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Original Article

Quantitative accuracy of positron emission tomography/magnetic resonance and positron emission tomography/computed tomography for cervical cancer

ABSTRACT

With the spread of positron emission tomography/magnetic resonance (PET/MR), the question of comparability of studies becomes important. We aim to determine whether PET/MR and PET/computed tomography (PET/CT) are comparable for the case of cervical cancer. Fifteen cervical cancer patients identified by either a radiation oncologist or an oncologic surgeon had both PET/MR and PET/CT performed for initial staging within 3 weeks. We then compared the results both quantitatively (measuring standardized uptake values [SUVs] on visible lesions) as well as qualitatively (having radiologists and nuclear medicine physicians interprets the results). While interpretations between PET/MR and PET/CT varied in many cases, SUVs of primary lesions were similar to within 25% in all but one case, and correlation coefficient was 0.92. Maximum SUV ranged between 4.9 and 25.2 for PET-MR and between 5.8 and 30.4 for PET-CT for primary tumors and between 1.5 and 18.8 for PET-MR and between 1.8 and 20.8 for PET-CT for nodes. However, clinical reads often varied significantly between PET/MR and PET/CT. This suggests that SUV is similar on PET/MR and PET/CT although the differing anatomic modalities available for correlation may make the difference in terms of qualitative interpretation.

Keywords: Cervical cancer, positron emission tomography/computed tomography, positron emission tomography/magnetic resonance, standardized uptake value

INTRODUCTION

Both positron emission tomography/computed tomography (PET/CT) and magnetic resonance imaging (MRI) have important roles in staging of gynecologic cancers, with MRI being more useful in assessing primary tumor and local extension and PET/CT in assessing for nodal and distant metastatic disease.[1] PET/CT has also been used to assess response to therapy for chemotherapy, radiation, and surgery (detecting residual disease) in cervical cancer, although less commonly than in other tumors such as lymphoma (National Comprehensive Cancer Network). PET findings have been shown to correlate with survival when assessed before,[2] after,[3,4] as well as during[5-7] radiotherapy for cervical cancer for up to 5 years.[8]

PET/magnetic resonance (PET/MR) imaging is an emerging modality that combines PET with MR, hoping to marry the

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functional assessment of PET to the superior soft tissue contrast of MR. At present, it is still being validated. An important question is whether attenuation correction between MR and CT is similar.[9] PET/MR has been shown to have identical lesion visibility in cancers such as lymphoma,[10] with maximum standardized uptake value (SUV_{max}) on PET/MR about 15%–25% less than PET/CT.[11] PET/MR has been shown to have similar sensitivity to PET/CT and better local staging ability in small pilot studies of assorted gynecological cancers,[12,13] and it has even been suggested that biomarkers from PET/CT and MR could be combined to aid in prognostication.[14] Recently, a large study of over 2000 patients has shown that PET/MR and PET/CT have similar utility in a wide variety of cancers.[15] This study cited three previous studies[12,13,16] on a variety of gynecologic cancers, each with about seven to eight cervical cancer patients, which showed good correlation between PET/MR and PET/CT. We aim to assess the strength of correlation of PET/CT and PET/MR in cervical cancer in particular. The primary aim of this study was to look at the correlation of the two studies performed within a short time frame (<3 weeks).

SUBJECTS AND METHODS

Ethics

Informed consent was obtained from patients for this study, which was approved by the Institutional Review Board (IRB 12-1946) and was HIPAA compliant and in accordance with the Declaration of Helsinki, 1975.

Selection and description of participants

Eighteen women with at least stage IB cervical cancer and no prior treatment were consented for this trial. One patient refused (index number 1), and another could not complete the PET/MR examination due to claustrophobia (index number 7). Another (index number 17) did not have a PET/CT within a few weeks of the PET/MR. Patients ranged in age from 26 to 65 years, with a mean age of 45 years.

Technical information

Using a Siemens Biograph mMR, simultaneous acquisition of PET/MR images of the pelvis before initial treatment was obtained. MR and PET sequence data and protocol are given in Tables 1 and 2. Image acquisition was completed in about 35 min. PET images of the primary tumor were interpreted by a board-certified nuclear medicine physician.

In the majority of patients,[15] a PET/CT was obtained within 3 weeks of the PET/MR. A flowchart showing available data for each patient is given in Figure 1 (two patients, indices 8 and 9, were imaged using the same injection; patient 15 had same-day imaging with two different injections). Most

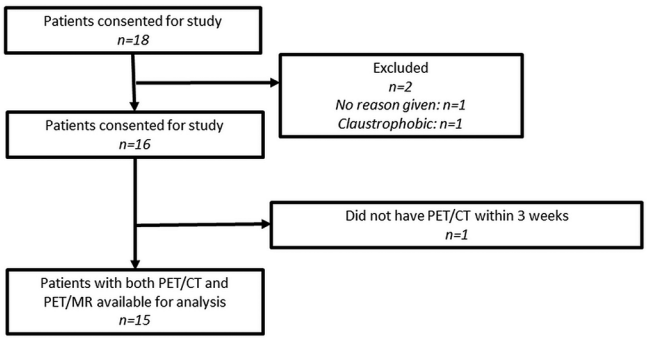

Figure 1: STARD diagram for our study

Table 1: Positron emission tomography sequence parameters

	PET/MR PET	PET/CT PET
Recon algorithms	OSEM 2 subsets, 21 iterations	OSEM 2 subsets, 8 iterations Time-of-flight reconstruction
Matrix size	172×172	168×168 (true point) 200×200 (mCT)
Filter	Gaussian, FWHM 4 mm	Gaussian, FWHM 5 mm
Time per bed position	4 min	2 min
Dose	259-481 MBq (based on weight)	259-481 MBq (based on weight)
Uptake time	59-198 min (mean 82, SD 38)	59-97 min (mean 76, SD 12)

SD: Standard deviation; PET: Positron emission tomography; mCT: Micro-computed tomography; MR: Magnetic resonance; OSEM: Ordered-subsets expectation maximization; FWHM: Full width at half maximum

PET/CTs were done using our standard PET/CT protocol on a Siemens Biograph micro-CT (patient with index 2 was compared to an outside PET/CT). Nondiabetic patients fasted for 6 h. Diabetic patients fasted and did not administer insulin. As per the standard PET routine, patients were asked to remain still in a relaxed setting and refrain from speaking. Further technical details are given in Table 1. Dose and uptake time were similar for the PET/CT and PET/MR protocol. No intravenous or oral contrast was given. The PET images were then reviewed to assess differences in attenuation correction and in some cases clinical planning. PET images were reinterpreted by the same nuclear medicine physician after a duration of 2 months for this study. SUV_{max} was calculated using MIMvista (MIM Software, Cleveland, Ohio, USA).

Statistics

The sample was too small for a reliable regression, but agreement could still be assessed through a correlation coefficient between PET/MR and PET/CT. Relative differences in SUV_{max} between PET/MR and PET/CT were also calculated to give a sense of whether the difference between PET/MR and PET/CT fell within the usual range of PET variability. Cohen's kappa was used to assess agreement between qualitative PET/MR and PET/CT reads.

RESULTS

Overall quantitative values of MR and PET findings are presented in Table 3. On two of the studies (indices 17 and 18), a primary tumor could not be visualized. Pretreatment examinations demonstrated maximum tumor size ranging from 1.7 to 8.7 cm, with SUV_{max} for the tumors ranging from 5.6 to 25.2. SUV_{max} ranged between 4.9 and 25.2 for PET-MR (mean 14.5, standard deviation [SD] 6.6) and between 5.8 and 30.4 for PET-CT (mean 15.5, SD 7.7) for primary tumors and between 1.5 and 18.8 for PET-MR (mean 4.8, SD 4.3) and between 1.8 and 20.8 for PET-CT (mean 5.6, SD 5.0) for nodes.

SUV_{max} was similar between PET/CT and PET/MR in the majority of cases for primary tumors [Table 4], in all but one being within 33%, and strongly correlated with $r = 0.92$ [Figure 2].

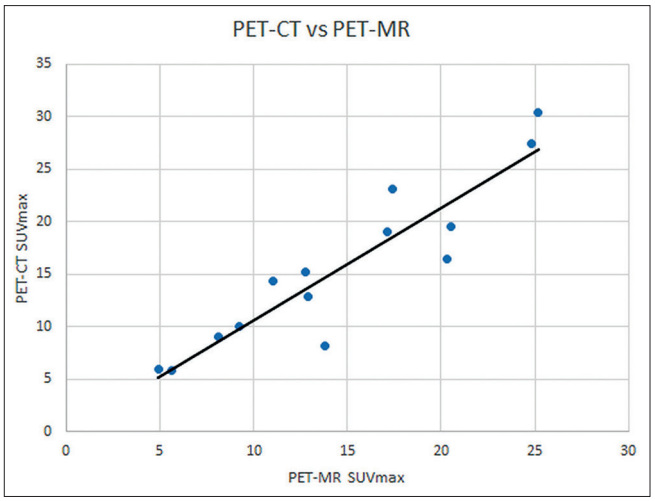

Figure 2: Positron emission tomography-magnetic resonance versus positron emission tomography-computed tomography. The values are strongly correlated, with maximum standardized uptake value for positron emission tomography-computed tomography being slightly higher

Table 2: Magnetic resonance sequences

Sequence	Orientation	Matrix size	Thickness (mm)	Slices	TR	TE	Other
Dixon	Coronal	192×128	3	128	3.6	1.2/2.5	
T2 TSE	Axial	320×320	3	50	4590	91	GRAPPA: 2
T2 TSE	Sagittal	320×320	4	30	4200	86	
T2 TSE	Coronal	320×320	5	31	1260	121	
T2 HASTE	Axial	256×208	8	24	2000	94	
T1 VIBE Dixon	Axial	320×200	3	64	4.1	1.2/2.5	GRAPPA: 2
T1 VIBE FS	Sagittal	288×232	3	64	5.6	2.5	GRAPPA: 2
T1 VIBE FS postcontrast	Sagittal	288×232	3	64	5.6	2.5	GRAPPA: 2
DWI	Axial	192×144	5	35	9200	85	GRAPPA: 2, b=50, 400, 800
PET	Axial	172×172	2	127	N/A	N/A	

N/A: Not available; PET: Positron emission tomography; DWI: Diffusion-weighted imaging; TR: Time to repetition; TE: Echo time; GRAPPA: Generalized autocalibrating partial parallel acquisition; TSE: Turbo spin echo; HASTE: Half-Fourier acquisition single-shot turbo spin echo imaging; VIBE: Volumetric interpolated breath-hold examination; FS: Fat saturation

Table 3: Positron emission tomography and magnetic resonance findings, primary tumor and nodes

Index	Tumor size, cm (MR)	Tumor SUV_{max} (PET-MR)	Nodes (MR)	Nodes (PET)	Node size, mm (MR)	Node SUV (PET)
2	5.2	12.8	Left EI	No	12	N/A
3	1.7	4.91	No	No	N/A	N/A
4	3.9	20.5	Right EI	No	7	N/A
5	6.1	17.4	Right EI	No	4	N/A
6	4.0	8.1	No	No	N/A	N/A
8	4.1	20.3	No	No	N/A	N/A
9	8.7	25.2	Left EI × 3, right EI × 2	Left EI	20, 9, 5 9, 6	19
10	4.8	11	Right EI × 4, left EI × 4	No	12, 11, 9, 7 11, 9, 7, 6	N/A
11	4.0	5.6	Right EI	No	5 (DWI only)	N/A
12	6.1	17.1	Left CI	No	8	N/A
13	3.8	24.8	No	No	N/A	N/A
14	2.3	9.2	No	No	N/A	N/A
15	5.9	12.9	Right EI	No	9	N/A
16	2.6	13.8	Left EI	No	8	N/A
17	1.3	N/A	No	Right EI, right CI, left EI	No	1.9, 2.3, 2
18	No	N/A	Left EI	No	12	N/A

EI: External iliac; CI: Common iliac; MR: Magnetic resonance; PET: Positron emission tomography; N/A: Not available; SUV_{max}: Maximum standardized uptake value; DWI: Diffusion-weighted imaging

Table 4: Maximum standardized uptake value, positron emission tomography-magnetic resonance versus positron emission tomography-computed tomography

Index	Tumor SUV_{max} (PET-MR)	Uptake time, min (PET-MR)	Tumor SUV_{max} (PET-CT)	Uptake time, min (PET-CT)	Days apart	Percentage difference
2	12.8	78	15.2	60	20	15.8
3	4.91	68	6	72	4	18.3
4	20.5	77	19.5	88	13	5.1
5	17.4	64	23.1	78	2	24.7
6	8.1	76	9.04	59	1	10.4
8	20.3	146*	16.5	67	0	23.0
9	25.2	198*	30.4	86	0	3.6
10	11	68	14.4	68	11	23.6
11	5.6	62	5.8	87	1	3.4
12	17.1	66	19	89	8	10.0
13	24.8	64	27.4	76	1	9.5
14	9.2	62	10	97	5	8.0
15	12.9	59	12.9	72	0	0.0
16	13.8	60	8.2	62	1	40.0
18	N/A	79	N/A	79	15	N/A

*Same-day imaging with one injection (PET-CT was done first). Patient with index 17 did not have a PET-CT available within 3 weeks. MR: Magnetic resonance; PET: Positron emission tomography; SUV_{max}: Maximum standardized uptake value; CT: Computed tomography; N/A: Not available

Interestingly, the two patients with wide discrepancies between PET-MR and PET-CT uptake times (patients 8 and 9) nonetheless had relatively close SUV_{max}. While this is unacceptable for quantitative applications in a scientific setting, in the clinical setting, most results were within the 20% study-to-study variation typical of PET.[17-19] SUV_{max} on nodes called by either PET-CT or PET-MR was also remeasured on both images [Table 5], and while more variable in relative terms (likely due to lower uptake) SUV_{max} on one modality was usually within 1.5 absolute SUV unit of the other. The most prominent example of increased variation is shown in Figure 3, where susceptibility effects corrupted the MR attenuation correction.

Approximately half of the patients had surgical confirmation (four who were treated surgically and three who had subsequent surgery). On several occasions, PET/MR interpretations were at variance with the PET/CT interpretations performed by the standard clinical team [Table 6]. In general, while the modalities agreed perfectly on the presence or absence of a primary tumor, and there was substantial agreement on the presence of nodal spread ($k = 0.667$) and moderate agreement on pelvic sidewall invasion ($k = 0.513$) and parametrial invasion ($k = 0.455$), there was slight to no agreement on bladder ($k = 0.167$) and rectal ($k = -0.129$) abutment and invasion of the upper two-thirds of the vagina ($k = 0.242$) (invasion of the lower third of the vagina was not detected in any patient). As the PET/CT was a whole-body image, there were additional incidental findings such as ovarian cysts (located superiorly enough not to be visualized on purely pelvic imaging) and a small lung nodule (unchanged 5 months later at last cross-sectional imaging) that were not visualized on a pelvic MR. Hydronephrosis was similarly seen on three PET/CTs, but not on PET/MR, simply due to the larger coverage.

Table 5: Positron emission tomography-computed tomography and positron emission tomography-magnetic resonance of nodes (where detected)

Patient index	Days apart	Percentage difference	Nodal SUV_{max} (PET-MR)	Nodal SUV_{max} (PET-CT)
4	13	25.7	*OB: 2.6*	OB: 3.5
9	0	9.6	EI: 18.8	EI: 20.8
9	0	29.4	*LLQ: 3.6*	LLQ: 5.1
9	0	−18.8	*RP: 3.8*	RP: 3.2
10	11	−44.8	*Pelvic: 4.2*	Pelvic: 2.9
10	11	−11.4	*3.9*	3.5
10	11	12.1	*5.8*	6.6
10	11	8.2	*4.5*	4.9
10	11	46.7	*4.0*	7.5
10	11	5.1	*3.7*	3.9
10	11	31.3	*2.2*	3.2
10	11	18.4	*LEI: 10.2*	Left EI: 12.5
11	1	9.1	*Left OB: 2.0*	Left OB: 2.2
11	1	16.7	*Right OB: 1.5*	Right OB: 1.8
16	1	−60.0	*Left SW: 3.2*	Left SW: 2.0

Italics denote nodes not described on formal PET-MR read, but detected on secondary review. EI: External iliac; LLQ: Left lower quadrant; RP: Retroperitoneal; OB: Obturator; SW: Sidewall; MR: Magnetic resonance; PET: Positron emission tomography; SUV_{max}: Maximum standardized uptake value; CT: Computed tomography

DISCUSSION

In terms of key findings, in general, the relative similarity of quantitative interpretation did not carry through to interpretive agreement with PET/CT. However, surgical and pathologic confirmation was available in only in four cases.

In two cases, the PET/CT interpretation identified multiple nodes that were not called on PET/MR; these may have been metabolically active ovaries (harder to identify on PET/CT) or actual new nodes. If identifiable on both, the nodes were usually similar [Table 6] in SUV_{max}, with two exceptions. In one patient (index 10), the nodes all had SUV_{max} on PET-CT similar to their PET-MR values, except one node which had a much lower PET-MR value near a susceptibility artifact from a hip replacement [Figure 4]. In the other patient (index 16), the node was off by the same factor of about 40% as the primary tumor, suggesting a systematic error (the time may have been recorded incorrectly). The general pattern is thus that measurements are quantitatively preserved but may vary significantly based on interpretation of the accompanying anatomic (CT or MR) modality. We were able to acquire a complete PET-MR of the pelvis in 30 min, and further refinements may be possible (we made little use of the diffusion-weighted sequences, for instance).

In terms of strengths and limitations, we do have a relatively sample focused specifically on cervical cancer on PET/MR. As far as limitations go, the small sample size naturally limits the power and sensitivity of the results as does the lack of

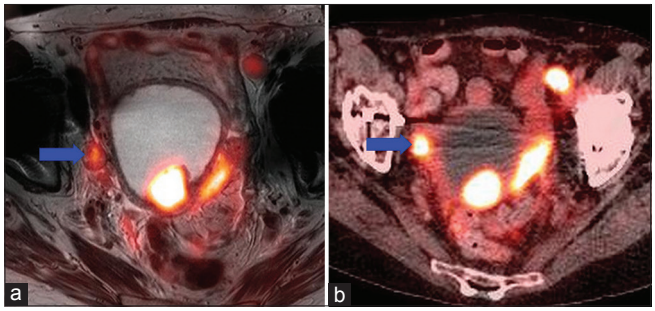

Figure 3: Positron emission tomography/magnetic resonance (a) showing less intense uptake of nodal metastasis (blue arrow) compared to positron emission tomography/computed tomography (b) likely due to errors in attenuation correction resulting from susceptibility artifacts around a hip arthroplasty

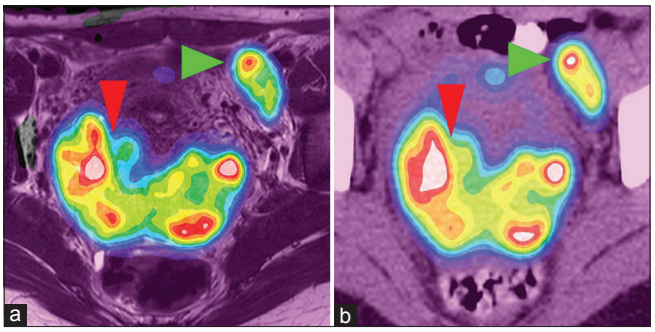

Figure 4: Positron emission tomography/magnetic resonance (a) and positron emission tomography/computed tomography (b) showing similar uptake patterns in primary tumor (red arrowhead, maximum standardized uptake value 25.2 vs. 30.4) and nodal metastasis (green arrowhead, 18.8 vs. 20.8). Each color represents an standardized uptake value range of 2, pink representing a standardized uptake value over 20

Table 6: Positron emission tomography-computed tomography and positron emission tomography-magnetic resonance interpretations

Index	Days apart	PET-MR read	PET-CT read	Sx path (if available)
2	20	Parametrial invasion	Upper vagina, parametrial invasion, bladder and rectal abutment	
3	4	Local only	Right pelvic node	No ext, 0/19 nodes
4	13	Upper vagina, parametrial invasion	Upper vagina, parametrial invasion	
5	2	Right EI, pararectal, pelvic nodes; upper vagina and parametrial invasion	Right EI, pelvic nodes; upper vagina and parametrial invasion, bladder abutment	Uterine, vaginal extension
6	1	Upper vagina and parametrial and pelvic sidewall invasion	Local only	Cone, margins+
8	0	Upper vagina and parametrial and pelvic sidewall invasion, bladder and rectal abutment	Upper vagina and parametrial invasion, bladder abutment, left hydronephrosis	
9	0	Right EI node, bladder abutment	Right EI node, upper vagina and parametrial and pelvic sidewall invasion, bladder and rectal abutment	Vaginal extension, 1/7 nodes
10	11	Multiple pelvic nodes, parametrial invasion, bladder abutment	Multiple pelvic nodes, upper vagina, parametrial, and pelvic sidewall invasion, rectal abutment	
11	1	Bladder abutment	Upper vagina invasion, bladder and rectal abutment	Cone, margins+
12	8	Upper vagina and parametrial invasion, bladder abutment	Parametrial invasion, left hydronephrosis	
13	1	Bladder abutment	Parametrial invasion	No ext, 1/26 nodes
14	5	Local only	Local only	No ext, 0/17 nodes
15	0	Upper vagina invasion	Upper vagina invasion, parametrial invasion, bladder and rectal abutment, left hydronephrosis	
16	1	Parametrial invasion, fibroids	Parametrial invasion, adnexal cyst, fibroids	
18	15	No visible lesion	No visible lesion	No ext, 0/17 nodes

Patient with index 17 did not have a PET-CT available within 3 weeks. PET: Positron emission tomography; CT: Computed tomography; MR: Magnetic resonance; EI: External iliac

pathologic confirmation in most cases. The reconstruction algorithms for PET/MR and PET/CT differed considerably, and this may have introduced additional error into a parameter such as SUV_{max} which is prone to being affected by differences in processing. However, this also further suggests that quantitation between PET/MR and PET/CT remains robust even with these differences taken into account.

With time elapsing between the PET/MR and PET/CT, it is possible some clinically important event may have occurred between one and the other (no treatment was done between one and the other in our study, however). PET varied widely in assessing bladder and rectal abutment as well as local invasion of the upper vagina, although PET is generally not used for local staging in most tumors. Since our protocol only allowed for pelvic MR, the rest of the body could not be staged, and hence, congruence with PET/CT in the chest and abdomen could not be assessed, although more extensive protocols are available for cancer staging.

Future research directions might include larger sample sizes, acquiring PET/CT and PET/MR after the same injection, and focusing on other gynecologic cancers.

CONCLUSION

PET/MR gives reasonably similar results to PET/CT for quantitative purposes. For qualitative interpretation, the correlation with the anatomic imaging modality may become more important.

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Conflicts of interest
There are no conflicts of interest.

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