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Review Article

PET/CT and SPECT/CT for the assessment and management of primary and metastatic tumors of the spine

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Abstract: This review evaluates nuclear imaging techniques used to assess primary and metastatic spinal tumors. The imaging techniques investigated include positron emission tomography (PET) and single-photon emission computed tomography (SPECT), both integrated with computed tomography (CT). These techniques provide metabolic information that addresses several limitations of MRI, and they offer improved lesion localization, characterization, and treatment planning. PET enables sensitive detection of early metastases, determination of tumor burden, and monitoring of intervention response, while SPECT/CT improves diagnostic confidence and reduces indeterminate findings compared with planar scintigraphy or SPECT alone. Together, these modalities help distinguish benign from malignant lesions, identify areas of pain, and clarify equivocal structural findings. We compare the two modalities directly, summarize the evidence for radiotracers beyond ^{18}F-FDG, including ^{18}F-NaF, prostate-specific membrane antigen ligands, somatostatin receptor ligands, and fibroblast activation protein inhibitors, and review the false-positive and false-negative patterns that arise from degenerative, inflammatory, infectious, and postoperative change. Most spine-specific data come from case reports and small retrospective series, and no validated quantitative threshold separates benign from malignant vertebral lesions. Molecular imaging nonetheless holds an established place in the clinical evaluation of spinal tumors, and integrated multidisciplinary care together with emerging tracers should further strengthen early detection, staging, and treatment.

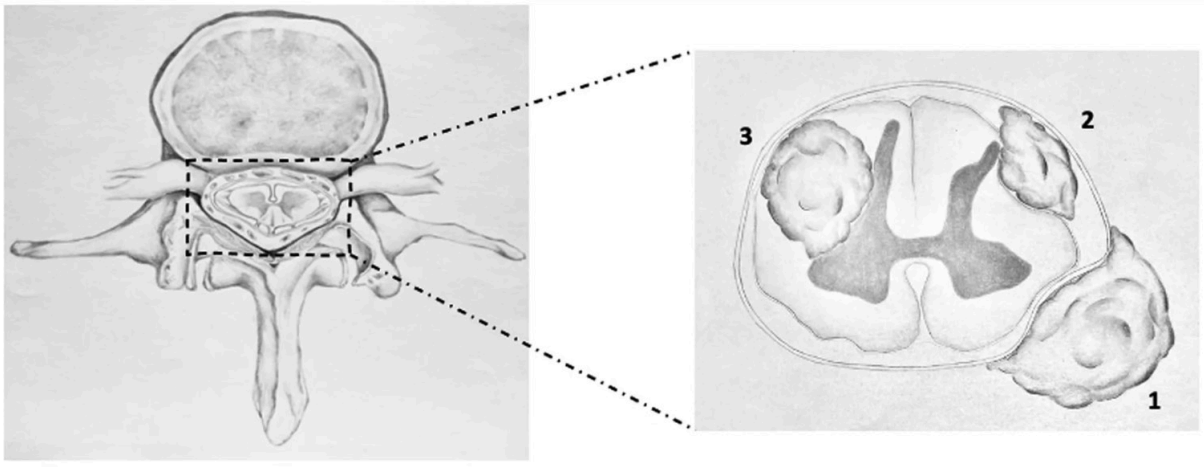
Keywords: Spinal tumors, metastatic disease, diagnosis, evaluation, Positron emission tomography (PET), Single-photon emission computed tomography (SPECT)

Introduction

Spinal cord tumors of primary origin are rare and account for 4-8% of central nervous system tumors [1]. In contrast, spinal metastases are found in 20% of individuals diagnosed with cancer and contribute to 97% of total spinal tumors [2, 3]. Spinal tumors are broadly classified by origin and anatomic location, yielding the categories of primary and metastatic disease and of extradural and intradural disease. Intradural tumors are divided further into intradural extramedullary and intradural intramedullary lesions [4]. Extradural tumors are the most common and arise outside the dural sac. Extradural metastases are often seen, although primary lesions such as lymphoma, multiple myeloma, chondrosarcoma, and Ewing sarcoma have also been reported [4, 5]. Intradural extramedullary tumors grow outside the spinal cord within the subdural space and are most often schwannomas, meningiomas, or neurofibromas [6]. Intradural intramedullary tumors are the rarest, arise within the spinal cord itself, and are most often ependymomas, astrocytomas, gangliogliomas, or hemangioblastomas [7]. These anatomical distinctions, in conjunction with histologic features and imaging characteristics, are incorporated into tumor staging and inform clinical decision making (**Figure 1**). This framework sets the basis for imaging evaluation, in which modalities that include positron emission tomography (PET) and single-photon emission computed tomography (SPECT) support accurate localization and tumor staging.

Initial tumor evaluation often begins with plain radiographs to estimate lesion location; however, diagnostic utility in this circumstance is limited, as up to 40% of metastatic lesions may go undetected [8]. New bone formation at the lesion site can lead to increased tracer uptake, a feature that can be detected in complementary screening tools such as bone scintigraphy [9]. Aside from these applications, magnetic resonance imaging (MRI) and computed tomography (CT) operate as the primary imaging techniques for diagnosis and staging. MRI is generally regarded as the gold standard for spinal tumor evaluation because of its soft tissue contrast and its depiction of bone marrow infiltration. CT provides excellent visualization of bone and demonstrates efficacy in detecting metastatic involvement up to 6 months before radiographic changes become apparent [8, 10]. Beyond detection, MRI also helps define disease extent, monitor treatment response, and guide surgical and radiotherapeutic planning [11]. The principal features of each modality are compared in **Table 1**.

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1 Extradural tumors

- Mostly attributed to *Metastases* (>90%)
  - most common: breast, lung, renal, prostate, thyroid, melanoma, myeloma, lymphoma and colorectal cancer
- *Primary tumors of the vertebral column* (rare)
  - Sarkoma, Osteosarkoma, Chordoma etc. overall > 70 entities

2 Intradural extramedullary tumors

- Mostly primary spinal tumors
  - Spinal meningioma, spinal nerve sheath tumors (schwannomoma, neurofibroma)
- *Spinal leptomeningeal metastases* (rare)

3 Intradural intramedullary tumors

- *Mostly primary spinal tumors*
  - Spinal ependymoma, pilocytic astrocytoma, hemangioblastoma, spinal gangioglioma, spinal primitive neuroectodermal tumors
- *Intramedullary metastases* (rare)
  - Lymphoma/leukemia, solid tumors

Figure 1. Classification System of primary and metastatic spinal tumors featuring anatomical compartments: extradural, intradural extramedullary, and intradural intramedullary. This research was originally published in *Frontiers in Surgery*. Nevzati E, Poletti N, Spiessberger A, Bäbler S, Studer G, Riklin C, Diebold J, Chatain GP, Finn M, Witt JP, Moser M, Mariani L. *Establishing the Swiss Spinal Tumor Registry (Swiss-STR): a prospective observation of surgical treatment patterns and long-term outcomes in patients with primary and metastatic spinal tumors. Front Surg.* 2023;10:1222595. Published by Frontiers Media SA. © 2023 [87].

Even though MRI has proven to be valuable, one of its key limitations in spinal oncology is its lack of specificity in identifying pain-generating lesions [12]. Although highly sensitive for detecting structural abnormalities, MRI cannot reliably distinguish painful from incidental findings [13, 14]. To address these limitations, supplementary nuclear imaging methods such as 2-deoxy-2-[18F]fluoro-D-glucose (^{18}F-FDG) PET/CT and single-photon emission computed tomography (SPECT)/CT have been explored. PET/CT detects regions of increased metabolism and can help localize pain sources when MRI findings are inconclusive, especially in cases of complex metastatic disease [15]. SPECT/CT addresses several limitations of bone scintigraphy by improving tracer localization and diagnostic accuracy [16]. While MRI remains the standard for spinal imaging, its limitations highlight the need for complementary metabolic approaches such as PET/CT and SPECT/CT. There is limited literature on the direct comparison between PET/CT and SPECT/CT in spinal oncology, and their roles in disease detection, treatment planning, and post-therapy monitoring remain underexplored. In this review article, we assess the effectiveness of PET and SPECT for the identification and management of primary and metastatic spine tumors. We compare the two modalities directly, summarize the evidence for radiotracers beyond ^{18}F-FDG, describe the interpretive pitfalls that limit specificity, and outline where quantitative thresholds remain undefined.

PET/CT

PET is a nuclear imaging modality that measures variations in metabolic activity, which supports the evaluation of disease status and functional assessment [17, 18]. In spinal oncology, PET with FDG identifies metabolically active lesions, including those responsible for pain, because tracer accumulation tracks glucose metabolism [19]. PET uses radiotracers labeled with positron-emitting radionuclides, allowing high contrast resolution, sensitive visualization, and precise identification of tracer uptake around lesions [20]. However, PET alone lacks anatomic localization of abnormalities, and the integration of CT provides essential structural context to improve diagnostic accuracy (**Figure 2**) [21, 22].

^{18}F-FDG is the tracer used most often in clinical studies of spinal tumors because it identifies early metabolic changes in primary and metastatic lesions [20]. Additional tracers, such as ^{18}F-sodium fluoride (NaF) and prostate-specific membrane antigen (PSMA), have shown promise for characterizing osteoblastic metastases and prostate cancer spread respectively, although their application in spinal oncology remains limited [20].

Table 1. Comparison of imaging modalities for the assessment of primary and metastatic spinal tumors

Feature	CT	MRI	Bone scintigraphy with SPECT/CT	^{18}F-FDG PET/CT
Signal source	X-ray attenuation by mineralized bone	Proton density and relaxation in marrow and soft tissue	^{99m}Tc-MDP uptake reflecting osteoblastic activity and blood flow	Glucose transport and hexokinase activity in viable tumor
Spatial resolution	0.5 to 1 mm	0.5 to 1 mm in plane	10 to 15 mm at spinal depth	4 to 6 mm
Principal strength	Cortical detail, matrix mineralization, fracture and stability assessment, surgical planning	Soft tissue contrast, marrow infiltration, cord and nerve root involvement, epidural extension	Wide availability, low cost, whole-skeleton survey with anatomic correlation at the level of interest	Whole-body metabolic staging in one examination, detection of marrow disease before cortical change, response assessment
Principal limitation	Less sensitive than MRI for marrow-confined disease; no functional information	Cannot reliably separate painful from incidental lesions; degraded by spinal instrumentation; long acquisition	Uptake is not tumor specific; photopenic in purely lytic disease such as myeloma; limited field of view for the SPECT component	False positives from degeneration, infection, fracture, and postoperative change; reduced sensitivity in sclerotic metastases
Reported performance for spinal metastases	Moderate sensitivity, high specificity for cortical destruction	Highest sensitivity for marrow-based disease; comparable to PET in pooled analyses	Planar imaging alone performs least well; adding SPECT/CT raises accuracy and specificity toward PET	Pooled sensitivity 91.8% and specificity 84.6%, with wide confidence intervals
Quantification	Hounsfield units; well standardized	Semiquantitative; ADC and signal ratios not standardized across vendors	SUV-like metrics feasible with CT-based attenuation correction; no validated thresholds	SUV_{max} and SUV_{peak}; harmonized through EANM and EARL; PERCIST for response
Typical effective dose	5 to 10 mSv for a diagnostic spine or body CT	None	4 to 8 mSv including the CT component	7 to 14 mSv including the CT component
Acquisition time	Under 5 minutes	30 to 60 minutes per region	2 to 4 hour uptake delay plus 20 to 40 minutes tomography	60 minute uptake delay plus 15 to 25 minutes acquisition
Availability and relative cost	Universal; lowest cost	Widely available; intermediate cost	Widely available including non-tertiary centers; low cost	Restricted to centers with a cyclotron supply chain; highest cost
Preferred clinical situation	Structural characterization, fracture risk, and operative planning	First-line for any suspected spinal tumor and for cord compression	Indeterminate focus on a prior bone scan, solitary vertebral lesion, sclerotic disease, pain generator localization	FDG-avid primary, whole-body staging, occult primary, marrow disease, metabolic response assessment

ADC, apparent diffusion coefficient; CT, computed tomography; EANM, European Association of Nuclear Medicine; EARL, EANM Research Ltd.; FDG, fluorodeoxyglucose; MDP, methylene diphosphonate; MRI, magnetic resonance imaging; PERCIST, PET Response Criteria in Solid Tumors; PET, positron emission tomography; SPECT, single-photon emission computed tomography; SUV, standardized uptake value.

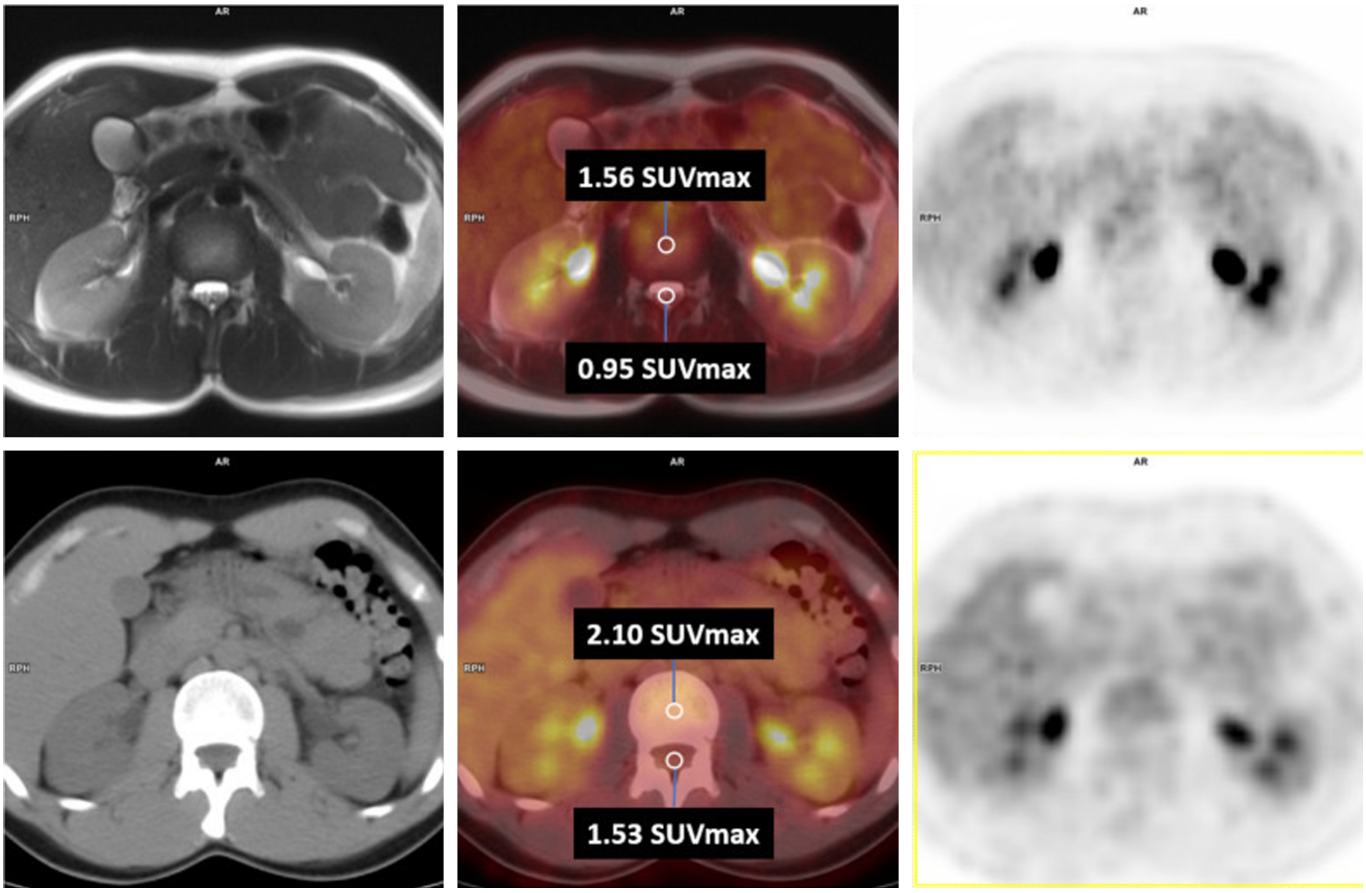


Figure 2. A region of interest (ROI) centered on the spinal cord and bone marrow at T12. Top row from left to right (MRI, PET/MRI, PET); bottom row from left to right (CT, PET/CT, PET). Localization within the ROI is demonstrated on the PET/MRI and PET/CT using SUVmax measurements. This research was originally published in *EJNMMI Research*. Aiello M, Alfano V, Salvatore E, Cavaliere C, Picardi M, Della Pepa R, Nicolai E, Soricelli A, Vella A, Salvatore M, Mascalchi M. *[18F]FDG uptake of the normal spinal cord in PET/MR imaging: comparison with PET/CT imaging. EJNMMI Res.* 2020;10:91. Published by Springer Nature [88].

Radiotracers beyond ^{18}F-FDG

^{18}F-sodium fluoride (^{18}F-NaF) is a bone-seeking PET agent whose uptake reflects regional blood flow and osteoblastic activity at sites of increased bone turnover. Because it images the osseous reaction to a lesion and not tumor glycolysis, it performs well in sclerotic metastases that show little ^{18}F-FDG uptake, which makes it useful in prostate and breast cancer. In men with high-risk prostate cancer, ^{18}F-NaF PET/CT identified more vertebral metastases than planar bone scintigraphy and SPECT, and the addition of CT resolved many of the equivocal foci seen on PET alone [23]. A prospective comparison of ^{99m}Tc-diphosphonate planar scintigraphy and whole-body SPECT/CT with ^{18}F-NaF PET/CT reported higher sensitivity for the fluoride studies, although specificity was similar once CT correlation was available [24]. The main constraint is that ^{18}F-NaF shares the limitations of any bone-turnover agent, since degenerative facet disease, endplate change, and healing fractures also produce intense uptake in the spine [25, 26].

Prostate-specific membrane antigen (PSMA) ligands such as ^{68}Ga-PSMA-11, ^{18}F-DCFPyL, and ^{18}F-PSMA-1007 bind a transmembrane glycoprotein that is overexpressed in prostate adenocarcinoma [27]. In a randomized comparison with conventional imaging that combined CT and bone scintigraphy, PSMA PET/CT achieved substantially higher accuracy for pelvic nodal and distant metastatic disease in men with high-risk prostate cancer and changed management in a meaningful proportion of patients [28]. In the spine, PSMA PET/CT detects marrow-based deposits before they produce sclerotic or lytic change on CT, which matters when a solitary vertebral lesion determines whether treatment is directed at oligometastatic or systemic disease. Interpretation requires care because PSMA ligands also accumulate in Paget disease, healing fractures, fibrous dysplasia, and vertebral hemangioma, and ^{18}F-PSMA-1007 produces benign bone uptake of uncertain origin at a rate high enough to affect staging [29].

Somatostatin receptor ligands labeled with ^{68}Ga, including ^{68}Ga-DOTATATE and ^{68}Ga-DOTATOC, target somatostatin receptor subtype 2 [30, 31]. Their established role in spinal disease is the detection of vertebral metastases from well-differentiated neuroendocrine tumors, where sensitivity exceeds that of ^{18}F-FDG for low-grade lesions

and where uptake also identifies candidates for peptide receptor radionuclide therapy [32-34]. Spinal meningiomas express somatostatin receptor 2 strongly, so somatostatin receptor PET can separate meningioma from schwannoma at the same intradural extramedullary location and can define target volumes for radiotherapy when the interface with cord and nerve root is difficult to see on MRI. The spine-specific evidence for these agents is confined to small series and case reports.

Fibroblast activation protein inhibitors (FAPI) labeled with ^{68}Ga target the cancer-associated fibroblast compartment of the tumor stroma [35]. Physiologic uptake in normal bone marrow is low, so tumor-to-background contrast in the vertebral column is high, and uptake does not depend on tumor glycolysis or on the blood glucose level at the time of injection. Comparative studies across several cancer types report that ^{68}Ga-FAPI detects more bone metastases than ^{18}F-FDG, with the largest differences in tumors of low FDG avidity such as differentiated thyroid, hepatocellular, and gastric carcinoma [36]. Series in bone and soft tissue sarcoma, a group that includes the chordomas and chondrosarcomas encountered in the spine, show uptake in lesions that are FDG-negative. The published experience consists of single-center series, and no study has used a spine-specific reference standard [37, 38].

In practice, tracer selection follows the histology of the primary tumor and the clinical question. ^{18}F-FDG remains the default for staging and response assessment in lymphoma, lung cancer, sarcoma, and most solid tumors with high glycolytic activity. ^{18}F-NaF and bone scintigraphy address the osseous reaction and retain a role where sclerotic disease predominates. PSMA and somatostatin receptor ligands are selected when the primary tumor expresses the corresponding target, and FAPI remains investigational. None of these agents has been evaluated in a prospective trial designed around spinal endpoints, so the comparative data summarized in **Table 2** are extrapolated from whole-body studies in which vertebral involvement was one finding among many.

Diagnosis of primary spinal tumors

The application of PET/CT in identifying primary spinal tumors in large retrospective and prospective studies remains understudied. However, several case reports have indicated the significance of FDG PET/CT in tumor assessment. Feng et al. reported a case of a 46-year-old man with a primary malignant giant cell tumor of the bone and lumbosacral pain, where FDG PET/CT showed increased ^{18}F-FDG uptake in the lumbar and sacral vertebrae (**Figure 3**) [39].

Similarly, Shen et al. presented a 47-year-old woman with possible primary spinal glioblastoma in which ^{18}F-FDG PET/CT characterized tumor metabolism and confirmed its primary origin [40]. In a study of 26 patients with spinal intramedullary lesions, ^{18}F-FDG PET/CT differentiated between high-grade and low-grade malignancies [41]. ^{18}F-FDG PET/CT has also demonstrated potential for detecting occult primary tumors and the origin of metastatic spread, with a reported detection accuracy of 24-53% [42]. Gutzeit et al. investigated 45 patients with cervical adenopathy or extracervical metastases, where PET/CT accurately detected primary tumors in 33% of patients [43]. Similarly, Kwee et al. conducted a meta-analysis assessing the diagnostic performance of ^{18}F-FDG PET/CT in localizing the primary site in patients with cancer of an unknown origin, reporting a pooled sensitivity of 84% (95% CI 78-88%) and specificity of 84% (95% CI 78-89%) [44]. A separate study demonstrated that ^{18}F-FDG PET/CT outperformed contrast-enhanced CT and CT/MR imaging in primary tumor localization, with higher overall sensitivity and accuracy [22]. Overall, PET/CT appears to be a valuable supplementary imaging technique for characterizing intramedullary spinal lesions and detecting occult primary tumors, and it warrants further evaluation in larger prospective studies.

The evidence supporting ^{18}F-FDG PET/CT in primary spinal tumors rests almost entirely on case reports and small single-center retrospective series. The largest spine-specific study cited above enrolled 26 patients, and the reports of occult primary detection drew on mixed cancer populations in which spinal lesions formed a small subgroup. No prospective trial has evaluated PET/CT for the diagnosis of a primary spinal neoplasm, blinded histopathologic reference standards are rarely reported, and the case report literature is subject to publication bias toward positive findings. The level of evidence in this area is therefore low, and the findings summarized above should be read as hypothesis generating until larger prospective cohorts with defined reference standards become available.

Diagnosis of metastatic spinal tumors

^{18}F-FDG PET/CT is frequently utilized in the staging and reassessment of metastatic involvement [45]. Early metastases can be identified by FDG PET/CT through increased glucose metabolism in occult bone marrow infiltration, which is otherwise not evident on conventional imaging (**Figure 4**) [18].

FDG PET is more sensitive for osteolytic metastases than for osteoblastic metastases because osteoblastic lesions show low glucose uptake [8, 46]. A meta-analysis by Harlianto et al. recorded the pooled sensitivity and specificity of FDG PET/CT for detecting spinal metastases at 91.8% (95% CI 54.0-99.1%) and 84.6% (95% CI 55.2-96.1%) [47]. Moreover, ^{18}F-FDG PET has demonstrated utility in differentiating benign from metastatic tumors of the spine. In a study of 22 cancer patients with a combined 214 vertebral lesions, ^{18}F-FDG PET/CT correctly identified 128 of 129 metastases and 83 of 85 benign lesions [48]. Collectively, these findings indicate a useful

Table 2. Positron emission tomography radiotracers applicable to the assessment of spinal tumors

Radiotracer	Molecular target	Role in spinal disease	Advantages	Limitations and level of evidence
^{18}F-FDG	Glucose transporters and hexokinase	Staging and response assessment in FDG-avid primaries; characterization of intramedullary lesions; detection of occult primary	Widest availability and evidence base; whole-body coverage; validated response criteria	Low specificity in degenerative, infective, and postoperative change; reduced sensitivity in sclerotic metastases; meta-analytic estimates with wide confidence intervals
^{18}F-NaF	Hydroxyapatite exchange at sites of bone turnover	Detection of sclerotic and mixed skeletal metastases where FDG uptake is low	Higher lesion detection than planar bone scintigraphy and SPECT; rapid blood clearance and high bone uptake	Uptake reflects the osseous reaction and not the tumor; degenerative disease and healing fracture cause false positives; no soft tissue staging
PSMA ligands (^{68}Ga-PSMA-11, ^{18}F-DCFPyL, ^{18}F-PSMA-1007)	Prostate-specific membrane antigen	Detection of vertebral marrow metastases in prostate carcinoma; selection of patients for metastasis-directed therapy	Higher accuracy than CT with bone scintigraphy in randomized comparison; detects marrow deposits before cortical change	Benign uptake in Paget disease, fracture, fibrous dysplasia, and hemangioma; ^{18}F-PSMA-1007 shows unexplained benign bone uptake; spine-specific data limited
^{68}Ga-DOTATATE and ^{68}Ga-DOTATOC	Somatostatin receptor subtype 2	Vertebral metastases from well-differentiated neuroendocrine tumors; characterization of spinal meningioma; radiotherapy target delineation	High sensitivity in low-grade neuroendocrine disease; identifies candidates for peptide receptor radionuclide therapy	Restricted to receptor-expressing histologies; low sensitivity in dedifferentiated tumors; spinal evidence confined to small series and case reports
^{68}Ga-FAPI	Fibroblast activation protein in tumor stroma	Investigational detection of bone metastases and of sarcomas including chordoma and chondrosarcoma	Low physiologic marrow uptake gives high vertebral contrast; independent of blood glucose; no uptake-delay requirement	Uptake also occurs in fibrotic, inflammatory, and degenerative tissue; single-center series only; no spine-specific reference standard

DCFPyL, 2-(3-{1-carboxy-5-[(6-fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid; DOTATATE, DOTA-Tyr3-octreotate; DOTATOC, DOTA-Tyr3-octreotide; FAPI, fibroblast activation protein inhibitor; FDG, fluorodeoxyglucose; NaF, sodium fluoride; PSMA, prostate-specific membrane antigen.

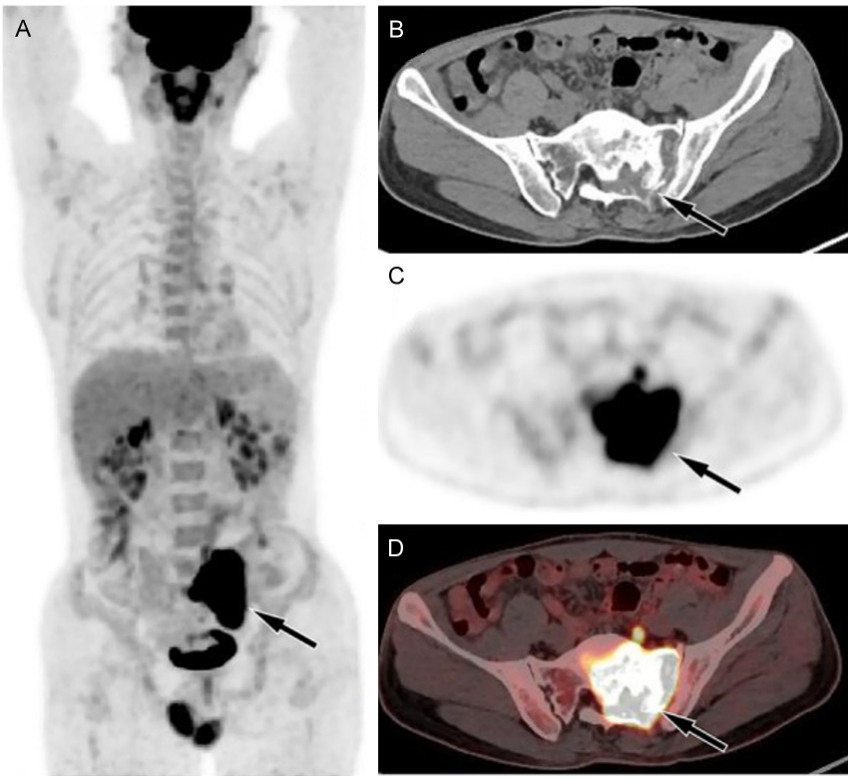


Figure 3. ^{18}F-FDG PET/CT imaging of a 46-year-old man with primary malignant giant cell tumor from the fifth lumbar vertebra to the second sacral vertebra. (A) Increased uptake can be seen in the pelvic area (arrow). (B) The lesion is localized in the left region of the sacrum. Increased ^{18}F-FDG uptake of the lesion can be seen in the axial PET (C) and the PET/CT (D). Feng Z, Yu R, Hu X. ^{18}F-FDG PET/CT revealed primary malignant giant cell tumor of the sacrum: a case report. *Front Med (Lausanne).* 2025;12:1653522. doi:10.3389/fmed.2025.1653522 [39].

diagnostic yield for ^{18}F-FDG PET/CT in evaluating spinal metastases, with improved sensitivity and specificity compared with structural imaging alone.

The confidence intervals around these pooled estimates are wide and reflect substantial heterogeneity between the contributing studies. Sources of variation include patient selection, the histology of the primary tumor, the reference standard used to confirm metastasis, and whether the analysis was performed per patient or per lesion. Series enriched for osteolytic disease report higher sensitivity than series that include a large proportion of sclerotic prostate or breast metastases, and studies that accept imaging follow-up as the reference standard report higher accuracy than those that require histology. The timing of imaging relative to systemic therapy adds further variation, since treatment suppresses glycolysis and lowers measured uptake. These factors should be weighed before the pooled figures are applied to an individual patient.

Management of spinal tumors

PET provides insight into tumors at the molecular level, which may hold clinical value for predicting therapeutic response. For instance, variations in ^{18}F-FDG uptake between pretherapeutic and post-therapeutic imaging have been correlated with histologic treatment response, progression-free survival, and overall survival in patients with osteosarcoma [49]. Soliman et al. and Patil et al. demonstrated that PET/CT can track metabolic activity levels, complement MRI findings, and overcome image distortion caused by spinal hardware [46, 50]. Choi et al. found that radiation therapy significantly reduced maximum and mean standardized uptake values (SUV_{max} and SUV_{mean}) in spinal metastases, which shows a further use of PET/CT in monitoring early treatment effects [51]. Similarly, long-term PET/CT follow-up after stereotactic body radiation therapy (SBRT) has been used to monitor changes in metabolism across multiple metastatic sites, though scans performed too soon after treatment can be affected by post-radiation inflammation [52, 53]. To avoid this effect, the first scan should be delayed 2 to 3 months after SBRT [54]. FDG PET/CT provides a metabolic perspective that complements anatomical imaging and enables more accurate evaluation of treatment efficacy and earlier identification of disease progression in patients with spinal tumors.

FDG PET/CT can also change the initial treatment management. Reinert et al. reported that 71 of 155 patients had a change in their intended treatment approach based on PET/CT results [55]. Combining PET/CT with MRI improves diagnostic accuracy for suspected metastatic spinal lesions, reduces equivocal findings, and prevents unnecessary procedures, allowing for more appropriate treatment planning [56]. Kuah et al. emphasized that whole-body PET/CT supports comprehensive staging and treatment planning for metastatic spinal cord compression, defining the extent of disease that guides surgery, radiation, and management decisions [57].

SPECT/CT

SPECT/CT is a nuclear imaging modality that combines functional imaging of SPECT with anatomical detail from CT, which enables precise localization and improved diagnostic accuracy compared with planar scintigraphy or SPECT alone (**Figure 5**) [58, 59].

SPECT is conducted through the detection of gamma photons emitted by radiotracers such as technetium-99m, which accumulate in target tissues based on biological activity [60]. A rotating gamma camera captures

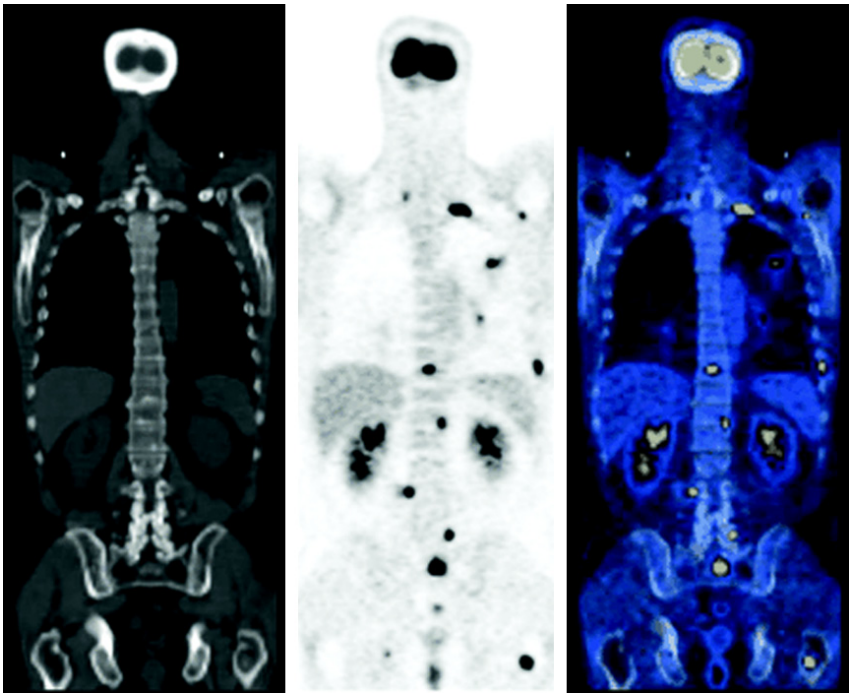


Figure 4. A 52-year-old man with lung cancer and multiple bone marrow spinal metastases. The metastases are seen only in PET and not in CT. From left to right, images are produced by CT, PET, and PET/CT. This research was originally published in *JNM*. Metser U, Lerman H, Blank A, Lievshitz G, Bokstein F, Even-Sapir E. *Malignant Involvement of the Spine: Assessment by ^{18}F-FDG PET/CT. J Nucl Med.* 2004;45:279-284. © SNMMI [45].

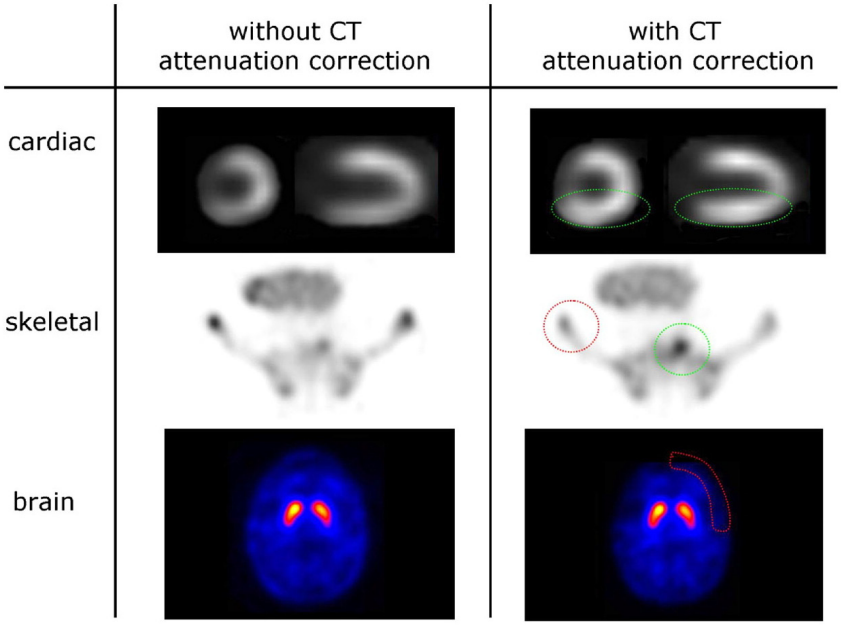


Figure 5. Effect of CT-based attenuation correction on SPECT imaging. Top row: myocardial perfusion SPECT; apparently reduced uptake in the inferior wall without correction appears normal after CT attenuation correction (green circles). Middle row: skeletal SPECT; a sacral metastasis is better localized after correction (green circle). Bottom row: brain SPECT without and with CT attenuation correction. Without correction, background activity in peripheral structures may be overestimated (red circles) and can approach the intensity of true lesions. This research was originally published in *JNM*. Buck AK, Nekolla S, Ziegler S, Beer A, Krause BJ, Herrmann K, Scheidhauer K, Wester HJ, Rummeny EJ, Schwaiger M, Drzezga A. *SPECT/CT. J Nucl Med.* 2008;49:1305-1319. © SNMMI [59].

emissions from multiple angles, which are reconstructed into three-dimensional tomographic images representing regional tracer distribution [61]. The fusion of metabolic and structural data enhances specificity, reduces equivocal findings, and increases confidence in distinguishing benign from malignant abnormalities, particularly in complex anatomical areas such as the spine [62]. As a result, SPECT/CT can improve localization of solitary tumors and spinal metastases compared with conventional nuclear medicine techniques [63].

Diagnosis of solitary and metastatic spinal tumors

SPECT/CT imaging demonstrates strong diagnostic performance for solitary spinal lesions, showing greater accuracy than SPECT alone. In a study consisting of 48 patients diagnosed with a solitary spinal abnormality, SPECT/CT detected 9 of 18 benign and 29 of 30 malignant lesions, whereas SPECT alone identified 6 of 18 benign and 28 of 30 malignant lesions [64]. Similarly, Sharma et al. reported that 36 of 90 solitary spinal lesions were determined equivocal by SPECT alone, compared with only 5 of 90 with SPECT/CT, demonstrating a reduction in indeterminate findings [65]. In an investigation of 80 patients with solitary spine lesions, the addition of SPECT/CT decreased equivocal findings and increased the proportion of lesions given a definitive characterization from 6.1% with planar bone scanning to 78.8%, which improved diagnostic confidence [66]. SPECT/CT also exhibits value in distinguishing spinal osteoblastoma from other osteogenic tumors, through accurate detection of uptake differences between benign and malignant sites (**Figure 6**) [67].

In a meta-analysis including 1,598 patients, Liu et al. demonstrated that bone scintigraphy with SPECT provides greater diagnostic accuracy and specificity while maintaining similar sensitivity on a per-patient basis for detecting vertebral metastases [10]. These findings indicate that SPECT/CT improves diagnostic accuracy, specificity, and reader confidence, which establishes it as a useful approach for evaluating both solitary and metastatic spinal lesions.

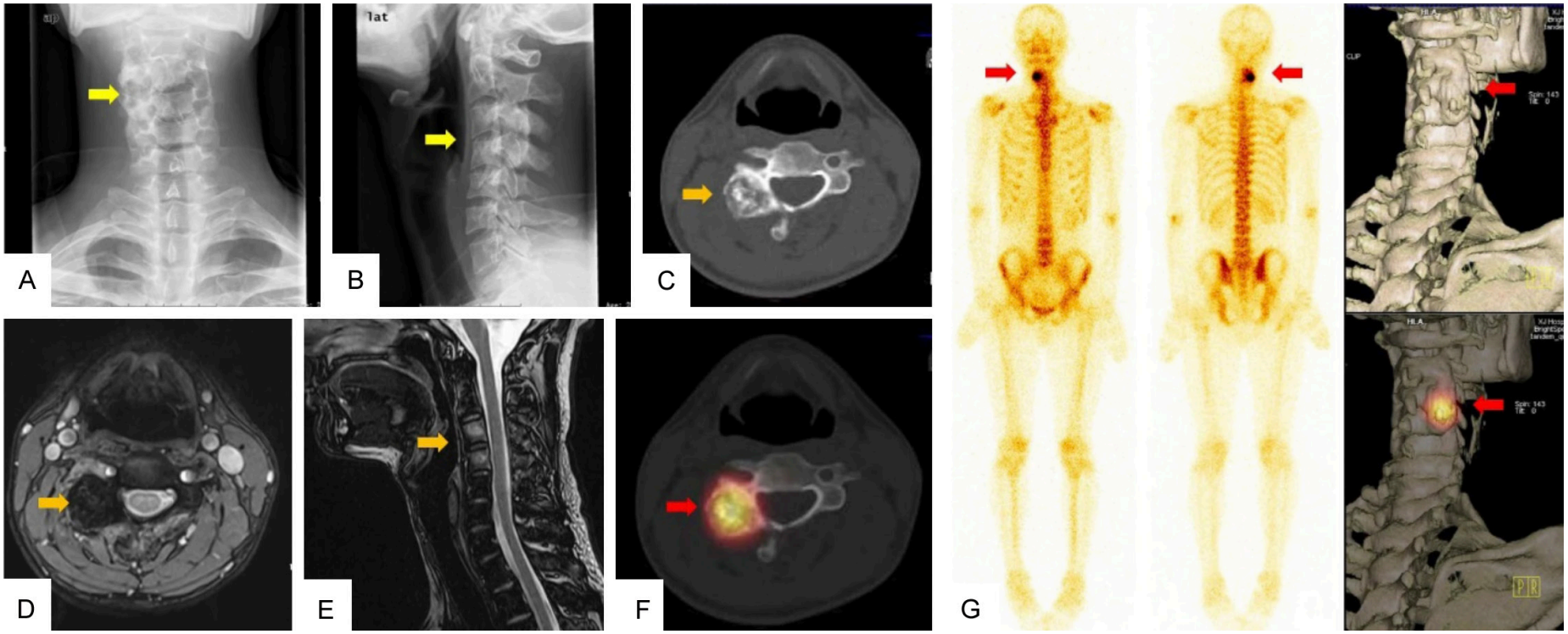


Figure 6. Osteoblastoma of C3-C4 in a 28-year-old man. Anteroposterior (A) and lateral (B) radiographs show bone destruction and hyperplasia at C3-C4 (yellow arrows). Axial CT (C), axial contrast-enhanced fat-suppressed T1-weighted MRI (D), and sagittal T2-weighted MRI (E) show a 20-mm osteogenic lesion involving the right transverse processes and laminae of C3-C4 (orange arrows). Fused SPECT/CT (F) and three-dimensional reconstructions (far right) localize the lesion (red arrows), and planar whole-body bone scintigraphy (G) shows high uptake at C3-C4 (red arrows). This research was originally published in JOSR. Ma W, Quan Z, Wang J, Li X, Li G. The one-in-all diagnostic value of ^{99m}Tc-MDP bone scan combining with single-photon emission tomography (SPECT)/CT imaging in spinal osteoblastoma. J Orthop Surg Res. 2020;15:181. Published by Springer Nature. © 2020 [67].

Management of spinal tumors

SPECT/CT contributes to the assessment of both primary and metastatic spinal tumors by combining functional and anatomical information to improve diagnostic accuracy and guide treatment decisions [16]. Whole-body scintigraphy has remained the accepted standard for evaluating skeletal metastatic disease because it identifies osseous lesions, but its localization is imprecise, which makes malignant and benign lesions difficult to separate without anatomical correlation [68]. Compared with planar scintigraphy, SPECT offers greater sensitivity for detecting vertebral lesions and improves identification of both benign and malignant spinal lesions, and accurate localization is essential for separating these conditions [69]. SPECT alone, however, remains insufficient for precise lesion characterization and requires correlation with anatomical imaging [63]. The integration of SPECT with CT addresses this limitation by providing high-resolution anatomical images and attenuation correction, which increases specificity compared with planar scintigraphy or SPECT alone [70]. Bahouth et al. noted that the contribution of SPECT/CT to planar bone scintigraphy in the management of spinal metastases can reduce false-positive and false-negative results and unreliable identification of spinal lesions, which aids the radiation oncologist and surgeon in evaluating individual bone lesions [71]. In oncology, SPECT/CT is used to clarify indeterminate hotspots and to confirm or exclude metastases, and it has been shown to increase reader confidence and correct lesion misclassification [72].

Monitoring treatment of spinal tumors

Treatment of spinal tumors includes surgery, radiation therapy, and targeted therapy with the main objective of improving the patient's quality of life [73]. The functional and metabolic information provided by SPECT/CT improves treatment monitoring and the assessment of disease progression [74]. Gherghe et al. demonstrated that quantitative SPECT/CT using SUV-like metrics provides a reproducible and objective method for monitoring treatment response in spinal bone metastases, showing strong correlation with traditional visual interpretation [75]. Their findings support the use of quantitative SPECT/CT as a standardized follow-up approach during systemic or local therapy. Meng et al. reported that two baseline ^{99m}Tc-MDP SPECT/CT features, nerve-root compression (NRC) and radioactive cold-zone lesions, predicted poor pain relief following ^{89}Sr therapy for bone metastases, with NRC showing 93.5% sensitivity and 89.5% specificity for treatment failure [76]. Lee et al. used active lesions identified on SPECT/CT together with the numerical rating scale to predict treatment outcomes in patients presenting with lower back pain [77]. The available evidence suggests that SPECT/CT can localize metabolically active lesions and predict therapeutic outcomes, which supports its use in the comprehensive evaluation and treatment of spinal tumors.

Comparison of PET/CT and SPECT/CT

PET/CT and SPECT/CT differ in detector physics, and these differences account for much of their clinical behavior. PET uses electronic collimation through coincidence detection of annihilation photons, which yields a system sensitivity one to two orders of magnitude higher than SPECT and a reconstructed spatial resolution of approximately 4 to 6 mm on current clinical scanners. SPECT relies on mechanical collimation, which discards most emitted photons and gives a spatial resolution of approximately 10 to 15 mm at the depths encountered in the spine [59, 61]. PET is quantitative by design because attenuation and scatter correction are well established and the standardized uptake value has an accepted definition [78]. Quantification in SPECT has become feasible with CT-based attenuation correction and calibrated iterative reconstruction, but it is applied less consistently across centers [58].

Practical considerations often determine which study is performed. Whole-body PET/CT is acquired in 15 to 25 minutes and covers the skull base to the thighs in a single examination, which is efficient when the clinical question includes extraskeletal disease. Bone scintigraphy with limited-field SPECT/CT requires a delay of 2 to 4 hours after tracer injection and adds 20 to 40 minutes for the tomographic acquisition over one or two bed positions. Effective dose is broadly comparable, in the range of 7 to 14 millisievert (mSv) for ^{18}F-FDG PET/CT and 4 to 8 mSv for ^{99m}Tc-MDP bone scintigraphy with SPECT/CT, and in both cases the CT protocol contributes a large share of the total. Gamma cameras with SPECT/CT capability are more widely available than PET/CT scanners, particularly outside tertiary centers, and the per-study cost of bone scintigraphy is a fraction of that of PET/CT [59].

Direct comparative data in the spine come mainly from meta-analyses of diagnostic accuracy. Yang et al. compared ^{18}F-FDG PET, CT, MRI, and bone scintigraphy for bone metastases and found that PET and MRI achieved the highest patient-level sensitivity and specificity, while planar bone scintigraphy performed least well [9]. Liu et al. restricted their analysis to vertebral metastases and reported that adding SPECT to bone scintigraphy raised diagnostic accuracy and specificity to a level approaching that of PET, with similar sensitivity [10]. Harlianto et al. reached broadly similar conclusions for spinal metastases specifically [47]. These analyses share important limitations, since few of the contributing studies imaged the same patients with both modalities, the reference standards differed, and the SPECT arms often did not include CT.

The two modalities answer different questions, and their preferred indications follow from that difference. PET/CT is preferred when the primary tumor is FDG-avid, when whole-body staging is required, when marrow-based metastases must be detected before cortical change

appears, when an occult primary is suspected, and when metabolic response to systemic or radiation therapy is being assessed. SPECT/CT is preferred when a bone scan has already been performed and one or more foci remain indeterminate, when a solitary lesion raises the question of benign or malignant origin, when sclerotic disease predominates, when a pain generator must be localized in a degenerative or postoperative spine, and when access or cost makes PET impractical. The two are complementary in the patient who has both degenerative change and known malignancy, where SPECT/CT characterizes the osseous reaction and PET/CT defines the extent of viable tumor. **Table 1** summarizes this comparison across CT, MRI, bone scintigraphy with SPECT/CT, and ^{18}F-FDG PET/CT.

Quantitative parameters and threshold standardization

Several of the studies discussed above report SUV_{max} as a discriminator between benign and malignant vertebral lesions, but no validated universal threshold exists. Reported cutoffs in the spine range from approximately 2.0 to 4.0, and the distributions of benign and malignant uptake overlap at every proposed value. Degenerative facet arthropathy, insufficiency fracture, and spondylodiscitis can all exceed an SUV_{max} of 4.0, while low-grade chordoma, well-differentiated chondrosarcoma, and treated sclerotic metastases can fall below 2.0. A threshold derived in one cohort therefore performs poorly when applied to a population with a different mix of pathology [79-81].

The measurement itself varies with factors unrelated to the lesion. Uptake time, injected activity, blood glucose, body habitus, reconstruction algorithm, and the use of point-spread-function or time-of-flight modeling all shift SUV_{max}, and small vertebral lesions are further affected by partial volume averaging and by respiratory motion in the thoracic spine. Harmonization programs such as the EANM procedure guidelines and the EARL accreditation framework were developed to control this variability, and multicenter studies of spinal disease should state whether they were followed [82, 83]. For response assessment, PERCIST provides a defined framework based on the change in lean-body-mass corrected peak SUV, and it is more reproducible across centers than any absolute cutoff [84].

Quantitative SPECT has followed a similar path more recently. CT-based attenuation correction, scatter correction, and calibration against a known source now permit SUV-like metrics from ^{99m}Tc-MDP SPECT/CT, and Gherghe et al. showed that these values correlate with visual interpretation and track treatment response in spinal bone metastases [75]. No threshold has been validated for separating benign from malignant vertebral uptake, and cross-vendor reproducibility has not been established. Until harmonized prospective data exist, quantitative values in the spine are best used as a within-patient measure of change on serial studies acquired on the same scanner with the same protocol, and absolute thresholds should be treated as center specific.

Diagnostic pitfalls and sources of error

The specificity of ^{18}F-FDG PET/CT in the spine is limited because glucose metabolism increases in any process with high cellular turnover. Degenerative disease is the most frequent source of error, and uptake is seen in facet arthropathy, active endplate change, Schmorl nodes, and synovial cysts. Infection produces intense uptake, so spondylodiscitis, epidural abscess, and infected instrumentation can all mimic tumors. Recent fracture, whether traumatic, osteoporotic, or pathologic, shows uptake during healing, and malignant collapse cannot be separated from benign collapse on uptake intensity alone. Postoperative changes that include granulation tissue, bone graft incorporation, and reaction around instrumentation persist for months. Radiation produces early inflammatory uptake within the treated volume followed by a later fall in marrow activity, which is the reason for the interval of 2 to 3 months recommended before post-treatment imaging. Diffuse marrow activation after granulocyte colony-stimulating factor or recent chemotherapy raises background uptake and can obscure focal disease. Brown adipose tissue in the paravertebral and supraclavicular regions is mistaken for nodal or osseous disease when the CT component is not examined [18, 85, 86].

False-negative findings arise in the opposite circumstances. Sclerotic metastases from prostate and breast carcinoma have low cellularity and low glycolytic activity, and they may show uptake at or below the level of normal marrow. Lesions smaller than approximately twice the reconstructed spatial resolution are subject to partial volume averaging and can be missed [78, 84]. Low-grade tumors that include chordoma, well-differentiated chondrosarcoma, and some low-grade gliomas are weakly FDG-avid. Hyperglycemia at the time of injection reduces tumor uptake, and imaging performed shortly after the start of systemic therapy may show metabolic suppression that does not reflect the true tumor burden.

Bone-seeking agents carry their own pitfalls because uptake reflects the osteoblastic response to a lesion and not the lesion itself. Degenerative facet and endplate disease, healing fractures, Paget disease, osteoid osteoma, and infection all produce focal vertebral uptake. Purely lytic lesions with little osteoblastic reaction, most notably multiple myeloma and some renal cell and thyroid metastases, can appear photopenic or normal. A transient increase in uptake during the first months of successful systemic therapy, known as the flare phenomenon, can be misread as progression. The CT component of SPECT/

CT resolves many of these situations by showing the morphology that underlies the hot focus, and the reductions in equivocal findings described earlier in this review derive largely from this mechanism.

Several measures reduce the effect of these pitfalls. The CT component should be reviewed in every case, since the morphologic pattern usually separates degenerative from neoplastic uptake. The clinical timeline should be established before interpretation, including the dates of surgery, radiation, systemic therapy, growth factor support, and any fracture. Post-treatment PET should be deferred for 2 to 3 months after radiation. Correlation with MRI is valuable when marrow signal and cord or nerve root involvement are in question. When imaging findings remain discordant with the clinical picture, biopsy remains the reference standard, and the decision to treat a solitary indeterminate vertebral lesion should not rest on uptake alone.

Limitations of the current evidence

The evidence base for hybrid imaging in spinal oncology has several consistent weaknesses that limit the strength of the conclusions drawn above. Most studies are retrospective and single center, and sample sizes are small, with several of the frequently cited spinal series including fewer than 50 patients. Reference standards are inconsistent, since some studies require histology while others accept imaging follow-up of variable duration, and the latter approach inflates apparent accuracy. Few investigations image the same patients with both PET/CT and SPECT/CT, so most comparisons between the two modalities are indirect. Reporting of technical parameters is incomplete, which prevents readers from judging whether quantitative values are comparable across studies. Case reports dominate the literature on primary spinal tumors and carry a well-recognized publication bias. Cost-effectiveness data are almost absent, and no study has examined whether the changes in management attributed to hybrid imaging translate into differences in survival or quality of life. These limitations should be considered whenever the pooled accuracy figures in this review are applied to an individual patient.

Proposed imaging strategy

Figure 7 outlines an imaging strategy that follows from the evidence reviewed above. For a suspected primary spinal tumor, contrast-enhanced MRI of the affected region remains the first study, since it defines the anatomic compartment, the relationship to cord and nerve roots, and the surgical approach. PET/CT is added when the lesion is intramedullary and the grade is uncertain, when staging of a known aggressive histology is required, when an occult primary is suspected, or when a biopsy target must be selected. For suspected metastatic disease, the pathway depends on the primary tumor. When the histology is FDG-avid, whole-body ^{18}F-FDG PET/CT provides staging and skeletal assessment in a single examination. When the primary is prostate carcinoma or a well-differentiated neuroendocrine tumor, a target-specific tracer is preferred. When bone scintigraphy has already been performed and a vertebral focus is indeterminate, regional SPECT/CT resolves most cases without further imaging. For post-treatment follow-up, MRI assesses structural change and cord compression, while PET/CT assesses metabolic response after an interval of at least 2 to 3 months from radiation. Biopsy is reserved for lesions that remain discordant after the appropriate combination of these studies.

Conclusion and future directions

The evaluation of spinal tumors remains difficult because of their diverse origins and complex anatomical presentations. However, advanced molecular imaging modalities have enhanced our knowledge of the metabolic and structural characteristics underlying both primary and metastatic spinal disease, contributing essential approaches for accurate diagnosis, staging, and treatment assessment. PET and SPECT imaging contribute substantially to differentiating malignant from benign lesions and to assessing therapeutic response across diverse tumor types. Integrating multimodal imaging approaches that include PET, SPECT, CT, and MRI offers a comprehensive evaluation of spinal anatomy, function, and tumor metabolism. Continued efforts should focus on longitudinal assessment, tracer standardization, and defining quantitative biomarkers for disease monitoring. The ongoing developments in hybrid imaging technologies and the emergence of novel radiotracers will further enhance early detection, individualized therapy planning, and outcome prediction. As research advances, molecular imaging will remain central to improving diagnosis, management, and prognosis for patients with spinal neoplasms.

Several specific steps would give effect to these priorities. Prospective cohorts that image the same patients with both PET/CT and SPECT/CT would allow the direct comparison that the current literature does not support. Registries of primary spinal tumors with linked imaging and histopathology would provide the sample sizes that single-center series cannot reach. Multicenter studies that follow the EANM and EARL harmonization frameworks would make quantitative values comparable and would allow thresholds for benign and malignant vertebral uptake to be derived in one cohort and validated in another. Trials of target-specific tracers designed around spinal endpoints, including the detection of marrow-based metastasis and the delineation of radiotherapy tar-

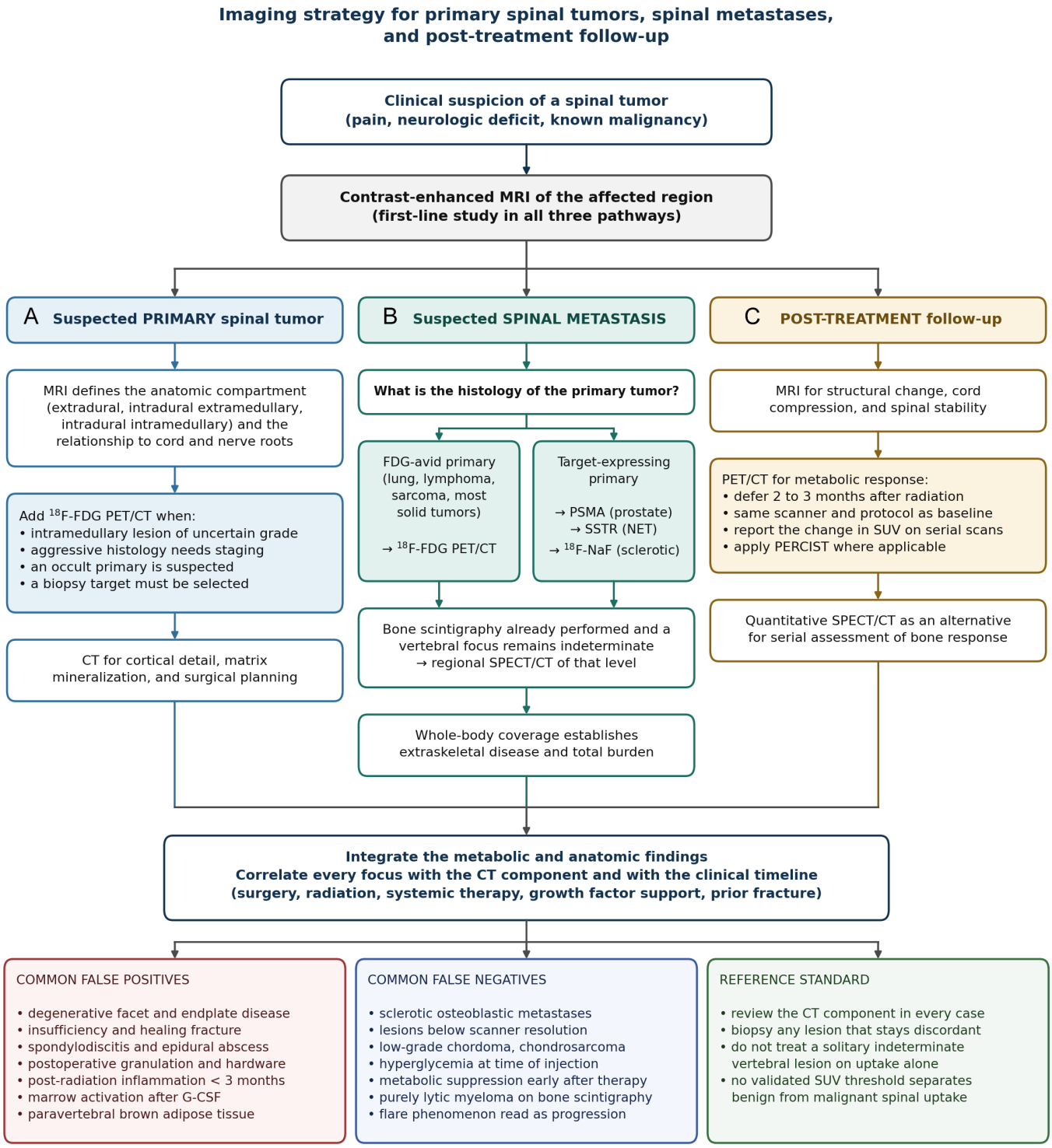


Figure 7. Proposed imaging strategy for a suspected primary spinal tumor (pathway A), suspected spinal metastases (pathway B), and post-treatment follow-up (pathway C). Contrast-enhanced MRI is the first study in every pathway, and tracer selection in (pathway B) follows the histology of the primary tumor. The lower panels list the interpretive pitfalls that most often affect the spine and the situations in which biopsy remains the reference standard. Figure created via Python 3.12.3 and matplotlib 3.10.8.

get volumes, would establish whether the advantages seen in whole-body studies apply to the spine. Studies that measure downstream outcomes such as change in management, complication rates, and quality of life would clarify the clinical value of these techniques beyond diagnostic accuracy.

Disclosure of conflict of interest

None.

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References

[1] Schellinger KA, Propp JM, Villano JL and McCarthy BJ. Descriptive epidemiology of primary spinal cord tumors. J Neurooncol 2008; 87: 173-179.

[2] Ciftdemir M, Kaya M, Selcuk E and Yalniz E. Tumors of the spine. World J Orthop 2016; 7: 109-116.

[3] Goodwin ML, Buchowski JM, Schwab JH and Sciubba DM. Spinal tumors: diagnosis and treatment. J Am Acad Orthop Surg 2022; 30: e1106-e1121.

[4] Van Goethem JW, van den Hauwe L, Ozsarlak O, De Schepper AM and Parizel PM. Spinal tumors. Eur J Radiol 2004; 50: 159-176.

[5] Kumar N, Tan WLB, Wei W and Vellayappan BA. An overview of the tumors affecting the spine-inside to out. Neurooncol Pract 2020; 7 Suppl 1: i10-i17.

[6] Amadasu E, Panther E and Lucke-Wold B. Characterization and treatment of spinal tumors. Intensive Care Res 2022; 2: 76-95.

[7] Samartzis D, Gillis CC, Shih P, O'Toole JE and Fessler RG. Intramedullary spinal cord tumors: part I-epidemiology, pathophysiology, and diagnosis. Global Spine J 2015; 5: 425-435.

[8] Shah LM and Salzman KL. Imaging of Spinal Metastatic Disease. Int J Surg Oncol 2011; 2011: 769753.

[9] Yang HL, Liu T, Wang XM, Xu Y and Deng SM. Diagnosis of bone metastases: a meta-analysis comparing 18FDG PET, CT, MRI and bone scintigraphy. Eur Radiol 2011; 21: 2604-2617.

[10] Liu T, Wang S, Liu H, Meng B, Zhou F, He F, Shi X and Yang H. Detection of vertebral metastases: a meta-analysis comparing MRI, CT, PET, BS and BS with SPECT. J Cancer Res Clin Oncol 2017; 143: 457-465.

[11] Lee KR. Interpretation of MR imaging of spinal metastasis: focus on the understanding of its pathophysiology and the next step toward a further clinical approach using MRI findings. Investig Magn Reson Imaging 2016; 20: 1-8.

[12] Elliott JM, Flynn TW, Al-Najjar A, Press J, Nguyen B and Noteboom JT. The pearls and pitfalls of magnetic resonance imaging for the spine. J Orthop Sports Phys Ther 2011; 41: 848-860.

[13] Tender GC, Davidson C, Shields J, Robichaux J, Park J, Crutcher CL and DiGiorgio AM. Primary pain generator identification by CT-SPECT in patients with degenerative spinal disease. Neurosurg Focus 2019; 47: E18.

[14] Adrian M. MRI: understanding its limitations. Br Columb Med J 2005; 47: 359-361.

[15] Caraceni A and Shkodra M. Cancer pain assessment and classification. Cancers (Basel) 2019; 11: 510.

[16] Koppula BR, Morton KA, Al-Dulaimi R, Fine GC, Damme NM and Brown RKJ. SPECT/CT in the evaluation of suspected skeletal pathology. Tomography 2021; 7: 581-605.

[17] Cook GJ and Fogelman I. The role of positron emission tomography in the management of bone metastases. Cancer 2000; 88 Suppl: 2927-2933.

[18] Patel PY, Dalal I and Griffith B. [^{18}F]FDG-PET Evaluation of spinal pathology in patients in oncology: pearls and pitfalls for the neuroradiologist. AJNR Am J Neuroradiol 2022; 43: 332-340.

[19] Nair C, Panikkar S and Ray A. How not to miss metastatic spinal cord compression. Br J Gen Pract 2014; 64: e596-e598.

[20] Ametamey SM, Honer M and Schubiger PA. Molecular imaging with PET. Chem Rev 2008; 108: 1501-1516.

[21] Townsend DW, Carney JP, Yap JT and Hall NC. PET/CT today and tomorrow. J Nucl Med 2004; 45 Suppl 1: 4S-14S.

[22] Lee JR, Kim JS, Roh JL, Lee JH, Baek JH, Cho KJ, Choi SH, Nam SY and Kim SY. Detection of occult primary tumors in patients with cervical metastases of unknown primary tumors: comparison of 18F FDG PET/CT with contrast-enhanced CT or CT/MR imaging-prospective study. Radiology 2015; 274: 764-771.

[23] Even-Sapir E, Metser U, Mishani E, Lievshitz G, Lerman H and Leibovitch I. The detection of bone metastases in patients with high-risk prostate cancer: 99mTc-MDP Planar bone scintigraphy, single- and multi-field-of-view SPECT, 18F-fluoride PET, and 18F-fluoride PET/CT. J Nucl Med 2006; 47: 287-297.

[24] Löfgren J, Mortensen J, Rasmussen SH, Madsen C, Loft A, Hansen AE, Oturai P, Jensen KE, Mørk ML, Reichkendler M, Højgaard L and Fischer BM. A prospective study comparing (99m)Tc-hydroxyethylene-diphosphonate planar bone scintigraphy and whole-body SPECT/CT with (18)F-fluoride PET/CT and (18)F-fluoride PET/MRI for diagnosing bone metastases. J Nucl Med 2017; 58: 1778-1785.

[25] Patil S, Lee W, Patel R, Gerlach A, Patel D, Kata R, Fanta O, Khan T, Jeevika F, Ayubcha C, Gujral J, Gandhi OH, Werner T, Wulff Christensen H, Høilund-Carlsen PF and Alavi A. Evaluation of physiological bone metabolic activity in the spine with 18F-fluorodeoxyglucose and 18F-sodium fluoride PET: associations with degenerative risk factors. Nucl Med Commun 2026; 47: 724-731.

[26] Gujral J, Gandhi OH, Amanullah AA, Dagli MM, Singh SB, Ayubcha C, Werner TJ, Revheim ME, Welch WC and Alavi A. The emerging role of ^{18}F-NaF PET/CT in osteoporosis: an emphasis on its application for the evaluation and management of lumbar spine osteoporosis. EJNMMI Res 2026; 16: 93.

[27] Pienta KJ, Gorin MA, Rowe SP, Carroll PR, Pouliot F, Probst S, Saperstein L, Preston MA, Alva AS, Patnaik A, Durack JC, Stambler N, Lin T, Jensen J, Wong V, Siegel BA and Morris MJ. A phase 2/3 prospective multicenter study of the diagnostic accuracy of prostate specific membrane antigen PET/CT with (18)F-DCFPyL in prostate cancer patients (OSPREY). J Urol 2021; 206: 52-61.

[28] Hofman MS, Lawrentschuk N, Francis RJ, Tang C, Vela I, Thomas P, Rutherford N, Martin JM, Frydenberg M, Shakher R, Wong LM, Taubman K, Ting Lee S, Hsiao E, Roach P, Nottage M, Kirkwood I, Hayne D, Link E, Marusic P, Matera A, Herschtal A, Iravani A, Hicks RJ, Williams S and Murphy DG; proPSMA Study Group Collaborators. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet 2020; 395: 1208-1216.

[29] Grünig H, Maurer A, Thali Y, Kovacs Z, Strobel K, Burger IA and Müller J. Focal unspecific bone uptake on [(18)F]-PSMA-1007 PET: a multicenter retrospective evaluation of the distribution, frequency, and quantitative parameters of a potential pitfall in prostate cancer imaging. Eur J Nucl Med Mol Imaging 2021; 48: 4483-4494.

[30] Gujral J, Gandhi OH, Amanullah AA, Singh SB, Ayubcha C, Patil S, Werner TJ, Revheim ME, Brem S and Alavi A. Soma-

tostatin receptor PET in meningioma: diagnosis, therapy, and surveillance. Nucl Med Commun 2026; 47: 491-502.
[31] Gujral J, Gandhi OH, Amanullah AA, Singh SB, Ayubcha C, Werner TJ, Revheim ME and Alavi A. Somatostatin receptor PET-guided treatment and artificial intelligence applications in meningioma: a comprehensive review. Am J Nucl Med Mol Imaging 2025; 15: 223-235.
[32] Bozkurt MF, Virgolini I, Balogova S, Beheshti M, Rubello D, Decristoforo C, Ambrosini V, Kjaer A, Delgado-Bolton R, Kunikowska J, Oyen WJG, Chiti A, Giammarile F, Sundin A and Fanti S. Guideline for PET/CT imaging of neuroendocrine neoplasms with (68)Ga-DOTA-conjugated somatostatin receptor targeting peptides and (18)F-DOPA. Eur J Nucl Med Mol Imaging 2017; 44: 1588-1601.
[33] Sadowski SM, Neychev V, Millo C, Shih J, Nilubol N, Herscovitch P, Pacak K, Marx SJ and Kebebew E. Prospective study of 68Ga-DOTATATE positron emission tomography/computed tomography for detecting gastro-entero-pancreatic neuroendocrine tumors and unknown primary sites. J Clin Oncol 2016; 34: 588-596.
[34] Albert NL, Preusser M, Traub-Weidinger T, Tolboom N, Law I, Palmer JD, Guedj E, Furtner J, Fraioli F, Huang RY, Johnson DR, Deroose CM, Herrmann K, Vogelbaum M, Chang S, Tonn JC, Weller M, Wen PY, van den Bent MJ, Verger A, Ivanidze J and Galldiks N. Joint EANM/EANO/RANO/SNMMI practice guideline/procedure standards for diagnostics and therapy (theranostics) of meningiomas using radiolabeled somatostatin receptor ligands: version 1.0. Eur J Nucl Med Mol Imaging 2024; 51: 3662-3679.
[35] Kratochwil C, Flechsig P, Lindner T, Abderrahim L, Altmann A, Mier W, Adeberg S, Rathke H, Röhrich M, Winter H, Plinkert PK, Marme F, Lang M, Kauczor HU, Jäger D, Debus J, Haberkorn U and Giesel FL. (68)Ga-FAPI PET/CT: tracer uptake in 28 different kinds of cancer. J Nucl Med 2019; 60: 801-805.
[36] Singh SB, Shrestha BB, Gandhi OH, Shah RP, Mukhtiar V, Ayubcha C, Desai V, Eberts CE, Paudyal P, Jha G, Singh A, Shi Y and Kumar T. The comparative utility of FAPI-based PET radiotracers over [(18)F]FDG in the assessment of malignancies. Am J Nucl Med Mol Imaging 2024; 14: 190-207.
[37] Chen H, Pang Y, Wu J, Zhao L, Hao B, Wu J, Wei J, Wu S, Zhao L, Luo Z, Lin X, Xie C, Sun L, Lin Q and Wu H. Comparison of [68Ga]Ga-DOTA-FAPI-04 and [18F] FDG PET/CT for the diagnosis of primary and metastatic lesions in patients with various types of cancer. Eur J Nucl Med Mol Imaging 2020; 47: 1820-1832.
[38] Kessler L, Ferdinandus J, Hirmas N, Bauer S, Dirksen U, Zarrad F, Nader M, Chodyla M, Milosevic A, Umutlu L, Schuler M, Podleska LE, Schildhaus HU, Fendler WP and Hamacher R. (68)Ga-FAPI as a diagnostic tool in sarcoma: data from the (68)Ga-FAPI PET prospective observational trial. J Nucl Med 2022; 63: 89-95.
[39] Feng Z, Yu R and Hu X. (18)F-FDG PET/CT revealed primary malignant giant cell tumor of the sacrum: a case report. Front Med (Lausanne) 2025; 12: 1653522.
[40] Shen G, Ma H, Pan L, Su M and Kuang A. FDG PET/CT and MRI in primary spinal cord glioblastoma. Clin Nucl Med 2020; 45: e144-e145.
[41] Naito K, Yamagata T, Arima H, Abe J, Tsuyuguchi N, Ohata K and Takami T. Qualitative analysis of spinal intramedullary lesions using PET/CT. J Neurosurg Spine 2015; 23: 613-619.
[42] Townsend DW and Cherry SR. Combining anatomy and function: the path to true image fusion. Eur Radiol 2001; 11: 1968-1974.
[43] Gutzeit A, Antoch G, Kühl H, Egelhof T, Fischer M, Hauth E, Goehde S, Bockisch A, Debatin J and Freudenberg L. Unknown primary tumors: detection with dual-modality PET/CT--initial experience. Radiology 2005; 234: 227-234.
[44] Kwee TC and Kwee RM. Combined FDG-PET/CT for the detection of unknown primary tumors: systematic review and meta-analysis. Eur Radiol 2009; 19: 731-744.
[45] Metser U, Lerman H, Blank A, Lievshitz G, Bokstein F and Even-Sapir E. Malignant involvement of the spine: assessment by 18F-FDG PET/CT. J Nucl Med 2004; 45: 279-284.
[46] Soliman M, Taunk NK, Simons RE, Osborne JR, Kim MM, Szerlip NJ and Spratt DE. Anatomic and functional imaging in the diagnosis of spine metastases and response assessment after spine radiosurgery. Neurosurg Focus 2017; 42: E5.
[47] Harlianto NI, van der Star S, Suelmann BBM, de Jong PA, Verlaan JJ and Foppen W. Diagnostic accuracy of imaging modalities for detection of spinal metastases: a systematic review and meta-analysis. Clin Transl Oncol 2025; 27: 2316-2326.
[48] Wafaie A, El-Liethy N, Kassem H and Kotb MH. A comparison between FDG PET/CT, CT and MRI in detection of spinal metastases and its impact on clinical management. Egyptian J Nucl Med 2013; 8: 30-44.
[49] Batouli A, Gholamrezanezhad A, Petrov D, Rudkin S, Matcuk G and Jadvar H. Management of primary osseous spinal tumors with PET. PET Clin 2019; 14: 91-101.
[50] Patil S, Patel R, Herpin L, Patel D, Gujral J, Gandhi OH, Gerlach A, Ghonim M, Ghonim M, Mhana SAA, Teichner E, Subtirelu R, Werner T, Høilund-Carlsen PF and Alavi A. (18)F-NaF and (18)F-FDG PET/CT imaging of spinal instrumentation: case report and review of the literature. Am J Nucl Med Mol Imaging 2026; 16: 125-130.
[51] Choi J, Kim JW, Jeon TJ and Lee IJ. The 18F-FDG PET/CT response to radiotherapy for patients with spinal metastasis correlated with the clinical outcomes. PLoS One 2018; 13: e0204918.
[52] Gandhi OH, Lee AE, Gujral J, Ismoilov M, Singh SB, Ghonim M, Ghonim M, Kim MY, Raynor WY, Case MJ, Siddiqi A, Yazdanpanah F, Werner TJ, Saboury B, Revheim ME, Chang YC and Alavi A. Maxillary sinus inflammation assessment using FDG-PET/CT in head and neck cancer patients with photon, proton, and combined radiation therapy. Am J Nucl Med Mol Imaging 2025; 15: 97-104.
[53] Gandhi OH, Gujral J, Amanullah A, Ismoilov M, Singh SB, Patil S, Ahmed M, Niazi SK, Motamedi N, Shrestha BB, Werner TJ, Revheim ME and Alavi A. Role of FDG-PET/CT in detecting metabolic changes in parotid glands following photon versus proton therapy. Am J Nucl Med Mol Imaging 2026; 16: 114-124.
[54] Youland RS, Packard AT, Blanchard MJ, Arnett AL, Wiseman GA, Kottschade LA, Dronca RS, Markovic SN, Olivier KR and Park SS. 18F-FDG PET response and clinical outcomes after stereotactic body radiation therapy for metastatic melanoma. Adv Radiat Oncol 2017; 2: 204-210.
[55] Reinert CP, Sekler J, La Fougère C, Pfannenberg C and Gatidis S. Impact of PET/CT on clinical management in patients with cancer of unknown primary-a PET/CT registry study. Eur Radiol 2020; 30: 1325-1333.

[56] Oh HS, Jeon BC, Park YS, Chun TS and Kim NK. The role of 18F-FDG PET/CT scan in suspected metastatic spine tumor. Korean J Spine 2005; 2: 193-198.
[57] Kuah T, Vellayappan BA, Makmur A, Nair S, Song J, Tan JH, Kumar N, Quek ST and Hallinan JTPD. State-of-the-art imaging techniques in metastatic spinal cord compression. Cancers (Basel) 2022; 14: 3289.
[58] Bailey DL and Willowson KP. An evidence-based review of quantitative SPECT imaging and potential clinical applications. J Nucl Med 2013; 54: 83-89.
[59] Buck AK, Nekolla S, Ziegler S, Beer A, Krause BJ, Herrmann K, Scheidhauer K, Wester HJ, Rummeny EJ, Schwaiger M and Drzezga A. SPECT/CT. J Nucl Med 2008; 49: 1305-1319.
[60] Kuwert T. Skeletal SPECT/CT: a review. Clin Transl Imaging 2014; 2: 505-517.
[61] Townsend DW. Multimodality imaging of structure and function. Phys Med Biol 2008; 53: R1-R39.
[62] Even-Sapir E. Imaging of malignant bone involvement by morphologic, scintigraphic, and hybrid modalities. J Nucl Med 2005; 46: 1356-1367.
[63] Hirsch BP, Sossamon J, Khan MA, Reitman C, Lawrence JP, Glaser J, Chun R, Gerald B, Baron E, Goldstein T, Baaj AA, Johnson JP, Elojeimy S and Ravinsky RA. Applications of SPECT/CT in the evaluation of spinal pathology: a review. Int J Spine Surg 2024; 18: 9-23.
[64] Jiang L, Han L, Tan H, Hu P, Zhang Y and Shi H. Diagnostic value of 99mTc-MDP SPECT/spiral CT in assessing indeterminate spinal solitary lesion of patients without malignant history. Ann Nucl Med 2013; 27: 460-467.
[65] Sharma P, Singh H, Kumar R, Bal C, Thulkar S, Seenu V and Malhotra A. Bone scintigraphy in breast cancer: added value of hybrid SPECT-CT and its impact on patient management. Nuclear Medicine Communications 2012; 33: 139-147.
[66] Iqbal B, Currie GM, Wheat JM, Raza H and Kiat H. The incremental value of SPECT/CT in characterizing solitary spine lesions. J Nucl Med Technol 2011; 39: 201-7.
[67] Ma W, Quan Z, Wang J, Li X and Li G. The one-in-all diagnostic value of 99mTc-MDP bone scan combining with single-photon emission tomography (SPECT)/CT imaging in spinal osteoblastoma. J Orthop Surg Res 2020; 15: 181.
[68] Cook GJ and Goh V. Functional and hybrid imaging of bone metastases. J Bone Miner Res 2018; 33: 961-972.
[69] Sedonja I and Budihna NV. The benefit of SPECT when added to planar scintigraphy in patients with bone metastases in the spine. Clin Nucl Med 1999; 24: 407-413.
[70] Israel O, Pellet O, Biassoni L, De Palma D, Estrada-Lobato E, Gnanasegaran G, Kuwert T, la Fougère C, Mariani G, Massalha S, Paez D and Giammarile F. Two decades of SPECT/CT - the coming of age of a technology: an updated review of literature evidence. Eur J Nucl Med Mol Imaging 2019; 46: 1990-2012.
[71] Bahouth SM, Yeboa DN, Ghia AJ, Tatsui CE, Alvarez-Breckenridge CA, Beckham TH, Bishio AJ, Li J, McAleer MF, North RY, Rhines LD, Swanson TA, Chenyang W and Amini B . Multidisciplinary management of spinal metastases: what the radiologist needs to know. Br J Radiol 2022; 95: 20220266.
[72] Jain A, Jain S, Agarwal A, Gambhir S, Shamshery C and Agarwal A. Evaluation of efficacy of bone scan with SPECT/CT in the management of low back pain: a study supported by differential diagnostic local anesthetic blocks. Clin J Pain 2015; 31: 1054-1059.
[73] Ouvrard E, Kaseb A, Poterszman N, Porot C, Somme F and Imperiale A. Nuclear medicine imaging for bone metastases assessment: what else besides bone scintigraphy in the era of personalized medicine? Front Med (Lausanne) 2024; 10: 1320574.
[74] Mariani G, Bruselli L, Kuwert T, Kim EE, Flotats A, Israel O, Dondi M and Watanabe N. A review on the clinical uses of SPECT/CT. Eur J Nucl Med Mol Imaging 2010; 37: 1959-1985.
[75] Gherghe M, Mutuleanu MD, Stanciu AE, Irimescu I, Lazar AM, Toma RV, Trifanescu OG and Anghel RM. Quantitative assessment of treatment response in metastatic breast cancer patients by SPECT-CT bone imaging-getting closer to PET-CT. Cancers (Basel) 2023; 15: 696.
[76] Meng B, Song J, Liu L, Chen L and Chen X. Added value of hybrid SPECT with CT imaging for predicting poor therapeutic efficacy of 89Sr in patients with bone metastasis. Sci Rep 2020; 10: 21207.
[77] Lee I, Budiawan H, Moon JY, Cheon GJ, Kim YC, Paeng JC, Kang KW, Chung JK and Lee DS. The value of SPECT/CT in localizing pain site and prediction of treatment response in patients with chronic low back pain. J Korean Med Sci 2014; 29: 1711-6.
[78] Ritt P, Vija H, Hornegger J and Kuwert T. Absolute quantification in SPECT. Eur J Nucl Med Mol Imaging 2011; 38 Suppl 1: S69-77.
[79] Lee N and Joo MW. Current position of nuclear medicine imaging in primary bone tumors. Diagnostics (Basel) 2025; 15: 2786.
[80] Even-Sapir E, Martin RH, Barnes DC, Pringle CR, Iles SE and Mitchell MJ. Role of SPECT in differentiating malignant from benign lesions in the lower thoracic and lumbar vertebrae. Radiology 1993; 187: 193-198.
[81] Takigawa T, Tanaka M, Sugimoto Y, Tetsunaga T, Nishida K and Ozaki T. Discrimination between malignant and benign vertebral fractures using magnetic resonance imaging. Asian Spine J 2017; 11: 478-483.
[82] Kaalep A, Sera T, Oyen W, Krause BJ, Chiti A, Liu Y and Boellaard R. EANM/EARL FDG-PET/CT accreditation - summary results from the first 200 accredited imaging systems. Eur J Nucl Med Mol Imaging 2018; 45: 412-422.
[83] Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, Verzijlbergen FJ, Barrington SF, Pike LC, Weber WA, Stroobants S, Delbeke D, Donohoe KJ, Holbrook S, Graham MM, Testanera G, Hoekstra OS, Zijlstra J, Visser E, Hoekstra CJ, Pruim J, Willemsen A, Arends B, Kotzerke J, Bockisch A, Beyer T, Chiti A and Krause BJ; European Association of Nuclear Medicine (EANM). FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging 2015; 42: 328-354.
[84] Wahl RL, Jacene H, Kasamon Y and Lodge MA. From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. J Nucl Med 2009; 50 Suppl 1: 122S-150S.
[85] Long NM and Smith CS. Causes and imaging features of false positives and false negatives on ^{18}F-PET/CT in oncologic imaging. Insights Imaging 2011; 2: 679-698.
[86] Rosenbaum SJ, Lind T, Antoch G and Bockisch A. False-positive FDG PET uptake--the role of PET/CT. Eur Radiol 2006; 16: 1054-1065.

[87] Nevzati E, Poletti N, Spiessberger A, Bäbler S, Studer G, Riklin C, Diebold J, Chatain GP, Finn M, Witt JP, Moser M and Mariani L. Establishing the Swiss Spinal Tumor Registry (Swiss-STR): a prospective observation of surgical treatment patterns and long-term outcomes in patients with primary and metastatic spinal tumors. Front Surg 2023; 10: 1222595.

[88] Aiello M, Alfano V, Salvatore E, Cavaliere C, Picardi M, Della Pepa R, Nicolai E, Soricelli A, Vella A, Salvatore M and Mascalchi M. [(18)F]FDG uptake of the normal spinal cord in PET/MR imaging: comparison with PET/CT imaging. EJNMMI Res 2020; 10: 91.