Breast Imaging Update

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Outline

• Breast cancer - the scope of the problem and who is at risk
• Breast cancer screening options - what is available and what is on the horizon
• Breast cancer screening recommendations - how to make sense of them
The Headlines

- “Shocking and unconscionable”
- “Incredibly flawed”
- “Will have deadly effects for women”
- “Countless American women will die needlessly”
- “Deliberate decisions to trade women’s lives for money”

November 17th, 2009 United States Preventative Services Task Force (USPSTF) new breast screening guidelines were released
U.S. Breast Cancer Facts
American Cancer Society 2011

• 230,480 new cases of invasive breast cancer
  – 28% of all cancer diagnoses in women
  – 57,650 cases of in situ breast cancer

• 39,520 breast cancer deaths
  – 15% of cancer deaths in women
Texas Breast Cancer Estimates for 2012

American Cancer Society 2012

• 15,050 women will be diagnosed with invasive breast cancer this year

• 2,650 women will die from breast cancer this year
Breast Cancer Incidence Trends


- 1980-1987: increased 4%/year
- 1987-1994: constant
- 1994-1999: increased 1.7%/year
  - increased screening, use of hormone replacement therapy (HRT), increased obesity rates, delayed childbearing
- 1999-2005: decreased 2.1%/year
  - Reduced use of HRT
  - Drop in mammography utilization
Breast Cancer Deaths

- 1975-1990: increased 0.4%/year
- 1990-1995: decreased 1.8%/year
- 1995-1998: decreased 3.2%/year
- 1998-2009: decreased 1.9%/year
  - Decline larger in women under age 50 years
  - Decrease likely due to earlier detection, improved treatment and decreased incidence
Lifetime probability of developing breast cancer is 12.15% (1 in 8)

Every woman’s risk is different
Breast Cancer Risk Factors

Relative risk >4.0

- Increasing age (>65)
- Known genetic risk factors
- Personal history of breast cancer
- Biopsy confirmed atypical hyperplasia
- Mammographically dense breasts
Age

Probability of developing cancer in next 10 years

- 20 year old: 1 in 1681 (0.06%)
- 30 year old: 1 in 232 (0.43%)
- 40 year old: 1 in 69 (1.45%)
- 50 year old: 1 in 42 (2.38%)
- 60 year old: 1 in 29 (3.45%)
- 70 year old: 1 in 27 (3.74%)
Genetic risk factors

• 5 to 10% of breast cancer patients have a hereditary form of the disease
• Genetic mutations BRCA-1 and BRCA-2
  – Lifetime breast cancer risk 36 to 85%
• Other disorders with increased risk
  – Ataxia-telangectasia (ATM), Li-Fraumeni (p53 and CHEK2), Cowden syndrome (PTEN), Hereditary diffuse gastric cancer syndrome (CDH1)
Breast Density

- The amount of fibroglanulardular parenchyma on a mammogram
- Mammogram reports describe density
  1. Almost entirely fat - <25% FG
  2. Scattered fibroglanulardular - 25-50% FG
  3. Heterogeneously dense - 51-75% FG
    Small lesions could be obscured
  4. Extremely dense - >75% FG
    May lower the sensitivity of mammography
Almost Entirely Fat
Heterogeneously Dense
Extremely Dense
Breast Density

- Breast cancer and breast parenchyma are both white
- Fat is nearly black
- The greater amount of fat, the easier it is to recognize a cancer
- Heterogeneously dense and extremely dense breasts can obscure a cancer, even a large cancer
Cancer in Fatty Breasts
Breast Density

• Cannot be predicted based on physical exam
  – Unrelated to breast size or consistency
• More common in younger women, during breast feeding, women using hormone replacement therapy
• 60% of women under 50, 40% of women in their 50s and 25% of women in their 60s have radiographically dense breasts
Breast Density

• Sensitivity and specificity reduced
  – Sensitivity 33 to 81%
  – False positives increased

• Breast density is a significant independent risk factor for breast cancer
  – 4-5x relative risk

• Texas law mandates patient notification concerning breast density – Henda’s Law
Henda’s Law (Texas House Bill 2102)

- Became effective September 1, 2011 and implemented by January 1, 2012
- The law states that the following information is to be conveyed (verbatim) by the mammography facility to each woman on completion of a mammogram in Texas:

“If your mammogram demonstrates that you have dense breast tissue, which could hide abnormalities, and you have other risk factors for breast cancer that have been identified, you might benefit from supplemental screening tests that may be suggested by your ordering physician.

Dense breast tissue, in and of itself, is a relatively common condition. Therefore, this information is not provided to cause undue concern, but rather to raise your awareness and to promote discussion with your physician regarding the presence of other risk factors, in addition to dense breast tissue.

A report of your mammogram results will be sent to you and your physician. You should contact your physician if you have any questions or concerns regarding this report.”
• The onus of providing the notice falls on the **mammography facility**, not with the physician. The ownership of the facility by a physician or physician group does not exempt the facility from the obligation.

• The goal is to inform a woman, so she is aware of her breast density and can thus have the opportunity to be proactive in her health care, if she so desires. This includes both screening and diagnostic examinations.

• The law leaves it to the **woman** to speak with her personal physician regarding the need and appropriateness of additional screening.
Breast Cancer Risk Factors

Relative risk 2.1 to 4

- Two first degree relatives with breast cancer
- High bone density (postmenopausal)
- High endogenous estrogen or testosterone levels
- Hx of high-dose radiation to chest
Breast Cancer Risk Factors

Relative risk 1.1-2.0

- Early menarche (<12 yrs)
- Late menopause (>55 yrs)
- Late first pregnancy (>30 yrs)
- No full-term pregnancies
- Never breastfed
- Hormone replacement therapy
- Obesity (postmenopausal)
- High socioeconomic status
- One 1\textsuperscript{st} degree relative with breast CA
- Personal history endometrial, ovarian or colon cancer
- Alcohol consumption
- Ashkenazi Jewish heritage
- Recent oral contraceptive use
- Height (tall)
Breast Cancer Prognosis

- Breast cancer is a progressive disease
- Early arrest of the disease improves survival
- Prognosis related to extent of disease
  - Localized-98% five year survival
  - Regional-84%
  - Distant-24%
  - Unknown-51%

Breast Cancer Prognosis

• Larger cancers more likely to metastasize
  – <1 cm - 10% spread to lymph node
  – 2 cm - 35%
  – 3 cm - 50%

• Median size of cancer found mammographically is 1-1.5cm
• Median size of cancer found at clinical breast exam 2-2.5 cm
Breast Cancer Screening

• Goal of screening is to reduce mortality
  – detect cancer early when treatment is more effective and has fewer morbidities
Early Detection

• Breast imaging
  – Mammography
  – Ultrasound
  – MRI
Mammography

• Mammography is the best screening tool available
  – Good sensitivity (90+%%) in fatty breasts
  – 80-90% sensitivity on average
  – Inexpensive
  – Widely available
Mammography

- Mammography is the only screening test which has been shown to reduce deaths due to breast cancer
  - 20-40% mortality reduction for women in the screened groups vs. control groups
Digital Mammography

• Improved breast cancer detection over analog (screen-film) mammography for:
  – Heterogeneously dense or extremely dense breasts (independent of age)
  – Women under 50
  – Pre- or perimenopausal women (LMP within 12 months of mammogram)

• Lower radiation dose

• No increase in false positive rate

• Expensive
Digital vs Screen-film mammography
Breast Ultrasound

• Diagnostic test for evaluation of mammographic and palpable abnormalities
  – Can differentiate cystic from solid (most of the time)
  – Characterize solid masses
  – Evaluate the axilla for metastatic disease
  – First exam for patients less than age 25 (at S&W)
Breast Ultrasound

• Screening ultrasound
  – No radiation, no compression
  – 29% increase cancer detection over mammography alone

• Not ready for widespread use
  – Low specificity, higher cost, lack of availability
  – Low sensitivity for calcifications of DCIS
  – High false positive rate = more bxs
Breast Ultrasound
Breast Ultrasound
Breast Ultrasound
Breast MRI

- Excellent tissue differentiation
- High sensitivity for breast cancer
- Not limited by breast density
- No ionizing radiation
Clinical applications of breast MRI

**Supported indications**
- Staging patient with recent breast cancer diagnosis
- Detection of occult, clinically-suspected cancer
- Screening certain high-risk populations
- Neoadjuvant chemotherapy monitoring
- Silicone implant evaluation

**Questionable indications**
- Characterizing indeterminate lesions seen on mammography or ultrasound
- Screening standard-risk population
Breast cancer staging

- MRI is the superior modality to determine tumor size, intraductal extension, chest wall invasion, nipple involvement
- Can identify multicentric tumors, contralateral tumors
  - May be present in 5-10% of patients
- Has important prognostic value and helps determine therapy
  - Especially in deciding breast-conserving therapy vs. mastectomy
Detecting occult cancer

• Breast MRI may be helpful in some patients with carcinoma of unknown primary
• If axillary adenopathy is a dominant feature (in women), then a breast carcinoma is likely
  – If mammogram is negative, MRI is indicated
  – Can help direct surgical therapy, if warranted
  – High negative predictive value for invasive cancer can preclude unnecessary mastectomy
High-risk screening

• MRI is helpful for screening in certain populations
  – Strong familial breast cancer history
    • May or may not have BRCA1 or BRCA2 mutations
    • Multiple first-order female relatives with breast carcinoma
    • Most supported indication for screening in literature
    • Should start early, typically by age 30 (peak incidence in BRCA1 carriers is age 40)
    • Typically performed in conjunction with mammography
      – Exception may be in BRCA1 carriers, increased radiosensitivity
High-risk screening

• MRI is helpful for screening in certain populations
  – Other high-risk populations
    • Personal history of breast carcinoma
    • Prior mediastinal radiation for Hodgkin’s disease
    • High-risk biopsy pathology
      – Lobular carcinoma in-situ
      – Atypical ductal/lobular hyperplasia
    • These indications are less-supported in literature
Important point

• MRI will detect lesions not seen on initial mammography or ultrasound
  – May perform second-look targeted ultrasound to detect up to 60% of these lesions
  – Necessitates the ability to perform MRI-guided biopsy
  – In general, an institution offering breast MRI should have the equipment and qualified radiologist to perform MRI-guided biopsy
Questionable indications
Indeterminate lesion characterization

• Generally, if a lesion is indeterminate on mammography or ultrasound, and does not fit into the criteria for a BI-RADS 3 lesion, then biopsy is recommended
  – NPV of MRI is good for invasive ductal carcinoma, but not high enough for other high-risk pathologies to serve in this capacity

• Does have value in determining scar vs. recurrent carcinoma in post-lumpectomy patients
Questionable indications
Standard risk screening

• Mammography sensitivity is reduced in women with dense breasts
• MRI clearly has greater sensitivity
• However, in the average risk population, the cost per cancer diagnosis may be prohibitively high, and will increase unnecessary biopsies
• Some insurance providers will cover this
Cancer in Dense Breasts
MRI Breast Cancer Screening

• Why not everyone?
  – Expense
  – Invasive procedure
  – Contraindicated in some patients
  – Lack of expertise and MRI availability
  – Low specificity results in excess biopsies and additional follow-up
Further Breast Imaging

- Breast scintigraphy
- Digital tomosynthesis
- Positron emission mammography (PEM)
- Computed Tomography (CT)
Breast Scintigraphy

- Molecular breast imaging (MBI), breast specific gamma imaging (BSGI), scintimammography
- Injection of radionuclide Tc99 Sestamibi
  - Radionuclide is taken up by cancers
  - Improved cancer detection in dense breasts
Breast Scintigraphy
Breast Scintigraphy

• High whole body radiation dose precludes use in screening
  – Dose may be reduced in future

• Problem solving tool
  – For uncertain clinical findings, mammogram, or ultrasound
  – For patients who cannot undergo MRI
Digital Breast Tomosynthesis

- Multiple low-dose, high-resolution images
- Dose similar to 2X screening mammogram
- Good for dense breasts
- Better sensitivity and characterization
- Lower recall rates
- Expensive, longer reading times, training
- Large clinical trials are underway
Digital Breast Tomosynthesis

Conventional Digital Image

Breast Tomosynthesis Image
Positron Emission Mammography

- Injection of fluorodeoxyglucose (FDG)
- Cancers take up FDG
- High specificity but lower sensitivity than MRI
- High radiation dose and expense preclude use in routine screening
- Assess extent of disease, response to treatment, evaluation for recurrence
Breast Computed Tomography

- Good resolution
- Improved patient comfort over mammography
- Higher radiation dose, expense and lack of availability makes widespread use unlikely
Breast Cancer Screening Recommendations

• American Cancer Society (ACS)
• United States Preventative Services Task Force (USPSTF)
Screening Guidelines ACS

- Women at average risk:
  - Ages 20 to 39
    - clinical breast examination at least every three years
  - Age 40 and over
    - annual screening mammography and clinical breast exam
  - Breast self-exam (BSE) is an option for women starting in their 20s
  - Elderly women
    - continue screening as long as woman is in reasonably good health and would be a candidate for cancer treatment
Screening Guidelines ACS

- Women at high (>20% lifetime) risk
  - Annual mammogram and MRI beginning at 30
- Women at moderate (15-20% lifetime) risk
  - Discuss with clinician the benefits and limitations of adding MRI to yearly screening
- Yearly MRI is not recommended for women with lifetime risk less than 15%
Screening Guidelines ACS
High Risk Patients

- Known BRCA1 or BRCA2 mutation
- First degree relative with BRCA1 or 2 and no testing themselves
- Radiation therapy to the chest between the ages of 10 and 30 yrs
- Have Li-Fraumeni, Cowden, or hereditary diffuse gastric syndromes, or a first degree relative with one of these syndromes
- Risk assessment tools > 20% lifetime
Screening Guidelines ACS Moderately Increased Risk

- Personal history of breast cancer, DCIS, lobular neoplasia, atypical ductal hyperplasia
- Have dense breasts at mammography
- Risk assessment tools 15-20% lifetime
Risk assessment tools

- Siteman Cancer Center’s Web site: yourdiseaserisk.wustl.edu
- National Cancer Institute’s Web site: cancer.gov/bcrisktool
- Gail and Claus Models
USPSTF Breast Cancer Screening Recommendations

- Against screening mammography before age 50
  - Decision to screen earlier is individual one
- Biennial screening mammography for women between the ages of 50 and 74
- Insufficient evidence for screening women 75 years and older
- Against teaching breast self-examination
- Insufficient evidence for clinical breast exam
- Insufficient evidence for digital mammography or MRI instead of film mammography for screening
USPSTF Recommendations

- No screening for women 40-49 years
  - Benefit of mortality reduction considered too small compared to harms of screening
- Biennial screening
  - Benefit of mortality reduction considered too small compared to harms of screening
- Recommendations based on meta-analyses of randomized controlled trials (RCT) and on computer generated models
USPSTF Analysis

• Based on review of RCTs
  – Screening mammography mortality reductions were
    • 15% for women in their 40s
    • 14% for women in their 50s
    • 32% for women in their 60s
USPSTF Recommendations

• Also noted “overdiagnosis” as potential drawback of screening mammography
• Statement does acknowledge there is no current, reliable method to stratify aggressiveness of cancers by imaging
Recommendation from American College of Radiology (ACR) and Society of Breast Imaging (SBI)

• Annual screening mammography beginning at age 40 for women at baseline risk of breast cancer
• Difference in position from USPSTF arises from methodology of supporting studies
Problems with USPSTF’s data

• USPSTF used metaanalysis of RCT’s with a fundamental flaw
  – The study groups consisted of women who were *offered* screening mammography, not those who *actually received* screening mammography.
    • Estimates are that only 70% of those offered mammograms receive them
  – The control groups consisted of women who were *not offered* screening mammography, not those who *did not receive* screening mammography.
    • Some women who were not offered screening mammograms may have opted to pursue it anyway
Problems with USPSTF’s data

• Resulted in an artificially diminished rate of early breast cancer detection and diminished estimate of improvements in morbidity and mortality from breast cancer
  – Even with these limitations, they estimated a 15% reduction in breast cancer death in women 40-49

• Also resulted in elevated survival numbers in the control (not offered screening) group, since some of these women were effectively screened, diagnosed and treated for breast cancer
ACR/SBI counterpoints

1. Benefit in breast cancer death reduction in women in their 40s grossly underestimated by USPSTF due to study design flaws
   - Population controlled studies from Sweden and British Columbia investigated those who actually received screening mammography
     - Sweden: 48% lower risk of breast cancer death
     - British Columbia: 39% lower risk of breast cancer death
ACR/SBI counterpoints

2. Vast majority of breast cancer deaths occur in women who have not received mammograms

- Massachusetts study:
  - 16% occur from cancers detected on mammogram
  - 10% occur from cancers not detected on mammogram
  - 70% occur in women who never had a mammogram

ACR/SBI counterpoints

• 3. Breast cancers occurring in younger women tend to be more aggressive
  – Preclinical, initially node-negative tumors that go on to have nodal disease within one year
  • 16% in women 40-49
  • 7% in women 50-59
  • 5% in women 60-69
ACR/SBI counterpoints

• 4. Annual screening mammograms lead to increased survival vs. longer intervals

Expected % of women with breast cancer whose lives will be saved by mammographic screening vs. no screening by age and interval

<table>
<thead>
<tr>
<th>Interval</th>
<th>40-49 yr. old</th>
<th>50-59 yr. old</th>
<th>60-69 yr. old</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>36%</td>
<td>46%</td>
<td>44%</td>
</tr>
<tr>
<td>2 year</td>
<td>18%</td>
<td>39%</td>
<td>39%</td>
</tr>
<tr>
<td>3 year</td>
<td>4%</td>
<td>34%</td>
<td>34%</td>
</tr>
</tbody>
</table>

ACR/SBI counterpoints

5. Screening in women older than 74 may be beneficial
   - USPSTF report noted insufficient evidence that screening mammograms improve survival after age 74
   - Studies they used did not invite women over age 74 to participate
   - Mortality benefit is seen 5-7 years after onset of screening
     • If there is reasonable expectation that a patient will survive this long, screening mammography is helpful
Summary

• Annual screening mammography beginning at age 40 has benefits
  – Incidence of cancer begins to rise in 40’s
  – Younger women may have more aggressive cancer
  – Effective treatments exist for early stage breast cancer

Breast Cancer Mortality

• Between 1990 - 2007 US breast cancer mortality has declined 2.2%/year
  – >30% reduction in mortality
  – Likely due to early detection and improved cancer treatment
  – % decline was larger among younger women
    • 3.2%/year for women <50
    • 2%/year for women >50
Conclusion

- Benefits of annual screening mammography beginning at age 40 outweigh the harms.
- New technologies are on the horizon.
- For now mammography is our best method for detecting small curable cancers in the general population.