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Whole-body MRI and PET-CT in the management of cancer patients

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Abstract Mortality rate, prognosis, and treatment outcome of cancer patients depend strongly on the detection of malignancy at an early stage and efficient monitoring of the disease. Multimodality diagnostic approaches are now widely applied for tumor detection, staging, and follow-up. However, the introduction of whole-body imaging modalities into clinical practice has substantially expanded diagnostic options. PET-CT has increased diagnostic accuracy by providing “anatomometabolic” information by fusing tumor glucose-uptake measures from the PET examination and accurate delineation of anatomical structures given by spiral CT. Since PET-CT is associated with high doses of ionizing radiation, it is used in mainly tumor staging and screening within the scope of tertiary prevention. Here promising results have been

reported for various tumor entities. MRI provides excellent tissue contrast, detailed morphological information and lack of ionizing radiation. MRI has been employed for the assessment of focal pathologies in specific anatomical regions. Whole-body MRI scanners using multiple receiver channels with parallel acquisition techniques now allow tumor screening from head to toe within substantially shorter examination times and without compromises in image resolution. We report our experience with these two novel techniques and discuss their benefits and drawbacks in terms of systemic tumor screening.

Keywords Screening · Oncology · Magnetic resonance imaging · Positron emission tomography · Computed tomography

Introduction

Malignant tumors are the third most common cause of death worldwide [1]. The clinical outcome of tumor patients depends crucially on accurate tumor detection, effective therapeutic management, and precise follow-up. The primary goal of an efficient tumor screening is to reduce overall patient mortality by detecting early stages of malignant diseases which are accessible to curative therapy or potentially have a better outcome in the case of a palliative approach. Secondary goals are increasing life quality of the patient and decreasing costs for the health

care system through shorter and more efficient patient management. An indispensable precondition for effective screening is high disease prevalence in the population (e.g., neoplasms), as the positive predictive value of a particular diagnostic test, according to Bayes' theorem, is strongly dependent on disease prevalence [2]. Additionally, high sensitivity of the diagnostic test is required to ensure that no malignant lesions are missed. At the same time specificity should be adequate to limit false-positive results, which create further unnecessary investigations and costs and unsettle the patient. Moreover, the test should be time- and cost-effective and easy to perform. Thus a

screening procedure is only justifiable with a continuous risk-benefit analysis.

Applications for whole-body MRI and PET-CT

The introduction of whole-body (WB) imaging has fundamentally changed diagnostic concepts for tumor patients in recent years. As alternative to multimodality imaging approaches, WB techniques are now increasingly applied to give more consideration to neoplastic disease as a systemic affection (Fig. 1).

Since its introduction in 2001 positron emission tomography (PET) computed tomography (CT) has produced record results for oncological imaging [3]. Within a few years the production of single PET scanners worldwide has dramatically decreased, and the vast majority of systems are now produced as combined PET-CT units. PET-CT

combines the advantages of two modalities by giving anatomometabolic information through a fusion of data provided by pathological tumor tracer uptake in the PET examination together with an accurate delineation of anatomical structures of spiral CT. Additionally, temporal and spatial differences between the two-image acquisitions are significantly reduced as the patient remains fixed in one position for both examinations. Various studies have reported a significant improvement in both diagnostic accuracy and lesion localization in various tumor entities [4–6]. The most frequently used tracer, [^{18}F]fluoro-deoxy-glucose (FDG) is a glucose analogue allowing imaging of increased glucose utilization, a process that is inherent to various tumors, thus making it a robust “all-round” tracer for oncological purposes. Recent hardware improvements in PET-CT imaging have focused on upgrading the CT component from the initial single-slice scanners to 16-slice dual-modality scanners resulting in faster acquisition times

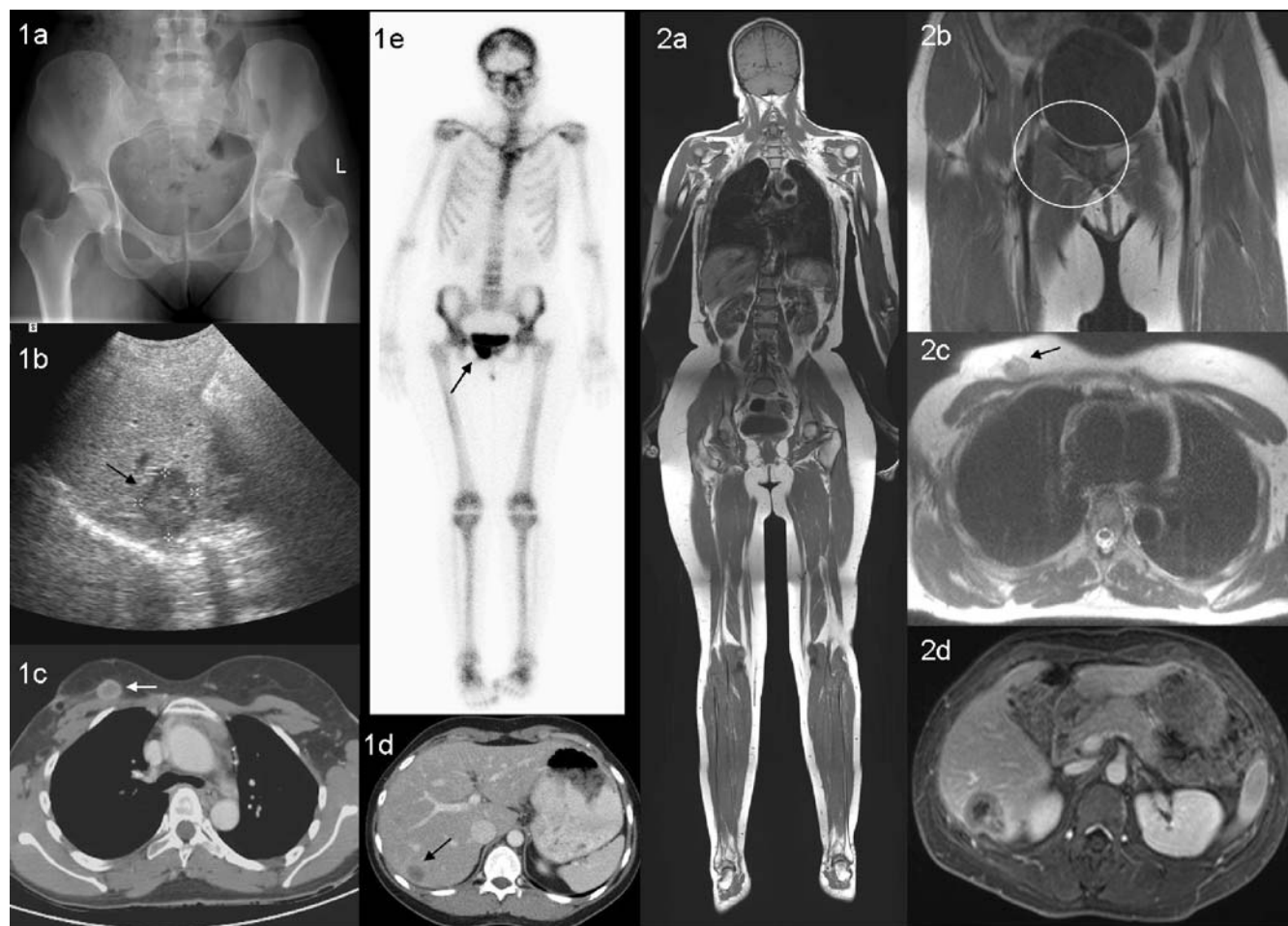


Fig. 1 From multimodality to single-step examination. Restaging in a 29-year-old woman treated for breast cancer and with newly elevated tumor markers and bone pain. **1a, 1b** Radiographs of the skeleton were normal, but bone scintigraphy showed a pathological tracer uptake in the right pubic bone (*arrow*). Abdominal ultrasound exhibited a suspicious mass. **1c, 1d** CT revealed tumor recurrence in

the right breast and confirmed hepatic metastasis. **2a, 2b** T1-weighted whole-body MRI depicted a metastasis in the right pubic bone (*circle*). **2c, 2d** HASTE images of the thorax showed the tumor recurrence in the right breast (*arrow*) and dynamic contrast enhanced studies of the abdomen unmasked the liver metastasis

and higher resolution. A state-of-the-art PET-CT now allows a complete WB examination within approx. 30 min. Another important benefit of dual systems is a marked reduction in the time-consuming PET scan as the CT data can be used for low-noise attenuation correction of the PET data. This has led to a decrease in acquisition time by 40% [7]. Attenuation correction can either be calculated by a low-dose CT prescan or directly from the diagnostic CT data. Figure 2 gives an overview of the PET-CT protocol used for WB oncological imaging at our institution.

Magnetic resonance imaging (MRI) with its excellent tissue contrast, high spatial resolution, and detailed morphological information also appears promising for tumor screening. Previously MRI has been employed for the assessment of focal pathologies in restricted anatomical regions or organ systems. The crucial problem in implementing WB MRI has been to integrate substantially different requirements in coil setup, contrast media application, slice positioning, and sequence design into a single comprehensive scan. WB imaging on a conventional scanner required at least one patient and coil repositioning, which substantially increased examination time far beyond 1 h.

Improvements in hard- and software, including a rolling platform (BodySURF, MR-Innovation, Essen, Germany) mounted on top of the scanner table for the first time overcame field of view restrictions and extended the scan range in the z-axis without repositioning. With this concept the patient glides in between a “coil sandwich” incorporating the body coil and the integrated spine coil. Barkhausen et al. [8] applied this system for axial WB tumor screening using true fast imaging with steady-state precession–gradient-recalled echo sequences and reduced examination times to that of a routine CT. However, considerable restrictions in spatial resolution had to be taken in account as the application of a body coil in the head/neck region or on peripheral body parts certainly represents a compromise.

An important development has been the introduction of parallel imaging techniques (PAT) [9, 10]. The basic principle of this is the use of the spatial information from different elements of multiple independent radiofrequency receiver coils to reconstruct the image [11]. This process substantially reduces scan time and results in shorter overall examination times without compromising spatial or temporal resolution.

The recent introduction of WB scanners using a system of multiple phased-array coils covering the entire body as a matrix allows, in combination with automated table movement, WB imaging with parallel imaging in all three spatial dimensions at a total field of view of 205 cm. Dedicated assessment of various organs by sequences with adequate soft tissue contrast, image orientation, spatial resolution, and contrast media dynamics can now be combined with WB anatomical coverage. A WB MRI tumor protocol should cover the pathways of metastatic spread and at the same time must guarantee a high diagnostic accuracy. It should also include state-of-the-art imaging techniques such as T1-weighted and short tau inversion recovery (STIR) imaging, which have proven highly efficient for the assessment of soft tissue and bone structures, fast high-resolution imaging of the lung (e.g., half-Fourier single-shot turbo spin echo, HASTE), as well as static and dynamic contrast-enhanced studies of the abdominal organs and of the brain. The total scan time of the protocol presented in Fig. 3 is 55 min.

A promising further development in parallel imaging techniques is the combination of sensitivity-encoding reconstruction algorithm with continuously moving table MRI for WB angiography and oncological applications. WB imaging has been successfully applied in vivo for continuous three-dimensional gradient echo imaging from head to toe within 77 s and without significant constraints in image quality [9–12].

Fig. 2 Whole-body PET-CT imaging on a two-detector row scanner (Gemini, Philips Medical Systems, Ohio, USA) using a low-dose CT prescan for attenuation correction

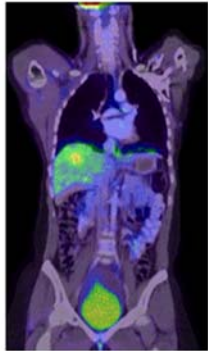
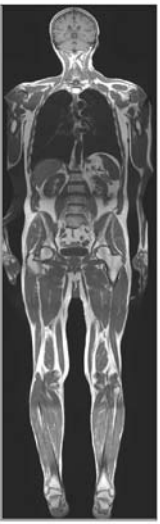
FOV	Whole body PET-CT protocol (Philips Gemini®)			
	<u>Patient preparation</u> <ul style="list-style-type: none"> • Fasting 6 hours before • 200 Mbq FDG • 20mg Furosemide i.v. • 20 mg butylscopolamine i.v. 	<u>Low dose CT</u> <ul style="list-style-type: none"> • 60 mA / 120 kV • collimation 2 x 5mm 	<u>Emission-scan</u> <ul style="list-style-type: none"> • RAMLA-3D • matrix 144 x 144 • 12 bed positions • 10cm FOV 	<u>Diagnostic-CT</u> <ul style="list-style-type: none"> • 130 mA / 130 kV • collimation 2 x 5mm • pitch 1,5 • 120 ml Iopromide 80 sec delay
	60 minutes	scan time = 43 minutes		

Fig. 3 MRI protocol for oncological whole-body imaging on a 32-channel whole-body scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) with the use of PAT. Total imaging time is 55 min

FOV		Whole-body MRI protocol					
 205 cm	STIR cor		T1 cor				T1+con T2 ax skull
	STIR cor	HASTE/STIR cor + ax lung	T1 cor	T1+STIR sag upper spine		T1 fs +con ax abdomen	
	STIR cor	T2 ax liver	T1 cor	T1+STIR sag lower spine	3D- VIBE liver		
	STIR cor		T1 cor				
	STIR cor		T1 cor				
scan time = 55 minutes							

Whole-body imaging in surveillance of cancer patients

By definition a screening examination is conducted either within the scope of secondary or tertiary prevention. Secondary tumor prevention aims at filtering cancerous disease from a primarily healthy population, meaning that it benefits mainly a small proportion of ill patients while negative side effects affect the entire examined population. Therefore a minimal incidence of side effects and strict selection criteria are indispensable to focus secondary screening on a preselected population with an increased risk profile. Thus far radiological procedures have played only a limited role in secondary tumor prevention. In the world's largest study of WB screening, the PLCO-Cancer Screening Trial, diagnostic imaging included only radiographic examinations of the chest and transvaginal ultrasound [13]. The primary domain today remains mammography screening. Although there still is conflicting evidence on the overall impact of mammography screening of large cohorts, positive effects concerning mortality and survival have been reported [14]. Recently multislice CT has been proposed for screening purposes, targeting early manifestations of colon and lung cancer [15, 16]. However, the European Union has passed legislation prohibiting the application of radiography for screening purposes except for mammography [17]. The high effective radiation dose of up to 25 mSv for a WB examination makes PET-CT a priori inadequate for secondary prevention screening, and its main applications and clinical impact are discussed below in the context of tertiary prevention [18].

WB MRI, on the other hand, with its lack of ionizing radiation is highly attractive for secondary prevention

purposes. Initial experience was with a combined cardiovascular and oncological multiorgan protocol in the context of a preventive health care program to employees. Goehde et al. [19] examined 298 asymptomatic individuals with the use of the previously described rolling platform system and a protocol comprising a WB MR-angiography, a functional assessment of the heart, morphological imaging of the brain and chest, and MR colonography. In addition to revealing manifestations of atherosclerotic disease in 21% of patients (including cerebral and myocardial infarctions), colonic polyps ($n=12$) and one renal cell carcinoma were detected. The mean room time was 63 min. A similar protocol has been adapted as an application for a multi-channel WB MR scanner using parallel imaging. Significant improvements in spatial and temporal resolution, especially for the depiction of lung, abdominal, vessel, and cardiac pathologies have been reported, with significantly shorter overall scan time than with sequential scan setups [20]. MR colonography is a promising application, as the time of latency from a benign polyp to malignant degeneration of up to 10 years makes colon cancer ideal for secondary screening purposes. Initial MR colonography studies have reported promising results for the detection of polyps larger than 10 mm compared with CT colonography and conventional colonography [21]. Despite these encouraging reports concerning diagnostic accuracy and important findings it must be emphasized that the described oncological findings in these studies were "accidental." As for any other screening program, long-term results must be awaited before conclusions can be drawn on positive effects for patients' health and cost-effectiveness. Certainly it must be advised against an

unsighted adoption of such multiorgan WB examinations. As mentioned above, an unfocused and uncontrolled screening of a healthy population would lead to a dramatic decrease in the positive-predictive rate and therefore certainly not be cost-effective. Another factor adding to costs is the danger of finding numerous equivocal findings (e.g., lung nodules of unknown cause) which may result in a chain of additional examinations for clarification and unsettle the patient. Furthermore, a cost- and time-effective WB screening protocol definitely cannot replace dedicated MRI examinations in specific organs such as the prostate, in which MRI with the use of an endorectal coil and MR spectroscopy remain the gold standard.

Whole-body screening for tertiary prevention

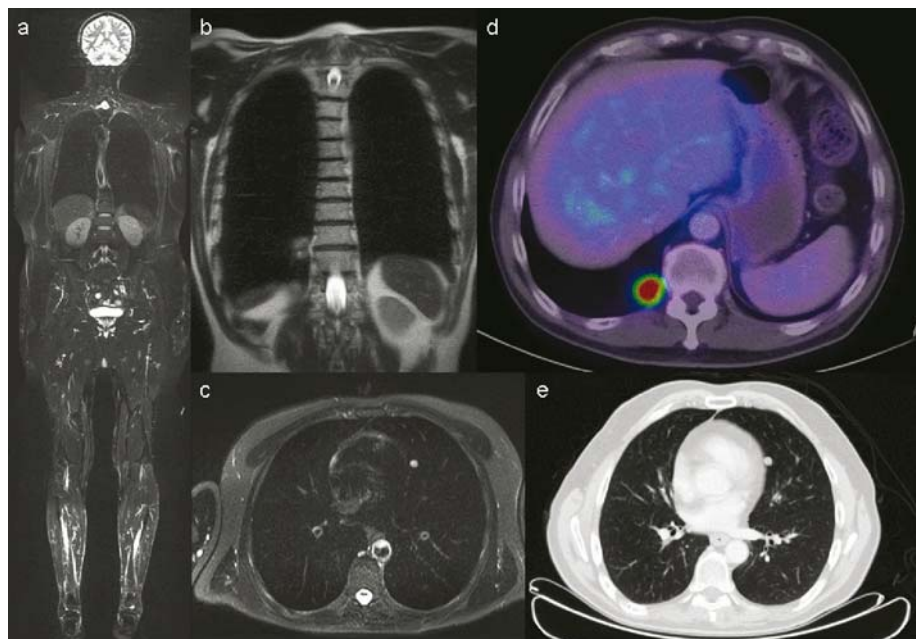
The primary goal of screening in tertiary prevention is to obviate aggravation of a preexisting chronic disease in a patient by early interventional measures or therapy changes. The main focus in the oncological patient is to detect a tumor recurrence or metastatic disease within restaging procedures and to exclude secondary complications due to disease progression. The TNM staging system of the American Joint Committee on Cancer has become the international standard for this purpose [22]. This triadic system addresses primary tumor growth (T stage), local lymph node involvement (N stage), and distant hematogenous metastatic spread (M stage). Tumor staging certainly represents the main domain for diagnostic imaging and multislice CT as a stand-alone examination is the most frequently used modality in clinical practice. CT of the neck, thorax, and abdomen/pelvis with multiplanar recon-

structions and recalculation of the bone and lung window setting is usually performed, thus covering the most important routes of lymphatic and hematogenous spread. However, a limitation of CT alone is its low soft-tissue contrast outside of the lung, which may result in problems when assessing distant metastases or tumor extension into adjacent structures. Various studies have documented greater efficacy in tumor staging of the anatomical-functional information provided by PET-CT than that of PET and CT alone [5, 6, 23]. MRI as a single modality has been found to be superior to CT in assessing parenchymal and osseous structures [24, 25]. Thus both PET-CT and WB MRI have great potential in tumor staging.

Whole-body MRI and PET-CT in the detection of primary or recurrent tumors

Only few studies have directly compared PET-CT with WB MRI concepts in imaging of oncological patients. For the first time the study group of Antoch et al. [26] examined 98 patients with various cancer entities with PET-CT and WB MRI and found a good overall diagnostic accuracy of 77% for correct TNM staging with PET-CT while that of WB MRI was only 54%. The main reason was a sensitivity of only 52% for the assessment of correct T stage achieved with WB MRI, compared to 80% with PET-CT. This reflects the ability of PET-CT to differentiate viable tumor from adjacent structures or postoperative scar tissue. However, it must be noted that the selected patient series with a high proportion of lung cancer patients favored PET-CT, as CT has obvious advantages over MRI due to better tissue contrast and lower susceptibility artifacts in this body

Fig. 4 **a** Whole-body MR study performed in a patient with cancer of unknown primary. **b** Coronal HASTE of the lung showed a suspicious paravertebral mass in the right lower lobe. **c** Axial STIR imaging revealed an additional lung node in the left upper lobe. **d** PET-CT confirmed a lung tumor with pathological tracer uptake. **e** CT also showed the node in the left lung; however, there was no tracer uptake. The tumor was biopsied and confirmed by histology as lung cancer of the right lower lobe with pulmonary metastasis



region. Notable differences in the applied protocols between the two modalities (e.g., thinner slices were used for PET-CT of the lung) and the use of the above slightly “outmoded” rolling platform system certainly further compromised diagnostic performance of the WB MRI examinations in this study. Furthermore, the proposed protocol comprised contrast-enhanced studies alone for specific body regions such as the neck.

A recent study at our institute subjected 41 patients with various primary tumors (two-thirds had tumors of the gastrointestinal tract) or cancer of unknown primary to PET-CT and WB MRI on a 32-receiver channel scanner with the use of parallel imaging (Figs. 3, 4). Overall diagnostic accuracy with TNM staging was 96% for PET-CT, compared to 91% with WB MRI, and the T stage was understaged only once by each modality [27]. However, most patients came for restaging after operative therapy, and therefore the prevalence of primary or recurrent tumors was low ($n=7$), thus hardly allowing a reliable interpretation of T stage results alone. Moreover, a recurrent carcinoma of the esophagus without visible morphological changes was missed in WB MRI while it was diagnosed in PET-CT due to the pathological tracer uptake (Fig. 5). Another study comparing PET-CT with PET and CT alone underlined the overall robust performance of PET-CT in assessing T stage and a diagnostic accuracy of 82% was obtained [28].

Between 5% and 10% of cancer patients are diagnosed with cancer of unknown primary, defined as histologically confirmed metastatic disease without a finding indicative of a primary tumor. The inability to localize the primary in the majority of patients restricts focused therapeutic interventions and significantly reduces patient prognosis. Various authors have reported that PET-CT offers better tumor localization than PET and CT alone [29]. However, a primary tumor was still found in only one-third of the examined patients. Unfortunately, there have been no reports on the performance of WB MRI or dedicated MRI in imaging of cancer of unknown primary.

Whole body MRI and PET-CT in the assessment of lymph node involvement

The impact of metabolic information provided by PET-CT becomes even more evident in the assessment of lymph node invasion by neoplastic cells. Depending on the anatomical region, morphological criteria for pathological lymph nodes vary between cutoff size of 10 to that of 15 mm. However, lymph node classifications based on size criteria alone have often proven unreliable. Recently there have been promising reports on WB MRI applications for the assessment of lymphoma patients as an alternative to WB CT alone [30, 31]. One study group has proposed WB FSE-STIR imaging as a sensitive technique for evaluating lymphoma patients with nodal involvement, as well as

affection of extranodal sites, especially the bone marrow [31]. Other authors confirmed the performance of WB MRI by detecting 92% of lymph node stations diagnosed positive in CT for nodes larger than 12 mm. However, detection dropped significantly down to 67% for nodes measuring 6–12 mm [30]. The problem of lymph node staging based on size alone are the borderline sized nodes; false-positive findings due to enlarged nodes in inflammatory processes or normal-sized nodes harboring micro-metastases often impair sensitivity and specificity of MRI and CT [6]. The functional information of PET-CT clearly facilitates both localization and characterization of equivocal lymph nodes (Fig. 5). Studies comparing a PET-based staging of lung cancer with CT demonstrates significantly higher accuracy in the assessment of N stage with PET [32]. The study by Antoch et al. [26] found that combined PET-CT achieved a diagnostic accuracy of 93% compared to 79% with WB MRI in lymph node assessment. Our own observations confirm the advantage of PET-CT over WB MRI by revealing an accuracy of 97% compared to 82% in evaluation of the N stage. In a lesion-by-lesion analysis an accuracy of 91% and 78% for correct node characterization has been calculated [27]. Lymph node imaging with MRI may also be limited by motion artifacts when they are located in the hilar, mediastinal, or retrocrural regions. However, the significant reduction in overall scan time using PAT has enabled more flexible scan protocols with implementation of fast high-resolution axial and coronal HASTE and STIR sequences of the lung. This may be the underlying reason for the better results in our study than those reported by Antoch et al. To improve diagnostic accuracy in detection of lymph node metastases obviously represents the key to further increase overall accuracy of WB MRI in tumor staging. Several concepts are presently being developed to enhance diagnostic accuracy: STIR echo planar imaging (EPI) diffusion sequences with adequate fat suppression has proven very promising for an enhanced display of pathological lymph nodes at high resolution [33]. Other authors have used the calculation of signal intensity ratios from turbo spin echo STIR images compared to a saline phantom and have reported excellent results for the detection of lymph node metastases in lung cancer [34].

Whole body MRI vs. PET-CT in the detection of distant metastases

WB MRI is highly effective in the detection of distant metastatic disease. Antoch et al. [26] reported an equally high diagnostic accuracy of 93% for WB MRI and 94% for PET-CT in correct assessment of the M stage. At our institute the detection of distant metastatic disease for both modalities was also evaluated on a lesion-by-lesion basis and revealed an advantage for MRI [27]. Overall diagnostic accuracy was higher in MRI with 92%, compared to 82% for PET-CT. However, the performance of both methods

must be placed in relation to the various affected organ systems. MRI is known to have a high sensitivity for the detection of bone and liver metastases [24, 25, 35]. Our observations confirm this with a WB MRI application and are well correlated with the observations of Antoch et al.: MRI has a higher sensitivity for bone and liver metastases than PET-CT [26, 27]. Dynamic contrast-enhanced studies improve the detection of abdominal metastases and uptake characteristics improve specificity of abdominal MR studies [24]. Our study showed reliable diagnosis of liver metastases at a cutoff size of 3 mm using dynamic three-dimensional volume-interpolated breath-hold examination sequence. These were invisible in PET-CT (cutoff size 5 mm) due to the low soft-tissue contrast of CT and the frequently normal FDG uptake in small lesions [27]. STIR imaging is efficient in the sensitive detection of skeletal and soft tissue lesions [25]. Compared to established imaging techniques for WB bone screening such as ^{99m}Tc -labeled skeletal scintigraphy, WB MRI based on STIR imaging has proven particularly sensitive for the detection of malignant bone disorders, even in younger patients [36]. PAT allows high-resolution coronary WB STIR-images at a scan time of 12 min. Combined with WB T1-weighted sequences our bone marrow screening protocol revealed smallest bone lesions with a cutoff size of 2 mm [27, 37] (Fig. 6). However, conflicting results have been reported by one study group on the use of WB MRI and PET in detecting skeletal metastases in children and adolescents [38]. PET alone showed a higher sensitivity of 90% than WB MRI with 82%. This may be due to the higher cellularity of normal bone marrow in this age group, leading to a lower signal in T1-weighted spin echo sequences with a hyperintense STIR signal, so that contrast of metastases within the bone marrow is reduced. Additionally, MRI was based on T1-weighted imaging alone in the majority of patients. Advantages for PET-CT over WB MRI were reported for the detection of lung metastases. Antoch et al. [26] found 89% sensitivity with PET-CT compared to 82% with WB MRI. The excellent lung tissue contrast in CT combined with PET and the lower susceptibility to motion artifacts provided better detection of lung pathologies than

MRI. However, our results indicate that fast HASTE imaging of the lung improves performance of MRI; only one metastasis was missed in the MRI studies ($n=36$) compared with PET-CT ($n=37$). Furthermore, lung metastases down to a size of 4 mm were visualized in WB MRI (PET-CT 2 mm) [27].

The field of view of a standard WB PET-CT examination ranges from the skull base to the proximal femoral bones, as the main routes of hematogenous and lymphatic spread are covered, thus avoiding additional radiation exposure and examination time through patient repositioning. WB MRI with its anatomical coverage from head to toe potentially reveals additional findings of therapeutic and prognostic importance. In our patient series 15 additional metastases were found in 6 patients, 9 cerebral metastases, and 6 bone metastases of the lower extremities. Especially, the finding of cerebral metastases is of decisive importance for patient survival and planning of therapy. Cerebral and skull metastases are particularly difficult to identify in PET-CT because of a high physiological tracer uptake in normal brain tissue.

Another study on WB assessing metastatic disease and using a similar protocol and the same multichannel MR scanner, compared to CT as the standard staging method, reported a considerable number of additional diagnoses, including previously unknown cerebral tumor spread and soft-tissue metastases. This led to a change in therapy in 6 of 63 patients (10%) [39].

Whole-body MRI and PET-CT in oncological imaging: pitfalls and limitations

Despite the excellent sensitivity of PET-CT in tumor detection interpretative pitfalls must be taken into account as FDG is not an entirely tumor-specific tracer, and pathological tracer accumulations may be present, for example, in inflammatory processes. In addition, physiologically increased FDG uptake is observed in brown fat or muscle tissue due to patient motion or speech activity (typically in the tongue base) during patient preparation



Fig. 5 A 55-year old patient post-colorectal carcinoma. **1a** Axial HASTE MRI showed a high signal intensity focus in the left hilus (arrow). **1b**, **1c** CT indicates a lymph node in the left hilus 10 mm in size. PET-CT revealed pathological tracer uptake indicative of lymph node metastasis

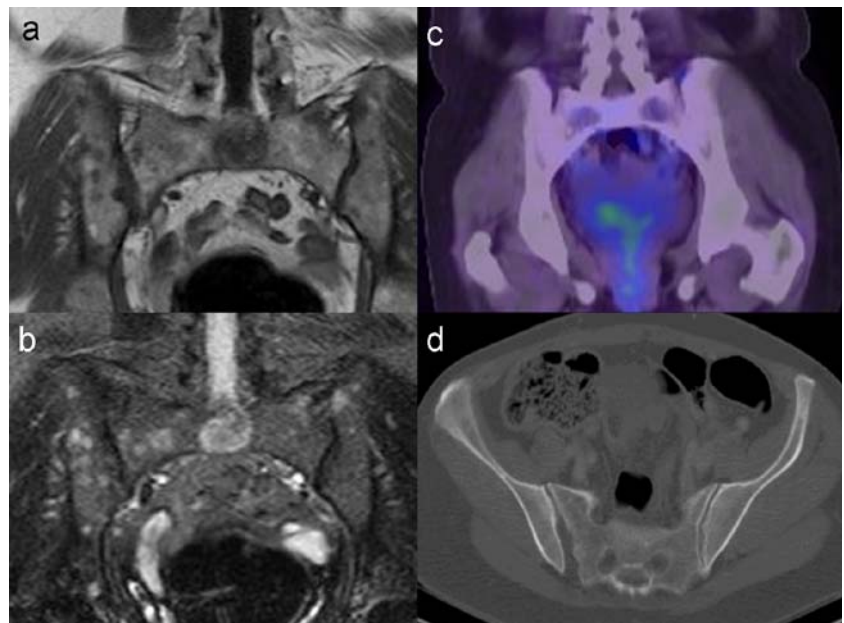
[40]. Furthermore, tracer accumulations in the urinary tract or due to bowel muscle activity may impair diagnostic performance. However, there is no doubt that the additional morphological information of CT with the ability correctly to attribute tracer uptake to normal organ structures has significantly reduced the number of these potential pitfalls. PET-CT specific pitfalls may occur when different breathing patterns are used for PET and CT image acquisition. This can lead to a misregistration of structures located near the diaphragm, such as pulmonary nodules in the lower lung fields or lesions in upper liver segments. Additionally, small lung or hepatic lesions may remain FDG occult due to “smearing” of the PET emission signal by organ motion (see Fig. 4). These problems can be minimized when CT is performed in normal expiration. In addition, respiratory gating techniques are currently being developed to further ameliorate image coregistration [41]. It has been reported that high-density contrast agents or metallic objects can lead to “hot spot” artifacts by overestimating PET activity when the CT data are used for attenuation correction. However, such artifacts can easily be recognized by analyzing the uncorrected images [42]. Moreover, it must be taken into account that there are various tumor entities which are not FDG amenable, such as renal cell carcinoma, prostate cancer, and low-grade soft-tissue malignancies. This may lead to false-negatives in early stage disease in the absence of pronounced morphological changes.

As discussed above, the major limiting factor of diagnostic accuracy in WB MRI is the lack of metabolic information when assessing lymph nodes or the postoperative status. Differentiating reactive lymph node enlargement (e.g., due to inflammatory processes) from malignant nodes or discriminating postoperative scar tissue from small tumor recurrence can cause problems when imaging

is based on morphology alone. A breakthrough development might be the recent application of fused “virtual PET-MRI” images using STIR sequences combined with high b-value diffusion-weighted breath-hold EPI sequences for further lesion characterization [43]. Despite significant improvements in image quality through the development of faster turbo spin echo sequences, assessment of regions with frequent metastatic spread, such as the mediastinum or retrocruial area, can be impaired by motion artifacts, potentially leading to a decrease in sensitivity. Moreover, protocols favoring WB MRI based on coronal studies may encounter diagnostic problems when lesions are located in peripheral sections of the body, for example, skin metastases. There have been reports that WB MRI performed this way tends to miss lesions in small curved flat bones, such as the ribs and skull [25, 35]. In a post-therapeutic setting it must be considered that necrotic bone metastases can remain virtually unchanged in morphology or signal after chemotherapy, which complicates evaluation of therapy response with MRI [31]. Frequently there is a delayed reduction in tumor size observed and sometimes a delayed contrast enhancement. On the other hand, MRI is particularly useful following radiation therapy, as irradiated lesions are easily distinguishable from new lesions because of the high signal of previously treated bone marrow in T1-weighted spin echo images.

The cost-effectiveness of WB imaging with PET-CT and WB MRI in oncological patients has not yet been fully explored. Since both methods allow replacement of a number of different imaging examinations and to provide diagnostic information on the whole body in which tumor manifestations may be present, targeted therapeutic measures can be initiated at an early stage. This approach may also reduce the psychological burden of patients who are

Fig. 6 A 62-year old woman previously treated for breast cancer. **a, b** Enlargement of coronary T1-weighted whole-body MRI showed multifocal hypointense lesions in the sacrum and iliac bones with a corresponding hyperintense signal in STIR. Lesions down to a size of 2 mm were depicted. **c** Coronal PET-CT reconstructions showed no tracer uptake at all in the pelvis and sacrum. **d** In the CT scan (bone window) no osseous destructions or sclerotic foci were found



exposed to numerous exams. Since neither PET-CT and WB MRI are 100% sensitive and specific, it must be further investigated how often dedicated follow-up tests are required.

Conclusion

With the introduction of WB MRI and PET-CT two modalities for systemic tumor screening have become more widely available that may represent promising alternatives to a multimodality approach in the near future, so that patients might benefit from early and accurate tumor detection and improved therapeutic options. Due to high radiation doses associated with WB PET-CT, PET-CT is not suitable for screening in secondary tumor prevention. The design and development of multiorgan, state-of-the-art

MRI protocols using image-acceleration techniques such as PAT offer new options for systemic secondary tumor prevention. However, despite promising reports on diagnostic performance, long-term results on prognostic relevance and on cost-effectiveness are yet not available, and cautious practice with these new methods is advised. Although there are individual pros and cons, initial experience shows a reliable performance of both PET-CT and WB MRI for tumor staging in tertiary prevention. In this setting patients may benefit from early and accurate staging facilitating planning of therapy. In various cancer entities PET-CT performs better in primary tumor detection and lymph node staging. In primary tumors with poor FDG uptake such as renal cell carcinoma and in the case of tumors with frequent metastatic spread to the bone, liver, or CNS (e.g., breast cancer), WB MRI represents a promising alternative to PET-CT.

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