Nipple Sparing Mastectomy

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BAPTIST HEALTH SOUTH FLORIDA

History

- Halsted’s radical mastectomy
- Modified radical mastectomy
- Skin sparing mastectomy
- Breast conserving surgery
- Nipple sparing mastectomy
  - Rise in genetic testing
  - Prophylactic surgery
  - “Angelina Jolie” effect

Technique

NSM is performed with the aim of removing all glandular breast tissue while leaving the NAC viable and intact

- Infiltration of the retroareola tissue with 10 mL saline
- Nipple delay procedure
- Separate nipple margin removed
- Immediate breast reconstruction
Nipple reconstruction vs NSM

• BRCA1/2 mutation carriers and high risk patients undergoing prophylactic mastectomy
• Breast conservation candidates that desire mastectomy
• Small, peripheral tumors
Contraindications

- Absolute
  - Skin or nipple involvement with tumor
  - Central tumors close to the nipple-areola complex
  - Blood-stained nipple discharge

- Relative
  - Diffuse calcifications
  - Tumor distance <2cm from nipple on imaging
  - Locally advanced disease requiring neoadjuvant chemotherapy
  - Smoking history
  - Larger breast size
  - Ptosis

Would you offer this patient NSM?

- 42 yo F presenting with suspicious microcalcifications bilaterally on screening MMG
  - R breast: DCIS, high grade, with comedo-type necrosis
  - L breast: ADH, proliferative fibrocystic changes
- Pt asking for bilateral nipple sparing mastectomy
- Final pathology- Invasive ductal carcinoma arising in association with high grade DCIS with an extensive intraductal component and DCIS involving the nipple ducts

Considerations & Complications

- Small incision, technically challenging
- Limited exposure, risk leaving breast tissue behind
- Traction injury
- Compromise of blood supply

- Skin desquamation
- Skin flap necrosis
- Nipple-areola complex necrosis
- Infection

Matsen et al. ASO 2015
• S/P bilateral prophylactic mastectomy in a BRCA+ patient
• Ultimately, the nipple was removed

Nipple-areola complex necrosis

Skin Flap Necrosis After Mastectomy With Reconstruction: A Prospective Study

• Of 606 consecutive procedures, 85 (14%) had some level of skin flap necrosis
• NSM was associated with higher rates of necrosis at every level of severity
• Other significant factors for moderate or severe necrosis included BMI, DM, specimen size, and expander size

Total Skin-Sparing Mastectomy in BRCA Mutation Carriers
Anne Warren-Peled, MD, Chetan S. Irwin, MD, E. Shelley Hwang, MD, Cheryl A. Ewing, MD, Michael Alvarez, MD, and Laura J. Esserman, MD

• 53 BRCA+ pts underwent bilateral NSM for prophylactic (n=26) or therapeutic (n=27) indications from 2001-2011, mean f/u was 51 mos and 37 mos for prophylactic and therapeutic groups respectively
  - Cases were age and stage matched with non-BRCA+ pts
  - Outcomes: NAC involvement, new breast cancer in pts who had prophylactic surgery, LRR in pts who underwent therapeutic surgery

<table>
<thead>
<tr>
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<th>Prophylactic, BRCA+ N=26</th>
<th>Prophylactic, BRCA- N=26</th>
<th>Therapeutic, BRCA+ N=27</th>
<th>Therapeutic, BRCA- N=27</th>
</tr>
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<tbody>
<tr>
<td>Cancer in NAC</td>
<td>1 (1.9%)</td>
<td>2 (3.8%)</td>
<td>0</td>
<td>2 (3.7%)</td>
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<tr>
<td>LRR</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>1 (3.7%)</td>
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NSM cases from June 2007-Dec 2012

- PT and tumor characteristics, complications, and recurrences collected
  - NSM performed on 645 breasts in 370 pts
  - 24 (3.7%) breasts had nipples removed as a result of a positive subareolar margin
  - LRR occurred in 4/156 (2.6%) breasts operated on for cancer at 22 mos f/u; none involved the nipple
  - The 4 local recurrences all occurred in cancer patients with gene mutations (2 pts with p53 mutations, 2 pts with BRCA1 mutations)

Increasing Eligibility for Nipple-Sparing Mastectomy
Suzanne B. Coopey, MD, Rong Tang, MD, Lan Lei, MD, Phoebe E. Freer, MD, Kari Kansal, MD, Amy S. Colwell, MD, Michele A. Gadd, MD, Michelle C. Specht, MD, Williams O. Senter J, MD, and Barbara L. Smith, MD, PhD

- 177 NSMs performed in 89 BRCA mutation carriers between Sept 2005-Dec 2013
  - 26 pts with early stage invasive disease (f/u 28 mos)
  - 63 pts had prophylactic mastectomy (f/u 26 mos), 8 were found to have incidental DCIS

Nipple-sparing mastectomy in patients with BRCA1/2 mutations and variants of uncertain significance

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<th>Prophylactic, BRCA+</th>
<th>Therapeutic, BRCA+</th>
<th>Total</th>
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<tr>
<td>Cancer in NAC</td>
<td>2 (8%)</td>
<td>2 (8%)</td>
<td>4 (4%)</td>
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<tr>
<td>LRR</td>
<td>0</td>
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Risk factors associated with recurrence after nipple-sparing mastectomy for invasive and intraepithelial neoplasia

- European Institute of Oncology - 934 NSM operated between March 2002-Dec 2007, median f/u 50 months
  - 772 with invasive cancer (Group A)
  - 162 with in situ carcinoma (Group B)
- Intra-op radiation (16 Gy linear accelerator, ELIOT) to the NAC + 1 cm margin
- Survival endpoints: breast related recurrences, LR in the breast and NAC recurrences
Risk factors associated with recurrence after nipple-sparing mastectomy for invasive and intraepithelial neoplasia

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<th>Group A (Invasive)</th>
<th>Group B (In situ)</th>
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<tr>
<td></td>
<td>n=772</td>
<td>n=162</td>
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<tr>
<td>In Breast Local Recurrence</td>
<td>28 (3.6%)</td>
<td>9 (4.9%)</td>
</tr>
<tr>
<td>NAC Recurrence</td>
<td>6 (0.8%)</td>
<td>9 (5.2%)</td>
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- NAC recurrence: Paget’s disease of the nipple associated with DCIS in the underlying ducts and 4 LR with invasive carcinoma
- 70 pts with negative intra-op frozen section, had positive final definitive histology. These pts decided to preserve their NAC, no LR was observed in these cases (all received RT)
- Number of positive lymph nodes, histotype, and Ki-67 index were significant prognostic factors for breast related occurrences
- Tumor size, receptor status, HER2/neu, grade and Ki-67 were associated with the risk of NAC recurrence after an invasive tumor

Overall Survival, Disease-Free Survival, Local Recurrence, and Nipple-Areolar Recurrence in the Setting of Nipple-Sparing Mastectomy: A Meta-Analysis and Systematic Review

- Primary outcomes: OS, DFS, LR, NAC recurrence
- 20 studies published from 2006-2014 met criteria for inclusion; 2,207 pts who underwent therapeutic NSM
- All pts had Stage 1 or 2 invasive ductal carcinoma
- 8 studies compared NSM to MRM/SSM (4,663 pts; 1398 NSM, 698 SSM, 2567 MRM)
- Subgroup analysis of studies with >5 yr follow-up showed no difference in OS, DFS, and LR

Overall Survival, Disease-Free Survival, Local Recurrence, and Nipple-Areolar Recurrence in the Setting of Nipple-Sparing Mastectomy: A Meta-Analysis and Systematic Review

- Studies with f/u >5 yrs had mean OS of 86.8%, DFS of 76.1%, LR of 11.4%, and NAR of 3.4%
- Pros: Large representative sample of 4,663 pts; all 8 studies showed uniform consistency in which NSM was not inferior to MRM/SSM
- Cons: Tumor subtype and treatment data missing, study level data, findings derived from observational studies, self-selection bias
Summary

- Patient selection criteria for NSM continues to evolve
- NSM is an oncologically acceptable option for high risk and BRCA-positive patients undergoing bilateral prophylactic mastectomy
- For women with in situ or invasive breast cancer who desire NSM, LRR rates vary in the literature from 0-11.4% and are limited to 5 years of follow-up
- Patients desiring NSM should be made aware of the limited follow-up data available and the risks (i.e., NAC necrosis, technical difficulty of procedure) involved with NSM