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Evaluation of Metabolic Abnormality in Brain Tumors by *In Vivo* ^{1}H MR Spectroscopy at 3 Tesla

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To investigate differences between the metabolic ratios of normal controls and brain tumors such as astrocytomas and glioblastoma multiforme (GM) by proton MR spectroscopy (MRS) at 3T high field system. Using 3T MRI/MRS system, localized water-suppressed single-voxel technique in patients with brain tumors was employed to evaluate spectra with peaks of N-acetyl aspartate (NAA), choline-containing compounds (Cho), creatine/phosphocreatine (Cr) and lactate. On the basis of Cr, these peak areas were quantificated as a relative ratio. The variation of metabolites measurements of the designated region in 10 normal volunteers was less than 10%. Normal ranges of NAA/Cr and Cho/Cr ratios were 1.67±018 and 1.16±0.15, respectively. NAA/Cr ratio of all tumor tissues was significantly lower than that of the normal tissues (P=0.005). Cho/Cr ratio of glioblastoma multiforme was significantly higher than that of astrocytomas (P=0.001). Lactate was observed in all tumor cases. The present study demonstrated that the neuronal degradation or loss was observed in all tumor tissues. Higher grade of brain tumors was correlated with higher Cho/Cr ratio, indicating a significant dependence of Cho levels on malignancy of gliomas. This results suggest that clinical proton MR spectroscopy could be useful to predict tumor malignancy.

Keyword : Brain tumors, Magnetic resonance, Spectroscopy

INTRODUCTION

The clinical challenge of managing primary brain tumors is still formidable. The need for prompt and accurate recognition of malignant brain tumor has given impetus to continued reassessment and to the search for novel neuroimaging methods.[1-3] Although computerized tomography (CT) and magnetic resonance imaging (MRI) can solve many diagnostic problems related to brain tumors, they do not provide the biochemical information critical to the appropriate management.[4, 5] Positron emission tomography (PET) provides insights into tumor cell metabolism and has emerged as a powerful method to assess the biological behavior of brain tumors,[6-8] however PET facilities are available in only a few specialized centers.

In recent years, in vivo proton magnetic resonance spectroscopy (^{1}H MRS) has been developed as a

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non-invasive technique that provides living biochemical information in situ.[9] This technique has shown great promise as a tool for cancer research and the clinical management of cancer. The proton spectrum of healthy human brain reveals resonances from creatine and phosphocreatine (Cr), choline containing compounds (Cho), and N-acetylaspartate (NAA), which is currently considered to be a neuronal specific metabolite.[10, 11] Improvements in localization, water-suppression techniques, and instrumentation for in vivo ^{1}H MRS and the relatively high MR sensitivity of protons have promoted a wide range of applications of in vivo ^{1}H MRS to the study of human brain tissue.[12, 13] Stimulated-echo acquisition mode (STEAM)[14-16] has been used as a means of localization of the volume of interest (VOI) in MRI. Hence, spatially localized in vivo ^{1}H MRS could provide a better quality of information on the biochemical changes in the brain tumors. Indeed, spectroscopic studies on brain tumors have attempted to characterize the histologic type and assess the degree of malignancy, which help in better treatment planning and management.[17-19]

The purpose of the present study was to evaluate ^{1}H MR spectroscopic characteristics of malignant brain tumors (glioblastoma multiforme : GM and astrocytoma) to provide diagnostic aids.

METHODS AND MATERIALS

1. Patient Characteristics

Ten patients, four men and six women (age range, 28-73 years; mean age, 52.2 years) were examined in Kangnam St. Mary's Hospital, Catholic University Medical College from January 2001 to June 2002. Their confirmed diagnoses were as follows; five glioblastoma multiforme (GM) and five astrocytomas. The clinical characteristics of patients are summarized in Table 1. All the patients underwent surgery to remove the tumors after the examination, and the complete histologic diagnosis of each tumor was provided by the pathologists. Tumors were included in the study only when we could locate at least 2.5 mL of VOI within the tumor body while avoiding the inclusion of macroscopic cysts and necrosis in the VOI. After complete description of the study to the subjects, written informed consent was obtained from each subject.

Table 1. Patients Characteristics (n=10) and metabolic ratios of tumor lesions

Patient#	Age/ Sex	Tumor Type and Location	Pathologic Finding	Lesion		
				Cho/Cr	NAA/Cr	Lac/Cr
1	F/49	Pilocytic astrocytoma, Lt. Frontal	KI-67 index:5-10%, GFAP: +	0.44	0.26	1.65
2	F/42	Astrocytoma, Lt. Temporal	Ki-67 index:less than1%	0.45	0.80	1.50
3	M/45	Astrocytoma, fibrillary type, low-grade, Lt. Fontal	Ki-67 index:less than1%, GFAP: +	0.91	0.67	1.30
4	F/28	Anaplastic astrocytoma	Ki-67 index: 27%	1.10	0.46	1.87
5	F/73	Anaplastic astrocytoma	Ki-67 index: 2-3%	1.76	0.94	1.30
6	F/55	Glioblastoma, Rt. Parietal	Ki-67 index: 40%	2.02	0.32	3.80
7	F/64	Glioblastoma, Rt. Temporoperiatal	GFAP: +	2.10	0.11	9.10
8	M/46	Glioblastoma, Rt. Frontal	Ki-67 index: 7-8%	2.11	1.17	4.95
9	M/59	Glioblastoma, Rt. Temporal	Ki-67 index: 30%	2.28	0.52	4.25
10	M/64	Glioblastoma, Rt. Temporal	Ki-67 index: 5%	3.80	0.90	5.58
Mean±SD				1.70± 1.02	0.62± 0.34	3.53± 2.54

2. Magnetic Resonance Spectroscopy

In vivo ^{1}H MRS examinations were performed on a Magnus 2.1 for Magnum 3 tesla MRI/MRS system (Medinus Co., LTD. Seoul, Korea) with a standard quadrature birdcage head coil. Localized single voxels (7-8 ml) centered on the volume of interested lesion in patients with brain tumors selected using the T2-weighted MR images (TR 2500 ms; TE 90 ms) with fast spin echo (FSE) with the echo train length of 8. A stimulated-echo acquisition mode (STEAM)[20] was used as the localization method in this study. Suppression of the water signal was performed by using a three-pulse chemical shift selective, or CHESS, sequence. Offsets of the higher order and linear shim coils were adjusted by the auto prescan (APS) for optimization of the homogeneities of the total and the localized volumes of the brain, respectively. The strength of the transmitter RF power, the receiver gains, and the three RF pulses for suppression of the water signal were also adjusted by the APS. After APS, typical line width (full width at half maximum; FWHM) was usually 2 to 4 Hz, which gave 97-99% of the suppression factor. Image guided STEAM spectra were obtained with a TE of 20 msec, TR of 2000 msec, data points of 2048, spectral bandwidth of 2500 Hz, and acquisition averages of 128.

The magnetic field over the VOI was homogenized by adjusting the linear shims to minimize water line width. Typical line width (full width at half maximum) was 3-4 Hz. Special attention was given to locating the water signal frequency to maximize the water suppression. An exponential line broadening (1-2 Hz) was used for apodization of the free induction delay. Time domain data were converted to frequency domain by Fourier transformation. Frequency domain spectra were phased by hand, with use of frequency-independent phase corrections only. Phased absorption spectra are reported directly without baseline correction or resolution enhancement. All of the ^{1}H MRS were plotted and analyzed in the absorption mode.

Proton resonances in the spectra obtained from brain tissues were assigned on the basis of prior assignments.[21] Resonance peak assignments of major proton metabolites were CH_3 of NAA, 2.00 ppm; N-CH_3 of Cr, 3.00 ppm; N-$(CH_3)_3$ of Cho, 3.20 ppm; doublets of CH_3 of Lac, 1.26 and 1.35 ppm. In order to obtain the relative metabolite ratios, Cr was used as a putative reference.

3. Statistical Analysis

Statistical analysis was performed using SPSS (SPSS for Windows, Version 6.0, SPSS Inc., Chicago, Illinois). The data were analyzed with two-tailed *t*-tests, where $P<0.05$ was considered significant to account for multiple comparisons. All the data are presented as group mean values±standard deviation (SD).

RESULTS

In vivo ^{1}H MR spectrum in tumor tissue was very different from that in normal brain tissues. The specific MRS features of brain tumors (GM and astrocytomas) showed a decrease of the NAA signal and an increase of the Cho and Lac signals relative to normal brain spectra. Fig. 1 shows the VOI in the temporal parietal white matter and the acquired spectrum in a typical volunteer. The variation of metabolites measurements of the designated region in 10 normal volunteers was less than 10%. Normal ranges of NAA/Cr and Cho/Cr were 1.67±0.18 and 1.16±0.15, respectively. The metabolite ratio of Cho/Cr in brain tumor (1.79±1.02) was significantly higher than that of normal brain (1.16±0.15) (P=0.001). The metabolite ratio of NAA/Cr in brain tumor (0.64±

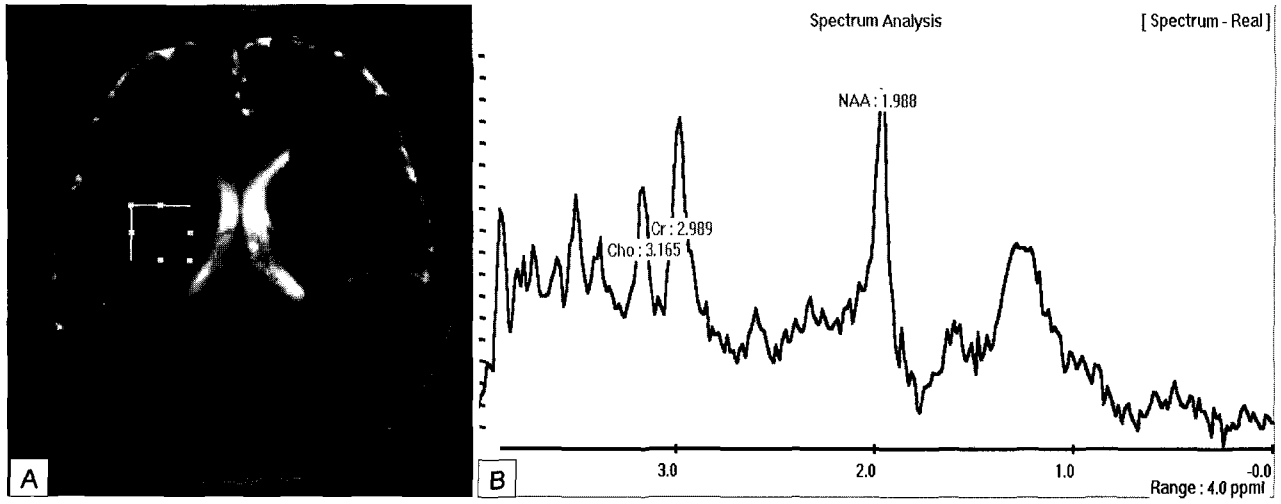

Fig. 1. MR imaging and ^{1}H MR spectrum of a normal volunteer.
A) T2-weighted axial MR imaging defining the volume of interest selected for localized in vivo ^{1}H-MRS.
B) The corresponding spectrum obtained from the VOI shown in A, acquired with STEAM. Chemical shifts are indicated in parts per million (ppm).

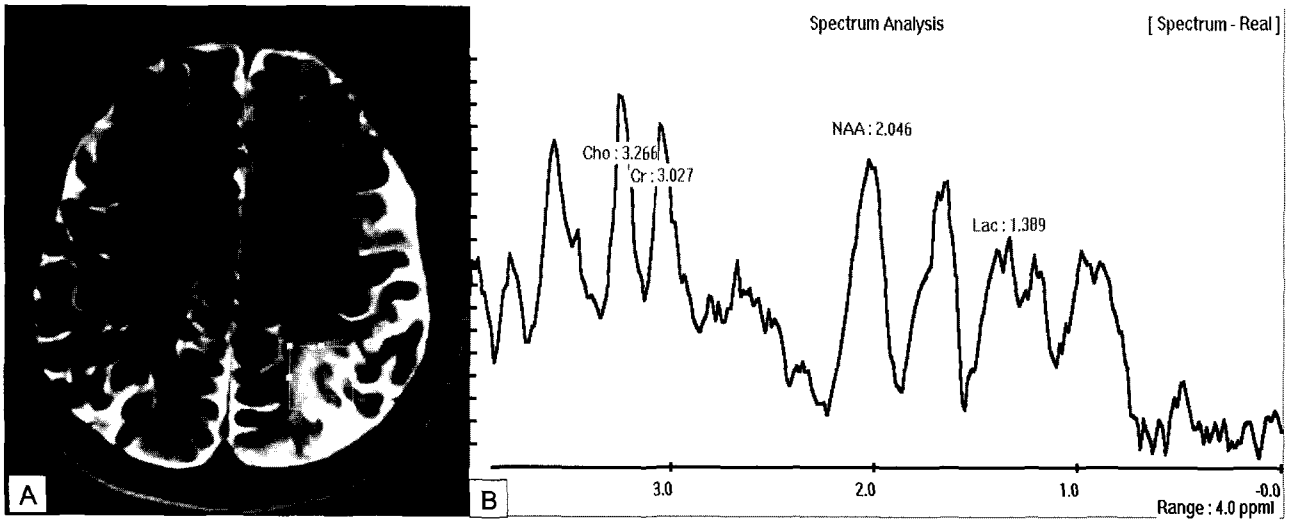

Fig. 2. MR imaging and 1H MR spectrum of a patient with anaplastic astrocytoma.
A) T2-weighted axial MR imaging defining the volume of interest selected for localized in vivo ^{1}H-MRS.
B) The corresponding spectrum obtained from the VOI shown in A, acquired with STEAM. Cho signal increased and NAA signal decreased. Also, lactate signal was observed. Chemical shifts are indicated in parts per million (ppm).

0.38) was significantly lower in normal brain (1.16 ± 0.15) (P<0.005). The signal intensity of Lac/Cr was greatly elevated (3.53±2.54) in brain tumor. High-grade gliomas (GM) showed elevated Cho/Cr ratio, while low-grade gliomas (anaplastic astrocytomas) had Cho/Cr values within the normal ranges (Table 1). All tumor cases showed the decreased NAA/Cr ratio. The decrease in the NAA peak was the actual cause of the low NAA/Cr ratio. However, NAA/Cr ratio was not correlated with malignancy. Statistically significant differences between low-grade gliomas and high-grade gliomas were shown in the levels of Cho/Cr and NAA/Cr (P=0.001). Lactate was more or less present in all the gliomas. A lactate signal has been detected in the all tumor spectra. The assignment of lactate is based upon its chemical

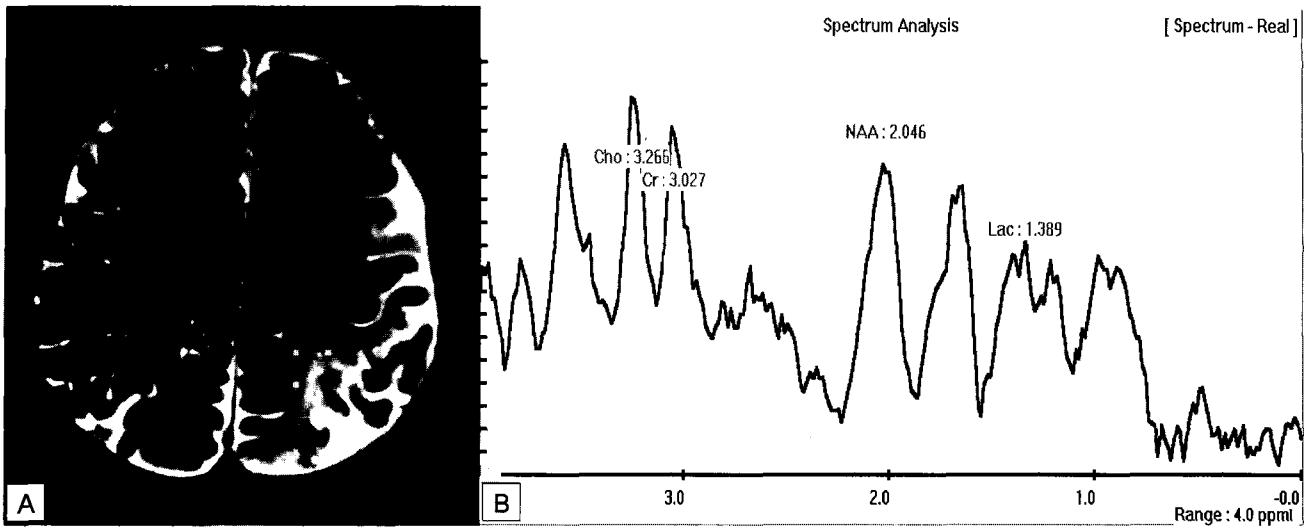

Fig. 3. MR imaging and ^{1}H MR spectrum of a patient with high-grade glioma, glioblastoma.
A) T2-weighted axial MR imaging defining the volume of interest selected for localized in vivo ^{1}H-MRS.
B) The corresponding spectrum obtained from the VOI shown in A, acquired with STEAM. Cho signal increased and NAA signal decreased. Also, lactate signal was observed. Chemical shifts are indicated in parts per million (ppm).

shift (1.30 ppm) and its coupling constant (about 7 Hz). High-grade gliomas tended to have higher lactate values than did low-grade gliomas. The representative cases are presented in Fig. 2 and 3. Fig. 2 shows increased signal intensity of Cho/Cr and hyperintense lactate signal in the neoplastic region (anaplastic astrocytoma) when comparing normal control brain. Fig. 3 shows increased signal intensity of Cho/Cr and hyperintense lactate signal, however decreased signal intensity of NAA/Cr in the neoplastic region (glioblastoma multiforme) when comparing the normal frontal area.

CONCLUSION & DISCUSSION

In vivo ^{1}H MRS is a major advance for noninvasive spectroscopic evaluation of biochemical changes since it allows appreciation of the regional heterogeneity of the chemical pathological changes. Also, in vivo ^{1}H-MRS can contribute to the monitoring of alterations of brain metabolites in the slice of whole brain and the understanding of the pathophysiology during the development of a disease. The use of in vivo MRS has generated considerable interest as a means for obtaining noninvasive biopsy information because obtaining biochemical information from brain tissue through repeated brain biopsies is not clinically feasible.

Establishing which compounds contribute to the Cho signal has been an area of active research in recent years. If the major water-soluble Cho-containing compounds in the brain are added together, their total concentration does no account for the large signal that is seen in vivo. This has led to the conclusion that relatively immobile lipid molecules, such as phosphatidylcholine, can be seen in vivo.[22] In the 1994 in vivo and in vitro study of the canine brain, the Cho signal was attributed predominantly to water-soluble glycerophosphocholine and phosphocholine.[23] A recent report on the patients with neoplastic and infectious brain lesions stated that the in vivo Cho signal correlated with in vitro measures of cellular density and water-soluble Cho-containing compounds (phosphocholine and glycerophosphocholine), but not with membrane-bound phosphatidylcholine.[24] All these Cho-containing compounds parti-

cipate in phospholipid metabolism. Thus, the increased Cho peak found in most of the 1H MRS studies of brain tumors has been attributed to a greater membrane synthesis, increased cellularity, or to a rapid cell turnover.[17, 25] Our observations are consistent with the results of Gill, Fulham and coworker.[17, 25] This elevation of Cho signal intensity was statistically significant.

NAA was unequivocally demonstrated in normal tissue, but its function remains unknown. One suggestion is that NAA donates its acetyl group for lipid synthesis, particularly during the developmental period corresponding to the myelination for neurons.[26, 27] Another suggestion is that NAA may play a role in the N-terminal nonribosomal synthesis of NAA-containing neuropeptides, including N-acetyl-aspartyl-glutamate,[28] or serve as an organic anion in neurons, similar to isothianate in the squid axon.[29] That the location of NAA is confined to neurons was confirmed using an antibody to NAA.[30] NAA is present in the millimolar range in nervous tissues but in contrast is very low in nonnervous tissues.[31] In our study, the reduced NAA signal was generally observed in GM and astrocytomas. If the NAA peaks were detected in a case, it would imply contamination of the nontumorous neuronal tissues surrounding the tumors (Fig. 1b). ^{1}H-MRS data indicated that decreases of NAA concentrations were more directly related to the tumor plus associated pathology. Nagendank showed that NAA is a neuronal marker[9] and its content decreases in many brain diseases including tumors, stroke, multiple sclerosis, and metabolic disorders.[32-36] A reduction in NAA is a nonspecific marker for anything that displaces normal brain tissue.

The relationship between lactate concentrations and brain tumors is complex. Although many clinical reports cited increased lactate levels in brain tumors,[32, 33] increased lactate levels may not fully characterize the nature or grading of primary brain tumors.[9] The lactate signal rises whenever the lactate producing anaerobic glycolytic pathway exceeds the capacity of the lactate catabolizing respiratory pathways, or when the cellular capacity for exporting lactate to the bloodstream is impaired.[37] In our study, lactate signal was increased highly in malignant brain tumors. The presence of lactate in brain tumors has been focused by several groups of authors,[17, 25, 30] and although lactate is more likely to be found in high grade gliomas, its importance as a potential predictor of malignancy is still being debated.[25, 30] Because of the well-known anaerobic glycolytic nature of tumor metabolism, it is reasonable to assume that many tumors should produce increased levels of lactate. Although lactate is detected in most tumors, its presence is not necessarily a direct indicator of anaerobic metabolism. Single-voxel ^{1}H-MRS can measure total quantity of lactate, however, it do not allow for distinguishing between lactate that is trapped in nonviable tissue and that which is produced by anaerobic metabolism in viable tissue. This may be associated, in part, with the difficulty of separating the lactate signals from those of lipids and macromolecules that are either within the tumor or that contaminate the tumor spectrum due to incomplete volumetric localization.

In the present analysis the metabolite signal intensities were measured in the tumor and the healthy control tissues. The proton spectrum of healthy human brain reveals resonances from Cr and Cho containing compounds, and NAA, which is currently considered to be a neuron-specific metabolite. ^{1}H-MRS has been shown to be capable of detecting metabolic changes in brain tumor comparing to normal brain tissue.

In conclusion, MRS may provide an additional information in cases in which differential diagnosis by neuroimaging is difficult, because it reflects low-molecular weight substances of tumor metabolism according to their origin. We anticipate that this

noninvasive method may play an important role for improving the management of patients with brain tumors, as well as accurate diagnosis.

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REFERENCES

1. Cairncroo JG, Laperriere NJ: Low-grade glioma. To treat or not to treat? Arch Neurol 46:1238-1239 (1987)
2. Piepmeier JM: Observations on the current treatment of low-grade astrocytic tumors of the cerebral hemispheres. J. Neurosurg 62:177-181 (1987)
3. Jaeckle KA: Clinical presentation and therapy of nervous system tumors. In: Bradley WG, Daroff RB, Fenichel GM, eds. Neurology in Clinical Practice: Principles of Diagnosis and Management. Vol 2. 1st ed. Boston: Butterworth-Heimann, 1991, pp.1008-1030.
4. Mimmerman RA: Imaging of adult central nervous system primary malignant gliomas. Staging and follow-up. Cancer 67:1278-1283 (1991)
5. Kondziolka D, Lunsford LD, Martinez AJ: Unreliability of contemporary neurodiagnostic imaging in evaluating suspected adult supratentorial (low-grade) astrocytoma. J. Neurosurg 79:533-536 (1993)
6. Coleman RE, Hoffman JM, Hanson MW: Clinical application of PET for the evaluation of brain tumors. J. Nucl. Med. 32:616-622 (1991)
7. Di Chiro G: Positron emmission tomography using [^{18}F]Fluorodeoxyglucose in brain tumors. A powerful diagnostic and prognostic tool. Invest Radiol. 22: 360-371 (1987)
8. Fulham MJ: PET with ^{18}F] Fluorodeoxyglucose (PET-FDG): An indispensable tool in the proper management of brain tumors. In: Hubner KF, Coolmann J, Buonocore E, eds. Clinical Positron Emission Tomography. Year Book. St. Louis: Mosby, 1992, pp.50-60
9. Negendank W: Studies of human tumors by MRS: A review. NMR Biomed. 5:303-324 (1992)
10. Gill S, Small R, Thomas D, Patel P, Porteous R, Bruggen N, Gadian D, Kauppinen R, Williams S: Brain metabolites as 1H NMR markers of neuronal and glial disorders. NMR Biomed. 2:196-200 (1989)
11. Koller K, Zaczek R, Coyle J: N-Acetyl-Aspartyl-Glutamate: Regional levels in rat brain and the effects of brain lesions as determined by a new HPLC method. J. Neurochem 43:1136-1142 (1984)
12. Choe BY, Suh TS, Choi KH, Bahk YW, Shinn KS: In vivo 1H MR spectroscopi imaging of human brain. J. Korean Rad. Soc. 31:185-190 (1994)
13. Tugnoli V, Tosi MR, Barbarella G, Bertoluzza A, Ricci R, Trevisan C: In vivo 1H MRS and in vitro multinuclear MR study of human brain tumors. Anticancer Res. 16:2891-2900 (1996)
14. Granot J: Selected volume excitation using stimulated echoes (VEST): applications to spatially localized spectroscopy and imaging. J. Magn. Reson. 70:488-492 (1986).
15. Kimmich R, Hoepfel D: Volume-selective multipulse spin-echo spectroscopy and imanging. J. Magn. Reson. 72:379-384 (1987)
16. Frahm J, Merboldt KD, Haenicke W: Localized proton spectroscopy using stimulated echoes. J. Magn. Reson. 72:502-508 (1987)
17. Gill SS, Thomas DG T, Bruggen NV, Gadian DG, Peden CJ, Bell JD, Cox IJ, Menon DK, Iles RA, Bryant DF, Coutts GA : Proton MR spectroscopy of intracranial Tumors: in vivo and in vitro studies. J. Comput. Assist. tomogr. 14:497-504 (1990)
18. Harada M, Tanouchi M, Nishitani H, Miyoshi H, Bandou K, Kannuki S: Non-invasive characterization of brain tumor by in-vivo proton magnetic resonance spectroscopy. Jpn J. Cancer Res. 86:329-332 (1995)
19. Tedeschi G, Lundbom N, Raman R, Bonavita S, Duyn JG, Alger JR, Chiro GD: Increased choline signal coinciding with malignant degeneration of cerebral gliomas: a serial proton magnetic resonance spectroscopy imaging study. J Neurosurg 87:516-524 (1997).
20. Aue WP: Localization methods for in vivo nuclear magnetic resonance spectroscopy. Rev. Magn. Reson.

Med. 1:21-72 (1986)
21. Frahm J, Bruhn H, Gyngell ML, Merboldt KD, Hanicke W, Sauter R: Localized high-resolution proton NMR spectroscopy using stimulated echoes: Initial applications to human brain in vivo. Magn. Reson. Med. 9:79-93 (1989)
22. Miller BL: A review of chemical issues in ^{1}H NMR spectroscopy: N-acetyl-aspartate, creatine and choline. NMR Biomed. 4:47-52 (1991).
23. Barker PB, Breiter SN, Soher BJ: Quantitative proton spectroscopy of canine brain: in vivo and invitro correlations. Magn. Reson. Med. 32:157-163 (1994)
24. Miller BL, Chang L, Booth R: In vivo ^{1}H-MRS choline: correlation with in vitro chemistry/histology. Life Sce. 58:1929-1935 (1996)
25. Fulham JM, Bizzi A, Dietz MJ, Shih HHL, Raman R, Sobering GS, Frank JA, Dwyer AJ, Alger JR, Di Cyhiro G: Mapping of brain tumor metabolites with proton MR spectroscopic imaging: Clinical relevance. Radiology 185:675-686 (1992)
26. D'Adamo AF, Gidez LI, Yatsu FM: Acetyl transport mechanism. Involvement of N-acetyl aspartic acid in de novo fatty acid biosynthesis in the developing rat brain. Exp Brain Res 5:267-273 (1968)
27. Shigematsu H, Okamura N, Shimeno H, Kishimoto Y, Kan L, Feselau C: Purification and characterization of the heat-stable factors essential for the conversion of lignoceric acid to cerebronic acid and glutamic acid: Identification of N-acetyl-L-aspartic acid. J. Neurochem 40:814-820 (1983)
28. Reichelt KL, Kvamme E, Histamine-dependent formation of N-acetyl-aspartyl peptides in mouse brain. J. Neurochem 21:849-859 (1973)
29. McIntosh JC, Cooper JR: Studies in the function of N-acetylaspartic acid in brain. J. Neurochem 12: 825-835 (1965)
30. Segebarth CM, Baleriaux DF, Luyten PR, den Hollander JA: Detection of metabolic heterogeneity of human intracranial tumors in vivo by ^{1}H NMR spectroscopy imaging. Magn. Reson. Med. 13:62-76 (1990)
31. Clarke DD, Lajtha AL, Maker HS: *Intermediary metabolism.* In: Siegel G, Agranoff B, Albers RW, Molinoff P, eds. Basic Neurochemistry. 4th ed. New York: Raven Press, 1973, pp.541-565.
32. Kugel H, Heindel W, Ernestus RI: Human brain tumors: spectral pattern detected with localized ^{1}H MRS spectroscopy. Radiology 183:701-709 (1992)
33. Herholz K, Heindel W, Luyten PR: In vivo imaging of glucose consumption and lactate concentration in human gliomas. Ann. Neurol. 31:319-327 (1992)
34. Bruhn H, Frahm J, Gyngel ML: Cerebral metabolism in man after acute stroke: new observations using localized proton MRS spectroscopy. Magn. Reson. Med. 9:126-131 (1989)
35. Matthews PM, Francis G, Antel J: Proton magnetic resonance spectroscopy for metabolic characterization of plaques in multiple sclerosis. Neurology 41:1251-1256 (1991)
36. Grodd W, Krageloh-Mann I, Klose U: Metabolic and destructive brain disorders in children: findings with localized proton MR spectroscopy. Radiology 181: 173-181 (1991)
37. Prichard JW: What the clinician can learn from MRS lactate measurement. NMR Biomed 4:99-102 (1991)

3T 양성자 자기공명분광에 의한 뇌종양의 대사물질 이상소견

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목 적 : 성상세포종과 다형성교모세포종과 같은 뇌종양에서 3T 양성자 자기공명분광법을 이용한 분광 소견을 알아보고, 이를 정상인 뇌의 분광소견과 비교하여, 그 차이를 알아보고자 하였다.

대상 및 방법 : 대상환자는 가톨릭의대 부속 강남성모병원에서 2001년 1월 1일부터 2002년 6월 1일까지 조직학적으로 확인된 astrocytoma 및 glioblastoma multiforme (GM) 환자들 중에서 양성자 자기공명분광을 시행한 10명의 환자를 대상으로 하였다. 연령분포는 28세에서 73세(평균: 52.2세), 남녀비는 4:6이었다. 양성자 자기공명분광법은 전신용 3T MRI/MRS 시스템(Medinus Co., LTD. Magnus 2.1)과 STEAM (stimulated echo acquisition mode) pulse sequence를 사용하였다. 획득한 자기공명분광 소견은 각각의 군에서 N-acetylaspartate (NAA), phosphocreatine and creatine (Cr), choline containing compounds (Cho) and lactate (Lac)와 같은 대사물질들을 Cr을 기준으로 대사산물 신호강도의 비율로 상대적으로 계측하였다. 각각의 군에서 상대적인 비율의 평균과 표준편차를 구하여 정상뇌와 뇌종양을 비교하였고, 종합적인 결과는 Student t-test로 통계처리하였다.

결 과 : 양성자 자기공명분광소견상 정상 뇌조직과 뇌종양의 Cho/Cr 평균값은 각각 1.16±0.15, 1.79±1.02로 측정되었고, NAA/Cr은 각각 1.67±0.18, 0.64±0.38로 측정되었다. Lactate는 정상 뇌조직에서는 거의 발견되지 않은데 비해 뇌종양에서는 모두 관찰되었고 그 양은 3.53±2.54로 높게 나타났다.

결 론 : 뇌종양(성상세포종, 다형성교모세포종)은 정상 뇌조직에 비해 Cho/Cr 비율이 현저히 증가하였으며, NAA/Cr 비율은 감소하였다. 또한 뇌종양에서는 강한 Lactate signal을 보여 주었다. 양성자 자기공명분광은 뇌종양에 대한 생화학적 정보를 얻을 수 있으므로, 임상적으로 비침습적인 방법을 통한 진단뿐 만 아니라 치료후 효과 판정이나, 뇌종양 재발 등의 감별진단에도 이용할 수 있을 것으로 사료된다.

중심단어 : Brain tumor, Astrocytoma, Glioblastoma multiforme (GM), ^{1}H magnetic Resonance Spectroscopy (^{1}H MRS)