Published in final edited form as:

Skeletal Radiol. 2014 April ; 43(4): 453–458. doi:10.1007/s00256-013-1795-0.

Correlation of PUV and SUV in the Extremities while using PEM as a High Resolution Positron Emission Scanner

Sania Rahim¹, Osama Mawlawi¹, Patricia Fox², Shree Taylor¹, Richelle Millican¹, Nancy M. Swanston¹, Elliott Brown³, and Eric M. Rohren¹

¹Division of Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX

²Division of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX

³Department of Radiology, Yale University Hospital, New Haven, CT

Abstract

Intro—Due to its unique configuration of two adjustable plate detectors Positron Emission Mammography, or PEM, could theoretically also function as a high resolution positron emission scanner for the extremities or neck. PEM quantitates its activity via a “PEM Uptake Value,” or PUV, and although its relationship to the Standardized Uptake Value, or SUV, has been demonstrated in the breasts, to our knowledge there are no studies validating PUV in other sites such as the extremities.

Materials/Methods—This was a retrospective chart review of two separate protocols of a total of 15 patients. The patients all had hypermetabolic lesions in the extremities or neck on imaging with PET/CT and were sent after their PET/CT to PEM for further imaging. Due to the sequential nature of these exams no additional radiotracer was administered.

Results—A spearman rank order correlation was calculated between the PUV max obtained from PEM images, and the SUVmax for all. The spearman rank order correlation for all sites was 0.42 which is not significantly different from 0 ($p=0.13$). When neck lesions were excluded from the group, there was a strong and statistically significant correlation between PUVmax and SUVmax, with a spearman rank correlation of 0.73 and significantly different from 0 ($p=0.0068$).

Discussion—The correlation of PUV and SUV in the extremities indicates the potential use of PEM as a semiquantitative, high resolution positron emission scanner and warrants further investigation especially in the realm of disease processes that often present in the extremities such as melanoma, osteomyelitis and arthritis as well as playing a role in the imaging of patients with metallic hardware post limb salvage surgery.

Keywords

Positron Emission Mammography; PEM; High Resolution Positron Emission Scanner; PUV; limb salvage imaging

Corresponding Author: Sania Rahim, MD, MPH MD Anderson Cancer Center 1400 Pressler FCT 16.6007 Houston, TX 77030 (Srahim@mdanderson.org; 832 969 7925).

Conflict of Interests: The authors declare that they have no conflict of interest.

Introduction

PEM, or Positron Emission Mammography, is a small portable device with two plate detectors, between which the site of interest is positioned. Like Whole Body Positron Emission Tomography, or WB PET, PEM utilizes the metabolism of F-18 FDG to demonstrate areas of hypermetabolism within the organ of interest. Also like WB PET/CT, PEM utilizes coincidence detection to help localize areas of increased radioactive tracer concentration within the breast. In order to provide a method of quantification, the manufacturers of the PEM created the PUV, or PEM uptake Value. Although the PUV, like SUV represents the activity concentration in the image, unlike the SUV, the calculation of PUV does not account for various data corrections such as attenuation or scattered photons [6]. Although validity of the PUV as a quantification metric has not been well documented a large single study published in the AJR[7] found a statistically significant correlation between SUV and PUV in the breast.

In theory the two adjustable arms of the PEM device may be positioned adjacent to any peripheral lesion. The superior spatial resolution of PEM[8], combined with the possibility of using PUV as a surrogate for SUV, demonstrate a new role for PEM in the evaluation of small, difficult to image, peripherally located lesions. Our institution submitted a protocol for the use of PEM in the evaluation of small, superficially located malignancies. The primary malignancies of 15 patients were evaluated with PET/CT and PEM in order to demonstrate a relationship between PUVmax and SUVmax. The effort to demonstrate a correlation between these two values was sought to evaluate the potential use of PUVmax as a validated surrogate for SUVmax in peripherally located malignancies.

Materials/Methods

This study was approved by our institutional review board. Due to the retrospective nature of this work, information was obtained via chart review. All of the patients who are part of this review had a biopsy proven malignancy and underwent ^{18}F -FDG PET/CT as part of their evaluation. Immediately after their PET/CT, patients were imaged with PEM. Due to the sequential nature of these exams no additional ^{18}F FDG was administered.

PET/CT

F-18 FDG was administered to the patients based on weight, with the administered activity in this patient group ranging from 325.6 – 495.8 MBq (8.8 – 13.4 mCi), with average administered activity of 418.1 MBq (11.3 mCi). Imaging was performed on an integrated PET/CT system (DSTe, RX, VCT, GE Medical Systems, Milwaukee, WI) approximately 60-80 minutes after injection. Noncontrast CT scanning was performed for attenuation correction and image registration. The extent of scanning was tailored to the indication, with inclusion of the extremities as needed.

PEM

PEM imaging was performed following completion of PET/CT. The device used was a PEMFlex Solo II High Resolution PET (Naviscan, San Diego, CA). PEM imaging was

performed between 1.5 and 2 hrs after tracer administration. Since PEM images were obtained immediately after PET/CT imaging no additional radiotracer was administered. The patient was seated in a comfortable position, and a trained technologist positioned the body part of interest between the two plate detectors of the PEM system. One of these detectors is fixed and provides stabilization, while the other adjusts for gentle compression of the body part being imaged. The positioning of these two plate detectors adjacent to the object of interest provides better spatial resolution and count sensitivity than with whole body PET/CT [6], with a reported in plane resolution of 2 mm [9].

PEM's use of two parallel plate detectors does not allow for true tomographic images. Instead, PEM must use limited angle image reconstruction algorithm that employs 3D MELM that results in 12 slices representing the volume between the two detectors. The images were acquired as anterior or lateral. Limited angle reconstruction results in spatial anisotropy, or the distortion of image geometry, particularly in the axial dimension (parallel to the two plate detectors) thus the exact geometry of the lesions was not consistent from view to view.

Image Analysis

PET/CT images were sent to an Advantage Windows AW reading station (GE, Milwaukee) where they were reviewed by an experienced reader. The lesion that had been previously seen on initial imaging or on biopsy was identified and a ROI was drawn to calculate its SUVmax (body weight calculation). The calculated SUV represents the ratio of concentration of the injected radiotracer activity within the ROI over the concentration of activity distributed throughout the body, normalized by body weight.

PEM images were sent to a work station with Naviscan's proprietary image analysis software. A board certified imager reviewed the 12 images for each view and selected the image with the best qualitative lesion to background ratio and placed an ROI around the lesion. The software supplied a PUV. A PUV to background ratio, although recommended by the manufacturer was not calculated due to the varying anatomical locations of the images and inability to standardize backgrounds.

Results

A spearman rank order correlation was calculated between the PUV max obtained from the frontal view and the SUVmax for all 15 patients. The spearman rank order correlation between the PUVmax and SUVmax for the patients was 0.42 which is not significantly different from 0 ($p=0.13$).

During the data review, two distinct outliers were found ; both neck lesions were found to have inconsistently low PUV values. When these results were excluded there was a strong and statistically significant correlation between PUVmax and SUVmax in the remaining 13 extremities patients with a spearman correlation of 0.73 which significantly different from 0 ($p=0.0068$).

Discussion

The benefits of using metabolic imaging as both a diagnostic and predictive tool has been extensively extolled in the literature. The imaging modality of choice has been WB PET/CT. However, the fundamental limitation of WB PET/CT remains its difficulty in accurately characterizing metabolic activity of lesions smaller than 2.5cm due to partial volume effects and smoothing[6]. The need for a new modality to accurately image and quantify the metabolic activity of lesions smaller than 2.5 cm is clear. PEM has been shown repeatedly to identify lesions smaller than those seen with WB PET/CT [9]; yet the validation of PEM as a means of semiquantitative assessment has been limited. There has only been a single series published by Wang and colleagues, which addresses the validity of PUV in relation to SUV [7]. This study was performed on lesions in the breast and showed a strong and statistically significant spearman correlation of 0.79 between PUV and.

To our knowledge there have been no reports of usage of PEM to semiquantitatively evaluate the extremities or the neck, although the adjustable detector heads allow for such imaging. Broadening the application of the PEM beyond the breast to use PUV as a quantitative metric must address several new considerations, namely the PEM uptake value's lack of standardization or correction. A phantom study found that quantitative accuracy of the PEM (based on administered dose) was affected by thickness of the phantom[10] if this finding were reproducible in vivo, then we would see variations in the correlation between SUV and PUV in smaller objects of interest such as the hands versus larger objects such as the thigh. Although our sample size was too small to appreciate such differences in a statistically significant way, this finding would be interesting to evaluate in a larger study. In addition, factors such as lesion size, attenuation and scatter have also been shown to affect the count density in PEM imaging, thereby influencing PUV [11].

In theory, the variable attenuation characteristics of adjacent bone and tissue would impact the accuracy of PUV when compared to the relative lack of attenuating tissues in the breast which could potentially explain the higher correlation of SUV and PUV in breast in the Wang study versus the correlation seen in the extremities in our study. Despite the multiple factors influencing PUV accuracy, our study demonstrated that there was an overall correlation of PUVmax values were correlative to SUVmax in the extremities group illustrating the potential of PUVmax to act as a surrogate for SUVmax in quantifying metabolic activity.

In our study PUVmax was measured on one view only per patient because positioning difficulties of the extremities prevented image acquisition from a second view in 4 patients. In addition, we chose to compare PUVmax directly to SUVmax without the use of a PUVmax-to-background ratio as recommended by the manufacturer and performed by the Wang study. This decision was made because of the heterogeneity in disease sites, which would have led to significant inconsistency in background measurements.

The lack of correlation between PUV and SUV in the neck was conspicuous and although we had a paucity of patients for which to compare to the extremities group (n=2). The rather suboptimal results seen in the neck were consistent with our understanding of PEM physics.

The absence of correction for scatter with the PUV resulted in scatter from the adjacent brain and heart to decrease count sensitivity in the neck; thereby underestimating the PUV with a resultant lack of correlation with SUVmax for those lesions.

The use of PEM as a high resolution dedicated positron emission scanner that is able to provide a quantified value of activity for disease in the extremities has multiple potential implications for oncology. The use of the SUVmax both as a prognostic factor [12] and as an indicator of response to therapy in cancer imaging [13, 14] has been widely discussed in the literature. The results of our study show that PUV has the potential to act as an SUV surrogate and could in theory function as a prognostic factor or as indicator of therapeutic response as well.

One scenario in which extremity imaging with PEM may be advantageous is in the assessment of peripherally located tumors, or lesions which are of a size which is below the threshold for reliable detection and/or characterization with PET/CT. An excellent example is a patient in this study who had a peripherally located melanoma as seen in Figure 1. The lesion was seen in the medial aspect of the patient's surgical stump and <2.5 cm in size. The PEM images had significantly improved spatial resolution for this lesion, and the uptake was easily quantified by PUV measurement. Although there has been little published work of the evaluation of melanoma with high resolution PET scanners, there has been some preliminary research on uveal melanomas and high resolution PET [15]. The use of high resolution dedicated PET in the form of PEM warrants further investigation in melanoma research.

PEM may also play a role in the imaging of the extremities post placement of metallic hardware in limb salvage surgeries. Although all metallic orthopedic hardware may theoretically heat up immediately prior to scanning, such hardware is generally safe to image with MR. However, the imaging of the extremities with metallic hardware is problematic with beam hardening artifact seen on CT and field distortion and signal voids on MR which can obscure the surgical site [16]. Hardware made out of ferromagnetic materials such as iron, cobalt and nickel produces more artifacts on MR than non-ferromagnetic material such as titanium and tantalum. Yet, on CT artifact is more proportional to the density of the metal hardware, making tantalum significantly more productive of artifact than titanium [17]. MDCT and the several techniques such as altering patient positioning on MR and using alternative sequences such as Fat suppression STIR are currently used to image patients after limb salvage; providing an appreciable improvement in imaging [17]. PEM provides metabolic data with excellent spatial resolution without the impingement of metallic artifact. Although on PET/CT hypermetabolic activity may be seen in the bone adjacent to weight bearing hardware because of increased osseous inflammation, one may presume that this level of activity would be lower and more diffuse than that of recurrent metabolically active disease. Several recent studies and case reports have reported abnormal or artifactual elevations of SUV when imaging patients with metallic prosthesis on PET/CT but these were the results of attenuation correction artifact from the CT [18-19]. Since PEM is not attenuation corrected this should not be an issue.

The potential uses for PEM in the evaluation of the extremities extend beyond oncology and may include other fields in which high spatial resolutions are important, such as infectious disease and rheumatology. Preliminary studies evaluating the use of high resolution PET in arthritis have already been published and a high resolution PET scanner may fulfill some of the objectives of PET/MR[20]. Of particular interest has been the potential usage of methyl-¹¹C-choline, a marker of cellular proliferation, to image the synovium in an effort to gauge active disease[21]. A recent study found that PET/CT was excellent at gauging response to therapy in joints affected by rheumatoid arthritis but the results of smaller joints may have been inaccurate due to low resolution [22]; demonstrating that the potential value of high resolution positron emission scanning in rheumatoid arthritis therapy and monitoring.

Our study is the first to evaluate the validity of PUV in extremity imaging. By demonstrating the correlation between PUV and SUV in the extremities it opens the door for further investigation of the use of PEM as a high resolution imaging device for use in small, peripherally located masses. The potential implications of such usage are vast as multiple disease processes, such as melanoma and lung cancer are often staged when the primary lesion is below the 2.5 cm threshold of SUVmax evaluation. As evidence grows that metabolic activity of primary lesions correlates with disease free survival in certain malignancies [23] the use of an SUV surrogate such as PUV becomes increasingly relevant.

References

1. Checka CM, et al. The relationship of mammographic density and age: implications for breast cancer screening. *AJR Am J Roentgenol.* 2012; 198(3):W292–5. [PubMed: 22358028]
2. Jackson VP, et al. Imaging of the radiographically dense breast. *Radiology.* 1993; 188(2):297–301. [PubMed: 8327668]
3. Berg WA, et al. Reasons women at elevated risk of breast cancer refuse breast MR imaging screening: ACRIN 6666. *Radiology.* 2010; 254(1):79–87. [PubMed: 20032143]
4. Kalles V, et al. The current status of positron emission mammography in breast cancer diagnosis. *Breast Cancer.* 2012
5. Avril N, et al. Breast imaging with positron emission tomography and fluorine-18 fluorodeoxyglucose: use and limitations. *J Clin Oncol.* 2000; 18(20):3495–502. [PubMed: 11032590]
6. MacDonald L, et al. Clinical imaging characteristics of the positron emission mammography camera: PEM Flex Solo II. *J Nucl Med.* 2009; 50(10):1666–75. [PubMed: 19759118]
7. Wang CL, et al. Positron emission mammography: correlation of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 status and 18F-FDG. *AJR Am J Roentgenol.* 2011; 197(2):W247–55. [PubMed: 21785049]
8. Eo JS, et al. Imaging sensitivity of dedicated positron emission mammography in relation to tumor size. *Breast.* 2012; 21(1):66–71. [PubMed: 21871801]
9. Schilling K, et al. Positron emission mammography in breast cancer presurgical planning: comparisons with magnetic resonance imaging. *Eur J Nucl Med Mol Imaging.* 2011; 38(1):23–36. [PubMed: 20871992]
10. Springer A, Mawlawi OR. Evaluation of the quantitative accuracy of a commercially available positron emission mammography scanner. *Med Phys.* 2011; 38(4):2132–9. [PubMed: 21626946]
11. Shkumat NA, et al. Investigating the limit of detectability of a positron emission mammography device: a phantom study. *Med Phys.* 2011; 38(9):5176–85. [PubMed: 21978062]

12. Koolen BB, et al. Association of primary tumour FDG uptake with clinical, histopathological and molecular characteristics in breast cancer patients scheduled for neoadjuvant chemotherapy. *Eur J Nucl Med Mol Imaging*. 2012
13. Koolen BB, et al. Relevance of Breast Cancer Subtypes in Response Monitoring with 18F-FDG PET/CT During Neoadjuvant Chemotherapy. *European Journal of Cancer*. 2012; 48:S42–S42.
14. Kurland BF, et al. Feasibility study of FDG PET as an indicator of early response to aromatase inhibitors and trastuzumab in a heterogeneous group of breast cancer patients. *EJNMMI Res*. 2012; 2(1):34. [PubMed: 22731662]
15. Beyer T, et al. Multi-modality imaging of uveal melanomas using combined PET/CT, high-resolution PET and MR imaging. *Nuklearmedizin*. 2008; 47(2):73–9. [PubMed: 18392316]
16. Fritz J, et al. Imaging of Limb Salvage Surgery. *AJR*. 2012; 198:647–660. [PubMed: 22358005]
17. White L, Buckwalter K. Technical Considerations :CT and MR Imaging in the Postoperative Orthopedic Patient. *Seminars in Musculoskeletal Radiology*. 2002; 6(1):5–17.
18. More Y, et al. Positron-emission tomography pitfalls related to oral prosthesis. *Laryngoscope*. Feb. 2013; 123(2):404–6. [PubMed: 22778055]
19. Abdoli M, Dierckx RA, Zaidi H. Metal artifact reduction strategies for improved attenuation correction in hybrid PET/CT imaging. *Med Phys*. Jun. 2012; 39(6):3343–60. [PubMed: 22755716]
20. Roivainen A, et al. Use of positron emission tomography with methyl-11C-choline and 2-18F-fluoro-2-deoxy-D-glucose in comparison with magnetic resonance imaging for the assessment of inflammatory proliferation of synovium. *Arthritis Rheum*. 2003; 48(11):3077–84. [PubMed: 14613269]
21. McQueen FM, Ostergaard M. Established rheumatoid arthritis - new imaging modalities. *Best Pract Res Clin Rheumatol*. 2007; 21(5):841–56. [PubMed: 17870031]
22. Roivainen A, et al. Correlation of (18)F-FDG PET/CT assessments with disease activity and markers of inflammation in patients with early rheumatoid arthritis following the initiation of combination therapy with triple oral antirheumatic drugs. *Eur J Nucl Med Mol Imaging*. 2013; 40(3):403–10. [PubMed: 23229747]
23. Bastiaannet E, et al. Prognostic value of the standardized uptake value for (18)F-fluorodeoxyglucose in patients with stage IIIB melanoma. *Eur J Nucl Med Mol Imaging*. 2012; 39(10):1592–8. [PubMed: 22801730]

Figure 1.

A) PEM Flex Solo II device B) Two adjustable detector heads which are positioned around the site of interest, one providing compression and the other stabilization. Image credit to Macdonald, et al.

Figure 2.

The patient is an 83 year old man with a history of invasive level IV melanoma of the right great toe, treated with nodal dissection and partial resection of the right great toe. Three years later the patient presented with recurrent invasive level IV melanoma at the surgical site. PET and PEM imaging was performed per protocol. PET images A) demonstrate hypermetabolism in the right great toe but limited spatial resolution of PET limits further evaluation of the lesion. PEM images B) clearly localize the hypermetabolism only to the medial aspect of the surgical stump.

Figure 3.

The patient is a 21 year old male with osteosarcoma of the ulna which was resected days prior to imaging. The PET image depicted in a) demonstrates linear appearing uptake which most likely corresponds to soft tissue but osseous activity cannot be excluded. The lateral PEM images in b) and the anterior PEM image in c) clearly depict hypometabolic activity only within the soft tissue and tracking adjacent to the bone consistent with post-surgical change.

Figure 4.

SUVmax and PUVmax for All Patients. Note: The two significant outliers seen in the non-breast group represent patients with neck imaging

SUV_{max}

Figure 5.
SUV_{max} and PUV_{max} for patients with lesions in the extremities (excluding neck imaging)

Table 1

Patient Histology and Site of Lesion of Interest.

Patient	Location of Imaged Lesion	Histology
1	Right foot	spindle cell sarcoma
2	Right femur	invasive ductal carcinoma
3	Left ulna	osteosarcoma
4	Left wrist	nonsmall cell lung cancer
5	Left fibula	invasive ductal carcinoma
6	Left tibia	osteosarcoma
7	Right tibia	invasive ductal carcinoma
8	Right great toe	melanoma
9	Right femur	diffuse large cell lymphoma
10	Head/neck	sebaceous carcinoma
11	Head/neck	melanoma
12	Left foot	melanoma
13	Left knee	melanoma
14	Right tibia	nonsmall cell lung cancer
15	Right arm	merkel cell carcinoma