Surgical management of breast cancer

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Silchar (Assam)
Multidisciplinary decision

- Surgical oncologist
- Radiation oncologist
- Medical oncologist
- Radiologist
- Pathologist
- Plastic surgeon, psychologist, physiotherapist, geneticist, and specialized breast nurse
- Patients and family involvement in decision making for surgery.
- Patient's choice should be clearly documented.
DO ALL PATIENTS NEED RADICAL SURGERY?
# Evolution of surgery

<table>
<thead>
<tr>
<th>Theory and Year</th>
<th>Spread from one source</th>
<th>Radical mastectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>The halstead theory(1894)</td>
<td></td>
<td>Radical mastectomy</td>
</tr>
<tr>
<td>The alternative theory(1980)</td>
<td>Systemic disease</td>
<td>Modified radical mastectomy, lumpectomy</td>
</tr>
<tr>
<td>The spectrum theory(1994)</td>
<td>Combination</td>
<td></td>
</tr>
</tbody>
</table>
Signs of inoperability

Skin ulceration
Chest wall fixity
Axillary nodes >2.5 cm
Edema of skin
Fixed axillary nodes
Inflammatory ca breast
Supraclavicular nodes
  edema of arm
Clinically involved internal mammary nodes
  satellite nodules in skin
• Patey's: Pectoralis minor removed.
• Scanlon: Pectoralis minor divided.
• Auchincloss: Pectoralis minor retracted.
Indications

- C/I for BCT
- Patient's choice (often depend on information provided by physician)
- Fear of recurrence (patient /surgeon)
- Post Neoadjuvant chemotherapy
Shrink pattern after NACT

- Type I: solitary (61%)
- Type II: Multifocal (33%)
- Type III: Patch like (6%)

TECHNICAL ASPECTS: INCISION

- Vertical elliptical
- Tranverse
- Oblique
Flaps are raised up to clavicle superiorly, inframammary folds up to rectus abdominis fascia inferiorly, sternal borders medially, anterior border of latissimus dorsi muscle laterally.
Breast tissue to be dissected along with Pectoralis fascia.
PRECAUTIONS

- Avoid very thin flaps
- Meticulous hemostasis
- Careful handling of flaps
- Dissect nerve to serratus and neurovascular pedicle to LD muscle carefully
Complications of Mastectomy

- Flap Necrosis
- Seroma
- Wound Infection
- Shoulder Dysfunction
Implant Reconstruction

Tissue Expansion Before and After
Goal of BCT

To provide survival equivalent to Mastectomy with preservation of the cosmesis

To achieve low rate of recurrence in treated breast
- Women who have BCS are more likely to have positive attitude towards life.
Surgeon characteristics and use of breast conservation surgery in women with early stage breast cancer

Ann Surg 2009 May; 249(5)

- one small study in women with early-stage breast cancer also suggests that patients seen by female surgeons are more likely to receive BCS than mastectomy

• the attitudes and beliefs of providers with whom they discuss surgical options may influence treatments. Such attitudes and beliefs may differ by physician specialty”

• It is possible that radiation oncologists and surgeons may differ in their attitudes regarding some of these issues.
Indications

T1/T2, N0, N1 tumors.

Selected patients with T3 tumors.
## Evidence for BCT

<table>
<thead>
<tr>
<th>Trials</th>
<th>No</th>
<th>Stage</th>
<th>Surgery</th>
<th>RT boost</th>
<th>FU</th>
<th>Overall survival</th>
<th>Local recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institute Gustave Roussy</td>
<td>179</td>
<td>1</td>
<td>2cm gross margin</td>
<td>15</td>
<td>15</td>
<td>73</td>
<td>65</td>
</tr>
<tr>
<td>Milan</td>
<td>701</td>
<td>1</td>
<td>quadrantectomy</td>
<td>10</td>
<td>20</td>
<td>42</td>
<td>41</td>
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<tr>
<td>NSABP B-06,18,23</td>
<td>1219</td>
<td>1,2</td>
<td>lumpectomy</td>
<td>none</td>
<td>20</td>
<td>46</td>
<td>47</td>
</tr>
<tr>
<td>NCI 24,25</td>
<td>237</td>
<td>1,2</td>
<td>Gross excision</td>
<td>15-20</td>
<td>18</td>
<td>59</td>
<td>58</td>
</tr>
<tr>
<td>EORTC 26,27</td>
<td>874</td>
<td>1,2</td>
<td>1 cm gross margin</td>
<td>25</td>
<td>10</td>
<td>65</td>
<td>66</td>
</tr>
<tr>
<td>Danish 28</td>
<td>904</td>
<td>1,2,3</td>
<td>Wide excision</td>
<td>10-25</td>
<td>6</td>
<td>79</td>
<td>82</td>
</tr>
</tbody>
</table>
Contraindications for BCT

Absolute: Radiation therapy during pregnancy

Diffuse suspicious or malignant appearing microcalcification

Wide spread disease that can not be incorporated by local excision through a single incision that achieves negative margins with a satisfactory cosmetic result

Persistent positive pathologic margin
- Relative: Prior radiation therapy to chest wall.
- Active connective tissue disease involving the skin (scleroderma and lupus)
- Tumors >5 cm
- Focally positive margin
- Women with known or suspected genetic predisposition in breast cancer
Techniques

- Wide local excision
- Curvilinear incision
- Radial incisions
- Circum-areolar incision
Basic Steps

- No skin excision unless anterior margin is very close
- Wide skin flaps to be raised
- Careful skin flap handling
- Meticulous hemostasis
- No slanting of margins
- Regular palpation and maintaining at least 1cm margin
- To go upto muscle
- Adequate light and retraction
- Marking of specimen
- Frozen section
- No drain at primary site?
- Approximate fat
- Mobilize fat off the muscle and off the skin
- In UOQ axillary dissection from same incision
Oncoplastic closure

- Volume displacement – mobilizing breast fat and approximating.
- Volume replacement – using flaps, preferably LD flap.
- Concept of leaving cavity for seroma to accumulate no more exist.
• oncplastic surgery is not a technique – it’s a way of thinking.
<table>
<thead>
<tr>
<th>Risk factors for LR after BCT</th>
<th>Patient factors:</th>
<th>Tumor factors:</th>
<th>Treatment risk factors:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
<td>Inherited susceptibility</td>
<td>Margin of resection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EIC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Use of a boost</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Use of adjuvant therapy</td>
</tr>
</tbody>
</table>
- Age: Young age is an independent risk factor
- Inherited susceptibility: BRCA1/BRCA2 mutation are at higher risk of contralateral breast cancer. (20% with mutation, 2% without mutation)
- EIC: young age and multiple close margins are a/w increased risk of IBTR and can be used to select patients who might benefit from re-excision.
- Margins of resection: negative margin : Absence of cancer cells at inked surface.
- Use of adjuvant systemic therapy
- Endocrine therapy NSABP B-14
- Stockholm breast cancer study group
- NSABP B-21
- Chemotherapy NSABP B-13
- Molecular subtype: most important significant determinant of LR after BCT (and mastectomy).
  
  TNBC > other subtypes

- Use of Radiation boost: EORTC trial of 5318 patients
MANAGEMENT OF AXILLA

- Positive axillary nodes are harbinger of systemic disease.
- Axillary dissection – prognostic implication. No survival benefit (NSABP B-04 trial)
- Standard of care is complete axillary clearance (level I, II and III)
- Minimum number of nodal yield -12
Lymph node levels
Problems with ALND

- 10% to 20% of patients exhibit decreased range of motion of the shoulder.
- 80% experience numbness in the distribution of the intercostobrachial nerve.
- 2% to 30% report arm edema.
- 15% to 50% experience breast edema.
- 5% seroma.
- Poor QOL
standard for staging the axilla.

Surgical excision of the axillary nodes represents the gold

examination of the axillary nodes in predicting nodal status.

No invasive technique is as accurate as pathologic

BUT...
AND.....

The impact of prophylactic axillary node dissection on breast cancer survival--a Bayesian meta-analysis.
*Orr RK.*

CONCLUSION- All six trials showed that prophylactic axillary node dissection: *average survival benefit of 5.4%.*
• Survival impact and predictive factors of axillary recurrence after sentinel biopsy

• From 1999 to 2013, 14,095 patients who underwent surgery for clinically N0 previously untreated breast cancer and had sentinel lymph node biopsy were analysed

• In multivariate analysis, overall survival was significantly lower in cases of AR (p < 0.0001), age >50, lymphovascular invasion, grade 3 disease, sentinel node (SN) macrometastases, tumour size >20 mm, absence of chemotherapy and triple-negative phenotype.

• Isolated AR is more common in Her2-positive/HR-negative triple-negative tumours with a more severe prognosis in triple-negative and Her2-positive/HR-negative tumours

*European journal of cancer*, May 2016, volume 58, pages 73-82
• Shift from ALND to SLNB
Concept

- If sentinel node is negative, unlikely that patient will have positive axillary node. Hence avoidance of axillary dissection.
- Concept has been validated in multiple randomised trials both single and multi-institutional.
- Has no impact on survival on long term follow-up of > than 10 years.
NSABP 04

Nodal Treatment and Survival
NSABP B04

Fisher B, NEJM 2002;347:567
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>5LN B</th>
<th>ALND</th>
<th>5LN B</th>
<th>ALND</th>
<th>5LN B</th>
<th>ALND</th>
<th>5LN B</th>
<th>ALND</th>
<th>5LN B</th>
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<tr>
<td>NSABP-B32</td>
<td>5611</td>
<td>2697</td>
<td>2619</td>
<td>8.0</td>
<td>14.0</td>
<td>8.1</td>
<td>31.1</td>
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<td>19.0</td>
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<td>N/A</td>
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<td>ALMANAC</td>
<td>954</td>
<td>478</td>
<td>476</td>
<td>5.0</td>
<td>13.0</td>
<td>11.0</td>
<td>31.0</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Milan</td>
<td>516</td>
<td>259</td>
<td>257</td>
<td>7.0</td>
<td>75.0</td>
<td>1.0</td>
<td>68.0</td>
<td>N/A</td>
<td>N/A</td>
<td>21.0</td>
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<tr>
<td>Purushotham et al</td>
<td>298</td>
<td>143</td>
<td>155</td>
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<td>64.0</td>
<td>N/A</td>
<td>66.0</td>
<td>N/A</td>
<td>14.0</td>
<td>N/A</td>
<td>21.0</td>
</tr>
<tr>
<td>5NAC</td>
<td>1083</td>
<td>544</td>
<td>539</td>
<td>2.8</td>
<td>4.2</td>
<td>N/A</td>
<td>2.5</td>
<td>4.4</td>
<td>36.0</td>
<td>17.0</td>
<td>36.0</td>
</tr>
<tr>
<td>GIVOM</td>
<td>697</td>
<td>345</td>
<td>352</td>
<td>10.0</td>
<td>5.0</td>
<td>8.0</td>
<td>15.0</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Z0011</td>
<td>744</td>
<td>371</td>
<td>373</td>
<td>6.0</td>
<td>11.0</td>
<td>9.0</td>
<td>39.0</td>
<td>N/A</td>
<td>6.0</td>
<td>14.0</td>
<td>N/A</td>
</tr>
</tbody>
</table>
SLNB for AXILLARY STAGING

- LESS MORBIDITY
- IMPROVE CHANCE OF DETECTION OF DISEASE IN LN
- CHANCE OF DETECTING NON AXILLARY LN METS
- NO SURVIVAL DIFFERENCE

For patients with

cNo
T1/ T2
Indications

- T1/T2 tumors, clinically node negative.
Contra-Indications

- T3,t4 tumors
- Clinically palpable nodes
- DCIS without mastectomy except large >than 5cm
  DCIS and high grade DCIS to avoid second
  procedure if invasive component discovered in final
  pathology
- Pregnancy
- Prior non oncologic surgery?
- Prior systemic treatment?
- inflammatory breast cancer
Techniques

Dye directed (Blue dye)

Radiotracer directed (Hot node)

Combination
Dye directed technique

Blue Dye Used
Iso sulphann blue; patent blue V, methylene blue
Route of administration
Intra parenchymal
Intra dermal
Sub dermal
Peri areolar
Sub areolar
Blue dye technique

Advantages
Simple, inexpensive, easy to identify a blue stained tract against yellow fatty background

Disadvantages
Strong learning curve (Giuliano)
Radiopharmaceuticals

Tc99m Sulfur colloid
Filtered Tc99m labeled colloidal albumin
Site of injection

- Sub dermal/Intradermal
- Peritumoral in deep seated lesions specially in medial quadrant
- Periareolar
- Subareolar
Dose and Volume

0.1-0.4 ml to 4-8 ml
300 - 400 μCi
500 μCi-1mCi
Filtered or unfiltered
Advantages of Radiotracer guided technique

• ‘Road map’ to the SN

• Detects SNs at unusual sites
  - Level III, sub pectoral, int. mammary
Special scenarios

- Old age
- Male breast cancer
- Locally advanced and inflammatory breast cancer
- Neoadjuvant chemotherapy
- Multicentric disease
- Ductal carcinoma insitu
- Pregnancy
- Previous breast or axillary surgery for nonmalignant conditions
SLN mapping of nonaxillary nodes

- Can identify non axillary nodes in 43%.
- Remain controversial
- Dissection is investigational
- May affect decisions regarding adjuvant systemic therapy and radiation field.
- Limitations: Interference
  - High rate of technical failure in patient with parasterna hot spot
  - Hot spots do not always represent metastatic disease
• Intra mammary node:
  1-28% of breast cancer
  same prognostic significance as axillary nodes
NSABP B-32

N = 5611
Lymphatic mapping was successful 97%
False negative rate 9.8%
No difference in OS or DFS in 8 yrs follow up
Coordination of Breast Cancer Care Between Radiation Oncologists and Surgeons: A Survey Study

Reshma Jagsi, M.D., D.Phil.,* Paul Abrahamse, M.S.,† Monica Morrow, M.D.,‡ Ann S. Hamilton, Ph.D.,§ John J. Graff, M.S., Ph.D.,¶ and Steven J. Katz, M.D., M.P.H.*
DO ALL PATIENTS WITH POSITIVE SLNB NEED ALND?
ACOSOG Z0011

A randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive SN

Principal Investigator: Armando E. Giuliano, MD
165 Investigators / 177 Institutions

Giuliano A, JAMA 2011;305:589
## Inclusion/Exclusion Criteria

<table>
<thead>
<tr>
<th>Eligibility</th>
<th>Ineligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clinical T1 T2 N0 breast cancer</td>
<td>• <em>Third field (nodal), irradiation</em></td>
</tr>
<tr>
<td>• H&amp;E-detected metastases in SN (AJCC 5th edition)</td>
<td>• <em>Metastases in SN detected by IHC only</em></td>
</tr>
<tr>
<td>• Lumpectomy with whole breast irradiation</td>
<td>• <em>Matted nodes</em></td>
</tr>
<tr>
<td>• Adjuvant systemic therapy by choice</td>
<td>• 3 or more involved SN</td>
</tr>
</tbody>
</table>
## Patient and Tumor Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intent-to-treat</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ALND n = 420</td>
<td>SLND n = 436</td>
<td></td>
</tr>
<tr>
<td>Median age</td>
<td>56 (24-92)</td>
<td>54 (25-90)</td>
<td></td>
</tr>
<tr>
<td>Clinical T1</td>
<td>68%</td>
<td>71%</td>
<td></td>
</tr>
<tr>
<td>ER+</td>
<td>83%</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>PR+</td>
<td>68%</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>LVI present</td>
<td>41%</td>
<td>36%</td>
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</table>
### Patient and Tumor Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intent-to-treat</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>ALND n = 420</td>
<td>SLND n = 436</td>
<td></td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>22%</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>49%</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>29%</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal</td>
<td>83%</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>Lobular</td>
<td>7%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11%</td>
<td>8%</td>
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</tr>
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</table>

## Adjuvant Systemic Therapy

<table>
<thead>
<tr>
<th></th>
<th>ALND</th>
<th>SLND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>57.9%</td>
<td>58.0%</td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td>46.4%</td>
<td>46.6%</td>
</tr>
<tr>
<td>Either/Both</td>
<td>96.0%</td>
<td>97.0%</td>
</tr>
</tbody>
</table>

\[ P = \text{N.S.} \]
Median Number of Lymph Nodes Removed

<table>
<thead>
<tr>
<th>ALND</th>
<th>SLND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent to Treat</td>
<td>N=420</td>
</tr>
<tr>
<td>Treatment Received</td>
<td>N=388</td>
</tr>
<tr>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

- ALND: 17 (Intent to Treat), 17 (Treatment Received)
- SLND: 2 (Intent to Treat), 2 (Treatment Received)

Median number of nodes removed:
- Intent to Treat: ALND = 17, SLND = 4
- Treatment Received: ALND = 17, SLND = 3
106 (27.4%) of patients treated with ALND had additional positive nodes removed beyond SN.
## Locoregional Recurrence Z11

<table>
<thead>
<tr>
<th></th>
<th>ALND n = 420</th>
<th>SN n = 436</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>15 (3.6%)</td>
<td>8 (1.8%)</td>
</tr>
<tr>
<td>Regional</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 F/u 6.3 yrs

p = 0.11

## Survival Outcomes Z11

**Median F/u 6.3 yrs**

<table>
<thead>
<tr>
<th></th>
<th>% DFS</th>
<th>% OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SN</td>
<td>83.9 (80.2-87.9%)</td>
<td>92.5 (90-95.1%)</td>
</tr>
<tr>
<td>ALND</td>
<td>82.2 (78.3-86.3%)</td>
<td>91.8 (89.1-94.5%)</td>
</tr>
<tr>
<td>HR</td>
<td>0.82 (0.58-1.17)</td>
<td>0.79 (.56-1.1)</td>
</tr>
<tr>
<td>Adjusted HR*</td>
<td>0.88 (0.62-1.25)</td>
<td>0.87 (.62-1.2)</td>
</tr>
</tbody>
</table>

Adjusted for age, adjuvant rx

 Giuliano A, JAMA 2011;305:589
SN only positive node in 70% of cases.

0.9% regional recurrence at 6.3 years completely consistent with other published studies.
Z11: Is it Practice Changing?

Yes, but not for:

- Clinically N+
- LABC
- Neoadjuvant Therapy
- Mastectomy
- PBI
Top 5 Things Critics Don’t Like About Z11

5. Follow-up isn’t long enough
4. Not enough ER negatives
3. Not enough young women
2. “Failed Study” — didn’t reach accrual goal
# 1 Thing Critics Don’t Like About Z11

Doesn’t seem right

To cut is to cure
(and I get paid for doing it)
Other factors

- Protocol noncompliance- 11 patients assigned to the SLNB only arm underwent an ALND, and 32 patients assigned to the SLNB +ALND didn't proceed with and ALND.
- Loss to follow up: almost 20% patients
- Lack of analysis the took into account the numbers of patients with isolated tumor cell clusters, micrometastases, or macrometastases in the two arms.
International Breast Cancer Study Group (IBCSG) 23-01 trial

- Patients with micrometastatic (2 mm) disease within the sentinel node.
- Included node negative young patients.
- Regional recurrence was <1% for the ALND arm and 1% for the no ALND arm
- No differences in DFS, cumulative incidence, or OS
In clinically node-negative patients undergoing BCT with macrometastases in the SN:

- Systemic Rx decision made
- ALND not necessary for local control
- ALND does not contribute to survival
CAN PATIENTS UNDERGO AXILLARY IRRADIATION INSTEAD OF AXILLARY SURGERY?
EORTC 10981-22023 AMAROS

(After Mappings of the Axilla: Radiotherapy Or Surgery?) trial
<table>
<thead>
<tr>
<th>Therapy</th>
<th>ALND Arm (n = 300)</th>
<th></th>
<th>ART Arm (n = 266)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>%</td>
<td>No. of Patients</td>
<td>%</td>
</tr>
<tr>
<td>None</td>
<td>23</td>
<td>8</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>Endocrine therapy</td>
<td>95</td>
<td>32</td>
<td>80</td>
<td>30</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>35</td>
<td>12</td>
<td>39</td>
<td>15</td>
</tr>
<tr>
<td>Chemotherapy plus endocrine therapy</td>
<td>140</td>
<td>47</td>
<td>123</td>
<td>46</td>
</tr>
<tr>
<td>Missing</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Radiotherapy (breast/chest wall)</td>
<td>257</td>
<td>86</td>
<td>237</td>
<td>89</td>
</tr>
<tr>
<td>Axillary radiotherapy</td>
<td>15</td>
<td>5</td>
<td>266</td>
<td>100</td>
</tr>
</tbody>
</table>

Abbreviations: ALND, axillary lymph node dissection; ART, axillary radiation therapy.
• Preliminary Analysis

Patients with a tumor-positive sentinel node, treating the axilla with radiation instead of lymph node dissection, and thus performing an incomplete axillary staging, does not appear to significantly influence the prescription of adjuvant systemic therapy.
AND THEN THERE WERE SOME...
NCIC-CTG MA.20 trial

MA20 Study Schema: A Phase III Study of Regional Radiation Therapy in Early-Stage Breast Cancer

Stratify
- Number of positive nodes (0, 1-3, >3)
- Number of nodes removed (<10, ≥10)
- Type of chemotherapy (i.e., anthracycline, other, none)
- Hormonal therapy (yes, no)
- Treatment center

Randomize
- Breast Alone Radiation Therapy
- Breast and Nodal Radiation Therapy
NCIC-CTG MA20 Eligibility Criteria

Inclusion Criteria

- Invasive, female breast cancer
- Breast conserving surgery plus Level I, II axillary dissection (or SLN only if node negative)
- Systemic therapy with chemotherapy, hormones, or both
- Moderate to high risk of regional recurrence on the basis of:
  - Involved axillary nodes
  - Or if node-negative, patients must have tumors $\geq 2.0$ cm in diameter, have $<10$ nodes dissected, and have either grade 3 histology, estrogen receptor-negative disease, or the disease present in lymphovascular spaces in the breast

• Planned accrual 1822 patients (actual 1832)
• Powered to detect 5% improvement in survival at 5 years
• DSMC approved plan for protocol specified interim analysis of patterns of recurrence, survival and toxicity at 5 year
• Based upon results at interim analysis, DSMC advised results be released

Whelan et al. ASCO 2011 LBA1003
## 5-Year Results

<table>
<thead>
<tr>
<th></th>
<th>WBI</th>
<th>WBI + RNI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated LR DFS*</td>
<td>94.5%</td>
<td>96.8%</td>
<td>.02</td>
</tr>
<tr>
<td>Distant DFS</td>
<td>87.0%</td>
<td>92.4%</td>
<td>.002</td>
</tr>
<tr>
<td>DFS</td>
<td>84.0%</td>
<td>89.7%</td>
<td>.003</td>
</tr>
<tr>
<td>OS</td>
<td>90.7%</td>
<td>92.3%</td>
<td>.07</td>
</tr>
</tbody>
</table>

*identical no. IBTR’s in each group

Whelan et al. ASCO 2011 LBA1003
<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>WBI</th>
<th>WBI + RNI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonitis ≥ grade 2</td>
<td>0.2%</td>
<td>1.3%</td>
<td>.01</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>4.1%</td>
<td>7.3%</td>
<td>.004</td>
</tr>
</tbody>
</table>

*Whelan et al. ASCO 2011 LBA1003*
Provocative Results!!

2% improvement in LRC translates into 5% improvement in DDFS and DFS at 5 years.
How should we interpret these findings given the results from Z-11?
Z-11  
patients randomized  
n=891  
\( \text{cl } T_{1,2} N_0 \)  
BCT  
SLND only  
n=446  
ALND  
n=445  
No difference in  
regional control,  
DFS, OS

MA-20  
patients randomized  
n=1832  
\( \text{cl } T_{1-3} N_{0-1} \) *  
BCT  
ALND  
n=916  
ALND+RNI  
n=916  
Significant benefit in  
regional control, DDFS,  
DFS

* 85% patients with 1-3 positive nodes
Statistical Issues

• MA-20 completed accrual; Z-11 did not
• Both underestimated survival, especially Z-11
  • *Z-11 based power of trial on 5x more deaths than number observed.*

  Due to overestimation of number of deaths, planned interim analyses abandoned. However, Type I error that SLND not inferior to ALND preserved. And while power was decreased, less of concern since positive trend in favor of SLND.

• MA-20: toxicity analysis at first interim analysis for survival
Trials asking different but related questions regarding regional control and impact on BCS.

• Tumor burden appears to be greater in patients enrolled on MA-20 but populations appear to be overlapping to some degree
• RT fields on MA-20. No RT fields discription in Z-11.
We need more information to better understand disparate results.

- **MA-20**: Outcome data by number positive nodes/involvement of micromets

- **Z-11**: Information regarding RT fields; outcomes by extent of nodal disease (beyond micromets); further follow-up since 83% had ER disease and late recurrences likely
PATIENTS REQUIRING AXILLARY DISSECTION

- When no sentinel node is identified.
- Clinically node positive disease.
- Three or more sentinel node positive.
- Extracapsular spread.
- 1-2 SLNB
- High grade tumor.
- Negative Er/Pgr receptor status.
- Young patients.
ROLE OF AUS AND INTRAOPERATIVE US

Recent studies dealing with AUS in breast cancer was to identify women with lymph node metastases (imaging N1[iN1]) to spare SLNB and refer them directly to ALND.
Sparing sentinel node biopsy through axillary lymph node fine needle aspiration in primary breast cancers

Yu-Shu Cheng¹, Shou-Jen Kuo¹,²,³ and Dar-Ren Chen¹,²,³

Abstract

Background: Axillary lymph node status is an important staging and prognostic factor in breast cancer. This study aimed to evaluate the efficacy of axilla fine needle aspiration cytology (FNAC) in primary breast cancer without a palpable node and even without image characteristics of a metastatic node.

Methods: From June 2008 to January 2012, 77 patients met the inclusion criteria of having received a FNAC procedure during the diagnostic protocol of primary breast cancer with the characteristic of impalpable axilla nodes, and of having received axillary surgery after that, according to the guidelines. The patients' characteristics, clinical-pathological features, pre-operative axillary lymph node FNAC findings, surgical lymph node report, and definite pathologic staging were reviewed.

Results: The FNAC procedures had a reported sensitivity of 58.82%, specificity of 100%, positive predictive value of 100%, negative predictive value of 72.55%, and accuracy of 80.28%. There were no false positives on FNAC; therefore, the positive likelihood ratio approached infinity. The negative likelihood ratio was 41.18%. Axillary lymph node FNAC is feasible in newly diagnosed breast cancer patients to evaluate metastatic lymph nodes even in those without clinical or ultrasonic evidence of lymphadenopathy.

Conclusions: FNAC can be a routine evaluation for most primary breast cancer patients with benefits in expediting treatment. For those patients with positive findings of the axilla, sentinel node biopsy can be avoided.

Keywords: Axillary lymph node, Breast cancer, Fine needle aspiration cytology


Two planned prospective trials are focusing on this topic:

- **SOUND** (Sentinel Node vs. Observation after axillary Ultrasound).

- **INSEMA-Trial**, an Intergroup study to compare axillary SLNB vs. no axillary surgery in patients with early primary breast cancer (Gentilini & Veronesi 2012).
Patients with newly diagnosed breast cancer routinely see surgeons, but the frequency and timing of consultation with radiation oncologists has not been well characterized. Therefore, this study seeks to answer several questions. First, when do radiation oncologists become involved in the care of patients with newly diagnosed breast cancer? Second, do radiation oncologists feel that they are involved in the care of the breast cancer patient at the appropriate time in the decision-making process? Third, are certain provider or practice characteristics associated with more coordinated multidisciplinary care? And finally, do surgeons and radiation oncologists have different opinions regarding optimal management in certain common breast cancer scenarios?
# Distribution of physician responses to items related to frequency and timing of radiation oncologist participation

<table>
<thead>
<tr>
<th>Responses</th>
<th>Share of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Few or almost none</td>
</tr>
<tr>
<td><strong>Surgeon responses</strong></td>
<td></td>
</tr>
<tr>
<td>Share of patients for whom surgeon discussed plan with radiation oncologist before definitive surgery</td>
<td>43.5</td>
</tr>
<tr>
<td>Share of patients who consulted with a radiation oncologist before definitive surgery</td>
<td>49.7</td>
</tr>
<tr>
<td><strong>Radiation oncologist responses</strong></td>
<td></td>
</tr>
<tr>
<td>Share of patients seen in consultation before definitive surgery</td>
<td>49.6</td>
</tr>
<tr>
<td>Share of patients for whom treatment plan was discussed with surgeon before definitive surgery</td>
<td>39.5</td>
</tr>
<tr>
<td>Share of patients for whom radiation oncologist discussed treatment plan with medical oncologist before initiating radiotherapy</td>
<td>9.7</td>
</tr>
<tr>
<td>Share of patients for whom radiation oncologist discussed treatment plan with plastic surgeon before initiating radiotherapy</td>
<td>78.8</td>
</tr>
</tbody>
</table>
- Multidisciplinary management
- More emphasis on conservative procedures, both breast and axilla
- Individualize the management of axilla
- ITC- Not indicated
- Micrometastasis: Not entirely clear
- Limited disease (1-2 nodes): Individualize
- > 3 positive nodes: ALND
It's not about you.

It's not about me.

It's about "we".

Working Together. As one.