Special Submission

BREAST CANCER IMAGING: A NEW ROLE OF Tc-99m SESTAMIBI PRONE SCINTIMAMMOGRAPHY FOR DIAGNOSIS OF BREAST CANCER

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According to current estimates, after the skin cancer, the breat cancer is the most frequently diagnosed malignancy in the United States, followed by cancer of the lung, rectum and prostate (1).

In 1993, the American Cancer Society estimated that 182,000 women would be diagnosed with breast cancer and that 46,000 women would die of this disease (2). It was also estimated that 1,000 men would be diagnosed with breast cancer in 1993, approximately 0.5% of the total number of cases estimated to be diagnosed this year. Among women, breast cancer acounts for 32% of all cancers detected and 18% of all cancer deaths (2). Until recently breast cancer was the leading cause of death from cancer among women, but since 1985 it has ranked second, after lung cancer (3).

Breast cancer received considerable public attention not only because of the magnitude of disease burden but also becuase of the clear potential to significantly reduce mortality through wide spread participation in breast cancer screening programs. Early detection of breast cancer decreases mortality and facilitates breast conserving therapy. Studies continue to prove that mammography is the most effective method for early breast cancer detection.

In 1973, the Breast Cancer Detection Demonstration Project (BCDDP) which was sponsored by the American Cancer Society and the National Cancer Institute, enrolled 280,000 women for annual screening by mammography and physical examination. In the five successive years of the BCDDP, mammography was shown to be superior to physical examination. This study demonstrates that mammography alone was responsible for diagnosing 32% of breast cancers in that protocol whereas only 9% were detected by physical examination alone (4,5). The Swedish study also confirmed the ability of screening to detect cancer at an early stage (6).

The number of cases of breast cancer detected at stage II was reduced by 25% among screened women. The Swedish trial

demonstrated 30% mortality reduction in women over 50 years of age who had screening mammography vs. controlled group that did not have mommography in the same period of time (7).

The American Cancer Society, the American College of Radiology, and eleven other professional medical societies have endorsed specific guidelines for early breast cancer detection and mammography. Mammography has been shown to be quite sensitive to detect breast cancer, but frequently it cannot be used to accurately differentiate benign from malignant lesions (8). The only definitive conformation of a suspicious lesion seen on mammography is excisional biopsy.

In recent years, the use of fine needle aspiration cytology and a stereotactic core biopsy of the breast have become more available in clinical use (9). These techniques, although fairly simple, require a trained cytopathologist and costly equipment to perform, nevertheless, they can have an important impact on eliminating some of the excisional biopsies which are more invasive and costly.

The true indication and efficacy in these techniques are still under investigation. This requires multicenter clinical trials on a population of patients with suspicious breast lesions who undergo a stereotactic fine needle aspiration cytology, core biopsy and confirmation with excisional biopsy. The National Cancer Institute in the U.S. is conducting such a trial, the results of which are not yet available.

The rate of lesion detection by modern mammography has been significantly improved over the past decade using dedicated mammography units, excellent film-screening combinations and dedicated processer. However, mammography lacks adequate specificity for cancer detection, and therefore, it has low positive predictive value for detection of breast cancer which is only 20-30% (10). Thus, only one out of four to six breast biopsies is positive for breast cancer.

One of the major reasons for such low positive predictive value is dense breast seen on mammography which obscures the identification of tumors. Radiologically dense breast are unique challenge to mammographic detection of early stage breast cancer. Approximately 25% of women have dense breast on mammogram so this is not a trivial problem (11). The other concern about mammogtraphy's routine use is its high false negative rate. In one report from New Mexico (12) the false negative rate was 45%. In another report from Canada (13) the false negative rate was 26% in women over 50 years of age and 40.9% in women who were under 50. The issue of observer variability is even more critical, although various authors have reported a high degree of correlation among different radiologists (14,15).

Recently, at Harbor-UCLA Medical Center, we conducted a retrospective study consisting of the interpretation of over 500 mammograms by three board certified radiologists highly skilled in mammography. Intra-observer variabilities among these physicians were 89.1%, 98/7% and 92.4% and inter-observer variabilities were similar, 83.6% (reader 1 vs. reader 2), 86.5% (reader 1 vs. reader 3), and 81.1% (reader 2 vs. reader 3) (unpublished data).

The following imaging techniques have been proposed to improve the specificity of mammograpy:

1. Magnetic resonance imaging (MRI) of the breast.

Breast images were among the first images of the human anatomy used by MRI (16,17). In recent publication, Harms et al. (18) performed MRI of the breast with rotation delivery of

excitation of resonance. In 30 breasts with 47 malignant lesions and 27 benign lesions, MRI has a sensitivity of 94% but a specificity of 37%. In this series, there were 11 patients with breast cancer seen on MRI that were not seen with mammography (11 out of 47 cancers). The lesions not seen on mammography varied in size from 3 mm to 12 cm. The authors concluded that the MRI of the breast can be used in patients with mommographically dense breast or in palients with silicone implants/injection, and to stage disease in patients who are candidates for lumpectomy (19).

2. Positron emission tomography (PET) imaging of the breast

Positron-emitter (fluorine-18)-labeled analogue of 2- deoxyglucose, 2-(F-18-fluoro-2-deoxy-D-glucose) has been used for imaging breast cancer (20). These sugars undergo phosphorylation by the intracellular hexokinase enzyme but are not further metabolized, and therefore, can be trapped in tumor cells. There are several reports in the PET literature on the utility of this modality for the diagnosis of primary breast carcinoma. Lillien reviewed the world PET literature through early 1993 which pertained to breast cancer detection. There were 97 cases of breast cancer patients reported using PET: overall sensitivity and specificity were 100% and 85%, respectively (personal communication with David Lillien, M.D.; New Port Beach California). Since most of these reports were performed on patients with known breast cancer, the sensitivity and specificity of this procedure for detection of breast cancer is probably an overestimate. Besides its high cost and limited availability, the number of patients that have been studied with PET for the diagnosis of primary breast cancer does not allow us to draw a conclusion as to its clinical application in the primary work up of patients with suspicious mammograms.

3. Radionuclide breast imaging using thallium (Tl-201)

The oncoimaging use of Tl-201 was first reported in 1976 from the Netherlands by Cox et al. (21). He incidentally identified a focal region of increased uptake in the lung of a 47-year-old male patient with a bronchial carcinoma of the left lung who was referred for Tl-201 evaluation of his heart. In the last decade, several investigators have reported the use of Tl-201 imaging for tumor imaging (22,23).

The first use of this agent for breast imaging was reported in 1978 by Hisada et al. in two patients with known breast cancer (24). This group evaluated 173 patients with malignant tumors and 76 benign lesions; there were two patients with known breast cancers in the series. The authors concluded that Tl-201 tumor imaging had a sensitivity and specificity of 64% and 61%, respectively in this pilot study. Subsequently, Sluyser and Hoefnagel (25) reported on the use of Tl-201 imaging in a series of 15 patients with known breast cancer in whom there was increased focal uptake with Tl-201 noted in their breast images. No conclusion can be made about the sensitivity and specificity in this group since all these patients had known breast cancer prior to imaging.

Recently, Waxman et al. (26) evaluated 81 female patients with Tl-201 scintigraphy of the breast because of palpable breast masses. In addition, 30 females with no palpable breast abnormalities were studied. Of 44 with palpable breast carcinomas, 42 (96%) abnormalities were detected using Tl-201. In 19 patients with palpable breast abnormalities shown on biopsy to be benign fibrocystic disease, no abnormalities were detected with Tl-201. This group concluded that Tl-201 scintigraphy of palpable breast lesions is an

effective test for evaluation of these masses. More recently, Lee et al. (27) evaluated 40 patients with breast abnormalities detected by mammography and/or physical examination. These patients underwent breast imaging with Tl-201 prior to biopsy. This group demonstrated overall sensitivity of 80% and the specificity of 96% for the detection of breast cancer.

It should be noted that these authors used a technique of supine imaging which is not optimal for imaging of the posterior aspect of the breast. Furthermore, Tl-201 is not the agent of choice for breast cancer imaging because it has significantly lower target to background ratio in tumor cells than Tc-99m sestamibi (28).

4. Radionuclide breast imaging using Tc-99m sestamibi

Tc-99m sestamibi, a lipophilic cationic complex of a new class of Tc-99m labeled isonitrile compounds, has some similar properties to Tl-201 thallous chloride (i.e., myocaridal accumulation), as well as dissimilar characteristics (i.e., lack of redistribution) (29). Following an intravenous injection at rest, the highest Tc-99m sestamibi concentration is found in the gallbladder and liver, followed by the heart, spleen and lungs. Within the first hour, liver activity decreased with excretion into the biliary system, while maximal accumulation in the gallbladder occurs at 60 minutes. Organ dosimetry of Tc-99m sestamibi demonstrates that a dose of 20 mCi delivers 3 rads to the large intestine which is the predominant target organ. The whole body dose is 0.3 rads (30).

Tc-99m sestamibi, manufactured by Dupont-Merck Pharmaceuticals is an FDA approved radiopharmaceutical since December, 1990 used predominately in patients with coronary disease to identify damaged cardiac muscle. Tc-99m sestamibi is greatly different from Tl-201 which exhibits redistribution in the myocardium. Tc-99m sestamibi is not metabolized and is predominantly bound to an intracellular protein resulting in a relatively fixed distribution.

The use of Tc-99m sestamibi in tumor imaging was first reprted by Hassan et al. in 1989 (31). This group reported the use of Tc-99m sestamibi uptake in 19 patients with lung leions (13 malignant and six benign). A localized increase of Tc-99m sestamibi uptake was observed in 10 patients with untreated malignant tumors of the lungs. No localized lung uptake was observed in the patient with untreated poorly differentiated squamous cell carcinoma, two patients with treated lung cancers, and two patients with fibrosing alveolitis. The authors conculded that the use of Tc-99m sestamibi uptake in malignant and benign lesions is a new area of research which warrants further study.

Subsequently, the use of Tc-99m sestamibi uptake for the diagnosis of osteosarcoma and its metastases to lymph nodes was described in one patient by Caner et al. (22). SPECT imaging of pediatric brain tumors with Tc-99m sestamibi was reported by O'Tuana et al. (23) in a 5-year-old patient with a brain stem astrocytoma which showed focal uptake of Tc-99m sestamibi at the site of tumor recurrence which was positive by biopsy.

The exact mechanism of cellular uptake of Tc-99m sestamibi by cancer cells is unknown. Recrent data suggests that 90% of the tracer activity is concentrated in the mitochondria (29). Delmon-Moingeon et al. (32) determined the uptake of Tc-99m sestamibi in nine tumor cells. The concentration of Tc-99m sestamibi after one hour incubation varied from 5% to 28% of the activity in the external medium. This group also examined normal cells (chinese hamster lung fibroblasts) and human peripheral blood mononuclear cells and showed the uptake of Tc-99m sestamibi to be

less than 2% of the activity in the medium. Preliminary reports indicate that this compound also may localize in vivo in primary malignant tumors and metastatic deposits from thyroid, lung, and bronchial carcinoma (33, 34). In a similar experiment, Maublant et al. (28) compared the in vitro uptake of Tl-201 and Tc-99m sestamibi in cultured normal cells and carcinoma lines in order to define their possible use for in vivo tumor imaging. Their results show that the mean uptake was 80% higher in tumors than in normal cells for Tl-201 and nearly four times higher for Tc-99m sestamibi. When the myocytes are excluded from the group of normal cells, the uptake is 112% higher in tumor than in normal cells for Tl-201 but it becomes nearly nine times higher for Tc-99m sestamibi. These experimental culture cell studies support the role for in vivo tumor imaging in humans with Tc-99m sestamibi. The concentration of Tc-99m sestamibi in tumor cells far exceeds that of Tl-201, and therefore, for this and other reasons mentioned above, it would appear that Tc-99m sestamibi is the radiopharmaceutical of choice for tumor imaging.

The technique of prone breast imaging using planar lateral views of the breast was developed at Harbor-UCLA Medical Center (35). This technique provides natural landmarks of breast contour that are necessary for localization of lesions. Planar prone breast imaging is more favorable than the supine position because of excellent separation of deep breast structures from the myocardium in the left breast, and excellent separation of the right breast from the liver and relaxation of the pectoralis muscle, thus improving the resolution of small deep-seated leions. SPECT images of breast lesions provide better contrast than planar images, however, the absence of landmarks renders localization efforts difficult and often inaccurate. For this reason, we selected prone planar breast imaging as the optimal imaging procedure.

Recently at Harbor-UCLA Medical Center, we conducted a study of 59 female subjects with 62 lesions (41 palpable and 21 non-palpable) for when abnormal mammogram and/or physical examination warranted breast biopsy and/or fine needle aspiration cytology of the breast (36,37). Each patient received 20 mCi of Tc-99m sestamibi intravenously in the arm contralateral to the breast with the suspected abnormality. Five and 60 minutes post-injection, planar breast images in lateral and posterior oblique view were obtained.

In 33 benign breast lesions, no increased uptake of Tc-99m sestamibi was noted in the breast. In 23 breasts with biopsy-confirmed breast cancer, the radionuclide breast imaging result was positive. Five other breasts with benign breast lesions had false positive scans. All had excisional biopsies for pathologic confirmation. The final diagnoses were three cases of fibrocystic disease and two cases of fibroadenomas. Hypercellularity with extensive hyperplasia florid and adenosis were common pathologic features in these patients. There was only one patient with an intraductal carcinoma and a cluster of microcalcifications on screening mammography without an associated mass for whom the Tc-99m, sestamibi scan was negative.

In the group of patients studied, the sensitivity of this procedure was 95.8%, specificty was 68.8%, positive predicitive value was 82.1%, and most importantly, the negative predictive value for the detection of breast cancer was 97.1%. We concluded from this pilot study that: Prone radionuclide breast imaging using Tc-99m sestamibi was a highly sensitive test which improved the specificity of conventional mammography for the detection of breast cancer.

Our more recent data were evaluated on

147 patients with 153 breast lesions (38). The results of scintimammography were correlated with the excisional biopsy and fine needle aspiration cytology of the breast. Prone scintimammography exhibits a very high negative predictive value of 95.5% and improved specificity of 88%. We have therefore concluded that the large number of unnecessary breast biopsy recommended after mammography can be reduced with use of scintimammography. Kao et al. (39) evaluated 38 women with palpable breast masses who underwent Tc-99m sestamibi breast imaging. The results showed that 27 of the 32 cases of breast carcinoma were correctly biopsied with this method. None of 6 benign lesions showed focal increased uptake with Tc-99m sestamibi. In this cohort group, the diagnostic sensitivity, specificity, and accuracy were 84%, 100%, and 87%, respectively. Scintimammography in this group was performed in supine position.

Our experience and data of others indicate that the overall, sensitivity and specificity of scintimammography for palpable masses are superior to nonpalpable lesions. In a group of 33 nonpalpable lesions, our sensitivity, specificity, positive predictive value and negative predictive value were 88%, 80%, 58%, and 95%, respectively (40). We have also observed that about 5% of our patients exhibit bilateral diffuse breast uptake with Tc-99m sestamibi (uniform or patchy). We consider this group "Probably normal". This finding is seen more often a week before and after womens menustrual period (41). The most single important finding on abnormal cases in our experience is when " focal " abnormal uptake is seen on scinti- mammogram. We have noted that the most optimal condition to interpret the result of scintimammography is directly from the computer screen rather than hard copy images.

We examined the contribution of breast density, as determined by mammography, to the intensity of uptake of Tc-99m sestamibi breast imaging in 578 breasts (42). We found the degree of uptake of Tc-99m sestamibi breast uptake is generally independent of breast density seen on mammograms. This finding is significant, given the observation for low mamographic sensitivity for detection of breast cancer in patients with dense breasts.

SUMMARY

Mammography remians the procedure of choice in screening asymptomatic women for breast cancer. However, in patients with symptoms, other types of imaging play an important role in the detection of malignancies. The high cost and lack of availability of PET and MRI largely precludes the use in this patient population. Tl-201 is not the imaging agent of choice because of its wash-out and redistribution mechanism in tumor cells; low photon energy also makes the agent less optimal for imaging. Tc-99m sestamibi scintimammography, on the other hand, has high sensitivity and improves the specificity of conventional mammography for the detection of breast cancer. In addition, the technique of prone breast imaging is superior to supine imaging bacause of excellent separation of deep breast structures from the myocardium in the left breast, excellent separation of the right breast from the liver and relaxation of the pectoralis muscle, ultimately improving the resoltion of small deep-seated lesions. For these reasons, Tc-99m sestamibi scintimammography deserves further study as a diagnostic technique to potentially reduce the number of mammographically "indicated" breast biopsies which yield negative results for cancer.

REFERENCES

1. American Cancer Society. Cancer facts and figures-1992. Atlanta : American Cancer Society, 1992.

2. Boring CC, Squires TS, Tong T. Cancer statistics, 1992.CA. 42: 19-38; 1992.

3. Ries LAG, Hankey BF, Miller BA, Hartman AM, Edwards BK. Cancer statistics review. 1973-88 NTH Publication no. 91 : 2780. Behesda, Md (USA); J. Natl. Cancer Ins., 1991.

4. Morrison AS, Brisson J Khalid N Breast cancer incidence and mortality in the Breast Cancer Dtection Demostration Project. J Natl Cancer Ins. 80: 1540-1547; 1988.

5. Shapiro S. Evidence on screening for breast cancer from a randomized trail. Cancer. 39 (suppl): 2772-2782; 1977.

6. Tabar L, Fagerberg CJG, Gad A et al. Reduction in mortality from breast cancer after mass screening with mammography: Randomized trial from the breast cancer screening working group of the Swedish Natl. Board of Health & Welfare. Lancet. 1: 829-832; 1985.

7. Tabar L, Fagerberg G, Duffy SW, Day NE. The swedish two county trial of mammographic screening for breast cancer: recent results and calculation of benefit. J Epidemiol Community Health. 43: 107-114; 1989.

8. Sickle WA. Mammographic features of 300 consecutive nonpalpable breast cancers. AJR. 146: 661-663; 1986.

9. Parker SH, Lovion JD, Jobe WF, Luethke JM, Hopper KD, Yakes Wf, Burke BJ. Stereotactic breast biopsy with a biopsy gun. Radiology. 176: 741-747; 1990.

10. Kopans DB. Positive predictive value of mammography. AJR. 158: 521-526; 1992.

11. Jackson VP, Hendrick RE, Kerg SA et al. Imaging of the Radiographically Dense Breast. Radiology. 1988: 297-301; 1993.

12. Polli RS, Mettler FA, Barstow SA, Moradian G, Moskowitz M. Occult breast cancer: Prevalence and radiographic detectability. Radiology. 163: 435-464; 1987.

13. Niloff PH, Shelner NM. False-negative mammograms in patients with breast cancer. Can J Surg. 24: 50-52; 1981.

14. Boyd NF, Wolfson C, Moskowitz M, Carlile T, Petitclerc c, Farri HA, Ry SL. Observer variation in classification of mammographic parenchymal patterns. J Chron Dis. 39: 465-472; 1986.

15. Vineis P, Sinisterero G, Temporelli A, Azzoni L, Bigo A, Burke P. Inter-observer variability in the interpretation of mammograms. Tumori. 74: 275-279; 1988.

16. Bovee WM, Creyghton JH, Getrever KW et al. NMR relaxation and images of human breast tumors in vitro. Philos Trans R. soc. Lond. (Biol). 289: 535-536; 1980.

17. Mansfield P., Morris PG, Ordidye R. Carcinoma of the breast : Imaging by NMR. Br. Radiol. 52; 242-267; 1979.

18. Harms SE, Flamig DP , Hesley KL et al. Fat-suppressed three-dimensional MR imaging of the breast. Radiographics. 13: 247-267; 1993a.

19. Harms SE, Falmig DP, Hesley KL et al. MR imaging of the breast with rotating delivery of excitation of resonance; clinical experience with pathological correlation. Radiology. 187: 439-501; 1993b.

20. Wahl RL, Cody RL, Huchins GD, Mudgett EE. Primary and metastatic breast carcinoma: initial clinical evaluation with PET with radiolabeled glucose analogue 2-(F-18)-Fluoro -2-deoxy-D-glucose. Radiology. 179: 765-770; 1991.

21. Cox PH, Belfer AJ, Van der Pompe WB. Thallium-201 chloride uptake in tumours, a possible implication in heart scintigraphy. Br J Radiol. 49: 767-768; 1976.

22. Cancer B, Kitapci M, Aras T, Erbengi G, Ugur O, Bekdik C. Increased accumulation of hexakis (2-methoxyisobutylisonitrile) technetium (I) in osteosarcoma and its metastatic lymph nodes. J Nucl Med. 32: 1977-1978; 1991.

23. O'Tuama LA, Packerd AB, Treves ST. SPECT imaging of pediatric brain tumor with hexakis (methoxyisobutylnitrile) technetium (I). J Nucl Med. 31: 2040-2041; 1990.

24. Hisada K, Tonami N, Miyamae T. clinical evaluation of tumor imaging with Tl-201 chloride. Radiology. 497-500; 1978.

25. Sluyser M and Hoefnagel CA. Breast carcinomas detected by thallium-201 scintigrapy. Cancer Letters. 40: 161-168; 1988.

26. Waxman AD, Ramanna L, Memsic LD, Foster CE, Silberman AW. Thallium scintigraphy in the evaluation of mass abnormalities of the breast. J Nucl Med. 34: 18-23; 1993.

27. Lee VW, Sax EJ, McAnency DB et al. complemetry role of Thallium-201 Scintigraphy with mammography in the diagnosis of breast cancer. J Nucl Med. 34: 2095-2100; 1993.

28. Mublant JC, Zheng Z, Rapp M, Olier M, Michelot J, Veyre A. In vitro uptake of TC-99m Texobotoxime in carcinoma cell lines and normal cell lines: comparison with Tc-99m sestamibi and thallium-201. j Nucl. Med. 34: 1949-1952; 1993.

29. Caralho PA, Chiu ML, Kronang JF et al. Subcellular distribution and analysis of Tc-99m MIBI in J Nucl Med. 33: 1516-1521; 1992.

30. Package insert. Cardiolite tmDupont Merck Pharmaceuticals. Billerica, MA. DRUG INSERT.

31. Hassan IM, Shaweil A, Constantinides C, Mahmoud A et al. Uptake and kinetics of Tc-99m hexakis 2-methoxy isobutyl isonitrile in benign and malignant lesions in the lungs. Clin. Nucl. Med. 14(5): 33-340; 1989.

32. Delmon-Mongeon LI, Piwnica- Worms D, Vander Abbeele AD, Holman BL, Davison A, Jones AG. Uptake of the cation hexakis (2-methoxyisobutylisonitrile) - technetium-99m by human carcinoma cell lines in vitro. Ca. Res. 50: 2198-2202; 1990.

33. Muller ST, Gut-Tougelides B, Creutzig H. Imaging of malignant tumors with Tc-99m MIBI SPECT. J Nucl Med. 28: 562 (abstract); 1987.

34. Muller ST, Reiners C, Pass M et al. Technetium-99m MIBI and Thallium-201 uptake in bronchial carcinoma.J Nucl Med. 33: 845 (abstract); 1989.

35. Khalkhali I, Mena I, Jouanne E et al. Breast cancer detection with Tc-99m sestamibi prone imaging: Its correlation with mammography and pathology. Clin Nucl Med. 17(9): 761 (abstract); 1992.

36. Kahlkhali I, Mena I, Jouanne E, Diggles L et al. (In press) Prone Scintimammography in patients with suspicion of breast cancer. J of American College of surgeons.

37. Kahlkhali I, Mena I, Diggles L. Review of Imaging techniques for a diagnosis of breast cancer: A new role of prone Scintimammography using Tc-99m sestamibi for Breast imaging. Eur J Nucl Med (In press)

38. Khalkhali I, Cutrone J, Mena I et al. Scintimammography mammography: Complementary role of Tc-99m sestamibi in the prone position for the diagnosis of breast carcinoma. Radiology. 193: 158 (abstract); 1994.

39. Kao CH, Wang SJ, Liu TJ. The use of tchnetium-99m methoxyisobutylisonitrile breast scintigraphy to evaluate palpable breast masses. European Journal of Nuclear Medicine. 21; 432-436; 1994.

40. Cutrone J, Khalkhali I, Mena I. et al. sestamibi breast imaging of nonpalpable mammographically suspicous breast lesions. Clin J Nucl Med. 19: 843 (abstract); 1994.

41. Diggles L, Mena I, khalkhali I. Bilateral increased uptake of TC-99m sestamibi in Scintimammography: Its correlation with the menstrual cycle. JNM Tech. 22: 111 (abstract); 1994.

42. Khalkhali I, Mena I, Diggles L. Limitations of mammography: The role of Tc-99m sestamibi Scintimammography in the diagnosis of breast cancer. Clin Nucl Med. 18-927 (abstract); 1993.