

RESEARCH ARTICLE

Comparison of Automated Breast Volume Scanning and Hand-Held Ultrasound in the Detection of Breast Cancer: an Analysis of 5,566 Patient Evaluations

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Abstract

Background: The purpose of this study was to compare the accuracy and effectiveness of automated breast volume scanning (ABVS) and hand-held ultrasound (HHUS) in the detection of breast cancer in a large population group with a long-term follow-up, and to investigate whether different ultrasound systems may influence the estimation of cancer detection. **Materials and Methods:** Institutional review board approval was obtained for this retrospective study, and informed consent was waived. From September 2010 to August 2011, a total of 1,866 ABVS and 3,700 HHUS participants, who underwent these procedures at our institute, were included in this study. Cancers occurring during the study and subsequent follow-up were evaluated. The reference standard was a combination of histology and follow-up imaging (≥ 12 months). The recall rate, cancer detection yield, diagnostic accuracy, sensitivity, specificity, and positive (PPV) and negative (NPV) predictive values were calculated with exact 95% confidence intervals. **Results:** The recall rate was 2.57 per 1,000 (48/1,866) for ABVS and 3.57 per 1,000 (132/3,700) for HHUS, with a significant difference ($p=0.048$). The cancer detection yield was 3.8 per 1,000 for ABVS and 2.7 per 1,000 for HHUS. The diagnostic accuracy was 97.7% for ABVS and 96.5% for HHUS with statistical significance ($p=0.018$). The specificity of ABVS and HHUS were 97.8%, 96.7%, respectively ($p=0.022$). **Conclusions:** ABVS shows a comparable diagnostic performance to HHUS. ABVS is an effective supplemental tool for mammography in breast cancer detection in a large population.

Keywords: Breast cancer - automated breast volume scanning - ultrasound - screening

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Introduction

Breast cancer screening with mammography is a standard imaging method and has been shown to decrease mortality. In Korea, mammography is implemented for breast cancer screening (Kim et al., 2011) with controversy in cost-effectiveness (Kang et al., 2013; Yoo et al., 2013). Mammography has well recognized limitations, such as reduced sensitivity of both screening and diagnostic mammography in dense breast tissue by as much as 50% compared with fatty breast tissue (Kolb et al., 2002; Berg et al., 2004; Boyd et al., 2007). The sensitivity is lower among women younger than 50 years and extremely dense breast tissue carries a higher risk for breast cancer: up to an 18-fold increase in interval cancer compared with fatty breast tissue (Boyd et al., 2007).

Ultrasound (US) has been demonstrated to be a supplemental screening tool for breast cancer and the sensitivity is less affected by breast density. Breast US is widely available, painless, well-tolerated, relatively

inexpensive, and does not involve ionizing radiation (Berg et al., 2008). Supplemental screening using breast US increased the detection of early, node-negative, invasive breast cancers not normally seen on mammography in women with dense parenchyma (Benson et al., 2004; Berg et al., 2004; Wang et al., 2013). However, the dependence on operator technique for hand-held ultrasound (HHUS) is a major concern when considering the widespread use of whole-breast US (Akbari et al., 2012; Lin et al., 2012). Automated breast volume scanning (ABVS), which can produce objective and reproducible images, has several advantages over HHUS-including more reproducibility, the capacity for gathering standardized views of the entire breast volume by lesser trained personnel, 3D capability through multiplanar reconstruction, shorter non-real-time review with delayed interpretation, and the potential for complete documentation (Cho et al., 2006; Chou et al., 2007). There are several previous studies that have demonstrated the feasibility of ABVS (Tozaki and Fukuma, 2010; Lin et al., 2012) and that showed

equal performances when comparing ABVS with HHUS (Chang et al., 2011; Shin et al., 2011). High reliability was obtained in the detection of breast lesions and in the reporting of lesion size and location for ABVS (Shin et al., 2011), and it could be used for not only follow-up of benign lesions, but also for the screening of breast cancer. ABVS has been proposed as a suitable technique for the screening of breast cancer in women with dense breast tissue (Kelly et al., 2010a; 2010b). However, there are few studies comparing ABVS and HHUS in a large group. Therefore, the purpose of this study was to retrospectively compare the accuracy and effectiveness of ABVS and HHUS in the detection of breast cancer in a large population group with a long-term follow-up, and to investigate whether different ultrasound systems may influence the estimation of cancer detection.

Materials and Methods

This retrospective study was approved by the institutional review board of our hospital for human investigation, and informed consent was waived for use of data.

Patients

We reviewed the computerized medical records, breast US images in our institution from September 2010 to August 2011. During this period total 16,894 breast US were performed. There are four HHUS and one ABVS units at our institution. ABVS commenced in our institute from August 2010 for asymptomatic women with benign findings (BI-RADS category 1, 2, and 3) follow-up who underwent previous HHUS at our institution, and we did not do ABVS in women with axillary lesions nor abnormalities detected by mammography, PET/CT or other modality. We included patients that could be assigned to two study groups: an ABVS group and a HHUS group. The ABVS and HHUS group was defined who undergone the ABVS or HHUS as the very first US tool in this period who underwent previous HHUS at our institution within 6 month to 1 year. The participants were randomly selected to undergo either ABVS or HHUS. Whether the ultrasound was interpreted in conjunction with prior mammography or not was evaluated. Cancers occurring during the study and subsequent follow-up were evaluated.

The reference standard was a combination of histology and follow-up imaging (≥ 12 months). The women who had reference standard under 12 months were excluded. Finally, 1,866 ABVS and 3,700 HHUS participants out of 5,566 women (age range, 19-82 years, mean age \pm SD: 47 \pm 9 years) were analyzed in the study.

US examination and image analysis

HHUS: Hand-held ultrasound was performed by one of five board certified radiologists who specialized in breast imaging with 1 to 11 years of experience using the IU22 instrument (Philips Medical System, Bothell, WA), equipped with a 50mm linear array transducer with a bandwidth of 5-12 MHz. The whole breast was scanned, starting from the right breast and using two perpendicular

scans (transverse and sagittal orientation). The patient was in a supine or supine-oblique position with her arm raised above the head. If an abnormal lesion was detected, its location according to breast, size, features, and the American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS) final assessment were recorded (Mendelson et al., 2003). The average time required to perform an ultrasound examination with a hand-held device per patient was approximately 20 minutes.

ABVS: Automated breast US was performed by two trained technologists, who had at least one month of experience with the technique, using an ACUSON S2000 system (Siemens Medical Solutions, Mountain View, CA) with a large-footprint wide-frequency bandwidth transducer (5–14 MHz with a 9 MHz center frequency). All patients were placed in the supine position on an examination table and positioned with the arm above the head. For scanning, a specific lotion for the ABVS unit was used for optimal imaging and to avoid contact artifacts. Customized presets were also used to optimize depth, gain, frequency, and view. A typical examination comprised three automated scans of each breast in the anteroposterior and both oblique positions. Occasionally, additional superior or inferior views were required for larger breasts. The whole nipple was included in each scan. Scan thickness was displayed at intervals of 0.5 mm without overlap. After volume data acquisition, the axial image series was automatically sent from the automated breast volume scanner to the workstation and reviewed in multiple orientations in a multiplanar reconstruction (MPR) display. The total acquisition time per patient was about 15 minutes.

The image review was completed by one of five board certified radiologists with 1 to 11 years of experience with HHUS. They reviewed the 3D volume ABVS data at the workstation, and each reader evaluated these data according to the ACR BI-RADS lexicon. The average time required to review the ABVS was approximately 10 minutes.

Data evaluation: HHUS and ABVS data were collected from a review of radiologic reports. For each modality, assessments were recorded according to the ACR BI-RADS assessment (Mendelson et al., 2003; D'Orsi et al., 2003) as follows: 0, incomplete; 1, negative; 2, benign; 3, probably benign; 4A, low suspicion; 4B, intermediate suspicion; 4C, moderate suspicion; or 5, highly suggestive of malignancy. A BI-RADS assessment of 0, 4A, 4B, 4C, or 5 was considered "positive", and a BI-RADS assessment of 1, 2, or 3 was considered "negative".

Reference standard information included a combination of pathology results, as well as 1 year clinical and imaging follow-up results. Pathology results revealing breast cancer, including ductal carcinoma in situ (DCIS), were considered "disease positive" and when breast cancer was detected, the lesion was removed surgically and a final pathological report was reviewed. The lesion was reviewed for histological type, invasive size, and lymphovascular invasion. The absence of a known diagnosis of breast cancer on a review of medical records at the 1 year follow-up for breast US was considered to

indicate “disease negative”.

Statistical analysis

After completing the reading session and receiving histopathological results, the recall rate, cancer detection yield (i.e., the number of women with a positive examination and positive reference standard per 1,000 patients), and performance characteristics of each method, including diagnostic accuracy, sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, were calculated with exact 95% confidence intervals. The Chi-square or Fisher’s exact test was used to compare the diagnostic yields between ABVS and HHUS. A p value less than 0.05 was considered statistically significant. All statistical analyses were performed with statistical software (SPSS for Windows, version 20.0; SPSS, Chicago, IL).

Results

The final series consisted of 1,866 participants from ABVS group and 3,700 participants from HHUS group. The mammography was performed in 3,303 participants in initial breast US; 1,038 participants in ABVS group and 2,265 participants in HHUS group. At the last follow up US, 3,819 patients performed mammography; 1,336 participants in ABVS group and 2,483 participants in HHUS group. The mean follow-up period of ABVS and HHUS was 13.79±3.31 months, 14.51±4.01 months, respectively.

The overall performance characteristics of ABVS and HHUS methods for breast cancer screening are listed in Table 1. The recall rate was 2.57 per 1,000 (48/1,866) for ABVS and 3.57 per 1,000 (132/3,700) for HHUS and showed statistically significant difference. Among the 1,866 subjects who underwent ABVS, seven cancers were detected with a cancer detection yield of 3.8 per 1,000; four with invasive ductal carcinoma (IDC), and three with

DCIS. Among the 3,700 subjects who underwent HHUS, 10 breast cancers were identified with a cancer detection yield of 2.7 per 1,000; six with IDC, two with DCIS, one with microinvasive ductal carcinoma, and one with mucinous carcinoma.

Two cases were identified as a false negative in ABVS group with a mean interval period of 11.4 month and they were one IDC and one microinvasive ductal carcinoma. In HHUS group, six cases were identified as a false negative with a mean interval period of 15.5 month and four with DCIS, one with IDC and one with microinvasive ductal carcinoma. Among these eight cases, seven cases were detected after stereotactic biopsy which were identified in only mammography and one case which was detected as IDC by excision after a probable benign HHUS. For all 25 cancers, including nine DCIS lesions, the mean size of the tumor was 17.9 mm (range, 5–37 mm) in ABVS group and 13.8 mm (range, 4–65 mm) in HHUS group, respectively. The mean size of the invasive cancer was 12.4 mm (range, 5–30 mm) and 12.7 mm (range, 6–19), respectively. No axillary lymph node metastasis was found.

The diagnostic accuracy for ABVS was 97.70% (95% CI, 97.01–98.38) and for HHUS was 96.54% (95% CI, 95.95–97.13); this difference reached statistical significance (p=0.018). The sensitivity of ABVS and HHUS was 77.78% (95% CI, 45.26–93.68) and 62.50% (95% CI, 38.64–81.52), and the specificity of ABVS and HHUS was 97.79% (95% CI, 97.02–98.37) and 96.69% (95% CI, 96.06–97.22), respectively; the specificity showed statistical significance (p=0.022). The PPVs of ABVS and HHUS were 14.58% (95% CI, 7.25–27.17) and 7.58% (95% CI, 4.17–13.38), and the NPVs of ABVS and HHUS were 99.89% (95% CI, 99.60–99.97) and 99.83% (95% CI, 99.63–99.92), respectively.

Discussion

In Korea, breast cancer has become the second most common cancer in women (Jung et al., 2012). Moreover, as Asian women have smaller breast volumes and less body fat, resulting in relatively dense breasts, it can be relatively difficult to detect breast cancer by mammography alone (Yoo et al., 2013). For these reasons, a supplemental screening tool in addition to mammography is needed to improve the detection of breast cancer among Asian women and more generally (Boonlikit, 2013; Suh et al., 2013). However, to date there is no scientific evidence that breast US screening reduces breast cancer mortality. Screening using breast US is also limited by the need for standardization of the scanning technique, the time required to perform a bilateral ultrasound, and cost.

In our current study, the PPV of ABVS and HHUS was 14.58% and 7.58%, respectively. This is not higher than the 33% PPV reported by the Breast Cancer Surveillance Consortium (BCSC) (Weaver et al., 2006), but is substantially higher than that reported in the previous ACRIN trial, which showed an 11% PPV (Berg, 2007). Considering the low recall rate of 2.57 per 1,000 and the high PPV of 14.58% in ABVS compared with HHUS, ABVS is a good supplemental tool for screening breast cancer. The cancer detection rate in our current study was

Table 1. Summary of the Performance Characteristics of ABVS and HHUS.

	ABVS	HHUS	p
Recall Rate (per 1,000)	48/1,866 2.57 (1.95, 3.39)	132/3,700 3.57 (3.26, 4.53)	0.048*
Cancer Detection-Yield (per 1,000)	7/1,866 3.8 (1.8, 7.7)	10/3,700 2.7 (1.5, 5.0)	0.503
Accuracy	1,823/1,866 97.70 (97.01, 98.38)	3,572/3,700 96.54 (95.95, 97.13)	0.018*
Sensitivity	7/9 77.78 % (45.26, 93.68)	10/16 62.50 % (38.64, 81.52)	0.661
Specificity	1,816/1,857 97.79 % (97.02, 98.37)	3,562/3,684 96.69 % (96.06, 97.22)	0.022*
Positive Predictive Value	7/48 14.58 % (7.25, 27.17)	10/132 7.58 % (4.17, 13.38)	0.160
Negative Predictive Value	1,816/1,818 99.89 % (99.60, 99.97)	3,562/3,568 99.83 % (99.63, 99.92)	0.725

(95% confidence intervals); ABVS, automated breast volume scanning; HHUS, hand-held ultrasound; *p < 0.05

3.8 per 1,000 in ABVS subjects, which is higher than both a previous study that showed 2.6 per 1,000 for a cancer detection rate with ABVS and the supplemental yield findings of earlier studies using HHUS (range, 2.7-4.6 per 1,000) (Berg, 2009).

In this study, the accuracy, sensitivity and specificity of ABVS was found to be 97.70%, 77.78%, and 97.79%, respectively. The diagnostic accuracy and specificity of ABVS was significantly higher than HHUS, although the absolute value was little different. This result was similar to previous studies (Kotsianos-Hermle et al., 2009; Wang et al., 2012). ABVS can be more complete than HHUS for evaluating breast lesions because ABVS could improve breast lesion analysis by additional coronal-plane image which shows better observation of lesion margin and each sectional plane of the saved volume can be visualized avoiding non-standardized documentation.

The size of a cancerous breast lesion plays an important role in its staging and subsequent treatment. In our current study, the mean size of the breast tumors was 17.9 mm in ABVS group and 13.8 mm in HHUS group, respectively. If defined to invasive cancer, the mean sizes of the tumors are 12.4 mm in ABVS group and 12.7 mm in HHUS group which indicate the benefits of detecting smaller lesions.

Of the 25 detected cancers in our current study subjects, seven cases were detected only by follow-up mammography. All cases underwent stereotactic mamotome biopsy for newly developing, or increasing microcalcifications, and the histologic types were four DCIS, two microinvasive ductal carcinoma and one IDC. The lesions in these cases were all difficult to detect by US. Although supplemental breast US increases the detection in western countries of early, node-negative invasive breast cancers in women with mammographically dense breast tissue (Kolb et al., 2002; Berg et al., 2008; Berg et al., 2012), our present findings still demonstrate the importance of mammography for screening breast cancer, especially microcalcifications.

There are some noteworthy limitations of our study. First, as it was a retrospective study, it may have an inherent bias in terms of patient selection. No participants undergone two different devices at the same time, and we compared the different devices of each study group. However, even though selection bias exists, our study could be representative; that is, large population was enrolled in the study and both study groups were randomly selected from the same condition. Second, both study groups were asymptomatic women with benign findings follow up without history of breast cancer or high risk lesion, not a population-based group. Third, the examinations were performed by a number of different breast examiners, especially for ABVS. Finally, at the initial assessment, we only analyzed US without considering whether assessment of mammography and follow-up mammography was completed in all subjects. Among 5,566 cases, only 3,827 subjects underwent mammography with various breast densities during the 1 year follow-up. In our current study, seven breast cancers were detected as microcalcifications at mammography, and some cancers may be missed in women who did not

undergo mammography.

In conclusion, ABVS shows comparable diagnostic performance when compared with HHUS and is a feasible supplemental tool for mammography when screening for breast cancer in a large population.

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