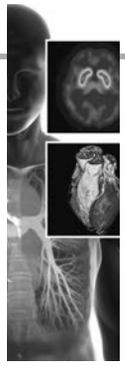

Image-guided percutaneous breast biopsies

Diagnosis of breast cancer at its earliest stage affords women the best prognosis. The role of the breast imager has evolved from cancer screening and detection to now include diagnosis and management with the widespread adoption of image-guided core biopsy. This article will briefly discuss the current image-guided biopsy techniques for the diagnosis of suspicious breast findings, specifically, stereotactic, ultrasound and MR-guided, and the evidence in the literature emphasizing proven efficacy for each. For those lesions which cannot undergo percutaneous biopsy, this report will also discuss the use of marker placement at the time of wire localization and excision for ensuring and verifying biopsy of the appropriate lesion.

KEYWORDS: biopsy ▪ breast ▪ breast cancer ▪ breast MRI ▪ false-negative ▪ stereotactic ▪ ultrasound ▪ vacuum-assisted

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An estimated 1.6 million breast biopsies are performed in the USA every year. In two studies auditing utilization practices for minimally invasive breast biopsies as the initial diagnostic procedure, it was found that approximately 30–40% of initial breast biopsies performed are actually open surgical biopsies. [1,2]. However, the accuracy of image-guided percutaneous needle or core biopsy is equivalent to open surgical biopsy, and expert opinion states that percutaneous core biopsy should essentially replace open surgical biopsy as the first diagnostic procedure for breast abnormalities [3]. The role of the breast imager has evolved from cancer screening and detection to now include diagnosis and management with the widespread adoption of image-guided core biopsy, primarily by stereotactic guidance or ultrasound (US) guidance, with 95% of percutaneous breast biopsies in the USA performed by radiologists [4].

A major benefit of image-guided percutaneous breast biopsy as the initial procedure, is the ability to establish a benign diagnosis in most cases, and the avoidance of an open surgical procedure. The overall cost of diagnosis is decreased, as well as morbidity. Less than 1% of percutaneous core biopsies are affected by severe complications, compared to 2–10% of open surgical procedures [5]. If the result is malignant, the percutaneous biopsy permits preoperative staging, acquisition of histologic and biomarker data, consultation with appropriate specialists, and planning for surgical resection and axillary nodal sampling [6,7], and overall allows the woman to undergo fewer surgeries during treatment [5].

The operator performing the core biopsy must be familiar with the imaging findings and the level of suspicion of the abnormality in question. Careful review of all prebiopsy images and correlation with the correct lesion is important. To maintain the high sensitivities and low false-negative rates with any percutaneous core biopsy program, proper preparation, technique, and histologic correlation with appropriate follow-up should be observed. In addition, quality improvement measures, including complication rates, should be monitored and documented.

Stereotactic core biopsy

The development of an automated biopsy device approximately 20 years ago that could be used with stereotactic mammography equipment, allowed for confident targeting of small lesions [8]. This procedure uses x-ray guidance to target the lesion, with the patient lying prone, and with her breast suspended through an aperture in the table, or use of an upright table. As with a mammogram, the patient's breast is in compression. A scout image and two stereotactic images are obtained 15° from midline to target the lesion. Although both masses and calcifications can be biopsied using stereotactic guidance, the majority of imaging abnormalities now biopsied with stereotactic technique contain calcifications [9].

Early experience with automated biopsy needles was without vacuum assistance. However, most are now performed with vacuum assistance given the superior tissue acquisition with these devices. There are seven to 14 gauge needles available and most biopsies are performed with

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11 gauge or larger. This is a single pass procedure and samples are taken in a directional fashion, allowing the operator to obtain samples from the lesion where the most diagnostic portion of the lesion may be. As most of the lesions biopsied by stereotactic guidance contain calcifications, documenting adequate sampling with specimen radiography is crucial (Figure 1). In the largest validation study of stereotactic needle core breast biopsies using vacuum assistance, Jackman *et al.* found a less than 1% overall false-negative rate, with a 4.4% rate for 14 gauge core needles and 0.45% for 11 gauge core needles, demonstrating a particular advantage for larger gauge needles. There was also more than 2 years of follow-up of benign lesions and minimal selection bias of lesions biopsied. Emphasizing the importance of documenting adequate lesion sampling, Jackman *et al.* found the highest false-negative rate of 25% were in those lesions in which no calcifications were documented in the specimen radiograph [9]. As the mammographic lesion can be completely removed with the biopsy, a radiopaque marker or microclip should be placed after tissue sampling [10], to document appropriate lesion sampling and for targeting of the suspicious area if further intervention is needed.

Limitations for stereotactic breast biopsies include discomfort from compression of the breast, as for a mammogram, and use of ionizing radiation. Lesions located far posteriorly or directly behind the nipple can be difficult to position. Occasionally, the breast may compress too thinly to accommodate the needle. However, manufacturers have developed various tools and different needle geometries to facilitate tissue acquisition under these circumstances.

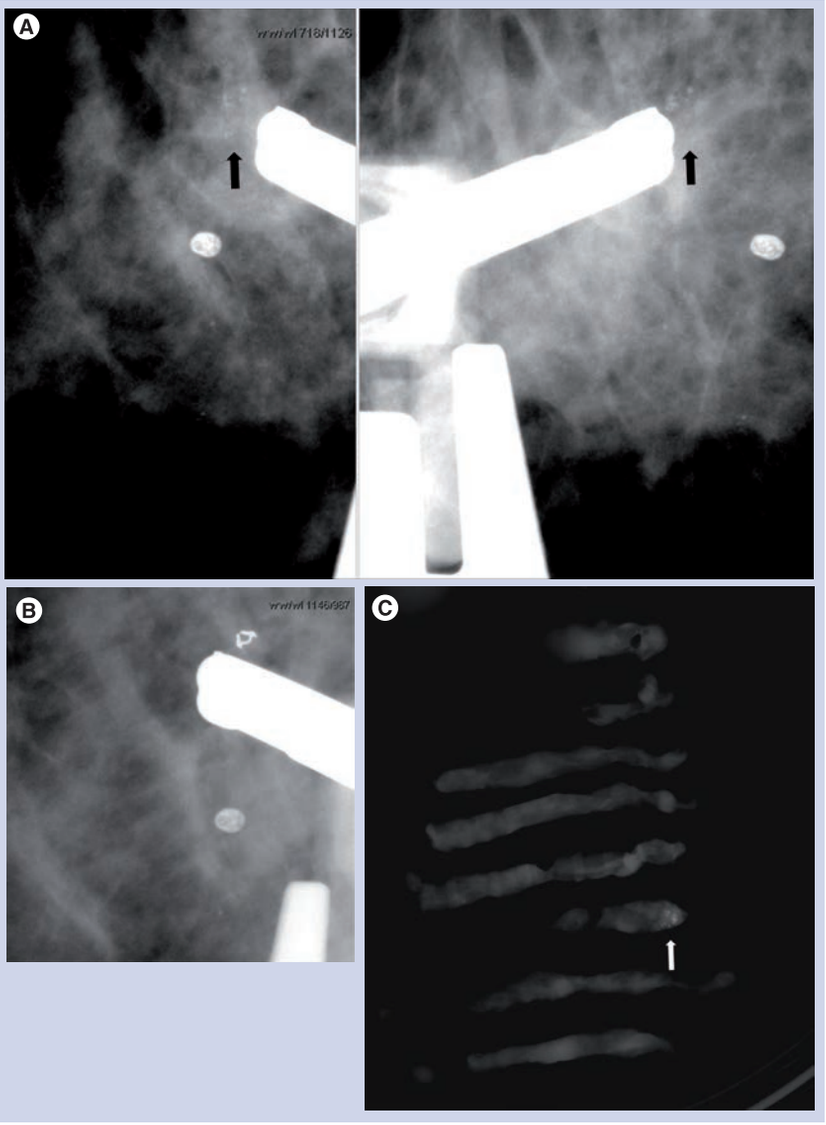

Figure 1. Stereotactic biopsy. (A) Stereotactic images targeting a cluster of calcifications (arrow). **(B)** Radiopaque marker placed through biopsy device. **(C)** Specimen radiograph documenting calcifications in the specimen (arrow).

US-guided core biopsy

For lesions clearly apparent by US, US-guided biopsy provides a quick and comfortable [11], as well as highly accurate way to obtain a tissue diagnosis of breast lesions. It is also a less expensive alternative to stereotactic core biopsy and excisional biopsy [12]. There is no exposure to ionizing radiation during the procedure and no need for compression of the breast as in stereotactic or MR-guided procedures. Unlike stereotactic core biopsies, US provides access to all areas of the breast, is faster and allows for real-time monitoring of the lesion. The operator can see and document needle placement, which can be particularly important for small, deep, mobile or vaguely palpable lesions. Many palpable breast lesions are biopsied by US guidance for these reasons [13,14]. The two largest validation studies to date of US-guided core biopsies, demonstrated false-negative rates of less than 3% and sensitivities of at least 98% [14,15].

Ultrasound machines with linear near field transducers with high resolution, of at least 7 MHz, should be used. Many machines now have a multidirectional 7–12 MHz transducer. For very deep lesions, a 5 MHz transducer may be helpful. Most of the literature on US-guided core breast biopsies describe using a 14 gauge, 22 mm throw, automated needle device [13–18]. Use of a handheld 11 gauge vacuum-assisted device has also been described [19]. Advantages of the 11 gauge handheld device with vacuum-assistance, as with stereotactic core biopsies, is the acquisition of larger tissue samples and the ability

to biopsy smaller lesions. However, no significant differences were found in outcomes between the 11 gauge vacuum-assisted biopsy devices and the 14 gauge automated device [20]. For lesions in very dense, glandular breasts, a coaxial system may be helpful to work through the tissue to the lesion, followed by insertion of the biopsy needle through the introducer [21].

Optimal visualization of both the needle and the lesion biopsied is essential for adequate sampling. Given that the most reflected echoes are obtained with the needle perpendicular to the US beam, the long axis of the transducer should remain aligned with the lesion and skin entry site. Very slight sweeping motions of the needle, while the transducer is held in position with the lesion visualized also helps facilitate needle visualization [22]. The transducer can also be angled to make the US beam more perpendicular to the needle, or the biopsy needle can be 'levered' down to a more horizontal plane maximizing the number of reflected echoes generated from the needle [22]. Alternatively, some US machines have a steerable beam which can change the incident angle to 90° so the beam will be perpendicular to the needle [23].

Once the biopsy device has been deployed, an orthogonal view should be taken to ensure the needle has traversed through the lesion. Documenting needle placement decreases the chance of a nondiagnostic biopsy (Figure 2). Fishman *et al.* analyzed the diagnostic yield for each specimen taken with a 14 gauge core needle, and correlated the findings with mass, procedural and specimen characteristics. A minimum of four specimens, those specimens that were not fragmented and those that sank when placed in formalin correlated with diagnostic tissue [17]. A marker should be placed if the lesion has greatly decreased in size or is no longer visualized. Marker placement also helps correlate with mammographic findings [24].

MRI-guided core biopsy

The use of breast MRI in the detection and management of breast cancer is increasing, particularly in women considered high risk (>20% lifetime risk). The sensitivity of breast MRI for the detection of invasive breast cancer has been found to be very high (approaching 100%), but of moderate specificity [25,26]. This high sensitivity allows for the detection of mammographically and sonographically occult cancer. As such, the need for MR-guided breast procedures for minimally invasive tissue sampling is rising. Key differences in MR-guided biopsies include the use of intravenous contrast material, and no real-time monitoring of tissue sampling with only immediate post biopsy MR images to determine adequacy of sampling, as MR specimen imaging is not possible. Although the breast is in compression, as in stereotactic biopsy, compression must be minimal to allow adequate contrast circulation. There can be fast contrast washout from lesions and increasing background enhancement of breast tissue, potentially making localization of lesions found at diagnostic MRI difficult [27], necessitating quick targeting and sampling (Figure 3). Nonvisualization of the lesion on the day of the procedure is well documented (12–13%) [28–32]. Puckering at the needle entry site can occur, changing the calculated depth of the lesion. The lesion may be displaced by hematoma or obscured by the needle or gas artifact [28,33,34]. These issues suggest MR-guided breast biopsies may not be as accurate as stereotactic or US-guided breast biopsies. To date, there are few studies with large numbers evaluating the accuracy and safety of MR-guided breast biopsies [5,29,31,33,35].

Given the larger tissue acquisition with vacuum-assisted devices, more recent studies describe the use of 11 gauge or larger needles for MR-guided breast biopsies. Despite the larger gauge needles, there is a relatively high discordancy rate for MR-guided breast biopsy (7% in the USA, and

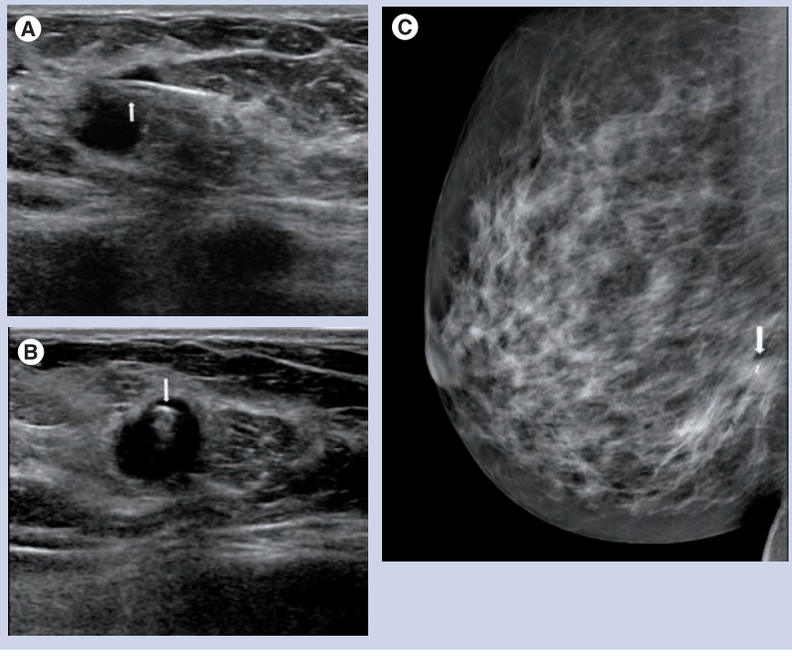

Figure 2. Ultrasound-guided biopsy. (A) Longitudinal view of the biopsy needle traversing the mass. **(B)** Orthogonal view of the needle placed through the mass (arrow). **(C)** Postbiopsy mammogram documenting marker placed within the mass (arrow).

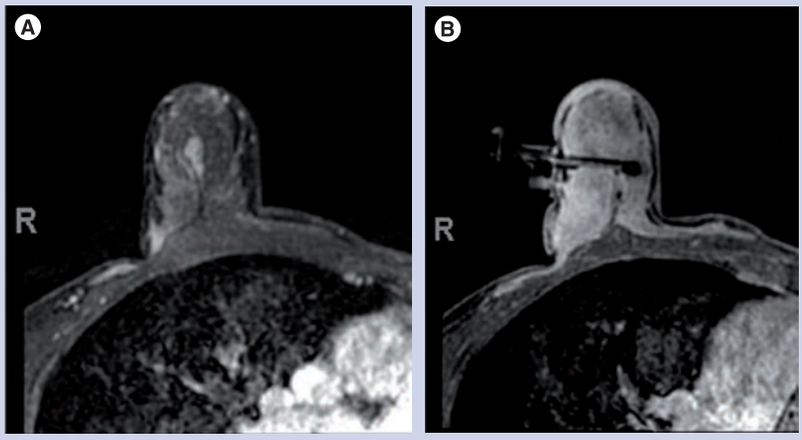

Figure 3. MR-guided breast biopsy. (A) Postcontrast-enhanced MR axial image demonstrating enhancing lesion and **(B)** lesion obscured by background enhancement and obturator.

9% in Europe vs 3% or less for stereotactic or US guidance) [30,32,36]. Of these discordant lesions that went to surgical excision, 36% were malignant, compared with less than 3% reported in the largest, recent studies for stereotactic and US guidance [9,14,15,30]. The higher cancer rate in discordant lesions for MR-guided biopsies may be due to the higher proportion of high risk women in these studies or other technical factors [30]. In the largest multicenter study assessing the accuracy, reliability and reproducibility of MR-guided breast biopsy, a 96% success rate was demonstrated. However, of those described as not successful, no histology or follow-up was given [29]. Therefore, exact false-negative rates cannot be determined. What the appropriate follow-up should be to avoid cancer misses and keep false-negative rates low for MR-guided breast biopsies is evolving. One study recommends for benign, concordant results, follow-up no sooner than 6 months, as cancers missed did not grow before this time, and none were greater than 1 cm or node positive [33]. In the USA, MRI is an expensive resource and insurance reimbursement for follow-up breast MR may be difficult. Optimal timing for postbiopsy follow-up will need further evaluation.

The best timing for breast MR is typically around midcycle for menstruating women, given the potential for increased background enhancement during menstruation [29]. Using the same coil, field strength and patient position as that used for the diagnostic exam is essential. The patient is prone with her breast suspended through a breast coil and in compression. MR compatible equipment is used. Needle grid or pillar and post biopsy devices are used for targeting the lesion. A coaxial sheath is placed into the breast to a calculated depth, the inner stylet removed and a localizing obturator is placed through the sheath. Sagittal or axial sequences are performed to confirm accurate targeting. The obturator is then removed and the biopsy device is inserted through the sheath and tissue sampling is then performed. Placement of MR compatible metallic markers, as with other percutaneous core biopsies, achieves easy subsequent preoperative localization. 'Second look' US may prove helpful to find MR detected abnormalities and use for US-guided biopsy. However, careful scanning technique is required as malignant lesions are often subtle [37].

Radiopaque marker placement at time of wire localization

For a small number of cases, percutaneous biopsy of a lesion may not be feasible. The lesion in question could potentially be difficult to biopsy percutaneously due to small size, bloody nipple discharge without clinical or mammographic mass, location in the breast or patient preference for excisional biopsy [38]. Some lesions that are predominantly cystic may be difficult to clearly biopsy if the cystic component is disrupted, leaving no clear soft tissue component to target [39]. Placement of a radiopaque marker or clip at the time of percutaneous US-guided biopsy to facilitate subsequent excision is well described, particularly in lesions less than 7 mm or in those that resolve after aspiration [40]. Sonographically guided marker placement into a lesion prior to preoperative chemotherapy has also proven useful, as the lesion may no longer be detected on imaging after treatment [41]. Sonographically guided marker placement at the time of wire localization for surgical excision has been described for ensuring and verifying biopsy of the appropriate lesion in certain circumstances [42,43]. Finally, marker placement at the time of ductography has been described for ensuring excision of intraductal lesions causing nipple discharge at the time of wire localization [44]. The added cost of marker placement is minimal under these circumstances, especially given the potential larger cost of inadequate excision.

Typically, specimen radiography or specimen sonography will be performed after wire localization and excision to confirm lesion retrieval. However, if the lesion is mammographically occult, confirmation on specimen radiography will be difficult. Also, the breast imaging center may not be in close proximity to the surgical suite, making specimen imaging impossible [42]. There are also additional limitations to specimen

sonography. Lesions less than 1 cm, particularly in a fatty background, may lead to false-negative specimen sonography [45]. Certain types of lesions, such as those with a significant fluid component that may be disrupted and disappear in the specimen can make sonographic, as well as radiographic, confirmation difficult [43,45]. Sonographically guided placement of a marker at the same time as wire localization has proven beneficial in ensuring surgical removal of lesions under these circumstances (Figure 4) [42,43].

The prevalence of cancer in women who present with pathologic nipple discharge is low, with the most common cause an intraductal papilloma [46]. Yet discharge may be the only symptom [47]. The sensitivity for US detection of intraductal abnormalities in the setting of nipple discharge is variable [48–51], and in two reports with patients with no clinical or mammographic abnormalities, the correct cause of the nipple discharge was sonographically identified in 10–26% of cases, with all malignant cases missed [52,53].

If mammographic and US evaluation are negative in the setting of nipple discharge, a ductogram or galactogram may be requested by the referring surgeon. Although the gold standard for diagnosis is major surgical duct excision, ductography may identify distal ductal abnormalities that may not be excised with routine subareolar duct excision. There are a few series with small numbers of patients describing US-guided or galactographic-guided stereotactic, large gauge vacuum-assisted biopsy of intraductal lesions causing nipple discharge, with limited results or variable follow-up [54,55]. Percutaneous biopsy of intraductal lesions could be attempted using these techniques. The surgeon may request wire localization of the ductographic abnormality

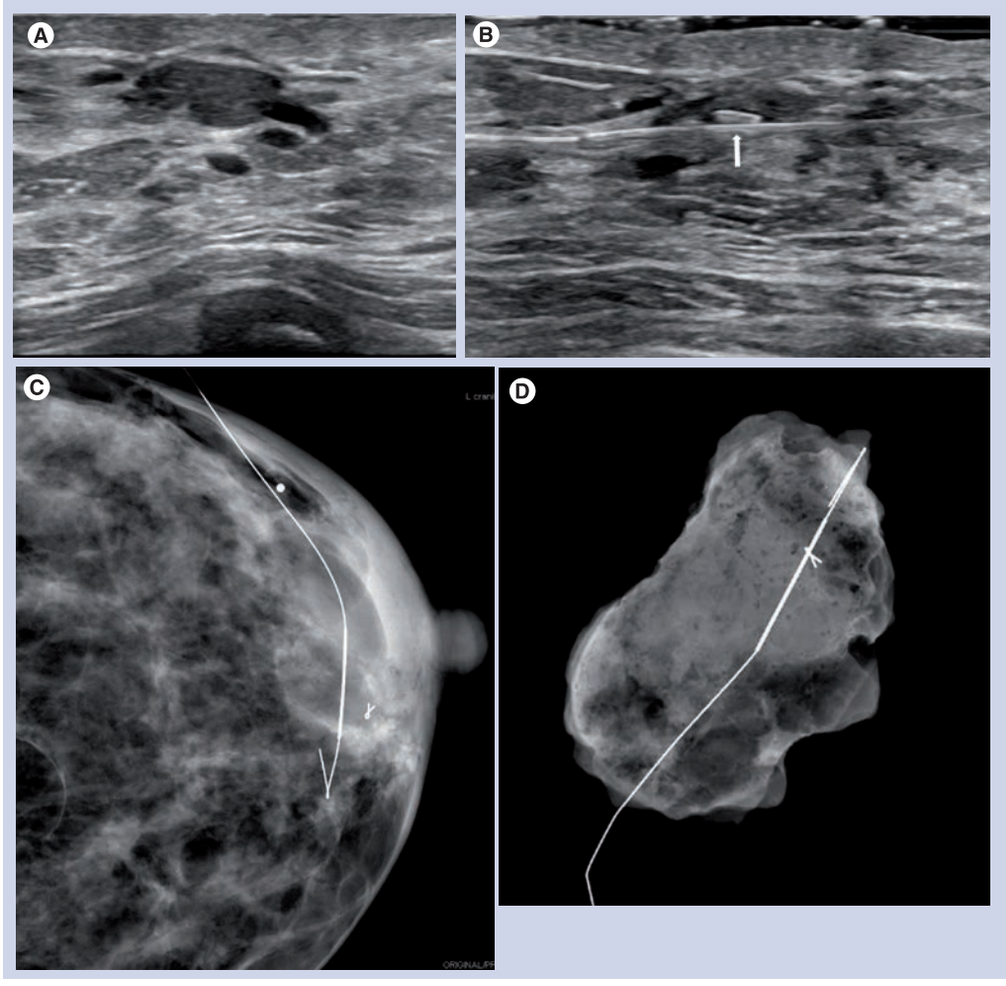

Figure 4. A 39-year-old lactating woman with a vaguely palpable breast mass presents for an excisional biopsy. (A) Ultrasound image demonstrating an intraductal lesion. **(B)** Marker and localizing wire in place (arrow). **(C)** Mammogram performed after marker and localizing wire placement. Note the mass is mammographically occult. **(D)** Specimen radiograph demonstrating the marker and wire. The mass is not apparent. Pathology revealed lactation changes.

for primary excision and treatment, as most will be papillary lesions. Clear guidelines for the management of papillary lesions have not been established and there remains a high association of atypia or malignancy of those diagnosed with percutaneous core biopsy [56]. However, ductography may not be successful for a variety of reasons at the time of surgery, such as inability to cannulate the duct, contrast extravasation, or there may be no discharge at the time of the examination.

If ductography can be performed at the time of wire localization, the suspicious finding can be targeted. However, intraductal lesions causing nipple discharge that can only be detected with ductography will also be very difficult to confirm retrieval on specimen sonography or radiography [44]. Once excision is performed, the contrast material will have been absorbed, or lost and no longer present in the specimen to confirm lesion removal on specimen radiography, and with the fluid component lost, specimen sonography may be negative [45]. Grid coordinate x-ray guided marker placement at the time of the diagnostic ductogram has been described to obviate the need for repeat duct injection at the time of wire localization (Figure 5). As in x-ray-guided wire localization, the lesion found at the time of ductography can be localized using a grid coordinate technique through a fenestrated paddle. The marker device can be placed through the fenestrated paddle and the depth is determined on the orthogonal mammographic view. In a study describing this technique, no patients were converted to a blind duct excision after marker placement and no surgeries were canceled [44].

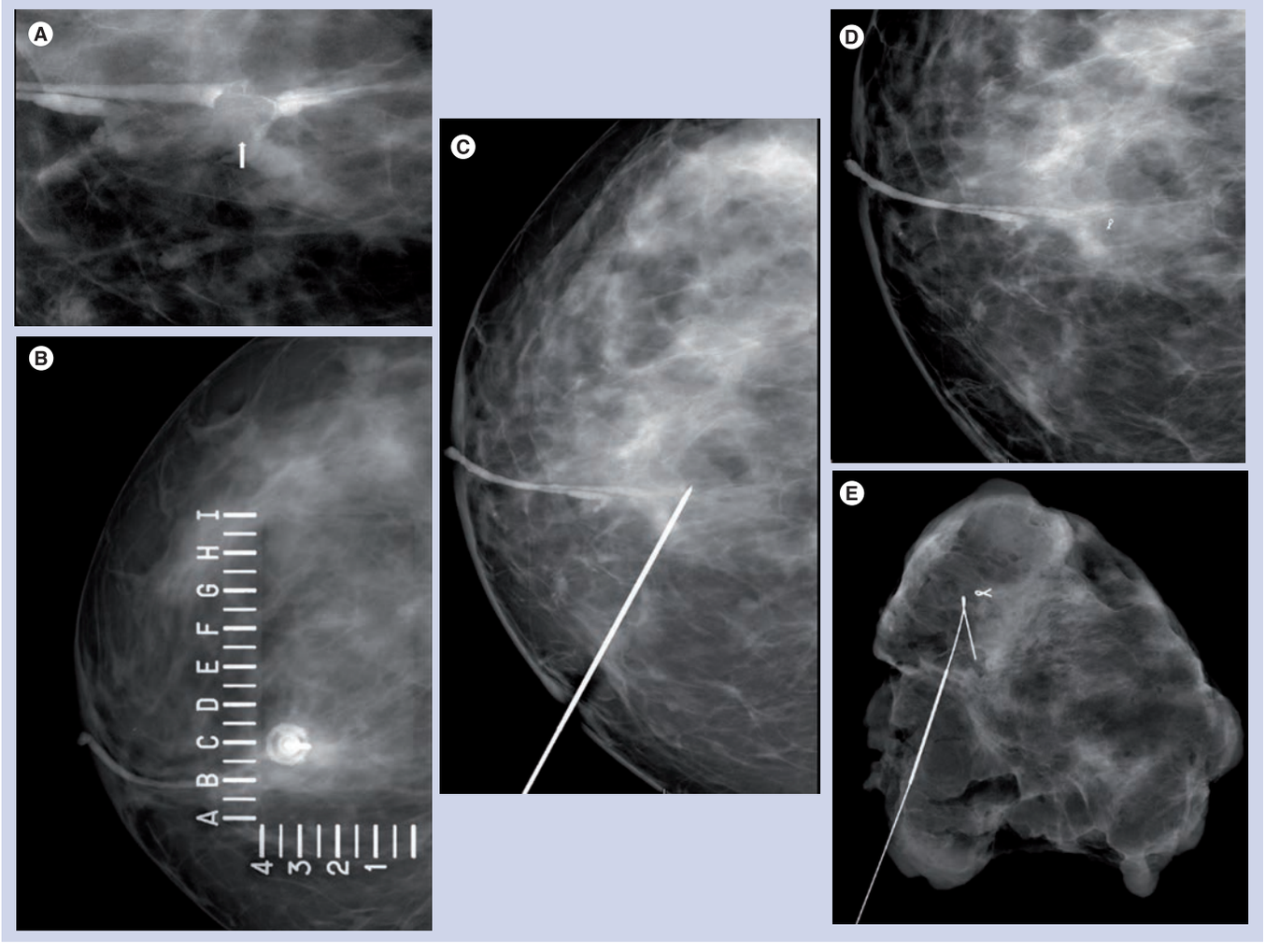

Figure 5. Marker placement at the time of ductography. (A) Contrast material from a ductogram outlines an intraductal lesion in a woman with bloody nipple discharge (arrow). Ultrasound at the time of ductography was negative. **(B)** The lesion is targeted with mammographic guidance using grid coordinate technique (note placement of marker device). **(C)** The orthogonal view demonstrates the depth for placement of the marker device. Note placement of the tip of the marker device at the level of the intraductal lesion. **(D)** Mammogram demonstrating marker placement. **(E)** Specimen radiograph demonstrating marker in place, verifying excision of the occult lesion. Pathology revealed intraductal papilloma.

Conclusion

With an aging population needing screening and evaluation for breast cancer, and over a million breast biopsies performed in the USA every year, there will be a continued need for image-guided breast biopsy procedures, benefiting the patient with a minimally invasive, safe and potentially lower cost work-up. Long term data reveal the safety and efficacy of stereotactic and US-guided core biopsies, with the data for MR-guided breast biopsies evolving. There is a role for percutaneous, sonographically guided marker placement at the time of wire localization for surgical excision under certain circumstances, to verify lesion retrieval and limit the likelihood of inadequate excision of breast abnormalities.

Future perspective

At the beginning of the 20th century, women had to endure more and more invasive and debilitating surgery for the diagnosis and treatment of breast cancer. With an improved understanding of the biology of breast cancer and its behavior, together with the development of medical adjuvant treatments and the refinement of techniques for early detection such as mammography, we are detecting breast cancer at its earliest stages and improving survival. There should be a continued push for minimally invasive approaches for diagnosis, leaving surgery for treatment and not diagnosis. For women with breast lesions detected by MRI, further validation studies are needed to assure the accuracy and efficacy of MR-guided breast biopsies.

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Executive summary

Stereotactic core biopsy

- Large gauge needles using vacuum-assistance afford superior tissue acquisition and overall low (<1%) false-negative rates. Documenting adequate sampling with specimen radiography is key.

Ultrasound-guided core biopsy

- Best tolerated procedure by patients, less expensive than stereotactic, no ionizing radiation used.
- With appropriate technique and pathologic correlation, false-negative rates are low.

MR-guided core biopsy

- High sensitivities of breast MR for the detection of invasive carcinomas that are mammographically and sonographically occult, but with moderate specificities, necessitates MR-guided procedures for minimally invasive tissue sampling.
- Problems with the use of intravenous contrast, such as fast washout from lesions found, no real-time imaging of the MR-guided biopsy and difficulty with determining adequacy of sampling are a few of the issues that suggest MR-guided breast biopsies may not be as accurate as stereotactic- or ultrasound-guided breast biopsies.
- To date, there are a few studies with large numbers evaluating the accuracy and safety of MR-guided procedures.

Radiopaque marker placement

- In a small number of cases, percutaneous core breast biopsy may not be possible.
- Sonographically guided marker placement at the time of wire localization has proven beneficial in confirming surgical removal of lesions that are mammographically occult, or that may become less sonographically apparent during surgery.
- Grid coordinate marker placement at the time of an abnormal ductogram can obviate the need for another ductogram at the time of wire localization for surgical removal in women with abnormal nipple discharge.

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