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ORIGINAL ARTICLE – BREAST ONCOLOGY

# Ultrasound-Guided Segmental Mastectomy and Excisional Biopsy Using Hydrogel-Encapsulated Clip Localization as an Alternative to Wire Localization

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## ABSTRACT

**Background.** Wire localization is currently the most widely used localization strategy for excision of nonpalpable breast lesions. Its disadvantages include patient discomfort, wire-related complications such as wire displacement/fracture, and operating room delays related to difficulties during wire placement. We have implemented the technique of intraoperative ultrasound-guided excision using hydrogel-encapsulated (HydroMARK) biopsy clips for lesion localization. We hypothesize that this method is as effective as wire localization for breast conserving therapy.

**Methods.** This is a retrospective review of 220 consecutive patients who underwent segmental mastectomy or excisional biopsy using wire localization or hydrogel-encapsulated clip localization from January 2014 to July 2015. Data were collected and analyzed. Statistical analyses for differences between groups were performed using *t* tests and Mann-Whitney rank-sum analyses.

**Results.** A total of 107 excisions were performed using hydrogel-encapsulated clip localization, and 113 excisions were performed using the traditional wire localization technique; 68 % of our patients underwent excision for malignant pathology. Wire placement took a mean of 46 minutes (range 20–180 min), compared with 5 minutes for ultrasound localization ($p < .001$). Successful intraoperative ultrasound localization and excision was performed on 100 % of patients. There was no difference in re-excision rates for positive margins or overall specimen size between the two groups.

**Conclusions.** Intraoperative ultrasound-guided excision of nonpalpable breast lesions using a hydrogel-encapsulated biopsy clip for breast conserving therapy is a safe and feasible alternative to the traditional preoperative wire localized excision. This technique will lead to improvement in patient experience, operative efficiency, and alleviate wire-related complications.

With the continued emphasis on breast cancer screening and the improvements in breast imaging technology, including the use of breast MRI, there has been an increase in the detection of nonpalpable breast lesions.[1,2] Currently, wire localization (WL) is the most common method used to localize nonpalpable breast lesions for surgical excision and is considered the gold standard.[3,4] There are numerous disadvantages to the WL technique including the need for an additional procedure the day of surgery, patient discomfort and distress, wire-related complications such as migration, fracture, or transection, as well as technical challenges during placement that lead to operative delays and interference with the surgical approach.[4,5] Several alternative strategies to WL have been proposed in the literature including radioactive seed localization (RSL), hematoma-guided and ultrasound (IOUS)-guided excision (HUG), and radio-guided occult lesion localization (ROLL). Similar to WL, there are several disadvantages to these techniques, including the unpredictability of locating the target hematoma in HUG either from no primary hematoma formation or subsequent hematoma resorption, as well as the persistent need for additional procedures in patients undergoing RSL, with the additional need to implement a process to handle and dispose of the radioactive seeds.[3,6]



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To overcome these challenges, our institution has implemented the technique of intraoperative ultrasound (IOUS)-guided excision using hydrogel-encapsulated (HydroMARK) biopsy clips. The HydroMARK clip is a biopsy clip placed at the time of the initial breast biopsy either stereotactically or sonographically. Once inserted, the clip absorbs water molecules from the surrounding breast tissue creating the formation of a hydrogel. The hydrogel creates an anechoic structure surrounding the clip allowing it to be visible on US and T2 weighted MRI for up to 15 months after its placement.[7] We hypothesize that this method is as effective as WL for excision of nonpalpable breast lesions. Additionally, using this method will lead to improvement in patient experience, perioperative workflow, and alleviate WL related complications.

## METHODS

This is an institutional review board approved retrospective review of all patients at a single institution who underwent either segmental mastectomy or excisional biopsy using WL or hydrogel-encapsulated clip localization between January 2014 and July 2015 for nonpalpable breast lesions. To be eligible for US-guided excision, the patient had to have had a hydrogel-encapsulated clip placed at the time of initial core needle biopsy. Whether the patient underwent US-guided excision versus WL excision was decided based on the presence of a hydrogel-encapsulated clip (HydroMARK) visible on US.

For WL, a standard technique was performed.[8] A wire was placed preoperatively in the radiology department under mammographic, US, or MRI guidance. The patient was taken to the operating room with the wire in place, and excision was performed using post-WL mammographic images for guidance. Specimens were sent for standard specimen radiograph to ensure removal of the complete wire, clip, and lesion if visible.

For the US-guided technique, the surgeon and radiologist together marked the lesion preoperatively using US to ensure visibility of the clip placed at the time of the original biopsy. The patient was then taken to the operating room; the clip was identified intraoperatively prior to incision with a sterile linear array US transducer. The margins of the lesion were mapped out on the skin surface with careful attention paid to depth of lesion. This is done by marking the ends of the transducer in both the transverse and longitudinal planes. An incision was subsequently made overlying the lesion of interest, in a cosmetically appropriate position, and skin flaps were developed based on lesion depth. The US probe was then switched to a hockey stick or finger transducer and placed within the breast flaps to facilitate the creation of margins on all sides of the lesion using either sharp or electrocautery dissection. The specimen was delivered from the cavity, and the ultrasound was used to confirm the clip is within the specimen and that margins are adequate. The specimen was oriented, and a specimen radiograph was obtained for confirmation that the biopsy clip and, if visible, the lesion of interest was removed. Additional shave margins were taken at the discretion of the operating surgeon based on type of malignancy and proximity of the lesion to the breast margins based on specimen radiograph.

Patient characteristics and demographic data were collected and analyzed, including data on margin status, specimen size, need for re-excision, complications, recurrence, procedure time for preoperative lesion localization, as well as use of neoadjuvant systemic therapy. Margins greater than 2 mm were routinely used for DCIS excision, and "no tumor present on ink" was used for invasive cancer. Statistical analyses for differences between groups were performed using *t* tests and Mann–Whitney rank-sum analyses when appropriate.

## RESULTS

A total of 220 consecutive patients underwent segmental mastectomy or excisional biopsy between January 2014 and July 2015. All patients with a hydrogel-encapsulated clip placed at the time of the initial breast biopsy were eligible for US-guided excision. After instituting the use of the hydrogel clip at our institution, all patients underwent placement of the hydrogel clip at the time of biopsy. Patients who underwent wire localization after implementation of the hydrogel clip were often patients who were biopsied at an outside institution with a standard clip, required bracketing of microcalcifications, or had clip migration at the time of initial biopsy. There were 107 excisions performed using hydrogel-encapsulated clip localization, and 113 excisions were performed using the traditional WL technique; 68 % of patients underwent excision for malignant pathology. There were no differences in patient or lesion characteristics between groups (Table 1). In 96 % of our patients, the HydroMARK clip was successfully visualized and in the appropriate position preoperatively. Four patients were converted from US localization to WL.

The average amount of time required for a single WL procedure was 46 min (range 20–180 min), compared with 5 min for US procedure (range 3–6 min) ($p < .001$) (Table 2). Successful intraoperative US localization and excision was performed on 100 % of patients, as confirmed by biopsy-site changes and pathology on permanent sections. There was no difference in the rate of re-excision for margin positivity or complications between patients undergoing traditional WL techniques compared with hydrogel-encapsulated clip guided excision (Table 2).

**TABLE 1** Patient and lesion characteristics

| | Wire localization | Intraoperative US-guided | *p* value |
|---|---|---|---|
| Age (mean) | 59.3 | 58.4 | .321 |
| Lesion type | | | .850 |
| Invasive cancer | 50 | 48 | NS |
| Ductal carcinoma in situ | 25 | 22 | NS |
| Benign | 38 | 37 | NS |
| Neoadjuvant | 8 | 5 | .452 |
| Follow-up, in months, median (range) | 12.5 (1–18) | 6 (1–19) | |

*NS* nonsignificant

**TABLE 2** Results

| | Wire localization | Intraoperative US-guided | *p* value |
|---|---|---|---|
| Number of excisions | 113 | 107 | |
| Re-excision rate (%) | | | |
| Malignant | 14 % | 16 % | .653 |
| DCIS | 39 % | 40 % | .796 |
| Complications (wound infection, hematoma, seroma) | 10 | 5 | .221 |
| Preoperative localization procedure time, in minutes, mean (range) | 46 (20–180) | 4.7 (3–6) | <.001 |

*NS* nonsignificant

There was no difference in re-excision rate between surgeons performing the procedure, nor was there difference in re-excision rates when comparing the first 9 months compared with the last 9 months of the study period.

The median follow-up was 12.5 months (range 1–18 months) for the WL group and 6 months (range 1–19 months) for the US group (Table 2). There were 5 patients who had the hydrogel-encapsulated clip placed at the time of their initial biopsy who subsequently underwent neoadjuvant chemotherapy, and 100 % of those patients were able to undergo successful intraoperative localization and excision of their lesion, on average 6.8 months (range 5.5–7.5 months) from time of biopsy (Fig. 1). We were unable to assess the specimen size as only 46 and 61 % of patients in the WL and US groups, respectively, had the lesion weight recorded in the pathology report.

## DISCUSSION

With more women undergoing routine breast cancer screening, early detection of nonpalpable breast lesions and early breast cancers is more common. Wire localization is currently the most widely used preoperative localization strategy for the excision of nonpalpable breast lesions and is considered the gold standard treatment.[3] The disadvantages of WL have been frequently discussed in the literature and include wire dislocation, migration, or fracture, the need for a separate procedure, scheduling difficulties when coordinating with the radiology department, as well as patient distress and discomfort.[4,9] Several alternative strategies to WL have been proposed. The 3 most prominent have included radio-guided occult lesion localization (ROLL), radioactive seed localization (RSL), and various methods of ultrasound-guided excision including the hematoma-guided excision (HUG) technique.[4,10,11] Although there have been no randomized controlled trials examining the efficacy of WL excision versus other techniques, there have been several meta-analyses, prospective analyses, and systemic reviews performed in the last decade that have proven these techniques to be as effective, if not superior to WL excision for nonpalpable breast lesions.[1,4]

Several recent articles have shown that RSL has comparable, if not superior, outcomes to WL for preoperative breast lesion localization when comparing rates of margin negativity and need for reoperation for close or positive margins.[1,5,12,13] Although RSL has been effective in eliminating many of the common disadvantages inherent to the WL technique, there are several downsides related to RSL that persist, which we believe are mitigated using IOUS-guided excision with the hydrogel encapsulated clip. Such downsides of RSL include an additional procedure performed prior to the surgery (usually 1–7 days) where an 18-gauge needle is used to inject the seed under either US or mammographic guidance, as well as the inability of patients to be in close proximity to infants, young children, or animals during the interval between radioactive seed placement and excision, both of which negatively affect patient experience. Furthermore, all surgeons, pathologists, and facilities involved in handling the seeds must have specific licensing and approval to do so, and protocols must be in place to track the seeds and dispose of nuclear material appropriately.[13]

Ultrasound-guided excision of nonpalpable breast lesions without hydrogel encapsulated clips has also been described in the literature both for lesions visible on US and using the HUG technique, in which the hematoma that is created at the time of initial biopsy is used to localize the lesion either preoperatively or intraoperatively for excision.[14,15] Downsides to this procedure are the resorption of the hematoma tends to occur in an average of 14 days and most hematomas are nearly completely absorbed by 5 weeks, making this form of localization unreliable for patients undergoing surgery outside of this time frame,

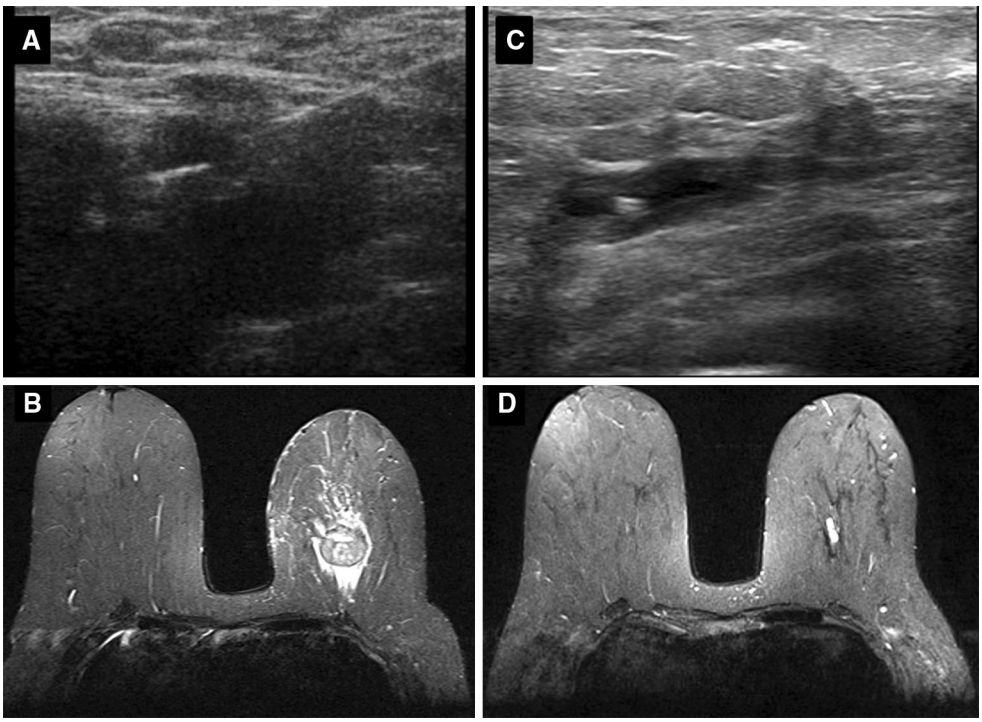


**FIG. 1** **a** Placement of hydrogel-encapsulated clip at time of initial US-guided biopsy. **b** Pre-neoadjuvant chemotherapy T2 weighted MRI image of clip within mass. **c** US image of clip at time of surgical marking day of surgery. **d** Post-neoadjuvant chemotherapy T2 weighted MRI image of clip without residual mass

such as neoadjuvant therapy patients.[16] Furthermore, these techniques have not been used in women who have multiple lesions biopsied in a single breast, due to the concern for incorrect lesion localization for excision. Ultrasound localization using hydrogel-encapsulated clip localization mitigates these downsides, as the hydrogel-encapsulated clip is typically visualized by ultrasound for 12–15 months, meaning that it can be placed prior to neoadjuvant chemotherapy.[7] The marker is also visualized by MRI during the T2 sequencing phase (Fig. 1), as well as being visible on standard specimen radiographs, which allows better evaluation of margin status in the operating room. Furthermore, this technique can be used to excise multiple lesions in the same breast or for en bloc resection of multifocal cancers.

The HydroMARK clip was originally developed in order to aid in wire localization and seed placement procedures for WL and RSL breast excision as an alternative to the use of mammography, as mammography is often more uncomfortable for the patient, as well as slower than US guidance. Surgeons have since realized that IOUS-guided excision using the clip alone may be feasible. Klein, et al. published a small series of 25 patients who underwent excision of nonpalpable breast lesions utilizing the HydroMARK clip and localization with IOUS, although only 6 patients underwent excision using IOUS alone.[9] Klein et al. reported migration or extrusion of the marker through the biopsy tract in half of the cases, which we did not experience in our series, likely secondary to improved clip design.[9] Furthermore, Blumencranz et al. published a large retrospective review of patients who underwent partial mastectomy and showed that the use of wire localization was more frequent in patients with standard biopsy markers placed, compared with those who had a hydrogel marker placed at the time of initial biopsy; however, hydrogel-guided excision was superior to wire localization.[17]

We believe that US-guided excision using the hydrogel-encapsulated clip provides an efficacious and precise method for preoperative localization of nonpalpable breast lesions. There are several small series in the literature that report the successful excision of benign and malignant lesions visible on US using IOUS alone; however, most of these involve excising lesions that are visible by US.[3,15,18–20] In 2009, James et al. reported a cohort study in which 93 patients with DICS were excised under IOUS guidance alone, using biopsy site changes or visible clips for guidance.[20] We report the largest series to date of patients undergoing IOUS-guided excision for both benign and malignant disease using a biopsy marker alone, rather than the lesion itself. We were successful in excising invasive and in situ cancer with similar re-excision rates to WL (Table 2). We have also demonstrated that we can successfully excise microcalcifications, tumors after neoadjuvant therapy, as well as lesions not

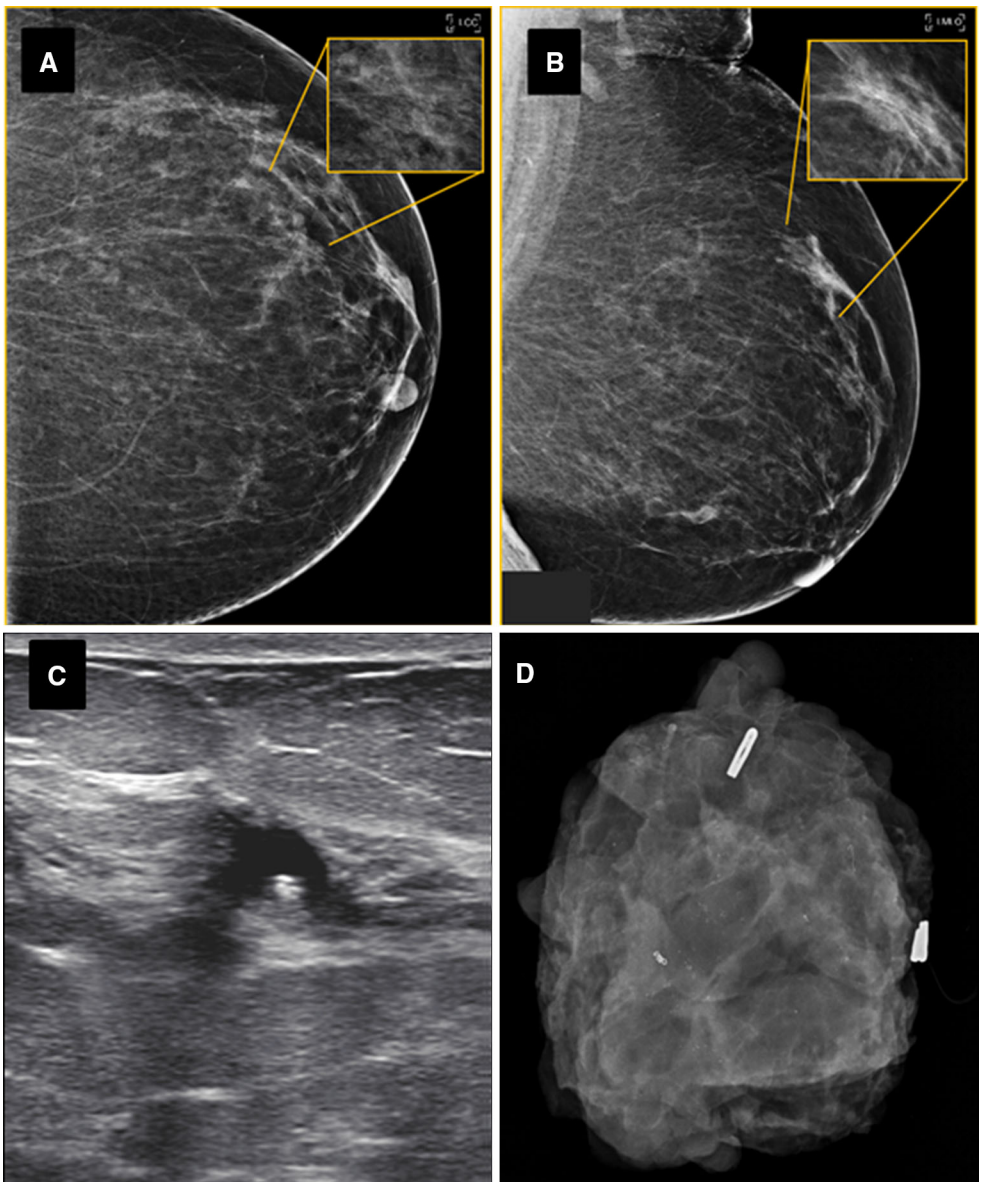


**FIG. 2** Successful use of the HydroMARK excision in a lesion that was not visible on US. **a** Diagnostic cranio-caudal (CC) view. **b** Diagnostic medio-lateral-oblique (MLO) view with magnification views showing suspicious microcalcifications. Core needle biopsy demonstrated ADH. **c** Preoperative US marking image of HydroMARK biopsy clip and lesion that is not visible by US. **d** Specimen radiograph after excision

visible on US (Fig. 2). In our series, 100 % of the lesions were successfully excised as evidenced by biopsy site changes or primary lesion presence in the specimen. We did not have postexcision-related complications. There was no difference in re-excision rates among the 2 surgeons performing the procedure, and there was not a steep learning curve that demonstrates the ease of clip utilization and implementation. Moreover, ultrasound courses are incorporated into general surgery training, fellowship training, as well as offered by national surgical societies that facilitate the comfort and use of bedside and intraoperative ultrasound.[21] Furthermore, ultrasound facilitates the creation of a uniform and precise specimen and likely reduces the amount of excessive benign breast tissue excised, in addition to offering the ability for improved cosmesis as incision can be made in an aesthetic location on the breast rather than guided by the location of the wire.

All in all, intraoperative ultrasound-guided excision of nonpalpable breast lesions using a hydrogel-encapsulated biopsy clip for breast conserving therapy is a safe and feasible alternative to the traditional preoperative wire localization excision. We believe this technique eliminates the need for extra procedures in the weeks prior to surgery, eliminates potential delays related to wire placement the

day of surgery, improves operating room efficiency, and most importantly improves patient experience.

**AUTHORS CONTRIBUTION** LFG contributed to the collecting and analysis of data and interpretation, conception, design, composition, drafting, and editing of the manuscript. AH contributed to data collection and editing of the manuscript. CMS contributed to conception, design, participated in procedures, and to the editing of the manuscript. AB contributed to IRB submission and approval process. EV contributed to the conception, design, and editing of the manuscript. JM contributed to the conception, design, and manuscript editing. LRPS contributed to the conception and design of the manuscript, data analysis and interpretation, and the composition/editing/writing of the manuscript.

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