information concerning the individual patient than a thorough physical examination combined with a noninvasive assessment of left-ventricular ejection fraction.

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TABLE 1. RATIOS OF FEMUR-TO-SOFT TISSUE (MEAN ± s.d.), AT 2 hr AFTER INJECTION IN NORMAL SUBJECTS AND IN PATIENTS WITH MALIGNANCIES

	N	Normals	Patients	N
MDP*	57	1.638 ± 0.279	1.756 ± 0.317	128
		n.s.	$p < 0.005$	
HMDP†	66	1.627 ± 0.207	1.655 ± 0.221	142
		$p < 0.005$	$p < 0.005$	
DPD‡	26	1.825 ± 0.385	1.885 ± 0.336	177

* MDP = methylene diphosphonate.
† HMDP = hydroxymethylene diphosphonate.
‡ DPD = dicarboxypropane diphosphonate.

Comparison of Tc-99m MDP, HMDP, and DPD with Respect to Bone-to-Soft Tissue Ratios

To close the gap between comparative studies, either open by design (*1-5*) or by number of patients (*1-3,5,6*), we would like to introduce some results illustrated in Tables 1 and 2. This study was designed to complete the comparison of bone imaging with Tc-99m dicarboxypropane diphosphonate (DPD) and Tc-99m methylene diphosphonate (MDP), published in 1982 (*4*), by including Tc-99m hydroxymethylene diphosponate (HMDP). Accordingly, selection of patients, methods, and aims were identical (*4*). Incubation time of Tc-99m in the diphosphonate vials was 45 min in all cases. HMDP was prepared from commercial kits.*

The results comparing the bone-to-soft tissue ratios showed that HMDP was very close to MDP and that differences between the three agents were very small (Tables 1, 2)—in particular the ratio between os sacrum (cancellous bone) and femoral soft tissue (Table 2). Moreover, as with MDP and DPD, HMDP revealed identical trends: ratios in patients were higher than in normals (this difference was most pronounced with MDP, Table 1) and sacrum-to-femoral soft-tissue ratios decreased with patient's age. Image contrast in patients without skeletal lesions was still the highest with DPD (Tables 1, 2). However, intra-individual comparison in patients with skeletal lesions revealed changes in this ranking (*6*).

Comparative intra-individual studies are bound to include a small number of patients due to ethical reasons. Therefore, small changes in preparation, selection, evaluation, and sequence of choice of agents may play a more important role than in the large number of patients included in inter-individual studies (596 patients in Table 1). On the other hand, it is more effective to compare uptake in lesions than in normal bone. To solve these problems created by an increasing number of bone-seeking diphosphonates similar in action but different in structure, more work is needed to explain the differences in biokinetics at the target, rather than solely to describe them.

TABLE 2. RATIOS OF SACRUM-TO-SOFT TISSUE (MEAN ± s.d.), AT 2 hr AFTER INJECTION, IN NORMALS AND IN PATIENTS WITH MALIGNANCIES

Years of age	N	DPD	Normals	HMDP	N	MDP
20 – 30	7	8.16 ± 3.25	13	7.04 ± 2.35	8	7.53 ± 1.94
40 – 49	6	6.63 ± 2.49	17	6.86 ± 2.03	11	5.93 ± 1.49
50 – 59	8	6.02 ± 1.11	10	5.33 ± 1.76	19	5.68 ± 1.47
60 – 69	5	5.02 ± 0.71	14	5.75 ± 1.62	10	4.78 ± 1.28
>70	—		12	4.61 ± 1.14	8	3.79 ± 1.14
			Patients			
20 – 39	30	7.16 ± 2.10	25	7.71 ± 2.40	11	6.62 ± 2.10
40 – 49	41	7.09 ± 2.27	33	6.56 ± 1.63	26	6.66 ± 1.98
50 – 59	40	6.36 ± 2.00	33	6.23 ± 1.42	33	5.80 ± 1.63
60 – 69	33	5.40 ± 1.56	32	5.18 ± 1.51	41	5.56 ± 1.88
>70	33	5.28 ± 1.36	19	4.82 ± 1.19	17	4.86 ± 1.00

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FOOTNOTE

* Proctor & Gamble by courtesy of Byk-Mallinckrodt, one vial contained 3.0 mg of HMDP and 0.24 mg of $SnCl_2$, five patients per vial, 10.8 mCi (400 MBQ) per patient.

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Reply

We can indeed welcome the additional data provided by Drs. Buell, Kirsch, Kleinhans, and Jager comparing Tc-99m hydroxymethylene diphosphonate (HMDP) and Tc-99m methylene diphosphonate (MDP). Since their comparative imaging data were obtained 2 hr following injection, and ours were obtained at 4 hr bone-to-soft tissue ratios are not strictly comparable. Also, we used the entire contents of a single reaction vial for each study rather than "loading" the reaction vial with a large amount of Tc-99m and dispensing several doses from one vial. Whether and how this may influence labeling efficiency or biodistribution is unknown.

Regarding our study, care was taken to prepare all radiopharmaceuticals in a similar manner and the order of administration was randomized.

The effect of incubation time on the biodistribution of MDP, demonstrated by Henkin and associates as well as Buell and associates (*1*,*2*), is of interest and deserves additional study.

We agree with the statement "more work is needed to explain the differences in biokinetics (of the various diphosphonates) at the target rather than solely describe them."

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Tc-99m MDP and Ga-67 Citrate Accumulation in Cutaneous Metastases from Colon Carcinoma

A 58-yr-old male who had undergone resection of an adenocarcinoma of the colon the previous spring, presented at our institution in the fall of 1982 with abdominal discomfort and multiple subcutaneous nodules on the thorax, abdomen, and lower extremities. Biopsy of these nodules revealed adenocarcinoma consistent with the patient's known colonic primary.

Whole-body bone scintigraphy was performed following intravenous injection of 20 mCi of Tc-99m MDP; gallium scintigraphy was performed 48 hr after intravenous injection of 5 mCi of Ga-67 citrate.

Bone imaging demonstrated abnormalities of the thoracolumbar spine and sternum without definite evidence of abnormal soft-tissue accumulation of the tracer in the thorax or abdomen (Figs. 1 and 2). Focal soft-tissue accumulation of the Tc-99m MDP was noted in both lower extremities, and these foci corresponded to the subcutaneous nodules (Fig 3).

On gallium scintigraphy, abnormal soft-tissue accumulation was seen in the left anterior hemithorax (Fig 1). The osseous abnormalities were less clearly appreciated on this study. Initially, no corresponding abnormality was seen on bone scintigraphy, but in retrospect such a focus could have been obscured by underlying rib activity. A solitary focus of abnormal gallium accumulation in the left flank (Fig 2) did not accumulate the bone agent; it was

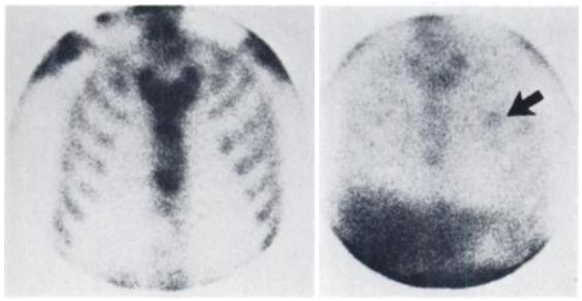

FIG. 1. Anterior thorax: Bone image (left): Irregular uptake of Tc-99m MDP in sternum—no definite abnormal soft-tissue activity. Gallium image (right): Abnormal accumulation of imaging agent in subcutaneous nodule (arrow); irregular uptake in sternum.

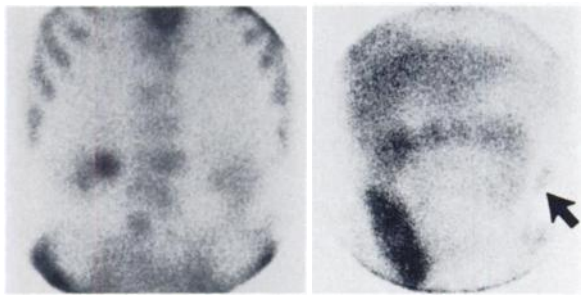

FIG. 2. Anterior abdomen: Bone image (left): No focal soft-tissue abnormality. Gallium Image (right): Abnormal activity in left flank nodule (arrow).