MRI OVERRATED IN BREAST CANCER

GRAND ROUNDS
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Epidemiology

• Approximately 178,480 American women are diagnosed with breast cancer annually
• 40,460 women die from this disease
• Breast cancer is
  – The most common female cancer in US
  – The 2nd most common cause of cancer death in women
  – The main cause of death in women ages 45 to 55.

Possible Uses of MRI in Breast Cancer

- Screening
- Coincident Lesions
- MRI for Suspicious Lesions on Mammography
- MRI to Change Surgical Plan Preop
- Occult Primary Disease
- MRI to Follow Cancer Patients Post Treatment
Cons Overview

• MRI Availability to the Masses
• Sensitive but not Specific
  – Screening low risk
  – Breast Conservation concerns
  – Unneeded biopsies and examinations
• Expensive
• NO PROVEN MORTALITY BENEFIT
MRI for Breast Cancer Screening
ACS Recommendations for Breast MRI Screening as Adjunct to Mammography

• Recommend Annual MRI screen if
  – Lifetime risk 20-25%
  – BRCA carrier or untested with relative
    – Above based on nonrandomized screening trials and observational studies
  – Radiation to Chest between age 10-30
  – Certain syndromes
    – Based on expert opinion
ACS Recommendations for Breast MRI Screening as Adjunct to Mammography

• Insufficient evidence to recommend for or against MRI Screening
  – Lifetime risk of 15-20%
  – LCIS or Atypical lobular hyperplasia
  – Atypical ductal hyperplasia
  – Heterogeneous or very dense breast on mammography
  – Women with personal history of Breast Cancer including DCIS
ACS Recommendations for Breast MRI Screening as Adjucnt to Mammography

• Recommend Against MRI Screening
  – Women with less than 15% lifetime risk
    – Based on expert opinion
Evidence for Screening Women at Increased Risk

- 6 Prospective nonrandomized studies in the 1990s to determine benefit of adding MRI to Mammography
- Participants in these studies had either documented BRCA 1 or 2 or a strong family history of breast cancer
- Overall MRI showed high sensitivity compared with mammography in these high risk populations
Evidence for Screening Women At Increased Risk - PROBLEMS

- Specificity of MRI compared to Mammography lower in all studies to date
- Thus More recalls and more biopsies
  - Additional imaging recall rate 8-17%
  - Biopsy rates 3-15%
- Positive predictive value of MRI 20-40%
- No evidence of decreased mortality
- Potentially justifiable in highest risk groups, but in low risk groups harms likely outweigh the benefits
Evidence for Screening Women At Increased Risk


Evidence for Screening - PROBLEMS

- Access to Appropriate MRI capabilities
  - Must have experienced radiologist
  - Must have biopsy capabilities
  - This year standardization guidelines are supposed to be developed
  - Some MRI technical aspects of the actual MRI specific for breast MRI
Evidence for Screening - PROBLEMS

- Cost Effectiveness
- Limited data available
- One recent Study modeled adding MRI to Mammography screening to women of differing age groups who carry BRCA 1 or 2 compared with mammography alone
- Authors felt cost effectiveness varied by age and was more effective for BRCA1 than 2

Cost Effectiveness

• Relative to screening with mammography alone, the cost per quality adjusted life year gained by adding MRI from ages 35 to 54 years is:
  • $55,420 for BRCA1 mutation carriers,
  • $130,695 for BRCA2 mutation carriers,
  • $98,454 for BRCA2 mutation carriers with dense breasts.
Cost Effectiveness

• UK study determined the incremental cost per cancer detected for women with 50% risk of carrying BRCA mutation was

  – $50,911 for MRI with mammography compared with mammography alone

Cost Effectiveness

• Problems with these studies
• Both are models based on assumptions
• In first study no study proven mortality benefit so they estimate benefit
• Range of 50-130K per cancer or QALY
• Specific groups have more cost effective return
• According to Feed the Hungry this would feed between 6250 - 16250 children for one month

• According to Doctors without Borders this would vaccinate over 100,000 people against meningitis, measles or polio
Evidence for Screening - PROBLEMS

- Psychological distress

- One UK study
  - 47% of women said still having intrusive thoughts about the exam 6 weeks afterward

  - 4% found breast MRI “extremely distressing”

Evidence for Screening - PROBLEMS

- Psychological distress
- Dutch Study
  - Found distress within normal limits in the 357 women in the study
  - Elevated breast cancer — specific stress related to screening was found certain subgroups that included 35% of their sample
  - They recommended addition psychological support for these groups
  - More Expense
Evidence for Screening - PROBLEMS

• No randomized trails showing reduction in mortality or size of diagnosed breast cancer comparing MRI to Mammography in screening women with dense breast

• Scant data available for screening women with personal history of breast cancer or other lesion increasing risk of cancer
Evidence for Screening - PROBLEMS

• In the ACS Guideline publication they say

• “…outcome data from screening MRI studies are not sufficient to form a solid basis for many of the recommendations. It was therefore necessary to relay on inferential evidence and expert opinion…”
Evidence for Screening - PROBLEMS

- Evidence may support increased sensitivity for MRI compared with mammography and possibly stage shift towards earlier tumor stages BUT

- **NO data on recurrence or survival rates**

MRI for Evaluation of Contralateral Coincident Lesions
MRI for Contralateral Breast Lesion

- Largest study of MRI for screening of the contralateral breast was conducted by the American College of Radiology Imaging Network and published in NEJM

- 969 women with a diagnosis of unilateral breast cancer within 60 days and no contralateral abnormalities on mammographic or clinical examination underwent breast MRI

- Women were then followed clinically for one year.
MRI for Contralateral Breast Lesion

- A biopsy was performed on the basis of an abnormal MRI finding in 121 women (12.5 percent),
  - of whom 30 (3.1 % of the study) had cancer diagnosed

- The positive predictive value of an abnormal MRI was 21 percent

- Specificity was significantly higher among postmenopausal as compared to premenopausal or perimenopausal women (31 versus 11 percent), and for those with fatty as compared to dense breasts

- MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. Lehman CD; Gatsonis C; Kuhl CK; Hendrick RE; Pisano ED; Hanna L; Peacock S; Smazal SF; Maki DD; Julian TB; DePeri ER; Bluemke DA; Schnall MD N Engl J Med. 2007 Mar 29;356(13):1295-303. Epub 2007 Mar 28.
MRI for Contralateral Breast Lesion

• No evidence of improved mortality benefit or recurrence rate

• Study authors themselves note:
  – ‘The current cost of MRI precludes its widespread use in general populations.’

• Specific subgroups benefit more

• These are my common themes
MRI for Ipsilateral Coincident Lesions
MRI Changing Surgical Planning

• Retrospective review of 267 patients with primary breast tumors who had MRI studies prior to undergoing definitive surgery.
• Planned surgical management was altered in 69 of 267 patients (26%);
  – 44 of 267 patients (16.5%) had conversion of planned breast conservation to mastectomy.
  – 11 patients (4%) underwent a wider surgical excision than was planned initially;
  – 14 patients (5%) underwent an additional, separate excisional biopsy to evaluate the area of MRI-detected abnormality.
MRI Changing Surgical Planning

• Of 69 patients who underwent these additional procedures to evaluate MRI abnormalities, there was pathologic verification of malignancy in the surgical specimen in 49 patients (71%),

• However, in 20 of 69 patients (29%), it was determined on final pathologic examination that additional suspicious areas seen on MRI studies were benign.
MRI Changing Surgical Planning

• Not data about local recurrence or mortality

• The identification of biologically insignificant disease may lead to overtreatment and a shift away from breast preservation. We need more data.

• Isabelle Bedrosian, Rosemarie Mick, Susan G. Orel, Mitchell Schnall, Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging, Cancer 98:3, 468-473; 2003
Detection of Residual Disease after Biopsy with MRI

In 70 of 267 patients who were had imaging studies after undergoing excision of the primary tumor, the sensitivity of MRI was diminished markedly for the detection of residual disease around the biopsy cavity.

- 60 of 70 patients had residual disease present around the biopsy cavity on final pathology,
- Overall, the sensitivity of MRI in this subgroup was 57% (34 of 60 patients) and the specificity was 60% (6 of 10 patients)
- Thirty-two patients who underwent prior biopsy had no MRI evidence of malignant disease; of these, 26 patients (81%) had residual disease confirmed on pathologic examination (negative predictive value 19%).

* Isabelle Bedrosian, Rosemarie Mick, Susan G. Orel, Mitchell Schnall, *Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging*, Cancer 98:3, 468-473; 2003
Detection of Residual Disease after Biopsy with MRI

• In patients with breast carcinoma who present after undergoing excisional biopsy with positive or close margins, the results of MRI studies should not be used to determine whether the patient should undergo reexcision for positive margins.
MRI for Patients with Mammographically or Clinically Suspicious Breast Lesions
MRI of the Breast Prior to Biopsy with Abnormal Mammogram

- Prospective multicenter investigation of the International Breast MR Consortium conducted at 14 university hospitals in North America and Europe from June 2, 1998, through October 31, 2001,
- 821 patients referred for breast biopsy for ACR category 4 or 5 mammographic assessment or suspicious clinical or ultrasound finding.
- MRI examinations performed prior to breast biopsy
MRI of the Breast Prior to Biopsy

- Among the 821 patients:
  - MRI correctly detected cancer in 356 of 404 cases
    - resulting in a sensitivity of 88.1% (95% CI, 84.6%-91.1%),
  - MRI correctly identified as negative for cancer 281 of 417 cases
    - resulting in a specificity of 67.7% (95% CI, 62.7%-71.9%).
  - The positive predictive values was 72.4%
  - Negative Predictive value of MRI 85.4%
MRI of the Breast Prior to Biopsy with Abnormal Mammogram

- Breast MRI had high sensitivity but only moderate specificity independent of breast density, tumor type, and menopausal status.

- Although the positive predictive value of MRI is greater than mammography,
  
  – MRI DOES NOT obviate the need for subsequent tissue sampling

- Magnetic resonance imaging of the breast prior to biopsy. Bluemke DA; Gatsonis CA; Chen MH; DeAngelis GA; DeBruhl N; Harms S; Heywang-Kobrunner SH; Hylton N; Kuhl CK; Lehman C; Pisano ED; Causer P; Schnitt SJ; Smazal SF; Stelling CB; Weatherall PT; Schnall MD JAMA 2004 Dec 8;292(22):2735-42.
Occult Primary Disease

- Data from several small series suggest that breast MRI can detect a primary breast cancer in a high percentage of women who present with axillary adenocarcinoma and a negative clinical examination and mammogram.
Occult Primary Disease

• However, breast MRI is also characterized by high false-positive rates (29 percent in one study)

• Use Selectively

  • Magnetic resonance imaging-guided biopsy of mammographically and clinically occult breast lesions. Bedrosian I; Schlencker J; Spitz FR; Örel SG; Fraker DL; Callans LS; Schnall M; Reynolds C; Czerniecki BJ Ann Surg Oncol. 2002 Jun;9(5):457-61.
MRI for post therapy Breast Cancer Surveillance

- There is no evidence that breast MRI improves outcomes when used as a breast cancer surveillance tool during routine post treatment follow-up in asymptomatic women.
- Breast MRI is not recommended for routine post treatment surveillance in women treated for an apparently sporadic primary breast cancer in guidelines from any expert group.
- Similar to routine screening, population characteristics dictate usage.

Summary

• Retrospective and some prospective evidence is accumulating for high sensitivity of MRI for the detection of breast cancer with variable specificity depending on the study
• MRI is expensive
• MRI not easily available in all communities
• May decrease breast conservation in certain situations where this is not warranted
• May increase numbers of evaluations and procedure a patient requires increasing both cost and risks.
• No mortality or recurrence rate improvement documented to date
• Use MRI as an adjunct to mammography and clinical exam in selected populations as dictated by a educated risk versus benefit discussion amongst patients and doctors