

Proton Magnetic Resonance Spectroscopic Imaging of Cerebral Gliomas: Correlation of Metabolite Ratios with Histopathologic Grading

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Background: Magnetic resonance spectroscopic imaging (MRSI) can provide spatially encoded metabolite information and improve tissue specificity in human brains. The major goal of this study was to evaluate the correlation of metabolite ratios measured by MRSI with histopathological grading of cerebral gliomas.

Methods: Twenty-seven patients with cerebral gliomas were referred consecutively for pre-surgical evaluation. The lesions included 10 grade II, 5 grade III, and 12 grade IV gliomas. MRSI data were acquired during the same session of conventional magnetic resonance imaging and analyzed in terms of N-acetylaspartate (NAA), creatine-phosphocreatine (Cr), choline-containing compounds (Cho), and lactate.

Results: There were significantly lower NAA/Cr and higher Cho/Cr, Cho/NAA and (Cho+Cr)/NAA ratios ($p < 0.001$) in gliomas than in normal tissues. There were significantly lower NAA/Cr and higher Cho/NAA and (Cho+Cr)/NAA ratios ($p \leq 0.05$) in World Health Organization (WHO) grade III or IV gliomas than in grade II gliomas. A significant correlation was identified between the (Cho+Cr)/NAA ratio and WHO grade ($p < 0.05$). There was no significant metabolite difference between grade III and grade IV tumors ($p > 0.1$), or significant difference in lactate occurrence rates among different grades ($p = 0.26$).

Conclusions: Proton MRSI can provide in vivo information about the metabolic status of cerebral gliomas, and the (Cho+Cr)/NAA ratio can discriminate different grades better than other metabolite ratios. However, substantial overlap of metabolite ratios among different severities of malignancy makes it impossible to confirm the WHO grade of a specific cerebral glioma by using clinical MRSI.

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Key words: brain, glioma, proton MR spectroscopy.

Brain tumors and related changes, including necrosis, perifocal edema, and mass effect on cerebral structures, can be readily demonstrated by conventional magnetic resonance imaging (MRI).⁽¹⁾

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Abnormal enhancement of cerebral gliomas after intravenous administration of contrast medium containing gadolinium due to brain-blood-barrier disruption and the resultant T1-shortening effect are well known.⁽¹⁾ However, tumor grading according to enhancing patterns revealed on conventional post-contrast MRI is unreliable. It has been shown that inhomogeneous intensity and enhancement can be seen in both high- and low-grade gliomas.⁽²⁾ In the hope of improving tumor characterization, magnetic resonance spectroscopy (MRS), which can detect the existence and quantify the intensity of major cerebral metabolites, has been widely applied to evaluate cerebral gliomas.⁽³⁻⁶⁾ The most common metabolites measured in MRS studies of cerebral gliomas include N-acetylaspartate (NAA), choline-containing compounds (Cho), creatine-phosphocreatine (Cr), and lactate. NAA is present in the neurons, neurogenic precursors and immature oligodendrocytes, and is absent in mature glial cells.⁽⁷⁾ It has been shown that NAA intensity correlates with neuronal density and viability in the brain.⁽⁸⁾ The intensity of Cho in cerebral proton MRS has major contributions from phosphocholine and glycerophosphocholine, involving the turnover of cell membranes and neurotransmitters.⁽⁹⁾ Cr serves as a reserve for high-energy phosphates in the cytosols of neurons and reflects high-energy metabolism in the brain.⁽⁹⁾ The Cr peak reflects the total pool of Cr and remains relatively stable under most conditions.⁽¹⁰⁾ So, it is commonly used as an internal reference with which to compare the level of other metabolites. Compared with normal tissues, cerebral gliomas consistently have reduced NAA intensity, which is attributed to a low density or an absence of neuronal cells in the tumor.⁽³⁾ Most studies found that there is an elevated Cho intensity in cerebral glioma, indicating an increase in membrane metabolism due to active turnover of tumor cells.⁽⁴⁻⁶⁾ Cr intensity was reported to be stable or only mildly changed in tumor spectra.⁽⁴⁻⁶⁾ The presence of cerebral lactate is always abnormal and indicates ineffectiveness of the cellular oxidative respiration cycle and carbohydrate catabolism.⁽¹⁰⁾

Basically, there are two different MRS techniques for acquisition of metabolic information: single voxel spectroscopy (SVS) and magnetic resonance spectroscopic imaging (MRSI), also known as chemical shift imaging.^(9,10) SVS detects the signal

from a single region during one measurement, while MRSI uses additional phase-encoding pulses to obtain spatially encoded signals from multiple regions simultaneously. MRSI has the advantage of providing direct comparisons between metabolites in the tumor region and those in normal tissue under exactly the same measurement conditions. Although data acquisition and processing are more sophisticated than in SVS, a modern automated MRSI system can accomplish spectral measurement with acceptable reproducibility during an examination time of less than 10 minutes.⁽¹¹⁾

Since proton MRS can demonstrate varieties of metabolism status and increase tissue specificity of cerebral pathologies, it has been evaluated as a non-invasive grading modality of cerebral gliomas. Generally speaking, high-grade gliomas tend to have lower NAA intensities and higher Cho intensities than low-grade gliomas.⁽⁴⁻⁶⁾ Lactate and lipids are found in necrotic regions of the tumors, and seem to be correlated with higher malignancy.^(6,12,13) Quantification of in vivo cerebral metabolite concentration using MRS is too complicated and time-consuming to be routinely applied for clinical service.⁽¹⁴⁾ On the other hand, metabolite ratios can be derived directly from the outputs of a clinical MRS system, without the necessity for correction for coil-loading and tissue characteristics. Therefore, most clinical MRS studies evaluated cerebral gliomas and related changes in terms of semiquantitative metabolite ratios rather than absolute concentrations. However, the relationship between metabolite ratios and histopathologic grading of gliomas is still an issue of debate.^(15,16) Compared with low-grade gliomas, decreased NAA/Cr⁽¹³⁾ and NAA/Cho^(12,17) and increased Cho/Cr^(6,12,13,17) ratios in gliomas of higher malignancy have been identified using SVS. However, absence of significant distinctions between low- and high-grade gliomas using NAA/Cr,^(15,18,19) NAA/Cho,^(15,18,19) NAA/(Cho+Cr),⁽¹⁹⁾ and Cho/Cr^(15,18) ratios was also noted in studies using SVS^(12,15,19) and MRSI.⁽¹⁸⁾ To the best of our knowledge, there is no in vivo MRSI study focusing on the evaluation of the correlation of metabolite ratios with different grades of cerebral gliomas. The major aim of the present study was to identify representative metabolite ratios which had significant correlations with tumor grading and to assess their ability to discriminate different grades of cerebral gliomas.

METHODS

From July 2001 to April 2003, 49 patients with brain tumors were recruited for conventional MRI and MRSI studies. A total of 27 patients (9 women, 18 men, 18-82 years old) had surgery to remove the tumor bulk and cerebral glioma was diagnosed. Conventional MRI and proton MRS studies were performed on a 1.5-tesla whole body MR scanner (Magnetom Vision; Siemens, Erlangen, Germany) with a standard circularly polarized head coil during the same examination session. After a series of orthogonal images for localization were obtained, a hybrid spectroscopic technique, point resolved spectroscopy MRSI, was then applied to avoid contamination from lipid signals in the skull. After automated transmitter and receiver adjustment, the water signal was automatically shimmed to within a linewidth of 10 to 15 Hz for MRSI acquisition. After pre-irradiation of water resonance by applying three chemical shift select pulses,⁽²⁰⁾ water-suppressed MRSI was then performed with the following parameters: TR/TE = 1500/135 msec, field of view = 16×16 cm², phase encoding = 16×16 , region of interest = $60 \times 60 \times 20 \sim 80 \times 80 \times 20$ mm³, voxel = $10 \times 10 \times 20$ mm³, number of acquisition = 1, data points = 1024, and scan time = 6 min 31 sec. The largest dimension of abnormal signal intensity of the tumors was greater than 20 mm as measured on conventional MRI, encompassing more than 1 voxel on MRSI.

Automated processing of the raw data was accomplished using a commercially available spectral analysis software package (Version B23A; Magnetom Vision, Siemens),⁽¹¹⁾ which included Fourier transformation with a k-space Hamming filter (50%), apodization with a Gaussian filter (center, 0.0 msec; width, 256 msec), subtraction of residual water signal, correction of frequency shift, baseline and phase, and integration of peak areas by Gaussian curve fit routines. The NAA peak was identified at 2.00 parts per million (ppm), the Cr peak at 3.02 ppm, and the Cho peak at 3.22 ppm. The presence of lactate was defined by an inverse doublet peak at 1.30 ppm. Metabolite ratios were then calculated in terms of NAA/Cr, Cho/Cr, Cho/NAA, and (Cho+Cr)/NAA ratios for each voxel. A spectrum was excluded for analysis if integration of any peak could not be accomplished using the automated analysis software. The voxels in the solid part of a tumor presenting

with the lowest NAA/Cr or the highest Cho/Cr, Cho/NAA, and (Cho+Cr)/NAA ratios were selected as the representative tumor voxels for further analysis. Metabolite ratios from the voxels in contralateral normal brain tissues at roughly the corresponding anatomic location were recruited as the normal control voxels (Fig. 1). A positive result for lactate was made when the lactate peak could be identified in any one of the voxels in the solid part of a tumor.

Comparison between different groups was assessed by using paired two-tailed Student's *t*-test or analysis of variance followed by the Tukey honestly significant difference test when appropriate. Relationship between metabolite ratios and histopathological grading was analyzed by using the Spearman correlation. The significance of discrimination between different grades by metabolite ratios was evaluated by using multinomial logistic regression. The level of significance was determined at a *p* value of 0.05.

RESULTS

Among the 27 patients with cerebral gliomas, according to the classification guidelines of the World Health Organization (WHO),⁽²¹⁾ there were 10 with grade II, 5 with grade III and 12 with grade IV gliomas in the present study. In the grade II glioma group (4 women, 6 men, 20-49 years old), there were 6 astrocytomas, 2 oligodendrogliomas and 2 oligoastrocytomas. In the grade III glioma group (1 woman and 4 men, 44-53 years old), there were 3 astrocytomas and 2 oligodendrogliomas. In the grade IV glioma group (4 women, 8 men, 18-82 years old), there were 7 primary and 5 recurrent glioblastoma multiformes. Since the neurosurgical navigation system was not applied in these patients, the histopathologic grading of a cerebral glioma was not obtained from a surgical specimen referenced on the representative MRSI voxels. Group comparison between tumor and normal voxels showed that NAA/Cr ratios of tumor voxels (0.42 ± 0.20) were significantly lower than those of corresponding normal voxels (1.61 ± 0.25) ($p < 0.001$), and Cho/Cr, Cho/NAA and (Cho+Cr)/NAA ratios of tumor voxels (2.42 ± 1.33 , 4.90 ± 2.83 , and 7.50 ± 3.95 , respectively) were significantly higher than those of corresponding normal voxels (0.84 ± 0.29 , 0.55 ± 0.18 , and 1.18 ± 0.25 , respectively) ($ps < 0.001$) (Table 1). Compared with

an individual's own healthy brain tissue, gliomas had 41%-89% ($73 \pm 12\%$) decreases in the NAA/Cr ratio, 7%-635% ($227 \pm 245\%$) increases in the Cho/Cr ratio, 127%-2012% ($841 \pm 582\%$) increases in the Cho/NAA ratio, and 60%-1526% ($543 \pm 350\%$) increases in the (Cho+Cr)/NAA ratio (Table 2).

There were significant differences in the NAA/Cr ($p=0.01$), Cho/NAA ($p=0.04$) and (Cho+Cr)/NAA ($p=0.005$) ratios among different grades of tumors, but not in the Cho/Cr ratio ($p>0.6$). Specifically, compared with grade II gliomas, there were significantly lower NAA/Cr

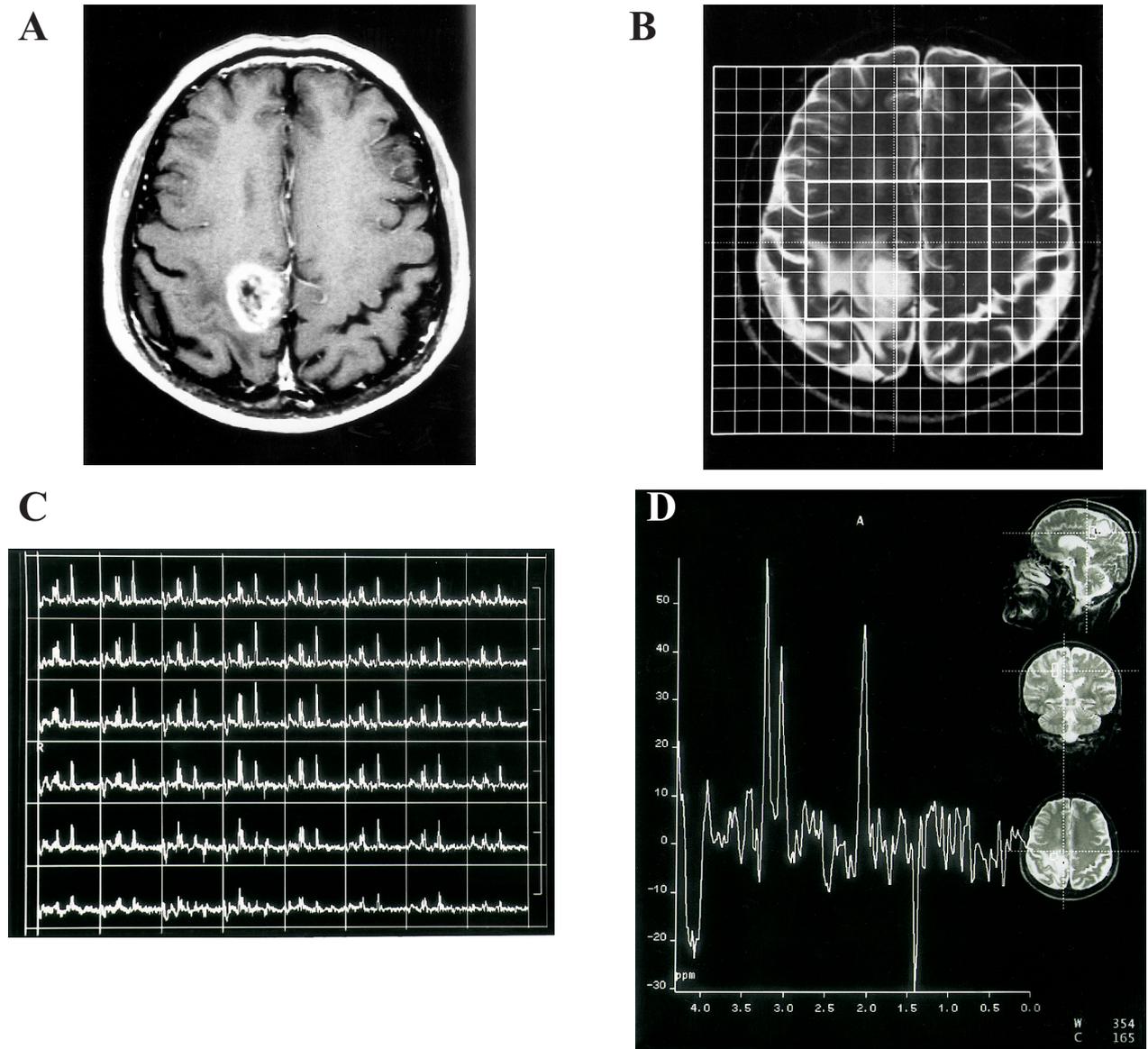


Fig. 1 An 82-year-old man with a glioblastoma multiforme (WHO grade IV). (A) A post-contrast T1-weighted image shows a heterogeneously enhancing tumor with perifocal white matter edema in the right frontal lobe. (B) Magnetic resonance spectroscopic imaging data were acquired from a $6 \times 8 \times 2$ cm region of interest (the rectangular area bound by thick white lines), overlying the T2-weighted localization image. (C) A total of 48 proton spectra are displayed in a 6×8 matrix, anatomically corresponding to the region of interest in the localization image. (D) A representative voxel at the solid part of the tumor shows reduced N-acetylaspartate intensity at 2.0 ppm, elevated choline intensity at 3.2 ppm, and an inverted lactate peak at 1.3 ppm.

($p < 0.02$) and higher Cho/NAA ($p = 0.04$) and (Cho+Cr)/NAA ratios ($p = 0.005$) in grade III gliomas, and significantly lower NAA/Cr ratios ($p = 0.05$) in grade IV gliomas (Fig. 1). There were no significant differences in any one of the metabolite ratios between grade III and grade IV gliomas ($ps > 0.1$). Using metabolite ratios in corresponding normal voxels as individual internal references, the magnitudes of decreases in the NAA/Cr and increases in the (Cho+Cr)/NAA ratios were significantly larger in grade III than in grade II gliomas ($ps < 0.05$) (Table 2).

Significant correlation was only identified between WHO grade and the (Cho+Cr)/NAA ratio

(coefficient of correlation = 0.04, $p < 0.05$). There was no significant correlation between WHO grades and the magnitudes of changes in metabolite ratios ($ps > 0.09$). Multinomial logistic regression analysis also showed that the (Cho+Cr)/NAA ratio was the most significant predictor for discrimination of different grades of gliomas ($p = 0.024$).

Lactate peaks were identified in one patient (10%) with a grade II glioma, in 2 patients (40%) with grade III gliomas, and in 6 patients (50%) with grade IV gliomas (Table 2). The chi-square test showed that there were no significant differences in the occurrence rates of lactate peaks among different grades of gliomas ($p = 0.26$).

DISCUSSION

The major findings of the present study are as follows: (1) there were significantly lower NAA/Cr and higher Cho/Cr, Cho/NAA and (Cho+Cr)/NAA ratios in gliomas than in normal tissues within individual patients; (2) only the (Cho+Cr)/NAA ratio had a significant correlation with WHO grade in cerebral gliomas; (3) there was no significant difference in metabolite ratios between grade III and grade IV gliomas, and (4) there were no significant differences in lactate occurrence rates among grade II, III and IV gliomas.

The present study showed that there were signif-

Table 1. Metabolite Ratios in 27 Patients with Cerebral Gliomas

	Tumor voxels	Normal voxels	<i>p</i>
NAA/Cr			< 0.001*
Mean (SD)	0.42 (0.20)	1.61 (0.25)	
Cho/Cr			< 0.001*
Mean (SD)	2.42 (1.33)	0.84 (0.29)	
Cho/NAA			< 0.001*
Mean (SD)	4.90 (2.83)	0.55 (0.18)	
Cho+Cr/NAA			< 0.001*
Mean (SD)	7.50 (3.95)	1.18 (0.25)	

Paired two-tailed Student's *t*-test.

Abbreviations: NAA: N-acetylaspartate; Cr: creatine-phosphocreatine; Cho: choline-containing compounds; SD: standard deviation.

Table 2. Metabolite Data of Grade II, III and IV Gliomas

	Grade II	Grade III	Grade IV	<i>p</i> * II vs III	<i>p</i> * II vs IV	<i>p</i> * III vs IV
NAA/Cr						
Tumor	0.55 ± 0.21	0.27 ± 0.13	0.37 ± 0.14	0.015	0.050	0.494
Tumor/Normal	32 ± 10%	16 ± 8%	25 ± 13%	0.044	0.352	0.311
Cho/Cr						
Tumor	2.24 ± 1.13	2.91 ± 2.28	2.37 ± 1.07	0.651	0.975	0.740
Tumor/Normal	274 ± 127%	396 ± 489%	342 ± 192%	0.654	0.805	0.914
Cho/NAA						
Tumor	3.32 ± 1.92	6.99 ± 3.59	5.34 ± 2.60	0.040	0.182	0.462
Tumor/Normal	661 ± 391%	1157 ± 784%	1042 ± 569%	0.144	0.264	0.749
Cho+Cr/NAA						
Tumor	4.88 ± 2.22	11.26 ± 4.94	8.11 ± 3.30	0.005	0.077	0.193
Tumor/Normal	439 ± 207%	906 ± 476%	702 ± 315%	0.032	0.146	0.456
Lactate						
Occurrence	10%	40%	50%		0.26†	

Abbreviations: NAA: N-acetylaspartate; Cr: creatine-phosphocreatine; Cho: choline-containing compounds.

Difference using analysis of variance and post hoc Tukey honestly significant difference test. †Chi-square test.

icantly lower NAA/Cr and higher Cho/Cr, Cho/NAA and (Cho+Cr)/NAA ratios in gliomas than in normal tissue, which is consistent with results in the literature.⁽³⁻⁶⁾ Furthermore, other than group comparison between healthy subjects and patients with brain tumors, the present study used MRSI to identify that a patient's cerebral glioma had a significantly different metabolite profiles compared with his or her own healthy brain tissue. Compared with an individual's own healthy brain tissue, gliomas had $73 \pm 12\%$ decreases in NAA/Cr, $227 \pm 245\%$ increases in Cho/Cr, $841 \pm 582\%$ increases in Cho/NAA, and $543 \pm 350\%$ increases in (Cho+Cr)/NAA ratios. The magnitudes of the metabolite changes in cerebral gliomas in our patients were similar to those reported in studies using SVS⁽¹⁵⁾ or MRSI techniques.⁽²²⁾ The changes in metabolite ratios indicated a decrease in NAA intensity and an increase in Cho intensity in cerebral gliomas, reflecting loss of normal neuronal cells, accelerated cell turnover and increased cellularity in the tumor region. A specific change in the Cr intensity in cerebral gliomas can not be inferred from the present study. Results concerning Cr changes in cerebral gliomas are controversial in the literature, and both mild decreases^(6,13,15,17) and increases⁽²³⁾ in Cr intensity have been reported.

Grade III and IV tumors are generally more cellular, more cytologically atypical, and more mitotically active than grade II gliomas.⁽²⁴⁾ Substitution or destruction of normal neuronal cells by tumor cells is expected to be more severe in grade III and grade IV tumors, resulting in more pronounced decreases in NAA intensity. The present study revealed that there were significantly lower NAA/Cr ratios in grade III and IV gliomas than in grade II gliomas. However, only the (Cho+Cr)/NAA ratio had significant correlation with WHO grades of cerebral gliomas. Furthermore, the (Cho+Cr)/NAA ratio discriminated different WHO grades of gliomas better than other metabolite ratios. Increased mitosis and cellularity in grade III and grade IV gliomas indicate that there is an acceleration of turnover of cell membrane and an expected increase in Cho intensity. However, there is always a suboptimal separation between Cho and Cr peaks in heterogeneous tissues, making quantification of each peak more variable. Therefore, the combination effects of increased cell membrane turnover and neuronal loss are expected to be more prominent and consistent in the (Cho+Cr)/NAA ratio than in the

other ratios. Similar results were reported in previous studies,^(12,17,25) but contrary findings were also noted.^(18,19,26) This may occur because of different numbers and criteria in patient recruitment, various techniques of spectral acquisition, and inherent histological heterogeneity of each type and grade of glioma.⁽¹⁷⁾ The voxel size applied for current clinical MRS acquisition is commonly between 1 cm³ and 8 cm³, much larger than the microscopic scales of histopathological examination, leading to various degrees of tissue contamination. Consequently, in vivo proton MRS studies always demonstrate substantial overlaps in spectral profiles among gliomas of all grades,^(15,27) even in those cases with apparently minimal tissue contamination,⁽¹⁵⁾ resulting in uncertainty in determination of tumor grading for an individual cerebral glioma.

Histopathologically, microvascular proliferation and necrosis are characteristic microscopic features of grade IV glioblastoma multiformes.⁽²⁴⁾ However, the present study did not reveal a significant difference in any one of the metabolite ratios between grade III and grade IV gliomas, which is similar to previous studies.^(15,17) These findings indicate that the histological grading criteria between WHO grade III and grade IV gliomas do not impose MRSI-detectable metabolite differences in the solid component of tumors. Although mobile lipid detection by ex vivo MRS has been shown to be correlated with microscopic cellular necrosis in high-grade astrocytomas,⁽²⁸⁾ application of lipid intensity detected by in vivo proton MRS for discrimination of grade III from grade IV gliomas has not been confirmed.

A lactate peak was identified more frequently in grade III and IV (~50%) than in grade II (10%) gliomas, however, there was no significant difference in the lactate occurrence rate among different grades. Lactate is a marker of abnormal cellular oxidative respiration and its occurrence seems to be more frequent in gliomas of higher malignancy.^(6,23) The usefulness of occurrence or intensity of lactate peak in glioma grading is controversial. Most studies found it was impossible to discriminate low- from high-grade gliomas based on the absence or presence of a lactate peak.^(19,23,29) To the best of our knowledge, only one study has reported that the lactate to water ratio can be used to distinguish grade II, III and IV gliomas.⁽⁶⁾ However, treatment-induced ischemia in a tumor may result in MRS-detectable lactate

intensity,⁽²³⁾ making direct comparison and interpretation of results from different studies more complicated. After the influence of the treatment effect was excluded, an *in vivo* MRS study in patients with primary gliomas showed prominent variability in the appearance of lactate across tumor grades.⁽³⁰⁾ Interestingly, in the present study, only 2 of the 5 (40%) patients with recurrent glioblastoma multiformes had MRSI-detectable lactate signals, and the incidence was in 4 of the 7 (57%) patients with primary untreated glioblastoma multiformes. The significance of existence or absence of a lactate peak in different grades of gliomas remains elusive.⁽¹⁶⁾

There are several limitations in the present study. First, the semi-quantitative metabolite ratio rather than the absolute concentration was used to evaluate the biochemical status of cerebral gliomas. The specific change in each metabolite in cerebral gliomas could not be calculated based on the results of metabolite ratios. Second, proton spectra with a long TE of 135 msec can readily identify the inverted lactate doublet at 1.3 ppm, but cannot assess metabolites with a short T2, such as myo-inositol. It has been shown using proton SVS that the myo-inositol to creatine ratio was higher in patients with low-grade gliomas and lower in those with anaplastic gliomas and glioblastoma multiformes than in control subjects.⁽³¹⁾ However, repeated proton MRSI acquisitions using both short and long TEs can prolong the examination time and were not applied in the present study. Third, complete separation of Cho and Cr peaks could not be achieved in most spectra by using a 1.5 tesla MR scanner. Application of a higher field scanner can discriminate each metabolite peak better and integrate the peak areas more accurately. This might improve the delineation between Cho and Cr peaks and resolve the discrepancy of the (Cho+Cr)/NAA ratio from the NAA/Cr and Cho/NAA ratios in predicting malignancy. Fourth, the number of patients recruited in the present study, especially those with grade III gliomas, was not large enough. A large cohort study is necessary to solidify these preliminary results and assess the relationship between tumor grading and specific metabolite changes. Furthermore, recruitment of more pathologies major in other brain tumors can help to explore the tumor differentiation ability of MRSI.

Taken together, *in vivo* MRSI could delineate significantly lower NAA/Cr and higher (Cho+Cr)/

NAA ratios in grade III or IV gliomas than in grade II gliomas, and the (Cho+Cr)/NAA ratio could discriminate gliomas of different WHO grades better than other metabolite ratios. However, substantial overlap of metabolite ratios among tumor grades was noted. Furthermore, the present study did not find significant differences in metabolite profiles between grade III and grade IV gliomas, nor in the lactate occurrence rates among different grades. In conclusion, although *in vivo* proton MRSI can provide valuable information about the metabolic status of cerebral gliomas, it is difficult to confirm the WHO grade of a specific cerebral glioma based on clinical MRSI.

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腦部膠質細胞瘤之質子磁振頻譜造影： 代謝物比率與組織病理分級之相關性

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背景：磁振頻譜造影可提供空間定位的代謝物資訊，改進腦部組織之特異性。本研究之主要目的，是評估磁振頻譜造影測量代謝物比率與腦部膠質細胞瘤組織病理分級之相關性。

方法：共有27位腦部膠質細胞瘤病患，於手術前接受磁振頻譜造影，包括10位II級，5位III級，12位IV級。振頻譜造影數據與一般磁振影像在同一次檢查中獲得。分析的代謝物為N-乙醯天門冬胺酸鹽(NAA)，肌胺酸-磷肌胺酸(Cr)，含膽鹼化合物(Cho)和乳酸。

結果：與正常腦組織比較，膠質細胞瘤有顯著較低的NAA/Cr，以及較高的Cho/Cr，Cho/NAA和(Cho+Cr)/NAA ($p < 0.001$)。與世界衛生組織分級為II級的膠質細胞瘤比較，III級或IV級的膠質細胞瘤有顯著較低的NAA/Cr，以及較高的Cho/NAA和(Cho+Cr)/NAA ($p \leq 0.05$)。(Cho+Cr)/NAA與世界衛生組織分級有顯著相關($p < 0.05$)。III級與IV級的膠質細胞瘤之間並無顯著的代謝物差異($p > 0.1$)。不同分級之間的乳酸出現率並無顯著差異($p = 0.26$)。

結論：質子磁振頻譜造影可提供膠質細胞瘤的代謝物資訊，而且(Cho+Cr)/NAA較其他代謝物比率更能區分不同惡性度的膠質細胞瘤。但是，不同級數之間的代謝物比率有相當大的重疊，無法以臨床磁振頻譜造影的結果判定單一膠質細胞瘤的世界衛生組織分級。

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關鍵字：腦部，膠質細胞瘤，質子磁振頻譜。

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