HHS Public Access

Author manuscript

Breast Cancer Res Treat. Author manuscript; available in PMC 2020 July 01.

Published in final edited form as:

Breast Cancer Res Treat. 2019 July ; 176(2): 401–406. doi:10.1007/s10549-019-05246-4.

Does every woman presenting with malignant calcifications require a post lumpectomy mammogram?

Hálio Rodrigues–Duarte[1,2], **Thiemo J. A. van Nijnatten**[1,3], **Tatiana Khoury**[1], **Hiram Cody**[1], **Stefanie Jacobs**[1], and **Maxine S. Jochelson**[1]

[1]Department of Radiology, Memorial Sloan Kettering Cancer Center, 300 East 66th Street, New York, NY 10065, USA [2]Department of Radiology, Instituto Português de Oncologia Francisco Gentil, Porto, Portugal [3]Department of Radiology and Nuclear Medicine, Maastricht University Medical Center, Maastricht, The Netherlands

Abstract

Purpose—Successful breast-conserving surgery (BCS) followed by radiation therapy (XRT) is dependent on complete removal of the cancer with clear surgical margins, providing survival rates equivalent to those observed following mastectomy. In patients who have cancers presenting with microcalcifications, post lumpectomy mammograms (PLM) prior to radiation (XRT) can be performed to ensure that no cancer has been left behind. The purpose of this study was to assess the benefit of PLM in patients with malignant breast tumors presenting with microcalcifications.

Methods—In this IRB-approved retrospective study, we reviewed medical records for patients with breast cancers presenting with microcalcifications who underwent BCS between February 2008 and June 2013. 198 patients who had a PLM prior to XRT for cancers presenting with microcalcifications were included.

Results—Histopathology of the initial lumpectomy revealed invasive carcinoma in 78/198 (39.4%) and DCIS alone in 120/198 (60.6%). 114/198 (58%) patients had negative surgical margins. 7/114 (6%) patients with negative margins had positive PLM and re-excisions that were positive for malignancy: sensitivity 88%, specificity 95%, PPV 58%, NPV 99%. 84/198 patients had positive surgical margins. The diagnostic performance of PLM in this group was: sensitivity 55%, specificity 71%, PPV 66%, NPV 61%.

Conclusion—PLM plays an important role in the evaluation of patients undergoing breast conservation for breast cancer presenting with microcalcifications. Residual malignancy was detected on positive PLM in 6% of patients with negative margins.

Maxine S. Jochelson jochelsm@mskcc.org.

Conflict of interest Author Maxine Jochelson has received a speaker honorarium from GE.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent As this was a retrospective study, the need for informed consent was waived.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Keywords

Mammography; Breast cancer; Breast conservative therapy; Radiation therapy

Purpose

Breast-conserving surgery (BCS) followed by radiation therapy (XRT) is a valid alternative to mastectomy in appropriately selected women [1–3]. The success of this approach is dependent on complete removal of the cancer with clear surgical margins, which provides local control and survival rates equivalent to those observed following mastectomy [4]. The definition of a negative surgical margin has evolved over the years—it is most recently defined as 2 mm for ductal carcinoma in situ (DCIS) [5] and no ink on tumor for women with invasive carcinoma [6]. As a result of the change in the definition of positive margins in invasive cancer, reexcision rates have gone down significantly [7].

In patients who have cancers presenting with microcalcifications, post lumpectomy mammograms (PLM) prior to XRT may be performed to ensure that no malignant calcifications have been left behind. This has classically been done in patients with positive and negative margins, in part because DCIS has been shown to skip areas of involvement [8–10]. However, recently some question the value of that mammogram. PLM is usually performed within the first few weeks after surgery, which may cause patient discomfort and anxiety. Additionally, these mammograms may have false-positive findings leading to stereotactic biopsies or additional surgery, even in patients with negative margins who would otherwise not require re-excision [10].

The purpose of this study was to assess the benefit of PLM in patients with malignant breast tumors presenting with microcalcifications to determine if there are any patients for whom PLM can be eliminated.

Methods

This HIPAA-compliant retrospective study was approved by the Institutional Review Board and the need for informed consent was waived. We reviewed medical records for patients with breast cancers presenting with microcalcifications who were treated with BCS between February 2008 and June 2013. Patients with a PLM prior to XRT for cancers presenting with microcalcifications alone or for cancers associated with a mass were included. The choice to perform PLM was based on the individual surgeon’s practice patterns without a specifically stated reason. Since our hospital is a referral center, most patients were referred from other hospitals prior to surgery.

Patients were excluded if the original mammogram or report was not available.

Specimen radiographs were performed on all patients. However, after each radiograph was performed, the surgeons circumferentially shaved the margins without obtaining another radiograph, so the specimen radiograph could not be used to determine the adequacy of removal of the malignant calcifications.

All patients had histologic confirmation of their imaging findings and follow-up biopsies by the pathology department at our institution.

The standard PLM included two standard views (craniocaudal and mediolateral oblique) and magnification views at the lumpectomy site in the craniocaudal and lateral projections. The presence or absence of suspicious calcifications was recorded as well as the method of obtaining histologic confirmation. Residual suspicious calcifications were a positive PLM whereas the absence of residual suspicious calcifications was considered to be a negative exam.

Clinical, pathologic, and demographic data were collected for analysis. Statistical analyses were performed using SPSS (Version 24, IBM, Armonk, New York, USA). Continuous data were compared by calculating the mean (including range) and comparing both subgroups with the independent samples *t* test. Categorical data were analyzed using the χ^2 test and if necessary Fisher's Exact Test. Statistical analyses included uni- and multivariable binary logistic regression analyses. Two-sided *p* values < 0.05 were considered statistically significant.

Results

General characteristics

One hundred and ninety-eight patients with a mean age of 56 years (34–79) were included. Of the total study population, 49% had heterogeneously dense breasts and 36% had scattered fibroglandular tissue. Histopathology of the initial lumpectomy revealed invasive carcinoma in 39% and DCIS alone in 61%. The mean pathologic size of the invasive cancers was 9 mm. Size was not reported for DCIS. A complete overview of the patient characteristics is provided in Table 1.

Diagnostic performance of PLM in patients with negative surgical margins

Of the total study population, 114/198 (57.6%) patients had negative surgical margins (Fig. 1). Of the patients determined to have negative surgical margins, 15/114 (13.2%) underwent re-excision, of whom 12/15 (80.0%) had abnormal findings on PLM. Of these, 7/12 (58.3%) had re-excisions that were positive for malignancy, with a detection rate of 7/114 (6.1%). In contrast, 5/12 (41.7%) with positive PLM showed no residual cancer. 3/114 (2.6%) patients with negative margins and negative PLM underwent re-excision for "close" margins (2 mm). One was positive and two were negative. Localization before re-excision was performed in 5/7 patients with positive PLM and negative margins. The overall diagnostic performance of PLM in patients with negative surgical margins was: sensitivity 88% (47–99%), specificity 95% (89–98%), positive predictive value (PPV) 58% (29–84%), and negative predictive value (NPV) 99% (94–100%) (Tables 2,3).

Diagnostic performance of PLM in patients with positive surgical margins

84/198 (42.4%) of the patients had positive surgical margins (Fig. 1). Of the patients determined to have positive surgical margins, 33/84 (39.3%) had positive PLM of whom 21/33 (63.6%) had cancer on re-excision while 11/33 (33.3%) did not. One of the 33 with

positive PLM did not undergo re-excision for an unknown reason. 44 patients with negative PLM underwent re-excision, solely for the positive margins with malignancy in 17/44 (38.6%) patients. 7/51 (13.7%) patients with negative PLM did not get re-excised despite positive margins for unknown reasons. Localization before re-excision was performed in 17 patients with positive margins to ensure that all the residual calcifications were removed since the PLM detected calcifications that may not be included in the routine reexcision. The overall diagnostic performance of PLM to detect remaining cancer was: sensitivity 67% (49–83%), specificity 71% (54–84%), PPV 66% (47–81%), and NPV 73% (56–86%) (Tables 2,3).

Statistical analysis

No significant differences in patient characteristics were found between patients with “negative” and “positive” PLM regarding age, breast density, type of biopsy performed, histopathology, size of invasive cancer, and receptor status. There was, however, an association between the extent of the calcifications at presentation and the presence of residual calcifications on PLM: patients with more extensive disease at presentation (extent of calcifications ≥ 5 cm) were more likely to have residual calcifications ($p = 0.011$). There was also an association between the presence of calcifications on PLM and positive surgical margins ($p < 0.001$) (Tables 2, 3, 4).

Discussion

This study evaluated the usefulness of mammography performed after BCS and before XRT in patients who had breast cancer presenting with calcifications, whether with positive or negative margins at the time of their original lumpectomies. The current practice of performing PLM is not consistent across institutions or among all surgeons within an institution. While several investigators advocate the routine use of PLM [11–13] despite negative surgical margins [13], this is not uniformly seen as the standard of care.

Our results show that a negative PLM can accurately rule out residual cancer in patients with negative surgical margins (NPV 99%) but is unable to do that in patients with positive margins. Of note, PLM identified residual cancer in 7/114 (6.1%) patients with negative surgical margins.

Teixidor et al. [14] reported an 8% incidence of residual calcifications at the surgical site found on PLM in a group of 120 patients with breast cancer. In their study, all patients had PLM regardless of the presence or absence of calcifications on preoperative mammography, which could explain the lower percentage of residual calcifications compared with our study. Of the 120 patients, 22/120 (18%) patients had PLM findings considered to be indeterminate or suspicious for neoplasm. 6/120 (5%) were malignant. The authors concluded that PLM even without a history of calcifications can provide useful information as a baseline prior to XRT and was helpful for the interpretation of post-treatment mammograms in 39/120 (32%) patients.

Waddell et al. [13] conducted a retrospective study in 67 patients with DCIS who underwent BCS and post-excision mammography. They identified residual suspicious calcifications in

16/67 (24%) patients, with residual DCIS found in 9/14 (64%) of the patients who underwent re-excision. Although the incidence of calcifications on PLM was comparable to what we found in our group of patients, they had a higher rate of residual cancer in re-excision (64% versus 51%). They concluded that PLM should be performed routinely in all patients with DCIS presenting with associated mammographic microcalcifications who were treated with BCS.

Aref et al. [15] retrospectively reviewed 90 patients treated for early-stage breast cancer presenting with calcifications. Seventy had negative margins and 13 had close margins. They found that 16/90 (18%) patients had residual calcifications on PLM. Re-excision was performed in 12/16 (75%) patients, 9 with initial clear margins, 2 with “close” margins (< 1 mm), and 1 with focally involved margin. Re-excision revealed residual malignancy in 8/12 (67%) patients; 6/8 (75%) who had had negative margins and 2/6 (33%) had their tumors resected with “close” margins.

In a series of 281 patients with DCIS who were treated with BCS, 144 patients underwent post lumpectomy mammograms at the discretion of the treating physician. Whaley et al. [16] found that 34/144 (24%) had residual calcifications. Of the patients with residual calcifications, 10/34 had negative surgical margins and 6/10 (60%) had residual malignancy. Despite that, they concluded that in institutions where careful assessment of pathologic margins is performed and specimen radiography is routinely performed, routine PLM is not warranted.

Patients with more extensive disease at presentation (extent of calcifications ≥ 5 cm) were more likely to have residual calcifications ($p = 0.011$), although the extent of calcifications at presentation did not seem to influence the percentage of patients with residual disease (Table 4).

Our study has a few limitations. First, it was a retrospective study of a relatively small number of patients and represented the experience of a single institution. Second, PLM was performed at the discretion of the treating physician without specifically stated reasons, a fact that could have led to selection bias since PLM was possibly more frequent in patients where clinicians were more concerned about the possibility of residual cancer. Since our study comprised only a subset of all breast conservation patients treated during this period, our results may not be representative for all breast conservation patients.

This individualization of practice both at our institution and elsewhere has been based on a paucity of data regarding the utility of PLM and was in fact the impetus to perform this study. If corroborated in larger trials, this may indicate more utility for PLM than originally expected.

Conclusion

We can conclude from this study that PLM plays an important role in the evaluation of patients undergoing breast conservation for breast cancer presenting with microcalcifications.

In patients with negative margins, PLM detected otherwise unsuspected cancer in 6% of the patients, which should lead to better local control. If corroborated in larger studies, this may indicate more utility for PLM than originally expected. In patients with positive margins in whom re-excision is necessary, the detection of calcifications on PLM sometimes detects calcifications that may not be included in routine re-excision for positive margins. These can be localized prior to surgery, thereby reducing the possibility of persistent positive margins.

Funding

This study was funded by the NIH/NCI Cancer Center Support Grant P30 CA008748 and a Grant from the Breast Cancer Research Foundation.

References

1. Fisher B, Bauer M, Margolese R et al. (1985) Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. N Engl J Med 312:665–673 [PubMed: 3883167]
2. Harris JR, Hellman S, Kinne DW (1985) Limited surgery and radiotherapy for early breast cancer. N Engl J Med 313:1365–1368 [PubMed: 4058531]
3. Nattinger AB, Gottlieb MS, Veum J, Yahnke D, Goodwin JS (1992) Geographic variation in the use of breast-conserving treatment for breast cancer. N Engl J Med 326:1102–1107 [PubMed: 1552911]
4. Morrow M, Strom EA, Bassett LW et al. (2002) Standard for breast conservation therapy in the management of invasive breast carcinoma. CA Cancer J Clin 52:277–300 [PubMed: 12363326]
5. Morrow M, Zee KJV, Solin LJ et al. (2016) Society of surgical oncology—American Society for Radiation Oncology—American Society of Clinical Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. J Clin Oncol 34:4040–4046 [PubMed: 27528719]
6. Buchholz TA, Somerfield MR, Griggs JJ et al. (2014) Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of Clinical Oncology Endorsement of the Society of Surgical Oncology/ American Society for Radiation Oncology Consensus Guideline. J Clin Oncol 32:1502–1506 [PubMed: 24711553]
7. Pilewskie M, Morrow M (2018) Margins in breast cancer: how much is enough? Cancer 124:1335–1341 [PubMed: 29338088]
8. Faverly DR, Burgers L, Bult P, Holland R (1994) Three-dimensional imaging of mammary ductal carcinoma in situ: clinical implications. Semin Diagn Pathol 11:193–198 [PubMed: 7831530]
9. Cheng L, Al-Kaisi NK, Gordon NH, Liu AY, Gebrail F, Shenk RR (1997) Relationship between the size and margin status of ductal carcinoma in situ of the breast and residual disease. J Natl Cancer Inst 89:1356–1360 [PubMed: 9308705]
10. Adkisson CD, McLaughlin SA, Vallow LA et al. (2013) Is postexcision, preradiation mammogram necessary in patients after breast-conserving surgery with negative margins. Ann Surg Oncol 20:3205–3211 [PubMed: 23975292]
11. Dershaw DD (1995) Mammography in patients with breast cancer treated by breast conservation (lumpectomy with or without radiation). AJR 164:309–316 [PubMed: 7839960]
12. Gluck BS, Dershaw DD, Liberman L, Deutch BM (1993) Microcalcifications on postoperative mammograms as an indicator of adequacy of tumor excision. Radiology 188:469–472 [PubMed: 8327699]
13. Waddell BE, Stomper PC, DeFazio JL, Hurd TC, Edge SB (2000) Postexcision mammography is indicated after resection of ductal carcinoma-in situ of the breast. Ann Surg Oncol 7:665–668 [PubMed: 11034243]
14. Teixidor HS, Chu FC, Kim YS, Levin TL (1992) The value of mammography after limited breast surgery and before definitive radiation therapy. Cancer 69:1418–1423 [PubMed: 1540879]

15. Aref A, Youssef E, Washington T, Segel M, Grigorian C, Bongers S, Bouwman D (2000) The value of postlumpectomy mammogram in the management of breast cancer patients presenting with suspicious microcalcifications. Cancer J Sci Am 6:25–27 [PubMed: 10696735]

16. Whaley JT, Lester-Coll NH, Morrissey SM, Milby AB, Hwang WT, Prosnitz RG (2013) Use of postexcision preirradiation mammography in patients with ductal carcinoma in situ of the breast treated with breast-conserving therapy. Pract Radiat Oncol 3:e107–e112 [PubMed: 24674371]

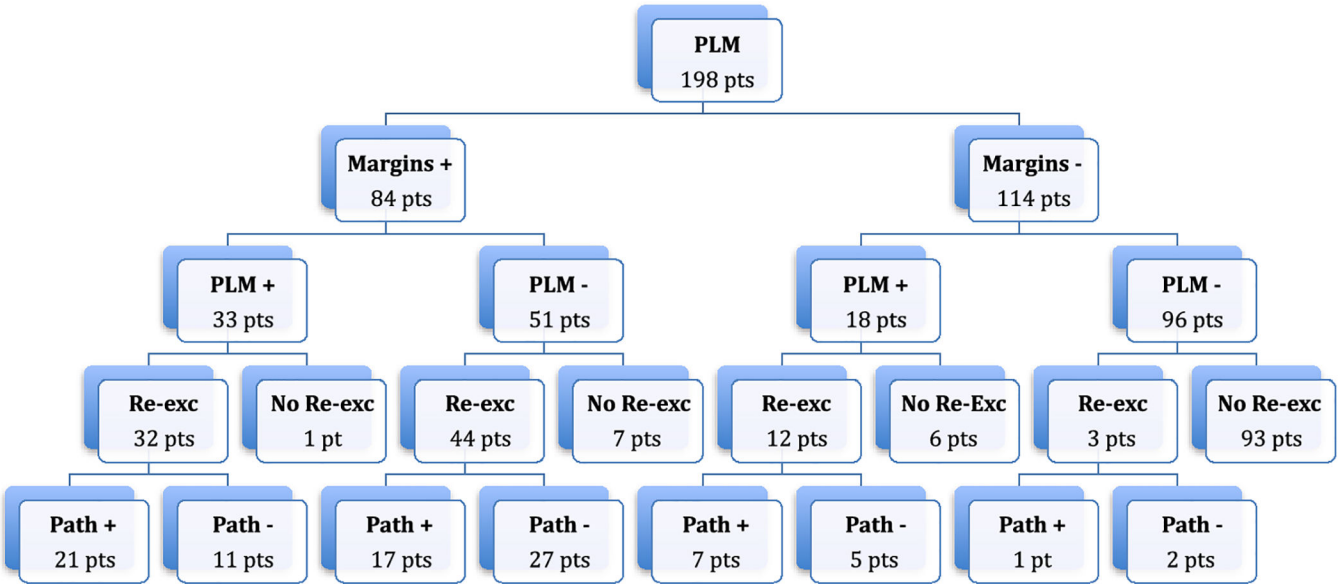

Fig. 1.
Diagnostic performance of PLM

Table 1

General patient characteristics

	***N* = 198**
Mean age (years) (range)	55.7 (34–79)
Breast density (%)	
Fatty	3 (1.5%)
Scattered fibroglandular	72 (36.4%)
Heterogeneously dense	96 (48.5%)
Extremely dense	27 (13.6%)
Extent calcifications at presentation (%)	
< 1 cm	56 (28.3%)
1–2.9 cm	81 (40.9%)
3–4.9 cm	40 (20.2%)
≥ 5 cm	14 (7.1%)
Unknown	7 (3.5%)
Type of biopsy (%)	
Stereotactic	154 (77.8%)
Ultrasound guided	27 (13.6%)
Surgical	10 (5.1%)
Unknown	7 (3.5%)
Histopathology (%)	
Invasive carcinoma NST	70 (35.4%)
Other invasive carcinoma	8 (4.0%)
DCIS only	120 (60.6%)
Mean size of invasive cancers (mm) (range)	9.3 (1–35)
Receptor status (%)	
ER positive	69 (34.8%)
PR positive	57 (28.8%)
HER2 positive	13 (6.6%)
Triple negative	5 (2.5%)

NST no special type, *ER* estrogen receptor, *PR* progesterone receptor, *HER2* human epidermal growth factor receptor 2

Table 2

General characteristics according to the presence/absence of calcifications on PLM

Characteristic	Calcs (*n* = 51)	No calcs (*n* = 147)	*p* value
Mean age (years) (range)	56 (39–76)	56 (34–79)	0.825
Breast density (%)			
Fatty	0	2.0	0.570
Scattered fibroglan- dular	41.2	34.7	0.407
Heterogenously dense	41.2	51.0	0.226
Extremely dense	17.6	12.2	0.333
Extent calcifications at presentation (%)			
< 1 cm	28.0	29.8	0.811
1–2.9 cm	30.0	46.8	0.039
3–4.9 cm	26.0	19.1	0.306
≥ 5 cm	16.0	4.3	0.011
Type of biopsy (%)			
Stereotactic	77.1	81.8	0.473
US guided	16.7	13.3	0.561
Surgical	6.2	4.9	0.714
Histopathology (%)			
Invasive carcinoma NST	35.3	35.4	0.992
Other invasive carcinoma	7.8	2.7	0.208
DCIS only	56.9	61.9	0.525
Mean size invasive cancer (mm) (range)	9 (1–25)	9 (1–35)	0.938
Receptor status (%)			
ER positive	95.8	85.2	0.261
PR positive	95.7	71.4	0.027
HER2 positive	9.5	25.6	0.191
Triple negative	0	10.0	0.167
Positive surgical margins	64.7% (33/51)	34.7% (51/147)	< 0.001
Reexcision performed	86.3% (44/51)	32.0% (47/147)	< 0.001
Histopathology reexcision			
Benign	36.4% (16/44)	60.9% (28/46)	0.020
DCIS	59.1% (26/44)	39.1% (18/46)	0.058
Invasive	4.5% (2/44)	0 (0/46)	0.236

Table 3

Uni- and multivariable logistic regression analyses according to the number of patients with reexcision

% Reexcision	Univariable OR (95% CI)	Univariable *p* value	Multivariable OR (95% CI)	Multivariable *p* value
Extent calcifications				
0.1–2.9 cm 41.6%	Reference		Reference	
3.0–5.0 cm 55.0%	1.715 (0.844–3.487)	0.136	1.557 (0.422–5.745)	0.506
≥ 5.0 cm 71.4%	3.509 (1.048–11.746)	0.042	1.233 (0.198–7.687)	0.822
Positive surgical margins				
No 13.2%	Reference	< 0.001	Reference	< 0.001
Yes 90.5%	62.700 (25.273–155.555)		143.520 (39.799–517.545)	
Post-op MG suspicious calcs				
No 32.0%	Reference	< 0.001	Reference	< 0.001
Yes 86.3%	13.374 (5.605–31.910)		43.633 (10.013–190.126)	

Table 4

Extent of microcalcifications at presentation versus presence of residual disease

Extent of calcifications at presentation	Re-excision pathology (%) (*N*)		
	Benign	**DCIS**	**IDC**
< 1 cm (*n* = 23)	52.2 (12)	43.5 (10)	4.3 (1)
1–2.9 cm (*n* = 34)	50.0 (17)	47.1 (16)	2.9 (1)
3–4.9 cm (*n* = 22)	40.9 (9)	59.1 (13)	0
≥ 5 cm (*n* = 10)	50.0 (5)	50.0 (5)	0

2 cases were not selected because extent of calcifications at presentation was unknown