PET and SPECT in Brain Tumors and Epilepsy

Laura L. Horky, MD, PhD[a,*], S. Ted Treves, MD[b]

KEYWORDS

• Molecular imaging • Positron emission tomography
• Brain tumor • Epilepsy

Molecular imaging with positron emission tomography (PET) plays an important role in the diagnosis and management of patients with brain tumors and epilepsy. Where applicable, single-photon emission computed tomography (SPECT) is also discussed.

OVERVIEW OF PET AND SPECT IN NEUROSURGERY: BRAIN TUMORS

Annually in the United States, more than 20,000 people are diagnosed with malignant brain tumors and approximately 13,000 die of primary brain tumors. Another 22,000 are diagnosed with nonmalignant primary brain tumors. Metastatic brain tumors, predominantly from breast, lung, and colon primary cancers are even more common, with approximately 140,000 patients diagnosed each year, and more than 100,000 deaths per year from symptomatic brain metastases.[1–3]

Nuclear molecular imaging can be used for the assessment of treated or untreated primary or metastatic brain tumors. PET is commonly used for assessing and grading brain tumors, assessing aggressiveness and prognosis, distinguishing between recurrence and postradiation necrosis, and guiding biopsy. Brain SPECT is also a useful technique in the assessment of brain tumor activity.

PET Technology

PET was developed in the 1970s by Phelps and Hoffman, as an in vivo imaging application of autoradiography, using radioactively labeled glucose.[4] Briefly, a positron-emitting radiotracer is injected into the patient and taken up selectively by cells possessing certain molecular characteristics, such as the presence of glucose or amino acid transporters. In the target tissue, the radiotracer decays, emitting positrons. The emitted positrons collide with nearby electrons and are annihilated, producing 2 high-energy (511 keV) photons, which are emitted 180° apart. The photons are detected by a PET scanner, which is a ring-shaped, high-energy coincidence detector that surrounds the patient. Registration of millions of coincidence events allows localization of the radiotracer distribution within the patient. The spatial resolution of PET is 4 to 10 mm, depending on the scanner type. It is generally accepted that assessment of lesions smaller than 7 to 8 mm in diameter or 0.5 cm^3 may be limited.

Hybrid PET/computed tomographic (CT) scanners have all but replaced the traditional PET-only scanners. The hybrid scanner uses low-dose multislice helical CT (approximately 10–40 mA and 130 kilovolt [peak]) for the dual purpose of anatomic localization and attenuation correction.[5] Once acquired, PET images may also be fused to a patient's magnetic resonance imaging (MRI). PET/MRI systems are currently under development, in which PET and MRI images are acquired simultaneously.[6]

PET Tracers: FDG

Fluorodeoxyglucose

2-Deoxy-2-(^{18}F)fluoro-D-glucose (^{18}F-FDG or FDG) is the most common clinical nuclear medicine imaging tracer used today to assess brain tumors.

[a] Division of Nuclear Medicine and Molecular Imaging, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA
[b] Division of Nuclear Medicine and Molecular Imaging, Department of Radiology, Children's Hospital Boston, 300 Longwood Avenue, Boston, MA 02115, USA
* Corresponding author.
E-mail address: lhorky@partners.org

Neurosurg Clin N Am 22 (2011) 169–184
doi:10.1016/j.nec.2010.12.003

FDG-PET was initially used for functional brain mapping and then became the first PET tracer used for the assessment of brain tumors.[7] An analogue of glucose, FDG uptake correlates with regional glucose metabolism. FDG readily crosses the blood-brain barrier and is transported intracellularly by glucose transporters. Once intracellular, it is phosporylated by glucose 6-hexokinase and trapped in the cell, because it cannot be metabolized. Brain tumors characteristically have a high concentration of glucose transporters and glucose 6-hexokinase and are therefore typically FDG avid.

The brain uses glucose as its main energy source, and glucose is transported by a group of glucose transporters (GLUTs). GLUT1s are expressed in glia, capillary endothelial cells, choroid plexus, and ependymal cells. GLUT3s are expressed in neurons. Gray matter uses 2 to 4 times more glucose than white matter.[8] In brain tumor imaging, the high rate of glucose transport within physiologically active normal brain can obscure the target to background ratio, particularly when the tumor is adjacent to physiologically active gray matter (**Fig. 1**).

TUMOR GRADING WITH FDG

FDG is useful for tumor grading because most high-grade tumors, such as high-grade gliomas, medulloblastoma, and primary central nervous system lymphoma, have high concentrations and activity of GLUTs.[9] Most low-grade tumors have lower concentrations of GLUTs and can be distinguished from high-grade gliomas by the lower FDG uptake on PET. FDG avidity of common benign and malignant primary and metastatic brain tumors is shown in **Box 1**.

As an exception to the rule, some low-grade tumors have a high FDG avidity, which is because of the high concentrations of GLUTs. In pilocytic astrocytomas, for example, the vascular density is high. In this case, glucose uptake does not represent the blood flow but is thought to represent the metabolic activity of the endothelial cells lining the tumor vasculature.[10–12] Endothelial proliferation and metabolism account for the high FDG avidity. Oligoastrocytomas also have variable FDG uptakes, even within the same tumor grade.

Measurements of tumor FDG uptake versus physiologic brain FDG uptake can be used to predict high- versus low-grade brain tumors, both primary and metastatic, with certain exceptions as noted earlier. Semiquantification of glucose uptake is performed using a standardized uptake value (SUV).[13,14] A tumor to gray matter uptake ratio of greater than 0.6 or a tumor to white matter uptake ratio of greater than 1.5 was, in 1 series by Delbeke and colleagues,[15] 100% sensitive and 67% specific for distinguishing high-grade gliomas from low-grade gliomas. Applying the same cutoffs to primary brain tumors and brain metastases yielded 94% sensitivity and 77% specificity. FDG avidity has also been inversely correlated with survival. For example, in a series of 165 patients with highly FDG avid brain tumors, 1-year survival was only 29%, as opposed to 94% in patients with tumors with low FDG avidity.[16]

Recurrence versus Postradiation Necrosis with FDG

In primary or metastatic tumors treated with radiotherapy, tumor growth as seen on contrast MRI

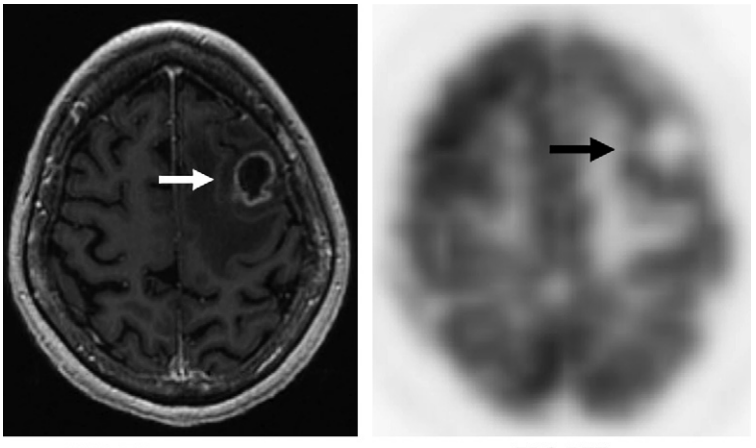

Fig. 1. A 62-year-old woman with metastatic lung cancer to the left frontal lobe 18 months after stereotactic radiosurgery. The ring-like contour of FDG avidity corresponding to the rim-enhancing lesion on MRI (*left*) could represent either the tumor or the surrounding gyrus. Biopsy demonstrated that the uptake corresponded to normal gyrus rather than to tumor.