What is the impact of MRI scanning on breast cancer treatment?

Ulrich Bick
Charité - Universitätsmedizin Berlin
Magnetic Resonance Imaging in Breast Cancer
One Step Forward, Two Steps Back?

Monica Morrow, MD

...breast cancer patients undergoing MRI should be advised that this step forward in technology may take them right back to the 1970s and result in a mastectomy for disease that can be controlled with radiation.
## Sensitivity of MRI in high-risk screening

<table>
<thead>
<tr>
<th>Country</th>
<th>Age</th>
<th>Cancers</th>
<th>Mx</th>
<th>US</th>
<th>MRI</th>
<th>ppv (MRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>44</td>
<td>1.6% (27/1679)</td>
<td>33%</td>
<td>37%</td>
<td>93%</td>
<td>0.48</td>
</tr>
<tr>
<td>(Kuhl 2010)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>45</td>
<td>3.3% (52/1592)</td>
<td>50%</td>
<td>52%</td>
<td>91%</td>
<td>0.56</td>
</tr>
<tr>
<td>(Sardanelli 2011)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>47</td>
<td>9.3% (22/236)</td>
<td>36%</td>
<td>33%</td>
<td>77%</td>
<td>0.46</td>
</tr>
<tr>
<td>(Warner 2004)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>40</td>
<td>1.1% (97/8760)</td>
<td>41%</td>
<td>-</td>
<td>71%</td>
<td>0.08</td>
</tr>
<tr>
<td>(Obdeijn 2010)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norway</td>
<td>41</td>
<td>2.9% (25/867)</td>
<td>50%</td>
<td>-</td>
<td>86%</td>
<td>-</td>
</tr>
<tr>
<td>(Hagen 2007)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>40</td>
<td>1.9% (35/1881)</td>
<td>40%</td>
<td>-</td>
<td>77%</td>
<td>0.07</td>
</tr>
<tr>
<td>(Leach 2005)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
39-year-old asymptomatic patient with known BRAC2 mutation in the family, first high-risk screening round
5-mm invasive carcinoma (NST) pT1a pN0(sn) G2
Sensitivity of MRI in high-risk patients without a known mutation

<table>
<thead>
<tr>
<th></th>
<th>Mammography</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 40</td>
<td>40 - 50</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>51%</td>
<td>57%</td>
</tr>
<tr>
<td>Specificity</td>
<td>95%</td>
<td>91%</td>
</tr>
<tr>
<td>PPV</td>
<td>5.1%</td>
<td>8.8%</td>
</tr>
</tbody>
</table>
preoperative MRI detects in around 16% (IQR 11% - 24%) of cases with localized breast cancer additional multifocal or multicentric malignant lesions (Houssami 2008)

detection of occult contralateral cancers in around 5% of cases (similar to contralateral prophylactic mastectomy)

additional cancer yield will vary substantially with type of cancer, individual patient risk factors, and quality of imaging
Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer

- 19 studies (including 3 RCTs) with a total of 85,975 subjects, of which 15,274 received pre-operative MRI
- No statistical evidence of an effect of MRI on the rates of re-excision, re-operation, or positive margins
- But increased odds of receiving mastectomy [OR 1.39 (1.23, 1.57); p < 0.001]
- And increased odds of receiving contralateral prophylactic mastectomy [OR 1.91 (1.25, 2.91); p = 0.003]
9 studies with a total of 3,252 women, of which 1,077 received pre-operative MRI

- no statistical differences in the proportion of women with positive margins (OR 0.80, P = 0.059; adjusted OR 1.10, P = 0.716), nor in the necessity of reoperation (OR 1.06, P = 0.759; adjusted OR 1.04, P = 0.844)

- MRI significantly increased the odds of having initial mastectomy (OR 1.72, P = 0.012; adjusted OR 1.76, P = 0.010)

- overall mastectomy rates did not differ significantly (OR 1.23, P = 0.340; adjusted OR 0.97, P = 0.881).
Why is it so difficult to show a benefit for the MRI

- Long-term prognosis dominated by the risk of distant metastasis from the primary cancer
- Local recurrence rates for stage 0 and I breast cancers after BCT in conjunction with adequate systemic therapy very low
- Re-excision rates influenced by a variety of (non-medical) factors
- Specificity of MRI for lesions less than 5 mm in size and for non-mass lesions relatively low
- Contrary to common believe, MRI cannot reliably differentiate between clinically relevant and irrelevant disease
48-year-old female with palpable invasive carcinoma (NST) confirmed by ultrasound-guided core biopsy (no oral contraceptives or HRT)
second (multicentric) 4-mm invasive carcinoma (NST)

Final surgical pathology:
*pT1b(m) pN0(sn) G2

on mastectomy additional extensive lobular neoplasia (LIN II) on the right with multifocal microinvasion

no cancer on the left after more than 5 years of follow-up under adjuvant endocrine therapy
Does MRI really find predominantly biological relevant disease?

<table>
<thead>
<tr>
<th>IDC Grade</th>
<th>Detected with Mammography</th>
<th>Contribution of Ultrasound</th>
<th>Contribution of MRI</th>
<th>Not detected by Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>21% (7/33)</td>
<td>46% (11/24)</td>
<td>57% (4/7)</td>
<td>38% (3/8)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>42% (14/33)</td>
<td>29% (7/24)</td>
<td>14% (1/7)</td>
<td>13% (1/8)</td>
</tr>
<tr>
<td>High</td>
<td>33% (11/33)</td>
<td>25% (6/24)</td>
<td>29% (2/7)</td>
<td>25% (2/8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3% (1/33)</td>
<td>-</td>
<td>-</td>
<td>25% (2/8)</td>
</tr>
<tr>
<td>All</td>
<td>46% (33/72)</td>
<td>33% (24/72)</td>
<td>10% (7/72)</td>
<td>11% (8/72)</td>
</tr>
</tbody>
</table>

ACRIN 6666 Trial: *tumor biology and mode of detection*

Berg et al. (2012) JAMA 307: 1394 - 1404
Reexcision/Reoperation rates

- Surgeon (Experience)
- Patient (Preference)
- Type of Surgery (lumpectomy, oncoplastic surgery)
- Country-specific Guidelines ("No ink on tumor")
Use of Preoperative Magnetic Resonance Imaging for Breast Cancer: A Canadian Population-Based Study

- 14.8% of patients (7,824 of 53,015) with primary operable breast cancer treated from 2003 to 2012 had a preoperative MRI
- During the 10-year study period, MRI use increased across all stages by 8-fold (from 3% to 24%; $P < .001$ for trend)
- Preoperative breast MRI was associated with higher likelihood of:
  - further confirmatory breast imaging (OR 2.09)
  - postdiagnosis breast needle biopsies (OR 1.74)
  - staging imaging to assess for distant metastatic disease (OR 1.51)
  - mastectomy (OR 1.73)
  - contralateral prophylactic mastectomy (OR, 1.48)
  - 30-day wait to surgery (OR 2.52)

Use of Preoperative Magnetic Resonance Imaging for Breast Cancer: A Canadian Population-Based Study

- factors associated with the use of preoperative MRI:
  - younger patient age
  - higher patient socioeconomic status
  - higher Charlson comorbidity score
  - higher stage
  - lobular histologic type
  - later year of diagnosis
  - having surgery in a teaching hospital
  - getting treatment in certain Local Health Integration Networks
  - surgeons with higher patient volumes
  - surgeons with less experience (in years)

Local tumor staging with MRI: Possible indications

- invasive lobular carcinoma
- additional pathologic risk lesions (FEA, lobular neoplasia)
- locally advanced breast carcinoma
- large DCIS high-grade prior to planned breast conserving surgery
- high-risk patients based on genetic abnormalities or family history
- young premenopausal patients
- limited value of mammography due to dense breast parenchyma or multiple calcifications
35-year old female with palpable abnormality on the left

bifocal invasive carcinoma (NST) with extensive high-grade DCIS treated with BCT
Follow-up after BCT for left breast cancer (pT2 pN3a G3) in 2008

diagnosis of a singular bone metastasis 6 years after BCT

diagnosis of multiple hepatic metastasis 7.5 years after BCT
When is MRI for local tumor staging NOT necessary?

- small DCIS associated with calcifications on mammography
- small invasive carcinoma (NST), well-defined on mammography and/or ultrasound
- long term survival rates of in-situ and stage I (pT1 pN0) breast cancers more than 98%
- risk of overdiagnosis/overtherapy particularly high in older women with breast cancer diagnosed during screening
64-year-old asymptomatic female with 13-mm invasive breast carcinoma (NST) in the right breast (pT1c pN0 G1)
Local Tumor Staging with MRI: *Survival Guide*

- MRI just one piece of the puzzle, along with risk constellation, clinical exam, mammography and ultrasound
- likelihood of malignancy for non-mass lesions on MRI higher in cases with a corresponding finding on ultrasound and/or MX
- as MRI may significantly overestimate tumor size, any conversion from BCS to mastectomy should (ideally) be based on histological confirmation
- short-term follow-up for non-specific contralateral MRI findings very helpful (optimal imaging conditions with endocrine therapy)
- Never perform the MRI on the day (evening) before surgery *(you can always schedule it after BCS and before RT if necessary)*
Increasing Role of MRI in the future

- defining the need for surgical excision in patients with risk lesions detected on percutaneous biopsy
- prior and during primary systemic therapy
- patient selection for partial breast irradiation
- as part of watch and wait strategies for low-grade disease
- identification of patients in whom axillary sampling is needed