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Case Report

^{18}F-NaF and ^{18}F-FDG PET/CT imaging of spinal instrumentation: case report and review of the literature

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Abstract: This report describes the ^{18}F-sodium fluoride (^{18}F-NaF) and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT imaging of spinal instrumentation incidentally found in a 71-year-old male with extensive degenerative spinal disease. Hardware was noted at L5-S1, a common site of lumbar degeneration and cause of radiculopathy. ^{18}F-NaF showed intense focal uptake at the instrumentation site, while ^{18}F-FDG demonstrated minimal uptake. These findings suggest remodeling of bone (^{18}F-NaF) at the site of instrumentation in the setting of benign physiological metabolic activity (^{18}F-FDG). Other signs of structural deterioration were observed in the cervical and thoracic regions, such as osteophytes and ossification of the posterior longitudinal ligament. We present these findings in the context of a literature review of published studies that utilized ^{18}F-NaF or ^{18}F-FDG PET imaging for the assessment and monitoring of patients with spinal instrumentation.

Keywords: Bone metabolism, degeneration, fluorodeoxyglucose, PET/CT, sodium fluoride, spine surgery

Introduction

Spinal instrumentation plays a central role in the surgical management of degenerative disc disease, spondylolisthesis, traumatic fractures, and other causes of spinal instability. Despite advances in surgical technique, complications after spinal fusion, including pseudarthrosis (failure to achieve bony union), loosening of hardware, and surgical site infection, continue to pose diagnostic and therapeutic challenges. When these problems go unrecognized, patients may experience ongoing back pain, radiculopathy, or progressive neurological deficits that ultimately require revision surgery [1-3].

Conventional imaging modalities such as plain radiographs, computed tomography (CT), and magnetic resonance imaging (MRI) are the standard workup for patients with suspected post-operative complications [4, 5]. Yet, each of these modalities has well-recognized limitations in sensitivity. These techniques rely on detecting gross anatomic changes and are unable to identify early metabolic bone alterations that may precede structural abnormalities. Additionally, postoperative edema, scar tissue, and metallic hardware artifacts can obscure or mimic pathology in CT/MRI results [6-8]. For example, radiographic criteria (such as presence of bridging bone or haloing around hardware) can be ambiguous or inconclusive [9]. Although considered the gold standard for assessing arthrodesis, CT may in some cases be misleading. In one series of cervical fusion patients, 41% of levels that appeared fused on CT were actually pseudarthrosis at surgery [10]. Taken together, these issues mean that standard imaging alone cannot always distinguish expected post-operative changes from true pathology such as infection or failed fusion.

Positron emission tomography/computed tomography (PET/CT) has emerged as a complementary tool that may address several of these shortcomings. Unlike conventional modalities, PET/CT provides functional imaging of the spine by using radiotracers such as fluorine-18 fluorodeoxyglucose (^{18}F-FDG) and fluorine-18 sodium fluoride (^{18}F-NaF) to assess glycolytic activity and osseous metabolism, respectively [11-14]. This case report explores the ^{18}F-NaF and ^{18}F-FDG PET/CT images of a patient who was incidentally found to have extensive degenerative spinal disease and lumbar instrumentation.

Case presentation

A 71-year-old man with hypertension, hypercholesterolemia, a BMI of 32.9 kg/m^2, past smoking history, and alcohol use was enrolled in the Cardiovascular Molecular Calcification Assessed by ^{18}F-NaF PET/CT (CAMONA) clinical trial [15]. The patient underwent ^{18}F-NaF and ^{18}F-FDG PET/CT imaging at least two weeks apart. The CAMONA trial was designed to evaluate cardiovascular molecular calcification; accordingly, ^{18}F-FDG PET/CT was acquired at a delayed time point of 180 min post-injection (4.0 MBq/kg) to optimize signal-to-noise for vascular imaging, while

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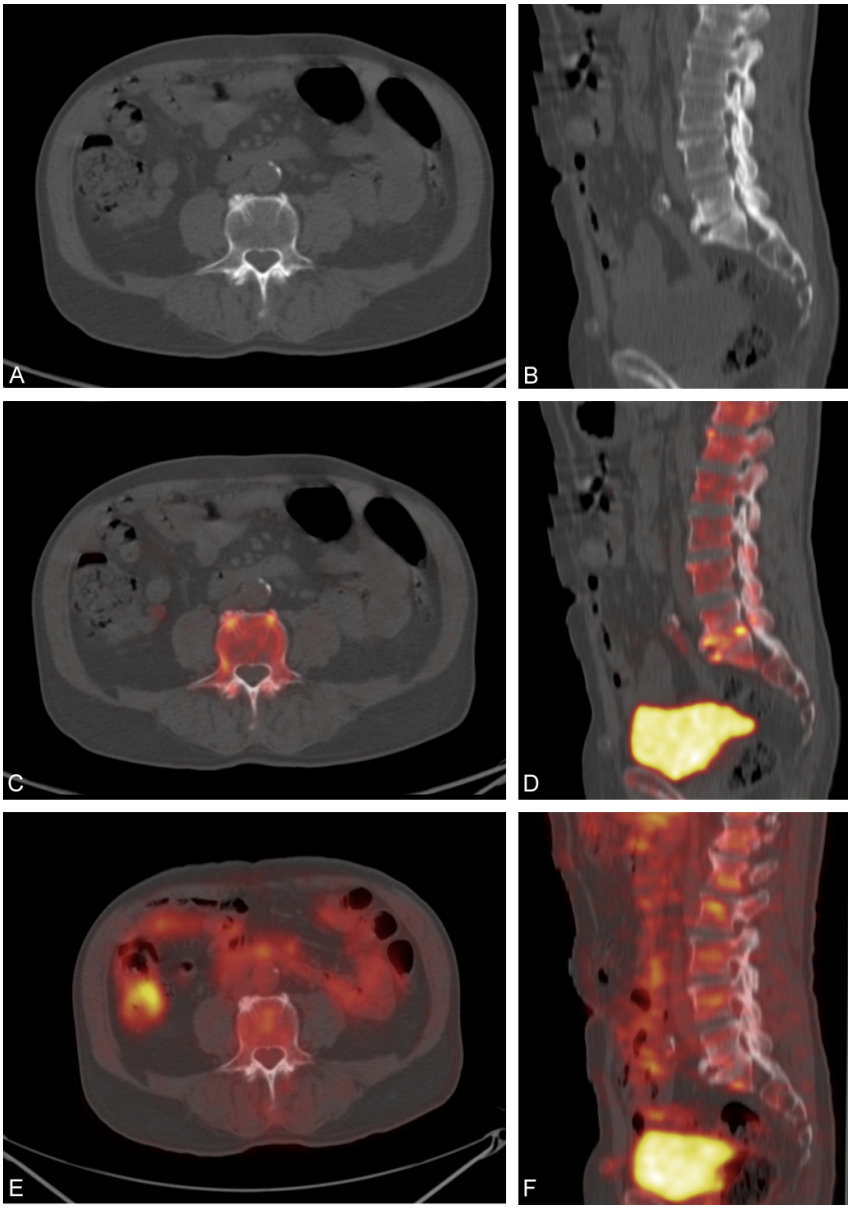

Figure 1. (A) Axial and (B) sagittal CT of the lumbar spine. (C) Axial and (D) sagittal ^{18}F-NaF PET/CT. (E) Axial and (F) sagittal ^{18}F-FDG PET/CT images. Surgical hardware is visible at L5-S1, with significant focal uptake of ^{18}F-NaF but not ^{18}F-FDG. White arrows indicate pedicle screws. Arrowheads in (C) and (D) denote areas of intense ^{18}F-NaF uptake surrounding the instrumentation.

^{18}F-NaF PET/CT was acquired at 90 min post-injection (2.2 MBq/kg) [14]. The spinal findings described herein were incidental to the primary cardiovascular objectives of the study.

Spinal instrumentation was incidentally found at L5-S1: the mean radiodensity of the screws on CT were 220 Hounsfield Units (HU) (**Figure 1**). The mean and max standardized uptake values (SUV_{mean}, SUV_{max}) of ^{18}F-NaF and ^{18}F-FDG at the site of instrumentation were determined by manually delineating a region of interest (ROI) around the vertebral bodies containing instrumentation. The vertebral arch and facet joints were excluded from the ROI. A single reader (S.P.) drew freehand volumetric ROIs on consecutive axial slices without applying an SUV threshold for boundary delineation. All quantitative imaging analysis was performed using OsiriX MD software (Pixmeo, Bernex, Switzerland).

^{18}F-NaF uptake at the instrumentation site was high (SUV_{mean} 6.67; SUV_{max} 18.33), with the highest activity appreciated around the screws. In contrast, ^{18}F-FDG uptake was only modest (SUV_{mean} 1.1; SUV_{max} 2.0). ^{18}F-FDG uptake at the site of instrumentation did not appear significantly different from the background metabolic activity of the vertebrae.

Extensive structural degeneration was also observed in the cervical and thoracic spine (**Figure 2**). An osteophyte at C5 demonstrated intense focal ^{18}F-NaF uptake (SUV_{mean} 15.4; SUV_{max} 40.3) with modest ^{18}F-FDG activity (SUV_{mean} 1.44, SUV_{max} 2.3). Ossification of the posterior longitudinal ligament was also found at the level of C4-C6 vertebrae, but uptake of ^{18}F-NaF or ^{18}F-FDG were not considered significant in this region of interest. Osteophytes at T9-T11 demonstrated similar patterns of high ^{18}F-NaF uptake (SUV_{mean} 4.9, SUV_{max} 32.8) with limited ^{18}F-FDG activity (SUV_{mean} 1.15, SUV_{max} 2.6).

Discussion and literature review

The present case illustrates ^{18}F-NaF and ^{18}F-FDG PET/CT imaging of a patient with extensive spinal degeneration and lumbar instrumentation. At the site of the hardware implant, sharp ^{18}F-NaF uptake with only modest ^{18}F-FDG uptake was observed. These findings suggest remodeling of bone (^{18}F-NaF) at the site of instrumentation and benign physiological metabolic activity (^{18}F-FDG). Due to the limited information available on this patient's surgical history, the clinical implications of these findings are unclear. We were unable to determine the approximate age of the hardware or the patient's current symptom status, as this was an incidental finding within a cardiovascular imaging trial. However, the absence of lucency around the screws on CT and the low mean radiodensity (220 HU) of the hardware are consistent with a chronic, well-integrated implant rather than a recently placed construct. The patient did not report spinal complaints at the time of enrollment. It should also be noted that the CAMONA protocol employed a delayed ^{18}F-FDG

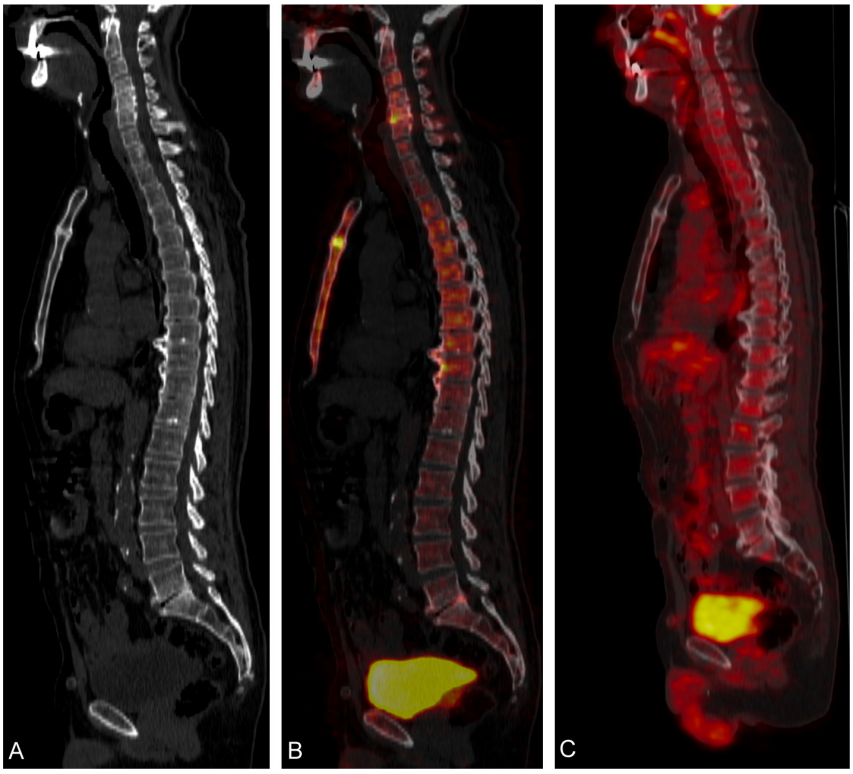

Figure 2. (A) Sagittal CT, (B) ^{18}F-NaF PET/CT, and (C) ^{18}F-FDG PET/CT of the entire spine. Degeneration of the cervical spine is observed with a metabolically active osteophyte at C5 and stable ossification of the posterior longitudinal ligament at C4-C6. In the thoracic spine, metabolically active osteophytes are visible at T9-T11. White arrows indicate the C5 osteophyte; dashed arrows mark the region of posterior longitudinal ligament ossification at C4-C6; arrowheads identify the T9-T11 osteophytes. L5-S1 instrumentation is visible at the base of (A).

acquisition time point (180 min post-injection) optimized for cardiovascular rather than musculoskeletal imaging, which may influence the absolute SUV values reported here; nonetheless, the same protocol has been successfully applied to evaluate non-cardiovascular musculoskeletal structures in prior CAMONA-based studies [14, 16-19]. The timing of PET/CT imaging after surgery is an important consideration, as radiotracer uptake could reflect either true instability (^{18}F-NaF) and inflammatory activity (^{18}F-FDG) in the acute post-surgical period or benign remodeling in the chronic setting [10].

To properly contextualize the present case, it is worth considering the expected trajectory of radiotracer uptake around stable spinal hardware. Normal post-operative bone healing involves an initial phase of robust osteoblastic activity that gradually diminishes as fusion matures. Studies employing bone scintigraphy and ^{18}F-NaF PET have shown that tracer uptake around instrumentation typically peaks in the first 6-12 months after surgery and then trends downward as the fusion consolidates [20, 21]. In patients with stable, well-integrated hardware imaged beyond one year, ^{18}F-NaF uptake is generally low or absent at the intragraft and extragraft regions [10]. Similarly, ^{18}F-FDG activity around hardware tends to normalize within months of surgery in the absence of infection or ongoing inflammation [22]. This expected decline provides a useful baseline against which the pathological states reviewed below - persistent uptake signaling pseudarthrosis or infection - can be compared. Importantly, a recent study of 120 subjects from the same CAMONA cohort established normal physiological vertebral uptake values, reporting a mean lumbar ^{18}F-NaF SUVmean of 5.5 ± 1.0 and lumbar 18F-FDG SUVmean of 1.4 ± 0.3 in non-pathologic vertebral bodies [14]. This provides a direct reference for interpreting the present patient's uptake values. In the present case, the high ^{18}F-NaF uptake coupled with minimal ^{18}F-FDG activity is more consistent with ongoing bone remodeling without a significant inflammatory component.

^{18}F-NaF is a bone-avid radiotracer that quantifies active ossification as dissociated ^{18}F ions incorporate into hydroxyapatite in regions of osteogenic or calcifying tissue [23]. Traditionally used to detect bone tumors, ^{18}F-NaF has emerged as a promising tool in the evaluation of non-oncologic osseous conditions such as osteoporosis and spinal degeneration [24]. Recent studies have investigated the application of ^{18}F-NaF PET/CT to evaluate bone metabolic changes occurring in the post-operative spine that precede structural alterations on CT [25]. In particular, this imaging modality has shown utility in detecting abnormal bone metabolic activity at sites of suspected pseudarthrosis in patients with recurrent back pain at least four months after fusion, accurately localizing the levels that required surgical revision [20]. Abnormal focal ^{18}F-NaF uptake was commonly observed around hardware in patients with persistent pain, and surgical exploration confirmed these sites as the underlying non-fused sites.

Building on these findings, El Yaagoubi et al. analyzed the ^{18}F-NaF PET/CT scans of 18 patients who underwent revision surgery for suspicion of pseudarthrosis and 5 control patients who were clearly fused on CT [21]. The time interval between initial surgery and ^{18}F-NaF PET/CT imaging was between 6 and 44 months (mean of 17 months). They reported significantly greater ^{18}F-NaF standardized uptake values and uptake ratios in the revision surgery group relative to controls, and that elevated ^{18}F-NaF uptake around intercorporal fusion material was associated with increased mobility. A separate study from El Yaagoubi et al. enrolled 30 patients undergoing anterior cervical discectomy and fusion (ACDF), consistent with a total of 40 surgical levels analyzed [10]. The time between initial ACDF and ^{18}F-NaF PET/CT ranged from 12

to 126 months (mean of 36 months). In cases of confirmed pseudoarthrosis on revision surgery, intragraft ^{18}F-NaF uptake was observed in all levels while 41% of these levels were rated as "fused" on pre-operative CT. One year after surgery, seven patients (consisting of 8 levels) had underwent repeat ^{18}F-NaF PET/CT for persistent or recurrent pain. There was no significant intragraft or extragraft radiotracer uptake in 7 levels that demonstrated fusion on follow-up CT. Notably, there was presence of intragraft uptake in the only level labeled as "nonfused" on CT, indicating that ^{18}F-NaF PET/CT may be useful in identifying sources of chronic pain and suspected pseudarthrosis following surgery.

Other nuclear medicine techniques such as single-photon emission computed tomography (SPECT) with ^{99m}Tc-labeled radiotracers have been used to analyze osteoblastic activity in the spine [26]. A study by Easton et al. demonstrated a sensitivity of 91% and specificity of 79% for pre-operative SPECT/CT to detect pseudoarthrosis in 60 surgical patients who underwent revision spinal fusion [27]. Shapovalov et al. assessed 23 patients with post-operative neck pain after 1 year of observation from prior cervical fusion, achieving a similar sensitivity of 94.4% and moderate specificity of 66.7% to detect segmental instability with SPECT/CT performed at an average of 5.5 ± 1.1 years post-surgery [28]. A study by Tender et al. evaluated the SPECT/CT images of 315 patients with chronic (i.e., ≥2 years) axial spine pain: 86 patients whose scans were focally positive at 2 or fewer areas were offered surgery [29]. The results demonstrated a significant reduction in the self-reported Visual Analogue Scale of 48 patients who underwent the fusion procedures.

While SPECT/CT demonstrates promising clinical utility in the field of spine surgery, ^{18}F-NaF PET/CT provides superior target-to-background ratio and spatial resolution [30]. It also offers shorter study times as ^{18}F-NaF binds minimally to protein and clears rapidly in plasma [31]. In a practical clinical setting, SPECT/CT may be a more cost-effective and accessible option.

Several studies have also investigated ^{18}F-FDG PET in the setting of suspected surgical site infection. Because ^{18}F-FDG reflects cellular metabolism and the degree of radiotracer uptake is particularly elevated within areas of inflammatory cell infiltrate [32]. The physiological metabolic activity of bone marrow hematopoiesis is relatively low which facilitates distinction of an inflammatory process via ^{18}F-FDG. A meta-analysis of 12 studies (396 patients) reported a sensitivity of 95% and specificity of 91% for ^{18}F-FDG PET/CT in the diagnosis of spinal infection [33]. In contrast to CT or MRI, the signal of ^{18}F-FDG PET is not affected by metal implant artifact, allowing for potentially improved visualization and more accurate diagnosis [8, 34]. Consistent with this view, Paez et al. demonstrated superior diagnostic performance when combining the results of MRI with ^{18}F-FDG PET/CT in 63 patients with suspected post-operative spinal infection [35].

However, elevated ^{18}F-FDG uptake in the post-operative spine may also reflect other non-infectious etiologies, thus limiting its specificity. Both aseptic inflammation and active post-operative healing can result in hypermetabolism. Post-surgical granulation tissue or mechanical stress around instrumentation can also cause elevated ^{18}F-FDG uptake [34]. In a study of 73 patients who underwent previous spine surgery (27 with implants), Winter et al. achieved a specificity of 65% with ^{18}F-FDG PET performed at a median time interval of 10 months in patients with instrumentation (vs 92% in those without hardware). Thus, a positive study in a patient with hardware must be interpreted with caution [22].

Conclusion

PET/CT enables the detection of post-operative molecular changes in bone metabolism and inflammatory activity that may precede structural alterations on conventional imaging modalities used in spine surgery. This can help clinicians aid in the early diagnosis of surgical complications such as pseudarthrosis and infection, and may also serve as a tool for monitoring long-term post-operative recovery. Further research, particularly longitudinal studies that correlate PET/CT findings to clinical outcomes, is necessary to evaluate the clinical applications of ^{18}F-NaF and ^{18}F-FDG PET/CT in spine surgery.

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Informed consent was obtained from each participant included in this study.

Disclosure of conflict of interest

None.

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