

Does PET/MR Imaging Improve Cancer Assessments? Literature Evidence from More Than 900 Patients

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Various integrated PET/MR imaging systems have recently been developed to provide improved clinical assessments of cancers in tissues that may be anatomically better characterized with MR imaging than with CT, to explore whether the combined anatomic and functional capabilities of MR imaging together with the molecular PET information provide new insights into disease phenotypes and biology, and to reduce radiation exposure to vulnerable populations such as children and women of child-bearing age. The following review summarizes the published studies and informs about the potential diagnostic advantages of this new technology.

Key Words: PET/MRI; oncology; cancer diagnosis; staging; PET/CT

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PET/CT using ¹⁸F-FDG serves as a diagnostic, prognostic, and intermediate endpoint biomarker in cancer patients (1). It is now recognized as a cornerstone in cancer patient management. It is relatively inexpensive and straightforward operationally, does not adversely affect cancer care expenditures (2), and, in many instances, has been shown to be cost-effective (3).

Relatively recently, various integrated PET/MR imaging systems have been developed and deployed with 3 major goals: first, to provide improved clinical assessments of cancers in tissues that may be anatomically better characterized with MR imaging than with CT; these tissues include the brain, head and neck, breast, liver, pancreas, bones and muscles, and prostate gland (4); second, to explore whether the combined anatomic and functional capabilities of MR imaging together with the molecular PET information provide new insights into disease phenotypes and biology (4); and, third, to reduce radiation exposure to vulnerable populations such as children and women of child-bearing age (5,6). The reduced risk of radiation exposure is relevant because a large retrospective study in pediatric patients reported a small but significantly increased risk for subsequent leukemia and brain tumors in children who undergo frequent CT scans (7). Reduced exposure is

likely much less relevant or even irrelevant in adult cancer patients who undergo multiple chemotherapy and radiation therapy sessions (8). Nevertheless, that MR imaging does not involve ionizing radiation is listed as a key advantage of this technology in virtually every PET/MR imaging publication.

Hybrid PET/MR imaging systems have some significant disadvantages. First, they are several times more expensive than PET/CT, ranging in price from \$5 million to \$6 million, excluding costs for infrastructure, compared with \$1 million to \$2 million for PET/CT; second, imaging protocols that provide functional in addition to anatomic information are difficult to complete in the time required for PET/CT acquisitions. Limited patient throughput is another disadvantage of PET/MR imaging systems. Thus, a viable economic model of PET/MR imaging has not been found. So it is not a coincidence that many more PET/MR imaging systems have been placed in public than in private health care environments.

A relatively small number of studies have compared the diagnostic performance of PET/MR imaging with that of PET/CT. Many of them have not used optimized PET/MR imaging or PET/CT protocols. A review of these studies appears warranted because the oncology and imaging communities want to be informed about the potential diagnostic advantages of this new technology.

We searched PubMed using key words such as *PET/MR imaging*, *oncology*, and key words for specific cancers. To sum up the results of this initial literature survey: PET/CT and PET/MR imaging appear to assess cancers with comparable accuracy.

The individual published reports that include more than 900 patients are briefly discussed in the following text.

MIXED CANCER POPULATIONS

Drzezga et al. (9) compared the diagnostic performance of integrated PET/MR imaging with that of PET/CT in 32 patients with a variety of malignancies including colon cancer, breast cancer, melanoma, pancreatic cancer, esophageal cancer, lymphoma, and leukemia. They concluded that whole-body PET/MR imaging is feasible. Lesion detection was comparable for both types of instruments.

A larger cohort of patients ($n = 80$) was studied by Quick et al. (10). Patients with a variety of cancers were injected with various PET probes (⁶⁸Ga-DOTATATE, ¹⁸F-FDOPA, ¹⁸F-FDG, ¹⁸F-choline). PET/CT was performed first, followed by an integrated PET/MR imaging study. Eight (10%) of 80 patients could not complete PET/MR imaging because of claustrophobia or discomfort. The PET image quality of PET/CT was slightly better than that of PET/MR imaging, but the detection of lesions was essentially identical.

Al-Nabhani et al. (11) reported a nearly identical diagnostic performance of integrated PET/MR imaging and PET/CT in 50

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patients with a variety of cancers. T staging appeared to be marginally improved by PET/MR imaging.

These studies in 162 patients showed that PET/MR imaging is feasible and provides diagnostic accuracy comparable to that of PET/CT.

HEAD AND NECK CANCERS

MR imaging is frequently considered the modality of choice for assessing head and neck cancers, despite the fact that metaanalyses have failed to show its diagnostic superiority (12–14). The clinical performance of PET/MR imaging has thus far been studied most extensively in head and neck cancers.

Using their trimodality system consisting of PET/CT and 3-T MR imaging, Kuhn et al. (15) studied 150 adult patients to compare the diagnostic performance of contrast-enhanced PET/MR imaging with that of PET/CT. The study population comprised patients who underwent initial and subsequent treatment strategy determinations. Although PET/CT image quality tended to be better than that of PET/MR imaging, the conspicuity of primary tumors was significantly better for T1- and T2-weighted, contrast-enhanced PET/MR imaging. This finding is relevant because tumor invasion of adjacent structures provides important information for therapy planning. In contrast, conspicuity of lymph node metastases was comparable for the two modalities. Diagnostic confidence appeared to be higher for PET/MR imaging. Overall, no diagnostic advantage of PET/MR imaging over PET/CT was shown. Primary tumors and lymph node metastases were detected with comparable accuracies. The authors concluded that PET/MR imaging may be a legitimate alternative to PET/CT.

Queiroz et al. (16) reported their initial experience with follow-up of 87 head and neck cancer patients. Again, almost identical accuracy between PET/CT and PET/MR imaging was reported. Lesion conspicuity appeared to be marginally better for PET/MR imaging.

Finally, an integrated PET/MR imaging system was used in a small prospective study of 17 head and neck cancer patients. Again, no diagnostic advantage over PET/CT was shown (17).

Taken together, the data obtained in 254 patients show that PET/MR imaging is feasible in head and neck cancer and may provide improved information on lesion conspicuity, but it provides no significant overall diagnostic advantage over PET/CT.

LUNG CANCER AND PULMONARY LESIONS

A recent pilot study compared the performance of integrated PET/MR imaging with that of PET/CT for the staging of 22 lung cancer patients (18). Both PET/CT and PET/MR imaging staged all primary tumors correctly. Similar results were reported in 10 patients with lung lesions (19).

Rauscher et al. (20) used PET/MR imaging and PET/CT to characterize lung lesions in 40 patients. PET image quality and the detection rate of ^{18}F -FDG-positive lung lesions was equivalent for CT and MR imaging. However, the detection rate of small, ^{18}F -FDG-negative lung lesions was inferior with MR imaging compared with CT. Similar results were reported by Stolzmann et al. (21) in another 40 patients with pulmonary nodules.

Thus, data from 112 patients with lung nodules or lung cancer revealed comparable diagnostic information from both modalities.

BREAST CANCER

A comparable performance of PET/MR imaging and PET/CT was reported in 36 breast cancer patients. The authors concluded that PET/MR imaging is feasible and could be used for clinical decision-making (22).

NEUROENDOCRINE TUMORS

PET/MR imaging using ^{68}Ga -DOTATOC was compared with PET/CT in 24 patients with neuroendocrine tumors (23). PET/MR imaging and PET/CT performed equally well with regard to image quality and diagnostic accuracy.

LIVER METASTASES

Using their trimodality system, Reiner et al. (24) compared ^{18}F -FDG PET/MR imaging and PET/CT for assessing suspected metastatic liver disease. Contrast-enhanced and unenhanced PET/CT images were analyzed and compared with a variety of PET/MR imaging protocols. One hundred twenty lesions were detected in 55 patients, 66% of which were considered malignant. Eighty percent of the malignant lesions exhibited increased ^{18}F -FDG uptake on PET/CT studies. ^{18}F -FDG-negative lesions were significantly smaller than positive lesions. Biopsy or follow-up imaging was the reference standard. As expected, the sensitivity of unenhanced PET/CT was lowest at 75%; T1- and T2-weighted PET/MR imaging detected liver lesions with an accuracy of 98% using contrast-enhanced PET/CT as the reference standard. The same accuracy was achieved when diffusion-weighted images were added to the PET/MR imaging study. Dynamic contrast-enhanced MR imaging sequences did not improve the overall diagnostic accuracy. However, using follow-up as the reference, dynamic contrast-enhanced MR imaging detected metastases that were undetected by contrast-enhanced PET/CT in 5 patients (undetected metastases in 3 patients, additional metastases in the other liver lobe in 2 patients). This finding resulted in a potential impact on management in 10% of patients. The impact on management analysis did not include false-positive findings that occurred more frequently with advanced MR imaging protocols (up to 15% of patients). Moreover, no state-of-the-art, multiphase, contrast-enhanced CT protocol was used.

In summary that study suggests that PET/contrast-enhanced CT and PET/MR imaging detect liver metastases with comparable accuracy. PET/dynamic contrast-enhanced MR imaging may have an impact on patient management by detecting more lesions; however, the lower specificity of PET/MR imaging may lead to incorrect management decisions.

PROSTATE CANCER

Wetter et al. (25) compared the ability of ^{18}F -choline PET/MR imaging with that of ^{18}F -choline PET/CT for the detection of prostate cancer recurrence. Thirty-six patients were included in the study. All lesions were seen with both modalities, and PET image quality was comparable.

In another study (26), a ^{68}Ga -labeled prostate-specific membrane antigen-targeted ligand was used to detect the site of cancer in 20 patients with biochemical prostate cancer recurrence. A variety of MR imaging sequences was acquired; a Dixon volume-interpolated breath-hold examination sequence was used for attenuation correction. PET/MR imaging was acquired after PET/CT, resulting in higher ligand accumulation in target tissues

and lower background activity when compared with the previously acquired PET/CT. The authors concluded that recurrent prostate cancer was detected more easily and more accurately with PET/MR imaging. However, the present data are unclear whether a delayed PET/CT scan resulting in further tracer accumulation in target tissue would have provided identical diagnostic information.

MALIGNANT BONE LESIONS

Because of its superior soft-tissue contrast, MR imaging in conjunction with PET may provide advantages in the assessment of malignant bone disease. This possibility was tested in 119 patients with hypermetabolic primary cancers who underwent ^{18}F -FDG PET/CT (one set of PET/CT data) followed by PET/MR imaging (two sets of PET/MR imaging: T1-weighted Dixon in-phase images and T1-weighted turbo-spin-echo images) (27). Ninety-eight bone lesions were identified in 33 of 119 patients. Although lesion identification was nearly identical for PET/CT and PET/MR imaging, anatomic delineation of lesions was significantly better accomplished with PET/MR imaging. The authors concluded in their preliminary study that PET/MR imaging may be superior to PET/CT for assessing primary bone tumors, early bone marrow infiltration, and tumors with low PET probe uptake.

PET/MR IMAGING IMPACT ON MANAGEMENT

The impact of ^{18}F -FDG PET/MR imaging on patient management was studied retrospectively by Catalano et al. (28). One hundred thirty-four patients with breast cancer, lymphoma, colorectal cancer, lung and uterine cancer, sarcoma, melanoma, and other cancers were included in the analysis. PET/CT and PET/MR imaging studies were performed with or without contrast material based on the preference of the referring physicians. Two reader pairs interpreted PET/CT and PET/MR imaging studies; after the image interpretation, the reader teams met to determine additional findings from one or the other modality that might affect patient management. The additional findings were reported to the referring physicians to determine their impact on patient management. PET/MR imaging revealed additional findings in 55 patients (41.0%) that were considered inconsequential in 31 patients (23.1%) but significant in 24 patients (17.9%). Overall, PET/MR imaging was superior to PET/CT for evaluating lymphadenopathy and was more sensitive for detecting bone and liver lesions, renal lesions, and incidental breast lesions. These retrospective data need to be confirmed in a larger prospective trial.

CONCLUSION

Data on the diagnostic performance of PET/MR imaging are still limited. PET/MR imaging is clearly feasible and reduces radiation exposure to patients, which is relevant in the pediatric population and in women of child-bearing age. However, in adult male and female cancer patients who undergo chemo- and radiation therapy, the radiation concerns are probably less relevant.

Studies in more than 900 patients have so far not shown a striking difference in diagnostic accuracy for cancer assessment. This is not surprising because both PET and MR imaging as stand-alone modalities provide highly accurate information. Moreover, because the diagnostic accuracy of PET/CT is

already high, studies including large numbers of patients are required to show a statistically significant difference for cancer detection.

We reviewed data acquired in more than 900 patients, all of whom underwent both PET/CT and PET/MR imaging. Thus, the number of studies comparing PET/CT and PET/MR imaging is still quite low. Moreover, these studies have focused on PET/MR imaging feasibility rather than on a systematic performance comparison using well-defined diagnostic reference standards. The current data show comparable diagnostic performance for PET/MR imaging and PET/CT. However, MR imaging is considered the anatomic imaging modality of choice in certain cancers. Therefore, it would be reasonable to convert these MR imaging scans to PET/MR imaging studies if scan durations are tolerable, whole-body protocols are well established, and costs and study methods are acceptable. Moreover, because of widespread radiation concerns, PET/MR imaging may develop into an important diagnostic modality in the pediatric population and in women of child-bearing age.

Future studies that exploit the functional MR imaging and molecular PET capabilities may reveal substantial contributions of PET/MR imaging for tumor phenotyping, treatment response predictions, and treatment monitoring.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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