

Breast parenchymal activity on scintimammography: Comparison between bone-seeking agents and ^{99m}Tc -sestamibi

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The aim of this study was to evaluate breast parenchymal activity on scintimammography with bone-seeking agents and ^{99m}Tc -MIBI. Scintimammography was performed with bone-seeking agents in 61 patients and with ^{99m}Tc -MIBI in 33 patients. Activity in the breast parenchyma contralateral to the suspected lesion was visually assessed by two independent observers. Increased breast parenchymal activity was shown in 19 of 61 patients examined with bone-seeking agents, while it was demonstrated in only two of 33 patients examined with ^{99m}Tc -MIBI. Breast parenchymal activity of bone-seeking agents was higher in patients aged 50 years or younger than in those older than 50. Increased parenchymal activity of bone-seeking agents may disturb visualization of primary breast cancer especially in relatively young patients. Low parenchymal activity is suggested to be a favorable characteristic of ^{99m}Tc -MIBI as a scintimammographic agent.

Key words: scintimammography, breast parenchyma, ^{99m}Tc -sestamibi, ^{99m}Tc -MDP

INTRODUCTION

SCINTIMAMMOGRAPHY is a nuclear medicine procedure that is of increasing interest. Various radiotracers have been employed as agents for scintimammography.¹ Among them, ^{99m}Tc -sestamibi (MIBI) is the most common agent in imaging primary breast cancer, and favorable diagnostic accuracy has been described for scintimammography with ^{99m}Tc -MIBI.²⁻⁹

Piccolo et al. reported that primary breast cancer was successfully depicted on images obtained soon after the administration of ^{99m}Tc -methylene diphosphonate (MDP), a bone-seeking agent.¹⁰ Breast cancer tends to metastasize to the skeletal system, and bone scintigraphy is often performed in patients with breast cancer to evaluate metastatic skeletal lesions. Scintimammography with ^{99m}Tc -MDP can be performed as an adjunct to bone scintigraphy

and may provide convenience in managing patients with breast cancer.

Breast cancer is delineated as a focal area of increased radioactivity on scintimammography, and high lesion-to-background contrast is required to clearly visualize a breast lesion. In addition to high radioactivity in breast cancer, low breast parenchymal activity is characteristic of optimal scintimammographic agents. In this study, we evaluated breast parenchymal activity on scintimammography with ^{99m}Tc -MIBI and bone-seeking agents.

MATERIALS AND METHODS

Subjects

Ninety-two women suspected of having breast cancer underwent scintimammography. The radiotracers used were ^{99m}Tc -MIBI and two bone-seeking agents, ^{99m}Tc -MDP and ^{99m}Tc -hydroxymethylene diphosphonate (^{99m}Tc -HMDP). Forty patients (age range 26-81 years; mean age 54.7 years) were studied with ^{99m}Tc -MDP, 21 patients (age range 34-76 years; mean age 54.5 years) with ^{99m}Tc -HMDP and 33 patients (age range 26-82 years; mean age 57.4 years) with ^{99m}Tc -MIBI. Two

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patients underwent examinations with ^{99m}Tc -MDP and ^{99m}Tc -MIBI. Consequently, 94 examinations were performed. No patient received hormonal medication prior to the examination. None of them had previous breast surgery or previous irradiation of the breast. Patients with bilateral breast lesions were excluded.

Table 1 Breast activity and tracer

Tracer	Breast activity			Total
	Grade 0	Grade 1	Grade 2	
MDP	30	6	4	40
HMDP	12	6	3	21
MIBI	31	2	0	33

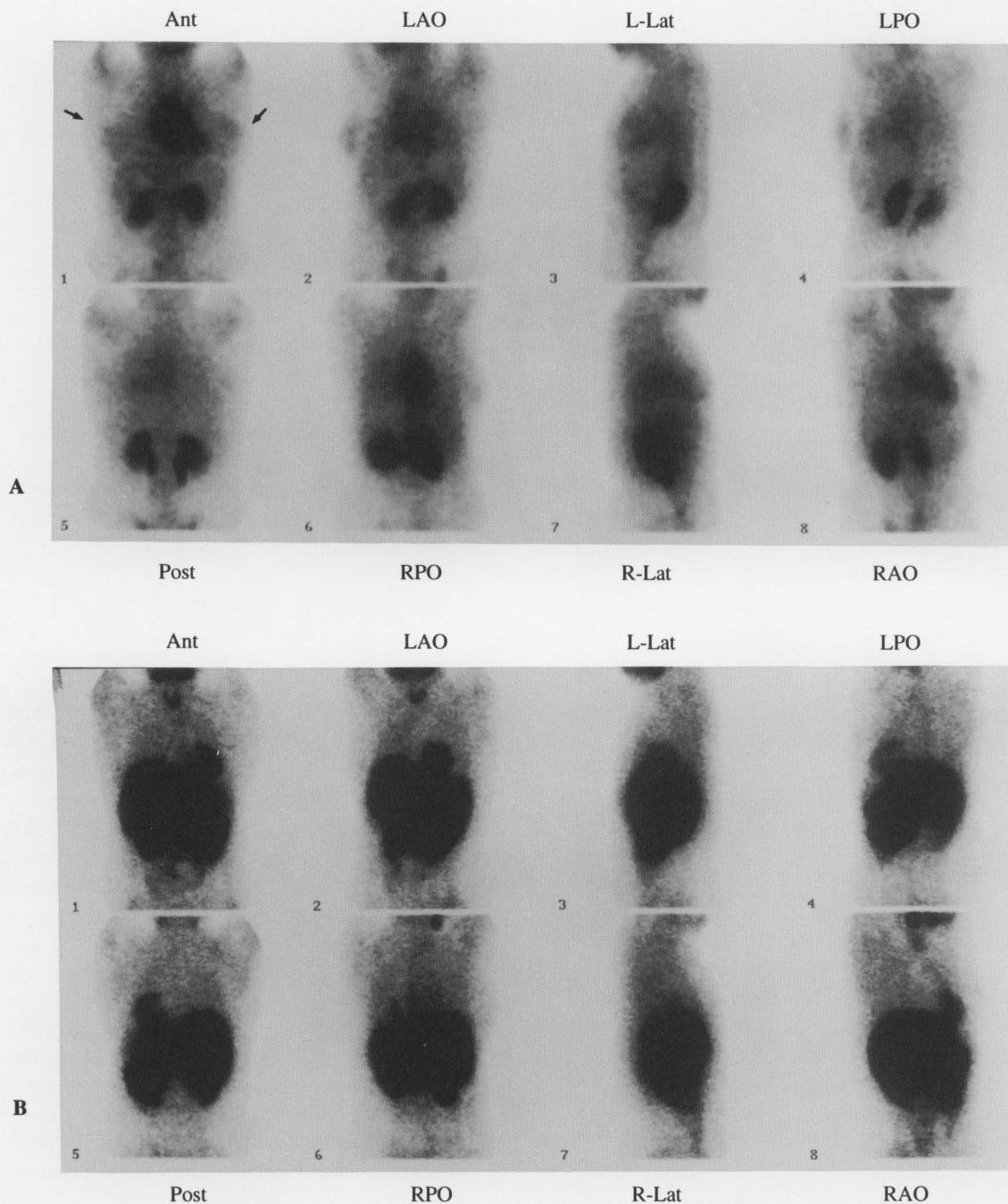


Fig. 1 A 26-year-old woman with left breast cancer. A. Scintimammography with ^{99m}Tc -MDP. Breast activity is elevated bilaterally (arrows), and was judged as grade 2. B. Scintimammography with ^{99m}Tc -MIBI. Increased breast parenchymal activity is not shown (grade 0).

Table 2 Age and breast activity of bone-seeking agents

Age (years)	Breast activity			Total
	Grade 0	Grade 1	Grade 2	
≤ 50	14	7	7	28
> 50	28	5	0	33

Imaging procedures

In scintimammography with ^{99m}Tc -MDP or ^{99m}Tc -HMDP, the injected dose was 740 MBq. SPECT of the chest was performed 5 min after the injection of a radiotracer. Sixty-four views over 360 degrees were acquired in a step mode at 15 sec per view. In patients studied with ^{99m}Tc -MIBI, SPECT was performed 15 min after the administration of 600 MBq of tracer. Sixty-four views were acquired at 30 sec per view. A single-head rotating gamma camera (RC-1500I, Hitachi) equipped with a low-energy high-resolution collimator interfaced to a minicomputer (RW-3000, Hitachi) was used. Data were obtained with the patients in the supine position.

Data analysis

Every two projection images were added together, and breast parenchymal activity was evaluated by visual inspection of the reframed images. Activity in the breast parenchyma contralateral to the suspected lesion was compared with activity in the adjacent chest wall, and was classified into three grades: grade 0 (equal to activity in the chest wall), grade 1 (mildly higher than chest wall activity), and grade 2 (definitely higher than chest wall activity). Visual interpretation was carried out independently by two radiologists (Y.I. and N.K.), and discrepancies were resolved by consensus between them. They were informed of the side of the lesion and blinded to the other information.

RESULTS

Breast activity of grade 1 or 2 was shown in 10 of 40 studies (25.0%) with ^{99m}Tc -MDP and in nine of 21 studies (42.9%) with ^{99m}Tc -HMDP (Table 1). On scintimammography with ^{99m}Tc -MIBI, breast activity was judged as grade 1 in two of 33 studies (6.1%) and as grade 0 in the remaining studies. Increased breast activity (grade 1 or 2) was less frequent with ^{99m}Tc -MIBI than with ^{99m}Tc -MDP ($p < 0.05$, chi-square test) or with ^{99m}Tc -HMDP ($p < 0.01$) (Fig. 1). Frequency of increased breast activity was not significantly different between ^{99m}Tc -MDP and ^{99m}Tc -HMDP ($p > 0.05$).

The relation between age and the breast parenchymal activity of bone-seeking agents is presented in Table 2. Breast activity of grade 1 or 2 was observed in 14 of 28 patients (50.0%) aged 50 years or younger and in five of 33 patients (15.2%) older than 50. Breast activity of grade 2 was demonstrated in seven of 28 patients (25.0%) aged

50 years or younger but in no patients older than 50. Increased breast activity of bone-seeking agents was less frequent in patients older than 50 years than those aged 50 years or younger ($p < 0.01$).

DISCUSSION

In this study, breast parenchymal activity was frequently high on scintimammography with bone-seeking agents. Increased parenchymal activity may disturb visualization of activity in primary breast cancer, and appears to constitute a drawback of this technique. Breast parenchymal activity was more prominent in patients aged 50 years or younger than in those older than 50. Although the actual effect of parenchymal activity on diagnostic ability remains to be evaluated, scintimammography with bone-seeking agents may be insensitive to breast cancer especially in relatively young patients.

Images are obtained in scintimammography with bone-seeking agents soon after the intravenous administration of a radiotracer,¹⁰ and appear to reflect mainly the distribution of the blood pool. Breast cancer is delineated as an area of increased radioactivity, probably because of its hypervascularity. Increased activity in breast parenchyma is considered to indicate high vascularity, and the result of this study suggests that high vascularity of normal breast parenchyma is not uncommon. The breast undergoes involutional changes with age.¹¹ Involution appears to decrease the blood pool in the breast and, consequently, breast parenchymal activity soon after the injection of bone-seeking agents.

High parenchymal enhancement has been found on dynamic contrast-enhanced magnetic resonance (MR) imaging of the breast.^{12,13} Contrast-enhancing foci may mimic breast cancer, and constitute a possible cause of false-positive findings.¹² High enhancement early after the injection of contrast material should reflect high vascularity. Patients older than 50 years have been shown to yield lower parenchymal enhancement than patients aged 35–50,¹³ consistent with our results for scintimammography with bone-seeking agents. A significant effect of the menstrual cycle on parenchymal enhancement has also been demonstrated in MR imaging of premenopausal subjects, and lower enhancement has been shown in the second and third weeks of the menstrual cycle.^{12,13} In the present study, the timing of the examination in the menstrual cycle was not taken into consideration. Scintimammography with bone-seeking agents performed in the second or third week may show low parenchymal activity and have high sensitivity to primary breast cancer. The relation between breast parenchymal activity and the menstrual cycle is a problem for future investigation.

Increased breast parenchymal activity was noted in only two of 33 patients who underwent scintimammography with ^{99m}Tc -MIBI. In the present study, parenchymal activity was assessed on projection images of SPECT,

which are obviously inferior in quality to usual static images. On SPECT images reconstructed with filtered backprojection, counts in the breast are inhomogeneous and visualization of the breast is sometimes distorted by artifacts due to high activity areas such as the heart.¹⁴ Classification of breast parenchymal activity on reconstructed images appeared to be unreliable, and projection images were used for analysis. Faint breast activity may have been missed because of the poor quality of projection images, and breast parenchymal activity may have been underestimated. However, it is strongly indicated that parenchymal activity is lower with ^{99m}Tc-MIBI than with bone-seeking agents.

It was demonstrated by *in vitro* studies that ^{99m}Tc-MIBI is retained in tumor cell lines to a much greater extent than in normal cell lines, and *in vivo* uptake of ^{99m}Tc-MIBI in the tumor is suggested to be associated with mitochondrial and plasma membrane potentials and cellular mitochondrial content in addition to regional blood flow.¹⁵⁻¹⁷ ^{99m}Tc-MIBI is considered to be a good marker of viable tumor tissue, and appears to be retained less efficiently in normal breast parenchyma than in breast cancer. It is inferred that increased vascular bed and increased blood flow in normal parenchyma causes increased delivery of ^{99m}Tc-MIBI to the tissue but does not necessarily induce high uptake because of the low retention efficiency. The low breast parenchymal activity of ^{99m}Tc-MIBI may aid in clearly delineating primary breast cancer, and appears to be a favorable characteristic of ^{99m}Tc-MIBI as a scintimammographic agent. ^{99m}Tc-MIBI may be used to assess breast cancer irrespective of age and the menstrual cycle.

In summary, we examined breast parenchymal activity in scintimammography with bone-seeking agents and ^{99m}Tc-MIBI. Increased parenchymal activity of bone-seeking agents was noted especially in patients aged 50 years or younger, and appeared to be a possible factor in reducing sensitivity to primary breast cancer. The activity of ^{99m}Tc-MIBI was low in breast parenchyma, supporting that ^{99m}Tc-MIBI is an excellent scintimammographic agent. The diagnostic ability of scintimammography depends on radioactivity in malignant and benign lesions in addition to breast parenchymal activity, and a comparative study should be conducted to determine whether ^{99m}Tc-MIBI is really preferable to bone-seeking agents as a tracer for scintimammography.

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