Clinical Comparison of Technetium-99m Diphosphonate and Pyrophosphate in Bone Scintigraphy: Concise Communication

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Thirty patients had bone scintigraphy with both Tc-99m pyrophosphate (Tc-PPi) and Tc-99m diphosphonate (Tc-HEDP). The images were given a composite rating for quality on the basis of three sets of criteria, and were also compared for the number of lesions detected by each agent. The two agents provided no difference in scan quality. Nevertheless, in ten of the 30 patients, at least two of the three readers detected with Tc-HEDP lesions that were not seen with Tc-PPi, and in two such cases all three readers considered the Tc-PPi scan normal. In another of these ten, two of three readers felt the Tc-PPi image was normal, whereas all three detected the lesion with Tc-HEDP. The reverse never occurred ($p < 0.01$).

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Although the introduction of Tc-99m polyphosphate (*1*) brought a new level of resolution and sensitivity to bone scintigraphy, Tc-99m pyrophosphate (Tc-PPi) and Tc-99m diphosphonate (Tc-HEDP) are currently the two radiopharmaceuticals in widest use for skeletal imaging. To date only one study, involving a small series of nine patients, has attempted to compare the clinical efficacy of these two agents in the same patient (*2*). We have undertaken to compare the quality of bone scintigrams and the number of lesions (foci of abnormally increased activity) detectable employing both Tc-HEDP and Tc-PPi in the same group of 30 patients.

MATERIALS AND METHODS

After informed consent, 30 patients referred for staging of biopsy-proven carcinoma were scanned with 15 mCi of Tc-HEDP* or Tc-PPi†. The radioagent given first was alternated in sequential pairs of studies. The sets of two scans on each of the 30 patients were obtained within 5–14 days of each other and never with intervening surgery, chemotherapy, or radiotherapy. Each pair of images was made on the same instrument, either a rectilinear scanner or gamma camera. With the latter, the same number of counts was collected for each member of a pair. All patients drank one-half liter of water within the 3 hr between injection and imaging.

Three experienced readers graded the 30 sets of scans on three semi-quantitative scales. The readers received the scans in random sequence and were unaware of which scans were performed on the same patient. The scores were related to the amount of soft tissue observable (Table 1), to the renal uptake relative to spine concentration (Table 2), and to the

TABLE 1. RATING SYSTEM FOR BONE SCANS. SOFT-TISSUE BACKGROUND (BLOOD POOL, MUSCLE OF ARM, LEG)

	Rating
None observable	3
Mild but not interfering with interpretation	2
Soft-tissue density = bone density	1

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TABLE 2. RATING SYSTEM FOR BONE SCANS. RENAL UPTAKE

Image density of kidney / Image density of spine	Rating
$\ll 1$	3
< 1	2
1	1
> 1	0

TABLE 3. RATING SYSTEM FOR BONE SCANS. GENERAL APPEARANCE—"DIAGNOSTIC POTENTIAL"

	Rating
Excellent; vertebrae, ribs, and other bones delineated	3
Good; all bones delineated, vertebral bodies and ribs not all separated	2
Fair; all bones delineated, ribs and/or spine homogeneous—separate bones not seen	1
Poor; unreadable	0

overall diagnostic potential of the scan (Table 3). These scores were summed (Table 4) and analyzed by three-way analysis of variance.

Finally each judge recorded the lesions detected on an anatomic diagram for each patient's two studies. The identity of the radiopharmaceutical employed for each scan was unknown to the judges throughout the image-grading and lesion-counting process.

RESULTS

Thirty sets of bone scintigrams rated by three readers yielded 180 judgments. The total and mean scores appear in Table 4 for each reader and radiopharmaceutical. Using three-way analysis of variance, two questions were asked:

1. Was there a difference in image quality between Tc-HEDP and Tc-PPi?

2. Was there a difference between the way the readers rated scans?

No significant difference was found, either between the two agents regarding scan-quality score ($p = 0.15$), or between the three readers regarding the scores produced ($p = 0.07$).

The third question posed by this study asked whether more lesions were detected by one agent as compared with the other. In ten of the 30 scans (33%) one or more metastases not detected on the Tc-PPi image were noted by at least two of the three readers with Tc-HEDP. The reverse never happened. This difference is significant by the sign test ($p < 0.01$). In two of these ten, tumor was seen with the Tc-HEDP but not with Tc-PPi by all three readers, and in a third case two of the three readers did not see any lesion with Tc-PPi, whereas all noted this abnormality with Tc-HEDP. One such case is illustrated in Fig. 1.

DISCUSSION

Seven studies of in-vivo clearance of Tc-HEDP against Tc-PPi in man (*3–9*), as well as numerous animal studies (*4,6,7,9–11*) have uniformly found Tc-HEDP to be more rapidly cleared from the blood than Tc-PPi. Furthermore, target-to-nontarget ratios between bone and soft tissue, or between normal and abnormal bone, have favored Tc-HEDP in all but one of these studies (*4*). In this latter work, uptake of the two agents by fractured and normal bone was about the same. These clearances and ratios have been obtained with many brands of Tc-HEDP or Tc-PPi, including the two we employed. In the only other study where each subject received both agents, but with only nine cancer patients studied, 18 lesions were found with Tc-HEDP and 11 with Tc-PPi (*2*). This difference, however, is not significant by McNemar's test for correlated proportions, perhaps because of the small number of patients involved. Moreover, in a recent comparison (*5*) there appeared no clear difference between the two agents in the detection of metastatic disease.

One study of 71 individuals, in which Tc-HEDP and Tc-PPi were not compared in the same patients, favored, by a slim margin, nonlyophilized HEDP over PPi, using scan-quality criteria similar to ours (*3*). The data were not statistically analyzed and no lesion counts were reported. Weber et al. (*4*), using

TABLE 4. SEMI-QUANTITATIVE BONE SCAN RATING OF Tc-99m-LABELED SKELETAL SCANNING AGENTS

	Reader 1		Reader 2		Reader 3	
	Tc-HEDP	Tc-PPi	Tc-HEDP	Tc-PPi	Tc-HEDP	Tc-PPi
Total	134	147	164	161	161	178
Mean	4.47	4.90	5.47	5.37	5.37	5.93

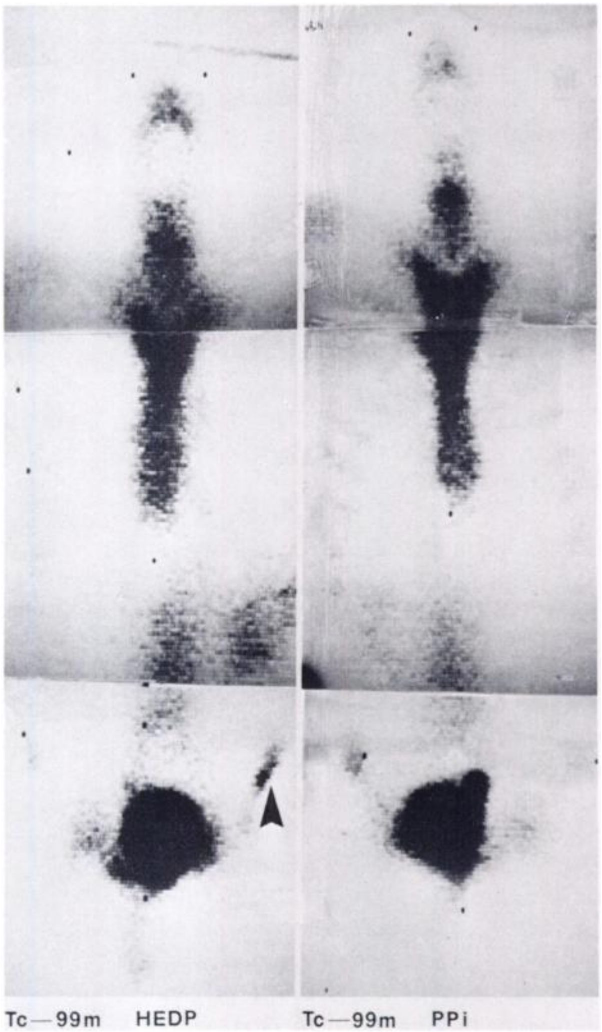

FIG. 1. Solitary ilial metastasis is seen with Tc-HEDP (arrow) but not with Tc-PPi.

Tc-HEDP and Tc-PPi from the same sources as this study, noted variable contrast between bone and soft tissue with Tc-HEDP but abnormal hepatic uptake with Tc-PPi. They preferred Tc-PPi but without any clearly defined supporting data. These authors did not scan each patient with both agents in this study, and their in-vitro data, in fact, favored Tc-HEDP. A very recent project studied 140 patients with Tc-HEDP, Tc-PPi, and a Tc-99m trimetaphosphate preparation (*12*). Several measures of bone definition were used, and HEDP appeared inferior to PPi. The agents, however, were not compared in the same patient.

CONCLUSION

What may one conclude from our data? First, despite data from many studies showing more rapid blood clearance and higher target-to-nontarget ratios favoring Tc-HEDP over Tc-PPi, and higher counting rates from Tc-PPi-injected patients (probably due to its slower blood and soft-tissue clearance), we found no difference in general scan quality when both agents were compared in each of 30 patients.

However, this series showed that lesions could be seen better with Tc-HEDP than Tc-PPi in ten of the patients studied. In fact, in three of 30 patients the Tc-PPi scan was falsely read as normal by at least two of three readers, whereas metastatic disease was found in these patients with Tc-HEDP.

FOOTNOTES

* Procter and Gamble Osteoscan containing 5.9 mg ethane-1 hydroxy-1, 1-diphosphonate, and 0.16 mg $SnCl_2$.

† Mallinckrodt Technescan-PPi containing 15.4 mg Sn-PPi equal to approximately 2.1 mg stannous ion and 13.3 mg PPi.

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