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EDITORIAL

Practice Based Evidence of the Beneficial Impact of PET in Patients with Brain Tumors

Homer A. Macapinlac,[1] Johannes Czernin,[2] Steven M. Larson[3]

[1]*The University of Texas, M. D. Anderson Cancer Center, Houston, TX, USA*
[2]*University of California, Los Angeles, CA, USA*
[3]*Memorial Sloan Kettering Cancer Center, New York, NY, USA*

This issue of the Journal of Molecular Imaging and Biology contains an important article by Hillner et al. [1]: "Impact of Dedicated Brain PET on Intended Patient Management in Participants of the National Oncologic PET Registry" which builds upon the previous landmark National Oncologic PET Registry (NOPR), sponsored by the Academy of Molecular Imaging and operated as a coverage with evidence development program by the Centers for Medicaid and Medicare Services (CMS), in patients with various tumor types not generally reimbursed by Medicare. The goal of this article is to assess the impact of dedicated brain positron emission tomography (PET) on intended management of patients from the NOPR dataset with primary and metastatic brain tumors. A major advantage of this study was its size, with a total of 509 dedicated brain PET scans in 479 patients analyzed from the NOPR cohort of 74,932 scans in 62,122 patients. This represents the largest dataset published to date to determine the impact of 2-deoxy-2-[^{18} F]fluoro-D-glucose (FDG)-PET on the management of brain tumor patients.

The strength of the data also stems from the innovative mechanism of Coverage with Evidence Development (CED) designed to develop sufficient data to allow appropriate CMS National Coverage Decisions. This study was designed with input from CMS including patient eligibility, end points, statistical analysis, plus coverage of the cost of services by CMS for the PET studies.

Despite having the large number of patients, brain tumor patients account for only 0.67% of the total number of NOPR PET scans. This reflects the clinical reality of the low incidence of brain tumors. This is of particular importance since multicenter trials of patients with rare diseases are difficult to design and conduct.

The glycolytic phenotype of brain cancers varies with tumor grade and aggressiveness. Low-grade tumors are not well detected largely due to the high background glycolytic activity of normal brain tissue. However, a low glycolytic phenotype of brain tumor might carry important prognostic information. Moreover, the specificity of magnetic resonance imaging (MRI) is limited since benign pathology can also lead to contrast enhancement as is the case in patients with radiation necrosis. FDG-PET is therefore an important modality for differentiating persistent or recurrent tumor from benign post-therapeutic tissue alterations [2, 3]. For example, when uptake within the tumor mass is greater >1.4× contralateral white matter, tumor recurrence rather than radiation necrosis is the likely diagnosis. [4]. Thus, despite its limited sensitivity for low-grade tumors, the current study demonstrates that FDG-PET has a substantial impact on intended patient management. The main finding of the study is that the frequency of intended management change using dedicated brain PET was similar to the rate found overall for the aggregate of all other cancers in the NOPR. Differences were noted, namely: (1) the changes in intended management from treatment to non-treatment was more common in the brain tumor patients; (2) there was less frequent initiation of therapy as a consequence of the PET study; and (3) the pre-PET plan of a biopsy was modified in 84% of the patients. This avoidance of a biopsy could potentially lead to cost savings. However, by design, NOPR was unable to address this issue since the registry did not monitor actual management changes and whether they affected patient outcome.

However, the NOPR design enabled the collection of important data that were acquired using state-of-the-art equipment. Moreover, academic and community practices in all 50 states participated in the registry. This alliance between the diagnostic imaging professionals, a scientific organization (AMI) and CMS is a great example of practice based evidence development which can provide a practical alternative to prospective randomized trials. The CED approach allows us to answer important clinical questions, such as whether and how dedicated brain PET imaging impacts management decisions including the initiation of therapy, changes in treatment, and performing biopsies.

Correspondence to: Homer Macapinlac; *e-mail:* hmacapinlac@mdanderson.org

In practical terms, whenever a clinical situation arises for which MR or CT imaging cannot assess the status of a patient regarding tumor grade/prognosis, residual or recurrent disease, dedicated brain PET could provide direction in managing these patients. A concrete example would be holding off on biopsy of a previously suspicious lesion if it demonstrates low or absent activity on the PET scan. Multimodality therapies for brain tumors continue to evolve resulting in better survival rates of patients. Glucose metabolic phenotyping with FDG-PET can be used to predict tumor grade, to identify appropriate biopsy sites, and to allow for outcome predictions. Moreover, risk-adapted treatment strategies can be initiated. Novel tracers with low background activity in the normal brain could be introduced to allow for more comprehensive non-invasive tumor phenotyping. The recent advent of PET/MRI brain devices might further improve the assessments of brain tumor patients. We now need to seek synergies between all imaging modalities to arrive at the most informed patient management decisions.

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