Imaging Surveillance in Women with a History of Treated Breast Cancer

Wei Tse Yang, M.D.
Breast Cancer

1. Extent
2. Response
3. Recurrence
Surveillance Breast Cancer

1. Extent
2. Response
Surveillance Breast Cancer

1. Extent
2. Response
3. Recurrence
62-year-old woman
Left BCT T2N0 ER(+) IDC + chemo 1997
New right ILC 2011
Followup at 18 months post APBI treatment (same patient) right breast

Grade 2 IDC-ILC, ER/PR(+), HER2 eq

Courtesy Wendie Berg, MD, PhD
Women with PHBC

Population increasing
• Gains life expectancy
• Population breast screening
• Improved cancer Tx
Early stage invasive breast cancer | BCT | long term FU
Develop IBR in the range of 0.5-1.0%/y\textsuperscript{1,2}
Reported actuarial rates of CBC\textsuperscript{3}
  6.1% at 10 ys
  12% at 20 ys
Risk approximates an annualized incidence rate of 0.6%\textsuperscript{3}

IBR: recurrence or a new primary BC
CBC: new primary BC

\textsuperscript{1}J Clin Oncol 2001;19:1688-97
\textsuperscript{2}Int J Radiat Oncol Biol Phys 2008;71:1014-21
\textsuperscript{3}Int J Radiat Oncol Biol Phys 2003;56:1038-45
The risk of developing a further breast cancer in the treated/previously unaffected breast varies according to:

- Tumor
- Therapeutic variables

Associated with the first breast cancer

Surveillance women with PHBC

Identify and manage health and QOL issues related to BC and its therapy of women previously treated (non-metastatic) initial dx stage I-II BC

General consensus

• Should have FU & screening mammography
• Frequency and duration of mammographic surveillance varies in guidelines and practice

Br J Cancer 2007;96:1625-32
Br J Cancer 2007;96:1632-41
Women with PHBC

Screening mammography
Breast density
Frequency surveillance
Screening MRI
Alternate strategies
Abstract

Context—Women with a personal history of breast cancer (PHBC) are at risk of developing another breast cancer and are recommended for screening mammography. Few high-quality data exist on screening performance in PHBC women.

Objective—To examine the accuracy and outcomes of mammography screening in PHBC women relative to screening of similar women without PHBC.


Participants—There were 58,870 screening mammograms in 19,078 women with a history of early-stage (in situ or stage I-II invasive) breast cancer and 58,870 matched (breast density, age group, mammography year, and registry) screening mammograms in 55,315 non-PHBC women.

Main Outcome Measures—Mammography accuracy based on final assessment, cancer detection rate, interval cancer rate, and stage at diagnosis.

Results—Within 1 year after screening, 655 cancers were observed in PHBC women (499 invasive, 156 in situ) and 342 cancers (285 invasive, 57 in situ) in non-PHBC women. Screening accuracy and outcomes in PHBC relative to non-PHBC women were cancer rates of 10.5 per 1000 screens (95%CI, 9.7–11.3) vs 5.8 per 1000 screens (95%CI, 5.2–6.4), cancer detection rate of 6.8 per 1000 screens (95%CI, 6.2–7.5) vs 4.4 per 1000 screens (95%CI, 3.9–5.0), interval cancer rate of 3.6 per 1000 screens (95%CI, 3.2–4.1) vs 1.4 per 1000 screens (95%CI, 1.1–1.7), sensitivity 65.4% (95% CI, 61.5%–69.0%) vs 76.5% (95% CI, 71.7%–80.7%), specificity 98.3% (95% CI, 98.2%–98.4%) vs 99.0% (95% CI, 98.9%–99.1%), abnormal mammogram results in 2.3% (95% CI, 2.2%–2.5%) vs 1.4% (95% CI, 1.3%–1.5%) (all comparisons P <.001). Screening sensitivity in PHBC women was higher for detection of in situ cancer (78.7%;95% CI, 71.4%–84.5%) than invasive cancer (61.1%; 95% CI, 56.6%–65.4%), P <.001; lower in the initial 5 years (60.2%; 95% CI, 54.7%–65.5%) than after 5 years from first cancer (70.8%;95% CI, 65.4%–75.6%), P = .006; and was similar for detection of ipsilateral cancer (66.3%; 95% CI, 60.3%–71.8%) and contralateral cancer (66.1%; 95% CI, 60.9%–70.9%), P = .96. Screen-detected and interval cancers in women with and without PHBC were predominantly early stage.

Conclusion—Mammography screening in PHBC women detects early-stage second breast cancers but has lower sensitivity and higher interval cancer rate, despite more evaluation and higher underlying cancer rate, relative to that in non-PHBC women.

breast cancer diagnosis, diagnosis date, cancer characteristics

PHBC women – mammogram matched to non-PHBC women

JAMA 2011 Feb 23; 305(8): 790-799
Screening Mammography PHBC

Outcome measures accuracy
  • final assessment
  • interval cancer detection rate
  • stage at diagnosis
58,870 screening mammograms
19,078 women
early, Tis Stage I-II invasive BC
58,870 matched screening mammograms
[breast density, age, mammography year]
55,315 non-PHBC women
Results (1)

PHBC: 655 cancers (499 inv, 156 is)
Non-PHBC: 342 cancers (285 inv, 57 is)
All results PHBC vs non-PHBC (P<.001)

Cancer rates:
10.5 per 1000 screens (95% CI, 9.7-11.3) vs 5.8 per 1000 screens (95% CI, 5.2-6.4)

Cancer detection rates:
6.8 per 1000 screens (95% CI, 6.2-7.5) vs 4.4 per 1000 screens (95% CI, 3.9-5.0)
Results (2)

Sensitivity:
65.4% (95% CI, 61.5%-69%) vs 76.5% (95% CI, 71.7%-80.7%)

Interval cancer rate:
3.6 per 1,000 screens (95% CI, 3.2-4.1) vs 1.4 per 1,000 screens (95% CI, 1.1-1.7)
• detects early-stage second breast cancers
• lower sensitivity
• higher interval cancer rate
despite more evaluation and higher underlying cancer rate relative to that in non-PHBC women
Sensitivity:
Higher IS CA (78.7%, 71.4-84.5%) invasive (61.1%; 56.5-65.4%) P<.001
Lower initial 5 years (60.2%; 54.7-65.5%) after 5 years (70.8%; 65.4-75.6%) P=.006
Similar for ipsilateral (66.3%; 60.3-71.8%) contralateral cancer (66.1%; 60.9-70.9%) P=.96
Meta-analyses

2263 subjects (13 studies) with recurrences
Pooled analyses: IBR CBC regional distant mets
Effect early detection potentially underestimated
58% recurrences detected early
Early detection: improved survival of women who experienced BC recurrence
Hazard ratio for late vs early detection of relapse: 1.68 (1.48-1.91)

Breast Cancer Res Treat 2009;114:403-12
Evidence based only studies on early detection of IBR/CBC (n=10)

** various surveillance strategies that include mammography

Study-specific HR: 0.1-0.86

Beneficial effect in the range of 90%-14% relative reduction in the hazard of BC death

Breast Cancer Res Treat 2009;114:403-12
Screening Mammography PHBC

Nested case-control; 65 years and older

1846 | Stage I-II invasive BC
Surveillance & mortality
Recurrence (B/N/DM) who died of BC (first 5ys of FU) compared with women who did not die
Protective association with M: OR = 0.69; 0.53-0.92
Each additional screening M 0.7x decrease in conditional odds for BC mortality
*Effect most evident stage I

J Clin Oncol 2007;25:3001-6
Screening Mammography PHBC

Houssami 1044 asymptomatic second BCs a/w

- Earlier detection
- More favorable stage
- Smaller IBR (P<0.001), CBC (P<0.001)
- Fewer nodal metastases (P=0.0001)
- HR: 0.53

Ann Oncol 2009;20:1505-10
Variability in how the accuracy of mammography interpretation is rendered

- Type clinical events considered in analysis
  - IBR/CBC/Both/Regional nodal recurrences
- Data for M-only detection or any method detection
Early detection IBC/CBC may not confer the anticipated benefit if the risk of mortality is large, or partly determined by the first breast cancer.

Specificity data sparse (unselected women with PHBC)

Sensitivity over-estimated
No RCTs examining the impact on mortality
Non-randomized studies:
lead-time and length-time bias
(over-estimate the benefit from screening)
Measured survival/FU time from the time of diagnosis of the 1\textsuperscript{st} and 2\textsuperscript{nd} BC
Estimates for the early detection of IBR/CBC are affected by length-time bias
Women with PHBC

Screening mammography
Breast density
Frequency surveillance
Screening MRI
Alternate strategies
Recurrence and Breast density

136 IC Cumulus 7.7yr follow-up$^1$
335 IC Wolfe 7-8yr follow-up$^2$*
392 DCIS Wolfe Planimetry (area) 11yr follow-up$^3$
935 DCIS Wolfe BI-RADS Planimetry (area) 8.6yr follow-up$^4$

$^1$International Journal of Radiation Oncology Biology Physics 2009:73(1);75-79
$^2$Cancer 2009:115(24);780-5787 *(examined IC recurrence only)
$^3$J Natl Cancer Inst 2004:96(19);1467-1472
$^4$Cancer Epidemiol Biomarkers Prev 2010:19(10);2488-2495
Recurrence and Breast density

Local/locoregional recurrence IC following BCT ≥75% density compared to <25% density
HR of 4.3-5.7

No association with distant recurrence/death

*Density was only predictive of increased risk when radiotherapy was not used

International Journal of Radiation Oncology Biology Physics 2009:73(1);75-79
*Cancer 2009:115(24);780-5787
Recurrence and Breast density

≥75% density compared to <25% density
RR of local recurrence of any cancer of 3.0
No significant risk increase for contralateral breast

Increased risk for cancer recurrence—in the contralateral breast (HR 3, 1.4 and 5 respectively).
No significant risk increase for ipsilateral breast.

J Natl Cancer Inst 2004:96(19);1467-1472
Cancer Epidemiol Biomarkers Prev 2010:19(10);2488-2495
Women with PHBC

Screening mammography
Breast density
Frequency surveillance
Screening MRI
Alternate strategies
Purpose
To provide recommendations on the follow-up and management of patients with breast cancer who have completed primary therapy with curative intent.

Methods
To update the 2006 guideline of the American Society of Clinical Oncology (ASCO), a systematic review of the literature published from March 2006 through March 2012 was completed using MEDLINE and the Cochrane Collaboration Library. An Update Committee reviewed the evidence to determine whether the recommendations were in need of updating.

Results
There were 14 new publications that met inclusion criteria: nine systematic reviews (three included meta-analyses) and five randomized controlled trials. After its review and analysis of the evidence, the Update Committee concluded that no revisions to the existing ASCO recommendations were warranted.

Recommendations
Regular history, physical examination, and mammography are recommended for breast cancer follow-up. Physical examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter. For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy. Thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed. The use of complete blood counts, chemistry panels, bone scans, chest radiographs, liver ultrasounds, pelvic ultrasounds, computed tomography scans, $[{^{18}}F]$fluorodeoxyglucose–positron emission tomography scans, magnetic resonance imaging, and/or tumor markers (carcinoembryonic antigen, CA 15-3, and CA 27.29) is not recommended for routine follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.

J Clin Oncol 31:961-965. © 2012 by American Society of Clinical Oncology
THE BOTTOM LINE

ASCO GUIDELINE UPDATE

Breast Cancer Follow-Up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update

**Intervention**
- Modes of surveillance for patients with breast cancer who have completed primary therapy with curative intent

**Target Audience**
- Medical oncologists, primary care providers, oncology nurses, surgical oncologists, pathologists, and nuclear medicine specialists

**Key Recommendations**
- Regular history, physical examination, and mammography are recommended
- Examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter
- For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy; thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed
- Use of CBCs, chemistry panels, bone scans, chest radiographs, liver ultrasounds, computed tomography scans, [18F]fluorodeoxyglucose–positron emission tomography scanning, magnetic resonance imaging, or tumor markers (carcinoembryonic antigen, CA 15-3, and CA 27.29) is not recommended for routine breast cancer follow-up in an otherwise symptomatic patient with no specific findings on clinical examination

**Methods**
- A comprehensive systematic review of the literature was conducted, and an Update Committee was convened to review the evidence and develop guideline recommendations

A Data Supplement (including evidence tables) and clinical tools and resources can be found at http://www.asco.org/guidelines/breastfollowup

**Key Recommendations**

• Regular history, physical examination, and mammography are recommended

• Examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter

• For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy; thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed
Purpose: To compare cancer recurrence outcomes on the basis of compliant semiannual versus noncompliant annual ipsilateral mammographic surveillance following breast conservation therapy (BCT).

Materials and Methods: A HIPAA-compliant retrospective review was performed of post-BCT examinations from 1997 through 2008 by using a deidentified database. The Committee on Human Research did not require institutional review board approval for this study, which was considered quality assurance. Groups were classified according to compliance with institutional post-BCT protocol, which recommends semiannual mammographic examinations of the ipsilateral breast for 5 years. A compliant semiannual examination was defined as an examination with an interval of 0–9 months, although no examination had intervals less than 3 months. A noncompliant annual examination was defined as an examination with an interval of 9–18 months. Cancer recurrence outcomes were compared on the basis of the last examination interval leading to diagnosis.

Results: Initially, a total of 10,750 post-BCT examinations among 2,329 asymptomatic patients were identified. Excluding initial mammographic follow-up, there were 8,234 examinations. Of these, 7,169 examinations were semiannual with 94 recurrences detected and 1,065 examinations were annual with 15 recurrences detected. There were no differences in demographic risk factors or biopsy rates. Recurrences identified at semiannual intervals were significantly less advanced than those identified at annual intervals (stage I vs stage II, \( P = .04 \); stage 0 + stage I vs stage II, \( P = .03 \)). Nonsignificant findings associated with semiannual versus annual intervals included smaller tumor size (mean, 11.7 vs 15.3 mm; \( P = .15 \)) and node negativity (98% vs 91%, \( P = .28 \)).

Conclusion: Results suggest that a semiannual interval is preferable for ipsilateral mammographic surveillance, allowing detection of a significantly higher proportion of cancer recurrences at an earlier stage than noncompliant annual surveillance.
Semiannual Ipsilateral Mammography

Retrospective Post BCT mammography
Semiannual ipsilateral 5 years
1997-2008

Compliant: 0-9, not < 3
Non-compliant: 9-18

Cancer recurrences compared basis last exam interval leading to outcome
Semiannual Ipsilateral

10,750 M  2,329 women  8,234 M
Semiannual:  7,169   94 recurrences
Annual:    1,065    15 recurrences
Stage
S I vs II, P=.04
S 0/I vs II, P=.03
Mean size NS  11.7 vs 15.3 mm
Node (-) NS   98% vs 91%
Table 1

Distribution of Mammographic Surveillance Mammographic Examinations

<table>
<thead>
<tr>
<th>No. of Examinations per Patient</th>
<th>No. of Patients</th>
<th>Total No. of Examinations*</th>
<th>Subsequent Examinations according to Interval†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Compliant Semiannual, 91–274 Days*</td>
</tr>
<tr>
<td>1</td>
<td>488</td>
<td>488</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>288</td>
<td>576</td>
<td>200</td>
</tr>
<tr>
<td>3</td>
<td>235</td>
<td>705</td>
<td>317</td>
</tr>
<tr>
<td>4</td>
<td>226</td>
<td>904</td>
<td>487</td>
</tr>
<tr>
<td>5</td>
<td>211</td>
<td>1055</td>
<td>638</td>
</tr>
<tr>
<td>6</td>
<td>187</td>
<td>1122</td>
<td>752</td>
</tr>
<tr>
<td>7</td>
<td>176</td>
<td>1232</td>
<td>908</td>
</tr>
<tr>
<td>8</td>
<td>199</td>
<td>1592</td>
<td>1267</td>
</tr>
<tr>
<td>9</td>
<td>177</td>
<td>1593</td>
<td>1327</td>
</tr>
<tr>
<td>10</td>
<td>92</td>
<td>920</td>
<td>788</td>
</tr>
<tr>
<td>11</td>
<td>39</td>
<td>429</td>
<td>372</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>108</td>
<td>92</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2329</strong></td>
<td><strong>10750</strong></td>
<td><strong>7169</strong></td>
</tr>
</tbody>
</table>

Note.—The protocol at our institution recommends semiannual surveillance.

* Total number of examinations include the first surveillance examination and examinations with intervals greater than 547 days (not shown).

† Mean number of days for compliant semiannual and noncompliant annual examinations were 190 days and 369 days, respectively. Subsequent examinations according to interval do not include the first surveillance examinations because there was no preceding surveillance examination from which an interval could be calculated.
<table>
<thead>
<tr>
<th>Detection Data</th>
<th>Compliant Semiannual Interval</th>
<th>Noncompliant Annual Interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cancer recurrences</td>
<td>94</td>
<td>15</td>
<td>.81</td>
</tr>
<tr>
<td>No. with stage 0*</td>
<td>31 (33)</td>
<td>4 (27)</td>
<td>.04†</td>
</tr>
<tr>
<td>No. with stage I*</td>
<td>57 (61)</td>
<td>7 (47)</td>
<td>.03‡</td>
</tr>
<tr>
<td>No. with stage II*</td>
<td>6 (6)</td>
<td>4 (27)</td>
<td>...</td>
</tr>
<tr>
<td>Mean invasive size (mm)$^§$</td>
<td>11.7 (7.4)</td>
<td>15.3 (8.8)</td>
<td>.15</td>
</tr>
<tr>
<td>≤1 cm*</td>
<td>42 (67)</td>
<td>4 (36)</td>
<td>.09</td>
</tr>
<tr>
<td>&gt;1 cm*</td>
<td>21 (33)</td>
<td>7 (64)</td>
<td>...</td>
</tr>
<tr>
<td>Node-negative invasive*</td>
<td>62 (98)</td>
<td>10 (91)</td>
<td>.28</td>
</tr>
</tbody>
</table>

* Numbers in parentheses are percentages.
† Stage I versus stage II.
‡ Stage 0 + stage I versus stage II.
$^§$ Mean invasive size excludes stage 0. Numbers in parentheses are standard deviations.
Women with PHBC

Screening mammography
Breast density
Frequency surveillance
Screening MRI
Alternate strategies
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)

ABSTRACT  New evidence on breast Magnetic Resonance Imaging (MRI) screening has become available since the American Cancer Society (ACS) last issued guidelines for the early detection of breast cancer in 2003. A guideline panel has reviewed this evidence and developed new recommendations for women at different defined levels of risk. Screening MRI is recommended for women with an approximately 20–25% or greater lifetime risk of breast cancer, including women with a strong family history of breast or ovarian cancer and women who were treated for Hodgkin disease. There are several risk subgroups for which the available data are insufficient to recommend for or against screening, including women with a personal history of breast cancer, carcinoma in situ, atypical hyperplasia, and extremely dense breasts on mammography. Diagnostic uses of MRI were not considered to be within the scope of this review.

TABLE 1 Recommendations for Breast MRI Screening as an Adjunct to Mammography

<table>
<thead>
<tr>
<th>Recommend Annual MRI Screening (Based on Evidence*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA mutation</td>
</tr>
<tr>
<td>First-degree relative of BRCA carrier, but untested</td>
</tr>
<tr>
<td>Lifetime risk ~20–25% or greater, as defined by BRCApro or other models that are largely dependent on family history</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommend Annual MRI Screening (Based on Expert Consensus Opinion†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation to chest between age 10 and 30 years</td>
</tr>
<tr>
<td>Li-Fraumeni syndrome and first-degree relatives</td>
</tr>
<tr>
<td>Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives</td>
</tr>
</tbody>
</table>

**Insufficient Evidence to Recommend for or Against MRI Screening‡**

| Lifetime risk 15–20%, as defined by BRCApro or other models that are largely dependent on family history |
| Lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH) |
| Atypical ductal hyperplasia (ADH)                                      |
| Heterogeneously or extremely dense breast on mammography              |
| Women with a personal history of breast cancer, including ductal carcinoma in situ (DCIS) |

<table>
<thead>
<tr>
<th>Recommend Against MRI Screening (Based on Expert Consensus Opinion )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women at &lt;15% lifetime risk</td>
</tr>
</tbody>
</table>

*Evidence from nonrandomized screening trials and observational studies.
†Based on evidence of lifetime risk for breast cancer.
‡Payment should not be a barrier. Screening decisions should be made on a case-by-case basis, as there may be particular factors to support MRI. More data on these groups is expected to be published soon.
Insufficient Evidence to Recommend for or Against MRI Screening‡

Lifetime risk 15–20%, as defined by BRCAPRO or other models that are largely dependent on family history

Lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH)

Atypical ductal hyperplasia (ADH)

Heterogeneously or extremely dense breast on mammography

Women with a personal history of breast cancer, including ductal carcinoma in situ (DCIS)

‡Payment should not be a barrier. Screening decisions should be made on a case-by-case basis, as there may be particular factors to support MRI. More data on these groups is expected to be published soon.
TABLE 2 Published Breast MRI Screening Study Results

<table>
<thead>
<tr>
<th></th>
<th>The Netherlands</th>
<th>Canada</th>
<th>United Kingdom</th>
<th>Germany</th>
<th>United States</th>
<th>Italy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of centers</td>
<td>6</td>
<td>1</td>
<td>22</td>
<td>1</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>No. of women</td>
<td>1,909</td>
<td>236</td>
<td>649</td>
<td>529</td>
<td>390</td>
<td>105</td>
</tr>
<tr>
<td>Age range</td>
<td>25–70</td>
<td>25–65</td>
<td>35–49</td>
<td>≥30</td>
<td>≥25</td>
<td>≥25</td>
</tr>
<tr>
<td>No. of cancers</td>
<td>50</td>
<td>22</td>
<td>35</td>
<td>43</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>80</td>
<td>77</td>
<td>77</td>
<td>91</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Mammogram</td>
<td>33</td>
<td>36</td>
<td>40</td>
<td>33</td>
<td>25</td>
<td>16</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>n/a</td>
<td>33</td>
<td>n/a</td>
<td>40</td>
<td>n/a</td>
<td>16</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>90</td>
<td>95</td>
<td>81</td>
<td>97</td>
<td>95</td>
<td>99</td>
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<tr>
<td>Mammogram</td>
<td>95</td>
<td>&gt;99</td>
<td>93</td>
<td>97</td>
<td>98</td>
<td>0</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>n/a</td>
<td>96</td>
<td>n/a</td>
<td>91</td>
<td>n/a</td>
<td>0</td>
</tr>
</tbody>
</table>

n/a = not applicable.
Breast MR Imaging Screening in Women with a History of Breast Conservation Therapy

**Purpose:** To retrospectively investigate the outcomes of single-screening breast magnetic resonance (MR) imaging in women who had a history of breast conservation therapy (BCT) for breast cancers and who had previous negative mammography and ultrasonographic (US) findings.

**Materials and Methods:** This study was institutional review board–approved and informed consent was waived. Between January 2008 and March 2012, 607 consecutive women (median age, 48 years; age range, 20–72 years) who underwent BCT for breast cancer, had negative mammography and US findings, and underwent subsequent screening breast MR imaging were studied. Of the study population, 91.8% (557 of 607) patients underwent preoperative MR examinations. Cancer detection rate, characteristics of detected cancers, positive predictive value (PPV), sensitivity, and specificity were assessed. Multivariate logistic regression analysis was performed to identify independent clinicalpathologic factors associated with women with cancers detected by using MR imaging.

**Results:** Eleven cancers (eight invasive, three ductal carcinoma in situ; median invasive size, 0.8 cm; range, 0.4–1.4 cm; all node negative) were additionally detected with MR imaging in 607 women (18.1 cancers per 1000 women). PPV for recall, PPV for biopsy, sensitivity, and specificity were 9.4% (11 of 117 examinations), 43.5% (10 of 23 examinations), 91.7% (11 of 12 examinations), and 82.2% (489 of 595 examinations), respectively. At multivariate analysis, the independent factors associated with women with Mrdetected cancers were age younger than 50 years at initial diagnosis ($P = .001$) and more than a 24-month interval between initial surgery and screening MR imaging ($P = .011$).

**Conclusion:** Single-screening MR imaging depicted 18.1 additional cancers per 1000 women with a history of BCT. Multivariate analysis revealed age younger than 50 years at initial younger than 50 years.
MRI screening following BCT

Single screening MRI in women (-) MRI/US
Jan 08 – March 12
607 consecutive women
Median age 48, (20-72)
557 (91.8%) had preoperative MRI
Cancer detection, Cancer characteristics
PPV, Sensitivity, Specificity
MRI screening following BCT

11 additional cancers
8 invasive, 3 DCIS
Median size 0.8 cm (0.4 – 1.4)
Node (-)
18.1 cancers per 1,000 women
## Table 2

**Clinical and Imaging Features of Second Breast Cancers Detected with Screening MR Imaging in Women with a History of Breast Conservation Therapy**

<table>
<thead>
<tr>
<th>Patient Age (y)</th>
<th>Initial Surgery Interval (mo)*</th>
<th>MR Examination Interval (mo)†</th>
<th>Site‡</th>
<th>BI-RADS Category§</th>
<th>Imaging Finding</th>
<th>Pathologic Finding</th>
<th>Size (cm)</th>
<th>Nodal Status</th>
<th>Hormonal Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial round of screening</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>25</td>
<td>25</td>
<td>Ipsilateral 4</td>
<td>Nonmass</td>
<td>DCIS</td>
<td>0.2</td>
<td>Negative</td>
<td>ER(−), PR(−), HER2(+)</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>43</td>
<td>No</td>
<td>Contralateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>1.4</td>
<td>Negative</td>
<td>ER(+), PR(+), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>14</td>
<td>14</td>
<td>Ipsilateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>0.7</td>
<td>Negative</td>
<td>ER(−), PR(−), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>26</td>
<td>26</td>
<td>Contralateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>0.4</td>
<td>Negative</td>
<td>ER(+), PR(+), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>32</td>
<td>33</td>
<td>Contralateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>0.7</td>
<td>Negative</td>
<td>ER(+), PR(+), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>56</td>
<td>56</td>
<td>Contralateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>0.8</td>
<td>Negative</td>
<td>ER(+), PR(+), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>50</td>
<td>50</td>
<td>Ipsilateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>0.8</td>
<td>Negative</td>
<td>ER(−), PR(−), HER2(+)</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>20</td>
<td>20</td>
<td>Ipsilateral 4</td>
<td>Mass</td>
<td>DCIS</td>
<td>1.5</td>
<td>Negative</td>
<td>ER(+), PR(−), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>56</td>
<td>56</td>
<td>Ipsilateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>1.1</td>
<td>Negative</td>
<td>ER(−), PR(−), HER2(+)</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>34</td>
<td>34</td>
<td>Ipsilateral 4</td>
<td>Mass</td>
<td>DCIS</td>
<td>3.7</td>
<td>Negative</td>
<td>ER(+), PR(−), HER2(−)</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>23</td>
<td>No</td>
<td>Contralateral 3</td>
<td>Mass</td>
<td>IDC</td>
<td>1.0</td>
<td>Negative</td>
<td>ER(+), PR(−), HER2(−)</td>
<td></td>
</tr>
<tr>
<td><strong>Second round of screening</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>64</td>
<td>40</td>
<td>13</td>
<td>Ipsilateral 4</td>
<td>Mass</td>
<td>IDC</td>
<td>1.7</td>
<td>Negative</td>
<td>ER(−), PR(−), HER2(+)</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>30</td>
<td>15</td>
<td>Ipsilateral 4</td>
<td>Nonmass</td>
<td>IDC</td>
<td>0.5</td>
<td>Negative</td>
<td>ER(+), PR(−), HER2(−)</td>
<td></td>
</tr>
</tbody>
</table>

Note.—DCIS = ductal carcinoma in situ, ER(−) = ER negative, ER(+) = ER positive, HER2(−) = HER2 negative, HER2(+) = HER2 positive, IDC = invasive ductal carcinoma, PR(−) = PR negative, PR(+) = PR positive.

* Interval between initial surgery and breast cancer observed by using MR imaging.
† Interval between most recent previous MR examination and breast cancer observed by using MR imaging.
‡ Second breast cancer site compared with initial breast cancer.
§ Final assessment at screening MR imaging.
MRI screening following BCT

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV Recurrence</td>
<td>9.4% (11/117)</td>
</tr>
<tr>
<td>PPV Biopsy</td>
<td>43.5% (10/23)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>91.7% (11/12)</td>
</tr>
<tr>
<td>Specificity</td>
<td>82.2% (489/595)</td>
</tr>
</tbody>
</table>
Table 1

Characteristics of Women with MR-detected Cancers and Those without MR-detected Cancers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women with Cancer Detected at MR Imaging*</th>
<th>Women without Cancer Detected at MR Imaging†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (y)‡</td>
<td>47 (29–58)</td>
<td>48 (20–72)</td>
<td>.704</td>
</tr>
<tr>
<td>Age at initial cancer diagnosis (y)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt;50</td>
<td>10 (14.9)</td>
<td>57 (85.1)</td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>1 (0.2)</td>
<td>539 (99.8)</td>
<td></td>
</tr>
<tr>
<td>BI-RADS breast density</td>
<td></td>
<td></td>
<td>.999</td>
</tr>
<tr>
<td>Category 1–2</td>
<td>2 (1.7)</td>
<td>118 (98.3)</td>
<td></td>
</tr>
<tr>
<td>Category 3–4</td>
<td>9 (1.8)</td>
<td>478 (98.2)</td>
<td></td>
</tr>
<tr>
<td>Stage of initial cancer</td>
<td></td>
<td></td>
<td>.906</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>2 (1.3)</td>
<td>150 (98.7)</td>
<td></td>
</tr>
<tr>
<td>Invasive, stage I</td>
<td>4 (1.7)</td>
<td>226 (98.3)</td>
<td></td>
</tr>
<tr>
<td>Invasive, stage II</td>
<td>4 (2.1)</td>
<td>189 (97.9)</td>
<td></td>
</tr>
<tr>
<td>Invasive, stage III</td>
<td>1 (3.1)</td>
<td>31 (96.9)</td>
<td></td>
</tr>
<tr>
<td>ER status</td>
<td></td>
<td></td>
<td>.014</td>
</tr>
<tr>
<td>Positive</td>
<td>4 (0.9)</td>
<td>433 (99.1)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>7 (4.1)</td>
<td>163 (95.9)</td>
<td></td>
</tr>
<tr>
<td>Progesterone receptor status</td>
<td></td>
<td></td>
<td>.117</td>
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<tr>
<td>Positive</td>
<td>4 (1.1)</td>
<td>369 (98.9)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>7 (3.0)</td>
<td>227 (97.0)</td>
<td></td>
</tr>
<tr>
<td>HER2 receptor status</td>
<td></td>
<td></td>
<td>.281</td>
</tr>
<tr>
<td>Positive</td>
<td>4 (2.8)</td>
<td>138 (97.2)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>7 (1.5)</td>
<td>458 (98.5)</td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td></td>
<td></td>
<td>.084</td>
</tr>
<tr>
<td>Performed</td>
<td>2 (8.7)</td>
<td>21 (91.3)</td>
<td></td>
</tr>
<tr>
<td>Not performed</td>
<td>9 (1.9)</td>
<td>475 (98.1)</td>
<td></td>
</tr>
<tr>
<td>Interval between initial surgery and</td>
<td></td>
<td></td>
<td>.021</td>
</tr>
<tr>
<td>screening MR imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24 mo</td>
<td>3 (0.8)</td>
<td>386 (99.2)</td>
<td></td>
</tr>
<tr>
<td>≥24 mo</td>
<td>8 (3.7)</td>
<td>210 (96.3)</td>
<td></td>
</tr>
<tr>
<td>Preoperative MR imaging</td>
<td></td>
<td></td>
<td>.227</td>
</tr>
<tr>
<td>With imaging</td>
<td>9 (1.6)</td>
<td>548 (98.4)</td>
<td></td>
</tr>
<tr>
<td>Without imaging</td>
<td>2 (4.0)</td>
<td>48 (96.0)</td>
<td></td>
</tr>
</tbody>
</table>

Note.—Data in parentheses are percentages except where otherwise indicated.
* n = 11
† n = 596
‡ Numbers in parentheses are range. Median age was based on age at time of initial cancer diagnosis.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adjusted Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at initial cancer diagnosis &lt; 50 years</td>
<td>1434.3 (129.0, 210961.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Estrogen receptor negativity</td>
<td>1.2 (0.1, 536.5)</td>
<td>.945</td>
</tr>
<tr>
<td>≥24-month interval between initial surgery and screening MR imaging</td>
<td>191.6 (2.9, 55038.4)</td>
<td>.011</td>
</tr>
</tbody>
</table>

Note.—Data in parentheses are 95% confidence intervals.
Screening MRI in Women With a Personal History of Breast Cancer

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Abstract

Background: Screening MRI is recommended for individuals at high risk for breast cancer, based on genetic risk or family history (GFH); however, there is insufficient evidence to support screening MRI for women with a personal history (PH) of breast cancer. We compared screening MRI performance in women with PH vs GFH of breast cancer.

Methods: We analyzed case-series registry data, collected at time of MRI and at 12-month follow-up, from our regional Clinical Oncology Data Integration project. MRI performance was compared in women with PH those with GFH. Chi-square testing was used to identify associations between age, prior history of MRI, and clinical indication with MRI performance; logistic regression was used to determine the combined contribution of these variables in predicting risk of a false-positive exam. All statistical tests were two-sided.

Results: Of 1521 women who underwent screening MRI from July 2004 to November 2011, 915 had PH and 606 had GFH of breast cancer. Overall, MRI sensitivity was 79.4% for all cancers and 88.5% for invasive cancers. False-positive exams were lower in the PH vs GFH groups (12.3% vs 21.6%, P < .001), specificity was higher (94.0% vs 86.0%, P < .001), and sensitivity and cancer detection rate were not statistically different (P > .99). Age (P < .001), prior MRI (P < .001), and clinical indication (P < .001) were individually associated with initial false-positive rate; age and prior MRI remained statistically significant in multivariable modeling (P = .001 and P < .001, respectively).

Conclusion: MRI performance is superior in women with PH compared with women with GFH. Screening MRI warrants consideration as an adjunct to mammography in women with a PH of breast cancer.
Screening MRI PHBC

High risk for BC based on genetic risk or family history (GFH)\(^1\)

Compared screening MRI in women with PH and GFH of breast cancer

\(\text{JNCI 2016;108(3): djv349}\)
Case series registry data
Collected at time of MRI & at 12 month FU
Age, PH MRI, clinical indication MRI (chi-sq)
Combined contribution of these variables in predicting risk of a FP (logistic regression)
Screening MRI PHBC – Results 1

915 PH vs 606 GFH
Overall sensitivity
  79.4% all cancers
  88.5% invasive cancers
FP: 12.3% vs 21.6%, P < .001
Specificity: 94.0% vs 86.0%, P < .001
Sensitivity, Cancer detection NS, P > .99
Age (P < .001)
Prior MRI (P < .001)
Clinical indication (P < .001)
Individually associated with initial false-positive rate (P = .001)
Age and prior MRI remained statistically significant in multivariate modeling (P < .001)
Screening MRI PHBC

Superior performance vs GFH
Breast MRI Screening of Women With a Personal History of Breast Cancer

OBJECTIVE. The purpose of this article is to determine the cancer detection and biopsy rate among women who have breast MRI screening solely on the basis of a personal history of breast cancer.

MATERIALS AND METHODS. This retrospective review of 1,699 breast MRI examinations performed from 1999 to 2001 yielded 144 women with prior breast cancer but no family history who commenced breast MRI screening during that time. Minimal breast cancer was defined as ductal carcinoma in situ (DCIS) or node-negative invasive breast cancer < 1 cm in size.

RESULTS. Of 144 women, 44 (31% [95% CI, 15–29%]) underwent biopsies prompted by MRI examination. Biopsies revealed malignancies in 17 women (12% [95% CI, 7–18%]) and benign findings only in 27 women (19% [95% CI, 13–26%]). Of the 17 women in whom cancer was detected, seven also had benign biopsy results. In total, 18 malignancies were found. One woman had two metachronous cancers. MRI screening resulted in a total of 61 biopsies, with a positive predictive value (PPV) of 39% (95% CI, 27–53%). The malignancies found included 17 carcinomas and one myxoid liposarcoma. Of the 17 cancers, 12 (71%) were invasive, five (29%) were DCIS, and 10 (59%) were minimal breast cancers. Of 17 cancers, 10 were detected by MRI only. The 10 cancers detected by MRI only, versus seven cancers later found by other means, were more likely to be DCIS (4/10 [40%] vs 1/7 [14%]; p = 0.25) or minimal breast cancers (7/10 [70%] vs 3/7 [43%]; p = 0.26).

CONCLUSION. We found that breast MRI screening of women with only a personal history of breast cancer was clinically valuable finding malignancies in 12%, with a reasonable biopsy rate (PPV, 39%).
Screening MRI PHBC

Retrospective chart review 1999-2001
144 women PHBC (no FHBC)
1699 breast MRIs

Determine the cancer detection & bx rate

Brennan AJR 2010
44 women (31%, 95% CI 15-29%): MRI Bxs
Malignant: 17 (12%; 7-18%)
Benign: 27 (19%; 13-26%)
Total: 18 Malignant lesions, 1 metachronous

Brennan AJR 2010
Screening MRI PHBC

MRI Bx: 61; PPV: 39%; 95%CI 27-53%
18 Malignancies: 17 CAs, 1 lipoSA
17 CAs: 12 Invasive (71%); 5 DCIS (29%)
10 minimal CAs
10 cancers detected by MRI-only
DCIS: 4/10 (40%) vs 1/7 (14%)
Minimal CAs: 7/10 (70%) vs 3/7 (43%)

Brennan AJR 2010
Benefit certain subsets of patients

- Have not had preoperative MRI at initial dx
- Have not taken hormonal therapy
- RCT prospective to best determine the cost-effectiveness
Use of Magnetic Resonance Imaging in Detection of Breast Cancer Recurrence: A Systematic Review

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Department of Academic Surgery, Cork University Hospital/University College Cork, Cork, Ireland

ABSTRACT

Background. Diagnosis of breast cancer recurrence can be difficult as a result of the presence of scar tissue in the breast. Magnetic resonance imaging (MRI) may be superior to traditional imaging in diagnosis of recurrence because of its ability to differentiate malignancy from scarring. Current guidelines on investigation of suspected breast cancer recurrence recommend MRI when other investigations have equivocal findings. We performed the first systematic review on this topic.

Methods. Literature search revealed 35 potentially relevant studies; 10 were included in final analysis. Included were clinical studies comparing MRI with another diagnostic modality for diagnosis of breast cancer recurrence, with at least 10 patients, in the English language. Data extraction focused on sensitivity and specificity of standard diagnostic modalities and MRI for diagnosis of local disease recurrence.

Results. In total 494 patients were assessed across 10 studies; all were case series. Sensitivity of MRI for detection of recurrence ranged 75–100 %, while specificity ranged 66.6–100 %. Both sensitivity and specificity increased when MRI was performed after a longer time interval from the original surgery, although the longest follow-up reported was only 36 months. A negative MRI can avoid the need for further biopsy.

Conclusions. Available data are based on clinically heterogeneous case series and superiority over standard triple assessment for breast cancer recurrence has not been proven. At present, MRI cannot be recommended in the routine diagnostic assessment for breast cancer recurrence but has a potentially useful role as a second-line investigation. A negative MRI is more useful than a positive MRI as positive MRIs require further investigation.

Screening MRI PHBC

35 clinical studies 1993-2006
Comparing MRI with another diagnostic modality for breast recurrence diagnosis
Sensitivity and specificity

Quinn Ann Surg Oncol 2012
Screening MRI PHBC

Abstracts: 67 + 7
Papers: 35
# patients: 13-140
Longest FU: 35 months
Screening MRI PHBC

Increase interventions in breast CA?
Increase radical Sx
Specificity (Breast CA recurrence): 66-100%
Mandates Preoperative Bx
Sensitivity (BCT or MX): 75-100%

Negative MRI conclusive
Omit need for repeat bx scarred tissue
Not first line diagnosis for breast recurrence
Screening MRI PHBC

Radiation therapy:
Greater parenchymal enhancement
Radiation fibrosis
Increase FN&FP (closer proximity RT)
Changes decrease with time
Best 1Y after Tx (scarring fibrosis vs recurrence)
Screening MRI PHBC

Data clinically heterogeneous
Meta-analysis precluded
• Broad range of patients
• Previous treatment types
• Poor descriptions of inclusion/exclusion criteria
• Variable MRI technique
Screening MRI PHBC

MRI: Expensive, resource intensive, delay time to further Tx
Cost analysis MRI use in the assessment breast cancer recurrence
Long term FU data on patients with (-) MRI
Alternate Imaging Strategies
Molecular Breast Imaging

Gamma-ray emitting radiotracers 99mTc-sestamibi and 99mTc-tetrofosmin
Post-therapy changes scar tissue
Limitation: low sensitivity for small BCs
High-resolution specific breast cameras detection sub-cm malignant lesions
Radiation

No RCT that examines the impact of breast cancer mortality achieved in the use of annual mammography
No other imaging modality (MRI) sufficient evidence to justify inclusion in the recommended surveillance of breast cancer survivors
Screening mammography: some suggestion of benefit systematic review small data sets
BC survivors tend to be younger (~20% new cases in the U.S. are diagnosed in women under 50 ys)
Conclusion (3)

Screening mammography
  Modality of choice
Breast density
  Risk factor
Frequency surveillance
  Annual vs 6 monthly
Screening MRI
  Warrants further investigation