Breast Cancer Diagnosis and Treatment

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Breast Cancer

- >200,000 new cases per year
- 4600 in Tennessee
- 40,000 deaths per year
- # one cancer in women
- # two in cause of cancer death
5 year Survival

Local disease only – 99%
Regional spread – 84%
Distant spread – 23%
Overall – 90%

Cancer Statistics, 2012
Risk Factors

- Age
- Early menarche
- Late menopause
- Nulliparity / late parity
- Previous breast cancer
- Proliferative histology on biopsy
- Family history
- Other
The most important thing to remember about risk factors is that 75 – 80% of women with breast cancer have no risk factors other than that they are women and have breasts.

All masses need to be thoroughly evaluated. Biopsy is the only way to be sure that a mass is not cancer.
<table>
<thead>
<tr>
<th>Symptom†</th>
<th>Diagnostic Exams</th>
<th></th>
<th></th>
<th></th>
<th>Screening Exams</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breast Cancer</td>
<td></td>
<td>Rate</td>
<td>OR (95% CI)</td>
<td>Breast Cancer</td>
<td></td>
<td>Rate</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>None</td>
<td>9,249</td>
<td>383</td>
<td>41</td>
<td>1.0</td>
<td>105,146</td>
<td>656</td>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>Any</td>
<td>4,275</td>
<td>283</td>
<td>66</td>
<td>2.0 (1.6, 2.3)</td>
<td>5,177</td>
<td>67</td>
<td>13</td>
<td>2.1 (1.6, 2.7)</td>
</tr>
<tr>
<td>Lump</td>
<td>2,745</td>
<td>229</td>
<td>83</td>
<td>2.8 (2.3, 3.4)</td>
<td>1,740</td>
<td>38</td>
<td>22</td>
<td>3.6 (2.6, 5.0)</td>
</tr>
<tr>
<td>Nipple discharge</td>
<td>470</td>
<td>25</td>
<td>53</td>
<td>1.5 (1.0, 2.3)</td>
<td>873</td>
<td>10</td>
<td>11</td>
<td>1.8 (1.0, 3.4)</td>
</tr>
<tr>
<td>Pain</td>
<td>287</td>
<td>15</td>
<td>52</td>
<td>1.4 (0.8, 2.4)</td>
<td>694</td>
<td>6</td>
<td>9</td>
<td>1.5 (0.7, 3.4)</td>
</tr>
<tr>
<td>Other</td>
<td>1,400</td>
<td>58</td>
<td>41</td>
<td>1.2 (0.9, 1.6)</td>
<td>2,672</td>
<td>20</td>
<td>7</td>
<td>1.2 (0.8, 1.9)</td>
</tr>
</tbody>
</table>

* Rate of breast cancer diagnoses per 1000 women per year.
† Adjusted for age, body mass index, family history of breast cancer, previous breast biopsy, and hormone therapy use.
‡ Symptom categories are not mutually exclusive.
A negative mammogram should not preclude biopsy of a new palpable mass.

10 - 15% of malignancies are not visible on mammogram.
Breast Mass
Tissue Diagnosis

- FNA
  - cytology
  - experienced cytopathologist
  - inadequate sample

- Core bx
  - histology
  - routine pathology
  - tumor markers
Image Guided Biopsy

- **Ultrasound**
  - patient supine
  - lesion must be visible on usg

- **Stereotactic**
  - patient prone
  - not good for deep / posterior lesions
  - weight limit on table
Ultrasound-guided biopsy
Needle passing through lesion
Stereotactic Biopsy
Pre & Post-biopsy Image

marker clip
Image Guided Biopsy

- 6 month follow-up imaging
- X-ray evaluation of specimen for microcalcifications
- Discordant pathology requires excision
MRI in Breast Oncology

ASBS Consensus Statement- 2010

- axillary met with no known primary
- ipsilateral extent or contralateral disease
- monitor response to neoadjuvant therapy
- screening in women at high risk
  - BRCA 1 or 2 mutations
  - history of chest wall XRT
  - others with a ≤ 20% risk of breast cancer
- indeterminate imaging and/or physical
MRI in Breast Oncology

NCCN Guidelines

- occult axillary met or Paget’s
- ipsilateral extent or multifocal/multicentric
- monitor response to neoadjuvant therapy
- mammographically dense

False positives common. Surgical decisions should not be based on MRI alone – additional tissue sampling is recommended.
MRI in Breast Oncology

Canadian Study

Compared MRI vs Conventional Screening in BRCA 1 and 2

1275 women for 3.2 years (median)

445 with MRI, 830 mammography alone

9.2% in each group developed cancer

DCIS or Stage I 13.8 vs 7.2 %

Stage II to IV 1.9 vs 6.6 %
Complete Clinical Response MRI
Triple Negative Breast Cancer
Therapy
Breast Conservation

Absolute Contraindications

- 2 or more tumors in diff quadrants*
- diffuse suspicious calcifications
- prior radiation
- pregnancy
- persistent positive margins

Relative Contraindications

- collagen vascular disease
- tumor > 5cm or tumor:breast size
- <35 yo with BRCA 1 or 2 mutation
Breast Cancer
Mastectomy

Does not:

change overall survival
change incidence of distant recurrence
change need for adjuvant therapy
chemo-, endocrine, or biologic
Breast Cancer
Reconstruction after mastectomy

- immediate vs delayed
- expander vs autogenous tissue
- may significantly affect quality of life
- chemotherapy can continue

Does not adversely affect long-term outcome
Sentinel Lymph Node Biopsy

ACOSOG Z0011

900 patients RCT patients w/ positive SN

SN + ALND vs SN alone

Compared local and regional recurrence

locoregional \( 4.1 \% \) vs \( 2.8 \% \)

local \( 3.6 \% \) vs \( 1.9 \% \)

regional \( 0.5 \% \) vs \( 0.9 \% \)

95\% received adjuvant systemic Rx

All received whole-breast XRT
SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB and IIIA T3, N1, M0

FNA or core biopsy positive

Axillary dissection level I/II

Clinically node positive at time of diagnosis

FNA or core biopsy negative

Sentinel node negative

Consider no further surgery (category 1)

Sentinel node positive

Meets ALL of the following criteria:
- T1 or T2 tumor
- 1 or 2 positive SLNs
- Breast conserving therapy
- Whole breast RT planned
- No neoadjuvant chemotherapy

Yes to all

Sentinel node not identified

Axillary dissection level I/II

Clinically node negative at time of diagnosis

Sentinel node mapping and excision

No
Breast Cancer
Adjuvant Therapy
Considerations

Tumor size and grade

Nodal status

N0, N 1 mi vs Node positive

Hormone receptor status

Her 2 status

Oncotype DX
NCCN Guidelines
Adjuvant Systemic Therapy

**Tumor size**

- \( \leq 0.5 \text{cm} \) if ER/PR +, consider endocrine Rx
  - if ER/PR -, no additional Rx
- \( > 0.5 - 1 \text{cm} \) adjuvant therapy if ER/PR – or Her 2 +
- \( > 1 \text{cm} \) adjuvant therapy
## NCCN Guidelines
### Adjuvant Systemic Therapy

**Nodal status**

<table>
<thead>
<tr>
<th>Nodal Status</th>
<th>Therapy Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>May need no additional therapy</td>
</tr>
<tr>
<td>N1 mi</td>
<td>Adjuvant therapy recommended (2B)</td>
</tr>
<tr>
<td>N1 or higher</td>
<td>Adjuvant therapy recommended (1)</td>
</tr>
</tbody>
</table>
Adjuvant Systemic Therapy
Chemo-, Hormonal or Biologic

Chemotherapy
Node positive *
ER/PR negative
Her 2 neu positive
Oncotype DX™ or Mammoprint™

Hormonal therapy
ER / PR positive

Biologic therapy
Her 2 positive
Standardized Quantitative Oncotype DX Assay

Recurrence Score in N-, ER+ patients

- Low Risk Group
- Intermediate Risk Group
- High Risk Group

21 gene array

**Lower RS’s**
- Lower likelihood of recurrence
- Greater magnitude of TAM benefit
- Minimal, if any, chemotherapy benefit

**Higher RS’s**
- Greater likelihood of recurrence
- Lower magnitude of TAM benefit
- Clear chemotherapy benefit

3) Paik et al JCO 2006, 4) Gianni et al JCO 2005
Adjuvant Therapy

Oncotype DX™

Score of 4
Distant Recurrence at 10 yrs 5%

RESULTS

Recurrence Score = \( \mathbf{4} \)

Test results should be interpreted using the information in the Clinical Experience section below, which applies only to patients consistent with this clinical experience.

CLINICAL EXPERIENCE

Patients with a Recurrence Score of 4 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 5\% (95\% CI: 2\% - 7\%)

The following results are from a clinical validation study with prospectively-defined endpoints involving 688 patients. The patients enrolled in the study were female, stage I or II, node negative, ER-positive, and treated with tamoxifen, *N Engl J Med* 2004; 351: 2817-26.

![Graph showing recurrence risk](graph.png)

*For Recurrence Scores > 50, group average rate of distant recurrence and 95% CI shown*
Breast Cancer
Neo-adjuvant Chemotherapy

Chemotherapy given before surgical intervention
Breast Cancer
Neo-adjuvant Chemotherapy

Indications

- Large clinical stage IIA (T2N0M0)
- Stage IIB (T2N1M0 or T3N0M0)
- Stage III A (T3 N1 M0)
- Tumors that meet criteria for BCT except for size

NCCN Guidelines
Breast Cancer

Neo-adjuvant Chemotherapy

- Convert to candidate for conserving surgery
- Evaluate tumor response to agents
- No survival advantage
Breast Cancer
Neo-adjuvant Chemotherapy

Lymph node evaluation
pretreatment
  clinically negative
  clinically positive
posttreatment
Preoperative Chemotherapy Guideline

PRIMARY TREATMENT

RESPONSE

No response after 3-4 cycles or progressive disease

- Partial response, lumpectomy not possible
- Partial response, lumpectomy possible or complete response

Preoperative chemotherapy (endocrine therapy alone may be considered for receptor positive disease in postmenopausal patients)

No response after 3-4 cycles or progressive disease

- Consider alternative chemotherapy

Partial response, lumpectomy not possible

Complete response or partial response, lumpectomy possible

See Mastectomy (BINV-13)

See Lumpectomy (BINV-13)

See Lumpectomy (BINV-13)
Breast Cancer Radiation Therapy

- breast conservation
- post mastectomy
  - 4 or more positive lymph nodes including supraclavicular
  - T3 (>5cm) or Stage 3 operable tumors
- internal mammary
  - insufficient evidence
Accelerated Partial Breast Radiation (APBI)

- Multicatheter technique
- Cavity device technique
- Intraop radiation therapy
- 3 - D Conformal
ABPI Criteria

ASBS

- N0*
- T: \( \leq 3 \) cm
- Age >45 (50 for DCIS)
- Margins: negative
APBI Criteria

ASTRO

- N0 or i+
- T: ≤ 2 cm (T1) (2.1 – 3)
- Age ≥ 60 (50 – 59)
- Margins: negative by at least 2 mm (<)
- Ductal Histology
  - no “pure DCIS” (pure DCIS ≤ 3cm)
    (invasive lobular)
- Unicentric
- No extensive DCIS or LVI (≤3cm)
  (“cautionary” criteria)
Interstitial Breast Brachytherapy

Multicatheter technique
Fig 2. MammoSite radiation therapy system. External appearance and sagittal view of balloon with dosimetric target coverage. Target is defined as tissue within 1 cm of balloon surface.
3-D Conformal therapy

Fig 3. Three-dimensional conformal external beam radiotherapy. Four-field beam arrangement and conformal, homogeneous dose coverage of the target. Target is shaded in purple.
IORT
Followup

Clinical exam q 3 – 6 months for 5 yrs then yearly
Mammogram 6 mths after XRT, then q 6 mths for 2 yrs, then yrly
annual on contralateral breast
On tamoxifen – annual GYN exam
On AI or w/ ovarian failure – bone health monitoring
Breast Cancer
During Pregnancy

1 in 3000 pregnancies
Most common malignancy assoc w/ preg
Diagnosis often delayed
Breast Cancer
During Pregnancy

Radiation contraindicated

Surgery
mastectomy in early stages
lumpectomy later stages

Chemotherapy
after first trimester
Pregnant patient with confirmed breast cancer diagnosis (core biopsy preferred) No distant metastases on staging

1st trimester → Discuss termination: Non-therapeutic → Continuing pregnancy → Mastectomy + axillary staging

2nd trimester/Early 3rd trimester → Mastectomy or breast-conserving surgery + axillary staging or Neoadjuvant chemotherapy, mastectomy or breast-conserving surgery + axillary staging post-partum

Late 3rd trimester → Mastectomy or breast-conserving surgery + axillary staging

Begin adjuvant chemotherapy in 2nd trimester, ± Adjuvant radiation therapy post-partum, ± Adjuvant endocrine therapy post-partum

Adjuvant chemotherapy, ± Adjuvant radiation therapy post-partum, ± Adjuvant endocrine therapy post-partum
Male Breast Cancer

- Less than 1% of breast cancers
- Majority ER positive
- Mastectomy, sentinel node
- Predisposing factors
  - Klinefelter’s
  - Previous radiation
Occult Primary Tumor

Axillary Node

- Less than 1% of all breast cancers
- Imaging w/ MRI will define primary in up to 70% of patients
- Treatment options w/ no primary
  - Mastectomy
  - Whole breast radiation
- Axillary dissection
- Adjuvant systemic therapy
Paget’s Disease

- 1 – 3% of cancers
- Eczematoid rash, itching, discharge
- Often treated as rash for months
- May be treated with mastectomy or breast conserving surgery

Margins may be a problem – cancer can be found deep within breast

Nipple areolar complex removed

Survival depends on stage
Paget’s Disease
Inflammatory Breast Cancer

- Not the same as locally advanced
- Erythema, edema
- Often treated as mastitis or cellulitis
- Pathology – dermal lymphatic invasion
Inflammatory Breast Cancer

- Neoadjuvant chemotherapy
- Mastectomy
- Radiation
What we say to dogs
Okay, Ginger! I've had it! You stay out of the garbage! Understand, Ginger? Stay out of the garbage, or else!

What they hear
blah blah GINGER blah
blah blah blah blah
blah GINGER blah
blah blah blah...
This is the second reminder that your program (University of Tennessee Program - 4404721324) has been scheduled to participate in the ACGME Resident Survey. The deadline for your program is 3/24/2013.

As of today, your program currently has a response rate of 36.0%. A 70% response rate is required for programs with 4 or more residents/fellows; programs with fewer than 4 residents/fellows should obtain a 100% response. Residents that started the program off-cycle (after Aug 31 of the current academic year) will not be asked to participate in this year's implementation.

Email received from ACGME 3/12/13