Clinical and Translational Imaging (2023) 11:351–364
https://doi.org/10.1007/s40336-023-00577-1

EXPERT REVIEW

The synergistic effect of PET/MRI in whole-body oncologic imaging: an Expert Review

Felipe S. Furtado[1,2,3] · Mina Hesami[1,2] · Shaunagh Mcdermott[1] · Harshad Kulkarni[4] · Alexander Herold[5] · Onofrio A. Catalano[1,2]

Received: 18 March 2023 / Accepted: 31 May 2023 / Published online: 13 July 2023

Abstract

Purpose Positron emission tomography (PET)/magnetic resonance imaging (MRI) is a hybrid imaging modality that combines MRI and PET imaging into a comprehensive modality for oncologic evaluation. MRI contributes with excellent soft tissue contrast resolution along with multiparametric information and PET with exquisite high sensitivity. Together they facilitate lesion detection and characterization, TNM staging, and assessment of treatment response. This review aimed to survey the published PET/MRI research findings for body oncology and reflect upon them.

Methods This narrative overview of the literature summarizes the findings of published research articles on PET/MRI for oncology (excluding neurologic applications) indexed in the online databases Google Scholar, PubMed, and Scopus, from its commercial introduction in 2011 to the present (2023).

Results The theoretical advantages of PET/MRI have been demonstrated in practice with studies showing PET/MRI has comparable or superior sensitivity and specificity to PET/CT and MRI in most cancers, with the advantage of being acquired in a single session. Limitations include the comparatively lesser availability and the higher cost, both of which are predicted to be offset by increased adoption.

Conclusions PET/MRI has the potential to become the standard test for staging and post-treatment evaluation of many primary tumors.

Keywords PET/MRI · PET/MR · Oncologic imaging · PET · Cancer · FAPI

Purpose

Simultaneous positron emission tomography (PET)/magnetic resonance imaging (MRI) is a hybrid imaging technique commercially introduced in 2011 [1], after the development of avalanche photodiodes [2], and most recently silicon photomultipliers, breakthroughs in engineering that allowed incorporation of PET detectors into the MRI system without meaningful interference [3]. Previously used photomultiplier tubes suffered interference from magnetic fields making such achievement impossible. PET/MRI promised to address some of the limitations of the current oncologic standard of care imaging, namely, PET/CT. These include the poor soft tissue contrast of CT [4], which is exacerbated when performed with low radiation doses for attenuation correction purposes only. Another shortcoming of the current PET/CT technology is that it cannot acquire PET and CT data at once, but rather does it sequentially. Usually, the attenuation correction CT is acquired first, only subsequently the PET data are obtained [5]. This may lead to misregistration artifacts due to motion, such as breathing and peristalsis [6–8]. These artifacts might result in missed lesions in sites adjacent to motion, such as the liver capsule. Moreover, the quantitative measurements extracted from PET, like the ubiquitous maximum standardized uptake value (SUV_{max}),

✉ Onofrio A. Catalano
onofriocatalano@yahoo.it

1 Department of Radiology, Massachusetts General Hospital, Harvard Medical School, 55 Fruit St, Boston, MA 02114, USA

2 Athinoula A. Martinos Center for Biomedical Imaging, 149 13Th St, Charlestown, MA 02129, USA

3 Medex, Rua da Gloria 344, Rio de Janeiro, RJ, Brazil

4 Medical University of Vienna, Spitalgasse 23, 1090 Vienna, Austria

5 BAMF Health, 109 Michigan St NW, Grand Rapids, MI 49503, USA

might be underestimated due to motion averaging [9]. PET/MRI introduces the simultaneous acquisition of PET and MRI and leverages MRI data to motion-correct PET events, resulting in more accurate measurements [10, 11]. MRI also allows protocol customization for specific primaries, adding sequences, such as diffusion-weighted imaging (DWI) and perfusion imaging to evaluate tumors beyond their anatomy. Given all the potential applications of PET/MRI in cancer staging and post-treatment evaluation, this review aims to consolidate the research findings on body oncologic applications of this diagnostic technology.

Methods

This narrative overview of the literature summarizes the findings of published research articles on PET/MRI for oncology (excluding neurologic applications) indexed in the online databases Google Scholar, PubMed, and Scopus, from its commercial introduction in 2011 to the present (2023). The same keyword combinations were used across these platforms. For each organ/system a combination of relevant terms on the topic, plus the term "PET/MRI," was entered in the appropriate search field. Detailed search queries for each topic are included in Table 1. The returned articles were curated by an expert in PET/MRI, with 12 years of clinical and research experience, and included in the manuscript according to scientific soundness and relevance of the findings. When relevant, the references from returned articles were also reviewed. The review is structured with the following outlines: Head and Neck, Thorax, Breast, Cholangiocarcinoma, Pancreas, Colon and Rectum, Genitourinary Cancer, and Gynecological Cancer.

Results

Head and neck

Head and neck cancers (HNC) comprise 3% of all malignancies, with 66,000 cases annually in the United States [12]. Histologically, most of them are squamous cell carcinomas. This anatomic region contains several critical structures. Hence, precise evaluation of the primary tumor size, as well as the involvement of regional lymph nodes, surrounding soft tissues, and osseous structures, is crucial for choosing the ideal treatment strategy. The superior soft tissue contrast of MRI makes it the preferred imaging modality for head and neck cancer evaluation, given its ability to delineate tumor invasion more accurately [13]. Metabolic imaging with 2-Deoxy-2-[18F]fluoroglucose ([18F]FDG) PET can enhance staging accuracy, identification of lymph node involvement, and differentiation of residual or recurrent disease [14]. Therefore, integrated PET/MRI, which combines the advantages of both methods, can meaningfully improve diagnostic accuracy (Fig. 1).

Previous studies show PET/MRI has a higher sensitivity and specificity in detecting HNC than stand-alone PET, CT, or MRI [15–18]. The high efficacy of PET/MRI in T staging of HNC has been demonstrated in several studies [19–21]. For example, PET/MRI showed high accuracy in the assessment of intracranial, retropharyngeal, skull, and prevertebral invasion, in addition to depicting perineural infiltration and

Table 1 Search queries for each review topic

Review topic	Search query
Head and Neck	("PET/MR" OR "PET/MRI") AND ("Head and Neck" OR "Cervical") AND ("Cancer" OR "Tumor" OR "Carcinoma")
Thorax	("PET/MR" OR "PET/MRI") AND ("Lung" OR "Bronchial") AND ("Cancer" OR "Tumor" OR "Adenocarcinoma" OR "Small-Cell -Carcinoma" OR "Non-Small-Cell Carcinoma" OR "Squamous Cell Carcinoma" OR "Large Cell Carcinoma")
Breast	("PET/MR" OR "PET/MRI") AND ("Breast") AND ("Lobular Carcinoma" OR "Ductal Carcinoma" OR "Cancer")
Cholangiocarcinoma	("PET/MR" OR "PET/MRI") AND ("Cholangiocarcinoma") OR (("Bile Ducts" OR "Bile Duct") and "Cancer")
Pancreas	("PET/MR" OR "PET/MRI") AND (("Pancreas" OR "Pancreatic") AND ("Cancer" OR "Carcinoma" OR "Adenocarcinoma" OR "Neuroendocrine Tumor")))
Colon and Rectum	("PET/MR" OR "PET/MRI") AND (("Colon" OR "Rectal" OR "Rectum" OR "Colorectal") AND ("Cancer" OR "Carcinoma" OR "Adenocarcinoma"))
Genitourinary cancer	("PET/MR" OR "PET/MRI") AND (("Renal Cell Carcinoma") OR (("Kidney" OR "Renal") AND "Cancer") OR ("Prostate" AND "Cancer")))
Gynecological cancer	("PET/MR" OR "PET/MRI") AND ("Cervical" OR "Uterine" OR "Ovarian" OR "Endometrial" OR "Vulvar" OR "Vaginal") AND ("Cancer" OR "Adenocarcinoma" OR "Squamous Cell Carcinoma" OR "Tumor")
Neuroendocrine tumors	("PET/MR" OR "PET/MRI") AND ("Neuroendocrine Tumor" OR "Carcinoid Tumor" OR "Pancreatic Neuroendocrine Tumor" OR "Gastrointestinal Neuroendocrine Tumor" OR "Lung Neuroendocrine Tumor" OR "Bronchial Neuroendocrine Tumor" OR "Small Intestinal Neuroendocrine Tumor" OR "Appendiceal Neuroendocrine Tumor")

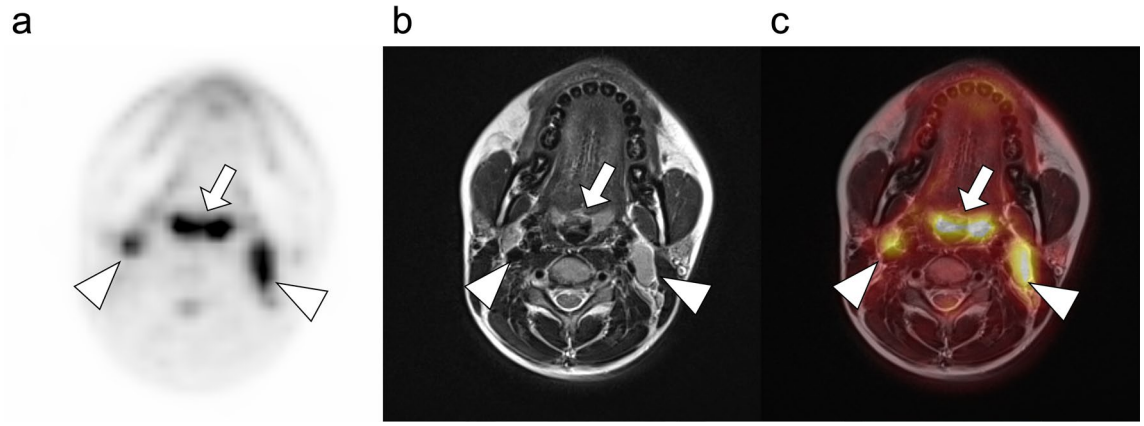

Fig. 1 Axial [18F]FDG-PET (**a**), corresponding level T2-weighted FSE (**b**), fused PET/MRI (**c**). Markedly avid head and neck cancer (arrow), infiltrating the soft palate, with associated bilateral cervical lymphadenopathy (arrowheads) are well depicted on both MRI and PET

muscular involvement [22, 23]. Another study reported a good imaging-pathological correlation between PET/MRI and surgical specimens in 67% of patients [24].

Before starting any therapy, assessment of nodal metastases is crucial since cervical lymph node involvement is common in HNC patients and is considered one of the most important predictors of prognosis. Nodal metastases are usually [18F]FDG avid. Thus, [18F]FDG-PET combined with DWI and dynamic contrast-enhanced MRI can be complementary to overcome the limitations of stand-alone MRI in detecting the small size and variable morphologic appearances of cervical lymph nodes [25].

Regarding M staging, the evaluation of lung and liver metastases is crucial, considering that those are the most common sites of spread in the 15% of patients who do develop distant metastases [26, 27]. While PET/MRI is superior in evaluating distant metastases from a range of primaries to a variety of organs, and especially to the bones, liver, lymph nodes, and peritoneum [28–32], it is limited in detecting lung metastases, especially if < 7 mm in maximal diameter [33]. Therefore, a dedicated chest CT needs to be obtained in those undergoing PET/MRI.

Thorax

Primary lung tumors

Tumors originating in the lung are highly lethal and are projected to account for 20% of cancer-related deaths in 2022 [12]. Non-small-cell lung cancer (NSCLC) comprises 85% of lung tumors and encompasses squamous cell carcinoma, adenocarcinoma, and large cell carcinoma [34]. For this group, [18F]FDG PET/MRI is comparable to [18F]FDG PET/CT in the initial staging [35]. Moreover, PET/MRI outperforms PET/CT in detecting brain and liver metastases [36]. The determination of tumor resectability is also adequately performed using [18F]FDG PET/MRI with a tailored protocol including breath-hold T1-weighted and respiratory-gated T2-weighted images [37]. Another prospective study with 50 patients showed a specificity of 92% and a sensitivity of 97% for [18F]FDG PET/MRI in determining primary tumor resectability [38] (Fig. 2).

A marked advantage of PET/MRI over PET/CT is the possibility of integrating a brain MRI into the whole-body scan. This integration saves time, contrast media, and is more convenient for the patient. The nervous system is the most common site of lung cancer metastases [39]; therefore, brain evaluation is of utmost importance in lung cancer staging.

Lung metastases

The lung is the third most common site of metastases for men and women [40]. Therefore, besides evaluating primary masses, it is essential to examine the lungs in the setting of any whole-body staging. In this regard, MRI is intrinsically limited due to low proton density and motion artifacts. Even though specialized MRI sequences, such as ultrashort echo time and zero-echo time, provide a better evaluation than standard Dixon images, MRI still falls short of CT performance for lung nodule detection [41–44]. PET/MRI inherits this deficiency, presenting subpar sensitivity for lung nodules ranging from 30 to 80% [33, 45–48]. This problem becomes more evident as nodule size decreases, with a sensitivity < 15% for ≤ 5 mm nodules [33]. However, in several types of malignancies, if metastatic disease is already detected elsewhere, diagnosing additional lung lesions may not change management. Thus, in most cases, [18F]FDG-PET/MRI is well positioned as a one-stop-shop modality for cancer staging (Fig. 3). Notwithstanding, in the specific cases where identifying a lung metastasis would result in management changes, PET/MRI should be complemented

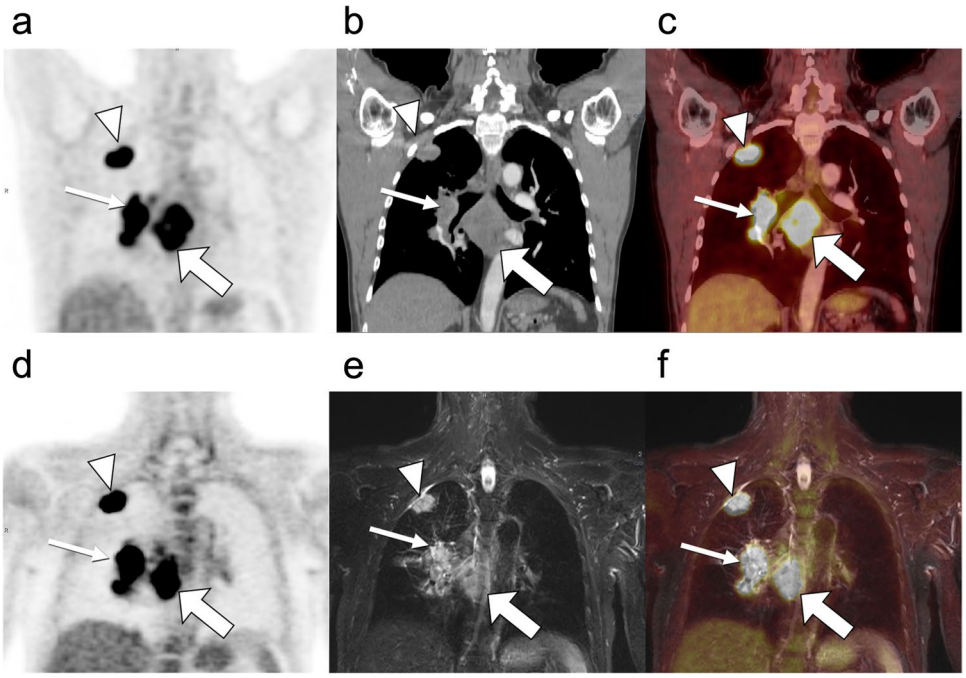

Fig. 2 Coronal [18F]FDG-PET from PET/CT (**a**), coronal CT (**b**), fused PET/CT (**c**), coronal [18F]FDG-PET from PET/MR (**d**), coronal STIR (**e**), fused PET/MRI (**f**). There is an [18F]FDG-avid mass in the right upper lobe (arrowhead), corresponding to primary lung cancer, with associated [18F]FDG avid right hilar (narrow arrow) and subcarinal (broad arrow) lymphadenopathy. Infiltration of the visceral pleura can be appreciated on STIR

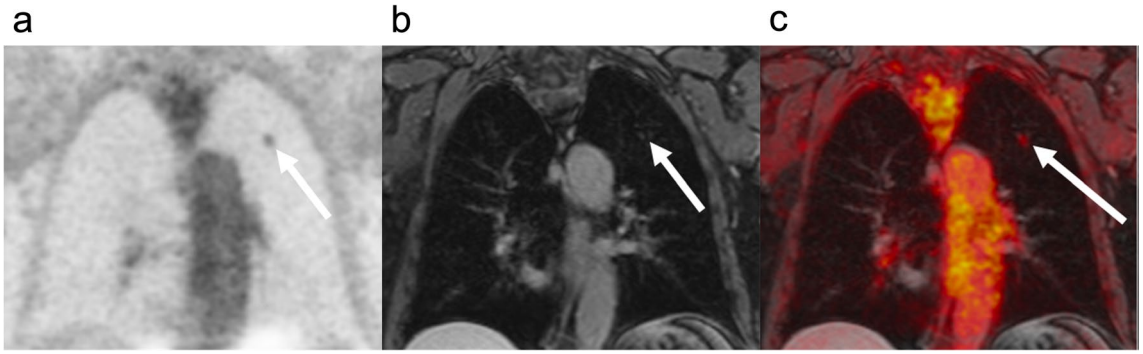

Fig. 3 Coronal [18F]FDG-PET (**a**), coronal T1-weighted fat saturated MRI (**b**), fused PET/MRI (**c**). An [18F]FDG-avid nodule (arrow), corresponding to pulmonary metastasis, in the left upper lobe is easily detected on PET. Detection on MRI might be challenging, given small size, in the absence of corresponding marked [18F]FDG avidity

by chest CT if negative for extrathoracic metastases and lung nodules.

Breast

Breast cancer is the most common neoplasm worldwide, and its annual incidence continues to increase in the United States [12]. MRI is the most accurate cross imaging modality for breast cancer evaluation, with a sensitivity of 99% and specificity of 89%, according to pooled data [49]. Regarding molecular imaging's role in breast cancer management, the National Comprehensive Cancer Network currently considers [18F]FDG PET/CT an optional test [50]. It is thought that PET/CT helps identify occult nodal or metastatic disease. By incorporating PET into the already best-in-class MRI, [18F]FDG PET/MRI might serve as a one-stop-shop modality in the staging of this disease. The proven diagnostic yield of MRI, combined with the incremental N and M staging performance delivered by PET, results in an even more robust test (Fig. 4). Case in point, [18F]FDG PET/MRI was superior to [18F]FDG PET/CT in whole-body staging [51, 52]. A retrospective study with 36 patients reported an increase in diagnostic confidence and changed the management in one-third of the cases when using [18F]FDG PET/MRI for the initial staging of invasive ductal carcinoma [53]. PET/MRI could detect additional nodal and distant metastases, which led to upstaging in 39% of the cases. A later meta-analysis found that this rate of change was lower when PET/CT was used for initial staging instead (25% for PET/CT vs. 39% for PET/MRI) [54]. In a prospective head-to-head

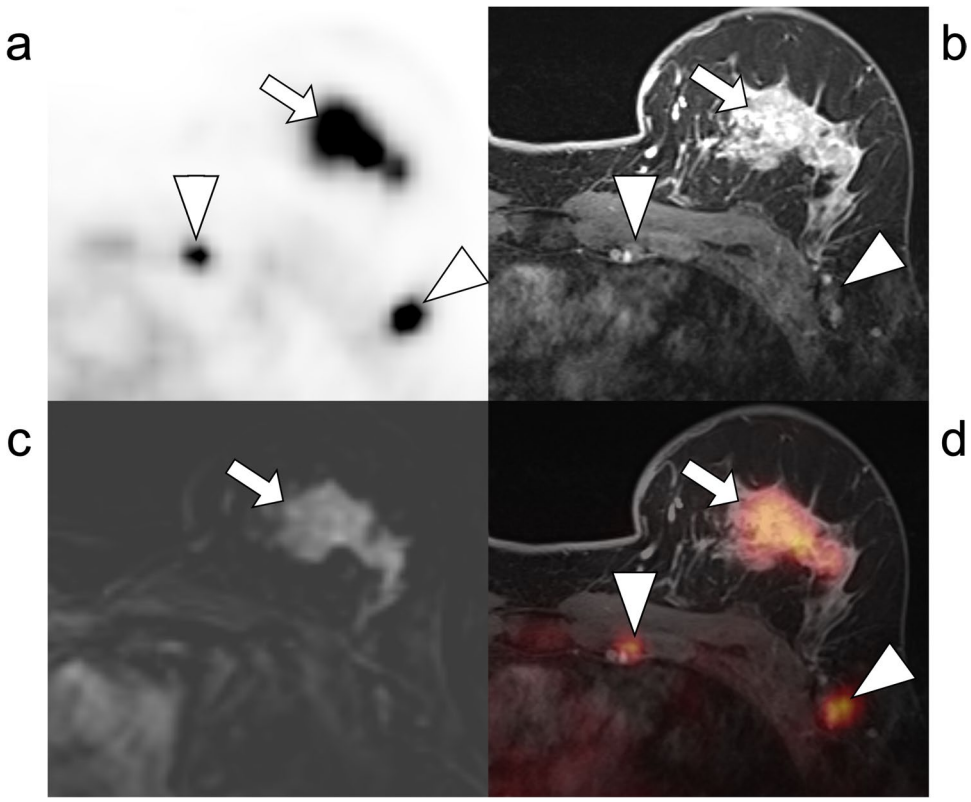

Fig. 4 Axial [18F]FDG-PET (**a**), axial high-resolution post-contrast T1-weighted MRI (**b**), subtraction early arterial phase T1-weighted dynamic contrast-enhanced MRI (**c**), fused PET/MRI (**d**). A large, [18F]FDG avid, markedly enhancing mass, corresponding to known invasive ductal carcinoma, infiltrates the left breast (arrows). [18F]FDG avidity improves detection of lymphadenopathy, including the small left internal thoracic lymphadenopathy (arrowheads)

comparison, [18F]FDG PET/MRI identified and correctly classified more lesions than [18F]FDG PET/CT [55]. In another direct comparison, PET/MRI was more effective than PET/CT in detecting bone metastases, presenting a sensitivity of 96% and a specificity of 99% [29]. [18F]FDG PET/MRI-derived biomarkers may also provide in-depth assessment of tumor biology and aggressiveness [56–58]. Ductal carcinoma has higher [18F]FDG uptake than lobular carcinoma. In the settings of lobular cancer, while detection of primary tumor, associated synchronous breast lesions, and overall local staging can be achieved by the MRI part of the study, [18F]FDG negative distant metastases in occult areas could be overlooked and may be better evaluated with other radiotracers discussed below [59]. In summary, in ductal breast cancer, [18F]FDG PET/MRI is an excellent tool to identify nodal and distant metastases, especially in younger patients and intermediate to high-grade tumors [53].

Fibroblast activation protein inhibitor (FAPI) has emerged as an alternative to [18F]FDG, targeting cancer-associated fibroblasts instead of increased glucose metabolism. A retrospective study reported [68Ga]Ga-FAPI uptake in 100% of the 19 primary breast tumors evaluated [60]. However, only 16% (3) of them had lobular carcinoma, which would be the histology in most need of a better radiotracer since [18F]FDG has already been proven effective for ductal carcinoma. For treatment response monitoring, the [68Ga]Ga-FAPI tumor-to-background ratio was associated with complete pathologic response [61]. Moreover, [68Ga]Ga-FAPI PET/MRI performed better than MRI alone for treatment response assessment in breast cancer [61]. PET/CT studies suggest that [68Ga]Ga-FAPI outperforms [18F]FDG in breast cancer, achieving a sensitivity of 100% and specificity of 96% versus 78% and 100%, respectively, for [18F]FDG. Further prospective PET/MRI studies are needed to determine if the same advantages are observed.

Abdomen

Cholangiocarcinoma

Cholangiocarcinomas are tumors arising from the biliary tree whose treatment is often surgical. Thus, careful evaluation of its relationship to adjacent vasculature and lymph node involvement is essential [62]. The majority of cholangiocarcinomas are perihilar, with extrahepatic disease representing 40% of the cases and intrahepatic tumors the other 10% [63]. Morphologically, cholangiocarcinoma may be mass forming, periductal infiltrating, intraductal, superficial spreading, or undefined [62]. The staging of cholangiocarcinoma often involves a multimodal strategy, including contrast-enhanced CT, MRI with MRCP, and PET/CT imaging to completely evaluate the tumoral extension, nodal involvement, and distant metastases, even though only the first two are listed in the National Comprehensive Cancer

Network guidelines [64–67]. The main limitations of such methods that can be overcome by PET/MRI are detecting small lesions, especially subcentimeter intrahepatic lesions, and peritoneal metastases [30].

[18F]FDG PET/MRI resulted in management changes in 30% of the cases with untreated, mass-forming intrahepatic cholangiocarcinoma when compared to the management that would have been proposed after conventional imaging [32]. Another study of [68Ga]Ga-FAPI PET/CT plus PET/MRI versus [18F]FDG in hepatic tumors, including 13 patients with cholangiocarcinoma, showed that [68Ga]Ga-FAPI was better than [18F]FDG for hepatic lesions, but was similar to MRI alone [68]. However, [68Ga]Ga-FAPI PET may contribute by identifying additional positive nodes and distant metastases. Therefore, the available data suggest that PET/MRI, especially when performed with [68Ga]Ga-FAPI, may perform better than CT, MRI, or PET alone in cholangiocarcinoma.

Pancreas

Pancreatic cancer is a lethal pathology with a rising incidence in the United States [69] and the 7th leading cause of cancer-related death worldwide [70]. Pancreatic cancer staging is usually performed with contrast-enhanced CT or MRI [71]. Notwithstanding, the use of [18F]FDG PET/MRI in the staging and post-treatment evaluation may be warranted since a retrospective study found that in 49% of cases [18F]FDG PET/MRI resulted in changes in management when compared to standard of care imaging [72]. Further, post-neoadjuvant therapy response is well correlated to [18F]FDG PET/MRI metrics, such as a change in SUV_{max} [73]. [68Ga]Ga-FAPI PET/MRI has also been used to successfully used to differentiate pancreatic cancer from IgG4-related pancreatitis in a case of ambiguous [18F]FDG PET imaging [74]. A prospective study with 33 patients comparing [68Ga]Ga-FAPI to [18F]FDG PET/CT showed a higher sensitivity for lymph node metastases but a lower detection rate for hepatic metastases for the former. While more studies are needed to provide more definitive conclusions, PET/MRI is positioned to become a staple in pancreatic cancer staging and restaging.

Colon and Rectum

Colorectal cancer is responsible for a major societal burden, being the third most prevalent cancer in males after prostate and lung and in females after breast and lung [12]. The standard of care for whole-body evaluation in colorectal cancer includes a pelvic MRI and a CT scan of the chest and abdomen. Whole-body [18F]FDG PET/MRI adds clinical value to this diagnostic process by detecting additional lesions and allowing better characterization of extracolonic lesions [75]. In the local staging of rectal tumors, PET/MRI improves T staging [76], the assessment of tumor size, and sphincteric infiltration [77], both of which may change surgical planning (Fig. 5). Moreover, PET/MRI presents better N staging versus MRI alone, thanks to the PET component, which can identify pathologic lymph nodes that do not meet cross sectional imaging size criteria for suspicion (Fig. 6). The M staging is also improved when using PET/MRI versus CT for liver metastases [28, 78, 79] (Fig. 7). This is especially important considering that the liver is the most common site of metastatic spread in colorectal cancer, and up to 25% of patients with colorectal cancer will develop liver metastases over the course of their disease [80, 81]. In oligometastatic colorectal cancer, [18F]FDG PET/MRI may change patient management in 19% of the cases (95% confidence interval 9–37%) [82]. Based on an initial study with [68Ga]Ga-FAPI PET/CT, [68Ga]Ga was superior to

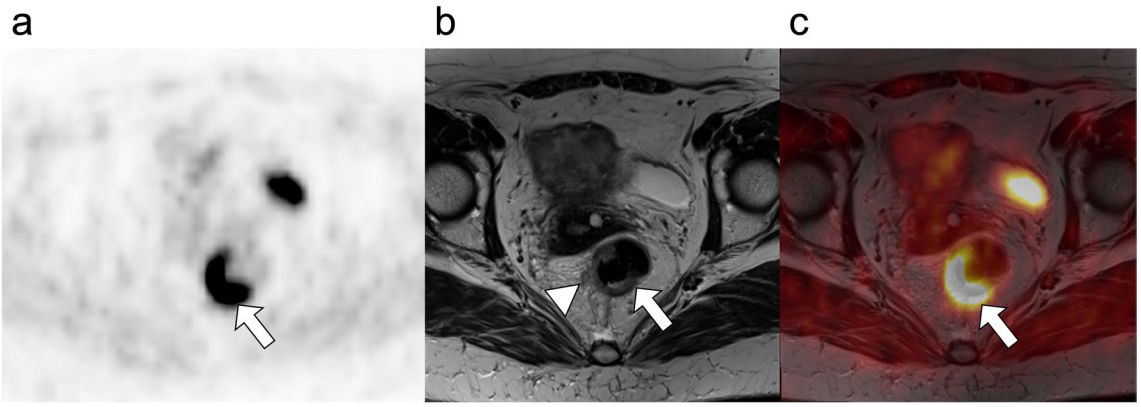

Fig. 5 Axial [18F]FDG-PET (**a**), axial T2-weighted high-resolution FSE MRI (**b**), fused PET/MRI (**c**). Semi-circumferential rectal wall thickening, corresponding to known rectal cancer, demonstrates intermediate signal intensity in (**b**) and marked [18F]FDG uptake in (**a**). Extension beyond the tunica muscularis (arrowhead) for about 10 mm (T3c) would have been missed on PET images but is well depicted on MRI

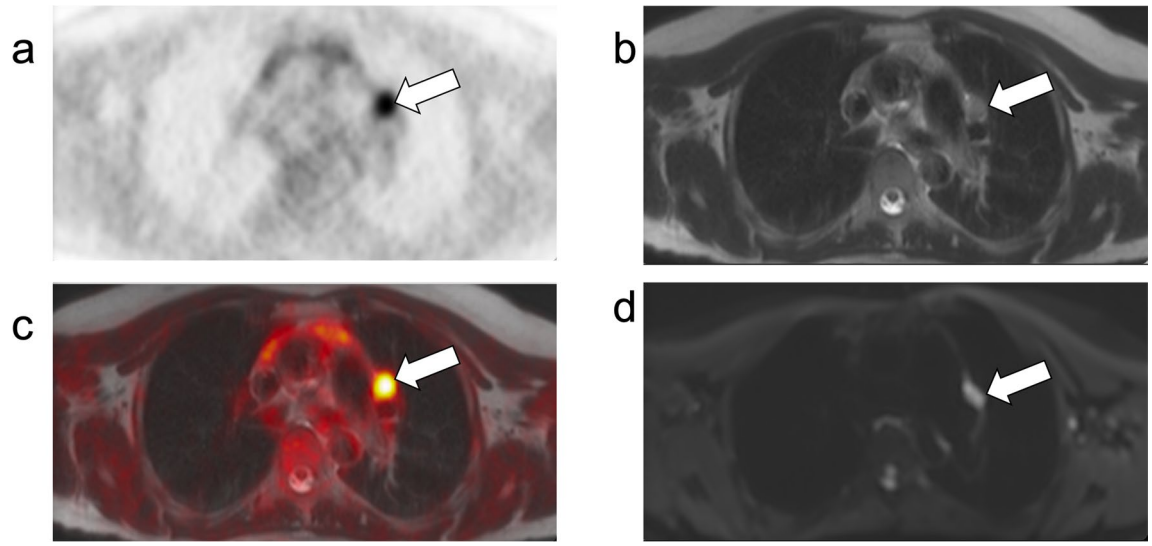

Fig. 6 Axial [18F]FDG-PET (**a**), T2-weighted SSFSE (**b**), fused PET/MRI (**c**), corresponding level DWI (**d**).Metastatic lymph node from colorectal cancer. On PET/MRI, metastatic lymph nodes (arrow) tend to concordantly demonstrate increased [18F]FDG avidity, heterogeneous internal signal and diffusion restriction as in this case. Note also exquisite delineation of lymph node from adjacent vasculature despite lack of IV contrast

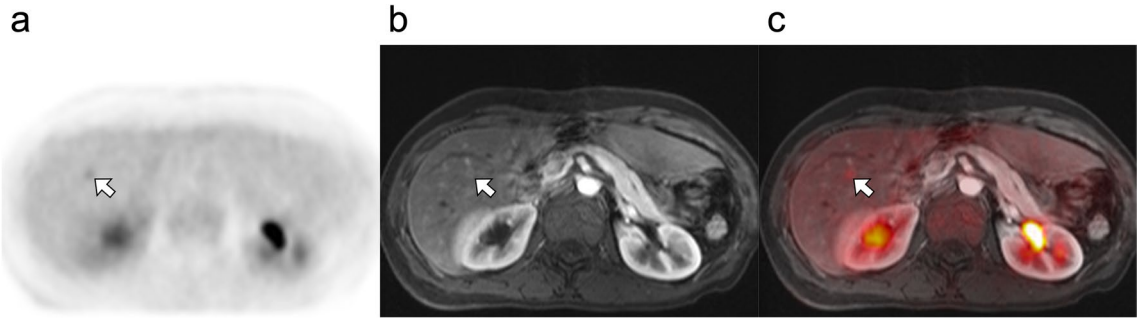

Fig. 7 Axial [18F]FDG-PET (**a**), axial fat saturated post-contrast T1-weighted MRI (**b**), fused PET/MRI (**c**). A subcentimeter, mildly [18F]FDG avid liver metastasis (arrow) might have been missed on stand-alone PET or stand-alone MRI; however, simultaneously acquired MRI and PET facilitate lesion detection and characterization

[18F]FDG in the detection of primary and metastatic lesions in gastric, duodenal, and colorectal cancers. Additionally, FAPI presented higher uptake in most lesions [83]. [68Ga] Ga-FAPI also led to upstaging when compared to the TNM-assigned stage by [18F]FDG PET/CT in 21% of the cases.

Musculoskeletal

Emerging studies on the role of PET/MRI in primary bone malignancies found it a promising modality that allows for precise local staging and detection of distant metastases with reduced patient exposure to radiation [84–87]. To evaluate musculoskeletal (MSK) malignancies, in addition to [18F] FDG, the most widely used radiopharmaceutical, one can use [18F]-sodium fluoride ([18F]-NaF) as a bone-seeking agent capable of detecting bone metastases, especially in tumors with low [18F]FDG affinity, like renal cell carcinoma and thyroid cancer [88]. Based on the published studies, PET/MRI is an excellent modality for the evaluation of soft tissue neoplasms. PET/MRI for T staging in sarcoma is equivalent to MRI, while the PET component improves N and M staging l [89]. MRI is an accurate tool for local staging in soft tissue sarcomas thanks to its ability for excellent delineation of tumor margins as well as detection of osseous and neurovascular invasion. Adding these potentialities of MRI to simultaneously acquire metabolic information from PET can yield a more accurate local staging [90]. The same applies regarding lymph node involvement since [18F]FDG-PET showed 96% sensitivity in the detection of involved lymph nodes compared with stand-alone CT and MRI [91].

Metastases detection by PET/MRI faces the aforementioned limitation of this modality for the assessment of pulmonary metastases, while it remains superior for detecting other distant metastases [4, 28, 33, 52, 92]. FAPI can overcome some of the limitations of [18F]FDG, such as the high [18F]FDG avidity of bone marrow and its low uptake in low-grade sarcoma. FAPI has an excellent tumor-to-background ratio in sarcomas. Therefore, FAPI-PET/MRI can be used as a single examination to provide all the necessary information regarding treatment and staging in affected patients [93, 94]. PET/MRI is also useful to guide treatment and identify biopsy targets in sarcomas [95]. The detailed anatomic (MRI) and functional (PET) information provided simultaneously on PET/MRI can yield more accurate and reliable TNM staging in both primary and metastatic MSK neoplasms. The diagnostic value of this modality may be optimized by the appropriate radiopharmaceutical and MRI protocol selection [96, 97].

Genitourinary

Prostate cancer

Prostate cancer is the most common cancer type in males and is projected to account for 27% of the newly diagnosed cancers in this patient population [12]. Prostate-specific membrane antigen (PSMA) is a transmembrane enzyme that is overexpressed in prostate adenocarcinoma; its degree of expression is usually correlated with tumor grade [98]. PSMA analogs have been developed to target prostatic cancers. Their use is particularly useful in patients with low serum PSA, whose lesions can be more subtle and missed by anatomic imaging alone or non-specific tracers, such as [18F]FDG. Examples of FDA-approved agents to date include [18F]DCFPyL and [68Ga]PSMA-11. [68Ga]PSMA PET/MRI was superior to PET alone and multiparametric MRI alone for prostate cancer localization (AUROCs of 0.88, 0.83, and 0.73, respectively) [99]. Compared to multiparametric pelvic MRI, the current standard of care, PSMA PET/MRI, increases the sensitivity (46% vs. 69%) of extracapsular extension evaluation at the expense of specificity (94% vs. 90%) [100]. PSMA PET/MRI may also improve nodal staging and distant metastasis evaluation, especially in the bones, where MRI is superior to CT [101–103] (Fig. 8). Besides initial staging, PSMA PET/MRI performs well in the setting of restaging/biochemical recurrence, with a sensitivity of 99% [104]. PSMA PET/MRI detection rate in biochemical recurrence is related to the PSA levels, with values < 0.5 ng/mL presenting significantly less lesions vs. PSA value ≥ 2 ng/mL [105]. However, even at low PSA levels, PSMA positivity is still relevant at 54.5%, and most of these patients had a distant recurrence in the lymph nodes or bones [106]. Notably, besides stellar performance for whole-body metastases detection, PSMA PET/MRI performs better than PSMA PET/CT to assess recurrent disease in the prostatectomy bed.

Kidney cancer

Renal tumors accounted for 4% of new cancer diagnoses in the United States in 2022 [12]. PSMA is a expressed in several tissues, including the small intestine, proximal renal tubules, and salivary glands [107]. Unfortunately,

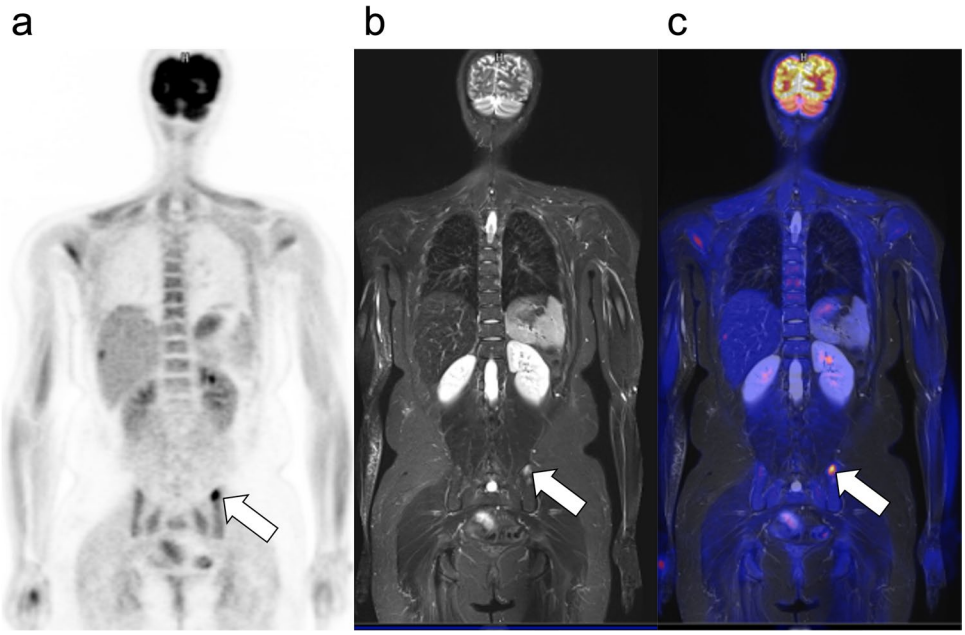

Fig. 8 Coronal [18F]FDG-PET (**a**), coronal STIR MRI (**b**), fused PET/MRI (**c**). An [18F]FDG-avid focus denotes a metastatic lesion in the left iliac bone, which matches an area of high signal on STIR

this expression, coupled with the urinary excretion of most PSMA ligands, makes imaging primary kidney tumors challenging with the radiopharmaceutical [108, 109]. However, in the characterization of primary renal cancers, [68Ga] PSMA PET/CT SUV_{max} has been shown to differentiate histologic tumor grade [110] and also differentiate benign and malignant tumors [111]. Finally, [18F]-PSMA PET/CT has been used to evaluate treatment response in patients with metastatic renal cell carcinoma undergoing immune checkpoint inhibitor therapy, detecting changes that were missed by RECIST [112]. [18F]DCFPyL has been successfully used in PET/CT imaging of metastatic renal cell carcinoma, detecting more lesions than CT or MRI [113–115]. PET/MRI is yet to be applied in the context of renal cancers, but we can expect similar or even better results than with PET/CT.

Gynecological cancer

Cervical, ovarian, and uterine cancer are among the ten most common cancers in females, and gynecologic cancers accounted for about 672,00 deaths in 2020 worldwide [116]. They are classified based on the anatomic origin, including cancers of the ovaries and fallopian tubes, uterine corpus, uterine cervix, endometrium, vagina, and vulva [117]. The risk of gynecologic cancer increases with age, and early diagnosis is paramount for the most effective treatment. PET/MRI showed similar efficacy in the evaluation of local tumor extent with that of contrast-enhanced pelvic MRI, which is a common modality for the evaluation of tumor size and local extension in gynecologic settings [118–121]. In two studies of cervical cancer, PET/MRI showed high accuracy for T staging (83.3%, 85%) and N staging (90%, 87%) [119, 120, 122] (Fig. 9). Another study using PET/MRI for ovarian cancer reported accuracies of 96.4%, 93.9%, and 100% for T, N, and M staging, respectively (Fig. 10). Additionally, PET/MRI allows better treatment planning due to its higher sensitivity for distant metastasis [122]. In comparison with PET/CT, PET/MRI was reported to be equivalent or more accurate for detecting lymph node metastases in cervical cancer [120, 123]. Moreover, as reported in a study of 30 patients with endometrial cancer, PET/MRI and PET/CT showed the same sensitivity, specificity, and accuracy (100%, 96.3%, and 96.7%, respectively) for detecting pelvic nodal metastases [124]. Another study specifically focused on the detection of deep myometrial invasion and lymph node involvement of Endometrial Cancer using PET/MRI reported good performance in preoperative staging (sensitivity of 0.8571, specificity of 0.9286, accuracy of 0.9143) [125]. Moreover, this study showed that MRI parameters, such as tumor volume, volume index, and tumor volume ratio, together with PET parameters, like total lesion glycolysis, may predict lymphovascular space invasion, with MRI parameters also being able to classify patients into low or high risk. Regarding distant metastases, PET/MRI showed a high sensitivity for the detection of metastatic liver lesions (95%) as well as peritoneal carcinomatosis (97%) [28, 30]. However, more studies are needed to confirm the role of PET/MRI in gynecological malignancies.

Neuroendocrine tumors

Neuroendocrine tumors can arise in different organs and share neuromarker expression, such as chromogranin A and synaptophysin; they also variably express different classes of somatostatin receptors [126]. The evaluation of neuroendocrine tumors is thus facilitated on PET/MRI due to the superb soft tissue contrast resolution of MRI paired with the ability to customize the PET scan by choosing different tracers according to the underlying tumor biology. In a pilot study with [68Ga]DOTATOC including 8 patients, PET/MRI was able to detect all malignant neuroendocrine

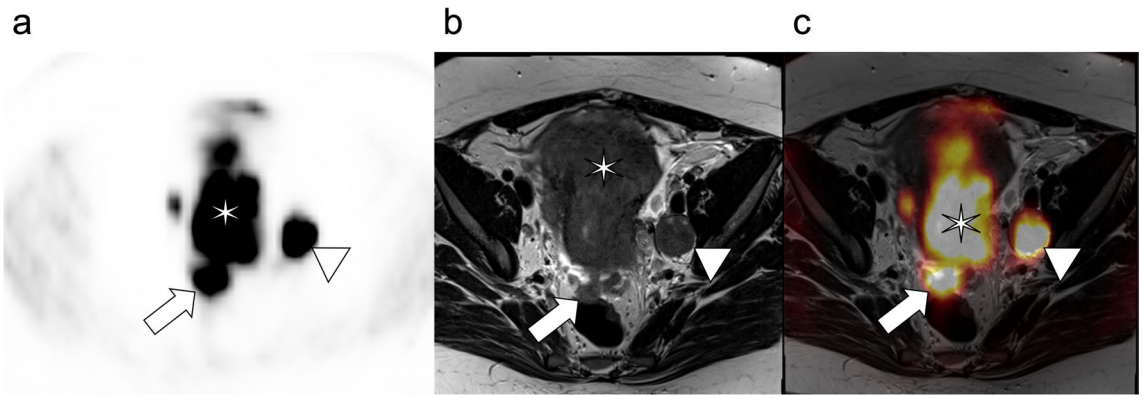

Fig. 9 Axial [18F]FDG-PET (**a**), axial T2-weighted MRI (**b**), fused PET/MRI (**c**). Large cervical cancer (asterisk) infiltrates the uterus, bilateral parametria, peritoneum (arrow) and metastasizes to pelvic lymph nodes (arrowhead). Note high-quality anatomic layout provided by MRI and perfect coregistration with PET, ensured by simultaneous PET/MR acquisition

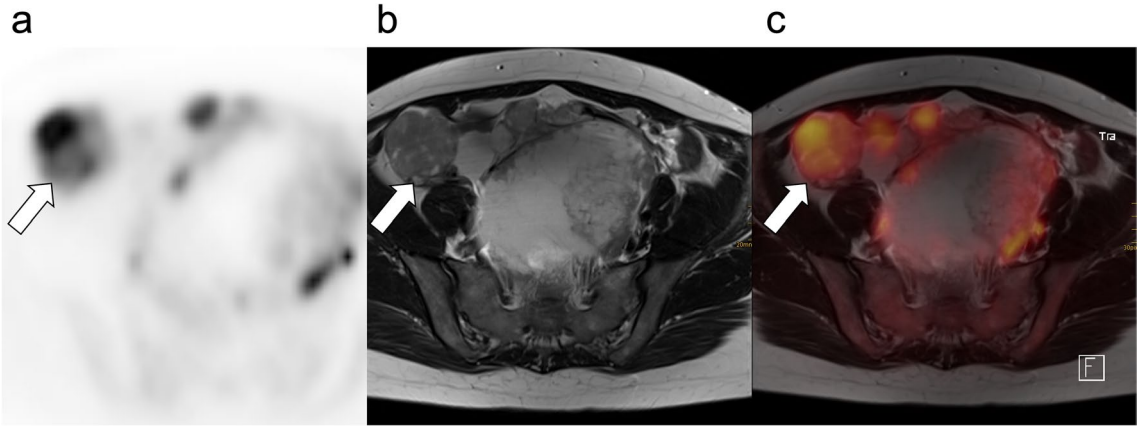

Fig. 10 Axial [18F]FDG-PET (**a**), axial T2-weighted high resolution FSE MRI (**b**), fused PET/MRI (**c**). Large ovarian cystadenocarcinoma occupies the entire pelvis. Solid components (arrow) demonstrate marked [18F]FDG avidity

lesions, although 4 benign and indeterminate lung lesions detected on PET/CT were not seen on PET/MRI [127]. A larger study assessed the performance of the same radiotracer in PET/CT and PET/MRI in 28 patients with neuroendocrine tumors, where PET/MRI outperformed PET/CT in liver lesion detection thanks to the possibility of performing hepatobiliary phase contrast-enhanced imaging and DWI that increased the sensibility beyond PET-positive lesions. In a separate study with similar design, review of 197 lesions in 30 patients showed a higher proportion of correctly classified neuroendocrine lesions on PET/MRI than on PET/CT (90.8% vs. 86.7%, $p = 0.031$), with PET/MRI also presenting better lesion conspicuity than PET/CT, with the caveat of only ~ 10% of the lesions having had pathological confirmation [128]. A third study with 12 patients comparing [68Ga] DOTATOC PET/MRI and PET/CT showed PET/MRI superiority in lesion detection (72.5% vs. 62.7%, respectively, $p = 0.01$) [129]. Overall, these results suggest PET/MRI is equivalent to or better than PET/CT for neuroendocrine tumor evaluation with DOTATOC. Another study using a different tracer, [68Ga]DOTANOC, showed a slight advantage of PET/MRI over PET/CT for neuroendocrine tumor imaging, with an overall accuracy for PET/MRI of 97% (95% CI, 94.4%–99.6%), versus 94.6% (95% CI, 91.2%–98.1%) for PET/CT [130]. Of note, as mentioned beforehand the evaluation of lung metastases can be compromised on PET/MRI due to MRI limitations for chest imaging, and this study replicated such deficit – three pulmonary lesions and one pleural metastasis were missed by PET/MRI, resulting in 0% sensitivity (95% CI, 0%–70.8%) for this segment. In a retrospective study, PET/MRI with [68Ga]DOTATATE PET/MRI detected additional lesions when compared to [68Ga]PET/CT, with better characterization of lesions in the liver, pancreas, and pelvis [131]. Even without using gadolinium contrast, PET/MRI can achieve a performance similar or superior to contrast-enhanced PET/CT, which is important in patients with risk factors for nephrogenic systemic fibrosis [132]. In summary, a variety of tumor-specific radiotracers have been developed for neuroendocrine tumor imaging, and PET/MRI explores these tracers with remarkable synergy thanks to the intrinsic soft tissue contrast of MRI coupled with protocol flexibility that allows for inclusion of sequences, such as DWI and hepatobiliary phase imaging.

Limitations and Pitfalls

Although a promising technology with several paradigm-shifting results as presented above, PET/MRI presents some drawbacks. Patients with ferromagnetic implants or other devices that are not compatible with MRI might be better suited for PET/CT evaluation. Even in MRI-compatible materials, the associated field inhomogeneity leads to significant image distortion and compromise attenuation correction [133, 134]. Moreover, a comprehensive lung evaluation as part of the whole-body PET/MRI is still suboptimal, especially in lesions measuring 6 mm or smaller. A dedicated chest CT should be considered in cases where sufficient suspicion of lung lesions is warranted. Finally, cost, accessibility, and personnel training remain significant barriers to PET/MRI adoption, despite some studies already showing a favorable cost-effectiveness profile for PET/RMI given appropriate indications [135].

Conclusions

PET/MRI is in a unique position to become the standard whole-body staging for body oncology by combining precise anatomic localization, functional and metabolic data in a single and simultaneously acquired study.

Authors contribution This article was conceptualized by OAC, FSF, MH, SM, HK, and AH performed the literature search and data analysis; FSF, MH, and OAC drafted the manuscript; and SM and OAC critically revised the work.

Funding No funding was received for conducting this study.

Declarations

Conflict of Interests The authors declare no competing interests.

Ethics approval This is a review study. This article does not contain any studies with human or animal subjects performed by the any of the authors. The Institutional Review Board has confirmed that no ethical approval is required.

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