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Original Article

만져지는 유방 병소를 평가하는데 있어 Tc-99m MIBI 유방스캔과 유방촬영술의 비교: 예비 결과

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The value of Dedicated Tc-99m MIBI Scintimammography in the Evaluation of Patients with Palpable Breast Lesions in Comparison with Mammography: Preliminary Result

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Purpose: There are few studies evaluating the usefulness of dedicated high-resolution scintimammography and no studies using delayed washout with this dedicated high resolution scintimammography for the evaluation of breast lesions. We underwent this study to evaluate the clinical usefulness of Tc-99m MIBI in evaluating patients with palpable breast lesions using dedicated high-resolution scintimammography. **Materials and Methods:** This study included 19 patients with 23 palpable breast lesions who underwent mammography. Tc-99m MIBI was taken to further characterize these lesions. Scintimammography images were acquired with standard craniocaudal and mediolateral oblique views and delayed images were additionally taken. Final conclusions were based on histopathology, either by biopsy or mastectomy results. **Results:** Eighteen lesions were malignant and five were benign. Mammography was indeterminate for thirteen lesions, nine of those were malignant. Mammography also categorized one lesion as benign in a dense breast, but scintimammography and pathology results showed malignancy. Of the five benign lesions, two were visible on scintimammography, but delayed images showed washout. **Conclusion:** Based on our preliminary results, dedicated high resolution scintimammography seems to be very useful in characterizing palpable lesions that were indeterminate or negative on mammography. (Nucl Med Mol Imaging 2009;43(1):48-54)

Key Words: Tc-99m MIBI, dedicated high-resolution scintimammography, breast cancer

Introduction

The incidence of breast cancer is rising in the western world, and with the westernization of lifestyles of Korean people, the incidence of breast cancer as well as the incidence of breast cancer in younger Korean women is on the rise.[1,2] Mammography is frequently used as the screening method of choice for breast cancer, with a reported high sensitivity of 85%-90% for fatty breasts.[3] However, in younger, pre-menopausal women with dense breasts, the reported sensitivities drop to about 70%.[4]

Functional imaging with scintimammography has the advantage of having higher lesion-to-background contrast compared to X-ray mammography in dense breasts. In a recent meta-analysis by Liberman et al.[5], the reported sensitivity and specificity for scintimammography was 85% and 86%, respectively. However, for non-palpable masses, the sensitivity was 67%. This implies that size is a concern when using general purpose gamma cameras in tumors less than 1 cm. Scopinaro et al.[6] recently

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evaluated breast tumors smaller than 1 cm using a dedicated high resolution gamma camera and reported an increase in sensitivity from 50% with Anger camera prone scintimammography to 81.2% with high-resolution-scintimammography. With the advent of high-resolution dedicated scintimammography, the additional clinical usefulness of these cameras needs to readdressed.

We underwent this study to evaluate the additional benefit of Tc-99m MIBI scintimammography in the evaluation of patients with palpable breast lesions.

Materials and Methods

1. Patient population and study design

This retrospective study reviewed 23 breast lesions in 19 patients (19 female, average age: 49.2 years old, range: 28-76) who underwent mammography for the evaluation of palpable breast lesions. All patients underwent subsequent Tc-99m MIBI scintimammography within 30 days of mammography (average 12 days, range 0-30 days) for further characterization. All patients then had ultrasonography guided biopsy, and patients diagnosed as cancer underwent subsequent partial or total mastectomy. The ethical committee in our institution approved this retrospective study.

2. Imaging techniques

1) Mammography

Eighteen women had mammography obtained with dedicated equipment (DMR, GE Healthcare, USA) in our hospital. Standard craniocaudal and mediolateral oblique views were routinely obtained, and additional mammographic views were obtained as needed. One patient had mammography obtained at an outside institution.

2) Scintimammography

Patients were injected with 25 - 30 mCi (925 - 1110 MBq) of Tc-99m MIBI in the ante-cubital vein of the contralateral arm of the breast lesion. In case of bilateral lesion, the injection was done in a vein of the leg. Imaging was performed 10 minutes after injection with a dedicated high-resolution, breast-specific gamma camera (Dilon 6800, Dilon Technologies, USA). Standard craniocaudal and mediolateral oblique views for each breast were obtained for five minutes each. Delayed craniocaudal images were then taken on the breast with the lesion 30 minutes after the injection. Images with the high-resolution camera were taken on a matrix size of 80×80 and photopeak was focused at 140 keV with a symmetrical 10% window.

3) Image interpretation

Mammography was assessed by an experienced radiologist according to the Breast Imaging Reporting and Data System (BI-RADS) classification. BI-RADS classification **1**: Normal; **2**: Benign- absence of any suspicious finding; **3**: Probably benign: neither category 2 nor category 4 or 5; **4**: Suspicious abnormality- one or more suspicious findings, not category 5; **5**: Highly suggestive of malignancy- two or more major suspicious findings; **6**: Known malignancy biopsy proven malignancy; **0**: Incomplete assessment- Further information is needed to make a final assessment.

Scintimammography images were visually analyzed by two experienced nuclear medicine physicians blinded to the patient history or radiological assessment according to uptake on the initial and delayed images on the high resolution display monitor. Positive findings were categorized as increased uptake on the initial images with persistent or further increased uptake on delayed images. Findings were categorized as negative if there were no uptake or any uptake that decreased on delayed images.

4) Analysis

Patients that were BI-RADS 0, 3, or 4 on mammography were categorized as "Indeterminate". Mammography that were BI-RADS 1 or 2 were categorized as "Negative"; BI-RADS 5 or 6 were categorized as "Positive", and these findings were correlated with scintimammography images to see if further characterization of the lesions was possible. Pathological results of malignancy and benign were then correlated with the image analysis to determine the sensitivity, specificity, and accuracy of scintimammography.

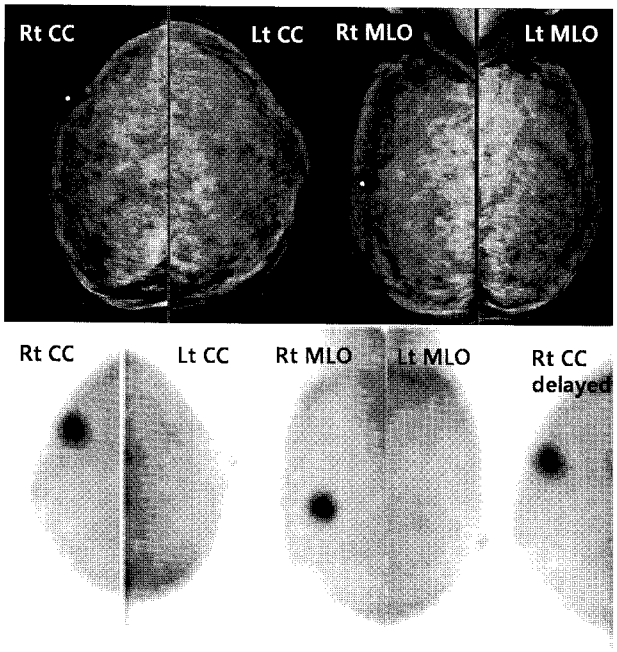

Figure 1. In a 28 year old female with right breast nodule, mammography categorized this lesion as BI-RAD 0 (incomplete assessment) (A). Scintimammography showed focal uptake in the right breast nodule without washout on delayed images, indicating malignancy (B). Final pathology was invasive ductal carcinoma. (CC; craniocaudal, MLO; mediolateral).

Results

1. Histopathology and Tc-99m MIBI uptake on scintimammography

Eighteen lesions were diagnosed as malignant by partial or total mastectomy. Five lesions were diagnosed as benign lesions by core- or needle-biopsy. Of the malignant lesions, there were thirteen lesions of invasive ductal carcinoma (IDC), one invasive apocrine cancer, one solid papillary cancer with mucin content, one infiltrating mucinous cancer, one ductal carcinoma in situ with lobular cancerization, and one IDC with micropapillary type. The average size of the malignant lesions was 2.1 cm (range 1.0-4.2 cm). Of the benign lesions, there was one fibroadenoma, one fibrocystic change, one fibroadenomatoid hyperplasia, one fibroadenomatous hyperplasia with stromal fibrosis, and one fibrocytic change and adenosis. The average size of the benign lesions was 1.4 cm (range: 1.0-2.4 cm).

Eighteen lesions were visually categorized as positive on scintimammography, and all the lesions were histologically confirmed as malignant (Fig. 1). Five lesions were categorized as negative on scintimammography. Three lesions did not show any uptake on scintimammography. Two lesions showed focal uptake which substantially reduced on delayed images (Fig. 2). All five lesions were pathologically confirmed as benign. Based on early images, we found a sensitivity of 100% and a specificity of 60% on dedicated scintimammography for the evaluation of palpable breast lesions. The use of short interval delayed images was useful in increasing the specificity from 60% to 100%.

2. Correlation of scintimammography with mammography

A total of 13 lesions in 10 patients had indeterminate results on mammography (BI-RADS 0 and 4). Nine lesions showed increased uptake on scintimammography, and were visually categorized as positive. Histopathology showed all of these lesions to be malignant. Four lesions were negative on scintimammography and were histologically diagnosed as benign lesions.

A total of 10 lesions in 10 patients had either positive or negative findings on mammography. Two lesions were categorized with BI-RADS 1, but scintimammography categorized one of the two lesions with malignancy, and histopathology confirmed the lesion to be IDC (Fig. 3). The other lesion showed no uptake on scintimammography and was confirmed as fibroadenoma. Eight lesions were categorized as BI-RADS 5, and all showed positive uptake on scintimammography and were confirmed to be malignant.

Fig. 4 represents the flow chart of these lesions from mammography to scintimammography to pathology.

Discussion

Most previous studies showed variable sensitivities (71-93%) and specificities (69-87%) for the diagnosis of breast cancer using Tc-99m MIBI scintimammography and conventional gamma cameras.[7-9] In a recent meta-analysis by Hussian et al.[10], 2424 patients in single-study trial groups showed an overall sensitivity of 85% (range 69-90%), and a specificity of 84% (range 71-94%). The

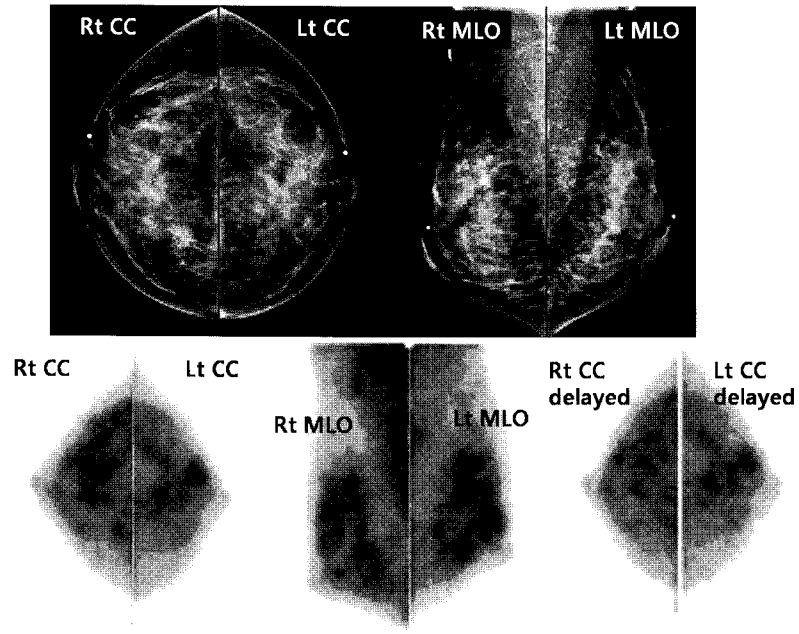

Figure 2. In a 43 year old female with a palpable nodule in each breast, mammography categorized both lesions as BI-RAD 0 (incomplete assessment) (A). Left breast showed a focal uptake with washout on delayed images (B). Right breast showed no focal uptake (B). Core biopsy in the right breast lesion showed fibroadenomatoid hyperplasia. Mammotome of the left breast lesion demonstrated adenosis with fibrocystic changes. (CC; craniocaudal, MLO; mediolateral).

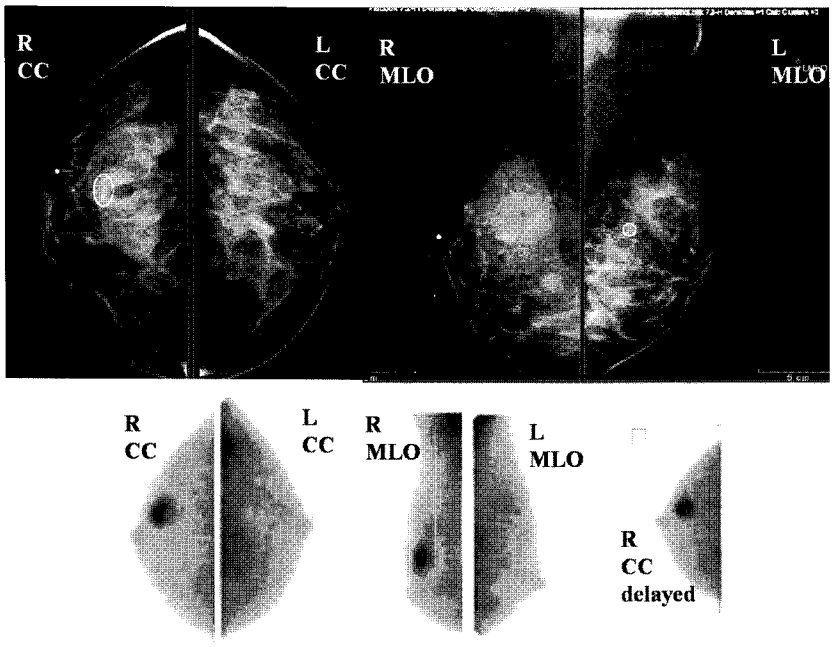

Figure 3. In a 49 year old female with infiltrating ductal carcinoma mixed with papillary type in the left breast, mammography categorized this lesion as BI-RADS 1 (normal) (A). Scintimammography correctly categorized this lesion as malignancy (B). (CC; craniocaudal, MLO; mediolateral).

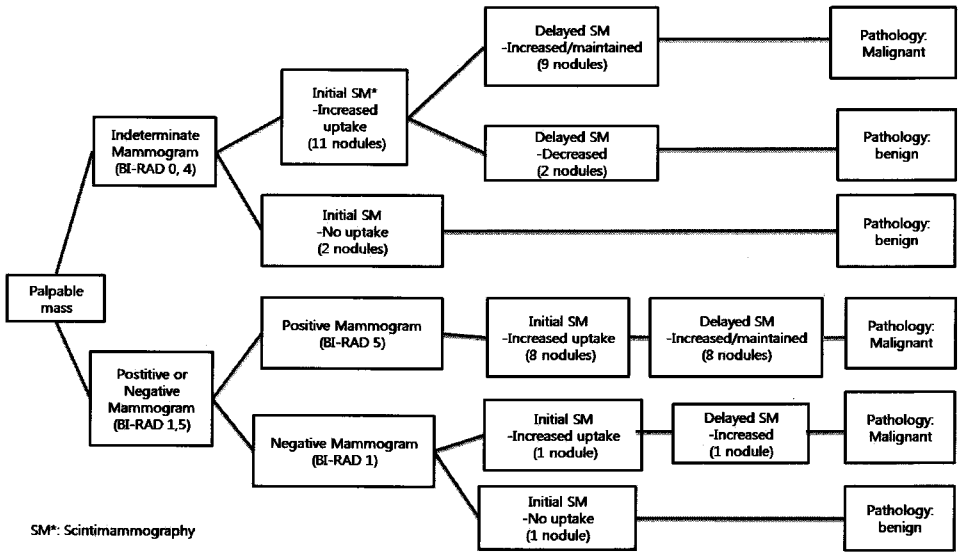

Figure 4. This is the diagnosis flow chart from mammography to scintimammography to pathology used in this study.

wide range of specificities and sensitivities in these studies could be due to a couple of factors. Size of the lesion is an inherent problem with conventional gamma cameras, with a low sensitivity for lesions smaller than 1 cm. Mekhmandarov et al.[11] reported that standard gamma cameras have poor sensitivity (55%) for lesions with a mean size of 1.34 cm. Distance from detector to lesion can also be a reason for low sensitivity. Khalkhali et al.[12] devised a prone lateral method of imaging that allowed the breast to hang away from the chest through a cut-off in the mattress, which would reduce the activity from the liver or the heart. Another major factor that may affect sensitivity and specificity of a lesion is the histopathology. Buscombe et al.[13] evaluated Tc-99m MIBI uptake with various breast malignancies and found that histological subtype is the dominant factor in uptake in vivo, with ductal carcinomas having a higher tumor to background ratio than benign lesions or other breast cancers.

The use of a high resolution scintimammography has several advantages over conventional gamma cameras, most notably the increased lesion sensitivity. In a comparison study between Anger camera prone scintimammography and high resolution scintimammography by Scopinaro et al.[6], the sensitivity of anger cameras was 50% compared to 81% for high resolution cameras for T1a-T2b breast cancers. Specificity was 86% for both techniques. Brem et al.[14] also evaluated the sensitivity of high resolution scintimammography who had normal mammographic and physical examination findings. Sixteen of the 94 women had abnormal scintimammography, and two patients were confirmed to have 9mm invasive carcinoma on pathology. Spanu et al.[15], using Tc-99m tetrofosmin showed that dedicated high resolution scintimammography showed 90.3% of sensitivity for ≤ 10-mm and 100% for lesions larger than 1 cm, with an overall sensitivity of 96.7% and specificity of 91.7%.

In this study, we found a 100% of sensitivity of breast dedicated scintimammography for the evaluation of patients with palpable breast lesions. Other than the use of high resolution technique, the facts that all of our lesions were large (>1 cm) lesions and that most of them were IDC, which has the highest Tc-99m MIBI uptake compared to other breast malignancies, could have contributed to the excellent sensitivity for the evaluation of the lesions.

A well-known false positive in scintimammography using Tc-99m MIBI is fibroadenomas, fibrocystic disease, and inflammatory lesions, which will compromise the specificity of scintimammography.[3,14,16,17] However, most fibrocystic diseases are generally diffuse than focal, often bilateral, and poorly delineated, which can help in differentiating from malignancies.[17] Another method that

could help in discriminating between benign and malignant lesions is the use of dual phase scintimammography. Various studies have evaluated the usefulness of this technique in evaluating breast lesions.[18-21] The assumption for performing early and delayed imaging to differentiate between benign and malignant diseases is that Tc-99m MIBI uptake by malignant tumors might persist on delayed images in contrast to that of benign lesions, which would fade away.

Kim et al.[18] evaluated 520 breast cancer patients using early (10 minutes) and delayed (3 hours) double phase scintimammography using Tc-99m MIBI. They found that early uptake was more valuable than delayed uptake. Paz et al.[20] using double phase Tc-99m MIBI acquired at immediately and 90±120 minutes later concluded that double phase be more specific but less sensitive than early phase in detecting breast cancer. Melloul et al.[19] showed that using double phase (immediate and 90-120 minutes delayed images) showed 100% of sensitivity in detecting tumors >1 cm, and an overall 88.9% of sensitivity and 88.3% of specificity. All of these studies used conventional gamma cameras in the evaluation of double phase studies. To our knowledge, this is the first study using double phased high resolution scintimammography in the evaluation of palpable breast lesions. Different from the previous studies, delayed imaging in this study was performed only 30 minutes after the injection to avoid the possibility of compromising the sensitivity of scintimammography. In this preliminary result, we had only two lesions (2/20) showing increased Tc-99m MIBI uptake on early images and a decrease in uptake on delayed images. Both of them were confirmed as benign on histopathology. Even though delay imaging in this study was done earlier than the previous studies, it still seems to have a value in increasing the specificity of scintimammography. However, further studies including a larger patient population are needed to elucidate the role of dedicated scintimammography with a short interval dual phase.

There were 13 lesions with indeterminate results on mammography. Dedicated scintimammography was extremely useful in characterizing those lesions. Therefore, the use of dedicated scintimammography may be helpful to select those lesions for further diagnostic evaluation using ultrasonography or ultrasonography guided biopsy. All of the 8 lesions considered malignant on conventional mammography eventually found to be malignant. However, of the 2 patients with negative mammography, one patient had a positive scintimammography and eventually turned out to have a malignant lesion.

Based on our preliminary results, dedicated high resolution scintimammography seems to be very useful in characterizing palpable breast lesions that were indeterminate or negative on mammography. It can play an important role in screening those patients who need further medical intervention. In this small series, delayed image seems to have a potential in improving the specificity. However, it needs to be validated by further studies with more patients.

요 약

목적: 기존의 Tc-99m MIBI 유방스캔은 유방암 진단에 어느 정도 유용하다고 알려져 있으나 작은 병변을 발견하는데 민감도가 낮은 것이 문제점이었다. 고해상도 유방 전용 스캔 또한 작은 병변에 대한 예민도에 한계가 있다. 본 연구에서는 1 cm이상의 촉지되는 병변에 대해서 고해상도 유방 전용 스캔의 유용성을 알아보고자 하였다. **대상 및 방법**: 19명의 만져지는 병변이 있은 환자를 대상으로 Tc-99m MIBI 유방스캔을 시행하였다. 약 925-1110 MBq을 투여한 10분 후에 조기 영상을 촬영하고, 30분 후에 지연 영상을 시행하였다. **결과**: 19명중 23개의 병변이 조직학적으로 진단되었고, 그 중 18개는 악성으로, 5개 병변은 양성으로 진단되었다. 고해상 유방스캔이 악성 병변을 찾는데 있어 민감도 100%로 매우 유용하였다. 다섯 개의 양성 중 2개는 초기 영상에서 섭취 증가를 보였으나 지연 영상에서 섭취 감소를 보여 양성으로 판단하였고 병변 진단에 지연 영상이 도움이 되었다. 유방 촬영술이 13개의 병변들에서 모호한 결과를 보였고 1개의 악성 병변을 양성으로 진단한 것에 비해 유방 전용 스캔은 악성 선별에 훨씬 우수한 결과를 보였다. **결론**: 본 연구에 의하면 고해상 유방 전용 스캔은 1 cm 이상의 만져지는 병변에서 악성 병변을 선별하는데 큰 도움이 될 것으로 기대된다. 이러한 결과는 좀 더 많은 환자를 대상으로 한 연구에 의해 검증되어야 하며 특히 지연 영상을 촬영하는 최적의 시간에 대해서도 비교 연구가 필요할 것으로 사료된다.

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