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Tissue-Specific Effects on Uptake of ^{99m}Tc-Sestamibi by Breast Lesions: A Targeted Analysis of False Scintigraphic Diagnoses

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The limited spatial resolution of γ-cameras is commonly considered the main reason for the low sensitivity of scintimammography in the detection of small carcinomas. The present study assessed whether uptake of ^{99m}Tc-sestambi is affected by certain tissue-specific parameters besides the size of the tumor. **Methods:** Surgical specimens from 75 patients (30 benign lesions, 8 of which had shown false-positive scintigraphic findings, and 45 carcinomas, 8 of which had shown false-negative scintigraphic findings) were subjected to a distinct histopathologic/immunohistochemical reevaluation. Tissue-specific parameters (lesion size, cellular density, vascularity, signs of inflammation, proliferative activity, multidrug resistance expression, and receptor status) were visually scored and correlated with the sestamibi uptake on scintimammograms. **Results:** A clear relationship was found between sestamibi uptake and tumor size. As previously assumed, a lesion size of less than 1 cm in diameter was found to be one reason for false-negative scintigraphic diagnoses. In addition, a low cell count, low vascularity, and absence of inflammation in carcinomas had a negative effect on uptake of the radiopharmaceutical. The decisive factor for increased tracer uptake by benign lesions was the presence of inflammatory changes. No correlation could be found between sestamibi uptake and proliferative cellular activity, multidrug resistance expression, or the receptor status of the tumor. **Conclusion:** Because all mentioned findings were statistically significant only in part, it is to be supposed that uptake of ^{99m}Tc-sestambi by breast lesions is determined by various tissue parameters in interaction.

Key Words: scintimammography; breast cancer; ^{99m}Tc-sestambi; histopathology

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Despite promising initial results, scintimammography with ^{99m}Tc-sestambi has failed to establish a position in the routine clinical diagnosis of breast carcinoma. The sensitivity of the method in initial studies was reported to range from 84% to 96%, with a specificity of 86%–100% (*1–7*), but has undergone significant downward revision after publication of more recent, partially multicenter studies (*8–11*). For example, in the European multicenter study, the sensitivity of scintimammography was reported as 71%, with a specificity of 69% (*9*). Our own studies of selected patients with unclear mammographic findings or suggestive microcalcifications have revealed a sensitivity of 62% and 63%, respectively, and a specificity of 83% and 85%, respectively (*8,10*). All studies have identified a correlation between sensitivity and the diameter of the tumor.

Explanations for the limitations of scintimammography may include the assumption that, whereas carcinomas do in fact show increased uptake of the radiopharmaceutical, technical limitations of the camera prevent the delineation of small tumors on the scintigram. On the other hand, the possibility must be considered that carcinomas not recognized at scintigraphy may show no or only slight uptake of the radiopharmaceutical and thus escape detection.

Based on these considerations, the objective of the present study was to assess whether uptake of ^{99m}Tc-sestambi is affected by tissue-specific parameters besides tumor size. A correlation between uptake and given histopathologic characteristics could then be proposed as an explanation for absence of ^{99m}Tc-sestambi uptake by malignant tumors or for increased uptake by benign lesions and thus explain false-negative or false-positive scintigraphic findings.

MATERIALS AND METHODS

To correlate uptake with certain tissue-specific parameters, we retrospectively selected 75 patients and subjected their surgical specimens to a distinct histologic reevaluation. Included in the study were patients whose planar scintigrams showed pathologic patterns of increased tracer uptake ($n = 45$), including 8 patients for whom suggestive increased uptake failed to receive histopathologic confirmation of malignancy. In addition, we selected patients for whom histopathology revealed malignant tissue despite unremarkable scintigraphic findings ($n = 8$). Finally, 22 patients were

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included for whom neither histopathology nor scintigraphy raised suspicion of malignant disease.

Specimens obtained surgically were fixed for histologic examination in buffered formalin and embedded in paraffin. These included 30 benign processes (19 cases of fibrocystic disease, 7 fibroadenomas, 2 cases of chronic mastitis, and 2 cases of papillomatosis) and 45 malignant lesions (8 DCIS, 29 ductal invasive tumors, and 8 lobular invasive tumors).

Scintigraphy

Scintimammography was performed according to the standard protocol with the patient lying prone. We used either a double- or a triple-head camera (PRISM 2000 or 3000; Picker International). Anterior and lateral planar images were acquired 5 min after intravenous injection of 740 MBq of ^{99m}Tc-sestambi, with an acquisition time of 10 min each. When the double-head camera was used for lateral views, images of both breasts could be acquired simultaneously. To avoid possible scatter originating from the opposite breast, we did not use a lead shield. For all patients, an imaging matrix of 256 × 256 pixels and a zoom factor of 1.1–1.6 were chosen. A low-energy high-resolution collimator was used.

The uptake pattern of ^{99m}Tc-sestambi was assessed visually on the lateral images and assigned to 1 of 2 categories. The first category included normal or slight, diffuse ^{99m}Tc-sestambi uptake and was considered to represent a benign situation; the second category included focal or significant, confluent unilateral increased uptake and was considered suggestive of malignancy. The histopathologic diagnoses of the enrolled patient population in relation to the scintimammographic uptake pattern are given in Table 1.

Histopathology/Immunohistochemistry

The paraffin blocks were sectioned into several slices with a thickness of 3 μm and mounted on a glass slide. The slides were stained by 2 methods (hematoxylin and eosin [HE] and van Gieson). HE staining assists with visualization of cells and cell components. Van Gieson staining (iron hematoxylin, picric acid, and acid fuchsin) particularly targets the connective tissue components of a specimen. In the next step, other slides were incubated with various antibodies (MIB-1, cluster designation [CD] 31, and multidrug resistance [MDR]-1). MIB antibody is a monoclonal antibody used primarily with immunohistochemical stains to identify actively proliferating cells. This identification results from the antibody's binding to the nuclear, proliferation-associated antigen Ki-67, which is expressed in all active phases of the cell cycle. The polyclonal MDR-1 antibody reacts with different peptides of the C-terminal, cytoplasmatic section of the P-glycoprotein (Pgp). The gene that codes for this protein sequence is the MDR-1 gene. Pgp is an intrinsic plasma membrane protein that is present in large numbers in tumor cells and that cross-reacts with numerous chemotherapeutic agents (e.g., vinblastine and doxorubicin). Thus, accumulation of drugs in cells with MDR expression is diminished. It has been suggested that Pgp acts as an energy-dependent pump that transports from the cell various substances that have entered. Because the radiopharmaceutical ^{99m}Tc-sestambi is also a lipophilic and cationically charged molecule, questions may be raised about whether ^{99m}Tc-sestambi reacts in the same way with Pgp and whether this reaction affects the uptake pattern of ^{99m}Tc-sestambi in MDR-positive cells.

The sectioned and stained specimens were submitted to 2 independent pathologists for microscopic examination. The proportion of cells characteristic of the respective disease and the presence of inflammation were assessed visually from the HE- and van Gieson–stained specimens. Three categories were formed for assessing cell count (low, moderate, and high), and 3 for inflammation (none, slight/moderate, and significant). A lesion was considered of low cell count when microscopic examination at the highest degree of magnification (high-power field [HPF]) revealed a cellular content of less than 30%. A lesion was considered of high cell count when more than 60% of 1 HPF consisted of lesion-specific cells. Similarly, the MIB-1–stained specimens were evaluated on the basis of the proportion of actively proliferating cells (no or few cells, a moderate proportion, or a high proportion). In addition, the vascular status of the tissue specimen was evaluated and scored as slight (0–2 vessels per HPF), moderate (3–5 vessels per HPF), or high (5 vessels per HPF). After reaction with the MDR-1 antibody, expression of Pgp was reported as absent/slight, moderate, or high. Finally, the estrogen and progesterone receptor status was determined.

The tissue-specific characteristics of the specimens were then correlated with the scintigraphically determined tracer uptake by the lesion. Correlation was determined statistically using the χ^2 multifield test. Significance was assigned for values of $P < 0.05$. Because a sufficient quantity of specimen had not been preserved for some patients, not all histopathologic and immunohistochemical parameters could be determined for all patients.

TABLE 1
^{99m}Tc-Sestamibi Uptake in Relation to Histopathologic Diagnosis

Histopathologic diagnosis	^{99m}Tc-sestamibi uptake	
	Normal/slightly increased	Suggestive
Invasive ductal carcinoma	5	24
Invasive lobular carcinoma	1	7
DCIS	2	6
Fibroadenoma	3	4
Papilloma	2	—
Fibrocystic disease	17	2
Mastitis	—	2

RESULTS

Tumor Size

Specimens from 47 patients were adequate for evaluation. The diameter of malignant tumors ($n = 40$) ranged from 0.3 to 6.8 cm (mean, 2.1 cm), and the diameter of benign tumors (fibroadenomas, papillomas) ranged from 1.0 to 6.0 cm (mean, 2.3 cm). Small tumors less than 1 cm in diameter showed suggestive tracer uptake in 7 patients (4 with ductal invasive carcinoma and 3 with lobular carcinoma), whereas in 6 patients (1 with ductal carcinoma in situ [DCIS], 3 with ductal invasive carcinoma, and 2 with fibroadenoma), scintigraphy revealed either normal or slightly increased tracer uptake.

Tumors between 1 and 2 cm in diameter were associated with pathologic sestamibi uptake in 12 patients (1 with DCIS, 9 with ductal invasive carcinoma, 1 with lobular

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carcinoma, and 1 with fibroadenoma) and with normal tracer uptake in 3 patients (1 with ductal invasive carcinoma, 1 with lobular carcinoma, and 1 with papilloma). Tumors larger than 2 cm, however, showed pathologic tracer uptake in 18 patients (1 with DCIS, 11 with ductal invasive carcinoma, 3 with lobular carcinoma, and 3 with fibroadenoma) but unremarkable tracer uptake in only 1 patient (with ductal invasive carcinoma). A clear relationship is seen between uptake pattern and tumor size (Fig. 1). Three DCIS were recognized only on exceeding a diameter of 1.8 cm, because of a markedly increased, confluent tracer uptake. Regarding the stage of invasive tumors, carcinomas in stage pT1a,b (≤1 cm) were identified with a sensitivity of 70%. Carcinomas in stage pT1c (1–2 cm) showed pathologically increased tracer uptake in 83% of cases, whereas in the group with carcinomas staged higher than pT2, 93% of tumors were correctly diagnosed on the basis of focally increased tracer uptake. The 4 cases of benign diseases in which focal tracer uptake was incorrectly interpreted as suggestive of malignancy were all fibroadenomas larger than 1 cm in diameter (1.3, 2.4, 3, and 6 cm).

Cellular Density

The proportion of cells characteristic of the respective pathologic entity could be determined in 59 patients. We assessed whether normal and pathologic tracer uptake at scintigraphy correlated in a statistically significant fashion with patients' respective cell counts. The absolute distribution of data is given in Figure 2. In all 23 patients with normal or slightly increased uptake, histopathologic examination revealed a cell count < 60% (<30% in 19 patients and 30%–60% in 4 patients). In 20 patients, lesions were benign (14 cases of fibrocystic disease, 4 fibroadenomas, 2 papillomas); only 3 patients had ductal invasive carcinoma (Fig. 3). Conversely, in all cases of high cell count ($n = 12$; ductal invasive carcinoma in all cases), scintigraphy revealed pathologically increased tracer uptake (Fig. 4). The opposite assumption, namely, that high tracer uptake at scintigraphy is necessarily associated with a high cell count, was not confirmed however: Five lesions with significant tracer uptake (2 lesions from cases of ductal invasive carcinoma, 1 from lobular carcinoma, 1 from DCIS, and 1 from chronic mastitis) showed only a moderate number of characteristic cells (30%–60%), and 19 other lesions with suggestive tracer uptake (4 lesions from cases of ductal invasive carcinoma, 3 from lobular carcinoma, 5 from DCIS, 4 from fibroadenomas, 2 from fibrocystic disease, and 1 from mastitis) showed low cell counts. In 16 of 19 patients, changes were associated with moderate to high vascularity, and 7 lesions (including lesions from patients other than those 16) revealed moderate to significant inflammatory signs. One would expect the pattern of tracer uptake at

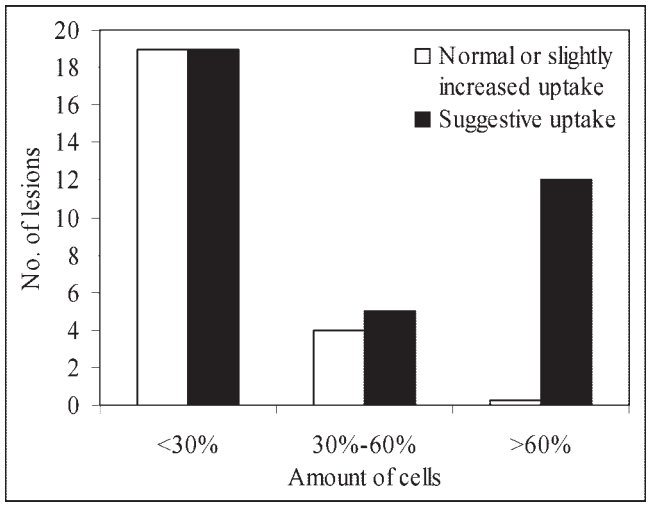


FIGURE 2. Sestamibi uptake by breast lesions in relation to cellular density.

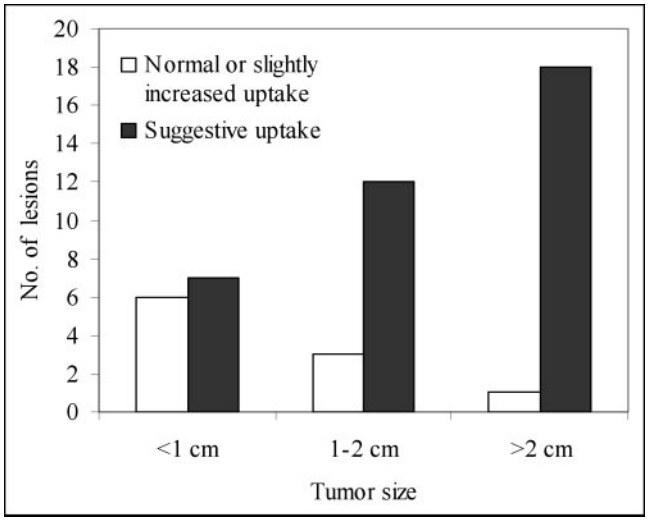


FIGURE 1. Sestamibi uptake by breast lesions in relation to tumor size.

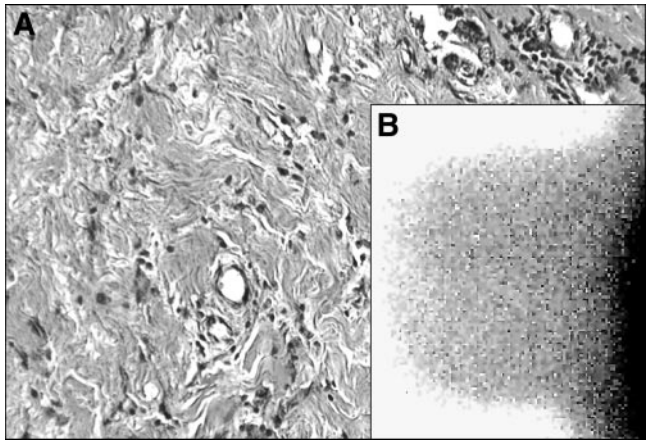


FIGURE 3. Ductal invasive carcinoma with a low cellular density. (A) HE-stained section shows a low proportion of carcinoma cells, compared with the surrounding connective tissue. (B) Scintimammography findings are false-negative, showing a normal and homogeneous distribution of the radiopharmaceutical.

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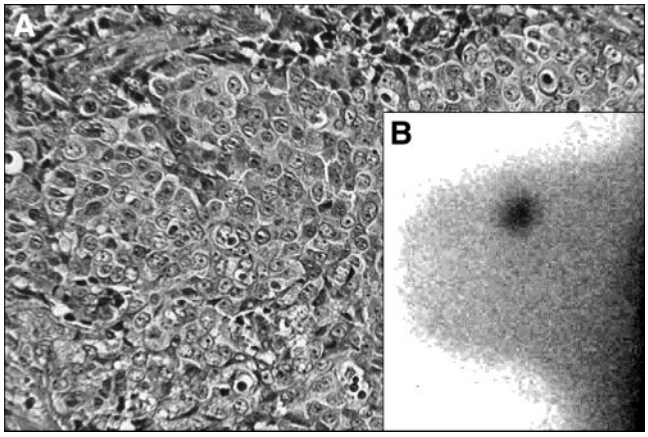


FIGURE 4. Ductal invasive carcinoma with a high cellular density. (A) HE-stained section shows a high proportion of carcinoma cells, compared with the surrounding connective tissue. (B) At scintigraphy, the carcinoma exhibited marked focal ^{99m}Tc-sestambi uptake.

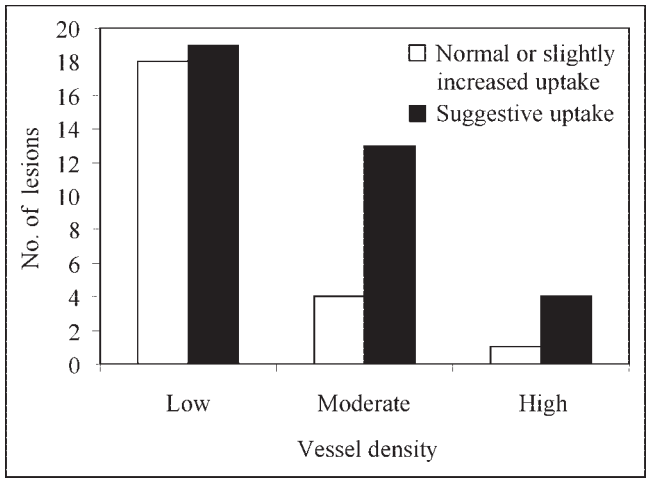


FIGURE 5. Sestamibi uptake by breast lesions in relation to vascularity.

scintigraphy to be affected, at least in part, by these changes. The χ^2 test revealed a significant difference between scintigraphically positive and negative lesions regarding their cell counts ($P < 0.05$). This difference is primarily due to the fact that all high-cell-count lesions showed increased ^{99m}Tc-sestambi uptake. Tracer uptake behavior did not differ significantly in the subgroup of patients whose lesions showed lower cell counts.

Vascularity/Angioneogenesis

A similar constellation was observed in the comparison between the number of vascular cross sections and ^{99m}Tc-sestamibi uptake ($n = 59$). Among patients in whom tracer uptake was interpreted as not suggestive of malignancy, 18 histologic specimens (12 of fibrocystic disease, 1 of fibroadenoma, 1 of papilloma, 3 of ductal invasive carcinoma, and 1 of DCIS) showed few vascular cross sections per HPF, 4 histologic specimens (2 of fibrocystic disease, 1 of fibroadenoma, and 1 of DCIS) showed a moderately increased number, and only 1 specimen (of papilloma) showed many (Fig. 5). Of cases in which increased uptake at scintigraphy was interpreted as suggestive of malignancy, 17 showed moderate to many vessels (8 cases of ductal invasive carcinoma, 1 of lobular carcinoma, 3 of DCIS, 1 of fibrocystic disease, 2 of fibroadenoma, and 2 of mastitis), whereas 19 showed only a few vessels (9 cases of ductal invasive carcinomas, 4 of lobular carcinoma, 3 of DCIS, 1 of fibrocystic disease, 1 of fibroadenoma, and 1 of mastitis). Lesions associated with normal or slightly increased tracer uptake tended to show fewer vascular cross sections; the differences, however, were statistically not significant. A correlation between vessel density and preoperative color duplex sonography results could not be performed, since color duplex sonography has not routinely been applied to the selected patient population.

Inflammation

In 22 of 23 lesions associated with normal scintigraphic findings or only slightly increased tracer uptake, histopathologic examination revealed no ($n = 16$) or only slight signs of inflammation (Fig. 6). In only 1 case (highly vascularized papilloma) were significant signs of inflammation present in the absence of increased ^{99m}Tc-sestambi uptake. In cases of significantly increased uptake ($n = 36$), the amount of inflammation was not uniform; 25 specimens showed no or only slight evidence of inflammation, whereas 11 specimens showed moderate ($n = 9$) or pronounced ($n = 2$) signs of inflammation. The constellation of significantly increased uptake coupled with moderate signs of inflammation was exhibited by 8 cases of carcinoma (2 of which were DCIS) and 1 of fibroadenoma. Two patients with significant ^{99m}Tc-sestambi uptake, and whose specimens were characterized by pronounced signs of inflammation, had chronic mastitis (Fig. 7). A comparison of lesions characterized by increased tracer uptake and lesions with normal scintigraphic findings

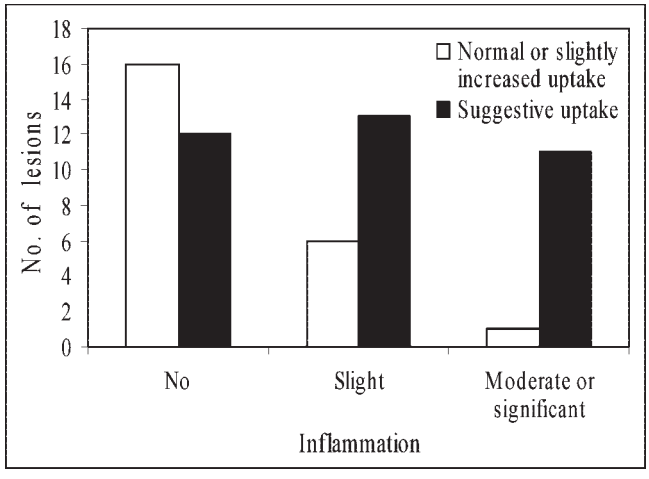


FIGURE 6. Sestamibi uptake by breast lesions in relation to inflammatory changes.

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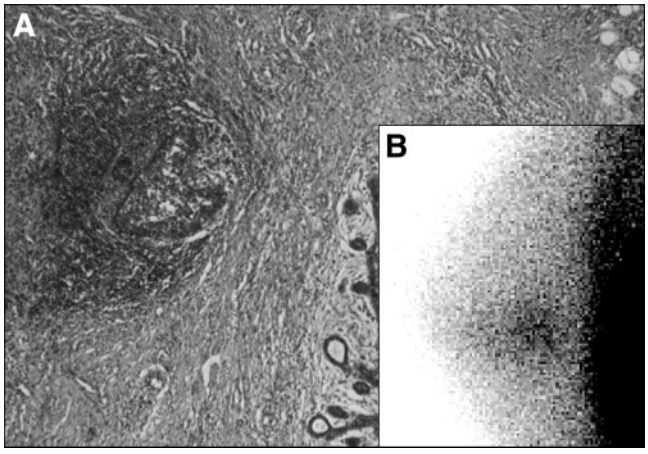


FIGURE 7. Chronic mastitis. (A) HE-stained section shows pronounced inflammatory components in the area of the milk ducts and surrounding connective tissue. (B) Scintimammography reveals significantly increased ^{99m}Tc-sestambi uptake, which is characteristic of malignancy.

for inflammation yielded statistically significant differences ($P < 0.05$). Thus, it would appear that besides the proportion of specific cells, the presence of inflammatory processes can produce an increased uptake of ^{99m}Tc-sestambi and could explain at least some of the false-positive findings.

Proliferative Activity

No statistically significant correlation was found between a high percentage of proliferating cells and high tracer uptake at scintigraphy. Only 8 of 32 patients with significant tracer uptake (7 with invasive carcinomas and 1 with fibroadenoma) showed a moderate to high proportion of MIB-1–positive cells, which corresponds to a high rate of proliferation. Twenty-four patients with no or only a slight rate of proliferation, however, did exhibit significant tracer uptake. In 13 of these patients, histologic examination revealed a high density of blood vessels. It can be assumed that the increased uptake of ^{99m}Tc-sestambi is due to the increased vascularization. Seventeen of 20 lesions with normal or only slightly increased ^{99m}Tc-sestambi uptake showed no or only a few MIB-1–positive cells. In no instance was highly active proliferation associated with normal ^{99m}Tc-sestambi uptake.

Receptor Status

No statistically significant correlation was found between patients' estrogen and progesterone receptor status and scintigraphic tracer uptake pattern. Among lesions exhibiting increased tracer uptake, positive receptor status for estrogen and progesterone was identified in 18 and 14, respectively, and negative receptor status in 16 and 20, respectively. Among lesions exhibiting normal or slight ^{99m}Tc-sestambi uptake, positive receptor status for estrogen and progesterone was identified in 5 and 2, respectively, and negative receptor status in 2 and 5, respectively.

MDR Status

Sixteen of 20 adequately sized preserved carcinoma specimens reacted positively to the MDR antibody. Fifteen of these specimens showed significantly increased ^{99m}Tc-sestambi uptake. The hypothesis that elimination of ^{99m}Tc-sestambi might be increased in cells exhibiting elevated expression of Pgp, as has been observed with certain chemotherapeutic agents, could not be confirmed by our data.

Analysis of False Scintigraphic Findings

The embedded specimens of 8 carcinomas that had escaped detection by scintigraphy (false-negative) were analyzed. Six of the 7 carcinoma lesions whose size could be determined from the embedded specimen (1 case of lobular carcinoma, 5 of ductal invasive carcinoma, and 1 of DCIS) showed a maximum diameter of 1.3 cm. Tumor size appears decisive in limiting the ability of scintigraphy to detect carcinoma, as underscored by the fact that 4 carcinomas escaping detection by scintigraphy exhibited histologic characteristics leading one to expect increased tracer uptake (moderately increased density of cells [$n = 2$], increased vascularization [$n = 1$], and signs of proliferation [$n = 1$]). The ductal invasive carcinoma with a diameter of 2.5 cm, which showed normal ^{99m}Tc-sestambi uptake at scintigraphy and was not considered suggestive of malignancy, was described as mucinous at histopathology. Histologic sections showed a low cell count, as well as a low level of inflammatory and proliferative activity, together with absence of angioneogenesis. Overall, of the carcinoma specimens that were associated with false-negative findings at scintigraphy and were sufficient for evaluation, 4 of 6 showed few cells; 4 of 5, few vascular cross sections; 5 of 5, absence of or low levels of inflammatory activity; and 3 of 4, absence of or low levels of proliferative activity.

Lesions that were incorrectly interpreted at scintigraphy as suggestive of malignancy (false-positive) included 8 benign processes (2 cases of fibrocystic disease, 4 of fibroadenoma, and 2 of chronic mastitis). The size of all 4 fibroadenomas could be determined and was greater than 1.3 cm in diameter. In 7 of the 8 benign lesions, various histopathologic parameters could be identified that, in addition to size, might possibly explain the increased uptake of radiopharmaceutical (a moderate to high density of vascular cross sections [$n = 5$], moderate to severe signs of inflammation [$n = 3$], and a moderate to high proportion of characteristic cells [$n = 1$] or proliferating cells [$n = 1$]).

DISCUSSION

To evaluate tissue-specific reasons for false-positive or false-negative scintigraphic findings, we correlated ^{99m}Tc-sestambi uptake by various breast disorders with a series of tissue-specific parameters. The study showed that, besides tumor diameter, parameters such as vascularity, cell density, and inflammation strongly influenced the intensity of tracer uptake. Uptake of the radiopharmaceutical depended on the extent of the inflammatory component of benign lesions.

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Only for a few specific histopathologic parameters, however, was a statistically significant correlation found with the uptake behavior of a lesion. Overall, the uptake pattern was determined by a combination of factors. Benign lesions frequently showed a low proportion of characteristic cells, with normal or only slightly increased tracer uptake. A significantly increased tracer uptake did not, however, correlate with a high cell density or vascularity, so that in these cases other factors, such as inflammation, were likely responsible for the increased uptake. We also found no correlation between tracer uptake and the respective estrogen or progesterone receptor status and Pgp expression.

The positive correlation between the size of the tumor and the extent of ^{99m}Tc-sestamibi uptake was also confirmed by Cwikla et al. (*12*). Analogous to our findings were their study results—for 85 patients with breast carcinoma—showing no correlation between ^{99m}Tc-sestamibi uptake and estrogen or progesterone receptor status. Absence of correlation between ^{99m}Tc-sestamibi uptake and receptor status was also reported by Maini et al. (*13*) and Tofani et al. (*14*). Their studies, which also investigated immunohistochemical parameters, found no correlation between ^{99m}Tc-sestamibi uptake and expression of Pgp-170 or the CD31 antigen. Tumors with absence of or low expression of the Her-2/*neu* oncogene and the proliferating cell nuclear antigen did show higher ^{99m}Tc-sestamibi uptake than did carcinomas with higher expression of these antigens, but the difference was not statistically significant.

In a study by Cutrone et al. (*15*), immunohistochemical staining was performed to assess neovascularity, desmoplasia, mitochondrial density, and cellular proliferation. In accordance with our findings, they found no correlation between ^{99m}Tc-sestamibi uptake and the degree of neovascularity. In addition, mitochondrial density did not significantly correlate with ^{99m}Tc-sestamibi uptake. Staining for α-actin antigen to determine collagen-producing myofibroblasts revealed a moderate correlation between the level of myofibroblast activity and the level of ^{99m}Tc-sestamibi uptake. Desmoplasia and fibroblastic activity around the tumor has been shown to be another cause of true-positive, but also false-positive, scintigraphic results. However, we did not stain for α-actin antigen.

Cayre et al. (*16*), in a study of 45 patients, evaluated the relevance of pretreatment scintigraphy using ^{99m}Tc-sestamibi for predicting tumor response to neoadjuvant chemotherapy. They tested the hypothesis that MDR expression is associated with reduced tracer uptake by the tumor or with accelerated elimination of tracer, resulting in less intense uptake at scintigraphy. The study was based on earlier investigations such as that of Piwnica-Worms et al. (*17*), according to which ^{99m}Tc-sestamibi is a substrate of the Pgp-modulated transport mechanism, and when disease is resistant to certain chemotherapeutic agents the tracer is more rapidly eliminated from cells rich in Pgp. Negative findings at pretreatment scintimammography predicted, with 100% specificity, resistance of the carcinoma to therapy. Uptake of the radiopharmaceutical correlated inversely with the MDR-1 expression of ductal invasive carcinomas (*16*).

Kao et al., in a retrospective study of 48 patients, showed that carcinomas not characterized by expression of Pgp or MDR-related protein showed significantly higher ^{99m}Tc-sestamibi uptake at scintimammography performed 10 min after tracer application (*18*).

The immunohistochemical investigations of the present study, on a smaller collective, failed to confirm the findings of Cayre et al (*16*), Piwnica-Worms et al. (*17*), and Kao et al. (*18*). In our study, 20 carcinomas exhibited heterogeneous uptake, independent of MDR status; the data failed to support any correlation between MDR expression and the degree of tracer uptake or lack thereof. A study by del Vecchio et al. also did not support the assertion that initial determination of ^{99m}Tc-sestamibi uptake correlates with the relative Pgp concentration within the tumor. Their results showed that, for prediction of resistance to chemotherapy, early and late (240 min) scintigraphy was necessary. In comparison with carcinomas with high Pgp expression (n = 9), carcinomas with low Pgp expression (n = 18) showed a lower efflux and, therefore, higher retention of the radiopharmaceutical in late images. The authors concluded that the determination of ^{99m}Tc-sestamibi retention is a simple test for estimating Pgp expression and, hence, for predicting resistance to chemotherapy (*19*). Retrospective determination of the ^{99m}Tc-sestamibi efflux rate was not feasible in our study, since late imaging at 240 min after tracer application had not been performed.

CONCLUSION

Our findings confirm that a lesion size of less than 1 cm in diameter is one reason for false-negative scintigraphic findings. In addition, parameters such as low cell count, low vascularity, and absence of inflammation in carcinomas may negatively affect uptake of the radiopharmaceutical and, hence, the rate of lesion detection. The decisive factor in false-positive increased tracer uptake by benign lesions, on the other hand, is probably the presence of inflammation. However, because these findings were statistically significant only in part, it is to be supposed that uptake of ^{99m}Tc-sestambi by breast lesions is determined by various tissue parameters in interaction.

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