Original article

Performance of synthetic mammography in the detection of architectural distortion: a comparison with conventional 2D digital mammography

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Objectives To compare the performance of synthetic mammography (SM) and conventional 2D digital mammography (DM) in the detection of architectural distortion (AD).

Methods A retrospective review was conducted by three breast imaging radiologists for DM and SM of 33 patients (16 distorted and 17 non-distorted) to identify the presence or absence of and the location of AD. The results were checked for consensus with the standard digital breast tomosynthesis (DBT) reference. STATA version 16.0 was used to analyze the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of each method. Logistic regression was used to calculate the Area Under the Curve (AUC) and the Chi-squared test was used to compare the AUC between the two methods.

Results The sensitivity, specificity, PPV, NPV and accuracy of detection of AD with DM versus SM were 62.5% vs 62.5%, 70.6% vs 88.2%, 66.7% vs 83.3%, 66.7% vs 71.4% and 66.7% vs 75.8%, respectively. The AUC (95% CI) of the SM technique for detection of AD was higher than the DM technique: 0.75 (0.61-0.90) compared with 0.67 (0.50-0.83) ($p = 0.32$).

Conclusion SM provides equal and potentially better diagnostic performance than DM in the detection of AD. **Chiang Mai Medical Journal 2020;59(4):207-15.**

Keywords: architectural distortion, synthetic 2D mammography, conventional 2D mammography, digital breast tomosynthesis

Introduction

Digital breast tomosynthesis (DBT) is a new breast cancer screening tool that involves the X-ray machine moving in an arc around the breast, making several low dose images (1). This technique produces an individual plane of the breast, minimizing the effect of overlapping breast tissue and can demonstrate some mammographic abnormalities more clearly than conventional 2D mammograms (DM) (2,3). In addition, the excellent software algorithm associated with the procedure can reconstruct a synthetic mammogram (SM) from a DBT data set (4). The use of SM can avoid the use of DM when used in combination with DBT which also gives some advantages such as decreased radiation dose, decreased acquisition time, smaller number of images, and lower interpretation time (5-7). In some mammography vendors, SM has also been approved by the FDA for use in combination with DBT for breast cancer screening, providing higher sensitivity and specificity and a lower recall rate than DM alone (8-11). We believe that the SM has the advantage of extracting information from the multiple projection views

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of the tissue structure which can result in the identification of subtle changes associated with breast cancer such as architectural distortion with greater efficacy than DM. The aim of this study was to compare the performance of SM with DM in terms of detection of architectural distortion.

Methods

Patients

A retrospective search for patients with architectural distortion (AD) using the database of the Breast Imaging Unit of the Women Health Center at the Center for Medical Excellence, Faculty of Medicine, Chiang Mai University for the three year period from October 2015 through September 2018 identified 50 patients with AD. Eight patients were excluded from our study because the AD was a result of previous surgery and hence defined as secondary AD. Other eight patients were also excluded due to incomplete imaging data on the picture archiving and communication system (PACS) review. We enrolled all patients who had all imaging data of three mammographic techniques including conventional 2D mammography (DM), synthetic mammography (SM) and digital breast tomosynthesis (DBT). Of that group, 18 patients who were found to have AD associated with mass on retrospective review were also excluded. Finally, 16 patients with primary AD were included in our study. We also randomly selected mammographic images of 17 other patients who had been reported as BIRADS1 or BIRADS2 without the presence of AD that performed at Breast Imaging Unit of the Women Health Center at the Center for Medical Excellence, Faculty of Medicine, Chiang Mai University, to randomly mix with the patients with AD group. Thus, the total number of sets of mammographic images for reviewing was 33.

Ethical approval

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University (study code: RAD-2561-05866). For this type of study formal consent of the patient is not required.

Mammographic machine and techniques

All 33 patients had had bilateral breast mammography performed with combo set protocol of DM and DBT using a Dimension 1.8.4.4, Hologic mammographic machine. The SM images were also reconstructed using Hologic reconstruction algorithm software, also being known as C-View. Four DM images from each patient were grouped as a DM data set, while four SM images from each patient were grouped as an SM data set. Four tomographic views from each patient were used as a standard reference of the presence of and the location of the AD.

Data collection and imaging evaluation

Patient age and pathological reports were collected. Of the 16 patients with AD, one had AD in both breasts, making a total of 17 AD lesions from 16 patients in our study. The flow chart of the study is shown in Figure 1.

Both DM and SM data sets were reviewed independently and retrospectively by three breast imaging radiologists. The DM data set was reviewed first and the SM data set was reviewed two weeks later to reduce recall bias. Each reviewer recorded the presence or absence of AD in each patient and, if it was evident, the location was recorded in a quadrant position. The results from all three reviewers were summarized into consensus results derived from the unanimous or majority opinion of the three reviewers for each case. The consensus results were checked with the standard reference DBT before concluding whether the results were correct or incorrect in each case. A correct result was defined as a case where the AD was correctly detected in at least one image view based on the consensus result. In the case of the single patient who had AD in both breasts, each AD had to be correctly detected on at least one image view to be considered a correct conclusion.

Statistical analysis

STATA version 16.0 was used for all analyses. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of

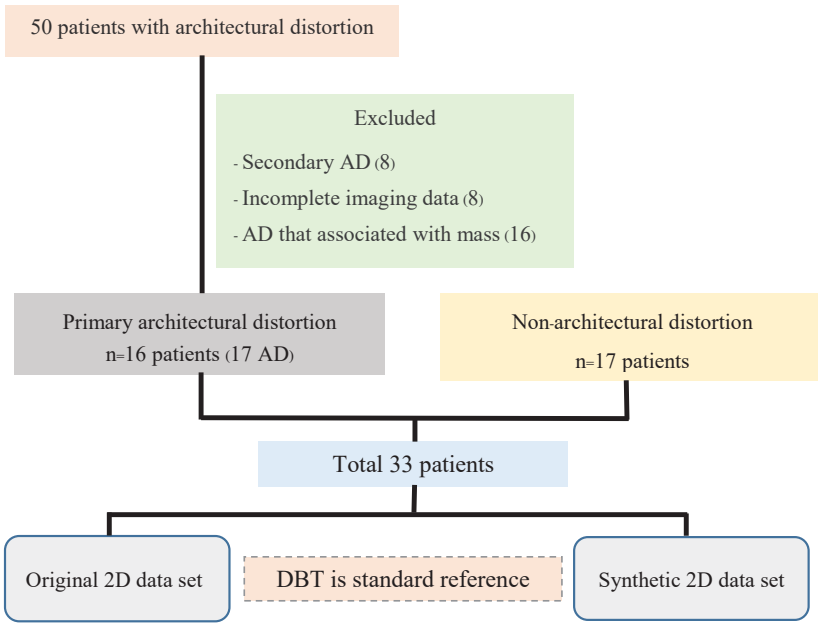


Figure 1. Flow chart of the study

each method were calculated as percentages. The agreement level between the reviewers was evaluated using the κ coefficient. Logistic regression was used to calculate the area under curve (AUC) and a Chi-squared test was used to compare the AUC between the two methods. The results were considered to be statistically significant if the *p*-value was less than 0.05.

Results

General data

The demographic data are shown in Table 1. There was no difference in age range between patients with AD and those without AD ($p = 0.112$). Most (11) of the incidences of AD in our study were found in the left breast with 4 in the right breast; only one patient had AD in both breasts. Nine AD lesions were determined to be malignant by pathological examination including 7 lesions of invasive ductal carcinoma and 2 lesions of invasive lobular carcinoma.

Inter-reader Agreement

The three reviewers were breast imaging radiologists with between 5 and 15 years of experience. Agreement between the three reviewers was assessed using Kappa coefficient analysis and ranged from slight to substantial for the DM technique and from moderate to substantial for the SM technique (Table 2).

Image analysis with conventional 2D mammography and with synthetic mammography

In the case of the DM data set, the reviewers correctly detected AD in 10 of 16 patients and correctly interpreted12 of 17 non-AD patients. In the SM data set, the reviewers correctly detected AD in 10 of 16 AD patients and correctly interpreted 15 of 17 non-AD patients.

The diagnostic performance of each mammographic technique was analyzed for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. The sensitivity of DM and SM techniques were equal at 62.5%, while specificity, PPV, NPV and accuracy were 70.6% vs 88.2%, 66.7% vs 83.3%, 66.7% vs 71.4% and 66.7% vs 75.8%, respectively (Table 3). The AUC (95% CI) with the SM technique for detection of AD was 0.75 (0.61-0.90) compared with 0.67 (0.50-0.83) with the DM technique ($p = 0.32$).

Table 1. Demographic data of patients included in the study

Clinical characteristic	Presence of architectural distortion (n=16)	Absence of architectural distortion (n=17)	Total (n=33)	*p*-value
Age range (years)	33-74	36-64	33-74	0.112
(mean)	(55.4)	(49.6)	(52.4)	
Site n (%)				
Right side	4 (25)			
Left side	11 (69)			
Bilateral	1 (6)			
Pathology n (%)				
Benign	5 (36)			
Malignant	9 (64)			
Invasive ductal carcinoma	7			
Invasive lobular carcinoma	2			
No/Unsatisfied	2			

Nine AD cases (52.9%) were correctly detected by reviewers using both the DM and SM techniques (Figure 2). There were five patients with a total of six AD lesions (35.3%) that could not be detected by the reviewers using either the DM or the SM technique. One lesion (5.9%) was detected by the reviewers using the DM technique in mediolateral oblique (MLO) view, but was not detected with the SM technique (Figure 3). One lesion (5.9%) was detected by reviewers using the SM technique but not the DM technique (Figure 4).

Discussion

Even though architectural distortion (AD) is a subtle sign of breast cancer, it is an important finding that should not be missed due to significant malignancy risk (12-14). This study found AD to be an infrequent finding, with only 24 patients with primary AD having been identified at the Breast Imaging Unit of Women Health Center at the Center for Medical Excellence, Faculty of Medicine, Chiang Mai University during the three-year period of this study.

A review of many previous studies found that 44-70% of cases of AD were due to malignant lesions, with the most frequent pathology of malignant AD being invasive carcinomas (94.5%), predominantly with invasive ductal carcinoma (12, 14). The malignancy rate of AD in this study was 64% which is in agreement with previous studies. This study found 100% of the cases of malignant AD were invasive carcinoma, a rate higher than that found in previous studies, although this difference may be due to the small sample size. Most of the malignant AD cases in this study were invasive ductal carcinoma (77.8%) and the rest were invasive lobular carci-

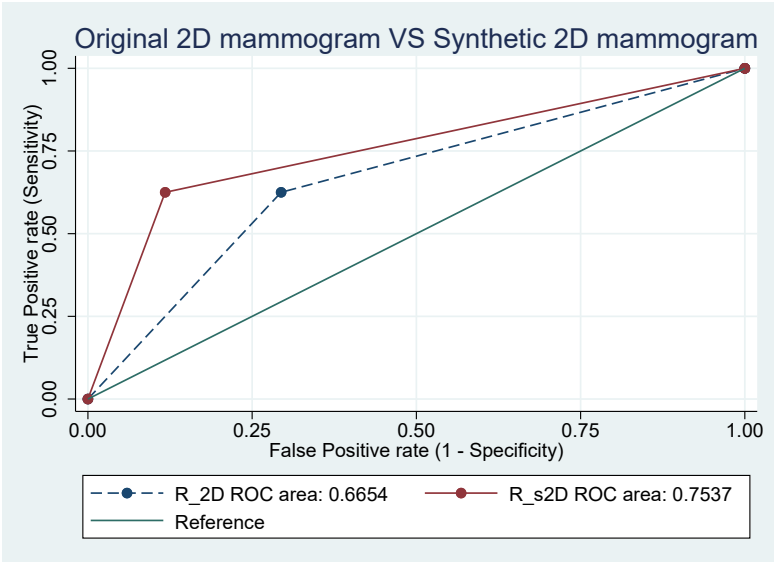
Table 2. Level of agreement among reviewers

	Conventional mammogram	Synthetic mammogram
R1 vs R2	k=0.15 (slight)	k=0.67 (substantial)
R1 vs R3	k=0.70 (substantial)	k=0.48 (moderate)
R2 vs R3	k=0.33	k=0.55 (moderate)

Table 3. Performance of conventional 2D mammography compared with synthetic mammography in the detection of architectural distortion

Characteristic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Conventional	62.5 (10/16)	70.6 (12/17)	66.7 (10/15)	66.7 (12/18)	66.7 (22/33)
Synthetic	62.5 (10/16)	88.2 (15/17)	83.3 (10/12)	71.4 (15/21)	75.8 (25/33)

Table 4. Area under the curve with conventional 2D and with synthetic mammography for the diagnosis of architectural distortion



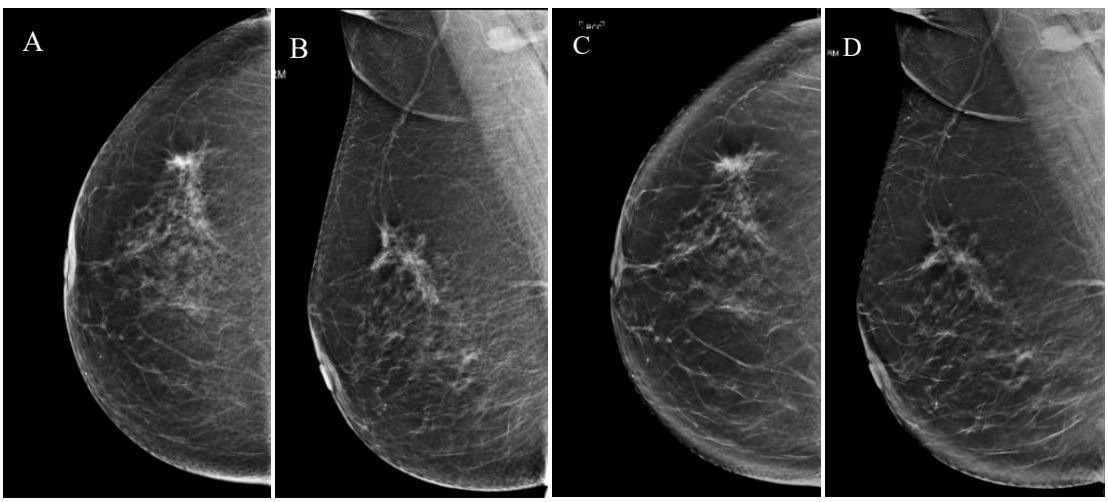


Figure 2. Example of AD lesion detected in both DM and SM. Screening mammogram of a 74-year-old woman. (A) The DM of right craniocaudal (CC) view; (B) right mediolateral oblique (MLO) view; (C) SM of right CC; (D) right MLO; AD at right upper outer quadrant (RUOQ) is clearly evident

noma (22.8%), a finding which also corresponds with previous studies.

In this study, there was slight to substantial variation in agreement among the reviewers. This result corresponds with previous studies which found that AD was the type of lesion with highest inter-observer variability (15,16). The reason why AD has high inter-observer variability may be due to differences in the experience of the reviewers, their level of familiarity with the imaging technique and misinterpretation of some spiculate lesions as AD rather than a spiculate mass. Agreement between reviewers was higher with the SM technique and appeared to be more coherent than with the DM technique. We believe that this result may be due to the images in the SM technique being reconstructed from multiple projection views of the soft tissue, helping the

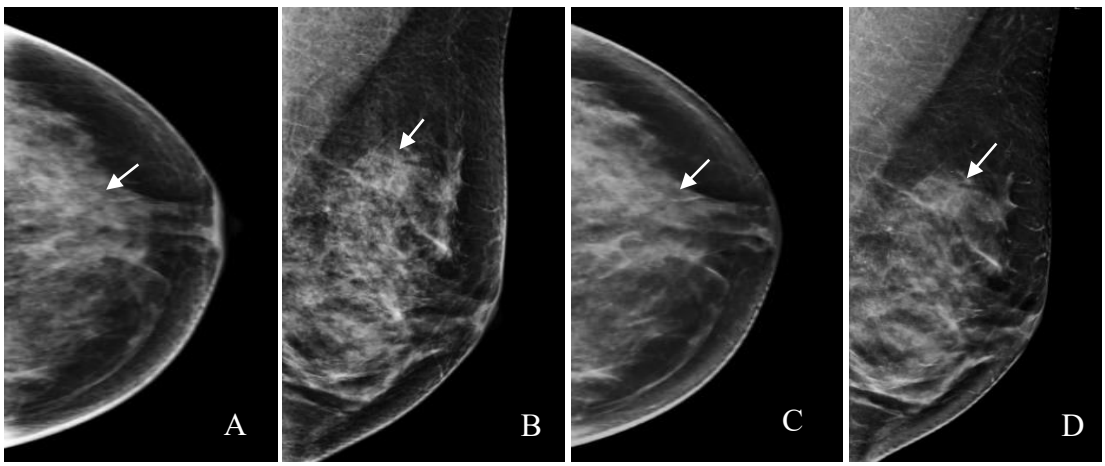


Figure 3. Example of AD lesion detected by all reviewers only in DM. A 45-year-old woman with right breast pain. DBT showed AD at upper central of left breast (not shown). (A) The DM of left CC; (B) left MLO; (C) SM of left CC; (D) left MLO. show faint AD at upper central left breast on retrospective review (arrows).

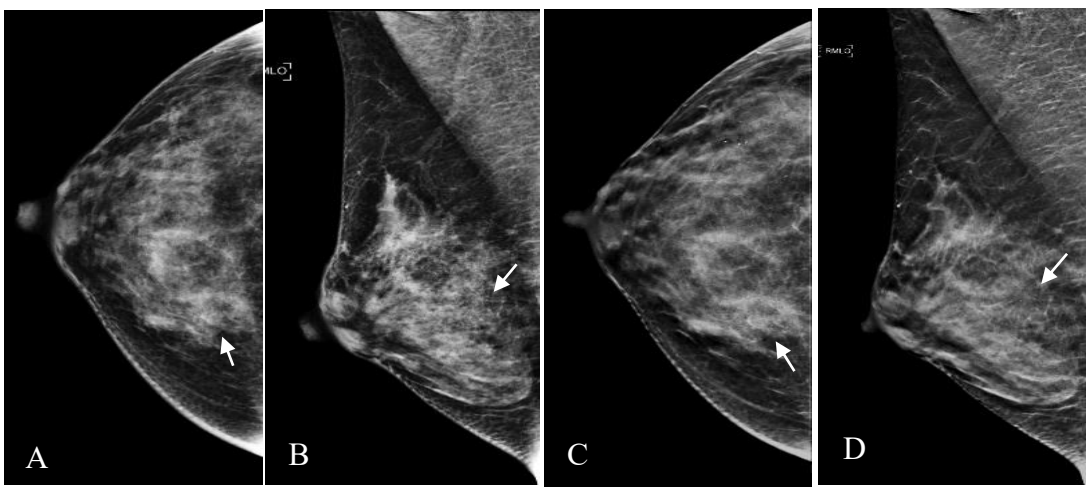


Figure 4. Example of AD lesion detected by all reviewers only in SM. A 33-year-old woman, screening mammogram. The DBT showed AD at inner central right breast (not shown). (A) The DM of right CC; (B) right MLO; (C) SM of right CC; (D) right MLO show AD at inner central right breast in both imaging techniques on retrospective review (arrows).

radiologist better differentiate between a spiculate mass and an AD lesion.

Two previous studies found that AD was a frequently missed lesion and that it could be mammographically occult in about 50% of cases (17,18). In this study, however, sensitivity in the detection of AD with the DM and SM techniques was equal at 62.5%; the mammographically occult AD incidence in this study was only 35.3%. The better detection rate and lower mammographically occult incidence of AD in this study may be due to our reviewers being aware of the research objective and therefore possibly more specifically focused than usual on the detection of AD.

The values of the remaining parameters, specificity, PPV, NPV and accuracy, in our study were higher and had a greater AUC with the SM technique than with the DM technique. Even though the findings differences were not statistically significant, perhaps as a result of the small sample size, but it is not unreasonable to infer that the SM technique provides more information from the

multiple projection plane of soft tissue than the DM technique. Additionally, the reconstruction software algorithm is continually being improved (7). Together, this may suggest that SM has a potentially better diagnostic performance than DM.

Our study had several limitations. First, it was a retrospective study and although the imaging reviewers were blinded to the images and, although they were not given the proportions of distorted and non-distorted cases in the study population, some detection bias could still have occurred. Second, we specifically limited the scope of the study only to the detection of AD from digital mammography and did not include other subtle findings which may have affected the diagnostic performance of each mammography technique. A third limitation was that we did not collect data on breast composition for each group, which could have affected the visualization of the AD. Fourth, we only had a small sample and reviewers were all from a single institution, so the results are not transferable. Results may differ in a larger study with a larger sample and reviewers from multiple institutions. Additionally, we only used data from a single manufacturer and SM from a single version of software from the same manufacturer; results with equipment from different manufacturers and different synthetic software algorithms may provide different results.

Conclusions

The SM technique provides equal or better diagnostic performance than the DM technique in the detection of AD. However, the SM technique should not be used alone, but always in combination with DBT. Although the results of the combination of DM plus DBT or DBT with SM reconstruction may not make a significant difference in clinical management but use of SM in place of the previously conventional method can reduce the radiation dose to patients.

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None

Conflicts of interest

None

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ประสิทธิภาพของภาพเอกซเรย์เต้านมที่สังเคราะห์จากภาพถ่ายเต้านมแบบสามมิติ (synthetic mammography; SM) ในการตรวจพบโครงสร้างเต้านมบิดเบี้ยว (architectural distortion; AD): โดยเทียบกับภาพถ่ายเอกซเรย์เต้านมแบบสองมิติ (conventional 2D digital mammography; DM)

ลลิตา ฮั่นตระกูล, สิรวิชญ์ อุดมพร, ไพลิน คงมีผล, จินตนา รุจิเวชพงศธร และ มาลัย มุตตารักษ์
ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ การศึกษานี้มีเป้าหมายเพื่อเปรียบเทียบประสิทธิภาพของ SM และ DM ในการตรวจพบการหดรั้งของเนื้อเยื่อเต้านม

วิธีการ เป็นการศึกษาแบบทบทวนย้อนหลัง โดยรังสีแพทย์สามคนทำการทบทวนภาพถ่ายเอกซเรย์เต้านมของผู้หญิง 33 ราย (16 รายมี AD และ 17 รายไม่มี AD) ผลการทบทวนภาพถ่ายทั้งหมดถูกนำมาตรวจสอบความถูกต้องโดยเทียบกับภาพเอกซเรย์เต้านมแบบสามมิติ (digital breast tomosynthesis; DBT) และใช้ STATA version 16.0 เพื่อคำนวนหาค่าความไว (sensitivity) ความจำเพาะ (specificity) ความถูกต้อง (accuracy) ค่าพยากรณ์ผลบวก (PPV) ค่าพยากรณ์ผลลบ (NPV) และใช้ logistic regression test เพื่อคำนวนค่า AUC ของทั้งสองวิธี แล้วนำมาเปรียบเทียบกันด้วย Chi-squared test

ผลการศึกษา ความไว ความจำเพาะ ความถูกต้อง ค่าพยากรณ์ผลบวก และค่าพยากรณ์ผลลบของการตรวจพบ AD ระหว่าง DM และ SM คิดเป็นร้อยละ 62.5 กับ 62.5, 70.6 กับ 88.2, 66.7 กับ 83.3, 66.7 กับ 71.4 และ 66.7 กับ 75.8 ตามลำดับ พบว่าค่า AUC (95% CI) ของ SM ในการตรวจพบ AD สูงกว่า DM: 0.75 (0.61-0.90) เทียบกับ 0.67 (0.50-0.83) (p = 0.32)

สรุป SM มีความสามารถเทียบเท่าและมีแนวโน้มที่จะมีประสิทธิภาพที่ดีกว่า DM ในการตรวจพบการหดรั้งของเนื้อเยื่อเต้านม **เชียงใหม่เวชสาร 2563;59(4):205-14.**

คำสำคัญ: การหดรั้งของเนื้อเยื่อเต้านม ภาพถ่ายเต้านมสังเคราะห์ ภาพถ่ายเต้านมแบบสองมิติ ภาพถ่ายเต้านมแบบสามมิติ