Quality of Bone Scans Compared with Time Between Dose and Scan

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The usual time interval between the administration of technetium-labeled bone-seeking radiopharmaceuticals and imaging varies among nuclear-medical departments. Pharmacokinetic data indicate that the interval could be as short as 2 hr. We have studied overall quality of bone detail in 280 bone scans performed at intervals varying from 2 to 5 hr following injection of technetium-99m diphosphonate. No significant qualitative difference was found between the studies performed at 2 hr and those done at later intervals.

J Nucl Med 18: 787–789, 1977

When technetium-99m labeled phosphates and phosphonates were introduced as skeletal imaging agents, the suggested time to elapse between intravenous administration of the agent and the beginning of imaging (scan-delay time, SDT) was assumed to be 3–4 hr. The delay was based on normal human blood-clearance data and was intended to allow sufficient clearance of the labeled agent from the blood and soft tissues so that optimal visualization of the skeleton and any bone lesion could be achieved. In the light of all the animal and human data on blood clearance currently available, however, the 3–4 hr scan-delay time seems longer than necessary. It is generally accepted that only a small fraction of a bone-seeker remains in the blood after one hour (*1–4*). Accordingly a clinical review of a number of recent scans was undertaken to determine whether bone-scan quality is improved significantly by extending the scan-delay time beyond 2 hr.

MATERIALS AND METHODS

A wide spectrum of SDTs had occurred inadvertently as a result of heavy workloads. This made it possible for us to carry out a retrospective analysis of bone-scan quality in 280 consecutive unselected patient studies performed with rectilinear scanners and scintillation cameras. The adult dose of 20 mCi of technetium-99m Sn-diphosphonate,* had been used for all studies performed during this 2-month period (*5*). The radiopharmaceutical was prepared in the same manner daily and was monitored by chromatographic analysis (silica gel–methanol extraction) of each vial prepared for dosing. Four-fifths of the studies were performed on a dual-detector scanner† with 5-in. focusing collimators, at an information density of 500 counts per cm^2 and with 10–15% background substraction but no enhancement. The remainder were on two commercial Anger cameras‡,|| both with parallel-hole collimation, obtaining 300,000–500,000 counts per image. Imaging in our clinical facility is performed using standardized protocols that tend to minimize the variability of technical factors that can alter scan quality.

For assessment of quality, the cases were randomly placed, 40 at a time, on an alternator viewer, without any indication of the scan-delay time. Two experienced observers independently scored the quality of the studies on a sliding scale of one to five, with one considered the best, five the worst, and three average. Normal bone definition, abnormal-to-normal bone contrast, and the level of background activity were the principal grading criteria (Fig. 1).

RESULTS

For the purpose of this analysis, the scans were separated into four groups, with Group 1 containing studies performed less than 2 hr after administration

Received Oct. 18, 1976; revision accepted Feb. 23, 1977.

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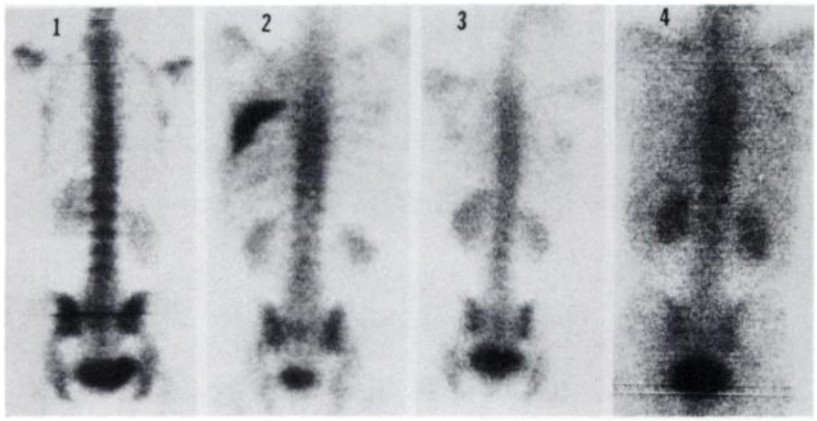

FIG. 1. Posterior bone scans in four patients. Numbers indicate quality rating given to each study. Image 1 shows excellent bone definition; excellent bone-to-background contrast. Image 2 shows bone definition and bone-to-background contrast still recognizable. Image 3 shows bone definition recognizable but lost in some areas; background activity masking ribs. Image 4 shows poor bone definition; many bones masked by background activity.

TABLE 1. BONE-SCAN QUALITY ANALYSIS

Time from agent administration to imaging in relation to patient population

Group	Time after administration, and average time		Average age (yr)	Sex distribution (%)		Age average (yr)	
				female	male	female	male
1	2 hr or less	(1 hr, 50 min)	52.5	53.6	46.4	52.8	52.2
2	2–2.5 hr	(2 hr, 15 min)	55.5	63.2	36.8	55.6	55.3
3	2.5–3.5 hr	(3 hr, 0 min)	58.4	54.2	45.8	53.3	64.3
4	Over 3 hr	(4 hr, 20 min)	55.1	50.0	50.0	54.7	55.5

of the radiopharmaceutical, Group 2 with scan-delay time of 2–2.5 hr, Group 3 delaying 2.5–3.5 hr, and Group 4 covering delays longer than 3.5 hr. Table 1 shows the distribution of patients in each group as to sex and age, and indicates the average interval between intravenous injection and start of imaging.

Table 2 presents an analysis of the grades assigned by the two observers, with the resultant means and standard deviations that each observer achieved for the four groups of scans. Student t test of validity is presented in Table 3. The data suggest that no appreciable improvement in bone-scan quality is evident when the scan-delay time is longer than 2 hr.

DISCUSSION

In bone imaging with technetium-labeled compounds, there is a trade-off between the greatest obtainable target-to-nontarget ratios on the one hand, and rapidly falling count rates on the other, due to the 6-hr half-life of technetium-99m. The blood and urine clearance rates of the various Tc-labeled bone agents (polyphosphate, pyrophosphate, and diphosphonate) are such as to indicate that imaging can be performed at about 2 hr after injection (*1–4*).

Approximately 50% of injected Tc-99m diphosphonate is cleared into the urine by the end of 2 hr, with an additional 25% cleared by the kidney over the next 4 hr, and there is a concomitant drop in technetium-99m blood levels in normal volunteers (*1*). The same article also reports that there is a

TABLE 2. SCAN-DELAY TIME VS. BONE-SCAN QUALITY

Group	Time after administration (hr) and No. of cases (280)		Scan quality, mean and s.d. (±)	
			Observer 1	Observer 2
1	2 or less	(56)	2.93 (0.87)	2.82 (0.94)
2	2–2.5	(76)	3.06 (0.68)	3.03 (0.83)
3	2.5–3.5	(96)	2.90 (0.66)	3.01 (0.75)
4	Over 3.5	(52)	2.88 (0.78)	2.83 (0.94)

TABLE 3. BONE-SCAN QUALITY ANALYSIS

Student t Test

Groups	Observer 1	Observer 2
1–2	$0.1 < p < 0.5$	$0.1 < p < 0.5$
2–3	$p > 0.5$	$0.1 < p < 0.5$
1–4	$p > 0.5$	$p > 0.5$
2–3	$0.1 < p < 0.5$	$p > 0.5$
2–4	$0.1 < p < 0.5$	$0.1 < p < 0.5$
3–4	$p > 0.5$	$0.1 < p < 0.5$

TABLE 4. BLOOD LEVELS OF Tc-99m DIPHOSPHONATE (HUMAN VOLUNTEERS AND PATIENTS)

Time after injection (min)	% of dose Mass. Gen. Hosp. NV	NP	AP	Subramanian, et al. (1) NV*
5	24.90 ± 6.73	21.23 ± 6.84	16.86 ± 6.39	45.4 ± 10.4
60	8.43 ± 2.57	6.74 ± 2.08	5.99 ± 3.22	12.4 ± 1.8

NV: Five normal volunteers; NP: 23 patients with normal bone scans; and AP: 13 patients with abnormal bone scans.
* Six normal volunteers.

70% drop in blood concentration (from 7 to 2%) in normal human volunteers between 2 and 6 hr. Similar results in human volunteers have been found in our laboratory (*2*, and Table 4), but the absolute blood levels were lower than those reported by Subramanian, et al. (*1*). The data in Table 4 also show that blood clearance appears to be faster in patients with abnormal positive bone scans (metastases, Paget's disease, etc.) than in patients and volunteers with normal bone scans (*2*).

Table 3 reveals that in this series no significant qualitative differences could be detected in the bone scans performed at times from slightly less than 2 hr to as great as 5 hr after the tracer injection. As in any nuclear medical clinic, there was great variability in the quality of the bone images on any one day, even though patients were dosed from the same vial of radiopharmaceutical. That may be attributed in part to the variable metabolic states of the skeletal system in hospitalized and ambulatory patients, the variable attenuation by various thicknesses of soft tissue between the skeleton and detector, and uncertain factors (e.g., medication and disease) within the patient population which might affect the kinetics of the radiopharmaceutical. In this series, no patient exhibited thyroid, gastric, or hepatic concentration of radioactivity, and the tracer had similar chromatographic characteristics from day to day, with labeling consistently greater than 95%.

In vivo qualitative measurements of the ratio of bone to soft tissue were made by Weber and coworkers using Tc-99m pyrophosphate (*3*). The ratio of normal bone to soft tissue increased slightly from 2 to 6 hr, but no significant temporal increase was noted in the ratio of abnormal bone to soft tissue. In a later report, the same laboratory reported that no additional lesions are found in patients with metastatic bone disease imaged sequentially at 2 and 6 hr (*4*).

Polyphosphate, pyrophosphate, and diphosphonate all have generally similar clearance rates from blood, urine, and body, although most investigators find the diphosphonates clearing slightly faster. The instructions for use of the various marketed products vary in their suggestions for scan-delay time. On the basis of our results with a Tc Sn-diphosphonate imaging agent, we now start all bone imaging as early as 2 hr after injection. Our results indicate that hospitals with heavy patient schedules for bone scanning can image the average patient (those who are not obese, or with impaired renal function, etc.) 2 hr after injection without any appreciable loss in scan quality in terms of decreased skeletal visualization or higher levels of soft-tissue background.

FOOTNOTES

* Procter & Gamble Osteoscan (stabilized).
† Ohio-Nuclear Model 84.
‡ Ohio-Nuclear Model 100.
|| Large-Field-of-View Searle Radiographics Camera.

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