

Local Control by Breast-conserving Surgery with Nipple Resection

JUN HORIGUCHI¹, YUKIO KOIBUCHI¹, KOTARO IJIMA¹, TAKASHI YOSHIDA¹,
DAISUKE TAKATA¹, NANA ROKUTANDA¹, RIN NAGAOKA¹, TETSUNARI OYAMA²,
YUICHI IINO³, HIDEYUKI SAKURAI⁴ and YASUO MORISHITA¹

¹Second Department of Surgery, ²Second Department of Pathology, ³Department of Emergency Medicine,
⁴Department of Radiation and Radiation Oncology, Gunma University Faculty of Medicine, Gunma, Japan

Abstracts. Local control was compared between patients who had undergone breast-conserving therapy with and without nipple resection. We explored whether there was any difference in local control between the two treatment methods for patients with early breast cancer. A total of 333 women with breast cancer, who had undergone breast-conserving therapy between 1991 and 2002, were included in this study. Surgery consisted of a wide local excision of the primary tumor with a 2-cm free margin as the minimum distance. When the tumor was located under the nipple or close to the nipple, breast-conserving surgery with nipple resection was selected. A total of 320 patients received breast-conserving surgery without nipple resection and radiation therapy (BCT) and 13 patients breast-conserving surgery with nipple resection and radiation therapy (BCT-NR). There were no significant differences in age, tumor size, nodal status, clinical stage, ER status, histological type or surgical margin status between the two groups. The surgical margin was positive in 55 (17.2%) out of 320 patients in the BCT group and in one (7.7%) out of 13 patients in the BCT-NR group. There was no significant difference in the breast-free survival between the two groups. In conclusion, breast-conserving surgery with nipple resection and radiation therapy may be the treatment of choice for early breast cancer patients with the tumor located under the nipple or very close to the areola.

Breast-conserving therapy is accepted as a standard treatment for early breast cancer. Ipsilateral breast recurrence is one of the serious problems for breast-conserving therapy, and thus complete resection of cancer cells is important to prevent ipsilateral breast recurrence (1-3). In the case of tumors close

to the nipple, achieving complete resection is difficult. Breast-conserving surgery with nipple resection was performed in patients who had invasive cancer or intraductal cancer components close to the nipple (4). In this study, local control of breast-conserving surgery accompanied by nipple resection and radiation therapy (BCT-NR) was compared with that of breast-conserving surgery and radiation therapy (BCT).

Patients and Methods

A total of 333 women with breast cancer, who had undergone breast-conserving therapy between 1991 and 2002, were included in this study. The surgical procedure consisted of a wide excision of the primary tumor with a level II or III lymph node dissection. The tumor was widely excised, with a 2-cm free margin as the minimum distance. When the tumor was close to the nipple and could not be excised with a 2-cm free margin, or when ductal spreading was extended to the nipple, breast-conserving surgery with nipple resection was selected. The operative method of breast-conserving surgery with nipple resection has been described in our previous paper (4). Excised specimens were histopathologically examined in consecutive 5-mm slices. Negative margins are defined as no tumor cells within the 5-mm surgical margin. All patients, in addition to breast-conserving surgery with or without nipple resection, also received whole breast irradiation. A daily dose of 2Gy calculated at the midplane of the breast was delivered through two opposing tangential fields (185°), designed to minimize lung exposure, with high-energy photons (6-MV X-ray). A total dose of 50Gy was delivered in 25 fractions for 5 weeks. A radiation boost of 10Gy in 2 fractions to the tumor bed was delivered to margin-positive patients with electron beam radiation. All patients received adjuvant chemotherapy and/or endocrine therapy; patients with hormone-sensitive tumors were treated with 20 mg tamoxifen daily for 2 years or longer. Patients were monitored every month for the first 6 or 12 months after surgery and in 2- or 3-month intervals for the following 2 years, and at a minimum of 6-month intervals thereafter. Biopsy was performed in order to histologically confirm all local recurrences.

Clinicopathological factors and surgical treatment were analyzed using the Student's *t*-test or the Chi-squared test. The actuarial result for breast-free survival was calculated using the Kaplan-Meier method. The log-rank test was used to compare the two survival curves.

Correspondence to: Jun Horiguchi, MD, Second Department of Surgery, Gunma University Faculty of Medicine, Showa-machi 3-39-15, Maebashi, Gunma 371-8511, Japan. Tel: +81-27-220-8245, Fax: +81-27-220-8255, e-mail: junhorig@showa.gunma-u.ac.jp

Key Words: Breast-conserving surgery, nipple resection, surgical margin and breast cancer.

Table I. Clinicopathological factor by surgery.

		BCT (N=320)	BCT-NR (N=13)	<i>p</i>
Age	Mean±SE	51.3±0.6	51.0±2.3	NS
Size	2.0 cm≥	177	7	NS
	2.0 cm<	143	6	
Nodal status	Negative	228	11	NS
	Positive	91	2	
Stage	0	1	0	NS
	I	168	6	
	II	151	7	
ER	Negative	138	6	NS
	Positive/Unknown	182	7	
Histology	DCIS	1	0	NS
	IDC	294	11	
	Lob	7	1	
	Others	18	1	
Surgical margin	Negative	265	12	NS
	Positive	55	1	

BCT; breast-conserving therapy, BCT-NR; breast-conserving therapy with nipple resection, ER; estrogen receptor, DCIS; ductal carcinoma *in situ*, IDC; invasive ductal carcinoma, Lob; invasive lobular carcinoma

Table II. Positive factor of surgical margin.

Positive factor	BCT	BCT-NR
Invasive and ductal spreading	3	0
Invasive	10	0
Ductal spreading	40	0
Lobular carcinoma <i>in situ</i>	1	1
Lymphatic	1	0

BCT; breast-conserving therapy, BCT-NR; breast-conserving therapy with nipple resection

Results

The patients' characteristics are provided in Table I. There was no significant difference in age, tumor size, nodal status, clinical stage, ER status, histological type or surgical margin status between the BCT and the BCT-NR groups. The surgical margin was positive in 55 (17.2%) out of 320 patients in the BCT group and only one (7.7%) out of 13 patients in the BCT-NR group. The positive factors of surgical margin are listed in Table II. Histopathological examination of the specimens by consecutive 5-mm slices in the BCT-NR group revealed that the distance from the tumor edge to the nipple was less than 5 mm in 3 patients and more than 5 mm in 10 patients. One patient in the BCT-NR group showed margin-positive on the lateral side. With a mean follow-up of

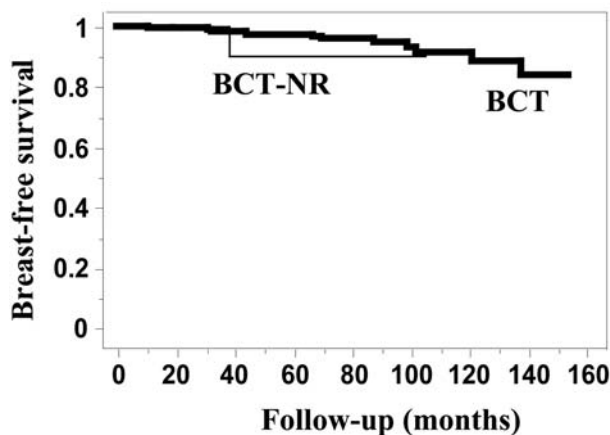


Figure 1. Ipsilateral breast recurrence-free survival curves were compared between the BCT and the BCT-NR groups. No difference in the survival rates between the two groups was found.

64 months, there has been only one ipsilateral breast recurrence (7.7%) in the BCT-NR group. There was no significant difference in breast-free survival curves between the BCT and the BCT-NR groups (Figure 1).

The cosmetic appearance of the breast in the BCT-NR group was evaluated according to the following criteria: excellent, the breast of a patient was basically unchanged compared to its preoperative condition because the wound edge located in the center of round-shaped areola resembled the nipple; good, skin retraction and unbalanced areola were not observed; not so good, observable skin retraction or unbalanced areola; poor, remarkable skin retraction and observable unbalanced areola. Eleven patients were regarded as excellent and 2 as good. An excellent case undergoing BCT-NR is shown in Figure 2.

Discussion

A modified radical mastectomy has generally been the treatment of choice for breast cancer patients with tumors close to the nipple or invading the nipple-areolar complex. We previously reported breast-conserving surgery with nipple resection for early breast cancer patients whose tumors were very close to the nipple (4). In this study, the local control of BCT and BCT-NR were compared in early breast cancer. Pezzi *et al.* (5) also reported breast conservation surgery with nipple-areolar resection for central breast cancers. Ten patients, who had subareolar cancers directly involving the nipple or areola, received breast conservation surgery using nipple-areolar resection. With a mean follow-up of 32 months, only one recurrence (7%) has been reported. In our study, 13 patients received BCT-NR and one (7.7%) had ipsilateral breast recurrence



Figure 2. Local findings of patient after BCT-NR. This case was considered to be excellent, because the breast appearance was scarcely changed compared to its preoperative condition, and the wound edge located in the center of round shape areola resembled the nipple.

with a mean follow-up of 64 months. The local control of our patients is in agreement with the result of Pezzi *et al*.

Margin status is reported to be a risk factor for breast recurrence after breast-conserving surgery, irrespective of radiation surgery (1-3). When the tumor is centrally located in the breast, a choice must be made whether to preserve the nipple or not. Dale *et al*. (6) reported nipple-areolar preservation during breast-conserving therapy for subareolar breast carcinomas. Two out of 25 patients in their study had positive surgical margins of resection. Dale *et al*. concluded that patients who have small subareolar primary breast carcinomas without evidence of nipple involvement are candidates for breast-conserving therapy with nipple-areolar preservation. In our study, when the tumor was close to the nipple and probably could not be excised with a 2-cm free margin, or when ductal spreading was extended to the nipple, breast-conserving surgery with nipple resection was selected. In these cases, 10 out of 13 patients had tumors close to the nipple, as determined pathologically. If BCT had been performed on these 13 patients, no less than 10 patients would have resulted in a positive surgical margin for the nipple side. Actually, the

surgical margin on the nipple side was negative in all 13 patients, while in one of 13 patients the margin on the other side was positive by intralobular component. It is thus critical to pay attention not only to the nipple side, but to the other side as well. This last patient later developed ipsilateral breast recurrence.

The cosmetic result in patients with BCT-NR was generally satisfactory. Furthermore, local control in the BCT-NR group was the same as the BCT group. We conclude that breast-conserving surgery with nipple resection and radiation therapy may be the treatment of choice for early breast cancer patients with the tumor located under the nipple or in close proximity to the areola.

References

- 1 Park CC, Mitsumori M, Nixon A, Recht A, Connolly J, Gelman R, Silver B, Hetelekidis S, Abner A, Harris JR and Schnitt SJ: 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* 18: 1668-1675, 2000.
- 2 Horiguchi J, Koibuchi Y, Takei H, Yokoe T, Yamakawa M, Nakajima T, Oyama T, Iino Y and Morishita Y: Breast-conserving surgery following radiation therapy of 50Gy in stages I and II carcinoma of the breast: the experience at one institute in Japan. *Oncol Rep* 9: 1053-1057, 2002.
- 3 Fredriksson I, Liljegren G, Palm-Sjovall M, Arnesson LG, Emdin SO, Fornander T, Lindgren A, Nordgren H, Idvull I, Holmqvist M, Holmberg L and Frisell J: Risk factors for local recurrence after breast-conserving surgery. *Br J Surg* 90: 1093-1102, 2003.
- 4 Iino Y, Maemura M, Takei H, Horiguchi J, Ishikita T, Koibuchi Y, Andoh T, Nagasawa M, Horii Y, Yokoe T, Ohwada S and Morishita Y: Breast conserving surgery with nipple resection. *Anticancer Res* 16: 3185-3188, 1996.
- 5 Pezzi CM, Kukora JS, Audet IM, Herbert SH, Horvick D and Richter MP: Breast conservation surgery using nipple-areolar resection for central breast cancers. *Arch Surg* 139: 32-37, 2004.
- 6 Dale PS and Giuliano AE: Nipple-areolar preservation during breast-conserving therapy for subareolar breast carcinomas. *Arch Surg* 131: 430-433, 1996.

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