Screening with Abbreviated Breast MRI (AB-MR)

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Outline

• History of our approach to screening
• Concept of screening
• MRI
• Concept of AB-MR
• EA1141 Trial
When women are screened with analog mammography...

~30% mortality reduction from breast cancer since mammography started

Based on poor quality mammography and invitation to screen!
2D Analog Screen Mammography

• 8 Randomized clinical trials

• Prior to:
  • Improved high-speed screen film techniques
  • CAD
  • Digital (FFDM)
  • Tomosynthesis
Improvements in Mammography

- High speed screen film combinations
- Computer Aided Detection (CAD)
- Full-field Digital Mammography (FFDM)
- Digital Breast Tomosynthesis (DBT)
CAD (Detection)

- Computer
- Radiologist
- Cancers
Digital Mammography
ACRIN-DMIST

- Digital Mammographic Imaging Screening Trial
- >49,000 women
- Multiple Digital Vendors
- Results presented 9/16/05 show overall no significant difference
- However, benefit for subgroups (age < 50, Dense breasts and peri-menopausal women)
Limitations of Mammography

1 year later
Digital Breast Tomosynthesis (DBT)
454,850 patients at 13 sites

Cancer Detection: 7058 MG
- MG: 4.2/1000
- MG+DBT: 5.4/1000

Recall rate:
- MG: 10.7%
- MG+DBT: 9.1%
Breast Density Legislation

1. Shortcomings of mammography has led to passage of breast density legislation in many states

2. Laws recommend women with dense breasts consider supplemental screening

3. Type of supplemental screening not specified
Breast Density Legislation

D.E.N.S.E.®
State Efforts

Click on your state to find information about "mandatory breast density notification" legislative efforts.

Whole Breast Screening Ultrasound

1. Default supplemental screening modality due to relatively low cost and wide availability

2. Supplemental cancer yield: 3-4/1000

3. Limitation of WBUS include:
   - Low PPV (8-9%)
   - High frequency of short-term follow recommendations
   - Time consuming
1. For many women with dense breasts, the standard is now annual DM or DBT plus WBUS
2. The combined cancer detection rate is approximately 7-9 cancers per 1000
3. Exact mortality reduction is unknown
4. Limitation of this approach include:
   – Low PPV (8-9%)
   – High frequency of short-term follow recommendations
   – Time consuming
   – Cost
Reservoir of Breast Cancer Present in 1000 Women Being Screened

- Is it 30, 40, 50, 60 or more breast cancers per 1000 women?
- Depends on risk of population
- Detection level (size and stage) depends on modality and frequency of screening
Reservoir of Breast Cancer Present in 1000 Women Being Screened

Current approach - Mammo plus WBUS
How we choose to screen is somewhat arbitrary

- How many of the cancers in the reservoir we choose to find and at what size is balanced by the cost and harms of the test.
Screening Tests

- **No Screen**: No detected particles.
- **Palpable**: Detected particles.
- **Test 1**: Screen detected particles.
- **Test 2**: Screen detected particles.
Mammography in Breast Cancer Screening

In 1956, Robert Egan introduced dedicated x-ray film for Mammography.
What have we done with breast cancer screening since 1956?

1939 1969 1975 2013
The most sensitive test we have is breast MRI

FFDM and MRI on same patient

8 mm IDC
The Use of MRI for Breast Cancer Screening

1. Not limited by breast density
2. No ionizing radiation
3. Most sensitive test for breast cancer screening
4. PPV similar to mammography
5. Preferentially detects higher grade lesions
Is MRI better than Mammography and US? – The untold story!

From: Detection of Breast Cancer With Addition of Annual Screening Ultrasound or a Single Screening MRI to Mammography in Women With Elevated Breast Cancer Risk
1. Kuhl et al. JCO 2014
   – Intermediate to slightly increased risk women
   – 18.3/1000 additional cancers
   – All were Tis or T1, N0, M0 and almost all were path or nuclear grade II/III.
   – Median tumor size was 8.4mm
Results: Tumor Histology and Grade by % of CA Seen on Each Modality
Why have we ignored MRI except for extremely high-risk women?

1. Cost
2. Time
3. Perceived low PPV
AB-MR is defined as a breast MRI fulfilling the following requirements:

1. Total scan time of less than 10 min (including localizer)
2. A localization scan
3. 1 pre- and 1 post-contrast gradient echo (GRE) axial acquisition; In-plane resolution of 1 mm or less
4. Slice thickness of 3 mm of less
5. Axial T2 weighted sequence with in-plane resolution matching the GRE sequences and 3 mm or less slice thickness
Comparison of Abbreviated Breast MRI and Digital Breast Tomosynthesis in Breast Cancer Screening in Women with Dense Breasts

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ECOG-ACRIN AB-MR Working Group
Objectives

Primary Endpoints

1. To compare the rates of detection of invasive cancers between the initial AB-MR and DBT.

Secondary Endpoints

1. To compare the positive predictive value (PPV) of biopsies, call back rates, and short-term follow up rates after AB-MR and DBT on both the initial and 1 year follow up studies.
2. To estimate and compare the sensitivity and specificity of AB-MR and DBT, using the 1 year follow up to define a reference standard.
3. To compare patient-reported short-term quality of life related to diagnostic testing with AB-MR and DBT using the Testing Morbidities Index.
4. To compare willingness to return for testing with AB-MRI vs DBT within the recommended screening interval and explore factors associated with willingness to return for screening.
5. To compare the tumor biologies of invasive cancers and DCIS detected on AB-MR and DBT.
6. To estimate the incident cancer rate during 3 years following the year-1 AB-MR/DBT when patients return to standard screening.
1. Exploration of the differences in the biological detection profiles (BDP) of Tomosynthesis and AB-MR. (PAM50 for invasive CA and DCIS score for DCIS)
1. Paired design: All patients undergo both DBT and AB-MR on the same day at year 0 and year 1.
2. Randomization is only done to determine which test is done first. Once randomized, the order of the tests should be done the same at year 0 and year 1.
3. After the year 1 DBT and AB-MR, patients return to their standard screening per site practice and are followed for breast cancer occurrence for 3 years.
4. For patients that consented for tissue submission, tissue from all cancers detected during the study period should be sent for genetic profiling per study protocol.
Women ages 40-75 with dense breasts already scheduled for routine screening DBT

**Randomization**

Arm A (DBT first)
- Years 0 and 1 DBT followed by AB-MR.
- Year 0 PRO/QOL assessments to be completed approximately 2 weeks after screening

Arm B (AB-MR first)
- Years 0 and 1 AB-MR followed by DBT.
- Year 0 PRO/QOL assessments to be completed approximately 2 weeks after screening

Return to routine mammographic screening and follow up for 3 years

Accrual Goal = 1450

1. Suspicious lesions detected on one or both of the modalities at the Year 0 or 1 time points will be biopsied as per local standard practice
2. Tissue collection and analysis for all cancers detected
1. The table shows that 1363 cases with complete data from both tests and pathology are needed to ensure power 90\% for a difference in the rates of invasive cancer detection as low as 9/1000.

2. Assuming that inadequate information will be available on up to 6\% of cases, a sample size of 1450 will provide power 90\% to compare the diagnostic yield in invasive cancer of the two modalities.

<table>
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<th>Power</th>
<th>Sample size</th>
<th>Difference in invasive cancer rates (ABMR –DBT)</th>
<th>Proportion of discordant cases</th>
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Main Eligibility Criteria

1. Patients must be women ages 40 to 75 years and scheduled for routine screening DBT
2. Patient’s breast density must be known; patients must have mammographically dense breasts (ACR BI-RADS Density categories 3 or 4) on their most-recent prior screening
3. Patient must be asymptomatic for breast disease and undergoing routine screening
4. Patient must have no known breast cancer (DCIS or invasive cancer), not currently undergoing treatment for breast cancer, or planning surgery for a high risk lesion (ADH, ALH, LCIS, papilloma, radial scar)
5. Patient must not be taking chemoprevention for breast cancer.
6. Patient must not have undergone breast ultrasound within 12 months prior to randomization
7. Patient must not have previously had a breast MRI or CEDM
8. Patient must not be suspected of being at high-risk for breast cancer, as defined by the ACS breast MR screening recommendations (lifetime risk of ≥ 20-25%).
9. Able to undergo breast MRI
10. Does not have breast implants

Please see protocol for complete list
AB-MR Working Group

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Interpretation Guidelines

Unique 4-5 mm Focus on Baseline AB-MR:
Single, dominant

CIRCUMSCRIBED MARGINS

- YES
  - RIM ENHANCEMENT
    - YES
      - INFLAMMATORY CYST
        - YES
          - BENIGN
        - NO
          - BX
    - NO
      - BX
  - NO
    - BENIGN

IRREGULAR SHAPE AND MARGINS

- YES
  - HIGH T2
    - YES
      - BENIGN
    - NO
      - 6 MO FU
- NO
  - BX
Interpretation Guidelines

Unique Mass on Baseline AB-MR

- Not Circumscribed:
  - BX
  - Not Benign
  - Classic Lymph Node
    - Homogeneous or Heterogeneous Enhancement
      - 6 MO FU
    - Rim Enhancement
      - BX
    - Homogeneous Enhancement
      - 6 MO FU

- Circumscribed:
  - High T2
    - Not Benign
    - Degenerated Fibroadenoma
      - Benign
  - Low T2
    - Inflammatory Cyst (Central High Pre-T1 or T2)
      - Benign

- bx

- 6 MO FU
Interpretation Guidelines

![Flowchart](Image)

1. Unique Non-Mass Enhancement on Baseline AB-MR
   - **Distribution:** Linear, Segmental
     - BX
   - **Internal Enhancement:** Clumped, Heterogeneous, Clustered Ring
     - BX

2. **Distribution:** Focal, Regional, Multiple Regions, Diffuse
   - **Internal Enhancement:** Homogeneous
     - Associated Fibrocystic Change on T2
       - NO: 6 MO FU
       - YES: Benign
In the End

• Access to MRI will be widely expanded
• Women with dense breasts will have a faster, more sensitive and more accurate option to WBUS.
• AB-MR every 2-3 years may prove to be a better stand alone test than mammography and ultrasound every year.
Thank you!