Localization for Breast Surgery

The Next Generation

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• ***Context.***—**Preoperative localization of nonpalpable breast lesions using image-guided wire placement has been a standard of breast imaging, diagnosis, and treatment since its development in the 1970s. With this technique, coordinated, same-day wire placement by the radiologist and surgery are required, which can lead to significant inefficiencies in workflow. Other disadvantages of wire localization (WL) include limitations in surgical incision and dissection route and protruding wires that can be both bothersome for the patient and have risk of displacement.**

Objective.—**To outline several recently developed techniques that could replace traditional WL and eliminate its disadvantages. The first developed was radioactive seed localization (RSL) using I-125, a technique adopted by many institutions during the last few years. The challenge to this method, however, is the strict nuclear regulatory requirements, which can be a significant burden and limitation. The disadvantages of WL and RSL have provided incentive for the development of other types of preoperative localization procedures. Two of these are recently US Food and Drug Administration–cleared, nonradioactive, non-wire location technologies emerging as alternatives to WL and RSL; SAVI SCOUT (Cianna Medical Inc, Aliso Viejo, California), which uses infrared light and a microimpulse radar reflector, and Magseed (Endomagnetics Inc, Austin, Texas), which uses a magnetic seed for localization.**

Data Sources.—**We review the published literature on non-wire location technologies for breast tissue resection.**

Conclusions.—**Non-wire location techniques are beneficial, allowing image-guided placement before the day of surgery and resulting in improved workflows. These techniques also eliminate bothersome protruding wires, risk of dislodging, and allow the incision site to be independent from the localization site.**

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In the 1970s, the development of screen-film mammography and publication of studies showing decrease in mortality from breast cancer in women who were offered screening led to the rise of mammography. With screening mammography, nonpalpable abnormalities were detected that required biopsy. Before the development of image-guided percutaneous biopsy, surgical excision was the only diagnostic biopsy method available. Clinically occult lesions required preoperative localization to guide appropriate excision. Wire localization (WL) techniques using mammographic, and later ultrasound guidance, were developed to assist in surgical excision of suspicious breast lesions.[1,2] These techniques allow the surgeon to use the wire as a guide to find and remove the targeted lesion; a radiograph of the tissue specimen confirms appropriate excision. The mammographic technique uses a compression paddle with a grid-coordinate system or fenestrations to visualize the lesion and map coordinates for precise localization. A needle containing a wire is placed through the target and when appropriate placement is confirmed with imaging, the needle is removed and the wire is left in the breast as a guide. The wire protrudes out of the skin, allowing the surgeon to dissect down to the end of the wire to the suspicious lesion. Although the advent of image-guided percutaneous core needle biopsy has decreased the number of WLs required for tissue diagnosis, localization is still required for guidance during breast conservation surgery for carcinoma or atypia or in lesions not amenable to image-guided core needle biopsy.

Although reliable, well tolerated, and cost effective, WL does have disadvantages. It requires close coordination of the surgery and breast imaging schedules, as the wire must be placed on the same day as the excision. This can limit the performance of wire-localized surgical cases early in the morning or require the patient and radiologist to be available for localization very early before surgery. Once placed, the wire protrudes from the skin until removal during surgery, which can be bothersome to the patient and is a risk for displacement. In addition, the placement route of the wire chosen by the radiologist often dictates the incision, which may not be that preferred by the surgeon.

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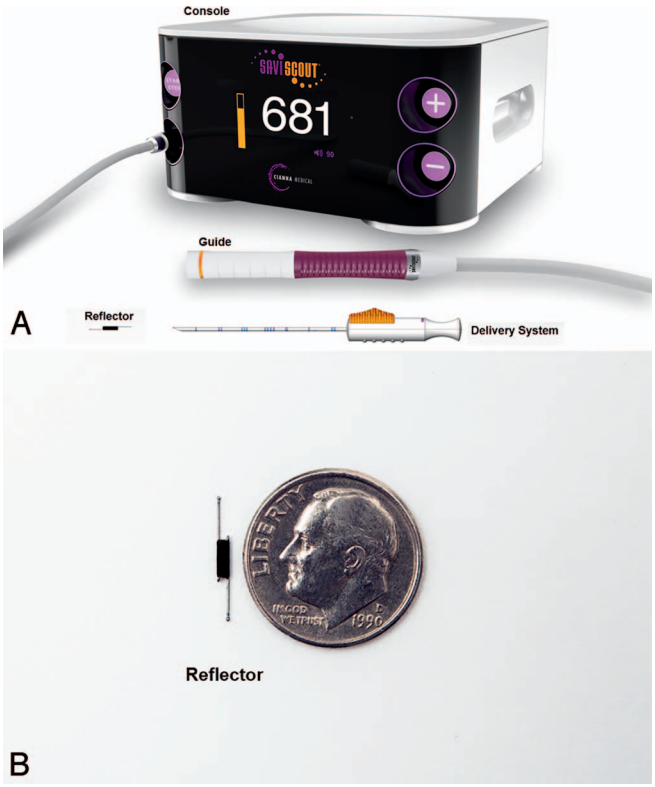

Figure 1. *The console detects the SAVI SCOUT (Cianna Medical Inc, Aliso Viejo, California) reflector by using a combination of radar and infrared light emitted by the guide. A, SAVI SCOUT system. B, SAVI SCOUT reflector. Printed with permission (Terry Hardin, director of marketing & technology for Cianna Medical Inc).*

Because of these disadvantages, there has been investigation into alternative localization techniques. The first of these uses an iodine-125 radioactive seed, which allows placement up to 5 days before surgery. This method has become popular and is the preferred localization technique for many hospitals throughout the world. However, it, too, has disadvantages related to the use of a radioactive material and the accompanying nuclear regulatory issues. This has generated a continued search for a better non-wire localization marker. As of 2017, two additional localizers have received US Food and Drug Administration (FDA) clearance: a radar reflector that uses microimpulse radar (SAVI SCOUT, Cianna Medical Inc, Aliso Viejo, California) and a magnetic seed (Magseed, Endomagnetics Inc, Austin, Texas).

RADIOACTIVE SEEDS

In 2001, Gray et al[3] described a novel technique using a titanium seed containing iodine-125 placed into a breast lesion for preoperative localization. Their randomized prospective trial compared women undergoing localization with either WL or radioactive seed localization (RSL). They found that RSL was an effective alternative that offered several advantages. In their study, fewer RSL patients required re-excision for positive margins, the radiologist and the surgeon could choose the best site of entry independently, and there was no displacement as there could be with a protruding wire. An even more important advantage was that the seed could be placed up to 5 days before surgery, allowing for independent scheduling of the localization and surgery.

The placement technique for RSL is similar to traditional wire placement. Guidance is either with the mammographic grid coordinate system with the patient in compression or with real-time ultrasound guidance for visualization of the targeted lesion. The seed can be loaded into an 18-G needle and the tip occluded with bone wax; alternatively, the seed can be placed with a preloaded needle. The seed is deposited in or adjacent to the targeted lesion through the needle, and position is confirmed on 2 view orthogonal radiographs. At the time of excision, the surgeon localizes the seed with a gamma probe, similar to the procedure for localizing a sentinel lymph node. After tissue excision, the surgeon uses the gamma probe to confirm that the seed is within the specimen. Additionally, a specimen radiograph confirms the presence of the targeted lesion and seed removal. Next, the pathology department retrieves the seed before standard tissue processing. If the seed is not grossly identified a gamma probe can aid in localization. Care must be taken not to damage the seed during dissection, as this could potentially release radioactive material.[4] The seed is placed in a lead-lined, marked container and given to the Radiation Safety Officer (RSO) for safe storage and disposal.[5,6]

Recent studies have confirmed that RSL is an effective alternative to WL. In 2015, Sharek et al[7] reported their data on 114 cases using RSL and 118 using WL. They found no significant differences in surgical outcomes between RSL and WL for lumpectomy and a significant improvement in efficiency, with increased breast imaging time slot utilization, decreased time spent scheduling, and reduction in operating room delays. In 2016 Dryden et al[8] showed the rates of close or positive margins, re-excision, and mastectomy were similar between 127 radioactive seeds and 533 WLs.

Starting and maintaining an RSL program requires strict adherence to the nuclear regulations and additional effort from all members of the breast care team. Establishing an RSL program takes approximately 9 months.[9] All personnel involved with the handling of the seed must have radiation safety training by the RSO or an authorized user who is board certified in diagnostic radiology or radiation oncology. Obtaining and maintaining proper licensing and meticulous tracking of the seed is mandatory. Every seed needs to be tracked, recovered, and properly disposed of to comply with nuclear regulatory licensing. A lost seed could result in loss of an institution's nuclear regulatory license.

For many institutions, the advantages of RSL have outweighed the regulatory disadvantages and it has become the localization procedure of choice at many institutions around the world. Formal courses offering instruction on how to start an RSL program have been available since 2009.[9] For many, however, the nuclear regulatory requirements present a significant obstacle. This has prompted research and development of nonradioactive localizers that have the benefits of non-wire localization without the nuclear regulatory disadvantages of RSL.

SAVI SCOUT

In 2014, the FDA cleared the first nonradioactive nonwire localizer, the SAVI SCOUT radar localization system from Cianna Medical Inc, for preoperative breast localizations. This system uses a radar reflector activated with infrared light. The reflector is passive until activated from the console by a hand piece (Figure 1, A and B). The SAVI SCOUT

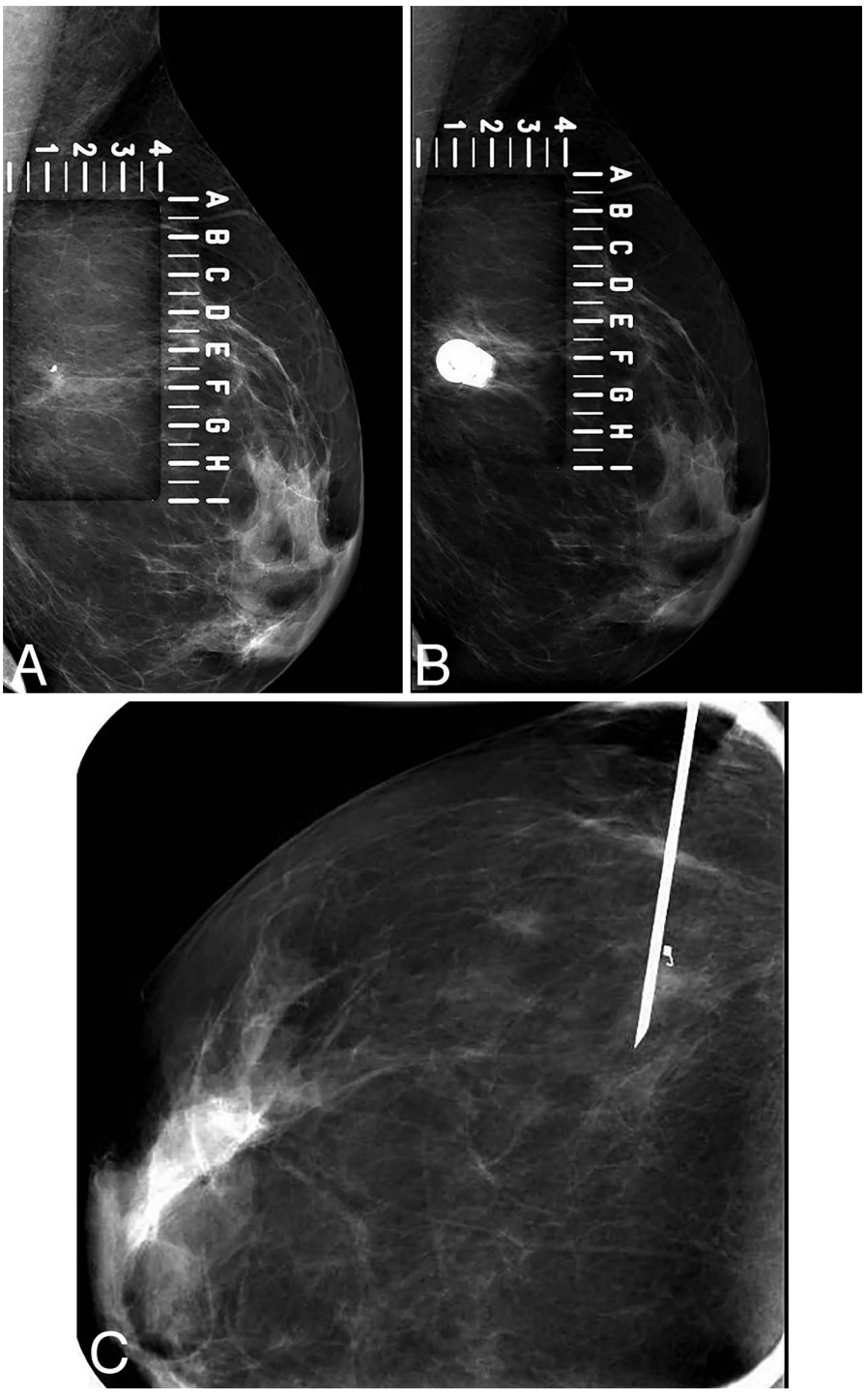

Figure 2. *Mammographically guided placement of SAVI SCOUT (Cianna Medical Inc, Aliso Viejo, California) using grid-coordinate technique. A, Targeting of biopsy clip marker. B, Appropriate placement of introducer superimposed over target. C, Orthogonal projection with introducer appropriately placed for reflector deployment.*

reflects the radar signal, which is then detected by the hand piece and console. The reflector is 12 mm in length, with a 4-mm body and 2 antennas each 4 mm in length, and can be inserted with either ultrasound or mammographic guidance through a preloaded 16-gauge introducer needle (Figures 2, A through C; 3, A and B; and 4, A through C). The reflector allows placement up to 30 days before surgery, maximizing flexibility of scheduling for the surgeon, radiologist, and patient. Immediately after placement, the reflector can be activated and detected with an audible signal and numerical indicator from the console; this can be done while the patient is still in the breast imaging department to verify detection from the skin surface (this is an optional step). Additionally, radiographs assess proximity of the reflector to the targeted lesion. At the time of surgery, the surgeon activates the reflector with the hand

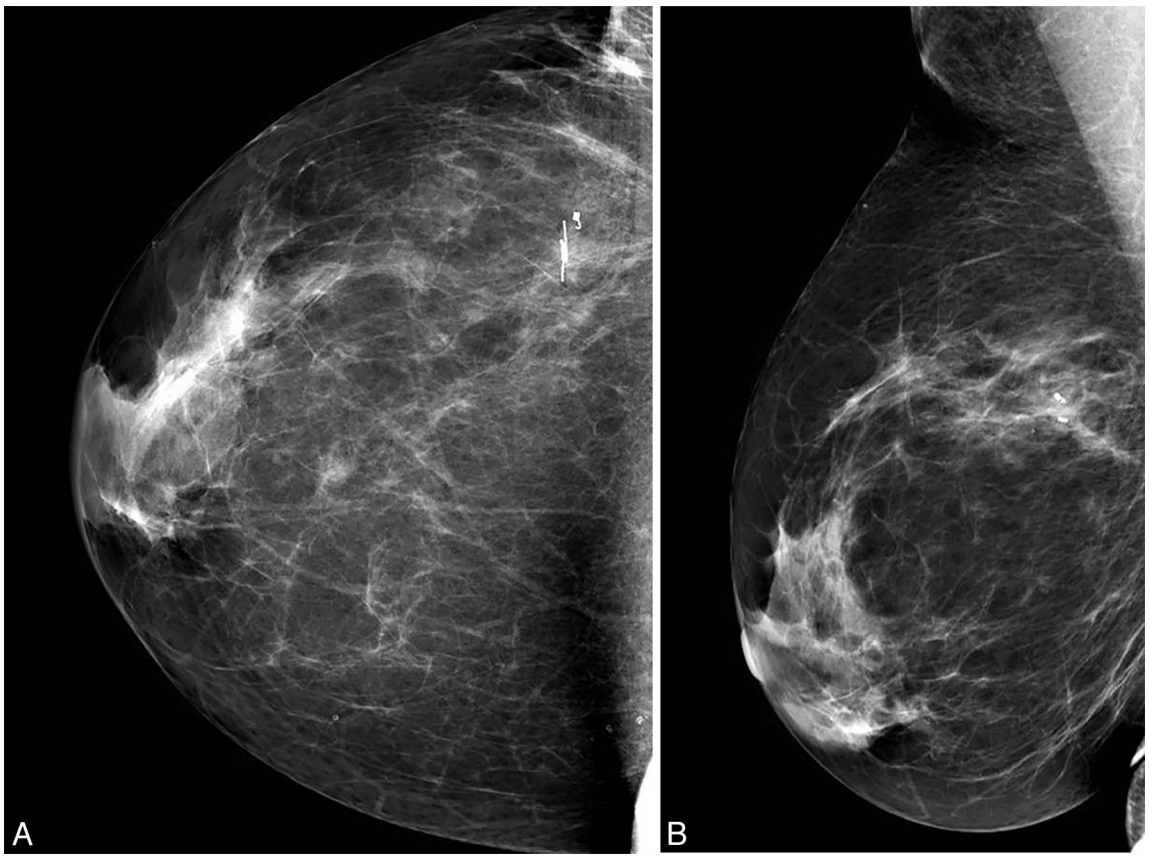

Figure 3. *SAVI SCOUT (Cianna Medical Inc, Aliso Viejo, California) reflector adjacent to biopsy clip marker. A, Craniocaudal mammogram. B, Lateral mammogram.*

piece and follows the signal to guide the excision. The audible and numerical signals change with increasing proximity to the lesion, directing precise localization.[10]

A pilot study by Cox et al[11] in June 2016 reported the use of the SAVI SCOUT system for preoperative breast localization in 50 patients. This showed that the system was safe and effective, with all of the lesions and reflectors successfully removed and no adverse outcomes. This was followed by a report in October 2016 by Mango et al,[12] confirming successful localization with SAVI SCOUT in a smaller group of 15 patients. Cox et al[13] later performed a prospective multisite study with 153 successful localizations. This study included feedback from surgeons, radiologists, and patients (via surveys) as well as data on the technical success of localization/excision and surgical margin status. A total of 154 patients were initially enrolled; in 1 case the SAVI SCOUT placement was remote from the targeted lesion and the localization was continued with traditional

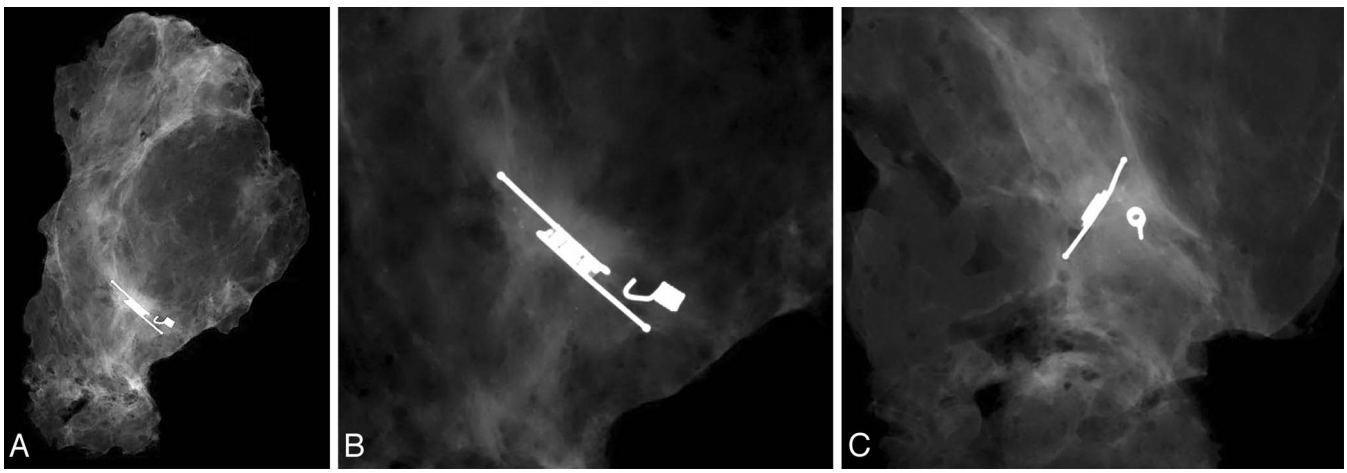

Figure 4. *A, Specimen radiograph shows SAVI SCOUT (Cianna Medical Inc, Aliso Viejo, California) within small mass with calcifications and adjacent to biopsy clip marker. B, SAVI SCOUT en face. C, SAVI SCOUT in profile.*

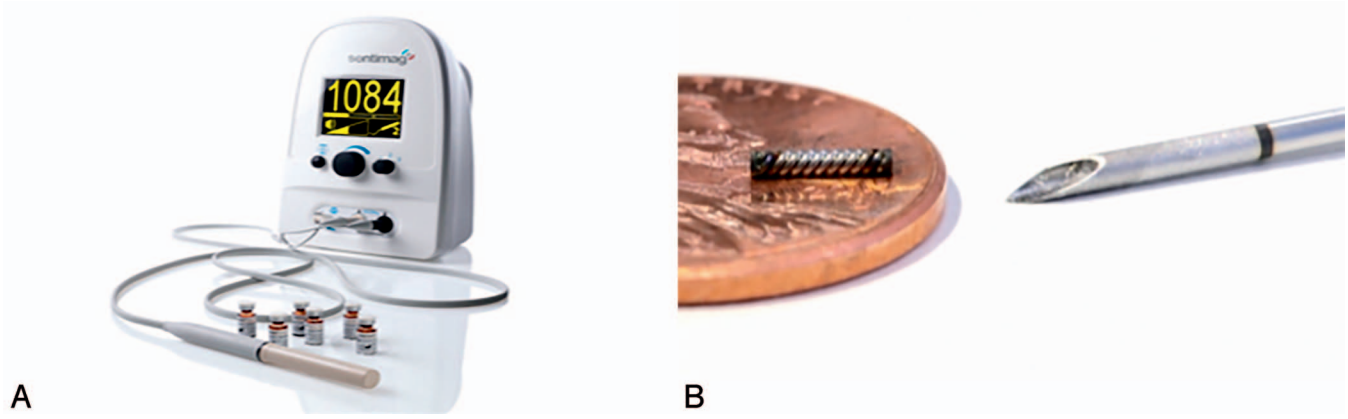

Figure 5. *A, Magseed (Endomagnetics Inc, Austin, Texas) detector. B, Magseed magnetic seed and introducer needle. Printed with permission (Eric Fryxell, executive sales representative, Leica Biosystems).*

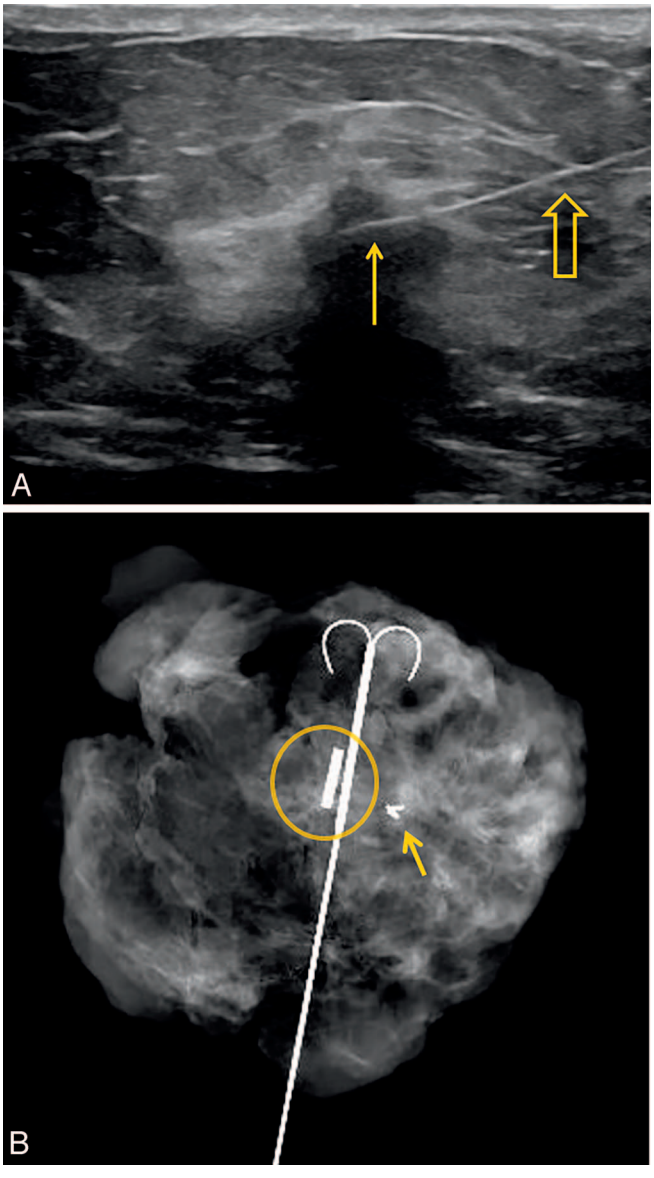

Figure 6. *A, Ultrasound image shows Magseed (Endomagnetics Inc, Austin, Texas) (solid arrow) within targeted shadowing lesion. Introducer (open arrow) has been retracted to deposit the seed. B, Specimen radiograph shows Magseed (circle) and adjacent Magseed-compatible wire (placed during initial phase of product use at our institution) and core biopsy clip marker (arrow).*

wire placement. In all cases, there was successful removal of both lesion and reflector. For the 101 patients undergoing lumpectomy for known cancer, 85% had negative surgical margins. This compares favorably with reported re-excision rates for RSL and WL.[7,8,14]

The multisite study surveyed the participating surgeons, radiologists, and patients for feedback on the procedure.[13] After each case, the surgeons and radiologists rated localization using SAVI SCOUT as it compared with traditional WL. Both localization and removal were rated the same or better than WL. Surgeons favored SAVI SCOUT over WL for incision site planning, tissue localization, confidence in removing the correct target, and ease of specimen removal. For survey questions about workflow, including ability to start cases earlier, patient wait times, and reduction in surgery schedule delays, the responses for SAVI SCOUT were significantly better than WL. Eleven of 13 radiologists (85%) who completed the survey also reported improved workflow with SAVI SCOUT over WL.

Patient experience was evaluated directly with postlocalization surveys and subjective ratings by the radiologists and surgeons. Of the 105 patients who responded to the survey, 75 (71%) were very satisfied, 14 (13%) were somewhat satisfied, 13 (12%) were neutral, and 3 (3%) were somewhat dissatisfied. The authors of the study did not report prior patient experience with WL. However, based on general patient population statistics, it is likely that most, if not all, did not have experience with an earlier WL procedure for comparison of the 2 procedures. The subjective physician impression of patient experience rated the SAVI SCOUT procedure more favorably than WL. Eighteen of the 36 participating study physicians (14 radiologists, 4 surgeons) rated the SAVI SCOUT better than WL for patient comfort, anxiety, and overall experience.[13]

The SAVI SCOUT does have some limitations, most notably, the potential to disable the reflector with direct contact by electrocautery. The reflector has been modified with the addition of an electrostatic discharge diode to minimize the risk of reflector inactivation; however, it does not eliminate the possibility. At our institution, radiologists have noted that the reflector insertion mechanism, which uses a rotating movement to unlock the deployment button and a withdrawing motion for deployment, can be cumbersome, particularly if a one-handed insertion is needed while holding an ultrasound probe. Although

uncommon, there is a risk of transection of the SAVI SCOUT antenna during dissection. Other limitations are inability to reposition the reflector once deployed and a recommended maximal detection depth of 4.5 to 5 cm.

MAGSEED

In 2016, the FDA cleared the Magseed system from Endomagnetics Inc for breast localization. For localization with this system, a 1 mm × 5 mm magnetic seed can be placed in the breast with either ultrasound or mammographic guidance up to 30 days before surgery (Figures 5, A and B; and 6, A and B). The company's Sentimag probe detects the magnetic signature of the seed.[15] A major challenge with the Magseed is that ferromagnetic instruments will interfere with the signal, so special nonferromagnetic surgical instruments are necessary. Electrocautery or other metallic equipment in the operating room can also interfere with the signal, requiring recalibration of the probe. Magseed has received recent FDA clearance; there are no studies reported in the literature evaluating its use and efficacy.

SUMMARY

The use of non-wire localization of nonpalpable breast lesions has substantial benefits. Being able to "uncouple" the image-guided localization from surgery allows for improved efficiency in both breast imaging and surgery scheduling, as well as improved workflow on the day of localization and on the day of surgery. The surgery schedule is no longer at risk of delays that might arise during localization (eg, due to vasovagal reactions or other unforeseen issues). The breast imaging schedule can also be optimized for placement when it is most convenient for the patient and radiologist. Additionally, non-wire localization techniques eliminate bothersome protruding wires, risk of dislodging, and allow the incision site to be independent from the localization site.

The first nonwire system using RSL has been widely adopted as the localization of choice for many institutions. However, the rigorous nuclear regulatory requirements are an obstacle for some institutions. Recently, new nonradioactive, non-wire localization technologies have been developed that have the benefits of RSL without the nuclear regulatory disadvantages. SAVI SCOUT has been available since 2014; several published studies have reported its efficacy. Magseed received FDA clearance in 2016; there is currently no literature available on this device. The interest in finding simple, effective non-wire localization systems will continue to inspire the future development of these new technologies.

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References

1. Hall FM, Kopans DB, Sadowsky NL, Homer MJ. Development of wire localization for occult breast lesions: Boston remembrances. *Radiology*. 2013; 268(3):622–627.

2. Joe BN, Sickles EA. The evolution of breast imaging: past to present. *Radiology*. 2014;273(2 suppl):S23–S44.

3. Gray RJ, Salud C, Nguyen K, et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. *Ann Surg Oncol*. 2001;8(9):711–715.

4. Gilcrease MZ, Dogan BE, Black DM, Contreras A, Dryden MJ, Jimenez SM. Transection of radioactive seeds in breast specimens. *Am J Surg Pathol*. 2016; 40(10):1375–1379.

5. Goudreau SH, Joseph JP, Seiler SJ. Preoperative radioactive seed localization for nonpalpable breast lesions: technique, pitfalls, and solutions. *Radiographics*. 2015;35(5):1319–1334.

6. Graham RP, Jakub JW, Brunette JJ, Reynolds C. Handling of radioactive seed localization breast specimens in the pathology laboratory. *Am J Surg Pathol*. 2012;36(11):1718–1723.

7. Sharek D, Zuley ML, Zhang JY, Soran A, Ahrendt GM, Ganott MA. Radioactive seed localization versus wire localization for lumpectomies: a comparison of outcomes. *AJR Am J Roentgenol*. 2015;204(4):872–877.

8. Dryden MJ, Dogan BE, Fox P, et al. Imaging factors that influence surgical margins after preoperative 125I radioactive seed localization of breast lesions: comparison with wire localization. *AJR Am J Roentgenol*. 2016;206(5):1112–1118.

9. Jakub J, Gray R. Starting a radioactive seed localization program. *Ann Surg Oncol*. 2015;22(10):3197–3202.

10. Cianna Medical Inc. SAVI SCOUT: precision and efficiency: what every patient, physican and CEO wants. 2016. https://ciannamedical.showpad.biz/share/wfYG4gHPjjEfwexcI6TU. Accessed September 27, 2016.

11. Cox CE, Garcia-Henriquez N, Glancy MJ, et al. Pilot study of a new nonradioactive surgical guidance technology for locating nonpalpable breast lesions. *Ann Surg Oncol*. 2016;23(6):1824–1830.

12. Mango V, Ha R, Gomberawalla A, Wynn R, Feldman S. Evaluation of the SAVI SCOUT Surgical Guidance System for localization and excision of nonpalpable breast lesions: a feasibility study. *AJR Am J Roentgenol*. 2016;207: W1–W4.

13. Cox CE, Russell S, Prowler V, et al. A prospective, single arm, multi-site, clinical evaluation of a nonradioactive surgical guidance technology for the location of nonpalpable breast lesions during excision. *Ann Surg Oncol*. 2016; 23(10):3168–3174.

14. Hughes JH, Mason MC, Gray RJ, et al. A multi-site validation trial of radioactive seed localization as an alternative to wire localization. *Breast J*. 2008; 14(2):153–157.

15. Endomagnetics Inc. Magseed. 2016. http://us.endomag.com/magseed. Accessed February 22, 2017.