GRAND ROUND
Breast Cancer
Evolving NCCN Guidelines

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4/24/14
BREAST CANCER

- American Cancer Society estimates in 2013:
  - 235,000 Americans be diagnosed
  - 40,000 will die of dz

- Incidence inc, but mortality dec

- Risk factors:
  - Female, Elderly
  - Family hx of Breast cancer at young age, BRCA 1/2
  - Early menarche, Late Menopause, older age at 1’st live birth
  - Chest Wall irradiation, HRT
  - Benign proliferative dz, inc breast density
Breast Cancer Awareness Campaigns:

- One in Eight.
- not correct
- One in Eight.
- more correct
## Staging

### NCCN Guidelines™ Version

**Breast Cancer**

Table 1 (continued)

<table>
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<th>ANATOMIC STAGE/PROGNOSTIC GROUPS</th>
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* T1 includes T1mi

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**T- Primary Tumor**

- **T0**: no evidence of 1’ tumor
- **Tis**: in situ
- **T1**: < 2cm
  - mi = <1mm
  - a = 1-5mm
  - b = 5mm-1cm
  - c = 1cm-2cm
- **T2**: 2cm to 5cm
- **T3**: >5cm
- **T4**: extends to chest wall or skin
  - a→c: including pec muscle + other; ulceration; both
  - d: Inflam Ca
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N- Regional Lymph Nodes

• N0= none
  • N0i+= isolated tumor cells <0.2mm, <200 cells

• N1= ipsilat level 1 or 2 (1-3 nodes)
  • N1mi= micrometastasis 0.2mm- 2mm, >200 cells

• N2= ipsilat level 1 or 2 & matted (4-9 nodes)
  • Or (+) Internal mammary LN

• N3= ipsilat infraclavicular LN
  • Or supraclavicular LN
  • Or >10 axillary nodes
  • Or Internal mammary LN with (+) level 1 or 2 axillary LN
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M- Distant Metastasis

- **M0**= none
- **M0(i+) =** <0.2mm Tumor cells in bone marrow, circulating, or found incidentally in other tissues
- **M1**= >0.2mm distant
M- Distant Metastasis

- M0= none
- M0(i+)= <0.2mm Tumor cells in bone marrow, circulating, or found incidentally in other tissues
- M1= >0.2mm distant
Updates to staging

- 2010 TNM staging:
  - Subdivided Stage 1A & 1B
    - N0 vs N0mi- Nodal micrometastasis <0.2mm
  - New M0(i+) category
    - <0.2mm Tumor cells in bone marrow, circulating, or found incidentally in other tissues
  - All invasive Ca need a histologic tumor grade
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Breast Cancer Grades

- Nottingham combined histologic grade
- Assesses Morphologic features:
  - Tubule formation= 1,2,3
  - Nuclear pleomorphism= 1,2,3
  - Mitotic count= 1,2,3
- Value given for each feature 1= favorable, 3= unfavorable
- Add together the scores of 3 categories:
  - Grade 1= 3-5 pts  GOOD
  - Grade 2= 6-7 pts
  - Grade 3= 8-9pts  BAD
Breast Cancer Grades

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Breast Cancer Awareness Campaigns:
**LCIS**

- Lobular Carcinoma In Situ, Stage 0 Tis
- Need H&PE & B MMG
- If core biopsy → Surgical excision
- If only LCIS:
  - Do not need neg margins
  - Counsel about risk reduction
  - Surveillance
- “Pleomorphic” LCIS - acts like DCIS
  - Rec complete excision with neg margins
  - No radiation
LCIS

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- “Pleomorphic” LCIS- acts like DCIS
  - Rec complete excision with neg margins
  - No radiation
DCIS

- Ductal Carcinoma In Situ, Stage 0 Tis
- Need H&P< B MMG, ER/PR
- Tx Options:
  - (BCT) Lumpectomy (needle loc?) + Whole Breast Radiation
    - Radiation reduces recurrence rates by 50%
    - Re-resection: + or <1mm margin
    - Rad Boost→ if <1mm @ chest wall or skin
  - Total Mastectomy, +/- SLN, +/- Reconstruction
  - Lumpectomy without Radiation
    - “Low” risk pts- nonpalpable, tiny, low grade, wide margins, age>50
DCIS

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DCIS

- Post op:
- 5 yrs of Tamoxifen if ER +
  - Risk Reduction Bilaterally
- 5 yrs of H&P q 6-12 mths
  - Then annually
- MMG annually
  - MMG 6 mths post op if BCT

* Of note, NSABP trial showed 75% reduction of Invasive Breast Ca in pts with atypical ductal hyperplasia treated with 5 yrs of tamoxifen. Benign breast disease also dec
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Stage 1

- H&P
- Labs: CBC, LFT’s + alk phos
- Imaging: B MMG & US, ?MRI
- Path review w ER/PR/HER2
- Genetic or fertility counseling if indicated
- Stage 1-2b: Image for sx and abn lab
  - Bone pain or inc alk phos= Bone scan
  - Abd pain, Inc LFT’s= CT A/P
  - Pulm sx= CT chest
Stage 1

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Stage 2 Breast Cancer

- Breastbone
- Lymph nodes

Cancer in 1 to 3 lymph nodes in the axilla or near the breastbone

Tumor is 2 cm or smaller

Tumor is larger than 2 cm but not larger than 5 cm

Stage 2
Stage 2

Stage IIA Breast Cancer

- Breastbone
- Lymph nodes
- Axilla

Cancer in 1 to 3 lymph nodes in the axilla or near the breastbone

Tumor is 2 cm or smaller
2 cm

Tumor is larger than 2 cm but not larger than 5 cm
5 cm
2 cm

Stage IIB Breast Cancer

- Breastbone
- Lymph nodes
- Axilla

Cancer in 1 to 3 lymph nodes in the axilla or near the breastbone

Tumor is larger than 2 cm but not larger than 5 cm
5 cm
2 cm

Clusters of cancer cells in lymph nodes

Tumor is larger than 5 cm
5 cm
**Stage 1-2b “Early Stage” Option 1**

- If T2 or T3, may use neoadj to dec size for BCT
- Follow with Radiation
  - Omit if all
    - >70yo
    - T1, N0
    - ER+
  - will take endocrine therapy
Stage 1-2b “Early Stage” Option 1

- If T2 or T3, may use neoadjuvant to dec size for BCT
- Follow with Radiation
  - Omit if all
    - >70yo
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    - ER+
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Stage 1-2b BCT

- If > 1 positive axillary LN → Whole Breast Radiation tx +/- boost
  - ALN diss if 3 or more (+) nodes
  - Rec include infra & supraclavicular LN & internal mammary LN
  - If > 4 + → systemic imaging, CT C/A/P, bone scan, PET/CT

- If Neg axilla → Whole or Partial Breast Radiation +/- boost
  - PBI- >60yo, BRCA (-), T1N0, unifocal, ER+, IDC, favorable, (-) margin

- Radiation AFTER chemo
Stage 1-2b
BCT

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- Radiation AFTER chemo
Surgical Staging of the Axilla

- ACOSOG Z0011 - Randomized trial
  - Compared SLN or ALN
    - >18yoF
    - T1-2 tumors, 1-2 (+) SLN
  - Undergoing BCT w Whole Breast Radiation
  - No neoadj treatment
  - No diff in LR, disease free survival or OS
  - Only dec OS in ER (-), <50yo, & no postop chemo
  - No signif difference in det (+) or (-) dz
  - More morbidity with ALN dis (level 1&2)
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BCT Contraindications:

- **Absolute:**
  - Radiation during pregnancy
  - Diffuse, Suspicious calcifications
  - Widespread disease & unable to get (-) margins with 1 incision with a good cosmetic result
  - Continued (+) margins after re-excisions

- **Relative:**
  - Prior radiation to breast or chest wall
  - Active connective tissue dz invol skin (lupus or scleroderma)
  - Tumors > 5cm
  - Focally + margin
  - BRCA +
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  - BRCA +
Stage 1-2b

- In BCT
- (+) Margins $\rightarrow$ re-excite
- If microscopically focally + without an Extensive Intraductal Component (EIC) $\rightarrow$ can Radiate with boost
  - EIC- IDC where $>$25% of tumor volume is DCIS & DCIS extends beyond the invasive Ca into surrounding normal breast tissue
Breast Cancer Awareness Campaigns:

save a life
grope
your wife
save the ta-tas
Stage 1-2b “Early Stage” Option 2

- With or without immediate reconstruction
- SLN instead in most cases
  - Stage 1-2b
  - FNA neg in axilla
- ALN diss if 3 or more (+) nodes
Stage 1-2b Post Mastectomy

- If > 1 positive axillary LN → Chest Wall Radiation
  - Rec Include infra & supraclavicular LN & internal mammary LN
- If > 4 + → systemic imaging, CT C/A/P, bone scan, PET/CT

- If neg axilla:
  - > 5cm tumor or + margins → Chest Wall Radiation + LN
  - < 5cm tumor & margins <1mm → Chest Wall Radiation
  - < 5cm tumor & margins >1mm → No radiation

- Radiation AFTER chemo
Stage 1-2b Post Mastectomy

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- Radiation AFTER chemo
Breast Cancer Awareness Campaigns:
Stage 3
“Locally Advanced”

- Clinical stage T3N1M0
- Advanced disease confined to breast & regional LN

- Usual Workup →
  Consider Imaging:
  - MRI or CT C/A/P
  - Bone Scan or PET/CT
Stage 3
Stage 3 Breast Cancer

Stage IIIB Breast Cancer
- Chest wall
- Ribs
- Muscle
- Fatty tissue
- Lymph nodes
- Cancer
- Breastbone

Stage IIIC Breast Cancer
- Collarbone
- Lymph nodes
- Axilla
- Cancer in 10 or more lymph nodes in the axilla
- Cancer in lymph nodes above or below the collarbone
- Cancer in lymph nodes in the axilla and near the breastbone

No tumor or tumor is any size
Stage 3

- Inoperable → Neoadj
  - Neoadj AC + taxane
  - If HER2 + add trastuzumab

- Operable: 1 or 2 Options
  1. Local therapy w lumpectomy + ALN
  2. MRM +/- immed reconstruction
     - Complete Chemo
     - Postop Rad chest wall + LN
     - +/- Endocrine tx +/- Biologic therapy (HER2)

- If doesn’t respond = palliative breast Radiation for local control
Stage 3

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Neoadj

- NSABP B-18 trial
  - BCT rate higher after preop chemo
- Breast: Core biopsy & mark w clip → begin neoadj
- 2 Options after neoadj:
  - Mastectomy +/- reconstruction
    - Progressive Dz on neoadj
    - Partial response & BCT impossible
  - Lumpectomy
    - Complete Response
    - Partial response & BCT possible
- Axilla: US & SLN or FNA/Core before neoadj
  - If (+) → Level 1&2 axillary dissection at surgery
  - If (-) → SLN if FNA (-) or nothing if SLN (-) at surgery
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NeoAdj

- Chemo
  - NSABP B-27
  - Higher complete response rate with this regimen:
    - 4 cycles of Pre-op Chemo AC
      - (doxorubicin/cyclophosphamide)
    - 4 cycles of preop Docetaxol
  - Local therapy
    - Lumpectomy or Mastectomy +/- immed reconstruction
    - ALN level 1&2 if pre-op SLN/FNA was (+)
NeoAdj

- HER 2 (+)
  - Higher complete response rate (26% vs 65.2%) with:
    - Preop trastuzumab with paxlitaxel
    - FEC cyclophosphamide/*epirubicin/Fluorouracil

- ER (+)
  - Postmenopausal= aromatase inhibitor anastrozole or letrozole
    - Superior to tamoxifen
    - “Menopause” definition- prior B oophorectomy, age > 60yr, < 60yr w 1 yr of amenorrhea, FSH & estradiol in postmenopausal range

*Cardiac toxicity inc with trastuzumab + doxorubicin
NeoAdj

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Surgical Staging of the Axilla

- **ALD**
  - **Indications:**
    - Stage 3 “locally advanced”
    - 3 or more (+) SLN
  - **Excise Level 1 & 2**
    - At least 10 LN
    - Level 3 only if gross dz in Level 2

- **Optional Axillary staging:**
  - Favorable tumors
  - Elderly
  - Multiple comorbid conditions
Surgical Staging of the Axilla

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Anatomical landmarks of the axilla

- Pectoralis major muscle
- Breast tissue
- Subclavian artery and vein
- Brachial plexus
- Pectoralis minor
- Axillary artery and vein
- Latissimus dorsi muscle
- Thoracodorsal bundle (nerve, artery, vein)
- Long thoracic nerve
Breast Cancer Awareness Campaigns:
Stage 4

- H&P
- CBC
- LFT’s + alk phos
- Chest CT
- Bone Scan
- CT/MRI abd
- X-ray of painful long bones
- Biopsy & Path for ER/PR/HER2

- B MMG & US
- Genetic counseling if indicated
- Additional Imaging based on sx,s,MRI brain
Metastatic Dz

- Bone Mets- Bisphosphonates, Denosumab, oral Ca + Vit D

- Begin Endocrine therapy
  - Regardless of ER/PR/HER2

- If progression or recurrence during endocrine tx-
  - Nonsteroidal aromatase inhibitor= anastrozole
  - Steroidal aromatase inhibitor= exemestane
  - Serum ER modulators= tamoxifen
  - ER down regulator= fulvestrant
  - Others= progestins, androgens, high dose estrogen, ovarian suppression & ablation
Metastatic Dz

- If refractory to endocrine tx or visceral dz-
  - Chemo- start with 1\textsuperscript{st} line tx

- Indications for Surgery:
  - Palliation of sxs, skin ulceration, bleeding, fungation
  - Only if complete clearance of tumor can be obtained and wound closed

- Radiation can be an option > surgery

- Retrospective studies suggest a Potential benefit from complete excision of breast tumor\textsuperscript{\rightarrow} Controversial
Metastatic Dz

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Inflammatory Breast Cancer

- Clinical dx- >1/3 skin erythema & dermal edema
  - 1-6% of breast cancers
  - Usually receptor neg HER2 pos & younger age
  - Blockage of dermal lymphatics by breast Ca tumor emboli

- Stage 3B, stage3C, or stage 4
  - T4d by definition +/- LN or mets, punch biopsy
  - CBC, LFT, bone scan, CT C/A/P

- Tx- Neoadj chemo → MRM → Chemo, Rad +/- endocrine
  - BCT in select cases: only after neoadj & skin clear
  - Immediate Reconstruction is contraindicated
Inflammatory Breast Cancer

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Breast Cancer Awareness Campaigns:
Reconstruction

- Immediate vs Delayed
  - Subpectoral expander or implant (saline &/or silicone)
  - Autogenous tissue, free, or pedicle flap
  - Composite reconstruction
  - NAC- immed vs delayed, preservation technique

- “Skin” sparing mastectomy
  - Retrospective studies= no inc local recurrence

- “Volume displacement” techniques
  - Shift breast tissue to fill defect

- Radiation Expected or IBC
  - Rec delayed or staged reconstruction
Reconstruction

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Who gets Post-op Chemo?

- Tumors over 1cm LN (-) or (+) >2mm ➔ chemo
  - Trastuzumab if HER2 (+)
  - Endocrine therapy after chemo if ER (+)
    - Premenopausal= Tamoxifen 5-10yr
    - Postmenopausal= Aromatase inhibit 5yr or combo
      - anastrozole, letrozole, exemestane

- Tumors up to 0.5cm, LN <2mm, N1mi ➔ -/+ chemo
  - Endocrine therapy if ER (+)
  - Trastuzumab if HER2 (+)

- Tumors up to 0.5cm, LN (-) ➔ no chemo
  - Endocrine therapy if ER (+)

- Tumors in between ➔ ?
  - Unfavorable/ high risk get chemo
Who gets Post-op Chemo?

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  - Trastuzumab if HER2 (+)
- Tumors up to 0.5cm, LN (-) → no chemo
  - Endocrine therapy if ER (+)
- Tumors in between → ?
  - Unfavorable/ high risk get chemo
Chemo

• 3 preferred regimens:
  • 1. Doxorubicin + cyclophosphamide (AC) then Paclitaxel
  • 2. AC then weekly paclitaxel
  • 3. Docetaxel + cyclophosphamide (TC)

• HER2 (+)
  • AC then paclitaxel with 1 yr of trastuzumab
Follow-Up

- H&P q 4-6 mths for 1st 5 yrs
  - Then q 1 yrs
- MMG q 1 yr
- S/E management-
  - Venlafaxine for hot flashes & depression
  - Women on Tamoxifen- yearly Gyn exams
  - Women on Aromatase Inhib- periodic BMD exam
- Healthy lifestyles (BMI 20-25) = less contralateral Cancer
Recurrence

- After BCT (Lumpectomy + Rad)
  - MRM or mastectomy w repeat SLN

- After Mastectomy + SLN or MRM (No Rad)
  - Resect local recurrence + Chest wall + LN Radiation

- After MRM + Rad
  - Resection + ? Additional radiation

  - If Unresectable → +/- Radiation

  - If LN recurrence → +/- Resection + Chest wall & LN Radiation
Recurrence

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- After MRM + Rad
  - Resection + ? Additional radiation

- If Unresectable ➔ +/- Radiation

- If LN recurrence ➔ +/- Resection + Chest wall & LN Radiation
MRI

- Limitations: High false positive findings

- Advantages: (when US/MMG inadequate)
  - Dense breasts for staging
  - Occult 1’ tumor with axillary nodal adenoCa or Paget’s
  - Evaluate chest wall
  - Monitor for neoadj or metastatic progression or regression

- F/U MRI screening should only be rec if recurrence breast CA risk> 20% or BRCA (+)

- Should have MRI guided sampling capability or wire localization capability
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Breast Cancer Awareness Campaigns:
Pregnancy

- Often delayed dx, ALN (+) larger Tumor, frequently ER/PR (-), 30% HER2 (+)
- MRM or BCT
  - SLN “safe” (some=No or >30wk) NO blue dye
  - Radiation & endocrine tx postpartum
- FAC Chemo- 2nd trimester to 35 wks
  - HER2 Trastuzumab only postpartum
- No breast feeding during chemo/endocrine
- Refer pts who desire future pregnancies to fertility specialists prior to chemo
- After treatment- No Oral Contraceptive Pills for Birth Control for any ER/PR/HER2 -/+
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Pregnancy

- **1st Trimester:** Terminate vs Continue
  - Mastectomy + SLN → Chemo in 2nd Tri
    - Postpartum: +/- Radiation & endocrine

- **2nd trimester:**
  - Mastectomy or BCT + SLN → chemo
  - Postpartum: +/- Radiation & endocrine
  - Neoadj chemo → Mastectomy or BCT + SLN
    - Finish chemo → Postpartum: +/- Rad & endo

- **Late 3rd Trimester:**
  - Mastectomy or BCT + SLN → chemo
    - Postpartum: +/- Rad & endocrine
Male Breast Cancer

- Rare, Avg age 71yo
- < 1% of breast cancers
- Delayed Presentation:
  - 6-10 mths from sx to dx
- BRCA 2= 6% lifetime risk
  - Avg 0.1% risk
- Tx. similar to women
  - BCT or Mastectomy
  - Use Tamoxifen post tx
Axillary Breast Cancer

- Bx of axilla- ER/PR/HER2 status
- MMG & US → MRI breast, CT C/A/P
- Stage 2a T0N1M0
  - 1. MRM
  - 2. Axillary nodal dissection + Whole breast +/- Axillary Rad
  - Chemo
- Stage 3 T0N2-3M0
  - Neoadj chemo → MRM → chemo, radiation + endocrine tx
Phyllodes of Breast

- Tumors of stromal & epithelial elements
  - Mean age 40, Painless mass
  - Enlarges rapidly, > 2cm
  - Misdiagnosed as fibroadenoma on US & core bx
  - Inc in Li Fraumeni syndrome

- Dx & Tx = Excisional bx w 1cm margins
  - Local recurrence = re excision & +/- post-op radiation
  - Metastasizes to lung
  - No role for endocrine, cytotoxic chemo, or SLN
Paget’s Disease

- Neoplastic cells in epidermis of the NAC
  - 80-90% Assoc with DCIS or cancer in the breast
- Sxs: Always at NAC
  - Eczema, bleeding, ulceration, & itching
- Dx: Punch biopsy
  - Obtain B MMG + US or MRI breast
  - Core Bx of breast lesion if present
- Tx: NAC resection + radiation + tamoxifen
  - Or Mastectomy + SLN
Breast Cancer Awareness Campaigns:

check them out
Hereditary Breast & Ovarian CA

- Breast Ca (incl DCIS) Dx<50yo
- Breast CA with >1 (1st-3rd degree) relative
  - breast CA <50
  - ovarian CA at any age
  - 2 relatives with Pancreatic or Breast CA
  - Ashkenazi Jew

- 2 breast cancer primaries
- Triple negative Breast CA
- Family member w Breast and “other” cancer

- Male Breast CA
  - Or fam hx of male breast CA
- Ovarian CA
- Family hx of BRCA +
  - 1st or 2nd degree relative with breast CA <45
- Family hx of
  - > 2 breast primaries in pt
  - Ovarian CA
  - 2 breast CA on same side of family
Breast Cancer Summary

- Evolving NCCN Guidelines will continue to evolve as research and trials continue...

- Questions?
Thank You!