Bone Imaging in Infections: Artefacts from Spectral Overlap Between a Tc-99m Tracer and In-111 Leukocytes

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In three patients with skeletal infectious disease, scintigrams with a Tc-99m bone-seeker and In-111-tagged leukocytes, made within 24 hr of each other, showed striking similarities. In two cases, the findings from the In-111 WBC images were ultimately determined to be artefacts due to Tc-99m crosstalk within the 173-keV photopeak of In-111. In the second case, the error was traced to failure to use a pure In-111 source for energy calibration: the camera had been peaked on the radiation from the patient himself, who had had an earlier Tc-99m bone scan.

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The diagnosis of infectious disease in the skeleton and joints is a common and difficult problem in clinical practice. Bone imaging with Tc-99m compounds has long been established as a sensitive method for the detection of osteomyelitis. In traumatic or postsurgical situations, however, the value of bone imaging is reduced because of its nonspecificity. In these cases, diagnosing skeletal infection becomes difficult and imaging with Ga-67 citrate has been added to increase specificity. Gallium, however, is a weak bone-imaging agent and behaves somewhat like the Tc-99m compounds, sharing their nonspecificity. Recently In-111-labeled leukocytes (In-111 WBCs) have been found reliable for diagnosis of various infections (*1–4*). The two gamma emissions of In-111, at 173 and 247 keV, are favorable for imaging with current instruments. A previous report suggests that combined scans with bone-seekers and labeled WBCs will aid in the differentiation between infection and the loosening of a prosthesis (*5*). A more recent report suggests that In-111 WBC scans are helpful in the detection of acute but not chronic infections of the skeleton (*6*). Whether In-111 WBC scans are superior to Ga-67 for detection of skeletal inflammatory disease remains to be proved. In our medical center we currently use Tc-99m bone-seekers and In-111 WBC imaging in evaluation of suspected infectious disease of the skeleton and joints. In order to expedite the evaluation of patients, In-111 WBC images are obtained within 24 hr of the Tc-99m bone scan. This sequence is followed when abnormal bone scans due to previous trauma and/or surgery are anticipated. Bone scans are obtained in all patients to identify skeletal abnormalities precisely and to provide landmarks that aid in subsequent In-111 WBC scan interpretation. We wish to present three recent cases in which abnormal results on the In-111 WBC scan were found to be artefacts.

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METHODS AND CASE PRESENTATION

The Tc-99m bone scan and the In-WBC studies are performed in our laboratory in the following manner: Blood is taken from the patient for initiation of WBC labeling with In-111, and 15 to 20 mCi of Tc-99m HMDP is administered through the same venepuncture. The patient then waits 3 hr before bone imaging is initiated. Immediately after the bone study, the white blood cells (labeled with ~400 to 500 μCi of In-111 oxine) are administered intravenously, and imaging is usually performed 24 hr later. However, imaging as early as 30 min after injection is performed when possible, since some investigators suggest that it provides good diagnostic information (*7*). Early imaging permits both scintigraphic procedures to be completed in one day if the In-111 WBC scan is positive at this early time. All In-111 WBC studies are initiated before antibiotic therapy is administered.

The bone scintigram was made on a gamma camera, either standard or large-field, in the usual manner. For the In-111 WBC imaging procedure a medium-energy collimator and two 20% energy windows were centered on the 173- and 247-keV energy peaks respectively.

Case 1 is a 57-yr-old female who presented with a 1-mo history of chills, fever, and pain, with edema of the right upper thigh and right hip. One year before admission the patient had a right total hip replacement (THR) to treat severe functional impairment

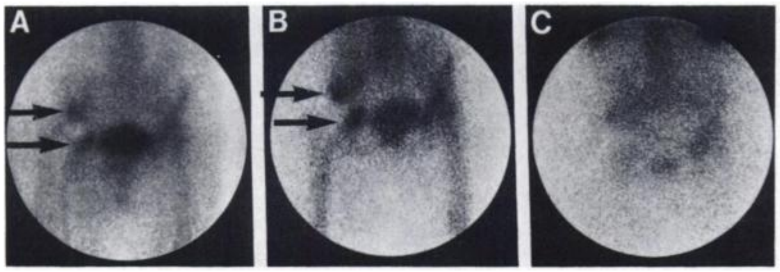

FIG. 1, Case 1. (A) Tc-99m bone scan showing increased uptake in superior and inferior aspects of right acetabulum (arrows); (B) 24-hr In-111 WBC image obtained next day shows similar uptake pattern (arrows), including bladder. (C) At 48 hr, In-111 WBC image shows no abnormal uptake apart from hip prosthesis.

stemming from tuberculous infection of the hip during childhood, with several subsequent operations. An infected prosthesis was suspected. All laboratory data were normal. Culture of the hip was not obtained. The radiographs of the hip failed to disclose evidence of infection or loosening. A bone scan (Fig. 1A) showed two areas of increased tracer uptake in the acetabular region of the right hip. A 24-hr In-111 WBC scan obtained the next day also demonstrated increased uptake in the right acetabular region (Fig. 1B), but followup In-111 images at 48 hr failed to show the same abnormalities (Fig. 1C). The patient's symptoms and signs resolved spontaneously without antibiotic therapy and she remains asymptomatic 16 mo after the initial episode.

Case 2 is a 67-yr-old male who had a history of bilateral THR 2 yr previously, now presenting with a 3-wk history of pain and decreased maneuverability of the right hip and leg. The question of infection versus loosening was raised and bone/indium scans were ordered. The bone scan (Figs. 2A & B) revealed increased uptake in the acetabulum and greater trochanter of the right hip. The left hip displayed changes secondary to the previous THR but was otherwise unremarkable. The 24-hr In-111 WBC scan, obtained the following day with revised gamma windows (20% window around the 247-keV In-111 peak, 10% around 173 keV), also revealed similar features including tracer concentration in the right hip and bladder (Fig. 2C). Investigation into this unexpected finding revealed that the dual pulse-height analyzers (PHAs) had been set up using the patient's own radiations (Tc-99m + In-111). Images obtained the same day, using identical window and energy settings but after calibration with a pure In-111 source, show no abnormal areas of increased uptake (Fig. 2D). Material obtained by needle aspiration failed to grow bacteria, thus confirming the true negative nature of the In-111 WBC study. This was further confirmed by the patient's 18-mo follow-up.

RESULTS AND DISCUSSION

The bone images and 24-hr In-111 WBC images showed identical skeletal patterns in the two cases in which the patients were ultimately proven by laboratory studies and clinical followup to be free of infection. The increased uptake on the In-111 images duplicated the Tc-99m scintigraphic pattern and corresponded to the clinically suspected areas of infection, suggesting that this diagnosis was likely. However, the similarity between the two sets of images was also disturbing.

In Case 1 (Fig. 1), scintigraphic patterns suggested that contributions from residual Tc-99m could be responsible for the image similarities noted at 24 hr but not at 48 hr. The 20% window widths centered around the Tc-99m 140-keV peak and In-111 173-keV peak involved discriminator levels bracketing 126–154 and 156–190 keV, respectively. Consequently, at least in theory, discriminator overlap was not the cause of the problem. Further investigations into our imaging methods revealed distinct technical problems. Energy resolution values (FWHM) were then determined for both radionuclides to search for possible crosstalk. A multichannel analyzer was used to obtain the FWHM of the Z pulses (energy information) from the camera. With the collimator removed, small sources of Tc-99m and In-111 at one meter were used to irradiate the crystal uniformly. The FWHM for Tc-99m was found to be 13.3%, and for In-111 at the 173-keV photopeak it was about 14%. The two gamma spectra are shown in Fig. 3. Clearly the Tc-99m photopeak "tail" contributes counts within the 20% window centered on 173 keV. Because only low-activity In-111 WBCs can be administered to the patient, images require long periods of time, typically 10 to 15 min. This factor, combined with the increased sensitivity of the medium-energy collimator used for In-111 imaging, results in some contribution of the Tc-99m peak to the In-111 images. By narrowing the 20% window around the 173-keV photopeak to 10%, the Tc-99m contribution is virtually eliminated, although In-111 sensitivity diminishes by approximately 35%.

These FWHM values prompted a service call to determine whether photomultiplier imbalance, gain drift, or other electronic problems could be corrected. Even though the experimentally determined values were within the acceptable levels stated by the manufacturer, improvement of the FWHM values would decrease and perhaps eliminate the Tc-99m and In-111 peak overlap.

Photomultiplier "tuning" (gain balancing) was then performed on the camera. This involved removing the collimator and placing a Tc-99m point source directly facing each photomultiplier tube. As before, a properly calibrated multichannel analyzer was used to observe the Z-pulse spectrum, and each phototube gain was

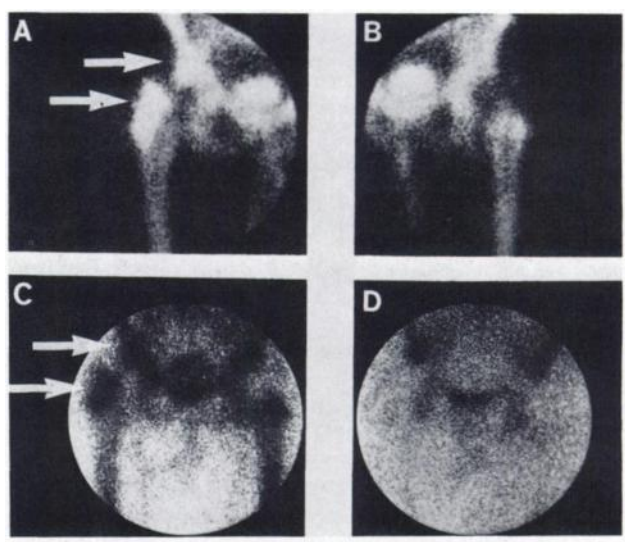

FIG. 2, Case 2. Tc-99m bone images (A) demonstrate increased uptake in right greater trochanter and acetabulum. Left hip image (B) shows prosthesis pattern with no other abnormalities. At 24-hr, In-111 WBC image (with PHA adjusted on patient's radiations) (C) also showed uptake in right greater trochanter and right acetabulum (arrows). After peaking over source of pure In-111, bilateral THR pattern appears (D) without other abnormalities.

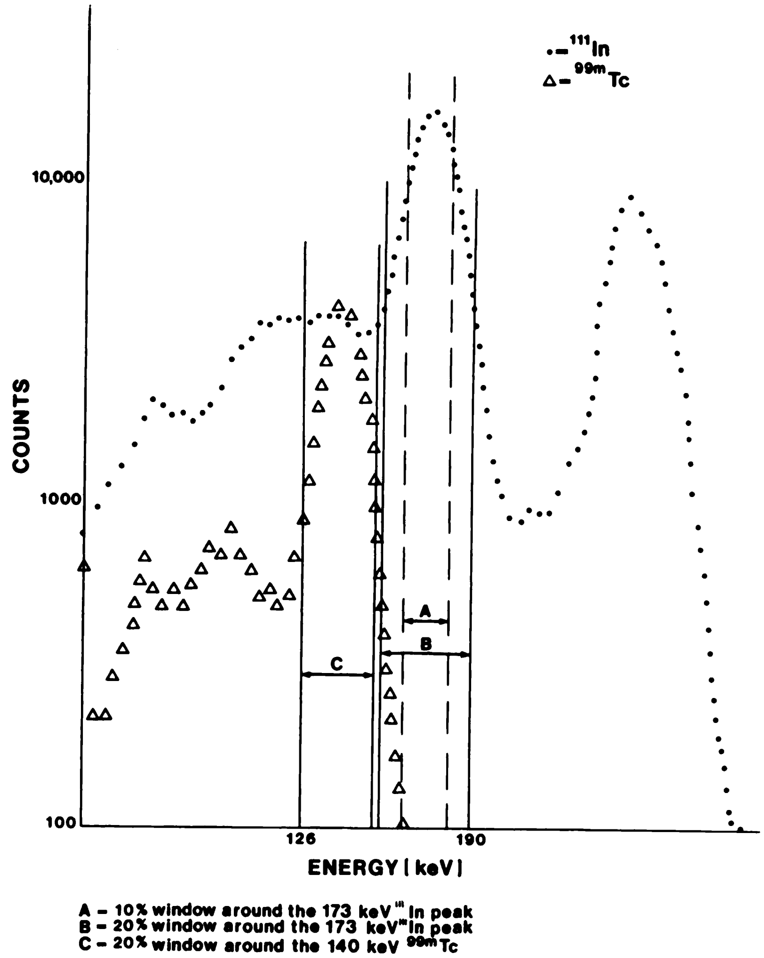

FIG. 3. Gamma spectra for Tc-99m and In-111, with 20% windows around Tc-99m (C) and 173-keV In-111 (B) photopeaks. Note spillage of technetium counts into 173-keV In-111 peak. The 10% window (A) essentially eliminates this problem.

adjusted so that the photopeak was centered over the channel corresponding to 140 keV. The 37 gains were thus trimmed. After these adjustments, the energy resolution improved to 11% FWHM for Tc-99m and 13% for In-111. The relationship was puzzling, however, since energy resolution of a NaI detector typically improves with increasing energy. Two reasons occur to us. First, the gain-balancing was done using a Tc-99m source and not an In-111 source. Second, Compton scatter from the upper gamma of In-111 causes a broadening of the 173-keV peak. At any rate even with the improved resolution, 20% windows centered at 140 and 173 keV may still permit some Tc-99m crosstalk, possibly inducing abnormal scintigraphic patterns.

We have found this true in subsequent cases, one of which is illustrated in Fig. 4. This patient had an open fracture of the left tibia and a closed uncomplicated fracture of the right femur treated with immobilizing cast alone. Two months later the patient was admitted for suspected osteomyelitis of the left tibia. Since infection of the right femoral fracture was clinically extremely unlikely, this provided a good opportunity to assess scintigraphic changes occurring in an uncomplicated fracture. The bone scan (Fig. 4A) showed prominent increased uptake in the shaft of the right femur. The In-111 WBC images obtained the next day (Fig. 4B), with 20% windows at 247 and 173 keV, showed increased uptake corresponding to the bone-scan abnormality. Repeat images, obtained immediately but with a 10% window at 173 keV and 20% at 247 keV, yielded no abnormalities in the right femur (Fig. 4C). We now use this window arrangement when imaging is performed within 24 hr after Tc-99m administration.

The second problem encountered was also related to the presence of residual Tc-99m in the patient. In this instance camera peaking using emissions from the patient (Tc-99m + In-111), rather than a pure In-111 source, was the technical factor that resulted in similarities between the Tc-99m and In-111 scintigrams (Fig. 2, A, B, & C).

Use of a coarse energy range of 120–185 on the camera permits a peak including the 140 keV Tc-99m as well as the 173 keV In-111

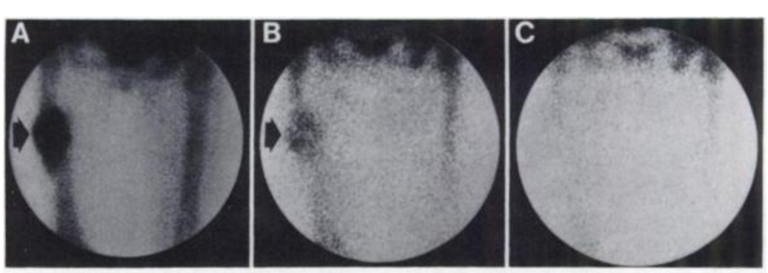

FIG. 4, Case 3. (A) Bone scan shows lesion in right femur (arrow). (B) In-111 WBC image obtained 24 hr later, with 20% window, also shows increased uptake (arrow) caused by Tc-99m contribution. (C) Repeat image with 10% and 20% windows around 173- and 247-keV peaks, respectively, is normal.

peak, depending on the adjustment of the control. By using the dual source (patient), the technologist inadvertently set the window "sill" to include some of the Tc-99m peak. The resulting scintigrams represented the Tc-99m distribution. Readjustment of the PHA using a pure In-111 source avoided the problem (Fig. 2D).

CONCLUSIONS

Suspected infectious disease of the skeleton and joints can be successfully evaluated by concomitant Tc-99m HMDP and In-111 WBC imaging. However, In-111 WBC imaging, when performed within 24 hr of the bone scan, is highly technique-dependent. To avoid artefacts of technical origin the following recommendations are suggested:

1. Energy resolution of the camera system must be optimized to prevent significant Tc-99m/In-111 crosstalk. Energy resolution should not deteriorate on camera imaging systems if stringent maintenance schedules are followed. Slight deterioration of energy resolution will not manifest itself in routine quality-assurance procedures. Uniformity-correction mechanisms can not be expected to maintain optimal energy resolution of a gamma camera. Hence, one should not imagine them to be a "cure-all" for degradation of camera performance and to take the place of FHWM determinations. Annual or bi-annual FWHM determinations should be considered as an adjunct to the routine quality-control procedures for imaging equipment.
2. Once energy resolution is optimized, a 10% window centered around the 173 keV In-111 photopeak may be used on the Picker Dynacamera 4/15 when In-111 WBC imaging is performed within 24 hr of a Tc-99m administration. Reduction of window width does conserve some sensitivity for indium imaging.
3. The PHAs must be adjusted using a pure In-111 source.

Failure to adhere to any of the above precautions may lead to artefactual and erroneous results. These artefacts may or may not prejudice other camera systems currently in use. Investigations of energy resolution, peak overlap, and peak adjustment must be initiated by individual users as they appear necessary.

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Erratum

The Erratum appearing in Volume 24, p. 443, 1983, should appear as follows:

[^{11}C]Spiroperidol: Synthesis, Specific Activity Determination, and Biodistribution in Mice. [*J Nucl Med* 23: 437–445, 1982]. J.S. Fowler, C.D. Arnett, A.P. Wolf, R.R. MacGregor, E.F. Norton and A.M. Findley.

Page 439. Line 19, ppm should read ppb.

Page 439. In "Synthesis of [^{11}C]Spiroperidol" line 6, 0.20 ml of 0.05 M NaOH should read 0.020 ml of 0.05 M NaOH