

Fewer Angle SPECT/CT (FASpecT/CT) Blood Pool Imaging for
Infection and Inflammation

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Abstract

Rationale: A new protocol for rapid SPECT/CT blood pool imaging consisting of fewer image angle acquisitions was evaluated for localization of focal sites of soft tissue inflammation, infection and osteomyelitis.

Methods: Immediately following dynamic flow and standard planar blood pool imaging with ^{99m}Tc-MDP, fewer angle SPECT/CT (FASpecT/CT) was performed with a dual head gamma camera consisting of 6 steps over 360°, 12 total images with 30° separation between angles and 30 seconds per image requiring a total imaging time of approximately 3 minutes. Images were reconstructed using ordered subset expectation maximization (OSEM) iterative reconstruction. Prior to use in a patient-care setting, various FASpecT/CT acquisition protocols were modeled using a phantom to determine the minimum number of stops and stop duration required to produce a reliable image.

Results: FASpecT/CT blood pool images provided excellent 3-dimensional localization of spine osteomyelitis, soft tissue infection of the foot and tendonitis of the hand and foot utilizing a 3 minute image acquisition time.

FASpecT/CT acquisition protocol required 1.3-3.5 minutes including camera movement time. This was a reduction of 72-90% when compared to the time required for the standard 60 angle, 20 second SPECT/CT acquisition.

Principal Conclusions: FASpecT/CT blood pool images help localize focal sites of hyperemia/inflammation which can increase exam sensitivity and specificity. Additionally, utilizing a FASpecT/CT imaging protocol decreases imaging time by up to 90%.

Key Words: SPECT/CT, FASpecT, blood pool imaging, inflammation, infection

Introduction:

Blood pool imaging is frequently performed as the second phase of three phases in scintigraphic bone scanning to demonstrate inflammation associated with osteomyelitis. Focal regions with increased activity on the 3 phases of flow, blood pool, and delayed imaging are deemed to be three-phase positive and consistent with a diagnosis of osteomyelitis, although this finding also occurs with fracture, recent orthopedic hardware placement and neuropathic joint (Charcot's arthropathy) [1, 2]. A challenge with standard planar blood pool images is that specific localization of the focal region of increased blood pool, i.e. hyperemia/inflammation, is not possible, limiting interpretation of the study. This is particularly true in regions with overlying normal hyperemic muscles and other soft tissues, such as the calf and spine. Blood pool localization is also poorly defined in the forefoot in which focal soft tissue blood pool activity cannot be readily distinguished from blood pool activity in the bone, primarily due to the small size of the anatomic structures.

This challenge of precise anatomic localization is found with all planar imaging in nuclear medicine, which has led to the rapid proliferation of exams utilizing single photon emission computed tomography with co-registered conventional computed tomography (SPECT/CT) [3]. SPECT/CT has been shown to increase sensitivity and specificity in three phase bone scan as well as result in changes in management versus planar imaging alone [4, 5]. The primary diagnostic limitation of SPECT/CT is patient motion and misregistration, which are due at least in part to the long acquisition times of SPECT, ranging from 20-30 minutes. Additionally, this long acquisition time is impractical for the blood pool phase of a three phase bone scan. Solutions to these problems have been posited including immobilizing the body part being imaged and reducing image acquisition time [6-10].

Advances in iterative reconstruction, now available in most nuclear medicine clinics [11], have played a significant role in enabling FASpecT and other reduced dose or rapid acquisitions. Iterative reconstruction of images composed of a greatly reduced number of angular image samples has also been described for reconstruction of 3D images in other image-based fields, such as photoacoustic imaging and cone-beam CT imaging [12, 13]. For example, iterative reconstruction of sparse-view (30 image angles as opposed to 900 image angles) cone-beam CT has been shown to produce high quality tomographic images [12], and photoacoustic imaging with iterative reconstruction derived from as few as 15 detectors has been shown to produce tomographic images similar to those using 120 detectors [13].

Our hypothesis was that it would be possible to develop an imaging protocol which would enable SPECT/CT imaging of the blood pool phase of the three phase bone scan in order to improve localization. In this article we describe a method of reducing SPECT/CT acquisition time to approximately 3 minutes, which we refer to as fewer angle single photon emission computed tomography with co-registered conventional computed tomography (FASpecT/CT). FASpecT/CT images were obtained of the blood pool phase of bone scans with a greatly reduced number of acquisition angles, specifically six steps over 360°, 12 total images with 30° separation between angles and 30 seconds per image requiring a total SPECT imaging time of approximately three minutes. The FASpecT images were acquired rapidly after ^{99m}Tc -MDP administration for specific localization of sites of inflammation and infection. FASpecT/CT has previously been reported as a method to decrease the required imaging time and/or increase the detection efficiency for radioiodine pre-therapy and post-therapy imaging [14].

Materials and Methods:

The study has been approved by the institutional review board, and the need for written informed consent was waived. Studies were initially performed with an image phantom for comparison of image characteristics of standard SPECT/CT and FASpecT/CT acquisitions with differing times and angle samples. Subsequently, FASpecT/CT was performed in four clinical patients to demonstrate the clinical use of FASpecT/CT for tomographic blood pool imaging.

Phantom Studies:

Phantom Description:

A phantom was used for comparison of images acquired with different times and angle sample parameters. This phantom consisted of 19 water filled glass cylinders containing 25 mL of water each which were mounted into a hexagonal configuration. All cylinders were fully filled with water and 6 of the outer cylinders were filled with 2.6 ± 0.07 MBq of ^{99m}Tc -MDP of activity. In the first phantom, the 6 cylinders were spaced evenly on the outer ring as seen in Figure 1. In the second phantom, the six cylinders were placed randomly in the outer ring with several of the cylinders being placed adjacent to each other as seen in Figure 2. This amount of activity (0.104 MBq per mL of water) was chosen in accordance with our medical physicist based on an approximation of blood pool activity anticipated at five minutes post-administration when a 925 MBq ^{99m}Tc -MDP bone dose is distributed within the average human clinical circulating blood volume of 5000 ml allowing for clearance from blood of approximately 50% of the activity.

SPECT image acquisition:

SPECT imaging studies were performed of each phantom using differing acquisition times and a differing number of total image angle samples for visual comparison of image quality. Images were acquired using a reduced number of angle samples consisting of SPECT images acquired with 8 views of 30 seconds per image sample, 12 views for 8 seconds, 15 seconds, 30 seconds, and 60 seconds per image sample. A standard SPECT acquisition parameters of 60 views and 20 seconds was obtained for comparison. SPECT processing was performed with both ordered subset expectation maximization (OSEM) iterative reconstruction and filtered back projection. The OSEM images were processed with a two iterations and 10 subsets using a Butterworth filter with critical frequency of 0.48 and power of 10. The filtered back projection images were processed using a Butterworth filter with a critical frequency of 0.48 and a power of 10. Transaxial images of all the different SPECT acquisitions with slices through the center of the cylinders are shown in figures 1 and 2.

Clinical Studies:

Immediately after injection of 925 MBq-1110 MBq of ^{99m}Tc -MDP in 4 different representative clinical patients, dynamic flow and planar blood pool image acquisitions were acquired over each patient's region of concern using a 128x128 matrix over three minutes. Immediately following these planar images, a rapid SPECT/CT was obtained of the blood pool phase using a dual head SPECT/CT camera (GE Infinia Hawkeye 4 dual head SPECT/CT camera) utilizing the FASpecT protocol described in Table 1 (i.e. six steps, 12 total images with 30 seconds per images). Immediately after acquisition of the FASpecT images, a CT was performed with the patient in the same position. Image reconstruction was performed with GE Xeleris Functional Imaging software using iterative reconstruction parameters specified for FASpecT in Table 1. Example FASpecT/CT blood pool images in clinical patients with spine osteomyelitis, soft tissue infection of the foot, and tendinitis of the wrist and foot are shown in Figures 3-6. Follow-up delayed 3-hour bone scan imaging was performed, and when appropriate, either gallium-67 (^{67}Ga) or indium-111 (^{111}In) white blood cell imaging as per standard clinical protocols was performed for comparison.

Results:

Phantom Studies:

Results for the phantom studies are shown in Figures 1 and 2 below. The phantom imaging results were compared visually by four board-certified nuclear medicine physicians. In all of the FASpecT images, the iterative

reconstruction images are visually superior to the filtered back projection images. In the images with 12 angle samples, image quality decreases as the acquisition time decreases, however, images with 12 angle samples acquired for 30 and 60 seconds compared favorably to images with standard SPECT acquisition parameters of 60 angles acquired for 30 seconds. The FASpecT acquisition protocol required 1.3-3.5 minutes including camera movement time. This was a reduction of 72-90% when compared to the time required for the standard 60 angle, 20 second SPECT acquisition. Images with only 8 angle samples were visually inferior to 12 angle samples with image artifacts and poor localization of the activity in the phantoms. The phantom studies with random placement of the activity demonstrated similar visual findings.

Clinical Studies:

Clinical blood pool FASpecT/CT images are shown in four different cases (figures 3-6), with descriptions in the figure legends. The specific localization of blood pool activity on the FASpecT/CT was found by the four reviewing providers to be clinically useful, providing diagnostic information not evident on planar blood pool imaging alone.

Discussion:

The FASpecT/CT blood pool imaging protocol described in this article provides specific localization of sites of hyperemia/inflammation that can facilitate arrival at specific clinical diagnoses and result in improved patient care. In this article, we have shown that that FASpecT/CT imaging has particular promise for the imaging and diagnosis of musculoskeletal pathologies. In figure 3, a precise focus of blood pool activity is noted in the spine at the lumbosacral joint using FASpecT/CT imaging that is not localized with planar spine blood pool imaging. This localization of infection was not affected by the metallic artifact from the patient's spinal fusion hardware. The ability to image specific sites of infection/inflammation in the spine with blood pool tomographic imaging has the potential to impact spine care and direct treatment specifically to sites of spinal inflammation. FASpecT/CT may prove to be an additional tool for improving the diagnosis and treatment of low back pain, the number one cause of musculoskeletal related disability in the developed world [15].

FASpecT/CT also has significant promise in evaluation of soft tissue and bone infections of the foot. In figure 4, the FASpecT/CT blood images demonstrate increased blood pool activity in soft tissue adjacent to the 2nd metatarsal bone, but not within the bone itself. By standard planar imaging alone, the region of the 2nd metatarsal bone scan would have been inappropriately called suspicious for osteomyelitis. Follow up ¹¹¹In-WBC SPECT/CT

confirms that the infection was only localized to the soft tissues of the foot adjacent to the 2nd metatarsal bone which was the same region with blood pool activity on the FASpecT/CT image.

In figure 5, FASpecT blood pool imaging demonstrates increased blood pool activity within the extensor pollicis brevis tendon supporting a diagnosis of de Quervain's tenosynovitis in which early diagnosis is important for proper treatment [16]. This diagnosis was not evident from the planar blood pool or delayed phase images.

In figure 6, FASpecT blood pool imaging demonstrates linear increased activity associated with the posterior tibial tendon. Again, this localization is not possible on planar images. Early diagnosis of this condition is important as it can progress from tendonitis at Stage I to deformity at Stage II and a severe disability in Stages III and IV [17].

The iterative reconstruction used for FASpecT image processing provides significantly improved image quality as compared to Filtered Back Projection (FBP) reconstruction when using a greatly reduced number angle samples. Although FBP reconstruction remains the most commonly used method for reconstructing SPECT myocardial perfusion images[9], iterative SPECT reconstruction methods have become more popular as a method to reduce image artifacts and noise. The most commonly used iterative reconstruction method used is Ordered Subset Expectation Maximization (OSEM), although recently other iterative methods are also being evaluated [18]. Currently, the main focus of research using iterative reconstruction methods has been on the reduction of administered doses in cardiac SPECT imaging and the development of faster imaging procedures [6-9]. A prior study iteratively reconstructed SPECT images containing either 30, 60, or 120 image angles while maintaining the pixel counts of reconstructed images constant. The SPECT images with 30 angle samples compared favorably with those SPECT reconstructions containing either 60 or 120 angles. This study concluded that a combination of iterative reconstruction with OSEM and a reduced number of angle samples may be a clinically useful method of reducing the time required for SPECT imaging [19]. Although iterative image reconstruction makes it possible obtain higher quality 3D images with using fewer angle samples, there have no prior reports of using few angle protocols to reduce acquisition time for SPECT blood pool imaging.

FASpecT/CT with greatly shortened imaging times may have applications for dynamic SPECT/CT acquisitions with radiopharmaceuticals other than ^{99m}Tc-MDP. SPECT/CT is used routinely in clinical practice for many other exams including parathyroid localization using ^{99m}Tc-Sestamibi, neuroblastoma evaluation using ¹²³I-MIBG, and Parkinson's evaluation using ¹²³I-Ioflupane, just to name a few. SPECT/CT with a traditional number of

imaging angles (60-120) has been described for occult gastrointestinal bleeding with ^{99m}Tc-labeled red blood cells [20] and for assessment of myocardial flow reserve using ^{99m}Tc-Sestamibi [21]. The use of rapidly acquired FASpecT/CT imaging may prove useful in these and in other new applications to greatly reduce imaging times which would have wide-ranging positive effects including reducing patient motion and increasing throughput.

Conclusion:

FASpecT/CT blood pool images help localize focal sites of hyperemia/inflammation which can increase exam sensitivity and specificity. Additionally, utilizing a FASpecT/CT imaging protocol decreases imaging time by up to 90%.

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Disclaimer

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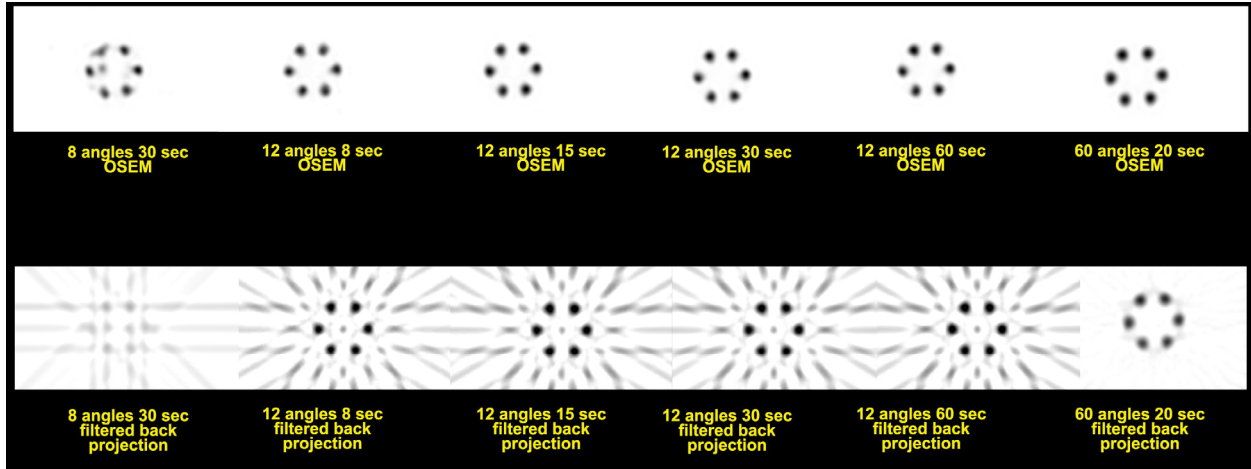


Figure 1

SPECT images of the phantom with symmetrically distributed cylinders acquired with various image angles and times are shown. SPECT acquisitions in the top row are processed with OSEM and the same SPECT images in the bottom row are processed with filtered back projection. The images are labeled with the number of images and times for the acquisitions as follows from left to right: 1) 8 angles-30 seconds per image, 12 angles-8 seconds per image, 12 angles-15 seconds per image, 12 angles-30 seconds per image, 12 angles-60 seconds per image, and the standard SPECT protocol of 60 angles-20 seconds per image.

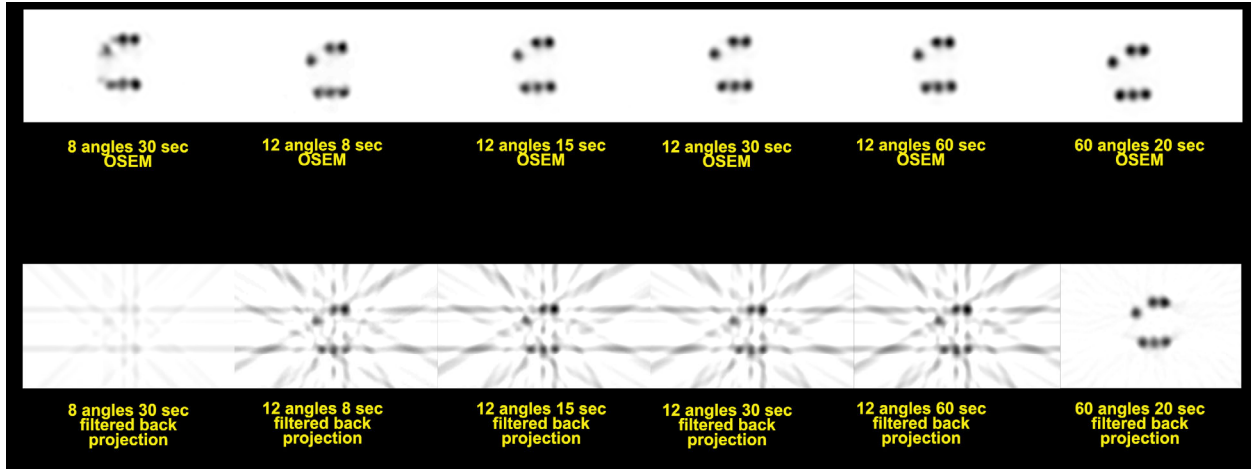


Figure 2

SPECT images are shown of the phantom containing randomly placed activity containing glass vial cylinders with the image parameters the same as in Figure 1 as labeled on the images.

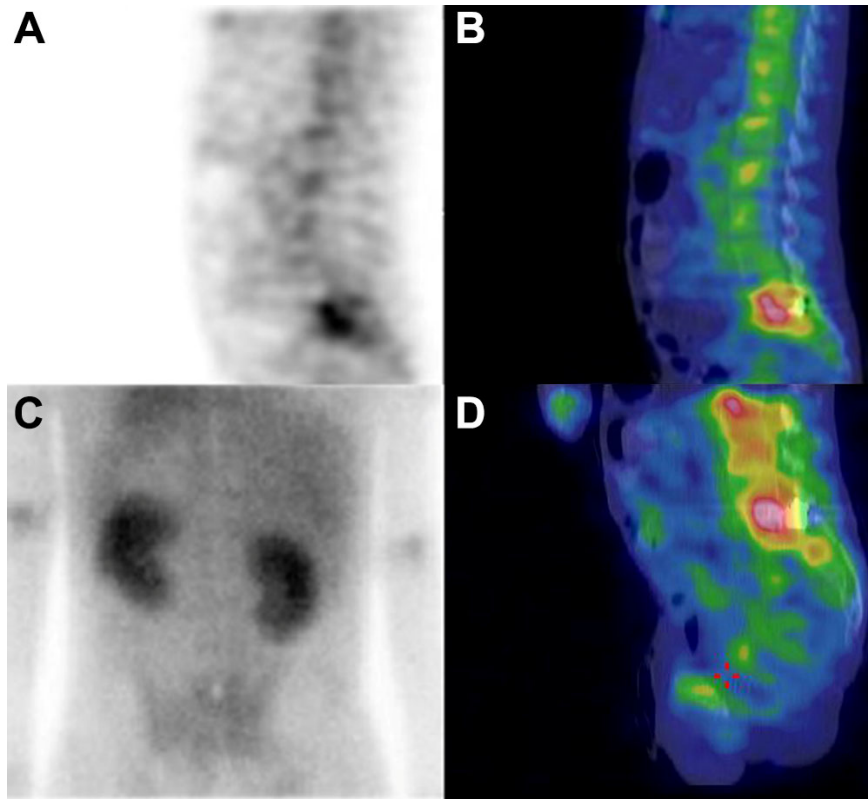


Figure 3

Blood Pool imaging of the spine with FASpecT/CT. FASpecT blood pool sagittal image (A), Fused FASpecT/CT blood pool sagittal image (B), posterior planar blood pool (C) and SPECT/CT of gallium-67 citrate sagittal image (D). The FASpecT /CT blood pool images (A and B) demonstrate intense focal increased uptake at the L5-S1 vertebra that is poorly localized on planar imaging (C). Subsequent gallium-67 citrate imaging (D) demonstrates the presence of infection corresponding to the region of increased blood pool on the FASpecT image (A and B).

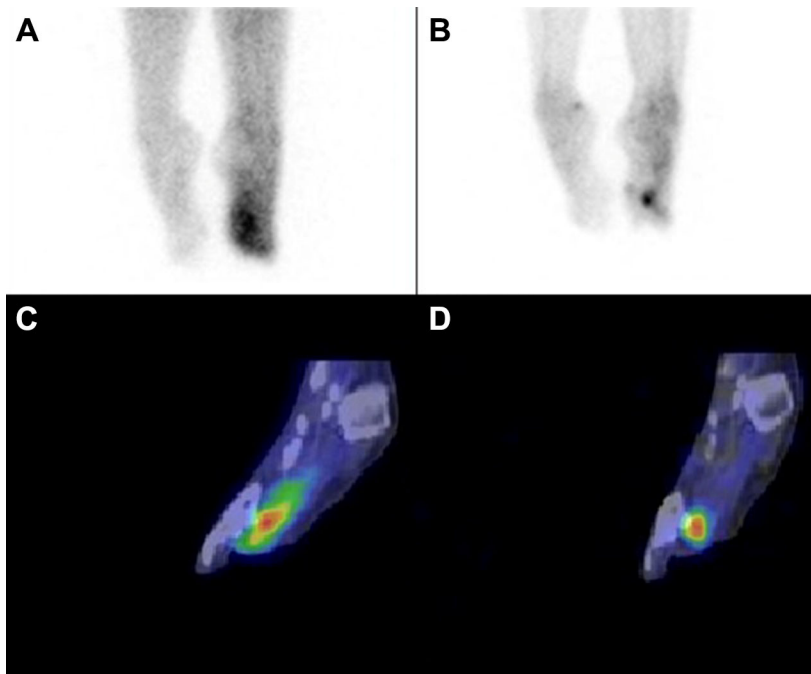


Figure 4

Blood Pool imaging of the foot with FASpecT/CT. Anterior planar blood pool of the feet (A), anterior planar delayed bone scan of the feet (B), FASpecT/CT blood pool sagittal image of the left foot (C), ^{111}In -WBC SPECT/CT sagittal image of the left foot (D). Planar blood pool imaging demonstrates diffuse increased blood pool activity that cannot be precisely localized. The delayed planar bone scan shows focal bone uptake consistent with 3 phase positivity of the region of the left distal 2nd metatarsal. However, FASpecT/CT blood pool imaging (C) demonstrates focal soft tissue blood pool activity of the left foot without apparent bone involvement. Subsequent ^{111}In -WBC SPECT/CT images (D) shows focal soft tissue activity without bone activity correlating with FASpecT/CT blood pool imaging.

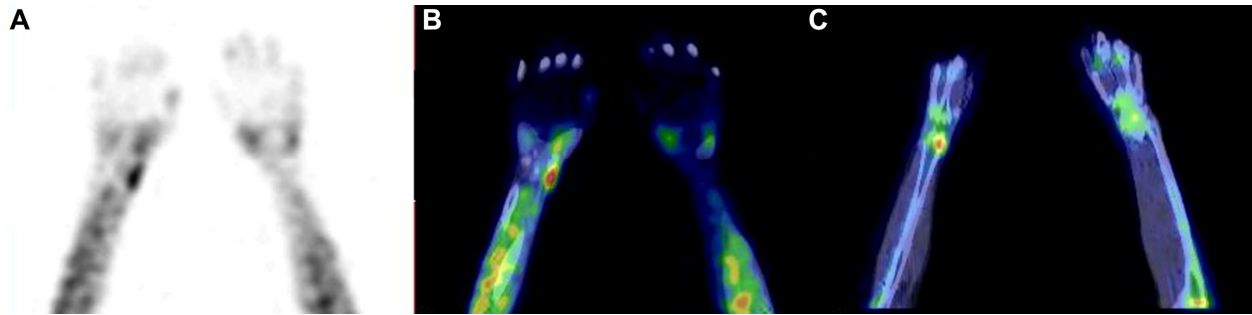


Figure 5

Blood Pool imaging of the hands with FASpecT/CT. FASpecT blood pool (A), fused FASpecT/CT blood pool (B), delayed bone scan SPECT/CT (C). FASpecT/CT blood pool images show increased linear blood pool activity along the distribution of the right extensor pollicis brevis tendon characteristic of De Quervain's tenosynovitis. Delayed bone scan imaging (C) shows focal increased uptake only in the distal radius at the origin of the extensor pollicis brevis tendon, most likely due to increased regional blood flow. Planar blood pool (not shown) had very minimal asymmetric increased blood pool in the right wrist that could not be localized.

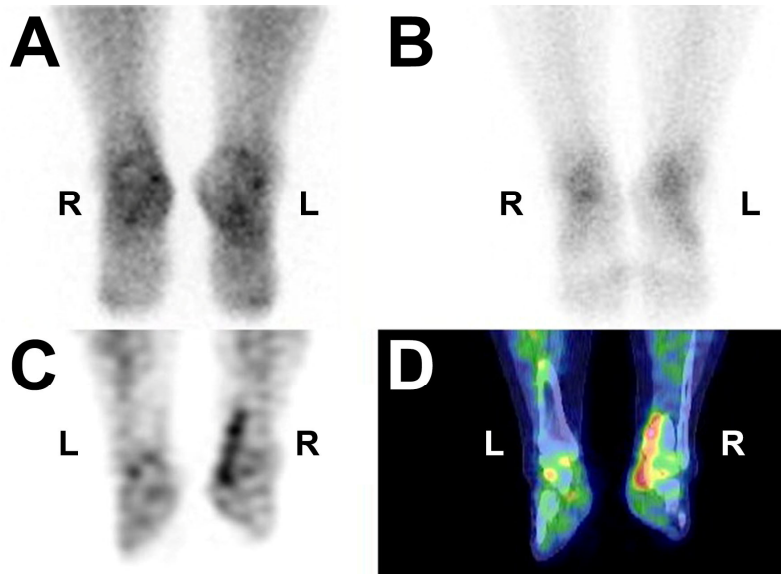


Figure 6

Blood Pool imaging of the ankles with FASpecT/CT. Posterior planar blood pool of the feet (A), posterior planar delayed bone scan of feet (B), FASpecT blood pool coronal images of feet (C), and coronal SPECT/CT blood pool coronal image of the feet (D). FASpecT/CT blood pool images demonstrate focal increased uptake along the posterior tibial tendon consistent with tendonitis. Note the delayed bone scan is essentially normal and the posterior planar blood pool scan shows asymmetry that cannot be localized.

Parameter	FASpecT/CT protocol	Standard SPECT/CT protocol
SPECT acquisition	30° steps and total angular range 360° with a dual head SPECT/CT camera	3-6° steps and total angular range of 360° with a dual head SPECT/CT camera
Acquisition time per projection	30 seconds	20-30 seconds
Total imaging time required	3:20 minutes	22-65 minutes
Number of steps	6	60
Total images acquired	12	60-120
Matrix size	128 x 128	64x64 or 128x128
Reconstruction	OSEM (2 iterations, 10 subsets)	Filtered Back Projection or OSEM
Post reconstruction filter	Butterworth; critical frequency 0.48, power 10	Butterworth with varying parameters

Table 1

FASpecT blood pool protocol acquisition and processing parameters compared to standard SPECT imaging