Paradigm Shifts in Breast Cancer Treatment

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Assistant Professor of Surgery

May 7, 2016
Introduction

• Controversies that Challenge Current Paradigms in Breast Cancer:
  o Mammography screening
  o Surgical Treatment of DCIS
  o Sentinel Lymph Node Biopsy in Early Breast cancer
  o Genetics
The Mammography Debate

- **Why I Won't Get a Mammogram**
- **False Positive Findings**
- **Overdiagnosis & Overtreatment**
- **Mammogram Debate**

**New Breast Cancer Screening Guideline for women with average risk**

- **Age 40**
  - Talk with your doctor about when to begin screening. Women should have the opportunity to begin screening if they choose.

- **Age 45**
  - Begin yearly mammograms by age 45.

- **Age 55**
  - Transition to mammograms every other year at age 55 or continue with annual mammography, depending on your preferences.

- **Age 55+**
  - Continue to have regular mammograms for as long as you're in good health.
The Mammography Debate

• Screening Mammogram:
  o The only breast imaging modality shown by RCT to reduce breast cancer mortality

• The Debate: Who and How Often?
  o Depends on who you ask....
The Mammography Debate

• Society of Breast Imaging, American College of Radiology, American Congress of Obstetricians and Gynecologists
  o Average-risk women: start age 40, annually
  o No age when screening should end (“as long as in good health”)
  o Clinical breast exam: q 3 years for age 20s-30s and q year for age ≥ 40
• US Preventive Services Task Force (USPSTF)
  o Screening of average-risk women: start age 50y, q 2 yr
  o Screening should end at age 74
  o Breast self-exams have little value
ACS Screening Recommendations

• For women at average risk:
  o Start age 45.
  o Annual screening: ages 45 to 54.
  o Biennial screening: age ≥ 55 years but have the opportunity to continue screening annually.
ACS Screening Recommendations

- Opportunity to begin annual screening between the ages of 40 - 44 yr.

- Continue as long as overall health is good and life expectancy ≥ 10 yr.

- Clinical breast examination is not recommended.
ACS Screening Recommendations
Screening Recommendations

• Based on:
  o RCTs (8) – reporting on mortality
  o Observational studies (200+; 81 directly address effectiveness)
  o Meta-analyses
# Breast Cancer-Specific Mortality: RCT Findings

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Breast Cancer Mortality Reduction: RR (95% CI)</th>
<th>Deaths Averted With Screening 10,000 Women Over 10 Years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>39-49</td>
<td>0.92 (0.75-1.02)</td>
<td>3 (0-9)</td>
</tr>
<tr>
<td>50-59</td>
<td>0.86 (0.68-0.97)</td>
<td>8 (2-17)</td>
</tr>
<tr>
<td>60-69</td>
<td>0.67 (0.54-0.83)</td>
<td>21 (11-32)</td>
</tr>
<tr>
<td>70-74</td>
<td>0.80 (0.51-1.28)</td>
<td>13 (0-32)</td>
</tr>
<tr>
<td>75+</td>
<td>Not Reported</td>
<td>Unknown</td>
</tr>
<tr>
<td>50-69</td>
<td>0.78 (0.68-0.90)</td>
<td>13 (6-20)</td>
</tr>
</tbody>
</table>

No trials included women 75 years of age and older
ACS Screening Recommendations

• Age to Begin Screening: Why draw the line at age 45?

<table>
<thead>
<tr>
<th>Ages</th>
<th>5-yr Risk</th>
<th>Incident Breast Cancers</th>
<th>Breast Cancer Death Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-44</td>
<td>0.6%</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>45-49</td>
<td>0.9%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>50-54</td>
<td>1.1%</td>
<td>12%</td>
<td>11%</td>
</tr>
</tbody>
</table>
ACS Screening Recommendations

- RCT of Swedish women who started screening at 40 vs. those who did not

- Overall 29% mortality reduction:
  - Age 40-44 years: 18%
  - Age 45-49 years: 32%

## Breast Cancer Mortality

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ACS Screening Recommendations

- Age 40-44 years: 18% mortality reduction
  - No mammogram necessary?

- USPSTF: acknowledged that more women would die of breast cancer if regular screening does not begin until age 50

The net benefit of screening mammography in women:

- Aged 50 to 74 years is moderate.
- Aged 40 to 49 years, while positive, is small.
- Aged 75 and over: insufficient evidence.
Screening Interval: Annual vs. Biennial

- No trials compared different screening intervals

- 2 observational studies showed no difference in BC mortality with annual versus biennial or triennial screening

- Modeling best approach to estimate trade-offs gained with different intervals
Screening Interval: Annual vs. Biennial

• Swedish Two County Trial – Women 40-49 have higher rate of interval cancers

• 2009 & 2016 CISNET analysis (USPSTF)
  o More cancer deaths averted:
    ▪ annual compared with biennial screening for all age groups
    ▪ when screening began before age 50 y
Screening Interval

• Biennial screening maintained ~80% of the mortality benefit of annual screening

• Annual screening and earlier screening incurred higher rates of FALSE-POSITIVES
False-Positives

- False positive recall: 16% at first; 10% subsequent
- Start age at 40, cumulative probability of 1 false positive after 10 years:
  - 61% for annual screening
  - 42% for biennial screening
- Biennial screening: increase in the proportion of late-stage cancers

False-Positives

• Comparison mammograms halved the odds of a false positive recall

• False-positive rates are similar when women begin screening at age 50 yr vs. age 40

False-Positives

Why are there so many more false-positives in mammography compared to other imaging subspecialties?
What Is Normal?

Why are there so many more false-positives in mammography compared to other imaging subspecialties?
Real or Not Real?

FP

Superimposition
Real or Not Real?

Superimposition

FP
Real or Not Real?

Invasive Lobular Carcinoma
False-Positives

Benign & Malignant Features Overlap
Benign & Malignant Features Overlap

- Dense Fibrous Stroma
- Fibroadenoma
- Fibroadenoma
- Invasive Ductal Carcinoma
- Sclerosing Adenosis
False-Positives

• “Harms” of False-Positives:
  o Cost
  o Anxiety
  o Discomfort of compression
  o Radiation dose
Radiation Dose

• Dose of radiation from a screening mammogram = avg amount of radiation from natural surroundings over 7 weeks

<table>
<thead>
<tr>
<th>Natural background radiation in the US in one year</th>
<th>3 mSv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dose for a typical mammogram with 2 views of each breast</td>
<td>0.4 mSv</td>
</tr>
</tbody>
</table>
Weakness of ACS & USPSTF Recommendations

• Did Not Account For:
  
  o Morbidity, personal grief & financial costs of breast cancers diagnosed in later stages
  
  o Benefit of less invasive and less disfiguring therapy
What Do I Say to My Patient?

- Discuss the harm-benefit trade-off
What Do I Say to My Patient?

• Annual screening yields larger reduction in breast cancer mortality than biennial screening

• More frequent screening also results in higher rate of recalls and biopsies
The DCIS Debate

• Ductal Carcinoma In Situ (DCIS):
The DCIS Debate

• Current Treatment of DCIS:
  o Surgery
  o Radiation
  o Hormonal Therapy

• DCIS can recur, but it is not life-threatening
  o Are We Overtreating DCIS?
Doubt Is Raised Over Value of Surgery for Breast Lesion at Earliest Stage

“...it now appears that treatment may make no difference in outcomes..”

Kolata G, *NY Times* 2015
Breast Cancer Mortality After a DCIS Diagnosis

- Observational study: 108,196 DCIS patients
- Age < 70 (mean age 53)
- Lumpectomy or unilateral mastectomy
- Mean follow up 7.5 yrs
- 20-yr breast cancer specific mortality: 3.3%; risk of invasive recurrence 6%

Narod SA et al., JAMA Oncol 2015
Breast Cancer Mortality After a DCIS Diagnosis

• Comparison of risk of breast cancer death in DCIS cohort to risk in age-matched cohort in general US population:
  • Risk of breast cancer death in patients with DCIS 1.8 times greater than general population
  • Risk of breast cancer death decreased with increasing age

Narod SA et al., JAMA Oncol 2015
“Patients with DCIS had close to the same likelihood of dying of breast cancer as women in the general population, and the few who died did so despite treatment, not for lack of it…”

“…it now appears that treatment may make no difference in outcomes..”

Kolata G, *NY Times* 2015
DCIS: What are the facts?

• Non-obligate precursor to invasive breast cancer
• Progression to invasive cancer may never occur in some cases
• Some DCIS diagnosed by needle biopsy may harbor invasive breast cancer
• No reliable means of distinguishing DCIS from invasive cancer other than surgery
DCIS: What are the facts?

- Known clinical factors associated with recurrence
  - Young age
  - High grade
  - Presence of necrosis
  - Extensive or multifocal
  - ER/PR-negative, Her2+
  - Positive margins
DCIS: Can Individualized Therapy Be Improved?

- Which DCIS is more likely to progress to invasive cancer and pose a risk of death?
- Which DCIS is more amenable to active surveillance without treatment?
  - Multi-gene expression assays
  - Ongoing randomized trials
Multi-gene Assay for predicting DCIS recurrence

- DCIS Score (12-gene assay) to predict recurrence risk of DCIS
- Genes selected based on 21-gene assay (Oncotype Dx) developed to predict recurrence risk in invasive breast cancer

Solin LJ et al., JNCI 2013
Multi-gene Assay for predicting DCIS recurrence

• 327 patients with “low-risk” DCIS treated with lumpectomy \textit{without} radiation

• 12-gene assay to calculate DCIS Score
  • 3 risk categories: Low, Intermediate, High

• DCIS score was significantly associated with risk of recurrence

Solin LJ et al., \textit{JNCI} 2013
Multi-gene Assay for predicting DCIS recurrence

Solin LJ et al., JNCI 2013
Conclusions:
• Traditional clinical and pathological criteria alone are insufficient to define a low-risk population
• DCIS Score predicted 10-y risk of recurrence
• May have utility in identifying patients for whom radiation may be omitted

Solin LJ et al., JNCI 2013
Multi-gene Assay for predicting DCIS recurrence

• Can radiation be avoided for DCIS with low risk scores?

   Well, maybe…
Alternatives to Surgery to Treat DCIS?

• Can I Safely Avoid Surgery for DCIS?

• CALGB 40903: Multicenter Phase II trial of Neoadjuvant Letrozole for Postmenopausal Women with ER+ DCIS
Alternatives to Surgery to Treat DCIS?

Aromatase Inhibitors

- Anastrozole
- Letrozole
- Exemestane

Adrenal Hormones

- Cortisol
- Androstenedione
- Aldosterone

Estrone
- Testosterone

Estradiol

Aromatase inhibitors block post-menopausal estrogen production
Alternatives to Surgery to Treat DCIS?

• Endpoints:
  o Radiographic response on MRI
  o Mammographic extent of disease
  o Breast conservation
  o Complete pathologic response
60 y old asymptomatic female presented with calcifications on MMG

- PMH: none, LMP at age 50
- FH: maternal aunt with breast cancer
- Exam: negative
CALGB 40903 Trial

6.8cm
• Core Biopsy:
  o Ductal carcinoma in situ
  o Intermediate to high nuclear grade with necrosis
  o ER 3+, PR 3+, Her2-
DCIS spans 6.4 cm
After 6 Months of Letrozole

DCIS spans 4.8 cm
Pathology:

LEFT BREAST, LUMPECTOMY:

- Ductal carcinoma in situ (DCIS), intermediate to high nuclear grade without necrosis, measuring **2.8 cm**
- No invasive carcinoma is identified
Alternatives to Surgery to Treat DCIS?

- *First clinical trial evaluating potential role for medical management of DCIS*

- Institutional PI: Armando Giuliano, MD
- Trial nationwide recently met accrual goal of 115
Is Active Surveillance Safe for Low Risk DCIS?

- LORD study: Prospective randomized Phase 3 non-inferiority trial
  - Women age ≥ 45 with asymptomatic low-grade DCIS diagnosed by calcifications
  - Life expectancy of >5 years
  - Excluded: BRCA mutation carriers, hx of prior breast cancer, symptomatic patients

Elshof LE et al., *Eur J Ca* 2015
LOLD Study

Low-Risk DCIS

Standard Arm
n = 620

Surgery (WLE or MX)
+/- Radiotherapy
+/- Hormonal therapy

Annual Mammography
for a period of 10 years

Experimental Arm
n = 620

Active Surveillance

Annual Mammography
for a period of 10 years

Elshof LE et al., Eur J Ca 2015
LORD Study

• Endpoints:
  o 10-y Ipsilateral invasive breast cancer-free survival
  o Regional & distant metastases
  o Death from breast cancer

Elshof LE et al., *Eur J Ca* 2015
Is Active Surveillance Safe for Low Risk DCIS?

- LORIS trial
- Women age 46-70
- Low grade DCIS or intermediate grade with low grade features
- Diagnosis by core biopsy of asymptomatic calcifications

Francis A et al., Eur J Ca 2015
LORIS Trial

Patient presents with screen detected or incidental microcalcification

Local diagnosis of non-high grade DCIS

Obtain informed consent for Central Histopathology Review

REGISTER

Yes

Low risk DCIS confirmed by Central Histopathology Review?

No

End of participation

Obtain informed consent for randomisation

RANDOMISE

SURGERY ARM

Surgery

Annual mammograms for 10 years

All randomised patients to complete QoL Questionnaires until 5 years post-randomisation

ACTIVE MONITORING ARM

New ipsilateral abnormality detected - follow Investigation Algorithm

Annual mammograms for 10 years

Invasive disease or grade migration beyond entry criteria:
  • Treat as newly diagnosed with surgery +/- adjuvant therapy
  • Continue follow up

All randomised patients to be followed-up for a minimum of 10 years

Francis A, *Eur J Ca* 2015
LORIS Trial

Primary objective
- To assess whether Active Monitoring is non-inferior to surgery, in terms of ipsilateral invasive breast cancer free survival

Primary outcome measure
- Ipsilateral invasive breast cancer free survival time

Secondary outcome measures
- Time to development of ipsilateral invasive breast cancer
- Time to development of any invasive breast cancer
- Time to development of contralateral invasive breast cancer
- Overall survival
- Time to mastectomy
- Time to surgery
- Quality of Life (QoL)
- Quality-adjusted life years

Translational Exploratory assessment of predictive biomarkers

Francis A, *Eur J Ca* 2015
Sentinel Node Biopsy in Early Breast Cancer
Surgical Treatment of Breast Cancer

• Paradigm shift:
• Maximum tolerable treatment  
  Minimum necessary treatment
Sentinel Node Biopsy in Early Breast Cancer

If SLN has no cancer → No ALND

If SLN has cancer → ALND in select cases
### Morbidity of Axillary Surgery

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>SLNB Lymphedema</th>
<th>ALND Lymphedema</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP-B32</td>
<td>5611</td>
<td>7%</td>
<td>14%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SNAC</td>
<td>1080</td>
<td>2%</td>
<td>4%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ALMANAC</td>
<td>476</td>
<td>5%</td>
<td>13%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Veronesi</td>
<td>257</td>
<td>11%</td>
<td>69%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ACOSOG Z0011</td>
<td>891</td>
<td>6%</td>
<td>11%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Sentinel Node Biopsy in Early Breast Cancer

- Standard means to evaluate lymph nodes in patients with early invasive cancer
  - Provides staging information
  - Guides treatment recommendations
  - Lower axillary morbidity
Can We Challenge Current Paradigm?

• Shift in therapy recommendations
  o Now guided more by tumor biology

• Biomarker profile: ER, PR, Her2
Can We Challenge Current Paradigm?

• Does every patient with early breast cancer have to have SLN biopsy?
  
  o 75% have *no* cancer in SLN
  
  o SLN status less critical in determining treatment plan
Sentinel Node Biopsy in Patients Over Age 70

- Breast cancer in patients over age 70:
  - 33% of breast cancer
  - Less aggressive
  - ER+
  - Lower rates of recurrence
  - Less likely to have chemotherapy
• Challenges in treatment in age ≥ 70:
  o Optimize therapy
  o Account for effects of treatment on function
  o Life expectancy & co-morbidities
    • Age 70-74 avg. 3 comorbidities
    • Age 75-84 avg. 4 comorbidities
Axillary Treatment vs. No Axillary Treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Treatment Arms</th>
<th>Survival Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP-B04</td>
<td>1159</td>
<td>RM-TM/RT-TM</td>
<td>NS</td>
</tr>
<tr>
<td>CRCWP</td>
<td>2243</td>
<td>TM/RT-TM</td>
<td>NS</td>
</tr>
<tr>
<td>Manchester</td>
<td>1022</td>
<td>TM/RT-TM</td>
<td>NS</td>
</tr>
<tr>
<td>Glasgow</td>
<td>322</td>
<td>RT/Chemo-RT</td>
<td>NS</td>
</tr>
<tr>
<td>Stockholm</td>
<td>644</td>
<td>MRM/RT-MRM</td>
<td>NS</td>
</tr>
<tr>
<td>ACOSOG Z0011</td>
<td>891</td>
<td>SNB/ALND</td>
<td>NS</td>
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</tbody>
</table>
Sentinel Node Biopsy in Patients Over Age 70

- Extent of axillary surgery not shown to impact survival in early breast cancer
- SNB may contribute to unnecessary morbidity
Sentinel Node Biopsy in Patients Over Age 70

• CSMC review of 140 patients age ≥70:
  o Clinical T1-2N0 invasive breast cancer
  o Breast conservative surgery
  o *No* axillary surgery
  o Median follow-up 4.5 y

Chung A et al., *JAMA Surg* 2015
Sentinel Node Biopsy in Patients Over Age 70

- Only 5/140 (4%) breast cancer events:
  - 1 axillary recurrence
  - 4 deaths from breast cancer

- 5-y OS and BCSS: 70%, 96%

Chung A et al., JAMA Surg 2015
Sentinel Node Biopsy in Patients Over Age 70

Chung A et al., JAMA Surg 2015
**Sentinel Node Biopsy in Patients Over Age 70**

Comparison to 439 patients who had SNB

<table>
<thead>
<tr>
<th>Outcome at 5 y</th>
<th>SLNB</th>
<th>No SLNB</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional Recurrence</td>
<td>3.0%</td>
<td>1.8%</td>
<td>NS</td>
</tr>
<tr>
<td>Disease Free Survival</td>
<td>94.7%</td>
<td>96.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Cancer-Specific Survival</td>
<td>97.5%</td>
<td>98.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>90.7%</td>
<td>72.1%</td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>
Conclusions:

• Omission of SNB in patients with early breast cancer age ≥ 70 does not impact survival

• Deaths occur more commonly from causes other than breast cancer

Chung A et al., JAMA Surg 2015
Prospective Clinical Trial evaluating Safety of Omitting SLNB in patients age ≥ 70

• Hypothesis: Omission of SNB in women age ≥ 70 with early ER+ invasive breast cancer treated with BCS does not impact survival.

• Endpoints:
  o Locoregional recurrence
  o Disease-free survival
  o Breast Cancer Specific Survival
  o Overall Survival
Prospective Clinical Trial evaluating Safety of Omitting SLNB in patients age ≥ 70

• Eligibility Criteria:
  o Early invasive breast cancer
  o Breast conserving surgery
  o ER+
  o Hormonal therapy and radiation planned
• Patients will be monitored for recurrence
Prospective Clinical Trial evaluating Safety of Omitting SLNB in patients age ≥ 70

• Potential benefits:
  o Shorter operative time
  o Fewer surgical complications
  o Lower rates of pain, numbness, lymphedema
  o Lower costs
Prospective Clinical Trial evaluating Safety of Omitting SLNB in patients age ≥ 70

• Open to accrual November 16, 2015
• PI: Alice Chung, MD
• Contact: Parisa Mirzadeghan
Genetics
Genetics Timeline

• December 1990 Discovery of gene encoding DNA repair enzyme involved in genetic susceptibility to breast cancer by King Lab

• October 1994 Gene cloned by scientists at Univ of Utah, NIEHS, and Myriad Genetics

• Nov 2011 King Lab (University of Washington) publish series of proof of principal papers on use of next generation sequencing for identification of germline mutations

• March 2012 Ambry Genetics Laboratory first in industry to offer NGS cancer susceptibility panels
Genetics Timeline

• May 2013- NYT article Angelina Jolie, the “Jolie Effect” begins

Angelina Jolie's announcement of BRCA1 gene risk scare story
Genetics Timeline

• June 12, 2013 - Supreme court overturns BRCA patent

• June 12, 2013 –Ambry Genetics begins offering BRCA testing

• Multiple labs begin offering BRCA testing and despite numerous lawsuits by Myriad, additional labs continue to enter marketplace

• December 2014 Myriad lawsuit against Ambry – court ruled against Myriad

• Today most labs providing hereditary cancer testing almost exclusively do extended panel testing
Genetics

Walsh T et al PNAS Nov 1, 2011 vol 108
Walsh, T et al PNAS July 13 2010 vol 107
High Penetrance Genes

- **BRCA1/BRCA2**: 41-87% lifetime risk of breast cancer, up to 63% risk of CBC. Also significant risk of ovarian, pancreatic, melanoma, prostate cancers.

- **PTEN**: 25-45% risk of breast cancer along with risks for endometrial, non-medullary thyroid cancers

- **STK11**: 45-50% risk of breast cancer. Also colorectal, small bowel, pancreatic, gastric, cervical, ovarian, lung cancers.
High Penetrance Genes

- **TP53**: 70-77% develop cancer. In descending frequencies: breast, soft tissue sarcoma, brain, osteosarcoma, adrenocortical carcinoma

- **CDH1**: 39-52% lifetime risk for lobular breast cancer as well as high risk of diffuse gastric cancer

- All have NCCN Guidelines for clinical criteria, diagnostic testing and management recommendations
Intermediate Penetrance Genes

• Many of these, include (in order of importance): *PALB2*, *CHEK2*, *ATM*, *NBN*, *NF1*
• *RAD50*, *BRIP1*, *BARD1*

• These variants often must be interpreted in the context of the family history
  ◦ *PALB2*: lifetime risk of developing breast cancer is 58% by age 70 with a family history of breast cancer, 33% by age 70 without a family history of breast cancer

• Be aware of ancestry!
Low Penetrance Genes/Limited Evidence

- NBN, RAD50, BRIP1, BARD1, and NF1
- AKT1, FAM175A, FANCC, MRE11A, MUTYH, PIK3CA, RAD51C, RAD51D, RINT1, SDHB, SDHD, and XRCC2

- Currently do not have a definitive clinical association, but may prove to be clinically significant in the future
# Breast and Ovarian Management Based on Genetic Test Results

<table>
<thead>
<tr>
<th>Intervention required based on gene and/or risk level</th>
<th>Recommend Breast MRI (≥20% risk of breast cancer)</th>
<th>Discuss Option of RRM</th>
<th>Recommend/Consider RRSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, STK11, TP53</td>
<td>BRCA1, BRCA2, CDH1, PTEN, TP53, PALB2</td>
<td>BRCA1, BRCA2, Lynch syndrome, BRIP1, RAD51C, RAD51D</td>
<td>BRCA1, BRCA2, Lynch syndrome, BRIP1, RAD51C, RAD51D</td>
</tr>
<tr>
<td>Insufficient evidence for intervention</td>
<td>BRIP1</td>
<td>ATM, CHEK2, STK11</td>
<td>PALB2</td>
</tr>
</tbody>
</table>

**RRM**: risk-reducing mastectomy  
**RRSO**: risk-reducing salpingo-oophorectomy
Conclusions
Mammography screening is here to stay

Treatment of DCIS is evolving

Sentinel Node Biopsy in certain patients may become a procedure of the past

Growing panels of susceptibility genes for Breast Cancer
THANK YOU

ACKNOWLEDGEMENTS:
• Bruce Gewertz, MD
• Armando Giuliano, MD
• Margie & Robert E. Peterson Foundation
• Samuel Oschin Cancer Center Institute
• Donald Cohen, MD
• Ora Gordon, MD
• Margaret Taghavi, MD
• Saul & Joyce Brandman Breast Center
Surgeons, Staff and PATIENTS

“Man, you’ve got to try this ‘walking upright’ stuff! – it’s like a total paradigm shift!”