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ORIGINAL ARTICLE – BREAST ONCOLOGY

Should Breast Density Influence Patient Selection for Breast-Conserving Surgery?

Nimmi S. Kapoor, MD[1], Anne Eaton, MS[2], Tari A. King, MD[1], Sujata Patil, PhD[2], Michelle Stempel, MS[1], Elizabeth Morris, MD[3], Edi Brogi, MD[4], and Monica Morrow, MD[1]

[1]Breast Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; [2]Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; [3]Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, NY; [4]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY

ABSTRACT

Background. In a previous study of the relationship between breast density and primary tumor features, we observed a higher mastectomy rate in patients with extremely dense breasts. Here we examine possible reasons for this finding.

Methods. Data were obtained from a prospectively maintained database of 1,056 invasive breast cancer patients from January 2005 to June 2007. Mammographic density was assigned by Breast Imaging-Reporting and Data System (BI-RADS) classification. Initial and final surgical procedures, and patient and tumor variables were recorded.

Results. Breast-conserving surgery (BCS) was attempted in 758 patients (72 %), 385 (51 %) of whom had preoperative magnetic resonance imaging (MRI). Initial BCS was less common among patients with the highest (BI-RADS 4) breast density compared to patients with less-dense breasts (52 vs. 74 %; $p < 0.0001$), but MRI use was more common (65 vs. 33 %; $p < 0.0001$). Adjusting for clinical and pathologic variables, patients with the highest breast density had 1.94-times (95 % confidence interval 1.44–2.62; $p < 0.0001$) the odds of initial mastectomy compared to patients with less-dense breasts. After initial BCS, 387 patients (51 %) had positive shaved margins, 96 (25 %) of whom converted to mastectomy. MRI did not correlate with the rate of positive margins overall or among those with dense breasts. Adjusting for clinical and pathologic variables, density did not predict margin status or conversion to mastectomy. In a multivariate model, age, histologic grade, extensive intraductal component, and multicentricity/multifocality were independently associated with conversion to mastectomy.

Conclusions. Density alone seems to influence the decision to proceed with initial mastectomy. When BCS was attempted, breast density was not associated with positive margins or conversion to mastectomy. A benefit of MRI in decreasing positive margins was not observed. These data do not support the use of breast density as a selection criterion for BCS.

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M. Morrow, MD
e-mail: morrowm@mskcc.org

INTRODUCTION

Increased breast density is associated with an increased risk of breast cancer development and decreased sensitivity of mammographic screening.[1–5] Despite these concerns, in a previous study investigating the relationship between breast density and the presenting features of malignancy, we found that patients with high breast density were more likely to have favorable tumors with an estrogen receptor (ER) positive, HER2 negative phenotype, compared to patients with less-dense breasts.[6] At the same time, we observed that patients with high breast density were significantly more likely to undergo mastectomy than their counterparts with less-dense breasts. The reason for this was unclear as breast density alone is not considered a contraindication for breast-conserving surgery (BCS).[7]

The purpose of this study was to determine whether the increased mastectomy rate observed in women with dense breasts can be explained by clinical factors necessitating initial mastectomy, such as multicentricity and presence of extensive intraductal component (EIC), or whether the high mastectomy rate was due to failed attempted BCS with a higher rate of positive margins leading to conversion to mastectomy in patients with dense breasts. In addition, we sought to determine whether magnetic resonance imaging (MRI) was beneficial in the subset of women with high breast density.

PATIENTS AND METHODS

After institutional review board approval, data were obtained from a prospectively maintained, registered database. Patients with stage 1–3 invasive breast cancer were eligible for inclusion if they were surgically treated at Memorial Sloan-Kettering Cancer Center (MSKCC) between January 2005 and June 2007. Patients were excluded if they received neoadjuvant chemotherapy, did not have a mammogram at the time of diagnosis available for review by the MSKCC breast imaging group, had initial surgical treatment of their breast cancer somewhere other than MSKCC, or had a surgical biopsy for diagnosis. Mammographic density was classified into 4 groups using the Breast Imaging-Reporting and Data System (BI-RADS) density definitions: 1 = almost entirely fatty (<25 % glandular); 2 = scattered fibroglandular densities (25–50 % glandular); 3 = heterogeneously dense (51–75 % glandular); or 4 = extremely dense (>75 % glandular). Outcomes in patients with extremely dense (BI-RADS density 4) breasts were compared to all others (BI-RADS densities 1–3).

In general, margins were inked and evaluated during the study time period using the shaved technique as previously described by Wright et al.[8] Briefly, shaved margins were 2–3 mm sections taken tangentially from the lumpectomy surface. A positive margin was defined as any tumor within the shaved specimen.

Tumor features, including histologic type, size, grade, ER and progesterone receptor (PR) status, HER2/neu status, multifocality and multicentricity, lymphovascular invasion (LVI), and the presence of an EIC were obtained from the pathology report of the definitive surgery. Multifocality and multicentricity were defined as the discontinuous growth of tumor in 1 quadrant of the breast or the presence of tumor in multiple quadrants of the breast, respectively. An EIC was defined as the presence of intraductal carcinoma both in the invasive tumor and in adjacent breast tissue that compromised more than 25 % of the tumor. Lymph-node positivity was defined by 7th Edition American Joint Committee on Cancer guidelines, with macrometastases (N1 or greater) and micrometastases (N1mic) included as lymph-node positive, and isolated tumor cells (N0i+) considered lymph-node negative.

Logistic regression models were used to evaluate associations between clinicopathologic and demographic variables and outcomes, including: (1) initial mastectomy versus BCS; (2) positive margin after BCS; and (3) conversion to mastectomy after a finding of positive margin, and to test the association between breast density and preoperative MRI. The association between lymph node status and initial mastectomy was not examined because lymph node status is not known preoperatively. Multivariate logistic regression models were built to adjust for factors known to be associated with outcomes that were significant on univariate analysis and our variable of interest: breast density. Overall, type III Wald tests were performed for variables in the multivariate models. Tumor type could not be included in the model for conversion because it was closely related to histologic grade. Generalized estimating equation models were used in all analyses to take into account correlation between outcomes from the same surgeon. Statistical analysis was performed by SAS version 9.1 (SAS Institute, Cary, NC), and *p*-values less than 0.05 were considered statistically significant.

RESULTS

A total of 1,056 patients were included in the study. The mean patient age at surgery was 57 years (range 29–91 years), and the mean tumor size was 1.70 cm (range 0.1–11.0 cm). Palpable tumors were present in 486 patients (46.0 %), 277 (26.2 %) had multifocal/multicentric tumors, and 151 (14.3 %) had an EIC. There were 951 patients (90.1 %) with BI-RADS 1–3 breast density, considered less dense, and 105 patients (9.9 %) with BI-RADS 4 breast density, the “extremely dense” group. Overall, 385 patients (36.5 %) had preoperative MRI. BCS was attempted in 758 patients (71.8 %), while 298 (28.2 %) had mastectomy as the initial surgical procedure. Initial mastectomy rate by surgeon ranged from 15 to 46 % (Table 1). Univariate associations between clinicopathologic and demographic variables, and initial mastectomy, adjusted for surgeon variation in mastectomy use, are shown in Table 2. Patients with extremely dense breasts were less likely to attempt BCS than those with less-dense breasts (52.4 vs. 73.9 %; $p < 0.0001$). On multivariate analysis, large tumor size, multifocality/multicentricity, presence of LVI, and high breast density were strong independent predictors of initial mastectomy, each conferring a twofold to threefold increase in the odds of initial mastectomy (Table 2). In addition, younger patient age, palpable tumor, preoperative MRI, and higher tumor grade were also significantly associated with initial mastectomy (Table 2).

After adjustment for patient, clinical, and tumor features, the odds ratio for mastectomy was 1.94 (95 % confidence interval 1.44–2.62; $p < 0.0001$) in the extremely dense group compared to the less-dense group (BI-RADS 1–3).

Of the 758 patients undergoing BCS, 387 (51.1 %) had positive shaved margins after their initial surgical procedure. Patients with extremely dense breasts were more likely to have positive margins compared to patients with less-dense breasts, with 65.5 % of BI-RADS 4 density patients having positive margins compared to 49.9 % of those with less-dense breasts; however, this difference was not statistically significant. After adjustment for age, tumor type, lymph node status, presence of EIC, multicentricity/multifocality, LVI, tumor size, and preoperative MRI, density still did not predict margin status ($p = 0.24$, Table 3). In multivariate analysis, tumor type, presence of EIC, and multicentric/multifocal tumors were associated with positive margin status (Table 3).

Preoperative MRI was performed in 242 patients (31.9 %) attempting BCS. Patients with extremely dense breasts were significantly more likely to have an MRI (64.8 vs. 33.3 %, $p < 0.0001$). MRI did not decrease the overall rate of margin positivity (57.9 % with MRI, 47.9 % without MRI), nor the rate of positive margins in those patients with extremely dense breasts (75.8 % with MRI, 50 % without MRI).

Overall, 120 (15.8 %) of 758 patients who attempted BCS were converted to mastectomy, including 96 (24.8 %) of 387 patients with positive margins. Of patients with a positive margin after initial attempt at BCS, clinical variables that significantly predicted conversion to mastectomy in a multivariate model included young patient age, histologic grade III tumors, presence of EIC, presence of multicentricity/multifocality, tumor size, and preoperative MRI (Table 4). Density, however, did not predict conversion to mastectomy after a positive margin.

TABLE 1 Initial mastectomy rate by surgeon

Surgeon	No. of initial mastectomies	No. of cases	Initial mastectomy rate (95 % confidence interval)
1	17	73	23 % (14–35)
2	21	71	30 % (19–42)
3	5	16	31 % (11–59)
4	32	116	28 % (20–37)
5	26	63	41 % (29–54)
6	33	98	34 % (24–44)
7	49	194	25 % (19–32)
8	41	102	40 % (31–50)
9	19	41	46 % (31–63)
10	34	144	24 % (17–31)
11	21	138	15 % (9.7–22.0)

DISCUSSION

In a prior study of the impact of breast density on the presenting features of malignancy, we found that breast density was related to cancer presentation, with patients with extremely dense breasts having more ER/PR positive, HER2 negative tumors, more lobular cancers, and more mammographically occult cancers than their counterparts with less-dense breasts.[6] Patients with extremely dense breasts were also significantly more likely to be treated with mastectomy. In this study, we investigated whether margin positivity and conversion to mastectomy after BCS could explain the higher mastectomy rate in patients with extremely dense breasts.

Although patients with extremely dense breasts were significantly more likely to undergo mastectomy compared to their counterparts with less-dense breasts, these mastectomies were more likely to be the first surgical procedure performed. We observed no difference in the rate of conversion from BCS to mastectomy after a positive margin on the basis of density. Factors that were predictive of conversion included the presence of an EIC, multifocality/multicentricity, and younger patient age—features that have previously been shown to be associated with higher rates of mastectomy.[9–11]

The finding that the initial mastectomy rate accounted for the greater use of mastectomy in patients with extremely dense breasts suggests that clinical judgment, surgeon and patient preference, and other subjective factors may have played a role in surgical decision making, a hypothesis supported by the variation in mastectomy rates from 15 to 46 % among the surgeons in this study. There are several areas of limited clinical data that could give rise to surgeon variation in initial mastectomy rates. The greater incidence of mammographically occult tumors in dense breasts may raise concerns about the ability to successfully perform BCS and to detect local recurrence.[4–6] However, Morrow et al.[12] have shown that patients with mammographically occult tumors are just as likely as those with mammographically evident tumors to be candidates for BCS, and that the success rate of BCS (defined as the ability to obtain negative margins) did not differ between groups. Yang et al.[13] examined outcomes of mammographically occult and evident breast cancers treated with BCS and irradiation. Two-thirds of the local recurrences observed in patients with an initial tumor that was mammographically occult were visible on mammogram, and there was no difference in the incidence of in-breast recurrence between those with mammographically occult and evident tumors after adjustment for other variables. In aggregate, these studies indicate that there is no reason to preferentially perform mastectomy because a cancer is not seen on a mammogram.

TABLE 2 Factors associated with initial mastectomy, adjusted for surgeon variation in mastectomy use ($n = 1056$)

Variable	Level	Initial M (n)	Initial BCS (n)	Univariate		Multivariate	
				OR (95 % CI)	p	OR (95 % CI)	p
Age at surgery	10 years[a]	–	–	0.72 (0.63–0.82)	<0.0001	0.86 (0.76–0.99)	0.0306
Histological tumor type	Ductal/mixed	261	658	1 (Ref.)	–	X	X
	Lobular	31	78	1.03 (0.62–1.73)	0.9021	X	X
	Special	6	22	0.69 (0.35–1.35)	0.2760	X	X
Mode of diagnosis	Image-detected	108	450	1 (Ref.)	–	1 (Ref.)[b]	–
	Physical finding	189	297	2.62 (2.07–3.31)	<0.0001	1.35 (1.12–1.61)	0.0012
	Incidental	1	11	0.44 (0.10–2.04)	0.2945	0.57 (0.16–2.00)	0.3792
Histologic grade	I/II	39	208	0.39 (0.27–0.56)	<0.0001	0.67 (0.49–0.91)[b]	0.0107
	III	222	451	1 (Ref.)	–	1 (Ref.)	–
	Not available	37	99	0.75 (0.57–0.99)	0.0445	0.87 (0.62–1.23)	0.4415
EIC	No	249	656	1 (Ref.)	–	X	X
	Yes	49	102	1.28 (0.79–2.07)	0.3194	X	X
Multicentric/focal	No	168	611	1 (Ref.)	–	1 (Ref.)	–
	Yes	130	147	3.11 (2.20–4.40)	<0.0001	2.67 (1.86–3.83)	<0.0001
LVI	No	138	582	1 (Ref.)	–	1 (Ref.)	–
	Yes	160	176	3.81 (2.80–5.17)	<0.0001	2.51 (1.60–3.94)	<0.0001
Tumor size	0.5 or less	26	83	1.13 (0.73–1.76)	0.5838	1.71 (1.03–2.86)[b]	0.0390
	0.5–1	31	194	0.60 (0.39–0.92)	0.0193	0.84 (0.57–1.24)	0.3719
	1–2	94	354	1 (Ref.)	–	1 (Ref.)	–
	>2	145	125	4.16 (3.41–5.08)	<0.0001	3.06 (2.41–3.89)	<0.0001
Subtype	ER+/PR+/HER2−	198	582	1 (Ref.)	–	1 (Ref.)[b]	–
	ER+/PR+/HER2+	31	45	2.03 (1.54–2.69)	<0.0001	1.35 (0.93–1.95)	0.1098
	ER−/PR−/HER2+	22	32	1.99 (1.13–3.50)	0.0166	1.35 (0.76–2.38)	0.3012
	ER−/PR−/HER2−	47	99	1.30 (0.91–1.86)	0.1431	0.95 (0.65–1.40)	0.8090
Preoperative MRI	No	155	516	1 (Ref.)	–	1 (Ref.)	–
	Yes	143	242	1.86 (1.27–2.72)	0.0014	1.56 (1.02–2.37)	0.0381
BI-RADS density	1–3	248	703	1 (Ref.)	–	1 (Ref.)	–
	4	50	55	2.60 (1.97–3.43)	<0.0001	1.94 (1.44–2.62)	<0.0001

All effects adjusted for surgeon variation in mastectomy use; $n = 1052$ for models that include tumor size. X indicates variables that were not included in the multivariate model

M mastectomy, *BCS* breast-conserving surgery, *OR* odds ratio, *CI* confidence interval, *EIC* extensive intraductal component, *LVI* lymphovascular invasion, *ER* estrogen receptor, *PR* progesterone receptor, *MRI* magnetic resonance imaging, *BI-RADS* Breast Imaging-Reporting and Data System

[a] Estimated change in odds of initial mastectomy associated with a 10-year increase in age

[b] Type III multivariate p-values for means of diagnosis, histologic grade, tumor size, and subtype are 0.0014, 0.0375, <0.0001, and 0.0539, respectively

Whether breast density increases the risk of local recurrence is uncertain. Cil et al.[14] retrospectively reviewed breast density in 335 patients undergoing BCS for invasive cancer and found that those with the highest breast density were significantly more likely to experience local recurrence compared to patients with low breast density. However, the association was only statistically significant for women who did not receive radiotherapy. In addition, over 11 % of patients in the study had positive final margins, only about half of the ER positive patients received tamoxifen, and fewer than 20 % of patients received chemotherapy, raising questions about the applicability of the findings to patients treated with modern multidisciplinary therapy. In contrast, Buist et al.[15] reported on the impact of density in a cohort of 17,286 breast cancer patients. Although those with dense breasts had an increased risk of new primary breast cancers, no trend toward an increased risk of recurrence on the basis of density was observed.

In addition to density, other factors related to an increased likelihood of initial mastectomy included younger patient age and having an MRI before surgery. It has been well documented that use of MRI leads to an increase in mastectomy rate, and this study reconfirms that MRI is an independent variable predictive of

TABLE 3 Factors associated with a positive margin after breast-conserving surgery ($n = 758$)

Variable	Level	Positive margin (n)	Negative margin (n)	Univariate		Multivariate	
				OR (95 % CI)	p	OR (95 % CI)	p
Age at surgery	10 years[a]	–	–	0.82 (0.71–0.95)	0.0101	0.93 (0.83–1.04)	0.2067
Histological tumor type	Ductal/mixed	338	320	1 (Ref.)	–	1 (Ref.)[b]	–
	Lobular	34	44	0.72 (0.47–1.11)	0.136	0.57 (0.37–0.88)	0.011
	Special	15	7	2.04 (1.01–4.12)	0.047	2.53 (1.11–5.81)	0.028
Mode of diagnosis	Image-detected	217	233	1 (Ref.)	–	X	X
	Physical finding	164	133	1.33 (0.91–1.95)	0.137	X	X
	Incidental	6	5	1.32 (0.62–2.81)	0.472	X	X
LN status	Negative	278	296	1 (Ref.)	–	1 (Ref.)	–
	Positive	109	75	1.60 (1.02–2.50)	0.0387	1.32 (0.87–1.99)	0.1870
Histologic grade	I/II	103	105	0.88 (0.64–1.22)	0.452	X	X
	III	237	214	1 (Ref.)	–	X	X
	Not available	47	52	0.81 (0.56–1.19)	0.281	X	X
EIC	No	317	339	1 (Ref.)	–	1 (Ref.)	–
	Yes	70	32	2.36 (1.52–3.66)	0.0001	2.02 (1.42–2.89)	0.0001
Multicentric/focal	No	280	331	1 (Ref.)	–	1 (Ref.)	–
	Yes	107	40	3.19 (2.29–4.43)	<0.0001	3.20 (2.37–4.34)	<0.0001
LVI	No	280	302	1 (Ref.)	–	1 (Ref.)	–
	Yes	107	69	1.68 (1.03–2.72)	0.0367	1.35 (0.85–2.15)	0.2087
Tumor size	0.5 or less	42	41	0.88 (0.59–1.31)	0.540	0.70 (0.41–1.21)[b]	0.2046
	(0.5,1)	85	109	0.67 (0.51–0.88)	0.004	0.72 (0.51–1.01)	0.0576
	(1,2)	190	164	1 (Ref.)	–	1 (Ref.)	–
	>2	70	55	1.11 (0.79–1.56)	0.549	0.93 (0.68–1.29)	0.6734
Subtype	ER +/PR +/HER2−	304	278	1 (Ref.)	–	X	X
	ER +/PR +/HER2+	23	22	0.95 (0.48–1.89)	0.894	X	X
	ER−/PR−/HER2+	18	14	1.17 (0.58–2.38)	0.657	X	X
	ER−/PR−/HER2−	42	57	0.67 (0.48–0.95)	0.023	X	X
Preoperative MRI	No	247	269	1 (Ref.)	–	1 (Ref.)	–
	Yes	140	102	1.51 (1.18–1.93)	0.0010	1.34 (0.98–1.84)	0.0703
BI-RADS density	1–3	351	352	1 (Ref.)	–	1 (Ref.)	–
	4	36	19	1.90 (0.85–4.26)	0.1197	1.61 (0.72–3.58)	0.2441

All effects adjusted for surgeon variation in margin positivity; $n = 756$ for models that include tumor size. X indicates variables that were not included in the multivariate model

R odds ratio, *CI* confidence interval, *LN* lymph node, *EIC* extensive intraductal component, *LVI* lymphovascular invasion, *ER* estrogen receptor, *PR* progesterone receptor, *MRI* magnetic resonance imaging, *BI-RADS* Breast Imaging-Reporting and Data System, *OR* odds ratio

[a] Estimated change in odds of positive margin associated with a 10-year increase in age

[b] Type III multivariate p-values for histologic tumor type and tumor size are 0.0181 and 0.1443, respectively

mastectomy.[16–19] Several studies have found that MRI does not decrease the rate of margin positivity or the need for reexcision.[16,19,20] In this study, we specifically examined the use of MRI in patients with very dense breasts, the group for which it is thought to be of greatest benefit, and did not observe a decrease in the positive margin rate. Breast density, young patient age, mammographically occult cancers, and the use of preoperative MRI are interrelated factors, but even after adjusting for these variables, breast density remained a significant predictor of an increased likelihood of initial treatment with mastectomy in our study. Patient participation in surgical decision making is strongly associated with mastectomy use, and it is possible that patients who have been advised that they are difficult to screen mammographically as a result of high breast density may opt for mastectomy in greater numbers than those with less-dense breasts.[21]

In patients attempting BCS, we did not observe a significant difference in margin positivity in women with extremely dense breasts after adjustment for other

TABLE 4 Factors associated with conversion to mastectomy after positive margins present after attempted breast-conserving surgery (n = 387)

Variable	Level	Conversion (n)	No conversion (n)	Univariate		Multivariate	
				OR (95 % CI)	p	OR (95 % CI)	p
Age at surgery	10 year[a]	–	–	0.76 (0.68–0.85)	<0.0001	0.80 (0.69–0.94)	0.0054
Histologic tumor type	Ductal/mixed	90	248	1 (Ref.)	–	X	X
	Lobular	3	31	0.36 (0.15–0.84)	0.018	X	X
	Special	3	12	0.84 (0.34–2.04)	0.694	X	X
Mode of diagnosis	Image-detected	50	167	1 (Ref.)	–	X	X
	Physical finding	44	120	1.13 (0.87–1.47)	0.363	X	X
	Incidental	2	4	1.40 (0.33–5.86)	0.647	X	X
LN status	Negative	61	217	1 (Ref.)	–	X	X
	Positive	35	74	1.33 (0.86–2.05)	0.1965	X	X
Histologic grade	I/II	15	88	0.40 (0.24–0.66)	<0.001	0.35 (0.19–0.62)[b]	<0.001
	III	72	165	1 (Ref.)	–	1 (Ref.)	–
	Not available	9	38	0.64 (0.45–0.89)	0.008	0.60 (0.38–0.92)	0.020
EIC	No	64	253	1 (Ref.)	–	1 (Ref.)	–
	Yes	32	38	2.97 (1.60–5.51)	0.0006	2.53 (1.40–4.57)	0.0021
Multicentric/focal	No	55	225	1 (Ref.)	–	1 (Ref.)	–
	Yes	41	66	2.37 (1.43–3.91)	0.0008	1.90 (1.04–3.48)	0.0365
LVI	No	65	215	1 (Ref.)	–	X	X
	Yes	31	76	1.20 (0.77–1.88)	0.4197	X	X
Tumor size	0.5 or less	18	24	2.44 (1.21–4.91)	0.013	2.45 (1.16–5.17)[b]	0.0187
	(0.5,1)	17	68	0.89 (0.49–1.64)	0.717	0.99 (0.55–1.78)	0.9660
	(1,2)	40	150	1 (Ref.)	–	1 (Ref.)	–
	>2	21	49	1.38 (0.93–2.03)	0.109	1.13 (0.68–1.89)	0.6306
Subtype	ER+/PR+/HER2−	74	230	1 (Ref.)	–	X	X
	ER+/PR+/HER2+	9	14	1.97 (0.92–4.22)	0.082	X	X
	ER−/PR−/HER2+	5	13	1.16 (0.36–3.75)	0.804	X	X
	ER−/PR−/HER2−	8	34	0.69 (0.31–1.53)	0.360	X	X
Preoperative MRI	No	54	193	1 (Ref.)	–	1 (Ref.)	–
	Yes	42	98	1.64 (1.17–2.30)	0.0039	1.58 (1.01–2.47)	0.0458
BI-RADS density	1–3	87	264	1 (Ref.)	–	1 (Ref.)	–
	4	9	27	1.10 (0.55–2.21)	0.7776	0.88 (0.40–1.96)	0.7550
Pathology at positive margin	Any invasive disease	64	183	1.05 (0.72–1.54)	0.7971	X	X
	DCIS only	32	108	1 (Ref.)	–	1 (Ref.)	–

All effects adjusted for surgeon variation in conversion rate. X indicates variables that were not included in the multivariate model

OR odds ratio, *CI* confidence interval, *LN* lymph node, *EIC* extensive intraductal component, *LVI* lymphovascular invasion, *ER* estrogen receptor, *PR* progesterone receptor, *MRI* magnetic resonance imaging, *BI-RADS* Breast Imaging-Reporting and Data System, *DCIS* ductal carcinoma-in-situ

[a] Estimated change in odds of conversion associated with a 10-year increase in age

[b] Type III multivariate p-values for histologic grade and tumor size are 0.0003 and 0.0882, respectively

variables. An association between breast density and margin positivity has been suggested in a few smaller studies. In a study examining the usefulness of wire bracketing in preoperative needle localization, Liberman et al.[22] found that 10 of 11 patients with dense breasts had tumor at the margin of an excision specimen compared to only 32 of 64 patients with less-dense breasts ($p < 0.02$ on univariate analysis). In a larger study of 565 patients, Bani et al. identified variables associated with reexcision for positive margins (defined as tumor within 1 mm of ink) and cited a 42 % reoperation rate for the 45 patients with BI-RADS 4 breast density compared to only 18 % for less-dense breasts (odds ratio 3.2; 95 % confidence interval 1.2–11.0; $p < 0.03$ on multivariate analysis controlling for tumor size, multifocality, and EIC, but excluding patient age).[23] However, after reexcision, 90 % of the patients in this study were able to have BCS, leading the authors to conclude that high breast density should not be used as a selection factor for mastectomy. In contrast, in a study of 357 patients undergoing BCS for invasive cancer, Malik et al. reported no difference in margin positivity among patients with the highest breast density compared to those with fatty or mixed breast density (multivariate analysis, 40 vs. 31 % or 37 %, respectively), an observation consistent with the results of our study.[24]

It is possible that an impact of density on margin positivity may have been obscured by the very high rate of margin positivity in our study (51 %). This can largely be attributed to the use of the shaved technique to evaluate margins. The switch from the more common perpendicular method of margin assessment to the shaved technique increased the rate of margin positivity from 15 to 49 % at our institution in the absence of any change in surgical technique.[8] The shaved margin technique has been abandoned. However, there is no reason to believe that the likelihood of identifying tumor in a shaved margin specimen is related to breast density, suggesting that our findings are valid.

In summary, density appears to be an independent selection factor for initial mastectomy. This study did not find an association between density and margin positivity or the decision to convert to mastectomy after attempted BCS. Preoperative MRI did not decrease the rate of positive margins—even in patients with extremely dense breasts—but did increase the rate of mastectomy. These data do not support the use of breast density as a selection criterion for BCS.

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