PET/MR imaging of neoplastic and inflammatory lesions

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Chapter 1

Introduction

From: An overview of PET/MR, focused on clinical applications.
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Imaging inflammation and cancer by PET/MR

PET/MR is an innovative hybrid imaging technique that allows acquiring and fusing anatomical and functional data from magnetic resonance (MR) with metabolic information from positron emission tomography (PET) (1,2). MR and PET may be acquired simultaneously (co-acquisition) or sequentially (1,2). In the setting of co-acquisition, the MR and PET components simultaneously image the same body region. This allows for complete spatial and temporal matching of MR and PET data (1).

Development of PET/MR has recently advanced with innovations such as larger bore MR scanners, magnetic field insensitive avalanche photodiodes, and cupper shielding (3).

Precise quantification of attenuation correction by PET/MR is challenging (3). A variety of methods such as Dixon-based tissue decomposition to atlas-based attenuation maps, to ultra-short echo time sequences (UTE), have helped but not completely resolved this issue (3–5).

PET/MR is the only hybrid imaging technology capable of co-acquisition of PET with morphologic imaging. This ensures temporal and spatial correlation of morphologic and functional data with one technique potentially complementing the other. In particular, PET quantification may be improved by MR anatomic information, which in turn may help *in vivo* validation of functional MR techniques (6). Moreover, MR-driven PET motion correction may reduce blurring and improve PET quantification in the case of patient motion, respiration, and bowel peristalsis (7).

PET/CT is the most accurate imaging technique for the staging of several solid organ neoplasms, with accuracy higher than CT or PET alone (8,9). PET detects metabolically active lesions and quantifies the amount of radiotracer uptake, expressed as standard uptake value (SUV), which might be helpful in evaluating treatment response (10,11). However, PET/CT is limited by the asynchronous acquisition of PET and CT, that induces potential miss-match between PET events and corresponding anatomic correlates, and by the ntrinsically low soft tissue contrast of CT. Moreover, background physiologic radiotracer activity in conjunction with the low soft tissue resolution of CT can compromise detection of lesions with a low metabolic rate (for example some low-grade lymphomas) (12–19).

On the contrary, PET and MR data can be acquired simultaneously in PET/MR, with an ideal matching of the metabolic data of PET and the morphofunctional information of MR. This optimizes anatomic correlates for PET events and can produce unique hybrid biomarkers to potentially investigate lesion histology (for example discriminating inflammatory from fibrotic strictures in Crohn disease) or explore the molecular profile of cancer. Moreover, PET/MR provides superior soft tissue contrast to noise ratio and signal to noise ratio,which are fundamental in evaluating soft tissue pathology commonly encounted in abdominopelvic and breast imaging (1,12,20). MR is also capable of providing functional information, like diffusion weighted imaging (DWI) and the resultant apparent diffusion coefficient

(ADC) that may further enhance PET performance. Meanwhile, PET can improve the specificity of DWI and of ADC values.

The synergism of PET/MR, and the possibility to obtain unique hybrid functional metabolic biomarkers, that could potentially provide insights into tissue composition and molecular features of lesions, inspired us to investigate PET/MR in oncology and in Crohn's disease (CD).

Role of [^{18}F]-FDG PET/CT in Crohn's disease

Several groups have evaluated the use of PET in Crohn disease (CD). Skehan *et al.* in 25 paediatric patients with suspected IBD, 15 of whom with CD, found that [^{18}F]-FDG PET had an overall sensitivity of 81% and a specificity of 85%. Moreover, when colonoscopy was limited, PET localized further inflammatory areas in the proximal large bowel. Authors concluded that PET is a useful technique in children and it may be used an adjunct to colonoscopy and barium studies when they are unsuccessful (21).

Several years later, the same group confirmed that PET identified active inflammatory disease in 81.5% of CD patients, according to endoscopic results. Therefore, although PET cannot replace conventional studies, it might be considered as an alternative technology in the appropriate clinical setting, keeping in mind the associated radiation exposure (22). Also, Loffler *et al.* performed FDG-PET in 23 paediatric patients, 17 of whom with CD, obtaining a sensitivity and specificity equal to 98% and 68% with histology as standard of reference, and 92% and 65% with endoscopy as standard of reference, respectively (23). They considered PET as a fast, non-invasive imaging method with low radiation exposure that allows the assessment of disease activity in children at an early stage.

Other authors evaluated the accuracy of FDG-PET to non-invasively assess inflammation in 43 CD patients, using ileocolonoscopy and magnetic resonance enterography (entero-MR) as reference standards. PET results were comparable to entero-MR for the assessment of the proximal ileum, and complementary to colonoscopy to assess the nature of strictures, suggesting PET as a promising non-

invasive technique for clinical management of CD (24). The same group compared PET to entero-MR and anti-granulocyte scintigraphy (GAB) in 59 patients with active CD. PET had the highest sensitivity (85%) followed by entero-MR (67%) and GAB (41%), while it demonstrated lower specificity (89%) than entero-MR (93%) and GAB (100%). Authors concluded that non-invasive detection of inflamed gut segments in CD with PET offers high sensitivity and specificity (25).

Berthold *et al.* (26) compared PET versus PET/CT in 23 children and adolescents, 19 of whom with CD, using endoscopy with biopsy and histology as gold standard. The authors demonstrated that, although CT provided additional anatomical information, only PET was able to locate the active disease in the gut segments. Moreover, PET detected extra intestinal inflammation, and allowed the assessment of the extent and degree of high-grade inflammation, especially in those small bowel segments that were not accessible to endoscopy. Several authors have investigated whether CT provides better anatomical details, improving the diagnostic accuracy of PET, for the assessment of inflammation in adult and paediatric patients with CD. Bettenworth et al. (27) performed PET/CT in 25 patients with histologically diagnosed Crohn's colitis. PET/CT was positive in 88% of extensive ulcerations, but only in 50% of superficial epithelial lesions. The author concluded that PET/CT is a non-invasive and promising translational method. Moreover, they found that the intestinal glucose uptake is variable and pathologic segments might be difficult to distinguish from normal ones. The same group compared [^{18}F]-FDG PET/CT, entero-MR and trans-abdominal ultrasound in order to evaluate the best non-invasive imaging method for the detection and differentiation of inflammatory and fibromatous stenoses in CD, using endoscopy and histology as reference standards. A combination of trans-abdominal ultrasound and PET/CT or entero-MR led to a 100% detection rate (28). Jacene et al. (29) preoperatively investigated the accuracy of PET/CT in CD patient with obstructive symptoms in comparison to postoperative histopathological analyses of these lesions. In their study, different lesions demonstrated FDG uptake, including inflammatory lesions, fibrotic strictures and muscle hypertrophy. The authors suggested that, although a qualitative PET analysis is sensitive, a semi-quantitative

analysis could help identifying patients with active inflammation, using the maximum lean standardized uptake value (SUL_{max}). Another group studied the clinical utility of PET/CT in 7 patients, 4 of whom with CD, and showed that PET/CT can be viewed as a useful imaging method in diagnosis, management and clinical decision-making of patients with known or suspected CD (30). Louis and colleagues in a prospective study, which included 22 patients with active CD, found that PET/CT detected 35 of 48 endoscopically affected segments, with a sensitivity and a specificity of 72.9% and 55.3%, respectively. Furthermore, severe endoscopic lesions, such as deep ulcers and strictures, were detected by PET/CT with a sensitivity of 100%, suggesting a direct correlation between PET sensitivity and clinical significativity. Overall, PET/CT scores correlated with clinical parameters, endoscopy and biological activity of CD (31). Meisner *et al.* conducted another study using PET/CT for the assessment of disease activity in 12 patients with IBD, 7 of whom with CD. In their study, PET/CT was positive in 59.4% of segments and there was 81.3% correlation between PET activity and clinical activity, demonstrating utility of PET as a non-invasive technique to identify active inflammatory regions in CD (32). The feasibility and potential clinical utility of [^{18}F]-FDG PET/CT for the assessment of CD activity was also investigated in a study performed by Saboury *et al.* in which 22 subjects underwent PET/CT followed by ileocolonoscopy in order to correlate imaging results with clinical and endoscopic findings. PET/CT detected 15 additional segments compared to those visualized by endoscopy and all global PET parameters correlated with standard clinical scores (CDAI), allowing a new quantitative analysis of regional and global CD activity using PET imaging (33). Recently, Russo and colleagues evaluated the role of [^{18}F]-FDG PET/CT as a marker of progression of inflammatory activity and its response to anti-TNF therapy in 22 patients with CD. PET/CT sensitivity and specificity were respectively 88% and 70%; moreover, SUV correlated with clinicopathological markers like C-reactive protein and Harvey-Bradshaw Index (34).

Other authors studied the CD activity combining [^{18}F]-FDG PET with CT enteroclysis or CT enterography. Das *et al.* included in a prospective study 17 patients, 9 of whom with CD, using PET/CT enteroclysis in order to obtain both

morphological and functional details. PET/CT enteroclysis outperformed barium studies and colonoscopy in detecting affected segments in the small and large bowel (50 versus 16 versus 17 segments respectively). Furthermore, PET/CT enteroclysis detected also extra-intestinal abnormalities and differentiated active from fibrostenotic CD (35). Ahmadi and colleagues examined the role of combined [^{18}F]-FDG PET/CT enterography (CTe) in active CD. CTe identified 48 abnormal small bowel segments as well as PET. The authors also found a correlation between CTe score and SUV_{max}, suggesting a similar sensitivity of both imaging methods; moreover, PET provided additional information quantifying the degree of inflammation in abnormal small bowel segments (36).

Groshar *et al.* performed [^{18}F]-FDG PET/CTe in 28 patients with known or suspected CD in order to correlate the CTe score and SUV_{max} for the assessment of the grade and severity of inflammation in abnormal segments. They detected 85 abnormal segments in 22 patients, with a good correlation between SUV_{max} and CTe measurements of mural thickness and enhancement, concluding that SUV_{max} might be a reliable parameter to quantify CD activity (37).

Finally, Shyn *et al.* compared [^{18}F]-FDG PET/CTe with CTe alone with the purpose of evaluating the diagnostic efficacy of the two imaging methods in 13 patients with CD. Different parameters such as CTe severity score, SUV_{max}, simplified endoscopic score, and clinical parameters correlated with pathology inflammation grade. In 3 patients, PET detected active inflammation and an enterocolonic fistula, not revealed by CTe alone. SUV_{max} strongly correlated with disease activity, suggesting that PET/CTe might improve the detection and grading of active inflammation in CD patients (38).

PET/MR in IBD: advantages and disadvantages

Hybrid PET/MR scanners are the most advanced, clinically approved devices available for in-vivo diagnostic imaging. They can simultaneously (co-acquisition)

or sequentially acquire metabolic data from positron emission tomography (PET) as well as functional and morphologic information from magnetic resonance (MR) (1,2).

In the setting of co-acquisition, the PET and MR components of this hybrid technology simultaneously image the same body region, allowing a nearly complete spatial and temporal matching of PET and MR data. This spatial and temporal matching is not achievable by sequential PET/MR scanners neither by PET/CT, with the latter being limited by the necessarily asyncronous acquisition of the PET events and the CT data (1). The matching of the PET and MR data translates into the possibility of exploring a queried lesion, for example a thickened bowel loop, with a large array of PET and functional MR (fMR) biomarkers that include, among others, SUVmax, metabolic volume (MV), apparent diffusion coefficient (ADC), and volume transfer coefficient (Ktrans). This would be precluded, due to bowel peristalsis and patient movements, in the case of sequentially acquired PET and MR scans.

Secondarily PET/MR co-acquisition may symbiotically overcome some limitations of each modality taken apart (6). Moreover, serially acquired high temporal resolution MR data can track and quantitate patient and bowel motion allowing for MR-assisted PET motion correction with subsequent reduction in PET related motion artifacts, noise, blurring, and increased contrast (6,7).

Another important advantage of PET/MR compared to PET/CT is the reduced radiation burden to the patient. PET/MR allows a 20% reduction in radiation exposure compared to PET/CT, when the CT component is used for attenuation correction only, or up to 60-73% if the CT part is employed both for attenuation correction and for producing diagnostic quality CT images (39,40).

The geometry of the PET components of the PET/MR scanners, with the resultant increased sensitivity in the center of the PET field of view (FOV), allows reducing activity to up to 30-50% of that required for comparable quality PET from PET/CT (41).

Moreover, the lengthier times required to acquire MR sequences might be used to prolong PET acquisition, improving the quality of the PET images and/or allowing a

lower activity. In a phantom study, increasing bed position time by a factor of 8, from 2 minutes to 16 minutes, allowed reducing to 1/8 (12.5%) the injected activity, with PET images displaying same signal to contrast ratio as those obtained from 100% activity while using 2 minutes per bed position (42).

This is extremely important in CD patients who are usually younger at presentation and will likely require several follow-up studies in the course of their disease.

A major disadvantage of PET/MR compared to PET/CT relies in its limits in quantifying the attenuation exerted by body tissues on the gamma-rays. While in PET/CT the density of the tissues, as measured by CT Hounsfield units, may be used to compute the linear attenuation correction (LAC), this is not the case of PET/MR where the signal intensity of the tissue does not have any direct relations with the LAC. Several techniques have been employed to address this issue, the most effective being tissue segmentation/decomposition and atlas based methods. However, this problem has not been resolved completely. But new approaches based on artificial intelligence seem very promising.

Another potential disadvantage of PET/MR, compared to PET/CT, is the lengthier acquisition time (23-30 minutes for a Crohn's PET/MR protocol versus 12-15 minutes for a Crohn's PET/CT study), with MR acquisition being the time limiting factor. However, neither PET nor MR quality should be compromised if intention is to maximize clinical benefit from PET/MR capabilities.

Most of the research efforts in clinical PET/MR have been deployed in neurologic and oncologic imaging. In selected indications, PET/MR has been proven advantageous over PET/CT, and also over PET and MR performed separately. For example, PET/MR improves staging of central nervous system cancers, detection of satellite brain lesions, residual disease, and evaluation of intratumoral heterogeneity (43–47).

In oncologic body imaging PET/MR has been demonstrated to be superior to PET/CT and also to MR in several respects, including evaluation of liver, peritoneal, bone, and lymph node metastases, and whole-body staging of different primary cancers. Moreover, PET/MR can also provide insights into the tumor biology, as in the case of breast cancer (48–57).

PET/MR has enormous potentialities also in the evaluation of Crohn's disease. However, it has been rarely used in this disease, with only two research manuscripts available in the literature (25,31,58-60).

PET/MR might increase the diagnostic confidence in assessing patients affected by Crohn's disease. It has been shown that MR enterography, PET/CT enterography, and PET/MR enterography had similar accuracy in detecting areas affected by Crohn's disease. However PET/MR enterography provided additional clinically relevant information due to its increased accuracy in assessing extra-luminal manifestations of the disease, that were associated with higher need for stoma [p = 0.022], and also distant localization [p = 0.002] (59).

PET/MR enterography was also useful in assessing the dominant nature of strictures. Strictures constitute one of the most important clinical challenges in Crohn's disease. They occur in about 11% of patients at presentation, and their prevalence increases over time. Moreover, they represent a major cause of morbidity in Crohn's disease (28,61,62).

While several medical options are available for predominantly inflammatory strictures, the fibrotic ones need to be treated more invasively, by surgery or mechanical dilatation. This pivotal information, however, is not usually available to the clinicians, due to the limits of current techniques, even in the case of endoscopic biopsy. Therefore patients are usually treated conservatively first, and in the case of failure, a surgical approach is pursued (28,61,62).

In two very recent PET/MR studies focused on this very specific topic, with surgical pathology as standard of reference, it was found that PET/MR could be useful to differentiate between fibrotic and inflammatory strictures.

PET/MR enterography was more accurate in detecting fibrosis compared with PET/CT enterography [p = 0.043] and with MR enterography [p = 0.024] (59).

Among the different PET/MR biomarkers that were investigated, the best discriminator between fibrosis and active inflammation was the hybrid PET/MR enterography biomarker ADC*SUVmax, that at a cutoff of less than 3000, was associated with accuracy, sensitivity, and specificity of 71%, 67%, and 73%, respectively for purely fibrotic strictures (60).

PET/MR in neoplastic patients: advantages and disadvantages

PET/MR has several potential advantages over PET/CT and over MR and PET standing alone in oncologic imaging. The simultaneous acquisition of PET and MR data allows for complete spatial and temporal matching of MR and PET data and makes it possible to compensate for motion both MR and PET data. This translates into the possibility to improve image quality, increase detection rate, provide more precise quantitative assessment of lesion pharmacokinetics and metabolism (1,58). Moreover, the high signal to noise and contrast to noise ratios of MR, and the resultant high quality anatomic layout, allow to better localize areas of abnormal metabolism detected by PET, especially in critical areas, like the subcapsular liver parenchyma and the pelvis, and to pin point lesions that, because of small size or critical location or high background activity or low intrinsic metabolism, might be missed by PET alone (58). This can be advantageous in improving clinical staging and restaging, ascertaining the benign or malignant nature of lesions, providing an anatomic-metabolic road map to the surgeons, and investigate the biology of cancers (57,58).

PET and MR together may play a pivotal role in several oncologic entities, complementing each other. One of this field might be neuro-oncology. Contrast enhanced MR, by itself, is the method of choice for the initial evaluation and follow up of brain tumors. However, contrast enhancement of lesions is imperfect being influenced by several factors related to tumor biology, e.g. blood flow and vessel permeability, and to brain physiology, e.g., the blood-brain barrier. Therefore, reduction of lesion enhancement after therapy does not always correlate with tumor response. Although PET can rely on specific tracers exploring selective features of tumor biology, like amino acid transport (^{11}C-methionine and ^{18}F-fluoroethyltyrosine), hypoxia (^{18}F-fluoromisonidazole), and proliferation (^{18}F-fluoroethylthymidine), it is influenced by blood perfusion to the affected areas and by local permeability. For example, MR can help PET to discriminate the transport and metabolic trapping of ^{18}F-fluoroethylthymidine allowing a better quantification

of tumor cell proliferation. It is expected that PET/MR can overcome the limitations of each technique when used separately (6). PET/MR may prove useful for a more accurate pre-surgical planning showing the relationships of the metabolic vital portions of brain tumors with adjacent white matter tracts, infiltration and displacement. Moreover, it is capable of highlighting functionally important areas that need to be spared such as Broca's area. It has already been demonstrated that PET/MR can change the radiation target volume when compared to stand alone MR or PET (63).

In the field of body oncology, PET/CT represents the gold standard technique for the staging of several solid organ neoplasms and it has been shown to allow a more accurate TNM staging than CT or PET alone (8,9). PET can detect metabolically active lesions and quantify the amount of radiotracer uptake, expressed as standard uptake value (SUV), with several cut off values proposed to discriminate malignant from benign lesions. Quantification of radiotracer uptake has also been shown helpful in assessing treatment response by following changes in lesion metabolism (10,11). Despite its attributes, PET/CT has limitations imposed by the low intrinsic soft tissue contrast of CT, and by physiologic radiotracer uptake in normal tissues that may render lesions with a low metabolic rate (e.g, well-differentiated hepatocellular carcinoma, mucinous adenocarcinomas, neuroendocrine tumors, and some low-grade lymphomas) difficult to detect. Neoplastic lesions in or adjacent to tissues with normally high metabolism (e.g., liver, kidneys) may be overlooked (12–19).

PET/MR couples the advantages of PET with the superior soft tissue contrast of MR allowing for the improved assessment of fine anatomical detail, and the clear depiction of lesion margins, local tumor infiltration, and the relationship of lesions to adjacent structures. One such application can be in evaluating extention of rectal cancers beyond the tunica muscularis and threatening of the mesorectal fascia that might be very hard to assess by PET/CT, unless extensive (1,12,20). Moreover, MR is also capable of providing functional information with diffusion weighted imaging (DWI), perfusion imaging, and spectroscopy which may be used for lesion detection and characterization.

DWI is particularly valuable in the assessment of lesion cellularity, and may be used as a whole-body screening technique for the detection of hyper-cellular neoplasms, including lesions less than 10mm in diameter (64,65). DWI greatly contributes to the sensitivity of PET/MR. In our experience it is equivalent to PET in identifying neoplastic metabolically active lesions and is superior to PET in identifying neoplastic lesions with low metabolic activity. While highly sensitive, DWI suffers from low specificity. Lesions detected at DWI may be better characterized with a combination of morpho-functional MR criteria and metabolic PET criteria leading to increased specificity and improved readers' confidence. These include similarity of signal intensity of the lesion with that of the primary neoplasm, areas of internal necrosis as on T2 weighted and on contrast enhanced images, apparent diffusion coefficient (ADC) values $<1.4x10^{-3}$mm/s for distant metastases and $<1.0x10^{-3}$mm/s for lymphadenopathy (66–68), SUV≥ 2.5 (10,11); satisfaction of these criteria allows to call a lesion as malignant (10,11,66–69). In our experience, the superior ability of PET/MR to characterize subcentimeter lesions as benign or malignant allows for increased staging accuracy over other modalities.

PET/CT may detect small foci of radionuclide uptake due to the PET component. However, due to the low soft tissue contrast of CT and the sequential nature of data acquisition inherent to PET/CT, lesion localization may suffer in some circumstances, and anatomic correlates for small PET findings may be overlooked. Conversely, concurrent data acquisition with PET/MR allows each modality to help the other in an additive manner. PET/MR will often help detecting small lesions that may be ignored by either modality alone. Specific instances include small peritoneal lesions that may be missed by MR or miss-interpreted by FDG-PET as non-specific intestinal uptake (e.g., small foci of carcinomatosis in the supramesocolic region) (70–72). In our experience, PET/MR is particularly helpful in evaluating lymph node, liver, bone, pelvic organ, and breast.

Size criteria are often used to differentiate benign from malignant lymph nodes on both MR and CT, with a short axis diameter of ≥ 10mm being a common threshold for malignancy (73). However, this method suffers from both low sensitivity and specificity as non-neoplastic conditions may result in "pathologic" lymph node

enlargement and small lymph nodes may harbor metastatic disease. In the setting of rectal cancer, up to 15% of pelvic lymph nodes less than 5mm are metastatic (69,74). MR-based morpho-functional indices, including lymph node T2-weighted characteristics, internal structure, shape, margin, and ADC value (ADC $<1.0x10^{-3}$mm/s suggesting malignancy), combined with metabolic PET data account for good performance figures of PET/MR in the assessment of lymph nodes below the 10mm threshold.

PET/MR is an ideal technique for oncologic liver imaging. MR alone, given its exquisite soft tissue resolution, is superior to CT alone in evaluating the liver parenchyma. PET improves the assessment of critical regions adjacent to the liver capsule and intrahepatic vasculature. Moreover PET facilitates the evaluation of areas that have undergone local regional therapies (e.g. TACE, thermal ablation, and SIRT) (75–77). Moreover, PET/MR value is not hampered by coexisting hepatic steatosis, a common limitation of CT in the setting of chemotherapy.

Sclerotic bone metastases are readily detected by CT, however, subtle lytic metastases, particularly those lacking cortical breakthrough, are often overlooked. The sensitivity of CT for the detection of bone metastases is further reduced in patients with osteopenia. FDG-PET will often identify pathologic FDG uptake in bone prior to the development of an anatomic CT correlate. PET/CT evaluation of bone is often confounded in the setting of increased hematopoietic bone marrow uptake from chemotherapy or colony stimulating factor administration, and is not sensitive in the detection of hypometabolic metastases (78–80). Specific radiotracers, such as ^{18}F-Fluoride, may be used to improve PET detection of bony metastases (81,82). PET/MR with FDG may identify subtle signal alterations on MR that provide anatomic correlates for otherwise indeterminate foci of FDG avidity, improving confidence in the diagnosis of bone metastases. STIR and DWI are sensitive for bone marrow edema; T1weighted imaging, including pre and post contrast imaging, is sensitive for sclerotic metastases as well as marrow replacing. In a comparative study it has been shown that whole body MR outperforms bone scintigraphy and targeted x-rays, being more sensitive for bone metastases from prostate cancer (sensitivity of 98-100% versus 86% respectively). However whole

body MR had similar specificity (specificity of 98-100% versus 98% respectively)(83).

PET/MR has the potential to greatly improve the care of patients with pelvic cancers, a rather common entity. For most pelvic cancers, accurate local staging is important for treatment planning. PET/CT imaging is limited in local staging due to the low soft tissue contrast and the presence of excreted radiotracer in the bladder that limits assessment of adjacent structures (84). MR alone is also limited, given the potentiality for metastatic disease in lymph nodes <10mm. PET/MR combines the improved T staging inherent to MR with the improved N staging of PET (85,86). Furthermore, the low sensitivity of MR for the detection of small peritoneal implants and recurrent/residual disease after treatment may be improved in the presence of concurrent PET data (84–87). From our initial clinical and research activities, we feel that PET/MR will prove superior to MR or PET alone in both initial staging of pelvic cancers and post treatment surveillance.

In our experience, PET/MR is extremely useful for breast cancer staging and follow up. The coaquisition of contrast enhanced MR and PET improves characterization of subcentimeter foci of non-mass like enhancement and improves the sensitivity for the detection of synchronous lesions.

Several factors have the potential to hamper PET/MR performance. These are often related to the MR component of PET/MR. They include issues with lesion localization due to motion artifact (particularly in the region of the diaphragm, heart and bowel), and issues with image degradation due to magnetic susceptibility artifacts. PET/MR requires appropriate patient cooperation and is longer than PET/CT (average length 50-80 minutes according to the protocols). For patients unable to perform breath holds or hold still, PET/CT is preferred.

Compared to CT, MR has lower temporal and spatial resolution, making PET/MR challenging in the setting of lung nodules less than 6mm in diameter. However, Stolzman *et al.* (88), using a trimodality scanner to evaluate lung nodules on CT, MR, and PET, both separately and in various combinations, found similar detection rates for lung nodules on PET/MR (83%) and PET/CT (85%). These results are in keeping with a comparative study of PET/MR and PET/CT which showed that

PET/MR did not miss clinically relevant lung nodules in 134 consecutive oncologic patients (55).

According to our preliminary clinical experience, PET/MR is not inferior to PET/CT in lung assessment and outperforms PET/CT in the detection and characterization of lymph nodes, bone metastases, and liver metastases, and in the staging of pelvic malignancies. Moreover, PET/MR can evaluate tumor regions such as the kidneys that are difficult to assess by PET/CT. PET/MT can also detect additional coexistent incidental neoplasms in the kidneys and breasts, not identified on PET/CT.

Finally PET/MR suffers of the same contraindications as per MR only, including claustrophobia, metallic foreign bodies, ferromagnetic implants and devices. Moreover, because it is a relatively novel technology, there are no consolidated clinical protocols for PET/MR.

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