Breast MRI Indications

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Background: Breast MRI

• Powerful tool for detection and evaluation of breast lesions
• High sensitivity, lower specificity
  – Advantage:
  • Detection of cancer occult on mammography or ultrasound
  – Disadvantage:
  • Additional benign biopsies, increased patient anxiety, increased health care costs

Indications

• High risk screening
• Preoperative staging
• Evaluation of treatment response
• Metastatic adenopathy of unknown primary
• Problem solving
• Implant evaluation

High Risk Screening

• Sensitivity depends on breast density

American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography

Saslow et al. CA Cancer J Clin 2007; 57:75-89

Based on evidence
• BRCA 1 or 2 mutation
• Untested first-degree relative of BRCA carrier
• Lifetime risk 20% or greater
  – defined by BRCAPRO
  – other models dependent on family history
High Risk Screening

<table>
<thead>
<tr>
<th>Author</th>
<th># CA detected/ # screened</th>
<th>MG Sensitivity (%)</th>
<th>US Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuhl</td>
<td>8.1% (43/529)</td>
<td>91% (19/21)</td>
<td>40% (17/43)</td>
</tr>
<tr>
<td>Warner</td>
<td>9.3% (22/236)</td>
<td>77% (17/22)</td>
<td>33% (7/21)</td>
</tr>
<tr>
<td>Podo</td>
<td>7.6% (8/105)</td>
<td>100% (8/8)</td>
<td>13% (1/8)</td>
</tr>
<tr>
<td>Tilanus-Linthorst</td>
<td>2.8% (3/109)</td>
<td>0%</td>
<td>100% (3/3)</td>
</tr>
<tr>
<td>Morris</td>
<td>3.8% (14/367)</td>
<td>100% (14/14)</td>
<td>—</td>
</tr>
<tr>
<td>Kriege</td>
<td>2.4% (45/1909)</td>
<td>71% (23/32)</td>
<td>—</td>
</tr>
<tr>
<td>Lehman</td>
<td>1.1% (4/367)</td>
<td>100% (4/4)</td>
<td>—</td>
</tr>
<tr>
<td>Leach</td>
<td>5.1% (33/649)</td>
<td>77% (25/32)</td>
<td>—</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4.0% (172/4271)</td>
<td>84% (144/172)</td>
<td>48% (144/297)</td>
</tr>
</tbody>
</table>

Cancer Yield of the Different Imaging Methods

EVA Trial
- Prospective, multicenter study
- Respective contribution of clinical exam, MG, US, and MRI
- 687 women with ≥20% lifetime risk
- 1679 annual screening rounds

Cancer Yield of MRI alone significantly higher
- Slightly improved with MG
- No improvement with US
- PPV:
  - MRI: 48%, MG: 39%, US: 36%
- MRI superior for both invasive CA and DCIS

Combined Screening with MG and MRI
- Retrospective review of women who underwent combined screening between 2005-2010
- 222 cancers diagnosed
  - MRI: 167 (75%)
    - 118 invasive CA (71%)
  - MG: 43 (19%)
    - 28 DCIS (65%)
  - Interval CA: 12 (5%)
    - 11 invasive CA (92%)

Comparison of Tumor Histology by Detection method
High Risk Screening MRI

- Multiple studies support MRI high risk screening
  - Prevalence screen: ~ 1-5%
  - Incidence screen: 0.6-4%
  - Sensitivity of mammography, esp in BRCA pts
    • Sensitivity of ~50%
  - 50% of CA had nodal involvement at the time of detection
- Supported by most major medical groups:
  - ACS (2007), NCCN, ACR, SBI, EUSOMA

When to Start Screening

- 5-10 yrs before earliest prior breast CA in family
- Between 25-35 years for BRCA pts
- ACS: “For most women at high risk, screening with MRI and mammograms should begin at age 30 years and continue for as long as a woman is in good health”

Any Benefit to Staggering MG and MR?

- No data to support simultaneous vs staggering screening
  - ? Staggering may decrease interval cancers
- Le-Petross et al:
  - 73 (mainly BRCA) patients
  - 13 CA in 11 women on MRI
  - 12/13 not seen on MG 6 months prior

ACS Guidelines: Annual Screening MRI

Based on expert consensus opinion
- Chest irradiation between ages 10-30
- Li-Fraumeni syndrome and 1st degree relatives
- Cowden and Bannayan-Riley-Ruvalcaba syndromes and 1st degree relatives

Screening: Chest Irradiation

- Increased risk of breast CA after ~ 8 years
- 12-20% develop breast CA by age of 40-45
- Current guidelines:
  - Annual screening MG and MRI starting 8 years after radiation but not before age of 25

ACS Guidelines: Annual Screening MRI

Insufficient Evidence to recommend for or against
- Lifetime risk 15-20%
- LCIS, ALH, ADH
- Dense breasts on mammography
- Personal history of breast cancer
**ACS Guidelines: Annual Screening MRI**

**Insufficient Evidence to recommend for or against**

- Lifetime risk 15-20%
- LCIS, ALH, ADH
- Dense breasts on mammography
- Personal history of breast cancer

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**Indications**

- High risk screening
- Extent of Disease/Preoperative staging
- Evaluation of treatment response
- Metastatic adenopathy of unknown primary
- Problem solving
- Implant evaluation

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**Potential Benefits**

**Extent of disease**

- Additional occult ipse- and contralateral disease
- Evaluation of adjacent structures
- Evidence of metastatic disease

This information could potentially result in:
- Improved surgical outcomes (fewer surgeries)
- Decreased recurrence rates

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**EOD: Known data from pathology**

- 282 mastectomies for unifocal invasive CA on mammography & physical
- 105 (37%) no additional cancer
- 56 (20%) within 2 cm
- 121 (43%) > 2 cm

Holland et al 1985

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**EOD: Ipsilateral Disease**

- Meta-analysis of 19 studies of women undergoing preoperative MRI
- Preoperative MRI detected additional disease in 16% (N = 2610).
- PPV of biopsy: 66%
- 11.3% converted from lumpectomy to more extensive surgery
  - 8% from WLE to mastectomy


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**Table: Contra lateral CA on MRI**

<table>
<thead>
<tr>
<th>Author/Year</th>
<th># of Pts</th>
<th># (%) with Contralateral CA on MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rieber, 1997</td>
<td>34</td>
<td>3 (8.8%)</td>
</tr>
<tr>
<td>Fischer, 1999</td>
<td>463</td>
<td>15 (3.2%)</td>
</tr>
<tr>
<td>Slavens, 2002</td>
<td>17</td>
<td>4 (23.5%)</td>
</tr>
<tr>
<td>Liberman, 2003</td>
<td>223</td>
<td>12 (5.4%)</td>
</tr>
<tr>
<td>Lee, 2003</td>
<td>182</td>
<td>7 (3.9%)</td>
</tr>
<tr>
<td>Vashwog, 2004</td>
<td>119</td>
<td>4 (3.4%)</td>
</tr>
<tr>
<td>Berg, 2004</td>
<td>111</td>
<td>3 (2.7%)</td>
</tr>
<tr>
<td>Lehman, 2005</td>
<td>103</td>
<td>4 (3.9%)</td>
</tr>
<tr>
<td>Pediconi, 2007</td>
<td>118</td>
<td>22 (18.8%)</td>
</tr>
<tr>
<td>Lehman, 2007</td>
<td>969</td>
<td>30 (3.1%)</td>
</tr>
<tr>
<td>Hawusinsk, 2002</td>
<td>101</td>
<td>2 (2.0%)</td>
</tr>
<tr>
<td>Baley, 2004</td>
<td>27</td>
<td>1 (3.7%)</td>
</tr>
<tr>
<td>Hollingsworth, 2008</td>
<td>603</td>
<td>22 (3.6%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>3070</td>
<td><strong>129 (4.2%)</strong></td>
</tr>
</tbody>
</table>

Lehman et al. JNCCN 2009;7: 193-201
Contralateral Breast Cancer

• 4% detection rate
  – 35% DCIS, 65% invasive cancer
• Majority of lesions early stage and small
  – pTis or pT1
  – Average size: 9 mm
  – Lymph node negative
• 48% positive predictive value

EOD: Pectoralis and Chest wall

• Pectoralis invasion:
  – Definite enhancement in the muscle
  • Increased vascularity through the muscle to the breast
    may be confused for muscle involvement
  – Loss of fat plane ≠ invasion
  – Does not change stage of the patient
• Chest wall invasion:
  – Invasion of structures posterior to pectoralis
  – Changes stage of the patient (IIIB)

EOD: Evidence of Metastatic Disease

• Lymph nodes
  – Axilla, subpectoral, internal mammary
  – Enlarged, irregular thickened cortex, spiculated margins, heterogeneous enhancement
  – Sensitivity 65%
• Other:
  – Bone, lung, etc

Summary of Clinical Trials

• MRI identifies additional unsuspected malignancy
• No clear differences in cancer yields in subgroups based on breast density, age or histology of index cancer

Controversies

• Impact on surgery?
• Impact on recurrence?
• Impact on survival?

Impact on Surgery: Does MR Reduce Positive Margins?

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>% Positive Margins No MRI</th>
<th>% Positive Margins MRI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleicher</td>
<td>290</td>
<td>14</td>
<td>22</td>
<td>NS</td>
</tr>
<tr>
<td>Pengel</td>
<td>355</td>
<td>19</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Schiller</td>
<td>730</td>
<td>18</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Hwang</td>
<td>472</td>
<td>14</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td>Grady</td>
<td>184</td>
<td>26</td>
<td>11</td>
<td>.04</td>
</tr>
<tr>
<td>MSKCC</td>
<td>348</td>
<td>46</td>
<td>30</td>
<td>.01</td>
</tr>
</tbody>
</table>
MRI and Surgical Outcomes

- Retrospective studies
- Selection bias:
  - Patients selected for MRI due to higher likelihood of benefit
  - Younger, dense breasts, lobular CA, difficult mammogram
- Findings on preoperative MRI not systematically linked to a specific change in surgical management

Impact on Surgery: COMICE

- Randomized clinical trial of 1623 women
  - Preop MR: 816, no preop MRI: 807
- Primary endpoint:
  - Further wide local excision, mastectomy within 6 months, or pathological avoidable mastectomy at initial surgery
- No difference in surgical outcomes
  - Preop MRI: WLE: 10.4%, total: 10.8%
  - No preop MRI: WLE: 11.2%, total: 19.3%

Limitations of COMICE

- Re-excision rate (10%) extremely low
  - MSKCC: ~25%
  - MRI may add little with large resection volumes
- High rate of mastectomy without pathological confirmation
  - 16/58 mastectomies did not have additional bx
  - Counted in reoperation rate
- Selection bias
- Image quality and interpretation:
  - Sensitivity of 50%, contralateral CA in 1.6%

Can MR Decrease Reoperative Rates?

- Data inconclusive
  - Variable quality of MRI and reader experience
  - No standardization of management of MRI results or surgical approach
  - What we see on imaging is currently near impossible to translate to the OR
  - Differences in patient positioning
  - Ability to localize irregular margins difficult

Impact on Recurrence

- Retrospective single institution trials – conflicting results

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Time</th>
<th>No MRI</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fischer et al</td>
<td>219</td>
<td>40 mo</td>
<td>7%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Solin et al</td>
<td>756</td>
<td>8 years</td>
<td>4%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Impact on Recurrence?

- Limitations:
  - Retrospective, nonrandomized analysis
  - No discussion of selection criteria for MRI
  - Insufficiently powered
- No compelling evidence to either support or disprove ability of MRI to decrease local recurrence rate
ACRIN 6694/ALLIANCE Z11101
Effect of Preoperative Breast MRI on Surgical Outcomes, Costs and Quality of Life
Isabelle Bedrosian, MD and Christopher Comstock, MD
• Primary Aim: To compare the rates of local recurrence after BCT in women with TN or HER-2 randomized to preop staging with MG vs MG + MRI
• Secondary Aim: To compare re-operation rates

Impact on Survival?
Even after histologic confirmation:
• Rate of MRI detected additional tumor is 2-3 times higher than the rate of recurrence in women who undergo breast conservation without pre-operative MRI
• Question remains: Whether the additional disease found on MRI if not treated differently would change clinical outcomes?

Future Role of Pre-op MRI: BCT with Multifocal Ipsilateral Breast Cancers
• 2-3 areas of CA separated by >2 cm of normal tissue
  – No more than 2 quadrants with bx proven CA
• Resect to negative margins, XRT, +/- chemo, endocrine therapy
• Aim: Assess local recurrence rates at 5 years

ECOG-ACRIN protocol, E4112: Prospective Study of Magnetic Resonance Imaging (MRI) and Multiparameter Gene Expression Assay in Ductal Carcinoma In Situ (DCIS)*
• To determine whether XRT can be avoided in subset of patients
• All patients with DCIS have breast MRI and DCIS score
  – Low score: No XRT
  – Intermediate or high score: XRT

Impact on Survival?
• No randomized prospective trials assessing the effect of breast MRI on long term outcomes such as recurrence rates or mortality.

Indications
• High risk screening
• Preoperative staging
• Evaluation of treatment response
• Metastatic adenopathy of unknown primary
• Problem solving
• Implant evaluation
Evaluation of Treatment Response: Neoadjuvant Chemotherapy

- Allows BCT in whom primary surgery not feasible
- HER2+ and TN breast CA highly chemosensitive
- Downstage the axilla to avoid full axillary dissection

Evaluation of Treatment Response

- **Extent of residual malignancy:**
  - More accurate than CBE, MG, or US
  - Sensitivity: 81%, specificity 93%
- **Mean imaging-path discrepancy:**
  - +/- 0.5 cm to +/- 3.9 cm
- **Better accuracy in more aggressive tumors:**
  - HR neg vs HR pos
  - HER2 post vs HER2 negative
  - Ki-67 pos vs ≤10% Ki-67

Evaluation of Treatment Response

- **Overestimation:**
  - Reactive inflammation, chemotherapy induced fibrosis
- **Underestimation:**
  - Small foci of invasive tumor, taxane containing regimens

Indications

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Metastatic Adenopathy of Unknown Primary

- <1% of all breast cancers
- Primary CA usually in ipsilateral breast
- Traditionally, mastectomy and axillary dissection recommended
- MRI detects primary CA in ~70-86%
  - Tumors usually < 2 cm
  - Lumpectomy, tailored chemotherapy
- Negative breast MR predictive of low tumor yield at mastectomy
Problem Solving

• Controversial application
• Most commonly for asymmetry or architectural distortion
• Is the NPV of MRI sufficiently high to exclude malignancy?
  – Likelihood of malignancy should be <2%

• Bluemke et al:
  – Multicenter trial
  – 812 pts with suspicious finding on CBE or MG prior to biopsy
  – NPV: 85% (48 CA/329 negative exams)
• Cilotti et al:
  – 55 patients with BI-RADS 3,4, or 5 calcifications
  – NPV: 76%

• Moy et al:
  – Retrospective study
  – Included 115 cases equivocal on MG
  – MR:
    • Sensitivity: 100%, specificity: 92%
    • NPV: 100%
    • 18/33 (54%) lesions incidental

• 353 BI-RADS 4 lesions on MG or US in 340 women
• If negative MR, followed for 18-24 months
  – FN for calcs: 12%
• Lesions excluding calcs:
  – Increased PPV from 18% to 78%
  – FN rate: 0%
• MR found additional 3 invasive CA

Summary

• MRI is the most sensitive imaging modality for breast cancer detection
• Important to understand the evidence supporting use of MRI for specific indications

• Use judiciously given lack of data and frequency of false positives
• Generally, an equivocal finding should be treated as suspicious and undergo biopsy
Summary

• Additional studies needed in multiple areas, especially long term outcomes

• MRI is most sensitive and specific imaging modality for detecting silicone implant rupture

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