Background

- Breast cancer is the most common form of cancer in women
- Mammography remains the mainstay of screening for breast cancer
- Breast CA mortality has declined overall by 28% since 1990; it is estimated that a little less than half this decline is due to early diagnosis with screening mammography
- Recommended age and frequency of screening mammography is variable across organizations
Increased breast density both increases the risk of breast cancer and decreases the sensitivity of mammography to detect small lesions.

Approximately 50% of women have “dense breasts” (BI-RADS density “c” or “d”).

Digital mammography has become the standard across the U.S., and is more sensitive than film for dense breasts.

The most important harms of mammography screening are false-positive results and over-diagnosis (detection of disease that would not have caused morbidity or mortality if not found).

Desirable Attributes of New Approaches to Screening Mammography*

- Decrease false positives
- Increase cancer detection
  - However, currently not possible to know whether any particular patient whose cancer is detected by mammography is or is not at risk of the cancer being “over-diagnosed.”
- Reasonable cost effectiveness

* More definitive studies of new approaches to mammography screening that evaluate mortality are unlikely to be undertaken.
Newer Approaches to Breast Cancer Screening

Digital Breast Tomosynthesis (DBT)
- Provides 3-D images and is a modification of digital mammography using a moving x-ray source and digital detector
- Approved in U.S. for breast CA screening when used in combination with mammography
- Newer tomosynthesis techniques do not significantly increase radiation exposure

Supplemental Modalities in Women with Dense Breast Tissue
- Magnetic resonance imaging (MRI)
- Hand-held ultrasound (HHUS)
- Automated whole breast ultrasound (ABUS)
Agency Medical Directors’ Concerns

- Safety = Low
- Efficacy = High
- Cost = High

Key Questions 1-3

1) What is the effectiveness of screening with digital breast tomosynthesis (DBT) vs. digital mammography among women aged 40-74 who are candidates for screening mammography?

2) What is the comparative effectiveness of handheld ultrasonography, automated ultrasonography, and magnetic resonance imaging when used as supplemental screening modalities in women with dense breast tissue and a negative mammogram or negative DBT result?

3) What are the documented and potential harms associated with these imaging tests, including overdiagnosis and overtreatment, unnecessary biopsy as a result of false-positive imaging, patient anxiety, and radiation exposure?
Key Questions 4 - 5

4) What is the differential effectiveness and safety of the tests of interest according to such factors as age, race or ethnicity, comorbidities, BMI, method of breast density classification, overall breast cancer risk, scan vendor, and imaging protocol (e.g., whether ultrasound is performed by a radiologist, technologist, or some combination of the two)?

5) What are the costs and cost-effectiveness (e.g., cost per cancer detected) of the imaging modalities of interest?

Current State Agency Policy

<table>
<thead>
<tr>
<th>Cancer Screening Using:</th>
<th>Medicaid</th>
<th>UMP</th>
<th>DOC</th>
<th>LNI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>PA</td>
</tr>
<tr>
<td>Breast Tomography</td>
<td>PA*</td>
<td>PA</td>
<td>PA</td>
<td>PA</td>
</tr>
<tr>
<td>Breast MRI</td>
<td>C</td>
<td>PA</td>
<td>PA</td>
<td>C</td>
</tr>
<tr>
<td>Breast Ultrasound</td>
<td>C</td>
<td>PA</td>
<td>PA</td>
<td>C</td>
</tr>
</tbody>
</table>

* Under unlisted (unspecified) procedure code.

C: Covered
NC: Not covered
PA: Prior authorization required
Appropriate Imaging for Breast Cancer: State Agency Utilization

### PEBB/UMP

#### All Mammograms by Age Groups, 2010-2013

- **Member Count**: 50,000
- **Client Count**: 30,000

#### Medicaid

#### All Mammograms by Age Groups, 2010-2013

- **Member Count**: 50,000
- **Client Count**: 30,000

### PEBB/UMP

#### Breast Tomography by Age Groups, 2010-2013

- **Member Count**: 2,000
- **Client Count**: 1,000

### Medicaid

#### Breast Tomography by Age Groups, 2010-2013

- **Member Count**: 2,000
- **Client Count**: 1,000
Appropriate Imaging for Breast Cancer: State Agency Utilization

**PEBB/UMP Breast MRI by Age Groups, 2010-2013**

- <40
- 40-49
- 50-74
- 75+

**Medicaid Breast MRI by Age Groups, 2010-2013**

- <40
- 40-49
- 50-74
- 75+

**PEBB/UMP Breast Ultrasound by Age Groups, 2010-2013**

- <40
- 40-49
- 50-74
- 75+

**Medicaid Breast Ultrasound by Age Groups, 2010-2013**

- <40
- 40-49
- 50-74
- 75+
Uncertainties

• For all technologies under consideration, sufficient follow-up data is lacking to estimate sensitivity and specificity
• No data on more definitive outcomes of morbidity and mortality
• MRI and HHUS studies have been done in high risk populations that happen to include women with dense breast tissue, and so results are not specific to women with dense breast tissue only
• Very limited data available on ABUS
• Study populations are heterogeneous and hence meta-analysis is not possible

Summary of Harms

• False positive test result
  – May impact psychological well being
  – Some patients will go on to unnecessary biopsy with attendant risk of complications (e.g. infection; bleeding)
• Radiation exposure from DBT now comparable to that of digital mammography along
## Summary: DBT

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography (Estimated yield)</th>
<th>DBT + DM (Estimated yield)</th>
<th>Uncertainty*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-160</td>
<td>80-140</td>
<td>Moderate-High</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>12-27</td>
<td>Moderate</td>
</tr>
<tr>
<td>Cancer detection rate per 1,000</td>
<td>3-5</td>
<td>4-6</td>
<td>Moderate-High</td>
</tr>
<tr>
<td>Positive biopsy among total biopsied (PPV3)</td>
<td>20-25%</td>
<td>25-30%</td>
<td>Low-Moderate</td>
</tr>
</tbody>
</table>

* Issues of study heterogeneity and comparability of populations result in higher uncertainty. Degree of uncertainty of recall rates is because two prospective studies are from outside of U.S. There are no prospective large studies with patient outcomes.

- DBT is a promising but as yet unproven approach to screening mammography. Available studies are of poor quality, and questions remain regarding rates of recall, biopsy and cancer detection, as well as test sensitivity and specificity.
- Available Economic modeling is limited
  - Available models suggest possible small benefit with likely substantial additional cost.
DBT: Private Payer Examples

• National private payers
  – DBT is considered experimental, investigational or unproven for any purpose by Aetna, CIGNA, Humana, UniCare, United Healthcare and Wellpoint/Anthem

• Regional payers
  – Premera and Health Net consider DBT investigational and do not cover it
  – Regence considers DBT to be incident to either screening or diagnostic mammogram and does not cover it

Centers for Medicare & Medicaid Services

• There are no published national or local coverage determinations for DBT
## Supplemental Screening with MRI

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography</th>
<th>Incremental Yield with MRI</th>
<th>Uncertainty*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-120</td>
<td>100-120</td>
<td>High</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>20-40</td>
<td>High</td>
</tr>
<tr>
<td>Cancer detection rate per 1,000</td>
<td>3-5</td>
<td>3-11</td>
<td>High</td>
</tr>
<tr>
<td>Positive biopsy among total biopsied (PPV3)</td>
<td>20-25%</td>
<td>22-48%</td>
<td>High</td>
</tr>
</tbody>
</table>

* There is a high level of uncertainty around these values b/c of the lack of direct evidence from studies of MRI in women with dense breast tissue and b/c of heterogeneity of findings in studies of high risk women.

## Supplemental Screening with Hand-Held Ultrasound (HHUS)

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography</th>
<th>Incremental Yield with HHUS</th>
<th>Uncertainty*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-120</td>
<td>30-100</td>
<td>High</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>30-60</td>
<td>Low-Moderate</td>
</tr>
<tr>
<td>Cancer detection rate per 1,000</td>
<td>3-5</td>
<td>2-4</td>
<td>Low</td>
</tr>
<tr>
<td>Positive biopsy among total biopsied (PPV3)</td>
<td>20-25%</td>
<td>5-7%</td>
<td>Low</td>
</tr>
</tbody>
</table>

* High level of uncertainty about recall rate b/c lack of direct evidence from studies of women with dense breasts and b/c heterogeneity of findings. Cancer detection rate based on three Connecticut studies.
Supplemental Screening with Automated Whole Breast Ultrasound (ABUS)

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography</th>
<th>Incremental Yield with HHUS</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-120</td>
<td>30-100</td>
<td>High</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>30-60</td>
<td>High</td>
</tr>
<tr>
<td>Cancer detection rate per 1,000</td>
<td>3-5</td>
<td>2-4</td>
<td>High</td>
</tr>
<tr>
<td>Positive biopsy among the total # biopsied (PPV3)</td>
<td>20-25%</td>
<td>5-7%</td>
<td>High</td>
</tr>
</tbody>
</table>

Summary: Supplemental Screening

- MRI
  - Very limited evidence in women with dense breast tissue but otherwise low risk
  - High relative cost

- HHUS
  - Inconclusive evidence across multiple studies esp. with respect to recall rates and cancer detection rates
  - HHUS as an adjunct to screening mammography in women with dense breasts may modestly increase cancer detection, but it increases the risk of false-positive findings leading to breast biopsies.

- ABUS
  - Inadequate evidence to comment
Economic Analysis

- Available Economic modeling is limited
- For MRI and HHUS:
  - Available models suggest possible small benefit with substantial additional cost
  - Benefit would likely be greatest in women with dense breast tissue who have additional risk factors as well

Third-Party Coverage for Supplemental Studies

Breast Ultrasound
- No information available from Health Net, Premera Blue Cross or Regence
- Cigna, Humana and United Healthcare consider breast ultrasound experimental for any type of screening

Breast MRI
- Humana and United Healthcare cover breast MRI as an adjunct to mammography when heterogeneous or extremely dense breast tissue is identified
- Aetna, UniCare, and WellPoint/Anthem cover MRI as an adjunct in women with dense breasts AND a personal history of breast cancer
Centers for Medicare and Medicaid

- No national or local coverage determination on use of breast ultrasound to supplement screening mammography
- No national or local coverage determination for breast MRI to supplement screening mammography

State Agency Recommendation

- **Digital Breast Tomography**
  - Non-coverage
- **MRI** supplementary to screening mammography in women with dense breasts
  - Non-coverage
- **Hand Held Ultrasound** supplementary to screening mammography in women with dense breasts
  - Non-coverage
- **Automated Breast Ultrasound** supplementary to screening mammography in women with dense breasts
  - Non-coverage
Questions?

More Information:

Dan Lessler, MD
Daniel.Lessler@hca.wa.gov
Order of Scheduled Presentations:

**Appropriate Imaging for Breast Cancer Screening in Special Populations**

<table>
<thead>
<tr>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
</tbody>
</table>

No requests to provide public comment on the technology review were received.
Appropriate Imaging for Breast Cancer Screening in Special Populations

Clinical Expert

Christoph I. Lee, MD, MSHS
Director, Breast Imaging Fellowship
Department of Radiology, Section of Breast Imaging
University of Washington School of Medicine
Disclosure

Any unmarked topic will be considered a "Yes"

<table>
<thead>
<tr>
<th>Potential Conflict Type</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Salary or payments such as consulting fees or honoraria in excess of $10,000.</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>2. Equity interests such as stocks, stock options or other ownership interests.</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>3. Status or position as an officer, board member, trustee, owner.</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>4. Loan or intellectual property rights.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Research funding.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6. Any other relationship, including travel arrangements.</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

I have received both grant funding and consulting fees from GE Healthcare related to digital mammography, ultrasound, and digital breast tomosynthesis.

<table>
<thead>
<tr>
<th>Potential Conflict Type</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

If yes to #7, provide name and funding sources:

________________________________________________________________________________________________________________________________________________________

________________________________________________________________________________________________________________________________________________________

________________________________________________________________________________________________________________________________________________________

If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may attach additional sheets explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

X. Christoph Lee

Date: 12/19/14

Print Name: Christoph Lee

So we may contact you regarding your presentation, please provide the following:

Mail Address: 825 Eastlake Avenue East, G3-200, Seattle WA 98109-1023

Phone Number: (206) 288-6783 office, (650) 796-5098 mobile
1. PERSONAL DATA

Name                      Christoph I. Lee, M.D., M.S.H.S.
Home Address            2250 70th Avenue SE
                        Mercer Island, WA 98040
                        (650) 796-5098
Work Address           Seattle Cancer Care Alliance
                        825 Eastlake Avenue East, G3-200
                        Seattle, WA 98109
                        (206) 288-6783
Date of Birth         December 19, 1976
Birthplace             Mississauga, Ontario, Canada
Citizenship            USA
Marital Status         Married

2. EDUCATION

1994-1998               A.B. *cum laude*
                        Princeton University, Princeton, NJ

2001-2005               M.D. *cum laude*
                        Yale University, New Haven, CT

2010-2011               M.S.H.S., Health Services Research and Policy
                        University of California, Los Angeles, CA

3. POSTGRADUATE TRAINING

2005-2006               Internship
                        Transitional Year
                        University of Hawaii, Honolulu, HI

2006-2010               Residency
                        Diagnostic Radiology
                        Stanford University, Palo Alto, CA
2010-2011  Fellowship
Breast Imaging
University of California, Los Angeles, CA

2010-2012  Fellowship
Health Services Research and Policy
Robert Wood Johnson Clinical Scholars Program, Los Angeles, CA

4. FACULTY POSITIONS HELD

2010-2012  Clinical Instructor
Department of Radiology, Section of Breast Imaging
UCLA David Geffen School of Medicine, Los Angeles, CA

2010-2012  Clinical Scholar
Department of Medicine, Division of General Internal Medicine
UCLA David Geffen School of Medicine, Los Angeles, CA

2011-2012  Attending Physician
Department of Radiology, Section of Acute Care Imaging
UCLA David Geffen School of Medicine, Los Angeles, CA

2012-present  Assistant Professor
Department of Radiology, Section of Breast Imaging
University of Washington School of Medicine, Seattle, WA

2012-present  Assistant Professor
Department of Radiology, Section of Health Services Research
University of Washington School of Medicine, Seattle, WA

2012-present  Faculty Investigator
Hutchinson Institute for Cancer Outcomes Research (HICOR)
Division of Public Health Sciences
Fred Hutchinson Cancer Research Center, Seattle, WA

2012-present  Faculty Investigator
Comparative Effectiveness, Cost & Outcomes Research Center
University of Washington, Seattle, WA

2013-present  Adjunct Assistant Professor
Department of Health Services
University of Washington School of Public Health, Seattle, WA

2013-present  Director, Breast Imaging Fellowship
Department of Radiology, Section of Breast Imaging
University of Washington School of Medicine, Seattle, WA
5. **HOSPITAL POSITIONS HELD**

See Post-Graduate Training and Faculty Positions

6. **HONORS**

1994 Los Angeles County Medical Association Scholarship

1994-1998 Robert C. Byrd Honors Scholarship

1995 Rotary International District Grant

1996 Princeton University Summer Service Award

1997 American Heart Association Summer Research Fellowship

1998 NCAA Division I Varsity Letter (Men's Tennis)

1998 Certificate in Spanish Language & Culture, Princeton University

1998 Departmental Honors, English, Princeton University

1998 Princeton AlumniCorps Public Interest Fellowship

2002 Etta S. Chidsey Award in Cancer Research, Yale School of Medicine

2005 Farr Scholar for Excellence in Research, Yale School of Medicine

2005 Overall Honors at Graduation, Yale School of Medicine

2006 Graduation Speaker, University of Hawaii Transitional Year

2009 AMA Foundation Excellence in Leadership Award

2010 Certificate in Health Policy, Finance & Economics, Stanford GME

2010-2012 NIH/NIMHD Loan Repayment Program Award

2011 ACR E. Stephen Amis, Jr., MD, Fellowship in Quality and Safety

2011 Recognition of Exceptional Manuscript Review, *JACR*

2012-2014 GE-AUR Radiology Research Academic Fellowship (GERRAF)

2012 *JACR* Best Article of 2012, Practice Management

2012 Recognition of Exceptional Manuscript Review, *JACR*
2012     Article Selection for Best RSNA Content of 2012
2012-2014 NIH/NIMHD Loan Repayment Program Renewal Award
2013     JACR Best Article of 2013, Health Services Research & Policy
2013     Radiology Editor’s Recognition Award with Special Distinction
2015-2019 American Cancer Society Mentored Research Scholar

7. BOARD CERTIFICATION

2010-potient American Board of Radiology, Board Certified Diplomate

8. CURRENT LICENSES TO PRACTICE

2005-2013 California State # A97106
2012-potient Washington State # MD60267813

9. PROFESSIONAL AND SERVICE ORGANIZATIONS

1994-1998 Princeton Community Service Committee
        Chairman, 1997-1998
1995-1998 Princeton University Student Health Program
        President, 1996-1997
1996-1998 Princeton Student Volunteer Journal (SVCommunicator)
        Editor-in-Chief, 1996-1998
1997-1998 Rowen Towers Afterschool Program (Trenton, NJ)
        President & Founder, 1997-1998
2001-2005 American Red Cross, Yale Medical Chapter
        President, 2001-2002
2001-2005 Yale History of Medicine Society (Nathan Smith Club)
        President, 2002-2003
2001-2005 Yale Migrant Health Clinic
        President, 2002-2003
2001-2005 Yale Radiology Interest Group
        President & Founder, 2001-2003
2001-present
American College of Radiology
   Member, ACR Radiologist Resources Committee, 2006-2010
   Member, ACR Reference Committee, Breast Imaging, 2012
   Member, ACR Reference Committee, Ultrasound, 2012
   Member, ACR Reference Committee, Nuclear Medicine, 2012
   Member, ACR Human Resources Commission, 2012-2014

2001-present
Radiological Society of North America
   Member, Health Services Research Committee, 2013-present

2005-present
American Medical Association
   Recipient, AMA Foundation Leadership Award, 2009

2006-2010
California Radiological Society
   Secretary, Resident & Fellow Section, 2006-2007

2006-present
American Roentgen Ray Society

2011-present
Association of University Radiologists (AUR)
   Faculty, Annual Meeting, 2013 and 2014
   Member, Scientific Program Committee, Annual Meeting, 2014
   Member, Scientific Program Committee, Annual Meeting, 2015

2011-present
Radiology Alliance for Health Services Research (RAHSR)
   Faculty, Annual Meeting, 2013 and 2014
   Member, Scientific Program Committee, Annual Meeting, 2014

2011-present
Society of Breast Imaging

10. TEACHING RESPONSIBILITIES

A. Research Mentorship

2003-2005
   Research mentee: Harry Flaster (Stanford medical student)
   Project: Institutional informed consent policies regarding CT scans

2008-2010
   Research mentee: Emily Tsai, MD (UCLA radiology resident)
   Project: Incidental findings on coronary CT, economic impact

2010-2012
   Research mentee: Jesse Jones, MD (UCLA radiology resident)
   Project: Primer on radiation dose in acute care imaging

2010-present
   Research mentee: Solveig Hofvind, PhD (Norway cancer registry)
   Project: Mammographic performance in population-based screening

2011-2013
   Research mentee: Warren Perry, MD (Yale ED resident)
   Project: Time-motion analysis of emergency radiologists
<table>
<thead>
<tr>
<th>Year</th>
<th>Research mentee</th>
<th>Project</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012-2013</td>
<td>Luke Grauke, MD (UW breast fellow)</td>
<td>Radiologists’ performance in ACR Breast MR course</td>
</tr>
<tr>
<td>2012-2013</td>
<td>Michele Rochelle, MD (UW breast fellow)</td>
<td>Variation in breast MRI BI-RADS in community settings</td>
</tr>
<tr>
<td>2012-2014</td>
<td>Aimee Lee, MD (UW radiology resident)</td>
<td>Concordance of breast MRI BI-RADS and management</td>
</tr>
<tr>
<td>2013-2014</td>
<td>Eni Obadina, MD (UW breast fellow)</td>
<td>Advanced breast imaging availability in U.S. by facility type</td>
</tr>
<tr>
<td>2013-2014</td>
<td>Diana Lam, MD (UW radiology resident)</td>
<td>Non-interpretive skills - imaging-based screening</td>
</tr>
<tr>
<td>2014-2015</td>
<td>Jessica Germino, MD (UW radiology resident)</td>
<td>Advanced breast imaging access among vulnerable women</td>
</tr>
<tr>
<td>2014-2015</td>
<td>Crystal Piper (Yale medical student)</td>
<td>30-year trend for women authorship in academic radiology</td>
</tr>
<tr>
<td>2015-2016</td>
<td>Jessica Germino, MD (UW radiology resident)</td>
<td>Access to supplemental screening among high-risk women</td>
</tr>
<tr>
<td>2015-2016</td>
<td>Diana Lam, MD (UW breast fellow)</td>
<td>Informing decision-making for radiation-induced cancer risks</td>
</tr>
<tr>
<td>2015-2016</td>
<td>Jessica Germino, MD (UW radiology resident)</td>
<td>Current controversies in imaging-based screening</td>
</tr>
</tbody>
</table>

**B. Course Faculty and Lectureships**

<table>
<thead>
<tr>
<th>Year</th>
<th>Lectureship</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011-2012</td>
<td>Lecturer, Senior Resident Board Review, David Geffen School of Medicine at UCLA, Department of Radiology</td>
</tr>
<tr>
<td></td>
<td>“Breast Imaging Oral Board Review” (2/29/2012)</td>
</tr>
<tr>
<td>2012-present</td>
<td>Faculty, ACR Education Center</td>
</tr>
<tr>
<td></td>
<td>Breast MRI and Guided Biopsy Course (11/1-2/2012)</td>
</tr>
<tr>
<td>2012-present</td>
<td>Faculty, Medical Student Clerkship, UW School of Medicine, Department of Radiology</td>
</tr>
<tr>
<td></td>
<td>“Breast Cancer &amp; Screening Mammography” (8/22/12, 10/17/12, 10/16/2013)</td>
</tr>
<tr>
<td></td>
<td>“Introduction to Diagnostic Breast Imaging” (8/22/12, 10/17/12, 10/16/2013)</td>
</tr>
</tbody>
</table>
### 2012-present
Faculty, UW Resident Monthly Noon Teaching Conferences, UW School of Medicine, Department of Radiology  
Breast imaging case-based conferences on quarterly basis

### 2012-present
Faculty and Examiner, UW Resident Practical Examination, UW School of Medicine, Department of Radiology  
“Breast Imaging Case Review” (10/16/2012)

### 2012-present
Faculty, Resident Annual Lecture Series, UW School of Medicine, Department of Radiology  
“Breast Cancer Screening Update” (3/14/2013)  
“Digital Breast Tomosynthesis” (3/13/2014)

### 2012-present
Faculty, Resident Journal Club, Section of Breast Imaging, UW School of Medicine, Department of Radiology  
Resident journal club in breast imaging on quarterly basis

### 2012-2013
Lecturer, Senior Resident Board Review, UW School of Medicine, Department of Radiology  
“Breast Imaging Oral Board Review” (1/25/2013)

### 2013-2014
Faculty and Examiner, Mock Oral Boards, UW School of Medicine, Department of Radiology  
“Mock Oral Boards: Breast Imaging” (4/30/2013)

### 2013-present
Lecturer, New ABR Core Exam Review, UW School of Medicine, Department of Radiology  
“New ABR Core Exam – Breast Imaging Review” (6/11/2013)  
“Breast Imaging Review for the New Boards” (2/25/2014)

### C. Clinical Teaching

### 2010-2012
Clinical Preceptor, David Geffen School of Medicine at UCLA, Department of Radiology, Sections of Acute Care Imaging and Breast Imaging  
Radiology Residents (2 per rotation, 2.5 days/week)

### 2012-present
Clinical Preceptor, UW School of Medicine, Department of Radiology, Section of Breast Imaging  
Medical Student (directed elective for Linda Chen, 10/2012)  
Radiology Residents (2-3 per rotation, 2.5 days/week)  
Fellows (3-4 per year, 2.5 days/week)

### 2013-present
Director, Breast Imaging Fellowship, University of Washington School of Medicine, Section of Breast Imaging  
Fellows (3 dedicated breast imaging fellows per year)
11. EDITORIAL RESPONSIBILITIES

2001-2003
Yale Journal of Health Policy, Law, & Ethics
Staff Editor, 2001-2002
Business Editor, 2002-2003
Member, Editorial Board, 2002-2003

2008-present
American Journal of Roentgenology (AJR)
Reviewer, Health Policy and Practice, 2008-present
Special Consulting Editor, Best Practices, 2013-present
Member, Editorial Board, 2013-present

2009-present
Journal of the American College of Radiology (JACR)
Reviewer, Health Services Research, 2009-present
Guest Editor, Special Issue on Screening, 2013
Member, Editorial Board, 2013-present

2011-present
Radiology
Reviewer, Health Policy and Breast Imaging, 2011-present

2013-present
Journal of the American Medical Association (JAMA)
Reviewer, Radiology and Health Policy, 2013-present

12. SPECIAL NATIONAL RESPONSIBILITIES

1998-2001
Princeton Project 55 Tuberculosis Initiative, Washington, DC
Manager, 1998-1999
Executive Board Member, 1998-2001
• Led global TB advocacy group, founded by Ralph Nader
• Briefed U.S. Congress foreign operations subcommittee
• Co-drafted TB Control Act of 1999 (Barbara Boxer, D-CA)

1999-2001
The Lewin Group, Boston, MA
Analyst, 1999-2001
• Consultant to major biotechnology and pharmaceutical firms
• Managed large phase IV clinical effectiveness trials

2012-present
RAND Corporation, Santa Monica, CA
Adjunct Scientist, RAND Health
• Evaluation of CMS Medicare Imaging Demonstration (MID)

2012-present
Castlight Health, San Francisco, CA
Member, Clinical Advisory Board
• Advisor for start-up dedicated to healthcare cost transparency

2012-2014  American College of Radiology, Reston, VA  
National Commission on Human Resources  
Chairman, Working Group on Citizenship, 2012-2013  
• Lead author of JACR manuscript on radiology citizenship

2013-2014  Centers for Medicare & Medicaid Services (CMS), Baltimore, MD  
Member, Working Group, Quality Performance Measurements  
• Developing performance measures for screening mammography

2014-2015  Institute for Clinical and Economic Review (ICER), Boston, MA  
Scientific Consultant  
• Clinical expert for review of breast imaging technologies

13. SPECIAL LOCAL RESPONSIBILITIES

2002-2004  Yale University School of Medicine, New Haven, CT  
Member, New Student Orientation Committee, 2002-2003  
Member, Pre-Clinical Evaluations Committee, 2002-2004

2006-2010  Stanford University School of Medicine, Palo Alto, CA  
Department of Diagnostic Radiology  
Member, Resident Education Committee, 2006-2007  
Member, Resident Operations Committee, 2008-2009  
Member, Resident Relations Committee, 2009-2010  
Office of Graduate Medical Education (Stanford Hospital)  
Member, Resident Leadership Certificate Committee, 2007-2008

2010-2012  David Geffen School of Medicine at UCLA, Los Angeles, CA  
Robert Wood Johnson Clinical Scholars Program  
Member, Fellowship Selection Committee

2012-2013  L.A. County Department of Health Services, Los Angeles, CA  
Senior Advisor, Erin Saleeby, MD, Director of Women’s Health

2012-present  University of Washington School of Medicine, Seattle, WA  
Department of Diagnostic Radiology  
Member, Resident Mentorship Program, 2012-present  
Member, HSR Seed Grant Selection Committee, 2012-present  
Member, Fellowship Education Committee, 2013-present  
Section of Breast Imaging  
Member, Fellowship Selection Committee, 2012-present  
Director, Breast Imaging Fellowship, 2013-present  
Member, Senior Faculty Search Committee, 2014-present
2012-present  Fred Hutchinson Cancer Research Center, University of Washington Cancer Consortium Research Program, Seattle, WA  
    Member, Cancer Imaging Program, 2012-present  
Hutchinson Institute for Cancer Outcomes Research (HICOR) 
    Faculty Investigator, 2013-present  
    Interviewer, New Faculty Selection Committee, 2013-present

14. RESEARCH FUNDING

Awarded

2010-2012  Funding Source: Robert Wood Johnson Foundation  
    Role: Principal Investigator  
    Direct Costs (Lee): $135,000  
    Project: Patients’ willingness to donate a biospecimen for future genetic research at screening mammogram.

2010-2014  Funding Source: NIH (NIMHD) L60 MD005349  
    Role: Principal Investigator  
    Direct Costs (Lee): $117,639  
    Project: Community level access and utilization of breast imaging technologies.

2012-2014  Funding Source: GE-AUR Radiology Research Academic Fellowship  
    Role: Principal Investigator  
    Direct Costs (Lee): $140,000  
    Project: Cost-effectiveness analysis of adjunct screening breast tomosynthesis for women with dense breasts.

2013-2014  Funding Source: AHRQ K72PCO3 25505  
    Role: Co-Investigator (PI: Sullivan)  
    Direct Costs (Lee): $26,925  
    Project: Imaging techniques for metastatic breast cancer

2012-2016  Funding Source: NIH (NCI) P01 CA154292  
    Role: Co-Investigator (PI: Miglioretti/Kerlikowske)  
    Direct Costs (Lee): $153,098 (estimated for 10% FTE)  

2014-2016  Funding Source: GE Healthcare 124.03-2013-GES-0003  
    Role: Co-Investigator (PI: Lehman)  
    Direct Costs (Lee): $34,031 (estimated for 5% FTE)  
    Project: Automated breast ultrasound and tomosynthesis screening in women with dense breasts.

2015-2019  Funding Source: American Cancer Society MRSG-14-160-01-CPHPS  
    Role: Principal Investigator
11

Direct Costs (Lee): $675,000
Project: Adoption of advanced breast imaging and access to screening mammography among vulnerable women

15. BIBLIOGRAPHY

A. Peer-Reviewed Journal Publications


14. Lee CI, Ponce NA, Ettner SL, Kahn KL, Bassett LW, Forman HP. Ordering of CT scans by


#trainee mentee
B. Medical Books


C. Book Chapters

1. Lee CI, Elmore JG. Radiation-related effects of imaging studies for screening and diagnosis. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA. 2011.


E. Editorials (Lay Press)


**F. Letters to the Editor**


**G. Abstracts**


H. Oral Presentations and Panel Discussions


Appropriate Imaging for Breast Cancer Screening in Special Populations

An Assessment of Comparative Clinical Effectiveness & Comparative Value

Presented to the Washington State Health Care Authority by Daniel A. Ollendorf, PhD
January 16, 2015

Overview

- Project Scope, Comparators, Outcomes of Interest
- Breast Density Legislation
- Systematic Review of Published Evidence
- Comparative Value
- Evidence Ratings
- Clinical Guidelines
- Payer Coverage Policies
- Summary
Background

- Breast cancer: most common form of cancer in women
  - ~240,000 new cases annually in U.S.
  - ~40,000 deaths
- Breast cancer mortality in decline for past 25 years
  - Most models suggest that about half of decline due to early detection from mammography, about half from improvements in therapy
  - Some controversy around these estimates, however

Background

- Screening mammography
  - Benefits of screening established in 9 RCTs of >600,000 women followed for 10-20 years
    - 20-25% reductions in mortality after 15 years of follow-up in women age 50-69
- Film mammography replaced by digital technology in mid-2000s:
  - Better image precision, including better contrast resolution in women with dense breast tissue
Digital Breast Tomosynthesis (DBT)

- An extension of digital mammography
- Acquires multiple images in an arc around the breast
  - Software reconstructs individual “slices” (tomograms) in addition to standard 2D mammogram
- Virtual 2D image can be created so that DBT radiation exposure ≈ digital mammography
- Rapid adoption of technology:
  - Likely to be accelerated by new CPT code (effective 1/1/15)

DBT vs. DM Image

Source: [http://ww1.prweb.com/prfiles/2010/11/27/4280464/Screenshot20101127at5.03.34PM.png](http://ww1.prweb.com/prfiles/2010/11/27/4280464/Screenshot20101127at5.03.34PM.png)
Breast Density

- Areas that absorb more x-ray energy and appear more “white” on mammography
- 4-category qualitative rating scale
  - heterogeneously dense: may obscure small masses
  - extremely dense: may lower sensitivity of mammography
- Density-related decrease in sensitivity of film mammography mitigated somewhat by digital mammography
- Density also an independent risk factor for breast cancer

Breast Density on Mammography

Breast Density Legislation

- National advocacy sparked by efforts of breast cancer survivor with missed cancer on mammography
- 19 states have passed legislation requiring notification of dense breast tissue with mammography
  - 2 of these require insurance coverage for supplemental screening
- State of Washington: bill introduced in January 2014, but never debated on House or Senate floors
- Major concern: legislative mandate that outpaces accumulation of scientific evidence

Supplemental Modalities in Women with Dense Breast Tissue

- Magnetic resonance imaging (MRI)
  - Similar process to DBT (reconstruction of detailed cross-sectional views) but using strong magnetic fields instead of x-ray energy
- Handheld ultrasound (HHUS)
  - Used for screening and also to visualize cyst aspiration and breast biopsy
- Automated whole breast ultrasound (ABUS)
  - Newest technology, uses an automated transducer rather than handheld probe for image acquisition
Key Questions

1. What is the effectiveness of screening with digital breast tomosynthesis (DBT) vs. digital mammography among women aged 40-74 who are candidates for screening mammography?

2. What is the comparative effectiveness of handheld ultrasonography, automated ultrasonography, and magnetic resonance imaging when used as supplemental screening modalities in women with dense breast tissue and a negative mammogram or negative DBT result?

3. What are the documented and potential harms associated with these imaging tests, including overdiagnosis and overtreatment, unnecessary biopsy as a result of false-positive imaging, patient anxiety, and radiation exposure?

4. What is the differential effectiveness and safety of the tests of interest according to such factors as age, race or ethnicity, comorbidities, BMI, method of breast density classification, overall breast cancer risk, scan vendor, and imaging protocol (e.g., whether ultrasound is performed by a radiologist, technologist, or some combination of the two)?

5. What are the costs and cost-effectiveness (e.g., cost per cancer detected) of the imaging modalities of interest?
Project Scope

Population:
- DBT: All asymptomatic women age 40-74 who are candidates for screening mammography every 1-2 years
- Supplemental screening: All asymptomatic women age 40-74 with heterogeneously or extremely dense breast tissue and normal mammography or DBT result

Supplemental Screening Tests:
- MRI
- HHUS
- ABUS

Comparators
- DBT: Digital mammography was primary comparator (film mammography studies were allowed)
- Supplemental screening: head-to-head, vs. no supplemental screening
- Also allowed comparisons to clinical/self exams or other forms of additional follow-up
Project Scope

Outcomes:
- Breast cancer mortality
- Health-related quality of life
- Cancers detected/missed
- Rates of recall and biopsy
- Other test characteristics (e.g., sensitivity and specificity, PPV)
- Harms (radiation, “overdiagnosis”, unnecessary workup)

Literature Search
- Published studies Jan 1990 – Nov 2014
- All study designs included, regardless of comparator(s) or duration of follow-up
- Excluded studies that focused only on technical performance (e.g., image precision)
Study Quality Ratings

- RCTs/Cohorts: USPSTF Criteria
- Diagnostic Accuracy Studies: QUADAS-2 with certain modifications
  - Use of digital vs. film mammography as reference standard
  - Method for classification of breast density
  - “Good”: consecutive sample, low withdrawal rate, sufficient follow-up
  - “Fair”: allowance for small differences between groups or loss to follow-up
  - “Poor”: insufficient follow-up, selection bias, substantial and/or differential loss to follow-up, inappropriate interval between test and reference standard

Overall Strength of Evidence

- Risk of bias: study design and quality
- Consistency: direction and magnitude of findings
- Directness: direct comparison of major interventions and/or direct measurement of key outcomes
- Precision: confidence interval around estimates of intervention effect
**PRISMA flowchart showing results of literature search**

2935 potentially relevant references screened

390 abstracts for assessment

109 references for full text review

33 references
  - 9 tomosynthesis
  - 1 MRI
  - 18 hand-held ultrasound
  - 5 automated ultrasound

538 duplicate citations excluded
2087 excluded: not screening, reviews, meeting abstracts only

177 references excluded
( Editorials, reviews, abstracts, no clinical outcomes)

76 references excluded: no primary data, multiple publications, reviews

**Findings**
Quality & Type of Evidence

- *No* studies directly measuring impact of testing on breast cancer morbidity and/or mortality
- *No* RCTs
- DBT: All studies rated poor
  - Insufficient follow-up for interval cancers and/or
  - Imbalanced patient groups and/or
  - Selection bias
- Few good-quality studies of supplemental tests
  - One RCT of MRI, but not in target population

KQ1: Effectiveness of DBT
<table>
<thead>
<tr>
<th>TEST</th>
<th>COMPARATOR</th>
<th>STRENGTH OF EVIDENCE</th>
<th>DIRECTION OF EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness of</td>
<td>DBT</td>
<td>Digital mammography;</td>
<td>Incremental test performance vs. DM; improved</td>
</tr>
<tr>
<td>Screening</td>
<td></td>
<td>film mammography</td>
<td>cancer detection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td>Incomplete follow-up precludes definitive conclusions</td>
</tr>
</tbody>
</table>

**DBT Studies**

- Earliest large studies came from Europe (Ciatto, 2013; Skaane, 2013)
  - 10-15% reductions in recall
  - 30-50% increase in cancer detection rate (~1-2 add’l cancers per 1,000)
- Largest US multicenter study was recently published (Friedewald, 2014) (N=~174,000 receiving DBT)
  - 17% reduction in recall but 7% increase in biopsy
  - 29% increase in cancer detection
- Only US study with complete follow-up had imbalanced groups and 20% loss to follow-up (Destounis, 2014)
Estimated Yield: DBT vs. DM

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital mammography</th>
<th>DBT+Digital mammography</th>
<th>SOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-160</td>
<td>80-140</td>
<td>Moderate</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>12-27</td>
<td>Low-moderate</td>
</tr>
<tr>
<td>CDR per 1,000</td>
<td>3-5</td>
<td>4-6</td>
<td>Low</td>
</tr>
<tr>
<td>PPV3</td>
<td>20-25%</td>
<td>23-30%</td>
<td>Low-moderate</td>
</tr>
</tbody>
</table>

CDR: cancer detection rate; PPV3: positive predictive value of biopsies actually performed

KQ2: Effectiveness of Supplemental Screening
### 0 RCTs, 24 Cohort Studies (18 HHUS, 5 ABUS, 1 MRI)

<table>
<thead>
<tr>
<th>TEST</th>
<th>COMPARATOR</th>
<th>STRENGTH OF EVIDENCE</th>
<th>DIRECTION OF EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHUS</td>
<td>Digital or film mammography alone</td>
<td>Low-moderate</td>
<td>Comparable: small increase in cancer detection vs. very high false-positive rate; substantial study heterogeneity</td>
</tr>
<tr>
<td>ABUS</td>
<td>Digital mammography alone</td>
<td>Insufficient</td>
<td>Substantial study heterogeneity; wide variation in study findings</td>
</tr>
<tr>
<td>MRI</td>
<td>Digital or film mammography alone</td>
<td>Low</td>
<td>Likely incremental to mammography but limited evidence in target population</td>
</tr>
</tbody>
</table>

*Single study in women with dense breast tissue and negative mammogram; others in women at very high breast cancer risk

### HHUS Studies

- 18 studies conducted worldwide in ~100,000 women with dense breast tissue and negative mammogram
  - Only 4 with digital mammography
  - High degree of between-study heterogeneity, results ranged *widely*
    - Recall 21-186 per 1,000: all prospective studies had recall rates >100 per 1,000
    - Cancer detection rate: 0.4-14 per 1,000 (median 3.2)
    - Biopsy rate: 12-114 per 1,000 (median 46); PPV3 on biopsy very low (range 3-18%)
ACRIN 6666 Trial

- Only prospective US-based trial of HHUS with multiple screening rounds (N=2,809)
  - But in *high-risk population only*
  - Women randomized to receive mammography alone or mammography-ultrasound in alternate order
  - Depending on screening round, HHUS arm saw increase in cancer detection of 4-6 per 1,000
  - However, in first screening round:
    - More than twofold increase in recall (266 vs. 115 per 1,000)
    - More than fourfold increase in biopsy (102 vs. 24 per 1,000) and PPV3 of only 6.8%
  - Similar patterns in subsequent screening rounds

Estimated Yield: HHUS+DM vs. DM

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography</th>
<th>Incremental Yield With HHUS</th>
<th>SOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-120</td>
<td>30-100</td>
<td>Low</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>30-60</td>
<td>Low-moderate</td>
</tr>
<tr>
<td>CDR per 1,000</td>
<td>3-5</td>
<td>2-4</td>
<td>Moderate-high</td>
</tr>
<tr>
<td>PPV3</td>
<td>20-25%</td>
<td>5-7%</td>
<td>High</td>
</tr>
</tbody>
</table>

CDR: cancer detection rate; PPV3: positive predictive value of biopsies actually performed
**ABUS Studies**

- 5 studies of 28,000 women; no RCTs
- Even more heterogeneity than seen with HHUS:
  - Recall 23-207 per 1,000
  - Cancer detection rate: 0-12 per 1,000
  - Biopsy rate: 12-36 per 1,000 (but not reported in 2 of the 5 studies)
  - PPV3: 0% and 9.8% in the 2 studies reporting these data

---

**Brem, 2014**

- Large, prospective, multinational study (N=~15,000) of fair quality
- 35% increase in cancer detection (7.3 vs. 5.4 per 1,000)
- Nearly twofold increase in recall (285 vs. 150 per 1,000)
- Biopsy rate of 36 per 1,000, PPV3 = 9.8%
- PPV1 (% of abnormal screening results resulting in cancer diagnosis) lower for ABUS+DM vs. DM alone (2.6% vs. 3.6% respectively)
### Estimated Yield: ABUS+DM vs. DM

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography</th>
<th>Incremental Yield With ABUS</th>
<th>SOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-120</td>
<td>30-100</td>
<td>Insufficient</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>30-60</td>
<td>Insufficient</td>
</tr>
<tr>
<td>CDR per 1,000</td>
<td>3-5</td>
<td>2-4</td>
<td>Insufficient</td>
</tr>
<tr>
<td>PPV3</td>
<td>20-25%</td>
<td>5.7%</td>
<td>Insufficient</td>
</tr>
</tbody>
</table>

CDR: cancer detection rate; PPV3: positive predictive value of biopsies actually performed

*Due to high uncertainty, yield estimates same as for HHUS*

### MRI Studies

- Only 1 study in target population (women with dense breasts and normal mammogram):
  - High sensitivity, specificity and PPV, but...
  - MRI used as third-line screen after normal DM and ultrasound; and
  - Population was very high risk (nearly half of women had personal history of breast cancer)
- Studies in other high risk populations added for context:
  - Sensitivity: 71-100%; Specificity: 76-98%
  - Cancer detection rate: 8-67 per 1,000
  - Biopsy rate: 29-157 per 1,000
    - PPV3: 17-89% (median 48%)*
### Estimated Yield: MRI+DM vs. DM

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Digital Mammography</th>
<th>Incremental Yield With MRI</th>
<th>SOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recall rate per 1,000</td>
<td>100-120</td>
<td>100-120</td>
<td>Low</td>
</tr>
<tr>
<td>Biopsy rate per 1,000</td>
<td>14-22</td>
<td>20-40</td>
<td>Low</td>
</tr>
<tr>
<td>CDR per 1,000</td>
<td>3-5</td>
<td>3-11</td>
<td>Low</td>
</tr>
<tr>
<td>PPV3</td>
<td>20-25%</td>
<td>22%-48%</td>
<td>Low</td>
</tr>
</tbody>
</table>

CDR: cancer detection rate; PPV3: positive predictive value of biopsies actually performed

### KQ3: Harms of General Population or Supplemental Screening
<table>
<thead>
<tr>
<th>TEST</th>
<th>COMPARATOR</th>
<th>STRENGTH OF EVIDENCE</th>
<th>DIRECTION OF EFFECT</th>
</tr>
</thead>
</table>
| All  | Digital or film mammography alone | Insufficient | General underreporting of harms  
(1) Magnitude of overdiagnosis unclear and controversial  
(2) Unnecessary biopsy—reported complications <1%, but patient anxiety also of concern  
(3) Only DBT involves radiation exposure, approximately equal to mammography* |

*Best estimates from modeling studies suggest <1 add’l cancer per 1,000 screened after 20 screening rounds with mammography or DBT

KQ4: Differential Effects of Screening in Key Subgroups
**KQ5: Costs and Cost-Effectiveness of Screening Tests of Interest**

*Arleo 2013: Recall rate dropped from 247 per 1,000 to 126 per 1,000 between first and third calendar quarters after implementation*
### 5 Studies

<table>
<thead>
<tr>
<th>TEST</th>
<th>COMPARATOR</th>
<th>STRENGTH OF EVIDENCE</th>
<th>DIRECTION OF EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs and Cost-effectiveness of Screening</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBT</td>
<td>DM</td>
<td>Insufficient</td>
<td>$50,000-$100,000 per QALY gained in single model-based study (biennial screening, dense breasts only)</td>
</tr>
<tr>
<td>HHUS</td>
<td>Digital or film mammography alone</td>
<td>Low</td>
<td>4 studies: $325,000 per QALY gained, $60,000-$200,000 per additional cancer detected</td>
</tr>
<tr>
<td>ABUS</td>
<td>Digital mammography alone</td>
<td>Insufficient</td>
<td>No studies in target population</td>
</tr>
<tr>
<td>MRI</td>
<td>Digital or film mammography alone</td>
<td>Insufficient</td>
<td>No studies in target population</td>
</tr>
</tbody>
</table>

### Economic Impact of Frontline and Supplemental Screening: Published Evidence

- **DBT+DM vs. DM:**
  - Single decision analysis of *biennial screening in women with dense breasts* (DBT premium: $50)
  - DBT: 0.5 fewer deaths and 405 fewer false positives per 1,000 after 12 screening rounds
  - Cost-effectiveness: $54,000 per QALY gained

- **Supplemental screening (HHUS+DM vs. DM alone):**
  - Four studies (one model, three single-center evaluations)
  - Modeled cost-effectiveness: $325,000 per QALY gained
  - Single-center studies: $60,000-$200,000 per additional cancer detected
Economic Impact of Frontline and Supplemental Screening: ICER Cohort Model

- Target Populations:
  - Asymptomatic Washington women age 40-74 eligible for general screening
  - As above but with dense breast tissue and negative mammogram or DBT

- Strategies:
  - DBT/DM vs. DM (frontline)
  - DM+HHUS, ABUS, or MRI vs. DM or DBT alone (supplemental)

- Costs
  - Medicare fee schedule

---

Economic Impact of Frontline and Supplemental Screening: ICER Cohort Model

- Outcomes and costs (per 1,000 tested) over 1 year:
  - Recalls, biopsies, false positives (with and without biopsy), cancers detected, cancers missed (interval cancers)
  - Costs of screening, recall, biopsy, and detection of interval cancers
  - Supplemental screening results stratified by overall breast cancer risk

- Key assumptions:
  - Perfect compliance with frontline and supplemental screening
  - Supplemental screening would occur immediately following negative DM or DBT result
  - All abnormal supplemental tests would result in biopsy
  - Assumed performance of certain tests in an average-risk population (e.g., MRI)
Screening-Eligible Washington Women, by Level of Breast Cancer Risk*

*Low, moderate, and high risk corresponds to 5-year risks of <1.7%, 1.7-3.0%, and >3.0% respectively

Comparison of DBT to Digital Mammography, per 1,000 Women Screened

<table>
<thead>
<tr>
<th>Outcome (per 1,000 screened)</th>
<th>Digital Mammography</th>
<th>DBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recalls</td>
<td>107.0</td>
<td>91.0</td>
</tr>
<tr>
<td>Biopsies Performed</td>
<td>18.1</td>
<td>19.3</td>
</tr>
<tr>
<td>Cancers Detected (True Positives)</td>
<td>3.6</td>
<td>3.7</td>
</tr>
<tr>
<td>False Positive (with Biopsy)</td>
<td>14.5</td>
<td>15.6</td>
</tr>
<tr>
<td>False Positive (without Biopsy)</td>
<td>83.3</td>
<td>67.2</td>
</tr>
<tr>
<td>Cancers Missed (Interval Cancers)</td>
<td>0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Cost (per Woman Screened, $)</td>
<td>189</td>
<td>245</td>
</tr>
<tr>
<td>Women w/Dense Breast Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recalls</td>
<td>130.6</td>
<td>114.6</td>
</tr>
<tr>
<td>Biopsies Performed</td>
<td>22.1</td>
<td>24.3</td>
</tr>
<tr>
<td>Cancers Detected (True Positives)</td>
<td>4.2</td>
<td>4.3</td>
</tr>
<tr>
<td>False Positive (with Biopsy)</td>
<td>17.9</td>
<td>20.0</td>
</tr>
<tr>
<td>False Positive (without Biopsy)</td>
<td>105.7</td>
<td>89.6</td>
</tr>
<tr>
<td>Cancers Missed (Interval Cancers)</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Cost (per Woman Screened, $)</td>
<td>194</td>
<td>249</td>
</tr>
</tbody>
</table>
**Total Cost per Woman Screened, at Different Payment Premiums for DBT**

- **$75**
- **$57**
- **$50**
- **$25**
- **$10**
- **$1**
- **$0**
- **DM**

<table>
<thead>
<tr>
<th>Outcome (per 1,000 screened)</th>
<th>DM Basecase</th>
<th>DBT Basecase</th>
<th>(A)</th>
<th>(B)</th>
<th>(C)</th>
<th>(D) 1 add'l cancer detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sn: 84.0 Sp: 90.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sn: 84.0 Sp: 91.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sn: 87.0 Sp: 93.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sn: 89.0 Sp: 95.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Sensitivity Analyses on Test Performance**

<table>
<thead>
<tr>
<th>Outcome (per 1,000 screened)</th>
<th>DM Basecase</th>
<th>DBT Basecase</th>
<th>(A)</th>
<th>(B)</th>
<th>(C)</th>
<th>(D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sn: Sensitivity; Sp: Specificity; DM: Digital mammography; DBT: Digital breast tomosynthesis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTES:** Recalls refer to positive mammograms or DBTs recalled for additional imaging and/or biopsy; findings may not sum perfectly due to rounding.
Supplemental Screening with HHUS, ABUS, or MRI: Results

- Rate of biopsy 3-4 times that of digital mammography alone
- 4-6 additional cancers detected over DM (but 1-2 of these have the potential to be overdiagnosed)
- All tests would identify nearly all of the cancers missed by mammography
- Incremental costs driven by cost of screening test: MRI ($602), ABUS ($243), HHUS ($159)
- Cancer yield greatest in higher-risk women

Supplemental Screening with HHUS, ABUS, or MRI: Results

- When DBT was considered the frontline test, total strategy costs were similar:
  - Fewer women recalled for additional imaging, but...
  - More women sent to supplemental screening as a result of initial negative test
- When DBT assumed to detect 1 add’l cancer per 1,000, biopsy rate declined
  - Incremental costs of supplemental screening reduced by 2-11%, depending on type of test
Costs of DBT or DM and Supplemental Screening Among Washington Women with Dense Breasts

Costs of DM and Supplemental Screening Among Higher-Risk Women Only
**Economic Impact of Frontline and Supplemental Screening in Washington: Summary**

- Comparison of DBT vs. digital mammography in all screening-eligible women suggests reductions in recall only offset a small % of additional screening costs:
  - Cost neutrality only approached with very small premium
  - Greater cost offsets seen with more optimistic scenarios for improved test performance
  - Reductions in recall would accumulate over longer time horizon
- Supplemental screening with any technology would substantially increase screening costs if performed in all women with dense breast tissue
  - Risk-based targeting results in much smaller increase

**Integrated Evidence Ratings**
### ICER Rating Matrix

<table>
<thead>
<tr>
<th>Superior: A</th>
<th>Ab</th>
<th>Ac</th>
</tr>
</thead>
<tbody>
<tr>
<td>B* a</td>
<td>B* b</td>
<td>B* c</td>
</tr>
<tr>
<td>Ba</td>
<td>Bb</td>
<td>Bc</td>
</tr>
<tr>
<td>Incremental: B*/B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparable: C*/C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C* a</td>
<td>C* b</td>
<td>C* c</td>
</tr>
<tr>
<td>Ca</td>
<td>Cb</td>
<td>Cc</td>
</tr>
<tr>
<td>Inferior: D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Da</td>
<td>Db</td>
<td>Dc</td>
</tr>
<tr>
<td>Promising but Inconclusive: P/I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pa</td>
<td>Pb</td>
<td>Pc</td>
</tr>
<tr>
<td>Insufficient: I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
</tbody>
</table>

**Comparative Value**

- a (if premium <$30)
- b (if premium $30-$60)
- c (if premium >$60)

### Evidence Ratings: DBT vs. DM

- **Comparative Clinical Effectiveness:** C+
- **Comparative Value:**
  - a (if premium <$30)
  - b (if premium $30-$60)
  - c (if premium >$60)
Evidence Ratings: Supplemental Screening

- Comparative Clinical Effectiveness:
  - MRI+DM vs. DM: B+ (A)*
  - HHUS+DM vs. DM: P (C+)*
  - ABUS+DM vs. DM: I

- Comparative Value:
  - MRI+DM vs. DM: c (b)*
  - HHUS+DM vs. DM: c (b)*
  - ABUS+DM vs. DM: N/A

*Rating in brackets reflects use in risk-targeted subgroup
Practice Guidelines

- DBT:
  - ACS and NCCN note promise of DBT but do not recommend it as of yet
  - ACR and Wash. State Radiological Society (WSRS) describe benefits of DBT and encourage reimbursement of test to enable collection of long-term data
  - American Society of Breast Disease (ASBD) notes limitations that still remain with digital mammography and consider DBT a major advancement

Practice Guidelines

- MRI (ACS, NCCN, ACR/SBI):
  - Recommended as adjunct to mammography in high-risk women (e.g., lifetime risk >20%, genetic mutations, history of chest radiation)

- HHUS:
  - ACS has no current recommendation for or against HHUS
  - NCCN does not recommend routine supplemental screening in women with dense breast tissue and no other risk factors
  - ACR/SBI recommends HHUS as an adjunct in MRI-eligible women who cannot have an MRI for any reason, and suggest consideration of HHUS in women with dense breast tissue

- ABUS:
  - No guidelines identified
Payer Coverage Policies

CMS

- HHUS/ABUS
  - Available NCD relates only to use for diagnosis
- MRI
  - Available NCD/LCDs relate only to use for diagnosis
- DBT
  - Final rule for 2015 relates only to separate payment for DBT, not to considerations of coverage
Private Payers

- HHUS/ABUS:
  - Considered investigational as a screening tool by Humana, United, and CIGNA
  - No available policies from other national or regional payers
- MRI:
  - Generally covered only for women considered at high risk for breast cancer
  - Humana and United consider dense breast tissue an indication for adjunct MRI screening, regardless of other risk factors
- DBT:
  - Covered by Regence, but at no additional payment currently
  - Considered investigational by other regional/national payers

Appendix: Quality Criteria
Quality Ratings: USPSTF criteria and QUADAS-2

Outcome Studies:

- **“Good”:**
  - Comparable groups with no or low attrition; intent-to-treat analysis used in RCTs
  - Reliable and valid measurement instruments used
  - Clear description of intervention and comparator(s)
  - All important outcomes considered
  - Attention to confounders in design and analysis

- **“Fair”:**
  - Generally comparable groups, some differential follow-up may occur; intent-to-treat analysis used in RCTs
  - Acceptable measurement instruments used
  - Some but not all important outcomes considered
  - Some but not all potential confounders are accounted for

- **“Poor”:**
  - Noncomparable groups and/or differential follow-up; lack of intent-to-treat analysis for RCTs
  - Unreliable or invalid measurement instruments used (including not masking outcome assessment)
  - Key confounders given little or no attention

Quality Ratings: USPSTF criteria and QUADAS-2

QUADAS-2 (Diagnostic Accuracy Studies):

- Designed to rate risk of bias and applicability in 4 key domains:
  - Patient selection
  - Index test
  - Reference standard
  - Flow and timing

- Rated in terms of % of studies with levels of bias risk or applicability concerns that are:
  - Low risk/concern
  - High risk/concern
  - Unclear
HTCC Coverage and Reimbursement Determination Analytic Tool

HTA’s goal is to achieve better health care outcomes for enrollees and beneficiaries of state programs by paying for proven health technologies that work.

To find best outcomes and value for the state and the patient, the HTA program focuses on three questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

**Principle One: Determinations are evidence-based**

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective as expressed by the following standards:

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

**Principle Two: Determinations result in health benefit**

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms:

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

---

1 Based on Legislative mandate: See RCW 70.14.100(2).
2 The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm
3 The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm
Using evidence as the basis for a coverage decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. **Availability of Evidence:**

   Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. **Sufficiency of the Evidence:**

   Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence using characteristics such as:
   - Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
   - The amount of evidence (sparse to many number of evidence or events or individuals studied);
   - Consistency of evidence (results vary or largely similar);
   - Recency (timeliness of information);
   - Directness of evidence (link between technology and outcome);
   - Relevance of evidence (applicability to agency program and clients);
   - Bias (likelihood of conflict of interest or lack of safeguards).

   Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

<table>
<thead>
<tr>
<th>Not Confident</th>
<th>Confident</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.</td>
<td>Very certain of evidentiary support. Further information is unlikely to change confidence</td>
</tr>
</tbody>
</table>

3. **Factors for Consideration - Importance**

   At the end of discussion a vote is taken on whether sufficient evidence exists regarding the technology’s safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:
   - Risk of event occurring;
   - The degree of harm associated with risk;
   - The number of risks; the burden of the condition;
   - Burden untreated or treated with alternatives;

---

4 Based on GRADE recommendation: [http://www.gradeworkinggroup.org/FAQ/index.htm](http://www.gradeworkinggroup.org/FAQ/index.htm)
- The importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- The degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- Value variation based on patient preference.

### HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

**Discussion Document:**
What are the key factors and health outcomes and what evidence is there?

<table>
<thead>
<tr>
<th>Safety Outcomes</th>
<th>Safety Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation</td>
<td></td>
</tr>
<tr>
<td>Over-diagnosis</td>
<td></td>
</tr>
<tr>
<td>Unnecessary work up</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Efficacy – Effectiveness Outcomes</th>
<th>Efficacy / Effectiveness Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
</tr>
<tr>
<td>Health related quality of life</td>
<td></td>
</tr>
<tr>
<td>Cancers detected/missed</td>
<td></td>
</tr>
<tr>
<td>Rates of recall and biopsy</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Special Population / Considerations Outcomes</th>
<th>Special Populations/ Considerations Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cost</th>
<th>Cost Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td></td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td></td>
</tr>
<tr>
<td>Cost-utility</td>
<td></td>
</tr>
</tbody>
</table>
Medicare Coverage and Guidelines

[From Page 35 of evidence report]

3. Medicare ...

3.1 Breast Ultrasound

Centers for Medicare and Medicaid Services (CMS)

The national coverage determination (NCD) for breast ultrasound relates only to its use for diagnosis rather than screening. There is also no current local coverage determination (LCD) for screening that covers the state of Washington. LCDs for Illinois (L26890) and Kentucky (L31856) on breast imaging relate only to breast ultrasound’s diagnostic use.

3.2 Breast MRI

Centers for Medicare and Medicaid Services (CMS)

The national coverage determination (NCD) for MRI relates only to its general diagnostic use rather than as a breast cancer screening method. There is no local coverage determination (LCD) for breast MRI screening that covers the state of Washington. LCDs for Illinois (L26890) and Kentucky (L31856) cover the use of breast MRI, but, as with ultrasound, indications are limited to diagnostic purposes only.

3.3 Digital Breast Tomosynthesis

Medicare

There are no published national or local coverage determinations for DBT.

[From Page 30 of evidence report]

2. Clinical Guidelines and Training Standards

2.1 Magnetic Resonance Imaging (MRI) of the Breast

The American Cancer Society (ACS) (2014)


The ACS recommends annual adjunctive MRI for women at high risk for breast cancer. This includes women whose lifetime risk of breast cancer is 20% to 25% or greater; women who have a known BRCA1 or BRCA2 gene mutation, or who have a first-degree relative with these genetic mutations if they have not been tested themselves; women who had radiation therapy to the chest between ages 10 and 30; and women who have Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome. The ACS recommends against MRI screening for women with a low lifetime risk of breast cancer, defined as less than 15%. The society suggests that there is not enough evidence to form MRI recommendations for women with moderate risk of developing breast cancer, or who may be at increased risk for breast cancer due to factors such as having extremely or heterogeneously dense breast tissue on mammogram, a personal history of breast cancer, ductal carcinoma in situ, lobular carcinoma in situ, atypical ductal hyperplasia, or atypical lobular hyperplasia.

National Comprehensive Cancer Network (NCCN) (2014)


The NCCN recommends MRI as an adjunct to mammography starting at age 30 for women with a lifetime risk of breast cancer greater than 20% (using Claus, BRCAPRO, BOADICEA, or Tyrer-Cuzick models), as well for women with mutations in BRCA1, BRCA2, TP53, or PTEN and their untested first-degree relatives. In addition,
they recommend annual screening MRI for those receiving radiation therapy to their chest between the ages of 10 to 30 years starting 8 to 10 years following the radiation therapy or at age 40, whichever comes first.

The NCCN guidelines also state that there is insufficient evidence to recommend for or against annual MRI screening for the following women: those with a 15% to 20% lifetime risk for breast cancer; those with a personal history of breast cancer, ductal carcinoma in situ, lobular carcinoma in situ, atypical ductal hyperplasia, atypical lobular hyperplasia; or those with heterogeneously dense or extremely dense tissue on mammography. NCCN recommends against MRI for women with a lifetime risk of less than 15%.

American College of Radiology / Society of Breast Imaging (2010)
http://www.jacr.org/article/S1546-1440(09)00480-3/fulltext

Joint guidelines from the American College of Radiology and the Society of Breast imaging recommend annual screening MRI examinations starting at age 30 for BRCA mutation carriers and their untested first degree relatives, for women with greater than a 20% lifetime risk for breast cancer on the basis of family history, women with a history of chest irradiation (usually for Hodgkin’s disease), and a single screen of the contralateral breast for women with newly diagnosed breast cancer (Lee et al., 2010). They recommend considering screening MRI for women with a lifetime risk between 15% and 20% on the basis of a personal history of breast or ovarian cancer or biopsy proven lobular neoplasia or atypical ductal hyperplasia.

The European Society of Breast Imaging (2007)

The European Society of Breast Imaging recommends annual MRI screening examinations for women with a BRCA mutation, first degree relatives of BRCA carriers, women with radiation to their chest wall between the ages of 10 and 30 years, women with Li-Fraumeni syndrome (TP53 mutation carriers) and their untested first degree relatives, and women with Cowden syndrome (PTEN mutation carriers) and their first degree relatives) (Mann et al., 2007).

2.2 Hand-held Ultrasonography (HHUS) of the Breast

The American Cancer Society (ACS) (2014)

The ACS has no recommendation on HHUS for breast cancer screening.

National Comprehensive Cancer Network (NCCN) (2014)

Under breast screening considerations, the NCCN guidelines state “Dense breasts limit the sensitivity of mammography. Dense breasts are associated with an increased risk for breast cancer, but there is insufficient evidence to support routine supplemental screening in women with dense breasts and no other risk factors” (NCCN, 2013). Under the same section they also note, “There are several studies supporting the use of ultrasound for breast cancer screening as an adjunct to mammography for high risk women with dense breast tissue.”

American College of Radiology / Society of Breast Imaging (2010)
http://www.jacr.org/article/S1546-1440(09)00480-3/fulltext

Joint guidelines from the American College of Radiology and the Society of Breast imaging recommend considering annual screening ultrasound examinations in addition to mammography for women eligible for
MRI screening who cannot have MRI for any reason (Lee et al., 2010). They recommend considering ultrasound in women with dense breast tissue as an adjunct to mammography.

2.3 Automated Whole Breast Ultrasonography (ABUS)

There are no guidelines currently recommending ABUS to screen for breast cancer from any major clinical society, including the American Cancer Society, the National Comprehensive Cancer Network, the American College of Radiology, and the Society of Breast Imaging.

2.4 Digital Breast Tomosynthesis (DBT)

American Cancer Society (ACS) (2014)


The ACS suggests that DBT “uses more radiation than most standard 2-view mammograms, but it may allow doctors to see [dense areas] more clearly. Some studies have suggested it might lower the chance that the patient will be called back for unnecessary tests. It may also be able to find more cancers.” ACS does not provide a recommendation for or against use of DBT.

American College of Radiology (ACR) (2014)

http://www.acr.org/About-Us/Media-Center/Position-Statements/Position-Statements-Folder/20141124-ACR-Statement-on-Breast-Tomosynthesis

While digital mammography is the only breast cancer screening procedure that has been proven to reduce mortality, tomosynthesis is a very promising technology that has been shown to reduce recall rates and increase cancer detection, thus having a positive impact on patient care. The ACR acknowledges the lack of studies demonstrating long-term benefits, and encourages payers to reimburse for tomosynthesis so that additional large-scale studies can be conducted.

American Society of Breast Disease (ASBD) (2013)


Despite the growing use of full-field digital mammography over film, screening mammography is still limited by overlapping breast tissue. The use of DBT has the potential to overcome these limitations and improve diagnostic accuracy of breast cancer. DBT has the potential to improve patient outcomes, particularly with regards to diagnostic work-up following screening. By increasing cancer detection and reducing recalls, DBT has utility as both a diagnostic and screening tool and may have the greatest impact on women with dense breast tissue.

National Comprehensive Cancer Network (NCCN) (2014)


Under breast screening considerations, the NCCN guidelines state that “Early studies show promise for DBT mammography. Two large trials showing a combined use of digital mammography and tomosynthesis resulted in improved cancer detection and decreased call back rates; of note, this is double the dose of radiation and is a factor in recommending this modality. Definitive studies are still pending” (NCCN, 2013).


http://www.wsrs.org/position_statements.html

Adding DBT to standard mammography screening programs would help overcome many of the current limitations of digital mammography, such as its inability to distinguish overlapping breast tissue. As evidenced by recent studies, the addition of DBT will likely result in the additional detection of one cancer for every
1,000 women screened. Moreover, it will reduce the number of unnecessary call-backs as well as decrease patient anxiety and lost productivity as a result of false-positive findings. DBT has the potential to both improve patient outcomes and decrease healthcare costs by identifying more early-stage cancers and expediting diagnostic workup. WSRS urges payers to reimburse for DBT so this advancement in breast cancer screening can be more widely utilized.

Clinical Committee Findings and Decisions

Efficacy Considerations

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value?
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests’ accuracy?
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices?

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
  - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
  - Adverse effect on health that can result in lasting harm or can be life-threatening?
- Other morbidity concerns?
- Short term or direct complication versus long term complications?
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?
Overall
- What is the evidence about alternatives and comparisons to the alternatives?
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?

Next Step: Cover or No Cover
If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions
If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
   - Refer to evidence identification document and discussion.
   - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
   - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
   - What are the known conditions/criteria and evidence state
   - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Clinical Committee Evidence Votes

First Voting Question
The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.
Is there sufficient evidence under some or all situations that the technology is:

<table>
<thead>
<tr>
<th></th>
<th>Unproven (no)</th>
<th>Equivalent (yes)</th>
<th>Less (yes)</th>
<th>More (yes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost-effective</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second Vote
Based on the evidence about the technologies’ safety, efficacy, and cost-effectiveness, it is

________ Not Covered _______ Covered Unconditionally _______ Covered Under Certain Conditions

Discussion Item
Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Next Step: Proposed Findings and Decision and Public Comment
At the next public meeting the committee will review the proposed findings and decision and consider any public comments as appropriate prior to a vote for final adoption of the determination.

1) Based on public comment was evidence overlooked in the process that should be considered?

2) Does the proposed findings and decision document clearly convey the intended coverage determination based on review and consideration of the evidence?

Next Step: Final Determination
Following review of the proposed findings and decision document and public comments:
Final Vote

Does the committee approve the Findings and Decisions document with any changes noted in discussion?

If yes, the process is concluded.

If no, or an unclear (i.e., tie) outcome Chair will lead discussion to determine next steps.