SPECT/CT Using ^{67}Ga and ^{111}In-Labeled Leukocyte Scintigraphy for Diagnosis of Infection

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The present study evaluated the role of SPECT/CT as an adjunct to ^{67}Ga (GS) or ^{111}In-labeled white blood cell (WBC) scintigraphy for diagnosis or localization of infection. **Methods:** Eighty-two patients (56 male and 26 female; mean age, 62 y) assessed for known or suspected infectious processes underwent 88 SPECT/CT studies. Forty-seven patients underwent GS SPECT/CT (13 with fever of unknown origin, 21 with suspected osteomyelitis, and 13 with suspected soft-tissue infection), and 35 patients underwent WBC SPECT/CT (24 with suspected vascular graft infection, and 11 with suspected osteomyelitis). Ninety-eight suggestive sites were identified (52 on GS and 46 on WBC). Additional information provided by SPECT/CT for diagnosis or localization of infection, as compared with planar and SPECT scintigraphy, was recorded. The SPECT/CT contribution was analyzed on a patient and site basis and was compared for the 2 tracers and clinical indications. **Results:** SPECT/CT provided additional information for infection diagnosis and localization in 39 (48%) of 82 patients and in 47 (48%) of 98 sites. SPECT/CT defined the extent of infection in 35 patients (43%) in 43 sites (44%) and excluded infection in 4 suggestive sites defined as physiologic bowel uptake on GS. SPECT/CT was incorrect in 2 suggestive sites (1 GS and 1 WBC). The contribution of SPECT/CT was significantly higher for WBC than for GS ($P < 0.05$)—in 63% versus 36% of patients, respectively, and in 61% versus 36% of sites, respectively. **Conclusion:** SPECT/CT made an incremental contribution to GS and WBC in 48% of patients with suspected infections, by improving diagnosis, localization, and definition of extent of disease. SPECT/CT has an important role mainly with highly specific, low-background infection-seeking tracers such as WBC.

Key Words: SPECT/CT; gallium scintigraphy; labeled leukocyte scintigraphy; infection

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A wide armamentarium of clinical, laboratory, and imaging tools is available today for diagnosis of infections. Anatomic imaging modalities such as CT or MRI provide a high-quality assessment of structural abnormalities related to infection (*1–3*). Scintigraphic studies have demonstrated early functional impairment due to an infectious process (*4*). Diagnosis and precise delineation of infection may be challenging in certain clinical scenarios, rendering decisions concerning further patient management difficult (*5,6*).

^{67}Ga scintigraphy (GS) and ^{111}In-labeled white blood cell scintigraphy (WBC) have been widely used in the assessment of suspected infection (*7,8*). However, their clinical applications may be limited by the relatively low spatial resolution and the lack of anatomic landmarks of scintigraphy. High ^{67}Ga uptake in the liver, colon, or kidneys may decrease the performance of GS in assessments of suspected abdominal-pelvic sites of infection. Defining the presence or absence of bone or vascular graft involvement by an adjacent soft-tissue infectious process may be impossible on WBC, a highly specific tracer with only scarce background uptake to use as a framework for orientation (*8–10*).

The complementary use of scintigraphic and anatomic imaging modalities can overcome many of the limitations in the assessment of infection (*7*). A SPECT/CT device that provides accurate online spatial fusion of functional (scintigraphic) and anatomic (low-dose CT) imaging data has been shown to be beneficial for the evaluation of endocrine and neuroendocrine tumors (*11–14*). There are only limited, preliminary reports evaluating the potential value of this new hybrid imaging modality for the assessment of infection (*15–17*).

The aim of the present study was to assess the role of SPECT/CT as an adjunct to GS and WBC in patients being evaluated for the presence of an infectious process or to localize an infectious process. We hypothesized that SPECT/CT localization of scintigraphic findings within anatomic structures would improve GS and WBC diagnosis and localization of infection. Such information may further have a clinical impact on the diagnostic and therapeutic management of patients with suspected infection.

MATERIALS AND METHODS

Patient Population

Ninety-one patients referred for GS or WBC for the evaluation of a known or suspected infectious process between October 1999

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and December 2002 underwent SPECT/CT studies in addition to routine scintigraphy. The decision to perform SPECT/CT and the selection of its field of view (FOV) were based on the need to evaluate an infectious process suspected because of clinical symptomatology, patient history, the results of prior imaging tests, or planar scintigraphy findings that were of uncertain nature or location. The Institutional Ethics Committee approved the use of SPECT/CT in addition to the routine scintigraphic protocol.

Follow-up data to confirm the scintigraphy results were not available for 9 patients, who were excluded from further analysis. The final study population included 82 patients, who were retrospectively evaluated. There were 56 male patients and 26 female patients, with a median age of 62 y (range, 7–91 y). GS was performed on 47 patients, including 13 patients who had fever of unknown origin (FUO), 21 who had suspected osteomyelitis, and 13 who had suspected visceral or soft-tissue infections. WBC was performed on 35 patients, including 24 with suspected vascular graft infection and 11 with suspected complicated bone osteomyelitis. Eighty-eight SPECT/CT studies were performed on these 82 patients: 15 studies of the chest, 21 of the abdomen, 31 of the pelvis, and 21 of the lower extremities.

Imaging Protocol

GS was performed 24 h after injection of ^{67}Ga citrate (185 MBq for adults; 1.85 MBq/kg for children). Planar scintigraphy was performed with a dual-head, variable-angle digital γ-camera (Millennium VG; GE Healthcare) using a medium-energy collimator and the 3 main energy peaks of ^{67}Ga: 93, 184, and 300 keV. Whole-body images were acquired for 240 s per FOV.

WBC was performed 24 h after injection of 18.5 MBq of ^{111}In-labeled mixed-culture leukocytes. Planar images were acquired for 20 min for each FOV on a dual-head, variable-angle γ-camera (Millennium VG) equipped with a medium-energy collimator and using the 2 energy peaks of ^{111}In: 172 and 245 keV.

SPECT/CT studies of both GS and WBC were performed after planar imaging using a dual-head, variable-angle γ-camera equipped with a low-power x-ray transmission system mounted on the same slip-ring gantry (Millennium VG and Hawkeye; GE Healthcare). The low-dose CT transmission scan was acquired for 16 s over 220° for each transaxial slice. Multiple slices were obtained by moving the table by a slice step before acquisition of the next slice. The full FOV consisting of 40 slices was completed in 10 min. The transmission data were reconstructed using filtered backprojection to produce cross-sectional images. The resolution of the CT scans was 2.2 mm, but localization images were produced on a 4.5-mm pixel size, similar to the nuclear medicine emission images. The CT scans were reconstructed into a 256 × 256 matrix. Transmission data were integrated into the emission database, using the nuclear medicine workstation (eNTEGRA; GE Healthcare).

After transmission, the SPECT component of the same FOV was acquired using a 128 × 128 matrix, 360° rotation, 6° angle step, and 50-s-per-frame acquisition time, for both GS and WBC. No attenuation correction was used. GS SPECT data were reconstructed by filtered backprojection using a Metz filter with parameters 3 and 14. WBC SPECT data were reconstructed by filtered backprojection using a Hanning filter. SPECT studies were viewed in the coronal, axial, and sagittal planes and in reprojection 3-dimensional cine mode.

Matching pairs of x-ray transmission and nuclear medicine emission images were fused using the eNTEGRA software, and hybrid images of overlying transmission (CT) and emission (SPECT) data were generated.

Interpretation Criteria

Two experienced nuclear medicine physicians aware of the patients' clinical history and the results of previously performed conventional imaging tests initially reviewed the scintigraphic data, including the planar and SPECT images, with regard to the presence and location of infection. SPECT/CT images were subsequently reviewed and interpreted in the same manner as for the scintigraphic (planar and SPECT) data. SPECT/CT images were visually inspected to exclude misregistration between the SPECT and CT components. Landmarks of reference included skeletal structures for GS and bone marrow or soft-tissue uptake for WBC SPECT/CT. No misalignment was found in the SPECT/CT studies of the 82 patients.

Descriptions of GS and WBC planar, SPECT, and SPECT/CT images included the location of any focus of abnormal tracer uptake and an assessment of whether it was caused by infection, was unrelated to the infectious process, or was of equivocal cause.

A focus of increased uptake recognized as part of the known physiologic tracer biodistribution was considered to be unrelated to the infectious process. A focus of increased uptake that could not be related to the normal physiologic biodistribution of the radiopharmaceutical and was in the suggestive region, based on clinical or prior imaging data, was considered to represent infection. In patients with FUO in whom no specific site was suggested before the current imaging assessment, any abnormal, nonphysiologic site of increased uptake was considered to represent infection. An equivocal focus of increased uptake was one that could not clearly be defined as either infectious or physiologic or whose location within 1 of several adjacent structures was uncertain.

A GS or WBC study was considered positive for infection when showing at least 1 focus of abnormal uptake considered to represent an infectious process. Study findings were considered negative when no sites of abnormal tracer uptake were shown. Studies showing only equivocal sites were defined as equivocal for infection.

For the site-based analysis, SPECT/CT was considered contributory when it provided data that could not be obtained from the assessment of planar and SPECT images concerning the presence of infection or its precise location. For the patient-based analysis, SPECT/CT was considered contributory if it provided incremental data for at least 1 suggestive site. Final diagnosis was verified by culture or surgery in 59 sites in 52 patients and by correlative imaging data or clinical follow-up of up to 24 mo in 39 sites in 30 patients.

Data Analysis

The number of patients and sites for which SPECT/CT changed the scintigraphic interpretation with respect to the presence or location of infection was recorded and used for comparison between the performance of SPECT/CT and scintigraphy (planar + SPECT). SPECT/CT-induced changes in GS and WBC interpretation were analyzed on a patient and site basis for the whole study group and separately for GS and WBC. The patient-based performance of SPECT/CT was compared for the different clinical indications, including FUO, osteomyelitis, soft-tissue infection, and vascular graft infection. For the site-based analysis, the comparison was based on the type of infection suspected in the site, including osteomyelitis, soft-tissue infection, or vascular graft infection.

The difference in SPECT/CT performance between GS and WBC, and for the different clinical indications, was assessed by the χ^2 test. P values of less than 0.05 were considered statistically significant.

RESULTS

Infection was diagnosed in 58 (71%) of 82 patients, including 31 patients who underwent GS and 27 who underwent WBC. Thirty patients had a soft-tissue infection, including soft-tissue abscesses ($n = 14$: 4 pelvic, 3 lung, 2 spleen, 2 liver, 1 paravertebral, 1 subdiaphragmatic, and 1 upper arm); wound infection ($n = 13$); and peritonitis, septic arthritis, or cellulitis ($n = 1$ patient with each). Twelve patients had osteomyelitis, 10 had a vascular graft infection, 4 had a urinary tract infection, 1 had subacute bacterial endocarditis, and 1 had brucellosis.

The final diagnosis indicated no evidence of infection in 24 patients (29%), including 16 patients who underwent GS and 8 who underwent WBC. In 20 patients, a different type of condition was diagnosed, including malignancy ($n = 5$: medulloblastoma, renal cell carcinoma, prostate carcinoma, lymphoma, and myeloma), degenerative spine disease ($n = 3$), drug fever ($n = 2$), or other orthopedic or inflammatory conditions ($n = 10$: compressed vertebral fracture, avascular necrosis of the femoral head, rupture of shoulder ligaments, arthritis, Behçet's disease, glomerulonephritis, exacerbation of chronic lung disease, postpericardiotomy syndrome, vascular graft pseudoaneurysm, and dislocation of a hip prosthesis). In 4 patients, clinical signs and symptoms resolved without further treatment, and they had an uneventful follow-up of 12–16 mo.

Patient-Based Analysis

Scintigraphy (planar + SPECT) and SPECT/CT showed concordant results for the diagnosis and location of infection in 41 (50%) of the 82 patients, including 29 GS and 12 WBC studies. Twenty-four studies (18 GS and 6 WBC) were positive for infection, and 17 studies (11 GS and 6 WBC) were negative. Infection was diagnosed in 22 of these patients (16 GS and 6 WBC). No infection was diagnosed in 19 patients (13 GS and 6 WBC).

Scintigraphy and SPECT/CT results were discordant for the diagnosis and location of infection in 41 (50%) of 82 patients (18 GS and 23 WBC). The clinical details of these patients and their scintigraphic results are presented in Tables 1 and 2. Infection was diagnosed in 34 of these patients (14 GS and 20 WBC). No infection was found in 7 patients (4 GS and 3 WBC). Five of the 41 discordant studies (all GS) differed with regard to diagnosis of infection, and SPECT/CT contributed to 4 studies. Thirty-six studies were discordant with regard to location of infection (13 GS and 23 WBC), and SPECT/CT contributed to 35 of these studies. SPECT/CT was incorrect in 2 patients (2%) for the diagnosis (1 GS) or location (1 WBC) of infection.

SPECT/CT was beneficial for diagnosis of infection on GS in 4 patients, including 2 patients with FUO, 1 with suspected osteomyelitis, and 1 with a suspected infected polycystic kidney. Planar and SPECT GS of these patients showed a single equivocal site of increased abdominopelvic tracer uptake. SPECT/CT excluded infection in these sites by localizing the suggestive focus within bowel loops, thus defining it as physiologic tracer uptake. This physiologic uptake was still present in 2 patients on delayed GS up to 10 d after injection. The final diagnosis of the 2 patients referred with FUO included drug-induced fever in 1 patient and central fever in the presence of recurrent medulloblastoma in the other. Multiple myeloma was diagnosed in the patient with suspected osteomyelitis. The fourth patient, assessed for a suspected infected polycystic kidney, was diagnosed with lower urinary tract infection, underwent a successful renal transplantation without prior nephrectomy, and had an uneventful follow-up of 19 mo.

SPECT/CT was misleading for the diagnosis of infection in 1 GS study. This patient, with fever and bilateral ovarian cystic lesions, had a left pelvic focus that was equivocal on scintigraphy but was shown to be within bowel loops on SPECT/CT and was considered to be physiologic uptake. Delayed images 7 d after injection showed persistent uptake in the same region. A left ovarian abscess was diagnosed on laparotomy.

SPECT/CT was beneficial for determining the precise anatomic location of infection in 35 (85%) of 41 discordant studies (13 GS and 22 WBC).

Of the 13 discordant GS studies, SPECT/CT defined ($n = 4$) or excluded ($n = 6$) osteomyelitis in 10 patients. SPECT/CT defined the precise anatomic location of soft-tissue infection in 3 patients, including 1 spleen abscess, 1 subdiaphragmatic abscess, and 1 infected abdominal surgical scar (Fig. 1). Of the 22 discordant WBC studies, SPECT/CT defined ($n = 9$) or excluded ($n = 7$) graft involvement by the infectious process in 16 patients with suspected vascular graft infection. In 6 patients with suspected complicated bone osteomyelitis, SPECT/CT defined ($n = 4$) or excluded ($n = 2$) skeletal infection (Fig. 2).

SPECT/CT was misleading for the location of infection in 1 WBC study. In this patient, presenting with a left inguinal surgical wound infection 6 wk after thrombectomy within a vascular graft, SPECT/CT localized the suggestive focus of increased tracer uptake to include both the infected soft tissue and the adjacent graft. Clinical signs and symptoms of infection resolved rapidly with antibiotic treatment, indicating no graft infection, and the patient had no further evidence of graft infection during a follow-up of 24 mo.

Overall, SPECT/CT provided more accurate data than did planar imaging and SPECT for the diagnosis and localization of infection in 39 (48%) of 82 patients. SPECT/CT contributed significantly more for WBC than for GS, improving the interpretation of 17 (36%) of 47 GS studies, compared with 22 (63%) of 35 WBC studies ($P < 0.05$) (Table 3). GS SPECT/CT was contributory in 48% of patients assessed for osteomyelitis, in 23% assessed for soft-tissue infection, and in 31% with FUO. WBC SPECT/CT

TABLE 1
Incremental Value of GS SPECT/CT: Clinical and Scintigraphic Details in 20 Discordant Suggestive Sites in 18 Patients

Site no.	Suspected infection	Planar + SPECT findings	SPECT/CT findings	SPECT/CT contribution	Final diagnosis
1	STI	Equivocal abdominal uptake	Physiologic bowel uptake	Exclusion of infection	Drug fever
2	STI	Equivocal abdominal uptake	Physiologic bowel uptake	Exclusion of infection	Central fever; (medulloblastoma)
3	STI	Equivocal abdominal uptake	Physiologic bowel uptake	Exclusion of infection	Myeloma
4	STI	Equivocal abdominal uptake	Physiologic bowel uptake	Exclusion of renal infection	Lower urinary tract infection
5	STI	Mid abdominal infectious process	Infected surgical scar	Localization to scar	Infected abdominal surgical scar
6	STI	L abdominal infectious process	Splenic abscess	Localization to spleen	Splenic abscess
7	STI	L abdominal infectious process	Subdiaphragmatic infection	Exclusion of spleen abscess	Subdiaphragmatic abscess
8	OM	Pelvic infection (susp. sacral OM)	Pelvic abscess	Exclusion of OM	Perianal abscess
9	OM	Infection in arm (susp. humerus OM)	STI only	Exclusion of OM	Soft-tissue abscess in upper arm
10	OM	Infection in thigh (susp. femur OM)	STI only	Exclusion of OM	Soft-tissue abscess in thigh
11	OM	Pelvic infection (susp. sacral OM)	Pelvic abscess and sacral OM	Defining extent of OM and STI	Pelvic abscess and sacral OM
12	OM	Paraspinal infection (susp. spine OM)	Paravertebral abscess	Exclusion of OM	Paravertebral abscess
13	OM	Pelvic infection (susp. sacral OM)	Pelvic abscess	Exclusion of OM	Pararectal abscess
14	OM	Pelvic infection (susp. sacral OM)	Pelvic abscess	Exclusion of OM	Pelvic abscess
15	OM	Paraspinal infection (susp. spine OM)	Thoracic vertebra OM	Localization to bone	Thoracic vertebra OM
16	OM	Infection in thigh (susp. femur OM)	STI and femoral OM	Defining extent of OM and STI	STI and femoral OM
17	OM	Paraspinal infection (susp. spine OM)	Thoracic vertebra OM	Localization to bone	Thoracic vertebra OM
18	OM	Infection in thigh (susp. infected hip prosthesis)	STI only	Exclusion of infected prosthesis	Cellulitis in thigh
19	OM	Lung abscess (susp. rib OM)	Lung abscess and OM of ribs	Defining extent of OM and STI	Lung abscess and OM of ribs
20	STI	Equivocal pelvic uptake	Physiologic bowel uptake	False exclusion of infection	Ovarian abscess

susp. = suspected; OM = osteomyelitis; STI = soft-tissue infection.

was contributory in 67% of patients with suspected vascular graft infection and in 55% assessed for osteomyelitis (Table 3).

Site-Based Analysis

The contribution of SPECT/CT over that of scintigraphy (planar + SPECT) for the diagnosis and localization of infection on GS and WBC was evaluated in 98 suggestive sites (52 sites on GS and 46 sites on WBC). Infection was diagnosed in 64 of 98 sites (29 GS and 35 WBC). There were 38 sites of soft-tissue infection (17 abscesses, 19 infected wounds, 1 case of septic arthritis, and 1 case of cellulitis), 13 sites of osteomyelitis, and 13 sites of vascular graft infection. No infection was found in 34 sites (23 GS and 11 WBC). The final diagnosis included malignancy ($n = 5$), degenerative spine changes or muscular strain ($n = 4$), arthritis ($n = 3$), a splenic cyst ($n = 2$), and 1 site each of inflammatory adenopathy, vertebral fracture, avascular necrosis, rupture of ligaments, vascular graft pseudoaneurysm, and hip prosthesis dislocation. Physiologic tracer uptake in the bowel was seen in 4 sites. No further evidence of disease was found in 10 sites, involving joint prostheses ($n = 4$), surgical scars ($n = 3$), a vascular graft ($n = 1$), a renal transplant ($n = 1$), and a pacemaker ($n = 1$).

Scintigraphy (planar + SPECT) and SPECT/CT showed concordant results for the diagnosis and localization of

TABLE 2
Incremental Value of WBC SPECT/CT: Clinical and Scintigraphic Details in 29 Discordant Suggestive Sites in 23 Patients

Site no.	Suspected infection	Planar + SPECT findings	SPECT/CT findings	SPECT/CT contribution	Final diagnosis
1	OM	Infection in calf (susp. tibial OM)	STI in calf	Exclusion of OM	Wound infection
2	OM	Infection in thigh (susp. femoral OM)	STI in thigh and femoral OM	Defining extent of OM and STI	STI of thigh and femoral OM
3	OM	Infection in calf (susp. tibial OM)	STI in calf	Exclusion of OM	Wound infection
4	OM	Infection in thigh (susp. femoral OM)	STI in thigh	Exclusion of OM	Wound infection
5	OM	Infection in thigh (susp. femoral OM)	STI in thigh and femoral OM	Defining extent of OM and STI	Wound infection and femoral OM
6	OM	Infection of foot (susp. metatarsal OM)	OM of metatarsus	Defining OM	OM of metatarsal bone
7	OM	Infection in thigh (susp. infected hip prosthesis)	Infected prosthesis	Defining OM	Infected hip prosthesis
8	VGI (fem-pop)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
9	VGI (aorto-b-fem)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
10	VGI (fem-pop)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
11	VGI (aorto-b-fem)	Infection in groin (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
12	VGI (fem-pop)	Infection in groin (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
13	VGI (fem-pop)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
14	VGI (fem-tibialis)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
15	VGI (fem-fem)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
16	VGI (fem-fem)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
17	VGI (fem-pop)	Infection in groin (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
18	VGI (fem-pop)	Infection in thigh (susp. VGI)	STI and graft infection	Defining extent of STI and graft	STI and VGI
19	VGI (fem-peroneal)	Infection in thigh (susp. VGI)	STI in thigh	Exclusion of graft infection	Wound infection
20	VGI (fem-peroneal)	Infection in thigh (susp. VGI)	STI in thigh	Exclusion of graft infection	Wound infection
21	VGI (fem-pop)	Infection in groin (susp. VGI)	STI in groin	Exclusion of graft infection	Wound infection
22	VGI (fem-pop)	Infection in groin (susp. VGI)	Uptake in inguinal adenopathy	Exclusion of graft infection	Inflammatory inguinal adenopathy
23	VGI (fem-pop)	Infection in groin (susp. VGI)	STI in groin	Exclusion of graft infection	Wound infection
24	VGI (aorto-b-fem and fem-pop)	Infection in groin (susp. VGI)	Wound infection	Exclusion of graft infection	Wound infection
25	VGI (fem-pop)	Infection in groin (susp. VGI)	Wound infection	Exclusion of graft infection	Wound infection
26	VGI (fem-pop)	Infection in groin (susp. VGI)	Wound infection	Exclusion of graft infection	Inflammatory scar reaction
27	VGI (aorto-b-fem)	Infection in groin (susp. VGI)	Wound infection	Exclusion of graft infection	Inflammatory scar reaction
28	VGI (fem-pop)	Infection in groin (susp. VGI)	Wound infection	Exclusion of graft infection	Inflammatory scar reaction
29	VGI (fem-fem)	Infection in thigh (susp. VGI)	STI and graft infection	Misleading for graft infection	Wound infection

susp. = suspected; OM = osteomyelitis; STI = soft-tissue infection; VGI = vascular graft infection; fem-pop = femoropopliteal bypass; aorto-b-fem = aortobifemoral bypass; fem-tibialis = femorotibialis bypass; fem-fem = femorofemoral bypass; fem-peroneal = femoroperoneal bypass.

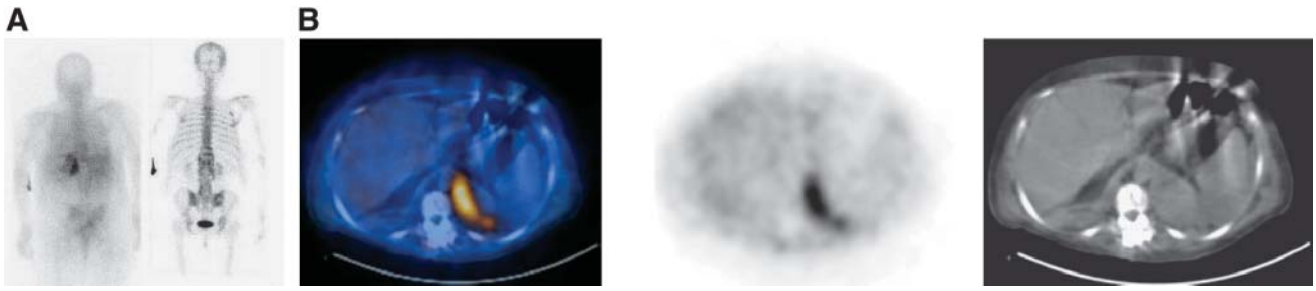

FIGURE 1. SPECT/CT for suspected bone infection on GS. A 56-y-old woman presented with fever, low back pain, and infected scar 1 mo after spinal surgery and was referred for GS for suspected vertebral osteomyelitis. (A) Planar posterior whole-body GS image (left) shows prominent abnormal uptake in left lower back, corresponding in part to regions of increased irregular uptake seen on planar posterior whole-body ^{99m}Tc-MDP image (right) along operated vertebrae. (B) Transaxial GS SPECT/CT image (left) localizes abnormal uptake on GS (center) to paravertebral soft-tissue abscess seen on corresponding CT image (right), thus defining soft-tissue infection without osteomyelitis. There was no evidence of vertebral osteomyelitis on follow-up CT 4 wk later.

infection in 49 (50%) of 98 sites, including 32 sites on GS and 17 on WBC. Thirty-seven sites (26 GS and 11 WBC) were positive for infection, and 12 sites (6 GS and 6 WBC) were negative. Infection was diagnosed in 23 sites (13 GS and 10 WBC). No infection was found in 26 sites (19 GS and 7 WBC).

Scintigraphy and SPECT/CT results were discordant for the diagnosis and localization of infection in 49 (50%) of 98 suggestive sites (20 GS and 29 WBC). The clinical and scintigraphic results in these 49 sites are detailed in Tables 1 and 2. Infection was diagnosed in 41 of 49 sites (16 GS and 25 WBC). No infection was found in 8 sites (4 GS and 4 WBC).

Scintigraphy and SPECT/CT differed in the diagnosis of infection in 5 sites (all GS) and in localization in 44 sites (15 GS and 29 WBC). SPECT/CT provided accurate data for diagnosis (4 GS) and for localization (15 GS and 28 WBC) of infection in 47 of these 49 sites (48% of the total 98 sites). SPECT/CT was misleading in the diagnosis (1 GS) and localization (1 WBC) of infection in 2 sites.

SPECT/CT was more beneficial than planar imaging and SPECT for the exclusion of infection in 4 sites of equivocal increased abdominopelvic ^{67}Ga uptake that had been localized by SPECT/CT within the bowel loops and thus defined as physiologic activity. SPECT/CT was misleading for the diagnosis of infection in 1 site on GS (as detailed in the patient-based analysis).

SPECT/CT defined the precise anatomic location of 43 infectious sites (44% of the total 98 sites) that had been equivocal or erroneous on scintigraphy (15 GS and 28 WBC). Of the 15 discordant sites on GS, SPECT/CT defined the precise anatomic location of soft-tissue infection in 3 sites, including 2 abscesses and 1 infected abdominal scar. SPECT/CT defined ($n = 5$) or excluded ($n = 7$) osteomyelitis in 12 sites. Of 28 discordant sites on WBC, SPECT/CT defined ($n = 11$) or excluded ($n = 10$) vascular graft infection near a surgical wound infection in 21 sites and defined ($n = 4$) or excluded ($n = 3$) osteomyelitis of complicated bones in 7 sites. SPECT/CT was misleading for infection location in 1 site on WBC (as detailed in the patient-based analysis).

Overall, SPECT/CT was more accurate than scintigraphy for the diagnosis and localization of infection in 47 (48%) of 98 suggestive sites. SPECT/CT contributed significantly more to the assessment of suspected sites on WBC than on GS, improving the interpretation of 28 (61%) of 46 sites on WBC, compared with 19 (36%) of 52 sites on GS ($P < 0.05$)

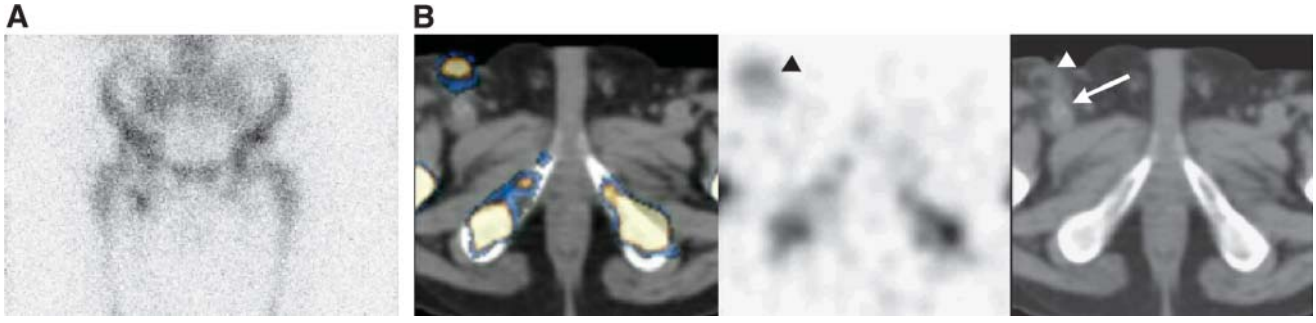

FIGURE 2. SPECT/CT for suspected vascular graft infection on WBC. A 54-y-old man, 2 y after left femoropopliteal bypass and 1 mo after right femoral-popliteal bypass, was referred for WBC for suspected vascular graft infection in presence of infected surgical wound in right groin. (A) Planar anterior WBC image shows focal uptake in right groin. Precise anatomic location of this lesion with regard to potential involvement of adjacent vascular graft could not be determined. (B) Transaxial WBC SPECT/CT image (left) shows that suggestive right inguinal uptake seen on WBC (center, arrowhead) is localized to subcutaneous fat blurring seen on corresponding low-dose CT image in region of surgical scar (right, arrowhead), with no involvement of adjacent vascular graft (right, arrow). Signs and symptoms of surgical wound infection resolved rapidly with systemic antibiotic and local treatment. Patient had no further evidence of wound or graft infection during follow-up of 10 mo.

TABLE 3
Contribution of SPECT/CT to Diagnosis and Localization of Infection: Patient-Based Analysis

Scintigraphy	Clinical indication	Total no. patients	Contributory SPECT/CT no. patients	*P*
GS	Osteomyelitis	21	10 (48)	NS*
	Soft-tissue infection	13	3 (23)	NS*
	FUO	13	4 (31)	NS*
	Total	47	17 (36)	
WBC	Vascular graft infection	24	16 (67)	NS*
	Osteomyelitis	11	6 (55)	NS*
	Total	35	22 (63)	
Total		82	39 (48)	<0.05†

*Comparison between different clinical indications for same scintigraphic method.
†Comparison between GS and WBC.
NS = nonsignificant.
Numbers in parentheses are percentage of total number of patients with this indication.

(Table 4). GS SPECT/CT had an incremental value in 39% of the sites suspected of being osteomyelitis and in 33% of sites assessed for soft-tissue infection. WBC SPECT/CT was of additional value in 68% of sites suspected of being vascular graft infection and in 47% of sites assessed for osteomyelitis (Table 4).

DISCUSSION

GS and WBC are modalities commonly used for the diagnostic workup of infectious processes (*7,8*). GS has been used for the assessment of FUO and for the diagnosis of vertebral osteomyelitis and lung infections. WBC has been used for the diagnosis of complicated osteomyelitis involving bones after fractures or surgery, vascular graft infections, and various soft-tissue infections (*4,6*). These scintigraphic modalities are, however, limited by their low image resolution and lack of anatomic landmarks. As demonstrated in 35 (43%) of 82 patients of the present study population, the main diagnostic difficulty was the inability to precisely localize an infectious focus within a specific organ. This difficulty is of major clinical significance when one needs to determine whether a bone or vascular graft is involved with an adjacent soft-tissue infection.

TABLE 4
Contribution of SPECT/CT to Diagnosis and Localization of Infection: Site-Based Analysis

Scintigraphy	Type of suspected infection	Total no. sites	Contributory SPECT/CT no. sites	*P*
GS	Osteomyelitis	31	12 (39)	NS*
	Soft-tissue infection	21	7 (33)	NS*
	Total	52	19 (36)	NS*
WBC	Vascular graft infection	31	21 (68)	NS*
	Osteomyelitis	15	7 (47)	NS*
	Total	46	28 (61)	NS*
Total		98	47 (48)	<0.05†

*Comparison between different clinical indications for same scintigraphic method.
†Comparison between GS and WBC.
NS = nonsignificant.
Numbers in parentheses are percentage of total number of sites with this indication.

Limited preliminary data have previously suggested a potentially promising role for hybrid SPECT/CT in the evaluation of infection. Horger et al. (*17*) showed that SPECT/CT changed the interpretation of radioimmunoscintigraphy with ^{99m}Tc-labeled antigranulocyte antibodies in 28% of suggestive foci evaluated in 27 patients in whom relapsing posttraumatic osteomyelitis was suspected. SPECT/CT correctly localized all foci of uptake detected on planar and SPECT images, thus accurately differentiating between soft-tissue infection, septic arthritis, and osteomyelitis.

In the present study, the precise anatomic localization of foci of abnormal tracer uptake by SPECT/CT was contributory in 48% of patients and in 48% of the suspected sites evaluated. SPECT/CT contributed to better diagnosis of infection in only a few patients (in GS studies demonstrating abdominal uptake of unclear significance). Physiologic bowel uptake of ^{67}Ga is a known obstacle in the interpretation of GS that is usually overcome by clearance on delayed imaging. The ability to localize abdominal uptake within the bowel by SPECT/CT enabled the correct exclusion of infection in 4 patients in our study. The inconvenience and cost of delayed imaging could have been spared in these patients. Nevertheless, it should be noted that defining ^{67}Ga uptake as physiologic by its localization within bowel loops may be misleading with the low-dose, unenhanced CT provided by the first-generation SPECT/CT system used in the study, as was the case in 1 patient. The recently introduced new SPECT/CT systems providing improved CT capabilities may further improve the performance of fused data for accurate characterization of equivocal abdominal scintigraphic findings.

However, the main value of SPECT/CT, observed in 43% of patients in our study, was related to the precise anatomic localization of an infectious process and the delineation of its extent after its diagnosis on scintigraphy.

SPECT/CT had a significantly higher incremental contributory value for WBC than for GS, contributing to the accurate identification of infection in 55% of patients suspected to have osteomyelitis and 67% of those suspected to have a vascular graft infection. This value can be explained by the high specificity of WBC with low background activity and therefore limited anatomic information. Although, in cases of suspected osteomyelitis, combined bone and bone

marrow scintigraphy can somewhat facilitate accurate image interpretation, such additional data cannot be obtained when vascular graft infection is suspected. Accurate spatial localization of abnormal foci to the graft or adjacent soft tissues may be impossible unless the images are combined with an anatomic road map. Precise alignment of the body region of interest during SPECT/CT acquisition is crucial to ensure accurate registration and anatomic localization of scintigraphic findings, particularly in the extremities, which are prone to patient motion between imaging sequences and which may harbor an infectious process in a structure that is very close to several other structures. With WBC, ensuring precise image coregistration may be difficult. Although sometimes difficult, using bone marrow or background uptake as a reference for image alignment in the extremities allowed us to verify the accuracy of registration in all SPECT/CT studies evaluated.

A relative bias in the patient selection criteria limited the present study. In the routine clinical setting, the decision to perform SPECT/CT is directed by clinical or prior conventional imaging diagnostic dilemmas or by equivocal planar scintigraphic findings. SPECT/CT is not performed routinely on all patients referred for suspected infection at our institution. The present study population was therefore representative of the performance of SPECT/CT as an adjunct to conventional scintigraphic assessment. Following these indications, hybrid imaging had an additional value in 48% of the assessed patients.

Present and future efforts in the development of more specific radiotracers for imaging of infection underscore the need and potential value of combined anatomic and functional assessments. The development of new, improved SPECT/CT devices will lead to improved diagnosis and localization of infection and subsequently to optimized treatment planning.

CONCLUSION

The results of the present study demonstrated that SPECT/CT is a valuable adjunct to GS and WBC in patients with suspected infections. The precise anatomic localization of suggestive foci of increased tracer uptake enabled the diagnosis of infection and, more frequently, the precise localization and delineation of its extent in 48% of patients and 48% of sites. SPECT/CT contributed significantly more to the assessment of the highly specific, low-background WBC, emphasizing the potential important role of hybrid imaging in other target-oriented scintigraphic modalities as well.

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