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Original Article

MOLLI Seed and Surgical Margin Status in Breast-conserving Surgery: An Exploratory Study

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Abstract

Background and objectives: Fine-wire-guided localization (FWGL) has traditionally been used for nonpalpable breast lesions although it can complicate specimen handling. Magnetic Occult Lesion Localization and Imaging (MOLLI) is a wire-free alternative for which comparative pathologic data remain limited. This exploratory study examined margin status, morphometry, and specimen integrity.

Methods: We retrospectively analyzed 109 consecutive lumpectomy specimens (83 MOLLI, 26 FWGL) at a single academic center between March 2022 and April 2023, comprising 108 primary excisions and one re-excision. The localization method was not randomly assigned and appears to have depended on surgeon preference. Secondary invasive-carcinoma analyses used Firth penalized logistic regression to adjust for potential confounding.

Results: After exclusion of 33 benign lesions, 76 carcinomas remained (62 invasive carcinomas and 14 cases of pure ductal carcinoma *in situ*), 75 with evaluable primary-excision margins. For the primary outcome, positive margins occurred in 13.8% (8/58) of MOLLI versus 17.6% (3/17) of FWGL cases (P = 0.70). In the secondary invasive-carcinoma analysis, positive margins occurred in 10.9% (5/46) versus 18.8% (3/16) (P = 0.41). Median specimen weight and volume did not differ significantly; specimen integrity was preserved in 98.8% (82/83) of MOLLI and 100% (26/26) of FWGL specimens.

Conclusions: In this exploratory study, MOLLI shows no detectable differences in margin status, morphometry, or specimen integrity relative to fine-wire localization. Unlike published data on a related magnetic-seed device, we observe no reduction in resected tissue volume, indicating that findings for one device should not be assumed to apply to another. The study is underpowered to detect small differences. These preliminary findings therefore require confirmation in larger studies.

Introduction

Breast-conserving surgery followed by adjuvant radiation therapy remains the standard of care for early-stage breast cancer. The central surgical objective of breast-conserving surgery is complete excision of the neoplastic lesion with microscopically clear margins. Consensus guidelines define an adequate margin for invasive carcinoma as no ink on tumor[1]; a positive margin—invasive or *in situ* carcinoma extending to the inked surface of the specimen—typically mandates re-excision. Re-excision increases patient morbidity and psychological distress, delays adjuvant therapy, adds cost, and can compromise cosmetic outcome.[2,3] Minimizing positive margins is therefore a key quality metric in breast surgical oncology and surgical pathology.

As screening mammography and high-resolution ultrasonography have advanced, an increasing proportion of breast carcinomas are detected at a nonpalpable stage, making precise preoperative and intraoperative localization essential. For decades,

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fine-wire-guided localization has served as the institutional reference standard. In this approach, a percutaneous hook-wire is deployed into or adjacent to the target lesion under imaging guidance, usually on the morning of surgery. Although effective, this localization method has recognized limitations.[4] Clinically, the protruding wire limits patient mobility, can cause discomfort, and creates scheduling dependencies between radiology and the operating room. From a pathology perspective, a rigid transfixing wire can complicate grossing: it may require careful dissection prior to sectioning, can distort specimen orientation, and constitutes a sharps hazard at the grossing bench.

Several wire-free technologies have emerged in response, including radioactive seed localization, radiofrequency identification tags, radar reflectors, and magnetic seeds.[4,5] Magnetic Occult Lesion Localization and Imaging (MOLLI), developed at the Sunnybrook Odette Cancer Centre, uses a small (approximately 3.2 mm) passive magnetic seed that can be implanted into the target lesion days to weeks before surgery. Intraoperatively, a handheld magnetometer probe detects the magnetic signature and provides continuous three-dimensional spatial feedback to guide dissection.[6,7] By decoupling localization from the day of surgery and removing the external wire, MOLLI has the potential to improve patient experience and streamline both radiology and pathology workflows.

First-in-human and early clinical experience established the safety and feasibility of the MOLLI system,[7] and larger multicenter and comparative evaluations of magnetic seed localization have reported margin and re-excision outcomes comparable to those of wire localization.[8,9] MOLLI-specific clinical evidence, however, remains sparse: to date, only a 20-patient phase 1 feasibility study and a single-arm 145-patient series have been reported.[7,10] A Canadian health technology assessment appraised MOLLI on the basis of a single noncomparative case series and identified no comparative data for the device,[11] and a recent international systematic review likewise noted that MOLLI evidence rests on one feasibility study.[12] Data addressing detailed pathologic endpoints—margin clearance stratified by tumor histology and gross specimen morphometry—within routine surgical pathology practice are likewise lacking. We therefore undertook this exploratory, retrospective, single-center study to compare the pathological outcomes of MOLLI seed-guided and fine-wire-guided excisions, focusing on positive-margin rates and corresponding gross specimen characteristics. We deliberately restricted the scope to endpoints that are measured in the pathology laboratory, since these have received comparatively little attention in the localization literature; we recognize that this leaves broader clinical outcomes, including operative measures, patient-reported outcomes, and long-term recurrence, outside the scope of the present analysis.

Materials and methods

Study design and cohort

This retrospective, single-center cohort study analyzed 109 consecutive breast-conserving lumpectomy specimens accessioned at St. Paul's Hospital, Providence Health Care, Vancouver, British Columbia, between March 2022 and April 2023, a period corresponding to the initial implementation of MOLLI at our institution. Of these, 108 were primary breast-conserving excisions and one was a re-excision specimen. Cases were identified sequentially from the institutional pathology archives without selection; each specimen corresponded to a distinct patient, with no bilateral or synchronous cases. Breast-conserving surgery was performed by five surgeons during the study period; case-level attribution to individual surgeons was not recorded, so stratification by surgeon was not possible. Allocation was not randomized and not governed by a written eligibility protocol: no formal size-, subtype-, or location-based criteria determined MOLLI use, and method selection appears to have depended substantially on surgeon preference and familiarity with the newly introduced system. In total, 83 specimens were localized with MOLLI magnetic seeds and 26 with fine-wire localization. The number of localization devices was documented in 100 specimens: a single device was placed in 91 specimens (75 MOLLI and 16 fine-wire), and more than one device was used for bracketing in 9 specimens (6 MOLLI and 3 fine-wire). Device-number information was unavailable for the remaining 9 specimens (2 MOLLI and 7 fine-wire). All localizations were captured irrespective of final diagnosis; 33 specimens yielding benign or other non-carcinomatous lesions (24 MOLLI, 9 fine-wire) were excluded from diagnosis-dependent analyses, leaving a carcinoma cohort of 76 specimens (59 MOLLI, 17 fine-wire) comprising 62 invasive carcinomas and 14 cases of pure ductal carcinoma *in situ* (DCIS). The re-excision specimen (a MOLLI case with residual intermediate-grade DCIS) was excluded from the margin analysis, having no primary-excision margin to assess, leaving 75 margin-evaluable primary-excision carcinomas (58 MOLLI, 17 fine-wire). The complete cohort flow is summarized in Figure 1. Data were extracted by cross-referencing gross dictations with final diagnostic reports.

Data extraction and morphometric variables

A structured data matrix captured macroscopic and microscopic parameters for each specimen: localization method, patient age and sex, and the pathologists' assistant responsible for grossing. To assess tissue-sparing and surgical precision, the following morphometric variables were recorded. Specimen weight (g) was obtained directly from the laboratory balance, and specimen volume (mL) was derived from three-dimensional macroscopic measurements taken prior to sectioning. Gross tumor size (cm) was determined by visual or palpatory assessment in the gross room, and microscopic tumor size (mm) was measured on the final histologic sections. Specimen integrity was documented to assess whether the localization method contributed to fragmentation.

Pathologic processing and margin assessment

All specimens were processed according to standardized institutional breast grossing protocols. Our routine pathway is image-guided core biopsy with placement of a tissue marker clip, followed by preoperative localization with either a fine wire or a MOLLI seed and subsequent excision. Specimens were oriented using surgical sutures or clips, and the external surfaces were differentially inked to permit three-dimensional margin mapping. Gross morphometric assessment was performed at the bench as part of routine grossing: specimen weight was measured on a calibrated balance, three orthogonal specimen dimensions (mediolateral, superoinferior, and anteroposterior) were recorded, and spe-

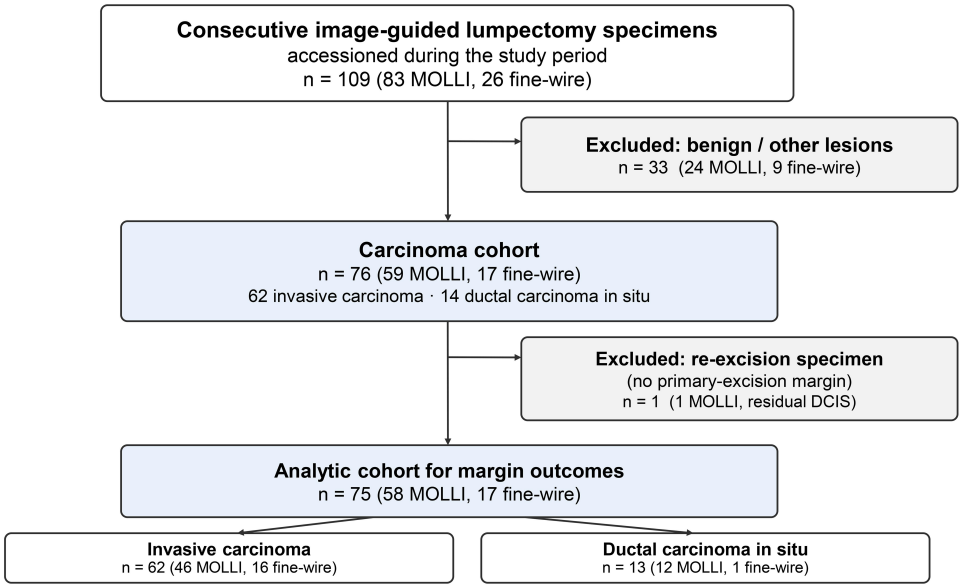


Fig. 1. Cohort flow. Consecutive image-guided lumpectomy specimens were captured irrespective of final diagnosis; benign and other non-carcinomatous lesions were excluded from diagnosis-dependent analyses, and one re-excision specimen (residual DCIS), which by definition has no primary-excision margin, was excluded from the margin analysis. DCIS, ductal carcinoma *in situ*; MOLLI, Magnetic Occult Lesion Localization and Imaging.

cimen volume was calculated as their product, a rectangular-prism approximation. Because lumpectomy specimens are irregular, this is a geometric estimate rather than a direct volumetric measurement. Specimen integrity was defined as receipt of the specimen as a single intact, orientable structure suitable for standard margin assessment. For fine-wire specimens, the wire was carefully dissected free before sectioning to avoid blade damage and tissue distortion. For MOLLI specimens, the magnetic seed was identified visually or by palpation during serial sectioning and its location documented (e.g., within the mass, adjacent to the lesion, or loose within the container). Final margin status was based on standard gross and microscopic pathological assessment of the excised specimen. No intraoperative margin-assessment adjuncts were used at our institution during the study period: neither specimen radiography (including Faxitron imaging) nor intraoperative ultrasound was performed, and routine cavity shave margins were not taken. Representative gross and histologic images of the seed within the specimen were obtained for illustrative purposes (Fig. 2). Generative artificial intelligence tools were used solely for language proofreading and copyediting of this manuscript; they were not used to generate, analyze, or interpret data, and are not listed as authors.

Margin status was defined microscopically, consistent with consensus guidelines of the Society of Surgical Oncology and the American Society for Radiation Oncology for invasive carcinoma and DCIS.[1,13] The primary margin outcome was any invasive carcinoma or DCIS at the inked surgical margin (distance = 0 mm) among all margin-evaluable primary-excision carcinomas. Histology-stratified analyses were secondary. For invasive carcinoma, any measurable distance between tumor and the inked margin was classified as negative (no ink on tumor). For DCIS, a margin was classified as positive when DCIS was present at the inked margin. When DCIS was not present at ink, the distance from the inked margin was measured microscopically and categorized as <2 mm or ≥2 mm to assess guideline-based margin adequacy separately. Thus, the 2-mm threshold was not used to define the primary margin outcome, and a DCIS margin of <2 mm was not classified as positive in the primary analysis. DCIS margin distance was additionally categorized as <2 mm or ≥2 mm for descriptive assessment and was not used to define positive margins in the primary or histology-stratified analyses. Receptor biomarker profiles (estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2)) and Nottingham histologic grade were recorded as descriptive cohort characteristics.

Statistical analysis

Continuous variables were summarized as medians with interquartile ranges (IQRs), or means ± standard deviations where distributions were approximately symmetric, and compared using the Mann–Whitney U or independent-samples t test as appropriate. Two-by-two categorical comparisons, including the primary outcome of any invasive carcinoma or DCIS at ink among all margin-evaluable primary-excision carcinomas, were assessed with the Fisher exact test. Distributions across more than two categories were compared using the Fisher–Freeman–Halton exact test. In the secondary invasive-carcinoma analysis, effect estimates were reported as an odds ratio, and multivariable adjustment used Firth penalized logistic regression rather than standard maximum-likelihood estimation, because the small number of positive-margin events produces unstable estimates and, when tumor grade is included, complete separation (no high-grade case had a positive margin); Firth's method reduces small-sample bias and remains well defined under separation.[14,15] Confidence intervals for these models were calculated by

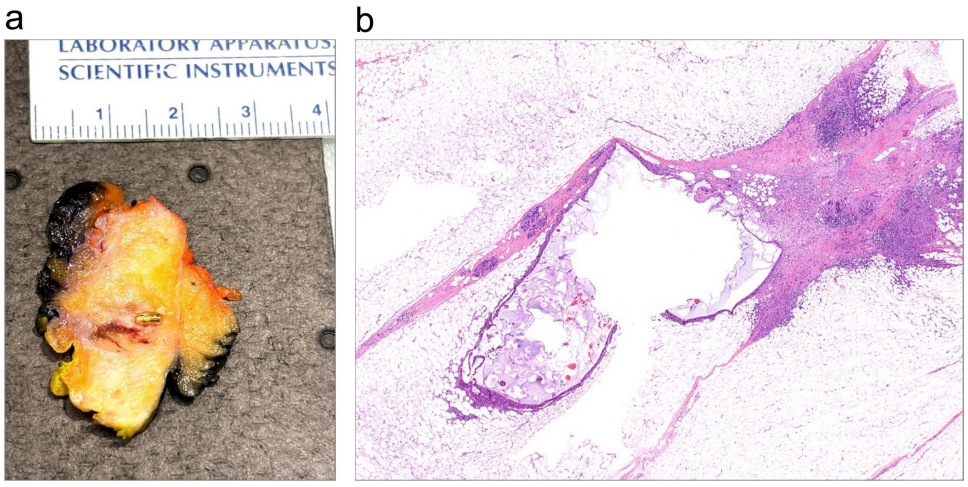


Fig. 2. MOLLI magnetic seed within a breast-conserving surgical specimen. (a) Gross appearance at the grossing bench: the magnetic seed is identified within the lumpectomy specimen during serial sectioning, without disruption of specimen orientation or margin inking. (b) Corresponding histologic appearance of the seed site (hematoxylin and eosin, original magnification ×20). MOLLI, Magnetic Occult Lesion Localization and Imaging.

penalized profile likelihood rather than Wald approximation. The number of covariates such a model can support is limited by the number of outcome events rather than the sample size; with 8 positive-margin events, and the conventional requirement of at least ten events per variable, the data support only minimal adjustment. Age was selected as the adjustment variable for the principal adjusted analysis because it was recorded for every patient and so preserves the full analytic set, whereas Nottingham grade was missing in 24.2% of invasive cases. Specimen weight and volume were not entered as covariates: they are determined by the excision itself and therefore lie downstream of the localization method on the causal pathway, so adjusting for them would constitute overadjustment. Rather than stacking covariates into a single model, remaining candidate confounders were entered one at a time alongside localization method as sequential sensitivity analyses. Even so, these models contain only three to four events per variable and therefore remain below the conventional threshold; this is precisely why penalized estimation with profile-likelihood intervals was used, and why the adjusted estimates are presented as tests of the robustness of the unadjusted comparison rather than as definitive adjusted effects. Analyses were restricted to complete cases, with no imputation, and the extent of missing data is reported. The multivariable analyses and the post-hoc power calculation were performed after peer review, at the editors' request, and are reported as such. A two-sided P value < 0.05 was considered statistically significant. Given the exploratory nature of the analysis, no adjustment for multiple comparisons was applied, and comparisons involving very small subgroups are reported descriptively.

Results

Cohort and baseline characteristics

A total of 109 consecutive image-guided lumpectomy specimens were identified: 83 MOLLI seed-guided and 26 fine-wire-guided procedures, comprising 108 primary excisions and one re-excision. Each specimen corresponded to a distinct patient; no bilateral or synchronous cases were present. A total of 33 specimens (30.3%) yielded benign or other non-carcinomatous lesions (24 MOLLI, 9 fine-wire) and were excluded from diagnosis-dependent analyses, leaving a carcinoma cohort of 76 specimens (59 MOLLI, 17 fine-wire), of which 62 were invasive carcinomas (46 MOLLI, 16 fine-wire) and 14 were pure DCIS (13 MOLLI, 1 fine-wire). Among the invasive carcinomas, 7 were invasive lobular carcinoma (6 MOLLI, 1 fine-wire) and 55 were invasive ductal or other non-lobular subtypes (40 MOLLI, 15 fine-wire); no specimen contained both invasive ductal and invasive lobular carcinoma. A DCIS component was present alongside invasive carcinoma in 32 specimens (21 MOLLI, 11 fine-wire). No statistically significant difference in the overall distribution of histologic categories was detected between localization groups ($P = 0.31$). The single re-excision specimen was excluded from the margin analysis, leaving 75 margin-evaluable primary-excision carcinomas (58 MOLLI, 17 fine-wire) for the primary outcome analysis (Fig. 1).

Baseline characteristics are summarized in Table 1. Mean patient age was 59.3 ± 12.7 years for MOLLI and 56.9 ± 14.7 years for fine-wire cases ($P = 0.41$), and all patients were female. Among invasive carcinomas, mean microscopic tumor size was 15.9 ± 9.1 mm for MOLLI and 19.0 ± 16.8 mm for fine-wire ($P = 0.36$). No statistically significant differences in baseline variables were detected between groups; however, given the small fine-wire group and the substantial missingness in biomarker data described below, the absence of a detected difference should not be taken as evidence that the cohorts were equivalent at baseline.

Gross specimen morphometry

Morphometric endpoints were assessed across the full cohort of 109 specimens and, as a sensitivity analysis, in the 76 carcinomas. Specimen weight, volume, and integrity reflect the localization method and excision rather than histologic diagnosis; therefore,

Table 1. Baseline demographic and tumor characteristics

Characteristic	MOLLI	Fine-wire	*P* value
All patients			
Number of specimens	83	26	—
Age, years (mean ± SD)	59.3 ± 12.7	56.9 ± 14.7	0.41
Age range, years	38–89	28–89	—
Female sex, *n* (%)	83 (100)	26 (100)	NE
Histologic distribution, n			0.31
Invasive carcinoma	46	16	
Ductal carcinoma *in situ*	13	1	
Benign/other	24	9	
Invasive carcinoma characteristics			
Invasive carcinoma with DCIS component, n	21	11	
Microscopic size, mm (mean ± SD)	15.9 ± 9.1	19.0 ± 16.8	0.36
Nottingham grade, n			> 0.99
Grade 1	10	5	
Grade 2	17	9	
Grade 3	4	2	
Grade not recorded	15	0	
Biomarker data availability			
ER result not available, *n* (%)	22/46 (47.8)	1/16 (6.3)	
PR result not available, *n* (%)	22/46 (47.8)	1/16 (6.3)	
HER2 result not available, *n* (%)	23/46 (50.0)	1/16 (6.3)	

Continuous variables were compared using the t test; 2 × 2 categorical comparisons by Fisher exact test; multicategory distributions (histology, Nottingham grade) by Fisher–Freeman–Halton exact test, with the *P* value shown on the variable heading row. Sex is not estimable because both cohorts were 100% female. No *P* value is given for the number of specimens or the age range, which are descriptive. Receptor positivity is not tabulated or compared: biomarker assays are generally performed on the diagnostic core biopsy and were often not recorded with the excision specimen, so availability was incomplete and unevenly distributed between groups. The proportion of cases without an available result is shown instead. DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MOLLI, Magnetic Occult Lesion Localization and Imaging; NE, not estimable; PR, progesterone receptor; SD, standard deviation.

results for both cohorts are reported. Diagnosis-dependent endpoints remain restricted to carcinomas.

Gross specimen characteristics did not differ significantly between localization methods. Distributions were right-skewed in both cohorts and are therefore summarized as median [IQR]. Across the full cohort, median specimen weight was 15.1 g for MOLLI and 13.9 g for fine-wire cases ($P = 0.78$ by Mann–Whitney U) and median specimen volume was 26.5 mL versus 25.3 mL ($P = 0.89$). In the carcinoma-only sensitivity analysis, median specimen weight was 20.0 g [12.6–41.6] for MOLLI versus 18.5 g [11.4–32.1] for fine-wire ($P = 0.90$), median specimen volume was 35.8 mL [19.4–66.6] versus 25.3 mL [17.7–64.3] ($P = 0.62$), and median gross tumor size was 1.8 cm [1.2–2.5] versus 1.5 cm [1.1–2.2] ($P = 0.43$). Neither analysis showed evidence of systematically larger excisions in either group (Table 2). Because preoperative imaging-based tumor size was not available, these data cannot establish whether either method achieved more precise excision relative to lesion size.

Tumor biology and biomarker profile

Tumor grade is summarized in Table 1. Receptor results are not compared between groups because, although ER, PR, and HER2 testing is performed routinely in all cases, the assay is usually carried out on the diagnostic core biopsy rather than repeated on the excision specimen, and those results were frequently not captured in this specimen-based dataset. Results were not available for 47.8% of MOLLI versus 6.3% of fine-wire invasive carcinomas for ER, 47.8% versus 6.3% for PR, and 50.0% versus 6.3% for HER2. Nottingham grade was likewise not recorded in 15 of 46 MOLLI cases and none of the fine-wire cases. Because availability is so unbalanced between groups, any comparison of receptor positivity would reflect which results happened to be captured rather than underlying tumor biology, and no such comparison is reported. Analyses throughout were restricted to complete cases, and denominators reflect cases with available results.

Table 2. Gross specimen morphometry for the full cohort (*n* = 109) and carcinoma specimens (*n* = 76). Values are medians [interquartile ranges]; *P* values are from the Mann–Whitney U test, except for specimen integrity (Fisher exact test)

Parameter	MOLLI	Fine-wire	*P* value
Full cohort (*n* = 109)			
Specimen weight, g — median [IQR]	15.1 [9.2–29.3]	13.9 [9.2–27.7]	0.78
Specimen volume, mL — median [IQR]	26.5 [16.5–54.0]	25.3 [17.7–35.2]	0.89
Intact specimen, *n* (%)	82/83 (98.8)	26/26 (100)	> 0.99
Carcinoma only (*n* = 76)			
Specimen weight, g — median [IQR]	20.0 [12.6–41.6]	18.5 [11.4–32.1]	0.90
Specimen volume, mL — median [IQR]	35.8 [19.4–66.6]	25.3 [17.7–64.3]	0.62
Gross tumor size, cm — median [IQR]	1.8 [1.2–2.5]	1.5 [1.1–2.2]	0.43

Values are medians [interquartile ranges]. *P* values for specimen weight, specimen volume, and gross lesion size from the Mann–Whitney U test, given right-skewed distributions; specimen integrity from the Fisher exact test. Denominators differ by variable because not every measurement was recorded. Full cohort: specimen weight 83/83 MOLLI and 26/26 fine-wire; volume 83/83 and 23/26. Carcinoma-only subset: specimen weight and volume 59/59 MOLLI and 17/17 fine-wire; gross lesion size 51/59 and 16/17. Gross lesion size was unavailable when no discrete lesion was visible or palpable at the bench. IQR, interquartile range; MOLLI, Magnetic Occult Lesion Localization and Imaging.

Primary outcome: Any carcinoma component at ink

The primary outcome was any invasive carcinoma or DCIS at ink among all margin-evaluable primary-excision carcinomas. Positive margins occurred in 13.8% (8/58) of MOLLI-guided cases and 17.6% (3/17) of fine-wire-guided cases ($P = 0.70$). In the secondary invasive-carcinoma analysis, positive margins occurred in 10.9% (5/46) of MOLLI-guided cases and 18.8% (3/16) of fine-wire-guided cases ($P = 0.41$). The unadjusted odds ratio was 0.51 (95% confidence interval, 0.12–2.46), and the age-adjusted odds ratio was 0.52 (95% confidence interval, 0.13–2.08). Among pure DCIS cases, positive margins occurred in 25.0% (3/12) of MOLLI cases and 0% (0/1) of fine-wire cases. Because the fine-wire group included only one pure DCIS case, this comparison was considered descriptive (Table 3).

Specimens with a positive invasive margin were substantially smaller than those with a negative margin: median weight 9.3 g [IQR 8.9–14.5] versus 26.3 g [15.2–46.2] ($P = 0.003$) and median volume 21.4 mL [15.6–26.9] versus 45.9 mL [21.8–75.8] ($P = 0.023$). Specimen size was not significantly different between localization groups (weight $P = 0.78$, volume $P = 0.89$), although residual confounding cannot be excluded; it is reported descriptively and was not used as an adjustment variable.

A DCIS component was present in 45 primary-excision specimens, all of which had a recorded DCIS margin status. DCIS was on ink in 5 specimens (4 MOLLI, 1 fine-wire). The remaining 40 had a negative DCIS margin, with a recorded distance of < 2 mm in 16 (11 MOLLI, 5 fine-wire) and ≥ 2 mm in 19 (13 MOLLI, 6 fine-wire); in 5, all MOLLI cases from the earliest part of the series, the margin was negative but the distance was not recorded, so documentation was not balanced between groups. The margin categories are summarized in Table 4. Among pure DCIS specimens alone, all 13 evaluable cases were classifiable (MOLLI: 3 on ink, 4 < 2 mm, 5 ≥ 2 mm; fine-wire: 1 ≥ 2 mm). Given the small numbers per stratum, these data are descriptive and were not compared statistically.

Specimen integrity and grossing observations

Specimen integrity was preserved in 98.8% (82/83) of MOLLI and 100% (26/26) of fine-wire cases ($P > 0.99$); one MOLLI specimen was received with a loose fragment in the same container. No seed, wire, or biopsy clip extrusion was recorded in either group, and no wire-related sharps incidents were documented. In MOLLI cases, the seed was identified during serial sectioning and did not impede inking, orientation, or sectioning; these grossing observations are anecdotal and unquantified, as no time-based or throughput metrics were collected. The gross and corresponding microscopic appearance of the magnetic seed within the lumpectomy specimen is illustrated in Figure 2.

Discussion

In this exploratory, retrospective, single-center analysis of 109 consecutive lumpectomy specimens, margin positivity, gross specimen morphometry, and specimen integrity did not differ significantly between MOLLI seed-guided and fine-wire-guided localization. For the primary outcome, positive-margin rates were 13.8% and 17.6%, respectively ($P = 0.70$). In the secondary invasive-carcinoma analysis, positive-margin rates were 10.9% and 18.8%, respectively ($P = 0.41$), and the confidence interval around the effect estimate was wide (odds ratio 0.51, 95% confidence interval, 0.12–2.46). Because the study was underpowered, these data should not be read as demonstrating equivalence between the two methods; they establish only that no difference was detected in a cohort of this size.

Our margin-positivity rates are broadly in line with the published literature, in which pooled analyses of magnetic-seed and other wire-free devices have not shown higher positive-margin rates than wire guidance; one meta-analysis reported 12.3% versus 14.9%.[8,16,17] MOLLI-specific data are more limited: the phase 1 study of 20 patients reported no positive margins,[7] and the only prior MOLLI cohort (145 patients) reported 17.3%,

Table 3. Primary margin outcome and secondary histology-stratified positive-margin rates

Margin status	MOLLI	Fine-wire	*P* value
Primary outcome: all carcinomas			
Positive margin, *n*/*N* (%)	8/58 (13.8)	3/17 (17.6)	0.70
Negative margin, *n*/*N* (%)	50/58 (86.2)	14/17 (82.4)	
Secondary analysis: invasive carcinoma			
Positive margin, *n*/*N* (%)	5/46 (10.9)	3/16 (18.8)	0.41
Negative margin, *n*/*N* (%)	41/46 (89.1)	13/16 (81.3)	
Secondary analysis: ductal carcinoma *in situ*			
Positive margin, *n*/*N* (%)	3/12 (25.0)	0/1 (0)	> 0.99[a]
Negative margin, *n*/*N* (%)	9/12 (75.0)	1/1 (100)	

N denotes evaluable primary-excision cases with recorded margin status; one MOLLI DCIS re-excision specimen was excluded because it had no primary-excision margin to assess. A specimen was counted as positive if invasive carcinoma or DCIS was present at the inked margin; the combined row sums the two mutually exclusive groups. All *P* values were calculated using Fisher's exact test. [a]The DCIS comparison includes only one fine-wire case; the test therefore has essentially no power and the resulting *P* value should be regarded as uninformative rather than as evidence of equivalence. This subgroup is presented descriptively. DCIS, ductal carcinoma *in situ*; MOLLI, Magnetic Occult Lesion Localization and Imaging.

Table 4. Ductal carcinoma *in situ* margin status by distance category (all DCIS-containing primary-excision specimens; *n* = 45)

DCIS margin category	MOLLI	Fine-wire	Total
DCIS on ink	4	1	5
Negative, < 2 mm from margin	11	5	16
Negative, ≥ 2 mm from margin	13	6	19
Negative, distance not recorded	5	0	5
Total	33	12	45

DCIS, ductal carcinoma *in situ*; MOLLI, Magnetic Occult Lesion Localization and Imaging. DCIS margin was recorded as positive when DCIS was present at the inked margin; where DCIS was not at ink, the distance to the closest margin was recorded and grouped as < 2 mm or ≥ 2 mm. Distances were not separately documented in five specimens, all MOLLI cases from the earliest part of the series. Numbers within strata are small and are presented descriptively; no statistical comparison was performed.

though it classified tumor within 2 mm as positive and pooled invasive and *in situ* disease, so its figures are not directly interchangeable with ours.[10] Under our histology-stratified, no-ink-on-tumor definition, the MOLLI invasive rate of 10.9% sits at the favorable end of this range and the fine-wire rate of 18.8% is congruent with wire-guided experience. The absence of a statistically significant difference in our series reflects limited power and does not demonstrate equivalence. A 2026 systematic review and meta-analysis likewise concluded that magnetic seed localization is a safe and effective alternative to wire guidance, reporting lower re-excision rates for positive margins,[18] though that analysis pooled studies of the Magseed device.

From a surgical pathology perspective, the morphometric findings merit comment. Two prior comparative series have reported significantly smaller resections with magnetic seed than with wire guidance: Redfern and Shermis found lower total resected volume (13.7 versus 17.1 mL) and lower calculated resection ratios with a magnetic seed,[19] and Moreno-Palacios *et al.*,[20] in the largest such series (149 magnetic-seed versus 76 wire cases), likewise reported significantly smaller specimen volumes with the magnetic marker. Both of those studies, however, evaluated the Magseed system. Although MOLLI and Magseed are both magnetic-seed devices, they are not identical products, and in our MOLLI cohort we observed no such difference: median specimen weight and volume were nearly identical between groups for lesions of similar microscopic and gross size, with no reduction in tissue removal detected. Several device-level differences could plausibly influence how much tissue a surgeon removes and may account for this divergence: the two markers differ in physical dimensions, in the design and sensitivity of their detection probes, and in the spatial feedback they provide during dissection, any of which could affect a surgeon's confidence in approaching the lesion closely. Differences in implantation timing, lesion selection, and institutional grossing practice may contribute as well. Whatever the explanation, our finding cautions against assuming that a resection-volume advantage demonstrated for one magnetic-seed product necessarily extends to another. This point applies to the pooled evidence as well: the most recent meta-analysis of magnetic seed versus wire localization drew its conclusions from studies of Magseed,[18] so its findings cannot be assumed to describe MOLLI, for which directly comparative data remain scarce.

These observations point to a broader limitation of gross morphometry as currently practiced. Weight, dimensions, and calculated volume are recorded manually, are influenced by fixation, handling, and the prosector, and reduce a three-dimensional excision to a few scalar values. Calculated volume assumes a regular geometry that lumpectomy specimens rarely have, and cannot describe the shape of an excision or the position of the lesion within it. This matters here, because the question is not only how much tissue was removed but whether it was well centered on the target: two excisions of identical volume may differ in how much normal parenchyma was sacrificed and how narrowly the lesion was approached. Specimen imaging with automated or machine-learning analysis could allow geometric reconstruction, quantification of lesion eccentricity, and observer-independent measurement; linked to preoperative imaging it would permit a resection ratio reflecting precision rather than size alone. We regard this as a realistic direction for future work rather than a developed method.

To our knowledge, this is the first study to compare the MOLLI device directly with fine-wire localization using pathological endpoints: histology-stratified margins for invasive carcinoma and DCIS, specimen integrity, and gross morphometry recorded directly from the specimens. We note that magnetic-seed localization more broadly has been compared with wire localization in several prior series,[8,16,17,19,20] and we do not claim novelty for that comparison. The existing comparative literature has, however, been reported largely from a surgical standpoint, with resection volume and reoperation as the principal endpoints,[19,20] and it is this pathology-based framing, applied to a device for which only two prior clinical reports exist,[7,10] that we regard as the limited contribution of the present work. A direct MOLLI-versus-wire comparison has previously been identified as a gap by health technology assessment.[11] Given the exploratory design and limited size of this series, these observations are intended to inform the design of a larger comparative study rather than to support conclusions about device performance.

The clearance of *in situ* disease remains a distinct challenge. DCIS spreads discontinuously along the ductal system, is not palpable, and requires a 2 mm margin by consensus guidelines,[13] so its control depends on accurate target mapping rather than intraoperative palpation.[21] In our series, MOLLI pure-DCIS cases had a positive-margin rate of 25.0%. The graded margin data requested by the editors add context: of the 45 DCIS-containing specimens, DCIS was on ink in 5 and lay within 2 mm of the margin in a further 16. The distribution appeared similar between groups, although the small sample precludes attributing difficulty clearing DCIS to its ductal spread rather than the localization device. Binary margin classification also provides an incomplete description of *in situ* disease. The single fine-wire DCIS case precludes direct comparison, and larger DCIS-enriched cohorts are needed.

Beyond oncologic endpoints, wire-free localization offers workflow and safety benefits in the pathology laboratory. A percutaneous wire must often be dissected free before sectioning to avoid dulling grossing blades, a step that can distort the specimen and poses a sharps hazard. The 3.2 mm magnetic seed presents no comparable barrier: assistants can ink, orient, and section tissue with the seed *in situ* and retrieve it readily. In our cohort, specimen integrity was preserved in nearly all cases in both groups, with no wire-related incidents.

Limitations

This study has several important limitations. It was retrospective and single-center, and allocation was not randomized; the method-selection criteria were not recorded, so confounding by surgeon preference during early implementation cannot be excluded, and with no written eligibility protocol the two groups cannot be assumed comparable at baseline. The cohorts were unequal (fine-wire $n = 26$; 16 invasive carcinomas) and the study was underpowered: achieved power was 12.0%, and roughly 314 patients per group would be needed for 80% power. Subgroup analyses were correspondingly limited, most acutely for DCIS, where a single fine-wire case rendered that comparison uninformative. Several variables were not captured: case-level attribution to individual surgeons, so that with only five contributing surgeons operative technique cannot be separated from the effect of the device; operating-room time; any formal assessment of a learning curve; the distance between the localization device and the biopsy clip; and preoperative imaging measurements, including lesion size and the span of calcifications, so excision volume cannot be related to lesion size. Receptor data were incomplete and unbalanced (ER unavailable for 47.8% of MOLLI versus 6.3% of fine-wire invasive carcinomas; HER2 50.0% versus 6.3%), as assays are usually performed on the diagnostic core biopsy and not recorded with the excision specimen; a DCIS-specific margin distance was likewise undocumented in five specimens, all MOLLI cases from early in the series. No quantified workflow measure was collected, so observations about bench handling remain anecdotal, and the study captures pathological endpoints only, without patient-reported outcomes, cost, or long-term outcomes such as local recurrence.

Conclusions

In this exploratory, single-center study, MOLLI seed-guided and fine-wire-guided localization show no statistically significant differences in surgical margin positivity, gross specimen morphometry, or specimen integrity. The study is underpowered to detect differences in margin positivity, and the numerically lower rate observed with MOLLI cannot be interpreted as evidence of superiority or of equivalence. These preliminary findings, together with the pathology-based endpoints described here, may inform the design of a larger, adequately powered comparative study of the two localization methods.

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Conflict of interest

Dr. Wei Xiong has been an editorial board member of the *Journal of Clinical and Translational Pathology* since May 2021. The authors declare no other conflicts of interest.

Author contributions

Study concept and design (MC, WX), acquisition of data (LO, SMW, NH), analysis and interpretation of data (LO, SMW, MC, HY, WX), drafting of the manuscript (LO, SMW), critical revision of the manuscript for important intellectual content (NH, MC, HY, AB, WX), surgical and clinical input (AB), and study supervision (WX). All authors made significant contributions to this study and have approved the final manuscript.

Ethical statement

This project was reviewed by the Chair of the Providence Health Care Research Ethics Board and was determined to be a quality improvement project exempt from research ethics approval, in accordance with University of British Columbia Human Research Policy LR9 and Article 2.5 of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2); an exemption letter was issued. No approval number is assigned to projects determined to be exempt from REB review. The study was carried out in accordance with the Declaration of Helsinki (as revised in 2024). Written informed consent was not required for this retrospective analysis of de-identified specimen data, the project having been determined exempt from research ethics review. A copy of the exemption letter is available from the corresponding author upon reasonable request.

Data sharing statement

The dataset used in support of the findings of this study is available from the corresponding author at wei.xiong@ubc.ca upon reasonable request.

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