COMPARISON OF ^{99m}Tc-POLYPHOSPHATE AND ^{18}F. II. IMAGING

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Comparison has been made between ^{99m}Tc-polyphosphate (Tc-PP) and ^{18}F in clinical imaging studies. The normal skeletal structure was better delineated with Tc-PP than with ^{18}F. The sternum, sternoclavicular joint, iliac crests, and inferior angle of the scapulas appear more prominently with Tc-PP. The degree of renal concentration of Tc-PP seems to have good correlation with renal parenchymal function and poor correlation with ^{18}F. In men, the scrotum and penis normally concentrate Tc-PP more avidly than ^{18}F and so may contribute to a false-positive pelvic bone scan. Bone lesions are better delineated with Tc-PP than with ^{18}F. A few lesions not seen with ^{18}F are clearly delineated with Tc-PP. With Tc-PP, scintillation camera images are superior to rectilinear scans. In the scintillation camera, high-resolution collimator images are superior to high-sensitivity collimator images. Even though study time with the high-resolution collimator is relatively longer than that with the high-sensitivity collimator, the superior resolution of the high-resolution collimator more than compensates for its longer study time. It is concluded that the best skeletal images are obtained with Tc-PP and a scintillation camera equipped with a high-resolution collimator.

In 1971 Subramanian and McAfee introduced ^{99m}Tc-labeled sodium triphosphate for skeletal imaging (*1*). A year later, they again introduced a new preparation, a synthetic linear long-chain polyphosphate labeled with ^{99m}Tc (*2*). The ^{99m}Tc-polyphosphate (Tc-PP) was shown in animals to have a blood background radioactivity lower than that of ^{99m}Tc-labeled triphosphate and higher than that of ^{85}Sr. To date, much of the published physiologic data on Tc-PP have been obtained with animals and comparative studies have focused on ^{85}Sr. Earlier studies have shown, in humans as well as in animals, that ^{18}F is more effective than either ^{85}Sr or ^{87m}Sr (*3*). It is thus essential to compare all newer skeletal imaging agents with ^{18}F before claiming superiority over previous agents. Consequently, we have undertaken a clinical study to compare Tc-PP with ^{18}F (*4*). In this paper bone images obtained with ^{18}F and Tc-PP are compared using different instruments: a standard rectilinear scanner and a scintillation camera equipped variously with a high-sensitivity and with a high-resolution collimator. Variations and similarities in images obtained with ^{18}F and Tc-PP using different equipment are analyzed. An attempt is made to establish the ideal scanning time and equipment for imaging the skeleton using Tc-PP.

MATERIALS AND METHODS

Twenty patients with suspected bone lesions were studied first with intravenous injections of 2–4 mCi ^{18}F, and a day or two later with an intravenous injection of 15 mCi ^{99m}Tc-labeled polyphosphate (Tc-PP). (The polyphosphate kits were supplied through the courtesy of Diagnostic Isotopes, Inc., Upper Saddle River, N.J. and New England Nuclear Corporation, North Billerica, Mass.). Blood samples were obtained in test tubes containing anticoagulant at 10 min, 1, 2, 3, and 4 hr into the postinjection period. Urine was collected for 4 hr. No special patient preparation was used although patients were allowed fluids ad libitum.

With ^{18}F, only rectilinear scans (no minification) were obtained, using either a Picker 5-in. crystal Magnascanner Mark III fitted with a 19-hole, high-energy collimator or a Searle Radiographics 5-in.

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crystal Pho/Dot V scanner fitted with a 37-hole collimator (Model 520-821918).

A day or two after the ^{18}F study, the bone images (1:1) were repeated after the injection of 15 mCi of Tc-PP. Imaging was started 2–2½ hr postinjection. All the views obtained with ^{18}F were also obtained with Tc-PP using the same rectilinear scanner, fitted this time with a low-energy collimator. The scan speed was adjusted to obtain an information density of 300/cm^2 with ^{18}F and 900/cm^2 with Tc-PP. Maximum and minimum counting rate regions were selected, respectively, over the lumbar spine and buttocks. The contrast between maximum and minimum count was set at 40–50%. Following the rectilinear scans, bone scintiphotos were obtained with the Anger scintillation camera (Searle Radiographics) using high-sensitivity (Model 820-821713) and high-resolution (Model 820-821742) collimators. Each of these collimators has 15,000 parallel holes. Counts of 500,000 were accumulated for each view and the time required for each view was noted. All views obtained with the scanner were also obtained with the camera. The rectilinear scans were obtained 1 hr postinjection with ^{18}F and 2–2½ hr postinjection with Tc-PP. The scintillation camera images were usually obtained 4 hr after the injection of Tc-PP.

For purposes of correlation, complete roentgen bone surveys and serum calcium, phosphorus, alkaline, and acid phosphatase levels were obtained. Clinical history and physical findings were recorded at the time of the scan. Rectilinear scans and the scintillation camera studies were evaluated qualitatively by eight to ten nuclear medicine physicians during the weekly conference time. The physicians were asked to evaluate the bone anatomic detail obtained with ^{18}F and Tc-PP and also to compare the details of the Tc-PP bone scintiphotos obtained with high-resolution and high-sensitivity collimators. The consensus was accepted in the final evaluation of the studies.

RESULTS

Twelve of the 20 patients had normal bone scans with both ^{18}F and Tc-PP. Coincidentally, the first consecutive ten patients had normal bone scans with both agents, providing an opportunity to appreciate the normal skeletal image with Tc-PP. Eight patients had abnormal skeletal images with both agents. Figure 1 shows a normal skeletal image obtained with ^{18}F and Tc-PP. With Tc-PP, the normal sternum, sternoclavicular joint, and anterior iliac crest were better delineated. The radioactivity over the shoulder joint was as intense as, or slightly more intense than, that over the upper thoracic ribs. Normal kidneys were well delineated in every case studied with Tc-PP but not with ^{18}F. Patients with normal serum BUN and creatinine who showed good kidney visualization with Tc-PP sometimes failed to show good kidney images with ^{18}F. Kidney delineation with Tc-PP did not interfere with axial skeletal visualization.

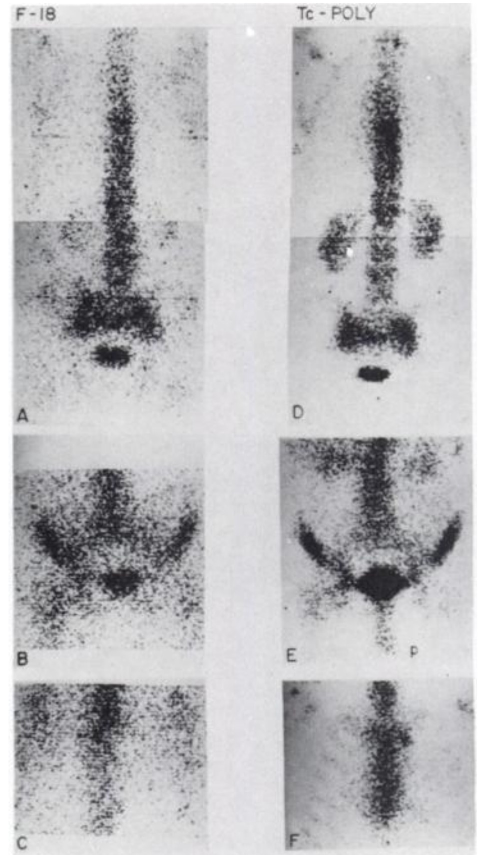

FIG. 1. Normal skeletal image with ^{18}F and ^{99m}Tc-polyphosphate as shown in rectilinear scan. Note more prominent sternoclavicular joints, iliac crests, kidneys, and genitalia in Tc-PP images. P represents genitalia.

Of the two patients who showed abnormal kidney images with Tc-PP, one had had a left nephrectomy and a normal-functioning right kidney and the other had a nonfunctioning left kidney and a normal right kidney. In the latter patient, the left kidney was visualized very faintly during Tc-PP bone imaging and the right kidney appeared normal whereas with ^{18}F neither kidney was visualized (Fig. 2). The penis and scrotum were seen regularly with Tc-PP in most male patients and sometimes radioactivity over the penis was much more intense than that over the anterior pubic bones or the upper part of the femur (Fig. 3). Contamination of the area with radioactive urine was excluded by repeat scanning after cleansing of the area. Penile radioactivity, when overlying the pubic bone or the femur in the anterior scan of the pelvis, resulted in a "false-positive" bone scan with Tc-PP (Fig. 2).

In patients with osteoarthritis, the involved joints were delineated better with Tc-PP than with ^{18}F. Shoulder joint radioactivity was much more intense than that over the upper thoracic ribs and hip joint radioactivity was much more intense than that of anterior superior iliac spine (Fig. 4).

All the bone lesions seen with ^{18}F were also seen with Tc-PP. In addition, Tc-PP showed a few lesions not seen with ^{18}F. The delineation of abnormal and normal bone structure was much more detailed with Tc-PP than with ^{18}F (Figs. 5 and 6).

With Tc-PP, scintillation camera bone images were better than images obtained with the rectilinear scanner. The bone anatomy was much more detailed in the camera studies, showing each rib and vertebral body clearly. The bone anatomy was less clear with ^{18}F. With the scintillation camera, the resolution of the studies performed with an HR collimator was better than that with an HS collimator (Fig. 7). The time required for study with the HR collimator was two to three times that required with the HS collimator. Both normal and abnormal bone anatomy was better delineated with the HR collimator. In studying abnormal bone anatomy, the site of the lesion could be localized more precisely to each individual rib and vertebra with the HR collimator than with the HS collimator (Fig. 7).

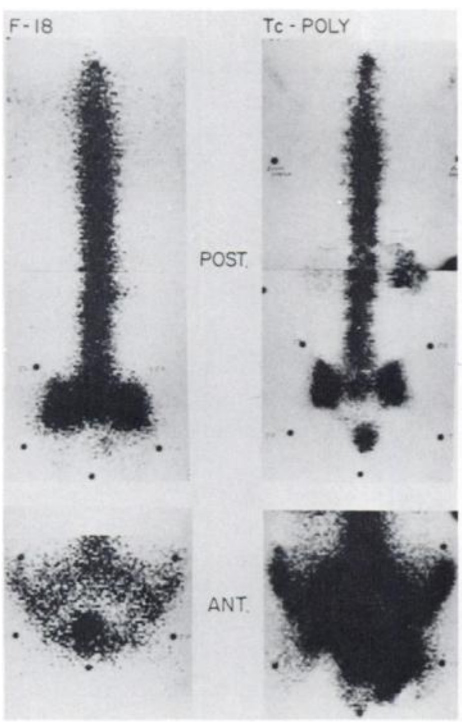

FIG. 2. Note complete nonvisualization of both kidneys with ^{18}F but their relatively clear demonstration with Tc-PP. Genitalia are not seen with ^{18}F but are seen overlying normal pubic bone with Tc-PP. Serrations along margin of vertebral column with Tc-poly are due to delineation of intervertebral disc spaces.

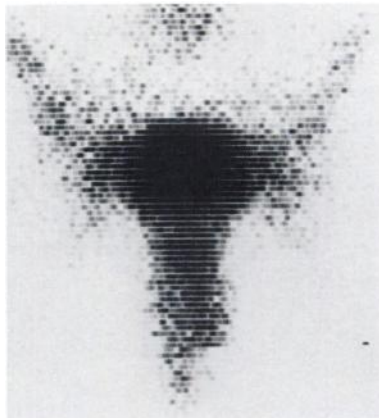

FIG. 3. Note marked uptake of Tc-PP by genitalia. Increased activity in genitalia almost obscures normal pelvic bone and upper part of both femurs.

DISCUSSION

Of present day instruments used in nuclear medicine, the scintillation camera is best suited for radionuclides having a gamma photon energy between 100 and 200 keV. One of the main disadvantages of ^{18}F is its high gamma photon energy (511 keV), requiring specially designed collimators. The scintillation camera could not be used with its regular collimators; even with specially designed collimators there was image aberration. The image aberration was shown to be due to the collimator septa, which had to be thick to prevent penetration of the 511-keV photon energy of ^{18}F. In addition, the improved resolution of the scintillation camera phototubes resulted in delineation of the collimator septa, which produced aberration of the images obtained (*5,6*). Thus the rectilinear scanner remains the ideal instrument for bone scanning with ^{18}F (*5*).

The introduction of ^{99m}Tc-labeled phosphate compounds for skeletal imaging has literally revolutionized bone imaging technology. First, radiopharmaceutical cost for bone imaging has been reduced enormously, from the \$35–\$75 cost for an individual patient dose of ^{18}F to the \$2–\$10 cost for Tc-PP depending on the number of patients studied from each commercially available kit. Second, the gamma photon energy of ^{99m}Tc is ideal for present-day instruments, especially the scintillation camera.

Comparison of ^{18}F and ^{99m}Tc-polyphosphate rectilinear scans. The normal bone image is adequately delineated with ^{18}F. The entire vertebral column and the pelvic bones are well visualized. Little radioactivity is seen in the region of the shoulder joints, ribs, or scapulas (Fig. 1). The entire vertebral column is seen as a single solid band with no serrations along the margins to indicate intervertebral disc spaces. In the pelvis, both sacroiliac joints and ischial tuberosities are seen. Urinary bladder radioactivity is clearly separated from the tip of the coccyx. In the anterior scan of the pelvis, both iliac crests, acetabular rims, and the upper part of the femurs are seen. Urinary bladder radioactivity is seen superimposed over the pubic bone (Fig. 1B, and Fig. 2). In the anterior scan of the thorax, the sternum and thoracic cage ribs are seen faintly. The ribs are not discernible individually and show decreased radioactivity in the costal cartilage region adjoining the sternum (Fig. 1C). No appreciable radioactivity is seen over the penis or scrotum (Figs. 1 and 2).

In the ^{99m}Tc-polyphosphate rectilinear scan, the vertebral column appears as a vertical band with a serrated margin delineating intervertebral disc spaces (Fig. 1D and Fig. 2, Tc-PP). Shoulder joints and spine and inferior angle of scapulas are more often visualized with Tc-PP than with ^{18}F. In the lumbar region, the normal-functioning kidneys are always well delineated. The renal image does not interfere in any way with the visualization of adjacent vertebral body images. As with ^{18}F, urinary bladder radioactivity in the posterior scan of the pelvis is well separated from the tip of the coccyx and both sacroiliac joints (Fig. 1D). In the anterior view of the pelvis, the iliac crests, acetabular ridges, and upper ends of both femoral heads are seen more clearly

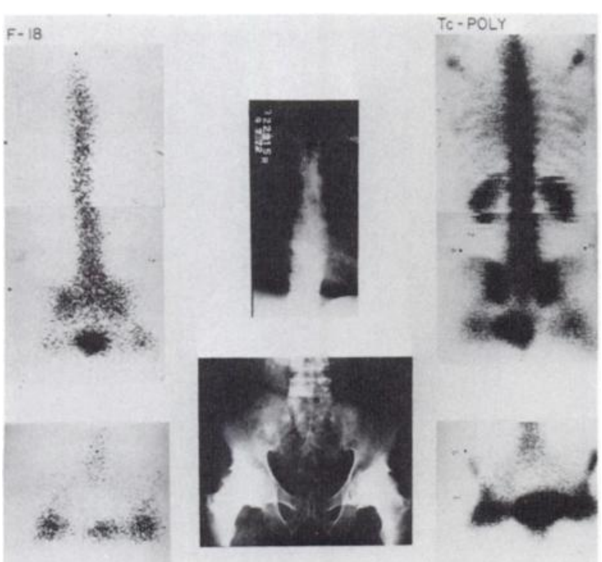

FIG. 4. Distribution of ^{18}F and Tc-PP in patient with generalized osteoarthritis. Note increased uptake of Tc-PP in hip and shoulder joints and clear demonstration of normal renal image; with ^{18}F activity over shoulder joints and kidneys is not evident. Roentgenogram of pelvis showed osteoarthritis of shoulder and hip joints.

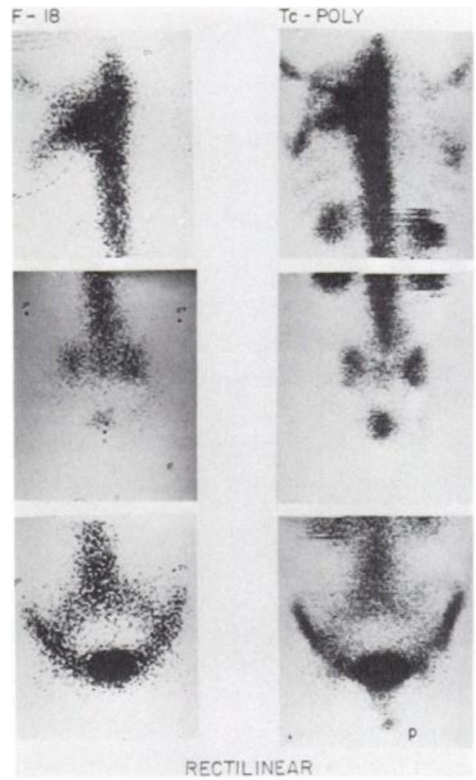

FIG. 5. Rectilinear scans of patient receiving ^{60}Co irradiation for bronchogenic cancer in left lung. Note that inferior scapular angle shown on right side in Tc-PP scan, not seen in the ^{18}F scan, mimics rib lesion. Again note disparity in renal images obtained with both agents. P represents Tc-PP activity in genitalia.

with Tc-PP than with ^{18}F. The urinary bladder is superimposed over the pubic bone. In contrast to the ^{18}F scan, the Tc-PP scan always delineates the penis and scrotum. As with ^{18}F, the sternum and anterior thoracic ribs are seen with Tc-PP but the sternoclavicular joint always appears more prominent with Tc-PP.

The delineation of the renal images with Tc-PP deserves a few comments. We have regularly noticed that normal-functioning kidneys are always delineated with Tc-PP but not necessarily with ^{18}F (Fig. 2). In Fig. 1 normal-functioning kidneys are seen with both ^{18}F and Tc-PP, but the renal image is far superior with Tc-PP. In Fig. 2, a hypofunctioning left kidney and a normal-functioning right kidney are not seen with ^{18}F but are readily demonstrated on the Tc-PP scan. Correlation of the Tc-PP renal image with other renal function tests is underway in our laboratory (*7*). Preliminary studies seem to indicate good correlation of Tc-PP renal concentration with renal function. This was not the case with ^{18}F scans, for which renal function had no relation to ^{18}F concentration. Similar results were noted in a study by Sharma and Quinn (*8*). They studied 27 patients with ^{18}F scans in the dehydrated state and concluded that the degree of renal concentration bore no relation to kidney disease.

Another striking difference between ^{18}F and Tc-PP images lay in the visualization of the penis. In all male patients, the penis was delineated regularly with Tc-PP and not with ^{18}F. The cause of penile uptake of Tc-PP is not evident; however, two possible explanations may be given. First, with Tc-PP there is relatively more radioactivity in the blood and urine, which may contribute to the penile image. Normally, the penile urethra is free of urine at all times except during voiding. However, since the anterior pelvic scan is obtained after voiding, the radioactive urine coating the urethral passage may contribute to some extent to penile visualization. The fact that the whole penis and not just the penile urethra is delineated suggests that there may be active uptake of Tc-PP by the corpora cavernosa and corpora spongiosa. The further fact that other highly vascular structures such as the heart and aorta are not delineated suggests that it is not just the blood in the penile tissue, but active uptake of Tc-PP that plays a major part in penile visualization.

The delineation of the genitalia in the anterior pelvic scan creates some technical difficulty. The genitalia, if they overlie the pubic bone or upper part of the thighs, may result in increased radioactivity over the underlying bone structures, suggesting a bone lesion (Fig. 2). This problem is easily overcome by marking the position of the penis on the scan.

The anatomic detail obtained with Tc-PP is far superior to that obtained with ^{18}F. This may all be a function of total dose. The ^{18}F images were obtained with 2–4 mCi, the Tc-PP images with 15 mCi. It appears from animal studies that more than 70% of the injected dose of ^{18}F is taken up by bone (*9*) in contrast with about 50% with Tc-PP (*2*).

The increased amount of Tc-PP in bone and the increased efficiency of the instrument for detecting gamma photons of ^{99m}Tc result in superior image resolution. In patients with osteoarthritis, increased radioactivity surrounding the involved joints was evident with both radiopharmaceuticals but Tc-PP provided far superior delineation. In Fig. 4, osteoarthritis of the hip joint was evident with both agents but the involvement of the shoulder joint was evident only with Tc-PP. The shoulder joint radioactivity was more intense than that over the thoracic ribs.

Several abnormal bone lesions not delineated with ^{18}F were well visualized with Tc-PP. In Fig. 5, a patient with bronchogenic cancer receiving tumor irradiation showed diffuse rib lesions in the upper part of the left posterior thoracic cage and none on the right side. In addition, the inferior angle of the right scapula was seen mimicking a rib lesion (Fig. 5). In this patient, again the normal-functioning kidneys were not seen with ^{18}F but were seen very clearly with Tc-PP. Cardiac blood pool or aorta were not seen in our study. One patient who showed increased radioactivity adjoining the cardiac region

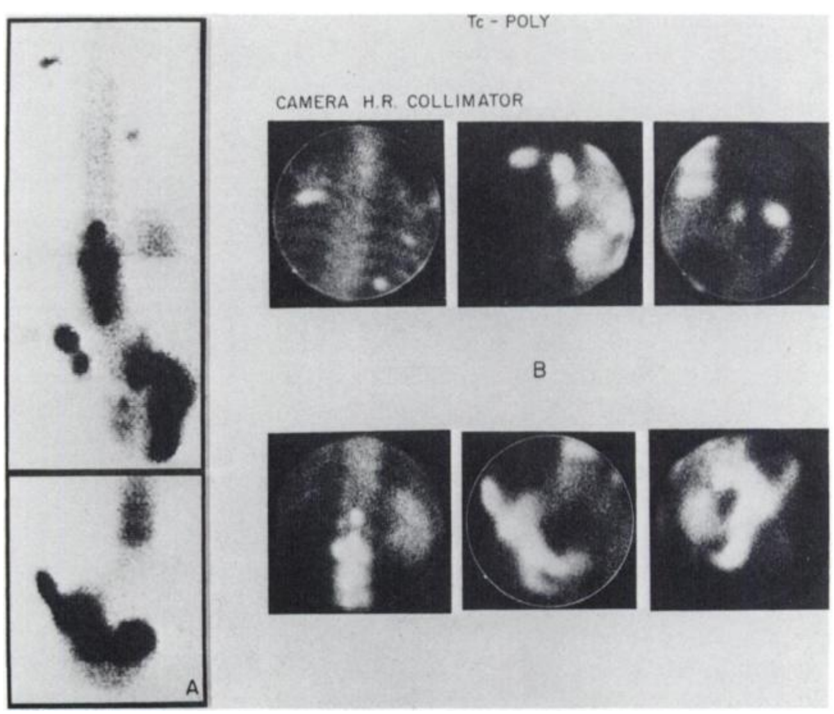

FIG. 6. Tc-PP rectilinear scan and scintillation camera images. Note superior resolution of normal and abnormal bone scintillation camera images with high-resolution collimator. Each individual lesion can be ascribed to definite anatomic site in camera image (B), but not in rectilinear scan (A). (This patient had left nephrectomy for renal cell cancer.)

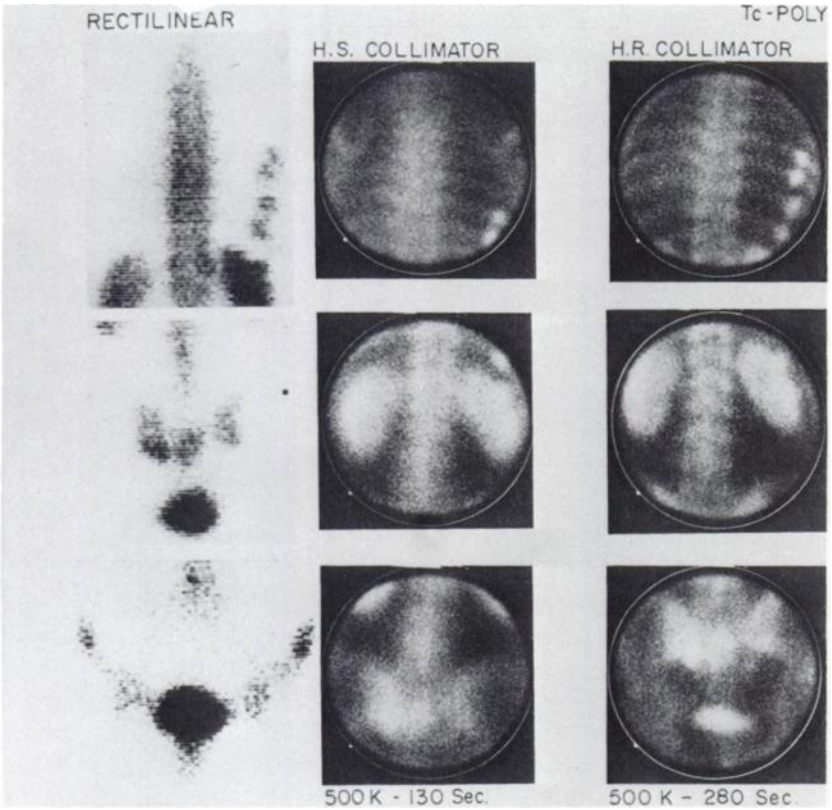

FIG. 7. Tc-PP bone image of patient with bronchogenic cancer with multiple osseous metastases. Note that right rib lesions are seen but cannot be ascribed to any particular anatomic site in the images obtained with rectilinear scanner or camera with high-sensitivity collimator. However, each lesion is anatomically definable in images obtained with high-resolution collimator. Note that time taken with high resolution collimator is twice time taken with high-sensitivity collimator for accumulating identical number of counts. Individual ribs, vertebral canal, and intervertebral disc spaces are well-defined in high-resolution collimator image.

had bronchogenic cancer in the left hilar region. It has been shown recently that Tc-PP does accumulate in many soft-tissue malignancies (*10*). Charkes, et al have reported the delineation of the cardiac blood pool occasionally in normal subjects (*11*).

Comparison of Tc-PP rectilinear scan and scintillation camera image. With Tc-PP, the scintillation camera images were far superior to the rectilinear scans. The resolution of camera studies is so fine that bone lesions can be ascribed to a definite anatomic region such as a particular rib, the vertebral body, or even a part of the vertebra. Many lesions not delineated on the rectilinear scan were clearly seen with the camera. In Fig. 6, a patient with left nephrectomy for transitional cell tumor showed only two rib lesions, one on either side (A), that could not be ascribed to any particular rib. With the camera study, the lesion on the left side could be ascribed to the second thoracic rib, the lesion on the right side to the third thoracic rib, and one more, which was not seen with the rectilinear scan, to the right sixth rib (B). In the pelvis, discrepancies between the images obtained with the two instruments were again evident—the camera studies showing a larger number of lesions that could be ascribed to a particular anatomic structure or region. This shows how scanning can miss a lesion due to "peaking problems" or by setting the scanner on an area with excessive radioactivity.

Comparison of Tc-PP high-sensitivity and high-resolution collimator camera images. Each collimator, as noted earlier, has 15,000 parallel holes. Imaging time required with the high-resolution collimator (90–300 sec) was two to three times that with the high-sensitivity collimator (45–180 sec), the total counts accumulated for each view with each collimator remaining constant. The total study can be completed in 30–50 min with the high-sensitivity collimator and in 40–80 min with the high-resolution collimator. Image resolution was far superior with the high-resolution collimator. The anatomy of each individual vertebra and rib was clearly delineated. The spinal canal and intervertebral disc spaces too were seen clearly. The exact anatomic localization of a bone lesion could be made. Such anatomic delineation was not possible with the high-sensitivity collimator. It was thought that although the high-sensitivity collimator is adequate for clinical purposes, the superior resolution obtained with the high-resolution collimator compensates for the longer time necessary to complete the study.

High-sensitivity collimator images are comparable to rectilinear scans. As noted, they provide clinically useful information but lack the resolution of the high-resolution collimator images (Fig. 7). In our opinion, the best skeletal images are obtained with Tc-PP using the scintillation camera equipped with a high-resolution collimator.

Imaging interval. The ideal imaging time with ^{18}F was found to be 3 hr postinjection when blood background radioactivity is minimal; but clinically useful studies can be obtained as early as 1 hr postinjection. The ideal time for imaging with Tc-PP is 4 hr postinjection; however, useful studies can be obtained as early as 2–2½ hr postinjection using a rectilinear scan and usually after 4 hr when the scintillation camera is used. In camera studies obtained earlier than 4 hr, the high background radioactivity prevented superior skeletal images. This was probably due to the nonfocusing nature of the parallel-hole collimator, which does not discriminate very efficiently between the background and bone radioactivity. With rectilinear scans, the focusing nature of the collimator results in better delineation of bone image against the background radioactivity.

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