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Original Research

Preoperative Localization of Breast MRI Lesions: MRI-guided Marker Placement With Radioactive Seed Localization as an Alternative to MRI-guided Wire Localization

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Abstract

Objective: Preoperative MRI-guided wire localization (MWL) presents challenges to both the physician and patient. In this study, we examined the efficiency and outcome of MRI-guided marker placement followed by mammographic-guided radioactive seed localization (MMP/RSL) as an alternative localization method. The primary outcome parameter was pathology upon excision. The secondary outcome parameters were total procedure time and clinical indication for localization.

Methods: A retrospective review of a large tertiary cancer center's breast imaging database was performed. Records of 21 patients with MMP/RSL (24 markers) from August 2013 to January 2019 were compared with 34 patients receiving MWL (48 wires) from January 2016 to January 2019. Multiple factors, including age, prelocalization pathology, postsurgical pathology, concordance, re-excision rates, and total procedure time required for each technique, were compared. Univariate and descriptive statistical analyses were performed.

Results: Mean patient age in years (MMP/RSL = 54.1 ± 13.1, MWL = 55.1 ± 10.8, $P = 0.389$), time in MR scanner in minutes (MMP/RSL = 31.7 ± 12.0, MWL = 35.8 ± 13.1, $P = 0.678$), and postsurgical pathology malignancy rates (MMP/RSL = 71.4%, MWL = 65.7%, $P = 0.7715$) were similar without statistically significant differences. As expected, the mean total procedure time was slightly longer without a statistically significant difference (47.3 ± 19.8 min versus 35.8 ± 13.1 min, $P = 0.922$) for the MMP/RSL group. All patients in both groups underwent successful localization with 100% radiologic-pathology concordance. Re-excision rates were lower for the MMP/RSL group (9.5%) versus the MWL group (16.7%); however, they were not found to be statistically significant ($P = 0.7104$).

Conclusion: MMP/RSL is a feasible alternative to MWL and may alleviate many challenges presented by MWL. Further studies are needed.

Key words: wire localization; radioactive seed localization; breast cancer; breast surgery; breast magnetic resonance imaging.

Introduction

Improvements in breast cancer detection have led to a steady increase in the number of breast cancer patients with nonpalpable breast disease (1). Consequently, in recent years, more women are opting for breast conservation surgery for many of these earlier stage breast cancers (2–5). The

Key Messages

- Preoperative MRI-guided marker placement followed by radioactive seed localization is a feasible alternative to MRI-guided wire localization.
- While mean procedure time to perform MRI-guided marker placement followed by radioactive seed localization is longer, the difference is not statistically significant, and other patient/physician benefits outweigh this potential drawback.
- While highly suspicious lesions ipsilateral to a known cancer yielded malignancy in 75% of cases on surgical excisional biopsy, a thoughtful clinical approach to such lesions and further study is advised.

challenge for the radiologist and surgeon is to accurately localize the nonpalpable lesions for optimal surgical outcome.

Wire-guided localization (WL) has been the standard of care for preoperative localizations and is widely used (6, 7); however, it has several disadvantages, including a wide range of positive margin rates and potential for wire migration prior to and during surgery (8). A less often discussed limitation is the tedious coordination between multiple departments (radiology, surgery, anesthesia, etc.) and operating room schedules (9). Due to the disadvantages of WL, various alternative methods have been investigated (10, 11). Radioactive seed localization (RSL) with a radioactive iodine-125 seed has been demonstrated to be an effective alternative to WL for guiding breast conservation surgery of nonpalpable breast cancer (12, 13). First described by Gray et al in 2001 (12), RSL was found to be at least equivalent to WL in terms of surgical technical ease, volume of breast tissue excised, and avoidance of reoperation. RSL also allows for more flexibility in scheduling, as the seed can be inserted up to 30 days prior to surgical excision given its 60-day half-life; however, it is most commonly inserted up to 5 days prior to surgery in the United States (9).

There are occasions where MRI is necessary to guide localization. In such occasions, MRI-guided wire localization (MWL) is performed, most often on the day of surgery. MWLs are warranted preoperatively, particularly in cases in which disease extent is underestimated on either ultrasound and mammography, in which there is biopsy marker migration, or in which marker deployment was not previously performed at the time of MRI-guided biopsy. MWL may also be a viable alternative if a lesion is not technically amenable to MRI-guided biopsy due to the location or size of the breast (14).

To date, there is a paucity of literature on MRI-guided nonwire localizations, with only a single case report describing MRI-guided radioactive seed placement (15). The hypothesis for this study is that while preoperative MWL presents many limitations to the physician, ancillary staff, and patient, MRI-guided marker placement followed by mammographic-guided radioactive seed localization (MMP/RSL) may prove to be an effective alternative to alleviate some of these limitations. Thus, the objective in this study was to examine the efficiency and outcome of MMP/RSL compared with the standard practice of MWL. The primary outcome parameter was pathology upon excision. The secondary outcome parameters were total procedure time and clinical indication for localization.

Methods

An institutional review board–approved, Health Insurance Portability and Accountability Act–compliant retrospective review of breast imaging records was performed from August 2013 to January 2019, yielding 21 patients who underwent MMP/RSL (24 markers total). For the WL group, consecutive breast records from January 7, 2016, to October 10, 2018, were evaluated with 34 patients who underwent MWL (48 wires total) (Table 1). Two patients in the WL group with outside localization images were excluded because time stamp data was not included on the available images.

One patient who underwent MMP was excluded because the patient ultimately opted for mastectomy, so localization was deferred. All other marker placements followed by localizations were included.

All localizations included were performed by fellowship-trained breast radiologists with years of practice ranging from 2 to 22.

Medical records were reviewed for demographic information, clinical indication for localization, pathology prior to localization (if available), target of localization, postsurgical specimen pathology, need for re-excision, and rad-path concordance.

Time (in minutes) within the MRI scanner was calculated by subtracting the time on the last MR image from the time on the first MR image. For the MMP/RSL group, total procedure time (in minutes) was calculated by adding the time required to perform the radioactive seed localization to the time in the MRI scanner. Radioactive seed localization time was calculated by subtracting the time on the last postradioactive seed localization mammogram from the time on the first scout image taken during the RSL. Time was calculated inclusive of all localizations, meaning the times were taken based on the first and last images of the procedure regardless of whether it was a single or multiple site marker placement or localization.

Statistical Analysis

Descriptive statistics were computed for the two groups. Means, standard deviations, and ranges were calculated for continuous variables. Frequencies and percentages were computed for categorical variables.

Univariate analysis was performed to determine associations between the type of localization and each outcome of interest. Wilcoxon rank sum test and *t*-test were used to compare continuous variables between the two localization groups. Fisher's exact test was used to compare categorical

Table 1. Patient Characteristics

Characteristic	MMP/RSL Group (*n* = 21 patients)	MWL Group (*n* = 34 patients)	*P*-value
Age (years)			
Mean ± SD	54.1 ± 13.1	55.1 ± 10.8	.389
Range	29–76	35–86	
Time (min)			
In MRI scanner	31.7 ± 12.0	35.8 ± 13.1	.678
In RSL	15.6 ± 9.4	n/a	
Total procedure time (min)	47.3 ± 19.8	35.8 ± 13.1	.922

Abbreviations: MMP, MRI-guided marker placement; MWL, mammographic-guided wire localization; n/a, not applicable; RSL, radioactive seed localization.

variables between the two localization groups with a level of statistical significance being $P < 0.05$. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

In total, there were 21 patients (mean age 54.1 years, range 29–76) with 24 sites localized by MMP/RSL (Tables 1 and 2) (Figures 1 and 2). These patients were compared with 34 patients (mean age 55.1, range 35–86) with 48 sites localized by MWL.

Eleven patients had multiple marker or wire localizations (Table 2). Of the 11 patients, 9 patients had bracketing with pathology reported as a single lumpectomy site. For this reason, we reported these localizations as a single final pathology. The two remaining patients (both in the MWL group) had localizations that were reported as two separate pathology sites. The first patient had a two-site bracketing of a known left invasive lobular carcinoma and noncontiguous but adjacent nonmass enhancement. This patient also had suspicious nonmass enhancement in the right breast that was localized for excisional biopsy at time of the left lumpectomy. The right nonmass enhancement returned benign results, and this three-site wire localization was reported as two separate pathologies, one malignant (left) and one benign (right). The second patient had known right ductal carcinoma in situ (DCIS) with a displaced biopsy marker and a more posterior mass, both localized with wires. Both the DCIS and mass returned DCIS and invasive ductal carcinoma, respectively, and this was reported as two separate pathology sites. Final pathology results totaled 21 for the MMP/RSL group and 36 for the MWL group. Imaging and pathology concordance were determined by the breast radiologist who performed the localization procedure.

Clinical Indication for Localization

Indications for MRI-guided localization are listed in Table 3. The most common reasons for MRI-guided localization were biopsy marker migration or nondeployment at the time of MRI-guided biopsy (29.2% MWL vs. 16.7% for MMP/RSL) and bracketing of confluent nonmass enhancement with known cancer or high-risk lesion (37.5% MWL vs. 45.8% MMP/RSL). Another common reason was to localize a target that was highly suspicious for a satellite lesion seen on MRI only (12.5% MWL vs. 25% MMP/RSL). There was no significant difference in localization indication between the two localization groups ($P = 0.666$).

Table 2. Number of Localizations Per Patient

	MMP/RSL Group (*n* = 21 patients) (%)	MWL Group (*n* = 34 patients) (%)
Number of localizations per patient		
1	19 (90.5)	25 (73.5)
2	1 (0.05)	5 (14.7)
3	1 (0.05)	3 (0.09)
4	0 (0.00)	1 (0.03)
Total localizations	24	48

Abbreviations: MMP, MRI-guided marker placement; MWL, mammographic-guided wire localization; RSL, radioactive seed localization

Sixteen of the 21 patients who underwent MMP/RSL had the procedures simultaneously on the same day. One of the five patients without same-day localization following marker placement received neoadjuvant chemotherapy prior to surgery (Figure 1). Two patients had MRI-guided biopsies separate from their known cancers, where a marker was additionally placed at the known cancer (displaced original marker) and at a highly suspicious satellite nodule. One patient had the marker placed at our institution and then had it localized and excised at an outside institution by our surgeon. One patient had 10 days in between marker placement and localization for unknown reasons.

Table 3 also shows the final pathologic outcomes by MR localization indication. In 32 lesions, a biopsy of a BI-RADS 4 (suspicious) or 5 (highly suspicious) lesion was deferred in favor of surgical excision, and the lesion was localized with surgical pathology showing malignancy in 24/32 (75%) of the lesions as listed in Table 3. The lesions considered suspicious or highly suspicious were masses or areas of nonmass

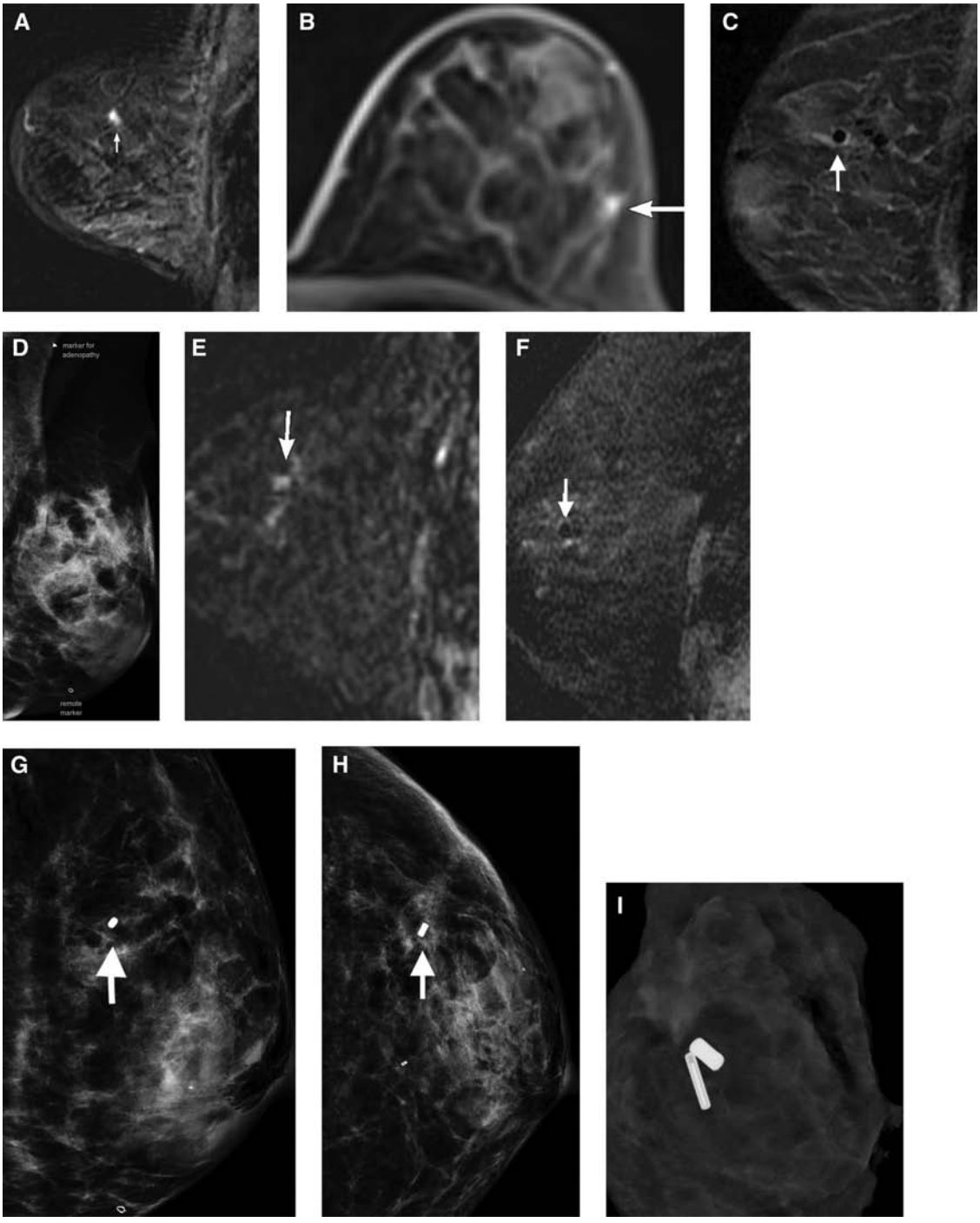

Figure 1. 49-year-old female presented with a palpable left axillary mass. Fine-needle aspiration yielded metastatic invasive lobular breast cancer without suspicious findings on mammography or ultrasound. Postcontrast sagittal (**A**) and axial (**B**) T1 image shows focal clumped nonmass enhancement (arrows). Sagittal image from MRI-guided biopsy performed at an outside institution (**C**) demonstrates introducer at target (arrow), but postprocedure mediolateral oblique mammogram (**D**) shows no biopsy marker deployment from MRI biopsy. Of note, marker in the axilla denotes a metastatic lymph node and marker in the inferior breast is from a remote biopsy. Scout postcontrast sagittal T1, fat saturated image (**E**) from MRI-guided marker placement demonstrates residual nonmass enhancement (arrow). Subsequent sagittal image (**F**) demonstrates introducer at target (arrow). Postprocedural mammogram mediolateral (**G**) and craniocaudal (**H**) views show deployment of cork marker in the expected location (arrow). Specimen radiograph (**I**) contains the radioactive seed and cork marker.

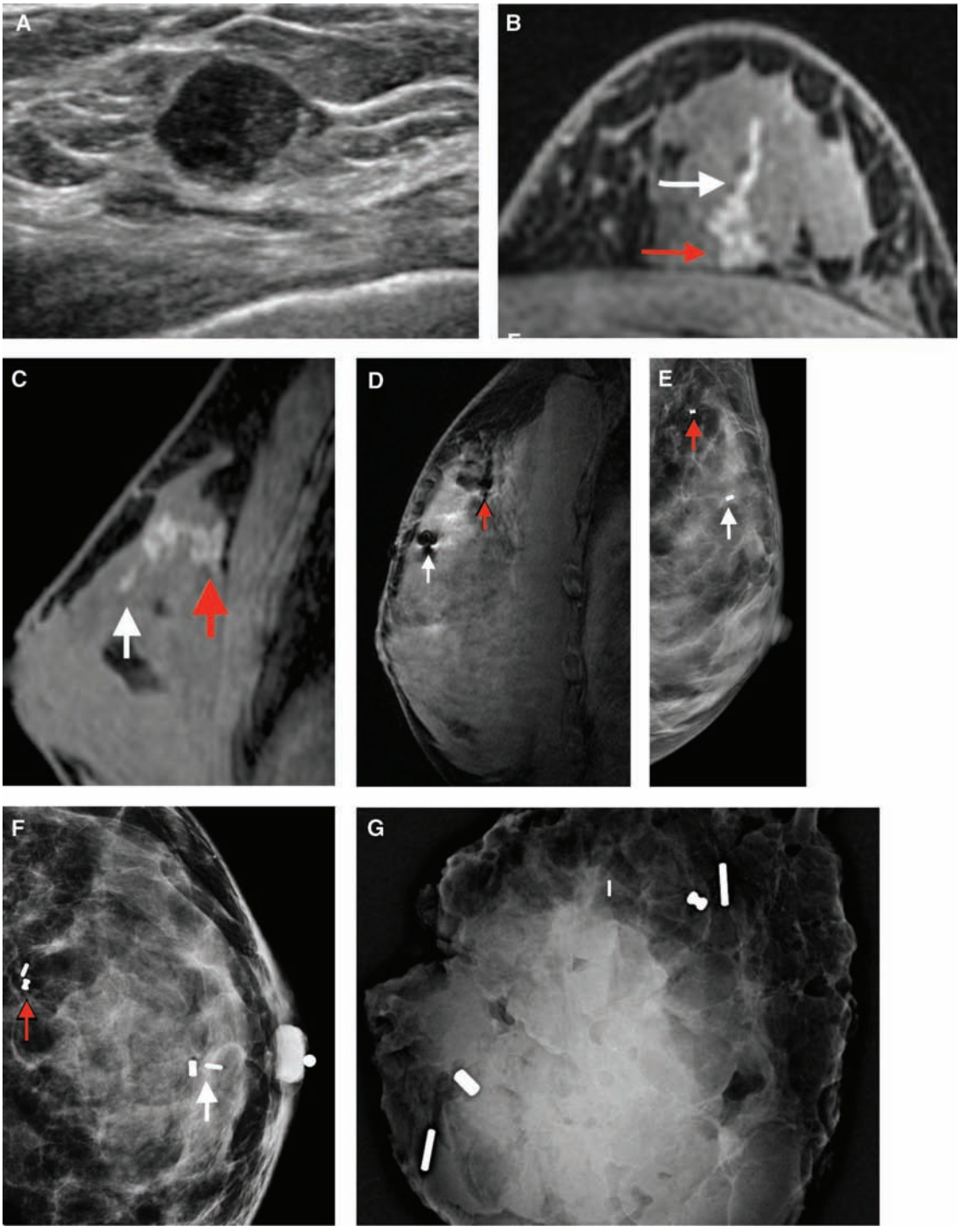

Figure 2. 61-year-old female presented to an outside institution with a palpable left breast mass. Ultrasound (**A**) shows an irregular hypoechoic mass corresponding to palpable abnormality. Ultrasound-guided core-needle biopsy yielded invasive ductal carcinoma. Per report, no marker was placed at the time of biopsy given the palpable nature of mass. Subsequent MRI postcontrast axial (**B**) and sagittal (**C**)T1 images demonstrate an irregular homogenously-enhancing mass (red arrow) with contiguous linear nonmass enhancement (white arrow). Sagittal image (**D**) from MRI-guided marker placement demonstrates two introducers at the mass (red arrow) and anterior aspect of nonmass enhancement (white arrow). Postprocedural mammogram mediolateral view (**E**) shows deployment of cork (white arrow) and hourglass (red arrow) markers in the expected locations. Subsequent mammographic radioactive seed localization (**F**) was performed with seeds adjacent to cork (white arrow) and hourglass (red arrow) markers. Specimen radiograph (**G**) contains both radioactive seeds as well as hourglass and cork markers.

Table 3. Indications for MR Localization

Indication	MMP/RSL Localizations (*n* = 24) (%)	MWL Localizations (*n* = 48) (%)	*P*-value	Final Pathologic Outcome: Benign (*n* = 19) (%)	Final Pathologic Outcome: Malignant (*n* = 38) (%)	*P*-value
Displaced biopsy marker OR no marker deployment	4 (16.7)	14 (29.2)	0.666	5 (0.26)	11 (0.29)	.001
Suspicious mass/NME						-
Suspicious mass/NME bracketing confluent with known cancer/high-risk lesion	11 (45.8)	18 (37.5)	-	1 (0.05)	18 (0.47)	-
Suspicious mass/NME along prior lumpectomy site at follow-up imaging OR along known positive margin	1 (0.04)	4 (8.33)	-	5 (0.26)	2 (0.05)	-
Suspected satellite lesion	6 (25.0)	6 (12.5)	-	2 (0.11)	4 (0.10)	-
Excisional biopsy						-
Suspicious lesion in contralateral noncancer breast	0	2 (4.16)	-	3 (0.16)	0 (0.00)	-
Suspicious lesion in ipsilateral breast with high-risk lesion	0	1 (2.08)	-	1 (0.05)	2 (0.05)	-
Position not amenable to biopsy	2 (0.08)	3 (6.25)	-	2 (0.11)	1 (0.03)	-

Abbreviations: MMP, MRI-guided marker placement; MWL, mammographic-guided wire localization; RSL, radioactive seed localization; NME, non-mass enhancement; OR, operating room.

enhancement confluent with known cancer (Figure 2) or high-risk lesion (18/19 [94.7%] were malignant), masses or areas of nonmass enhancement along prior lumpectomy site at follow-up imaging and/or along known positive margin (2/7 [28.6%] were malignant), and suspected satellite lesions (4/6 [66.7%] were malignant). The small sample size limited the power to detect statistically significant associations or make definitive conclusions.

Procedure Time

MRI-guided marker placement followed by mammographic-guided radioactive seed localization was performed successfully in all 24 lesions (100%). MRI-guided wire localization was performed successfully in all 48 lesions (100%). As shown in Table 2, the average time in the MRI scanner to perform the MRI-guided marker placement was 31.7 ± 12.0 minutes, compared with an average of 35.8 ± 13.1 minutes to perform MWL. Total average procedure time for the MMP/RSL group was slightly longer given that the additional radioactive seed localization procedure took an average of 15.6 ± 9.4 minutes. The overall mean total procedure time for the MMP/RSL group was 47.3 ± 19.8 minutes, and the overall mean total procedure time for the MWL group was 35.8 ± 13.1 minutes ($P = 0.922$).

Margin Outcomes/Re-excision

Two patients from the MMP/RSL group and 9 patients from the MWL group had multisite localizations, for a total of 11 multisite localizations (Table 2). As detailed above, 9 of the 11 multisite patients were performed for bracketing and were reported as a single pathology site at final lumpectomy, and in total, there were 21 final pathology results for the MMP/RSL group and 36 for the MWL group.

As shown in Table 4, prelocalization pathology was available for 6/21 of the MMP/RSL targets and 19/36 of the MWL targets. At final pathology, 15/21 (71.4%) of the MMP/RSL targets were malignant and 6/21 (28.6%) were benign, while 23/36 (63.9%) of the MWL targets were malignant and 13/36 (36.1%) were benign. Rad-path concordance was 100% for both groups. Re-excision due to positive margins was performed in 9.5% (2 patients) and 16.7% (6 patients) of the MMP/RSL and MWL groups, respectively.

Discussion

In the setting of conservative breast surgical management, precise preoperative tumor localization is important to facilitate adequate breast conservation surgery with clear margins. Compared with wire localization, nonwire localization has proven to be noninferior in surgical outcomes (11, 16, 17) while proving beneficial in overcoming limitations such as migration prior to and during surgery (8, 13, 18–23). In addition, nonwire localization may alleviate tight scheduling parameters limiting operational flexibility and improve overall patient satisfaction. However, there is limited data

Table 4. Pathology by Localization Method

	MMP/RSL Pathology Sites (*n* = 21) (%)	MWL Pathology Sites (*n* = 36) (%)	*P*-value
Pathology prior to localization[a]	-	-	0.364
Malignant	5 (23.8)	11 (30.6)	-
Benign	1 (4.76)	8 (22.2)	-
Postsurgical pathology	-	-	0.772
Malignant	15 (71.4)	23 (63.9)	-
Benign	6 (28.6)	13 (36.1)	-
Re-excision	2 (9.5)	6 (16.7)	-
Concordance[b]	21 (100)	36 (100)	-

Abbreviations: MMP, MRI-guided marker placement; MWL, mammographic-guided wire localization; RSL, radioactive seed localization.
[a]Not all patients had pathology available prior to localization.
[b]All patients with bracketing who underwent a single lumpectomy were reported as one pathology site, and two patients in the MWL group were reported with two pathology sites, for a total of 36 final pathology results.

with respect to MRI-guided nonwire localization techniques, with a single case study reporting experience with MRI-guided RSL (15).

To our knowledge, the present study is the first single-center retrospective review comparing the surgical outcomes and procedure time of MMP/RSL and MWL. MRI-guided marker placement followed by mammographic-guided radioactive seed localization was noninferior to MWL with lower re-excision rates in the MMP/RSL group (9.5% vs. 16.7%), with both MMP/RSL and MWL groups showing a 100% radpath concordance rate. The MWL group re-excision rate of 16.7% is within the expected range given reported clear margins with a wire-guided excision range from 70.8%–87.4% (10). The lower re-excision rates in the MMP/RSL group support previously reported outcomes when comparing RSL versus WL (12, 20).

A potential concern with an MRI-guided biopsy is that it may delay surgery. In 32 cases in our study, a biopsy of a highly suspicious lesion was deferred in favor of surgical excision and the lesion was localized. Excisional biopsy yielded malignancy in 24/32 specimens (75%). The decision for localization of highly suspicious MR lesions ipsilateral to a known cancer may be an individualized choice based on surgeon preference, patient tolerance for additional biopsies, proximity to the biopsied cancer, and level of suspicion for malignancy. Our study demonstrates that while these areas are very likely to be malignant, they are benign 25% of the time, and therefore a thoughtful clinical approach would be advisable. Of note, in the cases in which localization was performed along a lumpectomy site at follow-up imaging or preoperative localizations for positive margins were performed, only 2/7 (29%) were malignant. Since the patient is undergoing re-excision for the positive margins, the localization may not be necessary. Additionally, abnormal enhancement associated with a recent lumpectomy bed may warrant biopsy or follow-up imaging rather than excision. The small sample size limited the power to detect statistically significant associations or make definitive conclusions; therefore, more study needs to be done before recommendations can be made.

In addition to the known benefits of RSL versus WL, we hypothesized that RSL may ease the scheduling of patients for the radiology department and operating room and improve overall patient satisfaction. While WL is generally performed the day of surgery, which can prolong the operating day for the patient, radioactive seeds can be placed in the breast up to 30 days in advance, providing flexibility in radiology and surgery schedules. Radioactive seeds can be placed on the same day as other presurgical testing and appointments, allowing for less travel time and minimizing time off from work for the patient. In our study, although the overall procedure time was more for the MMP/RSL group, the difference was not statistically significant, and both techniques have a mean performance time less than an hour. The proximity of the MR machine to the mammography departments and subsequent transit time of moving from one department to the next is not accounted for and will vary across institutions.

In past studies that evaluated patient satisfaction, the widened scheduling interval has resulted in improved patient satisfaction. Bloomquist et al (24) demonstrated higher patient convenience scores for RSL versus WL; specifically, 85% of the RSL patients rated the convenience of the RSL procedure as very good to excellent compared with 44% of the WL patients. These results emulated those from Gray et al (20), who reported that patients whose seed was placed at least one day prior to surgery rated the convenience of the RSL procedure significantly higher than those whose seed was placed on the day of surgery. Furthermore, WL has been associated with increased reported patient discomfort compared with RSL (19, 24). The patient's inability to physically visualize the radioactive seed externally following RSL may contribute to the perception of less pain associated with the RSL procedure. Additional studies have also reported that surgeons find RSL more convenient because of the ease of surgical scheduling, the ability to avoid operating room delays, and the ability to have earlier operating start times (23).

Strengths of our study include 100% radiologic-pathologic concordance rates for both techniques, indicating that proper localization occurred, as this confirms the

targeted lesions were successfully excised. Additionally, the postsurgical pathology of the targets localized under MMP/RSL demonstrated malignancy in 71.4%, which validates the importance of an available MRI-guided localization technique. This high rate of malignancy is higher than that seen in image-guided biopsies and demonstrates surgical excision at these sites was medically indicated (25).

There are several limitations of this study. First, this was a retrospective review with a relatively small number of cases. Secondly, the results reflect the localization practice of one institution's physicians, who are all subspecialists in breast imaging, and, therefore, the results may not be generalizable to other groups. Additionally, the elapsed time between the MMP and RSL was not included in the total time equation, which introduces a wide array of time variation depending on scheduling and turnover time.

In conclusion, MMP/RSL is a viable alternative to MWL, with at least equivalent surgical outcomes. In addition to providing equivalent surgical outcomes, the ability to localize patients prior to the day of surgery with radioactive seeds may improve patient satisfaction as suggested by prior studies. MRI-guided marker placement followed by mammographic-guided radioactive seed localization avoids the radiation safety concerns of MRI-guided radioactive seed placement until a commercially available MR-compatible Geiger counter becomes available. Given the equivalent surgical outcomes, the benefits of MMP/RSL outweigh its slightly longer procedure time compared with MWL. Thus, MMP/RSL should be considered a feasible alternative when MRI-guided localization is necessary.

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Conflict of interest statement

None declared.

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