Breast Cancer: An overview.
Grand Round 7/6/10
Praveen Vikas, M.D.
Fellow, Oncology
East Tennessee State University

Case Report
- 60 yr. old female had a routine screening mammograms, that showed a developing density in the right breast and was reported as BI-RADS 0.
- Patient was then sent for Diagnostic Digital Mammogram and was found to have suspicious mass in the 10 o’clock position of the right breast.
- Focused ultrasound was performed throughout the right upper-outer quadrant and a hypo-echoic focus measuring 1.2 x 1.0 x 1.0 cm was noted.
- Patient had USG guided Vacuum assisted core biopsy of the right breast lump and pathology was consistent with invasive ductal carcinoma.

Case report Contd.
- Patient was then evaluated by surgical oncologist and had lumpectomy done along with sentinel lymph node biopsy of 3 LNs. Intraoperative assessment demonstrated no evidence of metastatic disease.
- Pathology findings were consistent with Invasive ductal cancer, G II, tumor size of 1.3 cm, ER/PR 100 % +, Her 2 non-amplified by FISH. Pathological margins were negative for malignancy or DCIS/LCIS.
- Patient was then send to medical oncology and radiation oncology clinic for consideration of adjuvant treatment.
Pertinent History.
- No personal or family history of breast cancer.
- Smoked ½ pack for around 10 yrs. No alcohol use.
- Age at Menarche was 14 and age at Menopause was 50.
- Patient had used OCPs for around 5 yrs.
- Obstetrics history : G3P3A0.
- She did use topical estrogen for around 4 years after menopause.
- Patient’s BMI was 23.

Treatment course.
- Patient was tested for Oncotype DX™ 21-gene assay and her 10 year distant recurrence score was 25.
- Patient was treated with 4 cycles of Adriamycin and Cyclophosphamide (AC) q 3 weeks.
- Patient then received radiation therapy as part of breast conservation protocol and was started on hormonal therapy with Tamoxifen 4 weeks after finishing radiation treatment.

Screening/ ACS guidelines.
- The American Cancer Society recommends screening mammogram every year after age 40.
- SBE after age 20, breast examined by a healthcare provider at least once every three years after age 20, and every year after age 40.
- Women at high risk ( > 20% lifetime risk) should get an MRI in addition to Mammogram.

USPSTF Recent Update to 2002 recommendation
Ann Intern Med November 17, 2009
- Recommends against routine screening mammography in women aged 40 to 49 years.
- Biennial screening mammography for women between the ages of 50 and 74 years.
- Current evidence is insufficient to assess the additional benefits /harms of screening in women 75 yrs. or older.
- Current evidence is insufficient to assess the additional benefits and harms of clinical breast examination beyond screening mammography in women 40 years or older.
- Recommends against clinicians teaching women how to perform breast self-exams.
- Current evidence is insufficient to assess additional benefits and harms of either digital mammography or MRI instead of film mammography as screening modalities.
Mammogram

- Screening Mammogram: It usually takes 2 x-ray pictures (views) of each breast. The goal of a screening mammogram is to find cancer when it is still too small to be felt by a woman or her doctor (asymptomatic).
- Today, about half of mammography units are screen-film units, which means they produce the picture on x-ray film and other half are newer full-field digital mammography units, which produces digital format for viewing on a computer screen.
- Diagnostic Mammogram: x-ray exam of the breast in a woman who either has a breast problem (a breast lump, nipple discharge, etc.) or has had changes on screening mammogram.

Breast Imaging Reporting and Data System (BI-RADS).

- **Assessment is incomplete**
  - Category 0: Needs additional imaging evaluation and/or comparison.
- **Assessment is complete**
  - Category 1: Negative
  - Category 2: Benign (non-cancerous) finding
  - Category 3: Probably benign finding -- Follow-up in a short time frame is suggested
  - Category 4: Suspicious abnormality -- Biopsy should be considered
  - Category 5: Highly suggestive of malignancy -- Appropriate action should be taken
  - Category 6: Known biopsy-proven malignancy -- Appropriate action should be taken

Other Imaging Modalities

- **Ultrasound**: Takes a closer look at some breast masses, and is the only way to tell if a suspicious area is a cyst. It is also used to guide biopsy.
- **MRI**: For certain women at high risk for breast cancer, screening MRI is recommended along with a yearly mammogram. It also helps in better evaluation of locally advanced breast cancer and resectability.
- **Scintimammography**: A radioactive contrast agents are injected into a vein and the image of the breast is taken with a special camera, which detects the radiation (gamma rays) emitted by the dye. Tumor cells, which contain more blood vessels than benign tissue, collect more of the dye and project a brighter image.
- **Positron emission tomography (PET) scanning**: It can be useful in evaluating distant metastases and lymphatic spread.

Biopsy methods.

- **Surgical biopsy**: For years, excisional (surgical) biopsy was the only option.
- **Wire localization** is a procedure used to guide a surgical breast biopsy of a small mass.
- **Needle biopsy**
  - Fine needle aspiration (FNA) biopsy uses a very thin, hollow needle to remove fluid and tiny bits of tissue. *Not very favored.*
  - Core needle biopsy (CNB) uses a larger needle to remove a bigger piece of tissue.
- **Image guided/ Stereotactic Biopsy**
- The Mammatome® is a type of vacuum-assisted biopsy
- The ABBI method (Advanced Breast Biopsy Instrument)
Pathological Types

- **Infiltrating (invasive) ductal carcinoma.** Starts in the ducts of the breast and invade through the wall into the surrounding tissue in the breast. Most common form of breast cancer, 80% of cases.

- **Ductal carcinoma in situ, DCIS, (stage 0),** the disease is confined to the milk ducts and has not invaded nearby breast tissue. If untreated, DCIS may become invasive cancer. It is almost always curable.

- **Infiltrating (invasive) lobular carcinoma.** Begins in the lobules of the breast but has spread to surrounding tissues, accounts for 10% to 15% of breast cancers.

- **Lobular carcinoma in situ (LCIS),** is not considered cancer, It is a risk factor for breast cancer, in both or either breasts.

Rare types

- **Inflammatory Breast cancer** is a faster-growing type of cancer that accounts for about 1% to 5% of all breast cancers. It is diagnosed clinically by an intense, irregular redness and edema of the skin with or without an underlying lump. *Peau d’Orange* appearance. It may be misdiagnosed as a breast infection because there is often swelling of the breast and redness of the breast skin.

- **Paget's disease** is a type of in situ cancer that can begin in the ducts of the nipple. Nipple excoriations, scaling and itching are the features.

- Less common cancers of the breast include metaplastic, mixed medullary, papillary, tubular and mucinous (colloid) breast cancer.

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### SEER INCIDENCE

Based on cases diagnosed in 2003-2007 from 17 SEER geographic areas.

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td>All races</td>
<td>122.9 per 100,000 women</td>
</tr>
<tr>
<td>White</td>
<td>126.5 per 100,000 women</td>
</tr>
<tr>
<td>Black</td>
<td>118.3 per 100,000 women</td>
</tr>
<tr>
<td>Asian/pacific Islander</td>
<td>90.0 per 100,000 women</td>
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<tr>
<td>American Indian/Alaska Native</td>
<td>76.4 per 100,000 women</td>
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<tr>
<td>Hispanic</td>
<td>86.0 per 100,000 women</td>
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### Stage Distribution and 5-year Relative Survival by Stage at Diagnosis for 1999-2006, All Races, Females . NCI/SEER DATABASE.

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>Stage Distribution (%)</th>
<th>5-year Relative Survival (%)</th>
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</thead>
<tbody>
<tr>
<td>Localized (confined to primary site)</td>
<td>60</td>
<td>98.0</td>
</tr>
<tr>
<td>Regional (spread to regional lymph nodes)</td>
<td>33</td>
<td>83.6</td>
</tr>
<tr>
<td>Distant (cancer has metastasized)</td>
<td>5</td>
<td>23.4</td>
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<tr>
<td>Unknown (upstaged)</td>
<td>2</td>
<td>57.9</td>
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</table>

<table>
<thead>
<tr>
<th>TREND</th>
<th>PERIOD</th>
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<tbody>
<tr>
<td>-0.5</td>
<td>1975-1980</td>
</tr>
<tr>
<td>3.9 *</td>
<td>1980-1987</td>
</tr>
<tr>
<td>-0.1</td>
<td>1987-1995</td>
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<tr>
<td>2.7</td>
<td>1995-1998</td>
</tr>
<tr>
<td>-1.7 *</td>
<td>1998-2007</td>
</tr>
</tbody>
</table>

Factors that increase the risk.

1. Inherited BRCA 1 and 2 Mutation.
2. 1st degree relative with Breast or ovarian cancer.
3. Old age
4. < 12 yr of age at first menstrual period.
5. > 30 yr of age at the time of birth of first child.
6. Older age at menopause
7. Hyperplasia with atypia on breast biopsy
8. Hyperplasia without atypia on breast biopsy.
9. Hormone replacement therapy, estrogen and progestin
10. Alcohol intake
11. Increased breast density on mammogram
12. Obesity
13. Nocturnal light exposure/ night shift work
14. Increased bone density

Hereditary breast cancer
- About 5-10% of breast cancer cases are hereditary.
- Women who carry the BRCA1 and BRCA2 have up to an 85% chance of developing breast cancer in their lifetime.
- These mutations are present in far less than 1% of the general population.
- BRCA1 and BRCA2 are human genes that belong to a class of genes known as tumor suppressors.
- Men with harmful BRCA1 mutations also have an increased risk of breast cancer and, possibly, of pancreatic cancer, testicular, and early-onset prostate. However, male breast cancer, pancreatic cancer, and prostate cancer appear to be more strongly associated with BRCA2 gene mutations.
- Mutations in several other genes, including TP53, PTEN, STK11/LKB1, CDH1, CHEK2, ATM, MLH1, and MSH2, have been associated with hereditary breast and/or ovarian tumors.

Genetic testing/ ACS.

Ashkenazi Jewish descent:
- Any 1st degree relative diagnosed with breast or ovarian cancer or two 2nd degree relatives on the same side of the family diagnosed with breast or ovarian cancer.

Not of Ashkenazi Jewish descent:
- Two 1st degree relatives with breast cancer, one of whom was diagnosed at age 50 or younger.
- Three or more 1st degree or 2nd degree relatives diagnosed with breast cancer regardless of their age at diagnosis.
- A combination of 1st and 2nd degree relatives diagnosed with breast cancer and ovarian cancer.
- A 1st degree relative with bilateral breast cancer.
- A combination of two or more 1st or 2nd degree relatives with ovarian cancer regardless of age at diagnosis.
- An 1st or 2nd degree relative diagnosed with both breast and ovarian cancer regardless of age at diagnosis.
- Breast cancer diagnosed in a male relative.
Women’s Health Initiative: Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women.


A randomized controlled primary prevention trial (planned duration, 8.5 years) in which 16608 postmenopausal women aged 50-79 years with an intact uterus at baseline were recruited by 40 US clinical centers in 1993-1998.

- Participants received conjugated equine estrogens, 0.625 mg/d, plus medroxyprogesterone acetate, 2.5 mg/d, in 1 tablet (n = 8506) or placebo (n = 8102).
- The primary outcome was coronary heart disease (CHD) (nonfatal myocardial infarction and CHD death), with invasive breast cancer as the primary adverse outcome.
- On May 31, 2002, after a mean of 5.2 years of follow-up, the data and safety monitoring board recommended stopping the trial of estrogen plus progestin vs. placebo because the test statistic for invasive breast cancer exceeded the stopping boundary for this adverse effect.

Effects of Conjugated Equine Estrogen in Postmenopausal Women With Hysterectomy. WHI Randomized trial.

JAMA. 2004;291:1701-1712

- Enrolled were 10,739 postmenopausal women, aged 50-79 years, with prior hysterectomy, including 23% of minority race/ethnicity.
- Women were randomly assigned to receive either 0.625 mg/d of conjugated equine estrogen (CEE) or placebo.
- The use of CEE increases the risk of stroke, decreases the risk of hip fracture, and does not affect CHD incidence in postmenopausal women with prior hysterectomy over an average of 6.8 years.
- Invasive breast cancer, the primary safety outcome for this trial, was diagnosed at a 23% lower rate in the CEE group than in the placebo group (26 vs. 33 per 10,000 person-years) and this comparison narrowly missed statistical significance (<i>P = .06</i>).
- The trend toward a reduction in breast cancer incidence was unanticipated and is opposite of that observed in the WHI estrogen plus progestin trial, which reported a 24% increased risk.

WILLIAM STEWART HALSTED 1852-1922

- The first Radical Mastectomy for breast cancer was performed by Halsted in 1882.
- Halsted was named the first chief of the Department of Surgery at Johns Hopkins Hospital when it opened in May 1889.
- Halsted radical mastectomy, an en bloc removal of the breast, muscles of the chest wall, and contents of the axilla, was the “established and standardized operation for cancer of the breast in all stages, early or late” for most of the 20th century.
Halsted WS. The results of radical operations for the cure of carcinoma of the breast. Ann Surg 1907;46:1-19

- Halstedian theory proposed that breast cancer begins as a strictly local disease and that tumor cells spread over time in a contiguous manner away from the primary site through lymphatics. Even distant metastasis are the result of direct extensions of local involvement.
- The halstedian approach thus dictated that aggressive local therapy for control of disease in the breast, chest wall, and regional lymph nodes would have a substantial effect on survival.
- Even though Halstead carried out drastic surgical procedures on ladies with advanced breast cancer in an era without having antibiotics, enough ladies survived that the Halstead radical mastectomy continued to become the regular of care until the late 1970s.

Alternative Hypothesis
Dr. Bernard Fischer

- By mid 1960s, dissatisfaction started growing among the surgeons about the halstedian hypothesis, since disease developed at distant sites in many women, even though the primary cancer was well controlled locally with aggressive surgery.
- Breast cancer is considered a systemic disease at time of diagnosis, a condition requiring treatment of the entire patient rather than just the source organ.
- Ultimate manifestation of systemic (metastatic) disease is the result of tumor and patient heterogeneity and the complex interactions between them.


- Alternative hypothesis was tested, beginning in 1961, in a series of carefully planned clinical trials by the National Surgical Breast Adjuvant Project (NSABP), a cooperative group created in 1957, of which Dr Fisher was chairman for many years.
- Dr Fisher’s many accomplishments include the promotion of the scientific process and the randomized clinical trial to obtain answers to questions directly affecting clinical care.

TWENTY-FIVE-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING RADICAL MASTECTOMY, TOTAL MASTECTOMY, AND TOTAL MASTECTOMY FOLLOWED BY IRRADIATION

- To determine whether less extensive surgery with or without radiation therapy was as effective as the Halsted radical mastectomy.
- Between July 1971 and September 1974, 1765 women with primary operable breast cancer were randomly assigned to treatment. One third of those with clinically negative axillary nodes underwent Halsted radical mastectomy and axillary dissection, one third underwent total mastectomy without axillary dissection but with regional irradiation, and one third underwent total mastectomy alone.
  One half of the women with clinically positive nodes underwent radical mastectomy; the other half underwent total mastectomy and regional irradiation.
- Results: No significant differences were observed among the three groups of women with negative nodes or between the two groups of women with positive nodes with respect to disease-free survival, relapse-free survival, distant-disease-free survival, or overall survival.
TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION FOR THE TREATMENT OF INVASIVE BREAST CANCER
BERNARD FISHER, M.D., et al.

Between August 8, 1976, and January 27, 1984, a total of 2163 women with invasive breast tumors that were 4 cm or less in their largest diameter and with either negative or positive axillary lymph nodes (stage I or II breast cancer) were randomly assigned to one of three treatments:

- Total mastectomy
- Lumpectomy
- Lumpectomy plus irradiation

Axillary nodes were removed regardless of the treatment assignment.

The cumulative incidence of recurrent tumor in the ipsilateral breast was 14.3 percent in the women who underwent lumpectomy and breast irradiation, as compared with 39.2 percent in the women who underwent lumpectomy without irradiation (P<0.001).

No significant differences were observed among the three groups of women with respect to disease-free survival, distant-disease–free survival, or overall survival.

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED STUDY COMPARING BREAST-CONSERVING SURGERY WITH RADICAL MASTECTOMY FOR EARLY BREAST CANCER

Randomized trial to compare the efficacy of radical (Halsted) mastectomy with that of breast-conserving surgery.

From 1973 to 1980, 701 women with breast cancers measuring no more than 2 cm in diameter were randomly assigned to undergo radical mastectomy (349 patients) or breast-conserving surgery (quadrantectomy) followed by radiotherapy to the ipsilateral mammary tissue (352 patients).

After 1976, patients in both groups who had positive axillary nodes also received adjuvant chemotherapy with cyclophosphamide, methotrexate, and fluorouracil.

30 women in the group that underwent breast-conserving therapy had a recurrence of tumor in the same breast, whereas 8 women in the radical-mastectomy group had local recurrences (P<0.001).

The survival rate was the same in both groups, even though the rate of local recurrences was higher in the group that received breast-conserving therapy, supports the original basis of the trial — namely, that the prognosis of breast cancer is linked to the presence or absence of occult distant foci of metastatic cells and not to the extent of local surgery.
Less is better...

- Halsted hypothesis, remained the established paradigm for almost 100 years until a consensus meeting of the National Institutes of Health (NIH) in 1979 determined that since rates of survival and recurrence were essentially the same for the total mastectomy and the modified total mastectomy, the modified version was preferable.
- Eleven years later another NIH consensus meeting determined that breast preservation with lumpectomy and radiation yielded results equivalent to modified radical mastectomy.
- Now, conventional axillary dissection is being replaced by the sentinel node biopsy, which has lesser morbidity.

Adjuvant Treatment / NCCN Guidelines.

- Small tumors (up to 0.5cm, T1a) that don’t involve the LNs are so favorable that adjuvant therapy is not recommended.
- Tamoxifen may be considered to reduce the risk of a second contralateral breast cancer, especially in those with ER positive disease.
- Lymph node involvement or tumors greater than 1 cm need chemotherapy (Category 1).
- Tumor greater than 1 cm and ER+ should get Chemotherapy and Endocrine therapy (Category 1).
- Tumor size 0.5 cm-1 cm and no lymph node involvement may be divided into patients with a low risk of recurrence and those with unfavorable prognostic features that warrant adjuvant treatment.
- Tumor 0.6-1.0 cm, consider chemotherapy if Triple Negative or ER/PR Negative (Category 1).

- 6 months of anthracycline-based polychemotherapy (e.g., with FAC or FEC) reduces the annual breast cancer death rate by about 38% for women younger than 50 years of age when diagnosed and by about 20% for those of age 50-69 years when diagnosed, largely irrespective of the use of tamoxifen and of estrogen receptor (ER) status, nodal status, or other tumor characteristics.

Such regimens are significantly more effective than CMF chemotherapy.

- For ER-positive disease only, allocation to about 5 years of adjuvant tamoxifen reduces the annual breast cancer death rate by 31%, irrespective of the use of chemotherapy and of age, progesterone receptor status, or other tumor characteristics.

Adjuvant Chemotherapy for Breast Cancer-30 Years Later

- In 1976, Bandanna and his colleagues published the results of their landmark trial of adjuvant chemotherapy and showed that 12 months of postoperative chemotherapy consisting of cyclophosphamide, methotrexate, and fluorouracil (CMF) decreased the risk of recurrence of breast cancer in women with positive axillary lymph nodes.

- The meta-analysis reported by the Early Breast Cancer Trialists’ Collaborative Group in 1998 showed that, as compared with CMF, anthracycline-containing chemotherapy was associated with significant reductions in the rates of recurrence and death.

- In individual trials, CMF and doxorubicin plus cyclophosphamide were equivalent in terms of relapse-free and overall survival.


- Recent trials have shown that the addition of paclitaxel after the administration of AC was associated with a better outcome than doxorubicin plus cyclophosphamide alone, and a dose-dense regimen consisting of four cycles of paclitaxel after doxorubicin plus cyclophosphamide (administered every 2 weeks) was better than the standard schedule of doxorubicin plus cyclophosphamide followed by paclitaxel.

- The addition of trastuzumab to chemotherapy is a recent exciting development.

Dennis Slamon

- He and his team identified over-expression of Her2-neu oncogene in aggressive breast cancer and worked to develop targeted antibodies to control the disease.

- Dr. Slamon initially had trouble finding support for his research.

- His work exemplifies the value of translational research and has helped transform one of the most lethal forms of breast cancer into a manageable one.

- The movie “Living Proof” is about Dr. Dennis Slamon and his work with breast cancer patients.

Herceptin /Trastuzumab

- In breast cancer, human epidermal growth factor receptor 2 (HER2) over-expression is usually associated with a more aggressive tumor phenotype and poor overall prognosis. It is found in approximately 25-30 percent of invasive cancer patients.

- Trastuzumab (Herceptin), a humanized monoclonal antibody against the extracellular domain of HER2, is established as the foundation of care for HER2-positive breast cancer and, in metastatic breast cancer (MBC), is indicated in combination with taxane chemotherapy or as monotherapy.
USE OF CHEMOTHERAPY PLUS A MONOCLONAL ANTIBODY AGAINST HER2 FOR METASTATIC BREAST CANCER THAT OVEREXPRESSES HER2.

NEJM March 15, 2001, Dennis J. Slamon, MD, PhD, et al

- The addition of trastuzumab to chemotherapy was associated with a longer time to disease progression (median, 7.4 vs. 4.6 months), a higher rate of objective response (50% vs. 32%), a longer duration of response (median, 9.1 vs. 6.1 months), a lower rate of death at 1 year (22% vs. 33%), longer survival (median survival, 25.1 vs. 20.3 months).

- The most important adverse event was cardiac dysfunction, which occurred in 27% of the group given an anthracycline, cyclophosphamide, and trastuzumab; 8% of the group given an anthracycline and cyclophosphamide alone; 13% of the group given paclitaxel and trastuzumab; and 1% of the group given paclitaxel alone.

- Herceptin is now incorporated in adjuvant setting in Her2+ patients and is also being considered in neo-adjuvant settings.

A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer

Soonmyung Paik, M.D et al.
NEJM 351;27 www.nejm.org December 30, 2004

- Tested RT-PCR assay of 21 prospectively selected genes in paraffin-embedded tumor tissue to find the correlation of the likelihood of distant recurrence in patients with node-negative, tamoxifen-treated breast cancer who were enrolled in the NSABP clinical trial B-14.

- Gives a recurrence score from 0 to 100, categorizing them in to low risk (18 or less), intermediate risk (19-50) and high risk (31 and above). The proportions of patients categorized as having a low, intermediate, or high risk by the RT-PCR assay were 51, 22, and 27 percent, respectively.

- The Kaplan-Meier estimates of the distant recurrence at 10 years in the low-risk, intermediate-risk, and high-risk groups were 6.8 percent, 14.3, and 30.5 percent, respectively.

- TAILORx (Trial Assigning Individualized Options for Treatment), sponsored by the NCI, is designed to find out if women with intermediate range Oncotype DX scores benefit from chemotherapy.

In-Situ cancers.

All patients with DCIS need to be treated to avoid the development of invasive cancer.

- Lumpectomy with radiation therapy or mastectomy.
- May be followed by treatment with tamoxifen.
- Removal of axillary lymph nodes is not generally needed.

LCIS, Lobular Carcinoma In Situ: Needs only regular follow up with clinical exam and imaging. Can consider Tamoxifen for risk reduction.
Radiation therapy.

- Essential part of Breast conservation therapy to prevent local recurrence. Small/ No benefit in OS.
  RT may be omitted in those with 70 yr. or older with Clinical node negative, T1 tumors that are ER positive and can get adjuvant endocrine Rx.

- Radiation therapy after mastectomy, if positive axillary LN, Tumor size >5cm, positive margin or inadequate margin( <1mm).

- Newer radiation techniques are incorporating IMRT and Brachytherapy aimed at less toxicity and morbidity while maintaining the efficacy.

NCI ‘S SIMPLIFIED GAIL MODEL

1. Does the woman have a medical history of any breast cancer or of DCIS/LCIS ?
2. Woman’s age
3. Age at Menarche
4. Age at first live birth
5. How many of the woman's first-degree relatives - mother, sisters, daughters have had breast cancer?
6. Has the woman ever had a breast biopsy.
7. Has the woman had at least one breast biopsy with atypical hyperplasia.
8. What is the woman's race/ethnicity.

Women who have a Gail risk score of 1.66 or higher have a higher than average risk for developing breast cancer.

CARE model appears to offer more valid and usually larger estimates of invasive breast cancer risk for African American women.

Prevention Trials

- 1998: The NSABP’s first Breast Cancer Prevention Trial, P-1, compared tamoxifen against placebo in 13,388 women at increased risk for developing breast cancer ( 5 yr. predicted breast cancer risk score of 1.66 or more, based on modified GAIL model.).
  Tamoxifen could reduce the occurrence of breast cancer by 49% making it effective in significantly reducing the incidence of both invasive and non-invasive breast tumors in women at increased risk for the disease.

- 2006 : The NSABP’s second breast cancer prevention trial, the Study of Tamoxifen and Raloxifene (STAR), enrolled 19,747 postmenopausal women at increased risk for developing breast cancer
  Raloxifene was just as effective as tamoxifen in reducing their risk of developing invasive breast cancer, by about 50% but has better side effect profile.
Ongoing/Future research.

- Treatment based on molecular subtypes, tailored treatment, deviating from “one-size-fits-all” approach.
- Preventive agents for ER Negative breast cancers.
- More effective agents for metastatic breast cancer.
- More effective agents for Triple Negative breast cancer.
- Newer targeted agents.

Questions?