10 March 2012

Controversial Issues In the Surgical Management of Early-Stage Breast Cancer

Nipple Sparing Mastectomy

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Memorial Sloan-Kettering Cancer Center
Key Facts in This Case

- Patient has DCIS
- Patient has known deleterious BRCA1 mutation
What Type of Mastectomy for DCIS?

- Conventional
- Skin sparing
- Nipple sparing
Outcome of Mastectomy in DCIS

Metaanalysis: 21 studies
1574 patients

Local Recurrence: 1.4% (0.7 – 2.1%)

Boyages, Cancer 1999;85:616
<table>
<thead>
<tr>
<th>Author</th>
<th>No. of Cases</th>
<th>Mean f/u (mo)</th>
<th>% LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubio</td>
<td>95</td>
<td>44</td>
<td>3.1</td>
</tr>
<tr>
<td>Slavin</td>
<td>26</td>
<td>45</td>
<td>3.8</td>
</tr>
<tr>
<td>Spiegel</td>
<td>44</td>
<td>118</td>
<td>0</td>
</tr>
<tr>
<td>Greenway</td>
<td>28</td>
<td>49</td>
<td>0</td>
</tr>
<tr>
<td>Carlson</td>
<td>223</td>
<td>82</td>
<td>3.1</td>
</tr>
</tbody>
</table>
What About Nipple Sparing Mastectomy?

Concerns

• NSM leaves behind ductal tissue + breast tissue in order to preserve blood supply.

• Occult nipple involvement present in 6-31% of cancers.

• Most studies of NSM are in invasive cancer.
Outcomes of NSM

Assessing outcomes is difficult due to:

- Heterogeneity of inclusion criteria
- Variable surgical technique
- Retrospective studies
- Under-reporting of complications
- Small numbers

This Is Not Standard Practice
Concerns in NSM

- Occult cancer retained in NAC
- New cancer developing in retained breast tissue
What Is the Risk of Nipple Involvement with Carcinoma?

- Older reports range from 0-58%.
- Studies prior to era of BCT likely underestimate risk of nipple involvement since patients undergoing mastectomy today often have extensive disease precluding BCT.
What Is the Incidence of Occult Nipple Involvement with Carcinoma?

- Prospective study 316 consecutive mastectomy specimens at MGH
- Nipples grossly normal
- Multiple histologic sections
- 232 therapeutic mastectomies
  - Median age 55 yrs, 62% postmenopausal
- 84 prophylactic mastectomies
  - Median age 46 yrs

Brachtel EF, JCO 2009;27:4948
What Is the Incidence of Occult Nipple Involvement with Carcinoma?

Median distance tumor → nipple: 4 cm

21% involved with invasive ca or DCIS

62% of involved nipples had DCIS

Brachtel EF, JCO 2009;27:4948
# Predictors of Nipple Involvement

## Multivariate analysis

<table>
<thead>
<tr>
<th>Feature</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T size</td>
<td>.0126</td>
</tr>
<tr>
<td>Tumor — nipple distance</td>
<td>.0176</td>
</tr>
<tr>
<td>HER amplification</td>
<td>.0047</td>
</tr>
</tbody>
</table>

Brachtel EF, JCO 2009;27:4948
Can Nipple Involvement Be Predicted by Frozen Section of Subareolar Tissue?

n = 45 involved nipples

36/45 subareolar tissue contained cancer
9/45 only nipple involved

Sensitivity = 80%  NPV 96%

Brachtel EF, JCO 2009;27:4948
Intraoperative Assessment of Nipple Margin

- Nipple involvement on final pathology in 2.8-20% of patients selected based on T size, distance from nipple.

- Frozen section false-negative rates 1-3% in smaller studies.

- Petit (n = 1001) false-negative rate 8.6%

Can MRI Better Predict Nipple Areola Involvement?

<table>
<thead>
<tr>
<th></th>
<th>Overall (125 pts)</th>
<th>Invasive ca (67 ID 17 IL)</th>
<th>DCIS (41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>57%</td>
<td>75%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Specificity</td>
<td>85.5%</td>
<td>86.1%</td>
<td>84.4%</td>
</tr>
<tr>
<td>Positive PV</td>
<td>44.4%</td>
<td>47.4%</td>
<td>37.5%</td>
</tr>
<tr>
<td>Negative PV</td>
<td>90.8%</td>
<td>95.4%</td>
<td>75%</td>
</tr>
</tbody>
</table>

Sacchini V, 2011
Is the Retained NAC at Risk for Future Cancer Development?

- 15/62 (24%) NACs in BRCA1/2 carriers had TDLUs.
- Only one-third of these were in the nipple papilla.

Reynolds C, Ann Surg Oncol 2011;18:3102
Oncologic Concerns

• Retained NAC is not the only risk factor for local recurrence.

• Exposure is more difficult than with SSM increasing the risk of residual breast tissue.
### Clinical Outcomes NSM
European Institute of Oncology 3/02-12/07

Median f/u: 50 months
All patients received 16 Gy to NAC

<table>
<thead>
<tr>
<th></th>
<th>Invasive Cancer</th>
<th>DCIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># Cases</strong></td>
<td>772</td>
<td>162</td>
</tr>
<tr>
<td><strong>5yr LR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>3.6%</td>
<td>4.9%</td>
</tr>
<tr>
<td>NAC</td>
<td>0.8%</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

*CAUTION: At 20 mo f/u, no NAC recurrences, 1.4% LR*

Petit JY, Ann Oncol 2012 (Epub ahead of print)
Petit JY, Br Ca Res Treat 2009;117:333
Recurrence in the NAC

- 5/6 recurrences in invasive cancer had an EIC.
- 5/6 invasive cancers overexpressed HER2.
- 64% of NAC recurrences were Paget’s disease.

Lohsiriwat V, Ann Surg Oncol 2012 (Epub ahead of print)
Prophylactic NSM

- Cancer in NAC rare.
- Subsequent breast cancer uncommon, but:
  1) Follow-up is short
  2) Limited experience very high-risk women (BRCA carriers)
Non-Oncologic Issues

- Nipple necrosis
- Nipple sensation
- Cosmetic outcome
NIPPLE AND AREOLA COMPLICATIONS

Partial Necrosis (1/3 involvement)
14/205 (6.6%)

Partial Necrosis (2/3rd involvement)
4/205 (1.9%)

Total Necrosis requiring excision
3/205 (1.5%)
Factors Predicting Nipple Necrosis

<table>
<thead>
<tr>
<th><strong>Patient</strong></th>
<th><strong>Technical</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (usually older)</td>
<td>Thin areolar flap</td>
</tr>
<tr>
<td>Smoking</td>
<td>Circumareolar incisions</td>
</tr>
<tr>
<td></td>
<td>Flap or permanent implant reconstruction</td>
</tr>
</tbody>
</table>

Algaithy ZK, Eur J Surg Oncol 2012;38:125
Rusby JE, Br J Surg 2010;97:305
Nipple Sensation

Scale 0-10

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Petit</td>
<td>414</td>
<td>2.0</td>
<td>Yueh</td>
<td>17</td>
</tr>
<tr>
<td>Yueh</td>
<td>17</td>
<td>2.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sensation present

- 15% at 1 year
- Denewer: 37/41
- Nahabedian: 6/14 ↓ quality
Cosmetic Satisfaction

- Rates of satisfaction among small patient samples are high.
- Whether cosmetic satisfaction is improved over SSM + nipple reconstruction cannot be determined from existing data.
Prospective Evaluation NSM: MDACC

54 NSM, 33 patients
37 prophylactic

NAC necrosis: Partial 20.4%, Total 7.4%

Cosmetic Outcome

<table>
<thead>
<tr>
<th></th>
<th>Breast</th>
<th>NAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable</td>
<td>73%</td>
<td>55.8%</td>
</tr>
<tr>
<td>Poor</td>
<td>13.5%</td>
<td>28.8%</td>
</tr>
<tr>
<td>Unacceptable</td>
<td>13.5%</td>
<td>15.4%</td>
</tr>
</tbody>
</table>

Wagner JL, Ann Surg Oncol 2011
Trends in NSM at MSKCC

n = 353
(3.9% of all mastectomies)

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of NSMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000–02</td>
<td>7</td>
</tr>
<tr>
<td>2003–04</td>
<td>24</td>
</tr>
<tr>
<td>2005–06</td>
<td>59</td>
</tr>
<tr>
<td>2007–08</td>
<td>88</td>
</tr>
<tr>
<td>2009–10</td>
<td>175</td>
</tr>
</tbody>
</table>
MSKCC Experience NSM

Patient Characteristics

**Therapeutic**  $n = 157$
- 21% DCIS
- 75% of invasive cancers Stage I
- Median T size 1.1 cm
- Positive nodes 5.5%

**Prophylactic**  $n = 79$
- Known BRCA1  20%
- Known BRCA2  8%
- Occult DCIS  8 cases, invasive 3

Median f/u 10 months — no local recurrence

Nipple Sparing Mastectomy

Inferior Incision
Bilateral Nipple Sparing Mastectomy

Inferior Incision
Lateral Breast Excision

Partial Necrosis of Left Nipple
Current NSM Experience MSKCC

353 NSM, 200 patients
196 prophylactic

OR debridement skin necrosis: 3.3%  NAC necrosis: 0.2%
Implant loss: 1%
Infection: 2%

de Alcantara-Filho P, Ann Surg Oncol 2011;18:3117
Other Questions

• Is there an indication for RT?
  Data-free zone, but RT does not prevent the development of new cancers
  Standard indications for PMRT

• Can imaging evaluate residual breast tissue?
  Data-free zone
  Low sensitivity for nipple involvement
  preop, unlikely to be beneficial postop
Conclusions

• The literature on NSM does not allow firm conclusions regarding oncologic safety or superiority of cosmetic outcomes.

• The risk of subsequent cancer after prophylactic NSM in BRCA mutation carriers is unknown.
Conclusions

- Sensation, erectile function, and pigmentation of the NAC are altered after NSM.
- Extent of alteration may be related to amount of breast tissue preserved.
Conclusions

• High-quality studies and long-term follow-up are sorely needed.

• NSM is an option for highly selected patients with favorable cancers, but is NOT the standard of care at this time.

• Patient education regarding risks, uncertainties, and nipple alteration is critical.
MSKCC NSM Criteria  
(Adopted 2011)

**Absolute contraindications**
- Clinical suspicion of nipple involvement
- DCIS, invasive cancer or unsampled indeterminate calcifications < 1-2 cm from the nipple
- T4, T3, T2 > 3 cm
- Extensive DCIS necessitating mastectomy

**Relative**
- Recurrent carcinoma (invasive or DCIS) after BCS + RT
What do I really think about NSM?

It’s a great operation for a woman who doesn’t actually need a mastectomy.
MÓDULO
TRATAMENTO LOCAL

MODERADOR
RUFFO FREITAS JR.

DISCUSSÃO