Journal of
Nuclear Medicine & Radiation Therapy

Case Series Open Access

^{18}F Sodium Fluoride PET Bone Scan: Initial Experience

Geoff Currie[1]*, John Barlow[2], Elizabeth Brettschneider[2] and Michael Crook[2]

[1]Charles Sturt University, NSW, Australia
[2]Queensland Xray, QLD, Australia

Abstract

A number of ^{99}Mo shortages in Australia in 2018 and 2019 drove lobbying for substitution of some PET procedures as equivalent for the same Medicare rebate/reimbursement approved for general nuclear medicine. Approval of ^{18}F NaF bone PET as a substitute for bone scans in all pathologies had the largest impact with respect to patient numbers and relieving ^{99m}Tc utilisation. This review provides a case-based insight into the initial experience of using ^{18}F NaF PET bone scanning as a substitute for ^{99m}Tc based bone scanning on a gamma camera; highlighting application in a variety of pathologies.

Keywords: PET; NaF; Sodium fluoride; Bone scan

Introduction

The nuclear médicine bone scan using ^{99m}Tc diphosphonate radiopharmaceuticals has been a key diagnostic procedure in a wide range of pathological conditions; trauma, metastatic spread of cancer, avascular disease, metabolic disease, degenerative disease, infection to list a few. Indeed, In Australia and no doubt many countries around the globe, the ^{99m}Tc bone scan is the most frequently performed nuclear medicine scan. Early gamma camera-based radiopharmaceuticals included ^{67}Ga citrate and ^{18}F sodium fluoride (NaF). ^{67}Ga citrate has weak calcium analogue properties that were enhanced by inclusion of carrier in previous production methods. Today, carrier free ^{67}Ga citrate sees insufficient bone accumulation for adequate bone scanning, however, from time to time enhanced bone accumulation may be noted following gadolinium enhanced MRI imaging that provides an insight into the limited capabilities of the former tracer. ^{18}F NaF was approved in the 1970s by the USA FDA and, despite enhanced localisation properties, suffered the poor sensitivity of imaging 511 keV gamma emissions on a gamma camera compared to the 140 keV of ^{99m}Tc. The global ^{99m}Tc crisis has been widely reported and discussed, and is associated with dated reactors and lack of new reactor installations in the northern hemisphere leading to recurring ^{99m}Tc supply stress [1]. In Australia, high production capabilities in the new OPAL reactor at ANSTO generally mean there is no shortage of ^{99m}Tc [1]. Moreover, when faults invariably occur in high end technology, Australia has had a partnership with the South African facility (NTP) that has seen ^{99}Mo bulk transported to Australia to create an almost seamless ^{99m}Tc supply locally. Nonetheless, in early 2010 Australia suffered a ^{99m}Tc crisis with the national reactor closed for routine maintenance causing 'shock waves' through the nuclear medicine community [1]. On 16 June 2018, ANSTO experienced a mechanical failure on the ^{99}Mo/^{99m}Tc generator production line and the 10-day repair evolved into a 7-month shortage. A 2-week window of decreased activity occurred in June 2019 following an accidental high exposure to staff. Production quickly returned to normal domestic supply. On 6 September 2019, a valve failure in the recently commissioned ANM facility (extraction hot cell) brought ^{99}Mo/^{99m}Tc generator production to a halt once again. During the 2018 crisis, lobbying for substitution of some PET procedures as equivalent for the same Medicare rebate/reimbursement began. While there was little traction, the acute crisis of September heralded an awareness that national ^{99m}Tc supply lack security and provided some momentum to argue for substitution as a safety net. The Federal Government approved the following funded PET substitutions (irrespective of pathology):

- ^{18}F FDG brain scans as a substitute for cerebral perfusion SPECT in all pathologies.
- ^{18}F NaF bone PET as a substitute for bone scans in all pathologies.
- ^{68}Ga galligas/^{68}Ga MAA as a substitute for ventilation perfusion lung scans.
- PET myocardial perfusion as a substitute for SPECT myocardial perfusion in all pathologies.

Prior to this decision, none of the applications for PET were approved or rebatable. Indeed, ^{18}F NaF PET was not rebatable even in the evaluation of metastatic spread of cancer. The basic premise of these substitutions is that, during scarce supply of ^{99m}Tc, the PET based substitution for those departments with PET provides a pathway to manage workload and accommodate urgent patients, without increasing tension on the ^{99m}Tc market. Furthermore, the use of PET substitution for those with PET increases the availability of ^{99m}Tc for those sites without PET. This review provides a case-based insight into the initial experience of using ^{18}F NaF PET bone scanning as a substitute for ^{99m}Tc based bone scanning on a gamma camera; highlighting a variety of pathologies.

Method

The protocol generally followed was that defined by the Society of Nuclear Medicine and Molecular Imaging [2] and European Association of Nuclear Medicine [3]. Unfasted, well hydrated patients were administered approximately 250 MBq of ^{18}F NaF intravenously and scanned 30-120 minutes post injection. Our initial experience with early imaging times at 30 minutes demonstrated poor uptake in long bones and, thus, the protocol was adjusted to be a minimum of 60-90 minutes post injection for commencement of scanning. This observation and protocol adjustment is in keeping with observations

***Corresponding author:** Currie G, Associate Professor in Nuclear Medicine, School of Dentistry and Health Sciences, Charles Sturt University, Wagga Wagga, Australia, Tel: 61269332822; E-mail: gcurrie@csu.edu.au

Received October 24, 2019; **Accepted** November 22, 2019; **Published** November 30, 2019

Citation: Currie G, Barlow J, Brettschneider E, Crook M (2019) ^{18}F Sodium Fluoride PET Bone Scan: Initial Experience. J Nucl Med Radiat Ther 10: 409.

Copyright: © 2019 Currie G, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

and recommendations of both the SNMMI [2] and EANM [3]. Whole body PET/CT was performed on either a GE Discover 690 or Siemens Biograph mCT Flow with the arms down using 15 bed positions to cover head through to toes over 15-22.5 minutes using between 1 and 1.5 minutes per bed position. Specifically, a low dose CT was performed for localization and attenuation correction followed by whole body PET in 3D mode. All data was reconstructed using iterative reconstruction (OSEM) with time of flight. Attenuation corrected images were displayed in sectional planes, rotating MIP and with and without co-registered CT.

Case Description

The first week of substitution saw a number of patients undergo ^{18}F NaF bone PET as an alternative to the conventional ^{99m}Tc based bone scan. While these cases do not provide the most significant disease or the larger volume of studies performed using substitution nation-wide, they do provide a glimpse at the quality and various clinical applications of ^{18}F NaF bone PET in malignant (Figure 1) and benign disease. A comparison of the ^{18}F NaF PET scan with the previous ^{99m}Tc diphosphonate bone scan demonstrates the enhanced image quality provided by PET (Figure 2). It should be noted that the PET images displayed are pooled for comparison with the traditional bone scan. The advantages of assessing the whole body PET in slices, including co-registered with CT, are not evident from these images (Figure 3). A number of benign applications of ^{18}F NaF PET bone imaging are also reported including an evaluation of a sclerotic 5th rib (Figure 4A), evaluation of flank and buttock pain in a patent with normal CT and MRI (Figure 4B), assessment of back pain (Figure 4C), evaluation of suspected sacroiliac joint arthropathy (Figure 4D), suspected osteomyelitis of a finger (Figure 5), and assessment of thigh pain in a patient with hyperparathyroidism (Figure 6). From a technical perspective, Figure 4A provides an example of a high quality axial scan performed with 247 MBq of NaF and scanned 28 minutes after administration with corresponding poor appendicular uptake. In contrast, Figure 4B is a 249 MBq dose of NaF scanned at 92 minutes post administration demonstrating improved appendicula accumulation but corresponding decrease in quality post radionuclide decay. Non traumatic pain and previous trauma can be evaluated (Figure 7), evaluation of the joint prosthesis can be undertaken (Figure 8), and challenges of assessing widespread metastatic disease progression in significant scoliosis/kyphosis (Figure 9) can be overcome.

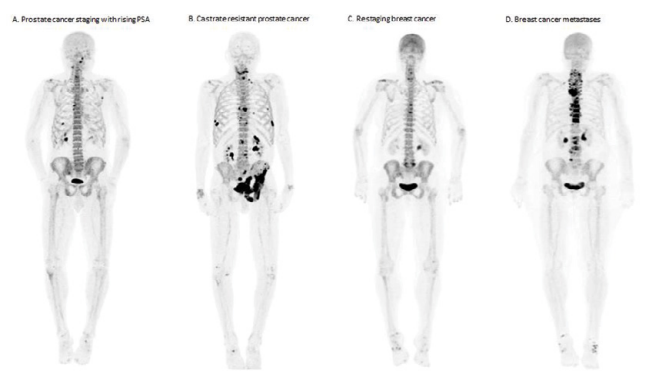

Figure 1: Application of ^{18}F NaF PET bone imaging in malignancy for prostate cancer staging (A) or re-staging (B), and breast cancer restaging (C) and monitoring progress (D).

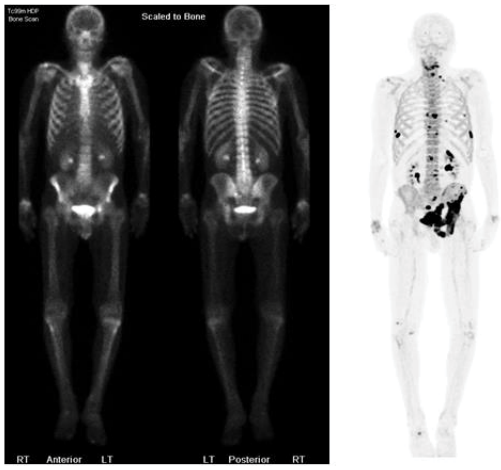

Figure 2: A patient with metastatic castrate resistant prostate cancer with significant osseous bony disease in the pelvis and left proximal femur. The ^{18}F NaF PET scan (right) demonstrates enhanced image quality over the previous wholebody scan (left). It should be noted that the PET images are pooled for comparison with the traditional bone scan and the advantages of assessing the whole body in slices, including co-registered with CT, are not evident from this comparison.

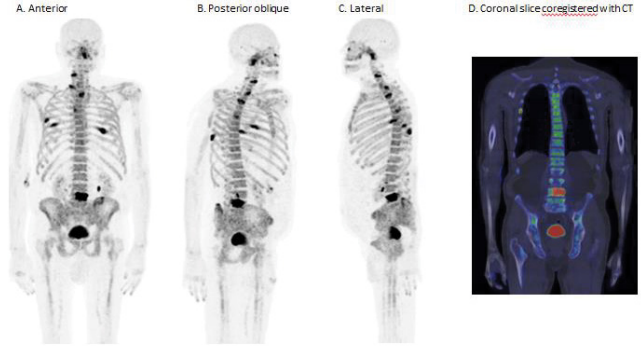

Figure 3: Pooled data displayed and reorientated for anterior (A), posterior oblique (B) and lateral (C) projections. PET studies can be displayed sliced into traditional or custom planes and co-registered with the CT. A coronal slice is co-registered with CT to deepen insight into the lumbar lesion (D).

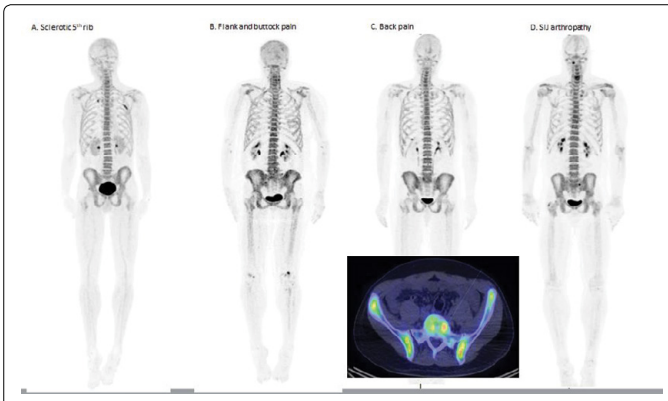

Figure 4: A number of benign applications of ^{18}F NaF PET bone imaging including an evaluation of a sclerotic 5th rib thought to be benign with on-going Ct surveillance recommended (A), evaluation of flank and buttock pain in a patent with normal CT and MRI provided no physiological evidence of non-degenerative disease (B), assessment of back pain after previous microdiscectomy demonstrated a Schmorl's node on the left at L5/S1 (C), and evaluation of suspected right sacroiliac joint arthropathy demonstrated degenerative osteophytosis in L5/S1 and C5/6 degeneration but no sacroiliac pathology (D).

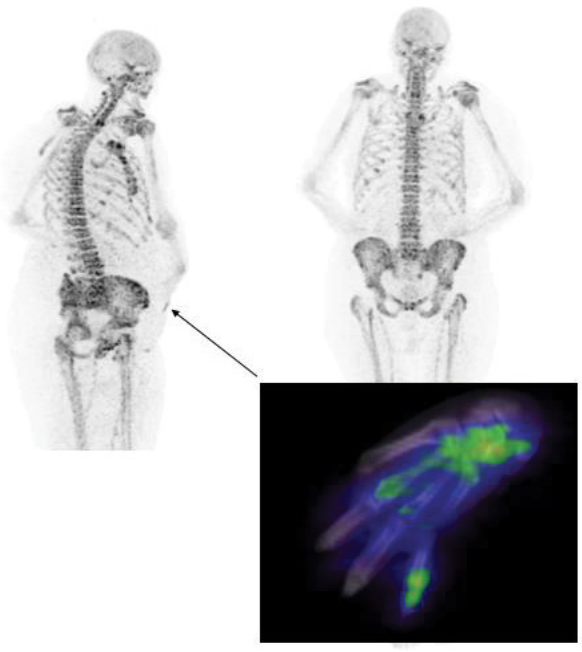

Figure 5: The patient presented with a reddened small left finger to rule out osteomyelitis. There were limitations for PET for this particular indication as blood flow and pool images were not able to be obtained. The traditional palmar views that also would have been acquired were not possible due to the level of patient pain and discomfort.

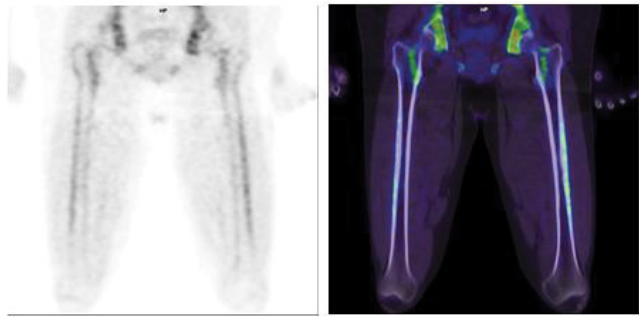

Figure 6: A patient presented with thigh pain with a history of hyperparathyroidism. Low grade, diffuse bilateral femoral uptake of NaF was thought to be periostitis.

Discussion

Since the early limitations of ^{18}F NaF PET, there has been a re-emergence of the technique specifically for the evaluation of bone metastasis and this has been driven by the wider availability of PET, the role PET plays in staging, re-staging and monitoring progression or response to therapy, and the enhanced diagnostic utility of hybrid imaging with PET/CT [4,5]. Beyond metastatic evaluation, the British Nuclear Medicine Society recommends ^{18}F NaF PET bone imaging in a variety of benign and malignant diseases for selected patients [4] and this may reflect responsiveness to the more chronic strain on ^{99m}Tc availability. While there has been general support for the use of ^{18}F-NaF PET/CT for skeletal metastases, the framework for widespread replacement of the conventional bone scan is absent due to limited availability of PET/CT relative to conventional gamma camera technology (particularly penetrating into smaller communities), and

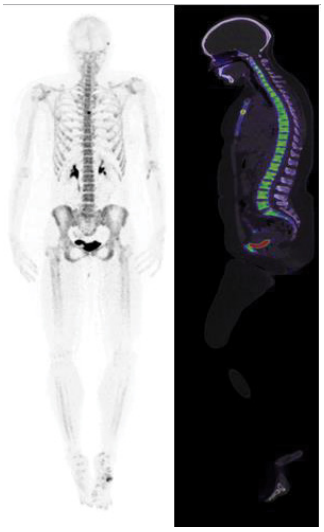

Figure 7: A patient presented with sternal pain but no history of trauma. Focally intense NaF accumulation was demonstrated in the sterno-manubrial joint. CT demonstrated corresponding sclerosis with no erosions or fracture. The differential diagnosis of stress changes or inflammatory arthropathy was reported. Inflammatory accumulation was noted in the left temporal bone and left foot accumulation was correlated with previous trauma.

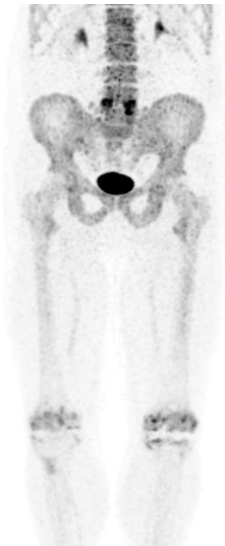

Figure 8: The patient presented with left knee pain and a history of bilateral total knee replacements. Patchy low to moderate grade NaF uptake was noted in both knees suggestive of osseous remodelling or low grade stress reaction rather than infection or loosening. Moderate NaF accumulation in L4/L5 associated with facet joint arthropathy was also noted.

the lack of funding for the procedures in many developed economies including Australia, USA and UK. Nonetheless, ^{18}F NaF has been used sparingly in clinical practice and interest in its use appears to be growing. These cases highlight not only the value and versatility of ^{18}F NaF in metastatic bone disease but also in other bone pathologies. Perhaps a limitation of more widespread adoption of ^{18}F NaF for bone PET is the reliance on cyclotron production (simple chemistry) and short half-life for transportation (110 min). This also highlights the enormous value of the ^{99}Mo/^{99m}Tc generators system in providing high quality, reliable and regular access to the versatile ^{99m}Tc radionuclide.

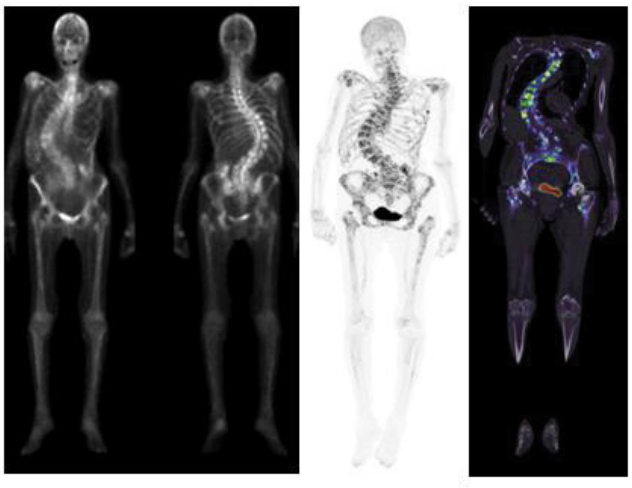

Figure 9: The patient presented with a history of metastatic breast cancer for a progress scan. The previous ^{99m}Tc based bone scan (left) was performed 3 months prior. Interval increase in size and number of widespread sclerotic lesions in axial and appendicula skeleton was noted on the current PET/CT NaF scan (right). Bilateral hip replacement was also noted as was significant scoliosis / kyphosis.

The pharmacokinetics of ^{18}F NaF are more favorable than ^{99m}Tc diphosphonate radiopharmaceuticals with almost 100% extraction into bone on first pass after intravenous injection leading to localization rates that are not only twice that of ^{99m}Tc diphosphonates but also occurring much early [4-6]. The ^{18}F NaF also has much lower plasma protein binding (0% compared to 30% for ^{99m}Tc diphosphonates) which leads to more rapid clearance (kidney) from soft tissues further enhancing image quality [4-6]. The rapid clearance of ^{18}F NaF from soft tissue follows a biphasic model with 0.5 hour and 2.6 hour half-lives [5]. At 60 minutes post intravenous administration of ^{18}F NaF, only 10% of the injected dose remains in the vascular compartment [5,6]. These factors combined allow ^{18}F NaF imaging to commence 45-60 minutes after intravenous administration (matched with short half-life). While ^{18}F NaF localizes in bone in a similar fashion as ^{99m}Tc based diphosphonates, specifically, ion exchange with hydroxyl ions on hydroxyapatite crystals forms fluorapatite which reflects blood flow, binding sites (osteoblastic) and remodelling [4-6]. The argument against the more widespread use of ^{18}F NaF bone PET as an alternative to traditional bone scans is that with the increased sensitivity comes a decrease in specificity. ^{18}F NaF detects more lesions but causes more false positives where the increased lesion detection may not change staging or patient management. With respect to bone metastases, ^{99m}Tc diphosphonate imaging has been reported to have a sensitivity of 70% and specificity of 57% which improved to 92% and 82% respectively with the addition of SPECT [7]. The same study reported ^{18}F NaF PET with 100% sensitivity but only 62% specificity which improved to 100% and 100% with the addition of PET/CT typical of current study protocols [7]. ^{18}F NaF PET has been reported to have higher overall accuracy than ^{99m}Tc diphosphonate bone scans in both malignant and benign skeletal conditions [5]. ^{18}F NaF has been reported spine and pelvis pain, stress and sports injuries, bone viability, inflammatory processes (including 3 phase studies), and metabolic disease with the advantage of potential quantitation [5,6].

Conclusion

This article provides an insight into the use of ^{18}F-NaF in a variety of skeletal pathologies as an alternative to traditional ^{99m}Tc based bone scanning with specific applications in meeting clinical demands during periods of ^{99m}Tc shortage. While a number of false positive lesions might be detected, the addition of the co-registered CT enhances specificity. ^{18}F NaF is unlikely to universally replace ^{99m}Tc based bone scanning, especially given the limited availability and increased cost of PET, but substitution funding provides an essential safety net during times of ^{99m}Tc shortage that allows continuation of patient care and management.

References

1. Currie G, Kiat H, Wheat J (2010) Global contrast in nuclear medicine. J Nucl Med Technol 38: 115-116.
2. Segall G, Delbeke D, Stabin MG (2010) SNM practice guideline for ^{18}F-fluoride PET/CT bone scans. J Nucl Med 51:1813-1820.
3. Beheshti M, Mottaghy FM, Payche F (2015) ^{18}F-NaF PET/CT: EANM procedure guidelines for bone imaging. Eur J Nucl Med Mol Imaging 42:1767-1777.
4. Kulshrestha RK, Vinjamuri S, England A, Nightingale J, Hogg P (2016) The role of ^{18}F-Sodium Fluoride PET/CT bone scans in the diagnosis of metastatic bone disease from breast and prostate cancer. J Nucl Med Technol 44: 217-222.
5. Grant FD, Fahey FH, Packard AB, Davis RT, Alavi A, et al. (2008) Skeletal PET with ^{18}F-Fluoride: applying new technology to an old tracer. J Nucl Med 49: 68-78.
6. Czernin J, Satyamurthy N, Schiepers C (2010) Molecular mechanisms of bone ^{18}F-NaF deposition J Nucl Med 51: 1826-1829.
7. Sapir EE, Metser U, Mishani E, Lievshitz G, Lerman H, et al. (2006) The detection of bone metastases in patients with high risk prostate cancer: ^{99m}Tc-MDP planar bone scintigraphy, single- and multi-field-of-view SPECT, ^{18}F-fluoride PET, and ^{18}F-fluoride PET/CT. J Nucl Med 47: 287-297.