Diagnostic Breast Evaluation: When to Refer and What the Results Really Mean

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Abstract

Diagnostic breast imaging is an important tool in evaluating abnormal physical examination findings and assessing incomplete screening mammographic results. It is imperative for primary care providers to be knowledgeable regarding which patients would benefit from this evaluation in order to provide optimal healthcare.
Introduction

Misdiagnoses of breast malignancies and delayed treatment of breast cancer is the second leading cause of medical malpractice cases in the United States\(^1\). On the other hand, approximately $20 billion is spent annually in the United States for breast cancer screening and treatment\(^2\). Given that breast cancer is the second leading cause of cancer death in American women, appropriate referral is vital to ensure that actions to further assess breast lesions are adequately employed, if needed, but are not implemented unnecessarily\(^3\).

Obtaining a Comprehensive History

A comprehensive breast evaluation is an important and necessary part of both screening examinations and diagnostic assessments. For the primary care provider, the conundrum is to differentiate benign and/or hormonally related breast changes from suspicious and potential malignant changes. Eliciting an accurate history is imperative and beneficial when assessing, diagnosing, treating, and possibly referring breast conditions.

Pertinent factors that impact a woman’s risk of breast cancer which should be addressed in a focused comprehensive history include use of oral contraceptives and/or hormone replacement therapy, previous chest radiation, diethylstilbestrol (DES) exposure, alcohol use, body mass index, menstrual, pregnancy, and breastfeeding histories, personal history of breast conditions or breast cancer, breast density, family history of breast cancer, and genetic risk factors\(^4,5\). Women who use oral contraceptives have a slightly greater risk of breast cancer than women who have never used them\(^4\). Combined hormone replacement therapies (estrogen and progesterone) for women experiencing symptoms of menopause have also been found to increase the risk of developing breast cancer\(^4\). Those women who have had radiation therapy to the chest for the treatment of other types of cancer have a significantly increased risk of acquiring breast cancer.
cancer while those exposed to DES during pregnancy have a slightly increased risk of developing breast cancer\(^4\). Alcohol use has been associated with the elevated risk of breast cancer as well as obesity, early menarche and/or late menopause\(^4\). Nulliparous women or women having their first child after the age of 30 have a somewhat enhanced risk of breast cancer occurrence while some studies indicate that breastfeeding, especially for at least 1 ½ to 2 years, may decrease breast cancer risk\(^4\).

Personal history of breast disease may affect breast cancer risk. A woman’s history of pathologically diagnosed benign breast disease without atypia (e.g., complex fibroadenoma, sclerosing adenosis, papilloma, and radial scar) increases her risk of breast cancer slightly (1 ½ to 2 times normal)\(^4\). Lesions with atypia, including atypical ductal and atypical lobular hyperplasia, raise a woman’s risk of developing breast cancer 4 to 5 times\(^4\). Breast density is an important consideration and can be evaluated by both physical examination and mammography\(^3\). Dense breasts have more glandular tissue than fatty tissue, and breast cancers tend to develop within this dense tissue\(^3\).

Hereditary factors also impact the possibility of breast cancer occurrence. Approximately 20% to 30% of women with breast cancer have a family member with breast cancer. Nevertheless, most women (70% to 80%) who get breast cancer have no family history of this disease\(^4\). Knowing if a patient has any genetic mutations, especially BRCA1 and BRCA2 gene mutations, affects screening protocols and guides referrals to specialists.

Genetics counselors should be consulted if a patient is found to have or is suspected to have a genetic mutation in order for appropriate counseling and screening protocols to be outlined and instigated. Patients with BRCA gene mutations should have a clinical breast
examination every 6 months beginning at age 20 and magnetic resonance imaging (MRI) alternating with mammography every 6 months beginning at age 25.

In patients presenting with a specific complaint, additional questions specific to the problem should be addressed. For breast masses, key points such as mass duration, onset, and associated pain, redness, fever, or discharge should be covered. With issues of nipple discharge, the spontaneity of the discharge along with, color, site/location (i.e., unilateral or bilateral; one duct or multiple ducts), past medical history (i.e., thyroid, pituitary, hypothalamic disorders), current/recent pregnancy or breastfeeding, and medications (psychiatric drugs, antihypertensives, opiates, oral contraceptives/hormone replacement therapy) should be reviewed. The presence or absence of these particular endocrine disorders, as well as the use of certain prescribed medications, must be considered in the assessment of nipple discharge from non-malignant causes.

A relationship between menstrual cycles (if not menopausal) and breast pain should be established. Description of the pain (diffuse or focal; unilateral or bilateral) as well as aggravating and relieving factors should be evaluated. History of trauma, past breast surgeries, pregnancy, and exogenous hormone and caffeine intake are also important considerations. Skin and/or nipple/areolar changes (i.e., thickening, lesions, rash, discoloration) should be assessed in the context of onset, duration, associated factors such as trauma or piercings, and history of radiation therapy. Pertinent past medical history that might predispose patients to skin changes of the breast such as diabetes, eczema, or hidradenitis suppurativa should be assessed in order to differentiate benign skin changes versus those of Paget’s disease.

Physical Examination

The clinician should also conduct a thorough examination of the breasts. Complete physical assessment is necessary to differentiate referrals for diagnostic mammographic
evaluation versus screening mammography. According to the American College of Radiology (ACR), patients should be referred for a diagnostic mammogram for a mass, axillary lymphadenopathy, some types of nipple discharge, skin and/or nipple/areolar changes, and focal pain/tenderness\(^9\).

**Masses**

Palpable breast or axillary masses or asymmetries on physical exam should be referred for further diagnostic evaluation\(^9,8\). Masses most associated with malignancy include firm or fixed masses as well as those with indistinct borders\(^9\). Smooth, mobile masses with defined borders are more often related to masses of benign origin\(^9\). While being aware of these characteristics will assist the provider in educating, counseling, and/or reassuring the patient, masses are not definite or mutually exclusive. Further assessment of patients 30 years and older with diagnostic mammography and those younger than 30 with ultrasound are needed to explicitly assess for benign or suspicious features\(^9\).

**Nipple Discharge**

Nipple discharge is a common complaint in women, and adequate assessment is essential for evaluation, diagnosis, and treatment. Nipple discharge can be divided into two categories: discharge concerning for the presence of a pathologic process versus discharge that is benign or physiologic. Pathologic nipple discharge should be referred for diagnostic imaging and is commonly characterized as unilateral, single duct, spontaneous (e.g., woman wakes up with discharge on her clothing), bloody, clear, or purulent\(^8\). Physiologic nipple discharge is usually bilateral, multi duct, non-spontaneous (i.e., occurs with stimulation) and may be milky, brown, yellow, green, or black\(^9\). If the provider is unable to illicit nipple discharge at the time of the
visit, the patient should return at the time of next nipple discharge\textsuperscript{11}. The provider should be able to actually see the discharge for complete evaluation.

\textit{Pain}

Physical examination of the breast with regards to pain in the premenopausal woman must be carefully considered in relation to the menstrual cycle. Pain that is cyclic, associated with menses, and is accompanied by diffuse, bilateral nodularity (i.e., no discrete, palpable mass) and tenderness is usually physiologic and benign\textsuperscript{8}. If there is any uncertainty regarding the presence of nodularity, the patient can be re-evaluated one to weeks after menses to establish resolution of this finding or referred for diagnostic radiologic evaluation if these findings persist. Any woman (pre- or postmenopausal) with new onset, focal, and/or persistent pain or pain associated with a palpable mass or skin, nipple/areolar change [i.e., lesions, erythema, edema, skin discoloration, nipple inversion, peau d’orange (dimpled, edematous appearance of the overlying surface of the breast, resembling the skin of an orange)] on physical examination should be referred for diagnostic radiologic evaluation\textsuperscript{10}.

\textit{Skin Changes}

Skin changes of the breast should be considered carefully. Women with new onset inflammatory skin changes of the breast can be given a 10-day trial of antibiotics with a repeat clinical breast examination\textsuperscript{11}. If all signs and symptoms resolve, then the patient may resume routine clinical follow-up and screening. If any changes persist, referral for diagnostic imaging evaluation should take place\textsuperscript{11}. Nipple/areolar rashes or inversion should be directly referred for diagnostic imaging\textsuperscript{10}. Table 1 illustrates some common findings which are hormonally related versus findings concerning for malignancy.
Table 1 Physical Examination of the Breast

<table>
<thead>
<tr>
<th>Common Benign Breast Changes</th>
<th>Findings Warranting Further Evaluation</th>
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<tbody>
<tr>
<td><strong>Masses</strong></td>
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<tr>
<td>Nodularity related to menses, resolves following menses; Smooth, mobile, definite borders</td>
<td>No resolution following menses; new or persistent; firm, fixed to underlying tissue or muscle, indiscrte margins</td>
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<tr>
<td><strong>Nipple Discharge</strong></td>
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<tr>
<td>Bilateral, milky, nonspontaneous, multiduct</td>
<td>Unilateral, bloody, spontaneous, uniduct</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td></td>
</tr>
<tr>
<td>Diffuse, bilateral, cyclic</td>
<td>New, unilateral, not associated with menses; associated with mass or skin changes</td>
</tr>
<tr>
<td><strong>Skin Changes</strong></td>
<td></td>
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<tr>
<td>Associated with pregnancy or oral contraceptive pills/hormone replacement therapy; inflammatory changes that resolve completely with antibiotics</td>
<td>Nipple/areolar inversion or rashes; inflammatory changes that do not resolve with trial of antibiotics; peau d’orange</td>
</tr>
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Differences Between Screening and Diagnostic Mammography

Understanding the difference between a diagnostic and screening breast evaluation is significant in initiating a timely and appropriate referral. A screening mammogram is a two-view (4 views total – 2 views of each breast), radiologic evaluation of the breast. The patient does not see a doctor, and no other assessment is performed. The standard two-views consist of a craniocaudal and a mediolateral-oblique. According to the Mammography Quality Standards Act (MQSA), the radiologist must provide a written report to the clinician within 30 days of the examination being performed.

Diagnostic mammography consists of the mammogram itself with supplementary additional views, if needed, and must be evaluated by the radiologist on the same day of the procedure. Further assessment practices might include (a) physical breast examination, (b) ultrasound, (c) ductogram, (d) cyst aspiration, (e) ultrasound guided core biopsy, and (f)
sterotactic biopsy. The physician and/or nurse practitioner in the radiology department will determine if these additional assessment modalities are needed.

Guidelines For Screening and Diagnostic Mammography

The United States Preventive Services Task Force (USPSTF) now advocates that women at average-risk for breast cancer should begin biennial mammographic screening between the ages of 50 to 74. To date, no changes have been made to the American College of Radiology guidelines or to the American Cancer Society recommendations. The debate continues among professional organizations and the USPSTF regarding these recently published proposals. Table 2 provides a description of the differences among these recommendations.

Table 2 USPSTFa Recommendations Versus ACSb Guidelines

<table>
<thead>
<tr>
<th>USPSTF Recommendations</th>
<th>ACS Guidelines</th>
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<tbody>
<tr>
<td>Biennial screening mammography for women 50 to 74 years of age.</td>
<td>Annual screening mammography for women age 40 and older.</td>
</tr>
<tr>
<td>Evidence is insufficient to assess the additional benefits of screening mammography in women 75 years of age and older.</td>
<td>Annual screening mammography as long as a woman is in good health and continues to be an appropriate candidate for imaging.</td>
</tr>
<tr>
<td>Recommends against teaching breast self-examination</td>
<td>Women should be educated regarding benefits and limitations of breast self-examination.</td>
</tr>
<tr>
<td>Evidence is insufficient to assess the benefits and harms of clinical breast examination outside screening mammography in women 40 years of age and older.</td>
<td>Women in their 20’s and 30’s should have clinical breast examination at least every 3 years. At age 40 years and greater, women should have clinical breast examination annually.</td>
</tr>
<tr>
<td>Evidence is insufficient to assess the additional benefits of digital mammography or MRI versus film mammography as methods of screening for breast cancer.</td>
<td>Women with greater than 20% lifetime risk of breast cancer should get a mammogram and MRI every year.</td>
</tr>
</tbody>
</table>

a United States Preventive Services Task Force
b American Cancer Society

In 2008, the ACR provided the following guidelines for the performance of screening and diagnostic mammography. Women who are asymptomatic from a breast standpoint with a
negative clinical breast evaluation and age 40 years and older should have a screening mammographic evaluation annually. The age these examinations should end is dependent on the health of the patient and agreement between the woman and her provider. Women with breast implants should also undergo annual screening mammographic evaluations. Depending on specific facility protocols, a diagnostic mammogram can be performed in these particular patients. Women with a family history of breast cancer (first degree relative(s), especially with a history of premenopausal diagnosis) should begin screening earlier than age 40 (ideally 10 years before breast cancer occurrence in the family) and be referred to a genetic counselor to discuss options for genetic testing, screening, and prevention\textsuperscript{9,15}.

Diagnostic mammography is carried out when a problem is detected on screening mammography or by the patient or her provider. Conditions that are appropriate for diagnostic mammographic referral include, but are not limited to, palpable mass or induration, skin changes, certain types of nipple discharge (discussed above), and continual or focal pain or tenderness. Diagnostic mammography is also performed on patients with a prior Breast Imaging Reporting Data System (BIRADS) 3 mammographic study. This is probably indicative of a benign breast imaging category with recommendation for short interval follow-up. Patients with a history of breast cancer may also be appropriate for diagnostic breast imaging, depending on the institution’s protocol. The American Society of Clinical Oncology (ASCO) recommends a 6 month follow-up mammogram post treatment in patients with breast cancer followed by 12 month follow-up intervals if findings remain stable\textsuperscript{16}.

A general assessment of the patient referred for a diagnostic mammogram is initially based on the patient’s age. In women less than 30 years of age, the ACR proposes the initial evaluation of a breast mass begin with an ultrasound followed by a mammogram if the
ultrasound findings are suspicious for malignancy\textsuperscript{17}. In women 30 years of age and older, the initial assessment should begin with a mammogram followed by an ultrasound to ensure correspondence with the mammographic imaging and to potentially guide further interventions\textsuperscript{17}.

What is the BIRADS?

Breast Imaging Reporting Data System is a mammogram reporting method used by the ACR. BIRADS was created in order to promote the transmission of accurate and comprehensible reports with the purpose of fulfilling high-quality mammography federally mandated in the MQSA of 1994\textsuperscript{12}. It is a system of standardized language for classifying mammographic findings\textsuperscript{18}. There are 7 assessment categories included in the BIRADS\textsuperscript{10}. Table 3 is a compilation of these classifications, including the role of the provider in evaluating the assessment findings, indicated by this system.

Table 3 BIRADS Categories

<table>
<thead>
<tr>
<th>BIRADS Category</th>
<th>Description</th>
<th>Provider Follow-up</th>
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<tbody>
<tr>
<td>0</td>
<td>Additional imaging (mammography views, ultrasound, or previous studies) is necessary in order for the diagnostic evaluation to be completed\textsuperscript{a}. The goal of this assessment is to determine if a true abnormality exists that needs to be serially followed and/or biopsied.</td>
<td>Ensure the patient has an appointment with mammography for the diagnostic work-up to be completed. The patient should understand that an area of concern exists and further imaging is necessary before an official and final reading can be rendered by the radiologist.</td>
</tr>
<tr>
<td>1</td>
<td>Negative\textsuperscript{a}. The study is completely normal. The breasts are symmetric with no suspicious or concerning findings\textsuperscript{b}.</td>
<td>Ensure the patient continues to receive annual mammographic evaluations or follow-up appropriate for the patient’s age and/or family history.</td>
</tr>
<tr>
<td></td>
<td>Benign finding(s)\textsuperscript{a}. This is a normal study; however, the</td>
<td>Ensure the patient continues to receive annual mammographic evaluations or follow-up appropriate for the patient’s age and/or family history.</td>
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2. The radiologist chooses to depict a clearly benign finding such as, but not limited to, a calcified fibroadenoma, a lipoma, or a benign inframammary lymph node which have characteristically benign features and can be confidently labeled as such.

3. **Probably benign**. This study finding has less than a 2% risk of malignancy. A biopsy is recommended in order to establish stability of the specific mass/lesion of concern. The usual follow-up regimen is a unilateral mammogram of the side of concern 6 months from the initial evaluation, a bilateral mammogram 12 months from the initial evaluation, and a second bilateral mammogram 24 months from the initial evaluation (if all imaging studies show no interval changes).

4. **Suspicious abnormality**. This type of finding has a probability of malignancy between 2-95%. A biopsy and correlation of pathology results with imaging is necessary for diagnostic purposes.

5. **Highly suggestive of malignancy**. This type of finding has a high probability of malignancy (>95%). A biopsy for pathologic diagnosis is warranted.

6. **Known biopsy proven malignancy**. This type of lesion has been biopsied with pathologic evaluation proving malignancy. This category is utilized to describe the imaging studies of those patients treated with neoadjuvant chemotherapy.

Provider follow-up: Ensure the patient has appropriate oncologic and recommended mammographic evaluation regimen follow-up.

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a American College of Radiology

b Per radiologist review.
Adjunct Radiographic Assessment – Magnetic Resonance Imaging

While mammography remains the gold standard for detecting breast cancer, magnetic resonance imaging (MRI) provides an adjunct radiographic assessment to mammography, which can be particularly beneficial for certain kinds of lesions. MRI can be used for screening of high-risk, asymptomatic women or diagnosis of women with breast abnormalities. According to the ACR, patients should be referred for a screening MRI after evaluation by a genetic counselor. Women who have been found to have more than a 20% lifetime risk of breast cancer (e.g., genetic predisposition or history of mantle radiation for Hodgkin’s disease) are those who would most benefit from screening MRI from a genetics standpoint.

The ACR does not recommend routine screening of the general, asymptomatic, average risk woman with MRI. MRI is not advocated for all patients due to its large false positive rate leading to potential over diagnosis and treatment. The current ACR recommendations for MRI include, but are not limited to, assessing the contralateral breast in patients with a new diagnosis of breast cancer. Contralateral cancer has been detected in up to 10% of patients with unilateral breast cancer. MRI has been shown to be useful in detecting clinically and mammographically occult breast cancer in the contralateral breast of patients within this population. Evaluating extent of disease (i.e., margins of tumor, presence of multifocality and multicentricity), residual disease, and response to neoadjuvant chemotherapy are also supported uses of MRI. In addition, MRI is helpful in assessing patients with a suspected breast cancer that is mammographically and sonographically occult, characterizing lesions in which mammography and/or ultrasound are inconclusive, and evaluating for suspected recurrence in patients who have undergone postoperative tissue reconstruction.
Role of the Nurse Practitioner

Nurse practitioner (NP) experts have recently forged new roles in the field of diagnostic radiology. With the direction of physicians who specialize in radiology, NPs are able to provide care to patients in this type of setting. Required skills include proficient performance of preliminary evaluation of mammographic studies with presentation to the radiologist for discussion, clinical breast examination, ultrasound evaluation, and the execution of ultrasound guided core and stereotactic biopsies.

At Parkland Health and Hospital System, the NP collaborates with the attending radiologist in evaluation of patients referred for diagnostic breast imaging. The NP summarizes conclusions of initial mammographic images prior to consultation with the radiologist. Collaboration with the physician then leads to constructing a plan for further mammographic imaging, physical examination, and/or ultrasound. If a biopsy is found to be necessary, the NP is able to perform the procedure. Pathology results are then discussed with the physician to determine needed referrals and follow-up. The NP educates patients and provides anticipatory guidance regarding diagnosis implications and subsequent plans for referral to appropriate specialties as needed. The use of the NP in this specialized setting promotes efficient workflow within the diagnostic clinic, allowing for increased numbers of patients to receive high-quality care.

Conclusion

Breast cancer is the second leading cause of cancer death in women. If detected and treated early, women have a much greater chance of long term survival. Understanding who to screen and when diagnosis is warranted is imperative in order for proper and timely referrals to be initiated by the primary care practitioner. A complete history and thorough physical
examination are vital tools in completing this assessment. MRI, ultrasound and other diagnostic procedures (i.e., biopsy, ductogram) are additional modalities available to detect the presence of breast abnormalities.

Professional organizations currently do not agree regarding the guidelines for breast evaluation in the female population. While this is a source of confusion for providers and patients, continued detailed evaluation (i.e., obtaining thorough family history, past medical history; performing complete physical examination) along with patient education by the healthcare provider will promote healthy behaviors and high quality care. Because of their education and training in primary care, NPs are integral pieces of this system. NPs are also forging new ground with specialization in diagnostic technologies. This area of expertise will allow the NP a broader practice arena in order to positively affect the quality of healthcare today and in the future, decreasing preventable deaths from breast cancer through promotion of early malignancy detection.
References


