Radiology

Supplemental Screening Breast US in Women with Negative Mammographic Findings:

Effect of Routine Axillary Scanning[1]

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Purpose: To evaluate the effect of routine axillary scanning when supplemental screening breast ultrasonography (US) is performed in women with negative mammographic findings.

Materials and Methods: This retrospective review included 12 844 screening breast US examinations performed in 8664 asymptomatic women aged 40 years or older with dense breasts and negative results for cancer at mammography performed between January 2012 and December 2014. Bilateral whole-breast US was performed with a handheld device by one of 10 experienced radiologists. The bilateral axillae were routinely scanned, and representative images were documented in all examinations. The abnormal interpretation rate (AIR), cancer detection rate (CDR), and positive predictive value (PPV) of screening breast US with and without axillary scanning were calculated. The 95% confidence intervals (CIs) were calculated for cancer detection after an abnormal finding at screening US.

Results: The frequency of positive axillary findings was 3.5 per 1000 (14 of 4009) baseline screening US examinations and 2.2 per 1000 (19 of 8835) subsequent screening US examinations. Of the 33 women with 33 positive axillary findings, 11 had positive breast findings; none were diagnosed with breast cancer. The remaining 22 women showed positive findings only in the axilla. The axillary findings revealed no malignancy at biopsy (n = 12) or during 22–54-month follow-up (n = 21) (95% CI: 0%, 10.6%). Without routine axillary scanning, the AIR of screening US decreased from 15.2% (610 of 4009 examinations) to 15.0% (602 of 4009 examinations) at baseline US and from 8.1% (714 of 8835 examinations) to 7.9% (700 of 8835 examinations) at subsequent US examinations, and the PPV for biopsy performed increased from 6.0% (five of 83 examinations) to 6.4% (five of 78 examinations) at baseline US and from 7.6% (13 of 170 examinations) to 7.9% (13 of 164 examinations) at subsequent US examinations, without a change in the CDR.

Conclusion: Routine axillary scanning during screening breast US had no effect on additional cancer detection, but rather increased the number of false-positive results. However, the conclusions based on these findings must be tempered by the low rate of positive findings.

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Mammography is the only screening method that has been proven in randomized controlled trials to reduce breast cancer–related mortality (1,2). However, the sensitivity of mammography has been reported to be as low as 30%–48% in women with dense breasts (3,4) and the risk of developing breast cancer is higher in women with dense breast tissue than in those without dense breast tissue (5,6). Breast ultrasonography (US) and tomosynthesis are the most commonly used supplemental screening modalities in women with dense breasts and no other risk factors (7). Breast US has many advantages in that it is widely available, is well tolerated by women, and requires no ionizing radiation. Supplemental screening breast US can depict small mammographically occult cancers and reduce the number of interval cancers (8–15). In most previous studies, handheld US was used for breast screening. However, implementation of handheld US as a screening tool remains controversial because of its false-positive rate, the variability among operators, and the considerable physician time required for image acquisition (7). Recently, three-dimensional automated breast US is being investigated as a potential solution for women with heterogeneously and extremely dense breasts. Some studies (16,17) have demonstrated significantly improved cancer detection with the addition of automated breast US to screening mammography.

The axillary region can be included when breast US is performed with a handheld device. Scanning of the axilla is considered optional because it may increase scanning time and result in more false-positive findings (18,19). However, the bilateral axillae are routinely scanned and representative images are documented in many institutions when handheld breast US is performed because breast cancers have been known to manifest as an isolated axillary nodal metastasis without any clinically or radiologically detectable breast tumors (20), and various lesions, both benign and malignant, can develop in the accessory breast tissue, which is present in 0.6%–6% of the general population (21). In addition, scanning of the axilla reinforces the importance of scanning of the posterior breast when performing breast US with a handheld device (19). Conversely, axillary regions cannot be covered with automated breast US owing to its wide field-of-view transducer, so when automated breast US is performed, questions remain as to whether additional axillary US should be included. Yet despite these considerations, relatively little is known about the effects of routine bilateral axillary scanning during screening breast US.

Therefore, the purpose of this study was to evaluate the effect of routine axillary scanning during supplemental screening breast US in women with negative mammographic findings.

Advances in Knowledge

- The frequency of positive axillary findings at screening US in women with negative mammographic findings was 3.5 per 1000 (14 of 4009) baseline US examinations and 2.2 per 1000 (19 of 8835) subsequent US examinations; biopsy (n = 12) and at least 22 months of follow-up (n = 21) for the 33 positive axillary findings in 33 women revealed no malignancy (95% confidence interval [CI]: 0%, 10.6%).
- Supplemental screening breast US depicted 1.5 cancers (95% CI: 0.5, 3.3) per 1000 baseline examinations and 2.2 (95% CI: 1.4, 3.4) per 1000 subsequent examinations with or without axillary scanning; without routine axillary scanning, the abnormal interpretation rate of screening US decreased from 15.2% (610 of 4009 examinations) to 15.0% (602 of 4009 examinations) at baseline US and from 8.1% (714 of 8835 examinations) to 7.9% (700 of 8835 examinations) at subsequent US examinations, and the positive predictive value for biopsy performed increased from 6.0% (five of 83 examinations) to 6.4% (five of 78 examinations) at baseline US and from 7.6% (13 of 170 examinations) to 7.9% (13 of 164 examinations) at subsequent US examinations.

Implications for Patient Care

- Routine axillary scanning during screening breast US does not provide additional breast cancer detection, but rather increases the number of false-positive results leading to recall examinations and biopsies.
- Additional axillary US may not be necessary when automated breast US or breast US with a handheld device is performed in women with negative findings at screening mammography.

Materials and Methods

Study Population

This study was approved by our institutional review board, and the requirement to obtain informed consent was waived. A search of our institutional database identified 23 846 consecutive

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Abbreviations:
AIR = abnormal interpretation rate
BI-RADS = Breast Imaging Reporting and Data System
CDR = cancer detection rate
CI = confidence interval
PPV = positive predictive value
PPV_1 = PPV for abnormal interpretation
PPV_2 = PPV for biopsy recommendation
PPV_3 = PPV for biopsy performed

Author contributions:
Guarantors of integrity of entire study, S.H.L., W.K.M.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, S.H.L., W.K.M.; clinical studies, S.H.L., A.Y., J.M.C., N.C., W.K.M.; statistical analysis, S.H.L., M.J.J.; and manuscript editing, S.H.L., J.M.C., W.K.M.

Conflicts of interest are listed at the end of this article.

Figure 1

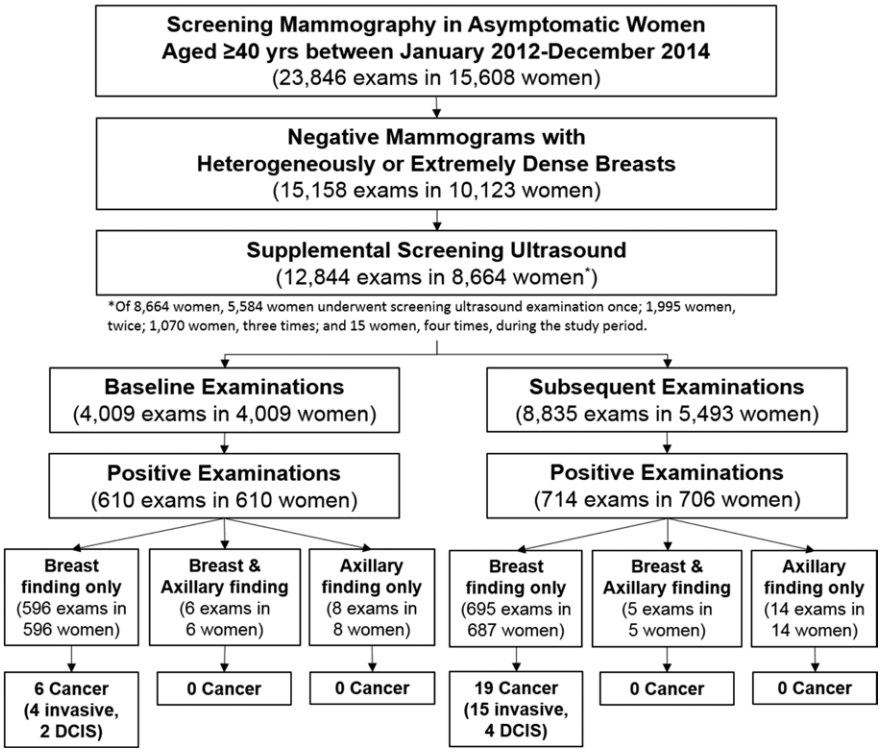


Figure 1: Study flow diagram.

screening mammography examinations performed in 15608 asymptomatic women aged 40 years or older at Seoul National University Hospital Healthcare System Gangnam Center from January 2012 to December 2014. Among them, 15158 screening mammography examinations showed heterogeneously or extremely dense breast tissue and negative results for cancer. Supplemental screening with bilateral whole-breast US was performed within 6 months after mammography in 12844 (84.7%) examinations. We retrospectively reviewed results from all 12844 screening US examinations in 8664 women; 4009 (31.2%) were baseline US examinations and 8835 (68.8%) were subsequent US examinations (Fig 1).

Screening Mammography

Mammography was performed with a dedicated digital mammography unit (Senographe 2000D; GE Medical Systems, Milwaukee, Wis). Standard craniocaudal and mediolateral oblique views were routinely obtained. Screening mammograms were interpreted by one of 10 board-certified and breast fellowship–trained radiologists with 3–20 years of experience (including S.H.L., A.Y., J.M.C., N.C., and W.K.M.). Mammographic breast density was classified as grade a (almost entirely fat), b (scattered fibroglandular densities), c (heterogeneously dense), or d (extremely dense) according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) lexicon (22). Women with initial BI-RADS assessment category 1 (negative) or 2 (benign) at screening mammography and with heterogeneously dense (grade c) or extremely dense (grade d) breast tissue were assigned to undergo supplemental screening breast US.

Screening Breast US

Screening breast US was performed on the same day as mammography in 12779 of 12844 examinations (99.5%) and after a median of 26 days after mammography (range, 1–181 days) in the remaining examinations. Screening breast US was performed and interpreted by one of 10 dedicated breast radiologists with 3–20 years of experience in breast imaging (including S.H.L., A.Y., J.M.C., N.C., and W.K.M.) and with knowledge of the mammographic results and clinical information by using a standardized technique (13). Bilateral whole-breast US examinations were performed with a handheld device (EUB-8500, Hitachi Medical, Tokyo, Japan; Acuson S2000, Siemens Medical Solutions, Mountain View, Calif) equipped with a 6–14- or 6–18-MHz linear-array transducer. The bilateral axillae were routinely scanned, and representative images from all examinations were documented. If the axillary US image showed benign-appearing lymph nodes only, a single view of a representative axillary lymph node was obtained. If there were positive axillary findings assessed as BI-RADS category 3 or higher, two orthogonal view images of the axillary finding were acquired. Time to perform examinations was not recorded, but in our experience it takes approximately 5–20 minutes per patient to perform bilateral breast and axillary scanning. BI-RADS category 1, 2, 3, 4A, 4B, 4C, or 5 was recorded for each breast and axillary finding. Axillary lymphadenopathy with a round shape, cortical thickness greater than 3 mm, or loss of fatty hilum detected in women without a history of rheumatoid arthritis or systemic lupus erythematosus was assessed as BI-RADS category 4 (biopsy recommendation) or 3 (short-term follow-up recommendation) at the radiologist's discretion (23,24).

Data Collection

Demographic and imaging data were obtained from a prospectively maintained institutional database. For positive screening US examinations, defined as BI-RADS category 3, 4A, 4B, 4C, or 5, the reports were reviewed to determine whether the positive findings were in the breast, the axilla, or both. For negative screening examinations, the results for the breast and

axilla were recorded as negative. Our institutional pathology database was searched for biopsy or surgery performed within 1 year of the screening US examination in all women, and the results were reviewed. Primary breast cancers diagnosed within 1 year were identified and classified as invasive or ductal carcinoma in situ. Cancers containing mixed invasive and in situ components were classified as invasive. Women with only lobular carcinoma in situ were not considered to have cancer. For all women with positive screening US results in the breast and/or axilla, an additional medical record review was performed to determine clinical outcomes during the follow-up period. If no tissue diagnosis of cancer was made within 1 year, the result was considered to be disease negative.

Outcome Measurements and Statistical Analysis

All analyses were conducted by using the screening examination as the unit of analysis; women may have undergone more than one breast US examination during the study period. Differences in demographics and breast density between women who underwent screening US and those who did not undergo screening US were assessed by using the χ^2 test or Fisher exact test for categorical variables and the *t* test for continuous variables. The abnormal interpretation rate (AIR), the cancer detection rate (CDR), and the positive predictive value (PPV) for abnormal interpretation (PPV_1), PPV for biopsy recommendation (PPV_2), and PPV for biopsy performed (PPV_3) were calculated separately for baseline and subsequent US examinations according to BI-RADS guidelines (25). Exact 95% confidence intervals (CIs) were calculated for AIR and CDR. To determine the hypothetical performance of screening breast US without routine axillary scanning, the outcome measures were calculated in two ways: with combined data for the breast and axilla and with data for the breast only. Two-sided $P < .05$ was indicative of a statistically significant difference.

Table 1

Demographic Characteristics of Women with and without Supplemental Screening US after Negative Mammographic Findings

Characteristic	With Supplemental Screening US (*n* = 12844)	Without Supplemental Screening US (*n* = 2314)	*P* Value
Mean age ± SD (y)	51.2 ± 7.2	50.0 ± 7.9	<.001
Age group (y)	…	…	<.001
40–49	5809 (45.2)	1269 (54.8)	…
50–59	5449 (42.4)	770 (33.3)	…
≥60	1586 (12.3)	275 (11.9)	…
Family history of breast cancer*	…	…	<.001
No	12411 (96.6)	2282 (98.6)	…
Yes	433 (3.4)	32 (1.4)	…
Personal history of breast cancer	…	…	.459
No	12732 (99.1)	2298 (99.3)	…
Yes	112 (0.9)	16 (0.7)	…
Breast density	…	…	.037
Heterogeneously dense	9169 (71.4)	1701 (73.5)	…
Extremely dense	3675 (28.6)	613 (26.5)	…
Type of screening US	…	…	NA
Baseline	4009 (31.2)	NA	…
Subsequent	8835 (68.8)	NA	…

Note.—Except where indicated, data are numbers of examinations, with percentages in parentheses. NA = not applicable, SD = standard deviation.

* Family history of breast cancer in first-degree relatives.

Statistical analyses were performed with software (SAS for Windows, version 9.3; SAS Institute, Cary, NC).

Results

Demographics of the Study Population

The mean age (±standard deviation) of women at the time of screening US was 51.2 years ± 7.2 (Table 1). Of the 12844 women, 12411 (96.6%) had no family history of breast cancer in first-degree relatives and 12732 (99.1%) had no personal history of breast cancer. Mammographic breast density was classified as heterogeneously dense (BI-RADS grade c) in 9169 of the 12844 women (71.4%) and as extremely dense (BI-RADS grade d) in 3675 (28.6%). Women who underwent supplemental screening breast US after negative mammographic findings had a higher mean age and higher incidence of family history of breast cancer than did women who did not undergo screening breast US ($P < .001$ for both).

Axillary Findings at Screening US in Women with Negative Mammographic Findings

The frequency of positive findings in the axilla at supplemental screening US was 3.5 per 1000 (14 of 4009) baseline US examinations and 2.2 per 1000 (19 of 8835) subsequent US examinations (Table 2). Of the 33 positive axillary findings in 33 women (median age, 51 years; age range, 41–77 years), 23 were unilateral lymph node enlargements, six were bilateral lymph node enlargements, three were soft-tissue masses in the axillary fossa, and one was a mass in the accessory breast tissue (Table 3). Of 33 women with abnormal axillary findings, nine patients had previously undergone one US examination with negative findings, and one patient had previously undergone two US examinations with negative findings. The remaining 23 women underwent screening US examination once during the study period.

There was no known current malignancy in the 33 women with abnormal

Table 2

Results of Screening US for Breast and Axilla in Combination or Alone

Finding	Breast and Axilla	Breast	Axilla
Baseline screening US (n = 4009)			
Negative (BI-RADS 1, 2)	3399 (0)	3407 (0)	3995 (6)
Positive	610 (6)	602 (6)	14 (0)
BI-RADS 3	501 (1)	499 (1)	8 (0)
BI-RADS 4A	105 (4)	99 (4)	6 (0)
BI-RADS 4B	3 (1)	3 (1)	0 (0)
BI-RADS 4C	1 (0)	1 (0)	0 (0)
BI-RADS 5	0 (0)	0 (0)	0 (0)
Subsequent screening US (n = 8835)			
Negative (BI-RADS 1, 2)	8121 (3)	8135 (3)	8816 (22)
Positive	714 (19)	700 (19)	19 (0)
BI-RADS 3	527 (6)	519 (6)	12 (0)
BI-RADS 4A	179 (11)	173 (11)	7 (0)
BI-RADS 4B	6 (0)	6 (0)	0 (0)
BI-RADS 4C	1 (1)	1 (1)	0 (0)
BI-RADS 5	1 (1)	1 (1)	0 (0)

Note.—Data are numbers of examinations. Data in parentheses are numbers of women diagnosed with breast cancer within 1 year after screening US examination.

Table 3

US Features of 33 Positive Axillary Findings at Screening US

Axillary Finding	Lesion Size (mm)	Round Shape*	Cortical Thickness (mm)	Loss of Fatty Hilum*
Lymph node enlargement (n = 29)				
Unilateral (n = 23)				
BI-RADS 3 (n = 14)	11.4 (5.4–21.3)	4	4.0 (2.8–7.4)	4
BI-RADS 4A (n = 9)	15.3 (6.2–24.3)	0	5.3 (3.0–7.9)	2
Bilateral: BI-RADS 3 (n = 6)	9.6 (6.6–22.9)	0	3.9 (3.0–5.4)	0
Soft-tissue mass (unilateral): BI-RADS 4A (n = 3)	16.2 (11.1–18.0)	NA	NA	NA
Mass in the accessory breast (unilateral): BI-RADS 4A (n = 1)	17.6	NA	NA	NA

Note.—Unless otherwise indicated, data are medians, with ranges in parentheses. NA = not applicable.

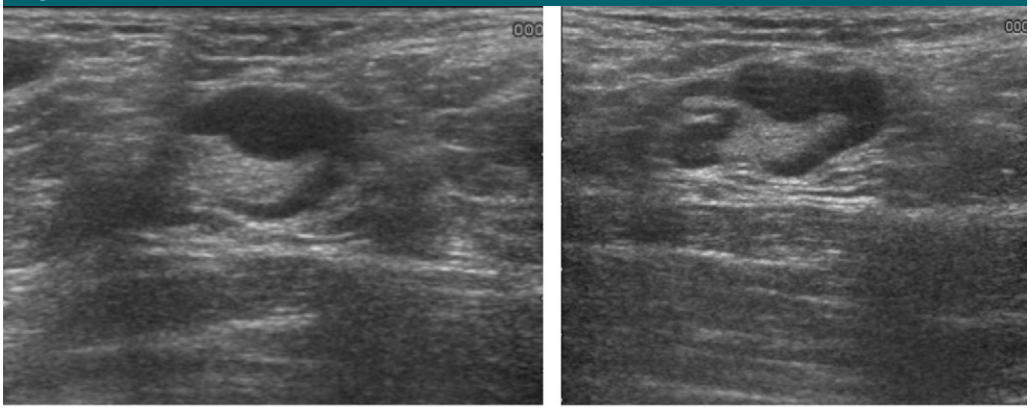
* Data are numbers of cases.

axillary findings, but two women had a history of breast cancer. Eleven of the 33 women had positive breast findings at breast US (BI-RADS category 3 masses in seven women and category 4A masses in four women); none were diagnosed with breast cancer. The other 22 women showed positive findings only in the axillae. Biopsy (n = 13) or follow-up (n = 20) was recommended for the 33 axillary findings. One lesion, unilateral axillary lymphadenopathy, had decreased in size at the time of biopsy and was considered benign; therefore, biopsy was cancelled. The woman had no evidence of malignancy after 22 months of clinical follow-up. Of the 12 axillary lesions that were sampled for biopsy, 11 were sampled with US-guided 16-gauge core needle biopsy and the findings were reactive hyperplasia (n = 5) (Fig 2), lymphoid tissue with no tumor (n = 1), fibroadipose tissue only (n = 3), and fibrocystic change (n = 2). With regard to the finding of only fibroadipose tissue at biopsy, the images and pathologic findings were considered to be concordant in two women with axillary soft-tissue masses and not concordant in one woman with unilateral axillary lymphadenopathy that had disappeared at follow-up US after 25 months. US-guided fine-needle aspiration biopsy was performed for unilateral axillary lymphadenopathy in one woman, and the result was negative for malignant cells. Of the 20 axillary lesions assessed as BI-RADS category 3, 11 remained stable or had disappeared at follow-up US (median 32 months; range, 22–48 months). The other nine axillary lesions were considered benign because there was no evidence of malignancy in the nine affected women after a median clinical follow-up of 32 months (range, 26–54 months). The rate of cancer among those with positive axillary findings was 0% (95% CI: 0%, 10.6%). The findings at axillary screening US were negative in all 25 women with breast cancers detected at supplemental screening US, including two invasive cancers with axillary lymph node metastases found at surgery.

Screening Outcomes for Breast US with and without Axillary Scanning

Baseline screening breast US with routine axillary scanning showed an AIR of 15.2% (95% CI: 14.1%, 16.4%) and enabled detection of an additional 1.5 (95% CI: 0.5, 3.3) cancers per 1000 examinations when the bilateral axillae were routinely scanned (Table 4). The PPV_1 was 1.0% (six of 610 examinations), PPV_2 was 4.6% (five of 109 examinations), and PPV_3 was 6.0% (five of 83 examinations). Subsequent screening breast US with routine axillary scanning showed an AIR of 8.1% (95% CI: 7.5%, 8.7%) and a CDR of 2.2 cancers per 1000 examinations (95% CI: 1.4, 3.4). When outcome measures of screening US were calculated by using the breast data to determine the hypothetical performance of screening breast US without routine axillary scanning, the AIR was 15.0% (95% CI: 13.9%, 16.2%) at baseline screening and 7.9% (95% CI: 7.4%, 8.5%) at subsequent screening. Incremental CDR was not changed with axillary scanning for either baseline or subsequent screening examinations. Without axillary scanning, the PPV_2 and PPV_3 of screening US increased;

Figure 2



a. b.

Figure 2: US images show axillary lymphadenopathy detected at supplemental screening US in 53-year-old woman with negative findings at mammography. **(a, b)** Two orthogonal views in left axilla at axillary screening US show 18.7-mm lymph node with eccentric cortical thickening (cortical thickness, 5.3 mm; preserved fatty hilum). US-guided 16-gauge core needle biopsy was performed in left axillary lymph node; result was reactive hyperplasia.

the PPV_3 of baseline and subsequent screening US increased from 6.0% (five of 83 examinations) to 6.4% (five of 78 examinations) and from 7.6% (13 of 170 examinations) to 7.9% (13 of 164 examinations), respectively.

Characteristics of Cancers Detected with Screening US

Of the 25 cancers detected with supplemental screening US, six (24.0%) were ductal carcinoma in situ and 19 (76.0%) were invasive. Among the invasive cancers for which the size was known, the mean size was 8 mm (median, 8 mm; range, 1–15 mm). Of the 17 invasive cancers with known nodal status, 15 (88.2%) had no axillary lymph node metastasis and two (11.8%) had metastases in one axillary lymph node. Three interval cancers were identified in our study population. Two of the three interval cancers were invasive (mean size, 15 mm), and none involved metastasis in axillary lymph nodes.

Table 4

Outcomes of Screening Breast US with and without Axillary Scanning

Outcome Measure	Supplemental Screening US of Breast and Axilla	Supplemental Screening US of Breast Alone
Baseline screening US		
AIR (%)	15.2 (610/4009) [14.1, 16.4]	15.0 (602/4009) [13.9, 16.2]
CDR (‰)	1.5 (6/4009) [0.5, 3.3]	1.5 (6/4009) [0.5, 3.3]
PPV_1(%)	1.0 (6/610)	1.0 (6/602)
PPV_2 (%)	4.6 (5/109)	4.9 (5/103)
PPV_3 (%)	6.0 (5/83)	6.4 (5/78)
Subsequent screening US		
AIR (%)	8.1 (714/8835) [7.5, 8.7]	7.9 (700/8835) [7.4, 8.5]
CDR (‰)	2.2 (19/8835) [1.4, 3.4]	2.2 (19/8835) [1.4, 3.4]
PPV_1 (%)	2.7 (19/714)	2.7 (19/700)
PPV_2 (%)	7.0 (13/187)	7.2 (13/181)
PPV_3 (%)	7.6 (13/170)	7.9 (13/164)

Note.—Numbers in parentheses are raw data; numbers in brackets are 95% CIs.

Discussion

According to our study findings, routine axillary scanning performed during supplemental screening breast US had no effect on additional cancer detection, but instead increased the number of false-positive results. Supplemental screening US enabled detection of 25 mammographically occult breast cancers (19 invasive), and all of these cancers were diagnosed as positive findings in the breast. Axillary screening US would have increased the additional CDR if it had depicted axillary metastases in women with occult primary breast tumors at screening breast US or primary cancers occurring in accessory axillary breast tissue; however, there were no such patients in our study population (n = 12 844), which was gathered from a single high-volume screening center for 3 consecutive years. In contrast, 33 positive findings detected at axillary screening US in 33 women were all benign (95% CI for the rate of cancer among those with positive axillary findings: 0%, 10.6%) in our study.

The yield for the detection of axillary metastasis is expected to be low with axillary screening US because screening US–detected breast cancers are mostly small, node-negative invasive

cancers (8–14). In our study,15 of 17 invasive cancers that had been detected at supplemental screening US and had undergone staging (88.2%) were node-negative, similar to the findings of the American College of Radiology Imaging Network ACRIN 6666 trial (89% [eight of nine]) and Japan Strategic Anti-cancer Randomized Trial J-START (86% [47 of 55]) (8,14). Even if metastases are present in the axillary lymph nodes, small metastases without enlargement of the node or replacement of the fatty hilum can have a normal appearance at US (26). The sensitivity of US for the detection of axillary metastases is known to be moderate (26.4%–79.5%) when morphologic criteria are used (27). In our study, two invasive cancers were detected at supplemental screening US and axillary metastases were found at surgery; however, neither showed suspicious findings at axillary screening US. Primary cancers occurring in accessory axillary breast tissue are very rare and are less likely to be diagnosed at screening US; palpable symptoms in the axilla or abnormal findings at mammography, including calcifications in accessory axillary breast tissue, are usually accompanied by other findings (28).

Many studies (23,26,27) have evaluated the usefulness of US in assessing axillary lymph nodes in patients with known breast cancer; however, studies evaluating the clinical importance of axillary lymphadenopathy encountered at axillary scanning during screening breast US are few. In one such study, Kim and Park (29) found that no malignancy was diagnosed in nonpalpable axillary lymphadenopathies identified at breast US in patients without known malignancy, despite frequent manifestations of suspicious US features including loss of the fatty hilum, round shape, abnormal cortical thickening, and marked hypoechogenicity. Our results support their conclusion that short-term follow-up imaging rather than immediate biopsy can be recommended for nonpalpable lymphadenopathy in patients without known malignancy. However, in the study by Kim and Park, only 13 of 73 US examinations (17.8%) were performed for screening purposes. Our study included 12844 supplemental screening US examinations in women with negative mammographic findings, and the frequency of positive axillary findings at screening US was 3.5 per 1000 baseline examinations and 2.2 per 1000 subsequent examinations. The recall rate for the axilla was higher at baseline screening US than at subsequent screening because comparisons with axillary findings from previous US examinations can reduce unnecessary recall examinations. Without routine axillary scanning, the AIR of screening US decreased and the PPV_2 and PPV_3 of screening US increased for both baseline and subsequent examinations.

Our study had several limitations. First, this study was a single-center retrospective analysis, which limits the generalizability of the study results. Most of our study population (96.6%, 12411 of 12844 women) had no family history of breast cancer in first-degree relatives. Second, the number of women in our study population with abnormal axillary findings at screening US was small (n = 33). The upper limit of the rate of cancer among those with positive axillary findings was 10.6%. Further studies with larger patient populations appear to be warranted. Third, a positive screening US finding was defined as a final BI-RADS assessment category of 3 or higher based on the report and did not strictly follow the audit guidelines of the fifth edition of BI-RADS (25). This was because our study period preceded the publication and implementation of the new edition of BI-RADS, in which a screening US examination is considered positive if both standard (a single image of each breast quadrant plus a retroareolar image and, if a benign finding is present, a single representative image of that finding) and additional (diagnostic) images are recorded, independent of the assessment rendered. Screening US was performed by radiologists in our study, and additional diagnostic US images were acquired for breast and axillary lesions assessed as BI-RADS category 3 or higher.

In conclusion, routine axillary scanning during supplemental screening breast US did not provide additional breast cancer detection, but rather increased the number of false-positive results leading to recall examinations and biopsies. However, the conclusions based on these findings must be tempered by the low rate of positive findings (CI for cancer detection after axillary scanning: 0%, 10.6%). Our study results suggest that additional axillary US may not be necessary when automated breast US or breast US with a handheld device is performed in women with negative findings at screening mammography.

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