# Predictors of Successful Nipple-Sparing Mastectomy After Neoadjuvant Chemotherapy

**Tracy-Ann Moo, MD,1,2,3, Carolina Saccarelli, MD,1,2, Elizabeth Sutton, MD,1,2, Varadan Sevilmedu, MBBS, DPH,1,2 Kate Pawloski, MD,1,2 Tim Dalfonso, MD,1,2 Mary Hughes, MD,2, Amir Blumentreich, MD, PhD,2 Elizabeth Morris, MD,2, Audree B. Tadros, MD,1, Monica Morrow, MD,1 Mary L. Gemignani, MD, MPH, Virgilio Sacchini, MD,1

1 Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2 Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY; 3 Biostatistics Service, Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY; 4 Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY

**Background**

- Neoadjuvant chemotherapy (NAC) is increasingly used for operable breast cancer, and rates of pathologic complete response have increased with targeted therapy.1–3
- Nipple-sparing mastectomy (NSM) utilization after NAC is increasing.1–3
- A 1 cm tumor-to-nipple distance (TND) is often used for NSM eligibility in the primary surgical setting, but its suitability after NAC is not well defined.

**Study Objective**

To examine factors associated with nipple involvement and evaluate the accuracy of TND ≥ 1 cm in predicting negative nipple pathology (NS-). In a cohort of women having total mastectomy after NAC.

**Methods**

- Retrospective review of women with invasive breast cancer treated with NAC between 8/2014–8/2018
- Underwent total mastectomy after NAC
- Pre- and post-NAC MRIs available
- Excluded: Women with clinical T4 tumors, clinical nipple involvement, or pathologic nipple discharge
- Mammogram and pre/post-NAC MRIs were reviewed by a dedicated breast radiologist
- Findings suggestive of nipple involvement such as retraction/invasion, mass and non-mass enhancement on MRI, or suspicious calcifications on mammogram were included in TND measurement
- Patients were stratified based on TND < 1 cm, 1-2 cm, or > 2 cm
- Association of clinicopathologic imaging variables, and TND with nipple involvement was examined using t-test or Wilcoxon’s rank test for continuous variables, and Chi-square or Fisher’s exact test for categorical variables
- Accuracy of ≥ 1 cm TND for estimating probability of nipple involvement was determined

**Results**

- 175 eligible women undergoing 179 mastectomies met criteria and were analyzed
- 18 nipples were positive on final pathology

**Table 1. Clinicopathologic characteristic of breasts with and without pathology nipple involvement**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>N=45</th>
<th>N=70</th>
<th>N=134</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic nipple involvement</td>
<td>Positive</td>
<td>38 (84%)</td>
<td>62 (89%)</td>
<td>90 (67%)</td>
<td>0.89</td>
<td>0.77</td>
<td>0.79</td>
<td>0.87</td>
</tr>
<tr>
<td>Histologic grade</td>
<td>I/II</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>27 (60%)</td>
<td>44 (63%)</td>
<td>71 (53%)</td>
<td>0.70</td>
<td>0.91</td>
<td>0.97</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>11 (24%)</td>
<td>17 (24%)</td>
<td>28 (21%)</td>
<td>0.68</td>
<td>0.91</td>
<td>0.97</td>
<td>0.67</td>
</tr>
<tr>
<td>Tumor histology</td>
<td>Lobular</td>
<td>12 (27%)</td>
<td>23 (33%)</td>
<td>35 (26%)</td>
<td>0.91</td>
<td>0.68</td>
<td>0.97</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>Mixed ductal/lobular</td>
<td>14 (31%)</td>
<td>21 (30%)</td>
<td>35 (26%)</td>
<td>0.89</td>
<td>0.79</td>
<td>0.79</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>19 (42%)</td>
<td>20 (29%)</td>
<td>39 (29%)</td>
<td>0.85</td>
<td>0.77</td>
<td>0.77</td>
<td>0.67</td>
</tr>
<tr>
<td>Histologic type</td>
<td>DCIS</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Invasive ductal</td>
<td>45 (100%)</td>
<td>70 (100%)</td>
<td>134 (100%)</td>
<td>0.89</td>
<td>0.77</td>
<td>0.79</td>
<td>0.87</td>
</tr>
<tr>
<td>ER status</td>
<td>Positive</td>
<td>5 (11%)</td>
<td>10 (14%)</td>
<td>15 (11%)</td>
<td>0.89</td>
<td>0.77</td>
<td>0.79</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>40 (90%)</td>
<td>60 (86%)</td>
<td>119 (89%)</td>
<td>0.94</td>
<td>0.84</td>
<td>0.87</td>
<td>0.91</td>
</tr>
</tbody>
</table>

**Conclusions**

- A ≥ 1 cm TND on pre-NAC imaging had an NPV of 97% for NS- compared to 96% for post-NAC imaging.
- In 13 women with TND of < 1 cm on pre-NAC imaging and a complete response on post-NAC imaging, all had NS- (p = 0.4).

**Selected References**


**Figure 1. Pathologic nipple status based on increasing TND pre- and post-NAC imaging**

On univariate analysis, increasing number of positive nodes, pre-NAC nipple retraction on MRI, and TND < 1 cm were associated with nipple involvement (p < 0.05). On multivariable analysis, increasing number of positive nodes, pre-NAC nipple retraction on MRI, and TND < 1 cm were associated with nipple involvement (p < 0.05).

**Figure 2. Pathologic nipple status based on size of TND cut-off 1 cm pre-vs post-NAC imaging**

On univariate analysis, nipple involvement was associated with lower grade, HR+/HER2-, pT3, pN+, greater number of positive nodes, and a number of imaging variables such as greater tumor extent on pre- and post-NAC MRI, and multifocality/multicentricity on post-NAC MRI (p-values < 0.05) (Table 1).