

BREAST CANCER DETECTION WITH ^{99m}Tc MIBI IMAGING AND MAMMOGRAPHY

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ABSTRACT

Screening mammography in female patients provides good sensitivity in the detection of breast abnormalities but low specificity for the diagnosis of breast carcinoma. Thus many patients end up with unnecessary biopsy and/or lumpectomy. The use of nuclear medicine methods in detection of malignancy has been widely studied with various radiopharmaceuticals. The objective of this study was to study the efficacy ^{99m}Tc -MIBI scintimammography and mammography in the detection of breast carcinoma. The diagnosis would be made by pathological findings of the tissue or clinical follow up for at least 6 months. There were 33 female patients included in the study, among these there were 7 cases with known carcinoma of breast and clinically suspected of recurrent. Of all 33 cases, 14 cases was diagnosed as breast carcinoma and 19 cases as benign disease of the breasts. The results showed that sensitivity, specificity, accuracy, positive predictive value and negative predictive value of ^{99m}Tc -MIBI scintimammography in the diagnosis of breast carcinoma were 93%, 100%, 97%, 100% and 95% respectively. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of mammography were 100%, 63%, 79%, 67% and 100% respectively. We concluded that ^{99m}Tc -MIBI scintimammography has a good efficacy and increase specificity of mammography in the diagnosis of breast carcinoma. We suggested that patients should have mammography performed first, if the lesion is indeterminated by mammography then ^{99m}Tc -MIBI scintimammography will be the next step for investigation.

INTRODUCTION

Breast cancer is a very common neoplasm in women around the world. In the year 1993, International Agency for Research on Cancer reported that breast cancer ranked the third most common neoplastic disease in Thai women after cervix cancer and liver cancer with incidence rate of 11.9/100,000 population¹. In the same year 208 breast cancer patients were treated in Chulalongkorn Hospital². It comprised of 14.77%

of all cancer patients and ranked the second after cervix cancer.

Most patients present with palpable breast mass. However, physical examination alone usually unreliable for the differentiation between benign and malignant mass³. Mammography is an accepted method of choice both for screening and diagnosis of breast cancer. However, one paper reported false negative findings of up to 26.8%⁴. Further-

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more the sensitivity of mammography is lower in young patients, dense breasts, fibrocystic disease, evaluation after biopsy, surgery or radiotherapy⁵. ^{99m}Tc-methoxyisobutyl isonitrile (MIBI) is a tracer that is widely used for myocardial perfusion imaging. It has been found that ^{99m}Tc-MIBI can be used to detect different types of neoplasms such as brain gliomas, bone cancer, thyroid cancer, lung cancer, etc⁶. In 1992, there are reports of ^{99m}Tc-MIBI in the diagnosis of breast cancer^{7,8} and since then, various authors have studied the possible usefulness of ^{99m}Tc-MIBI scintimammography in the evaluation of breast cancer^{9,10,11}.

The aims of this study were to evaluate the locally produced ^{99m}Tc-MIBI in Thai women with suspicious of breast cancer and to determine whether a diagnostic protocol based on the joint use of mammography and scintimammography is capable of increasing the sensitivity and specificity in the detection of breast cancer.

MATERIAL AND METHODS

We prospectively studied 33 women of age range 30-67 years (mean \pm sd. = 46.9 \pm 8.4 years). Mammography and ^{99m}Tc-MIBI scintimammography were performed in all subjects. Inclusion criteria consisted of: a) women who were suspected of having breast cancer by physical examination and/or mammography, b) known cases of treated breast cancer with suspected of recurrence. Final diagnosis was established by biopsy or fine needle aspiration or clinical follow up for at least 6 months.

Subject was examined by surgeon then mammography and scintimammography were performed within 1 week. Mammography was performed in all subjects in craniocaudal and mediolateral oblique views. And if necessary, additional projections including magnification or spot compression techniques were used. The mammogram was evaluated by radiologist according to the findings, and the studies were divided into three group representing positive, negative or indeterminate for malignancy.

MIBI, which was produced by the Office of Atomic Energy for Peace, Thailand, was labeled with Tc-99m in the Nuclear Medicine Division, Chulalongkorn Hospital. Twenty mCi (740 MBq) was injected into patient's arm vein on the contralateral side of the affected breast. When there were clinical suspicions of having bilateral breast masses, the injection was made in the dorsal vein of foot. The same imaging sequence was performed in all subjects, beginning with the lateral view of the affected breast, followed by the contralateral breast and the anterior view of both breasts. For the lateral view, subject lied on the scanning bed on her side with gamma camera head placed underneath the bed. Planar image acquisition began 5 minutes after radiopharmaceutical administration using low-energy parallel hole, high-resolution collimator, 128x128 matrix size and 20% window centered at 140 KeV. Each image acquisition time was 10 minutes.

All focal accumulation of ^{99m}Tc-MIBI higher than the surrounding background of the breast was considered an abnormal increased uptake. Then, in such a case, "tumor uptake ratio (TUR)" was calculated.

$$\text{Tumor uptake ratio} = \frac{\text{average count per pixel in area of increased tracer accumulation}}{\text{average count per pixel in surrounding background area}}$$

RESULTS

Of 33 subjects included in this study, 26 were suspicious of primary breast cancer and 7 were suspicious of recurrent disease. Among these subjects, final diagnoses were established by surgical biopsy in 21 cases, by fine needle aspiration in 7 cases and by 8-15 months clinical follow up in 5 cases. There were 14 malignant and 19 benign conditions. One subject was diagnosed as bilateral invasive ductal carcinoma. Details of the final diagnoses were shown in table 1.

In 14 subjects with malignant disease, mammography gave positive, negative and indeterminate results in 10, 0 and 4 cases respectively. Scintimammography showed abnormal increased uptake in 13 cases with TUR between 1.48 - 3.05 (mean \pm s.d. = 2.16 ± 0.15). The size of the lesion varied from 0.5 - 5cm. The smallest mass detected by scintimammography was 1 cm. Figure 1 was a sample of a 40 years old patient with final diagnosis of invasive ductal carcinoma, scintimammography show an area of increased radiotracer accumulation in right breast with TUR of 2.0. One case with negative scintimammography, the mass size was 0.5 cm. and mammography also gave indeterminate result (Table 2). Among 7 cases of suspected recurrent, one case was found to have recurrent of ductal carcinoma with palpated mass

of 1 cm. Scintimammography result in TUR 1.8 but the lesion was indetermined by mammography (Fig. 2).

In 19 subjects with benign conditions, mammography gave positive, negative and indeterminate results in 1, 12 and 6 cases respectively. Scintimammography showed no abnormal uptake in 12 cases but 7 cases showed abnormal increased uptake with TUR between 1.13 - 1.33 (mean \pm s.d. = 1.26 ± 0.07). Figure 3 was a sample of a 46 years old patient with final diagnosis of fibroadenoma, scintimammography show an area of faintly increased radiotracer accumulation in left breast with TUR of 1.3. One case of chronic inflammation with fat necrosis, mammography gave positive result but no abnormal uptake by scintimammography (Table 3).

If we considered TUR value of 1.40, which was the value of mean \pm 2 s.d. of benign condition, as diagnostic cut off value for malignant lesion, scintimammography will give only 1 false negative without false positive case (Table 2, 3). Then sensitivity and specificity of scintimammography for the diagnosis of malignancy will be 93% and 100% respectively.

Table 1 Final diagnoses in 33 subjects included into the study.

Diagnosis	number
Ductal carcinoma	14
Fibrocystic disease	4
Chronic inflammation / Fat necrosis	3
Fibroadenoma	2
Granuloma	2
Mammary dysplasia	1
No evidence of malignancy	7
Total	33

Table 2 Showed diagnostic results of mammography and scintimammography in patients with malignant diseases.

	Scintimammography		No abnormal uptake
	Abnormal increased uptake		
Mammography	TUR > 1.40	TUR < 1.40	
Positive	10	-	-
Negative	-	-	-
Indetermined	3	-	1

Table 3 Showed diagnostic results of mammography and scintimammography in patients with benign conditions.

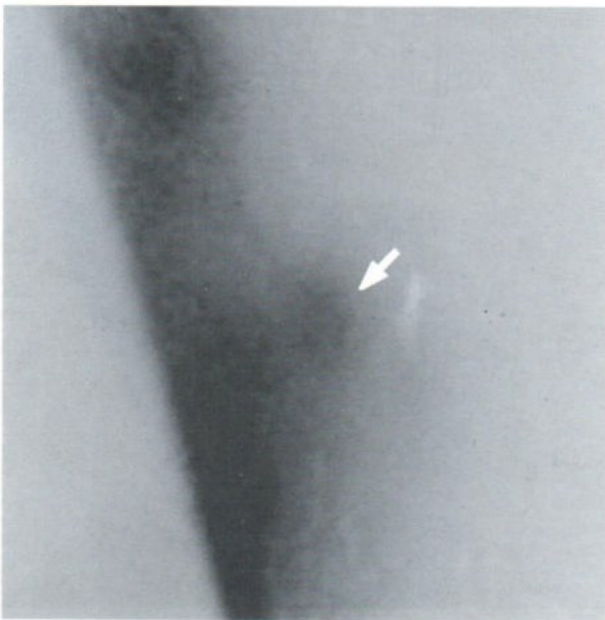
	Scintimammography		No abnormal uptake
	Abnormal increased uptake		
Mammography	TUR > 1.40	TUR < 1.40	
Positive	-	-	1
Negative	-	3	9
Indetermined	-	4	2



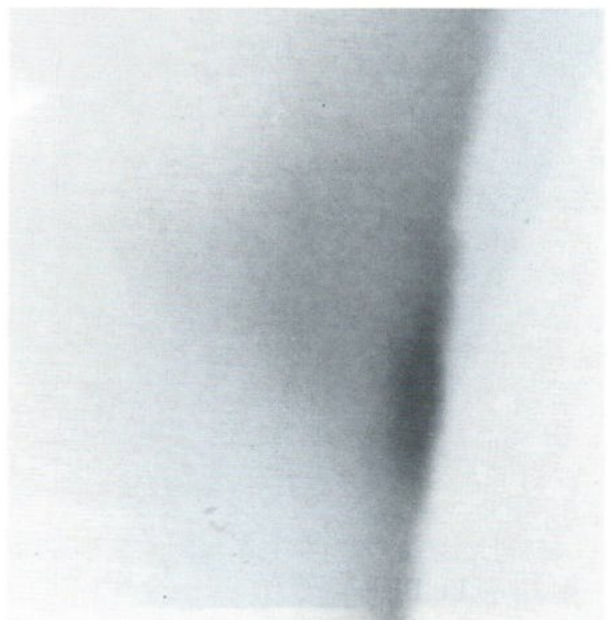
1A.



1B.



1C.



1D.

Fig. 1 A 40 years old patient with final diagnosis of invasive ductal carcinoma, mammogram of right breast (CC and MLO views) showed a microlobulated mass with spiculated border at right upper outer quadrant being highly suspicious of malignancy (A = right CC, B = right MLO). Scintimammography show a round area of increased radiotracer accumulation in right breast (arrow) with TUR of 2.0 (C = right breast, D = left breast).
MLO = mediolateral oblique, CC = craniocaudal

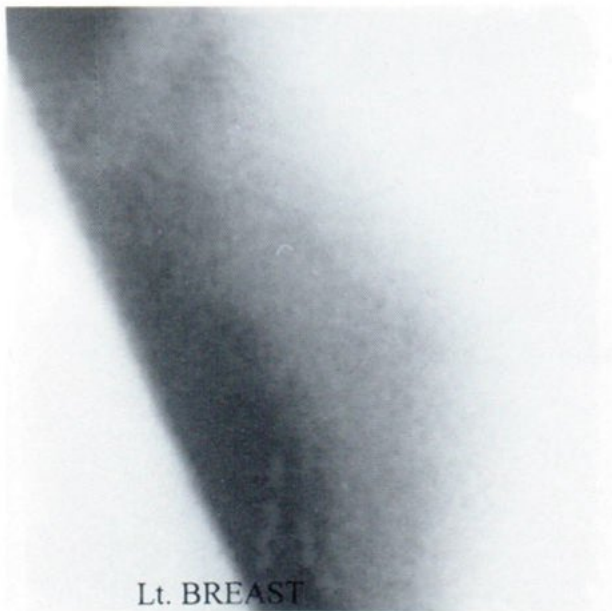
Rt. BREAST



2A.



2B.

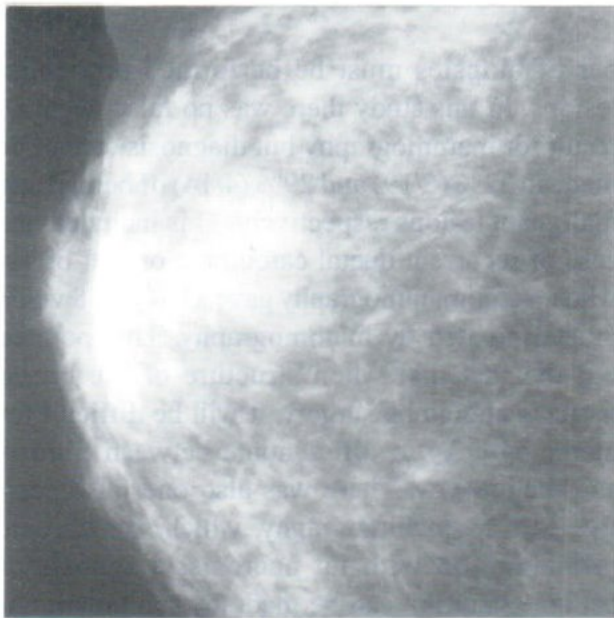


2C.



2D.

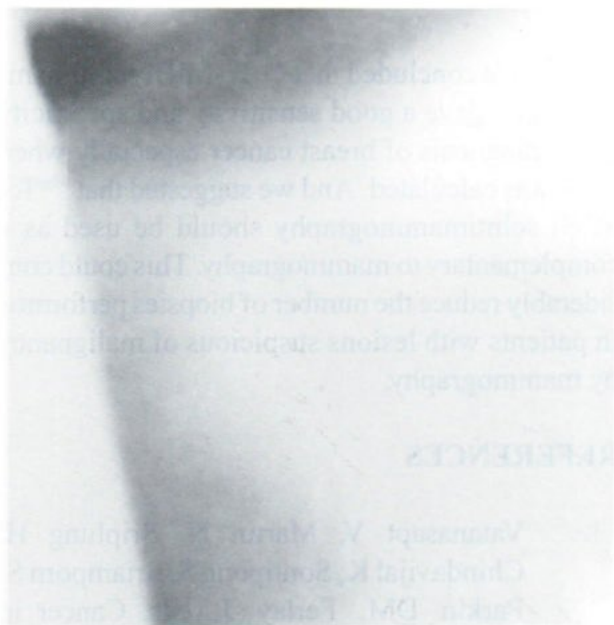
Fig. 2 A 41 years old patient who had wide excision done for breast carcinoma, on follow up recurrent of malignancy was suspected. Mammogram of left breast (CC and MLO views) showed an ill-defined opacity with radiating fibrosis strands at left upper outer quadrant, post-operative scar is possible but residual tumor cannot be definitely excluded (A = left CC, B = left MLO). Scintimammography show a round area of increased radiotracer accumulation in left breast (arrow) with TUR of 1.8 (C = right breast, D = left breast).



3A.



3B.



3C.



Lt. BREAST

3D.

Fig. 3 A 46 years old patient with final diagnosis of fibroadenoma, mammogram of left breast (CC and MLO views) showed a lobulated well-defined border soft tissue mass at left upper middle quadrant without hypodensity rim, fibroadenoma is suspected but malignancy cannot be definitely excluded (A = left CC, B = left MLO). Scintimammography show an oval area of faintly increased radiotracer accumulation in left breast (arrow) with TUR of 1.3 (C = right breast, D = left breast).

DISCUSSION

During the past several years, many studies have reported the successfulness of using ^{99m}Tc -MIBI in the evaluation of breast lesions.¹²⁻¹⁷ The results of this technique in the detection of breast cancer, in general, were good with a sensitivity between 67%¹⁸ and 94%¹⁹ and a specificity between 72%²⁰ and 100%²¹. In this study the sensitivity and specificity were 93% and 63% respectively if TUR were not taken into consideration. However, if TUR of equal to or greater than 1.40 were used as the diagnostic criteria for malignancy, specificity would dramatically improve to 100%. This was because, as generally known that the accumulation of ^{99m}Tc MIBI will increase in some benign conditions with hypercellularity such as fibrocystic disease and fibroadenoma²²⁻²⁵. Such conditions have been found to be the risk of breast cancer^{26,27}. There were 2 cases of fibrocystic disease and 1 case of fibroadenoma in this study, which resulted in positive scintimammography. We also found histologically hypercellularity in each case of mammary dysplasia and chronic inflammation. However, TUR in all these cases were not greater than 1.33. In all other reports, the TUR in all but one malignant tumor were greater than 1.48. Tallifer R.²⁸, Maurer DF.²⁹, and Khalkhali I.³⁰ reported TUR for their breast cancer subjects equal to $2.2 + 0.7$, $1.82 + 0.95$ and $2.13 + 0.93$ respectively. One false negative case was invasive ductal carcinoma with a mass size of 0.5 cm. Most reports also found the smallest mass that could be detected by ^{99m}Tc -MIBI scintimammography was 0.8-1.0 cm³¹⁻³³

Mammography is an accepted technique in screening for breast cancer. However, in many occasions, distinguishing between benign and malignant lesion is unreliable. For example patient with breast prosthesis, some cases of fat necrosis and women with dense breast³⁴. And because the positive predictive value of mammography is approximately 15%-30%³⁵, a large num-

ber of biopsies must be performed on benign lesions. In this study there was no false negative result for mammography but diagnosis cannot be made in 32% (6/19) and 29% (4/14) of benign and malignant lesions respectively. This included one case of recurrent ductal carcinoma on left breast whose scintimammography gave TUR of 1.8 while indetermined by mammography. This pointed out the fact that when structure of the breast tissue is altered by surgery, it will be difficult for mammography to differentiate between fibrosis and malignancy. There was also one false positive case by mammography, which was chronic inflammation with fat necrosis, diagnosis of benign condition can be made by scintimammography.

CONCLUSION

We concluded that ^{99m}Tc -MIBI scintimammography gave a good sensitivity and specificity in the diagnosis of breast cancer especially when TUR was calculated. And we suggested that ^{99m}Tc -MIBI scintimammography should be used as a complementary to mammography. This could considerably reduce the number of biopsies performed in patients with lesions suspicious of malignancy by mammography.

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