Breast Cancer Screening and Surgery

April 26, 2018
Ashley B. Simpson, DO
Objectives

• Breast cancer screening

• Common breast complaints

• Surgical management of breast cancer
Breast Screening
Question 1

- At what age and frequency should women begin screening mammography?
  - A. Every 2 years at age 40
  - B. Every 2 years at age 50
  - C. Annually at age 40
  - D. Annually at age 50
  - E. none of the above
Introduction

• Breast cancer is the leading form of cancer in women.
• In 2017 nearly 30% of cancers diagnosed in women were breast cancers.
• Since 1989 deaths from breast cancer have steadily declined
  - screening mammography leading to earlier detection
Who Should Be Screened?
Risk Stratification- How?

Tyrer Cuzick Model
- Most useful model
- Takes into account 1-3\textsuperscript{rd} degree family members with breast / ovarian cancer
- Age of menarche and menopause, AFLB, breastfeeding, BMI, previous biopsies of atypia, known BRCA mutations within the family
- Calculates lifetime risk, risk of a BRCA mutation
Woman's age is 40 years.
Age at menarche was 14 years.
Age at first birth was 30 years.
Person is premenopausal.
Height is 5 ft 5 ins.
Weight is unknown.
Woman has never used HRT.
Woman has had hyperplasia without atypia.

Risk after 10 years is 8.474%.
10 year population risk is 1.606%.
Lifetime population risk is 9.736%.
Lifetime risk is 44.33%.
Probability of a BRCA1 gene is 0.062%.
Probability of a BRCA2 gene is 2.292%.
Risk Stratification- How?

Gail Model
- Calculates 5 year risk
- More limited- low sensitivity and specificity
- Cannot be used to assess role for genetic testing
- Women must be at least 35 to use this model
Average Risk

- No personal history of biopsy proven atypia or cancer
- No known genetic predisposition to cancer,
- Less than 20% lifetime risk of cancer based on risk models.

Currently, regardless of the model used, there is no method for determining that a patient has a “low” risk patient for breast cancer.
Average Risk Recommendations

- Breast self-awareness and clinical breast exam along with digital mammography
- Annual mammogram at age 40
- Begin clinical exam every three years before age 40 and annually after 40
- Practice *self breast awareness*
Moderate Risk

- Personal history of biopsy-proven atypia or lobular carcinoma in situ (LCIS)
  - ADH 30% risk of developing breast cancer (NEJM)
- First-degree relatives with breast or ovarian cancer
- History of radiation to the chest wall before age 30
Moderate Risk Recommendations

- Mammography ten years prior to the earliest first-degree relative but not before age 25
- Begin screening 8 years after treatment for patients with chest radiation
- Magnetic Resonance Imaging (MRI) in addition to annual digital mammography screening
High Risk

• High-risk women have a significantly increased lifetime risk of developing breast cancer
  - > 20% lifetime risk
• Important to discuss all options available for reducing risk
• Lifetime risk is as high as 87% and the risk of ovarian cancer can be as high as 54% with a BRCA 1/2 gene mutation
High Risk Recommendations

• Initial screening should begin with MRI at the age of 25 and mammogram at age 30.
• Annual MRI until the age of 75
• In women with a known BRCA mutation:
  - Ovarian cancer screening
  - Consider risk reducing mastectomy
  - Consider risk reducing BSO
Which Test is the Right Test?

- Mammogram
  - Screening
  - Diagnostic
- Ultrasound
- MRI
- Other Modalities
Patient Education

• Self Breast Awareness
  - Optimal on days 7-15 of menstrual cycle
  - “Know Your Normal”

• Modifiable Risk Factors
  - Obesity
  - More than 1 alcoholic beverage / day
  - HRT
  - Nulliparous / AFLB > 30
Provider Education

• Annual clinical breast exams
• Obtain detailed family history
  - Type of cancer
  - Age of diagnosis
  - Include several generations
• Identify patients who may benefit from enhanced screening options
Common Breast Complaints
Question 2

- What percentage of patients who present with nipple discharge will have breast cancer?
  - A. 0.5%
  - B. 2%
  - C. 7%
  - D. 10%
  - E. 15%
Answer: B

• Roughly 2% of breast cancers present with nipple discharge.
Topics

• Nipple Discharge
• Focal Pain
• Skin Changes
Case 1

• LH is a 48 year old female presents with single duct brown discharge that is spontaneous
• No FH breast cancer.
• Never had a mammogram
• No risk factors for breast cancer
Nipple discharge

• Most common complaints
• 50-80% women have had some sort of fluid
• 5-7% referred to surgeons
• Most common etiology is BENIGN
Nipple Discharge: Evaluation

• Goals: distinguish between benign or pathologic
  - Papilloma, cancer, high risk lesions

• History is most helpful:
  - Benign – bilateral, multiductal, occurs with manipulation
  - Concerning – unilateral, uniductal, spontaneous, bloody
Types of Discharge

• Lactational

• Physiologic

• Pathologic
Lactational Discharge

- Postpartum discharge can last at least 6 months after cessation of breastfeeding

- Bloody discharge can be seen in 20% of women during pregnancy and is usually benign (ductal hyperplasia)

- Bloody discharge seen in 15% of lactating women. Self-limiting, if not refer to a surgeon.
Physiologic Discharge

• Non pathologic, Unrelated to pregnancy or breastfeeding

• Galactorrhea – milky discharge involving multiple ducts bilaterally.
  - Neurogenic stimulation
  - Breast compression
  - Stresses affecting dopamine release
Physiologic Discharge

• Absence of Galactorrhea
  - Multiple ducts – elicited, bloody or non bloody, bilateral, black or clear, green
  - Fibrocyctic changes or ductal ectasia
  - Green nipple discharge is textbook for fibrocyctic changes (not molded milk!)
  - Reassurance
Duct Ectasia

- Major subareolar ducts dilate during aging
- Nipple discharge common
- Scarring due to periductal inflammation
  - most common cause of benign acquired nipple inversion
  - On exam if nipple can be easily everted there is no malignancy
## Medications that cause hyperprolactinemia

<table>
<thead>
<tr>
<th>Medication class</th>
<th>Frequency of prolactin elevation</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipsychotics, first generation</strong></td>
<td></td>
<td></td>
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<tr>
<td>Chlorpromazine</td>
<td>Moderate</td>
<td>Dopamine D₂ receptor blockade within hypothalamic tuberoinfundibular system</td>
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<tr>
<td>Fluphenazine</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Loxapine</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Perphenazine</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Pimozide</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Thiothixene</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics, second generation</strong></td>
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<tr>
<td>Aripiprazole</td>
<td>None or low</td>
<td>Dopamine D₂ receptor blockade</td>
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<td>Asenapine</td>
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<tr>
<td>Clozapine</td>
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<td>Biperidone</td>
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<tr>
<td>Lurasidone</td>
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<td>Olanzapine</td>
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<td>Paliperidone</td>
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<td>Quetiapine</td>
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<td>Risperidone</td>
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<tr>
<td>Ziprasidone</td>
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<tr>
<td><strong>Antidepressants, cyclic</strong></td>
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<tr>
<td>Amitriptyline</td>
<td>Low</td>
<td>Not well understood. Possibly by GABA stimulation and indirect modulation of prolactin release by serotonin.</td>
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<tr>
<td>Desipramine</td>
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<tr>
<td>Clomipramine</td>
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<td></td>
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<tr>
<td>Nortriptyline</td>
<td>None</td>
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<tr>
<td><strong>Antidepressants, SSRI</strong></td>
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<tr>
<td>Citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline</td>
<td>None or low (rare reports)</td>
<td>Same as for cyclic antidepressants</td>
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<tr>
<td><strong>Antidepressants, other</strong></td>
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<tr>
<td>Bupropion, venlafaxine, mirtazapine, nefazodone, bazedone</td>
<td>None</td>
<td>Not applicable</td>
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<tr>
<td><strong>Antimetic and gastrointestinal</strong></td>
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<tr>
<td>Metoclopramide</td>
<td>High</td>
<td>Dopamine D₂ receptor blockade</td>
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<tr>
<td>Domperidone (not available in United States)</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine</td>
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<tr>
<td><strong>Antihypertensives</strong></td>
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<tr>
<td>Verapamil</td>
<td>Low</td>
<td>Not well understood. Specific to verapamil. May involve calcium influx inhibition within tuberoinfundibular dopaminergic neurons.</td>
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<tr>
<td>Methyldopa</td>
<td>Moderate</td>
<td>Decreased conversion of L-dopa to dopamine; Suppression of dopamine synthesis</td>
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<tr>
<td>Most other antihypertensives (including other calcium channel blockers)</td>
<td>None</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Opioid analgesics</strong></td>
<td></td>
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<tr>
<td>Methadone, morphine, others</td>
<td>Transient increase for several hours following dose</td>
<td>Potentially an indirect effect of mu opiate receptor activation</td>
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</tbody>
</table>

Medication induced hyperprolactinemia can cause decreased libido and erectile dysfunction in men and galactorrhea and amenorrhea in women.

GABA: gamma-aminobutyric acid; SSRI: selective serotonin reuptake inhibitor.

* Frequency of increase to abnormal prolactin levels with chronic use: high >50 percent; moderate: 25 to 50 percent; low: <25 percent; none or low: case reports. Effect may be dose-dependent.
## Causes of Nipple Discharge

### General Causes and Frequency of Nipple Discharge, Palpable Mass, and Age Distribution in 204 Patients

<table>
<thead>
<tr>
<th>Histologic Disease</th>
<th>Cases</th>
<th>Milky</th>
<th>Greenish</th>
<th>Serous</th>
<th>Bloody</th>
<th>Total (n)</th>
<th>Palpable Tumor (n)</th>
<th>Range</th>
<th>Mean</th>
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</thead>
<tbody>
<tr>
<td>Fibrocystic disease</td>
<td>65</td>
<td>3</td>
<td>24</td>
<td>16</td>
<td>22</td>
<td>65 (32%)</td>
<td>14</td>
<td>20–58</td>
<td>43</td>
</tr>
<tr>
<td>Mammary duct ectasia</td>
<td>23</td>
<td>3</td>
<td>7</td>
<td>13</td>
<td></td>
<td>23 (11%)</td>
<td>5</td>
<td>20–73</td>
<td>53</td>
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<tr>
<td>Papilloma</td>
<td>68</td>
<td>20</td>
<td>48</td>
<td></td>
<td></td>
<td>68 (33%)</td>
<td>5</td>
<td>28–81</td>
<td>51</td>
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<tr>
<td>Papillomatosis</td>
<td>30</td>
<td>8</td>
<td>22</td>
<td></td>
<td></td>
<td>30 (15%)</td>
<td>3</td>
<td>36–77</td>
<td>53</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>18</td>
<td>3</td>
<td>15</td>
<td></td>
<td></td>
<td>18 (9%)</td>
<td>7</td>
<td>40–78</td>
<td>59</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>204</td>
<td>3</td>
<td>27</td>
<td>54</td>
<td>120</td>
<td>204 (100%)</td>
<td>29</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pathologic Discharge

- Unilateral, single duct, persistent, spontaneous, associated with mass
- Serous, sanguinious, serosanguinious
- Most common reason: papilloma
  - (52-57%)
- Papillomas may harbor atypia or DCIS
- Malignancy in 5-15% pathologic discharge
Pathologic Discharge

- Age is predictive of cancer risk with nipple discharge
  - <40 – 3%
  - 40-60 – 10%
  - >60 – 32%
Clinical evaluation

NCCN Guidelines Version 1.2015
Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/ SYMPTOMS

DIAGNOSTIC FOLLOW-UP

Non-spontaneous or multi-duct

Nipple discharge, no palpable mass

Persistent and reproducible on exam, spontaneous, unilateral, single duct, serous, sanguineous, or serosanguineous

Age < 40 y

Age ≥ 40 y

Mammographic Evaluation
(See BSCR-15)

Screening
(See BSCR-1)

Benign

Malignant

Duct excision

Suspicous progression

Stable/ resolves

6-mo follow-up physical exam and imaging for 1–2 y

Screening
(See BSCR-1)

Benign

Clinical correlation to determine need for duct excision

Malignant

BI-RADS® category 4–5

Tissue biopsy

See NCCN Guidelines for Breast Cancer Treatment

MRI (optional)

BI-RADS® category 1–3

BI-RADS® category 0

(See BSCR-15)

BI-RADS® category 1–3

Ductogram (optional)

BI-RADS® category 4–5

Age < 30 y ultrasound ± diagnostic mammogram

Age ≥ 30 y ultrasound ± diagnostic mammogram

Observation

Educate to stop compression of the breast and report any spontaneous discharge

Educate to stop compression of the breast and report any spontaneous discharge

1See Assessment Category Definitions (BSCR-C).
2Mammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997.62:55986).
3A list of drugs that can cause nipple discharge (not all-inclusive): Psychoactive drugs, antihypertensive medications, opiates, oral contraceptives, and estrogen
4If BI-RADS Category 3 finding is unrelated to nipple discharge, manage mammographic finding by BSCR-15.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Evaluation

• History and Physical
• Diagnostic Evaluation: Bilateral diagnostic mammogram and retroareolar ultrasound
• Referral to a surgeon: spontaneous, unilateral, single duct discharge, bloody, or clear, or reassurance
• Cytologic examination not necessary
Intraductal papilloma
Case 1

- Patient underwent diagnostic imaging and retroareolar ultrasound that showed a retroareolar mass
- Minimally invasive biopsy showed an intraductal papilloma with atypia
- On excisional biopsy, the patient was shown to have DCIS
Case 2

- 52 year old with focal pain in the right upper inner quadrant breast
- Diagnostic mammogram (tomosynthesis) was negative
- CBE 1.5 cm mobile irregular mass in the upper inner quadrant breast
Diagnostic Mammogram
Ultrasound
Breast Pain

• Cyclical
  - hormonal changes with menstrual cycle
  - bilateral and more common in UOQ

• Noncyclical – unilateral
  - Pendulous breasts, diet/lifestyle
  - HRT, ductal ectasia, mastitis, breast cancer
  - hidradenitis suppurativa
  - pregnancy, trauma, cysts, medications
Evaluation

• History and Physical
• Focal pain with or without a mass
  - diagnostic imaging
• Most breast pain is benign
  - 0.5-3.3% breast pain associated with cancer.
• Refer for any concern despite negative imaging
Approach to the Patient with Breast Pain

- Patient presents with breast pain
  - Perform physical examination
    - Mass palpated
      - Order imaging and refer to breast surgeon
    - No mass palpated
      - Focal pain
      - Patient younger than 30 years
        - Targeted ultrasonography
        - Normal
        - Nonsteroidal anti-inflammatory drugs (topical or oral) and/or well-fitted brassiere
      - Patient 30 years or older
        - Targeted ultrasonography
      - Patient does not have risk factors
        - No imaging indicated; provide reassurance
        - Persistent pain
        - Consider mammography
Case 2

• Patient underwent a minimally invasive biopsy that showed a malignancy
Skin Changes

• Nipple Areolar Eczema vs. Paget’s

• Infection vs. Inflammatory

• Sebaceous cyst vs. Malignancy
Eczema

- Characterized by thickened skin, increased skin markings (lichenification), and excoriated, fibrotic papules.
- Involvement of nipple may mimic Paget’s
- Generally bilateral, possible systemic
Skin Changes

Nipple eczema

Paget's
Paget’s Disease
Paget’s Disease of the Breast

- Scaly, raw, vesicular, or ulcerated lesion that begins on the nipple and then spreads to the areola
- Occasionally bloody discharge is present
- Usually unilateral
- Nipple retraction
- Symptoms lasting months
  - May have delay in diagnosis
Infection

• Lactational: commonly seen in first pregnancy and first 12 weeks of postpartum, weaning
  - Cracked nipple / skin abrasion – leading to edema of ducts and poor milk drainage leading to increased number of organisms
  - Sx: Pain, erythema, swelling, possible fluctuant mass
Lactational Infection

• Management: antibiotics and breast feeding
• Improvement usually seen in 48-72 hours
• If a fluctuant mass – drain the abscess - Needle aspiration
• Reevaluate in 72 hours
Non-lactational Abscess

• Central or periareolar infection
• Common in Cigarette smokers (Zuska’s)
  - damages the wall of the subareolar ducts
• Causes periductal inflammation leading to periductal mastitis
• *Short* onset of central breast pain, mass, possible nipple retraction, purulent nipple discharge
Management

- Antibiotics and drainage
- Encourage smoking cessation
- Rule out inflammatory breast cancer if persistent redness
- Peripheral abscesses seen less common and may assoc with DM, rheumatoid arthritis, steroids, trauma
Periareolar abscess. Large incisions are not necessary for the drainage of a breast abscess.

Courtesy of Michael J Dixon, MD.
Granulomatous Lobular Mastitis

- Non caseating granulomata and microabscesses.
- Causes: Autoimmune, sarcoidosis, Wegener's, arthritis, foreign body, TB, mycotic, parasitic, idiopathic,
- Firm mass – similar to malignancy
Inflammatory Breast Cancer

- Red, warm, slightly indurated, tender breast with peau d’orange appearance
- Dermal lymphatics containing tumor emboli
- Vascular congestion and tissue edema
- *Onset over weeks*
Inflammatory breast cancer

It is important to rule out inflammatory breast cancer if a suspected breast infection does not respond to antibiotics.
Breast Infections

• Quick onset, painful
• Start abx, **REEXAMINE** in 72 hours
• Ultrasound to evaluate for abscess
• Alternative diagnoses such as inflammatory breast cancer should also be considered
Surgical Management of Breast Cancer
Question 3

Which statement is most accurate regarding mastectomy compared to breast conservation therapy (BCT)?

- A. Rate of recurrence for mastectomy is lower than lumpectomy alone
- B. There is no difference in overall survival with mastectomy compared to BCT
- C. Tumors with aggressive biology are best treated with mastectomy
- D. All of the above
- E. A&B
- F. A&C
Answer: E

• Long term data has proven partial mastectomy (lumpectomy) combined with whole breast radiation is equivalent to mastectomy to overall survival.

• Lumpectomy alone carries a ~40% risk of recurrence compared to mastectomy (10%)

• Tumor biology alone should not direct surgical management
Historical Perspective

• NSABP
  - B-04
  - B-06

Twenty-Five-Year Follow-up of a Randomized Trial Comparing Radical Mastectomy, Total Mastectomy, and Total Mastectomy Followed by Irradiation

Bernard Fisher, M.D., Jong-Hycon Jeong, Ph.D., Stewart Anderson, Ph.D., John Bryant, Ph.D., Edwin R. Fisher, M.D., and Norman Wolmark, M.D.
BCT vs Mastectomy?
Potential Contraindications

• Collagen vascular disease  
  - Lupus, sclerodema

• Pregnancy (1st & 2nd trimester)

• Pacemakers

• History of previous breast/chest radiation

• Significantly compromised pulmonary / cardiac function
Tumor To Breast Ratio

- Neoadjuvant chemo can be used to shrink large tumors for patients who desire BCT
  - TNBC
  - HER2
Tumor to Breast Ratio

• 20% breast tissue removal results in deformity of the breast

• Oncoplastic surgery involves resection of the tumor with rearrangement of the breast tissue to correct deformity.
Oncoplastic Surgery
Oncoplastic Surgery- Wise Pattern
Multi Centric Breast Cancer

- Synchronous tumors within different quadrants
- Significant deformity with BCT
- Best served with mastectomy
Inflammatory Breast Cancer

- Rare < 5% breast cancers
- Aggressive
- Neoadjuvant chemo
- Modified radical mastectomy
- PMRT
Surgical Options

**BCT**
- Oncoplasty
- APBI
- IORT

**Mastectomy**
- Nipple Sparing
- Direct to implant
- Autologous recon
Nipple Sparing Mastectomy

Bilateral Hidden Scar Mastectomy
Photograph courtesy of Beth DuPree, MD,
Holy Redeemer Health System,
Meadowbrook, PA
IORT

**Step 1:** INTRABEAM IORT is delivered during the lumpectomy procedure, immediately following tumor removal.

**Step 2:** After the surgeon has removed the tumor, the radiation oncologist positions the INTRABEAM applicator in the area of the breast where the tumor was located.

**Step 3:** Low energy radiation is delivered locally to the targeted tissue in the tumor bed, minimizing healthy tissue exposure to radiation.

**Step 4:** After 20-30 minutes of radiotherapy, the applicator is removed and the surgeon then closes the incision.
APBI Mammosite
Contralateral Prophylactic Mastectomy
American Society of Breast Surgeons

Five Things Physicians and Patients Should Question

Released June 27, 2016

1. Don’t routinely order breast MRI in new breast cancer patients.
   After a new diagnosis of breast cancer, breast MRI can be useful in selected patients to aid treatment decisions. However, there is a lack of evidence that routine use of MRI reduces cancer recurrence, death from cancer or the need for re-operation after lumpectomy surgery. The routine use of MRI is associated with an increased need for subsequent breast biopsy procedures, delays in time to treatment and higher cost of care. Increased mastectomy rates can occur if the MRI finds additional cancers or indeterminate findings cause patient anxiety, leading to patient requests for mastectomy.

2. Don’t routinely excise all the lymph nodes beneath the arm in patients having lumpectomy for breast cancer.
   After a new diagnosis of invasive breast cancer, most patients undergoing partial breast removal (lumpectomy) benefit from a sentinel node (SN) biopsy, a procedure that removes a small number of lymph nodes beneath.
We Can Do It!
Cleveland Clinic

Every life deserves world class care.