The added value of SPECT/CT in complicated osteomyelitis

By

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ABSTRACT

Background: The detection of bone infection can be very difficult especially in bone with altered structure due to prior trauma or surgical procedures. Complicated osteomyelitis (COM) is becoming a public health problem especially with the difficult choice between, high cost surgery and prolonged courses of intravenous or oral antibiotic therapy, as well as the social and psychological effect of long-term disease and disability of the patient. The correct localisation of especially bone infection is still a challenge for the clinician. The single photon emission computed tomography/low dose computed tomography (SPECT/CT), by fusing the functional information with the anatomical parts, is a well-established tool used in many nuclear medicine studies. This improves the overall quality of the study with more clear answers. The aim of the study was to determine the added value of SPECT/CT in the management of complicated osteomyelitis (COM) in patients with endo-prosthesis, post traumatic osteomyelitis with and without metal implants and diabetic foot.

Methods: This was a prospective study, between February 2010 and February 2012. Patients with suspected COM who fulfilled the selection and inclusion criteria were included. All had abnormal three phase bone scan followed by infection imaging with ^{99m}Tc labelled white blood cells and ^{99m}Tc -colloid if the ^{99m}Tc labelled white blood cell study was abnormal. ^{67}Ga citrate was used in vertebral involvement. Planar and SPECT/CT images were reviewed for presence of abnormal uptake and for its localization in bone and soft tissue. Scan results were defined as positive or negative. Both planar and SPECT/CT images were compared regarding diagnosis and precise localization of infection. The final diagnosis was obtained from surgical specimen or microbiological culture as well as clinical follow-up of all patients.

Results: There were 72 patients, 29 male and 43 female with mean age of 57 yrs [range 27-88].There were 24 patients with prosthesis, 16 with hip prosthesis (PH=16), and 8 with knee prosthesis (PK=8). There were 44 patients with post traumatic osteomyelitis, 26 with metal implants (TOM=26) and 18 without metal implants (TOWM= 18). Four patients had diabetic foot (DF= 4). Infection was diagnosed in 19/72 patients on planar images and in 21/72 on SPECT/CT. Infection was diagnosed in 4 patients with prosthesis, 16 patients with post traumatic injury and one diabetic foot patient. The four patients with prosthesis, SPECT /CT added diagnostic value by excluding osteomyelitis in 3 patients and by defining the exact extent and localizing soft tissue and bone infection (STI/OM) in one patient. In 16 patients with post traumatic OM on planar images, SPECT /CT added diagnostic

value, by excluding OM in 4 patients and confirming only STI, better localisation of the uptake in bone and soft tissue in 5 patients, of them 2 patient was negative on planar, and in 7 patients, confirmed and defined the exact extent of

both OM and STI. One diabetic foot was positive for STI on the planar, the SPECT/CT added diagnostic value by defining the extent of the infection.

 In summary the added value of SPECT/CT was:

- a. Overall infection:
    1. Exclusion of osteomyelitis by confirming only soft tissue involvement: 7 patients (10%)
    2. Better localization in bone and soft tissue: 6 patients (8%)
    3. Better delineation of extent of infection: 9 patients (12%)
    4. None: 50 patients (70%)
- b. In positive cases only:
    1. Exclusion of osteomyelitis by confirming only soft tissue involvement: 7 patients (33%)
    2. Better localization in bone and soft tissue: 5 patients (24%)
    3. Better delineation of extent of infection: 9 patients (43%)
    4. None: 0 patients

The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy for infection, on planar was 90%, 100%, 100%, 97%, 97%, respectively and for SPECT/CT 100%, 100%, 100%, 100%, 100%. For OM on planar, the sensitivity, specificity , positive predictive value, negative predictive value and accuracy was 100%, 89%, 53%, 100%, 90%, respectively and for SPECT/CT 100%, 100%, 100%, 100%, 100%.

Conclusion:

In complicated osteomyelitis, SPECT/CT is useful in localizing, defining the exact extent of infection where the planar images are abnormal, with no added value if the planar images are negative. We recommend in clinical practice the routine use of hybrid SPECT/CT imaging in complicated osteomyelitis when planar images are abnormal.

ABSTRAK

Agtergrond: Die opspoor van beeninfeksie is veral moeilik in been wat as gevolg van vorige trauma of chirurgiese prosedures misvorm is. Gekompliseerde osteomiëlitis word 'n gesondheidsprobleem veral as gevolg van die moeilike keuse tussen hoë koste chirurgie en langdurige kursusse binneaarse of orale antibiotika, asook die sosiale en sielkundige gevolge van langstaande siekte en die gestremdheid van die pasiënt.

Die korrekte lokalisering van veral beeninfeksie is steeds 'n uitdaging vir die geneesheer. Enkel foton emissie rekenaartomografie / lae dosis rekenaartomografie (SPECT/CT), die kombinasie van funksionele en anatomiese inligting, is 'n goed gevestigde metode in baie kerngeneeskunde ondersoeke. Dit verbeter die algemene kwaliteit van die studie met 'n meer spesifieke antwoord. Die doel van hierdie studie was om die bykomende waarde van SPECT/CT in die hantering van gekompliseerde osteomiëlitis in pasiënte met endo-protese, post traumatise osteomiëlitis met en sonder metaal prosteses asook diabetiese voet te bepaal.

Metode: 'n Prospektiewe studie is tussen Februarie 2010 en Februarie 2012 gedoen. Pasiënte met vermoedelik gekompliseerde osteomiëlitis wat aan die keuse en insluitingskriteria voldoen het, is ingesluit. Almal het abnormale drie-fase beenflikkergramme gehad, gevolg deur infeksiebeelding met ^{99m}Tc gemerkte witselle en ^{99m}Tc kolloïed indien die ^{99m}Tc gemerkte witselstudie abnormaal was.

^{67}Ga sitraat is gebruik wanneer daar werwelaantasting teenwoordig was. Die planare en SPECT/CT beelde is vergelyk ten opsigte van diagnose en presiese lokalisering van die infeksie. Die finale diagnose is met behulp van chirurgiese monsters en mikrobiologiese kweking asook die kliniese opvolg van alle pasiënte bepaal.

Resultate: Die studie het 72 pasiënte, 29 mans en 43 vroue, met gemiddelde ouderdom van 57 jaar [27 – 88 ingesluit]. Daar was 24 pasiënte met prosteses, waarvan 16 met heupprosteses (PH= 16) en 8 met knieprosteses (PK= 8). Van die 44 pasiënte met post traumatiese osteomiëlitis, het 26 metal prosteses (TOM= 26) en 18 geen metaalprosteses gehad nie (TOWM= 18). Vier pasiënte het diabetiese voet gehad (DF= 4). By 19/72 van die pasiënte is infeksie op die planare beelde gediagnoseer en in 21/72 op die SPECT/CT beelde. Die bykomende twee gevalle was 1 met TOM en 1 met TOWM.

Infeksie is by 4 pasiënte met prosteses, 16 pasiënte met post traumatiese besering en 1 met diabetiese voet gediagnoseer. In die vier pasiënte met prosteses, het SPECT/CT 'n diagnostiese bydrae gelewer om osteomiëlitis by 3 van die pasiënte uit te skakel en die presiese omvang en

lokalisering van sagte weefsel en beeninfeksie (STI/OM) in een pasiënt te bepaal. In 16 pasiënte met post traumatise osteomiëlitis op die planare beelde, was SPECT/CT van diagnostiese waarde, waar osteomiëlitis in 4 pasiënte uitgesluit is, en slegs STI bevestig is. Beter lokalisering van die opname in been en sagte weefsel was in 5 pasiënte moontlik, van wie 2 op die planare beelde negatief was, en in 7 pasiënte bevestig en die presiese omvang met beide OM en STI gedefinieer is. Een diabetiese voet was positief vir STI op die planare beelde, maar die SPECT/CT het diagnostiese waarde verbeter deur die omvang van die infeksie beter te toon.

Ter opsomming, was die waarde van die SPECT/CT:

1. Uitsluiting van osteomiëlitis deur slegs van sagte weefsel aantasting te bevestig:
    7 pasiënte 10%
2. Beter lokalisering in been en sagte weefsel: 5 pasiënte 7%
3. Beter definisie van omvang van infeksie: 9 pasiënte 12%
4. Geen bykomende waarde: 51 pasiënte 71%

Die algehele sensitiwiteit, spesifisiteit, positiewe voorspellingswaarde, negatiewe voorspellingswaarde en akkuraatheid vir die opspoor van infeksie vir die planare beelde was 90%, 100%, 100%, 97%, 97%, onderskeidelik en vir die SPECT/CT 100%, 100%, 100%, 100% en 100%. Vir osteomiëlitis was sensitiwiteit, spesifisiteit, positiewe voorspellingswaarde, negatiewe voorspellingswaarde en akkuraatheid van planare beelde 100%, 89%, 53%, 100%, 90%, onderskeidelik en die van SPECT/CT 100%, 100%, 100%, 100%, 100%.

Gevolgtrekking: SPECT/CT is nuttig in die lokalisering en definiëring van die presiese omvang van die infeksie in gekompliseerde osteomiëlitis in gevalle waar die planare beelde abnormaal is, met geen bykomende waarde wanneer planare beelde negatief is nie. Ons beveel SPECT/CT beelding as roetine in kliniese praktyk aan wanneer planare beelde in gekompliseerde osteomiëlitis abnormaal is.

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Abbreviation

BDI: Better delineation of extent of infection

BL: Better localization in bone and soft tissue

COM: Complicated osteomyelitis

CRP: C-reactive protein

CT: Computer tomography

DF: Diabetic foot

EOM: Exclusion of osteomyelitis by confirming only soft tissue involvement

ESR: Erythrocyte sedimentation rate

FN: False negative

HIV: Human immunodeficiency virus

MRI: Magnetic resonance imaging

NEG: Negative

NI: No infection

OM: Osteomyelitis

PH: Prosthesis hip

PK: Prosthesis knee

POS: Positive

SPECT/CT: Single photon emission computed tomography/low dose computed tomography

STI: Soft tissue infection

TOM: Traumatic osteomyelitis with metal

TOWM: Traumatic osteomyelitis without metal

WBC: White blood cell

WCC: White cell count

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INTRODUCTION AND LITERATURE REVIEW

The detection of bone infection can be very difficult, especially in bone with altered structure due to prior trauma or surgical procedures. The presence of predisposing factors such as scarred tissue, bone necrosis, foreign body and diabetes increases the chance of bone infection. Infection following joint-replacement surgery is relatively low (0.5–3%); however, the number of patients who need joint prosthesis is increasing.[1][2][3] In the scenario of diabetic foot, osteomyelitis (OM) represents approximately 20% of all types of foot infection and many patients undergo unnecessary amputations because of improper diagnostic and therapeutic approaches.[4][5]

Complicated osteomyelitis (COM) is becoming a public health problem, especially with the difficult choice between high-cost surgery and prolonged courses of intravenous or oral antibiotic therapy, as well as the social and psychological effect of long-term disease and disability of the patient.[6][7][8][9]

Nuclear medicine imaging provides useful information about bone metabolism and infectious processes, particularly in patients with orthopaedic devices.[10][11][12][13][14][15] ^{99m}Tc-labelled leukocyte scintigraphy has proven to be clinically useful for diagnosing infections.[16] ^{67}Ga citrate is used in spine infection as the sensitivity of ^{99m}Tc-labelled leukocyte in spinal infection is poor. In addition, ^{67}Ga citrate has shown better accuracy in post-traumatic OM with metallic implants or other conditions than anatomical imaging such as magnetic resonance imaging (MRI).[17][18][19][20][21]

Planar images alone are usually not accurate to assess the exact extent of disease and to distinguish between soft tissue and bone infection, which influences patient management. SPECT/CT imaging, which is the fusion of functional (SPECT) and anatomical (CT) images, has shown to increase the accuracy in identification and characterisation of many different abnormalities. SPECT/CT increases the sensitivity and improves the localisation over the planar alone. In a study by Utsunomiya et al,[23] the additional diagnostic value in fused SPECT and CT images for the assessment of possible bone metastases was evaluated, and it was found that SPECT/CT provides increased diagnostic confidence. Strobel et al,[22] compared planar, SPECT and SPECT/CT in focal bone lesion, and found that SPECT/CT significantly increased the certainty of diagnosis. In a study by Sharma et al,[24] planar bone scan and SPECT/CT in skull base OM were compared, and they emphasised that SPECT/CT increased the confidence and the accuracy of diagnosis of skull base OM compared to planar alone. Mariani et al,[25] showed that SPECT/CT improved accuracy in identifying the anatomical site and extent of disease, increasing the specificity and overall accuracy of diagnostic nuclear medicine procedures. Many studies have proven that SPECT/CT is more accurate than planar imaging in the evaluation of orthopaedic disorders.[26][27][28][29][30][31]

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In a recent study by Heiba et al,[32] it was found that SPECT/CT imaging with ^{99m}Tc-labelled leukocytes in patients with diabetic foot provided accurate anatomic localisation and precise definition of the extent of infection. In a study by Filippi et al,[33] in which ^{99m}Tc-labelled leukocytes were used in a population sample with similar conditions as in this study, patients with suspected OM with or without orthopaedic implants, SPECT/CT provided accurate anatomical localisation and precise definition of the extent of infection.

AIM OF THE INVESTIGATION

The aim of the study was to determine the added value of SPECT/CT in management of complicated osteomyelitis in patients with endo-prosthesis infection, post traumatic osteomyelitis with and without metal implants and diabetic foot.

MATERIALS AND METHODS

Patient selection

This was a prospective study conducted between February 2010 and February 2012. A total number of 174 patients were referred to the department for infection imaging, of which 72 patients with suspected COM were recruited who complied with the inclusion and exclusion criteria below.

Inclusion criteria:

- Patient's ≥ 18 years.
- Clinical suspected osteomyelitis based on:
  - ✓ Recent clinical symptoms: pain, fever, redness, swelling, tenderness.
  - ✓ Recent laboratory findings of infection: WCC, ESR, and or CRP.
  - ✓ Radiological finding: X-ray, CT, MRI.
- Abnormal 3-phase bone scans.
- Prosthetic and metal implants; imaging was performed at least 3 months post-intervention.

Exclusion criteria:

- Leucocyte count less than 2000, in case of ^{99m}Tc labelled WBC.
- Patients with bone and soft-tissue cancer or metastases.
- Pregnancy and lactation.
- HIV positive.
- Patient < 18 years were excluded from the study.

All patients had abnormal three phase bone scans followed by infection imaging with ^{99m}Tc labelled leukocytes and ^{99m}Tc-colloid when ^{99m}Tc labelled leukocyte scan was positive. ^{67}Ga citrate was used in vertebral involvement.

The study was conducted in accordance with established ethical guidelines and was approved by the Health Research Ethics Committee (HREC) of Stellenbosch University (Ref #N09/02/057).

Clinical data

Information regarding previous trauma, surgery, medical management or orthopaedic hardware was obtained from all patients. The data were recorded using a standardised clinical assessment sheet

Anatomical, Biological, and Pathological Results:

Most recent, WCC, ESR, and/or CRP at time of the scan were obtained. Where available the pathology, blood culture and anatomical finding were recorded.

Image acquisition

Three phase bone scan:

Was performed according to SNM guideline. [34]

Dose: 740 MBq-1000 MBq of ^{99m}Tc- MDP (according to the body weight).

Flow-phase:

Obtained for 2 min: 2 sec/frame for 60 frames on 128x128 matrix, over the area of interest .

Blood pool images:

Whole body, continuous at 120 sec/pixel on 256x256 matrix, and statics for 1000K counts on 256x256 matrix.

Delayed images:

Planar whole body: continuous at 240 sec/pixel on 256x256 matrix.

Planar static: 700K counts on 256x256 matrix for axial skeleton. 300K counts on 256x256 matrix for appendicular skeleton

White Blood Cell scan:

 White blood cells were labelled using in-vitro technique described in the protocol suggested by MRC Cyclotron Unit, Hammersmith Hospital, London UK.

Dose: 370 MBq -555 MBq ^{99m}Tc labelled WBC. (Dependent on cell availability/cells harvested).

Whole body or spot views of the chest and abdomen 30 min post IV injection for QC.

Planar whole body:

Continuous at 350 and (5 cm/min) on 256x256 matrix at 3-4 h and 24 h respectively.

Planar static:

1000K counts or 10 minutes/spot view on 256x256 matrix.

SPECT/CT of the suspected region:

SPECT:

 Low energy high resolution collimator with a 128x128 matrix, using step and shoot mode. Projections of 3˚ each with 30 seconds per projection.

Low dose CT:

Hawkeye 1, 140 KV, 2.5 mA, slice thickness 10 mm, matrix 256x256.

No contrast media was used.

In case of positive ^{99m}Tc labelled WBC scan a ^{99m}Tc colloid (bone marrow scan) scan was performed to exclude physiological reactive or displaced bone marrow uptake.

Colloid scan:

Dose: 370 MBq of ^{99m}Tc -colloid (at least 72 h after the WBC injection).

Scan at 30 min post-injection.

Planar whole body:

Continuous at 5 cm/min on 256x256 matrix.

Planar static:

10 minutes/spot view (depending on image quality) on 256x256 matrix.

^{67} Ga citrate scan:

Dose: 185 MBq

Scan at 48 h post injection.

 Planar whole body:

Continuous at 400 sec/pixel on 256x256 matrix.

Planar static:

10 minutes/spot view on 256x256 matrix.

SPECT/CT of the suspected region:

SPECT:

A medium energy all-purpose collimator with a 64x64 matrix, using step and shoot mode. Projections of 3˚ each with 30 seconds per projection.

Low dose CT:

Hawkeye, 140 KV, 2.5 mA, slice thickness 10 mm, matrix 256x256.

No contrast media was used.

Equipment: Infinia Hawkeye 1 and Infinia Hawkeye 4 SPECT/CT system (GE healthcare, Milwaukee, USA).

All acquired images were transferred via network to a HERMES workstation for storage, processing and interpretation

Image interpretation

All the planar and SPECT/CT images were evaluated by two nuclear medicine physicians together, blinded to clinical information, with interpretation by consensus for presence of abnormal uptake and for its localisation in bone and soft tissue. First the planar images were evaluated, followed by the SPECT/CT images. The abnormal uptake was identified on both planar and SPECT/CT, then categorised as OM, OM/STI or only STI.

Lastly the added value of SPECT/CT over Planar was classified, into four categories:

1. Exclusion of osteomyelitis by confirming only soft tissue involvement.
2. Better localization in bone and soft tissue.
3. Better delineation of extent of infection.
4. None.

When the SPECT/CT localised the uptake on the WBC scan to probably bone/ bone marrow , a colloid scan was done to exclude reactive/ displaced bone marrow.

Validation

The final diagnosis was obtained from surgical specimens or microbiological culture where available, as well as clinical information and follow-up of all patients.

Statistical analysis

The STATA 12 statistical software was used for descriptive analysis. Categorical data were summarised as percentages. Age was summarised using mean and range. In univariate analysis, we estimated diagnostic parameters for each test (i.e. planar and SPECT/CT): sensitivity, specificity, predictive values and accuracy with regard to correct detection of the infection. We used 95% confidence intervals (CI) to estimate population parameters

RESULTS

Over a period of 2 years, between February 2010 and February 2012, a total of 174 consecutive patients were referred to the nuclear medicine department with clinical suspicion of infection. Only 72 patients with suspected complicated osteomyelitis were recruited who fulfilled the inclusion and exclusion criteria.

Demographics

Of the 72 patients with suspected OM that were reviewed, there were 29 males and 43 females, with mean age of 57 yrs [range 27-88].

Fifty eight WBC scans with 20 positive for infection and 14 ^{67}Ga citrate scans with 1 positive for infection were acquired. OM was positive in 7 WBC scans and in 1 ^{67}Ga citrate scan.

There were 24 patients with prosthesis, 16 with hip prosthesis, and 8 with knee prosthesis.

There were 44 patients with post traumatic osteomyelitis, 26 with metal implants and 18 without metal implants.

Four patients had diabetic foot.

Infection was positive in 21, and negative in 51 patients. Thirteen patients had STI only (18%), 6 OM/STI (8%), and 2 OM (3%). From the total of 72 patients only 8 patients had OM (10%).

Type of case	Number of cases	Percentage	Type of infection			
			STI	OM/STI	OM	NI
PH	16	22%	2	1	-	13
PK	8	11%	1	-	-	7
TOM	26	36%	3	4	2	17
TOWM	18	25%	6	1	-	11
DF	4	6%	1	-	-	3
Total	72	100%	13(18%)	6 (8%)	2 (3%)	51(71%)

Table 1: Type and number cases (PH = prosthesis hip, PK = prosthesis knee, TOM = traumatic osteomyelitis with metal, TOWM = traumatic osteomyelitis without metal, DF = diabetic foot)

Pathology and management findings

All patients were followed up clinically. From the 72 patients in the study, 18 patients had pus swab or bone biopsy to confirm or exclude OM. This was done in five patients who had a negative planar or SPECT/CT scan and in 12 patients with a positive planar and SPECT/CT scan, and one patient where the planar was negative but SPECT/CT was positive.

In the 13 patients with a positive SPECT/CT scan:

- 8 had bone biopsy and tissue culture.
- 5 had pus swab.

Type of scan	Type of case	Diagnosis on planar	Diagnosis on SPECT/CT	Final diagnosis
1/WBC	TOWM	OM/STI	STI	Bone biopsy and tissue culture negative
2/WBC	TOM	OM/STI	OM/STI	Bone biopsy and tissue culture positive
3/WBC	PH	OM/STI	STI	Bone biopsy and tissue culture negative
4/WBC	TOWM	OM/STI	OM/STI	Pus swab positive
5/WBC	DF	STI	STI	Pus swab positive
6/WBC	TOWM	STI	STI	Pus swab positive
7/WBC	PH	OM/STI	OM/STI	Bone biopsy and tissue culture positive
8/WBC	TOM	OM/STI	OM/STI	Bone biopsy and tissue culture positive
9/WBC	TOWM	STI	STI	Pus swab positive
10/WBC	TOWM	OM/STI	STI	Bone biopsy and tissue culture negative Pus swab of the wound positive
11/WBC	TOM	OM/STI	OM/STI	Pus swab positive
12/WBC	TOWM	NI	STI	Bone biopsy and diagnostic CT positive
13/WBC	TOM	OM/STI	OM/STI	Bone biopsy and tissue culture positive
14/WBC	TOWM	NI	NI	Bone biopsy and tissue culture negative
15/WBC	PH	NI	NI	Bone biopsy and tissue culture negative
16/WBC	PH	NI	NI	Bone biopsy and tissue culture negative
17/ ^{67}Ga	TOM	NI	NI	Bone biopsy and tissue culture negative
18/ ^{67}Ga	TOWM	NI	NI	Bone biopsy and tissue culture negative

Table 2: The final diagnosis in 18 patients who had pathology procedure.

Imaging findings

Colloid scan

Of the 58 WBC scans that were done, colloid scan were acquired in 22. Seven scans were positive for OM.

In 5 patients with OM, the SPECT/CT localised uptake in bone, but only after the colloid scan confirmed it to be OM and not displaced bone marrow.

In remaining 2 patients with OM, bone marrow images were not acquired.

Detection and localization

1. Hip prosthesis (PH)

Planar*:* 3 patients were positive for OM/STI.

SPECT/CT*:* 3 patients were positive for infection, 2 with STI and 1 with OM/STI.

Both planar and SPECT/CT were negative in 13 patients

2. Knee prosthesis (PK)

Planar: 1 patient positive for OM/STI.

SPECT/CT: one patient positive for STI only.

Both planar and SPECT/CT were negative in 7 patients

3. Traumatic osteomyelitis with metal (TOM)

Planar: 8 patients were positive for infection, 7 for OM/STI and 1 with only STI.

SPECT/CT: 9 patients were positive for infection, 4 with OM/STI, 3 with only STI, and 2 with OM only.

Both planar and SPECT/CT were negative in 17 patients

4. Traumatic osteomyelitis without metal (TOWM)

Planar: 6 patients were positive for infection, 4 patients with OM/STI and 2 with only STI.

SPECT/CT: 7 patients were positive for infection, 1 with OM/STI and 6 with only STI.

Eleven patients were negative on both planar and SPECT/CT.

5. Diabetic foot (DF)

Planar: 1 positive patient for only STI.

SPECT/CT: 1 positive patient for only STI.

Planar and SPECT/CT were negative in 3 patients.

Added value of SPECT/CT

1. Hip prosthesis (PH)

SPECT/CT excluded osteomyelitis by confirming only STI in 2 patients and in 1 patient better delineated the infection in bone and soft tissue.

2. Knee prosthesis (PK)

SPECT/CT excluded OM by confirming only STI in 1 patient.

3. Traumatic osteomyelitis with metal (TOM)

SPECT/CT excluded osteomyelitis by confirming only STI in 1 patient. It better localized the uptake in bone and/or soft tissue in 2 patients of which one appeared to have both OM/STI on planar, but only OM on SPECT/CT, the other patient who was negative on the planar images showed focal STI on SPECT/CT. In the remaining 6 patients, SPECT/CT better delineated the extent of infection.

4. Traumatic osteomyelitis without metal (TOWM)

SPECT/CT excluded osteomyelitis by confirming only STI in 3 patients, better localized the uptake in bone and/or soft tissue in 4 patients, including the patient which was negative on the planar images, and better delineated the extension of infection in 1 patient.

5. Diabetic foot (DF)

In the 1 patient with STI, SPECT/CT better delineated the extent of infection.

Overall infection

1. Exclusion of osteomyelitis by confirming only soft tissue involvement: 7 patients (10%)
2. Better localization in bone and soft tissue: 6 patients (8%)
3. Better delineation of extent of infection: 9 patients (12%)
4. None: 50 patients (70%)

In positive cases only

1. Exclusion of osteomyelitis by confirming only soft tissue involvement: 7 patients (33%)
2. Better localization in bone and soft tissue: 5 patients (24%)
3. Better delineation of extent of infection: 9 patients (43%)
4. None: 0 patients

	Added value of SPECT/CT				
	None	EOM	BDI	BL	Total
Overall infection	50	7	9	6	**72**
	70%	10%	12%	8%	**100%**
In positive cases only	-	7	9	5	**21**
	-	33%	43%	24%	**100%**

Table 3: The added value of SPECT/CT in overall infection and positive cases only.

Sensitivity, specificity, predictive values, and accuracy:

Infection (STI and OM):

Nineteen (19) patients were positive on planar and SPECT/CT, 2 were negative on planar but positive on SPECT/CT.

 The overall sensitivity, specificity and accuracy for infection OM or/and STI:

a. Planar: sensitivity 90%, specificity 100%, positive predictive value 100%, negative predictive value 97% and accuracy 97%. Table 4.

b. SPECT/CT : sensitivity 100%, specificity 100%, positive predictive value 100%, negative predictive value 100%, and accuracy 100%, Table 5.

	Final diagnosis for infection(OM and STI)	
	Positive	Negative
	TP=19	FP=0
PLANAR	FN=2	TN=51
	Sensitivity	90%	95% CI (69.6 to 98.8)
	Specificity	100%	95% CI (93 to 100)
	Positive predictive value	100%	95% CI (82.3 to 100)
	Negative predictive value	97%	95% CI (87 to 99.5)
	Accuracy	97%	95%CI (88.5 to 99.5)

Table 4: Sensitivity, specificity, predictive values, and accuracy of planar for infection, when using planar imaging only.

SPECT/CT	Final diagnosis for infection(OM and STI)		
	Positive	negative	
	TP=21	FP=0	
	FN=0	TN=51	
	Sensitivity	100%	95% CI (83.8 to 100)
	Specificity	100%	95% CI (93 to 100)
	Positive predictive value	100%	95% CI (83.8 to 100)
	Negative predictive value	100%	95% CI (93 to 100)
	Accuracy	100%	95% CI (91.2 to 100)

Table 5: Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of SPECT/CT for infection, when using SPECT/CT.

Osteomyelitis (OM)

Only 8 patients were diagnosed with OM in this study. Fifteen patients were positive on planar for OM, of whom only 8 patients had OM on SPECT/CT, with 7 false positive.

c. Planar: sensitivity 100%, specificity 89%, positive predictive value 53%, negative predictive value 100% and accuracy 90%. Table 6.

d. SPECT/CT : sensitivity 100%, specificity 100%, positive predictive value100%, negative predictive value 100%, and accuracy 100%, Table 7.

	Final diagnosis for OM		
	Positive	Negative	
	TP=8	FP=7	
Planar	FN=0	TN=57	
	Sensitivity	100%	95% CI (63.0 to 100)
	Specificity	89%	95% CI (78.7 to 95.4)
	Positive predictive value	53%	95% CI (26.5 to 78.7)
	Negative predictive value	100%	95% CI (93.7 to 100)
	Accuracy	90%	95% CI (77.9 to 96.4)

Table 6: Sensitivity, specificity, predictive values, and accuracy of planar for OM, when using planar imaging only.

SPECT/CT	Final diagnosis for OM		
	Positive	Negative	
	TP=8	FP=0	
	FN=0	TN=64	
	Sensitivity	100%	95% CI (63 to 100)
	Specificity	100%	95% CI (94.4 to100)
	Positive predictive value	100%	95% CI (63 to 100)
	Negative predictive value	100%	95% CI (94.4 to 100)
	Accuracy	100%	95% CI (92.8 to 100)

Table 7: Sensitivity, specificity, predictive values, and accuracy of SPECT/CT for OM, when using SPECT/CT.

DISCUSSION

SPECT/CT has shown to improve the accuracy of scintigraphic images when the tracer gives good-quality images, but with very poor anatomical localisation. ^{67}Ga citrate and ^{99m}Tc-labelled WBC scans are commonly used for imaging bone and joint infections. [15] [16] [19] [20] However, the correct localisation of especially bone infection is still a challenge to the clinician.

In this study, on the planar images, the sensitivity for overall infection was 90%, 95% CI(69.6 to 98.8) vs 100%, 95% CI(83.8 to 100) for SPECT/CT, but the specificity was 100% for both, 95% CI (93 to 100)and (83.8 to 100) for planar images and SPECT/CT respectively, The negative predictive value of planar was 97%,95% CI (87 to 99.5)and SPECT/CT 100%, 95% CI (93 to 100), however, the positive predictive value of planar was 100%, 95% CI (82.3 to 100), similar to SPECT/CT 100%, 95% CI (83.8 to 100). For OM, both planar and SPECT/CT had a sensitivity of 100%, 95% CI (63 to 100)but the specificity was higher for SPECT/CT, namely 100%, 95% CI (94.4 to 100) vs 89%, 95% CI (78.7 to 95.4) compared to the planar images The negative predictive value of planar was 100% ,95% CI (93.7 to 100)and SPECT/CT 100%, 95% CI (94.4 to 100), the positive predictive value of planar was53% , 95% CI(63 to 100) , vs SPECT/CT 100%, 95% CI (63 to 100). SPECT/CT did not increase the detection of OM or detected new sites compared to the planar images, but improved the specificity by providing accurate anatomical localisation of infection. This is consistent with a study by Horger et al,[35] in 31 patients suspected of bone infection. The sensitivity of the planar and SPECT/CT was 78%, and the specificity was 50% vs 86%. Although the specificity of the WBC scan is higher than the bone scan for bone infection, the study by Horger et al is consistent with our study, in which the sensitivity is similar, but the specificity is significantly different between SPECT/CT and planar for OM.

In this study, only eight patients were diagnosed with OM from 21 positive scans. SPECT/CT excluded OM and confirmed only soft tissue infection in seven (33%) patients. These patients avoided unnecessary long-term antibiotic therapy or orthopaedic surgery. In nine patients (43%), SPECT/CT better delineated the extent of infection, including the six patients with OM on planar images. It better localised the uptake in five patients (24%). It is not always possible to differentiate soft tissue infection from OM on the planar, and our results indicate that SPECT/CT is a useful adjunct in these situations. Similar results were found by Bar-Shalom et al [21] who evaluated the additional value of SPECT/CT in 82 patients, with suspicion of infection but of uncertain location. SPECT/CT provided additional information for infection diagnosis and localisation in 39 (48%) of 82 patients, defined the extent of infection in 35 patients (43%), and concluded that SPECT/CT made an incremental contribution to ^{67}Ga and WBC in 48% of patients with suspected infections by improving diagnosis, localisation and definition of extent of disease.

In this study, we found that SPECT/CT was positive in two patients where the planar images were negative, overall SPECT/CT did not contribute in 50 (70%) of the total number of patients. Our findings are supported by Filippi et al. [30] in 2006, using ^{99m}Tc-labelled WBC scans in 28 patients; 15 with suspected bone infection without orthopaedic implant (Group 1) and 13 with suspected orthopaedic implant infection (Group 2). They found that SPECT/CT did not contribute to the evaluation of patients with negative planar images.

SPECT/CT has shown good diagnostic accuracy in the evaluation of orthopaedic disorders affecting the extremities.[27] In this study, we had 44 (61%) patients with traumatic injury, 30 patients with suspected COM of the extremities, seven were diagnosed with OM. Six out of the seven had orthopaedic hardware. The diagnosis of OM in patients with orthopaedic hardware is extremely difficult with anatomical imaging.

The use of prosthetic joint replacement is increasing, especially with increasing mean age of old people. Complications of prosthetic joint surgery are relatively uncommon; however infection is still a major complication and a cause of prosthesis failure. Graute et al [36] compared planar images with SPECT/CT using ^{99m}Tc-labelled antigranulocyte. In 31 patients with suspected lower-grade infection, they found that SPECT/CT increased the sensitivity and specificity of their study. In this study, 24 patients (33%) with suspected OM had joint prosthesis. Four patients on planar were suspected of having OM. SPECT/CT excluded OM in three patients by localising the uptake to soft tissue and diagnosing OM in one patient with hip prosthesis (PH).

In 2009, Filippi et al.[37] Investigated the added value of SPECT/CT in diabetic foot, using ^{99m}Tc-labelled WBC. They had 17 patients with 19 clinically suspected sites of infection. Leukocyte scanning was positive in 16 of 19 lesions and negative in three. SPECT/CT changed the interpretation of the planar and SPECT images of 10 of 19 suspected sites (52.6%). It excluded OM in six cases, revealed bone infection in one case, and revealed both bone and soft tissue infection in three cases. The number of diabetic foot in this study was extremely small, with only four patients recruited. Only one patient was positive for STI, SPECT/CT better delineated the extent of infection with no added value in the negative cases.

The localisation of bone marrow in prior destructed bone is unexpected, which make the interpretation of the WBC scan without a colloid scan difficult.[35][36] SPECT/CT cannot rule out displaced/reactive bone morrow. In this study, SPECT/CT improved the localisation of activity in bone and soft tissue, but was unable to distinguish between displaced/reactive bone marrow and OM without the colloid scan.

Love et al.[17] compared the accuracies of bone and ^{67}Ga scintigraphy and MRI for diagnosing spinal OM in 22 patients, with 24 sites of possible spinal OM. Eleven sites of spinal OM were identified. Bone /^{67}Ga SPECT was significantly more accurate (92%) than both planar bone/ ^{67}Ga (75%) and bone SPECT. ^{67}Ga SPECT was as accurate as SPECT bone/^{67}Ga and as sensitive as MRI (91%). The radionuclide study was slightly but not significantly more specific (92% vs. 77%) than MRI. They concluded that the SPECT bone/ ^{67}Ga can be used as a reliable alternative when MRI cannot be performed and as well as an adjunct in patients where the diagnosis is uncertain. In this study, 14 patients had a ^{67}Ga scan, only one was positive for OM. The patient had severe scoliosis, the anatomy was significantly distorted and there were significant artefacts from the orthopaedic hardware on anatomical imaging. SPECT/CT contributed significantly in this patient by better localising and delineating the extent of OM.

LIMITATIONS

The limitations of the study included the following:

- Too few patients in this study had OM (8/72); diabetic foot (4) and ^{67}Ga scans (14). This made it difficult to determine the statistical significance.
- Lack of gold standard. Only 18 from 72 patients had bone biopsy, tissue culture or pus swabs.
- Two patients with OM could not return for the colloid scan.

CONCLUSION

In complicated osteomyelitis, SPECT/CT is useful in:

- Localising and defining the exact extent of infection where the planar images are abnormal;

- Increasing the specificity of the study;

- Did not add clear value in cases of negative planar images.

- Bone marrow scan are necessary when SPECT/CT localises the WBC uptake to the bone marrow to determine whether it is OM or displaced/reactive bone marrow.

We recommend in clinical practice the routine use of hybrid SPECT/CT imaging in COM when planar images are abnormal.

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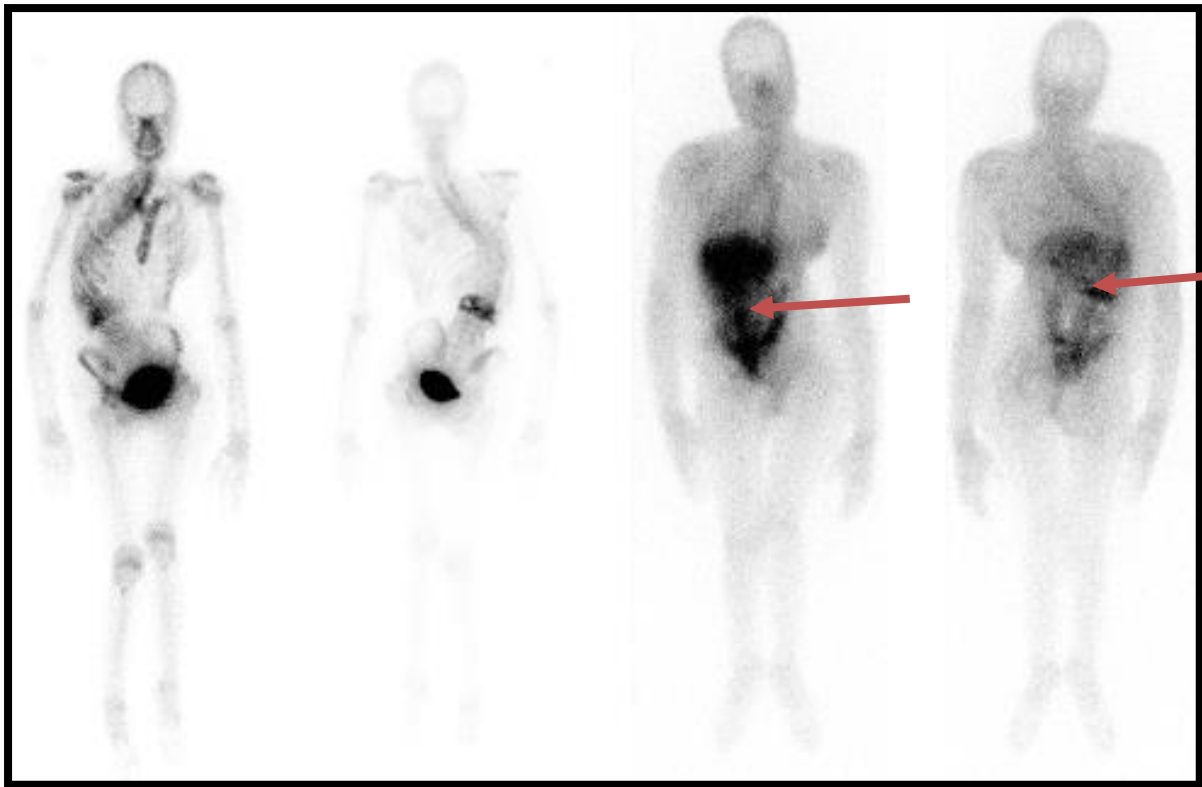
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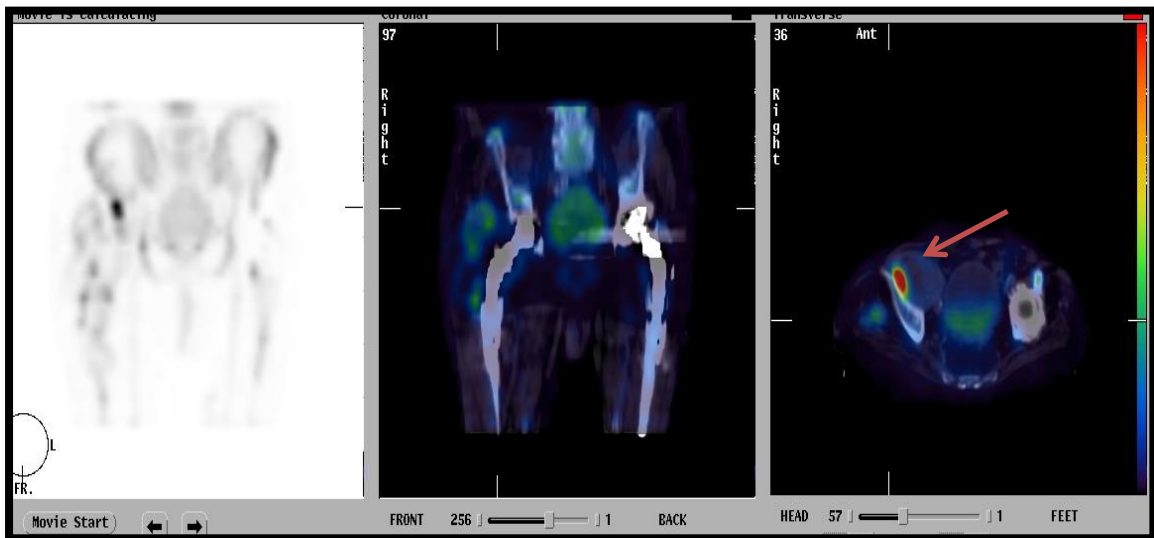
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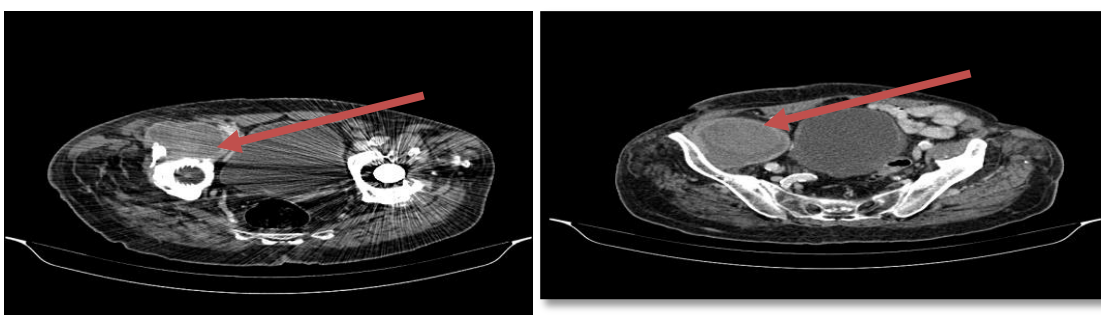
(C)

Figure 1: Planar and SPECT/CT images of 88 year old male known with PH, complain of pain to the right hip area, the planar images **(A),** demonstrate equivocal finding with focal uptake probably right iliac bone (red arrow) . On SPECT/CT **(B)** this uptake localised to soft tissue abscess, [confirmed on the diagnostic CT **(C)**], with surrounding soft tissue infection and no OM.
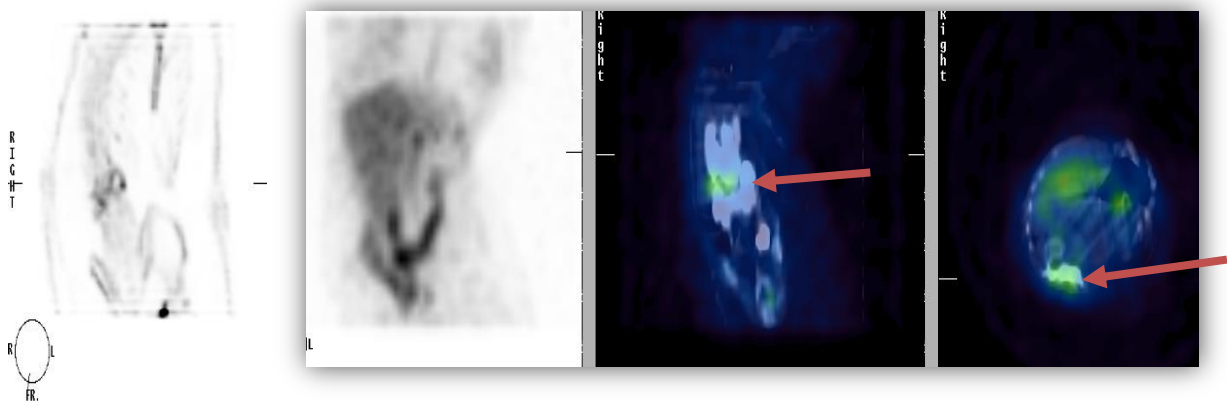
Figure 2: Planar and SPECT/CT images of 30 year old femal e known with scoliosis , had spinal surgery with orthpedic hardware in 2004, complain of chronic back pain, the planar demonstrate equivocal finding due to overlap with bowel activity . On SPECT/CT this uptake localised to bone and was interpreted as spatially discordant with MDP uptake in keeping with OM.