

GUAM BREAST AND CERVICAL CANCER EARLY DETECTION PROGRAM

SCREENING GUIDELINES FOR BREAST CANCER

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INTRODUCTION

The purpose of these guidelines is to provide service providers with brief, easy-to-use tools to help ensure the consistent provision of screening and diagnostic procedures for patients eligible under the Guam Breast and Cervical Cancer Program (GBCCEDP). These guidelines have been developed for early detection of breast and cervical cancer that can help reduce the morbidity and mortality of these diseases.

The BCCEDP adopted the *Breast Cancer Diagnostic Algorithms for Primary Care Providers*, Cancer Detection Section, California Department of Health Services, 2005. These algorithms were developed for Primary Care Providers (PCPs) who provide breast cancer screening services. These clinicians are the critical providers to ensure that women receive timely and appropriate screening and diagnostic services, including the highest quality initial screening, appropriate referral of abnormal findings, and follow-up with other breast specialists.

PCPs are encouraged to use these algorithms to aid clinical decision-making. As with all medical protocols and algorithms, they are intended to serve as an adjunct, not as a replacement for clinical judgment applied to individual cases. Excellent communication must always be maintained among PCPs and radiologists, surgeons, pathologists, and other breast specialists.

The following guidelines are based on the policies and procedures established by the National Breast and Cervical Early Detection Program (NBCCEDP) of the Centers for Disease Control in Atlanta. It may be amended from time to time as needed.

OVERVIEW

Health history and assessment of risk, physical examination of the breast, mammographic imaging and documentation should be performed routinely for all patients and are described in this section.

These algorithms graphically describe a logical progression of services designed to facilitate the work-up of a patient presenting with breast symptoms or abnormal breast screening. The management of any patient will vary according to age, clinical history and clinical findings.

The graphics provide a visual presentation of decision points throughout the process as well as recommendations or indications for the timing of a referral to a breast specialist for definitive risk assessment, diagnosis, staging and/or treatment.

Notes for each algorithm provide additional information on the assessment and decision-making guiding principles, including selected terminology, rationales, alternative approaches, and controversies.

Graphic Designations	Abbreviations
 Starting point for algorithm	ADH = Atypical Ductal Hyperplasia
 Decision point	ALH = Atypical Lobular Hyperplasia
 Process or procedure	BI-RADS® = Breast Imaging Reporting and Data System
 Endpoint - decision finished for that algorithm	CBE = Clinical Breast Examination
 Direction for further work-up or connector to another algorithm	DCIS = Ductal Carcinoma in Situ
 Flowchart note marker	DX = diagnosis
	FNA = Fine Needle Aspiration
	F/U = Follow-up
	HX = Patient History
	LCIS = Lobular Carcinoma In Situ
	NCI = National Cancer Institute

ASSESSMENT OF RISK - ALGORITHM 1

A woman's risk of developing breast cancer should be assessed at each routine screening visit since her personal risk factors will change over time. The Assessment of Risk Algorithm provides a basic guide for primary care providers to follow and can help identify women at greater risk of breast cancer than the general population. A sample [Breast Cancer History and Risk Assessment Form](#) can be used as a tool to help collect relevant patient information at every breast cancer screening visit.

Risk assessment for breast cancer effectively engages the PCP and the patient in a discussion about breast cancer prevention, educates a woman about her specific risk factors, and helps guide a personalized plan for risk reduction and early detection. For the woman with high risk determined by a risk assessment algorithm, a referral to a risk assessment counselor can be helpful in further defining the risk, identifying possible genetic risks, and recommending appropriate risk reduction strategies.

Risk is the probability or likelihood that an event will occur. Risk can be expressed in several ways, the most common being relative risk and lifetime risk. Relative risk is the ratio of the risk of disease (in this case breast cancer) among those exposed to a risk factor to the risk of disease among those not exposed to the risk factor. For breast cancer, important risk factors include age, gender, family history, age at menarche, other reproductive factors, use of hormone replacement therapy, radiation exposure, alcohol use, and previous breast biopsies – especially those with abnormal findings. See Appendix A-2 for details on relative risk estimates associated with certain risk factors. Absolute risk describes the risk of disease in the context of time, such as the lifetime risk for a disease or risk by a certain age. The Gail Model estimates the absolute risk of breast cancer for a woman over the next five years and over her lifetime based on certain risk factors for the disease. It is an excellent breast cancer risk assessment tool for most women. However, it may underestimate risk for women with a family history of cancer. The Claus Tables provide a better estimate of absolute risk for women with a family history of cancer. These tables estimate breast cancer risk based on the family history of breast cancer and/or ovarian cancer taking into account the age of onset of the disease.

Algorithm #1 is intended to assist PCPs with the identification of women at increased risk for developing breast cancer. Breast cancer risk assessment should be performed as part of routine screening, and it should be repeated annually since risk factors for breast cancer change over time. Certain breast cancer risk factors are more significant than others, and generally, there are interactions between these major risk factors. The interactions make true risk assessment difficult to calculate. This algorithm attempts to incorporate the risk factors that have epidemiologic evidence of significant risk; it does not include all possible risk factors or assess absolute risk for combinations of risk factors. Rather, the algorithm provides a qualitative assessment of risk based on personal history, family history, medical/pathological/genetic factors, with the outcome of either normal or increased risk for breast cancer.

Pathological factors:

A personal history of breast cancer increases the general risk of a second primary breast cancer either in the contralateral breast or the ipsilateral breast if there is remaining tissue. For most

women, this risk is estimated to be 0.7% to 1.0% per year for the first 10 years with a 20-year cumulative risk of 4%-20%. However, the personal risk of another primary breast cancer depends to a great extent on the presence of risk factors. For example, a BRCA1 or BRCA2 mutation is associated with a 10-year cumulative risk of 43% and 34% respectively (Metcalf et al., 2004).

Ductal carcinoma in situ (DCIS) confers a risk similar to invasive breast cancer (Yen, 2003). Other pathological features that increase breast cancer risk include: lobular carcinoma in situ (LCIS), atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), fibroadenoma with complex features, moderate or florid hyperplasia and solitary papillomas without coexistent hyperplasia.

Genetic and family history risk factors:

Inherited **mutations** in breast cancer susceptibility genes are associated with a very high risk of the occurrence of breast cancer. The breast cancer susceptibility genes identified to date include: *BRCA1/BRCA2*, associated with the diagnoses of hereditary breast-ovarian cancer and hereditary site-specific breast cancer.

- *PTEN*, associated with the diagnosis of Cowden syndrome.
- *STK11*, associated with the diagnosis of Peutz-Jeghers syndrome
- *MLH1/MSH2/MSH6*, associated with hereditary non-polyposis, colorectal carcinoma and breast cancer in certain families.
- *ATM*, associated with a 4-fold increase in risk among heterozygotes.
- *CHK2*, associated with a 2-fold increase in risk among heterozygotes.
- *TP53*, 50% risk of breast cancer by age 50.

A family history of breast cancer significantly increases the risk of breast cancer for the individual if the cancer occurs in first- and/or second-degree biological relative(s) – parents, siblings, children, grandparents, aunts, uncles, nieces and nephews. Red flags suggestive of genetic susceptibility to breast cancer include:

- One or more first- or second-degree relatives with breast cancer at an early age (less than 40-50 years of age).
- Breast cancer and a second primary cancer in a close relative, especially ovarian cancer. (Other cancers that may be associated with an increased genetic risk include: thyroid, colorectal, prostate, endometrial, pancreatic, adrenocortical carcinoma, melanoma, childhood sarcoma, leukemia/lymphoma, and brain tumors.)
- Male breast cancer in a close relative.
- Two or more relatives with breast cancer at any age.
- If of Ashkenazi Jewish descent, a biological relative with breast cancer diagnosed before age 50 or ovarian cancer at any age.

Personal risk factors:

- Gender is the most obvious and important risk factor for breast cancer. Females have a 100-fold increase in risk as compared to males. However, the ACS estimates that in 2005

there will be 1,690 new cases of invasive breast cancer diagnosed among men in the United States. (Male breast cancer is a red flag for a possible genetic susceptibility.)

- Age – breast cancer risk increases with age; 96% of breast cancers occur in women age 40 and older (ACS, 2003-2004). Most women face a lifetime risk of 12-13%.
- Race – Caucasian women have a greater risk of breast cancer than other racial groups.
- Prolonged exposure to endogenous estrogen and progestins (U.S. Preventive Services Task Force, 2005).
- Exposure to exogenous combined estrogen and progestin therapy in hormone replacement therapy for postmenopausal women has been shown to slightly increase the risk for breast cancer. It is controversial whether or not exogenous estrogen alone in estrogen replacement therapy for postmenopausal women affects the risk for breast cancer. (U.S. Preventive Services Task Force, 2005.)
- Alcohol use – greater than 27 drinks per week. (Gronback, 2004.)
- Obesity – obese women with BMI >30 had estrogen concentrations between 60% and 219% higher than thin women and the risk of Brest cancer increased as BMI increased at an average rate of about 18% per 5-point increase in BMI. (Journal of National Cancer Institute, 2003.)
- Radiation exposure to the upper torso (e.g. treatment of Hodgkin’s lymphoma). (Preston, 2002.)

The table below reveals changes in breast cancer risk across a woman's lifetime.

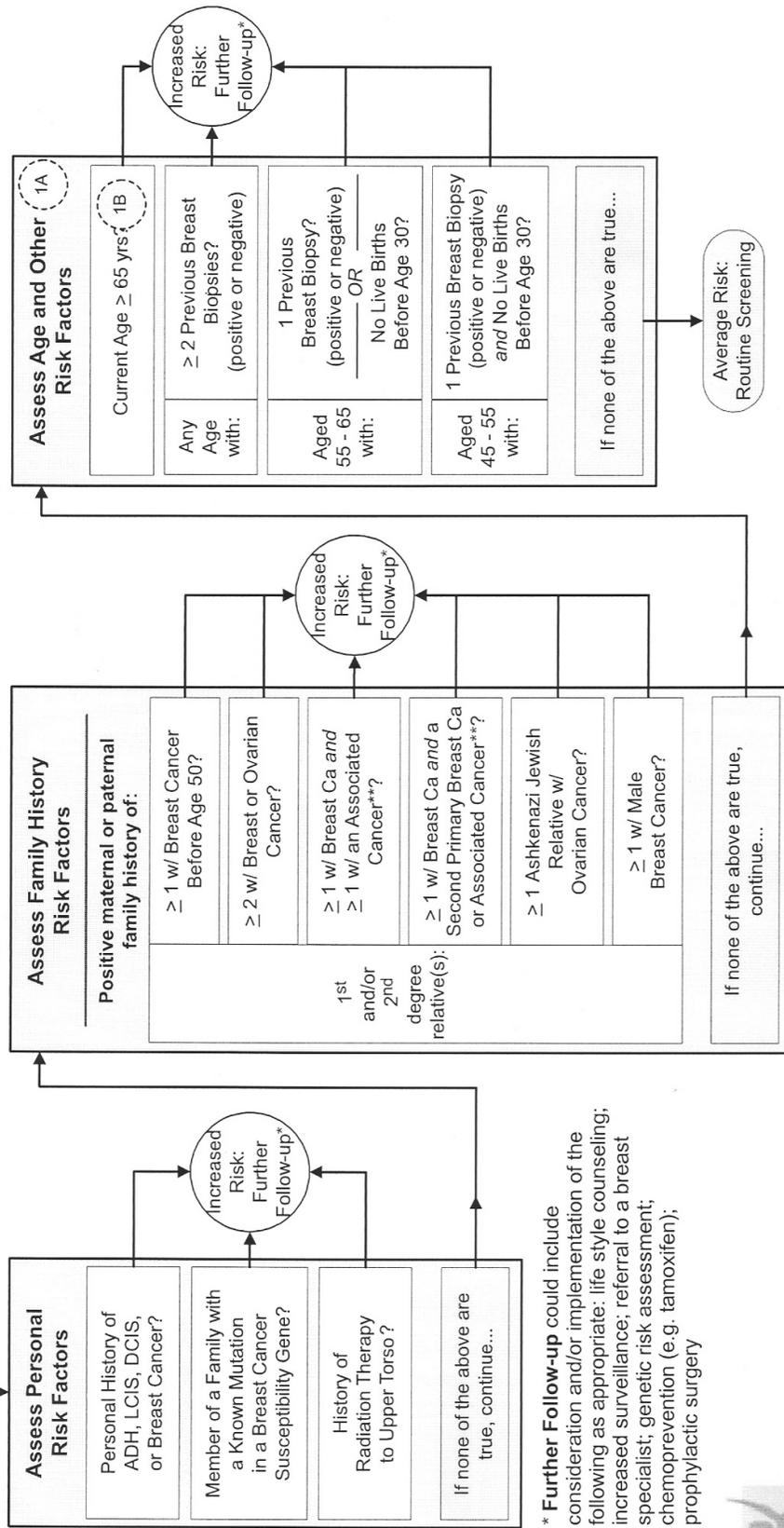
Age-Specific Probability of Developing Breast Cancer*		
If current age is...	Probability of developing breast cancer in next 10 years is:**	Or 1 in:
20	0.05%	2,152
30	0.40%	251
40	1.45%	69
50	2.78%	36
60	3.81%	26
70	4.31%	23

American Cancer Society, Surveillance Research, 2003.

* Among those free of cancer at the beginning of the age interval. Based on breast cancer cases diagnosed 1988-2000. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.

** Probability derived using NCE DEVCAN software.

Algorithm 1: Assessment of Risk



* **Further Follow-up** could include consideration and/or implementation of the following as appropriate: life style counseling; increased surveillance; referral to a breast specialist; genetic risk assessment; chemoprevention (e.g. tamoxifen); prophylactic surgery

** **Associated cancers:** ovarian; thyroid; colorectal; prostate; endometrial; pancreatic; adrenocortical; melanoma; childhood sarcoma; leukemia/lymphoma; brain tumor



Flowchart Notes and Footers

NOTE 1A: After ruling out the presence of *Personal Risk Factors* and *Family History Risk Factors* listed in Algorithm #1, assessment of *Age and Other Risk Factors* will identify most women at increased risk for breast cancer, but may over-estimate risk for some women. For a more accurate risk-estimate, calculate breast cancer risk using the National Cancer Institute (NCI) Risk Assessment Tool (Gail Model) instead of using the Algorithm's *Age and Other Risk Factors* criteria. A five-year risk of >1.7 % should be considered **Increased Risk**. NCI's online risk assessment tool is available at <http://bcra.nci.nih.gov/brc/>

NOTE 1B: A Caucasian woman aged 65 with *average* risk factors has a 2% risk of developing breast cancer within the next 5 years according to the Gail Model . Therefore, women 65yrs or older should have their *personal* risk evaluated on an individual basis using the Gail Model if possible. Women with a 5-year risk of >1.7% meet FDA criteria for receipt of approved chemoprevention (e.g., Tamoxifen). However, the potential benefit of treatment must be weighed against the associated risk of serious side effects for the individual woman.

*Further Follow-up could include consideration and/or implementation of the following as appropriate: life style counseling; increased surveillance; referral to a breast specialist; genetic risk assessment; chemoprevention (e.g. tamoxifen); prophylactic surgery

**Associated cancers: ovarian; thyroid; colorectal; prostate; endometrial; pancreatic; adrenocortical; melanoma; childhood sarcoma; leukemia/lymphoma; brain tumor

NEW PALPABLE MASS - ALGORITHM 2

A new palpable mass identified during a women's clinical breast exam must always receive a complete diagnostic work-up before concluding whether or not the mass is a benign finding. While the CBE alone is not a diagnostic procedure, a negative diagnostic mammogram result is insufficient to conclude that a palpable mass is not malignant and further follow-up is necessary. The guidance provided by this algorithm can help ensure the complete work-up of a new palpable breast mass.

Introduction to the work-up of a New Palpable Mass - Algorithm 2

Management of the patient with a breast mass varies according to age, history and clinical findings. Detection of a breast mass often creates anxiety for the woman and her family, requiring sensitive provider/patient communication. Important questions to consider when assessing the index of suspicion of a breast mass (lesion) detected on CBE include:

- Is it an asymmetrical finding in both breasts?
- Is it a three dimensional discrete palpable mass?
- What is the location and depth?
- Is it mobile or fixed?
- What is the size and shape?
- What is the consistency?
- Is it tender or non-tender?

Normal glandular tissue is generally mirrored in the contralateral breast. A discrete palpable mass is three-dimensional, different from surrounding tissues and usually asymmetric. Clinical signs that are suggestive of benignity, but are not diagnostic, include a mass that is soft, rubbery and mobile. Features suggestive of malignancy include a mass that feels firm or hard, is fixed, has an irregular shape, is solitary, and feels much different from the surrounding breast tissue (Barton, 1999; Goodson, 1996).

CBE is a screening method, not a diagnostic test. Regardless of age, every clinically suspicious lesion requires further evaluation. *CBE finds 4% to 7% of cancers that are normal or benign on mammography* (Green 2003, Bobo 2000, Beyer 2003, Georgian-Smith 2000). **Thus, an abnormal CBE in the presence of a negative mammogram requires further follow-up.** *The leading cause of physician delay in the diagnosis of breast cancer continues to be inappropriate judgment that a mass is benign without performing a biopsy.* Reducing delay in diagnosis requires less reliance on CBE to determine the benignity of a mass as well as less reliance on benign mammographic reports in deciding not to biopsy a mass (Goodson, 2002). Physical exam alone is approximately 70% accurate; mammography alone is approximately 85% accurate; minimally invasive tissue diagnosis alone is approximately 95% accurate. While physical exam and mammogram alone can detect many cancers, no single test by itself allows for detection of all breast cancers. The best clinical approach to the diagnosis and management of patients with a palpable mass is the combination of all three tests – physical exam, radiographic imaging and pathology (biopsy or FNA). This diagnostic triad is known as the "**triple test.**" The diagnostic accuracy of these three tests taken together approaches 100% (Morris, 2002; Vetto, 2003).

Clinicians should select the "triple test" method as it helps make an evidence-based decision about clinical management. If one of the "triple test" components is discordant, the entire diagnosis is uncertain and each of the "triple test" findings will need to be reviewed before proceeding.

Pre-menopausal

Women

In patients younger than 30 years of age, or patients who are pregnant, ultrasound may be the first or sole breast imaging modality performed (Mehta, 2003 and Baker, 2000). For patients 30-49 years of age with a new palpable mass, a cyst is the most likely diagnosis and can be confirmed or ruled-out by fine needle aspiration (FNA) or ultrasound (a diagnostic imaging modality). If the degree of suspicion is very low (the palpable mass is a "ridge" and is two-dimensional, rather than three-dimensional), it is acceptable to repeat the screening CBE at a more optimal time of the menstrual cycle. Any palpable mass that persists and has not been proven to be a simple cyst, must receive additional diagnostic work-up until a final diagnostic status is determined.

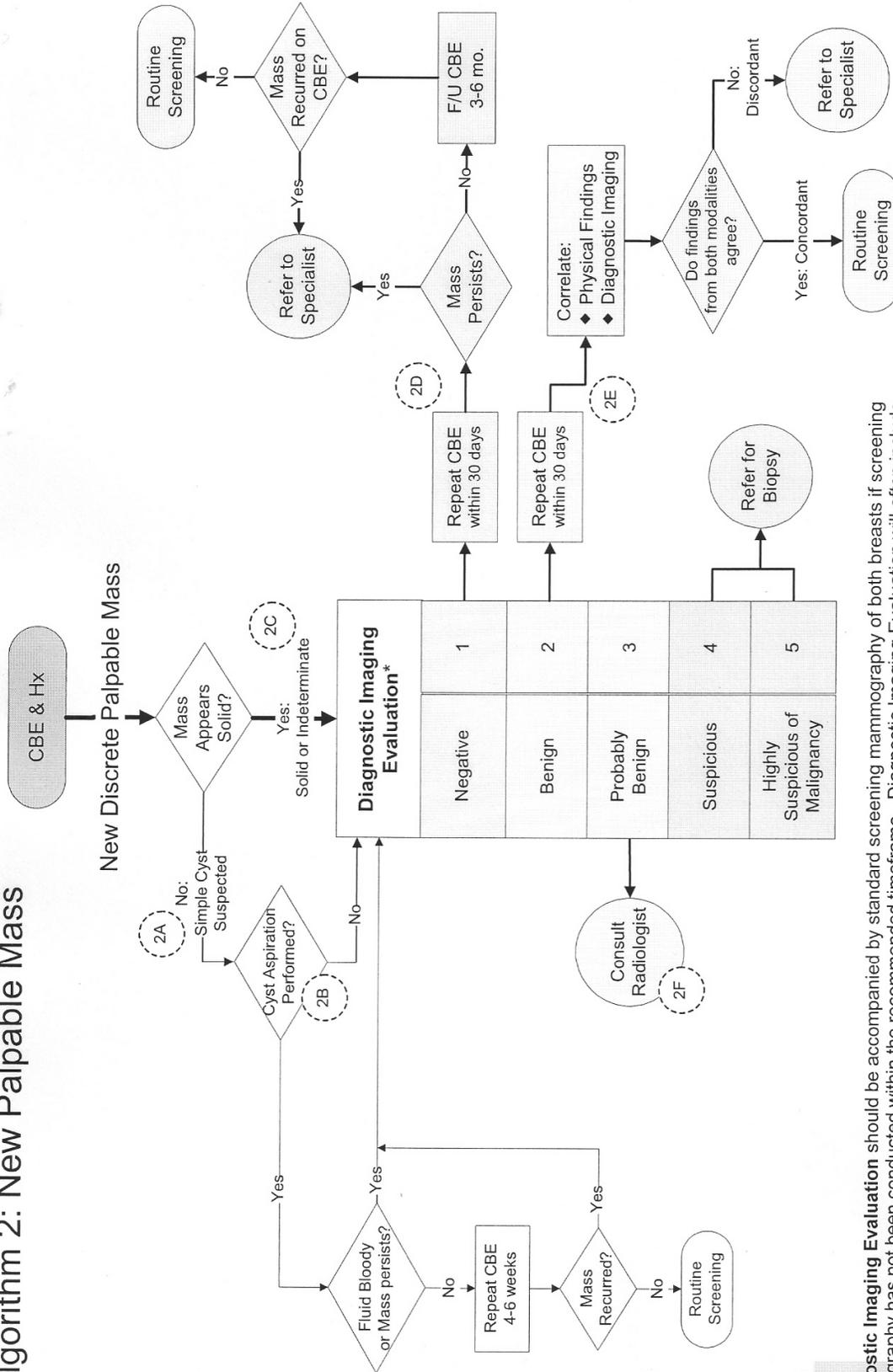
Post-menopausal

Women

Since the risk of breast cancer increases with age, clinicians need to be more suspicious of a dominant mass or asymmetric thickening in the breasts of postmenopausal women. Cystic findings decrease after menopause, although cysts, pain, and discharge can be found in women taking hormone replacement therapy. Diagnostic imaging evaluation is usually the first-line investigation of a palpable breast mass in postmenopausal women.

Regardless of age, it is important to request a **diagnostic** imaging evaluation for a palpable mass, and NOT a screening mammogram.

Algorithm 2: New Palpable Mass



* **Diagnostic Imaging Evaluation** should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed. California Department of Health Services, 2005

ABNORMAL SCREENING MAMMOGRAM WITH NORMAL CBE - ALGORITHM 3

With improved imaging techniques, screening mammograms are enabling detection of earlier breast cancers. If an abnormality is suspected with screening mammography, the radiologist performs additional mammographic views and/or ultrasound. After the imaging work-up is complete, the radiologist assigns a BI-RADS® category 1-6 as the final imaging result.

Introduction to the work-up of an Abnormal Screening Mammogram with Normal CBE ~ Algorithm 3

With improved imaging techniques, screening mammograms are enabling detection of earlier breast cancers. If an abnormality is suspected with screening mammography, the radiologist performs additional mammographic views and/or ultrasound. After the imaging work-up is complete, the radiologist assigns a BI-RADS® category 1-6 as the final imaging result.

Final Imaging Results – Negative or Benign (BI-RADS® Categories 1 or 2)

Routine clinical follow-up is appropriate for Negative and Benign (BI-RADS® category 1 and 2) mammographic imaging results.

Final Imaging Result – Probably Benign (BI-RADS® Category 3)

A Probably Benign, BI-RADS® category 3 lesion generally will require a repeat CBE in 3-6 months and repeat mammography in six months to ensure concordance between the CBE findings and the radiographic lesion. If the woman is at increased risk for breast cancer, immediate follow-up is recommended with a breast specialist. Women with average risk may be referred for repeat CBE and imaging in six months (short-term follow-up). If the initial six-month short-term follow-up (unilateral mammogram) is stable, another bilateral mammogram in 6 months may be recommended by the radiologist (ACR, 2003 and Kerlikowske, 2003). If there is still no change, the patient should be rescreened at one-year intervals for two years. While a lesion's radiographic stability over time suggests benignity, a lack of change in features cannot completely reassure the PCP and patient that a lesion is benign. There have been reports of microcalcifications, which are stable on radiologic exam, yet are later found to be malignant in 8-63 months (Michell, 2003). Some lesions classified mammographically as probably benign may be biopsied depending on the recommendations of the breast specialist and the preferences of the patient.

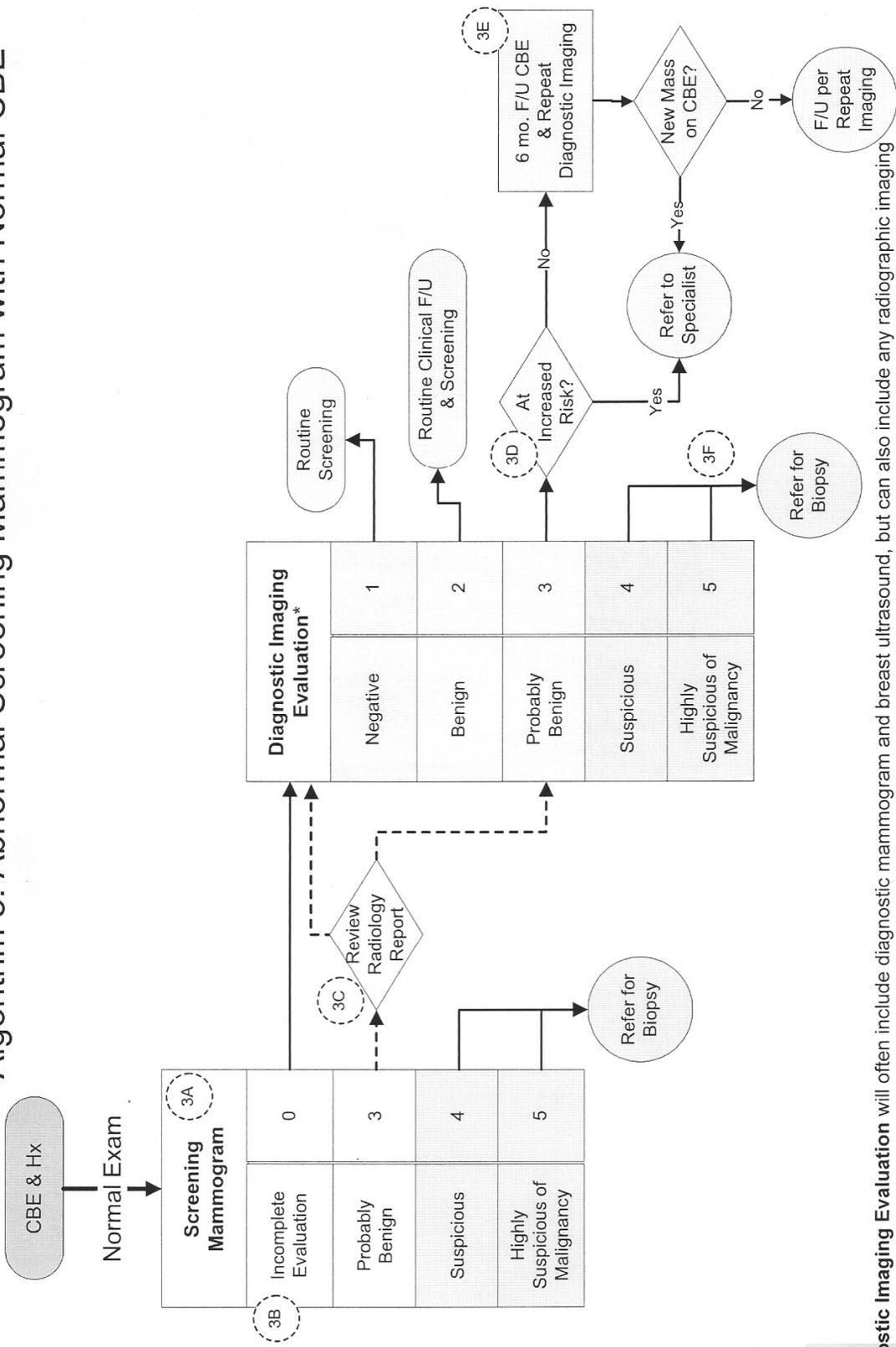
Final Imaging Results – Suspicious Abnormality or Highly Suggestive of Malignancy (BI-RADS® Categories 4 or 5)

All mammograms showing a Suspicious Abnormality or a lesion that is Highly Suggestive of Malignancy (BI-RADS® category 4 or 5) should result in biopsy.

Categories 3, 4, and 5 always require further evaluation despite the normal clinical breast exam. A reasonable percentage (50-90%) of category 4 and 5 lesions will be shown to be cancerous (ACR, 2003). In fact, it is the detection of these small or pre-invasive cancers by mammography that significantly contributes to the reduction in breast cancer mortality .

The false-negative rate for screening mammography is 8% to 10% (Shaw de Paredes, 2000). Breast density can compromise the ability of a mammogram to detect a mass, and lesions located near the sternum can be difficult to visualize (Mandelson, 2000). Over a 10 year period approximately 24% of women getting an annual mammogram will have at least one false positive mammogram.

Algorithm 3: Abnormal Screening Mammogram with Normal CBE



* **Diagnostic Imaging Evaluation** will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

Flowchart Notes and Footer

NOTE 3A: Screening mammogram results of Negative (BI-RADS® category 1) and Benign (BI-RADS® category 2) prompt routine rescreening for women with normal CBE exams.

NOTE 3B: Lesions identified with a screening mammogram **require** a diagnostic "work-up" (additional views and/or ultrasound) before a *final* imaging result can be assigned (ACR, 2003). Prior to assigning the final imaging result, a BI-RADS® category 0 may be temporarily assigned to indicate that additional views or tests are needed, or that previous mammographic results need to be reviewed.

NOTE 3C: The American College of Radiology does not recommend the assignment of a BI-RADS® 3 result to a *screening* mammogram. If you should receive a *screening* mammogram report with this result, refer the woman for additional *diagnostic* imaging. If a diagnostic evaluation has already been completed, continue work-up based on that *diagnostic* imaging result.

NOTE 3D: A patient with a final imaging result of BI-RADS® category 3 who is at increased risk for breast cancer (See Algorithm #1) should be immediately referred to a breast specialist. Referral to a breast specialist can be offered to women who are concerned about their results and do not want to wait six months for further follow-up.

NOTE 3E: For BI-RADS® category 3, the vast majority of findings will be managed with an initial short-term follow-up examination in 3-6 months, followed by additional examinations until stability is demonstrated (2 years or longer). There may be occasions when a biopsy is done (i.e. patient request or clinical concerns). Evidence from all the published studies indicates the need for biopsy if the lesion increases in size or undergoes morphologic change (ACR, 2003).

NOTE 3F: A BI-RADS® category 4 lesion should lead to biopsy, and a BI-RADS® category 5 lesion requires biopsy (ACR, 2003). If the lesion is definitively diagnosed as benign after core biopsy and is consistent (concordant) with the radiological findings, excisional biopsy is not required (See Algorithm #7). The methods of biopsy include stereotactic or ultrasound-guided core biopsy** for definitive diagnosis or needle localization followed by excisional biopsy with intraoperative confirmation of negative margins.

Footer:

*Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

**Ultrasound-sound guided biopsy could be done by the radiologist. The radiologist however needs to discuss the procedures, alternative and risk with the patient and the patient's primary care provider.

SPONTANEOUS UNILATERAL NIPPLE DISCHARGE ~ ALGORITHM 4

Nipple discharge is a common breast problem that has been reported in 10-15% of women with benign breast disease and in 2.5-3% of women with breast cancer (Morrow, 2000). A nipple discharge should be of concern when a woman reports it as unilateral and spontaneous (not in response to stimulation) and staining her bra, bed sheet, or sleeping garment.

Introduction to the work-up of Spontaneous Unilateral Nipple Discharge ~ Algorithm 4

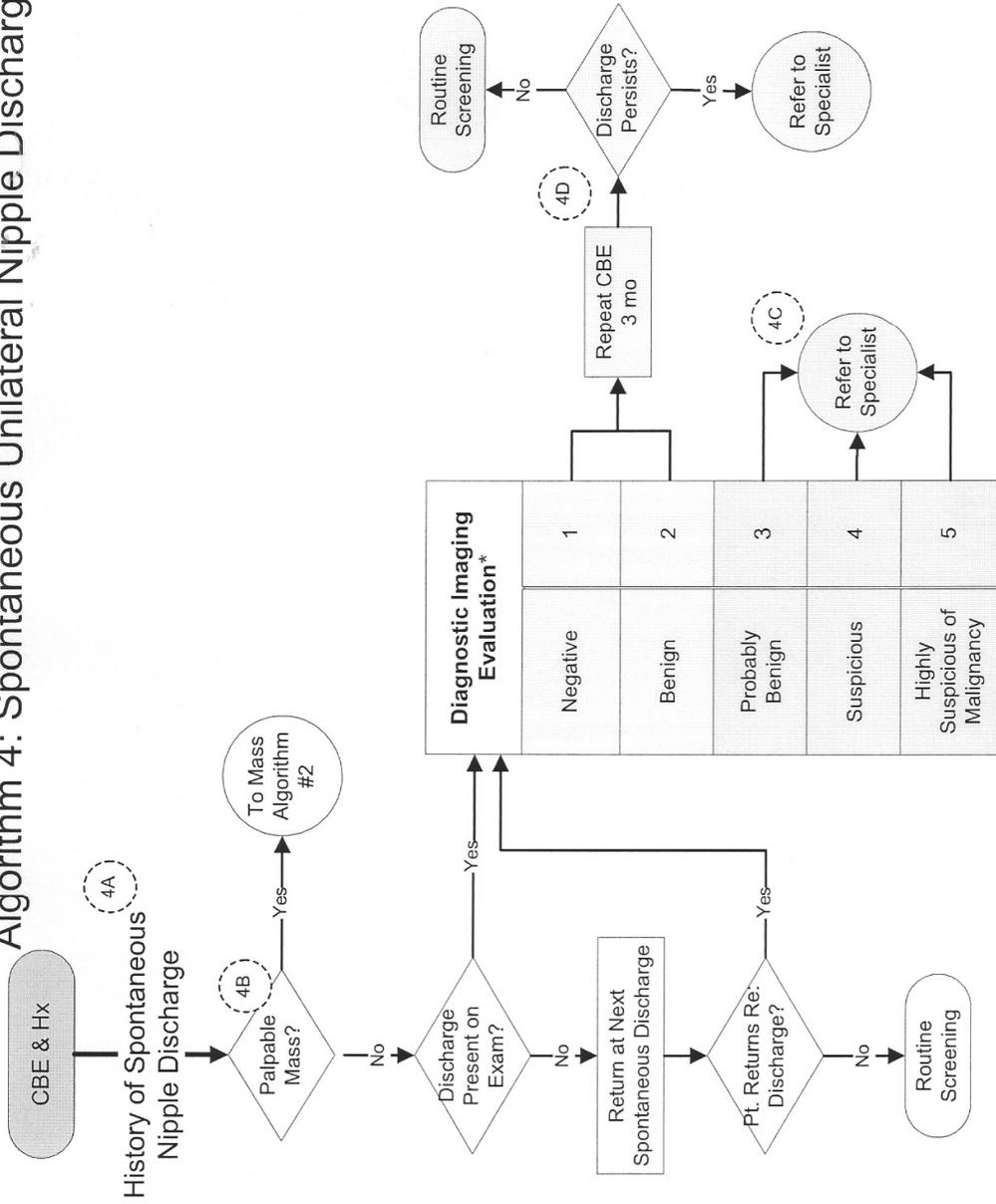
Nipple discharge is a common breast problem that has been reported in 10-15% of women with benign breast disease and in 2.5-3% of women with breast cancer (Morrow, 2000). A nipple discharge should be of concern when a woman reports it as unilateral and spontaneous (not in response to stimulation) and staining her bra, bed sheet, or sleeping garment. Directly squeezing the nipple to express fluid promotes discharge and is not a routine part of the screening CBE in asymptomatic women. Using an aspiration pump will elicit a discharge from 50 to 80% of women without breast disease. Women should be advised to avoid checking themselves for discharge since benign discharge may resolve when the nipple is left alone (Morrow, 2000).

A number of conditions result in nipple discharge. Endocrine causes of galactorrhea include pregnancy, hypothyroidism and amenorrhic syndromes. Medications such as antihypertensives, oral contraceptives, phenothiazines, and tranquilizers may also cause nipple discharge. Milky discharge could be due to medications and the provider may want to consider ruling out this etiology prior to referral to a breast specialist.

Bilateral nipple discharge usually has a physiological cause, such as hyperprolactinemia leading to galactorrhea. It can also occur in breast disease that is bilateral, such as mammary duct ectasia. This is a benign condition occurring in postmenopausal women, characterized by dilation of the ducts, nipple secretions and periductal inflammation.

Every woman with a unilateral, spontaneous, clear, watery, serous, or bloody discharge should be referred for diagnostic imaging evaluation. Most mammograms in such instances are normal and should NOT deter surgical referral. Any discharge from a **single duct** is of concern. Multiple duct discharges are rarely caused by cancer (Florio, 2003). Any mammographic abnormality should correspond with the quadrant of the breast from which the discharge originates for it to be considered relevant to the cause of the discharge. Cytology in the assessment of nipple discharge is controversial and is generally not recommended as a first line investigation due to the high number of false negative results.

Algorithm 4: Spontaneous Unilateral Nipple Discharge



* **Diagnostic Imaging Evaluation** should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

California Department of Health Services, 2005

Flowchart Notes and Footer

NOTE 4A: A non-spontaneous discharge is not usually significant. It is more clinically relevant if a history of a spontaneous discharge is elicited. The patient should be asked whether she has noticed staining of her clothing. A true nipple discharge originates in one or more duct(s) (Apantaku, 2000). Inverted nipples, eczema, infection, etc can cause pseudo-nipple discharges.

NOTE 4B: It is important to determine if the nipple discharge is associated with a palpable mass. Any mass noted within 2 cm of the nipple is considered correlative (Sheen-Chen, 2001). Immediate referral for diagnostic imaging followed by surgical consultation is appropriate.

NOTE 4C: The diagnostic imaging abnormality should correspond with the quadrant from which the discharge originates (i.e. a radiographic abnormality that does not correlate to the discharge quadrant may represent a separate lesion). It is important to realize that a mammographic abnormality that corresponds to a palpable lesion may be a separate lesion that is not associated with the discharge. It may need a separate work-up and referral to a breast specialist.

NOTE 4D: Clinical re-evaluation of a woman with a BI-RADS® category 1 or 2 is recommended at 3 months and is intended to assure that the nipple discharge has resolved.

Footer:

*Diagnostic Imaging Evaluation should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

BREAST SKIN CHANGES/NIPPLE RETRACTION ~ ALGORITHM 5

A thorough history and CBE are important in the assessment of the patient who presents with skin changes (e.g. inflammation, scaling) or skin/nipple retraction.

Introduction to the work-up of Breast Skin Changes/Nipple Retraction ~ Algorithm 5

A thorough history and CBE are important in the assessment of the patient who presents with skin changes (e.g. inflammation, scaling) or skin/nipple retraction. Important questions to consider include:

- How long has the change been present?
- Is there an associated palpable mass or mammographic abnormality?
- Is it a unilateral finding?

Timing of onset of nipple retraction is of paramount importance; congenital nipple inversion is insignificant, whereas recent nipple retraction has more serious implications. Unilateral nipple retraction, even slight, is also more suspicious than bilateral nipple inversion.

Skin changes that may signify carcinoma include skin erythema, retraction, dimpling, nipple excoriation or crustiness. Asymmetry of the breasts that indicate a recent change should be noted along with other findings, particularly any masses. Inflammatory breast cancer (IBC) symptoms include diffuse erythema, edema involving more than two-thirds of the breast, peau d'orange, tenderness, induration, warmth, enlargement of the breast, and diffuseness (or absence) of a tumor on palpation (Cristofamilli, 2004).

Signs of inflammation can be treated with a 10-day course of antibiotics that cover aerobic and anaerobic skin bacteria (typical of those in the mouth and vagina), but if not completely (100%) resolved, inflammatory carcinoma must be suspected and diagnostic imaging is required. A possible treatment regimen could be cephalexin plus metronidazole. Nipple retraction can be managed in the case of suspected periductal mastitis or deep tissue infections. A lack of a complete (100%) response requires further diagnostic imaging work-up.

There are many dermatologic causes of red, oozing and crusted nipples, including psoriasis, seborrheic dermatitis, contact dermatitis, neurodermatitis and atopic dermatitis. Eczema can be localized or can involve the complete nipple-areolar complex and must be distinguished from the non-eczematous conditions of Paget's disease of the nipple. Because Paget's disease is a very serious but commonly missed diagnosis, a thorough history and physical examination are important for every patient who presents with skin and/or nipple changes of the breast. Paget's disease comprises 1-3% of all primary breast cancers (Marcus, 2004). Paget's disease is manifested by progressive eczematoid changes of the areola with persistent soreness or itching (Lev-Schelouch, 2003). A mass is often associated with Paget's disease (NCI, 2002) and those patients with a palpable mass have a worse survival rate than do patients with a nonpalpable mass (Fu, 2001).

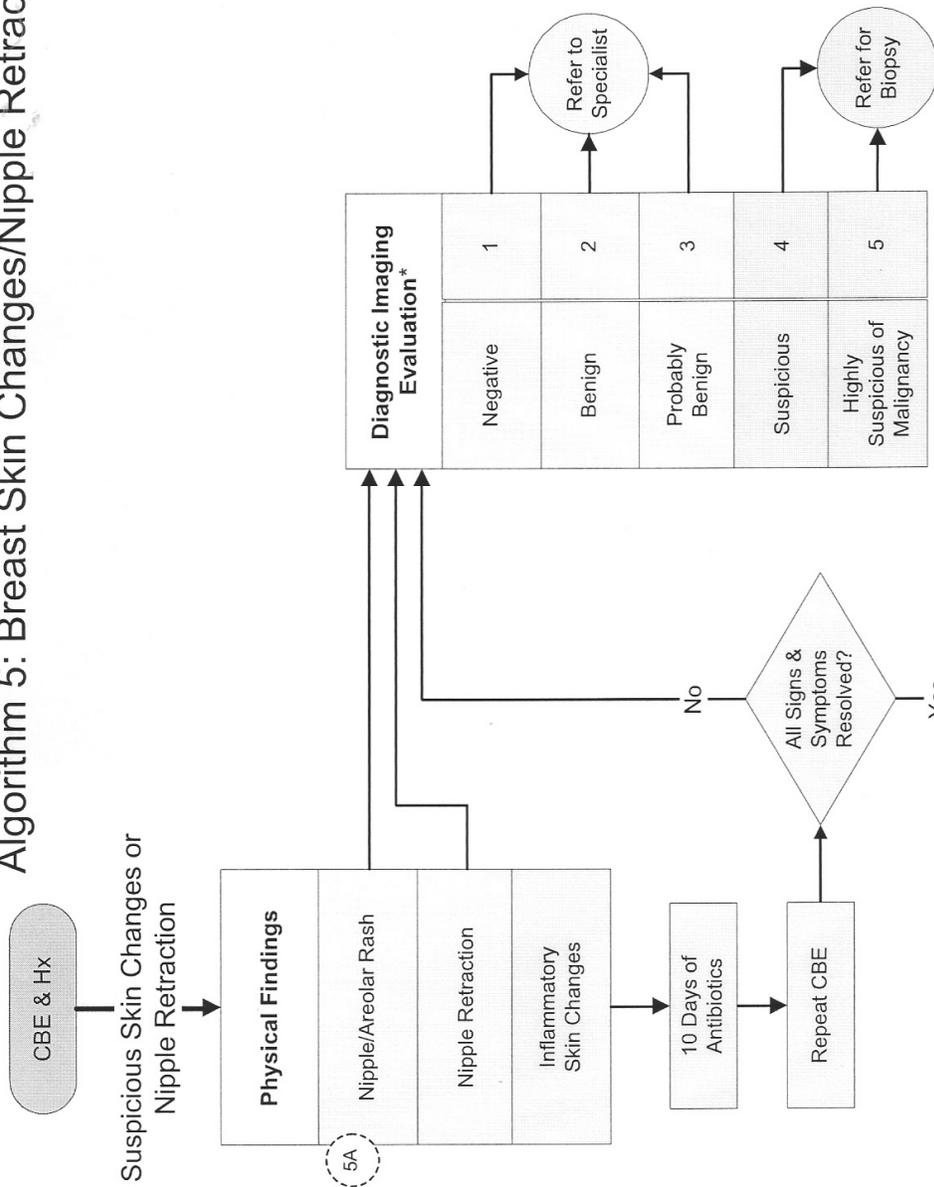
Eczema	Paget's Disease of the Nipple
Usually bilateral	Unilateral
Intermittent history with rapid evolution	Continuous history with slow progression
Moist	Moist or dry
Indefinite edge	Irregular but definite edge
Nipple may be spared	Nipple always involved and disappears in advanced cases
Itching common	Itching common

From Hughes LE et al. *Benign Disorders and Diseases of the Breast: Concepts and Clinical Management*. London, Ballière Tindell, 1989.

Despite some of these clinical differences, it is important to consider Paget's disease until proven otherwise. Nipple scaling may respond to a short course of topical steroids, but a follow-up appointment is critical to assess responsiveness. Sometimes Paget's will transiently respond to steroid cream, so if used, follow-up exam is required. Paget's disease with a palpable breast mass is likely to be accompanied by an invasive ductal carcinoma and has a poor prognosis (Sun Q, 2003).

Diagnostic imaging is the first line investigation when there are skin or nipple changes, even if no mass is palpable on CBE. However, a negative diagnostic imaging work-up for a clinical abnormality of the breast must not preclude referral to a breast specialist. Patients with any nipple complaint require further evaluation.

Algorithm 5: Breast Skin Changes/Nipple Retraction



* **Diagnostic Imaging Evaluation** should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.



Flowchart Notes and Footer

NOTE 5A: There is some controversy over the use of a topical steroid cream for nipple symptoms indicative of Paget's disease. Some surgeons now advocate referral for examination and possible biopsy prior to any use of steroid cream.

Footer:

*Diagnostic Imaging Evaluation should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

BREAST PAIN IN A NON-LACTATING WOMAN ~ ALGORITHM 6

- Mastalgia (breast pain) is the most common breast-related complaint at both primary care clinics and breast referral centers.

Introduction to the work-up of Breast Pain in a Non-Lactating Woman ~ Algorithm 6

Mastalgia (breast pain) is the most common breast-related complaint at both primary care clinics and breast referral centers. Most of these complaints are cyclic in nature. Cyclic pain usually is normal in menstruating women or in postmenopausal women on hormone replacement therapy. Fibrocystic changes represent the most common cause of cyclic breast pain and symptoms are typically bilateral and described as diffuse, dull, full, achy, and heavy.

Non-cyclic causes include a ruptured cyst, a non-ruptured cyst under tension, fat necrosis, cervical radiculitis, intercostal neuritis, shingles, Tietze's Syndrome (costochondritis), mastitis/abscess, Mondor's disease, trauma, post-radiation syndrome and **rarely** cancer. Non-cyclic pain tends to be unilateral and described as localized, sharp, throbbing, stabbing, or burning.

The differential diagnosis of breast pain requires a CBE and careful assessment:

- Is it cyclic or non-cyclic?
- Is it bilateral or unilateral?
- Is the pain diffuse or focal?
- Is it associated with a mass?
- Is hormone replacement therapy ongoing?
- Is there a history of trauma?

Non-cyclic pain is initially investigated with a diagnostic imaging evaluation. If the patient is a young woman, an ultrasound may be the preferred imaging modality. Additional follow-up depends on the diagnostic imaging final assessment category. The risk of most cancer after a negative clinical and imaging evaluation for breast pain is less than 1% (ICSI, 2003).

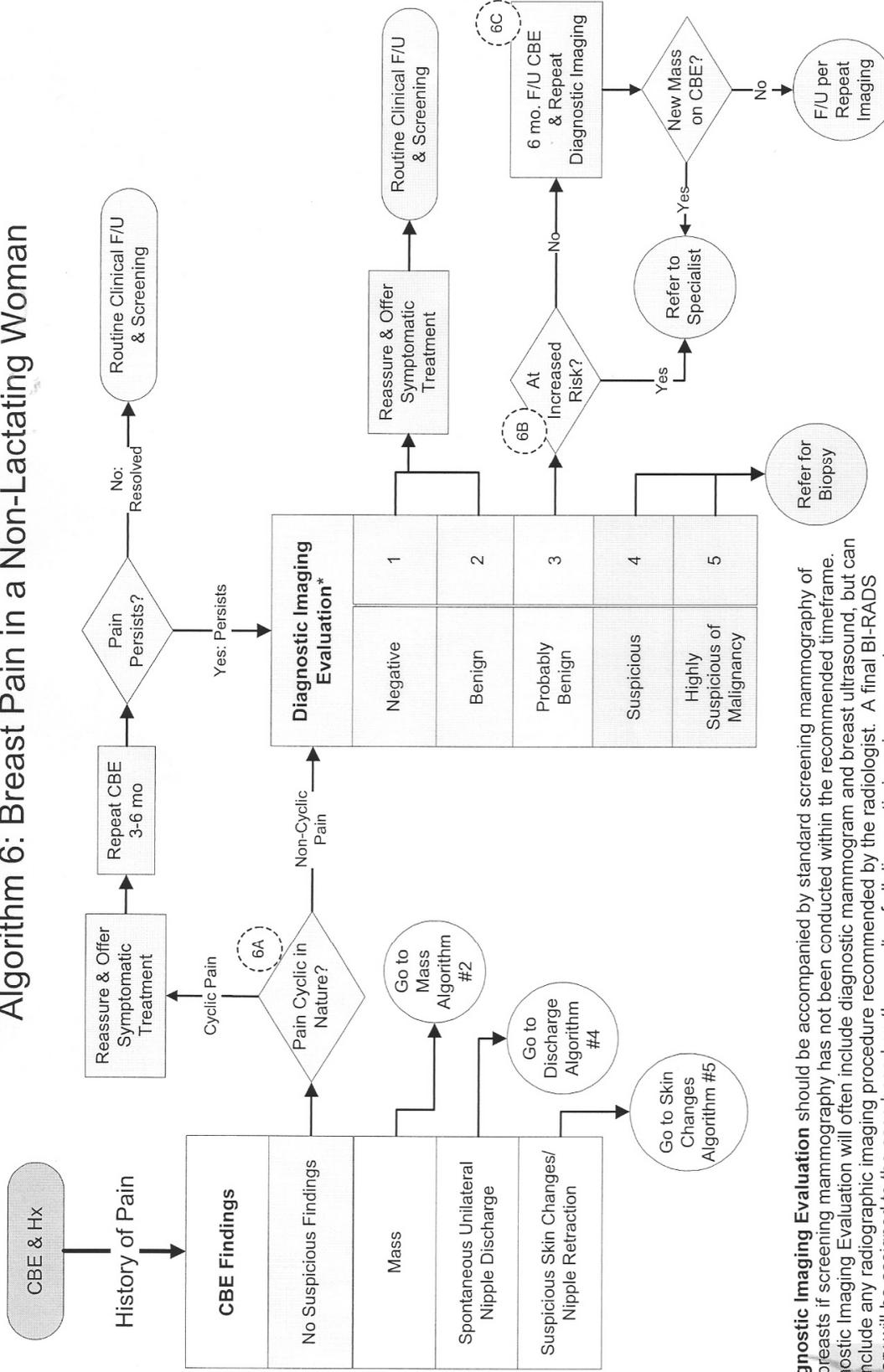
Mastalgia is reported by up to 15% of women diagnosed with breast cancer, and 7% present with pain alone (Morrow, 2000). Therefore, a diagnosis of cancer must be considered in patients with well-localized breast pain of recent onset. The pain associated with breast cancer is often unilateral, persistent, and constant in position.

If there are changes consistent with mastitis such as erythema, fever >102 degrees, skin tenderness, abscess, or pus expressed from the nipple, refer to Algorithm #5 on skin changes/nipple retraction.

Although this algorithm addresses the non-lactating woman, a similar work-up of breast pain in the lactating woman is recommended. However, the lactating woman may need referral to a breast specialist.

For most women presenting with breast pain, treatment consists of relieving symptoms and reassuring the patient that there is no underlying carcinoma or other serious disorder. Non-narcotic analgesics and supportive bras may be helpful. Some women may find relief by using oil of primrose (3 grams a day). Elimination of caffeine, chocolate or salt from the diet has not been scientifically proven to be beneficial. The etiology of breast pain remains unclear, and no satisfactory treatment exists for some women (Khan, 2002).

Algorithm 6: Breast Pain in a Non-Lactating Woman



* **Diagnostic Imaging Evaluation** should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

Flowchart Notes and Footer

NOTE 6A: Distinguish between cyclic and non-cyclic breast pain. Cyclic pain is typically bilateral and described as diffuse, dull, full, achy, and heavy. Non-cyclic pain tends to be unilateral and described as localized, sharp, throbbing, stabbing, and burning.

NOTE 6B: As with other algorithms, a BI-RADS® category 3 result requires a differential assessment of risk. See Algorithm #1, Risk Assessment, to determine if the patient is at increased risk for breast cancer. If so, refer to a breast specialist.

NOTE 6C: For BI-RADS® category 3, the vast majority of findings will be managed with an initial short-term follow-up imaging examination in 3-6 months, followed by additional examinations until stability is demonstrated (2 years or longer). There may be occasions where biopsy is done (i.e. patient request or clinical concerns). Evidence from all the published studies indicates the need for biopsy of a lesion that increases in size or undergoes morphologic change (ACR, 2003).

Footer:

*Diagnostic Imaging Evaluation should be accompanied by standard screening mammography of both breasts if screening mammography has not been conducted within the recommended timeframe. Diagnostic Imaging Evaluation will often include diagnostic mammogram and breast ultrasound, but can also include any radiographic imaging procedure recommended by the radiologist. A final BI-RADS category will be assigned to the case based on the results of all diagnostic imaging procedures. Women should return to routine screening once the diagnostic and/or treatment cycle is completed.

MANAGEMENT OF BREAST BIOPSY RESULTS ~ ALGORITHM 7

- Definitive diagnosis of a breast mass can only be established through fine needle aspiration biopsy (FNAB), core needle biopsy, or excisional biopsy. Most experts agree that if a mass persists for three months, a sampling of the lesion is warranted.

Introduction to the Management of Breast Biopsy Results ~ Algorithm 7

Definitive diagnosis of a breast mass can only be established through fine needle aspiration biopsy (FNAB), core needle biopsy, or excisional biopsy. Most experts agree that if a mass persists for three months, a sampling of the lesion is warranted. Further delay in work-up is not prudent unless the diagnostic imaging evaluation shows a concordant benign lesion. Generally speaking, the best option depends on whether the mass is palpable, the availability of resources and expertise, the degree on CBE of suspected invasiveness and patient's demand for a rapid diagnosis.

The pathologic findings from a biopsy must fully explain the clinical and/or the imaging findings that prompted the biopsy ("triple test"). Clinical/ radiologic/ histologic discordance occurs when the CBE and/or imaging findings are not explained by the final pathology. When repeat imaging studies or clinical exam indicate that the original radiographic or clinical finding may not have been adequately sampled ("discordant triple test result"), further biopsy is needed. Clinical/radiologic/histologic discordance carries a rate of malignancy that can be as high as 40-50% (Morris, 2003). Therefore, if the results are discordant, or if the clinician is not sure, the patient must undergo further evaluation by a breast specialist. Various options are available for obtaining concordance. These include radiology consultation, repeat image-guided biopsy, or surgical consultation. For example, a woman with a palpable mass within 2 cm of visual nipple retraction and a pathology result of normal or fibrocystic change represents **discordance** between the clinical findings and the pathology report (regardless of the diagnostic imaging result). The patient needs a repeat biopsy.

Core Needle Biopsy

Core needle biopsy of the breast provides a solid cylinder(s) of tissue for histologic evaluation and when properly done in appropriately selected patients is a safe, well-tolerated and cost-effective alternative to surgical biopsy. Large core needle biopsy specimens do not require subspecialty pathologist expertise for histologic diagnosis. Core biopsy may also have a 7.6% (with a range of 3.3 to 22.2% depending on the gauge of needle employed) risk of false negative diagnosis which is chiefly due to sampling error. Sampling error is reduced with the use of larger gauge needles and by obtaining multiple core biopsy samples (Shah, 2003). When core biopsy yields a result that is discordant with the clinical or imaging impression, it is incumbent on the provider to pursue the situation with repeat core biopsy or surgical biopsy. Radiologic-guided core biopsy (see below) is useful in the evaluation of the palpable breast mass that is small, deep, mobile, vaguely palpable, or multiple (Lieberman, 2000). Core biopsy needle sizes may be 8, 11 or 14 gauge depending on operator preference, usually in a spring-loaded instrument, to extract several cores of tissue through a 3-5mm incision. Core biopsy is a sampling technique and is not intended to remove the lesion.

*Radiologically-Guided Percutaneous Core Biopsy ***

A nonpalpable mass detected via imaging study can be percutaneously biopsied by a **radiologist** or other physician with special skills using ultrasound or mammographic (stereotactic) guidance. Stereotactic core needle biopsy is performed using special mammographic apparatus. A core biopsy needle (either an automated spring-loaded or vacuum-assisted biopsy instrument) is inserted into the lesion. Multiple tissue samples are obtained. In most centers, large core needle biopsy is replacing open surgical biopsy for the diagnosis of nonpalpable mammographic lesions.

Pre-Operative Needle (or wire) Localization Biopsy

In pre-operative needle (or wire) localization biopsy a radiologist inserts a wire through a needle into the breast to mark nonpalpable lesions detected mammographically or by ultrasound. The wire guides the surgeon to the lesion for tissue removal during an excisional biopsy; hence it is a combined radiographic and surgical technique. Today, this technique is mainly therapeutic rather than diagnostic as the majority of breast lesions have had a prior diagnosis by a radiologically guided percutaneous biopsy. For nonpalpable abnormalities the localized biopsy has less than a 2% failure rate (Bassett, 2002).

Excisional Biopsy (Lumpectomy)

Surgical removal of a breast lesion is the gold standard against which all other diagnostic techniques are compared. Excisional biopsy surgically removes the entire lesion and should include a zone of normal tissue surrounding it. The procedure requires a sterile operating room setting and leaves a small (2-4 cm) scar.

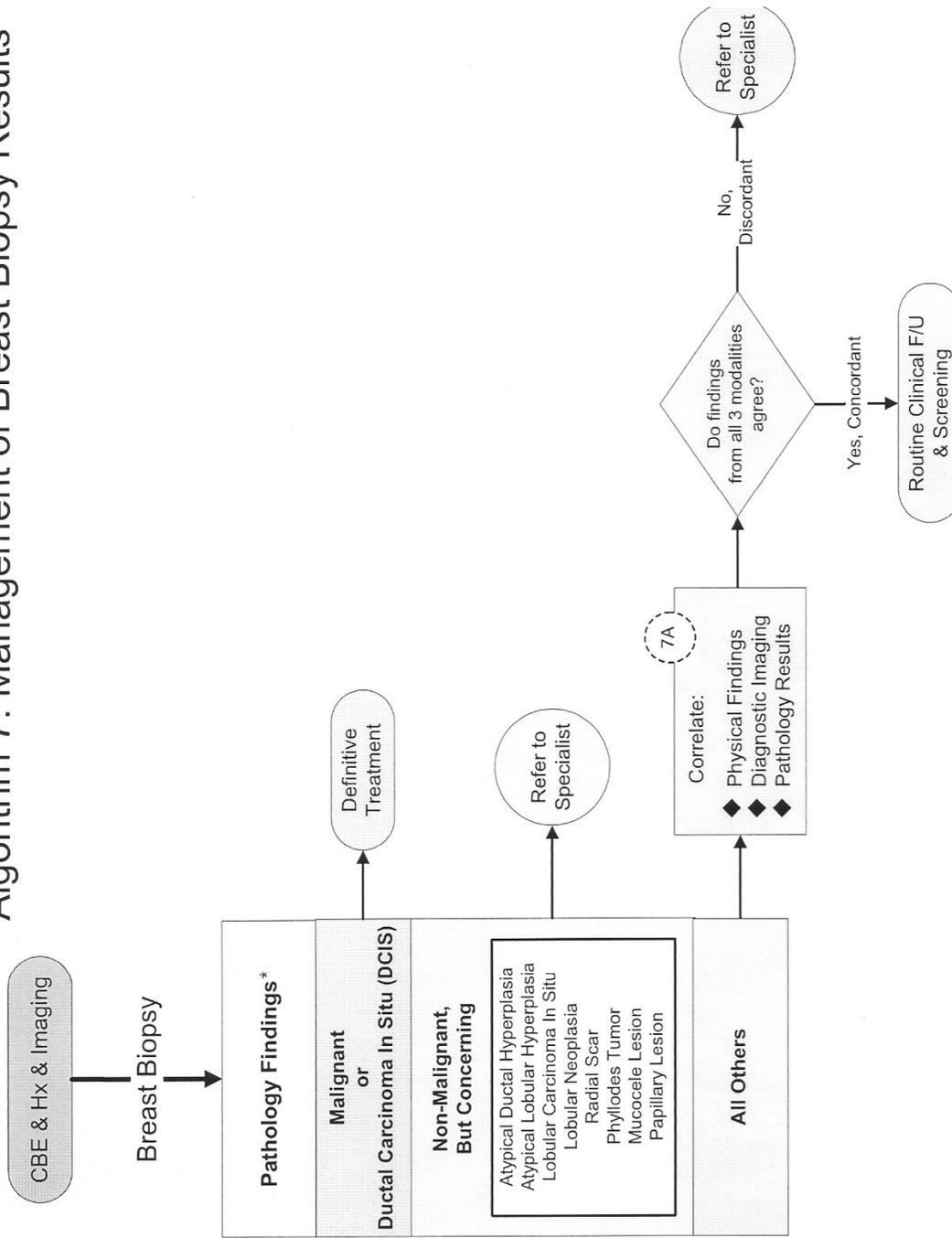
Fine Needle Aspiration Biopsy

FNA** biopsy is safe, accurate and better tolerated with less bleeding and infectious complications than either large core or surgical biopsy. However, it is a highly operator-dependent procedure, requires subspecialty expertise for interpretation, and cannot distinguish invasive from non-invasive disease. Compared to other biopsy methods, FNA biopsy has a higher rate of false negative results (chiefly due to sampling error) and suspicious results (chiefly due to interpretative challenges), (Salami, 1999; Shah, 2003). When FNAB yields a result that is discordant with the clinical or imaging impression, it is incumbent on the provider to pursue the situation with a different diagnostic procedure. The use of FNA biopsy may be limited since the special expertise required to perform and interpret this form of biopsy may not be available in all areas

*** Radiologically-Guided Percutaneous Core Biopsy ***

and Fine Needle Aspiration (FNA) could be done by the radiologist. The radiologist however needs to discuss the procedures, alternative and risk with the patient and the patient's primary care provider.

Algorithm 7: Management of Breast Biopsy Results



* Definitions of pathologic terms can be found in Appendix A-5: Glossary of Terms.

Flowchart Notes

NOTE 7A: If physical findings and/or diagnostic imaging results are suspicious for a malignancy then a "negative" biopsy must be considered "discordant" and may represent a false negative result. The patient should be referred to a breast specialist for further evaluation.

Footer:

*Definitions of pathologic terms can be found in Appendix A-5: Glossary of Terms

Digital Mammography

Reimbursement for digital mammography is capped at the conventional film mammography reimbursement rate.

Computer-Aided Detection (CAD)

Reimbursement of CAD is not permitted.

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