Trends in the surgical management of invasive breast cancer

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Brigham and Womens Hospital
Associate Professor of Surgery
Harvard Medical School
The Quest for Optimal Local Regional Therapy

- Radical Mastectomy (Halsted)
- Extended Radical Mastectomy (Urban)
- Fisher “systemic dz”
- NSABP B04
- NSABP B06
- Breast Conservation
- Sentinel Node Biopsy
The Quest for Optimal Local Regional Therapy in the New Millennium

Do all SLN+ pts need an axillary dissection?

Is SLN biopsy accurate after neoadjuvant tx?
SLN biopsy is the standard of care in node negative patients

- NSABP B32: Randomized phase III clinical trial
- No difference in OS, DFS, or regional control with SN alone vs SN + ALND

<table>
<thead>
<tr>
<th>Node Negative Patient Outcomes</th>
<th>SN + ALND N=1975</th>
<th>SN only N=2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
<td>85.4%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Disease Free survival</td>
<td>77.0%</td>
<td>76.4%</td>
</tr>
<tr>
<td>Local-regional recurrence*</td>
<td>84 (4.3%)</td>
<td>81 (4.0%)</td>
</tr>
</tbody>
</table>

NSABP B-32: False negative rate 9.8%

Krag et al. Lancet 2010;11:927-33
Julian ASCO 2013
10 yr update NSABP B-32: Local-Regional Recurrence - 1st events

<table>
<thead>
<tr>
<th>Node Negative Patient Outcomes</th>
<th>SN + ALND N=1975</th>
<th>SN only N=2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>75 (3.8%)</td>
<td>66 (3.3%)</td>
</tr>
<tr>
<td>Axillary</td>
<td>3 (0.2%)</td>
<td>9 (0.4%)</td>
</tr>
<tr>
<td>Extra-axillary</td>
<td>6 (0.3%)</td>
<td>6 (0.3%)</td>
</tr>
</tbody>
</table>

300/1960 (15.3%) pts in SN only arm had occult mets

Julian ASCO 2013
Not all microscopic disease will become clinically apparent...
NSABP B-04

~1/2 of patients with untreated “presumed positive” nodes in mastectomy arm presented with axillary failure

<table>
<thead>
<tr>
<th>Radical Mastectomy</th>
<th>Total Mastectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 362</td>
<td>n = 365</td>
</tr>
<tr>
<td>Median nodes removed: 16</td>
<td></td>
</tr>
<tr>
<td>40% positive axillary nodes</td>
<td>18.5% delayed axillary dissection</td>
</tr>
</tbody>
</table>

Fisher B, NEJM 1985;312:674
ACOSOG Z0011
local and regional recurrence

- clinical T1-2 N0 breast cancer and with 1-2 positive SLN, randomized to ALND or observation
- In ALND group, 97 (27.3%) pts had additional positive nodes

<table>
<thead>
<tr>
<th></th>
<th>ALND N=420</th>
<th>SLN only N=436</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>15 (3.6%)</td>
<td>8 (1.8%)</td>
</tr>
<tr>
<td>Regional recurrence</td>
<td>2 (0.5%)</td>
<td>4 (0.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>17 (4.1%)</td>
<td>12 (2.8%)</td>
</tr>
</tbody>
</table>

Median followup 6.3yrs
Local regional recurrence = 29 (3.4%) population

International Breast Cancer Study Group Trial 23-01

• Phase III randomized trial ALND vs SLN only
• cT1-2 N0 patients with micromets (≤ 2mm) in ≥ 1 SLN
• In ALND group, 59 (13%) pts had additional positive nodes

<table>
<thead>
<tr>
<th></th>
<th>ALND N=464</th>
<th>SLN only N=467</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>10 (2%)</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>Regional recurrence</td>
<td>1 (&lt;1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Distant</td>
<td>34 (7%)</td>
<td>25 (5%)</td>
</tr>
</tbody>
</table>

Median followup 5.0 yrs (IQR 3.6-7.3)

Galimberti et al Lancet Oncol 2013
AATRM 048/13/2000 Trial

- Multi-center prospective RCT, 2001-2008, cALND vs SLN only
- cT <3.5cm N0 patients with micromets (≤ 2mm) in SLN
- In cALND group, 15 (13%) had additional positive nodes

<table>
<thead>
<tr>
<th></th>
<th>ALND N=123</th>
<th>SLN only N=124</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local-regional recurrence</td>
<td>1/108 (1%)</td>
<td>2/119 (1.7%)</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>0</td>
<td>1 (0.8%)</td>
</tr>
</tbody>
</table>

Median f/u 62 months (24-107mos)

Solá M et al Ann Surg Oncol 2013
The Quest for Optimal Local Regional Therapy in the New Millennium

Do all SLN+ pts need an axillary dissection?

Is SLN biopsy accurate after neoadjuvant tx?
ACOSOG Z0011

- clinical T1-2 N0 breast cancer and 1-2 positive SLN
- BCS with whole breast RT
- no improvement in regional control with ALND and no impact on survival

<table>
<thead>
<tr>
<th></th>
<th>ALND</th>
<th>SLN only</th>
<th>Absolute difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>5yr overall survival</td>
<td>91.8% (95% CI 89.1-94.5)</td>
<td>92.5% (95% CI 90.0-95.1)</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

- Does not apply to: clinically node positive, locally advanced breast cancer, patients having mastectomy, patients having partial breast irradiation

Giuliano et al. JAMA 2011; 305: 569-575
International Breast Cancer Study Group Trial 23-01

- cT1-2 N0 patients with micromets (≤ 2mm) in ≥ 1 SLN
- no improvement in regional control with ALND and no impact on survival

<table>
<thead>
<tr>
<th></th>
<th>ALND N=464</th>
<th>SLN only N=467</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 yr DFS%</td>
<td>84.4</td>
<td>87.8</td>
<td>0.78 (0.55-1.11)</td>
<td>0.16</td>
</tr>
<tr>
<td>5 yr OS %</td>
<td>97.6</td>
<td>97.5</td>
<td>0.89 (0.52-1.54)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

9% of patients in each arm had mastectomy

Galimberti et al Lancet Oncol 2013
AATRM 048/13/2000 Trial

- Multi-center prospective RCT, 2001-2008
- cT <3.5cm N0 patients with micromets (≤ 2mm) in SLN
- In cALND group, 15 (13%) had additional positive nodes
- 5 yr DFS 98.2%, no differences by cALND (p=0.33)

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Median f/u 62 months (24-107mos)
7 % of patients in SLN only arm and 9% cALND arm had mastectomy

Solá M et al Ann Surg Oncol 2013
Not all patients with 1-2 + SLN need cALND...

What about axillary RT?
AMAROS
Radiotherapy or Surgery of the Axilla after a Positive SLN

- randomized trial ALND vs AxRT only
- cT1b-2 N0 patients with ≥ 1 pos SLN, BCT or mastectomy
- In ALND group, 244 (32.8%) pts had additional positive nodes

<table>
<thead>
<tr>
<th></th>
<th>ALND N=744</th>
<th>AxRT N=681</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axillary recurrence</td>
<td>0.43%</td>
<td>1.19%</td>
</tr>
</tbody>
</table>

Axillary recurrence in SLN negative pts: 0.72%

Median f/u 6.1yrs  Rutgers E. ASCO 2013
AMAROS
No difference in DFS or OS

**Disease Free Survival**
AxSN+ ITT

- HR: 1.17; 95CI: 0.85-1.62

**Overall Survival**
AxSN+ ITT

- HR: 1.18; 95CI: 0.93-1.15

Rutgers E. ASCO 2013
Decreased Lymphedema with AxRT

Clinical Observation: 1,3 and 5 yrs after axillary treatment

Treatment for Lymphedema: 1,3 and 5 yrs after axillary treatment
Do all pts with a positive SLN need axillary dissection?

• Modern study (2001-2010) T1b-2 cN0 pts, when all other clinical and treatment characteristics are equal, AxRT is equivalent to ALND in patients undergoing BCT or mastectomy

• Decreased lymphedema with AxRT in first 5 yrs

• Longer followup to assess late effects of AxRT on lymphedema, shoulder dysfunction and QOL
Axillary management T1-2cN0?

- Largely same population as Z0011: postmenopausal, grade I-II, appropriate systemic therapy

<table>
<thead>
<tr>
<th></th>
<th>Z0011</th>
<th>AMAROS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median number SN removed</td>
<td>2</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>Macrometastases in SN</td>
<td>50%</td>
<td>60%</td>
</tr>
<tr>
<td>Additional positive nodes ALND</td>
<td>27.3%</td>
<td>32.8%</td>
</tr>
<tr>
<td>Axillary recurrence: ALND</td>
<td>0.5%</td>
<td>0.43%</td>
</tr>
<tr>
<td>Axillary recurrence: other tx</td>
<td>0.9%</td>
<td>1.19%</td>
</tr>
<tr>
<td>Median follow-up</td>
<td>6.3yrs</td>
<td>6.1yrs</td>
</tr>
<tr>
<td>Breast Conservation</td>
<td>100%</td>
<td>82%</td>
</tr>
</tbody>
</table>
Axillary management T1-2cN0?

- Based on Z0011 – both ALND and AxRT could have been avoided in 82% of patients in AMAROS
  - Lymphedema: AND 28%
  - AxRT 14%
  - SLN 5-8%\(^1\)

- MSKCC experience\(^2\): applying Z0011 criteria to consecutive patients having BCT - 84% spared ALND
  - Both AMAROS and Z0011 represent “real world” breast cancer patients
  - Median f/u 30 months, no isolated axillary recurrences!

- Both fewer recurrences than expected – interplay between systemic tx and local tx in local control

\(^1\)NSABP B32, ACOSOG Z0010/11, ALMANAC  \(^2\) Dengel et al. Ann Surg Oncol 2013
How do we incorporate the results of these studies into clinical practice

• Accepting the results of Z11 means recognizing that some patients will have positive nodes which are not removed or specifically targeted with AxRT.

• There is NO role for nomograms to predict the likelihood of additional positive nodes or PET scans to look for additional positive nodes.

• There is NO role for routine IHC to look for isolated tumor cells or micromets
Clinical Implications

In clinically node-negative patients undergoing BCT found to have macrometastases in 1 or 2 SLN:

- Systemic Rx decision made
- ALND not necessary for local control
- ALND does not contribute to survival
Concerns About Z11

• Follow-up isn’t long enough – need more time
• Not enough ER negatives – doesn’t apply?
• Not enough young women – doesn’t apply?
• Radiation oncologists treated the axilla?
Concerns About Z11

- Follow-up isn’t long enough—need more time
  - Axillary recurrence is an early event
    - 14-30 mos. in reported series; f/u Z011 75.6 mos.

- Not enough ER negatives—doesn’t apply?
  - ER status not a predictor of nodal failure
    - Size of nodal mets, # of nodes, grade and adjuvant tx

- Not enough young women—doesn’t apply?
  - Age predicts IBTR, not nodal failure

Yates L, IJROBP 2011
Z011 Radiation Field Design?

Detailed RT records for 228/856 (27%) pts included in the intention to treat analysis
Favorable Z011 results cannot be explained by increased use of axillary RT

Jagsi R et al JCO 2014
Implementing a Policy of Individualized Axillary Management

cT1 T2 N0 – Undergoing BCT

• No routine Frozen section of SN

• Patients ≥ 3 involved SN on final pathology returned to OR for axillary dissection

• Whole breast RT with standard tangents
The Quest for Optimal Local Regional Therapy in the New Millennium

Do all SLN+ pts need an axillary dissection?

Is SLN biopsy accurate after neoadjuvant tx?
Axillary Management
Neoadjuvant Chemotherapy

• NAC downstages axilla ~ 40% of patients (tumor subtype specific)

• Potential to consider SLNB after NAC – avoid ALND

• Should management dependent on pre-treatment clinical nodal stage?
  – Clinically node negative
  – Clinically node positive
Axillary Node Downstaging
Neoadjuvant Chemotherapy
NSABP B18

<table>
<thead>
<tr>
<th></th>
<th>Surgery first (n = 743)</th>
<th>Chemo first (n = 735)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall node +</td>
<td>57%</td>
<td>41%</td>
</tr>
<tr>
<td>1-3 nodes +</td>
<td>30%</td>
<td>24%</td>
</tr>
<tr>
<td>4-9 nodes +</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>&gt; 10 nodes +</td>
<td>10%</td>
<td>4%</td>
</tr>
</tbody>
</table>

$p < 0.001$

Can we do SLN biopsy after NAC and avoid ALND?

Sentinel Lymph Node Biopsy
Neoadjuvant Therapy

Clinically node negative; before or after?

Identification rate?
False neg rate?
Decisions about RT?
Prognostic value?
## SLN Biopsy Before or After NAC clinically node negative

<table>
<thead>
<tr>
<th></th>
<th>SLN Identification rate</th>
<th>False-negative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEFORE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McMasters et al (2000)</td>
<td>86% and 90%‡</td>
<td>5.8 and 11.8%‡</td>
</tr>
<tr>
<td>ALMANAC trial (2006)</td>
<td>96.1%</td>
<td>6.7%</td>
</tr>
<tr>
<td>NSABP B32 (2007)</td>
<td>97.2%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Kim et al* (2006)</td>
<td>96% (41-100%)</td>
<td>7.3% (0-29%)</td>
</tr>
<tr>
<td><strong>AFTER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSABP B27 (2005)</td>
<td>85%</td>
<td>10.7%</td>
</tr>
<tr>
<td>Hunt et al (2009)</td>
<td>97.4%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Xing et al**(2006)</td>
<td>90% (72-100%)</td>
<td>12% (0-33%)</td>
</tr>
<tr>
<td>Kelly et al*** (2009)</td>
<td>89.6% (95%CI 86.0-92.3)</td>
<td>8.4 (95%CI 6.4-10.9)</td>
</tr>
</tbody>
</table>

‡ single agent vs dual agent
*Metaanalysis 69 trials, 8059 pts; **metaanalysis 21 trials, 1273 pts; ***metaanalysis 24 trials, 1799 pts
SLN Biopsy After Neoadjuvant Chemotherapy

MDACC 1994-2007, T1-3, cN0, n = 3746pts

<table>
<thead>
<tr>
<th></th>
<th>SLN found</th>
<th>SLN false negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLN before chemo</td>
<td>98.7%</td>
<td>4.2% (23/542)</td>
</tr>
<tr>
<td>n = 3171</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLN after chemo</td>
<td>97.4%</td>
<td>5.9% (5/84)</td>
</tr>
<tr>
<td>n = 575</td>
<td>(p = 0.02)</td>
<td>(p = 0.48)</td>
</tr>
</tbody>
</table>

No difference in LRR
(median f/u 47 mos)

Hunt KK, Ann Surg 2009;250:558
Neoadjuvant Chemotherapy Decreases Axillary Dissection

MDACC 1994-2007, T1-3, cNO, n = 3746pts

<table>
<thead>
<tr>
<th></th>
<th>SN first</th>
<th>Chemo first</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>19.0</td>
<td>12.7</td>
<td>0.2</td>
</tr>
<tr>
<td>T2</td>
<td>36.5</td>
<td>20.5</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>T3</td>
<td>51.4</td>
<td>30.4</td>
<td>0.04</td>
</tr>
</tbody>
</table>

No difference in LRR (median f/u 47 mos)

Hunt KK, Ann Surg 2009;250:558
Predictors of LRR after NAC pre- vs post-treatment nodal status

NSABP B-18 (AC)/B-27 (AC-T)

MVA: Predictors of LRR combined dataset at 10yrs

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 50 yrs vs &lt; 50yrs</td>
<td>0.78 (0.63-0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>Clin. Tumor Size &gt; 5 cm vs ≤ 5cm</td>
<td>1.51 (1.19-1.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clin. Node (+) vs. Clin. Node (-)</td>
<td>1.61 (1.28-2.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ypNode(-)/No breast pCR vs. ypNode(-)/breast pCR</td>
<td>1.55 (1.01-2.39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ypNode(+) vs. ypNode(-)/breast pCR</td>
<td>2.71 (1.79-4.09)</td>
<td></td>
</tr>
</tbody>
</table>

Mamounas E et al JCO 2012
LRF by Path Nodal Status and pCR B-18/B-27: cN0 Lumpectomy pts

Low rates of regional recurrence all patients irrespective of path nodal and pCR status

Mamounas E et al JCO 2012
LRF by Path Nodal Status and pCR B-18/B-27: cN0 Mastectomy pts

No PMRT Allowed

Low rates regional recurrence all groups; increased CW recurrence node + after tx

Mamounas E et al JCO 2012
Sentinel Lymph Node Biopsy
Neoadjuvant Therapy
A Practical Approach

• Clinically node negative
  – SLN biopsy after NAC
  – Intraoperative Frozen Section of SLN
  – cALND for failed mapping
  – cALND for any positive LN including micrometastatic disease
  – Radiation tx decisions made on final node status and pCR status
Clinically node positive pt that converts to cN0?

Identification rate?
False neg rate?
Eligible
T0-T4, N1-2, M0
Biopsy Proven
Nodal disease

n = 663 cN1

SN ID rate 95%

649 SN → ALND

≥ 2 SN identified
n = 525, 79%

FNR
12.6% (9.9, 16.1)

Failed to meet primary endpoint
FNR ≤ 10%

Boughey JC, JAMA 2013
ACOSOG Z1071 – cN1 patients

How do we translate these findings in clinical practice???

<table>
<thead>
<tr>
<th># SN Removed</th>
<th>1</th>
<th>2</th>
<th>≥ 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Cases</td>
<td>12</td>
<td>24</td>
<td>47</td>
</tr>
<tr>
<td>False Negative Rate</td>
<td>32%</td>
<td>21.1%</td>
<td>9.1%</td>
</tr>
</tbody>
</table>

Boughey JC, JAMA 2013
## SLN Biopsy After Neoadjuvant Therapy cN1 convert cN0

<table>
<thead>
<tr>
<th></th>
<th>ACOSOG Z1071</th>
<th>SENTINA</th>
<th>SN FNAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>649</td>
<td>592(cN+)*</td>
<td>153</td>
</tr>
<tr>
<td>Mapping</td>
<td>Dual recommended (79%)</td>
<td>Technetium required</td>
<td>Technetium required, IHC</td>
</tr>
<tr>
<td>Pre-op biopsy?</td>
<td>Yes</td>
<td>Not required (biopsy =25%)</td>
<td>Yes</td>
</tr>
<tr>
<td>Nodal pCR</td>
<td>41%</td>
<td>52% ypN0 (?)</td>
<td>35%</td>
</tr>
<tr>
<td>IR</td>
<td>92.7%</td>
<td>80.1%</td>
<td>87.6%</td>
</tr>
<tr>
<td>FNR (Overall)</td>
<td>12.6%</td>
<td>14.2%</td>
<td>8.4%</td>
</tr>
<tr>
<td>1 SLN</td>
<td>31.5%</td>
<td>24.3%</td>
<td>18.2%</td>
</tr>
<tr>
<td>2 SLN</td>
<td>21.1%</td>
<td>18.5%</td>
<td>4.9%</td>
</tr>
<tr>
<td>≥3SLN</td>
<td>9.1%</td>
<td>7.3%</td>
<td></td>
</tr>
</tbody>
</table>

*1737 patients enrolled in 4 arm multicenter trial. 592 ARM C were cN+ to cN0
SLN After Neoadjuvant Chemotherapy
cN+ convert to cN0

<table>
<thead>
<tr>
<th># of SN</th>
<th>ACOSOG Z1071 N=649</th>
<th>SENTINA N=592</th>
<th>SN-FNAC N=153</th>
<th>GANEA 2 N=270</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>24</td>
<td>18.2</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>19</td>
<td>4.9</td>
<td>-</td>
</tr>
<tr>
<td>≥ 3</td>
<td>9</td>
<td>7</td>
<td>-</td>
<td>12</td>
</tr>
</tbody>
</table>

- Consistent unacceptable FNR unless ≥ 3 SN removed
- Residual disease resistant to treatment?
  - No data on LRR in this setting
- Do know importance of path node status in predicting LRF in patients that start out cN+ ... *implications for RT*
Pre- vs post-treatment nodal status impact on LRR

Updated Analysis NSABP B-18 (AC)/B-27 (AC-T)

Mamounas E et al JCO 2012
Suggestions to minimize the FNR

- Dual agent mapping
- Normal exam after chemotherapy
- Remove $\geq 3$ SN
- Include IHC detected disease as node positive
- Leave a clip at time of biopsy and localize for SLN
Sentinel Lymph Node Biopsy Neoadjuvant Therapy
A Practical Approach

• Clinically node positive converts to node neg
  – SLN biopsy after NAC w/ dual mapping agents
  – Remove at least 3 SLN
  – Intraoperative Frozen Section of all SLN
  – cALND for
    • failed mapping
    • fewer than 3 SLN
    • any positive LN including micrometastatic disease/ITCs (unless on trial)
Post NAC Trials of Axillary Management cN1 to cN0

### ALLIANCE A11202 Schema

- **Clinical T1-3 N1 M0 BC**
- **Neoadjuvant Chemotherapy**
- **BCT or Mastectomy Sentinel Lymph Node Surgery**
  
  **SLN Negative**
  - Randomization
  - **ALND**
    - Breast/chest wall and nodal XRT (no Axillary RT)

  **SLN Positive**
  - Randomization
  - **No further axillary surgery. Breast/chest wall and nodal XRT (incl. Axilla)**

### NSABP B-51/RTOG 1304 (NRG 9353) Schema

- **Clinical T1-3 N1 M0 BC**
- **Axillary nodal involvement (FNA or core needle biopsy)**
- **Neoadjuvant chemo (+ Anti-HER-2 therapy for HER-2 neu pts)**

  **Definitive surgery with histologic documentation of negative axillary nodes** (by axillary dissection or by SLNB axillary dissection)

  - **Stratification**
    - Type of surgery (mastectomy vs lumpectomy)
    - ER status (+ vs -), HER-2 status (+ vs -)
    - pCR in breast (yes vs no)

  - **Randomization**

  **No Regional Nodal XRT with breast XRT if BCS & No chest wall XRT if mastectomy**

  **Regional Nodal XRT with breast XRT if BCS and chest wall XRT if mastectomy**
Post NAC Trials of Axillary Management cN1 to cN0

ALLIANCE A11202 Schema

- Clinical T1-3 N1 M0 BC
- Neoadjuvant Chemotherapy
- BCT or Mastectomy Sentinel Lymph Node Surgery

SLN Positive

Randomization

Can axillary RT replace ALND?

NSABP B-51/RTOG 1304 (NRG 9353) Schema

- Clinical T1-3 N1 M0 BC
- Axillary nodal involvement (FNA or core needle biopsy)
- Neoadjuvant chemo (+ Anti-HER-2 therapy for HER-2 neo pts)

Definitive surgery with histologic documentation of negative axillary nodes (by axillary dissection or by SLNB) axillary dissection

Randomization

Can response to NAC be used to select patients who do not need PMRT or extended nodal field RT?
Thank You