# Relative Lesion Detection Ability of Tc-99m HMDP and Tc-99m MDP: Concise Communication

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**To compare the efficacy of Tc-99m HMDP and Tc-99m MDP to define skeletal lesions, 28 adult patients were examined in a double-blind, randomized, crossover study. Each patient was imaged with both agents over a period of 7–14 days. Both quantitative and qualitative evaluations were performed on the resulting images. Both agents detected the same number of skeletal lesions, and the number of lesions detected was the same whether the imaging was performed 2 or 4 hr after injection. Relative uptake of the tracer in the lesion relative to normal bone was also the same for both agents. Lesions were easier to see at 4 hr after injection than at 2 hr, presumably because soft-tissue levels were lower. Retention of tracer in bone compared with soft tissue was greater, and image quality was judged to be better, with Tc-99m HMDP than with Tc-99m MDP.**

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Skeletal imaging agents are used primarily to detect skeletal lesions. However, considerable emphasis is placed on obtaining images that are of excellent overall quality (*1*). Pharmaceutical manufacturers have developed agents with high skeletal uptake and rapid soft-tissue clearance to provide the users with the high-quality images they desire (*2*). Fogelman has been critical of the trend toward agents with higher skeletal uptake because of the potential this provides for masking lesions (*3*). He has also reported (*4*) that the newest skeletal image agent, based on HMDP, has a 21% higher skeletal retention than MDP. The present study was conducted to compare the qualities of images produced with MDP and HMDP and to determine whether the higher skeletal uptake of HMDP interferes with its ability to detect skeletal lesions.

## METHODS

**Study design.** This was a controlled, double-blind, crossover study in adult patients who had or were suspected of having skeletal metastases. After obtaining written informed consent, patients were enrolled in the study and were randomly assigned to be imaged with either Tc-99m HMDP or Tc-99m MDP. Approximately 90 min after injection, the imaging procedure was initiated and images of the skeleton were obtained over a period of about 1 hr.

Approximately 3½ hr after injection of the imaging agent, a second imaging procedure was started. After these procedures were completed, quantitative evaluation of the images was performed to obtain ratios for normal bone-to-soft tissue and lesion-to-normal bone in those patients with skeletal metastases. Patients whose skeletal images were read as normal were removed from the study, and their data were not included for analysis. Patients whose skeletal images suggested the presence of metastases returned to the nuclear medicine department 7–14 days later and received a second injection of imaging agent. If the agent used in the first imaging procedure was Tc-99m HMDP, the agent used in the second was Tc-99m MDP, and vice versa. The same procedures used to evaluate images were followed after the second imaging. No new drug therapy or changes in

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drug therapy that could influence the biodistribution of the imaging agents were instituted during the interval between imaging procedures.

**Preparation of imaging agent.** Both agents used in this study were prepared by reconstituting commercial kits with 50 ± 5 mCi Tc-99m per vial. A standard dose of 15–20 mCi was used for all imaging procedures. All doses were drawn up and injected within 45 min of reconstitution. All kits of MDP and HMDP were from the same manufacturer's lot. Vials were checked by TLC after preparation and before administration of imaging agent, and were found to be satisfactorily tagged (>98%).

**Image evaluation.** Skeletal images were recorded on radiographic film, and selected views were also stored in computer memory. After acquisition, quantitative evaluation was performed to obtain the following ratios: femur-to-thigh muscle (F/M), lumbar spine-to-muscle (LS/M), and lesion-to-contralateral or adjacent normal bone (L/M). The F/M ratio was obtained by determining the gross count rate per pixel over the femur and adjacent muscle tissue. The same procedure was used for the LS/N ratio with the muscle count rate being determined in the soft tissues between the kidney and pelvis. These ratios were determined for both the 2- and 4-hr images with both agents and, when possible, L/N was usually obtained from more than one site per patient. Additionally, the number of lesions detected in each image was determined. When the lesions were too numerous to count, the images were inspected to determine whether any lesions were observed with one agent and not with the other.

Qualitative image evaluation was performed at the end of the study. In these evaluations both the 2-hr and 4-hr images of each patient with both agents were placed on a view box. All images lacked any identification with respect to imaging agent used, time from injection to imaging, and patient name. Physician graders then assigned a numerical value to each image with respect to overall image quality and ease of visualization of areas of altered osteogenesis. The details of the grading system are given elsewhere (*6*).

**Statistical analysis.** Each outcome was analyzed according to the statistical method for crossover designs presented by Grizzle (*7*), Koch (*8*), and Taulbee (*9*), using a two-sided, 5% level of significance.

**TABLE 1. RESULTS OF QUANTITATIVE LESION COUNTING EVALUATION**

| Imaging time (hr after injection) | Number of patients | Number of lesions detected per patient | |
|---|---|---|---|
| | | HMDP | MDP |
| 2 | 10 | 9.8 | 9.8 |
| 4 | 10 | 10.4 | 10.8 |

**TABLE 2. RATIO OF TRACER UPTAKE IN LESION COMPARED WITH CONTRALATERAL NORMAL BONE (L/N)**

| Imaging time (hr after injection) | Number of patients evaluated | L/N | |
|---|---|---|---|
| | | HMDP | MDP |
| 2 | 26 | 1.91 ± 0.09 | 1.93 ± 0.09 |
| 4 | 26 | 1.99 ± 0.11 | 2.04 ± 0.13 |

## RESULTS

A total of 28 patients with skeletal metastases were imaged with both Tc-99m HMDP and Tc-99m MDP in this study. The results for the number of lesions observed are given in Table 1. Lesions were counted on ten of the 28 sets of patient images acquired. There were no significant differences between HMDP and MDP in the number of lesions detected at either 2 or 4 hr after injection. Visual inspection of the images from the 18 patients who had lesions considered too numerous to count yielded results consistent with the quantitative counting evaluation.

A comparison of the relative lesion uptakes (L/N) of Tc-99m HMDP and Tc-99m MDP is given in Table 2. A total of 26 patients had these evaluations performed. In many cases ratios for several lesions were obtained on the same patient. Thus, the averages reported represent many more determinations of L/N than the number of patients evaluated. Analysis of the data fails to demonstrate any quantitative differences in the relative abilities of Tc-99m HMDP and Tc-99m MDP to detect lesions when imaging is performed at either 2 hr or 4 hr after injection. Additionally, the L/N ratios do not change significantly between the 2- and 4-hr scintigrams.

The results of the visual evaluation are given in Table 3. Whereas the L/N ratio is quantitative, the visual grading is subjective and integrates subjective variables, such as image quality and soft-tissue levels, into the ratings. The grading system uses a scale of 1 to 4 with 1 being the best visualization and 4 being the poorest. Consistent with the quantitative measurements, there

**TABLE 3. VISUAL GRADING OF LESION VISUALIZATION**

| Imaging time (hr after injection) | Number of patients evaluated | Rating (1 = excellent, 4 = poor) | |
|---|---|---|---|
| | | HMDP | MDP |
| 2 | 28 | 2.15 ± 0.15 | 2.29 ± 0.15 |
| 4 | 28 | 1.86 ± 0.12 | 1.75 ± 0.12 |

**TABLE 4. BONE-TO-SOFT-TISSUE RATIOS**

| Imaging time (hr after injection) | Number of patients evaluated | Bone-to-soft-tissue ratios | | | |
|---|---|---|---|---|---|
| | | Femur | | Lumbar spine | |
| | | HMDP | MDP | HMDP | MDP |
| 2 | 25 | 2.34* ± 0.19 | 2.09 ± 0.16 | 4.61 ± 0.43 | 4.68 ± 0.49 |
| 4 | 12 | 2.71† ± 0.33 | 2.35 ± 0.22 | 5.68‡ ± 0.68 | 4.58 ± 0.48 |

* $p < 0.002$ by paired t-test, compared with MDP at 2 hr.
† $p < 0.07$ by paired t-test, compared with MDP at 4 hr.
‡ $p < 0.01$ by paired t-test, compared with MDP at 4 hr.

are no significant differences between Tc-99m HMDP and Tc-99m MDP in their abilities to delineate lesions when imaging is performed at either 2 hr or 4 hr after injection. However, the average grades for both agents are lower at 4 hr than at 2 hr. Because the quantitative study showed no differences in L/N between the 2-hr and 4-hr images, the visual ratings suggest that the overall quality of the images was influencing the grader's sense of lesion visibility.

Both subjective and objective assessments of image quality were performed for all images obtained. The objective assessment of image quality was the ratio of uptake in the skeleton compared with retention in soft tissue. Table 4 gives the ratios for bone-to-soft tissue (B/ST) in images at 2 and 4 hr after injection. This measurement of contrast gives higher B/ST for Tc-99m HMDP than for Tc-99m MHDP. Unlike the lesion-to-normal-bone ratios, the bone-to-soft-tissue ratios are better at 4 hr after injection than at 2 hr.

The results of the subjective assessment of image quality are given in Table 5. Here the 2-hr Tc-99m HMDP images were judged to be of better quality than those with Tc-99m MDP. The quantitative contrast differences observed at 4 hr (Table 4) were not detected by this subjective evaluation.

## DISCUSSION

Actual counting of lesions and quantitative determination of relative tracer activity in lesions (L/N) demonstrates that there are no significant differences in the definition of lesions with Tc-99m HMDP and Tc-99m MDP. Since Tc-99m HMDP has been shown to have a 21% greater retention in the skeleton than Tc-99m MDP (*4*), we conclude that increased skeletal retention does not have an adverse effect on lesion detection.

The visual grading gives similar results: no significant differences regarding lesion visualization. However, the visual grading shows that lesions are easier to see with either agent at 4 hr after injection than at 2 hr. Since the L/N ratio shows no difference between 2 and 4 hr, this suggests that the higher soft-tissue background in 2-hr images interferes with the visual evaluation of the image, or that graders prefer to view images of better quality and thus grade the lesions as better visualized. This seems to justify the physicians' desire to produce the best-quality image for evaluating patient status. Quantitative evaluation of the distribution of Tc-99m HMDP and Tc-99m MDP (B/ST) are consistent with previously reported data (*6,10*). The higher skeletal retention of Tc-99m HMDP results in higher B/ST at 4 hr in both the lumbar spine and femur, and in the femur at 2 hr. Visual evaluation of the images is more subjective, and statistically significant differences in image quality are observed only at 2 hr after injection.

**TABLE 5. IMAGE QUALITY EVALUATION**

| Imaging time (hr after-injection) | Number of patients evaluated | Image quality grade (1 = excellent, 8 = poor) | |
|---|---|---|---|
| | | HMDP | MDP |
| 2 | 28 | 2.78* ± 0.11 | 3.11 ± 0.14 |
| 4 | 28 | 2.37 ± 0.16 | 2.29 ± 0.16 |

* $p < 0.05$, t-test compared with MDP at 2 hr.

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All letters and applications should be addressed to:

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