PET/MRI: Emerging Clinical Applications in Oncology

Tyler J. Fraum, MD, Kathryn J. Fowler, MD, Jonathan McConathy, MD, PhD

Abbreviations and Acronyms

AC attenuation correction

CHO [^{11}C]choline

CMS Centers for Medicare & Medicaid Services

CT computed tomography

DWI diffusion-weighted imaging

FACBC *anti*-1-amino-3[^{18}F]fluorocyclobutyl-1-carboxylic acid

FDG 2-deoxy-2-[^{18}F]fluoro-D-glucose

FDOPA 6-[^{18}F]fluoro-3,4-dihydroxy-phenylalanine

FET *O*-(2-[^{18}F]fluoro-ethyl)-L-tyrosine

FMISO [^{18}F]fluoromisonidazole

MET L-[^{11}C]methionine

MRI magnetic resonance imaging

OMs osseous metastases

PET positron emission tomography

Positron emission tomography (PET), commonly performed in conjunction with computed tomography (CT), has revolutionized oncologic imaging. PET/CT has become the standard of care for the initial staging and assessment of treatment response for many different malignancies. Despite this success, PET/CT is often supplemented by magnetic resonance imaging (MRI), which offers superior soft-tissue contrast and a means of assessing cellular density with diffusion-weighted imaging. Consequently, PET/MRI, the newest clinical hybrid imaging modality, has the potential to provide added value over PET/CT or MRI alone. The purpose of this article is to provide a comprehensive review of the current body of literature pertaining to the clinical performance of PET/MRI, with the aim of summarizing current evidence and identifying gaps in knowledge to direct clinical expansion and future research. Multiple example cases are also provided to illustrate the central findings of these publications.

Key Words: PET/MRI; PET/MR; Oncology; mMR; Whole-body imaging.

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From the Mallinckrodt Institute of Radiology, Washington University, Campus Box 8131, 510 S. Kingshighway Blvd., Saint Louis, MO, 63110. Received August 8, 2015; revised August 8, 2015; accepted September 27, 2015. Funding acknowledgements: Support for the [18F]FDOPA-PET/MRI study was supported through grant K08CA154790 from the National Cancer Institute and by Grant #ACS IRG-58-010-55 from the American Cancer Society. **Address correspondence to:** T.J.F. e-mail: fraumt@mir.wustl.edu

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PSA
prostate-specific antigen

PSMA
prostate-specific membrane antigen

SCC
squamous cell carcinoma

SUV
standardized uptake value

SUVmax
maximum SUV

TSE
turbo spin echo

INTRODUCTION

Positron emission tomography (PET) has revolutionized the imaging evaluation of numerous oncologic conditions by exploiting biochemical and physiologic differences between tumor cells and normal tissues (1). Often performed in conjunction with computed tomography (CT), PET utilizing the glucose analog 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) has become the standard of care for the initial staging and the subsequent assessment of treatment response for many malignancies (2,3). Tumor uptake of FDG reflects the increased rates of aerobic glycolysis that occur in many cancer cells (the Warburg effect) relative to most normal tissues and benign lesions. The resulting distribution of FDG thereby allows for anatomic delineation of local and distant tumor spread by PET/CT and provides a measure of a key aspect of cancer metabolism. Many PET tracers have also been developed to take advantage of other distinctive tumor properties, such as elevated amino acid transport or altered receptor expression (4).

Despite its proven utility, FDG-PET/CT has important limitations, especially with respect to local tumor staging and the characterization of certain incidental lesions. In such situations, further evaluation with magnetic resonance imaging (MRI) may be indicated to achieve optimal clinical management. The superb soft-tissue contrast of MRI and its capacity to assess cellular density by diffusion-weighted imaging (DWI) constitute powerful supplements to the molecular and metabolic data of PET. Consequently, PET/MRI, the newest clinical hybrid imaging modality, has significant potential to improve the diagnosis, initial staging, and subsequent restaging of numerous cancers. However, studies demonstrating such benefits are needed to support the routine clinical use of PET/MRI, particularly to justify the added expense and complexity of PET/MRI instead of PET/CT. This review aims to summarize the current body of evidence in support of PET/MRI, as well as current challenges and gaps in knowledge, and to identify oncologic conditions likely to benefit from its clinical use. We also present case examples to illustrate specific advantages of PET/MRI. Overall, this article should familiarize the reader with the current clinical applications of PET/MRI in oncology and provide an overview of the specific scenarios in which PET/MRI may provide added value over PET/CT or MRI alone.

CURRENT CHALLENGES

Technical Considerations

Before delving into the clinical evidence, it is essential to discuss briefly the technical development of PET/MRI, so as to understand some of the inherent advantages, challenges, and limitations. The earliest approach to combining PET and MRI data was through software fusion of PET or PET/CT images with separately acquired MRI. The first combined apparatuses were *sequential* PET/MRI systems that consisted of individual PET and MRI elements connected by a common table. The newer *integrated* PET/MRI systems acquire PET and MRI data simultaneously in the same bore. This latter strategy may improve scanning efficiency and reduce misregistration (5) but requires technical adaptations of the PET components; additionally, both *sequential* and *integrated* PET/MRI systems require a novel method to correct for the attenuation of PET photons (6–8).

Whereas the CT component of PET/CT directly provides electron density information that can be readily used to generate attenuation-corrected PET images, the MRI signal acquired during simultaneous PET/MRI instead correlates with proton density and tissue T1/T2 properties. Current approaches to MRI-based attenuation correction (AC) include segmentation-based and atlas-based methods (6,7). Segmentation-based AC is used clinically and relies on the Dixon method to classify voxels as soft tissue (i.e., muscle and solid organs), fat, lung, or air. In contrast to the atlas-based method, which fits pre-existing averaged imaging data sets to an acquired study and is currently used mainly in the research setting, the segmentation-based method uses each patient's own imaging data and thus can account for large tumors, postsurgical changes, anatomic variants, and other findings not readily incorporated into imaging atlases. However, segmentation-based AC has its own set of limitations. Cortical bone, which attenuates PET photons more than soft tissue,