



^{18}F -NaF PET/CT in Presumed Aseptic Pseudarthrosis after Spinal Fusion: Correlation with Findings at Revision Surgery and Intraoperative Cultures

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Abstract

Background Conventional imaging is useful to assess interbody fusion by showing complete trabecular bony bridging, but has a low positive predictive value for pseudarthrosis. Because alterations of bone metabolism may precede structural anatomical changes on computed tomography (CT), we aimed to investigate the ability of fluorine 18 sodium fluoride positron emission tomography/computed tomography (^{18}F -NaF PET/CT) to identify pseudarthrosis after spinal fusion using surgical revision as the reference standard.

Methods We retrospectively reviewed ^{18}F -NaF PET/CT scans performed between February 2019 and September 2020 in patients experiencing pain after spinal fusion. We included the 18 patients who underwent revision surgery for suspicion of pseudarthrosis. Five consecutive patients who were clearly fused on CT served as the control group.

Results In the revision surgery group ($n = 18$), visual assessment by ^{18}F -NaF PET/CT revealed that all 22 cages with an increased ^{18}F -NaF uptake around intercorporeal fusion material had mobility at revision surgery, whereas none of the fused patients ($n = 5$) showed uptake around cage/intervertebral disk space. Among the 18 patients with presumed aseptic pseudarthrosis, intraoperative cultures revealed surgical site infection (SSI) caused by *Cutibacterium acnes* (*C. acnes*) in seven patients (38.9%). There was a statistically significant difference in standardized uptake values and uptake ratios

Keywords

- ▶ fluorine-18 sodium fluoride
- ▶ positron emission tomography/computed tomography
- ▶ spinal fusion
- ▶ pseudarthrosis
- ▶ *Cutibacterium acnes*

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between the revision surgery and control groups ($p = 5.3 \times 10^{-6}$ and $p = 0.0002$, respectively).

Conclusions ^{18}F -NaF PET/CT imaging appeared as a useful tool to identify pseudarthrosis following spinal fusion. The unexpectedly high prevalence (38.9%) of SSI caused by *C. acnes* found in presumed aseptic patients supports the utility of intraoperative cultures in revision cases for pseudarthrosis, even without preoperative clinical suspicion of SSI.

Introduction

In the therapeutic management of back pain, spinal fusion can be considered after failed conservative measures. Following spinal fusion, persistent or recurrent pain is reported in a significant proportion of patients, and up to 14% of patients may require an additional operation within 4 years.¹ Failed spinal fusion is a well-known cause of persistent or recurrent pain after fusion surgery. Pseudarthrosis is defined as the absence of solid bony fusion at a minimum follow-up of 6 months after spinal surgery,^{2,3} and may occur in 30 to 40% of spinal fusion patients.^{4,5} Revision surgery is the preferred treatment in patients suffering from symptoms due to pseudarthrosis. As patient outcome following surgical reintervention may be worse than that with primary surgery, identifying the accurate cause of pain in these patients is crucial to select those who will benefit from revision surgery.

Standard evaluation of recurrent symptoms after spinal fusion surgery usually consists of physical examination and conventional imaging. If computed tomography (CT) has developed into the preferred method of assessing interbody fusion by showing complete trabecular bony bridging,⁶ it can also demonstrate extensive and nonspecific postoperative changes, especially in the early postoperative phase.⁷ It has been stated that bone metabolism may precede structural anatomical changes on CT.⁸ These data suggest a potential usefulness of nuclear medicine techniques in patients following spinal fusion surgery.

Fluorine-18 sodium fluoride (^{18}F -NaF) was already used as a clinical radiopharmaceutical for bone scintigraphy in the early 1960s. However, due to technical and availability reasons, it was not largely utilized and $^{99\text{m}}\text{Tc}$ -labeled tracers like $^{99\text{m}}\text{Tc}$ -methylene diphosphonate (MDP) were preferred for bone scanning. With the development of positron emission tomography/computed tomography (PET/CT) systems and ^{18}F -labeled tracers since the early 1990s, there is a renewed interest in the use of ^{18}F -NaF as a tracer. Depicting osteoblastic activity, the physiology of ^{18}F -NaF is similar to that of $^{99\text{m}}\text{Tc}$ -MDP used in traditional bone scanning, but ^{18}F -NaF PET/CT is faster and provides superior detector sensitivity and spatial resolution compared with bone scan.^{9,10} To date, few studies investigated the role of ^{18}F -NaF PET/CT in pseudarthrosis after spinal fusion surgery,¹¹⁻¹⁴ but direct comparison against the gold standard of surgical evaluation of the stability of the fusion material is limited.

The current work aimed to investigate the ability of ^{18}F -NaF PET/CT to identify pseudarthrosis after spinal fusion surgery and therefore help surgeons select patients who would benefit from revision surgery. Validation of ^{18}F -NaF PET/CT results was based on findings at revision surgery, which is considered the gold standard, and intraoperative cultures.

Materials and Methods

Patients

This compliant study received a local institutional review board approval. Written informed consent was waived due to the retrospective nature of this study.

We retrospectively reviewed ^{18}F -NaF PET/CT scans performed between February 2019 and September 2020 in patients experiencing persistent or recurrent pain after spinal fusion surgery, without an obvious clinical and/or conventional imaging explanation. We included the patients who underwent revision surgery for suspicion of symptomatic pseudarthrosis following ^{18}F -NaF PET/CT. A total of 18 patients (10 women, 8 men; age range: 33–84 years) met the inclusion criteria (revision surgery group). Because none of these patients had clinical signs or laboratory parameters suggesting surgical site infection (SSI), suspected pseudarthrosis was presumed to be aseptic. Time interval between initial fusion surgery and ^{18}F -NaF PET/CT was 6 to 44 months (mean: 17 months, median interval: 12 months). Initial indication of spinal fusion was degeneration in 17/18 patients (94.4%) and isthmic spondylolisthesis in 1/17 patients (5.6%). In all 18 patients (100%), only polyetheretherketone (PEEK) cages ($n = 22$) had been implanted, associated with autograft for lumbar fusion and synthetic bone graft substitute for cervical fusion (► **Table 1**).

As a control group, five consecutive patients who underwent ^{18}F -NaF PET/CT for persistent or recurrent pain after spinal fusion surgery, but were clearly fused on CT (trabecular bony bridging across the disk space), were also included. Time interval between initial fusion surgery and ^{18}F -NaF PET/CT was 6 to 15 years (mean 10.4 years, median interval: 11 years). Initial indication of spinal fusion was degeneration in 5/5 (100%) patients. In 3 of 5 patients (60%), PEEK cages (with autograft) had been implanted and 2 of 5 patients (40%) had osteosynthesis with transpedicle screws with rods but without cage implantation (► **Table 2**).

Table 1 Key findings in revision surgery group

Patient	Levels fused	Type of hardware	Bone graft material	Time between spinal fusion surgery and ¹⁸ F-NaF PET/CT (months)	Imaging results			Time between ¹⁸ F-NaF PET/CT and revision surgery (months)	Findings on revision surgery	Intraoperative cultures
					¹⁸ F-NaF PET/CT findings	SUV _{max} around cage	Ratio cage / first normal adjacent vertebra			
1	C5-C6	PEEK	SBGCS	7	Increased uptake around cage at C5-C6	44.3	3.4	1	Pseudarthrosis at C5-C6	Negatives
2	L4-L5	PEEK	Autograft	13	Increased uptake around cage at L4-L5	41.5	3	0	Pseudarthrosis at L4-L5	Negatives
3	L5-S1	PEEK	Autograft	31	Increased uptake around cage at L5-S1	52.9	2.8	7	Pseudarthrosis at L5-S1	Negatives
4	L4-L5 and L5-S1	PEEK and PEEK	Autograft	10	Increased uptake around cages at L4-L5 and L5-S1	13.1 and 17	1.3 and 1.7	3	Pseudarthrosis at L4-L5 and L5-S1	Positives (<i>Curibacterium acnes</i>)
5	L4-L5	PEEK	Autograft	35	Increased uptake around cage at L4-L5	34.5	3.5	0	Pseudarthrosis at L4-L5	Positives (<i>Curibacterium acnes</i>)
6	L4-L5 and L5-S1	PEEK and PEEK	Autograft	12	Increased uptake around cages at L4-L5 and L5-S1	23.5 and 29	2.2 and 2.7	1	Pseudarthrosis at L4-L5 and L5-S1	Negatives
7	L4-L5	PEEK	Autograft	13	Increased uptake around cage at L4-L5	31.8	3.1	5	Pseudarthrosis at L4-L5	Positives (<i>Curibacterium acnes</i>)
8	L4-L5	PEEK	Autograft	7	Increased uptake around cage at L4-L5	46.3	3.9	7	Pseudarthrosis at L4-L5	Negatives
9	L4-L5	PEEK	Autograft	6	Increased uptake around cage at L4-L5	34.2	2.2	1	Pseudarthrosis at L4-L5	Positives (<i>Curibacterium acnes</i>)
10	C5-C6	PEEK	SBGCS	8	Increased uptake around cage at C5-C6	35.5	2.6	6	Pseudarthrosis at C5-C6	Positives (<i>Curibacterium acnes</i>)
11	C5-C6	PEEK	SBGCS	41	Increased uptake around cage at C5-C6	19.8	1.5	0	Pseudarthrosis at C5-C6	Negatives
12	C5-C6	PEEK	SBGCS	15	Increased uptake around cage at C5-C6	36.2	2.8	1	Pseudarthrosis at C5-C6	Negatives
13	L4-L5	PEEK	Autograft	6	Increased uptake around cage at L4-L5	28.2	3.2	11	Pseudarthrosis at L4-L5	Negatives
14	C5-C6 and C6-C7	PEEK and PEEK	SBGCS	21	Increased uptake around cages at C5-C6 and C6-C7	49.5 and 75.3	4.6 and 7	4	Pseudarthrosis at C5-C6 and C6-C7	Negatives
15	C6-C7	PEEK	SBGCS	23	Increased uptake around cage at C6-C7	51.5	3.7	1	Pseudarthrosis at C6-C7	Negatives
16	C5-C6 and C6-C7	PEEK and PEEK	SBGCS	10	Increased uptake around cage at C5-C6 and C6-C7	33.2 and 37.9	2.7 and 3.1	3	Pseudarthrosis at C5-C6 and C6-C7	Negatives
17	C5-C6	PEEK	SBGCS	11	Increased uptake around cage at C5-C6	31.9	2.3	0	Pseudarthrosis at C5-C6	Positives (<i>Curibacterium acnes</i>)
18	C5-C6	PEEK	SBGCS	44	Increased uptake around cage at C5-C6	58.6	3.8	1	Pseudarthrosis at C5-C6	Positives (<i>Curibacterium acnes</i>)

Abbreviations: ¹⁸F-NaF PET/CT, fluorine 18 sodium fluoride positron emission tomography/computed tomography; PEEK, polyetheretherketone; SBGB, synthetic bone graft substitute; SUV_{max}, maximum standardized uptake value.

Table 2 Key findings in control group

Patient	Initial indication for spinal fusion	Levels fused	Type of hardware	Bone graft material	Time between spinal fusion surgery and ¹⁸ F-NaF PET/CT (years)	Imaging results			
						Conventional CT scan findings at cage/ intervertebral disk space	¹⁸ F-NaF PET/CT Findings	SUV _{max} around intervertebral disk space	Ratio between cage/intervertebral disk space and first normal adjacent vertebra
19	Degeneration	L4-L5 and L5-S1	Osteosynthesis with transpedicle screws with rods but without cage implantation	...	11	Bony bridging across the disk space at L4-L5 and L5-S1	No abnormally increased uptake around intervertebral disk space at L4-L5 and L5-S1 Increased uptake around disk space at L3-L4, suggestive of ASD	9.8 and 12.9	0.8 and 0.9
20	Degeneration	L5-S1	PEEK	Autograft	15	Bony bridging across the disk space at L5-S1	No abnormally increased uptake around cage at L5-S1 Slightly increased uptake around disk space at L4-L5, suggestive of ASD Increased uptake around disk space at L2-L3, suggestive of degenerative disc disease	11	0.9
21	Degeneration	L4-L5	Osteosynthesis with transpedicle screws with rods but without cage implantation	...	9	Bony bridging across the disk space at L4-L5	No abnormally increased uptake around intervertebral disk space at L4-L5 Increased uptake around disk space at L5-S1, suggestive of ASD	11.2	0.9
22	Degeneration	L4-L5	PEEK	Autograft	6	Bony bridging across the disk space at L4-L5	No abnormally increased uptake around cage at L4-L5 Slightly increased uptake around disk space at L3-L4, suggestive of ASD Increased uptake around disk space at L2-L3, suggestive of degenerative disc disease	9	0.8
23	Degeneration	L4-L5	PEEK	Autograft	11	Bony bridging across the disk space at L4-L5	No abnormally increased uptake around cage at L4-L5 Increased uptake around disk space at L3-L4, suggestive of ASD	9.5	0.9

Abbreviations: ASD, adjacent segment disease; ¹⁸F-NaF PET/CT, fluorine 18 sodium fluoride positron emission tomography/computed tomography; PEEK, polyetheretherketone; SBGB, synthetic bone graft substitute; SUV_{max}, maximum standardized uptake value

Scanning

All patients underwent PET/CT imaging 60 minutes after ^{18}F -NaF intravenous injection (2,2 MBq/kg). The PET/CT images were obtained using an integrated PET/CT scanner (Discovery IQ; GE-Healthcare, Milwaukee, Wisconsin, United States). After a low-dose CT acquisition (120 kV, 30 mAs, slice thickness 4mm) for attenuation correction, whole-body three-dimensional PET scan was acquired at 2 minute/bed position. This was immediately followed by a noncontrast-enhanced diagnostic CT scan (16-slice helical, 100–140 kV, 80–200 mAs, 2,5 mm slice thickness).

Interpretation

The PET/CT images were visually reviewed using Advantage Window Volume Viewer software (GE-Healthcare, Milwaukee, Wisconsin, United States), providing multiplanar reformatted images of PET alone, CT alone and fused PET/CT. Images were analyzed in consensus by two board-certified nuclear medicine physicians (Y E Y and C P A). Physicians were not blinded to the clinical and imaging information of the patients obtained before ^{18}F -NaF PET/CT, but were blinded to the data of revision surgery. Attenuation-corrected PET images as well as fused PET/CT images were used for analysis, using the CT for anatomical correlation. Visual assessment of increased uptake around cage/intervertebral disk space higher than background recorded from the first normal adjacent vertebra was interpreted as positive, even without abnormality on fusion CT. Visual assessment of uptake around cage/intervertebral disk space lower or equal than background recorded from the first normal adjacent vertebra was interpreted as negative. Image data were also quantitatively analyzed by the maximum standardized uptake value (SUV_{max}) as an index of ^{18}F -NaF uptake, and the ratio between the cage/intervertebral disk space and background recorded from the first normal adjacent vertebra was calculated. For the control group, conventional CT scan was interpreted by a radiologist blinded to the results of ^{18}F -NaF PET/CT.

Clinical Management

^{18}F -NaF PET/CT results were compared with the gold standard of surgical evaluation of the stability of the fusion

material at sites of abnormal tracer activity. Surgical exploration consisted of the surgeon probing and manually testing the exact region for hardware failure at the sites of abnormal tracer uptake. Further, at least three intraoperative cultures were obtained from bone tissue and/or extracted hardware.

Statistics

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, Illinois, United States, version 21). p -Values less than 0.05 were considered statistically significant. Nonparametric analyses were performed using the Mann–Whitney U test.

Results

Between February 2019 and September 2020, 18 patients underwent revision surgery for suspicion of symptomatic pseudarthrosis following ^{18}F -NaF PET/CT. On the other hand, five consecutive fused patients who underwent ^{18}F -NaF PET/CT for persistent or recurrent pain after spinal fusion surgery were used as a control group.

In the revision surgery group ($n = 18$), visual assessment by ^{18}F -NaF PET/CT revealed that all 22 cages with an increased ^{18}F -NaF uptake around intercorporeal fusion material had mobility at revision surgery, hence confirming the diagnosis of pseudarthrosis (► Figs. 1 and 2). In some patients with lumbar fusion material, cage mobility was associated with elevated activity around screws suggestive of hardware loosening, which was also surgically confirmed (► Fig. 3). Time interval between ^{18}F -NaF PET/CT and revision surgery was 0 to 11 months (mean: 2.9 months, median interval: 1 month). The SUV_{max} of foci around cages ranged from 13.1 to 75.3 (average: 37.5, median: 35). The ratio between the uptake around the cage and the background recorded from the first normal adjacent vertebra ranged from 1.3 to 7 (average: 3, median: 2.9). Interestingly, among these 18 patients with presumed aseptic pseudarthrosis, intraoperative cultures revealed that pseudarthrosis was complicated with *Cutibacterium acnes* (*C. acnes*) infection in 7 patients (38.9%) (► Figs. 4 and 5). To rule out the possibility of contamination, diagnosis of *C. acnes*

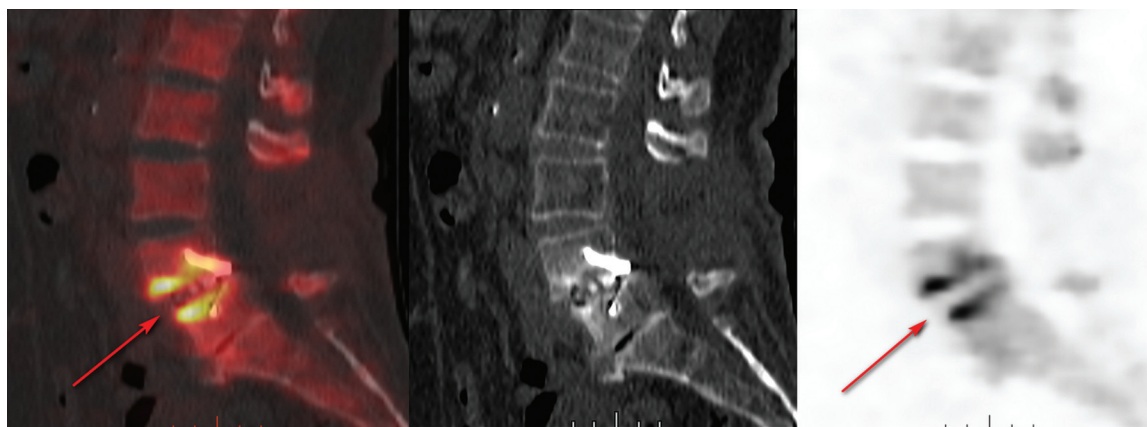


Fig. 1 Positron emission tomography/computed tomography (PET/CT) fusion, noncontrast CT, and PET images in patient 13. Sagittal PET/CT fusion, noncontrast CT, and PET show intense increased uptake around cage at L4-L5 (red arrow, maximum standardized uptake value = 28.2), suggestive of pseudarthrosis. Cage mobility was confirmed on revision surgery. Intraoperative cultures were negatives.



Fig. 2 Positron emission tomography/computed tomography (PET/CT) fusion, noncontrast CT, and PET show intense increased uptake around cage at C5-C6 (red arrow, maximum standardized uptake value = 36.2), suggestive of pseudarthrosis. Cage mobility was confirmed on revision surgery. Intraoperative cultures were negatives.

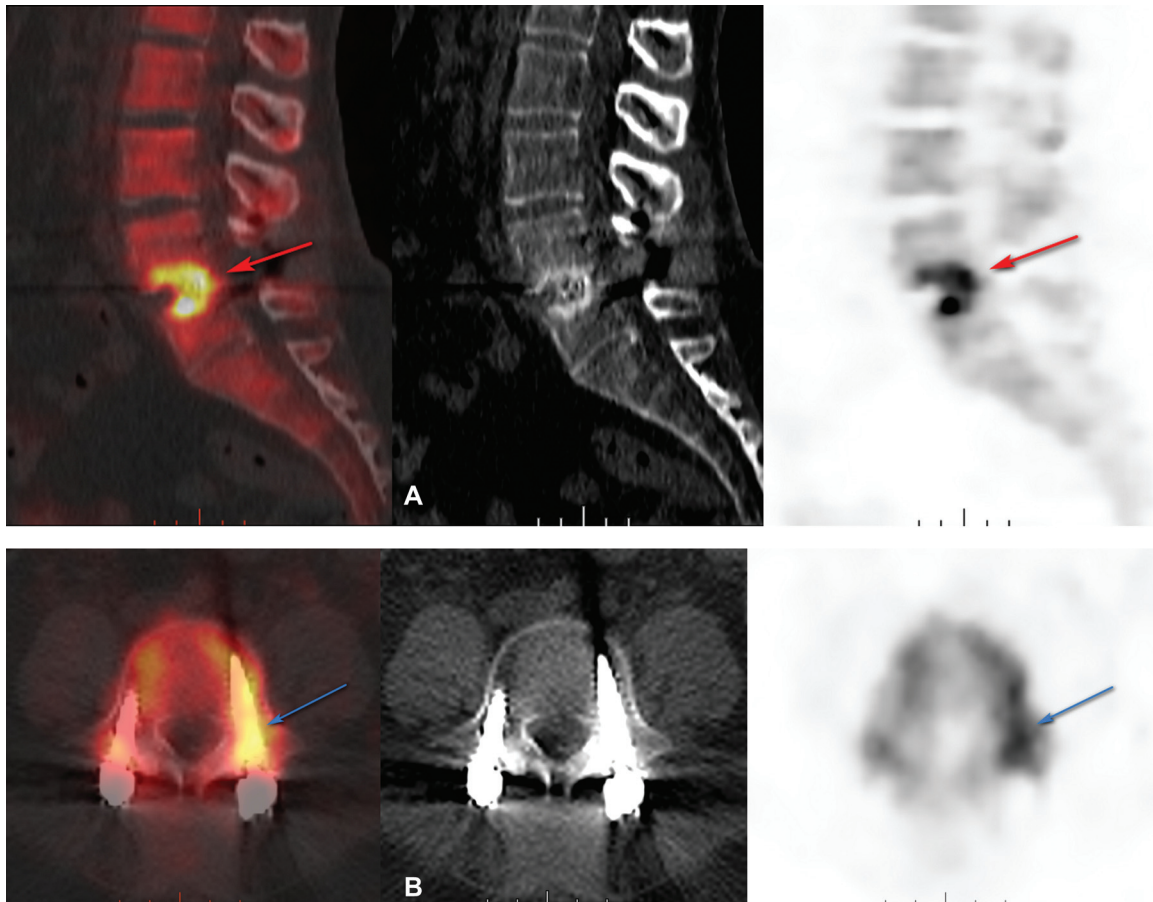


Fig. 3 Positron emission tomography/computed tomography (PET/CT) fusion, noncontrast CT, and PET images in patient 8. (A) Sagittal PET/CT fusion, noncontrast CT, and PET show intense increased uptake around cage at L4-L5 (red arrow, maximum standardized uptake value [SUV_{max}] = 46.3), suggestive of pseudarthrosis. Cage mobility was confirmed on revision surgery. (B) Axial PET/CT fusion, noncontrast CT, and PET show increased fluorine-18 sodium fluoride activity around left L4 screw (blue arrow, SUV_{max} = 19.2), suggestive of screw loosening, which was also confirmed on revision surgery. Intraoperative cultures were negatives.

infection was made only if at least two positive intraoperative cultures of the same *C. acnes* were isolated.^{15,16} Visual assessment of distribution of increased uptake around cage was similar in patients that were *C. acnes* positive versus *C. acnes* negative. Hence, it was not possible to distinguish the two groups of patients (► **Table 1**).

In the control group of fused patients (*n* = 5), visual assessment by ¹⁸F-NaF PET/CT did not reveal any uptake

around cage/intervertebral disk space (► **Figs. 6–8**). The SUV_{max} around cage/intervertebral disk space ranged from 9 to 11.2 (average: 10.2, median: 10.2) and the ratio between the uptake around the cage/intervertebral disk space and the background recorded from the first normal adjacent vertebra ranged from 0.8 to 0.9 (average: 0.87, median: 0.9). Additionally, in all five fused patients (100%), ¹⁸F-NaF PET/CT showed increased uptake on an adjacent level, suggestive of

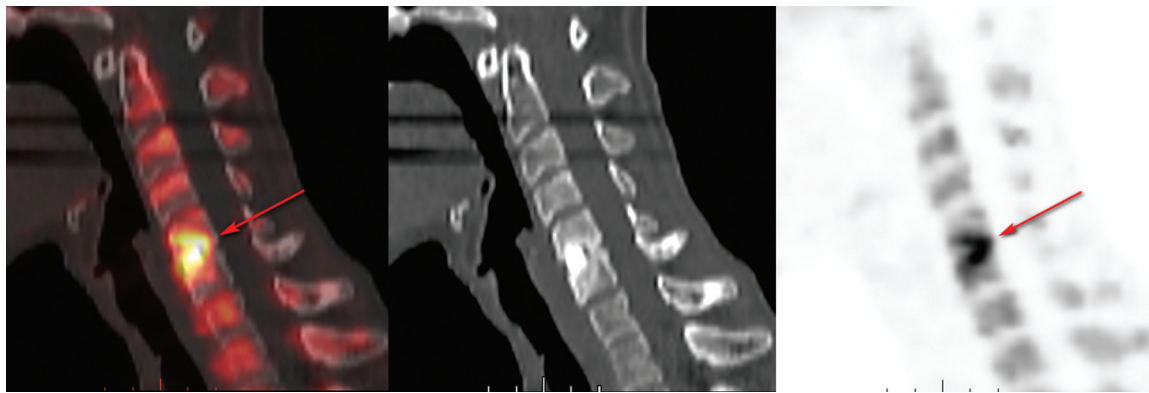


Fig. 4 Positron emission tomography/computed tomography (PET/CT) fusion, noncontrast CT, and PET images in patient 17. Sagittal PET/CT fusion, noncontrast CT, and PET show intense increased uptake around cage at C5-C6 (red arrow, maximum standardized uptake value = 31.9), suggestive of pseudarthrosis. Cage mobility was confirmed on revision surgery. Three of 3 intraoperative cultures grew *Cutibacterium acnes*.

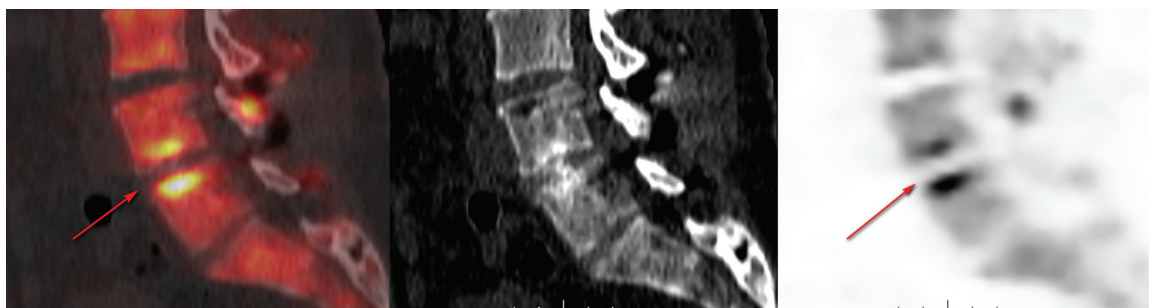


Fig. 5 Positron emission tomography/computed tomography (PET/CT) fusion, noncontrast CT, and PET images in patient 9. Sagittal PET/CT fusion, noncontrast CT, and PET show intense increased uptake around cage at L4-L5 (red arrow, maximum standardized uptake value = 34.2), suggestive of pseudarthrosis. Cage mobility was confirmed on revision surgery. Five of 5 intraoperative cultures grew *Cutibacterium acnes*.

adjacent segment disease, which could potentially help to explain persistent or recurrent pain (→Table 2).

There was a statistically significant difference in SUV_{max} values (around cage/intervertebral disk space) and uptake ratios between the revision surgery and control groups ($p = 5.3 \times 10^{-6}$ and $p = 0.0002$, respectively).

Discussion

^{18}F -NaF PET/CT imaging appeared as a useful adjunctive diagnostic tool to identify pseudarthrosis in patients with persistent or recurrent pain after spinal fusion surgery when standard conventional imaging remains inconclusive, especially in the early postoperative phase. Specifically, in the revision surgery group, 18 of 18 patients were correctly identified by PET/CT as having failed spinal fusion at surgical exploration. Interestingly, seven of these 18 patients (38.9%) had occult and unexpected SSI caused by *C. acnes*. Moreover, in the control group, none of the five fused patients had increased uptake around cage/intervertebral disk space. To our knowledge, this is the largest cohort of patients whose ^{18}F -NaF PET/CT imaging was directly compared with findings at revision surgery, which is considered the gold standard, and the first study to correlate ^{18}F -NaF PET/CT results with intraoperative cultures.

Despite considerable advances in spinal fusion surgery over the last one to two decades, the proportion of patients

with persistent or recurrent pain remains high, and pseudarthrosis is well known as a leading cause of pain postoperatively. Standard conventional imaging by CT or magnetic resonance imaging (MRI) is widely used to identify the cause of pain after spinal fusion surgery. CT has become the preferred imaging to assess interbody fusion by showing complete trabecular bony bridging,⁶ but is of limited value for detecting nonunion in the early postoperative phase, with a low positive predictive value for pseudarthrosis.¹⁷ MRI, although superior in assessment of soft tissue, is subject to limitations due to metallic artifacts from implant material.⁶ But it should be noted that more modern titanium implants and application of specific sequences may reduce these artifacts.¹⁸

Imaging of alteration of bone metabolism by ^{99m}Tc -labeled tracers has proved to be very sensitive in various bone pathologies, but it has also been criticized for its lack of specificity.¹⁹ Although several studies investigated the usefulness of planar and single-photon emission computed tomography (SPECT) bone scan for evaluating postoperative spine,^{20,21} few included more recent SPECT/CT systems, which should increase specificity because the CT allows identifying the exact localization of the abnormal uptake.²² A study by Damgaard et al suggested a possible utility of bone SPECT/CT for detecting loosening of metallic fusion material, using surgical evaluation as gold standard, but this retrospective study suffered from the smallness of the cohort that comprised only nine patients.²³ In their

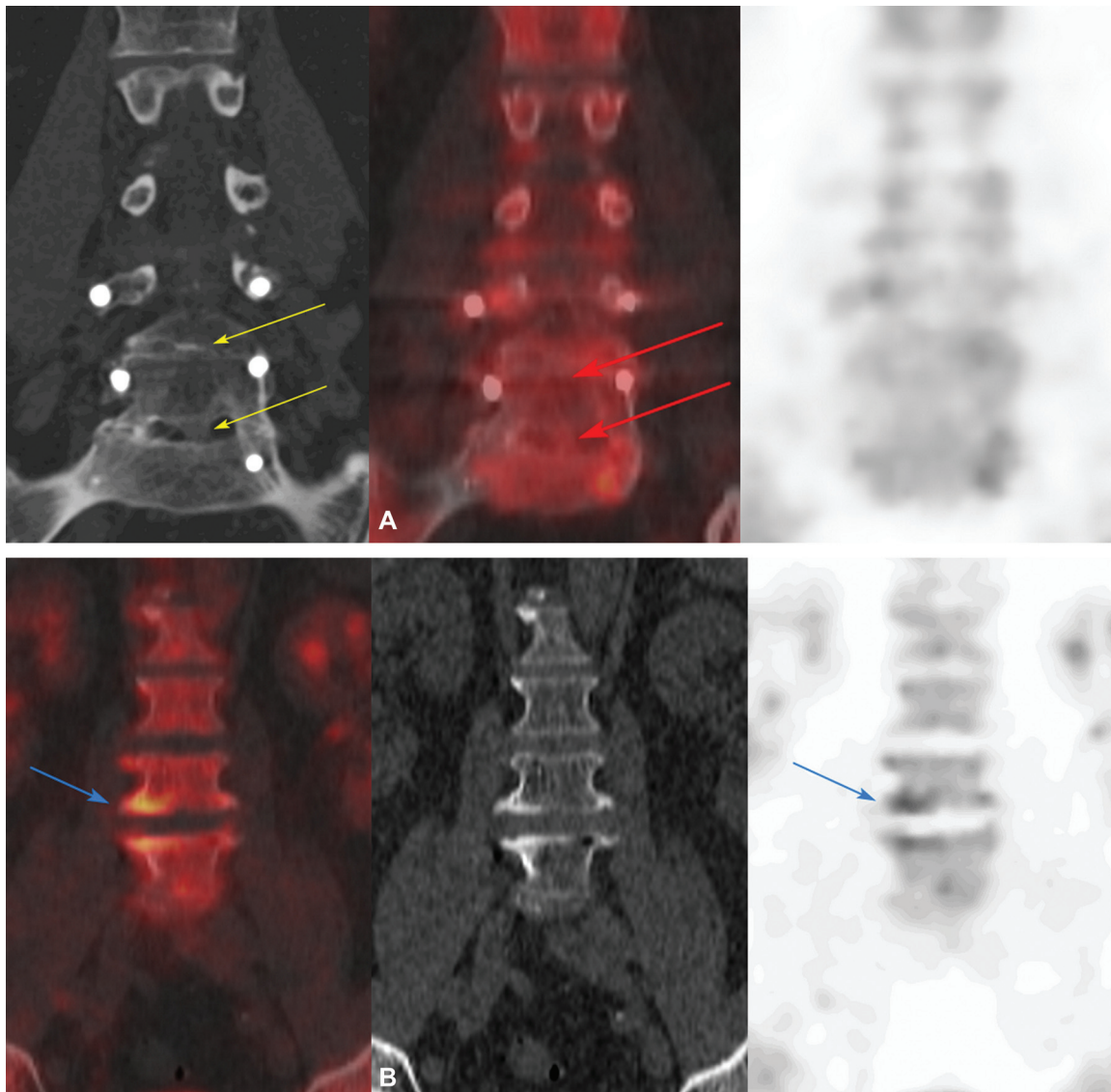


Fig. 6 Imaging findings in patient 19. (A) Coronal conventional computed tomography (CT) scan demonstrates bony bridging across the disk space at L4-L5 and L5-S1 (*yellow arrows*) without abnormally increased uptake detected on positron emission tomography/computed tomography (PET/CT) fusion and PET (*red arrows*). (B) Coronal PET/CT fusion, noncontrast CT, and PET show increased uptake around disk space at L3-L4 (*blue arrow*), suggestive of adjacent segment disease.

case series of 10 patients with suspicion of pseudarthrosis after lumbar spinal fusion, Rager et al reported that bone SPECT/CT seems to increase specificity for detection of non-union of interbody devices compared with CT alone.³ Recently, guidelines from the American College of Radiology stated that bone SPECT/CT helps detect and localize painful pseudarthrosis, and can be useful for anatomic localization and problem solving.²⁴

There is a more limited number of published articles on the utility of ^{18}F -NaF PET/CT for evaluating the postoperative spine. Only one study of 22 patients by Quon et al correlated ^{18}F -NaF PET/CT results with findings at revision surgery for 16 patients, 6 others being evaluated by clinical follow-up.¹³ ^{18}F -NaF PET/CT accurately determined lesions (cage failure, screw loosening, graft fracture) in 15 of the 16 patients, and authors reported only one false-positive scan in a patient at 4 months after spinal fusion surgery. Thus, ^{18}F -NaF PET/CT

correctly identified patients requiring surgical management. Fischer et al showed the potential of ^{18}F -NaF PET/CT imaging in patients with persistent pain after cervical or lumbar fusion.¹¹ They found that even 10 years after fusion surgery, there was an increased uptake around 8 of 17 cages, suggesting unsuccessful fusion due to increased stress and micro-instability. However, this study of 20 patients lacked correlation between ^{18}F -NaF PET/CT abnormalities and surgical exploration or outcome data. In a retrospective study, Peters et al measured uptake in the vertebral end plates and discs in 36 patients after lumbar spinal fusion.¹⁴ They showed that the degree of uptake was correlated with the clinical measure of pain reported by the patient, hence suggesting the possible usefulness of ^{18}F -NaF PET/CT in postoperative pain. Similarly, this study was limited by a lack of correlation to the gold standard of surgical exploration.

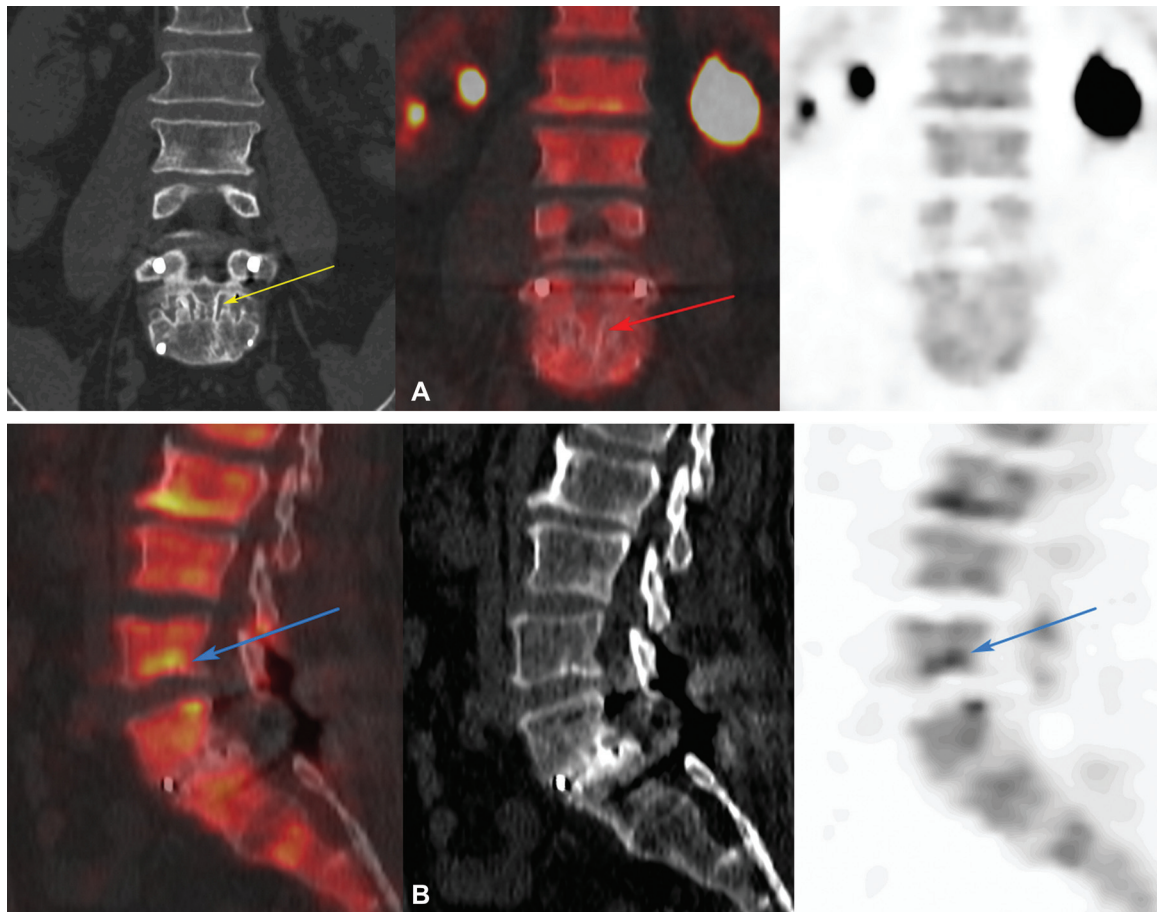


Fig. 7 Imaging findings in patient 20. (A) Coronal conventional computed tomography (CT) scan demonstrates bony bridging across the disk space at L5–S1 (yellow arrow) without abnormally increased uptake detected on positron emission tomography/computed tomography (PET/CT) fusion and PET (red arrow). (B) Sagittal PET/CT fusion, noncontrast CT, and PET show slightly increased uptake around disk space at L4–L5 (blue arrow), suggestive of adjacent segment disease.

It should be noted that we cannot deduce from our study the timing of ^{18}F -NaF uptake after spinal fusion in the early postoperative phase, which can reflect either the physiological remodeling after surgery or instability of the cage. Indeed, if the ^{18}F -NaF PET/CT is performed too soon after fusion surgery, PET/CT results can be falsely positive, as was the case for the only false-positive scan reported by Quon et al at only 4 months after fusion surgery.¹³ In this study, others patients found to be true positives at revision surgery were explored by ^{18}F -NaF PET/CT at least 8 months after spinal fusion. In our institution, ^{18}F -NaF PET/CT is preferentially performed at least 12 months after spinal fusion surgery, except in the case of severe pain, as was the case for 8 of the 18 patients who underwent ^{18}F -NaF PET/CT within 1 year of surgery.

On the other hand, among the 18 patients included in our study for suspicion of pseudarthrosis on ^{18}F -NaF PET/CT, thought to be aseptically preoperatively, intraoperative cultures at revision surgery unexpectedly revealed occult SSI caused by low virulence *C. acnes* in 7 patients (38.9%). It should be noted that visual assessment of distribution of increased uptake around cage was similar in patients that were *C. acnes* positive versus *C. acnes* negative. Thus, it was not possible to distinguish the two groups of patients.

SSI after spinal surgery is an infrequent complication with a mean incidence of 2 to 3%.²⁵ Diagnosis of SSI after spinal surgery can be challenging. Because delay in diagnosis can lead to higher morbidity and mortality, prompt diagnosis appears crucial.²⁶ Diagnostic criteria are essentially based on the microbiology but deep cultures are rarely obtained before revision surgery and blood cultures are of low relevance in postoperative instrumented spine infection.²⁷ Moreover, clinical signs and laboratory parameters can be ambiguous, especially in low-grade and chronic infections.²⁸ Therefore, complementary medical imaging can be necessary. MRI is the gold standard imaging method when spinal infection is suspected because this technique can show pathological abnormalities in the disc and adjacent bone marrow.²⁹ Nevertheless, MRI diagnostic accuracy is limited in the postoperative spine by the nonspecific signal characteristics, reflecting either active infection or reparative tissue processes.³⁰ In addition, metallic artifacts from implant material can also negatively affect diagnostic accuracy of MRI.⁶

Several studies have demonstrated the usefulness of ^{18}F -fluorodeoxyglucose (FDG) PET/CT in SSI after spinal surgery, suggesting the possible dominance of ^{18}F -FDG PET/CT over MRI.^{27,31,32} Some authors reported a negative

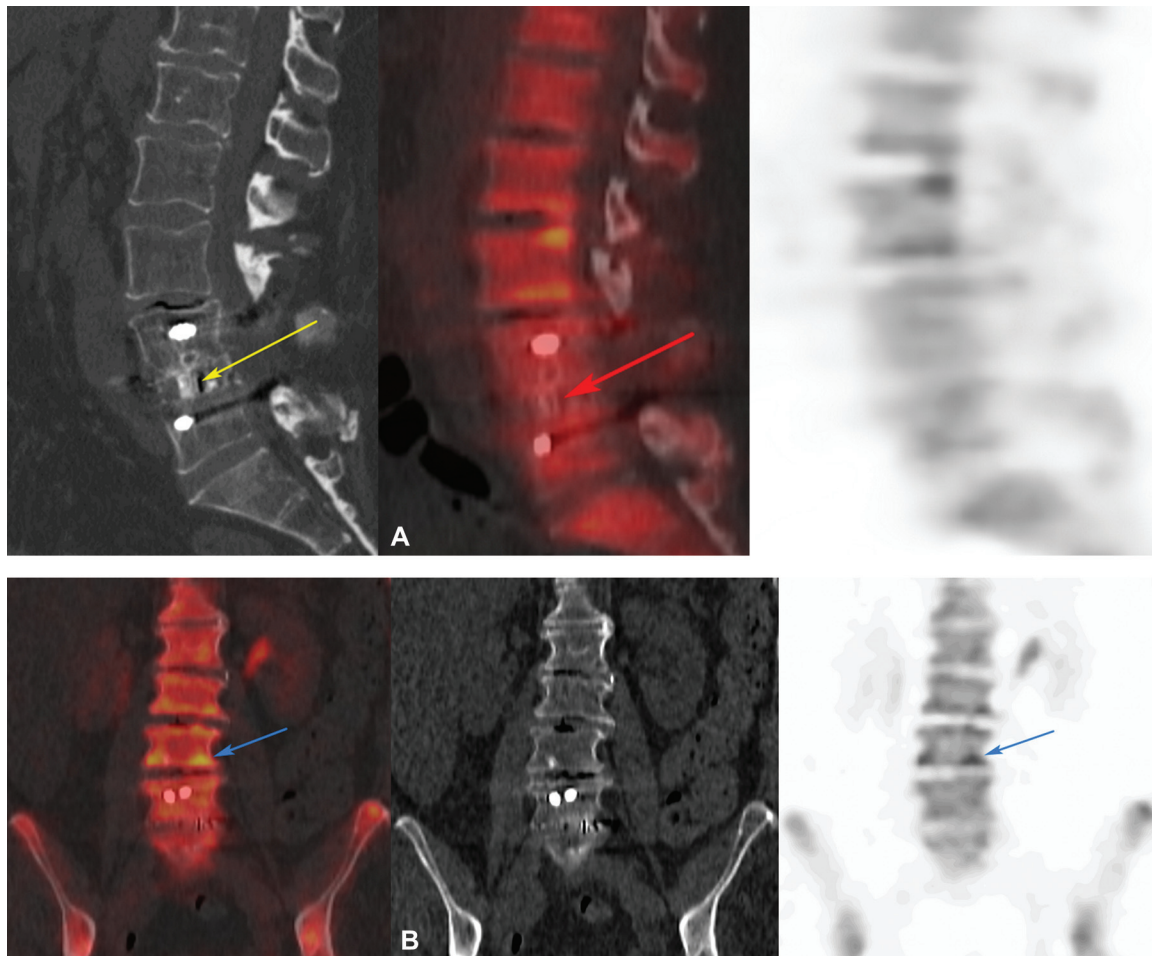


Fig. 8 Imaging findings in patient 22. (A) Sagittal conventional computed tomography (CT) scan demonstrates bony bridging across the disk space at L4-L5 (yellow arrow) without abnormally increased uptake detected on positron emission tomography/computed tomography (PET/CT) fusion and PET (red arrow). (B) Coronal PET/CT fusion, noncontrast CT, and PET show slightly increased uptake around disk space at L3-L4 (blue arrow), suggestive of adjacent segment disease.

predictive value close to 100% of ^{18}F -FDG PET/CT in spinal infection and concluded that a negative ^{18}F -FDG PET/CT can exclude infection with a high degree of confidence.^{33,34} However, recent studies have highlighted the possibility of false-negative ^{18}F -FDG PET/CT in SSI caused by some bacteria like *C. acnes* or *Staphylococcus epidermidis*.^{27,35} Absence of ^{18}F -FDG uptake, which reflect glucose metabolism, may be explained by the low-virulence of these bacteria. In a study of foreign-body-associated infection in a rabbit model, Lankinen et al demonstrated lower ^{18}F -FDG uptake in infection with the low-virulence bacteria *Staphylococcus epidermidis* compared with the highly virulent *Staphylococcus aureus*.³⁶

Pseudarthrosis is a leading cause of persistent or recurrent pain after spinal fusion surgery, and can be related to patient factors (tobacco use, diabetes, others), surgical technique (inadequate graft placement or poor fusion bed preparation), or mechanical factor (hardware failure, inadequate stabilization).³⁷ Revision surgery is the preferred treatment in patients suffering from symptomatic pseudarthrosis. These patients should undergo an infectious workup preoperatively because deep infection can lead to pseudarthrosis. When SSI is not suspected by clinical signs or laboratory tests

(blood counts, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]), diagnosis of “aseptic pseudarthrosis” is made.³⁷ However, because of its low-virulence, recent studies highlighted *C. acnes* as a possible cause of some presumed aseptic pseudarthrosis, suggesting that ongoing infection may affect local osteogenesis.^{16,38,39} *C. acnes* has a particularly long incubation period, with cultures held for at least 14 days, as it can be missed if not held for enough time.⁴⁰ SSI after spinal fusion surgery caused by low-virulent *C. acnes* is difficult to detect because patients may have an indolent clinical picture. Back pain remains the main symptom reported, and most of patients are afebrile.¹⁵ Moreover, level of ESR and CRP may be normal or only slightly elevated, and the absence of inflammatory markers cannot rule out infection.⁴¹ In their retrospective review of 578 revision surgeries, Shifflet et al reported that *C. acnes* was cultured in 54.2% of cases with the primary diagnosis of aseptic pseudarthrosis, suggesting that, in revision surgery, cultures should be held for *C. acnes*, particularly in the setting of pseudarthrosis.¹⁶ These data have also been widely discussed in the shoulder literature,^{42,43} although it is not clear whether positive cultures constantly translate into clinical infection.⁴⁴

These data may explain, at least in part, the high prevalence (38.9%) of SSI caused by *C. acnes* unexpectedly found in the group of patients who underwent revision surgery for suspicion of presumed aseptic pseudarthrosis on ^{18}F -NaF PET/CT. Our results support the utility of intraoperative cultures in revision cases for pseudarthrosis, even without preoperative clinical suspicion of SSI.

This study had several limitations, including its retrospective nature. First, it was not a pure control study. Although the SUV_{max} values were significantly higher in the revision surgery group, the small number of patients made receiver operating characteristics curve analysis statistically irrelevant. Thus, the true value of ^{18}F -NaF PET/CT scanning in the assessment of painful interbody pseudarthrosis remains undetermined. Moreover, if physicians were blinded to the data of revision surgery, they were not blinded to the clinical and imaging information of the patients obtained before ^{18}F -NaF PET/CT. Finally, in our institution, only patients suffering from substantial pain with a high suspicion of pseudarthrosis are surgically explored, which may introduce a bias in the patient population.

On the other hand, it was not possible to evaluate the impact of the different types of hardware (implant, bone graft) on ^{18}F -NaF uptake due to the limited number and as only PEEK cages, associated with autograft for lumbar fusion and synthetic bone graft substitute for cervical fusion, were used in the revision surgery group. Additionally, the control group was not homogeneous since three of the five fused patients had PEEK cages (with autograft), and two patients underwent osteosynthesis with transpedicle screws with rods but without cage implantation. Consequently, the value of ^{18}F -NaF PET/CT remains unknown for others types of implant materials like titanium or bone graft materials such as bone morphogenetic protein, which has been reported in a retrospective study by Heimbürger et al to cause false positive SPECT/CT bone scans in some patients.⁴⁵

Regarding the radiation safety, the effective dose equivalent for ^{18}F -NaF radiotracer is 0.023 mSv/MBq, which corresponds to a maximum effective dose equivalent of approximately 2.3 to 4.6 mSv (administered activity of 100–200 MBq). The radiation burden of a ^{18}F -NaF PET/CT is slightly superior to conventional SPECT/CT bone scan.⁴⁶

Conclusions

^{18}F -NaF PET/CT imaging is a useful tool to identify pseudarthrosis in patients with persistent or recurrent pain after spinal fusion surgery when standard conventional imaging remains inconclusive, especially in the early postoperative phase. Although further studies with a larger number of patients are required, ^{18}F -NaF PET/CT may help stratify patients and select those who would most likely benefit from revision surgery. Unexpectedly, we found a high prevalence (38.9%) of SSI caused by *C. acnes* in the group of patients who underwent revision surgery for suspicion of presumed aseptic pseudarthrosis. These data support the utility of intraoperative cultures in revision cases for symptomatic

pseudarthrosis, even without preoperative clinical suspicion of SSI.

Conflict of Interest

None.

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