Breast Basics, Boards and Bottomline!

A community guide to maintaining breast health and what to do if concerns arise.

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  - I have no relevant relationships with ineligible companies to disclose within the past 24 months.

- Objectives:

  - Objective 1- Discuss early detection of breast cancers through screening and diagnostic imaging
  - Objective 2- Breast biomarkers and treatment discussion
  - Objective 3- Strategies to maintain optimal health and correlate this to modifiable risk factors for breast cancer

- Basic Anatomy:
  - male and female breast
  - Female breast anatomy
  - Breast Lymphatic Anatomy
- Objective 1: Review the value of self breast awareness and self breast exam with discussion of potential findings/concerns
- Techniques of Breast Self Exam
  - Inspection
    - Peau d'orange (French for orange peel) is characterized by edema and pitting and results from blockage of lymphatic drainage with or without associated stromal infiltration. The most common cause of breast peau d'orange is **inflammatory breast cancer**.
    - Inspection: Visually identifying changes to the skin
      Mastitis vs Inflammatory Breast Cancer
    - Paget's Disease
    - Abnormal Lesions & Skin Infections
    - Nipple Discharge
    - Nipple Inversion & Skin Dimpling

  - Palpation

- Lump
- Fibrocystic Breasts
    - Management of fibrocystic changes and breast pain
        - Decrease caffeine
        - Stop using tobacco
        - Decrease alcohol intake
        - Wear a supportive bra

- Cysts
- Tumor (malignancy)

- **Explore early detection of breast concerns through breast screening and diagnostic imaging including a brief overview of breast imaging modalities**

    - Screening Recommendations for women of **average** risk:
        - Different agencies may make different recommendations from various guidelines. At the James we continue to follow NCCN guidelines (National Comprehensive Cancer Network)
    - For women at **average risk**, NCCN/James:
        - Age 25-39 years, clinical encounter, ongoing breast cancer risk assessment, risk reduction counseling, CBE every 1-3 years+SBE
        - >40 years annual clinical encounter w/ongoing breast cancer risk assessment, risk reduction counseling, CBE, SBA, annual mammography, +/-tomo
        - Upper age limit to stop is not defined
        - NCCN MS-6 Breast Cancer Screening/Diagnosis

    - Individuals at High Risk for Breast Cancer
        - This is an important conversation to have with your practitioner-and is an important component to annual/ongoing **breast cancer risk assessment**
        - There are various standardized tools available to practitioners to assist with the evaluation breast cancer risk. A healthcare professional will determine the most appropriate model based upon an individual's history
        - Examples include:
            - The Gail model
            - Claus
            - Tyrer-Cuzick

        - NCCN, MS12
          Individuals at High Risk for Breast Cancer are managed according to NCCN guidelines. NCCN, MS12

- **Imaging/diagnostics**

- Screening Mammograms
  - **CC image**
  - **MLO image**

- Diagnostic Mammograms- Additional views are obtained to evaluate and characterize the area of concern. These may include:
  - True Lateral Views
  - Spot Compression Views
  - Magnification Views
  - Tangential Views
  - Rolled Views
  - Cleavage Views

- Tomosynthesis-3D imaging
  - Shows images of the breast in 3D vs. 2D
  - Stacks multiple pictures of different sections instead of one whole image
  - Beneficial for patients with dense breast tissue
  - Increases ability to find smaller lesion
  - Decreases call back rates

- Breast Sonography
  - Persistent masses following diagnostic mammography are evaluated with sonography.
  - Used to characterize masses to aid in accurate BI-RADS categorization.
  - Location is correlated with mammographic views and documented using clock stations and distance from nipple.

  - Evaluated Features

    Mammography
    - Mass features
    - Calcifications
    - Architectural distortion
    - Special cases

    Sonography
    - Shape and orientation
    - Margins
    - Lesion boundary
    - Echogenicity
    - Posterior acoustic features
    - Effect on surrounding tissue
    - Calcifications
    - Vascularity

- Special cases

- MRI

- BI-RADS Categories

0-Need additional imaging evaluation and/or prior mammograms for comparison
1-Negative
2-Benign findings
3-Probably benign findings, short-interval follow-up suggested
4-Suspicious abnormality, biopsy should be considered
5-Highly suggestive of malignancy, appropriate action should be taken
6-Known biopsy proven malignancy, appropriate action should be taken

- **Strategies to maintain optimal health and correlate this to non modifiable risk factors and modifiable risk factors for breast cancer.**

  - Let's start with the Non Modifiable Risk Factors:
    - Female
    - Increasing Age
    - Race/Ethnicity
    - Dense breast tissue
    - Benign Breast conditions such as ALH
    - Family Hx/Heredity
    - Gene Mutations
    - Reproductive history factors
    - #prior breast biopsies
    - Prior thoracic radiation therapy
  - Modifiable Risk Factors
    - Having children
    - Current or prior estrogen or progesterone use
    - Hormone therapy after menopause
    - Breastfeeding (lowers risk)
    - Alcohol use (alcohol can increase levels of estrogen, decrease absorption of nutrients). Limit to one drink/day
    - Diet
    - Overweight/Obesity
    - Lack of physical activity

- **Occurrence of Breast Cancer in Men and Women. The most recent information.**

- Breast Cancer in Men:
  - The American Cancer Society estimates for breast cancer in men in the United States for 2021 are:
    - About 2,650 new cases of invasive breast cancer will be diagnosed
    - About 530 men will die from breast cancer
    - Breast cancer is about 100 times less common among white men than among white women. It is about 70 times less common among Black men than Black women
    - As in Black women, Black men with breast cancer tend to have a worse prognosis.
    - For men, the lifetime risk of getting breast cancer is about 1 in 833.
      - American Cancer Society's Cancer Statistic Center, cancerstatisticscenter.cancer.org/
- Breast Cancer in Women:
  - Breast Cancer is the most common cancer in American women, EXCEPT for skin cancers
  - The average risk of a women in the United States developing breast cancer sometime in her life is about 13%. This means there is a 1 in 8 chance she will develop breast cancer. This also means there is a 7 in 8 chance she will never have the disease.
  - Current year estimates
    - About 281,550 new cases of invasive breast cancer
    - About 49,290 new cases of DCIS
    - About 43,600 women will die from breast cancer
- Breast Cancer in Women:
  - At this time there are more than 3.8 million breast cancer survivors in the United States
  - Breast cancer is the 2nd leading cause of cancer death in women (only lung cancer kills more women each year)
  - This includes women that still being treated or those who have completed treatment

- **Review discuss the most basic types of breast cancer inclusive of a broad overview with emphasis on the uniqueness of each breast cancer diagnosis and treatment plan**

- **Breast Cancer Basics:**
  - If breast diagnostics are completed and there is still concern, a biopsy will be recommended. This can be completed in multiple ways (US, Stereotactic, MRI guided)
  - Even though the imaging was suspicious, the biopsy may return as benign
  - If there is a breast cancer it will be described by the anatomic location (most commonly "ductal" or "lobular") and whether or not is has breached that structure
  - It will also be described by its biology (ER/PR/HER2)

- **Breast Cancer Treatments are various**
  - There are many variables that are taken into consideration when determining breast cancer treatment
    - Age/Functional status
    - Overall health (pre-existing conditions)
    - ER/PR positivity or ER/PR negativity
    - HER2 positivity or HER2 negativity
    - Lack of positivity to any of the above receptors (TNBC)
    - Changes to the DNA/proteins of the cancer

- **Breast Cancer Staging 0-4**
  - Stage 0: Tis, N0, M0 (Surgery/+/-XRT to reduce recurrence/Endocrine therapy)
  - Stage 1
  - Stage 2
  - Stage 3
  - Stage 4:spread to other parts of the body, most often bones, lungs, liver, brain
  - Pathologic Staging: Pt has undergone surgery
  - Clinical Staging: Utilized in the neoadjuvant setting (annotated with yp)
  - TNM Staging "M"
    - M0: No clinical or radiographic evidence of distant mets
    - cM1: Distant mets detected by clinical and radiographic means
    - pM1: Any histologically proven metastases in distant organs or if non regional nodes, metastases greater than 0.2 mm

- Biomarkers: Estrogen, Progesterone, Her2

- Ductal Carcinoma In Situ (DCIS):
  Lobular Carcinoma In Situ (LCIS):
  - Stage 0 (Carcinoma In Situ)
  - There are two kinds of breast carcinoma in situ:
  - (DCIS) is a condition in which abnormal cells are found in the breast duct lining. These abnormal cells are noninvasive, which means they have not spread outside the duct to other breast tissues. In some cases. DCIS may become invasive and spread to other tissue

- Lobular carcinoma in situ (LCIS) is a condition in which abnormal cells are found in the breast lobules. LCIS rarely becomes an invasive cancer. Having LCIS in one breast, however, does increase the risk of developing breast cancer in the other breast.

- Breast Cancers:
  - Invasive Ductal Carcinoma
  - Invasive Lobular Carcinoma
  - Inflammatory Breast Cancer
  - Recurrent or Metastatic Breast Cancer (MBC): in regards to MBC even if the tumor is located in a different location it will still histologically be a breast cancer)
  - Other Breast Processes include:
    - Phyllodes tumor-very rare breast tumor that begins in the connective tissue of the breast, different than carcinomas that start in the ducts or lobules
    - Paget's disease-rare tumor that begins in the ducts, spreads to the nipple, then spreads to the areola
  - Invasive Carcinomas include NOS, ductal, inflammatory, medullary NOS, medullary with lymphoid stroma, mucinous, Papillary (predominantly micropapillary pattern, tubular, lobular, Paget Disease and infiltrating, undifferentiated, squamous cell, adenoid cystic, secretory cribriform)

- **Breast Cancer Grades+Stages:**
  - Breast Cancer Grade is Different than Stage
  - Pathology specimen grading
    - G1, G2, G3 (G3=poorly differentiated)

- **Broad overview of approaches to breast cancer treatment**
  - Local treatment:
    - Surgery-excision/LN sampling. Careful consideration given regarding the size of the cancer, size of the breast, timing of surgery, the ability of the individual to heal, reconstructive considerations, or any risk reducing strategies that may be desirable
    - Radiation-high energy particle waves that pass through the targeted tissue to damage the DNA of cancer cells and keeps them from duplicating/growing/functioning. There are different types of radiation
  - Systemic Treatment
    - Hormonal Therapy-indicated in hormone+ breast cancer. Examples include but are not limited to Tamoxifen or Anastrazole
    - Targeted therapy for HER2 positivity
    - Chemotherapy
    - Immunotherapy

- CDK 4/6 inhibitors for metastatic disease-advertisements frequently seen on television
- Other agents, including targeted therapy w/PARP inhibitors, Albelisib for PIK3CA, etc

- **Endocrine Therapy**
  - **SERMS:** Tamoxifen. Works to prevent the action of estrogen by blocking estrogen from binding to receptors inside the cancer cell. (oral daily)
  - **Ovarian Suppression:** Goserelin/Leuprolide. Stops the ovaries from making estrogen over a period of time in premenopausal women, is an injection. Some women consider oophorectomy.
  - **Aromatase Inhibitors:** Anastrazole/Letrozole/Exemestane. Blocks the aromatase enzyme from making estrogen in postmenopausal women and in premenopausal women that are using Ovarian Suppression
  - **Estrogen Receptor Downregulator:** Fulvestrant. Reduces the action of estrogen by blocking estrogen from binding to receptors inside the cancer cell and destroys estrogen receptors. Fulvestrant is only used for advanced stage breast cancer in postmenopausal women, premenopausal women who are using ovarian suppression, and men in combination with a medicine to suppress production of androgens, including testosterone by the testes. Given by injection.
  - Bicalutamide: AR positivity (TNBC)
- **HER2: Human epidermal growth factors receptor 2**
  - HER2: A growth promoting protein on the outside of all breast cells. In about 1 in every 5 breast cancers, cancer cells have an unusually high amount
  - HER2-positive breast cancers have overexpression/amplification of the HER2 receptor.
  - These cancers are typically treated with surgery and HER2-targeting antibodies. Often, chemotherapy is also recommended to decrease the chance that the cancer will return.
  - Drug example: Trastuzumab is a type of targeted cancer therapy called a "monoclonal antibody". Another name for this medicine is Herceptin. Trastuzumab seeks out cancer cells and attaches to the HER2 receptors, to prevent the cells from dividing and making new cancer cells. Can be given IV or SQ, Echo prior to dosing and about every 3 months while on therapy or an Echo about every 6 months in the metastatic setting.

- **General supportive care and consideration for those diagnosed with breast cancer:**
  - Anti emetics, growth factor support, scalp cooling, medications to prevent hypersensitivity reactions
  - Fertility considerations/pregnancy status (Fertility counseling, egg preservation, ovarian suppression)
  - Psychosocial Oncology

- Licensed individuals to assist with the specific needs of those diagnosed with breast cancer (fear of recurrence, “new normal”)
- Sexual Health/Body Image
- AYA (addressing the needs of the younger population diagnosed with cancer)
- Spiritual Needs
- Financial Assistance-financial toxicity associated with cancer diagnosis
- Smoking cessation
- Geriatric concerns

- Multidisciplinary approach at SSCBC
  - Surgical Oncology
  - Medical Oncology with Lab (1^{st}/4^{th} floor)+Infusion availability
  - Plastic Surgery/Reconstruction
  - Radiation Oncology
  - Psychosocial Oncology
  - Chaplain
  - Social Services
  - Medication Assistance
  - Expert nursing support in all disciplines listed above
  - Multimodality Conference
  - Hope’s Boutique
  - Radiology, inclusive of breast diagnostic imaging, CT, MRI, Echo, XRay

- References:

- Huff, J. The Sonographic Findings and Differing Clinical Implications of Simple, Complicated and Complex Breast Cysts. Journal of National comprehensive Cancer Network,2009;17, 1101-1105
- Johns Hopkins Medicine. (2018, June 7). Retrieved from: www.hopkinsmedicine.org/healthlibrary/conditions/breast_health/normal_breast_development_and_changes_85,P00151.
- Tang, S. & Gui, G. (2014) Nipple discharge and the role of ductoscopy in breast diseases. Dixon, J. Michael, Breast Surgery 5th edition, (44-50). Edinburgh; New York: Saunders/Elsevier.
- Zanotel M, Bednarova I, Londero V, Linda A, Lorenzon M, Girometti R, Zuiani C. Automated breast ultrasound: basic principles and emerging clinical applications. Radiol Med. 2018 Jan;123(1):1-12. doi: 10.1007/s11547-017-0805-z .Epub 2017 Aug 28. PMID: 28849324.
- Chong A, Weinstein SP, McDonald ES, Conant EF. Digital Breast Tomosynthesis: Concepts and Clinical Practice.,
- Radiology.292(1):1-14. doi: 10.1148/radiol.2019180760. 2019 July

- Phi XA, Tagliafico A, Houssami N, Greuter MJW, de Bock GH. Digital breast tomosynthesis for breast cancer screening and diagnosis in women with dense breasts - a systematic review and meta-analysis. BMC Cancer.18(1):380. doi: 10.1186/s12885-018-4263- PMID: 29615072. 2018 April 3

- As always you are welcome to join us in Step Up for Stefanie or Pelotonia! Questions?
- Adoption/Egg donation
- Discussed baseline testing to asses ovarian reserve, disruption of endocrine therapy, suppression, contraception, sexual function

- CM, continued
- Met with radiation oncology
- Discussed options for local regional treatment. Advised that mastectomy and breast conservation w/lumpectomy+radiation yield equivalent local control and survival
- Discussed risk for permanent complications from radiation including skin/pigment change, appearance-fibrosis, radiation pneumonitis when a portion of the ipsilateral lung is included in the field, and risk for secondary cancer (<0.1%)
- CM, continued
- Met with Plastic Surgery
- Discussed that this is an optional process
- Options include implant based reconstruction, Autologous abd based reconstruction, Latissimus/implant based reconstruction
- Pt remains considering lumpectomy without oncoplastic rearrangement
- Awaiting genetic results
- CM, continued
- B/L breast MRI completed.
- MRI with spiculated mass with non mass enhancement in LIQ left breast, additional indeterminate small focus lower outer left breast. If breast conservation is being considered, bx recommended.
- Pt advised that is she desired breast conservation than 2 additional MRI guided biopsies will be needed. Still considering surgical plan. Genetics remains pending.
- Pt now interested in mastectomy and SLNBx based on MRI findings.
- Genetics reveals a VUS in the SDHA gene and she does NOT carry a pathologic mutation.

- Ongoing meetings with fertility
- Now scheduled for a LEFT mastectomy SLNBx with DIEP flap August 2021

- CM, continued
- PostOp Pathology:
- Invasive Ductal Carcinoma **4.5 cm** in greatest dimension ER+ PR+ HER2-. Surgical margins negative. Nodal assessment demonstrated 1/8 lymph nodes. Total #nodes: 8, Sentinel Nodes: 2, #micromets: 1
- Cancer Staging:
    - Clinical Stage: cT1c, cN0, cM0, ER+, PR+, HER2-
    - Pathologic Stage: Stage IIa pT2pN1b(sn), cM0, G3, ER+ PR+, HER2-
- CM, continued
- Return to medical oncology, recovering from surgery and has completed egg harvesting and fertility treatment
- Now Planned for weekly Taxol, Adriamycin, Cytoxan and Zoladex
- Plan for port placement, ?scalp cooling, echo, labs, staging scans, give any vaccines that are needed prior to tx start if pt amenable
- Eval post op healing prior to chemo start, drains out, well approximated
- Unfortunately, pt developed flap necrosis and returned to the operating room for debridement w/plastics September 2021. Given delay in treatment to allow for wound healing, **anastrazole started**
- Staging scans were negative for distanct disease, Echo wnl
- **End of October 2021**, started weekly paclitaxel with scalp cooling and Leupron and experienced mild infusion reaction
- CM, continued
- So how does this patient respond when her active treatments are completed and she moves on to survivorship? How will she feel when she returns to her "new normal?"
- What is "survivorship"
- Cancer survivorship begins the day of diagnosis and continues throughout your lifetime. Survivorship care provides support for the physical, emotional, and practical issues (job, insurance, financial) of living with cancer. Our goal at The James Cancer Hospital is to help manage these issues to optimize your quality of life, longevity and general wellbeing.

- References:

- National Comprehensive Cancer Network (NCCN), NCCN.org
- James Comprehensive Cancer Center, https://search.osumc.edu/Pages/onesourceresults.aspx?k=breast%20cancer