Evaluation of Renal-Skeleton Ratio of Technetium-99m Phosphonate in Multiple Myeloma

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The kidneys were evaluated on [^{99m}Tc]phosphonate bone scans using 35 studies from 23 individuals with multiple myeloma; these images were compared with those from 50 controls. In each case, the kidneys could be visualized and calculation was made of the renal:skeleton ratio. Two myeloma patients showed an elevated renal:skeleton ratio. One was due to reduced vertebral uptake of [^{99m}Tc]phosphonate following therapeutic radiation. In the second case, the elevated ratio was related to renal uptake of the tracer (independent of urinary retention), and was consistent with nephrocalcinosis. No significant correlation between the renal:skeleton ratio and the degree of hypercalcemia, proteinuria, or renal impairment was found. We conclude that bone scintigraphy represents a safe, simple means of demonstrating renal presence and activity in multiple myeloma patients. However, calculation of the renal:skeleton ratio is not directly helpful in clarifying the events of calcium metabolism.

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Multiple myeloma can be associated with increased urinary excretion of calcium and proteins. Renal damage due to parenchymal deposition of calcium and/or the toxic tubular effects of light chain excretion is frequent, occurring in up to 50% of patients (*1*). Increased renal uptake of the technetium-99m (^{99m}Tc) phosphonates has been reported in isolated cases of multiple myeloma and in hypercalcemic individuals (*2,3*). We, therefore, performed a study to determine a possible role for radionuclide bone studies in the evaluation of renal function in patients with multiple myeloma.

MATERIALS AND METHODS

A retrospective review was performed. Images of the urinary system were studied in patients who had bone imaging with [^{99m}Tc]methylene diphosphonate (MDP) or [^{99m}Tc]HDP. We sought information on three topics: (a) to gauge renal presence and function in multiple myeloma; (b) to compare renal uptake of tracer with that in the skeleton; and (c) to determine whether any patient had suffered adverse urinary tract reactions following use of the bone imaging agent.

The study group consisted of 23 patients (35 scans) with multiple myeloma who were referred for skeletal scintigraphy at our institutions. The diagnosis was, in each case, based on the criteria established by the Southwest Oncology Group (*4*). The patients with multiple myeloma (12 men, 11 women) had a mean age of 69 yr. The chart of each patient was reviewed to determine the serum creatinine values prior to and after bone scintigraphy. When these laboratory values were not available, the record was examined for other evidence of renal function including BUN determinations, urine volumes, 24-hr creatinine values and/or narrative comments.

Fifty consecutive scintigrams, which had been read as normal, were used as controls. These had no regions of abnormally increased or decreased skeletal uptake of ra-

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diotracer. The mean age of the control group (47 men, 3 women) was 58 yr.

None of these individuals had evidence of renal disease. Twenty of the control patients had complained of focal pain (without known malignancy), while 29 had documented malignancies (primaries in lung, oral cavity, prostate, breast, bladder) and one had a soft-tissue infection.

Bone scans of each of the 50 control patients, and the 35 studies in the 23 multiple myeloma patients, were obtained 2-4 hr after i.v. administration of 15-20 mCi of either [^{99m}Tc]MDP or [^{99m}Tc]HDP. Three different gamma cameras were utilized. Each image was examined for renal presence and activity, as well as the renal:skeleton ratio (*5,6*). This was accomplished by transilluminating the images and employing a densitometer.* The optical densities of the renal cortices and vertebrae were determined. Vertebral uptake was defined as the averaged optical densities of the T9 and L2 vertebrae. When patients with multiple myeloma showed myelomatous involvement of these vertebrae, T10 and/or L3 were substituted. Soft-tissue activity was measured between the kidneys and the iliac crests, and subtracted from the raw data (*6*). The relationship between optical density and counts was established for each of the three gamma cameras, using the film employed with that machine. A cobalt-57 flood source was placed at the surface of the all-purpose, low-energy collimator utilized for the bone studies. Film exposure settings were maintained identical to those used for bone scintigraphy. By sequentially increasing the duration of exposure, a plot of counts versus optical density was generated for each of the three films employed† (Fig. 1). It was apparent from the close linear fit which resulted that, over the optical density range of ~0.01 to 0.8, optical density was proportional to the total counts accumulated (*5*). A relative measure of renal and vertebral counts could then be determined from measured optical densities, and a renal:skeleton ratio calculated.

RESULTS

The 50 control patients had normal renal function. These individuals showed a mean renal:skeleton ratio of 0.66. A range of 0.16 to 1.16 represented 2 s.d.s from the mean. One control patient had a renal:skeleton ratio slightly above the 1.16 ratio (Fig. 2, left). Two of the studies in patients with multiple myeloma produced renal:skeleton ratios which exceeded the upper limit of the normal range (Fig. 2, right). One of these patients, who had received radiation therapy to the vertebrae, had decreased uptake in the vertebrae. Hence, the renal:skeleton ratio was elevated due to a low skeleton value. The second patient, with the highest renal:skeleton ratio, had intense renal parenchymal uptake of the radiotracer without intense activity in the urine (Fig. 3). This individual had mild renal impairment and is shown on line 10 of Table 1. Both the patient's serum total calcium (3.18 mmol/l) and ionized calcium (1.8 mmol/l) were elevated at the time of bone scintigraphy. Monoclonal lambda light chain excretion in the urine was documented. One patient with multiple myeloma had a renal:skeleton ratio which fell slightly below the lower limit of 0.16. He had normal renal function at the time of the study, and the bone images did not reveal any evidence of intraskeletal abnormality.

A total of five patients with multiple myeloma (including the one mentioned above) had mildly decreased renal function at the time of bone imaging (Table 1). None of these had any significant change in serum creatinine following the bone scintigraphy. Four patients were hyper-

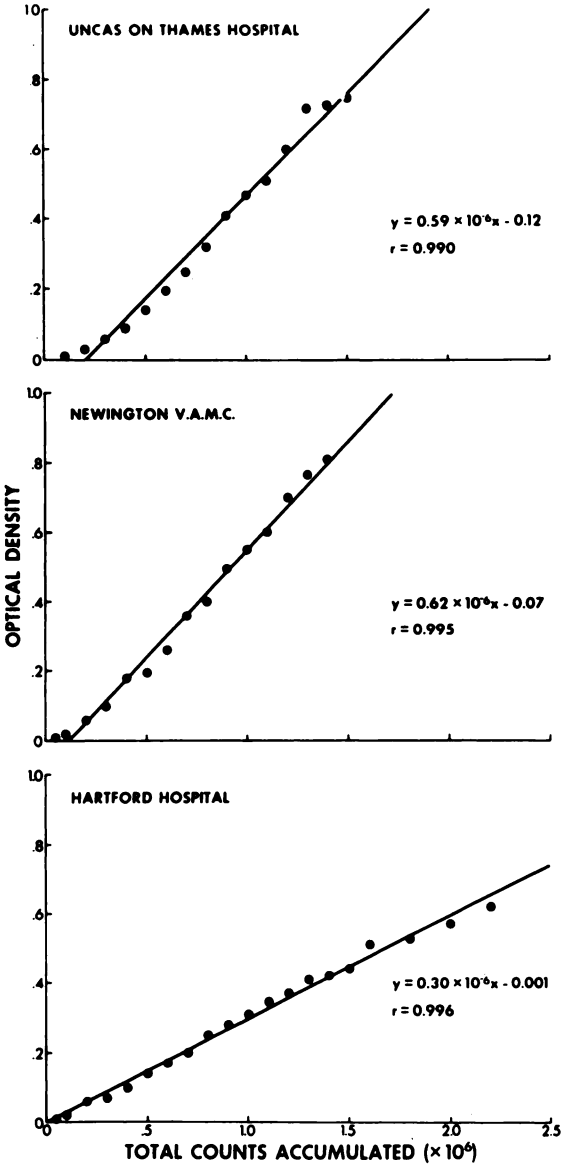

FIGURE 1
Optical density vs. counts was plotted for each of three cameras used. Good linear fit was obtained over experimental range. Differences in slopes of lines are consistent with variations in exposure characteristics (gray scales) of different films employed

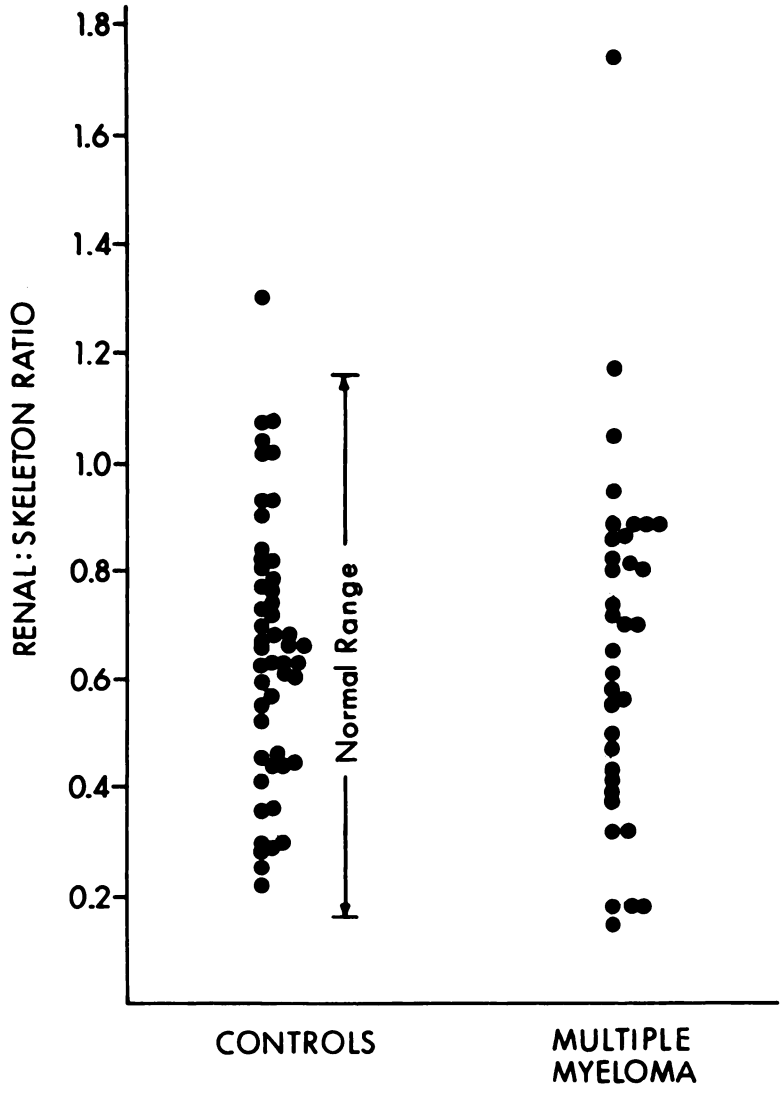

FIGURE 2
Distribution of renal:skeleton ratio in 50 control individuals as well as 35 images obtained in 23 patients with multiple myeloma

calcemic. Bence Jones proteinuria was documented in six cases. No significant correlation between the renal:skeleton ratio in these patients and the degree of proteinuria, hypercalcemia, or renal impairment was found.

DISCUSSION

An elevated renal:skeleton ratio may result from (a) increased renal accumulation of radiotracer or (b) decreased skeletal uptake of radiotracer. Among the recognized causes of increased renal localization of [^{99m}Tc]-MDP are hypercalcemia and, rarely, multiple myeloma (*2*, *3*). In this study, one multiple myeloma patient had intense renal parenchymal uptake of tracer. He was hypercalcemic, with an elevated serum creatinine at the time of scanning. Three other myeloma patients (Nos. 14, 15, 21 in Table 1) were hypercalcemic when scanned, but had normal serum creatinine values. One patient (No. 18) was normocalcemic at the time of bone scintigraphy, but his renal functions were mildly abnormal. None of these patients exhibited increased renal content of bone agent. Increased parenchymal uptake of radiotracer in the kidneys of multiple myeloma patients, then, is most likely consistent with nephrocalcinosis and associated renal damage. The second case of abnormally increased renal:skeleton ratio involved a patient who had had radiation treatment of the spine because of myeloma involvement. In this patient, decreased skeletal uptake of the bone agent was the etiology of the abnormal ratio.

A decreased renal:skeletal uptake ratio may result from increased skeletal uptake (due to diffuse metastases, diffuse metabolic disease, hematologic disease, or fibrous dysplasia), or from decreased kidney uptake due to renal failure (*6*). One myeloma patient had faint visualization of the kidneys on scintigrams, but had normal renal function. As there was no intraskeletal shift of activity into the extremities or axial skeleton, this patient's poor renal uptake may represent a normal variant (within 3 s.d.s of the mean).

In this study, the renal:skeleton ratio did not prove use-

TABLE 1
Data on 23 Patients (35 scans) with Multiple Myeloma*

Patient no.	Days prior to scan	Total calcium	Serum CR	BUN	Bence Jones proteinuria	Renal:skeleton ratio
1	—	—	—	—	—	0.50
2	4	2.53	1.0	—	—	0.80
3	3	—	1.6	26	—	0.94
	2	2.52	1.7	31	—	0.88
	—	—	—	—	—	0.81
4	21	2.53	1.3	17	—	0.88
	1	2.43	1.0	11	—	1.17
5	7	—	1.5	18	—	0.70
6	—	—	—	—	—	0.65
	—	—	—	—	—	0.70
7	7	2.18	1.2	31	—	0.88
8	3	2.40	2.0	27	Yes	0.74
	—	—	—	—	Yes	0.80
	—	—	—	—	Yes	0.61
	—	—	—	—	Yes	0.56
9	14	2.35	0.9	19	—	1.05
10	0	3.18	2.1	—	Yes	1.74
11	2	—	1.2	14	—	0.82
12	3	2.37	—	17	—	0.48
13	—	—	—	—	—	0.85
	—	—	—	—	—	0.86
14	4	3.3	1.2	—	Yes	0.18
15	0	2.6	1.1	21	—	0.15
16	—	—	—	—	—	0.32
	—	—	—	—	—	0.39
	—	—	—	—	—	0.71
	—	—	—	—	—	0.88
17	—	—	—	—	—	0.55
18	1	—	—	23	—	0.18
	—	—	—	—	—	0.41
19	5	2.29	—	—	—	0.39
20	—	—	—	—	—	0.33
21	0	2.60	0.9	13	Yes	0.58
22	2	2.42	1.0	18	Yes	0.43
23	0	—	2.0	33	Yes	0.18

*Normal serum calcium = 2.20–2.58 mmol/l.
Normal serum creatinine = 0.8–1.4 mg/dl.
Normal blood urea nitrogen = 6–22.

ful in predicting variations in serum calcium or the presence of proteinuria or mild renal impairment in multiple myeloma patients. This is not surprising as renal failure due to any cause, including the development of proteinaceous tubular casts, would be expected to decrease the renal:skeleton ratio, while hypercalcemia has been found to increase renal content of bone agent. Where both conditions are present in mild degree, the result should be normalization of the renal:skeleton ratio.

Use of radiographic contrast media has been implicated in the development of acute renal failure in multiple myeloma patients (*4, 7-12*). Since the introduction of diatrizoate, the incidence of contrast nephropathy has decreased, possibly due to decreased protein binding by the newer contrast agent (*8*). Nevertheless, Myers and Witten reported two cases of contrast nephropathy in patients with multiple myeloma and poor renal function prior to the x-ray procedure. It was inferred that the risk of contrast induced renal failure was increased in myeloma patients with pre-existing renal disease (*7, 8*). In this study, no adverse effect of the bone-seeking radiopharmaceutical on renal function could be discerned in myeloma patients with normal or mildly abnormal renal function at the time of scintigraphy. Given the overall poor prognosis of multiple myeloma patients with renal failure (*9*), it can be concluded that nuclear medicine studies may have an important role to play in determining renal presence and activity in these high risk cases.

This study indicates that radionuclide study of the kidneys during [^{99m}Tc]phosphonate bone imaging represents a safe and simple means of determining renal presence and activity in multiple myeloma patients, with or without

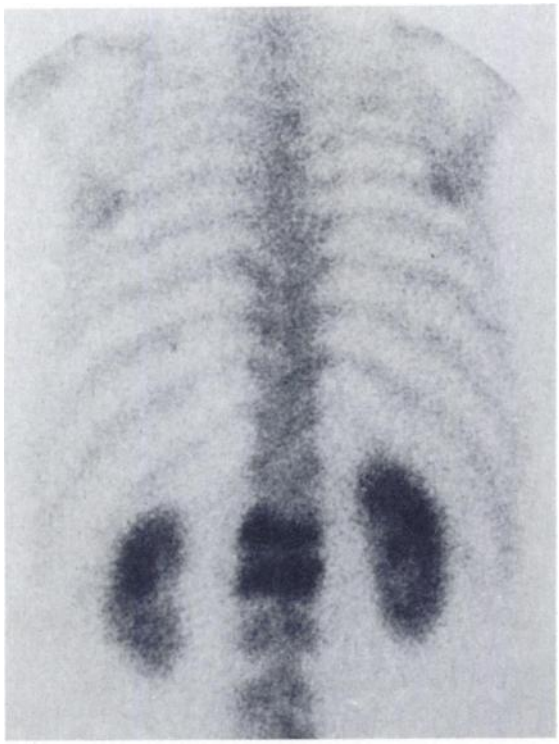

FIGURE 3
This is posterior image obtained in patient with multiple myeloma, following i.v. administration of [^{99m}Tc]MDP. In addition to involvement of two lumbar vertebrae, intense uptake can be seen in kidneys, independent of urinary activity

pre-existing renal disease. Calculation of the renal:skeleton ratio was not found helpful in further defining renal physiology in the myeloma patient.

ACKNOWLEDGMENT

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FOOTNOTES

*Sakura PDA-85.
†Sakura x-ray, Sakura UC, Kodak XRP-1.

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