimethyl amine group として報告されているものは、GPC、PC、free choline、クロルジアゼポキシドコリン、ACho、一部の PtdCho である。細胞膜に豊富な PtdCho は MRS では検出(unvisible)できず、MRS の信号への寄与は GPC と PC が大きい。PC や GPC は細胞膜の生合成や異化の過程で産出される代謝産物であり、これらの物質の濃度を測定することにより非腫瘍性病変との鑑別や腫瘍性病変の悪性度診断に用いることが可能である。

さらに MRS では、壊死前に出現する乳酸や壊死巣で検出される mobile lipid の検出に有用である。腫瘍性病変においては病理学的に壊死の存在は高い増殖性を示唆するものとして知られている。われわれは髄膜腫においてこの mobile lipid と壊死巣との関係を詳細に検討した。mobile lipid が検出された髄膜腫のすべてに病理学的に壊死が認められたこと、塞栓術後に乳酸に引き続いて mobile lipid の信号が出現し、摘出標本で壊死巣を確認できたことは、mobile lipid の由来が壊死巣であることを示唆している。また、画像では判り難い壊死巣が MRS で検出可能であったことは重要である。われわれの症例のうち、病理検査で4つの髄膜腫に腫瘍内壊死が認められたが、この中の1つは画像上壊死巣の存在はわからず、benign と診断された。しかしながら、この髄膜腫の MRS では、mobile lipid が検出され、trimethyl amine group の信号も高かった。また、乳酸が認められた髄膜腫では、G₀期以外の細胞核に出現する抗原を認識する抗体である MIB-1 の陽性率が通常のものよりも高かった。

放射線治療後に出現する遅発性放射線壊死は、画像診断上脳腫瘍の再発と鑑

別することは極めて困難である。放射線壊死巣は MRI 上、悪性神経膠腫に極めて類似している。遅発性放射線壊死の場合にはステロイドを投与することに改善する場合があるが、再発腫瘍の場合には化学療法や放射線治療を追加するといった治療法が必要となる。これら2つの病変の鑑別には、生検手術が必要である。あるいは、MRI をくり返し検査し、ステロイドへの反応性や経過を観察する必要がある。しかしながら、こうした診断法には手術侵襲、ステロイドの副作用、診断に時間がかかるといった問題がある。放射線壊死巣を MRS で検査すると特徴的なパターンが認められる。まず、trimethyl amine group の信号が検出濃度以下か極めて低いレベルにある。これは、病巣が増殖性でなく壊死巣であることと矛盾しない。次に、壊死部に存在する mobile lipid、特にメチレン基の信号が特異的に強いことが観察される。これらのことから、MRS は放射線壊死の診断に極めて有用である。

脳膿瘍の特異性は、通常の炎症性病巣と異なり、全身の炎症反応があまり表出されないことである。これは、脳には血液脳関門が存在し炎症反応は局所に限局するためと思われる。脳腫瘍か脳膿瘍の鑑別には、項部硬直、髄液の細胞数、白血球増加や CRP 反応の亢進が参考になるが、これらの検査結果がすべて陰性であっても脳膿瘍である患者は少なくない。また、脳膿瘍と悪性神経膠腫は画像診断上極めてまぎらわしいことがあり、生検ではじめて画像診断の誤りに気付く場合もある。MRS で脳膿瘍は、trimethyl amine group の信号の増加はなく、放射線壊死巣に類似したパターンを示す。また、起因菌の約半数はアセテートを生成するため、この信号が認められる場合にはまず脳膿瘍と言って間違いはない。

MRS において重要で忘れてならないのは、この検査は全く侵襲のないことである。検査は MRI の画像診断に引き続き施行可能であり、必要な時間も 20 分程度である。また、市販の MR 装置で検査可能であり、最近の技術の進歩により操作も非常に簡便化されている。既に保有している MRI 装置のパルスシーレンスをコンピューター上で変更するだけで技術的には検査可能となる。こうしたことから、MRS は臨床検査として極めて有用・普及可能な方法と考えている。

研究組織

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研究成果

Noninvasive evaluation of malignant potential of intracranial meningiomas by proton magnetic resonance spectroscopy

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Running head: Meningioma grade and MR spectroscopy

Key Words: magnetic resonance, spectroscopy, MIB-1, malignancy, meningioma

Abstract

Object. Controversy exists as to correlations between histologic tumor grade and magnetic resonance spectroscopy (MRS) data. We studied single-voxel proton MRS as a noninvasive way to evaluate grade of malignancy in intracranial meningiomas.

Methods. We compared results of MRS and MIB-1 staining index (SI) in 29 meningiomas. Proton MRS was performed using STEAM and VAPOR sequences before surgery or other therapy.

Conclusions. Twenty-four tumors were histologically benign (13 meningothelial, 3 fibrous, 4 transitional, 3 angiomatous and 1 chordoid); 4 were atypical (grade II), and 1 was papillary (grade III). Mean MIB-1 SI in the benign group was significantly lower than in the others ($P=.0041$). Mean Cho/Cr ratios in benign and nonbenign groups were 2.56 ± 1.26 and 7.85 ± 3.23 respectively ($P=.0002$). A significant linear correlation was observed between the Cho/Cr ratio and MIB-1 SI ($r_{0.05}=0.740$, $P<.001$). Necrosis was present histologically in 4 of the 5 meningiomas classified either as atypical or papillary. On MRS these meningiomas showed a methylene signal not detected in benign meningiomas. Of 5 meningiomas showing a lactate signal only, 2 were benign and MIB-1 SI in these 2 benign meningiomas was higher than the mean value for the benign group. Alanine, detected in only 7 of 30 meningiomas, did not correlate with tumor grade or Cho/Cr ratio.

Proton MRS is a useful diagnostic method for determining proliferative or malignant potential of meningiomas in terms of the Cho/Cr ratio. A lactate and/or methylene signal suggests a high-grade tumor.

Key Words: magnetic resonance, spectroscopy, MIB-1, malignancy, meningioma

Introduction

Intracranial meningiomas are frequently occurring tumors that grow slowly and usually are amenable to surgical treatment. Nevertheless, 5 to 20% of meningiomas show atypical³⁵ and 1.4 to 11.1% show malignant histologic features.^{13,20,21} These nonbenign meningiomas grow rapidly, invade adjacent brain, tend to recur, and sometimes result in a poor outcome despite aggressive treatment. Patients with an incidental finding of meningioma or imaging studies sometimes may be followed clinically without surgical intervention. However, some highly aggressive tumors will require surgical treatment, even if small and found in elderly patients. Reliable noninvasive preoperative evaluation of tumor grade is therefore a very important goal.

Computed tomography (CT) and magnetic resonance imaging (MRI) are generally excellent studies for diagnosis of meningiomas. While these imaging modalities also contribute to assessment of malignancy or tumor grade, these studies have only limited ability to evaluate tumor growth rate.³⁸ We believe that biochemical evaluation of meningiomas using magnetic resonance spectroscopy (MRS) offers a more accurate means of estimating growth rate. An immunohistologic method of identifying cell proliferation using MIB-1 antibody staining has proven very useful for evaluating proliferative and malignant potential in tumors specimens,^{4,10,23,27,32} and in the present study we used a MIB-1 staining index (MIB-1 SI) as a standard for evaluating preoperative MRS in determination of the proliferative potential of meningiomas. We also used MRS to evaluate specific characteristics of atypical meningiomas.

Subjects and Methods

Subjects were recruited from among 62 patients with meningiomas who were admitted to the Department of Neurosurgery at Shiga University of Medical Science from August 1990

to March 1992 and from September 1993 to December 1998. A total of 32 patients with meningiomas sufficiently large for MRS assessment were enrolled in this study. Of the 32 patients, 3 had postoperative tumor recurrences. One of these 3 patients was studied twice, at the time of initial presentation and again at tumor recurrence. The study was approved by the University Ethics Committee. A written explanation of the objectives and methodology of the study was provided to all patients and their families. Tumors were excised surgically from all patients. To reduce intraoperative bleeding, 7 patients underwent preoperative embolization with 50 to 200- μ m polyvinyl alcohol (PVA) particles via a microcatheter superselectively introduced into feeding vessels.

MRI and MRS were performed with a 1.5-T whole-body MRI device (General Electric, Milwaukee, WI) using a conventional birdcage head coil. Patients who had received any previous radiotherapy or chemotherapy were excluded from this study. The imaging protocol included T1-weighted spin-echo images (TR/TE=500/30 msec) with and without intravenous injections of 0.2 mL/kg of gadolinium (Gd)-DTPA as well as T2-weighted images (TR/TE=2400/100 msec). To minimize the effects of Gd-DTPA on MRS results, MRS studies were carried out before or at least 24 h after the administration of contrast agent. For determining the volume of interest (VOI) in each case, three-dimensional T1-weighted images (TR/TE= 600/ 20 msec) were obtained immediately before spectroscopy to avoid any areas not part of the tumor. Within that constraint, VOI size was set as large as possible, ranging from a minimum of 8 cm³ to a maximum of 27 cm³. Cases in which tissue other than tumor was included in the VOI due to peculiarities of tumor configuration or location were excluded from further data analysis. Proton MR spectroscopy was performed with a STEAM sequence, which generates a stimulated echo of the magnetization within the volume of interest (VOI) using three selective radiofrequency pulses under orthogonal gradients. For water suppression, a sequence dubbed VAPOR (volume localized, solvent attenuated, proton NMR)

with an eight-step phase cycle of the slice-selective pulses was used, resulting in excellent water suppression factors of over 750. Shimming was achieved manually over the selected volume by observing the proton MR signal of tissue water, resulted in a line widths of 2 to 4 Hz. Slice selection refocusing gradients also were adjusted manually. MRS parameters were as follows: echo time, 19 and 135 msec; middle interval, 10.8 msec; repetition time, 2000 msec; number of acquisitions, 64 to 128. The entire examination was usually completed in 50 min or less.

A processing scheme designed to exclude operator bias, described elsewhere,³⁷ was employed to analyze the spectra. Data were extracted randomly and processed by a single investigator (A.S.) who was unaware of the clinical diagnosis, using a Sun Sparc 10/30 workstation (Sun Microsystems, Mountain View, CA) with Omega software (version 6.0.2, General Electric, Milwaukee, WI). The free-induction decay was apodized with an exponential line-broadening (1 Hz), zero filling to 2000 complex points, and Fourier transformation with manual zero- and first-order phase correction. An additional baseline correction with polynomial interpolation was performed for the purpose of presentation. Metabolite peaks were identified by their chemical shift and coupling pattern as described in the literature p¹¹: methyl -CH₃, 0.9 ppm; methylene -(CH₂)-, 1.3 ppm (singlet); lactate -CH₃, 1.3 ppm (doublet); alanine -CH₃, 1.5 ppm (doublet); glutamate/glutamine -γCH₂, 2.3-2.5 ppm (multilet); creatine/phosphocreatine (Cr) -NCH₃, 3.0 ppm; choline/phosphocholine/glycerophosphocholine (Cho) -N(CH₃), 3.2 ppm. Peak areas were calculated by automatic curve fitting with a simplex method using software programmed in our laboratory for use with an IBM personal computer.²⁶ Unfortunately, we needed to exclude glutamate/glutamine peak from curve fitting because of technical difficulties in measurement of peak area.

During the early stage of this study the spectrum was obtained with two echo times (19 and 135 msec), but later 19 msec alone adopted to minimize examination time. An echo time of 135 ms was added if the presence of lactate was suspected to invert the doublets with spin-spin coupling at about 7.35 Hz. Proton MR spectra of meningiomas usually show prominent Cho resonance, while the Cr signal is small. Short echo time is advantageous for detection of Cr and aliphatic signals since the T1 of these compounds is shorter than that of others. At a short echo time, sufficient signal is available, and the phase and amplitude errors associated with *J* modulation of signal intensity are minimized.

Proliferative potentials evident in excised meningiomas were studied using MIB-1 antibody staining against the Ki-67 antigen. Details of MIB-1 staining index (SI) determination are described elsewhere.²⁸ Briefly, paraffin sections cut at 5- μ m thickness were deparaffinized and incubated with MIB-1 antibody (Immunotech, Marseille, France). Specimens were immunostained with an LSAB kit (DAKO, Carpinteria, CA) and developed with diaminobenzidine. MIB-1 SI was calculated as the percentage of MIB-1-positive cells among all tumor cells in the microscopic fields examined. At least 2000 tumor cells were counted in randomly chosen fields, then percentages of positively staining cells were calculated.

Statistical analyses, including establishment of a regression line, calculation of a correlation coefficient, and determination of significance of regression between MIB-1 SI and Cho/Cr values, were performed on a Macintosh computer (Cupertino, CA) with StatView IV (Abacus Concepts, Berkeley, CA).

Results

No definite signal peak could be identified in 3 of the 32 cases evaluated by MRS. Data from these 3 patients was excluded from further consideration. One patient who had a

tumor recurrence about 1 year after the first operation underwent MRS twice, at the time of initial symptoms and at the time of tumor recurrence. Thus, we evaluated 30 MRS studies in 29 patients. All patients were diagnosed with meningioma on the basis of surgically excised tissue specimens. The 29 patients (10 men and 19 women) ranged in age from 22 to 81 years (mean \pm SD, 57.6 \pm 14.1).

Histopathologic Diagnosis

We used the histopathologic classification of meningioma subtypes established by the World Health Organization (WHO) in 1993.¹⁶ Pre-1993 specimens were reclassified in accordance with the 1993 criteria. The number of patients with each subtype was as follows: meningothelial, 13; fibrous, 3; transitional, 4; angiomatous, 3; chordoid, 1; atypical, 4; and papillary, 1. The atypical (grade II) and papillary (grade III) meningiomas were considered as a nonbenign group, while the other subtypes were taken as the benign group. The recurrent tumor studied by MRS twice was atypical. Necrosis was demonstrated histologically in 4 of the 5 meningiomas classified as either atypical or papillary. None of the meningiomas in the benign group, with the exception of cases where preoperative embolization was performed, showed any necrosis on histopathologic examination. The subtype of the three recurrent meningiomas did not change.

Results of Magnetic Resonance Spectroscopy

A Cr signal at 3.0 ppm and a Cho signal at 3.2 ppm were present in all 30 MRS studies. In 26 of the 29 patients, an overlapping glutamate/glutamine multiplet was present at 2.3 to 2.5 ppm. An alanine signal was observed in 12 cases, and a lactate signal in 5. An undefined signal at 1.9 ppm was thought to represent acetate.

The mean Cho/Cr ratio was 7.85 ± 3.23 in the nonbenign meningiomas and 2.56 ± 1.26 in the benign meningiomas. Statistical analysis confirmed a significantly higher Cho/Cr ratio in the nonbenign meningiomas ($P = .0002$, Mann-Whitney U test).

Of the tumors showing a signal at 1.3 ppm, this represented a singlet from methylene (CH_2) resonance in five. Four of these five tumors were atypical meningiomas, and necrotic foci were found on histopathologic examination. The remaining tumor was angiomatous. Because preoperative embolization had been performed in the latter case, determination of whether necrosis had been present before embolization was not possible. A doublet signal of lactate was present in five tumors, two of these were meningothelial, while the other three were nonbenign.

Comparisons between MIB-1 Staining Index and MRS

Because the MIB-1 SI is affected by tissue changes following embolization,²⁹ 7 cases with preoperative embolization were excluded from MIB-1 SI data analysis. The remaining 23 meningiomas, representing 22 cases, were evaluated with respect to MIB-1 SI. MIB-1 SI values of histopathologically benign meningiomas ranged from 0.15 to 4.58 (mean \pm SD, 1.34 ± 1.32). MIB-1 SI values of the atypical and papillary meningiomas ranged from 2.43 to 4.63 (mean \pm SD, 3.46 ± 0.95). MIB-1 SI in the nonbenign group was significantly higher than that in the benign group ($P = .0041$, Mann-Whitney U test).

Figure 1 depicts the regression line for the Cho/Cr ratio in meningiomas vs. MIB-1 SI; the correlation coefficient was 0.740 ($P < .001$), indicating a significant linear correlation. In the patient with a recurrent atypical meningioma, MIB-1 SI and Cho/Cr ratio at initial presentation were 2.43% and 7.2, respectively; MIB-1 SI and Cho/Cr ratio at the time of

recurrence were 4.63% and 13.9, respectively. MIB-1 SI and Cho/Cr ratio both were approximately 1.9 times higher at the time of recurrence than at initial presentation.

Figure 2 shows the time course of spectrum evolution after embolization in a representative case. Immediately after embolization, a lactate signal appeared and Cho and Cr signals decreased. On days 5 to 8 a MRS-detectable aliphatic signal indicating mobile lipid was seen. Histopathologic examination revealed intratumor necrosis caused by embolization.

Discussion

Preoperative prediction of meningioma grade is clinically important. Jääskeläinen and colleagues have reported 5-year recurrence rates for benign, atypical, and malignant meningiomas of 3%, 38%, and 78%, respectively, following complete surgical excision.¹² Other authors have reported similar high rates of recurrence for high-grade meningiomas. Therefore, if preoperative examinations suggest a high grade, surgical planning and procedures should address a suspected malignant lesion, including wider resection margins and adequate intraoperative biopsy of margins. Conversely, if the tumor is suggested to have a very low proliferative potential, partial excision sometimes may achieve a satisfactory postoperative course especially in elderly patients.

MIB-1 is an antibody that recognizes nuclear antigens appearing in cell-cycle phases other than G_0 .¹⁹ The MIB-1 positivity rate is thought to be nearly equal to the fraction of the tumor that is actively growing. The statistically significant correlation between the Cho/Cr ratio measured by MRS and MIB-1 SI demonstrated in this study suggests that MRS is a useful noninvasive method for predicting the proliferation potential of meningiomas. Reports to date concerning CT and MRI indicate that absence of calcification, heterogeneous enhancement, intratumoral necrosis, irregular margins, and a mushrooming pattern are frequent findings suggesting a nonbenign meningioma.^{2,5,31,38,40} However, these

neuroimaging patterns, even together with findings from angiography, are not sufficient in themselves to predict malignancy of meningiomas. MRS provides further diagnostically useful information by virtue of its ability to biochemically predict proliferative potential of tumors. As shown by the case represented in Figure 3, a meningioma that appears benign by MRI may nonetheless prove to be atypical. In such cases, MRS offers a more accurate means of predicting tumor proliferative potential.

Resonance at 3.2 ppm is a signal that can represent various metabolic products including trimethylamine groups. Reported metabolites include glycerophosphocholine (GPC), phosphocholine (PC), free choline, chlordiazepoxidecholine, acetylcholine (ACh), and sometimes phosphatidylcholine (PtdCho).³ PtdCho, which is abundant in cell membranes, is not generally detectable by MRS.²⁴ Free choline, PC, and GPC are major contributors to the peak at 3.2 ppm in *in vivo* proton MRS of human brain tumors. These compounds are the metabolites produced during biosynthesis and catabolism of cell membranes. The main pathways of free choline involve synthesis of ACh and PC, and PC is used to synthesize PtdCho via the Kennedy pathway.²⁵ The concentration of choline-containing compounds that are visible on proton MRS is thought to correlate with increased membrane biosynthesis and/or increased cellularity.^{1,8} In gliomas, several reports have shown a correlation between high concentrations of choline-containing compounds and malignancy when necrotic areas can be excluded from the VOI.^{9,14,15} One reason for the positive correlation between MIB-1 SI and Cho/Cr ratio in our study is probably an increased pool of choline-containing compounds involved in membrane turnover.

The major contributors to 3.0 ppm resonance detectable on MRS are creatine and phosphocreatine.³ Since neurons and muscle consume ATP at a high rate, phosphocreatine, a temporary storage form of high-energy phosphate, is abundant in these cells. In contrast, the total Cr concentration of meningiomas is only approximately one fifth of that found in normal

brain.¹⁴ This results in difficulty in obtaining an adequate Cr signal from meningiomas, but the short echo time of 19 msec employed in this study elicited a sufficient Cr signal. The Cr peak sometimes is used as an internal standard, since it is relatively stable despite various diseases. However, in tumors, total creatine is decreased relative to nonneoplastic tissues^{14,15,22,30}; rat meningeal cells show increased PC concentration and decreased Cr concentration in comparison to human meningiomas.⁷ Similarly, the Cr concentration in human gliomas is also lower than that in normal brain.^{14,39} In addition, Cr concentration reportedly tends to decrease correlating with increasing degree of malignancy.¹⁴ These observations suggest that decreased Cr concentrations also contributed to the increased Cho/Cr ratios that we have observed. Semiquantitative measurement using external standards will help to clarify influence of changes in individual substances on the overall increased Cho/Cr ratio. Unfortunately, this will extend the time required to study each patient by 50%.

The most likely source of the methylene (CH₂) signal at 1.3 ppm in meningiomas is mobile lipid.^{17,36} The intensity of this aliphatic signal has been found to correlate with extent of necrosis and tumor malignancy.^{18,30,33} All of our meningioma cases showing this aliphatic signal had necrosis by histologic examination, and no necrosis was found histologically in any meningioma from which no methylene signal was detected by MRS. This signal also was seen in embolized meningiomas with resulting necrosis. As shown in Figure 2, a lactate signal appeared immediately after embolization and was superseded by a methylene signal after 3 to 4 days. Production of lactate occurs only when viable cell metabolism is underway in the form of anaerobic glycolysis, which suggests ischemic change in the tumor. The cell then is likely to die from ischemia, and the spectral change from lactate to methylene signal may reflect this event.

Without prior embolization, the presence of necrosis is highly suggestive of tumor malignancy.^{16,34} In the present study, MRS shows promise as a clinically important means of

detecting tumor necrosis, which sometimes is missed by conventional imaging studies. Histopathologic examination revealed intratumoral necrosis in four of our meningioma cases, while routine imaging studies in these cases failed to reveal any necrosis and appeared consistent with a benign diagnosis. Nevertheless, MRS examination of these meningiomas detected the presence of mobile lipid and high Cho/Cr ratios, and subsequently tissue sections of these tumors contained scattered areas of micronecrosis. One reason that necrotic change in a meningioma is difficult to reliably detect by conventional neuroimaging is that in themselves in homogeneous imaging patterns do not necessarily indicate tumor necrosis or malignancy.

The presence of lactate represents a precursor stage leading to tumor necrosis. However, two of the five meningiomas in which lactate was detected proved to be benign on histopathologic examination. Thus, the presence of lactate does not necessarily preclude a benign tumor. Nonetheless, the MIB-1 SI in the two benign meningiomas showing lactate signals on MRS were 2.95 and 2.30, values exceeding mean MIB-1 SI values for the benign group as a whole. One of these two meningiomas has not recurred for 2 years but the other recurred after 1 year. The presence of lactate therefore is suggestive of an increased tumor proliferation rate. Importantly, while signals of mobile lipid and lactate sometimes can be distinguished from each other on MRS, these signals not infrequently very difficult to separate completely.

Glutamate concentrations in human meningiomas are reported to be three times higher than those in rat meninges.⁷ In the present study, most of the meningiomas showed signals from 2.1 ppm to 2.5 ppm that were thought to be derived from glutamine and glutamate. However, no definitive correlation emerged between these signals and tumor malignancy. Interestingly, while the presence of an alanine signal is fairly specific for meningiomas,³³ our study demonstrated that the absence of such a signal on MRS does not exclude the presence

of a meningioma. Furthermore, the presence of alanine did not correlate with proliferation potential of meningiomas.

Conclusion

MIB-1 SI and histologic grade of meningiomas could be predicted by noninvasively measuring Cho/Cr ratio using proton MRS. A methylene signal in proton MRS was highly correlated with intratumoral necrosis, presumably resulting from an ischemic event or a degenerative process.

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Figure legends

Fig. 1. Scatter plot showing regression line for Cho/Cr ratio and MIB-1 staining index. Open and closed circles respectively represent benign and nonbenign meningiomas.

Meningiomas showing a methylene signal are marked by an asterisk. The dashed line represents the 95% confidence interval. Cho, choline containing compounds. Cr, creatine and phosphocreatine.

Fig. 2. A representative series of spectra in a meningioma before embolization and 1, 5, and 8 days after embolization. Lactate signal increased immediately after embolization of feeding vessels and gave place to a methylene signal several days later. Choline and creatine signals decreased immediately after embolization, although the glutamine/glutamate and methyl signals did not. Spectra were obtained with an echo time of 19 ms, and were averaged from 128 acquisitions. Cho, choline containing compounds. Cr, creatine and phosphocreatine.

Fig. 3. Illustrative cases of meningioma. A, gadolinium-enhanced T1-weighted image of a parasagittal meningioma suggesting that it might be atypical. The tumor showed bone destruction, a moderately irregular margin, heterogeneous enhancement, and marked peritumoral edema. Magnetic resonance spectroscopy of this meningioma suggested a benign histology, because the tumor showed no methylene signal and the choline containing compounds (Cho)/creatine+phosphocreatine (Cr) ratio was not high (2.06). The histopathologic diagnosis was meningothelial meningioma with no atypical features. B, T1-weighted, gadolinium-enhanced MR image of a recurrent meningioma of the cerebral convexity. The spectrum included a methylene signal and showed a high Cho/Cr ratio (6.53). The MIB-1 staining index was 3.75 %, and the histopathologic diagnosis was

atypical meningioma with xanthomatous change and micronecrosis. Cho, choline containing compounds. Cr, creatine and phosphocreatine.

Figure 1

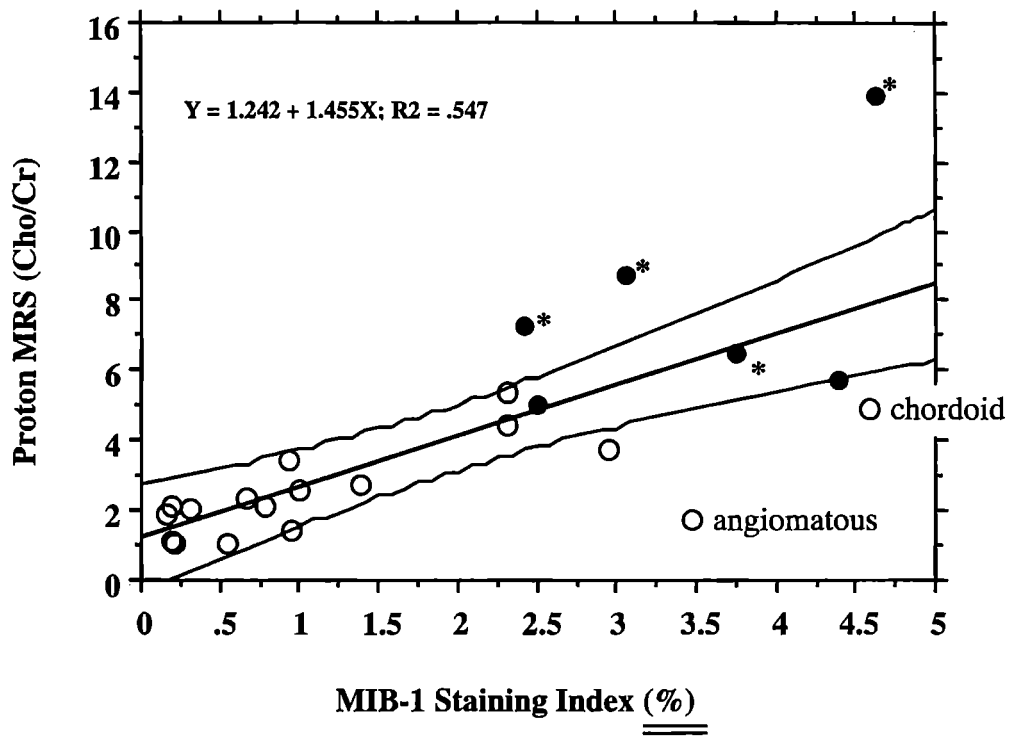
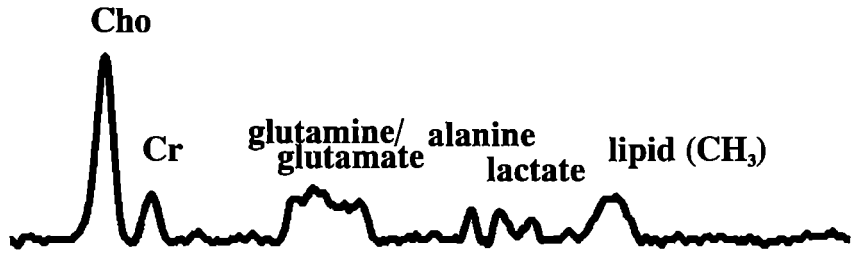


Figure 2

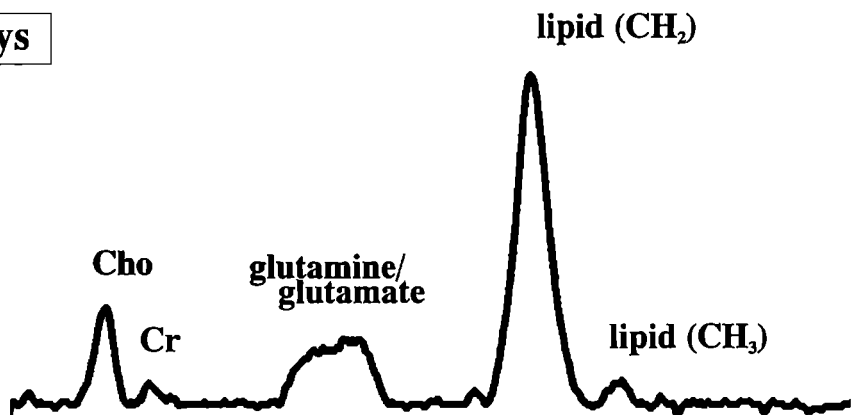
before embolization



1 day



5 days



8 days

