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EDITORIAL

Thallium-201 SPECT in the Evaluation of Gliomas

There is a growing body of literature which suggests that ^{201}Tl is useful in evaluating cerebral tumors (*1–5*).

Kaplan et al. reported that ^{201}Tl planar brain scans correlated better with residual glioma tissue than CT, ^{99m}Tc-gluconate or ^{67}Ga scans in 29 patients with grade 3 and 4 gliomas, thus proving that ^{201}Tl scanning is an indicator for viable tumor burden (*3*). Mountz et al. developed a method to quantify ^{201}Tl uptake in high-grade astrocytomas by assessing the tumor-to-cardiac uptake ratio and concluded that this uptake ratio, when tested serially, could provide an accurate estimate of residual viable tumor burden or recurrence during or after therapy.

Black and Kim et al. utilized ^{201}Tl SPECT to obtain a semiquantitative ^{201}Tl uptake index of brain tumor counts normalized to homologous contralateral hemisphere activity. They showed that this ^{201}Tl index was useful in separating high-grade from low-grade gliomas. This technique can reduce unrecognized sampling errors during needle biopsies of high-grade tumors misdiagnosed as low-grade tumors due to inadequate biopsy materials (*4,5*). It is essential to accurately define glioma grade since the survival of patients with grades 3 and 4 is considerably shorter than that of patients with low-grade glioma.

PET with ^{18}F-fluorodeoxyglucose or [^{11}C]methyl-L-methionine has been shown to correlate with glioma grade and therefore predict patient survival (*6–8*). However, PET is expensive and not widely available. With the exception of PET studies, other imaging modalities such as CT and MRI are not very reliable in distinguishing high-grade from low-grade gliomas.

In this issue of the *Journal*, Oriuchi et al. report on ^{201}Tl brain SPECT imaging in patients with supratentorial gliomas. The authors correlate the imaging findings with proliferative activity of the tumors and prognosis (*9*). This group obtained a semiquantitative ^{201}Tl index of the tumor to normal brain tissue and in 28 presurgical patients observed a significant correlation between the ^{201}Tl index and bromodeoxyuridine (BUdR)-positive cells in excised tumor specimens ($r = 0.67$, $p < 0.001$) after administering BUdR. This method seems to be effective in evaluating tumor cell proliferation and therefore can aid in select-

Received Aug. 18, 1993; accepted Aug. 24, 1993.
For correspondence or reprints contact: Norihisa Tonami, MD, Dept. of Nuclear Medicine, Kanazawa University School of Medicine, 13-1 Takara-Machi, Kanazawa 920, Japan.

ing specific therapies and may predict response to therapy.

Oriuchi et al. provide two meaningful cases demonstrating low ^{201}Tl and low BUdR labeling indices prior to malignant degeneration. When the initial studies are compared with post-malignant degeneration studies, increases in ^{201}Tl and BUdR labeling indices are significant. These cases display the utility of ^{201}Tl SPECT in the evaluation of malignant degeneration of low-grade gliomas. If these findings can be observed in a large number of cases, this method may be adopted as a promising diagnostic tool for guiding the management of low-grade gliomas.

The natural history of a low-grade glioma is not predictable from the histological picture of an individual case. There are reports that malignant degeneration occurs in 13%–50% of low-grade astrocytomas (*10–12*). Once malignant degeneration of a glioma does occur, more aggressive therapies are often required due to the change in tumor behavior.

Thallium-201 uptake is thought to be related to changes in blood-brain barrier permeability, regional blood flow and increased pumping of ^{201}Tl directly into malignant cells by the sodium potassium ($Na+/K+$) adenosine triphosphatase pump (*1*). We suppose that ^{201}Tl uptake by tumors represents the combined circumstances of cell density and cell viability. Cell density is related to the malignancy grade of gliomas, whereas cell viability may reveal the proliferative activity of the tumor. In patients with pulmonary lesions due to suspected lung cancer, we observed that the ^{201}Tl retention index (degree of retention in the lesion) rather than the ^{201}Tl uptake ratio helped differentiate malignant from benign lesions (*13*). This retention index may provide useful information for grading gliomas.

As for the semiquantitative measurement of the ^{201}Tl index, Kim et al. have shown that the ^{201}Tl index can be influenced by lesion size (effect of partial volume) and by the attenuation correction method in SPECT systems (*5*). If the object of interest is less than twice the system's FWHM, the apparent concentration of activity within the object may be underestimated. On the other hand, large tumors containing metabolically inactive areas such as necrosis will show a lower ^{201}Tl index. Also, since uptake in the normal brain tissues is quite low, different techniques of measurement may result in different ^{201}Tl indices. Evaluating the response of malignant gliomas to treatment is often required to differentiate remaining viable tumor from necrosis or surrounding brain edema associated with radiation therapy. CT and MRI studies are unable to distinguish residual tumor and tumor recurrence from tumor necrosis. Kosuda et al. reported that postoperative ^{201}Tl SPECT was very useful in differentiating recurrence of brain tumor from radiation necrosis in 10 patients with brain tumors (*14*). There is little uptake of ^{201}Tl in normal brain and radiation necrosis or resolving hematomas.

Another useful application of ^{201}Tl, proposed by Waxman et al., is the intraoperative assessment of brain malignancies. Since it is often difficult to separate areas of glioma from normal brain tissues during surgery, ^{201}Tl monitoring may assist the neurosurgeon in complete removal of the tumor (*15*).

Recently, ^{99m}Tc-methoxyisobutylisonitile (MIBI) has been reported to show results comparable to ^{201}Tl for the evaluation of childhood brain tumors and of recurrent brain tumors (*16,17*). Since both radiopharmaceuticals have different mechanisms of tumor uptake, further studies are needed to evaluate the behavior of the tracers that may improve in grading and therapeutic efficacy. Thallium-201 SPECT now appears to be the method of choice for grading gliomas, assessing residual viable glioma tumors following radiation therapy, and detecting malignant degeneration of low-grade gliomas.

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Kinichi Hisada
Kanazawa University School of Medicine
Kanazawa, Japan

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