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Whole-Body Positron Emission Tomography-Magnetic Resonance in Breast Cancer

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Whole-Body Magnetic Resonance Technology

Hybrid positron emission tomography (PET)-magnetic resonance (MR) technology has recently been introduced into the market, appearing in the clinical setting in 2007.[1,2] Whether designed as a sequential or simultaneous system, the hybrid PET-MR produces high-resolution anatomical, biological, and functional imaging. Given the limited approved indications of PET/computed tomography (CT) in patients with breast cancer, it is understandable that the potential role of PET-MR in such patients remains to be determined. The impetus to develop whole-body MR imaging (WB-MRI) scanning techniques lies in its advantages over CT. Namely, MRI makes no use of ionizing radiation, provides exceptional soft tissue contrast, and offers the ability to perform multisequence and multiplanar imaging, which allows for improved lesion characterization. The feasibility of a hybrid PET-MR scanner to evaluate the WB was dependent on the development of WB-MR sequences that could be conducted within a reasonable period while providing diagnostic images. The development of such sequences has been made possible by hardware innovations including multireceiver channel WB scanners as well as acquisition acceleration techniques.[3] Such advances allow the assessment of multiple organ systems during 1 scan to be conducted in an efficient and clinically applicable manner.[3,4] In terms of clinical applications, WB-MRI holds promise in evaluating tumors with frequent metastatic spread to the bone, liver, and central nervous system, such as lung cancer, colorectal cancer, prostate cancer, melanoma, and definitively breast cancer.[3] The recent advent of WB-MRI Dixon-based sequences has further reduced the time necessary for WB scans.[5]

Moreover, with the introduction of diffusion-weighted imaging (DWI), which identifies tumors based on the restricted diffusion of water molecules owing to their increased nuclear-cytoplasmic ratio and hypercellularity,[6] it also improved the sensitivity for lesion detection. This is particularly helpful in using the WB-DWI with background body signal suppression (DWIBS) under free breathing, which overcomes the challenges offered by breath holding and respiratory triggered scanning, and allowing for thin slices with multiple signal averaging within an efficient acquisition time.[7] Although early work with DWI in patients with breast cancer has shown potential in evaluating axillary lymph nodes,[8] WB-DWI alone cannot be recommended as a WB staging alternative given its high false-positive rate.[9] Thus, the combination of DWI with conventional sequences has been shown to increase the sensitivity and specificity of WB-MRI,[10] and a promising area of research is how the metabolic information of fluorodeoxyglucose (FDG)-PET can be used with DWI (Fig. 1).

Taken together, the advances in WB-MRI has been an invaluable step in the maturation of hybrid PET-MR systems.

Regardless of whether the hybrid PET-MRI system acquires images in a sequential or simultaneous fashion, dedicated MRI sequences are used for attenuation correction of PET data, a necessary step to account for differences in the attenuation of photons by different tissues of the body. Precise and reproducible attenuation correction is necessary to determine accurate quantification of FDG activity and allow for standardized uptake value (SUV) reporting. In PET/CT, attenuation coefficients of tissues at x-ray energies are obtained from the CT data itself, which directly provides data to allow for maps to 511-keV photon attenuation coefficients.[11] As MR images are determined by tissue hydrogen density and relaxation properties, the data cannot be directly converted into attenuation maps. Instead, MR attenuation maps rely on automated tissue segmentation methods.[12,13]

Despite the differences in attenuation methods between PET/CT and PET-MR, initial studies to date have shown both

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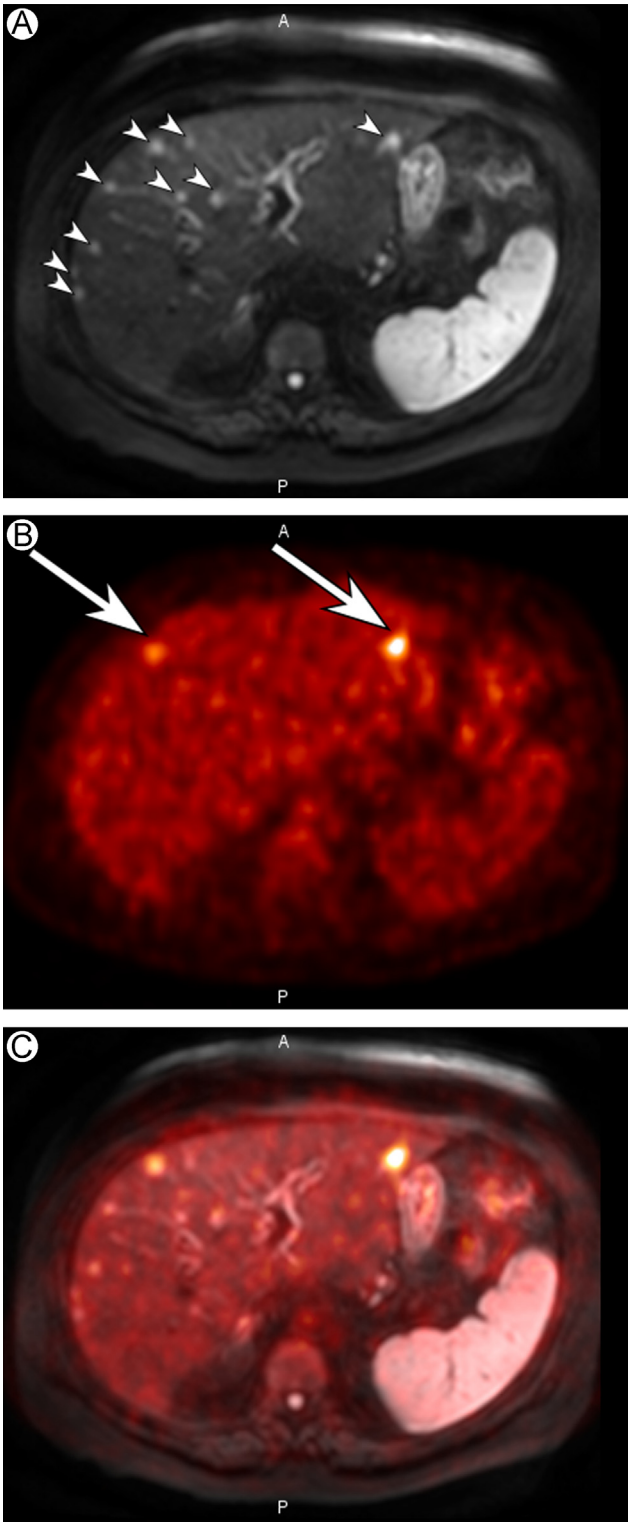

Figure 1 Metastatic breast cancer in a 63-year-old woman. (A) Diffusion-weighted MR image, obtained with a *b* value of 1000, demonstrates multiple foci of diffusion restriction (arrowheads). (B) Axial FDG-PET images obtained at the same level demonstrate 2 intense hypermetabolic foci; the remainder of the lesions seen in (A) are not well appreciated above background hepatic uptake. (C) Fused FDG-PET-MR images clearly illustrate the extent of disease. (Color version of figure is available online.)

overall good correlation between SUV values and similar detection rates between the 2 modalities.[14-16] The most significant differences in SUV values tend to be seen in osseous lesions[17,18] likely explained by current segmentation models not accounting for bone attenuation.[12,13]

PET/CT is now established as the imaging modality of choice in many clinical conditions, particularly in oncology.[19] It has to be noticed that a hybrid PET-MRI examination can generate more than 10,000 slices not all of which would necessarily cover the whole field of view or be isotropic, as opposed to modern multislice PET/CT data.

As of today, although PET-MRI provides unparalleled structural, metabolic, and functional information, an improvement in diagnostic accuracy, a change in management, or a change in patient outcome has not been demonstrated compared with PET/CT. In the clinical routine, more integrated PET-MRI considerations and protocols will need to be improved to optimize their workflow and imaging protocols.[20]

FDG-PET WB Staging

The introduction of integrated PET/CT systems led to an increase in diagnostic confidence and accuracy of restaging patients with suspected metastasis.[21] Furthermore, in patients previously treated for breast cancer and presenting with suspected recurrence, FDG-PET/CT has proven to be highly sensitive, specific, and accurate.[22-24] Multiple studies have sought to evaluate the effectiveness of FDG-PET and FDG-PET/CT on staging and management of patients with breast cancer.[22,25-28] Yap et al found that FDG-PET resulted in changes in clinical stage in 36% of the patients. Furthermore, in 53% of those patients whose stage was not altered by FDG-PET, management was changed because of the additional information provided.[26] These results are concordant with those from Mahner et al[28] who found that FDG-PET is superior to conventional imaging for the detection of distant metastases.

Although FDG-PET has shown a higher sensitivity than conventional imaging in the detection of metastatic disease, the effect of increased sensitivity on patient care and outcome has not been demonstrated.[29] Furthermore, prior studies of patients with stage I or early stage II disease have demonstrated that extensive imaging examinations are unnecessary in most patients with newly diagnosed breast cancer and result in a high degree of false positives and associated economical and emotional distress of patients.[30] Per the current National Comprehensive Cancer Network guidelines, when imaging is recommended for staging, CT or bone scintigraphy or both are the initial studies of choice. However, at the early stage of disease, lesions may remain invisible in the absence of an osteoblastic response. Furthermore, misinterpretation of tracer uptake in healing fractures or degenerative disease may lead to false-positive findings.[14] FDG-PET/CT is currently helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.[31]