Radiographic and Radionuclide Imaging in Multiple Myeloma: The Rôle of Gallium Scintigraphy: Concise Communication

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Eighteen patients with multiple myeloma were studied using radiographs of the skeletal system, technetium phosphate bone scans, and gallium-67 scintigraphy. A total of 94 sites were used as the basis for comparison in these 18 patients. Radiographic sensitivity on a patient basis was 94%, and was 82% on a site basis. Bone scans were positive in 78% of patients and in 46% of sites. Gallium scans were positive in 56% of patients and in 40% of sites. In five of the 18 patients, gallium scans showed activity in abnormal sites with a greater lesion-to-nonlesion ratio than did the bone scan. In this subgroup of patients, the disease was fulminant, and all died within 3 mo of their study. The finding of high gallium uptake in osseous sites that are normal or only slightly abnormal on bone scan has served to identify a subgroup of patients with rapidly progressive disease who may benefit from alternative treatment modalities such as radiation therapy.

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Radionuclide imaging in multiple myeloma has dealt mainly with detection of osseous abnormalities using bone-scanning agents, such as strontium-85, strontium-87m and, more recently, the technetium phosphate compounds (*1–7*). In general, these studies conclude that the bone scan will often detect osseous myeloma, but the sensitivity is considerably less than that of radiographic techniques.

Hübner et al. studied 23 myeloma patients with radiography, technetium bone scan, and gallium-67 (*6*). Despite gallium localization in some soft-tissue abnormalities and in solitary myelomas of bone, this group concluded that gallium uptake by multiple myeloma is probably the exception and is not a useful diagnostic aid in the evaluation of the myeloma patient.

The purpose of the current study was to compare the bone scan, radiograph, and gallium scan in multiple myeloma, with an attempt to define the relevance of each modality with respect to disease detection, and possibly the interrelationships of scan patterns with disease activity and/or prognosis.

MATERIALS AND METHODS

Eighteen patients with biopsy-proven multiple myeloma were studied with radiographs of the skeletal system, technetium phosphate bone scans, and gallium-67 citrate scintigraphy. Delayed bone scans were performed 2–4 hr after the injection of 15–20 mCi of Tc-99m diphosphonate or methylene diphosphonate. Gallium scans were performed 48–96 hr after injection of 4–6 mCi of gallium-67 citrate. The bone and gallium scans were performed using either a large-field-of-view Anger camera, a dual-headed rectilinear scanner, or a multiplane tomographic scanner. On any given patient, both the gallium and bone scan were performed on the same instrument for purposes of comparison.

The radiographic evaluation included views of the skull, thoracic spine, lumbar spine, pelvis, humeri, and femora. In addition, a routine PA and lateral chest projection was obtained. Additional areas were radiographed when appropriate.

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A positive site was defined as an abnormal region detected by one or more of the imaging modalities.

The diagnosis of myeloma was substantiated by tissue confirmation in all patients. Tissue confirmation of extraosseous sites was possible in three patients (three sites).

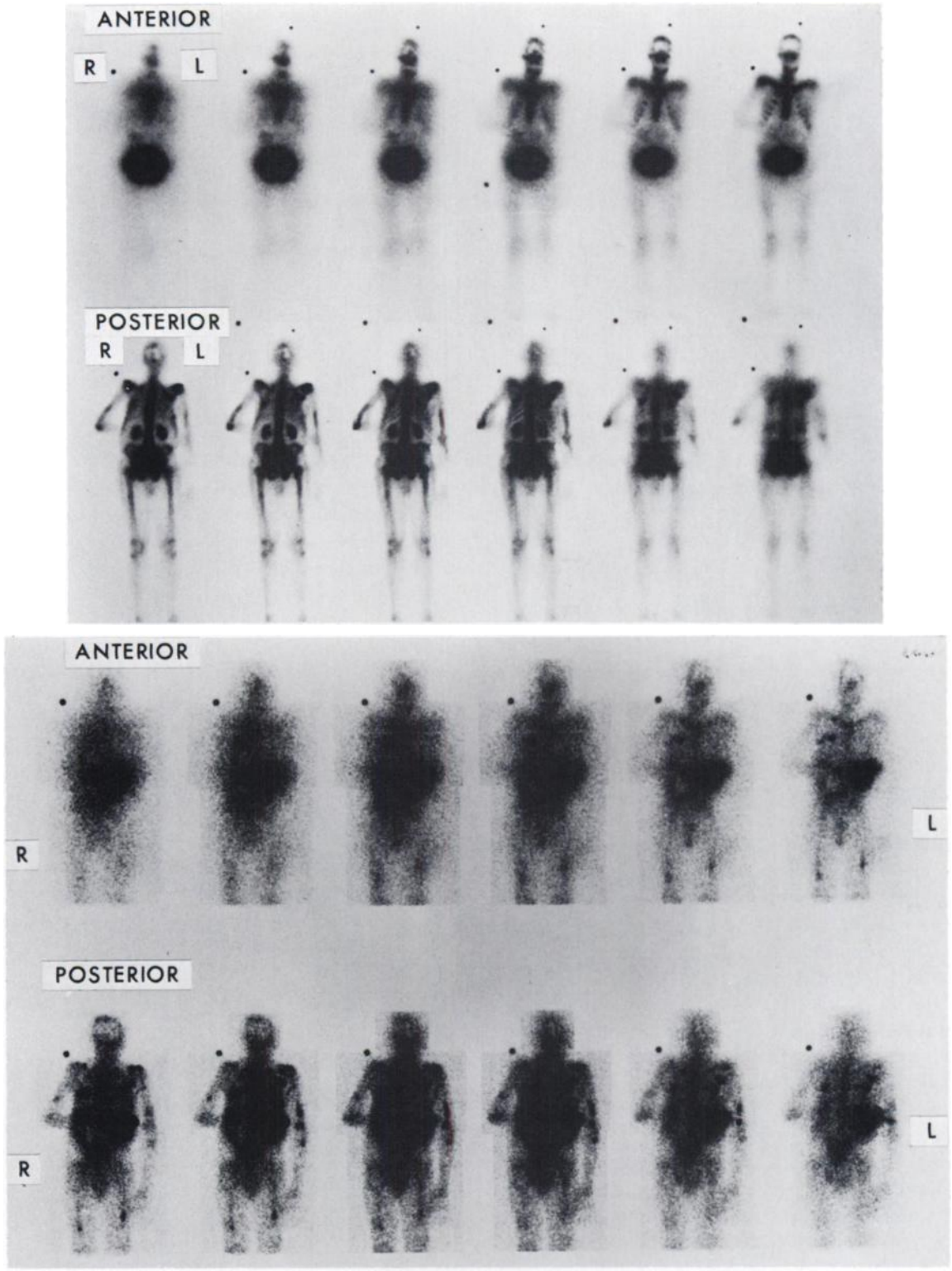

FIG. 1. (Top) Multiplane scintigraphic bone scan in patient with multiple myeloma. Note single large abnormality in left upper rib cage posteriorly. (Bottom) Same patient as above. Gallium multiplane study shows multiple focal abnormalities in rib cage and extremities. In addition, note left upper quadrant soft-tissue abnormality later shown to be a plasmacytoma.

TABLE 1.
POSITIVE SITES BY IMAGING MODALITY*

Patient	Radiograph	TcP bone scan	Gallium bone	Gallium soft tissue
1	3	4	0	
2	6	1	1	
3	3	2	2	
4	5	0	0	
5	6	4	3	
6	8	5	4	
7	1	3	0	
8	4	4	0	
9	2	0	0	
10	2	0	0	
11	0	3	0	Hilum
12	2	5	5	
13	3	0	0	
14	10	2	7	
15	9	3	8	Chest wall, abdomen
16	5	3	3	lung, abdomen
17	1	1	1	Hilum
18	7	3	4	
Total	77	43	38	

Total no. of patients = 18
Total no. of sites = 94

* A regional osseous abnormality on either radiograph, bone scan, or gallium scan defines a positive site.

TABLE 2. SITE-BY-SITE COMPARISON OF RADIOGRAPHIC AND SCAN FINDINGS IN MULTIPLE MYELOMA

Study combination	No. of sites
Radiograph + Bone Scan + Ga (osseous) +	15 (16%)
Radiograph + Bone Scan + Ga (osseous) −	15 (16%)
Radiograph + Bone Scan − Ga (osseous) −	31 (33%)
Radiograph + Bone Scan − Ga (osseous) +	16 (17%)
Radiograph + Bone Scan + Ga (osseous) +	3 (3%)
Radiograph − Bone Scan + Ga (osseous) −	10 (11%)
Radiograph − Bone Scan − Ga (osseous) +	4 (4%)
Radiograph − Bone Scan − Ga (osseous) − Ga (Soft Tissue) +	6 (6%)

RESULTS

Results are summarized in Tables 1–4.

Table 1 shows the distribution of positive studies for each imaging modality. It is clear that radiography was the most sensitive technique with respect to both patients and sites. Only one patient with osseous myeloma had a completely normal radiographic bone survey. The gallium scan was helpful in detecting extraosseous concentrations of myeloma. In addition, the gallium scan was helpful in determining activity of disease as judged by the intensity of gallium activity relative to radiographic and/or bone-scan findings. An example of a patient with significant gallium abnormalities of the osseous system, but with only minimal evidence of disease on bone scan, is shown in Fig. 1. Radiographs demonstrated irregular lytic changes in the extremities.

Table 2 summarizes a site-by-site analysis of the results of radiography, bone scan, and gallium scan of the osseous system. The most common pattern observed was that of a positive radiograph associated with a negative bone scan and a negative gallium scan. Of interest is the gallium-67 detection of six soft-tissue sites that were not observed on radiograph.

Table 3 is a case and site analysis in which only one imaging modality was found to be positive. In four patients (22%) the radiograph gave the only positive finding. In a single patient, the bone scan was the only positive imaging modality.

Table 4 compares the relative bone and gallium uptakes using a subjective estimate of lesion to surrounding bone as the basis for comparison. Twenty-one sites in five patients showed gallium to have a higher lesion-to-bone level than Tc-99m MDP. These five patients died within 3 mo of the study.

Figure 2 gives an example of a patient with high gallium-to-bone levels in multiple sites, who died 6 days after the study.

TABLE 3. CASES OR SITES IN WHICH ONLY ONE IMAGING MODALITY WAS POSITIVE

Study	Number of cases	Number of sites
Radiograph	4 (22%)	31 (33%)
Bone scan	1 (6%)	10 (11%)
Gallium scan (osseous)	0	4 (4%)

TABLE 4. RELATIVE GALLIUM-TO-BONE UPTAKE IN SCANS OF OSSEOUS LESIONS DUE TO MYELOMA

	Ga > TcP	Ga = TcP	Ga < TcP
No. of sites	21	9	27

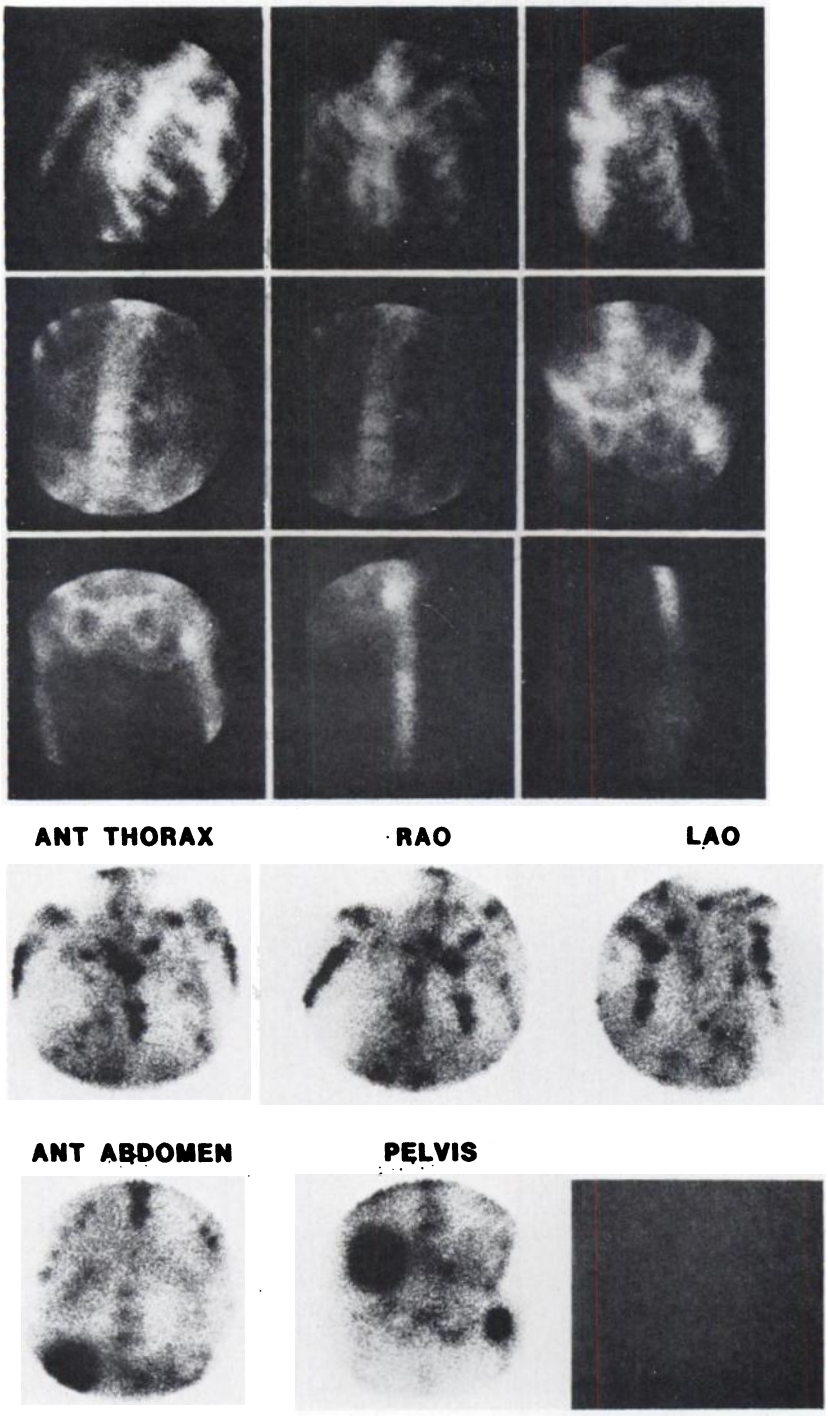

FIG. 2. (Top) Tc-MDP bone scan in patient with fulminant multiple myeloma. Note minimal changes in anterior projections of chest and pelvis. Increased activity is noted in left femur. (Bottom) Gallium scan of the same patient as above. Note extensive abnormalities demonstrated by gallium, which were poorly defined by Tc-MDP. Patient died 6 days later.

DISCUSSION

Previous reports have shown the radiograph to be the most sensitive imaging modality in detecting abnormalities due to multiple myeloma (*5–7*). Woolfenden et al. have recently reported on a study comparing the sensitivity of the emission bone scan in 51 patients with radiographically evident multiple myeloma (*7*). This group concluded that the scintigram was relatively insensitive in detecting myeloma. In 289 sites, the sensitivity of scintigraphy for myeloma was 60% compared with 75% for radiography. This correlates with the sensitivity figure of 46% for bone scintigraphy in this series, with a 77% sensitivity for radiography. In addition, the Woolfenden study showed that 40% of the sites were found only on radiography and 25% only on the bone scan. The current study shows 33% of sites were found only on radiography, and only 11% by bone scan.

Hübner recently evaluated osseous myeloma using gallium-67 citrate as well as a technetium phosphate bone scan (*6*). Using a site-by-site comparison, this group found that 52% of radiographically evident ab-

normalities were seen on the bone scan. However, 70% (seven of ten patients) were read as abnormal in at least one site. These figures are similar to ours. The Oak Ridge group found that 35% of patients with radiographically evident myeloma showed evidence of disease on gallium scan.

They also found that gallium abnormalities were detected in 22 of 87 sites (25%). Their data suggested that gallium accumulation occurred infrequently in myeloma and was probably not useful in this disease.

The number of patients who were examined by both radiography and gallium studies in their series numbered 17, six were positive by gallium and the remainder negative. Our series included 18 patients, of whom ten were considered positive on the gallium study. When one applies Fisher's exact test to the comparison of both data sets, the p value is 0.315. Thus, there is no significant difference between the percentage of patients that were positive by gallium in the previously published series and that in the current series. The power calculation yielded a value of 0.23, indicating that the numbers of patients in the two series are too small to conclude whether or not a significant difference was present.

The current series indicated that 56% of the patients studied with radiographically evident myeloma had abnormal gallium scans. In addition, 40% of abnormal sites were also gallium-positive. Thus, within the current series gallium appears to be a useful test in the evaluation of myeloma.

Table 5 compares the number of sites detected by radiograph, bone scan, and gallium scan for each of the 18 patients. Using these data, and applying Friedman's nonparametric analysis of variance, $p < 0.005$. This indicates that the numbers of sites detected by the three techniques are different. Using the Newman-Keuls test for nonparametric multiple comparisons, the radiograph was clearly superior to the bone scan in the number of sites detected ($p < 0.05$). There was no statistically significant difference in the sites detected between the bone scan and gallium scan.

In five patients, the gallium-to-bone ratio was significantly higher than the ratio of technetium phosphate to bone. All five patients in this study died within 3 mo after the study, indicating the presence of a fulminant disease process. Since gallium uptake is largely dependent upon cellular mechanisms and not on reactive bone, it appears that the relative gallium-to-bone scan activity may be important in predicting the presence of a high tumor burden, which has been shown to be associated with a poor prognosis (*8*).

This study again demonstrates the technetium phosphate bone scan to be a relatively insensitive indicator of the osseous myelomatous process when compared with radiography. However, in this study, 11% of bony abnormalities were detected by bone scintigraphy only.

In this series the gallium scan was the least sensitive of all imaging modalities in the detection of osseous myeloma. However, the sensitivity on a site-by-site as well as a patient basis was demonstrated to be higher than that reported by Hübner et al. (*6*). As discussed, this may be a function of the small patient population in both the Hübner series and ours. Additional patient studies appear needed to resolve this issue. While the sensitivity of gallium scintigraphy is less than that of radiography, and probably less than the bone scans, the findings of a high gallium-to-bone ratio, especially when coupled with a normal or minimally abnormal bone scan, indicated the presence of a fulminant process. The ultimate utility of this finding may be in defining a subpopulation of myeloma patients with a need for alternative therapies, such as localized radiation.

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