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CLINICAL TRIAL

Microchipping the breast: an effective new technology for localizing non-palpable breast lesions for surgery

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Abstract

Purpose Use of a wire to localize a non-palpable breast lesion for surgery is standard but archaic. We sought to evaluate a new radiofrequency localization system (RFLS) as an effective, non-radioactive alternative to the wire.

Methods Patients who required surgical excision of a non-palpable breast lesion were consented for the study. Patients underwent localization with a radiofrequency Tag and surgical removal guided by the handheld LOCalizer probe. The primary study endpoint was successful placement and retrieval of the Tag, and secondary endpoints included marker migration; days prior to surgery of Tag insertion; patient, radiologist, and surgeon experience; distance of Tag from skin; and positive margin and re-excision rates for cancer.

Results Fifty patients had successful placement and retrieval of the radiofrequency Tag. Likert questionnaire data revealed that most patients thought the procedure went smoothly and was easier than expected. Radiologists and surgeons thought that the Tag was as reliable as the wire. Of the 33 patients who had surgery for in situ or invasive cancer, one had a positive margin on final pathology (3%) and two underwent re-excision (6%).

Conclusions Data from this pilot study suggest that the RFLS is an effective localization system for non-palpable breast lesions intended for surgical removal. Unlike most other technologies, the LOCalizer probe detects distance from the Tag, and this unique feature may have contributed to the low positive margin rate seen in this study. The RFLS appears to offer advantages over current localization procedures and should be explored as an alternative to wire. ClinicalTrials.gov Identifier: NCT03202472.

Keywords Radiofrequency Tag · Breast surgery · Wire-free localization

Abbreviations

RFLS	Radiofrequency identification localization system
WL	Wire localization
RSL	Radioactive seed localization
RFID	Radiofrequency identification
FDA	Food and Drug Administration

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Introduction

Despite the patient inconveniences and logistical issues, wire localization (WL) has been the standard localization technique for guiding surgical excision of non-palpable breast lesions for over 20 years [1–3]. With widespread screening, mammography is diagnosing non-palpable breast lesions at much higher rates, increasing the number of image-guided localizations necessary to guide surgical resections. WL has proven effective in localizing the intended target with failure rates between 1 and 7% [4–6] but it carries risks inherent in the technique of placing a wire into a patient's breast. For one, a portion of the wire must reside outside of the breast, so the surgeon can use the trajectory of the wire to guide the surgical resection. In this case, the wire can be inadvertently dislodged at any point following its placement and before removal in the operating room [7]. In addition, given its external component, patients must undergo the WL procedure on the same day of surgery, which can delay surgical start times and impede operating room efficiency. Because they arrive at the facility on an empty stomach, patients can also experience lightheadedness and become vasovagal during the localization procedure. With these limitations and the increased demand, more efficient and convenient methods of localization are needed.

Radioactive seed localization (RSL) has been the most widely studied alternative thus far. Unlike the wire, the radioactive seed is implanted entirely within the breast at any time within 5 days of surgery. Studies have demonstrated the effectiveness of RSL in appropriately targeting the lesion for removal [8, 9]. In addition, RSL appears to equal if not improve the negative margin rate and re-excision rate for lumpectomies for breast cancer compared to WL [10–12]. Nonetheless, RSL has not been easy to adopt across all institutions given the regulations necessary to manage and track the radioactive seeds, the special licensing necessary for handling radioactive material, and the coordination necessary between the different departments.

Other alternatives for lesion localization are under investigation, including the Magseed, which generates a detectable magnetic field [13, 14], and the SAVI Scout [15–20], which utilizes radar technology. Each comes with its own initial challenges, including interference with detection of the Magseed from the metal surgical instruments used during surgery and concern for MRI compatibility. For the SAVI Scout, the cautery can disrupt the signal if it contacts the Scout device. The size of the probe for both the Magseed and SAVI Scout systems could also limit visualization if using a smaller incision.

Our pilot study evaluated a Radiofrequency Identification (RFID) Localization System (RFLS) as a wire-free, non-radioactive alternative for targeting non-palpable breast lesions for surgery. Unlike that with the Magseed and SAVI Scout systems, the RFID Surgical Probe is the size of a standard pencil, and the Reader is portable, handheld, and used in sterile fashion on the operating field. The RFLS also continuously measures distance of the probe from the Tag in millimeters.

Methods

This study was an institutional review board (IRB)-approved, prospective, single-institution pilot study. Patients over the age of 18 who required breast surgery for benign or malignant disease and required preoperative localization of a clip or non-palpable imaging finding were consented for the study between August 2017 and January 2018. Patients who were pregnant or breast-feeding or had multi-centric or Stage IV breast cancer were excluded. Informed consent was obtained from all individual participants included in the study.

The Food and Drug Administration (FDA)-approved RFLS is comprised of a Tag Applicator with a preloaded RFID Tag with a unique identifier, LOCalizer Reader, and Surgical Probe. The LOCalizer Reader transmits a weak unmodulated signal at 134 kHz that completes a circuit with the Tag enabling the LOCalizer Reader to detect the Tag. The Tag itself is passive and has no internal energy source, unlike the radioactive seed. The LOCalizer Reader measures distance in millimeters to the Tag, and Tag location is also indicated by an audible sound, of which the pitch and volume increases with proximity.

The RFLS Tag is intended for percutaneous placement in the breast to temporarily (< 30 days) mark a lesion intended for surgical removal. The LOCalizer Reader is portable and battery-operated and can be used on the operating field with the sterile Probe to locate the Tag and guide surgical excision of breast tissue around the Tag.

Consented patients underwent image-guided placement of the radiofrequency Tag by breast radiologists, either by mammographic or sonographic guidance, within 30 days of surgery. After placement, radiologists used the LOCalizer Reader to confirm appropriate placement and record the unique identifier of the Tag.

Patients and radiologists completed questionnaires anonymously in a private room immediately after the RFID Tag placement procedure and no later than 24 h. Adverse event reports were completed within 24 h of Tag placement for the first 25 patients.

The patients underwent surgery as planned, and the surgeons used the handheld LOCalizer Reader to locate the Tag during surgery and to measure the distance from the skin at the site directly over the Tag to determine Tag depth. Surgeons also recorded the radial distance of the Tag from the proposed incision site with a sterile ruler. Radiofrequency-guided surgery was then performed using the Surgical Probe to guide the dissection, measuring distance from the Tag in millimeters and using the audible cues to determine proximity to the Tag. Once the surgeon removed the specimen, a specimen radiograph was performed per standard protocol to confirm retrieval of the Tag and to evaluate for Tag migration based on comparison with post-placement radiography. Surgeons completed the surgeon questionnaire within 24 h of the breast surgery.

Primary endpoints for the study were percentage of patients with successful placement of the RFID Tag under radiographic guidance and successful retrieval of the Tag confirmed by specimen radiography. Secondary endpoints included patient, radiologist, and surgeon experience; percentage of patients with positive margins after lumpectomy; percentage of patients undergoing re-excision; volume of tissue removed; days prior to surgery of Tag insertion; and percentage of patients with Tag migration.

Data from all patients enrolled were included in the statistical analyses. Continuous variables were summarized with mean, standard deviation, median, and range. Categorical variables were summarized with frequency count and percentages. Exact confidence bounds were calculated for all endpoint proportions. For the three Likert questionnaires, a total score was computed for each and summary statistics (mean, standard deviation, median, range) were reported for the total score, and the summary statistics as well as the proportion of patients with each category 1,2,3,4,5 was calculated for each questionnaire item.

Table 1 Lesion and procedure characteristics

Variable	Category	# (% of 50)
Lesion diagnosis	Benign	17 (34.0)
	Cancerous	33 (66.0)
Pathology	Atypical ductal hyperplasia	3 (6.0)
	Fibroadenoma with atypia	1 (2.0)
	Benign phyllodes	1 (2.0)
	Glomus tumor	1 (2.0)
	Lobular neoplasia	1 (2.0)
	Papilloma	3 (6.0)
	Radial scar	5 (10.0)
	Stromal fibrosis	2 (4.0)
	DCIS	5 (10.0)
	DCIS with microinvasion	1 (2.0)
	Encapsulated papillary carcinoma	1 (2.0)
	Tubular carcinoma	4 (8.0)
	Invasive ductal carcinoma	19 (38.0)
	Invasive lobular carcinoma	3 (6.0)
Imaging modality	Mammogram	26 (52.0)
	Ultrasound	24 (48.0)

Results

Fifty-five patients were consented for the study and 50 completed treatment. Five patients were removed from the study prior to Tag placement because of either patient or surgeon considerations. Two surgeons enrolled most of the patients (49/50). The average patient age was 59.2 years. Most patients (33/50) had a diagnosis of breast cancer (Table 1), and the remaining were operated on for benign disease (17/50). Radiologists used mammogram (26/50) and ultrasound (24/50) almost equally for Tag placement. No adverse events occurred.

All 50 patients underwent successful placement and retrieval of the Tag (100%) with no migration identified. Tags were placed on average 1.4 days prior to surgery with the earliest placed 14 days prior. Average Tag depth was 1.9 cm with the greatest depth at 6.0 cm. Average radial distance of the Tag from the incision was 2.2 cm, with the greatest distance measured at 12.0 cm. Approximately 13.4 g of tissue and 30.7 cm^3 of tissue volume were removed. For patients with breast cancer (33/50), only 1 had a positive margin on final pathology (3.0%), and 2/33 underwent re-excision for a close or positive margin (6.1%) (Table 2). Volume of tissue removed did not differ significantly based on imaging modality used to guide placement of the Tag (mammogram, 27.4 cm^3 versus ultrasound, 34.4 cm^3, $p = 0.361$). However, as might be expected, more tissue was removed

Table 2 Endpoint summary

Primary endpoint	# (% of 50)	Exact CI[a]
Successful placement of RF Tag	50 (100)	92.9–100%
Successful retrieval of RF Tag	50 (100)	92.9–100%
Secondary endpoints—all patients	**# (% of 50)**	**Exact CI**
Migration of RF Tag	0 (0)	0–7.1%
	Mean ± Std	**Median [range]**
Days prior to surgery of insertion of Tag	1.4 ± 2.8	0.0 [0.0–14.0]
Closest depth measurement of Tag from skin (cm)	1.9 ± 1.1	1.8 [0.1–6.0]
Radial distance of Tag from incision (cm)	2.2 ± 2.1	2.0 [0.0–12.0]
Tissue weight (g)	13.4 ± 11.4	10.0 [1.6–60.0]
Tissue volume cm^3	30.7 ± 26.4	25.0 [3.8–159.3]
Secondary endpoints—patients with cancer	**# (% of 33)**	**Exact CI**
Positive margins on final pathology	1 (3.0)	0.1–15.8%
Patients with cancer requiring re-excision	2 (6.1)	7.4–20.2%

[a]Clopper Pearson 95% Exact Confidence Intervals for binary data

for a cancer diagnosis than for benign disease, and this was statistically significant (36.3 cm^3 vs. 20.0 cm^3, $p=0.013$).

Secondary endpoints also included patient and radiologist experience with image-guided placement of the RFID Tag and surgeon experience using the RFLS to guide surgical resection. The patient and physician assessments were captured using Likert-type questionnaires. Individual question responses for the patient and physician questionnaires ranged from 1 to 5 with a score of 5 representing the maximum positive or favorable response to each question (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree).

Most patients agreed or strongly agreed (94%) that the procedure went smoothly and agreed or strongly agreed (78%) that the procedure was easier than expected. Radiologists and surgeons suggested that the RFID Tag was as fast and reliable as the wire-localized procedure. Surgeons also generally agreed or strongly agreed that the distance gauge was helpful to guide the surgical dissection (Fig. 1). Patients who underwent ultrasound localization and radiologists who placed under ultrasound guidance had significantly more positive views of the process; the surgeon scores were not significantly different between the modalities.

Discussion

With the widespread use of screening mammography, significant breast lesions requiring surgical removal are often non-palpable and require preoperative localization to facilitate surgical removal. Localization methods using the standard wire, with its patient inconveniences and logistical inefficiencies, are quickly becoming anachronistic. As technology improves, wire-free localization methods are emerging that appear to offer advantages over standard wire and should be explored.

Our study is the first to prospectively evaluate a radiofrequency localization system in lieu of a wire to localize benign and malignant breast lesions for surgery. Unlike the radioactive seed, the RFID Tag is not radioactive, so special handling and tracking of the device and signal decay are of no concern. Radiofrequency technology is also already in widespread use outside of medicine, most commonly in the microchipping of pets for identification, and our study demonstrates that this technology can be effectively and safely applied for the localization of non-palpable breast lesions for surgery.

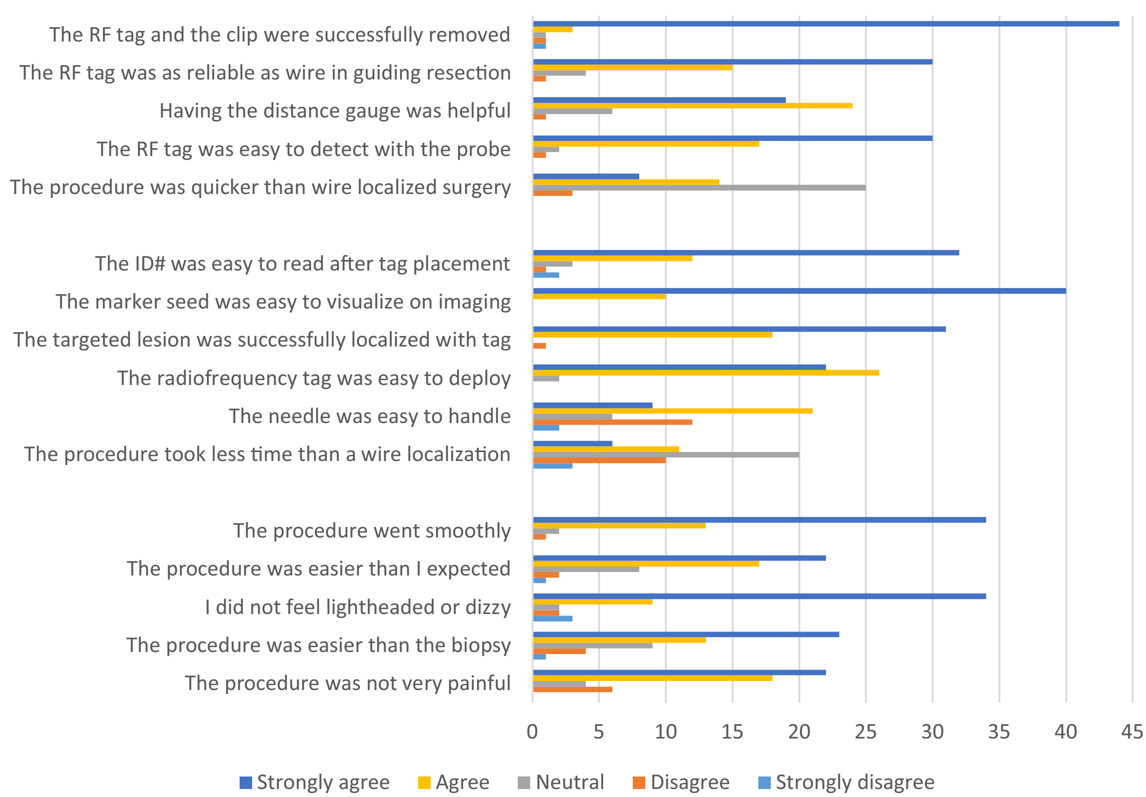

Fig. 1 Surgeon, radiologist, and patient responses to Likert questionnaires. Individual bars represent the number of responses out of 50 for each question with each color representing a different response. The blue bars depict "strongly agree" responses and the yellow bars represent "agree" responses

As a wire-free, non-radioactive alternative, the RFID Tag can be placed up to 30 days prior to surgery, which not only improves operating room efficiency but also provides more flexibility for patients in scheduling the localization procedure. Standard practice in the US necessitates placement of the radioactive seed within 5 days of surgery and, of course, radiologists must place the wire on the same day of surgery. In our study, patients underwent Tag placement as early as 14 days prior to surgery with successful retrieval and no migration noted. This ability to uncouple the localization procedure from the surgery also circumvents the very real problem with patient satisfaction of transporting a patient with a wire from the imaging center to the surgery suite, especially at centers where these two facilities are not co-located in the same building.

Our study also captured self-reported outcomes from patients, radiologists, and surgeons, which demonstrated that this technology is easy to adopt with good tolerance by patients and essentially no learning curve for the physicians. For the breast imagers, this procedure resembles placement of a biopsy microclip more than placement of a wire for pre-operative localization. For patients with cancer, the positive margin rate and need for re-excision was low. At the time of the study, the RFLS was the only technology that measured distance from the Tag in real-time, allowing for feedback and guidance to the surgeon during the surgical dissection. The surgeons found this to be a helpful feature, which may have contributed to the low positive margin rate noted in the study. The significance of this observation will need to be validated in a larger study.

To date, three primary non-radioactive alternatives to the wire exist that have been studied and each appears to perform similarly in terms of effectiveness in localizing the intended target for surgical removal. The SAVI Scout, Magseed, and now the RFLS all utilize a non-radioactive device the size of a grain of rice that can be placed completely within the breast. This allows uncoupling of the localization procedure from the surgery, and this alone has great potential for improving operating room efficiency and patient satisfaction. As we accumulate more data regarding safety and feasibility, wire-free localization options will undoubtedly become more suitable alternatives to explore.

From an institutional standpoint, the costs of adopting a wire-free approach could easily be shared between the surgical facilities and the imaging facilities. Both would benefit from this approach in terms of improving scheduling flexibility and operational flow, not to mention patient satisfaction. In terms of which technology to adopt, the subtleties of each system should be assessed and evaluated by the breast imagers and the breast surgeons at each institution. From our standpoint, the advantages of the RFLS include a pencil-sized probe which can be used in smaller incisions without obscuring visualization, and a portable, handheld reader that measures distance of the probe from the Tag and can be used directly on the operating field.

As a pilot study, our data demonstrate that the RFLS is an effective, non-radioactive, wire-free alternative for localizing breast lesions for surgery and is a suitable alternative to wire localization for patients requiring breast surgery. RFLS should be considered by surgeons and institutions who prefer a wire-free approach.

Conclusion

Radiofrequency technology to localize non-palpable breast lesions for surgery is an effective and desirable non-radioactive alternative to the wire and appears to have some user advantages over the other wire-free approaches.

Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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