Breast Cancer Screening: Who gets what??

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Disclosures:

ACRIN PA 4006 (P.I. Conant): comparison of Full-Field Digital Mammography with Digital Breast Tomosynthesis Acquisition in Relation to Screening Call-Back Rate

Scientific Advisory Board, Lecturer Hologic Inc., Bedford, Mass

NIH Grant: 5U54CA163313-03; Penn Center for Innovation in Personalized Breast Screening
Outline

Who gets what?
– Current recommendations
– What may change in the near future?

Future of “Precision Screening”
– How we can integrate our knowledge into patient-centered, personalize screening paradigms to improve outcomes...
## Screening Recommendations

<table>
<thead>
<tr>
<th>Organization</th>
<th>Guidelines</th>
</tr>
</thead>
</table>
| American Cancer Society                  | • Annual mammography age 40 and over  
• Clinical breast exam every 2-3 yrs 20-40, annually age 40 and over  
• Annual MRI for women > 20% lifetime risk |
| National Cancer Institute                | • Mammogram every 1-2 yrs for women age 40 and over  
• Clinical breast exam every one to two yrs.                           |
| U.S. Preventative Services Task Force    | • Mammography every two years 50-74 yrs  
• Breast exam not recommended                                           |
The Screening Process

General Population

Population with Disease
How Should Women Be Screened?

What does the USPSTF suggest that patients do?
Screening mammography should not be done routinely for all women age 40 to 49 years. Women and their doctors should base the decision to start mammography before age 50 years on the risk for breast cancer and preferences about the benefits and harms. Women aged 50 to 74 years should have mammography every 2 years. More evidence is needed for the USPSTF to recommend for or against screening mammography after age 74 years. The
Comparing Screening Modalities...
Screening with MRI - What is the Evidence?

American Cancer Society expert panel Aug. 2007:

- Review literature on MRI screening published 2002-2006
- Mid to late 1990s, at least 6 prospective, non-randomized studies to determine benefit of adding annual MRI to mammo for women at *increased risk of breast cancer*
  - Defined as > 20% lifetime risk or genetic mutation carriers
American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography

Debbie Saslow, PhD, Carla Boetes, MD, PhD, Wylie Burke, MD, PhD, Steven Harms, MD, Martin O. Leach, PhD, Constance D. Lehman, MD, PhD, Elizabeth Morris, MD, Etta Pisano, MD, Mitchell Schnall, MD, PhD, Stephen Sener, MD, Robert A. Smith, PhD, Ellen Warner, MD, Martin Yaffe, PhD, Kimberly S. Andrews, Christy A. Russell, MD for the American Cancer Society Breast Cancer Advisory Group

CA Cancer J Clin 2007; 57:75-89
## Cancer Yields in High Risk Screening

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Cancers/n</th>
<th>Mammo</th>
<th>MRI ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tilanus-Linthorst, 2000</td>
<td>2.8% (3/109)</td>
<td>0% (0)</td>
<td>2.8% (3)</td>
</tr>
<tr>
<td>Podo et al, 2002</td>
<td>7.6% (8/105)</td>
<td>1.0% (1)</td>
<td>6.7% (7)</td>
</tr>
<tr>
<td>Morris et al, 2003</td>
<td>3.8% (14/367)</td>
<td>0% (0)</td>
<td>3.8% (14)</td>
</tr>
<tr>
<td>Kriege et al, 2004</td>
<td>2.4% (45/1909)</td>
<td>0.9% (18)</td>
<td>1.2% (22)</td>
</tr>
<tr>
<td>Warner et al, 2004</td>
<td>9.3% (22/236)</td>
<td>3.4% (8)</td>
<td>3.0% (7)</td>
</tr>
<tr>
<td>Kuhl et al, 05</td>
<td>8.1% (43/529)</td>
<td>2.6% (14)</td>
<td>3.6% (19)</td>
</tr>
<tr>
<td>Leach et al, 05</td>
<td>5.1% (33/649)</td>
<td>2.2% (14)</td>
<td>2.9% (19)</td>
</tr>
<tr>
<td>Lehman et al, 05</td>
<td>1.1% (4/367)</td>
<td>0.3% (1)</td>
<td>0.8% (3)</td>
</tr>
<tr>
<td>Lehman et al, 05</td>
<td>3.5% (6/171)</td>
<td>1.2% (2)</td>
<td>2.3% (4)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>4.0%</strong> (178/4442)</td>
<td><strong>1.3%</strong> (58/4442)</td>
<td><strong>2.2%</strong> (98/4442)</td>
</tr>
</tbody>
</table>

Lehman CD. JMRI 2006; 24:964-70.
## Comparative Sensitivities in High Risk Screening

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Mammo</th>
<th>US</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tilanus-Linthorst, 2000</td>
<td>0% (0/3)</td>
<td>NA</td>
<td>100% (3/3)</td>
</tr>
<tr>
<td>Podo et al, 2002</td>
<td>13% (1/8)</td>
<td>13% (1/8)</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>Kriege et al, 2004</td>
<td>40% (18/45)</td>
<td>NA</td>
<td>71% (32/45)</td>
</tr>
<tr>
<td>Warner et al, 2004</td>
<td>36% (8/22)</td>
<td>33% (7/22)</td>
<td>77% (17/22)</td>
</tr>
<tr>
<td>Kuhl et al, 2005</td>
<td>33% (14/43)</td>
<td>40% (17/43)</td>
<td>91% (39/43)</td>
</tr>
<tr>
<td>Lehman, 2005</td>
<td>33% (2/6)</td>
<td>17% (1/6)</td>
<td>100% (6/6)</td>
</tr>
<tr>
<td>Leach et al, 2005</td>
<td>40% (14/35)</td>
<td>NA</td>
<td>77% (27/35)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>35% (57/162)</td>
<td>34% (25/73)</td>
<td><strong>81% (132/162)</strong></td>
</tr>
</tbody>
</table>
Current ACS Recommendations for MRI Screening

Recommend annual screening for high risk groups (based on evidence)*:

– BRCA mutation
– First-degree relative of BRCA carrier, but untested
– Lifetime risk ~20–25% or greater, using BRCAPRO or models that are largely dependent on family history

Also (based on consensus) *:
– Radiation to chest between age 10 and 30 years
– Li-Fraumeni syndrome and first-degree relatives
– Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives

Current ACS Recommendations for MRI Screening

Insufficient evidence to recommend *for or against*:

- Moderate risk: lifetime risk 15-20%
- High risk biopsy: ADH, ALH, LCIS
- Heterogeneously or extremely dense breasts on mammogram
- Personal history of breast cancer

Recommended *against* screening (*based on consensus*):

- Average risk or < 15%

MRI for Women with a Personal History (PH) of Treated Breast Cancer?

At elevated risk, early detection of 2nd cancers with mammography known to decrease mortality

- Mammography important but imperfect, sensitivity 50-65*

Initial studies* suggest MRI performance in pts with PHx alone may be ≥ to women with genetic FH
- Higher cancer yield and specificity

*G. Kalish. RSNA 2010
MRI for Women with a Personal History of Breast Cancer

New study Gweon, et al (Radiology online, April 15th)
- 607 consecutive women prior breast conservation
- 92% had had pre-op or staging breast MRs

Significant number of addit’l cancers detected
- 18.1/1000
  - Node negative 73% or DCIS 27.3%
- Factors associated with MR detected cancers:
  - Age<50
  - More than 24 mos after surgery and staging MR
What about MRI for Women with history of LCIS?

Sung et al (Radiology Nov. 2011)
- 670 studies performed in women with hx of LCIS
  - 9% biopsy rate
  - Of bxs, 20% were malignant
  - 4.5% increase in cancer detection
    - 17 cancers in 14 pts
      - 12 on MR only (9 invasive, 3 in situ)
Who is “high risk”?

High Risk is defined as > 20% lifetime risk
  • Known mutation carriers, strong family hx

But, most women are not at high risk!
  • Lifetime risk of 1 in 7 by age 85
    • 14% lifetime risk at age 85
    • Lower if younger age

What about moderate risk women?
  – Women with a personal hx breast cancer ~ 3x↑ risk
  – Women with ADH, ALH, LCIS?
  – Women with increased breast density have ~ 4x↑ risk
So, who should be screened with supplemental imaging?

And, should it be ultrasound or MRI?
## Cost of US versus MR

<table>
<thead>
<tr>
<th>Study</th>
<th>Medicare Payment*</th>
<th>Private Billing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening digital mammo</td>
<td>$140</td>
<td>$300</td>
</tr>
<tr>
<td>Breast ultrasound</td>
<td>$150</td>
<td>$390</td>
</tr>
<tr>
<td>Bilateral pre and post CE-MRI</td>
<td>$534</td>
<td>$3,000</td>
</tr>
</tbody>
</table>

*2013 CMS National Medicare Payment: Hospital outpatient
www.gehealthcare.com/reimbursement
ACRIN 6666: Mammo plus US
( High Risk patients)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Cancer Yield/1000 Screened</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Round 1:</td>
</tr>
<tr>
<td>Mammo alone</td>
<td>7.5</td>
</tr>
<tr>
<td>Ultrasound alone</td>
<td>9.0</td>
</tr>
<tr>
<td>Mammo plus Ultrasound</td>
<td>12.8</td>
</tr>
</tbody>
</table>

Ultrasound gives supplemental yield of 3.7 cancers/1000

### Recall Rate (%)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Round 1:</th>
<th>Round 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammo alone</td>
<td>11.5</td>
<td>9.4</td>
</tr>
<tr>
<td>Ultrasound alone</td>
<td>20.9</td>
<td>10.7</td>
</tr>
<tr>
<td>Mammo plus Ultrasound</td>
<td>26.6</td>
<td>16.8</td>
</tr>
</tbody>
</table>

*7-8% absolute increase in recall rate*

### Short Term Follow-up Rate (%)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Round 1:</th>
<th>Round 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammo alone</td>
<td>3.2</td>
<td>1.6</td>
</tr>
<tr>
<td>Ultrasound alone</td>
<td>11.1</td>
<td>3.9</td>
</tr>
<tr>
<td>Mammo plus Ultrasound</td>
<td>13.8</td>
<td>5.3</td>
</tr>
</tbody>
</table>
Is MRI better than Mammo with US?

<table>
<thead>
<tr>
<th></th>
<th>Mammo plus US</th>
<th>Mammo plus US plus MRI</th>
<th>Difference (p value)</th>
<th>Mammo alone</th>
<th>Mammo plus MRI</th>
<th>Difference (p value)</th>
<th>MRI alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Yield/1000</td>
<td>11.4</td>
<td>26.1</td>
<td>14.7 (.004)</td>
<td>8.2</td>
<td>26.1</td>
<td>18.0 (&lt;.001)</td>
<td>22.9</td>
</tr>
<tr>
<td>#/total</td>
<td>7/612</td>
<td>16/612</td>
<td></td>
<td>5/612</td>
<td>16/612</td>
<td></td>
<td>14/612</td>
</tr>
</tbody>
</table>

No doubt...

Method:
- 687 asymptomatic women with elevated risk (20% lifetime) underwent 1,679 annual screening rounds:
  - CBE, Mammo, ultrasound, and MRI
  - Read independently and in differing combinations
  - Mean and median follow-up was 29.18 and 29.09 mos.
EVA Trial continued...
Conclusion for screening high risk women:

- Quality-assured MRI shifts distribution of screen-detected breast cancers toward pre-invasive stage.

- Neither mammo, nor annual or half-yearly US or CBE will add to cancer yield achieved by MRI alone.

Can we create a “faster”, more efficient MRI while preserving the tests sensitivity?
Kuhl et al. ASCO 10/2013:
443 women at high risk with neg. mammo
- FAST scan: first post contrast sub imaging (T1, Fat sat) and MIP
- Full Scan – conventional 3 post contrast sequences

Results:
- Times:
  - Both TABLE time and READ time decreased
    - TABLE: 3mins FAST versus 21 min for FULL
    - READ time: 2.8 sec for MIP, 28 sec for sub images versus
- Cancer detection: 11 cancers diagnosed
  - 10 on FAST scan, 11 when Full protocol added
  - MIP alone positive in 9/11 scans
- Sensitivity and Specificity identical in two sets
  - 18.2 additional cancers detected per 1000 scanned
Abbreviated Breast Magnetic Resonance Imaging (MRI): First Postcontrast Subtracted Images and Maximum-Intensity Projection—A Novel Approach to Breast Cancer Screening With MRI

Christiane K. Kuhl, Simone Schrading, Kevin Strobel, Hans H. Schild, Ralf-Dieter Hilgers, and Heribert B. Biedling

Rethinking Breast Cancer Screening: Ultra FAST Breast Magnetic Resonance Imaging

Elizabeth A. Morris, Memorial Sloan Kettering Cancer Center, New York, NY

See accompanying article doi: 10.1200/JCO.2013.52.5386
Abridged or FAST MRI

Pre contrast

Post contrast – 1st dynamic only

Subtraction image

MIP: fused image of all subs

Kuhl et al. 6/23/2014 as 10.1200/JCO.2013.52.5386
Incorporating Imaging in Risk Assessment:  
Moving towards Personalized Screening...

Who? When? How often?

General Population

Population with Disease

General Population

Population with Disease
What’s a woman to do?
Journal of Cancer 2014: Conceptual Model of Breast Cancer Screening

**Screening Awareness**
- **Screening Discussion**
  - Provider knowledge
  - Patient perception & preferences
  - Decision-making tools
- **Determine Risk Level**
  - Age
  - Breast density
  - Genetics
  - Hx: Family, reproductive, breast, hormone use, screening

**Detection**
- **Screening Imaging**
  - Imaging type (Mammo, Ultrasound, tomosynthesis, MRI)
  - Breast density
- **Diagnostic Imaging**
  - Imaging type (Mammo, Ultrasound, tomosynthesis, MRI)
  - Clinical findings
- **BI-RADS 1 & 2:** Return for routine follow-up
- **BI-RADS 3:** Short term follow-up
- **BI-RADS 4 & 5:** Biopsy
- **Symptomatic patients**

**Diagnosis**
- Benign High risk
- Malignant Tumor markers

**Process Measures**
- Risk assessment performed
- Screening rates, risk-based modality, timeliness
- Utilization, intensity, timeliness
- Timeliness, adherence, care coordination

**Outcome Measures**
- Risk score (Lifetime & 5 year)
- Sensitivity, specificity, PPV, cancer detection rate, recall rate
- Biopsy yield, stage, EOD, tumor characteristics, PPV
- Quality of life, follow-up for cancer & death

**Treatment & Survivorship**
- Comorbidities
- Functional status
- Pt preferences
- Treatment plan (Surgery, XRT, chemo, palliation)
As Radiologists, how can we use our knowledge to help improve screening?

Screening Discussion
- Provider knowledge
- Patient perception & preferences
- Decision-making tools

Determine Risk Level
- Age
- Genetics
- Family Hx,
- Reproductive Hx,
- Breast Bx, HRT use
- Breast Density/Complexity,
- Screening Hx

Screening Awareness

Test availability, Cost, patient preference

Recommend Screening?
Integrated Risk Assessment Platform

Breast Complexity Index

“Quantitative Imaging Reading Room of the Future”

Kontos, Keller, Conant et al. RSNA 2012
Making Decisions:
Should I have a mammogram?

A decision aid for women thinking about having mammograms

Start the decision aid ➔

This decision aid was developed by researchers at the University of Pennsylvania
Making Decisions:
Should I have a mammogram?

A decision aid for women thinking about having mammograms

Welcome to the mammogram decision aid.

A mammogram is an x-ray picture of your breast. Mammograms are used as a screening test for breast cancer in healthy women who have no signs or symptoms of the disease.

Women in their 30s and 40s should think about whether to have mammograms in their 40s or wait until they are 50-years-old. This decision aid will provide you with information about having mammograms in your 40s so that you can make a decision for yourself.

This decision aid will take about 25 minutes to complete.

Courtesy of M. Schapira, MD
Why is there a decision to make about when to have mammograms?

Health experts have different opinions about whether women in their 40s should have mammograms. This is because there are pros and cons to having mammograms before age 50. The table below shows the recommended guidelines for mammography from two expert groups:

<table>
<thead>
<tr>
<th>Ages</th>
<th>American Cancer Society</th>
<th>U.S. Preventive Services Task Force</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 40 - 49</td>
<td>mammogram every year</td>
<td>talk to your doctor</td>
</tr>
<tr>
<td>Ages 50 - 74</td>
<td>mammogram every year</td>
<td>mammogram every two years</td>
</tr>
<tr>
<td>Ages 75+</td>
<td>mammogram every year</td>
<td>talk to your doctor</td>
</tr>
</tbody>
</table>
When women have mammograms there are both positive and negative outcomes.

This graph shows the outcomes for 1000 women who have mammograms every two years between the ages of 40 and 50 (a 10 year period):

- 12 women have breast cancer detected by a mammogram
- 9 women have breast cancer that is not detected by a mammogram, because it develops between mammograms
- 239 women do not have breast cancer, but have extra tests, biopsies, or surgery following abnormal mammograms
- 740 women do not have breast cancer and have normal mammograms

Courtesy of M. Schapira, MD
Patient-Level Decision Making

Breast Density/Complexity Assessment

Supplemental Screening? Screening Intervals?

Average Risk
- low
- high

Moderate Risk
- low
- high

High Risk
- low
- high

No.
Discuss screening intervals based on personal preference

Yes?
Discuss supplemental screening based on personal preference

Yes.
Discuss risk reduction interventions based on personal preference
Thank you!

Pablo Picasso, Girl Before a Mirror, 1932