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Technetium Tc99m Tetrofosmin Single-Photon Emission CT for the Assessment of Glioma Proliferation

We read the interesting recent article by Kato et al¹ concerning the assessment of glioma metabolic activity by positron-emission tomography (PET).¹ The authors evaluated the type, grade, and proliferation index of 95 primary glioma cases by simultaneous [¹⁸F] fluorodeoxyglucose (18F-FDG), [¹¹C]-methionine (MET) and [¹¹C]-choline (CHO) PET. Their results in astrocytic tumors showed a significant correlation between all tracer uptake and both tumor grade and proliferation activity (as assessed by the Ki-67/Mib-1 immunohistologic index). Nonetheless, in oligodendrogliomas and in mixed oligoastrocytic tumors, only CHO-PET demonstrated a significant correlation between tracer uptake and tumor grade. As regards visual image evaluation, MET-PET was proved superior due to its insignificant uptake by normal brain tissue.¹

The proliferation potential of gliomas is important for patient management and has significant prognostic implications. Its assessment currently requires tissue sampling through biopsy or over the course of a surgical procedure. A major objective of nuclear medicine is, therefore, the development of new radio-labeled tracers to evaluate, noninvasively, tumor proliferation in vivo. Aside from PET, which is relatively expensive and not widely available, single-photon emission CT (SPECT) with various radiotracers has also been evaluated. Thallium-201 (²⁰¹Tl) was one of the first tracers used. Technetium Tc99m-labeled compounds have also been studied; they were proved advantageous over ²⁰¹Tl, due to the 140 keV γ -ray energy, higher photon flux, higher spatial resolution, less radiation burden to the patient, and excellent availability.

We are currently investigating the brain tumor imaging properties of Tc99m tetrofosmin (Tc99m-TF), a lipophilic diphosphine routinely used for myocardial perfusion imaging, which also displays tumor-seeking properties. Its uptake mechanism depends mainly on blood-brain-barrier (BBB) disruption, regional blood flow, and cell membrane integrity, thus reflecting on cellular metabolic status and viability. Given that Tc99m-TF does not cross the intact BBB, every

brain lesion disrupting BBB and selectively accumulating the radio-tracer can be easily identified against negligible tracer uptake in normal background. We have recently described a strong correlation between Tc99m-TF uptake and cellular proliferation, as assessed by the Ki-67 index and by flow cytometry analysis, in both gliomas and meningiomas.^{2,3} We also found that Tc99m-TF can reliably distinguish between glioma recurrence and radiation necrosis.⁴ This correlation between Tc99m-TF uptake and glioma proliferation allows us to consider this initial evidence as adequate to substantiate further research regarding the clinical utility of Tc99m-TF SPECT. The wider availability and favorable cost of this imaging technique, compared with PET, also constitute a considerable advantage.

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