Breast imaging and Breast Cancer Updates

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Primary Methods of Breast Cancer Detection

Digital Mammogram Machine

3D Tomosynthesis Mammogram

Mammogram

Computer Aided Diagnosis (CAD)

- The computer will annotate masses (see circle around mass, top of photo)
- The computer will annotate calcifications (see dots, lower photo)
- Can help Radiologist find lesions
What do we look for on a Mammogram

- Masses
- Calcifications
- Distortion

Mass on Mammogram

Distortion on Mammogram

Calcifications

Making the Diagnosis of Breast Cancer

- Radiology biopsy (Preferred - 95%)
  - ultrasound guided core needle biopsy
  - mammogram/ computer guided, also called a stereotactic biopsy
- Surgical excisional biopsy

Stereotactic Breast Biopsy

- Uses mammographic imaging
- Computer guided probe
- Vacuum assisted with pulsed anesthetic
- As little as 10 minute "table time"
- Good cosmesis/no stitches
- No change in Mammogram
- Can get bleeding/bruising
Stereotactic Breast Biopsy

Mammography is proven to save lives but can we save more?
- Mammography has been proven to save lives by finding cancers while they are small enough to treat.
- But, mammography isn’t perfect, it is:
  - Less sensitive in dense breasts
  - Unable to distinguish between deadly cancers and those less threatening
  - Uncomfortable
  - Involves radiation

Recommendations are creating confusion

2017 JAMA study
- Breast density is the leading common risk factor for development of breast cancer over:
  - family history
  - personal history of benign lesions
  - first full term pregnancy over age 30
  - other

Breast cancer screening
- Screening mammography is an accepted approach to breast cancer mortality reduction
- Breast cancer mortality reduction ranges from 20-44%
- Non-screen-detected cancers, found when clinical symptoms develop, are:
  - Larger
  - Higher grade (more node positive disease)
  - Poorer prognosis

Breast density classifications
- Breast density is a qualitative assessment graded by ACR standards determined by the interpreting radiologists
- BI-RADS* Labeling

Mammography is an effective screening tool, but cancers are still missed.
Breast cancer screening effectiveness

Effectiveness of screening mammography
- All women
  - Sensitivity 85%
  - Mortality reduction
- Women with dense breasts
  - Sensitivity 65%
  - More than 1/3 of breast cancers not mammographically visible in women with dense breasts

Every other cancer is missed in extremely dense breasts

Limitations of mammography in dense breasts
- Masking Effect: “The Snowball in a Snowstorm”
- Sensitivity of Mammography in Dense Breasts ≤ 65%

Ultrasound more sensitive in dense breast tissue

Ultrasound can find additional mammographically occult breast cancers
- Ultrasound has demonstrated a 50% increase in sensitivity vs. mammography
- On average 40% of women in the USA have dense breast tissue, 70% of Asian women

Breast density awareness

Factors that may influence breast density
- Pre vs. postmenopausal status
- Parity
- Increase breast density is associated with multiparity and late age at first birth
- Family history
- Density may be associated with a family history of breast cancer
- Benign breast disease
- Women with benign breast disease have a greater risk of cancer if they also have dense breast tissue

Diet
- Dietary patterns may lead to an increased risk of dense breast tissue
- Giants in childhood
- Alcohol intake
- High alcohol intake is associated with increased breast density
- Environment
- Predominantly urban areas
- Hormone Replacement Therapy (HRT)
- Chronic low-level inflammation

Factors affecting breast density
- Body mass index
- Obesity
- Obesity increases breast density
- Ethnicity
- Ethnicity increases breast density
- Estrogen levels
- Estrogen levels in menstruating women
- Menopause
- Menopause increases breast density

The risk of having dense breasts is real

- 71% of cancers are in dense breasts
- 2X risk of development of contralateral breast cancer
- Increased odds of developing an interval breast cancer
Breast Ultrasound

- No radiation
- Comfortable
- Good for masses, palpable lesions
- Useful in dense breasts
- Solid vs. Cystic

Breast US Indications

- Palpable mass
- F/U to Mammogram or MRI
- Women < 30 y/o, palpable mass
- Work up of calcification or distortion in dense breasts
- Implants

Classic Cyst

- Black (anechoic)
- Nice Wall (circumscribed)
- White Tail (posterior acoustic enhancement)

Solid Mass on Ultrasound

- Angular margins (spiculated)
- Tall or irregular in shape
- Black tail (shadowing)

Malignant Mass on US
Ultrasound Guided Breast Biopsy

- More operator dependent
- Can be vacuum assisted
- Can watch biopsy "real time"

Invenia ABUS 2.0
- Sole manufacturer of ultrasound systems FDA-approved for screening women with dense breast tissue.
- The Invenia® ABUS 2.0 is indicated as an adjunct to mammography for breast cancer screening in asymptomatic women for whom screening mammography findings are normal or benign, with dense breast parenchyma, and have not had previous clinical breast intervention.
- The device is intended to increase breast cancer detection in the described patient population.
- The Invenia ABUS 2.0 may also be used for diagnostic ultrasound imaging of the breast in symptomatic women.

Supported by strong clinical results

Separates acquisition and interpretation
- Acquire images
  - Automated one-button image acquisition
  - 15 to 20 minutes
  - Re-site, re-dilate, core biopsy
  - Less than 3-minute scan for each breast
  - Total exam time: 15 minutes
- Interpret images
  - Supports image interpretation
  - Review 3D image sets
  - Read entire case in 1.3 minutes
Advancements in automation technology
- Invenia™ ABUS 2.0 cSound™ Imageform
- Operation-independent
- Extraordinary image quality
- Faster scan times
- Patented Reverse Curve™ Transducer
- The design conforms to female anatomy
- Intelligent Imaging Algorithms
- Single button optimization helps provide reproducibility

Reverse Curve™ transducer
Shaped to match female anatomy
- Uniform compression across the entire breast
- 15 cm wide field of view
- 6-15 MHz wide bandwidth
- Designed for patient comfort

Benefits of ABUS for the patient
- Minimal compression
- Can breathe normally
- No ionizing radiation
- Non-invasive test - no contrast

Breast MRI

MRI with CAD stream

BREAST MRI INDICATIONS American College Radiology
- Screening high risk pts (greater than 20% lifetime risk to develop breast cancer)
- Newly diagnosed breast cancer; evaluation of extent of disease and contralateral breast
- Breast Augmentation
- Extent of Disease, F/U Breast surgery with positive margins, chest wall involvement, chemo response
- Recurrence, Mets, Lesion characterization, Bx
Mass on MRI

MRI and Breast Cancer

All are useful for Breast Cancer detection

- Mammography, ultrasound, MRI and clinical exam all useful for Breast Cancer detection
- Different ways of detecting breast cancer with different strengths and weaknesses
- One not necessarily better than another

Breast Cancer

Breast

Impact of breast cancer in the USA

1 in 8 Women will be diagnosed with Breast Cancer in their lifetime.

Breast cancer is the most common cancer among women worldwide.
Breast Cancer

- The leading cause of malignancy related death among American women 15 to 54 years of age
- 75% of all breast cancers are sporadic (a patient with no family history of breast cancer)
- 1% of all breast cancers occur in men

Breast Cancer-Epidemiology

- Incidence and Mortality rates in US are 5x higher than in many Asian and African countries.
- Incidence increases as a woman gets older.
- 1400 men per year diagnosed in US.
The Numbers Can Be Misleading
• 1/8 women born today will develop breast cancer.

Breast Cancer Risk Assessment

Perspective
• A lot of women over estimate their risk of developing breast cancer but underestimate their risk of heart disease
  • Breast Cancer = (1/8) 43,000 deaths annually
  • Heart disease = (1/3) 505,000 deaths annually

Chance of Developing Breast Cancer by Age
(Average Risk)

<table>
<thead>
<tr>
<th>Age</th>
<th>Chance of Developing Cancer</th>
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<tbody>
<tr>
<td>By age 25</td>
<td>one in 19,608</td>
</tr>
<tr>
<td>By age 30</td>
<td>one in 2,525</td>
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<tr>
<td>By age 35</td>
<td>one in 622</td>
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<tr>
<td>By age 40</td>
<td>one in 217</td>
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<td>By age 85</td>
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<tr>
<td>Ever</td>
<td>one in 8</td>
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</tbody>
</table>

Source: NCI Surveillance Program

Breast Cancer Risk Factors
• Aging
• Early menarche
• Late menopause
• Nulliparity (no children)
• Later age of first pregnancy
• Number of first degree relatives
• Previous cancer
• Premalignant breast disease (atypical ductal hyperplasia)
Lifestyle Risk Factors

<table>
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<tr>
<th>Changeable</th>
<th>Non-changeable</th>
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<tbody>
<tr>
<td>Smoking</td>
<td>Height</td>
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<tr>
<td>Alcohol</td>
<td>Menarche</td>
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<tr>
<td>Weight</td>
<td>Menopause</td>
</tr>
<tr>
<td>First Pregnancy age</td>
<td>Age</td>
</tr>
<tr>
<td>Oral Contraceptives</td>
<td></td>
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</tbody>
</table>

LCIS
Lobular Carcinoma in-Situ
( NOT CANCER)

Options

- Surveillance
  - 30% risk in next 20 years
  - Risk factors additive (e.g., Family history)

- Prevention
  - BCT: NSABP P1 (13338 pts.)
    - tamoxifen vs. placebo
    - 49% cancer risk reduction
  - STAR: NSABP P2 (19000 pts.)
    - tamoxifen vs. evista (reloxifene)

- Prophylactic surgery
  - >90% reduction in the risk of getting and/or dying from cancer of the breast.*

* Hartmann NEJM 1999

Breast Cancer Types

- Invasive: Ductal vs. Lobular
- Non-invasive: DCIS (Ductal Carcinoma in-situ)
- Inflammatory Cancer

DCIS: Ductal Carcinoma in-Situ

DCIS: Presentation

Incidental
Mammographic Ca**
Palpable Mass
Nipple Discharge
Pagets Disease
DCIS: Facts and Figures

- From 1973-1996 incidence rates for DCIS have increased 7 times faster than for invasive ca.
- With aggressive screening non-invasive cancer accounts for 30% of the total breast cancers.

DCIS Incidence continues to rise (1975-2008)

Epidemiology of DCIS

- Ductal carcinoma in situ, precursor, non-invasive cancer
- Estimated incidence of DCIS: around 60,000 new cases annually
- Usually diagnosed by calculations on mammography in asymptomatic patients
- DCIS risk comprises over 20% of all mammographically detected breast cancer
- Nonobligate precursor of invasive cancer; rate and likelihood of progression are unknown

Invasive Breast Cancer
Historical Background

• 1889 – Halstead – radical mastectomy
  • Advanced disease
  • Includes pectoral muscles and extensive axillary dissection
• 1970s – modified radical mastectomy
  • Does not remove muscles
• 1980s – breast conservation
• 1990s – sentinel node biopsy

Breast Conservation Therapy (BCT)

- Requires multidisciplinary approach for best outcomes
  • Diagnostic imaging – define extent of disease
  • Surgery – excise disease with negative margins and assess nodal status
  • Pathology – margin assessment and node eval
  • Plastic surgery – optimal cosmesis/reconstruct
  • Medical oncology – systemic therapy

Surgery

• Segmental Mastectomy vs. Total Mastectomy
• Axillary Lymph Node Evaluation
  - sentinel lymph node biopsy and complete axillary dissection

Wire Localization
Wire localized Segmental Mastectomy

Clip localization

Savi clip  Savi Scout Probe

Lumpectomy Specimen Orientation

Ink Lumpectomy Specimen
Positive Margins Remain a Challenge

Despite significant advancements in Screening, Breast Conserving Surgery, Radiation and Medical Therapy, despite the advancements, positive margin rates remain high.

Clinical Need
Real-time identification of residual microscopic cancer and DCIS at the margins.

Clinical Challenge
Single DCIS duct or invasive cancer measuring down to 1mm in size.

Despite significant advancements in Screening, Breast Conserving Surgery, Radiation and Medical Therapy, Intra-Operative Margin Assessment has received little advancement and positive margin rates remain high.

MARGINPROBE®
Only FDA approved method for intraoperative margin assessment.
- Proprietary radio frequency (RF) based cancer detection algorithms, and databases enable detection of cancerous tissue.
- Identifies positive margins in real time - positive margins of excised lumpectomy specimens.
- Identifies residual microscopic disease at the margin enabling immediate surgical resection during initial surgery.
- Reduces likelihood of re-resection.

MARGINPROBE® Intraoperative Use
- Device used on excised tissue in operating room.
- All six margins evaluated.
- Surgeon covers each margin with 5-8 measurements.
- Margin indicated as positive if it has at least one positive measurement.

MARGINPROBE® Algorithm
- At the margin, we do not expect to find cancer tissue that fully covers the MARGINPROBE footprint. We expect to find only a tiny amount of residual cancerous tissue on a large background of normal tissue.
- Algorithm designed to provide binary output guiding surgeon to "take more tissue" if MarginProbe detects even small amount (1 mm) of residual cancer or DCIS, or "no need to take more tissue" if MarginProbe detects no cancer.

Pathology
Lumpectomy Serial Sections

lumpectomy
**lumpectomy**

*Hide surgical scar when feasible*

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**Mastectomy**

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**Modified Radical Mastectomy**

- Removes all the breast tissue including nipple and areola complex
- Includes full axillary dissection
- Indicated for operable advanced disease

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**Total or Simple Mastectomy**

- Removes all breast tissue and nipple areola complex
- Lymph nodes are not removed
- Used for ductal carcinoma in situ or prophylactic mastectomy

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**Prophylactic Mastectomy**

- Increased risk for contralateral cancer
  - High risk (LCIS, family history or genetic mutation)
- Patient preference
  - Desire for symmetry
  - High anxiety
- Bilateral – deleterious genetic mutation

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**Immediate Reconstruction**

- Early breast cancer
- Does not:
  - Compromise primary operation
  - Alter survival
  - Interfere with the detection and treatment of tumor recurrence
Implant or Tissue Expander Reconstruction

- Saline or Silicone
- Less surgery, short recovery
- No donor site morbidity

Nipple – Areolar Complex Sparing Mastectomy

- Subcutaneous mastectomy – removes breast tissue but preserves nipple and small amount tissue beneath nipple-areola
- Prophylactic mastectomy
- Early stage cancer (stage 0, 1 or 2)
- Tumor > 2.5 cm from nipple
- No microcalcifications extending to nipple
Axillary Dissection

Disadvantages of full dissection

Patient Complications

Sentinel Node Concept...

Sentinel Lymph Node Biopsy with Sub-areolar Blue Dye
Radiation Therapy

- Generally, 30 to 33 treatments over 6 weeks
- Treatment only to breast and/or local regional lymph nodal basins
- No systemic side effects (nausea, hair loss, etc)
- Side effects—may be “sunburn” type of skin reaction and fatigue (multiple trips for treatment)

Historical Perspective

Interstitial Radium Brachytherapy for Breast Cancer, 1917

Radiotherapy for Breast Cancer, London Hospital, c. 1917
Radiotherapy Treatment: Whole Breast XRT

Chemotherapy
- Usually more than one agent
- Typically 4 to 8 treatments, usually one treatment every 2 to 4 weeks as an outpatient
- Side effects: may have nausea/vomiting, hair loss (will grow back), increased risk of infections, anemia (low blood count), or dry skin
- Fatigue
- Fertility difficulties

Hormonal Therapy
- Tamoxifen- Estrogen receptor blocker
- Aromatase inhibitors- blocks the bodies fat cells from making estrogen
- LHRH analogs- blocks ovarian production of estrogen in premenopausal women

Adjunctive “Things” that may help
- Eat well balanced meals
- Exercise
- Gather knowledge- read
- Relaxation/ Stress Management techniques, massage, breathing exercises, meditation

The End