^{18}F-Flourodeoxy-Glucose PET/Computed Tomography in Brain Tumors

Value to Patient Management and Survival Outcomes

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KEYWORDS

• Central nervous system neoplasm • PET • PET/computed tomography • Brain • Tumor • Cancer • Survival outcomes • Patient management

KEY POINTS

- ^{18}F-flourodeoxy-glucose (FDG) PET/computed tomography (CT) is useful in the diagnosis, pretherapy prognosis, and response to therapy evaluation in primary central nervous system lymphoma.
- FDG avidity correlates with tumor grade in gliomas.
- FDG PET/CT can be used to identify nonenhancing, low-grade gliomas undergoing malignant transformation.
- FDG PET/CT can differentiate radiation therapy effect from tumor recurrence.

INTRODUCTION

The annual incidence of intracranial central nervous system (CNS) tumors in the United States is 21.4 per 100,000 persons.[1] The 5-year survival rate of all primary brain tumors is 34%.[2] There are many types of primary brain tumors. Gliomas account for greater than 80% of adult primary brain tumors. Less frequent types, such as primary CNS lymphoma, represent 3% of adult primary brain tumors.[3] Metastatic disease to the CNS occurs much more frequently than primary CNS lesions, with an estimated incidence 10 times greater.

The initial presentations for all CNS lesions are similar, manifesting as seizures, headaches, and focal neurologic deficits related to the anatomic site of involvement. The course of disease, however, differs greatly and is influenced by the patterns of growth and anatomic location. Treatment is generally dictated by histopathologic classification. Biopsy is mandatory and key to diagnosis and treatment planning. Although tissue sampling is crucial, it represents a short stop along the pathway from diagnosis to outcome. The standard of care requires a multimodality approach of complementary imaging utilizing dedicated computed tomography (CT), MR imaging, and PET/CT examinations to provide the highest quality assessment.[4]

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MR IMAGING

As per National Comprehensive Cancer Center (NCCN) guidelines, MR imaging is the gold standard of brain imaging, providing high soft-tissue contrast and high-resolution anatomic images.[5]

In addition to anatomy, new developments in MR imaging technique allow functional and metabolic analysis through perfusion-weighted, diffusion-weighted sequences and MR spectroscopy. Although MR imaging does have some limitations - such as availability, cost, and artifacts, it is critical in the diagnostic evaluation and post-therapy assessment of all brain tumors. MR imaging is utilized for anatomic localization, delineation of tumor extent, determination of involvement of higher cortical structures, identifying optimal biopsy sites, tumor grading, assessment of response to therapy, and identifying recurrent/progressive disease.[6–10]

^{18}F-FLOURODEOXY-GLUCOSE PET/COMPUTED TOMOGRAPHY

Traditionally, ^{18}F-flourodeoxy-glucose (FDG) PET/CT has played a vital complementary role to MR imaging, supplementing interpretation in areas where MR imaging tended to be equivocal. FDG PET/CT has been shown to correlate with tumor grade, demonstrate malignant transformation, and differentiate tumor from radiation necrosis.[11,12] This article provides an up-to-date assessment of the value of FDG PET/CT to patient management and survival outcomes in primary brain tumors.

GLIOMAS

FDG uptake is typically increased in high-grade tumors.[13] Histologic grading is a means of predicting the biological behavior of a neoplasm, and in the case of gliomas, it is a key factor in diagnosis, prognosis, and treatment selection. Grading is based on the World Health Organization (WHO) criteria and divided into 4 grades. Grades I and II are considered low grade, and grades III and IV are considered high grade. The differentiation reflects not only proliferative activity but also a distinct change in survival outcomes and recurrence rates.

PATIENT MANAGEMENT AND SURVIVAL OUTCOME

Low-grade tumors, such as infiltrative astrocytomas and oligodendrogliomas, have a low proliferative potential, and depending on risk factor stratification, have a median overall survival outcome of 3.9 years for high risk and 10.8 years for low risk.[14] Diffuse astrocytomas were traditionally considered benign but are now considered malignant, because they may dedifferentiate and undergo malignant transformation over time.[15] Low-risk features include age less than 40 years, Karnofsky performance status of at least 70, minor or no neurologic deficits, oligodendroglioma or mixed oligoastrocytoma, tumor dimension less than 6 cm, 1p and 19q co-deletion, and IDH1/2 mutations.[5]

High-grade tumors, such as anaplastic astrocytomas and glioblastomas, demonstrate histologic evidence of malignancy with nuclear atypia and increased mitotic activity. Anaplastic astrocytomas have a 27% 5-year survival rate, and glioblastomas have less than a 5% 5-year survival rate.[16] These high-grade tumors infiltrate adjacent parenchyma, resulting in significant peri-lesional edema, frequently causing symptoms related to their size and subsequent increased intracranial pressure.

Temozolomide is now the standard of care with postoperative radiation therapy (RT) in younger patients with good performance status (PS), showing improved survival when compared with RT alone.[17] Current NCCN guidelines recommend gross tumor resection whenever possible. Aggressive surgery has been shown in multiple studies to be associated with a good prognosis.[18] Adjuvant chemoradiation therapies are based on grade, status of the 1p 19q loci, performance status, and age. Procarbazine, lomustine, and vincristine (PCV) with fractionated external beam radiation therapy (EBRT) are recommended for anaplastic oligodendroglioma or oligoastrocytoma with 1p 19q co-deletion.[19] For glioblastoma in patients younger than 70 with good PS, temozolomide with fractionated RT is given. For glioblastoma in older age patients with poor PS, the regimen vary.

IMAGING EVALUATION: TUMOR GRADE

In the evaluation of a primary CNS tumor, as per NCCN guidelines, MR imaging is performed first to aid diagnosis, then postoperatively within 72 hours, and every 3 to 6 months for 5 years.[5] As grading is a critical factor in patient management and survival outcome, noninvasive radiologic determination of grade has potential to add great value to patient care. The principle that MR imaging exploits to determine enhancement is directly related to the integrity of the blood–brain barrier (BBB). Breakdown of the BBB allows contrast to enter, and this manifests as enhancement. Typically high-grade gliomas are associated with breakdown of the BBB and show enhancement, while low-grade gliomas do not show enhancement. However, this does not always hold true. Some glioblastomas do not show enhancement