Debate
Axillary dissection
- con

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Goals of discussion

- Data from the literature
- Factors associated with axillary node involvement
- Results of axillary node interventions
- Adverse effects of axillary lymph nodes interventions
- Adjuvant treatment decisions
- Changing role of radiation therapy in era of sentinel lymph node biopsy (SLNB)
Data from literature

Axillary lymph node dissection vs no directed treatment
# Trials of ALND vs no directed axillary therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Axillary status</th>
<th>Follow-up</th>
<th>Study interventions</th>
<th>Sample size</th>
<th>Recurrence %</th>
<th>Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP B-04 Fisher 2002</td>
<td>Palpable, suspicious nodes on examination</td>
<td>Mean, 20 y</td>
<td>Radical mastectomy</td>
<td>292</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total mastectomy + RT</td>
<td>294</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>NSABP B-04 Fisher 2002</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Mean, 20 y</td>
<td>Radical mastectomy</td>
<td>362</td>
<td>4</td>
<td>19</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Total mastectomy + RT</td>
<td>352</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total mastectomy</td>
<td>365</td>
<td>6</td>
<td>19</td>
</tr>
<tr>
<td>Greco 2000</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 5.1 y</td>
<td>Partial mastectomy or mastectomy with no ALND + RT if age &lt; 70 y</td>
<td>401</td>
<td>5</td>
<td>NE</td>
</tr>
<tr>
<td>Martelli 2010</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 15 y</td>
<td>BCT + ALND</td>
<td>109</td>
<td>0</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT alone</td>
<td>110</td>
<td>1.8</td>
<td>94</td>
</tr>
<tr>
<td>Hughes 2004</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 5 y</td>
<td>BCT + Tamoxifen</td>
<td>200</td>
<td>0</td>
<td>87</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Partial mastectomy + Tamoxifen</td>
<td>204</td>
<td>1</td>
<td>86</td>
</tr>
<tr>
<td>Rudenstam 2006</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 6.6 y</td>
<td>Mastectomy or BCT + ALND</td>
<td>234</td>
<td>1</td>
<td>75</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Mastectomy or BCT with no axillary surgery</td>
<td>239</td>
<td>3</td>
<td>73</td>
</tr>
</tbody>
</table>
NSABP B-04: Randomized management of the axilla

- Axilla treated by either surgery, XRT or observation in clinically negative nodes; in clinically positive nodes, treatment either by surgery or XRT.

- Radical mastectomy = removal of entire breast, level 1 and 2 axillary nodes, pectoralis major and minor muscles
- Total mastectomy = removal of all breast tissue with preservation of pectoralis muscles and axillary nodes
NSABP B-04: Results

- XRT achieved similar local control as surgery in clinically negative axilla while it was inferior to surgery in clinically positive axilla.
- Patients who had 6 or more nodes removed did not have axillary recurrence.
- No difference in survival with respect to treatment in either arm.
- Those patients treated with radical mastectomy had almost double the risk of lymphedema than those treated with radiation therapy or total mastectomy.
## Trials of Complete ALND vs Radiation Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Axillary status</th>
<th>Follow-up</th>
<th>Study interventions</th>
<th>Sample size</th>
<th>Recurrence %</th>
<th>Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johansen 1990</td>
<td>Palpable, suspicious nodes &lt; 2.5 cm or no palpable, suspicious nodes on examination</td>
<td>Mean, 50 y</td>
<td>Total mastectomy + RT</td>
<td>219</td>
<td>NR</td>
<td>1% (65% breast cancer-specific deaths)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Extended radical mastectomy</td>
<td>206</td>
<td>NR</td>
<td>2% (64% breast cancer-specific deaths)</td>
</tr>
<tr>
<td>Louis-Sylvestre 2004</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 5 y</td>
<td>BCT + ALND</td>
<td>326</td>
<td>0.6</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT + RT to axilla</td>
<td>332</td>
<td>1.8</td>
<td>74</td>
</tr>
<tr>
<td>Hoebers 2000</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 3.4 y</td>
<td>BCT + RT to axilla and supraclavicular nodes</td>
<td>105</td>
<td>2</td>
<td>83</td>
</tr>
<tr>
<td>Veronesi 2005</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 5.2 y</td>
<td>BCT alone</td>
<td>214</td>
<td>1.5</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT + RT to axilla</td>
<td>221</td>
<td>0.5</td>
<td>97</td>
</tr>
</tbody>
</table>
Other randomized data: French trial

- Randomized 658 pts with clinically negative nodes to axillary dissection (AXD) or axillary radiation. Enrollment from 1982-87.
- Fifteen years follow-up showed slight increase in axillary recurrence with XRT (3% vs. 1%).
- No difference in recurrence rates in the breast or supraclavicular and distant metastases
- No difference in overall survival or disease free survival.

JCO 22:97-101, 2004
Changes of management since 1987

- As a consequence of increasing use of adjuvant chemotherapy the role of axillary dissection shifted from therapeutic to prognostic value.
- Sentinel lymph node biopsy has largely replaced ALND for nodal staging.
Axillary involvement prediction factors

- **Size**: Any size tumor can have + nodes. Reports show an 11% risk of + nodes in T1a tumors, rising to 15-20% in T1b.
- **Age**: A variety of cutoffs but the younger the patient, the greater the chance of + nodes.
- **LVSI**: Risk rises to 50-60% in its presence and decreases to 15-25% without it.
- **Histology**: Ductal and lobular appear equal while tubular and medullary appear to have lower risks.
# Trials of ALND vs SLN Biopsy

<table>
<thead>
<tr>
<th>Study</th>
<th>Axillary status</th>
<th>Follow-up</th>
<th>Study interventions</th>
<th>Sample size</th>
<th>RR %</th>
<th>Surv. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veronesi 2010</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Mean, 7.9 y</td>
<td>BCT + negative SLN biopsy result</td>
<td>167</td>
<td>1.2</td>
<td>89</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BCT + SLN biopsy and completion ALND if positive SLN</td>
<td>92</td>
<td>0</td>
<td>89</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BCT + SLN and complete ALND regardless of SLN</td>
<td>257</td>
<td>0</td>
<td>89</td>
</tr>
<tr>
<td>Canavese 2009</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 5.5 y</td>
<td>BCT or mastectomy + negative SLN biopsy result</td>
<td>79</td>
<td>0</td>
<td>94</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + SLN biopsy and completion ALND if positive SLN</td>
<td>31</td>
<td>0</td>
<td>90</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + SLN and complete ALND regardless of SLN</td>
<td>115</td>
<td>0.9</td>
<td>90</td>
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<tr>
<td>Mansel 2006</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Mean, 1 y</td>
<td>BCT or mastectomy + negative SLN biopsy result</td>
<td>368</td>
<td>0.8</td>
<td>98</td>
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<td></td>
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<td></td>
<td>BCT or total mastectomy + complete ALND</td>
<td>496</td>
<td>0.6</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or total mastectomy + SLN biopsy + completion ALND</td>
<td>83</td>
<td>0</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or total mastectomy + SLN biopsy + axillary RT if positive SLN biopsy result</td>
<td>33</td>
<td>0</td>
<td>98</td>
</tr>
<tr>
<td>Zavagno 2008</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 4.6 y</td>
<td>BCT or mastectomy + negative SLN biopsy result</td>
<td>218</td>
<td>0.4</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + SLN biopsy + completion ALND</td>
<td>94</td>
<td>0</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + SLN biopsy + complete ALND</td>
<td>352</td>
<td>0</td>
<td>89</td>
</tr>
<tr>
<td>Krag 2010 NSABP B-32</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Mean, 7.9 y</td>
<td>BCT or mastectomy + negative SLN biopsy result</td>
<td>1978</td>
<td>0.4</td>
<td>83</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + negative SLN biopsy result and complete ALND</td>
<td>2011</td>
<td>0.7</td>
<td>84</td>
</tr>
</tbody>
</table>
NSABP B-32

- 2807 women were randomized to receive SLN biopsy followed by complete ALND
- 2804 women were randomized to receive SLN biopsy followed by observation if the SLN biopsy result was negative (n = 2011) or completion axillary node dissection if the SLN biopsy found metastases (n = 793)
- Recurrence of axillary node metastases was seen in 0.4% cases for complete ALND and in 0.7% cases for completion ALND only for nodal metastases
- There was no significant difference in survival between groups.
<table>
<thead>
<tr>
<th>Study</th>
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<th>Follow-up</th>
<th>Study interventions</th>
<th>Sample size</th>
<th>RR %</th>
<th>Surv. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giuliano 2011 ACOSOG Z0011</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 6.3 y</td>
<td>BCT + positive SLNB result + completion ALND</td>
<td>388</td>
<td>0.5</td>
<td>88.8</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BCT + positive SLNB result</td>
<td>425</td>
<td>0.9</td>
<td>89.9</td>
</tr>
<tr>
<td>Straver 2014 AMAROS</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 6.1 y</td>
<td>BCT or mastectomy + negative SLNB result</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + SLNB + completion ALND</td>
<td>2402</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + positive SLNB result + axillary RT</td>
<td>681</td>
<td>1.19</td>
<td>NA</td>
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<td></td>
<td></td>
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<td>BCT or mastectomy + positive SLNB result + completion ALND</td>
<td>744</td>
<td>0.43</td>
<td>NA</td>
</tr>
<tr>
<td>Galimberti 2013 IBCSG 23-01</td>
<td>No palpable, suspicious nodes on examination</td>
<td>Median, 5 y</td>
<td>BCT or mastectomy + positive SLNB result + completion ALND</td>
<td>464</td>
<td>0.2</td>
<td>87.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCT or mastectomy + positive SLNB result alone</td>
<td>467</td>
<td>0.8</td>
<td>84.4</td>
</tr>
</tbody>
</table>
ACOSOG Z0011

- Patients had clinical T1 to T2 N0 M0 cancer and undergone partial mastectomy with SLNB
- Patients found to have SLN metastases were randomized to observation vs completion axillary node dissection
- All patients received adjuvant whole breast radiation and 97% received adjuvant systemic therapy per local institutional standard
- Study endpoints were survival and recurrence
- After a median follow-up of 6.3 years, 0.5% of patients with ALND had a recurrence of axillary node metastases vs 0.9% in SLNB alone group
- 5-year overall survival was 91.8% for ALND vs 92.5% for SLNB alone
- 5-year disease-free survival was 82.2% for ALND vs 83.9% for SLNB alone
ACOSOG Z0011

The results from ACOSOG Z0011 are potentially practice changing and ALND may no longer be routinely required for patients who meet all of the following criteria:

- T1-2 tumors
- One to two positive SLNs without extracapsular extension
- Patient acceptance and completion of whole breast radiation therapy without extended fields of radiotherapy
- Patient acceptance and completion of adjuvant therapy (hormonal, cytotoxic or both)
- No neoadjuvant therapy

The results from ACOSOG Z0011 are not directly applicable for:

- T3 tumors
- More than 2 positive nodes
- Patients undergoing mastectomy
- Patients undergoing partial breast irradiation

SLN micrometastases detected only by IHC staining are clinically insignificant

The American Society of Breast Surgeons, aug 2011
IBCSG 23-01

- Randomized 934 patients with micrometastases in the SLNB to ALND vs SLNB alone
- After a median follow-up of 5 years regional recurrence was seen in 1% of the SLNB group vs 0.2% of the ALND group
- No statistically significant differences in disease-free survival were noted in spite of the fact that 13% of patients in the ALND arm had additional nodal metastases
1425 SLN positive patients having breast-conserving surgery or mastectomy were randomized to ALND vs radiotherapy to the axillary and supraclavicular nodes.

The axillary recurrence rates were 0.43% after ALND and 1.19% after radiotherapy, in spite of the finding that 32.8% of patients having ALND had additional positive nodes.

Disease-free survival after ALND was not significantly improved (HR 1.18 95%CI 0.93-1.15).
The incidence of lymphedema at 5 years was significantly higher in patients receiving ALND (22% vs 14%, p<0.0001)

Trial suggests that in patients to whom it is clear that postmastectomy radiotherapy is indicated on the basis of primary tumor characteristics and the finding of a positive sentinel node, ALND can be avoided.
## Trials of axillary dissection versus less surgery

<table>
<thead>
<tr>
<th>Trial</th>
<th>% RT</th>
<th>% Systemic therapy</th>
<th>Additional positive nodes at ALND (%)</th>
<th>Axillary recurrence, no ALND (%)</th>
<th>Ratio axillary recurrence to positive nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP B04</td>
<td>0</td>
<td>0</td>
<td>40</td>
<td>18.5</td>
<td>2.2</td>
</tr>
<tr>
<td>NSABP B32</td>
<td>82</td>
<td>84</td>
<td>9.8</td>
<td>0.7</td>
<td>14</td>
</tr>
<tr>
<td>IBCSG 23-01</td>
<td>71 (exclude IORT)</td>
<td>96</td>
<td>13.0</td>
<td>1.0</td>
<td>13</td>
</tr>
<tr>
<td>ACOSOG Z0011</td>
<td>89</td>
<td>97</td>
<td>27.4</td>
<td>0.9</td>
<td>30</td>
</tr>
<tr>
<td>AMAROS 2014</td>
<td>47.78</td>
<td>90</td>
<td>33</td>
<td>1.19</td>
<td>NR</td>
</tr>
</tbody>
</table>
Effect of RT after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomized trials

Lancet 2014; 383: 2127-35
Previous meta-analysis
Mastectomy and axillary clearance: N negative

There were 1400 women with mastectomy, axillary clearance, and N-ve disease in trials of ±RT
RT was generally to the chest wall and regional lymph nodes

5-year local recurrence risks:
- 2% vs 6% (reduction 4%)

15-year breast cancer mortality risks:
- 31.3% vs 27.7% (increase 3.6%, SE 3.6, 2p=0.01)

15-year overall mortality risks:
- 42.4% vs 38.2% (increase 4.2%, SE 2.7, 2p=0.0002)
Previous meta-analysis
Mastectomy and axillary clearance: N positive

There were 8500 women with mastectomy, axillary clearance, and N+ve disease in trials of ±RT. RT was generally to the chest wall and regional lymph nodes.

5-year local recurrence risks:
- 6% vs 23% (reduction 17%)

15-year breast cancer mortality risks:
- 54.7% vs 60.1% (reduction 5.4%, SE 1.3, 2p=0.0002)

15-year overall mortality risks:
- 59.8% vs 64.2% (reduction 4.4%, SE 1.2, 2p=0.0009)
Proportional and absolute reductions produced by radiotherapy

Radiotherapy produced similar proportional reductions in local recurrence in all women (irrespective of age or tumour characteristics) and in all major trials of ±RT (recent or older; with or without systemic therapy), so large absolute reductions in local recurrence were seen only if the control risk was large.
EBCTCG 2014 meta-analysis

For 700 women with axillary dissection and no positive nodes, radiotherapy had no significant effect on

- locoregional recurrence (two-sided significance level [2p]>0.1),
- overall recurrence (rate ratio [RR], irradiated vs not, 1.06, 95% CI 0.76–1.48, 2p>0.1),
- breast cancer mortality (RR 1.18, 95% CI 0.89–1.55, 2p>0.1).
For 1314 women with axillary dissection and one to three positive nodes, radiotherapy reduced
- locoregional recurrence ($2p<0.00001$),
- overall recurrence (RR 0.68, 95% CI 0.57-0.82, $2p=0.00006$), and
- breast cancer mortality (RR 0.80, 95% CI 0.67-0.95, $2p=0.01$).

For 1133 of these 1314 women were in trials in which systemic therapy was given in both trial groups, RT again reduced
- locoregional recurrence ($2p<0.00001$),
- overall recurrence (RR 0.67, 95% CI 0.55-0.82, $2p=0.00009$),
- breast cancer mortality (RR 0.78, 95% CI 0.64-0.94, $2p=0.01$)
For 1772 women with axillary dissection and four or more positive nodes, RT reduced
- locoregional recurrence (2p<0.00001),
- overall recurrence (RR 0.79, 95% CI 0.69-0.90, 2p=0.0003),
- breast cancer mortality (RR 0.87, 95% CI 0.77-0.99, 2p=0.04).

After mastectomy and axillary dissection, radiotherapy reduced both recurrence and breast cancer mortality in the women with one to three positive lymph nodes in these trials even when systemic therapy was given.
Factors associated with axillary node involvement
Data from NSABP B-32

- In 61% of patients, the + sentinel node is the only + node; therefore, even without the completion dissection; the procedure is therapeutic in 61% of patients.
- Risk of + non-sentinel node is increased by size of tumor and presence of LVSI.
- Risk of + non-sentinel node is decreased by increased number of nodes removed (＞4).
- Morbidity is low and there is a learning curve that each surgeon (institution) needs to go through.
A Validated Nomogram for Risk Estimation of SLN metastasis based on:

- Age
- Tumor size
- Histology type
- Location
- LVI
- Multifocal
- Nuclear grade
- ER status
- PR status

Special type= colloid, medullary or tubular

Nomograms for predicting non-sentinel lymph node involvement

- Helpful in deciding who needs completion ALND.
- Based on information available after final pathology is complete.
Results of axillary node interventions
Risk of developing symptomatic axillary recurrence

- Recurrence of axillary lymph node metastases can negatively affect quality of life. In particular, axillary metastatic disease that involves the chest wall, brachial plexus, or pectoralis musculature may not be amenable to surgery and has the potential to result in significant pain and disability.

- An increased risk of recurrence of axillary lymph node metastases is seen in patients who have diagnoses at a younger age, have higher-grade tumors, have estrogen/progesterone receptor–negative tumors, and have not had radiation.

- Complete axillary node dissection is still supported by data for patients
  - with palpable, suspicious axillary nodes (even if there is a good response to neoadjuvant chemotherapy);
  - undergoing mastectomy with a positive SLN biopsy result;
  - with a positive SLN biopsy result who cannot get radiation therapy;
  - with a positive SLN biopsy result who will not get adjuvant systemic therapy;
  - who would not meet inclusion criteria for the ACOSOG Z11 trial.
Survival

- NSABP B-04 trial randomized 1079 patients with breast cancer who had no palpable, suspicious axillary nodes to receive radical mastectomy, total mastectomy with axillary radiation, or total mastectomy alone.
  - With a mean follow-up of 20 years, there were no differences in disease-free, distant disease-free, or overall survival.

- Rudenstam et al randomized 473 women aged 60 years or older with breast cancer and no palpable, suspicious axillary nodes to receive complete axillary node dissection or no axillary treatment.
  - With a median follow-up of 6.6 years, disease-free and overall survival were nearly identical.
Survival

- Martelli et al randomized 219 women with breast cancer and no palpable, suspicious axillary nodes to complete axillary dissection or no axillary treatment.
  - After 5 years of follow-up, there was no difference in disease-free or overall survival.

- Several randomized trials have compared axillary dissection with SLN biopsy in patients with no suspicious, palpable axillary nodes. None reported a difference in disease-free or overall survival. All studies demonstrated that in patients without suspicious, palpable nodes, complete axillary node dissection does not affect survival compared with SLN biopsy.

- No trials exist assessing survival in women with suspicious palpable nodes randomized to a no-axillary-intervention group.
Adverse effects of axillary node interventions
Adverse outcomes with axillary surgery

- Axillary node dissection was associated with significant reductions in shoulder flexion and abduction at 1 month but range of motion had returned to near baseline by 12 months.
- Similarly, 62% of women reported arm pain or numbness at 1 month and 31% still reported these symptoms at 12 months. Clinicians rated these symptoms as severe in only 1% at 12 months.
- Women may develop measurable arm swelling after axillary surgery without symptoms; consequently, lymphedema rates are generally higher for studies that measure arm volumes or circumferences than for studies that rely on patient-reported symptoms.
Adverse outcomes with axillary surgery

- Unlike other shoulder and arm symptoms, the prevalence of lymphedema generally increases over time. Subjective lymphedema is reported by 14% of patients following axillary dissection, 4% of patients following axillary radiation, and 5% to 7% of patients following SLN biopsy.

- Randomized prospective clinical trials consistently report reduced rates of shoulder and arm morbidity for SLN biopsy compared with axillary dissection.
Adverse outcomes with axillary radio-surgery

- Breast LE is an often-overlooked area of breast cancer treatment-related side effects. Breast edema occurs in 6–48% of patients after receiving surgery and radiation therapy for breast cancer.

- The incidence rate of breast lymphedema after a lumpectomy alone is 6%. This rate drastically increases with nodal dissection and radiation therapy. The incidence of breast lymphedema after a sentinel lymph node biopsy and radiation therapy is 23%; with an axillary lymph node dissection and radiation therapy is 35% in node negative patients; and 48% in node positive patients.
Adverse outcomes with axillary radio-surgery

- The incidence of ipsilateral upper extremity LE increases with combined surgery and radiation to the regional lymphatics.
- The occurrence of LE after a SLNB alone is 2.6–3.0%. With this patient population, the tumor location in the upper outer quadrant was identified as a risk factor for the development of LE.
- If an ALND is performed alone, the incidence rate of LE rises. It has been reported that after a level I/II ALND the incidence of LE of the upper arm was 14%, 12% in the forearm, and 16% in the hand utilizing a diagnostic scale of a circumference difference greater than 5%.
- The incidence rate of upper extremity LE after an ALND and/or radiation therapy ranges from 6.0–33.5%.
Adverse outcomes with axillary radiotherapy

AMAROS results

- At 1 year following treatment, lymphedema rates were lower in women who had radiotherapy compared with lymph node dissection or removal (15% vs 25%; $P < 0.001$).
- Women who had both radiotherapy and a dissection or removal had an even higher incidence of lymphedema compared with those who received radiotherapy alone (59%; $P < .001$).
- After 5 years, these rates were 10%, 21%, and 58%, respectively ($P < .001$).
- Independent risk factors for lymphedema within the first year of treatment were lymph node dissection, combination of a dissection plus radiotherapy, a body mass index of greater than 25, premenopausal state, and treatment on the dominant side.
- No significant differences in shoulder mobility were seen between the lymph node dissection and lymph node radiotherapy groups.
- 10% of patients in the lymph node dissection group had paresthesia of the arm compared with 9% of those in the radiotherapy group.
- Complications occurred in 23% of patients who received a lymph node dissection compared with 9% in patients undergoing radiotherapy ($P < .001$).
Adverse effects of axillary node interventions

Long-term Rates of Adverse Outcomes Associated With Axillary Operations

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Axillary Lymph Node Dissection, %</th>
<th>Sentinel Node Biopsy Alone, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphedema</td>
<td>10-20</td>
<td>5-7</td>
</tr>
<tr>
<td>Quality-of-life reduction</td>
<td>35</td>
<td>23</td>
</tr>
<tr>
<td>Arm pain/ numbness</td>
<td>31</td>
<td>11</td>
</tr>
</tbody>
</table>

Breast cancer patients prefer radiation to axillary lymph node dissection
Adjuvant therapy decisions
Adjuvant therapy decisions

- In the past, axillary nodal status was a critical factor considered in adjuvant systemic therapy decisions. With the validation of SLN biopsy, the same staging information is obtained with less morbidity.

- Now, in the era of personalized therapy, decisions regarding adjuvant treatments are often guided by molecular tumor profiling, making it necessary to continue assessing the value of surgical axillary staging.

- These commercially available genomic assays, along with traditional pathologic tumor markers, often drive decisions regarding adjuvant chemotherapy, sometimes irrespective of nodal status. One of the genomic assays is able to provide information regarding recurrence risk in estrogen receptor–positive tumors based on 16 cancer genes. It was developed specifically to determine what benefit may be obtained from adding chemotherapy to a treatment regimen.

- There remain, however, clinical scenarios in which additional nodal metastases may influence decisions on systemic therapy; for these patients, a tailored approach with completion axillary node dissection is appropriate.
Discuss changing role of radiation in era of sentinel lymph node biopsy (SLNB)
Summary

- In the era of SLNB, most patients should have nodes evaluated.
- Purpose of nodal evaluation and removal is still both prognostic and therapeutic.
- If the patient cannot have ALND or SLNB, XRT will provide adequate local control in the clinically negative axilla.
- The hard question: Who needs the supraclavicular nodes radiated when the completion ALND is not done?
Management for No axillary surgery

- If no axillary surgery, axilla would be included in tangents if probability of nodal involvement is above 10%.
- Supraclavicular fossa would be included if patient’s condition could tolerate fibrosis of lung in that field.
Management for SLNB but no ALND

- If only 1 + node and no LVSI (especially if >4 nodes removed in SLNB), the axilla would be included in the tangents.
- If more than 1 node and/ or LVSI, suprclavicular fossa would be included.
Management for SLNB + ALND

- If 1 + node, no regional XRT.
- If >4 + nodes, XRT to axilla and supraclav.
- If >4+ nodes and upper inner quadrant, XRT to axilla, supraclav and IMN.
- If 2-3 nodes positive and NR>25%, XRT to axilla and supraclav.
Conclusion

- Among patients with breast cancer but no palpable lymph nodes, complete axillary node dissection provides no survival benefit compared with SLN biopsy but reduces the risk of recurrence of axillary node metastases by 1 - 3%.

- However, complete axillary node dissection is associated with a 14% risk of lymphedema compared with only 5% to 7% in patients undergoing SLN biopsy.

- In the future, multimodal treatment will be dependent on primary tumor features, including molecular markers, potentially rendering the staging information obtained via axillary lymph node dissection inconsequential.
Conclusion

- Radiation oncologists and surgeons must exercise caution when applying the findings of the Z0011 trial to patients with a positive sentinel lymph node biopsy and poor prognostic factors.

- If a patient had a > 15% risk of finding additional non-sentinel lymph nodes, then levels 1 and 2 were treated.

- If a patient had a > 15% chance of finding 4 or more lymph nodes, then level 3 and the supraclavicular field were treated.

- Currently, we prescribe comprehensive nodal irradiation for all macroscopically node positive patients and strongly consider it for younger patients with high grade ER/PR negative and HER2/neu positive tumors or those with a lesion in a medial/central location.
NCCN Guidelines Version 2.2015
Invasive Breast Cancer

SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB, and IIIA T3, N1, M0

Clinically node positive at time of diagnosis\(^1\)

- FNA or core biopsy positive
  - Axillary dissection level III
    - See Axillary Lymph Node Staging (BINV-E)

- FNA or core biopsy negative

  - Sentinal node mapping and excision\(^2,3\)
    - Sentinal node negative\(^3\)
      - No further axillary surgery (category 1)

  - Sentinal node positive\(^3\)
    - Meets ALL of the following criteria:
      - T1 or T2 tumor
      - 1 or 2 positive sentinel lymph nodes
      - Breast-conserving therapy
      - Whole-breast RT planned
      - No neoadjuvant chemotherapy
      - See Axillary Lymph Node Staging (BINV-E)

- Sentinal node not identified

Clinical Stage I, IIA, IIB and IIIA T3, N1, M0

- Clinically node negative at time of diagnosis

\(^1\) Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound-guided FNA or core biopsy in determining if a patient needs axillary lymph node dissection.

\(^2\) Sentinel lymph node mapping injections may be peritumoral, subareolar, or subdermal. However, only peritumoral injections map to the internal mammary lymph node(s).

\(^3\) Sentinel lymph node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.

\(^4\) For patients with clinically negative axillae who are undergoing mastectomy and for whom radiation therapy is planned, axillary radiation may replace axillary dissection level III for regional control of disease.
Thank you