^{99M}Tc-sestamibi scintimammography in detection of recurrent breast cancer

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Abstract

The aim of this study was to asses the accuracy of ^{99m}Tc-sestamibi scintimammography in patients with suspected recurrent breast cancer in the breast or loco regional tissues. After routine analyses in twenty-eight women (clinical examination, ultrasound, X-ray mammography, and fine needle aspiration biopsy) they were examined by scintimammography. All patients with suspected recurrent cancer in the breast or loco regional tissues (19) undergone surgery and the final diagnosis was determined by histopathological examination. Another 9 patients were followed 6-24 months. The scintigraphic studies were correlated with radiological findings and/or with histopathology. There were 19 patients with recurrent tumours (15 with loco-regional recurrent and 4 in another breast). X-ray mammography identified 13 of these cancers. 99mTc-sestamibi scintimammography identified seventeen of recurrent breast cancers. In the seven out of nine patients without cancer, scintimammography were reported as having no changes consistent with cancer. X-ray mammography showed suspected cancer lesions in four out of nine patients without cancer. There were two false-positive scintimammograms and one false negative. Axillary lymph node recurrence occurred in four patients. All of them were positive on scintimammography. 99mTc-sestamibi scintimammography showed higher sensitivity, specificity and accuracy per patient than did X-ray mammography (90,9% vs. 63,6%, 71,4% vs. 57,1% and 83,3% vs. 61,1%, respectively). To identifying recurrent breast cancer disease is better to use scintimammoraphy than X-ray mammography.

KEY WORDS: scintimammography, sestamibi, MIBI, recurrent breast cancer, mammography

Introduction

Breast cancer is the most common malignant tumor among women. In many countries it is the leading cause of death from the malignant diseases among women. According to the data of most countries of the world, except Asia, the incidence and mortality increases with age. The highest rate being among women over 85 where the incidence is over 350/100000. More women die from breast cancer than from all other disease put together. According to the data from 1990 in the USA every 15th minute 4,28 new cases of breast cancer are registered and within the same period of time one woman dies from breast cancer (1). Conservative surgery followed by breast irradiation has replaced modified radical mastectomy as the preferred treatment for early-stage invasive breast cancer. Public education and proactive screening programs have contributed to the early detection of small tumors in a greater percentage of women. Studies have shown that women diagnosed at early stages of invasive breast cancer have equivalent outcomes when they are treated by lumpectomy and radiation therapy or modified radical mastectomy (2,3). The probability of recurrent tumour increases in conserving surgery. Post-surgery and radiotherapy changes as fibrosis and/or inflammation have reduced the accuracy of convectional method of breast imaging as X-ray mammography. Scintimammography is independent of tissue density and being a functional imaging technique (4). The aim of this study is to asses the accuracy of 99mTc-MIBI scintimammography in patients with suspected recurrent breast cancer in the breast or loco regional tissues.

Patient and Methods

Twenty-eight (28) women (median age 44,6 years, range 21-82 years) with suspected recurrent breast cancer in the breast or loco regional tissues were investigated. Six patients had undergone mastectomy, so that a total of 40 breasts were studied. After routine analyses (clinical examination, ultrasound, X-ray mammography, and fine needle aspiration biopsy) they were examined by scintimammography. Scintimammography was performed using one-had gamma camera equipment with a high resolution collimator. The energy pick was centered at 140 KeV with a 10% window. Images were acquired on matrix 128x128. Each image was acquired for 10 minutes and 3 minutes with marker. The distance between the breast and the detector was kept minimal. A dose of 740 MBq of ^{99m}Tc sestamibi was injected into a vein in the foot followed by 10 ml saline flush. The patient was placed in a prone position on an imaging couch design that allowed the breast to be freely dependent of the imaging couch and with lead between breasts. Imaging was performed 10 minutes after injection beginning with affected breast. Lateral views of breasts and axillaae were acquired with patient lying prone. Anterior view of the breasts and both axillaea was performed with patients in supine position with her arms raised behind her had. Delay scintigraphy in prone position (lateral view) was done 60 minutes after injection. Two independent, experienced nuclear medicine physicians analyzed all scintimammograms. Focal accumulation of sestamibi uptake in the breast on early and delay scintigrams was interpreted to represent malignancy. All patients with suspected recurrent cancer in the breast or loco regional tissues (19) undergone surgery and the final diagnosis was determined by histopathological examination. Another 9 patients were followed 6-24 months. The scintigraphic studies were correlated with radiological findings and/or with histopathology. Sensitivity was defined as true positives (TP)/TP+false negatives (FN), specificity as true negative (TN)/TN+false positive (FP), positive predictive values (PPV) as TP/(TP+FP), negative predicative values (NPV) as TN/(TN+FN), and accuracy as (TN+FP)/overall patients.

Results

Table 1. summarizes the ^{99m}Tc sestamibi scintimammography, mammography and histopathologic diagnoses of 19 patients who underwent operation. 15

Histopathological findings	Number	*Scintimammography*		*Mammography*	
		Positive	Negative	Positive	Negative
Malignant findings	18	17	1	13	5
Invasive ductal carcinoma	14	14	0	11	3
Invasive lobular carcinoma	3	3	0	1	2
Ductal carcinoma in situ	1	0	1	1	0
Benign findings	1	1	0	0	1
Fibroadenoma	1	1	0	0	1

TABLE 1. Histopathological, scintimammography and mammography findings in patients undergone operation

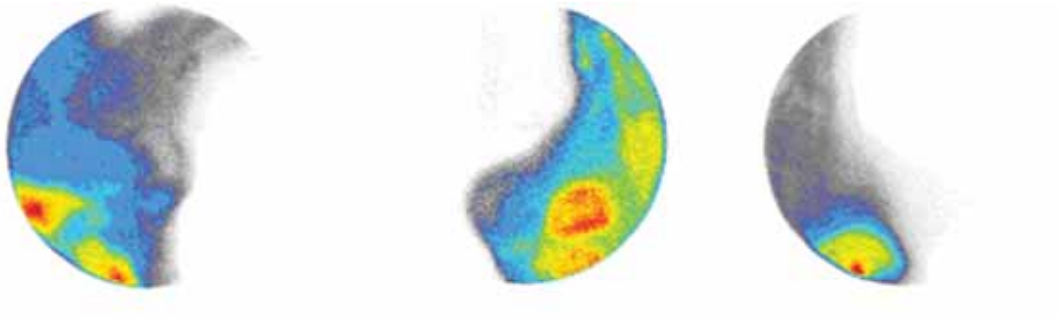

FIGURE 1. ^{99m}Tc sestamibi scintimammography in recurrent breast cancer (left anterior, left lateral and right lateral position)

of them have loco-regional recurrent and 4 in another breast. X-ray mammography identified 13 of these cancers. 99mTc-sestamibi scintimammography identified seventeen of eighteen recurrent breast cancers. One lesion on histopathological finding was fibroadenoma. The one cancer not seen on scintimammography was positive on X-ray mammography. In the seven out of nine patients without cancer, scintimammography were reported as having no changes consistent with cancer. X-ray mammography showed suspected cancer lesions in four out of nine patients without cancer. There were two false-positive scintimammograms and one false negative. Axillary lymph node recurrence occurred in four patients. All of them were positive on scintimammography. Among all lesions with true-positive results confirmed on pathohistology findings, scintimammography demonstrated focal areas of increased 99mTc uptake that corresponded to breast carcinoma (Figure 1). ^{99m}Tc-sestamibi showed higher sensitivity, specificity and accuracy per patient than did X-ray mammography (Table 2).

Discussion

A long time ago, mastectomy or removal of the entire breast was always used to establish local control of breast cancer. But now, in many cases, women can keep their breasts by careful surgery to remove all signs of breast cancer followed by radiotherapy, called "breast conserving surgery" or "lumpectomy". Conservative surgery followed by breast irradiation has replaced modified radical mastectomy as the preferred treatment for early-stage invasive breast cancer. With the increasing demand for breast conservation surgery, the probability of recurrent tumor within the breast increases (5). Mammography is the most useful diagnostic imaging method for screening and diagnostic breast cancer. It still has some limitations. Its sensitivity decreased in some circumstances such as dense breast, breast prosthesis or following radiation, surgery or biopsy. Post-surgery and radiotherapy changes as fibrosis, inflammation have reduced the accuracy of mammography in diagnosing of recurrent breast cancer (6). In our study the accuracy of mammography was also low (47%) due to the high number of false positive and false negative cases. Surgery and radiation therapy changed the structure of breast and mammography was not able to see thought this changes of breasts. Various diagnostic procedures have been used in an attempt to resolve some of limitations of mammography. Thus, with the "anatomic based" diagnostic procedures, we can cite ultrasound, color Doppler ultrasound, digital mammography, computed tomography and magnetic resonance imaging. But, still the problem exists. It is very difficult to see the character of the lesion in changed breast tissue. As the "functional based" diagnostic procedures we can cite scintimammography (7). ^{99m}Tc sestamibi is the single photon tracer of choice in the study of breast cancer. ^{99m}Tc sestamibi is not related with breast tissue density or with the presence of scar tissue. The biological principle of the technique is simply based on the fact that specific radiopharmaceuticals are absorbed at higher rates by malignant cells in comparison to normal cells. Its precise uptake mechanism into the tumor cells is still not clearly understood. More than 90% of the activity is located in the mitochondria. Exper-

	scintimammography	*mammography*
sensitivity	95%	68%
specificity	78%	56%
positive predictive value	90%	76%
negative predictive value	87%	45%
accuracy	89%	47%
Fibroadenoma	1	1

TABLE 1. Statistical parameters of scintimammography and mammography

imental studies suggest that the main factor that appears to intervene in the uptake of the radiopharmaceutical is the electrostatic attraction between the positive charge of the ^{99m}Tc sestamibi and the negative charge of the mitochondria. Other factors that have been suggested to apparels in the uptake are tumour perfusion, histological type, metabolic request or passive membrane diffusion (8). For these reasons scintimammography could have higher accuracy in the detection of recurrent breast cancer than mammography. It has also been shown that scintaimammography be reproducible with inter and intra-observer correlation of 0,94 or more (9). Yildiz et al. (10) in his prospective study determine the role of ^{99m}Tc-sestamibi scintigraphy in the evaluation of recurrence and metastases in breast cancer patients with mastectomy and/or radiotherapy. In 36 patients with suspected recurrent breast cancer the scintigraphic studies were correlated with radiological findings and/or with histopathology. The sensitivity and the specificity of sestamibi imaging were 89%, 81%, in other conventional radiological imaging methods were 95%, 65%, respectively. ^{99m}Tc-sestamibi scintigraphy using SPECT imaging may provide useful complementary information in patients with suspected recurrence breast cancer (10). Bongers and al. have shown that ^{99m}Tc tetrofosmin scintimammography accurately detected 100% of the local recurrences independently of the extent of the preceding surgical intervention. The sensitivity and specificity of the technique for the detection of regional recurrent disease were 93% and 90%, respectively. These results are substantially higher than those of other imaging modalities (11). Kolasinska et al. analyzed 101 women with suspected of loco-regional recurrence breast cancer. During the study the patients did not receive any treatment other then hormonotherapy. All patients undergone mammography and scintimamography. The results of each type of imaging compared with histology. In the ROC curve analysis 5 points of certainty were used: from 1 being definitely normal to 5 being definitely cancer; grades 4 and 5 were counted as positive. The overall sensitivity value of scintimamography was 84% and specificity was 85%, compared with a sensitivity of 52% for mammography and a specificity of 84%. Analysis of areas under ROC curves provides statistically significant difference between scintimammography and mammography ($p < 0,05$). Combining the two tests did not significantly improve the diagnostic accuracy of sequence imaging over scintimammography. ROC curve analysis demonstrates that scintimammography should be the primary investigation in suspected local recurrence following breast conservation surgery (12). In our study scintimammography also showed an excellent sensitivity and specificity, 85%, 78%, in patients with recurrent breast cancer. In all patients with recurrent breast cancer scintimmagraphy with ^{99m}Tc sestamibi were positive. Cwikla et al. showed one new dimension of scintimammography. They also analyzed the accuracy of Tc-99m sestamibi scintimammography in 63 women with suspected recurrent breast cancer in the breast and/or locoregional tissues. Recurrent breast cancers were identified by scintimammography in 78%, by mammography in 42% and in 90% were positive on one test or the other. In addition Tc-99m sestamibi scintimammography identified 63% of axillary lymph nodes with recurrent tumour and 4/6 sites of recurrent tumour present elsewhere. They concluded that scintimammography can identify locoregional recurrence outside of the breast and as other authors it is more accurate in identifying recurrent disease in the breast than mammography (13). In our study axillary lymph node recurrence occurred in four patients and all of them were positive on scintimammography. Scintimammography showed false positive findings in a case of inflammation. Bongers et al. reported fourth patient with 99mTc tetrofosmin uptake in the scar, which appeared to be an inflammatory lesion, proven by a histopathological biopsy and 1 year clinical follow-up (11). Our two cases of false positive scintimammography with increase uptake in the scar were result of inflammation. It is important to exclude the inflammation, because scintimamography is positive in this case. In our study scintimammography was false negative in one case with ductal carcinoma in situ. The lesion was nonpalpable, located in the medial part of the breast, which is further away from detector. Therefore, it is reasonable to believe that location, size and histological structure of this lesion may explain the false negative results.

Conclusion

^{99m}Tc-sestamibi scintimammography has high sensitivity, specificity and accuracy in patients with suspected recurrence of cancer in the breast or loco-regional tissues after conserving surgery. To identifying recurrent breast cancer disease after conserving surgery is better to use scintimammoraphy than X-ray mammography.

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