ISSN: 2469-4096

Gratis

Integrative Biomedical Sciences

Research Article

The Promising Role of Dynamic ^{18}F-NaF PET-CT in Diagnosing Symptomatic Joint Prosthesis

Olu Adesanya[1*], Pedro Foguet[2] and Charles Hutchinson[1]

[1]University of Warwick, Coventry, CV4 7AL, England, UK
[2]University Hospitals Coventry and Warwickshire NHS Trust, Clifford Bridge Road, 31 Walsgrave, Coventry, CV2 2DX, UK

Received: May 26, 2015; Accepted: June 12, 2015; Published: June 15, 2015

Abstract

Our purpose was to establish proof of principle case study for the use of dynamic ^{18}F-NaF PET-CT in the assessment of knee and hip prostheses. Approval was granted by the research ethics committee and informed consent was obtained. This is a case study investigating the role of dynamic ^{18}F NaF PET-CT in a patient with bilateral knee prostheses (1 symptomatic/painful and 1 asymptomatic). Both knees were studied with dynamic ^{18}F-NaF PET-CT technique to demonstrate the different pattern of uptake in normal/asymptomatic joint as well as painful joints with aseptic loosening. In addition, a knee aspirate was obtained from the symptomatic knee and serum C-reactive protein and erythrocyte sediment rate levels as well as a peripheral white cell count were obtained in addition to 12 month clinical follow up. Images were obtained with multi-sequential dynamic image acquisition in list mode using GE Healthcare® volume imaging protocol (ViP) after an intravenous injection of 250 MBq ^{18}F-NaF. The images were interpreted as normal, loosening or septic loosening based on the graphical pattern of tracer uptake produced at the bone-prosthesis interface. A final diagnosis was made by a combination of joint aspiration microbiology and clinical follow-up for 1 year; in addition to C-reactive protein and erythrocyte sediment rate levels as well as peripheral white cell count. NaF PET results were compared with 3-phase dynamic bone scan results and plain radiographs. The degree of uptake in the symptomatic joint exceeded background levels and also levels of uptake in the asymptomatic knee. The pattern of uptake and curve slope in both the asymptomatic and symptomatic joints matched the pattern of uptake in our hypothesis. Dynamic ^{18}F-NaF PET-CT is a useful imaging modality for assessing painful joint prosthesis. It can differentiate between asymptomatic joints and aseptic loosening. However, more work is required for the detection of septic loosening.

Introduction

As the population ages and the average body mass index rises, lower limb arthroplasty will become more common [1]. A significant number of these patients may go on to experience pain at the site of arthroplasty at some point after surgery. Arthroplasty pain can signal biomechanical failure, peri-prosthetic infection or septic loosening of the joint [1]. Approximately 10% of lower limb arthroplasties need surgical revision because of the pain [1].

***Correspondence:** Olu Adesanya, University of Warwick, Coventry, CV4 7AL, England, UK, E-mail: adesanya@doctors.org.uk

Materials and Methods

Our patient was a 72 year old female with a painful left knee total knee replacement studied with dynamic ^{18}F-NaF PET-CT. She had underwent routine clinical and laboratory studies for the evaluation of painful prostheses, in addition to the dynamic NaF PET-CT scan. The NaF PET-CT scan was were obtained more

than 12 months after joint replacement surgery. The interval between arthroplasty and PET-CT was 8 years. The patient gave written informed consent for the study. 18F-NaF PET-CT - Dynamic 18F-NaF PET-CT images were acquired using a GE Discovery ST with 16 slice CT (GE Healthcare®) volume imaging protocol (ViP) [2]. The patient fasted for at least 6 hours before receiving the injection. CT images of the joints were acquired, followed by dynamic PET image acquisition in list mode from the time of injection till 30 to 40 minutes after bolus intravenous administration of 250 MBq ^{18}F NaF [2]. The images were reconstructed using ordered-subset expectation maximization, and images were corrected for attenuation.

Image Interpretation – two experienced radiologists read the studies independently, and in the case of discrepancies, a consensus was reached following discussion. When an area of increased uptake was detected in the bone-prosthesis interface of the knee arthroplasty in comparison with adjacent bone and soft tissue, the region of interest was assessed using time-activity curves with simple standardized uptake value (SUV) analysis and background subtraction [3]. Graphical interpretation was performed using our hypothesis to determine the presence of infection, aseptic loosening or neither (Figure 1). The CT images were analysed for malignment of the prosthesis.

Follow-up - The final diagnosis was made by joint aspiration and clinical follow-up for 1 year. Arthroplasties were considered infected if aspiration cultures grew organisms, if infection was clinically obvious or if microbiological samples demonstrated infection or elevated neutrophils. Arthroplasties were considered aseptic if the preceding investigations were negative and this was backed by normal C-reactive protein and erythrocyte sediment rate levels as well as a normal peripheral white cell count. Furthermore, arthroplasties that did not require surgical exploration during the follow-up period were considered uninfected.

Results

The dynamic ^{18}F-NaF PET-CT scan correctly revealed a normal asymptomatic right knee and aseptic loosening in the symptomatic left knee (Figure 2 a-e). The degree of uptake in the symptomatic joint exceeded background levels and also levels of uptake in the asymptomatic knee. The pattern of uptake and curve slope in both the asymptomatic and symptomatic joints matched the pattern of uptake in our hypothesis based on the understood pattern of uptake in dynamic bone scans [4] and the relatively higher degree of ^{18}F-NaF uptake in infection [5]. There is a steeper slope and higher plateau of uptake in the symptomatic loose knee prosthesis, when compared with asymptomatic knee prostheses (Figure 2 d-e).

Discussion

^{18}F-NaF PET-CT has been used extensively for the detection of bone metastases. However, ^{18}F-NaF uptake is not specific for bone malignancy and increased bone uptake may occur with any other condition resulting in increased blood flow and increased bone turnover [6], hence lowering ^{18}F-NaF specificity. ^{18}F-NaF accumulation is well recognised in fractures and a variety of metabolic bone disease such as renal osteodystrophy, Paget's disease and fibrous dysplasia [7] as well as infection or inflammation [8]. This study demonstrates that the use of dynamic ^{18}F-NaF for diagnosing the presence or absence of prosthetic loosening is viable. Larger multi-centre trials are required, especially to prove the role of this novel technique for the detection of peri-prosthetic infection. Pre-surgical accurate diagnosis or elimination of periprosthetic infection significantly allows clinical teams to accurately plan management [1], because current assessment methods often require the combination of clinical signs, laboratory findings and often several sequential imaging studies [9] to differentiate loosening from post-operative change and infection with an acceptable sensitivity and specificity [10]. Although the plain radiograph gives important information regarding joint stability, malrotation and malignment as well as the choice of the type of prosthesis [11]; the role of plain radiographs in the diagnosis of infection associated with prostheses is limited because of nonspecific findings common to both septic and aseptic loosening [1]. Joint aspiration or biopsy is a valuable preoperative diagnostic tool for the detection of sepsis, with a sensitivity and specificity ranging from 50% to 93%

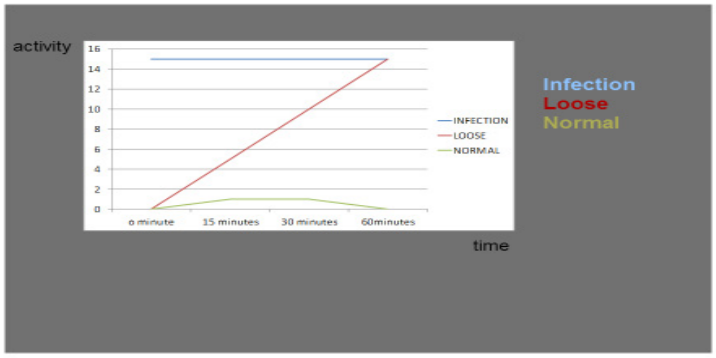

Figure 1: Sequential multiphase pattern of uptake in ^{18}F-NaF PET-CT in the Dynamic Imaging of Joint Prostheses.

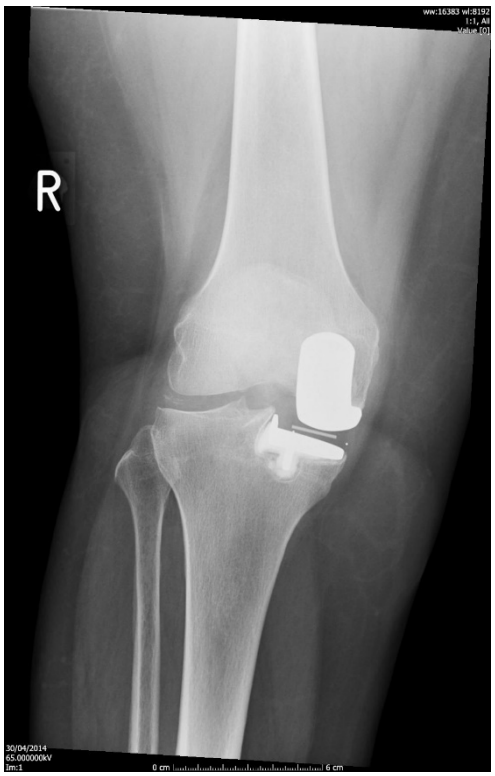

Figure 2a: Asymptomatic right knee with no osteolysis.

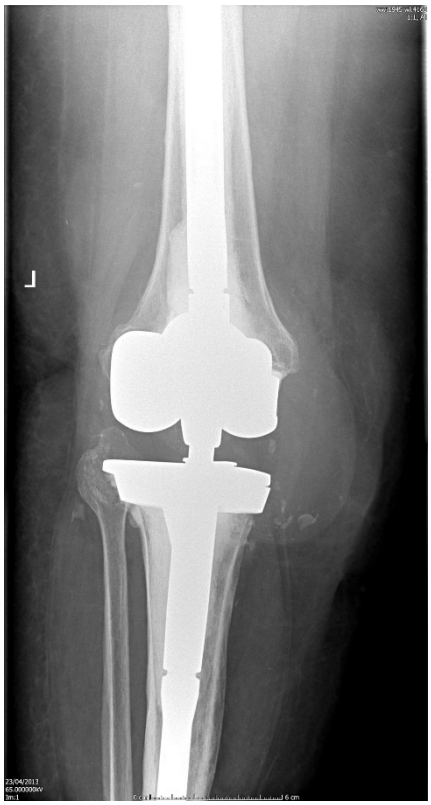

Figure 2b: Symptomatic left knee showing periprosthetic osteolysis.

and from 82% to 97%, respectively [1], but this degree of accuracy remains too low to exclude sepsis with certainty [1] and prior antibiotic administration may further reduce sensitivity [1]. Nuclear medicine imaging therefore has a valuable role to play in assessing joint prosthesis for infection. The 3-phase radionuclide bone scan is the most common nuclear medicine investigation for the assessment of joint prosthesis sepsis [12]. However, the presence of orthopaedic hardware reduces the sensitivity of bone scans [10]. Two other limitations are the lengthy examination time and the cost of the examinations [1]. Sequential bone and gallium scans were the first combined studies used to diagnose osseous infection [10] and have been

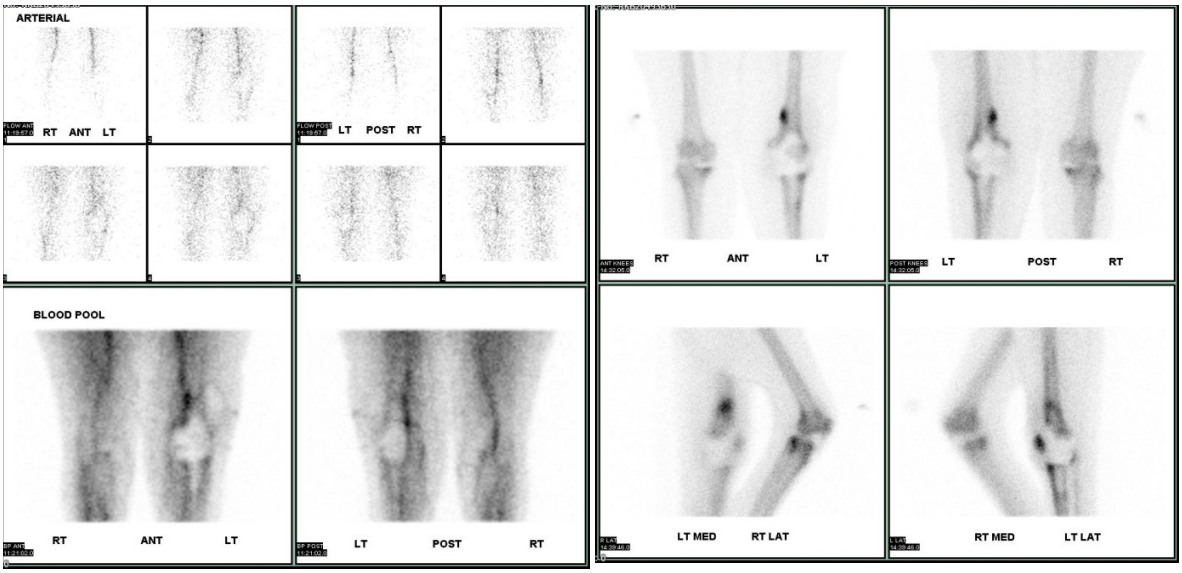

Figure 2c: Arterial & venous phase images showing minimally increased uptake in the symptomatic left knee prosthesis. Subsequent delayed phase images showing marked uptake in left femoral and tibial components in the symptomatic left knee.

applied to painful lower limb prosthesis since the 1970s [1], but are less favoured due to reported low sensitivity of 38% at the lower end of the spectrum in literature [1] or overall accuracy of 65 to 80% at the more optimistic end [10]. Other nuclear medicine studies such as 111In-labeled white blood cell scanning combined with 99mTc- sulphur colloid bone marrow imaging has a sensitivity, specificity, and accuracy of 86%-100%, 89%-94%, and 89%-96%, respectively [1]. Disadvantages of Indium-labelled leukocyte imaging include the demanding man-hours required for vitro labelling with resultant increasing opportunities for iatrogenic errors [1] and the requirement for delayed imaging at 24 hours post-injection [1]. Occasionally, there is a requirement for additional bone marrow imaging, resulting in relatively higher radiation exposure. Attempts have been made with limited success to replace 111Indium-labelled white cell imaging with 99mTechnetium-labelled murine monoclonal antigranulocyte antibody fragments. Tc-99m–labelled murine monoclonal antibody of the immunoglobulin bind with high affinity to CD-15 receptors present on the surface membrane of human polymorphonuclear leukocytes [13] and do not require in vitro labelling process. Antibody fragment imaging has a high negative predictive value [14], but murine antibodies have a reduced plasma half-life of few hours when compared with human IgG half-life of 3 weeks [15]. In addition, the murine IgG invokes a HAMA response that results in faster removal of the mouse IgG, and may also result in anaphylactic hypersensitivity response [15]. The decreased circulating half-life requires increasing administered doses (which can then lead to increasing risk of HAMA, or a reduced effectiveness of the study [15]. Early attempts to justify the use of FDG PET as a single, cost-effective method of diagnosing periprosthetic infection [1,16] have since been proven to be incorrect due to false positive nonspecific peri-prosthetic uptake [17]. The cost of ^{18}F-NaF PET-CT is substantially lower than the combined costs of sequential studies comprising 2 to 3 commonly performed radionuclide scans (mainly 111In-labeled white blood cell scans, bone scans and bone marrow scans) [1,18]. Furthermore, tomographic images with PET provide better spatial resolution than planar conventional nuclear medicine modalities [1], significantly improving test accuracy [1,18]. Dynamic ^{18}F-NaF PET-CT can be completed within an hour, compared with 4 hours to 2 days for other nuclear medicine methods [1].

Figure 2d, 2e shows a patient who had clear evidence of aseptic loosening. Dynamic ^{18}F-NaF PET-CT curve revealed a gentle upslope in the left prosthesis corresponding to osteolysis on the radiograph and delayed the increased uptake on the planar bone scan. The simplicity of the diagnostic criteria proposed

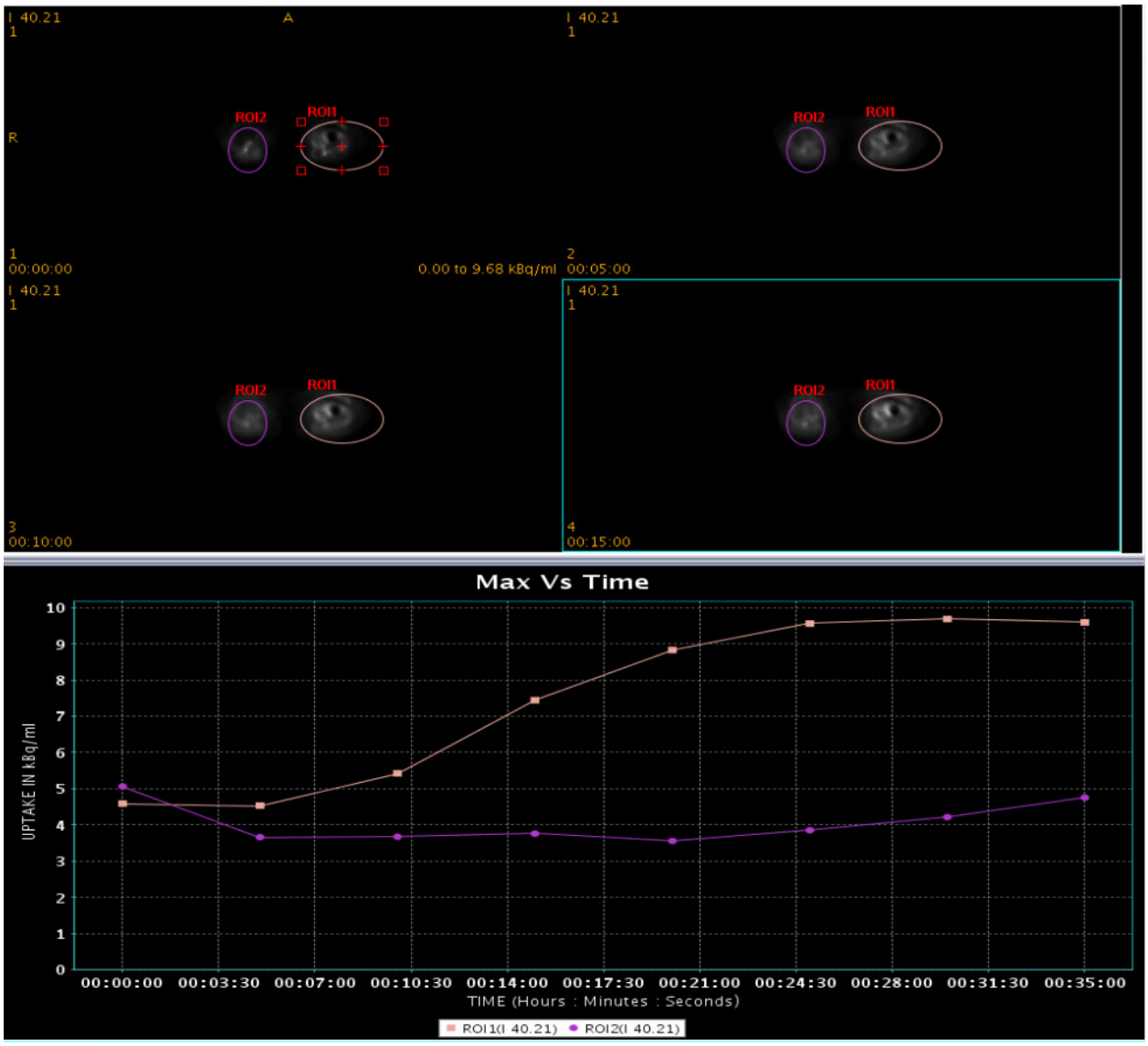

Figure 2d: NaF SUV vs sec. Symptomatic knee (pink) & asymptomatic knee (purple)

CRP, ESR, WCC and Knee aspirate all normal.
Outcome of long-term clinical follow up was loosening.

should reduce potential inter-observer variation and increase the accuracy of interpretation [19]. The interval between surgery and ^{18}F-NaF PET-CT was more than 1 year. Further research is required to confirm this proof of concept for uptake of ^{18}F-NaF in painful prosthesis as well as clearly define the appearance of infection using this promising technique. One of the major advantages of ^{18}F-NaF PET-CT over conventional nuclear medicine techniques is the simplicity of the approach and the timely availability of results within an hour [1].

Conclusion

This preliminary data demonstrates early proof of the principle that dynamic ^{18}F-NaF PET-CT can detect aseptic loosening of lower limb prosthesis and perhaps may reveal peri-prosthetic infection but has some limitations. Dynamic ^{18}F-NaF PET-CT may be more useful than 3 phase bone scans in the assessment of painful hip and knee prosthesis. Routine clinical use should not be engaged until the accuracy of dynamic

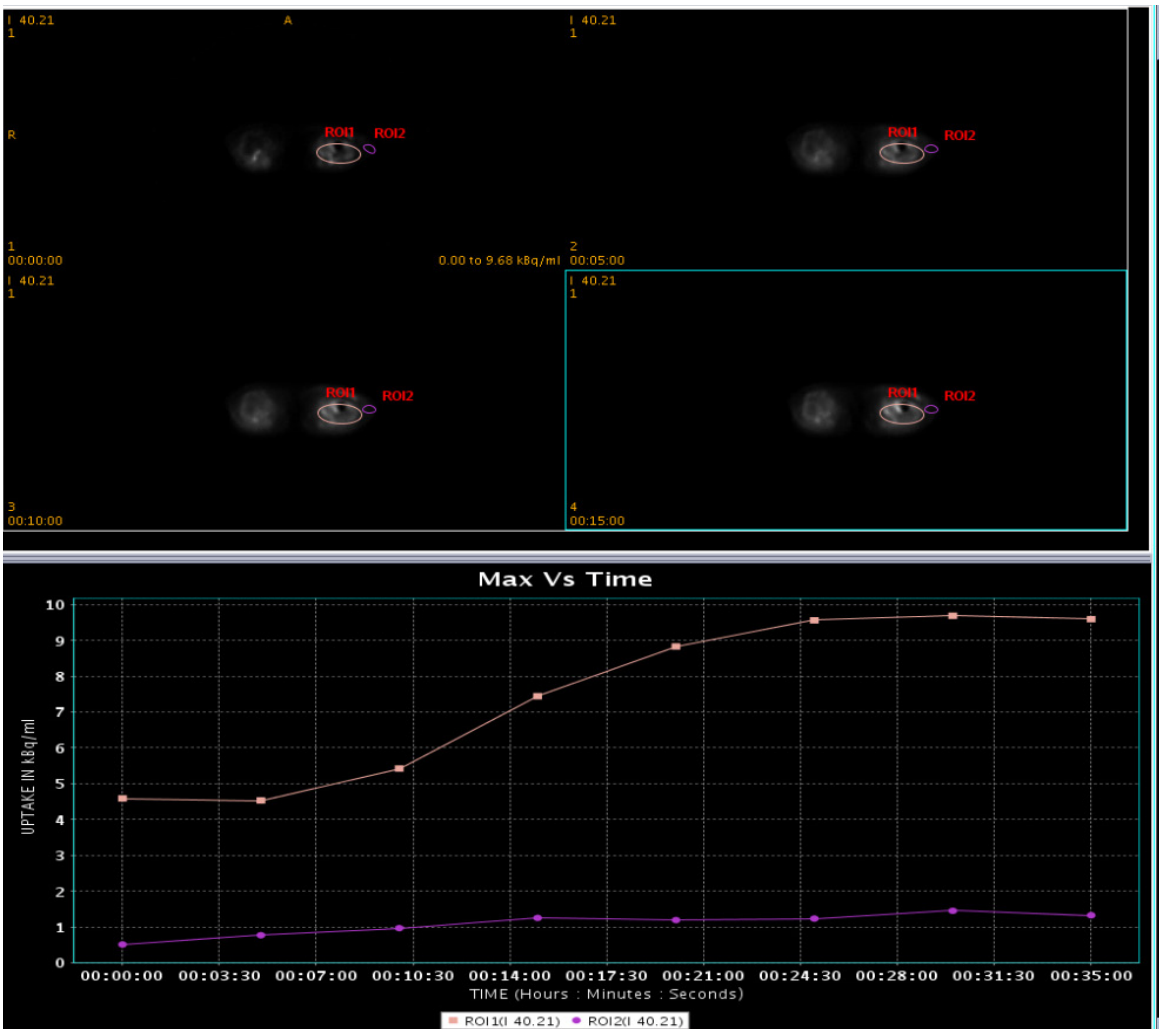

Figure 2e: Symptomatic knee (uptake (pink) & soft tissue background (purple).

^{18}F-NaF PET-CT is fully validated. Future multi-centre research is required to establish a role for dynamic ^{18}F-NaF PET-CT for detecting aseptic loosening and septic loosening. Dynamic ^{18}F-NaF PET-CT provides quicker higher resolution images with anatomic correlation from CT. Further prospective studies using larger cohorts of patients is needed to better understand the role of dynamic ^{18}F-NaF PET-CT in diagnosing symptomatic joint prosthesis.

Acknowledgments

This study was supported in part by Siemens PETNET Solutions and by a research grant from the NIHR Clinical Research Network.

References

1. Zhuang H, Duarte PS, Pourdehnad M, Maes A, Van Acker F, et al. (2001) The promising role of 18F-FDG PET in detecting infected lower limb prosthesis implants. J Nucl Med 42: 44-48.

2. Park SJ, Ionascu D, Killoran J, Mamede M, Gerbaudo VH, et al. (2008) Evaluation of the combined effects of target size, respiratory motion and background activity on 3D and 4D PET/CT images. Phys Med Biol 53: 3661.

3. Wong KK, Piert M (2013) Dynamic Bone Imaging with 99mTc-Labeled Diphosphonates and 18F-NaF: Mechanisms and Applications. J Nucl

Med 54: 590-599.

4. Love C, Marwin SE, Palestro CJ (2009) Nuclear medicine and the infected joint replacement. Semin Nucl Med 39: 66-78.

5. Kobayashi N, Inaba Y, Choe H, Ike H, Fujimaki H, Tezuka T, et al. (2011) Use of F-18 Fluoride PET to Differentiate Septic From Aseptic Loosening in Total Hip Arthroplasty Patients. Clin Nucl Med 36: E156-E61.

6. Czernin J, Satyamurthy N, Schiepers C (2010) Molecular mechanisms of bone 18F-NaF deposition. J Nucl Med 51: 1826-1829.

7. Ryan PJ, Fogelman I (1997) editors. Bone scintigraphy in metabolic bone disease. Semin Nucl Med 27: 291-305.

8. Segall G, Delbeke D, Stabin MG, Even-Sapir E, Fair J, et al. (2010) SNM practice guideline for sodium 18F-fluoride PET/CT bone scans 1.0. J Nucl Med 51: 1813-1820.

9. Cyteval C, Bourdon A (2012) Imaging orthopedic implant infections. Diagn Interv Imaging 93: 547-557.

10. Palestro CJ, Love C, Schneider R (2009) The evolution of nuclear medicine and the musculoskeletal system. Radiol Clin North Am 47: 505-532.

11. Athwal KK, Hunt NC, Davies AJ, Deehan DJ, Amis AA (2014) Clinical biomechanics of instability related to total knee arthroplasty. Clin Biomech (Bristol, Avon) 29: 119-128.

12. Love C, Palestro CJ (2004) Radionuclide imaging of infection. J Nucl Med Technol 32: 47-57.

13. Love C, Tomas MB, Marwin SE, Pugliese PV, Palestro CJ (2001) Role of Nuclear Medicine in Diagnosis of the Infected Joint Replacement. Radiographics 21: 1229-1238.

14. Iyengar KP, Vinjamuri S (2005) Role of 99mTc Sulesomab in the diagnosis of prosthetic joint infections. Nucl Med Commun 26: 489-496.

15. Blaine Templar Smith (2012) Introduction to Diagnostic and Therapeutic Monoclonal Antibodies. UNM College of Pharmacy 17: 1-34.

16. Stumpe KD, Nötzli HP, Zanetti M, Kamel EM, Hany TF, et al. (2004) FDG PET for Differentiation of Infection and Aseptic Loosening in Total Hip Replacements: Comparison with Conventional Radiography and Three-Phase Bone Scintigraphy. Radiology 231: 333-341.

17. Glaudemans AWJM, Signore A (2010) FDG-PET/CT in infections: the imaging method of choice? Eur J Nucl Med Mol Imaging 37: 1986-1991.

18. Gary JR Cook, Ignac Fogelman, Ora Israel (2006) PET Imaging of the Skeleton. Positron Emission Tomography 317-335.

19. Adesanya O, Sprowson A, Masters J, Hutchinson C (2015) Review of the role of dynamic 18F-NaF PET in diagnosing and distinguishing between septic and aseptic loosening in hip prosthesis. J Orthop Surg Res 10: 5.