



Digital Breast Tomosynthesis as a Breast Cancer Screening Tool for Women with Gynecologic Cancer

부인암을 가진 여성에서 유방암의 선별검사로서의 디지털 유방단층 촬영술

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Purpose The purpose of our study was to evaluate digital breast tomosynthesis as a breast cancer screening modality for women with gynecologic cancer.

Materials and Methods This retrospective study included patients with underlying gynecologic malignancies who underwent screening digital breast tomosynthesis for breast cancer. The cancer detection rate, recall rate, sensitivity, specificity, and positive predictive value (PPV) were calculated. PPV1 was defined as the percentage of all positive screening exams that have a tissue diagnosis of cancer within a year. PPV2 was defined as the percentage of all diagnostic exams (and Breast Imaging Reporting and Data System category 4, 5 from screening setting) with a recommendation for tissue diagnosis that have cancer within a year. PPV3 was defined as the percentage of all known biopsies actually performed that resulted in a tissue diagnosis of cancer within the year. For each case of screen-detected cancer, we analyzed the age, type of underlying gynecologic malignancy, breast density, imaging features, final Breast Imaging Reporting and Data System assessment, histologic type, T and N stages, molecular subtype, and Ki-67 index.

Results Among 508 patients, 7 with breast cancer were identified after a positive result. The cancer detection rate was 13.8 per 1000 screening exams, and the recall rate was 17.9%. The sensitivity was 100%, and the specificity was 83.2%. The false negative rate was 0 per 1000 exams. The PPV1, PPV2, and PPV3 were 7.7, 31.8, and 31.8, respectively.

Conclusion Digital breast tomosynthesis may be a promising breast cancer screening modality for women with gynecologic cancer, based on the high cancer detection rate, high sensitivity, high PPV, and high detection rate of early-stage cancer observed in our study.

Index terms Breast Neoplasms; Breast; Mass Screening; Gynecology;
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INTRODUCTION

Mammography as a screening tool has played an essential role in reducing breast cancer mortality. The identification of cancerous lesions by mammography before the lesions are clinically presented can allow early intervention, resulting in long-term survival (1). Despite this advantage, mammography has been criticized due to limited sensitivity, lots of false positive (FP) results, and the risk of overdiagnosis of clinically insignificant lesions (2, 3).

The sensitivity of screening mammography for average-risk women has been reported to range from 68% to 88% (4, 5). However, screening mammography for high risk groups of breast cancer had a lower sensitivity than average risk groups (6-11). In recent years, new approaches to breast imaging have been developed. One of them is the use of digital breast tomosynthesis (12). Tomosynthesis acquires multiple projection images from an X-ray source that moves at variable angles in a limited range, and these images are reconstructed into thin slices to reduce the effect of overlapping breast structures. In previous studies (12-14), the usefulness of digital breast tomosynthesis as a screening test has been demonstrated. However, there was a limited published data on the effectiveness of screening digital breast tomosynthesis for women at high risk of breast cancer (15). But, in the previous study, they did not observe a statistically significant increase in the cancer detection rate compared with the rate of the average-risk group (15).

Patients with underlying gynecologic malignancies also have a higher risk of breast cancer due to well-known gene mutations such as Breast Cancer Susceptibility Gene (BRCA) mutations, hormone effects, and other associated risk factors (16-19). While there is very few studies on screening digital breast tomosynthesis for high-risk groups of breast cancer, screening digital breast tomosynthesis for only patients with underlying gynecologic malignancies has not been evaluated. Therefore, in this study, we retrospectively reviewed and evaluated the breast cancer detection rates and recall rates among patients with gynecologic cancer (including ovarian cancer, endometrial cancer, and cervical cancer) who underwent screening digital breast tomosynthesis.

MATERIALS AND METHODS

STUDY POPULATION

This retrospective study was approved by the Institutional Review Board, and informed consent was waived (IRB No. 2019-06-027-004). Between July 2013 and July 2017, 921 patients underwent digital breast tomosynthesis. In our institute, there were three common indications of digital breast tomosynthesis. First, it used as the screening modality for underlying gynecologic malignancies. Second, for patients with previous suspicious mammographic findings (such as asymmetry or architectural distortion), it used as additional tool. Third, for patient taken outside mammography, it was performed as additional study. Among the 921 patients, 508 female patients (mean age, 54.4 years; age range, 24-92 years) with underlying gynecologic malignancies underwent digital breast tomosynthesis for the screening of breast cancer (Table 1). There were several types of underlying gynecologic malignancies; 232 patients (45.7%) had uterine cervical cancer, 156 patients (30.7%) had endometrial cancer, 113

Table 1. Characteristics of the Study Population

Study Population	<i>n</i> = 508
Age, years	54.4, 24–92
< 50	179 (35.2)
≥ 50	329 (64.8)
Type of gynecologic cancer	
Uterine cervical cancer	232 (45.7)
Endometrial cancer	156 (30.7)
Ovarian cancer	113 (22.2)
Other gynecologic malignancies*	7 (1.4)

Data are reported as the *n* (%) or mean (range) of patients unless indicated otherwise.

*Other gynecologic malignancies included vulvar cancer, vaginal cancer, placenta-related malignancy, fallopian tube cancer, and peritoneal or retroperitoneal malignancy.

patients (22.2%) had ovarian cancer, and the remaining 7 patients (1.4%) had other gynecologic malignancies including vaginal cancer, placenta-related malignancy, fallopian tube cancer, and peritoneal or retroperitoneal malignancy (Table 1). In 377 patients performed initial digital breast tomosynthesis, previous history of screening examination for breast cancer was reviewed as follows: 95 patients without screening examination and 282 patients with screening mammography. Among 508 patients, only 19 patients performed the genetic study for BRCA mutations. A total of 5 patients (26.3%) were identified as BRCA mutation carriers; 4 (80.0%) of them were BRCA1 mutation carriers, and 1 (20.0%) of them were BRCA2 mutation carriers.

IMAGE ACQUISITION AND ANALYSIS

All patients enrolled in our study underwent digital breast tomosynthesis for breast cancer screening. Digital breast tomosynthesis included craniocaudal and mediolateral oblique projections of each breast using a commercially available system (Dimension; Hologic, Bedford, MA, USA). In addition, we obtained synthetic 2D images generated from the digital breast tomosynthesis dataset for each patient using C-View image processing software (Hologic). The device was composed of a custom-designed high-power (mA) tungsten (W) anode X-ray tube with aluminum, rhodium, and silver X-ray filters. The filters produced optimal X-ray spectra based on the thickness and composition of each breast using automatic exposure control. While the breast was compressed, the X-ray tube moved over a 15° arc, taking serial ultra-low-dose mammographs. The average currents for digital breast tomosynthesis were 114 and 56 mA, the tube voltages were 28 and 29 kVp, and the mean glandular doses were 1.2 and 1.5 mGy, respectively.

One of four board-certified radiologists (E.S.C., J.E.L., J.H.K, and J.C.) who had more than 9 years of experience in breast imaging randomly interpreted the digital breast tomosynthesis images. According to the American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS) lexicon (20), breast density, imaging features, and final assessments were recorded in the radiologic reports (Table 2). Radiologic findings were based on the original radiographic reports. Based on the ACR BI-RADS lexicon (20), the four categories of

Table 2. Radiographic Findings Used for Screening Digital Breast Tomosynthesis

Factors	n = 508 (%)
Breast composition	
Almost entirely fatty breasts (a)	88 (17.3)
Scattered areas of fibroglandular density (b)	157 (30.9)
Heterogeneously dense breasts (c)	207 (40.7)
Extremely dense breasts (d)	56 (11.0)
Imaging features	
Mass or asymmetry without calcifications	149 (29.3)
Calcifications only	90 (17.7)
Mass or asymmetry with calcifications	8 (1.6)
Architectural distortion	4 (0.8)
Negative finding	257 (50.6)
BI-RADS category	
1	256 (50.4)
2	161 (31.7)
4A	9 (1.8)
4B	1 (0.2)
4C	1 (0.2)
5	0 (0.0)
0	80 (15.7)

Percentages may not equal 100 because of rounding.

BI-RADS = Breast Imaging Reporting and Data System

breast density for each patient were as follows: almost entirely fatty (a), scattered areas of fibroglandular density (b), heterogeneously dense (c), and extremely dense (d). Radiologic features were divided into five groups: mass or asymmetry without calcification, calcification only, mass or asymmetry with calcification, architectural distortion, and negative finding. Although there were mixed features in some cases, the dominant feature and the most suspicious lesion determined group by the reviewers. The BI-RADS initial and final assessments for digital breast tomosynthesis were retrospectively reviewed based on radiologic reports. Initial BI-RADS category was determined after screening digital breast tomosynthesis. Among the patients with initial BI-RADS category 0, final BI-RADS category was determined after additional study. The patients with initial BI-RADS category 1, 2, 3, 4, 5 had same final BI-RADS category. The BI-RADS assessment in each case was defined and categorized as follows: category 0 (incomplete study, the additional imaging evaluation needed), category 1 (negative finding), category 2 (benign finding), category 4A (low suspicion for malignancy), category 4B (moderate suspicion for malignancy), category 4C (high suspicion for malignancy), and category 5 (highly suggestive of malignancy) (20).

DETERMINATION OF REFERENCE STANDARDS

According to the ACR BI-RADS lexicon (20), negative cases were defined as BI-RADS category 1 or 2, and cases with BI-RADS category 0, 4, or 5 were considered as positive. Negative cases were not suspicious; thus, recall or biopsy was not required. However, positive cases on

screening setting included recalled cases. If the cases were initially assessed as BI-RADS category 0, the radiologists recommended recall. As these recalled cases were suspicious, additional imaging was necessary; however, biopsy was not warranted. Positive cases with BI-RADS category 4 or 5 were also suspicious and required both biopsy and recall. Cases with initial BI-RADS category 0, 4, and 5 required tissue confirmation or additional imaging studies including digital mammography and/or breast ultrasonography (US). Final standard references were biopsy and/or surgery. Follow-up imaging was performed for the remaining lesions without biopsy or surgery for at least 1 year. These remaining lesions were considered benign if they were stable on follow-up imaging. In cases of surgery, the T and N stage, hormone receptor expression status, and Ki-67 index were recorded based on the final pathological report.

STATISTICAL ANALYSIS

In the medical audit of breast imaging studies, the main outcome measurements included the sensitivity, specificity, positive predictive value (PPV), recall rate, and cancer detection rate. According to ACR BI-RADS definitions (20), true positive, true negative, FP, false negative (FN), sensitivity, specificity were analysed. PPV1 was defined as the percentage of all positive screening exams that have a tissue diagnosis of cancer within a year. PPV2 was defined as the percentage of all diagnostic exams (and BI-RADS category 4, 5 from screening setting) with a recommendation for tissue diagnosis that have cancer within a year. PPV3 was defined as the percentage of all known biopsies actually performed that resulted in a tissue diagnosis of cancer within the year. The three PPV were calculated using the BI-RADS method. Recall rates were defined as the number of abnormal screenings (BI-RADS category 0, 4, and 5) of the total screening tests. Cancer detection rates were defined as the number of cancers per 1000 screening tests. In this analysis, biopsy was not performed for all suspicious lesions that required tissue confirmation. However, in patients who underwent biopsy, all pathologic results of them were reported. If cancer was detected at biopsy, it was considered as a “screen-detected cancer.” Only 1 patient with initial BI-RADS category 4A performed follow-up US without biopsy. This lesion was stable after 2 years of follow-up US, so we considered the lesion as benign.

HISTOLOGY AND IMMUNOHISTOCHEMISTRY

Based on the biopsy or surgical specimens, the histologic type of invasive breast cancer, histologic grade, and axillary lymph node status were determined. The status of estrogen receptor (ER) and progesterone receptor (PR) was scored using the Allred scoring system (21). The scores were based on the proportion (range, 0–5) and intensity (range, 0–3) of immunostained cells. The total scores (the sum of the proportion and intensity scores) were in the range of 0–8. The positivity of ER or PR was defined as a total score of more than 2. The expression status of human epidermal growth factor receptor-2 (Her-2) was initially determined by immunohistochemical staining. According to the proportion and the intensity of cell membrane staining, the Her-2 expression was scored (0, ≥ 1 , ≥ 2 , and ≥ 3) and grouped as negative (0, ≥ 1 , and ≥ 2) or positive (≥ 3). For the Ki-67 index, a nuclear staining of 14% or more indicated a high level of expression (22). Based the hormone receptor expression sta-

tus and Ki-67 index, the breast cancer was categorized into four molecular subtypes as follows: luminal A-like, luminal B-like, Her-2 positive, and triple-negative. Luminal A-like cancers were ER-positive or PR-positive (or both) and Her-2-negative with a low Ki-67 index. Luminal B-like cancers were ER-positive or PR-positive (or both) and Her-2-negative with a high Ki-67 index [or ER-positive or PR-positive (or both) and Her-2 positive irrespective of the Ki-67 index]. Her-2 enriched cancers were ER-negative, PR-negative, and Her-2-positive. Triple-negative cancers were ER-negative, PR-negative, and Her-2-negative.

RESULTS

STUDY COHORT

Between July 2013 and July 2017, 508 patients having underlying gynecologic malignancies underwent digital breast tomosynthesis for screening in our facility. Their age ranged from 24 to 92 years (mean age, 54.4 years) (Table 1). They were divided into two age groups; most of the patients (64.8%) were more than 50 years old (Table 1). According to ACR guideline (20), screening mammography or digital breast tomosynthesis is not recommend for patients under 40 years of age. However, we allowed our patients to perform at least once for the screening of breast cancer and detection of calcification, after diagnosis of gynecologic cancers. Among 508 patients, 65 patients (12.8%) were under 40 years old. In this study, all 7 patients with screen-detected cancer underwent breast-conserving surgery. A total of 26 patients with lesions underwent only biopsy (including 3 patients with lesions who underwent vacuum-assisted biopsy). All patients had 2 years of follow-up imaging.

RADIOLOGIC FINDINGS

Between July 2013 and July 2017, the number of digital breast tomosynthesis for each patient ranged from 1 to 5. Only initial imaging was performed for 377 patients (74.2%). On the other hand, imaging was performed two times for 114 patients (22.4%) and three times for 17 patients (3.3%). In this study, 508 cases were categorized based on the breast composition, imaging features, and initial BI-RADS assessment (Table 2). The breast composition was classified into four groups based on ACR BI-RADS definitions (20). The majority of patients (207 patients) had heterogeneously dense breasts. The number of patients with denser breasts (including heterogeneously dense breasts and extremely dense breasts) was slightly higher than that of the other patients (including almost fatty breasts and scattered fibroglandular breasts). More than half of the patients with positive findings had a mass or asymmetry without calcification. In the initial BI-RADS assessment, 80 patients (15.7%) were considered as category 0 (Table 2). Additional US was performed for 70 of them, and additional magnification views were taken for 9 of them; only 1 patient had both.

PERFORMANCE MEASURES

Table 3 summarizes the results of screening exams using digital breast tomosynthesis for 508 patients with underlying gynecologic malignancies. The Table 3 includes the results for the cancer detection rate, recall rate, sensitivity, specificity, FN rate, and PPV. Among 508 cases, 7 breast cancer cases were detected after a positive result. Therefore, the cancer detection

Table 3. Performance Measures Used for Screening Digital Breast Tomosynthesis

Measurement	n/Total n (%)
Supplemental cancer detection rate (raw data)	7/508 (1.38)
Per 1000 exams	13.8/1000 (1.38)
Recall rate	91/508 (17.9)
Sensitivity	7/7 (100)
Specificity	417/501 (83.2)
FN rate (raw data)	0/508 (0)
Per 1000 exams	0/1000 (0)
PPV1, abnormal interpretations	7/91 (7.7)
PPV2, biopsy recommended	7/22 (31.8)
PPV3, biopsy performed	7/22 (31.8)

FN = false negative, PPV = positive predictive value

Table 4. Summary of the Cases Showing Screen-Detected Cancers

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age (years)	54	59	41	39	58	40	58
Gynecologic cancer	CX	CX	EM	OV	EM	CX	CX
Breast density*	b	b	b	b	c	c	c
DBT finding [†]	M + C	C	M	M	C	M	M
BI-RADS category [‡]	4C	4A	4A	4A	4A	4B	4B
Histologic type	DCIS	DCIS	DCIS	DCIS	DCIS	IDC	IDC
T stage	Tis	Tis	Tis	Tis	Tis	T1b	T1c
N stage	N0	N0	N0	N0	N0	N1	N0
Molecular subtype	H	A	B	A	B	B	B
Ki-67 index (%)	17	9	2	7	13	16	21

*Breast density was scored as follows: a, b, c, and d.

[†]DBT finding was categorized as follows: C, M + C, M, and D.

[‡]BI-RADS category means final BI-RADS category.

A = luminal A-like cancer, a = almost fatty, B = luminal B-like cancer, b = scattered fibroglandular, BI-RADS = Breast Imaging Reporting and Data System, C = calcification only, c = heterogeneously dense, CX = cervical cancer, D = architectural distortion, d = extremely dense, DBT = digital breast tomosynthesis, DCIS = ductal carcinoma in situ, EM = endometrial cancer, H = Her-2 enriched cancers, IDC = invasive ductal carcinoma, M = mass or asymmetry without calcification, M + C = mass or asymmetry with calcification, OV = ovarian cancer

rate was 13.8 per 1000 screening exams. The invasive cancer detection rate was 3.9 per 1000 screening exams. The number of abnormal interpretations was 91, and the recall rate was 17.9%. The sensitivity of screening digital breast tomosynthesis was 100%, and the specificity was 83.2%. Because the case of FN was not observed, the FN rate was 0 per 1000 exams. Out of 91 cases with initial BI-RADS category 0, 4, or 5, 7 cancer were detected, for a PPV1 of 7.7. Out of 22 patients with a final BI-RADS category 4 or 5, 7 cancers were diagnosed, for a PPV2 of 31.8. Out of 22 patients with a final BI-RADS category 4 or 5 with biopsy, 7 cancers were diagnosed, for a PPV3 of 31.8.

SCREEN DETECTED CANCERS

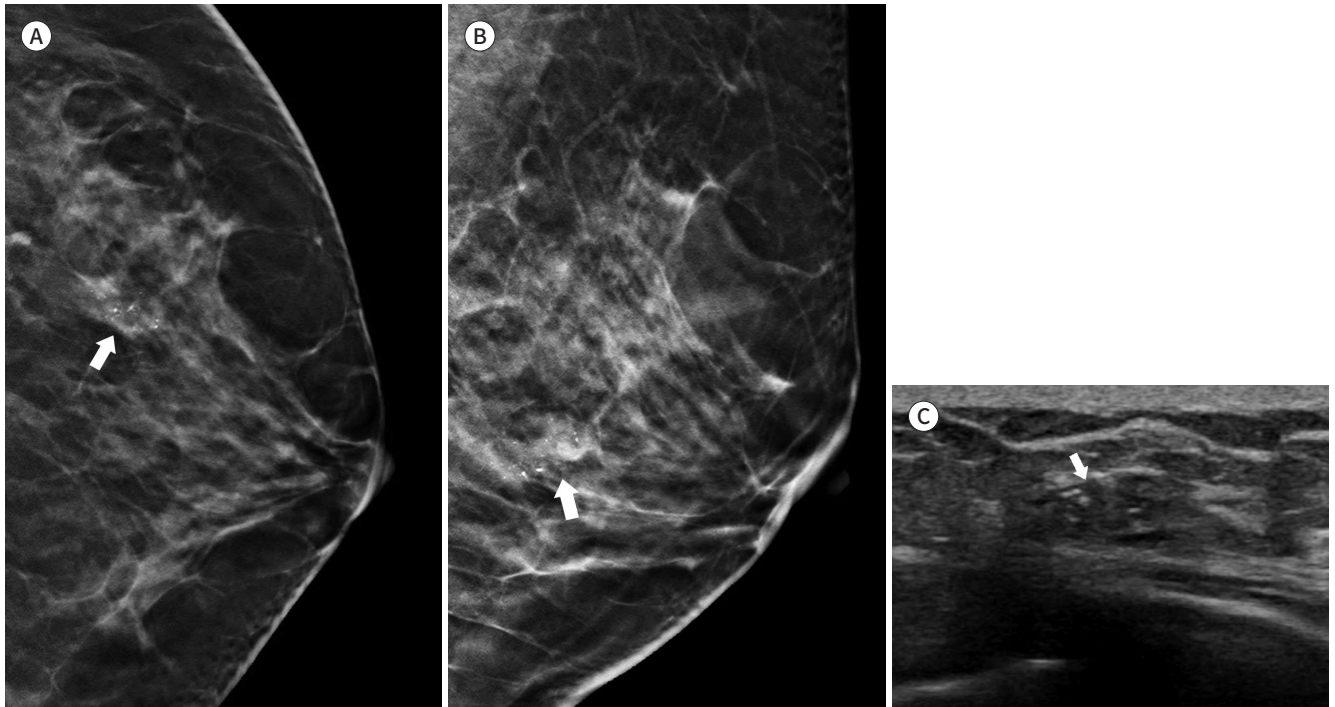
Table 4 shows a summary of screen-detected cancers including the patient's age, type of un-

Fig. 1. Screening digital breast tomosynthesis and additional US findings in a 54-year-old woman with ductal carcinoma in situ (Case 1 in Table 4).

A, B. Views of tomosynthesis (projection images) reveal focal asymmetry with fine pleomorphic calcifications (arrows).

C. Grayscale US reveals an irregular-shaped iso- to hypoechoic mass with calcifications on the left breast (3 o'clock direction), corresponding to the tomosynthesis image (arrow).

US = ultrasonography



derlying gynecologic malignancy, breast density, digital breast tomosynthesis imaging features, final BI-RADS assessment, histologic type of breast cancer, T stage, N stage, molecular subtype based on the expression status of the hormone receptor, and Ki-67 index. For patients with screen-detected cancer, the age range was 39–59 years, and the mean age was 49.9 years, which was lower than the average age of all patients ($n = 508$). Overall, 4 patients had cervical cancer, 2 patients had endometrial cancer, and 1 patient had ovarian cancer. All patients belonged to the scattered fibroglandular group or heterogeneous dense group of breast density. All cases of invasive breast cancer were detected in patients with denser breasts but not patients with less dense breasts. The radiologic findings of 4 patients were a mass or asymmetry. Calcification only was observed for 2 patients, and a mass or asymmetry with calcification was observed for 1 patient (Fig. 1). The final BI-RADS assessment of most patients was category 4A. There were 2 patients with BI-RADS category 4B and 1 patients with BI-RADS category 4C. All patients of BI-RADS category 4A were diagnosed with ductal carcinoma in situ (DCIS), and all patients with BI-RADS category 4B were diagnosed with invasive ductal carcinoma. In addition, 1 patients with BI-RADS category 4C were found to have DCIS. The final BI-RADS category appeared to be higher in cases of invasive cancer compared with DCIS. Of the 7 breast cancer cases detected with digital breast tomosynthesis, 5 cases (71.4%) were DCIS, and 2 cases (28.6%) were invasive cancer. More than half of all screen-detected cancers were diagnosed as DCIS (Tis). There were 2 cases of T1 stage breast cancer. The axillary lymph node was

positive for malignancy in only 1 case (Case 6 in Table 4). Luminal B-like cancer was detected in 4 patients, and triple-negative breast cancer was not detected. All patients with invasive cancer had a high Ki-67 index, whereas almost all patients with DCIS (except 1 patient) had a low Ki-67 index. All of them were not tested for BRCA gene mutations.

DISCUSSION

According to the American Cancer Society (ACS), women with a high risk of breast cancer are defined as women with genetics-based increased risk (and their untested first-degree relatives), women with a calculated lifetime risk of 20% or more or a history of chest radiation therapy at a young age, women with personal histories of breast cancer and dense tissue or those diagnosed by age 50, and women with atypia at biopsy (23). However, patients with gynecologic cancer also have a higher risk of breast cancer (16-19). BRCA mutations, which are well-known gene mutations that result in a high risk of breast cancer, also contribute to predisposition to ovarian cancer. In addition to BRCA mutations, mutations in the CHEK2, ATM, and PALB2 genes have been reported as risk factors of breast cancer and ovarian cancer (16). Hereditary nonpolyposis colorectal cancer or Lynch syndrome is an autosomal dominant genetic disorder that is associated with endometrial and ovarian cancer. Some breast cancers are associated with Lynch syndrome (16, 17). Peutz-Jeghers syndrome is an autosomal dominant genetic disorder that can increase the risk of developing carcinomas of the breasts, ovaries, and uterus and sex cord-stromal tumors with annular tubules in the ovaries (18). In addition to genetic factors, hormone effects such as late menopause, late age at first childbirth, and common risk factors such as obesity can affect the risk of breast and gynecologic cancers (19). Therefore, for patients with gynecologic cancer, the research to find suitable screening tool is needed.

In previous studies (6-11), it was found that women with a high risk of breast cancer based on their family history or genetic testing could benefit strongly from breast MRI. Furthermore, in comparison with mammography and/or US, screening breast MRI for women with a high risk of breast cancer has a significantly higher cancer detection rate, higher sensitivity, and lower interval invasive cancer rate (6-11). According to the ACS, supplemental breast MRI after conventional mammography is recommended as a screening tool adjunctive to mammography for women with a high risk of breast cancer (24). However, breast MRI as a screening tool has several disadvantages (25). It can lead to too many positive imaging findings including clinically insignificant lesions. In addition, screening breast MRI requires an extended period of time, which may disrupt the schedule of patients, technologists, and radiologists. The biggest obstacle is that breast MRI is too expensive to conduct annually. Therefore, breast MRI should be replaced with a suitable alternative. In contrast to breast MRI, digital breast tomosynthesis is a practical and time-saving approach; thus, many radiologists have recommended digital breast tomosynthesis as a screening modality for patients with an average risk.

Previous studies have reported that digital breast tomosynthesis plus conventional screening mammography could reduce the recall rate for additional imaging and increase breast cancer detection (14, 15). According to recommended benchmarks for screening mammography interpretations from the Breast Cancer Surveillance Consortium (BCSC) using 401548

mammograms from 2007 to 2013 (26), the recommended cancer detection rate is 4.8. The cancer detection rates of BI-RADS benchmarks are as follows: 3.7 in screening breast US and 20–30 in screening breast MRI (high-risk group) (20). The cancer detection rate in our study was 13.8. This was superior to other reported values (around 8) of digital breast tomosynthesis (average-risk group) (14, 15). However, this did not exceed the cancer detection rate in the benchmark of screening breast MRI. The BCSC benchmarks for PPV1, PPV2, and PPV3 are 4.4%, 25.2%, and 27.9%, respectively; in this study, they were 7.7%, 31.8%, and 31.8%, respectively. Therefore, there was an increase in PPV1, PPV2 and PPV3. In addition, there was a higher sensitivity (100%), lower specificity (83.2%), and lower FN rate (0%) compared with BCSC benchmarks (86.9%, 88.9%, and 0.7%, respectively). In contrast to populations with an average risk of breast cancer, screening mammography is not recommended for high-risk populations because of the relatively low sensitivity and significantly higher interval invasive cancer rate (6-11). Therefore, the high sensitivity observed in our study demonstrated the advantage of the screening tool compared with conventional mammography.

The potential benefit of digital breast tomosynthesis is higher sensitivity in dense breasts rather than conventional mammography (27). In this study, the breast density was lower than that of Korean population (28, 29), so the benefit of this DBT might be less reflected. The lower breast density of our groups may be caused due to hormone suppression therapy for gynecologic cancers. Out of 508 patients, 298 patients (58.7%) performed hormone suppression therapy or hysterectomy with bilateral salpingo-oophorectomy. And, the 0% FN rate and 100% sensitivity of our study might be related to lower rate of dense breast.

A previous study has suggested that digital breast tomosynthesis could be useful for early-stage breast cancer (30). Another study reported that screening digital breast tomosynthesis resulted in a mean time point shift to earlier cancer detection of at least 15 months (31). In our study, most screen-detected cancers were in the early T stage such as the Tis or T1 stage. There were 7 cases of node-negative invasive cancer (N0 stage). Although few patients participated in this study, the results demonstrated the possibility of a mean time point shift to earlier cancer detection for high-risk patients. The early detection of breast cancer in the high-risk group suggests that digital breast tomosynthesis can be a useful screening modality compared with mammography; the high interval invasive cancer rate is the cause of the failure of screening mammography in the high-risk group.

Although digital breast tomosynthesis has been suggested to reduce the recall rate, our recall rate was rather high (17.9%). This value was higher than that of previous studies (6.1–9.2%) (15, 30, 31). It should be noted that the published data were based on an average-risk population, whereas our recall rate was based on a high-risk population. Because the estimated value of our positive results was higher than average-risk groups, our recall rate might be increased. Moreover, this study was conducted in a specialized academic center and not a local hospital, which could result in a selection bias and a higher recall rate. Other studies have reported that recall rates in screening MRI range from 8% to 16% (7, 8, 10, 32, 33). Although these studies were performed with high-risk populations, their lower recall rate compared with the rate in our study might be associated with BI-RADS category 0. In BI-RADS assessment, it is recommended to avoid category 0 in breast MRI after screening mammography. However, there is no such restriction for screening digital breast tomosynthesis. In our study, the num-

ber of BI-RADS category 0 cases accounted for more than half of the number of abnormal interpretations. There are some limitations in our study. First, our results were reviewed retrospectively, and this study was performed at a single, large academic center equipped with specialized breast imagers; these factors may cause bias. The second limitation is the lack of genetic information. Tests for genetic mutations are costly if they are not covered by the national health insurance system. Among 508 patients, only 19 patients underwent genetic testing for BRCA mutations; 4 of them were BRCA1 mutation carriers, and 1 of them were BRCA2 mutation carriers. Third limitation is too short follow-up data (at least 2 year) to observe interval cancer. However, digital breast tomosynthesis is emerging modality, thus almost previous studies for screening digital breast tomosynthesis have at least 1 year follow-up period (12-15, 28, 34, 35). Screening breast MRI is recommended for women with a high risk of breast cancer. However, because of the retrospective study design, we cannot directly compare the performance measures of screening breast MRI. Future studies should be performed prospectively in a multicenter setting with sufficient genetic information about the risk of breast cancer. And future studies are needed for the long-term follow-up period.

In conclusion, digital breast tomosynthesis may be a promising breast cancer screening modality for women with gynecologic cancer based on the high cancer detection rate, high sensitivity, high PPV, and high detection rate of early-stage cancer observed in our study.

Author Contributions

Conceptualization, C.J., K.D.; data curation, C.J., K.D.; formal analysis, C.J., K.D.; funding acquisition, C.J.; investigation, all authors; methodology, C.J., K.D.; project administration, C.J., K.D.; resources, C.J., K.D.; software, C.J., K.D.; supervision, C.J.; validation, C.E., L.J.E., K.J.H.; visualization, C.E., L.J.E., K.J.H.; writing—original draft, K.D., C.J.; and writing—review & editing, K.D., C.J.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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부인암을 가진 여성에서 유방암의 선별검사로서의 디지털 유방단층 촬영술

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목적 본 연구는 부인암을 가진 여성에서 유방암의 선별검사로서의 디지털 유방단층 촬영술을 평가하였다.

대상과 방법 부인암을 가진 환자들 중 검진 목적으로 디지털 유방단층 촬영술을 촬영한 환자들을 대상으로 후향적 연구를 시행하였으며 유방암 발견율, 소환율, 민감도, 특이도, 양성예측도를 계산하였다. 양성예측도 1은 모든 양성 선별검사 중 1년 이내에 조직 검사에서 유방암을 진단받은 환자의 백분율로 정의되었다. 양성예측도 2는 진단 검사에서 조직검사의 필요 판정을 받은 후(그리고 선별 검사에서 Breast Imaging Reporting and Data System 카테고리 4, 5를 받은 후) 1년 이내에 조직검사에서 유방암을 진단받은 환자의 백분율로 정의되었다. 양성예측도 3은 실제로 조직검사를 시행 받은 환자 중 1년 이내에 조직검사에서 유방암을 진단받은 환자의 백분율로 정의되었다. 검진으로 발견된 암의 각 경우에 대해 환자의 나이, 부인암의 종류, 유방 밀도, 영상의 특징, 최종 Breast Imaging Reporting and Data System 평가, 조직학적 유형, T 및 N 병기, 분자아형 및 Ki-67 지수를 분석했다.

결과 전체 508명 중 7개의 유방암이 발견되었으며 유방암 발견율은 1000건 당 암 13.8이었다. 민감도는 100%, 특이도는 83.2%였으며 위음성률은 1000건 당 0이었다. 양성예측도 1, 양성예측도 2, 양성예측도 3은 각각 7.7, 31.8, 31.8이었으며 소환율은 17.9%였다.

결론 본 연구에서 디지털 유방단층 촬영술은 높은 유방암 발견율, 높은 민감도, 높은 양성예측도를 보이며 T, N 병기가 낮은 초기 암에 대해 높은 발견율을 보였다. 따라서 부인암 환자와 같은 고위험군에서 유방암의 선별검사로서 디지털 유방단층 촬영술이 유용할 수 있다.

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