ARTICLE IN PRESS

The American Journal of Surgery xxx (xxxx) xxx

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Original Research Article

Does surgeon-performed intraoperative wire localization allow for lower margin positivity rates compared to radiologist-performed preoperative localization in early breast cancer?

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A B S T R A C T

Background: This study compares positive margin rates in breast conserving surgery (BCS) for early breast cancer using two localization techniques: surgeon-performed intraoperative ultrasound-guided wire localization (IOWL) versus radiologist-performed preoperative wire localization (POWL).

Methods: Patients with unifocal breast cancer undergoing BCS with follow-up at a single institution were retrospectively identified. Factors associated with positive margins were identified.

Results: 177 patients underwent IOWL (N = 85) or POWL (N = 92). There was a significantly lower rate of positive margins for IOWL vs. POWL (7.1 % vs. 23.9 %, p = 0.002) and a corresponding lower rate of re-excision for IOWL vs. POWL (5.9 % vs. 18.5 %, p = 0.011). Presence of DCIS was associated with positive margins (p = 0.015). After adjusting for presence of DCIS, tumor size, and volume of tissue removed, the positive margin rate was significantly lower in the IOWL group compared to the POWL group (aOR 0.34, 95 % CI 0.13–0.93).

Conclusions: In this study, adjusted analysis favored IOWL in achieving negative tumor margins. Prospective studies are needed to further explore the impact of IOWL on quality, cost-effectiveness, and patient experience.

1. Introduction

Breast cancer is a substantial public health burden, with an estimated 281,550 new cases expected in the United States in 2024.[1,2] Early-stage breast cancer accounts for a majority of disease burden, with its prevalence reported at 88.4 per 100,000 women in the United States in 2022.[2] Breast-conserving surgery (BCS), also known as a lumpectomy or partial mastectomy, is the most common treatment option for early-stage breast cancer.[3] A critical determinant of successful BCS is achieving clear surgical margins, which reduces the need for re-excision and improves long-term outcomes for patients.[4]

In the majority of screen-detected breast cancers, the lesion cannot be palpated and thus requires that the imaging abnormality is localized for surgical excision. The localization procedure involves placing a wire or other localizing device into the lesion using image guidance with either ultrasound, mammogram, or magnetic resonance imaging (MRI). This localization procedure is most commonly performed pre-operatively by a radiologist. A meta-analysis of 10 studies with 591 cases of wire-guided localization for breast-conserving surgery reported an average positive margin rate of 35.1%, with studies in the analysis ranging from 0% to 47.7%.[5] Several studies have evaluated the benefit of surgeon-performed intraoperative ultrasound guidance (IOUS) for breast tumor localization showing lower rates of margin positivity and re-excision as well as being more cost efficient.[6,7,8]

Recently, our group described the use of surgeon-performed intraoperative ultrasound-guided wire localization (IOWL) as an alternative to IOUS for tumor localization with a margin positivity rate of 7.3%.[9] Before implementing the IOWL technique as a standard localization method across multiple surgeons at our institution, we sought to gather additional comparative data. The goal of this study is to compare the positive margin and re-excision rates between surgeon-performed intraoperative ultrasound-guided wire localization (IOWL) and radiologist-performed preoperative wire localization (POWL) in patients undergoing upfront BCS for early breast cancer.

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https://doi.org/10.1016/j.amjsurg.2024.115986
Received 7 July 2024; Received in revised form 15 September 2024; Accepted 20 September 2024

2. Methods

2.1. Study design

Patients with unifocal biopsy-proven breast cancer and planned BCS were retrospectively identified from a single institution who had post-operative follow-up for BCS between 2022 and 2023. Patients who underwent IOWL underwent surgery with a single surgeon (NSK) at multiple facilities, while those who underwent POWL were limited to those who had surgery with four surgeons at a single facility, in order to identify a similar number of patients. Patients with multifocal or bilateral tumors (n = 79) and those receiving neoadjuvant therapy (n = 12) were excluded to eliminate confounding factors that could impact margin positivity. Those undergoing BCS without any localization method (e.g., palpation-guided resection only) (n = 12) or wire-free localization devices, such as Savi Scout (n = 20) were excluded in order to minimize additional variability between the two groups. In addition, patients with lumpectomy volumes over 100g were also excluded to prevent over-estimation of negative margin rates (n = 8). This included exclusion of 8 patients in the IOWL group, while no patients in the POWL group needed to be excluded.

2.2. Localization techniques

IOWL is performed after the patient is sedated by anesthesia and prior to the usual surgical preparation. A linear-array ultrasound transducer probe is employed to locate the target breast lesion of either an ultrasound-visible mass, ultrasound-visible biopsy clip, or hematoma cavity. The area of skin next to the probe is sterilized, and a 22-gauge needle containing a 5 cm wire is inserted into the lesion. The needle is oriented parallel to the probe to ensure continuous visualization of its tip throughout the process. Once the needle is correctly positioned within the lesion, the wire is advanced by 1cm and the needle is withdrawn. The patient then undergoes the standard surgical sterile preparation and draping. After the wire is in place, the ultrasound is generally not needed again during the surgery.

POWL localization is completed by radiologists and performed prior to surgery with the awake patient in the Radiology department. Lesions are identified with one of three imaging modalities: mammography, ultrasound, or MRI. After sterile skin preparation, local anesthesia with 2 % lidocaine is administered then a 20-gauge 5cm needle-wire localization device is advanced toward the target with appropriate positioning confirmed in the orthogonal projection. The hook wire is deployed and 0.5 cc of methylene blue is injected. Post-localization mammographic images are taken to show the path of the wire. The patient is then transferred back to the preoperative waiting area.

2.3. Margin and postoperative assessments

Positive margins for invasive cancer were defined as no tumor on ink per final pathology report. Positive margins for ductal carcinoma in situ (DCIS) without presence of invasive disease were defined as no tumor within ≤2 mm of margin. All surgeons routinely performed shaved cavity margin excisions from around the perimeter of the lumpectomy cavity. Volume of tissue excised was recorded from the pathology report and collected for all excisions greater than or equal to 10g. For smaller volumes, including margin specimens, volume was calculated by measured tissue dimensions (length x width x height) when provided for best accuracy. Post-operative complications up to 30 days following initial BCS were recorded, including seroma formation, hematoma formation and infections requiring antibiotic treatment.

2.4. Data collection and statistical analysis

Patient demographics, clinical characteristics, and pathology results were collected. Patients were identified using the hospital's electronic medical records system. All eligible patients within the specified time-frame who met the inclusion and exclusion criteria were included in the study. The study was found exempt by our institutional review board (IRB 23–000376).

Univariate analyses using Pearson's Chi-Square were used to compare patient, tumor and treatment characteristics across treatment groups, IOWL v. POWL, and across margin outcomes, positive v. negative. Multivariate logistic regression analysis was performed to adjust for potential confounding variables. Statistical analysis was conducted using SPSS statistics software, version 28.

3. Results

A total of 177 patients were included in the study, 85 patients had IOWL, and 92 patients had POWL. Patient and tumor characteristics for both groups are shown in Table I. The median patient age was 69 years and mean tumor size was 1.2 cm. Preoperative magnetic resonance imaging (MRI) was performed in 61.6 % of patients. Invasive cancer was present in 75.1 % of patients, of which 62.1 % had associated DCIS. 23.7 % of patients had DCIS only and 1.1 % of patients had benign findings on final pathology. Between IOWL and POWL groups, there were no significant differences between tumor palpability, use of preoperative MRI, final tumor size, volume of tissue excised, or ratio of tumor size to volume of tissue excised (Table I). However, more patients in the POWL group underwent stereotactic-guided needle biopsy compared to the IOWL group, (41.3 % vs 15.3 %, respectively, p = 0.000) and more patients in the POWL group had DCIS on final pathology compared to the IOWL group (79.3 % vs 60.0 %. respectively, p = 0.005).

In total, 28 patients (15.5 %) had positive margins and positive margin rates were significantly lower in the IOWL group compared to the POWL group (7.1 % vs 23.9 % respectively, p = 0.002) on univariate analysis. Within the POWL group, there was no significant difference in margin positivity rates between surgeons (mean and median positivity rates 25.0 % and 18.5 %, respectively, p = 0.795). Additionally, fewer patients in the IOWL group underwent re-excision (5.9 % vs. 18.5 %, p = 0.011). Compared to patients with negative margins, patients with positive margins were more likely to have any DCIS on pathology, 89.3 % vs 66.4 %, respectively, p = 0.015 (Table 2). On regression analysis, adjusting for the presence of DCIS, tumor size, and volume of tissue removed, the positive margin rate remained lower in the IOWL group compared to the POWL group (aOR) of 0.34, 95% confidence interval [CI] 0.13–0.93, p = 0.036) (Table 3).

4. Discussion

In this retrospective analysis, we evaluated the rate of margin positivity after wire localization with two distinct methods: standard preoperative radiologist performed localization (POWL) and surgeon performed intraoperative localization (IOWL). We identified a significantly higher rate of positive margins in the POWL group at 23.9 % compared to the IOWL group at 7.1 %. Even after adjusting for DCIS, tumor size, and volume of excision, the positive margin rate was significantly lower in the IOWL group compared to the POWL group (aOR 0.34, 95 % confidence interval [CI] 0.13–0.93, p = 0.036).

Clinically, reduced positive margin rates are associated with fewer re-excision surgeries, as demonstrated by our findings, with re-excision rates of 5.9 % in the IOWL group vs 18.5 % in the POWL group. Eliminating the need for re-excision procedures can allow for accelerated recovery times and potentially earlier initiation of crucial adjuvant therapies factors that are pivotal in improving overall patient outcomes in the management of early-stage breast cancer.[1,10] Of note, margin positivity does not always translate to margin re-excision as was the case for 6 patients in this study, including 1 of 6 patients with technically "positive" margins in the IOWL group and 5 of 22 patients in the POWL group. This is often due to several reasons including: surgeon consideration of location of positive margin such as anterior location at or

Table 1
Characteristics by treatment group.

	IOWL N = 85	POWL N = 92	Overall N = 177	p-value
Age (yr); Median (Range)	70 (39–92)	65 (40–90)	69 (39–92)	p = 0.060
Race; % (N)				p = 0.000
Asian/Pacific Islander	10.6 %[9]	17.4 %[16]	14.1 %[25]	
Black/African American	2.4 %[2]	6.5 %[6]	4.5 %[8]	
White/Caucasian	60.0 % (51)	39.1 % (36)	49.2 % (87)	
Other	2.4 %[2]	27.2 %[25]	15.3 %[27]	
Unknown	24.7 %[21]	9.8 %[9]	16.9 % (30)	
Ethnicity; % (N)				p = 0.000
Hispanic/Latinx	2.4 %[2]	10.9 %[10]	6.8 %[12]	
Non Hispanic/Latinx	65.9 % (56)	80.4 % (74)	73.4 % (130)	
Unknown	31.8 %[27]	8.7 %[8]	19.8 % (35)	
Palpable; % (N)				p = 0.408
No	77.6 % (66)	82.6 % (76)	80.2 % (142)	
Yes	22.4 %[19]	17.4 %[16]	19.8 % (35)	
Preoperative MRI; % (N)				p = 0.677
No	40.0 % (34)	37.0 % (34)	38.4 % (68)	
Yes	60.0 % (51)	63.0 % (58)	61.6 % (109)	
Localization for Core Needle Biopsy; % (N)				p = 0.000
Mammographic/Stereotactic	15.3 %[13]	41.3 % (38)	28.8 % (51)	
US-guided	83.5 % (71)	51.1 % (47)	66.7 % (118)	
MRI	1.2 %[1]	7.6 %[7]	4.5 %[8]	
Pathology on Core Needle Biopsy; % (N)				p = 0.000
DCIS Only	15.3 %[13]	35.9 % (33)	26.0 % (46)	
Invasive Tumors	84.7 % (72)	64.2 % (59)	73.9 % (131)	
IDC	70.6 % (60)	50.0 % (46)	59.9 % (106)	
ILC	10.6 %[9]	3.3 %[3]	6.8 %[12]	
Other	3.5 %[3]	10.9 %[10]	7.2 %[13]	
CNB: Presence of DCIS on Pathology; % (N)				p = 0.000
Not Present	74.1 % (63)	37.0 % (34)	54.8 % (97)	
Present	25.9 %[22]	63.0 % (58)	45.2 % (80)	
Tumor Size (mm); Median (Range)	12 (0–50)	11 (0–43)	12 (0–50)	p = 0.319
Pathology on Final Surgical Excision; % (N)				p = 0.055
Benign	1.2 %[1]	1.1 %[1]	1.1 %[2]	
DCIS Only	14.1 %[12]	32.6 % (30)	23.7 % (42)	
Invasive Tumors	84.7 % (72)	66.3 % (61)	75.1 % (133)	
IDC	71.8 % (61)	53.3 % (49)	62.1 % (110)	
ILC	8.2 %[7]	6.5 %[6]	7.3 %[13]	
Other	4.7 %[4]	6.5 %[6]	5.6 %[10]	
Presence of DCIS on Final Pathology; % (N)				p = 0.005
Not Present	40.0 % (34)	20.7 %[19]	29.9 % (53)	
Present	60.0 % (51) (39)	79.3 % (73) (44)	70.1 % (126) (83)	

Table 1 (*continued*)

	IOWL N = 85	POWL N = 92	Overall N = 177	p-value
Present with Associated Invasive Tumors				
Invasive Tumors Pathology: Nuclear Grade; % (N)	**N = 72**	**N = 61**	**N = 133**	p = 0.397
0	0.0 % (0)	1.6 %[1]	0.8 %[1]	
1	22.2 %[16]	31.1 %[19]	26.3 % (35)	
2	65.3 % (47)	59.0 % (36)	62.4 % (83)	
3	12.5 %[9]	8.2 %[5]	10.5 %[14]	
DCIS Pathology: Nuclear Grade; % (N)	**N = 51**	**N = 73**	**N = 124**	p = 0.478
1	21.6 %[11]	13.7 %[10]	16.9 %[21]	
2	58.8 % (30)	61.6 % (45)	60.5 % (75)	
3	19.6 %[10]	24.7 %[18]	22.6 % (28)	
Localization for Surgical Excision; % (N)				p = 0.000
Mammographic/Stereotactic	0.0 % (0)	62.0 % (57)	32.2 % (57)	
MRI	0.0 % (0)	2.2 %[2]	1.1 %[2]	
US-guided	100 % (85)	35.9 % (33)	66.7 % (118)	
Invasive Tumors: Estrogen Receptor; % (N)	**N = 72**	**N= 61**	**N = 133**	p = 0.624
Negative	6.9 %[5]	4.9 %[3]	6.0 %[8]	
Positive	93.1 % (67)	95.1 % (58)	90.4 % (125)	
Invasive Tumors: Progesterone Receptor; % (N)	**N = 72**	**N= 61**	**N = 133**	p = 0.801
Negative	18.1 %[13]	16.4 %[10]	17.3 %[23]	
Positive	81.9 % (59)	83.6 % (51)	82.7 % (110)	
Invasive Tumors: HER2 Receptor; % (N)	**N = 72**	**N = 61**	**N = 133**	p = 0.152
Negative	87.5 % (63)	85.2 % (52)	86.5 % (115)	
Positive	12.5 %[9]	9.8 %[6]	11.3 %[15]	
Not Available	0.0 % (0)	4.9 %[3]	2.3 %[3]	
Excised Volume (g); Median (Range)	19 (7.5–83)	16 (3–87)	17.92 (3–87)	p = 0.407
Ratio of Volume: Size; Median (Range)	1.76 (0–30)	1.64 (0–25.7)	1.67 (0–30)	p = 0.368
Margins; % (N)				p = 0.002
Negative	92.9 % (79)	76.1 % (70)	84.2 % (149)	
Positive	7.1 %[6]	23.9 %[22]	15.5 % (28)	
Margin pathology: Invasive Disease; % (N)				p = 0.780
Negative	96.5 % (82)	95.7 % (88)	96.0 % (170)	
Positive	3.5 %[3]	4.3 %[4]	4.0 %[7]	
Margins pathology: DCIS; % (N)	**N = 52**	**N = 73**	**N = 125**	p = 0.001
Negative	56.5 % (48)	58.7 % (54)	57.6 % (102)	
Positive	4.7 %[4]	20.7 %[19]	13.0 %[23]	
Re-excision; % (N)				p = 0.011
No	94.1 % (80)	81.5 % (75)	87.6 % (155)	
Yes	5.9 %[5]	18.5 %[17]	12.4 %[22]	

including the skin margin, posterior location when including fascia overlying pectoralis fascia; patient consideration and plan for post-operative radiation; as well as type and amount of disease at the margin such as a focal site of DCIS within 1–2 mm. For these reasons, it is important to identify both margin positivity and margin re-excision rates to understand clinical consequences and downstream implications of

Table 2
Characteristics by margin outcome

	Negative Margins	Positive Margins	Overall	p-value
	N = 149	N = 28	N = 177	
Age (yr); Median (Range)	69 (39–92)	68 (42–88)	69 (39–92)	p = 0.525
Palpable; % (N)				p = 0.811
No	80.5 % (120)	78.6 %[22]	80.2 % (142)	
Yes	19.5 % (29)	21.4 %[6]	19.8 % (35)	
Preoperative MRI; % (N)				p = 0.749
No	38.9 % (58)	35.7 %[10]	38.4 % (68)	
Yes	61.1 % (91)	64.3 %[18]	61.6 % (109)	
CNB: Localization Type; % (N)				p = 0.269
Mammographic/ Stereotactic	26.8 % (40)	39.3 %[11]	28.8 % (51)	
MRI	4.0 %[6]	7.1 %[2]	4.5 %[8]	
US-guided	69.1 % (103)	53.6 %[15]	66.7 % (118)	
Final Pathology; % (N)				p = 0.126
Benign	1.3 %[2]	0.0 % (0)	1.1 %[2]	
DCIS Only	20.1 % (30)	42.9 %[12]	23.7 % (42)	
Invasive Tumors	78.50 % (117)	57.2 %[16]	75.0 % (133)	
IDC	64.4 % (96)	50.0 %[14]	62.1 % (110)	
ILC	8.1 %[12]	3.6 %[1]	7.3 %[13]	
Other	6.0 %[9]	3.6 %[1]	5.6 %[10]	
Presence of any DCIS on Pathology; % (N)				**p = 0.015**
Not Present	33.6 % (50)	10.7 %[3]	29.9 % (53)	
Present	66.4 % (99)	89.3 %[25]	70.1 % (126)	
Final Pathology Size (mm); Median (Range)	12 (0–43)	12.5 (1–50)	12 (0–50)	p = 0.454
Excised Volume (g); Median (Range)	18 (3–87)	15 (4.54–43.3)	17.92 (3–87)	p = 0.297
Ratio of Volume: Size; Median (Range)	1.71 (0–30)	1.033 (0.34–16)	1.67 (0–30)	p = 0.343
Treatment Group; % (N)				**p = 0.002**
IOWL	53 % (79)	21.4 %[6]	48.0 % (85)	
POWL	47 % (70)	78.6 %[22]	52.0 % (92)	

Table 3
Regression analysis.

	Odds Ratio	95 % CI	p-value
Crude Model for Positive Margins across Treatment Groups (IOWL v POWL)	0.242	(0.09–0.63)	p = 0.004
Adjusted Model for Positive Margins across Treatment Groups (IOWL v POWL)	0.342	(0.13–0.93)	p = 0.036

Variables: Volume of tissue excised (g), Final pathology size (mm), Presence of any DCIS, $r^2 = 0.110$.

margin positivity.

Factors known to be associated with positive margins include accuracy of tumor size on preoperative imaging, volume of tissue excised, presence of DCIS, and routine use of cavity shave margins.[11–16] In the current study, 61.6 % of patients underwent preoperative MRI and this was similar between both POWL and IOWL groups. Use of preoperative MRI was not associated with positive margins. While all surgeons in this study employed routine use of cavity shave margins, there can be variability of this technique so to further attempt to control for this variable, volumes of margin excisions were calculated and included in final volumes. Furthermore, comparison of margin positivity between surgeons who utilized POWL in this study did not differ significantly. Additionally, to further control for volume of tissue excised, we compared tumor size to volume ratio and excluded patients with large volume excisions (>100g). Even after adjusting for these potential confounding factors, our analysis revealed a significant odds ratio favoring the IOWL technique over POWL.

In our study, we did identify a significant association between any DCIS on pathology and positive margin outcomes (p = 0.015), correlating with previous research on the impact of DCIS on surgical margins in early-stage breast cancer.[11] Indeed, more patients undergoing POWL underwent stereotactic guidance for both biopsy and localization, however, 14 patients in the IOWL group underwent either core needle biopsy with either stereotactic guidance (13/85, 15.3%) or MRI-guidance (1/85, 1.2%). Furthermore, there was no difference in margin positivity between method of core biopsy diagnosis. Nonetheless, presence of DCIS is a critical feature of positive margins and selection of appropriate patient candidates for IOWL must take this into consideration.

To date, only one other study to our knowledge has compared surgical outcomes between POWL and IOWL.[6] In this retrospective study out of Korea, patients undergoing IOWL had shorter operation times and smaller volume:tumor size ratios than those undergoing POWL, but no difference in margin positivity rates between the groups was identified. This is likely due to the fact that, unlike the current study, the Korean study excluded patients with DCIS and required that all patients underwent US-guided imaging biopsy and localization. The decision to include such patients in the current study is important to note as, while method of localization for biopsy was not a factor related to positive margins, 16.5 % of patients underwent IOWL who had non-ultrasound-guided biopsy but could still have an intraoperative ultrasound localization procedure performed due to the visibility of either a biopsy clip or hematoma cavity. Furthermore, even though 51.1 % of patients in the POWL group underwent US-guided core needle biopsy, only 35.9 % of patients in this group underwent US-guided POWL at time of surgery. These differences are possibly related to scheduling or radiology preferences and technique.

Technically, IOWL provides the operating surgeon with real-time ultrasound imaging guidance, enhancing the precision of tumor localization and subsequent surgical excision.[10] Unlike POWL, which requires time between wire placement and surgical excision, IOWL ensures immediate and accurate localization. This eliminates the potential risks associated with prolonged time intervals, such as patient discomfort, migration of the wire during patient transport, and logistical challenges for surgery scheduling.[8,10,17]

Additionally, intraoperative localization techniques have demonstrated a substantial cost benefit by avoiding an extra preoperative procedure with radiology.[8,9] Other studies have shown reducing re-excision surgeries through more precise initial excision, as facilitated by IOWL, results in significant financial savings for healthcare institutions.[18,19] These savings include not only direct medical costs, but also indirect expenses incurred by patients, such as lost productivity and transportation expenses related to additional hospital visits.[20,21] Thus the adoption of IOWL in breast-conserving surgery has economic potential for improving healthcare resource utilization.

Cost should also be considered with the more recent adoption of wire-free localization methods such as Savi Scouts and Magseed that have gained popularity due to advantages in convenience and accuracy compared to traditional wire localization methods.[22,23] Wire-free localization has advantages over POWL in providing potentially better operative experience by decoupling localization from surgery and an improved patient experience, but similar positive margin outcomes of 18 % or more have been reported for these groups in contemporary studies.[23,24] Despite the routine use of wire-free localization at our institution, wire localization continues to be used with regularity either due to more streamlined patient care the day-of surgery for those who need to travel long distances to receive care at our institution, or due to surgeon preference of POWL over wireless localization methods. Wire-free techniques also face unique complications not found with IOWL, such as device migration, inactivation, or displacement.[25] In contrast, intraoperative localization offers other patient experience advantages by allowing patients to forgo the pain and anxiety associated with the awake device insertion procedure and by eliminating the burden of a separate preoperative visit, especially for patients who face social barriers such as those having to travel long distances and those with limited post-operative support at home. Intraoperative localization also benefits the healthcare facility by reducing procedural logistics for hospital staff and management. Further research is needed to directly compare IOWL with wire-free localization techniques.

4.1. Strengths and limitations

This retrospective study is limited by potential patient selection bias by inadvertently excluding patients in the IOWL group due to need for localization of calcifications or other non-visible lesions with POWL or other radiology-performed localization. IOWL cannot be applied to these patients routinely, so IOWL as a technique is limited by this factor. Additionally, at the time of the current study, only one surgeon at our institution was routinely employing IOWL, limiting the overall generalizability of results. Despite these limitations and the small sample size, the study's strengths include the similarity of patient populations and a significant difference in margin positivity rates, even after controlling for confounding factors. Prospective studies controlling for patient, tumor, facility, and surgeon variability will be needed to further understand the benefit and uses of IOWL. In addition, an inherent limitation in the broad applicability of IOWL is surgeon training and access to ultrasound. To that point, we have published recommendations for developing and establishing a breast ultrasound program that incorporates stakeholder engagement, surgeon champions, standard operating procedures, and quality assurance metrics to enable surgeons a pathway to attaining and utilizing ultrasound in their practice.[26]

4.2. Future directions

At the time of this study, only one faculty member who recently joined our institution was routinely performing IOWL. Since our trainees and other faculty were motivated to incorporate IOWL into their skillset more routinely, the current study provides baseline evidence to continue to incorporate this technique. Both our faculty and our trainees have now had opportunity for additional training in IOWL to facilitate the uptake of this skillset into practice.[27] Planned future studies include prospective analysis of feasibility of IOWL for multiple surgeons and ultimately a randomized study to assess margin positivity differences and patient reported outcomes between various localization techniques.

5. Conclusion

In conclusion, surgeon-performed intraoperative wire localization demonstrates promising outcomes with low margin positivity rates compared to POWL for patients undergoing BCS. As a result of our research on IOWL, we have started to integrate IOWL training into our surgical education program to expand its use amongst our breast surgeons so as to evaluate its impact on broader surgical practices and patient outcomes. When properly applied, IOWL could potentially be more cost effective and more accurate in achieving negative margins for BCS. Prospective trials of IOWL are needed.

CRediT authorship contribution statement

Reeta Asmai: Writing – original draft, Formal analysis, Data curation. **Tess Huy:** Writing – review & editing, Data curation, Conceptualization. **Jennifer L. Baker:** Writing – review & editing, Methodology, Conceptualization. **Hong-Ho Yang:** Writing – review & editing, Methodology, Formal analysis. **Carlie K. Thompson:** Conceptualization, Methodology, Writing – review & editing. **Nimmi S. Kapoor:** Writing – review & editing, Methodology, Data curation, Conceptualization.

Declaration of competing interest

Dr. Nimmi Kapoor disclosures:
Past consultant for Myriad Genetics and Guidepoint Consulting.
No other authors have any disclosures.

Acknowledgements

Research reported in this publication was supported by the Biomedical Informatics Program (BIP) at UCLA CTSI funded by the National Institution of Health (NIH) through the National Center for Advancing Translational Sciences (NCATS) Grant (#UL1TR001881).

References

1. American Cancer Society. *Breast Cancer Facts & Figures 2022-2024*. Atlanta: American Cancer Society, Inc.; 2022.
2. SEER*Explorer. *An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program*. National Cancer Institute; 2024 Apr 17 [cited 2024 Jun 18]. Available from: https://seer.cancer.gov/statistics-network/explorer/.Datasource(s):SEERIncidenceData,November2023Submission(1975-2021. SEER 22 registries.
3. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*. 2002;347(16):1233–1241. https://doi.org/10.1056/NEJMoa022152.
4. Medina-Franco H, Vasconez LO, Fix RJ, et al. Factors associated with local recurrence after skin-sparing mastectomy and immediate breast reconstruction for invasive breast cancer. *Ann Surg*. 2002;235(6):814–819. https://doi.org/10.1097/00000658-200206000-00008.
5. Ahmed M, Douek M. Intra-operative ultrasound versus wire-guided localization in the surgical management of non-palpable breast cancers: systematic review and meta-analysis. *Breast Cancer Res Treat*. 2013;140(3):435–446. https://doi.org/10.1007/s10549-013-2639-2.
6. Shin YD, Choi YJ, Kim DH, et al. Comparison of outcomes of surgeon-performed intraoperative ultrasonography-guided wire localization and preoperative wire localization in nonpalpable breast cancer patients undergoing breast-conserving surgery: a retrospective cohort study. *Medicine (Baltim)*. 2017;96(50):e9340. https://doi.org/10.1097/MD.0000000000009340.
7. Krekel NM, Haloua MH, Lopes Cardozo AM, et al. Intraoperative ultrasound guidance for palpable breast cancer excision (COBALT trial): a multicentre, randomised controlled trial. *Lancet Oncol*. 2013;14(1):48–54. https://doi.org/10.1016/S1470-2045(12)70527-2.
8. Konen J, Murphy S, Berkman A, Ahern TP, Sowden M. Intraoperative ultrasound guidance with an ultrasound-visible clip: a practical and cost-effective option for breast cancer localization. *J Ultrasound Med*. 2020;39(5):911–917. https://doi.org/10.1002/jum.15172.
9. Huy T, Graham DS, Baker JL, et al. Safety and margin positivity rates of surgeon-performed intraoperative ultrasound-guided wire localization for breast cancer. *Surgical Oncology Insight*. 2022. https://doi.org/10.1016/j.soi.2024.100057, 2024.
10. Wire-Free. Nonradioactive localization techniques to guide surgical excision of nonpalpable breast tumours: a health technology assessment. *Ont Health Technol Assess Ser*. 2023;23(2):1–139.
11. Barentsz MW, Postma EL, van Dalen T, et al. Prediction of positive resection margins in patients with non-palpable breast cancer. *Eur J Surg Oncol*. 2015;41(1):106–112. https://doi.org/10.1016/j.ejso.2014.08.474.
12. Gommers JJJ, Duijm LEM, Bult P, et al. The impact of preoperative breast MRI on surgical margin status in breast cancer patients recalled at biennial screening mammography: an observational cohort study. *Ann Surg Oncol*. 2021;28(11):5929–5938. https://doi.org/10.1245/s10434-021-09868-1.
13. Ocal K, Dag A, Turkmenoglu O, Gunay EC, Yucel E, Duce MN. Radioguided occult lesion localization versus wire-guided localization for non-palpable breast lesions: randomized controlled trial. *Clinics*. 2011;66(6):1003–1007. https://doi.org/10.1590/s1807-59322011000600014.
14. Landercasper J, Borgert AJ, Fayanju OM, et al. Factors associated with reoperation in breast-conserving surgery for cancer: a prospective study of American society of

breast surgeon members. *Ann Surg Oncol*. 2019;26(10):3321–3336. https://doi.org/10.1245/s10434-019-07547-w [published correction appears in Ann Surg Oncol. 2019 Dec;26(Suppl 3):891. doi: 10.1245/s10434-019-07799-6].
15. Chagpar AB, Killelea BK, Tsangaris TN, et al. A randomized, controlled trial of cavity shave margins in breast cancer. *N Engl J Med*. 2015;373(6):503–510. https://doi.org/10.1056/NEJMoa1504473.
16. Vicini FA, Eberlein TJ, Connolly JL, et al. The optimal extent of resection for patients with stages I or II breast cancer treated with conservative surgery and radiotherapy. *Ann Surg*. 1991;214(3):200–205. https://doi.org/10.1097/00000658-199109000-00002.
17. Chang S, Brooke M, Cureton E, et al. Rapid implementation of intraoperative ultrasonography to reduce wire localization in the permanente medical group. *TPJ*. 2019;23(3):18–73. https://doi.org/10.7812/TPP/18-073.
18. Merrill AY, Ochoa D, Klimberg VS, et al. Cutting healthcare costs with hematoma-directed ultrasound-guided breast lumpectomy. *Ann Surg Oncol*. 2018;25(10): 3076–3081. https://doi.org/10.1245/s10434-018-6596-1.
19. Banys-Paluchowski M, Rubio IT, Karadeniz Cakmak G, et al. Intraoperative Ultrasound-Guided Excision of Non-Palpable and Palpable Breast Cancer: Systematic Review and Meta-Analysis. Intraoperative Sonographie zur Entfernung von nicht-palpablen und palpablen Mammakarzinomen: systematisches Review und Meta-Analyse. *Ultraschall der Med*. 2022;43(4):367–379. https://doi.org/10.1055/a-1821-8559.
20. Grant Y, Al-Khudairi R, St John E, et al. Patient-level costs in margin re-excision for breast-conserving surgery. *Br J Surg*. 2019;106(4):384–394. https://doi.org/10.1002/bjs.11050.
21. Metcalfe LN, Zysk AM, Yemul KS, et al. Beyond the margins—economic costs and complications associated with repeated breast-conserving surgeries. *JAMA Surg*. 2017;152(11):1084–1086. https://doi.org/10.1001/jamasurg.2017.2661.
22. Ahmed M, Douek M. Radioactive seed localisation (RSL) in the treatment of non-palpable breast cancers: systematic review and meta-analysis. *Breast*. 2013;22(4): 383–388. https://doi.org/10.1016/j.breast.2013.04.016.
23. Lovrics PJ, Goldsmith CH, Hodgson N, et al. A multicentered, randomized, controlled trial comparing radioguided seed localization to standard wire localization for nonpalpable, invasive and in situ breast carcinomas. *Ann Surg Oncol*. 2011;18(12): 3407–3414. https://doi.org/10.1245/s10434-011-1699-y.
24. Srour MK, Kim S, Amersi F, Giuliano AE, Chung A. Comparison of wire localization, radioactive seed, and Savi scout® radar for management of surgical breast disease. *Breast J*. 2020;26(3):406–413. https://doi.org/10.1111/tbj.13499.
25. Cheang E, Ha R, Thornton CM, Mango VL. Innovations in image-guided preoperative breast lesion localization. *Br J Radiol*. 2018;91(1085):20170740. https://doi.org/10.1259/bjr.20170740.
26. Labora AN, Kapoor NS. The evolution of breast ultrasound in surgical practice: current applications, missed opportunities, and future directions. *Surg Oncol Insight*. 2024;1(3):100084. https://doi.org/10.1016/j.soi.2024.100084.
27. Huy TC, Thompson CK, Deranteriassian A, et al. Successful use of a cadaver model to teach ultrasound-guided breast procedures to surgical trainees. J Surg Res. Published online August 7, 2024. doi:10.1016/j.jss.2024.07.055.