

Clinical utility of PET/MRI in multiple myeloma

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ABSTRACT

Introduction: This study aimed to evaluate the clinical utility of positron emission tomography/magnetic resonance imaging (PET/MRI), especially in comparison with PET/computed tomography (CT), which has been widely used in clinical practice in multiple myeloma.

Method: F-18 fluorodeoxyglucose PET/MRI and PET/CT studies were done at baseline and when at least a partial response to treatment was achieved. These were done for newly-diagnosed myeloma patients who have not had more than 1 cycle of anti-myeloma treatment, or for relapsed and/or refractory myeloma patients before the start of next line of therapy.

Results: PET/MRI correlated significantly with PET/CT, in terms of number of lesions detected, standardised uptake value (SUVmean and SUVmax, both at baseline and post-treatment. PET/MRI and PET/CT correlated with survival at baseline, but not post-treatment.

Conclusion: In this study, PET/MRI was more sensitive in detecting early disease and disease resolution post-treatment, compared with PET/CT. However, PET/MRI was less sensitive in detecting lesions in the ribs, clavicle and skull.

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INTRODUCTION

Multiple myeloma (MM) is a haematological malignancy characterised by abnormal accumulation of malignant plasma cells and is associated with anaemia, renal impairment, hypercalcemia and bone lesions. A sensitive method to detect bone lesions is crucial as it could determine the decision to start treatment. In this era, the International Myeloma Working Group (IMWG) consensus recommends low-dose whole-body computed tomography (CT) over the conventional skeletal survey, in view of its increased sensitivity in detecting osteolytic bone lesions.¹

More advanced imaging techniques, such as positron emission tomography/computed

CLINICAL IMPACT

What is New

- This study showed that PET/MRI correlated well with PET/CT in multiple myeloma.
- PET/MRI was more sensitive in detecting early disease and disease resolution post-treatment, compared with PET/CT, though less sensitive in detecting lesions in the ribs, clavicle and skull.

Clinical Implications

- Given that PET/MRI is more sensitive in detecting early disease compared with PET/CT, it can be a better modality for diagnostic evaluation of myeloma.

tomography (PET/CT) and whole-body magnetic resonance imaging (MRI), are even more sensitive and able to determine not only bone destruction, but also disease burden and disease activity. In particular, focal lesions could only be detected by MRI and PET scans. These focal lesions are different from the osteolytic lesions where bone destruction has occurred—a process that can be detected by CT alone or conventional skeletal survey.¹

Studies have also shown that residual lesions on PET/CT and MRI were related to poorer outcomes.²⁻⁴ Imaging modality has also been incorporated into the MM response assessment criteria by the IMWG, in which the imaging plus minimal residual disease (MRD)-negative response category requires both MRD and PET/CT negativity.⁵

MRI has excellent soft tissue contrast⁶ and can evaluate abnormal infiltration in the tissue, including bone marrow, with high sensitivity, while PET-imaging evaluates the tissue metabolic activity to assess the viability of the focal lesions.^{1,7} Thus, MRI and PET provide complementary evaluation for increased sensitivity in MM imaging. This

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study aimed to evaluate the role of PET/MRI, which combines the benefits of both MRI and PET-imaging, especially in comparison with PET/CT that has been widely used in clinical practice.

METHOD

Study design and patients

Newly-diagnosed MM patients who have not had more than 1 cycle of anti-myeloma treatment, or relapsed and/or refractory MM patients before the start of next line of therapy, were recruited. PET/MRI and PET/CT studies were done at baseline and when at least a partial response to treatment as defined by IMWG,⁵ was achieved. All patients gave written informed consent. The study protocol was approved by the institutional ethics review board (Study Reference Number: 2015/00254).

Image acquisition

Participants underwent a single F-18 fluorodeoxyglucose (FDG) injection, followed by dual-imaging protocol including a whole-body PET/CT, followed by a PET/MRI scan. The baseline scans were done with 186 ± 4.53 MBq (5.02 ± 0.12 mCi) F-18 FDG injection, while the post-treatment scans were done with 188.90 ± 4.20 MBq (5.10 ± 0.11 mCi) F-18 FDG injection. Eight subjects had both baseline and end-of-treatment scans, while 4 subjects only had baseline scans performed. All reconstructed PET images were converted to standardised uptake value (SUV) images using the measured activity concentration, injected dose and body weight: $\text{SUV} = \text{tissue concentration [MBq/kg]} / (\text{injected dose [MBq]} / \text{body weight [kg]})$.

PET/CT scan was performed on a Biograph mCT (Siemens Healthcare, Germany) 60 min post-injection from the skull base to the knees, with an imaging duration of 5 min per bed position. The PET images were reconstructed into 400×400 matrix size with voxel size of $2.04 \times 2.04 \times 2.03$ mm³ using three-dimensional ordinary Poisson ordered-subset expectation maximisation (OP-OSEM3D) algorithm, with resolution modelling and point-spread-function and time-of-flight correction, and using 3 iterations and 21 subsets. Low-dose CT protocol (120 kVp, 150 mA, pitch 1.5, careDose) was utilised for attenuation correction of the PET data and image fusion.

Simultaneous PET/MRI scan was then performed on Biograph mMR (Siemens Healthcare, Germany), approximately 1 hour after the PET/CT scan, from skull to mid-thigh. Magnetic resonance (MR) images were acquired with 3T whole-body MRI and shielded whole-body gradient coil system, with the respective imaging parameters for the different MR sequences in Table 1. The PET images

were reconstructed into 344×344 matrix size with voxel size of $2.01 \times 2.01 \times 2.03$ mm³ using OP-OSEM3D. Similarly, all corrections were applied, with resolution modelling using 3 iterations and 24 subsets. For attenuation correction, a Dixon volume interpolated breath-hold examination sequence was performed to generate the attenuation map used during the data reconstruction.

Table 1. Imaging parameters for MR sequences.

Imaging parameters	T1-weighted	T2-weighted	DWI
TR (ms)	660	2000	17,300
TE (ms)	8.8	86	74
TI (ms)	Nil	240	180
Flip angle (°)	140	160	Nil
Matrix size	384 x 256	320 x 320	134 x 134
Field of view (mm)	450	450	430
Slice thickness (mm)	4	4	5
Inter-slice gap (mm)	0	0	0
Bandwidth (kHz)	310	781	2332

DWI: diffusion-weighted imaging; MR: magnetic resonance; TE: echo time; TI: inversion time; TR: repetition time

Image analysis

Image analysis was performed by 2 nuclear medicine radiologists by viewing the images in the transaxial, coronal and sagittal planes.

Osseous foci presenting with significant F18 FDG uptake above that of blood pool and adjacent uninvolved marrow, and unlikely to be attributed to a benign aetiology (e.g. degenerative change, inflammation or trauma) were considered as positive for MM. Extra-osseous foci were also evaluated in the same manner for extra-osseous involvement of MM. Quantitative evaluation was performed using SUVmax and SUVmean computed from volumes of interest (VOI) placed over the foci of increased F18 FDG uptake. A reference SUVmax for each patient was obtained from the marrow at the iliac ala that demonstrated no MM lesions, as well as the right hepatic lobe.

Morphologically, lesions that did not show significant FDG-avidity but demonstrated morphological features compatible with MM were also considered positive for MM. A measurable lucent marrow lesion was defined as a lesion of more than 5 mm in diameter on CT images, or lesion appearance on MRI with low T1 signal or exhibiting restricted diffusion on high b-value

diffusion-weighted imaging (DWI). Lesion characterisation was based on both functional (PET) and morphological (MRI/CT) criteria.

Four main patterns of bone marrow FDG uptake were identified: (1) normal FDG distribution with no abnormal focal FDG uptake to indicate MM involvement; (2) focal FDG-avid bone lesions identified and consistent with MM involvement; (3) diffusely increased, intense FDG uptake within the marrow without focal lesions but suspicious for extensive marrow disease infiltration; and (4) mixed pattern of focally FDG-avid bone lesions on a background of diffusely increased FDG uptake within the marrow.

Statistical analysis

Statistical analysis was done using the RStudio version 1.2.5042 software (RStudio, Boston, MA, US) on Mac OS Catalina version 10.15.5 (Apple Inc, Cupertino, CA, US). The statistical evaluation was performed using the Spearman's rank for correlation analysis, and Kaplan-Meier with log-rank test for survival analysis. All reported *P* values were evaluated at the conventional 5% significance level.

RESULTS

Baseline characteristics

From April 2016 to Jan 2019, a total of 40 whole-body F-18 FDG PET/CT and PET/MRI scans of 12 patients were conducted. Of the 12 patients in this study, 10 patients were newly diagnosed MM patients, 1 patient was newly-diagnosed with amyloid light-chain (AL) amyloidosis and 1 patient was a relapsed MM patient.

The demographics of the patients are presented in Table 2.

Radiological findings and correlation

All 12 patients underwent PET/CT and PET/MRI studies at baseline, and 8 out of 12 patients underwent post-treatment PET/CT and PET/MRI studies. Of the 4 patients who did not undergo post-treatment studies, 2 were due to the logistic issue of time unavailability and 2 died. Although the patients were planned to have the baseline imaging done at baseline or within cycle 1 of MM treatment, 2 of the enrolled patients (patients ID 9 and 10, Table 1) had their scans done during cycle 2 of MM treatment due to difficult logistic arrangements.

Table 2. Patient demographics.

Patient ID	Age	Sex	Disease	Presence of lytic lesion (skeletal survey)	ISS Stage	High-risk FISH	R-ISS Stage
1	46	Male	Newly diagnosed MM	Yes	1	No	1
2	60	Female	Newly diagnosed MM	Yes	1	Yes (17p del)	2
3	60	Male	Newly diagnosed MM	Yes	2	No	3
4	59	Female	Newly diagnosed MM	Yes	2	No	2
5	59	Male	Newly diagnosed MM	Yes	3	No	2
6	65	Male	Newly diagnosed MM	Yes	3	No	3
7	63	Female	Newly diagnosed MM	No	2	No	2
8	61	Female	Newly diagnosed MM	Not available	2	No	2
9	73	Male	Relapsed MM	Not available	3	Yes t(4;14)	3
10	65	Female	Newly diagnosed MM	Not available	2	No	2
11	54	Male	Newly diagnosed MM	Yes	2	No	2
12	54	Male	AL amyloidosis ^d	No	2	No	2

AL amyloidosis: immunoglobulin light chain amyloidosis; FISH: fluorescence in situ hybridisation; ISS: International Staging System; MM: multiple myeloma; R-ISS: Revised International Staging System; t(4;14)=translocation (4;14); 17p del: deletion 17p

Both PET/CT and PET/MRI images were of adequate diagnostic quality. Based on the evaluation of FDG marrow uptake pattern, at baseline, 2 patients demonstrated normal FDG distribution, 3 patients demonstrated focal FDG-avid bone lesions, 4 patients demonstrated diffuse bone marrow disease infiltration and 3 patients

demonstrated a mixed pattern (Table 3). Maximal intensity projection images of the 4 patterns of bone marrow FDG uptake are shown in Fig. 1.

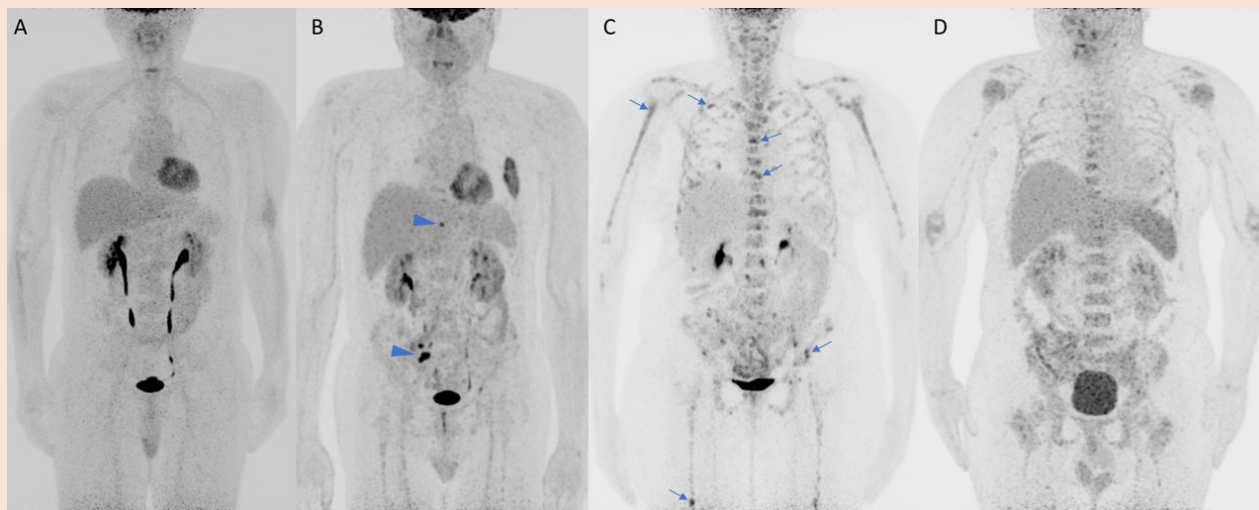
Post-treatment scans of the 8 patients demonstrated resolution of the abnormal patterns (patterns 2, 3 and 4) of marrow FDG uptake in 6

Table 3. Bone involvement pattern.

Patient ID	Pre-treatment FDG-uptake pattern	Pre-treatment morphological pattern	Post-treatment FDG uptake pattern	Post-treatment morphological pattern
1	Mixed, predominantly diffuse with focal lesions	MRI: focal lesions CT: mottled appearance with focal lytic lesions	FDG uptake resolved	MRI: focal lesions resolved CT: no change
2	Predominantly diffuse also involving long bones	MRI: diffuse marrow replacement CT: innumerable lytic lesions	FDG uptake resolved, especially in long bones	MRI: marrow lesions resolved CT: innumerable lytic lesions, more sclerosis
3	Focal lesions Some FDG-avid lesions are not seen on MRI or CT	MRI: focal lesions, some lesions not FDG avid CT: lytic lesions	Not done	Not done
4	Diffuse marrow uptake	MRI: diffuse marrow change with focal lesions CT: innumerable lytic lesions	Diffuse marrow uptake resolved	MRI: resolved CT: lytic lesions are less in number, new areas of sclerosis likely treated disease
5	Diffuse marrow uptake, no focal lesions except at T12/L1 fractures	MRI: diffuse marrow replacement CT: mottled appearance, no focal lytic lesion	FDG uptake resolved	MRI: resolved, fatty conversion CT: no change
6	Innumerable lesions	MRI: Diffuse marrow replacement CT: innumerable lytic lesions	Died	
7	Diffuse mild marrow uptake Focal extraosseous right axillary node	MRI: diffuse marrow replacement, no focal lesions CT: no focal lytic lesion	FDG uptake resolved Extraosseous right axillary node resolved	MRI: resolved CT: no change
8	Mixed Focal on diffuse	MRI: diffuse marrow replacement, DWI multiple focal lesions CT: lytic lesions	Not done	Not done
9	Mixed Focal on diffuse	MRI: innumerable focal lesions, DWI same CT: innumerable lytic lesions	Died	
10	No FDG avid lesions Insufficiency fractures with FDG uptake	MRI: multiple T1-hypointense lesions with no FDG-avidity, DWI shows multiple lesions with no FDG-avidity CT: multiple fractures, no focal lytic lesions	FDG unchanged, normal	MRI: overall less vertebral involvement by T1-hypointense and DWI intense lesions. CT: unchanged
11	Focal right humerus	MRI: dominant right humerus lesion, several tiny lesions on MRI (right iliac wing) too small for PET CT: dominant right humerus, innumerable lytic lesions.	FDG uptake resolved but many more sites of extraosseous nodal disease	MRI: both the lesions at the right humerus and the right iliac bone resolved CT: unchanged
12	Normal	No lesions on MRI or CT	Normal scan	No lesions on MRI or CT

CT: computed tomography; DWI: diffusion-weighted imaging; FDG: fluorodeoxyglucose; MRI: magnetic resonance imaging; PET: positron emission tomography

Fig. 1. F-18 fluorodeoxyglucose (FDG) positron emission tomography maximum-intensity-projection images demonstrating (A) normal FDG distribution, (B) focal FDG-avid lesions, (C) focal FDG-avid lesions on a background of diffusely increased marrow FDG uptake, and (D) diffuse pattern of increased marrow FDG uptake.



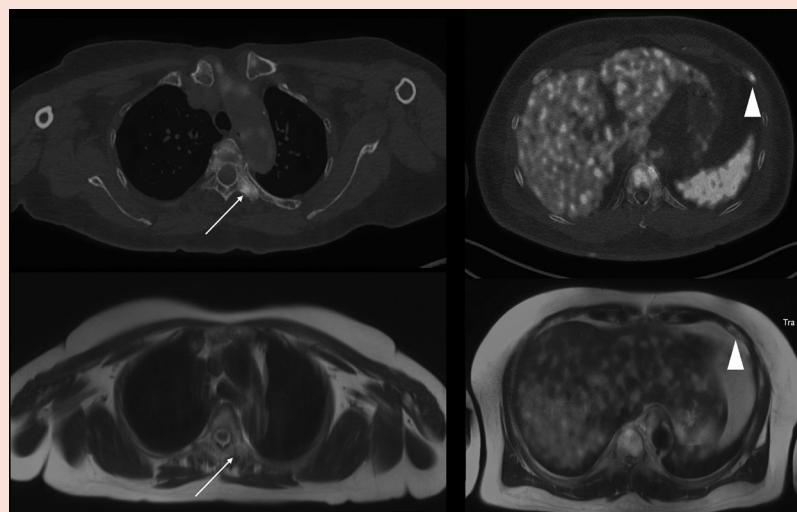
patients, while 2 patients with normal distribution of FDG on baseline scans had no discernible change on their post-treatment scans.

A total of 80 lesions were identified with PET/MRI and a total of 95 lesions were identified with PET/CT. For the number of lesions detected, PET/MRI correlated significantly with PET/CT, both at baseline and post-treatment with $r=0.84$ ($P<0.001$) and $r=0.79$ ($P=0.019$), respectively. However, there were some observable disparities. The largest disparity of lesions detected with PET/CT that was not detected on PET/MRI occurred for patient 2. In this patient, the majority of the lesions

detected on PET/CT had relatively low FDG-avidity, with SUVmax and SUVmean values equal to or below the reference liver SUVmax and SUVmean (Fig. 2). One important caveat to note is that the PET/CT and PET/MRI scans were performed sequentially after a single F-18 FDG injection leading to different uptake periods.

In patient 4, both PET/MRI and PET/CT demonstrated a mixed pattern of focal FDG-avid bone lesions on a background of diffusely increased marrow FDG uptake. In addition, there was a focal FDG-avid left cervical level V lymph node that was initially deemed indeterminate. On post-treatment scans,

Fig. 2. Fused positron emission/computed tomography (PET/CT) (top) and PET/magnetic resonance (MR) (bottom) images demonstrating fluorodeoxyglucose-avid lesions at the left transverse process of T4 (arrows) and the left 10th rib (arrowheads), which have an SUVmax and SUVmean equal to that of the liver on PET/CT but lower than the liver on PET/MR, accounting for the disparity in detection of bone lesions in this patient.



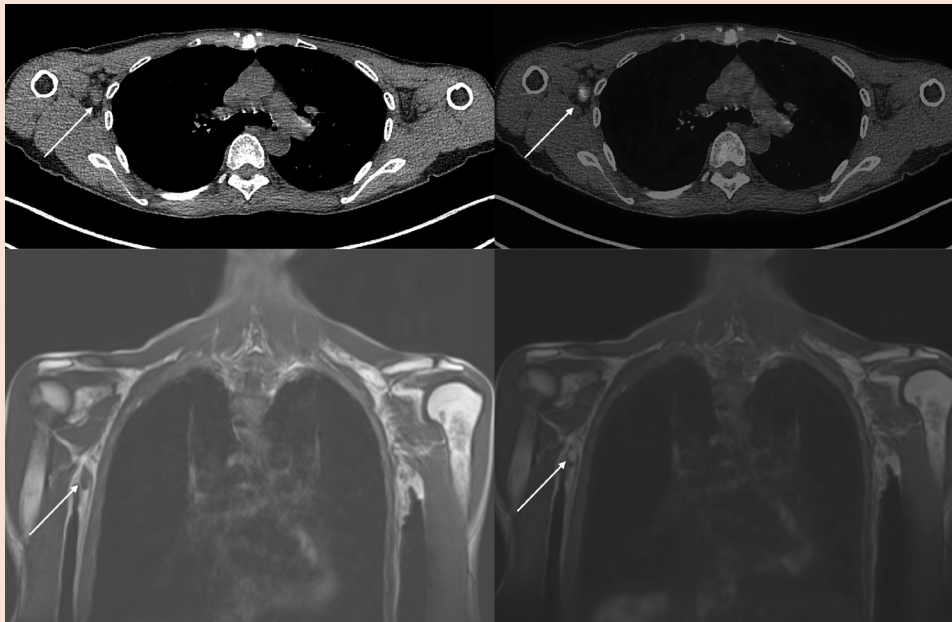
both PET/MRI and PET/CT showed a decrease in the number and FDG-avidity of bone lesions, but a discordant increase in the FDG-avidity of the left cervical level V lymph node. It was concluded that the lymph node was unlikely to represent a site of extramedullary disease. This might have contributed to the slight increase in SUV on the post-treatment scans.

For patient 7, both PET/MRI and PET/CT demonstrated a diffuse pattern of FDG uptake in the marrow without any focal signal abnormalities

on MRI or lytic lesions on CT. In addition, both PET/MRI and PET/CT identified an enlarged and FDG-avid right axillary lymph node that was deemed to be a possible site of extramedullary disease. On post-treatment scans, both PET/MRI and PET/CT showed resolution of the diffuse pattern of FDG uptake in the marrow as well as resolution of the right axillary lymphadenopathy (Fig. 3).

For patient 10, neither PET/MRI or PET/CT detected any FDG-avid bone lesions that were deemed as positive for MM involvement. Furthermore, there

Fig. 3. Top: Both axial positron emission tomography/computed tomography (PET/CT) and coronal PET/magnetic resonance (MR) demonstrate the FDG-avid lymph node in the right axilla, suspicious for a focus of extramedullary myelomatous disease. Bottom: (A) Pre-treatment coronal T1-weighted MR and fused PET/MR images demonstrate a diffuse hypointense marrow signal in the spine with (B) diffusely increased FDG uptake. (C) Post-treatment scans demonstrate restoration of normal signal intensity on T1-weighted MR images (D) as well as resolution of the diffusely increased FDG uptake.



were multiple vertebral compression fractures that did not demonstrate significant FDG-avidity, as well as evidence of prior healed fractures in the pubic rami and left femoral neck. Hence, these changes were deemed to be more likely attributable to insufficiency fractures from osteoporosis (Fig. 4).

For patient 11, PET/MRI detected more lesions than PET/CT (5 versus 3, respectively). In this patient, several tiny lesions were observed in the right iliac bone on MRI, which were probably too small for PET detection and demonstrated no abnormality on CT imaging (Fig. 5). Incidentally, both PET/MRI and PET/CT demonstrated FDG-avid lymphadenopathy, predominantly above the diaphragm. Post-treatment PET/MRI and PET/CT showed metabolic resolution of the dominant lesion at the right humerus, although there was an increase in the number and FDG-avidity of lymphadenopathy, which also progressed to involve the pelvic nodal stations. Due to the discordance of these findings, the FDG-avid lymphadenopathy was deemed unlikely to be related to MM.

Patient 12 had primary AL amyloidosis with low level plasma cells in the bone marrow and did not have any bone lesions.

Quantitative evaluation of SUVmax and SUVmean derived from VOIs drawn around MM lesions was performed. The SUVmax and SUVmean analysis for

both PET/CT and PET/MRI studies are summarised in Table 4.

The SUVmean and SUVmax of the positive lesions at baseline on PET/MRI and PET/CT showed significant correlations of $r=0.83$ ($P=0.001$) and $r=0.82$ ($P=0.002$). Similarly, the SUVmean and SUVmax of the positive lesions post-treatment on PET/MRI and PET/CT showed significant correlations of $r=0.84$ ($P=0.018$) and $r=0.84$ ($P=0.018$), respectively. For baseline scans, the average SUVmean and SUVmax were 2.85 and 4.96 for PET/CT, and 2.14 and 3.37 for PET/MRI. For post-treatment scans, the average SUVmean and SUVmax were 1.75 and 3.06 for PET/CT, and 2.14 and 3.37 for PET/MRI.

Clinical correlation

Baseline

For the evaluation of the number of lesions, we divided the patients into 6 groups (group 1 = 0 lesion, group 2: 1–3 lesions, group 3: 4–6 lesions, group 4: 7–9 lesions, group 5: 10–12 lesions and group 6: 22–24 lesions). We excluded the 1 relapsed MM patient from this survival analysis.

For the evaluation of SUVmean and SUVmax, we divided the patients into 9 groups, consisting of group 1: no lesion, group 2: SUV 0.1–1.9, group

Fig. 4. F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) maximum-intensity-projection image demonstrates normal FDG distribution in this patient. Sagittal fused PET/magnetic resonance (MR) image demonstrates compression fractures of the lumbar vertebrae (arrowheads) without significant FDG uptake. Axial fused PET/MR and T1-weighted MR images demonstrate linear hypointense signal at both sides of the sacral promontory with mildly increased FDG uptake (arrows). These lesions were deemed to be more likely attributable to insufficiency fractures secondary to osteoporosis than myelomatous disease involvement.

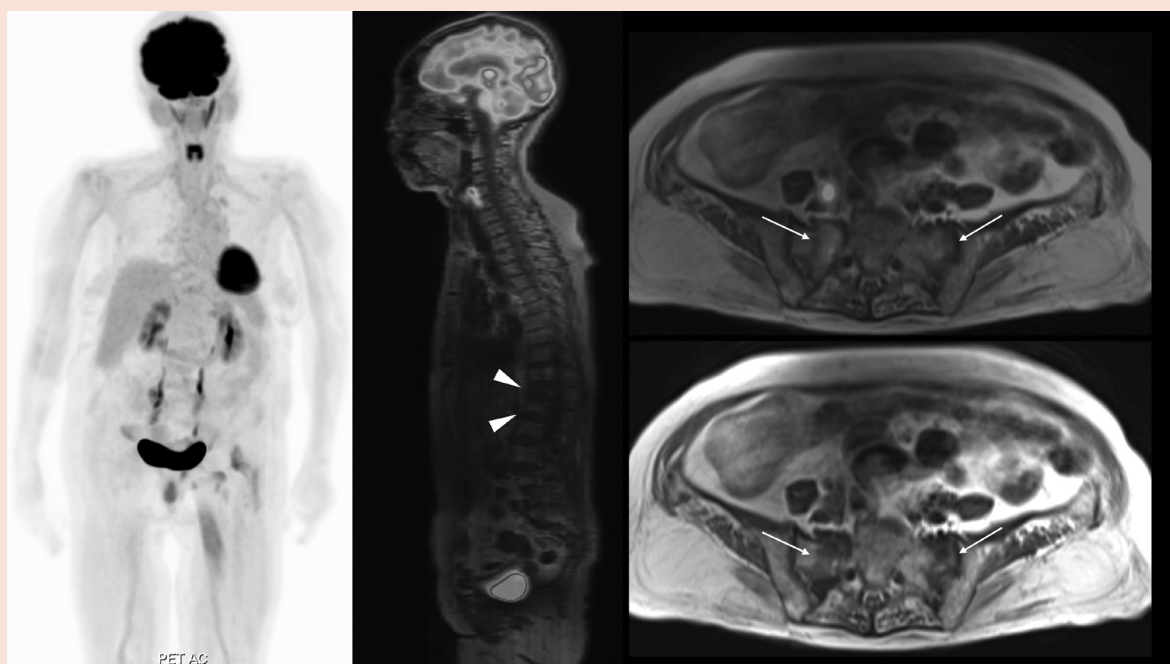
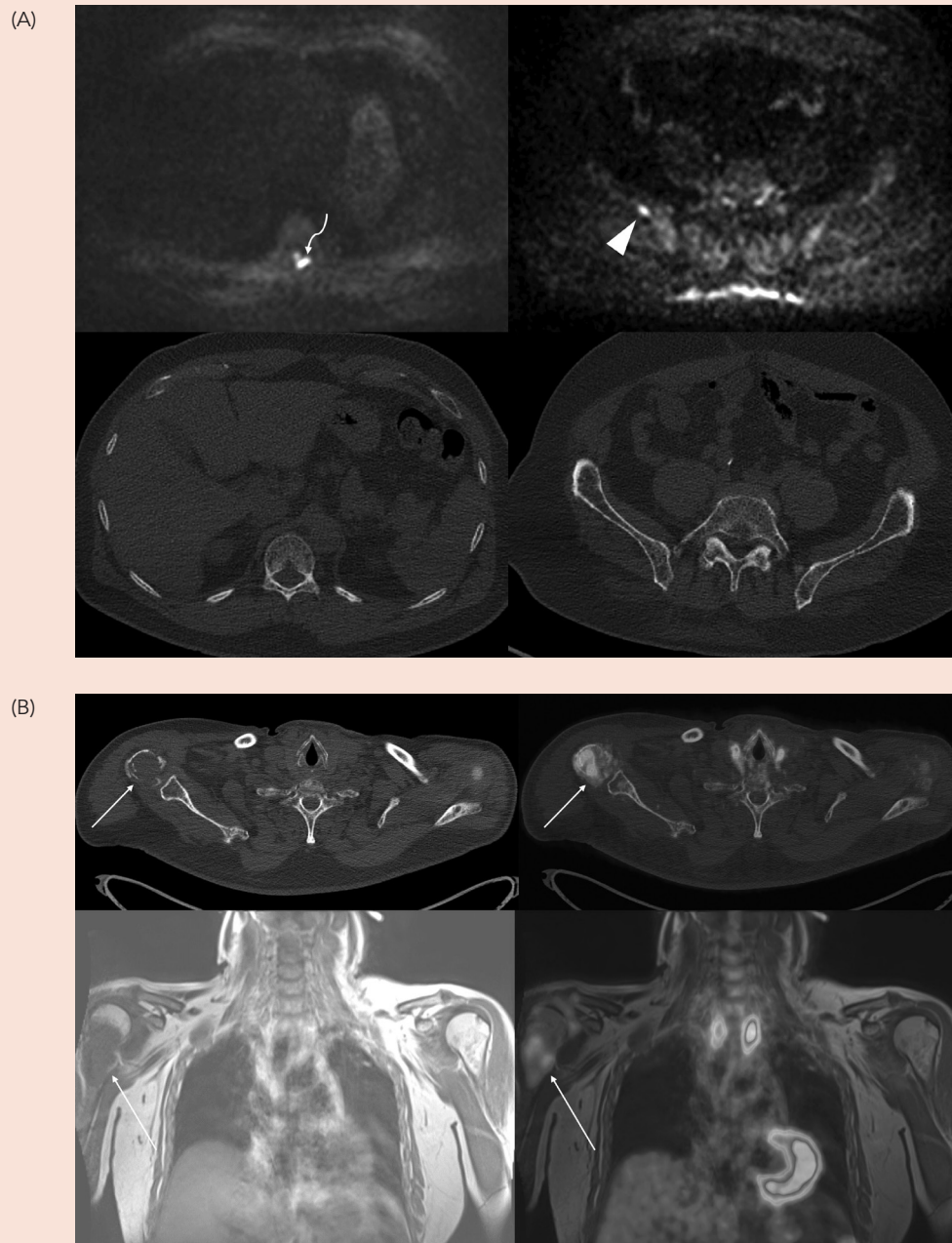


Fig. 5. (A) Diffusion-weighted imaging (DWI) in this patient demonstrated tiny lesions at the left lamina of T11 (arrow) and the right iliac wing (arrowhead) with no lytic change on the corresponding CT images. (B) Both axial positron emission tomography/computed tomography (PET/CT) and coronal PET/magnetic resonance (MR) demonstrate the dominant fluorodeoxyglucose-avid lesion involving the proximal right humerus (arrows) with lytic destruction of bone on CT imaging and a markedly hypointense marrow lesion on T1-weighted MR images.



3: SUV 2–2.9, group 4: SUV 3–3.9, group 5: SUV 4–4.9, group 6: SUV 5–5.9, group 7: SUV 6–6.9, group 8: SUV 7–7.9, and group 9: SUV 8 and above.

On the survival analysis, the number of lesions on PET/MRI at baseline correlated significantly with progression-free survival (PFS) ($P=0.02$) and overall survival (OS) ($P=0.04$). The number of lesions on PET/CT at baseline correlated significantly with PFS ($P=0.02$), but not for OS ($P=0.08$). Both

the SUVmean and SUVmax on the baseline PET/MRI correlated significantly with PFS ($P=0.02$ and $P=0.02$ respectively). On the other hand, both the SUVmean and SUVmax at baseline PET/CT did not show significant correlation with PFS ($P=0.2$ and $P=0.1$, respectively). The SUVmean and SUVmax of both baseline PET/MRI and PET/CT did not show significant correlation with OS ($P=0.8$ and $P=0.8$ for PET/MRI and $P=0.8$ and $P=0.9$ for PET/CT).

Table 4. Number of lesions and standardised uptake value (SUV)mean and SUVmax on positron emission tomography (PET/CT) and PET/magnetic resonance imaging (MRI).

(A) Baseline scans.

Patient	PET/CT			PET/MRI		
	No. of lesions	SUVmean	SUVmax	No. of lesions	SUVmean	SUVmax
1	8	3.1	5.6	4	1.7	2.8
2	8	2.9	4.4	1	3.2	4.4
3	6	4.2	7.1	5	3.5	5.7
4	10	2.4	4.0	9	1.6	2.4
5	2	3.8	6.6	2	2.8	4.8
6	22	2.7	4.4	22	1.7	2.3
7	1	2.6	4.4	1	1.7	2.7
8	6	5.6	9.7	6	4.5	7.2
9	12	3.0	6.3	11	2.6	4.1
10	Not avid	Not avid	Not avid	Not avid	Not avid	Not avid
11	3	4.0	7.2	5	2.4	4.0
12	0	0	0	0	0	0

(B) Post-treatment scans.

Patient	PET/CT			PET/MRI		
	No. of lesions	SUVmean	SUVmax	No. of lesions	SUVmean	SUVmax
1	1	1.9	3.7	1	0.8	1.4
2	3	2.3	4.0	0	0	0
3	-	-	-	-	-	-
4	3	2.5	4.5	3	1.2	1.9
5	0	0	0	0	0	0
6	-	-	-	-	-	-
7	0	0	0	0	0	0
8	-	-	-	-	-	-
9	-	-	-	-	-	-
10	Not avid	Not avid	Not avid	Not avid	Not avid	Not avid
11	10	7.3	12.3	10	3.1	4.9
12	0	0	0	0	0	0

Post-treatment

We divided the patients into 2 groups based on the presence and absence of positive lesions.

Survival analysis showed that the presence and absence of positive lesions on both PET/MRI and PET/CT post-treatment did not correlate significantly

with PFS ($P=0.3$ and 0.4 , respectively). The OS analysis could not be performed as all patients with post-treatment scans available are still alive. Both the SUVmean and SUVmax on the post-treatment PET/MRI did not correlate significantly with PFS ($P=0.3$ and $P=0.3$, respectively). The

SUVmean and SUVmax on post-treatment PET/CT did not correlate significantly with PFS ($P=0.5$ and $P=0.5$, respectively) as well.

DISCUSSION

To our knowledge, our study is the first to compare changes in PET/MRI in MM pre- and post-treatment along with survival correlation, and the second to compare the utility of PET/MRI and PET/CT in MM.

Our study showed that PET/MRI is not inferior to PET/CT. For detection of positive lesions, PET/MRI has significant correlation with the lesions on PET/CT. The SUVmean and SUVmax on PET/MRI also had good correlation with those of PET/CT, both at baseline and post-treatment. Similar findings were also noted in a previous study that showed significant correlation between these 2 modalities.⁸

With superior lesion contrast in the marrow and soft tissue, MRI could detect MM lesions presenting as marrow signal abnormalities, before bone destruction could be identified on CT. Hence, PET/MRI is the more sensitive imaging technique compared with PET/CT, especially in early disease.⁷ Also, MRI has far superior sensitivity for diffuse marrow infiltration, which is potentially morphologically undetectable on CT imaging.^{8,9} This finding is in keeping with a previous study, which reported that MRI showed abnormalities in 30% patients with negative PET/CT scan, especially of the diffuse pattern.¹⁰ Similarly, another study also reported that whole-body MRI showed significantly more extensive disease than whole-body multidetector CT (MDCT), with many false-negative MDCT findings being found in cases with diffuse marrow infiltration, which might not necessarily be associated with the destruction of trabecular or cortical bone.¹¹

However, although PET/MRI is sensitive for lesions in the vertebrae and pelvis, it is less sensitive for lesions in the ribs, clavicles and skull. This would explain why PET/MRI detected fewer lesions than PET/CT in patients 1 and 2, both of whom had most lesions involving the ribs. Interestingly, a systematic review that compared modern and conventional imaging techniques in MM reported that modern imaging techniques, including CT, MRI and FDG-PET detected fewer lesions in the skull and ribs, and recommended that additional conventional X-ray of the ribs and skull be performed if clinically relevant. For MRI, this mainly concerned lesions of the ribs; with a study reporting a 4.3 times higher detection of rib lesions by X-ray. FDG-PET or FDG-PET-CT and CT missed lesions in the ribs (by 7–33%) and skull (by 4–9%).¹²

In the post-treatment setting, PET/MRI has the

added benefit of evaluating treatment response.¹³ Along with FDG-PET, which is known to be useful in the assessment of treatment response,¹⁴ the MRI component complements metabolic changes detected on FDG-PET. Changes in morphological findings on MRI correlate with response to therapy. Morphological evidence of treatment response on MRI includes complete resolution of signal abnormalities, replacement of myeloma lesions with fatty marrow signal or a conversion of a diffuse pattern of marrow infiltration into a pattern of focal lesions in patients with a partial response. In some of our patients with diffuse marrow involvement at baseline, post-treatment MRI images demonstrated restoration of the normal marrow signal. In patients with focal disease, post-treatment MRI demonstrated fatty conversion of myeloma lesions. Many of these lesions remained lytic on CT images. Although no dedicated studies have been published, PET/MRI might be useful in the diagnosis and disease monitoring of oligosecretory and nonsecretory MM.¹³

Both SUVmax and SUVmean of MM lesions were significantly higher on PET/CT than on PET/MRI. This might be contributed by the additional waiting time between PET/CT and PET/MRI acquisitions, which were obtained sequentially in all patients. This would result in lesions demonstrating relatively lower FDG-avidity being more difficult to be identified on PET/MRI than on PET/CT. A similar study that compared both modalities, with PET/CT performed sequentially followed by PET/MRI, showed similar results.⁸

Compared with PET/CT, PET/MRI has the additional benefit of minimising ionising radiation exposure to the patient. However, PET/MRI is not without problems. MRI is contraindicated in patients with metallic implants or implantable devices that are not MRI-compatible. MRI is also far more time-consuming compared with CT, and in patients with significant bone pain or claustrophobia, the shorter scan acquisition time achievable in PET/CT would be preferred.

In terms of clinical correlation, at baseline, the number of focal lesions on both PET/MRI and PET/CT showed significant clinical correlation with PFS. In addition, PET/MRI has an additional significance of clinical correlation with OS. This is in keeping with the results of previous studies, which showed that the number of focal lesions was associated with survival.^{15–17} However, contrary to the result of previous studies, on post-treatment scans, both the evaluation of PET/MRI and PET/CT did not correlate significantly with PFS.^{3,4} This might be partly related to the small number of patients who had post-treatment scans, and the unrelated changes that might affect the SUVs as described

earlier. Another study showed that PET/MRI could predict bone marrow abnormalities and correlated with known biochemical prognostic markers.¹⁸

Functional MRI sequences (DWI) were obtained for some patients, including patients 5 (post-treatment only), 7 (post-treatment only), 8, 9, 10, 11 and 12. In these patients, PET/MRI detected an equal number of, or more lesions compared to PET/CT. In particular, functional MRI identified 2 bony lesions in patient 11, which were missed on PET/CT. If functional MRI sequences were routinely performed, it is likely that we would be able to detect more bony lesions, such as in the ribs, which were missed on conventional MRI sequences.

One limitation of our study is that PET/MRI was performed later than PET/CT after a single FDG injection, which might make the SUV values for PET/MRI less reliable. It might have been better if an independent injection was administered prior to each scan. Another limitation of our study is the small number of patients recruited. However, even with this small number of patients, significant correlation could be detected.

In conclusion, PET/MRI correlates well with PET/CT, with PET/MRI being more sensitive in detecting early disease compared with PET/CT. PET/MRI at baseline correlates with clinical outcomes and could identify disease resolution better than PET/CT. The cost-effectiveness of PET/MRI should be explored.

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Disclosure

No relevant conflicts of interest to disclose.

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