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Do LORIS trial eligibility criteria identify a ductal carcinoma in situ (DCIS) patient population at low risk of upgrade to invasive carcinoma?

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Abstract

Background—The Surgery versus Active Monitoring for Low-Risk DCIS (LORIS) trial is studying the safety of monitoring core-biopsy diagnosed low-risk ductal carcinoma in situ (DCIS) without excision. We sought to determine the incidence and characteristics of synchronous invasive carcinoma found in LORIS-eligible women who underwent excision, as this knowledge is essential in assessing the safety of observation alone.

Methods—Women meeting LORIS eligibility criteria (age ≥ 46 years, screen-detected calcifications, non-high–grade DCIS diagnosed by core-biopsy, absence of nipple discharge, or strong family history of breast cancer) who underwent surgical excision from 2009–2012 were identified. Histologic findings of excision specimens were reviewed.

Results—296 LORIS-eligible cases were identified; 58 (20%) had invasive carcinoma on final pathology (90% invasive ductal, 78% >1 mm size, 21% high grade, 3% triple negative, 9% HER2 amplified). Of these, 18 (31%) were pT1b or larger and 3 (5%) were pN1. Among eligible upgraded cases, 90% received radiation, 89% received endocrine therapy, and 18% were recommended chemotherapy. Women upgraded to invasive carcinoma were more likely to have intermediate-grade DCIS on core biopsy and to have undergone mastectomy.

Conclusions—Among LORIS-eligible women, 20% had invasive carcinoma at surgical excision that was heterogeneous in grade, size, and receptor status. Information gained from surgical excision influenced receipt of adjuvant radiation and endocrine therapy in most, and indicated benefit from chemotherapy in 18%. Surgical excision is warranted until additional risk stratification is available to identify a cohort of DCIS patients at lower risk for clinically significant synchronous invasive carcinoma.

Keywords

ductal carcinoma in situ; DCIS; invasive carcinoma; breast cancer; upgrade

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INTRODUCTION

Ductal carcinoma in situ (DCIS) represents a heterogeneous pre-invasive breast lesion which harbors the potential for the progression to invasive carcinoma.[1] While the natural history of untreated DCIS is not well studied, 2 early studies reported a 40–50% rate of progression to invasive disease by 10–15 years among women with unrecognized low-grade DCIS diagnosed as benign disease in an excisional biopsy.[2,3] Given that nearly half of patients with DCIS may not be at risk for disease progression, there is increasing concern regarding the potential overtreatment of this pre-invasive lesion[4], resulting in significant interest in identifying patients at very low risk for disease progression who may safely omit surgery and radiation therapy. The Surgery versus Active Monitoring for Low-Risk DCIS (LORIS)[5] trial is studying the safety of observation alone for a select cohort of patients with non-high–grade DCIS diagnosed by core needle biopsy. The primary outcome of the trial is the difference in invasive breast-cancer–free survival at 5 years among women treated with observation alone compared to standard surgical excision.

Identifying patients with DCIS who harbor undiagnosed synchronous invasive carcinoma is essential in assessing the safety of observation alone. A meta-analysis reported an overall 21% rate of upgrade to invasive cancer at the time of surgical excision among patients with non-high–grade DCIS diagnosed on needle biopsy[6], but the rate of upgrade for women meeting all LORIS study eligibility criteria is currently unknown. We sought to determine the upgrade rate to invasive carcinoma for women with non-high–grade DCIS diagnosed by core needle biopsy who meet all clinical and pathologic LORIS trial eligibility criteria.

METHODS

Following Memorial Sloan Kettering Cancer Center (MSKCC) institutional review board approval, all women with core needle biopsy-proven non-high–grade DCIS alone who underwent breast surgery at our institution between 2009 and 2012 were identified. During this time period, vacuum-assisted core needle biopsy was routinely used. Figure 1 summarizes the inclusion and exclusion criteria for the LORIS trial; these characteristics were used to select the current study patient population. Women age ≥ 46 years with screen-detected calcifications and non-high–grade DCIS diagnosed by vacuum-assisted core needle biopsy were selected. Among this cohort of patients with screen-detected mammographic calcifications, some did undergo additional breast imaging with US or MRI, including 106 who underwent breast US and 104 who underwent MRI. Women were excluded for the presence of a mass component on any breast imaging modality, nipple discharge, strong family history of breast cancer, or a personal history of invasive breast cancer or ipsilateral DCIS. For this study, strong family history was defined as 2 or more first- and/or second-degree relatives with a history of breast cancer.

Clinicopathologic factors were collected, including age at diagnosis, menopausal status, family history of breast cancer, BRCA testing results, core needle biopsy type, core needle biopsy DCIS grade and histology, breast surgery type (breast-conserving surgery [BCS], mastectomy), and axillary lymph node surgery (sentinel lymph node biopsy [SLNB],

axillary lymph node dissection [ALND]). If present on final pathology, details of the invasive cancer component were analyzed, including histology, grade, receptor status, presence of lymphovascular invasion, nodal stage, and, if appropriate, results of a 21-gene recurrence score (Oncotype DX®) (Genomic Health, Redwood City, CA). Clinicopathologic features were compared between women with and without an upgrade to invasive carcinoma at surgical excision. Characteristics of the invasive carcinomas found at surgical excision were described. Continuous variables were summarized using median and range, and compared using the Wilcoxon test. Categorical variables were summarized using frequency and percentage, and compared using Fisher's exact test. All statistical analysis was done in R 3.1.1 (R Foundation, Vienna, Austria), and p-values less than 0.05 were considered significant.

RESULTS

296 cases were identified with non-high–grade DCIS diagnosed by core needle biopsy and meeting all LORIS trial eligibility criteria during this 4-year time period. Table 1 summarizes the clinicopathologic characteristics of the entire cohort. Median patient age was 57 years (range 46–84 years). No patient had a known BRCA mutation, and 44% had one first- or second-degree family member with a history of breast cancer. Among the 296 cases, information regarding the type of core needle biopsy performed at the time of DCIS diagnosis was available for 254 (86%) cases, all of whom underwent a vacuum-assisted core needle biopsy. The gauge of the biopsy needle was 8 or 9 in 141 (62%), 10 or 11 in 81 (36%), 12 or 14 in 5 (2%), and unknown in 69. The majority of patients had mixed architecture (83%) and intermediate-grade (82%) DCIS.

Among 296 cases meeting all LORIS trial eligibility criteria, 58 (20%) were upgraded to invasive cancer at the time of surgical excision. Table 1 compares patients with and without an upgrade to invasive cancer. Women upgraded to invasive cancer at surgical excision were more likely to have intermediate-grade DCIS on core needle biopsy (93% versus 79%, $p = 0.013$) and were more likely to have undergone mastectomy (48% versus 24%, $p < 0.001$) compared to women without an upgrade.

Table 2 lists the characteristics of the 58 patients found to have invasive carcinoma at surgical excision. Among these upgraded patients, the overall median invasive tumor size was 0.3 cm (range 0.1–4 cm). A subset of patients had high-risk invasive carcinoma features, including 3 (5%) with lymphovascular invasion, 2 (3%) triple-negative tumors, 5 (9%) HER2-overexpressing tumors, and 3 patients (5%) with pN1 disease. In addition, 7 of the 50 hormone receptor-positive, HER2 negative tumors had high nuclear grade. Treatment recommendations for 57 of the 58 women upgraded to invasive carcinoma were available and included radiation therapy for 27 of 30 (90%) patients who underwent BCS, and endocrine therapy for 47 of 53 (89%) women with estrogen receptor (ER) positive tumors (Table 3). Among 19 women with node-negative, ER positive invasive cancer ≥ 5 mm in size, 13 had data available from the 21-gene recurrence score (OncotypeDX®); 4 women had intermediate- or high-risk recurrence scores, while 9 had low-risk scores. In total, 45% (26/58) of cases had tumor pathology that warranted genomic profiling or consideration for chemotherapy. Ten of 57 (18%) patients with treatment information available were

recommended to undergo chemotherapy for either high or intermediate genomic profile scores, node-positive disease, HER2 amplified or triple-negative tumors, or a combination of high-risk tumor features.

DISCUSSION

In our experience, LORIS eligibility criteria did not identify a population of women with DCIS at low risk for upgrade to invasive carcinoma at surgical excision, with an overall upgrade rate of 20% even among this highly selected patient population. While one study by Soumian et al reported zero upgrades to invasive cancer among a small cohort of 19 patients with low-grade DCIS on core biopsy who met LORIS criteria[7], our reported upgrade rate is nearly identical to that found by Brennan et al[6] in a meta-analysis reporting on 1736 patients diagnosed with DCIS by core needle biopsy. The overall reported upgrade was 26% (range 23%–30%) among all patients; with a 21% (range 15%–28%) upgrade to invasive carcinoma seen specifically among patients selected only for the presence of non-high–grade DCIS on core needle biopsy.

While others have reported an increased risk of upgrade to invasive carcinoma with the presence of clinical high-risk features such as a mass on imaging[8] or younger age[9], our analysis excluded such patients. Our population of patients diagnosed with non-high–grade DCIS by screen-detected mammographic calcifications without the presence of symptoms or a strong family history, at age 46 or older, retained a clinically significant rate of upgrade to invasive carcinoma at the time of surgical excision. Only intermediate-grade DCIS and treatment by mastectomy were associated with a statistically significant increased rate of upgrade. Among this patient population meeting all LORIS trial eligibility criteria, 23% of those with intermediate-grade DCIS on core-biopsy were upgraded to invasive carcinoma at surgical excision. In contrast, among the 53 patients with low-grade DCIS alone on core-biopsy, only 4 women (7%) were upgraded to invasive carcinoma on final pathology. The finding that patients undergoing mastectomy were more prone to harboring a synchronous invasive carcinoma is likely related to the extent of disease at initial presentation. Extent of calcifications has previously been shown to be associated with the risk for upgrade to invasive carcinoma among women with core biopsy-proven DCIS.[9-12] The LORIS trial is enrolling women with both low- and intermediate-grade DCIS on core needle biopsy and does not include a size limitation for mammographic calcifications. Our results suggest that within this population, there remains a spectrum of risk for the presence of synchronous invasive carcinoma. Interestingly, the LORD (LOw Risk Dcis)[13] study is a second European trial now accruing patients with a similar objective to the LORIS trial, but with slightly different eligibility criteria. The LORD study is limited to women with screen-detected low-grade DCIS on core-biopsy, excluding those with intermediate-grade lesions. Furthermore, additional eligibility criteria are included to better assess larger areas of calcifications, including additional mandatory core biopsies for patients with microcalcifications spanning > 4 cm or multicentric disease. Based on our findings, these additional inclusion criteria may result in a select population of patients with DCIS at lower risk for synchronous invasive carcinoma.

An important consequence of the identification of invasive carcinoma at the time of surgical excision is the potential change in adjuvant therapy recommendations. Unlike the situation in invasive carcinoma, radiation therapy after BCS for DCIS does not improve survival[14] and the acceptance of endocrine therapy is substantially lower among women with DCIS than in those with invasive cancer. Furthermore, chemotherapy and targeted anti-HER2 therapy are not utilized for the management of DCIS. We have previously reported adjuvant therapy use among larger cohorts of patients with DCIS treated at our institution, with utilization of radiation therapy in recent years for women with DCIS following BCS at approximately 60%, and the use of endocrine therapy substantially lower, at approximately 23%, with no patients receiving chemotherapy.[15-17] Similar utilization of adjuvant therapy for patients with DCIS has been reported from national database reviews. According to National Cancer Institute Surveillance Epidemiology and End Results (SEER) data, approximately 35%–40% of women managed with BCS for DCIS in 2005 did not receive adjuvant radiation therapy[18], and in a review of over 206,000 women with DCIS reported to the National Cancer Database between 2005 and 2012, the minority of women (37%) received adjuvant endocrine therapy.[19] Among the 59 cases with an upgrade to invasive carcinoma in the current study, nearly 90% of eligible patients received adjuvant endocrine therapy and radiation therapy—rates far greater than that seen for women with DCIS alone.

It is often felt that if non-high–grade DCIS progresses to invasive carcinoma, the resulting invasive component is correspondingly indolent.[20] This assumption supports the notion that if non-high–grade DCIS is managed with observation alone, any invasive component will be low-grade, detected on subsequent imaging at an early stage, and unlikely to require chemotherapy. Interestingly, the invasive cancers identified among this population of women with non-high–grade DCIS on core needle biopsy meeting all LORIS eligibility criteria were heterogeneous in regards to tumor grade, size, and receptor status. 6% of the entire study population had poor prognostic invasive tumor features, including triple-negative, HER2 overexpressing, high-grade, T2, presence of lymphovascular invasion, or node-positive disease identified at the time of surgical excision. In addition to the standard recommendations for radiation therapy or endocrine therapy in the setting of invasive carcinoma, 45% of the upgraded cases had tumor pathology that warranted genomic profiling or consideration for chemotherapy, and, ultimately, 18% (n = 10) of patients with invasive carcinoma were recommended to receive adjuvant chemotherapy. Of the 10 patients recommended to receive chemotherapy, follow-up is missing for 1 patient, and 1 patient refused any additional therapy. The remaining 8 patients received chemotherapy. While patients with features warranting chemotherapy likely benefited from the finding of invasive carcinoma, the remainder of patients with an upgrade likely benefited from the findings on final pathology as well as over 90% of these patients received additional adjuvant therapy with radiation and/or endocrine therapy, treatments known to improve survival among women with invasive breast cancer. Interestingly, the 4 tumors identified in patients with low-grade DCIS on core biopsy in this study were all sub-centimeter, hormone receptor positive, HER2 negative cancers, while the patients with intermediate-grade DCIS on core biopsy were found to have a mix of tumor features on final pathology.

As noted, considerable interest exists regarding the study of lesser treatment for low-risk DCIS, including the omission of surgical excision.[5,13,21] While the goal of managing a non-

invasive breast lesion must be balanced with the risk of the proposed therapy, the risk of surgical excision is low, with rates of short-term complications reported at < 2% among 6600 women reported to the American College of Surgeons NSQIP database who underwent BCS and sentinel lymph node biopsy[22], and therefore the associated surgical morbidity is likely even lower following excision alone. While postoperative complications are rare, there is potential for long-term morbidity following breast surgery, including chronic post-surgical pain and dissatisfaction with cosmesis.[23,24] However, given the overall 20% rate of upgrade to invasive carcinoma and the heterogeneity of the identified tumors, initial management of non-high–grade DCIS diagnosed by core-biopsy should remain surgical excision until additional risk stratification is available to identify a population at lower risk for clinically significant synchronous invasive carcinoma. Our data suggest that the LORIS criteria do not adequately define such a low risk DCIS population.

Our study is limited by the retrospective nature and lack of central radiology and pathology re-review. However, all pathology slides were interpreted, or in the case of biopsies performed elsewhere, re-reviewed by high-volume dedicated breast pathologists. The same practice was employed for imaging review

Conclusion

Women with screen-detected non-high–grade DCIS diagnosed by core-biopsy meeting all LORIS trial eligibility criteria have a 20% risk of upgrade to invasive carcinoma at the time of surgery excision. For nearly all of these, standard systemic and radiation therapy was influenced by the findings at excision. Outside of a clinical trial, given the clinically relevant rate of upgrade and the heterogeneity of the invasive carcinomas identified, surgical excision is warranted until additional risk stratification is available which identifies a population at lower risk for clinically significant synchronous invasive carcinoma.

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REFERENCES

1. Burstein HJ, Polyak K, Wong JS, et al. Ductal carcinoma in situ of the breast. N Engl J Med. 2004; 350(14):1430–41. [PubMed: 15070793]
2. Rosen PP, Bruan DW, Kinne DE. The clinical significance of preinvasive breast carcinoma. Cancer. 1980; 46:919–25. [PubMed: 7397668]
3. Sanders ME, Schuyler PA, Dupont WD, et al. The natural history of low-grade ductal carcinoma in situ of the breast in women treated by biopsy only revealed over 30 years of long-term follow-up. Cancer. 2005; 103(12):2481–4. [PubMed: 15884091]
4. Alvarado M, Ozanne E, Esserman L. Overdiagnosis and overtreatment of breast cancer. Am Soc Clin Oncol Educ Book. 2012:e40–5. [PubMed: 24451829]
5. Francis A, Thomas J, Fallowfield L, et al. Addressing overtreatment of screen detected DCIS; the LORIS trial. Eur J Cancer. 2015; 51(16):2296–303. [PubMed: 26296293]
6. Brennan ME, Turner RM, Ciatto S, et al. Ductal carcinoma in situ at core-needle biopsy: meta-analysis of underestimation and predictors of invasive breast cancer. Radiology. 2011; 260(1):119–28. [PubMed: 21493791]

7. Soumian S, Verghese ET, Booth M, et al. Concordance between vacuum assisted biopsy and postoperative histology: implications for the proposed Low Risk DCIS Trial (LORIS). Eur J Surg Oncol. 2013; 39(12):1337–40. [PubMed: 24209431]
8. Dillon MF, McDermott EW, Quinn CM, et al. Predictors of invasive disease in breast cancer when core biopsy demonstrates DCIS only. J Surg Oncol. 2006; 93(7):559–63. [PubMed: 16705731]
9. Yen TW, Hunt KK, Ross MI, et al. Predictors of invasive breast cancer in patients with an initial diagnosis of ductal carcinoma in situ: a guide to selective use of sentinel lymph node biopsy in management of ductal carcinoma in situ. J Am Coll Surg. 2005; 200(4):516–26. [PubMed: 15804465]
10. Tunon-de-Lara C, Chauvet MP, Baranzelli MC, et al. The Role of Sentinel Lymph Node Biopsy and Factors Associated with Invasion in Extensive DCIS of the Breast Treated by Mastectomy: The Cinnamome Prospective Multicenter Study. Ann Surg Oncol. 2015
11. Huo L, Sneige N, Hunt KK, et al. Predictors of invasion in patients with core-needle biopsy-diagnosed ductal carcinoma in situ and recommendations for a selective approach to sentinel lymph node biopsy in ductal carcinoma in situ. Cancer. 2006; 107(8):1760–8. [PubMed: 16977650]
12. Tan JC, McCready DR, Easson AM, et al. Role of sentinel lymph node biopsy in ductal carcinoma-in-situ treated by mastectomy. Ann Surg Oncol. 2007; 14(2):638–45. [PubMed: 17103256]
13. Elshof LE, Tryfonidis K, Slaets L, et al. Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ - The LORD study. Eur J Cancer. 2015
14. Early Breast Cancer Trialists' Collaborative G. Correa C, McGale P, et al. Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. J Natl Cancer Inst Monogr. 2010; 2010(41):162–77. [PubMed: 20956824]
15. Van Zee KJ, Subhedar P, Olcese C, et al. Relationship Between Margin Width and Recurrence of Ductal Carcinoma In Situ: Analysis of 2996 Women Treated With Breast-conserving Surgery for 30 Years. Ann Surg. 2015; 262(4):623–31. [PubMed: 26366541]
16. Pilewskie M, Olcese C, Eaton A, et al. Perioperative breast MRI is not associated with lower locoregional recurrence rates in DCIS patients treated with or without radiation. Ann Surg Oncol. 2014; 21(5):1552–60. [PubMed: 24385207]
17. Subhedar P, Olcese C, Patil S, et al. Decreasing Recurrence Rates for Ductal Carcinoma In Situ: Analysis of 2996 Women Treated with Breast-Conserving Surgery Over 30 Years. Ann Surg Oncol. 2015; 22(10):3273–81. [PubMed: 26215193]
18. Zujewski JA, Harlan LC, Morrell DM, et al. Ductal carcinoma in situ: trends in treatment over time in the US. Breast Cancer Res Treat. 2011; 127(1):251–7. [PubMed: 20931276]
19. Flanagan MR, Rendi MH, Gadi VK, et al. Adjuvant Endocrine Therapy in Patients with Ductal Carcinoma In Situ: A Population-Based Retrospective Analysis from 2005 to 2012 in the National Cancer Data Base. Ann Surg Oncol. 2015; 22(10):3264–72. [PubMed: 26202556]
20. Ozanne EM, Shieh Y, Barnes J, et al. Characterizing the impact of 25 years of DCIS treatment. Breast Cancer Res Treat. 2011; 129(1):165–73. [PubMed: 21390494]
21. Esserman L, Alvarado M. Setting a research agenda for ductal carcinoma in situ that meets the current need for change. Ann Intern Med. 2014; 160(7):511–2. [PubMed: 24566896]
22. Chatterjee A, Pyfer B, Czerniecki B, et al. Early postoperative outcomes in lumpectomy versus simple mastectomy. J Surg Res. 2015
23. Al-Ghazal SK, Blamey RW, Stewart J, et al. The cosmetic outcome in early breast cancer treated with breast conservation. Eur J Surg Oncol. 1999; 25(6):566–70. [PubMed: 10556000]
24. Bruce J, Thornton AJ, Powell R, et al. Psychological, surgical, and sociodemographic predictors of pain outcomes after breast cancer surgery: a population-based cohort study. Pain. 2014; 155(2): 232–43. [PubMed: 24099954]

Synopsis

Of women eligible for the LORIS trial (evaluating the safety of monitoring low-risk DCIS diagnosed by core biopsy without excision), 20% had invasive carcinoma at excision, with 21% being high grade, 12% HER2-amplified or triple negative, and 5% node-positive.

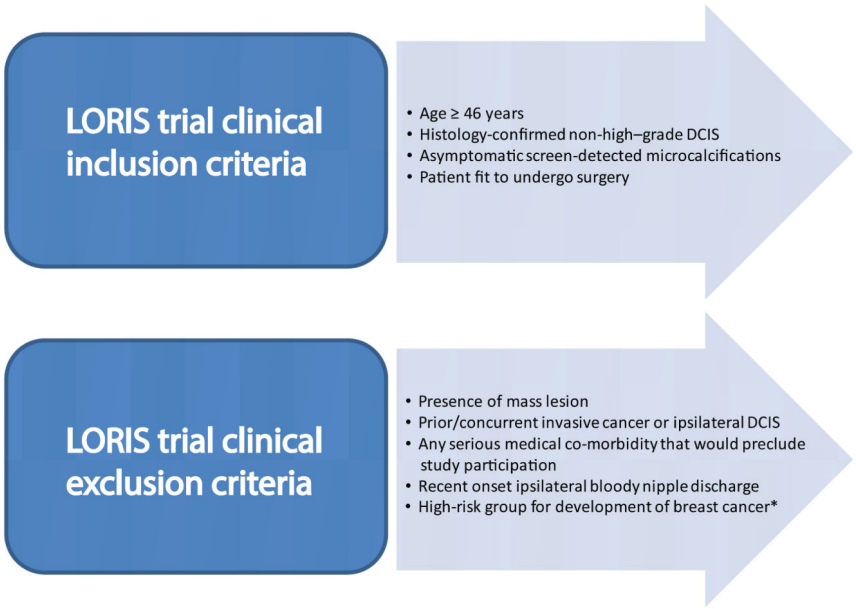

Fig. 1.

LORIS trial eligibility criteria

*Defined by The National Institute for Health and Care Excellence (United Kingdom) guidelines for familial breast cancer

DCIS, ductal carcinoma in situ

Table 1

Clinicopathologic features of the entire study population (n = 296) and among women with (n = 58) and without an upgrade (n = 238) to invasive carcinoma at surgical excision

Variable	Entire Population (n = 296)	Final Pathology Results		P-value
		Upgrade to Invasive Carcinoma (n = 58)	DCIS Alone (n = 238)	
Age, years, median (range)	56.9 (46.0–84.5)	55.7 (46.3–79.6)	57.2 (46.0–84.5)	0.2
Menopausal status				0.9
Pre/perimenopausal	92 (31%)	19 (33%)	73 (31%)	
Postmenopausal	204 (69%)	39 (67%)	165 (69%)	
Family history of breast cancer in 1 first- or second-degree relative	130 (44%)	30 (52%)	100 (42%)	0.2
DCIS grade on core needle biopsy				0.01
Low	53 (18%)	4 (7%)	49 (21%)	
Intermediate	244 (82%)	54 (93%)	189 (79%)	
DCIS architecture on core needle biopsy				0.07
Mixed	246 (83%)	51 (88%)	195 (82%)	
Cribriform	21 (7%)	1 (2%)	20 (8%)	
Solid	12 (4%)	4 (7%)	8 (3%)	
Micropapillary	2 (1%)	0	2 (1%)	
Papillary	1 (< 1%)	1 (2%)	0	
Non-specified	14 (5%)	1 (2%)	13 (6%)	
Breast surgery				< 0.001
Lumpectomy	213 (72%)	30 (52%)	182 (76%)	
Mastectomy	84 (28%)	28 (48%)	56 (24%)	
Vacuum-assisted core biopsy				1
Yes	254 (100%)	49 (100%)	205 (100%)	
No	0	0	0	
Missing	42	9	33	
Core needle gauge				0.2
8-9G	141 (62%)	24 (55%)	117 (64%)	
10-11G	81 (36%)	18 (41%)	63 (34%)	
12-14G	5 (2%)	2 (5%)	3 (2%)	
Missing	69	14	55	

DCIS, ductal carcinoma in situ

Table 2

Tumor characteristics of cases upgraded to invasive carcinoma at surgical excision

Invasive Tumor Pathology	n = 58
Invasive tumor size, cm, median (range)	0.3 (0.1–4)
Invasive carcinoma nuclear grade	
Low	5 (12%)
Intermediate	29 (67%)
High	9 (21%)
Missing	15
Lymphovascular invasion present	3 (5%)
Invasive carcinoma histology	
Ductal	52 (90%)
Lobular	4 (7%)
Other	2 (3%)
Estrogen receptor	
Positive	54 (95%)
Negative	3 (5%)
Missing	1
Progesterone receptor	
Positive	43 (77%)
Negative	13 (23%)
Missing	2
HER2 status	
Not amplified	48 (91%)
Amplified	5 (9%)
Missing	5
Receptor profile (n = 57)	
ER+/HER2− *	50 (88%)
ER+/HER2+	4 (7%)
ER−/HER2+	1 (2%)
ER−/PR−/HER2−	2 (3%)
Final T stage	
pT1mi	13 (22%)
pT1a	27 (47%)
pT1b	14 (24%)
pT1c	3 (5%)
pT2	1 (2%)
Final N stage	
pN0	55 (95%)
pN1mi	1 (2%)
pN1	2 (3%)
Final stage	

Invasive Tumor Pathology	n = 58
IA (T1N0)	54 (93%)
IB (T1N1mi)	1 (2%)
IIA (T1N1, T2N0)	3 (5%)

[*] 4 patients with ER+ disease had insufficient tumor size for HER2 testing

ER, estrogen receptor; PR, progesterone receptor

Table 3

Adjuvant management for women with invasive carcinoma at surgical excision

Invasive Upgrades (n = 57)*	Proportion	%
Radiation therapy†	27/30	90%
Endocrine therapy‡	48/54	89%
21-gene Recurrence Score-eligible§	19/58	33%
21-gene RS intermediate or high (n = 13)	4/13	31%
Chemotherapy‖	10/57	18%
Adjuvant treatment recommended	53/57¶	93%

*treatment information missing for 1 patient

†for women undergoing breast-conserving surgery

‡for women with estrogen receptor positive tumors

§tumor characteristics including size ≥ 5 mm, pN-, estrogen receptor positive, and HER2 negative

‖indications for chemotherapy included high or intermediate 21-gene recurrence score, node positive or HER2 amplified disease, triple-negative tumors, or combination of high-risk tumor features

¶4 patients with T1mic or T1a, node-negative tumors who underwent mastectomy were not recommended to undergo adjuvant systemic therapy secondary to patient co-morbidities or physician preference

RS, recurrence score