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Outcome of multiple-wire localization for larger breast cancers: do multiple wires translate into additional imaging, biopsies, and recurrences?

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Abstract

BACKGROUND: Breast conservation is possible in breast cancer patients whose mammographic lesions are large enough to require multiple localizing wires for excision.

METHODS: A retrospective review of 112 patients who underwent multiple-wire and 160 controls who underwent single-wire lumpectomy for breast cancer. Rates of in-breast recurrence, metastasis, and additional imaging and biopsy procedures were calculated.

RESULTS: The median follow-up was 24 months. One multiple-wire and 2 single-wire patients developed in-breast recurrences ($P = .84$). No distant metastases developed among the multiple-wire patients. Additional follow-up imaging was obtained in 29% of multiple-wire and 22% of single-wire cases ($P = .1$). Seven (6%) of the multiple-wire and 11 (6%) of the single-wire cases underwent biopsy ($P = .94$).

CONCLUSIONS: We found no increased risk of early local recurrence, metastasis, or additional imaging or biopsies in patients requiring multiple-wire localization for lumpectomy. Breast conservation should be considered a safe option even for patients with mammographically extensive lesions.

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Stringent tumor size guidelines are not routinely applied in determining eligibility for breast-conserving surgery. Rather, surgeons consider breast-conserving surgery a via-

ble treatment option when negative margins can be obtained while also achieving a cosmetically acceptable result.

Multiple localizing wires are often used to bracket larger areas of nonpalpable tumor or calcifications to allow for breast conservation in cases that otherwise would have mandated mastectomy.¹⁻³ Ideally, the use of multiple wires permits the surgeon to excise the entire lesion with a minimum volume of tissue. Another salient goal in undertaking breast-conserving surgery with multiple localizing wires is

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to minimize re-excisions. Although it has recently been shown by O'Sullivan et al⁴ that multiple re-excision procedures do not increase the rate of locoregional recurrence, they do contribute to increased patient anxiety, add to health care costs, and can delay the initiation of adjuvant therapy.

Recently, we showed that the use of multiple localizing wires permits a more precise excision of larger areas of known ductal carcinoma in situ (DCIS) or invasive cancer. Although the volume of tissue excised was greater in the multiple-wire group, 77% of these women were successfully treated with breast-conserving surgery.⁵ In addition, re-excision rates were significantly lower (28% vs 36%) than those of patients undergoing single-wire localized breast-conserving surgery ($P < .01$).

There are little data on the long-term safety of multiple-wire localized breast-conserving surgery for mammographically extensive cancers. There is also little information as to whether such extensive multiple-wire excisions lead to an increased need for subsequent imaging and biopsy procedures, both of which may diminish the relative benefit of breast conservation. In the present study, we sought to examine whether breast-conserving surgery with multiple localizing wires was associated with any elevation in recurrence rate or led to more frequent postoperative imaging studies or biopsies when compared with lumpectomies for lesions small enough to require only the standard approach of a single localizing wire.

Methods

We previously performed an institutional review board-approved retrospective review of 153 patients who underwent multiple-wire localized breast-conserving surgery and 196 controls who underwent single-wire localized breast-conserving surgery for a known breast cancer between May 2000 and November 2006.⁵ Among this cohort of patients, 112 multiple-wire patients and 160 single-wire patients had successful breast-conserving surgery and comprise the current study population. All patients carried a biopsy-proven diagnosis of DCIS and/or invasive breast cancer before the index procedure. The single-wire control group included sequential patients undergoing single-wire localization, half beginning in May 2000 and working forward and the other half sequentially beginning in November 2006 and working backward to create a cohort with median follow-up similar to that of the multiple-wire experimental group.

Patients were eligible for multiple wire localized breast-conserving surgery if the targeted area incorporated $<25\%$ of the breast volume.⁵ Multiple wires were used for lesions that were believed to be too large or eccentric in 3 dimensions to be successfully excised with 1 wire. All wire placements in the study were performed in a single-breast imaging department by a group of 6 dedicated breast radiologists. Surgical procedures were performed by a small group of high-volume breast surgeons throughout the duration of the

study. The decision as to whether to use single or multiple wires was guided by standard breast-imaging department policies throughout the duration of the study and was not altered for individual surgeons.

Medical records for all patients were reviewed for the age of the patient, the number of localizing wires, volume and maximum dimension of wire-localized lumpectomy specimen, tumor histology, and tumor estrogen and HER2 receptor status. Specimen volumes were calculated based on the 3 measurements of length, width, and depth provided in pathology reports. Fisher exact t test analyses were performed to analyze differences between the 2 groups with respect to the previously described parameters.

Margins of ≥ 2 mm were considered negative, and re-excision was directed to margins that were close or positive. All specimens were all examined by dedicated breast pathologists. Per institutional standards, all patients, including those with DCIS, received a recommendation for radiation after lumpectomy with the exception that some women over 70 with estrogen receptor positive tumors were offered surgery and endocrine therapy without radiation. The use of adjuvant systemic therapy was determined by the treating physicians.

Rates of in-breast tumor recurrence, metastasis, and frequency of additional ipsilateral imaging and biopsy procedures were calculated among the population of multiple- and single-wire patients who were successfully treated with lumpectomy. Patients who ultimately required mastectomy for treatment of their primary tumor were excluded from these calculations. Imaging or biopsy was considered additional if indicated for palpable or radiographic findings or if prompted by physician or patient concern about the treated breast. Screening mammography, screening magnetic resonance imaging, or imaging obtained as part of another research protocol was not considered additional. Differences in local recurrence rate were evaluated by using the log-rank test of differences. Fisher exact tests were performed to evaluate differences in the frequency of postoperative imaging and biopsy procedures.

Results

In our previously identified cohort of 349 patients who underwent needle-localized lumpectomy for biopsy-proven breast cancer,⁵ we identified 272 patients in whom breast conservation was successful, 112 patients with multiple-wire localization and 160 with single-wire localization. The remaining patients required mastectomy and are not included in the current analysis because our goal was to compare the rates of local failure and additional imaging with a multiple-wire approach to the widely accepted approach of single-wire lumpectomy. In the multiple-wire group, 2 wires were used in 94 cases, 3 wires in 17 cases, and 4 wires were used in the remaining 1 case.

The mean patient age was 56 years in the multiple-wire group (range 37–86) and 59 years (range 27–92) in the

Table 1 Tumor and specimen characteristics

	Single-wire group, % n = 160	Multiple-wire group, % n = 112
Pathologic tumor type		
DCIS	28	38
DCIS + IDC	49	47
IDC	13	8
DCIS + ILC	2	4
ILC	6	3
DCIS + IDC + ILC	2	0
Receptor status		
ER positive	79	54
HER2 positive	6	8

IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma.

single-wire group. Most tumors contained DCIS alone or in combination with invasive ductal carcinoma (Table 1). In the multiple-wire group, histology showed DCIS without invasion in 38% of patients, with an additional 51% showing DCIS in combination with an invasive carcinoma. The remaining 11% of multiple-wire cases had invasive cancer without DCIS. In the single-wire group, histology showed DCIS without invasion in 28%, with an additional 53% showing DCIS in combination with an invasive carcinoma. The remaining 19% had invasive cancer without DCIS. Significantly fewer tumors were estrogen receptor positive (ER+) in the multiple- versus the single-wire group (Table 1), suggesting that the more extensive lesions were those more likely to be estrogen receptor negative.

The mean specimen volumes were significantly higher in the multiple-wire group compared with the single-wire group (Table 2). The mean volume of tissue excised in the multiple-wire group was 75 mL compared with 49 mL for the single-wire group ($P = .005$). The mean maximal single specimen dimension was also significantly larger in the multiple-wire group (mean 6.2 cm) compared with the single-wire group (5.2 cm) ($P < .002$, Table 2).

The median follow-up was 24 months (range 0–85.6) and did not differ between multiple- and single-wire groups ($P = .19$, Wilcoxon 2-sided t test). The follow-up interval was calculated from the time of the initial wire localized

Table 2 Volume of specimen and number of localizing wires

	Single-wire group	Multiple-wire group	P value (t test)
Mean specimen volume (mL)			
	49.0	75.2	.005
Range (mL)			
	1–200.9	1.4–600	
Mean maximum dimension (cm)			
	5.2	6.2	<.002
Range (cm)			
	0.9–10	2–12	

Table 3 Outcomes after single-wire vs multiple wire breast-conserving surgery

	Single wire (%) n = 160	Multiple wire (%) n = 112	P value
Median follow-up (mo)	24.3	23.8	.19
Local recurrences	2 (1)	1 (1)	.84
Distant metastasis	2 (1)	0 (0)	.51
Additional imaging	36 (22)	32 (29)	.10
Ipsilateral biopsies	11 (7)	7 (6)	.94

lumpectomy to the time of the patient's most recent clinic visit. One multiple-wire patient (1%) and 2 single-wire patients (1%) developed a biopsy proven in-breast recurrence ($P = .84$) (Table 3). The multiple-wire patient, age 47 at the time of her primary diagnosis, had a recurrence of DCIS 12.1 months after primary excision using 3 localizing wires (Table 4). The primary DCIS was grade 3 and estrogen and progesterone receptor (ER/PR) negative. Margins from the primary excision were focally <2 mm, and a decision was made at the time not to perform a re-excision. One single-wire patient, age 35 at the time of her primary diagnosis, developed a recurrence of invasive lobular carcinoma (ER/PR+, HER2–) at 51.4 months after primary excision. Another single-wire patient, age 43, developed a recurrence of grade 1 DCIS (ER/PR+) 22.1 months following primary excision. All 3 patients with local recurrences had undergone whole-breast irradiation during the treatment of their primary carcinoma. All 3 patients underwent mastectomy for the treatment of their recurrent carcinomas and remain alive at 44.7 months, 68.7 months, and 55.7 months, respectively.

Distant metastases developed in 2 single-wire lumpectomy patients (Table 3). One patient was found to have bone metastases 48 months after treatment for a $<.5$ cm grade I DCIS (ER/PR+). She had received both whole-breast irradiation and tamoxifen as adjuvant therapy. She developed a local in-breast recurrence at 22.1 months (as noted previously) and a contralateral invasive ductal carcinoma with bony metastases at 48 months. The other patient developed bone metastases 48 months after treatment for invasive ductal carcinoma with DCIS (ER/PR+ and HER2+). Both patients remain alive to date. No distant metastases have developed among the multiple-wire lumpectomy patients ($P = .51$ vs single-wire patients).

There was no significant difference in the frequency of additional postoperative imaging studies obtained during the follow-up of multiple- versus single-wire localized patients treated with breast-conserving surgery. Additional diagnostic imaging (excluding routine screening mammography, screening breast magnetic resonance imaging, and imaging obtained for purposes of another research protocol) was obtained in 29% of multiple-wire cases and 29% of single-wire cases ($P = .1$) (Table 3).

Table 4 Local recurrences after breast-conserving surgery tumor characteristics

Recurrence	Wires	Primary tumor	Hormone receptors	Margins	Recurrence	mo to Recurrence
Patient 1	3	DCIS	ER/PR-	Focal <2 mm	DCIS	12.1
Patient 2	1	ILC	ER/PR+ Her2-	>2 mm	ILC	51.4
Patient 3	1	DCIS	ER/PR+	>2 mm	DCIS	22.1

There was no significant difference between multiple- versus single-wire groups with respect to the frequency of additional breast biopsies performed during the follow-up period in those treated with breast-conserving surgery (Table 3). Seven multiple-wire patients (6%) and 11 single-wire patients (7%) underwent ipsilateral breast biopsy ($P = .94$). One of the 7 multiple-wire biopsies and 2 of 11 single-wire biopsies revealed cancer.

Comments

Most patients presenting with invasive or in situ breast carcinoma are candidates for breast conservation. Although no strict size criteria exclude a particular patient population from breast-conserving surgery, many surgeons recommend mastectomy rather than primary breast-conserving surgery for tumors larger than 4-5 cm or for those tumors consuming >25% of the volume of a woman's breast.^{6,7} Eligibility is based on the achievement of negative margins, the ability to deliver adjuvant radiotherapy, and the likelihood of a cosmetically acceptable outcome.⁸ In addition, many surgeons are reluctant to perform breast-conserving surgery for extensive areas of calcifications on mammography previously documented to be DCIS or invasive carcinoma. With the advent of multiple-wire localization techniques to bracket these more extensive lesions, breast conservation has become more commonplace for large mammographic lesions in our institution and others.^{1,2,9,10} We recently showed that breast preservation is possible for most patients undergoing multiple-wire localized lumpectomy for larger areas of breast cancer identified on mammography.⁵ In addition, fewer re-excisions were necessary to achieve clear margins in comparison to single-wire localized lumpectomies, likely because of a more precise localization provided by multiple wires as well as the fact that larger volumes of tissue were excised in these cases.

Although breast preservation is an important goal, the prevention of in-breast recurrence and distant disease is of paramount importance when contemplating breast-conserving surgery. To date, there have been no data evaluating the long-term safety of multiple-wire localized breast-conserving surgery for mammographically extensive cancers. In our study, we found no significant difference in either the early locoregional recurrence rate or the frequency of metastatic disease among patients undergoing multiple- versus single-wire breast-conserving surgery. We found that our recur-

rence rate was approximately 1% over a median follow-up interval of 24 months, which is well within the accepted range shown by other studies.¹¹⁻¹⁴ One limitation of our study, however, is the short median follow-up interval. Given that the majority of in-breast recurrences are observed within 5 years of initial diagnosis, it will be important to review our data with longer follow-up to confirm that recurrence rates remain similar between groups.

Our 3 local recurrences occurred in 2 cases of DCIS and one of invasive lobular carcinoma. Cellini et al¹⁵ showed that when the primary tumor histology was DCIS or invasive lobular carcinoma, more residual cancer was found in re-excised specimens, suggesting that additional occult microscopic disease may be present despite the achievement of seemingly clear margins. It has also been shown that residual disease is increased in frequency with increasing size and grade of DCIS, which describes 2 of our 3 recurrences.¹⁶⁻¹⁸ The 2 cases of recurrence within the single wire group (1 DCIS and 1 invasive lobular carcinoma) both underwent re-excision during the course of initial treatment and had clear margins with these re-excisions. In the 1 multiple wire case of DCIS that recurred, margins from the primary excision were focally <2 mm, and a decision was made at the time not to perform a re-excision. The finding of a potentially microscopically positive margin suggests that this recurrence among our multiple wire group may not have occurred had a re-excision been performed.

There was a small but not statistically significant increase in the frequency of additional, nonroutine, postoperative imaging performed among our multiple wire localized patients. This could be driven by several potential factors, including the fact that a greater proportion of these were DCIS and characterized by areas of calcifications that either the surgeon and/or radiologist wished to confirm were all excised at the time of surgery or to monitor for change if still present postoperatively. Additionally, one can speculate that a greater degree of scarring may occur with the excision of greater volumes of tissue and/or with parenchymal mobilization during oncoplastic closure. This scarring could potentially lead to mammographic abnormalities that call for close short-term follow-up or biopsy. Overall, the observed increase in additional imaging was small enough that we do not think that it is a contraindication to multiple wire localized lumpectomy.

The goal of achieving negative margins with the fewest number of procedures while still preserving the breast presents cosmetic challenges as well. Although we previously

found that larger specimen volumes were excised with multiple wire localization, many in our practice use oncoplastic techniques of breast parenchymal mobilization and advancement flap closure to achieve acceptable cosmetic results. In future studies, we plan to examine the long-term cosmetic outcomes from both the patient and physician's perspectives after breast-conserving surgery in our study population.

Conclusions

We have found that performing multiple wire localized lumpectomy in cases of larger mammographic lesions does not lead to an increased rate of early local or distant recurrence or an increased rate of imaging studies or biopsies during the early postoperative period. A longer follow-up is underway to confirm that recurrence rates after multiple wire localized lumpectomy remain low.

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