
Simultaneous Dual Isotope Studies in the Diagnosis of Infection

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A simultaneous dual isotope technique incorporating computer subtraction for the diagnosis of bone, joint, or soft-tissue infection using [^{67}Ga]citrate and [$^{99\text{m}}\text{Tc}$]MDP or sulfur colloid is described. Comparison of this technique with visual congruence or noncongruence of the two radionuclide images in 41 patients shows that the two techniques have identical sensitivity (93%) and specificity (92%) but the computer technique gave additional information in 17% of all cases (44% of abnormal) concerning the anatomic location of the infective focus which aided in the subsequent surgical management of the patient.

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Handmaker, Leonards, and Giammona originally suggested the use of the gallium-67 (^{67}Ga) scan as an adjunct to the bone scan in the diagnosis of osteomyelitis and joint infection (1,2). Since then there have been numerous reports in the sequential use of these scans in the diagnosis of bone, joint, and soft-tissue infection (3-6). Simultaneous dual isotope studies with varying subtraction techniques have been used in the past for eliminating liver activity in pancreas scans by subtracting the gold-198 (^{198}Au) photopeak from that of selenium-75 (^{75}Se) (7), for differentiating malignant from benign hepatic lesions using ^{67}Ga and [$^{99\text{m}}\text{Tc}$]sulfur colloid (8) and in the detection of Hodgkin's disease and lymphoma by using ^{67}Ga and one or more of liver, bone, or lung scanning $^{99\text{m}}\text{Tc}$ agents (9). However, the experience in the detection of infection appears to be limited with only sporadic reports in the literature (10,11) and, more recently, the work of Ravekamp et al. who reported their experience in the use of indium-111-labeled leukocytes with [$^{99\text{m}}\text{Tc}$]colloid subtraction technique in the diagnosis of upper abdominal infection (12).

An increased ^{67}Ga activity may occur in many conditions other than infection, Rosenthal et al. (4) advocated the use of noncongruence or congruence in the distribution pattern of [$^{99\text{m}}\text{Tc}$]pyrophosphate and ^{67}Ga as a way of distinguishing infection from noninfection, respectively, with a recent caveat that this method may

not be useful in differentiating infective from noninfective hypertrophic pseudo-arthritis (13).

The purpose of the present work was to see if there was any improvement in (a) sensitivity and specificity using the simultaneous dual isotope study with a computer subtraction technique as compared to visual comparison of the ^{67}Ga and $^{99\text{m}}\text{Tc}$ images for congruence or noncongruence, and (b) anatomic location of the infective abnormality in order to guide further diagnostic studies or surgical exploration, as suggested by Dahawan et al. (11).

MATERIALS AND METHODS

Forty-one consecutive hospital inpatients, 17 females and 24 males of 4 to 78 yr of age (mean age 50 yr) in whom there was clinical suspicion of infection were studied. In 32 patients the suspect sites were bone, joint, and adjacent soft tissue and in nine there was a suspicion of abdominal sepsis. In none of the patients had a definite diagnosis been made on clinical, laboratory, radiologic, or ultrasound findings.

Simultaneous ^{67}Ga and $^{99\text{m}}\text{Tc}$ images of the region of interest (ROI) were obtained in multiple projections at ~48 and 2 hr following the i.v. injection of ^{67}Ga citrate and [$^{99\text{m}}\text{Tc}$] MDP, respectively, or 48 hr and 10 min following the i.v. injection of the ^{67}Ga and [$^{99\text{m}}\text{Tc}$] sulfur colloid, respectively. Adults received 4 mCi of [^{67}Ga]citrate and 2 mCi of [$^{99\text{m}}\text{Tc}$]sulfur colloid or 5 mCi of [$^{99\text{m}}\text{Tc}$]MDP. Children were given appropriately lesser doses depending on body weight.

A parallel-hole, medium-energy collimator was used. The pulse height analyzer was set at 140 keV for $^{99\text{m}}\text{Tc}$

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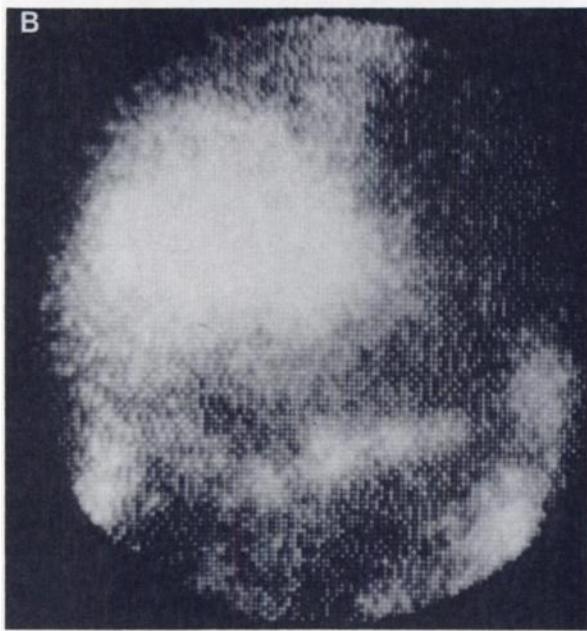
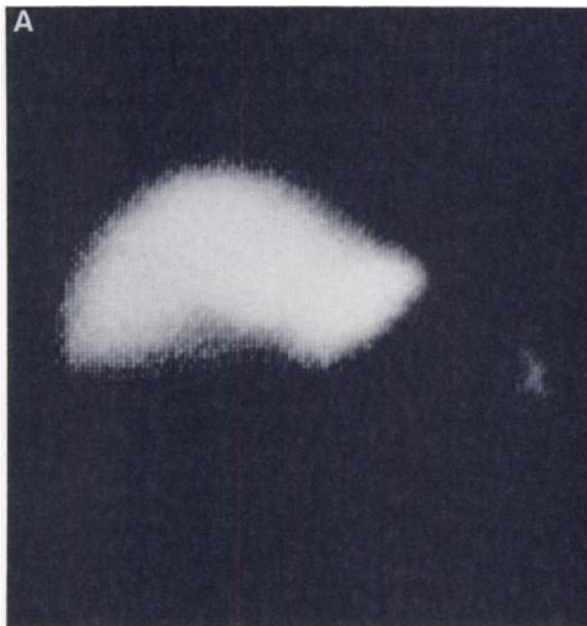


TABLE 1
Sensitivity, Specificity, and Predictive Value

n : 41

	D†+	D-
T*+	14	2
T-	1	24

Sensitivity $P(T+/D+) = 14/15$ (93%)
 Specificity $P(T-/D-) = 24/26$ (92%)
 Positive Predictive Value $P(D+/T+) = 14/16$ (87%)
 Negative Predictive Value $P(D-/T-) = 24/26$ (96%)

* T: Dual isotope study.

† D: Final diagnosis.

with a 20% symmetric window and 185 keV for ^{67}Ga with a 15% symmetric window and total of 1.5 to 2 million counts were obtained using gamma camera-computer imaging system.* The ratio of $^{99\text{m}}\text{Tc}$ to ^{67}Ga counts ranged from 5:1 to 20:1.

Data processing and analysis was done by displaying the ^{67}Ga and $^{99\text{m}}\text{Tc}$ images in a dual buffer display and noting if any abnormality was present in either of the images and if so, whether this was visually congruent or noncongruent. The ^{67}Ga image was typically normalized using the ROI method by determining the ratio of the $^{99\text{m}}\text{Tc}$ to ^{67}Ga counts in the contralateral region to the site of abnormality in paired structures or a part of an organ where no obvious visual abnormality was seen in unpaired structures. No attempt was made to correct the down-scatter in the $^{99\text{m}}\text{Tc}$ image. The $^{99\text{m}}\text{Tc}$ image was then subtracted from the normalized ^{67}Ga image and a note made of whether there was any excess of ^{67}Ga in the ROI and the location of this abnormality. Finally, using either two different color tables or the gray scale for the $^{99\text{m}}\text{Tc}$ image and a color table in the black and white mode for the normalized ^{67}Ga minus $^{99\text{m}}\text{Tc}$ image, the two images were overlayed so as to show excess ^{67}Ga in relationship to the $^{99\text{m}}\text{Tc}$ image. This was done with the hope that utilization of the better resolution of the $^{99\text{m}}\text{Tc}$ image would allow a relatively more accurate anatomic location of the ^{67}Ga abnormality.

RESULTS

Positive dual isotope studies

Of the 41 patients studied 16 (39%) showed both

FIGURE 1

77-yr-old male, postcholecystectomy, and closure of duodenal fistula with technically unsatisfactory ultrasound examination. Anterior upper abdomen view: Noncongruent A: [$^{99\text{m}}\text{Tc}$]sulfur colloid and B: ^{67}Ga Image. C: Normalized ^{67}Ga - $^{99\text{m}}\text{Tc}$ subtraction image with overlay of [$^{99\text{m}}\text{Tc}$]sulfur colloid liver image shows large collection of ^{67}Ga consistent with right subphrenic abscess confirmed at surgery

ity as well as excess ^{67}Ga in the subtracted image indicating active infection. In 13 of these patients the diagnosis of infection was confirmed at surgery or needle aspiration. In one patient there was spontaneous drainage of subhepatic abscess by way of a previous surgery incision. In two patients the final diagnosis was noninfective synovitis confirmed in one case at surgery and in one case by trial of antiinflammatory agents with successful resolution of the symptoms.

Negative dual isotope studies

In 25 patients (61%) there was congruence of the ^{67}Ga and $^{99\text{m}}\text{Tc}$ images as well as absence of any excess ^{67}Ga in the subtracted image. In 24 patients the final diagnosis was absent infection, confirmed in seven cases by surgery or needle aspiration and in 17 cases by clinical follow-up of at least 2 mo duration. In one patient a pyogenic granuloma was found at surgery.

The sensitivity and specificity (Table 1) of the visual and computer subtraction technique was the same at 93 and 92%, respectively, as was the predictive value of the positive and negative test at 87 and 96%, respectively, for a disease prevalence of 34%; but in seven out of 16 patients (44%) in whom there was noncongruence of the ^{67}Ga and $^{99\text{m}}\text{Tc}$ study visually, the computer subtraction image either allowed the diagnosis of infection to be made with greater confidence (Fig. 1) or indicated the exact location of the infection (Figs. 2 and 3) which was not apparent on visual examination of the ^{67}Ga and $^{99\text{m}}\text{Tc}$ images alone, and which played a significant role in the subsequent management of the patient.

DISCUSSION

Although the overall accuracy of the simultaneous dual isotope study with computer subtraction was found to be similar to visual inspection of the ^{67}Ga and [$^{99\text{m}}\text{Tc}$]MDP sulfur colloid imaged (92%), the former technique gave substantial additional information in 44% of the patients in whom visually noncongruent abnormality was found or in 17% of the total number of patients studied. This moderate gain is considered sufficient to continue using the study in patients in whom a probable noncongruent abnormality is seen but either its exact significance or its location is uncertain.

The relatively high specificity found in the present study is considered related to the fact that only hospital inpatients who, in the main, were relatively seriously ill

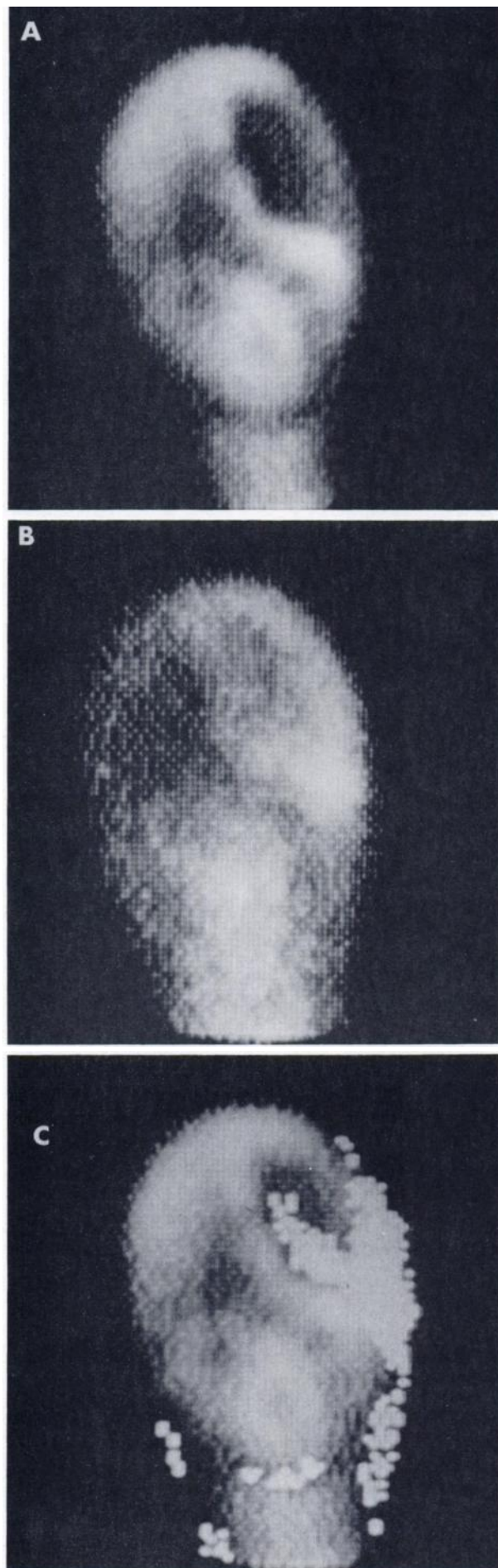
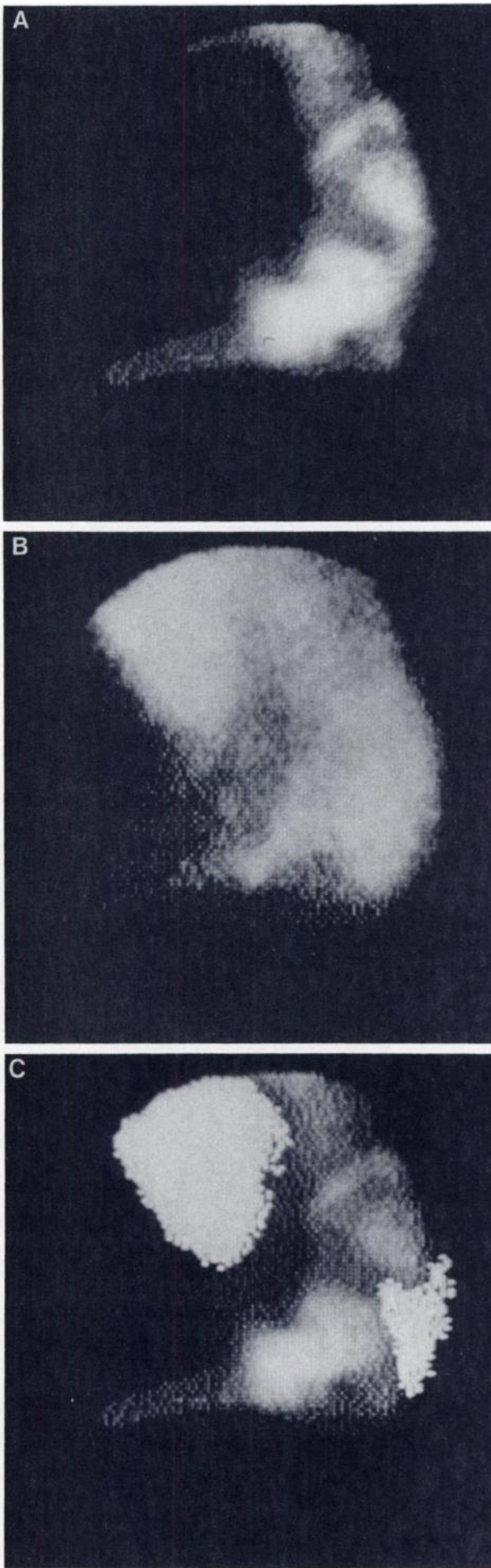


FIGURE 2

50-yr-old female with acrylic left skull plate due to previous bone infection following cerebral aneurysmectomy presented with pyrexia and soft fluctuant swelling superficial to the plate. CT examination of skull technically not feasible. Anterior skull view: Congruent A: [$^{99\text{m}}\text{Tc}$]MDP and B: ^{67}Ga images. C: Normalized ^{67}Ga - $^{99\text{m}}\text{Tc}$ subtraction image with overlay of [$^{99\text{m}}\text{Tc}$]MDP image shows excess ^{67}Ga both superficial and deep to plate, pus in these regions confirmed at subsequent surgery



and in whom there was a high clinical pretest probability of infection were included, as well as the use of clinical follow-up with its associated uncertainty in the designation of true negative in 17 out of 25 dual isotope studies.

FOOTNOTE

* General Electric 400 Maxicamera, Digital Equipment Corporation GAMMA-11 computer system.

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FIGURE 3

13-yr-old paraplegic male with large decubitus sacral ulcer unresponsive to treatment including appropriate antibiotics. Left lateral pelvis: Noncongruent A: ^{99m}Tc and B: ^{67}Ga images. C: Normalized ^{67}Ga - ^{99m}Tc subtraction image with overlay of [^{99m}Tc]MDP image shows excess of ^{67}Ga both superficial and within sacrum indicating bone infection, confirmed at subsequent surgery and by culture from sacral bone chip