

BONE SCINTIGRAPHY—COMPARISON OF ^{99m}Tc -POLYPHOSPHATE AND ^{99m}Tc -DIPHOSPHONATE

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Eighteen patients were randomly administered either ^{99m}Tc -diphosphonate or ^{99m}Tc -polyphosphate and then restudied within 1 week using the alternative agent. Although both have a high affinity with bone, differences in their in vivo biologic behavior have been reported. These factors do not appear to be significant clinically in their sensitivity in detecting bone lesions although qualitative and quantitative differences in the bone scans were demonstrated. The presence of free technetium in the prepared product appears to be the most important factor contributing to these differences.

Recent developments in bone-imaging radiopharmaceuticals have greatly improved the sensitivity of detecting reactive bone lesions. With the choice of a variety of ^{99m}Tc -labeled compounds such as polyphosphates, diphosphonates, and pyrophosphates, the need for adequate comparative studies in a clinical setting has become apparent. Although all have a high affinity with bone, differences in their in vivo biologic behavior have been reported (1,2). Diphosphonates are believed to be more stable than polyphosphates and have been shown to have a more rapid blood clearance. The clinical significance of these differences on detectability of bone lesions is not known.

Eighteen patient volunteers were recruited for this study. Patients were randomly administered either ^{99m}Tc -diphosphonate (Medi-Physics or Procter and Gamble) or ^{99m}Tc -polyphosphate (New England Nuclear) and then restudied within 1 week using the alternate agent. The results of these 36 studies were compared quantitatively and qualitatively.

MATERIALS AND METHODS

Each product was prepared as outlined by the manufacturers' instructions. The same source of methyl ethyl ketone (MEK)-extracted ^{99m}Tc -per-

technetate was used in the preparation of the ^{99m}Tc -Sn-EHDP (diphosphonate) and ^{99m}Tc -polyphosphate. Fifteen millicuries of the freshly prepared radiopharmaceutical were administered for each study. To ensure hydration, 1,000 cc of water were given to the patient after administration of the agent. Patients were asked to void prior to imaging to minimize interference from the bladder. Imaging was initiated at 3 hr postinjection. Whole-body images were obtained utilizing a commercially available Anger scintillation camera with a whole-body imaging system and low-energy, high-sensitivity collimator (Dyna Camera 2C with omniview whole-body imaging table). Both anterior and posterior projections were performed with the field of view selected to encompass the entire skeleton by means of three longitudinal passes.

The detector position was set as close as possible to the body and the distance was recorded in each instance. Exposure control was determined by positioning the camera over the chest so that the sternum could be used as a reference point. Profile controls were set for a slice through this reference point and, with the camera console in the digital mode, the time required to accumulate 100 counts in the data processor memory was recorded. This time was multiplied by 8 so that an acceptable information density of 800 counts/cm² was obtained. This was done to ensure visualization of lesions with the higher information density possible on the multiple single-exposure views.

Using the table-speed nomogram, the proper table-speed control was selected to obtain this information density. The total time to perform each view, anterior and posterior, the total counts in each view, and the whole-body profile were recorded for

Received April 16, 1974; revision accepted June 26, 1974.

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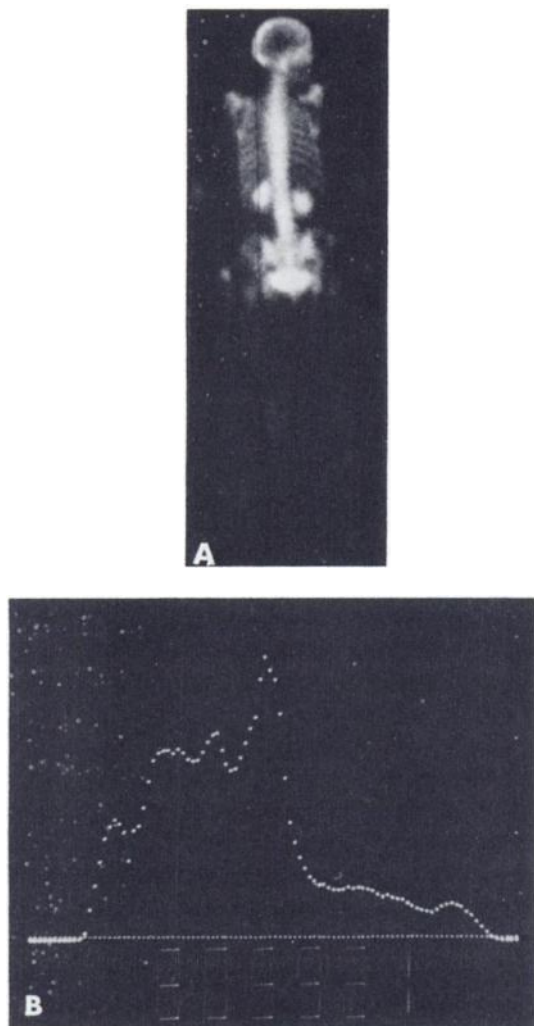


FIG. 1. (A) Patient AM demonstrating posterior whole-body camera study and (B) whole-body count profile with 805,921 total counts being recorded.

each patient (Fig. 1). Prior to repositioning the patient for the posterior view, multiple single-exposure camera views were obtained. In each view a total of 500,000 counts were obtained and the time recorded. This was repeated once the posterior whole-body camera image had been completed.

Following this, at recorded times postinjection, certain regions of interest of abnormal bone, normal bone, and background soft tissues were selected and quantified utilizing the Dyna Camera regions of interest and data processor capabilities (Fig. 2). The regions of interest chosen varied from case to case depending on the location of the target areas. However, regions that could be easily selected such as lumbar or thoracic vertebrae were utilized whenever possible. The coordinates of the regions of interest were recorded and a Polaroid photo of the monitoring oscilloscope was then taken to demonstrate the position of the areas of interest. This material

would be used as a reference when repositioning the patient over the areas of interest for the repeat study. This yielded relative ratios of selected regions of normal or abnormal bone compared with adjacent background areas. Within 1 week of the initial study, the alternate radiopharmaceutical was injected and the above-mentioned study repeated.

INTERPRETATION OF DATA

The ^{99m}Tc -diphosphonate and ^{99m}Tc -polyphosphate scans were separated into two groups that were interpreted independently. The total number of lesions detected in each study was recorded and a general subjective qualitative evaluation of the study was given with emphasis being placed on discreteness of lesions, target-to-nontarget comparisons, and areas of ectopic or soft-tissue accumulations.

In addition, the quantitative data included the computed ratios of the same selected site of interest for each study together with a comparison of the total time and counts recorded in both the anterior and posterior whole-body profile for each isotope at comparable intervals of time, postinjection.

RESULTS

The numerical data are listed in Tables 1 and 2. Seven patients had normal bone scans with no evidence of reactive bone formation. Eleven patients had abnormal bone scans with 29 individual areas showing evidence of reactive bone formation. All lesions were demonstrable with both radiopharmaceuticals; however, the quality of scans was not comparable in all cases. Averaged over all studies performed in this series, the total whole-body counts with ^{99m}Tc -diphosphonate were approximately 10% lower than the corresponding total whole-body counts with ^{99m}Tc -polyphosphate. In many cases, the ratios for ^{99m}Tc -polyphosphate were essentially equal to the ratios for diphosphonate. However, in half

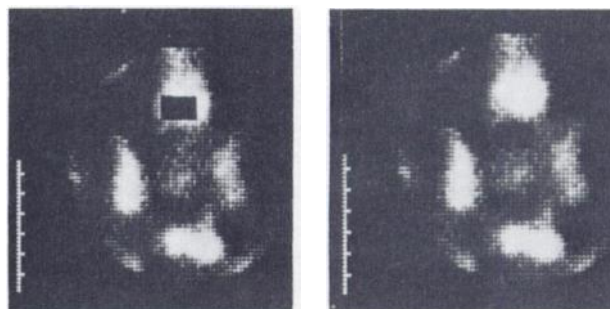


FIG. 2. At recorded times postinjection regions of interest of abnormal bone, normal bone, or background soft tissues were selected and quantified. This was then expressed as a ratio, e.g., abnormal bone cpm/normal bone cpm.

TABLE 1. NORMAL STUDIES

Patient	^{99m} Tc-EHDP				^{99m} Tc-polyphosphate				Diff. in ratio (%)
	Total whole-body counts		Total duration of study (sec)	Ratio	Total whole-body counts		Total duration of study (sec)	Ratio	
	Ant.	Post.			Ant.	Post.			
AM	1,060,741	745,695	2,343	4.05	1,010,021	1,039,657	2,500	4.13	-2.0
SD	887,631	807,484	1,756	1.85	1,329,627	1,251,519	2,207	1.86	-0.5
DK	709,206	742,735	2,278	2.90	954,010	1,063,503	1,924	1.74	+40.0
AM	807,472	805,921	2,342	2.60	1,106,801	1,316,167	2,491	2.32	+11.0
DJ	961,209	871,351	2,471	1.27	935,058	884,088	2,071	1.19	+6.3
MB	1,061,146	1,134,184	2,462	4.38	924,876	932,818	2,434	4.60	-5.0
CS	793,898	730,090	2,032	5.49	808,710	758,402	2,134	4.22	+23.0

TABLE 2. ABNORMAL STUDIES

Patient	^{99m} Tc-EHDP				^{99m} Tc-polyphosphate				Diff. in ratio (%)
	Total whole-body counts		Total duration of study (sec)	Ratio	Total whole-body counts		Total duration of study (sec)	Ratio	
	Ant.	Post.			Ant.	Post.			
EH	1,059,208	1,050,241	2,045	1.00	1,094,338	954,296	1,871	1.00	0.0
AH	878,787	847,627	2,354	1.45	1,194,446	1,177,212	2,311	1.12	+23.0
SA	1,036,390	939,418	2,405	3.80	1,113,468	1,017,543	2,524	3.90	-2.5
MF	825,155	1,001,542	2,440	2.30	1,073,091	1,015,364	2,927	1.60	+30.0
EG	748,464	714,171	2,399	1.34	892,484	891,064	2,220	1.12	+16.0
LG	1,209,962	1,033,144	2,476	1.74	1,021,258	1,135,331	2,328	1.51	+13.0
LG	1,353,356	1,126,881	2,984	2.74	1,277,217	1,131,459	2,398	2.68	+2.4
SH	1,033,344	985,219	2,260	2.35	1,043,347	1,141,943	2,027	2.34	+0.4
AK	1,357,309	1,235,211	2,279	3.00	1,213,284	1,121,684	2,019	2.44	+19.0
JS	941,673	859,565	2,247	1.69	1,006,447	1,028,846	2,319	1.64	+3.0
MW	675,562	829,202	2,921	17.67	613,398	698,592	2,471	13.67	+23.0

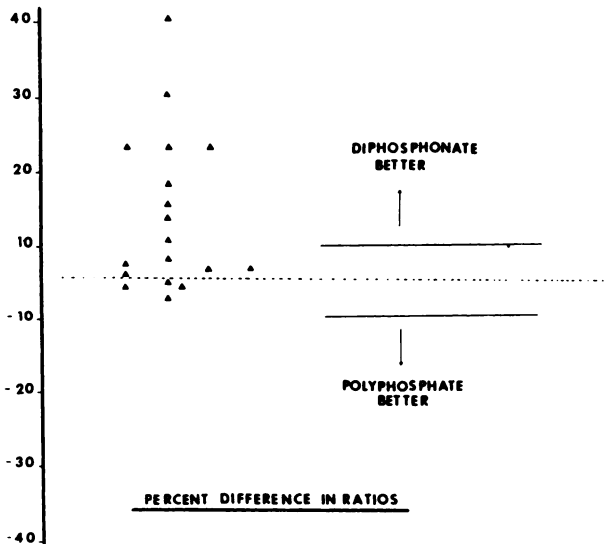


FIG. 3. Percentage difference between ^{99m}Tc-polyphosphate and ^{99m}Tc-diphosphonate. In 50% of patients ratios with ^{99m}Tc-diphosphonate were significantly different.

of the cases the ratios obtained with ^{99m}Tc-polyphosphate were much lower than with ^{99m}Tc-diphosphonate and the difference in the ratios was greater than 10% (Fig. 3). The reverse situation did not occur. The qualitative intercomparison correlated with the above findings.

When the area-of-interest ratios were the same, the overall qualitative appearance of the two studies was similar (Fig. 4). On the other hand, where the areas-of-interest ratios were significantly different, this was reflected in the qualitative appearance and in the interpretation of the study, higher ratios being associated with better definition of lesions (Figs. 5 and 6). Ascending paper chromatography (Whatman 3M developed in 70% methanol and in methyl ethyl ketone) of the freshly prepared skeletal-imaging agent demonstrated the presence of free technetium more frequently in those patients with the poorest target-to-background ratios.

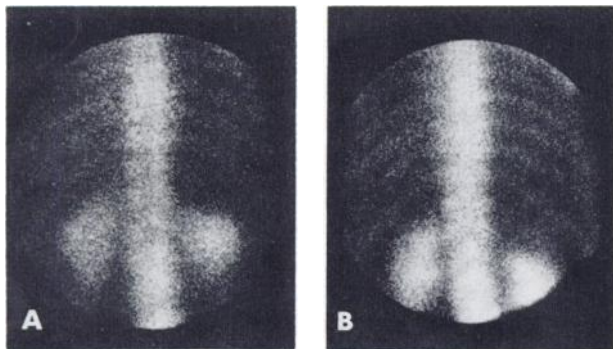


FIG. 4. (A) Normal ^{99m}Tc -polyphosphate scan having same overall qualitative appearance as (B) ^{99m}Tc -diphosphonate scan done on same patient (DJ). Difference in ratio over same areas of interest 6.3%.

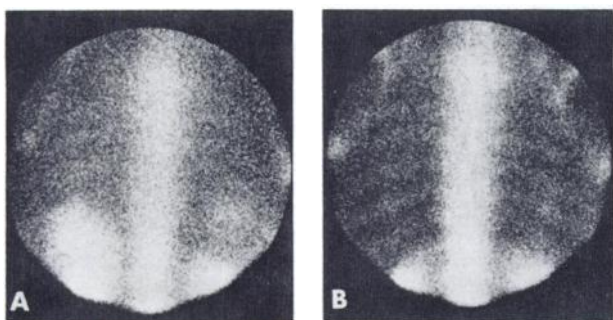


FIG. 5. (A) Normal ^{99m}Tc -polyphosphate scan qualitatively not as good as (B) ^{99m}Tc -diphosphonate done on same patient (CS). Difference in ratios over same areas of interest 23%.

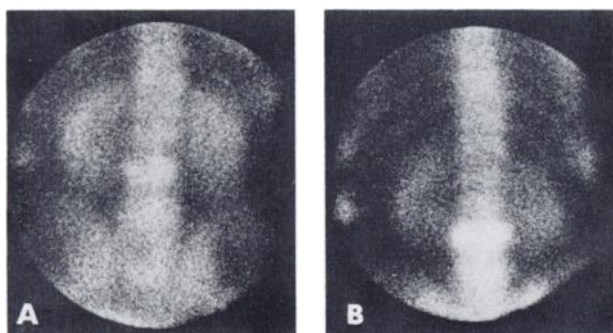


FIG. 6. (A) Abnormal ^{99m}Tc -polyphosphate scan qualitatively not as good as (B) ^{99m}Tc -diphosphonate, done on same patient (MF). Difference in ratios over same areas of interest 30%.

DISCUSSION

In half of the cases from this study, the measured target-to-background ratios as well as the qualitative evaluations were essentially equal for polyphosphate and diphosphonate. In the remainder of the cases, diphosphonate provided greater target-to-background contrast at 3 hr postinjection. Despite the difference in contrast, all of the lesions identified in this study could be visualized with either preparation.

The variability in results obtained from the polyphosphate preparation can be caused by several factors. The more rapid rate of excretion of diphospho-

nate has been previously emphasized as a possible cause of lower soft-tissue background. This fact was reflected in this study by the consistently lower whole-body counting rate at 3 hr postinjection obtained with diphosphonates. This, however, did not entirely explain the variability in target-to-background ratios. Another factor which has recently been investigated (5) is that the rate of uptake by bone and excretion also varies with chain length and molecular weight (5). Polyphosphate compounds with a P—O—P bond are also readily hydrolyzed in vivo by phosphatases whereas diphosphonates are not biodegradable (6). Finally, the preparation of the compounds could result in imperfect labeling and the presence of free technetium. This latter cause was identified in this study as the most important effect in those cases having the poorest target-to-background ratios. This appears to occur despite the careful following of the manufacturer's instructions in the preparation of the product. This problem was not observed as frequently with the diphosphonate preparations in this study.

In this study better results were achieved most consistently with ^{99m}Tc -diphosphonate compounds. Results of equal quality could often be achieved with ^{99m}Tc -polyphosphate regardless of several known factors which may affect the polyphosphate compound in vivo. The variability in results achieved with polyphosphate was due largely to the presence of varying amounts of free technetium in the preparation prior to injection. The resulting image degradation was, nevertheless, not so severe as to obscure any of the 29 lesions identified in this study.

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