Original Study

Review of Variables Associated With Positive Surgical Margins Using Scout Reflector Localizations for Breast Conservation Therapy

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Abstract

The aim of this study is to evaluate factors contributing to positive surgical margins associated with reflector guidance for patients undergoing breast conserving therapy for malignancy. We retrospectively reviewed 254 cases of Scout device pre-surgical localizations. There is a statistically significant decrease in the positive surgical margins with concomitant use of intraoperative ultrasound but increase in positive margins with the presence of ductal carcinoma in situ. These results add new information with regard to achieving better surgical outcomes for breast conserving surgery to treat breast cancer.

Objective: To evaluate factors contributing to positive surgical margins associated with reflector guidance for patients undergoing breast conserving therapy for malignancy. **Materials and Methods:** A retrospective IRB-approved review of our institutional database was performed for malignant breast lesions preoperatively localized from January 1, 2018 to December 31, 2020. The following data was recorded using electronic medical records: lesion type and grade, lesion location, reflector and wire placement modality, use of intraoperative ultrasound, margin status, patient age, family history, BMI, and final pathology. Statistical analysis was performed with univariate summary statistics and logistic regression. $P < .05$ was significant. **Results:** A total of 606 image-guided pre-surgical localizations were performed for lumpectomies of breast malignancies. A total of 352 of 606 (58%) wire localizations and 254 of 606 (42%) SCOUT reflector localizations were performed. Sixty out of 352 (17%) of wire-localized patients had positive surgical margins, whereas forty-eight out of 254 (19%) of reflector-localized patients had positive surgical margins. (OR = 1.12, *P* value: .59). For reflector guided cases, the use of intraoperative ultrasound (IOUS) was associated with decreased positive margin status (OR = 0 .28, 95% CI = [0.14, 0.58]) while in situ disease was associated with increased positive margin status (OR = 1.99, 95% CI = [1.05, 3.75]). No association between modality used for localization (mammography vs. ultrasound) and positive margin status was observed (OR = 0.63, 95% CI = [0.33, 1.19]). No association between positive margins and age, family history, tumor location and BMI was observed. **Conclusion:** For reflector guided surgeries, the use of IOUS was associated with decreased positive margins, by contrast the presence of ductal carcinoma in situ was associated with increased positive margins. There was no statistically significant difference in surgical outcomes for reflector-guided localization compared to wire localizations of the breast.

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Introduction

Over recent decades, breast-conserving surgery (BCS) has been utilized with the aim of reducing morbidity and improving cosmetic outcome. The goal of BCS is complete resection of the malignancy with negative margins. Approximately 50% of breast cancer patients will undergo BCS.[1] Risk of local recurrence is twice as likely with positive margins, as compared to those with negative margins.[2] The reoperation rates are widely variable (range 10%-40%).[28] Additional surgery for re-excision is associated with risks of anesthesia, postoperative complications, and increased costs.

Pre-operative localization is performed by the radiologist to demarcate as precisely as possible the coordinates of a malignant lesion to aid the surgeon in achieving satisfactory margins during BCS.[3] Wire localization has been a reliable and cost-effective procedure for over 40 years.[4] However since the wire localization must

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be performed on the day of the surgery to prevent wire displacement, operating delays, and inefficiencies are inherent. There is often patient dissatisfaction due to the anxiety of having to undergo an additional procedure on the day of their cancer surgery and discomfort from having a wire protruding from the skin.[5] Vasovagal events during placement have been reported to occur in 20% of patients.[13] The wire may dislocate, be transected during dissection and remain retained in the breast. Wire localization limits the choice of incision, resulting in unnecessarily large excision volumes which predicts poor cosmetic outcome [6] since the entry point to target distance is variable. When these points are close to one another, the surgeon will generally make an incision beginning at wire entry; when there is a significant distance between these points (> 3 cm), the surgeon places the incision closer to the target, dissecting down to the wire, and resecting the tissue around the wire.

Non–wire localization techniques have been developed recently and allow image-guided placement day's before surgery resulting in improved workflows. These techniques eliminate protruding wires, risk of dislodging, and allow the incision site to be independent from the skin entry site.[7] SCOUT (Cianna Medical, Merit Medical Systems, Inc South Jordan, UT) is a Food and Drug Administration (FDA)-cleared breast lesion localization tool that uses micro-impulse radar to localize and direct the removal of non–palpable breast lesions. The reflector is deployed within or adjacent to the target under mammographic or sonographic guidance. The reflector provides the surgeon with exact location of the target allowing for better planning and excision of less uninvolved tissue. The FDA has approved implantation of the reflector for an indefinite time. Bracketing is possible with reflectors as close as 1.5 cm.[8]

Use of IOUS for breast conservation was first reported in 1988 by Schwartz et al.[9] IOUS is used before making an incision which enables the surgeon to appraise the distance from tumor to the skin and the chest wall. The reflector location within the tumor can be visualized as well as the dimensions of the tumor which are incorporated into planning of the surgical approach. In the COBALT trial, Krekel et al.[10] showed that the IOUS for palpable tumors is associated with 15% reduction in positive margins. Pan et al. [11] performed a meta-analysis and systemic review for the use of IOUS and found that it is an accurate method for localization of non–palpable and palpable breast cancers. They reported high proportion of negative margins and optimum resection volumes. Colakovic et al.[12] showed a negative margin rate of above 88% with lower volume of excision of healthy breast tissue to preserve cosmetic outcome. Intraoperative ultrasound (IOUS) guidance for BCS has consistently shown the potential to improve surgical accuracy for breast cancer treatment.[6,13,15]

The purpose of this study was to compare the rates of positive margins between wire localization versus reflector localizations of malignant breast lesions undergoing BCS. The second aim was to identify patient, lesion or technique related factors associated with positive surgical margins following SCOUT reflector localizations.

Methods

This study was approved by our institutional review board, which granted a waiver of consent. The study was compliant with the Health Insurance Portability and Accountability Act.

Study Population

A retrospective review of our MagView (Fulton, MD) database identified patients who had preoperative image-guided localization of breast lesions from January 1, 2018 to December 31, 2020. SCOUT reflector localizations began in October 2018. The patient selection for reflector localization was determined after a discussion between the breast imaging radiologist and the breast surgeon. Although SCOUT localizations were performed for patients with high-risk lesions and discordant benign pathologic diagnosis, we evaluated the margin status for malignancies and pleomorphic lobular carcinoma in situ (pLCIS). Wire localizations were performed for cases where the lesion was deeper than 6 cm from the skin due to difficulty in detecting reflector signal in deep lesions, or needed bracketing for lesions spanning < 2 cm distance.

Wire or Reflector Placement and Surgical Removal

All wire and reflector placements were performed at a single academic breast center by 1 of 6 breast imaging radiologists (6-27 years of experience). Surgical excision was performed by 1 of 3 dedicated breast surgeons (12-20 years of experience). For each localization procedure, the breast imaging radiologist performed a pre-procedure review to identify the target and choose the best modality for optimal localization. In challenging cases, such as those involving bracketing an extensive area of disease, a discussion took place between the surgeon and the radiologist to ensure the most appropriate placement of reflectors or wires to facilitate surgery.

Wire Localizations

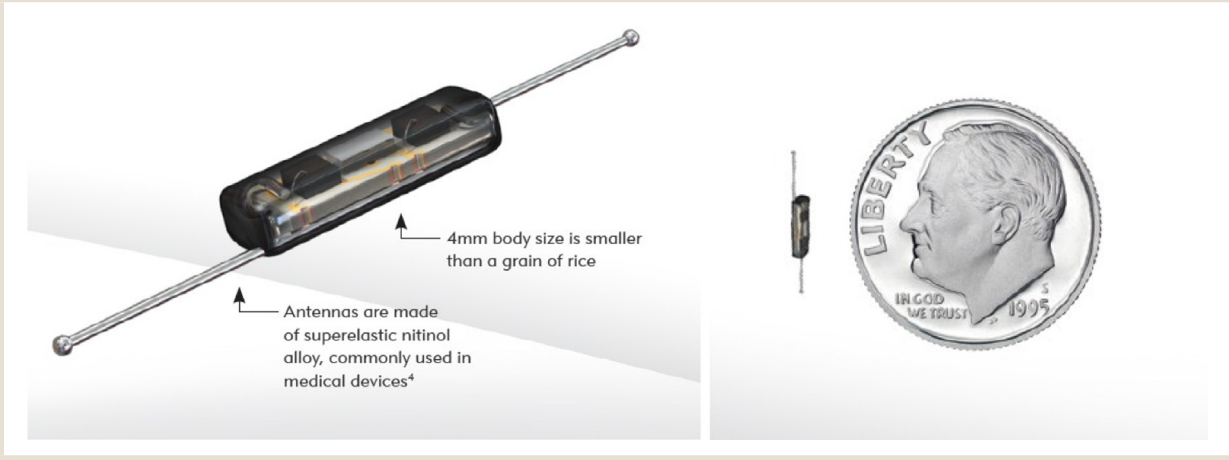
Each wire(s) was placed percutaneously into the breast using imaging guidance and deployed into the target lesion using an introducer needle (20g Kopans needle). Approximately 4 to 10 cm of wire protruded from the skin. The wire was secured with tape and the patient was transported to the operating room.

Reflector Localizations

A Scout reflector is pre-loaded into a 16-g introducer needle and deployed by withdrawing the release button into the breast. A console is used to ensure that the audible signal is heard immediately after placement with the patient in a supine position, mimicking the position that they will be lying in the operating suite. The intraoperative detector console provides the reflector location information by both audible with progressively increased cadence when the probe is directly over the device and visual feedback which provides the surgeon a measurement of depth. The reflector device is 1.2 cm in length which includes 2 antennae, an infrared light receptor, and a transistor switch.[14] (Figure 1).

In the operating room, the surgeon reviews the patient's post-localization mammography images which are displayed during the procedure for visual-spatial reference. Intraoperative ultrasound (IOUS) is used at the discretion of the surgeon but generally used for lesions that are > 1 cm which are visible by ultrasound. IOUS is rarely used for extent of microcalcifications associated with DCIS because in most cases these are not well seen by ultrasound. The breast surgeons in this study had 12 to 20 years of experience with ultrasound. If ultrasound is utilized, this is usually done before incision. Using a sterilely draped, multi-frequency 10-MHz linear

Figure 1 Components of a radar reflector localization system. (Images reprinted, with permission, from Cianna Medical.)



array transducer, the breast is scanned, and the tumor identified. Ultrasound is used to assess the tumor depth and extent. During transverse scanning, the center of the tumor is marked on the skin. Tumor location is confirmed by scanning in a sagittal plane. A cosmetically optimal incision, including skin if the anterior extent of the cancer is within 5 mm of the dermis, is marked on the overlying skin of the breast. The information provided by ultrasound exam including the depth of the tumor from the skin and the distance from chest wall are used to guide flap thickness and extent. After the incision is made, the surgeon relies on the localization device(s) for guidance. The reflector device provides continuous feedback which aids with the identification of resection margins; tissue free of signal are generally at a safe distance from the cancer. After removal of the targeted lesion, the specimen is marked with sutures for orientation, and fixed to a grid.

Using the Faxitron Trident HD Specimen Radiography System (Tucson, AZ), a specimen radiograph is taken and reviewed by the surgeon and remotely by the breast imaging radiologist. The specimen images are reviewed for inclusion of the index lesion, biopsy clip, wire or reflector. For malignant lesions, any radiographic findings that suggest an involved surgical margin is communicated to the surgeon in the operating room, allowing the surgeon to take additional margins if necessary.

Data Extraction

The list of all patients who had pre-surgical device placements were obtained from a search of the MagView (Fulton, MD) database. Each patients' demographics, radiology, surgical, and pathology reports from the electronic medical record system were reviewed by AC and RI. Correlation with imaging findings was performed using the Philips PACS system (Koninklijke Philips N.V.) by AC. This data was recorded in REDCap. Malignant cases included invasive cancers with or without ductal carcinoma in situ (DCIS) and pure DCIS. Although pLCIS is considered a high-risk lesion, the treatment is similar to DCIS. We included 1 case of pLCIS in our data. According to the guidelines by European Society of Medical Oncology,[30] "the pleomorphic variant of lobular neoplasia may behave similarly to DCIS and should be considered from a treatment perspective as high-grade DCIS." Surgical margins were considered positive when invasive lesions involved any inked margins and < 2 mm for DCIS and for pLCIS.

Statistical Analysis

Univariate summary statistics were computed for clinical and demographic variables of interest. Categorical variables were summarized using counts and percentages, while means and standard deviations were computed for quantitative variables. Contingency tables were used to display counts when comparing pairs of categorical variables. Odds ratios (ORs) were computed to assess the magnitude and direction of the association between pairs of binary categorical variables. In brief, the odds ratio function in the epitools R package (https://CRAN.R-project.org/package=epitools) was applied to calculate conditional maximum likelihood estimates of the ORs along with the corresponding 95% confidence intervals and *P*-values. The Cochran Armitage Test function in the Desc Tools R package (https://github.com/AndriSignorell/DescTools/) was used to apply the Cochran Armitage trend test. Statistical significance was assessed at the 0.05 level. All statistical analyses were performed with R 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria. 2020. https://www.R-project.org.)

Results

Our database identified 606 image-guided pre-surgical localizations for malignant lumpectomies from January 1, 2018 to December 31, 2020. A total of 352of 606 (58%) wire localizations and 254 of 606 (42%) SCOUT localizations were performed. 60 of 352 (17%) of wire-localized patients had positive surgical margins, whereas 48 of 254 (19%) of reflector-localized patients had positive surgical margins. (OR = 1.12, *P* value: .59).

124 of 254 (49%) SCOUT localizations were performed under ultrasound guidance and 130 of 254 (51%) were performed using mammographic guidance. Intraoperative ultrasound (IOUS) was

Table 1 Lesions Evaluated for Margins With SCOUT Localizations

Invasive lobular carcinoma	20
Invasive ductal carcinoma	138
Invasive ductal carcinoma and DCIS	46
Ductal Carcinoma in-situ	45
Adenocarcinoma	1
Encapsulated papillary carcinoma	1
Adenoid cystic carcinoma	2
Pleomorphic lobular carcinoma in-situ	1
Total	254

used in 117/254 (46%) cases of SCOUT localized malignant lumpectomies. There were 17/117 palpable lesions for which IOUS was used. Table 1 summarizes the pathologic findings for these cases.

Contingency tables displaying bivariate counts for positive margin status and select variables of interest for patients who received reflector localizations are shown in Table 2 along with odds ratios and corresponding 95% confidence intervals. No association between imaging modality (mammography vs. ultrasound) guidance and positive margin status was observed (OR = 0.63, 95% CI = [0.33, 1.19]). The use of intraoperative ultrasound was associated with decreased positive margin status (OR = 0 .28, 95% CI = [0.14, 0.58]), while in situ disease was associated with increased positive margin status (OR = 1.99, 95% CI = (1.05, 3.75)). These were statistically significant. Although neither of the odds ratios for tumor grade were statistically significant, the results suggest that the likelihood of positive margin status increases with tumor grade. This observation is supported by the fact that results from a Cochran Armitage test bordered on statistical significance ($P = .066$). No association between positive margins and age or BMI was observed (Figure 2). Likewise, there was no association between positive margins and family history or tumor location.

Discussion

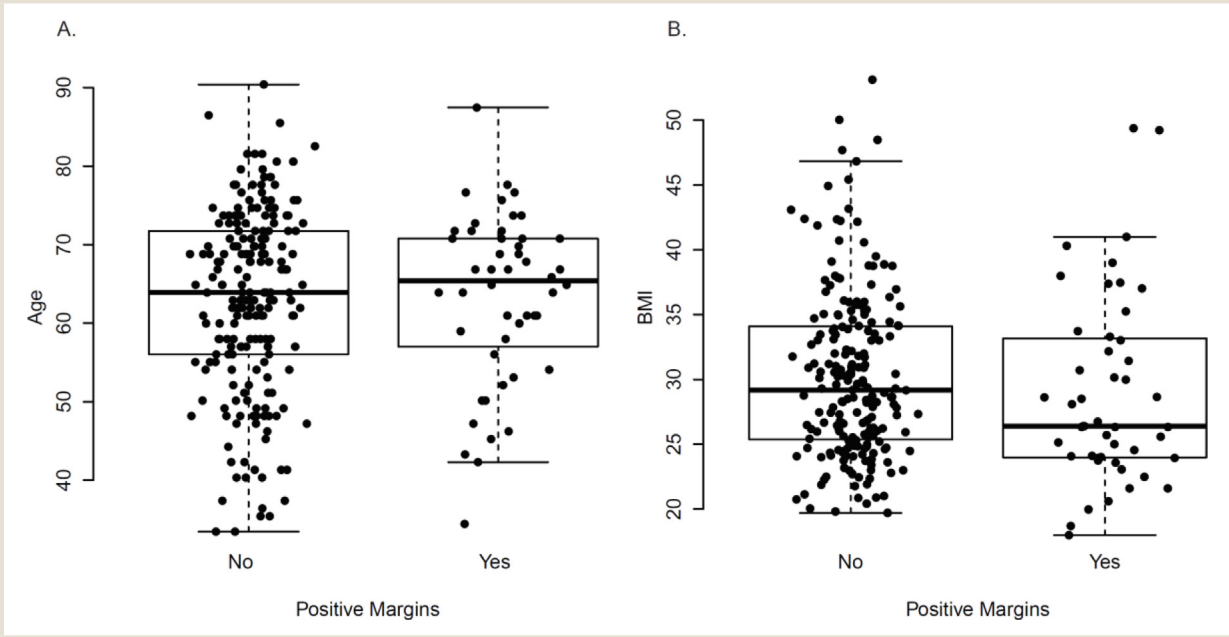
Breast conserving surgery (BCS) is a preferred option for many women diagnosed with early breast cancers. BCS offers cancer treatment which avoids mastectomy improving psychological outcome and self-esteem, however, the oncologic goal remains margin-negative surgery. Although local recurrence after BCS is related to several factors including tumor size, tumor grade, and multifocal or multicentric disease, margin status is the strongest predictor for recurrence.[16] Intraoperative assessment of surgical margins will help reduce positive margin status. This may be achieved by specimen radiography, frozen section or intraoperative ultrasound (IOUS).

Table 2 Summary of Factors Reviewed for SCOUT Localizations

	Margin Status					
Localization modality						
	Negative	Positive	Odds Ratio	Lower 95% CI	Upper 95% CI	*P*
Mammography	101	29	1	NA	NA	NA
Ultrasound	105	19	0.63	0.33	1.19	0.16
Intraoperative Ultrasound						
	Negative	Positive	Odds Ratio	Lower 95% CI	Upper 95% CI	*P*
No	100	37	1	NA	NA	NA
Yes	106	11	0.28	0.14	0.58	< .001
In-Situ Disease						
	Negative	Positive	Odds Ratio	Lower 95% CI	Upper 95% CI	*P*
No	137	24	1	NA	NA	NA
Yes	69	24	1.99	1.05	3.75	0.033
Tumor Grade						
	Negative	Positive	Odds Ratio	Lower 95% CI	Upper 95% CI	*P*
1	61	8	1	NA	NA	NA
2	99	24	1.85	0.78	4.37	0.16
3	44	14	2.43	0.94	6.28	0.063
Locality in breast						
	Negative	Positive	Odds Ratio	Lower 95% CI	Upper 95% CI	*P*
Central	71	19	1	NA	NA	NA
LIQ	11	3	1.02	0.26	4.02	> .99
LOQ	20	2	0.37	0.08	1.74	0.24
UIQ	20	10	1.87	0.75	4.65	0.22
UOQ	81	14	0.65	0.3	1.38	0.34

Abbreviations used: LIQ = lower inner quadrant; LOQ = lower outer quadrant; UIQ = upper inner quadrant; UOQ = upper outer quadrant; NA = not applicable.

Figure 2 Patient age and body mass index by positive margin status. Boxplot displays show patient age (panel A) and body mass index (BMI, panel B) in groups defined by positive margin status. Wilcoxon rank sum tests suggest that the values of age ($P = .89$) and BMI ($P = .11$) are similar in the 2 groups



Research has shown that IOUS improves oncological efficacy with smaller resection volumes. In a recently published article by Rahman et al.[17] which reviewed 945 breast cancer patients at a university-based Breast Center, the re-excision rate with wire localization was 14.5% versus 4.9% with ultrasound guidance. In our clinical practice, the use of IOUS helped to localize non–palpable lesions and even palpable lesions allowing the surgeon to better gauge the optimal extent of resection by skin-marking the approximate central portion of the tumor. This helped to improve negative margin resection rates with an adequate but not excessive amount of surrounding healthy breast tissue. Our results show that there is a statistically significant reduction in the positive margin rates of BCS with the use of IOUS.

The use of IOUS in resections of palpable cancers has been shown to result in smaller volumes of breast tissue excised while lowering re-excision rates.[10,18] Our results show that IOUS is useful in palpable and non–palpable cancers by lowering re-excision rates. Visualization of the cancer prior to incision can be especially critical if the reflector device is inadvertently inactivated during the excision which can occur if the reflector comes into contact with cautery. IOUS, like any other ultrasound, is operator dependent and requires adequate training and experience. Krekel et al.[19] reported that surgeons can gain expertise in ultrasound in a fairly short training period. The American Society of Breast Surgeons together with the American College of Radiology has developed a certification in breast ultrasound for breast surgeons.

The presence of ductal carcinoma in situ is independently associated with a higher rate of positive margins at lumpectomy as compared to invasive breast cancer.[20, 21] Our data analysis found that there is a statistically significant association with positive surgical margins when DCIS is present. Although DCIS most commonly presents as abnormal calcifications on mammography, not all DCIS is associated with calcifications. Approximately 85% of comedo and/or solid DCIS is visible as calcifications, however, only 50% of micropapillary and/or cribriform disease may be evident on specimen radiographs.[21] Specimen radiographs can help identify close margins when DCIS is associated with calcification, but will not help with assessment of positive margins when the DCIS is not associated with calcifications. DCIS also often presents with skipped areas of disease which can further compromise the ability to obtain clear margins on the first surgery. While we support the use of specimen imaging, we acknowledge its limitations. Lee and Carter[22] reported only a 49% sensitivity of specimen radiographs for detecting margin positivity.

Given the significant correlation of positive margins when DCIS is present, information should be discussed with the patient during pre-operative surgical consultation. Incorporating the specific DCIS pathology into the discussion with the patient with respect to risk for positive margins may be helpful because participation in shared decision making (SDM) is considered a keystone in the achievement of sustainable high-quality cancer care. SDM has been shown to increase the satisfaction of the patient, improve cost-effectiveness and reduce malpractice lawsuits.[29]

There was no correlation with patient demographics and positive margin status. There was no association between positive margin status and tumor locality, family history, age or BMI. There was no

Table 3 Published Outcomes Data of SCOUT Localizations for Malignant Lesions

Authors	Number of SCOUT cases	Malignant Lesions	Positive Margins n/N (%)	Number of Re-excisions
Mango[14] (2016)	15	5	0/5 (0)	0
Cox[23] (2016)	50	41	3/41 (7.3)	3
Cox[24] (2016)	153	101	17/101 (16.8)	17
Mango[25] (2017)	123	54	4/54 (7.4)	4
Patel[26] (2018)	42	42	4/42 (9.5)	3
Jadeja[27] (2018)	90	39	4/39 (10.3)	4
Kuzmiak[8] (2020)	111	66	14/66 (21.2)	14
Tingen[7] (2020)	320	320	18/320 (5.6)	17
Total	904	668	64/668 (9.5)	62

significant difference in the outcomes when comparing the mode of deployment of the wire or reflector markers. There is likelihood of positive margin status with higher tumor grade, however, this was not statistically significant. Table 3 is a summary of previous publications showing that SCOUT device is an effective method for preoperative localization of early-stage breast cancers. Our clinical experience supports this finding.

Our data also supports previous findings that there is no significant difference in the surgical outcomes using wire localizations versus SCOUT localizations; the advantages of wire free localizations include ease of scheduling by unlinking the localization from the day of surgery and decreasing patient discomfort.[5,7]

When clinically indicated and feasible, the use of IOUS in patients with Scout placement is recommended to reduce positive surgical margins. To our knowledge, the use of IOUS, and reflector localizations in BCS has not been previously studied. Our results add new information for improving re-excision rates with the use of IOUS in conjunction with reflector localizations for patients undergoing breast conservation therapy.

Study Limitations

This is a retrospective review performed at a single academic institution. There may be selection bias for SCOUT localizations versus wire localizations and for the use of IOUS. Further study is needed to validate the use of IOUS in the setting of BCS using wire or other types of localizations.

Clinical Practice Points

- Reflector localization offers an effective alternative to wire localizations.
- The use of intraoperative ultrasound in conjunction with reflector localization reduces positive surgical margins for breast conserving therapy.
- The presence of DCIS increases the rate of positive surgical margins.
- The mode of localization guidance, age, body mass index, and tumor locality were not associated with surgical margin status.

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