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Original article

Is higher dose radiation necessary for positive resection margin after breast-conserving surgery for breast cancer?

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ABSTRACT

Background: A positive resection margin after breast-conserving surgery (BCS) usually requires re-excision, which impairs cosmetic outcomes and causes considerable distress. This study aimed to evaluate the prognosis of patients with positive resection margin after BCS and the role of radiation therapy (RT) in these patients.

Materials and methods: We analyzed 297 patients who underwent BCS for breast cancer and had invasive carcinoma or ductal carcinoma in situ (DCIS) within less than 1 mm from the resection margin in Samsung Medical Center from January 2000 to June 2012. The association between RT dose and the incidence rate of ipsilateral breast tumor recurrence (IBTR) was examined.

Results: After a median follow-up of 78 months, the incidence rate of IBTR in all patients was 4.6% after 5 years. In the multivariate analysis, the unfavorable factors associated with IBTR were age < 40 years ($p = 0.019$), RT dose (<60 Gy vs. > 66 Gy, $p = 0.012$; 60–66 Gy vs. > 66 Gy, $p = 0.017$), and discontinuation of hormone therapy ($p = 0.001$).

Conclusions: Among the patients with invasive carcinoma or DCIS within less than 1 mm from the resection margin, adjuvant RT with higher dose > 66Gy EQD2 might improve local control. Further prospective studies are warranted to validate the benefit and risk of a high dose boost after BCS in patients with a positive resection margin.

1. Introduction

Breast cancer is the most common malignancy in women worldwide [1]. Breast-conserving surgery (BCS) followed by adjuvant radiation therapy (RT) is a standard treatment for patients with breast cancer [2]. The use of breast-conserving treatment is increasingly preferred due to its superiority in terms of cosmetic results and low risk of developing complications while maintaining oncologic safety [3]. Complete excision with a clear resection margin is required for a successful BCS, and re-excision is recommended if incomplete resection is suspected. Examination of the resection margin via frozen biopsy has been suggested, in spite of its several limitations [4,5]. However, some patients with negative margin turned out to have positive margin in the final pathologic examination. Re-excision has considerable disadvantages, which include worse cosmetic outcomes, psychological distress, and delay in adjuvant treatment [6]. Meanwhile, previous studies have reported that 24%–80% of patients with resection margin involvement did not present with residual disease when re-excision specimen is used [7]. In relation to these reasons, the need for re-excision and the role of high-dose RT as an alternative strategy to re-excision has been addressed.

Adjuvant whole-breast RT reduces local recurrence by 70% in invasive cancer and 50% in ductal carcinoma in situ (DCIS) [8]. An additional dose of 10–16 Gy to the tumor bed further reduced the incidence of ipsilateral breast tumor recurrence (IBTR) and cancer-related death in invasive cancer whereas boost to tumor bed reduced the incidence rate of IBTR without survival benefit in pure DCIS [9–11]. However, the optimal RT dose for patients with positive resection margin has not been established yet. Without a specific guideline regarding optimal RT dose in patients with resection margin involvement, various RT strategies are being used depending on the clinicians' decision. Our institution has also utilized various boost doses in patients with tumor involvement less

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than 1 mm from the resection margin after BCS.

Thus, this study aimed to evaluate the outcomes of patients with resection margin < 1 mm after BCS and the role of RT on local relapse in these patients.

2. Materials and methods

We identified 5694 patients who have been diagnosed as invasive ductal carcinoma of breast and underwent BCS in Samsung Medical Center from January 2000 to June 2012. Among them, 300 had invasive ductal carcinoma or DCIS within less than 1 mm from the resection margin in the final pathologic evaluation. After excluding patients (n = 3) who lacked information about RT dose, 297 were finally included in the analysis. This study was approved by the institutional review board of Samsung Medical Center, and the need for informed consent was waived.

All patients underwent breast ultrasonography and mammography, which are the initial work-up for breast cancer. Preoperative breast magnetic resonance imaging (MRI) was performed in 98.3% (292/297) of the patients. Specimen mammography was routinely performed to confirm if the suspected lesions had been successfully removed during surgery. Decision-making regarding adjuvant treatment after primary surgery was made by the multidisciplinary tumor board composed of pathologists, radiologists, surgeons, medical oncologists, and radiation oncologists. The RT dose to the whole breast was 50 Gy with 25 fractions or 50.4 Gy with 28 fractions. The median dose of the tumor bed boost was 15.0 (9.0–17.5) Gy. Among the patients, 16 (5.4%) and 188 (63.3%) received neoadjuvant chemotherapy and adjuvant chemotherapy. Among the hormone receptor (HR)-positive patients (n = 232), 230 (99.1%) received hormone therapy. Among the HER2-positive patients (n = 58), 34 (58.6%) received HER2-targeted therapy. Of all patients, 94.3% (280/297) received any systemic treatment.

The time to IBTR was defined as the time between the date of surgery and the date of IBTR. Disease-free survival (DFS) was defined as the time from surgery to any relapse or death. We used the Kaplan–Meier method to calculate the cumulative incidence of IBTR and log-rank test to compare the cumulative incidence curves between the different subgroups. The factors with a p value < 0.1 were included in the multivariate analysis. The Cox proportional hazards model was used in the multivariate analysis to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). A p value < 0.05 was considered statistically significant. All analyses were conducted using the Statistical Package for the Social Sciences software version 20 (SPSS Inc., IBM, USA).

3. Results

3.1. Characteristics of the patients

The median age of the patients was 47 (27–79) years. The characteristics of all the patients are depicted in Table 1. The pathologic tumor stage was pT0-1 in 199 (67.0%) patients and pT2-3 in 98 (33.0%) patients. The nodal stage was pN0 in 172 (57.9%) patients. HR + HER2- was the most common subtype (n = 201, 67.7%), followed by HR-HER2- (n = 38, 12.8%), HR + HER2+ (n = 31, 10.4%), and HR-HER+ (n = 27, 9.1%). Resection margin less than 1 mm was observed in 171 (57.6%) patients with DCIS and in 126 (42.4%) patients with invasive carcinoma. The location of the involved resection margin was superficial in 40 (13.5%), deep in 59 (19.9%), radial in 109 (46.8%), nipple in 10 (3.4%), and multiple in 45 (15.2%) patients. Most of the patients (243/297, 81.8%) had tumor on inked margin while 18.2% had tumors within less than 1 mm margin without tumor on ink. Re-excision was conducted in 55 (18.5%) patients. Of these patients, 17 (5.7%) and 38 (12.8%) underwent total mastectomy and partial mastectomy, respectively. No residual tumor was observed in 28 (50.9%) of 55 patients who underwent re-excision. However, residual invasive tumor and DCIS were found in 7 (12.7%) and 10 (18.2%) patients, respectively.

Table 1
Characteristics of all the patients.

	N (%)
Median age (range, years)	47 (27-79)
Age	
< 40 years	59 (19.9%)
≥ 40 years	238 (80.1%)
pT stage	
pT0-1	199 (67.0%)
pT2-3	98 (33.0%)
pN stage	
pN0	172 (57.9%)
pN1	98 (33.0%)
pN2	19 (6.4%)
pN3	8 (2.7%)
Nuclear grade	
Low	77 (25.9%)
Intermediate	136 (45.8%)
High	82 (27.6%)
Unknown	2 (0.7%)
Mean value of Ki-67	26.29%
Ki-67	
≤14%	108 (36.7%)
>14%	177 (59.6%)
Unknown	12 (4.0%)
Lymphovascular invasion	
Yes	190 (64.0%)
No	104 (35.0%)
Unknown	3 (1.0%)
Multifocality	
Yes	86 (29.0%)
No	211 (71.0%)
Extensive intraductal component	
Yes	147 (49.5%)
No	150 (50.5%)
Subtypes	
HR + HER2+	31 (10.4%)
HR + HER2-	201 (67.7%)
HR-HER2+	27 (9.1%)
HR-HER2-	38 (12.8%)
Pathology of the resection margin	
Carcinoma in situ	171 (57.6%)
Invasive cancer	126 (42.4%)
Location of the involved resection margin	
Superficial	40 (13.5%)
Deep	59 (19.9%)
Radial	139 (46.8%)
Nipple	10 (3.4%)
Multiple	45 (15.2%)
Unknown	4 (1.3%)
Tumor on ink	
Yes	243 (81.8%)
No	54 (18.2%)
Axillary management	
Sentinel lymph node biopsy	176 (59.3%)
Axillary lymph node dissection	121 (40.7%)
Re-excision	
No	242 (81.5%)
Total mastectomy	17 (5.7%)
Partial mastectomy	38 (12.8%)
Chemotherapy	
Yes	204 (68.7%)
No	93 (31.3%)
Hormone therapy	
Yes	230 (77.4%)
No	67 (22.6%)
Any systemic treatment	
Yes	280 (94.3%)
No	17 (5.7%)

Abbreviation: HR, hormone receptor.

3.2. Treatment outcomes and prognostic factors in all patients

After a median follow-up of 78 (15–265) months, the incidence rate of IBTR was 4.6%, and that of DFS was 91.1% after 5 years. In the univariate analysis of the prognostic factors associated with IBTR, age ($p = 0.012$), subtypes ($p = 0.005$), and hormone therapy ($p < 0.001$) were the significant factors (Table 2). Meanwhile, pT-stage, pN-stage, histologic grade, lymphovascular invasion (LVI), or pathology of the involved resection margin (DCIS vs. invasive carcinoma) were not significant factors of IBTR. None of the patients who underwent re-excision developed IBTR within 5 years. Fig. 1 shows the IBTR graph between patients who did not undergo re-excision, who received re-excision, and who did total mastectomy.

3.3. Effect of RT dose

The prognostic factors of IBTR and DFS were assessed in patients who did not undergo re-excision (n = 242). Table 3 shows the results of the univariate and multivariate analyses of IBTR in patients who did not undergo re-excision. In the univariate analysis, age < 40 years ($p = 0.034$), HR negativity ($p < 0.001$), HER2 receptor positivity ($p = 0.045$), and lower RT dose ($p = 0.060$) were the unfavorable factors of IBTR. The multivariate analysis of IBTR included significant clinical factors ($p < 0.1$), including age, HER2 receptor positivity, RT dose, and administration of hormone therapy. Hormone receptor positivity was excluded in the multivariate analysis due to its multicollinearity with hormone therapy. The multivariate analysis found that age < 40 years (HR: 4.184, 95% CI: 1.269–13.889, $p = 0.019$), RT dose (<60 Gy vs. > 66 Gy: HR: 9.801, 95% CI: 1.654–58.075, $p = 0.012$; 60–66 Gy vs. > 66 Gy: HR: 4.213, 95% CI: 1.298–13.672, $p = 0.017$), and discontinuation of hormone therapy (HR: 6.858, 95% CI: 2.125–22.132, $p = 0.001$) were the unfavorable factors of IBTR. Fig. 2 describes a survival graph of IBTR rates according to the RT dose.

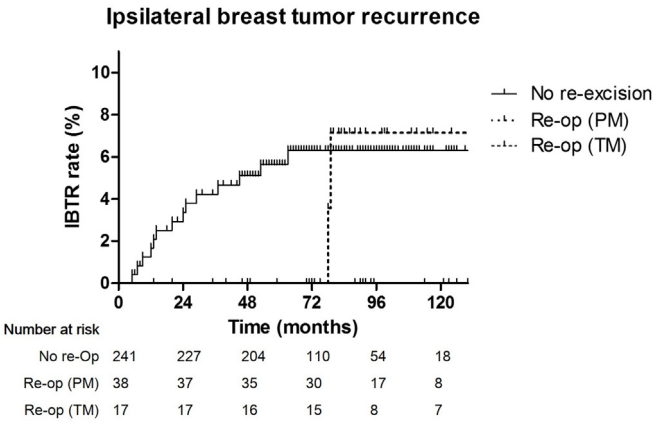

Fig. 1. Incidence rate of ipsilateral breast tumor recurrence according to re-excision.

Table 2
Univariate analysis of the prognostic factors of ipsilateral breast tumor recurrence in all patients.

Characteristics	5-year IBTR (%)	*p* value
Age		*0.012*
<40 years	10.4%	
≥40 years	2.6%	
pT stage	4.6%	*0.450*
pT0-1	4.3%	
pT2-3		
pN stage	5.0%	*0.220*
pN0-1	0	
pN2-3		
Histologic grade	3.9%	*0.866*
I-II	6.3%	
III		
Ki-67		*0.227*
≤14%	3.1%	
>14%	5.2%	
Lymphovascular invasion	7.0%	*0.457*
Yes	3.3%	
No		
Subtypes	3.3%	*0.005*
HR + HER2+	2.7%	
HR + HER2-	15.6%	
HR-HER2+	7.9%	
HR-HER2-		
Pathology of the resection margin	3.8%	*0.599*
Ductal carcinoma in situ	5.7%	
Invasive ductal carcinoma		
Location of the involved resection margin	7.8%	*0.193*
Superficial	8.6%	
Deep	2.2%	
Radial	0	
Nipple	4.9%	
Multiple		
Tumor on ink	3.8%	*0.995*
No	4.8%	
Yes		
Re-excision	5.6%	*0.544*
No	0	
Total mastectomy	0	
Partial mastectomy		
Chemotherapy	4.6%	*0.507*
Yes	4.4%	
No		
Hormone therapy	2.3%	*< 0.001*
Yes	12.4%	
No		

Abbreviation: IBTR, ipsilateral breast tumor recurrence; HR, hormone receptor.

4. Discussion

In the largest randomized trial that investigated the benefit of higher dose to positive resection margin, local control in patients treated with a dose of 26 Gy was not significantly higher than that in patients treated with a dose of 10 Gy [12]. However, only 40%–60% of the patients received systemic therapy in the study, and the effect of the involved resection margin and role of RT must be re-evaluated in modern systemic therapy. In the present study, 94.3% of all patients received any systemic treatment. After adjusting for administration of systemic therapy, a higher dose > 66 Gy EQD2 to the tumor bed remained a significant factor for local control in the multivariate analysis.

In this study, recurrence rate was extremely low among the patients who underwent total mastectomy for the involved resection margin, supporting that re-excision with total mastectomy results in satisfactory oncologic outcomes. The IBTR rate following re-BCS was lower than those without re-excision, however, the difference disappeared after more than 5 years follow-up. This study showed that young age (<40 years) and absence of hormone therapy were associated with a higher local relapse in the multivariate analysis. This result suggests that second surgery could be considered for young patients and/or those who are not able to receive adjuvant hormone therapy and total mastectomy might be preferred rather than re-BCS in order to benefit from re-excision. The benefit of re-BCS in margin-positive breast cancer patients following BCS needs to be further investigated.

Several studies have shown that positive resection margin after BCS is associated with a higher risk of developing IBTR [13,14], while other studies reported that positive or close resection margin

Table 3
Univariate analysis of the prognostic factors of ipsilateral breast tumor recurrence in patients who did not undergo re-excision (n = 242).

	Univariate analysis		Multivariate analysis	
	5-year IBTR	*p value*	HR (95% CI)	*p value*
Age		*0.034*		*0.019*
<40 years (n = 50)	12.2%		4.184 (1.269-13.889)	
≥40 years (n = 192)	3.2%		1	
Hormone receptor		*< 0.001*		
Negative (n = 52)	14.0%			
Positive (n = 190)	3.4%			
HER2 receptor		*0.045*		*0.401*
Negative (n = 189)	4.4%		1	
Positive (n = 53)	9.9%		1.660 (0.509-5.417)	
Histologic grade		*0.682*		
I-II (n = 173)	4.9%			
III (n = 67)	7.7%			
Ki-67		*0.430*		
≤14%	4.2%			
>14%	6.0%			
pT stage		*0.945*		
pT0-1 (n = 160)	5.8%			
pT2-3 (n = 82)	5.3%			
pN stage		*0.232*		
N0-1 (n = 217)	6.2%			
N2-3 (n = 23)	0			
LVI		*0.528*		
Yes (n = 88)	8.3%			
No (n = 151)	4.1%			
Pathology of the resection margin		*0.563*		
DCIS (n = 139)	3.7%			
IDC (n = 103)	17.0%			
Location of the involved margin		*0.580*		
Superficial (n = 39)	8.0%			
Deep (n = 58)	8.8%			
Radial (n = 103)	3.0%			
Nipple (n = 7)	0			
Multiple (n = 32)	13.5%			
Tumor on ink		*0.610*		
Yes (n = 195)	94.1%			
No (n = 47)	95.6%			
RT dose (EQD2)		*0.060*		*0.015*
<60 Gy (n = 13)	16.1%		9.801 (1.654-58.075)	*0.012*
60–66 Gy (n = 75)	8.5%		4.213 (1.298-13.672)	*0.017*
>66 Gy (n = 154)	3.3%		1	
Hormone therapy		*0.001*		*0.001*
Yes (n = 188)	2.8%		1	
No (n = 54)	15.1%		6.858 (2.125-22.132)	
Chemotherapy		*0.859*		
Yes (n = 160)	5.9%			
No (n = 82)	5.0%			

Abbreviation: IBTR, ipsilateral breast tumor recurrence; HR, hazard ratio; CI, confidence interval; LVI, lymphovascular invasion; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; RT, radiation therapy.

is not associated with worse prognosis [12]. These inconsistent results might be attributed to the heterogeneous descriptions of positive resection margin and a variety of relevant factors associated with resection margin [15–17]. The extent of margin involvement is associated with residual disease and higher risk of local relapse [15,18]. The concept of "focally positive resection margin" is defined as tumor involvement with < 4 mm of margin width, and several studies suggest that re-excision could be safely omitted in these cases [19,20]. The location of the resection margin is another factor that should be considered. Park et al. have reported that the presence of cancer cells in the superficial margin does not increase the risk of local relapse, whereas the radial margin positivity is associated with a higher risk of local relapse [21]. The effect of resection margin pathology (DCIS vs. invasive cancer) on local relapse has not been properly addressed as well. In cases of pure DCIS, 2 mm margin is considered adequate margin in the current guideline [22]. The American SSO guideline recommends that IDC or DCIS on inked margin could be equally considered as resection margin-positive [23]. This study also showed that IBTR rate was not affected by whether the resection margin is involved by IDC or DCIS.

Although this study suggested the potential dose-response relationship in patients with resection margin less than 1 mm, the benefit of higher dose should be weighed against possible side effects before applying the results in clinic. Although a re-excision deteriorates cosmetic outcome, we have learned from the Young Boost trial that a high boost dose also worsens cosmetic outcome. Although this study could not report the toxicities due to its retrospective nature, more evidence about optimal radiation dose which could reduce recurrence while minimizing toxicities needs to be accumulated.

This study had several limitations. First, the retrospective nature of this study might have caused substantial selection bias. Second, the details of the extent of the involved margin (focal or extensive) was not available in this study. Third, since documentation about toxicities of RT was not available in the medical records, we could

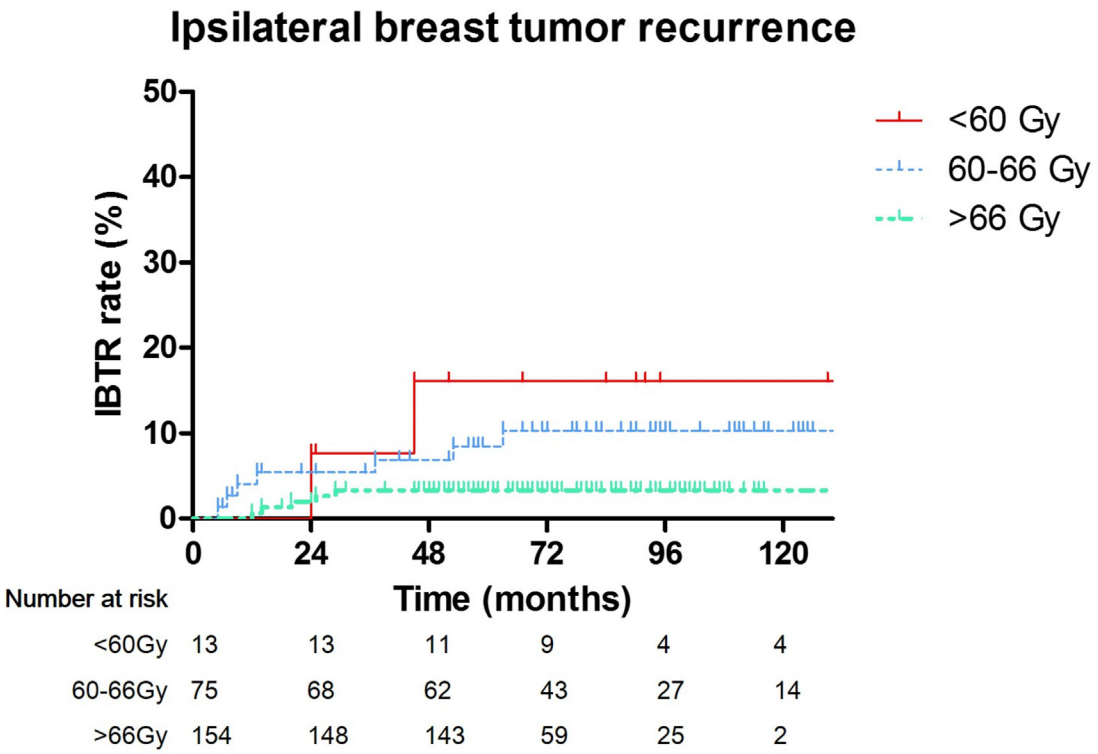

Fig. 2. Incidence rate of ipsilateral breast tumor recurrence according to RT dose in all patients who did not undergo re-excision.

not evaluate the toxicities according to RT dose. Prospective trials with detailed information about the characteristics of the resection margin and RT toxicities are needed to provide sufficient evidence to justify high dose boost.

In conclusion, this study showed that higher dose > 66Gy EQD2 might improve local control in patients with < 1 mm tumor free margin. Further prospective studies should be conducted to investigate the benefit and risk of a high dose boost after BCS in patients with a positive resection margin.

Conflicts of interest statement

There are no conflicts of interest relevant to this article.

Ethical approval

This study was approved by the Institutional Review Board at Samsung Medical Center (IRB No. 2017-12-117-005).

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References

[1] Jemal A, Ward EM, Johnson CJ, Cronin KA, Ma J, Ryerson B, et al. Annual report to the nation on the status of cancer, 1975-2014, featuring survival. J Natl Cancer Inst 2017:109.

[2] Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans V, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;366:2087–106.

[3] NIH consensus conference. Treatment of early-stage breast cancer. Jama 1991;265:391–5.

[4] Landercasper J, Attai D, Atisha D, Beitsch P, Bosserman L, Boughey J, et al. Toolbox to reduce lumpectomy reoperations and improve cosmetic outcome in breast cancer patients: the American society of breast surgeons consensus conference. Ann Surg Oncol 2015;22:3174–83.

[5] Esbona K, Li Z, Wilke LG. Intraoperative imprint cytology and frozen section pathology for margin assessment in breast conservation surgery: a systematic review. Ann Surg Oncol 2012;19:3236–45.

[6] Olsen MA, Nickel KB, Margenthaler JA, Wallace AE, Mines D, Miller JP, et al. Increased risk of surgical site infection among breast-conserving surgery Re-excisions. Ann Surg Oncol 2015;22:2003–9.

[7] Rivere AE, Chiasson KF, Corsetti RL, Fuhrman GM. An assessment of margins after lumpectomy in breast cancer management. Am Surg 2016;82:156–60.

[8] Correa C, McGale P, Taylor C, Wang Y, Clarke M, Davies C, et al. Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. J Natl Cancer Inst Monogr 2010;2010:162–77.

[9] Bartelink H, Maingon P, Poortmans P, Weltens C, Fourquet A, Jager J, et al. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol 2015;16:47–56.

[10] Bartelink H, Horiot JC, Poortmans P, Struikmans H, Van den Bogaert W, Barillot I, et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. N Engl J Med 2001;345:1378–87.

[11] Moran MS, Zhao Y, Ma S, Kirova Y, Fourquet A, Chen P, et al. Association of radiotherapy boost for ductal carcinoma in situ with local control after whole-breast radiotherapy. JAMA Oncol 2017;3:1060–8.

[12] Jones HA, Antonini N, Hart AA, Peterse JL, Horiot JC, Collin F, et al. Impact of pathological characteristics on local relapse after breast-conserving therapy: a subgroup analysis of the EORTC boost versus no boost trial. J Clin Oncol 2009;27:4939–47.

[13] Houssami N, Macaskill P, Marinovich ML, Dixon JM, Irwig L, Brennan ME, et al. Meta-analysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. Eur J Cancer 2010;46:3219–32.

[14] Houssami N, Macaskill P, Marinovich ML, Morrow M. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. Ann Surg Oncol 2014;21:717–30.

[15] DiBiase SJ, Komarnicky LT, Schwartz GF, Xie Y, Mansfield CM. The number of

positive margins influences the outcome of women treated with breast preservation for early stage breast carcinoma. Cancer 1998;82:2212–20.
[16] Park CC, Mitsumori M, Nixon A, Recht A, Connolly J, Gelman R, et al. Outcome at 8 years after breast-conserving surgery and radiation therapy for invasive breast cancer: influence of margin status and systemic therapy on local recurrence. J Clin Oncol 2000;18:1668–75.
[17] Santiago RJ, Wu L, Harris E, Fox K, Schultz D, Glick J, et al. Fifteen-year results of breast-conserving surgery and definitive irradiation for Stage I and II breast carcinoma: the University of Pennsylvania experience. Int J Radiat Oncol Biol Phys 2004;58:233–40.
[18] Wazer DE, Schmidt-Ullrich RK, Ruthazer R, Schmid CH, Graham R, Safaii H, et al. Factors determining outcome for breast-conserving irradiation with margin-directed dose escalation to the tumor bed. Int J Radiat Oncol Biol Phys 1998;40:851–8.
[19] Vos EL, Siesling S, Baaijens MHA, Verhoef C, Jager A, Voogd AC, et al. Omitting re-excision for focally positive margins after breast-conserving surgery does not impair disease-free and overall survival. Breast Canc Res Treat 2017;164:157–67.
[20] Park S, Park HS, Kim SI, Koo JS, Park BW, Lee KS. The impact of a focally positive resection margin on the local control in patients treated with breast-conserving therapy. Jpn J Clin Oncol 2011;41:600–8.
[21] Park S, Ahn SD, Choi EK, Kim SS. The effect of escalating the boost dose for patients with involved resection margin after breast-conserving surgery. Jpn J Clin Oncol 2018;48:272–7.
[22] Morrow M, Van Zee KJ, Solin LJ, Houssami N, Chavez-MacGregor M, Harris JR, et al. 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 2016;34:4040–6.
[23] Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol 2014;32:1507–15.