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MODALITY-BASED (US, CT, MRI, PET-CT) IMAGING

ORIGINAL ARTICLE

Correlation of ^{18}F-FDG PET/CT uptake with severity of MRI findings and epidural steroid injection sites in patients with symptomatic degenerative disease of the lumbar spine: a retrospective study

Michelle Lam
Christopher J. Burke
William R. Walter

PURPOSE
We aimed to retrospectively correlate ^{18}F-fluorodeoxyglucose (^{18}F-FDG) metabolic activity with lumbar spine magnetic resonance imaging (MRI) findings and epidural steroid injection sites in patients with symptomatic degenerative disease of the lumbar spine.

METHODS
A database search was conducted for patients receiving epidural injections <12 months after a positron emission tomography/computed tomography (PET/CT). Maximum standard uptake values (SUVmax) were measured at the facet joints, neural foramina, and spinal canal. Severity of facet arthrosis, disc degeneration, neuroforaminal, and canal stenosis was determined on MRI using previously described grading scales. Spearman rank coefficient assessed association between PET/CT FDG uptake and severity of MRI findings. The SUVmax was also compared with injection sites.

RESULTS
Twenty-five patients were included, comprising MRI (n=19) and injection (n=22 patients; 18 interlaminar, 8 transforaminal) groups. Injections were performed an average of 2.6 months after PET/CT. The greatest SUVmax occurred at the L5-S1 spinal canal (mean SUVmax = 2.25). A statistically significant, positive correlation between uptake and grade of spinal canal stenosis was seen only at L4-L5 (r=0.60, p = 0.007). No other significant association was found with spinal canal or neuroforaminal stenosis, or grade of facet joint or disc degeneration. All patients reported symptomatic improvement after injections with mean pain score improvement of 4.4 on a 10-point scale (SD, 2.9). There was moderate agreement between sites of epidural injection and highest SUVmax (κ= 0.591, p < 0.001).

CONCLUSION
^{18}F-FDG metabolic activity on PET/CT corresponds with MRI findings about the lumbar spinal column, but there is no significant correlation between severity of MRI findings and radiotracer uptake. Given the moderate agreement between metabolic activity and levels of symptomatic spinal stenosis, further studies are warranted to fully evaluate the diagnostic potential of FDG PET/CT as a surrogate for guiding epidural injections.

^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is useful to detect osseous metastases; however, uptake within the musculoskeletal system is frequently incidentally observed related to non-malignant degenerative or inflammatory disease 1-4). Chronic low back pain is extremely common worldwide, with a prevalence of 19.6% among people 20–59 years of age. Image-guided epidural steroid injections can be targeted to address symptomatic focal spinal stenosis (5, 6).

Previous studies have examined incidental FDG uptake in the musculoskeletal system in general (1, 7–9) and the spine in particular (10–13), although few have systematically evaluated non-neoplastic uptake as it pertains to patient symptoms. Incidental FDG metabolic activity in the spine is most frequently due to degenerative etiologies involving the intervertebral discs or facet joints (11) with the most common site of uptake at the thoracolumbar junction (10, 13). Despite this, to our knowledge, no study has correlated patterns of radiotracer uptake with MRI findings and patient symptoms.

From NYU Langone Health (M.L.), New York University School of Medicine, New York, USA; Department of Radiology (C.J.B., W.R.W. ✉ *walter@nyumc.org*), NYU Langone Health, Musculoskeletal Division Langone Orthopedic Hospital, New York, USA.

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The purpose of our study was therefore to detect possible correlations between FDG metabolic activity and severity of lumbar spine MRI findings as well as epidural injection sites among symptomatic patients.

Methods

Patient selection

Our institutional review board approved this retrospective study and informed consent was waived (Protocol s17-00198). A picture archiving and communication system (PACS) database search identified patients who had epidural steroid injection of the lumbar spine 12 months or less following a whole-body PET/CT, performed between 2014 and 2017. Patients were excluded for incomplete imaging, lumbar spine hardware, compression fractures, and bony or epidural neoplastic involvement. Electronic medical record review was performed for patient demographics, tumor type, lumbar spine MRI within 1 year of PET/CT, epidural steroid injection technique, and patient-reported pain scores. Patients with qualifying MRIs or epidural injections were included in the MRI group or the injection group, respectively. See the flowchart in Fig. 1 for details of patient inclusion and exclusion.

^{18}F-FDG PET/CT scans

Whole-body PET/CTs were performed from skull base to mid-thigh using a Biograph PET/CT scanner (Siemens Healthcare). A standard two-dimensional PET protocol was used with 5-minute emission period per bed position, imaging patients 45 minutes after intravenous injection of 10–15 mCi ^{18}F-FDG radiotracer (12.62±1.52 mCi). Patients fasted for a 6-hour period prior to imaging and serum glucose levels were confirmed to be <150 mg/dL.

Main points

- Increased FDG metabolic uptake on PET/CT can be seen in association with multiple non-neoplastic findings in the lumbar spine including facet joint arthritis and degenerative disc disease.
- The degree of FDG metabolic uptake does not necessarily correlate with severity of non-neoplastic findings as graded on MRI.
- There is a moderate agreement between foci of FDG metabolic uptake and sites of therapeutic epidural steroid injection.

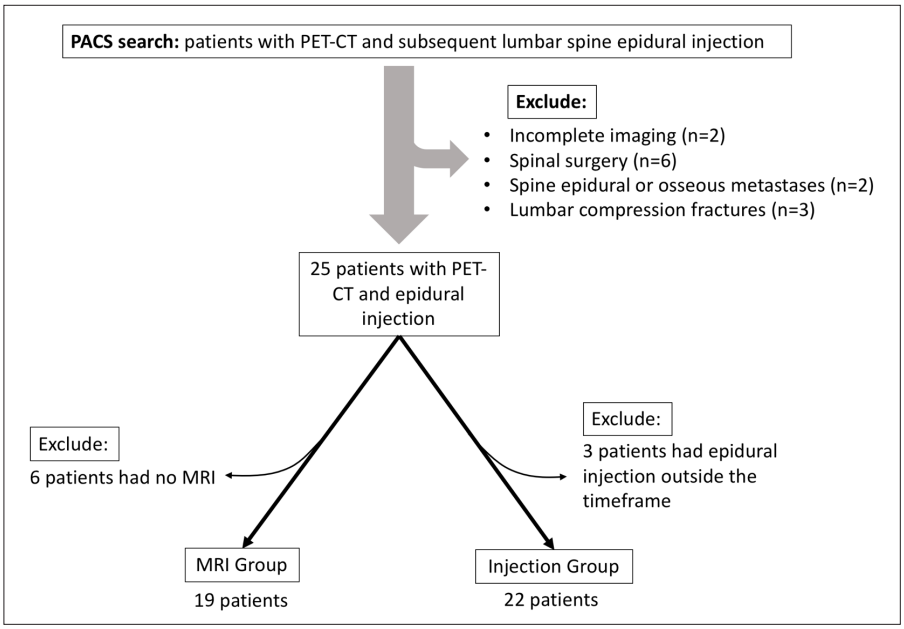

Figure 1. Flowchart illustrating patient inclusion and exclusion as well as the composition of the MRI and injection groups.

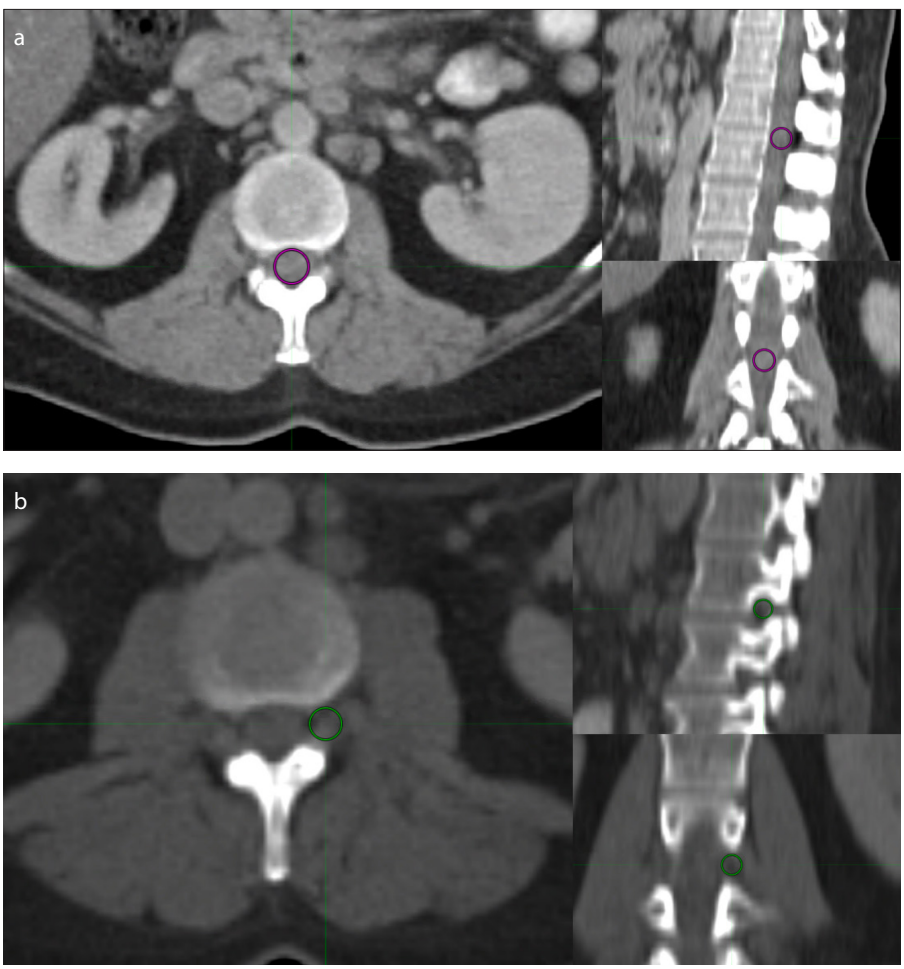

Figure 2. a, b. A 43-year-old male with history of pulmonary nodule. Axial CT image **(a)** from diagnostic PET/CT with sagittal and coronal reconstructions demonstrates ROI placement in the spinal canal *(purple circle)* at L1-L2. Axial CT image **(b)** from diagnostic PET/CT with sagittal and coronal reconstructions demonstrates ROI placement *(green circle)* over the left L2-3 neural foramen.

Table 1. Highest SUVmax sites and associated MRI grades

			MRI grades at vertebral level*					
Patient #	Level(s) of highest SUVmax	ROI(s) of highest SUVmax	Canal	RNF	LNF	Right facet	Left facet	Disc
1	L5-S1	Total	1	2	3	2	3	4
2	L3-L4	Left neural foramen	3	1	3	3	3	2
3	L5-S1	Total	0	1	1	2	2	3
4	L3-L4	Left facet	0	0	0	1	1	2
5	L5-S1	Right neural foramen	0	3	3	3	2	5
6	L4-5	Right facet	2	0	0	3	3	4
7	L5-S1	Total; Right neural foramen	1	0	1	2	3	3
8	L2-3	Total	2	3	2	2	2	5
9	L4-5	Left facet	0	2	2	2	2	2
10	L5-S1	Total	1	0	2	2	2	2
11	L4-5	Right neural foramen	1	0	0	3	3	2
	L5-S1	Right neural foramen	0	0	0	3	3	5
12	L2-3	Left neural foramen	1	1	1	1	1	5
13	L4-5	Right facet	2	2	2	3	3	4
14	L5-S1	Right neural foramen	1	2	1	3	3	4
15	L1-2	Total	0	0	0	0	0	4
	L2-3	Left neural foramen	0	0	0	0	0	2
16	L5-S1	Total	0	0	0	0	0	1
17	L4-5	Total	3	3	3	3	3	5
18	L4-5	Total	2	3	3	3	3	5
19	L3-4	Right facet	3	1	1	3	3	5

SUVmax, maximum standard uptake value; ROI, region of interest; MRI, magnetic resonance imaging; RNF, right neural foramen; LNF, left neural foramen.
*Grading scales are as detailed in the Methods, utilizing previously described scales for spinal canal stenosis (15), neuroforaminal stenosis (16), facet joint osteoarthritis (17), and degenerative disc disease (18, 19).

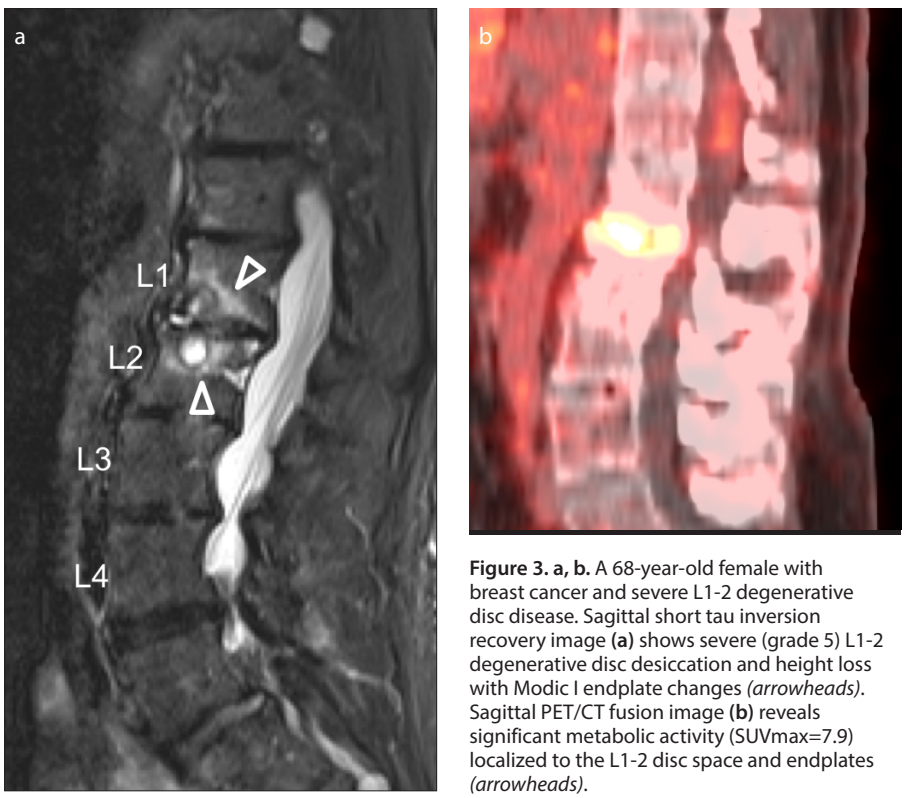

Figure 3. a, b. A 68-year-old female with breast cancer and severe L1-2 degenerative disc disease. Sagittal short tau inversion recovery image **(a)** shows severe (grade 5) L1-2 degenerative disc desiccation and height loss with Modic I endplate changes *(arrowheads)*. Sagittal PET/CT fusion image **(b)** reveals significant metabolic activity (SUVmax=7.9) localized to the L1-2 disc space and endplates *(arrowheads)*.

MRI scans

Our standard lumbar spine MRI protocol was performed using either a 1.5 T (Aera, Espree, Magnetom, Sonata (Siemens Healthcare); or Signa Excite (GE Healthcare) or 3 T (Skyra, Biograph mMR, Prisma, or Verio; Siemens Healthcare). A spine coil was used to obtain sagittal T1-weighted (TR/TE, 800.0/11.0; slice thickness, 4.0 mm; FOV, 280 mm), T2-weighted (TR/TE, 3500.0/90.0; slice thickness, 4.0 mm; FOV, 280 mm), and STIR (TR/TE, 3550.0/25.0; slice thickness, 4.0 mm; FOV, 280 mm), as well as axial T1-weighted (TR/TE, 2710.0/9.7; slice thickness, 4.0 mm; FOV, 200 mm) and T2-weighted (TR/TE, 5000.0/100.0; slice thickness, 4.0 mm; FOV, 200 mm) sequences.

Epidural steroid injections

Only patients who received epidural steroid injections <12 months after PET-CT were included in the injection group. Patients underwent standard informed consent. Epidural injection was facilitated by intermittent C-arm fluoroscopic guidance

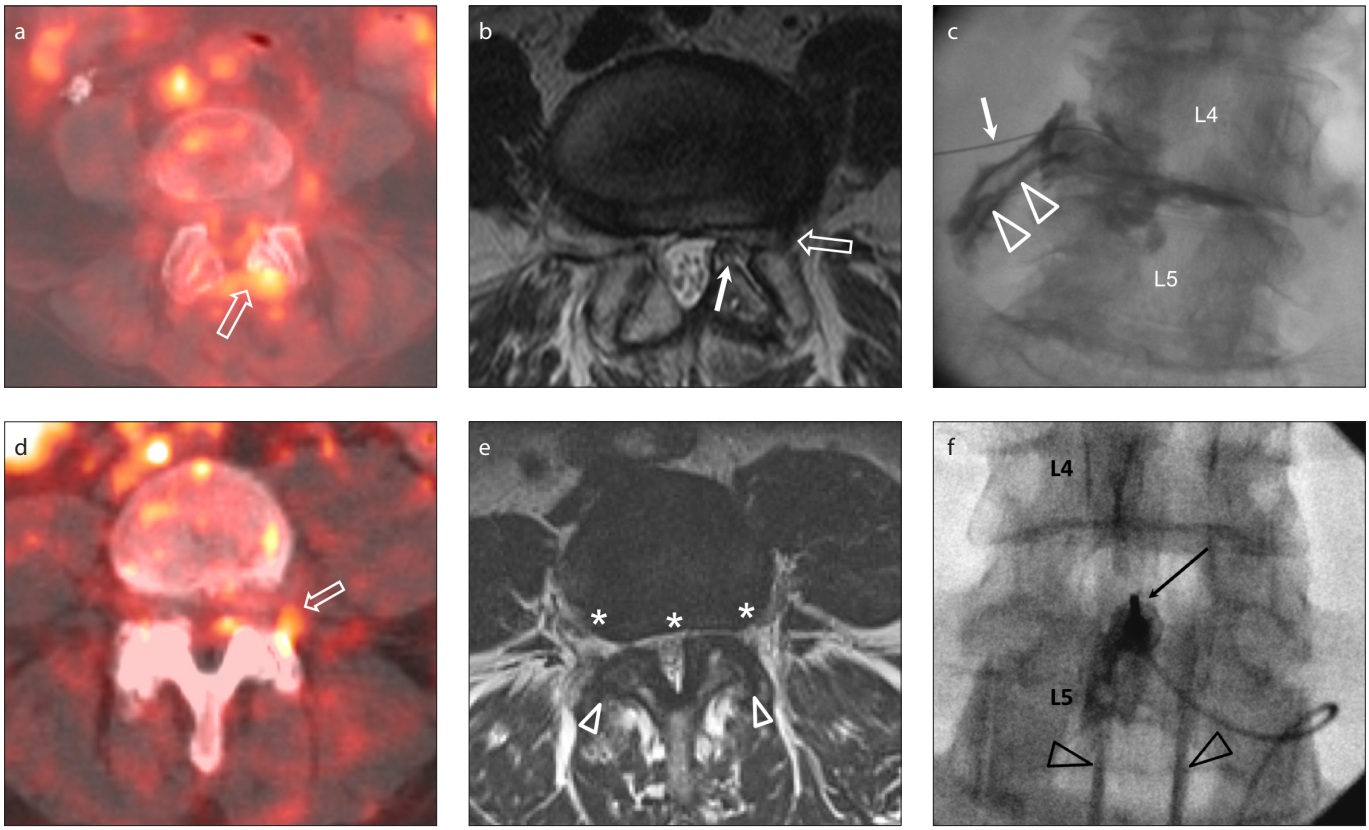

Figure 4. a–f. A 74-year-old female with non-small cell lung cancer status post left upper lobectomy with severe facet joint osteoarthritis **(a–c)**. Axial PET/CT fusion image **(a)** through the L4 vertebral body shows severe left facet joint osteoarthritis with prominent FDG-avidity along the margins of the joint *(arrow)* where the SUVmax measures 3.94. An axial T2-weighted image **(b)** demonstrates severe left lateral recess and left neuroforaminal stenosis on the basis of a complex synovial cyst *(solid arrow)* protruding anteromedially and a foraminal disc bulge *(hollow arrow)*. Prone fluoroscopic spot image **(c)** shows a spinal needle *(arrow)* advanced into the left L4-5 neural foramen and perineural spread of injected iodinated contrast *(arrowheads)* for a transforaminal epidural steroid injection. A 71-year-old male with non-small cell lung cancer and multilevel degenerative changes **(d–f)**. Axial PET/CT fusion image **(d)** through the level of L4 shows focal left asymmetric neuroforaminal FDG avidity *(arrow)* (SUVmax measures 3.82). A corresponding T2-weighted axial image **(e)** shows severe bilateral L4-5 facet joint osteoarthritis *(arrowheads)* and a large disc osteophyte complex *(asterisks)* causing spinal canal and neuroforaminal stenosis. Prone fluoroscopic image **(f)** demonstrates interlaminar insertion of a spinal needle inserted at L4-5 *(arrow)* with epidural spread of injected contrast *(arrowheads)*.

using sterile technique and a 22-gauge spinal needle via standard transforaminal or interlaminar approaches (6, 14). Epidural placement was confirmed by contrast injection (Isovue-200, GE Healthcare), followed by injection of triamcinolone (40 mg/mL) or dexamethasone (10 mg/mL) with anesthetic (1% lidocaine or 0.5% bupivacaine). The level and laterality of injection was selected based on radiculopathy symptoms and MRI analysis of canal or neuroforaminal stenosis (6). Subjective pain scores were reported by the patient immediately prior to and after injections, rated on a discrete scale from 0 ("no pain") to 10 ("worst pain of life").

Retrospective image review

Image review was performed by a board-certified subspecialty-trained musculoskeletal radiologist with 6 years of radiology experience (W.R.W.) who was blinded to clinical history and MRI findings when obtaining SUVmax measurements. MRIs were reviewed in a separate session where the reviewer was blinded to the SUVmax data and clinical history, to decrease the likelihood of recall bias.

PET/CTs were retrospectively reviewed using MIM v.6.4 software (MIM Software). Maximum standard uptake values (SUVmax), adjusted for lean body mass, were measured at 5 regions of interest (ROIs): 1) spinal canal, 2) left and 3) right neural foramina, and 4) left and 5) right facet joints (Fig. 2). ROIs were drawn by a single investigator in every case for consistency and the SUVmax values confirmed by the senior author (W.R.W.). Spherical ROIs were drawn with the largest diameter possible, excluding the vertebral bodies to avoid variable uptake levels of the bone marrow. For subsequent comparisons to epidural injection location, the PETMax was defined as: 1) the level with the highest spinal canal SUVmax, and 2) the side (left or right) with the highest neuroforaminal SUVmax at that level.

Lumbar spine MRIs were retrospectively reviewed for spinal canal stenosis, graded on a previously described (15) discrete scale from 0 (no stenosis) to 3 (complete obliteration of the cerebrospinal fluid). Neuroforaminal stenosis was also graded on a discrete scale from 0 (no stenosis) to 3 (foraminal nerve deformation) as described by Lee et al. (16). Facet joint osteoarthritis was graded on a discrete scale according to Pathria et al. (17), from 0 (normal) to 3 (facet joint space loss, large osteophytes, and periarticular cysts). Degenerative disc disease was graded on a 5-point scale according to the system described by Pfirrmann et al. (Fig. 3) (18, 19).

Table 2. Association of PET/CT metabolic activity and MRI grades

		MRI severity grade			
		Corresponding site on MRI		Disc	
Spine level	PET ROI	r	*p*	r	*p*
L1	Left facet	-0.24	0.323	0.11	0.663
	Left neural foramen	-0.18	0.459	0.31	0.200
	Right facet	-0.27	0.260	0.12	0.631
	Right neural foramen	-0.09	0.714	0.11	0.663
	Spinal canal	-0.26	0.282	0.27	0.267
L2	Left facet	-0.29	0.229	0.00	0.994
	Left neural foramen	-0.22	0.368	-0.03	0.918
	Right facet	-0.18	0.468	0.12	0.631
	Right neural foramen	-0.26	0.291	0.17	0.474
	Spinal canal	-0.10	0.691	0.18	0.458
L3	Left facet	-0.18	0.462	0.23	0.350
	Left neural foramen	0.26	0.276	-0.19	0.448
	Right facet	0.11	0.645	0.32	0.188
	Right neural foramen	0.36	0.133	0.16	0.503
	Spinal canal	-0.09	0.715	-0.02	0.937
L4	Left facet	0.03	0.895	-0.07	0.779
	Left neural foramen	0.18	0.462	0.07	0.772
	Right facet	0.10	0.689	0.15	0.552
	Right neural foramen	0.45	0.050	0.26	0.278
	Spinal canal	0.60	0.007	0.42	0.076
L5	Left facet	0.16	0.508	0.02	0.941
	Left	-0.12	0.625	0.00	1.000
	Right facet	0.10	0.692	-0.16	0.526
	Right neural foramen	0.01	0.981	0.14	0.560
	Spinal canal	0.23	0.340	-0.02	0.926

Spearman rank correlations (r) and *p* values given for associations between SUVmax measurements and MRI grades.
PET/CT, positron emission tomography/computed tomography; MRI, magnetic resonance imaging; ROI, region of interest.

Statistical analysis

The Spearman rank correlation was used to derive (r) and *p* values for associations between SUVmax measurements with severity of findings on MRI. Statistical tests were conducted at the two-sided 5% significance level using SAS 9.3 software (SAS Institute). Cohen's κ coefficient was used to determine agreement between PETmax and epidural injection site using SPSS Statistics for Windows (version 23.0, IBM) (20, 21). κ values were defined as nearly perfect (≥0.81), substantial (0.61–0.80), moderate (0.41–0.60), fair (0.21–0.40), slight (0.01–0.20), or poor (≤ 0.00) agreement (22).

Results

Twenty-five patients (15 female, 10 male) with a mean age of 70±11 years were ultimately included in the study. Nineteen of these patients had a lumbar spine MRI within 1 year of PET/CT and were thus included in the MRI group. Twenty-two patients who had a lumbar spine epidural injection less than 12 months after PET/CT were included in the injection group (Fig. 1).

The median time difference between PET/CT and MRI was 63 days (range, 3–380 days). The mean time-difference between PET/CT and spinal epidural injection was 66 days (range, 4–365 days). The most frequent primary tumors in our study population were lung (n=5 patients), lymphoma (n=4), and colorectal (n=4).

The locations of maximal FDG uptake in each patient are summarized in Table 1. The highest SUVmax was measured at L5-S1 in 9 patients. Overall, the highest mean SUVmax was found in the L5-S1 spinal canal (median, 2.04; range, 1.73–6.37). Associations between SUVmax measurements and MRI findings are assessed in Table 2, with a positive association between FDG uptake and grade of spinal canal stenosis only at L4-5 (r=0.60, $p = 0.007$). Otherwise, no statistically significant association was found regarding spinal canal or neuroforaminal stenosis or grade of disc or facet joint degeneration (Table 2).

Epidural injections and their comparison with PETmax sites are summarized in Table 3. Side-specific radiculopathy was explicitly reported in 9 patients (41%). Including multiple injections in the same patient, 18 interlaminar and 8 transforaminal injections were performed. All patients reported at least partial improvement in their pain, with a mean (±standard deviation) change in pain score of 4.4±2.9 points. Epidural injection and PETmax sites were concordant in terms of both level and laterality for 9 patients (41%) (Fig. 4). Concordance with PETmax in terms of level but not laterality was found in 2 additional patients (9.1%). Both level and laterality were discordant in 5 patients (22.7%). Cohen's κ statistic for agreement between either level or laterality for epidural injection and PETmax was moderate (κ=0.591, $p < 0.001$).

Discussion

Our study analyzed associations between FDG uptake on PET/CT and symptomatic MRI findings. Patients with symptomatic lumbar spine degenerative disease had increased ^{18}F-FDG metabolic activity corresponding to degenerative disc disease and facet joint arthrosis. However, the degree of facet joint degeneration and spinal canal or neuroforaminal stenosis assessed by MRI does not necessarily correlate with magnitude of SUV on PET/CT. Moderate agreement was found between maximal FDG metabolic activity and location of epidural spinal injections, suggesting a correlation with clinically significant spinal stenosis.

Many common non-neoplastic causes of increased FDG uptake in the spine have been reported, including discitis-osteomyelitis, inflammatory spondylitis, and osteoarthritis (1, 23). Hypermetabolic age-related degenerative disease is thought to be mediated by inflammation (24) and osteocyte replication, seen at sites of degenerative bone production (25). Most patients in

Table 3. Comparison of lumbar spine epidural injection site with PETmax and MRI grades

			MRI grades at epidural level*					
Patient #	Epidural injection site(s)	PETmax	Canal	RNF	LNF	Right facet	Left facet	Disc
1	5R	5R	1	2	3	2	3	4
2	3R	3R	N/A	N/A	N/A	N/A	N/A	N/A
3	4B	3L	N/A	N/A	N/A	N/A	N/A	N/A
4	2R	2R	N/A	N/A	N/A	N/A	N/A	N/A
5	5R	3L	2	2	2	3	3	2
6	5B	5R	0	1	1	2	2	3
7	4L	3L	1	0	0	2	2	1
8	5R	4L	0	3	3	3	2	5
9	5L	5L	0	1	0	3	3	4
10	4B	5R	3	2	3	3	3	5
	5B		1	0	1	2	3	3
11	5R	2R	2	3	3	3	3	5
12	4R	5R	0	2	2	2	2	2
13	5B	5L	1	0	2	2	2	2
14	4R, 5R	1R	N/A	N/A	N/A	N/A	N/A	N/A
15	5L	5L	1	0	0	3	3	5
16	5L	1R	1	2	1	3	3	4
17	4L	1L	1	2	2	1	1	5
	5L		0	1	2	1	1	5
18	5R	5R	0	0	0	0	0	1
19	3L	1R	N/A	N/A	N/A	N/A	N/A	N/A
20	4R	4L	N/A	N/A	N/A	N/A	N/A	N/A
21	4L	4R	2	3	3	3	3	5
	5L		1	1	1	2	2	5
22	4B	3R	3	1	2	3	3	5

LNF, left neural foramen; RNF, right neural foramen; R, right; L, left; B, bilateral, N/A, not applicable.
*Level is denoted as L1-L2=1, L2-L3=2, L3-L4=3, L4-L5=4, L5-S1=5.

our study had the highest spinal canal SUVmax within the lower lumbar levels. This finding is concordant with the current understanding that more caudal vertebral levels are subject to greater loading forces and more severe degeneration (26). Other less common, benign hypermetabolic processes have been reported in the literature as potential mimics of neoplastic disease both in and outside of the spine, including a sequestered vertebral disc fragment, osteonecrosis, and pigmented villonodular synovitis (27, 28), necessitating caution when interpreting unusual or unexpected FDG metabolic activity depicted on PET-CT.

While spinal cord uptake is less commonly mentioned in the literature, previous reports have confirmed increased FDG uptake in the spinal cord at the thoracolumbar junction to be a normal variant in a cohort of oncology patients (13). However, FDG avidity in the spinal cord should be carefully evaluated as it can indicate neoplastic or metastatic disease. An unusual distribution or intensity of FDG uptake in the spinal cord or spinal canal should prompt the radiologist to recommend further investigation, such as with MRI (29).

The lack of correlation between SUV magnitude and severity of degenerative MRI findings in our study is not entirely unexpected. Nishimatsu et al. (30) evaluated Baastrup's disease-related FDG avidity and concluded that increased uptake on PET/CT occurred only temporarily and in the earlier stages of degeneration, before morphologic changes on CT. Analogous phenomena involving degenerative disc disease or facet arthrosis may account for discrepancies in our study between severe but chronic imaging findings and FDG uptake. Interestingly, varying metabolic activity during the evolution and growth of some malignant tumors has also been described, resulting in variable levels of uptake over time. This is attributed in part to tumor cell hypoxia, which promotes greater ^{18}F-FDG uptake compared to normoxic cancer cells (31).

At our institution, epidural injection site selection depends upon severity, quality, and location of the patient's symptoms, and physical examination to corroborate imaging findings of spinal stenosis. Symptomatic spinal stenosis associated with nerve impingement results in what Floeth et al. (32) termed "compression-induced neuroinflammation", attributed to

glucose-consuming macrophages, lymphocytes, and neutrophils entering the damaged neural elements (16). The prospect of visualizing this neuroinflammation with metabolic imaging techniques is an intriguing target for future research. The moderate agreement level in our study suggests that FDG metabolic activity is more likely to be seen in association with symptomatic MRI findings. Therefore, PET/CT may have the potential to serve as a surrogate for guiding epidural injection sites, but further prospective validation measuring clinical outcomes would be required.

This retrospective study has several limitations. Variably increased FDG metabolic activity within the vertebral bodies (e.g., post-treatment uptake) could confound our SUVmax measurements. We therefore excluded bone from the ROIs; we also excluded patients with destructive osseous lesions, compression fractures, or epidural disease. SUV ratios to liver or blood pool were not obtained in this study, which may limit the generalizability of the data across patients and scans; future studies could generate more robust SUV data using ratios between spine uptake and a reference organ. We used spinal epidural injections as a proxy for symptomatic lumbar spine pathology, an imperfect method for inferring the exact source of symptomatology.

In conclusion, FDG uptake measured on PET/CT can be associated with site-specific locations but not the severity of abnormality seen on lumbar spine MRI. There is a moderate agreement between metabolic FDG focus and site of therapeutic epidural steroid injection.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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