Breast Imaging: A Clinician’s Perspective

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Disclosures

• The authors have no financial conflicts of interest to disclose
Objectives

1. To provide a general overview of current breast diagnosis and treatment

2. To highlight some of the pertinent information that imaging can provide in guiding diagnosis and treatment
Outline

• Introduction
• Understanding the TNM staging
• A general overview of breast cancer therapy
• Understanding different types of breast surgery
• Understanding different types of adjuvant radiation therapy
Introduction

• As there is a growing advocacy for multidisciplinary approach to patient care, the role of the radiologist is becoming more essential

• In order to become an active participant in patient care and provide value, it is important for the radiologist to understand the management of breast cancer from the clinician’s perspective
TNM classification

- A cancer classification system by the American Joint Committee on Cancer\(^1\)
- Estimates the prognosis of a newly diagnosed breast cancer and the risk of distant recurrence and death after therapy
- Used to guide therapy with an aim to prevent futile therapy
- Recently updated in January 2018 8\(^{th}\) edition
  - Now includes biological factors as part of the staging system:
    - ie. tumor grade, hormone receptor status, human epidermal growth factor, gene expression
Role of imaging in TNM staging

- In order to be included in a patient’s TNM staging, imaging needs to be performed **within 4 months of diagnosis or completion of surgery**

- Mammography and ultrasound are the most common modalities used

- Indications for MR imaging in a newly diagnosed breast cancer:
  - Axillary nodal metastasis with occult primary
  - To determine candidacy for breast conserving therapy
  - Screening for contralateral breast cancer, especially in the setting of dense breasts or invasive lobular carcinoma
  - Evaluation of neoadjuvant chemotherapy response following treatment
  - Evaluation of residual cancer following positive surgical margins

- Information that **imaging should provide**:
  - Size of the primary lesion
  - Presence or absence of chest wall invasion
  - Presence or absence of regional or distant metastases
  - Extension of the primary tumor to the ipsilateral nipple, overlying skin, or underlying chest wall
Size of the cancer in the largest contiguous dimension

Small satellite foci of noncontiguous tumor are not included

<table>
<thead>
<tr>
<th>T</th>
<th>Description</th>
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<tbody>
<tr>
<td>T1</td>
<td>20 mm or less</td>
</tr>
<tr>
<td>T2</td>
<td>&gt; 20 mm but ( \leq 50 ) mm</td>
</tr>
<tr>
<td>T3</td>
<td>&gt; 50 mm</td>
</tr>
<tr>
<td>T4</td>
<td>Extension to the chest wall or skin</td>
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</table>

Axial postcontrast T1 subtraction MR image. 63-year-old female with right breast cancer that invades the chest wall. There is enhancement of the right pectoralis and intercostal muscles and also the right parietal pleura, making this a T4 disease.
Often determined by physical examination

Routine use of imaging is controversial
- Evidence shows ultrasound evaluation detects about half of clinically occult axillary nodal metastases

If performed, imaging should include at least ipsilateral axillary levels I and II nodes
- If level I or II lymphadenopathy is present, consider imaging of level III axillary, internal mammary chain, and supraclavicular lymph nodes
### N (Nodes)

<table>
<thead>
<tr>
<th>N1</th>
<th>Ipsilateral level I, II nodes, movable</th>
</tr>
</thead>
<tbody>
<tr>
<td>N2a</td>
<td>Ipsilateral level I, II nodes, matted/fixed to each other</td>
</tr>
<tr>
<td>N2b</td>
<td>Ipsilateral internal mammary nodes in the absence of level I, II node metastasis</td>
</tr>
<tr>
<td>N3a</td>
<td>Level III node with or without level I, II involvement</td>
</tr>
<tr>
<td>N3b</td>
<td>Ipsilateral internal mammary node and axillary nodes</td>
</tr>
<tr>
<td>N3c</td>
<td>Ipsilateral supraclavicular node with or without axillary or internal mammary node involvement</td>
</tr>
</tbody>
</table>
Three major routes of breast lymphatics: axillary, interpectoral, and internal mammary

- Intrammary lymph nodes are categorized as axillary lymph nodes for staging
- Supraclavicular lymph nodes are categorized as regional lymph nodes
- Cervical or contralateral internal mammary are categorized as distant metastases

- Ultrasound (US) – both long and short axis measurements
- Cross-sectional imaging (CT/MRI) – short axis measurement

- Suspicious imaging features\(^2\)
  - Increased short- and long-axis diameter
  - Increased cortical thickness, > 3 mm\(^3\)
  - Absence of fatty hilum

Grayscale US image of left axilla. 45-year-old patient with an abnormal left axillary lymph node. The node is rounded with marked cortical thickening and loss of the fatty hilum
57-year-old female with right breast invasive ductal carcinoma.

a) Grayscale US image showing eccentric cortical thickening and diminutive fatty hilum
b) Axial MIP and c) axial postcontrast T1 fat-sat MR images showing corresponding abnormal right axillary level I lymph node, seen lateral to the pectoralis minor muscle.
Axial STIR (a) and postcontrast T1(b) MR images. Prominent left Rotter's node measuring 13 mm. Also incidentally seen are silicone granulomas in the bilateral anterior breast. Evidence has shown that up to one-fifth of breast cancer patients, or even one-third of those with positive axillary metastasis can have positive Rotter's node that goes undiagnosed. As Rotter's node involvement can change surgical management, it is important to mention it in MRI read.

Axial postcontrast T1 MR image. Conglomerate nodal mass measuring 31 x 13 mm in the right level III, medial to the pectoralis muscle. Ipsilateral level III node metastasis indicates N3 disease.
Decision to obtain imaging for M staging depends largely on patient history and physical examination. For example, large nodal disease or clinical abnormalities that raise the possibility of metastases (i.e. abnormal liver function test, bone pain, etc).

As mentioned before, cervical or contralateral internal mammary are categorized as distant metastases.
Axial postcontrast T1 subtraction MR image. In addition to two large right breast masses, there is enhancement of the intercostal muscles and chest wall that also involves the right sternum, consistent with osseous metastasis.
<table>
<thead>
<tr>
<th>Neoadjuvant therapy&lt;sup&gt;5&lt;/sup&gt;</th>
<th>Adjuvant therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time course</strong></td>
<td><strong>Before local therapy (surgery)</strong></td>
</tr>
<tr>
<td><strong>Candidate</strong></td>
<td>Locally advanced* and invasive breast cancer</td>
</tr>
</tbody>
</table>
| **Goal**                      | • Decrease the extent of primary lesion and regional metastases  
• Reduce the extent of surgery  
• Evaluate in vivo assessment of response to treatment | • Reduce the risk of distant and local recurrence by treating micro-metastatic disease<sup>6</sup>  
• To improve overall survival |

**Regimen is tailored to each patient** by:
- Tumor-specific factors (tumor size, node metastasis)
- Tumor biology
- Patient-specific factors (age, comorbidities, patient preference, etc)

*Locally advanced breast cancer<sup>7</sup>*
- Tumor > 5 cm in diameter with regional lymphadenopathy (N1-N3)
- Tumors of any size with direction extension to the chest wall and/or skin (includes ulcer or satellite nodules)
- Presence of regional lymphadenopathy regardless of tumor stage (ipsilateral axillary, infra/supraclavicular, internal mammary)
- Absence of metastases
Hormone receptors (HR)
- Estrogen receptor (ER), progesterone receptor (PR)
- HR-positive cancers tend to grow more slowly
- For HR-positive cancers, hormonal/endocrine therapy drugs are given in addition to systemic chemotherapy

Her2/neu (Human epidermal growth factor type)
- Overexpressed in some breast cancers
- Targeted therapy for Her2/neu+ cancers can also be given in addition to systemic chemotherapy

Ki67
- Nuclear protein expressed during the cell cycle
- Correlates with tumor cell proliferation rate
- Can serve as prognostic and predictive marker in HR-positive breast cancer
- Higher Ki67 is associated with poor prognosis
- Predicts the magnitude of chemotherapy benefit
**Major molecular subtypes of breast cancer**

Each subtype has different risk factors for incidence, therapeutic response, disease progression, and preferential organ sites of metastases\(^9\)

<table>
<thead>
<tr>
<th>Luminal type</th>
<th>HR</th>
<th>HER2</th>
<th>Ki-67</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>+</td>
<td>-</td>
<td>&lt; 14%</td>
<td>Slow-growing, less aggressive, more responsive to hormonal interventions</td>
</tr>
<tr>
<td>B</td>
<td>+</td>
<td>+</td>
<td>≥ 14%</td>
<td>Poorer prognosis than type A</td>
</tr>
<tr>
<td>HER2-enriched</td>
<td>-</td>
<td>+</td>
<td>Any</td>
<td>Poor prognosis</td>
</tr>
<tr>
<td>Basal-like</td>
<td>-</td>
<td>-</td>
<td>Any</td>
<td>Also known as triple negative, poor prognosis, no targeted therapy</td>
</tr>
<tr>
<td>Treatment type</td>
<td>Candidate</td>
<td>Drug type</td>
<td>Drug names</td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------</td>
<td>--------------------</td>
<td>-------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy (systemic) therapy</td>
<td>All</td>
<td>Anthracyclines</td>
<td>Doxorubicin (Adriamycin) Epirubicin (Ellence)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Taxanes</td>
<td>Paclitaxel (Taxol) Docetaxel (Taxotere)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Others</td>
<td>Cyclophosphamide Methotrexate Fluorouracil</td>
<td></td>
</tr>
<tr>
<td>Endocrine (hormonal) therapy</td>
<td>ER and/or PR+</td>
<td>ER and/or PR modulator</td>
<td>Tamoxifen</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Aromatase inhibitor</td>
<td>Letrozole Anastrozole Exmestane</td>
<td></td>
</tr>
<tr>
<td>Targeted therapy</td>
<td>Her2/neu+</td>
<td>Monoclonal antibodies</td>
<td>Trastuzumab (Herceptin) Pertuzumab (Perjeta)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kinase inhibitors</td>
<td>Laptinib (Tykerb) Neratinib (Nerlynx)</td>
<td></td>
</tr>
</tbody>
</table>
Different surgical approaches have been developed over the years with continued efforts to obtain better cosmetic outcome and reduce the morbidity of an invasive surgery while maintaining low rates of recurrence.

Breast cancer surgery is broadly categorized into mastectomy and lumpectomy (partial mastectomy).

<table>
<thead>
<tr>
<th>Surgical approach</th>
<th>Tissue removed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mastectomy</strong></td>
<td></td>
</tr>
<tr>
<td>Radical mastectomy</td>
<td>Skin, Breast tissue, Pectoralis muscles</td>
</tr>
<tr>
<td>Modified radical mastectomy</td>
<td>Skin, Breast tissue</td>
</tr>
<tr>
<td>Skin sparing mastectomy</td>
<td>Breast tissue, Nipple areola</td>
</tr>
<tr>
<td>Nipple sparing mastectomy</td>
<td>Breast tissue</td>
</tr>
<tr>
<td><strong>Breast conserving approach</strong></td>
<td></td>
</tr>
<tr>
<td>Lumpectomy (Partial mastectomy)</td>
<td>Lesion, A small margin of normal tissue</td>
</tr>
</tbody>
</table>
Axial postcontrast T1 fat-sat (a) and MIP (b) MR images of a 64-year-old female with a large left breast invasive ductal carcinoma.

Because of the large size of the tumor occupying a large volume of the breast and its proximity to the skin surface, breast conserving approach would not be ideal.

c) Axial postcontrast T1 subtraction MR image of the patient’s breast after modified radical mastectomy following completion of neoadjuvant chemotherapy.
Skin sparing mastectomy

Less ideal for:
- Tumor close to the skin surface
- Extensive malignant microcalcifications beneath the skin
- Inflammatory breast cancer\textsuperscript{10,11}

Axial postcontrast T1 subtraction (a) and postcontrast T1 fat-sat (b) MR images. 48-year-old female with right breast cancer and diffuse overlying soft tissue thickening and enhancement. Due to the extensive skin involvement, skin sparing mastectomy would not be an option.
Nipple sparing mastectomy

- Breast MRI is performed prior to surgery to determine if there is tumor involvement of the nipple and retroareolar complex

- Preferably performed on\textsuperscript{12,13}:
  - Younger patient (<45 years of age)
  - Tumor size <2.5 cm
  - Tumor nipple distance > 2cm

Axial T1 MR images showing postsurgical changes of bilateral nipple sparing mastectomy.
Adjuvant radiation therapy

Given after mastectomy or breast conserving surgery to reduce locoregional failures and target potential microscopic disease

<table>
<thead>
<tr>
<th>Type of radiation</th>
<th>Treatment duration</th>
<th>Indications</th>
<th>Radiation field</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Whole breast radiation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>External beam radiation(^{14,15})</td>
<td>3-6 weeks</td>
<td>Four or more positive lymph nodes</td>
<td>Chest wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Primary tumor &gt; 5 cm</td>
<td>Undissected high axilla (level III), supraclavicular, internal mammary lymph nodes(^{11})</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin or chest wall invasion</td>
<td>Often crosses the midline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multicentric cancer</td>
<td>Additional boost dose is sometimes given to the tumor bed</td>
</tr>
<tr>
<td><strong>Partial breast radiation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balloon (intraluminal) brachytherapy(^{16})</td>
<td>5 days</td>
<td>&lt; 3 cm</td>
<td>Lumpectomy cavity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low grade to intermediate grade tumor</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative nodes</td>
<td></td>
</tr>
<tr>
<td>Intraoperative radiation therapy (IORT)(^{17,18})</td>
<td>Single dose during surgery</td>
<td>&gt; 40-45 years old</td>
<td>Lumpectomy cavity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Early stage breast cancer</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tumor &lt;3.5 cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative lymph nodes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No metastases</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>May also be combined with whole breast radiation</td>
<td></td>
</tr>
</tbody>
</table>
Balloon (intraluminal) brachytherapy

- A balloon catheter is inserted into the lumpectomy cavity and inflated with saline solution. Radiation is delivered through a tiny bead that is inserted through the catheter.

- There needs at least 7 mm between the skin and fully inflated balloon to keep the skin dose low and prevent skin damage.\(^\text{19}\)

Axial STIR MR images of a Mammosite balloon catheter in the lumpectomy cavity (a) and its catheter external to patient’s body (b).
BioZorb tissue marker\textsuperscript{20}

- A 3D tumor bed marker that is placed within the lumpectomy cavity during surgery
- Facilitates more accurate delivery of boost radiation to the tumor bed
- Contains six titanium markers in a bioabsorbable helix polymer

a) Radiation planning axial CT image showing the BioZorb helix within the lumpectomy bed
b) A year after treatment, the helix polymer has been absorbed, leaving behind titanium markers
c) Mammographic image showing remaining titanium markers within the lumpectomy cavity
Summary

1. Imaging provides information that is important for TNM staging, such as the size of the primary lesion, presence of chest wall invasion, and metastasis.
2. Neoadjuvant/adjuvant therapy depends on the tumor-specific factors, tumor biology, and patient-specific factors. MRI imaging is often performed after neoadjuvant chemotherapy to assess in vivo response to treatment.
3. Relevant imaging findings for surgical planning include tumor involvement of the nipple, distance of the tumor from the skin surface, and presence of microcalcifications beneath the skin.
4. As there is increasing use of partial breast irradiation, the radiologist should be familiar with different types of systems used and their expected appearance on imaging.
References