SURGICAL MANAGEMENT OF DUCTAL CARCINOMA IN SITU

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FINANCIAL DISCLOSURE

- Susan G. Komen for the Cure®
- European School of Oncology (ESO)
- Pan American Health Organization (PAHO)
- Sheikh Mohammed Hussein Al-Amoudi Center of Excellence in Breast Cancer
- American Society of Clinical Oncology (ASCO)
- Navidea Biopharmaceuticals
- GE Healthcare
- Sanofi-Aventis
DUCTAL CARCINOMA IN SITU

Outline

- Diagnosis and extent of disease evaluation
- Breast conservation vs. mastectomy
- Surgical margins and nipple-sparing
- Adjuvant radiation and endocrine therapy
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SCREENING MAMMOGRAM:
Cranio-Caudal (CC) View
U.S. FEMALE CANCER INCIDENCE RATES, 1973-2005

Age-adjusted Incidence Rate per 100,000 Females

- Breast
- Colon and Rectum
- Lung and Bronchus
- Uterine Corpus
- Non-Hodgkin Lymphoma
- Ovary

Year of Diagnosis

YEAR OF DIAGNOSIS

1982

“LOCAL” (NODE-NEGATIVE)

“REGIONAL” (NODE-POSITIVE)

NONINVASIVE (DCIS)
U.S. FEMALE CANCER DEATH RATES, 1930-2005

Age-adjusted Death Rate per 100,000 Females

Year of Death


- **Increased Screening**
- **Decreased Mortality**

1982 1990

Cancers:
- **Breast**
- **Colon and Rectum**
- **Stomach**
- **Ovary**
- **Uterus**
- **Pancreas**

INCREASED SCREENING
DECREASED MORTALITY
DIAGNOSTIC MAMMOGRAM:

Cranio-Caudal (CC) View
CORE NEEDLE BIOPSY:
IN SITU BREAST CANCER

DCIS with Comedo Necrosis
Vacuum Assisted Biopsy System
**NCCN Guidelines Version 1.2012**

**Breast Cancer**

**DIAGNOSIS**

- Ductal carcinoma in situ (DCIS)
- Stage 0
- Tis, N0, M0

**WORKUP**

- History and physical exam
- Diagnostic bilateral mammogram
- Pathology review
- Determination of tumor estrogen receptor (ER) status
- Genetic counseling if patient is high risk for hereditary breast cancer

**PRIMARY TREATMENT**

- Lumpectomy without lymph node surgery + whole breast radiation therapy (category 1)
- or
- Total mastectomy with or without sentinel node biopsy ± reconstruction
- or
- Lumpectomy without lymph node surgery without radiation therapy (category 2B)

DCIS-1
Ductal tree follows segmental distribution

Breast cancers often follow anatomy of ductal tree

Collateral circulation permits lumpectomy without necrosis
SEGMENTAL BREAST ANATOMY

- Going and Moffat, 2002 University of Glasgow
- 2mm serial sections of autopsied breast
- 3-D computer model reconstruction
- Segmental ductal anatomy observed

J Pathol. 2004;203(1):538-44
SEGMENTAL BREAST ANATOMY

- Sir Astley Cooper (1768-1841)
- Gross autopsy breast specimens
- Wax / mercury ductal injections
- Segmental ductal anatomy observed
BREAST CANCER PATTERNS: Disease Distribution Categories

- Localized
- Segmentally Extended
- Irregularly Extended

Amano et al., Breast Cancer Res Treat: 60:43, 2000
BREAST CANCER PATTERNS: Localized

Amano et al., Breast Cancer Res Treat: 60:43, 2000
BREAST CANCER PATTERNS: Segmentally Extended

Amano et al., Breast Cancer Res Treat: 60:43, 2000
BREAST CANCER PATTERNS: Irregularly Extended

Amano et al., Breast Cancer Res Treat: 60:43, 2000
BREAST CANCER PATTERNS:
Partial Mastectomy Selection

- Localized - lumpectomy
- Segmentally Extended - oncoplastic
- Irregularly Extended – mastectomy

Amano et al., Breast Cancer Res Treat: 60:43, 2000
MRI FOR EXTENT OF DISEASE: Additional Biopsies

111 consecutive women with 121 cancerous breasts
- Median age 48.7yrs; 50% had palpable disease
- Mammographic sensitivity 100% in fatty breasts

Biopsy before definitive surgery
- MRI: 145 additional biopsies: 66 were benign; 12 were atypical
- Mammography: 43 biopsies: 20 were benign; 6 were atypical
- Ultrasound: 93 biopsies: 42 were benign; 6 were atypical

Berg, et al., Radiology 233:830,2004
MRI FOR EXTENT OF DISEASE: Impact on Surgical Management

8.1% (95% CI, 5.9 –11.3) of all women eligible for breast-conserving surgery were treated with mastectomy because of MRI-only detection of additional disease.

Additional 5.5% (95% CI, 3.1–9.5) of women had more extensive surgery (wider excision or mastectomy) because of false-positive findings on MRI including 1.1% (95% CI, 0.3–3.6) who converted to mastectomy.

Houssami and Hayes, CA Cancer J Clin 59:290, 2009
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EVOLUTION IN CANCER TREATMENT

Potential for cure vs. Risk of Procedure
BREAST CONSERVING SURGERY

Pectoralis major

Latissimus dorsi

Incision
BREAST CONSERVING RADIATION THERAPY
BREAST CONSERVATION: Long-term validation

The New England Journal of Medicine

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION FOR THE TREATMENT OF INVASIVE BREAST CANCER

Bernard Fisher, M.D., Stewart Anderson, Ph.D., John Bryant, Ph.D., Richard G. MargoIese, M.D., Melvin Deutsch, M.D., Edwin R. Fisher, M.D., Jong-Hyeon Jeong, Ph.D., and Norman Wolmark, M.D.

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED STUDY COMPARING BREAST-CONSERVING SURGERY WITH RADICAL MASTECTOMY FOR EARLY BREAST CANCER

Umberto Veronesi, M.D., Natale Cascarini, M.D., Luigi Mariani, M.D., Marco Greco, M.D., Roberto Saccuzzi, M.D., Alberto Luini, M.D., Marisel Aguilar, M.D., and Ettore Marubini, Ph.D.
NSABP B-06: Effect of Lumpectomy v. Mastectomy on Recurrence

CUMULATIVE INCIDENCE

YEAR

All Patients

Node Negative

Node Positive

No. of patients / No. of recurrences

Lumpectomy: 570/210 361/121 209/89
Lumpectomy + XRT: 567/62 375/50 192/12
NSABP B-06:
Effect of Lumpectomy v. Mastectomy on Survival

DISTANT DISEASE-FREE SURVIVAL (%)

Cohort A  Cohort B  Cohort C

YEAR

No. of patients / No. of recurrences

Total Mastectomy: 692/265  569/233  494/192
Lumpectomy: 699/302  634/282  520/236
Lumpectomy + XRT: 714/278  628/253  515/204
**DIAGNOSIS**
- Ductal carcinoma in situ (DCIS)
  - Stage 0
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DCIS-1
AXILLARY NODE DISSECTION: Complication Rates

- Lymphedema
  - Acute: 40%
  - Chronic: 15-20%
- Paraesthesia: 40%
- Need for a drain: 100%
- Seroma formation: 10%
SENTINEL NODE CONCEPT
SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB, and IIIA T3, N1, M0

Clinical Stage I/II

Clinically node positive at time of diagnosis

FNA or core biopsy positive → Axillary dissection level I/II

FNA or core biopsy negative

Sentinel node negative

Sentinel node not identified

Sentinel node positive

Meets all of the following criteria:
- T1 or T2 tumor
- 1 or 2 positive SLNs
- Breast conserving therapy
- Whole breast RT planned
- No neoadjuvant chemotherapy

Consider no further surgery (category 1)

Yes to all

No

Clinically node negative at time of diagnosis

Sentinel node mapping and excision

Axillary dissection level I/II
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  or
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DCIS-1
241 mastectomy specimens dissected

Correlated pathologic-radiologic mapping

Residual carcinoma >2 cm from edge of primary tumor found in
- 29% without EIC
- 59% with EIC

Holland et al, JCO 8:113, 1990
## Known Distribution of Disease

### Table 1. Probability of Finding Cancer Remaining in the Breast After Simulated Local Excision Related to the Distance From the Edge of the Primary Tumor Exclusive of LCIS

<table>
<thead>
<tr>
<th>Distance From Edge of Primary Tumor</th>
<th>&gt; 0.5 cm</th>
<th>&gt; 2 cm</th>
<th>&gt; 4 cm</th>
<th>&gt; 6 cm</th>
<th>&gt; 8 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any residual carcinoma*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIC +</td>
<td>74%</td>
<td>59%</td>
<td>32%</td>
<td>21%</td>
<td>9%</td>
</tr>
<tr>
<td>EIC -</td>
<td>42%</td>
<td>29%</td>
<td>12%</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>( P = )</td>
<td>.00001</td>
<td>.00004</td>
<td>.0009</td>
<td>.01</td>
<td>.09</td>
</tr>
<tr>
<td>Invasive carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIC +</td>
<td>36%</td>
<td>20%</td>
<td>12%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>EIC -</td>
<td>19%</td>
<td>12%</td>
<td>7%</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>( P = )</td>
<td>.006</td>
<td>.14</td>
<td>.19</td>
<td>.68</td>
<td>.52</td>
</tr>
<tr>
<td>Intralymphatic carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIC +</td>
<td>18%</td>
<td>11%</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>EIC -</td>
<td>11%</td>
<td>7%</td>
<td>4%</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>( P = )</td>
<td>.18</td>
<td>.42</td>
<td>1.0</td>
<td>6.7</td>
<td>1.0</td>
</tr>
<tr>
<td>Intraductal carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIC +</td>
<td>71%</td>
<td>58%</td>
<td>32%</td>
<td>21%</td>
<td>8%</td>
</tr>
<tr>
<td>EIC -</td>
<td>28%</td>
<td>19%</td>
<td>5%</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>( P = )</td>
<td>&lt; .00001</td>
<td>&lt; .00001</td>
<td>&lt; .00001</td>
<td>.0001</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviation: LCIS, lobular carcinoma in situ.

Holland et al, JCO 8:113, 1990
SURGICAL MARGINS: DCIS – Residual Disease

Neuschatz, Cady et al, Cancer 94:1917, 2002
MARGIN STATUS IN DCIS

Substantial controversy exists regarding the definition of a negative pathologic margin in DCIS. Controversy arises out of the heterogeneity of the disease, difficulties in distinguishing the spectrum of hyperplastic conditions, anatomic considerations of the location of the margin, and inadequate prospective data on prognostic factors in DCIS.

Margins greater than 10 mm are widely accepted as negative (but may be excessive and may lead to a less optimal cosmetic outcome).

Margins less than 1 mm are considered inadequate.

With pathologic margins between 1-10 mm, wider margins are generally associated with lower local recurrence rates. However, close surgical margins (<1 mm) at the fibro glandular boundary of the breast (chest wall or skin) do not mandate surgical re-excision but can be an indication for higher boost dose radiation to the involved lumpectomy site (category 2B).
MARGIN STATUS IN DCIS

● Margins greater than 10 mm are negative.

● Margins less than 1 mm are considered inadequate.

● With pathologic margins between 1-10 mm, wider margins are generally associated with lower local recurrence rates.
Skin-Sparing Mastectomy

Slide Credit: K. Calhoun
Skin-Sparing Mastectomy

- Introduced in 1991: Toth & Lappert
- Preserve skin envelope
- Reconstruction options: Expander/implant
  - Tissue: DIEP/TRAM
  - Latissimus flap
- Equivalent cancer outcome
- Only 36% satisfied with nipple reconstructions

Slide Credit: K. Calhoun
Nipple-Sparing Mastectomy

Slide Credit: K. Calhoun
Nipple-Sparing Mastectomy

- Introduced in 2003: Gerber
- Preserves native nipple
- First used for risk reduction (prophylactic) mastectomies
- Nipple recurrence rare
  Only 1 reported NAC cancer recurrence with prophylactic mastectomy

Slide Credit: K. Calhoun
Nipple-Sparing Mastectomy

- Introduced in 2003: Gerber
- Preserves native nipple

USE WITH CANCER?
- Nipple involvement
- Patient selection
- Local recurrence risk

Slide Credit: K. Calhoun
Nipple-Sparing Mastectomy
Patient Selection

- T0 or T1/T2 (< 4.5 cm)
- Peripheral location
- Distance from NAC:
  - Total NAC: 1-2 cm
  - Nipple center: 4 cm
- Exclusions
  - Paget’s
  - Bloody nipple discharge
  - Skin retraction

Slide Credit: K. Calhoun
### Nipple-Sparing Mastectomy
### Nipple-Areolar Complex (NAC) Involvement

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Number Patients</th>
<th>NAC involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sookhan et al.</td>
<td>2008</td>
<td>18</td>
<td>0%</td>
</tr>
<tr>
<td>Voltura et al.</td>
<td>2008</td>
<td>36</td>
<td>5.9%</td>
</tr>
<tr>
<td>Petit et al.</td>
<td>2009</td>
<td>1001</td>
<td>5.8%</td>
</tr>
<tr>
<td>Jensen et al.</td>
<td>2011</td>
<td>99</td>
<td>14%</td>
</tr>
<tr>
<td>Filho et al.</td>
<td>2011</td>
<td>156</td>
<td>3.1%</td>
</tr>
<tr>
<td>Boneti et al.</td>
<td>2011</td>
<td>293</td>
<td>2.5%</td>
</tr>
<tr>
<td>Spear</td>
<td>2011</td>
<td>49</td>
<td>10%</td>
</tr>
</tbody>
</table>

*Slide Credit: K. Calhoun*
## Nipple-Sparing Mastectomy

### Tumor to NAC Distance

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Number Patients</th>
<th>Average Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sookhan et al.</td>
<td>2008</td>
<td>18</td>
<td>4.8 cm</td>
</tr>
<tr>
<td>Voltura et al.</td>
<td>2008</td>
<td>36</td>
<td>4.9 cm</td>
</tr>
<tr>
<td>Petit et al.</td>
<td>2009</td>
<td>1001</td>
<td>&gt; 1 cm</td>
</tr>
<tr>
<td>Gerber et al.</td>
<td>2009</td>
<td>246</td>
<td>2 cm</td>
</tr>
<tr>
<td>Filho et al.</td>
<td>2011</td>
<td>156</td>
<td>&gt; 1 cm</td>
</tr>
</tbody>
</table>
Nipple-Sparing Mastectomy
Nipple Margin Analysis

- Mandatory margin measurement:
  - Separate core of nipple base
  - Sharp dissection to avoid trauma

- Intraoperative assessment
  - Frozen section
  - Nipple removed if positive
  - False negative rates 1-3%

- Postoperative assessment
  - No false positives or negatives
  - Requires reoperation if positive

Slide Credit: K. Calhoun
<table>
<thead>
<tr>
<th>Study and Year</th>
<th>Patients</th>
<th>Total Recurrence</th>
<th>NAC specific</th>
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<tbody>
<tr>
<td>Sookhan et al., 2008</td>
<td>18</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Voltura et al., 2008</td>
<td>36</td>
<td>5.9%</td>
<td>0%</td>
</tr>
<tr>
<td>Gerber et al., 2009</td>
<td>246</td>
<td>10.4%</td>
<td>2.1% (n=1)</td>
</tr>
<tr>
<td>Petit et al., 2009</td>
<td>1001</td>
<td>1.4%</td>
<td>0%</td>
</tr>
<tr>
<td>Jensen et al., 2011</td>
<td>99</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Filho et al., 2011</td>
<td>156</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Boneti et al., 2011</td>
<td>293</td>
<td>4.6%</td>
<td>0%</td>
</tr>
<tr>
<td>Spear et al., 2011</td>
<td>49</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Nipple-Sparing Mastectomy
Surgical Approaches

“Optimizing the Total Skin Sparing Mastectomy”, Arch. Surg., 2008, L. Esserman
# Nipple-Sparing Mastectomy

## Nipple Viability

<table>
<thead>
<tr>
<th>Study and Year</th>
<th>Patient(s)</th>
<th>Nipple necrosis</th>
<th>Incision</th>
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</thead>
<tbody>
<tr>
<td>Sookhan et al., 2008</td>
<td>18</td>
<td>10%</td>
<td>Areolar/IMF</td>
</tr>
<tr>
<td>Petit et al., 2009</td>
<td>1001</td>
<td>5.5%- partial 3.5%- full</td>
<td>N/S</td>
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<tr>
<td>Jensen et al., 2011</td>
<td>99</td>
<td>6.3%</td>
<td>Lateral</td>
</tr>
<tr>
<td>Filho et al., 2011</td>
<td>156</td>
<td>0.2%</td>
<td>Lateral/periareolar</td>
</tr>
<tr>
<td>Boneti et al., 2011</td>
<td>293</td>
<td>2.1%</td>
<td>IMF</td>
</tr>
<tr>
<td>Spear et al., 2011</td>
<td>49</td>
<td>1.8%</td>
<td>Periareolar with lateral extension</td>
</tr>
</tbody>
</table>
Nipple-Sparing Mastectomy
Nipple Viability

Slide Credit: K. Calhoun
NIPPLE SPARING MASTECTOMY: University of Arkansas, 2011

- Retrospective Review 1998-2010
  - 293 patients underwent 508 procedures:
    - 281 TSSMs (nipple sparing) / 227 SSMs
    - 215 bilat operations / 78 unilat operations

- Comparable complication rates:
  - TSSM 7.1% [20 of 281]
  - SSM 6.2% [14 of 227] (p=0.67)

NIPPLE SPARING MASTECTOMY: University of Arkansas, 2011

- Retrospective Review 1998-2010
  - 293 patients underwent 508 procedures:
  - 281 TSSMs (nipple sparing) / 227 SSMs
  - 215 bilat operations / 78 unilat operations

- Comparable locoregional recurrence rates:
  - TSSM 6% [7 of 152]
  - SSM 5.0% [7 of 141] (p = 0.89)

NIPPLE SPARING MASTECTOMY: University of Arkansas, 2011

- Retrospective Review 1998-2010
  - 293 patients underwent 508 procedures:
    - 281 TSSMs (nipple sparing) / 227 SSMs
    - 215 bilat operations / 78 unilat operations

- Superior cosmesis with TSSM:
  - TSSM score 9.2 ± 1.1
  - SSM score 8.3 ± 1.9 (p=0.04)

NIPPLE SPARING MASTECTOMY: University of Arkansas, 2011

- Retrospective Review 1998-2010
  - 293 patients underwent 508 procedures:
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    - 215 bilat operations / 78 unilat operations

- AUTHORS’ CONCLUSION:
  - TSSM appears to be oncologically safe with superior cosmesis and can be offered to patients with stages I and II breast cancer

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### DIAGNOSIS

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  or
  
  Total mastectomy with or without sentinel node biopsy ± reconstruction
  
  or
  
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---

**DCIS-1**
BREAST CONSERVATION: Radiation Therapy Concepts

- Surgical lumpectomy: removes tumor bulk
- Radiation therapy after surgery: eradicates residual microscopic cancer
- POSTOPERATIVE RADIATION TREATMENT DECREASES LOCAL RECURRENCE RISK OF BREAST CANCER FROM 30-40% to 10%
LOCAL RECURRENCE WITH BCT

Huston and Simmons, *Amer J Surg* 189:229, 2005
### Table 3. Distribution by Pathologic Characteristics of DCIS and Hazard Rates of IBT According to Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lumpectomy</th>
<th></th>
<th>Lumpectomy + irradiation</th>
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<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. at risk</td>
<td>No. IBT</td>
<td>Hazard rate/100</td>
<td>No. at risk</td>
<td>No. IBT</td>
<td>Hazard rate/100</td>
</tr>
<tr>
<td>Nuclear grade</td>
<td></td>
<td></td>
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<td>No. at risk</td>
<td>No. IBT</td>
<td>Hazard rate/100</td>
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<td>Poor</td>
<td>128</td>
<td>22</td>
<td>5.62</td>
<td>147</td>
<td>10</td>
<td>2.09</td>
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<td>Good</td>
<td>146</td>
<td>16</td>
<td>3.08</td>
<td>152</td>
<td>5</td>
<td>0.90</td>
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<td></td>
<td>No. at risk</td>
<td>No. IBT</td>
<td>Hazard rate/100</td>
</tr>
<tr>
<td>Moderate/marked</td>
<td>123</td>
<td>24</td>
<td>6.48</td>
<td>131</td>
<td>7</td>
<td>1.63</td>
</tr>
<tr>
<td>Absent/slight</td>
<td>151</td>
<td>14</td>
<td>2.59</td>
<td>168</td>
<td>8</td>
<td>1.32</td>
</tr>
<tr>
<td>Unknown</td>
<td>15</td>
<td>2</td>
<td>5.49</td>
<td>17</td>
<td>1</td>
<td>1.97</td>
</tr>
<tr>
<td>Pathologic tumor size</td>
<td></td>
<td></td>
<td></td>
<td>No. at risk</td>
<td>No. IBT</td>
<td>Hazard rate/100</td>
</tr>
<tr>
<td>&lt;1.0 cm</td>
<td>236</td>
<td>32</td>
<td>4.11</td>
<td>263</td>
<td>14</td>
<td>1.54</td>
</tr>
<tr>
<td>≥1.0 cm</td>
<td>32</td>
<td>6</td>
<td>4.70</td>
<td>31</td>
<td>1</td>
<td>0.96</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lumpectomy margins</td>
<td></td>
<td></td>
<td></td>
<td>No. at risk</td>
<td>No. IBT</td>
<td>Hazard rate/100</td>
</tr>
<tr>
<td>Free</td>
<td>223</td>
<td>25</td>
<td>3.33</td>
<td>249</td>
<td>10</td>
<td>1.18</td>
</tr>
<tr>
<td>Uncertain/involved</td>
<td>51</td>
<td>13</td>
<td>8.09</td>
<td>50</td>
<td>5</td>
<td>2.68</td>
</tr>
</tbody>
</table>

Table 4. Adjusted Estimates of the Relative Risk of Second Ipsilateral Breast Tumors Related to Comedo Necrosis and Status of Lumpectomy Margins

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative risk</th>
<th>95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comedo necrosis*</td>
<td>1.94</td>
<td>1.12–3.36</td>
<td>0.019</td>
</tr>
<tr>
<td>Margin status†</td>
<td>2.33</td>
<td>1.32–4.12</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*Moderate/marked vs. absent/ slight, adjusted for margin status and treatment.
†Free vs. uncertain/involved, adjusted for comedo necrosis and treatment.

Table 5. Average Annual Hazard Rate of Second Ipsilateral Breast Tumor Related to Margins of Resection and Comedo Necrosis

| Specimen margins | Comedo necrosis     | Lumpectomy N = 274 | | | | Lumpectomy + irradiation N = 299 | | |
|------------------|---------------------|-------------------|---|---|---|-----------------|---|---|---|
|                  | No. at risk | No. of events | Avg. annual rate/100 | No. at risk | No. of events | Avg. Annual rate/100 |
| Free             | Absent/slight | 125 | 9 | 1.97 | 144 | 6 | 1.18 |
| Free             | Moderate/marked  | 98 | 16 | 5.44 | 105 | 4 | 1.18 |
| Uncertain/involved | Absent/slight | 26 | 5 | 5.95 | 24 | 2 | 2.10 |
| Uncertain/involved | Moderate/marked | 25 | 8 | 10.46 | 26 | 3 | 3.28 |

“Most clinical investigators now agree that local recurrences after lumpectomy for DCIS most likely reflect residual disease and further that the acceptance of minimally clear margins is inadequate for local control.”

David Page and Michael Lagios

Breast Cancer

**DIAGNOSIS**
- Ductal carcinoma in situ (DCIS)
  - Stage 0
  - Tis, N0, M0

**WORKUP**
- History and physical exam
- Diagnostic bilateral mammogram
- Pathology review
- Determination of tumor estrogen receptor (ER) status
- Genetic counseling if patient is high risk for hereditary breast cancer

**PRIMARY TREATMENT**
- Lumpectomy without lymph node surgery + whole breast radiation therapy (category 1) or
- Total mastectomy with or without sentinel node biopsy ± reconstruction or
- **Lumpectomy without lymph node surgery without radiation therapy (category 2B)**
THE INFLUENCE OF MARGIN WIDTH ON LOCAL CONTROL OF DUCTAL CARCINOMA IN SITU OF THE BREAST

MELVIN J. SILVERSTEIN, M.D., MICHAEL D. LAGIOS, M.D., SUSAN GROSHEN, PH.D., JAMES R. WAISMAN, M.D., BERNARD S. LEWINSKY, M.D., SILVANA MARTINO, D.O., PARVIS GAMAGAMI, M.D., AND WILLIAM J. COLBURN, M.D.

BREAST CONSERVATION: Van Nuys Scale and Margins

BREAST CONSERVATION: Van Nuys Scale and Margins

BREAST CONSERVATION: Van Nuys Scale and Margins

Probability of Freedom from Recurrence

Years after Diagnosis

Excision (n=93)
Excision + radiation (n=40)

P=0.92
Margins $\geq 10$mm

“If wide margins are obtained, regardless of other factors, the probability of local recurrence remains small. With greater than 10-mm margins, the probability of remaining recurrence free at 8 years is greater than 90% without postoperative radiotherapy.”

DUCTAL CARCINOMA IN SITU
Lumpectomy without XRT

● Prospective, single arm trial:
  - DCIS of predominant grade 1 or 2
  - Mammographic extent of 2.5 cm
  - Final margins 1 cm or re-excision without residual DCIS

● Trial closed July 2002 at 158 patients:
  - Thirteen pts local recurrence at 7 to 63 months
  - Ipsilateral local recurrence 2.4% per patient-year
  - 5-year recurrence rate 12% (10/13 in same quadrant)

Wong (Joint Centers), et al., JCO 24:1031, 2006
DUCTAL CARCINOMA IN SITU
Multidisciplinary Selection

10 yr single institution experience
- Group 1: ≥5-mm margin and received radiation
- Group 2: ≥10-mm margin and received no radiation

152 patients (153 cancers); median F/U 8.2 years
- Overall, 6 recurrences (3.92%);
  - 1 of 71 recurred in group 1 (1.40%)
  - 5 of 82 recurred in group 2 (6.01%).

CONCLUSION: A subgroup of DCIS patients can be identified in which radiation can be safely avoided.

CANCER PREVENTION
METHODS

Prophylactic surgery
Chemoprevention
Behavior modification

FUTURE: Gene therapy?
BCPT SCHEMA

ELIGIBLE PARTICIPANTS

RANDOMIZATION (n=13,388)

TAMOXIFEN 5 YEARS (n= 6681)

PLACEBO 5 YEARS (n = 6707)
Invasive Breast Cancer

<table>
<thead>
<tr>
<th></th>
<th>Events</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>175</td>
<td>43.4</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>89</td>
<td>22.0</td>
</tr>
</tbody>
</table>

P < 0.00001

NSABP
Noninvasive Breast Cancer

<table>
<thead>
<tr>
<th>Events</th>
<th>Rate /1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>69</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>35</td>
</tr>
</tbody>
</table>

Rate /1000

YRS.0 1 2 3 4 5

P < 0.002

Placebo
Tamoxifen

NSABP
### P-2 STAR

**Cumulative Incidence of Invasive Breast Cancer**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>At Risk by Year</th>
<th># of Events</th>
<th>Rate/1000 at 6 yrs.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen</td>
<td>9726 6653 809</td>
<td>163</td>
<td>25.1</td>
<td>0.83</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>9745 6703 833</td>
<td>168</td>
<td>24.8</td>
<td></td>
</tr>
</tbody>
</table>

**Graph Details**

- **Y-axis:** Cumulative Incidence (per 1000)
- **X-axis:** Time Since Randomization (months)
- **Legend:**
  - Circle (Tamoxifen) 9726 6653 809
  - Triangle (Raloxifene) 9745 6703 833

**Legend:**

- **0 3 6 Events at 6 yrs.**
- **P-value**
P-2 STAR
Cumulative Incidence of Invasive Breast Cancer

<table>
<thead>
<tr>
<th>Treatment</th>
<th>At Risk by Year</th>
<th># of Events</th>
<th>Rate/1000 at 6 yrs.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen</td>
<td>9726 6633 805</td>
<td>57</td>
<td>8.1</td>
<td>0.052</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>9745 6667 828</td>
<td>80</td>
<td>11.6</td>
<td></td>
</tr>
</tbody>
</table>

Cumulative Incidence (per 1000)

Time Since Randomization (months)
P-2 STAR
Average Annual Rate and Number of Invasive Breast Cancers

Av Ann Rate per 1000

<table>
<thead>
<tr>
<th></th>
<th>Gail Model Projection</th>
<th>TAM</th>
<th>Raloxifene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av Ann Rate per 1000</td>
<td>312*</td>
<td>163</td>
<td>168</td>
</tr>
</tbody>
</table>

* # of events
P-2 STAR
Average Annual Rate And Number Of Non-invasive (In Situ) Cancers

Relative risk = 1.40
95% Confidence Interval: 0.98 to 2.00

Av Ann Rate per 1000

2

3

Relative risk = 1.40
95% Confidence Interval: 0.98 to 2.00

Av Ann Rate per 1000

1

2

3

TAM

80

Raloxifene

57*

* # of events
DCIS POSTSURGICAL TREATMENT

Risk reduction therapy for ipsilateral breast following breast conserving surgery:

Consider tamoxifen for 5 years for:
• Patients treated with breast-conserving therapy (lumpectomy) and radiation therapy (category 1), especially for those with ER-positive DCIS. The benefit of tamoxifen for ER-negative DCIS is uncertain
• Patients treated with excision alone

Risk reduction therapy for contralateral breast:
• Counseling regarding risk reduction

See also NCCN Breast Cancer Risk Reduction Guidelines

SURVEILLANCE/FOLLOW-UP

• Interval history and physical exam every 6-12 mo for 5 y, then annually
• Mammogram every 12 mo (and 6-12 mo postradiation therapy if breast conserved [category 2B])
• If treated with tamoxifen, monitor per NCCN Breast Cancer Risk Reduction Guidelines

DCIS-2
DUCTAL CARCINOMA IN SITU

Summary 1

- Minimally invasive percutaneous sampling should be used initially to make DCIS diagnosis.
- The extent of disease is the primary determinate of candidacy for breast conservation surgery.
- Standard imaging (mammo/US) should be used for EOD work-up; the role of MRI is controversial.
- SLN biopsy should be considered with mastectomy, in the event occult invasive cancer is found.
- The role of nipple-sparing mastectomy for DCIS is controversial, because patient selection is unclear.
DUCTAL CARCINOMA IN SITU
Summary 2

- Surgical margins for DCIS are a concern because of known residual disease and local recurrence risk.
- Oncoplastic techniques can assist in the resection of segmentally distributed cancers.
- Radiation therapy helps compensate for narrow (but not positive) surgical margins.
- Patient selection for lumpectomy alone (no XRT) is challenging and significant disagreements abound.
- Endocrine therapy reduces risk recurrence of ER+ DCIS, and may help patients who forego XRT.
Skin bridge at seroma cavity is too narrow (2mm) for accelerated partial breast irradiation (APBI)
RIGHT 9 O’CLOCK KNOWN IDC

RIGHT LEVEL 1 AXILLA KNOWN METASTATIC LAN

SLIDE CREDIT: Wendy Demartini

LEFT 3 O’CLOCK NMLE 23 MM MRI BX = DCIS