22. Mansi L, Rambaldi PF, Procaccini E, et al. Scintimammography with ^{99m}Tc-tetrofosmin in the diagnosis of breast cancer and lymph node metastases. *Eur J Nucl Med* 1996;23:932–939.
23. Adalet I, Demirkol O, Muslumanoglu M, et al. Technetium-99m-tetrofosmin scintigraphy in the evaluation of palpable breast masses: preliminary results [Abstract]. *Eur J Nucl Med* 1995;22(suppl):742.
24. Soriceli A, Cuocolo A, Tedeschi E, et al. Evaluation of brain tumors with ^{99m}Tc-tetrofosmin and ^{201}Tl: a preliminary report [Abstract]. *Eur J Nucl Med* 1994;21(suppl):6.
25. Piwnica-Worms D, Holman LB. Noncardiac application of hexakis(alkyl-isonitrile) ^{99m}Tc complexes [Editorial]. *J Nucl Med* 1990;31:1161.
26. Chiu ML, Kronauge JF, Piwnica-Worms D. Effect of mitochondrial and plasma membrane potentials on accumulation of hexakis (2-methoxyiso-butylisonitrile) technetium (I) in cultured mouse fibroblast. *J Nucl Med* 1990;31:1646–1653.
27. Higley B, Smith FW, Smith T, et al. Technetium-99m-1,2-bis(bis(2-ethoxyethyl)phosphino) ethane: human biodistribution, dosimetry and safety of a new myocardial perfusion imaging agent. *J Nucl Med* 1993;34:30–38.
28. Kelly JD, Forster AM, Higley B, et al. Technetium-99m-tetrofosmin as a new radiopharmaceutical for myocardial perfusion imaging. *J Nucl Med* 1993;34:222–227.
29. Piwnica-Worms D, Chiu ML, Budding M, Kronauge JF, Kramer RA, Croop JM. Functional imaging of multidrug-resistant p-glycoprotein with an organotechnetium complex. *Cancer Research* 1993;53:977–984.
30. Moretti JL, Azaloux H, Boisseron D, Kouyoumdjian JC, Vilcoq J. Primary breast cancer imaging with ^{99m}Tc-sestamibi and its relation with p-glycoprotein overexpression. *Eur J Nucl Med* 1996;23:980–986.
31. Derebek E, Kirkali Z, Dogan AS, et al. Technetium-99m-MIBI scintigraphy in metastatic renal cell carcinoma: clinical validation of the relationship between ^{99m}Tc-MIBI uptake and p-glycoprotein expression in tumours tissue. *Eur J Nucl Med* 1996;23:976–979.
32. Ballinger JR, Bannerman J, Boxen I, et al. Accumulation of ^{99m}Tc-tetrofosmin in breast tumor cells in vitro: role of multidrug-resistance p-glycoprotein [Abstract]. *J Nucl Med* 1995;36(suppl):202.
33. de Jong M, Bernard HF, Ensing G, Bakker WH, Visser TJ, Krenning EP. Uptake of ^{99m}Tc-MIBI, ^{99m}Tc-Myoview and ^{99m}Tc-Q12 into human breast cancer cell lines. [Abstract]. *J Nucl Med* 1996;37(suppl):190.
34. Atasever T, Gokcora N, Vural G, Cetin N, Ozturk C, Unlu M. Evaluation of malignant and benign lung lesions with ^{99m}Tc-tetrofosmin. *Nucl Med Commun* 1996;17:557–582.
35. Basoglu T, Sahin M, Coskun C, Koparan A, Bernay I, Erkan L. Technetium-99m tetrofosmin uptake in malignant lung tumors. *Eur J Nucl Med* 1995;22:687–689.
36. Novoa N, Tabuenca MJ, Varela A, Mar-Cordoba M, Ortiz-Berrocal JL, Montz R. The usefulness of ^{99m}Tc-tetrofosmin in the diagnosis of pulmonary tumors. A preliminary assessment. *Arch Bronconeumol* 1995;31:410–414.
37. Schillaci O, Volpino P, Tavolaro R, et al. Detection of primary lung cancer with ^{99m}Tc-tetrofosmin [Abstract]. *J Nucl Med* 1996;37(suppl):35.
38. Ohtake E, Kido Y, Hasegawa H, Sakamoto H, Numata H, Fukuda T. Utility of ^{99m}Tc-tetrofosmin SPECT for detecting small pulmonary nodules [Abstract]. *J Nucl Med* 1996;37(suppl):111.
39. Mansi L, Rambaldi PF, Di Lieto E, et al. Technetium-99m-tetrofosmin SPECT in primary lung tumor [Abstract]. *J Nucl Med* 1996;37(suppl):264.
40. Yurekli Y, Ertay T, Sayit E, et al. Technetium-99m-tetrofosmin uptake in lung cancers: a comparative study with ^{201}Tl [Abstract]. *Eur J Nucl Med* 1995;22(suppl):832.

Radionuclide-Guided Stereotatic Prebiopsy Localization of Nonpalpable Breast Lesions with Normal Mammograms

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Scintimammography with ^{99m}Tc-sestamibi can be used as a complementary technique to improve the mammogram's sensitivity and specificity for detection of breast carcinoma. We have observed in some patients focal areas of increased ^{99m}Tc-sestamibi uptake with no corresponding abnormalities on physical examination or mammogram. A phantom device and a special needle were designed to stereotactically localize these lesions before biopsy. **Methods:** After intravenous injection of 30 mCi (1110 MBq) of ^{99m}Tc-sestamibi, a prone lateral image of the abnormal breast was obtained. With the patient in the prone position, the breast was compressed with two fenestrated plates in the prone position. The x and y coordinates of the abnormal hot spot of the breast were determined. The z coordinate of focal ^{99m}Tc-sestamibi uptake was determined by advancing a localizer needle through a selected predetermined hole of the fenestrated plate using real-time visualization on the persistence monitor. The tip of the opturator inside the needle is welded with ^{57}Co to determine the depth of the hot spot in the breast. **Results:** Three women, all of whom had normal mammograms and breast physical examinations, were studied using ^{99m}Tc-sestamibi prone breast imaging. Pre-excisional biopsy needle localization of abnormal focal uptake was performed. Two women demonstrated infiltrative ductal carcinoma, and the third had proliferative fibrocystic disease of the breast. **Conclusion:** Our initial experience demonstrates that nuclear medicine-guided stereotactic needle biopsy of the breast in patients with positive scintimammograms is technically feasible. In the future, this technology will enable us to detect breast carcinoma in the absence of clear-cut clinical and mammographic findings.

Key Words: breast biopsy; scintimammography; breast cancer; technetium-99m-sestamibi

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Mammography and physical examination combined have a sensitivity of 85% for the detection of breast carcinoma. Mammography also has a positive predictive value of 15%–30%. (*1*) Initial data indicate that ^{99m}Tc-sestamibi can be used as a complementary technique to improve mammography's sensitivity and specificity for breast cancer detection (*2*).

We have observed that some patients have abnormal focal areas of ^{99m}Tc-sestamibi uptake with no abnormalities on physical examination or mammography to serve as a guide for biopsy. Because of the reported higher specificity of ^{99m}Tc-sestamibi uptake for breast cancer, our experience indicates such uptake is more likely to be due to malignancy than benign lesions and probably requires tissue diagnosis (*3–5*). We designed and manufactured a prototype of a stereotactic-guided prebiopsy needle localization device which enables us to localize the abnormality on the scintimammogram using nuclear medicine techniques (*6*). In this article, we demonstrate the clinical utility of this device in three women with normal mammograms and physical breast examinations who had focal areas of abnormal increased ^{99m}Tc-sestamibi breast uptake. These lesions were subsequently localized and biopsied with our stereotactic device. Two women had invasive ductal carcinoma, and the third had a proliferative type of fibrocystic disease.

MATERIALS AND METHODS

Scintimammography

Five minutes after intravenous injection of 20 mCi (740 MBq) ^{99m}Tc-sestamibi, prone lateral planar images of each breast were acquired followed by an anterior upright image of the chest. The procedure has been previously described in detail (*7*). Focal

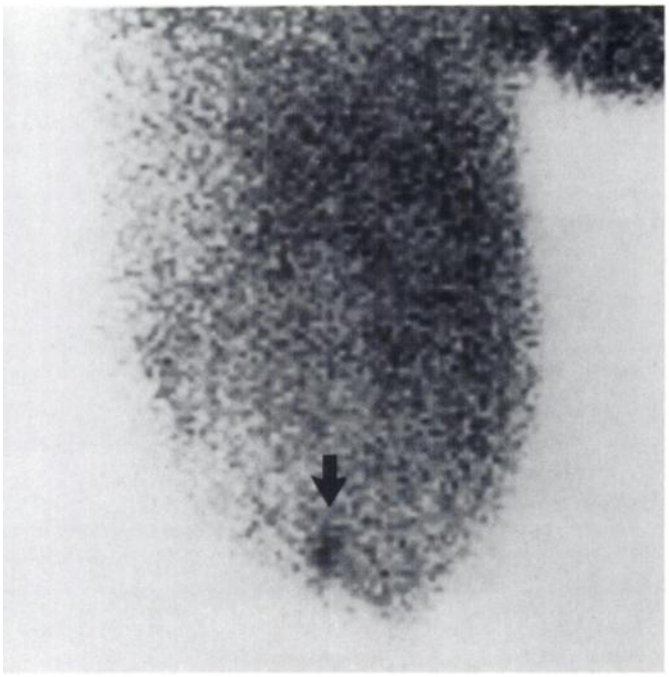

FIGURE 1. Prone lateral scintimammogram of the left breast of Patient 1, acquired without compression 5 min after intravenous injection of ^{99m}Tc-sestamibi, demonstrates a focal area of increased uptake in the retroareolar region (arrow).

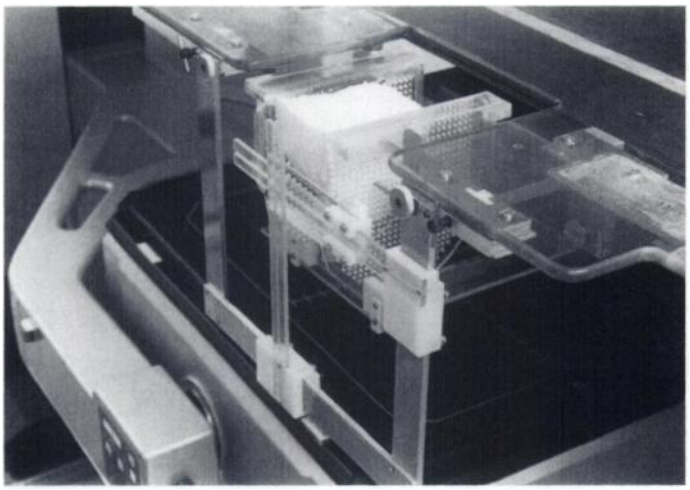

FIGURE 2. Nuclear medicine-guided stereotactic biopsy device attached to the imaging table (Reprinted with permission from Mena F, et al.) *Nucl Med Commun* 1996;17:717–723. A breast phantom is compressed between fenestrated paddles.

increased ^{99m}Tc-sestamibi breast uptake was seen, which resulted in scintigraphy-guided prebiopsy needle localization of the lesion. Biopsy was performed 2–6 wk after scintimammography (Fig. 1).

Prebiopsy Needle Localization

After an intravenous injection of 30 mCi (1110 MBq) of ^{99m}Tc-sestamibi, the patient was placed prone on the imaging table. The dependant breast was positioned in a previously described device designed for prebiopsy localization (*6*) (Fig. 2). This device has been patented by Harbor-UCLA Research and Education Institute Inc.

To immobilize the breast, mild cranial-caudad compression was applied using two fenestrated plastic paddles. A 1-min anterior image with the camera beneath the prone patient was acquired and used to accurately position a 296-kBq ^{57}Co line source oriented parallel to the patient's long axis and horizontal to the floor over the area of focal increased MIBI breast uptake (Fig. 3A, 3B). A 5-min image was acquired using dual windows: one centered at 122 keV for the ^{57}Co and the other at 140 keV for ^{99m}Tc. This image was used to determine the x (medial/lateral) axis coordinate of the lesion. The detector was then positioned lateral to the breast and an image was acquired to position the ^{57}Co line source parallel to the patient's long axis and parallel to the floor at the y (anterior/posterior) coordinate. The second cobalt line source perpendicular to the floor and perpendicular to the patient's long axis was superimposed over the lesion to determine the z (superior/inferior) coordinate of the lesion (Fig. 4A, 4B). A stainless steel needle guide and a 20-gauge breast localization needle fitted with an obturator tipped with 592 Bq of ^{57}Co were positioned at the x, y coordinates in the fenestrated paddle. Using real-time visualization on the persistence monitor, the needle was advanced in the breast until the radioactive tip reached the z coordinate of focal MIBI uptake. An image was acquired to confirm the correct position of the needle (Fig. 5A, 5B). The radioactive obturator was then removed, and 0.6 cc methylene blue dye was injected through the needle to mark the tissue for surgical removal. Finally, a J-hook wire was passed through the needle and secured in the breast. The breast was released from the localization device, and routine excisional biopsy was then performed using the hook wire and dye trail as guides.

Postbiopsy Specimen Radiograph and Image

After surgical excision of the breast lesion, the specimen was radiographed to determine location of the wire. A 10-min scintigraphic image of the specimen, on a plastic tray, was made to ascertain the presence of focal, increased ^{99m}Tc-sestamibi uptake (Fig. 6).

RESULTS

We studied three patients with our stereotactic unit.

Patient 1. A 56-yr-old woman presented with a questionable palpable mass above the left areola. Bilateral film screen

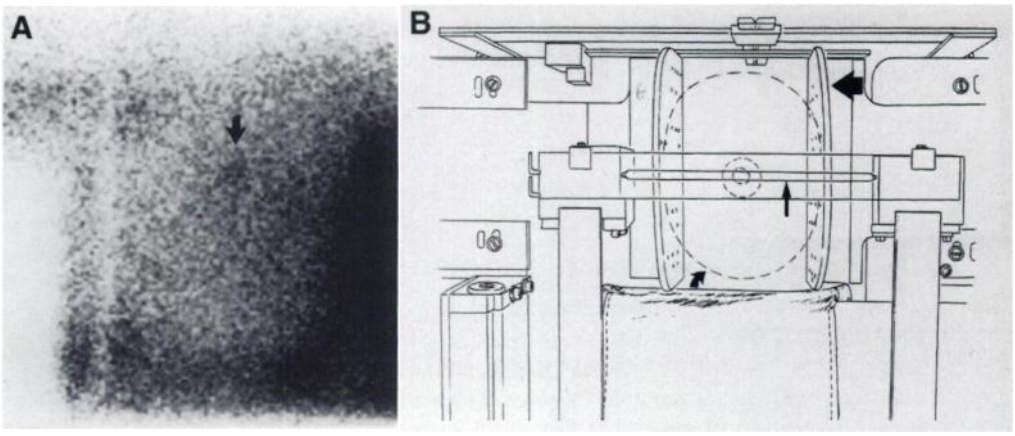

FIGURE 3. (A) Prone anterior scintimammogram of Patient 1 with a focal increased ^{99m}Tc-sestamibi uptake in the left breast (arrow). The mammogram and physical examination were normal. The breast is compressed in the craniocaudal axis. (B) Artist's drawing of 3A as seen from underneath with the left breast (curved arrow) compressed between two fenestrated paddles (large arrowhead). A ^{57}Co line source (thin arrow) is superimposed parallel to the patient's long axis to identify the medial/lateral coordinate of the area of focal increased uptake.

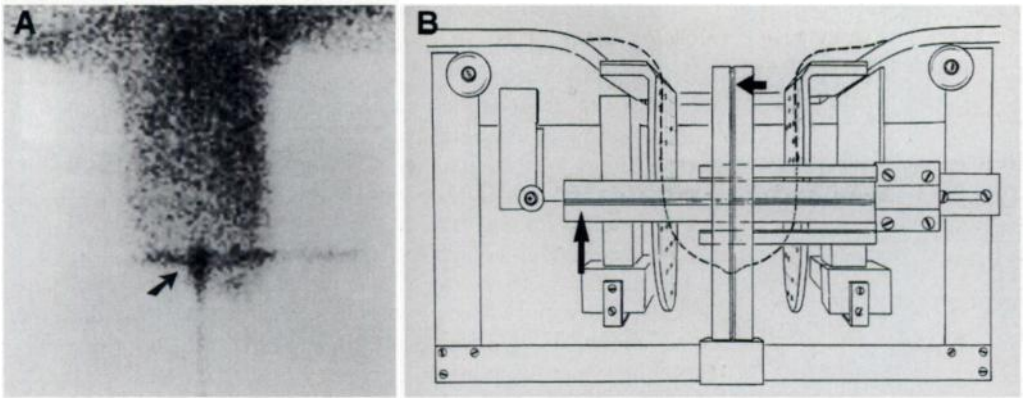

FIGURE 4. (A) Prone lateral scintimammogram shows two ^{57}Co "crosshair" line sources superimposed along the anterior/posterior and superior/inferior (arrow) coordinates of the focal area of increased uptake of ^{99m}Tc-sestamibi uptake. (B) Artist's drawing of 4A demonstrating the breast in the prone position (compressed as in Fig. 3) as viewed from the lateral side. Cobalt-57 line sources in the anterior/posterior (long arrow) and superior/inferior positions (short arrow) are seen superimposed over the breast (dotted outline).

mammography was normal. Scintimammography using ^{99m}Tc-sestamibi demonstrated a focal area of increased uptake above the left areola (Figs. 1 and 3A). The patient was scheduled for excisional biopsy. On the day of the biopsy, the surgeon was unable to palpate the suspicious lesion. Therefore, the lesion was localized with a stereotactic nuclear medicine device. The specimen scan, postbiopsy, showed a focal area of intense uptake, confirming the excision of the abnormal uptake noted on her prebiopsy scintimammogram (Fig. 6). Histopathology revealed infiltrating moderately differentiated ductal carcinoma, which was a 0.7-cm lesion with microscopically negative margins. The patient underwent lumpectomy followed by radiation therapy.

Patient 2. A 50-yr-old woman presented with a left axillary mass with an otherwise normal breast physical exam. Fine-needle aspiration cytology of the axillary mass revealed adenocarcinoma. Routine bilateral mammography showed no abnormalities. Scintimammography demonstrated a focal area of increased uptake in the left breast as well as focal intense uptake in the left axilla corresponding to the left axillary mass. Prebiopsy stereotactic needle localization using nuclear medicine was performed as described above. A postbiopsy image of the excised tissue demonstrated intense focal uptake in the specimen. Histopathology revealed invasive ductal carcinoma. The patient underwent lumpectomy and axillary node dissection followed by radiation therapy.

Patient 3. A 32-yr-old woman was referred for breast reduction. Each breast weighed approximately 32 pounds, causing back pain and some disability for the patient. Breast physical exam was unremarkable. Bilateral film screen mammography performed with great difficulty showed fatty breasts and no abnormality. Due to her unusually large breasts and difficulty performing mammography, as well as a history of breast cancer in her sister, scintimammography was requested. The study revealed a focal area of increased uptake in her left breast which was localized with the stereotactic device. An image of the tissue specimen confirmed excision of the area of focal uptake. Histopathology revealed a proliferative type of fibrocystic disease with hyperplasia and no atypia.

DISCUSSION

Needle localization biopsies for suspicious nonpalpable breast lesions have been performed using radiologic mammographic techniques. Stereotactic large-core needle biopsy of nonpalpable lesions also plays a significant role in obtaining appropriate tissue for histopathologic examination when a suspicious, nonpalpable lesion is seen on mammograms (*8*). Such devices have been developed and reported with MRI (*9,10*). Our experience, and that of others, demonstrates the usefulness of ^{99m}Tc-sestamibi scintimammography for improving mammographic sensitivity and specificity in women with questionable mammographic abnormalities and/or breast physical examination (*2–5*). It is often difficult to detect breast carcinoma in women with dense breasts with mammography. We have demonstrated that the degree of ^{99m}Tc-sestamibi breast uptake is independent of dense, fibroglandular tissue seen on mammography (*11*) and thus potentially improves breast cancer detection in women with dense breasts (*12*). However, once a nonpalpable lesion is identified by scintimammography in a patient with an unremarkable mammogram, pathologic confirmation is warranted. This prompted us to design a device to stereotactically localize areas of abnormal uptake in women with a normal mammogram and normal physical breast examination.

Currently, it is difficult to gather a larger population of patients with these characteristics, because we are not using scintimammography as a screening technique for breast cancer.

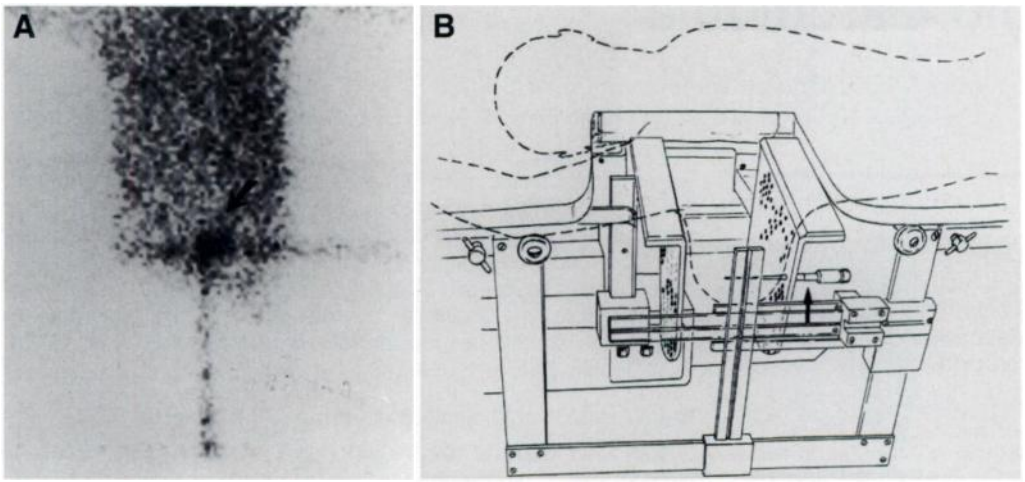

FIGURE 5. (A) Prone lateral scintimammogram as in Figure 4A. The radioactive tip of a guide wire is seen superimposed over the previously identified coordinates of the focal area of increased uptake (arrow). (B) Artist's drawing shows the prebiopsy localization needle inserted into the breast through a preselected hole in the caudal fenestrated paddle (arrow).

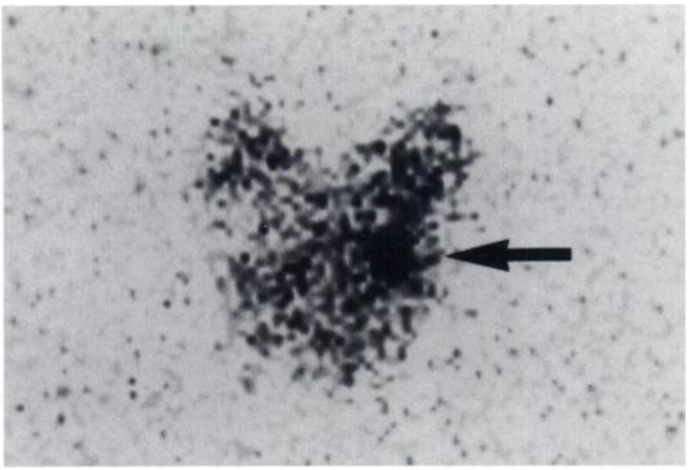

FIGURE 6. Scan of the excisional biopsy specimen from Patient 1 demonstrates an intense focal area of ^{99m}Tc-sestamibi uptake (arrow). Histopathology revealed a 0.7-cm infiltrating ductal carcinoma with microscopically negative margins. This image confirms the accurate localization and resection of the region of abnormal breast uptake.

It is possible that the biologic characteristics of ^{99m}Tc-sestamibi will localize a focus of breast carcinoma before anatomical changes that are evident on a mammogram. The patients reported here demonstrate that abnormalities not seen on mammograms can be visualized by scintimammography with ^{99m}Tc-sestamibi. The advantage of nuclear medicine-guided stereotactic prebiopsy localization is to locate and biopsy suspicious lesions seen on scintimammograms when mammography fails to define abnormalities.

The disadvantages of this approach include cost, patient discomfort, radiation exposure and false-positive scintimammograms that would result in "unnecessary" biopsies. This was observed in Patient 3 in this study because of her huge breasts. Mammography and breast physical examination were extremely difficult due to breast size. Each breast required 18 mammographic films to obtain a mammogram. The uncertainty of complete imaging of the breasts as well as the patient's anxiety because a sister had breast cancer prompted the referring physician to request scintimammography before breast reduction surgery. Inspite of the increased focal uptake noted on the scintimammogram, the histopathologic diagnosis was proliferative fibrocystic disease. Therefore, biopsy can be considered to be unnecessary.

Future experience with this technique in a larger cohort is necessary to define its clinical utility. Postbiopsy specimen scintigraphy should be a routine part of scintigraphy-guided biopsy, as is specimen radiography after prebiopsy needle localization of an abnormal, nonpalpable mammographically detected lesions. This image will confirm removal of suspicious areas of increased uptake seen on the scintimammogram. In all three patients, focal increased uptake was noted on the postbiopsy specimen scintigram. Since there is minimal photon attenuation seen on the specimen scintigram as well as increased proximity of the lesion to the nuclear medicine detector, we observed significant improvement in the target-to-background counting rate.

CONCLUSION

Our initial experience demonstrated that nuclear medicine-guided stereotactic prebiopsy needle localization is feasible. Further experience with this technology will enable us to biopsy breast cancer before clinical and mammographic findings, thereby further reducing mortality from this disease.

REFERENCES

1. Kopans DB. The positive predictive value of mammography. *AJR* 1992;158:521–526.
2. Khalkhali I, Mena, Jouanne E, et al. Prone scintimammography in patients with suspicion of carcinoma of the breast. *J Am Coll Surg* 1994;178:491–497.
3. Khalkhali I, Cutrone JA, Mena I, et al. Scintimammography: the complementary role of ^{99m}Tc-sestamibi prone breast imaging for the diagnosis of breast carcinoma. *Radiology* 1995;196:421–426.
4. Taillefer R, Robidoux A, Lambert R, et al. Technetium-99m-sestamibi prone scintimammography to detect primary breast cancer and axillary lymph node involvement. *J Nucl Med* 1995;36:1758–1765.
5. Khalkhali I, Cutrone J, Mena I, et al. Technetium 99m-sestamibi scintimammography of breast lesions: clinical and pathological follow-up. *J Nucl Med* 1995;36:1784–1789.
6. Mena F, Mena I, Diggles L, Khalkhali I. Design and assessment of scintigraphy-guided biplane localization technique of breast tumors: a phantom study. *Nucl Med Commun* 1996;17:717–723.
7. Diggles L, Mena I, Khalkhali I. Technical aspects of prone dependent-breast scintimammography. *J Nucl Med Technol* 1994;22:165–170.
8. Parker S, Burbank F, Jackman R, et al. Percutaneous large core breast biopsy: a multi-institutional experience. *Radiology* 1994;193:359–364.
9. Hussman K, Renslo R, Phillips J, et al. MR mammographic localization: work-in-progress. *Radiology* 1993;189:915–917.
10. Farria D, Gorczyca D, DeBruhl N, Sullenberger P, Sinha S, Bassett L. MR-guided breast lesion localization: validation study [Abstract]. *Radiology* 1995;197(suppl): 461P.
11. Khalkhali I, Mena I, Diggles L. Limitations of mammography: the role of technetium-99m-sestamibi scintimammography in diagnosis of breast cancer [Abstract]. *Clin Nucl Med* 1993;18:927.
12. Khalkhali I, Cutrone J, Mena I. The usefulness of scintimammography in patients with dense breast on mammogram [Abstract]. *J Nucl Med* 1995;36(suppl):52.

Frontal Sinus Mucocele Mimicking a Metastasis of Papillary Thyroid Carcinoma

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Radioiodine scans are highly specific for detecting metastases of well-differentiated thyroid carcinomas. However, false-positive ^{131}I whole-body scans may occur as illustrated in the following case report. In a 53-yr-old patient, abnormal ^{131}I uptake was found in the right frontal skull 4 wk after total thyroidectomy and radioiodine therapy for papillary thyroid cancer. Bone scans and planar x-rays of the skull were unremarkable, and the serum thyroglobulin level was within normal limits. X-ray CT revealed a small nodule in the right frontal sinus corresponding to the pathological focus of ^{131}I uptake. Surgical removal and histopathological examination of this lesion yielded a mucocele, a slow-growing lesion of the paranasal sinuses accumulating mucous material. The postoperative ^{131}I scan was unremarkable. The possibility of a false-positive finding on radioiodine scans should be considered, particularly when the serum thyroglobulin level is not elevated.

Key Words: thyroid carcinoma; iodine-131; mucocele

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