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Comparative study of two whole-body imaging techniques in the case of melanoma metastases: Advantages of multi-contrast MRI examination including a diffusion-weighted sequence in comparison with PET-CT

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ABSTRACT

The aim of our study was to compare whole-body MRI (Magnetic Resonance Imaging) with a multi-contrast protocol including a DW (Diffusion Weighted) sequence to PET-CT (Positron Emission Tomography) using ^{18}FDG (18F-fluoroDeoxyGlucose) for staging advanced melanoma. In a first part, we compared the respective overall accuracy of each modality. We analyzed in a second part the benefits of a DW sequence added to the standard whole-body MRI protocol. Among the population of the 35 patients who experienced the two examinations of our prospective blinded study, we were able to detect 120 lesions and 70 of them were found malignant. The sensitivity and specificity for whole-body MRI were respectively 82% and 97%, while PET-CT reached 72.8% and 92.7%. DW sequence allowed the detection of 14 supplementary malignant lesions (20%) in comparison with standard MRI protocol. Moreover, this technique has been shown to be the most accurate for detecting metastases in the liver, bone, subcutaneous and intra-peritoneal sites. Consequently, a DW sequence should be added systematically to the standard whole-body MRI oncologic protocol because of its high added-value for metastasis detection.

1. Introduction

In the case of advanced melanoma, a reliable and highly accurate tumor staging encompassing the entire body is a fundamental prerequisite for choosing the best therapeutic approach between surgical and palliative treatment and it is of vital importance when assessing patient prognosis.

As a consequence, an exhaustive investigation of the tumoral spread requires several different imaging techniques to be achieved.

The introduction of PET-CT scanners has given access to a new type of whole-body imaging that combines, in a single examination, functional data of PET with the detailed anatomic information yielded by CT. Thus, the fusion between these two modalities improves the diagnostic accuracy of the tumoral lesions, and shows promising results for staging different oncologic diseases compared to either PET or CT alone.

On the other hand, PET-CT can also suffer from false positives arising from the increase of ^{18}FDG uptake in muscle or tissue, or from imprecise localization of the tumors caused by an inadequate fusion between PET and CT data; the mismatch resulting most of the time from respiratory motions. In addition, PET-CT has two major limitations that are spatial resolution (lesion size must be at least 5 mm) and uptake, the latter being dependent on the histological type of the tumor. Nevertheless, PET-CT is currently considered as the most sensitive imaging modality for detecting metastases measuring more than 1 cm in diameter.

MRI (Magnetic Resonance Imaging) benefits from its lack of ionizing radiation, excellent soft tissue contrast, and high spatial resolution. Therefore, it is an excellent candidate for evaluating metastatic disease spread [1] since MRI imaging allows the combination of the advantages listed above with entire body coverage while maintaining high image quality and a reasonable acquisition time using T_2 and T_1 weighted sequences [2–5].

Several preliminary studies show that DW-MRI (Diffusion Weighted MRI) can have non-neurological applications such as whole-body examinations, this novel technique appearing to be very interesting in oncologic applications [6–10].

To the best of our knowledge, there does not yet exist any published study comparing whole-body MRI examination including a DW sequence with PET-CT. We propose here a prospective blinded study dealing with patients affected by advanced melanoma in order to determine the benefit of including a DW sequence in the

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whole-body MRI protocol on one hand and, on the other hand, to compare the respective staging accuracies of whole-body MRI (with a DW sequence) and PET-CT.

2. Materials and methods

2.1. Patient selection

From August 2006 to April 2007, 35 consecutive patients affected by cutaneous melanoma and presenting a risk of metastatic spread were referred to the department of dermatology for staging by PET-CT and whole-body MRI. They were included according to the usual contraindications to MRI (cardiac pace maker, metal devices in the body, allergy to contrast medium, restricted renal function, pregnancy, claustrophobia) and to PET-CT (pregnancy). All examinations were performed within a 24–72 h time interval. The Local Ethics Committee of the Faculty of Medicine of Nancy approved the study. The patients gave their written consent after the study had been explained to them in detail.

2.2. PET-CT imaging

PET-CT examinations were made on an integrated PET-CT Scanner Biograph (Siemens, Erlangen, Germany) combining a 2-row CT SOMATOM Emotion Duo CT and a LSO-based PET imager. CT scan was performed under free breathing and without using any oral or injected contrast agent. A helical acquisition mode has been used, the related experimental parameters being 75 mAs and 130 kV, the coverage being from the top of the head to the toes. Reconstruction has been made in axial plane with a slice thickness of 4 mm and a slice interval of 3.4 mm. PET acquisition coverage was the same as for CT with 14–16 bed positions. The examination started approximately 60 min after the injection of 5.5 MBq per kilogram of body weight of ^{18}F-FDG (Flucis, CIS bio, Saclay, France) with an acquisition time of 3 or 4 min by bed position (according to the patient weight). The mean effective dose was 10 mSv for the PET acquisition and 10 mSv as well for the CT part. Patients were asked to have not eaten anything for 6 h before the examination.

2.3. Whole-body MRI

MRI examinations were made on a 1.5T GE Signa HDx scanner (General Electric HealthCare, Waukesha, WI, USA). The protocol was composed of a 2D STIR (Short Time Inversion Recovery) sequence, a DW sequence and a 3D T_1 sequence with injection of a contrast agent (0.2 ml/kg with no specific flow rate) (Fig. 1). The 2D STIR and 3D T_1 weighted sequences were performed in coronal plane in such a way that five stations using a FOV (Field Of View) of 45 cm each were needed to investigate the entire body, the slice thickness being 8 mm (with a gap of 1 mm for the 2D STIR). For both sequences and all stations, the voxel dimensions remained fixed at 1.5 mm × 3 mm × 8 mm. The DW sequence used a diffusion factor b fixed at 600 s/mm^2 and provided two sets of images, one for the expected b value and the other one for $b = 0$. These two sets enabled us to discriminate between malignant and benign lesions. The acquisition was done in axial plane, using a FOV of 36 cm and a slice thickness of 7 mm with no gap, with an in-plane resolution of 3 mm × 5 mm. Seven stations were needed to cover the whole-body from the top of the head to the toes. The b factor was fixed at 600 s/mm^2 because this value constituted the best compromise between SNR (Signal to Noise Ratio) and lesion detection sensitivity on our MRI system. All sequences were performed in free breathing, except for STIR and T_1 sequences at the abdominal level for which they were respectively done triggered on respiration and with breath hold. Concerning the instrumental part, the body coil was systematically used for emission and reception, except for the abdominal station for which a 12-element phased-array coil was systematically used with parallel imaging technique (ASSET, factor 2). The gradient amplitude was 33 mT/m. The duration of the entire examination was about 1 h.

2.4. Methodology for interpreting examinations

In a first time, each examination was interpreted independently. Two specialists in nuclear medicine were in charge of PET-CT examinations whereas two practiced radiologists interpreted MR scans. The nuclear physicians did not consider the non-attenuation corrected images.

The readers were blind to the results of the other imaging technique. In the following week, results of MRI and PET-CT were re-evaluated in consensus by all specialists.

For each patient and for each modality, lesion size, site-based localization, number of lesions and their characteristic (benign, malignant or indeterminate) were recorded. In addition, the largest lesion diameter measured with PET-CT and MRI was evaluated as well.

2.5. Benefits of Diffusion Weighted MRI

MRI examinations were interpreted in consensus by two experienced radiologists without (session 1) and with (session 2) DW images so as to determine the actual benefit of the DW sequence.

DW images were analyzed qualitatively by focusing on the signal intensity. The latter was classified by using visual assessment (hypo-intensity or hyper-intensity) in comparison with the signal intensity of adjacent tissues. The same window level was used for all examinations. During session 2, the two radiologists noted intensity abnormalities and then they compared them with the two other conventional sequences to determine whether lesions were benign or malignant. A malignant lesion appeared hyper-intense on STIR images and displayed a signal enhancement on T_1 (with gadolinium) sequence. In any other case, the lesion is considered as benign from a MRI point of view. The results obtained during sessions 1 and 2 were compared with the standard of reference.

2.6. Gold standard

The standard of reference was established according either to histology, or to imaging or clinical follow-up including tumors markers (S100 and lactate dehydrogenase) proven to be specific of melanoma. A given lesion was considered malignant whether it was proven by histology or an increase of the lesion size was revealed by clinical or imaging follow-up. In the case of none of these criteria was fulfilled, the lesion was considered as benign.

False negative was considered as soon as a given lesion was shown benign by MRI or PET-CT examination whereas either follow-up indicated a progression or histology proved the malignity of the lesion. On the contrary, false positive occurred when a lesion was considered malignant by MRI or PET-CT whereas there was no progression on follow-up or histological proof.

Patients were observed for six months. A physician unaware of the results of PET-CT and MRI collected all data related to the standard of reference.

2.7. Statistical analysis

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy value were calculated by using the software SAS (SAS Institute Inc., North Carolina, USA). Whole-body MRI and

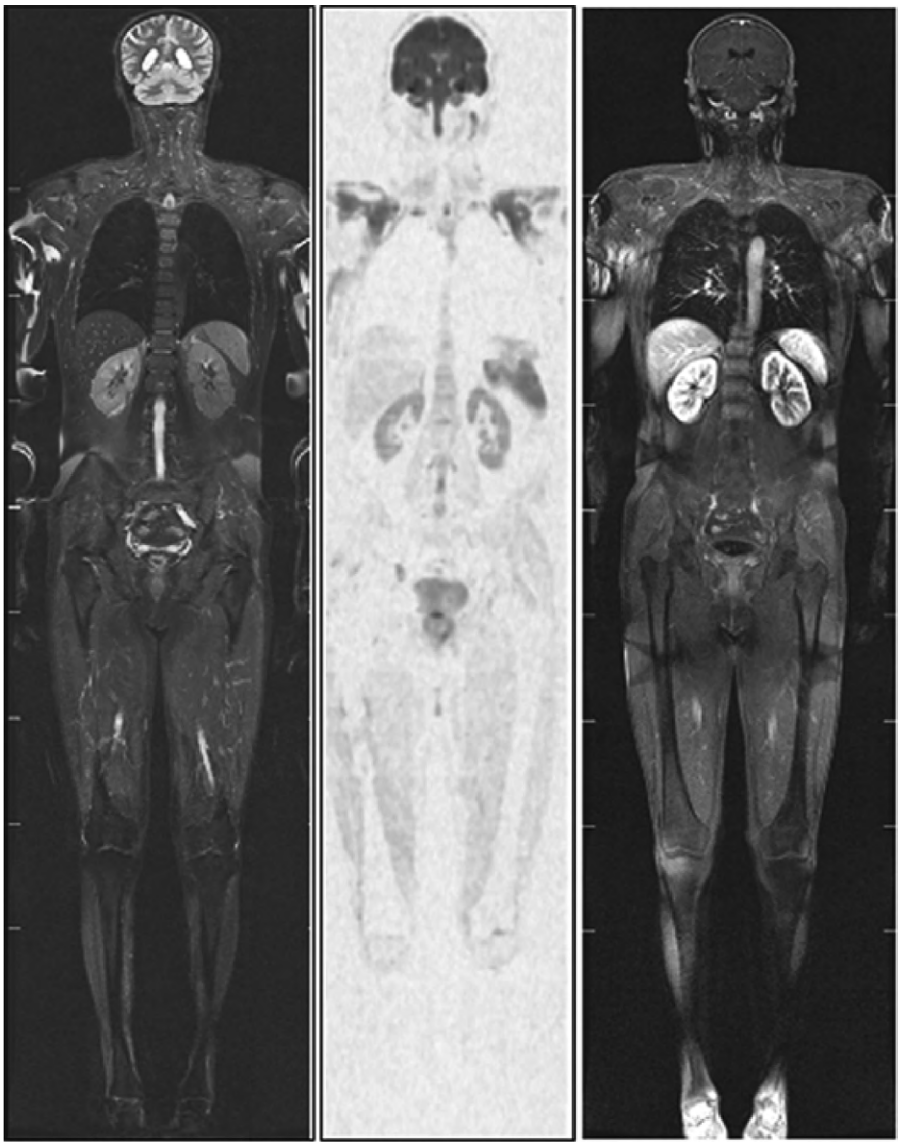

Fig. 1. Examples of images representing the three types of contrast used for whole-body MRI examination. The three sequences used are STIR (on the left), diffusion (center) and 3D T_1 (on the right). The STIR and 3D T_1 sequences are usually acquired in coronal plane while diffusion sequence is performed in axial plane and reconstructed in coronal.

PET-CT were compared lesion by lesion. A p-value smaller than 0.05 was considered as statistically significant.

3. Results

3.1. Overall accuracy

A total number of 120 lesions were spotted in the population of 35 patients that we considered for the present study. Each lesion was validated with respect to the standard of reference defined previously, the detailed analysis revealing that 32 were confirmed by histology, 43 by imaging follow-up and 45 by clinical follow-up. According to the standard of reference, 70 lesions were proven to be melanoma metastases (all the results are summarized in Table 1).

3.2. Analysis of staging for specific metastatic sites

The comparison of whole-body MRI with PET-CT for each specific metastatic site pointed out a significant difference between their respective sensitivities. The related results are enclosed in Table 2.

All hepatic lesions were correctly identified by whole-body MRI, while PET-CT missed two malignant lesions. The most accurate method for classifying bone lesions was whole-body MRI with a noteworthy difference compared with PET-CT; whole-body MRI detected indeed more subcutaneous metastases. One patient developed one cerebral metastasis that was missed by all the readers (PET-CT and MRI) on the first interpretation session, but the retrospective evaluation showed that this lesion was nevertheless detectable on the MRI examination.

Table 1
Sensitivity, specificity, positive predictive value and negative predictive value obtained for each modality in the case of the overall accuracy evaluation.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	p	Kappa
MRI	82.6%	97.6%	98.3%	76.9%	0.0023	0.76
PET-CT	72.9%	92.7%	94.4%	66.7%	0.0006	0.61

Table 2
Sensitivity and specificity obtained for each metastatic site considered in our study. The number of true positive, false negative and false positive has been reported to allow a more convenient comparison between modalities.

	True positive	False negative	False positive	Sensitivity	Specificity
Lung					
MRI	8	5	0	61.5%	100%
PET-CT	4	9	0	30.7%	100%
Bone					
MRI	13	1	0	82.8%	100%
PET-CT	10	4	0	71.4%	100%
Liver					
MRI	4	0	0	100%	100%
PET-CT	2	2	0	50%	100%
Lymph nodes					
MRI	26	3	1	89.6%	N/A
PET-CT	24	5	0	82.7%	100%

3.3. Impact of Diffusion Weighted imaging on the overall accuracy

The combination of a DW sequence with the usual STIR and contrast-enhanced T_1 sequences increased dramatically the sensitivity of the MRI examination. This protocol allowed the detection of 14 lesions (one in the hepatic parenchyma, 2 bone lesions, 3 adenopathies, 7 subcutaneous and a last located in the intraperitoneal area) that were not revealed when interpretation was made without taking the DW sequence into consideration (session 1). In terms of detection, a difference of 14 lesions can be considered statistically significant.

4. Discussion

A prior study comparing the accuracy of whole-body MRI with whole-body CT in the case of patients affected by advanced melanoma reported the superiority of the form [11]. Another study dealing with the same disease and contrasting whole-body MRI with PET-CT concluded that PET-CT has an overall accuracy of 86.7% compared to 78.8% for whole-body MRI ($p = 0.0007$) [12]. The respective specificities have been found different as well, for both specific and overall values. Indeed, PET-CT is more efficient for N-staging and detection of skin and subcutaneous metastases, while whole-body MRI is more sensitive for detecting liver, bone and brain metastases [12]. On the contrary, it was pointed out that whole-body MRI is less sensitive but more specific than PET-CT for classifying pulmonary lesions.

4.1. Overall accuracy

The results of our prospective study demonstrated the potential of whole-body imaging techniques for staging metastatic melanoma. Whole-body modalities simplify and shorten the clinical investigation of patients affected by melanoma by replacing the conventional multimodality imaging approach. DW sequence can be easily implemented for whole-body examinations.

In the population of patients that we considered for this study, whole-body MRI was significantly more accurate than PET-CT except for adenopathies. Nevertheless, a more detailed analysis of all metastatic sites underlines that sensitivity and specificity of PET-CT and whole-body MRI notably differ between from one site to another site.

The comparison of diagnostic performance of PET-CT with whole-body MRI in the case of patients experiencing a melanoma or another oncologic disease has already been studied, but without including a DW sequence in the MRI protocol [13–18].

Three studies have concluded that PET-CT provides a better diagnostic than MRI.

In 2003, Antoch et al. [19] collated results provided by whole-body MRI and PET-CT for TNM staging of a population of 98 patients affected by various malignant diseases. Global performance of PET-CT was 95% for sensitivity and 79% for specificity, while diagnostic performance of whole-body MRI was respectively evaluated at 79% and 78%. This study demonstrated the superiority of PET-CT but, the considered population being mainly composed of patients presenting pulmonary tumors, it can be argued that, in this specific case, tumor localization is obviously better performed with CT than with MRI. Due to their respective scan length, MRI is indeed much more sensitive to respiratory motions than CT and, as a consequence, it provides worse results than CT at the chest level.

Schmidt et al. [20] compared whole-body MRI to PET-CT for metastasis detection in the case of 41 patients affected by various oncologic diseases. The resulting overall accuracy for TNM classification was 95% for PET-CT, and 91% for MRI. The difference of accuracy between the two modalities is likely due to their respective accuracy concerning adenopathies.

Finally, we can mention a study concerning malignant melanoma led by Pfannenberg et al. [12] that proposed a comparison between PET-CT and MRI. The sensitivity of PET-CT was also evaluated at 86.7% whereas MRI reached a value of 78.8%.

The study that we carried out demonstrated that the modality providing the best results for staging patients affected by melanoma was whole-body MRI including a DW sequence. This result can be explained by the use of the DW sequence that improved significantly the diagnostic sensitivity. Indeed, we showed that whole-body MRI examinations interpreted without DW images yield the same conclusion as the 3 other studies cited previously, *i.e.* the superiority of PET-CT versus MRI; but as soon as the DW sequence was taken into account for interpreting MRI examinations, it appeared that PET-CT was outperformed.

4.2. Accuracy of N-staging

The major drawback of the MRI concerning adenopathies is that staging solely based on size is not applicable in numerous cases. The characterization of all lymph nodes is the biggest challenge for the future in such a way that it can change the therapeutic approach in many oncologic diseases. Radiology plays an important role for staging lymph nodes. A sub-microscopic metastasis can indeed exist in a small lymph node while a large lymph node can be only inflammatory. Consequently, the single size criterion cannot be considered as pertinent.

PET-CT provides additional information that seems to be a great advantage over other imaging modalities, but unfortunately it remains some false positives that are problematic as well. These false positives arise from inflammatory lymph nodes uptaking the ^{18}FDG molecule. Then, it cannot be considered as specific. In addition, one has to take into account that metastatic necrotic lymph nodes are not spotted by PET-CT because they do not uptake ^{18}FDG. Finally, it must be noticed that sub-microscopic metastases cannot be seen as well because of the poor spatial resolution of the current PET-CT scanners.

A last drawback that is common to all imaging modalities is the lack of histopathological control for each adenopathy. Thus, a relevant gold standard for the most of adenopathies is very difficult to obtain.

Antoch et al. [19] and Schmidt et al. [20] achieved a diagnostic accuracy from 91% up to 93% with PET-CT and from 79% up to 78% with whole-body MRI for the proper assessment of N-staging. Pfannenberg et al. [12] considered that the difference in performance was the most significant in the assessment of lymph nodes with a clear superiority of PET-CT, with an overall accuracy of 86% in comparison with 69.6% obtained with whole-body MRI.

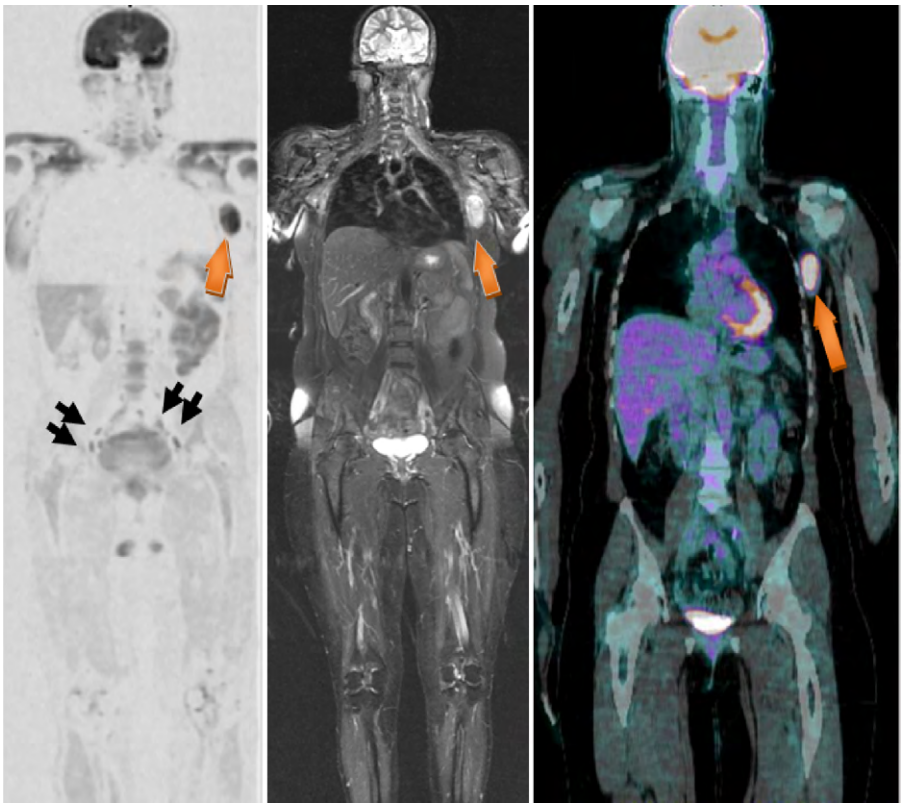

Fig. 2. 65 years old woman. DWI, STIR and PET-CT images are respectively depicted from the left to the right. The left axillar lymph node is well visualized by both MRI and PET-CT (orange arrows). Its size is around 25 mm. On the contrary, small bilateral iliac lymph nodes, whose size is 5–7 mm, are only displayed on DWI sequence (black arrows).

In our study, whole-body MRI seemed to be similar to PET-CT for adenopathy. The first explanation of these differences is the absence of a DW sequence in the previous studies. Therefore, with only STIR and T_1 sequences, spatial resolution is not optimal (between 3 and 5 mm for both sequences). With DW-MRI, all lymph nodes can be individualized whatever their size because this sequence permits the differentiation of abnormal signal intensities from surrounding organs. The remarkable difference in contrast between lymph nodes and surrounding adjacent tissue enables detection of lymph nodes (Fig. 2). We considered that abnormal signal intensity of lymph nodes reflects a decrease of ADC (Apparent Diffusion Coefficient) due to a high cellularity and to a T_2 shine-through effect. Nonetheless, these assumptions still need to be verified.

The second explanation given by Antoch et al. [19] is that frequent locations of metastatic lymph nodes were the hilum and the mediastinum because most of the patients in this study had lung cancer. These regions cannot be well studied by MRI because of respiratory motion artifacts. Another factor reducing accuracy is the low specificity caused by borderline sized lymph nodes that represents a significant issue for MRI investigation. Our study did not include hilar and mediastinal adenopathies. Three false negatives were yielded by MRI (concerning axillar, inguinal and retroperitoneal areas, 10 mm in diameter) whereas we obtained five false negatives with PET-CT (soeliac and retroperitoneal areas). The single false positive of the whole study concerned MRI and was actually a sus-clavicular adenopathy which did not appear on any other examinations.

4.3. Staging accuracy for specific metastatic sites (M-staging)

Antoch et al. [19] found an overall accuracy of 94% for PET-CT and 93% for whole-body MRI. For the same characteristic, the study

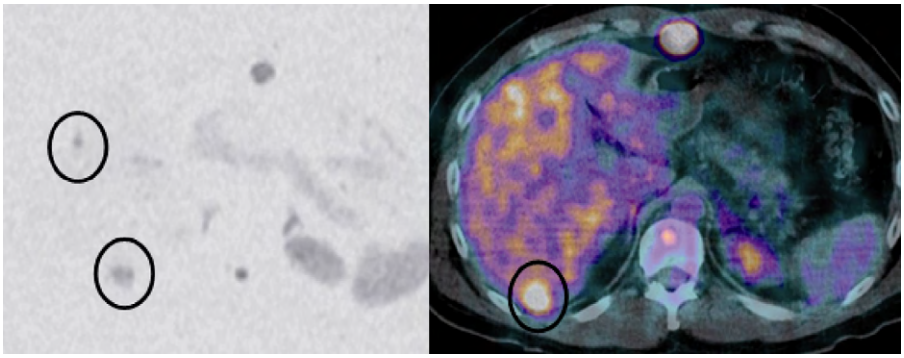

Fig. 3. 58 years old woman. Case of two secondary hepatic metastases (segments V and VI) clearly observed on a DW sequence (on the left). The lesion located in the segment V is not seen by PET-CT (on the right) because of a moderate physiological hyper-metabolism. One can notice an anterior intra-peritoneal node properly shown by the two techniques.

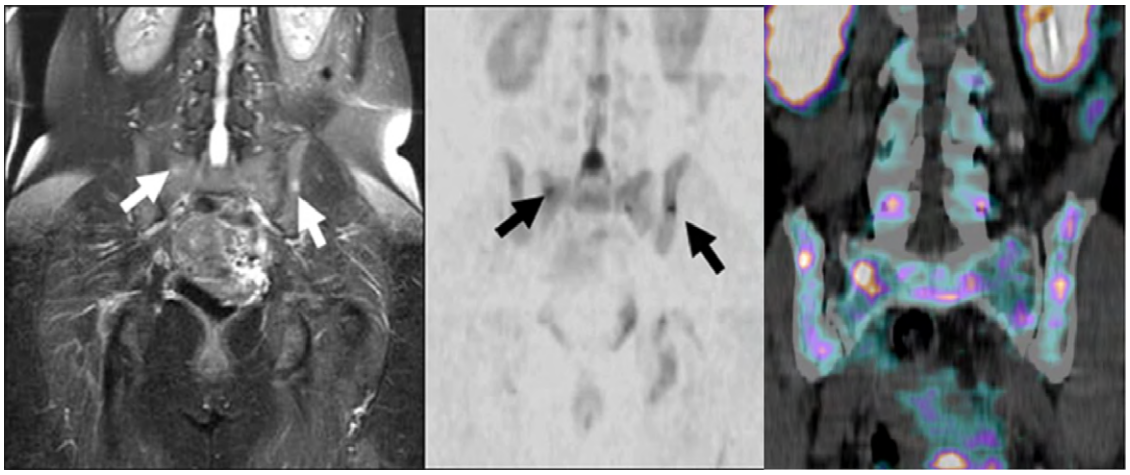

Fig. 4. 27 years old man. Examples of secondary distant bone metastases only visible on the MRI examination. These metastases are clearly seen as abnormal hyper-signal areas on the STIR sequence (on the left, white arrows) while they appear as hypo-signal areas on the DW sequence visualized in negative contrast (middle image, black arrows). On the right, no significant ^{18}FDG uptake can be visualized on PET-CT.

carried out by Schmidt in 2005 established 92% for whole-body MRI and 82% for PET-CT, but if the M-staging was considered solely whole-body MRI reached a value of 96% and PET-CT 82%.

Our study did not consider the so-called "global" M-staging but only the specific metastatic sites, because we considered that some areas such as lungs are too difficult to investigate by MRI. In addition, M-staging should not be considered, from our point of view, as the most relevant criterion for comparing these two techniques insofar as performances of PET-CT and whole-body MRI differ greatly from a given specific metastatic site to another.

4.3.1. Pulmonary metastases

Antoch et al. [19] showed that PET-CT was more reliable for pulmonary metastasis detection than whole-body MRI. On the contrary, Pfannenberg et al. [12] demonstrated that PET was the less accurate whole-body imaging modality for lungs.

Likewise, we showed that PET-CT provided the worst results with a sensitivity of 30.7% compared to 61.5% for MRI. In comparison, a sensitivity value of 26.4% for PET was reached in Pfannenberg's study.

In our case, the apparent below-average performance of MRI can be explained by the fact that we were committed to use the body coil for the thorax study (the phased-array coil was dedicated to the abdominal level and our scanner did not allow the use of several phased-array coils at the same time) and, as a consequence, we were unable to avoid motion artifacts by means of short apnea or respiratory trigger because the body coil was compatible neither with such a device or parallel imaging technique.

The lack of sensitivity of PET-CT can be related to the lesion size criterion, the size having to be superior to 5 mm to allow detection and, on the other hand, to the fact that some pulmonary lesions are known to not fix ^{18}FDG independently of their size.

We encountered five false negatives with MRI and nine with PET-CT.

4.3.2. Hepatic metastases (Fig. 3)

We found that MRI was the best modality for staging liver metastases considering that it allowed us to detect all hepatic metastases. The use of the DW sequence enabled to bring out one additional lesion that was not revealed by both STIR and T_1.

Two lesions were not detected by PET-CT. It turns out that the main problem of this technique remains the detection of small lesions because of a moderate physiologic uptake of ^{18}FDG in the liver. It is commonly admitted that lesions that have a size inferior to 10 mm are not detected by PET-CT, and this is precisely the reason for which these two hepatic metastases were not revealed. Their size was effectively measured smaller than 10 mm. Antoch's et al. [19] studies considered that MRI was the best modality as well and revealed 132 hepatic metastases for 13 patients compared with 117 lesions for 12 patients in the case of PET-CT.

Schmidt et al. [20] detected 15 hepatic metastases by means of MRI and only 8 by using PET-CT. All lesions missed by PET-CT had a mean size of 7 mm, whereas the mean size of detected lesions was 16 mm. In comparison, the smallest lesion detected on MRI images measured 5 mm.

MRI allowed Pfannenberg et al. [12] to discover 35 lesions whereas 33 were revealed by PET-CT on the same population. The two hepatic metastases missed by PET-CT measured less of 10 mm in diameter.

Our results confirmed the observations made by the three other mentioned studies that indicated a higher accuracy of whole-body MRI in comparison with PET-CT for hepatic [12] metastases.

MRI examinations did not display false negatives. On the contrary, PET-CT yielded 2 false negatives in segments IV and V concerning lesions measuring respectively 12 mm and 7 mm.

4.3.3. Bone and skeletal metastases (Fig. 4)

Antoch's study [19] showed that PET-CT failed to detect bone metastases twice. Incorrect M-staging is likely due to histological characteristics of the tumors on one hand, and to the metastasis size on the other hand. It is indeed commonly admitted that micrometastases cannot be seen no PET-CT images because of the poor spatial resolution of this technique. Schmidt et al. [20] and Pfannenberg et al. [12] demonstrated as well the superiority of whole-body MRI over PET-CT (in spite of the lack of DW sequence in the MRI protocol).

In our case, whole-body MRI showed 13 lesions and PET-CT only 10. For these metastatic sites, DW sequence appeared to be crucial in that sense that it allowed the detection of 2 additional lesions.

Numerous studies have already stated the superiority of MRI for detecting skeletal metastases [10,21–24] over skeletal scintigraphy. Several recent studies comparing ^{18}FDG PET-CT and whole-body MRI confirmed as well our observations and stressed the high sensitivity of MRI for bone marrow imaging and thus for detecting skeletal metastases. For instance, Schmidt et al. [22] proved that whole-body MRI allowed to detect more bone metastases than PET-CT did and whole-body MRI including a DW sequence has been shown to be superior to skeletal scintigraphy for detecting

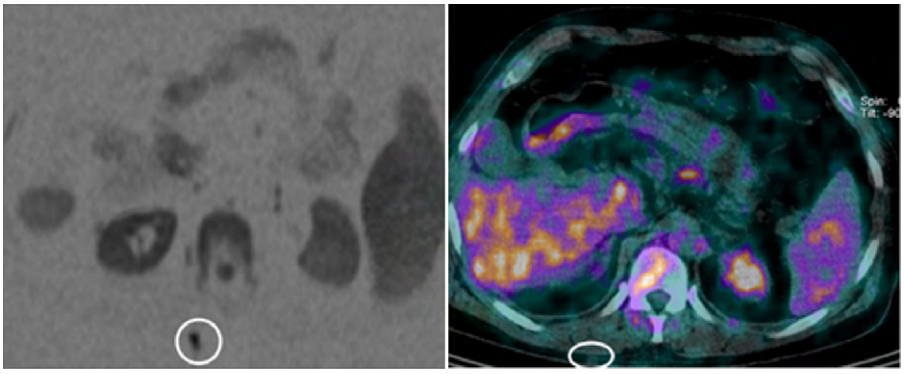

Fig. 5. 42 years old man. On the left: lumbar subcutaneous metastatic node (white circle) as seen by DW-MRI. On the right: the corresponding PET-CT image on which the node is not visible because of the lack of ^{18}FDG uptake.

bone metastasis [10]. The latter fact was confirmed in the present study considering that the DW sequence enabled us to detect 2 additional marrow lesions. This fact can be easily explained by the high contrast between tissues provided by a diffusion-weighted contrast, making therefore possible the detection of small lesions.

MRI provided only 1 false negative (T6, 10 mm in diameter). Four false negatives had to be considered for PET-CT (3 in the iliac bone and 1 in the sacrum).

4.3.4. Subcutaneous metastases (Fig. 5)

Schmidt et al. [20] and Pfannenberg et al. [12] considered that PET-CT was the most accurate modality, whereas we found that, on the contrary, whole-body MRI was the most accurate.

Pfannenberg's study showed that PET-CT revealed twice as many lesions as MRI did. An explanation might be the coronal orientation chosen for whole-body MRI imaging. The coronal plane can cause the miss or the misinterpretation of lesions that are localized superficially in the skin and subcutaneous tissues. Thus, they can be considered as vessel structures or as so-called partial volume phenomena. This is the reason for which we consider that the coronal orientation may be more difficult to interpret than the axial plane for detecting small subcutaneous metastases.

DW sequence that we used in our standard MRI protocol had here the benefit of its native axial acquisition plane. In this way, we had access at the same time to the most relevant acquisition plane for detecting subcutaneous lesions and to an excellent contrast between lesions and surrounding tissues due to diffusion phenomenon on one hand, and to the absence of fat signal on the other hand, the DW sequence we used being based on a selective water peak excitation. For the sake of convenience, DW sequence was reconstructed in coronal plane so as to be simultaneously interpreted with STIR and T_1 images. This technique enabled us to detect 7 additional subcutaneous lesions.

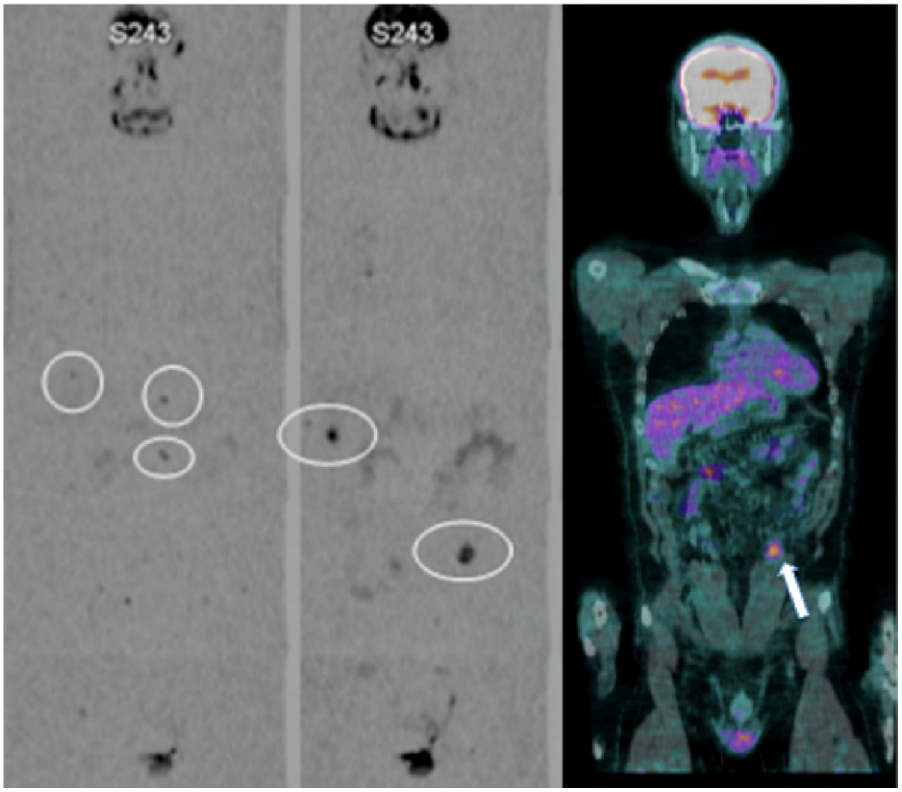

Fig. 6. 38 years old man. Examples of multiple subcutaneous and intra-peritoneal nodes well visualized on a coronal reconstruction of the DW sequence (images on the left and on the middle, white circles) with a size inferior to 7 mm. Only one node was detectable on the images provided by PET-CT examination (image on the right, white arrow).

4.3.5. Central nervous system metastases

It is important to mention that MRI is the best imaging modality for detecting tumor of the central nervous system. In the population we studied, there was only a single brain metastasis that was missed by both PET-CT and MRI. As previously mentioned, a retrospective analyze showed that it was detectable on MRI images only.

Several studies showed that the most accurate modality for brain metastasis detection was MRI because of normal uptake of ^{18}FDG into the brain that leads to a great uncertainty in terms of detection with PET-CT.

4.3.6. Intra-peritoneal metastases

A single patient was concerned by an intra-peritoneal carcinomatosis (Fig. 6). The latter was only seen on the DW sequence, likely due to the very small size of intra-peritoneal nodes (inferior to 4 mm). PET-CT examination was negative.

4.3.7. Partial conclusion about M-staging

To sum up, the comparison between our results and those obtained by Antoch et al. [19], Schmidt et al. [20] and Pfannenberg et al. [12] showed that the use of a DW sequence in the MRI protocol improves significantly the capability of detecting secondary lesions; especially in bone, liver, subcutaneous areas and intra-peritoneal carcinomatosis. As a matter of fact, DW sequence allowed us to finally detect 14 additional malignant lesions among the considered population of 35 patients. These lesions were mainly small (inferior to 10 mm) and were found in the bone marrow, in the liver, and in the subcutaneous and intra-peritoneal areas.

Another point of discussion in the future is certainly the cost and the availability of whole-body imaging. PET-CT costs twice as much or more than a whole-body MRI. Moreover, PET-CT is associated with X-ray exposure and the tracer production, transport and its application are more labor and cost-effective. Sensitivity and specificity of PET-CT depend on three major points that are tumor histology, localization and lesion size.

Diffusion-weighted sequence seems to be required in addition to the standard oncologic protocol composed by STIR and T_1 weighted sequences. Among the advantages of DW-MRI, one can cite the fact that this technique is totally non-invasive and cost-effective. Moreover, DW-MRI does not require any radiation exposure, any oral or intravenous administration of contrast material and does not cause patient discomfort. It can also be easily added to the standard MRI protocol to improve examination efficiency. We suggest that DW images should be analyzed before STIR and T_1 weighted sequences because it is not helpful for differential diagnosis between malign and benign tissues in any circumstances. In this last particular case, it can be just used to depict abnormal lesions because of its high sensitivity but poor specificity. Lichy et al. [25] suggested that the computation of ADC maps could help to solve differential diagnosis.

The study we made yielded interesting results, but it has several limitations. First, the population studied was relatively small and the results we obtained need to be confirmed with another study taking into account more than 35 patients. The second point is that the PET-CT we used (performed without any contrast agent) has only two channels for its CT part, which is rather poor compared to the current PET-CT scanners available. The results provided by using our devices are likely worse than results which would be obtained with an up-to-date device (at least for the CT part). The last limitation that we can point out is the following up results for the lymph nodes.

5. Conclusion

Finally, it appears that none of the methods ensured 100% staging accuracy, preventing that way from using only one modality as the sole basis for diagnosis. Our data suggest that whole-body MRI including a DW sequence is the most accurate method for detecting secondary lesions; particularly for liver, bone marrow and subcutaneous area. In the case of adenopathies, the problem remains that all modalities are sensitive, but not enough specific to clearly evaluate the presence of metastases.

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