Biopsy Techniques in Non-palpable or Palpable Breast Lesions

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William C. Dooley

Abstract

Diagnostic breast biopsy is one of the most common medical procedures, and a variety of methods have been developed in the last 30 years to augment classic surgical incisional and excisional biopsies. Fine-needle aspiration (FNA) has an important historical role and remains among the most cost-effective methods but is limited by the weakness of current breast cytology to adequately reproduce all information provided by traditional histopathology. FNA continues to play an important role in assessing risk. Core biopsies ranging from the use of simple needle cores to larger coring devices to remove spaghetti- to macaroni-sized pieces have become the mainstay of current biopsy techniques for most palpable and non-palpable lesions. Surgical incisional and excisional biopsies, which are the classic standards, are reserved for a few exceptional circumstances, including the removal of symptomatic benign lesions or when coring biopsy tools fail to provide adequate diagnostic information and material. Ductoscopy, which was initially developed as a tool to investigate pathological nipple discharge, is an evolving technology that may have an increasing role in research and prevention as tools and techniques become more refined. Failure of biopsy to accurately diagnose breast problem remains a small but persistent problem requiring the diligent methodical use of biopsy methods and the careful consideration of issues such as sample bias when the entire lesion is not removed and there is discordance between clinical expectations and biopsy pathology.

Keywords

Breast biopsy • Breast cancer • Core biopsy • FNA • Surgical breast biopsy • Breast cytology • Ductoscopy • Mammoscopy • Breast diagnosis

W.C. Dooley, MD, FACS
Department of Surgery and OU Breast Institute,
The University of Oklahoma Health Sciences Center,
G. Rainey Williams Pavilion, Suite 2290, 920 Stanton
L. Young Blvd., Oklahoma City, OK 73103, USA
e-mail: william-dooley@ouhsc.edu

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Fine-Needle Aspiration Biopsy–Core Needle Biopsy

Fine-Needle Aspiration (FNA) Biopsy

Fine-needle aspiration has a long history in breast cancer diagnosis. It has been popularized as a part of the "triple test" for the evaluation of palpable abnormalities preceding the modern mammographic screening era [1]. FNA is a common tool in many European clinics where breast cytology is a more refined and practiced art. One of the inherent weaknesses of breast cytology is the substantial overlap in cytological appearance of many very early lesions and malignant, premalignant, and common benign lesions [2]. Further, if cancerous cells are observed, FNA cannot be used alone with cytology to definitively determine if the lesion is in situ or invasive [3, 4]. These critical issues have limited its use in the USA in favor of coring needle techniques. Globally, however, FNA remains a cost-effective tool with much value and efficiency.

FNA is typically performed to evaluate palpable abnormalities and asymmetric breast tissue in a perceived high-risk situation, to screen high-risk patients for biological markers indicative of current active proliferation to evaluate temporal breast cancer risk, or to monitor trials of prevention agents. FNA is typically performed with a 22–25 G needle on a 10 cc syringe. Local anesthesia is induced by dermal injection and installation into the region of biopsy. Rigorous rapid jiggling of the biopsy needle in and out under vacuum and releasing the vacuum before extracting the needle provides the best specimen and can be rapidly mastered by the immediate evaluation of specimen cellularity by the operator (Fig. 1.1). Initially, air-dried smears were prepared, but increasingly, the aspirate material is injected into a liquid transport fixative such as those used for cervical cytology. The cellular architecture is often less disrupted in liquid media [5]. Occasionally, the pH of the local anesthesia may impact the cellular appearance. This can be minimized by buffering the initial local anesthetic immediately prior to injection. The specimens can be adequate for routine cytology, immunohistochemistry, and molecular techniques in both clinical and research settings. Usually, FNA results are considered highly specific but variably sensitive.

The use of FNA for non-palpable abnormalities is more complex. When aspirating under image guidance, there is a slightly increased risk of parallax issues in which the aspiration is immediately in front or behind the target lesion. Because this leads to insufficient removal of the target for image confirmation, much hope is placed on the initial accuracy of the first few

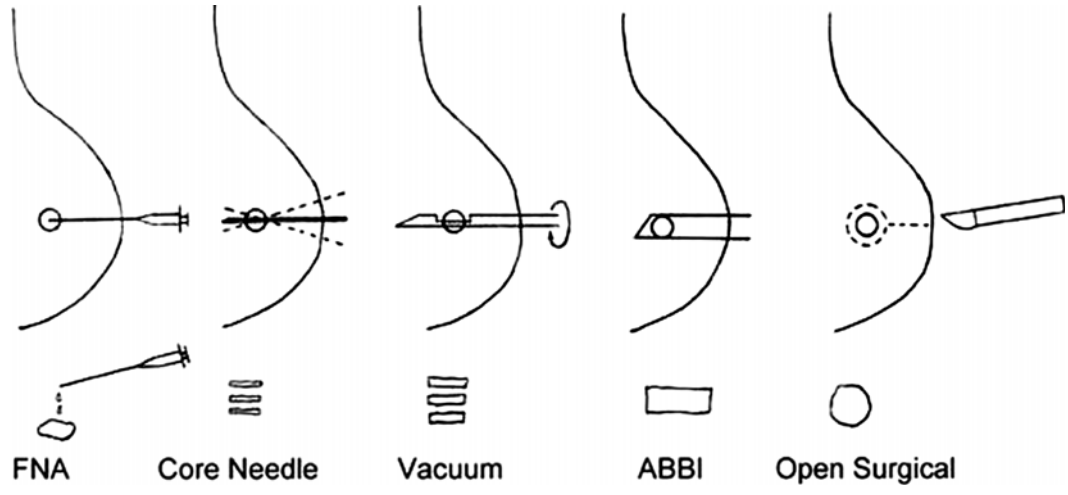

Fig. 1.1 Different types of biopsies (Reproduced with kind permission from Imaginis, Copyright 2000, Imaginis.com)

needle passes. The local anesthesia and hematoma from the biopsy typically rapidly interfere with imaging quality as the FNA continues. The results for non-palpable lesions are always confounded by these issues.

The most important use of FNA remains as a part of the triple test [1]. This technique has stood the test of time as highly reliable predating mammographic screening through the current plethora of new imaging technologies to evaluate palpable breast lesions. Most palpable breast lesions will have imageable lesions, which are then amenable to coring biopsy techniques. However, there are always some patients with odd asymmetric thickening, regionally focused reproducibility, worrisome history, or other factors that make the breast clinician suspicious of a significant abnormality in spite of negative breast imaging [6]. In this situation, the use of FNA as the third and final arm of a triple test is well justified by the medical literature and is considered highly accurate. Under this circumstance, the goal of screening is to confirm the presence or absence of significant glandular proliferation. If proliferative cells are not observed in an adequate cellular specimen, the probability of breast cancer is exceedingly low. If, however, proliferative ductal epithelial cells are observed, open surgical biopsy of the region is required to exclude an image-occult neoplastic change.

Core Needle Biopsy

Core needle biopsies were developed as a limited method of performing an incisional biopsy for diagnosis. Early coring needle technologies were cumbersome and were often used primarily for tiny biopsies of solid organs, such as the liver and kidney. In the late 1980s, the technology improved substantially with the introduction of automated coring needles. These needles typically cored 14 G, 16 G, or 18 G samples approximately 1–2 cm in length [7]. With improving mammographic imaging and increased facility with breast ultrasound, these new coring needles were applied to breast diagnostic work in the early 1990s. A series of trials demonstrated that these mini incisional biopsies by needle under image guidance could accurately diagnose many breast lesions. Because of the small diameter and rapid fixation of these biopsies, the time from biopsy to diagnosis began to decrease rapidly [8]. Establishing the diagnosis prior to the initial surgical procedure dramatically improved the chances of obtaining surgically clear margins during the initial operation and expanded the use of breast conservation dramatically. This was a crucial event in the evolution of the diagnostic process for breast cancer [9, 10].

Core biopsy methods vary slightly in specific needle design and the imaging used to direct the biopsy. As the popularity of core biopsy has increased, this method is now used not only for non-palpable lesions but also for palpable lesions combined with imaging to ensure biopsy of the center of the target lesion. After pressing a button or trigger, each of the coring needles usually throws out a coring section up to 2 cm in length and then rapidly covers the entire coring section and tissue core with a larger hollow needle of the final core size. This basic mechanism underlies many of the shortcomings of this method. The rapid-fire mechanism can allow a hard lesion in the midst of soft breast tissue to bounce off, and thus, the core will be of the tissue side of the target and not the target itself. Similarly, the cores are relatively small in the imaged lesions, and imaging is usually inadequate to visualize the actual hole or tract after needle removal. This introduces two possibilities: that the target bounced off the needle or that the parallax issues of imaging led to a false assurance of central target biopsy. A single core in the center of the target should be histologically adequate for nearly all lesions except borderline atypia vs. in situ disease. Clearly, early experience demonstrated that one core was not adequate, and multiple cores are now obtained to reduce the possibility of underdiagnosis due to sampling bias [11–13]. Based on specific histologies and imaging characteristics, 4–15 cores to assure an adequate diagnosis are common [14] (Figs. 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 1.10, 1.11, and 1.12). However, when substantial proliferative changes, such as atypia and papillary changes,

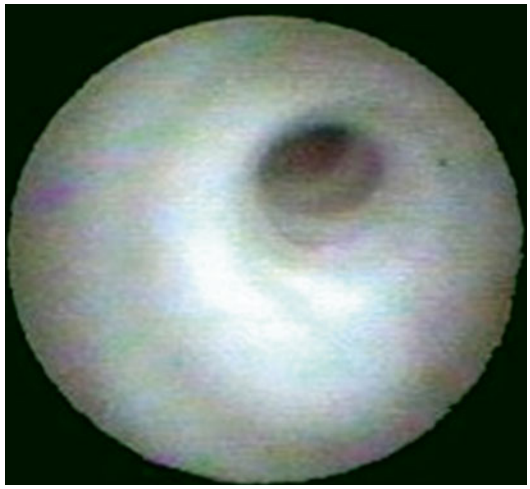

Fig. 1.2 Clean duct

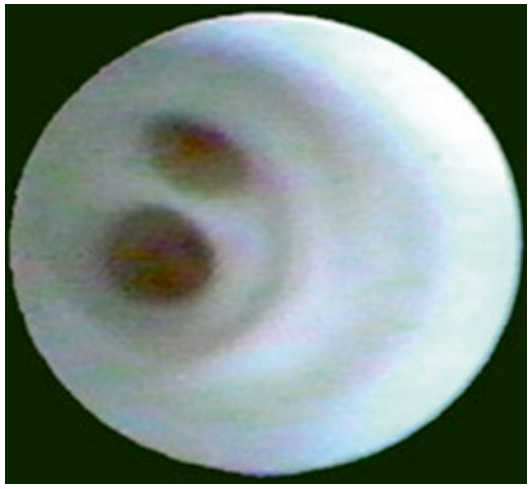

Fig. 1.3 Bifurcation

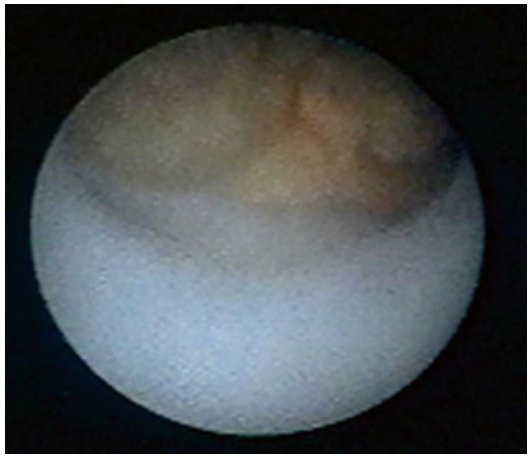

Fig. 1.4 Papilloma

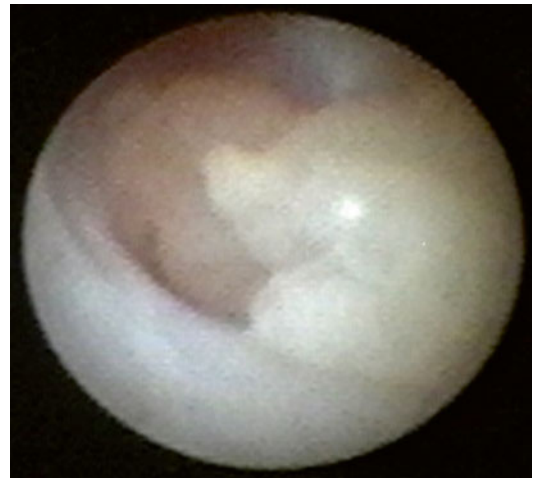

Fig. 1.5 Papillomas

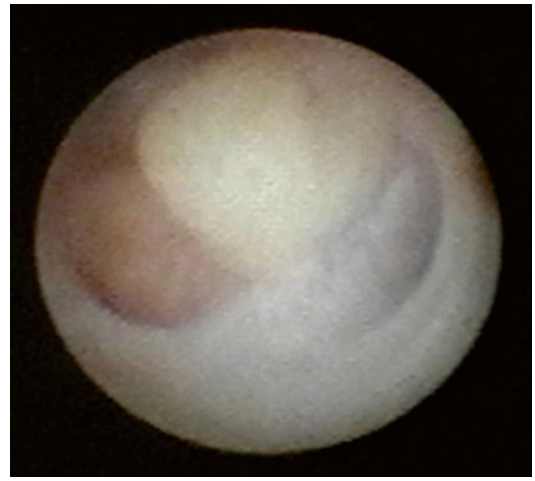

Fig. 1.6 Papillomas

Fig. 1.7 DCIS

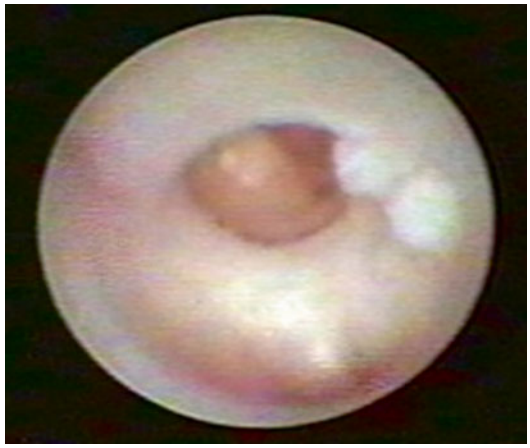

Fig. 1.8 Low-grade DCIS

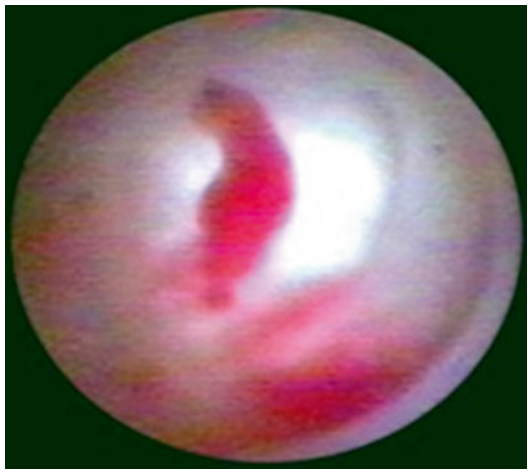

Fig. 1.9 High-grade DCIS

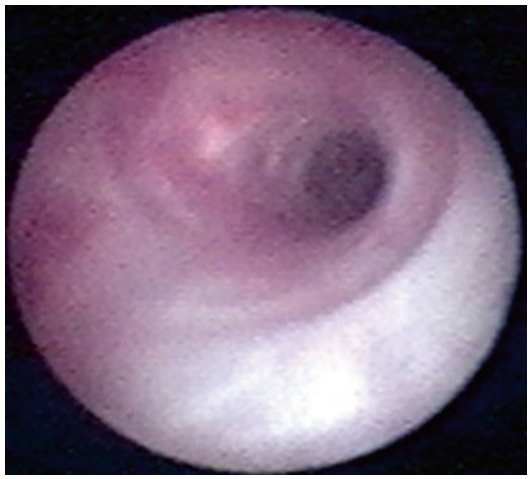

Fig. 1.10 DCIS

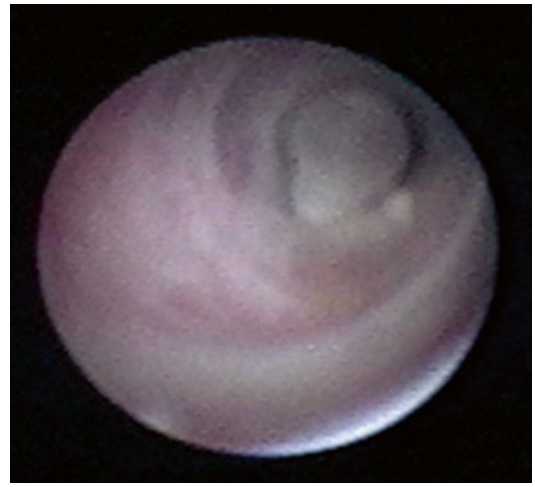

Fig. 1.11 DCIS

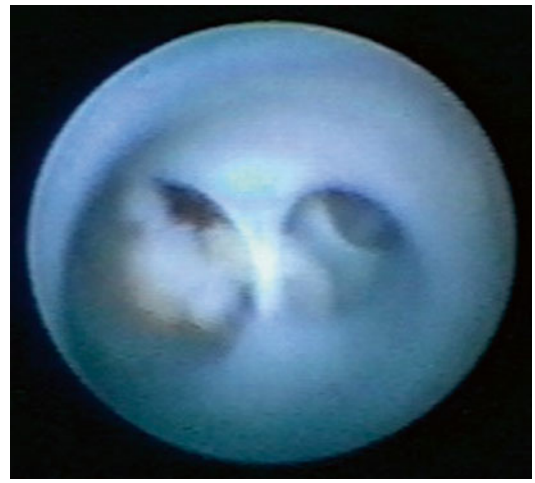

Fig. 1.12 High-grade DCIS

are observed, the core diagnosis is not reliable and requires open surgical excisional biopsy.

Core biopsy needles today are usually used in larger and advanced tumors where issues of sample bias are markedly diminished. Their importance in the evolution of modern breast diagnostic biopsy cannot, however, be understated. Reducing the number of breast cancers diagnosed by surgical biopsy has dramatically increased successful breast conservation and revolutionized the last two decades of breast cancer care in North America and Europe [15].

Vacuum-Assisted Breast Biopsy, Rotating Core Biopsy, and Radiofrequency Minimal Access Incisional Biopsy

The problem of throwing cores limited the safe use of older core needles to the axilla close to vessels or close to the chest wall. A new generation of coring devices have been developed to address the movement of the coring needle during biopsy to allow visualization of the biopsy in real time and increase the volume of tissue removed, thereby reducing the number of cores required to make a diagnosis and increasing the percentage of cores with actual pieces of the target lesion [12] (Fig. 1.12). The first versions were 10 G or larger solid-appearing needles inserted into the breast. Once inserted into or beside the target lesion, a trap door opens, allowing suction to be applied to pull tissue into the center of the needle. A rotating core inside the needle is then deployed to remove a larger core of tissue. Most of these needles allow the outer needle shaft to be left in place as cores are pulled out and new cores are taken. Reduced movement of the coring needle clearly reduces issues of biopsy pain but also allows sufficient excision of tissue in one location to confirm the adequacy of sampling by imaging before needle withdrawal.

This technique works well, but some of the hardest lesions within the softest breast tissue still cannot be sucked into the vacuum section of the needle. Alternatives, such as the insertion of a 19 G cold core needle into the lesion, followed by freezing of the lesion with liquid CO_2 and removal of a larger rotating core around the central needle within the ice ball, enable the biopsy of even the hardest lesions. Another approach to small hard lesions is to use radiofrequency (cautery) with an excision device introduced thru a large needle with a hole 5–8 mm in diameter. Rings of RF wire are deployed from the tip of such devices and under image control can be used to excise pieces of tissue up to 2 cm in diameter. Such techniques approach minimal access surgical incisional biopsy. Early enthusiasts believed that surgical lumpectomy might be accomplished on small subcentimeter lesions; success of this type has been limited, which likely reflects the joint technical limitations of the RF devices and real-time imaging in 3-D during the biopsy.

These techniques have dramatically reduced the number of cores required for diagnostic accuracy. However, more than one core is still required in the majority of cases, and when there is histological atypia or worrisome changes, wide excision of the region surgically is required to prevent missed cancers. All of these techniques can be performed stereotactically with mammography or MRI. Because of their complexity and logistical setup issues and positioning, using mammography or MRI extends the duration of each biopsy procedure to 40–60 min, with multiple staff to support the equipment and patient needs. As ultrasound imaging has improved, the majority of image non-palpable lesions can be observed sufficiently well to direct one of these coring techniques without difficult patient positioning and minimal additional staff. The vast majority of breast biopsies today of palpable or non-palpable lesions are ultrasound-directed and continuously imaged vacuum core biopsies. Although small lesions less than 1 cm may be completely removed, imaging cannot be used to adequately predict which patients have received adequate histological excision without actually examining the exterior margin of an intact en bloc resection or its equivalent.

Surgical Biopsy: Incisional Biopsy–Excisional Biopsy

Excisional surgical biopsy of palpable or non-palpable image-visible lesions will always be considered the gold standard. Even when surgical excision occurs, the missed cancer rate is approximately 2 % or 1/50. Because breast biopsy is one of the most common medical procedures, this rate translates into many missed cancers. Even when the palpable lesion is obvious or the image lesion is clearly observed in specimen radiography, it is always necessary to ensure all potential abnormal targets are identified. In the case of palpable lesions, this requires adequate pre- and

postoperative imaging to ensure any allied lesions are removed and never assuming that the imaged lesion is the palpable lesion without adequate proof. In the case of imaged lesions, the surgeon must carefully bimanually palpate the surrounding breast tissue to ensure all abnormalities have been identified. Similarly, postoperative imaging within 6 months or sooner revealing no additional lesions or residual lesions is needed.

Surgical incisional biopsy has been commonly used for more than a century for the diagnosis of large breast lesions and lesions that involve the skin [15]. Coring tools can often replace formal open surgical biopsies. There are circumstances in which incisions are still required, such as a mass coexistent with an abscess for which diagnostic biopsy can be accomplished by incision of the wall of the abscess during abscess drainage. Inflammatory breast cancer is a clinical diagnosis, but it is occasionally useful for clinical practice or research stratification to determine the involvement of dermal lymphatics. Such involvement was typically determined with an incision in a small region of inflamed skin. Today, 3–5-mm dermal punch core biopsy tools allow a "needle-like" approach to these diagnostic biopsies. Because a smaller sample is taken, sample bias is introduced, as with needle core biopsies. The region most likely to have dermal lymphatic involvement is the skin at the areolar edge in the same quadrant as the inflammatory lesion. Small core biopsies in this region can avoid the removal of skin requiring suturing required in older times. Similarly, these same dermal cores can be used to assess lesions of the nipple papilla for both Paget's disease and nipple adenomas.

Surgical excisional biopsy can be directed by palpation or use of an imaging adjunct. Ultrasound provides an almost direct extension of physical exam and can often localize well the majority of non-palpable abnormalities. For years, the ultrasound equipment available in imaging suites has had much greater resolution than those available in operating rooms. As more surgeons become adequately trained to use ultrasound equipment, intraoperative imaging with the highest quality devices has transformed breast surgery and especially added to our ability to achieve adequate margins during the initial therapeutic operation. When the target lesion is not clearly visible by ultrasound or palpable, we must resort to some marking of the target region that can be used by the surgeon because excision between plates of a mammogram device or in the magnet of an MRI is difficult. The core biopsy world has introduced a series of markers to leave behind for future imaging post biopsy. Any of these markers can be used in this circumstance, the most useful of which are ultrasound-visible post-core markers that can be intraoperatively imaged with ultrasound during the surgical procedure. The classic method, however, has been to deploy a wire, needle, and/or dye injection into the target region under image guidance for the surgeon to use to find the lesion in question. In the case of malignant core biopsies, this has even evolved into leaving a small radioactive bead in the biopsy cavity to guide later wide excision lumpectomy. Whichever method is used, imaging the extracted tissue or the residual breast immediately post-procedure is the best but not an absolutely infallible method to assure the excision of the correct tissue target. The most efficient method is to either ultrasound the specimen or radiograph the specimen in the operating room. Using this immediate image information, the surgeon can most likely identify and remove the target lesion even if the first specimen was inadequate.

Ductoscopy

Mammary ductoscopy has evolved from initial experimentation in Japan, where pathological nipple discharge is a more common symptom of early-stage breast cancer [16]. American innovations in submillimeter endoscopes and the recognition of the safety and improved endoscopic potential when saline distension is used have prompted new interest in this technique to identify some of the earliest lesions in situ long before traditional imaging would allow detection. It is now possible to find nearly all lesions intraductally that give rise to bloody nipple discharge, atypical cells in nipple fluid, or extensive intraductal carcinoma around small early-stage breast

cancers [17–22]. Biopsy tools and scope modifications that can allow biopsy under direct vision are being developed. Currently, clinically clear indications are relatively restricted. However, researchers now have a method that will repeatedly allow access to the ductal epithelium in high-risk patients. As molecular markers begin to replace traditional cytology, which has limitations as discussed before with FNA, we can expect anatomic mapping of the field defects of genetic changes that predispose to cancer and a crucial new understanding of how anatomy and molecular events interact in breast carcinogenesis [23–28]. These new understandings will hopefully shape the future of breast cancer prevention, which is beginning to replace our current standards of screening and treatment.

The most common indication for mammary ductoscopy is solitary duct spontaneous bloody nipple discharge. Occasionally, high-risk women produce abundant nipple fluid. Some prior research trials have indicated that there is increased risk if a non-lactating female is easily producing fluid [26, 29, 30]. If these high-risk women have nipple fluid cytology that is suspicious, this may appear sinister even in the absence of any imaging findings. The ducts that are producing fluid are usually quite large and can be easily cannulated with lachrymal duct probes and/or sutured with 22–24 G angiocaths. First, the duct is anesthetized and dilated by topical local anesthesia distention. Ductoscopy is readily performed with any available submillimeter endoscope. Most series of pathological nipple discharge reveal that 7–9 % are related to cancer [18, 19, 30].

Many stage 0–2 breast cancers (particularly if the invasive component is <2.5 cm) will have expressible nipple fluid [16, 28]. These ducts may produce less fluid, but if identified, can usually be used to locate the cancer and its allied proliferative changes in the region. Core biopsies performed on the nipple side of the target lesion usually disrupt the ducts making fluid, so if ductoscopy is of interest, it is important that diagnostic biopsies be performed from the deep non-nipple side of the target lesion. With some practice, ductoscopy at the time of therapeutic lumpectomy can be an important adjunct to achieving clear margins and can theoretically aid the selection of patients with limited region disease that may be ideal for partial-breast irradiation techniques.

Final Considerations

It is important to remember the 2 % miss rate of diagnostic breast biopsy in the USA. No biopsy procedure should be considered complete without a metachronous physical exam and repeat imaging after healing of the biopsy procedure. These procedures are usually performed after 6 months, and scientific data suggest that there is no decrease in survival if missed lesions are identified and removed within that initial 6-month period. This is of most crucial importance in image-guided non-palpable lesion biopsies. Any smaller incisional technique that yields pathological information that is unexpected or discordant with clinical expectations requires immediate confirmation by surgical excisional biopsy. Any surgical excision that does not clearly contain the lesion on specimen radiograph is difficult to resolve. Immediate postoperative (within the first month) imaging can be used, but edema and healing changes may substantially interfere with accurate target detection. If the pathology is concordant in these cases, 6-month imaging and exam follow-up seem prudent.

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