Radiation Indications in the setting of Neoadjuvant chemotherapy for Breast Cancer

Lauren Colbert, MD, MSCR
Faculty Mentor: Benjamin Smith, MD

UT MD Anderson Cancer Center
• 37 year old female who presents with self-palpated breast mass.
• History: No past medical history. G1P0A1, previously used OCP’s but currently not. Works as a waitress and is a graduate student. Denies drug or alcohol use, never smoker. Family history of cervical cancer (mother) and ovarian cancer (maternal aunt)
• On exam, appreciable fullness of left breast with mild overlying erythema. Multiple palpable, mobile lymph nodes in left axilla
• Ultrasound reveals mass corresponds to 5.1 x 3.2 x 4.0 cm heterogeneous hypoechoic mass with punctate hyperechogenicity.

• Mammogram demonstrates high density, irregular mass with associated pleomorphic calcifications and palpable finding in the left breast upper hemisphere at 12 o'clock. The central nidus is located approximately 2 cm from the nipple. The **calcifications extend to the nipple base** and to within 0.4 cm of the anterosuperior skin.

• US-guided core biopsy reveals high grade invasive ductal carcinoma, ER 94.8% positive, PR 96%; Her2/neu 3+, Ki-6 53.6%. FISH amplified (Her2/CEP17 ratio >11.8).

• US of left nodal basins demonstrates >10 left axillary nodes in level 1, 2-3 level 2 nodes. The index level 1 node was biopsied and clip was placed, and positive for malignancy.

• Next steps?
• Clinical Stage?
Careful Pre-Treatment Evaluation

• Imaging:
  • Mammogram
  • Ultrasound with careful assessment of all lymph node basins (Infraclavicular, supraclavicular, internal mammary nodes)
  • If node positive, then cross-sectional imaging (CT Chest/ neck, PET/CT)

IM Node in the absence of Axillary Node
Ipsilateral Infraclavicular nodes
Ipsilateral IM node + Axillary Nodes
Ipsilateral SCV

Courtesy of B. Smith
• In clinical Stage III, ultrasound identified N2b/N3 nodal disease in 37% (325/865) of patients, leading to change in radiation field design and/or dosing
  • 32% infraclavicular
  • 16% supraclavicular
  • 11% internal mammary
• In clinical Stage II-III, PET/CT identified N2b/N3 nodal disease in 16% (40/255) of patients.
Review Images Carefully

Biopsy-proven axillary disease  Suspicious IM node

Report: “Postoperative changes. No evidence of distant metastasis”.

Courtesy of B. Smith
For our patient...

- Clinical Stage T3N1
- Multidisciplinary evaluation with breast medical oncology, surgical oncology, radiation oncology, oncofertility service and cancer genetics
- Does patient have inflammatory breast cancer? No – based on timeline of symptom onset and skin findings.
- Dispositioned to neoadjuvant chemotherapy with ddAC x4, followed by THP x4 and trastuzumab to complete one year.
Post-chemotherapy Evaluation

- Repeat imaging
- Carefully evaluate pathology – Treatment response may help predict locoregional recurrence risk

**Z1071**

(Haffty et al, ASTRO 2016)

- Study design
  - N=701
  - cT1-3, N1-2 breast cancer
  - Pathologically confirmed nodal involvement -> Neoadjuv chemo -> Surgery
  - Radiation standard after BCS, at discretion of MD after mastectomy

- Residual Cancer Burden strongly correlated with LRR risk
  - RCB 0    HR 1 (referent)
  - RCB 1    HR 1.38 (0.15-12.4)
  - RCB 2    HR 2.25 (0.66-7.7)
  - RCB 3    HR 4.65 (1.53-14.1)
Making Treatment Decisions

**Indications for PMRT/RNI after NCT**

- Don’t Treat
- Treat

15% LRR risk

- Clinical Characteristics
- Pathologic Characteristics
- Response to neoadjuvant therapy

Risk of LRR

Courtesy of B. Smith
## Estimating Locoregional Recurrence Risk

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Pathologic Stage</th>
<th>LRR Risk WITHOUT RT</th>
<th>General Recommendation for PMRT/ RNI</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/T2, N0</td>
<td>ypT0-2 N0</td>
<td>6% at 10 years (NSABP B-18/27)</td>
<td>-</td>
</tr>
<tr>
<td>T1/T2, N1</td>
<td>ypT0-2, N0</td>
<td>0%-11% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)</td>
<td>= (NRG B-51)</td>
</tr>
<tr>
<td>T3, N+</td>
<td>ypT0-3, N0</td>
<td>0%-9% at 10 years (NSABP B18/27)</td>
<td>= (NRG B-51)</td>
</tr>
<tr>
<td>T1/2, N1</td>
<td>ypT0-2, N+</td>
<td>13% to 40% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)</td>
<td>+</td>
</tr>
<tr>
<td>T3, N+</td>
<td>ypT0-3, N+</td>
<td>22% at 10 years (NSABP B18/27)</td>
<td>+</td>
</tr>
<tr>
<td>T4 or N2/N3</td>
<td>Any</td>
<td>33% to 52%</td>
<td>+</td>
</tr>
</tbody>
</table>
Our patient

- Pathology: ypTisN0 (21 nodes), negative margins
- Locoregional Recurrence Risk: 0% to 9% at ten years
- Candidate for NRG B-51 trial, treated with PMRT/ RNI

Is this pathologic CR? Yes. pCR is defined as no residual invasive cancer.
NSABP B-51

- Clinical T1-T3 N1 M0 breast cancer → Axillary nodal involvement (FNA or core needle biopsy) → Neoadjuvant chemotherapy → Definitive surgery with negative axillary nodes (axillary dissection or SLNB +/- ALND) → Stratified by type of surgery, ER status, Her2 status, pCR status → Randomize to:

  **No Regional Nodal XRT**
  - Breast XRT if breast-conserving surgery, but no chest wall XRT if mastectomy

  **Regional Nodal XRT**
  - With breast XRT if breast-conserving surgery or chest wall XRT if mastectomy
What if there was residual disease in nodes?

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Pathologic Stage</th>
<th>LRR Risk WITHOUT RT</th>
<th>General Recommendation for PMRT/ RNI</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/T2, N0</td>
<td>ypT0-2 N0</td>
<td>6% at 10 years (NSABP B-18/27)</td>
<td>-</td>
</tr>
<tr>
<td>T1/T2, N1</td>
<td>ypT0-2, N0</td>
<td>0%-11% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)</td>
<td>= (NRG B-51)</td>
</tr>
<tr>
<td>T3, N+</td>
<td>ypT0-3, N0</td>
<td>0%-9% at 10 years (NSABP B18/27)</td>
<td>= (NRG B-51)</td>
</tr>
<tr>
<td>T1/2, N1</td>
<td>ypT0-2, N+</td>
<td>13% to 40% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)</td>
<td>+</td>
</tr>
<tr>
<td>T3, N+</td>
<td>ypT0-3, N+</td>
<td>22% at 10 years (NSABP B18/27)</td>
<td>+</td>
</tr>
<tr>
<td>T4 or N2/N3</td>
<td>Any</td>
<td>33% to 52%</td>
<td>+</td>
</tr>
</tbody>
</table>
LRR is much higher with residual nodal disease

- Recurrence Free Survival with residual axillary disease (60%) vs with axillary pCR (87%) (Hennessy et al, 2005)
- Haffty et al, PROC ASTRO 2016
- Huang et al, J Clin Oncol 22:4691-4699, 2004
Summary

• In the setting of neoadjuvant chemotherapy for breast cancer, pre-treatment evaluation is very important
• Pay attention to residual cancer burden at surgery (nodal or primary)
• Current standard of care for T1-T3, N1 patients with nodal CR is NSABP B-51
• Treatment decisions regarding nodal irradiation/ PMRT should be made with the goal of balancing LRR with risks of treatment.