Comparing thallium-201 spect mammoscintigraphy and ultrasonography to detect breast cancer in mammographical dense breasts

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The aim of our study was to compare the usefulness of thallium-201 (Tl-201) single photon emission computed tomography (SPECT) mammoscintigraphy and ultrasonography to detect breast cancer in mammographical dense breasts. This study included 32 Taiwanese female patients with indeterminate mammographic probability of malignancy due to mammographical dense breasts. Both Tl-201 SPECT mammoscintigraphy and ultrasonography were performed for each patient. Then, all of the 32 breast masses undervent biopsies or operations to obtain finally pathological diagnoses. Based on the finally pathological diagnoses, 24 masses were breast cancer and 8 masses were benign breast tumors among the 32 patients. Twenty-two cancers and one benign tumor had positive Tl-201 SPECT mammoscintigraphic findings. The sensitivity, specificity, and accuracy were 92%, 88%, and 91%. Twenty-two cancers and 5 benign tumors had positive ultrasonographic findings. The sensitivity, specificity, and accuracy were 92%, 38%, and 78%, respectively. To detect breast cancer in patients with non-diagnostic mammogram because of mammographically dense breasts, Tl-201 SPECT mammoscintigraphy and ultrasonography have the same sensitivity to screen breast masses. However, due to its higher specificity, Tl-201 SPECT mammoscintigraphy should be useful to confirm the ultrasonographic findings.

Key words: Thallium-201, single photon emission computed tomography, mammoscintigraphy, ultrasonography, breast cancer, dense breast.

Breast cancer, the leading causes of cancer related death in women in Taiwan, still poses a challenge to diagnostic procedures. The early detection of breast cancer relies on patient self-examination and physician physical examination. Besides physical examination, the most widely used tool for detection of breast cancer is radiographic mammography [3, 12]. Despite technical improvements and major advantages associated with the use of mammography, this procedure has some limitations in clinical practice. However, mammography is limited and less effective in women with dense breasts [17, 20]. On the average, Taiwanese women have smaller and denser breasts than western women. Therefore, other complementary imaging techniques such as breast ultrasonography [6, 14, 18] and mammoscintigraphy with technetium-99m sestamibi (Tc-MIBI) [10, 22] have evolved and gained clinical acceptance over the decades to solve this problem.

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Thallium-201 (Tl-201) has almost the same value as Tc-99m MIBI in detectability of breast cancers [2]. In addition, because of its fast clearance from circulation, Tl-201 seems to have a higher contrast than Tc-99m MIBI to detect breast cancer [2, 4]. However, no definite results of Tl-201 with single photon emission computed tomography (SPECT) to detect breast cancer in mammographically dense breasts were presented when compared with ultrasonography in Taiwan. Therefore, the aim of the present descriptive study was to compare the usefulness of Tl-201 SPECT scintimammography and ultrasonography to detect breast cancer in Taiwanese women with mammographically dense breasts.

Patients and methods

Patients. This study included 32 Taiwanese female patients (aged: 44.6 ± 10.6 years old) with indeterminate probability of malignancy on mammography because of

Table 1. Detailed data of the patients in this study

Patient No.	Age (Years)	Ultrasonography Findings	Ultrasonography Results	Tl-201 SPECT scintimammography Findings	Tl-201 SPECT scintimammography Results	Pathology Findings	Pathology Results
1	29	Negative	TN	Negative	TN	Fibroadenoma	Benign
2	36	Negative	TN	Negative	TN	Fibroadenoma	Benign
3	38	Negative	FN	Negative	FN	Infiltrating ductal ca	Malignant
4	58	Negative	TN	Negative	TN	Fibroadenoma	Benign
5	65	Negative	FN	Positive	TP	Infiltrating ductal ca	Malignant
6	32	Positive	FP	Negative	TN	Fibroadenoma	Benign
7	39	Positive	FP	Negative	TN	Intraductal papilloma	Benign
8	41	Positive	TP	Negative	TP	Infiltrating ductal ca	Malignant
9	45	Positive	FP	Negative	TN	Adenomyonegative epithelioma	Benign
10	48	Positive	FP	Negative	TN	Fibroadenoma	Benign
11	48	Positive	TP	Negative	TP	Infiltrating ductal ca	Malignant
12	57	Positive	TP	Negative	FN	Infiltrating ductal ca	Malignant
13	28	Positive	FP	Positive	FP	Fibroadenoma	Benign
14	30	Positive	TP	Positive	TP	Intraductal comendocarcinoma	Malignant
15	30	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
16	32	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
17	36	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
18	37	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
19	41	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
20	41	Positive	TP	Positive	TP	Medullary ca	Malignant
21	42	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
22	44	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
23	45	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
24	46	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
25	47	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
26	48	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
27	48	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
28	53	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
29	59	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
30	60	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
31	61	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant
32	62	Positive	TP	Positive	TP	Infiltrating ductal ca	Malignant

Tl-201 – thallium-201, SPECT – single photon emission computed tomography, TP – true-positive, TN – true-negative, FP – false-positive, FN – false-negative.

mammographical dense breast. All of the 32 breast masses were palpable and detected on physical examinations by experienced breast surgeons. Before excision biopsies or operations, both Tl-201 SPECT mammoscintigraphy and breast ultrasonography were performed for each patient. Mammography was performed using a mammography unit (BENNETT M-CTR BMC 28195 M-145 95480-05 100KHZ) with Kodak Min-R 2000 film in standard craniocaudal and mediolateral projections; if necessary, oblique and axillary tail views were taken. All mammography findings were interpreted indeterminate due to dense breasts through agreement of at least two out of three experienced radiology physicians. Then, excision biopsies or operations were performed to obtain finally pathological diagnoses for all patients.

Tl-201 SPECT mammoscintigraphy. Tl-201 SPECT of the chest and breasts were performed with a Vertex dual-head gamma camera (ADAC, Milphas, CA) equipped with low-energy, high-resolution collimators 10–15 min after intravenous injection of 150 MBq Tl-201 chloride. Acquisition was based on 360 noncircular rotation with 7 step angles, 60 sec per frame, 64 x 64 x 64 matrix, zoom factor 1.85. Reconstruction was performed with Butterworth filter, order 5, cutoff 0.35; one-pixel images, obtained in the sagittal, coronal and transverse planes. All Tl-201 SPECT mammoscintigraphic findings were independently interpreted by the agreement of at least two of three experienced nuclear medicine physicians without knowledge of final histopathological diagnoses. Scans were classified as positive (abnormal focal accumulation of tracer uptake at the tumor site) or negative (no abnormal tracer uptake at the tumor site).

Ultrasonography. Ultrasonographic examination of the breast was performed in all patients. An aloka 650 (Aloka, Tokyo, Japan) ultrasonography with a high-resolution (7.5 mhz) mechanical sector probe for direct skin contact was used. The patients were placed in the supine oblique position with the side to be examined raised slightly to distribute the breast tissue evenly over the pectoral muscle. The ipsilateral arm was raised to tense the breast as much as possi-

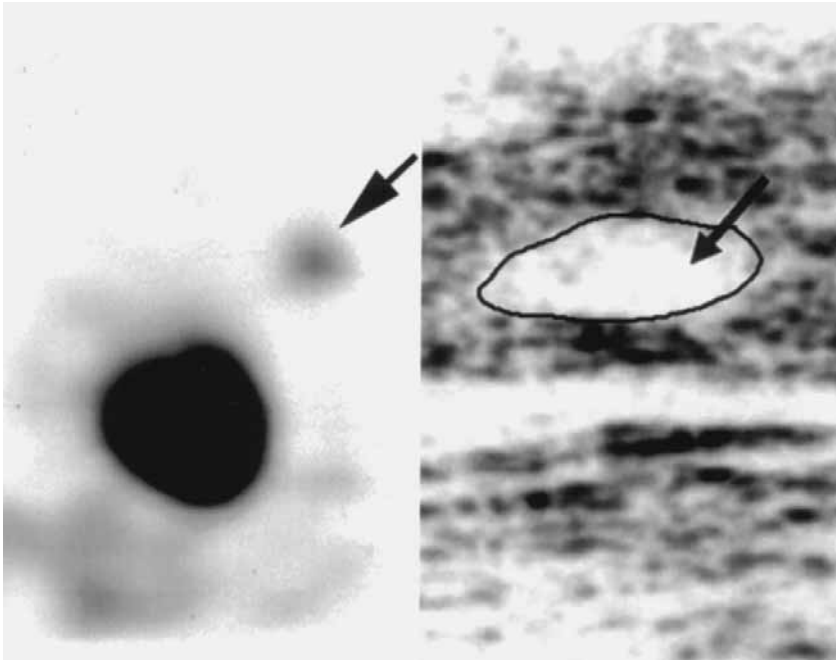

Figure 1. In a 65 year-old female patient (case no. 32) with a palpable mass in the left breast the pathologic finding demonstrated an infiltrating ductal carcinoma. Tl-201 SPECT scintimammography (left) revealed a lesion with increased Tl-201 uptake in the left breast (arrow) and was considered as a true-positive finding. Ultrasonography (right) revealed a cyst (arrow) in the left breast and was considered as a false-negative finding.

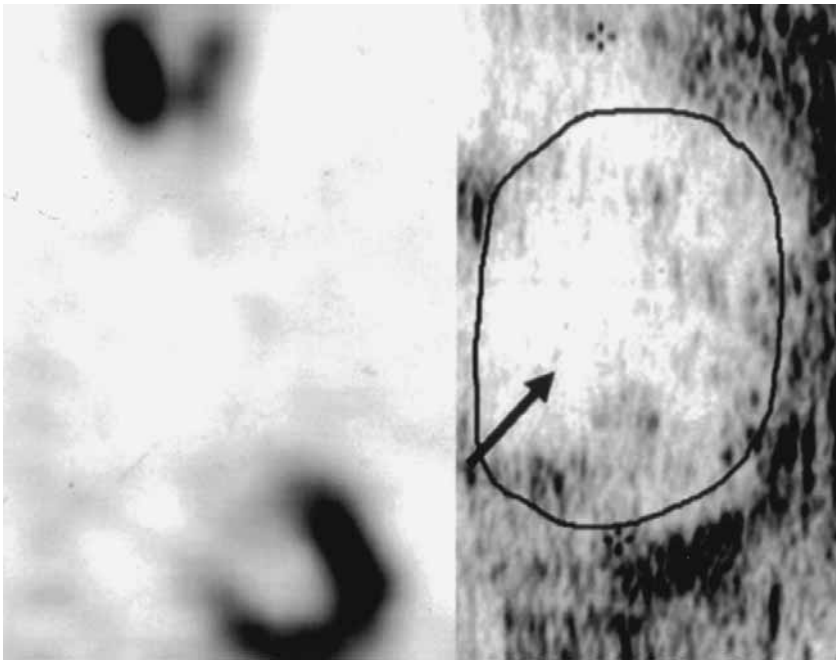

Figure 2. In a 32 year-old female patient (case no. 5) with a palpable mass in the left breast the pathologic finding demonstrated a fibroadenoma. Tl-201 scintimammography (left) revealed no definitely abnormal Tl-201 uptake in the left breast and was considered as a true-negative finding. Ultrasonography (right) revealed a hypoechoic nodule (arrow) in the left breast and was considered as a false-positive finding.

ble. Scans were obtained both transversely and longitudinally, taking special care to examine the periphery to avoid missing any occult lesions. All breast ultrasonographic findings were independently interpreted by agreement of at least two of three experienced physicians without knowledge of final histopathological diagnoses. All breast lesions demonstrated on ultrasonography were scored as malignant or benign.

Results

Detailed patients' data are shown in Table 1. Based on the final histopathological diagnoses, Tl-201 SPECT mammoscintigraphy revealed 22 true-positive cases (Fig. 1), 1 false-positive case, 7 true-negative cases (Fig. 2), and 2 false-negative cases (Fig. 3). The diagnostic sensitivity, specificity, and accuracy rates of Tl-201 SPECT mammoscintigraphy were 91.7%, 87.5%, and 90.6%, respectively, in detecting breast cancer from the 32 patients with mammographic dense breasts and indeterminate probability of malignancy. In addition, no Tl-201 SPECT mammoscintigraphy related discomfort or side effects were found in the 32 female patients. Ultrasonography revealed 22 true-positive cases, 5 false-positive cases (Fig. 2), 3 true-negative cases, and two false-negative cases (Fig. 3). The sensitivity, specificity and accuracy were 92%, 38% and 78%, respectively.

Discussion

Certainly, early detection would improve survival rates of women suffering from breast cancer. Many studies have demonstrated that mammography is the most effective tool and is superior to physical examination alone to early detect breast cancer [12, 19]. Mammography has a relatively high sensitivity in the range of 85% to 90%, especially in the examination of fatty breasts. Unfortunately, mammography is limited and less reliable to detect breast cancer in women with dense breasts [15, 17, 20]. Therefore, there is

a need for the development of new and reliable diagnostic imaging methods to complement mammography to detect breast cancer in patients with mammographical dense breasts.

Ultrasonography of breast is another imaging method that is non-invasive, convenient and most breast tumors can be visualized on ultrasonography [7, 8, 11]. However, diagnostic efficacy depends on the type of equipment and the size of the breast mass. In addition, many other factors can influence the results of ultrasonography, especially the skill level of the examiners. In our study, although ultrasonography had the same sensitivity that of Tl-201 SPECT mammoscintigraphy, nevertheless more false-positive cases were found on ultrasonography (Tab. 1). Therefore, due to no radiation, ultrasonography is thought to be more suitable to screen breast masses than Tl-201 SPECT mammoscintigraphy in patients with indeterminate mammographic probability of malignancy due to dense breasts.

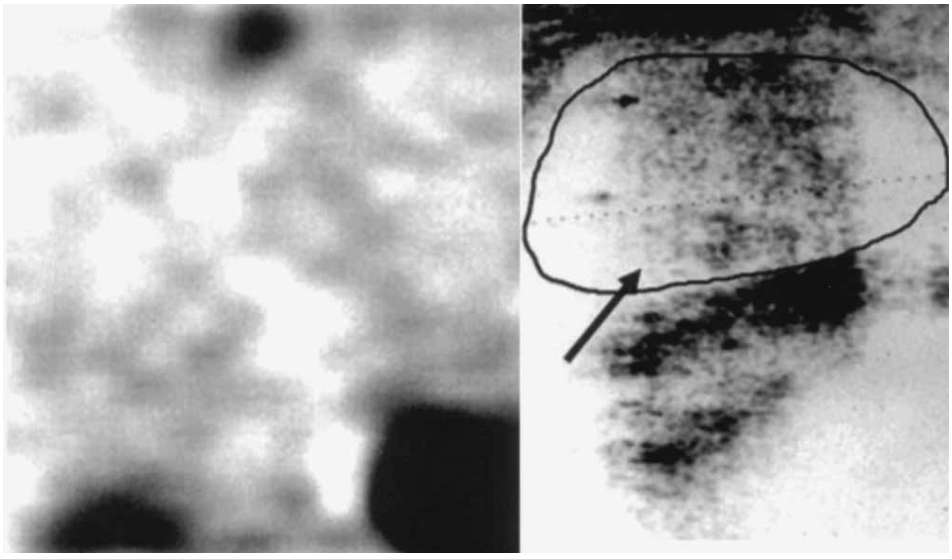

Figure 3. In a 41 year-old female patient (case no. 14) with a palpable mass in the right breast the pathologic finding demonstrated an infiltrating ductal carcinoma. Tl-201 SPECT scintimammography (left) revealed no definitely abnormal Tl-201 uptake in the right breast and was considered as a false-negative finding. Ultrasonography (right) revealed an irregular heterogenous mass (arrow) in the right breast and was considered as a true-positive finding.

The primary mechanism of Tl-201 tumor uptake is thought to be linked to Na,K-ATPase pump in the cell membrane. Biologically, Tl-201 is thought to act similarly to potassium and competes with potassium for intracellular transporter across the cell membrane via the Na,K-ATPase system [23]. Previous studies have suggested that areas of fibrotic tissuess do not accumulate Tl-201 due to nonfunctioning of the ATPase cell membrane pump [9]. This prevents active transport of Tl-201 into areas of fibrotic tissues. Thus, Tl-201uptake appears to reflect the viability of the metabolic activity of tumor cell [9]. Therefore, Tl-201 SPECT is considered superior to mammography to detect breast cancer (increased Tl-201 uptake) from benign lesions (without Tl-201 uptake) in dense breasts.

In 1988, Sluyser and Hoefnagel firstly reported on Tl-201 for detection of breast cancer and metastases [21]. Since then, few other studies have demonstrated that Tl-201 imaging had high accuracy in detecting the breast cancer in comparison with mammography or ultrasonography [5, 13]. However, the major limitation of Tl-201 scintimammography to detect breast cancer is the smaller size of the lesion than 1.5–2.0 cm [22, 23], because most of the studies with Tl-201 mammoscintigraphy were performed with planar imaging. Therefore, in this study, we used SPECT imaging to increase the imaging resolution and detection sensitivity. In this study, the results of diagnostic sensitivity, specificity, and accuracy of Tl-201 SPECT mammoscintigraphy were 91.7%, 87.5%, and 90.6%, respectively, to detect breast cancer in the patients with mammographically dense breasts and indeterminate probability of malignancy. There was only one patient with a benign breast lesion who had a false-positive Tl-201 SPECT mammoscintigraphic finding. This false-positive result may have been due to an inflammatory process or a highly cellular adenoma. Two patients with malignant breast lesions had false-negative Tl-201 SPECT mammoscintigraphic findings. The possible causes of these false-negative results include smaller tumor size (all breast tumors found by Tl-201 SPECT mammoscintigraphy were larger than 1 cm in diameter and no breast tumor with a diameter smaller than 1 cm could be demonstrated by Tl-201 SPECT mammoscintigraphy in this study) (Tab. 1).

In conclusion, Tl-201 SPECT mammoscintigraphy is a higher specific imaging technique, to complement ultrasonography, to detect breast cancer in patients with difficulties interpreted mammogram due to dense breast in Taiwanese females.

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