Jpn. J. Cancer Res. 86, 329–332, March 1995

Non-invasive Characterization of Brain Tumor by *in-vivo* Proton Magnetic Resonance Spectroscopy

Masafumi Harada,[1,4] Miki Tanouchi,[1] Hiromu Nishitani,[1] Hirokazu Miyoshi,[2] Kazuhiko Bandou[3] and Seiji Kannuki[3]

Department of [1]Radiology, [3]Neurosurgery, School of Medicine, and [2]Department of Radiological Technology, School of Medical Science, The University of Tokushima, 3-18-15 Kuramoto-cho, Tokushima 770

We studied the feasibility of characterizing brain tumor tissue by localized proton magnetic resonance spectroscopy (^{1}H-MRS). Twenty-six newly diagnosed tumors were examined by *in-vivo* ^{1}H-MRS. The NAA (N-acetylaspartate)/Cho (choline) ratio of Grade 2 astrocytoma was higher than that of Grade 4. The Cho/Cr (creatine and phosphocreatine) ratio of meningioma was considerably higher than that of glioma of all grades. We have experienced only two cases of ependymoma and the Cho/Cr ratios of both were lower than that of glioma. It seems likely that ^{1}H-MRS can be used to differentiate Grade 2 from Grade 4 in most cases of astrocytoma based on the NAA/Cho ratio, though a few cases will overlap. Meningioma can be distinguished easily from glioma, and the results of our study suggest that ependymoma shows a characteristic pattern on ^{1}H-MRS, different from those of other brain tumors.

Key words: ^{1}H-MRS — Brain tumor — Glioma — Meningioma — Ependymoma

Proton magnetic resonance spectroscopy (^{1}H-MRS) can detect biochemical changes in tissue non-invasively and there have been many reports concerning the utility of this method.[1)] We have already reported that ^{1}H-MRS of brain abscess differs appreciably from that of glioblastoma, and the method is useful for establishing the biochemical status of tissue.[2)] We have now conducted ^{1}H-MRS on patients with primary brain tumor and studied the feasibility of characterizing brain tumor tissue by ^{1}H-MRS.

OBJECTS AND METHODS

The 25 patients in this study were admitted to the University Hospital of Tokushima and all patients underwent tumor resection. Pathological diagnosis was conducted on all patients and the grades of all gliomas were determined. Fifteen cases were astrocytoma, including six cases of Grade 2, one case of Grade 3 and nine cases of Grade 4 (glioblastoma). Four cases were diagnosed as meningioma. Other tumors were oligodendroglioma in 2 cases, ependymoma in 2 cases, and craniopharyngioma in 1 case.

Proton MR imaging and MRS were carried out on a Magnetom H-15SP (1.5 Tesla) with the head coil using the PRESS sequence (spin echo sequence with three 180 degree pulses). The measurement conditions were as follows: repetition time (TR) = 1500 ms, echo time (TE) = 270 ms, 60 Hz width Chess pulse for water suppression, voxel of interest (VOI) = 15.6 ml, sum of free induction decays (FIDs) = 200. Spectral processing included zero filling and phase correction without smoothing function. VOI was placed on the center of the tumor or enhanced area of the brain tumor by GD-DTPA. Signal intensity ratios were used for quantitative comparison as follows: NAA/Cho ratio = intensity of NAA (N-acetylaspartate)/intensity of choline (Cho); NAA/Cr ratio = intensity of NAA/intensity of creatine and phosphocreatine (Cr); Cho/Cr ratio = intensity of Cho/intensity of Cr. Lactate was not estimated in this study because its intensity was highly variable depending on the measurement area and it was sometimes difficult to distinguish from the signal of lipid. Student's *t* test and the Wilcoxon test were used for statistical analysis.

RESULTS

Fig. 1 shows typical ^{1}H-MR spectra of high-grade astrocytoma, low-grade astrocytoma and meningioma. The observed peaks were derived from NAA, Cho and Cr. High-grade astrocytoma revealed a high doublet peak of lactate, but it was difficult to confirm whether there was a peak of lactate or lipids in the spectra of low-grade astrocytoma and meningioma. We found that each tumor had a characteristic pattern on ^{1}H-MRS. Fig. 2 shows the NAA/Cho ratio in the cases of glioma. The ratio of Grade 2 had a higher value than that of the other grades. The values of the ratio of Grade 4 were scattered and those of 2 cases were at the same level as that of Grade 2. However, the other 7 cases of Grade 4 had lower values

[4] To whom correspondence should be addressed.

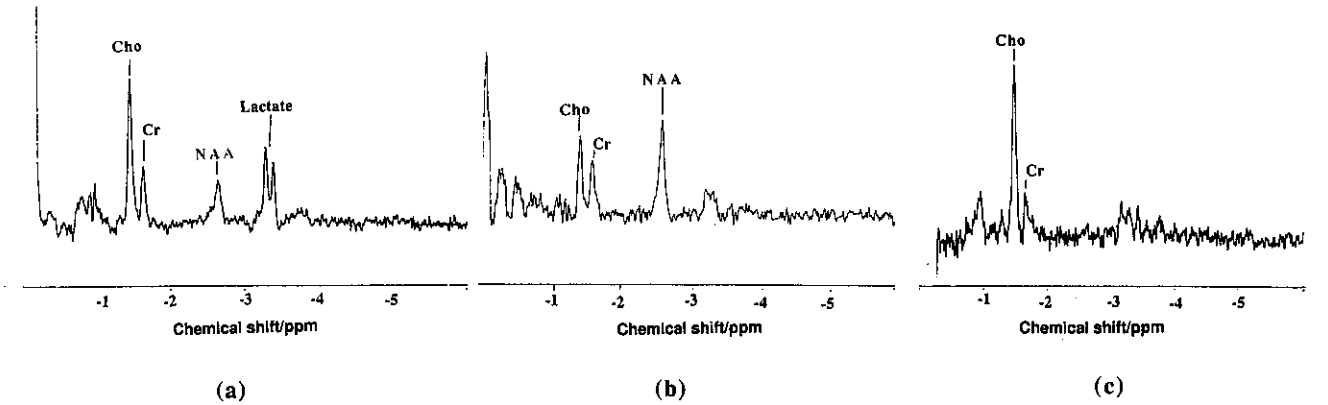

Fig. 1. ^{1}H magnetic resonance spectroscopy of a high-grade astrocytoma (a), a low-grade astrocytoma (b) and a meningioma (c). NAA, Cr and Cho mean N-acetylaspartate, creatine including phosphocreatine, and choline-containing components.

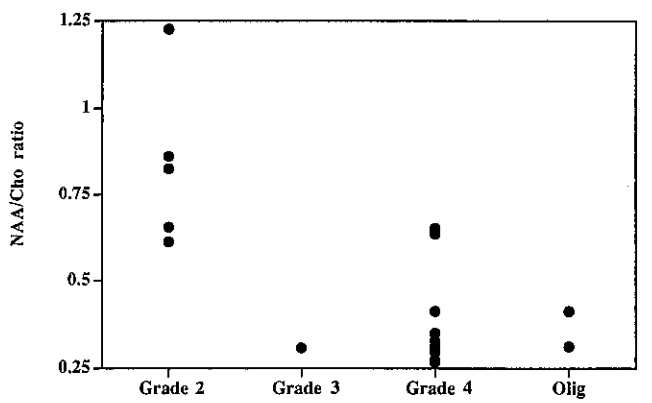

Fig. 2. NAA/Cho ratio of gliomas. Grades 2, 3 and 4 are astrocytoma and "Olig" means oligodendroglioma.

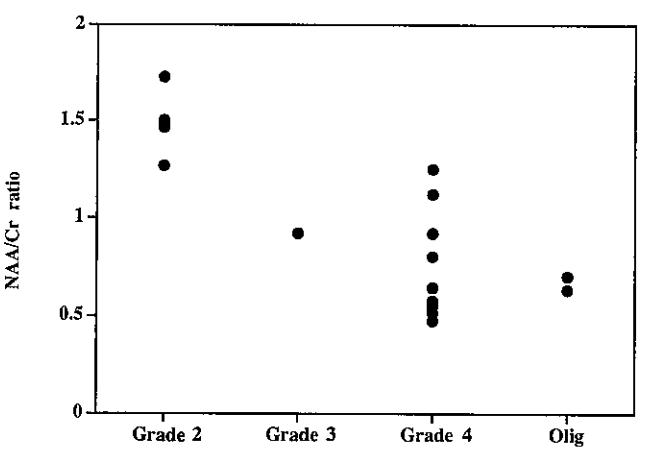

Fig. 3. NAA/Cr ratio of gliomas. Grades and "Olig" have the same meaning as in Fig. 2.

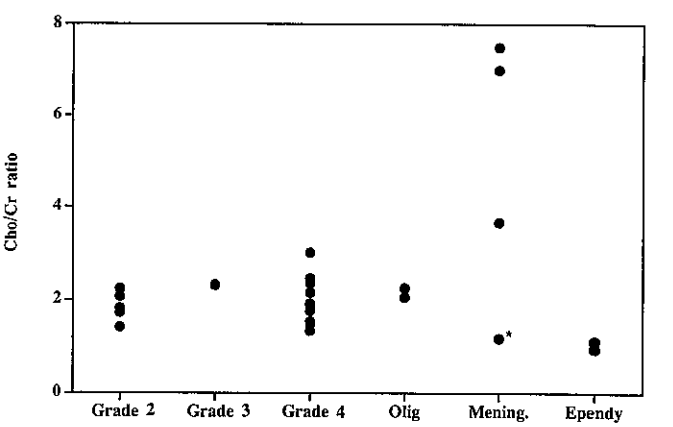

Fig. 4. Cho/Cr ratio of all brain tumors in this study. "Mening." and "Ependy" mean meningioma and ependymoma, respectively. One case of meningioma (*) with the low Cho/Cr ratio was a malignant meningioma which had deeply invaded the cerebral parenchyma.

than Grade 2, and a statistically significant difference ($P<0.01$) was found between them. Oligodendroglioma and Grade 3 had almost the same value.

Fig. 3 shows the NAA/Cr ratio in the cases of glioma. The dispersion of the NAA/Cr ratio of Grade 4 was a little larger than that of the NAA/Cho ratio, but the same tendency was found as for the NAA/Cho ratio described above.

In most cases of meningioma, the intensity of NAA was very low or undetectable. The Cho/Cr ratio was used for the comparison of all groups of brain tumors (Fig. 4). This ratio of meningioma was remarkable higher than that of the other groups of tumors except for one case, which was diagnosed as malignant meningioma. This

tumor was located in the left parietal region and exhibited invasion diffusely to the cerebral parenchyma with brain edema. In all grades of astrocytoma and oligodendroglioma, no differences in the Cho/Cr ratio were apparent. There were only two cases of ependymoma in this study, possibly derived from the fourth ventricle. The diameters of the two ependymomas were more than 3 cm and the voxel for ^{1}H-MRS was located in the center of each tumor. The volume of each tumor was sufficient for measuring ^{1}H-MRS. The Cho/Cr ratios of two ependymomas were lower than those of the four groups of glioma. The craniopharyngioma had a large cystic component and this ^{1}H-MRS showed only the peak of lipid.

DISCUSSION

Gill *et al.* conducted an *in-vitro* proton MR spectroscopic study of intracranial tumors and reported that the NAA/Cr ratio differed significantly in all grades from its value in normal white matter and that the Cho/Cr ratio differed significantly in Grade 4 tumors from its value in the other grades.[3] They also conducted an *in-vivo* MR study of a small number of cases and reported that the spectra *in vivo* were consistent with the *in-vitro* results from the same patients. However, their measurement was conducted with a large volume (64 ml) and their sequence differed slightly from ours. We found a difference in the NAA/Cho and NAA/Cr ratios between Grades 2 and 4 astrocytoma. The level of Cho/Cr ratio was almost the same in all grades of astrocytoma and oligodendroglioma. These results suggest that there is a marked decrease in NAA in Grade 4, while the changes in choline are not large. Though these results differed slightly from those of Gill *et al.*, heterogeneity in the tumor and contamination from normal or edematous parenchyma could not be evaluated in either their study or ours. Ott *et al.* reported that intraindividual differences between the spectra of one tumor at different locations were often larger than differences between the spectra of tumors with different histologic characteristics.[4] The tumor heterogeneity and contamination from surrounding parenchyma make spectral interpretation very difficult. Fulham *et al.* reported that tumor necrosis exhibited a different biochemical status from tumor cells.[5] They found that solid high-grade gliomas had higher normalized Cho values than did solid low-grade gliomas, but the normalized Cho value was not a discriminator of tumor grade, since necrotic high-grade lesions had reduced Cho values. Our result on the Cho/Cr ratio is consistent with that of Fulham *et al.* However, Gill's report and our study suggest that low-grade astrocytoma has different NAA/Cho and NAA/Cr ratios from those of high-grade astrocytoma. Furuya *et al.* observed the same tendency in the tumor spectra as seen in our study, but they used variable sequences (SE and STEAM) and the comparison was conducted in the spectra of different TR and TE.[6] We suggest that ^{1}H-MRS might be useful to differentiate Grade 2 from high-grade gliomas, though a few cases will overlap. Furthermore, we found that typical meningioma showed a characteristic ^{1}H-MRS pattern if there was no contamination from other tissues. The typical ^{1}H-MRS of meningioma was a remarkable high Cho peak, low Cr peak and remarkably reduced NAA peak. Kugel *et al.*[7] found a similar spectral pattern of meningioma to ours and the *in-vitro* study of Gill *et al.* supports these findings.[3] However, in our case of malignant meningioma, the spectrum resembled that of malignant glioma and was completely different from that of typical meningioma. We considered that information derived from tumor cells and invaded brain parenchyma would be mixed, in addition to the biochemical differences arising from malignant change. Our two cases of ependymoma had the lowest Cho/Cr ratio among all of the tumors and this ratio may be useful for the diagnosis of ependymoma. However, to our knowledge, there is no other report concerning the ^{1}H-MR spectra of ependymoma. Further studies should be conducted to establish the characteristic spectral pattern of ependymoma. In a report on a workshop held in Oxford, 1992, Gadian *et al.* stated that while ^{1}H-MRS of intracranial tumors can be a rich source of information, the problem of spectral interpretation has not yet been resolved.[8] Although there are several papers concerning ^{1}H-MRS of brain tumors, a consensus on the usefulness of this method has not yet been reached. Moreover, the meaning of an elevated Cho, lipid signal in relation to tumor biology, and the extent to which spectral changes can aid planning of therapy remain obscure. In order to answer these questions, extensive studies of tumor models and clinical cases and a comparison of the results of *in-vivo* measurement with those of *in-vitro* studies are needed. We consider that long-term observation by ^{1}H-MRS is necessary to establish its diagnostic and prognostic usefulness.

(Received October 4, 1994/Accepted December 15, 1994)

REFERENCES

1) Ross, B. D., Merkle, H., Hendrich, K., Staewen, R. S. and Garwood, M. Spatially localized *in vivo* ^{1}H magnetic resonance spectroscopy of an intracerebral rat glioma. *Magn. Reson. Med.*, **23**, 96–108 (1992).
2) Harada, M., Tanouchi, M., Miyoshi, H., Nishitani, H. and Kannuki, S. Brain abscess observed by localized proton

magnetic resonance spectroscopy. *Magn. Reson. Imaging,* **12,** 1269–1274 (1994).
3) Gill, S. S., Thomas, D. G. T., Bruggen, N. V., Gadian, D. G., Peden, C. J., Bell, J. D., Cox, I. J., Menon, D. K., Iles, R. A., Bryant, D. J. and Coutts, G. A. Proton MR spectroscopy of intracranial tumours: *in vivo* and *in vitro* studies. *J. Comput. Assist. Tomogr.,* **14,** 497–504 (1990).
4) Ott, D., Hennig, J. and Ernst, T. Human brain tumors: assessment with *in vivo* proton MR spectroscopy. *Radiology,* **186,** 745–752 (1993).
5) Fulham, M. J., Bizzi, A., Dietz, M. J., Shih, H. H. L., Raman, R., Sobering, G. S., Frank, J. A., Dwyer, A., Alger, J. R. and Chiro, G. D. Mapping of brain tumor metabolites with proton MR spectroscopic imaging: clinical relevance. *Radiology,* **185,** 675–686 (1992).
6) Furuya, S., Naruse, S., Ide, M., Yamashita, M., Murakami, K., Ikejiri, M., Kakoi, N., Tanaka, C., Horikawa, Y., Ueda, S., Miyazaki, T. and Yamamoto, T. Development of ^{1}H-magnetic resonance spectroscopic imaging method and clinical application for brain tumors and other brain diseases. *Jpn. J. Magn. Reson. Med.,* **12,** 77–87 (1992) (in Japanese).
7) Kugel, H., Heindel, W., Ernestus, R. I., Bunke, J., Mesnil, R. and Friedmann, G. Human brain tumors: spectral patterns detected with localized H-1 MR spectroscopy. *Radiology,* **183,** 701–709 (1992).
8) Gadian, D. G., Shaw, D., Moonen, C. T. W. and Zijl, P. Advances in proton magnetic resonance spectroscopy of the brain. *Magn. Reson. Med.,* **30,** 1–3 (1993).