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3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts

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Disclosure and Thanks

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Many thanks to the members of the SIS ad-hoc committee E B Mendelson and WA Berg for their advice, to B Wilzcek for image material from the Easy study and to GE for providing images of the new Invenia system.
3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts

Outline

- Background
- ABUS – how to perform and what is it good for?
- Handheld Ultrasound (HHUS) – results of the literature
- Automated Breast US (ABUS) – results of the literature
- Advantages and disadvantages
- Conclusion
- Take home messages
3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts
Personalized breast cancer screening and management

Framing – why talking on this topic?

Individual variation in susceptibility to breast cancer

- Individualized risk stratification
- Risk communication
- Revined screening strategies

Improving early detection and diagnosis of breast cancer
Supplemental Ultrasound detects mammographically occult breast cancers

Sensitivity of HH-US and Mx depending on the breast density

US > Mx

Mx > US

<table>
<thead>
<tr>
<th>Modality</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>2-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>98.0</td>
<td>82.9</td>
<td>64.4</td>
<td>47.8</td>
<td>64.4</td>
</tr>
<tr>
<td>US</td>
<td>NP</td>
<td>65.9</td>
<td>81.4</td>
<td>76.1</td>
<td>75.3</td>
</tr>
<tr>
<td>PE</td>
<td>22.0</td>
<td>31.7</td>
<td>28.8</td>
<td>34.8</td>
<td>31.5</td>
</tr>
</tbody>
</table>

### BCSC Mammography Screening Benchmarks (Data 1996 -2005)

<table>
<thead>
<tr>
<th>Category</th>
<th>BCSC (1996-2005)</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer detection rate (per 1,000 examinations)</td>
<td>4.7</td>
<td>3.7</td>
</tr>
<tr>
<td>Median size of invasive cancers (in mm)</td>
<td>14.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Percentage node-negative of invasive cancers</td>
<td>77.3%</td>
<td>96%</td>
</tr>
<tr>
<td>Percentage minimal cancer</td>
<td>52.6%</td>
<td>TBD</td>
</tr>
</tbody>
</table>

### Notes
- Original article describes methodology in detail.
- BCSC data are updated periodically and reported at [http://breastscreening.cancer.gov/data/benchmarks/screening/](http://breastscreening.cancer.gov/data/benchmarks/screening/). Updated data are presented in this table, comprising 4,032,556 screening mammography examinations, 1996-2005, collected from 152 mammography facilities and 803 interpreting physicians that serve a geographically and ethnically representative sample of the United States population. Average data are presented here, but the source material also includes data on ranges and percentiles of performance.
- Minimal cancer is invasive cancer ≤ 1 cm or ductal carcinoma in situ.
- Sensitivity and specificity are measured with reasonable accuracy only if outcomes data are linked to breast cancer data in a regional tumor registry.

There are insufficient rigorous data at this time to address benchmarks for diagnostic breast MRI and US examination.
### Populations included in screening ultrasound studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Years of study</th>
<th>Study design</th>
<th>Location</th>
<th>Number of women</th>
<th>Mean age, y</th>
<th>Mammographic breast density</th>
<th>Mammogram result</th>
<th>Family history, %</th>
<th>Prior breast cancer, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHUS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brancato et al, 2007[^16^]</td>
<td>2003-2006</td>
<td>NR</td>
<td>Italy</td>
<td>5227</td>
<td>51.9</td>
<td>Heterogeneously and extremely dense</td>
<td>Negative</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Berg et al, 2008[^18^] (ACRIN 6666)</td>
<td>2004-2006</td>
<td>Prospective</td>
<td>United States</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parris et al, 2013[^22^]</td>
<td>2009-2010</td>
<td>Retrospective</td>
<td>United States</td>
<td>5519</td>
<td>52</td>
<td>Heterogeneously and extremely dense</td>
<td>Allowed positive mammogram</td>
<td>42</td>
<td>6</td>
</tr>
<tr>
<td>Girardi et al, 2013[^23^]</td>
<td>2009-2010</td>
<td>Retrospective</td>
<td>Italy</td>
<td>9960</td>
<td>51</td>
<td>Heterogeneously and extremely dense</td>
<td>Negative</td>
<td>NR</td>
<td>10</td>
</tr>
<tr>
<td>Giuliano and Giuliano, 2013[^25^]</td>
<td>2010-2011</td>
<td>Prospective</td>
<td>United States</td>
<td>3418</td>
<td>57</td>
<td>Heterogeneously and extremely dense</td>
<td>Allowed positive mammography</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

ABUS, automated breast ultrasound; ACRIN, American College of Radiology Imaging Network; HHUS, handheld ultrasound; NR, not reported.

[^14^]: Includes women reporting either family relatives with breast cancer or a genetic predisposition.
[^15^]: Women with family history or personal history of breast cancer were not separately reported.
[^16^]: Analysis on women with heterogeneously and extremely dense breasts extracted from study data that included all breast densities (n = 22,131).

3D Automated Breast Ultrasound

ABUS – 3-d approach of Ultrasound

- ABUS – how to perform and what is it good for?
ABUS extends 3-d ultrasound to a global view of the breast.

Using 3d volume and multiple planes access for each track.

Supplemental tool to stage breast cancer accurately and non-invasively prior to surgery.

<table>
<thead>
<tr>
<th>Transducer</th>
<th>L14-6XW linear</th>
<th>C15-6XW Reverse Curve (concave)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ergonomics</td>
<td>manual compression</td>
<td>mechanical Compression Assist</td>
</tr>
<tr>
<td>Imaging Architecture</td>
<td>Siemens Antares 5.0</td>
<td>Proprietary Invenia Imaging Architecture</td>
</tr>
<tr>
<td>User Interface</td>
<td>stylus</td>
<td>touch</td>
</tr>
<tr>
<td>Workflow/Acq.</td>
<td>20-30 min. /patient</td>
<td>15 min/patient</td>
</tr>
<tr>
<td></td>
<td>60 sec. acquisition /view</td>
<td>~40 sec. acquisition /view</td>
</tr>
<tr>
<td>Performance</td>
<td>frame rate limited (~4Hz)</td>
<td>faster frame rate (~10 Hz)</td>
</tr>
<tr>
<td>Diagnostic and Screening</td>
<td></td>
<td>Diagnostic and Screening</td>
</tr>
</tbody>
</table>
Fibroadenoma
ABUS (Automated breast ultrasound)

AVUS (Automated breast volume ultrasound)

ABVS (Automated breast volume scanning)

S 2000
Three scanning tracks or projections
Or more per breast

Anterior-posterior  Lateral  Medial

Nipple  Nipple  Nipple

Right hand side
Scanning track or projection

Automated movement of transducer for acquisition of 3-d data
Reverse Curve*

Transducer | L14-6XW linear | C15-6XW Reverse Curve (concave)
3D Automated Breast Ultrasound – what is it?

Principle of volume scanning

- Linked with transducer by mechanical arm
- **Automated** standardized scanning tracks
- Acquisition of a three-dimensional data set using defined speed of scanning
- Coregistration of US echo information with voxel 3-d position in the breast
3D Automated Breast Ultrasound – what is it?

Data acquisition

Technician

- Positioning of patient
- Positioning of transducer
- Mechanical coupling with gel
- Starting and repeating the procedure
Compression Assist

Innovative mechanical design for patient and operator comfort

• Multi-level compression with one-touch operation

• Promotes comprehensive acquisition and study reproducibility
3D Automated Breast Ultrasound - how does it work?

Technical specifications – GE Invenia

Transducer and system

- Uniform compression across the breast
- 15 cm wide field of view
- 6-15 MHz wide bandwidth
- 3 d dataset with 340 images per acquisition
- 3 (to 5) acquisitions per breast
- 15 min examination time
3D Automated Breast Ultrasound - how does it work?

Technical specifications – GE Invenia

- 3-5 min reading time
- Sleek 24” display
- 2 megapixel monitor
- Multi-slice, 3D viewing
- Viewing algorithms
- Supports DICOM® 3.0

DICOM is a registered trademark of the National Electrical Manufacturers Association. Third party trademarks are the property of their respective owners.
3D Automated Breast Ultrasound – what is it good for?

Supplemental tool in addition to Mx

- **Screening** ultrasound supplemental to mammography in asymptomatic women with dense breasts
- **Diagnostic** ultrasound in symptomatic women
3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts

- HHUS – results of the literature
# Handheld Ultrasound – screen detected cancer rates

## Supplemental screening

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Incidental Screens</th>
<th>Screen Detected Cancer Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single Center Studies – Physicians</strong>(^1)</td>
<td>27 403</td>
<td>3.4/ 1000</td>
</tr>
<tr>
<td><strong>Multicenter Studies – Physician</strong>(^2)</td>
<td>16 630</td>
<td>4.1/ 1000</td>
</tr>
<tr>
<td><strong>Multicenter Studies – Technicians</strong>(^3)</td>
<td>16 676</td>
<td>2.5/ 1000</td>
</tr>
</tbody>
</table>

---


* Increased risk
47 y-o; 13mm NOS cancer, seen on ABUS only at 7:30; right
Corresponding HHUS, palpable retrospectively

Courtesy of B Wilczek
Mammogram and ultrasound sensitivity, specificity, receiver operating ROC area and prevalence of breast cancer in women attending symptomatic breast clinics by breast parenchymal pattern.

Wolfe

<table>
<thead>
<tr>
<th>Parenchymal pattern</th>
<th>N</th>
<th>Prevalence (%)</th>
<th>Sens. (%)</th>
<th>Specif. (%)</th>
<th>ROC area</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mammography</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>1310</td>
<td>13</td>
<td>90.1</td>
<td>99.1</td>
<td>0.95</td>
</tr>
<tr>
<td>P1</td>
<td>2532</td>
<td>13</td>
<td>72.5</td>
<td>99.6</td>
<td>0.86</td>
</tr>
<tr>
<td>P2</td>
<td>4556</td>
<td>10</td>
<td>60.6</td>
<td>99.9</td>
<td>0.80</td>
</tr>
<tr>
<td>DY</td>
<td>2125</td>
<td>6.3</td>
<td>45.9</td>
<td>99.7</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>Ultrasound</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>615</td>
<td>27</td>
<td>95.2</td>
<td>97.3</td>
<td>0.96</td>
</tr>
<tr>
<td>P1</td>
<td>1452</td>
<td>22</td>
<td>86.0</td>
<td>98.7</td>
<td>0.92</td>
</tr>
<tr>
<td>P2</td>
<td>3077</td>
<td>15</td>
<td>81.7</td>
<td>99.6</td>
<td>0.91</td>
</tr>
<tr>
<td>DY</td>
<td>1683</td>
<td>7.8</td>
<td>72.0</td>
<td>99.2</td>
<td>0.86</td>
</tr>
</tbody>
</table>

3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts

- **ABUS –**
  results of the literature
## 3D Automated Breast Ultrasound – performance

### Supplemental screening and diagnostic studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study setting</th>
<th>No. of patients</th>
<th>Machine</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Kelly et al., 2010     | Screening     | 4,419           | SonoCine  | Doubles overall cancer detection  
Triple the 1 cm-or-less invasive cancers                                   |
| Kelly et al., 2010     | Screening     | 102             | SonoCine  | Improved callback rates                                                  |
| Golatta et al., 2015   | Mixed         | 983             | Somo-V    | NPV: 98%, Specificity:85%, Sensitivity: 74%                             |
| Shin et al., 2011      | Diagnostic    | 55              | Acouson S2000 | ABUS shows that detection of lesions larger than 1.2 cm was reliable and substantial agreement was obtained for lesion description and final assessment |
| Wojcinski et al., 2013  | Diagnostic    | 100             | Acouson S2000 | Sensitivity of 83% and fair interobserver concordance (k=0.36). But, ABUS shows a high number of false-positive results |
| Li et al., 2013         | Diagnostic    | 33              | Acouson S2000 | Size of pure DCIS shows a higher correlation coefficient with histopathology |
| Chae et al., 2013      | Diagnostic    | 58              | Acouson S2000 | Can Reliably detect additional suspicious lesions                         |

Cyst

Invenia image
### 3D Automated Breast Ultrasound – performance

**ABUS in supplemental screening – recent studies**

<table>
<thead>
<tr>
<th>ABUS Studies</th>
<th>Incidental Screens</th>
<th>Screen Detected Cancer Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brem RF 2014</td>
<td>15 318</td>
<td>2.2/1000</td>
</tr>
<tr>
<td>Choy WJ 2014</td>
<td>1866</td>
<td>3.8/1000</td>
</tr>
<tr>
<td>Wilczek B 2014</td>
<td>1666</td>
<td>2.8/1000</td>
</tr>
</tbody>
</table>
47 y-o; cancer seen on ABUS only at 7:30; right side

Lateral track, frontal thick slice

Lateral track, transverse slice

Lateral track, sagittal slice

Courtesy of B Wilczek
NOS cancer G2

Invenia image
3D Automated Breast Ultrasound

ABUS vs HH Ultrasound in supplemental screening - synchrone

Patients randomly selected to have HHUS and ABUS, mixed collective with asymptomatic and symptomatic patients

- 983 patients (1966 breasts); 6% breasts had cancer
- 1638/1966 (83%) agreement HHUS, ABUS (κ 0.31)
- 88/119 (74%) breasts with cancer identified by ABUS
47 y-o; NOS cancer G2 with surrounding fibrosis seen on diagnostic MX and ABUS at 2:00, left side.
## 3D Automated Breast Ultrasound – Recall Rate

### ABUS versus Hand Held Ultrasound in supplemental screening

<table>
<thead>
<tr>
<th>Study</th>
<th>Single Center Studies</th>
<th>Incidental Screens</th>
<th>Additional Recall Rate for US only</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABUS Studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brem RF 2015</td>
<td>27,403</td>
<td>5.9%</td>
<td>HH Studies</td>
</tr>
<tr>
<td>Wilczek B 2014</td>
<td>16,630</td>
<td>10.1%</td>
<td></td>
</tr>
<tr>
<td>Choy WJ 2014</td>
<td>15,318</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>

### Multicenter Studies

- Incidental Screens: 16,660
- Additional Recall Rate for US only: 2.6%

- HH Studies: 10.1%
47 y-o; NOS cancer G2 with surrounding fibrosis seen on diagnostic MX and ABUS
Breast ultrasound – biopsy rate

High variability

Variability of biopsy rates across adjunct screening ultrasound studies

Crystal 2003
De Felice 2007
Brancato 2007
Corsetti 2008
Berg 2008
Leong 2012
Hooley 2012
Weigert 2012
Parris 2013
Kelly 2010

Number of Biopsies per 1,000 Examinations

Median

Societal recommendations for adjunct screening US

Based on the sparse data currently available regarding the potential benefits and harms of screening US in women with dense breast tissue and no other known risk factors, at this time, no medical organization recommends adjunct screening in women based on breast density alone (Table 3). The American College of Radiology and the Society of Breast Imaging recommend screening US as an adjunct to mammography only in a very selective subgroup of high-risk women (>20% lifetime risk) who cannot tolerate MRI.

Comment

Our systematic review of the available literature found that adjunctive screening US increases cancer detection compared with mammography screening alone and is also associated with a substantial number of false-positive biopsies. Previously, a systematic review by Nothacker et al analyzed 6 studies from 2000 to 2008 and reported the performance of adjunctive screening US. Our study extends the summary of evidence by including 7 additional studies published since 2008 on adjunctive screening US; 2 of the studies included in our systematic review also

Citation from:
Scheel JR, Lee JM, Sprague BL, Lee CI, Lehman CD
Screening ultrasound as an adjunct to mammography in women with mammographically dense breasts.
Advantages and disadvantages

3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts
ABUS

Advantages compared to HHUS (focal and whole breast)

- Better detection of retraction phenomenon and hyperechoic rim in the coronal plane
- Less examiner independent and more reproducible
- Complete, non selective documentation
- Better determination of the 3 d lesion localisation
- Digital data allow CAD
- Delayed interpretation and second reading at workstation with 3-d capability optimizing the reading environment
NOS cancer G1

Invenia image
Disadvantages compared to HHUS (whole breast)

- Less flexible in coupling transducer according to anatomy
- More shadowing artifacts at periphery
- Higher rate of false positive cases and higher recall rates
- Probably 10% lower sensitivity, lower cancer detection rate of last generation ABUS systems
- „One-stop-shop“ only for negative cases
- Need for supplementary characterization of a lesion by handheld Doppler, elastography or US-guided biopsy
Total reflection

Reduced total reflection

Fibroadenoma

Invenia image
# ABUS

## Questions & answers

<table>
<thead>
<tr>
<th>Question</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROC Interobserver variability</td>
<td>AUC 0.59 – 0.9; sensitivity 35-100%</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>Inter Class Correlation 0.34 – 0.99</td>
</tr>
<tr>
<td>Time dependent recall rate</td>
<td>25% 1st month; 13% 2nd month</td>
</tr>
<tr>
<td>Time to perform and to read</td>
<td>15 - 30 min and 5 to10 min</td>
</tr>
<tr>
<td>Added biopsy and detection rate</td>
<td>32.8 to 71.0 and 1.8 to 4.6 per 1000</td>
</tr>
</tbody>
</table>

2. Chang JM et al Acta Radiologica 2014
4. Arleo EK et al Clinical Imaging 2014
5. HJ Shin Ultrasonography 2015
41 y-o; NOS cancer G3, 2.2 cm with surrounding DCIS G3 3.5 cm, left side
Contralateral DCIS left side

Contralateral left side CC spot

DCIS ABUS neg

Courtesy of B Wilczek
### Screening approach for women with dense breasts

#### How effective is supplemental imaging in intermediate high risk?

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Additional Cancers / 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>HH US</td>
<td>3 – 4</td>
</tr>
<tr>
<td>AB US</td>
<td>2</td>
</tr>
<tr>
<td>Tomosynthesis</td>
<td>2</td>
</tr>
<tr>
<td>MRI</td>
<td>10</td>
</tr>
<tr>
<td>MBI</td>
<td>7 – 8</td>
</tr>
</tbody>
</table>

*No population-based screening tools*
ABUS and DBT are approaching supplementary screening women with dense breasts
Boths, ABUS and DTB are tomographic. ABUS differs to mammography also by physics.
Take home message 3

3D Automated Breast Ultrasound – a new multimodality approach for screening women with dense breasts

The Invenia ABUS image quality has closed up with HHUS. Time has come for a prospective study comparing DBT, ABUS and HHUS!
Thank you very much for your attention!
Save the dates

May 10th 2016: 40th SIS ANNIVERSARY
Senologic International Society in Strasbourg

19th SIS World Congress On Breast Healthcare
SAVE THE DATE
May 5-8, 2016 | Warsaw, Poland

www.siscongress.org