CLINICAL, RADIOGRAPHY AND GENETICS: UPDATES IN BREAST CANCER

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OBJECTIVES

- History of breast cancer
- Brief overview of breast cancer and epidemiology
- Breast cancer screening
- Chemoprevention
- Clinical Management of Breast Cancer
- Survivorship
- Genetics of breast cancer

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HISTORY OF BREAST CANCER

- "Thus, for 3,000 years and more, this disease has been known to the medical profession. And for 3,000 years and more, humanity has been knocking at the door of the medical profession for a cure" – Fortune Magazine, March 1937.
- Imhotep, an ancient Egyptian scientist, lived in 2625 BC and described the first breast tumor "bulging mass in the breast, cool, hard and dense spreading insidiously under the skin".
- Atossa, Queen of Persia, lived in 440 BC and had a bleeding lump in her breast removed by her slave, Democedes.
- "Cancer is a disease of double negative, it becomes common only once all other killers have been killed"

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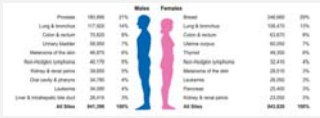
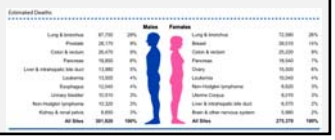
OVERVIEW OF BREAST CANCER

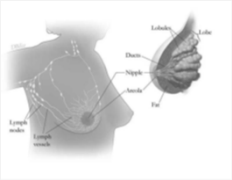
- Most common cancer in women in the United States
  - 1/8 lifetime risk of developing breast cancer
- Second most common cause of cancer death in women
  - 3% lifetime chance of death from breast cancer
- Steady decline in death since 1980s
- 2000 men will be diagnosed annually





TYPES OF BREAST CANCER

- Invasive lobular
- Invasive ductal (80%)
- Inflammatory
- Hormonal Status
- HER-2 Status



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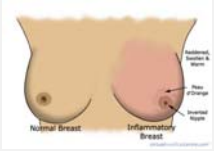
SIGNS AND SYMPTOMS



- Lump, inverted nipple, change to the nipple, nipple discharge, pain, lymphadenopathy, peau d'orange
- Negative mammogram in a patient with a palpable breast mass doesn't exclude cancer
- Mastitis can masquerade as breast cancer
- Breast cancer of neglect/denial/socioeconomic hardship

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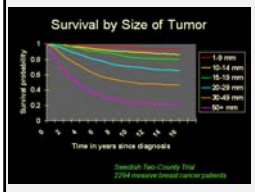
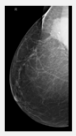
BREAST CANCER EPIDEMIOLOGY

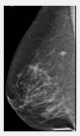


- 75% of women who are diagnosed are >50 years old
  - Inversely – 25% of women are <50 years old…
- 5-year survival rate is now ~98% for women caught with early stage I disease
  - Point of reassurance for women ambivalent about screening



← 5.5cm tumor

0.7cm tumor →



CURRENT SCREENING GUIDELINES

- Women aged 40 and older should have a mammogram every year and should continue to do so for as long as they are in good health
- Based on scientific evidence which demonstrates a 20-49% from breast cancer in women who are invited or actually have screening mammograms vs those who don't

American College of Surgeons
Inspiring Quality: Highest Standards, Better Outcomes

CURRENT BREAST CANCER SCREENING GUIDELINES

- **ACR/SBI/NCCN/ACOG**
  - Annual screening mammography starting at age 40 years and continuing for as long as the woman is in good health
- **USPSTF 2016 Guidelines**
  - Biennial (Every 2 years) screening mammography for women aged 30-74 years (Cat B)
  - The deicion to start screening mammography before age 50 should be an individual one (Cat C)
    - Women who place higher value on the potential benefitsthan the potential harms may chose to begin biennial screening between age 40-49 years.
  - The current evidence is insufficient to assess the balance of benefits and harms of screening women aged 75 and older.
- **ACS 2015 Guidelines**
  - The ACS recommends that women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years.
  - Women aged 45 to 54 years should be screened annually.
  - Women aged 55 and older should transition to biennial screening or have the opportunity to continue screening annually.
  - Women should have the opportunity to begin screening between aged 40 and 44
  - Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or longer

DEEP BREATH…

- Everyone got that. Great. Moving on.

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CURRENT BREAST CANCER SCREENING GUIDELINES

- There is a clear mortality benefit of beginning annual screening starting at age 40.
- All major groups agree on this statement.

REGIMEN	%MORT REDUC
ANNUAL 40-84	40%
ANNUAL 40-49, BIENNIAL 50-84	33%
BIENNIAL 50-84	29%

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BREAST CANCER SCREENING GUIDELINES

- However there is disagreement on the relative harms and benefits of screening mammography

BENEFITS	HARMS
REDUCED MORTALITY	FALSE POSITIVES
REDUCED, LESS TOXIC CHEMO	ANXIETY
LESS INVASIVE SURGERY	OVERDIAGNOSIS
COST OF TREATMENT	RADIATION INDUCED BREAST CANCER

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BREAST CANCER SCREENING AGE 40-50

- Breast cancer is the leading cause of death among women age 40-50
- 50% of all breast cancer deaths occur in women aged under 50 years old
- 70% of breast cancer deaths occur in the 20% of women not participating in screening
- The problem: low sensitivity and high rate of false positives

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BREAST CANCER RISK ASSESSMENT RECOMMENDATIONS

- Any woman of color should be risk assessed for breast cancer by age 30, particularly African American and Ashkenazi Jewish women
- Tools: Tyrer Cuzick and Gail Model
- If deemed greater than 20% lifetime risk, annual mammogram and MRI are recommended alternating every 6 months
- Additional Risk Factors for consideration:
  - Personal/Family history of breast cancer/ovarian cancer
  - Previous breast biopsy
  - Dense breasts
  - First child age >30 or G0
  - Early menstruation, Late menopause, HRT
  - Obesity, sedentary life style, excess alcohol

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TYRER CUZICK

- http://www.ems-trials.org/riskevaluator/

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GAIL MODEL

- Age
- First Menstrual Period
- First Live Birth
- First-Degree Relatives with breast cancer
- Previous Breast Biopsy
- Race

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CHEMOPREVENTION

- Consider chemoprevention in high risk patients
  - Defined as >1.7% five-year risk on the Gail model
- Tamoxifen and Raloxifene are the two medications currently indicated
- 5 years of preventative therapy resulted in 43% reduction in breast cancer risk
- Side effects generally manageable. Education on risk of endometrial cancer required.

- Future considerations:
  - Development of High-Risk Breast Cancer Program with Missouri Cancer Associates/Boone Hospital Center.
  - Gail model being performed at POC while getting mammograms

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SO THE MAMMOGRAM IS ABNORMAL, NOW WHAT?

- Most facilities offer biopsy within a day of abnormal mammogram findings, however some places will refer that on to other facilities
- Turn around for pathology of 2-3 days, however markers take ~1 week
- Appointment with oncology varies
- Referral to oncology vs surgery vs both, depends on provider.
- Important to offer reassurance during the waiting period.
- Unless high degree of suspicion for metastatic disease I recommend holding off on systemic imaging prior to pathology results.

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CLINICAL MANAGEMENT OF EARLY STAGE BREAST CANCER

- Bedrock of treatment consists of surgery – regardless of pathology (invasive cancer vs DCIS)
- Further treatment pends both on pathology prior to and from surgery
- Typically involves some combination of radiation, chemotherapy and endocrine/hormonal therapy
- Recent advent of Oncotype and Mammaprint have dramatically reduced the role of chemotherapy in early stage breast cancer

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TREATMENT OF ADVANCED BREAST CANCER

- Chemotherapy in a hormone negative patient
- Endocrine therapy in the hormone positive patient
- Anti-HER2 therapy in HER2 positive patients

- Prognosis completely varies based on subtype
  - Median OS still around 1 year for TNBC
  - Median OS now >3 years for hormone positive breast cancer
  - Median OS for HER2 positive breast cancer >4 years

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SURVIVORSHIP

- ***"A 'Cancer Survivor' is defined by the National Coalition for Cancer Survivorship as anyone with a history of cancer, from the time of diagnosis and for the remainder of life, whether that is days or decades."***
- Survivors are at risk for a wide range of late physical effects of their primary treatment
- Compared with matched controls, cancer survivors have a substantially increased burden of illness:
  - Days lost from work, inability to work
  - General health perception
  - Need for help with daily activities
- Anxiety over the diagnosis lasts for a lifetime

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BREAST CANCER FOLLOW UP:

- American Society of Clinical Oncology: Routine labs, tumor markers, CT scans and bone scans are not necessary or indicated
- Routine mammogram (provided the patient has breast tissue) should be continued as they normally would, consideration of high risk screening regimen

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SPECTRUM OF TOXICITIES IN SURVIVORS

- Depression
- Weight gain
- Fatigue
- GU symptoms
- Arthralgias
- Osteoporosis
- Sexual dysfunction
- Hot flashes
- Alopecia
- Neuropathy
- Infertility
- Cardiotoxicity
- Premature menopause

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TAMOXIFEN

- SERM
- Typically used in premenopausal females or in females unable to tolerate AI's
- Be careful about antidepressants - - - CYP2D6
- Monitor for:
  - Endometrial cancer – primary concern among patient's taking TAM
  - Increased risk of DVT/PE/Strokes
    - 29% increased risk of stroke
    - 3 fold increase risk of DVT/PE
  - Hot flashes and night sweats
  - Irregular periods, vaginal discharge
  - Is not birth control

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AROMATASE INHIBITORS

- Letrozole, anastrozole and exemestane
- Duration: 5 years vs… every conceivable other option.
- Monitor for:
  - Arthralgias: #1 complaint of patients on an AI. May resolve…
  - Osteoporosis:
    - Routine DEXA Q2-3 years while on an AI
    - Routine Calcium/Vitamin D
    - Bisphosphonate therapy in patient's with osteoporosis at baseline
  - Hot flashes and night sweats

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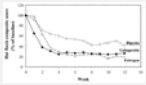
VASOMOTOR SYMPTOMS

- History of breast cancer should serve as a contraindication to HRT indefinitely
- Gabapentin – generally is titrated up quickly for maximal results



- SNRI's – venlafaxine
- SSRI's – watch out for interaction with tamoxifen
- CBT
- Soy – no benefit in most RCTs
- Black Cohosh – mixed results

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SEXUAL DYSFUNCTION

- 40 to 100% (depending on study) report some form of sexual dysfunction
  - 34% of women after mastectomy and chemotherapy lacked sexual interest
  - 25% reported difficulty with arousal, orgasm or lubrication
- Multiple dimensions:
  - Psychological
  - Body image
  - Hormonal and chemotherapy
- Open ended question important
- Communication with both partners
- Vaginal Dryness
  - Non-estrogenic lubricants are treatment of choice
  - Hot button issue about topical estrogens. Generally reserved.

SURVIVORSHIP COUNSELING

- Weight loss:
  - Clearly established that in **post**menopausal women there is increased risk of breast cancer
    - 5 point increase in BMI equates to 12% increase in risk
    - Obese pts have 20-40% increase risk of breast cancer compared to normal wt control
  - BWEL study ongoing
- Breast Exams?
- Regular colonoscopy and Gyn AHM exams
- Smoking cessation
- Physical activity

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REFERENCES

- Amy Patel, MD – Breast Radiologist and Medical Director of Liberty Hospital