Evaluation of Abnormal Mammography Results and Palpable Breast Abnormalities

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Background: **Because approximately 1 in 10 women with a breast lump or abnormal mammography result will have breast cancer, a series of decisions must be taken by a primary care practitioner to exclude or establish a diagnosis of breast cancer among these women.**

Purpose: **To determine the most accurate and least invasive means to evaluate an abnormal mammography result and a palpable breast abnormality.**

Data Source: **MEDLINE search (January 1966 to March 2003) for articles and reviews describing the accuracy of clinical examination, biopsy procedures, and radiographic examination for patients with abnormal mammography results or palpable breast abnormalities.**

Study Selection: **The authors reviewed abstracts and selected articles that provided relevant primary data. Studies were included if 1) mammography, fine-needle aspiration biopsy, or core-needle biopsy was performed before a definitive diagnosis was obtained; 2) the study sample included 100 or more women; and 3) breast cancer status was determined from histopathology review of excisional biopsy specimens, from linkage with a state cancer registry or the Surveillance, Epidemiology, and End Results program, or from clinical follow-up of 95% or more of the study sample.**

Data Extraction: **One investigator abstracted results. Methods were evaluated for major potential biases, but methodologic scoring was not performed.**

Data Synthesis: **Likelihood ratios for first screening mammography were 0.1 for the Breast Imaging Reporting and Data System (BI-RADS) assessment category "negative or benign finding," 1.2 for "probably benign finding," 7 for "need additional imaging evaluation," 125 for "suspicious abnormality," and 2200 for "highly suggestive of malignancy." For fine-needle aspiration biopsy of a palpable lump performed by formally trained physicians, the likelihood ratio was infinity for an assessment of "malignant," 2.6 for "atypical/suspicious," and 0.02 for "benign." When diagnostic mammography was used to evaluate a palpable lump or nonpalpable breast abnormality, the positive likelihood ratios were 5.6 and 9.4, and the negative likelihood ratios were 0.15 and 0.19, respectively.**

Conclusions: **Women whose screening mammography results are interpreted as "suspicious abnormality" or "highly suggestive of malignancy" have a high risk for breast cancer and should undergo core-needle biopsy or needle localization with surgical biopsy. Women whose screening mammography results are interpreted as "need additional imaging evaluation" have a moderate risk for breast cancer and should undergo diagnostic mammography or ultrasonography to decide whether a nonpalpable breast lesion should be biopsied. Women whose screening mammography results are interpreted as "probably benign finding" have a low risk for breast cancer and can undergo follow-up mammography in 6 months. Either fine-needle aspiration biopsy or ultrasonography is recommended as the first diagnostic test of a palpable breast abnormality to distinguish simple cysts from solid masses. Fine-needle aspiration biopsy also allows characterization of a solid mass. Diagnostic mammography does not help determine whether a palpable breast mass should be biopsied and should not affect the decision to perform a biopsy.**

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Professional organizations recommend that women at the age of 40 or 50 years start undergoing screening mammography every 1 to 2 years (1–5). Primary care practitioners order most screening mammography examinations and must decide how to evaluate women who have an abnormal result. Evaluation of women with an abnormal mammography result is a common problem because even good-quality mammography facilities generally interpret 5% to 10% of all screening examinations as abnormal. About 90% of women with abnormal results do not have breast cancer (6–9); therefore, a safe and efficient evaluation is crucial.

Breast symptoms are also a common problem; primary care practitioners receive approximately 20 presentations per 1000 person-years for the investigation of a breast symptom (10, 11). A breast lump is the most common symptom associated with breast cancer; between 9% and 11% of breast lumps result in a diagnosis of breast cancer (10, 12, 13). The prevalence of breast cancer among women who present with a breast lump increases with age from 1% for women 40 years of age and younger to 9% for women between 41 and 55 years of age to 37% for women age 55 years and older (12).

Given that about 1 in 10 women with a breast lump or abnormal mammography result will have breast cancer, primary care practitioners must make a series of decisions to exclude or establish a diagnosis of breast cancer in these women. We review the literature on the evaluation of an abnormal screening mammography result and palpable breast abnormality and present an evidence-based approach with which to evaluate these two common problems.

METHODS

We searched for published manuscripts determining the accuracy of screening and diagnostic mammography, fine-needle aspiration biopsy (FNAB), and core-needle biopsy to detect breast cancer among women with nonpalpable and palpable breast lesions. We systematically searched MEDLINE from January 1966 to March 2003

Table 1. **American College of Radiology Breast Imaging Reporting and Data System***

BI-RADS Assessment	Assessment	Definition	Examples of Type of Findings or Lesions
1	Negative	Breasts appear normal	
2	Benign finding	A negative mammogram, but the interpreter wishes to describe a finding	Calcified fibroadenoma, secretory calcifications, fat-containing lesion (such as an oil cyst) or intramammary lymph node
3	Probably benign finding	A mammogram with a lesion with a high probability of being benign	A discrete, extremely well-defined round mass
0	Need additional imaging evaluation	A mammogram with a lesion for which additional imaging evaluation is needed; used almost always in a screening situation	Indeterminate calcification, mass, or breast density
4	Suspicious abnormality	A mammogram with a lesion for which the radiologist has sufficient concern to recommend a biopsy	Punctate, linear, or amorphous calcifications; ill-defined mass; asymmetric breast density
5	Highly suggestive of malignancy	A mammogram with a lesion that has a high probability of being cancer	Spiculated mass, malignant-appearing microcalcifications

* BI-RADS = Breast Imaging Reporting and Data System.

using the Medical Subject Heading terms or key words *mammography*, *sensitivity*, *specificity*, *screening* combined with *breast cancer* or *breast neoplasm*; or *fine-needle biopsy*, *sensitivity*, *specificity*, *palpable mass* combined with *breast cancer* or *breast neoplasm*; or *core needle biopsy*, *sensitivity*, *specificity*, *palpable mass* combined with *breast cancer* or *breast neoplasm*. We manually searched bibliographies of original and review articles identified in MEDLINE. Studies were included if 1) mammography, FNAB, or core-needle biopsy was performed before a definitive diagnosis was obtained; 2) the study sample included 100 or more women; and 3) breast cancer status was determined from histopathology review of excisional biopsy specimens, from linkage with a state cancer registry or the Surveillance, Epidemiology, and End Results program, or from clinical follow-up of 95% or more of the study sample. Studies of mammography, FNAB, or core-needle biopsy were considered high quality if they had a study sample that was population-based or consecutively sampled and if they determined cancer status in 95% or more of the study sample 1 or more years after the imaging or biopsy test was performed in order to determine the false-negative rate of the test (6, 9, 13–22). The major limitations of studies not considered high quality were incomplete follow-up, convenience study sample, and results that were not age adjusted.

We primarily used results of three high-quality studies to describe optimal management strategies to evaluate nonpalpable and palpable breast lesions (13–15). Only one study (14) that evaluated the accuracy of screening mammography reported likelihood ratios or results to calculate likelihood ratios for the six American College of Radiology Breast Imaging and Reporting Data System (BI-RADS) assessment categories (23) for both first and subsequent screening examinations. A study of the accuracy of diagnostic mammography was the only population-based study to report results for nonpalpable and palpable breast lesions (15). The study of the accuracy of FNAB was the only study that gave results that allowed calculation of likelihood ratios for the four cytology assessment categories (13).

Evaluation of Abnormal Screening Mammography Examination

Screening mammography is performed in asymptomatic women with the goal of discovering invasive breast cancer at an early, curable stage. Screening mammography typically includes two views of each breast (craniocaudal and mediolateral oblique). The sensitivity of mammography ranges from 74% to 95%, and the specificity ranges from 89.4% to 99.1% (9, 14, 16, 17, 24). Sensitivity and specificity are higher for women more than 50 years of age, whereas sensitivity is lower and specificity higher for subsequent examinations compared with first screening examinations (9, 14, 16, 17, 24).

The most common (and most worrisome) mammographic abnormalities that are found on screening examinations and that require further evaluation are masses and calcifications. The differential diagnosis for a mammographic mass includes cyst, benign nonproliferative lesions, benign proliferative lesions with or without atypia, fibroadenoma, radial scar, intramammary lymph node, lipoma, galactoceles, ductal carcinoma in situ, and invasive cancer. The differential diagnosis for a mammographic calcification includes benign nonproliferative lesions, benign proliferative lesions with or without atypia, fat necrosis, atherosclerosis, dermal lesion, ductal carcinoma in situ, and invasive cancer. No specific mammographic findings are associated with lobular carcinoma in situ. However, when mammographic calcifications are biopsied, lobular carcinoma in situ has been identified adjacent to histologic calcifications located in normal epithelium. Of note, although the differential diagnosis for a mass or calcification is long, all diagnoses other than ductal carcinoma in situ and inva-

sive cancer are benign and require no further evaluation. Radiologists generally describe both masses and calcifications in terms of location, size, and other characteristics (such as shape, borders, and pattern). In addition to describing findings, radiologists make an assessment and recommendation (25). The American College of Radiology recommends one of six assessments for interpretation of a mammographic screening examination (**Tables 1** and **2**) (23). Abnormal screening mammography assessments are evaluated with diagnostic mammography, ultrasonography, and biopsy.

Diagnostic Mammography and Ultrasonography of Nonpalpable Lesions

Diagnostic mammography is a comprehensive radiologic examination of a breast abnormality that may allow the radiologist to more definitively classify a finding; it can sometimes be done during the same visit as the screening examination. Diagnostic mammography consists of multiple specialized views, including magnification views or spot compression views. Results of diagnostic mammography are reported by using one of five assessment categories by the American College of Radiology: negative, benign finding, probably benign finding, suspicious abnormality, or highly suggestive of malignancy (23). About 15% of women with nonpalpable cancer will have a diagnostic mammography examination that shows no evidence of cancer (**Table 3**) (15). Negative likelihood ratios for a normal mammography result in women with a nonpalpable lesion are approximately 0.2 (**Table 3**). Ultrasonography is of particular value in distinguishing a cyst from a solid lesion on screening or diagnostic mammography. Ultrasonography is 98% to 100% accurate in diagnosing simple cysts when four rigorous sonographic criteria are used to evaluate the lesion (oval or lobulated shape; anechoic, well-defined posterior border; increased through-transmission; and no alteration of surrounding breast parenchyma) (26, 27).

Biopsy

For mammographic abnormalities that are nonpalpable and that require biopsy, image-guided tissue sampling is necessary. Tissue for diagnosis can be obtained by mammography, ultrasonography-guided FNAB, or core-needle biopsy or by open surgical biopsy with needle localization. The sensitivity of needle-localized excisional biopsy is 99% for nonpalpable lesions (28). The most common reason for missing the carcinoma is erroneous placement of the needle guidewire.

Image-guided FNAB or core-needle biopsy is quicker, cheaper, and easier than standard-needle localization open biopsy (29–31). For image-guided FNAB or core-needle biopsy, a mammographic x-ray tube is angled to produce two views of the lesion, and the position of the lesion is calculated from the apparent movement of the lesion relative to a fixed reference grid. With use of this information, a needle is placed in the lesion; needle position is confirmed on repeated stereotactic x-ray views. Alternatively, high-resolution ultrasonography can be used to position the needle in real time within the lesion. A fine needle (22- to 25-gauge), an automated core needle (14- to 18-gauge), or a vacuum-assisted biopsy probe (11-gauge) can be used to obtain a sample of breast tissue. With nonpalpable lesions, core-needle biopsy is usually preferred over FNAB because the core sample provides adequate tissue for histologic diagnosis and is more accurate (32, 33). The accuracy of FNAB for nonpalpable lesions varies more than that of core-needle biopsy (sensitivity, 77% to 97%; specificity, 78% to 98%) (32–34); FNAB is also highly operator dependent and more often produces insufficient diagnostic material (33% for FNAB vs. 1.5% for core-needle biopsy) (18, 19). Image-guided FNAB allows safe sampling of very thin breast tissue and of lesions situated close to the chest wall or the skin, where core biopsy is not technically feasible. High sensitivity and specificity of FNAB have been reported in settings with a high level of expertise in both sampling technique and microscopic interpretation (33). State-of-the-art core-needle biopsy is almost as accurate as surgical biopsy (sensitivity, 93% to 98%; specificity, 95% to 100%) for nonpalpable masses (19, 20, 28, 32, 35–38). Core-needle biopsy for small foci of highly suspicious mi-

Table 2. **Frequency of Screening Mammographic Results and Risk for Breast Cancer Based on Mammographic Result***

BI-RADS Assessment	Assessment	Mammography Examinations, %†	Risk for Breast Cancer†	Likelihood Ratio‡	
				First Screening	Subsequent Screening
1 or 2	Negative or benign finding	87–93	0.0005–0.001	0.1§	0.3§
3	Probably benign finding	1–2	0.003–0.018	1.2‖	3.1‖
0	Need additional imaging evaluation	6–8	0.02–0.10	7§	27§
4	Suspicious abnormality	0.3–1.4	0.10–0.55	125§	315§
5	Highly suggestive of malignancy	0.1	0.6–1.0	2200§	∞§

* BI-RADS = Breast Imaging Reporting and Data System.
† Data are from the University of California Mobile Mammography Screening Program from 1985 to 1992. Adapted with permission from Kerlikowske et al. (6) (JAMA 1993;270(20):2446; Copyrighted 1993, American Medical Association.) Data are also from the New Mexico Mammography Project, 1991–1993 (Rosenberg et al. [22]) (Cancer. Vol. 78, No. 8, 1996. p. 1735. Copyright© 1996 American Cancer Society. Reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.)
‡ Likelihood ratio is the ratio of diseased to nondiseased persons for a given test result.
§ Data are from the University of California Mobile Mammography Screening Program from 1985 to 1991. Adapted with permission from Kerlikowske et al. (14). (JAMA. 1996;276(1):42. Copyrighted 1996, American Medical Association.)
‖ Data are from the San Francisco Mammography Registry of the University of California, San Francisco, from 1985 to 1999.

crocalcifications with no associated mass is less beneficial because sampling errors are more common and local excision provides definitive treatment (35). If atypical ductal hyperplasia, ductal carcinoma in situ, lobular neoplasia, benign intraductal papillomas, or a radial scar is found on core-needle biopsy, excisional biopsy should be considered because surgical specimens of these lesions yield more serious diagnoses 15% to 40% of the time (19, 28, 35, 37, 39, 40).

Core-needle biopsy has less morbidity than excisional biopsy; the chance for infection or hematoma requiring additional surgical or medical intervention is 0.1% (36, 41). Complications associated with excisional biopsies include hematomas, infection, and scarring; vasovagal reactions from wire localization itself (7%); and, rarely, prolonged bleeding (1%) and extreme pain (1%) (42). Core-needle biopsy with either ultrasonography or stereotactic guidance of nonpalpable breast lesions is cheaper ($385 to $610) than excisional breast biopsy ($1332) (10, 30, 43, 44).

Management Strategies

Women who have an assessment of "negative" (BI-RADS 1) or "benign finding" (BI-RADS 2) are considered to have a normal mammography result. Negative and benign findings are associated with a low risk for cancer (**Tables 2** and **4**). Therefore, women with either a negative or benign assessment should have routine screening mammography in 1 to 2 years.

"Probably benign finding" assessments (BI-RADS 3) are associated with a slightly higher risk for breast cancer than are negative or benign assessments (**Tables 2** and **4**), but the risk for cancer is low (46–55). Typically, a repeated diagnostic examination of the breast with the probably benign lesion is suggested in 6 months to determine if the lesion is truly benign (**Figure 1**). When mammography is repeated in 6 months, the radiologist should decide whether the lesion has progressed or remained stable. Lesions that have progressed generally require immediate evaluation, whereas those that remain stable are generally benign. Women with stable lesions are usually evaluated at an additional 6-month interval and, if the lesion has still not progressed, the woman can resume a regular screening interval.

With an assessment of "need additional imaging evaluation" (BI-RADS 0), the risk for breast cancer is between 2% and 10% (**Table 2**). Most abnormal screening mammography examinations are classified as "need additional imaging evaluation" and are associated with positive likelihood ratios for breast cancer of about 7 for first screening mammography and 28 for subsequent screening mammography (**Table 2**). For examinations interpreted as "need additional imaging evaluation," the risk for breast cancer after mammography is primarily influenced by a woman's age-specific risk for breast cancer before mammography (**Table 4**). There is no consensus on the "best" next test to evaluate screening examinations that fall into the "need additional imaging evaluation" category. Clinicians may have the woman return for a clinical breast examination, which is carefully directed to the area of abnormality on the mammographic examination to determine whether the lesion is palpable. For nonpalpable lesions, the choice of next test generally includes diagnostic mammography or ultrasonography (**Figure 1**) (56). For lesions that are still suspicious after diagnostic mammography, ultrasonography might be helpful if the radiologist thinks that the lesion has the appearance of a cyst. Because simple cysts are always benign, a lesion that is cystic on ultrasonography needs no further evaluation. A suspicious mass that is solid on ultrasonography requires biopsy.

Women whose mammograms are interpreted as "suspicious abnormality" (BI-RADS 4) or "highly suggestive of malignancy" (BI-RADS 5) should undergo a biopsy of the lesion (**Figure 1**). Positive likelihood ratios for breast cancer associated with screening mammography interpreted as "suspicious abnormality" or "highly suggestive of malignancy" are very high (approximately 125 for suspicious abnormality and 2200 for highly suggestive of malignancy) and substantially increase the risk for breast cancer, regardless of age (**Table 4**) (14).

Table 3. **Accuracy of Diagnostic Mammography in Women with a Nonpalpable Lesion or Breast Lump***

Measurement	Nonpalpable Abnormality	Lump
Sensitivity (95% CI), %	82.3 (78.1–85.9)	87.3 (84.4–89.7)
Specificity (95% CI), %	91.2 (90.1–92.2)	84.5 (83.1–85.8)
Positive predictive value (95% CI), %†	17.5 (15.6–19.6)	26.8 (24.5–29.2)
Positive likelihood ratio‡	9.4	5.6
Negative likelihood ratio‡	0.19	0.15

* Data are from the Breast Cancer Surveillance Consortium. Adapted from Barlow et al. (15). Performance of diagnostic mammography for women with breast signs or symptoms. JNCI. 2002;94(15):1155. By permission of Oxford University Press.
† Positive predictive value is defined as the proportion of women with an abnormal mammography result who have invasive cancer or ductal carcinoma in situ.
‡ Likelihood ratios are the ratio of diseased to nondiseased persons for a given test result.

EVALUATION OF PALPABLE BREAST ABNORMALITIES

Palpable breast abnormalities are usually described as lumps or breast thickenings (57). Investigation of women who present with a symptom of a breast abnormality starts with a history and physical examination. The clinical history should establish how long the abnormality has been noted; whether any change has been observed; and whether there is a history of atypical hyperplasia, lobular carcinoma in situ, ductal carcinoma in situ, or invasive breast cancer, factors that substantially increase the likelihood of breast cancer (58). However, the presence or absence of risk factors for breast cancer, including age, should not influence the decision to further investigate an abnormality. This investigation is needed because the prevalence of breast cancer is relatively high (10%) among women with a breast

Table 4. **Risk for Breast Cancer Based on Age and Mammographic Interpretation***

Age and Type of Screening Examination	Risk for Breast Cancer before Mammography†	Risk for Breast Cancer Based on Age and Mammographic Interpretation (BI-RADS Assessment)				
		Probably Benign Finding (3)	Need Additional Imaging Evaluation (0)	Suspicious Abnormality (4)	Highly Suggestive of Malignancy (5)	Normal or Benign Finding (1 or 2)
40–49 y						
First screening	0.003	0.004	0.02	0.30	0.87	0.0004
Subsequent screening	0.0015	0.0046	0.04	0.32	1.0	0.0004
50–59 y						
First screening	0.006	0.007	0.05	0.39	0.92	0.0004
Subsequent screening	0.0028	0.009	0.07	0.46	1.0	0.0008
60–69 y						
First screening	0.013	0.016	0.07	0.54	0.90	0.0008
Subsequent screening	0.0037	0.011	0.09	0.53	1.0	0.001
≥70 y						
First screening	0.014	0.017	0.07	0.63	0.97	0.001
Subsequent screening	0.0037	0.001	0.09	0.53	1.0	0.001

* BI-RADS = Breast Imaging Reporting and Data System.
† Based on the prevalence of breast cancer per 1000 first screening examinations for first screening (6); on Surveillance, Epidemiology, and End Results cancer statistics for incidence of invasive breast cancer for subsequent screenings (45); and on estimated likelihood ratios. Adapted with permission from Kerlikowske et al. (14). (JAMA. 1996; 276(1):42. Copyrighted 1996, American Medical Association).

lump compared with those who are asymptomatic at presentation for screening mammography (**Table 4**).

The most valid criteria in deciding whether a reported palpable breast abnormality is significant and warrants evaluation is whether the abnormality is dominant on clinical breast examination. A dominant breast abnormality is defined as a lump or suspicious change in breast texture that is discrete and distinctly different from the rest of the surrounding breast tissue and the corresponding area in the contralateral breast (59). Abnormalities that are less smooth and less mobile, with poorly defined margins, increase the suspicion of carcinoma but are not specific for breast cancer (60). Other criteria associated with malignancy include Paget-like lesions of the nipple, nipple discharge, and dimpling of the skin, all of which are rare.

The differential diagnosis of a dominant breast abnormality commonly includes cysts, fibroadenoma, benign nonproliferative lesions, benign proliferative lesions with or without atypia, fat necrosis, ductal carcinoma in situ, and invasive cancer. The initial objective is to distinguish simple cysts from solid masses because simple cysts are benign and do not require further evaluation (26, 61, 62). About 20% to 25% of palpable breast abnormalities are a simple cyst (13). Cysts are a common cause of dominant breast lumps in premenopausal women 40 to 49 years of age; 63% of cysts are detected among these women (61). Cysts cannot be reliably distinguished from solid masses by clinical breast examination or mammography (26, 63), but both FNAB and ultrasonography are highly accurate. Fine-needle aspiration biopsy, ultrasonography, diagnostic mammography, and core-needle biopsy are used to evaluate palpable breast abnormalities.

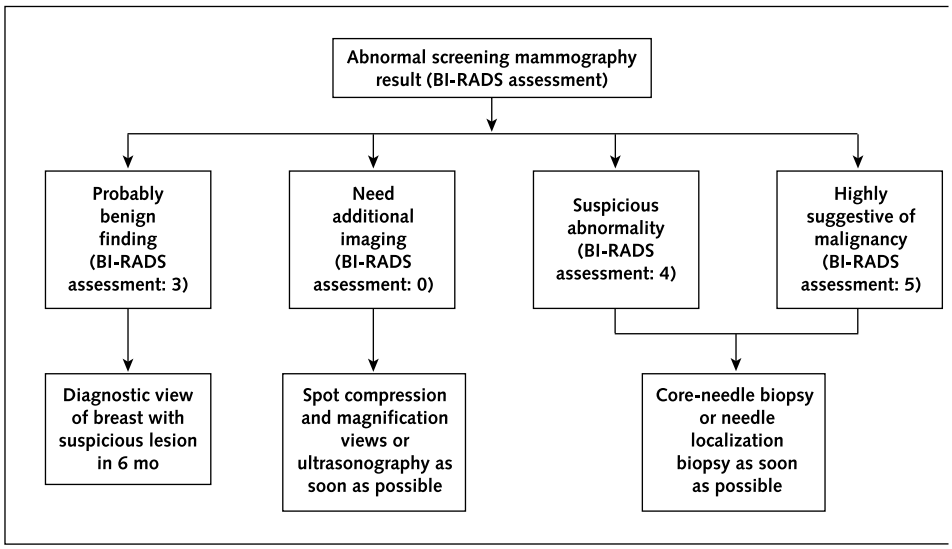
Fine-Needle Aspiration Biopsy

Fine-needle aspiration biopsy uses a small-gauge needle (21- to 25-gauge) to obtain fluid and cellular material from a breast lump or suspicious area of breast texture. Samples are obtained from the entire lump or suspicious area by multiple passes with one puncture. Sensitivity ranges from 65% to 98%, and specificity ranges from 34% to 100% (64). The sensitivity is lower in women younger than 40 years of age, when the tumors are small (≤10 mm) (65), and when untrained personnel perform the procedure (**Table 5**) (13, 66–68). Fine-needle aspiration biopsy that is performed and interpreted by an experienced cytologist (**Table 5**) has a sensitivity between 92% and 98% (13, 65, 69–73) and a low negative likelihood ratio between 0.02 and 0.11 (13, 74). In addition, specificity for specimens categorized as "malignant" approaches 100%, with a correspondingly very high positive likelihood ratio (13, 69, 75). When sampling or cytology evaluation is performed by personnel without formal training in FNAB, the accuracy of the test may decrease to unacceptable levels (sensitivity, 75%) (13, 66–68). Studies have shown that untrained personnel have a low sensitivity, primarily because of inadequate sampling (13, 67). When sampling is inadequate, physicians without formal training refer almost four times more patients with benign lesions for surgery than do trained physicians (13). Before ordering FNAB, practitioners should check with the cytologist who evaluates breast aspirates to ensure that the person has had formal training in sampling technique and microscopic interpretation and can provide satisfactory specimens for cytologic examination in 90% to 95% of cases (13, 76).

Ultrasonography

Ultrasonography is a noninvasive alternative to fine-needle aspiration of a palpable breast abnormality to distinguish a cyst from a solid mass. As noted earlier, ultrasonography is 98% to 100% accurate in diagnosing simple cysts when rigorous sonographic criteria are used for evaluation of the lesion (26, 27). Thus, if a mass is a simple cyst on ultrasonography, FNAB is not necessary. If a mass

Figure 1. **Flow diagram for evaluation of an abnormal screening mammography result in a woman without breast symptoms.**



BI-RADS = Breast Imaging Reporting and Data System.

is solid, ultrasonography must be followed by FNAB, core-needle biopsy, or excisional biopsy. Ultrasonography also may be helpful when a lump is too small or deep to offer a reliable target for FNAB. Attempts have been made to use ultrasonography to distinguish benign from malignant solid lesions, but little evidence supports the use of ultrasonography for this purpose.

Diagnostic Mammography

In addition to being used to further evaluate nonpalpable lesions detected on screening mammography, diagnostic mammography is performed to further evaluate solid masses, complex cysts, or bloody cystic fluid detected on FNAB or ultrasonography. Diagnostic mammography is usually performed after FNAB or ultrasonography because mammography cannot accurately distinguish a cyst from a solid mass. If diagnostic mammography is performed before FNAB or ultrasonography and a noncalcified mass is seen, FNAB or ultrasonography is required to determine whether the lesion is a cyst or solid mass. Performing FNAB or ultrasonography before diagnostic mammography will eliminate the need for diagnostic mammography in about 20% to 25% of women with simple cysts (13, 26). Diagnostic mammography can be performed after FNAB on the same day without interfering with mammographic interpretation (77). It can provide findings that support the suspicion of a malignant lesion on FNAB or ultrasonography, document the extent of a malignant lesion, and identify other nonpalpable suspicious areas in either breast that might require evaluation. When diagnostic mammography is being ordered, the request should clearly describe the size and location of the breast abnormality that is to be evaluated.

About 15% of women with palpable cancer will have a diagnostic mammography examination that shows no evidence of cancer (**Table 3**) (15). Negative likelihood ratios for a normal mammography result for women with a breast lump are approximately 0.2 (**Table 3**). Thus, a negative mammography result in the face of continued unexplained breast abnormalities on clinical breast examination does not rule out breast cancer and a biopsy should be performed (78). Women with an abnormal diagnostic mammography result should undergo tissue sampling because the risk for cancer is relatively high (**Table 3**).

Triple Test

The "triple test" (66, 70, 79, 80), which consists of tissue sampling, mammography, and clinical breast examination, has been advocated to evaluate breast abnormalities (81). If clinical breast examination does not suggest

Table 5. **Accuracy of Fine-Needle Aspiration Biopsy for Breast Lumps according to Cytologic Diagnosis and Level of Training of Physician Performing the Procedure***

Measurements†	Formally Trained	Not Formally Trained
Sensitivity (95% CI), %	98.2 (88.8–99.9)	75.0 (60.1–85.9)
Specificity (95% CI), %	91.4 (89.0–93.8)	88.8 (83.1–94.5)
Positive predictive value (95% CI), %	54 (44.2–63.8)	74 (61.8–86.2)
Positive likelihood ratio‡	11.4	6.8
Malignant	∞	∞
Atypical/suspicious	2.6	5.2
Nondiagnostic	0	0.27
Negative likelihood ratio‡		
Benign	0.02	0.28

* Specimens were collected between 1 January and 31 December 1992 in three San Francisco hospitals. Adapted from Ljung et al. (13). (Cancer. Vol. 93, No. 4, 2001. p. 266. Copyright© 2001 American Cancer Society. Reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.)
† Abnormal is defined as malignant or atypical/suspicious.
‡ Likelihood ratio is the ratio of diseased to nondiseased persons for a given test result.

cancer, if mammography results are negative, and if cytologic evaluation is benign, the chance of breast cancer is low (0.7%). If clinical breast examination is highly suggestive of breast cancer, if mammography results are suspicious for malignancy, and if cytologic evaluation is suspicious, the risk for breast cancer is very high (99%). There is no standardized reporting system for communicating the results of a clinical breast examination or what constitutes a clinical breast examination that is not suggestive of cancer versus one that is suggestive of cancer. Including clinical breast examination as a component of the triple test is confusing because by definition the presence of a dominant breast abnormality identified on clinical breast examination requires further evaluation (82); if no dominant breast abnormality is identified on clinical breast examination, then FNAB and diagnostic mammography are not indicated. Compared with FNAB and diagnostic mammography (**Tables 3** and **5**), the sensitivity (48% to 60%) and positive predictive value (1.5% to 4.3%) of clinical breast examination are lower (83–85). Therefore, together, FNAB and diagnostic mammography are the two most informative and accurate tests, and this "double test" should be used to evaluate a dominant breast abnormality (76). Clinical breast examination is best used to identify the presence or absence of a dominant breast abnormality that requires evaluation and to clinically follow a breast abnormality that is not clearly dominant or a simple cyst that has been aspirated to determine whether the cyst recurs or a residual lump is present at the aspiration site (**Figure 2**).

Core-Needle Biopsy

Core-needle biopsy is performed with a large-diameter needle (14- to 18-gauge) to obtain tissue cores for histologic diagnosis. Core-needle biopsy has gained in popularity over FNAB for evaluation of breast lumps because FNAB cannot consistently distinguish benign proliferative lesions with and without atypia and ductal carcinoma in situ from invasive disease (81, 86). For example, when results from FNAB are reported as "atypical," a subsequent core-needle biopsy can be used to obtain a more definitive histologic diagnosis because it includes surrounding architecture that can help to differentiate atypical ductal hyperplasia, carcinoma in situ, and infiltrating carcinoma (21). However, the superiority of core-needle biopsy over FNAB for breast lumps has not been established (81, 87). Only two studies have compared the accuracy of core-needle biopsy and FNAB for the same breast lumps (21, 88). In these studies, FNAB had a slightly higher sensitivity than did core-needle biopsy (96.7% to 97.5% vs. 85% to 90.0%) and a similar specificity (99.6% to 100% vs. 100%). As with FNAB, the accuracy of clinically guided core-needle biopsy is greater when the palpable mass is large. In one study of 150 core biopsies of palpable lumps, sensitivity was 89% overall and increased to 94% for lesions more than 2.5 cm in diameter (89).

As with FNAB, the accuracy of core-needle biopsy depends on the nature of the breast lesion, the skill of the person obtaining the sample, and the skill of the pathologist interpreting the specimens. Sampling errors are the main cause of a false-negative diagnosis with core-needle biopsy. Sampling errors may be due to difficulty in immobilizing the mass, monodirectional sampling of the lesion, imprecise needle localizaton due to using a spring-loaded device, and sampling a small mass with a coring device that pushes the lesion out of the biopsy needle pathway.

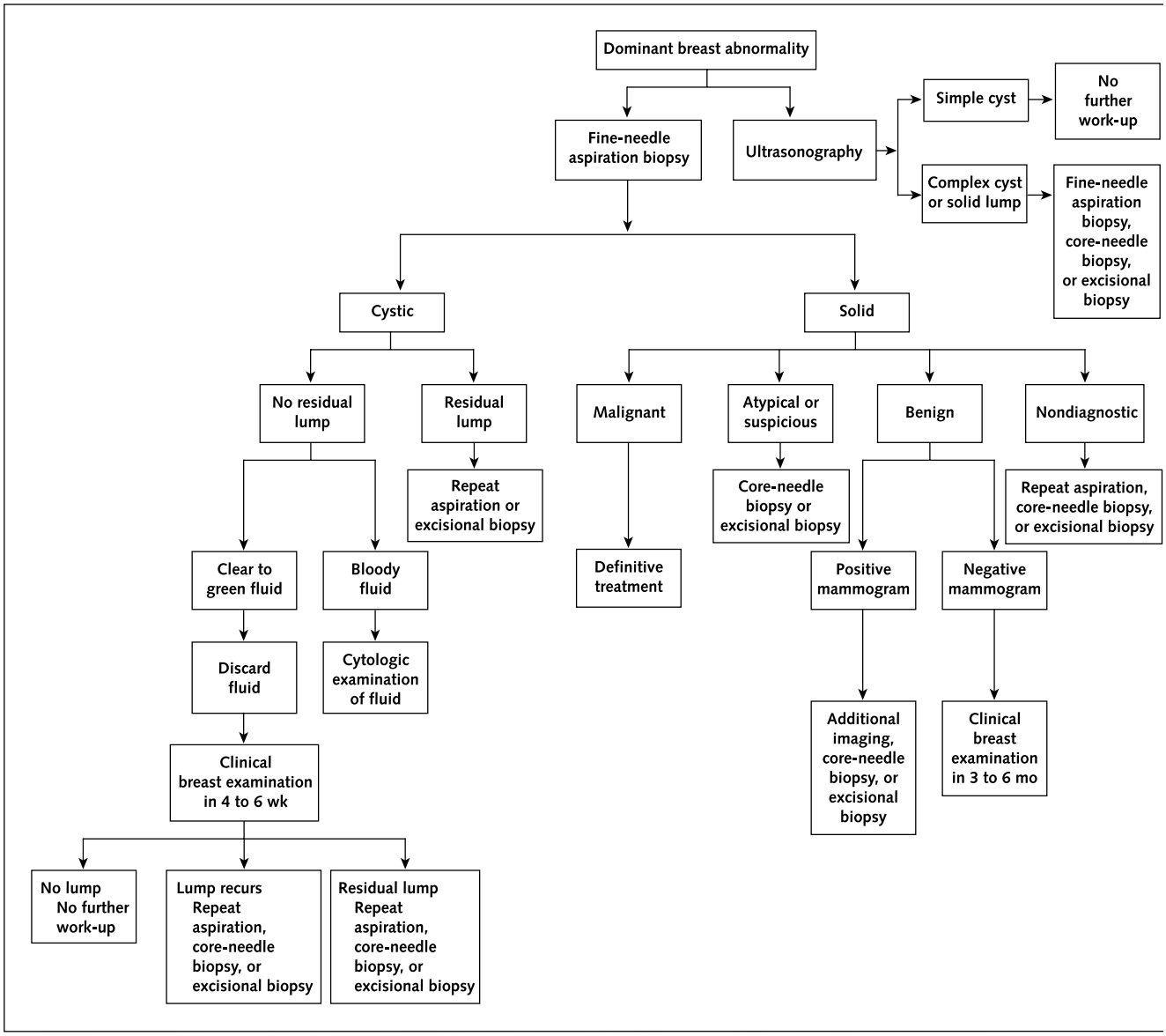
In summary, when well-trained providers perform core-needle biopsy, the sensitivity and specificity are high and similar to FNAB. Core-needle biopsy can more often distinguish benign proliferative lesions with and without atypia and ductal carcinoma in situ from invasive disease than can FNAB. Benign proliferative lesions or ductal carcinoma in situ may be categorized as atypical or suspicious by FNAB, thereby requiring core-needle biopsy or excisional biopsy to exclude or establish a diagnosis of invasive cancer. Because core-needle biopsy requires use of larger-diameter needles than does FNAB, the procedure tends to cause more patient discomfort and local bleeding and is less suitable for targets in certain anatomical positions (for example, close to the chest wall or in the nipple complex), small superficial targets, and small movable targets in the axillary area. Given that most patients with symptomatic breast abnormalities do not have breast cancer (89% to 91%) (10, 12, 13), if providers are well trained in both FNAB and core-needle biopsy, the requirement for core-needle biopsy is reduced by the use of FNAB as the first diagnostic step in evaluating a palpable breast abnormality, particularly in the context of benign disease. Core-needle biopsy is more expensive ($452 to $571) than FNAB ($85 to $131) but cheaper than excisional breast biopsy (10, 43, 44).

Management Strategies

Performing FNAB as the first diagnostic step in evaluating a palpable breast abnormality can be therapeutic, diagnostic, and cost-efficient and is the least invasive way to obtain tissue. Although ultrasonography is similar in cost to FNAB ($68 to $95 vs. $85 to $131) (10, 43), FNAB is cheaper overall as the first diagnostic step in evaluation of a palpable breast abnormality because 80% of abnormalities are not simple cysts on ultrasonography and require subsequent FNAB or tissue biopsy. In addition, FNAB can be a therapeutic measure for cysts that cause breast discomfort. If FNAB cannot be performed and interpreted by an experienced cytologist, performing ultrasonography before core-needle biopsy will eliminate the need for core-needle biopsy in about 20% to 25% of women with simple cysts (13, 26).

When straw-colored or grey-green fluid is obtained by FNAB and the lump completely disappears, the diagnosis is a simple cyst (**Figure 2**). The fluid should not be sent for analysis because the risk for cancer is exceedingly small. Of 6782 cytologic examinations of nonbloody breast cyst fluid aspirates, no breast cancers were identified (61). If the fluid is bloody or otherwise unusual, it should be sent for cyto-

Figure 2. **Flow diagram for evaluation of a dominant breast abnormality.**



logic examination because about 7% of bloodstained aspirates contain cancer (61, 90). If fluid is obtained by aspiration and a lump remains, the needle may have missed a solid mass next to the cyst or entered both a solid mass and a cyst, thus diluting the aspirated cells with cyst fluid. In this situation, the remaining lump should be immediately reaspirated and material sent for cytologic evaluation.

Women with simple cysts should undergo clinical breast examination 4 to 6 weeks after cyst aspiration to determine whether the cyst has recurred or whether a residual lump is present at the aspiration site (**Figure 2**). One study (90) of 401 women who underwent cyst aspiration found that 44 women had a recurrent cyst and 20 had a solid mass at the aspiration site within 6 to 8 weeks of the initial aspiration; of these 20, 2 had breast cancer (0.5% of cysts). If a simple cyst recurs several times after aspiration in a short period, the cyst should be excised.

If a solid mass is aspirated, the cellular material should be sent for cytologic evaluation. The classification of FNAB specimens sent for cytologic evaluation falls into one of four categories (**Figure 2**): 1) malignant—the cellular findings are diagnostic of malignancy, 2) atypical or suspicious—the cellular findings are not clearly benign or are suggestive of malignancy, 3) benign—no evidence of malignancy, and 4) nondiagnostic or unsatisfactory—findings indicate scant cellularity, air drying, a distortion artifact, obscuring blood, or inflammation (91).

The level of risk for breast cancer determines the management strategy for each category. The proportion of women with breast cancer ranges from very high for ma-

lignant (99.2% to 100%) and atypical or suspicious (50% to 70%) to much lower and more variable for benign (0.2% to 15.2%) and nondiagnostic (5.0% to 22.2%) categories (13, 66, 69, 71, 92, 93). If the cytologic diagnosis is malignant, women should be referred to a breast surgeon for definitive therapy (**Figure 2**). Atypical or suspicious cytology results should be followed by core-needle biopsy or excisional biopsy. Women with benign cytology results should undergo diagnostic mammography. Negative likelihood ratios for a benign cytology result are low at 0.02 (**Table 4**) among well-trained physicians (13). Benign cytology results in the setting of a normal or benign mammography result require no further diagnostic tests, but they should be followed by careful clinical breast examination within 3 to 6 months (**Figure 2**). In women age 35 years or younger with benign cytology results, such as fibroadenoma or lymph node, diagnostic mammography is not required because the chance of cancer is very low (94). If the mammography result is suspicious or malignant, core-needle biopsy or excisional biopsy should be performed despite benign aspiration cytology results. A nondiagnostic cytologic evaluation is inconclusive and reaspiration of the lump, core-needle biopsy, or surgical excision is indicated.

Discussion

Diagnostic mammography is most helpful in deciding whether a nonpalpable breast lesion should be biopsied but not whether a palpable breast abnormality should be biopsied. Fine-needle aspiration biopsy or core-needle biopsy is preferred for palpable masses, whereas core-needle biopsy or needle localization with surgical biopsy is usually preferred for nonpalpable lesions. Ultrasonography can be used for palpable and nonpalpable lesions to determine whether a lesion is a simple cyst and, therefore, benign.

When an abnormality is detected on screening mammography, clinical evaluation and thorough radiologic work-up are needed to determine the significance. The likelihood of cancer is high when the mammographic assessment is "suspicious abnormality" or "highly suggestive of malignancy"; tissue sampling of the lesions by image-guided biopsy or excisional biopsy is required. The likelihood of cancer is low when the mammographic assessment is "probably benign finding," and abnormalities may be evaluated by repeated imaging performed two times at 6-month intervals; if the abnormality is stable, a woman can return to routine screening examinations. Women with a mammographic assessment of "need additional imaging evaluation" are at intermediate risk for breast cancer. These women should have a clinical evaluation and radiologic work-up first to determine the significance of the lesion and minimize the number of unnecessary biopsies of radiologic findings that have a low probability of being cancer.

Breast symptoms are a common medical problem; a breast lump represents the most serious breast abnormality that requires evaluation. The initial objective is to distinguish simple cysts from solid lesions, which can be accomplished by performing a FNAB or ultrasonography. A solid mass requires a tissue diagnosis. A malignant FNAB result on cytologic examination is sufficient to refer a woman for definitive treatment. An atypical, suspicious, or nondiagnostic cytologic result requires a tissue biopsy, either a core-needle or excisional biopsy, of the palpable breast abnormality. A benign cytologic result on FNAB or benign histologic result on core-needle biopsy and negative mammography assessment require close clinical follow-up of the breast abnormality because neither test can exclude the possibility of breast cancer in a woman with persistent breast symptoms. Women who present with a breast lump and have an abnormal diagnostic mammography examination have a relatively high risk for cancer and should undergo tissue sampling of the lump. When FNAB, core-needle biopsy, or diagnostic mammography provides inconsistent or inconclusive results or a breast abnormality remains suspicious for cancer on close clinical follow-up, excisional tissue biopsy of the abnormality should be done.

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