MRI techniques such as diffusion- and perfusion-weighted imaging and MR spectroscopy have been suggested to have increased sensitivity and accuracy, compared with conventional imaging (*2*); however, these techniques have certain limitations in cases of mixed necrosis and recurrence, and overlap between tumor recurrence and radiation necrosis groups has also been noted (*3*).

Functional metabolic imaging by PET and SPECT has been also evaluated. Nonetheless, PET studies are often cost-prohibitive and not widely available. Therefore, there has been much interest in using SPECT as a feasible alternative imaging technique. The major tumor-seeking radiotracers that have been extensively evaluated are ^{201}Tl and ^{99m}Tc-sestamibi. Furthermore, several in vitro studies on glioma cell lines have substantiated a potential superiority of ^{99m}Tc-tetrofosmin (^{99m}Tc-TF) over ^{99m}Tc-sestamibi for brain tumor imaging, since ^{99m}Tc-TF accumulation is independent of the multidrug-resistance phenotype of the cell (*4,5*). On the basis of these reports, we investigated the in vivo imaging properties of ^{99m}Tc-TF in tumors of the central nervous system. ^{99m}Tc-TF is a tumor-seeking diphosphine that does not cross the intact blood–brain barrier, and uptake of ^{99m}Tc-TF depends on regional blood flow and cell membrane integrity, thus reflecting cellular metabolic status and viability. We fount that ^{99m}Tc-TF could successfully differentiate tumor recurrence from radiation injury (*6*). We also evaluated the relationship between glioma and meningioma proliferation (as assessed by the immunohistologic index Ki-67 and flow cytometry) and ^{99m}Tc-TF uptake. In both tumor types, we verified a strong positive linear correlation between tracer uptake and tumor proliferative potential and aggressiveness (*7–9*). Furthermore, we reported that ^{99m}Tc-TF SPECT could hold a role in differentiating neoplastic from nonneoplastic intracerebral hemorrhage (*10*). Thus, we propose that metabolic brain imaging by ^{99m}Tc-TF SPECT can contribute considerably to the management of patients who undergo radiotherapy and develop new lesions or symptoms. Comparative studies with other metabolic imaging techniques such as ^{11}C-MET would be valuable to evaluate this critical issue.

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REPLY: We thank Dr. Alexiou and his colleagues for their thoughtful comments regarding our article evaluating the diagnostic accuracy of PET with L-methyl-^{11}C-methionine (^{11}C-MET) in differentiating recurrent brain tumors from radiation necrosis after radiotherapy (*1*).

Although several studies show the utility of SPECT in distinguishing recurrent brain tumors from radiation necrosis, PET is known to be superior to SPECT in spatial resolution and ability to be quantified. Furthermore, our previous study evaluating brain tumors using ^{11}C-MET and ^{201}Tl-chloride suggested that ^{11}C-MET PET is more useful than ^{201}Tl SPECT for that purpose (*2*). On the basis of these findings, we have recently preferred ^{11}C-MET PET to ^{201}Tl SPECT, and our paper demonstrated that quantitative values determined from ^{11}C-MET PET data can differentiate recurrent brain tumors from radiation necrosis with acceptable diagnostic accuracy (*1*).

However, the use of ^{11}C-MET is often limited to facilities equipped with a cyclotron because the half-life of ^{11}C-MET is relatively short, thus making it costly. In contrast, SPECT is a less costly imaging technique and widely available. Nevertheless, a definitive SPECT radiotracer for the differentiation of recurrent brain tumors from radiation necrosis has not yet been established. We have examined patients with brain tumors using both ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi SPECT in clinical settings but have not yet obtained sufficient data to draw any conclusions. In the field of SPECT, ^{99m}Tc-tetrofosmin may be a promising radiotracer for the differentiation of recurrent brain tumors from radiation necrosis (*3*) and is the area in which we are most interested. We agree with the statement by Dr. Alexiou and his colleagues that comparative studies between these 2 imaging techniques with ^{11}C-MET PET and ^{99m}Tc-tetrofosmin SPECT are most interesting and helpful.

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