



**TITLE: Three-Dimensional Ultrasound for Screening and Diagnosis of Breast Cancer: Clinical and Cost Effectiveness**

**DATE:** 9 March 2012

## **RESEARCH QUESTIONS**

1. What is the clinical effectiveness of three-dimensional ultrasound for screening and diagnosis of breast cancer?
2. What is the cost effectiveness of three-dimensional ultrasound for screening and diagnosis of breast cancer?

## **KEY MESSAGE**

Seven clinical studies were identified pertaining to the clinical effectiveness of three-dimensional ultrasound for screening and diagnosis of breast cancer. No cost-effectiveness information was identified.

## **METHODS**

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 2), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2007 and February 27, 2012. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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## RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies and economic evaluations.

Seven non-randomized studies were identified regarding the clinical effectiveness of three-dimensional (3D) ultrasound for screening and diagnosis of breast cancer. No relevant health technology assessment reports, systematic reviews, meta-analyses, randomized controlled trials, or economic evaluations were identified.

## OVERALL SUMMARY OF FINDINGS

Seven non-randomized studies<sup>1-7</sup> suggested the following regarding the clinical effectiveness of 3D ultrasound for screening and diagnosis of breast cancer:

- 3D ultrasound may serve as a useful tool in distinguishing between benign and malignant breast tumors<sup>1,5,6,7</sup>
- of handheld ultrasound-detected cancers, only 57.1- 78.6% were also identified with 3D automated breast ultrasound<sup>2</sup>
- automated 3D ultrasound imaging appears to be similar to hand-held ultrasound in terms of diagnostic quality<sup>3,4</sup> but the sensitivity of mammography was significantly lower than of each ultrasound method.<sup>4</sup>

No relevant literature was identified pertaining to the cost-effectiveness of 3D ultrasound for screening and diagnosis of breast cancer; therefore, no summary has been provided on this topic.

## REFERENCES SUMMARIZED

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

No literature identified.

### Randomized Controlled Trials

No literature identified.

### Non-Randomized Studies

1. Chang JM, Moon WK, Cho N, Park JS, Kim SJ. Radiologists' performance in the detection of benign and malignant masses with 3D automated breast ultrasound (ABUS). *Eur J Radiol.* 2011 Apr;78(1):99-103.

[PubMed: PM21330080](#)

**OBJECTIVES: To retrospectively evaluate the detection performance of benign and malignant breast masses using 3D volume data obtained by ABUS and to determine lesion variables which affect detectability.** **METHODS:** Between November and December of 2007, bilateral whole breast US images were obtained using ABUS in 67 consecutive women who were scheduled to undergo US-guided needle biopsy due to suspicious breast masses. Twenty-four invasive ductal cancers in 23 breasts, 46 benign breast lesions in 44 breasts and 38 normal breasts were included. **Three breast radiologists (experience range, 8-16 years) who did not perform the examinations and were blinded to the histology independently reviewed the ABUS data of the 105 breasts to detect suspicious solid masses with pathology as the standard of reference.** Sensitivity and specificity in detecting benign and malignant masses were calculated, and lesion characteristics affecting detectability were analyzed. **RESULTS:** Sensitivities for benign and malignant mass detections were 65.2% (30/46), 95.8% (23/24) for reader 1 (p=0.007), 66.7% (31/46), 87.5% (21/24) for reader 2 (p=0.087), and 56.3% (24/46), 91.7% (22/24), for reader 3 (p=0.001), respectively. Logistic analysis showed that mass size (odds ratio, 95% CI; 1.12, 1.02-1.24), surrounding tissue changes (odds ratio, 95% CI; 0.11, 0.02-0.47), and shape of the mass (odds ratio, 95% CI; 3.12, 1.02-9.55) were the variables associated with detectability at ABUS. **CONCLUSION: In reader studies using ABUS data, significantly higher sensitivity was noted for malignant breast masses than for benign masses.**

2. Chang JM, Moon WK, Cho N, Park JS, Kim SJ. Breast cancers initially detected by hand-held ultrasound: detection performance of radiologists using automated breast ultrasound data. *Acta Radiol.* 2011 Feb 1;52(1):8-14.

[PubMed: PM21498319](#)

**BACKGROUND:** Ultrasonography (US) has been used as an important adjunct to mammography (MG), and automated breast US (ABUS) scanners were originally designed to effectively examine the breast in its entirety. **PURPOSE: To retrospectively assess the performance of radiologists in the detection of breast cancers, initially detected by hand-held ultrasound (HHUS), using 3D breast volume data obtained from a commercial ABUS system.** **MATERIAL AND METHODS:** Bilateral whole breast

US was performed using ABUS in 61 consecutive women who were scheduled to undergo US-guided needle biopsy due to suspicious breast masses detected during screening HHUS. Fourteen cancers in 13 women and 48 normal breasts of 48 women with benign disease in the contralateral breast were selected. Three radiologists who had not performed the HHUS examinations independently reviewed the 3D ABUS data for any lesions that required recall for further evaluation. Sensitivities and false-positive rates were calculated. **RESULTS: The sensitivities of the three readers for cancer detection were 78.6% (11/14), 78.6%, and 57.1% (8/14), respectively, with false-positive rates of 20.8% (10/48), 12.5% (6/48) and 8.3% (4/48). Seven cancers were detected by all three readers, four cancers by two readers, and one cancer by one reader. Two invasive cancers were not detected by any reader. CONCLUSION: Of HHUS-detected cancers, only 57.1-78.6% were identified with ABUS.** A substantial level of experience and training is necessary to improve cancer detection by ABUS.

3. Stoblen F, Landt S, Stelkens-Gebhardt R, Sehoul J, Rezai M, Kummel S. First evaluation of the diagnostic accuracy of an automated 3D ultrasound system in a breast screening setting. *Anticancer Res.* 2011 Aug;31(8):2569-74.  
[PubMed: PM21778306](#)

**BACKGROUND/AIM: Automated ultrasound examination of suspicious findings can reduce the physician's workload in screening mammography. The present study examines the diagnostic accuracy of this method in comparison to mammography as the reference standard for the first time.** PATIENTS AND METHODS: A total of 304 patients underwent automated 3D ultrasound examination after screening mammography. Mammograms and ultrasound images were assessed by independent examiners, and sensitivity, specificity and the degree of agreement between both methods were calculated. **RESULTS: The degree of agreement was moderate (Cohen's kappa=0.130 for all and 0.153 for positive/negative ratings), mainly owing to a high percentage of false-positive ultrasound results. However, the results of sonographical re-examination of suspicious mammograms were favorable. The only two undetected proven malignant lesions were microcalcified, and in three more cases with disagreement, the ultrasound diagnosis was correct.** **CONCLUSION: Automated 3D ultrasound imaging appears to be on a par with hand-held ultrasound in terms of diagnostic quality.**

4. Kotsianos-Hermle D, Hiltawsky KM, Wirth S, Fischer T, Friese K, Reiser M. Analysis of 107 breast lesions with automated 3D ultrasound and comparison with mammography and manual ultrasound. *Eur J Radiol.* 2009 Jul;71(1):109-15.  
[PubMed: PM18468829](#)

**OBJECTIVES: Our aim was to investigate the diagnostic potential of an automated ultrasound (US) breast scanner prototype and compare it with manual US and mammography.** METHODS: Ninety-seven patients with a total of 107 breast lesions had mammograms, manual US and an automated breast US scan. Multiplanar reconstructions in coronal, axial and the sagittal view were reconstructed from the automated dataset and visualized. After biopsy, all lesions were confirmed histologically. The data were evaluated according to the BIRADS (Breast Imaging Reporting and Data System) classification. The sensitivity and specificity were analyzed. **RESULTS: The BIRADS criterion "margin" was significantly related to the overall BIRADS classification, independently of the US method being used. The sensitivity of mammography was significantly lower**

than of each US method (Fisher's exact test with  $p < 0.05$ ). There were no significant differences between the US methods. **CONCLUSIONS: The reconstructed third (axial) image plane of the whole breast, which corresponds to a craniocaudal mammogram, can give additional information about both, site and differential diagnosis of a lesion. Although image quality was sufficient, automated US is not good enough to replace manual US at this time.**

5. Hsiao YH, Kuo SJ, Liang WM, Huang YL, Chen DR. Intra-tumor flow index can predict the malignant potential of breast tumor: dependent on age and volume. *Ultrasound Med Biol.* 2008 Jan;34(1):88-95.  
[PubMed: PM17720297](#)

**The aim of this study was to assess tumor vascularity through three dimensional (3D) power Doppler breast ultrasound (US) and propose a decision model for the classification of benign and malignant breast tumors.** Patient recruitment for this study was performed consecutively during a 13-mo period (January 2003 to February 2004). A total of 102 benign and 93 malignant solid breast images were analyzed. Three-dimensional power Doppler US imaging was performed using a Voluson730 ultrasound system equipped with a relative stopping power index (RSP) 6 to 12 transducer. The Virtual Organ Computer-aided Analysis (VOCAL)-imaging program (version 2.1) was used to analyze the stored volume. Histogram indices of the vascularization index (VI), flow index (FI) and vascularization-flow index (VFI) for the intra-tumor and for shells with a thickness of 3 mm surrounding the breast lesion were calculated and showed that for both, **malignancy had a higher VI, FI and VFI than benignancy, with statistical significance. Multivariate and stepwise logistic regression revealed the model (including patient age, volume and intra-tumor FI in 3D power Doppler vascularity) to be the best choice for malignant breast tumor characterization.** The receiver operating characteristics (ROC) index for the performance of the model was 0.926. **Histogram indices for the intra-tumor FI in the 3D power Doppler scan are a good choice of parameter for differentiating between malignant and benign tumors with respect to the power of sensitivity, no matter whether one index is suggested or the patients' age and volume are considered.**

6. Kuo SJ, Hsiao YH, Huang YL, Chen DR. Classification of benign and malignant breast tumors using neural networks and three-dimensional power Doppler ultrasound. *Ultrasound Obstet Gynecol.* 2008 Jul;32(1):97-102.  
[PubMed: PM18521971](#)

**OBJECTIVES: To evaluate the use of three-dimensional (3D) power Doppler ultrasound in the differential diagnosis of solid breast tumors using a neural network model as a classifier.** **METHODS:** Data from 102 benign and 93 malignant breast tumor images that had pathological confirmation were collected consecutively from January 2003 to February 2004. We used 3D power Doppler ultrasound to calculate three indices (vascularization index (VI), flow index (FI) and vascularization flow index (VFI)) for the tumor itself and for the tumor plus a 3-mm shell surrounding it. These data were applied to a multilayer perception (MLP) neural network model and we evaluated the model as a classifier to assess the capability of 3D power Doppler sonography to differentiate between benign and malignant solid breast tumors. **RESULTS: The accuracy of the MLP model for classifying malignancy was 84.6%, the sensitivity was 90.3%, the specificity was 79.4%, the positive predictive value was 80.0% and the negative**

predictive value was 90.0%. When the neural network was used to combine the three 3D power Doppler indices, the area under the receiver-operating characteristics curve was 0.89. CONCLUSIONS: 3D power Doppler ultrasound may serve as a useful tool in distinguishing between benign and malignant breast tumors, and its capability may be increased by using a MLP neural network model as a classifier.

7. LeCarpentier GL, Roubidoux MA, Fowlkes JB, Krucker JF, Hunt KA, Paramagul C, et al. Suspicious breast lesions: assessment of 3D Doppler US indexes for classification in a test population and fourfold cross-validation scheme. *Radiology*. 2008 Nov;249(2):463-70. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC265786>  
[PubMed: PM18936310](#)

**PURPOSE: To assess the diagnostic performance of various Doppler ultrasonographic (US) vascularity measures in conjunction with grayscale (GS) criteria in differentiating benign from malignant breast masses, by using histologic findings as the reference standard.** MATERIALS AND METHODS: Institutional Review Board and HIPAA standards were followed. Seventy-eight women (average age, 49 years; range, 26-70 years) scheduled for breast biopsy were included. Thirty-eight patient scans were partially analyzed and published previously, and 40 additional scans were used as a test set to evaluate previously determined classification indexes. In each patient, a series of color Doppler images was acquired and reconstructed into a volume encompassing a suspicious mass, identified by a radiologist-defined ellipsoid, in which six Doppler vascularity measures were calculated. Radiologist GS ratings and patient age were also recorded. Multivariable discrimination indexes derived from the learning set were applied blindly to the test set. Overall performance was also confirmed by using a fourfold cross-validation scheme on the entire population. RESULTS: **By using all cases (46 benign, 32 malignant), the area under the receiver operating characteristic curve (A(z)) values confirmed results of previous analyses: Speed-weighted pixel density (SWPD) performed the best as a diagnostic index, although statistical significance (P = .01) was demonstrated only with respect to the normalized power-weighted pixel density. In both learning and test sets, the three-variable index (SWPD-age-GS) displayed significantly better diagnostic performance (A(z) = 0.97) than did any single index or the one two-variable index (age-GS) that could be obtained without the data from the Doppler scan.** Results of the cross validation confirmed the trends in the two data sets. CONCLUSION: **Quantitative Doppler US vascularity measurements considerably contribute to malignant breast tissue identification beyond subjective GS evaluation alone.** The SWPD-age-GS index has high performance (A(z) = 0.97), regardless of incidental performance variations in its single variable components.

### Economic Evaluations

No literature identified.

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